Gold and BINOL-Phosphoric Acid Catalyzed Enantioselective Hydroamination/N-Sulfonyliminium Cyclization Cascade

Alex W. Gregory,† Pavol Jakubec,† Paul Turner‡ and Darren J. Dixon*†

†Department of Chemistry, Chemistry Research Laboratory, University of Oxford, Mansfield Road, Oxford OX1 3TA (UK) and ‡ Mereside, Alderley Park, AstraZeneca R&D Macclesfield, Cheshire SK10 4TG (UK).
darren.dixon@chem.ox.ac.uk

Contents

1. General Experimental

General Experimental Techniques

For reactions requiring anhydrous conditions, glassware was dried in an oven at 100 °C and reactions were carried out under a nitrogen or argon atmosphere. Room temperature (rt) refers to 20-25 °C. Temperatures of 0 °C were achieved using an ice-bath. All compounds were named using ACD IUPAC name predictor.

Solvents and Reagents

Commercial reagents were used as purchased without any further purification unless otherwise stated. Chiral Brønsted acids (**BPA-1A** to **BPA-1D** and **BPA-2A**) were synthesised by Dr Michael Muratore and Dr Lie Shi following standard literature procedure.[1,2,3] Bulk solutions were concentrated under reduced pressure using a Büchi rotary evaporator. Anhydrous toluene, tetrahydrofuran and dichloromethane were obtained by filtration through activated alumina (powder ~150 mesh, pore size 58Å, basic, Sigma-Aldrich) columns. Dichloroethane and acetonitrile were distilled over calcium hydride. Petroleum ether (PE) refers to distilled light petroleum with boiling points in the range of 40 °C – 60 °C. Tryptamine derivatives 2-(1*H*-indol-3-yl)ethanamine, 2-(5-methyl-1*H*-indol-3-yl)ethanamine and 2-(5-methoxy-1*H*-indol-3-yl)ethanamine were used as provided from commercial suppliers. Known tryptamine derivatives were made following literature methods.[4,5,6,] 5-cyano-tryptamine, 4-chloro-tryptamine and 7-bromo-tryptamine were synthesised as described.

Chromatography

All reactions were monitored by thin-layer chromatography (TLC) where appropriate using Merck Kiesel gel 60 F_{254} (230-400 mesh) silica plates which were visualised by UV-light (250 nm) or by staining using aqueous potassium permanganate solutions or vanillin, sulphuric acid in ethanol where appropriate. Column chromatography was carried out using Merck Kieselgel 60 silica gel (230-400 mesh). Enantiomeric excesses were determined using high performance liquid chromatography (HPLC) performed on a Hewlett-Packard 1050 Series system or Agilent 1200 Series system (column and solvent conditions are given with the compound).

Spectroscopy and Characterisation

All ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were collected on either a Bruker DPX400 (400 MHz ^{1}H, 100 MHz ^{13}C), Bruker DQX400 (400 MHz ^{1}H, 100 MHz ^{13}C) or Bruker AVC500 (500 MHz ^{1}H, 125 MHz ^{13}C) and in the deuterated solvent stated. Chemical shift values (δ) are reported relative to tetramethylsilane (δ = 0 ppm) using the solvent residual as an internal reference. ^{1}HNMR peak splitting (multiplicity) and coupling constants are quoted as seen in the spectra and are not compared to theoretically expected multiplicity. Assignments were aided by COSY and HSQC experiments.

Low resolution mass spectrometric (*m/z*) data was acquired by electrospray ionisation (ESI) on an LCT Premier instrument.. High resolution mass spectra (accurate mass) were recorded on a Bruker Micromass GCT spectrometer.

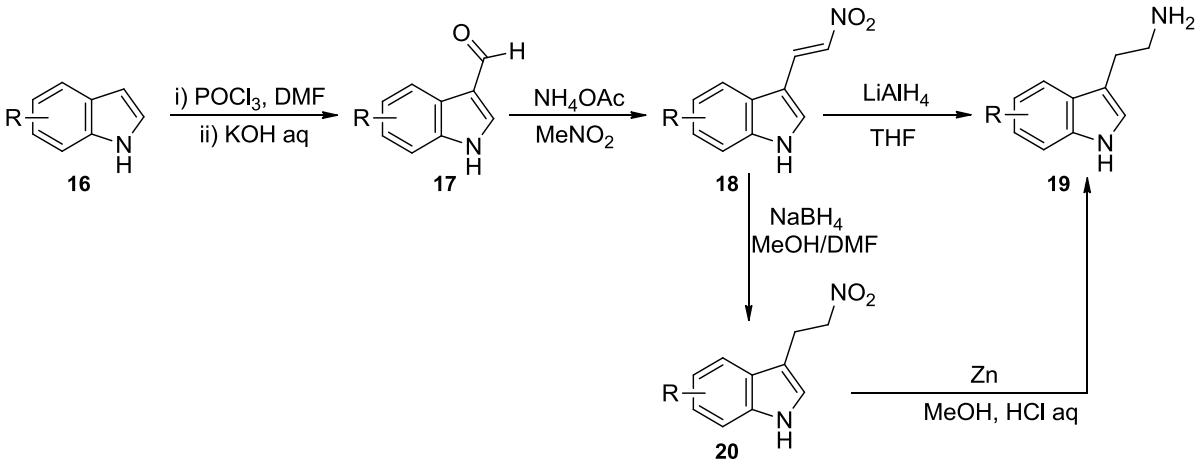
Infrared spectra (ν_{max}) were recorded (wavenumber cm^{-1}) from a thin film on a PIKE diamond ATR module. Only selected maximum absorbances are reported.

Optical rotations were recorded using an Optical Activity AA-1000 polarimeter or a Perkin-Elmer 241 polarimeter; specific rotation (SR) ($[\alpha]_D^T$) are reported in 10^{-1} deg.cm^2.g^{-1}; concentrations (*c*) are quoted in g/100 ml; *D* refers to the *D*-line of sodium (589 nm); Temperatures (*T*) are given in degrees Celsius (°C).

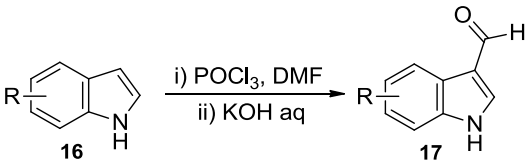
Melting points were measured on a Leica Galen III microscope apparatus, samples were measured mounted on a cover glass window.

2. Preparation and Characterisation

2.1. Preparation and characterisation of tryptamine derivatives



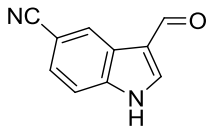
2.2. General procedure A for the preparation of indole carbaldehydes (17)



Phosphorus oxychloride (2.5 eq) was added dropwise to dry dimethyl formamide (5 ml per 1 ml of $POCl_3$) with ice-bath cooling under nitrogen. The mixture was stirred for 5 minutes before the chosen indole (1 equivalent) was added in dimethyl formamide (10 ml per 1 g of indole). The mixture was then allowed to warm to room temperature and stirred for 3 hours. The reaction became a thick suspension that required vigorous stirring. Potassium hydroxide solution (3.8 M, 10 eq) was added v*ia* dropping funnel and the mixture was heated at reflux for 14-16h. The solution was cooled to room temperature before adding a saturated sodium hydrogen carbonate solution and ethyl acetate until the mixture became clear and the organic layer was separated. The aqueous layer was extracted with ethyl acetate and the combined organic layers were dried over sodium sulphate, filtered and concentrated *in vacuo* to furnish the desired aldehyde that required no further purification.

2.2.1. Preparation and characterisation of 17g

3-formyl-1*H*-indole-5-carbonitrile

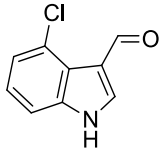


The title compound **17g** was synthesised according to general procedure **A** in 97% yield as an off white solid.

m.p. 230-233 °C; **FT-IR** ν_{max} 3207 (N–H), 2221 (C≡N), 1648 (C=O); **^{1}H NMR** (d_6-DMSO, 400 MHz) δ_H 12.54 (br s, 1H, ArNH), 9.99 (s, 1H, ArCHO), 8.49 (s, 1H, ArCH), 8.45 (d, 1H, ArCH, *J* 2.0 Hz), 7.69 (d, 1H, ArCH, *J* 8.5 Hz), 7.62 (dd, 1H, ArCH, *J* 8.5 Hz, 2.0 Hz); **^{13}C NMR** (d_6-DMSO, 100 MHz) δ_C 186.2 (C=O), 141.1 (ArCH), 139.7 (ArC_{quat}), 127.2 (ArCH), 126.6 (ArCH) 124.8 (ArC_{quat}), 120.8 (ArC_{quat}), 118.9 (ArCN), 114.8 (ArCH), 105.2 (ArC_{quat}); ***m/z*** (ES−) 169 ($[M-H]^-$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{10}H_6N_2NaO^+$) requires *m/z* 193.0372, found 193.0368.

2.2.2. Preparation and characterisation of 17b

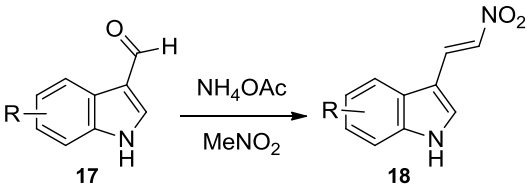
4-chloro-1*H*-indole-3-carbaldehyde



The title compound **17b** was synthesised according to general procedure **A** in 85% yield as a light brown solid.

m.p. 147-148 °C; **FT-IR** ν_{max} 1636 (C=O); **^{1}H NMR** (d_6-DMSO, 400 MHz) δ_H 12.57 (br s, 1H, ArNH), 10.49 (s, 1H, CHO), 8.30 (s, 1H, ArCH), 7.52 (d, 1H, ArCH, *J* 8.0 Hz), 7.30 (d, 1H, ArCH, *J* 8.0 Hz), 7.23 (t, 1H, ArCH, *J* 8.0 Hz); **^{13}C NMR** (d_6-DMSO, 125 MHz) δ_C 185.6 (C=O), 139.1 (ArC_{quat}), 134.9 (ArCH), 125.4 (ArC_{quat}), 124.4 (ArCH), 123.8 (ArC_{quat}), 123.4 (ArCH), 118.7 (ArC_{quat}), 112.8 (ArCH); ***m/z*** (ES−) 178 ($[M-H]^-$, 100%), **HRMS** (ES-) exact mass calculated for $[M-H]^-$ ($C_9H_5ClNO^-$) requires *m/z* 178.0065 & 180.0036 found *m/z* 178.0065 & 180.0033.

2.3. General procedure B for the synthesis of nitro-olefins 18

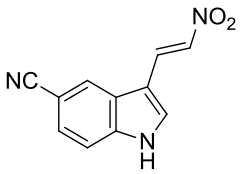


17 18

A mixture of the corresponding aldehyde **17** (1 eq), and ammonium acetate (dried under reduced pressure until the crystals became free flowing) (3 eq) in nitromethane (20 ml per 1 g of aldehyde) were heated at reflux under nitrogen for 1 hour (behind a blast shield). The reaction mixture was then allowed to cool to room temperature. **Two purification methods: 1)** The solvent was removed *in vacuo* and the residue washed with water and filtered. The filtration cake was pre-absorbed onto silica gel and purified by flash column chromatography (PE:ethyl acetate, 2:1) to furnish the desired nitro-olefin. **2)** The reaction was allowed to cool to room temperature and left to crystaillize for 14-16 h. The solid was filtered, washed with water and dried over phosphourous pentoxide in a vacuum dessicator affording the desired nitro-olefin **18**.

2.3.1. **Preparation and characterisation of 18g**

(*E*)-3-(2-nitrovinyl)-1*H*-indole-5-carbonitrile

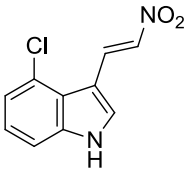


The title compound **18g** was synthesised according to general procedure **B** in 98% yield as a yellow solid.

m.p. 142 °C (decomposition); **FT-IR** 2222 (C≡N), 1621 (C=C), 1528 ($NO_{2(asy)}$), 1340 ($NO_{2(sy)}$); **^{1}H NMR** (d_6-DMSO, 400 MHz) δ_H 12.6 (br s, 1H, ArNH), 8.66 (s, 1H, ArCH), 8.40 (d, 1H, O_2NCHCH, *J* 13.5 Hz), 8.38 (s, 1H, ArCH), 8.22 (d, 1H, O_2NCHCH, *J* 13.5 Hz), 7.67 (d, 1H, ArCH, *J* 8.5 Hz), 7.61 (d, 1H, ArCH, *J* 8.5 Hz); **^{13}C NMR** (d_6-DMSO, 100 MHz) δ_C 140.2 (ArC_{quat}), 138.3 (ArCH), 134.0 (O_2NCH=CH) 134.0 (ArC_{quat}), 127.0 (O_2NCH=CH), 126.9 (ArCH), 125.3 (ArCH), 120.9 (ArCN), 114.8 (ArCH), 109.5 (ArC_{quat}), 104.8 (ArC_{quat}); ***m/z*** (ES−) 212 ($[M-H]^-$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{11}H_7N_3NaO_2^+$) requires ***m/z*** 236.0430, found ***m/z*** 236.0430.

2.3.2. **Preparation and characterisation of 18b**

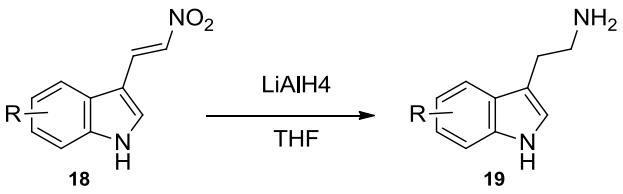
(*E*)-4-chloro-3-(2-nitrovinyl)-1*H*-indole



The title compound **18b** was synthesised according to general procedure **B** in 98% yield as a orange solid.

m.p. 158-160 °C (decomposition); **FT-IR** ν_{max} 3258 (N–H), 1605 (C=C), 1491 ($NO_{2\ (asy)}$), 1293 ($NO_{2(sy)}$); **^{1}H NMR** (d_6-DMSO, 400 MHz) δ_H 12.57 (br s, 1H, ArNH), 8.92 (d, 1H, O_2NCH=CH, *J* 13.5 Hz), 8.53 (s, 1H, ArCH), 8.12 (d, 1H, O_2NCH=CH, *J* 13.5 Hz), 7.50 (dd, 1H, ArCH, *J* 7.6 Hz, 1.5 Hz), 7.23 (m, 2H, ArCH); **^{13}C NMR** (d_6-DMSO, 100 MHz) δ_C 139.2 (ArC_{quat}), 134.4 (O_2NCHCH), 133.4 (O_2NCHCH), 132.6 (ArCH), 125.4 (ArC_{quat}), 124.5 (ArCH), 123.6 (ArC_{quat}), 123.5 (ArCH), 113.1 (ArCH), 107.8 (ArC_{quat}); ***m/z*** (ES−) 221 ($[M-H]^-$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{10}H_7ClN_2NaO_2^+$) requires ***m/z*** 245.0088 & 247.0059 found ***m/z*** 245.0084 & 247.0056.

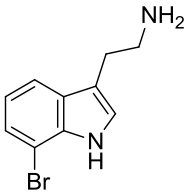
2.4. General procedure C for the synthesis of tryptamines 19



A solution nitro olefin **18** (1 equivalent) in tetrahydrofuran (10 ml per 1 mmol of nitro olefin) was added to a stirred slurry of lithium aluminium hydride powder (6 equivalents) in tetrahydrofuran (equal mass to volume, e.g. 1 g ($LiAlH_4$):1ml (tetrahydrofuran)) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 36 hours. The reaction was cooled to 0 °C and was quenched by dropwise addition of water until effervescence ceased. The mixture was then filtered and the solid washed with ethylacetate, the filtrate was concentrated *in vacuo* to furnish the desired tryptamine **19** which was purified by flash column chromatography or acidic extraction from CH_2Cl_2 solution followed by addition of solid KOH until the PH measures 14 (by universal indicator paper) and extracted with CH_2Cl_2 dried over $NaSO_4$ and concentrated.

2.4.1. Preparation and characterisation of 19m

2-(7-bromo-1*H*-indol-3-yl)ethanamine

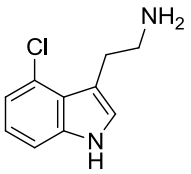


The title compound **19m** was synthesised according to general procedure **C** from known nitro-olefin[7] after acid base extraction isolated as a orange solid (50% yield).

m.p. 89-99 °C; **FT-IR** ν_{max} 3556 (NH_2), 3293 (ArN–H); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 8.67 (br s, 1H, ArNH), 7.55 (d, 1H, ArCH, *J* 8.0 Hz), 7.35 (d, 1H, ArCH, *J* 8.0 Hz), 7.07 (s, 1H, ArCH), 7.00 (t, 1H, ArCH, *J* 8.0 Hz), 3.04 (t, 2H, NCH_2, *J* 6.5 Hz), 2.90 (t, 2H, $ArCH_2$, *J* 6.5 Hz), 1.58 (br s, 2H, NH_2); **^{13}C NMR** (d_6-DMSO, 100 MHz) δ_C 135.1 (ArC_{quat}), 128.8 (ArC_{quat}), 124.3 (ArCH), 122.7 (ArCH), 120.4 (ArCH), 118.1 (ArCH), 114.9 (ArC_{quat}), 104.8 (ArCBr), 42.3 (NCH_2), 29.5 ($ArCH_2$); ***m/z*** (ES+) 239 ($[M+H]^+$, 100 %), **HRMS** (ES+) exact mass calculated for $[M+H]^+$ ($C_{10}H_{12}BrN_2^+$) requires ***m/z*** 239.0187 & 241.0158 found ***m/z*** 239.0178 & 241.0157.

2.4.2.**Preparation and characterisation of 19b**

2-(4-chloro-1*H*-indol-3-yl)ethanamine

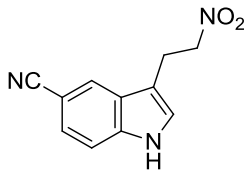


The title compound was synthesised from **19b** according to general procedure **C** and purified by flash column chromatography (DCM ramping to DCM : MeOH : NEt_3, 85 : 10 : 5) in 57% yield as a orange solid.

m.p. 83-93 °C; **FT-IR** ν_{max} 3351 (NH_2), 3294 (ArN–H); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 9.02 (br s, 1H, ArNH), 7.22 (dd, 1H, ArCH, *J* 6.5 Hz, 2.5 Hz), 7.08-7.02 (m, 2H, ArCH), 6.99 (s, 1H, ArCH), 3.13 (t, 2H, NCH_2, *J* 6.5 Hz), 3.06 (t, 2H, $ArCH_2$, *J* 6.5 Hz) 1.72 (br s, 2H, NH_2); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ_C 138.1 (ArC_{quat}), 126.3 (ArC_{quat}), 124.1 (ArC_{quat}), 123.9 (ArCH), 122.3 (ArCH), 120.3 (ArCH), 113.7 (ArC_{quat}), 110.0 (ArCH), 43.5 (NCH_2), 30.4 ($ArCH_2$); ***m/z*** (ES+) 195 ($[M+H]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+H]^+$ ($C_{10}H_{12}ClN_2^+$) requires ***m/z*** 195.0684 & 197.0654 found ***m/z*** 195.0681 & 197.0656.

2.4.3.**Preparation and characterisation of 20g[8]**

3-(2-nitroethyl)-1*H*-indole-5-carbonitrile

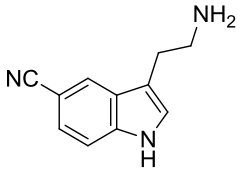


Sodium borohydride (25.8 mmol, 11 eq) was added portionwise to a solution of nitro-olefin **18b** (2.35 mmol, 1 eq) in dimethylformamide (20 ml) and methanol (20 ml). The reaction mixture was stirred at room temperature until the reaction reached completion (complete consumption of starting material by TLC analysis). Hydrochloric acid solution (2M) was added until the pH of the solution reached pH 7. The mixture was extracted with dichloromethane (3 × 30 ml) and the organic layer was washed with brine and dried over sodium sulfate filtered and concentrated *in vacuo*. Purification by column chromatography afforded the title compound XX as a off white solid (70 % yield)

m.p. 134-136 °C; **FT-IR** ν_{max} 3290 (ArN–H), 2222 (C≡N),1539 ($NO_{2\ (asy)}$), 1369 ($NO_{2(sy)}$); **^{1}H NMR** (CD_3OD, 400 MHz) δ_H 8.05 (s, 1H, ArC<u>H</u>), 7.49 (d, 1H, ArC<u>H</u>, *J* 8.5 Hz), 7.40 (d, 1H, ArC<u>H</u>, *J* 8.5 Hz), 7.30 (s, 1H, ArC<u>H</u>), 4.79-4.71 (m, 2H, $NO_2C\underline{H}_2$), 3.50-3.45 (m, 2H, $ArC\underline{H}_2$); **^{13}C NMR** (CD_3OD, 100 MHz) δ_C 138.8 ($Ar\underline{C}_{quat}$), 127.1 ($Ar\underline{C}_{quat}$), 125.9 (Ar<u>C</u>H), 124.4 (Ar<u>C</u>H), 124.1 (Ar<u>C</u>H), 120.8 (Ar<u>C</u>N), 112.6 (Ar<u>C</u>H), 111.1 ($Ar\underline{C}_{quat}$), 101.7 ($Ar\underline{C}_{quat}$), 75.8 ($O_2N\underline{C}H_2$), 23.0 ($Ar\underline{C}H_2$) ; ***m/z*** (ES+) 238 ([M+Na]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{11}H_9N_3NaO_2^+$) requires ***m/z*** 238.0587 & 239.0620 found ***m/z*** 238.0589 & 239.0627.

2.4.4. **Preparation and characterisation of 19g**

3-(2-aminoethyl)-1*H*-indole-5-carbonitrile

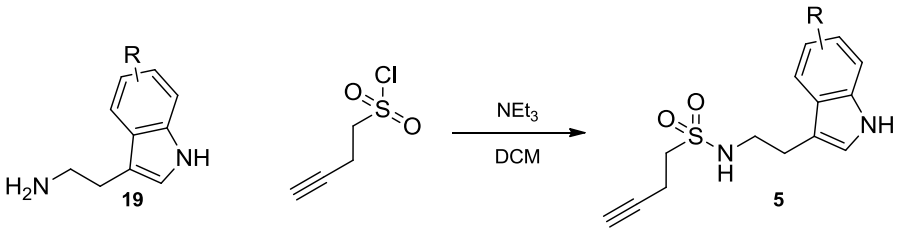


A solution of nitroalkane **20**g (1.53 mmol, 10 eq) in methanol (45 ml) was added to a mixture of zinc (35 mmol, 23 eq) in hydrochloric acid solution (2M, 45 ml) and heated to reflux over 2 hours. The reaction was cooled to room temperature and filtered. Sodium hydroxide (1M) was added the filtrate until the solution reached pH 11. The solution was extracted with a dichloromethane : methanol (95 : 5) solution and dried over $NaSO_4$. Concentration afforded the title compound **19g** as a light brown solid (88% yield).

m.p. 114-125 °C; **FT-IR** ν_{max} br 3224 (ArN–H, NH_2), 2216 (C≡N); **^{1}H NMR** (CD_3OD, 400 MHz) δ_H 8.03 (br s, 1H, ArC<u>H</u>), 7.47 (d, 1H, ArC<u>H</u>, *J* 8.5 Hz), 7.38 (d, 1H, ArC<u>H</u>, *J* 8.5 Hz), 7.28 (br s, 1H, ArC<u>H</u>), 2.95 (br s, 4H, $NC\underline{H}_2$, $ArC\underline{H}_2$); **^{13}C NMR** (CD_3OD, 100

MHz) δ_C 139.0 (Ar<u>C</u>$_{quat}$), 127.9 (Ar<u>C</u>$_{quat}$), 125.3 (Ar<u>C</u>H), 124.3 (Ar<u>C</u>H), 124.1 (Ar<u>C</u>H), 121.0 (ArC<u>C</u>N), 113.7 (Ar<u>C</u>$_{quat}$), 112.5 (Ar<u>C</u>H), 101.2 (Ar<u>C</u>CN), 42.0 (N<u>C</u>H$_2$), 27.8 (Ar<u>C</u>H$_2$); ***m/z*** (ES−) 186 ([M+H]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+H]$^+$ ($C_{11}H_{12}N_3^+$) requires ***m/z*** 186.1026 & 187.1059 found ***m/z*** 186.1032 & 187.0944.

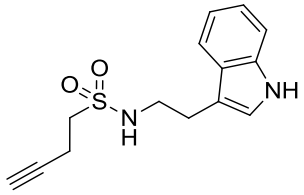
2.5. General procedure D for preparation of 5



To a stirred solution of sulfonylchloride[9] (1.1 eq) in dichloromethane (5 ml/mmol of tryptamine) under argon at -78 °C was added the desired tryptamine derivative **19** (1 eq) and triethyamine (1.1 eq) in dichloromethane (7 ml/mmol of tryptamine). The mixture was stirred at -78 °C for 5 to 10 mins then concentrated *in vacuo* (in a room temperature water bath) to give the crude product. The residue was purified by flash column chromatography (CH_2Cl_2:Et_2O, 1:0 to 8:2) to give the desired sulfonamide derivative **5**.

2.5.1. Preparation and characterisation of 5a

N-[2-(1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide



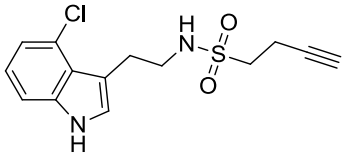
The title compound **5a** was synthesised according to general procedure **D** to give **5a** as an off white solid (90% yield). Recrystallization from ethanol gives thin white crystalline plates.

m.p. 122.4-122.5 °C; **FT-IR** ν_{max} 3419 (N–H), 3409 (N–H), 1306 (S=$O_{(as)}$), 1126 (S=$O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 8.10 (bs, 1H, ArN<u>H</u>), 7.60 (d, 1H, ArC<u>H</u>, *J* 8.0 Hz), 7.39 (d, 1H, ArC<u>H</u>, *J* 8.0 Hz), 7.23 (t, 1H, ArC<u>H</u>, *J* 8.0 Hz), 7.16 (t, 1H, ArC<u>H</u>, *J* 8.0 Hz), 7.1 (d, 1H, ArC<u>H</u>, *J* 2.5 Hz), 4.34 (t, 1H, CH_2N<u>H</u>, *J* 6.0 Hz), 3.46 (q, 2 H, ArCH_2C<u>H</u>$_2$, *J* 6.0 Hz), 3.11 (t, 2H, SC<u>H</u>$_2$, *J* 7.0 Hz), 3.07 (t, 2H, ArC<u>H</u>$_2$, *J* 6.5 Hz), 2.59 (td, 2H, SCH_2C<u>H</u>$_2$, *J* 7.0 Hz, 3.0 Hz), 1.65 (t, 1H, C≡C<u>H</u>, *J* 3.0 Hz); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ: 136.4 (Ar<u>C</u>$_{quat}$), 126.9 (Ar<u>C</u>$_{quat}$), 122.8 (Ar<u>C</u>H), 122.5 (Ar<u>C</u>H), 119.7 (Ar<u>C</u>H), 118.6 (Ar<u>C</u>H), 111.7 (Ar<u>C</u>$_{quat}$), 111.4 (Ar<u>C</u>H), 79.8 (HC≡<u>C</u>),

70.5 (C≡CH), 49.9 (SCH_2), 43.3 ($NHCH_2$), 26.2 ($ArCH_2$), 14.1 ($HCCCH_2$); ***m/z*** (ES+) 299 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{16}N_2NaO_2S^+$) requires *m/z* 299.0825, found *m/z* 299.0822.

2.5.2. Preparation and characterisation of 5b

N-[2-(4-chloro-1H-indol-3-yl)ethyl]but-3-yne-1-sulfonamide

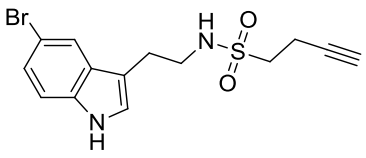


The title compound **5b** was synthesised according to general procedure **D** to give **5b** as an off white solid (80% yield). Recrystallization from ethanol gives thin white crystalline plates.

m.p. 84-85 °C; **FT-IR** ν_{max} 3381 (N–H), 3280 (N–H), 1312 ($S=O_{(as)}$), 1129 ($S=O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 8.21 (br s, 1H ArNH), 7.29 (dd, 1H, ArCH, *J* 5.5 Hz, 3.0 Hz), 7.03 (d, 1H, ArCH, *J* 2.0 Hz), 7.06-7.12 (m, 2H, ArCH), 4.33 (t, 1H, SNH, 3.51 (q, 2H, NCH_2, *J* 6.5 Hz), 3.27 (t, 2H, $ArCH_2$, *J* 6.5 Hz), 3.14 (t, 2H, SCH_2, *J* 7.0 Hz), 2.63 (td, 2H, SCH_2CH_2, *J* 7.0 Hz, 3.0 Hz), 1.69 (t, 1H, C≡CH, *J* 3.0 Hz); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ_C 138.0 (ArC_{quat}), 126.0 (ArC_{quat}), 124.6 (ArCH), 123.8 (ArC_{quat}), 122.9 (ArCH), 120.7 (ArCH), 112.0 (ArC_{quat}), 110.2 (ArCH), 79.8 (HC≡C), 70.5 (C≡CH), 49.8 (SCH_2), 44.6 (NCH_2), 27.1 ($ArCH_2$), 14.1 (SCH_2CH_2); **m/z** (ES+) 333 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{15}ClN_2O_2SNa^+$) requires *m/z* 333.0435 & 335.0406 found 333.0431 & 335.0401.

2.5.3. Preparation and characterisation of 5c

N-[2-(5-bromo-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide

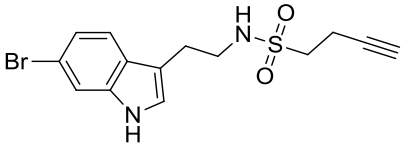


The title compound **5c** was synthesised according to general procedure **D** to give **5c** as a brown solid (25% yield). Recrystallization from ethanol gives an off white solid.

m.p. 68-70 °C; **FT-IR** ν_{max} 3415-3394 (N–H and ArN–H), 1305 ($S=O_{(as)}$), 1132 ($S=O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ_H 8.12 (bs, 1H, ArNH), 7.71 (d, 1H, ArCH, *J* 1.5 Hz) 7.31 (dd, 1H, ArCH, *J* 8.5 Hz, 2.0 Hz), 7.27 (d, 1H, ArCH, *J* 8.5 Hz), 7.13 (d, 1H, ArCH, *J* 2.0 Hz), 4.29 (t, 1H, SNH, *J* 6.0 Hz), 3.45 (q, 2H, NCH_2, *J* 6.5 Hz), 3.15 (t, 2H, SCH_2, *J* 7.0 Hz), 3.03 (t, 2H, NCH_2CH_2, *J* 6.5 Hz), 2.63 (td, 2H, SCH_2CH_2, *J* 7.0 Hz, 2.5 Hz), 1.75 (t, 1H, C≡CH, *J* 3.0 Hz); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ_C 135.0 (ArCBr), 128.7 (ArC_{quat}), 125.4 (ArCH), 123.9 (ArCH), 121.2 (ArCH), 113.0 (ArC_{quat}), 112.8 (ArCH), 111.5 (ArC_{quat}), 79.8 (HC≡C), 70.5 (HC≡C), 50.0 (SCH_2), 43.1 ($SNCH_2$), 26.1 (NCH_2CH_2), 14.1 (SCH_2CH_2); ***m/z*** (ES+) 377 ($[M+Na]^-$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{15}BrN_2O_2SNa^+$) requires *m/z* 376.9930 & 378.9909, found *m/z* 376.9925 & 378.9904.

2.5.4. **Preparation and charactarisation of 5d**

***N*-[2-(6-bromo-1H-indol-3-yl)ethyl]but-3-yne-1-sulfonamide**

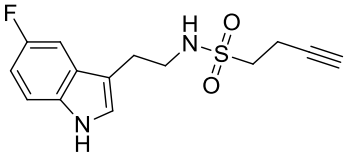


The title compound **5d** was synthesised according to general procedure **D** to give **5d** as an off white solid (73 % yield). Recrystallization from ethanol gives an off white solid.

m.p. 110-112 °C; **FT-IR** ν_{max} 3416 (N–H), 3290 (ArN–H), 1301 ($S=O_{(as)}$), 1127 ($S=O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H; 8.10 (br s, 1H, ArNH), 7.55 (s, 1H, ArCH), 7.45 (d, 1H, ArCH, *J* 8.5 Hz), 7.25 (d, 1H, ArCH, *J* 8.5 Hz), 7.09 (s, 1H, ArCH), 4.31 (t, 1H, SNH, *J* 6.5 Hz), 3.44 (q, 2H, NCH_2, *J* 6.5 Hz), 3.12 (t, 2H, SCH_2, *J* 7.0 Hz), 3.04 (t, 2H, $ArCH_2$, *J* 6.5 Hz), 2.61 (td, 2H, SCH_2CH_2, *J* 7.0 Hz, 2.5 Hz), 1.73 (t, 1H, C≡CH, *J* 2.5 Hz); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ_C; 137.2 (ArC_{quat}), 125.9 (ArC_{quat}), 123.3 (ArCH), 123.0 (ArCH), 119.8 (ArCH), 116.0 (ArCBr), 114.4 (ArCH), 112.0 (ArC_{quat}), 79.8 (HC≡C), 70.5 (C≡CH), 50.0 (SCH_2), 43.3 (NCH_2), 26.1 ($ArCH_2$), 14.1 ($HCCCH_2$); **m/z** (ES+) 377 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{15}BrN_2O_2SNa^+$) requires *m/z* 376.9930 & 378.9909, found *m/z* 376.9926 & 378.9905.

2.5.5. **Preparation and characterisation of 5e**

***N*-[2-(5-fluoro-1H-indol-3-yl)ethyl]but-3-yne-1-sulfonamide**

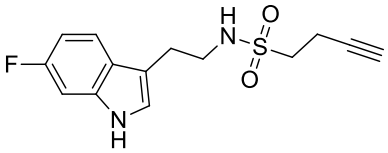


The title compound **5e** was synthesised according to general procedure **D** to give **5e** as an off white solid (57% yield). Recrystallization from ethanol gives thin white crystalline plates.

m.p. 99-101 °C; **FT-IR** ν_{max} 3419 (N–H), 3294 (ArN–H), 1300 (S=$O_{(as)}$), 1126 (S=$O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H; 8.17 (br s, 1H, ArNH), 7.30 (dd, 1H, ArCH, *J* 9.0 Hz, 4.0 Hz), 7.22 (dd, 1H, ArCH, *J* 9.5 Hz, 2.0 Hz), 7.14 (d, 1H, ArCH, *J* 2.0 Hz), 6.97 (td, 1H, ArCH, *J* 9.0 Hz, 2.5 Hz), 4.40 (t, 1H, SNH, *J* 6.0 Hz), 3.43 (q, 2H, NHCH_2, *J* 6.5 Hz), 3.12 (t, 2H, SCH_2, *J* 7.0 Hz), 3.01 (t, 2H, ArCH_2, *J* 6.5 Hz), 2.61 (td, 2H, SCH_2CH_2, *J* 7.0 Hz, 3.0 Hz), 1.73 (t, 1H, C≡CH, 2.5 Hz) **^{13}C NMR** ($CDCl_3$, 100 MHz) δ_C; 157.8 (d, ArCF, *J* 236 Hz), 132.9 (ArC_{quat}), 127.3 (d, ArC_{quat}, *J* 10 Hz), 124.6 (ArCH), 112.1 (d, ArCH, *J* 10 Hz), 111.8 (d, ArC_{quat}, *J* 4.8 Hz), 110.8 (d, ArCH, *J* 26 Hz), 103.5 (d, ArCH, *J* 24 Hz), 79.8 (HC≡C), 70.5 (C≡CH), 49.9 (SCH_2), 43.1 (SNCH_2), 26.2 (ArCH_2), 14.1 (SCH_2CH_2); **^{19}F NMR** ($CDCl_3$, 376 MHz), -124.0 (ArF); **m/z** (ES+) 317 ([M+Na]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{14}H_{15}FN_2O_2SNa^+$) requires *m/z* 317.0730 & 318.0763, found *m/z* 317.0724 & 318.0764.

2.5.6. Preparation and characterisation of 5f

N-[2-(6-fluoro-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide

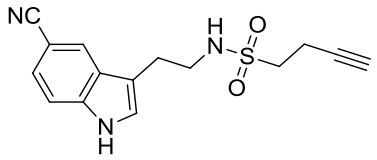


The title compound **5f** was synthesised according to general procedure **D** to give **5f** as an off white solid (46% yield). Recrystallization from ethanol gives thin white crystalline plates.

m.p. 98-99 °C; **FT-IR** ν_{max} 3419 (N–H), 3307 (ArN–H), 1301 (S=$O_{(as)}$), 1127 (S=$O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H; 8.15 (br s, 1H, ArNH), 7.49 (dd, 1H, ArCH, *J* 9.0 Hz, 5.0 Hz), 7.07 (m, 2H, ArCH), 6.92 (td, 1H, ArCH, *J* 9.0 Hz, 2.0 Hz), 4.39 (t, 1H, SNH, *J* 6.0 Hz), 3.44 (q, 2H, NCH_2, *J* 6.5 Hz), 3.11 (t, 2H, SCH_2, *J* 7.0 Hz), 3.03 (t, 2H, ArCH_2, 6.5 Hz), 2.60 (td, 2H, SCH_2CH_2, *J* 7.0 Hz, 2.5 Hz), 1.74 (t, 1H, C≡CH, *J* 3.0 Hz) **^{13}C NMR** ($CDCl_3$, 100 MHz) δ_C; 160.1 (d, ArCF, *J* 239 Hz), 136.3 (d, ArC_{quat}, *J* 12 Hz), 123.6 (ArC_{quat}), 123.0 (d, ArCH, *J* 3 Hz)), 119.3 (d, ArCH, *J* 10 Hz) 111.8 (ArC_{quat}), 108.5 (d, ArCH, *J* 24 Hz), 97.7 (d, ArCH, *J* 26 Hz) 79.8 (HC≡C), 70.5 (C≡CH), 49.9 (SCH_2), 43.3 (NCH_2), 26.2 (ArCH_2), 14.1 (SCH_2CH_2); **^{19}F NMR** ($CDCl_3$, 376 MHz), -120.4 (ArF); **m/z** (ES+) 317 ([M+Na]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{14}H_{15}FN_2O_2SNa^+$) requires *m/z* 317.0730 & 318.0763, found *m/z* 317.0727 & 318.0766.

2.5.7. Preparation and characterisation of 5g

N-[2-(5-cyano-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide

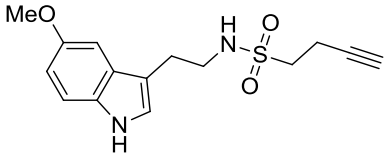


The title compound **5g** was synthesised according to general procedure **D** to give **5g** as an off white solid (42% yield). Recrystallization from ethanol gives thin white crystalline plates.

m.p. 135-136 °C; **FT-IR** ν_{max} 3339 (N–H), 3294 (ArN–H), 2225 (C≡N), 1318 (S=$O_{(as)}$), 1136 (S=$O_{(sy)}$); **^{1}H NMR** (d_6-DMSO, 400 MHz) δ_H 11.46 (br s, 1H, ArNH), 8.09 (s, 1H, ArCH), 7.51 (d, 1H, ArCH, *J* 8.0 Hz), 7.44-7.39 (m, 2H, ArCH), 7.26 (t, 1H, SNH, *J* 6.0 Hz), 3.23 (td, 2H, NCH_2, *J* 7.0 Hz, 6.0 Hz), 3.15 (t, 2H, SCH_2, *J* 7.5 Hz), 2.93 (t, 1H, C≡CH, *J* 3.0 Hz), 2.90 (t, 2H, $ArCH_2$, *J* 7.0 Hz), 2.50[(signal hidden under DMSO peak, confirmed by HSQC and COSY)] (m, 2H, $HC{\equiv}CCH_2$, *J* 7.5 Hz, 3.0 Hz); **^{13}C NMR** (d_6-DMSO, 100 MHz) δ_C 138.7 (ArC_{quat}), 127.9 (ArC_{quat}), 126.7 (ArCH), 125.1 (ArCH), 124.5 (ArCH), 121.8 (ArCN), 113.5 (ArCH), 113.5 (ArC_{quat}), 101.2 (ArC_{quat}), 82.0 (HC≡C), 73.4 (C≡CH), 50.2 (SCH_2), 43.9 (NCH_2), 26.4 ($ArCH_2$), 14.2 (SCH_2CH_2); **m/z** (ES+) 324 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{15}H_{15}N_3O_2SNa^+$) requires *m/z* 324.0777 & 325.0810, found *m/z* 324.0770 & 325.0812.

2.5.8. **Preparation and charactarisation of 5h**

***N*-[2-(5-methoxy-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide**

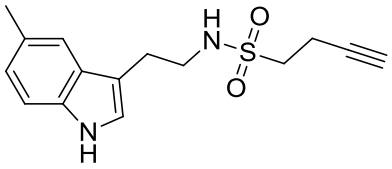


The title compound **5h** was synthesised according to general procedure **D** to give **5h** as an off white solid (81% yield). Recrystallization from ethanol gives an off white solid.

m.p. 70-72 °C; **FT-IR** ν_{max} 3405 (SN–H), 3282 (ArN–H), 1317 (S=$O_{(as)}$), 1134 (S=$O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 8.04 (br s, 1H, ArNH), 7.27 (d, 1H, ArCH, *J* 8.5 Hz), 7.05 (d, 1H, ArCH, *J* 1.5 Hz), 7.03 (d, 1H, ArCH, *J* 2.5 Hz), 6.89 (dd, 1H, ArCH, *J* 8.5 Hz, 2.5 Hz), 4.42 (t, 1H, SNH, *J* 6.5 Hz), 3.88 (s, 3H, OCH_3), 3.44 (q, 2H, NCH_2, *J* 6.5 Hz), 3.11 (t, 2H, SCH_2, *J* 7.0 Hz), 3.02 (t, 2H, $ArCH_2$, *J* 6.5 Hz), 2.59 (td, 2H, SCH_2CH_2, *J* 7.0 Hz), 1.72 (t, 1H, C≡CH, *J* 2.8 Hz); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ_C 154.2 (ArCOMe), 131.5 (ArC_{quat}), 127.4 (ArC_{quat}), 123.5 (ArCH), 112.6 (ArCH), 112.2 (ArCH), 111.4 (ArC_{quat}), 100.5 (ArCH), 79.8 (HC≡C), 70.5 (C≡CH), 56.0 (OCH_3), 49.9 (SCH_2), 43.3 (NCH_2), 26.2 ($ArCH_2$), 14.1 (SCH_2CH_2); **m/z** (ES+) 329 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{15}H_{18}N_2O_3SNa^+$) requires *m/z* 329.0930 & 330.0963, found *m/z* 329.0921 & 330.0969.

2.5.9.**Preparation and characterisation of 5i**

***N*-[2-(5-methyl-1H-indol-3-yl)ethyl]but-3-yne-1-sulfonamide**

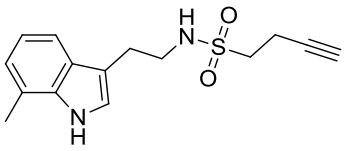


The title compound **5i** was synthesised according to general procedure **D** to give **5i** as an off white solid (72% yield). Recrystallization from ethanol gives an off white solid.

m.p. 112-114 °C; **FT-IR** ν_{max} 3412 (N–H), 3300 (ArN–H), 1307 (S=$O_{(as)}$), 1127 (S=$O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 7.99 (br s, 1H, ArNH), 7.37 (s, 1H, ArCH), 7.28 (d, 1H, ArCH, *J* 7.0 Hz), 7.06 (d, 1H, ArCH, *J* 1.5 Hz), 7.05 (dd, 1H, ArCH, *J* 7.0 Hz, 1.5 Hz), 4.32 (t, 1H, SNH, *J* 6.5 Hz), 3.45 (q, 2H, NCH_2, *J* 6.5 Hz), 3.11 (t, 2H, SCH_2, *J* 7.5 Hz), 3.04 (t, 2H, $ArCH_2$, *J* 6.5 Hz), 2.59 (td, 2H, SCH_2CH_2, *J* 7.0 Hz, 2.5 Hz), 2.47 (s, 3H, $ArCH_3$), 1.64 (t, 1H, C≡CH, *J* 2.5 Hz); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ_C 134.8 (ArC_{quat}), 129.0 (ArCMe), 127.2 (ArC_{quat}), 124.0 (ArCH), 122.9 (ArCH), 118.2 (ArCH), 111.1 (ArCH), 111.0 (ArC_{quat}), 79.8 (HC≡C), 70.5 (C≡CH), 49.9 (SCH_2), 43.3 (NCH_2), 26.2 ($ArCH_2$), 21.5 ($ArCH_3$), 14.1 ($HCCCH_2$); **m/z** (ES+) 313 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{15}H_{18}N_2NaO_2S^+$) requires *m/z* 313.0981 & 314.1014 found 313.0973 & 314.1009.

2.5.10. **Preparation and characterisation of 5j**

***N*-[2-(7-methyl-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide**



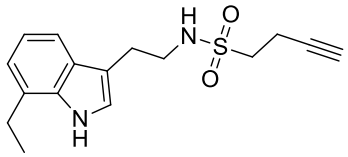
The title compound **5j** was synthesised according to general procedure **D** to give **5j** as an off white solid (95% yield). Recrystallization from ethanol gives an off white solid.

m.p. 113-117 °C; **FT-IR** ν_{max} 3400 (N–H), 3291 (ArN–H), 1303 (S=$O_{(as)}$), 1127 (S=$O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 8.05 (br s, 1H, ArNH), 7.45 (d, 1H, ArCH, *J* 7.5 Hz), 7.10 (d, 1H, ArCH, *J* 2.0 Hz), 7.08 (t, 1H, ArCH, 7.5 Hz), 7.03 (d, 1H, ArCH, *J* 7.5 Hz), 4.36 (t, 1H, SNH, *J* 6.0 Hz), 3.46 (q, 2H, NCH_2, *J* 6.0 Hz), 3.09 (t, 2H, SCH_2, *J* 7.0 Hz), 3.06 (t, 2H, $ArCH_2$, *J* 6.0 Hz), 2.57 (td, 2H,

$SCH_2\underline{C}H_2$, *J* 7.0 Hz, 3.0 Hz), 2.50 (s, 3H, $ArC\underline{H}_3$), 1.68 (t, 1H, C≡C$\underline{H}$, *J* 3.0 Hz); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ_C 136.1 ($Ar\underline{C}_{quat}$), 126.5 ($Ar\underline{C}_{quat}$), 122.9 (Ar$\underline{C}$H), 122.5 (Ar$\underline{C}$H), 120.6 ($Ar\underline{C}CH_3$), 119.9 (Ar$\underline{C}$H), 116.3 (Ar$\underline{C}$H), 112.1 ($Ar\underline{C}_{quat}$), 79.8 (HC≡$\underline{C}$), 70.5 (C≡$\underline{C}$H), 49.9 ($S\underline{C}H_2$), 43.3 ($N\underline{C}H_2$), 26.3 ($Ar\underline{C}H_2$), 16.6 ($Ar\underline{C}H_3$), 14.1 ($SCH_2\underline{C}H_2$); ***m/z*** (ES+) 313 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{15}H_{18}N_2O_2SNa^+$) requires *m/z* 313.0981 & 314.1014, found *m/z* 313.0977 & 314.1018.

2.5.11. **Preparation and characterisation of 5k**

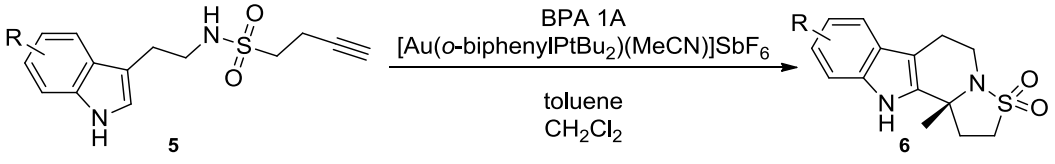
***N*-[2-(7-ethyl-1H-indol-3-yl)ethyl]but-3-yne-1-sulfonamide**



The title compound **5k** was synthesised according to general procedure **D** to give **5k** as an off white solid (25% yield). Recrystallization from ethanol gives thin white crystalline plates.

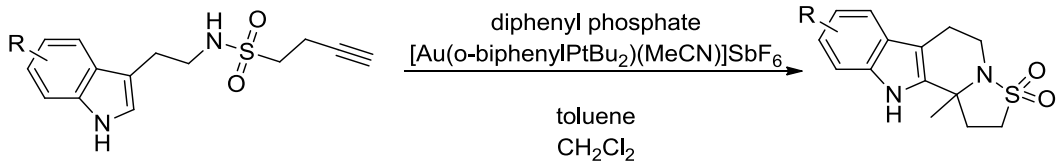
m.p. 109-112 °C; **FT-IR** ν_{max} 3404 (N–H), 3297 (ArN–H), 1312 ($S{=}O_{(as)}$), 1129 ($S{=}O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ_H 8.04 (br s, 1H, $ArN\underline{H}$), 7.45 (d, 1H, $ArC\underline{H}$, *J* 7.5 Hz), 7.11 (d, 1H, $ArC\underline{H}$, *J* 3.0 Hz), 7.11 (t, 1H, $ArC\underline{H}$, *J* 7.5 Hz), 7.07 (d, 1H, $ArC\underline{H}$, *J* 7.5 Hz), 4.31 (t, 1H, $SN\underline{H}$, *J* 6.5 Hz), 3.46 (q, 2H, $NC\underline{H}_2$, *J* 6.5 Hz), 3.11 (t, 2H, $SC\underline{H}_2$, *J* 7.5 Hz), 3.07 (t, 2H, $NCH_2C\underline{H}_2$, *J* 6.5 Hz), 2.87 (q, 2H, $ArC\underline{H}_2CH_3$, *J* 7.5 Hz), 2.59 (td, 2H, $SCH_2C\underline{H}_2$, *J* 7.5 Hz, 3.0 Hz), 1.65 (t, 1H, C≡C$\underline{H}$, *J* 3.0 Hz), 1.37 (t, 3H, $ArCH_2C\underline{H}_3$, *J* 7.5 Hz); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ_C 135.3 ($Ar\underline{C}_{quat}$), 126.8 ($Ar\underline{C}_{quat}$), 126.7 ($Ar\underline{C}_{quat}$), 122.4 (Ar$\underline{C}$H), 121.0 (Ar$\underline{C}$H), 120.1 (Ar$\underline{C}$H), 116.3 (Ar$\underline{C}$H), 112.1 ($Ar\underline{C}_{quat}$), 79.7 (HC≡$\underline{C}$), 70.4 (C≡$\underline{C}$H), 49.9 ($S\underline{C}H_2$), 43.3 ($N\underline{C}H_2$), 26.3 ($NCH_2\underline{C}H_2$), 24.0 ($Ar\underline{C}H_2CH_3$), 14.1 ($SCH_2\underline{C}H_2$), 13.8 ($ArCH_2\underline{C}H_3$); **m/z** (ES-) 303 ($[M-H]^-$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{16}H_{20}N_2O_2SNa^+$) requires *m/z* 327.1138 & 328.1171, found *m/z* 327.1134 & 328.1170.

2.6. General procedure E for preparation of 6



To a solution of the desired sulfonamide **5** (1 eq) and **BPA-1A** (0.1 eq) in toluene (14 ml per 0.1 mmol of sulfonamide) at 60 °C in a foil covered flask was added [Au(o-biphenylPtBu$_2$)(MeCN)]SbF_6 (**8**) (0.005 eq) in dichloromethane (0.67 ml per 1 mmol of sulfonamide). The reaction was allowed to stir at 60 °C for 1 to 12 hours. Upon completion the mixture was concentrated *in vacuo* and purified by flash column chromatography (CH_2Cl_2:MTBE ($CH_3OC(CH_3)_3$) 1:0 to 9:1).

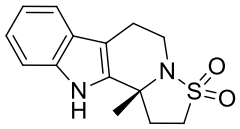
2.7. General procedure F for preparation of racemic derivatives 6



To a solution of the desired sulfonamide **5** (1 eq) and diphenylphosphate (0.1 eq) in toluene (14 ml per 0.1 mmol of sulfonamide **5**) at 60 °C in a foil covered flask was added [Au(o-biphenylPtBu$_2$)(MeCN)]SbF$_6$ (**8**) (0.05 eq) in dichloromethane (0.67 ml per 1 mmol of sulfonamide). The reaction was allowed to stir at 60 °C for 1 to 12 hours. Upon completion the mixture is concentrated *in vacuo* and purified by flash column chromatography (CH_2Cl_2:MTBE ($CH_3OC(CH_3)_3$), 1:0 to 9 : 1).

2.7.1. Preparation and characterisation of 6a

(*R*)-11b-methyl-1,2,5,6,11,11b-hexahydroisothiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide



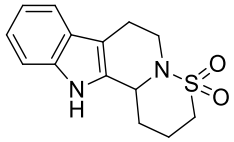
The title compound **6a** was synthesised according to general procedure **E** providing **6a** as a white solid (84% yield, 88% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220 nm, major t_R = 6.0 min, minor t_R = 15.4 min); **$[\alpha]_D^{21}$=** +113.8 (*c* 0.16, 1:1 MeOH:CH_2Cl_2)..

Racemic-6a was synthesised according to general procedure **F** as an off white solid.

m.p. 279-283 °C; **FT-IR** ν_{max} 3397 (N–H), 1289 (S=O$_{(as)}$), 1145 (S=O$_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ_H 7.78 (br s, 1H, ArN<u>H</u>), 7.50 (d, 1H, ArC<u>H</u>, *J* 8.0 Hz), 7.35 (d, 1H, ArC<u>H</u>, *J* 8.0 Hz), 7.22 (ddd, 1H, ArC<u>H</u>, *J* 8.0 Hz, 7.0 Hz, 1.0 Hz) 7.15 (ddd, 1H, ArC<u>H</u>, *J* 8.0 Hz, 7.0 Hz, 1.0 Hz), 4.05 (dd, 1H, SNC<u>H</u>$_a$H$_b$, *J* 14.5 Hz, 5.0 Hz), 3.33 (ddd, 1H, SNCH$_a$<u>H</u>$_b$, 15.0 Hz, 12.0 Hz, 4.5 Hz), 3.19 (m, 2H, ArC<u>H</u>$_a$H$_b$, SC<u>H</u>$_a$H$_b$), 2.90 (ddd, 1H, SCH$_a$<u>H</u>$_b$, *J* 12.0 Hz, 11.0 Hz, 7.0 Hz), 2.65 (m, 3H, ArCH$_a$<u>H</u>$_b$, SCH$_2$C<u>H</u>$_a$<u>H</u>$_b$), 1.73 (s, 3H, CC<u>H</u>$_3$); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ_C 135.9 (Ar<u>C</u>$_{quat}$), 133.9 (Ar<u>C</u>$_{quat}$), 126.8 (Ar<u>C</u>$_{quat}$), 122.8 (Ar<u>C</u>H), 120.1 (Ar<u>C</u>H), 118.7 (Ar<u>C</u>H), 111.9 (Ar<u>C</u>H), 109.7 (Ar<u>C</u>$_{quat}$), 59.1 (N<u>C</u>CH$_2$), 46.0 (NS<u>C</u>H$_2$), 38.1 (SN<u>C</u>H$_2$), 33.6 (NSCH$_2$<u>C</u>H$_2$), 28.2 (C<u>C</u>H$_3$), 19.9 (Ar<u>C</u>H$_2$); (ES+) 299 ([M+Na]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{14}H_{16}N_2O_2SNa^+$) requires *m/z* 299.0825 & 300.0858, found *m/z* 299.0821 & 300.0861.

2.7.2. Preparation and characterisation of 7[a]

2,3,6,7,12,12b-hexahydro-1*H*-[1,2]thiazino[2',3':1,2]pyrido[3,4-b]indole 4,4-dioxide

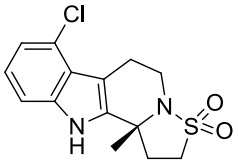


The title compound **7a** was isolated along side **6a** according to general procedure **E** providing a white solid (8% yield).

m.p. 261-265 °C (decomposition); **FT-IR** ν_{max} 3412 (N–H), 1323 (S=$O_{(as)}$), 1149 (S=$O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ_H 7.73 (br s, 1H, ArNH), 7.51 (d, 1H, ArCH, *J* 8.0 Hz), 7.34 (d, 1H, ArCH, *J* 8.0 Hz), 7.21 (t, 1H, ArCH, *J* 8.0 Hz), 7.14 (t, 1H, ArCH, *J* 8.0 Hz), 4.97 (d, 1H, NCHCH$_2$, *J* 11.0 Hz), 3.68 (m, 1H, SNCH_aH_b), 3.60 (m, 1H, SNCH_aH_b), 3.21 (dt, 1H, NSCH_aCH_b, *J* 13.5 Hz, 3.5 Hz), 3.02 (td, 1H, NSCH_aH_b, *J* 13.5 Hz, 4.0 Hz), 2.95 (m, 1H, ArCH_aH_b), 2.89 (dt, 1H, ArCH_aH_b, *J* 15.5 Hz, 4.5 Hz), 2.44 (qt, 1H, NSCH$_2$CH_aH_b, *J* 14.0 Hz, 3.5 Hz), 2.24 (dt, 1H, NSCH$_2$CH_aH_b, *J* 14.0 Hz, 3.5 Hz), 2.05 (dq, 1H, NSCH$_2$CH$_2$CH_aH_b, *J* 14.5 Hz, 3.0 Hz), 1.84 (m, 1H, NSCH$_2$CH$_2$CH_aH_b); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ_C 136.2 (ArC$_{quat}$), 132.0 (ArC$_{quat}$), 126.5 (ArC$_{quat}$), 122.4 (ArCH), 120.0 (ArCH), 118.4 (ArCH), 110.9 (ArCH), 108.7 (ArC$_{quat}$), 55.5 (NCCH$_2$), 46.8 (NSCH$_2$), 39.8 (SNCH$_2$), 27.8 (NSCH$_2$CH$_2$CH$_2$), 22.8 (NSCH$_2$CH$_2$), 21.4 (ArCH$_2$); ***m/z*** (ES+) 299 ([M+Na]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{14}H_{16}N_2O_2SNa^+$) requires *m/z* 299.0825 & 300.0858, found *m/z* 299.0819 & 300.0863.

2.7.3. Preparation and characterisation of 6b

(*R*)-7-chloro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide



The title compound **6b** was synthesised according to general procedure **E** providing a white solid (77% yield, 95% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220 nm, major t_R = 5.8 min, minor t_R = 8.1 min); **$[\alpha]_D^{25}$=** +94.3 (*c* 0.21, 1:1 MeOH:CH_2Cl_2).

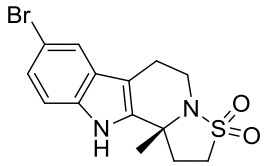
Racemic-6b was synthesised according to general procedure **F** as an off white solid,

m.p. 208 °C (decomposition); **FT-IR** ν_{max} 3321 (N–H), 1303 (S=$O_{(as)}$), 1136 (S=$O_{(sy)}$); **^{1}H NMR** (CD_3OD, 500 MHz) δ_H 7.25 (dd, 1H, ArCH, *J* 8.0 Hz, 1.0 Hz), 7.03 (t, 1H, ArCH, *J* 8.0 Hz), 6.96 (d, 1H, ArCH, *J* 7.5 Hz), 3.92 (dd, 1H, NCH_aH_b, *J* 15.0 Hz, 5.5 Hz), 3.37 (ddd, 1H, NCH_aH_b, *J* 15.0 Hz, 12.0 Hz, 4.5 Hz), 3.32-3.23 (m, 2H, NCH$_2$CH_aH_b, SCH_aH_b), 3.09 (ddd, 1H, NCH$_2$CH$_a$CH_b, *J* 15.5

Hz, 4.0 Hz, 1.0 Hz), 2.92 (ddd, 1H, SCH_aH_b, *J* 12.5 Hz, 10.0 Hz, 7.0 Hz), 2.77 (ddd, 1H, $SCH_2CH_aH_b$, *J* 13.5 Hz, 7.0 Hz, 5.5 Hz), 2.60 (ddd, 1H, $SCH_2CH_aH_b$, 13.5 Hz, 10.0 Hz, 6.5 Hz), 1.72 (s, 3H, $NCCH_3$); **^{13}C NMR** (CD_3OD, 125 MHz) δ_C 139.1 (ArC_{quat}), 137.4 (ArCCl), 126.9 (ArC_{quat}), 125.2 (ArC_{quat}), 123.4 (ArCH), 120.6 (ArCH), 111.0 (ArCH), 108.8 (ArC_{quat}), 60.6 ($NCCH_3$), 47.0 (SCH_2), 38.7 (NCH_2), 34.3 (SCH_2CH_2), 28.0 (NCH_2CH_2), 23.0 ($NCCH_3$); **m/z** (ES+) 333 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{15}ClN_2O_2SNa^+$) requires *m/z* 333.0435 & 335.0406, found *m/z* 333.0435 & 335.0405.

2.7.4. Preparation and characterisation of 6c

(*R*)-8-bromo-11b-methyl-1,2,5,6,11,11b-hexahydroisothiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide



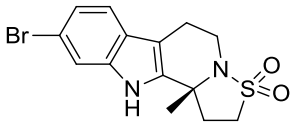
The title compound **6c** was synthesised according to general procedure **E** as a white solid (82% yield, 90% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220 nm, major t_R = 10.0 min, minor t_R = 27.2 min); **$[\alpha]_D^{21}$=** +101.6 (*c* 0.25, 1:1 MeOH:CH_2Cl_2).

Racemic-6c was synthesised according to general procedure **F** as an off white solid.

m.p. 266 °C (decomposition); **FT-IR** ν_{max} 3410 (N–H), 1301 ($S=O_{(as)}$), 1143 ($S=O_{(sy)}$); **^{1}H NMR** (d_6-acetone, 500 MHz) δ_H 10.42 (br s, 1H, ArNH), 7.63 (d, 1H, ArCH, *J* 2.0 Hz), 7.31 (d, 1H, ArCH, *J* 8.5 Hz), 7.23 (dd, 1H, ArCH, *J* 8.5 Hz, 2.0 Hz), 3.91 (dd, 1H, SCH_aH_b, *J* 15.0 Hz, 6.0 Hz), 3.37 (ddd, 1H, SCH_aH_b, *J* 15.0 Hz, 12.5 Hz, 5.0 Hz), 3.28 (dt, 1H, NCH_aH_b, *J* 12.5 Hz, 6.0 Hz), 3.05 (ddd, 1H, $SCH_2CH_aH_b$, *J* 15.5 Hz, 12.5 Hz, 6.0 Hz), 2.95-2.80 (m, 2H, NCH_aH_b, $ArCH_aH_b$), 2.65-2.60 (m, 2H, $ArCH_aH_b$, $SCH_2CH_aH_b$), 1.72 (s, 3H, CH_3); **^{13}C NMR** (d_6-acetone, 125 MHz) δ_C 138.2 (ArCBr), 136.0 (ArC_{quat}), 129.6 (ArC_{quat}), 125.2 (ArCH), 121.6 (ArCH), 113.8 (ArCH), 112.7 (ArC_{quat}), 108.6 (ArC_{quat}), 59.8 ($NCCH_2$), 46.7 (NCH_2), 38.1 (SCH_2), 34.0 ($ArCH_2$), 28.0 (CH_3), 20.5 (SCH_2CH_2); ***m/z*** (ES−) 355 ($[M-H]^-$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{15}BrN_2O_2SNa^+$) requires *m/z* 376.9930 & 378.9909, found *m/z* 376.9922 & 378.9900.

2.7.5. Preparation and characterisation of 6d

(*R*)-9-bromo-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide



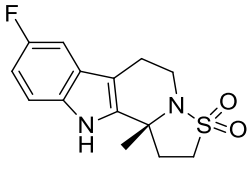
The title compound **6d** was synthesised according to general procedure **E** providing a white solid (81% yield, 91% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220 nm, major t_R = 8.3 min, minor t_R = 32.0 min); **[α]$_D^{25}$=** +148.2 (*c* 0.23, 1:1 MeOH:CH_2Cl_2).

Racemic-6d was synthesised according to general procedure **F** as an off white solid.

m.p. 228 °C (decomposition); **FT-IR** ν_{max} 3369 (N–H), 1295 (S=$O_{(as)}$), 1135 (S=$O_{(sy)}$); **^{1}H NMR** (CD_3OD, 500 MHz) δ_H 7.48 (d, 1H, ArC<u>H</u>, *J* 1.5 Hz), 7.34 (d, 1H, ArC<u>H</u>, *J* 8.5 Hz), 7.14 (dd, 1H, ArC<u>H</u>, *J* 8.5 Hz, 1.5 Hz), 3.94 (dd, 1H, NC<u>H$_a$</u>H$_b$, *J* 15.0 Hz, 6.0 Hz), 3.38 (ddd, 1H, NCH$_a$<u>H$_b$</u>, *J* 15.0 Hz, 12. Hz, 4.5 Hz), 3.34-3.27$^{(signal\ hidden\ under\ methanol\ peak,\ confirmed\ by\ HSQC\ and\ COSY)}$ (m, 1H, SC<u>H$_a$</u>H$_b$), 3.05 (ddd, 1H, NCH$_2$C<u>H$_a$</u>H$_b$, *J* 15.5 Hz, 12.0 Hz, 6.0 Hz), 2.92 (ddd, 1H, SCH$_a$<u>H$_b$</u>, *J* 12.5 Hz, 10.0 Hz, 7.0 Hz), 2.76 (ddd, 1H, SCH$_2$C<u>H$_a$</u>H$_b$, *J* 13.5 Hz, 7.0 Hz, 5.5 Hz), 2.63-2.56 (m, 2H, NCH$_2$CH$_a$<u>H$_b$</u>, SCH$_2$CH$_a$<u>H$_b$</u>, 1.70 (S, 3H, C<u>H$_3$</u>); **^{13}C NMR** (CD_3OD, 125 MHz) δ_C 138.6 (Ar<u>C$_{quat}$</u>), 137.1 (Ar<u>C$_{quat}$</u>), 127.0 (Ar<u>C$_{quat}$</u>), 123.3 (Ar<u>C</u>H), 120.5 (Ar<u>C</u>H), 116.1 (Ar<u>C</u>Br), 114.9 (Ar<u>C</u>H), 109.1 (Ar<u>C$_{quat}$</u>), 60.7 (N<u>C</u>CH$_3$), 47.0 (S<u>C</u>H$_2$), 38.6 (N<u>C</u>H$_2$), 34.2 (SCH$_2$<u>C</u>H$_2$), 27.9 (NC<u>C</u>H$_3$), 20.8 (NCH$_2$<u>C</u>H$_2$); **m/z** (ES+) 377 ([M+Na]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{14}H_{15}BrN_2O_2SNa^+$) requires *m/z* 376.9930 & 378.9909, found *m/z* 376.9928 & 378.9906.

2.7.6. **Preparation and characterisation of 6e**

(*R*)-8-fluoro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide



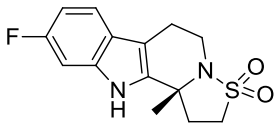
The title compound **6e** was synthesised according to general procedure **E** providing a white solid (85% yield, 93% e.e.).Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220 nm, major t_R = 8.5 min, minor t_R = 26.9 min); **[α]$_D^{25}$=** +164.3 (*c* 0.21, 1:1 MeOH:CH_2Cl_2).

Racemic-6e was synthesised according to general procedure **F** as an off white solid.

m.p. 205 °C (decomposition); **FT-IR** ν_{max} (N–H), 1299 (S=$O_{(as)}$), 1135 (S=$O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ_H 7.74 (br s, 1H, ArN<u>H</u>), 7.25 (dd, 1H, ArC<u>H</u>, *J* 9.0 Hz, 4.5 Hz), 7.31 (dd, 1H, ArC<u>H</u>, *J* 9.0 Hz, 2.5 Hz), 6.95 (td, 1H, ArC<u>H</u>, *J* 9.0 Hz, 2.5 Hz), 4.05 (dd, 1H, NC<u>H</u>$_a$H$_b$, *J* 14.5 Hz, 5.5 Hz), 3.32 (ddd, 1H, NCH$_a$<u>H</u>$_b$, *J* 14.5, 12.0 Hz, 4.5 Hz), 3.23 (ddd, 1H, SC<u>H</u>$_a$H$_b$, *J* 12.0 Hz, 6.5 Hz, 5.0 Hz), 3.13 (ddd, 1H, NCH$_2$C<u>H</u>$_a$H$_b$, *J* 15.5 Hz, 12.0 Hz, 5.5 Hz), 2.91 (ddd, 1H, SCH$_a$<u>H</u>$_b$, *J* 12.0 Hz, 10.5 Hz, 7.0 Hz), 2.68 (ddd, 1H, SCH$_2$C<u>H</u>$_a$H$_b$, *J* 13.0 Hz, 7.5 Hz, 4.5 Hz), 2.65-2.54 (m, 2H, SCH$_2$CH$_a$<u>H</u>$_b$, NCH$_2$CH$_a$<u>H</u>$_b$), 1.72 (s, 3H, NCC<u>H</u>$_3$); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ_C 157.7 (d, Ar<u>C</u>F, *J* 237.5 Hz), 135.8 (Ar<u>C</u>$_{quat}$), 132.3 (Ar<u>C</u>$_{quat}$), 127.3 (d, Ar<u>C</u>H, *J* 9.5 Hz), 111.5 (d, Ar<u>C</u>H, *J* 9.5 Hz), 111.0 (d, Ar<u>C</u>H, *J* 26.7 Hz), 109.8 (d, ArC$_{quat}$, *J* 5.0 Hz), 103.9 (d, Ar<u>C</u>H, *J* 24.0 Hz), 59.0 (N<u>C</u>CH$_3$), 45.9 (S<u>C</u>H$_2$), 37.9 (NCH$_2$), 33.5 (SCH$_2$<u>C</u>H$_2$), 28.1 (NC<u>C</u>H$_3$), 19.9 (NCH$_2$<u>C</u>H$_2$); **^{19}F NMR** ($CDCl_3$, 376 MHz), -123.7 (ArF); **m/z** (ES+) 317 ([M+Na]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{14}H_{15}FN_2O_2SNa^+$) requires *m/z* 317.0730 & 318.0763, found *m/z* 317.0724 & 318.0763.

2.7.7. **Preparation and characterisation of 6f**

(*R*)-9-fluoro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide



The title compound **6f** was synthesised according to general procedure **E** providing a white solid (85% yield, 83% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220 nm, major t_R = 7.4 min, minor t_R = 25.1 min); **$[\alpha]_D^{25}$=** + 138.1 (*c* 0.24, 1:1 MeOH:CH_2Cl_2).

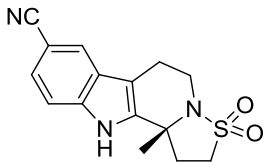
Racemic-6f was synthesised according to general procedure **F** as an off white solid: Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220, major t_R = 7.2 min, minor t_R = 24.2 min);

m.p. 220 °C (decomposition); **FT-IR** ν_{max} 3318 (N–H), 1280 (S=$O_{(as)}$), 1122 (S=$O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ_H 7.80 (br s, 1H, ArN<u>H</u>), 7.39 (dd, 1H, ArC<u>H</u>, *J* 8.5 Hz, 5.0 Hz), 7.03 (dd, 1H, ArC<u>H</u>, *J* 9.5 Hz, 2.0 Hz), 6.90 (ddd, 1H, ArC<u>H</u>, *J* 9.5 Hz, 8.5 Hz, 2.0 Hz), 4.04 (dd, 1H, NC<u>H</u>$_a$H$_b$, *J* 14.5 Hz, 5.5 Hz), 3.32 (ddd, 1H, NCH$_a$<u>H</u>$_b$, *J* 14.5 Hz, 12.0 Hz, 4.5 Hz), 3.23 (ddd, 1H, SC<u>H</u>$_a$H$_b$, *J* 12.0 Hz, 6.0 Hz, 4.5 Hz), 3.14 (ddd, 1H, NCH$_2$C<u>H</u>$_a$H$_b$, *J* 15.5 Hz, 12.0 Hz, 6.0 Hz), 2.91 (ddd, 1H, SC<u>H</u>$_a$H$_b$, *J* 12.0 Hz, 10.5 Hz, 7.0 Hz), 2.68 (ddd, 1H, SCH$_2$C<u>H</u>$_a$H$_b$, *J* 13.0 Hz, 7.0 Hz, 5.0 Hz), 2.64-2.57 (m, 2H, SCH$_2$CH$_a$<u>H</u>$_b$, NCH$_2$CH$_a$<u>H</u>$_b$), 1.72 (s, 3H, NCC<u>H</u>$_3$); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ_C 160.2 (d, Ar<u>C</u>F, *J* 237.0 Hz), 135.9 (d, Ar<u>C</u>$_{quat}$, *J* 12.5 Hz), 134.1 (d, Ar<u>C</u>$_{quat}$, *J* 4.0 Hz), 123.4 (Ar<u>C</u>$_{quat}$), 119.4 (d, Ar<u>C</u>H, *J* 10.5 Hz), 109.7 (Ar<u>C</u>$_{quat}$), 108.7 (d, Ar<u>C</u>H, *J* 25.0 Hz), 97.6 (d, Ar<u>C</u>H, *J* 26.5 Hz), 59.0 (N<u>C</u>CH$_3$), 45.9 (S<u>C</u>H$_2$), 37.9 (N<u>C</u>H$_2$), 33.4 (SCH$_2$<u>C</u>H$_2$), 28.1 (NC<u>C</u>H$_3$), 19.8 (NCH$_2$<u>C</u>H$_2$); **^{19}F NMR** ($CDCl_3$, 376 MHz), -119.6 (ArF); **m/z** (ES+) 317

([M+Na]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{14}H_{15}FN_2O_2SNa^+$) requires *m/z* 317.0730 & 318.0763, found *m/z* 317.0728 & 318.0767.

2.7.8. **Preparation and characterisation of 6g**

(*R*)-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole-8-carbonitrile 3,3-dioxide



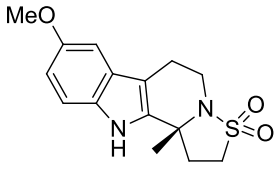
The title compound **6g** was synthesised according to general procedure **E** providing a white solid (60% yield, 96% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220 nm, major t_R = 13.1 min, minor t_R = 53.6 min); **$[\alpha]_D^{25}$=** +95.9 (*c* 0.16, 1:1 MeOH:CH_2Cl_2).

Racemic-6g was synthesised according to general procedure **F** as an off white solid.

m.p. 210 °C (decomposition); **FT-IR** ν_{max} 3316 (N–H), 2219 (C≡N), 1302 (S=$O_{(as)}$), 1134 (S=$O_{(sy)}$); **^{1}H NMR** (CD_3OD, 500 MHz) δ_H 7.90 (s, 1H, ArC<u>H</u>), 7.46 (d, 1H, ArC<u>H</u>, *J* 8.5 Hz), 7.43 (dd, 1H, ArC<u>H</u>, *J* 8.5 Hz, 1.5 Hz), 3.97 (dd, 1H, NC<u>H_a</u>H_b, *J* 15.0 Hz, 5.5 Hz), 3.41 (ddd, 1H, NCH_a<u>H_b</u>, *J* 15.0 Hz, 11.5 Hz, 4.5 Hz), 3.35-3.30$^{(signal\ hidden\ under\ methanol\ peak,\ confirmed\ by\ HSQC\ and\ COSY)}$ (m, 1H, SC<u>H_a</u>H_b), 3.09 (ddd, 1H, NCH_2C<u>H_a</u>H_b, *J* 15.5 Hz, 12.0 Hz, 6.0 Hz), 2.94 (ddd, 1H, SCH_a<u>H_b</u>, *J* 12.5 Hz, 9.5 Hz, 7.0 Hz), 2.78 (ddd, 1H, SCH_2C<u>H_a</u>H_b, *J* 13.0 Hz, 7.0 Hz, 5.5 Hz), 2.71-2.59 (m, 2H, SCH_2CH_a<u>H_b</u>, NCH_2CH_a<u>H_b</u>), 1.72 (s, 3H, NCC<u>H_3</u>); **^{13}C NMR** (CD_3OD, 125 MHz) δ_C 139.7 (Ar<u>C</u>$_{quat}$), 139.2 (Ar<u>C</u>$_{quat}$), 128.0 (Ar<u>C</u>$_{quat}$), 125.9 (Ar<u>C</u>H), 124.9 (Ar<u>C</u>H), 121.8 (Ar<u>C</u>CN), 113.2 (Ar<u>C</u>H), 110.0 (Ar<u>C</u>N), 102.8 (Ar<u>C</u>$_{quat}$), 60.5 (N<u>C</u>CH_3), 47.0 (S<u>C</u>H_2), 38.4 (N<u>C</u>H_2), 34.1 (SCH_2<u>C</u>H_2), 27.8 (NC<u>C</u>H_3), 20.7 (NCH_2<u>C</u>H_2); **m/z** (ES+) 324 ([M+Na]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{15}H_{15}N_3O_2SNa^+$) requires *m/z* 324.0777 & 325.0810, found *m/z* 324.0775 & 325.0818.

2.7.9. **Preparation and characterisation of 6h**

(*R*)-8-methoxy-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide



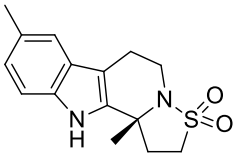
The title compound **6h** was synthesised according to general procedure **E** providing a white solid (75% yield, 80% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220 nm, major t_R = 8.2 min, minor t_R = 14.3 min); **$[\alpha]_D^{25}$=** 93.2 (*c* 0.734, 1:1 MeOH:CH_2Cl_2).

Racemic-6h was synthesised according to general procedure **F** as an off white solid.

m.p. 210-220 °C (decomposition); **FT-IR** ν_{max} 3365 (N–H), 2506 (ArOC–H), 1298 (S=$O_{(as)}$), 1137 (S=$O_{(sy)}$); **^{1}H NMR** (CD_3OD, 500 MHz) δ_H 7.21 (d, 1H, ArC<u>H</u>, *J* 9.0 Hz), 6.92 (d, 1H, ArC<u>H</u>, *J* 2.5 Hz), 6.77 (dd, 1H, ArC<u>H</u>, *J* 9.0 Hz, 2.5 Hz), 3.93 (dd, 1H, NC<u>H</u>$_a$H$_b$, *J* 14.5 Hz, 5.5 Hz), 3.82 (s, 3H, OC<u>H</u>$_3$), 3.38 (ddd, 1H, NCH$_a$<u>H</u>$_b$, *J* 14.5 Hz, 12.0 Hz, 4.5 Hz), 3.28 (dt, 1H, SC<u>H</u>$_a$H$_b$, *J* 12.0 Hz, 6.0 Hz), 3.05 (ddd, 1H, NCH$_2$C<u>H</u>$_a$H$_b$, *J* 15.5 Hz, 12.0 Hz, 6.0 Hz), 2.90 (ddd, 1H, SCH$_a$<u>H</u>$_b$, *J* 12.5 Hz, 10.0 Hz, 7.0 Hz), 2.77 (ddd, 1H, SCH$_2$CH$_a$<u>H</u>$_b$, *J* 13.0 Hz, 7.0 Hz, 5 Hz), 2.58 (m, 2H, SCH$_2$CH$_a$C<u>H</u>$_b$, NCH$_2$CH$_a$<u>H</u>$_b$), 1.70 (s, 3H, NCC<u>H</u>$_3$); **^{13}C NMR** (CD_3OD, 125 MHz) δ_C 155.3 (Ar<u>C</u>O), 136.8 (Ar<u>C</u>$_{quat}$), 133.0 (Ar<u>C</u>$_{quat}$), 128.3 (Ar<u>C</u>$_{quat}$), 112.9 (Ar<u>C</u>H), 112.7 (Ar<u>C</u>H), 108.6 (Ar<u>C</u>$_{quat}$), 101.2 (Ar<u>C</u>H), 61.0 (N<u>C</u>CH$_3$), 56.3 (O<u>C</u>H$_3$), 47.1 (S<u>C</u>H$_2$), 38.8 (N<u>C</u>H$_2$), 34.3 (SCH$_2$<u>C</u>H$_2$), 28.1 (NC<u>C</u>H$_3$), 21.0 (NCH$_2$<u>C</u>H$_2$); **m/z** (ES-) 305 ([M-H]$^-$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{15}H_{18}N_2O_3SNa^+$) requires *m/z* 329.0930 & 330.0963, found *m/z* 329.0917 & 330.0965.

2.7.1. **Preparation and characterisation of 6i**

(*R*)-8,11b-dimethyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide



The title compound **6i** was synthesised according to general procedure **E** providing a white solid (84% yield, 87% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220 nm, major t_R = 6.7 min, minor t_R = 14.0 min); **$[\alpha]_D^{25}$=** 101.3 (*c* 0.20, 1:1 MeOH:CH_2Cl_2).

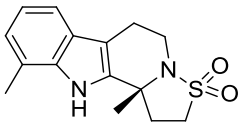
Racemic-6i was synthesised according to general procedure **F** as an off white solid.

m.p. 220 °C (decomposition); **FT-IR** ν_{max} 3390 (N–H), 1300 (S=$O_{(as)}$), 1141 (S=$O_{(sy)}$); **^{1}H NMR** (CD_3OD, 500 MHz) δ_H 7.21 (br s, 1H, ArC<u>H</u>), 7.20 (d, 1H, ArC<u>H</u>, *J* 8.0 Hz), 6.95 (dd, 1H, ArC<u>H</u>, *J* 8.0 Hz, 1.5 Hz), 3.93 (dd, 1H, NC<u>H</u>$_a$H$_b$, *J* 14.5 Hz, 5.5 Hz), 3.42-

3.35 (m, 1H, $NCH_a\underline{H}_b$), 3.35-3.26 (m, 1H, $SC\underline{H}_aH_b$), 3.05 (ddd, 1H, $NCH_2C\underline{H}_aH_b$, *J* 15.5 Hz, 12 Hz, 6.0 Hz), 2.91 (ddd, 1H, $SCH_a\underline{H}_b$, *J* 12.0 Hz, 10.0 Hz, 7.0 Hz), 2.78 (ddd, 1H, $SCH_2C\underline{H}_aH_b$, *J* 13.5 Hz, 7.0 Hz, 5.0 Hz), 2.62-2.54 (m, 2H, $SCH_2CH_a\underline{H}_b$, $NCH_2CH_a\underline{H}_b$), 2.41 (s, 3H, $ArC\underline{H}_3$), 1.70 (s, 3H, $NCC\underline{H}_3$); **^{13}C NMR** (CD_3OD, 125 MHz) δ_C 136.2 (ArC_{quat}), 136.1 (ArC_{quat}), 129.2 (ArC_{quat}), 128.3 (ArC_{quat}), 124.4 (ArCH), 118.7 (ArCH), 111.7 (ArCH), 108.3 (ArC_{quat}), 61.0 ($NCCH_3$), 47.1 (SCH_2), 38.8 (NCH_2), 34.3 (SCH_2CH_2), 28.1 ($NCCH_3$), 21.6 ($ArCH_3$), 20.9 (NCH_2CH_2); **m/z** (ES+) 313 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{15}H_{18}N_2O_2SNa^+$) requires *m/z* 313.0981 & 314.1014, found *m/z* 313.0973 & 314.1008.

2.7.2. Preparation and characterisation of 6j

(*R*)-10,11b-dimethyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide



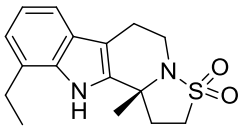
The title compound **6j** was synthesised according to general procedure **E** providing a white solid (85% yield, 92% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220 nm, major t_R = 5.0 min, minor t_R = 6.1 min); **$[\alpha]_D^{25}$=** +182.1 (*c* 0.25, 1:1 MeOH:CH_2Cl_2).

Racemic-6j was synthesised according to general procedure **F** as an off white solid.

m.p. 195 °C (decomposition); **FT-IR** ν_{max} 3338 (N-H), 1296 ($S{=}O_{(as)}$), 1125 ($S{=}O_{(sy)}$); **^{1}H NMR** (CD_3OD, 500 MHz) δ_H 7.25 (dd, 1H, ArC$\underline{H}$, *J* 7.0 Hz, 2.0 Hz), 6.94 (t, 1H, ArC$\underline{H}$, *J* 7.0 Hz,), 6.91 (d, 1H, ArC$\underline{H}$, *J* 7.0 Hz), 3.93 (dd, 1H, $NC\underline{H}_aH_b$, *J* 15.0 Hz, 5.5 Hz), 3.38 (ddd, 1H, $NCH_a\underline{H}_b$, *J* 15.0 Hz, 12.0 Hz, 4.5 Hz), 3.28 (m, 1H, $SC\underline{H}_aH_b$), 3.07 (ddd, 1H, $NCH_2C\underline{H}_aH_b$, *J* 15.5 Hz, 12.0 Hz, 6.0 Hz), 2.94-2.83 (m, 2H, $SCH_a\underline{H}_b$, $SCH_2C\underline{H}_aH_b$), 2.65-2.56 (m, 2H, $NCH_2CH_a\underline{H}_b$, $SCH_2CH_a\underline{H}_b$), 2.50 (s, 3H, $ArC\underline{H}_3$), 1.74 (s, 3H, $NCC\underline{H}_3$); **^{13}C NMR** (CD_3OD, 125 MHz) δ_C 137.2 (ArC_{quat}), 135.9 (ArC_{quat}), 127.7 (ArC_{quat}), 123.6 (ArCH), 121.6 (ArC_{quat}), 120.4 (ArCH), 116.7 (ArCH), 109.2 (ArC_{quat}), 61.1 ($NCCH_3$), 47.1 (SCH_2), 38.7 (NCH_2), 34.2 (SCH_2CH_2), 28.0 ($NCCH_3$), 21.1 (NCH_2CH_2), 17.1 ($ArCH_3$); **m/z** (ES+) 313 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{15}H_{18}N_2O_2SNa^+$) requires *m/z* 313.0981 & 314.1014, found *m/z* 313.0974 & 314.1017.

2.7.3. Preparation and characterisation of 6k

(*R*)-10-ethyl-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide



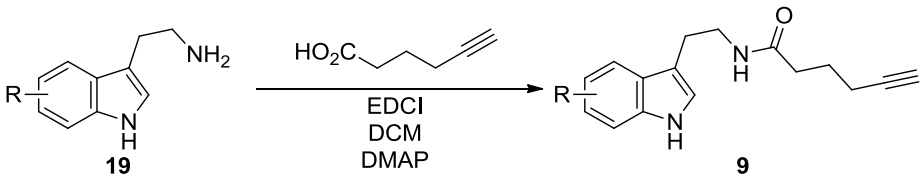
The title compound **6k** was synthesised according to general procedure **E** providing a white solid (83% yield, 95% e.e.).Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220 nm, major t_R = 7.9 min, minor t_R = 10.2 min); **$[\alpha]_D^{25}$=** +204.4 (*c* 0.09, 1:1 MeOH:CH_2Cl_2).

Racemic-6k was synthesised according to general procedure **F** as an off white solid: Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220, major t_R = 8.0 min, minor t_R = 10.3 min);

m.p. 190 °C (decomposition); **FT-IR** ν_{max} 3341 (N–H), 1296 (S=$O_{(as)}$), 1124 (S=$O_{(sy)}$); **^{1}H NMR** (CD_3OD, 500 MHz) δ_H 7.25 (dd, 1H, ArC<u>H</u>, *J* 7.0 Hz, 2.5 Hz), 6.99-6.94 (m, 2H, ArC<u>H</u>), 3.93 (dd, 1H, NC<u>H</u>$_a$H$_b$, *J* 15.0 Hz, 5.5 Hz), 3.39 (ddd, 1H, NCH$_a$<u>H</u>$_b$, *J* 15.0 Hz, 12.0 Hz, 4.5 Hz), 3.29 (dd, 1H, SC<u>H</u>$_a$H$_b$, *J* 11.5 Hz, 7.0 Hz, 5.0 Hz), 3.07 (ddd, 1H, NCH_2C<u>H</u>$_a$H$_b$, *J* 15.5 Hz, 12.0 Hz, 6.0 Hz), 2.95-2.83 (m, 4H, Ar<u>C</u>H$_2$CH$_3$, SCH_2<u>C</u>H$_a$H$_b$, SCH$_a$<u>C</u>H$_b$), 2.65-2.57 (m, 2H, SCH_2CH_a<u>C</u>H$_b$, NCH_2CH_a<u>C</u>H$_b$), 1.74 (s, 3H, NCC<u>H</u>$_3$), 1.34 (t, 3H, $ArCH_2C$<u>H</u>$_3$, *J* 7.5 Hz); **^{13}C NMR** (CD_3OD, 125 MHz) δ_C 136.4 (Ar<u>C</u>$_{quat}$), 135.8 (Ar<u>C</u>$_{quat}$), 128.1 (Ar<u>C</u>$_{quat}$), 127.9 (Ar<u>C</u>$_{quat}$), 121.7 (Ar<u>C</u>H), 120.5 (Ar<u>C</u>H), 116.7 (Ar<u>C</u>H), 109.2 (Ar<u>C</u>$_{quat}$), 61.1 (N<u>C</u>CH$_3$), 47.1 (S<u>C</u>H$_2$), 38.7 (N<u>C</u>H$_2$), 34.2 (SCH_2<u>C</u>H$_2$), 28.0 (NC<u>C</u>H$_3$), 25.1 (Ar<u>C</u>H$_2$CH$_3$), 21.1 (NCH_2<u>C</u>H$_2$), 14.9 ($ArCH_2$<u>C</u>H$_3$); **m/z** (ES+) 327 ([M+Na]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{16}H_{20}N_2O_2SNa^+$) requires *m/z* 327.1138 & 328.1171, found *m/z* 327.1135 & 328.1180.

2.8. Methodology extention for amide derivitives

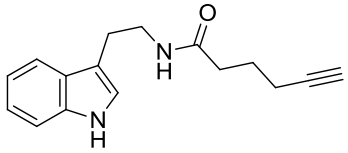
2.9. General procedure G for the preparation of 9



Hexynoic acid (1 eq) was added in one portion to a suspension of (1.5 eq) and DMAP (0.04 eq) in dichloromethane (3 ml/mmol of hexynoic acid) under argon and the mixture was stirred for 5 mins. A solution of tryptamine **19** (1.4 eq) in dichloromethane (7 ml/mmol of hexynoic acid) was added to the solution. The reaction mixture was stirred at rt for 12 h. Upon completion hydrochloric acid solution (1M, 10 ml) was added. The layers were separated and the aqueous was extracted with dichloromethane (2 × 20 ml). The combined organics were washed with brine, dried over sodium sulfate and concentrated *in vacuo.* The residue was purified by flash column chromatography (CH_2Cl_2:Et_2O, 1:0 to 7:3).

2.9.1. Preparation and characterisation of 9a

N-[2-(1*H*-indol-3-yl)ethyl]hex-5-ynamide

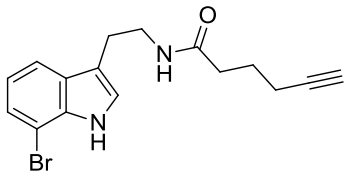


The title compound **9a** was synthesis according to general procedure **G** as a white solid (86% yield) and re-crystallized from ethanol.

m.p. 89-91 °C; **FT-IR** ν_{max} 3403 (N–H), 3286 (ArN–H), 1641 (C=O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 8.29 (br s, 1H, ArNH), 7.62 (d, 1H, ArCH, *J* 8.0 Hz), 7.39 (d, 1H, ArCH, *J* 8.0 Hz), 7.23 (t, 1H, ArCH, *J* 7.5 Hz), 7.14 (t, 1H, ArCH, *J* 7.5 Hz), 7.04 (d, 1H, ArCH, *J* 2.0 Hz), 5.63 (br s, 1H, OCNH), 3.62 (q, 2H, NCH_2, *J* 6.5 Hz), 2.99 (t, 2H, NCH_2CH_2, *J* 6.5 Hz), 2.25 (t, 2H, $OCCH_2$, *J* 7.5 Hz), 2.22 (td, 2H, $HC{\equiv}CCH_2$, *J* 7.5 Hz, 2.5 Hz), 1.94 (t, 1H, C≡CH, *J* 2.5 Hz), 1.84 (quin, 2H, $OCCH_2CH_2$, *J* 7.5 Hz); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ_C 172.2 (CO), 136.4 (ArC_{quat}), 127.3 (ArC_{quat}), 122.2 (ArCH), 122.1 (ArCH), 119.5 (ArCH), 118.7 (ArCH), 112.9 (ArC_{quat}), 111.3 (ArCH), 83.6 (HC≡C), 69.2 (C≡CH), 39.7 (NCH_2), 35.1 ($OCCH_2$), 25.3 (NCH_2CH_2), 24.2 ($OCCH_2CH_2$), 17.8 ($HC{\equiv}CCH_2$); ***m/z*** (ES+) 277 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{16}H_{18}N_2NaO^+$) requires *m/z* 277.1311 & 278.1345, found *m/z* 277.1316 & 278.1346.

2.9.2. **Preparation and characterisation 9b**

of *N*-[2-(7-bromo-1*H*-indol-3-yl)ethyl]hex-5-ynamide

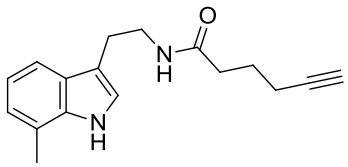


The title compound **9b** was synthesis according to general procedure **G** as a brown solid (65% yield) trituration (Et_2O and re-crystallized from ethanol.)

m.p. 87-89 °C; **FT-IR** ν_{max} 3400 (N–H), 3300 (ArN–H), 1636 (C=O); **^{1}H NMR** (DMSO-d_6, 400 MHz) δ_H 11.05 (br s, 1H, ArNH), 7.93 (t, 1H, OCNH, *J* 6.5 Hz), 7.55 (d, 1H, ArCH, *J* 7.5 Hz), 7.28 (d, 1H, ArCH, *J* 7.5 Hz), 7.21 (d, 1H, ArCH, *J* 2.0 Hz), 6.94 (t, 1H, ArCH, *J* 7.5 Hz), 3.32 (q, 2H, NCH_2, *J* 6.5 Hz), 2.80 (t, 2H, $OCCH_2$, *J* 7.5 Hz), 2.78 (t, 1H, C≡CH, *J* 2.5 Hz), 2.18-2.10 (m, 4H, $ArCH_2$, $HC{\equiv}CCH_2$), 1.65 (quin, 2H, $OCCH_2CH_2$, *J* 7.5 Hz);**^{13}C NMR** ($CDCl_3$, 100 MHz) δ_C 172.2 (CO), 135.3 (ArC_{quat}), 129.9 (ArC_{quat}), 124.9 (ArCH), 124.3 (ArCH), 120.6 (ArCH), 118.8 (ArCH), 114.3 (ArC_{quat}), 105.1 (ArCBr), 85.0 (HC≡C), 72.3 (C≡CH), 41-39.7$^{(signal\ hidden\ under\ DMSO\ peak,\ confirmed\ by\ HSQC\ and\ COSY)}$ (NCH_2) 35.1 ($ArCH_2$), 26.0 ($OCCH_2$) 25.1 ($OCCH_2CH_2$), 18.3 ($HC{\equiv}CCH_2$); ***m/z*** (ES+) 355 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{16}H_{17}N_2BrNaO^+$) requires *m/z* 355.0416 & 357.0397, found *m/z* 355.0404 & 357.0385.

2.9.3. **Preparation and Characterisation of 9c[10]**

***N*-[2-(7-methyl-1*H*-indol-3-yl)ethyl]hex-5-ynamide**

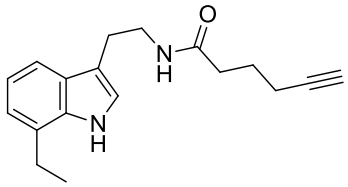


The title compound **9c** was synthesis according to general procedure **G** as a white solid (56% yield) and re-crystallized from ethanol.

m.p. 76-77 °C; **FT-IR** ν_{max} 3402 (ArNH), 3288 (NH), 1648 (C=O); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ_H 8.00 (br s, 1H, ArNH), 7.47 (d, 1H, ArCH, *J* 7.5 Hz), 7.07 (t, 1H, ArCH, *J* 7.5 Hz), 7.07 (d, 1H, ArCH, *J* 2.5 Hz), 7.03 (d, 1H, ArCH, *J* 7.5 Hz), 5.55 (br s, 1H, OCNH), 3.62 (q, 2H, NCH_2, *J* 6.5 Hz), 2.98 (t, 2H, NCH_2CH_2, *J* 6.5 Hz), 2.50 (s, 3H, $ArCH_3$), 2.25 (t, 2H, $OCCH_2$, *J* 7.5 Hz), 2.23 (td, 2H, $HC{\equiv}CCH_2$, *J* 7.5 Hz, 2.5 Hz), 1.93 (t, 1H, C≡CH, *J* 2.5 Hz), 1.84 (quin, 2H, $OCCH_2CH_2$, *J* 7.5 Hz); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ_C 172.0 (CO), 136.0 (ArC_{quat}), 126.8 (ArC_{quat}), 122.8 (ArCH), 121.7 (ArCH), 120.4 (ArC_{quat}), 119.8 (ArCH), 116.4 (ArCH), 113.6 (ArC_{quat}), 83.6 (HC≡C), 69.1 (HC≡C), 39.7 (NCH_2), 35.1 ($OCCH_2$), 25.5 (NCH_2CH_2), 24.1 ($OCCH_2CH_2$), 17.8 ($HC{\equiv}CCH_2$), 16.6 ($ArCH_3$); ***m/z*** (ES+) 291 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{17}H_{20}N_2NaO^+$) requires *m/z* 291.1468 & 292.1501, found *m/z* 291.1470 & 292.1503.

2.9.4. **Preparation and Characterisation of 9d**

-[2-(7-ethyl-1*H*-indol-3-yl)ethyl]hex-5-ynamide

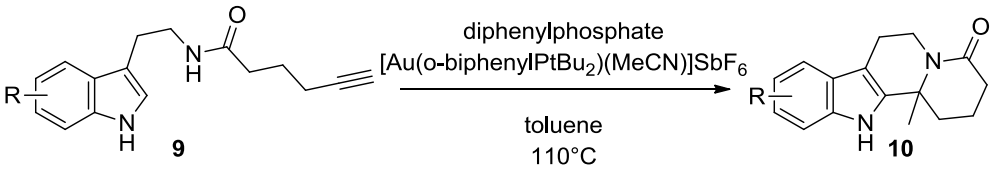


The title compound **9d** was synthesis according to general procedure **G** as a yellow oil (45% yield).

FT-IR ν_{max} 3404 (NH), 3289 (ArN–H), 1649 (C=O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 8.17 (br s, 1H, ArNH), 7.48 (d, 1H, ArCH, *J* 7.5 Hz), 7.11 (t, 1H, ArCH, *J* 7.5 Hz), 7.07 (d, 1H, ArCH, *J* 7.5 Hz), 7.05 (d, 1H, ArCH, *J* 2.0 Hz), 5.61 (br s, 1H, OCNH), 3.62 (q, 2H, NCH_2, *J* 6.5 Hz), 2.98 (t, 2H, NCH_2CH_2, *J* 6.5 Hz), 2.88 (q, 2H, $ArCH_2CH_3$, *J* 7.5 Hz), 2.25 (t, 2H, $OCCH_2$, *J* 7.5 Hz), 2.23 (td, 2H, $HC{\equiv}CCH_2$, *J* 7.5 Hz, 2.5 Hz) 1.94 (t, 1H, C≡CH, *J* 2.5 Hz), 1.84 (quint, 2H, $OCCH_2CH_2$, *J* 7.0 Hz), 1.38 (t, 3H, $ArCH_2CH_3$, *J* 7.5 Hz) ;

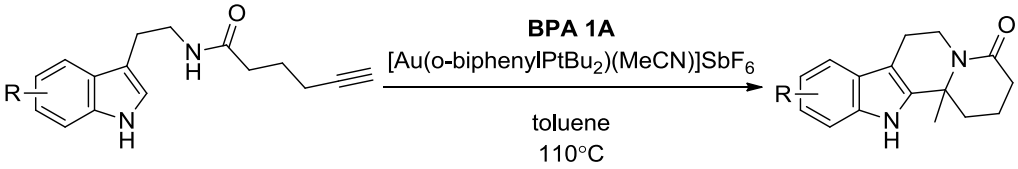
^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 172.2 (<u>C</u>O), 135.3 (Ar<u>C</u>$_{quat}$), 127.1 (Ar<u>C</u>$_{quat}$), 126.7 (Ar<u>C</u>$_{quat}$), 121.7 (Ar<u>C</u>H), 120.8 (Ar<u>C</u>H), 119.8 (Ar<u>C</u>H), 116.5 (Ar<u>C</u>H), 113.4 (Ar<u>C</u>$_{quat}$), 83.6 (HC≡<u>C</u>), 69.1 (C≡<u>C</u>H), 39.7 (N<u>C</u>H_2), 35.1 (OC<u>C</u>H_2), 25.5 (NCCH_2<u>C</u>H_2), 24.2 (OCCH_2<u>C</u>H_2), 24.0 (Ar<u>C</u>H_2CH_3), 17.8 (HC≡C<u>C</u>H_2), 13.8 (ArCH_2<u>C</u>H_3); ***m/z*** (ES+) 305 ($[M+H]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{18}H_{22}N_2NaO^+$) requires *m/z* 305.1624 & 306.1658, found *m/z* 305.1624 & 306.1661.

2.10. General procedure H for the racemic preparation of cyclic amides 10



To a foil covered flask [Au(o-biphenylPtBu_2)(MeCN)]SbF_6 (**8**) (0.05 eq), diphenylphosphate (0.1 eq) and desired amide derivative (**9**) (1 eq) were added and placed under nitrogen atmosphere. Toluene (14 ml/1 mmol of **9**) was added in one portion and the reaction was heated to 110 °C and left for 48 to 72 hours. The solvent was removed *in vacuo* and purified by flash column chromatography (CH_2Cl_2 : Et_2O, 1 : 0 to 7 : 3).

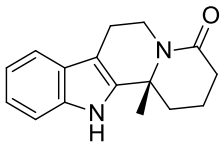
2.11. General procedure I for the Enantioselective preparation of cyclic amides 10



To a foil covered flask [Au(o-biphenylPtBu_2)(MeCN)]SbF_6 (**8**) (0.01 eq) was added in dichloromethane (1 ml/ 0.15 mmol of **9**), the dichloromethane was subsequently removed *via* stream of nitrogen. **BPA 1A** (0.1 eq) and desired amide derivative (**9**) (0.15 mmol, 1 eq) was added and placed under nitrogen atmosphere. Toluene (21 ml) was added in one portion and the reaction was heated to 110 °C typically for 20 to 72 h until TLC shows consumption of starting material. The solvent was removed *in vacuo* and purified by flash column chromatography (DCM : Et_2O, 1 : 0 to 7 : 3).

2.11.1. Preparation and characterisation of 10a

(*R*)-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one



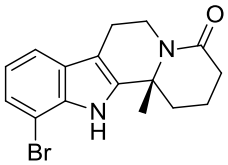
The title compound **10a** was synthesis according to general procedure **I** as a white solid (86% yield, 66% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220, major t_R = 5.1 min, minor t_R = 11.8 min); **$[\alpha]_D^{25}$=** +157.7 (*c* 0.26, CH_2Cl_2).

Racemic-10a was synthesised according to general procedure **H** as a white solid.

m.p. 180 °C (decomposition); **FT-IR** ν_{max} 3254 (N–H), 1606 (C=O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 8.38 (br s, 1H, ArN<u>H</u>), 7.51 (d, 1H, ArC<u>H</u>, *J* 7.5 Hz), 7.34 (d, 1H, ArC<u>H</u>, *J* 7.5 Hz), 7.19 (t, 1H, ArC<u>H</u>, *J* 7.5 Hz), 7.13 (t, 1H, ArC<u>H</u>, *J* 7.5 Hz), 5.13 (dd, 1H, NC<u>H</u>$_a$H$_b$, *J* 12.5 Hz, 5.0 Hz), 3.04 (td, 1H, NCH$_a$<u>H</u>$_b$, *J* 12.5 Hz, 4.5 Hz), 2.85 (ddd, 1H, NCH$_2$C<u>H</u>$_a$H$_b$, *J* 15.5 Hz, 11.5 Hz, 5.0 Hz), 2.76 (dd, 1H, NCH$_2$CH$_a$<u>H</u>$_b$, *J* 15.5 Hz, 5.0 Hz), 2.61 (dd, 1H, OCC<u>H</u>$_a$H$_b$, *J* 17.0 Hz, 5.0 Hz), 2.44 (ddd, 1H, OCCH$_a$<u>H</u>$_b$, *J* 18.0 Hz, 10.5 Hz, 7.0 Hz), 2.32 (m, 1H, OCCH$_2$CH$_2$C<u>H</u>$_a$H$_b$), 2.09-1.84 (m, 3H, OCCH$_2$CH$_2$C<u>H</u>$_a$H$_b$, OCCH$_2$C<u>H</u>$_a$H$_b$), 1.70 (s, 3H, NCC<u>H</u>$_3$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ_C 169.3 (<u>C</u>O), 138.5 (Ar<u>C</u>$_{quat}$), 136.1 (Ar<u>C</u>$_{quat}$), 126.7 (Ar<u>C</u>$_{quat}$), 122.0 (Ar<u>C</u>H), 119.7 (Ar<u>C</u>H), 118.4 (Ar<u>C</u>H), 110.9 (Ar<u>C</u>H), 108.0 (Ar<u>C</u>$_{quat}$), 56.7 (N<u>C</u>CH$_3$), 36.5 (N<u>C</u>H$_2$), 35.5 (OCCH$_2$CH$_2$<u>C</u>H$_2$), 32.1 (OC<u>C</u>H$_2$), 26.0 (C<u>C</u>H$_3$), 21.3 (NCH$_2$<u>C</u>H$_2$), 16.8 (OCCH$_2$<u>C</u>H$_2$); ***m/z*** (ES+) 277 ([M+Na]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{16}H_{18}N_2NaO^+$) requires *m/z* 277.1311 & 278.1345, found *m/z* 277.1306 & 278.1335.

2.11.2. **Preparation and Characterisation of 10b**

(*R*)-11-bromo-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one



The title compound **10b** was synthesis according to general procedure **I** as a white solid (99% yield, 93% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220, major t_R = 5.1 min, minor t_R = 6.6 min); **$[\alpha]_D^{25}$**= +164.0 (*c* 0.15, CH_2Cl_2)

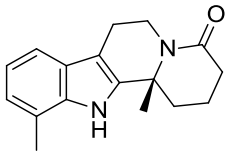
Racemic-10b was synthesised according to general procedure **H** as a white solid: Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220, major t_R = 5.1 min, minor t_R = 6.7 min);

m.p. 130-137 °C; **FT-IR** ν_{max} 3190 (N–H), 1606 (C=O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 8.09 (br s, 1H, ArN<u>H</u>), 7.44 (d, 1H, ArC<u>H</u>, *J* 8.0 Hz), 7.33 (d, 1H, ArC<u>H</u>, *J* 8.0 Hz), 7.01 (t, 1H, ArC<u>H</u>, *J* 8.0 Hz), 5.12 (dd, 1H, NC<u>H</u>$_a$H$_b$, *J* 13.0 Hz, 4.5 Hz), 3.01 (td, 1H, NCH$_a$<u>H</u>$_b$, *J* 12.5 Hz, 4.5 Hz), 2.83 (ddd, 1H, NCH$_2$C<u>H</u>$_a$H$_b$, *J* 15.5 Hz, 12.0 Hz, 5 Hz), 2.71 (dd, 1H, NH$_2$CH$_a$<u>H</u>$_b$, *J* 15.0 Hz, 4.0 Hz),

2.60 (br d, 1H, OCC$\underline{H}_a H_b$, *J* 17.0 Hz), 2.50-2.33 (m, 2H, OCC$H_a\underline{H}_b$, OCCH_2CH_2C$\underline{H}_a H_b$), 2.10-1.85 (m, 3H, OCCH_2CH_2C$H_a\underline{H}_b$, OCCH_2C$\underline{H}_a H_b$), 1.71 (s, 3H, NCC$\underline{H}_3$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ_C 169.2 (C=O), 139.2 (Ar$\underline{C}_{quat}$), 134.7 (Ar$\underline{C}_{quat}$), 128.0 (Ar$\underline{C}_{quat}$), 124.5 (Ar$\underline{C}$H), 121.0 (Ar$\underline{C}$H), 117.7 (Ar$\underline{C}$H), 109.6 (Ar$\underline{C}_{quat}$), 104.5 (Ar$\underline{C}_{quat}$), 56.7 (N$\underline{C}CH_3$), 36.2 (N$\underline{C}H_2$), 35.5 (OCH_2C$H_2\underline{C}H_2$), 32.1 (NC$H_2\underline{C}H_2$), 26.0 (NC$\underline{C}H_3$), 21.4 (OC$\underline{C}H_2$), 16.7 (OC$H_2\underline{C}H_2$); ***m/z*** (ES+) 355 ([M+Na]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{16}H_{17}BrN_2NaO^+$) requires *m/z* 355.0416 & 357.0397, found *m/z* 355.0409 & 357.0392.

2.11.3. **Preparation and Characterisation of 10c**

(*R*)-11,12b-dimethyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one



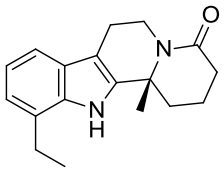
The title compound **10c** was synthesis according to general procedure **I** as white solid (90% yield, 90% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220, major t_R = 4.4 min, minor t_R = 5.4 min); $[\alpha]_D^{25}$= +167.6 (*c* 0.34, CH_2Cl_2).

Racemic-10c was synthesised according to general procedure **H** as a white solid.

m.p. 140-145 °C (decomposition); **FT-IR** ν_{max} 3265 (N–H), 1605 (C=O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 8.05 (br s, 1H, ArN$\underline{H}$), 7.36 (d, 1H, ArC$\underline{H}$, *J* 7.5 Hz), 7.06 (t, 1H, ArC$\underline{H}$, *J* 7.5 Hz), 7.00 (d, 1H, ArC$\underline{H}$, *J* 7.5 Hz), 5.12 (dd, 1H, NC$\underline{H}_a H_b$, *J* 12.5 Hz, 4.5 Hz), 3.03 (td, 1H, NC$H_a\underline{H}_b$, *J* 12.5 Hz, 4.5 Hz), 2.84 (ddd, 1H, NC$H_2\underline{C}H_a H_b$, *J* 15 Hz, 11.5 Hz, 4.5 Hz), 2.74 (dd, 1H, NCH_2C$H_a\underline{H}_b$, *J* 15.0 Hz, 4.5 Hz), 2.60 (br d, 1H, OCC$\underline{H}_a H_b$, *J* 17.5 Hz), 2.51 (s, 3H, ArC$\underline{H}_3$), 2.49-2.34 (m, 2H, OCC$H_a\underline{H}_b$, OCCH_2C$H_2\underline{C}H_a H_b$), 2.09-1.86 (m, 3H, OCCH_2CH_2C$H_a\underline{H}_b$, OCC$H_2\underline{C}H_a H_b$), 1.71 (s, 3H, NCC$\underline{H}_3$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ_C 169.2 (C=O), 138.2 (Ar$\underline{C}_{quat}$), 135.6 (Ar$\underline{C}_{quat}$), 126.3 (Ar$\underline{C}_{quat}$), 122.8 (Ar$\underline{C}$H), 120.2 (Ar$\underline{C}_{quat}$), 120.0 (Ar$\underline{C}$H), 116.1 (Ar$\underline{C}$H), 108.7 (Ar$\underline{C}_{quat}$), 56.8 (N$\underline{C}CH_3$), 36.4 (N$\underline{C}H_2$), 35.6 (OCH_2C$H_2\underline{C}H_2$), 32.1 (OC$\underline{C}H_2$), 26.0 (NC$\underline{C}H_3$), 21.3 (NC$H_2\underline{C}H_2$), 16.79 (Ar$\underline{C}H_3$), 16.78 (OC$H_2\underline{C}H_2$); ***m/z*** (ES+) 291 ([M+H]$^+$, 100%), **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{17}H_{20}N_2NaO^+$) requires *m/z* 291.1468 & 292.1501, found *m/z* 291.1467 & 292.1499.

2.11.4. **Preparation and Characterisation of 10d**

(*R*)-11-ethyl-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one



The title compound **10d** was synthesis according to general procedure **I** white solid (60% yield, 86% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220, major t_R = 4.1 min, minor t_R = 4.9 min); $[\alpha]_D^{25}$= +120.6 (*c* 0.34, CH_2Cl_2)

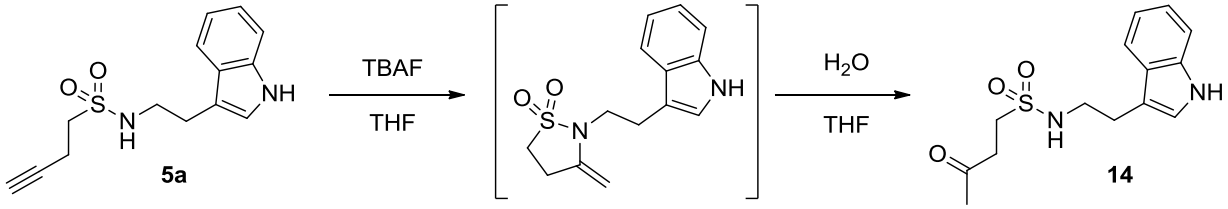
Racemic-10d was synthesised according to general procedure **H** as a white solid.

m.p. 127-129 °C; **FT-IR** ν_{max} 3277 (N–H), 1605 (C=O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ_H 8.00 (br s, 1H, ArNH), 7.37 (d, 1H, ArCH, *J* 7.5 Hz), 7.10 (t, 1H, ArCH, *J* 7.5 Hz), 7.05 (d, 1H, ArCH, *J* 7.5 Hz), 5.12 (dd, 1H, NCH_aH_b, *J* 13.0 Hz, 4.5 Hz), 3.03 (td, 1H, NCH_aH_b, *J* 12.5 Hz, 4.5 Hz), 2.88 (q, 2H, $ArCH_2CH_3$, *J* 7.5 Hz), 2.84 (td, 1H, $NCH_2CH_aH_b$, *J* 12.0 Hz, 5.0 Hz), 2.74 (dd, 1H, $NCH_2CH_aH_b$, *J* 15.0 Hz, 4.0 Hz), 2.60 (br d, 1H, $OCCH_aH_b$, *J* 17.0 Hz), 2.49-2.31 (m, 2H, $OCCH_aH_b$, $OCCH_2CH_2CH_aH_b$), 2.08-1.85 (m, 3H, $OCCH_2CH_2CH_aH_b$, $OCCH_2CH_aH_b$), 1.71 (s, 3H, $NCCH_3$), 1.38 (t, 3H, $ArCH_2CH_3$, *J* 7.5 Hz); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ_C 169.2 (CO), 138.1 (ArC_{quat}), 134.8 (ArC_{quat}), 126.5 (ArC_{quat}), 126.4 (ArC_{quat}), 120.7 (ArCH), 120.1 (ArCH), 116.2 (ArCH), 108.7 (ArC_{quat}), 56.7 ($NCCH_3$), 36.4 (NCH_2), 35.6 ($OCH_2CH_2CH_2$), 32.1 ($OCCH_2$), 26.0 ($NCCH_3$), 24.0 ($ArCH_2CH_3$), 21.3 (NCH_2CH_2), 16.8 $OCCH_2CH_2$), 13.9 ($ArCH_2CH_3$); ***m/z*** (ES+) 305 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{18}H_{22}N_2NaO^+$) requires *m/z* 305.1624 & 306.1658, found *m/z* 305.1626 & 306.1661.

2.12. Optimization, Derivative for X-ray and Control reactions.

2.13. Preparation and characterisation of 14

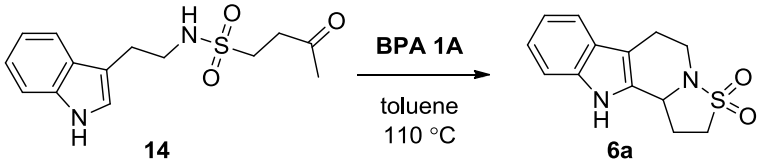
N-[2-(1H-indole-3-yl)ethyl]-3-oxobutane-1-sulfonamide



To a stirred solution of sulfonamide **5a** (500 mg, 1.81 mmol) in dry THF (20 ml), a solution of TBAF (9.1 ml, 1M in THF) was added under nitrogen and heated to reflux for 13 hours. The reaction was monitored by ^{1}HNMR ($CDCl_3$ passed through a short pad of K_2CO_3 prior to use). Upon completion, water (20 ml) was added and the solution was stirred for 1 h. The aqueous layer was separated and the organic layer was washed with water 5 times. Purification by flash column chromatography (silica) afforded **14** (230 mg, 25%)

m.p. 108-109 °C; **FT-IR** ν_{max} 3346 (ArN–H, broad), 3252 (SN–H) 1707 (C=O) 1313 ($S=O_{(as)}$), 1138 ($S=O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ_H 8.12 (br s, 1H, ArNH), 7.60 (d, 1H, ArCH, *J* 7.6 Hz), 7.39 (d, 1H, ArCH, *J* 8.2 Hz), 7.23 (t, 1H, ArCH, *J* 7.6 Hz), 7.15 (t, 1H, ArCH, *J* 7.9 Hz), 7.09 (s, 1H, ArCH), 4.26 (br s, 1H, SNH), 3.45 (q, 2H, $SNCH_2$, *J* 6.0 Hz), 3.19 (t, 2H, SCH_2, *J* 7.3 Hz), 3.05 (t, 2H, $ArCH_2$, *J* 6.0), 2.77 (t, 2H, SCH_2CH_2, *J* 7.1 Hz), 2.11 (s, 3H, $COCH_3$); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ_C 204.5 (CO) 136.5 (ArC quat), 127.0 (ArC quat), 122.8 (ArCH), 122.5 (ArCH), 119.8 (ArCH), 118.6 (ArCH), 111.7 ($ArCCH_2$), 111.5 (ArCH), 46.7 (SCH_2), 43.3 ($SNCH_2$), 37.3 (SCH_2CH_2), 29.9 ($COCH_3$), 26.2 ($ArCH_2$); ***m/z*** (ES+) 317 ($[M+Na]^+$, 100%), **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{18}N_2NaO_3S^+$) requires *m/z* 317.0930, found *m/z* 317.0927.

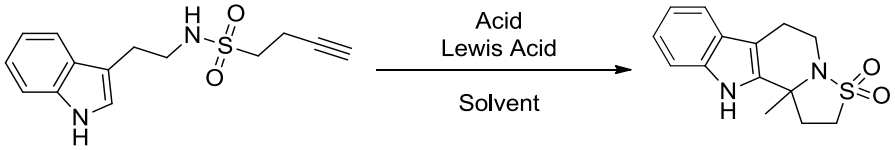
2.13.1. **Mechanistic evidence for *N*-sulfonylimminium 13**



14 **6a**

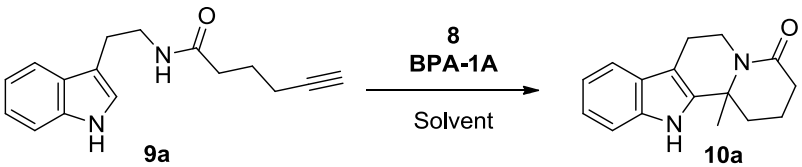
To a flask containing ketone **14** (0.1 mmol, 1 eq), and **BPA-1A** (0.01 mmol, 0.1 eq) under nitrogen atmosphere was added toluene at 90 °C rapidly *via* canula. The reaction mixture was stirred at reflux for 1 hour then cooled to room temperature. Concentration *in vacuo* and purification by flash column chromatography furnished the title compound (99 % yield, 92 % e.e.).

2.13.2. **General Proceedure for optimization in the preparation of 11b-methyl-1,2,5,6,11,11b-hexahydroisothiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 5a.**



To an aluminium foil covered flask alkyne **5a** (0.15 mmol, 1eq) and **BPA-1A** (0.015 mmol, 0.1 eq) were dissolved in solvent (21 ml/0.15 mmol of alkyne **5a**) under nitrogen the mixture was then heated to the desired temperature and the Lewis acid was added in DCM (1 ml). The reaction mixture was then stirred at the desired temperature until the reaction reached completion (monitoring by TLC and ^{1}HNMR). The reaction mixture was concentrated *in vacuo* and purified by FCC.

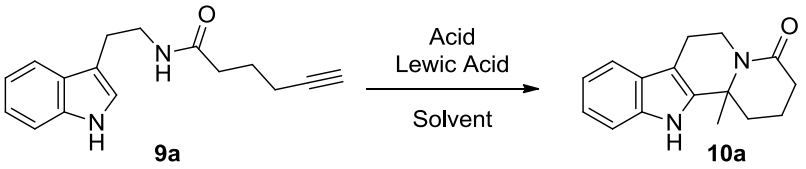
2.13.3. **General proceedure for optimization in the preparation of 10a.**



9a **10a**

To an aluminium foil covered flask [Au(o-biphenylPtBu_2)(MeCN)]SbF_6 (**8**) (0.0015 mmol, 0.01 eq) was added in dichloromethane (1 ml) and the dichloromethane was removed under nitrogen stream. Amide **9** (0.15 mmol, 1 eq) and **BPA-1A** (0.015 mmol, 0.1 eq) were added and were dissolved in toluene (21 ml/0.15 mmol of **9**) under nitrogen. The mixture was then heated to reflux and monitored (by TLC) until the reaction reached completion. The reaction was concentrated *in vacuo* and purified by FCC.

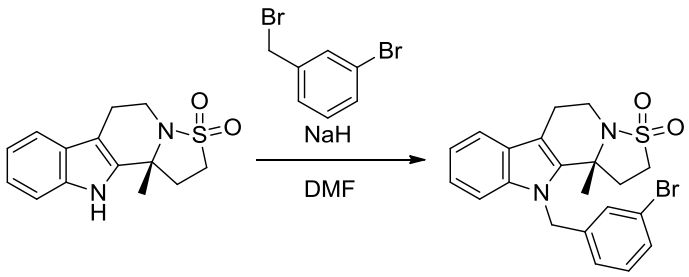
2.13.4. **Optimisation table for the preparation of 10a.**



Entry	Acid (**BPA**)	Acid (mol %)	**8** (mol %)	Solvent	Temp (°C)	Yield (%)	e.e.(%)
1	**1A**	10	5	toluene	60	47	66
2	**1A**	10	5	toluene	110	79	50
3	**1A**	10	3	toluene	110	99	62
4	**1A**	10	1	toluene	110	86	66
5	**1A**	10	0.5	toluene	110	81	68

2.13.5. **Preparation and characterisation of 15a**

11-(3-bromobenzyl)-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide



6a (0.12 mmol, 1 eq) was dissolved in DMF (1 ml/0.12 mmol of **6a**) under argon and added to a dried flask containing sodium hydride (1.6 mmol, 1.3 eq) in an ice bath. The mixture was stirred at 0°C for 10 mins and then allowed to warm to room temperature stirring for a further 10 mins. 3-bromobenzylbromide (0.37 mmol, 3 eq) was added to the mixture in one portion and allowed to stir at room temperature for 3 h. The reaction was diluted with water (5 ml/0.12 mmol of **6a**) and extracted with ethyl acetate (3 x 5 ml/0.12 mmol of **6a**). The combined organics were washed with brine, dried over sodium sulfate and concentrated *in vacuo*. Purification by FCC to gave **XX** as a white solid (68% yield). Recrystallization from ether by slow evaporation gave crystals of high enough quality for single crystal x-ray diffraction (<99% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220, major t_R = 12.0 min, minor t_R = 18.1 min).

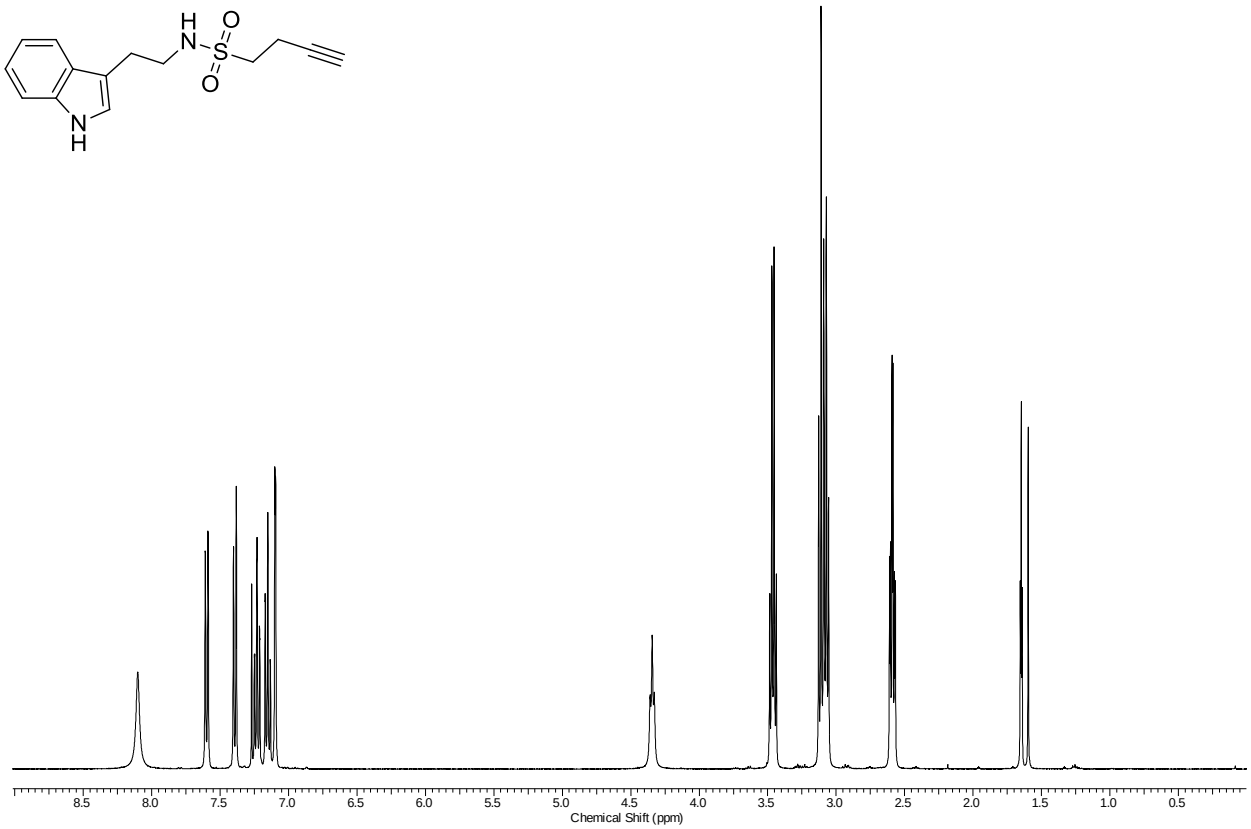
Racemic-15a was synthesised according to the same procedure as a white solid: Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220, major t_R = 12.0 min, minor t_R = 18.0 min);

m.p. 195-196 °C; **FT-IR** ν_{max} 1291 ($S{=}O_{(as)}$), 1134 ($S{=}O_{(sy)}$); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ_H 7.55 (m, 1H, ArC<u>H</u>), 7.39 (d, 1H, PhC<u>H</u>, *J* 7.9 Hz), 7.20-7.15 (m, 3H, 2 × ArC<u>H</u>, PhC<u>H</u>, *J* 8.2 Hz), 7.12 (t, 1H, ArC<u>H</u>, *J* 7.9 Hz), 7.03 (m, 1H, ArC<u>H</u>), 6.62 (d, 1H, PhC<u>H</u>), 5.43 (d, 1H, NC<u>H$_a$</u>H$_b$Ph, *J* 18.0 Hz), 5.38 (d, 1H, NCH$_a$<u>H$_b$</u>Ph, *J* 18.0 Hz), 4.08 (dd, 1H, NC<u>H$_a$</u>CH$_b$C<u>H$_2$</u>, *J* 14.5 Hz, 5.5 Hz), 3.34 (ddd, 1H, NCH$_a$<u>H$_b$</u>C<u>H$_2$</u>, *J* 14.5 Hz, 12.5 Hz, 4.5 Hz), 3.27-3.15 (m, 2H, SC<u>H$_a$</u>H$_b$, ArC<u>H$_a$</u>H$_b$), 3.01 (dt, 1H, SC<u>H$_a$</u>H$_b$, *J* 6.0 12.5 Hz, 7.0 Hz), 2.78 (dd, 1H, ArCH$_a$<u>H$_b$</u>, *J* 15.5 Hz, 4.0 Hz), 2.64 (m, 1H, SCH$_2$C<u>H$_a$</u>H$_b$), 2.56 (m, 1H, SCH$_2$C<u>H$_a$</u>H$_b$), 1.67 (s, 3H, NCC<u>H$_3$</u>); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ_C 139.5 (Ar<u>C$_{quat}$</u>) 136.9 (Ar<u>C$_{quat}$</u>), 135.3 (Ar<u>C$_{quat}$</u>), 130.8 Ph<u>C</u>H), 130.6 (Ph<u>C</u>H), 128.5 (Ph<u>C</u>H), 126.6 (Ar<u>C$_{quat}$</u>), 123.9 (Ph<u>C</u>H), 123.2 (Ph<u>C</u>Br), 123.0 (Ar<u>C</u>H), 120.2 (Ar<u>C</u>H), 118.9 (Ar<u>C</u>H), 109.7 (Ar<u>C</u>H), 109.6 (ArC$_{quat}$), 59.6 (N<u>C</u>CH$_3$), 47.3 (N<u>C</u>H$_2$Ph), 45.4 (S<u>C</u>H$_2$), 36.4 (N<u>C</u>H$_2$), 32.7 (SCH$_2$<u>C</u>H$_2$), 27.6 (NC<u>C</u>H$_3$), 20.9 (Ar<u>C</u>H$_2$); **HRMS** (TOF MS FI+) exact mass calculated for $[M]^+$ ($C_{21}H_{21}BrN_2O_2S^+$) requires *m/z* 444.0507 and 446.0488, found *m/z* 444.0519 and446.0502

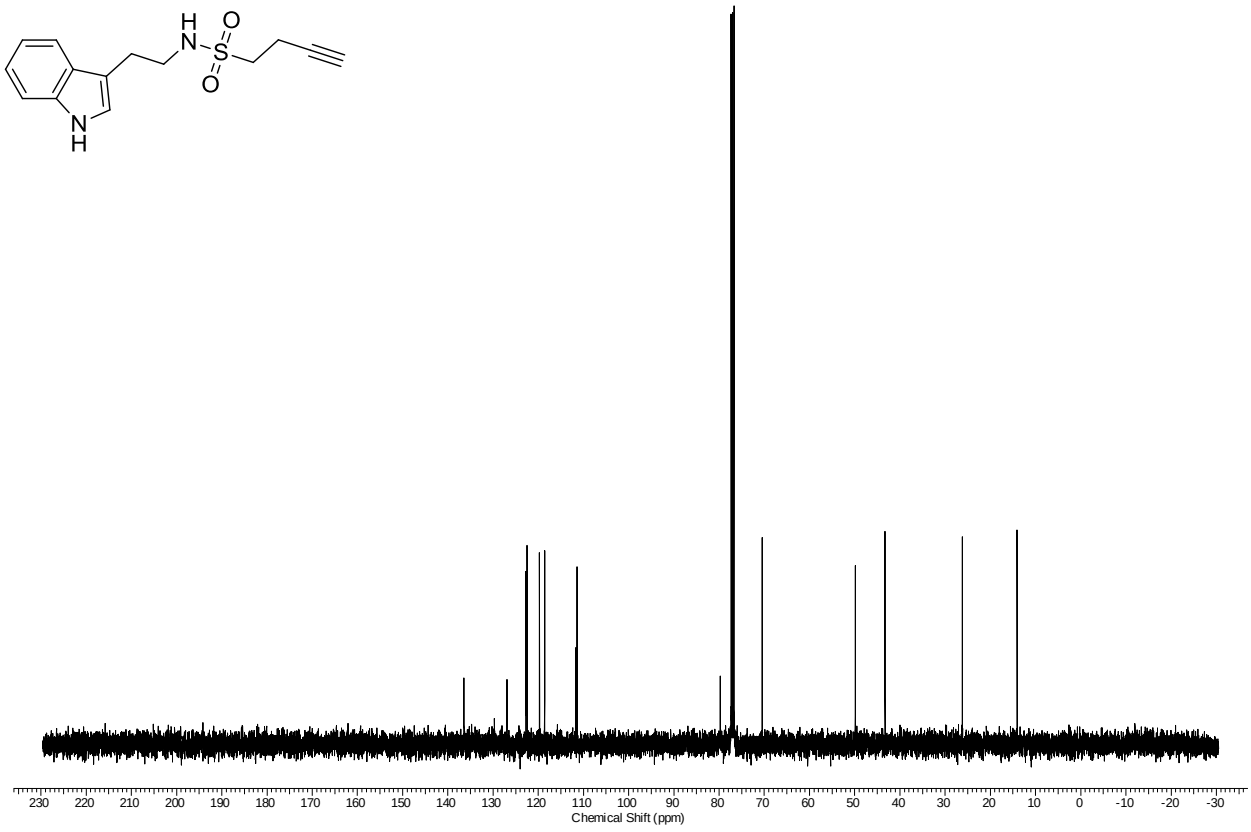
3. ^{1}HNMR and ^{13}CNMR spectra

3.1. Sulfonamide starting material 5

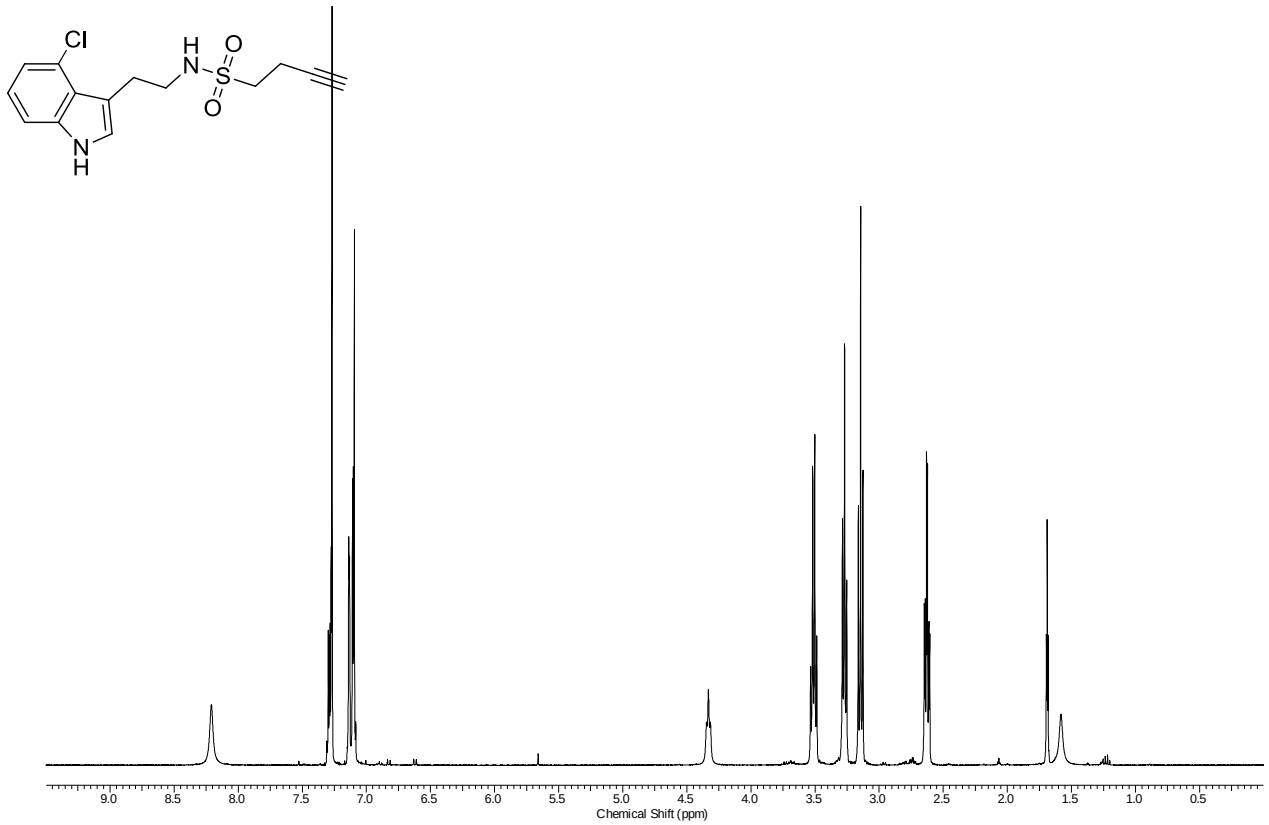
3.1.1. ^{1}HNMR spectra for *N*-[2-(1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5a



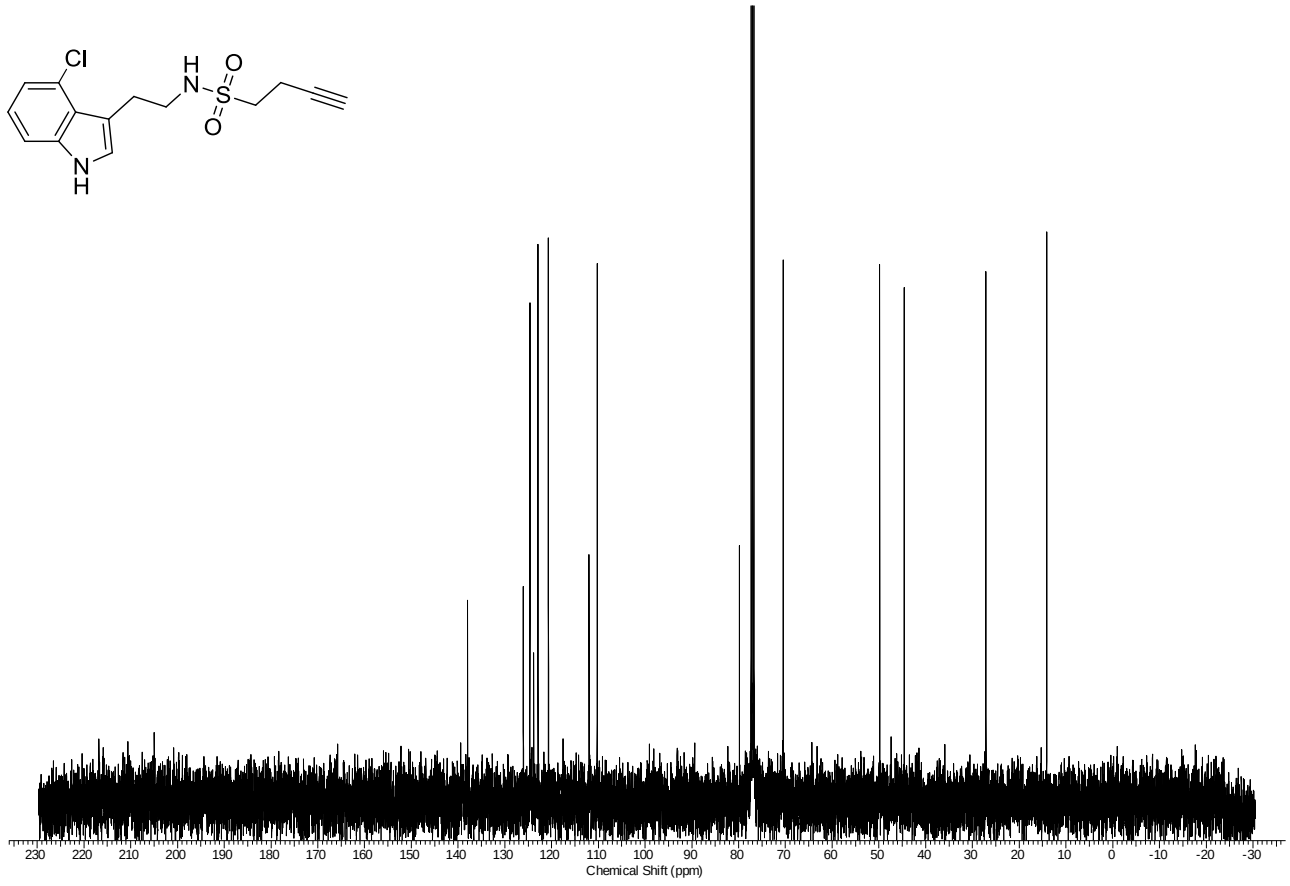
3.1.2. ^{13}CNMR spectra for *N*-[2-(1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5a



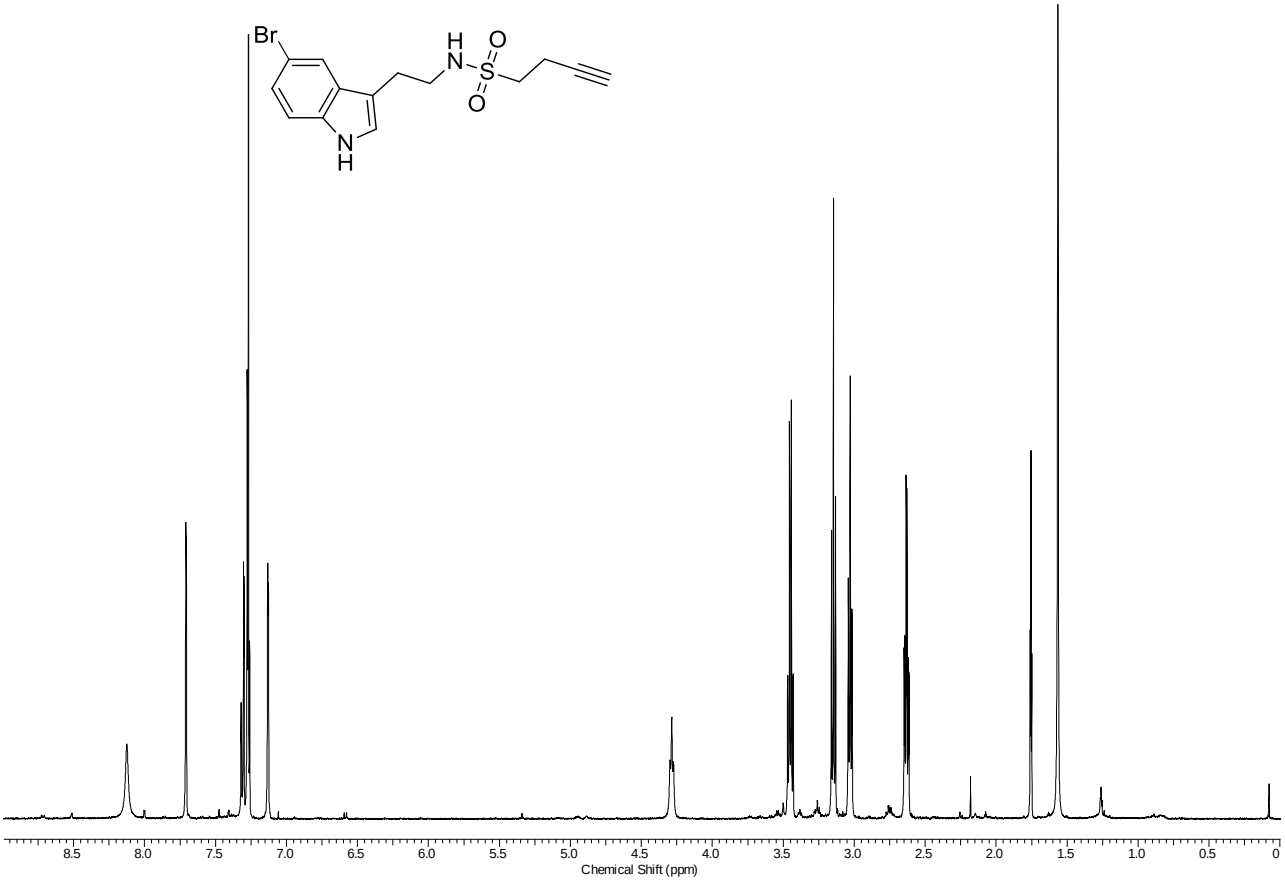
3.1.3. ^{1}HNMR spectra for *N*-[2-(4-chloro-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide **5b**



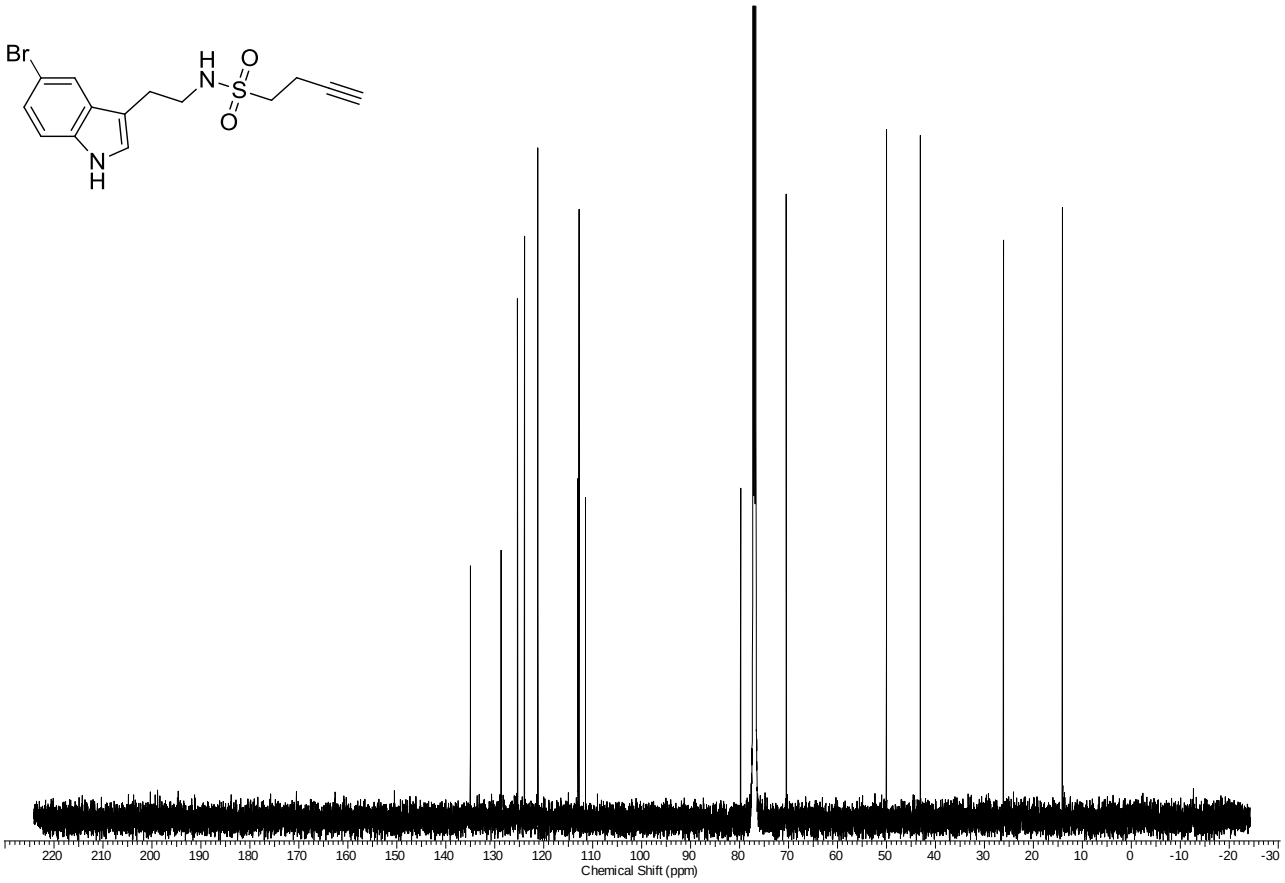
3.1.4. ^{13}CNMR spectra for *N*-[2-(4-chloro-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide **5b**



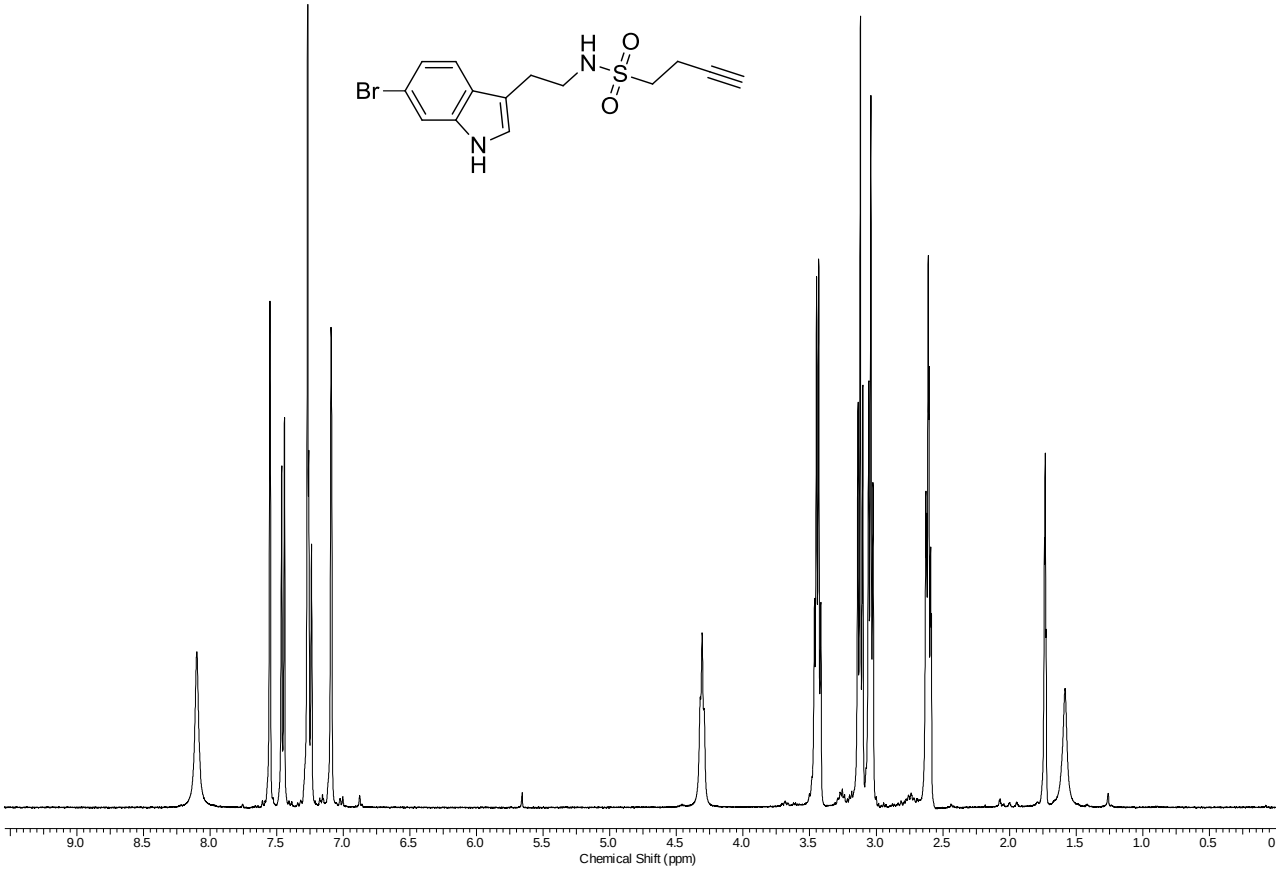
3.1.5. ^{1}HNMR spectra for *N*-[2-(5-bromo-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5c



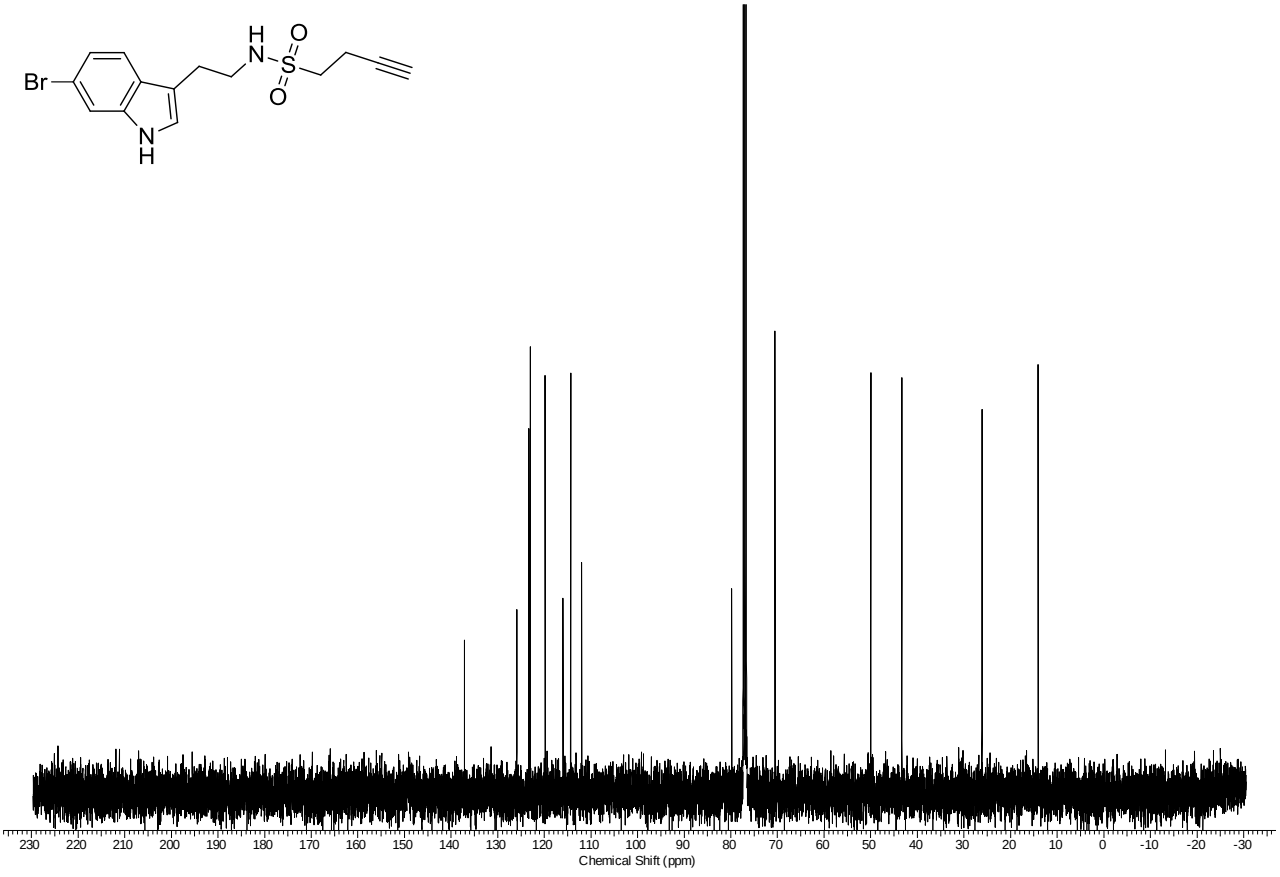
3.1.6. ^{13}CNMR spectra for *N*-[2-(5-bromo-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5c



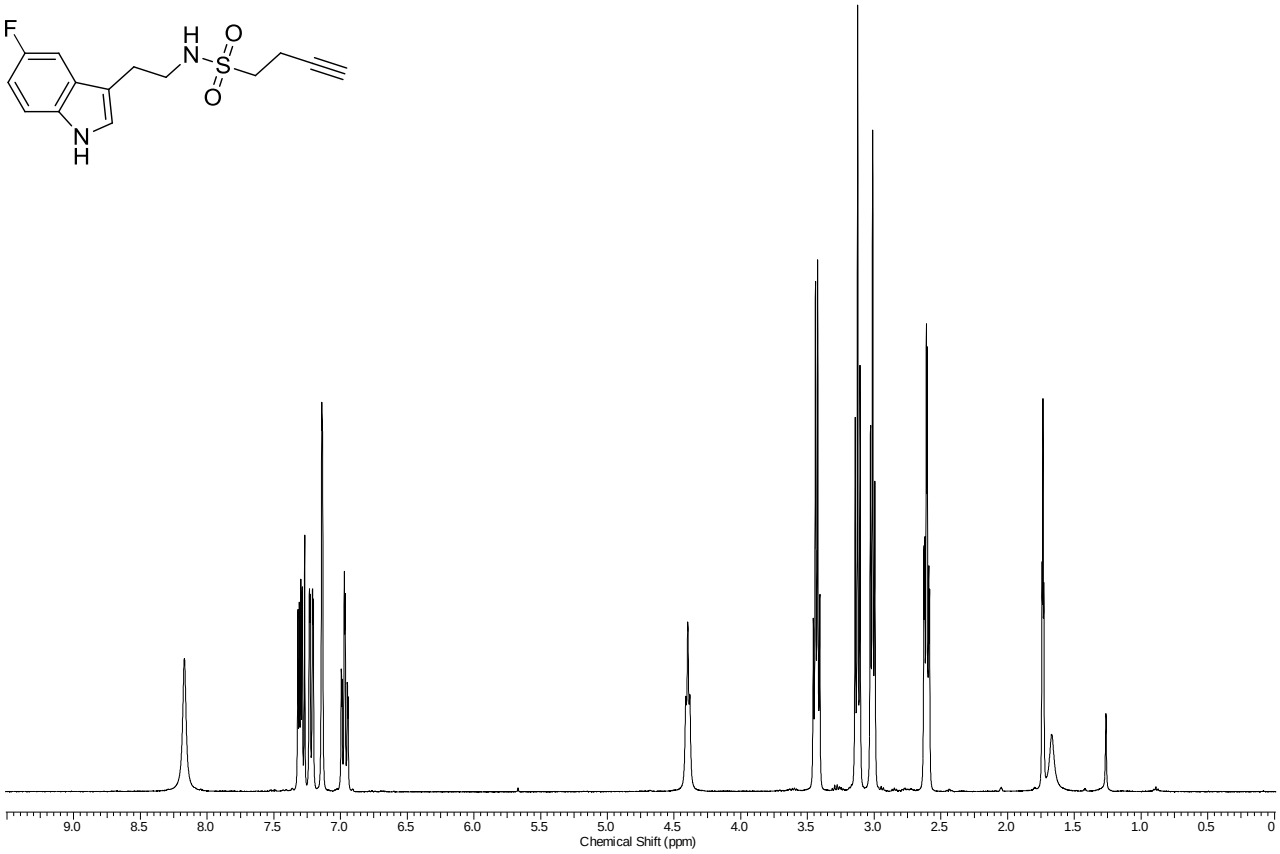
3.1.7.[1]HNMR spectra for *N*-[2-(6-bromo-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5d



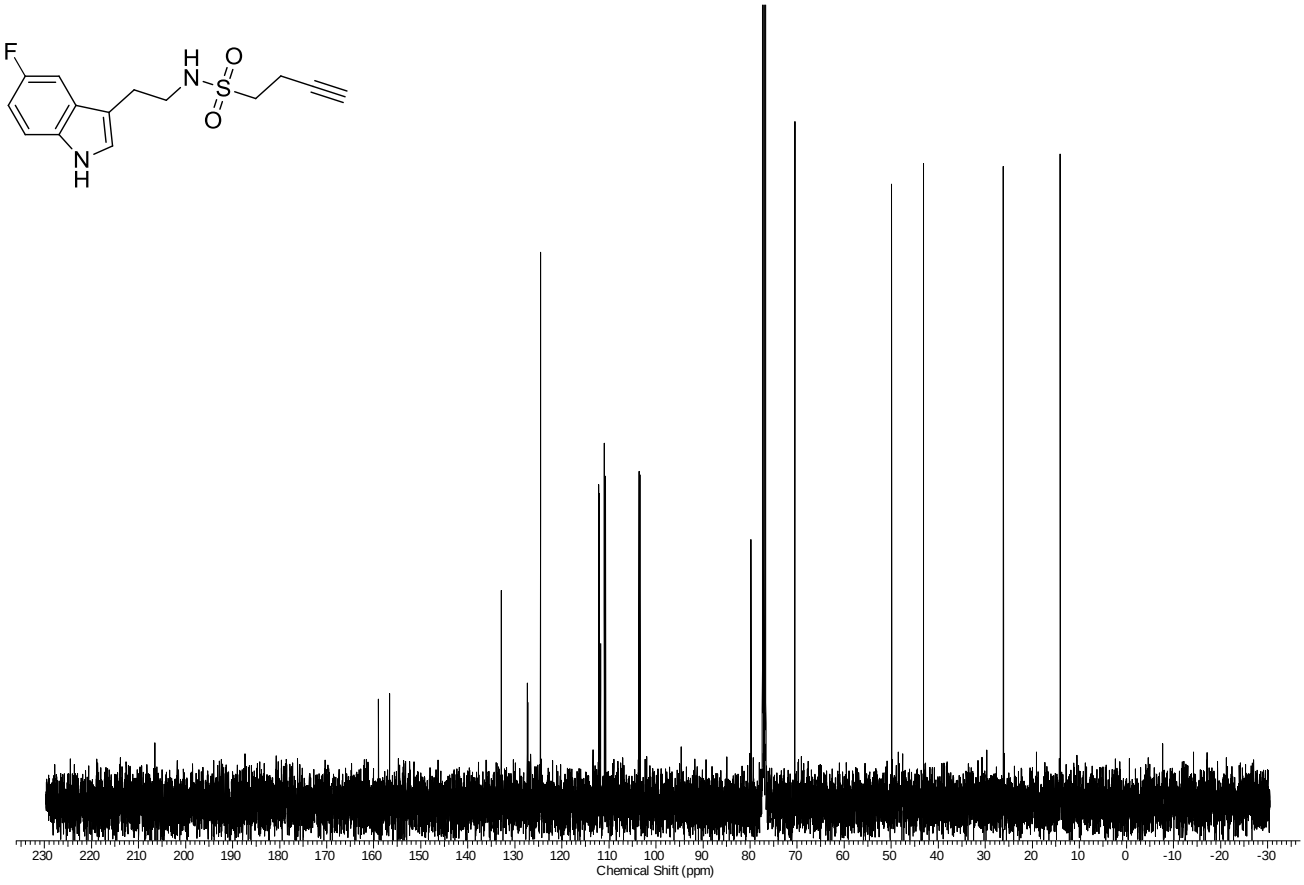
3.1.8.[13]CNMR spectra for *N*-[2-(6-bromo-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5d



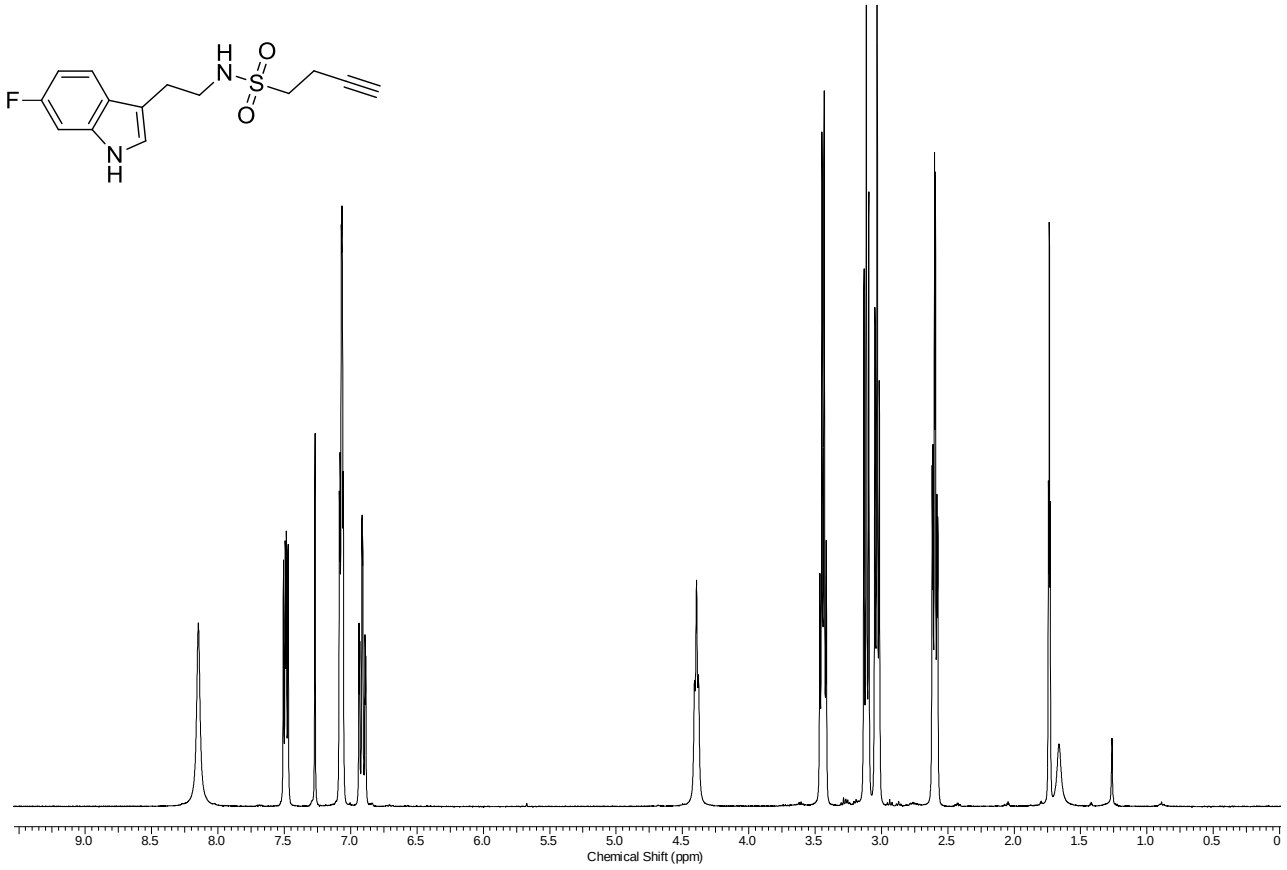
3.1.9. ^{1}HNMR spectra for *N*-[2-(5-fluoro-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide **5e**



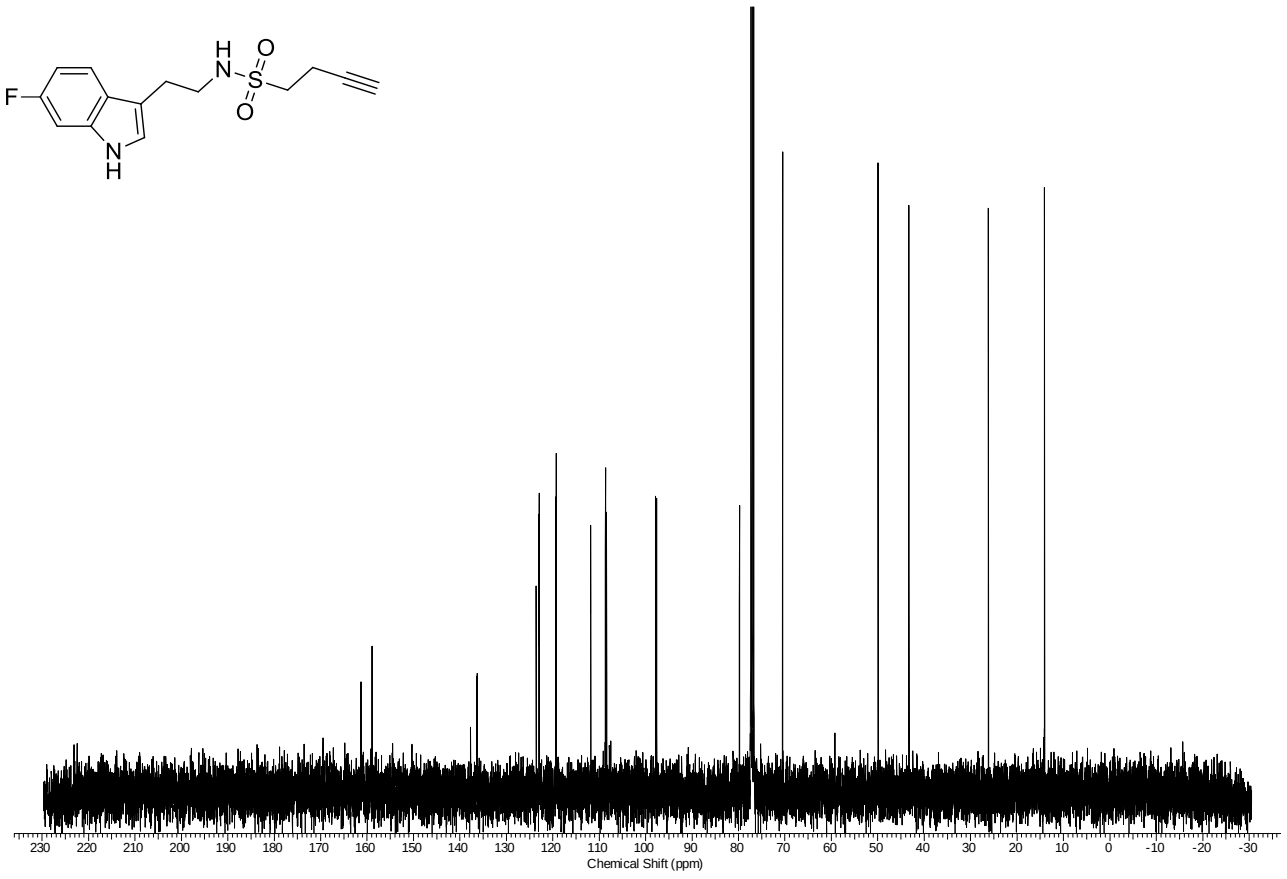
3.1.10. ^{13}CNMR spectra for *N*-[2-(5-fluoro-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide **5e**



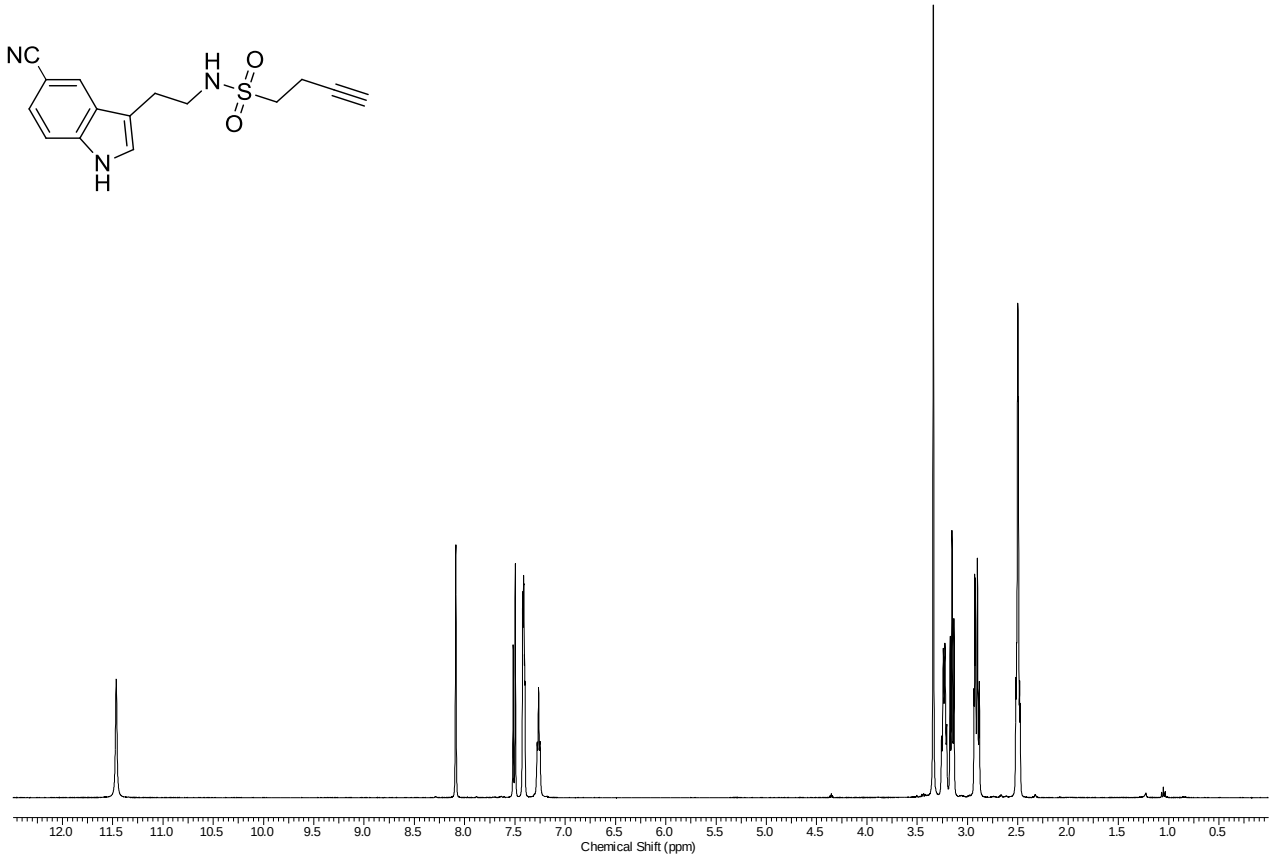
3.1.11. ^{1}HNMR spectra for *N*-[2-(6-fluoro-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5f



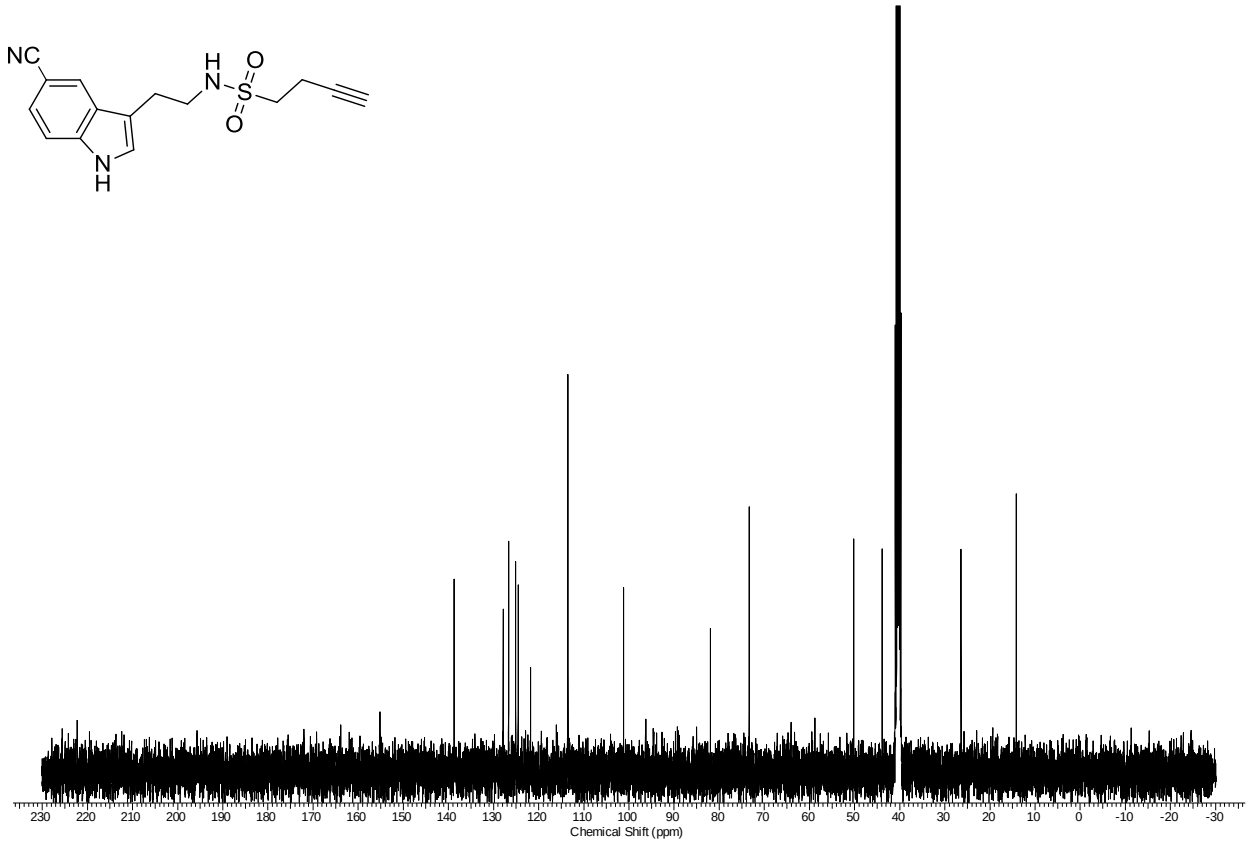
3.1.12. ^{13}CNMR spectra for *N*-[2-(6-fluoro-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5f



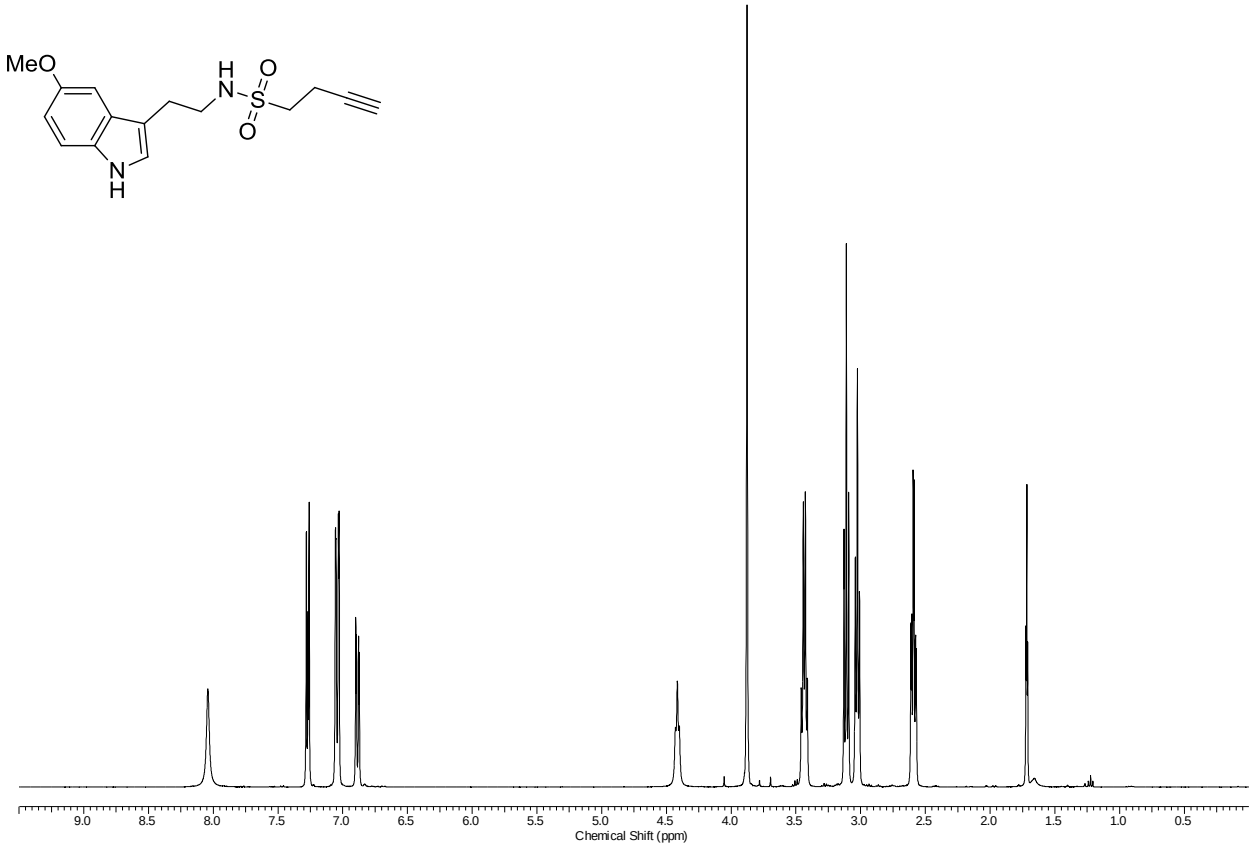
3.1.13. ^{1}HNMR spectra for *N*-[2-(5-cyano-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide **5g**



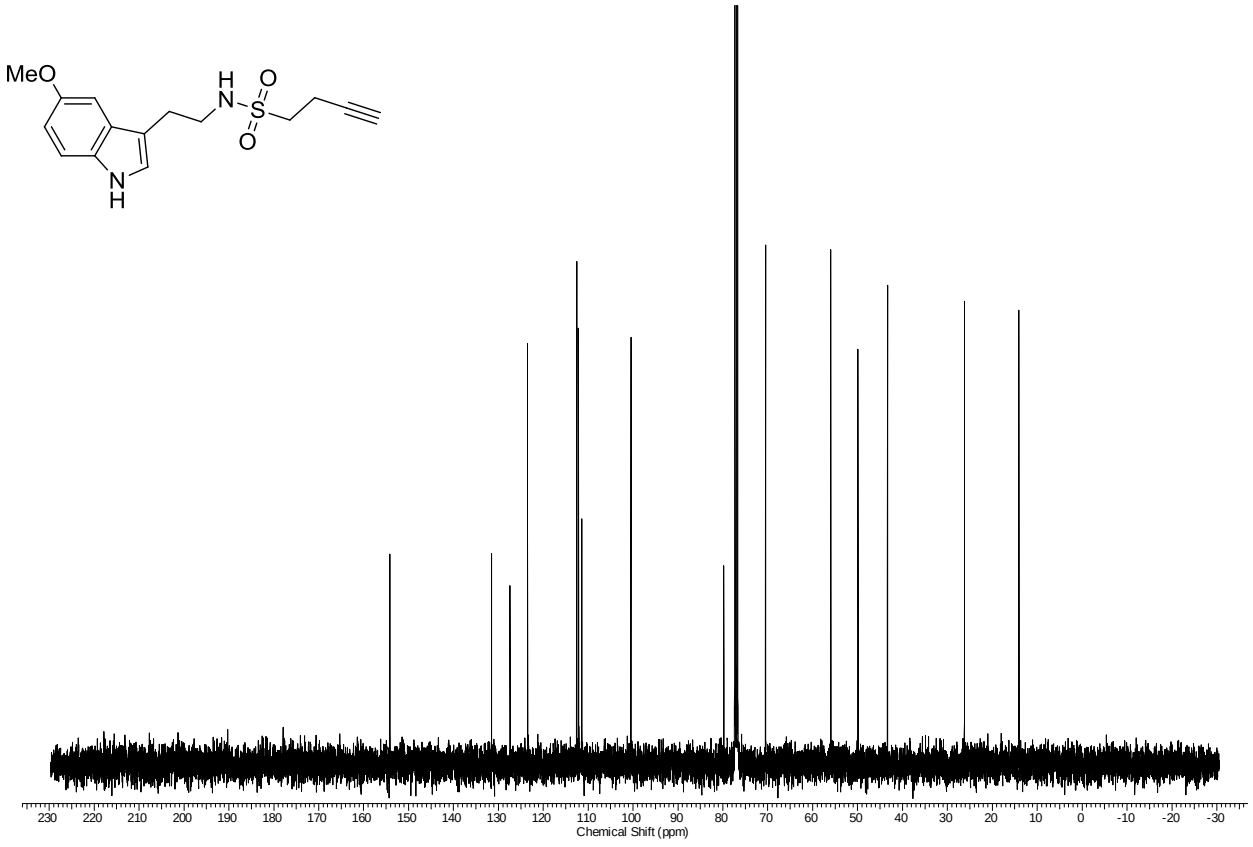
3.1.14. ^{13}CNMR spectra for *N*-[2-(5-cyano-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide **5g**



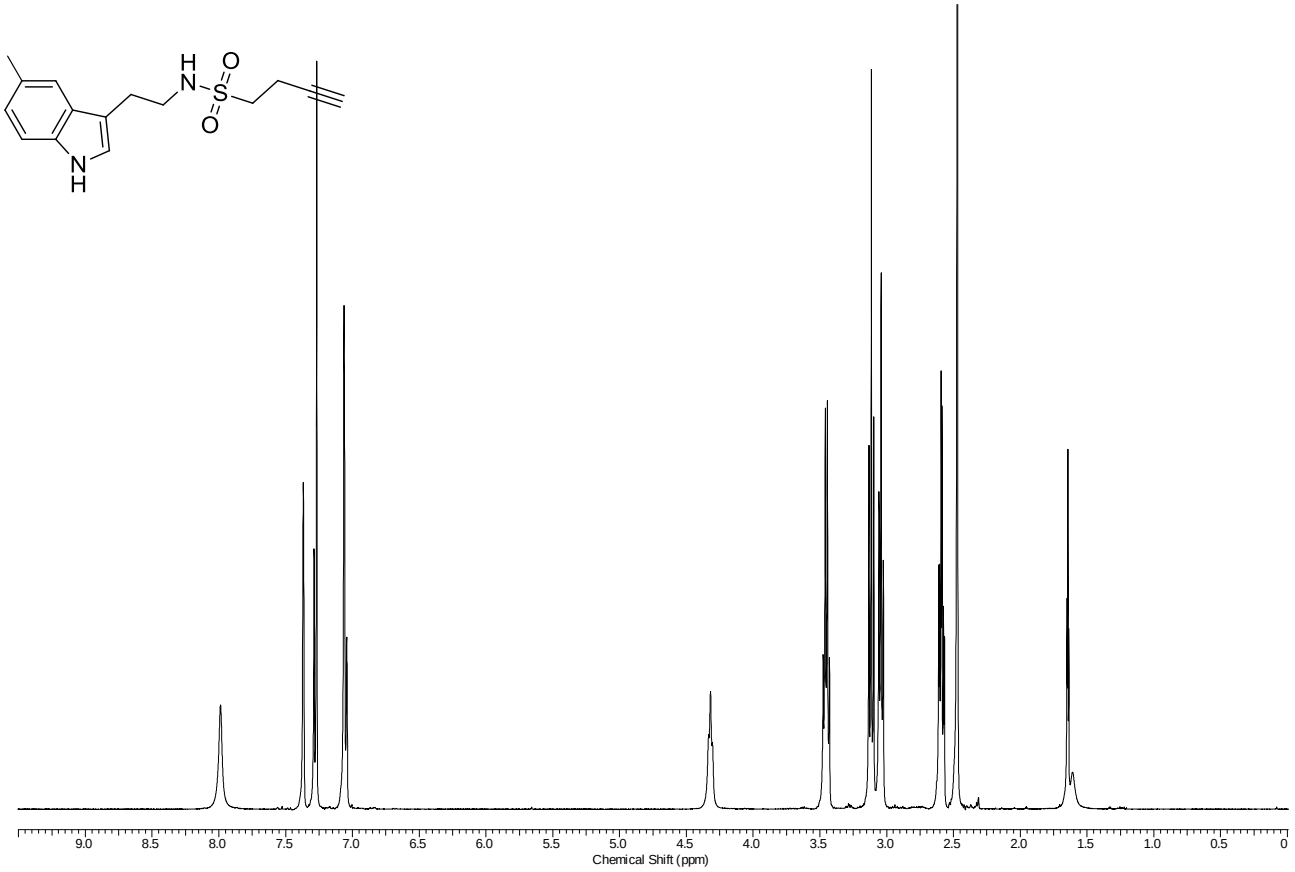
3.1.15. **^{1}HNMR spectra for N-[2-(5-methoxy-1H-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5h**



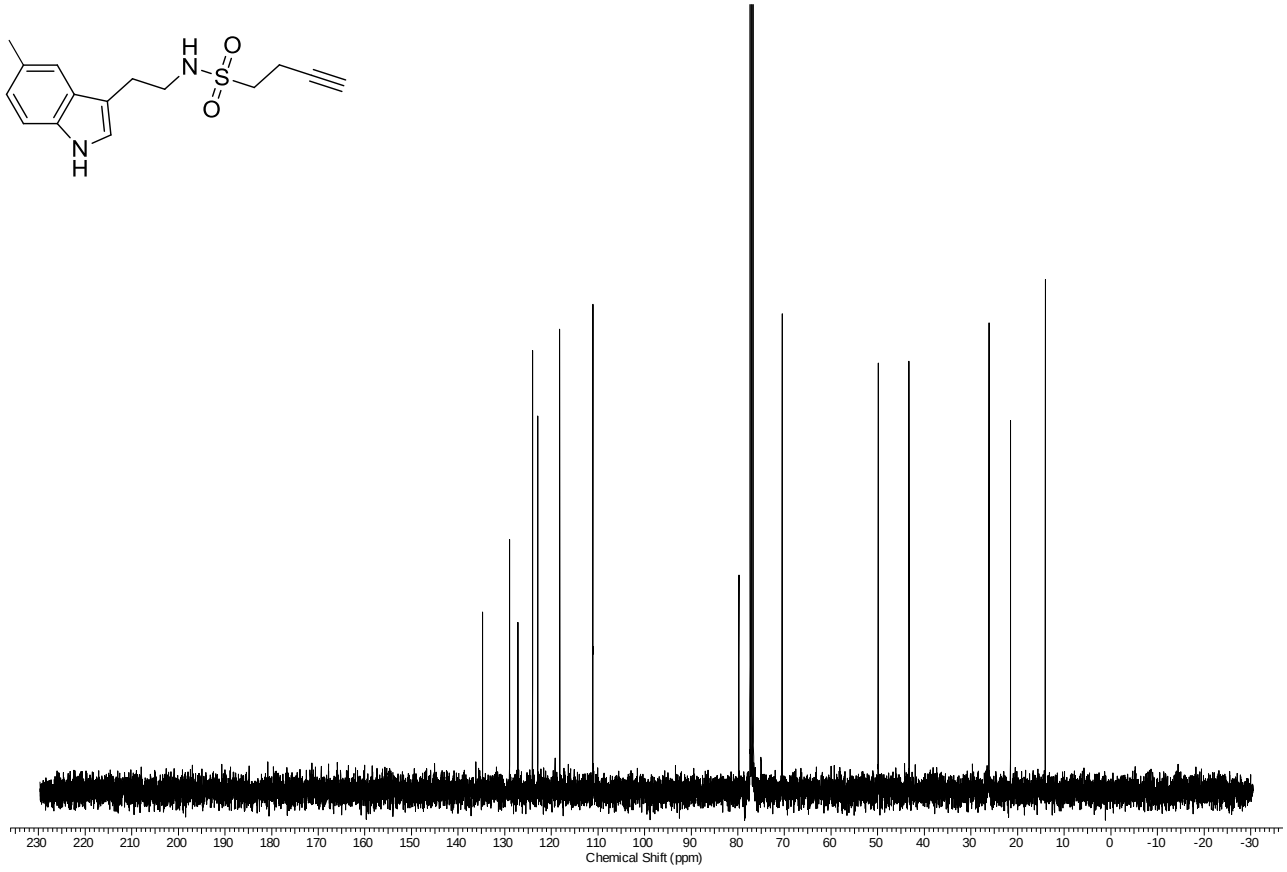
3.1.16. **^{13}CNMR spectra for N-[2-(5-methoxy-1H-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5h**



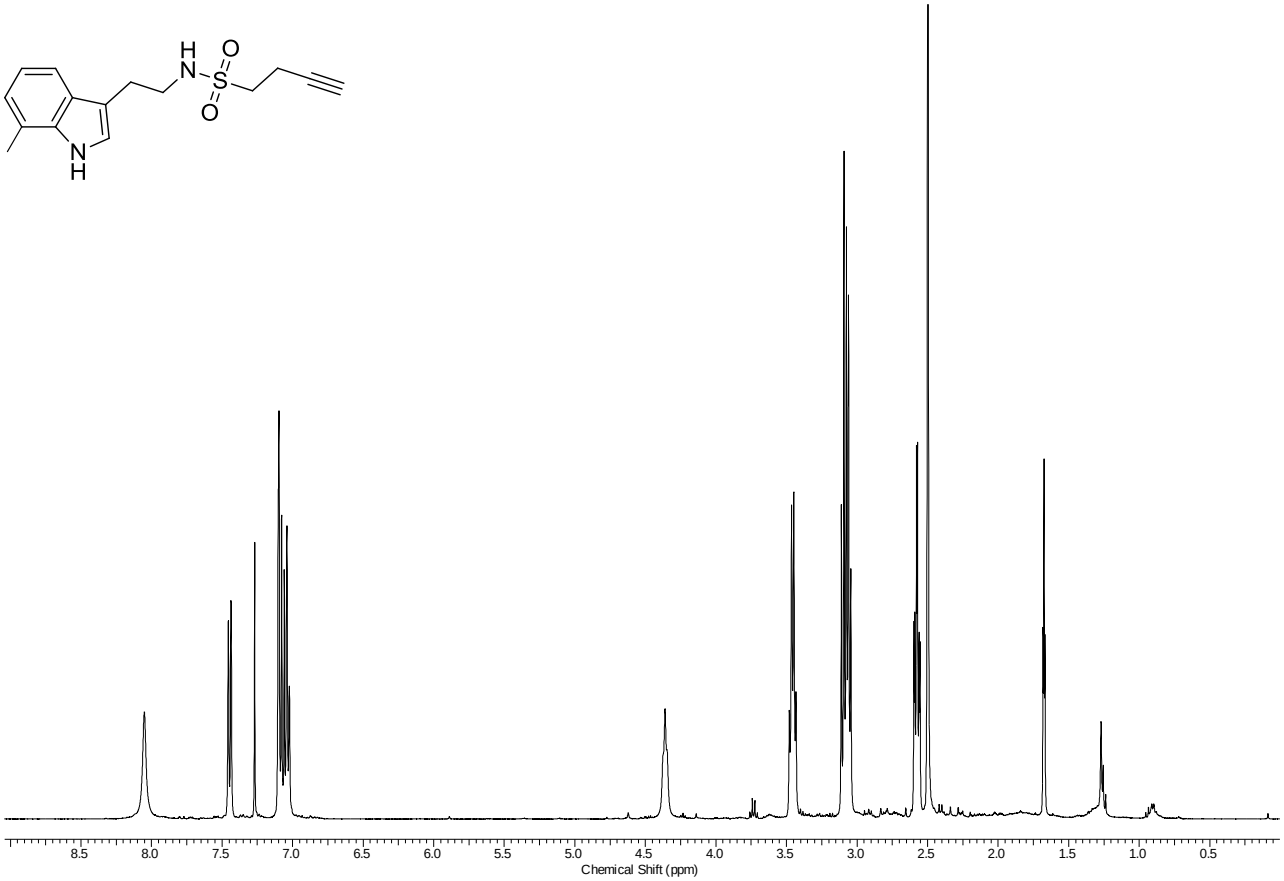
3.1.17. ^{1}HNMR spectra for *N*-[2-(5-methyl-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide **5i**



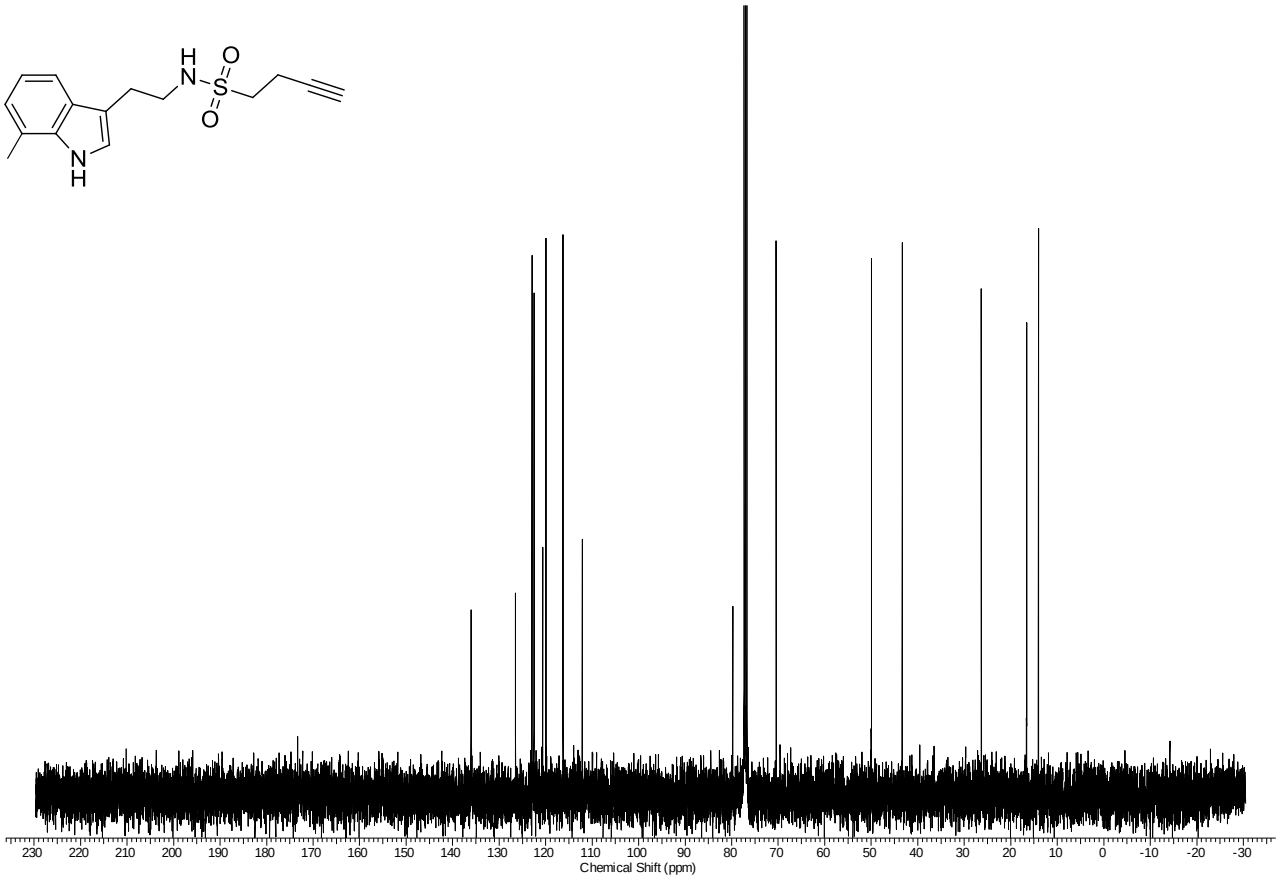
3.1.18. ^{13}CNMR spectra for *N*-[2-(5-methyl-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide **5i**



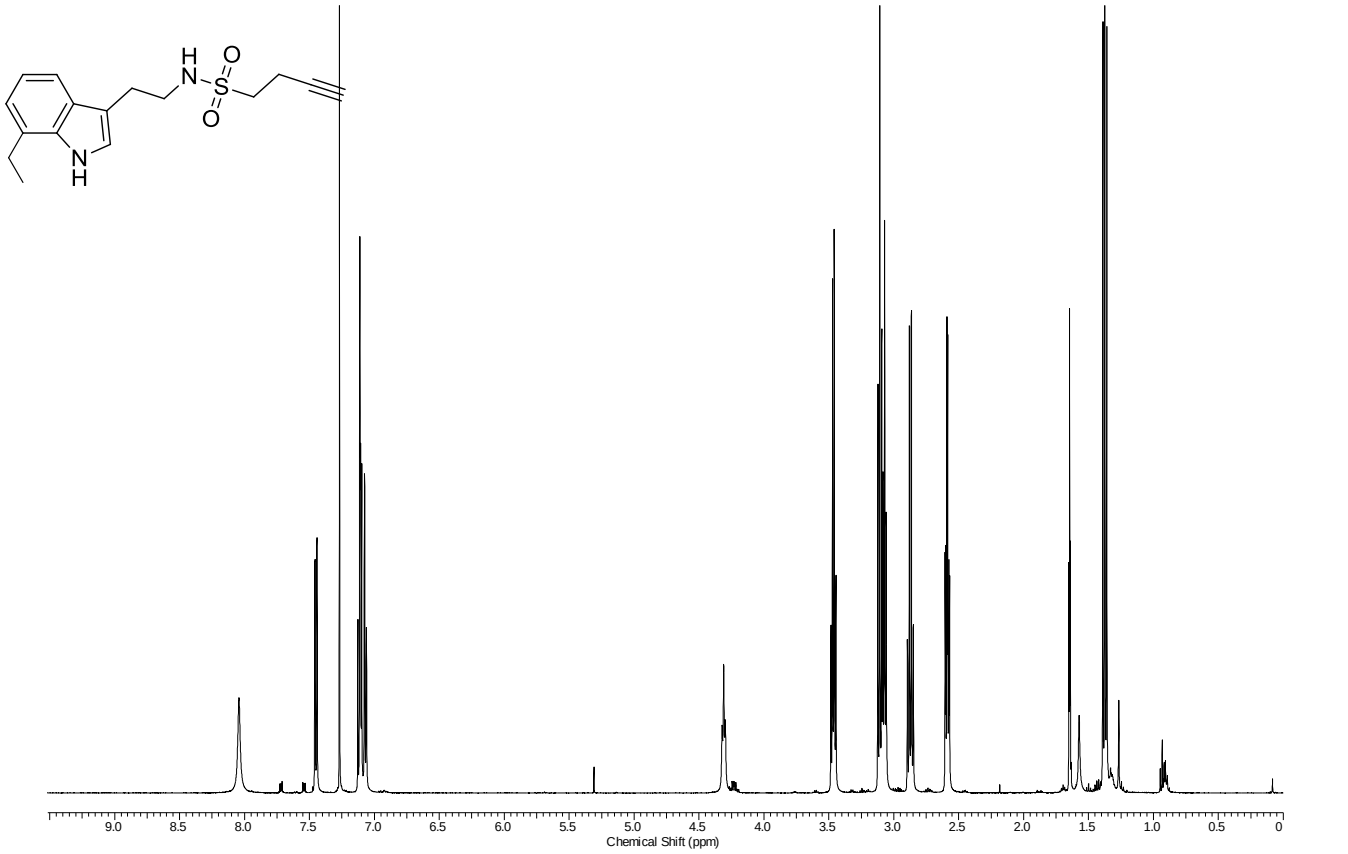
3.1.19. **^{1}HNMR spectra for *N*-[2-(7-methyl-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5j**



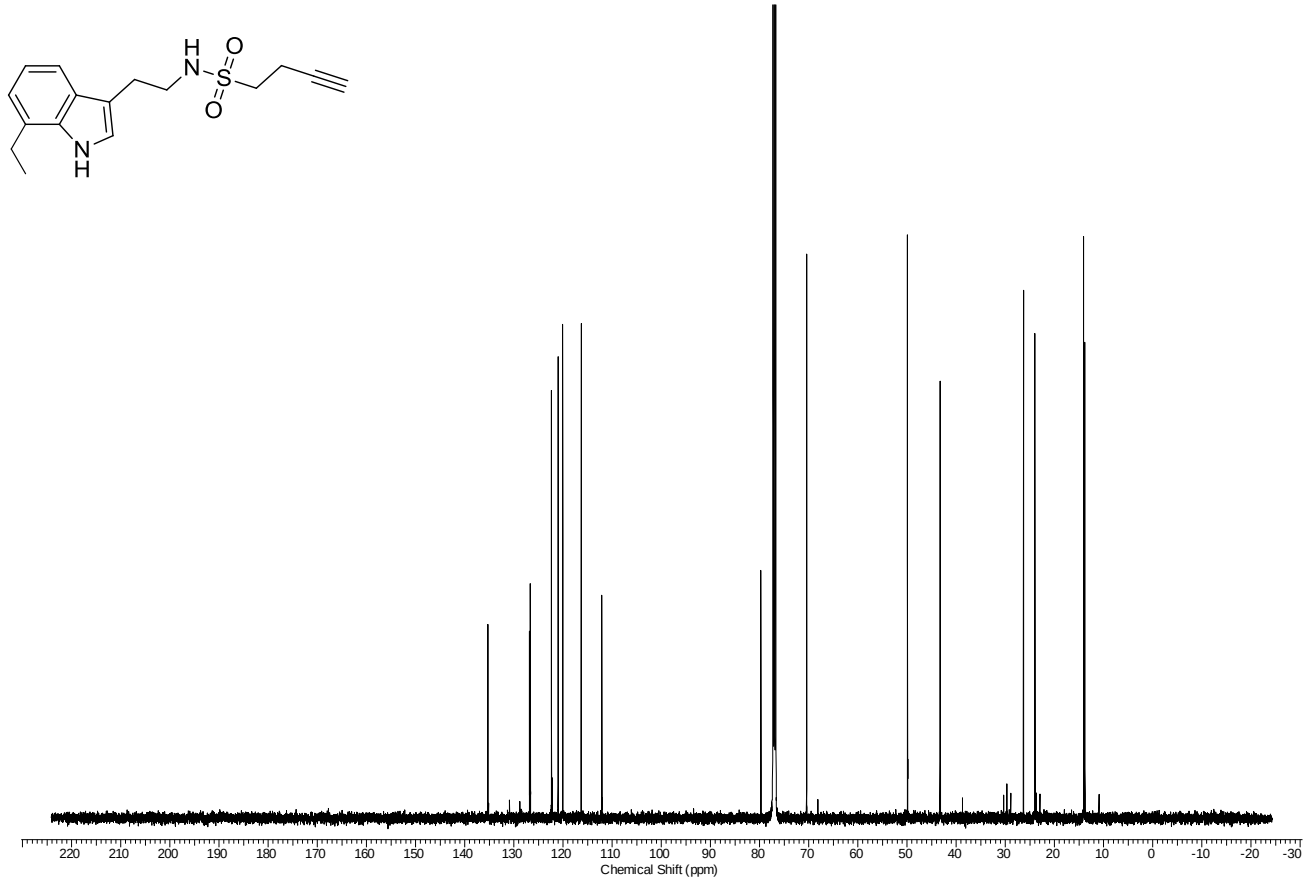
3.1.20. **^{13}CNMR spectra for *N*-[2-(7-methyl-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5j**



3.1.21. ^{1}HNMR spectra for *N*-[2-(7-ethyl-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide **5k**

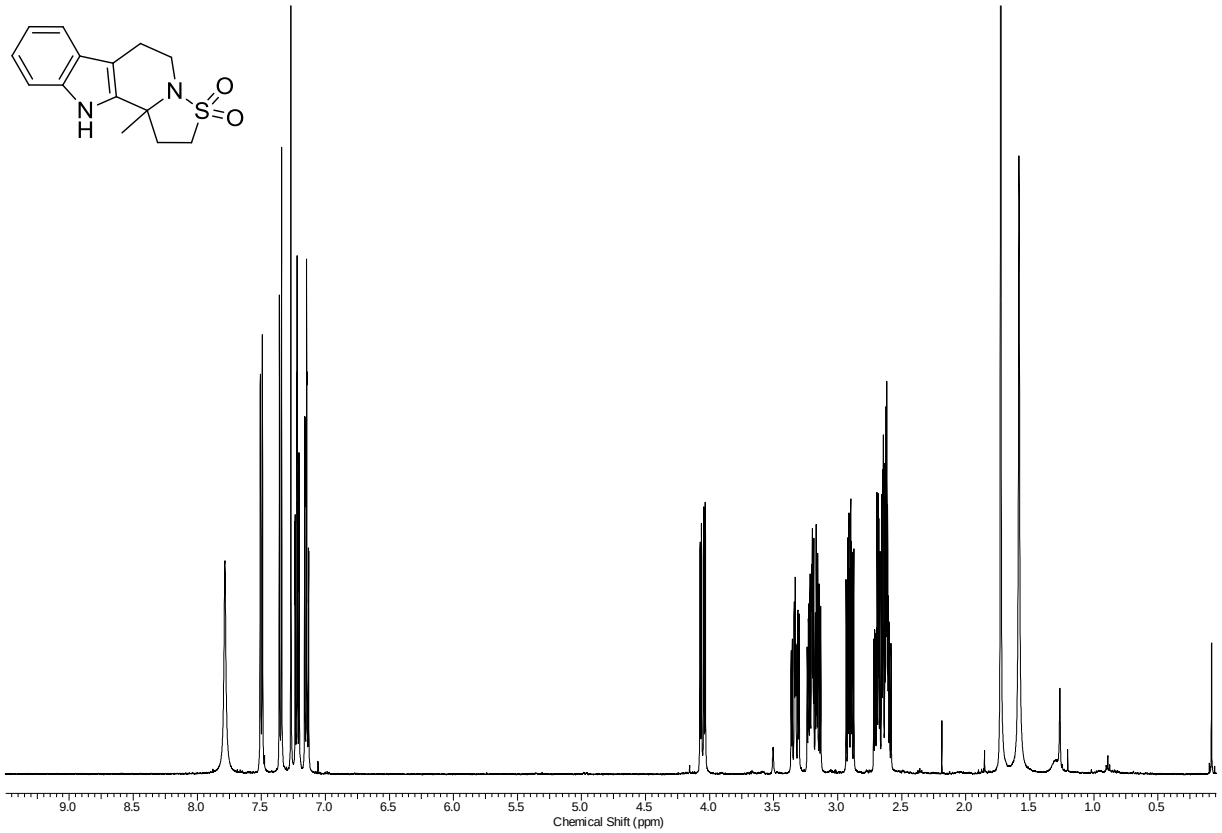


3.1.22. ^{13}CNMR spectra for *N*-[2-(7-ethyl-1*H*-indol-3-yl)ethyl]but-3-yne-1-sulfonamide **5k**

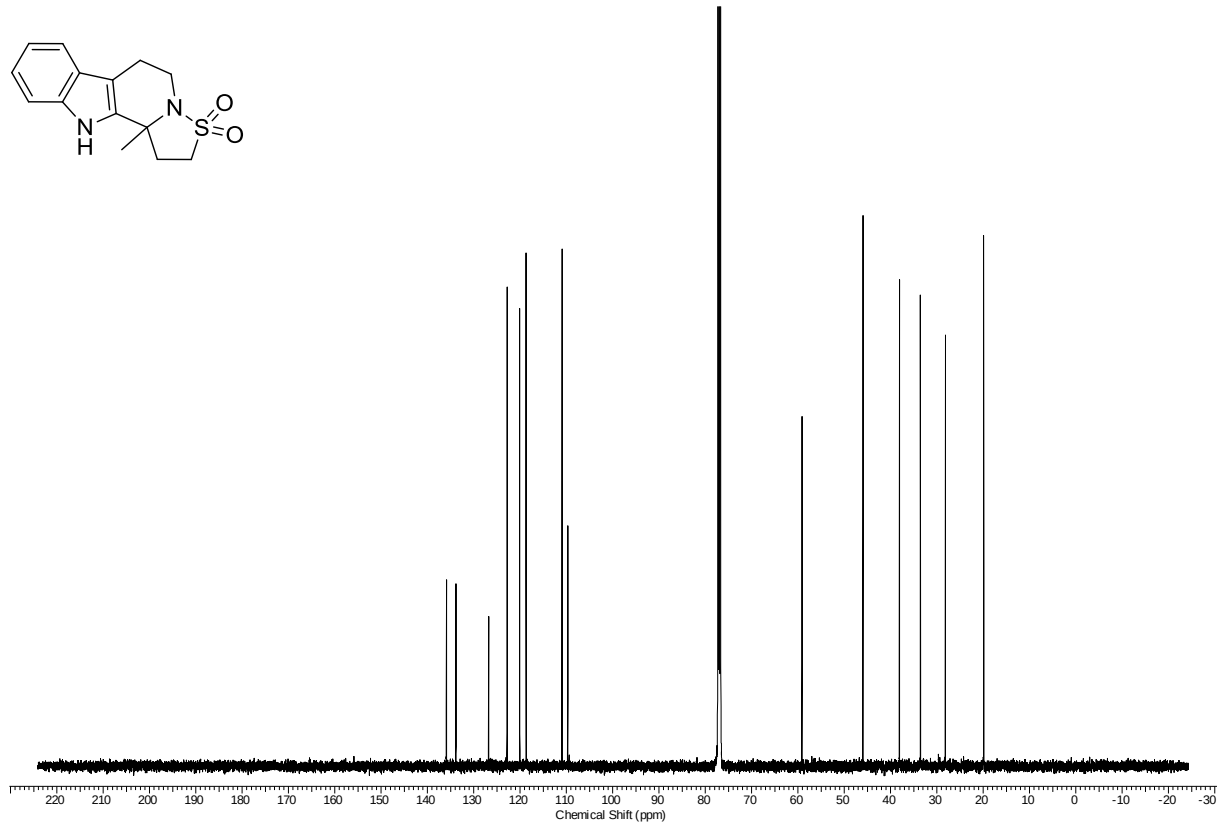


3.2. Sulfonamide cyclization products

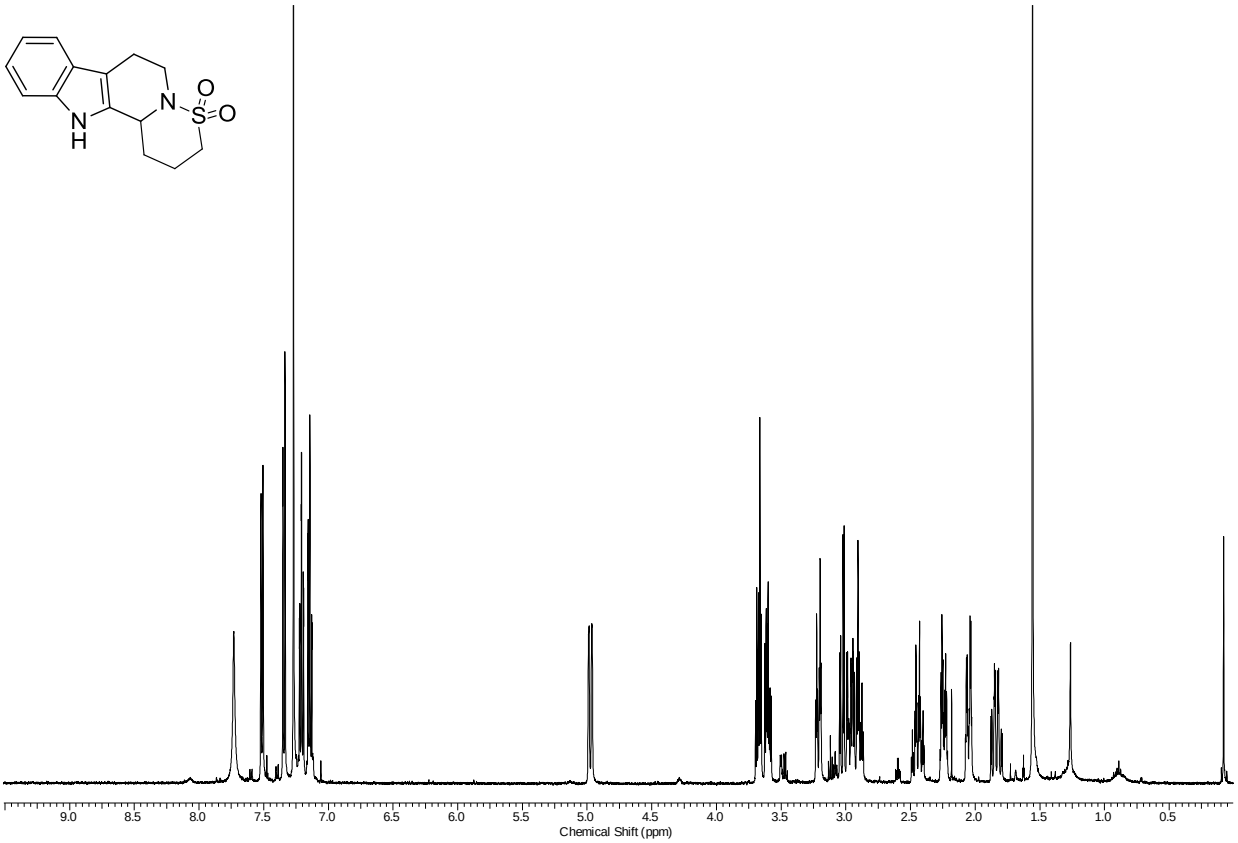
3.2.1. ^{1}HNMR spectra for 11b-methyl-1,2,5,6,11,11b-hexahydroisothiazolo[2',3':1,2]pyrido[3,4-b]indole-3,3-dioxide 6a



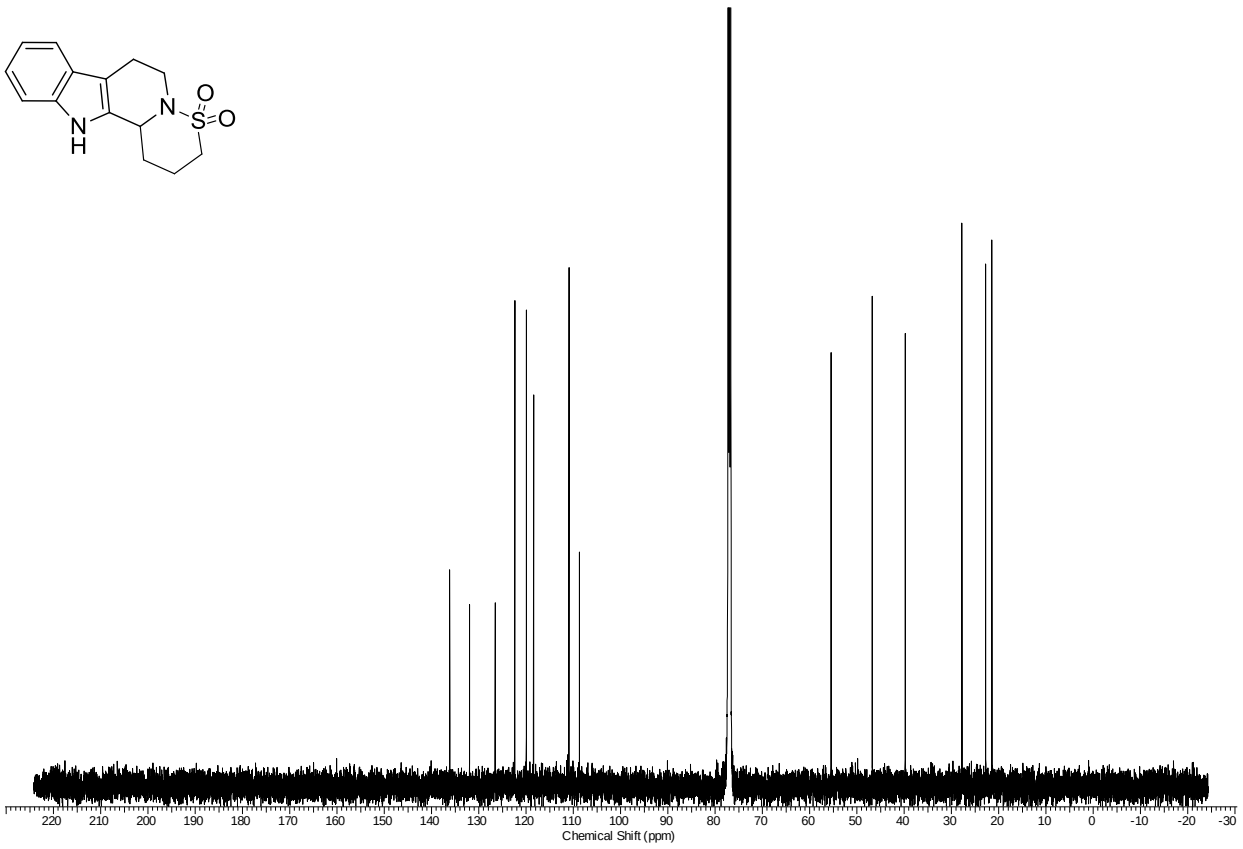
3.2.2. ^{13}CNMR spectra for 11b-methyl-1,2,5,6,11,11b-hexahydroisothiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 6a



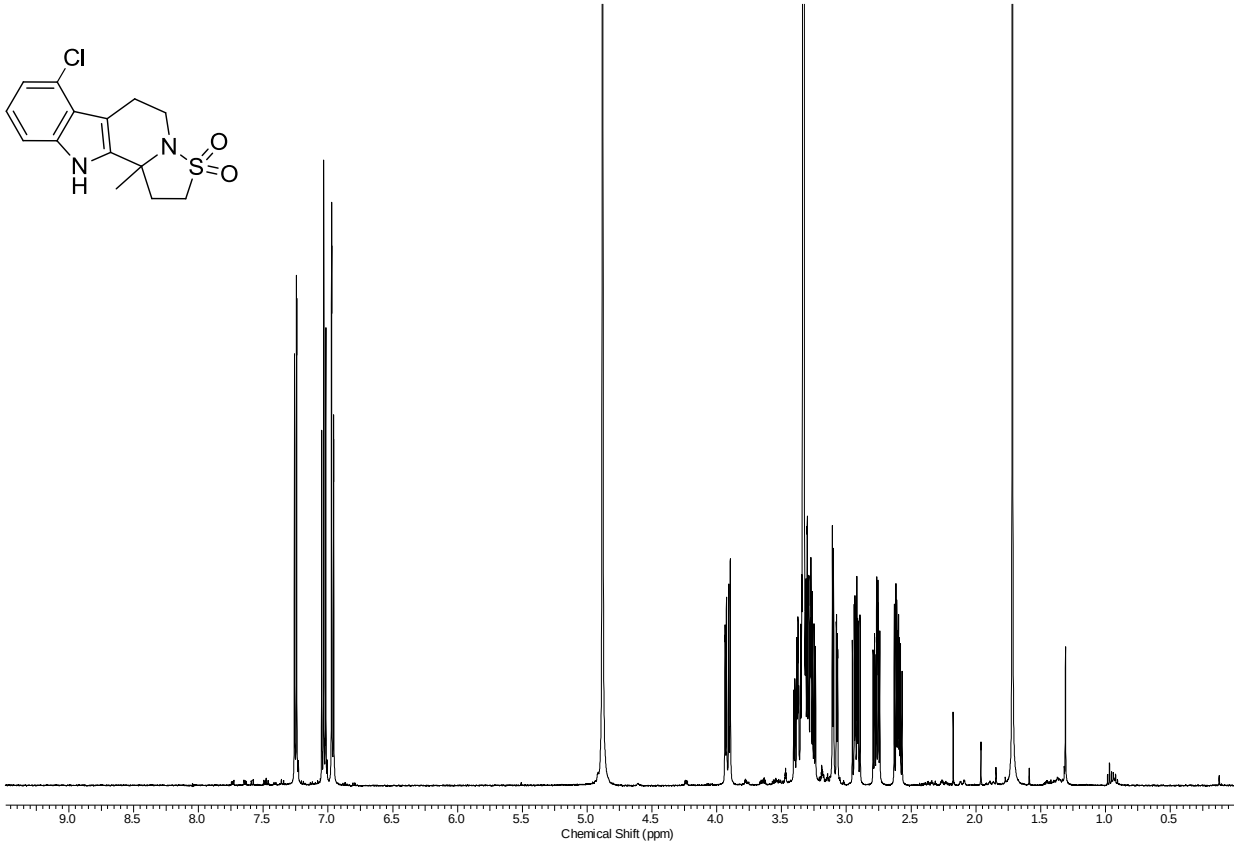
3.2.3.[1]**HNMR spectra for 2,3,6,7,12,12b-hexahydro-1*H*-[1,2]thiazino[2',3':1,2]pyrido[3,4-b]indole 4,4-dioxide 7a**



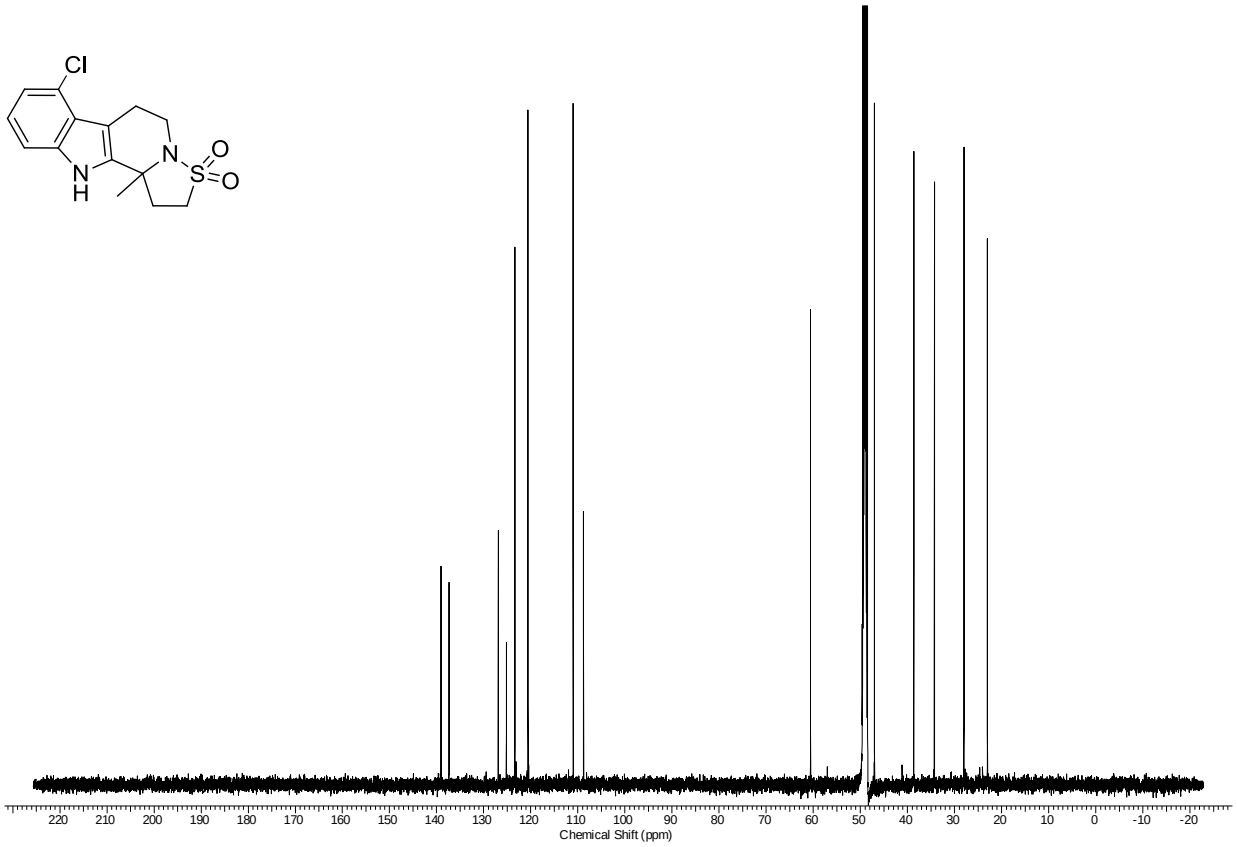
3.2.4.[13]**CNMR spectra for 2,3,6,7,12,12b-hexahydro-1*H*-[1,2]thiazino[2',3':1,2]pyrido[3,4-b]indole 4,4-dioxide 7a**



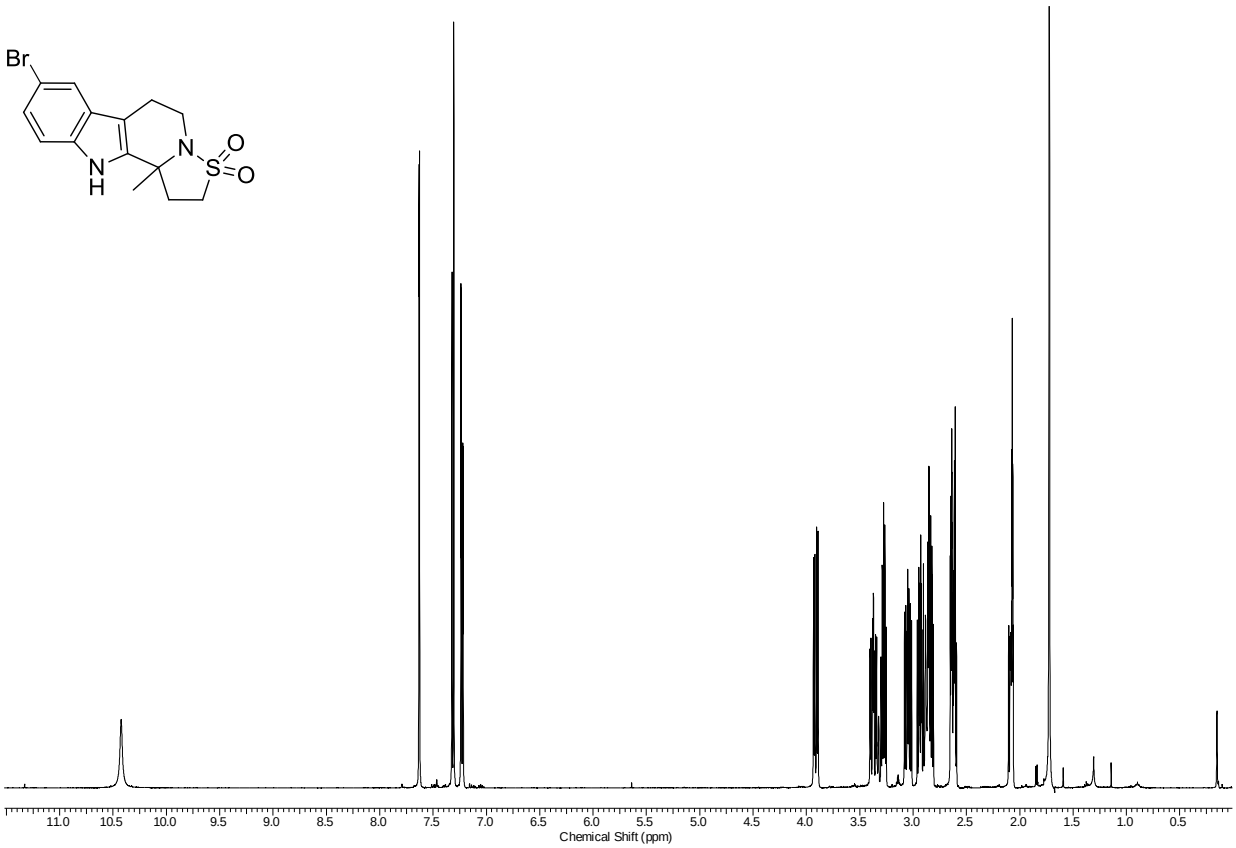
3.2.5.[1]**HNMR spectra for 7-chloro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6b**



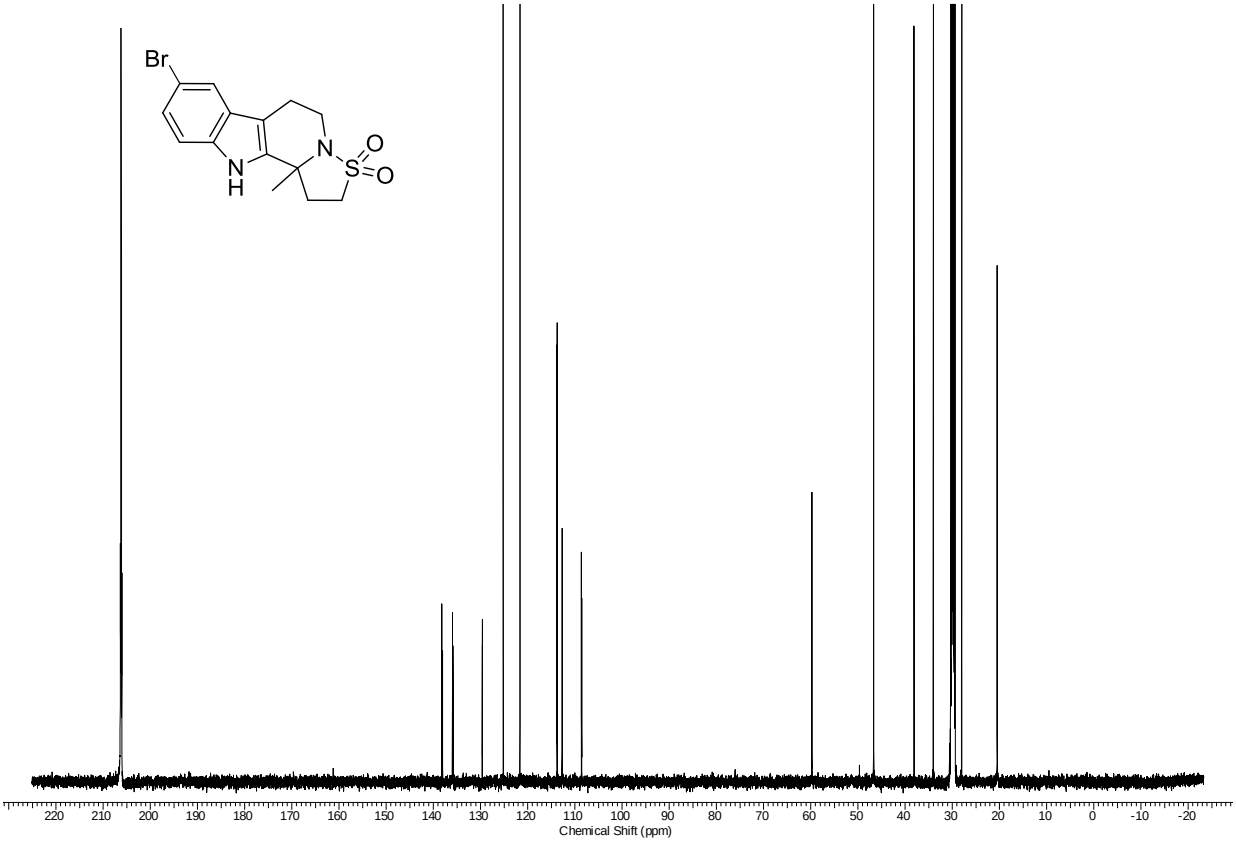
3.2.6.[13]**CNMR spectra for 7-chloro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6b**



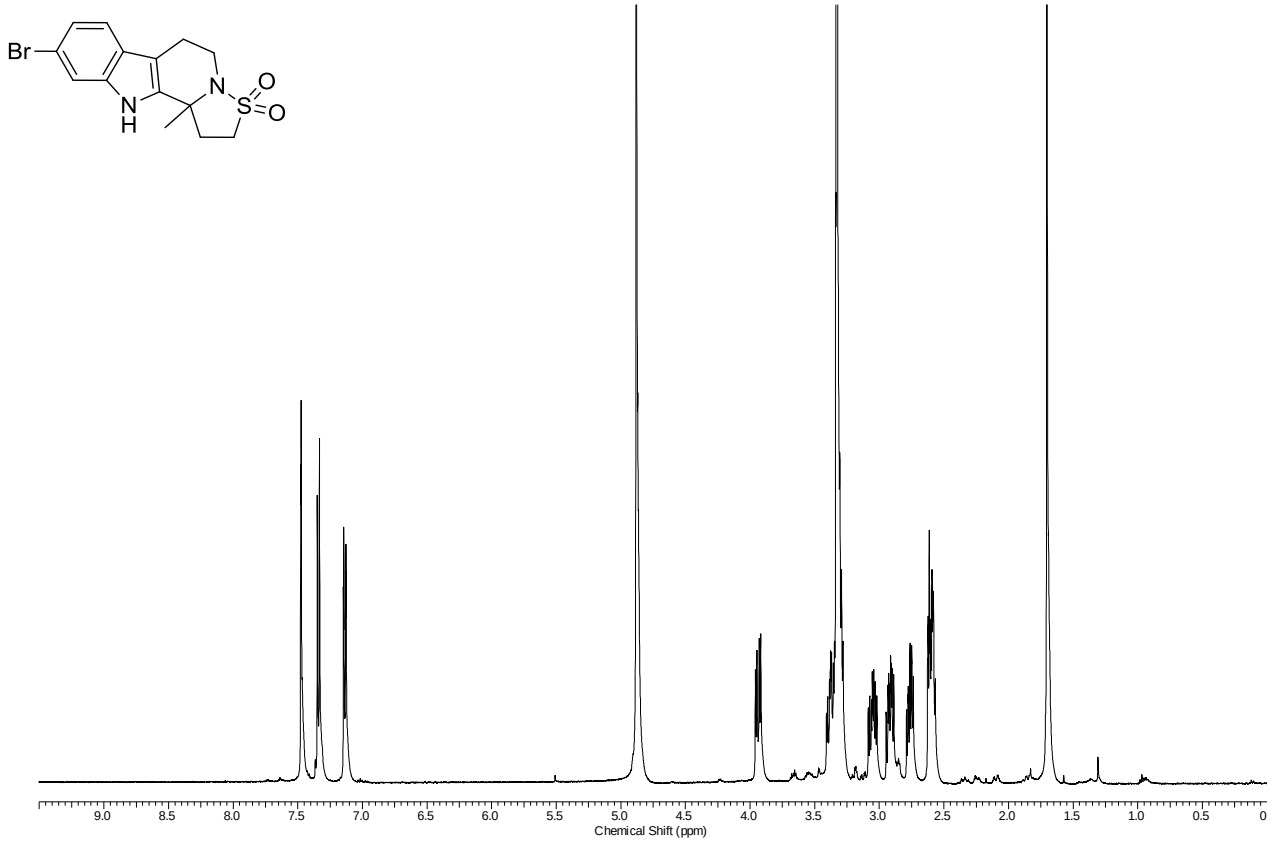
3.2.7.[1]**HNMR spectra for 8-bromo-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6c**



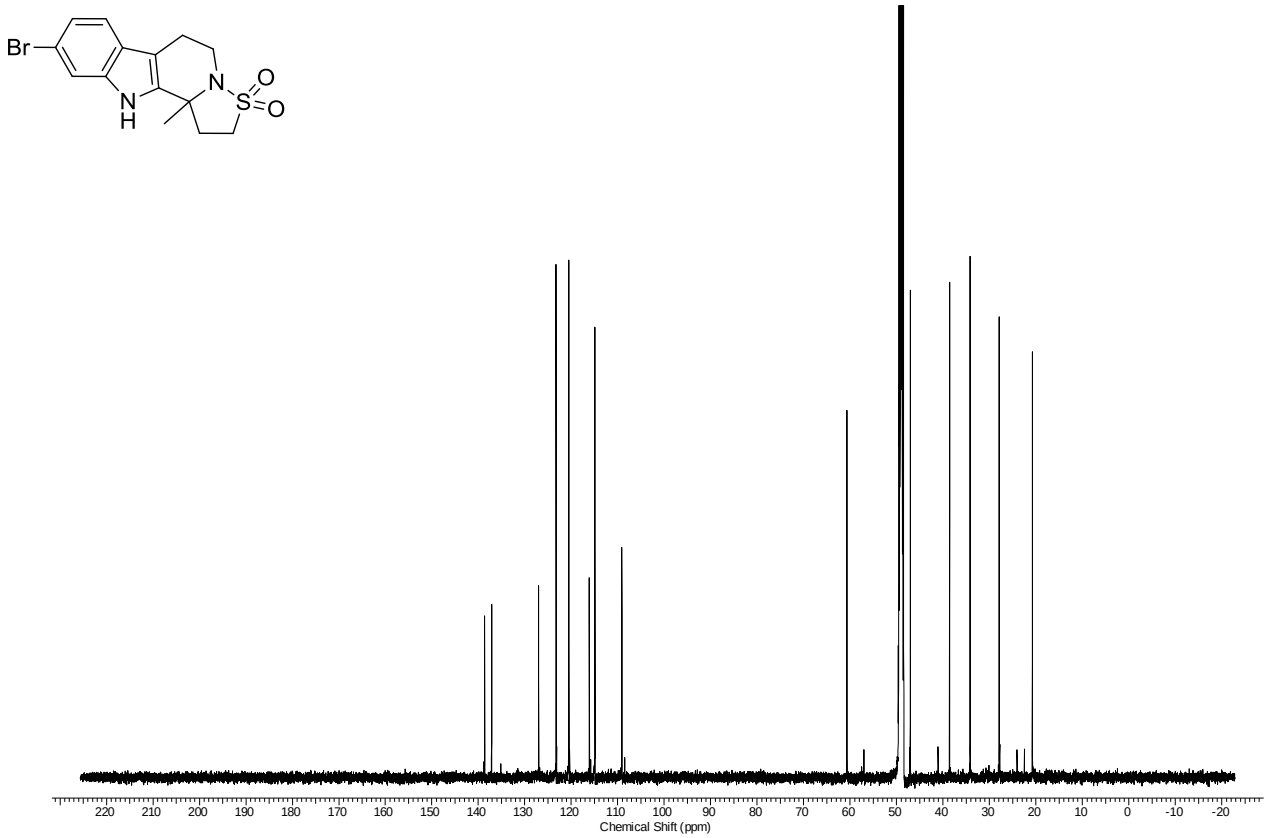
3.2.8.[13]**CNMR spectra for 8-bromo-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6c**



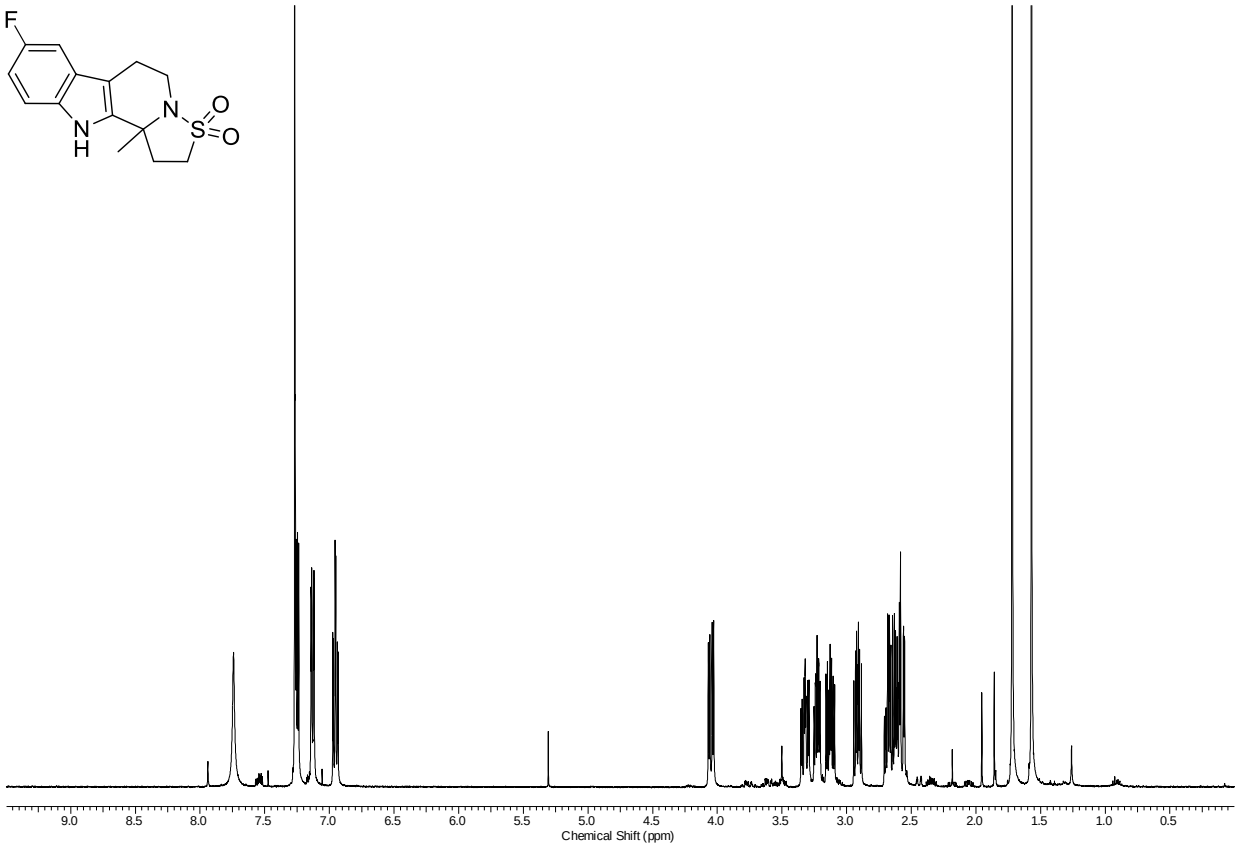
3.2.9.**^{1}HNMR spectra for 9-bromo-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6d**



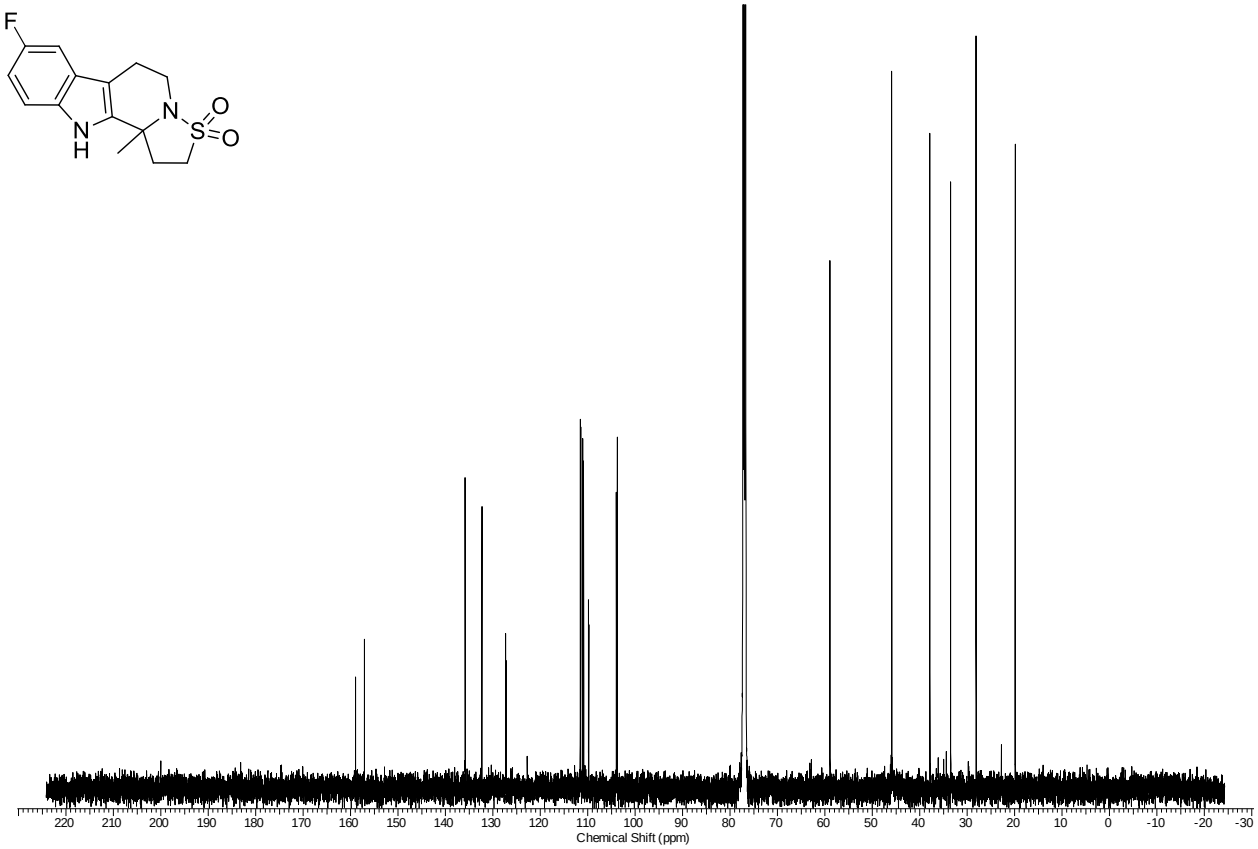
3.2.10. **^{13}CNMR spectra for 9-bromo-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6d**



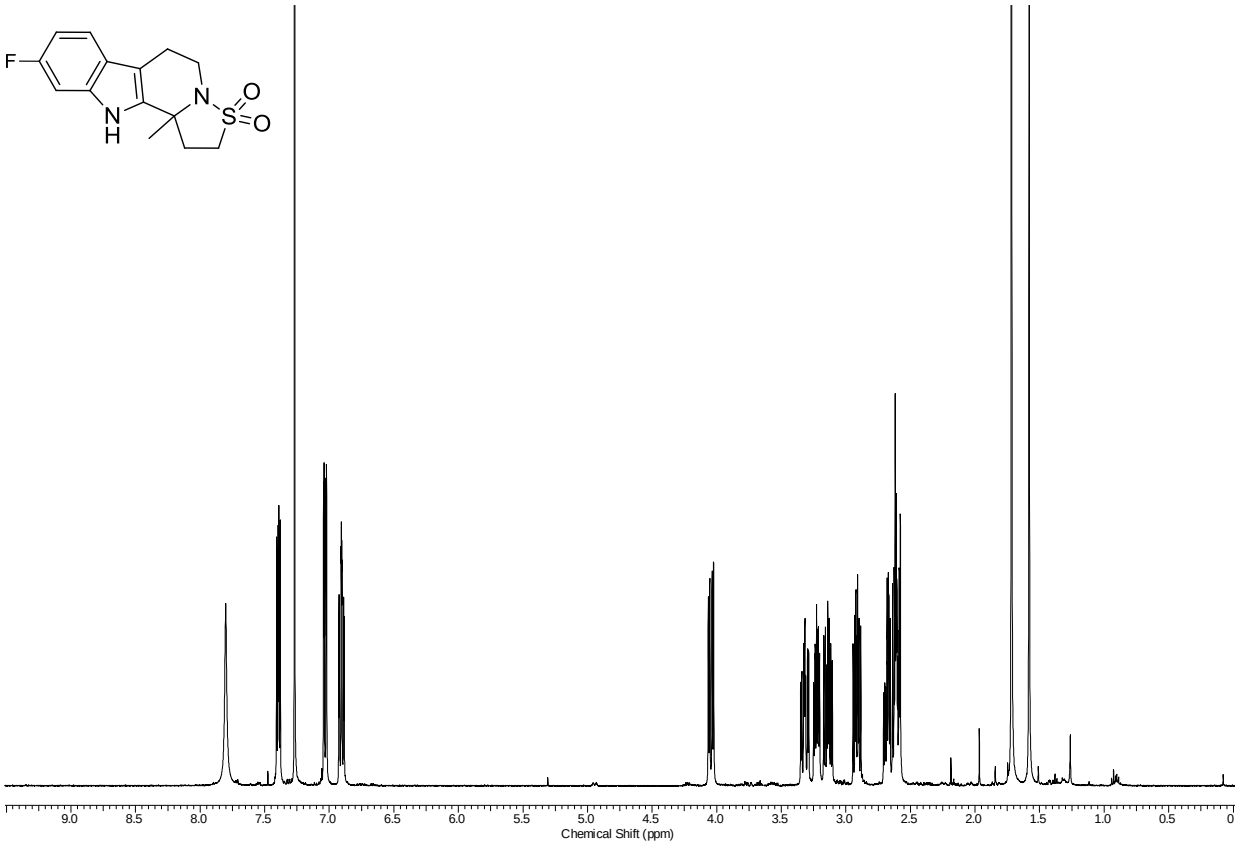
3.2.11. **^{1}HNMR spectra for 8-fluoro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6e**



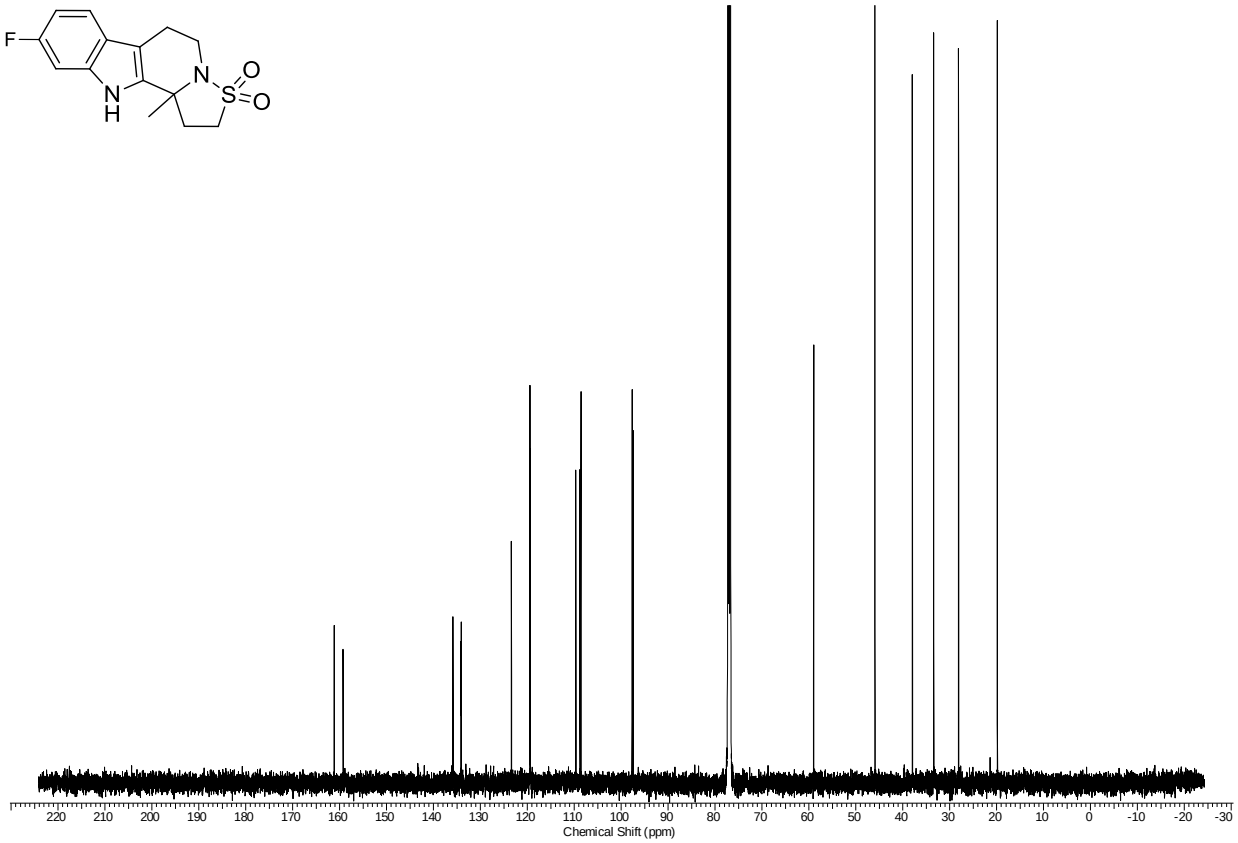
3.2.12. **^{13}CNMR spectra for 8-fluoro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6e**



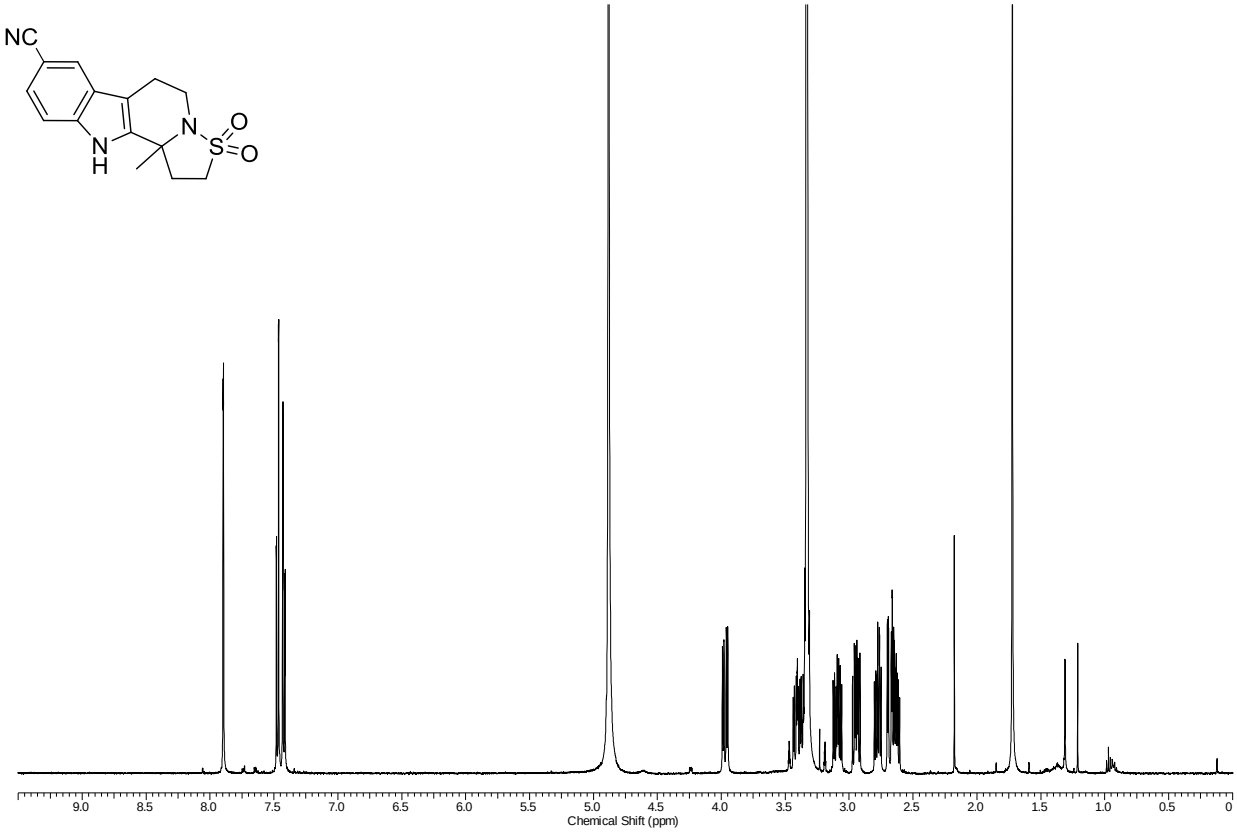
3.2.13. **^{1}HNMR spectra for 9-fluoro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6f**



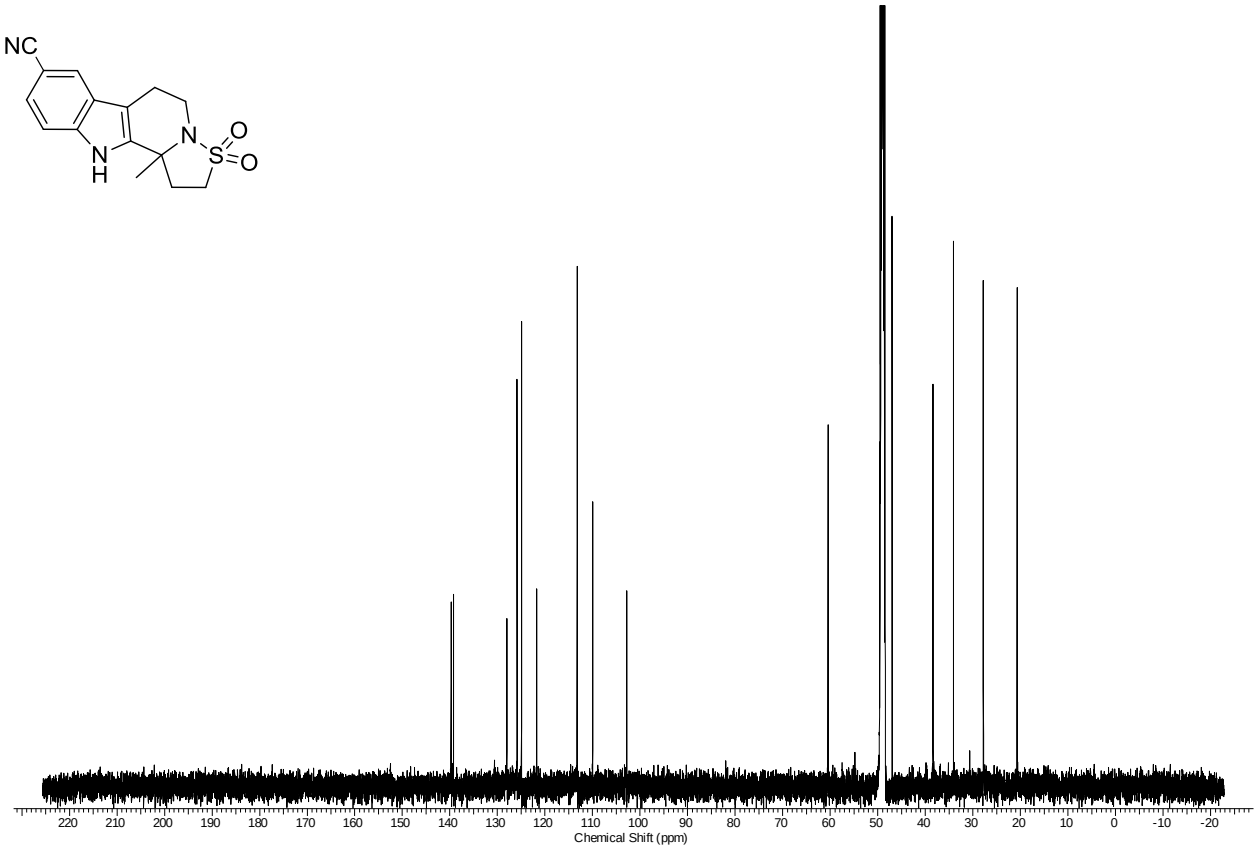
3.2.14. **^{13}CNMR spectra for 9-fluoro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6f**



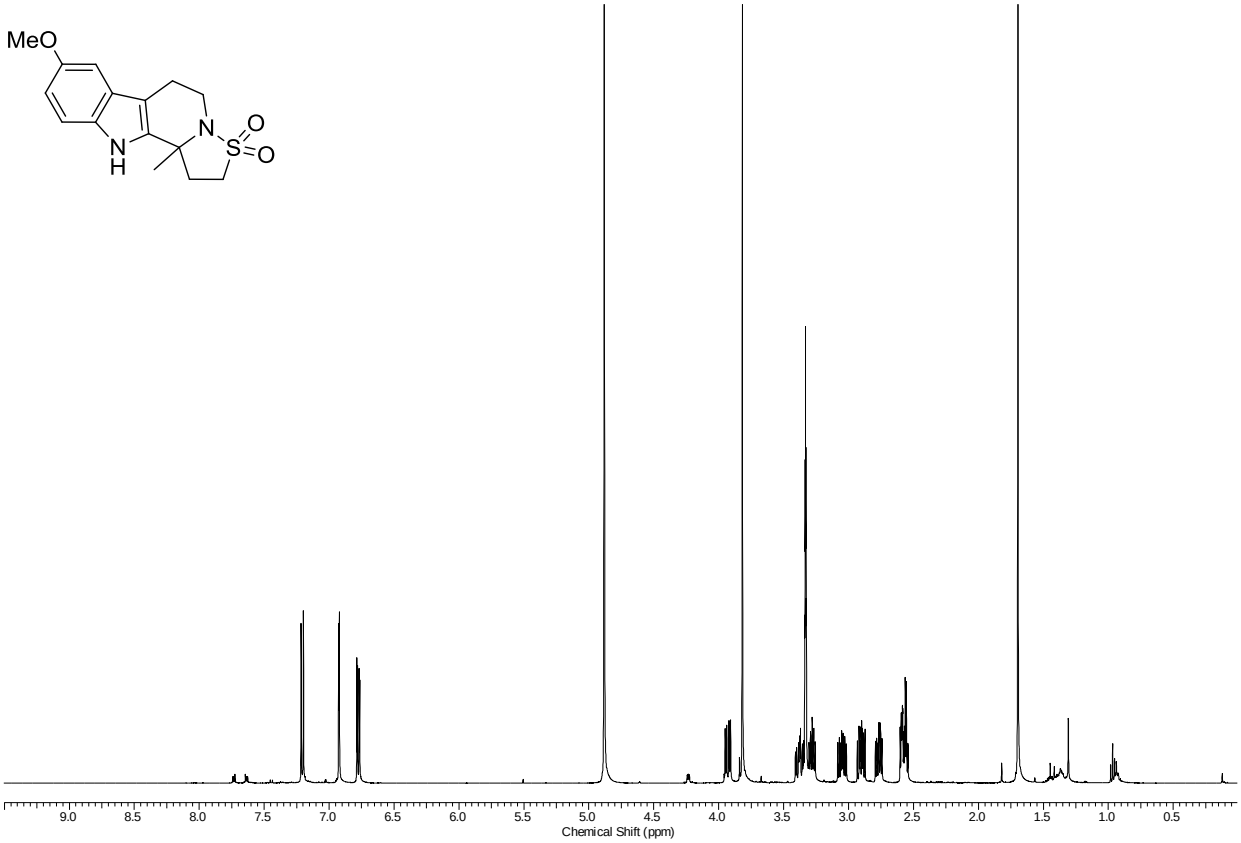
3.2.15. **^{1}HNMR spectra for 11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole-8-carbonitrile 3,3-dioxide 6g**



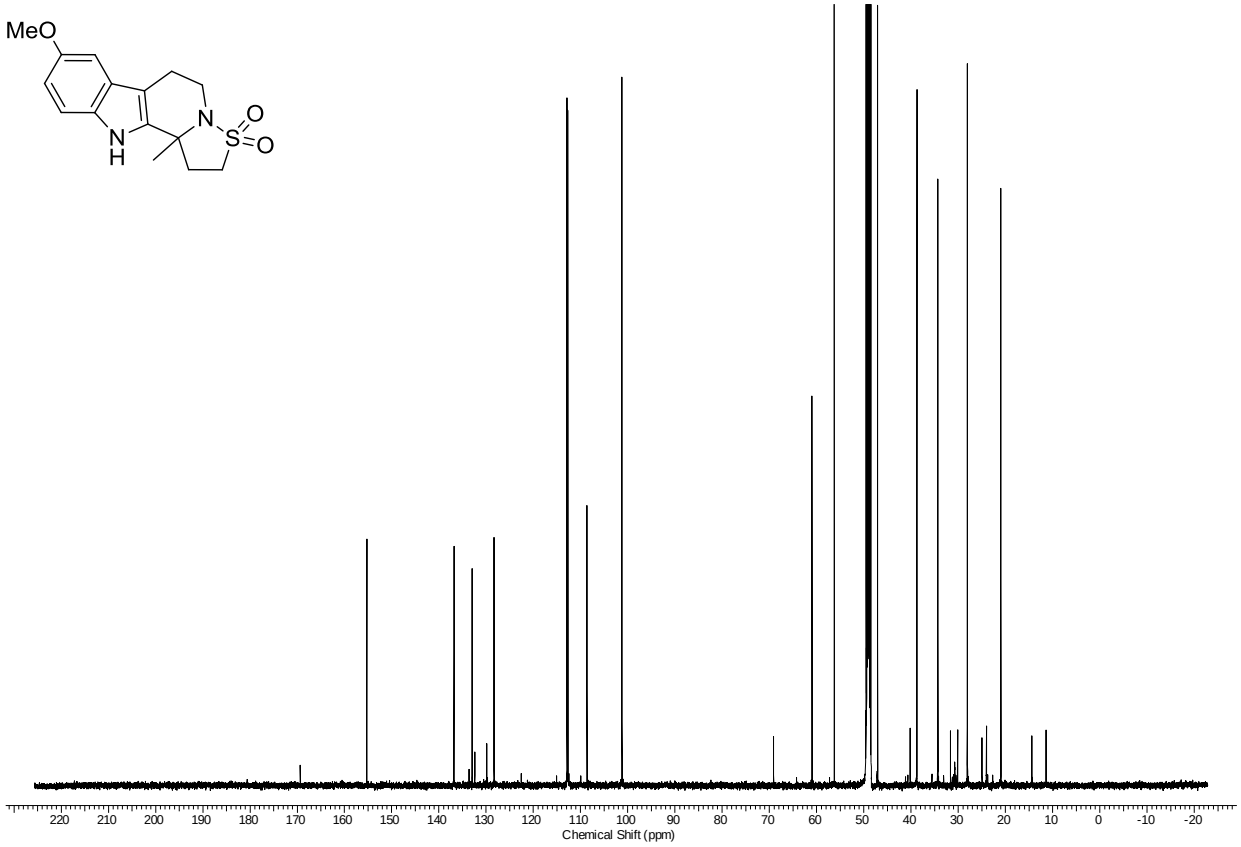
3.2.16. **^{13}CNMR spectra for 11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole-8-carbonitrile 3,3-dioxide 6g**



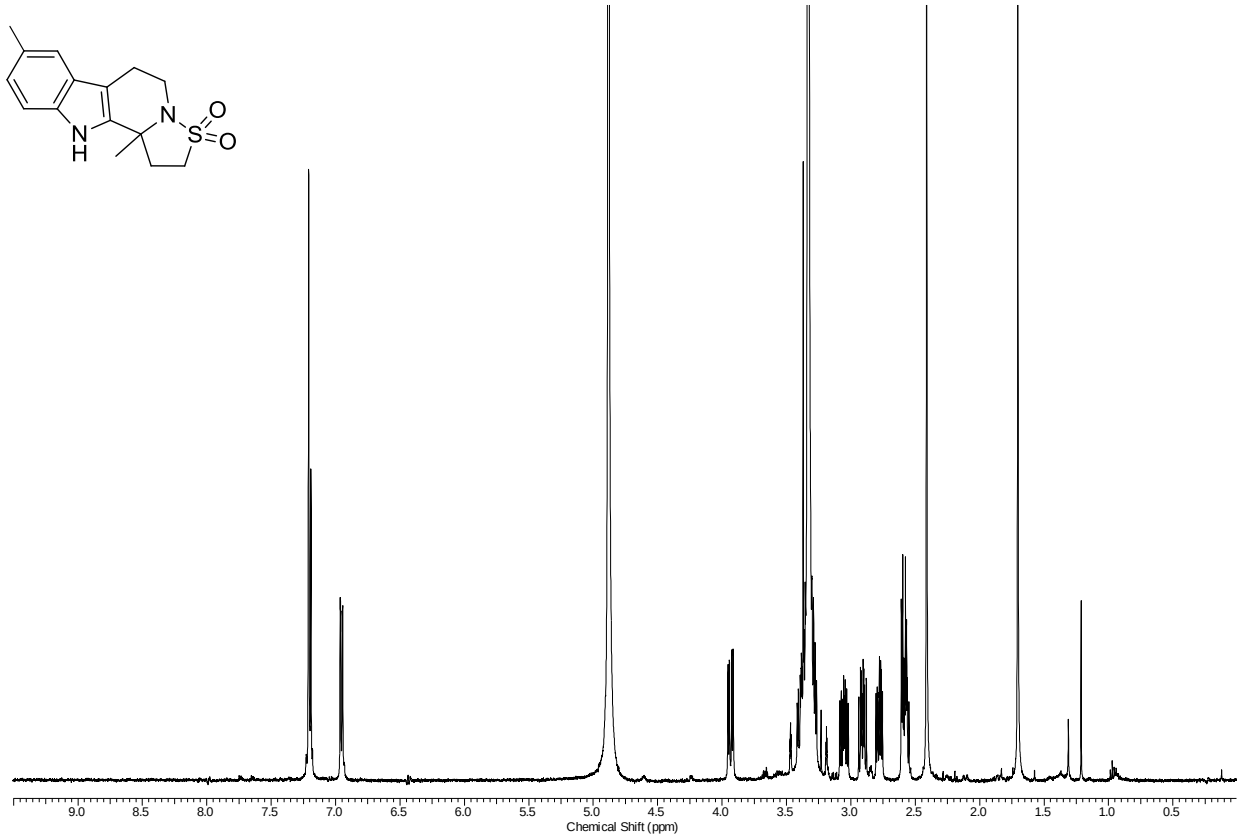
3.2.17. **^{1}HNMR spectra for 8-methoxy-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 6h**



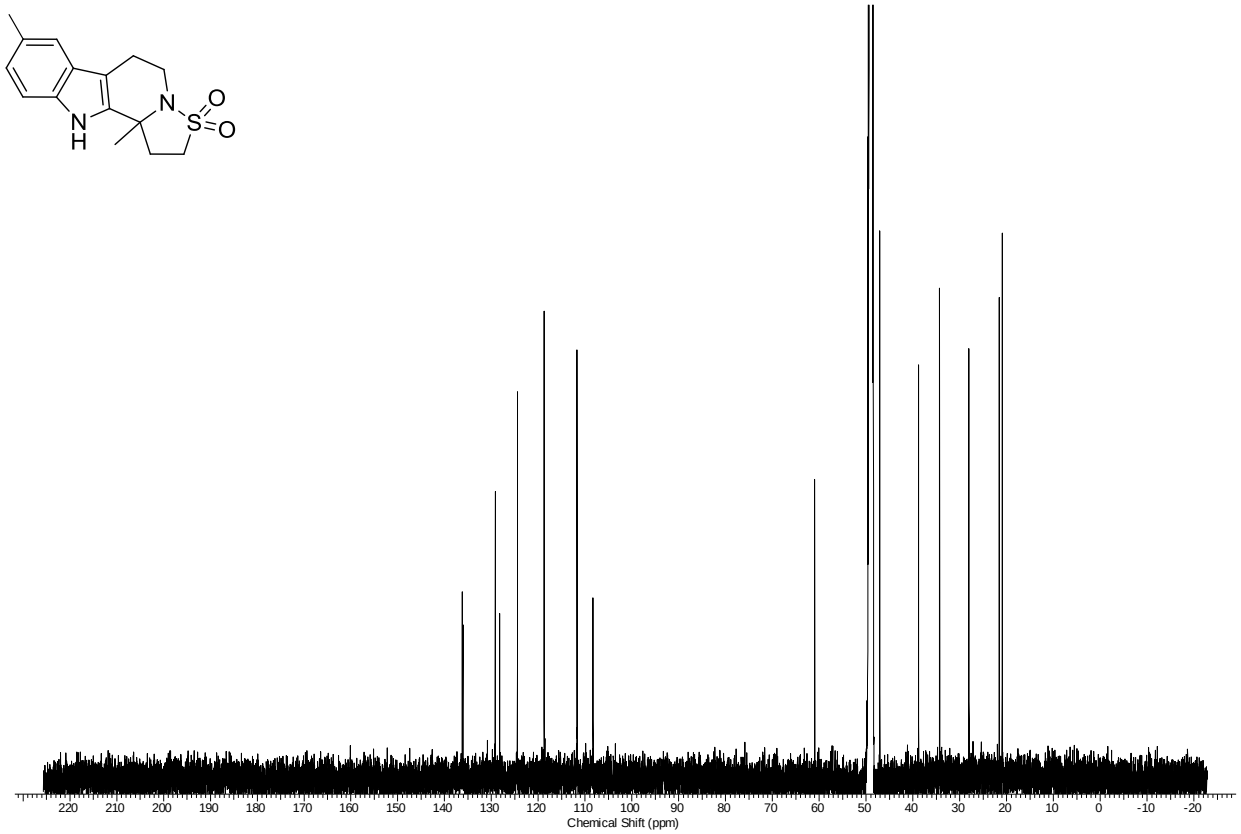
3.2.18. **^{13}CNMR spectra for 8-methoxy-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 6h**



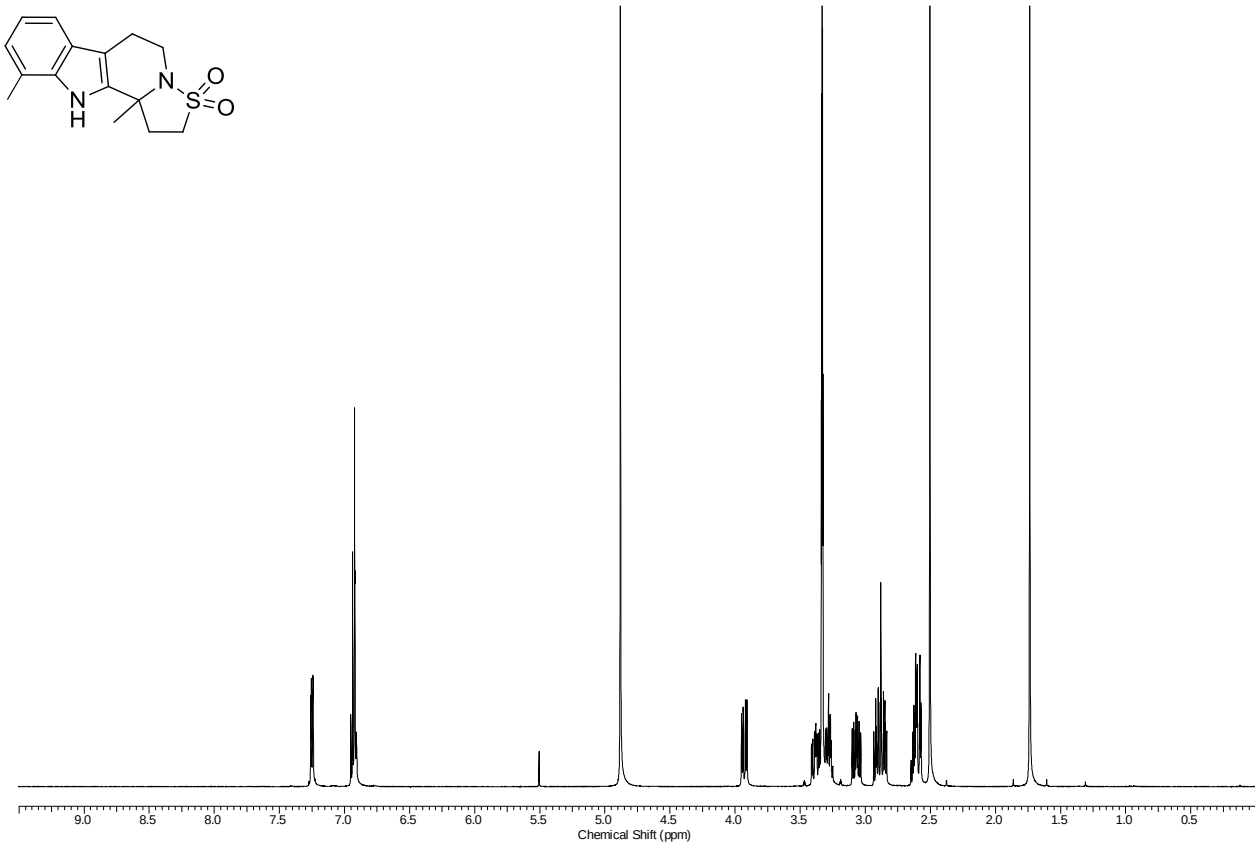
3.2.1.[1]**HNMR spectra for 8,11b-dimethyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6i**



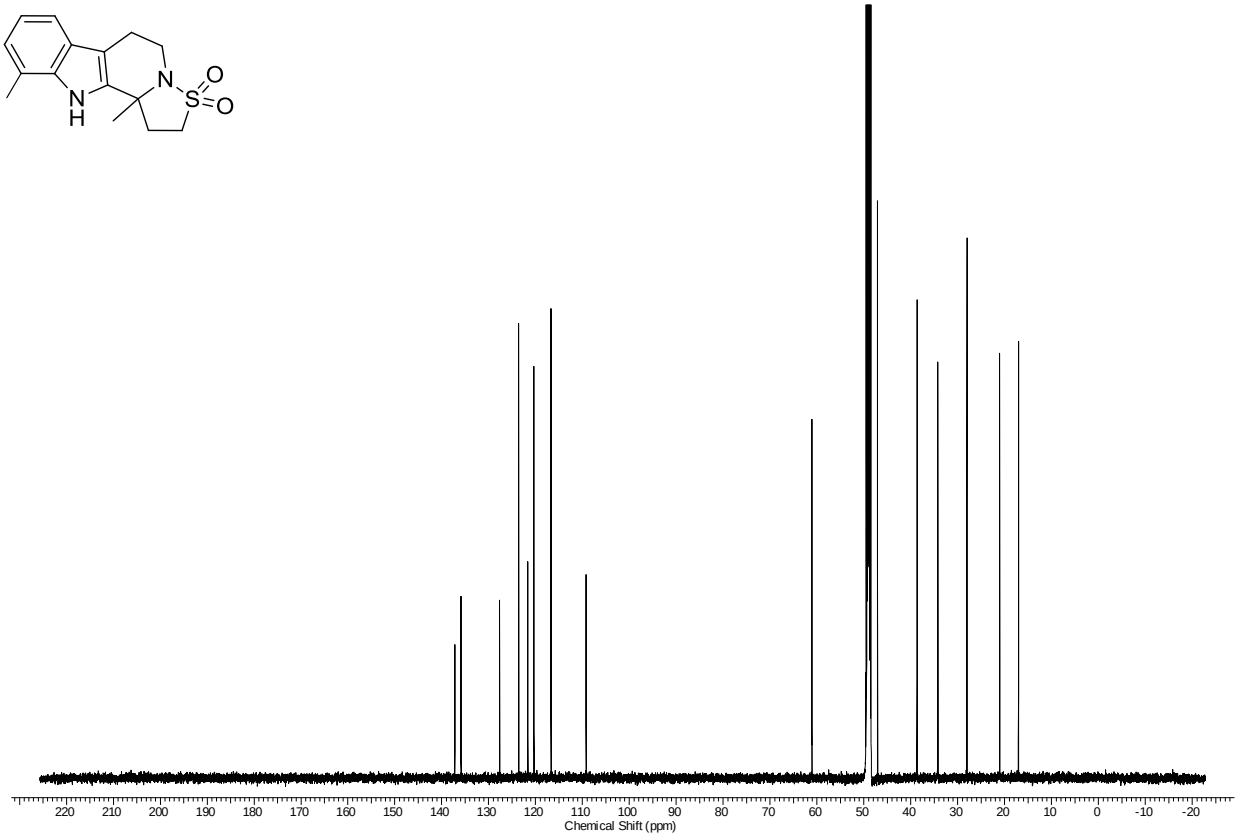
3.2.2.[13]**CNMR spectra for 8,11b-dimethyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6i**



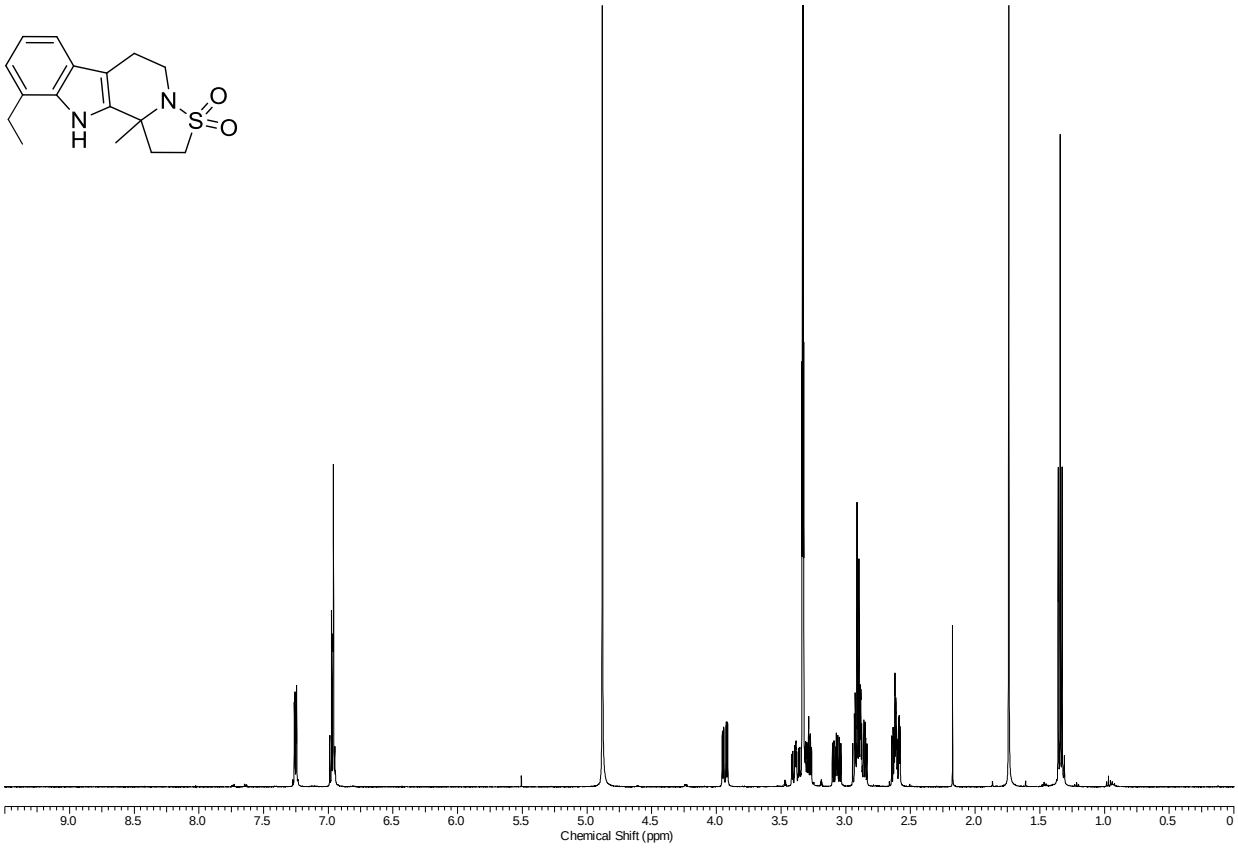
3.2.3. ^{1}HNMR spectra for 10,11b-dimethyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6j



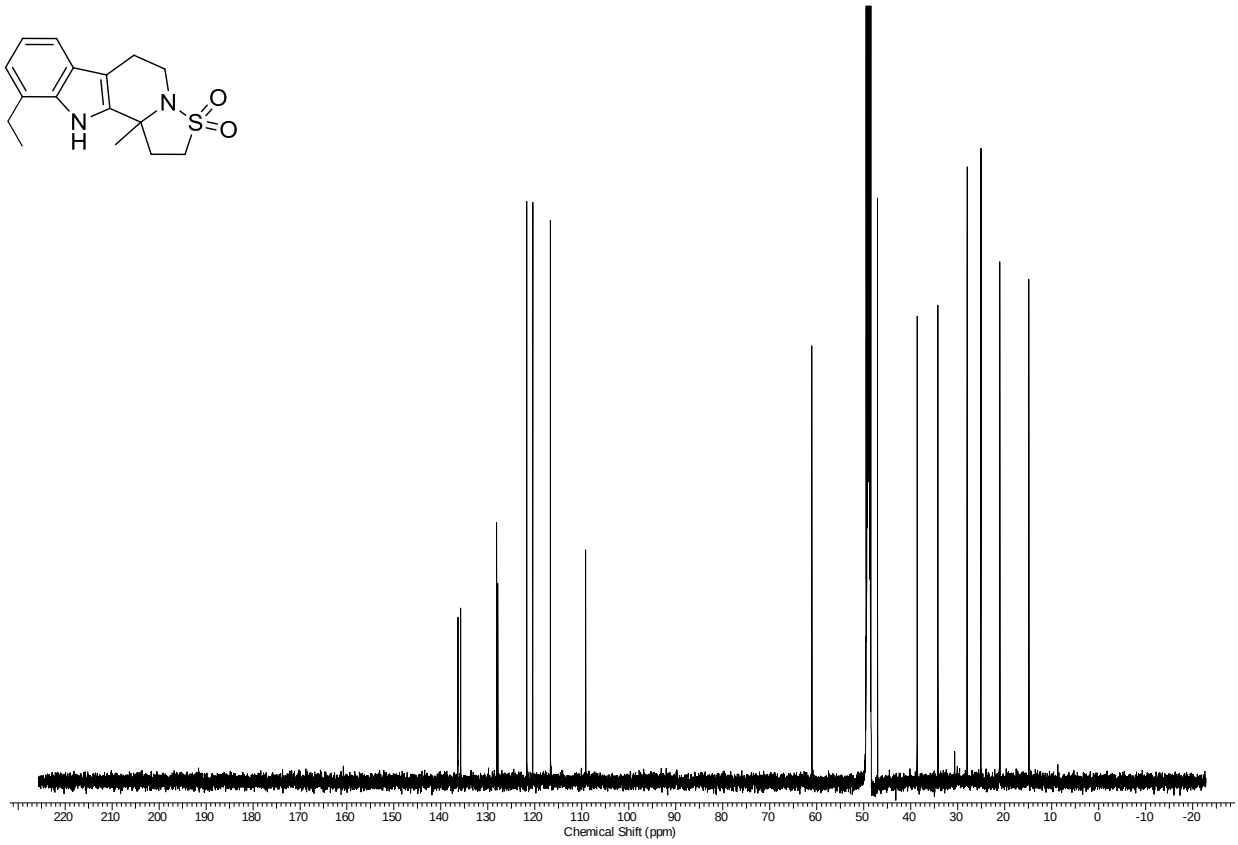
3.2.4. ^{13}CNMR spectra for 10,11b-dimethyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6j



3.2.5.[1]HNMR spectra for 10-ethyl-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6k

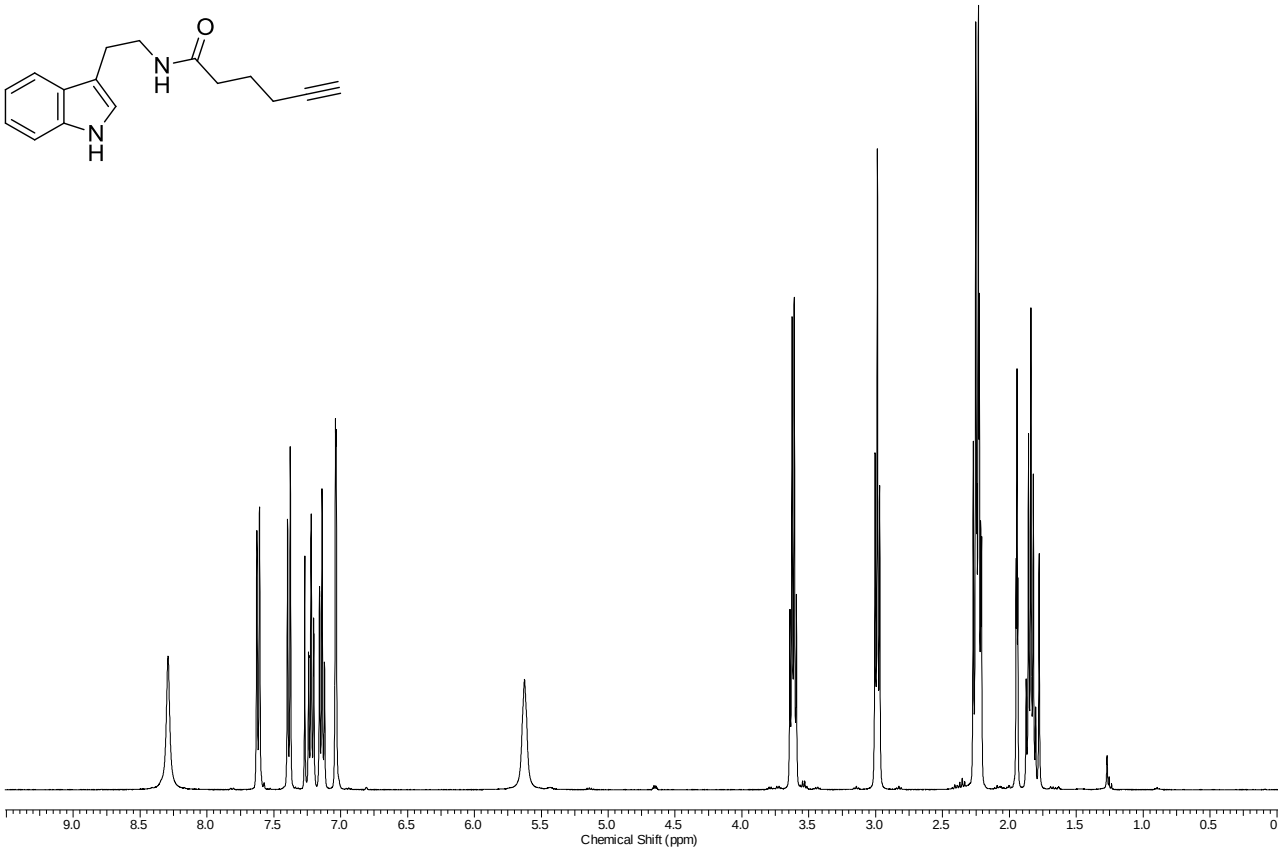


3.2.6.[13]CNMR spectra for 10-ethyl-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6k

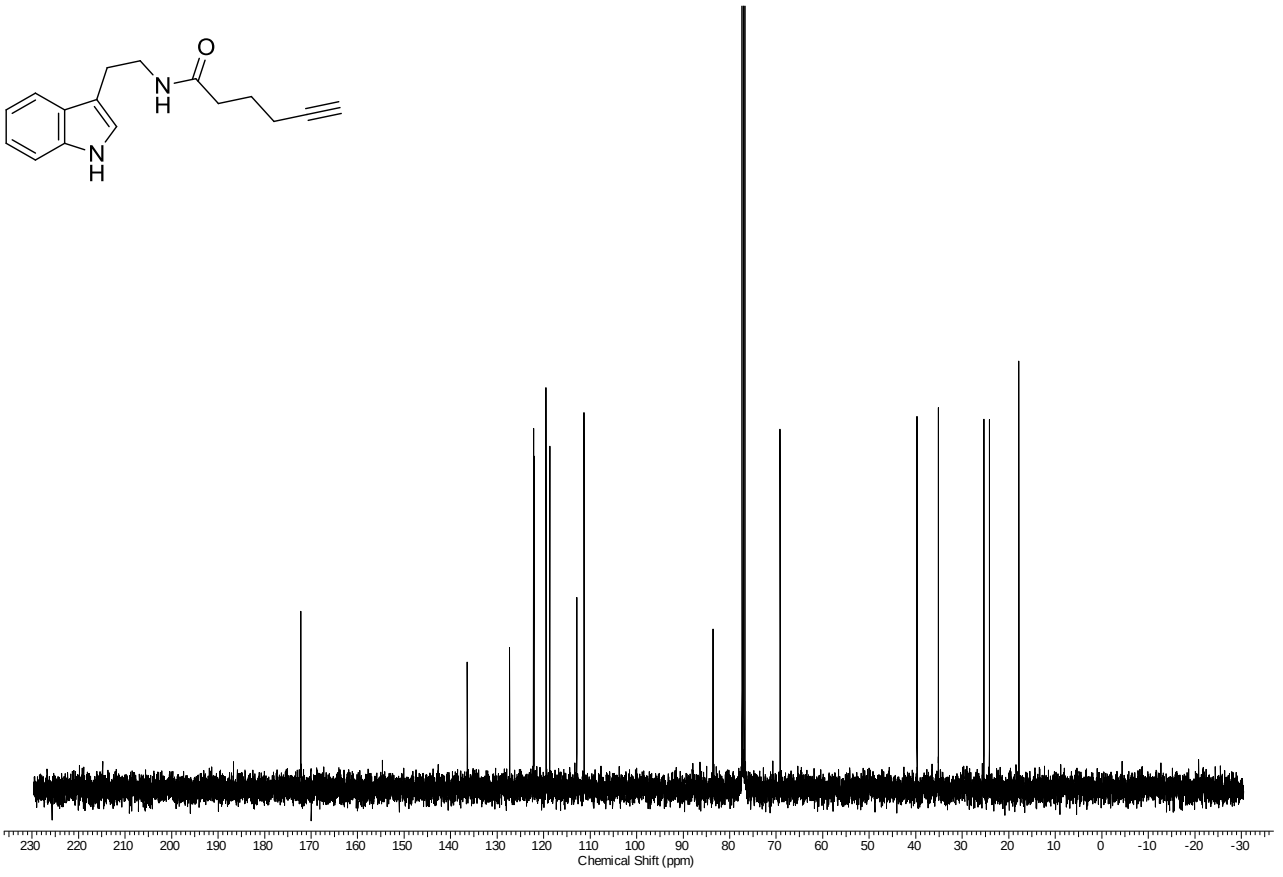


3.3. Amide starting material

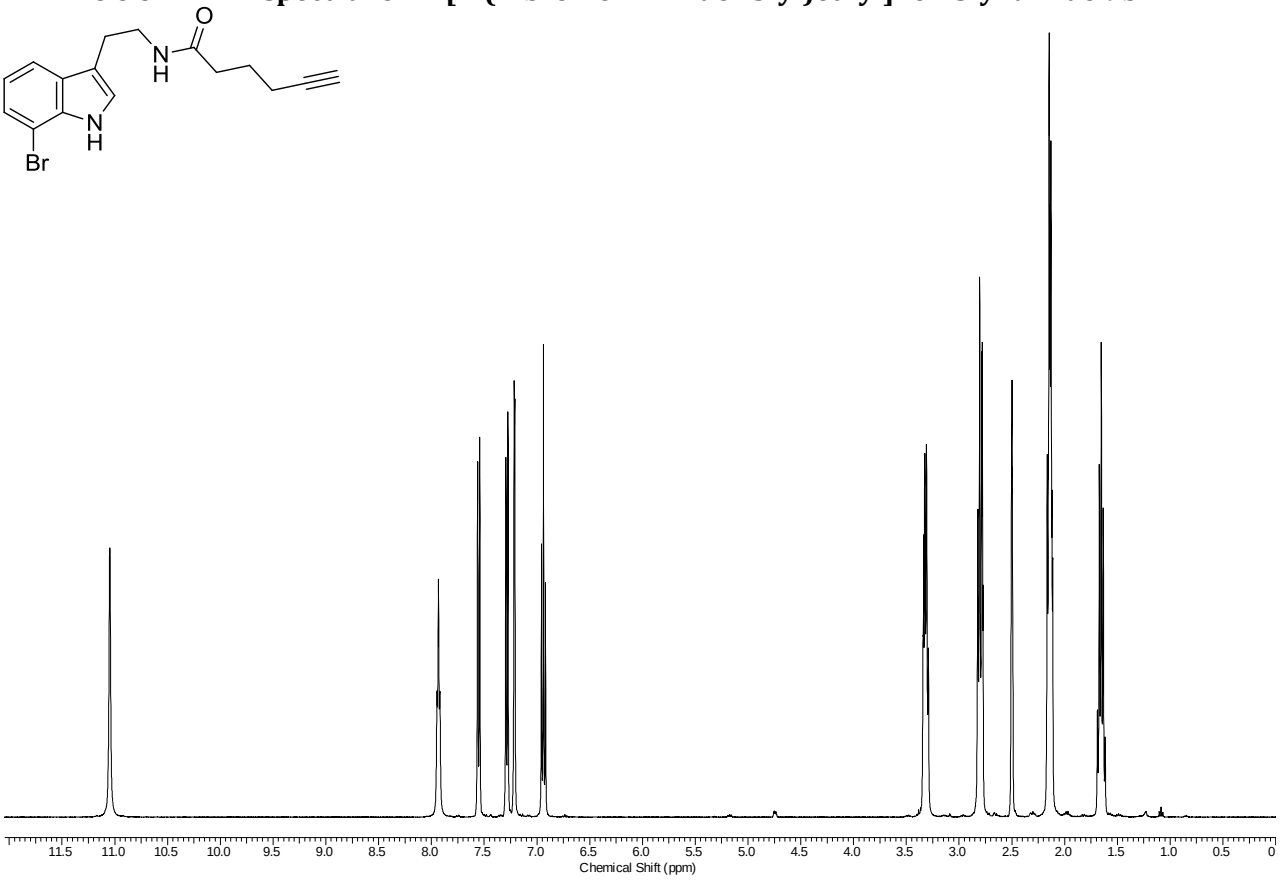
3.3.1. ^{1}HNMR spectra for *N*-[2-(1*H*-indol-3-yl)ethyl]hex-5-ynamide 9a



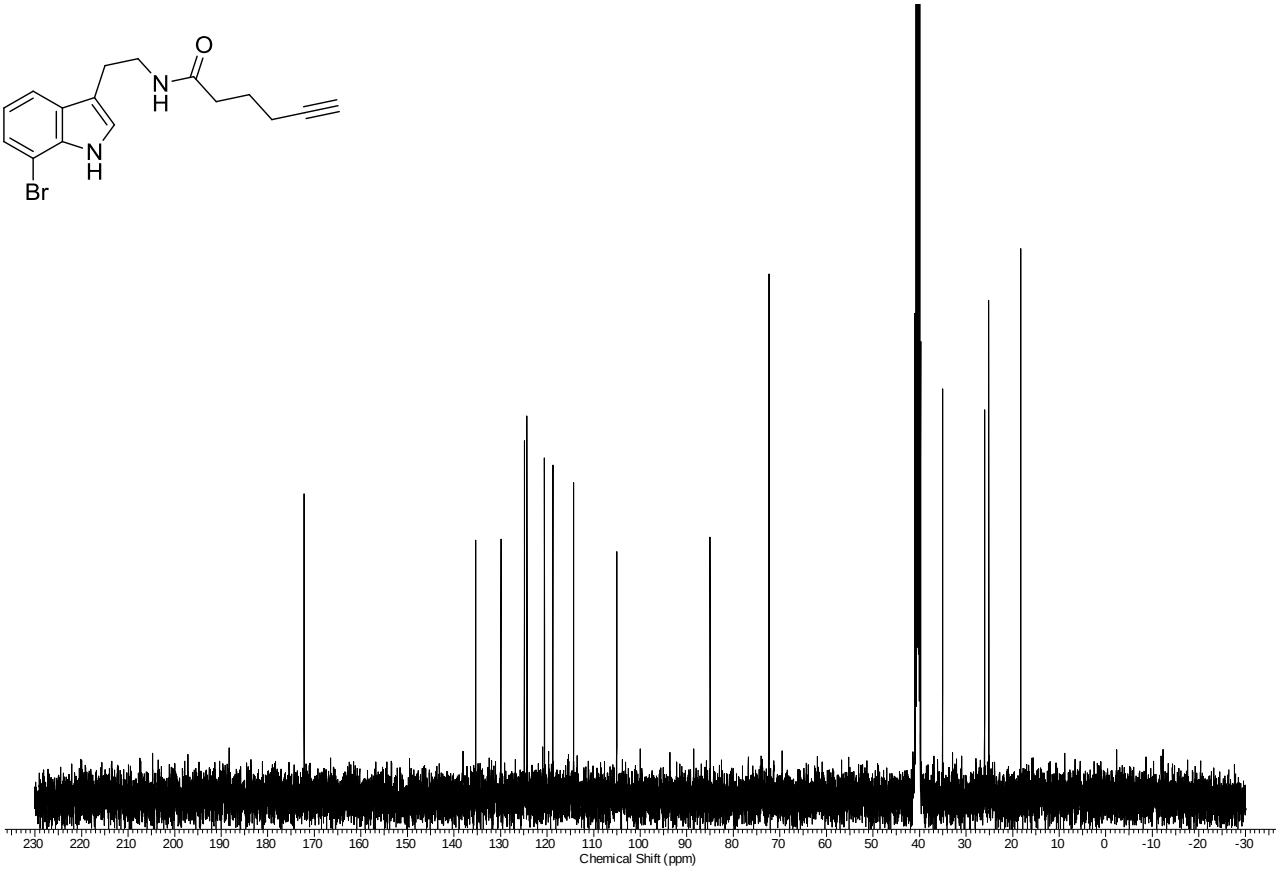
3.3.2. ^{13}CNMR spectra for *N*-[2-(1*H*-indol-3-yl)ethyl]hex-5-ynamide 9a



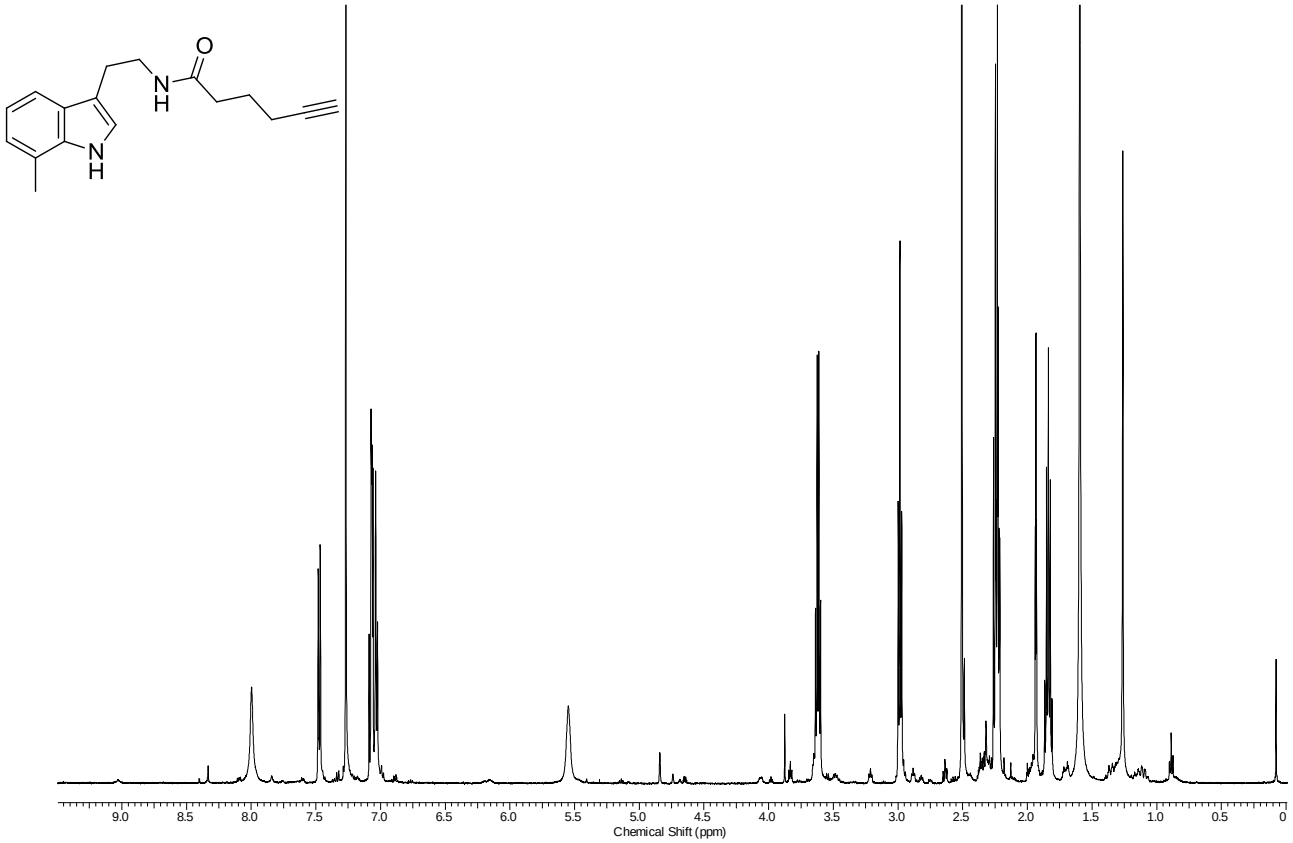
3.3.3. ^{1}HNMR spectra for *N*-[2-(7-bromo-1*H*-indol-3-yl)ethyl]hex-5-ynamide 9b



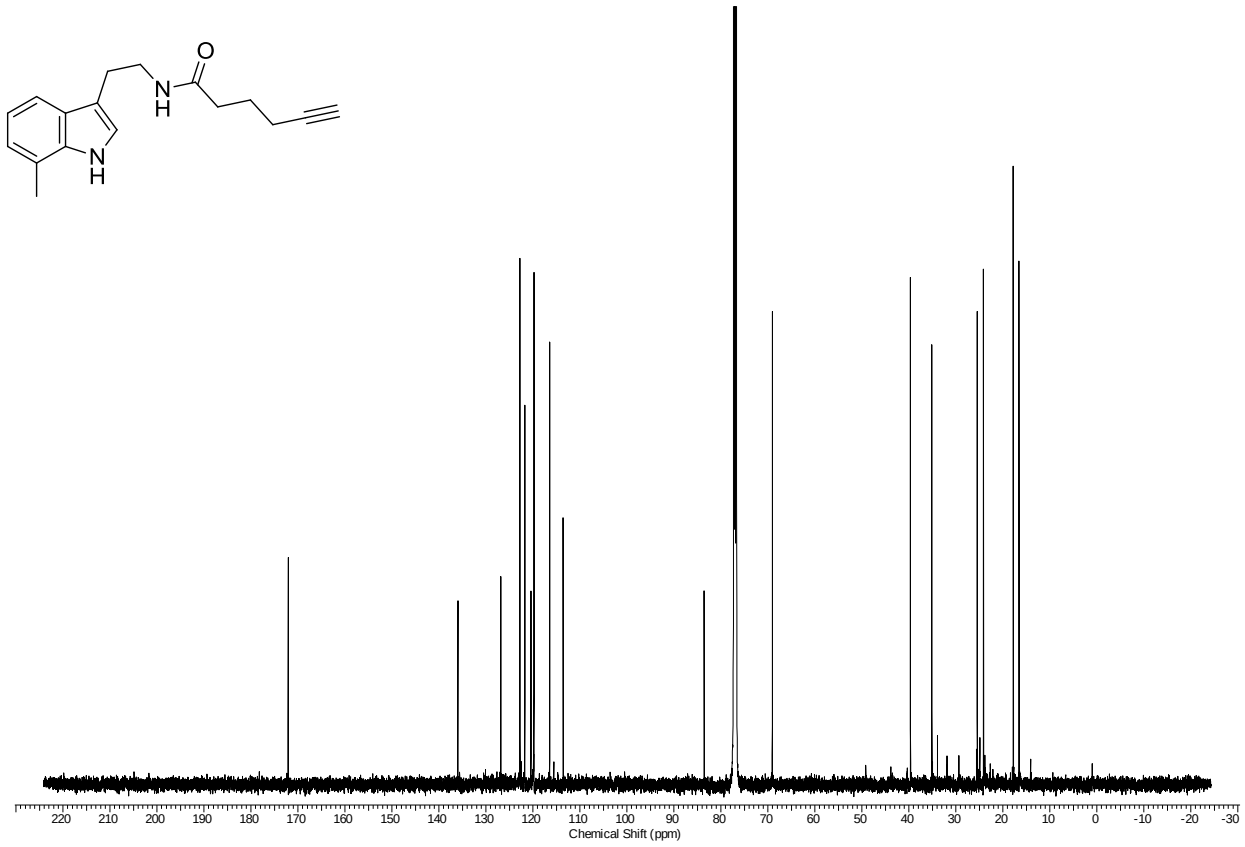
3.3.4. ^{13}CNMR spectra for *N*-[2-(7-bromo-1*H*-indol-3-yl)ethyl]hex-5-ynamide 9b



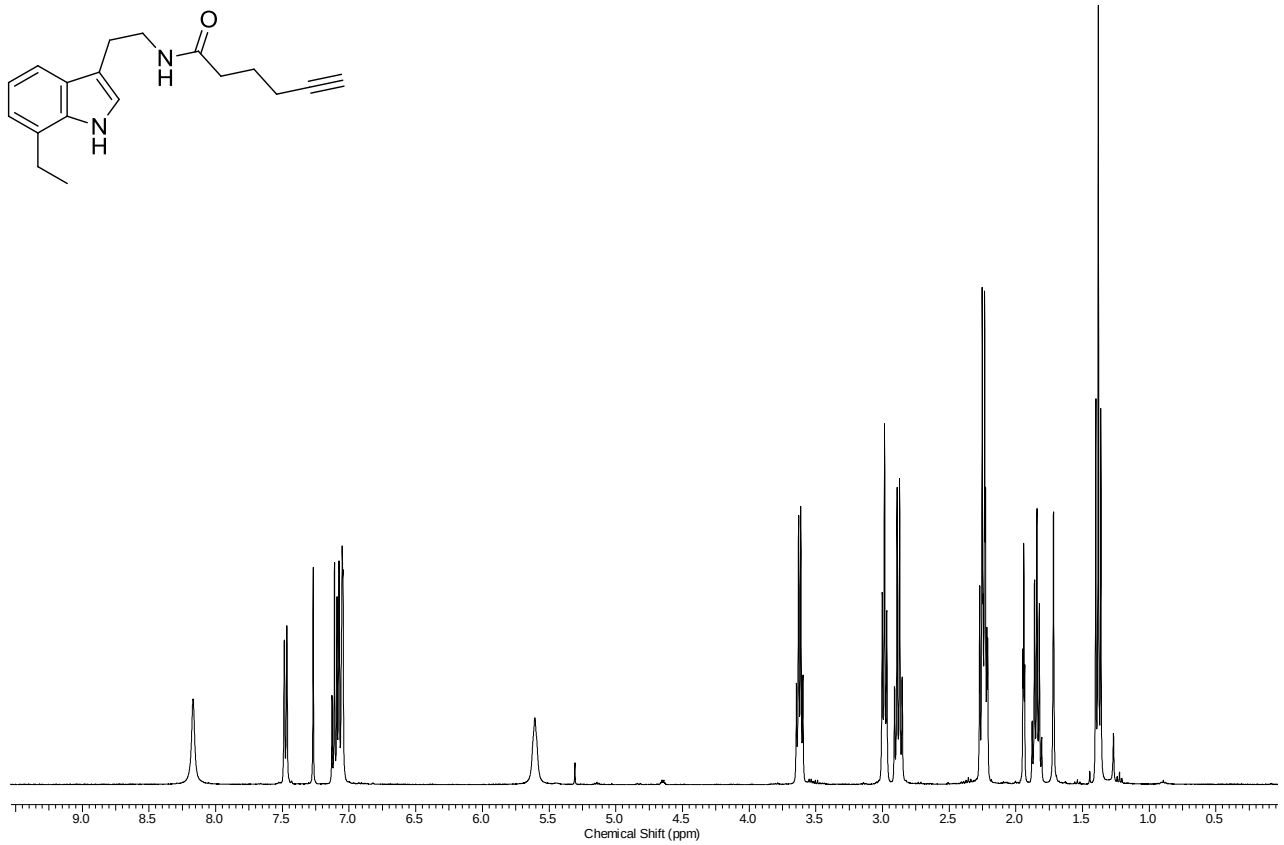
3.3.5.[1]HNMR spectra for *N*-[2-(7-methyl-1*H*-indol-3-yl)ethyl]hex-5-ynamide 9c



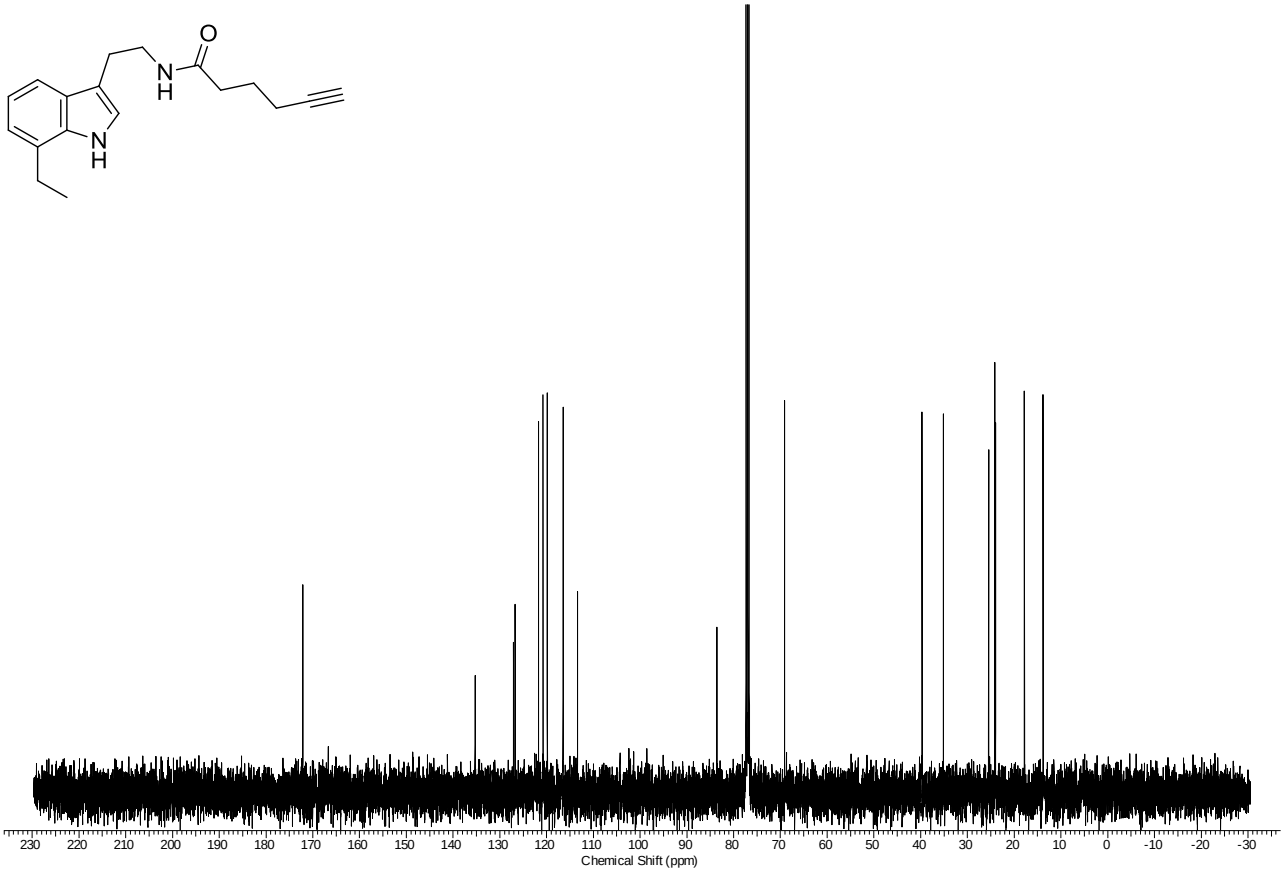
3.3.6.[13]CNMR spectra for *N*-[2-(7-methyl-1*H*-indol-3-yl)ethyl]hex-5-ynamide 9c



3.3.7.^{1}HNMR spectra for *N*-[2-(7-ethyl-1*H*-indol-3-yl)ethyl]hex-5-ynamide 9d

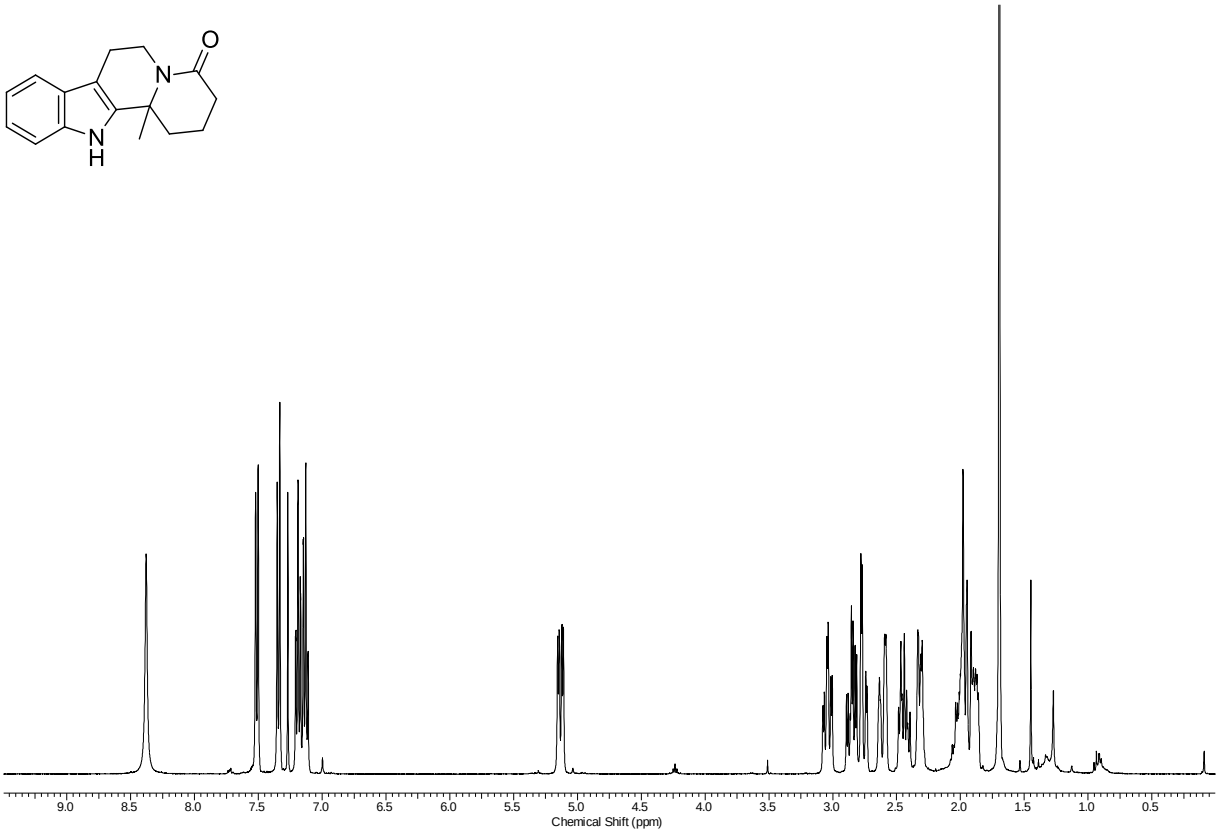


3.3.8.^{13}CNMR spectra for *N*-[2-(7-ethyl-1*H*-indol-3-yl)ethyl]hex-5-ynamide 9d

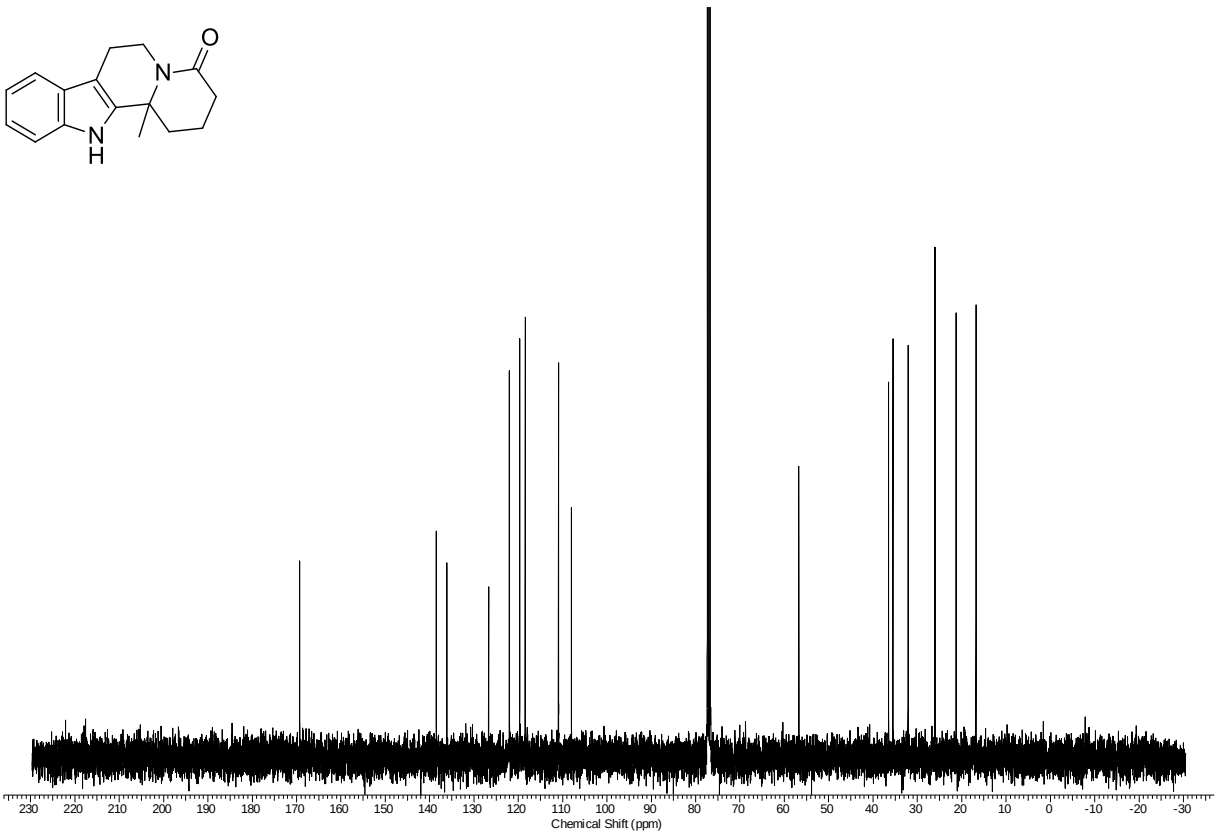


3.4. Amide cyclization products

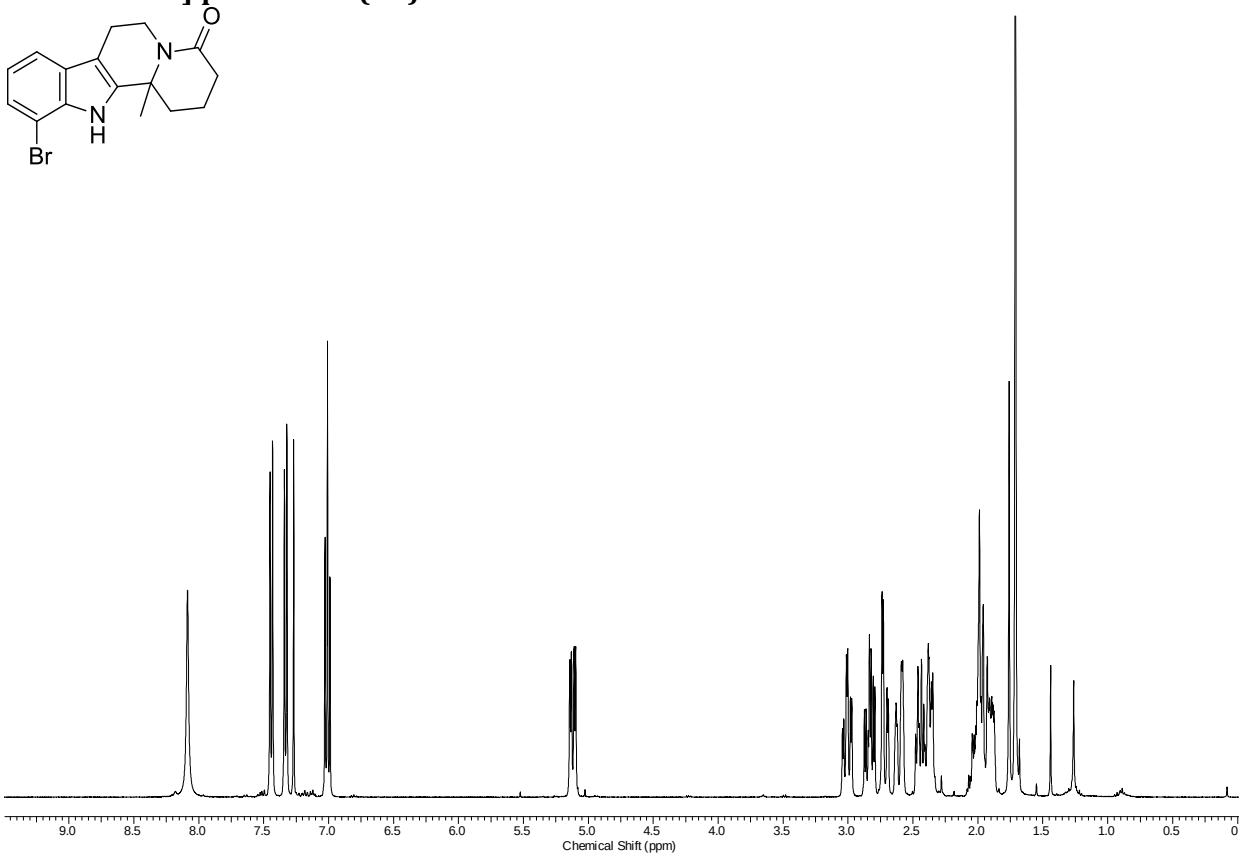
3.4.1. **1HNMR spectra for 12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-a]quinolizin-4(1H)-one 10a**



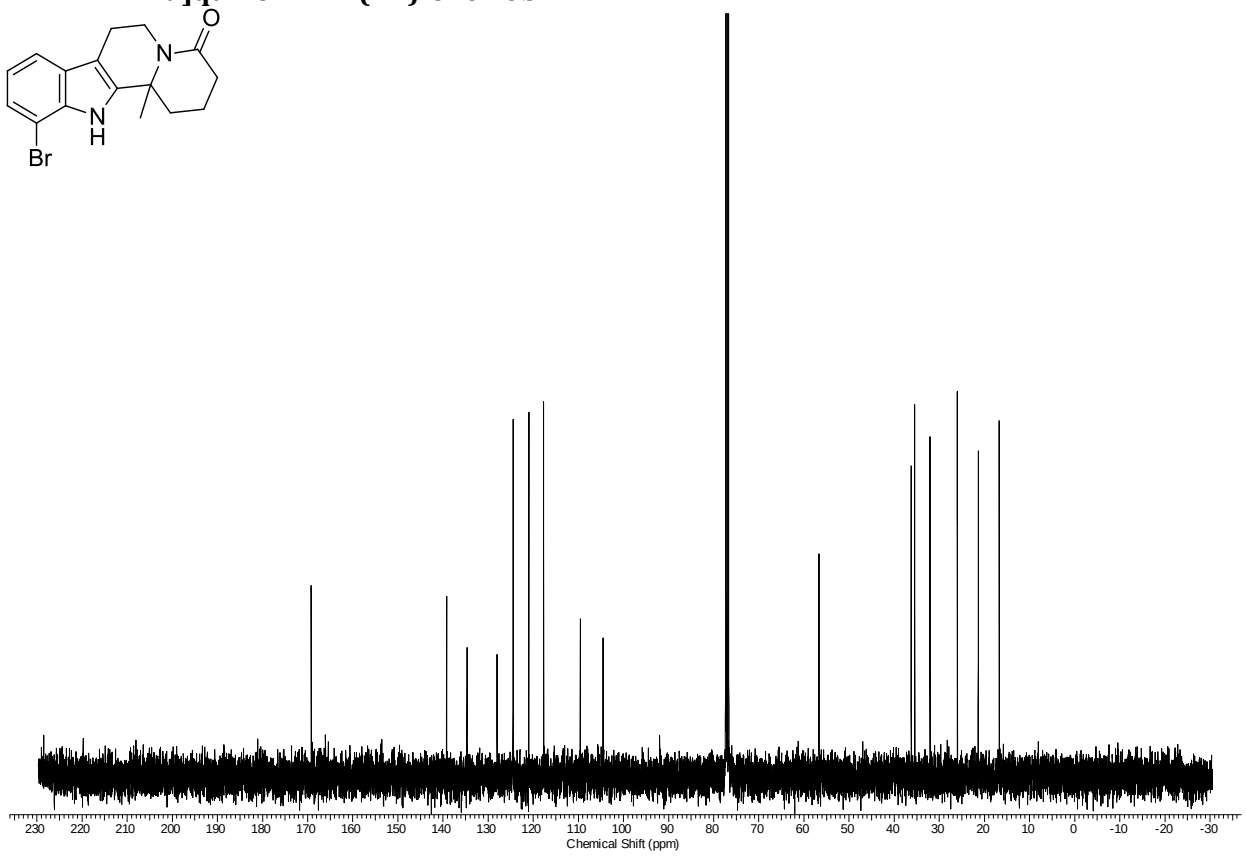
3.4.2. **^{13}CNMR spectra for 12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10a**



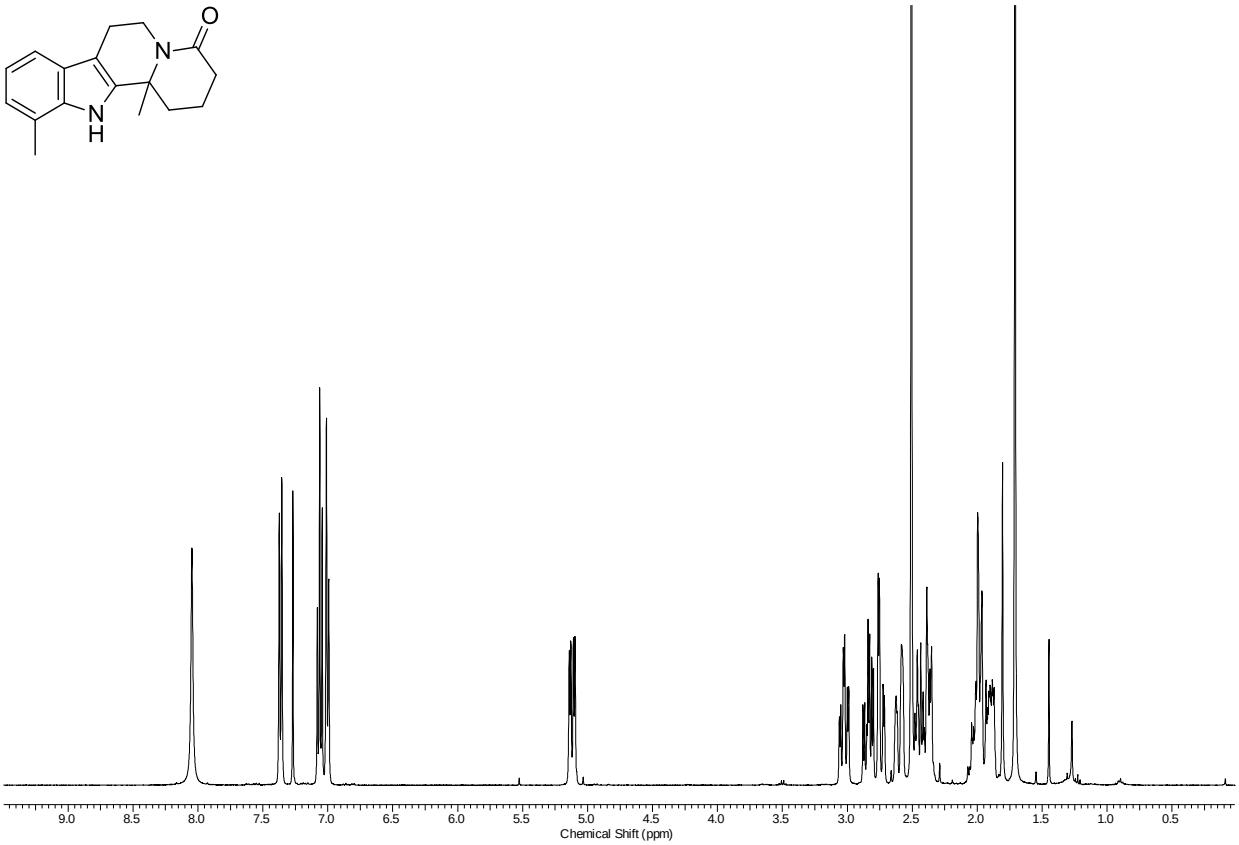
3.4.3.^{1}**HNMR spectra for 11-bromo-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10b**



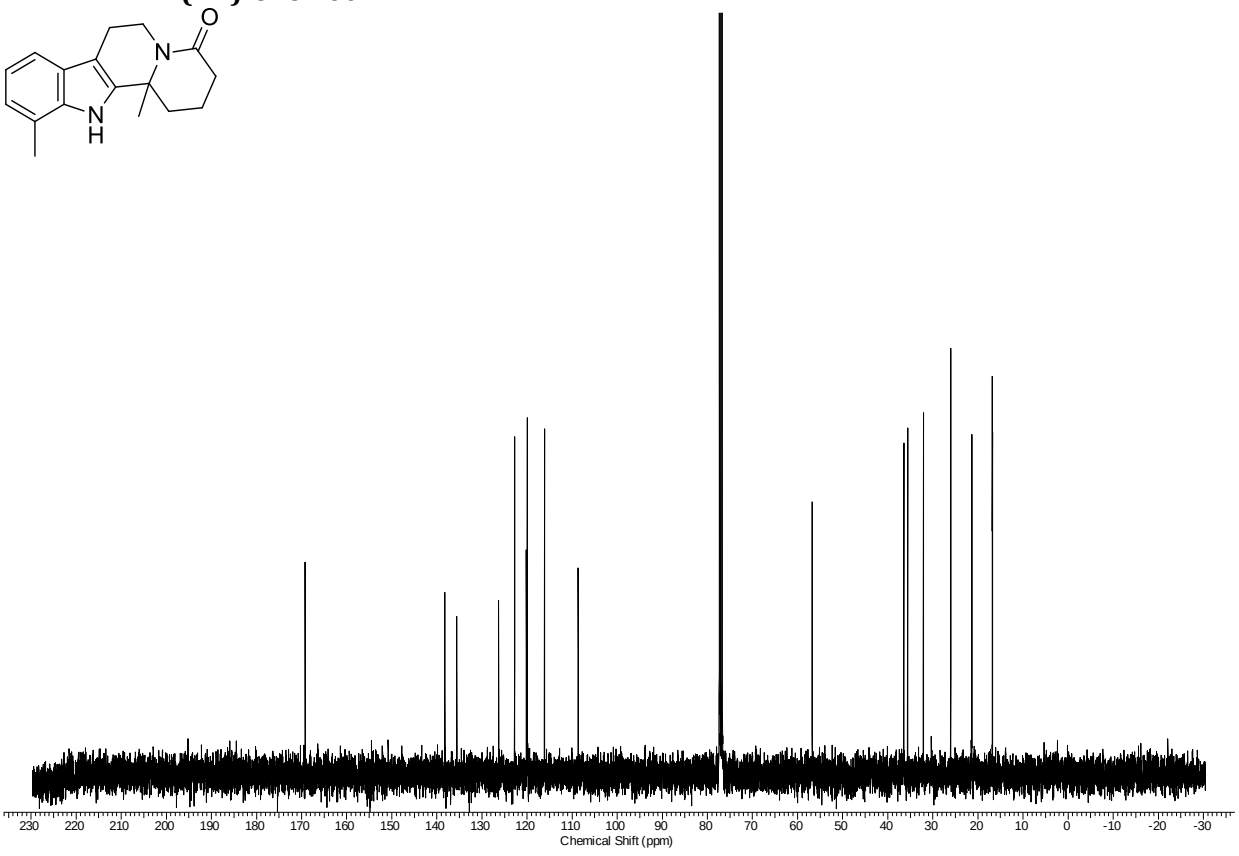
3.4.4.^{13}**CNMR spectra for 11-bromo-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10b**



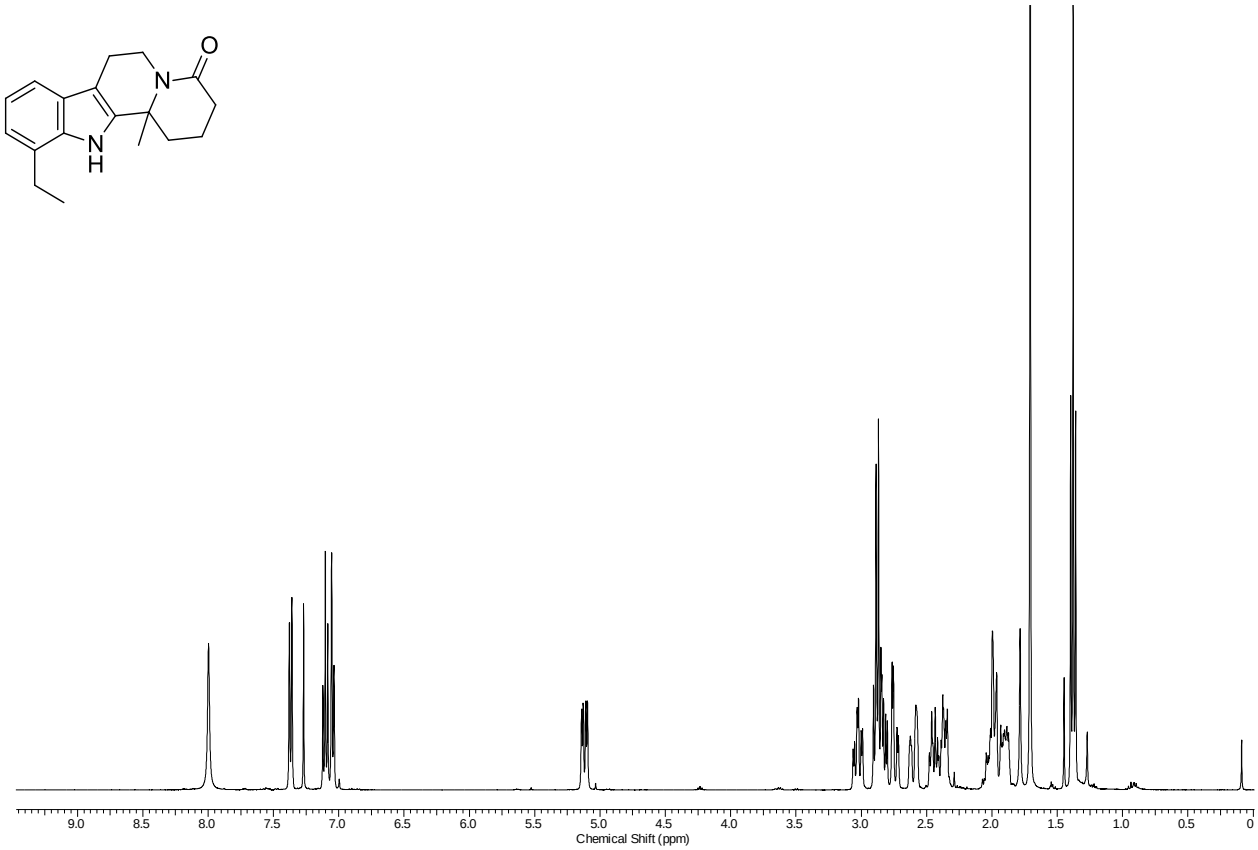
3.4.5.**^{1}HNMR spectra for 11,12b-dimethyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10c**



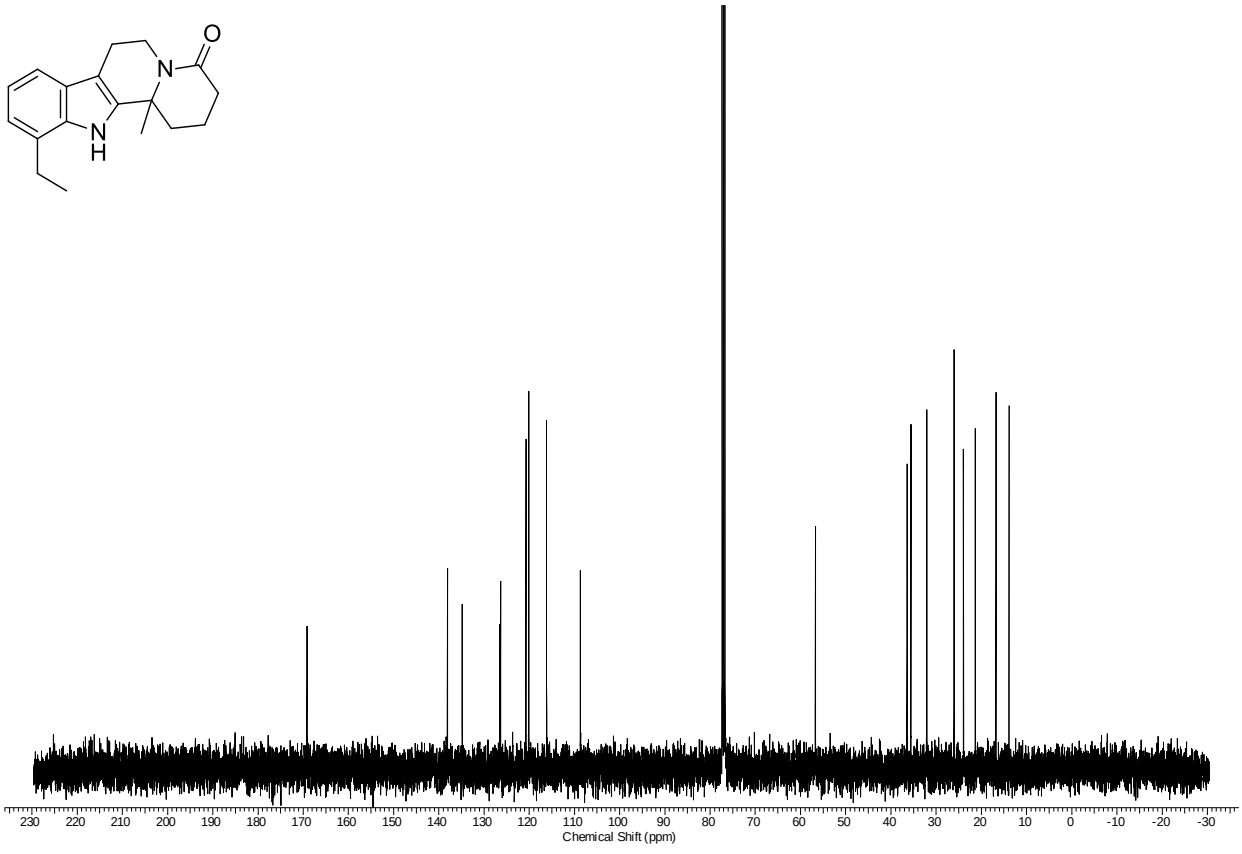
3.4.6.**^{13}CNMR spectra for 11,12b-dimethyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10c**



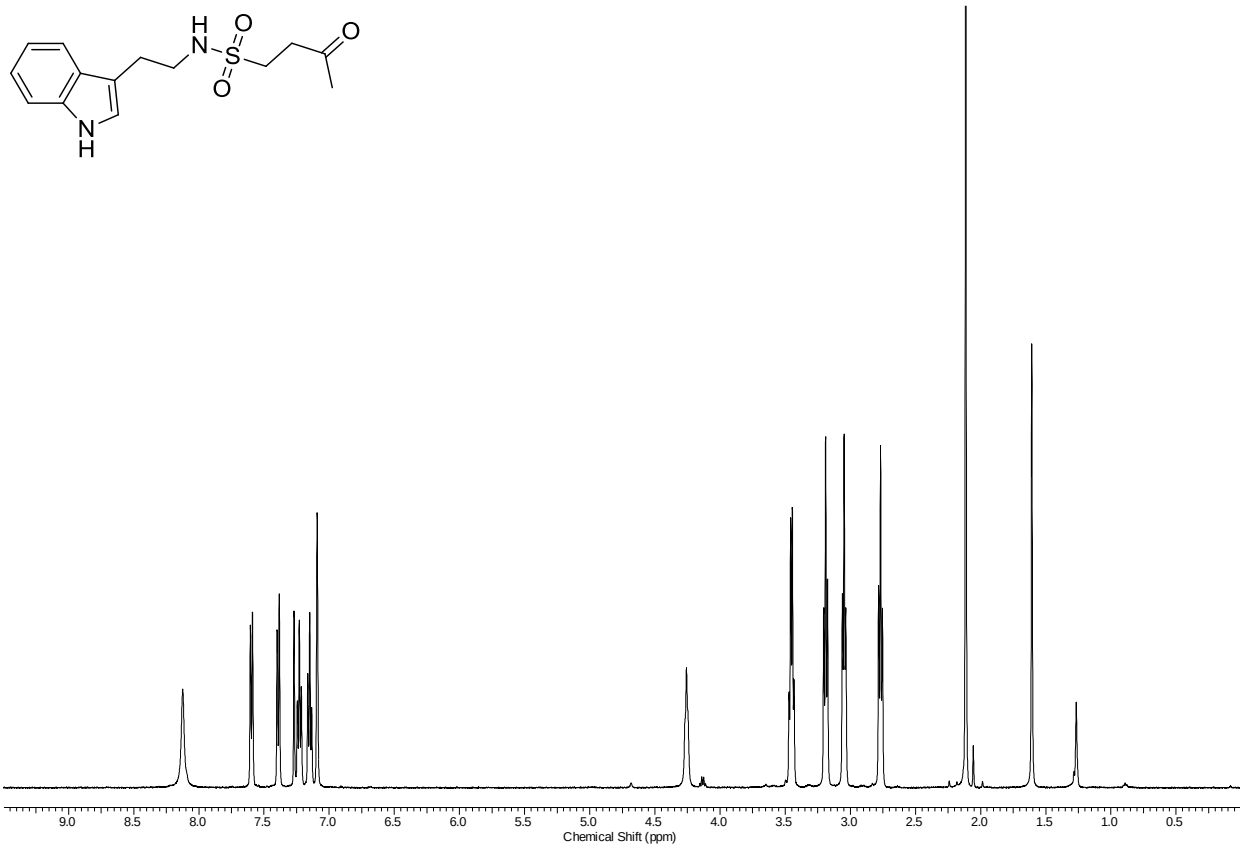
3.4.7.[1]**HNMR spectra for 11-ethyl-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10d**



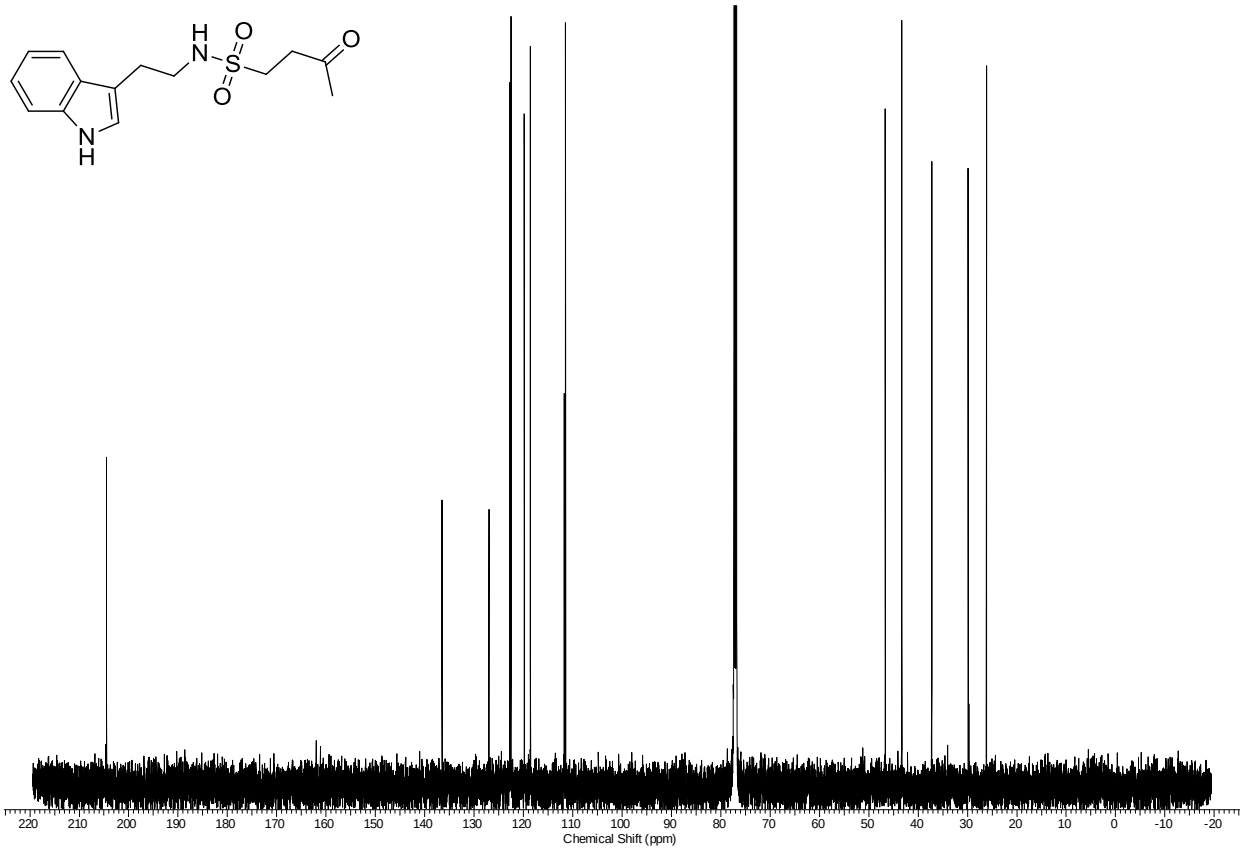
3.4.8.[13]**CNMR spectra for 11-ethyl-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10d**



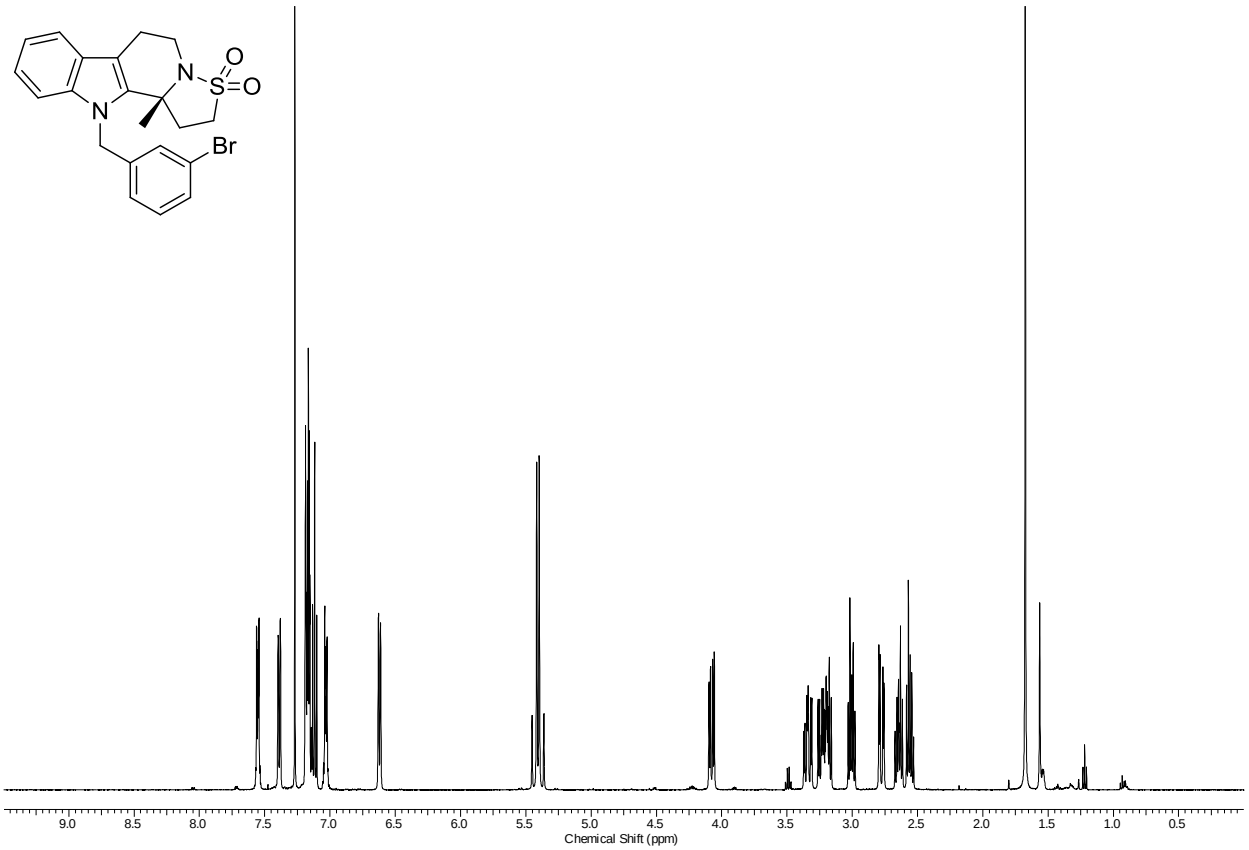
3.4.9.**^{1}HNMR spectra for *N*-[2-(1H-indole-3-yl)ethyl]-3-oxobutane-1-sulfonamide 14**



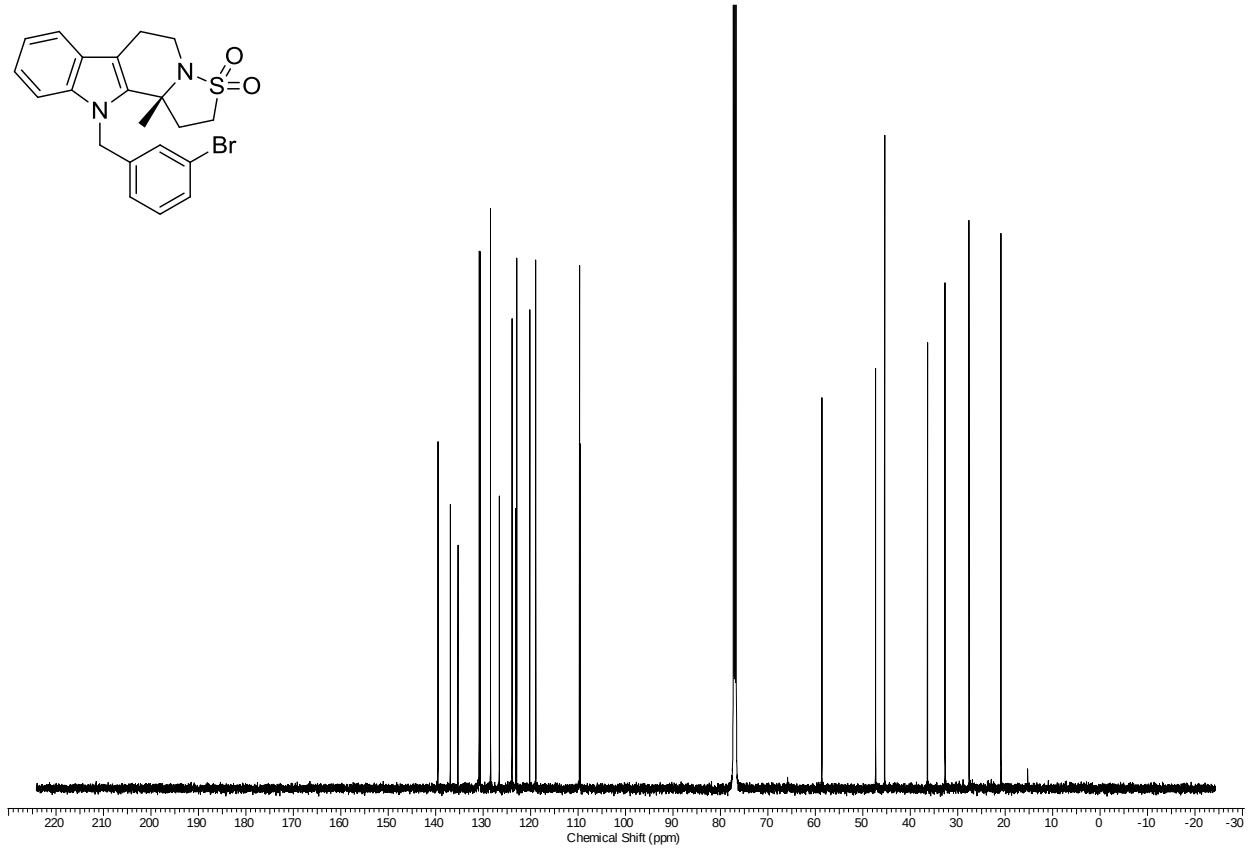
3.4.10. **^{13}CNMR spectra for *N*-[2-(1H-indole-3-yl)ethyl]-3-oxobutane-1-sulfonamide 14**



3.4.11. **1HNMR spectra for 11-(3-bromobenzyl)-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 15a**



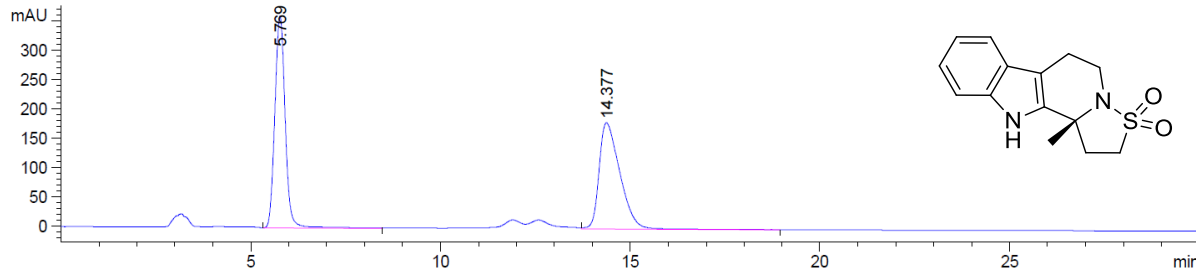
3.4.12. **^{1}HNMR spectra for 11-(3-bromobenzyl)-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 15a**



4. HPLC reports

4.1. Sulfonamide cyclization products

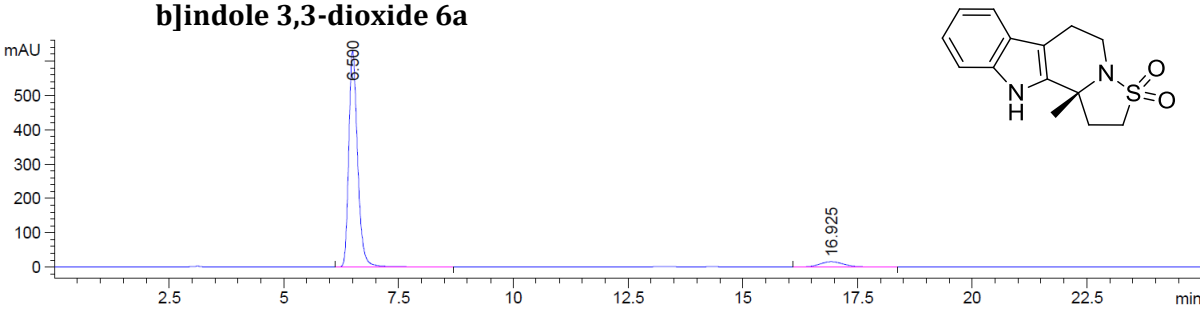
4.1.1. HPLC trace of racemic 11b-methyl-1,2,5,6,11,11b-hexahydroisothiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 6a



Signal 2: DAD1 B, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.769	VV	0.2996	6929.40234	361.55801	49.9763
2	14.377	VB	0.5818	6935.96973	181.50195	50.0237
Totals :				1.38654e4	543.05997	

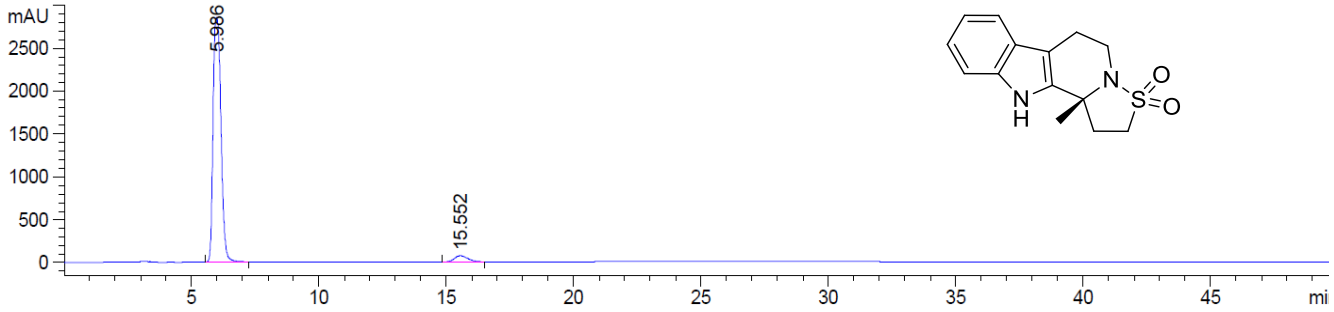
4.1.2. HPLC trace of 11b-methyl-1,2,5,6,11,11b-hexahydroisothiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 6a



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.500	BB	0.2088	8450.49805	628.89789	93.7254
2	16.925	BB	0.5624	565.73688	15.62640	6.2746
Totals :				9016.23492	644.52429	

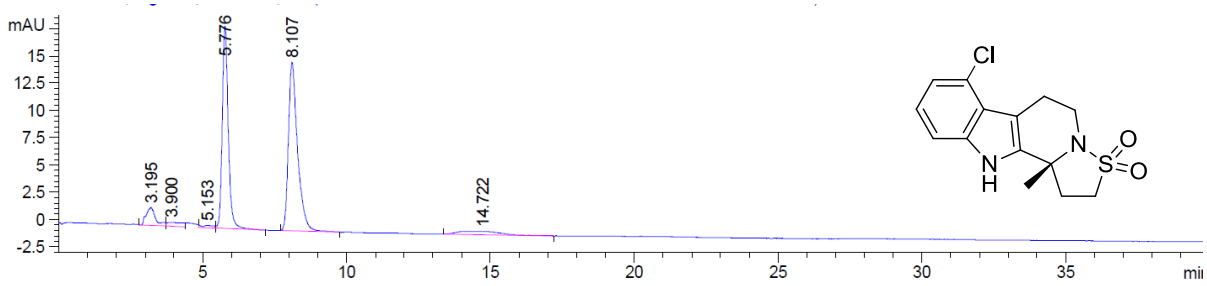
4.1.3. **HPLC trace of 11b-methyl-1,2,5,6,11,11b-hexahydroisothiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide fom ketone starting material 6a**



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.986	BB	0.3429	6.13641e4	2853.56030	95.9480
2	15.552	BB	0.5588	2591.48804	71.51179	4.0520
Totals :				6.39556e4	2925.07209	

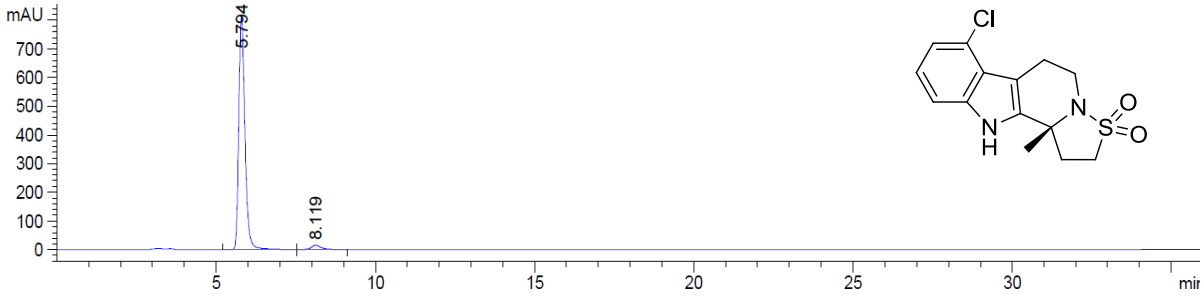
4.1.4.HPLC trace of Racemic 7-chloro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6b



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.776	VV	0.2205	1610.56543	111.51776	44.0052
2	8.106	VV	0.3295	2049.37549	92.85419	55.9948
Totals :				3659.94092	204.37196	

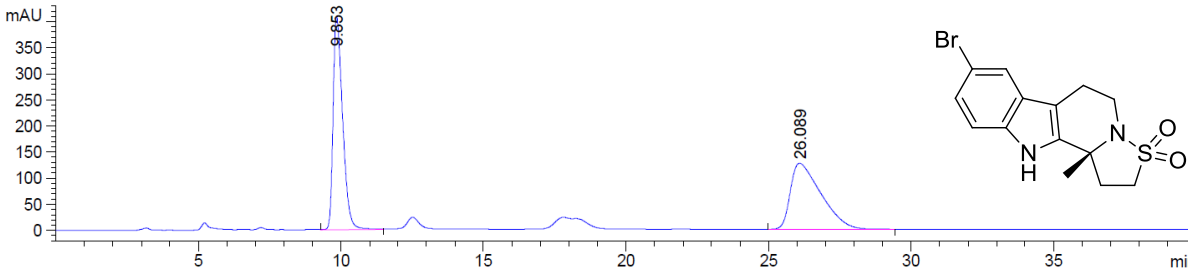
4.1.5.HPLC trace of 7-chloro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6b



Signal 2: DAD1 B, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.792	BB	0.2062	1.09271e4	816.11572	97.4035
2	8.118	BB	0.3032	291.29129	14.32851	2.5965
Totals :				1.12184e4	830.44423	

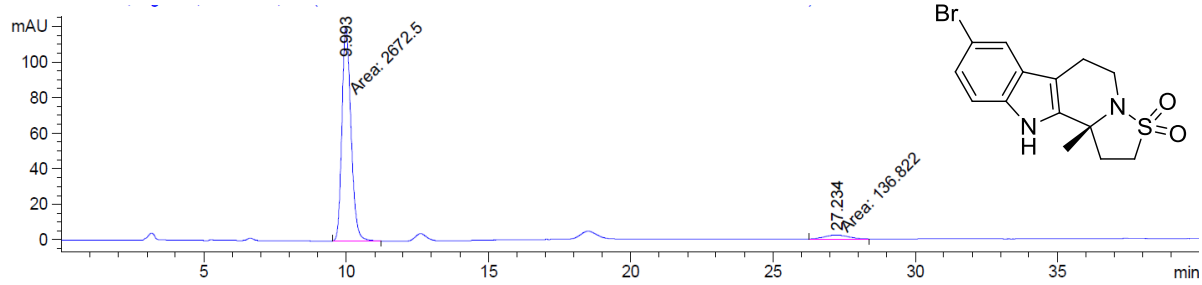
4.1.6. HPLC trace of racemic 8-bromo-11b-methyl-1,2,5,6,11,11b-hexahydroisothiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 6c



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.853	VB	0.3545	9467.04687	408.36649	50.1600
2	26.089	BB	1.1205	9406.65527	126.36646	49.8400
Totals :				1.88737e4	534.73294	

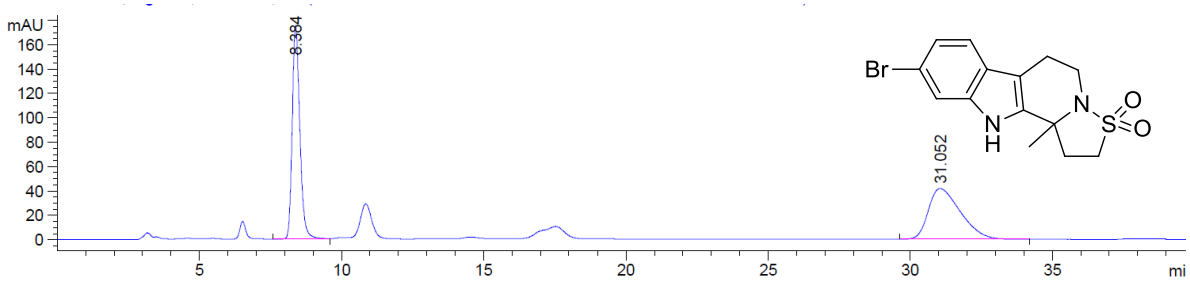
4.1.7. HPLC trace 8-bromo-11b-methyl-1,2,5,6,11,11b-hexahydroisothiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 6c



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.993	MM	0.3699	2672.50220	120.41589	95.1297
2	27.234	MM	1.0019	136.82187	2.27602	4.8703
Totals :				2809.32407	122.69190	

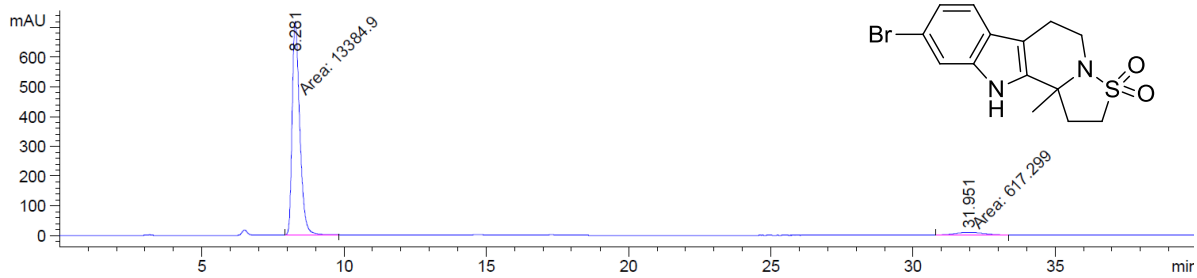
4.1.8. HPLC trace of Racemic 9-bromo-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6d



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.384	BV	0.2880	3306.75732	175.39285	50.2104
2	31.052	BB	1.1967	3279.05029	41.73261	49.7896
Totals :				6585.80762	217.12546	

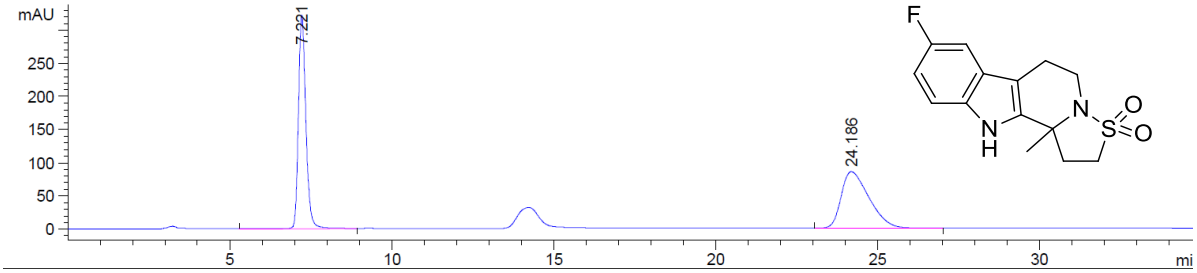
4.1.9. HPLC trace of 9-bromo-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6d



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.281	MM	0.3102	1.33849e4	719.05499	95.5914
2	31.951	MM	1.1629	617.29950	8.84681	4.4086
Totals :				1.40022e4	727.90180	

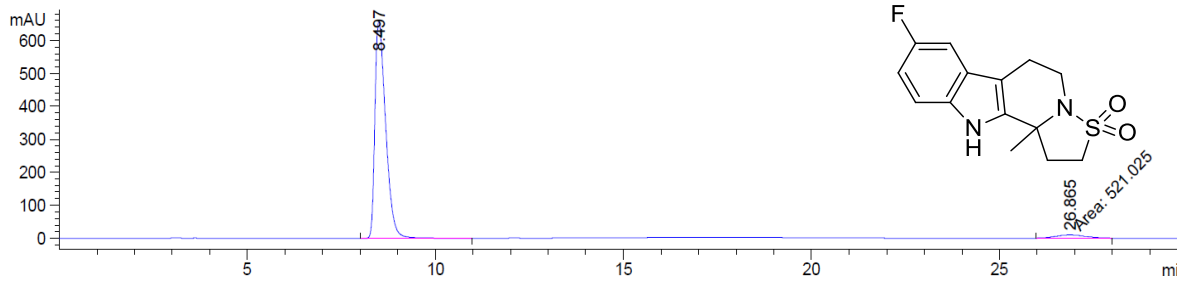
4.1.10. **HPLC trace of Racemic 8-fluoro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6e**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.221	VV	0.2477	5179.71240	321.97113	50.4178
2	24.186	BB	0.9163	5093.87256	85.34870	49.5822
Totals :				1.02736e4	407.31983	

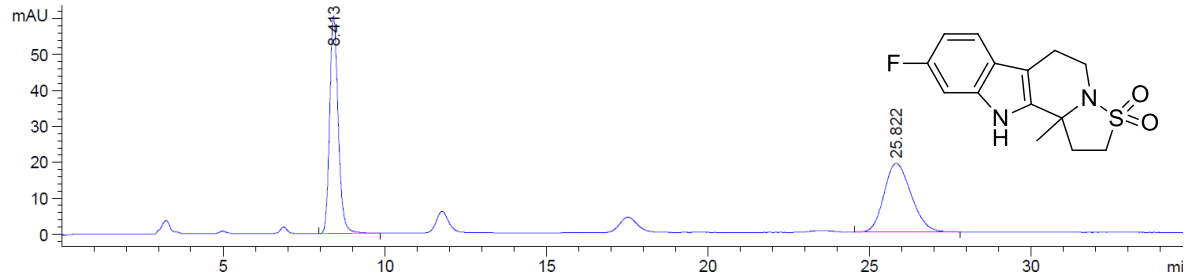
4.1.11. **HPLC trace of 8-fluoro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6e**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.497	VB	0.3021	1.30236e4	660.19110	96.1533
2	26.865	MM	0.9136	521.02521	9.50467	3.8467
Totals :				1.35446e4	669.69577	

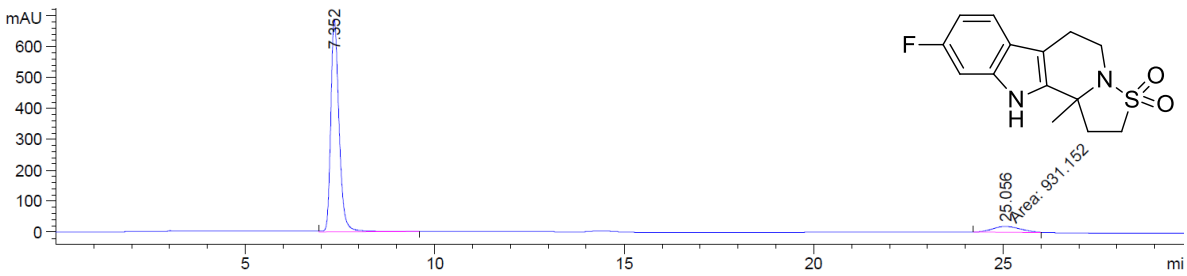
4.1.12. **HPLC trace of Racemic 9-fluoro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6f**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.413	BB	0.2888	1124.35437	60.50667	50.0497
2	25.822	VB	0.9079	1122.12244	19.14278	49.9503
Totals :				2246.47681	79.64946	

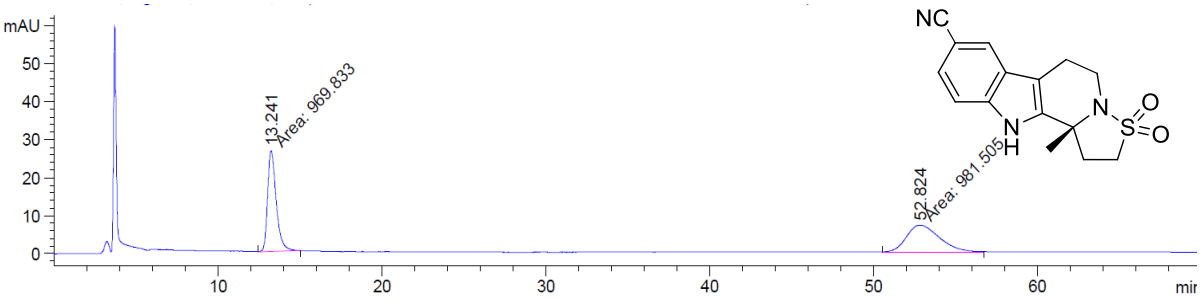
4.1.13. **HPLC trace of 9-fluoro-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6f**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.352	VB	0.2388	1.05252e4	686.87543	91.8722
2	25.056	MM	0.8457	931.15240	18.35109	8.1278
Totals :				1.14564e4	705.22652	

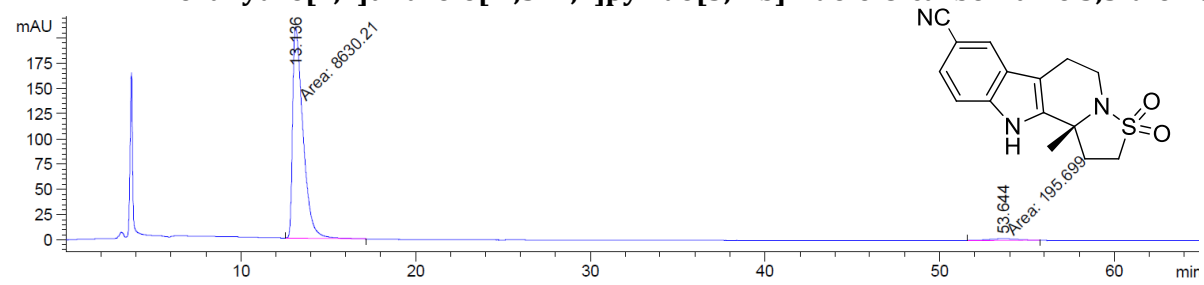
4.1.14. **HPLC trace of Racemic 11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole-8-carbonitrile 3,3-dioxide 6g**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.241	MM	0.6082	969.83325	26.57452	49.7009
2	52.824	MM	2.3171	981.50507	7.05992	50.2991
Totals :				1951.33832	33.63444	

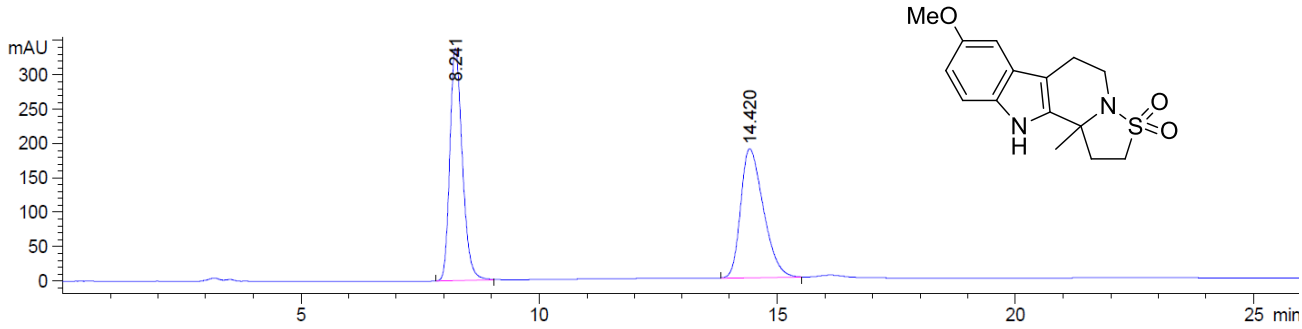
4.1.15. **HPLC trace of 11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole-8-carbonitrile 3,3-dioxide 6g**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.136	MM	0.6861	8630.20508	209.65181	97.7827
2	53.644	MM	2.0044	195.69910	1.62725	2.2173
Totals :				8825.90417	211.27906	

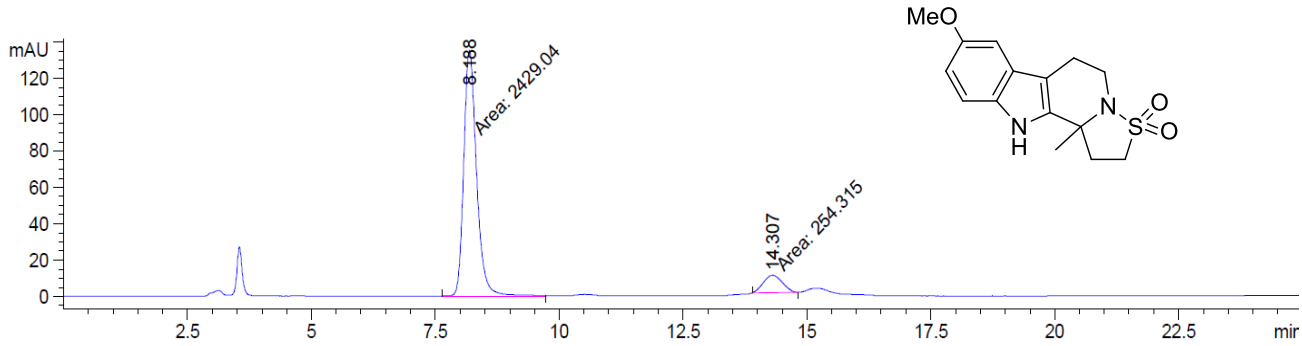
4.1.16. **HPLC trace of 8-methoxy-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 6h**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.241	BB	0.2805	6153.22998	337.82938	49.7137
2	14.420	BB	0.5110	6224.09473	187.62210	50.2863
Totals :				1.23773e4	525.45148	

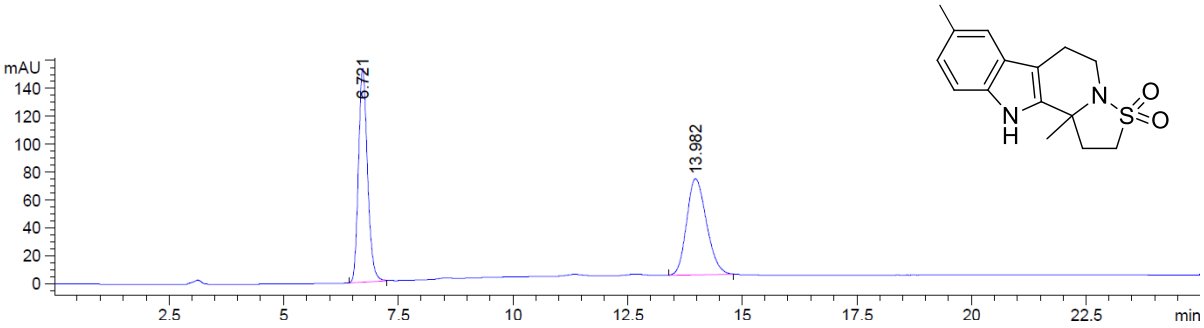
4.1.17. **HPLC trace of 8-methoxy-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 6h**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.188	MM	0.2998	2429.04248	135.01501	90.5225
2	14.307	MM	0.4439	254.31540	9.54864	9.4775
Totals :				2683.35788	144.56366	

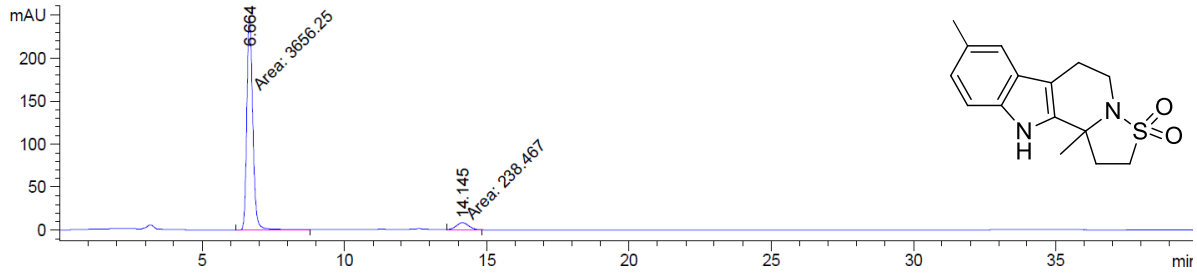
4.1.18. **HPLC trace of Racemic 8,11b-dimethyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6i**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.721	BB	0.2099	2099.92603	153.23482	50.1598
2	13.982	BB	0.4707	2086.54614	69.01322	49.8402
Totals :				4186.47217	222.24804	

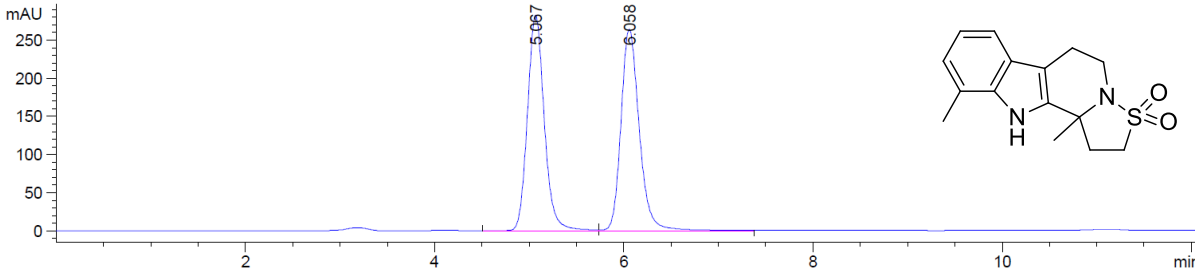
4.1.19. **HPLC trace of 8,11b-dimethyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6i**



Signal 2: DAD1 B, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.664	MM	0.2447	3656.24561	249.06523	93.8772
2	14.145	MM	0.4921	238.46709	8.07716	6.1228
Totals :				3894.71269	257.14240	

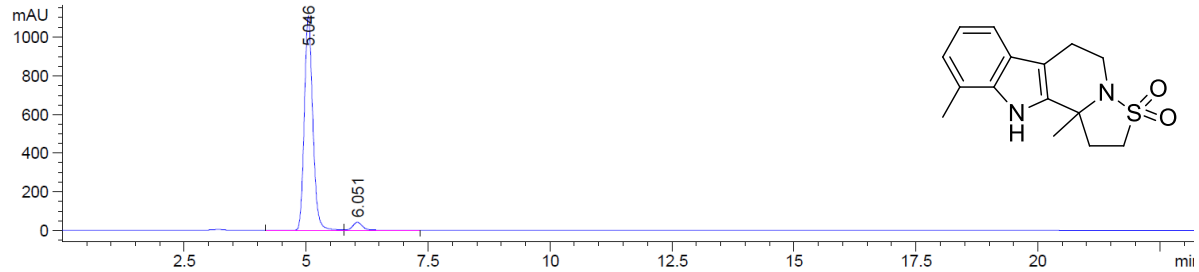
4.1.20. **HPLC trace of Racemic 10,11b-dimethyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6j**



Signal 2: DAD1 B, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.067	VV	0.1930	3511.04712	282.56686	49.6121
2	6.058	VB	0.2096	3565.95630	263.95245	50.3879
Totals :				7077.00342	546.51932	

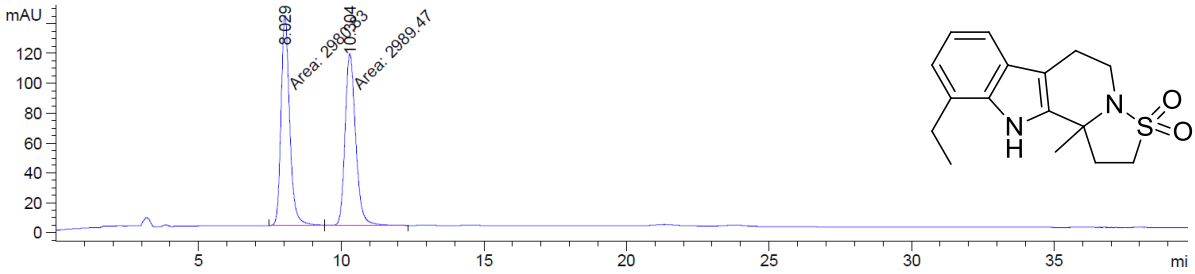
4.1.21. **HPLC trace of 10,11b-dimethyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6j**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.046	BV	0.1894	1.34379e4	1108.46716	95.6662
2	6.051	VB	0.2224	608.75525	41.67521	4.3338
Totals :				1.40466e4	1150.14238	

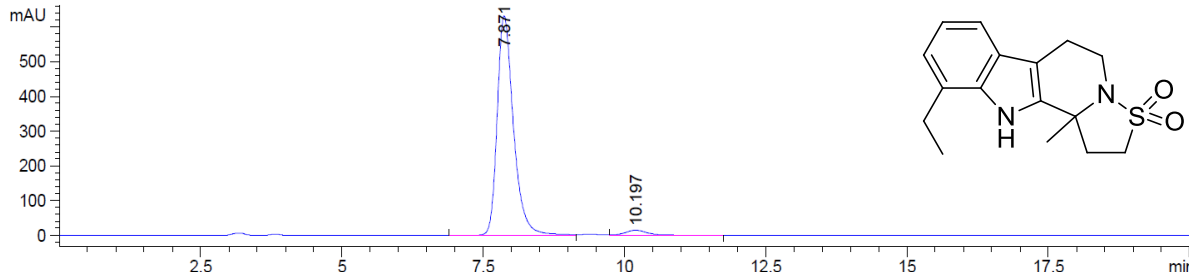
4.1.22. **HPLC trace of Racemic 10-ethyl-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6k**



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.029	MF	0.3528	2980.82861	140.81139	49.9277
2	10.304	FM	0.4335	2989.46655	114.93775	50.0723
Totals :				5970.29517	255.74914	

4.1.23. **HPLC trace of 10-ethyl-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-*b*]indole 3,3-dioxide 6k**

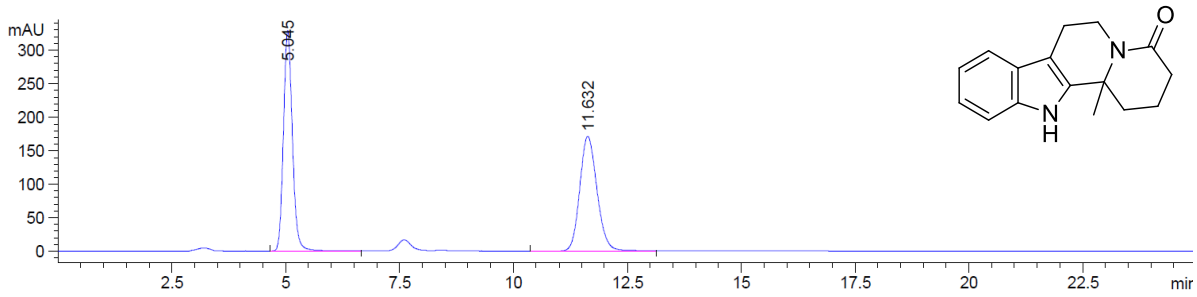


Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.870	BB	0.3043	1.25748e4	631.57336	97.4176
2	10.196	BB	0.3804	333.34106	13.58081	2.5824
Totals :				1.29081e4	645.15418	

Amide

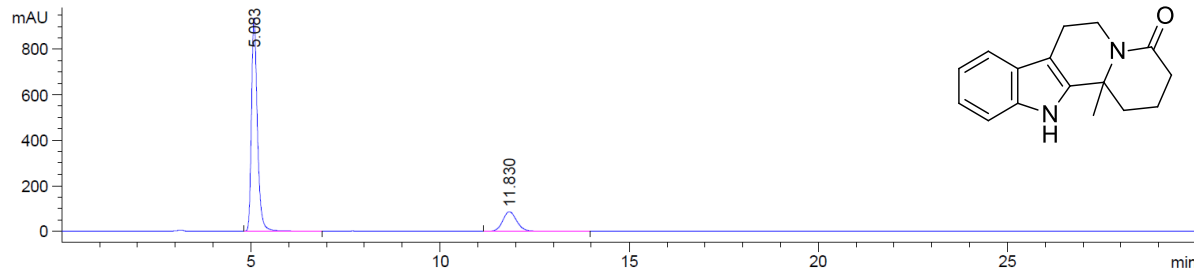
HPLC trace of Racemic 12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10a



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.045	VV	0.2131	4544.93945	329.05899	49.9785
2	11.632	BB	0.4097	4548.85742	171.38036	50.0215
Totals :				9093.79688	500.43935	

HPLC trace of 12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10a

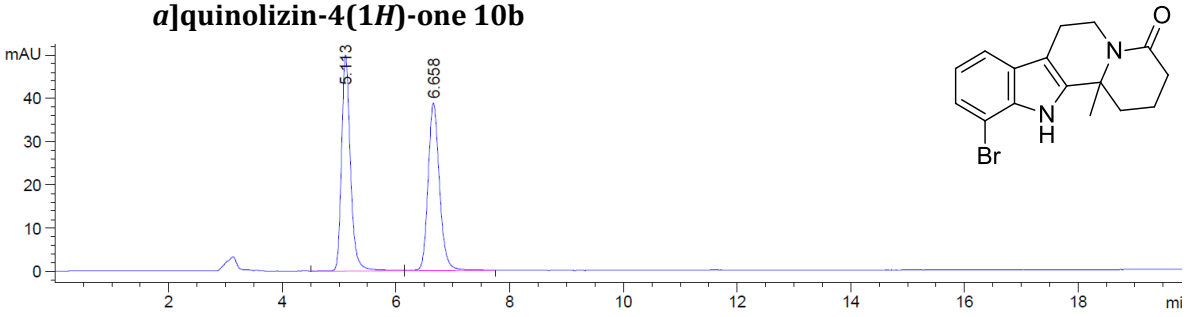


Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.082	MM	0.1846	1.04069e4	939.76501	82.8246
2	11.829	MM	0.4200	2158.08838	85.64144	17.1754
Totals :				1.25650e4	1025.40646	

4.2. Amide cyclization products

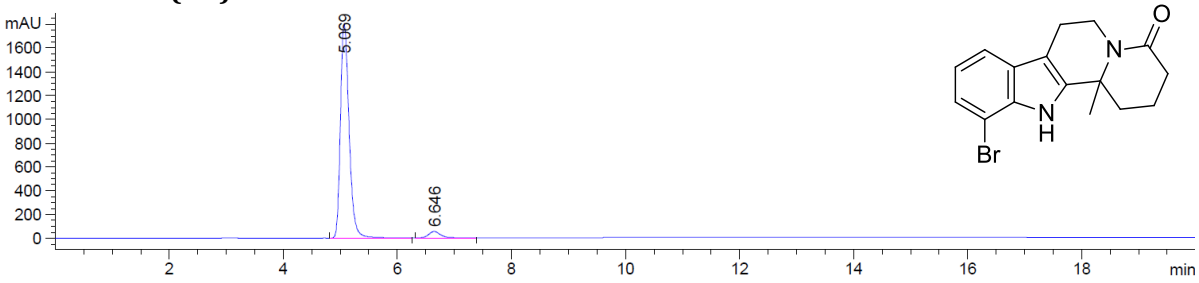
4.2.1. HPLC trace of Racemic 11-bromo-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10b



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.113	VV	0.1718	545.88226	49.84857	50.1874
2	6.658	VB	0.2154	541.80627	38.68854	49.8126
Totals :				1087.68854	88.53711	

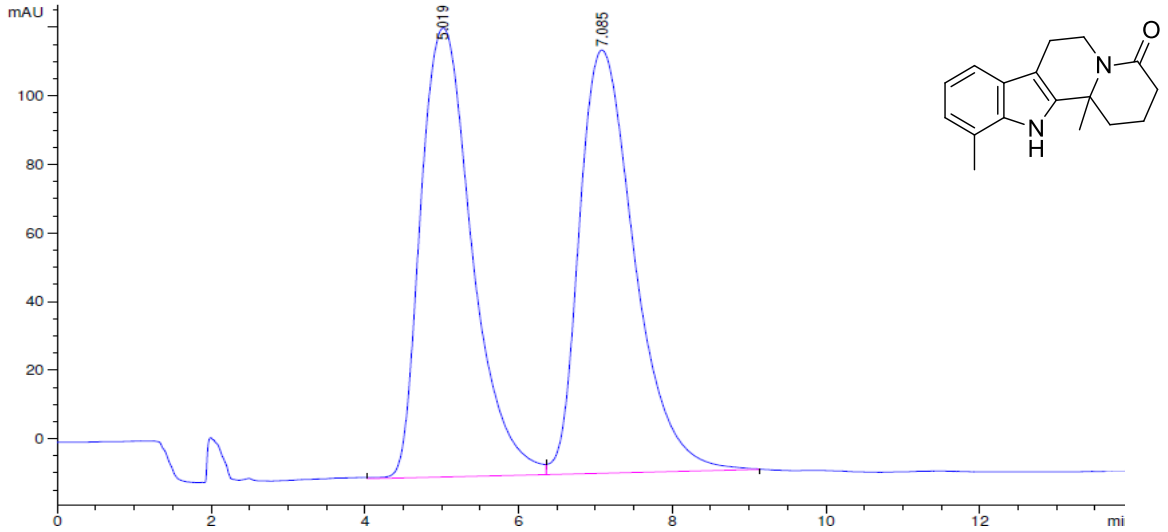
4.2.2. HPLC trace of 11-bromo-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10b



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.067	VB	0.1602	1.88902e4	1803.75488	96.3498
2	6.645	BB	0.2103	715.64355	52.73191	3.6502
Totals :				1.96059e4	1856.48679	

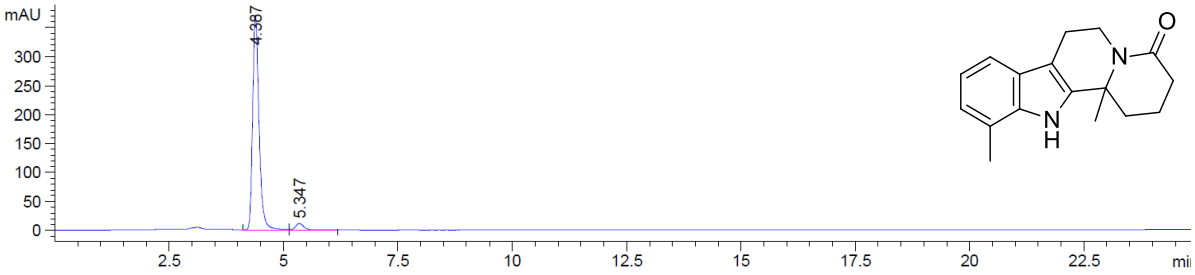
4.2.3.**HPLC trace of racemic 11,12b-dimethyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10c**



Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.019	VV	0.5596	6079.96680	130.96616	49.6528
2	7.085	VB	0.7037	6164.99609	123.44200	50.3472

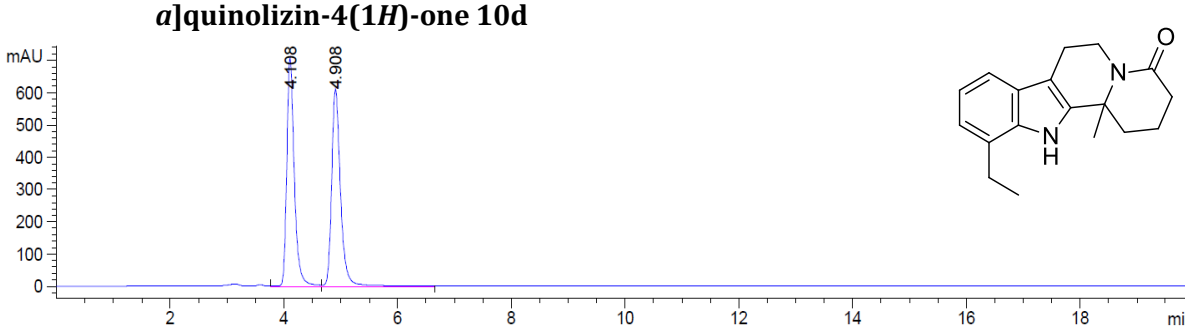
4.2.4.**HPLC trace of 11,12b-dimethyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10c**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.385	BB	0.1487	3578.53735	370.48203	96.5189
2	5.347	BB	0.1754	129.06354	11.12429	3.4811
Totals :				3707.60089	381.60631	

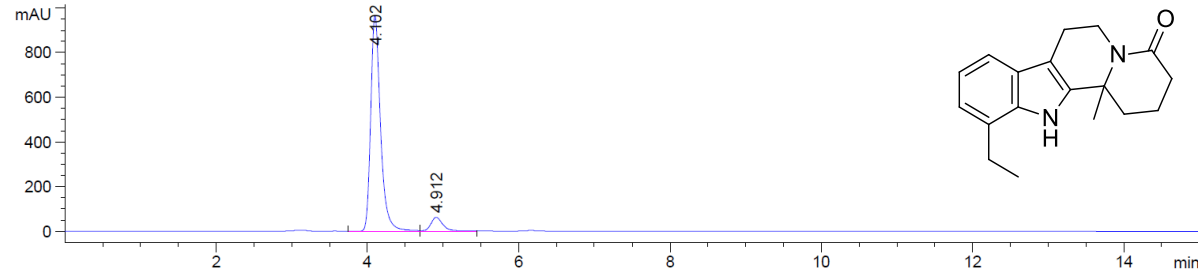
4.2.5.**HPLC trace of racemic 11-ethyl-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10d**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.108	VV	0.1432	6486.74707	706.11816	49.4928
2	4.908	VB	0.1667	6619.69873	609.59180	50.5072
Totals :				1.31064e4	1315.70996	

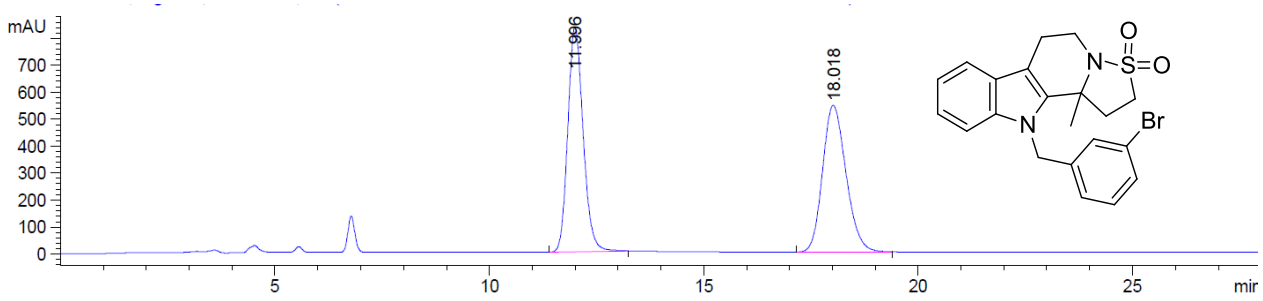
4.2.6.**HPLC trace of 11-ethyl-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one 10d**



Signal 2: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.100	BV	0.1379	8776.01367	966.42841	92.8026
2	4.911	VB	0.1657	680.63605	62.18039	7.1974
Totals :				9456.64972	1028.60880	

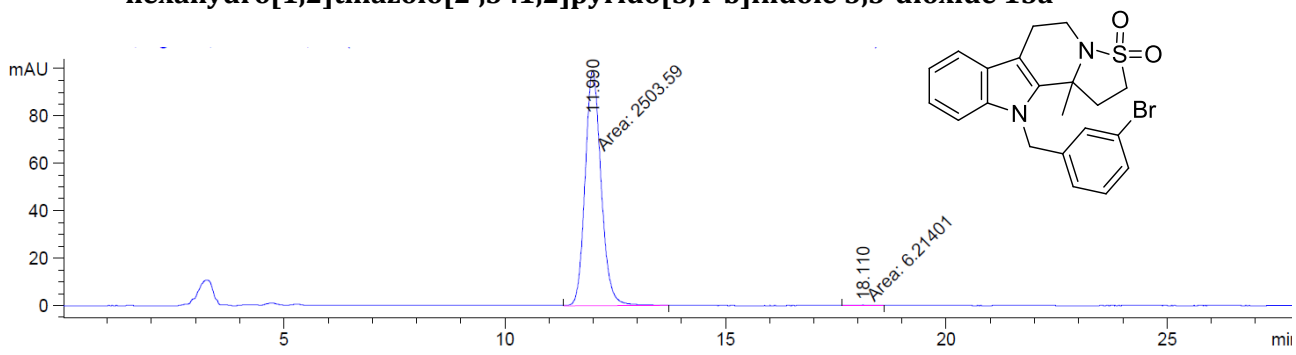
4.2.7. HPLC trace of racemic 11-(3-bromobenzyl)-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 15a



Signal 2: DAD1 B, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.996	BB	0.3824	2.07558e4	833.93286	50.0573
2	18.018	BB	0.5878	2.07083e4	544.39233	49.9427
Totals :				4.14642e4	1378.32520	

4.2.8. HPLC trace of 11-(3-bromobenzyl)-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide 15a



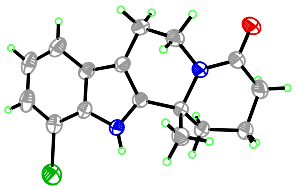
Signal 2: DAD1 B, Sig=220,16 Ref=360,100

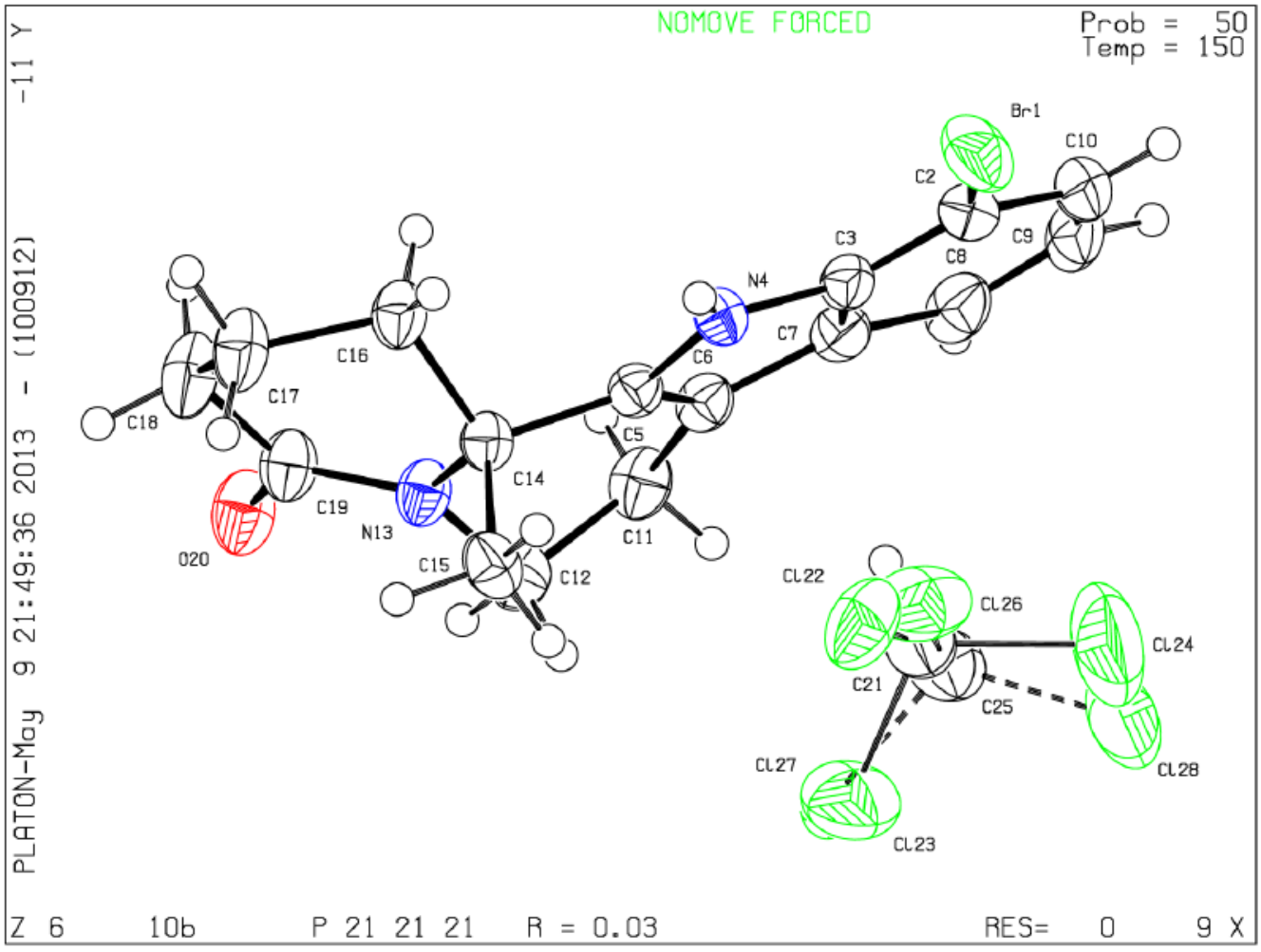
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.990	MM	0.4209	2503.59058	99.12993	99.7524
2	18.110	MM	0.5144	6.21401	2.01351e-1	0.2476
Totals :				2509.80458	99.33128	

5. Xray Data[11]

5.1. X-ray data for compound 10b

11-bromo-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-*a*]quinolizin-4(1*H*)-one





(10b)

Crystal data

$C_{16}H_{17}BrN_2O{\cdot}CHCl_3$
M_r = 452.60
Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab

D_x = 1.567 Mg m^{-3}
Melting point: not measured K
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 83413 reflections

a = 11.0236 (2) Å	θ = 5–27°
b = 12.9544 (2) Å	μ = 2.57 mm^{-1}
c = 13.4366 (2) Å	T = 150 K
V = 1918.80 (5) $Å^3$	Block, Clear_pale_colourless
Z = 4	0.62 × 0.38 × 0.30 mm
F(000) = 912	

Data collection

Nonius KappaCCD diffractometer	4092 reflections with $I > 2.0\sigma(I)$
Graphite monochromator	R_{int} = 0.087
ω scans	θ_{max} = 27.5°, θ_{min} = 5.2°
Absorption correction: Multi-scan *DENZO*/*SCALEPACK* (Otwinowski & Minor, 1997)	h = −14→14
T_{min} = 0.17, T_{max} = 0.46	k = −16→16
56832 measured reflections	l = −17→17
4361 independent reflections	

Refinement

Refinement on F^2	Hydrogen site location: Difference Fourier map
Least-squares matrix: Full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.034	Method, part 1, Chebychev polynomial, (Watkin, 1994, *P*rince, 1982) [*w*eight] = 1.0/[A_0*T_0(x) + A_1*T_1(x) ⋯ + A_{n-1}]*T_{n-1}(x)] where A_i are the Chebychev coefficients listed below and x = *F* /*F*max Method = Robust Weighting (*P*rince, 1982) W = [*w*eight] * [1-(delta*F*/6*sigma*F*)^2]^2 A_i are: 69.2 115. 71.6 31.4 7.79
$wR(F^2)$ = 0.083	$(\Delta/\sigma)_{max}$ = 0.002
S = 1.00	$\Delta\rho_{max}$ = 0.42 e $Å^{-3}$
4361 reflections	$\Delta\rho_{min}$ = −0.44 e $Å^{-3}$
255 parameters	Absolute structure: Flack (1983), 1893 Friedel-pairs
162 restraints	Flack parameter: −0.007 (8)
Primary atom site location: Other	

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($Å^2$)

	x	*y*	*z*	U_{iso}*/U_{eq}	Occ. (<1)
Br1	0.65201 (3)	0.67046 (3)	1.08633 (3)	0.0538	
C2	0.6812 (2)	0.65084 (19)	0.9491 (2)	0.0375	
C3	0.5948 (2)	0.60131 (18)	0.89063 (19)	0.0304	
N4	0.48228 (17)	0.56306 (15)	0.91457 (17)	0.0289	
C5	0.4336 (2)	0.51801 (19)	0.82999 (17)	0.0269	
C6	0.5127 (2)	0.52769 (19)	0.75153 (19)	0.0299	
C7	0.6164 (2)	0.58180 (19)	0.78843 (19)	0.0321	
C8	0.7263 (2)	0.6159 (2)	0.7450 (2)	0.0424	
C9	0.8085 (3)	0.6668 (3)	0.8039 (3)	0.0480	
C10	0.7884 (2)	0.6833 (2)	0.9055 (3)	0.0454	
C11	0.4861 (3)	0.4819 (2)	0.65142 (19)	0.0377	

C12	0.3845 (3)	0.4028 (2)	0.66363 (19)	0.0366	
N13	0.28353 (19)	0.44722 (18)	0.72179 (15)	0.0318	
C14	0.3093 (2)	0.47060 (19)	0.82822 (17)	0.0274	
C15	0.3064 (3)	0.3708 (2)	0.88971 (19)	0.0361	
C16	0.2171 (2)	0.5493 (2)	0.8680 (2)	0.0348	
C17	0.0883 (3)	0.5161 (3)	0.8449 (2)	0.0433	
C18	0.0731 (3)	0.5135 (3)	0.7325 (2)	0.0475	
C19	0.1766 (2)	0.4651 (2)	0.6760 (2)	0.0360	
O20	0.16200 (19)	0.44316 (18)	0.58674 (15)	0.0457	
C21	0.6761 (2)	0.3428 (2)	0.9014 (2)	0.0530	0.739 (8)
Cl22	0.5983 (2)	0.3334 (2)	1.01359 (14)	0.0620	0.739 (8)
Cl23	0.6434 (4)	0.2372 (4)	0.8252 (3)	0.0789	0.739 (8)
Cl24	0.83178 (19)	0.3520 (3)	0.9223 (3)	0.1103	0.739 (8)
C25	0.7068 (7)	0.3351 (4)	0.8686 (6)	0.0653	0.261 (8)
Cl26	0.6526 (11)	0.3566 (4)	0.9885 (5)	0.0775	0.261 (8)
Cl27	0.6276 (5)	0.2345 (8)	0.8120 (6)	0.0449	0.261 (8)
Cl28	0.8619 (7)	0.3086 (6)	0.8709 (8)	0.0923	0.261 (8)
H81	0.7411	0.6060	0.6779	0.0511*	
H91	0.8809	0.6888	0.7744	0.0580*	
H101	0.8460	0.7155	0.9432	0.0539*	
H111	0.5574	0.4481	0.6240	0.0450*	
H112	0.4596	0.5355	0.6043	0.0454*	
H121	0.4164	0.3434	0.7000	0.0432*	
H122	0.3531	0.3786	0.6004	0.0436*	
H151	0.2278	0.3397	0.8850	0.0533*	
H152	0.3263	0.3876	0.9579	0.0534*	
H153	0.3649	0.3239	0.8652	0.0533*	
H161	0.2277	0.5547	0.9386	0.0418*	
H162	0.2337	0.6164	0.8380	0.0419*	
H171	0.0313	0.5647	0.8702	0.0517*	
H172	0.0713	0.4491	0.8731	0.0517*	
H181	0.0687	0.5825	0.7066	0.0583*	
H182	0.0010	0.4749	0.7145	0.0575*	
H211	0.6492	0.4053	0.8682	0.0639*	0.739 (8)
H251	0.6951	0.3976	0.8291	0.0778*	0.261 (8)
H41	0.4494	0.5652	0.9709	0.0352*	

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Br1	0.05236 (17)	0.05674 (18)	0.05220 (17)	−0.01281 (15)	−0.00665 (15)	−0.01813 (14)
C2	0.0338 (13)	0.0294 (12)	0.0493 (14)	−0.0009 (9)	−0.0014 (10)	−0.0007 (10)
C3	0.0248 (10)	0.0280 (11)	0.0384 (13)	0.0008 (8)	0.0029 (9)	0.0030 (9)
N4	0.0265 (9)	0.0308 (9)	0.0296 (9)	−0.0035 (7)	0.0008 (8)	0.0000 (8)
C5	0.0273 (11)	0.0266 (10)	0.0268 (11)	0.0007 (9)	0.0003 (9)	0.0009 (8)
C6	0.0280 (11)	0.0317 (11)	0.0300 (11)	0.0023 (9)	0.0047 (9)	0.0034 (9)
C7	0.0298 (12)	0.0283 (11)	0.0383 (12)	0.0008 (9)	0.0069 (9)	0.0066 (9)
C8	0.0327 (13)	0.0425 (15)	0.0519 (16)	0.0041 (11)	0.0126 (12)	0.0144 (13)
C9	0.0264 (12)	0.0435 (14)	0.074 (2)	−0.0011 (12)	0.0071 (12)	0.0162 (15)
C10	0.0295 (12)	0.0356 (13)	0.0710 (19)	−0.0050 (10)	−0.0010 (14)	0.0032 (15)

C11	0.0330 (13)	0.0502 (15)	0.0299 (12)	0.0037 (11)	0.0059 (10)	−0.0006 (11)
C12	0.0365 (13)	0.0437 (14)	0.0297 (11)	0.0059 (10)	−0.0013 (10)	−0.0064 (10)
N13	0.0276 (10)	0.0424 (11)	0.0256 (9)	0.0032 (8)	−0.0018 (8)	−0.0006 (8)
C14	0.0255 (11)	0.0329 (11)	0.0239 (10)	−0.0003 (9)	−0.0005 (8)	0.0000 (8)
C15	0.0358 (12)	0.0379 (12)	0.0345 (13)	−0.0085 (10)	−0.0042 (10)	0.0052 (10)
C16	0.0262 (12)	0.0447 (14)	0.0335 (12)	0.0011 (10)	0.0023 (10)	−0.0025 (11)
C17	0.0260 (13)	0.067 (2)	0.0373 (14)	0.0027 (12)	0.0013 (10)	−0.0036 (13)
C18	0.0296 (13)	0.073 (2)	0.0398 (14)	0.0070 (13)	−0.0048 (11)	−0.0062 (14)
C19	0.0314 (13)	0.0475 (14)	0.0291 (12)	0.0015 (10)	−0.0041 (10)	0.0027 (10)
O20	0.0391 (10)	0.0690 (12)	0.0290 (8)	0.0048 (9)	−0.0072 (9)	−0.0025 (9)
C21	0.0506 (19)	0.0427 (18)	0.066 (2)	−0.0010 (16)	−0.0121 (18)	0.0043 (17)
Cl22	0.0550 (10)	0.0807 (10)	0.0502 (7)	0.0210 (8)	−0.0150 (6)	−0.0013 (8)
Cl23	0.089 (2)	0.0648 (14)	0.0833 (17)	−0.0014 (16)	0.0082 (15)	−0.0288 (13)
Cl24	0.0523 (9)	0.127 (2)	0.151 (3)	−0.0348 (11)	−0.0107 (13)	0.022 (2)
C25	0.071 (4)	0.050 (4)	0.075 (4)	−0.001 (3)	−0.030 (4)	−0.005 (3)
Cl26	0.111 (5)	0.059 (2)	0.063 (3)	0.019 (3)	−0.030 (3)	−0.0177 (19)
Cl27	0.0318 (19)	0.047 (3)	0.056 (3)	0.0025 (14)	−0.0096 (16)	−0.0139 (19)
Cl28	0.065 (3)	0.081 (3)	0.131 (5)	−0.026 (2)	−0.034 (3)	0.014 (3)

Geometric parameters (Å, º)

Br1—C2	1.889 (3)	N13—C19	1.349 (3)
C2—C3	1.391 (4)	C14—C15	1.534 (3)
C2—C10	1.384 (4)	C14—C16	1.536 (3)
C3—N4	1.374 (3)	C15—H151	0.958
C3—C7	1.416 (4)	C15—H152	0.967
N4—C5	1.385 (3)	C15—H153	0.945
N4—H41	0.840	C16—C17	1.516 (4)
C5—C6	1.374 (3)	C16—H161	0.957
C5—C14	1.502 (3)	C16—H162	0.977
C6—C7	1.429 (4)	C17—C18	1.520 (4)
C6—C11	1.499 (4)	C17—H171	0.952
C7—C8	1.415 (4)	C17—H172	0.966
C8—C9	1.371 (5)	C18—C19	1.507 (4)
C8—H81	0.926	C18—H181	0.961
C9—C10	1.399 (5)	C18—H182	0.969
C9—H91	0.936	C19—O20	1.244 (3)
C10—H101	0.914	C21—Cl22	1.738 (3)
C11—C12	1.527 (4)	C21—Cl23	1.746 (3)
C11—H111	0.972	C21—Cl24	1.743 (3)
C11—H112	0.984	C21—H211	0.972
C12—N13	1.477 (3)	C25—Cl26	1.740 (5)
C12—H121	0.976	C25—Cl27	1.743 (5)
C12—H122	0.968	C25—Cl28	1.744 (5)
N13—C14	1.489 (3)	C25—H251	0.976
Br1—C2—C3	119.8 (2)	N13—C14—C15	110.0 (2)
Br1—C2—C10	121.2 (2)	C5—C14—C16	109.1 (2)
C3—C2—C10	119.0 (3)	N13—C14—C16	110.1 (2)
C2—C3—N4	130.7 (2)	C15—C14—C16	111.0 (2)
C2—C3—C7	121.0 (2)	C14—C15—H151	109.7

N4—C3—C7	108.3 (2)	C14—C15—H152	108.4
C3—N4—C5	108.0 (2)	H151—C15—H152	111.2
C3—N4—H41	126.0	C14—C15—H153	109.9
C5—N4—H41	125.9	H151—C15—H153	108.9
N4—C5—C6	110.2 (2)	H152—C15—H153	108.7
N4—C5—C14	122.6 (2)	C14—C16—C17	111.1 (2)
C6—C5—C14	127.2 (2)	C14—C16—H161	108.2
C5—C6—C7	106.6 (2)	C17—C16—H161	109.8
C5—C6—C11	121.9 (2)	C14—C16—H162	108.8
C7—C6—C11	131.5 (2)	C17—C16—H162	110.1
C6—C7—C3	106.8 (2)	H161—C16—H162	108.7
C6—C7—C8	134.0 (3)	C16—C17—C18	108.3 (2)
C3—C7—C8	119.2 (3)	C16—C17—H171	110.9
C7—C8—C9	118.5 (3)	C18—C17—H171	107.3
C7—C8—H81	120.6	C16—C17—H172	110.8
C9—C8—H81	120.8	C18—C17—H172	110.4
C8—C9—C10	122.1 (3)	H171—C17—H172	109.0
C8—C9—H91	117.7	C17—C18—C19	115.2 (2)
C10—C9—H91	120.1	C17—C18—H181	110.1
C9—C10—C2	120.1 (3)	C19—C18—H181	104.1
C9—C10—H101	120.0	C17—C18—H182	110.5
C2—C10—H101	119.8	C19—C18—H182	106.4
C6—C11—C12	108.2 (2)	H181—C18—H182	110.4
C6—C11—H111	111.1	C18—C19—N13	120.3 (2)
C12—C11—H111	109.4	C18—C19—O20	118.8 (2)
C6—C11—H112	110.9	N13—C19—O20	120.9 (3)
C12—C11—H112	109.0	Cl22—C21—Cl23	110.61 (6)
H111—C11—H112	108.2	Cl22—C21—Cl24	110.54 (6)
C11—C12—N13	110.4 (2)	Cl23—C21—Cl24	110.61 (6)
C11—C12—H121	108.5	Cl22—C21—H211	107.9
N13—C12—H121	108.3	Cl23—C21—H211	108.7
C11—C12—H122	112.6	Cl24—C21—H211	108.5
N13—C12—H122	108.7	Cl26—C25—Cl27	110.58 (6)
H121—C12—H122	108.3	Cl26—C25—Cl28	110.60 (6)
C12—N13—C14	116.3 (2)	Cl27—C25—Cl28	110.59 (6)
C12—N13—C19	119.0 (2)	Cl26—C25—H251	108.9
C14—N13—C19	124.7 (2)	Cl27—C25—H251	108.4
C5—C14—N13	105.81 (19)	Cl28—C25—H251	107.6
C5—C14—C15	110.8 (2)		

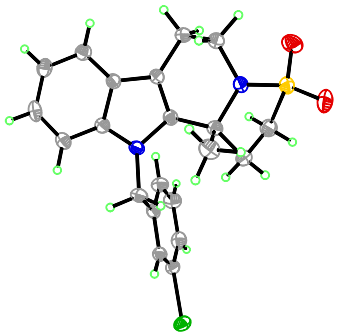
Hydrogen-bond geometry (Å, º)

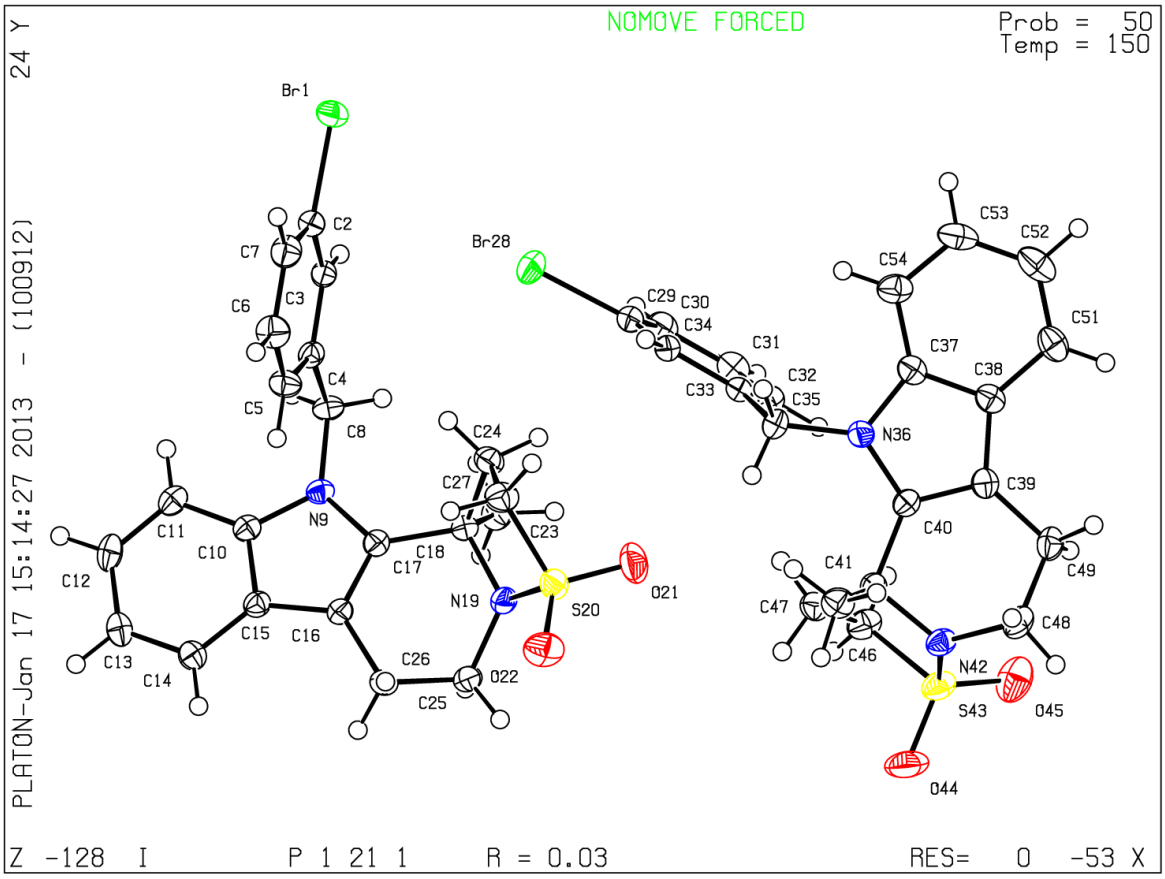
D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C16—H161···O20^{i}	0.96	2.33	3.229 (4)	155 (1)
C21—H211···C7	0.97	2.55	3.511 (4)	170 (1)
C25—H211···C7	1.11	2.55	3.517 (4)	145 (1)
C25—H251···C7	0.98	2.60	3.517 (4)	157 (1)
N4—H41···O20^{i}	0.84	1.99	2.809 (4)	166 (1)

Symmetry code: (i) −*x*+1/2, −*y*+1, *z*+1/2.

5.2. X-Ray data for compound 15a

11-(3-bromobenzyl)-11b-methyl-1,2,5,6,11,11b-hexahydro[1,2]thiazolo[2',3':1,2]pyrido[3,4-b]indole 3,3-dioxide





(15a)

Crystal data

$C_{21}H_{21}BrN_2O_2S$ $F(000) = 912$

M_r = 445.38
Monoclinic, $P2_1$
Hall symbol: P 2yb
a = 10.4507 (1) Å
b = 16.2752 (2) Å
c = 11.5043 (1) Å
β = 101.0903 (5)°
V = 1920.19 (3) Å^3
Z = 4

D_x = 1.541 Mg m^{-3}
Melting point: not measured K
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 4512 reflections
θ = 5–27°
μ = 2.27 mm^{-1}
T = 150 K
Block, Clear_pale_colourless
0.50 × 0.30 × 0.15 mm

Data collection

Nonius KappaCCD diffractometer
Graphite monochromator
ω scans
Absorption correction: Multi-scan *DENZO/SCALEPACK* (Otwinowski & Minor, 1997)
T_{min} = 0.54, T_{max} = 0.71
35947 measured reflections
8412 independent reflections

7894 reflections with $I > 2.0\sigma(I)$
R_{int} = 0.063
θ_{max} = 27.5°, θ_{min} = 5.1°
h = −13→13
k = −21→19
l = −14→14

Refinement

Refinement on F^2
Least-squares matrix: Full
$R[F^2 > 2\sigma(F^2)]$ = 0.029
$wR(F^2)$ = 0.064
S = 0.99
8412 reflections
488 parameters
1 restraint
Primary atom site location: Structure-invariant direct methods

Hydrogen site location: Difference Fourier map
H-atom parameters constrained
Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.03P)^2 + 1.16P]$, where $P = (\max(F_o^2,0) + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 1.11 e Å^{-3}
$\Delta\rho_{min}$ = −0.93 e Å^{-3}
Absolute structure: Flack (1983), 3898 Friedel-pairs
Flack parameter: 0.010 (4)

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
Br1	1.41297 (2)	0.38134 (3)	0.34172 (2)	0.0285
C2	1.3005 (2)	0.46900 (15)	0.2792 (2)	0.0226
C3	1.1759 (2)	0.45052 (14)	0.2192 (2)	0.0208
C4	1.0911 (2)	0.51396 (14)	0.1758 (2)	0.0205
C5	1.1330 (2)	0.59512 (15)	0.1918 (2)	0.0256
C6	1.2588 (3)	0.61223 (16)	0.2519 (2)	0.0295
C7	1.3438 (2)	0.54976 (17)	0.2968 (2)	0.0287
C8	0.9538 (2)	0.49079 (14)	0.1142 (2)	0.0228
N9	0.86899 (18)	0.56083 (12)	0.08136 (17)	0.0205
C10	0.8749 (2)	0.60797 (14)	−0.0176 (2)	0.0206
C11	0.9386 (2)	0.59243 (16)	−0.1112 (2)	0.0245

C12	0.9203 (3)	0.64855 (17)	−0.2034 (2)	0.0276
C13	0.8431 (2)	0.71881 (16)	−0.2021 (2)	0.0263
C14	0.7847 (2)	0.73585 (15)	−0.1068 (2)	0.0247
C15	0.8018 (2)	0.68067 (14)	−0.0121 (2)	0.0211
C16	0.7523 (2)	0.67577 (14)	0.0958 (2)	0.0209
C17	0.7947 (2)	0.60349 (14)	0.1504 (2)	0.0201
C18	0.7553 (2)	0.56948 (14)	0.2609 (2)	0.0213
N19	0.66573 (19)	0.63045 (12)	0.30024 (17)	0.0222
S20	0.72133 (6)	0.66744 (5)	0.43267 (5)	0.0261
O21	0.6787 (2)	0.61696 (14)	0.51981 (17)	0.0420
O22	0.6911 (2)	0.75361 (12)	0.43494 (18)	0.0378
C23	0.8865 (3)	0.64467 (16)	0.4315 (2)	0.0296
C24	0.8725 (3)	0.56237 (15)	0.3669 (2)	0.0263
C25	0.5806 (2)	0.68198 (16)	0.2122 (2)	0.0268
C26	0.6594 (2)	0.73246 (16)	0.1396 (2)	0.0266
C27	0.6827 (3)	0.48793 (16)	0.2380 (3)	0.0307
Br28	0.97901 (3)	0.32754 (3)	0.39862 (3)	0.0391
C29	0.8383 (2)	0.32493 (17)	0.4816 (2)	0.0267
C30	0.7437 (3)	0.26470 (16)	0.4539 (2)	0.0289
C31	0.6397 (3)	0.26565 (16)	0.5129 (2)	0.0274
C32	0.6313 (2)	0.32589 (16)	0.5970 (2)	0.0230
C33	0.7276 (2)	0.38529 (16)	0.62490 (18)	0.0207
C34	0.8335 (2)	0.38422 (16)	0.56645 (19)	0.0224
C35	0.7227 (2)	0.45407 (15)	0.7126 (2)	0.0227
N36	0.64904 (19)	0.43309 (12)	0.80417 (17)	0.0219
C37	0.6932 (2)	0.37513 (16)	0.89065 (19)	0.0228
C38	0.6024 (2)	0.36932 (15)	0.9660 (2)	0.0233
C39	0.4999 (2)	0.42615 (15)	0.9219 (2)	0.0229
C40	0.5304 (2)	0.46350 (14)	0.8242 (2)	0.0210
C41	0.4522 (2)	0.53135 (14)	0.7525 (2)	0.0216
N42	0.32641 (19)	0.53898 (13)	0.79549 (18)	0.0241
S43	0.20060 (6)	0.50210 (5)	0.70227 (6)	0.0298
O44	0.1293 (2)	0.56807 (15)	0.63536 (19)	0.0477
O45	0.1262 (2)	0.44851 (15)	0.76296 (19)	0.0450
C46	0.2931 (2)	0.45221 (17)	0.6100 (2)	0.0296
C47	0.4093 (2)	0.50934 (15)	0.6192 (2)	0.0253
C48	0.3300 (3)	0.53143 (17)	0.9239 (2)	0.0290
C49	0.3814 (2)	0.44762 (16)	0.9713 (2)	0.0271
C50	0.5235 (3)	0.61384 (15)	0.7699 (2)	0.0287
C51	0.6273 (3)	0.31427 (16)	1.0623 (2)	0.0300
C52	0.7391 (3)	0.26805 (17)	1.0798 (2)	0.0363
C53	0.8298 (3)	0.27482 (17)	1.0041 (2)	0.0339
C54	0.8077 (2)	0.32787 (17)	0.9083 (2)	0.0299
H31	1.1491	0.3960	0.2068	0.0270*
H51	1.0756	0.6379	0.1623	0.0299*
H61	1.2857	0.6670	0.2623	0.0363*
H71	1.4282	0.5614	0.3364	0.0342*
H81	0.9166	0.4571	0.1684	0.0282*
H82	0.9589	0.4601	0.0431	0.0281*
H111	0.9921	0.5464	−0.1109	0.0302*

H121	0.9601	0.6385	−0.2681	0.0355*
H131	0.8301	0.7549	−0.2672	0.0273*
H141	0.7350	0.7834	−0.1051	0.0321*
H231	0.9229	0.6857	0.3847	0.0360*
H232	0.9390	0.6411	0.5113	0.0359*
H241	0.8532	0.5197	0.4199	0.0333*
H242	0.9514	0.5494	0.3388	0.0331*
H251	0.5302	0.7191	0.2529	0.0329*
H252	0.5226	0.6463	0.1588	0.0332*
H262	0.7075	0.7748	0.1883	0.0328*
H261	0.6021	0.7573	0.0731	0.0329*
H272	0.6491	0.4727	0.3074	0.0469*
H271	0.6120	0.4938	0.1716	0.0470*
H273	0.7424	0.4459	0.2212	0.0471*
H301	0.7504	0.2247	0.3964	0.0338*
H311	0.5751	0.2252	0.4965	0.0308*
H321	0.5599	0.3262	0.6348	0.0293*
H341	0.9011	0.4224	0.5859	0.0268*
H351	0.6820	0.5011	0.6698	0.0308*
H352	0.8113	0.4677	0.7496	0.0309*
H462	0.2456	0.4477	0.5289	0.0352*
H461	0.3205	0.3981	0.6406	0.0348*
H472	0.3853	0.5577	0.5718	0.0322*
H471	0.4803	0.4814	0.5922	0.0319*
H481	0.2415	0.5390	0.9379	0.0329*
H482	0.3877	0.5736	0.9652	0.0330*
H491	0.4041	0.4489	1.0576	0.0331*
H492	0.3152	0.4064	0.9474	0.0330*
H501	0.4693	0.6565	0.7280	0.0460*
H502	0.5448	0.6273	0.8528	0.0461*
H503	0.6027	0.6101	0.7397	0.0461*
H511	0.5675	0.3105	1.1133	0.0423*
H521	0.7544	0.2303	1.1425	0.0472*
H531	0.9059	0.2427	1.0187	0.0368*
H541	0.8669	0.3322	0.8573	0.0380*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Br1	0.02460 (11)	0.03028 (12)	0.02933 (12)	0.00474 (10)	0.00169 (9)	0.00640 (11)
C2	0.0225 (11)	0.0244 (11)	0.0212 (11)	0.0034 (9)	0.0049 (9)	0.0025 (9)
C3	0.0221 (11)	0.0198 (11)	0.0216 (11)	0.0010 (9)	0.0071 (9)	0.0010 (9)
C4	0.0211 (11)	0.0217 (12)	0.0193 (11)	0.0015 (9)	0.0053 (9)	−0.0025 (9)
C5	0.0250 (12)	0.0211 (12)	0.0296 (13)	0.0010 (10)	0.0022 (10)	0.0006 (10)
C6	0.0307 (13)	0.0213 (12)	0.0357 (14)	−0.0051 (10)	0.0047 (11)	−0.0021 (10)
C7	0.0239 (12)	0.0358 (14)	0.0255 (12)	−0.0033 (11)	0.0029 (10)	−0.0023 (11)
C8	0.0211 (11)	0.0190 (11)	0.0275 (12)	0.0031 (9)	0.0028 (9)	−0.0028 (9)
N9	0.0204 (9)	0.0188 (9)	0.0222 (10)	0.0031 (8)	0.0039 (8)	−0.0018 (8)
C10	0.0181 (10)	0.0222 (11)	0.0208 (11)	−0.0010 (9)	0.0019 (8)	−0.0024 (9)
C11	0.0217 (11)	0.0272 (12)	0.0252 (12)	−0.0006 (10)	0.0062 (9)	−0.0054 (10)

C12	0.0286 (13)	0.0353 (14)	0.0207 (12)	−0.0091 (10)	0.0097 (10)	−0.0070 (10)
C13	0.0293 (13)	0.0282 (13)	0.0221 (12)	−0.0063 (11)	0.0063 (10)	0.0017 (10)
C14	0.0261 (12)	0.0227 (11)	0.0256 (12)	−0.0009 (10)	0.0059 (10)	0.0021 (10)
C15	0.0206 (11)	0.0223 (11)	0.0204 (11)	0.0013 (9)	0.0040 (9)	−0.0022 (9)
C16	0.0207 (11)	0.0223 (11)	0.0204 (11)	0.0025 (9)	0.0056 (9)	−0.0001 (9)
C17	0.0197 (11)	0.0213 (11)	0.0191 (11)	−0.0005 (9)	0.0033 (9)	−0.0020 (9)
C18	0.0211 (11)	0.0206 (11)	0.0224 (11)	0.0025 (9)	0.0051 (9)	0.0006 (9)
N19	0.0223 (10)	0.0258 (10)	0.0189 (9)	0.0033 (8)	0.0052 (8)	−0.0012 (8)
S20	0.0333 (3)	0.0253 (3)	0.0204 (3)	0.0026 (3)	0.0068 (2)	−0.0016 (2)
O21	0.0581 (13)	0.0468 (12)	0.0250 (10)	0.0043 (10)	0.0174 (9)	0.0065 (9)
O22	0.0465 (12)	0.0251 (10)	0.0408 (11)	0.0051 (9)	0.0060 (9)	−0.0097 (8)
C23	0.0278 (13)	0.0338 (14)	0.0250 (13)	0.0028 (11)	−0.0009 (10)	−0.0035 (10)
C24	0.0294 (13)	0.0262 (12)	0.0224 (12)	0.0048 (10)	0.0031 (10)	0.0026 (10)
C25	0.0240 (12)	0.0345 (14)	0.0225 (12)	0.0092 (10)	0.0055 (9)	0.0019 (10)
C26	0.0300 (13)	0.0259 (12)	0.0251 (12)	0.0092 (10)	0.0083 (10)	0.0045 (10)
C27	0.0299 (13)	0.0255 (13)	0.0386 (15)	−0.0049 (10)	0.0113 (11)	−0.0017 (11)
Br28	0.04223 (16)	0.04041 (15)	0.04193 (16)	0.01248 (13)	0.02604 (12)	0.00676 (13)
C29	0.0299 (12)	0.0266 (11)	0.0256 (12)	0.0087 (11)	0.0104 (9)	0.0067 (10)
C30	0.0406 (15)	0.0255 (12)	0.0206 (12)	0.0056 (11)	0.0056 (10)	−0.0031 (10)
C31	0.0311 (13)	0.0233 (12)	0.0257 (12)	−0.0036 (10)	0.0004 (10)	−0.0011 (10)
C32	0.0221 (11)	0.0242 (11)	0.0229 (11)	0.0000 (10)	0.0045 (9)	0.0030 (10)
C33	0.0203 (10)	0.0216 (10)	0.0198 (10)	0.0025 (10)	0.0032 (8)	0.0033 (10)
C34	0.0206 (10)	0.0237 (11)	0.0235 (10)	0.0018 (10)	0.0061 (8)	0.0046 (10)
C35	0.0211 (11)	0.0245 (12)	0.0238 (12)	−0.0027 (9)	0.0076 (9)	−0.0021 (9)
N36	0.0241 (10)	0.0210 (10)	0.0210 (10)	0.0024 (8)	0.0056 (8)	0.0009 (8)
C37	0.0288 (11)	0.0205 (11)	0.0176 (10)	−0.0001 (11)	0.0012 (8)	−0.0038 (9)
C38	0.0268 (11)	0.0230 (12)	0.0185 (10)	−0.0006 (10)	−0.0001 (9)	−0.0027 (9)
C39	0.0251 (12)	0.0239 (12)	0.0193 (11)	−0.0024 (9)	0.0036 (9)	−0.0024 (9)
C40	0.0204 (11)	0.0214 (11)	0.0213 (11)	−0.0007 (9)	0.0044 (9)	−0.0035 (9)
C41	0.0252 (12)	0.0207 (11)	0.0193 (11)	0.0018 (9)	0.0056 (9)	−0.0021 (9)
N42	0.0234 (10)	0.0258 (10)	0.0230 (10)	0.0036 (8)	0.0044 (8)	−0.0047 (8)
S43	0.0215 (3)	0.0392 (4)	0.0274 (3)	0.0046 (3)	0.0012 (2)	−0.0061 (3)
O44	0.0384 (11)	0.0639 (15)	0.0374 (11)	0.0288 (11)	−0.0014 (9)	−0.0022 (10)
O45	0.0324 (10)	0.0618 (14)	0.0418 (11)	−0.0150 (10)	0.0094 (9)	−0.0119 (10)
C46	0.0263 (13)	0.0342 (14)	0.0270 (13)	0.0038 (11)	0.0021 (10)	−0.0089 (11)
C47	0.0301 (13)	0.0265 (12)	0.0185 (11)	0.0045 (10)	0.0032 (9)	−0.0013 (9)
C48	0.0285 (13)	0.0356 (14)	0.0242 (12)	0.0016 (11)	0.0082 (10)	−0.0088 (10)
C49	0.0254 (12)	0.0358 (14)	0.0208 (12)	−0.0038 (11)	0.0063 (9)	−0.0017 (10)
C50	0.0325 (13)	0.0211 (12)	0.0326 (13)	0.0005 (10)	0.0068 (11)	−0.0024 (10)
C51	0.0403 (14)	0.0284 (13)	0.0198 (11)	−0.0037 (11)	0.0022 (10)	−0.0004 (10)
C52	0.0541 (18)	0.0255 (13)	0.0247 (13)	0.0014 (12)	−0.0037 (12)	0.0015 (10)
C53	0.0378 (15)	0.0278 (13)	0.0309 (14)	0.0115 (11)	−0.0060 (11)	−0.0032 (11)
C54	0.0316 (13)	0.0286 (12)	0.0275 (12)	0.0061 (11)	0.0007 (10)	−0.0062 (11)

Geometric parameters (Å, º)

Br1—C2	1.900 (2)	Br28—C29	1.901 (2)
C2—C3	1.385 (3)	C29—C30	1.386 (4)
C2—C7	1.392 (4)	C29—C34	1.381 (4)
C3—C4	1.389 (3)	C30—C31	1.387 (4)

C3—H31	0.933	C30—H301	0.940
C4—C5	1.393 (3)	C31—C32	1.392 (4)
C4—C8	1.521 (3)	C31—H311	0.936
C5—C6	1.390 (4)	C32—C33	1.388 (3)
C5—H51	0.938	C32—H321	0.934
C6—C7	1.383 (4)	C33—C34	1.401 (3)
C6—H61	0.936	C33—C35	1.514 (3)
C7—H71	0.931	C34—H341	0.935
C8—N9	1.449 (3)	C35—N36	1.460 (3)
C8—H81	0.967	C35—H351	0.963
C8—H82	0.969	C35—H352	0.968
N9—C10	1.384 (3)	N36—C37	1.384 (3)
N9—C17	1.397 (3)	N36—C40	1.395 (3)
C10—C11	1.394 (3)	C37—C38	1.406 (3)
C10—C15	1.416 (3)	C37—C54	1.404 (3)
C11—C12	1.384 (4)	C38—C39	1.432 (3)
C11—H111	0.934	C38—C51	1.410 (3)
C12—C13	1.401 (4)	C39—C40	1.368 (3)
C12—H121	0.935	C39—C49	1.500 (3)
C13—C14	1.382 (4)	C40—C41	1.519 (3)
C13—H131	0.941	C41—N42	1.497 (3)
C14—C15	1.396 (3)	C41—C47	1.554 (3)
C14—H141	0.934	C41—C50	1.529 (3)
C15—C16	1.437 (3)	N42—S43	1.642 (2)
C16—C17	1.367 (3)	N42—C48	1.475 (3)
C16—C26	1.495 (3)	S43—O44	1.442 (2)
C17—C18	1.515 (3)	S43—O45	1.436 (2)
C18—N19	1.493 (3)	S43—C46	1.765 (3)
C18—C24	1.557 (3)	C46—C47	1.517 (4)
C18—C27	1.526 (3)	C46—H462	0.972
N19—S20	1.637 (2)	C46—H461	0.971
N19—C25	1.475 (3)	C47—H472	0.963
S20—O21	1.432 (2)	C47—H471	0.971
S20—O22	1.4389 (19)	C48—C49	1.528 (4)
S20—C23	1.768 (3)	C48—H481	0.977
C23—C24	1.525 (4)	C48—H482	0.975
C23—H231	0.980	C49—H491	0.976
C23—H232	0.976	C49—H492	0.965
C24—H241	0.971	C50—H501	0.964
C24—H242	0.966	C50—H502	0.962
C25—C26	1.522 (3)	C50—H503	0.960
C25—H251	0.978	C51—C52	1.372 (4)
C25—H252	0.969	C51—H511	0.938
C26—H262	0.966	C52—C53	1.409 (4)
C26—H261	0.964	C52—H521	0.938
C27—H272	0.964	C53—C54	1.384 (4)
C27—H271	0.960	C53—H531	0.940
C27—H273	0.970	C54—H541	0.933
Br1—C2—C3	118.66 (18)	Br28—C29—C30	119.17 (19)

Br1—C2—C7	119.59 (18)	Br28—C29—C34	118.45 (19)
C3—C2—C7	121.7 (2)	C30—C29—C34	122.4 (2)
C2—C3—C4	119.4 (2)	C29—C30—C31	118.1 (2)
C2—C3—H31	120.6	C29—C30—H301	120.3
C4—C3—H31	120.0	C31—C30—H301	121.6
C3—C4—C5	119.7 (2)	C30—C31—C32	120.5 (2)
C3—C4—C8	117.6 (2)	C30—C31—H311	119.7
C5—C4—C8	122.8 (2)	C32—C31—H311	119.8
C4—C5—C6	119.9 (2)	C31—C32—C33	120.8 (2)
C4—C5—H51	119.5	C31—C32—H321	119.4
C6—C5—H51	120.6	C33—C32—H321	119.8
C5—C6—C7	121.1 (2)	C32—C33—C34	119.0 (2)
C5—C6—H61	119.1	C32—C33—C35	123.6 (2)
C7—C6—H61	119.8	C34—C33—C35	117.4 (2)
C2—C7—C6	118.2 (2)	C33—C34—C29	119.2 (2)
C2—C7—H71	121.0	C33—C34—H341	120.5
C6—C7—H71	120.8	C29—C34—H341	120.3
C4—C8—N9	113.68 (19)	C33—C35—N36	113.44 (19)
C4—C8—H81	107.5	C33—C35—H351	108.4
N9—C8—H81	108.3	N36—C35—H351	108.2
C4—C8—H82	108.7	C33—C35—H352	108.1
N9—C8—H82	108.4	N36—C35—H352	109.2
H81—C8—H82	110.3	H351—C35—H352	109.5
C8—N9—C10	121.95 (19)	C35—N36—C37	121.92 (19)
C8—N9—C17	128.4 (2)	C35—N36—C40	130.2 (2)
C10—N9—C17	108.04 (18)	C37—N36—C40	107.90 (19)
N9—C10—C11	129.7 (2)	N36—C37—C38	108.5 (2)
N9—C10—C15	108.5 (2)	N36—C37—C54	129.4 (2)
C11—C10—C15	121.9 (2)	C38—C37—C54	122.1 (2)
C10—C11—C12	117.1 (2)	C37—C38—C39	106.6 (2)
C10—C11—H111	121.1	C37—C38—C51	118.8 (2)
C12—C11—H111	121.8	C39—C38—C51	134.6 (2)
C11—C12—C13	121.7 (2)	C38—C39—C40	107.6 (2)
C11—C12—H121	118.5	C38—C39—C49	129.2 (2)
C13—C12—H121	119.8	C40—C39—C49	123.2 (2)
C12—C13—C14	121.0 (2)	N36—C40—C39	109.4 (2)
C12—C13—H131	119.8	N36—C40—C41	124.8 (2)
C14—C13—H131	119.2	C39—C40—C41	125.7 (2)
C13—C14—C15	118.7 (2)	C40—C41—N42	107.20 (18)
C13—C14—H141	121.0	C40—C41—C47	113.02 (19)
C15—C14—H141	120.4	N42—C41—C47	103.86 (18)
C10—C15—C14	119.5 (2)	C40—C41—C50	111.70 (19)
C10—C15—C16	106.2 (2)	N42—C41—C50	108.67 (19)
C14—C15—C16	134.1 (2)	C47—C41—C50	111.9 (2)
C15—C16—C17	107.8 (2)	C41—N42—S43	113.44 (15)
C15—C16—C26	128.5 (2)	C41—N42—C48	117.98 (19)
C17—C16—C26	123.4 (2)	S43—N42—C48	119.11 (17)
N9—C17—C16	109.5 (2)	N42—S43—O44	110.06 (13)
N9—C17—C18	124.5 (2)	N42—S43—O45	110.16 (12)
C16—C17—C18	125.7 (2)	O44—S43—O45	116.07 (14)

C17—C18—N19	107.40 (18)	N42—S43—C46	95.66 (11)
C17—C18—C24	112.60 (19)	O44—S43—C46	107.95 (13)
N19—C18—C24	104.89 (19)	O45—S43—C46	115.04 (14)
C17—C18—C27	112.3 (2)	S43—C46—C47	101.51 (17)
N19—C18—C27	108.10 (19)	S43—C46—H462	112.0
C24—C18—C27	111.1 (2)	C47—C46—H462	111.6
C18—N19—S20	113.29 (15)	S43—C46—H461	110.9
C18—N19—C25	120.05 (18)	C47—C46—H461	110.7
S20—N19—C25	119.29 (16)	H462—C46—H461	109.9
N19—S20—O21	109.75 (12)	C41—C47—C46	106.6 (2)
N19—S20—O22	109.60 (11)	C41—C47—H472	111.4
O21—S20—O22	116.58 (13)	C46—C47—H472	110.1
N19—S20—C23	95.05 (11)	C41—C47—H471	109.3
O21—S20—C23	108.72 (13)	C46—C47—H471	109.9
O22—S20—C23	115.00 (13)	H472—C47—H471	109.4
S20—C23—C24	100.68 (17)	N42—C48—C49	111.8 (2)
S20—C23—H231	110.1	N42—C48—H481	108.2
C24—C23—H231	110.0	C49—C48—H481	109.4
S20—C23—H232	112.2	N42—C48—H482	108.9
C24—C23—H232	113.0	C49—C48—H482	108.2
H231—C23—H232	110.5	H481—C48—H482	110.3
C23—C24—C18	107.68 (19)	C48—C49—C39	109.4 (2)
C23—C24—H241	109.5	C48—C49—H491	110.1
C18—C24—H241	108.6	C39—C49—H491	109.5
C23—C24—H242	110.3	C48—C49—H492	109.6
C18—C24—H242	110.4	C39—C49—H492	109.2
H241—C24—H242	110.3	H491—C49—H492	109.0
N19—C25—C26	111.43 (19)	C41—C50—H501	110.0
N19—C25—H251	109.4	C41—C50—H502	110.1
C26—C25—H251	109.1	H501—C50—H502	109.5
N19—C25—H252	108.4	C41—C50—H503	109.2
C26—C25—H252	108.3	H501—C50—H503	109.2
H251—C25—H252	110.2	H502—C50—H503	108.8
C25—C26—C16	107.9 (2)	C38—C51—C52	119.1 (2)
C25—C26—H262	110.1	C38—C51—H511	119.2
C16—C26—H262	109.7	C52—C51—H511	121.7
C25—C26—H261	110.0	C51—C52—C53	121.5 (2)
C16—C26—H261	109.6	C51—C52—H521	119.1
H262—C26—H261	109.6	C53—C52—H521	119.4
C18—C27—H272	109.2	C52—C53—C54	120.8 (2)
C18—C27—H271	109.4	C52—C53—H531	119.5
H272—C27—H271	109.7	C54—C53—H531	119.7
C18—C27—H273	109.3	C37—C54—C53	117.6 (2)
H272—C27—H273	109.5	C37—C54—H541	121.1
H271—C27—H273	109.8	C53—C54—H541	121.2

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C12—H121···O44^{i}	0.94	2.54	3.390 (4)	152

C23—H232···O44[ii]	0.98	2.51	3.347 (4)	143
C35—H351···O21	0.96	2.55	3.430 (4)	152
C46—H461···O22[iii]	0.97	2.50	3.282 (4)	137

Symmetry codes: (i) *x*+1, *y*, *z*–1; (ii) *x*+1, *y*, *z*; (iii) –*x*+1, *y*–1/2, –*z*+1.

For both compounds, data collection: *COLLECT* (Nonius, 2001).; cell refinement: *DENZO*/*SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO*/*SCALEPACK* (Otwinowski & Minor, 1997). Program(s) used to solve structure: Superflip (Palatinus & Chapuis, 2007) for (10b); *SIR92* (Altomare *et al.*, 1994) for (15a). For both compounds, program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *CAMERON* (Watkin *et al.*, 1996); software used to prepare material for publication: *CRYSTALS* (Betteridge *et al.*, 2003).

5.3. X-ray references

Betteridge, P. W., Carruthers, J. R., Cooper, R. I., Prout, K. & Watkin, D. J. (2003). J. Appl. Cryst. 36, 1487.

Flack, H. D. (1983). Acta Cryst. A39, 876-881.

Nonius (2001). *COLLECT*. Nonius BV, Delft, The Netherlands.

6. References

[1] P. Wipf, J. K. Jung. *J. Org. Chem.* **2000**, 65, 6319-6337

[2] R. I. Storer, D. E. Carrera, Y. Ni, D. W. C. MacMillan. *J. Am. Chem. Soc.* **2006**, 128, 84-86

[3] K. Maruoka, T. Itoh, Y. Araki, T. Shirasaka, H. Yamamoto. *Bull. Chem. Soc. Jpn.* **1988**, 61, 2975-2976

[4] M. E. Muratore, C. A. Holloway, A. W. Pilling, R. I. Storer, G. Trevitt, D. J. Dixon. *J. Am. Chem. Soc.* **2009**, *131*, 31, 10796–10797

[5] M. E. Muratore, L. Shi , A. W. Pilling , R. I. Storer. D. J. Dixon. *Chem. Commun.* **2012**, Advance Article

[6] F. Hadjaz, S. Besret, S. Yous, S. Dilly, N. Lebegue, P. Chavatte, P. Berthelot, P. Carato, F. Martin-Nizard, P. Duriez. *European Journal of Medicinal Chemistry,* **2011** , 46, 6, 2575-2585

[7] T. Newhouse, C. A. Lewis, K. J. Eastman, P. S. Baran. *J. Am. Chem. Soc.* **2010**, 132, 20, 7119-7137

[8] Two step reduction for the preparation of 5-cyano-tryptamine: M. Somel, M. Wakida, T. Ohta. *Chem. Pharm. Bull.* **1988**, 34, 3, 1162-1168.

[9] Sulfonyl chloride formed following literature procedure: F. K. Cheung, A. M. Hayes, D. J. Morris, M. Wills. *Org. Biomol. Chem*, **2007**, *5*, 1093–1103

[10] S. Chang, M. Lee, D. Y. Jung, E. J. Yoo, S. H. Cho, S. K. Han. *J. Am. Chem. Soc.* **2006**. 128, 38, 12366-12367

[11] Single crystal X-ray diffraction data were collected using a Nonius Kappa CCD diffractometer and data were reduced using Denzo-SMN.[12] The structures were solved with SIR92/SuperFlip[13] and refined with CRYSTALS.[14] The Flack x parameter[15] refined to -0.007(8) and 0.010(4) for **10b** and **15a** respectively. For further information, see ESI (CIF); full crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC XXXXX-X, respectively. Copies of these data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[12] Otwinowski, Z.; Minor, W. *Processing of X-ray Diffraction Data Collected in Oscillation Mode, Methods Enzymol.* Carter, C. W, Sweet, R. M, Eds.; Academic Press. **1997**, 276,

[13] a) Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli, M.; *J. Appl. Cryst.* **1994**, 27, 435; b) Palatinus, L.; Chapuis, G. *J. Appl. Cryst.* **2007**, 40, 786.

[14] a) Betteridge, P. W.; Carruthers, J. R.; Cooper, R. I.; Prout, K.; Watkin, D. J. *J. Appl. Cryst.* **2003**, 36, 1487; b) Cooper, R. I.; Thompson, A. L.; Watkin, D. J.; *J. Appl. Cryst.* **2010**, 43, 1100.

[15] a) Flack, H. D. *Acta Cryst.* **1983**, A39, 876; b) Thompson, A. L.; Watkin, D. J. *J. Appl. Cryst.* **2011**, 44, 1017.