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

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4.2. Amide cyclization products

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5. Xray Data

5.1. X-ray data for compound 10b

5.2. X-Ray data for compound 15a

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6. References
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-(1H-indol-3-yl)ethanamine, 2-(5-methyl-1H-indol-3-yl)ethanamine and 2-(5-methoxy-1H-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 F254 (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 1H and 13C nuclear magnetic resonance (NMR) spectra were collected on either a Bruker DPX400 (400 MHz 1H, 100 MHz 13C), Bruker DQX400 (400 MHz 1H, 100 MHz 13C) or Bruker AVCS00 (500 MHz 1H, 125 MHz 13C) 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. 1HNMR 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 (νmax) 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) ([α]_D^20) are reported in 10⁻¹ deg.cm².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 POCl₃) 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 via 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-1H-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); 1H NMR (d6-DMSO, 400 MHz) δH 12.54 (br s, 1H, ArNH), 9.99 (s, 1H, ArC(O), 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); 13C NMR (d6-DMSO, 100 MHz) δC 186.2 (C=O), 141.1 (ArC), 139.7 (ArCquat), 127.2 (ArCH), 126.6 (ArCH) 124.8 (ArCquat), 120.8 (ArCquat), 118.9 (ArCN), 114.8 (ArCH), 105.2 (ArCquat); m/z (ES−) 169 ([M−H]−, 100%), HRMS (ES+) exact mass calculated for [M+Na]+ (C10H6N2NaO+) requires m/z 193.0372, found 193.0368.

2.2.2. Preparation and characterisation of 17b

4-chloro-1H-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); 1H NMR (d6-DMSO, 400 MHz) δH 12.57 (br s, 1H, ArNH), 10.49 (s, 1H, CH(O), 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); 13C NMR (d6-DMSO, 125 MHz) δC 185.6 (C=O), 139.1 (ArCquat), 134.9 (ArCH), 125.4 (ArCquat), 124.4 (ArCH), 123.8 (ArCquat), 123.4 (ArCH), 118.7 (ArCquat), 112.8 (ArCH); m/z (ES−) 178 ([M−H]−, 100%), HRMS (ES−) exact mass calculated for [M-H]− (C9H5ClNO−) 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
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 crystallize for 14-16 h. The solid was filtered, washed with water and dried over phosphorous pentoxide in a vacuum dessicator affording the desired nitro-olefin 18.

2.3.1. Preparation and characterisation of 18g

**(E)-3-(2-nitrovinyl)-1H-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 (NO₂(asy)), 1340 (NO₂(sy)); ¹H NMR (d₆-DMSO, 400 MHz) δH 12.6 (br s, 1H, ArNH), 8.66 (s, 1H, ArCH), 8.40 (d, 1H, O₂NCHCH = C = H), 8.38 (s, 1H, ArCH), 8.22 (d, 1H, O₂NCHCH = C = H J 13.5 Hz), 7.67 (d, 1H, ArCH, J 8.5 Hz), 7.61 (d, 1H, ArCH, J 8.5 Hz); ¹³C NMR (d₆-DMSO, 100 MHz) δC 140.2 (ArCquat), 138.3 (ArCH), 134.0 (O₂NCH=CH) 134.0 (ArCquat), 127.0 (O₂NCH=CH), 126.9 (ArCH), 125.3 (ArCH), 120.9 (ArC), 114.8 (ArCH), 109.5 (ArCquat), 104.8 (ArCquat); m/z (ES−) 212 ([M−H]−, 100%), HRMS (ES+) exact mass calculated for [M+Na]⁺ (C₁₁H₇N₃NaO₂⁺) requires m/z 236.0430, found m/z 236.0430.

2.3.2. Preparation and characterisation of 18b

**(E)-4-chloro-3-(2-nitrovinyl)-1H-indole**
The title compound 18b was synthesised according to general procedure B in 98% yield as an orange solid.

m.p. 158-160 °C (decomposition); FT-IR \( \nu_{\text{max}} \) 3258 (N–H), 1605 (C=C), 1491 (NO\(_2\) (asy)), 1293 (NO\(_2\) (sy)); \(^1\)H NMR (d\(_6\)-DMSO, 400 MHz) \( \delta_H \) 12.57 (br s, 1H, ArN\(_2\)H), 8.92 (d, 1H, O\(_2\)NCH=CCH\(_3\), J 13.5 Hz), 8.53 (s, 1H, ArCH), 8.12 (d, 1H, O\(_2\)NCH=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) \( \delta_C \) 139.2 (ArC\(_{\text{quat}}\)), 134.4 (O\(_2\)NCHCH), 133.4 (O\(_2\)NCHCH), 132.6 (ArCH), 125.4 (ArC\(_{\text{quat}}\)), 124.5 (ArCH), 123.6 (ArC\(_{\text{quat}}\)), 123.5 (ArCH), 113.1 (ArCH), 107.8 (ArC\(_{\text{quat}}\)); m/z (ES–) 221 ([M–H]– 100%), HRMS (ES+) exact mass calculated for [M+Na]\(^+\) (C\(_{10}\)H\(_7\)ClN\(_2\)NaO\(_2\)) 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\(_4\)) : 1 ml (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\(_2\)Cl\(_2\) solution followed by addition of solid KOH until the PH measures 14 (by universal indicator paper) and extracted with CH\(_2\)Cl\(_2\) dried over NaSO\(_4\) and concentrated.

### 2.4.1. Preparation and characterisation of 19m

2-(7-bromo-1H-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 an orange solid (50% yield).

\[
\text{m.p. } 89-99 \degree C; \text{ FT-IR } \nu_{\text{max}} 3556 (\text{NH}_2), 3293 (\text{ArNH}) \text{; } ^1H \text{ NMR (CDCl}_3, 400 \text{ MHz}) \delta_H 8.67 \text{ (br s, 1H, ArNH)}, 7.55 \text{ (d, 1H, ArCH, } J 8.0 \text{ Hz}), 7.35 \text{ (d, 1H, ArCH, } J 8.0 \text{ Hz}), 7.07 \text{ (t, 1H, ArCH, } J 8.0 \text{ Hz), 3.04 \text{ (t, 2H, NCH}_2, J 6.5 \text{ Hz), 2.90 \text{ (t, 2H, ArCH}_2, J 6.5 \text{ Hz), 1.58 \text{ (br s, 2H, NCH}_2); } ^{13}C \text{ NMR (d}_6\text{-DMSO, 100 MHz) } \delta_C 135.1 \text{ (ArCquat), 128.8 \text{ (ArCquat), 124.3 \text{ (ArCH), 122.7 \text{ (ArCH), 120.4 \text{ (ArCH), 118.1 \text{ (ArCH), 114.9 \text{ (ArCquat), 104.8 \text{ (ArBr), 42.3 \text{ (NCH}_2), 29.5 \text{ (ArCH); m/z } 239 ([M+H]^+, 100\%), HRMS (ES+) exact mass calculated for [M+H]^+ (C}_10\text{H}_{12}\text{BrN}_2^+) requires m/z 239.0187 & 241.0158 found m/z 239.0178 & 241.0157.}
\]

2.4.2. Preparation and characterisation of \(19b\)

\[
\text{2-[(4-chloro-1H-indol-3-yl)ethanamine}
\]

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 an orange solid.

\[
\text{m.p. } 83-93 \degree C; \text{ FT-IR } \nu_{\text{max}} 3351 (\text{NH}_2), 3294 (\text{ArNH}) \text{; } ^1H \text{ NMR (CDCl}_3, 400 \text{ MHz}) \delta_H 9.02 \text{ (br s, 1H, ArNH)}, 7.22 \text{ (dd, 1H, ArCH, } J 6.5 \text{ Hz, 2.5 Hz), 7.08-7.02 \text{ (m, 2H, ArCH), 6.99 \text{ (s, 1H, ArCH), 3.13 \text{ (t, 2H, NCH}_2, J 6.5 \text{ Hz), 3.06 \text{ (t, 2H, ArCH}_2, J 6.5 \text{ Hz), 1.72 \text{ (br s, 2H, NH}_2); } ^{13}C \text{ NMR (CDCl}_3, 100 \text{ MHz) } \delta_C 138.1 \text{ (ArCquat), 126.3 \text{ (ArCquat), 124.1 \text{ (ArCquat), 123.9 \text{ (ArCH), 122.3 \text{ (ArCH), 120.3 \text{ (ArCH), 113.7 \text{ (ArCquat), 110.0 \text{ (ArCH), 43.5 \text{ (NCH}_2), 30.4 \text{ (ArCH); m/z } 195 ([M+H]^+, 100\%), HRMS (ES+) exact mass calculated for [M+H]^+ (C}_10\text{H}_{12}\text{ClN}_2^+) requires m/z 195.0684 & 197.0654 found m/z 195.0681 & 197.0656.}
\]

2.4.3. Preparation and characterisation of \(20g\)

\[
\text{3-[(2-nitroethyl)-1H-indole-5-carbonitrile}
\]
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\textsubscript{max} 3290 (ArN–H), 2222 (C≡N), 1539 (NO\textsubscript{2} (asy)), 1369 (NO\textsubscript{2} (sy)); \textsuperscript{1}H NMR (CD\textsubscript{3}OD, 400 MHz) δ\textsubscript{H} 8.05 (s, 1H, ArC\textsubscript{H}), 7.49 (d, 1H, ArC\textsubscript{H}, J 8.5 Hz), 7.40 (d, 1H, ArC\textsubscript{H}, J 8.5 Hz), 7.30 (s, 1H, ArC\textsubscript{H}), 4.79-4.71 (m, 2H, NO\textsubscript{2}C\textsubscript{H}\textsubscript{2}), 3.50-3.45 (m, 2H, ArC\textsubscript{H}\textsubscript{2}); \textsuperscript{13}C NMR (CD\textsubscript{3}OD, 100 MHz) δ\textsubscript{C} 138.8 (ArC\textsubscript{quat}), 127.1 (ArC\textsubscript{quat}), 125.9 (ArC\textsubscript{H}), 124.4 (ArC\textsubscript{H}), 124.1 (ArC\textsubscript{H}), 120.8 (ArC\textsubscript{N}), 112.6 (ArC\textsubscript{H}), 111.1 (ArC\textsubscript{quat}), 101.7 (ArC\textsubscript{quat}), 75.8 (O\textsubscript{2}NCH\textsubscript{2}), 23.0 (ArC\textsubscript{H}); m/z (ES+) 238 ([M+Na]\textsuperscript{+}, 100%), HRMS (ES+) exact mass calculated for [M+Na]\textsuperscript{+} (C\textsubscript{11}H\textsubscript{9}N\textsubscript{3}NaO\textsubscript{2}\textsuperscript{+}) 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)-1H-indole-5-carbonitrile

A solution of nitroalkane 20g (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\textsubscript{4}. Concentration afforded the title compound 19g as a light brown solid (88% yield).

m.p. 114-125 °C; FT-IR ν\textsubscript{max} 3224 (ArN–H, NH\textsubscript{2}), 2216 (C≡N); \textsuperscript{1}H NMR (CD\textsubscript{3}OD, 400 MHz) δ\textsubscript{H} 8.03 (br s, 1H, ArC\textsubscript{H}), 7.47 (d, 1H, ArC\textsubscript{H}, J 8.5 Hz), 7.38 (d, 1H, ArC\textsubscript{H}, J 8.5 Hz), 7.28 (br s, 1H, ArC\textsubscript{H}), 2.95 (br s, 4H, NCH\textsubscript{2}), 2.05 (br s, 3H, ArC\textsubscript{H}); \textsuperscript{13}C NMR (CD\textsubscript{3}OD, 100 MHz) δ\textsubscript{C} 139.8 (ArC\textsubscript{quat}), 127.0 (ArC\textsubscript{quat}), 126.0 (ArC\textsubscript{H}), 124.4 (ArC\textsubscript{H}), 122.0 (ArC\textsubscript{N}), 111.2 (ArC\textsubscript{H}), 101.6 (ArC\textsubscript{quat}), 78.5 (O\textsubscript{2}NCH\textsubscript{2}), 23.0 (ArC\textsubscript{H}); m/z (ES+) 239 ([M+Na]\textsuperscript{+}, 100%), HRMS (ES+) exact mass calculated for [M+Na]\textsuperscript{+} (C\textsubscript{12}H\textsubscript{11}N\textsubscript{3}NaO\textsubscript{2}\textsuperscript{+}) requires m/z 239.0620 & 240.0624 found m/z 239.0627 & 240.0627.
MHZ) \( \delta_{C} 139.0 \) (Ar\( _{\text{quat}} \)), 127.9 (Ar\( _{\text{quat}} \)), 125.3 (Ar\( C \)), 124.3 (Ar\( C \)), 124.1 (Ar\( C \)), 121.0 (Ar\( C_{\text{CN}} \)), 113.7 (Ar\( _{\text{quat}} \)), 112.5 (Ar\( C \)), 101.2 (Ar\( C_{\text{CN}} \)), 27.8 (Ar\( CH_{2} \)); \text{m}/z (ES−) 186 ([M+H]\(^{+}\), 100\%)

2.5. General procedure D for preparation of 5

To a stirred solution of sulfonyl chloride\(^{9}\) (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 triethylamine (1.1 eq) in dichloromethane (7 ml/mmol of tryptamine). The mixture was stirred at -78 °C for 5 to 10 mins then concentrated \textit{in vacuo} (in a room temperature water bath) to give the crude product. The residue was purified by flash column chromatography (CH\( _{2} Cl_{2}:Et_{2}O, 1:0\) to 8:2) to give the desired sulfonamide derivative 5.

2.5.1. Preparation and characterisation of 5a

\textit{N}-(2-(1\textit{H}-indol-3-yl)ethyl]but-3-yn-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.

\textbf{m.p.} 122.4-122.5 °C; \textbf{FT-IR} \text{v}_{\text{max}} 3419 (N–H), 3409 (N–H), 1306 (S=O\( _{\text{sy}} \)), 1126 (S=O\( _{\text{as}} \)); \textbf{\( ^{1}H\) NMR} (CDCl\( _{3}, 400\) MHz) \( \delta_{H} 8.10 \) (bs, 1H, Ar\( NH_{2} \)), 7.60 (d, 1H, Ar\( C_{H} \), J 8.0 Hz), 7.39 (d, 1H, Ar\( C_{H} \), J 8.0 Hz), 7.23 (t, 1H, Ar\( C_{H} \), J 8.0 Hz), 7.16 (t, 1H, Ar\( C_{H} \), J 8.0 Hz), 7.1 (d, 1H, Ar\( C_{H} \), J 2.5 Hz), 4.34 (t, 1H, CH\( _{2}\)NH, J 6.0 Hz), 3.46 (q, 2H, Ar\( CH_{2}CH_{2} \), J 6.0 Hz), 3.11 (t, 2H, S\( CH_{2} \), J 7.0 Hz), 3.07 (t, 2H, Ar\( CH_{2} \), J 6.5 Hz), 2.59 (td, 2H, S\( CH_{2}CH_{2} \), J 7.0 Hz, 3.0 Hz), 1.65 (t, 1H, C=CH\( J \) 3.0 Hz); \textbf{\( ^{13}C\) NMR} (CDCl\( _{3}, 100\) MHz) \( \delta: 136.4 \) (Ar\( _{\text{quat}} \)), 126.9 (Ar\( _{\text{quat}} \)), 122.8 (Ar\( C \)), 122.5 (Ar\( C \)), 119.7 (Ar\( C \)), 118.6 (Ar\( C \)), 111.7 (Ar\( _{\text{quat}} \)), 111.4 (Ar\( C \)), 79.8 (HC\( \equiv C \)), 79.1 (HC\( \equiv C \))
70.5 (C≡CH), 49.9 (SC\textsubscript{2}H\textsubscript{2}), 43.3 (NH\textsubscript{2}CH\textsubscript{2}), 26.2 (Ar\textsubscript{2}CH\textsubscript{2}), 14.1 (HCC\textsubscript{2}H\textsubscript{2}); \textit{m/z} (ES\textsuperscript{+}) 299 ([M+Na\textsuperscript{+}], 100\%), \textbf{HRMS} (ES\textsuperscript{+}) exact mass calculated for [M+Na\textsuperscript{+}]\textsuperscript{+} (C\textsubscript{14}H\textsubscript{16}N\textsubscript{2}O\textsubscript{2}S\textsuperscript{2}Na\textsuperscript{+}) requires \textit{m/z} 299.0825, found \textit{m/z} 299.0822.

2.5.2. Prepar\textbf{ation and characterisation of 5b}

\textbf{N-[2-\{(4-chloro-1H-indol-3-yl)ethyl\}but-3-yn-1-sulfonamide}

\begin{center}
\includegraphics[width=0.5\textwidth]{5b.png}
\end{center}

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

\textbf{m.p.} 84-85 °C; \textbf{FT-IR} \nu\textsubscript{max} 3381 (\textit{N}-\textit{H}), 3280 (\textit{N}-\textit{H}), 1312 (S=O (as)), 1129 (S=O (sy)); \textbf{\textit{\textit{\textit{1H NMR}}} (CDCl\textsubscript{3}, 400 MHz)} \delta\textsubscript{H} 8.21 (br s, 1H ArN\textsubscript{H}), 7.29 (dd, 1H, ArCH\textsubscript{2}, J 5.5 Hz, 3.0 Hz), 7.03 (d, 1H, ArCH\textsubscript{2}, J 2.0 Hz), 7.06-7.12 (m, 2H, ArCH\textsubscript{2}), 4.33 (t, 1H, SN\textsubscript{H}), 3.51 (q, 2H, NC\textsubscript{2}H\textsubscript{2}, J 6.5 Hz), 3.27 (t, 2H, ArCH\textsubscript{2}, J 6.5 Hz), 3.14 (t, 2H, SCH\textsubscript{2}, J 7.0 Hz), 2.63 (td, 2H, SCH\textsubscript{2}CH\textsubscript{2}, J 7.0 Hz, 3.0 Hz), 1.69 (t, 1H, C≡CH, J 3.0 Hz); \textbf{\textit{\textit{\textit{13C NMR}}} (CDCl\textsubscript{3}, 100 MHz)} \delta\textsubscript{C} 138.0 (ArC\textsubscript{quat}), 126.0 (ArC\textsubscript{quat}), 124.6 (ArCH), 123.8 (ArC\textsubscript{quat}), 122.9 (ArCH), 120.7 (Ar\textit{CH}), 112.0 (ArC\textsubscript{quat}), 110.2 (ArCH), 79.8 (HC\textsubscript{≡}\textit{C}), 70.5 (C=\textit{CH}), 49.8 (SC\textsubscript{2}H\textsubscript{2}), 44.6 (NCH\textsubscript{2}), 27.1 (Ar\textit{CH}), 14.1 (SCH\textsubscript{2}CH\textsubscript{2}); \textit{m/z} (ES\textsuperscript{+}) 333 ([M+Na\textsuperscript{+}], 100\%), \textbf{HRMS} (ES\textsuperscript{+}) exact mass calculated for [M+Na\textsuperscript{+}]\textsuperscript{+} (C\textsubscript{14}H\textsubscript{15}ClN\textsubscript{2}O\textsubscript{2}SNa\textsuperscript{+}) requires \textit{m/z} 333.0435 & 335.0406 found 333.0431 & 335.0401.

2.5.3. Preparation and characterisation of \textbf{5c}

\textbf{N-[2-\{(5-bromo-1H-indol-3-yl)ethyl\}but-3-yn-1-sulfonamide}

\begin{center}
\includegraphics[width=0.5\textwidth]{5c.png}
\end{center}

The title compound \textbf{5c} was synthesised according to general procedure D to give \textbf{5c} as a brown solid (25\% yield). Recrystallization from ethanol gives an off white solid.
m.p. 68-70 °C; FT-IR νmax 3415, 3394 (N–H and ArN–H), 1305 (S=O (as)) cm⁻¹, 1132 (S=O (sy)) cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ₉ 8.12 (bs, 1H, Ar NH), 7.71 (d, 1H, Ar CH, 7.15 Hz), 7.31 (dd, 1H, Ar CH, J 8.5 Hz, 2.0 Hz), 7.27 (dd, 1H, Ar CH, J 8.5 Hz), 7.13 (1H, Ar CH, J 2.0 Hz), 4.29 (t, 2H, S CH₂, J 6.5 Hz), 3.45 (q, 2H, NCH₂, J 6.5 Hz), 3.15 (t, 2H, S CH₂, J 7.0 Hz), 3.03 (t, 2H, NCH₂CH₂, J 6.5 Hz), 2.63 (td, 2H, SCH₂CH₂, J 7.0 Hz, 2.5 Hz), 1.75 (t, 1H, C ≡ CH, J 2.5 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 135.0 (Ar C Br), 128.7 (Ar Cquat), 125.4 (Ar CH), 121.2 (Ar CH), 113.0 (Ar Cquat), 79.8 (HC≡C), 50.0 (S C H₂), 43.1 (N C H₂), 26.1 (NCH₂CH₂), 14.1 (NCH₂CH₂); m/z (ES+) 377 ([M+Na]+, 100%), HRMS (ES+) exact mass calculated for [M+Na]+ (C₁₄H₁₆BrN₂O₂SNa) requires m/z 376.9930 & 378.9909, found m/z 376.9925 & 378.9904.

2.5.4. Preparation and characterisation 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 νmax 3416 (N–H), 3290 (Ar–H), 1301 (S=O (as)) cm⁻¹, 1127 (S=O (sy)) cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δH 8.10 (br s, 1H, Ar NH), 7.55 (s, 1H, Ar CH), 7.45 (d, 1H, Ar CH, J 8.5 Hz), 7.25 (d, 1H, Ar CH, J 8.5 Hz), 7.09 (s, 1H, Ar CH), 4.31 (t, 1H, S NH, J 6.5 Hz), 3.44 (q, 2H, NCH₂, J 6.5 Hz), 3.12 (t, 2H, S CH₂, J 7.0 Hz), 3.04 (t, 2H, Ar CH₂, J 6.5 Hz), 2.61 (td, 2H, S CH₂CH₂, J 7.0 Hz, 2.5 Hz), 1.73 (t, 1H, C≡CH, J 2.5 Hz); ¹³C NMR (CDCl₃, 100 MHz) δC 137.2 (Ar Cquat), 125.9 (Ar Cquat), 123.3 (Ar CH), 123.0 (Ar CH), 119.8 (Ar CH), 116.0 (Ar CBr), 114.4 (Ar CH), 112.0 (Ar Cquat), 79.8 (HC≡C), 70.5 (HC≡C), 50.0 (SCH₂), 43.3 (NCH₂), 26.1 (Ar CH₂), 14.1 (HC≡CH₂); m/z (ES+) 377 ([M+Na]+, 100%), HRMS (ES+) exact mass calculated for [M+Na]+ (C₁₄H₁₃BrN₂O₂SNa) 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

- S- 17 - -
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<sub>max</sub> 3419 (N–H), 3294 (Ar=N–H), 1300 (S=O<sub>(as)</sub>), 1126 (S=O<sub>(v)</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>HN</sub>: 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 24 Hz), 3.43 (q, 2H, NHCH<sub>2</sub>, J 6.5 Hz), 3.37 (t, 2H, SCH<sub>2</sub>, J 7.0 Hz), 3.01 (t, 2H, ArCH<sub>2</sub>, J 6.5 Hz), 2.61 (td, 2H, SCH<sub>2</sub>CH<sub>2</sub>, J 7.0 Hz, 3.0 Hz), 1.73 (t, 1H, C=C=CH, J 2.5 Hz) <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ<sub>CN</sub>: 157.8 (d, Ar CF, J 236 Hz), 132.9 (Ar<sub>quat</sub>), 127.3 (d, Ar<sub>quat</sub>, J 10 Hz), 124.6 (Ar CH), 121.1 (d, Ar CH, J 10 Hz), 111.8 (d, Ar<sub>quat</sub>, J 4.8 Hz), 110.8 (d, Ar CH, J 26 Hz), 103.5 (d, Ar CH, J 24 Hz), 79.8 (HC=C), 70.5 (C=CH), 49.9 (SCH<sub>2</sub>), 43.1 (SNCH<sub>2</sub>), 26.2 (Ar CH<sub>2</sub>), 14.1 (SCH<sub>2</sub>CH<sub>2</sub>); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz), -124.0 (ArF); m/z (ES+) exact mass calculated for [M+Na]<sup>+</sup> (C<sub>14</sub>H<sub>16</sub>FN<sub>2</sub>O<sub>2</sub>SNa<sup>-</sup>) 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-1H-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<sub>max</sub> 3419 (N–H), 3307 (ArF); 3170 & 3180 (HC=C), 3294 (HC=C), 3170 & 3180 (HC=N), 1301 (S=O<sub>(as)</sub>), 1127 (S=O<sub>(v)</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>HN</sub>: 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 26 Hz), 3.44 (q, 2H, NHCH<sub>2</sub>, J 6.5 Hz), 3.11 (t, 2H, SCH<sub>2</sub>, J 7.0 Hz), 3.03 (t, 2H, ArCH<sub>2</sub>, J 6.5 Hz), 2.60 (td, 2H, SCH<sub>2</sub>CH<sub>2</sub>, J 7.0 Hz, 2.5 Hz), 1.74 (t, 1H, C=C=CH, J 3.0 Hz) <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ<sub>CN</sub>: 160.1 (d, Ar CF, J 239 Hz), 136.3 (d, Ar<sub>quat</sub>, J 12 Hz), 123.6 (Ar<sub>quat</sub>, 123.0 (d, Ar CH, J 3 Hz)), 119.3 (d, Ar CH, J 10 Hz) 111.8 (Ar<sub>quat</sub>, 108.5 (d, Ar CH, J 24 Hz), 97.7 (d, Ar CH, J 26 Hz), 79.8 (HC=C), 70.5 (C=CH), 49.9 (SCH<sub>2</sub>), 43.1 (SNCH<sub>2</sub>), 26.2 (Ar CH<sub>2</sub>), 14.1 (SCH<sub>2</sub>CH<sub>2</sub>); <sup>19</sup>F NMR (CDCl<sub>3</sub>, 376 MHz), -120.4 (ArF); m/z (ES+) exact mass calculated for [M+Na]<sup>+</sup> (C<sub>13</sub>H<sub>14</sub>FN<sub>2</sub>O<sub>2</sub>SNa<sup>-</sup>) 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-1H-indol-3-yl)ethyl]but-3-yne-1-sulfonamide**

- S 18 -
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\text{max} 3339 (N–H), 3294 (ArN–H), 2225 (C=\text{N}), 1318 (S=O\text{(aq)}), 1136 (S=O\text{(aq)}); ¹H NMR (d₆-DMSO, 400 MHz) δ\text{H} 11.46 (br s, 1H, ArNH), 8.09 (s, 1H, ArCH), 7.51 (d, 1H, ArCH\text{)}, \text{J} 8.0 Hz), 7.44-7.39 (m, 2H, ArCH); 7.26 (t, 1H, SNH, J 6.0 Hz), 3.23 (td, 2H, NCH₂, J 7.0 Hz, 6.0 Hz), 3.15 (t, 2H, SCH₂, J 7.5 Hz), 2.93 (t, 1H, C=CH₂, J 3.0 Hz), 2.90 (t, 2H, ArCH₂, J 7.0 Hz), 2.50 (signal hidden under DMSO peak, confirmed by HSQC and COSY) (m, 2H, HC=CCH₂, J 7.5 Hz, 3.0 Hz); ¹³C NMR (d₆-DMSO, 100 MHz) δ\text{C} 138.7 (Ar\text{C}≡\text{C}), 127.9 (Ar\text{C}≡\text{C}), 126.7 (Ar\text{C}≡\text{C}), 125.1 (Ar\text{C}≡\text{C}), 124.5 (Ar\text{C}≡\text{C}), 112.6 (Ar\text{C}≡\text{C}), 111.4 (Ar\text{C}≡\text{C}), 101.2 (Ar\text{C}≡\text{C}), 82.0 (HC≡\text{C}), 73.4 (C≡\text{C}), 50.2 (SC\text{H}_₂), 43.9 (NCH₂), 26.4 (ArCH₂), 14.2 (SC\text{H}_₂\text{CCH}_₂); m/z (ES⁺) 324 ([M+Na]⁺, 100%), HRMS (ES⁺) exact mass calculated for [M+Na]⁺ (C₁₃H₁₀N₂O₃SNa⁺) requires m/z 324.0777 & 325.0810, found m/z 324.0770 & 325.0812.

#### 2.5.8. Preparation and characterisation of 5h

**N-[2-(5-methoxy-1H-indol-3-yl)ethyl]but-3-yn-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\text{max} 3405 (SN–H), 3282 (ArN–H), 1317 (S=O\text{(aq)}), 1134 (S=O\text{(aq)}); ¹H NMR (CDCl₃, 400 MHz) δ\text{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, OCH₃), 3.44 (q, 2H, NCH₂, J 6.5 Hz), 3.11 (t, 2H, SCH₂, J 7.0 Hz), 3.02 (t, 2H, ArCH₂, J 6.5 Hz), 2.59 (td, 2H, SCH₂CH₂, J 7.0 Hz), 1.72 (t, 1H, C=CH₂, J 2.8 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ\text{C} 154.2 (Ar\text{C}≡\text{OMe}), 131.5 (Ar\text{C}≡\text{C}), 127.4 (Ar\text{C}≡\text{C}), 123.5 (Ar\text{C}≡\text{C}), 112.6 (Ar\text{C}≡\text{C}), 112.2 (Ar\text{C}≡\text{C}), 111.4 (Ar\text{C}≡\text{C}), 100.5 (Ar\text{C}≡\text{C}), 79.8 (HC≡\text{C}), 70.5 (C≡\text{C}), 56.0 (OCH₃), 49.9 (SC\text{H}_₂), 43.3 (NCH₂), 26.2 (ArCH₂), 14.1 (SC\text{H}_₂\text{CCH}_₂\text{CCH}_₂); m/z (ES⁺) 329 ([M+Na]⁺, 100%), HRMS (ES⁺) exact mass calculated for [M+Na]⁺ (C₁₃H₁₀N₂O₃SNa⁺) 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-yn-1-yl]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) \(\delta_{H}\): 7.99 (br s, 1H, ArN–H), 7.37 (s, 1H, ArC\(\equiv\)C), 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, SN–H, J 6.5 Hz), 3.45 (q, 2H, NC\(\equiv\)H\(_2\), J 6.5 Hz), 3.11 (t, 2H, SC\(\equiv\)H\(_2\), J 7.5 Hz), 3.04 (t, 2H, ArC\(\equiv\)CH\(_2\), J 6.5 Hz), 2.59 (td, 2H, SCH\(_2\)C\(\equiv\)H\(_2\), J 7.0 Hz, 2.5 Hz), 2.47 (s, 3H, ArC\(\equiv\)H\(_3\)), 1.64 (t, 1H, C\(\equiv\)C\(\equiv\)C, J 2.5 Hz); \(^1^C\) NMR (CDCl\(_3\), 125 MHz) \(\delta_{C}\): 134.8 (ArC\(\equiv\)quat), 129.0 (ArCMe), 127.2 (ArC\(\equiv\)quat), 124.0 (ArCH), 122.9 (ArCH), 118.2 (ArCH), 111.1 (ArCH), 111.0 (ArC\(\equiv\)quat), 79.8 (HC\(\equiv\)C), 70.5 (C\(\equiv\)CH\(_2\)), 49.9 (SC\(\equiv\)H), 43.3 (NC\(\equiv\)H\(_2\)), 26.2 (ArCH\(_2\)), 21.5 (ArCH\(_3\)), 14.1 (HCC\(\equiv\)C\(_2\)); m/z (ES+) 313 ([M+Na]\(^+\), 100%), HRMS (ES+) exact mass calculated for [M+Na]\(^+\) (C\(_{15}\)H\(_{18}\)N\(_2\)NaO\(_2\)S\(^+\)) requires m/z 313.0981 & 314.1014 found 313.0973 & 314.1009.

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

*N*-[[2-[(7-methyl-1H-indol-3-yl)ethyl]but-3-yn-1-yl]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) \(\delta_{H}\): 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, J 7.5 Hz), 7.03 (d, 1H, ArCH, J 7.5 Hz), 4.36 (t, 1H, SN–H, J 6.0 Hz), 3.46 (q, 2H, NC\(\equiv\)H\(_2\), J 6.0 Hz), 3.09 (t, 2H, SC\(\equiv\)H\(_2\), J 7.0 Hz), 3.06 (t, 2H, ArCH\(_2\), J 6.0 Hz), 2.57 (td, 2H,
SCH₂CH₂, J 7.0 Hz, 3.0 Hz), 2.50 (s, 3H, ArCH₃), 1.68 (t, 1H, C=CH₂, J 3.0 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 136.1 (Ar₃ quat), 126.5 (Ar₃ quat), 122.9 (ArCH), 122.5 (ArCH), 120.6 (ArCH₂), 119.9 (ArCH), 116.3 (ArCH), 112.1 (Ar₃ quat), 79.8 (H(C=CH)), 70.5 (C≡CH), 49.9 (SCH₂), 43.3 (N(CH₃)), 26.3 (ArCH₂), 16.6 (ArCH₂), 14.1 (SCH₂CH₂); m/z (ES+) 313 ([M+Na]⁺, 100%), HRMS (ES+) exact mass calculated for [M+Na]⁺ (C₁₅H₁₂N₂O₂SNa) 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(quat)), 1129 (S=O(qmt)); ¹H NMR (CDCl₃, 500 MHz) δ H 8.04 (br s, 1H, ArNH₂), 7.45 (d, 1H, ArCH J 7.5 Hz), 7.11 (d, 1H, ArCH J 3.0 Hz), 7.11 (t, 1H, ArCH J 7.5 Hz), 7.07 (d, 1H, ArCH J 7.5 Hz), 4.31 (t, 1H, SNH J 6.5 Hz), 3.46 (q, 2H, NCH₂), 3.58 (t, 2H, ArCH₂), 3.07 (t, 2H, NCH₂CH₂ J 6.5 Hz), 2.87 (q, 2H, ArCH₂CH₂ J 7.5 Hz), 2.59 (td, 2H, S CH₂CH₂ J 7.5 Hz, 3.0 Hz), 1.65 (t, 1H, C=CH J 3.0 Hz), 1.37 (t, 3H, ArCH₂CH₂ J 7.5 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ C 135.3 (Ar₃ quat), 126.8 (Ar₃ quat), 126.7 (Ar₃ quat), 122.4 (ArCH), 121.0 (ArCH), 120.1 (ArCH), 116.3 (ArCH), 112.1 (Ar₃ quat), 79.7 (C=CH), 70.4 (C=CH), 49.9 (SCH₂), 43.3 (N(CH₃)), 26.3 (NCH₂CH₂), 24.0 (ArCH₂CH₃), 14.1 (SCH₂CH₂), 13.8 (ArCH₂CH₃); m/z (ES-) 303 ([M–H]⁻, 100%), HRMS (ES-) exact mass calculated for [M–H]⁻ (C₁₅H₁₀N₂O₂SNa) 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-biphenylPtBu₂)(MeCN)]SbF₆ (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 (CH₂Cl₂:MTBE (CH₃OC(CH₃)₂) 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-biphenylPtBu₂)(MeCN)]SbF₆ (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 (CH₂Cl₂:MTBE (CH₃OC(CH₃)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 tₚ = 6.0 min, minor tₚ = 15.4 min); [α]D +113.8 (c 0.16, 1:1 MeOH:CH₂Cl₂).

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

m.p. 279-283 °C; FT-IR νmax 3397 (N–H), 1289 (S=O(as)), 1145 (S=O(sy)); ¹H NMR (CDCl₃, 500 MHz) δH 7.78 (br s, 1H, ArNH), 7.50 (d, 1H, ArCH, J 8.0 Hz), 7.35 (d, 1H, ArCH, J 8.0 Hz), 7.22 (ddd, 1H, ArCH, J 8.0 Hz, 7.0 Hz, 1.0 Hz) 7.15 (ddd, 1H, ArCH, J 8.0 Hz, 7.0 Hz, 1.0 Hz), 4.05 (dd, 1H, SNCH₂H₃, J 14.5 Hz, 5.0 Hz), 3.99 (ddd, 1H, SNCH₂H₃, 15.0 Hz, 12.0 Hz, 4.5 Hz), 3.19 (m, 2H, ArCH₂H₅, SCH₂H₅), 2.90 (ddd, 1H, SCH₂H₅, J 12.0 Hz, 7.0 Hz), 2.65 (m, 3H, ArCH₂H₅, SCH₂CH₂H₅), 1.73 (s, 3H, CH₃); ¹³C NMR (CDCl₃, 125 MHz) δC 135.9 (ArCquat), 133.9 (ArCquat), 126.8 (ArCquat), 122.8 (ArCH), 120.1 (ArCH), 118.7 (ArCH), 111.9 (ArCH), 109.7 (ArCquat), 59.1 (NCCH₂), 46.0 (NSCH₂), 38.1 (SNCH₂), 33.6 (NSCH₂CH₂), 28.2 (CCCH₂), 19.9 (ArCH₂); (ES+) 299 [(M+Na)+, 100%], HRMS (ES+) exact mass calculated for [M+Na]+ (C₁₄H₁₆N₂O₂SNa⁺) requires m/z 299.0825 & 300.0858, found m/z 299.0821 & 300.0861.

2.7.2. Preparation and characterisation of 7a
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\textsubscript{max} 3412 (N–H), 1323 (S=O (as)), 1149 (S=O (sy)); \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz) δ\textsubscript{H} 7.73 (br s, 1H, ArN–H), 7.51 (d, 1H, ArCH\textsubscript{3} J 8.0 Hz), 7.34 (d, 1H, ArCH\textsubscript{3} J 8.0 Hz), 7.21 (t, 1H, ArCH\textsubscript{3} J 8.0 Hz), 7.14 (t, 1H, ArCH\textsubscript{3} J 8.0 Hz), 4.97 (d, 1H, NC\textsubscript{H}CH\textsubscript{2} J 11.0 Hz), 3.68 (m, 1H, SNCH\textsubscript{a}H\textsubscript{b}), 3.60 (m, 1H, SNCH\textsubscript{a}H\textsubscript{b}), 3.21 (dt, 1H, NSC\textsubscript{H}aCH\textsubscript{b} J 13.5 Hz, 3.5 Hz), 3.02 (td, 1H, NSCH\textsubscript{2}CH\textsubscript{2} J 13.5 Hz, 4.0 Hz), 2.95 (m, 1H, ArCH\textsubscript{3}H\textsubscript{b}), 2.89 (dt, 1H, ArCH\textsubscript{3}H\textsubscript{b} J 15.5 Hz, 4.5 Hz), 2.44 (qt, 1H, NSCH\textsubscript{2}CH\textsubscript{2} J 14.0 Hz, 3.0 Hz), 1.84 (m, 1H, NSCH\textsubscript{2}CH\textsubscript{2}H\textsubscript{b}); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz) δ\textsubscript{C} 136.2 (ArC\textsubscript{quat}), 132.0 (ArC\textsubscript{quat}), 126.5 (ArC\textsubscript{quat}), 122.4 (ArCH), 120.0 (ArCH), 118.4 (ArCH), 110.9 (ArCH), 108.7 (ArC\textsubscript{quat}), 55.5 (NCH\textsubscript{2}CH\textsubscript{2}), 46.8 (NSCH\textsubscript{a}H\textsubscript{b}), 39.8 (SNCH\textsubscript{2}CH\textsubscript{2}), 27.8 (NSCH\textsubscript{2}CH\textsubscript{2}H\textsubscript{b}), 21.4 (ArCH); m/z (ES+) 299 ([M+Na]\textsuperscript{+}, 100%), HRMS (ES+) exact mass calculated for [M+Na]\textsuperscript{+} (C\textsubscript{14}H\textsubscript{16}N\textsubscript{2}O\textsubscript{2}SNa\textsuperscript{+}) 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\textsubscript{R} = 5.8 min, minor t\textsubscript{R} = 8.1 min); [\alpha]_{D}^{25} = +94.3 (c 0.21, 1:1 MeOH:CH\textsubscript{2}Cl\textsubscript{2}).

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

m.p. 208 °C (decomposition); FT-IR ν\textsubscript{max} 3321 (N–H), 1303 (S=O (as)); \textsuperscript{1}H NMR (CD\textsubscript{2}OD, 500 MHz) δ\textsubscript{H} 7.25 (dd, 1H, ArCH\textsubscript{3} J 8.0 Hz, 1.0 Hz), 7.03 (t, 1H, ArCH\textsubscript{3} J 8.0 Hz), 6.96 (d, 1H, ArCH\textsubscript{3} J 7.5 Hz), 3.92 (dd, 1H, NCH\textsubscript{2}H\textsubscript{b} J 15.0 Hz, 5.5 Hz), 3.37 (ddd, 1H, NCH\textsubscript{2}H\textsubscript{b} J 15.0 Hz, 12.0 Hz, 4.5 Hz), 3.32-3.23 (m, 2H, NCH\textsubscript{2}CH\textsubscript{2}H\textsubscript{b}, SCH\textsubscript{2}H\textsubscript{b}), 3.09 (ddd, 1H, NCH\textsubscript{2}CH\textsubscript{2}H\textsubscript{b} J 15.5...
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 tₗ = 10.0 min, minor tₗ = 27.2 min; [α]D = +101.6 (c 0.25, 1:1 MeOH:CH₂Cl₂).

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)); 1H NMR (d₆-acetone, 500 MHz) δH 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 (ddd, 1H, ArCH, J 8.5 Hz, 2.0 Hz), 3.91 (dd, 1H, SC₃H, J 15.5 Hz, 6.0 Hz), 3.37 (ddd, 1H, SC₃H, J 15.0 Hz, 12.5 Hz, 6.0 Hz), 2.95-2.80 (m, 2H, NC₃H, ArCH₂, 2.65-2.60 (m, 2H, ArCH₂, SCH₂CH₃), 1.72 (s, 3H, CH₃); 13C NMR (d₆-acetone, 125 MHz) δC 138.2 (ArBr), 136.0 (ArCquat), 129.6 (ArCquat), 125.2 (ArCquat), 121.6 (ArC), 113.8 (ArC), 112.7 (ArCquat), 108.6 (ArCquat), 59.8 (NC₃H), 46.7 (NC₃H), 38.1 (SC₃H), 34.0 (ArC), 28.0 (CH₃), 20.5 (SCH₂CH₃); m/z (ES−) 355 ([M–H]−, 100%), HRMS (ES+) exact mass calculated for [M+Na]⁺ (C₁₄H₁₅ClN₂OSNa⁺) 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)); ¹H NMR (CD_3OD, 500 MHz) δ_H 7.48 (d, 1H, ArC_H, J 1.5 Hz), 7.34 (d, 1H, ArC_H, J 8.5 Hz), 7.14 (dd, 1H, ArC_H, J 8.5 Hz, 1.5 Hz), 3.94 (dd, 1H, NC_H, J 15.0 Hz, 6.0 Hz), 3.38-3.27 (signal hidden under methanol peak, confirmed by HSQC and COSY) (m, 1H, SC_H), 3.05 (ddd, 1H, NCH_2C_H, J 15.5 Hz, 12.0 Hz, 6.0 Hz), 2.92 (ddd, 1H, SCH_2C_H, J 12.5 Hz, 10.0 Hz, 7.0 Hz), 2.76 (ddd, 1H, SCH_2C_H, J 13.5 Hz, 7.0 Hz, 5.5 Hz), 2.63-2.56 (m, 2H, NCH_2C_H, SCH_2C_H, 1.70 (s, 3H, C_H); ¹³C NMR (CD_3OD, 125 MHz) δ_C 138.6 (ArC_quat), 137.1 (ArC_quat), 127.0 (ArC_quat), 123.3 (ArC), 120.5 (ArC), 116.1 (ArCBr), 114.9 (ArC), 109.1 (ArC_quat), 60.7 (NCH_2), 47.0 (SCH_2), 38.6 (NCH_2), 34.2 (SCH_2C_H), 27.9 (NCH_3), 20.8 (NCH_2C_H); m/z (ES+) 377 ([M+Na]^+, 100%), HRMS (ES+) exact mass calculated for [M+Na]^+ (C_14H_15BrN_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.
**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<sub>r</sub> = 7.4 min, minor t<sub>r</sub> = 25.1 min; [α]<sup>D</sup> = +138.1 (c 0.24, 1:1 MeOH:CH₂Cl₂).

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<sub>r</sub> = 7.2 min, minor t<sub>r</sub> = 24.2 min;
([M+Na]⁺, 100%), HRMS (ES⁺) exact mass calculated for [M+Na]⁺ (C₁₄H₁₅FN₂O₂SNa⁺) 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 tᵣ = 13.1 min, minor tᵣ = 53.6 min; [α]ᵦ = +95.9 (c 0.16, 1:1 MeOH:CH₂Cl₂).

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

m.p. 210 °C (decomposition); FT-IR νmax 3316 (N–H), 2219 (C≡N), 1302 (S=O (as)), 1134 (S=O (sy)); ¹H NMR (CD₃OD, 500 MHz) δH 7.90 (s, 1H, ArCH), 7.46 (d, 1H, ArCH, J 8.5 Hz), 7.43 (dd, 1H, ArCH, J 8.5 Hz, 1.5 Hz), 3.97 (dd, 1H, NCH₂H₃, J 15.0 Hz, 5.5 Hz), 3.41 (ddd, 1H, NCH₂H₃, 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, SCH₂H₃), 3.09 (ddd, 1H, NCH₂CH₂H₃, J 15.5 Hz, 12.0 Hz, 6.0 Hz), 2.94 (ddd, 1H, SCH₂H₃, J 12.5 Hz, 9.5 Hz, 7.0 Hz), 2.78 (ddd, 1H, SCH₂CH₂H₃, J 13.0 Hz, 7.0 Hz, 5.5 Hz), 2.71–2.59 (m, 2H, SCH₂CH₂H₃, NCH₂CH₂H₃), 1.72 (s, 3H, NCH₂CH₂); ¹³C NMR (CD₃OD, 125 MHz) δC 139.7 (ArCH₃), 139.2 (ArCH₃), 128.0 (ArCH₂), 125.9 (ArCH), 124.9 (ArCH), 121.8 (ArCN), 113.2 (ArCH), 110.0 (ArCN), 102.8 (ArCH₂), 60.5 (NCH₂), 47.0 (SCH₂), 38.4 (NCH₂), 34.1 (SCH₂CH₂), 27.8 (NCH₂H₃), 20.7 (NCH₂CH₂); m/z (ES⁺) 324 ([M+Na]⁺, 100%), HRMS (ES⁺) exact mass calculated for [M+Na]⁺ (C₁₅H₁₅N₂O₂SNa⁺) 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

- S- 27 - -
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 $t_n = 8.2$ min, minor $t_n = 14.3$ min; $[\alpha]_D^{25} = 93.2$ (c 0.734, 1:1 MeOH:CH₂Cl₂).

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

m.p. 210-220 °C (decomposition); FT-IR $\nu_{max}$ 3365 (N–H), 1300 (S=O (as)), 1141 (S=O (sy)); $^1$H NMR (CD$_3$OD, 500 MHz) $\delta_H$ 7.21 (d, 1H, ArCH, J 9.0 Hz), 6.92 (d, 1H, ArCH, J 2.5 Hz), 6.77 (dd, 1H, ArCH, J 9.0 Hz, 2.5 Hz), 3.93 (dd, 1H, NCH$_2$H$_{2n}$, J 14.5 Hz, 5.5 Hz), 3.82 (s, 3H, OCH$_3$), 3.38 (s, 3H, OCH$_3$), 3.28 (dt, 1H, SCH$_2$H$_{2n}$, J 12.0 Hz, 6.0 Hz), 3.05 (ddd, 1H, NCH$_2$H$_{2n}$, J 15.5 Hz, 12.0 Hz, 6.0 Hz), 2.90 (ddd, 1H, SCH$_2$H$_{2n}$, J 12.5 Hz, 10.0 Hz, 7.0 Hz), 2.77 (ddd, 1H, SCH$_2$CH$_3$H$_{2n}$, J 13.0 Hz, 7.0 Hz, 5 Hz), 2.58 (m, 2H, SCH$_2$CH$_3$H$_{2n}$, NCH$_2$CH$_2$H$_{2n}$), 1.70 (s, 3H, NCCH$_3$); $^{13}$C NMR (CD$_3$OD, 125 MHz) $\delta_C$ 155.3 (ArCO), 136.8 (Ar$_{C_{quat}}$), 133.0 (Ar$_{C_{quat}}$), 128.3 (Ar$_{C_{quat}}$), 112.9 (ArCH), 112.7 (ArCH), 108.6 (Ar$_{C_{quat}}$), 101.2 (ArCH), 61.0 (NCCH$_3$), 56.3 (OCH$_3$), 47.1 (SCH$_2$H$_2$), 38.8 (NCH$_3$), 34.3 (SCH$_2$CH$_2$), 28.1 (NCCH$_3$), 21.0 (NCH$_2$CH$_2$); m/z (ES+) 305 ([M+H$^+$], 100%), HRMS (ES+) exact mass calculated for [M+Na$^+$] (C$_{19}$H$_{18}$N$_2$O$_3$SNa$^+$) 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 $t_n = 6.7$ min, minor $t_n = 14.0$ min; $[\alpha]_D^{25} = 101.3$ (c 0.20, 1:1 MeOH:CH₂Cl₂).

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

m.p. 220 °C (decomposition); FT-IR $\nu_{max}$ 3390 (N–H), 1300 (S=O (as)), 1141 (S=O (sy)); $^1$H NMR (CD$_3$OD, 500 MHz) $\delta_H$ 7.21 (br s, 1H, ArCH), 7.20 (d, 1H, ArCH, J 8.0 Hz), 6.95 (dd, 1H, ArCH, J 8.0 Hz, 1.5 Hz), 3.93 (dd, 1H, NCH$_2$H$_{2n}$, J 14.5 Hz, 5.5 Hz), 3.42-
3.35 (m, 1H, NCH$_2$H$_b$), 3.35-3.26 (m, 1H, SCH$_2$H$_b$), 3.05 (ddd, 1H, NCH$_2$CH$_2$H$_b$, J 15.5 Hz, 12 Hz, 6.0 Hz), 2.91 (ddd, 1H, SCH$_2$H$_a$, J 12.0 Hz, 10.0 Hz, 7.0 Hz), 2.78 (ddd, 1H, SCH$_2$CH$_2$H$_b$, J 13.5 Hz, 7.0 Hz, 5.0 Hz), 2.62-2.54 (m, 2H, SCH$_2$CH$_2$H$_b$, NCH$_2$CH$_2$H$_b$), 2.41 (s, 3H, ArCH$_3$), 1.70 (s, 3H, NCC$_2$H$_5$); $^{13}$C NMR (CD$_2$OD, 125 MHz) $\delta$C 136.2 (Ar$_{\text{quat}}$), 136.1 (Ar$_{\text{quat}}$), 129.2 (Ar$_{\text{quat}}$), 128.3 (Ar$_{\text{quat}}$), 124.4 (ArCH), 118.7 (ArCH), 111.7 (ArCH), 108.3 (Ar$_{\text{quat}}$), 61.0 (NCC$_2$H$_5$), 47.1 (SCH$_2$), 38.8 (NCH$_3$), 34.3 (SCH$_2$CH$_2$), 28.1 (NCC$_2$H$_5$), 21.6 (ArCH$_3$), 20.9 (NCH$_2$CH$_2$); m/z (ES$^+$) 313 ([M+Na]$^+$, 100%), HRMS (ES$^+$) exact mass calculated for [M+Na]$^+$ (C$_{13}$H$_{18}$N$_2$O$_3$SNa$^+$) 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 $t_a = 5.0$ min, minor $t_a = 6.1$ min); $[\alpha]_D^{2\theta} = +182.1$ (c 0.25, 1:1 MeOH:CH$_2$Cl$_2$).

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

m.p. 195 °C (decomposition); FT-IR $\nu_{\text{max}}$ 3338 (N-H), 1296 (S=O$_{\text{a}}$), 1125 (S=O$_{\text{v}}$); $^1$H NMR (CD$_2$OD, 500 MHz) $\delta$H 7.25 (dd, 1H, ArCH, J 7.0 Hz, 2.0 Hz), 6.94 (t, 1H, ArCH, J 7.0 Hz), 6.91 (d, 1H, ArCH, J 7.0 Hz), 3.93 (dd, 1H, NCH$_2$H$_b$, J 15.0 Hz, 5.5 Hz), 3.38 (ddd, 1H, NCH$_2$H$_a$, J 15.0 Hz, 12.0 Hz, 4.5 Hz), 3.28 (m, 1H, SCH$_2$H$_b$), 3.07 (ddd, 1H, NCH$_2$CH$_2$H$_b$, J 15.5 Hz, 12.0 Hz, 6.0 Hz), 2.94-2.83 (m, 2H, SCH$_2$H$_b$, SCH$_2$CH$_2$H$_b$), 2.65-2.56 (m, 2H, NCH$_2$CH$_2$H$_b$, SCH$_2$CH$_2$H$_b$), 2.50 (s, 3H, ArCH$_3$), 1.74 (s, 3H, NCC$_2$H$_5$); $^{13}$C NMR (CD$_2$OD, 125 MHz) $\delta$C 137.2 (Ar$_{\text{quat}}$), 135.9 (Ar$_{\text{quat}}$), 127.7 (Ar$_{\text{quat}}$), 123.6 (ArCH), 121.6 (Ar$_{\text{quat}}$), 120.4 (ArCH), 116.7 (ArCH), 109.2 (Ar$_{\text{quat}}$), 61.1 (NCC$_2$H$_5$), 47.1 (SCH$_2$), 38.7 (NCH$_3$), 34.2 (SCH$_2$CH$_2$), 28.0 (NCC$_2$H$_5$), 21.1 (NCH$_2$CH$_2$), 17.1 (ArCH$_3$); m/z (ES$^+$) 313 ([M+Na]$^+$, 100%), HRMS (ES$^+$) exact mass calculated for [M+Na]$^+$ (C$_{13}$H$_{18}$N$_2$O$_3$SNa$^+$) requires m/z 313.0981 & 314.1014, found m/z 313.0973 & 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

- S- 29 - -
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; [α]_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)); ¹H NMR (CD_3OD, 500 MHz) δ_H 7.25 (dd, 1H, ArCH, J 7.0 Hz, 2.5 Hz), 6.99-6.94 (m, 2H, ArCH), 3.93 (dd, 1H, NC\_H_a\_H_b, J 15.0 Hz, 5.5 Hz), 3.39 (ddd, 1H, NCH_a\_H_b\_H_c, J 15.0 Hz, 12.0 Hz, 4.5 Hz), 3.29 (dd, 1H, SCH_a\_H_b, J 11.5 Hz, 7.0 Hz, 5.0 Hz), 3.07 (ddd, 1H, NCH_2\_H_a\_H_b, J 15.5 Hz, 12.0 Hz, 6.0 Hz), 2.95-2.83 (m, 4H, ArCH_2\_CH_3, SCH_2\_H_a, SCH_2\_H_b), 1.74 (s, 3H, NCH_3), 1.34 (t, 3H, ArCH_2\_C\_H_3, J 7.5 Hz); ¹³C NMR (CD_3OD, 125 MHz) δ_C 136.4 (Ar C\_quat), 135.8 (Ar C\_quat), 128.1 (Ar C\_quat), 127.9 (Ar C\_quat), 121.7 (Ar CH), 120.5 (Ar CH), 116.7 (Ar CH), 109.2 (Ar C\_quat), 61.1 (NCCH_3), 47.1 (SCH_2), 38.7 (NCCH_2), 34.2 (SCH_2CH_2), 28.0 (NC\_CH_3), 25.1 (ArCH_2CH_3), 21.1 (NCH_2\_CH_3), 14.9 (ArCH_3CH_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 extension for amide derivatives

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 x 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-(1H-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<sub>max</sub> 3403 (N–H), 3286 (ArN–H), 1641 (C=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ<sub>H</sub> 8.29 (br s, 1H, ArNH), 7.62 (d, 1H, ArCH<sub>2</sub>, J 8.0 Hz), 7.39 (d, 1H, ArCH<sub>2</sub>, J 8.0 Hz), 7.23 (t, 1H, ArCH<sub>2</sub>, J 7.5 Hz), 7.14 (t, 1H, ArCH<sub>2</sub>, J 7.5 Hz), 7.04 (d, 1H, ArCH<sub>2</sub>, J 2.0 Hz), 5.63 (br s, 1H, OCN), 3.62 (q, 2H, NCH<sub>2</sub>, J 6.5 Hz), 2.99 (t, 2H, NCH<sub>2</sub>, J 6.5 Hz), 2.25 (t, 2H, OCCH<sub>2</sub>, J 7.5 Hz), 2.22 (td, 2H, HC≡CCH<sub>2</sub>, J 7.5 Hz, 2.5 Hz), 1.94 (t, 1H, C≡CH<sub>2</sub>, J 2.5 Hz), 1.84 (quin, 2H, OCCH<sub>2</sub>, J 7.5 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ<sub>C</sub> 172.2 (C=O), 136.4 (Ar<sub>quat</sub>), 127.3 (Ar<sub>quat</sub>), 122.2 (ArCH), 122.1 (ArCH), 119.5 (ArCH), 118.7 (ArCH), 112.9 (Ar<sub>quat</sub>), 111.3 (ArCH), 83.6 (HC≡C), 69.2 (C≡C), 39.7 (NCH<sub>2</sub>), 35.1 (OCCH<sub>2</sub>), 25.3 (NCH<sub>2</sub>CH<sub>3</sub>), 24.2 (OCCH<sub>2</sub>CH<sub>3</sub>), 17.8 (HC≡CCH<sub>2</sub>); m/z (ES+) 277 ([M+Na]<sup>+</sup>), 100%, HRMS (ES+) exact mass calculated for [M+Na]<sup>+</sup> (C<sub>18</sub>H<sub>16</sub>N<sub>3</sub>BrNaO<sup>-</sup>) 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-1H-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<sub>2</sub>O and re-crystallized from ethanol.)

**m.p.** 87-89 °C; **FT-IR** ν<sub>max</sub> 3400 (N–H), 3300 (ArN–H), 1636 (C=O); <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz) δ<sub>H</sub> 11.05 (br s, 1H, ArNH), 7.93 (t, 1H, OCNH, J 6.5 Hz), 7.55 (d, 1H, ArCH<sub>2</sub>, J 7.5 Hz), 7.28 (d, 1H, ArCH<sub>2</sub>, J 7.5 Hz), 7.21 (d, 1H, ArCH<sub>2</sub>, J 2.0 Hz), 6.94 (t, 1H, ArCH<sub>2</sub>, J 7.5 Hz), 3.32 (q, 2H, NCH<sub>2</sub>, J 6.5 Hz), 2.80 (t, 2H, OCCH<sub>2</sub>, J 7.5 Hz), 2.78 (t, 1H, C≡CH<sub>2</sub>, J 2.5 Hz), 2.18-2.10 (m, 4H, ArCH<sub>2</sub>, HC≡CCH<sub>2</sub>), 1.65 (quin, 2H, OCCH<sub>2</sub>CH<sub>3</sub>, J 7.5 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ<sub>C</sub> 172.2 (C=O), 135.3 (Ar<sub>quat</sub>), 129.9 (Ar<sub>quat</sub>), 124.9 (ArCH), 124.3 (ArCH), 120.6 (ArCH), 118.8 (ArCH), 114.3 (Ar<sub>quat</sub>), 105.1 (Ar<sub>Br</sub>), 85.0 (HC≡C), 72.3 (C≡C), 41-39.7 (signal hidden under DMSO peak, confirmed by HSQC and COSY) (NCH<sub>3</sub>) 35.1 (ArCH<sub>3</sub>), 26.0 (OCCH<sub>2</sub>) 25.1 (OCCH<sub>2</sub>CH<sub>3</sub>), 18.3 (HC≡CCH<sub>2</sub>); m/z (ES+) 355 ([M+Na]<sup>+</sup>), 100%, HRMS (ES+) exact mass calculated for [M+Na]<sup>+</sup> (C<sub>18</sub>H<sub>18</sub>N<sub>3</sub>BrNaO<sup>-</sup>) requires m/z 355.0416 & 357.0397, found m/z 355.0404 & 357.0385.
2.9.3. Preparation and Characterisation of 9c

**N-[2-\{7-methyl-1H-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\text{max} 3402 (ArNH), 3288 (NH), 1648 (C=O); \textsuperscript{1}H **NMR** (CDCl\textsubscript{3}, 500 MHz) δ\textsubscript{H} 8.00 (br s, 1H, ArNH), 7.47 (d, 1H, ArCH\textsubscript{2}, J 7.5 Hz), 7.07 (t, 1H, ArCH\textsubscript{2}J 7.5 Hz), 7.07 (d, 1H, ArCH\textsubscript{2}, J 7.5 Hz), 7.03 (d, 1H, ArCH\textsubscript{2}, J 7.5 Hz), 5.55 (br s, 1H, OCN), 3.62 (q, 2H, NC\textsubscript{H}\textsubscript{2}, J 6.5 Hz), 2.98 (t, 2H, NCH\textsubscript{2}CH\textsubscript{3}, J 6.5 Hz), 2.50 (s, 3H, ArCH\textsubscript{3}), 2.25 (t, 2H, OCCH\textsubscript{2}, J 7.5 Hz), 2.23 (td, 2H, HCC\textsubscript{2}CH\textsubscript{3}, J 7.5 Hz, 2.5 Hz), 1.93 (t, 1H, C≡CH, J 2.5 Hz), 1.84 (quin, 2H, OCCH\textsubscript{2}CH\textsubscript{3}, J 7.5 Hz); \textsuperscript{13}C **NMR** (CDCl\textsubscript{3}, 125 MHz) δ\textsubscript{C} 172.0 (C\textsubscript{O}), 136.0 (Ar\textsubscript{quat}), 126.8 (Ar\textsubscript{quat}), 122.8 (ArCH), 121.7 (ArCH), 120.4 (Ar\textsubscript{quat}), 119.8 (ArCH), 116.4 (ArCH), 113.6 (Ar\textsubscript{quat}), 83.6 (HC≡C), 69.1 (HC≡C), 39.7 (NCH\textsubscript{2}), 35.1 (OCCH\textsubscript{2}), 25.5 (NCH\textsubscript{2}CH\textsubscript{3}), 24.1 (OCCH\textsubscript{2}CH\textsubscript{3}), 17.8 (HC≡CCH\textsubscript{3}), 16.6 (ArCH\textsubscript{3}); \textit{m/z} (ES\textsuperscript{+}) 291 ([M+Na\textsuperscript{+}], 100%), HRMS (ES\textsuperscript{+}) exact mass calculated for [M+Na\textsuperscript{+}]\textsuperscript{+} (C\textsubscript{17}H\textsubscript{20}N\textsubscript{2}NaO\textsuperscript{+}) requires \textit{m/z} 291.1468 & 292.1501, found \textit{m/z} 291.1470 & 292.1503.

2.9.4. Preparation and Characterisation of 9d

**-[2-\{7-ethyl-1H-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\text{max} 3404 (NH), 3289 (ArNH), 1649 (C=O); \textsuperscript{1}H **NMR** (CDCl\textsubscript{3}, 400 MHz) δ\textsubscript{H} 8.17 (br s, 1H, ArNH), 7.48 (d, 1H, ArCH\textsubscript{2}, J 7.5 Hz), 7.11 (t, 1H, ArCH\textsubscript{2}, J 7.5 Hz), 7.07 (d, 1H, ArCH\textsubscript{2}, J 7.5 Hz), 7.05 (d, 1H, ArCH\textsubscript{2}, J 2.0 Hz), 5.61 (br s, 1H, OCN), 3.62 (q, 2H, NCH\textsubscript{2}, J 6.5 Hz), 2.98 (t, 2H, NCH\textsubscript{2}CH\textsubscript{3}, J 6.5 Hz), 2.88 (q, 2H, ArCH\textsubscript{2}CH\textsubscript{3}, J 7.5 Hz), 2.25 (t, 2H, OCCH\textsubscript{2}, J 7.5 Hz), 2.23 (td, 2H, HCC\textsubscript{2}CH\textsubscript{3}, J 7.5 Hz, 2.5 Hz), 1.94 (t, 1H, C≡CH, J 2.5 Hz), 1.84 (quin, 2H, OCCH\textsubscript{2}CH\textsubscript{3}, J 7.0 Hz), 1.38 (t, 3H, ArCH\textsubscript{2}CH\textsubscript{3}, J 7.5 Hz);
$^{13}$C NMR (CDCl$_3$, 100 MHz) δ$_C$ 172.2 (C=O), 135.3 (Ar$_{quat}$), 127.1 (Ar$_{quat}$), 126.7 (Ar$_{quat}$), 121.7 (Ar_C), 120.8 (Ar_C), 119.8 (Ar_C), 116.5 (Ar_C), 113.4 (Ar$_{quat}$), 83.6 (HC≡C), 69.1 (C≡CH), 39.7 (NCH$_2$), 35.1 (OCCH$_2$), 25.5 (N$_2$CCH$_2$), 24.2 (OCCH$_2$), 17.8 (HC≡CH$_2$), 13.8 (ArCH$_2$CH$_3$); m/z (ES$^+$) 305 ([M+H]$^+$, 100%), HRMS (ES$^+$) exact mass calculated for [M+Na]$^+$ (C$_{18}$H$_{22}$N$_2$NaO$^+$) 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

![Chemical structure](image1)

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$_2$Cl$_2$ : Et$_2$O, 1 : 0 to 7 : 3).

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

![Chemical structure](image2)

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 (0.01 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$_2$O, 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(1H)-one

- S- 33 - -
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; \([\alpha]^{25}_{D} = +157.7 \) (c 0.26, CH\(_2\)Cl\(_2\)).

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

**m.p.** 180 °C (decomposition); **FT-IR** \( \nu_{\text{max}} \) 3254 (N–H), 1606 (C=O); **\(^1\)H NMR** (CDCl\(_3\), 400 MHz) \( \delta \) 8.38 (br s, 1H, ArNH), 7.51 (d, 1H, ArCH\(_3\) J 7.5 Hz), 7.34 (d, 1H, ArCH\(_3\) J 7.5 Hz), 7.19 (t, 1H, ArCH\(_3\) J 7.5 Hz), 7.13 (t, 1H, ArCH\(_3\) J 7.5 Hz), 5.13 (dd, 1H, NCH\(_2\)H\(_2\) J 12.5 Hz, 5.0 Hz), 3.04 (td, 1H, NCH\(_2\)H\(_2\) J 12.5 Hz, 4.5 Hz), 2.85 (ddd, 1H, NCH\(_2\)CH\(_3\) H\(_{10}\) J 15.5 Hz, 11.5 Hz, 5.0 Hz), 2.76 (ddd, 12H, NCH\(_2\)CH\(_3\) H\(_{10}\) J 15.5 Hz, 5.0 Hz), 2.61 (dd, 1H, OCCH\(_2\)H\(_3\) J 17.0 Hz, 5.0 Hz), 2.44 (ddd, 1H, OCCH\(_2\)H\(_3\) J 18.0 Hz, 10.5 Hz, 7.0 Hz), 2.32 (m, 1H, OCC\(_2\)CH\(_2\)CH\(_3\) H\(_{10}\)), 2.09-1.84 (m, 3H, OCC\(_2\)CH\(_2\)CH\(_3\) H\(_{10}\), OCC\(_2\)CH\(_2\)CH\(_3\) H\(_{10}\)), 1.70 (s, 3H, NCCH\(_3\)); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \( \delta \)C 169.3 (CO), 138.5 (Ar\(_{\text{qu}}\)), 136.1 (Ar\(_{\text{quat}}\)), 126.7 (Ar\(_{\text{qu}}\)), 122.0 (Ar\(_{\text{quat}}\)), 119.7 (Ar\(_{\text{quat}}\)), 118.4 (Ar\(_{\text{quat}}\)), 110.9 (Ar\(_{\text{quat}}\)), 108.0 (Ar\(_{\text{quat}}\)), 56.7 (NCCH\(_3\)), 36.5 (NCH\(_3\)), 35.5 (OCCH\(_2\)CH\(_2\)CH\(_3\)), 32.1 (OCCH\(_2\)), 26.0 (CC\(_{\text{quat}}\)), 21.3 (NCH\(_2\)CH\(_3\)), 16.8 (OCCH\(_2\)CH\(_3\)); **m/z** (ES+) 277 ([M+Na]\(^+\), 100%), **HRMS** (ES+) exact mass calculated for [M+Na]\(^+\) (C\(_{16}\)H\(_{12}\)N\(_2\)NaO\(^+\)) requires m/z 277.1311 & 278.1345, found m/z 277.1306 & 278.1335.

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**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(1H)-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; \([\alpha]^{25}_{D} = +164.0 \) (c 0.15, CH\(_2\)Cl\(_2\)).

**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** \( \nu_{\text{max}} \) 3190 (N–H), 1606 (C=O); **\(^1\)H NMR** (CDCl\(_3\), 400 MHz) \( \delta \) 8.09 (br s, 1H, ArNH), 7.44 (d, 1H, ArCH\(_3\) J 8.0 Hz), 7.33 (d, 1H, ArCH\(_3\) J 8.0 Hz), 7.01 (t, 1H, ArCH\(_3\) J 8.0 Hz), 5.12 (dd, 1H, NCH\(_2\)H\(_2\) J 13.0 Hz, 4.5 Hz), 3.01 (td, 1H, NCH\(_2\)H\(_2\) J 12.5 Hz, 4.5 Hz), 2.83 (ddd, 1H, NCH\(_2\)CH\(_3\) H\(_{10}\) J 15.5 Hz, 12.0 Hz, 5 Hz), 2.71 (dd, 1H, NH\(_2\)CH\(_2\)H\(_3\) J 15.0 Hz, 4.0 Hz),...
2.60 (br d, 1H, OCCH$_2$H$_6$, J 17.0 Hz), 2.50-2.33 (m, 2H, OCCH$_2$H$_6$, OCCH$_2$CH$_2$H$_6$), 2.10-1.85 (m, 3H, OCCH$_2$CH$_2$CH$_2$H$_6$, OCCH$_2$CH$_2$H$_6$), 1.71 (s, 3H, NCH$_3$); \(^13^C\) NMR (CDCl$_3$, 100 MHz) $\delta$: 169.2 (CO), 139.2 (Ar$_{quat}$), 134.7 (Ar$_{quat}$), 128.0 (Ar$_{quat}$), 124.5 (Ar$_{CH}$), 121.0 (Ar$_{CH}$), 117.7 (Ar$_{CH}$), 109.6 (Ar$_{quat}$), 104.5 (Ar$_{quat}$), 56.7 (NCH$_3$), 36.2 (NCH$_3$), 35.5 (OCCH$_2$CH$_2$H$_6$), 32.1 (NCH$_2$CH$_2$), 26.0 (NCH$_3$), 21.4 (OCCH$_2$), 16.7 (OCCH$_2$CH$_2$); $m/z$ (ES+) 355 ([M+Na]$^+$, 100%), HRMS (ES+) exact mass calculated for [M+Na]$^+$ (C$_{18}$H$_{27}$Br$_2$NaO$^+$) 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(1H)-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); [$\alpha$]$^D_{20}$ = +167.6 (c 0.34, CH$_2$Cl$_2$).

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

m.p. 140-145 °C (decomposition); FT-IR $v_{max}$ 3265 (N–H), 1605 (C=O); \(^1^H\) NMR (CDCl$_3$, 400 MHz) $\delta$: 8.05 (br s, 1H, ArNH), 7.36 (d, 1H, ArCH, J 7.5 Hz), 7.06 (t, 1H, ArCH, J 7.5 Hz), 7.00 (d, 1H, ArCH, J 7.5 Hz), 5.12 (dd, 1H, NCH$_2$H$_6$, J 12.5 Hz, 4.5 Hz), 3.03 (td, 1H, NCH$_2$H$_6$, J 12.5 Hz, 4.5 Hz), 2.84 (ddd, 1H, NCH$_2$CH$_2$H$_6$, J 15 Hz, 11.5 Hz, 4.5 Hz), 2.74 (dd, 1H, NCH$_2$CH$_2$H$_6$, J 15.0 Hz, 4.5 Hz), 2.60 (br d, 1H, OCCH$_2$H$_6$, J 17.5 Hz), 2.51 (s, 3H, ArCH$_3$), 2.49-2.34 (m, 2H, OCCH$_2$H$_6$, OCCH$_2$CH$_2$H$_6$), 2.09-1.86 (m, 3H, OCCH$_2$CH$_2$CH$_2$H$_6$, OCCH$_2$CH$_2$H$_6$), 1.71 (s, 3H, NCH$_3$); \(^13^C\) NMR (CDCl$_3$, 100 MHz) $\delta$: 169.2 (CO), 138.2 (Ar$_{quat}$), 135.6 (Ar$_{quat}$), 126.3 (Ar$_{quat}$), 122.8 (Ar$_{CH}$), 120.2 (Ar$_{quat}$), 120.0 (Ar$_{CH}$), 116.1 (Ar$_{CH}$), 108.7 (Ar$_{quat}$), 56.8 (NCH$_3$), 36.4 (NCH$_3$), 35.6 (OCCH$_2$CH$_2$H$_6$), 32.1 (OCCH$_2$), 26.0 (NCH$_3$), 21.3 (NCH$_2$CH$_2$), 16.79 (Ar$_{CH}$), 16.78 (OCCH$_2$CH$_2$); $m/z$ (ES+) 291 ([M+H]$^+$, 100%), HRMS (ES+) exact mass calculated for [M+Na]$^+$ (C$_{18}$H$_{27}$Br$_2$NaO$^+$) 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(1H)-one
The title compound 10d was synthesized according to general procedure I as a white solid (60% yield, 86% e.e.). Chiralcel AD, 80:20 Hexane/IPA, 1ml/min, 220, major tₘ = 4.1 min, minor tₙ = 4.9 min; [α]²⁵° +120.6 (c 0.34, CH₂Cl₂)

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); ¹H NMR (CDCl₃, 400 MHz) δH 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, NCH₂H, J 13.0 Hz, 4.5 Hz), 3.03 (td, 1H, NCH₂H, J 12.5 Hz, 4.5 Hz), 2.88 (q, 2H, ArCH₂CH₃, J 7.5 Hz), 2.84 (td, 1H, NCH₂CH₂H, J 12.0 Hz, 5.0 Hz), 2.74 (dd, 1H, NCH₂CH₂H, J 15.0 Hz, 4.0 Hz), 2.60 (br d, 1H, OCCH₂H, J 17.0 Hz), 2.49-2.31 (m, 2H, OCCH₂H, OCCH₂CH₂CH₂H), 2.08–1.85 (m, 3H, OCCH₂CH₂CH₂H, OCCH₂CH₂H), 1.71 (s, 3H, NCC₂H₃), 1.38 (t, 3H, ArCH₂CH₃, J 7.5 Hz); ¹³C NMR (CDCl₃, 100 MHz) δC 169.2 (CO), 138.1 (Ar₉quat), 134.8 (Ar₈quat), 126.5 (Ar₇quat), 126.4 (Ar₆quat), 120.7 (ArCH), 120.1 (ArCH), 116.2 (ArCH), 108.7 (Ar₅quat), 56.7 (NCC₂H₃), 36.4 (NCH₂), 35.6 (OCH₂CH₂CH₂), 32.1 (OCH₂), 26.0 (NCC₂H₃), 24.0 (ArCH₂CH₃), 21.3 (NCH₂CH₂), 16.8 (OCCH₂CH₂), 13.9 (ArCH₂CH₃); m/z (ES+) 305 ([M+Na]⁺, 100%), HRMS (ES+) exact mass calculated for [M+Na]⁺ (C₁₈H₂₂N₂NaO₂) 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

\[ N\text{-}[2\text{-}(1\text{-indole-3-yl})\text{ethyl}]\text{-3-oxobutane-1-sulfonamide} \]

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 ¹H NMR (CDCl₃ passed through a short pad of K₂CO₃ 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 \( \nu_{\text{max}} \) 3346 (ArN-H, br s), 3252 (SN-H), 1707 (C=O), 1313 (S=O (as)), 1138 (S=O (sy)); \(^1\)H NMR (CDCl\(_3\), 500 MHz) \( \delta \) 8.12 (br s, 1H, ArN-H), 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, SN-H), 3.45 (q, 2H, SNCH\(_2\)), 3.19 (t, 2H, SCH\(_2\)), 3.05 (t, 2H, ArCH\(_2\)), 2.11 (s, 3H, COCH\(_3\)); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \( \delta \) C 204.5 (CO), 136.5 (ArC quat), 127.0 (ArC quat), 122.8 (ArC), 119.8 (ArC), 118.6 (ArC), 111.7 (ArCCH\(_2\)), 111.5 (ArC), 46.7 (SCH\(_2\)), 43.3 (SNCH\(_2\)), 37.3 (SCH\(_2\)), 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\(_2\)NaO\(_3\)S\(^+\)) requires \( m/z \) 317.0930, found \( m/z \) 317.0927.

2.13.1. Mechanistic evidence for N-sulfonylimminium 13

![](image)

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 Procedure 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.

![](image)

To an aluminium foil covered flask alkyne 5a (0.15 mmol, 1 eq) 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 procedure for optimization in the preparation of 10a.

![](image)
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 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), 1134 (S=O); \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz) δ \text{H}: 7.55 (m, 1H, ArC_H), 7.39 (d, 1H, PhCH), 7.20-7.15 (m, 3H, 2 × ArCH), 7.12 (t, 1H, ArCH), 7.03 (m, 1H, ArCH), 6.62 (d, 1H, PhCH), 5.43 (d, 1H, NCH\textsubscript{2}H\textsubscript{3}Ph, J 18.0 Hz), 5.38 (d, 1H, NCH\textsubscript{2}H\textsubscript{3}Ph, J 18.0 Hz), 4.08 (dd, 1H, NCH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{3}, J 14.5 Hz, 5.5 Hz), 3.34 (ddd, 1H, NCH\textsubscript{2}CH\textsubscript{2}J 14.5 Hz, 12.5 Hz, 4.5 Hz), 3.27-3.15 (m, 2H, SCH\textsubscript{2}C\textsubscript{H}_{12}), 3.01 (dt, 1H, SCH\textsubscript{2}C\textsubscript{H}_{12}, J 6.0 12.5 Hz, 7.0 Hz), 2.78 (dd, 1H, ArCH\textsubscript{2}H, J 15.5 Hz, 4.0 Hz), 2.64 (m, 1H, SCH\textsubscript{2}CH\textsubscript{2}H), 2.56 (m, 1H, SCH\textsubscript{2}CH\textsubscript{2}H), 1.67 (s, 3H, NCCH\textsubscript{3}); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz) δ \text{C}: 139.5 (Ar\textsuperscript{quat}), 136.9 (Ar\textsuperscript{quat}), 135.3 (Ar\textsuperscript{quat}), 130.8 (PhCH), 130.6 (PhCH), 128.5 (PhCH), 126.6 (Ar\textsuperscript{quat}), 123.9 (PhCH), 123.2 (PhBr), 123.0 (ArCH), 120.2 (ArCH), 118.9 (ArCH), 109.7 (ArCH), 109.6 (Ar\textsuperscript{quat}), 59.6 (NCCH\textsubscript{3}), 47.3 (NCH\textsubscript{2}Ph), 45.4 (SCH\textsubscript{2}), 36.4 (NCH\textsubscript{2}), 32.7 (SCH\textsubscript{2}CH\textsubscript{2}), 27.6 (NCCH\textsubscript{3}), 20.9 (ArCH\textsubscript{2}); HRMS (TOF MS F+I) exact mass calculated for [M]^+ (C\textsubscript{21}H\textsubscript{21}BrN\textsubscript{2}O\textsubscript{2}S) 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-($1H$-indol-3-yl)ethyl]but-3-yn-1-sulfonamide 5a

![HNMR Spectra](image1.png)

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

![CNMR Spectra](image2.png)
3.1.3. $^1$HNMR spectra for \(N\{2\{4\text{-chloro-1\text{-H-indol-3-yl}}\text{ethyl}\}\text{but-3-ynesulfonamide 5b}\)

![HNMR Spectra](image)

3.1.4. $^{13}$CNMR spectra for \(N\{2\{4\text{-chloro-1\text{-H-indol-3-yl}}\text{ethyl}\}\text{but-3-ynesulfonamide 5b}\)

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

3.1.6. $^{13}$CNMR spectra for $N$-[2-{(5-bromo-1H-indol-3-yl)ethyl}but-3-yne-1-sulfonamide 5c
3.1.7. $^1$HNMR spectra for $N$-[2-$(6$-bromo-$1H$-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5d

3.1.8. $^{13}$CNMR spectra for $N$-[2-$(6$-bromo-$1H$-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5d
3.1.9. $^1$HNMR spectra for $N$-[(2-(5-fluoro-1H-indol-3-yl)ethyl]but-3-yn-1-sulfonamide 5e

3.1.10. $^{13}$CNR spectra for $N$-[(2-(5-fluoro-1H-indol-3-yl)ethyl]but-3-yn-1-sulfonamide 5e
3.1.11. $^1$HNMR spectra for $N$-[2-(6-fluoro-1H-indol-3-yl)ethyl]but-3-yn-1-sulfonamide 5f

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

![HNMR spectrum](image)

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

![CNR spectrum](image)
3.1.17. $^1$HNMR spectra for $N$-[2-(5-methyl-$1H$-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5i

![HNMR Spectra](image1)

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

![CNMR Spectra](image2)
3.1.19. $^1$HNMR spectra for $N$-[2-(7-methyl-1H-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5j

3.1.20. $^{13}$CNMR spectra for $N$-[2-(7-methyl-1H-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5j
3.1.21. $^1$HNMR spectra for $N$-[2-(7-ethyl-$1H$-indol-3-yl)ethyl]but-3-yne-1-sulfonamide 5k

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

3.2.1. $^1$H NMR 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. $^{13}$C NMR 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. \( ^{1} \)H NMR spectra for 2,3,6,7,12,12b-hexahydro-1H-[1,2]thiazino[2',3':1,2]pyrido[3,4-b]indole 4,4-dioxide 7a

3.2.4. \( ^{13} \)C NMR spectra for 2,3,6,7,12,12b-hexahydro-1H-[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

![HNMR spectrum](image)

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

![CNMR spectrum](image)
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 $\text{N-[2-}(1H\text{-indol-3-yl})\text{ethyl]hex-5-ynamide 9a}$

![HNMR Spectrum](image1.png)

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

![CNMR Spectrum](image2.png)
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-1H-indol-3-yl)ethyl]hex-5-ynamide 9c

3.3.6. $^{13}$CNMR spectra for $N$-[2-(7-methyl-1H-indol-3-yl)ethyl]hex-5-ynamide 9c
3.3.7. $^1$HNMR spectra for $N\{2-(7\text{-ethyl-1H-indol-3-yl})\text{ethyl}\}\text{hex-5-ynamide}$ 9d

3.3.8. $^{13}$CNMR spectra for $N\{2-(7\text{-ethyl-1H-indol-3-yl})\text{ethyl}\}\text{hex-5-ynamide}$ 9d
3.4. Amide cyclization products

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

3.4.2. 13C NMR spectra for 12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-a]quinolizin-4(1H)-one 10a
3.4.3. $^1$HNMR spectra for 11-bromo-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-
$\alpha$]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-
$\alpha$]quinolizin-4(1$H$)-one 10b
3.4.5. $^1$H NMR spectra for 11,12b-dimethyl-2,3,6,7,12,12b-hexahydroindolo[2,3-a]quinolizin-4(1H)-one 10c

3.4.6. $^{13}$C NMR spectra for 11,12b-dimethyl-2,3,6,7,12,12b-hexahydroindolo[2,3-a]quinolizin-4(1H)-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(1H)-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(1H)-one 10d
3.4.9. $^1$HNMR spectra for $N$-[(1H-indole-3-yl)ethyl]-3-oxobutane-1-sulfonamide 14

3.4.10. $^{13}$CNMR spectra for $N$-[(1H-indole-3-yl)ethyl]-3-oxobutane-1-sulfonamide 14
3.4.11. $^1$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

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 | Type | Width | Area  | Height | Area % |
|--------------|------|-------|-------|--------|--------|
| 1            | VV   | 0.2996| 6929.40234| 361.55801 | 49.9763 |
| 2            | 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 | Type | Width | Area  | Height | Area % |
|--------------|------|-------|-------|--------|--------|
| 1            | BB   | 0.2088| 8450.49805| 628.89789 | 93.7254 |
| 2            | 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 from ketone starting material 6a

![HPLC trace](image)

| # | RetTime [min] | Type | Width [min] | Area [mAUs] | 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 Type Width Area Height Area
# [min] [min] [mAU*s] [mAU] %
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 Type Width Area Height Area
# [min] [min] [mAU*s] [mAU] %
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 | Ret Time | Type | Width | 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 | Ret Time | Type | Width | 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

![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](image)

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

| Peak | RetTime | Type | Width | Area  | Height | 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

![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](image)

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

| Peak | RetTime | Type | Width | Area  | Height | 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

![HPLC trace image]

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

| Peak | RetTime | Type | Width | Area   | Height | 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

![HPLC trace image]

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

| Peak | RetTime | Type | Width | Area   | Height | 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 | Type | Width | Area   | Height | 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 | Type | Width | Area   | Height | 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 Type Width Area Height Area %
# [min] [min] [mAU*s] [mAU] %
---|-----|-----|-----|-----|-----|-----|
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 Type Width Area Height Area %
# [min] [min] [mAU*s] [mAU] %
---|-----|-----|-----|-----|-----|-----|
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 |

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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 Type | Width | Area       | Height | Area % |
|-------------------|-------|------------|--------|--------|
| #                 | [min] | [min] [mAU*s] [mAU] |        |
| 1                 |       | 6.721      | 0.2099 | 2099.92603 | 153.23482 | 50.1598 |
| 2                 | 13.982 |           | 0.4707 | 2086.54614 | 69.01322 | 49.8402 |

Totals: 4186.47217 222.24004

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 Type | Width | Area       | Height | Area % |
|-------------------|-------|------------|--------|--------|
| #                 | [min] | [min] [mAU*s] [mAU] |        |
| 1                 |       | 6.664      | 0.2447 | 3656.24561 | 249.06523 | 93.8772 |
| 2                 | 14.145 |           | 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

| Peak | RetTime | Type | Width | Area       | Height      | Area %   |
|------|---------|------|-------|------------|-------------|----------|
| 1    | 5.067   | VV   | 0.193 | 3511.04712 | 282.56686   | 49.6121  |
| 2    | 6.058   | VB   | 0.209 | 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

| Peak | RetTime | Type | Width | Area       | Height      | Area %   |
|------|---------|------|-------|------------|-------------|----------|
| 1    | 5.046   | BV   | 0.189 | 1.34379e4  | 1108.46716  | 95.6662  |
| 2    | 6.051   | VB   | 0.222 | 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

![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 | 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

![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 | 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]quinolin-4(1H)-one 10a

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

| Peak RetTime Type | Width | Area    | Height | Area % |
|------------------|-------|---------|--------|--------|
| #                | [min] | [min]   | [mAU*s] | [mAU]  |        |
| 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]quinolin-4(1H)-one 10a

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

| Peak RetTime Type | Width | Area    | Height | Area % |
|------------------|-------|---------|--------|--------|
| #                | [min] | [min]   | [mAU*s] | [mAU]  |        |
| 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]quinolinizin-4(1H)-one 10b

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

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

| Peak RetTime | Type | Width  | Area    | Height | Area % |
|--------------|------|--------|---------|--------|--------|
| #            | [min]| [min]  | [mAU*s] | [mAU]  |        |
| 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]quinolinizin-4(1H)-one 10b

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

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

| Peak RetTime | Type | Width  | Area    | Height | Area % |
|--------------|------|--------|---------|--------|--------|
| #            | [min]| [min]  | [mAU*s] | [mAU]  |        |
| 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(1H)-one 10c

Signal 1: VWD1 A, Wavelength=220 nm

| Peak | RetTime | Type | Width | Area  | Height | Area |
|------|---------|------|-------|-------|--------|------|
| 1    | 5.019   | VV   | 0.595 | 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(1H)-one 10c

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

| Peak | RetTime | Type | Width | Area  | Height | 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-α]quinolinizin-4(1H)-one 10d

![HPLC trace of racemic 11-ethyl-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-α]quinolinizin-4(1H)-one 10d]

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

| Peak RetTime | Width | Area       | Height    | Area %     |
|--------------|-------|------------|-----------|------------|
| #            | [min] | [min]      | [mAU*s]   | [mAU]      | %          |
|---------------|-------|------------|-----------|------------|------------|
| 1             | 4.108 | 0.1432     | 6486.74707| 706.11816  | 49.4928    |
| 2             | 4.908 | 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-α]quinolinizin-4(1H)-one 10d

![HPLC trace of 11-ethyl-12b-methyl-2,3,6,7,12,12b-hexahydroindolo[2,3-α]quinolinizin-4(1H)-one 10d]

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

| Peak RetTime | Width | Area       | Height    | Area %     |
|--------------|-------|------------|-----------|------------|
| #            | [min] | [min]      | [mAU*s]   | [mAU]      | %          |
|---------------|-------|------------|-----------|------------|------------|
| 1             | 4.100 | 0.1379     | 8776.01367| 966.42841  | 92.8026    |
| 2             | 4.911 | 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

| #  | Ret Time [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

| #  | Ret Time [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

5.1. X-ray data for compound 10b

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

Crystal data

$\text{C}_{16}\text{H}_{17}\text{BrN}_{2}\text{O} \cdot \text{CHCl}_{3}$

$M_r = 452.60$

Orthorhombic, $P 2_1 2_1 2_1$

Hall symbol: $P 2ac 2ab$

$D_x = 1.567 \text{ Mg m}^{-3}$

Melting point: not measured K

Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ Å}$

Cell parameters from 83413 reflections
Data collection

Nonius KappaCCD diffractometer
Graphite monochromator
ω scans
Absorption correction: Multi-scan
DENZO/SCALEPACK (Otwinowski & Minor, 1997)

4092 reflections with $I > 2.0\sigma(I)$
$R_{int} = 0.087$
$\theta_{\text{max}} = 27.5^\circ$, $\theta_{\text{min}} = 5.2^\circ$

Hydrogen site location: Difference Fourier map

Refinement

Refinement on $F^2$
Least-squares matrix: Full

$R[F^2 > 2\sigma(F^2)] = 0.034$
$wR(F^2) = 0.083$
$S = 1.00$

4361 reflections
255 parameters
162 restraints

Primary atom site location: Other

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

|          | $x$   | $y$   | $z$   | $U_{iso}/U_{eq}$ | 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 (19) | 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          |
| Atomic displacement parameters ($\AA^2$) |
|-----------------------------------------|
| $U_{11}$ | $U_{22}$ | $U_{33}$ | $U_{12}$ | $U_{13}$ | $U_{23}$ |
| 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 (9) |
| 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) |
|   | Geometric parameters (Å, °) |
|---|---------------------------|
|   |                           |
| C1 | 0.0330 (13)   0.0502 (15) 0.0299 (12) 0.0037 (11) 0.0059 (10) -0.0006 (11) |
| C2 | 0.0365 (13)   0.0437 (14) 0.0297 (11) 0.0059 (10) -0.0013 (10) -0.0064 (10) |
| N3 | 0.0276 (10)   0.0424 (11) 0.0256 (9)  0.0032 (8)  -0.0018 (8)  -0.0006 (8)  |
| C4 | 0.0255 (11)   0.0329 (11) 0.0239 (10) -0.0003 (9)  -0.0005 (8)  0.0000 (8)   |
| C5 | 0.0358 (12)   0.0379 (12) 0.0345 (13) -0.0085 (20) -0.0042 (10) 0.0052 (10)  |
| C6 | 0.0262 (12)   0.0447 (14) 0.0355 (12) 0.0011 (10) 0.0023 (10) -0.0025 (11) |
| C7 | 0.0260 (13)   0.067 (2)   0.0373 (14) 0.0027 (12) 0.0013 (10) -0.0036 (13) |
| C8 | 0.0296 (13)   0.073 (2)   0.0398 (14) 0.0070 (13) -0.0048 (11) -0.0062 (14)  |
| C9 | 0.0314 (13)   0.0475 (14) 0.0291 (12) 0.0015 (10) -0.0041 (10) 0.0027 (10)  |
| O1 | 0.0391 (10)   0.0690 (12) 0.0290 (8)  0.0048 (9)  -0.0072 (9)  -0.0025 (9)  |
| C20| 0.0506 (19)   0.0427 (18) 0.066 (2)   -0.0010 (16) -0.0121 (18) 0.0043 (17)  |
| C21| 0.0550 (10)   0.0807 (10) 0.0502 (7)  0.0210 (8)  -0.0150 (6)  -0.0013 (8)  |
| C22| 0.089 (2)     0.0648 (14) 0.0833 (17) -0.0014 (16) 0.0082 (15) -0.0288 (13) |
| C23| 0.0523 (9)    0.127 (2)   0.151 (3)   -0.0348 (11) -0.0107 (13) 0.022 (2)    |
| C24| 0.071 (4)     0.050 (4)   0.075 (4)   -0.001 (3)  -0.030 (4)  -0.005 (3)   |
| C25| 0.111 (5)     0.059 (2)   0.063 (3)   0.019 (3)   -0.030 (3)  -0.0177 (19) |
| C26| 0.0318 (19)   0.047 (3)   0.056 (3)   0.0025 (14) -0.0096 (16) -0.0139 (19) |
| C27| 0.065 (3)     0.081 (3)   0.131 (5)   -0.026 (2)  -0.034 (3)  0.014 (3)    |

**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** 119.2 (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
Hydrogen-bond geometry (Å, °)

| D—H···A     | D—H   | H···A  | D···A   | D—H···A |
|-------------|-------|-------|--------|---------|
| C16—H161···O20′ | 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′  | 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

\[ C_{21}H_{21}BrN_2O_2S \]

\[ F(000) = 912 \]
Mr = 445.38
Monoclinic, \(P2_1\)
Hall symbol: P 2yb
\(a = 10.4507 (1) \text{ Å}\)
\(b = 16.2752 (2) \text{ Å}\)
\(c = 11.5043 (1) \text{ Å}\)
\(\beta = 101.0903 (5)^\circ\)
\(V = 1920.19 (3) \text{ Å}^3\)
\(Z = 4\)

Data collection

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

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

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\(\text{Å}^2\))

| \(x\)     | \(y\)     | \(z\)     | \(U_{eq}\)/\(U_{\text{eq}}\) |
|-----------|-----------|-----------|-------------------------------|
| 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                        |
| At.   |    X   |   Y   |    Z   |  Ue1  |  Ue2  |  Ue3  |  Ue4  |
|-------|--------|-------|--------|--------|--------|--------|--------|
| 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) | 0.61969 (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)  | 0.39625 (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* |
| 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 | 0.5289  | 0.0352* |
| H462 | 0.2456 | 0.4477 | 0.6406  | 0.0348* |
| H461 | 0.3205 | 0.3981 | 0.6064  | 0.0322* |
| 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 (Å\(^2\))**

|   | \(U^{11}\)    | \(U^{22}\)    | \(U^{33}\)    | \(U^{12}\)    | \(U^{13}\)    | \(U^{23}\)    |
|---|----------------|----------------|----------------|----------------|----------------|----------------|
| 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)   |
### Geometric parameters (Å, °)

| Bond          | Length  | Angle       |
|---------------|---------|-------------|
| 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) |

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- S- 99 - -
| Bond                  | Distance (Å) | Bond                  | Distance (Å) |
|-----------------------|--------------|-----------------------|--------------|
| 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)  |
| Bond          | Distance (Å)  | Bond          | Distance (Å)  |
|---------------|---------------|---------------|---------------|
| Br1—C2—C7    | 119.59 (18)   | Br28—C29—C34 | 118.45 (19)   |
| C3—C2—C7    | 121.7 (2)     | C30—C29—C34  | 122.4 (19)    |
| C2—C3—C4    | 119.4 (2)     | C29—C30—C31  | 118.1 (2)     |
| C3—C2—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)   |
| Bond | Distance (Å) | Angle (°) |
|------|-------------|-----------|
| 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 | 113.0 | C48—C49—H492 | 109.6 |
| C18—C24—H242 | 113.0 | C39—C49—H492 | 109.2 |
| H241—C24—H242 | 110.3 | | |
| N19—C25—C26 | 114.43 (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 | 119.4 |
| H262—C26—H261 | 109.6 | C53—C52—H521 | 119.1 |
| 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, °)**

| D—H···A | D—H | H···A | D···A | D—H···A |
|----------|------|-------|-------|---------|
| C12—H121···O44\(i\) | 0.94 | 2.54 | 3.390 (4) | 152 |
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).

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