

## Palladium-catalyzed cyclization of bromoenynamides to tricyclic azacycles: Synthesis of trikentrin-like frameworks.

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## Supporting Information

### Contents

Experimental .....	2
1 a. General Experimental.....	2
1 b. General Procedures .....	4
2. Compound Characterisation .....	6
3. <sup>1</sup> H and <sup>13</sup> C NMR Spectra of cyclisation substrates and tricyclic products.....	20
4. References .....	33

## Experimental

### 1 a. General Experimental

#### NMR Spectra:

Proton ( $^1\text{H}$ ) and carbon ( $^{13}\text{C}$ ) NMR spectra were recorded on a Bruker AVII500 (500/126 MHz), Bruker DPX400 (400/101 MHz) or Bruker AV400 (400/101 MHz). Proton and carbon chemical shift ( $\delta_{\text{H}}$ ,  $\delta_{\text{C}}$ ) are quoted in ppm and referenced to tetramethylsilane ( $\delta_{\text{H}}$ ,  $\delta_{\text{C}}$  0.00).  $^1\text{H}$  NMR spectra were recorded using an internal deuterium lock for the residual protons in  $\text{CDCl}_3$  ( $\delta_{\text{H}}$  7.26).  $^{13}\text{C}$  NMR Spectra were recorded using an internal deuterium lock using solvent  $\text{CDCl}_3$  ( $\delta_{\text{C}}$  77.16). Assignments were made on the basis of chemical shift, coupling constants, COSY, HSQC, HMBC data and comparison with spectra of related compounds. Resonances are described using the following abbreviations; s (singlet), d (doublet), t (triplet), q (quartet), quin. (quintet), sext. (sextet), sept. (septet), m (multiplet), br. (broad), app. (apparent), dd (double doublet) and so on. Coupling constants ( $J$ ) are given in Hz and are rounded to the nearest 0.1 Hz. H and H' refer either to the numbering pattern specified schematically, or protons attached to the same carbon and imply no particular stereochemistry.

**Mass Spectra:** Low resolution mass spectra were recorded on a Micromass LCT Premier spectrometer (ESI). High resolution mass spectra were recorded by the Mass Spectrometry service of the Chemistry Research Laboratory, University of Oxford, using a Bruker Daltronics microTOF spectrometer (ESI).  $m/z$  values are reported in Daltons. High resolution values are calculated to four decimal places from the molecular formula, all found values being within a tolerance of 5 ppm.

**Infrared Spectra:** Infrared spectra were recorded on a Bruker Tensor 27 Fourier transform spectrometer, as a thin film on NaCl plates or a diamond ATR module. Absorption maxima ( $\nu_{\text{max}}$ ) are quoted in wavenumbers ( $\text{cm}^{-1}$ ).

**Melting Points:** Melting points were recorded on a Leica Galen III Compound microscope and are uncorrected.

**Chromatography techniques:** TLC was performed on Merck Kieselgel 60 F<sub>254</sub> 0.2 mm precoated plates and visualised using basic potassium permanganate dip, acidic vanillin dip or ultraviolet light. Retention factors are reported with the solvent system in parentheses. Column chromatography was performed on Merck Kieselgel 60  $\text{SiO}_2$  (40-63  $\mu\text{m}$ ) and the solvent system used is recorded in parentheses.

**Solvents** were either used as commercially supplied, or as purified by standard techniques. Pet. ether refers to the fraction of light petroleum ether boiling at 40-60 °C. Brine refers to a saturated aqueous solution of sodium chloride. Unless otherwise stated, reactions were carried out in oven-dried flasks under an atmosphere of dry argon or nitrogen.

## 1 b. General Procedures

### General Procedure A: Mitsunobu Coupling and N-Boc deprotection

#### Mitsunobu Coupling

To a solution of triphenylphosphine (2.0 equiv.), TsNHBoc (1.3 equiv.) and the appropriate alcohol (1.0 equiv.) in anhydrous THF (3 mL mmol<sup>-1</sup>) at 0 °C was added DIAD (1.5 equiv.) dropwise. Reaction was stirred at rt overnight before being concentrated *in vacuo*. The residue was dissolved in Et<sub>2</sub>O then sonicated for 5 min and the resulting precipitate (triphenylphosphine oxide) removed by filtration. To the filtrate was added hexanes which was further sonicated for 5 min and the resulting precipitate removed by filtration before being concentrated *in vacuo*. Purification *via* column chromatography (petroleum ether / EtOAc (20:1)) afforded the desired carbamate.

#### Deprotection

Carbamate product was taken up in CH<sub>2</sub>Cl<sub>2</sub> (2 mL mmol<sup>-1</sup>) before the dropwise addition of TFA (0.5 mL mmol<sup>-1</sup>) at 0 °C. The resulting reaction mixture was stirred at rt for 2-4 h before being cooled to 0 °C and slowly quenched by the dropwise addition of sat. *aq.* NaHCO<sub>3</sub>. The organic layer was separated and the aqueous layer further extracted with CH<sub>2</sub>Cl<sub>2</sub> and the organic layers combined, dried (MgSO<sub>4</sub>) and concentrated *in vacuo*. Purification *via* column chromatography (petroleum ether / EtOAc (10:1) → (5:1)) afforded the corresponding sulfonamides.

### General Procedure B: Bromination of terminal alkynes

**Method A:** To a stirred solution of the terminal alkyne (1.0 equiv.) in anhydrous THF (3 M) at -78 °C was added *n*-BuLi (2.5 M, 1.2 equiv.) dropwise. The resulting solution was stirred at -78 °C for 30 min before the dropwise addition of bromine (1.4 equiv.). The reaction mixture was then stirred for a further 15 min before being quenched with sat. *aq.* Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution. The reaction was extracted with Et<sub>2</sub>O, and the combined organic layers dried (MgSO<sub>4</sub>) and concentrated *in vacuo* (some THF not removed due to product volatility) to obtain the corresponding bromoalkynes which were used without further purification.

**Method B:** To a solution of terminal alkyne (1.0 equiv.) in acetone (2 mL mmol<sup>-1</sup>) was added AgNO<sub>3</sub> (0.1 equiv.). After stirring for 5 min, *N*-bromosuccinimide (1.1 equiv.) was added and the resulting mixture stirred for a further 2-4 h at rt. The reaction mixture was concentrated *in vacuo* before the addition of petroleum ether and filtration through cotton wool to remove the colourless precipitate. The resulting solution was concentrated *in vacuo* to obtain the corresponding bromoalkynes which were used without further purification.

**General Procedure C: Hsung route to ynamides**

To a mixture of sulfonamide (1.0 equiv.),  $K_3PO_4$  (2.0 equiv.),  $CuSO_4 \cdot 5H_2O$  (0.2 equiv.) and 1,10-phenanthroline (0.4 equiv.) was added a solution of bromoalkyne (1.5 equiv.) in toluene (4 mL mmol<sup>-1</sup>). The mixture was heated to 70 °C for 16 h before being cooled to rt and concentrated *in vacuo*. Purification *via* column chromatography afforded the corresponding bromoenynamide.

**General Procedure D: Bromoboration/protodeborylation and in-situ Boc-deprotection**

To  $BBr_3$  (1 M in  $CH_2Cl_2$ , 0.5 equiv.) under Ar at -78 °C was added dropwise a solution of the alkynyl Mitsunobu product (1.0 equiv.) in anhydrous  $CH_2Cl_2$  (0.57 M). The resulting reaction mixture was allowed to warm to rt over 4.5 h before the addition of glacial AcOH (2.14 mL mmol<sup>-1</sup> of  $BBr_3$ ). After stirring for a further 1 h the reaction was quenched by the addition of water and then extracted with  $CH_2Cl_2$  (×3). The combined organic layers were dried ( $MgSO_4$ ), filtered and concentrated *in vacuo*. Purification *via* column chromatography afforded the corresponding sulfonamides.

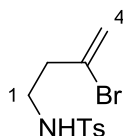
**General Procedure E: Intramolecular cascade cyclisation**

To an oven dried vial, equipped with a stirring bar, was added  $Pd(PPh_3)_4$  (5 or 10 mol%) in a glove box, and the vial sealed with a rubber septum. To this was added a degassed (Ar bubbling, 15 min) solution of the corresponding bromoenynamide (1.0 equiv.) and triethylamine (6.0 equiv.) in anhydrous MeCN (6.2 or 60 mL mmol<sup>-1</sup>). The rubber septum was replaced rapidly with a screw cap, and the reaction mixture heated to 80 °C until the reaction was complete as analysed by TLC (typically 8-16 h). On completion, the reaction was cooled to rt and concentrated *in vacuo*. Purification *via* column chromatography afforded the corresponding tricycles.

## 2. Compound Characterisation

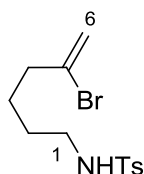
### Substrate precursors

#### ***N*-(5-Bromobut-3-en-1-yl)-4-methylbenzenesulfonamide **3a****



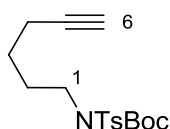
Prepared by General Procedure D using *tert*-butyl *N*-but-3-ynyl-*N*-(*p*-tolylsulfonyl)carbamate<sup>1</sup> **4a** (600 mg, 1.86 mmol, 1.0 equiv.). Purification *via* column chromatography (petroleum ether → petroleum ether / EtOAc (1:1)) afforded the title compound **3a** as a colourless semi-solid (350 mg, 1.15 mmol, 62%); *R*<sub>f</sub> 0.13 (petroleum ether / EtOAc (5:1)); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 7.76 (2H, d, *J* = 8.5 Hz, *TsH*), 7.32 (2H, d, *J* = 8.5 Hz, *TsH*), 5.60 (1H, app. s, H4), 5.48 (1H, d, *J* = 1.5 Hz, H4'), 4.83 (1H, br t, *J* = 6.0 Hz, NH), 3.16 (2H, t, *J* = 6.5 Hz, H1), 2.57 (2H, t, *J* = 6.5 Hz, H2), 2.43 (3H, s, *TsCH*<sub>3</sub>); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> 143.6, 136.9, 129.8, 129.6, 127.1, 120.0, 41.3, 41.0, 21.5. Data are in agreement with literature values.<sup>1</sup>

#### ***N*-(5-Bromohex-5-en-1-yl)-4-methylbenzenesulfonamide **3b****



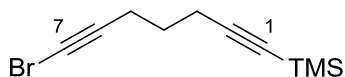
Prepared by General Procedure D using *tert*-butyl *N*-hex-5-ynyl-*N*-(*p*-tolylsulfonyl)carbamate **4b** (100 mg, 0.28 mmol, 1.0 equiv.). Purification *via* column chromatography (petroleum ether → petroleum ether / EtOAc (1:1)) afforded the title compound **3b** as a colourless oil (37 mg, 0.086 mmol, 30%). *R*<sub>f</sub> 0.10 (petroleum ether / EtOAc (10:1)); IR (thin film, ν<sub>max</sub> / cm<sup>-1</sup>) 3279, 2941, 2867, 1630, 1599, 1433, 1156, 1093, 887; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 7.75 (2H, d, *J* = 8.0 Hz, *TsH*), 7.32 (2H, d, *J* = 8.0 Hz, *TsH*), 5.52 (1H, app s, H6), 5.37 (1H, app s, H6'), 4.60 (1H, t, *J* = 6.0 Hz, NH), 2.96 (2H, q, *J* = 6.5 Hz, H1), 2.44 (3H, s, *TsCH*<sub>3</sub>), 2.37 (2H, t, *J* = 7.0 Hz, H4), 1.55- 1.46 (4H, m, H2 and H3); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> 143.5, 137.0, 133.8, 129.8, 127.1, 117.0, 42.9, 40.7, 28.3, 24.8, 21.6; HRMS (ES<sup>+</sup>) calc. for C<sub>13</sub>H<sub>18</sub>BrNNaO<sub>2</sub>S [M+Na]<sup>+</sup> 354.0134, found 354.0127.

### ***tert*-Butyl *N*-hex-5-ynyl-*N*-(*p*-tolylsulfonyl)carbamate **4b****



Prepared by General Procedure A (first step) using 5-hexyn-1-ol (1.00 g, 10.2 mmol). Purification *via* column chromatography (petroleum ether → petroleum ether / EtOAc (8:2)) afforded tosylcarbamate **4b** as a colourless solid (3.31 g, 9.43 mmol, 93%); **mp** 65–68 °C; **R<sub>f</sub>** 0.41 (petroleum ether / EtOAc (5:1)); **IR** (thin film,  $\nu_{\text{max}}$  /  $\text{cm}^{-1}$ ) 3286, 2979, 1724, 1598, 1456, 1352, 1289, 1256, 1184, 1087; **<sup>1</sup>H NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  7.78 (2H, d,  $J$  = 8.0 Hz, TsH), 7.30 (2H, d,  $J$  = 8.0 Hz, TsH), 3.85 (2H, t,  $J$  = 7.5 Hz, H1), 2.44 (3H, s, TsCH<sub>3</sub>), 2.26 (2H, td,  $J$  = 7.0, 2.5 Hz, H4), 1.97 (1H, t,  $J$  = 2.5 Hz, H6), 1.88 (2H, qu,  $J$  = 7.5 Hz, H2), 1.60 (2H, qu,  $J$  = 7.5 Hz, H3), 1.34 (9H, s, C(CH<sub>3</sub>)<sub>3</sub>); **<sup>13</sup>C NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  151.0, 144.1, 137.4, 129.2, 127.8, 84.2, 84.0, 68.7, 46.6, 29.3, 27.9, 25.6, 21.6, 18.1; **HRMS** (ES+) calc. for C<sub>18</sub>H<sub>25</sub>NNaO<sub>4</sub>S [M+Na]<sup>+</sup> 374.1397, found 374.1391.

### **7-Bromohepta-1,6-diynyl)trimethylsilane **5a****

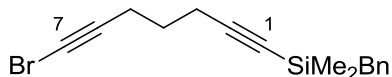


To a solution of 1,6-heptadiyne (750 mg, 8.14 mmol) in anhydrous THF (60 mL) at –78 °C was added 1.6 M *n*-BuLi (5.60 mL, 8.96 mmol) dropwise over 10 min. After dropwise addition of TMSCl (1.14 mL, 8.96 mmol) to the resulting light orange solution, the reaction was allowed to warm to rt and was stirred for 2 h. The reaction mixture was then poured into ice cold water (75 mL) and the residue extracted with Et<sub>2</sub>O (×3). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated *in vacuo* to afford the intermediate silyldiyne as a colourless liquid (628 mg, 47%). **<sup>1</sup>H NMR** (400 MHz,  $\text{CDCl}_3$ ) 2.35 (1H, t,  $J$  = 7.0 Hz, H7), 2.30 (2H, td,  $J$  = 7.0 Hz, H5), 1.96 (2H, t,  $J$  = 2.6 Hz, H3), 1.74 (2H, tt,  $J$  = 7.0, 6.9 Hz, H4), 0.15 (9H, s, Si(CH<sub>3</sub>)<sub>3</sub>). Data are in agreement with literature values.<sup>2</sup>

To a stirred solution of mono-trimethylsilyldiyne (441 mg, 2.68 mmol) in anhydrous THF (8 mL) at –78 °C was added dropwise *n*-BuLi (1.29 mL, 2.5 M solution in hexanes, 3.22 mmol). The resulting lithium acetylide solution was stirred at –78 °C for 30 min, and then bromine (0.19 mL, 3.75 mmol) was added dropwise until a red colour persisted. This light red solution was stirred at –78 °C for an additional 15 min. The solution was quenched with sat. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution and extracted with Et<sub>2</sub>O. The combined organic layers were dried (MgSO<sub>4</sub>) and the solvent was removed *in vacuo* to afford the desired bromoalkyne **5a** as a pale yellow liquid (646 mg, 99%); **<sup>1</sup>H NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  2.33 (2H, t,  $J$  = 6.9 Hz, H5), 2.32 (2H, t,  $J$  = 6.9 Hz, H3), 1.72 (2H, q,  $J$  = 6.9 Hz, H4), 0.14 (9H, s, Si(CH<sub>3</sub>)<sub>3</sub>); **<sup>13</sup>C**

**NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta_c$  105.9, 85.3, 79.4, 38.4, 27.3, 19.0, 0.1 Data are in agreement with literature values.<sup>3</sup>

**Benzyl(7-bromohepta-1,6-diyn-1-yl)dimethylsilane 5b**

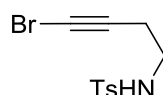


A solution of 1,6-heptadiyne (1.00 mL, 8.74 mmol) in anhydrous THF (4.1 mL) was cooled to  $-78^\circ\text{C}$ , under Ar, before the dropwise addition of LiHMDS (8.74 mL, 1 M in THF, 8.74 mmol). The reaction mixture was stirred for 45 min at  $-78^\circ\text{C}$  before a solution of BnMe<sub>2</sub>SiCl (1.9 mL, 10.5 mmol) in anhydrous THF (2.6 mL) was added. The resulting mixture was stirred for 1 h at  $-78^\circ\text{C}$ , and then at rt for 2 h, before quenching with sat. aq. NH<sub>4</sub>Cl and the addition of Et<sub>2</sub>O. After warming to rt the layers were separated and the aqueous layer extracted with Et<sub>2</sub>O (x2). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated *in vacuo*. Purification by column chromatography (petroleum ether  $\rightarrow$  petroleum ether / EtOAc (96:4)) afforded an inseparable 1:0.3 mixture (1.97 g, 82%) of the desired monoprotected diyne intermediate (63%) and the bisprotected diyne (19%) as a colourless oil;  $R_f$  0.63 (petroleum ether / EtOAc (30:1)); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta_H$  7.29-7.20 (2H, m, PhH), 7.15-7.00 (3H, m, PhH), 2.37 (2H, t,  $J = 7.0$  Hz, H3), 2.30 (2H, td,  $J = 7.0, 2.5$  Hz, H5), 2.19 (2H, s, SiCH<sub>2</sub>), 1.99 (1H, t,  $J = 2.5$  Hz, H7), 1.74 (1H, qu,  $J = 7.0$  Hz, H4), 0.12 (6H, s, Si(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta_c$  139.3, 128.5, 128.3, 124.4, 107.6, 83.8, 83.7, 69.0, 27.5, 26.6, 19.1, 17.6,  $-1.80$ . Data are in agreement with literature values.<sup>4,5</sup> Product used without further purification.

Desired bromoalkyne **5b** was obtained following General Procedure B, Method A using intermediate terminal alkyne (673 mg mono-silyldiyne, 2.80 mmol – 1.00 g mixture, 3.64 mmol). Purification *via* column chromatography (petroleum ether) afforded the desired bromoalkyne **5b** as a colourless oil (616 mg, 1.93 mmol, 69%);  $R_f$  0.46 (petroleum ether); IR (thin film,  $\nu_{\text{max}}$  / cm<sup>-1</sup>) 2958, 2175, 1600, 1493, 1452, 1251, 1208, 1156, 1057; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta_H$  7.26-7.07 (2H, m, PhH), 7.14-6.86 (3H, m, PhH), 2.32 (4H, dt,  $J = 10.5, 7.0$  Hz, H3 and H5), 2.18 (2H, s, SiCH<sub>2</sub>), 1.71 (2H, qu,  $J = 7.0$  Hz, H4), 0.02 (6H, d, Si(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta_c$  139.3, 128.5, 128.3, 124.4, 124.2, 107.5, 83.9, 79.5, 27.4, 26.6, 19.1, 18.9, 0.05,  $-1.79$ ; HRMS (EI+) calc. for C<sub>16</sub>H<sub>19</sub>BrSi [M]<sup>+</sup> 320.0420, found 320.0477.



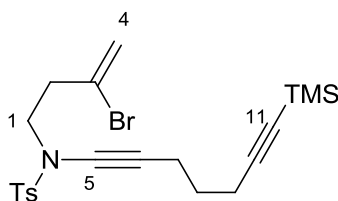
### ***tert*-Butyl (4-bromobut-3-yn-1-yl)(tosyl)carbamate **6****



Prepared by General Procedure B, Method B using *tert*-butyl *N*-but-3-ynyl-*N*-(*p*-tolylsulfonyl)carbamate<sup>1</sup> **4a** (1.00 g, 3.09 mmol). Mixture taken up in petroleum ether / EtOAc (1:1) and passed through a plug of silica to remove Ag salts, affording the crude intermediate bromoalkyne as a colourless solid (1.08 g, 87%); **mp** 93-94 °C. To a solution of *tert*-butyl (4-bromobut-3-yn-1-yl)(tosyl)carbamate (638 mg, 1.59 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (12 mL) was added TFA (3 mL) dropwise. Mixture was stirred for 1 h then poured into ice-water and extracted with CH<sub>2</sub>Cl<sub>2</sub> (×3). The mixture was dried (MgSO<sub>4</sub>), filtered and concentrated *in vacuo* to afford the crude tosylamide as a pale yellow paste (470 mg, 98%); **R<sub>f</sub>** 0.19 (petroleum ether / EtOAc (4:1)); **IR** (thin film)  $\nu_{\text{max}}$  = 3280, 3061, 2949, 2936, 1598, 1420, 1326, 1158, 1093, 815, 664; **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta_{\text{H}}$  7.76 (2H, d,  $J$  = 8.3 Hz, TsH), 7.32 (2H, d,  $J$  = 8.3 Hz, TsH), 4.71 (1H, t,  $J$  = 6.5 Hz, NH), 3.11 (2H, q,  $J$  = 6.5 Hz, NTsCH<sub>2</sub>), 2.44 (3H, TsCH<sub>3</sub>), 2.38 (2H, t,  $J$  = 6.5 Hz, NTsCH<sub>2</sub>CH<sub>2</sub>); **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta_{\text{C}}$  143.8, 137.0, 130.0, 127.2, 76.4, 41.6, 41.2, 21.7, 21.3; **HRMS** (ES+) calc. for C<sub>11</sub>H<sub>12</sub>BrNNaO<sub>2</sub>S [M+Na]<sup>+</sup> 323.9664, found 323.9671.

### *Cyclisation substrates*

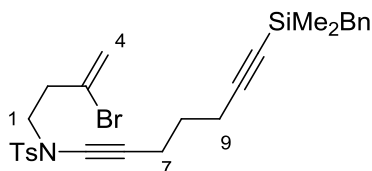
#### ***N*-(3-Bromobut-3-enyl)-4-methyl-*N*-(7-(trimethylsilyl)hepta-1,6-diynyl)benzenesulfonamide **1a****



Prepared by General Procedure C using sulfonamide **3a** (150 mg, 0.49 mmol) and bromoalkyne **5a** (236 mg, 0.74 mmol). Purification *via* column chromatography (petroleum ether / EtOAc (10:1)) afforded the desired ynamide **1a** as a pale yellow oil (278 mg, 60%); **R<sub>f</sub>** 0.38 (petroleum ether / ether (3:1)); **IR** (thin film)  $\nu_{\text{max}}$  = 2957, 2255, 2174, 1631, 1597, 1367, 1249, 1211; **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta_{\text{H}}$  7.79 (2H, d,  $J$  = 8.2 Hz, TsH), 7.35 (2H, d,  $J$  = 8.2 Hz, TsH), 5.64 (1H, appt s, H4), 5.45 (1H, d,  $J$  = 1.8 Hz, H4), 3.51 (2H, t,  $J$  = 7.1 Hz, H1), 2.72 (2H, t,  $J$  = 7.1 Hz, H2), 2.45 (3H, s, TsCH<sub>3</sub>), 2.39 (2H, t,  $J$  = 7.0 Hz, H7), 2.28 (2H, t,  $J$  = 7.0 Hz, H9), 1.69 (2H, qu,  $J$  = 7.0 Hz, H8), 0.15 (9H, s, Si(CH<sub>3</sub>)<sub>3</sub>); **<sup>13</sup>C NMR** (126

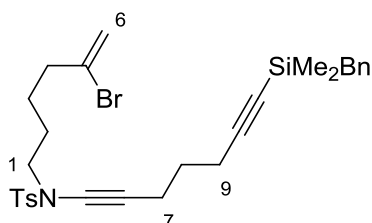
MHz)  $\delta_c$  144.7, 134.6, 129.9, 129.2, 127.8, 119.8, 106.3, 85.4, 73.5, 69.9, 49.8, 40.2, 28.0, 21.8, 19.1, 17.7, 0.3; **HRMS** (ES+) calc. for  $C_{21}H_{28}^{79}BrNNaO_2Si$   $[M+Na]^+$  488.0681, found 488.0686.

***N*-(7-(Benzyldimethylsilyl)hepta-1,6-diyn-1-yl)-*N*-(3-bromobut-3-en-1-yl)-4-methylbenzenesulfonamide **1b****



Prepared by General Procedure C using sulfonamide **3a** (150 mg, 0.49 mmol) and benzyl(7-bromohepta-1,6-diyn-1-yl)dimethylsilane **5b** (236 mg, 0.74 mmol). Purification *via* column chromatography (petroleum ether  $\rightarrow$  petroleum ether / EtOAc (10:1)) afforded the bromoenynamide **1b** as a colourless oil (139 mg, 0.25 mmol, 52%);  $R_f$  0.42 (petroleum ether / EtOAc (10:1)); **IR** (thin film,  $\nu_{max}$  /  $cm^{-1}$ ) 2957, 2173, 1699, 1599, 1494, 1358, 1250, 1163;  $^1H$  **NMR** (400 MHz,  $CDCl_3$ )  $\delta_H$  7.79 (2H, d,  $J$  = 8.5 Hz, TsH), 7.34 (2H, d,  $J$  = 8.0 Hz, TsH), 7.21 (2H, t,  $J$  = 7.5 Hz, PhH), 7.12-7.02 (3H, m, PhH), 5.64 (1H, d,  $J$  = 1.5 Hz, H4), 5.45 (1H d,  $J$  = 2.0 Hz, H4'), 3.52 (2H, t,  $J$  = 7.0 Hz, H1), 2.73 (2H, t,  $J$  = 7.0 Hz,  $CH_2$ ), 2.44 (3H, s, Ts $CH_3$ ), 2.37 (2H, t,  $J$  = 7.0 Hz,  $CH_2$ ), 2.28 (2H, t,  $J$  = 7.0 Hz,  $CH_2$ ), 2.18 (2H, s, Si $CH_2$ ), 1.68 (2H, qu,  $J$  = 7.0 Hz, H8), 0.11 (6H, s, Si( $CH_3$ ) $_2$ );  $^{13}C$  **NMR** (101 MHz,  $CDCl_3$ )  $\delta_c$  144.7, 139.3, 134.6, 129.9, 129.2, 128.5, 128.3, 127.8, 124.4, 119.8, 107.8, 83.8, 73.5, 69.9, 49.8, 40.2, 27.9, 26.6, 21.8, 19.1, 17.7, -1.76; **HRMS** (ES+) calc. for  $C_{27}H_{32}BrNNaO_2Si$   $[M+Na]^+$  564.0999, found 564.1001.

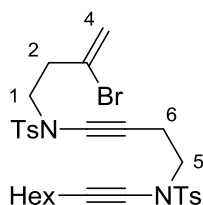
***N*-(7-(Benzyldimethylsilyl)hepta-1,6-diyn-1-yl)-*N*-(5-bromohex-5-en-1-yl)-4-methylbenzene sulfonamide **1c****



Prepared by General Procedure C using sulfonamide **3b** (163 mg, 0.49 mmol) and benzyl(7-bromohepta-1,6-diyn-1-yl)dimethylsilane **5b** (236 mg, 0.74 mmol). Purification *via* column chromatography (petroleum ether  $\rightarrow$  petroleum ether / EtOAc (10:1)) afforded the bromoenynamide **1c** as a colourless oil (106 mg, 0.18 mmol, 37%);  $R_f$  0.41 (petroleum ether / EtOAc

(10:1)); **IR** (thin film,  $\nu_{\max}$  /  $\text{cm}^{-1}$ ) 2953, 2173, 1695, 1599, 1355, 1249, 1161, 1088;  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  7.78 (2H, d,  $J$  = 8.5 Hz, TsH), 7.33 (2H, d,  $J$  = 8.0 Hz, TsH), 7.21 (2H, t,  $J$  = 7.5 Hz, PhH), 7.12-7.00 (3H, m, PhH), 5.56 (1H, d,  $J$  = 1.5 Hz, H6), 5.39 (1H, d,  $J$  = 1.5 Hz, H6'), 3.28 (2H, t,  $J$  = 6.5 Hz, H1), 2.49-2.40 (5H, m, TsCH<sub>3</sub> and CH<sub>2</sub>), 2.37 (2H, t,  $J$  = 7.0 Hz, CH<sub>2</sub>), 2.28 (2H, t,  $J$  = 7.1 Hz, CH<sub>2</sub>), 2.18 (2H, s,  $J$  = 7.5 Hz, SiCH<sub>2</sub>), 1.73-1.54 (6H, m, 3  $\times$  CH<sub>2</sub>), 0.16-0.04 (6H, m, Si(CH<sub>3</sub>)<sub>2</sub>);  **$^{13}\text{C}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  144.6, 139.3, 134.6, 134.0, 129.8, 128.5, 128.3, 127.8, 124.4, 117.1, 107.8, 83.7, 73.7, 69.4, 51.1, 40.8, 28.0, 26.6, 26.5, 24.6, 21.8, 19.1, 17.8, -1.76; **HRMS** (ES+) calc. for C<sub>29</sub>H<sub>38</sub>BrNNaO<sub>3</sub>SSi [M+Na]<sup>+</sup> 610.1417, found 610.1411.

***N*-(3-Bromobut-3-en-1-yl)-4-methyl-*N*-(4-(4-methyl-*N*-(oct-1-yn-1-yl)phenylsulfonamido)but-1-yn-1-yl)benzenesulfonamide 1d**

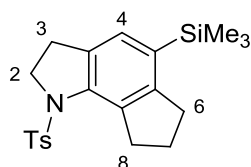


To a mixture of tosylamide **6** (100 mg, 0.331 mmol), K<sub>3</sub>PO<sub>4</sub> (140 mg, 0.662 mmol), CuSO<sub>4</sub>·5H<sub>2</sub>O (17 mg, 0.0662 mmol) and 1,10-phenanthroline (24 mg, 0.124 mmol) was added a solution of the 1-bromo-1-octyne (939 mg, 4.97 mmol) in toluene (2 mL). The mixture was heated at 80 °C for 16 h, then cooled to rt before filtration through cotton wool, eluting with Et<sub>2</sub>O. The organic fraction was concentrated *in vacuo*. Purification *via* column chromatography (petroleum ether / EtOAc (19:1) → petroleum ether / EtOAc (9:1)) gave the desired intermediate ynamide product as a colourless oil (60.0 mg, 44%) which was used immediately. To a mixture of the intermediate tosylamide (44.0 mg, 0.146 mmol), K<sub>3</sub>PO<sub>4</sub> (62.0 mg, 0.292 mmol), CuSO<sub>4</sub>·5H<sub>2</sub>O (7.0 mg, 0.0292 mmol) and 1,10-phenanthroline (11.0 mg, 0.0584 mmol) was added a solution of bromoalkyne **3a** (60 mg, 0.146 mmol) in toluene (0.45 mL). The mixture was heated at 80 °C for 2.5 h, then cooled to rt before filtration through cotton wool, eluting with Et<sub>2</sub>O. The organic fraction was concentrated *in vacuo*. Purification *via* column chromatography (petroleum ether / EtOAc (9:1)) gave the desired product **1d** as a colourless oil (56.2 mg, 0.0876 mmol, 60%); **R<sub>f</sub>** 0.28 (petroleum ether / EtOAc (4:1)); **IR** (thin film)  $\nu_{\max}$  = 2929, 2843, 2156, 1689, 1597, 1353, 1241, 1138, 1089;  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  7.79 (2H, d,  $J$  = 8.3 Hz, TsH), 7.76 (2H, d,  $J$  = 8.3 Hz, TsH), 7.35 (2H, d,  $J$  = 8.3 Hz, TsH), 7.33 (2H, d,  $J$  = 8.3 Hz, TsH), 5.68-5.62 (1H, m, C(Br)=CH<sub>A</sub>H<sub>B</sub>), 5.42 (1H, d,  $J$  = 1.7 Hz, C(Br)=CH<sub>A</sub>H<sub>B</sub>), 3.49 (1H, t,  $J$  = 7.0 Hz, H5), 3.37 (1H, t,  $J$  = 7.0 Hz, H1), 2.70 (2H, t,  $J$  = 7.0 Hz, H2), 2.62 (2H, t,  $J$  = 7.0 Hz, H6), 2.45 (3H, s, TsCH<sub>3</sub>), 2.44 (3H, s, TsCH<sub>3</sub>), 2.23 (2H, t,  $J$  = 7.1 Hz, N(Ts)C≡C-CH<sub>2</sub>), 1.50-1.40 (2H, m, C≡C-

$\text{CH}_2\text{CH}_2$ ), 1.37-1.20 (6H, m,  $\text{CH}_2 \times 3$ ), 0.88 (3H, t,  $J = 6.9$  Hz,  $\text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  144.8, 144.6, 134.7, 134.5, 130.0, 129.8, 129.1, 127.7 ( $\times 2$ ), 119.9, 74.7, 72.5, 71.1, 66.6, 50.5, 49.7, 40.0, 31.4, 28.9, 28.6, 22.7, 21.8, 21.8, 18.6, 18.5, 14.2; HRMS (ES+) calc. for  $\text{C}_{30}\text{H}_{38}\text{BrN}_2\text{NaO}_4\text{S}_2$   $[\text{M}+\text{H}]^+$  633.1451, found 633.1447.

### Cyclisation products

#### 1-Tosyl-5-(trimethylsilyl)-1,2,3,6,7,8-hexahydrocyclopenta[g]indole **2a**

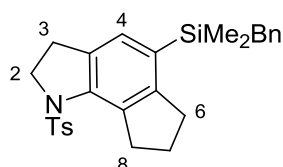


Prepared by General Procedure E (5 mol%  $\text{Pd}(\text{PPh}_3)_4$ , 0.16 M in MeCN) from ynamide **1a** (300 mg, 0.643 mmol) to afford the title compound **2a** as a colourless crystalline solid (217 mg, 88%); mp. 103 °C;  $R_f$  0.29 (petroleum ether /  $\text{Et}_2\text{O}$  (3:1)); IR (thin film)  $\nu_{\text{max}} = 2959, 1597, 1377, 1271, 1167, 1090, 996$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  7.47 (2H, d,  $J = 8.3$  Hz, TsH), 7.18 (2H, d,  $J = 8.1$  Hz, TsH), 7.00 (1H, s, H4), 3.97 (2H, t,  $J = 7.6$  Hz, H2), 3.21 (2H, t,  $J = 7.3$  Hz, H8), 2.97 (2H, t,  $J = 7.3$  Hz, H6), 2.40 (3H, s,  $\text{TsCH}_3$ ), 2.31 (2H, t,  $J = 7.6$  Hz, H3), 2.06 (2H, qu,  $J = 7.3$  Hz, H7), 0.28 (9H, s,  $\text{Si}(\text{CH}_3)_3$ );  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  151.5, 143.8, 140.1, 135.8, 135.6, 133.2, 132.7, 129.6, 128.0, 127.5, 52.6, 34.4, 32.5, 28.8, 26.4, 21.7, -0.4; HRMS (ES+) calc. for  $\text{C}_{23}\text{H}_{34}\text{N}_3\text{O}_2\text{SSi}$   $[\text{M}+\text{MeCN}+\text{NH}_4]^+$  444.2136, found 444.2127.

NB. Following procedure E using 10%  $\text{Pd}(\text{PPh}_3)_4$ , 0.017 M gave a yield of 90% after purification.

Following procedure E using 5%  $\text{Pd}(\text{PPh}_3)_4$ , 0.017 M gave a yield of 78% after purification.

#### 5-(Benzyldimethylsilyl)-1-tosyl-1,2,3,6,7,8-hexahydrocyclopenta[g]indole **2b**

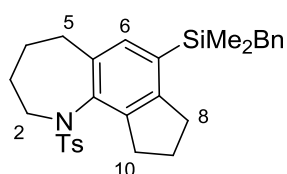


Prepared by General Procedure E (10 mol%  $\text{Pd}(\text{PPh}_3)_4$ , 0.16 M in MeCN) using bromoenynamide **1b** (20.0 mg, 0.036 mmol) with heating for 16 h. Purification *via* column chromatography (petroleum ether  $\rightarrow$  petroleum ether / EtOAc (9:1)) afforded the desired tricycle **2b** as a colourless oil (15.5 mg, 0.033 mmol, 90%);  $R_f$  0.28 (petroleum ether / EtOAc (10:1)); IR (thin film,  $\nu_{\text{max}}$  /  $\text{cm}^{-1}$ ) 2957, 1598,

1493, 1357, 1250, 1165, 1090, 909, 833;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  7.45 (2H, d,  $J = 8.5$  Hz, TsH), 7.19-7.14 (3H, m, TsH and PhH), 7.10-7.04 (2H, m, PhH), 6.93 (1H, s, H4), 6.89 (2H, d,  $J = 7.0$  Hz, BnH), 3.97 (2H, t,  $J = 7.5$  Hz, H2), 3.20 (2H, t,  $J = 7.5$  Hz, H6 or H8), 2.84 (2H, t,  $J = 7.5$  Hz, H6 or H8), 2.39 (3H, s,  $\text{TsCH}_3$ ), 2.30 (2H, s,  $\text{SiCH}_2$ ), 2.26 (2H, t,  $J = 7.5$  Hz, H3), 2.01 (2H, qu,  $J = 7.5$  Hz, H7), 0.25 (6H, s,  $\text{Si}(\text{CH}_3)_2$ );  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  151.9, 143.9, 140.3, 139.9, 136.0, 135.4, 133.3, 130.9, 129.6, 128.5, 128.4, 128.2, 127.5, 124.2, 52.6, 34.6, 32.5, 28.7, 26.4, 26.3, 21.8, -2.47; **HRMS** (ES+) calc. for  $\text{C}_{27}\text{H}_{31}\text{NNaO}_2\text{SSi}$   $[\text{M}+\text{Na}]^+$  484.1737, found 484.1731.

*NB.* Following procedure E using 10%  $\text{Pd}(\text{PPh}_3)_4$ , 0.017 M gave a yield of 73% after purification.

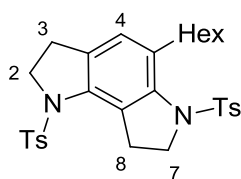
### 7-(Benzyldimethylsilyl)-1-tosyl-1,2,3,4,5,8,9,10-octahydroindeno[4,5-*b*]azepane **2c**



Prepared by General Procedure E (10 mol%  $\text{Pd}(\text{PPh}_3)_4$ , 0.16 M in MeCN) using bromoenynamide **1c** (20.0 mg, 0.035 mmol) with heating for 19 h. Purification *via* column chromatography (petroleum ether  $\rightarrow$  petroleum ether / EtOAc (9:1)) afforded the desired tricycle **2c** as a colourless oil (13.4 mg, 0.027 mmol, 78%);  $R_f$  0.28 (petroleum ether / EtOAc (10:1)); **IR** (thin film,  $\nu_{\text{max}}$  /  $\text{cm}^{-1}$ ) 2937, 1599, 1493, 1451, 1344, 1157, 1094, 1036, 908;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  7.67 (2H, d,  $J = 8.5$  Hz, TsH), 7.27 (2H, d,  $J = 7.5$  Hz, TsH), 7.18 (2H, t,  $J = 7.5$  Hz, PhH), 7.07 (1H, t,  $J = 7.5$  Hz, PhH), 6.92 (2H, d,  $J = 6.0$  Hz, PhH), 4.32 (1H, dt,  $J = 15.4, 3.2$  Hz, H2), 3.21-3.11 (1H, m, H8 or H10), 3.02 (1H, ddd,  $J = 14.5, 12.5, 2.5$  Hz, H2'), 2.97-2.82 (3H, m, H8 or H10, and H8' and H10'), 2.43 (3H, d,  $\text{TsCH}_3$ ), 2.37-2.28 (3H, m,  $\text{SiCH}_2$  and H5), 2.16 (1H, d,  $J = 13.0$  Hz, H5'), 2.10 (1H, ddt,  $J = 16.0, 8.0, 4.0$  Hz, H9), 1.89 (1H, ddt,  $J = 17.5, 12.0, 8.5$  Hz, H9'), 1.75-1.61 (2H, m, H3 and H4), 1.60-1.49 (1H, m, H3'), 1.16-1.07 (1H, m, H4'), 0.25 (6H, s,  $\text{Si}(\text{CH}_3)_2$ );  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  150.2, 144.9, 143.2, 139.9, 139.6, 139.2, 137.7, 134.2, 133.7, 129.7, 128.5, 128.2, 127.7, 124.2, 50.3, 34.8, 33.6, 40.00, 28.5, 26.3, 26.1, 25.8, 21.7, -2.64, -2.71; **HRMS** (ES+) calc. for  $\text{C}_{29}\text{H}_{35}\text{NNaO}_2\text{SSi}$   $[\text{M}+\text{Na}]^+$  512.2050, found 512.2049.

*NB.* Following procedure E using 10%  $\text{Pd}(\text{PPh}_3)_4$ , 0.017 M gave a complex mixture containing some desired product.

### 5-Hexyl-1,6-ditosyl-1,2,3,6,7,8-hexahydropyrrolo[2,3-*e*]indole **2d**



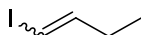
Synthesised from ynamide **1d** (36.0 mg, 0.0568 mmol) using Procedure E (5 mol% Pd(PPh<sub>3</sub>)<sub>4</sub>, 0.17 M in MeCN) to afford the title compound **2d** as a colourless oil (31.4 mg, 70%); *R<sub>f</sub>* 0.35 (petroleum ether / EtOAc (4:1)); **IR** (thin film)  $\nu_{\max}$  = 2926, 2856, 1598, 1493, 1403, 1355, 1210, 1165, 813, 709, 680; **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta_{\text{H}}$  7.60 (2H, d, *J* = 8.0 Hz, TsH), 7.29 (2H, d, *J* = 8.0 Hz, TsH), 7.25 (2H, d, *J* = 8.0 Hz, TsH), 7.23 (2H, d, *J* = 8.0 Hz, TsH), 6.88 (1H, s, H<sub>4</sub>), 3.97 (2H, t, *J* = 7.3 Hz, H<sub>7</sub>), 3.87 (2H, t, *J* = 7.6 Hz, H<sub>2</sub>), 2.99 (2H, dd, *J* = 7.6 and 0.3 Hz, ArCH<sub>2</sub>CH<sub>2</sub>), 2.52 (2H, t, *J* = 7.3 Hz, H<sub>8</sub>), 2.44 (3H, s, TsCH<sub>3</sub>), 2.34 (3H, s, TsCH<sub>3</sub>), 2.19 (2H, t, *J* = 7.6 Hz, H<sub>3</sub>), 1.65-1.55 (2H, m, ArCH<sub>2</sub>CH<sub>2</sub>), 1.38-1.25 (6H, m, CH<sub>2</sub>×3), 0.93-0.86 (3H, m, CH<sub>2</sub>CH<sub>3</sub>); **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta_{\text{C}}$  144.5, 144.3, 141.9, 136.8, 135.8, 135.3, 135.2, 134.8, 130.5, 129.7, 129.7, 129.6, 127.9, 127.4, 124.8, 53.6, 52.7, 32.4, 31.9, 30.4, 29.4, 29.4, 28.8, 22.8, 21.8, 21.8, 14.3 (*NB* Significant signal overlap observed); **HRMS** (ES<sup>+</sup>) calc. for C<sub>30</sub>H<sub>36</sub>N<sub>2</sub>NaO<sub>4</sub>S<sub>2</sub> [M+Na]<sup>+</sup> 575.2009, found 575.2001.

*NB.* Following procedure E using 10% Pd(PPh<sub>3</sub>)<sub>4</sub>, 0.017 M gave a yield of 49% after purification.

Following procedure E using 5% Pd(PPh<sub>3</sub>)<sub>4</sub>, 0.017 M gave a yield of 52% after purification.

### Hiyama cross-coupling compounds

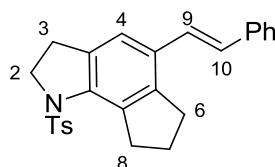
#### (*E*)-1-iodobut-1-ene and (*Z*)-1-iodobut-1-ene **7b**



To chromium(II) chloride (2.12 g, 17.22 mmol, 10.0 equiv.), dried under vacuum and heat, was added anhydrous THF (48 mL) and the resulting suspension stirred for 30 min at rt before being cooled to 0 °C. A solution of propionaldehyde (0.12 mL, 1.72 mmol, 1.0 equiv.) and iodoform (2.03 g, 5.16 mmol, 3.0 equiv.) in anhydrous THF (8 mL) was added *via* syringe. The resulting brown solution was stirred in the dark for 2.5 h at 0 °C before being diluted with Et<sub>2</sub>O and quenched with distilled water. The aqueous layer was extracted with Et<sub>2</sub>O (×2) and the combined organic layers washed sequentially with sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, brine, dried (MgSO<sub>4</sub>) and concentrated carefully *in vacuo* (no heat on water bath, lowest pressure 500 mbar). The solution was then carefully concentrated *in vacuo* by Kugelrohr distillation (80 °C at 200 mbar) to afford a 80:20 mixture of *E:Z*-**7b** in THF which was stored

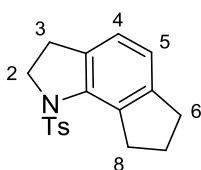
in the freezer in the dark (46 mg in THF, 0.25 mmol, 15%);  $R_f$  0.81 (petroleum ether); **(E)-7b**:  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_H$  6.53 (1H, dt,  $J = 14.5, 6.5$  Hz, H2), 5.95 (1H, dt,  $J = 14.5, 1.5$  Hz, H1), 2.10-2.01 (2H, m, H3), 0.98 (3H, t,  $J = 7.5$  Hz, H4); **(Z)-7b**:  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta_H$  6.18-6.07 (2H, m, H1 and H2), 2.17-2.08 (2H, m, H3), 1.00 (3H, t,  $J = 7.5$  Hz, H4). Data are in agreement with literature values.<sup>6</sup>

**(E)-5-Styryl-1-tosyl-1,2,3,6,7,8-hexahydrocyclopenta[*g*]indole 8a**



A modified procedure of Hirabayashi *et al.* was used for this preparation.<sup>7</sup> To a solution of the BDMS-substituted indoline **2b** (6.0 mg, 0.013 mmol, 1.0 equiv.) and commercial styrenyl iodide **7a** (4.4 mg, 0.019 mmol, 1.5 equiv.) in THF (0.04 mL) was added TBAF (0.14  $\mu\text{L}$ , 0.014 mmol, 1.1 equiv.) at 0  $^\circ\text{C}$ , and the resulting mixture stirred for 10 min. To this was added a pre-made solution of  $\text{Pd}(\text{PPh}_3)_4$  (0.8 mg, 0.65  $\mu\text{mol}$ , 5 mol%) and  $\text{Ag}_2\text{O}$  (3.2 mg, 0.014 mmol, 1.1 equiv.) in THF (0.1 mL) and the resulting mixture stirred at rt for 22 h. The reaction was diluted with EtOAc, filtered through a short silica plug and concentrated *in vacuo*. Purification *via* column chromatography (petroleum ether  $\rightarrow$  petroleum ether / EtOAc (10:1)) afforded the desired coupled product **8a** as a yellow oil (3.7 mg, 0.0088 mmol, 68%);  $R_f$  0.37 (petroleum ether / EtOAc (4:1)); IR (thin film,  $\nu_{\text{max}}$  /  $\text{cm}^{-1}$ ) 2924, 1597, 1454, 1355, 1249, 1164, 1090, 962;  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta_H$  7.51-7.38 (4H, m, TsH and PhH), 7.39-7.32 (2H, m, PhH), 7.28-7.23 (1H, m, PhH), 7.21-7.14 (4H, m, TsH, H4 and H9 or H10), 6.97 (1H, d,  $J = 16.5$  Hz, H9 or H10), 3.99 (2H, t,  $J = 7.5$  Hz, H2), 3.28 (2H, t,  $J = 7.5$  Hz, H6 or H8), 3.08-3.01 (2H, t,  $J = 7.5$  Hz, H6 or H8), 2.38 (3H, s, TsCH<sub>3</sub>), 2.28 (2H, t,  $J = 7.5$  Hz, H3), 2.11 (2H, dt,  $J = 14.5, 7.5$  Hz, H7);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta_C$  144.4, 144.0, 138.4, 137.7, 137.0, 135.3, 135.0, 131.4, 129.7, 129.0, 128.9, 127.8, 127.5, 126.6, 126.5, 119.0, 52.7, 33.2, 32.2, 28.7, 25.9, 21.7; HRMS (ES+) calc. for  $\text{C}_{26}\text{H}_{25}\text{NNaO}_2\text{S}$   $[\text{M}+\text{Na}]^+$  438.1498, found 438.1503.

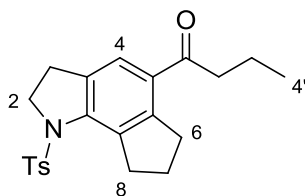
### 1-Tosyl-1,2,3,6,7,8-hexahydrocyclopenta[*g*]indole **B**



Isolated as a side-product using a modified procedure of Hirabayashi *et al.* for a Hiyama coupling.<sup>7</sup> To a solution of the BDMS-substituted indoline **2b** (6.0 mg, 0.013 mmol, 1.0 equiv.) and styrenyl iodide **7a** (3.5 mg, 0.019 mmol, 1.5 equiv.) in THF (0.04 mL) was added TBAF (0.14  $\mu$ L, 0.014 mmol, 1.1 equiv.) at 0 °C, and the resulting mixture stirred for 10 min. To this was added a pre-prepared solution of Pd(PPh<sub>3</sub>)<sub>4</sub> (0.8 mg, 0.7  $\mu$ mol, 5 mol%) and Ag<sub>2</sub>O (3.2 mg, 0.014 mmol, 1.1 equiv.) in THF (0.1 mL) and the resulting mixture stirred at rt for 17 h. The reaction was diluted with EtOAc, filtered through a short silica plug and concentrated *in vacuo*. Purification *via* column chromatography (petroleum ether  $\rightarrow$  petroleum ether / EtOAc (10:1)) afforded the desilylated indoline **B** as a colourless oil (2.7 mg, 0.0087 mmol, 67%); *R*<sub>f</sub> 0.60 (petroleum ether / EtOAc (4:1)); **IR** (thin film,  $\nu_{\text{max}}$  / cm<sup>-1</sup>) 2956, 1597, 1447, 1355, 1254, 1165, 1091, 908; **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta_{\text{H}}$  7.43 (2H, d, *J* = 8.5 Hz, TsH), 7.15 (2H, d, *J* = 8.0 Hz, TsH), 6.99 (1H, d, *J* = 7.5 Hz, H4), 6.83 (1H, d, *J* = 7.5 Hz, H5), 3.98 (2H, t, *J* = 7.5 Hz, H2), 3.24 (2H, t, *J* = 7.5 Hz, H6 or H8), 2.91 (2H, t, *J* = 7.5 Hz, H6 or H8), 2.37 (3H, s, TsCH<sub>3</sub>), 2.25 (2H, t, *J* = 7.5 Hz, H3), 2.06 (2H, qu, *J* = 7.5 Hz, H7); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta_{\text{C}}$  146.0, 143.9, 139.0, 136.9, 135.2, 134.1, 129.6, 127.5, 122.5, 122.1, 52.7, 33.3, 33.1, 28.7, 26.4, 21.7; **HRMS** (ES<sup>+</sup>) calc. for C<sub>18</sub>H<sub>19</sub>NNaO<sub>2</sub>S [M+Na]<sup>+</sup> 336.1029, found 336.1031.

### Bis(*desmethyl*)trikentrin compounds

#### 1-(1-Tosyl-1,2,3,6,7,8-hexahydrocyclopenta[*g*]indol-5-yl)butan-1-one **9**

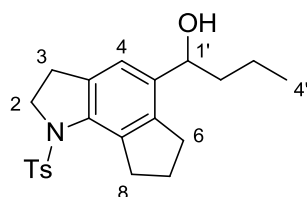


To a solution of AlCl<sub>3</sub> (375 mg, 2.81 mmol) and butyryl chloride (0.30 mL, 2.81 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (6.5 mL) was added a solution of indoline **2a** (217 mg, 0.563 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (6.5 mL). The reaction was stirred for 1 h at rt, quenched with sat. NaHCO<sub>3</sub> solution and extracted with CH<sub>2</sub>Cl<sub>2</sub> (×3). The combined organic layers were dried (MgSO<sub>4</sub>) and the solvent was removed *in vacuo*. Purification *via* column chromatography (petroleum ether / Et<sub>2</sub>O (10:1)) afforded the ketone **9** as a



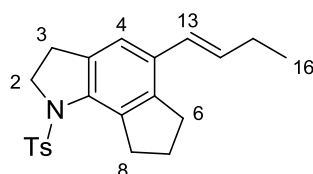
colourless solid (171 mg, 79%); **mp.** 108 °C; **R<sub>f</sub>** 0.12 (petroleum ether / Et<sub>2</sub>O (3:1)); **IR** (thin film)  $\nu_{\text{max}}$  = 2960, 1677, 1597, 1456, 1361, 1165, 1088; **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta_{\text{H}}$  7.45 (2H, d,  $J$  = 8.2 Hz, TsH), 7.36 (1H, s, H4), 7.17 (2H, d,  $J$  = 8.2 Hz, TsH), 4.04 (2H, t,  $J$  = 7.5 Hz, H2), 3.21 (4H, app t,  $J$  = 7.5 Hz, H6 + H8), 2.84 (2H, t,  $J$  = 7.5 Hz, H2'), 2.38 (3H, s, ArCH<sub>3</sub>), 2.37 (2H, t,  $J$  = 7.5 Hz, H3), 2.04 (2H, qu,  $J$  = 7.5 Hz, H7), 1.72 (2H, sextet,  $J$  = 7.5 Hz, H3'), 0.97 (3H, t,  $J$  = 7.4 Hz, H4'); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta_{\text{C}}$  201.8, 148.1, 144.2, 142.2, 138.1, 135.3, 134.2, 132.2, 129.8, 127.4, 123.3, 52.8, 42.4, 34.6, 32.8, 28.6, 26.4, 21.8, 18.0, 14.1; **HRMS** (ES<sup>+</sup>) calc. for C<sub>22</sub>H<sub>25</sub>NNaO<sub>3</sub>S [M+Na]<sup>+</sup> 406.1447, found 406.1443.

**1-(1-Tosyl-1,2,3,6,7,8-hexahydrocyclopenta[g]indol-5-yl)butan-1-ol 10**



To a stirred solution of ketone **9** (171 mg, 0.446 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (4.5 mL) and MeOH (3 mL) at 0 °C was added NaBH<sub>4</sub> (34 mg, 0.892 mmol). Upon completion by TLC analysis (~1 h), the reaction mixture was quenched with water and extracted with CH<sub>2</sub>Cl<sub>2</sub> (×3). The combined organics were dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo* to afford the title product **10** as a colourless solid (166 mg, 0.430 mmol, 96%); **mp.** 140-145 °C; **R<sub>f</sub>** 0.14 (petroleum ether / EtOAc (3:1)); **IR** (thin film)  $\nu_{\text{max}}$  = 3527, 2957, 1597, 1352, 1164, 1090, 1021; **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta_{\text{H}}$  7.41 (2H, d,  $J$  = 8.2 Hz, TsH), 7.14 (2H, d,  $J$  = 8.2 Hz, TsH), 6.98 (1H, s, H4), 4.80 (1H, t,  $J$  = 8.2 Hz, H1'), 3.97 (2H, m, H2), 3.23 (2H, t,  $J$  = 7.4 Hz, H6), 2.89 (2H, m, H8), 2.38 (3H, s, TsCH<sub>3</sub>), 2.25 (2H, t,  $J$  = 7.6 Hz, H3), 2.06 (2H, m, H7), 1.78-1.57 (2H, m, H2'), 1.50-1.24 (2H, m, H3'), 0.94 (3H, t,  $J$  = 7.4 Hz, H4'); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) 143.9, 142.4, 138.6, 138.0, 136.7, 135.1, 134.9, 129.5, 127.5, 119.4, 71.7, 52.7, 40.4, 32.9, 31.5, 28.7, 26.1, 21.7, 19.1, 14.1; **HRMS** (ES<sup>+</sup>) calc. for C<sub>22</sub>H<sub>27</sub>NNaO<sub>3</sub>S [M+Na]<sup>+</sup> 408.1604, found 408.1617.

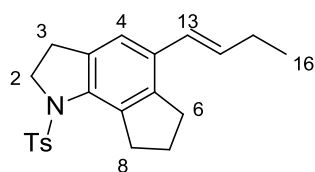
**(E)-5-(But-1-en-1-yl)-1-tosyl-1,2,3,6,7,8-hexahydrocyclopenta[g]indole 8b**



To a solution of 1-(1-tosyl-1,2,3,6,7,8-hexahydrocyclopenta[g]indol-5-yl)butan-1-ol **10** (200 mg, 0.519 mmol, 1.0 equiv.) in anhydrous toluene (2.4 mL) was added *p*-toluenesulfonic acid (10.0 mg,

0.0519 mmol, 0.1 equiv.) and a few 3 Å molecular sieves, and the resulting mixture heated at reflux for 16 h. The reaction was allowed to cool to rt, was quenched with sat. *aq.* NaHCO<sub>3</sub> solution and extracted with Et<sub>2</sub>O (×3). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated *in vacuo*. Purification *via* column chromatography (petroleum ether → petroleum ether / EtOAc (4:1)) afforded the desired product **8b** as a colourless oil (157 mg, 0.427 mmol, 82%) which solidified on standing; **mp.** 120-121 °C; **R<sub>f</sub>** 0.52 (petroleum ether / EtOAc (10:1)); **IR** (thin film,  $\nu_{\text{max}}$  / cm<sup>-1</sup>) 2959, 1597, 1454, 1355, 1250, 1164, 1090, 967; **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta_{\text{H}}$  7.45 (2H, d, *J* = 8.5 Hz, TsH), 7.16 (2H, d, *J* = 8.0 Hz, TsH), 6.99 (1H, s, H4), 6.43 (1H, d, *J* = 16.0 Hz, H13), 6.13 (1H, dt, *J* = 16.0, 6.5 Hz, H14), 3.97 (2H, t, *J* = 7.5 Hz, H2), 3.25 (2H, t, *J* = 7.5 Hz, H6 or H8), 2.94 (2H, t, *J* = 7.5 Hz, H6 or H8), 2.38 (3H, s, TsCH<sub>3</sub>), 2.30-2.19 (4H, m, H3 and H15), 2.07 (2H, qu, *J* = 7.5 Hz, H7), 1.09 (3H, t, *J* = 7.5 Hz, H16); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta_{\text{C}}$  143.8, 143.2, 137.6, 136.8, 135.2, 134.8, 133.3, 131.9, 129.6, 127.5, 126.7, 118.9, 52.7, 33.2, 32.1, 28.7, 26.5, 25.9, 21.7, 14.0; **HRMS** (ES+) calc. for C<sub>22</sub>H<sub>25</sub>NNaO<sub>2</sub>S [M+Na]<sup>+</sup> 390.1498, found 390.1500.

**(*E*)-5-(But-1-en-1-yl)-1,6,7,8-tetrahydrocyclopenta[*g*]indole [bis(desmethyl)trikentrin] 12**



*Preparation of sodium naphthalenide solution:*

To a solution of naphthalene (256 mg, 2.00 mmol) in anhydrous THF (10 mL) was added freshly cut sodium pieces (92 mg, 4.00 mmol). The mixture was sonicated at rt for 20 min with occasional swirling to afford a dark green solution of sodium naphthalenide (~0.2 M).

*Detosylation:*

To a -78 °C solution of (*E*)-5-(but-1-en-1-yl)-1-tosyl-1,2,3,6,7,8-hexahydrocyclopenta[*g*]indole **8b** (15.0 mg, 0.0410 mmol) in anhydrous THF (0.36 mL) was added sodium naphthalenide solution dropwise with swirling until the dark green colour persisted (~0.6 mL, ~0.12 mmol). After confirmation of completion by tlc (<2 min after dark green persistence), MeOH (0.1 mL) was added to quench the reaction and the mixture warmed to rt over 1 h. The mixture was concentrated *in vacuo* to afford the crude indoline product **12**, which was used **immediately**, minimising exposure to air.

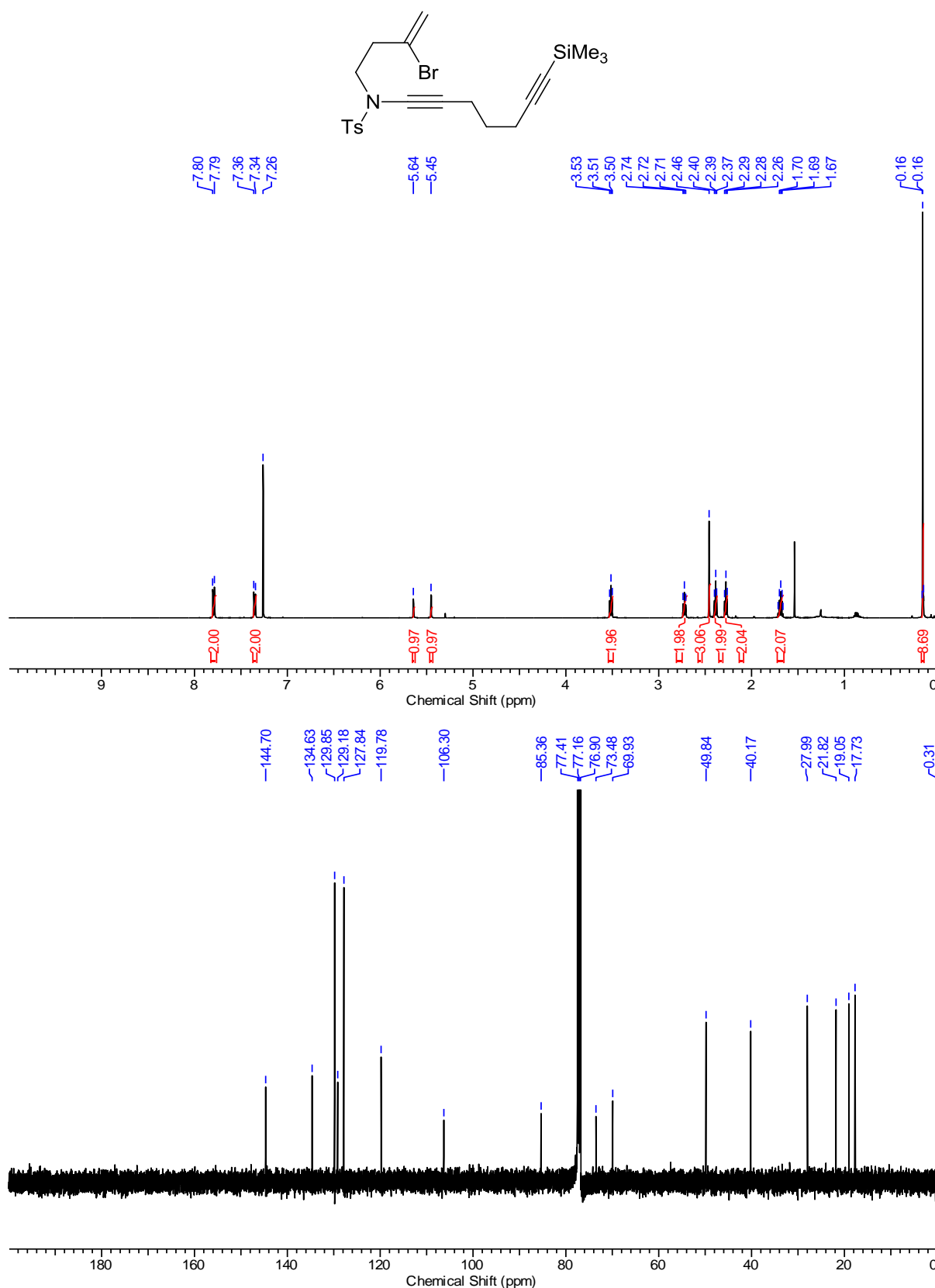
**NB.** The indoline intermediate **11** undergoes rapid aerobic decomposition, affording several aldehydes resulting from alkenyl chain cleavage.

*Dehydrogenation to the indole:*

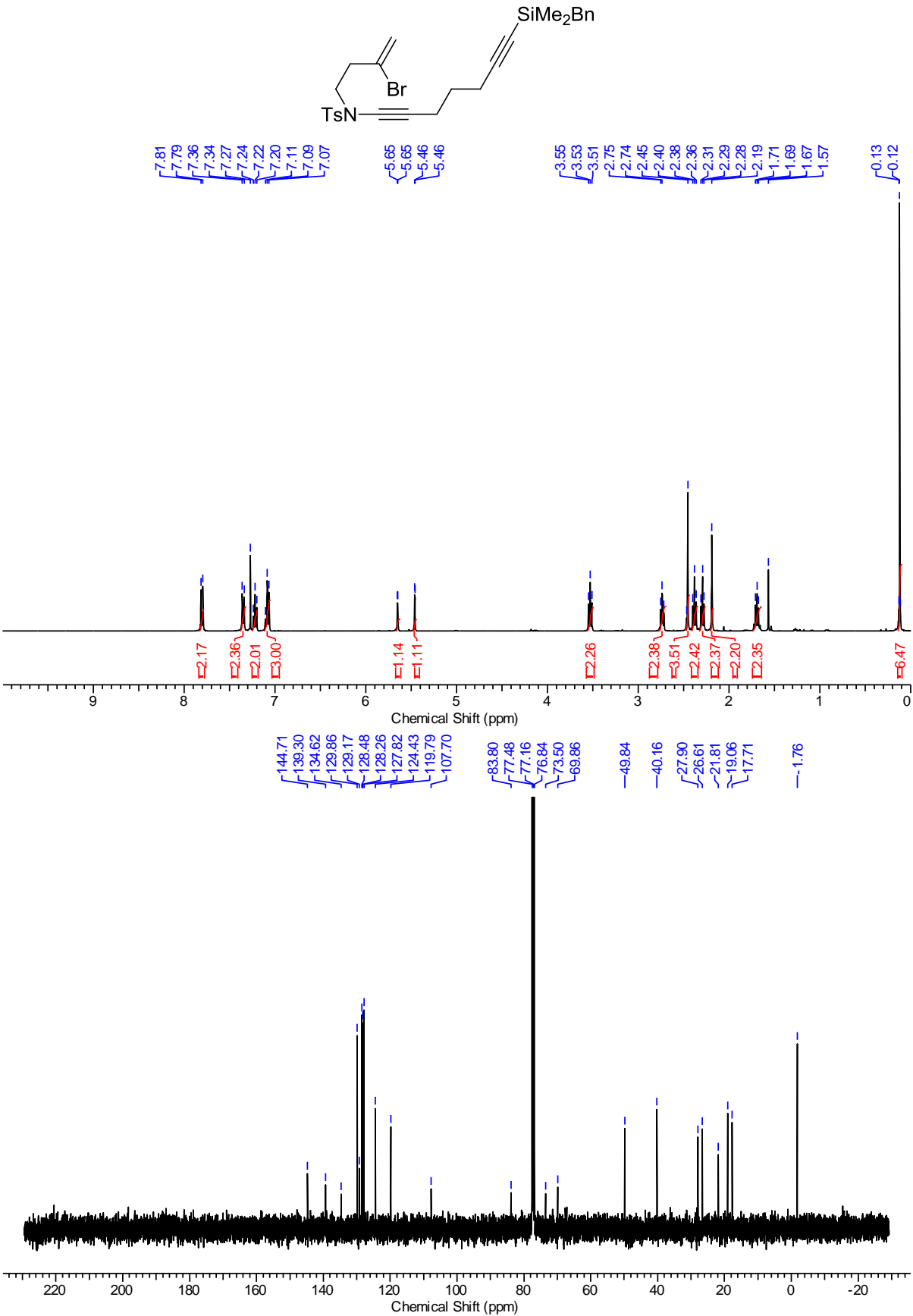
To the crude indoline mixture **11** was added Pd/C (98 mg, 10 wt/wt%, 0.0921 mmol) and anhydrous toluene (1 mL) and then heated to 85 °C for 4 h, cooled to rt, then filtered through Celite®, eluting with Et<sub>2</sub>O. The mixture was concentrated *in vacuo*, then purified *via* column chromatography (petroleum ether / Et<sub>2</sub>O (97:3) → petroleum ether / Et<sub>2</sub>O (95:5)) to afford the desired product **12** as a pale yellow oil (4.9 mg, 0.0230 mmol, 56%); *R*<sub>f</sub> 0.30 (petroleum ether / Et<sub>2</sub>O (9:1)); **IR** (thin film,  $\nu_{\text{max}}$  / cm<sup>-1</sup>) 3411, 2959, 2925, 2871, 2849, 1626, 1511, 1465, 1356, 1115, 1034, 965, 873; **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta_{\text{H}}$  8.03 (1H, br s, NH), 7.56 (1H, s, H4), 7.12 (1H, app. t, *J* = 2.7 Hz, H2), 6.54 (1H, br d, *J* = 15.8 Hz, H9), 6.51 (1H, dd, *J* = 2.8, 2.2 Hz, H3), 6.16 (1H, dt, *J* = 15.8, 6.6 Hz, H10), 3.05 (4H, app dt, *J* = 14.8, 7.4 Hz, H6,8), 2.28-2.16 (4H, m, H7,11), 1.10 (3H, t, *J* = 7.4 Hz, H12); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta_{\text{C}}$  136.9, 132.5, 131.2, 128.0, 127.4, 127.3, 125.2, 123.8, 115.1, 103.2, 32.3, 30.1, 29.8, 26.6, 25.2, 14.2; **HRMS** (ES<sup>-</sup>) calc. for C<sub>15</sub>H<sub>16</sub>N [M-H]<sup>-</sup> 210.1288, found 210.1279.

### 3. <sup>1</sup>H and <sup>13</sup>C NMR Spectra of cyclisation substrates and tricyclic products

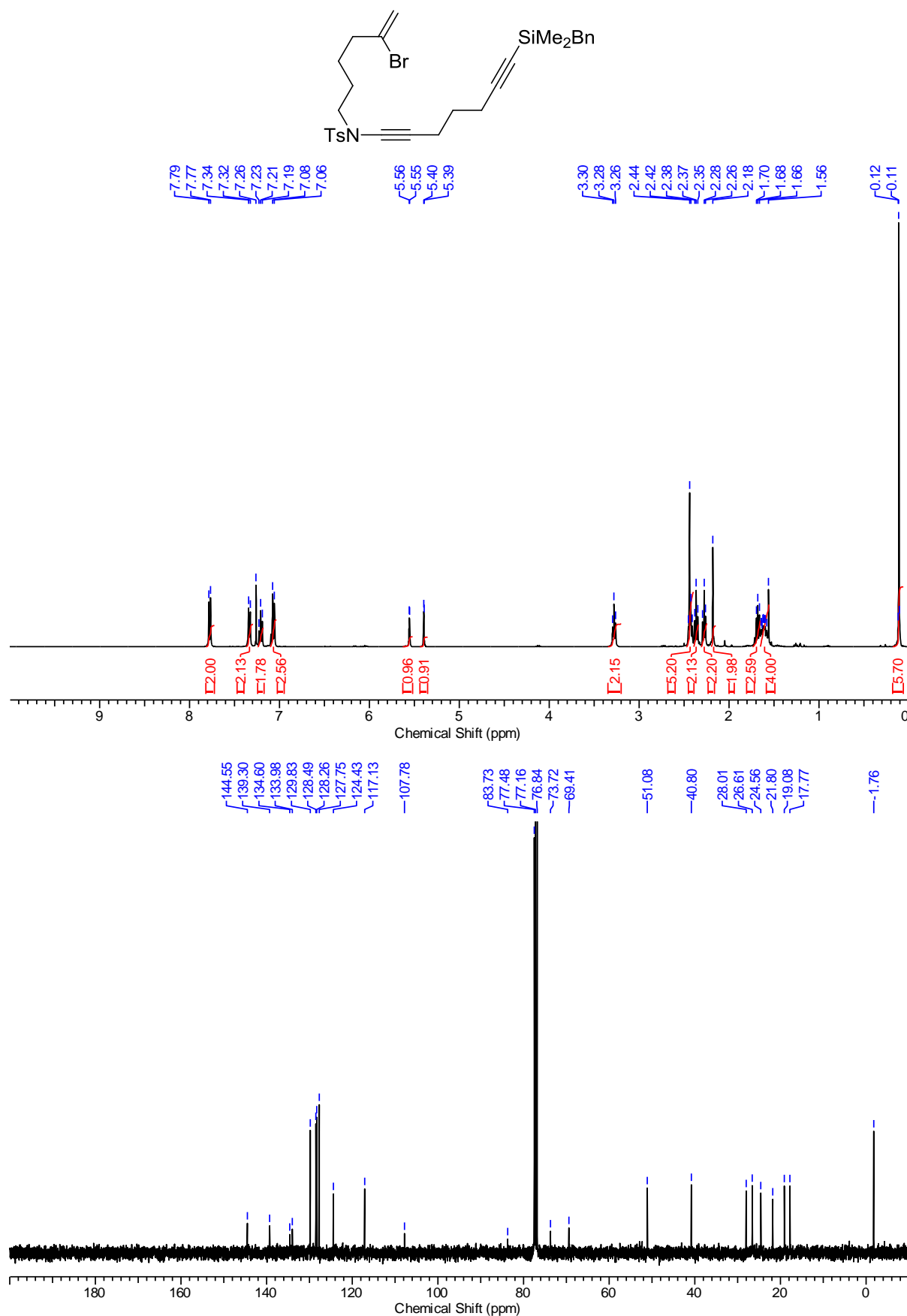
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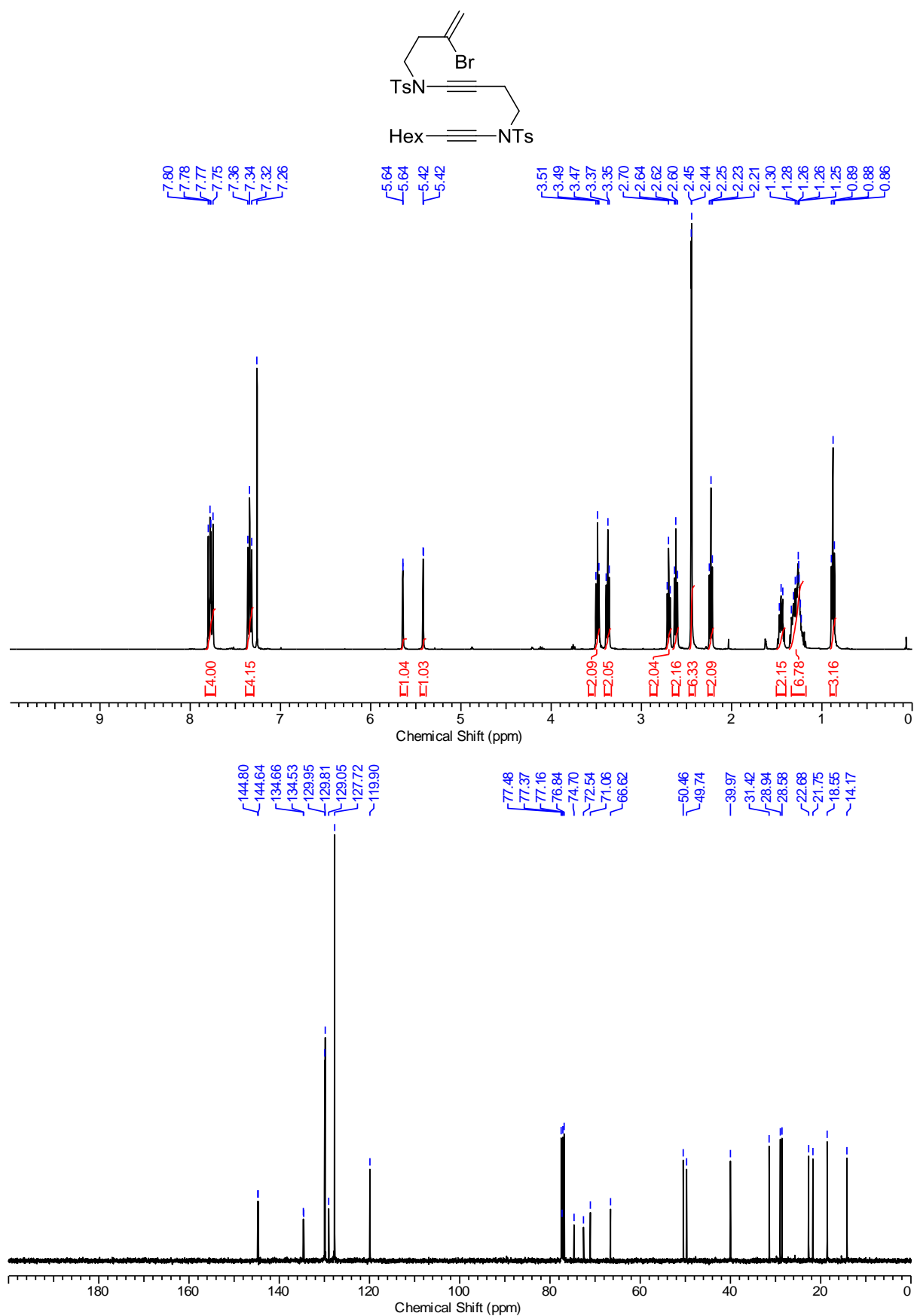
***N*-(7-(Benzyldimethylsilyl)hepta-1,6-diyn-1-yl)-*N*-(3-bromobut-3-en-1-yl)-4-methyl  
benzenesulfonamide 1b**



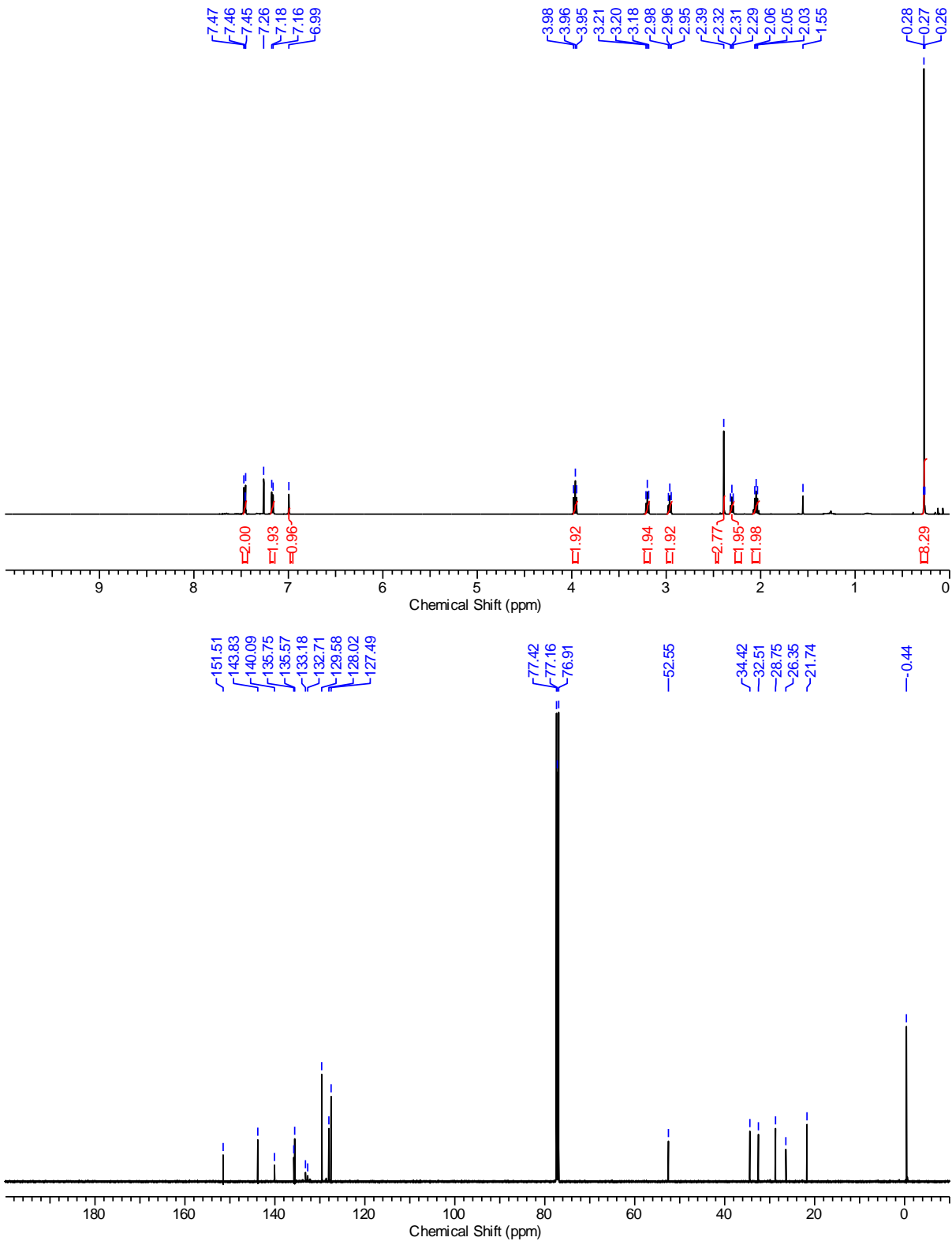
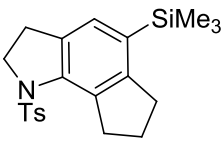
***N*-(7-(Benzyldimethylsilyl)hepta-1,6-diyn-1-yl)-*N*-(5-bromohex-5-en-1-yl)-4-methyl  
benzene sulfonamide 1c**



***N*-(3-Bromobut-3-en-1-yl)-4-methyl-*N*-(4-(4-methyl-*N*-(oct-1-yn-1-yl)phenylsulfonamido)but-1-yn-1-yl)benzenesulfonamide 1d**

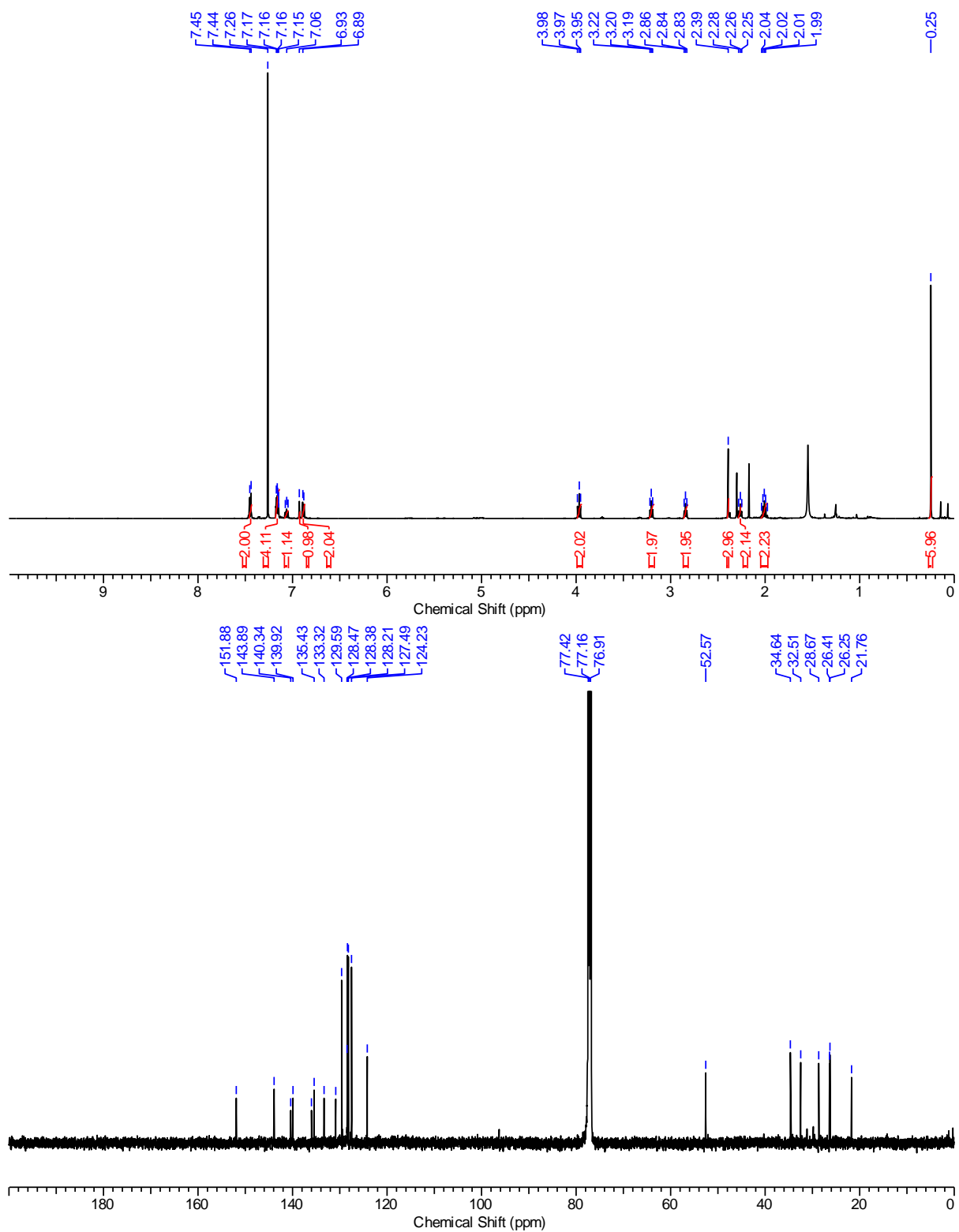


1-Tosyl-5-(trimethylsilyl)-1,2,3,6,7,8-hexahydrocyclopenta[g]indole 2a

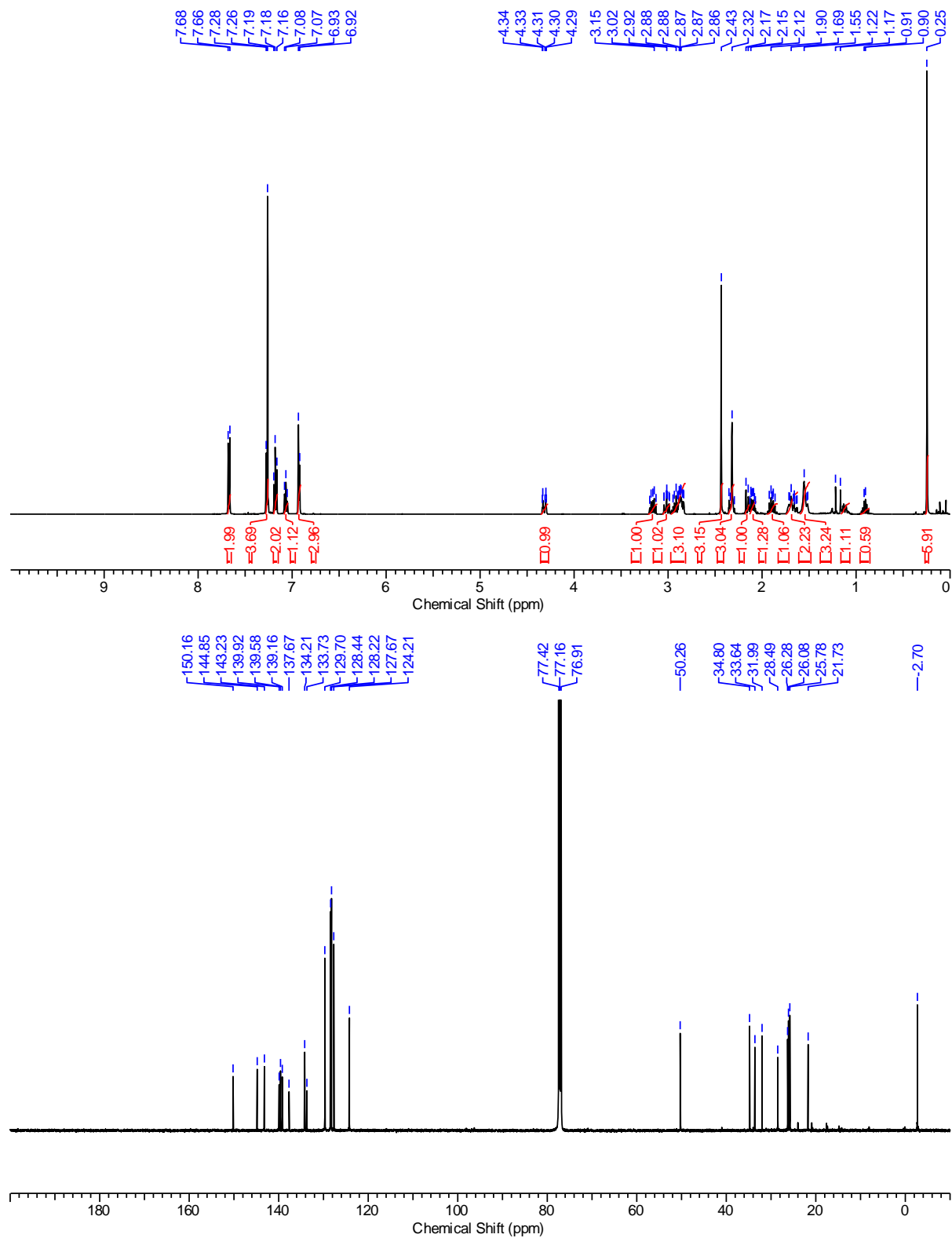
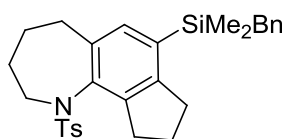




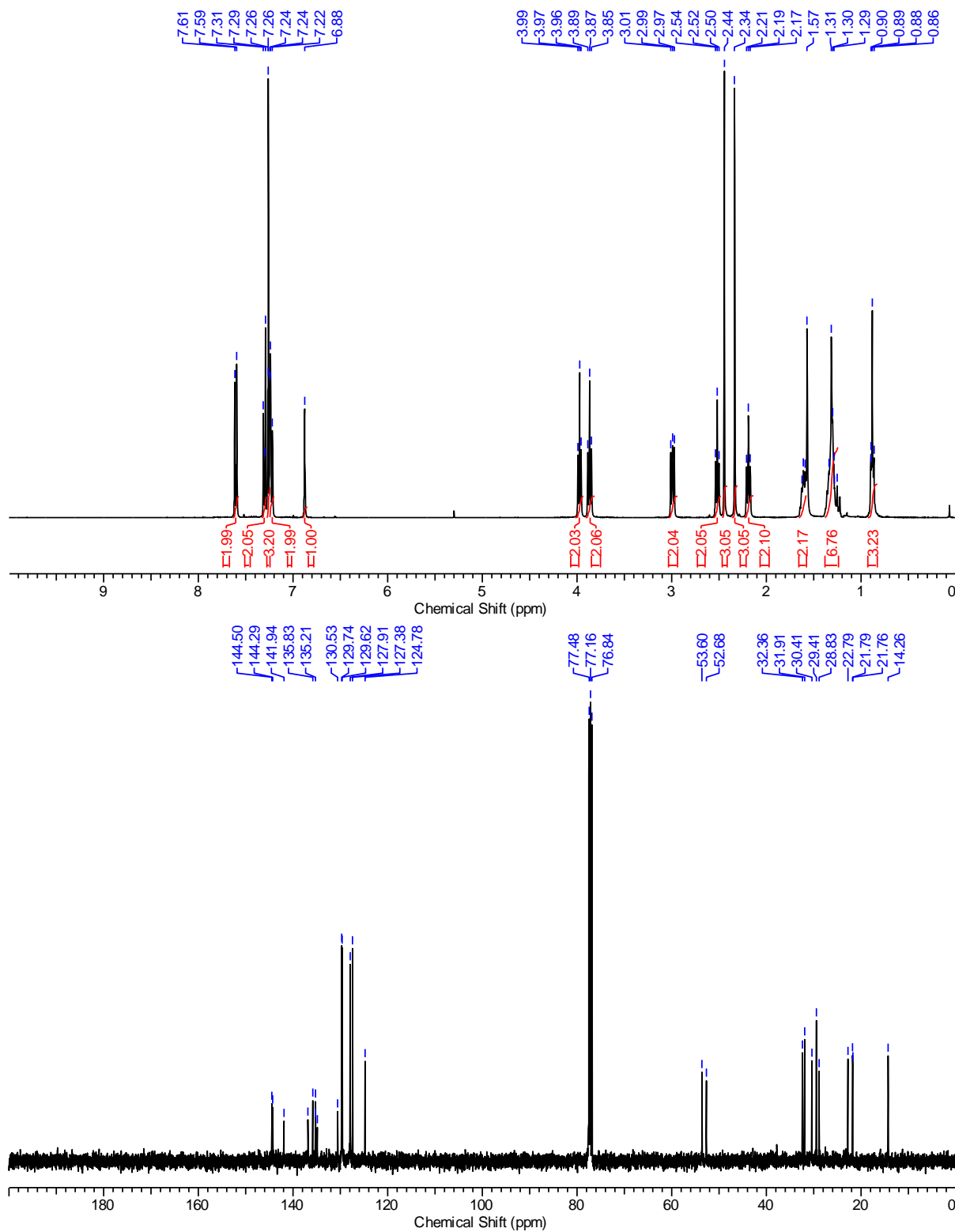
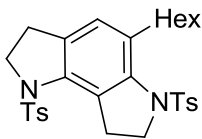
5-(Benzyldimethylsilyl)-1-tosyl-1,2,3,6,7,8-hexahydrocyclopenta[g]indole 2b



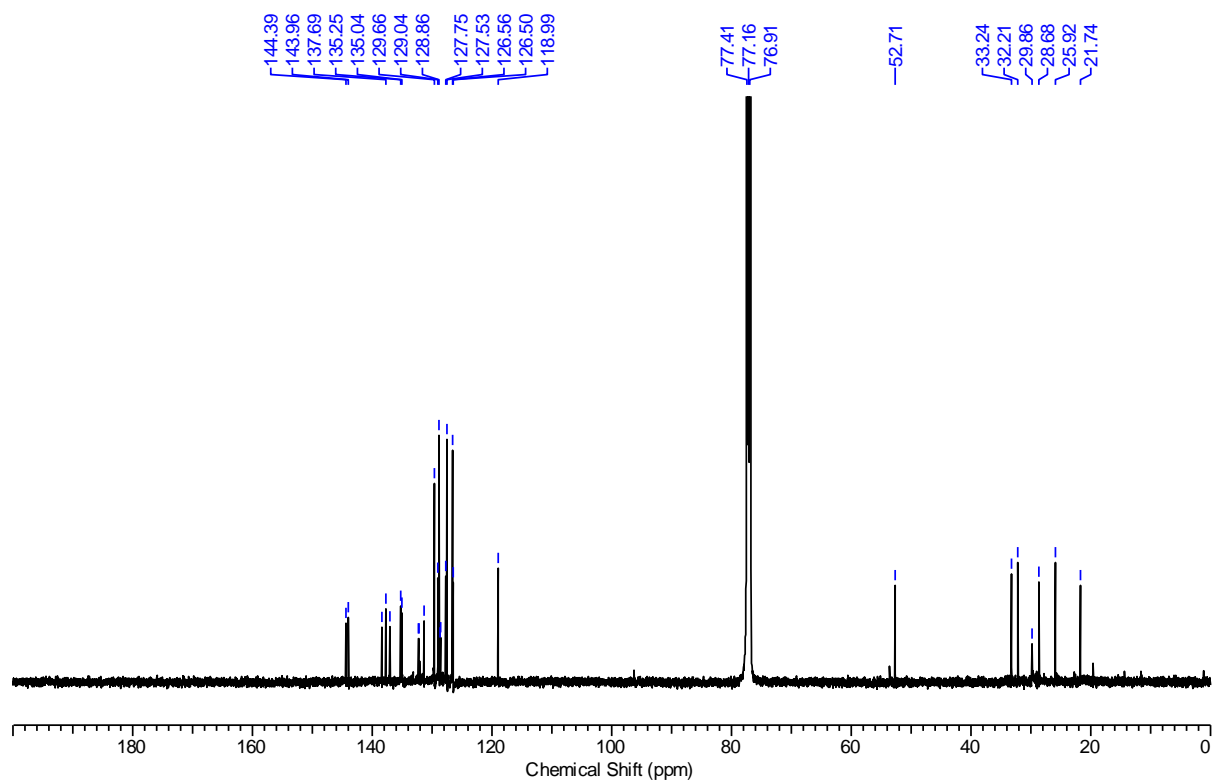
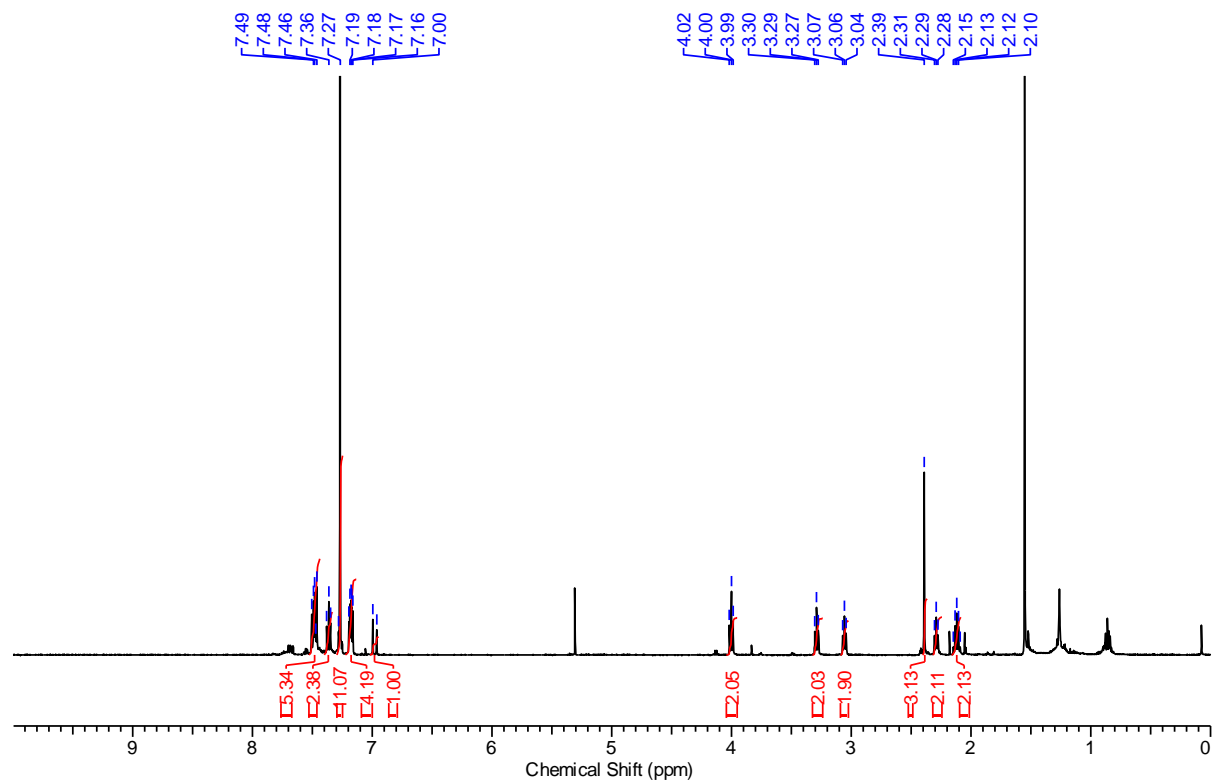
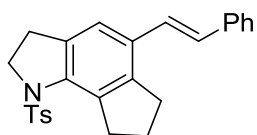
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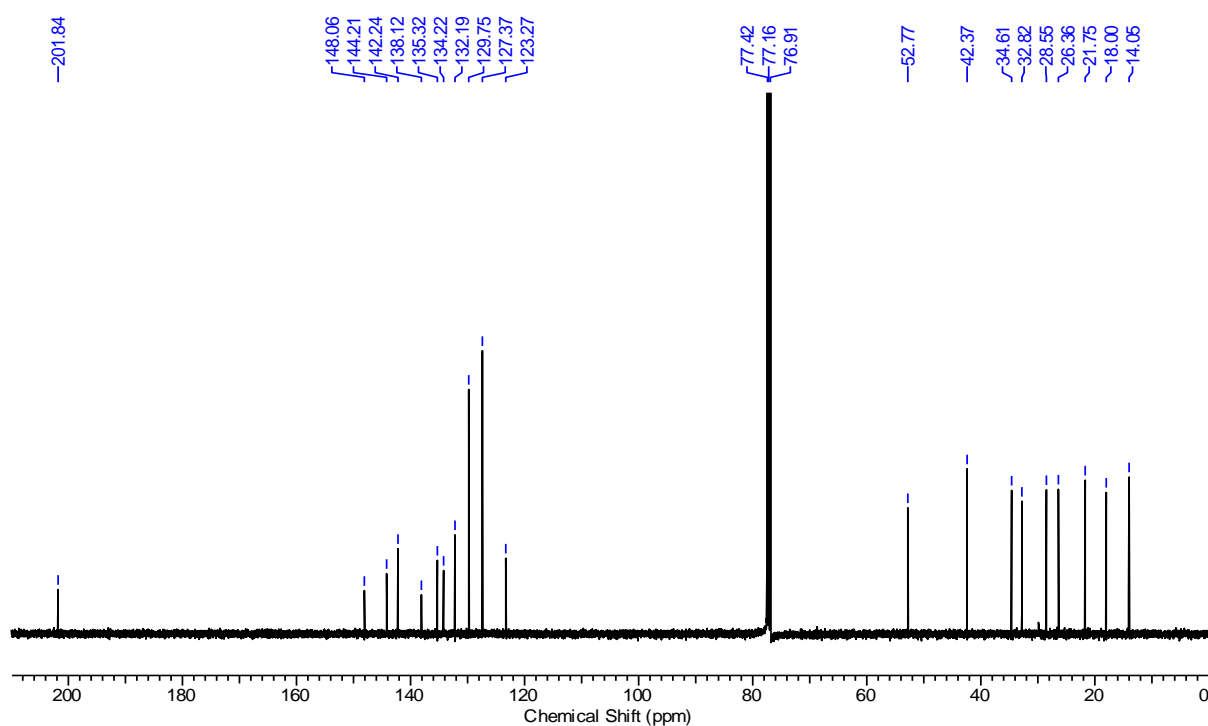
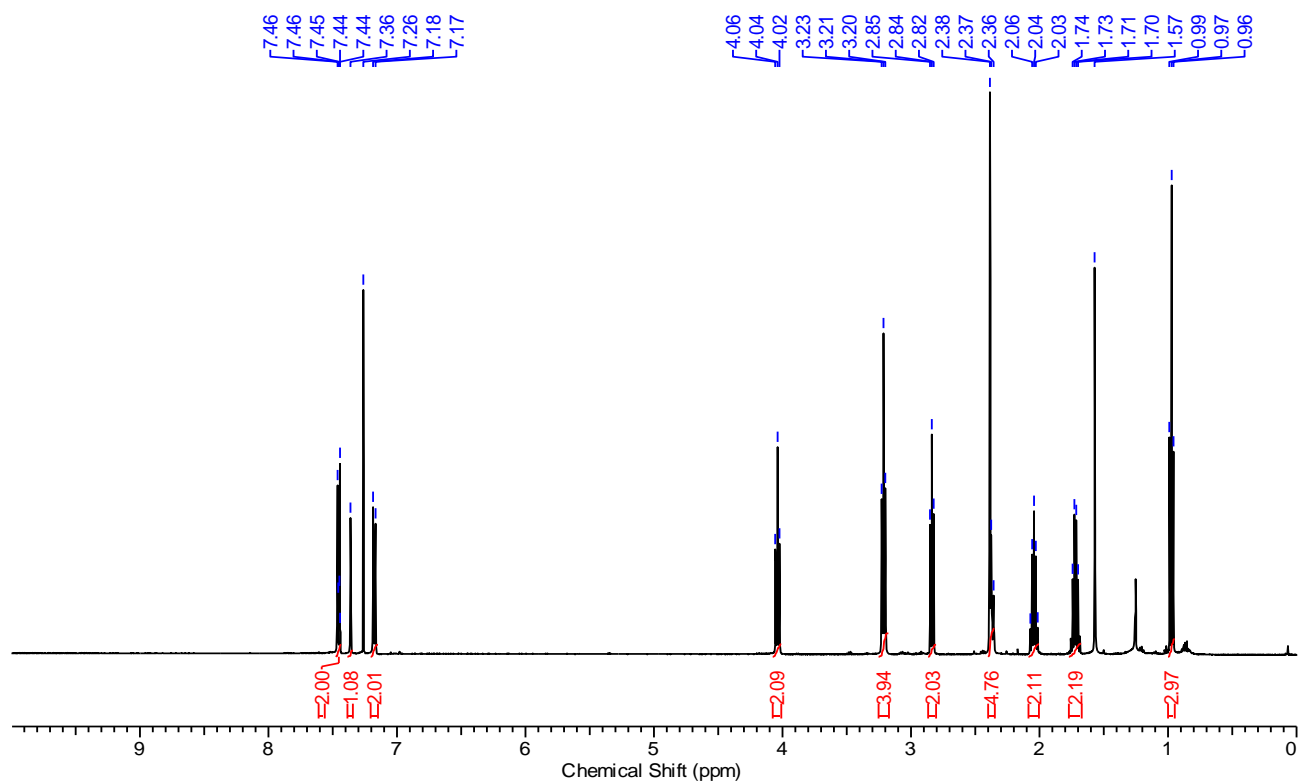
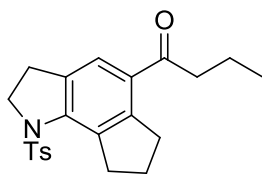
5-Hexyl-1,6-ditosyl-1,2,3,6,7,8-hexahydropyrrolo[2,3-*e*]indole 2d



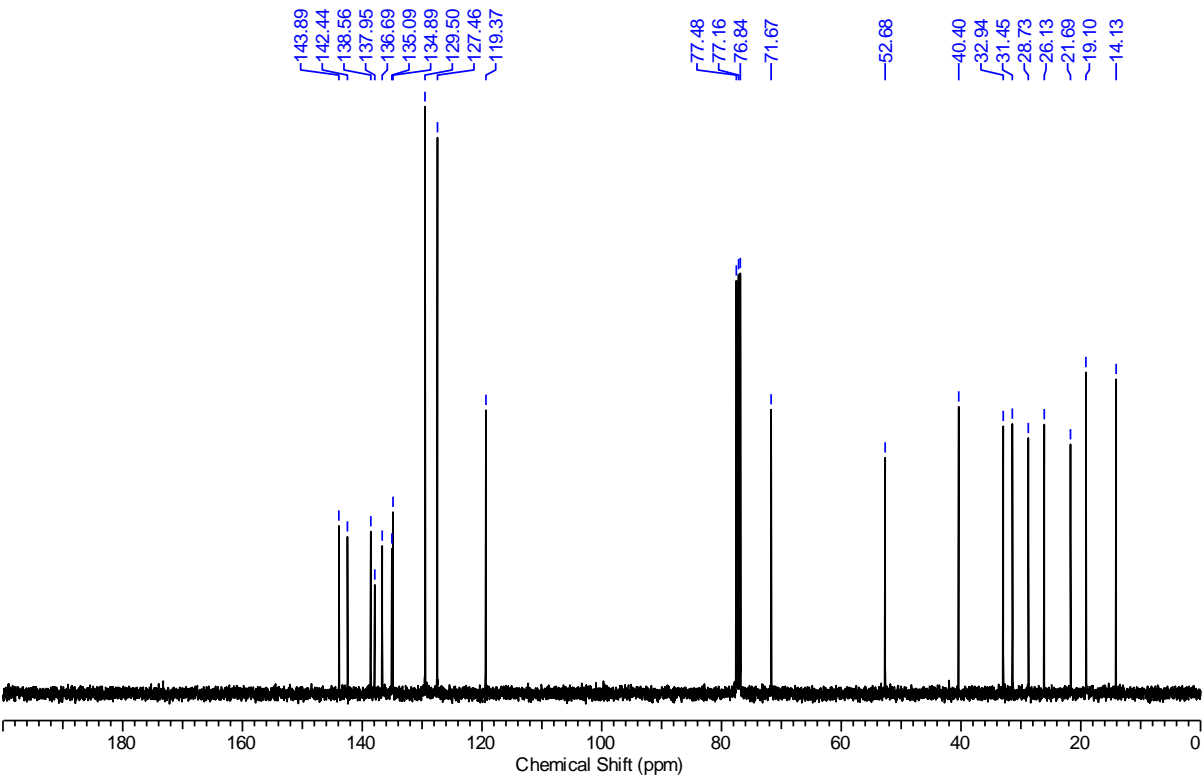
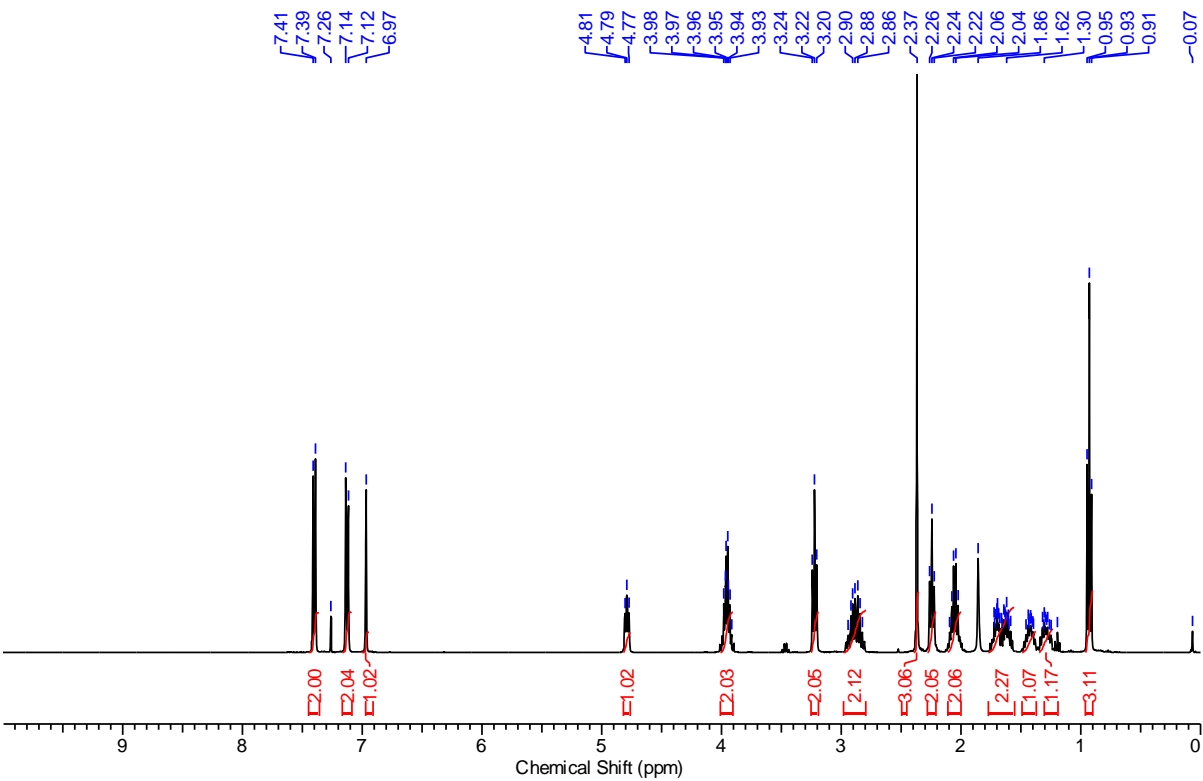
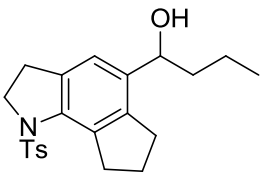
**(E)-5-Styryl-1-tosyl-1,2,3,6,7,8-hexahydrocyclopenta[g]indole 8a**



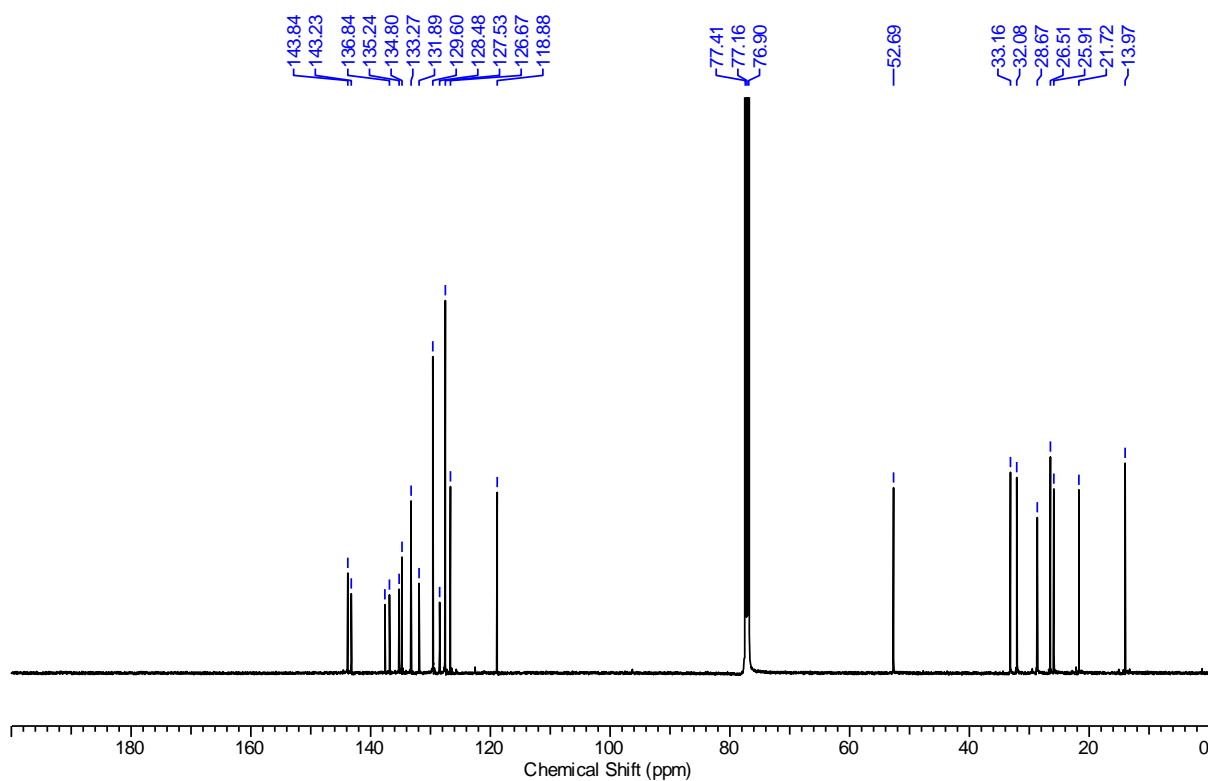
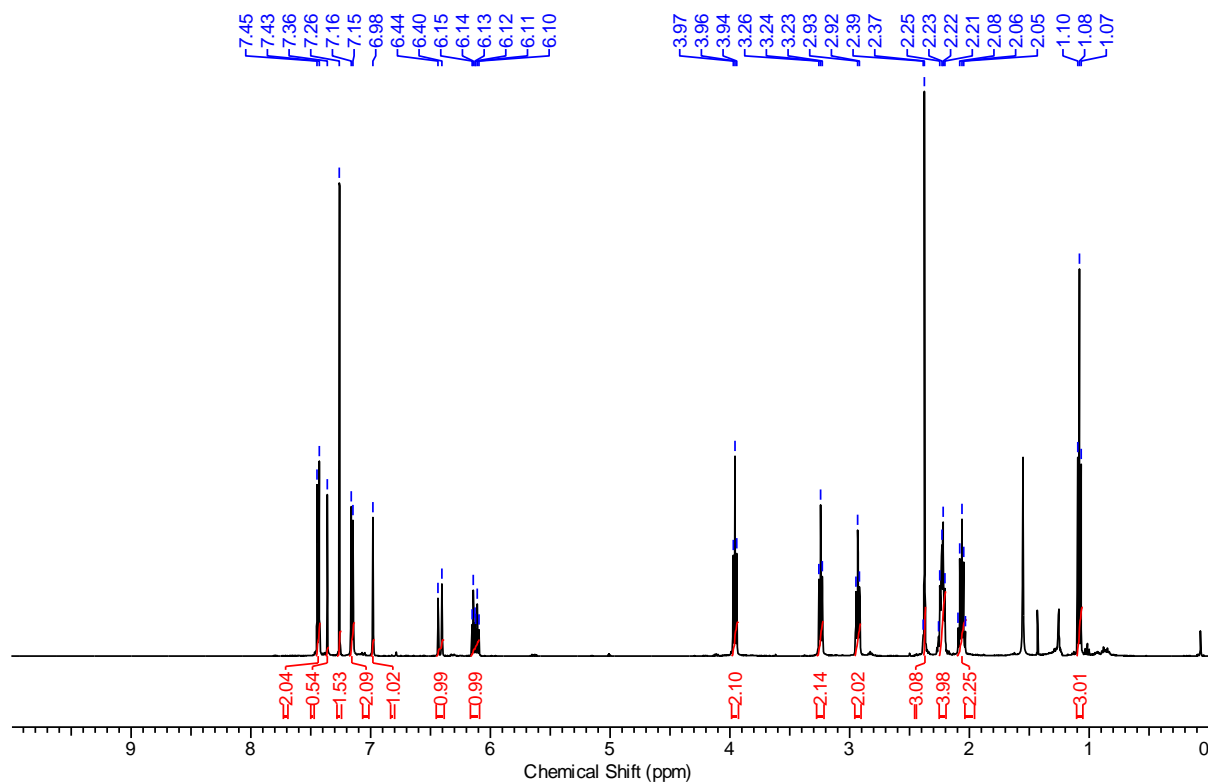
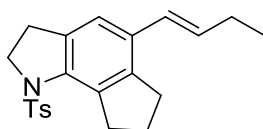
1-(1-Tosyl-1,2,3,6,7,8-hexahydrocyclopenta[*g*]indol-5-yl)butan-1-one 9



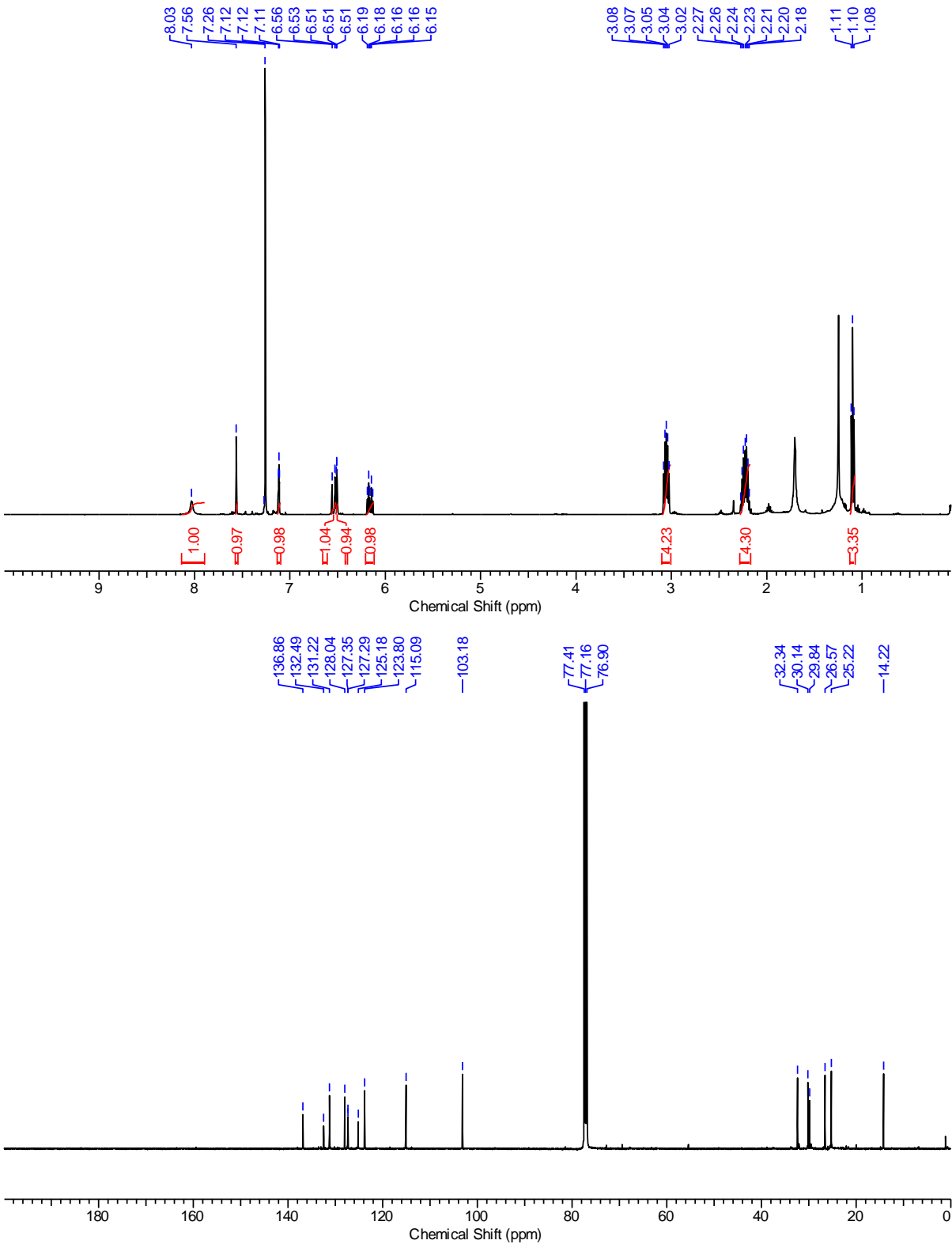
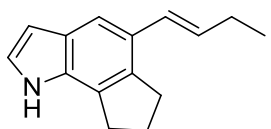
1-(1-Tosyl-1,2,3,6,7,8-hexahydrocyclopenta[*g*]indol-5-yl)butan-1-ol 10



**(E)-5-(But-1-en-1-yl)-1-tosyl-1,2,3,6,7,8-hexahydrocyclopenta[g]indole 8b**



(E)-5-(But-1-en-1-yl)-1,6,7,8-tetrahydrocyclopenta[g]indole [bis(desmethyl)trikentrin] 12





## 4. References

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