

# Supporting Information

## Facile Access to 5*H*-thiazolo[2',3':2,3]imidazo[4,5-*b*]indole derivatives by two-fold Cu-catalysed C-N coupling reactions

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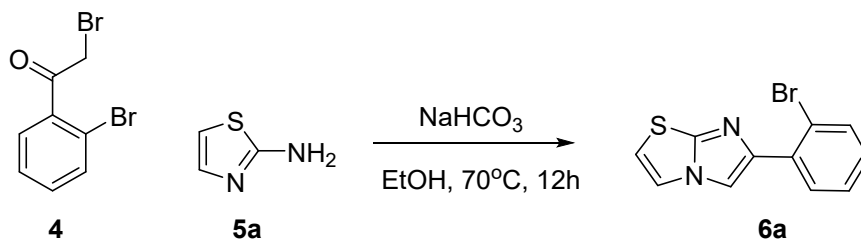
## 1. Experimental procedures

### Procedure for prepared of 2-bromo-1-(2-bromophenyl)ethan-1-one **2**[1]



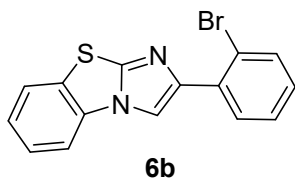
Dissolve 2'-bromoacetophenone (2 g, 10 mmol), *N*-bromosuccinimide (NBS) (1.8 g, 10 mmol) and *p*-toluenesulphonic acid (1.9 g, 10 mmol) in acetonitrile (20 mL). Stir the above solution for 8h at 80°C. Cool the reaction mixture to ambient temperature. Evaporate the volatiles in the reaction mixture. Extract the above solution with ethyl acetate and water. Dry the organic layer over anhydrous sodium sulfate. Evaporate the volatiles from the above solution to obtain 2-bromo-1-(2-bromophenyl)ethanone **4** as a light brown oil (2.74 g, 98%).

### General procedure A for prepared of 6-(2-bromophenyl)imidazo[2,1-*b*]thiazole **4** and 2-(2-bromophenyl)benzo[d]imidazo[2,1-*b*]thiazole **6a** [2]



Thiazol-2-amine **5a** (0.79g, 7.9 mmol) was added to a solution of 2-bromo-1-(2-bromophenyl)ethenone **4** (2g, 7.2 mmol) and sodium bicarbonate (0.6g, 7.2 mmol) in ethanol (15 mL). The reaction mixture was stirred at 80°C for 12 hours. Then the reaction was cooled to room temperature. The reaction mixture was extracted by ethyl acetate and water. Then, the organic layer was dried over anhydrous sodium sulfate. Evaporate the solution to dryness. The crude residue was purified by column chromatography (silica gel, Hexane/ethylacetate 4:1) to obtain 6-(2-bromophenyl)imidazo[2,1-*b*]thiazole **6a** as a white solid (1.6g, 80%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 8.17 (s, 1H), 8.07 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.63 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.42 (d, *J* = 4.5 Hz, 1H), 7.37 (ddd, *J* = 7.9, 7.3, 1.3 Hz, 1H), 7.12 (ddd, *J* = 8.0, 7.3, 1.8 Hz, 1H), 6.81 (d, *J* = 4.5 Hz, 1H). <sup>13</sup>C NMR (126

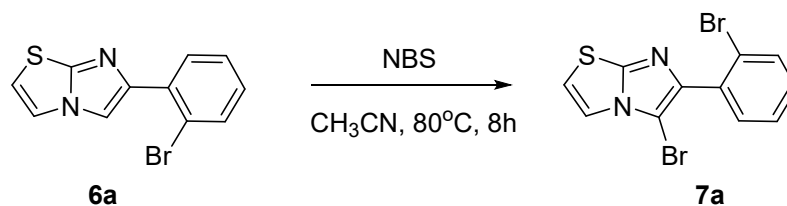
MHz,  $\text{CDCl}_3$ )  $\delta$  149.25, 145.04, 134.50, 133.71, 131.07, 128.42, 127.51, 120.77, 118.56, 112.81, 112.14.



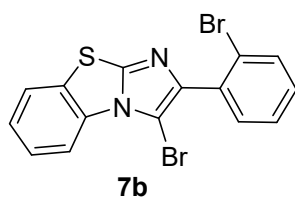
**2-(2-bromophenyl)benzo[d]imidazo[2,1-*b*]thiazole 6b** prepared following general procedure A using benzo[d]thiazol-2-amine **5b** (1.2g, 7.9 mmol) and 2-bromo-1-(2-bromophenyl)ethanone **4** (2g, 7.2 mmol). The product

was purified by column chromatography (silica gel, Hexane/ethylacetate 10:1) to yield **6b** (1.4 mg, 60 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.41 (s, 1H), 8.13 (dd,  $J = 7.9, 1.8$  Hz, 1H), 7.69 – 7.63 (m, 2H), 7.63 – 7.58 (m, 1H), 7.44 – 7.36 (m, 2H), 7.35 – 7.29 (m, 1H), 7.14 (ddd,  $J = 8.0, 7.3, 1.8$  Hz, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  147.22, 144.77, 134.19, 133.76, 132.18, 130.98, 130.39, 128.48, 127.54, 126.20, 125.02, 124.33, 120.71, 112.85, 111.08.

**General procedure B for prepared of 5-bromo-6-(2-bromophenyl)imidazo[2,1-*b*]thiazole 7a and 3-bromo-2-(2-bromophenyl)benzo[d]imidazo[2,1-*b*]thiazole 7b.**



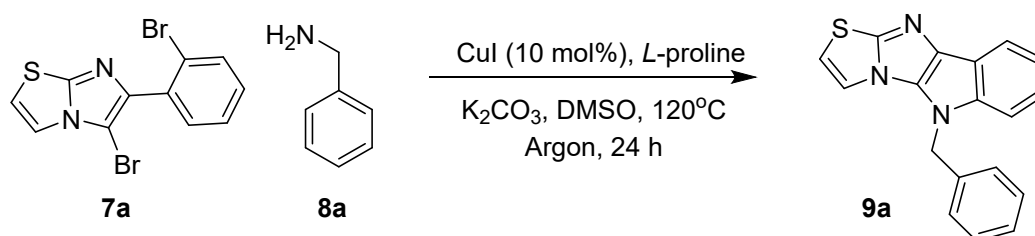
N-bromosuccinimide (1.3 g, 7.16 mmol) was added to a solution of 6-(2-bromophenyl)imidazo[2,1-*b*]thiazole **4** (2 g, 7.16 mmol) in acetonitrile (30 mL). This mixture was stirred at 80°C for 8 hours. The residue was extracted by ethyl acetate and water. Dry the organic layer over anhydrous sodium sulfate. Evaporate the solution to dryness. Then the crude residue was purified by column chromatography (silica gel, hexane/ethylacetate 4:1) to obtain 5-bromo-6-(2-bromophenyl)imidazo[2,1-*b*]thiazole **7a** as a white solid (2.1g, 82%).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.68 (dd,  $J = 8.1, 1.2$  Hz, 1H), 7.48 (dd,  $J = 7.6, 1.7$  Hz, 1H), 7.40 (d,  $J = 4.5$  Hz, 1H), 7.37 (td,  $J = 7.5, 1.2$  Hz, 1H), 7.28 – 7.23 (m, 1H), 6.93 (d,  $J = 4.5$  Hz, 1H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  148.39, 144.62, 134.01, 133.13, 132.41, 130.04, 127.12, 123.73, 117.55, 113.33, 92.91.



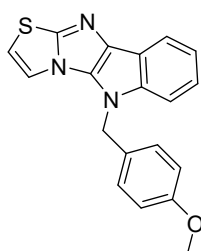
**3-bromo-2-(2-bromophenyl)benzo[d]imidazo[2,1-*b*]thiazole 7b** prepared following general procedure B using 2-(2-bromophenyl)benzo[d]imidazo[2,1-*b*]thiazole **6** (2g,

6 mmol) and N-bromosuccinimide (1.1 g, 6 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate 10:1) to yield **7b** (1.98 g, 80 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.39 (ddd,  $J = 8.2, 1.2, 0.6$  Hz, 1H), 7.75 – 7.68 (m, 2H), 7.52 – 7.45 (m, 2H), 7.40 (tdd,  $J = 7.5, 2.1, 1.2$  Hz, 2H), 7.28 (ddd,  $J = 8.1, 7.4, 1.8$  Hz, 1H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  147.63, 145.10, 133.81, 133.13, 132.94, 132.46, 130.27, 130.14, 127.14, 125.91, 125.33, 124.24, 123.98, 113.67, 94.53. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{15}\text{H}_8\text{Br}_2\text{N}_2\text{S}$  408.8833; found: 408.8767.

**General procedure C for double C-N coupling with amine derivatives, exemplified by 5-benzyl-5H-thiazolo[2',3':2,3]imidazo[4,5-*b*]indole **9a****

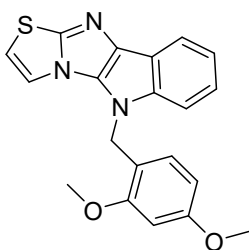


Compound **7a** (120 mg, 0.335 mmol), benzylamine **8a** (72 mg, 0.67 mmol), copper(I) iodide (6.38 mg, 0.034 mmol), *L*-proline (3.86 mg, 0.034 mmol), and  $\text{K}_2\text{CO}_3$  (139 mg, 1 mmol) were dissolved in DMSO (1 mL) and heated at  $120^\circ\text{C}$  for 24 h under Argon. After cooling, the reaction mixture was poured into water, extracted with ethyl acetate. The organic layer was dried over  $\text{Na}_2\text{SO}_4$ , filtered and the solvent was evaporated *in vacuo*. The brown residue was purified by column chromatography (silica gel, Hexane/ethylacetate 3:1) to yield 5-benzyl-5H-thiazolo[2',3':2,3]imidazo[4,5-*b*]indole **9a** (92 mg, 90%) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.99 – 7.94 (m, 1H), 7.34 – 7.30 (m, 1H), 7.30 – 7.26 (m, 3H), 7.26 – 7.20 (m, 2H), 7.17 – 7.12 (m, 2H), 6.46 (d,  $J = 4.6$  Hz, 1H), 6.43 (d,  $J = 4.6$  Hz, 1H), 5.29 (s, 2H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  148.12, 139.10, 136.57, 132.48, 130.38, 129.28, 128.38, 126.96, 121.93, 120.16, 118.74, 118.29, 116.05, 110.04, 109.88, 48.23. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{18}\text{H}_{13}\text{N}_3\text{S}$  304.0903; found: 304.0888.



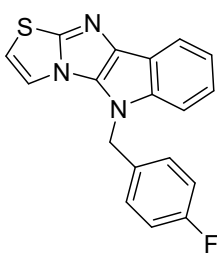
**5-(4-methoxybenzyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-*b*]indole **9b**** prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and 4-methoxybenzylamine (92 mg, 0.67 mmol). The product was purified by column

chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9b** (98 mg, 88 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 (ddd,  $J = 5.9, 2.2, 0.7$  Hz, 1H), 7.38 – 7.33 (m, 1H), 7.27 – 7.21 (m, 2H), 7.12 – 7.07 (m, 2H), 6.85 – 6.80 (m, 2H), 6.49 (d,  $J = 4.6$  Hz, 1H), 6.47 (d,  $J = 4.6$  Hz, 1H), 5.26 (s, 2H), 3.75 (s, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  159.66, 148.09, 139.11, 132.53, 130.40, 128.39, 128.30, 121.88, 120.09, 118.74, 118.27, 116.22, 114.65, 109.98, 109.91, 55.35, 47.78. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{19}\text{H}_{15}\text{N}_3\text{OS}$  334.1008; found: 334.0997.



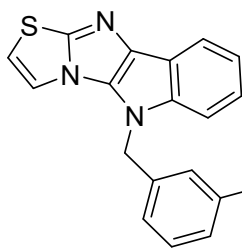
**5-(2,4-dimethoxybenzyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9c** prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and 2,4-dimethoxybenzylamine (112 mg, 0.67 mmol). The product was purified by column chromatography

(silica gel, Hexane/ethylacetate 3:1) to yield **9c** (110 mg, 90 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 – 7.91 (m, 1H), 7.44 – 7.39 (m, 1H), 7.27 – 7.18 (m, 3H), 6.94 (d,  $J = 8.4$  Hz, 1H), 6.64 (d,  $J = 4.6$  Hz, 1H), 6.44 (d,  $J = 2.4$  Hz, 1H), 6.35 (dd,  $J = 8.4, 2.4$  Hz, 1H), 5.38 (s, 2H), 3.74 (s, 3H), 3.71 (s, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  161.00, 158.15, 147.73, 138.84, 131.90, 130.97, 129.49, 121.60, 119.80, 118.77, 118.24, 116.98, 116.33, 110.17, 109.88, 104.36, 98.92, 55.41, 55.28, 43.63. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_2\text{S}$  364.1114; found: 364.1114.



**5-(4-fluorobenzyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9d** prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and 4-fluorobenzylamine (84 mg, 0.67 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9d**

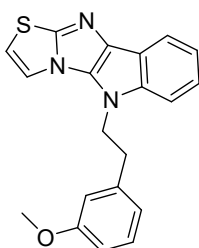
(86 mg, 80 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.99 – 7.93 (m, 1H), 7.33 – 7.27 (m, 1H), 7.27 – 7.20 (m, 2H), 7.14 – 7.07 (m, 2H), 7.02 – 6.94 (m, 2H), 6.64 (d,  $J = 4.6$  Hz, 1H), 6.53 (d,  $J = 4.6$  Hz, 1H), 5.29 (s, 2H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  162.55 (d,  $J = 247.6$  Hz), 148.18, 138.98, 132.59, 132.38 (d,  $J = 3.2$  Hz), 130.17, 128.48 (d,  $J = 8.2$  Hz), 122.03, 120.30, 118.82, 118.37, 116.23 (d,  $J = 21.7$  Hz), 115.71, 110.43, 109.80, 47.51. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{18}\text{H}_{12}\text{FN}_3\text{S}$  322.0808; found: 322.0806.



**5-(3-(trifluoromethyl)benzyl)-5H-**

**thiazolo[2',3':2,3]imidazo[4,5-*b*]indole 9e** prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and (3-(trifluoromethyl)phenyl)methanamine (117 mg, 0.67 mmol). The product was purified by column

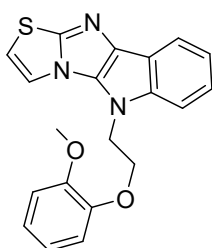
chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9e** (88 mg, 71 %) as a white solid. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 8.01 – 7.94 (m, 1H), 7.60 – 7.52 (m, 2H), 7.40 (t, J = 7.7 Hz, 1H), 7.30 (dt, J = 8.1, 2.9 Hz, 1H), 7.28 – 7.24 (m, 2H), 7.21 (d, J = 7.8 Hz, 1H), 6.79 (d, J = 4.6 Hz, 1H), 6.61 (d, J = 4.6 Hz, 1H), 5.44 (s, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 148.31, 139.02, 137.86, 132.76, 131.62 (q, J = 32.7 Hz), 130.10, 129.93, 129.86, 125.18 (q, J = 3.6 Hz), 123.75 (q, J = 272.4 Hz), 123.39 (q, J = 3.6 Hz), 122.22, 120.54, 119.00, 118.49, 115.32, 110.80, 109.76, 47.82. HRMS (ESI) m/z: [M+H]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>12</sub>F<sub>3</sub>N<sub>3</sub>S 372.0776; found: 372.0761.



**5-(3-methoxyphenethyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-**

**b]indole 9f** prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and 2-(3-methoxyphenyl)ethanamine (101 mg, 0.67 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate

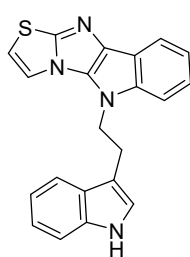
3:1) to yield **9f** (107 mg, 92 %) as a white solid. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.96 – 7.90 (m, 1H), 7.32 – 7.27 (m, 1H), 7.27 – 7.18 (m, 2H), 7.02 (dd, J = 8.3, 7.4 Hz, 1H), 6.74 (d, J = 4.6 Hz, 1H), 6.61 (ddd, J = 8.3, 2.6, 0.9 Hz, 1H), 6.53 – 6.44 (m, 2H), 6.23 (dd, J = 2.6, 1.6 Hz, 1H), 4.38 (t, J = 6.4 Hz, 2H), 3.47 (s, 3H), 2.98 (t, J = 6.4 Hz, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 159.77, 147.56, 139.94, 137.79, 131.36, 130.76, 129.72, 121.59, 120.90, 119.95, 118.92, 118.32, 115.01, 114.22, 112.73, 109.80, 109.77, 55.06, 46.76, 36.51. HRMS (ESI) m/z: [M+H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>17</sub>N<sub>3</sub>OS 348.1165; found: 348.1148.



**5-(2-(2-methoxyphenoxy)ethyl)-5H-**

**thiazolo[2',3':2,3]imidazo[4,5-*b*]indole 9g** prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and 2-(2-methoxyphenoxy)ethanamine (112 mg, 0.67 mmol). The product was purified by column chromatography (silica gel,

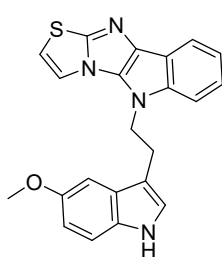
Hexane/ethylacetate 3:1) to yield **9g** (108 mg, 89 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 (ddd,  $J = 7.5, 1.5, 0.7$  Hz, 1H), 7.91 (d,  $J = 4.6$  Hz, 1H), 7.35 (dt,  $J = 8.3, 0.9$  Hz, 1H), 7.29 – 7.22 (m, 3H), 6.91 – 6.86 (m, 1H), 6.80 – 6.74 (m, 2H), 6.71 (d,  $J = 4.5$  Hz, 1H), 6.68 (dd,  $J = 8.4, 1.6$  Hz, 1H), 4.71 (t,  $J = 4.9$  Hz, 2H), 4.34 (dd,  $J = 5.2, 4.5$  Hz, 2H), 3.59 (s, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  149.71, 147.89, 147.67, 138.02, 131.83, 131.47, 122.32, 121.56, 120.73, 120.05, 119.10, 118.47, 117.36, 114.31, 111.99, 109.16, 108.97, 68.56, 55.32, 44.81. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_2\text{S}$  364.1114; found: 364.1093.



**5-(2-(1H-indol-3-yl)ethyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-**

**b]indole 9h** prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and tryptamine (107 mg, 0.67 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9h** (90 mg, 75 %) as a white solid.

$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.30 (s, 1H), 7.92 – 7.87 (m, 1H), 7.47 (dq,  $J = 7.8, 0.9$  Hz, 1H), 7.38 (dt,  $J = 8.2, 0.8$  Hz, 1H), 7.31 – 7.19 (m, 3H), 7.15 (ddd,  $J = 8.1, 7.0, 1.2$  Hz, 1H), 7.10 (ddd,  $J = 8.0, 7.0, 1.1$  Hz, 1H), 6.30 (d,  $J = 2.4$  Hz, 1H), 6.25 (d,  $J = 4.6$  Hz, 1H), 6.18 (d,  $J = 4.5$  Hz, 1H), 4.52 – 4.42 (m, 2H), 3.25 – 3.15 (m, 2H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  147.56, 137.82, 136.43, 131.18, 130.98, 126.68, 123.07, 122.24, 121.57, 119.91, 119.73, 118.84, 118.35, 117.78, 114.94, 111.76, 111.64, 109.86, 109.15, 45.80, 25.94. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{21}\text{H}_{16}\text{N}_4\text{S}$  357.1168; found: 357.1152.

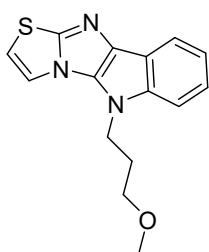


**5-(2-(5-methoxy-1H-indol-3-yl)ethyl)-5H-**

**thiazolo[2',3':2,3]imidazo[4,5-b]indole 9i** prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and 2-(5-methoxy-1H-indol-3-yl)ethanamine (128 mg, 0.67 mmol). The product was purified by column chromatography

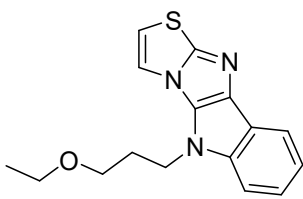
(silica gel, Hexane/ethylacetate 3:1) to yield **9i** (96 mg, 74 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.45 – 8.40 (m, 1H), 7.90 – 7.85 (m, 1H), 7.38 (dt,  $J = 8.1, 0.9$  Hz, 1H), 7.25 (ddd,  $J = 8.3, 7.2, 1.4$  Hz, 1H), 7.21 (ddd,  $J = 8.1, 7.2, 1.1$  Hz, 1H), 7.08 (dd,  $J = 8.8, 0.5$  Hz, 1H), 6.76 (dd,  $J = 8.8, 2.4$  Hz, 1H), 6.67 (d,  $J = 2.4$  Hz, 1H), 6.37 (d,  $J = 2.4$  Hz, 1H), 6.29 (d,  $J = 4.6$  Hz, 1H), 6.18 (d,  $J = 4.6$  Hz, 1H), 4.48 – 4.38 (m, 2H), 3.72 (s, 3H), 3.19 – 3.11 (m, 2H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  154.13, 147.51, 137.75, 131.56, 131.17, 131.00, 127.09, 123.66,

121.53, 119.88, 118.78, 118.24, 114.94, 112.40, 112.32, 111.71, 109.82, 109.10, 99.47, 55.81, 45.97, 25.97. HRMS (ESI)  $m/z$ :  $[M+H]^+$  Calcd for  $C_{22}H_{18}N_4OS$  387.1274; found: 387.1251.



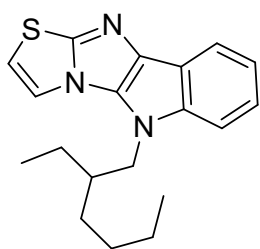
**5-(3-methoxypropyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-**

**b]indole 9j** prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and 3-methoxypropan-1-amine (60 mg, 0.67 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9j** (86 mg, 90 %) as a white solid.  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  7.94 (ddd,  $J = 7.5, 1.5, 0.7$  Hz, 1H), 7.65 (d,  $J = 4.6$  Hz, 1H), 7.33 (dt,  $J = 8.4, 0.9$  Hz, 1H), 7.28 – 7.19 (m, 2H), 6.74 (d,  $J = 4.6$  Hz, 1H), 4.41 (t,  $J = 6.4$  Hz, 2H), 3.17 (s, 3H), 3.16 – 3.13 (m, 2H), 2.11 – 2.03 (m, 2H).  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  147.74, 138.03, 131.46, 130.87, 121.57, 119.80, 118.73, 118.34, 116.03, 110.18, 109.74, 68.28, 58.42, 40.92, 29.68. HRMS (ESI)  $m/z$ :  $[M+H]^+$  Calcd for  $C_{15}H_{15}N_3OS$  286.1008; found: 286.0997.



**5-(3-ethoxypropyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-**

**b]indole 9k** prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and 3-ethoxypropan-1-amine (69 mg, 0.67 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9j** (89 mg, 89 %) as a white solid.  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  7.93 (ddd,  $J = 7.5, 1.5, 0.7$  Hz, 1H), 7.68 (d,  $J = 4.6$  Hz, 1H), 7.35 (dt,  $J = 8.3, 0.8$  Hz, 1H), 7.27 – 7.17 (m, 2H), 6.74 (d,  $J = 4.6$  Hz, 1H), 4.42 (t,  $J = 6.4$  Hz, 2H), 3.32 (q,  $J = 7.0$  Hz, 2H), 3.26 – 3.16 (m, 2H), 2.12 – 2.02 (m, 2H), 1.16 (t,  $J = 7.0$  Hz, 3H).  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  147.67, 138.11, 131.53, 130.83, 121.50, 119.75, 118.73, 118.33, 116.01, 110.13, 109.76, 66.25, 66.14, 41.04, 30.03, 15.08.

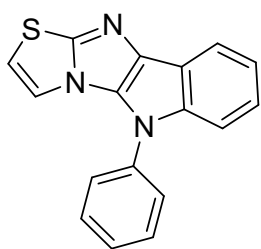


**5-(2-ethylhexyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole**

**9l** prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and 2-ethylhexan-1-amine (87 mg, 0.67 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9l** (87 mg, 80 %) as a white solid.  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  7.94 (d,  $J = 7.7$  Hz, 1H), 7.50 – 7.45 (m, 1H), 7.33 – 7.28 (m, 1H), 7.23 (dt,  $J = 25.1, 7.1$  Hz, 2H), 6.78 (d,  $J = 4.5$

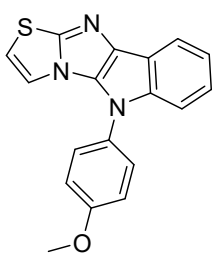


Hz, 1H), 4.15 – 4.00 (m, 2H), 1.89 (p,  $J = 6.1$  Hz, 1H), 1.42 – 1.13 (m, 10H), 0.96 – 0.73 (m, 7H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  147.60, 138.56, 131.65, 130.68, 121.53, 119.63, 118.43, 118.30, 115.29, 110.70, 109.85, 48.92, 40.81, 30.81, 28.73, 24.20, 22.95, 13.92, 10.88. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{19}\text{H}_{23}\text{N}_3\text{S}$  326.1685; found: 326.1669.



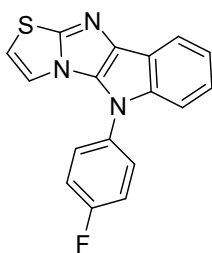
**5-phenyl-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9m**

prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and aniline (63 mg, 0.67 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9m** (57 mg, 59 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.02 – 7.96 (m, 1H), 7.65 – 7.57 (m, 2H), 7.57 – 7.50 (m, 3H), 7.44 (ddt,  $J = 8.7, 7.5, 1.2$  Hz, 1H), 7.32 – 7.20 (m, 3H), 6.73 (d,  $J = 4.6$  Hz, 1H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  148.24, 138.66, 137.03, 133.40, 130.15, 129.65, 127.20, 124.91, 122.49, 121.12, 119.50, 118.58, 116.20, 110.73, 110.64. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{17}\text{H}_{11}\text{N}_3\text{S}$  290.0746; found: 290.0735.



**5-(4-methoxyphenyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9n**

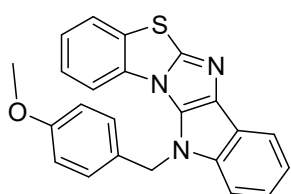
prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and 4-methoxyaniline (83 mg, 0.67 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9n** (71 mg, 66 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 – 7.95 (m, 1H), 7.45 – 7.39 (m, 3H), 7.30 – 7.19 (m, 2H), 7.16 (d,  $J = 4.6$  Hz, 1H), 7.12 – 7.06 (m, 2H), 6.69 (d,  $J = 4.6$  Hz, 1H), 3.89 (s, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  158.84, 147.98, 139.11, 132.72, 130.12, 129.62, 126.63, 122.25, 120.78, 119.15, 118.43, 115.92, 115.28, 110.64, 110.58, 55.67. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{18}\text{H}_{13}\text{N}_3\text{OS}$  320.0852; found: 320.0837.



**5-(4-fluorophenyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9o**

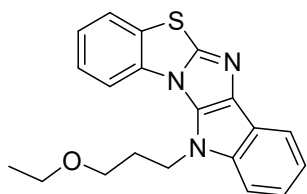
prepared following general procedure C using compound **7a** (120 mg, 0.335 mmol) and 4-fluoroaniline (75 mg, 0.67 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9o** (63 mg, 61 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 – 7.95 (m, 1H), 7.54 – 7.49 (m, 2H), 7.45 –

7.41 (m, 1H), 7.34 – 7.22 (m, 4H), 7.18 (d,  $J = 4.6$  Hz, 1H), 6.74 (d,  $J = 4.6$  Hz, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  161.47 (d,  $J = 248.3$  Hz), 148.30, 138.97, 133.32, 133.08 (d,  $J = 3.2$  Hz), 126.90 (d,  $J = 8.5$  Hz), 122.56, 121.21, 119.45, 118.61, 117.23, 117.05, 115.82, 110.92, 110.49. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{17}\text{H}_{10}\text{FN}_3\text{S}$  308.0652; found: 308.0635.



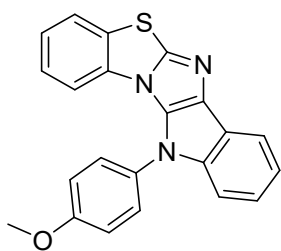
**11-(4-methoxybenzyl)-11H-benzo[4',5']thiazolo[2',3':2,3]imidazo[4,5-*b*]indole 9p**

prepared following general procedure C using 3-bromo-2-(2-bromophenyl)benzo[*d*]imidazo[2,1-*b*]thiazole **7b** (120 mg, 0.294 mmol) and 4-methoxybenzylamine (81 mg, 0.588 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9p** (90 mg, 80 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 – 7.91 (m, 1H), 7.62 – 7.57 (m, 1H), 7.52 – 7.47 (m, 1H), 7.30 – 7.26 (m, 1H), 7.26 – 7.17 (m, 4H), 7.06 – 7.01 (m, 2H), 6.80 – 6.75 (m, 2H), 5.64 (s, 2H), 3.69 (s, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  159.21, 145.83, 139.31, 132.38, 131.66, 131.16, 128.88, 128.49, 126.93, 126.09, 124.32, 124.22, 122.12, 120.47, 118.61, 118.02, 114.54, 112.68, 110.11, 55.23, 48.77. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{23}\text{H}_{17}\text{N}_3\text{OS}$  384.1165; found: 384.1146.



**11-(3-ethoxypropyl)-11H-benzo[4',5']thiazolo[2',3':2,3]imidazo[4,5-*b*]indole 9q**

prepared following general procedure C using 3-bromo-2-(2-bromophenyl)benzo[*d*]imidazo[2,1-*b*]thiazole **7b** (120 mg, 0.294 mmol) and 3-ethoxypropan-1-amine (61 mg, 0.588 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9q** (87 mg, 85 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (dt,  $J = 8.1, 0.8$  Hz, 1H), 7.92 (ddd,  $J = 7.7, 1.4, 0.7$  Hz, 1H), 7.68 (dd,  $J = 7.9, 1.2$  Hz, 1H), 7.48 – 7.41 (m, 2H), 7.35 – 7.30 (m, 1H), 7.29 – 7.24 (m, 1H), 7.22 (ddd,  $J = 8.1, 7.1, 1.1$  Hz, 1H), 4.71 (t,  $J = 7.2$  Hz, 2H), 3.39 – 3.26 (m, 4H), 2.18 (tt,  $J = 7.4, 5.5$  Hz, 2H), 1.18 (t,  $J = 7.0$  Hz, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  145.71, 138.89, 132.21, 131.54, 131.47, 128.64, 126.19, 124.39, 124.27, 121.76, 120.09, 118.44, 118.03, 113.14, 110.00, 66.71, 66.43, 43.12, 31.25, 15.18. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{20}\text{H}_{19}\text{N}_3\text{OS}$  350.1321; found: 350.1306.



**11-(4-methoxyphenyl)-11H-benzo[4',5']thiazolo[2',3':2,3]imidazo[4,5-b]indole 9r**

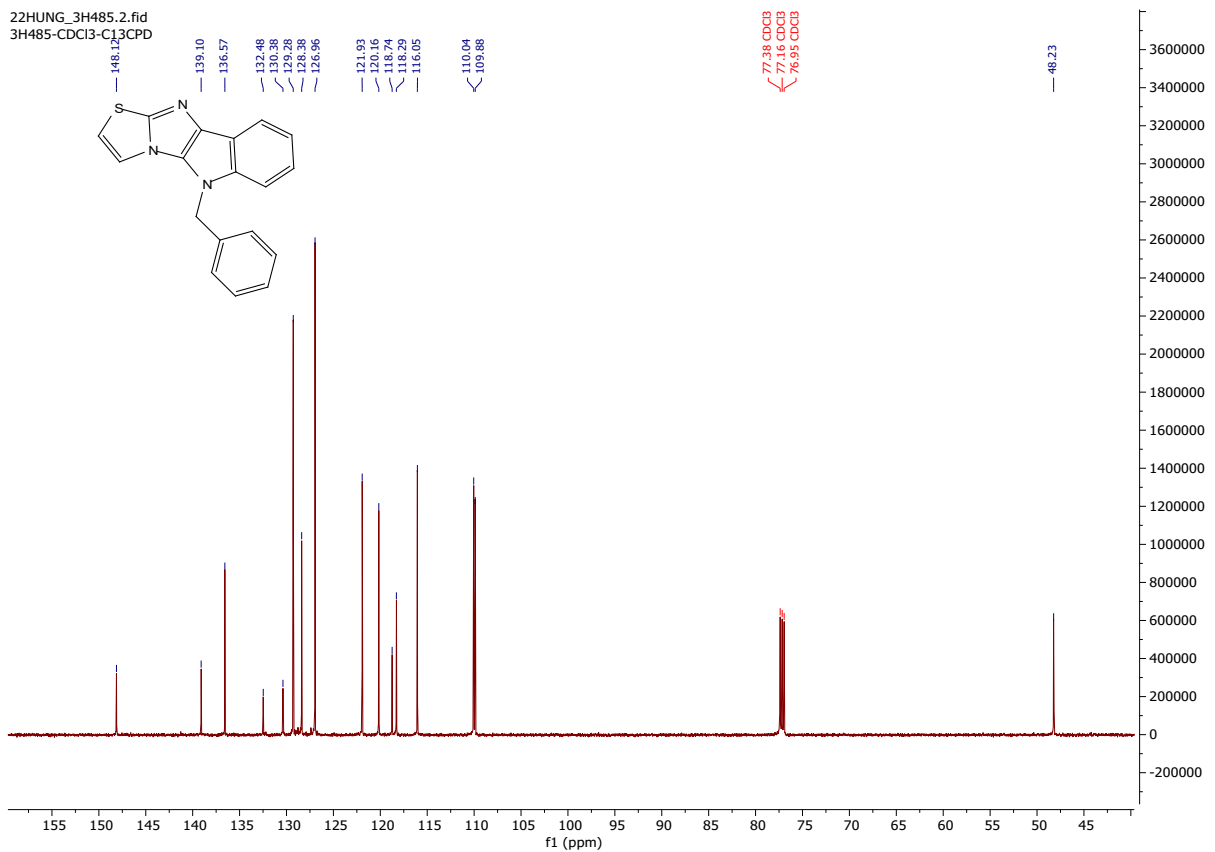
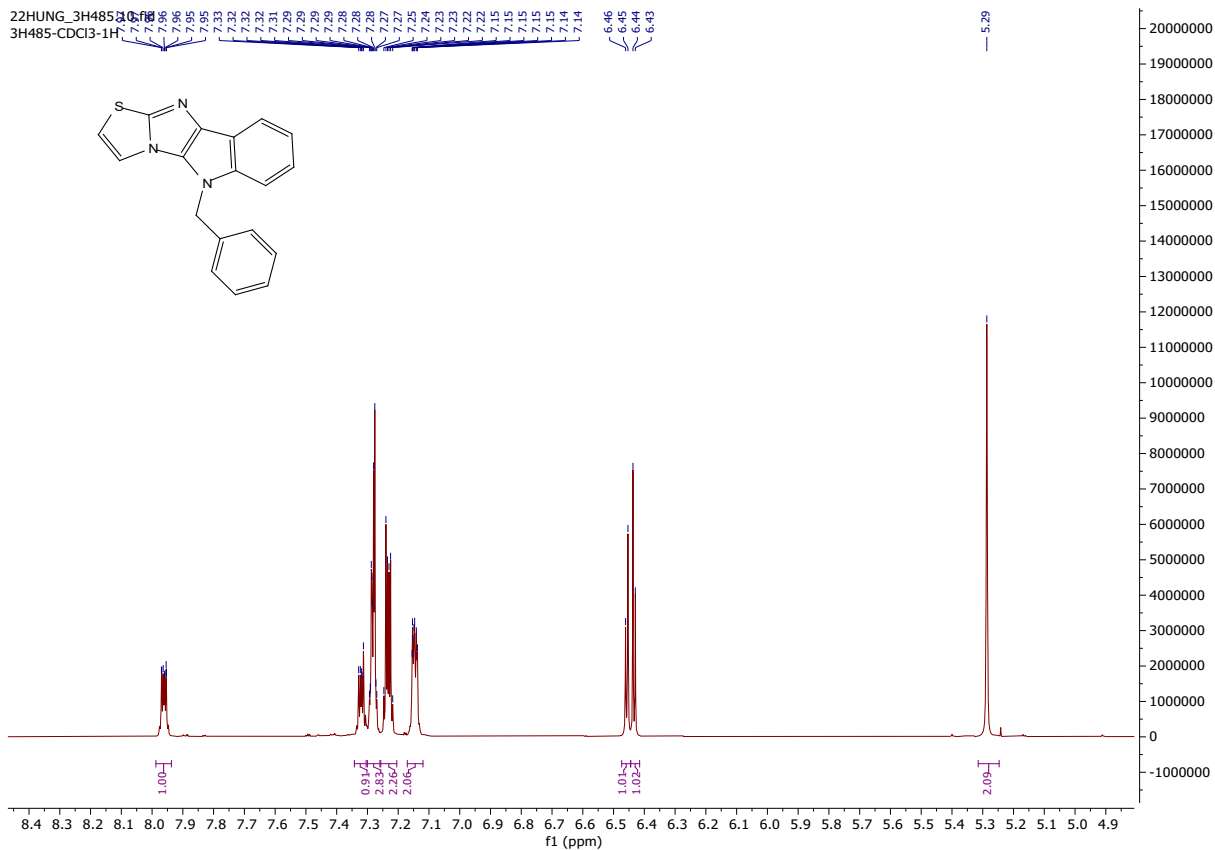
prepared following general procedure C using compound **7b** (120 mg, 0.294 mmol) and 4-methoxyaniline (72 mg, 0.588 mmol). The product was purified by column chromatography (silica gel, Hexane/ethylacetate 3:1) to yield **9r** (68 mg, 63 %) as a white solid.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.99 (dt,  $J = 7.8, 0.9$  Hz, 1H), 7.64 (ddd,  $J = 7.9, 1.2, 0.6$  Hz, 1H), 7.53 – 7.48 (m, 2H), 7.28 (ddd,  $J = 7.9, 6.1, 2.1$  Hz, 1H), 7.24 – 7.19 (m, 3H), 7.15 – 7.12 (m, 2H), 7.10 (ddd,  $J = 8.5, 7.5, 1.2$  Hz, 1H), 6.42 (ddd,  $J = 8.2, 1.1, 0.5$  Hz, 1H), 3.97 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  160.04, 145.70, 141.17, 132.65, 132.56, 131.37, 130.73, 129.73, 128.63, 125.90, 124.07, 124.02, 122.22, 120.97, 118.82, 118.06, 115.00, 113.58, 111.12, 55.76. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{22}\text{H}_{15}\text{N}_3\text{OS}$  370.1008; found: 370.0990.

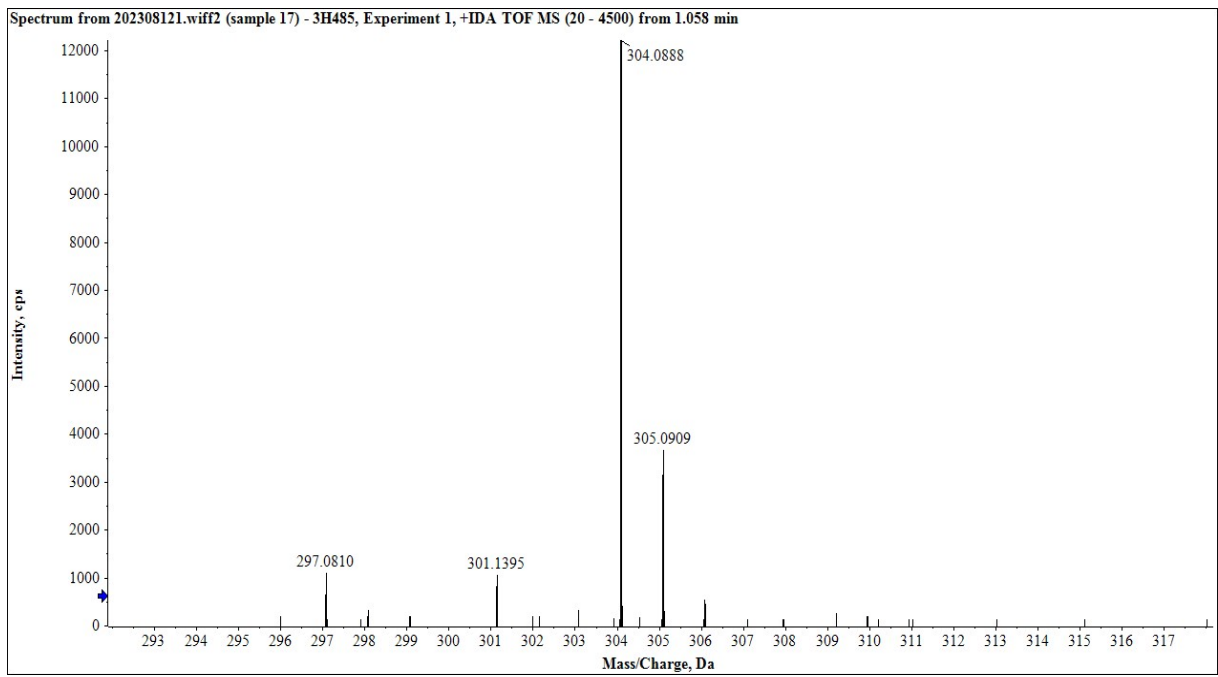
## REFERENCES

1. K. Pericherla, et al., *One-pot sequential C–N coupling and cross dehydrogenative couplings: synthesis of novelazole fused imidazo[1,2-a]pyridines*. *Chem. Commun.*, 2013, **49**, 2924-2926.
2. S.Thavasvelvan, and K. Parthasarathy, *Nickel-catalyzed [2 + 2 + 2] benzannulation of alkynes: a new route to the synthesis of highly substituted naphthalenes*. *Org. Biomol. Chem.*, 2022, **20**, 4309-4313.

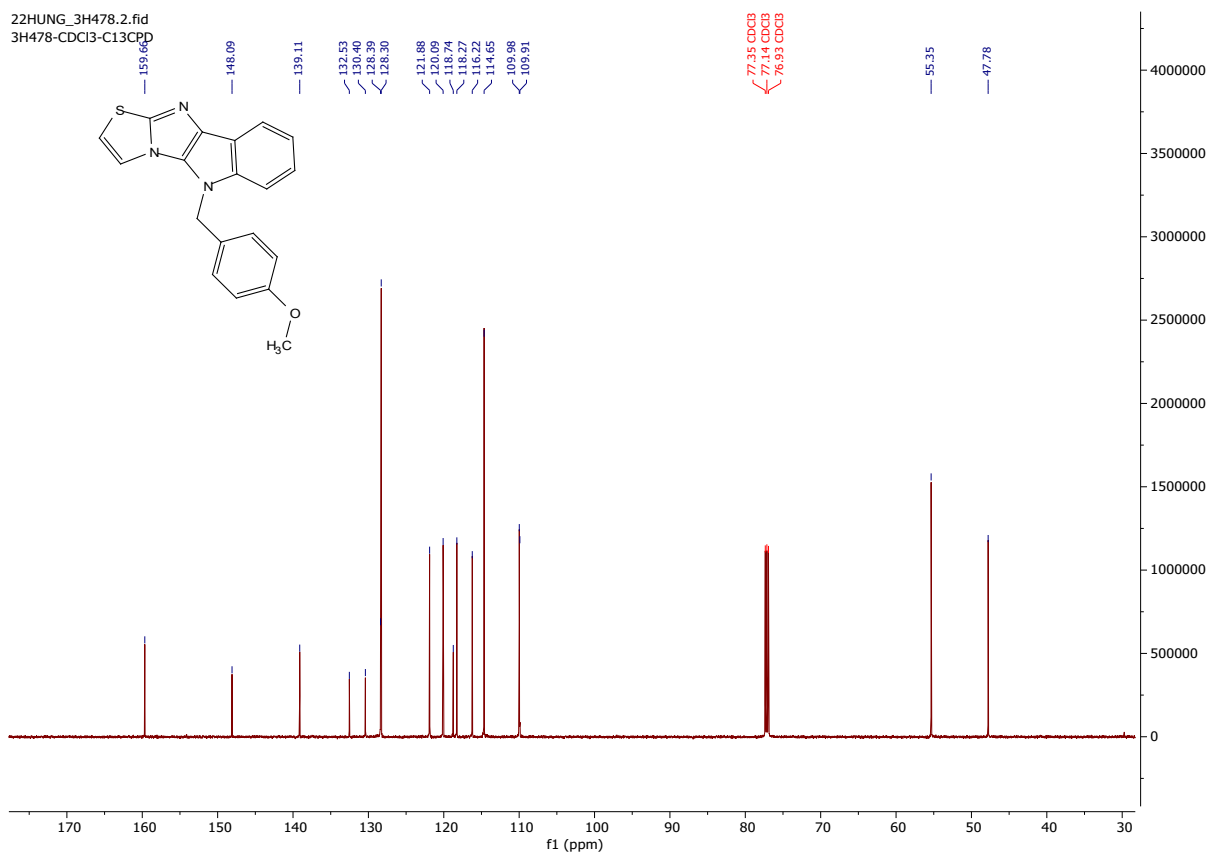
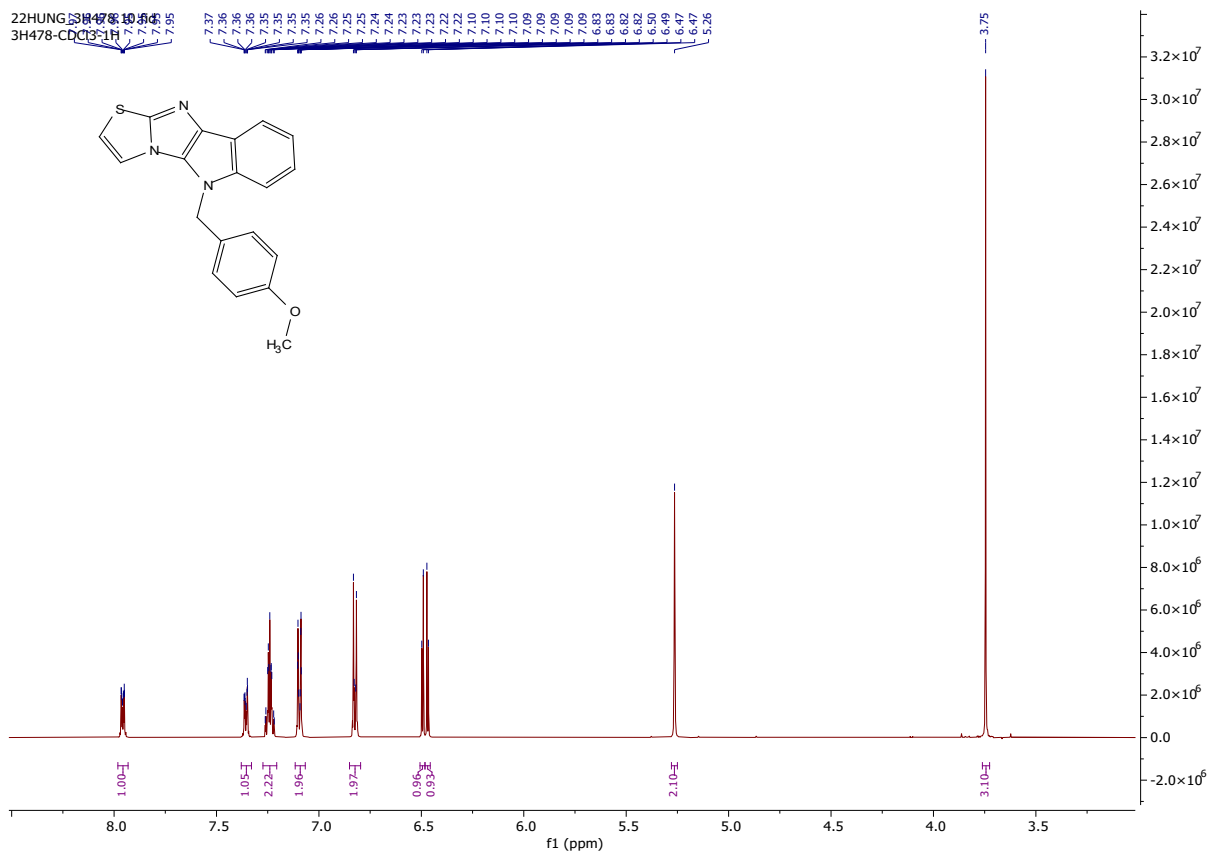
## 2. Copies of NMR spectra

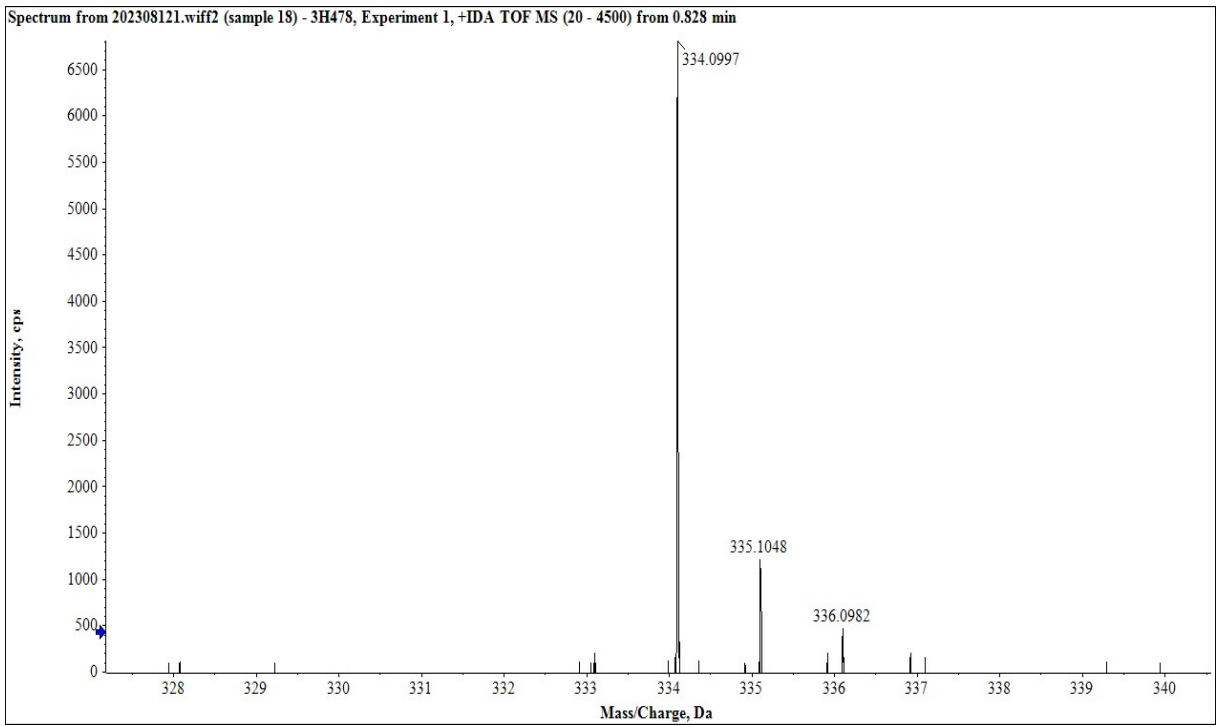
### 5-benzyl-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9a



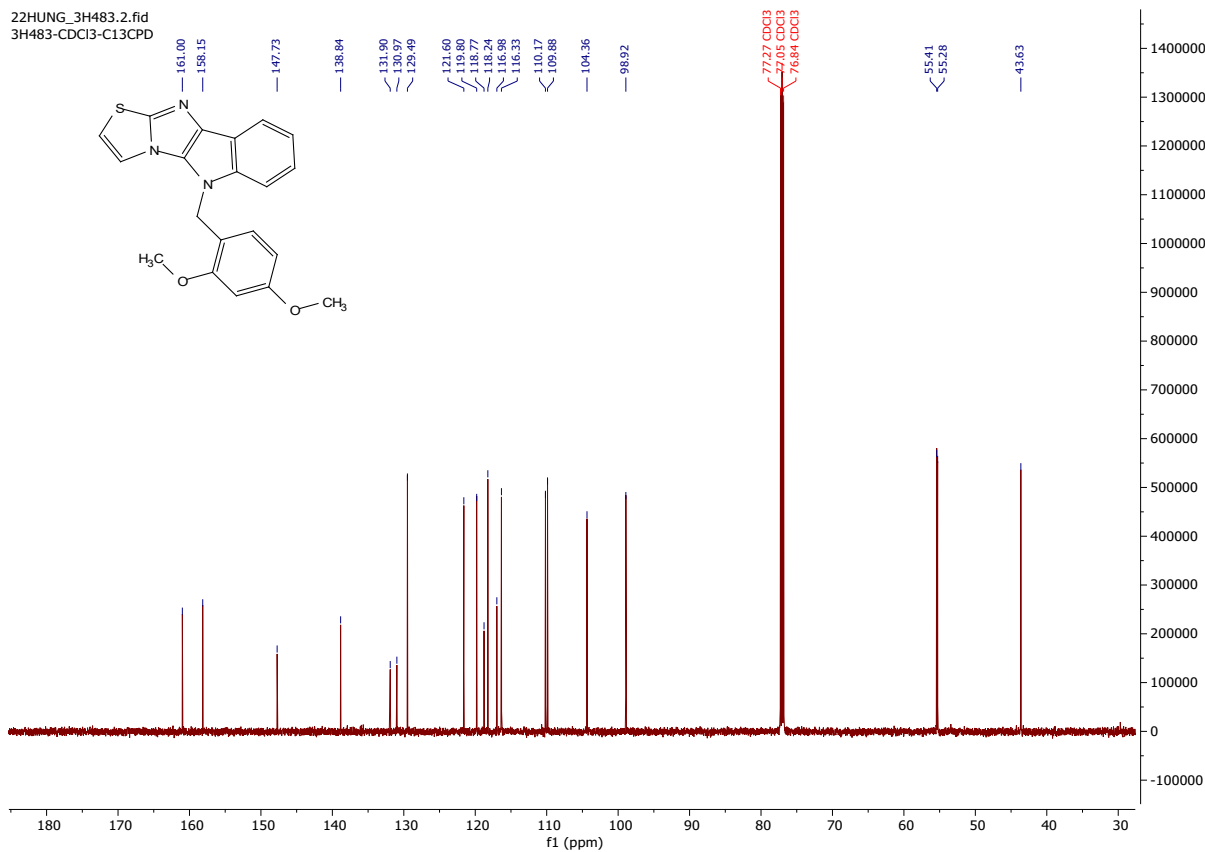
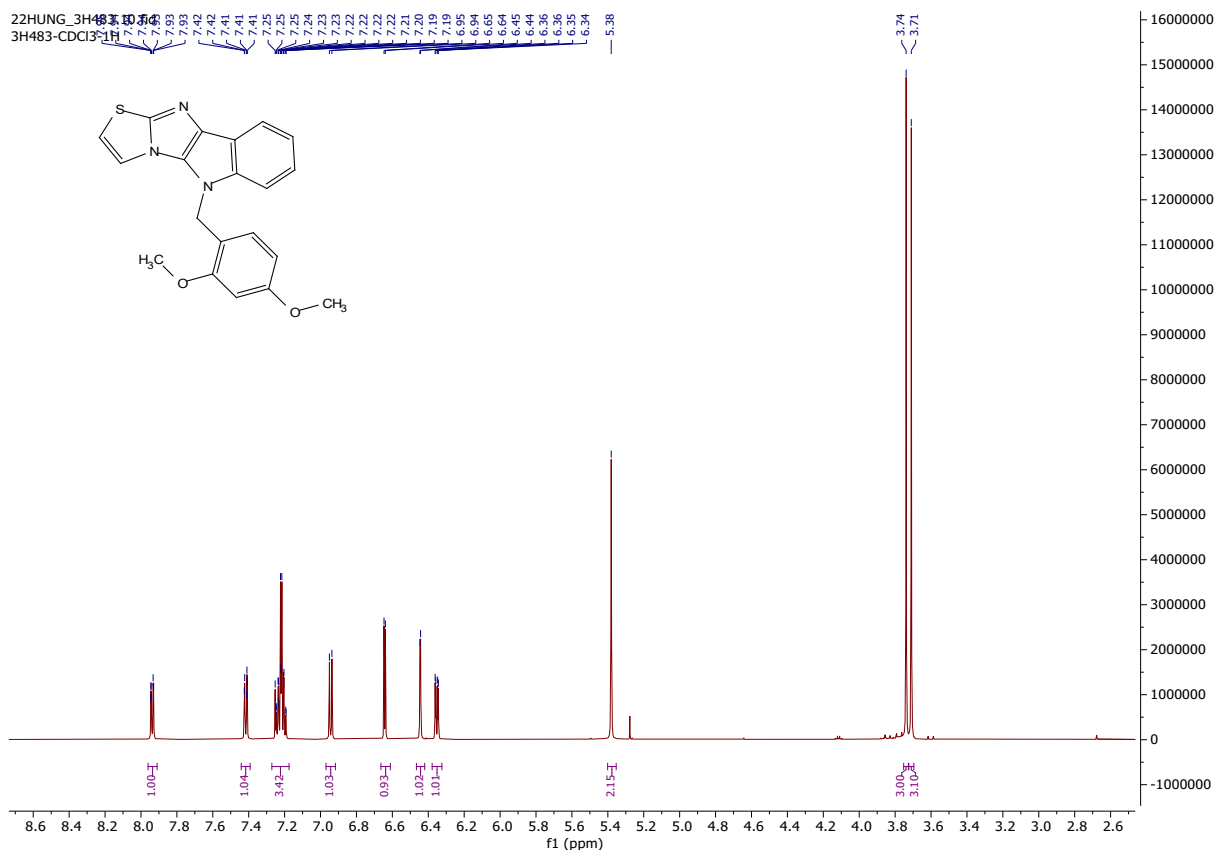


# 5-(4-methoxybenzyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9b

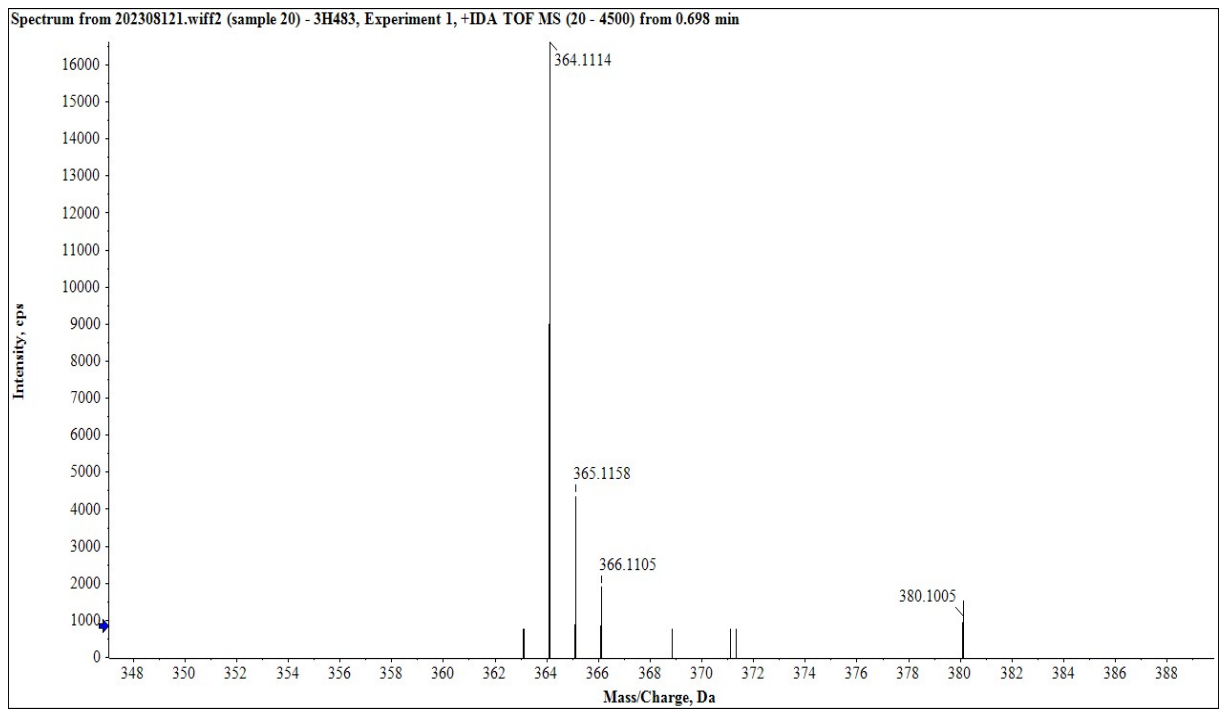




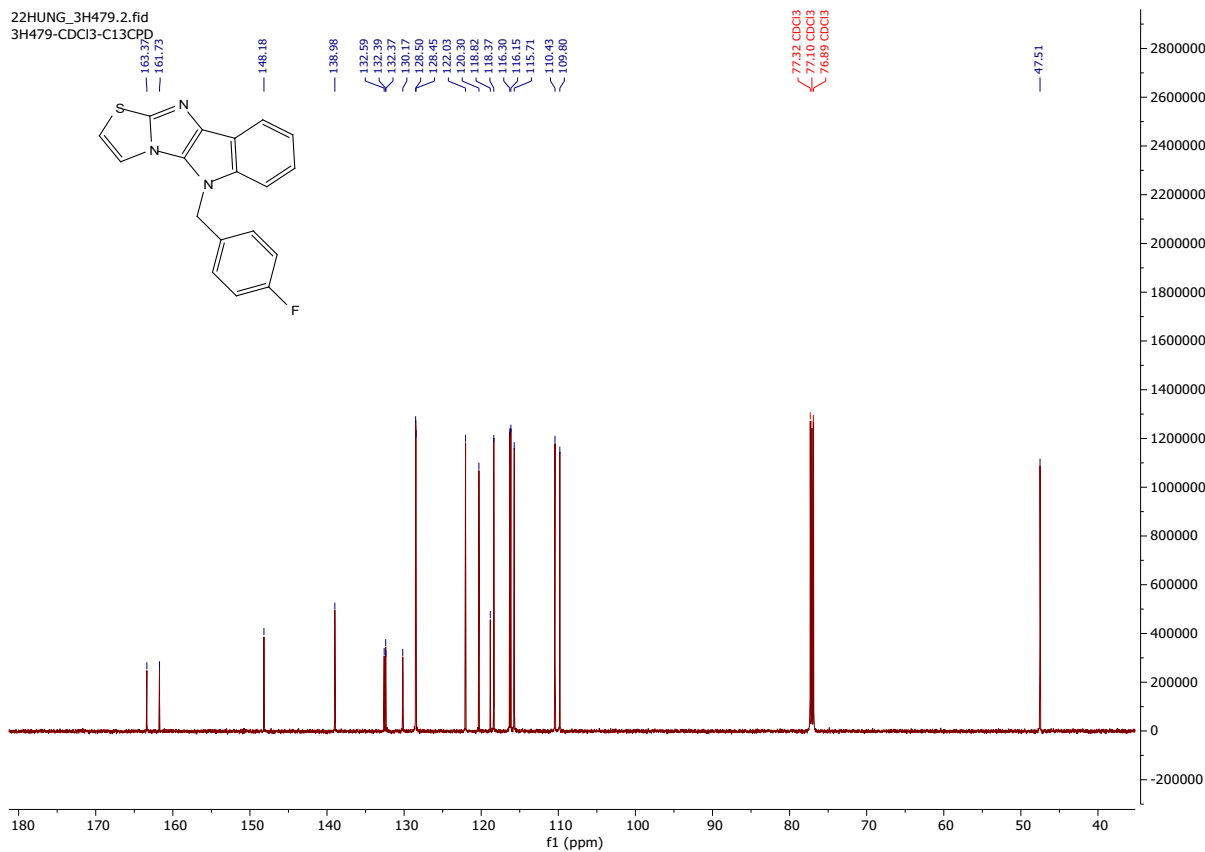
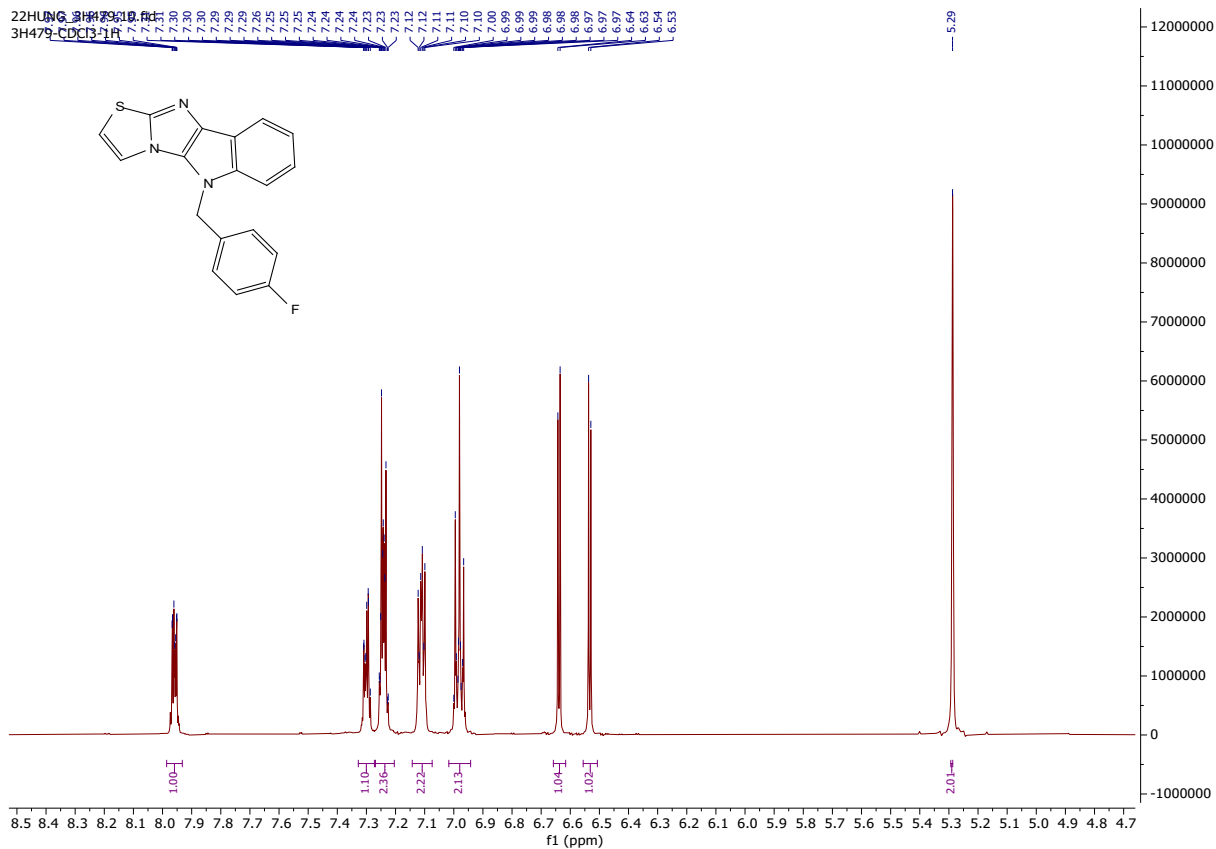
# 5-(2,4-dimethoxybenzyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9c

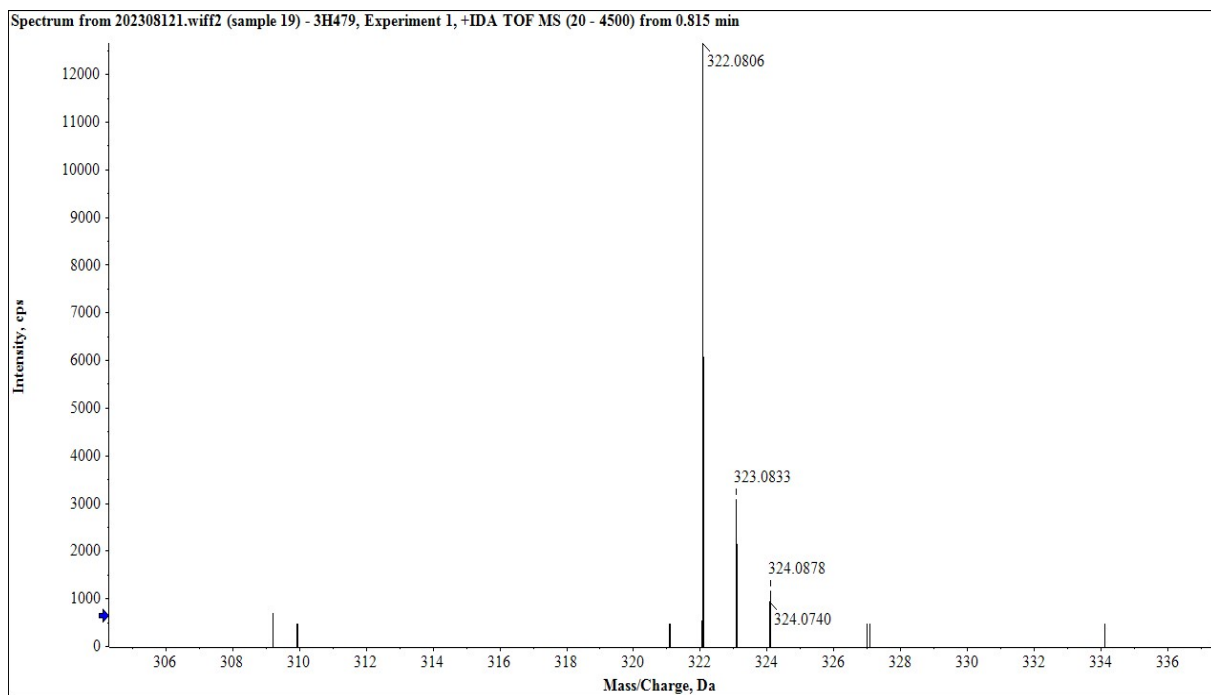




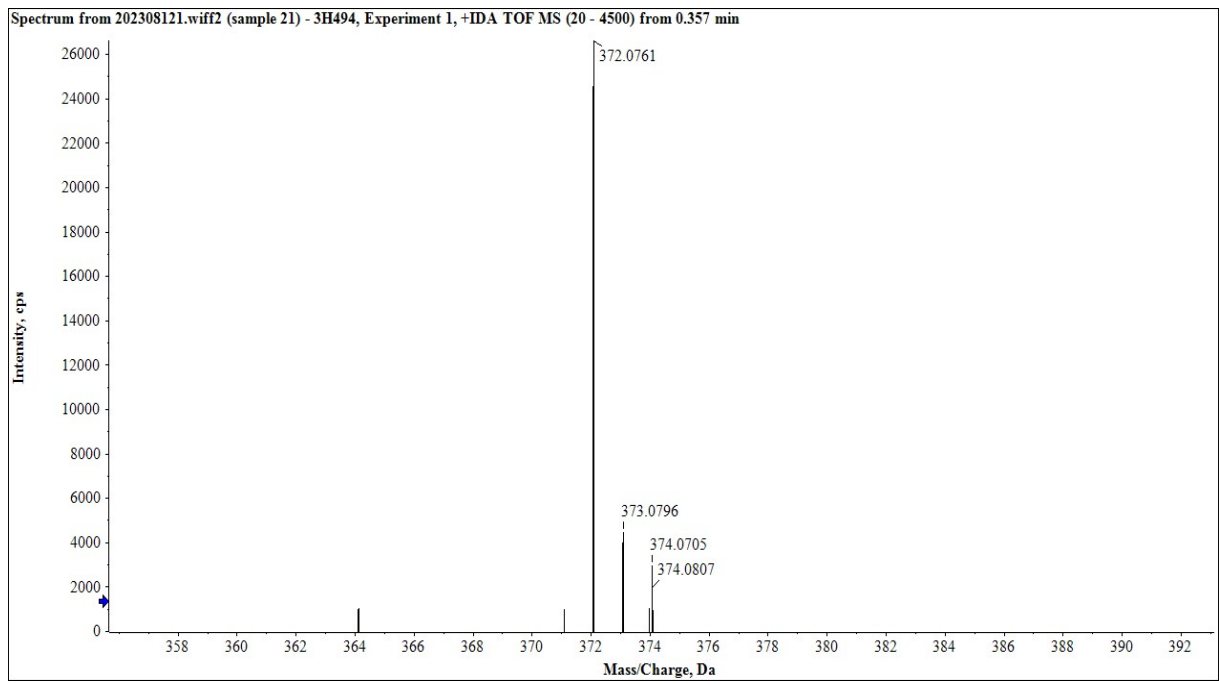


# 5-(4-fluorobenzyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9d

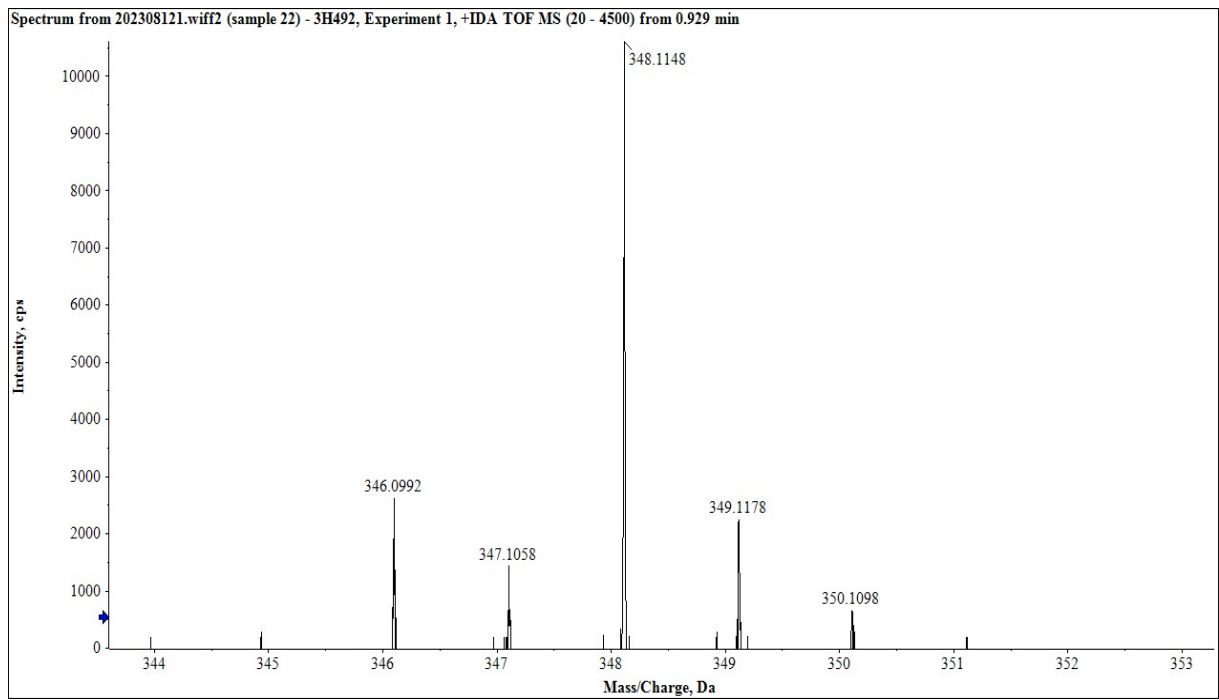






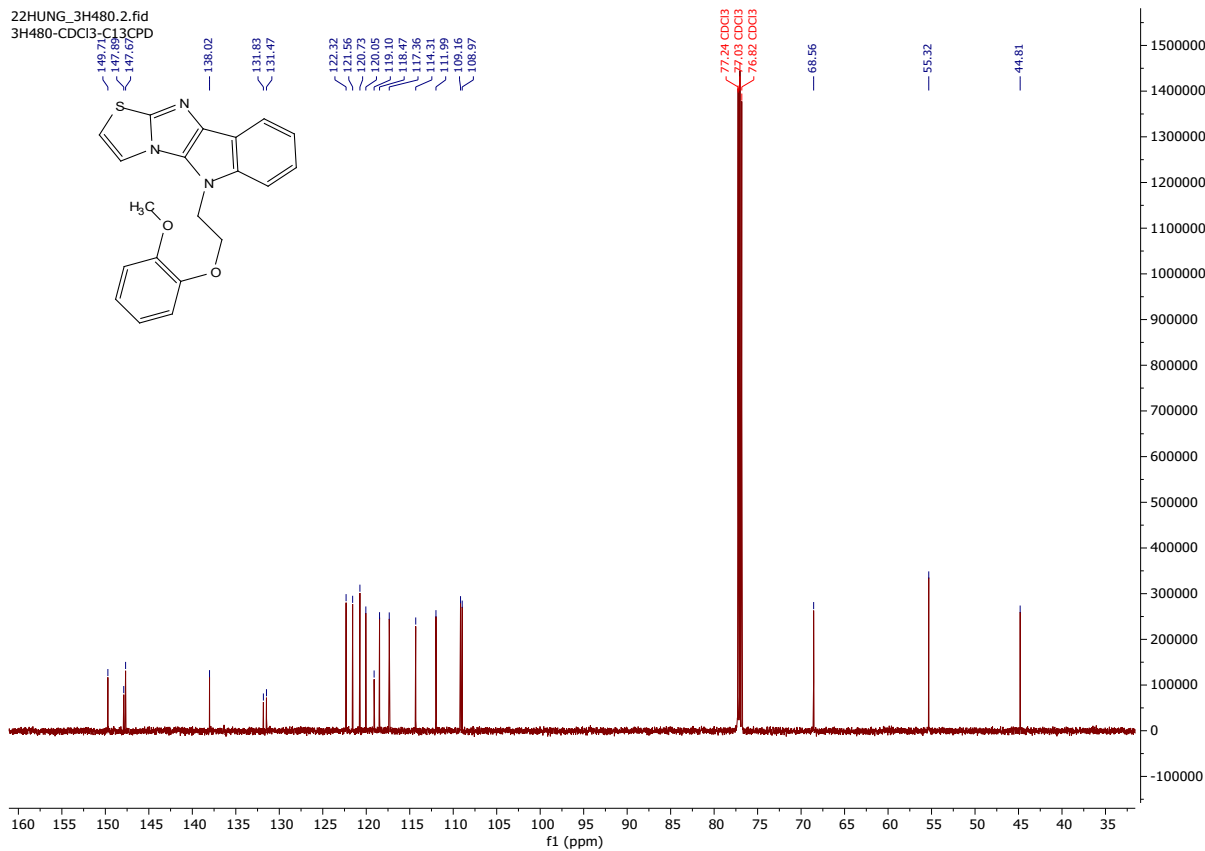
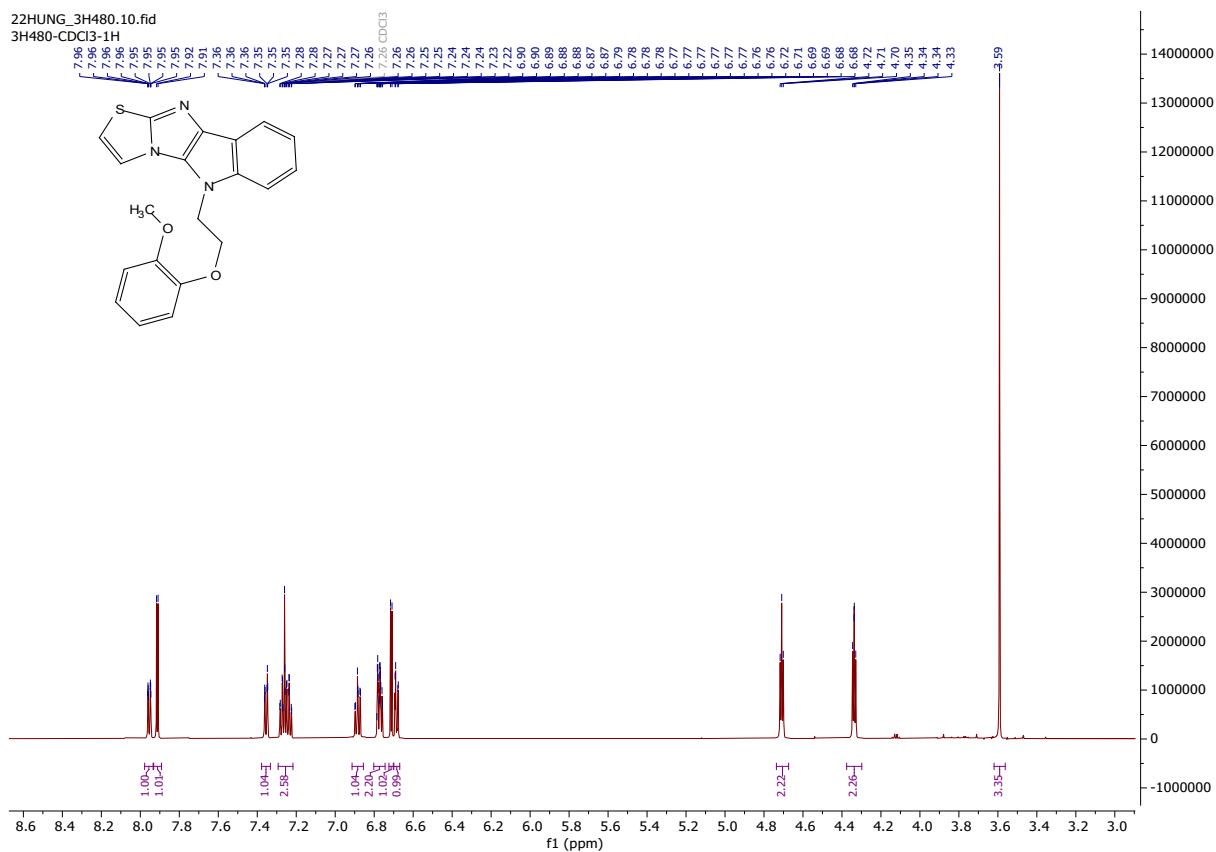






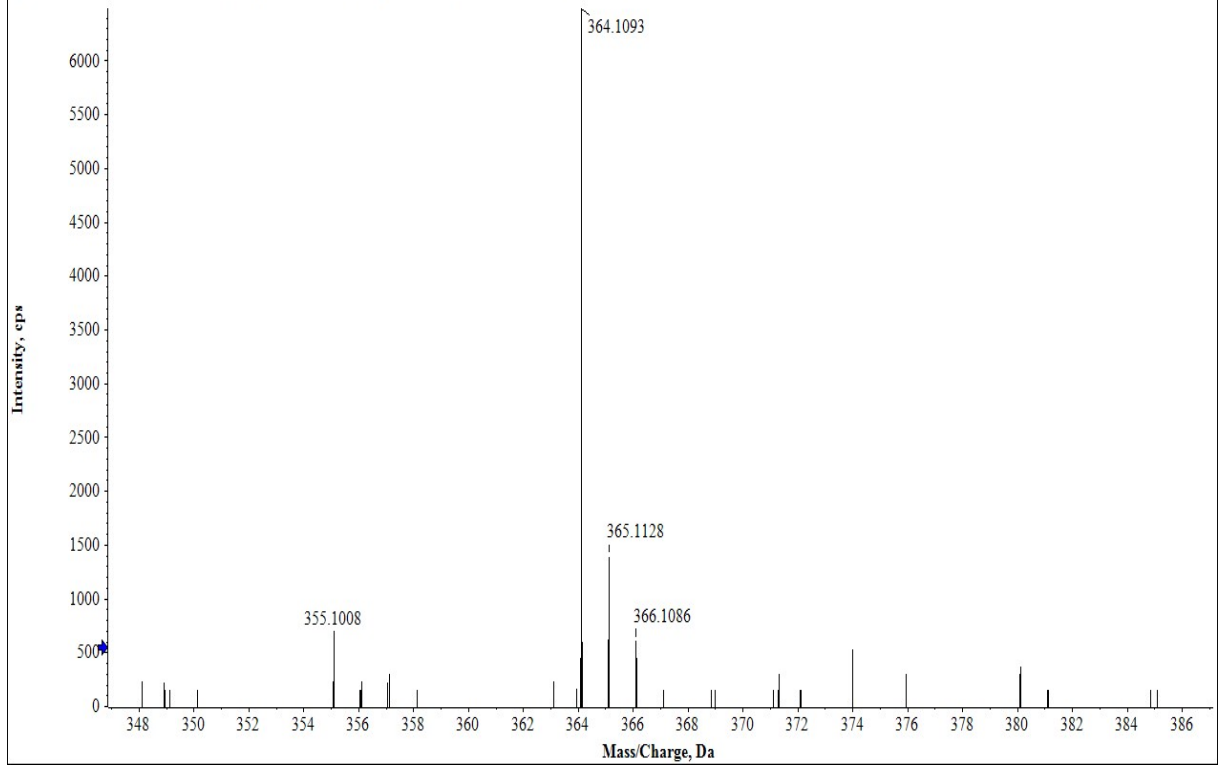
# 5-(2-(2-methoxyphenoxy)ethyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole

9g

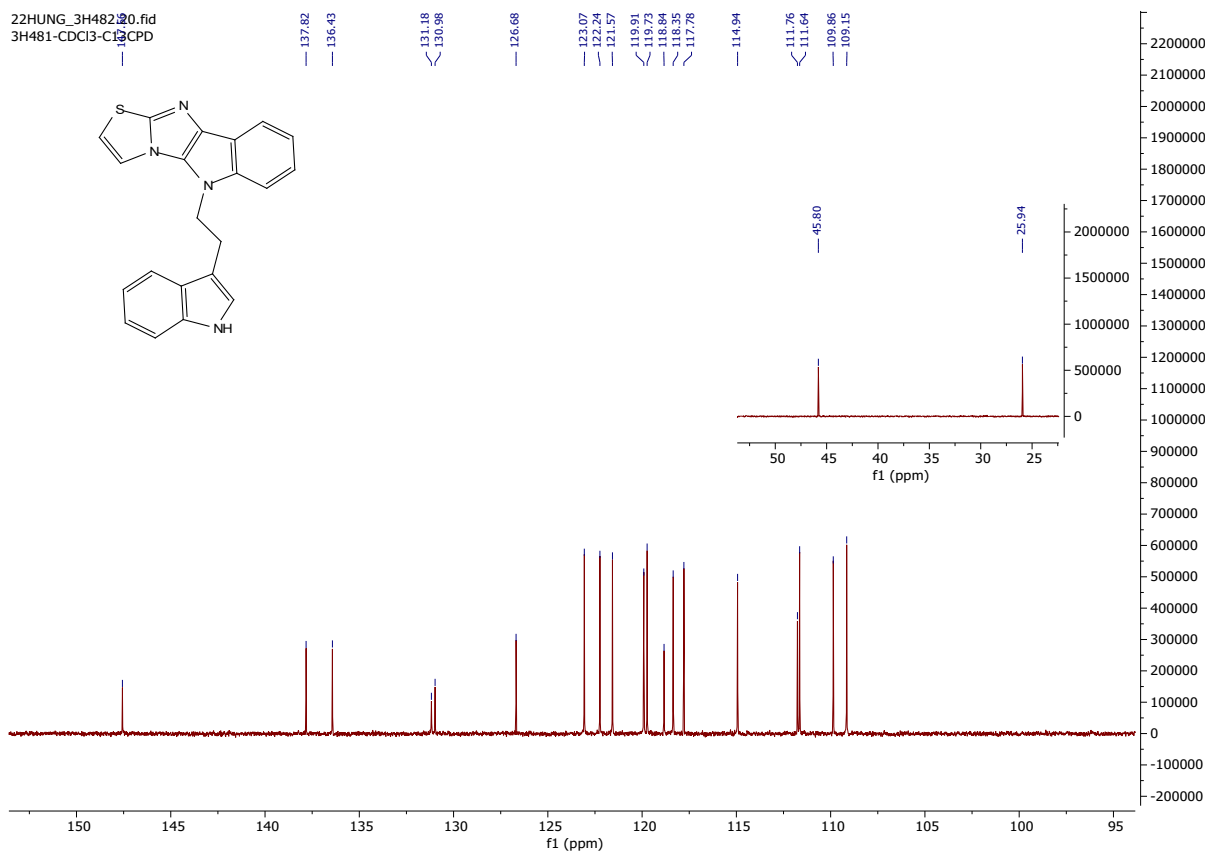
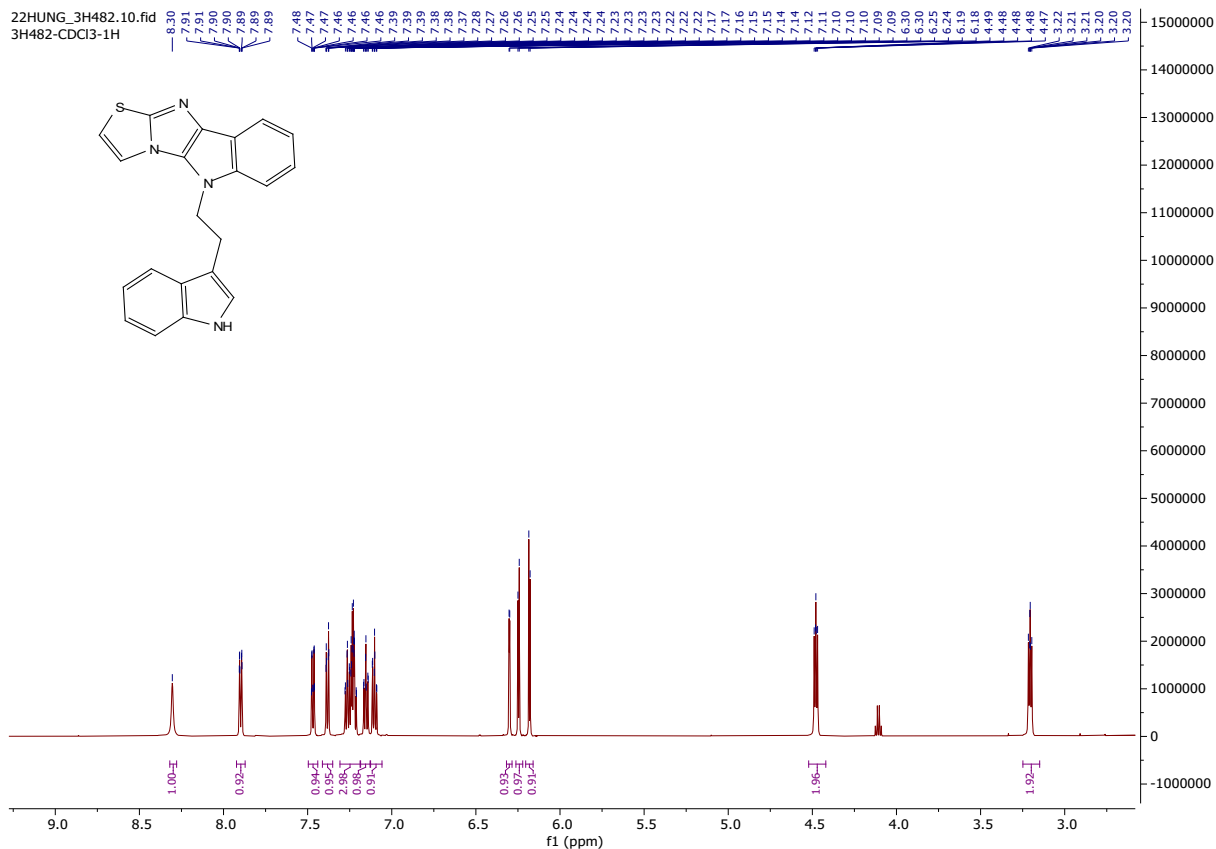


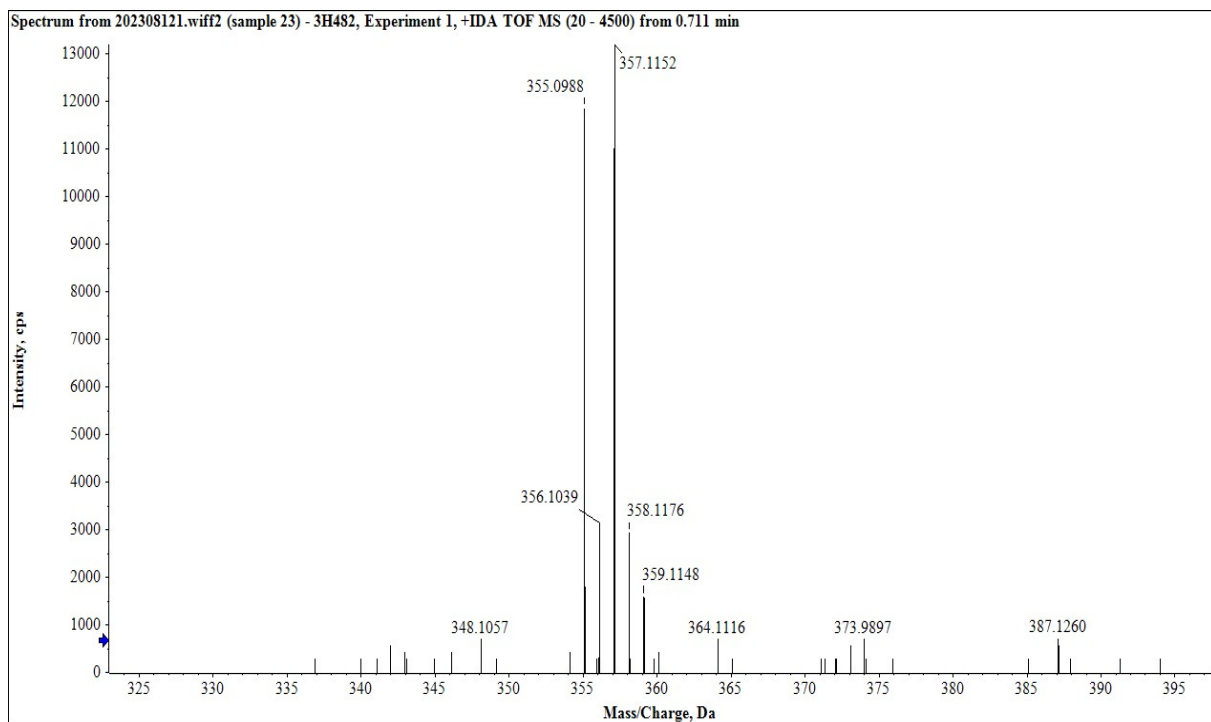


Spectrum from 202308121.wiff2 (sample 25) - 3H480, Experiment 1, +IDA TOF MS (20 - 4500) from 1.440 min

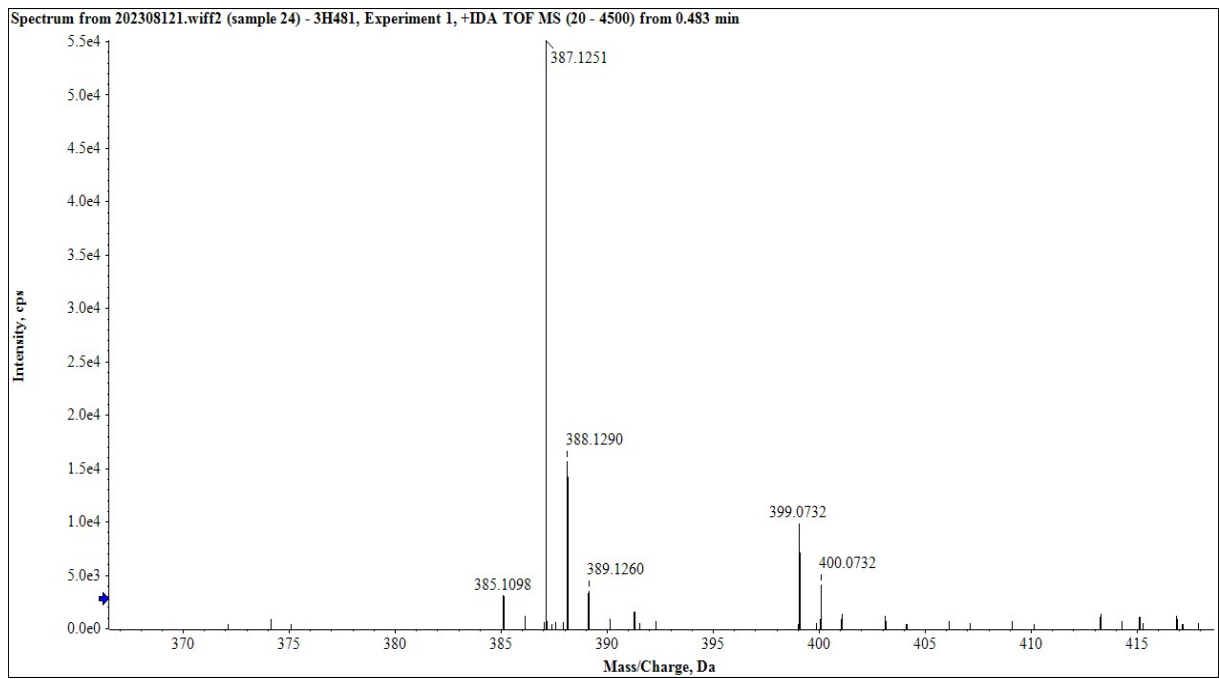


# 5-(2-(1H-indol-3-yl)ethyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9h

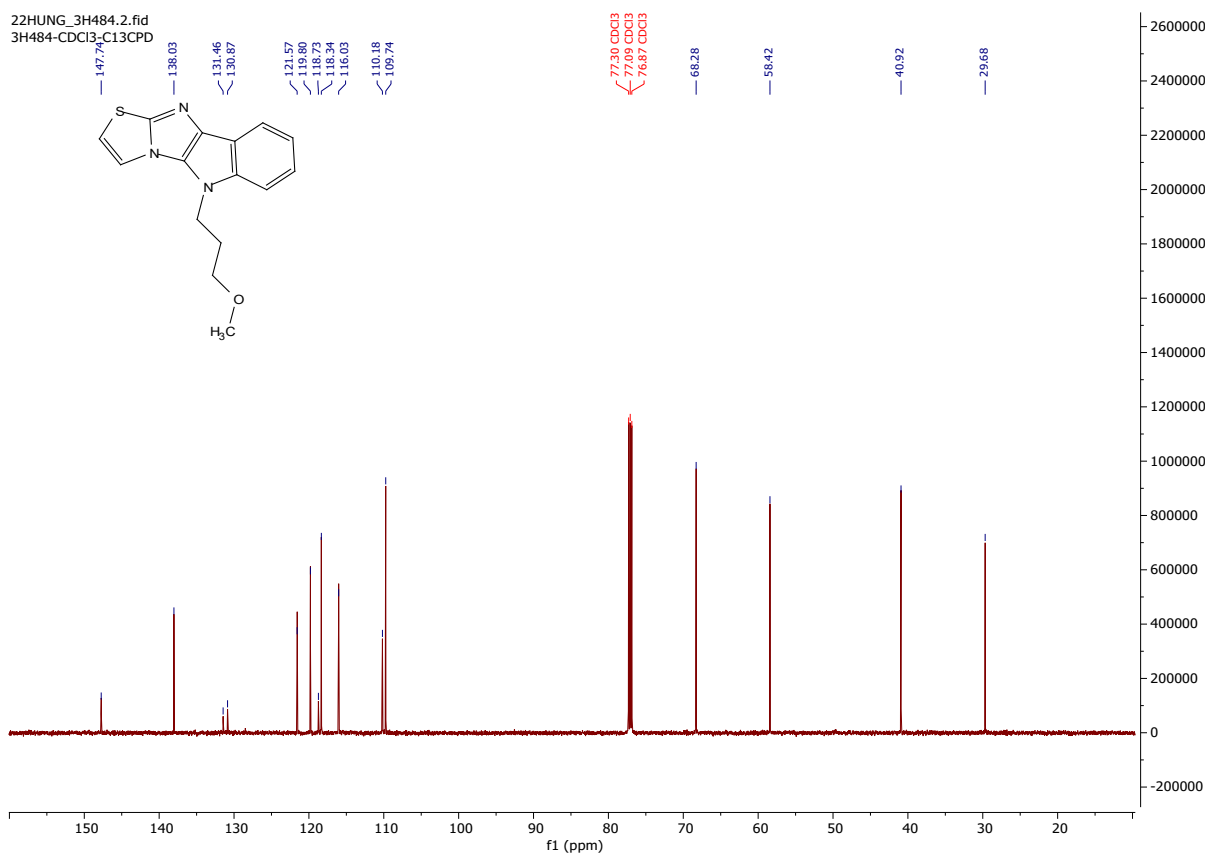
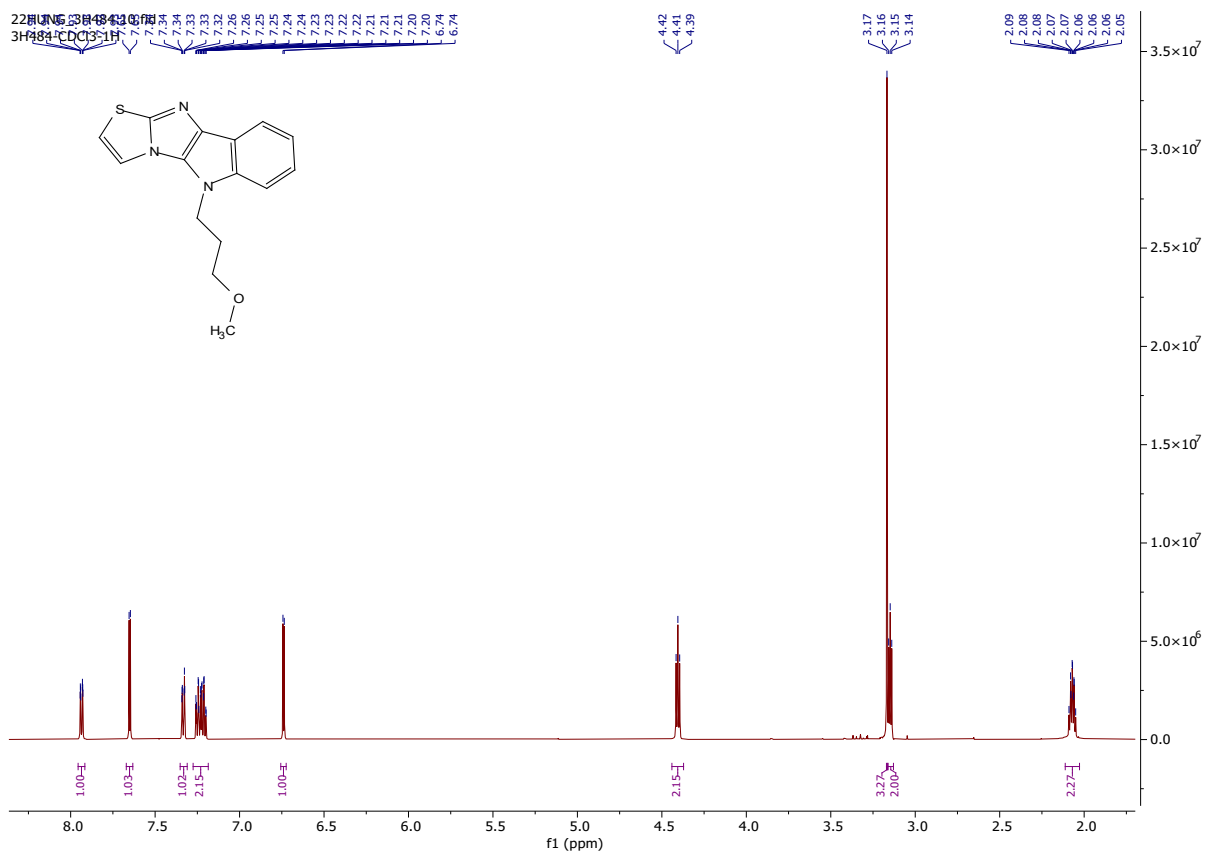


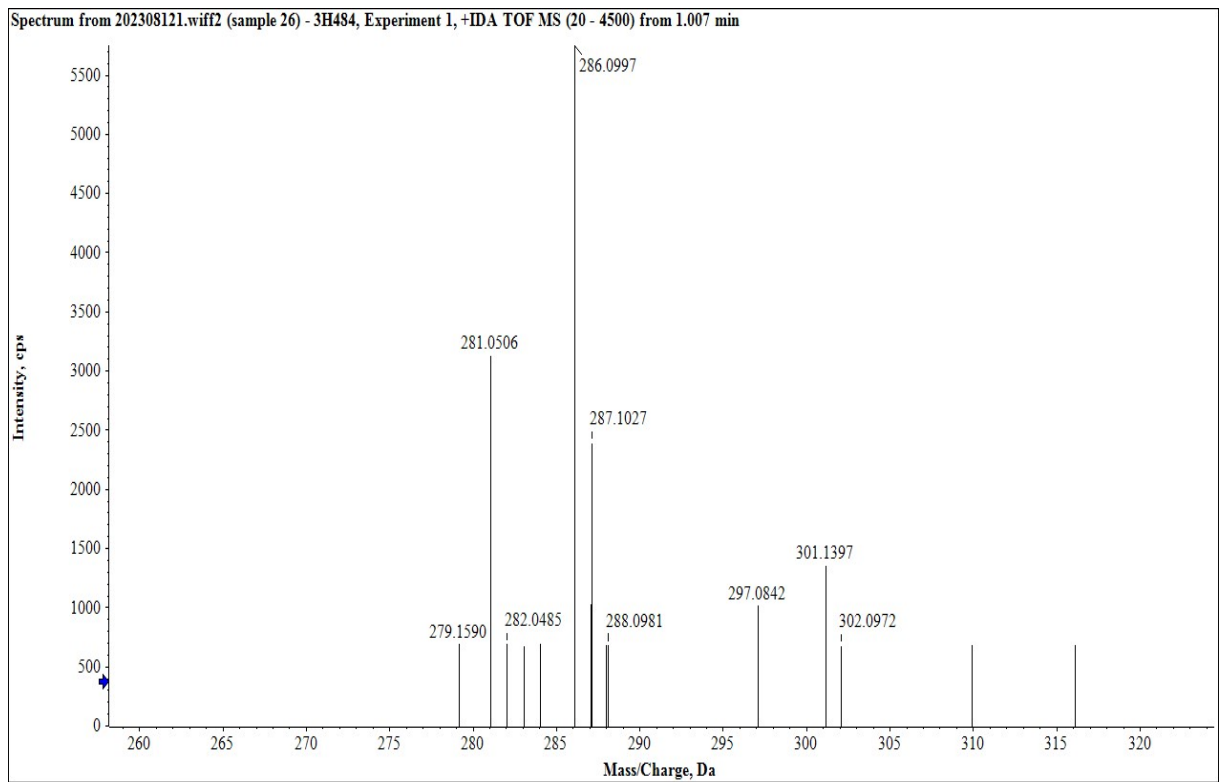




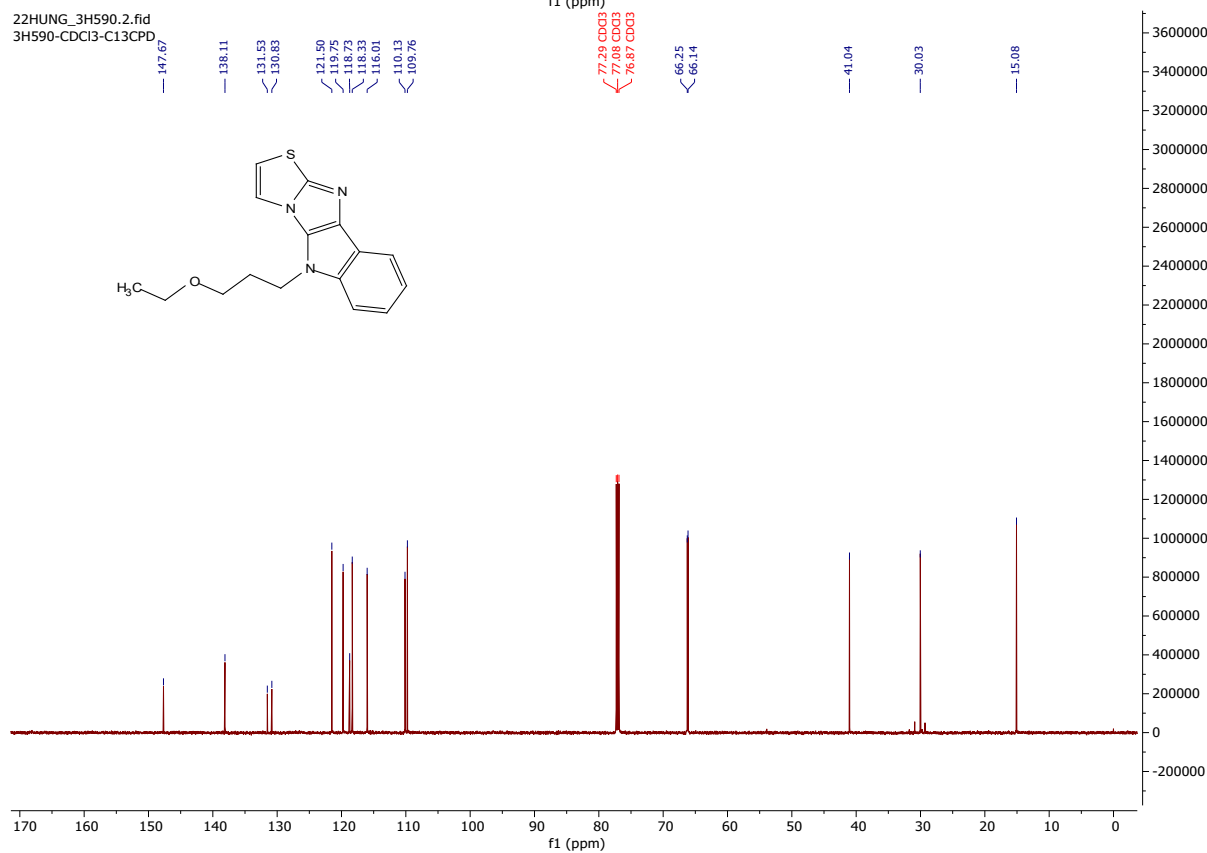
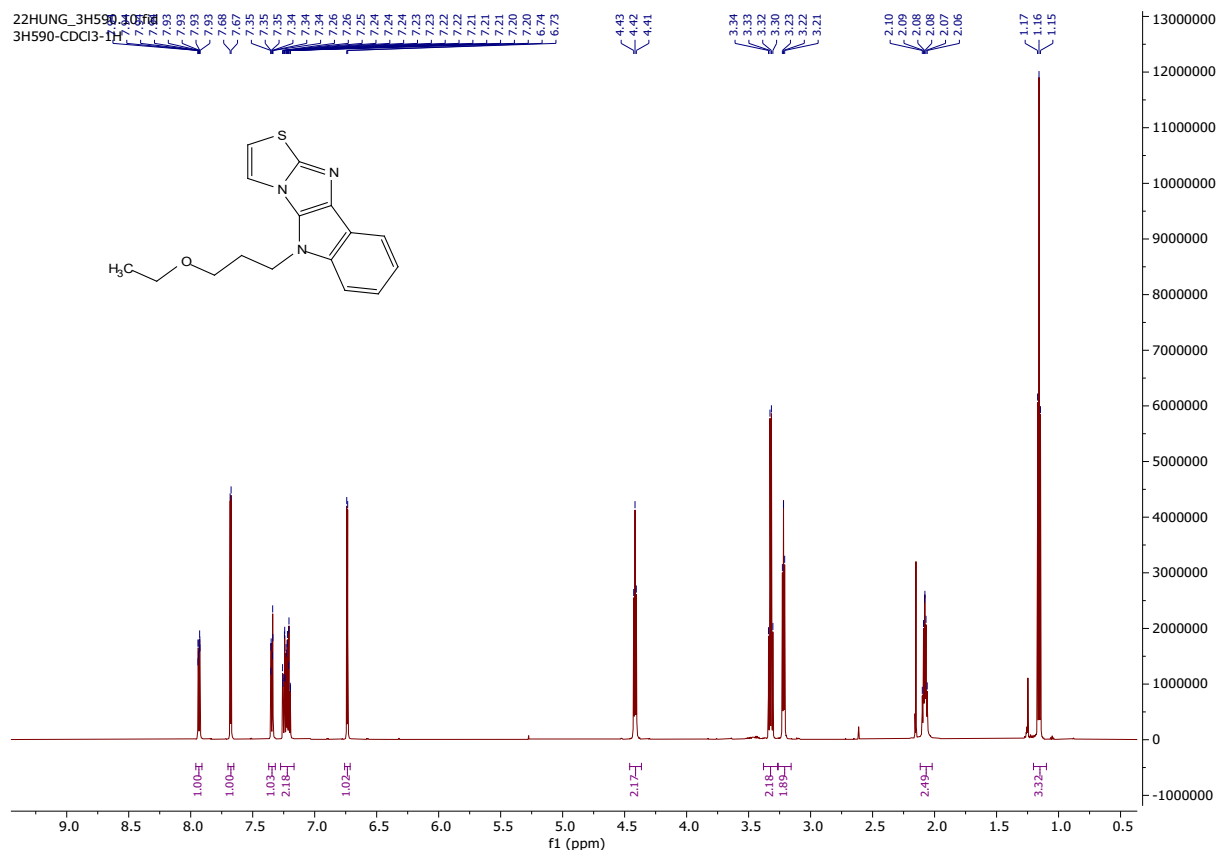


# 5-(3-methoxypropyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9j



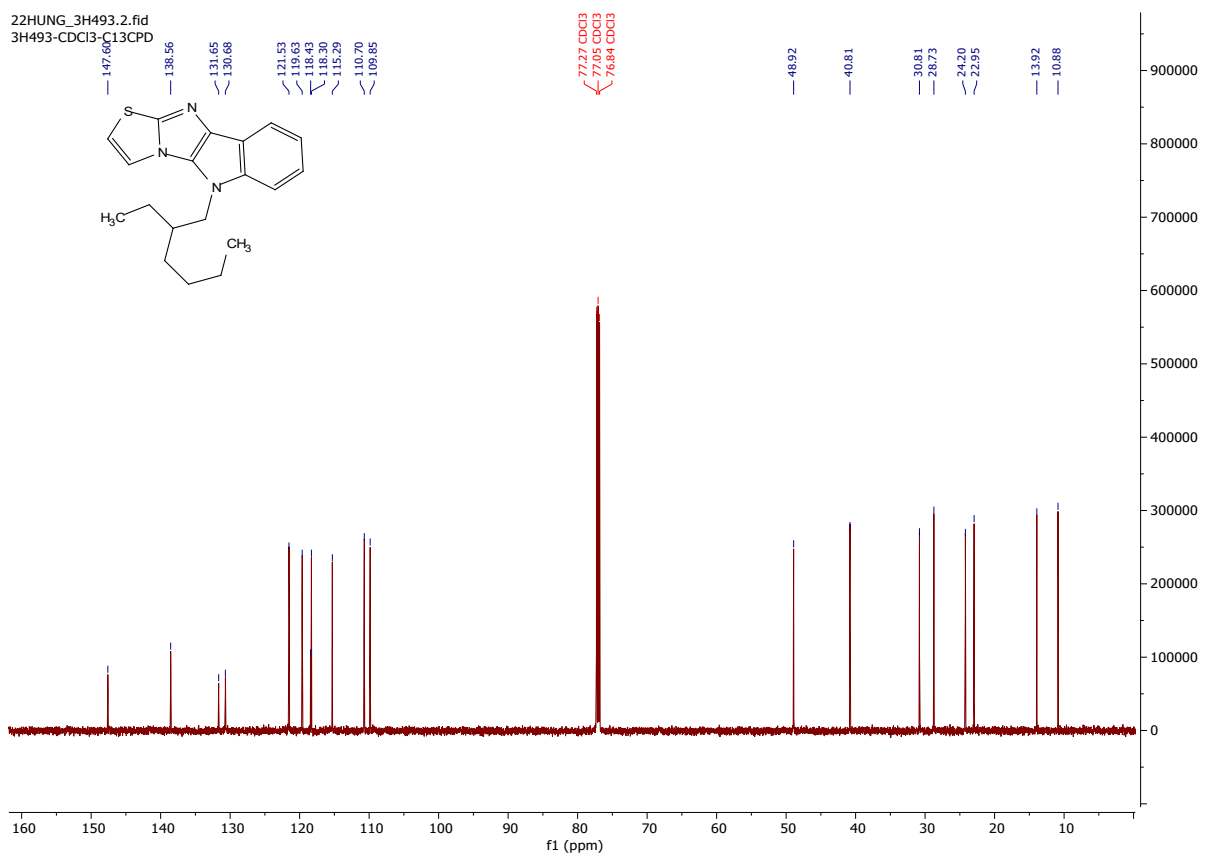
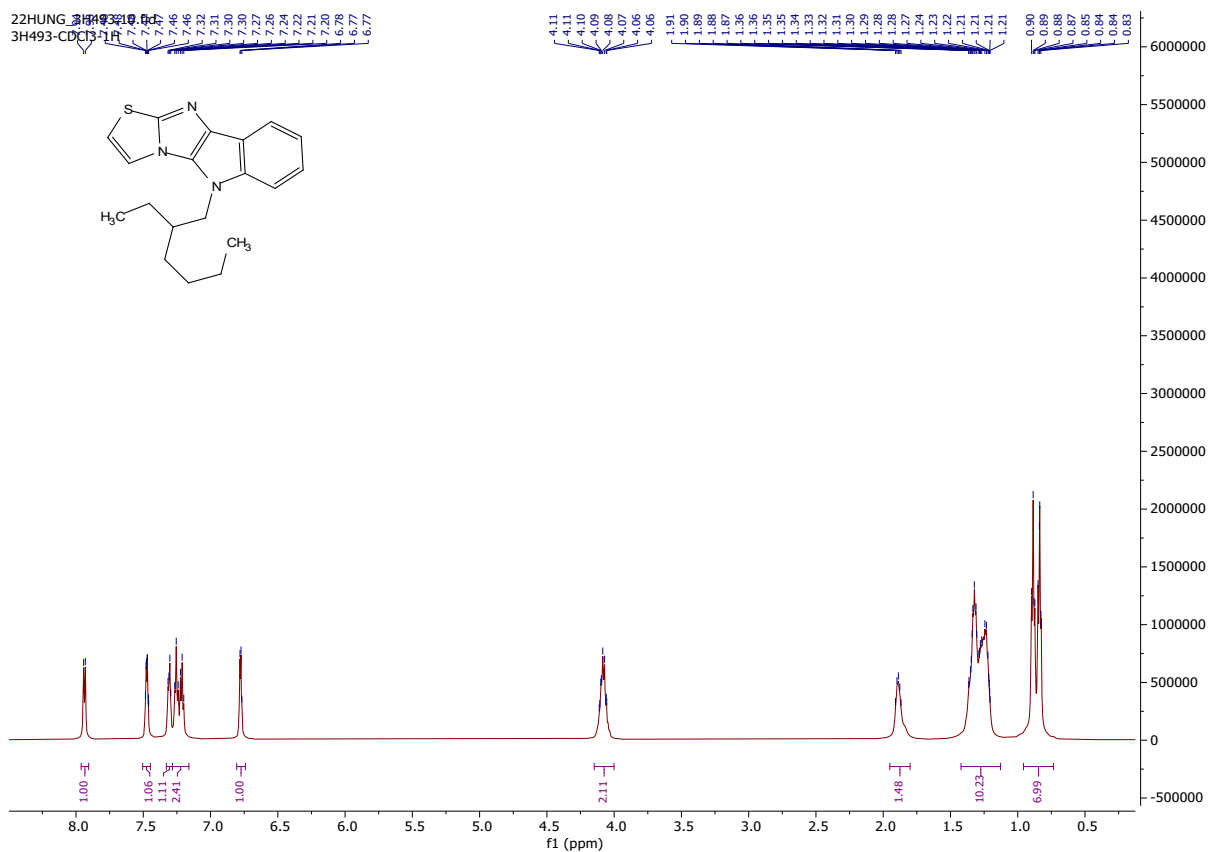


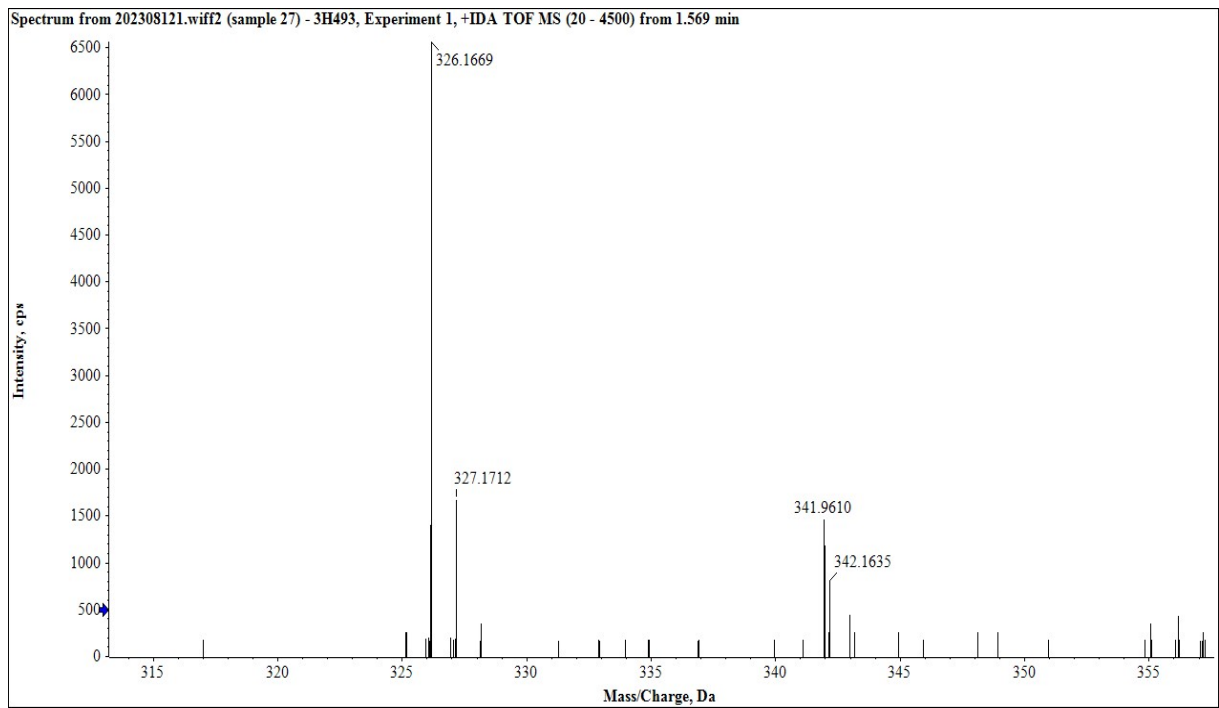
# 5-(3-ethoxypropyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9k



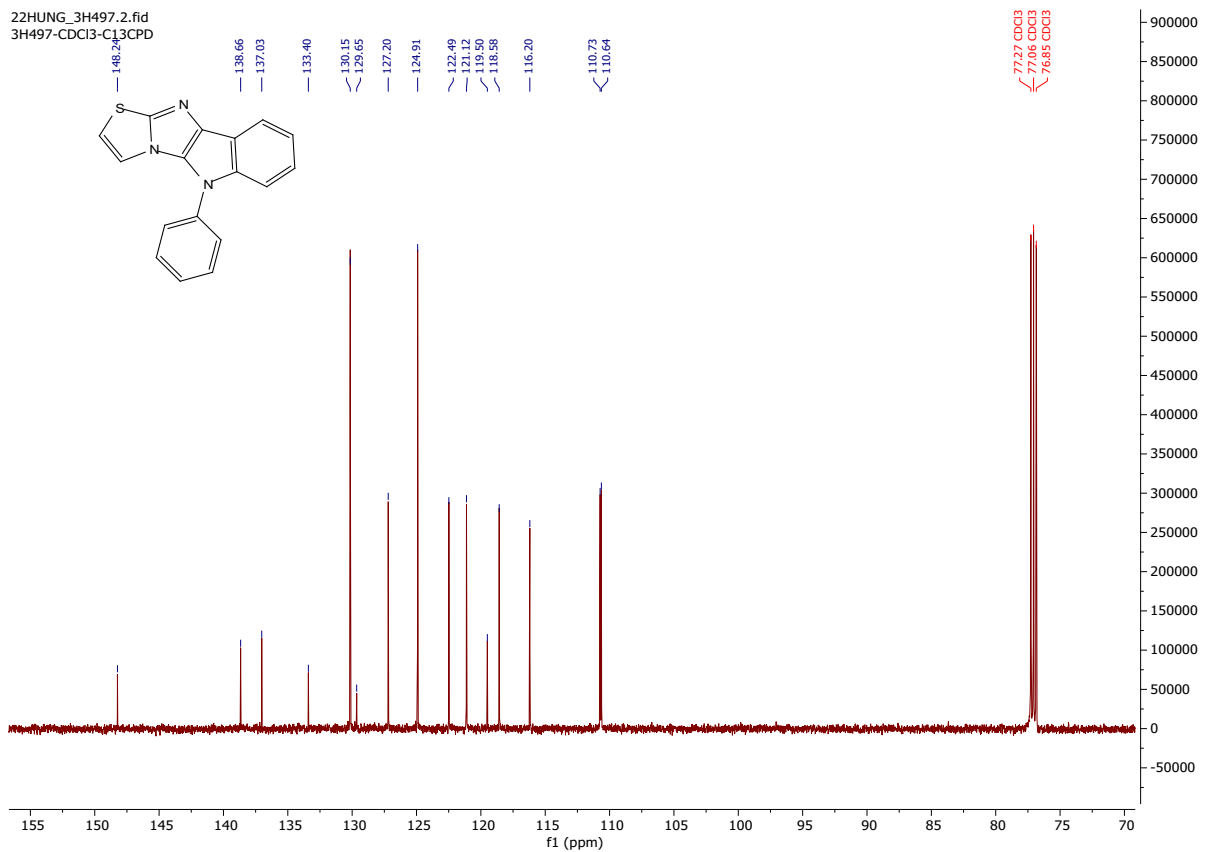
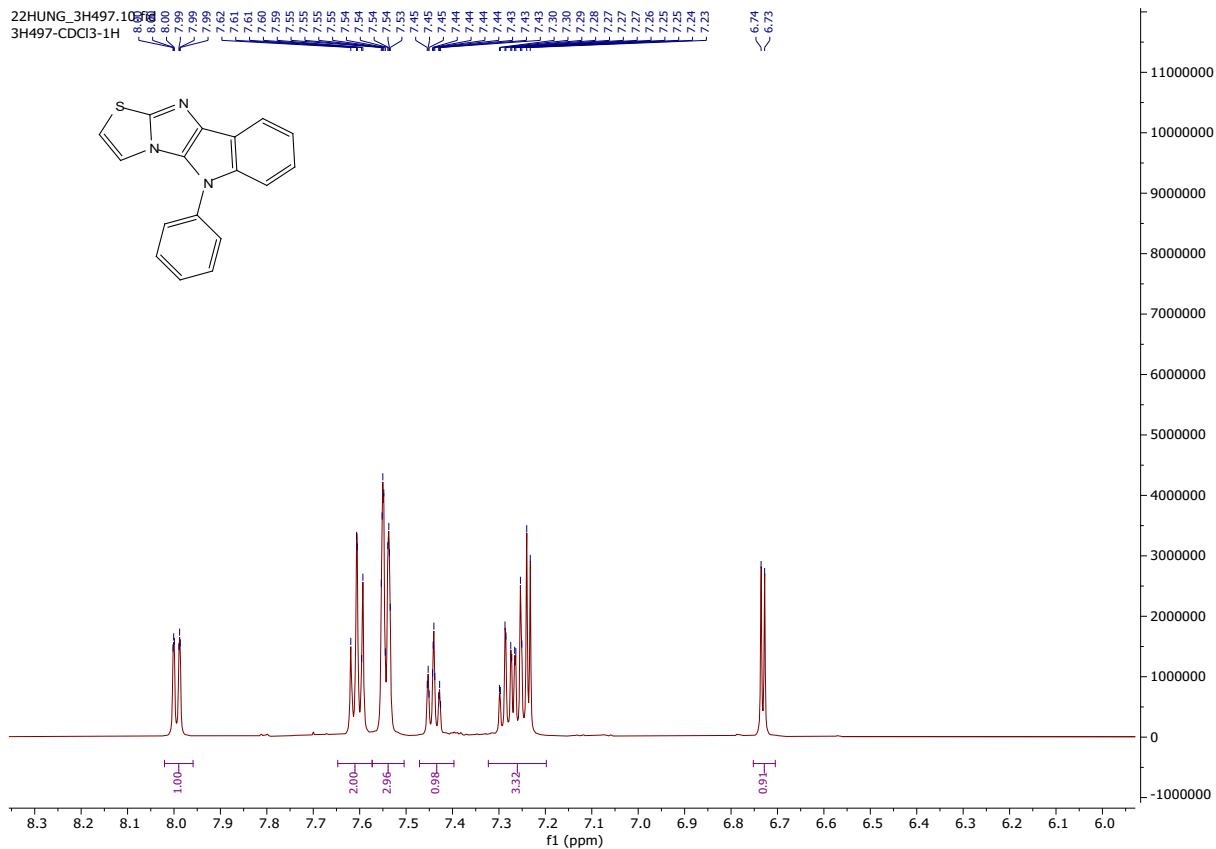


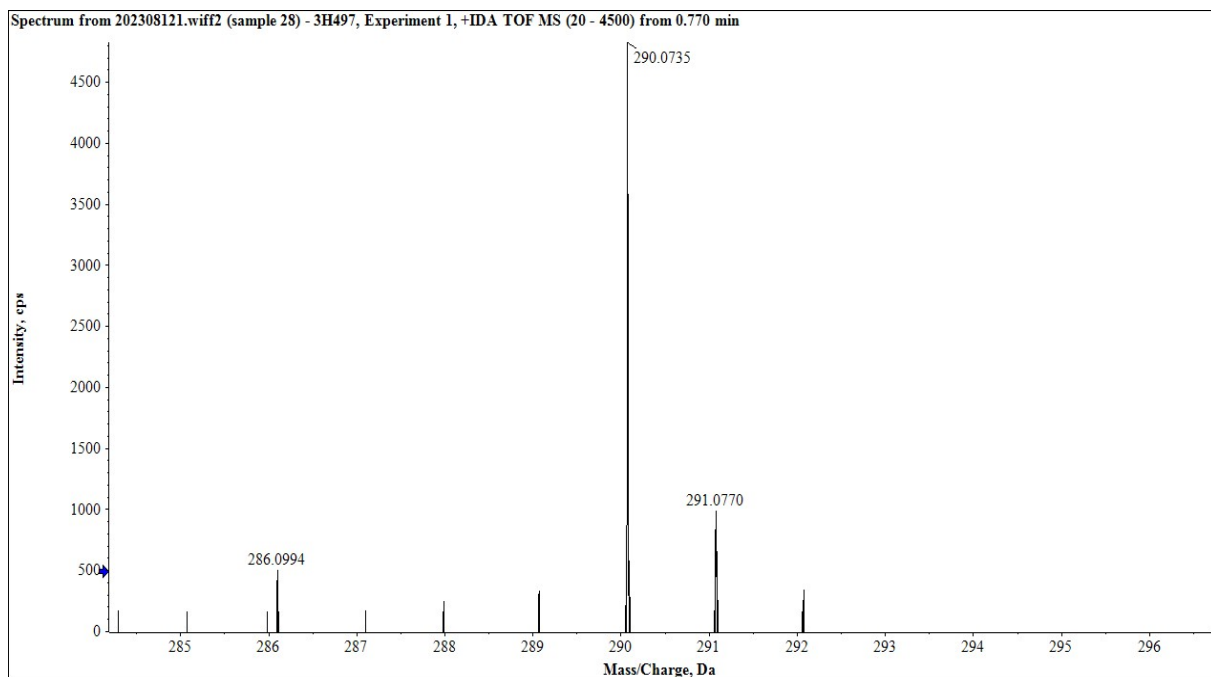
# 5-(2-ethylhexyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9l



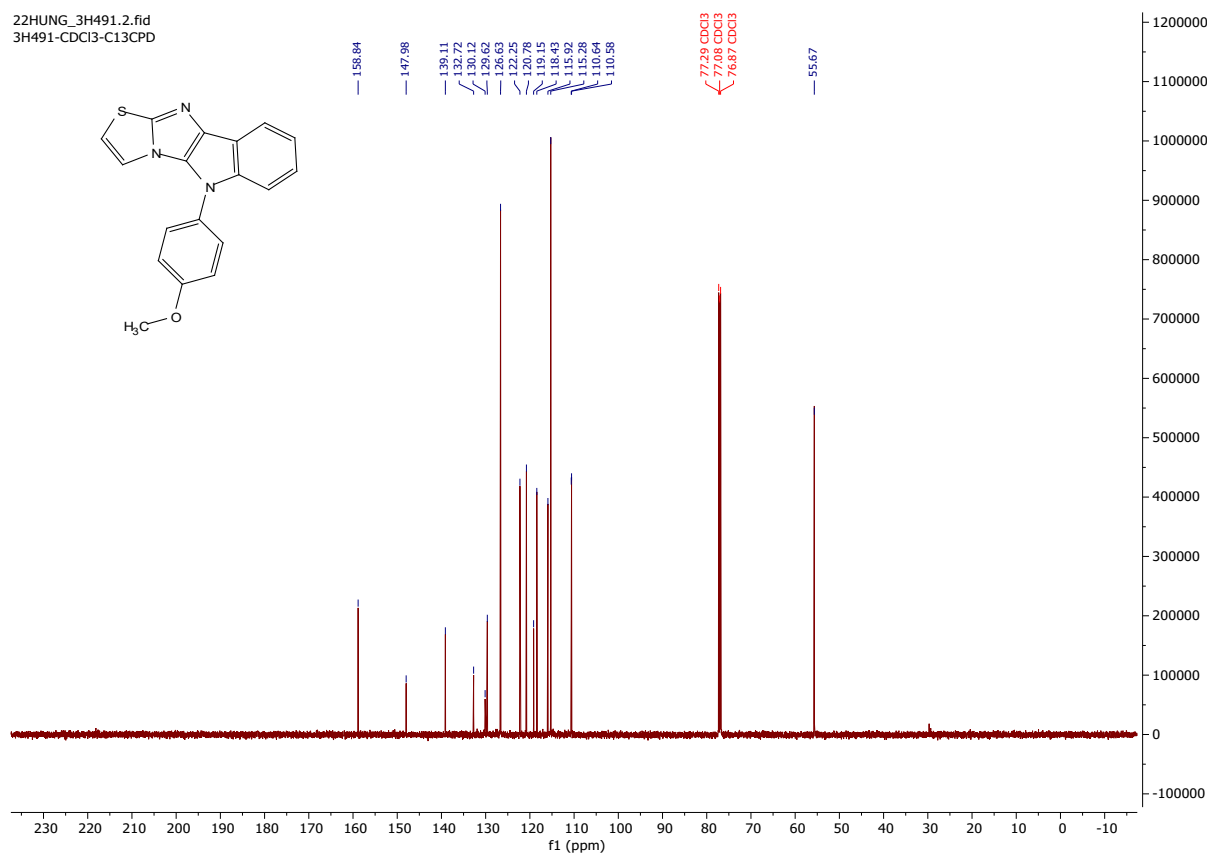
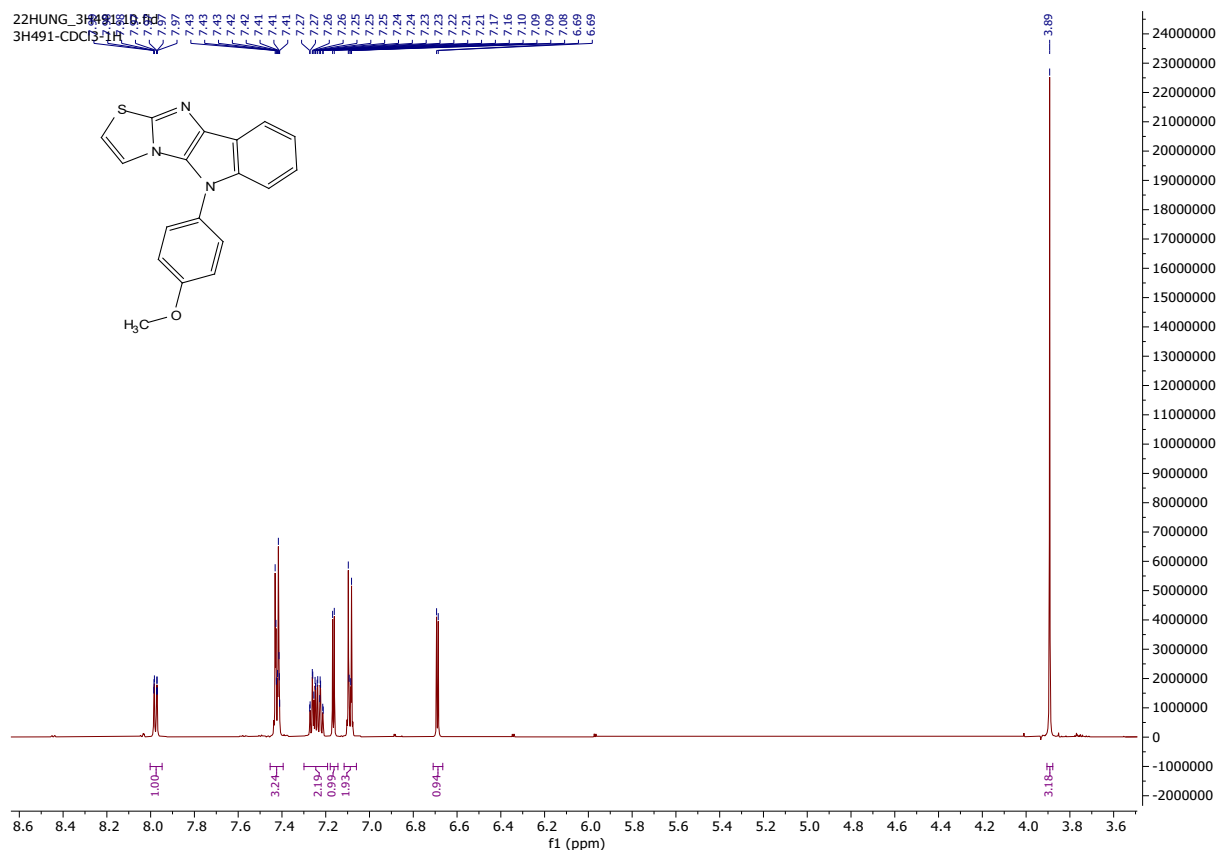


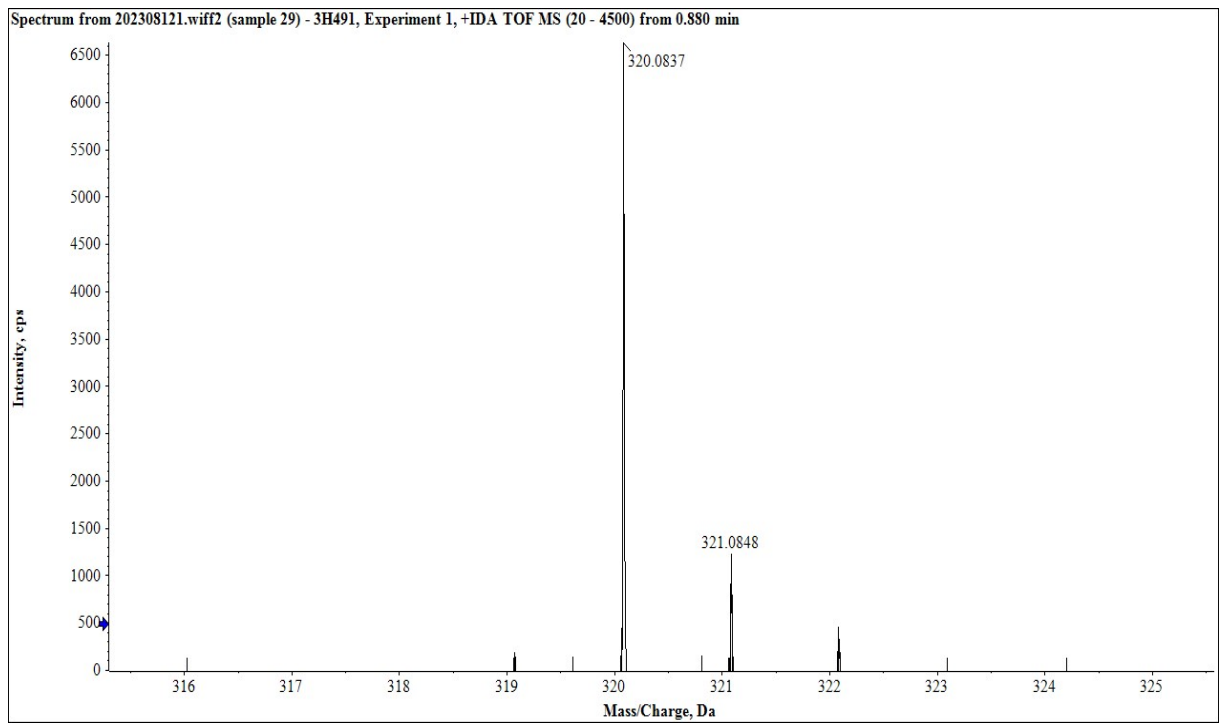
# 5-phenyl-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9m





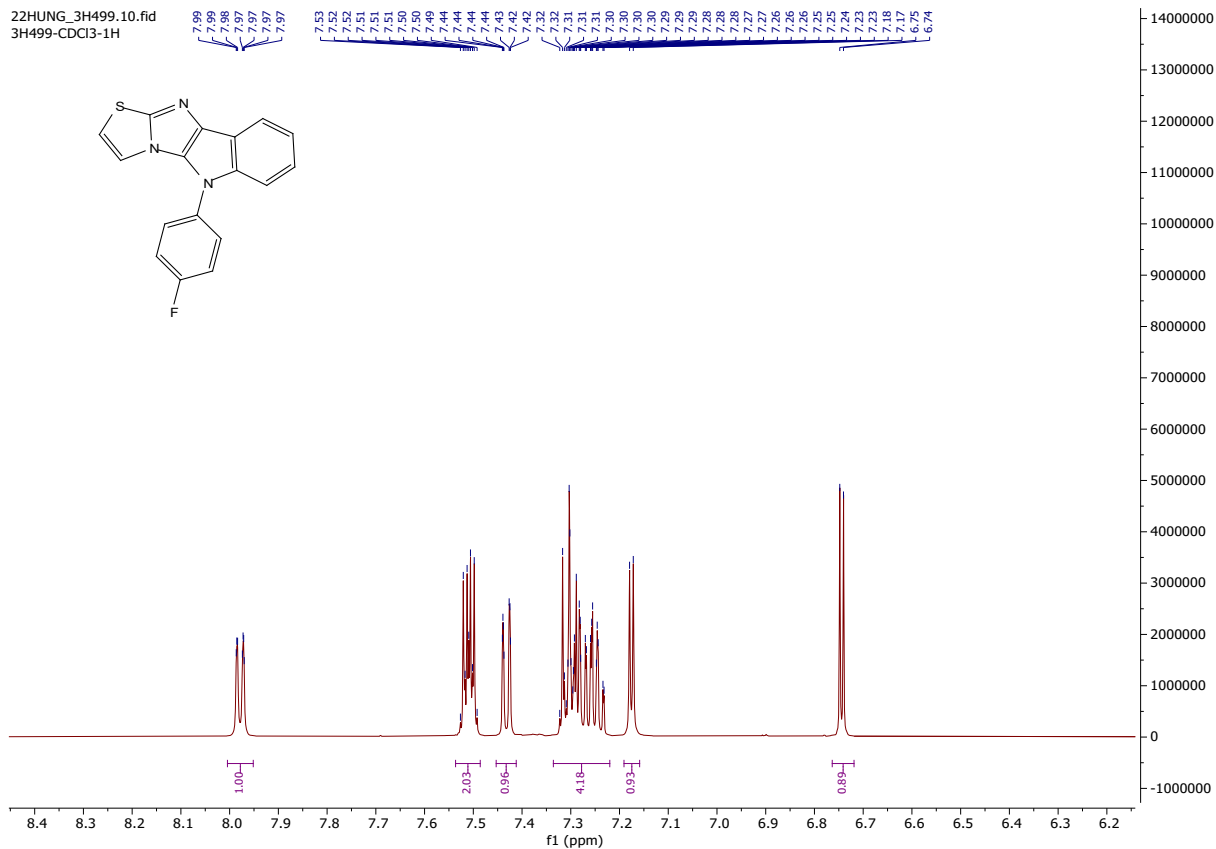
# 5-(4-methoxyphenyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9n



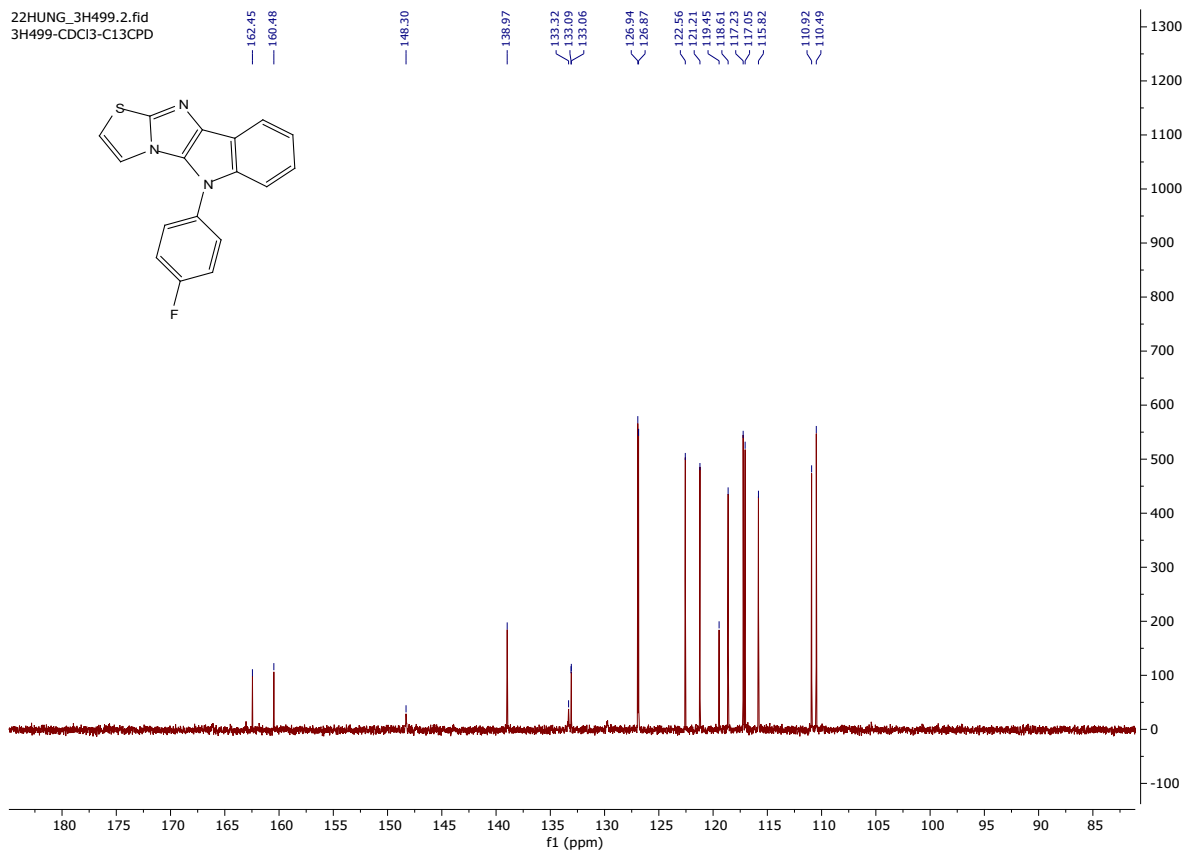


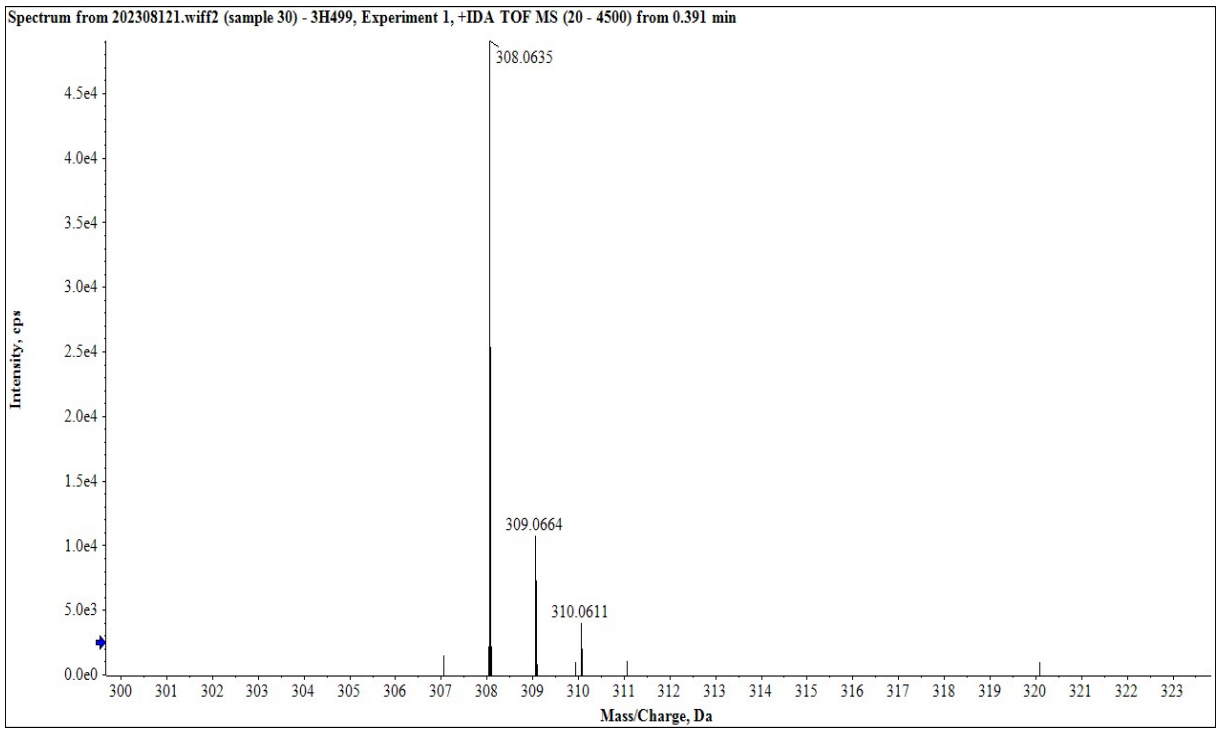
# 5-(4-fluorophenyl)-5H-thiazolo[2',3':2,3]imidazo[4,5-b]indole 9o

22HUNG\_3H499.10.fid  
3H499-CDCl3-1H



22HUNG\_3H499.2.fid  
3H499-CDCl3-C13CPD

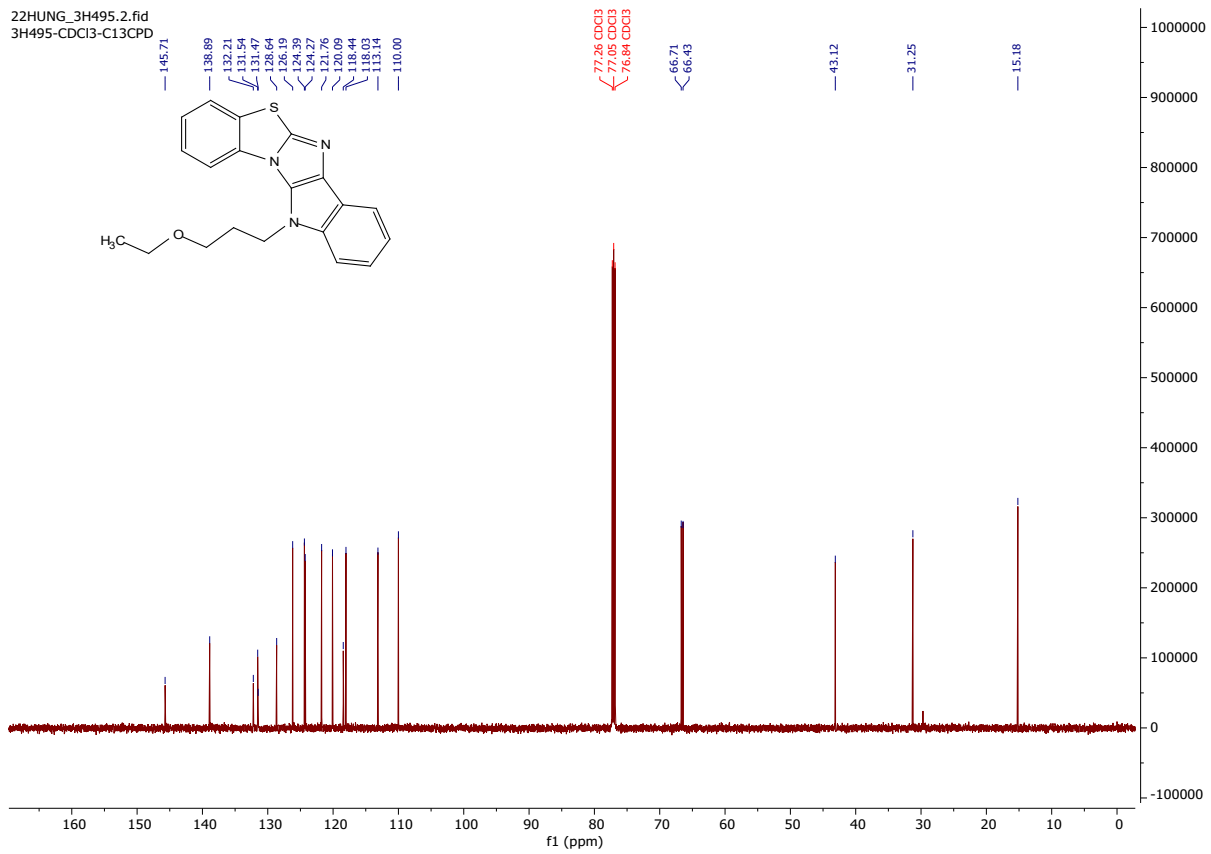
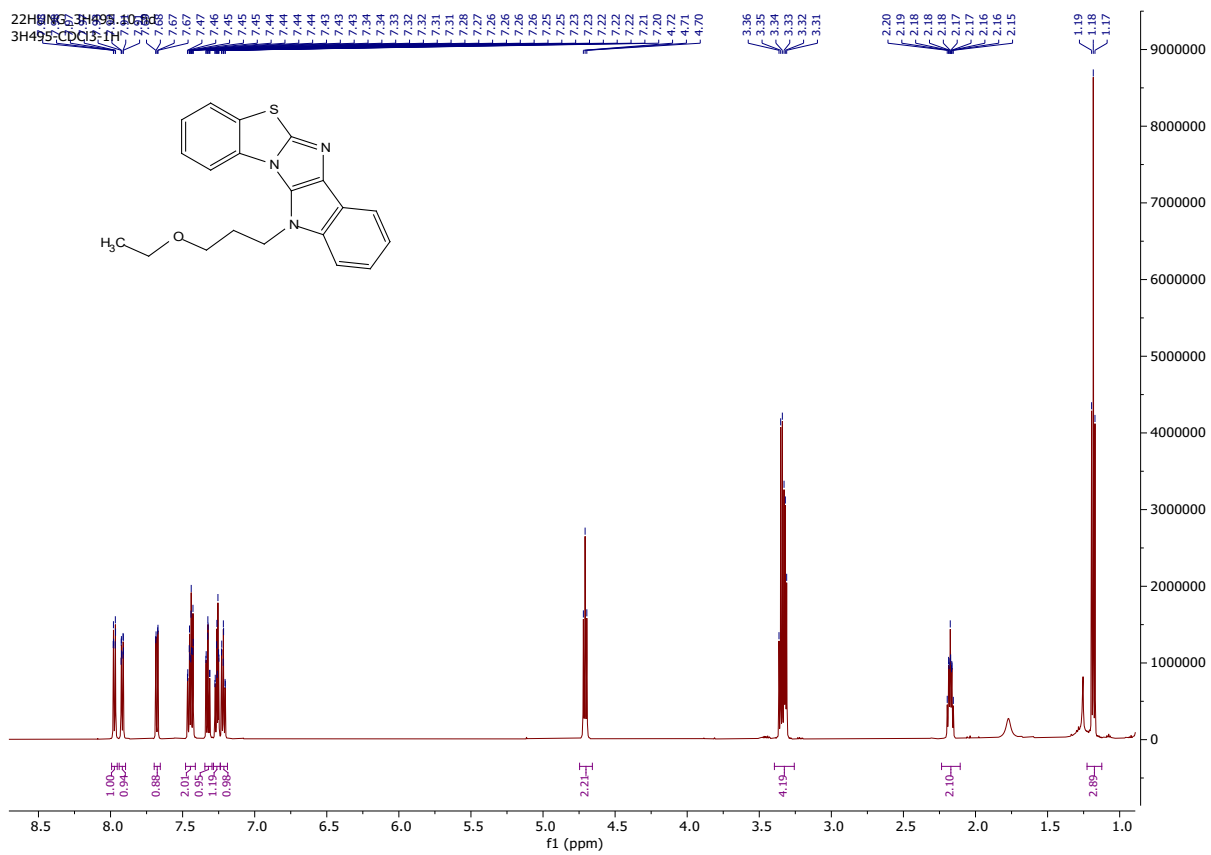


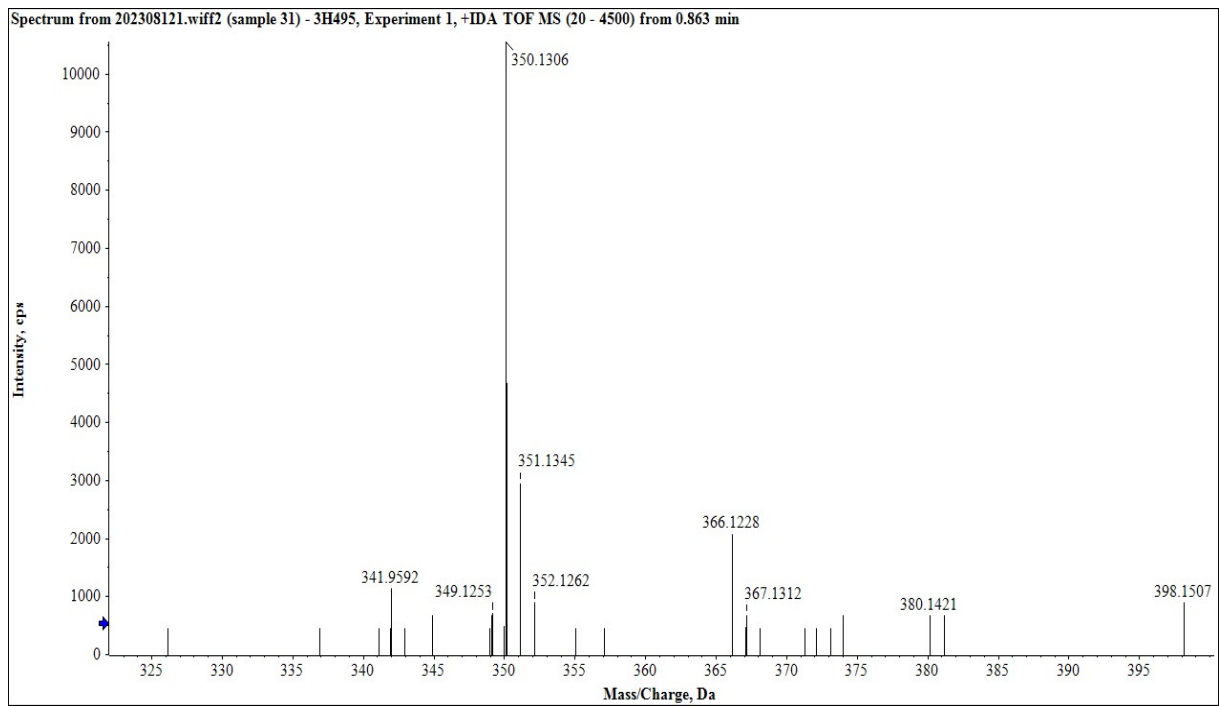




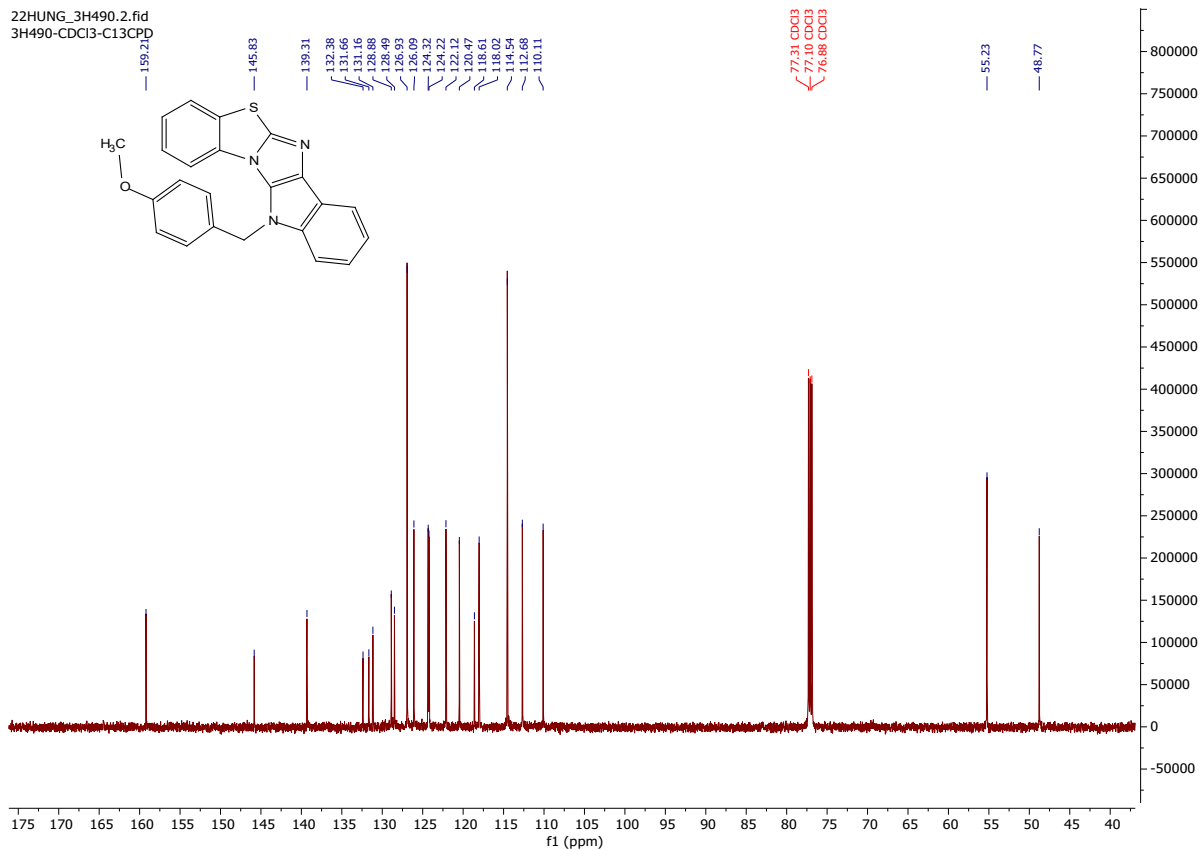
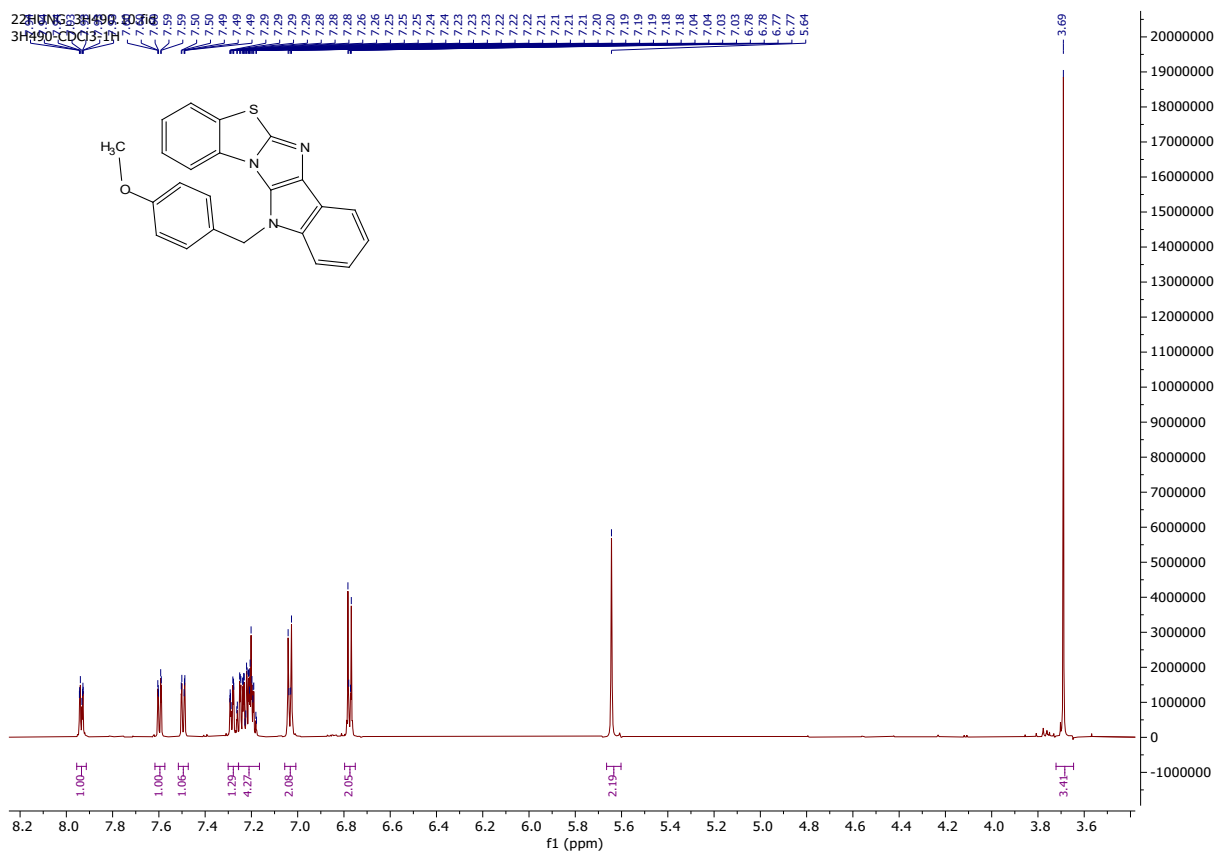
# 11-(3-ethoxypropyl)-11H-benzo[4',5']thiazolo[2',3':2,3]imidazo[4,5-b]indole

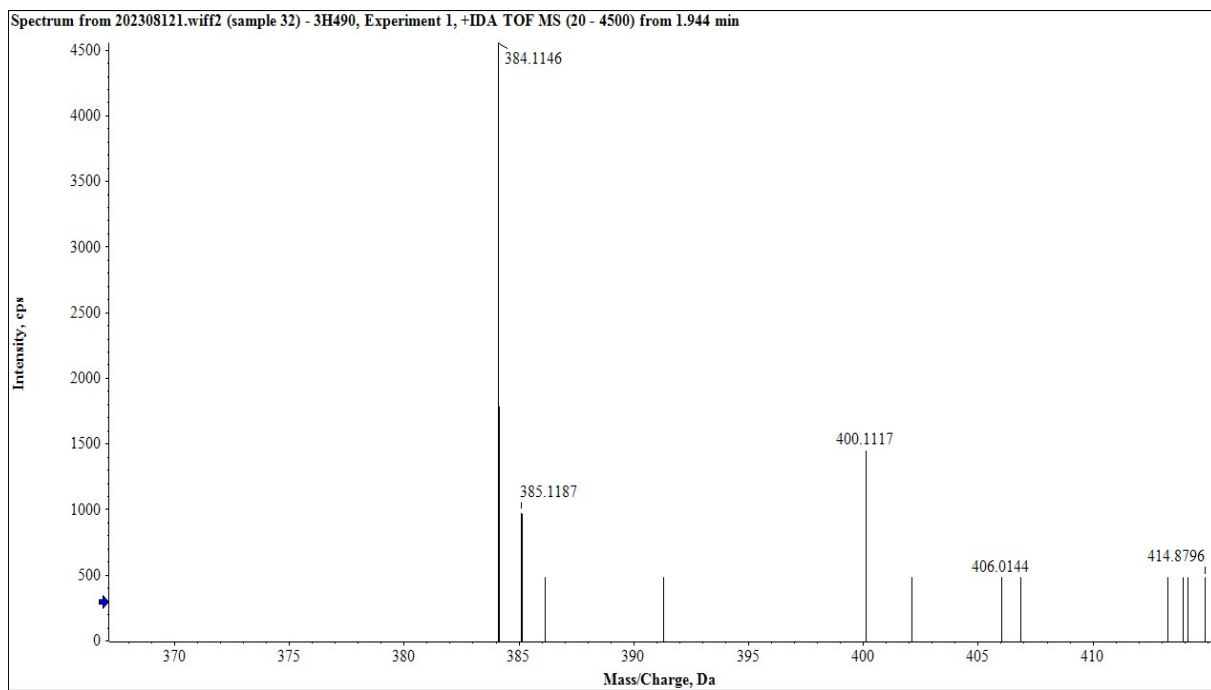
## 9o





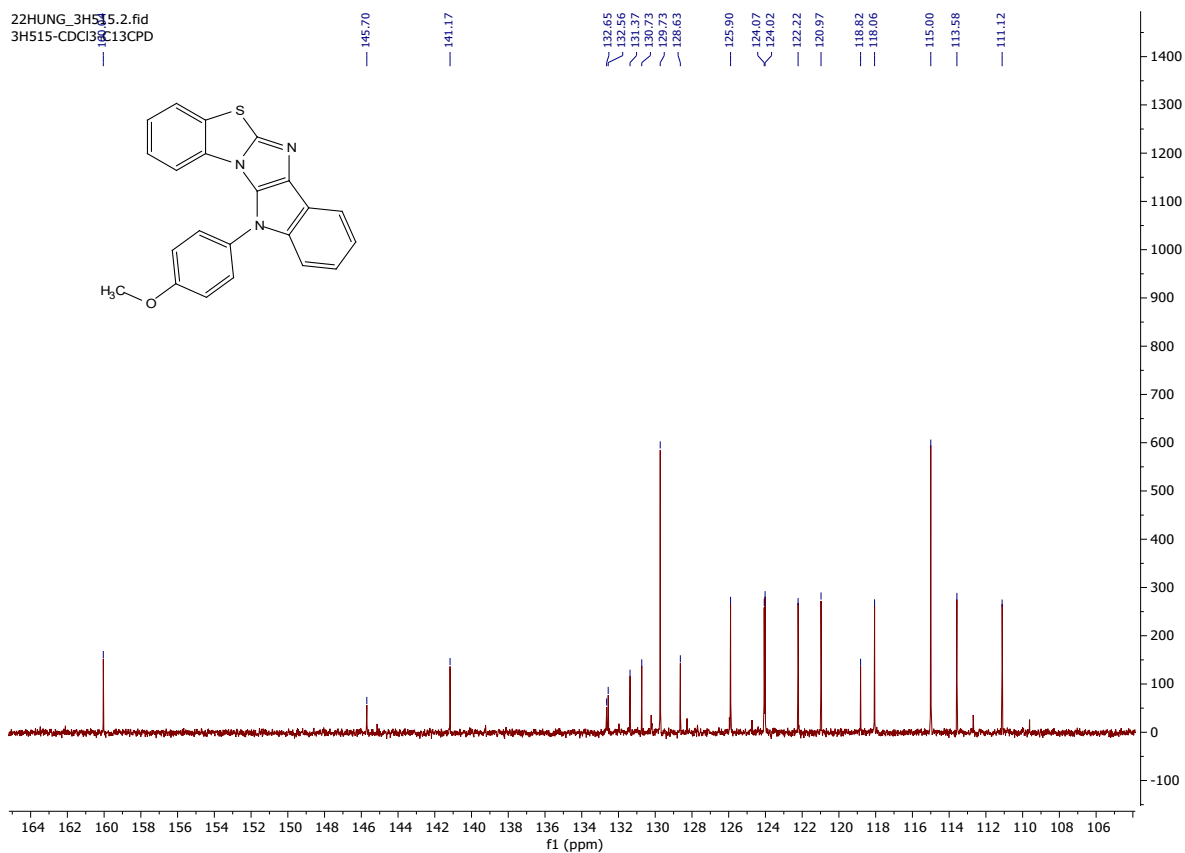
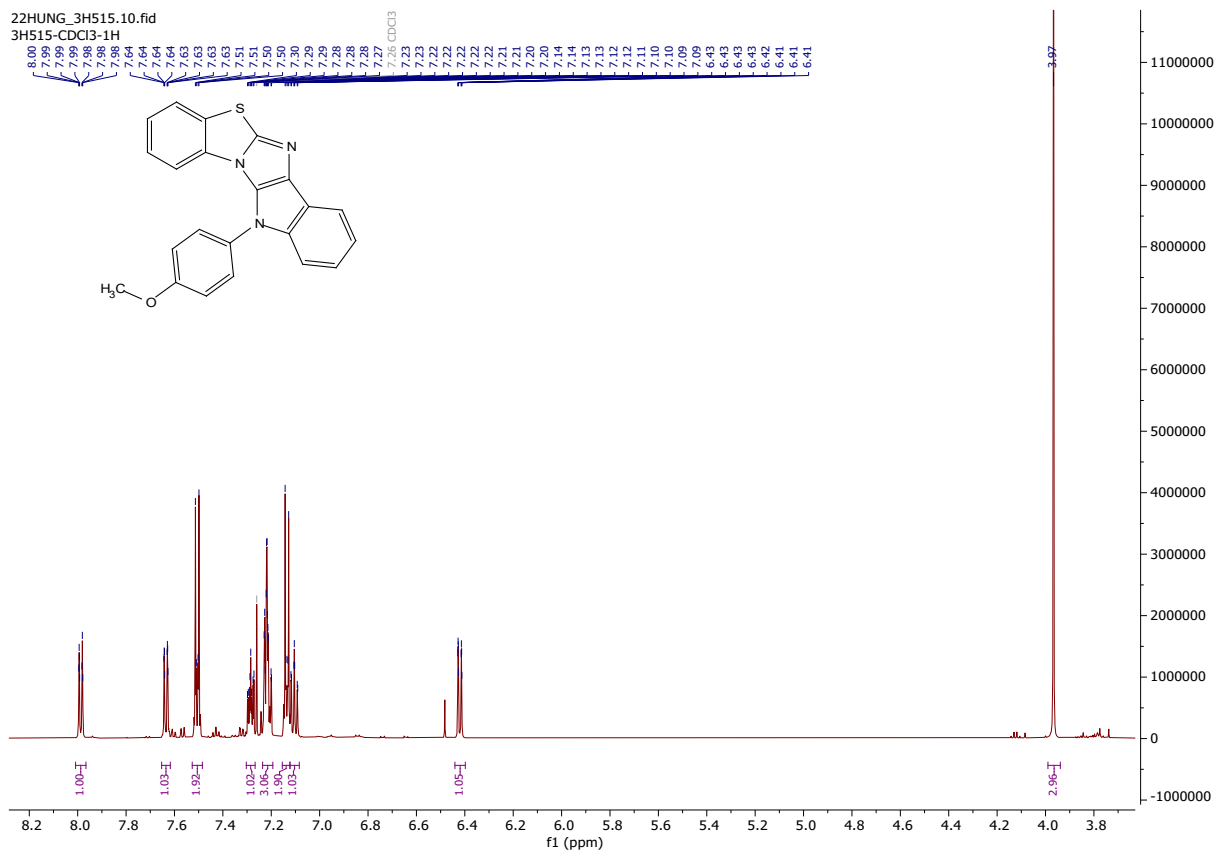
# 11-(4-methoxybenzyl)-11H-benzo[4',5']thiazolo[2',3':2,3]imidazo[4,5-b]indole 9p

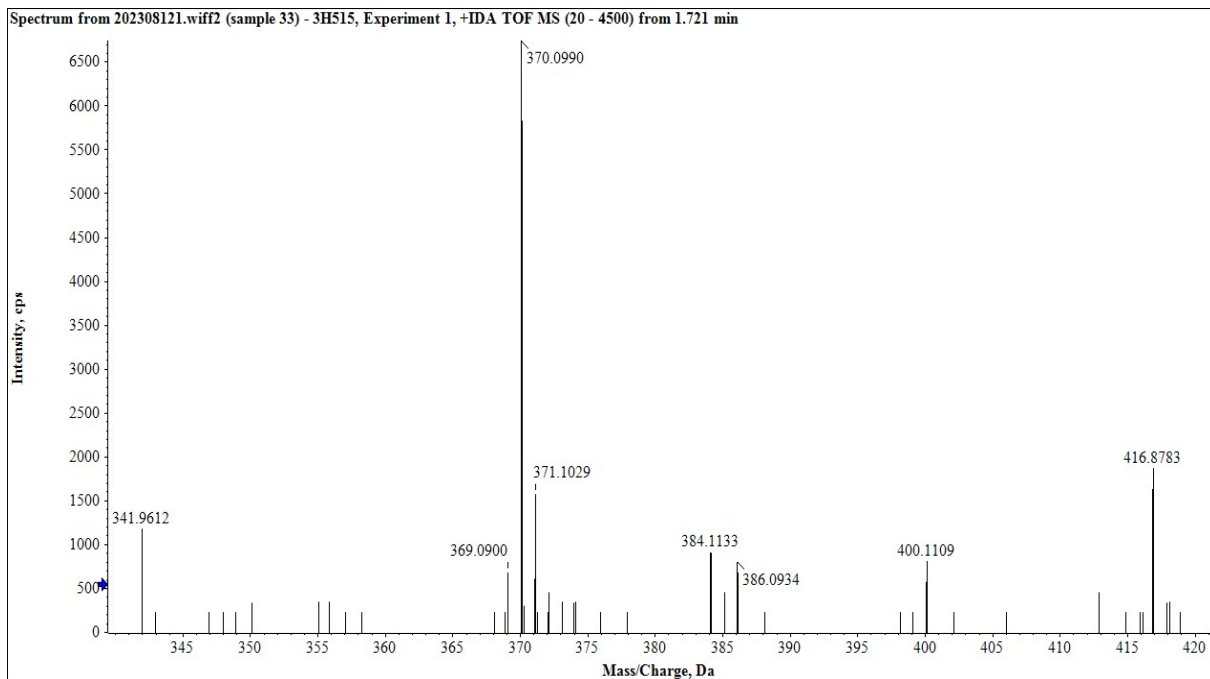




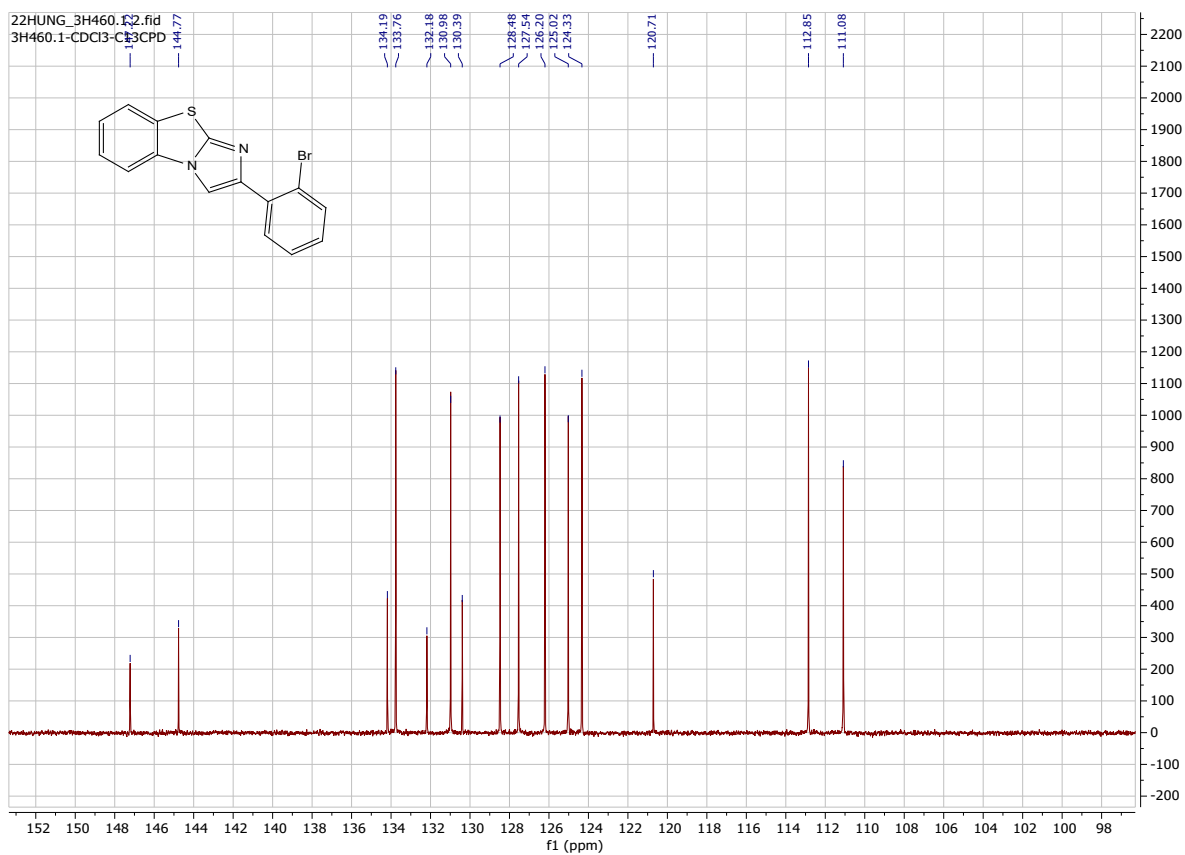
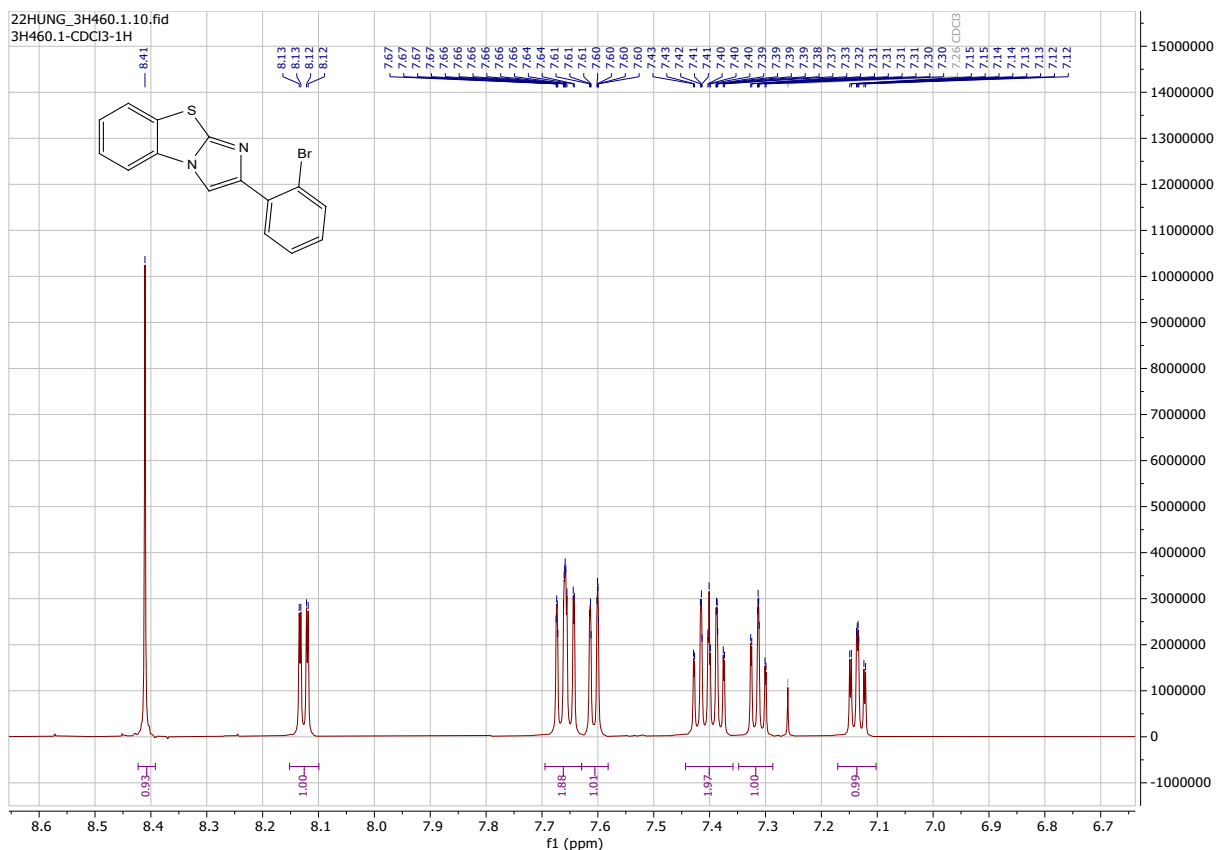
# 11-(4-methoxyphenyl)-11H-benzo[4',5']thiazolo[2',3':2,3]imidazo[4,5-b]indole

9q

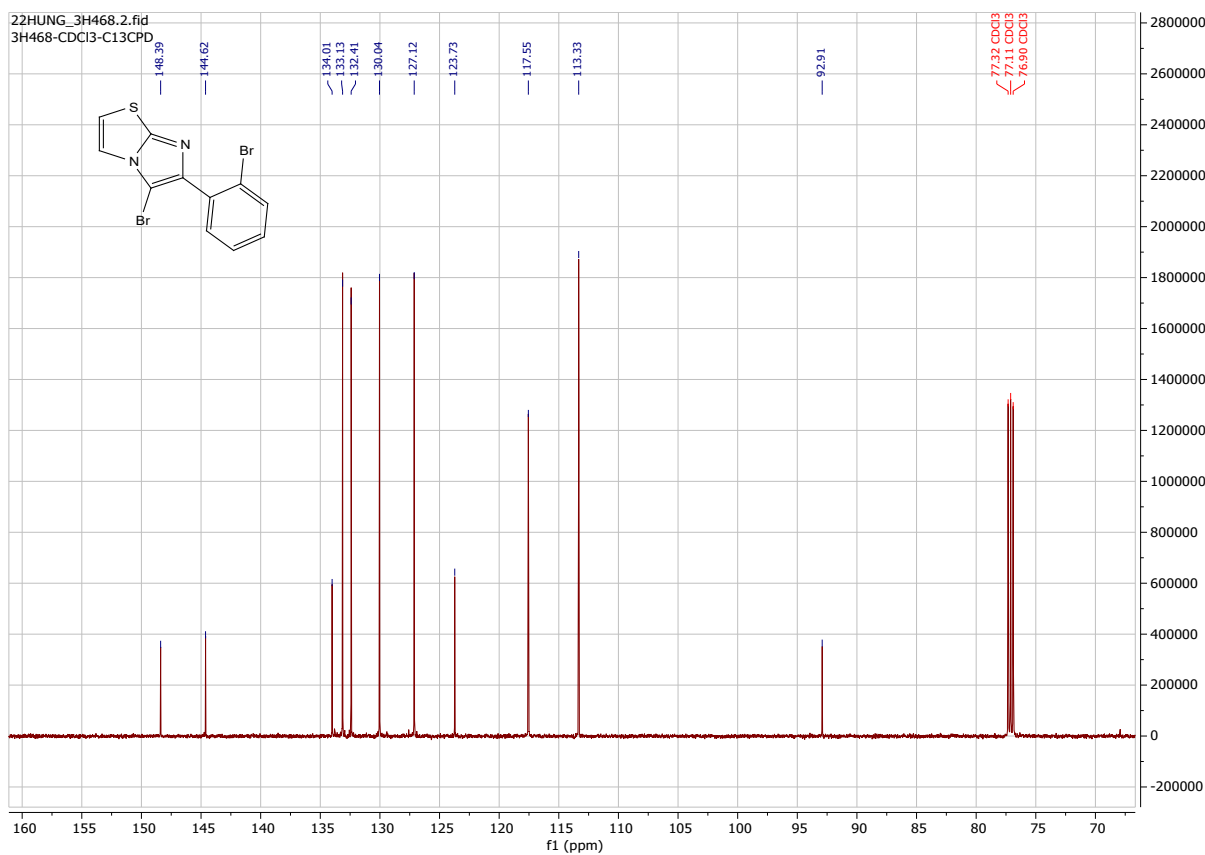
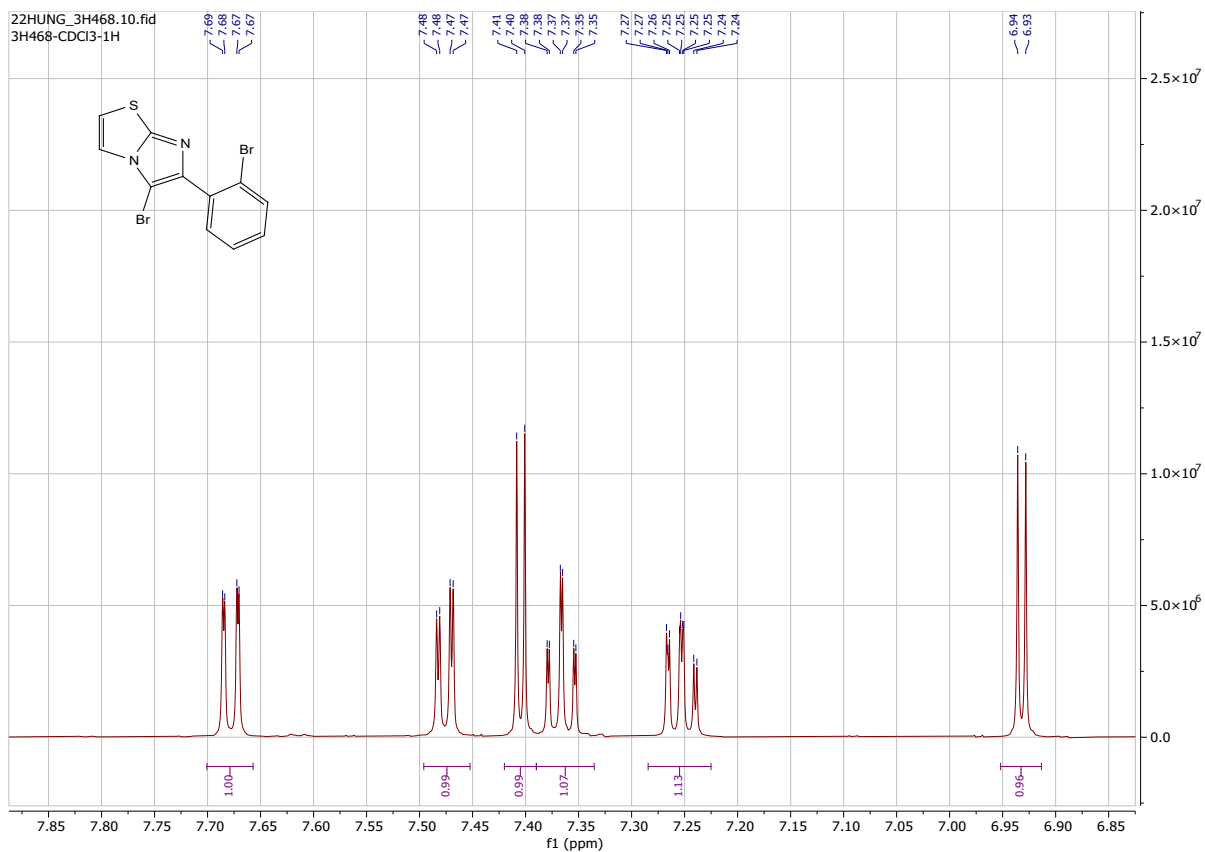




# 2-(2-bromophenyl)benzo[d]imidazo[2,1-b]thiazole 5

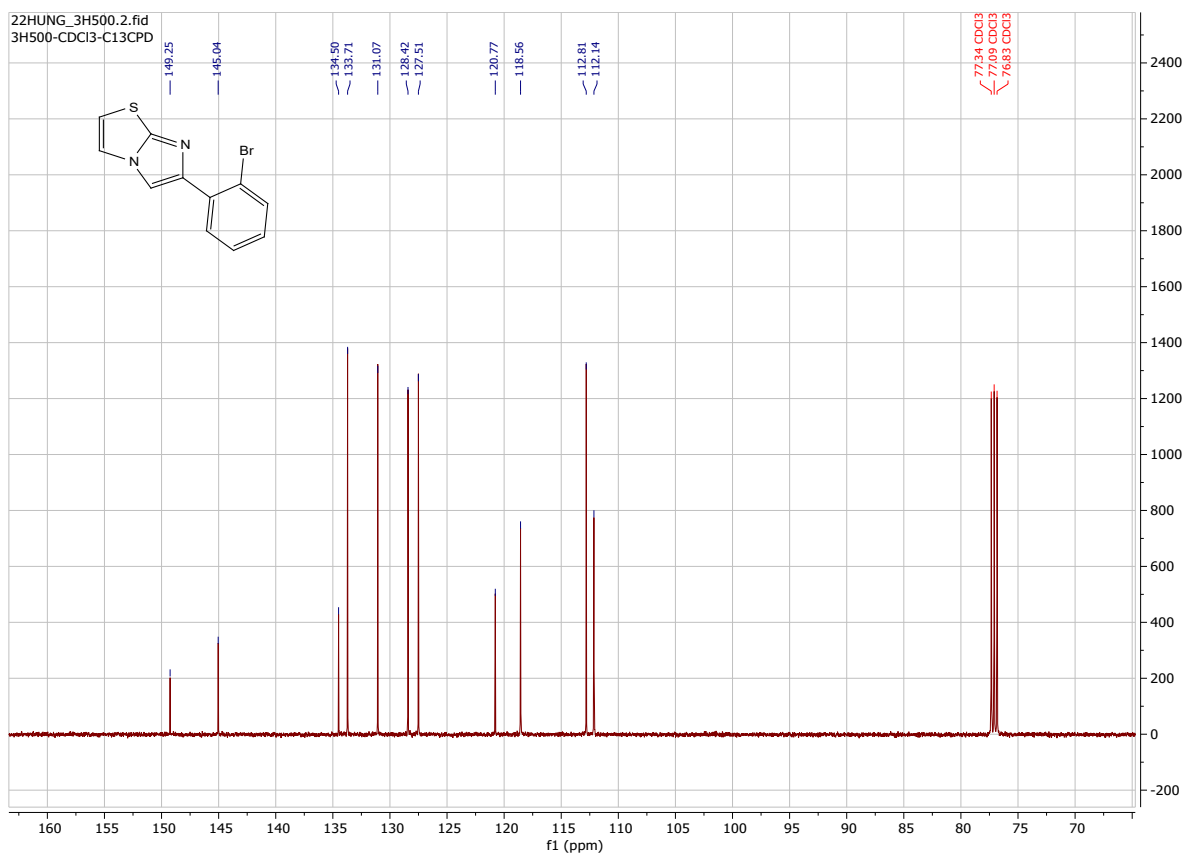
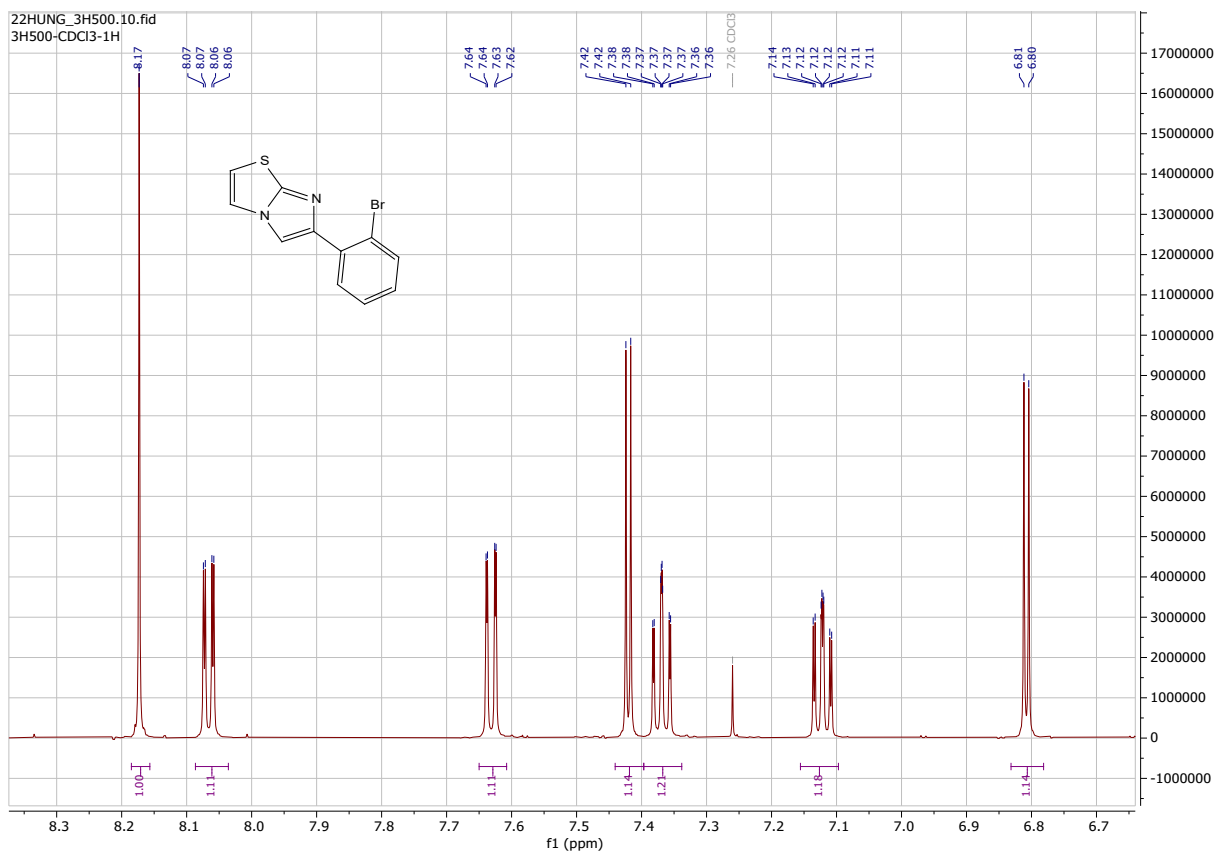


# 5-bromo-6-(2-bromophenyl)imidazo[2,1-b]thiazole 6





# 6-(2-bromophenyl)imidazo[2,1-b]thiazole 4



# 3-bromo-2-(2-bromophenyl)benzo[d]imidazo[2,1-b]thiazole 7

