

## Supporting Information

### **Divergent synthesis of pyrrolizine derivatives through C–H bond functionalization of pyrroles**

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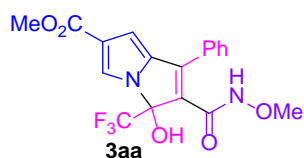
## I. General experimental information

Commercial reagents were used without further purification. *N*-Alkoxy carbamoyl pyrroles (**1**)<sup>[1]</sup>, trifluoromethyl ynones **2**<sup>[2]</sup> and [RhCp\*Cl<sub>2</sub>]<sub>2</sub><sup>[3]</sup> were prepared based on literature procedures. Melting points were recorded with a micro melting point apparatus and uncorrected. The <sup>1</sup>H NMR spectra were recorded at 400 MHz or 600 MHz. The <sup>13</sup>C NMR spectra were recorded at 100 MHz or 150 MHz. The <sup>19</sup>F NMR spectra were recorded at 376 MHz or 565 MHz. Chemical shifts were expressed in parts per million ( $\delta$ ), and were reported as s (singlet), d (doublet), t (triplet), dd (doublet of doublets), q (quartet), m (multiplet), etc. The coupling constants *J* were given in Hz. High resolution mass spectra (HRMS) were obtained *via* ESI-TOF mode. All reactions were monitored by thin layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm), and components were visualized by observation under UV light (254 and 365 nm).

## II. Experimental procedures and spectroscopic data

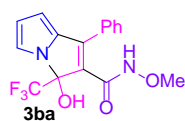
### 1. Typical procedure for the synthesis of 3aa and spectroscopic data of 3aa-3ta and 3ab-3at

To a reaction tube equipped with a stir bar were added with methyl 1-(methoxycarbonyl)-1*H*-pyrrole-3-carboxylate (**1a**, 39.6 mg, 0.2 mmol), KOAc (3.9 mg, 0.04 mmol), [RhCp\*Cl<sub>2</sub>]<sub>2</sub> (6.2 mg, 0.01 mmol), 1,1,1-trifluoro-4-phenylbut-3-yn-2-one (**2a**, 43.6 mg, 0.22 mmol) and CH<sub>3</sub>OH (2 mL). The tube was then sealed, and the mixture was stirred at room temperature under air for 3 h. Upon completion, it was quenched with saturated aqueous solution of NH<sub>4</sub>Cl, and then extracted with ethyl acetate (10 mL × 3). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate (2:1) as eluent to afford **3aa**. **3ba-3ta** and **3ab-3at** were obtained in a similar manner.



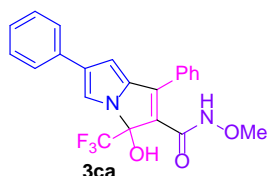
#### Methyl 3-hydroxy-2-(methoxycarbonyl)-1-phenyl-3-(trifluoromethyl)-3*H*-pyrrolizine-6-carboxylate (**3aa**)

Eluent: petroleum ether/ethyl acetate (2:1). White solid (62.3 mg, 79%), mp 183.0-183.9 °C. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ 11.32 (s, 1H), 9.13 (s, 1H), 7.76 (s, 1H), 7.68-7.67 (m, 2H), 7.55-7.54 (m, 3H), 6.71 (s, 1H), 3.76 (s, 3H), 3.57 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, DMSO-*d*<sub>6</sub>): δ 164.1, 159.1, 139.3, 136.8, 130.8, 130.3, 129.4, 128.5, 128.3, 123.9, 122.7 (q, <sup>1</sup>J<sub>C-F</sub> = 285.3 Hz), 121.2, 105.4, 90.4 (q, <sup>2</sup>J<sub>C-F</sub> = 33.2 Hz), 63.0, 51.6. <sup>19</sup>F NMR (376 MHz, DMSO-*d*<sub>6</sub>): δ -80.32 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>15</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>5</sub> 419.0825; Found 419.0823.



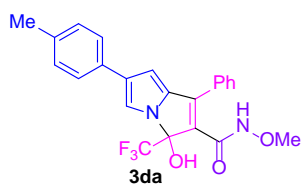
#### 3-Hydroxy-*N*-methoxy-1-phenyl-3-(trifluoromethyl)-3*H*-pyrrolizine-2-carboxamide (**3ba**)

Eluent: petroleum ether/ethyl acetate (2:1). White solid (56.7 mg, 84%), mp 151.4-152.0 °C.  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  11.06 (s, 1H), 8.62 (s, 1H), 7.64-7.63 (m, 2H), 7.53-7.50 (m, 3H), 7.16 (s, 1H), 6.30 (s, 2H), 3.54 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  159.7, 140.2, 136.1, 131.1, 130.4, 129.3, 128.5, 127.0, 123.1 (q,  $^1J_{\text{C-F}} = 285.5$  Hz), 119.6, 114.4, 105.5, 89.5 (q,  $^2J_{\text{C-F}} = 31.7$  Hz), 63.0.  $^{19}\text{F}$  NMR (565 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  -80.32 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{16}\text{H}_{13}\text{F}_3\text{N}_2\text{NaO}_3$  361.0770; Found 361.0768.



### 3-Hydroxy-*N*-methoxy-1,6-diphenyl-3-(trifluoromethyl)-3*H*-pyrrolizine-2-carboxamide (3ca)

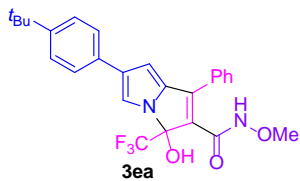
Eluent: petroleum ether/ethyl acetate (2:1). White solid (54.3 mg, 66%), mp 189.0-190.3 °C.  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  11.16 (s, 1H), 8.78 (s, 1H), 7.73-7.71 (m, 2H), 7.69 (s, 1H), 7.67 (d,  $J = 7.2$  Hz, 2H), 7.56-7.51 (m, 3H), 7.34 (t,  $J = 7.8$  Hz, 2H), 7.18 (t,  $J = 7.8$  Hz, 1H), 6.83 (s, 1H), 3.57 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  159.6, 140.0, 136.9, 135.1, 131.0, 130.5, 130.1, 129.3, 129.2, 128.6, 127.2, 126.5, 125.2, 123.1 (q,  $^1J_{\text{C-F}} = 284.4$  Hz), 116.3, 103.3, 90.0 (q,  $^2J_{\text{C-F}} = 33.9$  Hz), 63.0.  $^{19}\text{F}$  NMR (565 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  -80.10 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{22}\text{H}_{17}\text{F}_3\text{N}_2\text{NaO}_3$  437.1083; Found 437.1077.



### 3-Hydroxy-*N*-methoxy-1-phenyl-6-(*p*-tolyl)-3-(trifluoromethyl)-3*H*-pyrrolizine-2-carboxamide (3da)

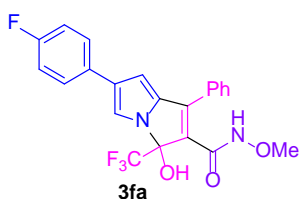
Eluent: petroleum ether/ethyl acetate (2:1). White solid (48.7 mg, 57%), mp 194.0-195.9 °C.  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  11.14 (br s, 1H), 8.73 (br s, 1H), 7.71 (dd,  $J_1 = 7.8$  Hz,  $J_2 = 1.8$  Hz, 2H), 7.62 (s, 1H), 7.56-7.51 (m, 5H), 7.14 (d,  $J = 7.8$  Hz, 2H), 6.78 (s, 1H), 3.56 (s, 3H), 2.28 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  159.6, 140.0, 136.8, 135.5, 132.2, 131.0, 130.5, 130.1, 129.7, 129.3, 128.6, 127.1, 125.1, 123.0 (q,  $^1J_{\text{C-F}} = 285.5$  Hz), 115.9, 103.2, 90.0 (q,  $^2J_{\text{C-F}} = 32.9$  Hz), 63.0, 21.1.  $^{19}\text{F}$  NMR (565 MHz,  $\text{DMSO-}d_6$ ):  $\delta$

-80.10 (s). HRMS (ESI) m/z:  $[M+Na]^+$  Calcd for  $C_{23}H_{19}F_3N_2NaO_3$  451.1240; Found 451.1231.



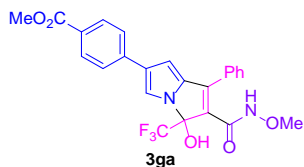
**6-(4-(*tert*-Butyl)phenyl)-3-hydroxy-*N*-methoxy-1-phenyl-3-(trifluoromethyl)-3*H*-pyrrolizine-2-carboxamide (3ea)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (69.2 mg, 74%), mp 210.2-211.2 °C.  $^1H$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  11.12 (s, 1H), 8.74 (s, 1H), 7.70 (dd,  $J_1 = 7.8$  Hz,  $J_2 = 1.2$  Hz, 2H), 7.62 (s, 1H), 7.58-7.52 (m, 5H), 7.35 (d,  $J = 8.4$  Hz, 2H), 6.76 (s, 1H), 3.56 (s, 3H), 1.28 (s, 9H).  $^{13}C\{^1H\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  159.6, 148.8, 140.1, 136.8, 132.2, 131.0, 130.5, 130.0, 129.3, 128.6, 127.2, 125.9, 125.0, 123.0 (q,  $^1J_{C-F} = 285.6$  Hz), 116.0, 103.2, 90.0 (q,  $^2J_{C-F} = 32.9$  Hz), 63.0, 34.6, 31.6.  $^{19}F$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -80.11 (s). HRMS (ESI) m/z:  $[M+Na]^+$  Calcd for  $C_{26}H_{25}F_3N_2NaO_3$  493.1709; Found 493.1704.



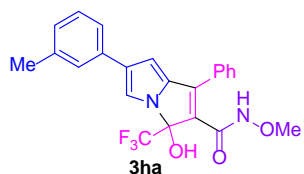
**6-(4-Fluorophenyl)-3-hydroxy-*N*-methoxy-1-phenyl-3-(trifluoromethyl)-3*H*-pyrrolizine-2-carboxamide (3fa)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (55.7 mg, 64%), mp 176.0-177.3 °C.  $^1H$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  11.16 (br s, 1H), 8.78 (br s, 1H), 7.73-7.71 (m, 4H), 7.69 (s, 1H), 7.56-7.52 (m, 3H), 7.16 (t,  $J = 9.0$  Hz, 2H), 6.82 (s, 1H), 3.57 (s, 3H).  $^{13}C\{^1H\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  161.2 (d,  $^1J_{C-F} = 240.6$  Hz), 159.6, 140.0, 136.9, 131.6 (d,  $^4J_{C-F} = 2.3$  Hz), 130.9, 130.5, 129.3, 129.1, 128.6, 127.3, 127.0 (d,  $^3J_{C-F} = 7.7$  Hz), 123.0 (q,  $^1J_{C-F} = 285.5$  Hz), 116.3, 115.9 (d,  $^2J_{C-F} = 20.9$  Hz), 103.4, 90.0 (q,  $^2J_{C-F} = 32.9$  Hz), 63.0.  $^{19}F$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -80.11 (s), -116.885 – -116.892 (m). HRMS (ESI) m/z:  $[M+Na]^+$  Calcd for  $C_{22}H_{16}F_4N_2NaO_3$  455.0989; Found 455.0991.



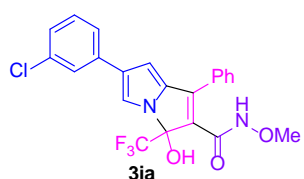
**Methyl 4-(3-hydroxy-2-(methoxycarbonyl)-1-phenyl-3-(trifluoromethyl)-3H-pyrrolizin-6-yl)benzoate (3ga)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (78.5 mg, 83%), mp 184.9-186.3 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.22 (br s, 1H), 8.88 (br s, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.90 (s, 1H), 7.86 (d, *J* = 8.4 Hz, 2H), 7.74-7.73 (m, 2H), 7.58-7.53 (m, 3H), 6.96 (s, 1H), 3.85 (s, 3H), 3.58 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 166.6, 159.5, 140.0, 139.8, 137.3, 130.8, 130.6, 130.2, 129.3, 128.9, 128.6, 127.5, 127.2, 125.1, 123.0 (q, <sup>1</sup>*J*<sub>C-F</sub> = 284.4 Hz), 117.8, 103.5, 90.2 (q, <sup>2</sup>*J*<sub>C-F</sub> = 32.9 Hz), 63.0, 52.4. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.11 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>24</sub>H<sub>19</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>5</sub> 495.1138; Found 495.1131.



**3-Hydroxy-*N*-methoxy-1-phenyl-6-(*m*-tolyl)-3-(trifluoromethyl)-3H-pyrrolizine-2-carboxamide (3ha)**

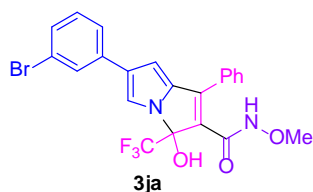
Eluent: petroleum ether/ethyl acetate (2:1). White solid (63.9 mg, 75%), mp 177.8-179.4 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.14 (s, 1H), 8.74 (s, 1H), 7.72-7.70 (m, 2H), 7.65 (s, 1H), 7.56-7.52 (m, 3H), 7.51 (s, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 1H), 7.00 (d, *J* = 7.8 Hz, 1H), 6.81 (s, 1H), 3.56 (s, 3H), 2.32 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 159.6, 140.0, 138.2, 136.8, 134.9, 131.0, 130.5, 130.1, 129.3, 129.0, 128.6, 127.2, 127.1, 125.9, 123.0 (q, <sup>1</sup>*J*<sub>C-F</sub> = 285.6 Hz), 122.3, 116.2, 103.3, 90.0 (q, <sup>2</sup>*J*<sub>C-F</sub> = 32.9 Hz), 63.0, 21.5. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.11 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>23</sub>H<sub>19</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub> 451.1240; Found 451.1242.



**6-(3-Chlorophenyl)-3-hydroxy-*N*-methoxy-1-phenyl-3-(trifluoromethyl)-3*H*-pyrrolizine-2-carboxamide**

**(3ia)**

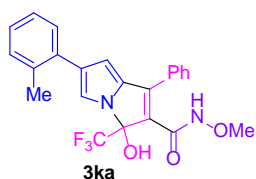
Eluent: petroleum ether/ethyl acetate (2:1). White solid (67.3 mg, 75%), mp 190.1-191.3 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.18 (s, 1H), 8.80 (s, 1H), 7.84 (s, 1H), 7.80 (t, *J* = 1.8 Hz, 1H), 7.73-7.71 (m, 2H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.56-7.52 (m, 3H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.22 (dd, *J*<sub>1</sub> = 7.8 Hz, *J*<sub>2</sub> = 1.2 Hz, 1H), 6.93 (s, 1H), 3.57 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 159.6, 139.8, 137.4, 137.0, 134.2, 130.9, 130.8, 130.6, 129.3, 128.64, 128.56, 127.4, 126.1, 124.8, 123.7, 123.0 (q, <sup>1</sup>*J*<sub>C-F</sub> = 284.4 Hz), 117.3, 103.5, 90.1 (q, <sup>2</sup>*J*<sub>C-F</sub> = 32.7 Hz), 63.0. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.09 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>16</sub>ClF<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub> 471.0694; Found 471.0689.



**6-(3-Bromophenyl)-3-hydroxy-*N*-methoxy-1-phenyl-3-(trifluoromethyl)-3*H*-pyrrolizine-2-carboxamide**

**(3ja)**

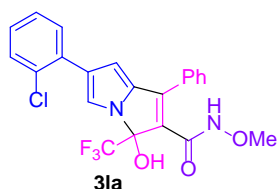
Eluent: petroleum ether/ethyl acetate (2:1). White solid (81.8 mg, 83%), mp 197.9-198.9 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.18 (s, 1H), 8.80 (s, 1H), 7.94 (s, 1H), 7.84 (s, 1H), 7.73-7.70 (m, 3H), 7.57-7.52 (m, 3H), 7.36-7.35 (m, 1H), 7.29 (t, *J* = 7.8 Hz, 1H), 6.94 (s, 1H), 3.57 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 159.6, 139.8, 137.6, 137.0, 131.2, 130.8, 130.6, 129.3, 129.0, 128.7, 128.5, 127.7, 127.4, 124.1, 123.0 (q, <sup>1</sup>*J*<sub>C-F</sub> = 284.4 Hz), 122.9, 117.3, 103.5, 90.1 (q, <sup>2</sup>*J*<sub>C-F</sub> = 32.9 Hz), 63.0. <sup>19</sup>F NMR (375 MHz, DMSO-*d*<sub>6</sub>): δ -80.15 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>16</sub>BrF<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub> 515.0189; Found 515.0190.





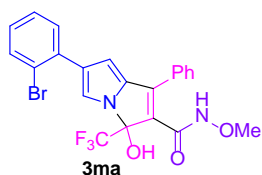
### 3-Hydroxy-*N*-methoxy-1-phenyl-6-(*o*-tolyl)-3-(trifluoromethyl)-3*H*-pyrrolizine-2-carboxamide (3ka)

Eluent: petroleum ether/ethyl acetate (2:1). White solid (65.4 mg, 76%), mp 184.3-186.3 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.12 (s, 1H), 8.77 (s, 1H), 7.71 (dd, *J*<sub>1</sub> = 7.8 Hz, *J*<sub>2</sub> = 1.8 Hz, 2H), 7.55-7.50 (m, 3H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.33 (s, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 6.6 Hz, 1H), 7.16 (td, *J*<sub>1</sub> = 7.2 Hz, *J*<sub>2</sub> = 1.2 Hz, 1H), 6.58 (s, 1H), 3.57 (s, 3H), 2.41 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 159.6, 140.2, 136.1, 135.0, 134.9, 131.1, 131.0, 130.5, 129.4, 129.33, 129.27, 128.6, 127.2, 126.8, 126.5, 123.1 (q, <sup>1</sup>*J*<sub>C-F</sub> = 284.3 Hz), 118.1, 106.1, 90.0 (q, <sup>2</sup>*J*<sub>C-F</sub> = 32.9 Hz), 63.1, 21.6. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.13 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>23</sub>H<sub>19</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub> 451.1240; Found 451.1237.



### 6-(2-Chlorophenyl)-3-hydroxy-*N*-methoxy-1-phenyl-3-(trifluoromethyl)-3*H*-pyrrolizine-2-carboxamide (3la)

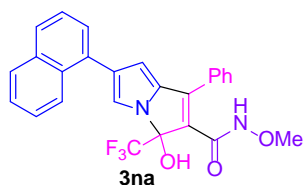
Eluent: petroleum ether/ethyl acetate (2:1). White solid (69.6 mg, 78%), mp 180.8-182.6 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.17 (s, 1H), 8.88 (s, 1H), 7.71 (d, *J* = 6.0 Hz, 2H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.63 (s, 1H), 7.56-7.53 (m, 3H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.26 (t, *J* = 7.2 Hz, 1H), 6.76 (s, 1H), 3.58 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 159.5, 140.0, 136.1, 133.5, 130.90, 130.88, 130.81, 130.77, 130.6, 129.4, 128.6, 128.3, 128.0, 127.4, 126.7, 123.0 (q, <sup>1</sup>*J*<sub>C-F</sub> = 285.5 Hz), 118.9, 105.9, 90.2 (q, <sup>2</sup>*J*<sub>C-F</sub> = 32.9 Hz), 63.1. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.13 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>16</sub>ClF<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub> 471.0694; Found 471.0693.



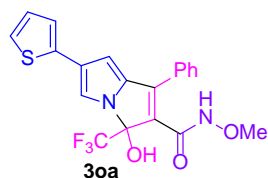
### 6-(2-Bromophenyl)-3-hydroxy-*N*-methoxy-1-phenyl-3-(trifluoromethyl)-3*H*-pyrrolizine-2-carboxamide

**(3ma)**

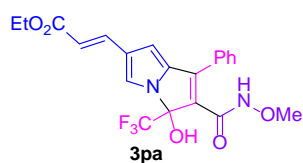
Eluent: petroleum ether/ethyl acetate (2:1). White solid (76.1 mg, 77%), mp 180.1-181.2 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.15 (s, 1H), 8.87 (s, 1H), 7.71-7.68 (m, 3H), 7.58-7.51 (m, 5H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 6.70 (s, 1H), 3.58 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 159.5, 140.0, 135.9, 135.7, 134.0, 131.4, 130.9, 130.6, 129.4, 128.7, 128.6, 128.4, 128.3, 127.4, 123.0 (q, <sup>1</sup>*J*<sub>C-F</sub> = 285.5 Hz), 121.5, 118.8, 106.2, 90.2 (q, <sup>2</sup>*J*<sub>C-F</sub> = 32.7 Hz), 63.1. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.13 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>16</sub>BrF<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub> 515.0189; Found 515.0191.

**3-Hydroxy-N-methoxy-6-(naphthalen-1-yl)-1-phenyl-3-(trifluoromethyl)-3H-pyrrolizine-2-carboxamide****(3na)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (66.3 mg, 71%), mp 178.6-178.8 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.22 (s, 1H), 8.85 (s, 1H), 8.23 (s, 1H), 7.92-7.87 (m, 5H), 7.78 (d, *J* = 6.6 Hz, 2H), 7.60-7.55 (m, 3H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.02 (s, 1H), 3.60 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 159.6, 140.0, 137.2, 134.1, 132.6, 132.2, 131.0, 130.6, 130.0, 129.4, 128.7, 128.6, 128.04, 128.01, 127.4, 126.7, 125.7, 124.5, 123.1 (q, <sup>1</sup>*J*<sub>C-F</sub> = 284.4 Hz), 122.7, 116.9, 103.5, 90.1 (q, <sup>2</sup>*J*<sub>C-F</sub> = 31.7 Hz), 63.1. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.03 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>26</sub>H<sub>19</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub> 487.1240; Found 487.1244.

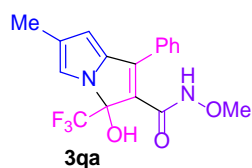
**3-Hydroxy-N-methoxy-1-phenyl-6-(thiophen-2-yl)-3-(trifluoromethyl)-3H-pyrrolizine-2-carboxamide****(3oa)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (50.5 mg, 60%), mp 197.4-198.3 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.19 (br s, 1H), 8.83 (br s, 1H), 7.68 (d, *J* = 6.6 Hz, 2H), 7.55-7.52 (m, 3H), 7.50 (s, 1H), 7.33 (d, *J* = 5.4 Hz, 1H), 7.29 (d, *J* = 3.6 Hz, 1H), 7.04-7.03 (m, 1H), 6.63 (s, 1H), 3.56 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 159.5, 139.8, 138.1, 136.9, 130.8, 130.6, 129.4, 128.5, 128.3, 127.6, 124.3, 123.4, 123.0 (q, <sup>1</sup>*J*<sub>C-F</sub> = 285.5 Hz), 122.7, 115.7, 103.5, 90.1 (q, <sup>2</sup>*J*<sub>C-F</sub> = 32.9 Hz), 63.0. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.14 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>15</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>3</sub>S 443.0648; Found 443.0645.



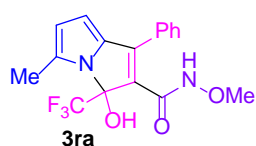
**Ethyl 3-(3-hydroxy-2-(methoxycarbonyl)-1-phenyl-3-(trifluoromethyl)-3H-pyrrolizin-6-yl)acrylate (3pa)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (74.0 mg, 85%), mp 86.0-86.8 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.22 (br s, 0.5H), 11.04 (br s, 1H), 8.90 (br s, 1.5H), 7.71 (s, 0.5H), 7.68-7.66 (m, 1H), 7.60 (d, *J* = 15.6 Hz, 1H), 7.55-7.49 (m, 6H), 7.25-7.23 (m, 2H), 6.87 (s, 0.5H), 6.77 (d, *J* = 3.0 Hz, 1H), 6.33 (d, *J* = 15.6 Hz, 0.5H), 6.22 (d, *J* = 16.2 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 1H), 4.05-4.01 (qd, dd, *J*<sub>1</sub> = 7.2 Hz, *J*<sub>2</sub> = 1.8 Hz, 2H), 3.56 (s, 1.5H), 3.43 (s, 3H), 1.23 (t, *J* = 7.2 Hz, 1.5H), 1.16 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 167.2, 166.7, 159.3, 158.5, 141.4, 139.4, 138.9, 137.6, 137.0, 135.7, 131.0, 130.7, 130.62, 130.60, 130.3, 129.3, 129.1, 128.9, 128.5, 128.0, 126.3, 123.3, 122.83 (q, <sup>1</sup>*J*<sub>C-F</sub> = 284.4 Hz), 122.81 (q, <sup>1</sup>*J*<sub>C-F</sub> = 285.5 Hz), 121.2, 116.7, 116.5, 114.7, 112.5, 103.6, 90.0 (q, <sup>2</sup>*J*<sub>C-F</sub> = 33.9 Hz), 89.7 (q, <sup>2</sup>*J*<sub>C-F</sub> = 33.9 Hz), 63.1, 63.0, 60.1, 60.0, 14.7, 14.5. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.14 (s), -80.21 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>19</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>5</sub> 459.1138; Found 459.1138.



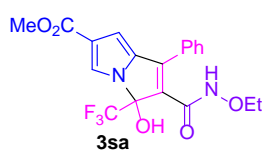
**3-Hydroxy-*N*-methoxy-6-methyl-1-phenyl-3-(trifluoromethyl)-3H-pyrrolizine-2-carboxamide (3qa)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (45.4 mg, 64%), mp 111.2-112.8 °C.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  11.03 (br s, 1H), 8.50 (br s, 1H), 7.62-7.61 (m, 2H), 7.50-7.49 (m, 3H), 6.93 (s, 1H), 6.15 (s, 1H), 3.54 (s, 3H), 2.06 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  159.8, 140.3, 136.0, 131.2, 130.4, 129.2, 128.5, 126.6, 124.4, 123.1 (q,  $^1J_{\text{C-F}} = 285.3$  Hz), 117.3, 107.0, 89.5 (q,  $^2J_{\text{C-F}} = 31.8$  Hz), 63.0, 12.6.  $^{19}\text{F}$  NMR (376 MHz, DMSO- $d_6$ ):  $\delta$  -80.38 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{17}\text{H}_{15}\text{F}_3\text{N}_2\text{NaO}_3$  375.0927; Found 375.0924.



### 3-Hydroxy-*N*-methoxy-5-methyl-1-phenyl-3-(trifluoromethyl)-3*H*-pyrrolizine-2-carboxamide (3ra)

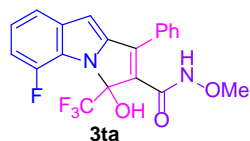
Eluent: petroleum ether/ethyl acetate (2:1). White solid (41.8 mg, 59%), mp 174.3-175.3 °C.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  10.96 (s, 1H), 8.51 (s, 1H), 7.59-7.57 (m, 2H), 7.49-7.48 (m, 3H), 6.13 (d,  $J = 3.0$  Hz, 1H), 5.98 (d,  $J = 2.4$  Hz, 1H), 3.53 (s, 3H), 2.33 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  159.8, 140.5, 135.8, 132.1, 131.3, 130.3, 129.2, 128.4, 125.7, 123.8 (q,  $^1J_{\text{C-F}} = 285.5$  Hz), 113.3, 105.5, 90.9 (q,  $^2J_{\text{C-F}} = 31.8$  Hz), 63.0, 12.6.  $^{19}\text{F}$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -76.88 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{17}\text{H}_{15}\text{F}_3\text{N}_2\text{NaO}_3$  375.0927; Found 375.0932.



### Methyl 2-(ethoxycarbonyl)-3-hydroxy-1-phenyl-3-(trifluoromethyl)-3*H*-pyrrolizine-6-carboxylate (3sa)

Eluent: petroleum ether/ethyl acetate (2:1). White solid (65.1 mg, 79%), mp 158.8-160.1 °C.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  11.19 (s, 1H), 9.08 (s, 1H), 7.73 (s, 1H), 7.67-7.66 (m, 2H), 7.54-7.53 (m, 3H), 6.68 (s, 1H), 3.79-3.76 (m, 2H), 3.75 (s, 3H), 1.08 (t,  $J = 6.6$  Hz, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  164.0, 159.3, 139.1, 136.9, 130.8, 130.4, 129.5, 128.4, 123.8, 122.7 (q,  $^1J_{\text{C-F}} = 285.5$  Hz), 121.1, 105.3, 90.4 (q,  $^2J_{\text{C-F}}$

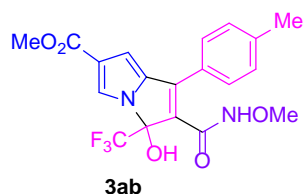
= 32.9 Hz), 70.7, 51.7, 13.8.  $^{19}\text{F}$  NMR (565 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  -80.29 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{19}\text{H}_{17}\text{F}_3\text{N}_2\text{NaO}_5$  433.0982; Found 433.0983.



### 5-Fluoro-3-hydroxy-*N*-methoxy-1-phenyl-3-(trifluoromethyl)-3*H*-pyrrolo[1,2-*a*]indole-2-carboxamide

(3ta)

Eluent: petroleum ether/ethyl acetate (3:1). White solid (32.2 mg, 40%), mp 178.9-179.4 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  12.26 (s, 1H), 10.99 (s, 1H), 7.69-7.66 (m, 2H), 7.56-7.52 (m, 3H), 7.34 (d,  $J = 8.0$  Hz, 1H), 7.26 (s, 1H), 7.09 (td,  $J_1 = 7.6$  Hz,  $J_2 = 4.8$  Hz, 1H), 6.98 (dd,  $J_1 = 11.6$  Hz,  $J_2 = 8.0$  Hz, 1H), 3.56 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  161.0, 150.1 (d,  $^1J_{\text{C-F}} = 242.9$  Hz), 146.0, 140.9, 137.1, 130.9, 130.2, 129.1, 128.8, 128.6 (d,  $^2J_{\text{C-F}} = 13.2$  Hz), 126.6 (d,  $^3J_{\text{C-F}} = 5.4$  Hz), 125.6 (q,  $^1J_{\text{C-F}} = 285.6$  Hz), 121.6 (d,  $^3J_{\text{C-F}} = 6.6$  Hz), 119.0, 115.4, 107.1 (d,  $^2J_{\text{C-F}} = 16.4$  Hz), 80.0 (q,  $^2J_{\text{C-F}} = 30.6$  Hz), 63.1.  $^{19}\text{F}$  NMR (376 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  -75.46 (s), -130.51 (dd,  $J_1 = 10.90$  Hz,  $J_2 = 4.14$  Hz). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{20}\text{H}_{14}\text{F}_4\text{N}_2\text{NaO}_3$  429.0833; Found 429.0829.

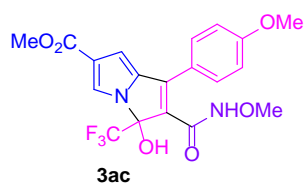


### Methyl 3-hydroxy-2-(methoxycarbonyl)-1-(*p*-tolyl)-3-(trifluoromethyl)-3*H*-pyrrolizine-6-carboxylate

(3ab)

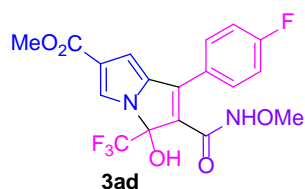
Eluent: petroleum ether/ethyl acetate (2:1). White solid (58.8 mg, 72%), mp 156.2-157.7 °C.  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  11.27 (s, 1H), 9.05 (s, 1H), 7.73 (s, 1H), 7.58 (d,  $J = 8.4$  Hz, 2H), 7.35 (d,  $J = 7.8$  Hz, 2H), 6.69 (s, 1H), 3.75 (s, 3H), 3.57 (s, 3H), 2.38 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  164.1, 159.3, 140.7, 139.1, 136.9, 130.0, 128.4, 127.6, 127.4, 123.7, 122.8 (q,  $^1J_{\text{C-F}} = 284.4$  Hz), 121.1, 105.4, 90.3 (q,  $^2J_{\text{C-F}}$

= 32.7 Hz), 63.1, 51.6, 21.4.  $^{19}\text{F}$  NMR (565 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  -80.29 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{19}\text{H}_{17}\text{F}_3\text{N}_2\text{NaO}_5$  433.0982; Found 433.0984.



**Methyl 3-hydroxy-2-(methoxycarbonyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3ac)**

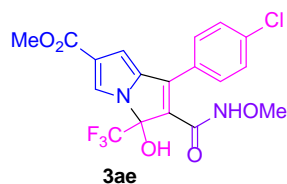
Eluent: petroleum ether/ethyl acetate (2:1). White solid (57.7 mg, 68%), mp 185.6-186.9 °C.  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  11.26 (s, 1H), 9.01 (s, 1H), 7.72 (s, 1H), 7.64 (d,  $J = 9.0$  Hz, 2H), 7.09 (d,  $J = 9.0$  Hz, 2H), 6.70 (s, 1H), 3.83 (s, 3H), 3.76 (s, 3H), 3.59 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  164.1, 161.3, 159.4, 138.8, 137.0, 130.2, 126.5, 123.6, 122.8 (q,  $^1J_{\text{C-F}} = 285.5$  Hz), 122.5, 121.1, 114.9, 105.4, 90.3 (q,  $^2J_{\text{C-F}} = 32.9$  Hz), 63.1, 55.8, 51.6.  $^{19}\text{F}$  NMR (565 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  -80.28 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{19}\text{H}_{17}\text{F}_3\text{N}_2\text{NaO}_6$  449.0931; Found 449.0936.



**Methyl 1-(4-fluorophenyl)-3-hydroxy-2-(methoxycarbonyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3ad)**

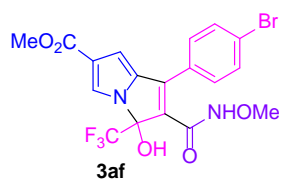
Eluent: petroleum ether/ethyl acetate (2:1). White solid (62.4 mg, 75%), mp 176.3-178.0 °C.  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  11.32 (br s, 1H), 9.13 (br s, 1H), 7.75 (s, 1H), 7.74-7.71 (m, 2H), 7.39 (t,  $J = 9.0$  Hz, 2H), 6.72 (s, 1H), 3.76 (s, 3H), 3.57 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  164.0, 163.5 (d,  $^1J_{\text{C-F}} = 247.2$  Hz), 159.0, 138.3, 136.7, 130.9 (d,  $^3J_{\text{C-F}} = 8.9$  Hz), 128.2, 126.7 (d,  $^4J_{\text{C-F}} = 2.3$  Hz), 123.9, 122.7 (q,  $^1J_{\text{C-F}} = 284.4$  Hz), 121.2, 116.5 (d,  $^2J_{\text{C-F}} = 21.9$  Hz), 105.5, 90.3 (q,  $^2J_{\text{C-F}} = 32.9$  Hz), 63.1, 51.7.  $^{19}\text{F}$  NMR (565 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  -80.31 (s), -109.95 – -110.00 (m). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{18}\text{H}_{14}\text{F}_4\text{N}_2\text{NaO}_5$

437.0731; Found 437.0730.



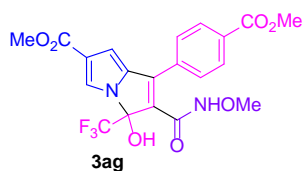
**Methyl 1-(4-chlorophenyl)-3-hydroxy-2-(methoxycarbonyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3ae)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (66.8 mg, 78%), mp 72.6-73.1 °C. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ 11.34 (br s, 1H), 9.16 (br s, 1H), 7.75 (s, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 6.72 (s, 1H), 3.76 (s, 3H), 3.57 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 164.0, 158.9, 138.2, 136.4, 135.5, 130.3, 129.6, 129.1, 128.7, 124.0, 122.7 (q, <sup>1</sup>*J*<sub>C-F</sub> = 285.5 Hz), 121.2, 105.5, 90.4 (q, <sup>2</sup>*J*<sub>C-F</sub> = 33.9 Hz), 63.1, 51.7. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.28 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>14</sub>ClF<sub>3</sub>N<sub>2</sub>NaO<sub>5</sub> 453.0436; Found 453.0440.



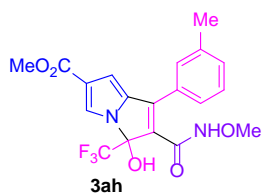
**Methyl 1-(4-bromophenyl)-3-hydroxy-2-(methoxycarbonyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3af)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (59.3 mg, 63%), mp 185.1-186.5 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.33 (br s, 1H), 9.16 (br s, 1H), 7.76-7.74 (m, 3H), 7.60 (d, *J* = 8.4 Hz, 2H), 6.71 (s, 1H), 3.75 (s, 3H), 3.57 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 164.0, 158.9, 138.3, 136.4, 132.5, 130.5, 129.4, 128.7, 124.2, 124.0, 122.7 (q, <sup>1</sup>*J*<sub>C-F</sub> = 284.4 Hz), 121.2, 105.5, 90.4 (q, <sup>2</sup>*J*<sub>C-F</sub> = 32.9 Hz), 63.1, 51.7. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.27 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>14</sub>BrF<sub>3</sub>N<sub>2</sub>NaO<sub>5</sub> 496.9930; Found 496.9922.



**Methyl 3-hydroxy-2-(methoxycarbonyl)-1-(4-(methoxycarbonyl)phenyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3ag)**

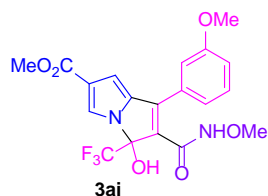
Eluent: petroleum ether/ethyl acetate (2:1). White solid (64.9 mg, 71%), mp 185.1-186.5 °C.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  11.37 (br s, 1H), 9.21 (br s, 1H), 8.11 (d,  $J = 8.4$  Hz, 2H), 7.80 (d,  $J = 8.4$  Hz, 2H), 7.77 (s, 1H), 6.74 (s, 1H), 3.90 (s, 3H), 3.76 (s, 3H), 3.56 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  166.1, 164.0, 158.7, 138.4, 136.3, 134.7, 131.4, 130.2, 129.8, 128.9, 124.1, 122.6 (q,  $^1J_{\text{C-F}} = 284.4$  Hz), 121.3, 105.6, 90.4 (q,  $^2J_{\text{C-F}} = 32.9$  Hz), 63.1, 52.8, 51.7.  $^{19}\text{F}$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -80.28 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{20}\text{H}_{17}\text{F}_3\text{N}_2\text{NaO}_7$  477.0880; Found 477.0871.



**Methyl 3-hydroxy-2-(methoxycarbonyl)-1-(*m*-tolyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3ah)**

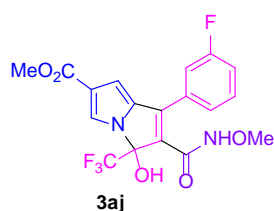
Eluent: petroleum ether/ethyl acetate (2:1). White solid (43.9 mg, 54%), mp 192.6-193.6 °C.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  11.27 (br s, 1H), 9.07 (br s, 1H), 7.73 (s, 1H), 7.46-7.40 (m, 3H), 7.34 (d,  $J = 7.2$  Hz, 1H), 6.68 (s, 1H), 3.75 (s, 3H), 3.55 (s, 3H), 2.38 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  164.1, 159.1, 139.3, 138.7, 136.9, 131.5, 130.3, 129.4, 128.8, 128.2, 125.6, 123.8, 122.7 (q,  $^1J_{\text{C-F}} = 284.4$  Hz), 121.1, 105.4, 90.3 (q,  $^2J_{\text{C-F}} = 33.9$  Hz), 63.0, 51.7, 21.4.  $^{19}\text{F}$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -80.31 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{19}\text{H}_{17}\text{F}_3\text{N}_2\text{NaO}_5$  433.0982; Found 433.0985.





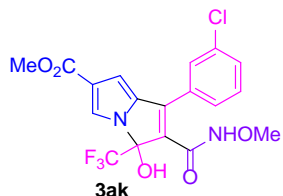
**Methyl 3-hydroxy-2-(methoxycarbamoyl)-1-(3-methoxyphenyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3ai)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (51.2 mg, 60%), mp 187.8-188.4 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.32 (br s, 1H), 9.11 (br s, 1H), 7.74 (s, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 7.8 Hz, 1H), 7.14 (s, 1H), 7.13-7.11 (m, 1H), 6.67 (s, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 3.57 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 164.0, 159.8, 159.1, 139.1, 136.8, 131.5, 130.7, 128.6, 123.9, 122.7 (q, <sup>1</sup>*J*<sub>C-F</sub> = 285.5 Hz), 121.2, 120.8, 116.4, 113.6, 105.3, 90.3 (q, <sup>2</sup>*J*<sub>C-F</sub> = 33.9 Hz), 63.1, 55.7, 51.7. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.30 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>17</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>6</sub> 449.0931; Found 449.0932.



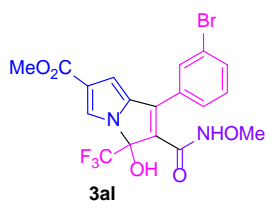
**Methyl 1-(3-fluorophenyl)-3-hydroxy-2-(methoxycarbamoyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3aj)**

Eluent: petroleum ether/ethyl acetate (20:1). White solid (41.7 mg, 50%), mp 171.4-172.2 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.36 (br s, 1H), 9.19 (br s, 1H), 7.75 (s, 1H), 7.62-7.58 (m, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.41-7.39 (m, 2H), 6.73 (s, 1H), 3.75 (s, 3H), 3.56 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 164.0, 162.5 (d, <sup>1</sup>*J*<sub>C-F</sub> = 242.9 Hz), 158.8, 138.2, 136.3, 132.3 (d, <sup>3</sup>*J*<sub>C-F</sub> = 8.7 Hz), 131.7 (d, <sup>3</sup>*J*<sub>C-F</sub> = 7.7 Hz), 129.3, 124.8, 124.1, 122.6 (q, <sup>1</sup>*J*<sub>C-F</sub> = 284.4 Hz), 121.3, 117.7 (d, <sup>2</sup>*J*<sub>C-F</sub> = 20.7 Hz), 115.1 (d, <sup>2</sup>*J*<sub>C-F</sub> = 23.0 Hz), 105.6, 90.4 (q, <sup>2</sup>*J*<sub>C-F</sub> = 33.9 Hz), 63.1, 51.7. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.31 (s), -112.14 – -112.15 (m). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>14</sub>F<sub>4</sub>N<sub>2</sub>NaO<sub>5</sub> 437.0731; Found 437.0726.



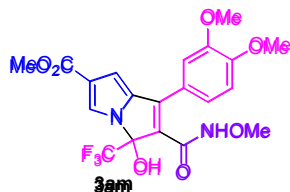
**Methyl 1-(3-chlorophenyl)-3-hydroxy-2-(methoxycarbonyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3ak)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (45.2 mg, 52%), mp 181.4-182.3 °C.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  11.38 (br s, 1H), 9.19 (br s, 1H), 7.76 (s, 1H), 7.64-7.57 (m, 4H), 6.71 (s, 1H), 3.75 (s, 3H), 3.56 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  164.0, 158.7, 138.0, 136.2, 134.0, 132.2, 131.5, 130.7, 129.4, 127.9, 127.3, 124.2, 122.6 (q,  $^1J_{\text{C-F}} = 284.4$  Hz), 121.3, 105.5, 90.4 (q,  $^2J_{\text{C-F}} = 32.9$  Hz), 63.0, 51.7.  $^{19}\text{F}$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -80.29 (s). HRMS (ESI) m/z:  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{18}\text{H}_{14}\text{ClF}_3\text{N}_2\text{NaO}_5$  453.0436; Found 453.0424.



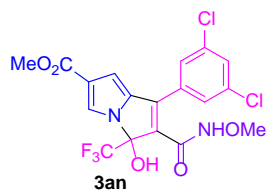
**Methyl 1-(3-bromophenyl)-3-hydroxy-2-(methoxycarbonyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3al)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (48.3 mg, 51%), mp 181.2-182.3 °C.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  11.38 (br s, 1H), 9.18 (br s, 1H), 7.76-7.73 (m, 3H), 6.68 (d,  $J = 7.8$  Hz, 1H), 7.52 (t,  $J = 7.8$  Hz, 1H), 6.70 (s, 1H), 3.75 (s, 3H), 3.56 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  164.0, 158.7, 137.9, 136.2, 133.6, 132.4, 131.8, 130.7, 129.4, 127.7, 124.2, 122.6 (q,  $^1J_{\text{C-F}} = 284.4$  Hz), 122.4, 121.3, 105.5, 90.4 (q,  $^2J_{\text{C-F}} = 32.9$  Hz), 63.1, 51.7.  $^{19}\text{F}$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -80.28 (s). HRMS (ESI) m/z:  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{18}\text{H}_{14}\text{BrF}_3\text{N}_2\text{NaO}_5$  496.9930; Found 496.9922.



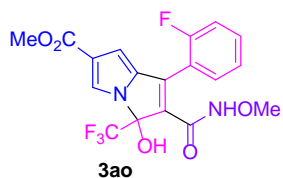
**Methyl 1-(3,4-dimethoxyphenyl)-3-hydroxy-2-(methoxycarbonyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3am)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (64.5 mg, 71%), mp 198.2-199.3 °C.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  11.27 (s, 1H), 9.02 (s, 1H), 7.72 (s, 1H), 7.29 (d,  $J = 8.4$  Hz, 1H), 7.15 (s, 1H), 7.11 (d,  $J = 8.4$  Hz, 1H), 6.71 (s, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.75 (s, 3H), 3.59 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  164.1, 159.6, 151.1, 149.1, 139.0, 137.0, 126.7, 123.7, 122.7 (q,  $^1J_{\text{C-F}} = 281.1$  Hz), 122.6, 121.8, 121.1, 112.3, 111.5, 105.3, 90.2 (q,  $^2J_{\text{C-F}} = 32.9$  Hz), 63.3, 56.1, 56.0, 51.7.  $^{19}\text{F}$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -80.26 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{20}\text{H}_{19}\text{F}_3\text{N}_2\text{NaO}_7$  479.1037; Found 479.1035.



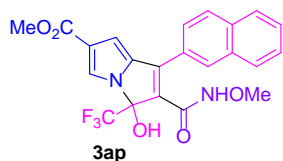
**Methyl 1-(3,5-dichlorophenyl)-3-hydroxy-2-(methoxycarbonyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3an)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (52.0 mg, 56%), mp 198.8-199.4 °C.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  11.40 (br s, 1H), 9.30 (br s, 1H), 7.83 (s, 1H), 7.76 (s, 1H), 7.57 (s, 2H), 6.74 (s, 1H), 3.76 (s, 3H), 3.56 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  163.9, 158.4, 137.1, 135.7, 135.2, 133.5, 130.4, 130.3, 126.9, 124.4, 122.6 (q,  $^1J_{\text{C-F}} = 285.5$  Hz), 121.4, 105.7, 90.4 (q,  $^2J_{\text{C-F}} = 32.9$  Hz), 63.0, 51.7.  $^{19}\text{F}$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -80.32 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{18}\text{H}_{13}\text{Cl}_2\text{F}_3\text{N}_2\text{NaO}_5$  487.0046; Found 487.0047.



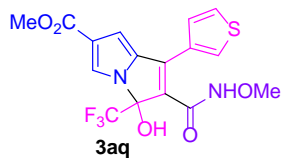
**Methyl 1-(2-fluorophenyl)-3-hydroxy-2-(methoxycarbonyl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3ao)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (44.8 mg, 54%), mp 89.1-90.4 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.13 (s, 1H), 9.25 (br s, 1H), 7.74 (s, 1H), 7.62-7.56 (m, 2H), 7.39-7.35 (m, 2H), 6.51 (s, 1H), 3.74 (s, 3H), 3.52 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 164.0, 159.8 (d, <sup>1</sup>J<sub>C-F</sub> = 249.5 Hz), 158.7, 136.7, 135.3, 132.8 (d, <sup>3</sup>J<sub>C-F</sub> = 7.7 Hz), 130.9, 130.4, 125.3, 123.9, 122.7 (q, <sup>1</sup>J<sub>C-F</sub> = 284.4 Hz), 121.2, 118.4 (d, <sup>2</sup>J<sub>C-F</sub> = 14.3 Hz), 116.7 (d, <sup>2</sup>J<sub>C-F</sub> = 20.9 Hz), 105.5, 90.4 (q, <sup>2</sup>J<sub>C-F</sub> = 32.9 Hz), 63.0, 51.7. <sup>19</sup>F NMR (367 MHz, CD<sub>3</sub>OD): δ -82.87 (s), -111.51 – -111.57 (m). HRMS (ESI) m/z: [M+Na]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>14</sub>F<sub>4</sub>N<sub>2</sub>NaO<sub>5</sub> 437.0731; Found 437.0722.



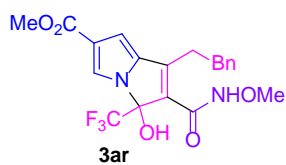
**Methyl 3-hydroxy-2-(methoxycarbonyl)-1-(naphthalen-2-yl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3ap)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (46.9 mg, 53%), mp 180.2-181.9 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.31 (br s, 1H), 9.15 (br s, 1H), 8.30 (s, 1H), 8.13 (d, *J* = 7.2 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.99 (d, *J* = 7.2 Hz, 1H), 7.78 (s, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.64-7.60 (m, 2H), 6.85 (s, 1H), 3.77 (s, 3H), 3.55 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 164.1, 159.2, 139.4, 136.8, 134.0, 133.1, 129.2, 128.9, 128.5, 128.4, 128.1, 128.0, 127.8, 127.4, 125.5, 123.9, 122.8 (q, <sup>1</sup>J<sub>C-F</sub> = 284.4 Hz), 121.2, 105.8, 90.4 (q, <sup>2</sup>J<sub>C-F</sub> = 32.8 Hz), 63.1, 51.7. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -80.24 (s). HRMS (ESI) m/z: [M+Na]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>17</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>5</sub> 469.0982; Found 469.0973.



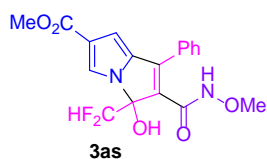
**Methyl 3-hydroxy-2-(methoxycarbonyl)-1-(thiophen-3-yl)-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3aq)**

Eluent: petroleum ether/ethyl acetate (2:1). White solid (47.9 mg, 60%), mp 182.0-183.0 °C.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  11.38 (br s, 1H), 9.05 (br s, 1H), 8.24 (s, 1H), 7.73-7.70 (m, 2H), 7.38 (d,  $J = 4.2$  Hz, 1H), 6.90 (s, 1H), 3.76 (s, 3H), 3.64 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  164.1, 159.4, 136.6, 133.4, 130.7, 129.2, 128.1, 127.1, 126.6, 123.6, 122.7 (q,  $^1J_{\text{C-F}} = 285.5$  Hz), 121.1, 105.5, 90.2 (q,  $^2J_{\text{C-F}} = 31.7$  Hz), 63.2, 51.7.  $^{19}\text{F}$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -80.28 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{16}\text{H}_{13}\text{F}_3\text{N}_2\text{NaO}_5\text{S}$  425.0389; Found 425.0393.



**Methyl 3-hydroxy-2-(methoxycarbonyl)-1-phenethyl-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (3ar)**

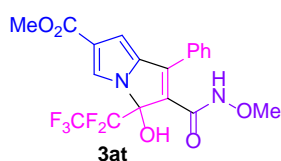
Eluent: petroleum ether/ethyl acetate (2:1). White solid (46.3 mg, 55%), mp 161.1-162.4 °C.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  10.92 (s, 1H), 9.11 (s, 1H), 7.66 (s, 1H), 7.30-7.28 (m, 4H), 7.23-7.19 (m, 1H), 6.72 (s, 1H), 3.75 (s, 3H), 3.67 (s, 3H), 2.96-2.86 (m, 4H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  164.1, 159.3, 145.0, 141.3, 138.1, 128.83, 128.79, 127.9, 126.6, 123.6, 122.8 (q,  $^1J_{\text{C-F}} = 285.5$  Hz), 121.1, 105.2, 90.0 (q,  $^2J_{\text{C-F}} = 32.9$  Hz), 63.7, 51.6, 34.5, 28.8.  $^{19}\text{F}$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -80.70 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{20}\text{H}_{19}\text{F}_3\text{N}_2\text{NaO}_5$  447.1138; Found 447.1147.



**Methyl 3-(difluoromethyl)-3-hydroxy-2-(methoxycarbonyl)-1-phenyl-3H-pyrrolizine-6-carboxylate**

### (3as)

Eluent: petroleum ether/ethyl acetate (2:1). White solid (55.0 mg, 73%), mp 163.9-164.2 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.16 (s, 1H), 8.41 (s, 1H), 7.71 (s, 1H), 7.61-7.60 (m, 2H), 7.53-7.52 (m, 3H), 6.64-6.46 (m, 2H), 3.75 (s, 3H), 3.57 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 164.3, 160.1, 138.3, 137.4, 130.5, 129.8, 129.3, 128.8, 124.6, 120.3, 115.2, 113.6 (t, <sup>1</sup>J<sub>C-F</sub> = 237.5 Hz), 104.7, 91.0 (t, <sup>2</sup>J<sub>C-F</sub> = 20.7 Hz), 63.1, 51.6. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -129.57 (dd, *J*<sub>1</sub> = 276.3 Hz, *J*<sub>2</sub> = 53.1 Hz, 1F), -137.35 (dd, *J*<sub>1</sub> = 275.7 Hz, *J*<sub>2</sub> = 55.4 Hz, 1F). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>16</sub>F<sub>2</sub>N<sub>2</sub>NaO<sub>5</sub> 401.0919; Found 401.0910.



### Methyl 3-hydroxy-2-(methoxycarbonyl)-3-(perfluoroethyl)-1-phenyl-3H-pyrrolizine-6-carboxylate (3at)

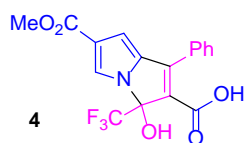
Eluent: petroleum ether/ethyl acetate (2:1). White solid (51.4 mg, 58%), mp 202.9-203.3 °C. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>): δ 11.13 (s, 1H), 9.23 (s, 1H), 7.72 (s, 1H), 7.65-7.64 (m, 2H), 7.56-7.53 (m, 3H), 6.65 (s, 1H), 3.75 (s, 3H), 3.55 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 164.0, 159.1, 139.9, 137.0, 130.7, 130.4, 129.4, 128.6, 128.5, 124.7, 121.1, 118.7 (qt, <sup>1</sup>J<sub>C-F</sub> = 286.5 Hz, <sup>2</sup>J<sub>C-F</sub> = 35.0 Hz), 112.5 (tq, <sup>1</sup>J<sub>C-F</sub> = 263.7 Hz, <sup>2</sup>J<sub>C-F</sub> = 36.2 Hz), 105.5, 91.0 (t, <sup>2</sup>J<sub>C-F</sub> = 25.2 Hz), 62.9, 51.7. <sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>): δ -78.67 (s, 3F), -120.94 (d, *J* = 276.3 Hz, 1F), -123.50 (d, *J* = 276.3 Hz, 1F). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>15</sub>F<sub>5</sub>N<sub>2</sub>NaO<sub>5</sub> 469.0793; Found 469.0789.

## 2. Structural elaborations

### 2.1 Synthesis of 4<sup>[4]</sup>

To a reaction tube equipped with a stir bar were added **3aa** (79.3 mg, 0.2 mmol), *tert*-butyl nitrite (28.5 μL, 0.24 mmol), H<sub>2</sub>O (18 μL) and DCE (2 mL). The tube was then sealed, and the mixture was stirred at room temperature under air for 2 h. Upon completion, it was concentrated under reduced pressure. The residue was

purified by column chromatography on silica gel with petroleum ether/ethyl acetate/acetic acid (30:6:1) as the eluent to give **4**.



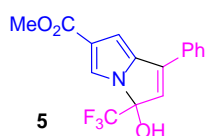
### 3-Hydroxy-6-(methoxycarbonyl)-1-phenyl-3-(trifluoromethyl)-3H-pyrrolizine-2-carboxylic acid (**4**)

Eluent: petroleum ether/ethyl acetate/acetic acid (30:6:1). Yellow solid (45.8 mg, 62%), mp 188.5-189.7 °C.

$^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  7.81 (s, 1H), 7.61-7.60 (m, 2H), 7.52-7.51 (m, 3H), 6.57 (s, 1H), 3.75 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  163.9, 163.7, 145.2, 137.2, 131.1, 130.6, 128.99, 128.97, 126.9, 124.6, 122.9 (q,  $^1J_{\text{C-F}} = 285.5$  Hz), 121.5, 106.5, 90.9 (q,  $^2J_{\text{C-F}} = 32.7$  Hz), 51.7.  $^{19}\text{F}$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -79.90 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $\text{C}_{17}\text{H}_{13}\text{F}_3\text{NO}_5$  368.0740; Found 368.0744.

## 2.2 Synthesis of **5**

To a reaction tube equipped with a stir bar were added **4** (36.7 mg, 0.1 mmol) and methanesulfonic acid (1 mL). The tube was then sealed, and the mixture was stirred at room temperature under air for 2 h. Upon completion, it was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (5:1) as the eluent to give **5**.



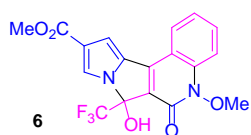
### Methyl 3-hydroxy-1-phenyl-3-(trifluoromethyl)-3H-pyrrolizine-6-carboxylate (**5**)

Eluent: petroleum ether/ethyl acetate (5:1). Yellow solid (18.1 mg, 56%), mp 157.9-158.8 °C.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ ):  $\delta$  8.79 (s, 1H), 7.91-7.89 (m, 2H), 7.72 (s, 1H), 7.53-7.49 (m, 3H), 7.85 (d,  $J = 1.2$  Hz, 1H), 6.83 (s, 1H), 3.76 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ ):  $\delta$  164.3, 139.8, 137.6, 130.7, 130.5, 129.6, 127.4, 123.7, 123.23, 123.21 (q,  $^1J_{\text{C-F}} = 283.4$  Hz), 120.8, 104.2, 89.6 (q,  $^2J_{\text{C-F}} = 32.7$  Hz), 51.6.  $^{19}\text{F}$  NMR (565 MHz, DMSO- $d_6$ ):  $\delta$  -81.11 (s). HRMS (ESI)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{16}\text{H}_{12}\text{F}_3\text{NNaO}_3$  346.0661; Found

346.0659.

### 2.3 Synthesis of **6**<sup>[5]</sup>

To a reaction tube equipped with a stir bar were added **3aa** (79.3 mg, 0.2 mmol), PIFA (103.2 mg, 0.24 mmol) and DCE (2 mL). The tube was then sealed, and the mixture was stirred at room temperature under air for 2 h. Upon completion, it was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (1:1) as the eluent to give **6**.

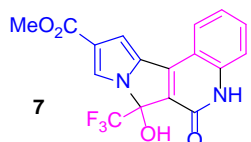


### Methyl 7-hydroxy-5-methoxy-6-oxo-7-(trifluoromethyl)-5,7-dihydro-6H-pyrrolizino[2,1-c]quinoline-10-carboxylate (**6**)

Eluent: petroleum ether/ethyl acetate (1:1). Yellow solid (63.2 mg, 80%), mp 278.4-278.6 °C. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): δ 7.98 (d, *J* = 7.8 Hz, 1H), 7.92 (s, 1H), 7.60 (t, *J* = 7.8 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.21 (s, 1H), 6.96 (br s, 1H), 3.87 (s, 6H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, CDCl<sub>3</sub>): δ 164.3, 154.2, 142.7, 139.2, 133.3, 132.1, 126.3, 125.4, 123.9, 123.6, 122.5, 122.4 (q, <sup>1</sup>*J*<sub>C-F</sub> = 284.4 Hz), 113.5, 112.8, 108.8, 89.4 (q, <sup>2</sup>*J*<sub>C-F</sub> = 36.2 Hz), 63.6, 51.6. <sup>19</sup>F NMR (565 MHz, CDCl<sub>3</sub>): δ -81.21 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>13</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>5</sub> 417.0669; Found 417.0665.

### 2.1 Synthesis of **7**<sup>[6]</sup>

To a reaction tube equipped with a stir bar were added **6** (39.4 mg, 0.1 mmol) and MeOH (2 mL). The tube was then sealed, and the mixture was stirred at room temperature under 10 W blue LED irradiation and argon atmosphere for 6 h. Upon completion, it was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (1:2) as the eluent to give **7**.





**Methyl 7-hydroxy-6-oxo-7-(trifluoromethyl)-5,7-dihydro-6H-pyrrolizino[2,1-c]quinoline-10-carboxylate**  
**(7)**

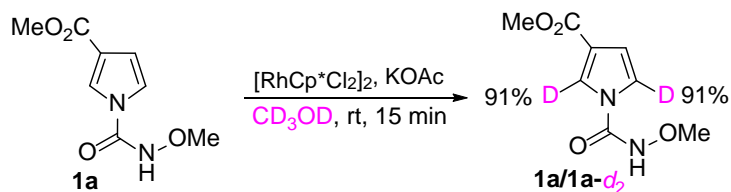
Eluent: petroleum ether/ethyl acetate (1:2). White solid (32.3 mg, 89%), mp 278.2-279.0 °C. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ 12.02 (s, 1H), 9.09 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.89 (s, 1H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.50 (s, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 3.81 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>): δ 164.0, 157.3, 143.0, 141.6, 133.2, 132.7, 126.5, 125.1, 124.7, 123.2, 123.0 (q, <sup>1</sup>*J*<sub>C-F</sub> = 285.5 Hz), 122.1, 116.3, 113.1, 108.5, 90.0 (q, <sup>2</sup>*J*<sub>C-F</sub> = 33.9 Hz), 51.8. <sup>19</sup>F NMR (376 MHz, DMSO-*d*<sub>6</sub>): δ -79.46 (s). HRMS (ESI) *m/z*: [M+Na]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>11</sub>F<sub>3</sub>N<sub>2</sub>NaO<sub>4</sub> 387.0563; Found 387.0561.

### 3. Gram-Scale Synthesis of **3aa**

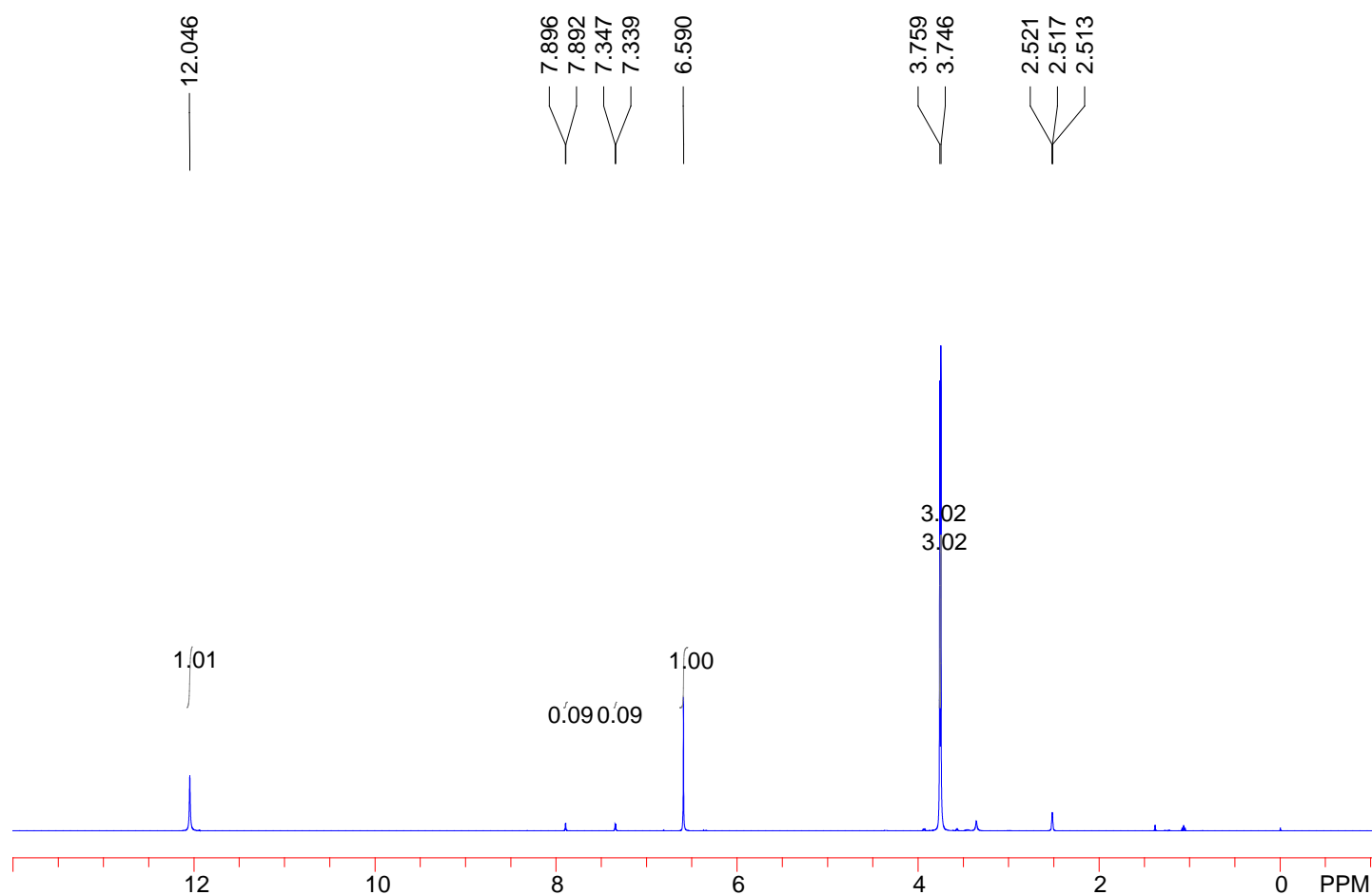
To a reaction tube equipped with a stir bar were added **1a** (990.9 mg, 5.0 mmol), KOAc (98.14 mg, 1.0 mmol), [RhCp\*Cl<sub>2</sub>]<sub>2</sub> (77.3 mg, 0.125 mmol), **2a** (1089.8 mg, 5.5 mmol) and CH<sub>3</sub>OH (20 mL). The tube was sealed, and the mixture was stirred at room temperature under air for 6 h. Upon completion, it was quenched with saturated aqueous solution of NH<sub>4</sub>Cl, and then extracted with ethyl acetate (40 mL × 3). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (2:1) as eluent to afford **3aa** (1.54 g, 78%).

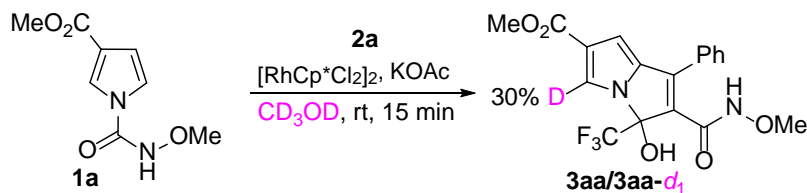
### III. Mechanism studies

#### 1. Studies on the reversibility of C–H bond activation

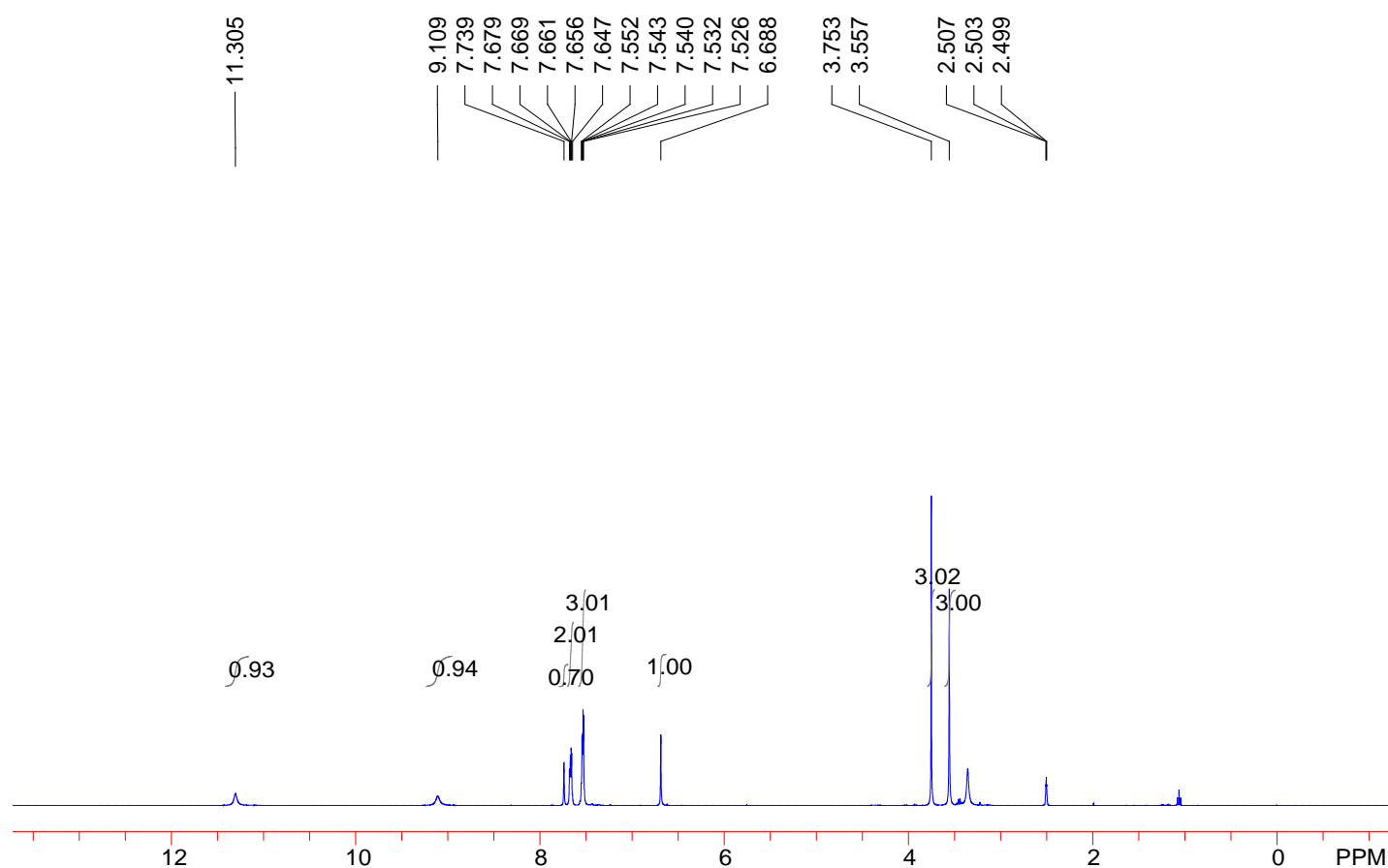


To a reaction tube equipped with a stir bar were charged with **1a** (39.6 mg, 0.2 mmol), KOAc (3.9 mg, 0.04 mmol),  $[\text{RhCp}^*\text{Cl}_2]_2$  (6.2 mg, 0.01 mmol) and  $\text{CD}_3\text{OD}$  (2 mL). The tube was then sealed, and the mixture was stirred at room temperature under air for 15 min. Afterwards, it was cooled to room temperature, filtered through a pad of celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate (5:1) as eluent to give a mixture of **1a** and **1a-d<sub>2</sub>**. Based on the  $^1\text{H}$  NMR of the mixture, 91% deuteration at the *ortho*-position of the pyrrole moiety was observed. This result indicates the occurrence of a reversible *ortho*-C–H bond cleavage.

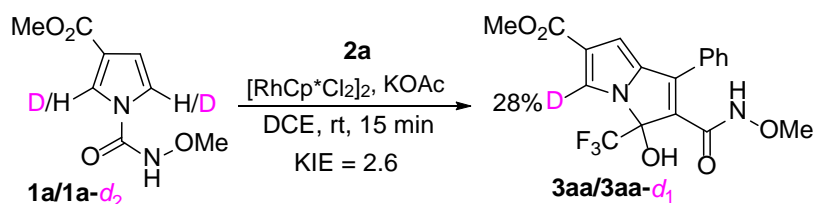




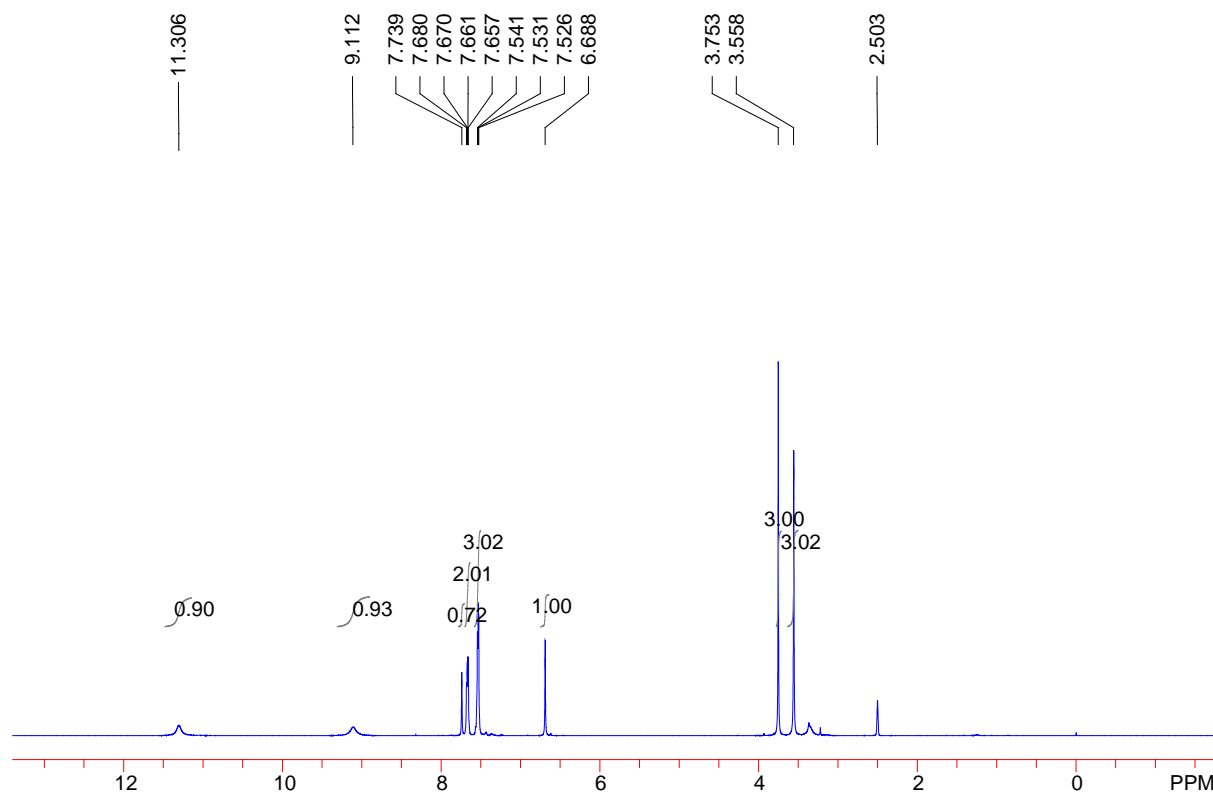
To a reaction tube equipped with a stir bar were added **1a** (39.6 mg, 0.2 mmol), KOAc (3.9 mg, 0.04 mmol), [RhCp\*Cl<sub>2</sub>]<sub>2</sub> (6.2 mg, 0.01 mmol), **2a** (43.6 mg, 0.22 mmol) and CD<sub>3</sub>OD (2 mL). The tube was then sealed, and the mixture was stirred at room temperature under air for 15 min. Afterwards, it was quenched with saturated aqueous solution of NH<sub>4</sub>Cl, and extracted with ethyl acetate (10 mL × 3). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate (2:1) as eluent to afford a mixture of **3aa** and **3aa-d<sub>1</sub>**. Based on the <sup>1</sup>H NMR of the resulting mixture, 30% deuteration at the unreacted *ortho*-position was observed. This result indicates that in the presence of **2a**, the *ortho*-C–H bond activation is still reversible.



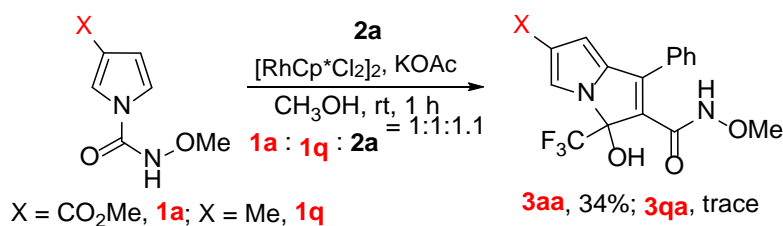
## 2. Kinetic isotope effect study



To a reaction tube equipped with a stir bar were added **1a-d<sub>2</sub>** (44.4 mg, 0.222 mmol, 91% deuteration), **1a** (35.3 mg, 0.178 mmol), KOAc (3.9 mg, 0.04 mmol),  $[\text{RhCp}^*\text{Cl}_2]_2$  (6.2 mg, 0.01 mmol), **2a** (39.6 mg, 0.2 mmol) and DCE (2 mL). The tube was then sealed, and the mixture was stirred at room temperature under air for 15 min. Afterwards, it was quenched with saturated aqueous solution of  $\text{NH}_4\text{Cl}$ , and extracted with ethyl acetate (10 mL  $\times$  3). The combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate (2:1) as eluent to afford a mixture of **3aa** and **3aa-d<sub>1</sub>**. Based on the  $^1\text{H}$  NMR of the resulting mixture, a  $k_{\text{H}}/k_{\text{D}}$  value of 2.6 was observed. This result showed that the *ortho*-C–H cleavage step has an obvious influence on the over-all reaction rate of this cascade reaction.

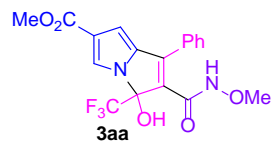
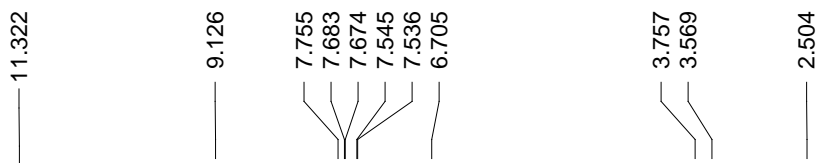


### 3. Competitive experiment between **1a** and **1q**

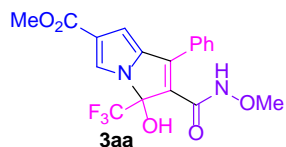
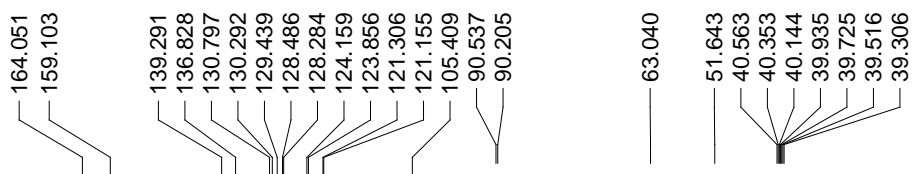
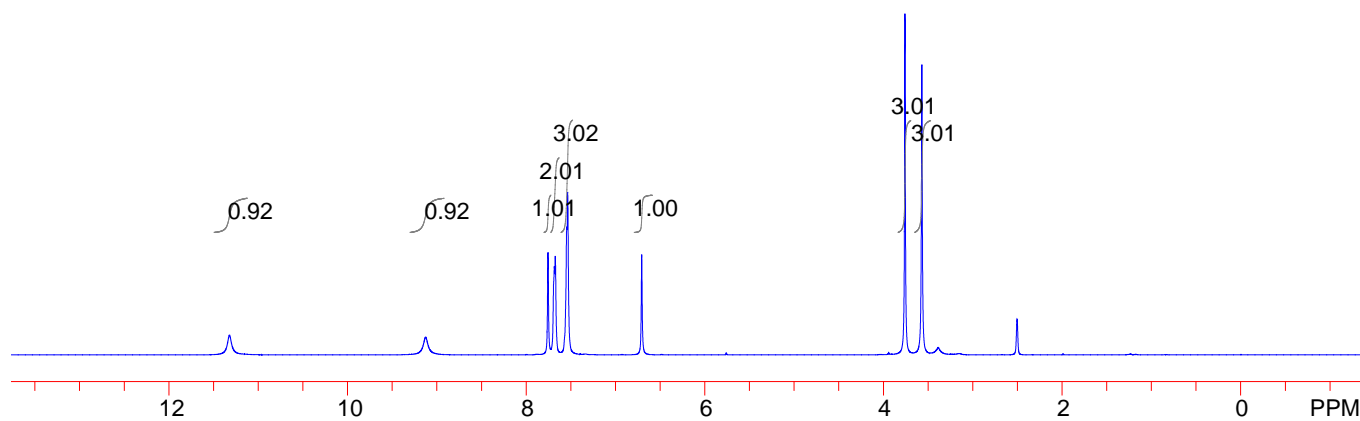


To a reaction tube equipped with a stir bar were added **1a** (39.6 mg, 0.2 mmol), **1q** (30.8 mg, 0.2 mmol), KOAc (3.9 mg, 0.04 mmol), [RhCp\*Cl<sub>2</sub>]<sub>2</sub> (6.2 mg, 0.01 mmol), **2a** (43.6 mg, 0.22 mmol) and CH<sub>3</sub>OH (2 mL). The tube was then sealed, and the mixture was stirred at room temperature under air for 1 h. Afterwards, it was quenched with saturated aqueous solution of NH<sub>4</sub>Cl, and then extracted with ethyl acetate (10 mL × 3). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate (2:1) as eluent to afford **3aa** (26.9 mg, 34%). Meanwhile, **3qa** was formed only in trace amount. This means that the presence of an electron-withdrawing ester group on the pyrrole moiety can facilitate this reaction obviously, indicating that the C–H bond cleavage step might occur *via* concerted metalation-deprotonation (CMD) process.

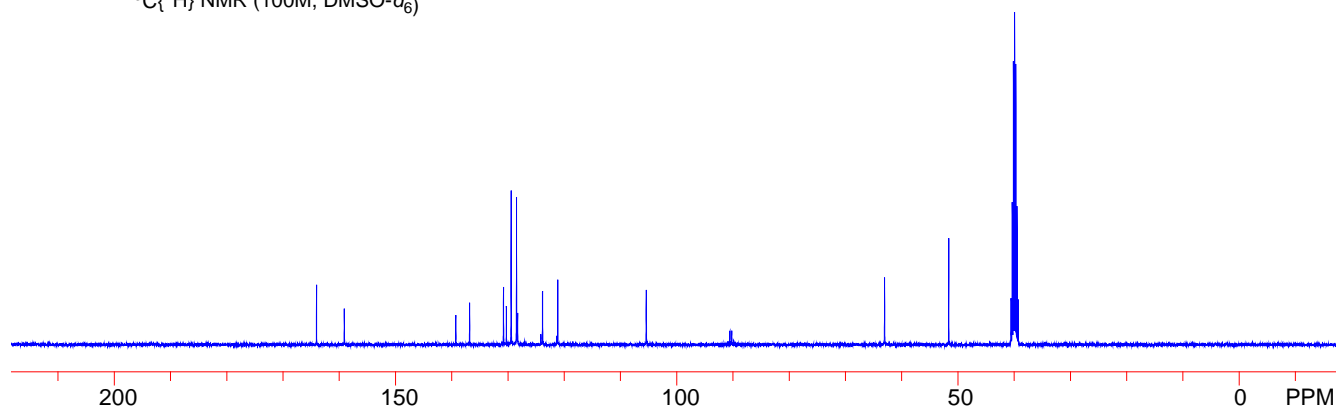
## IV. NMR spectra of 3aa-3ta and 3ab-3at



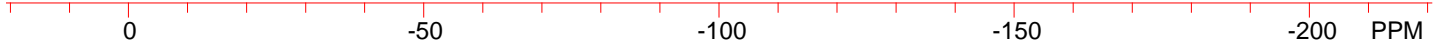
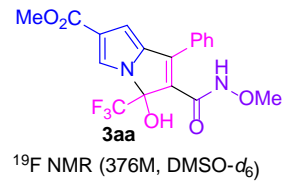
$^1\text{H}$  NMR (400M, DMSO- $d_6$ )

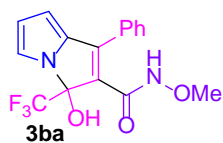


$^{13}\text{C}\{^1\text{H}\}$  NMR (100M, DMSO- $d_6$ )

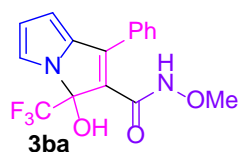
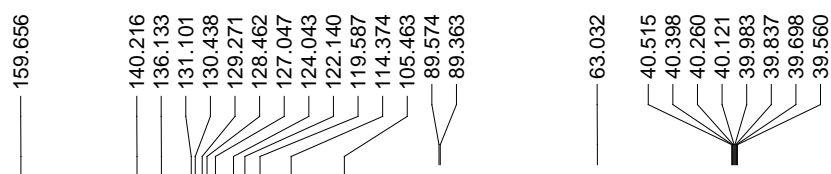
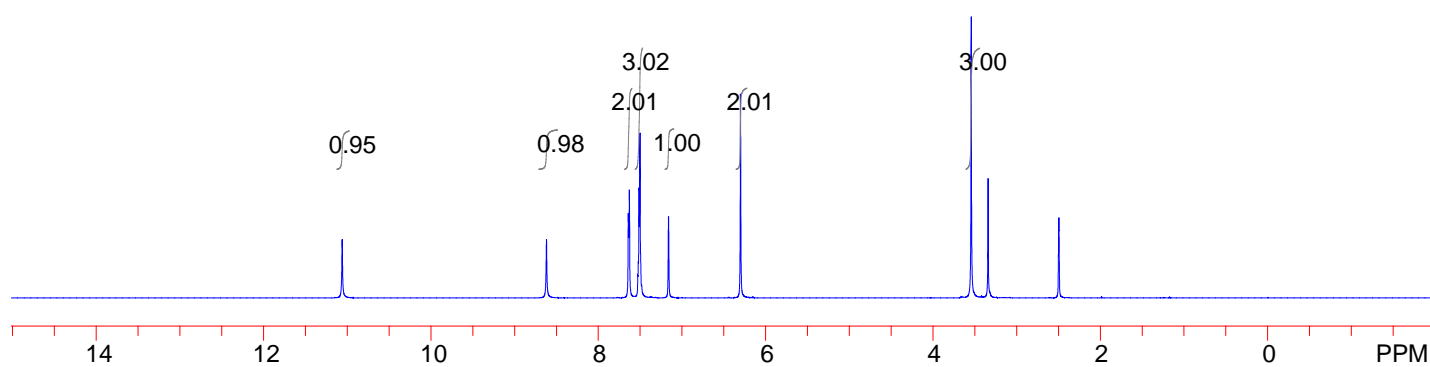
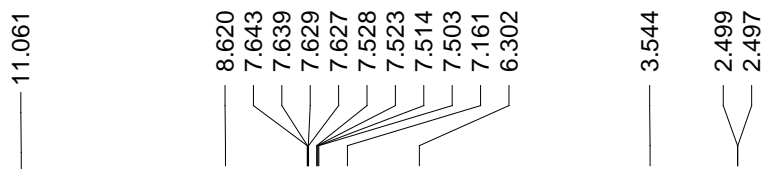


80.315

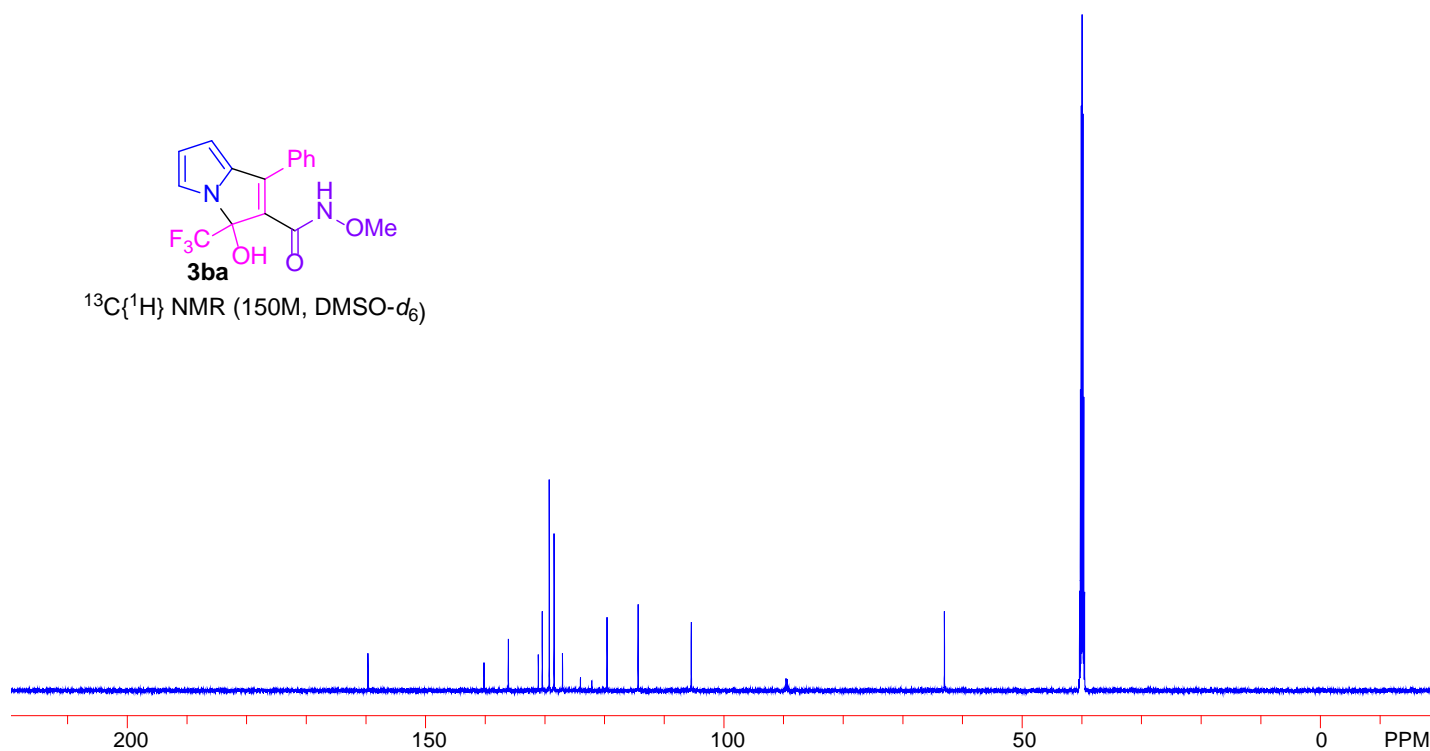




$^1\text{H}$  NMR (600M, DMSO- $d_6$ )

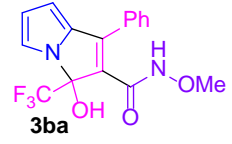


$^{13}\text{C}\{^1\text{H}\}$  NMR (150M, DMSO- $d_6$ )



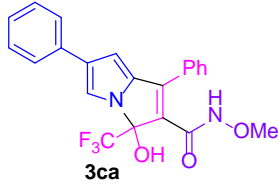
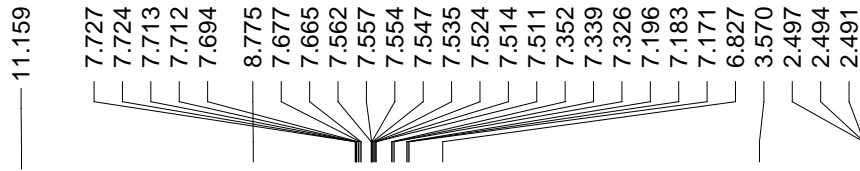


80.317

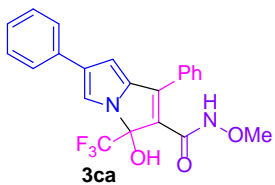
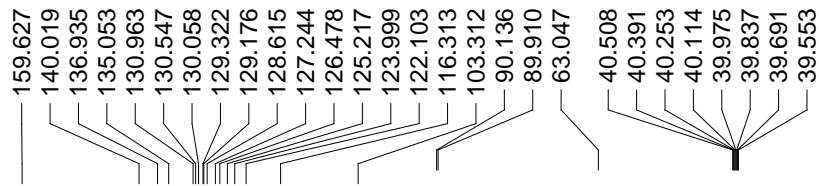
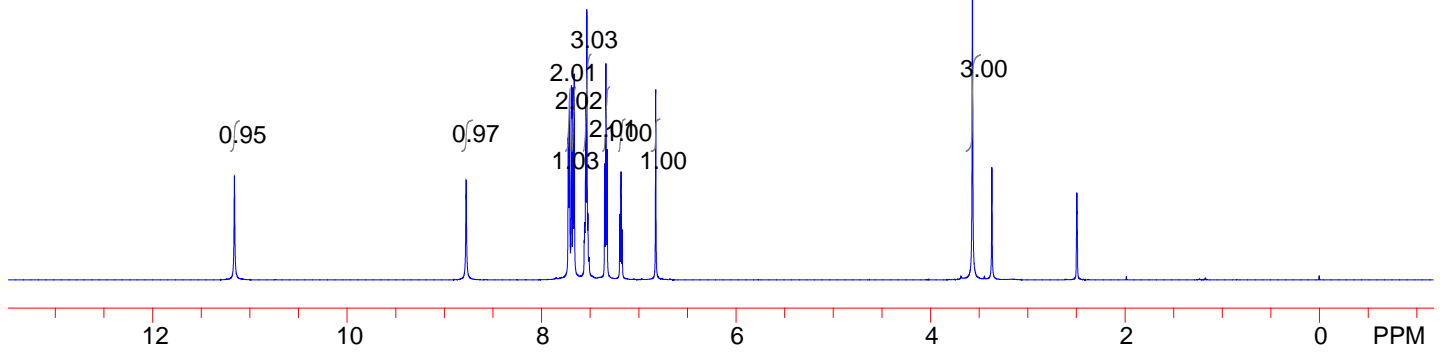


<sup>19</sup>F NMR (565M, DMSO-*d*<sub>6</sub>)

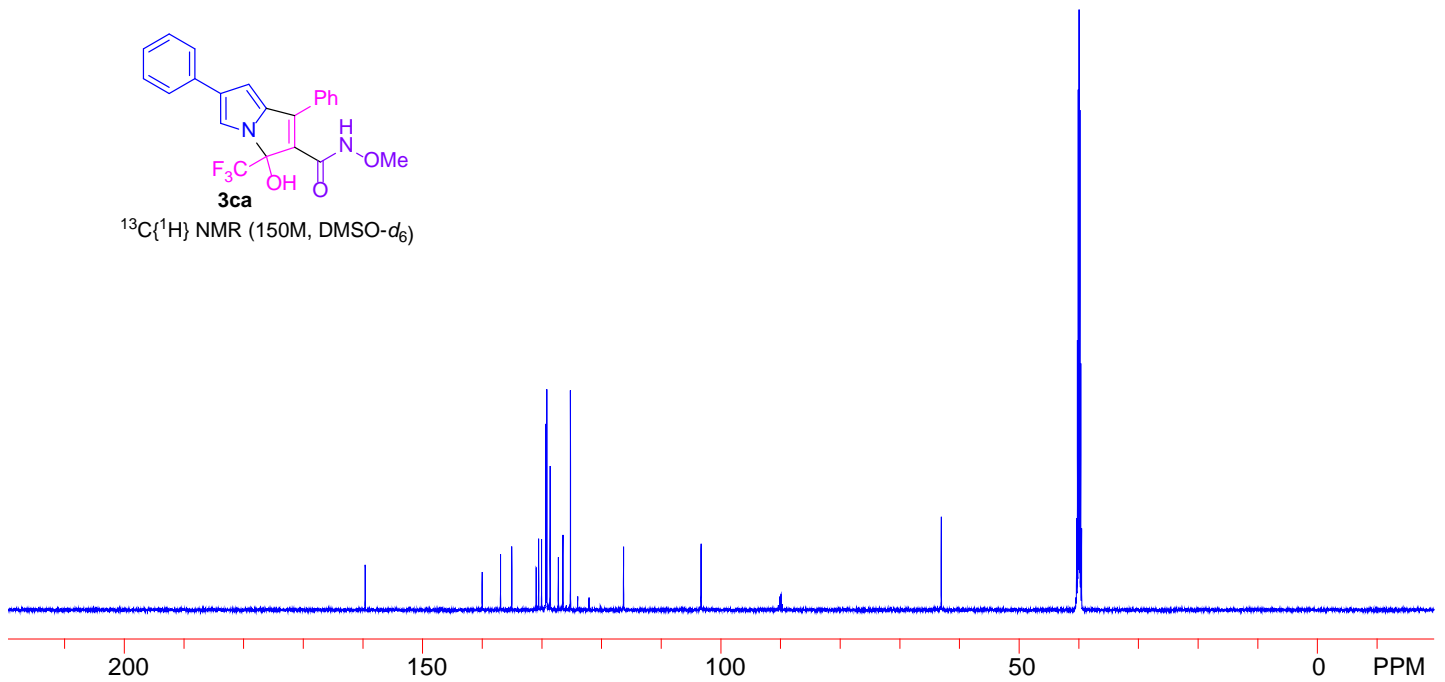
0 -50 -100 -150 -200 PPM



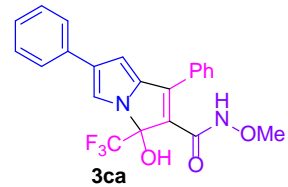
<sup>1</sup>H NMR (600M, DMSO-*d*<sub>6</sub>)



<sup>13</sup>C{<sup>1</sup>H} NMR (150M, DMSO-*d*<sub>6</sub>)

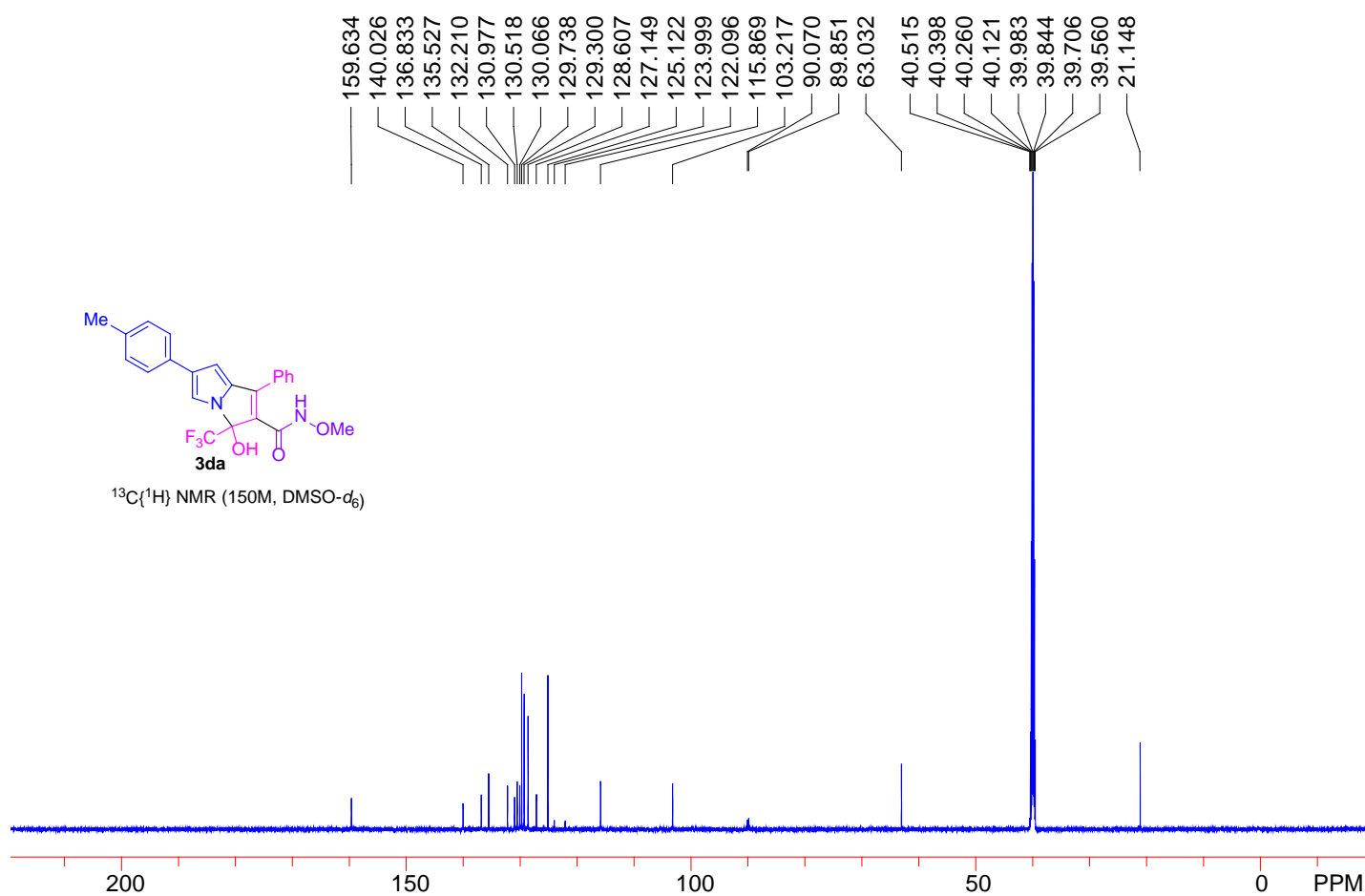
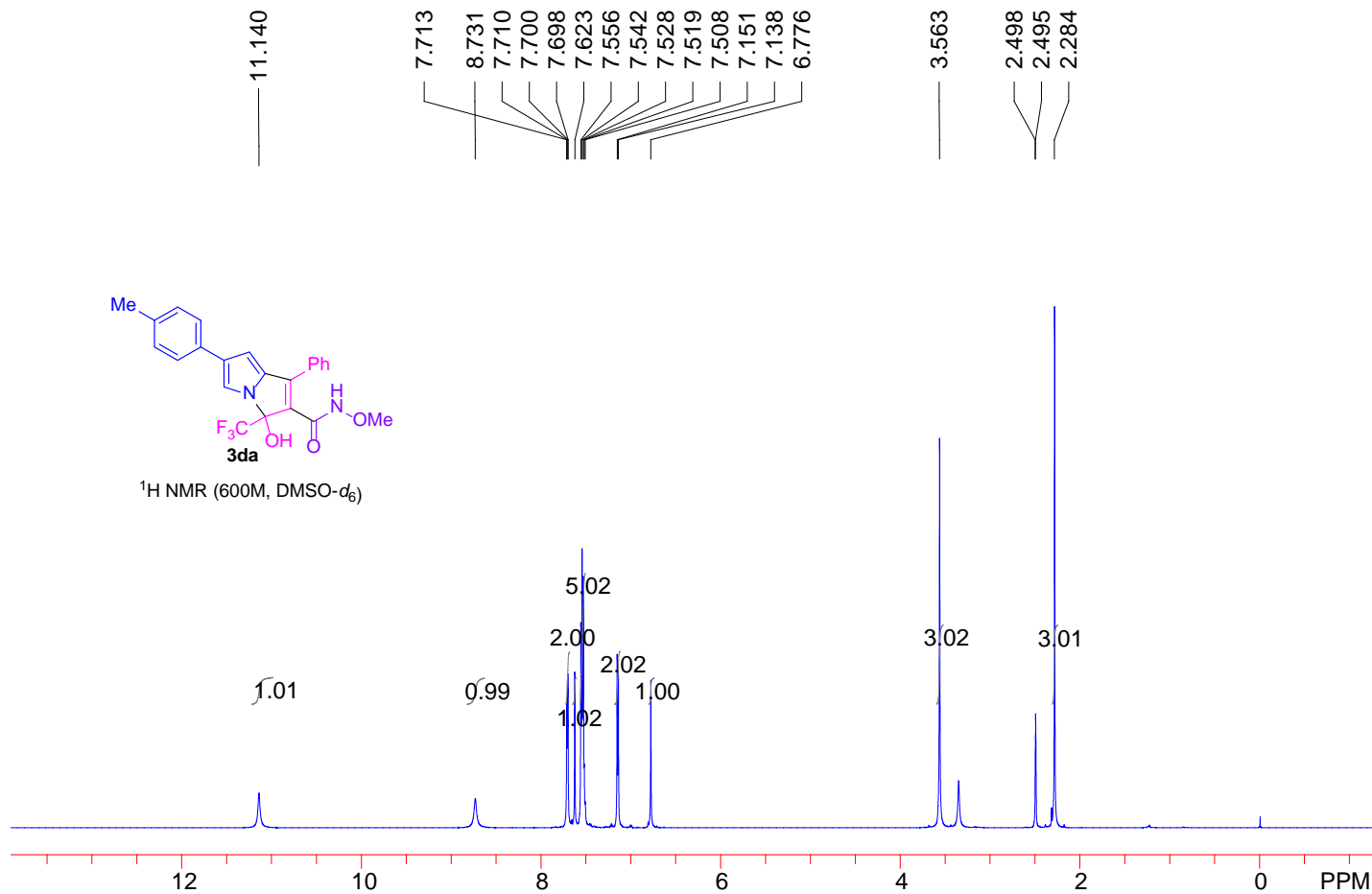


80.096

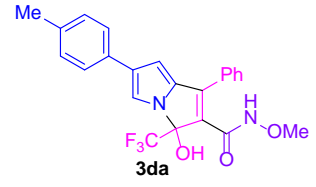


<sup>19</sup>F NMR (565M, DMSO-d<sub>6</sub>)

0 -50 -100 -150 -200 PPM

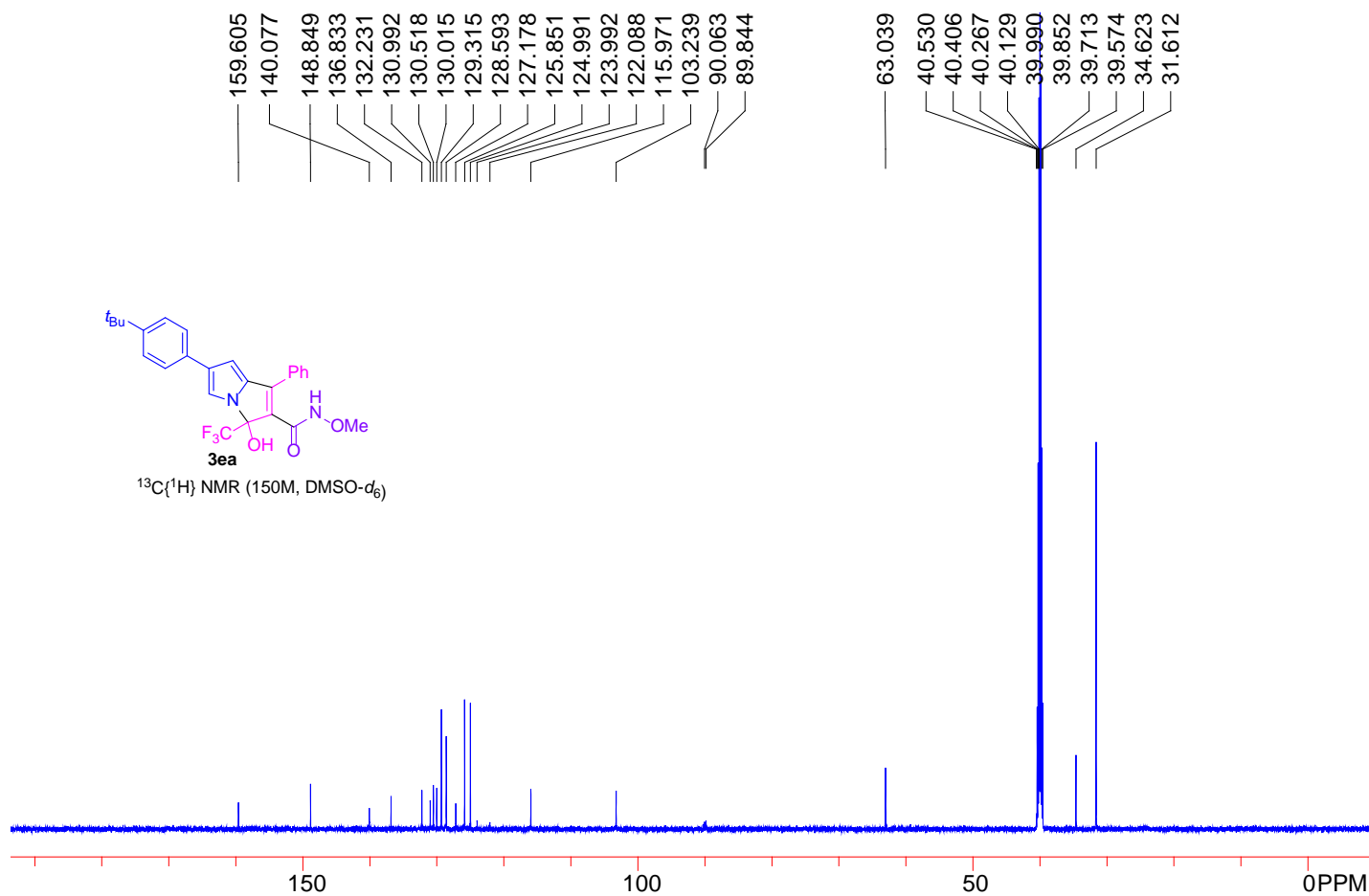
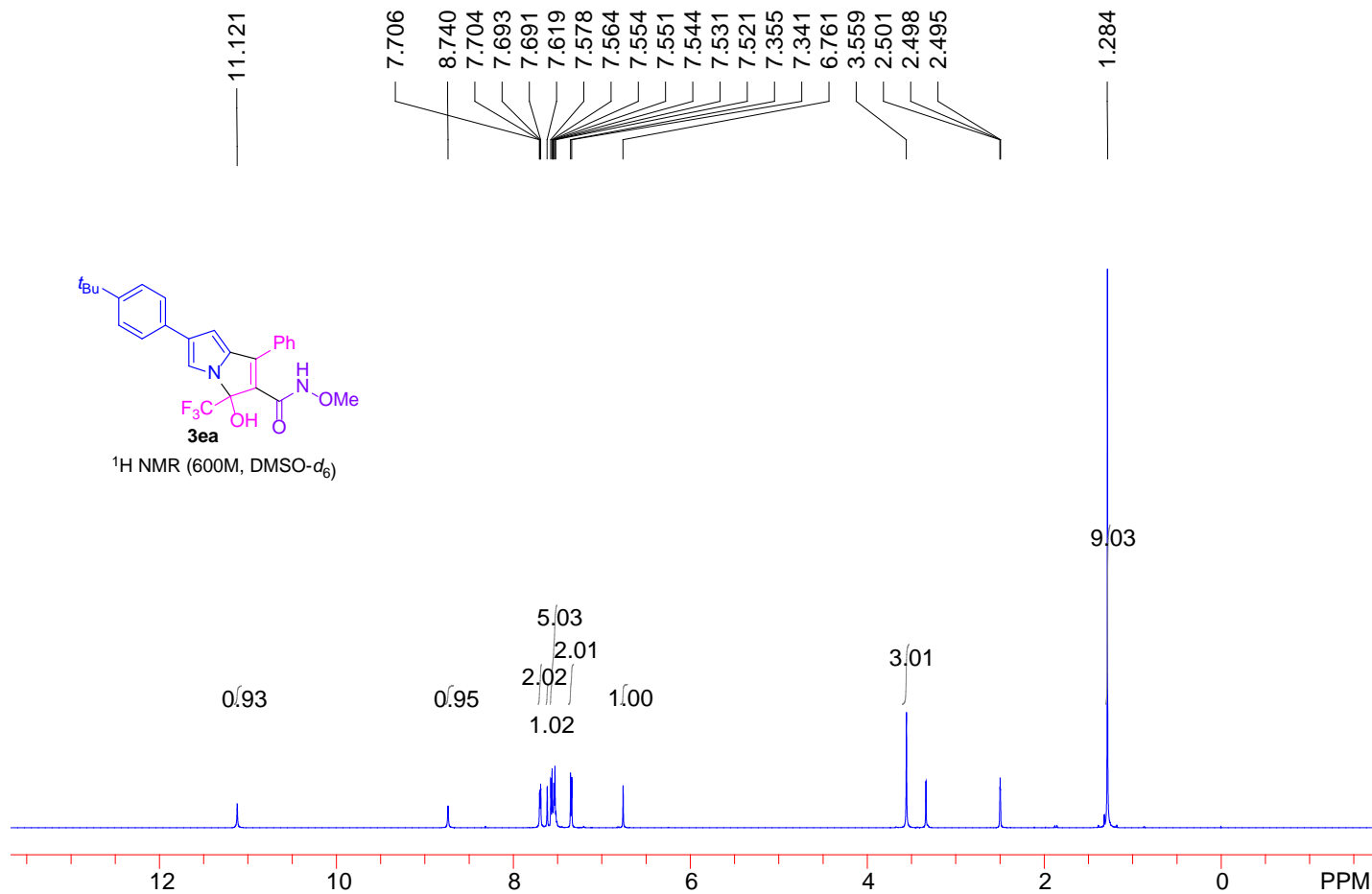


80.100

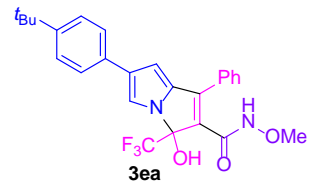


<sup>19</sup>F NMR (565M, DMSO-d<sub>6</sub>)

0 -50 -100 -150 -200 PPM

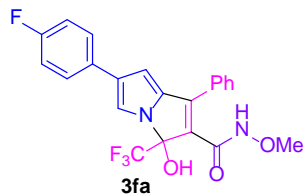


80.111

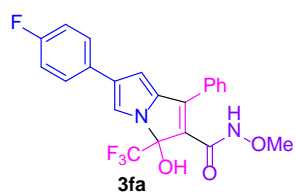
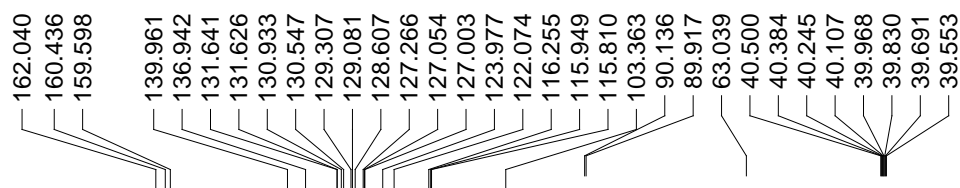
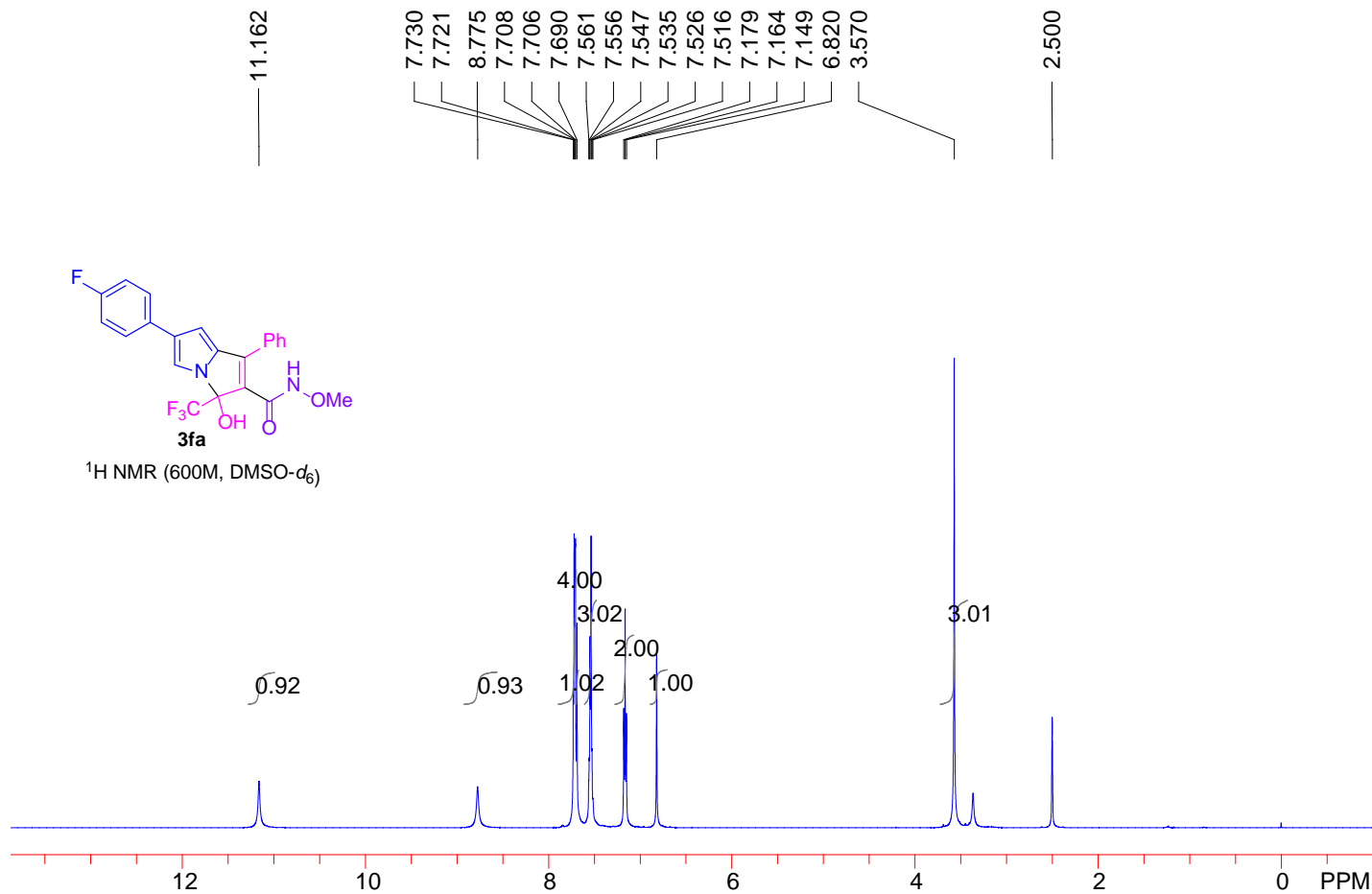


$^{19}F$  NMR (565M, DMSO- $d_6$ )

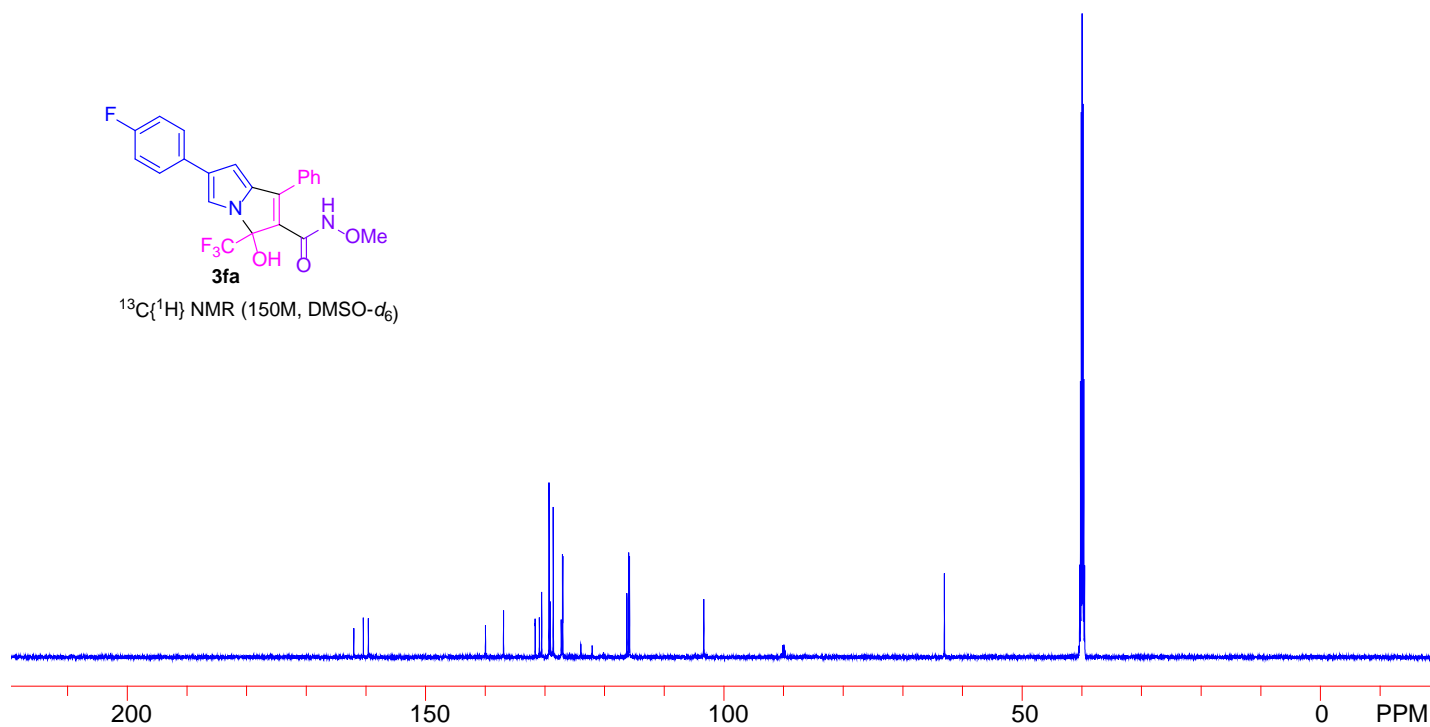
0 -50 -100 -150 -200 PPM



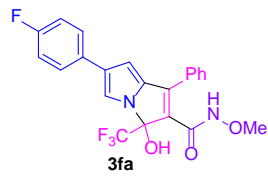
$^1\text{H NMR}$  (600M,  $\text{DMSO-}d_6$ )



$^{13}\text{C}\{^1\text{H}\}$  NMR (150M,  $\text{DMSO-}d_6$ )





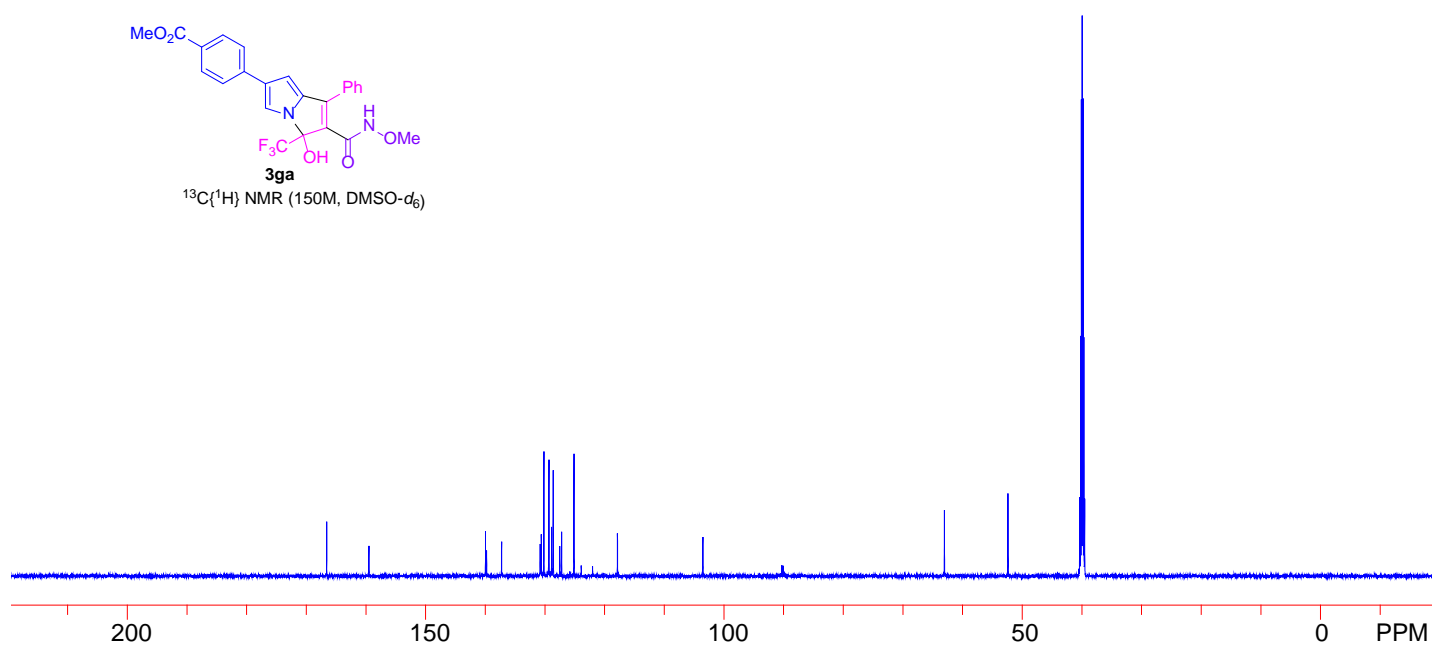
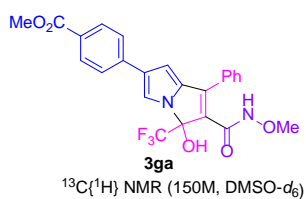
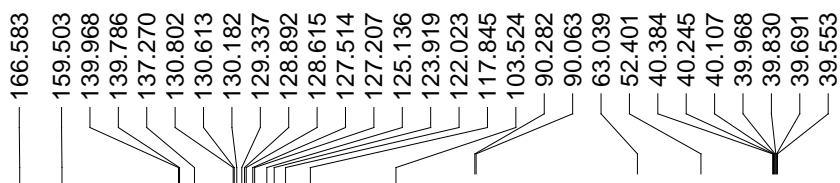
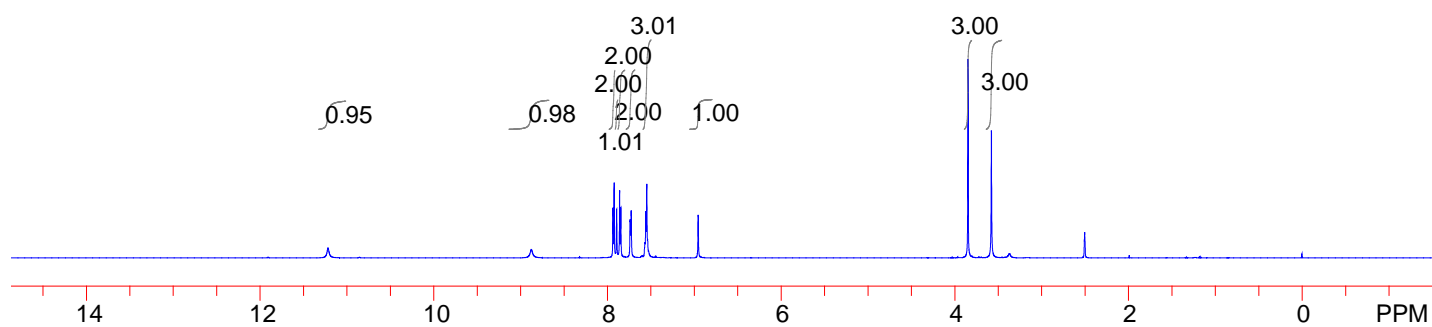
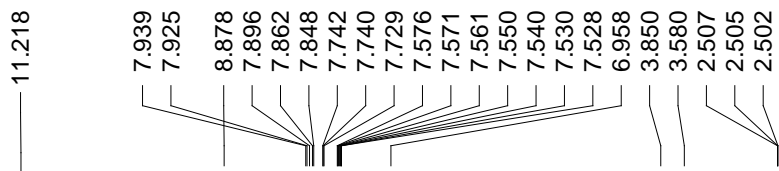
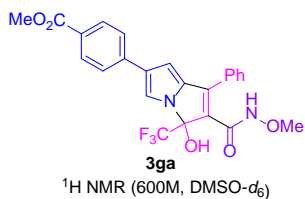


<sup>19</sup>F NMR (565M, DMSO-d<sub>6</sub>)

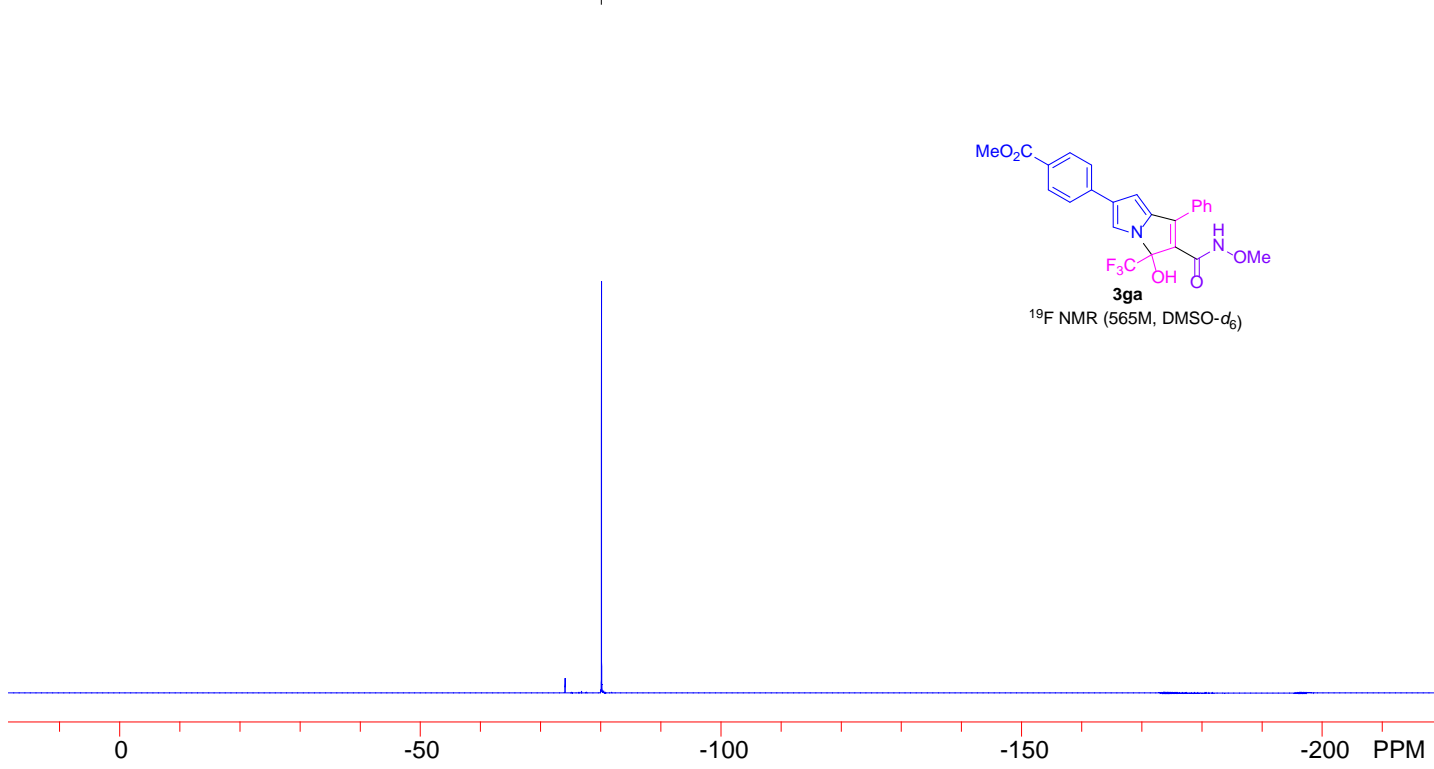
80.114

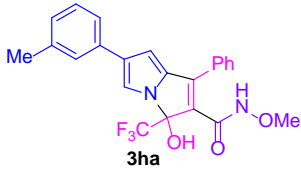
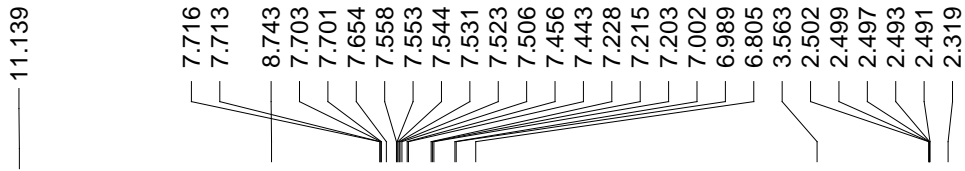
116.885  
116.892

0 -50 -100 -150 -200 PPM

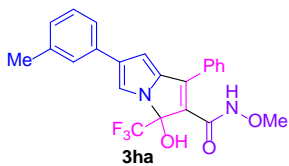
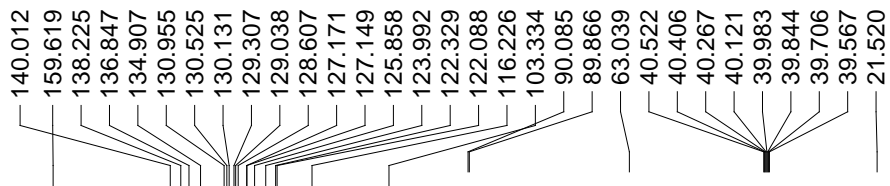
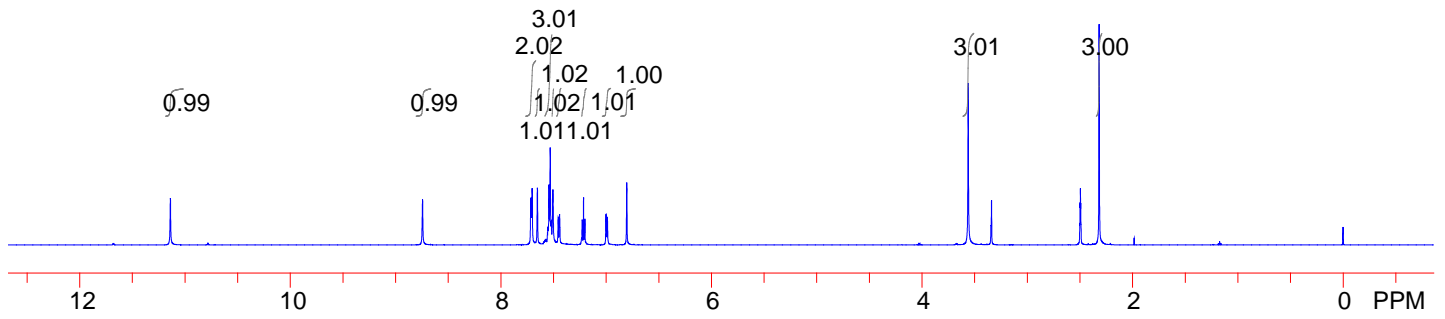


80.107

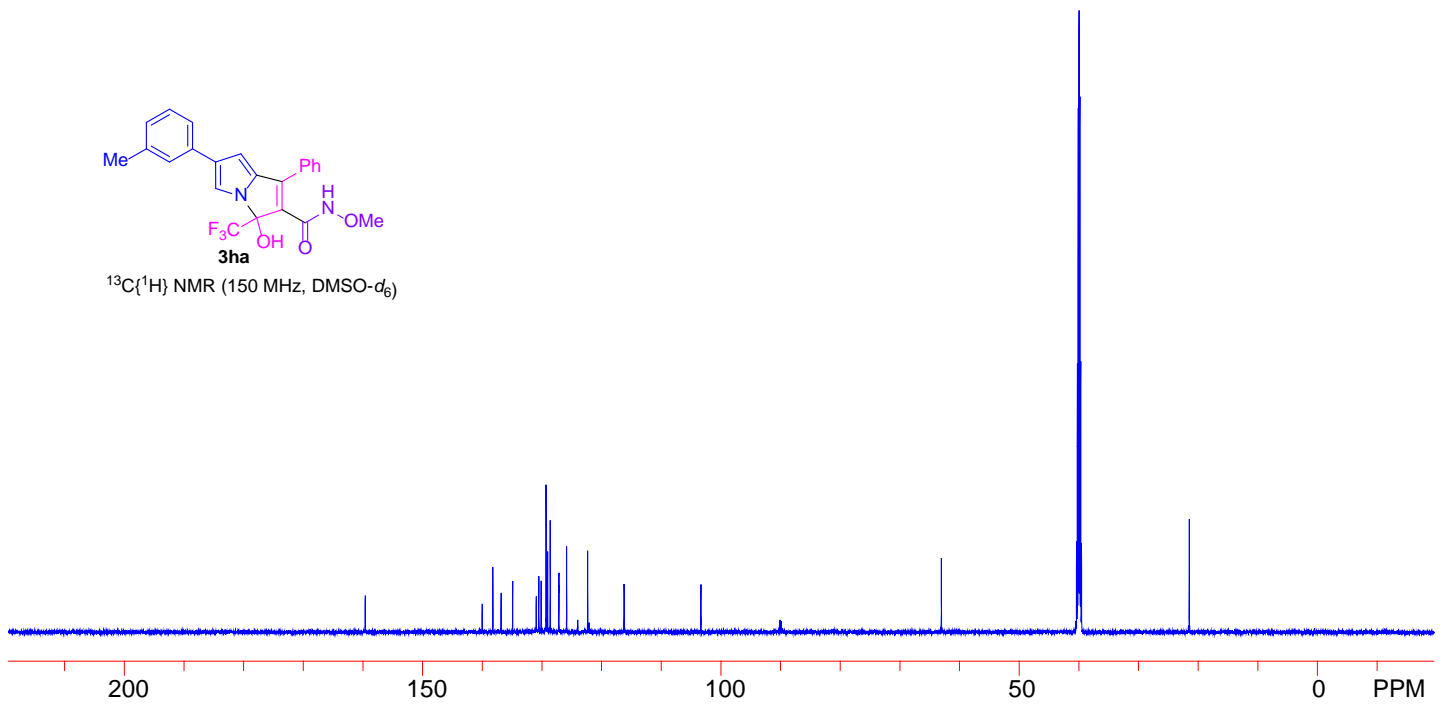




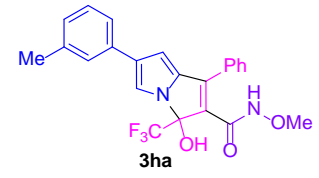
$^1\text{H}$  NMR (600 MHz,  $\text{DMSO}-d_6$ )



$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO}-d_6$ )

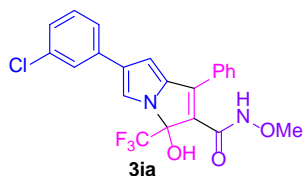
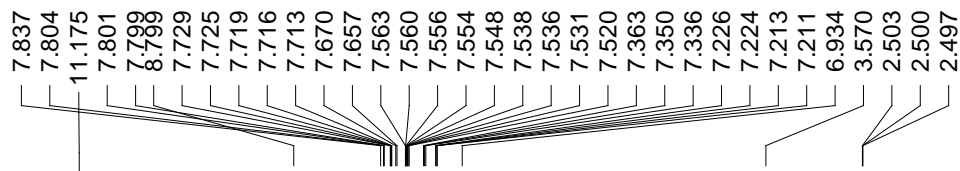


80.114

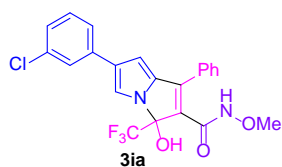
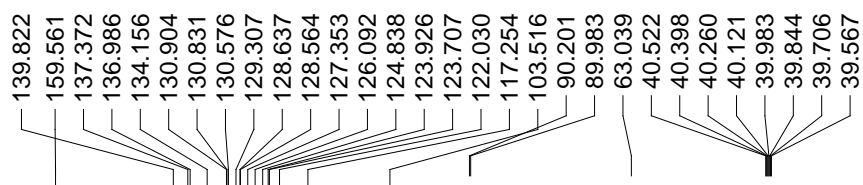
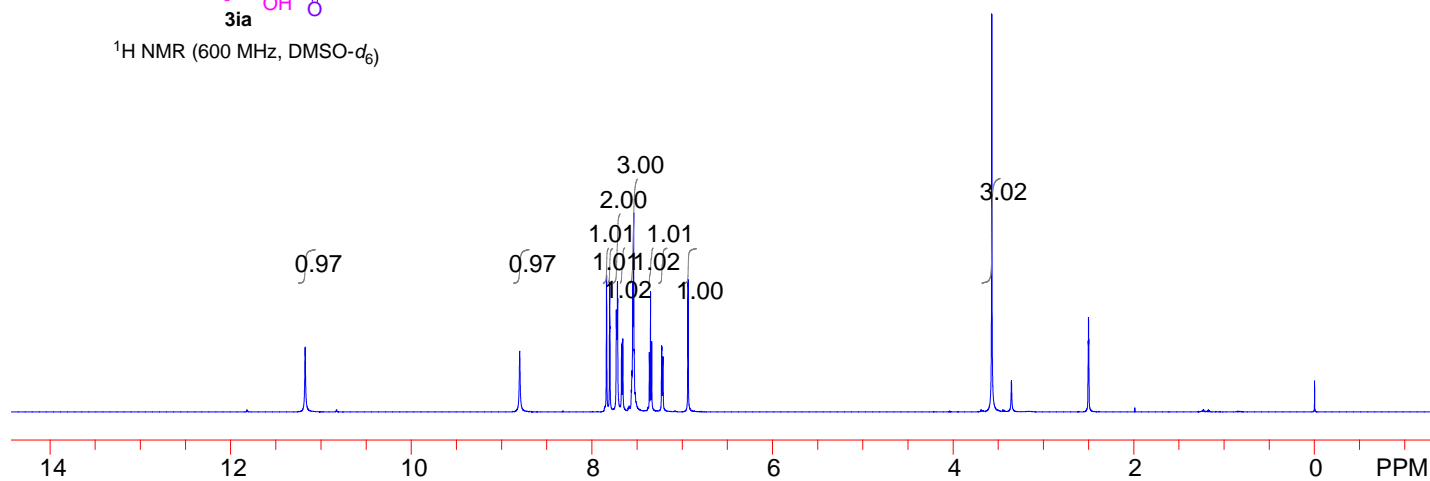


<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

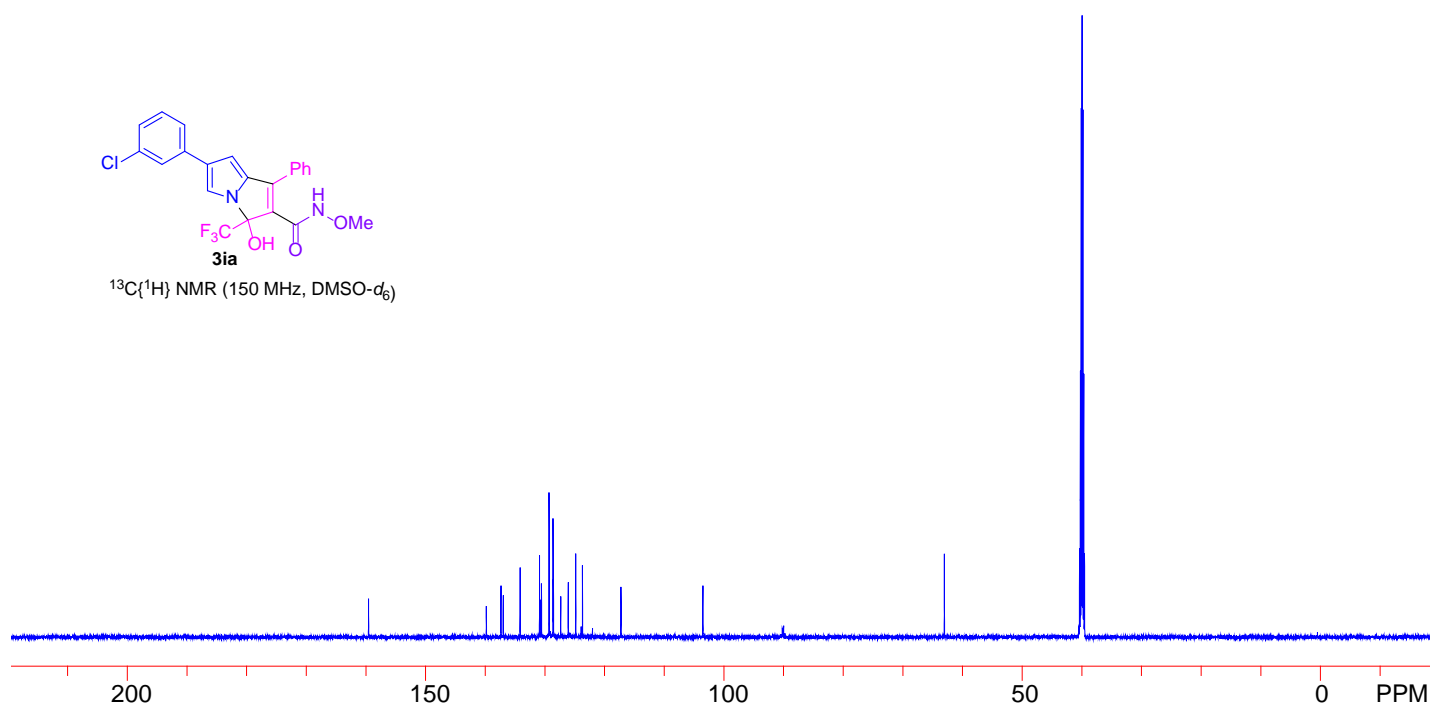
0 -50 -100 -150 -200 PPM



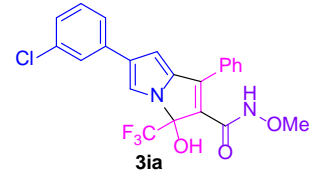
$^1\text{H NMR}$  (600 MHz,  $\text{DMSO-}d_6$ )



$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ )

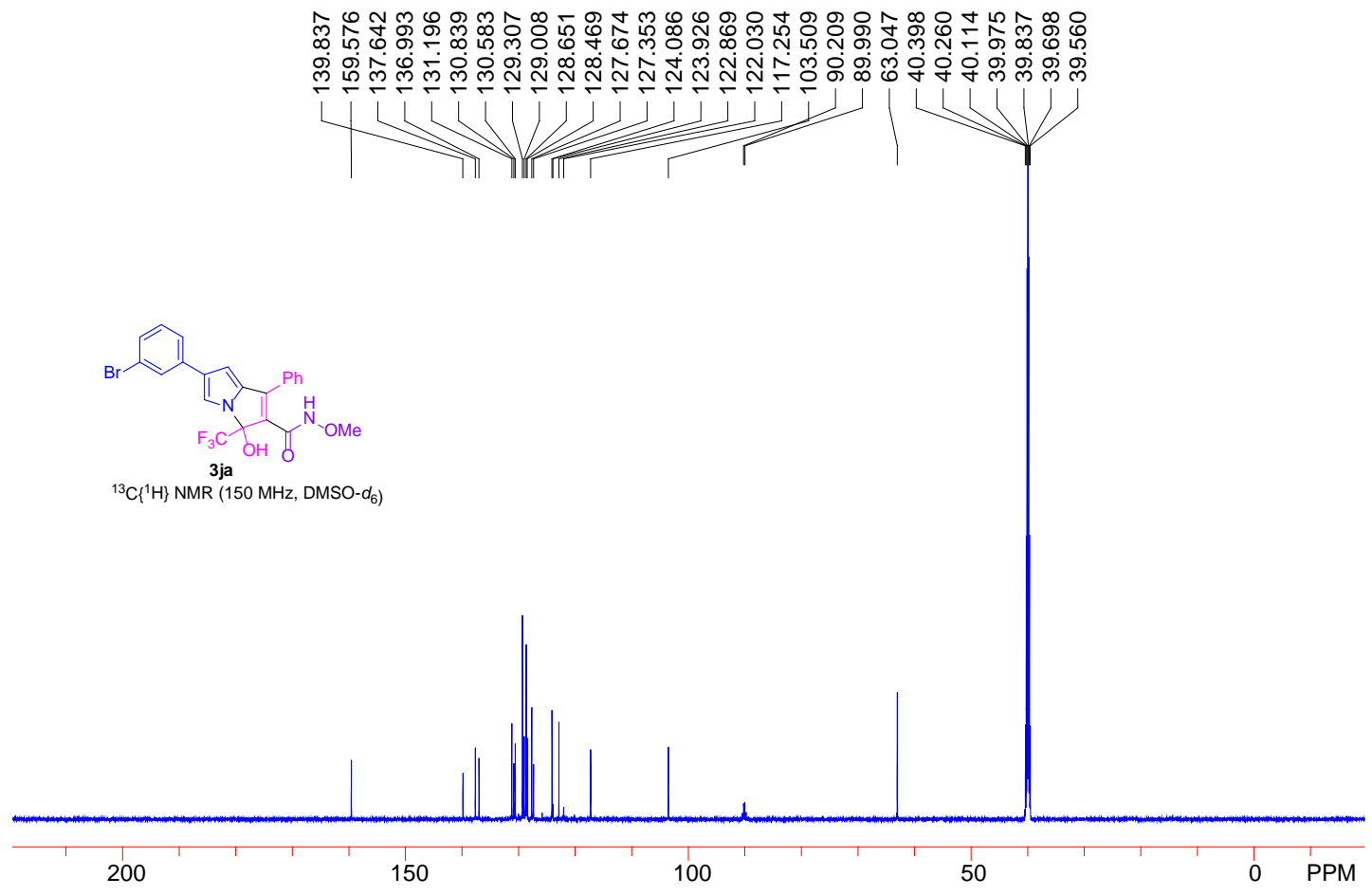
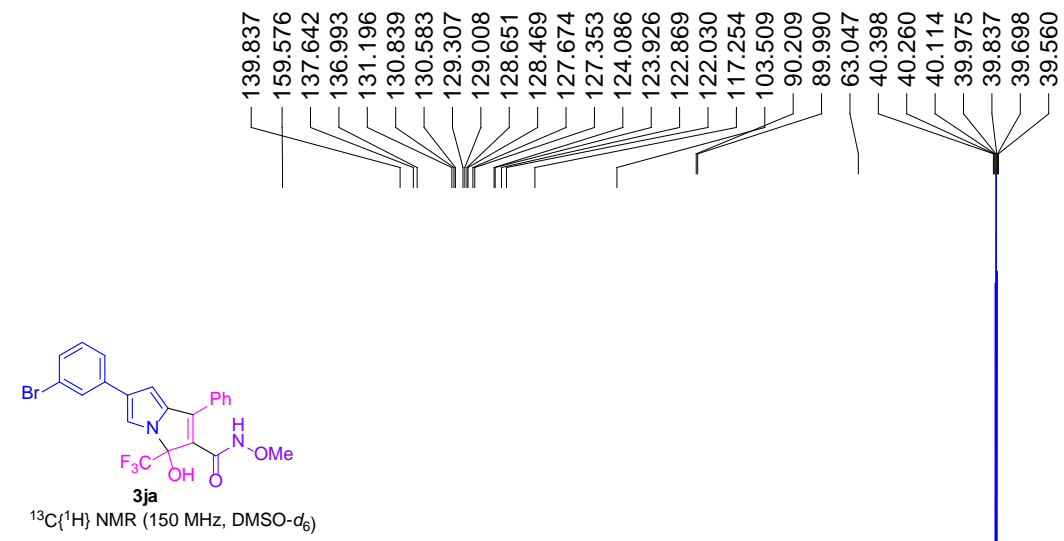
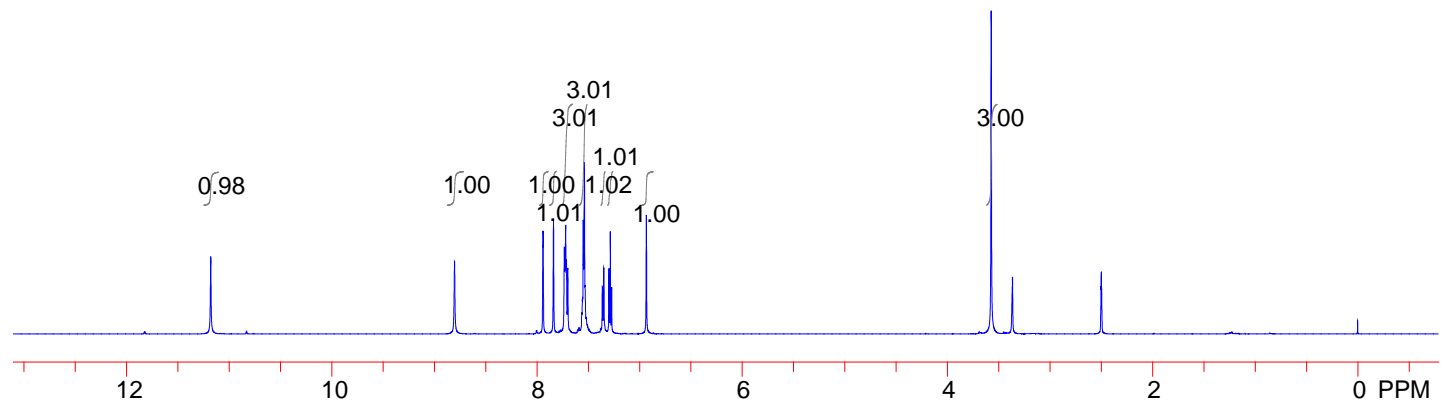
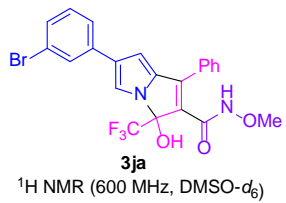
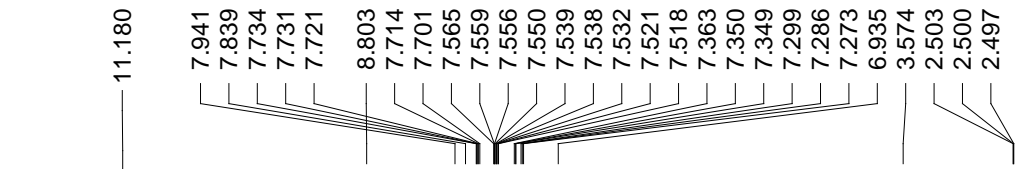


80.085



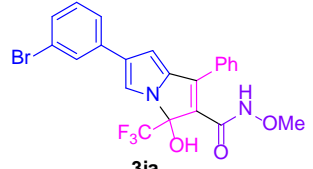
<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

0 -50 -100 -150 -200 PPM



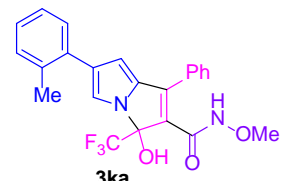
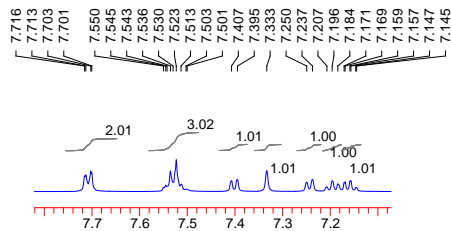
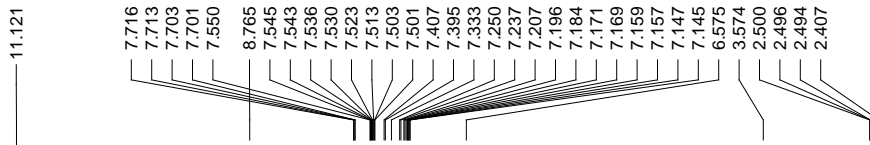


-80.146

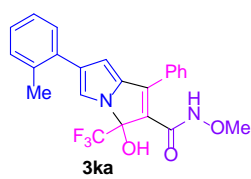
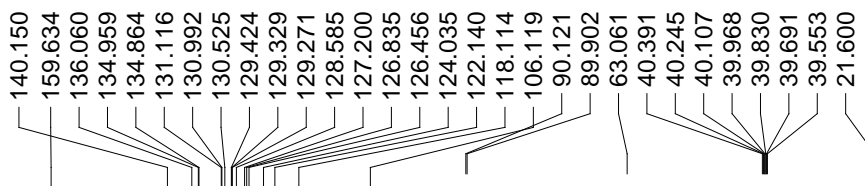
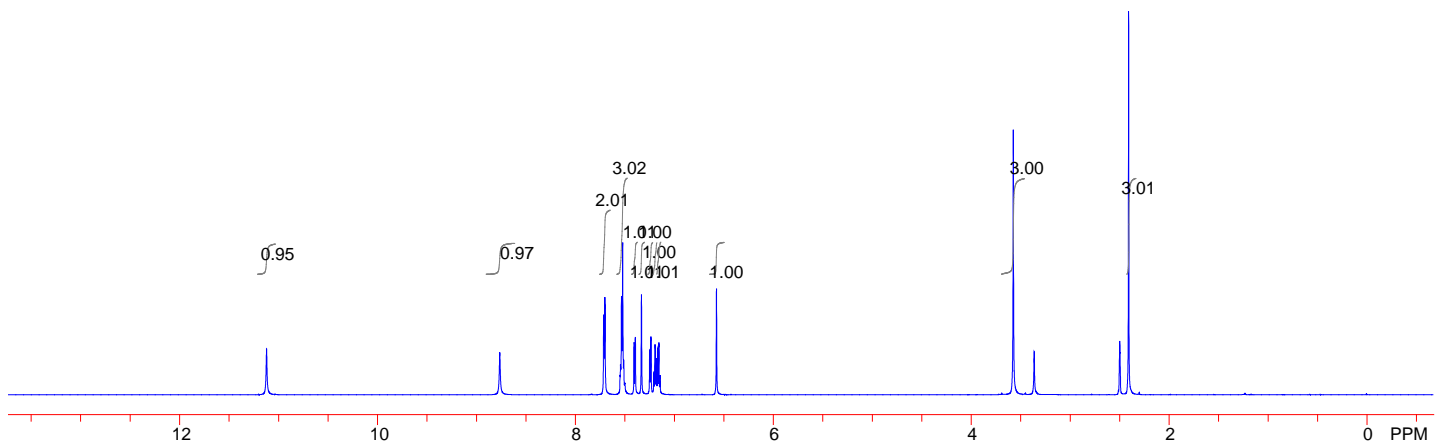


**3ja**  
<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

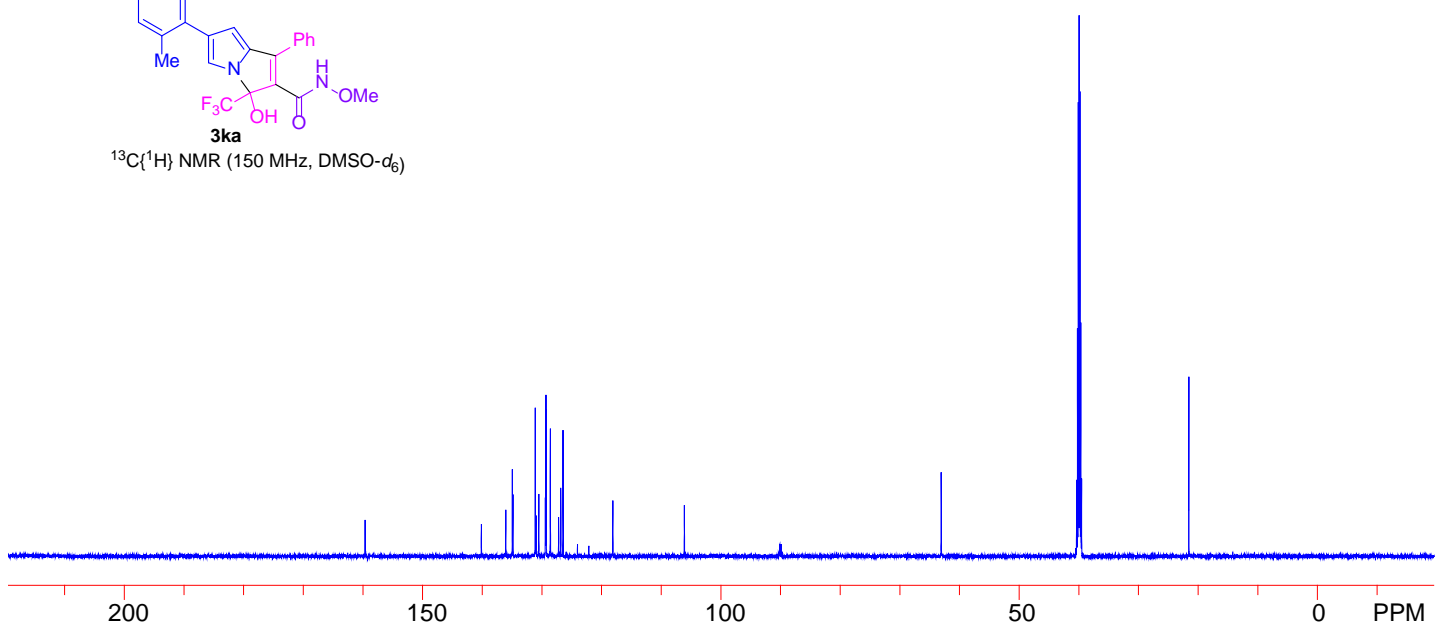
0 -50 -100 -150 -200 PPM



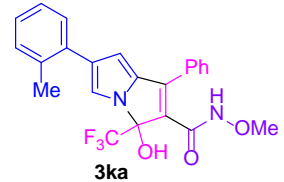
<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>)



<sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-d<sub>6</sub>)

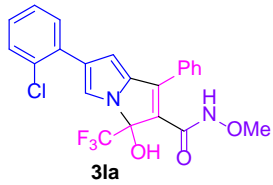
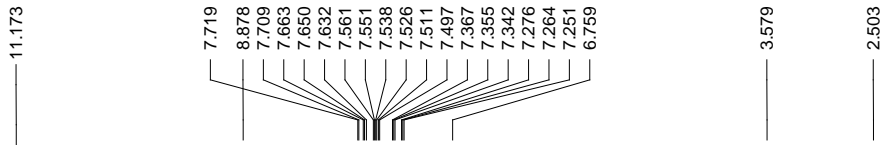


80.129

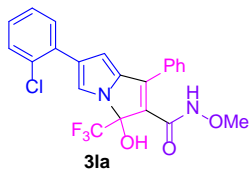
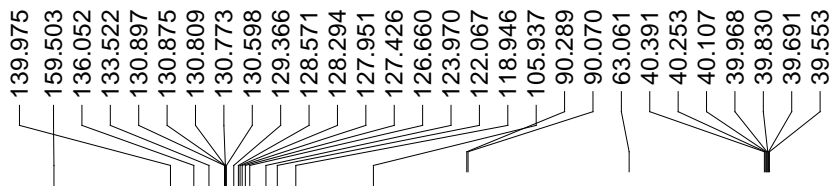
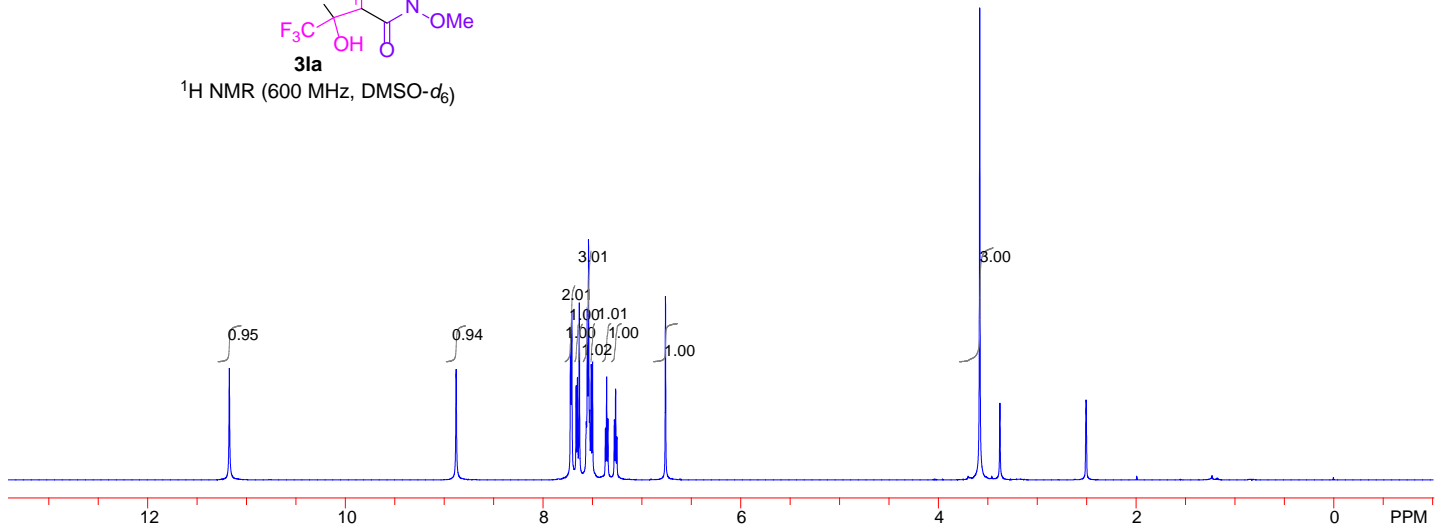


<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

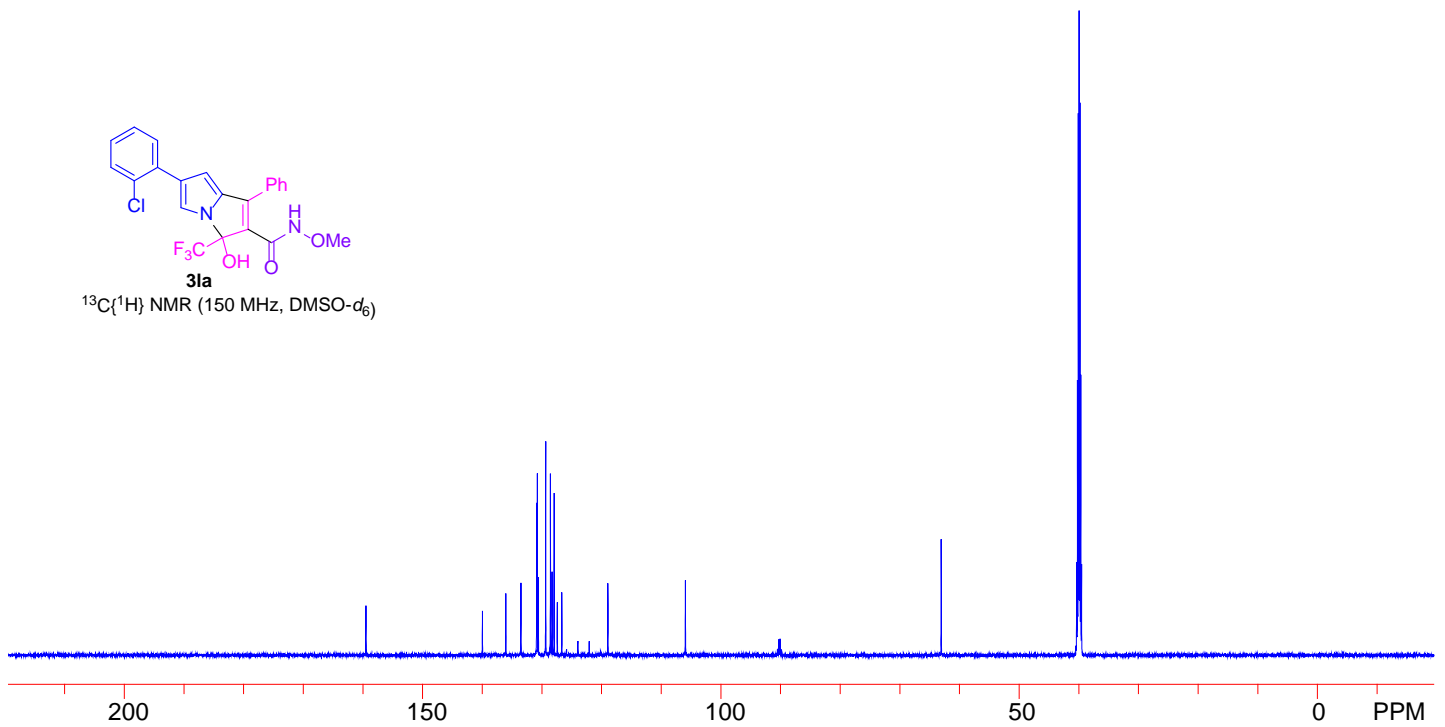
0 -50 -100 -150 -200 PPM



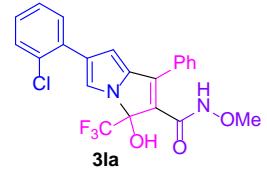
$^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )



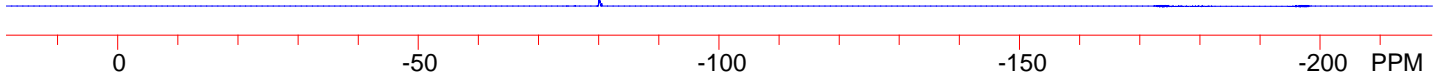
$^{13}\text{C}$  NMR (150 MHz, DMSO- $d_6$ )

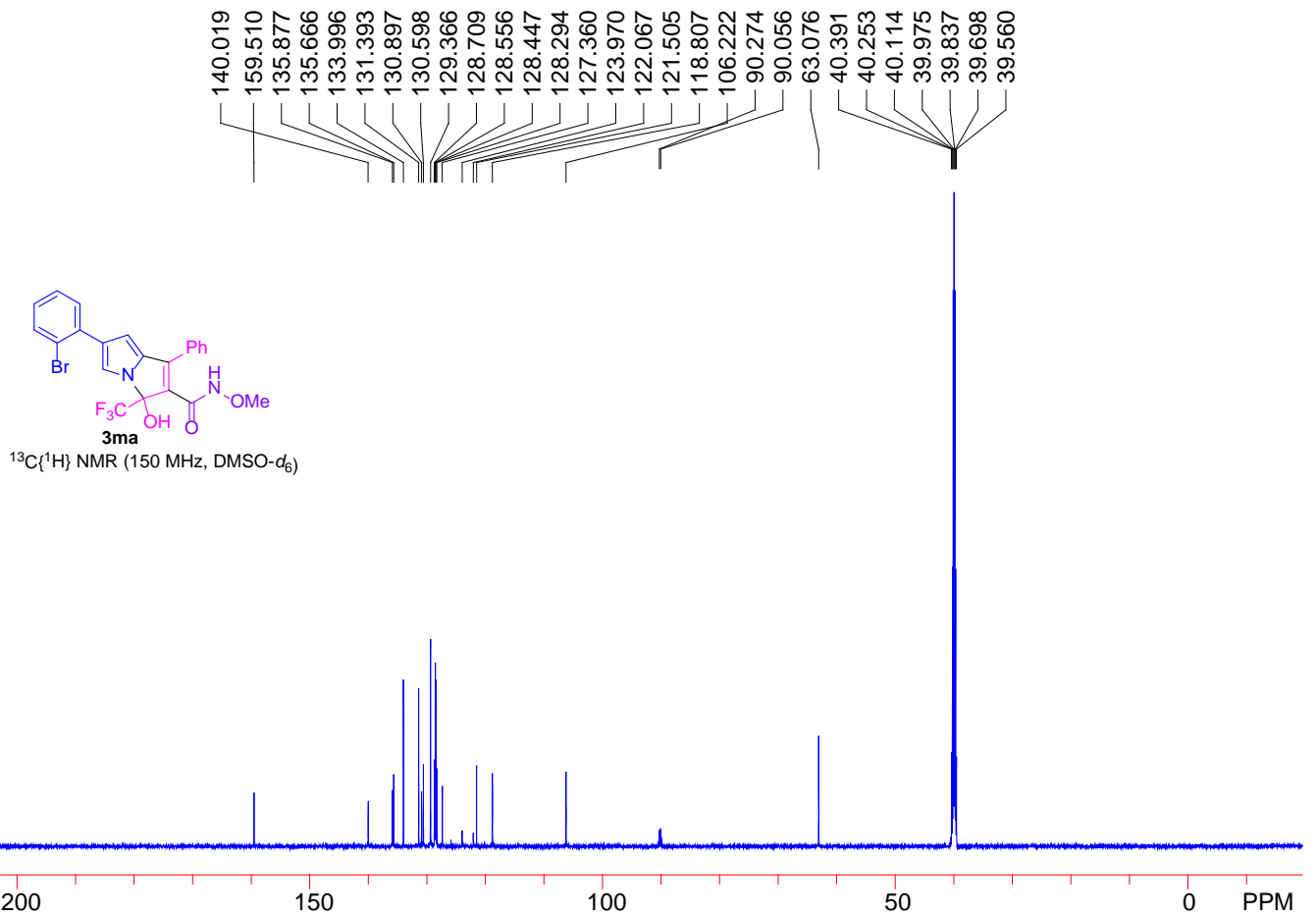
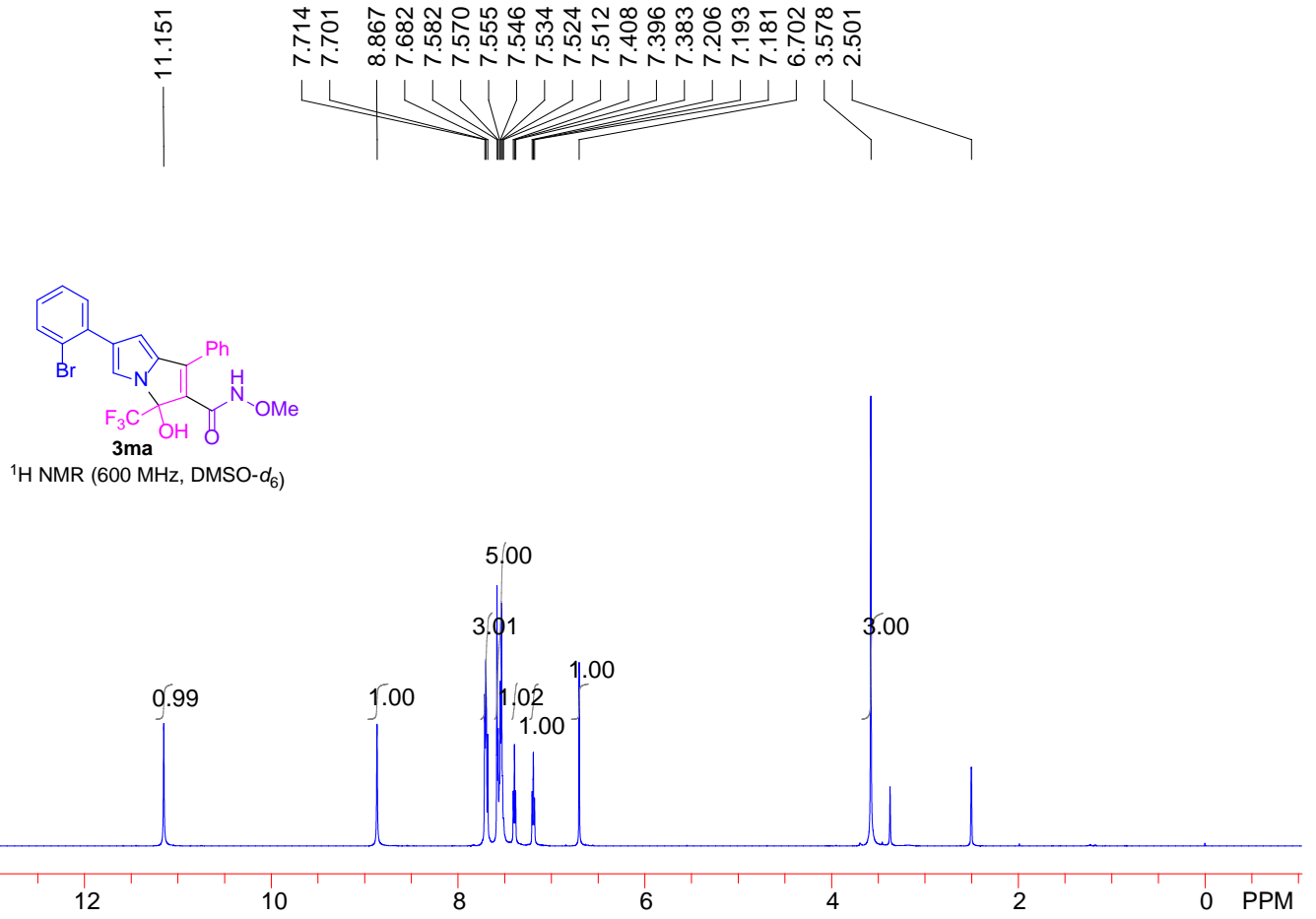


80.132

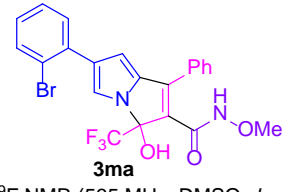


**3a**  
<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

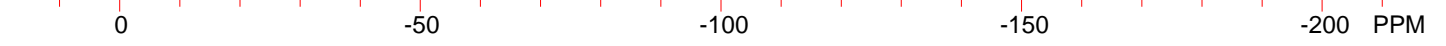


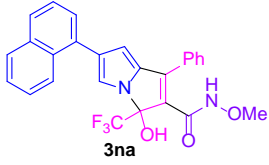
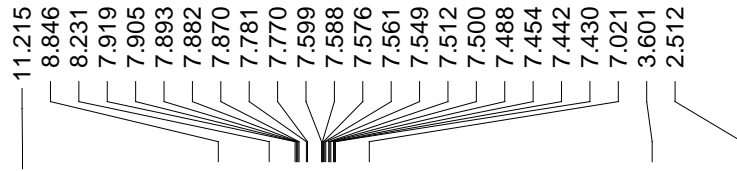


80.129

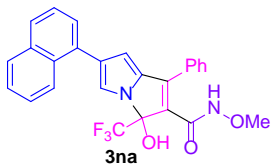
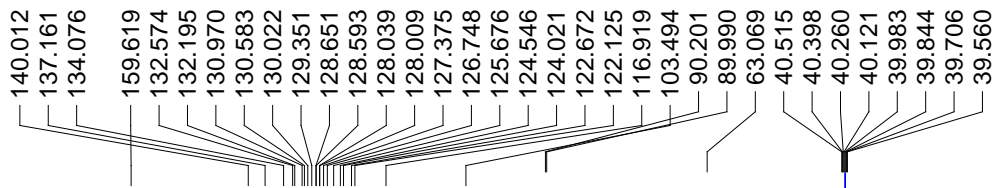
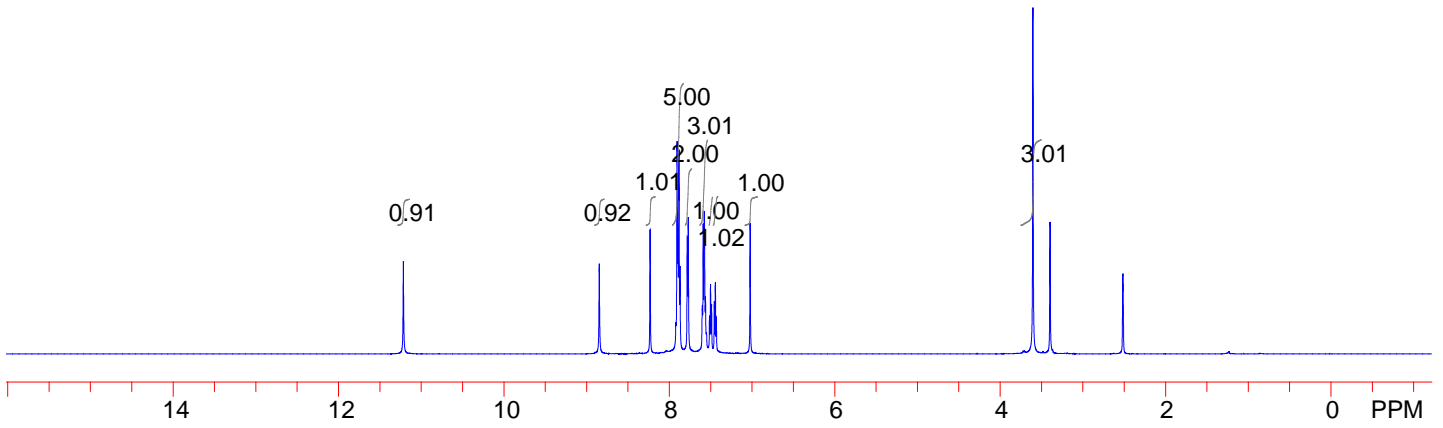


<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

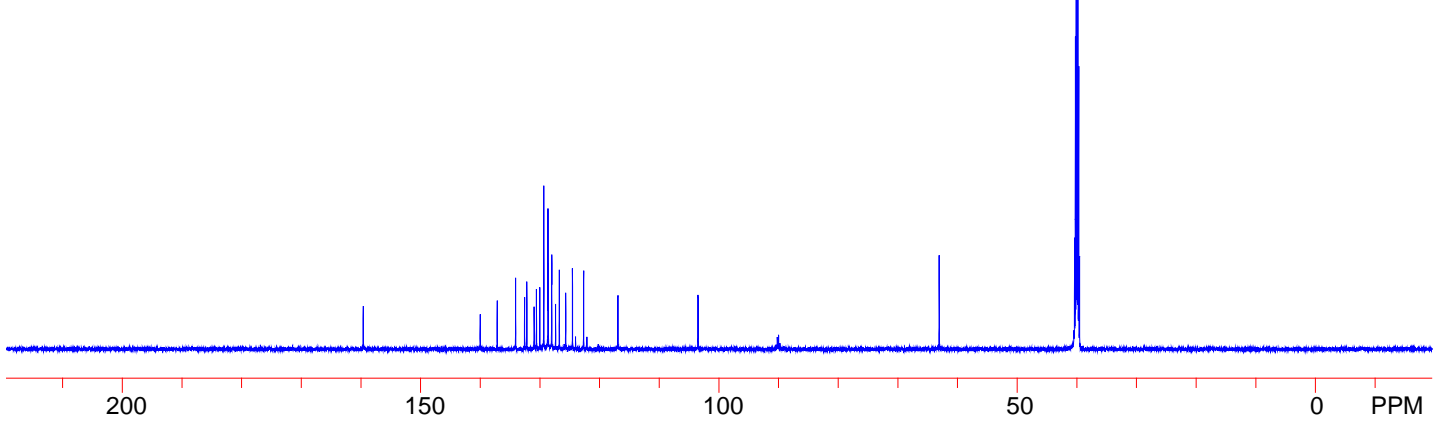




$^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )

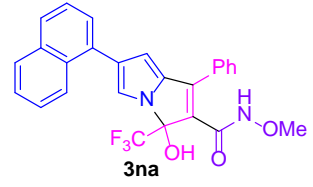


$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ )



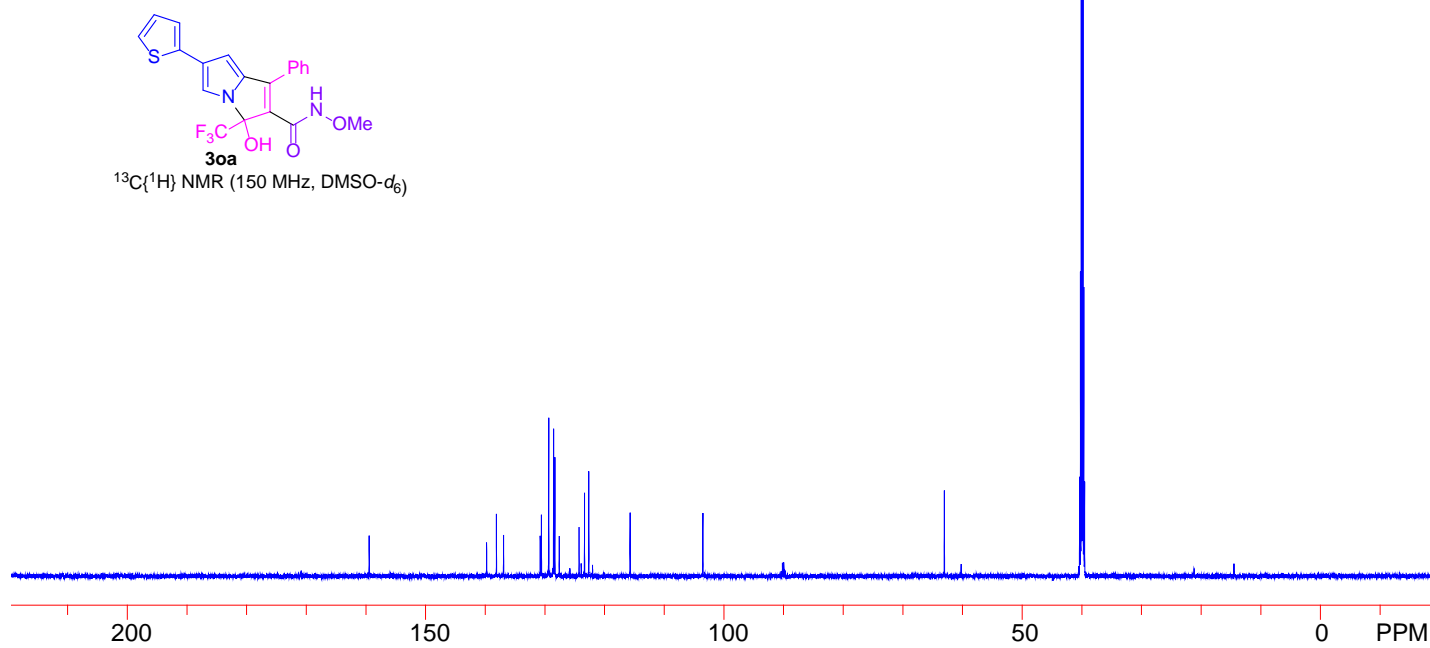
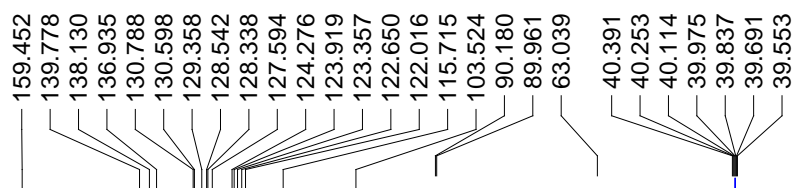
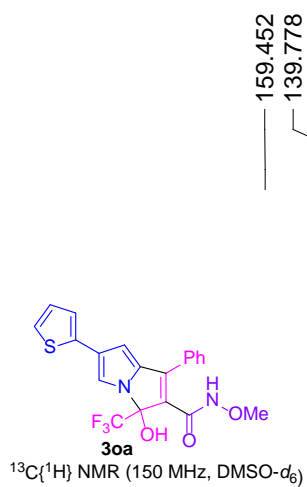
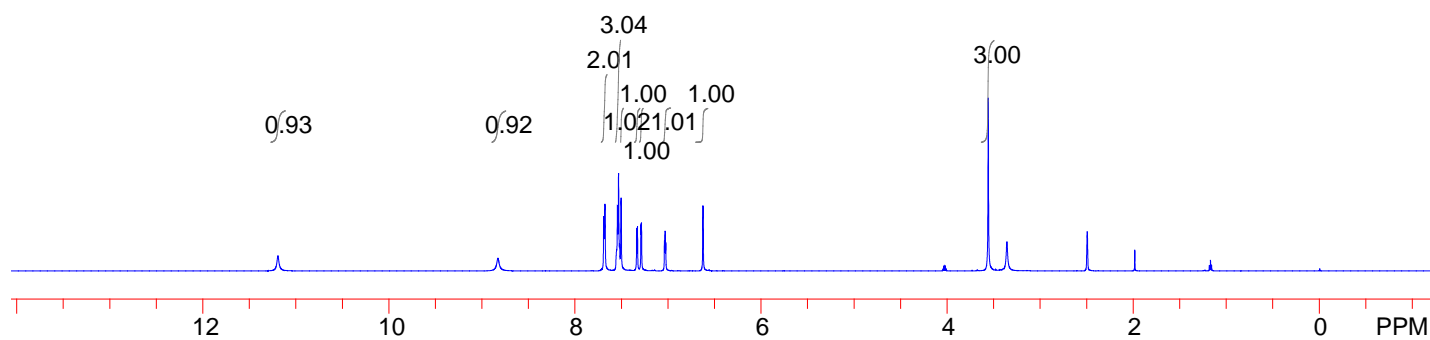
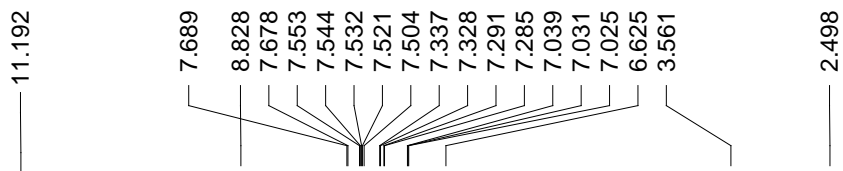
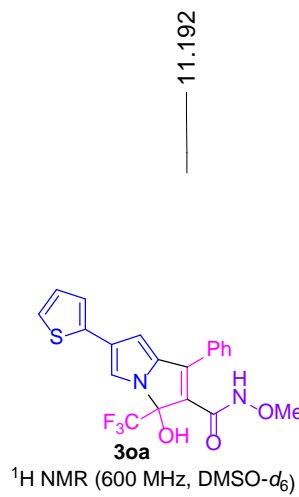


80.027

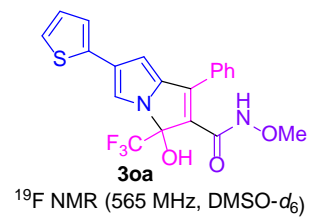


<sup>19</sup>F NMR (565 MHz, DMSO-d<sub>6</sub>)

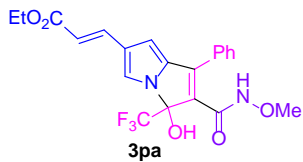
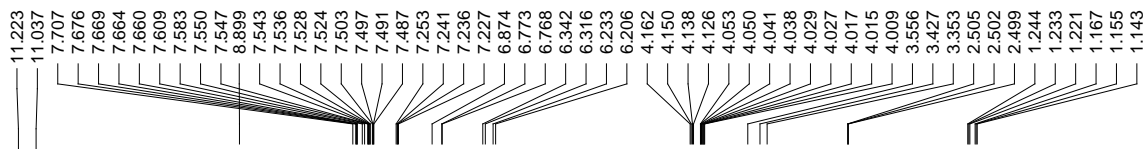
0 -50 -100 -150 -200 PPM



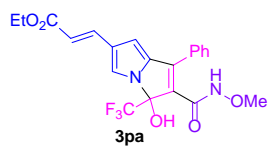
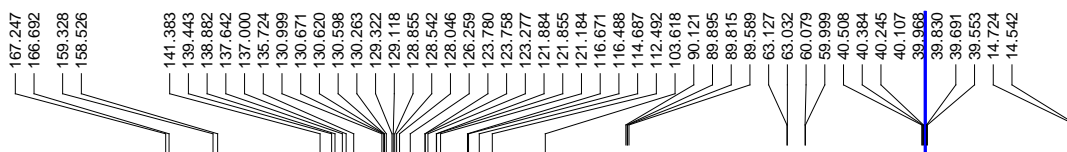
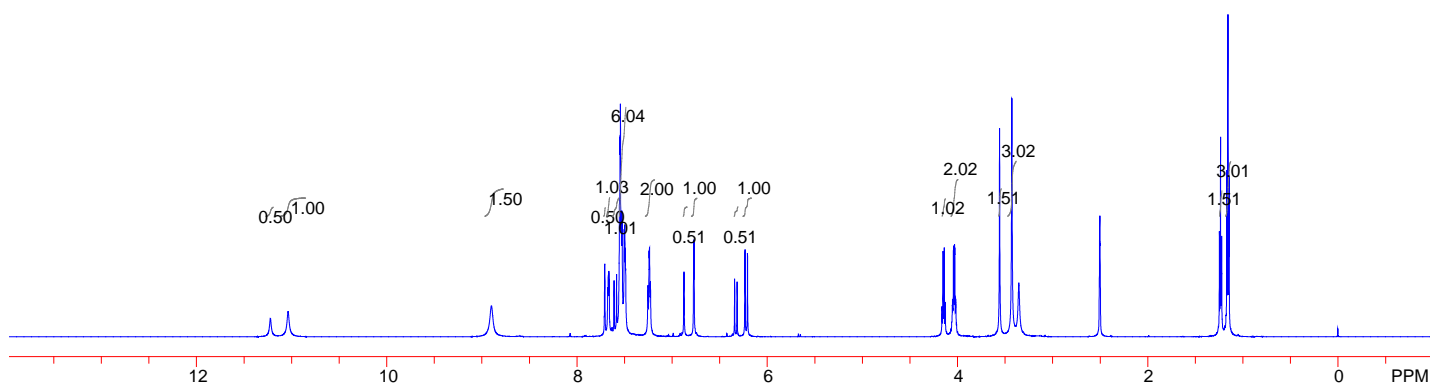
80.139



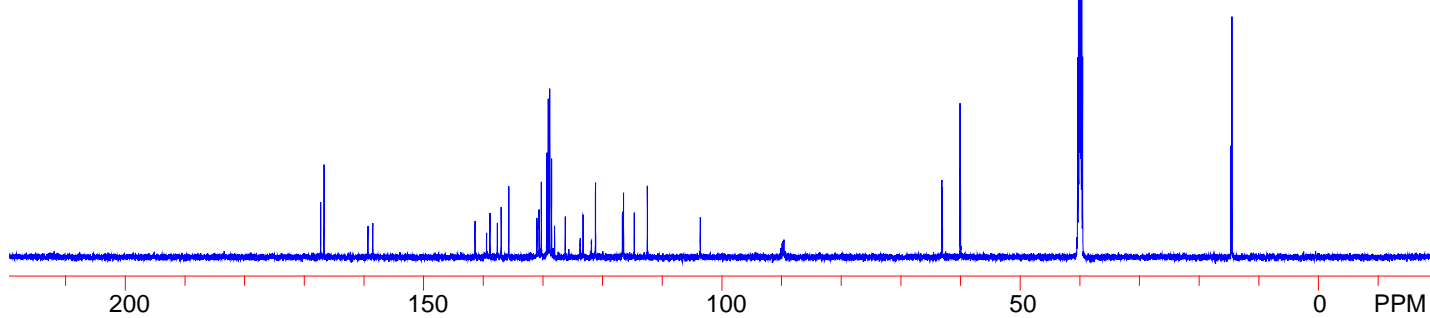
0 -50 -100 -150 -200 PPM



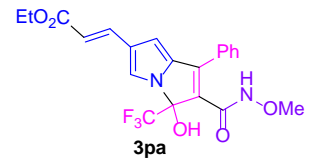
$^1\text{H}$  NMR (600 MHz,  $\text{DMSO}-d_6$ )



$^{13}\text{C}$  NMR (150 MHz,  $\text{DMSO}-d_6$ )

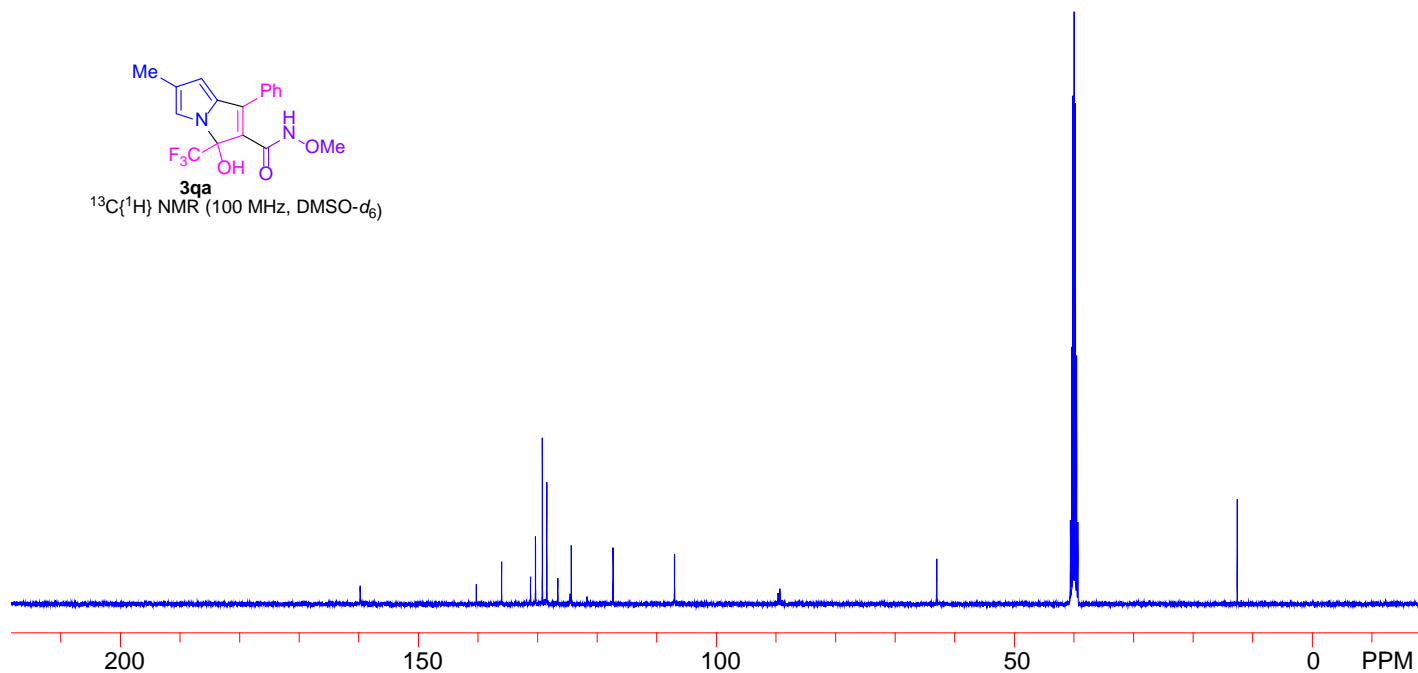
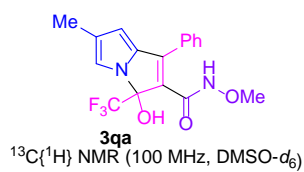
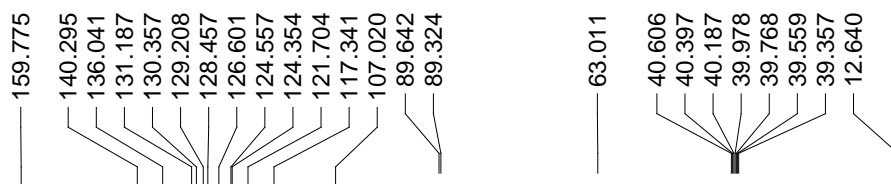
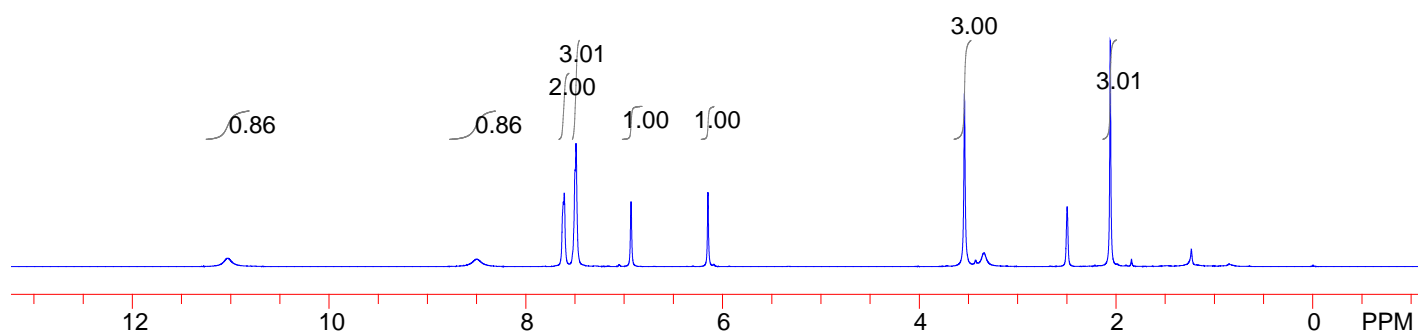
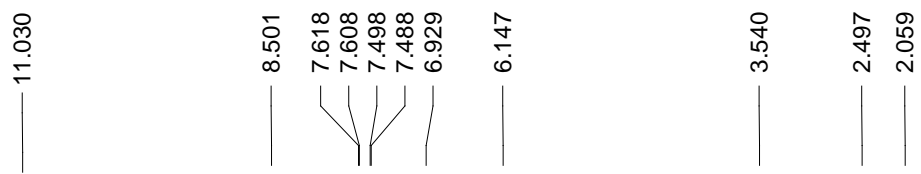
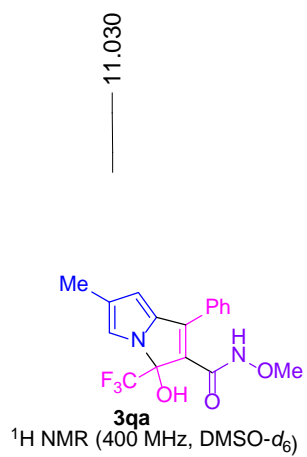


80.143  
80.208

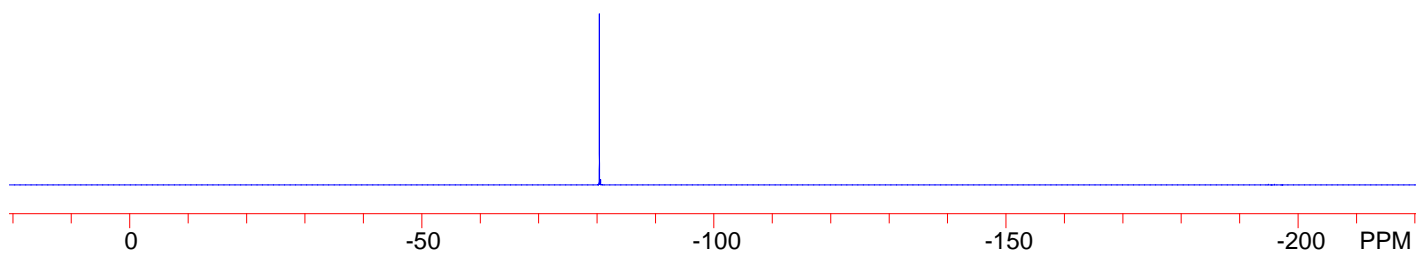
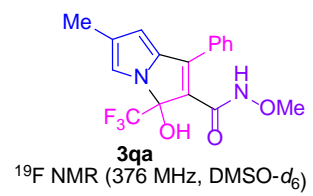


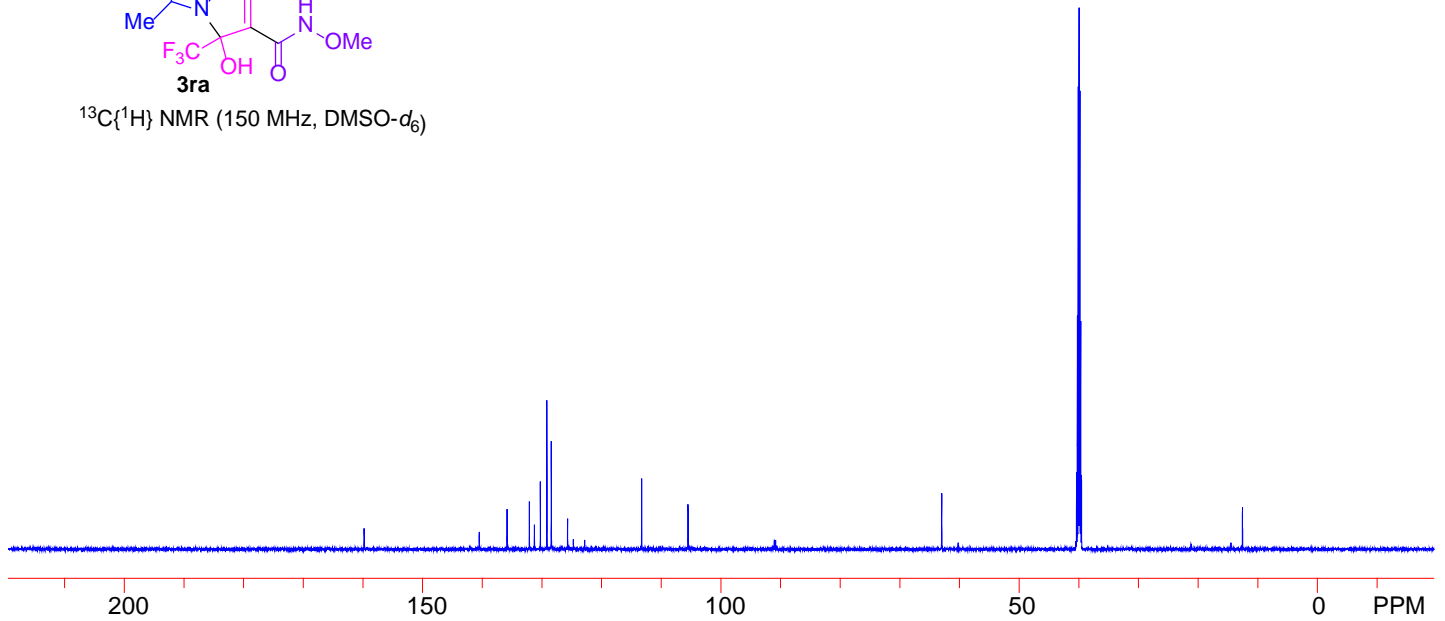
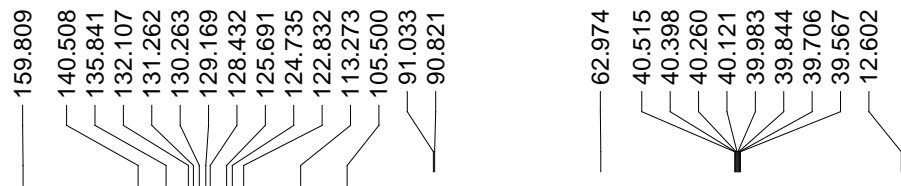
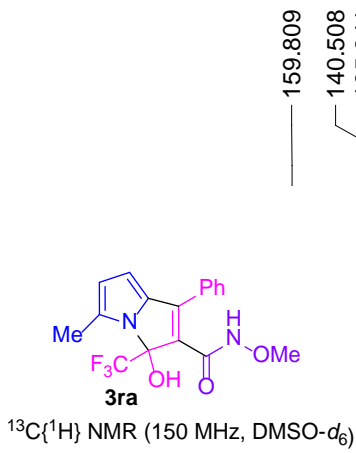
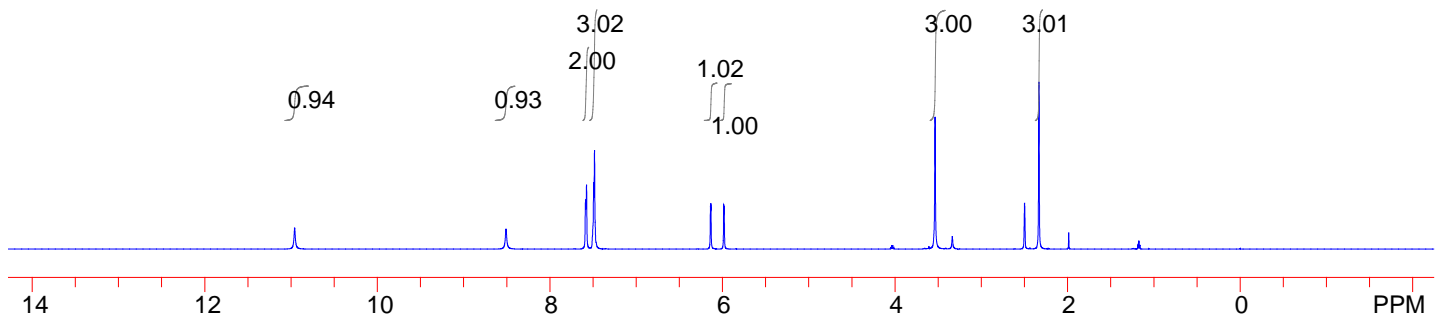
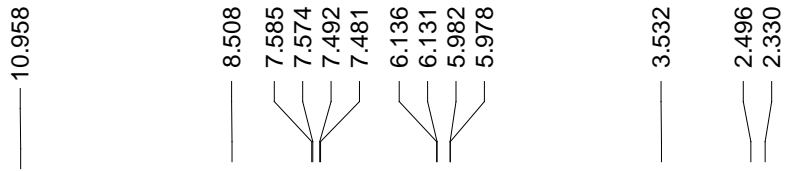
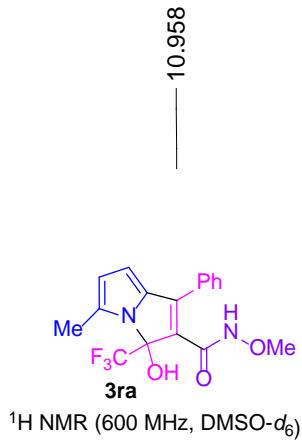
$^{19}F$  NMR (565 MHz,  $DMSO-d_6$ )

0 -50 -100 -150 -200 PPM



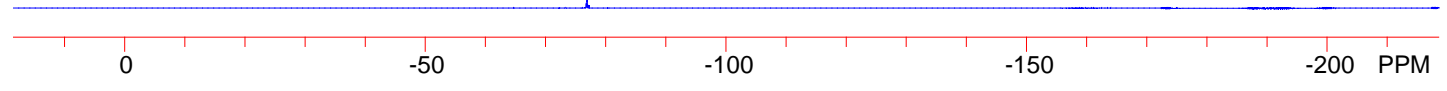
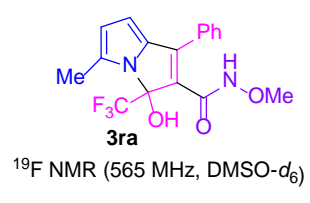
-80.375

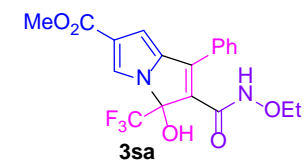




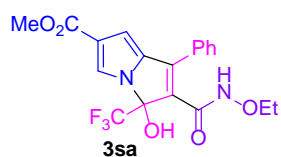
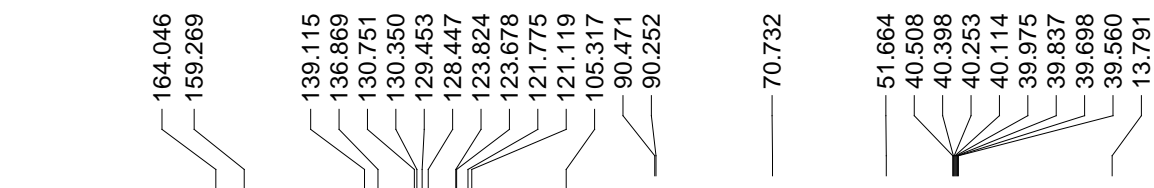
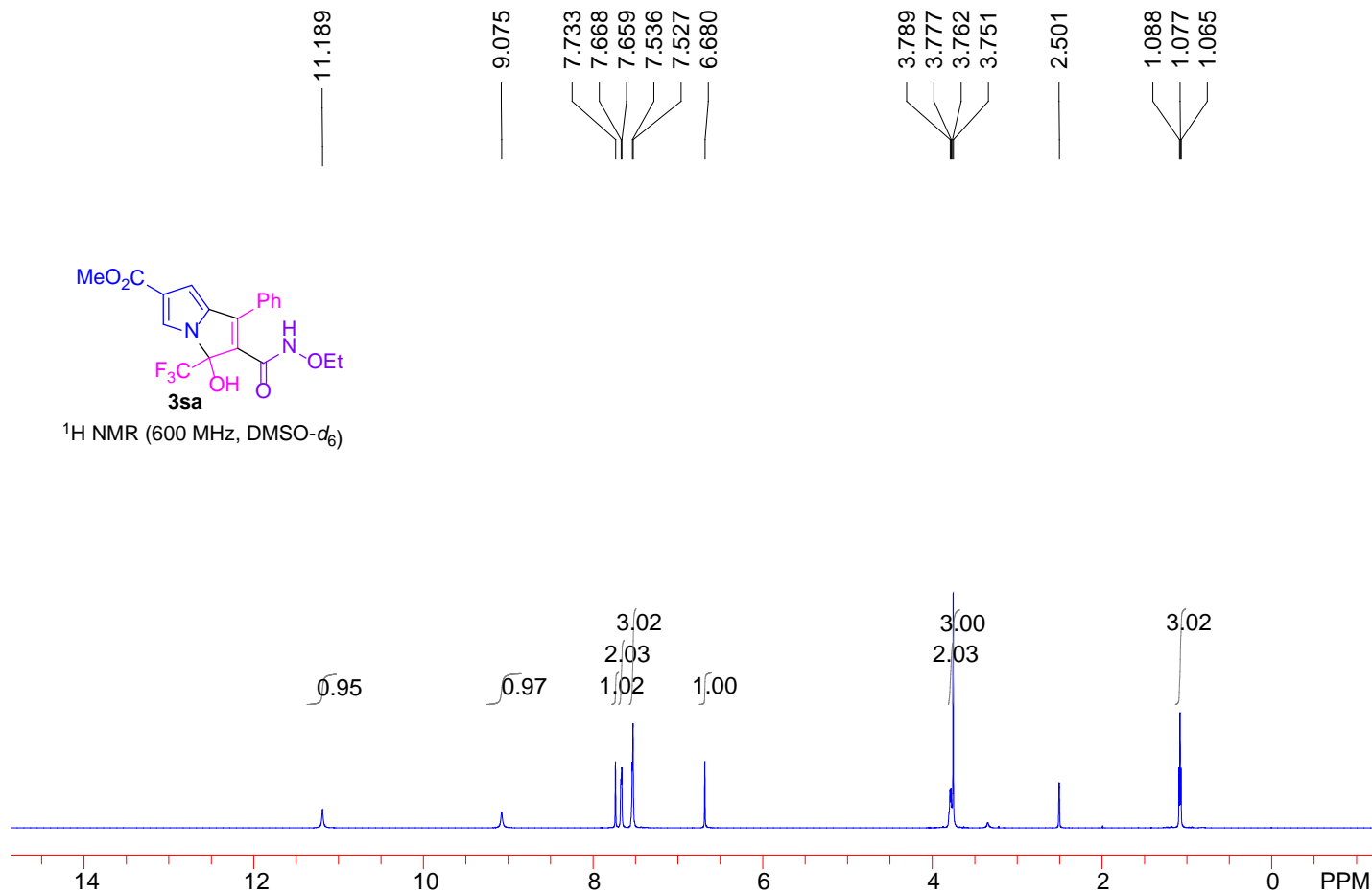


76.880

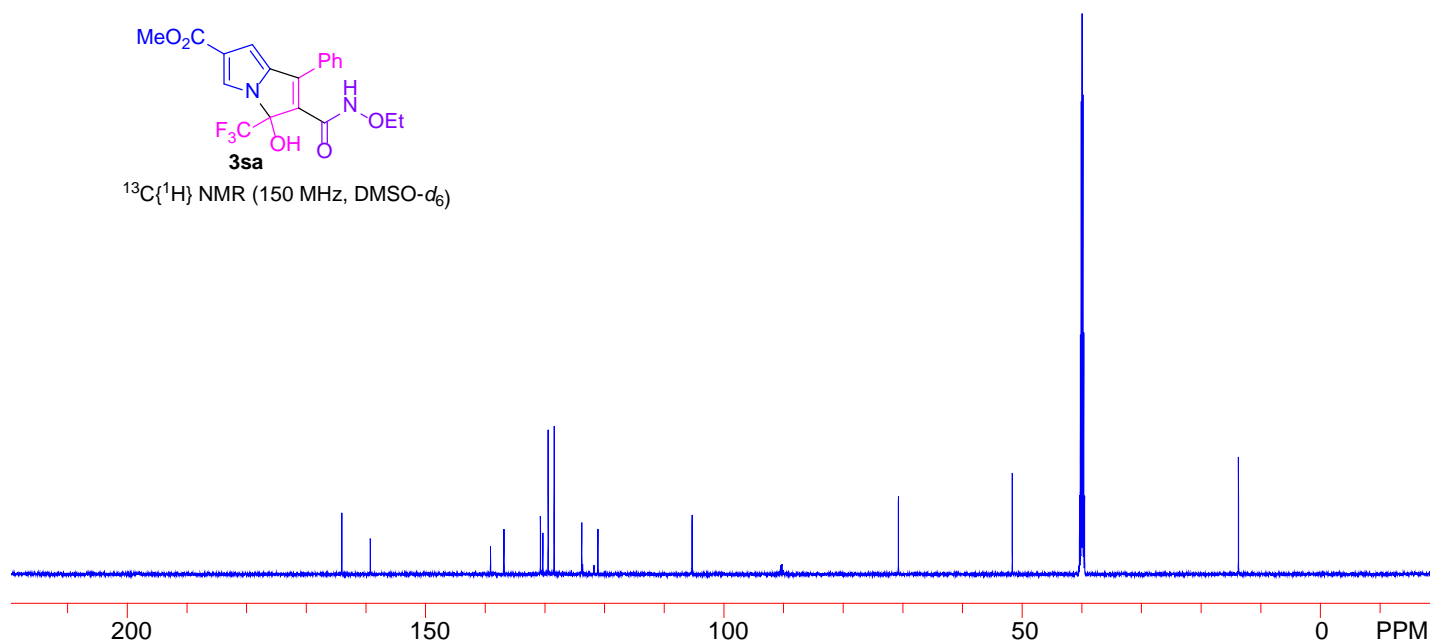




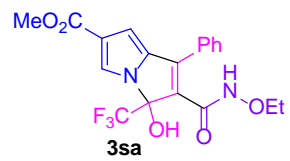
$^1\text{H}$  NMR (600 MHz,  $\text{DMSO-}d_6$ )



$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ )

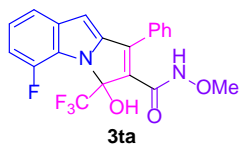
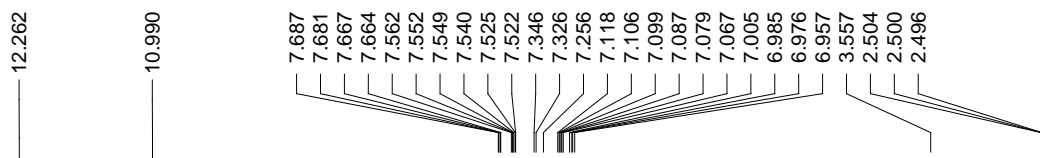


80.291

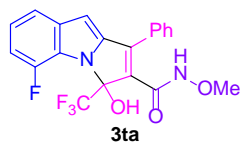
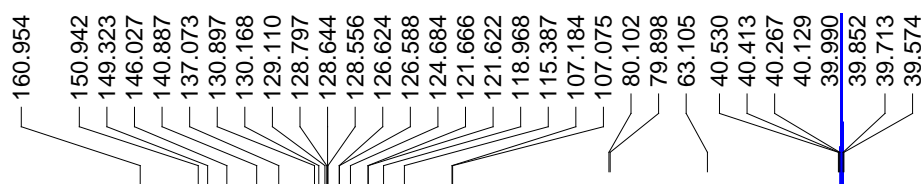
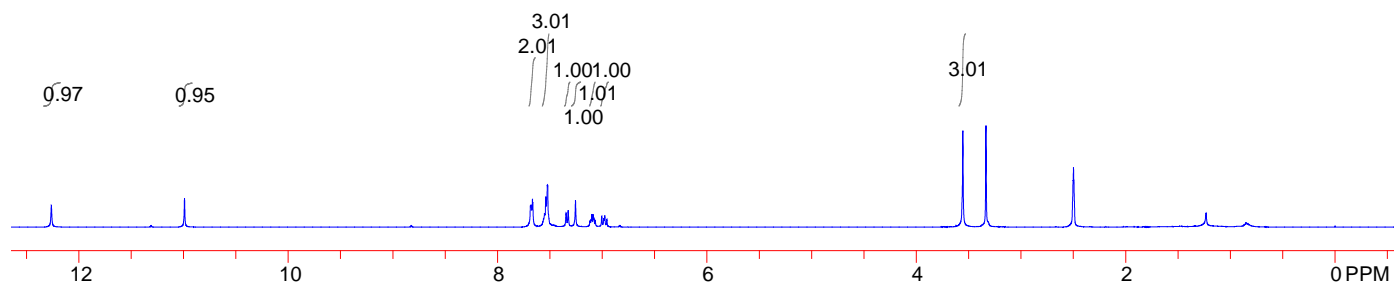


$^{19}\text{F}$  NMR (565 MHz,  $\text{DMSO-}d_6$ )

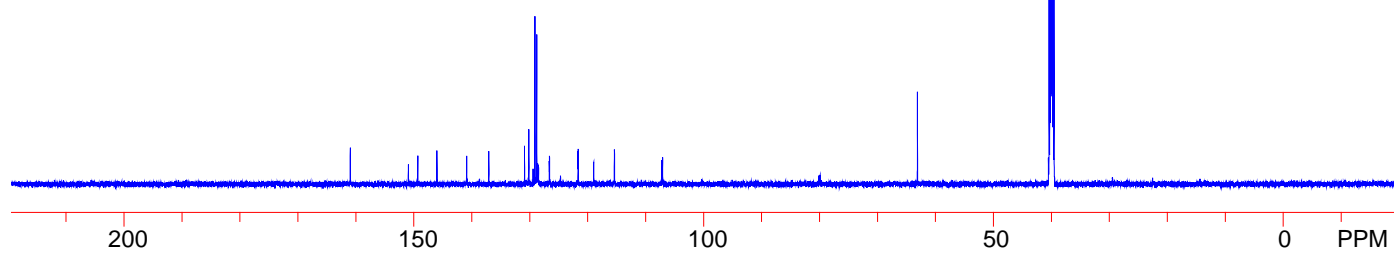
0 -50 -100 -150 -200 PPM

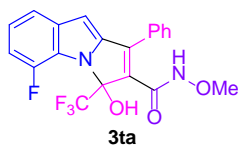


$^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )

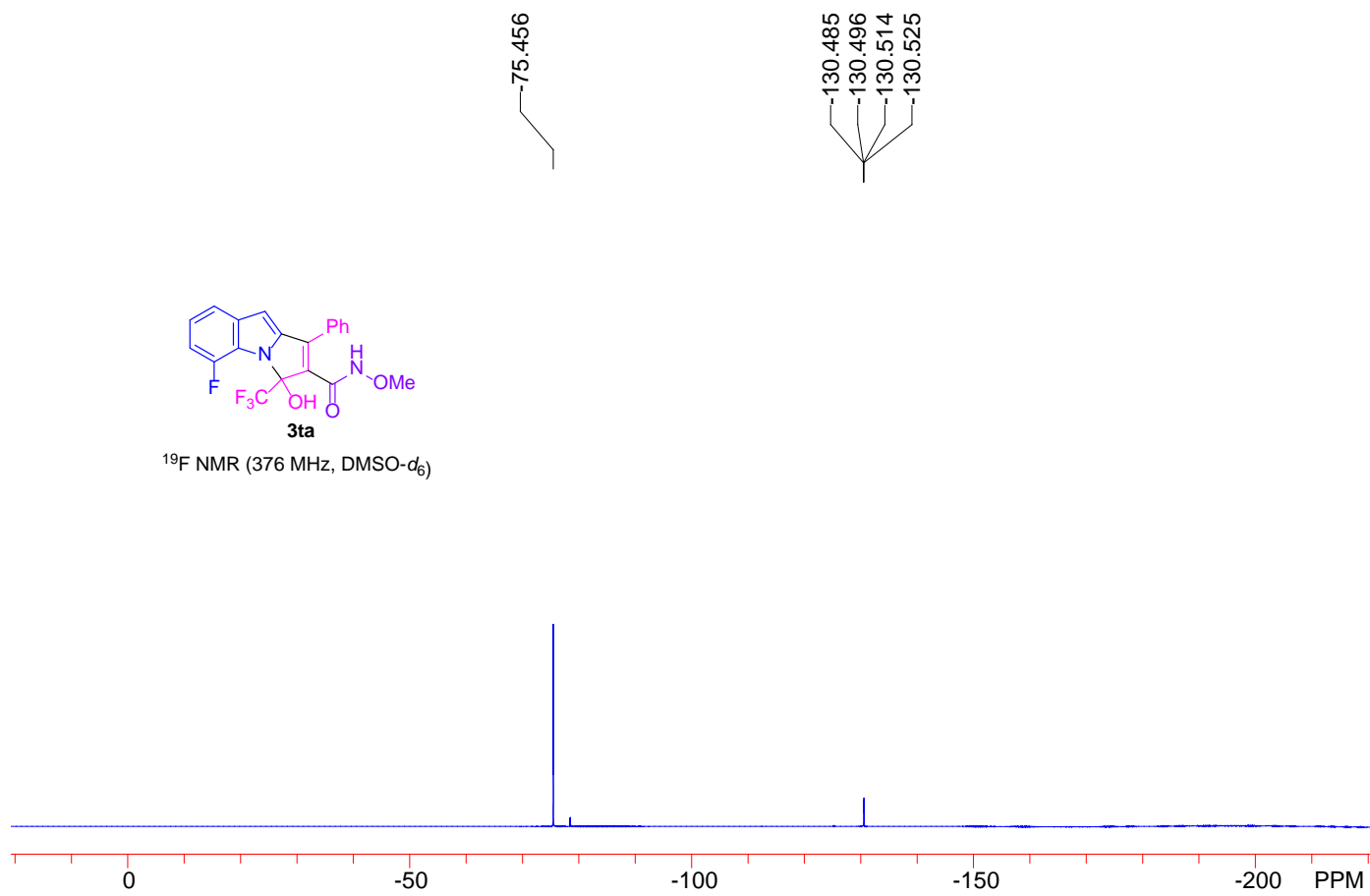


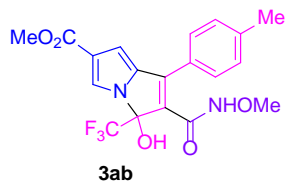
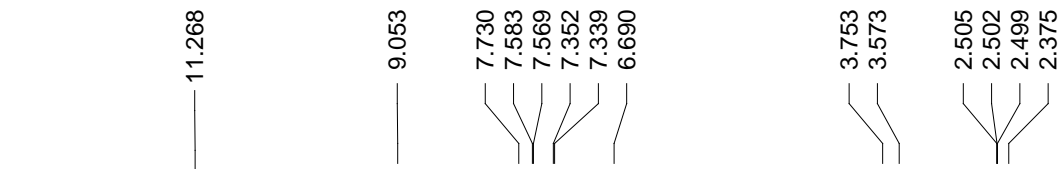
$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ )



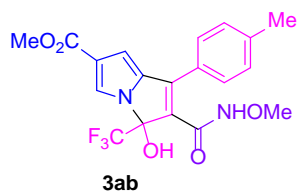
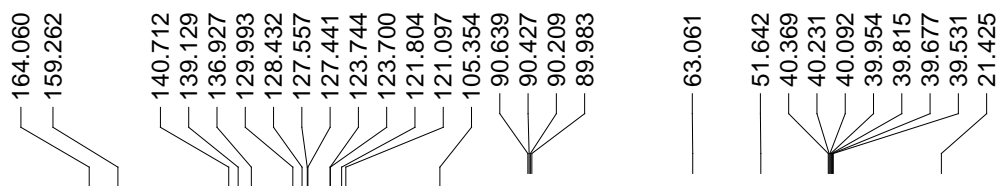
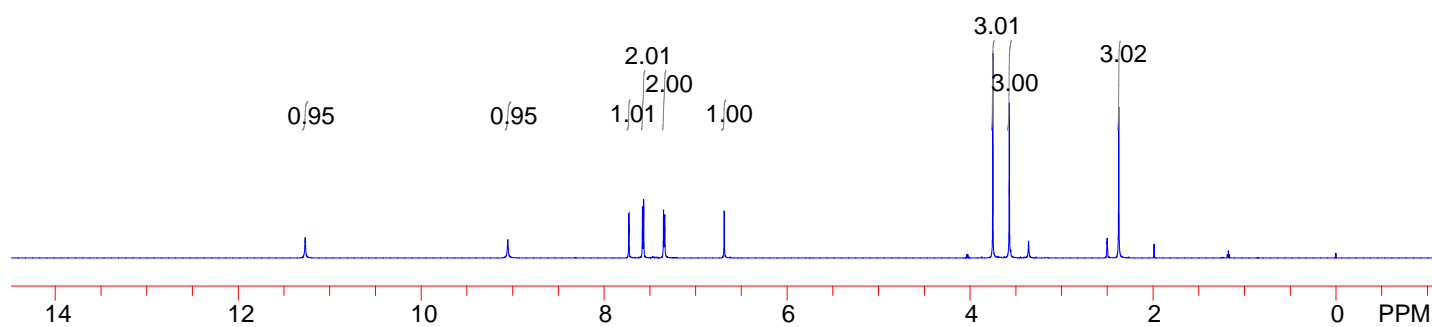


$^{19}\text{F}$  NMR (376 MHz,  $\text{DMSO-}d_6$ )

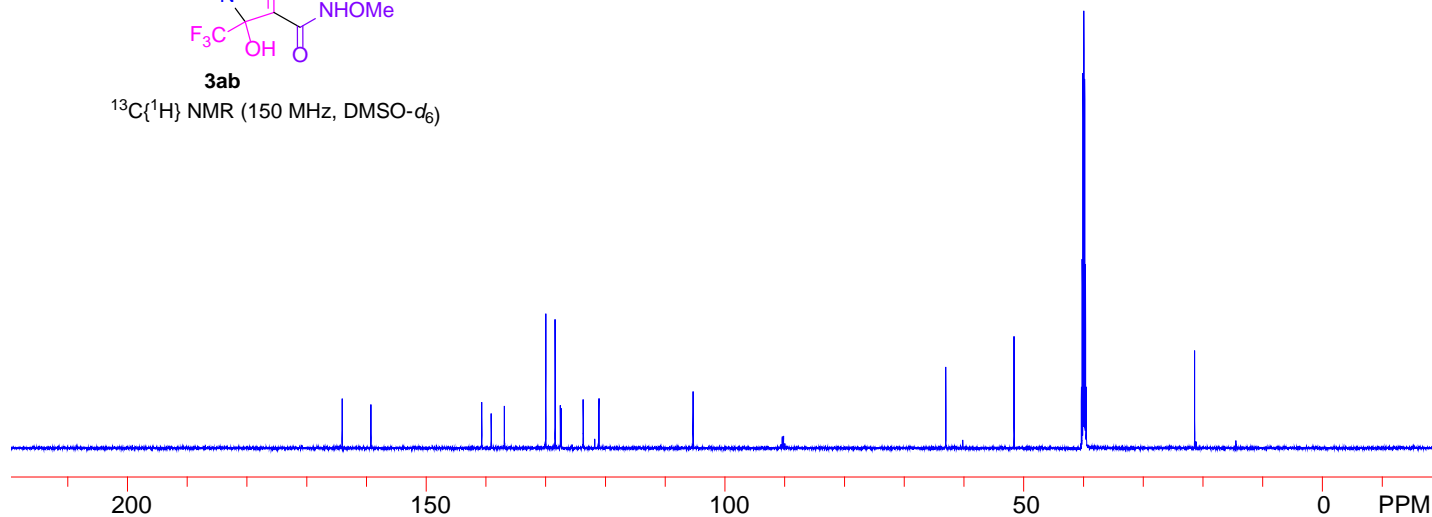




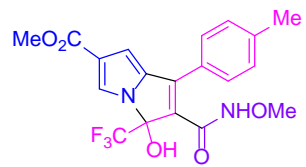
$^1\text{H}$  NMR (600 MHz,  $\text{DMSO-d}_6$ )



$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-d}_6$ )

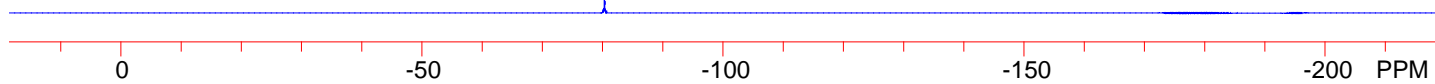


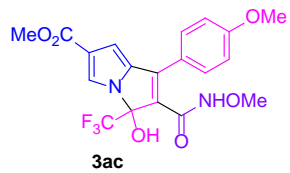
-80.288



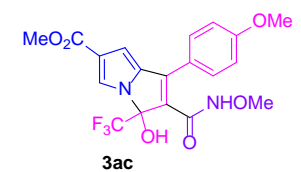
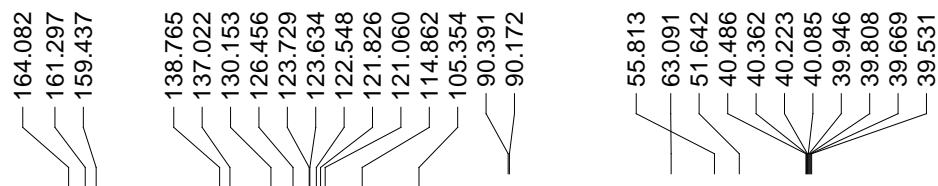
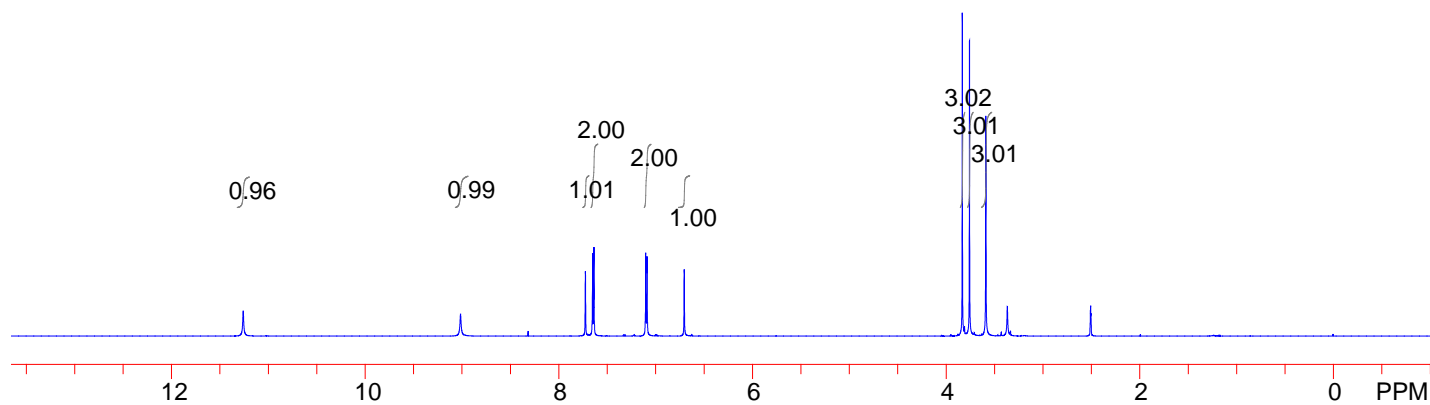
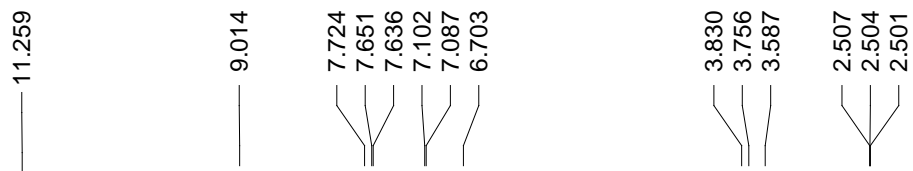
**3ab**

<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

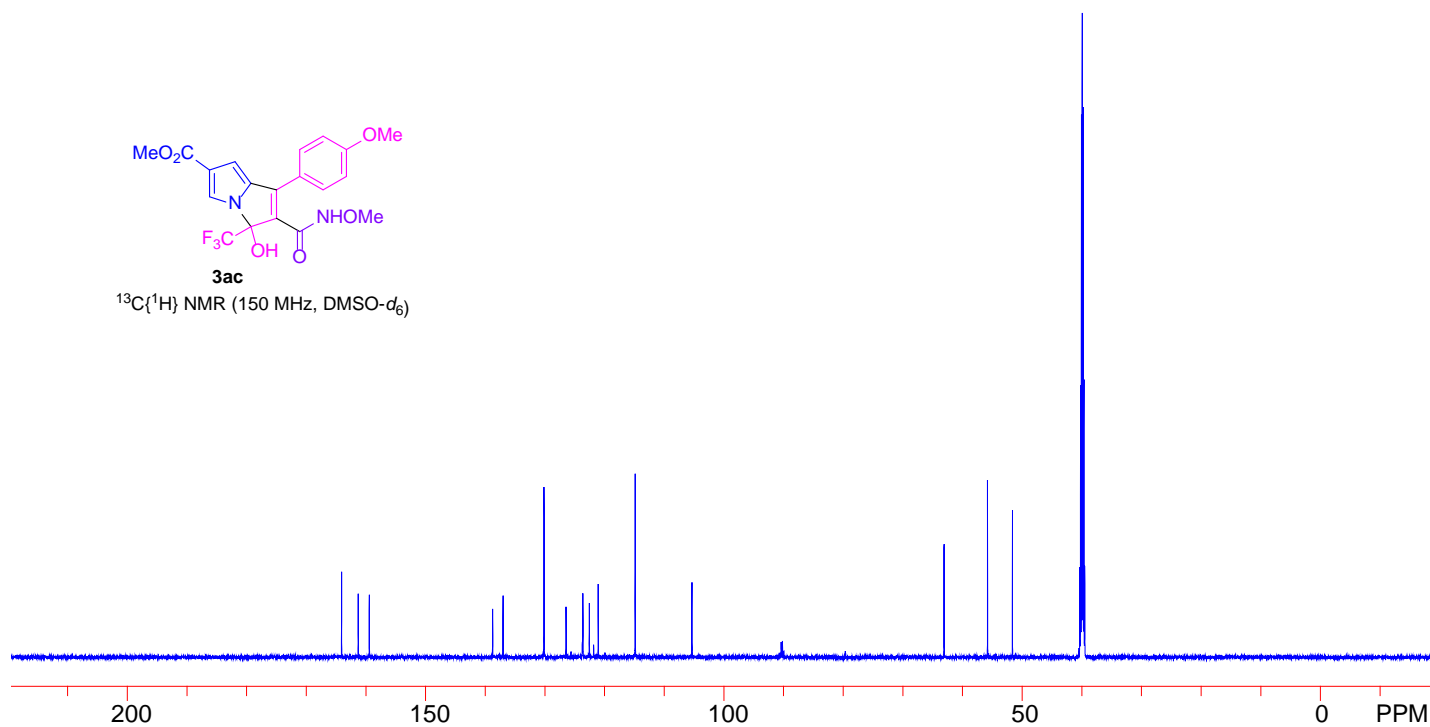




$^1\text{H NMR}$  (600 MHz,  $\text{DMSO-}d_6$ )

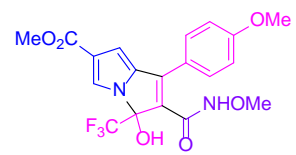


$^{13}\text{C}(^1\text{H}) \text{NMR}$  (150 MHz,  $\text{DMSO-}d_6$ )



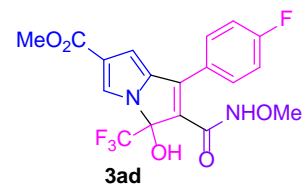
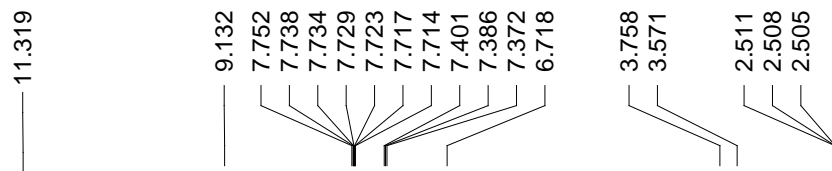


80.281

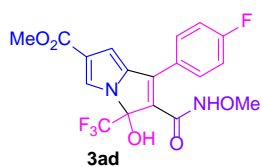
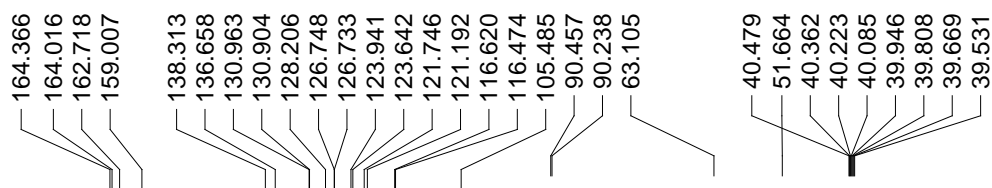
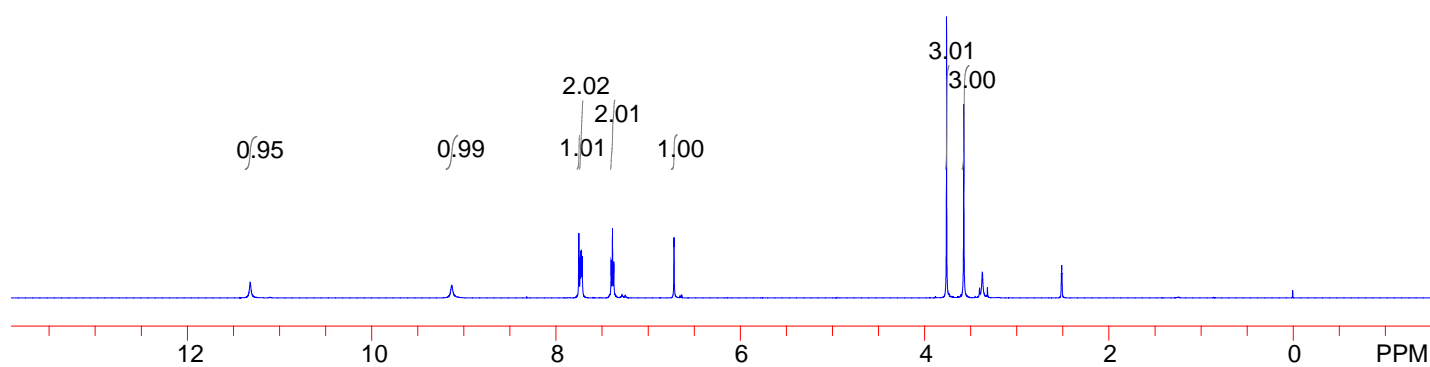


<sup>19</sup>F NMR (565 MHz, DMSO-d<sub>6</sub>)

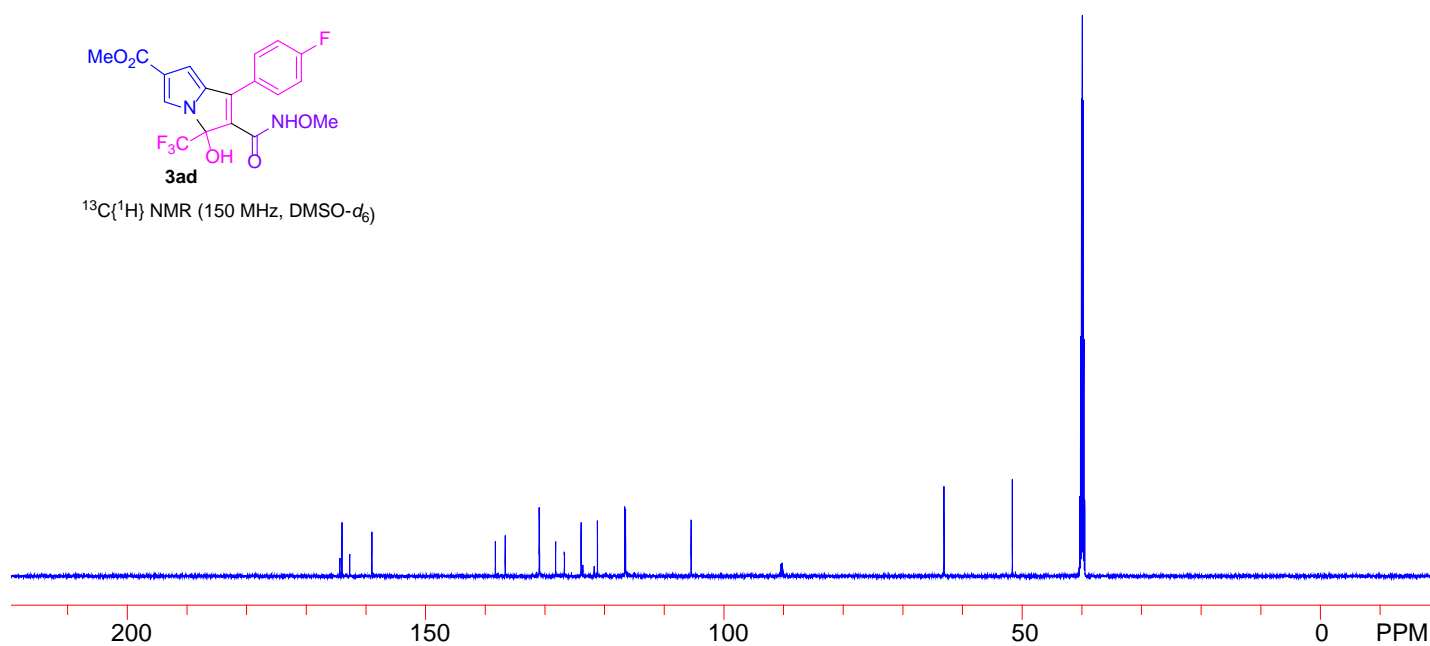
0 -50 -100 -150 -200 PPM

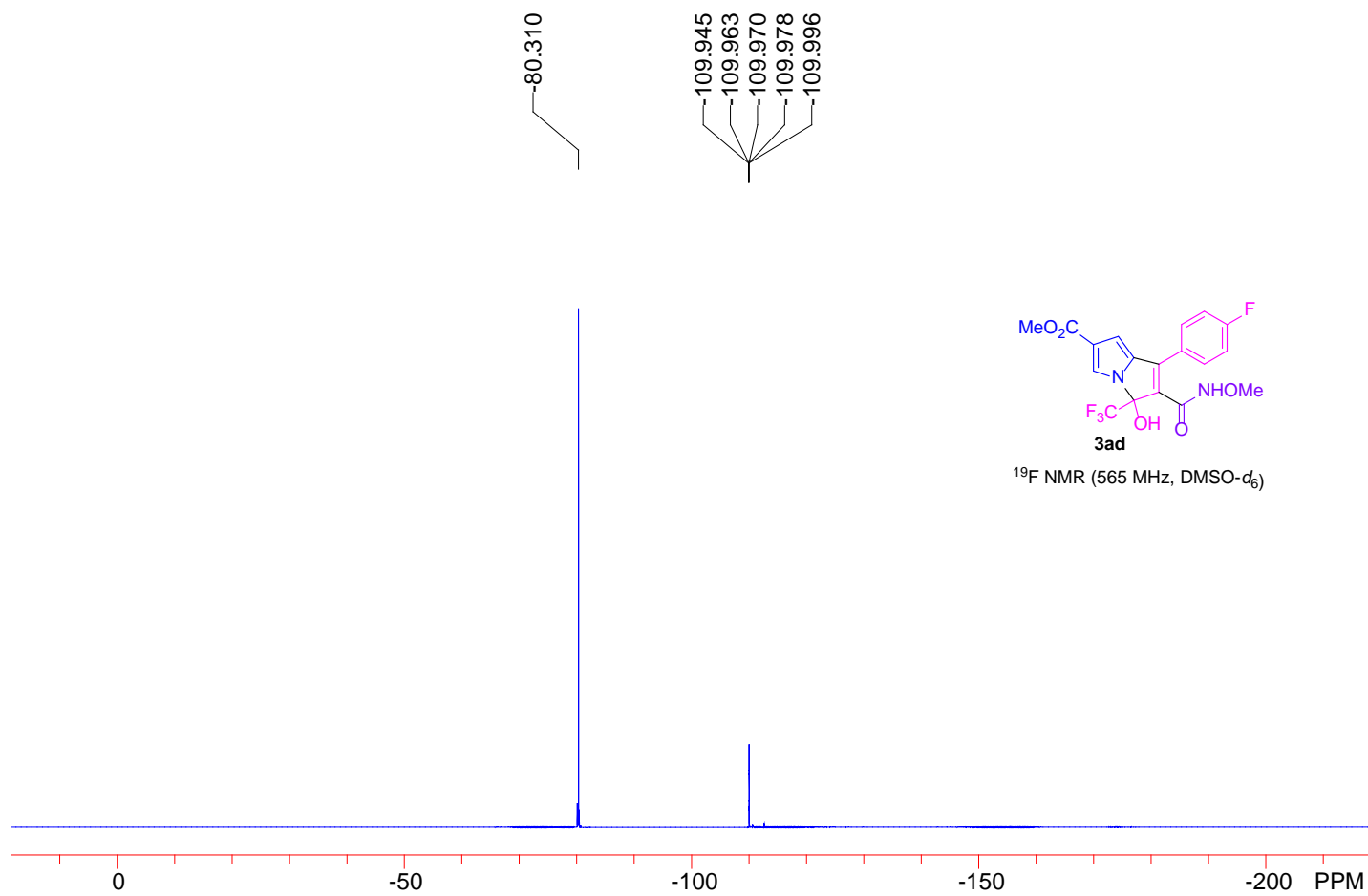


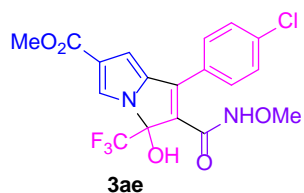
$^1\text{H}$  NMR (600 MHz,  $\text{DMSO-}d_6$ )



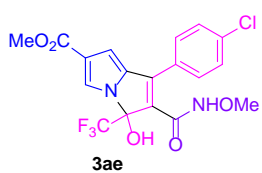
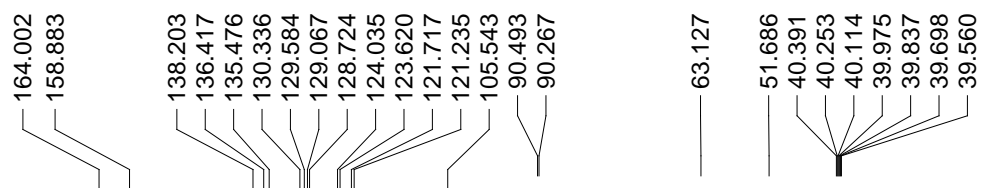
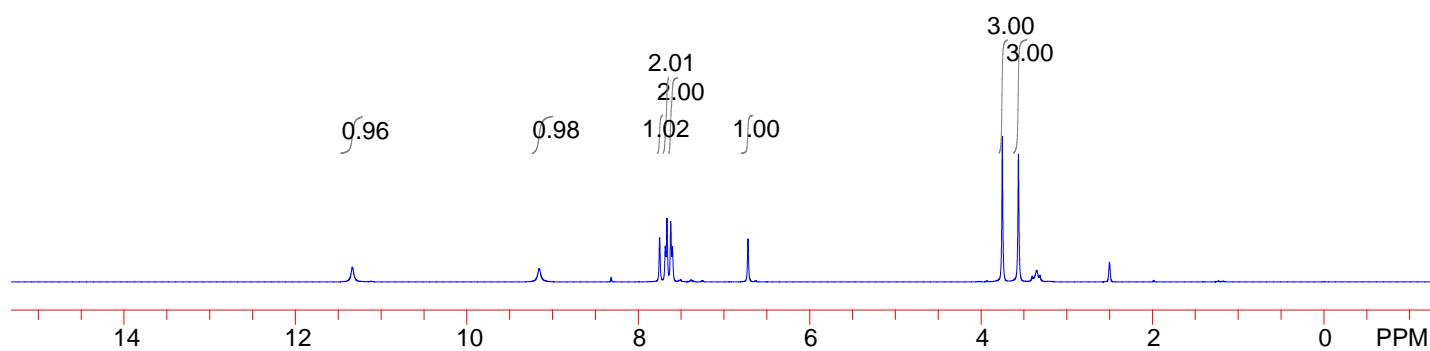
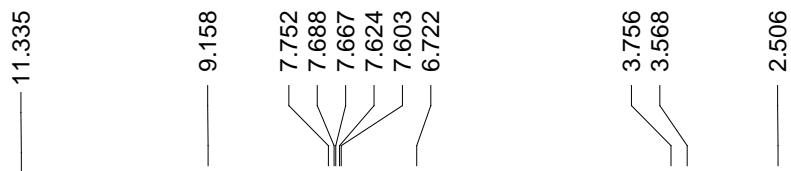
$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ )



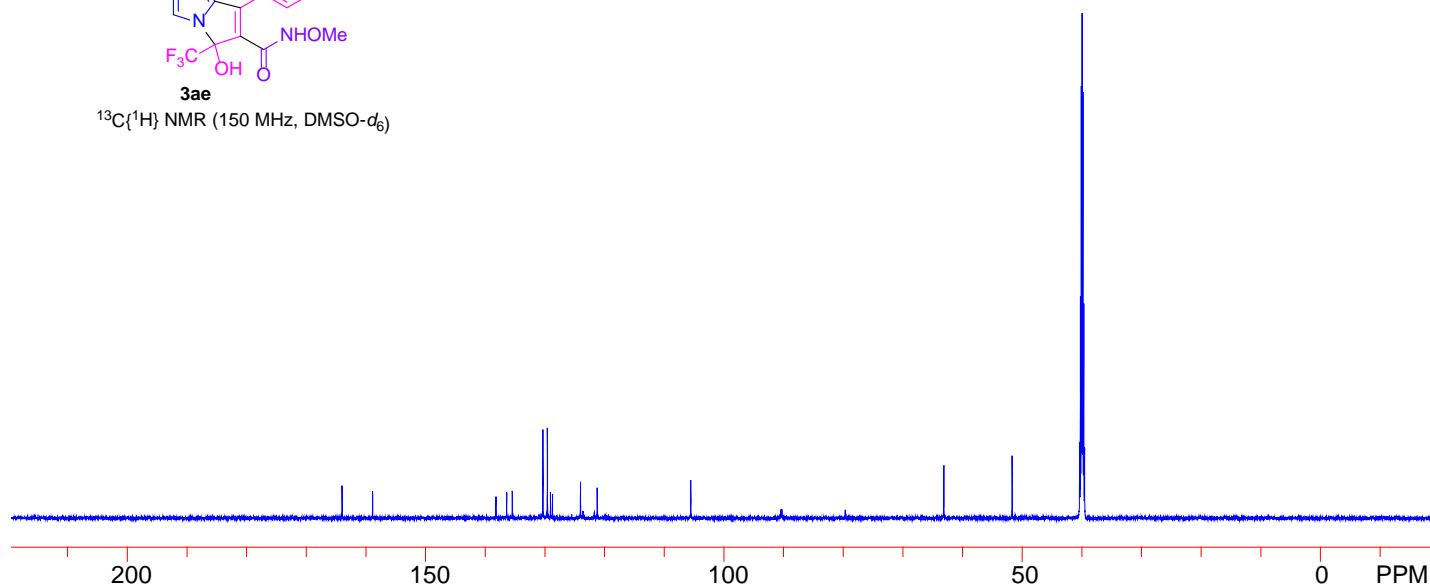




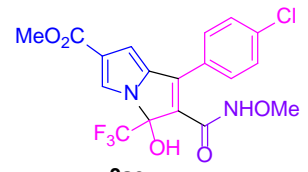
$^1\text{H NMR}$  (600 MHz,  $\text{DMSO-}d_6$ )



$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ )



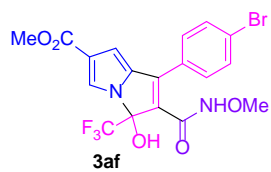
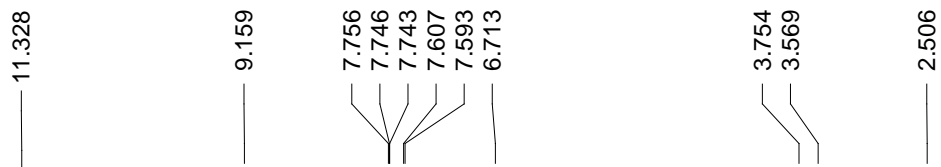
80.277



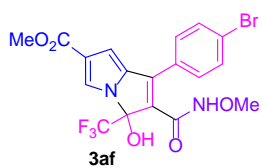
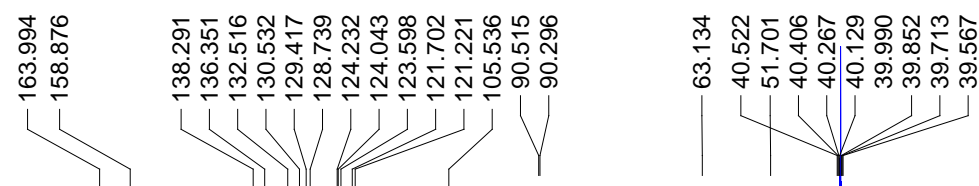
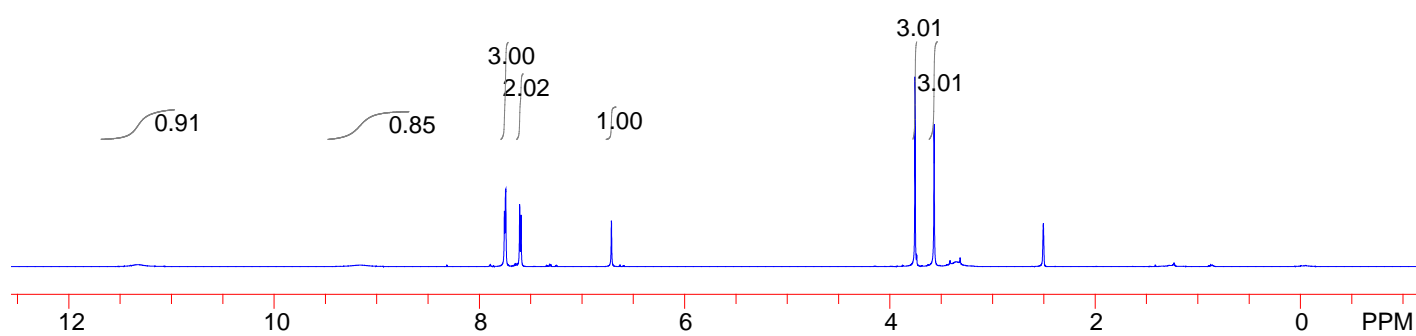
**3ae**

<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

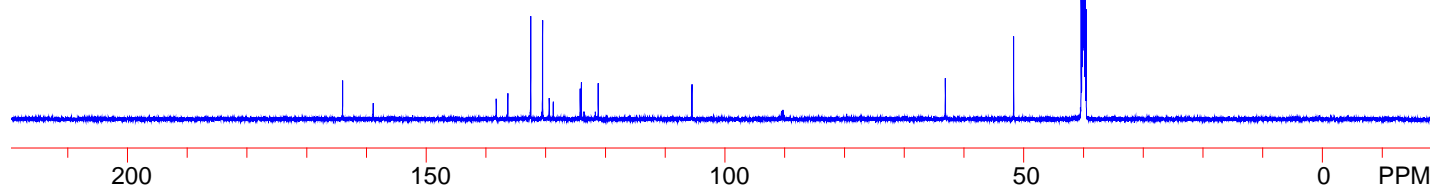
0 -50 -100 -150 -200 PPM



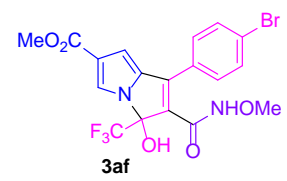
<sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)



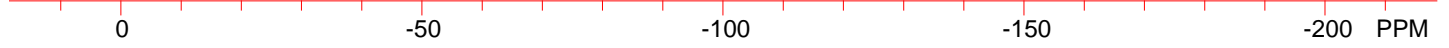
<sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>)

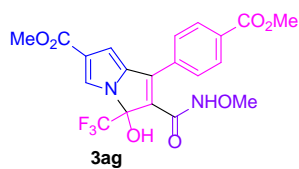


-80.270

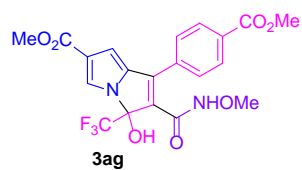
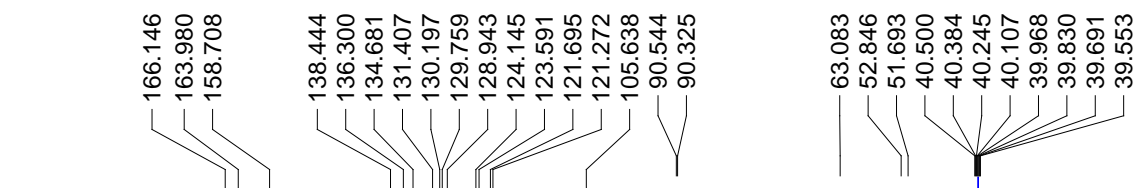
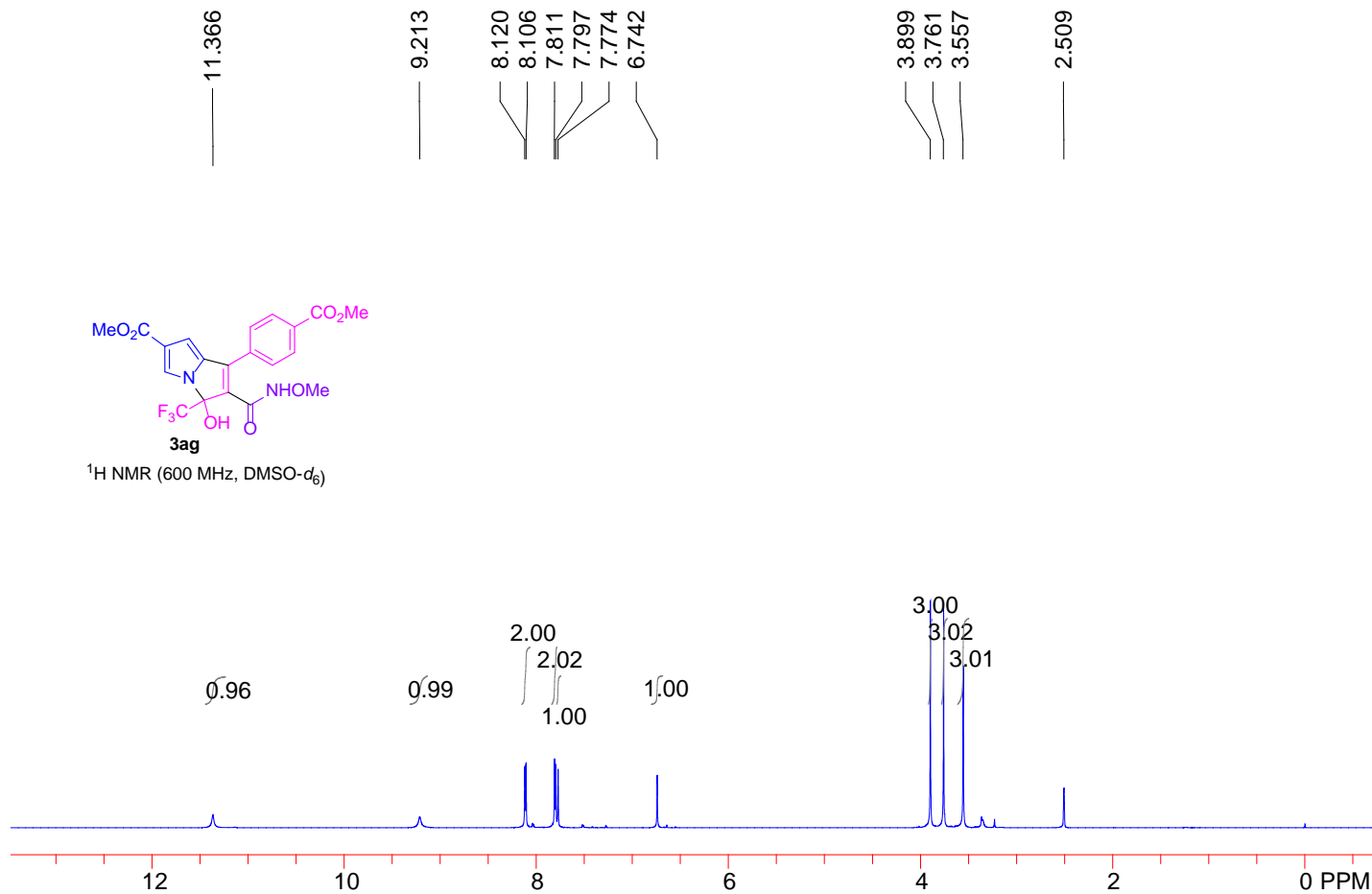


**3af**  
<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

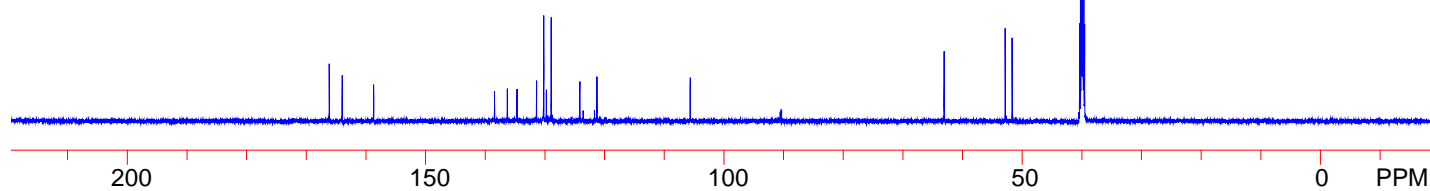




$^1\text{H NMR}$  (600 MHz,  $\text{DMSO-}d_6$ )

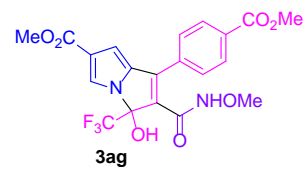


$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ )



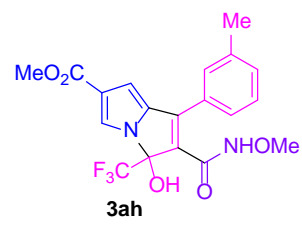
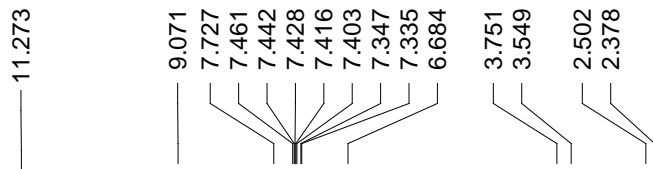


80.277

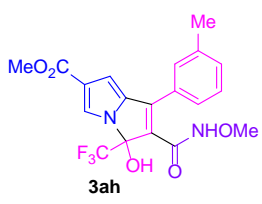
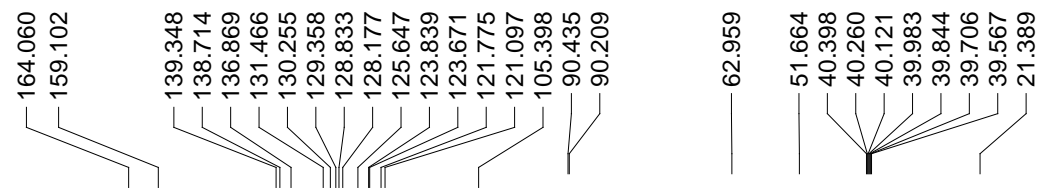
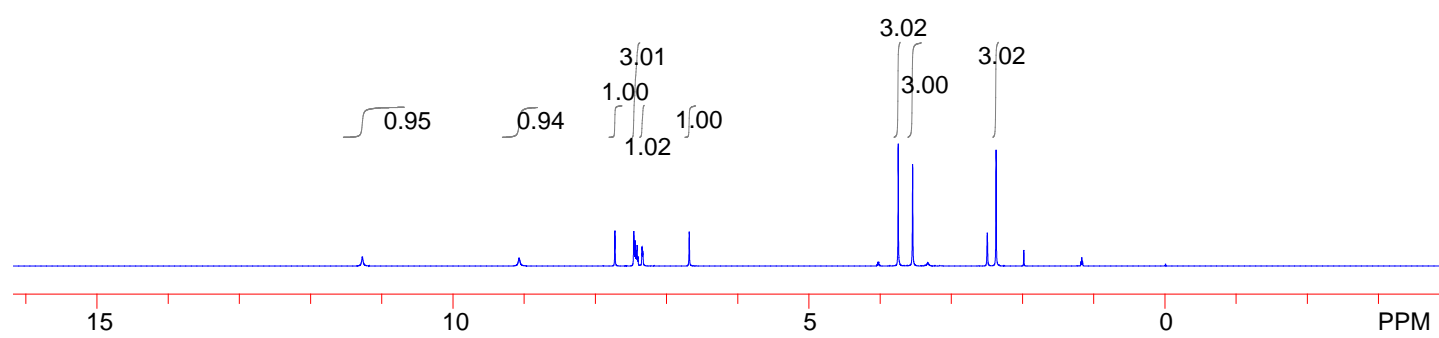


<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

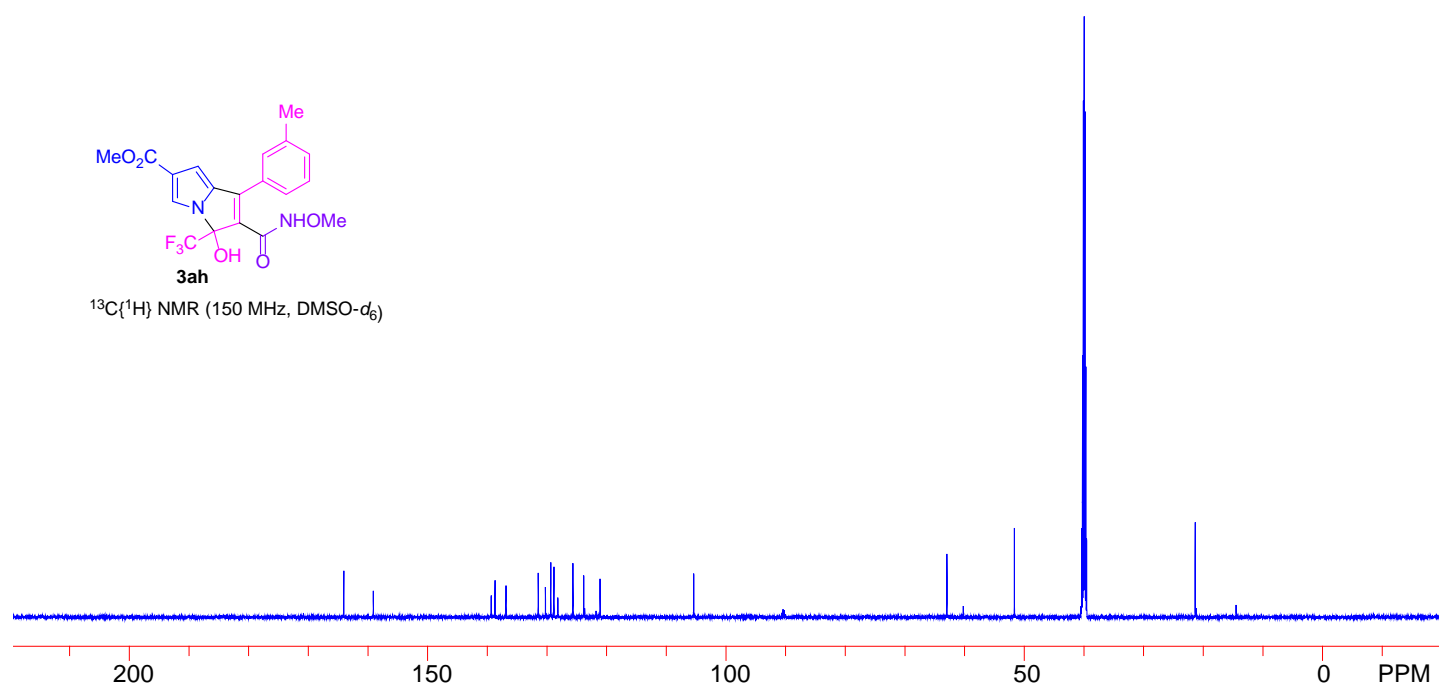




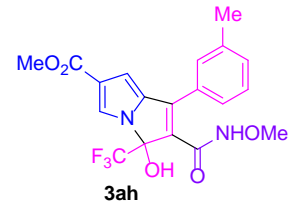
<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>)



<sup>13</sup>C(<sup>1</sup>H) NMR (150 MHz, DMSO-d<sub>6</sub>)

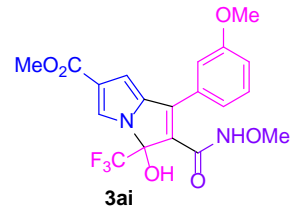
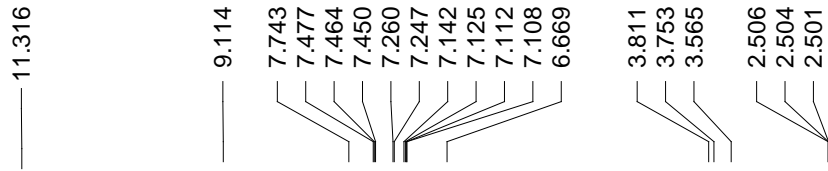


80.306

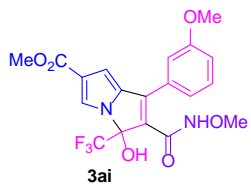
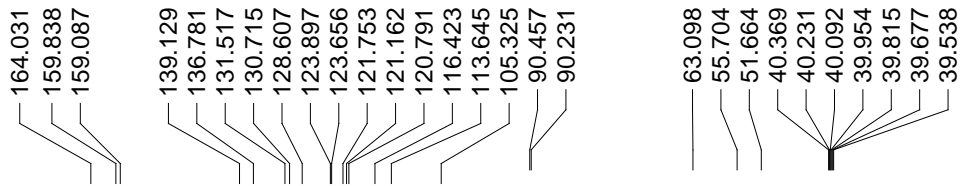
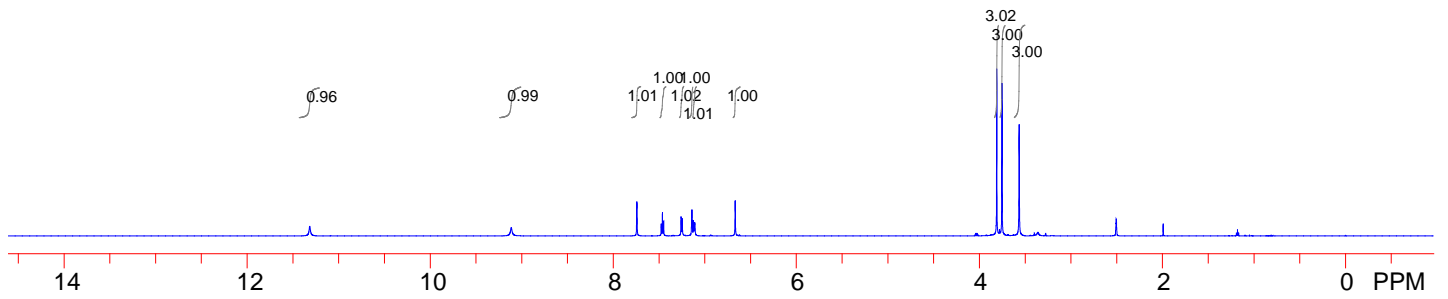


**3ah**  
<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

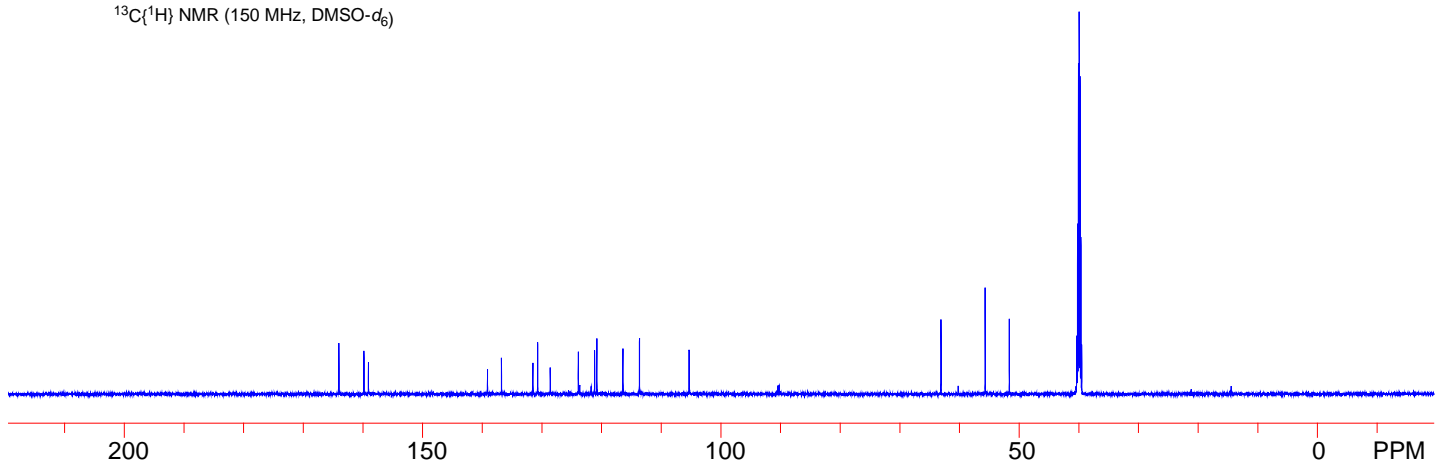
0 -50 -100 -150 -200 PPM



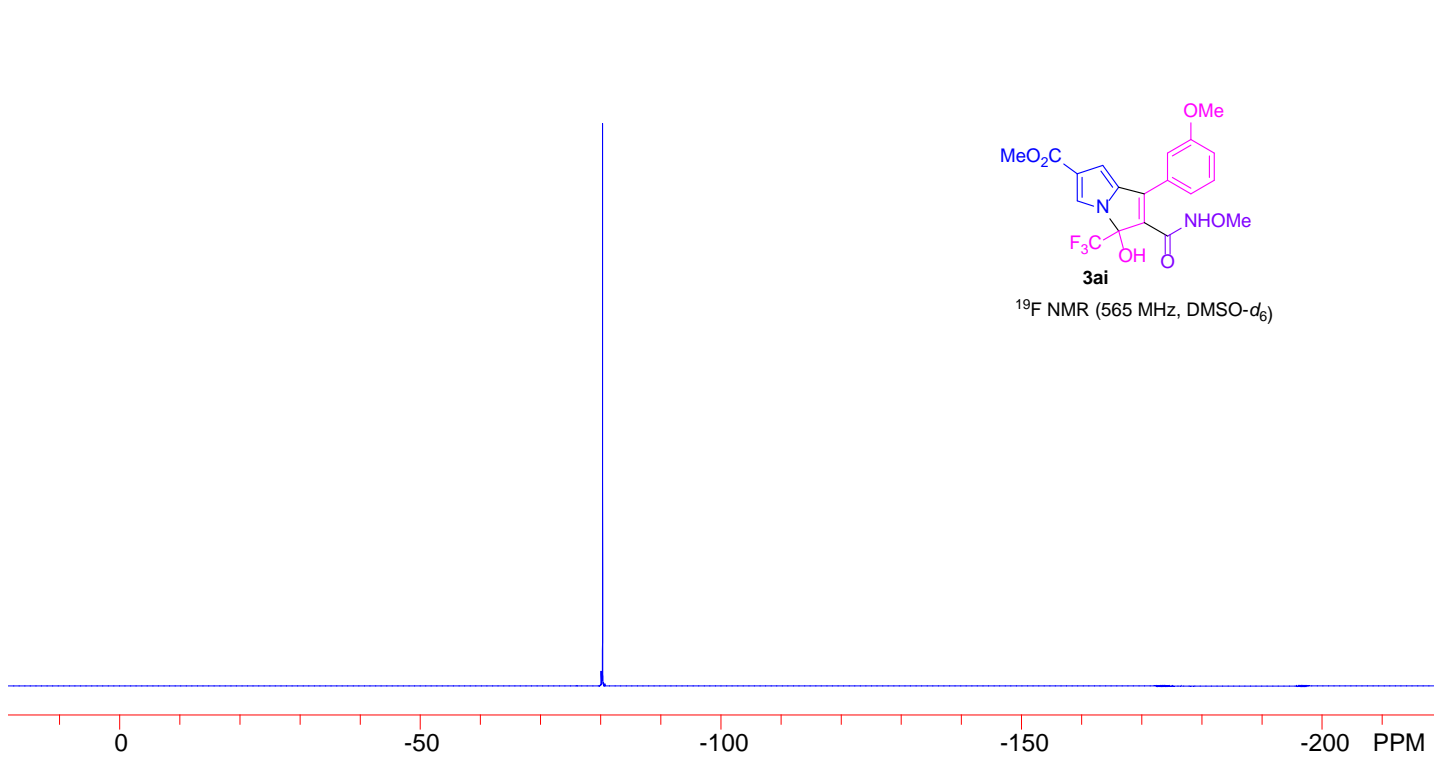
$^1\text{H}$  NMR (600 MHz,  $\text{DMSO}-d_6$ )

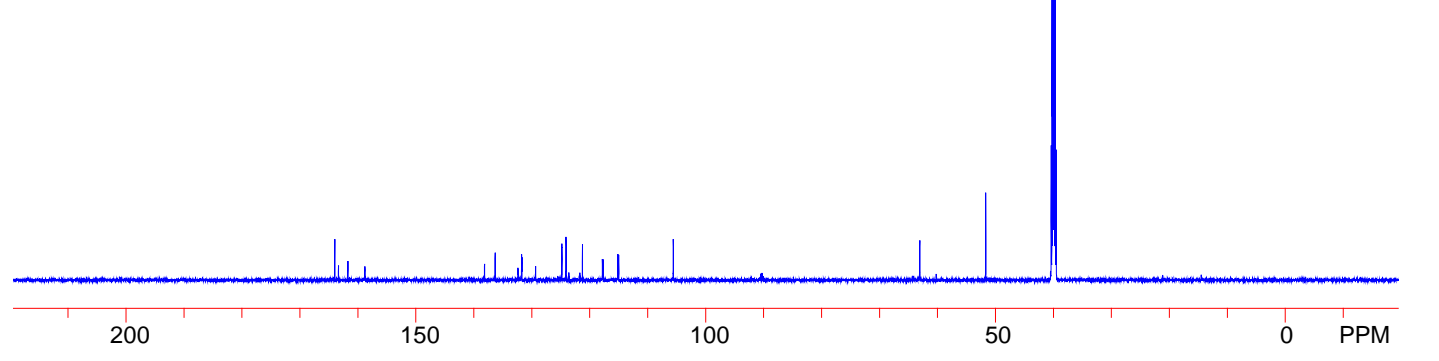
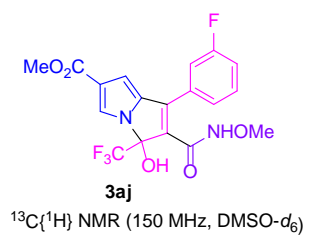
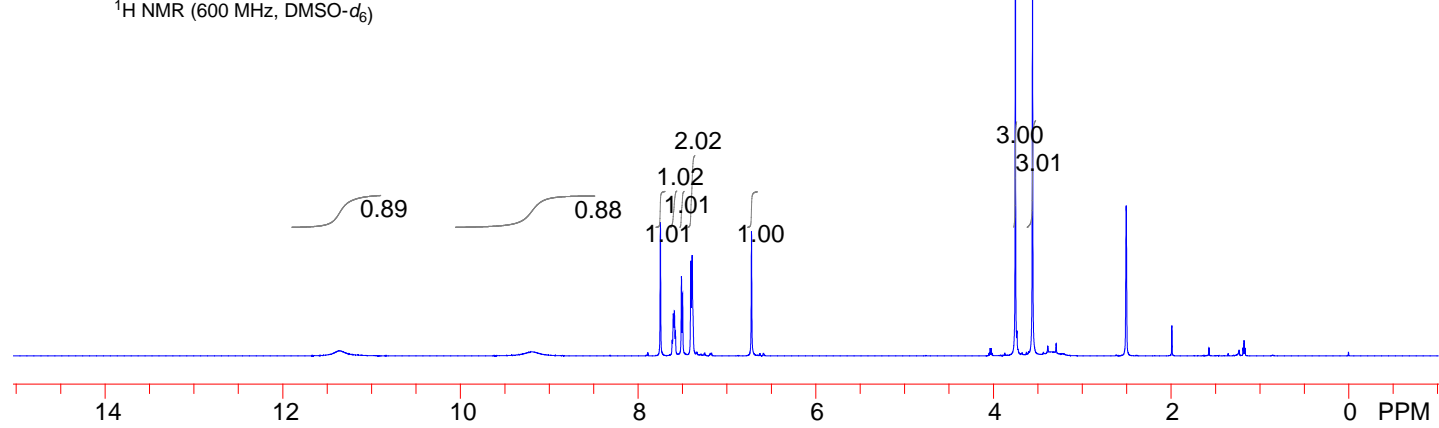
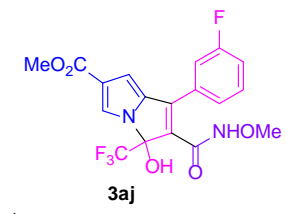
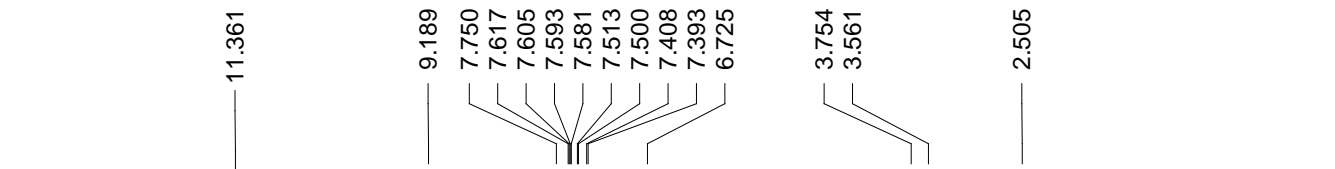


$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO}-d_6$ )



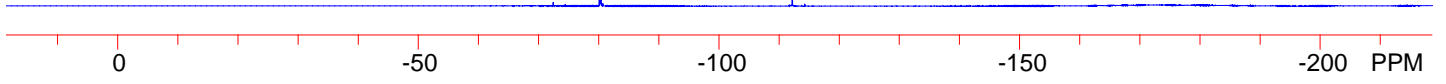
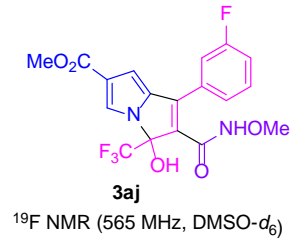
80.302

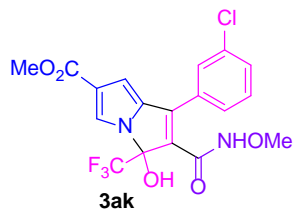
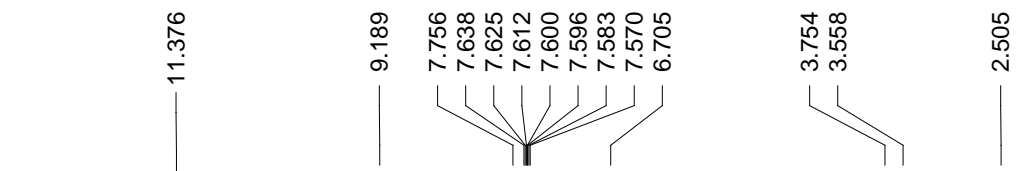




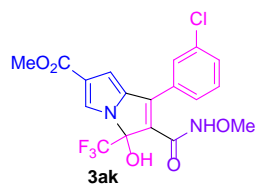
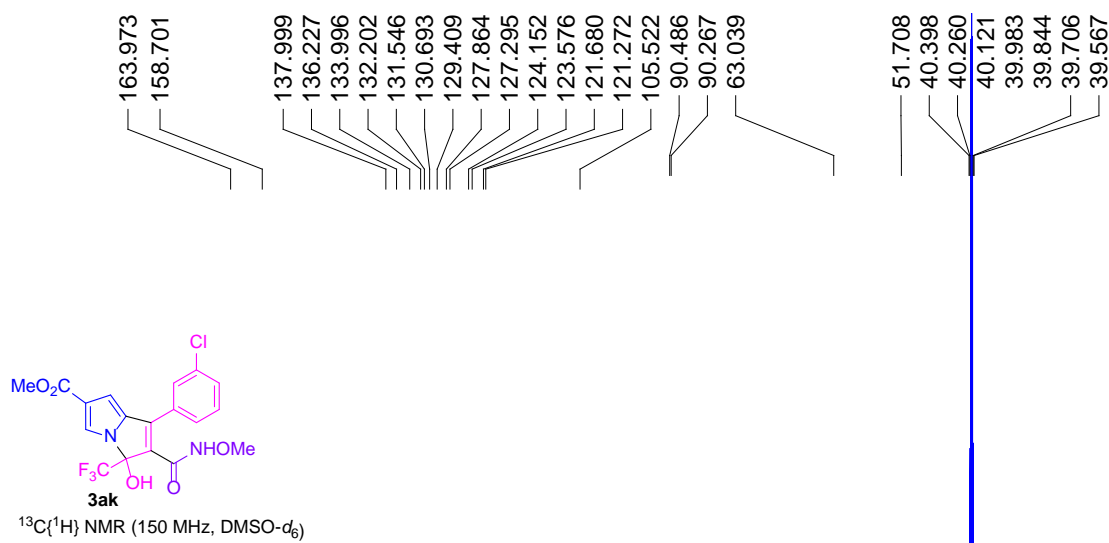
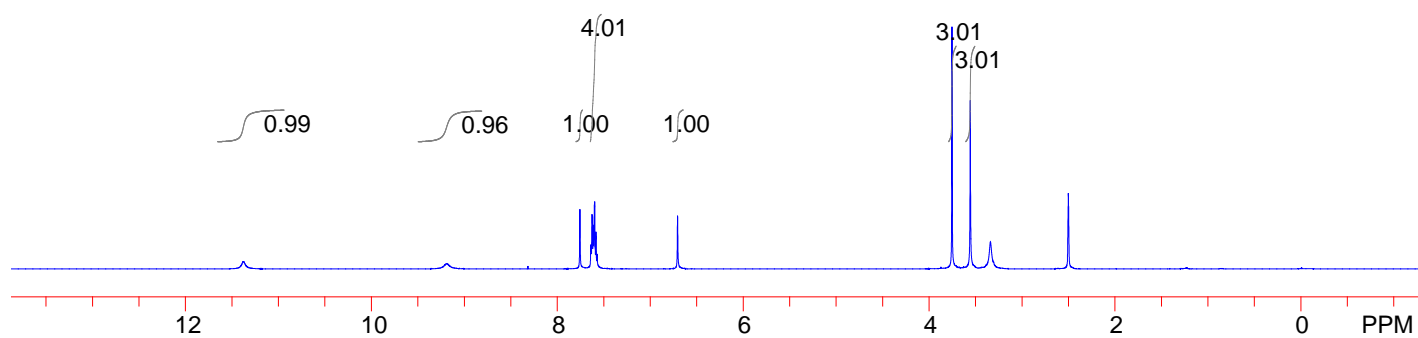
80.306

112.138  
112.149

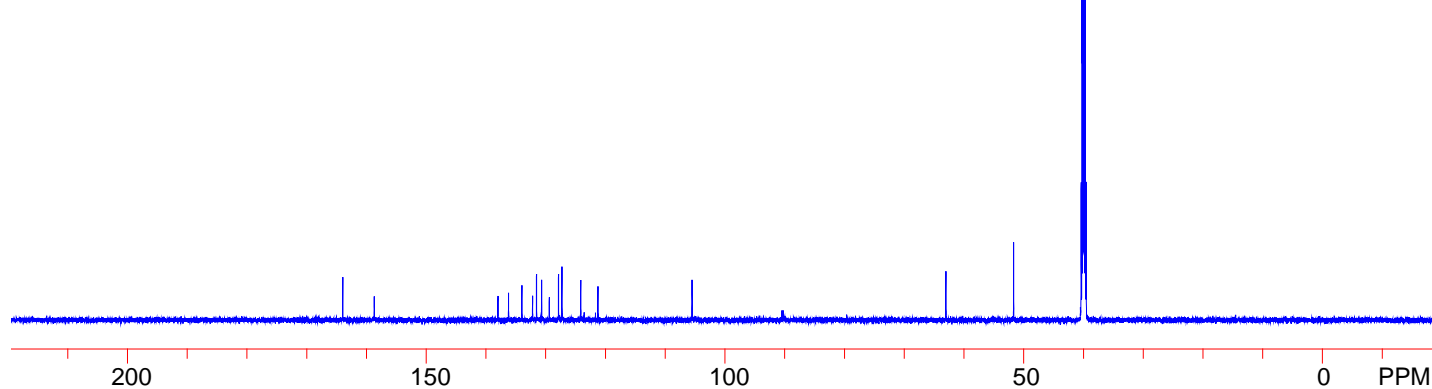




<sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)

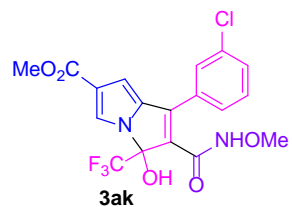
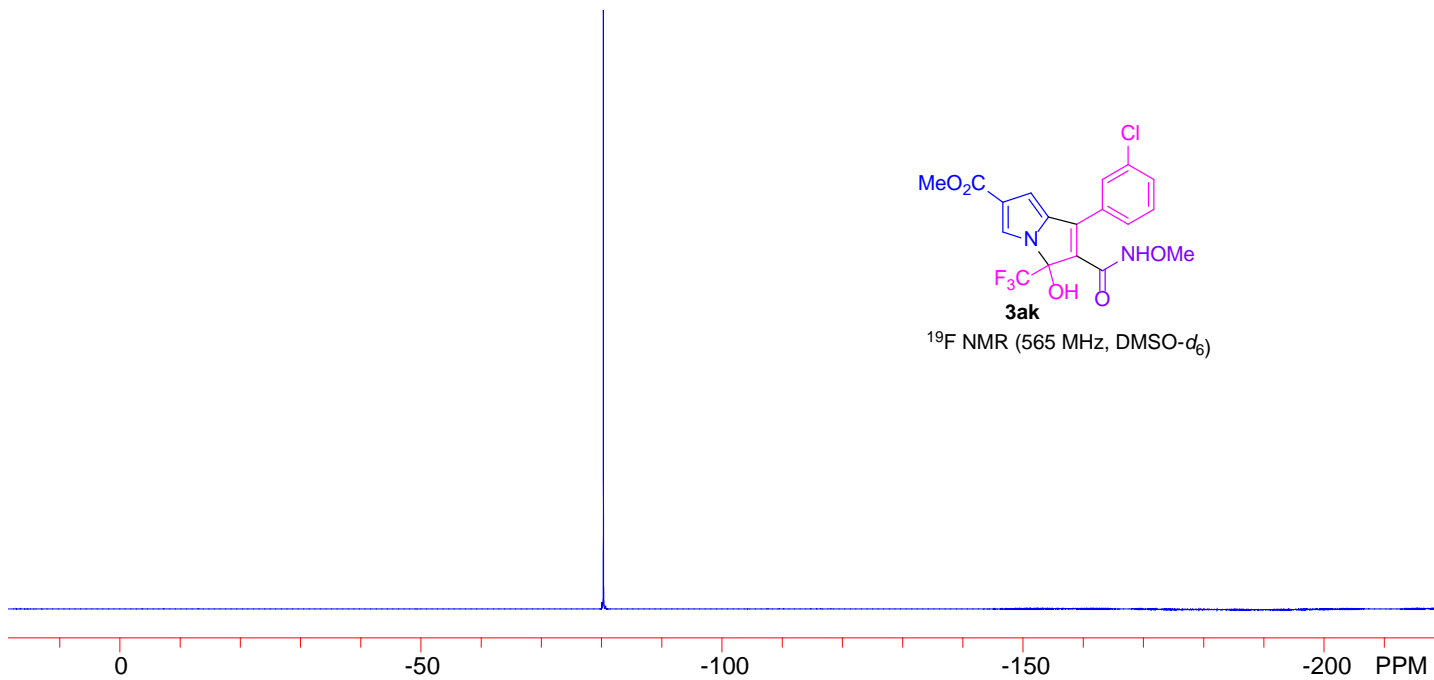


<sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>)

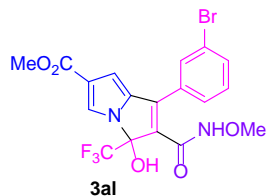
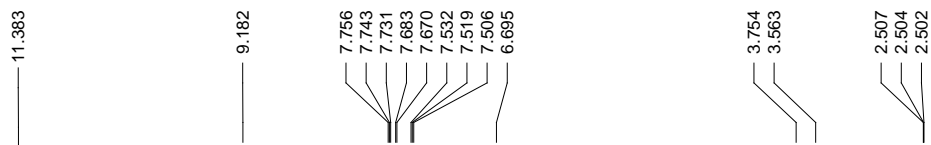




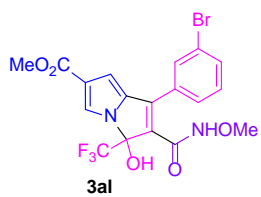
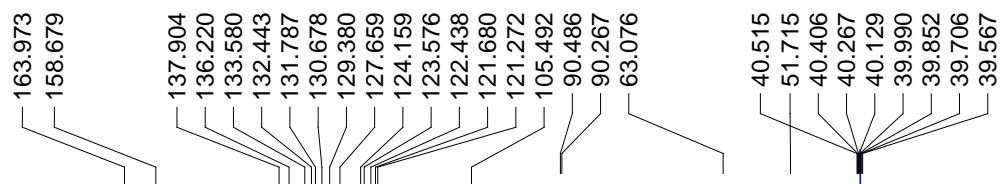
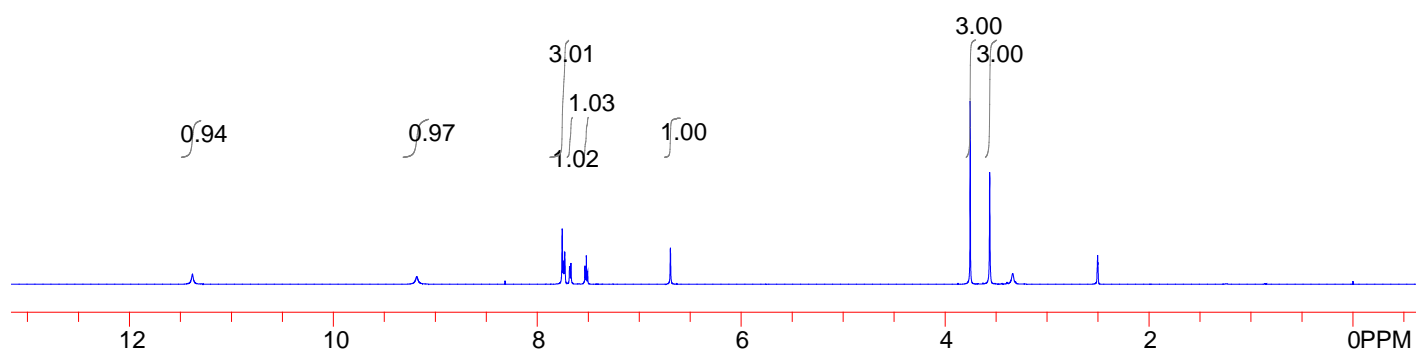
-80.291



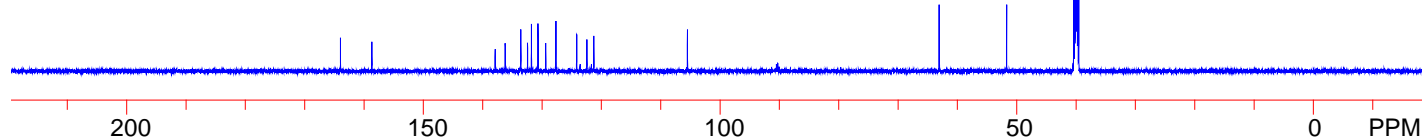
$^{19}\text{F}$  NMR (565 MHz,  $\text{DMSO-}d_6$ )



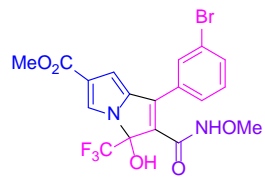
<sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)



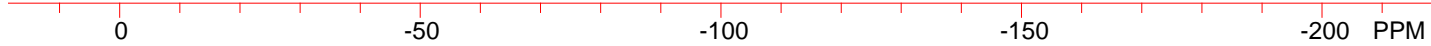
<sup>13</sup>C{<sup>1</sup>H} NMR (150 MHz, DMSO-*d*<sub>6</sub>)

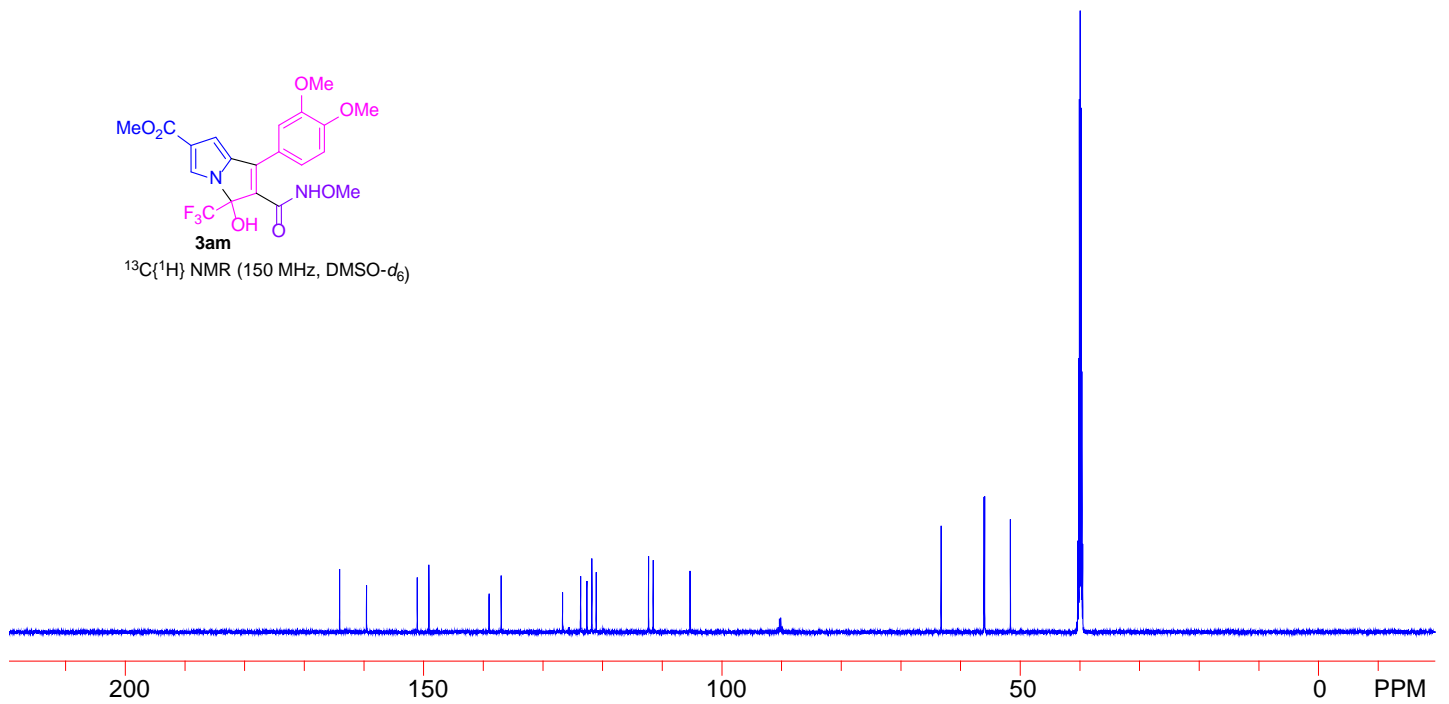
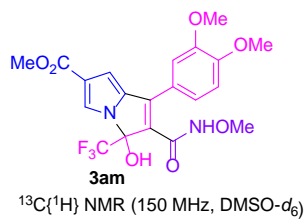
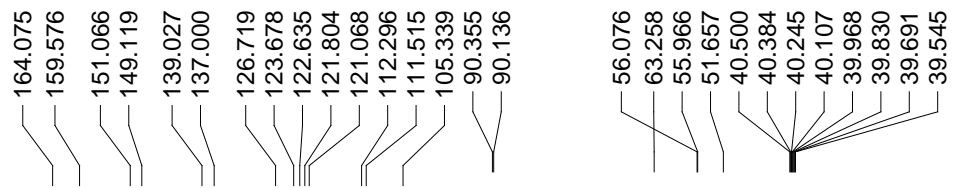
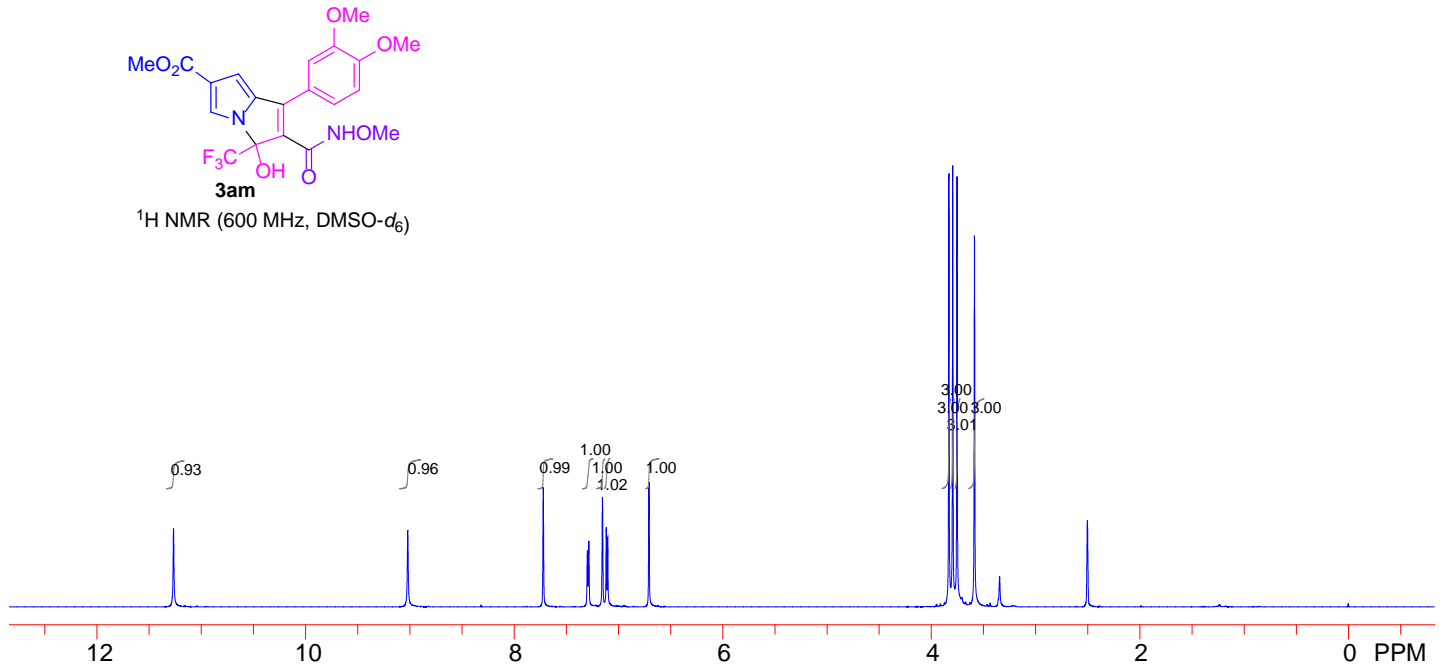
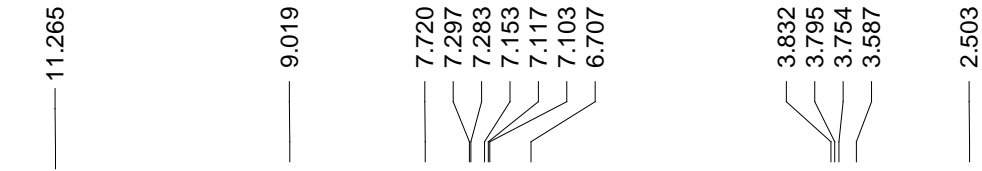


80.281

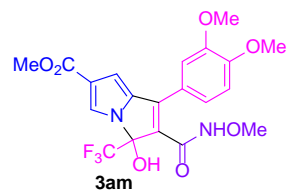


**3al**  
 $^{19}\text{F}$  NMR (565 MHz,  $\text{DMSO-}d_6$ )

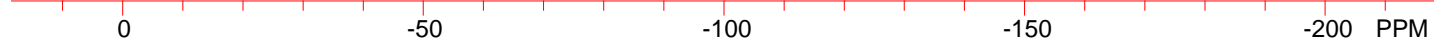


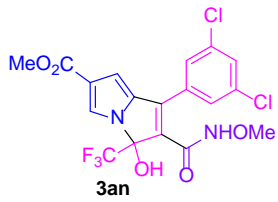


80.259

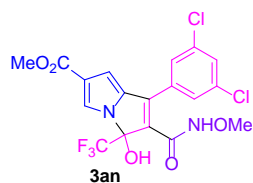
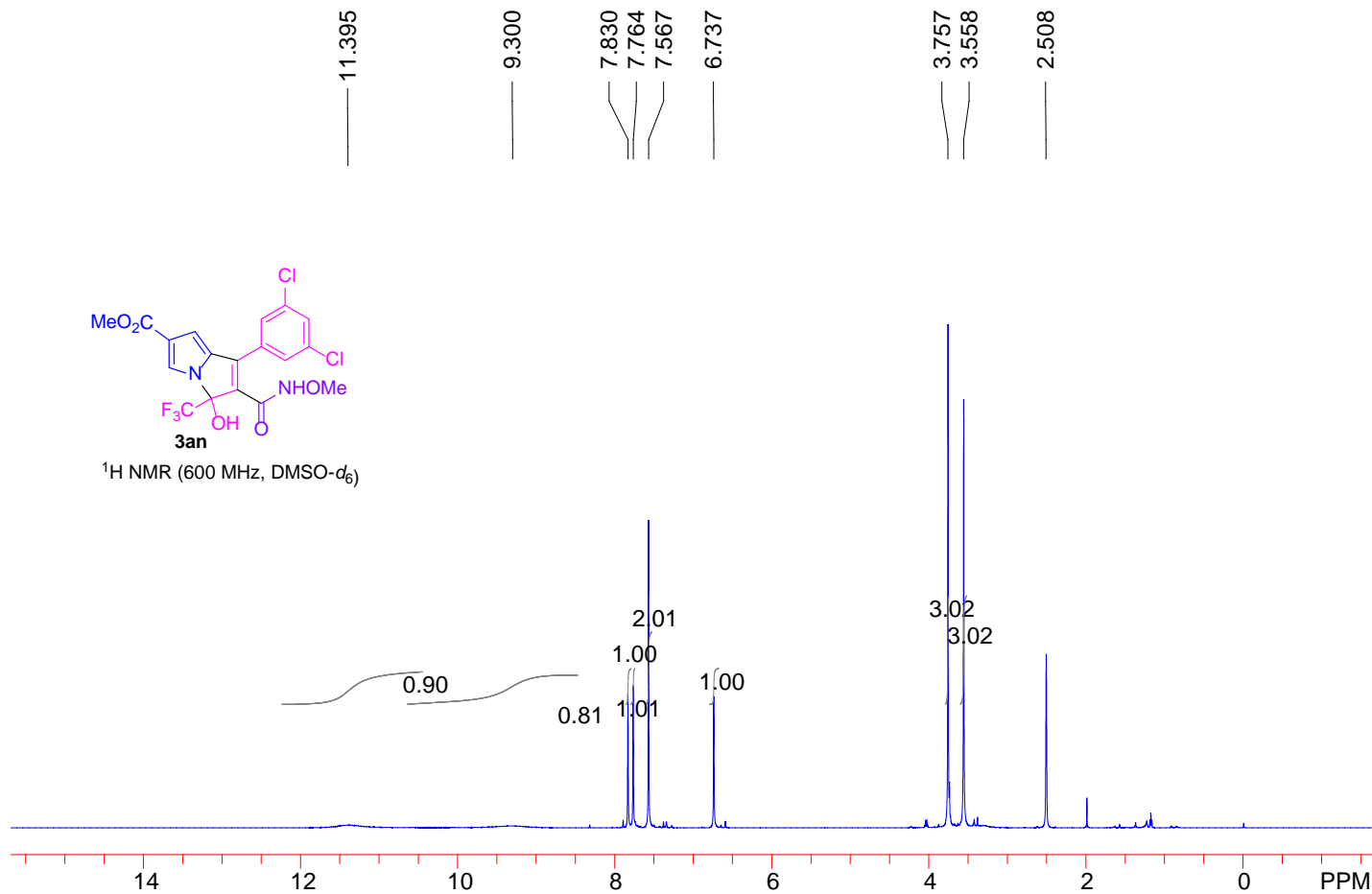


<sup>19</sup>F NMR (565 MHz, DMSO-d<sub>6</sub>)

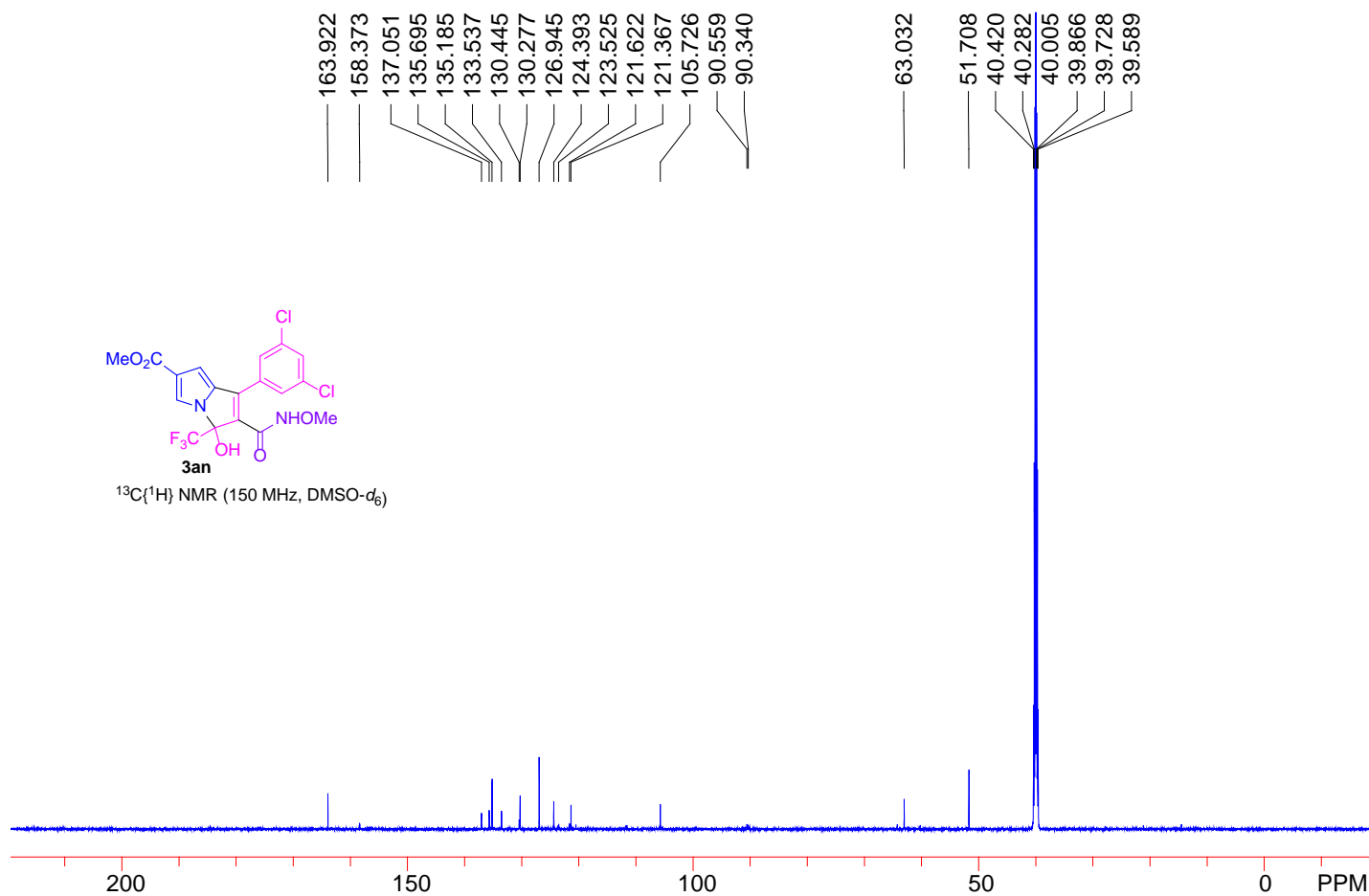




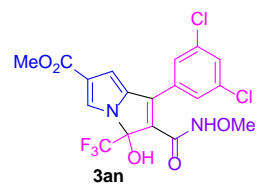
$^1\text{H NMR}$  (600 MHz,  $\text{DMSO-d}_6$ )



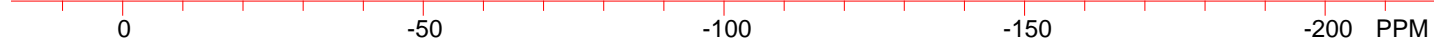
$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-d}_6$ )

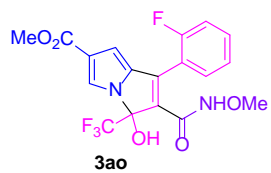


80.320

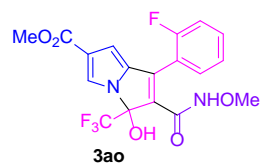
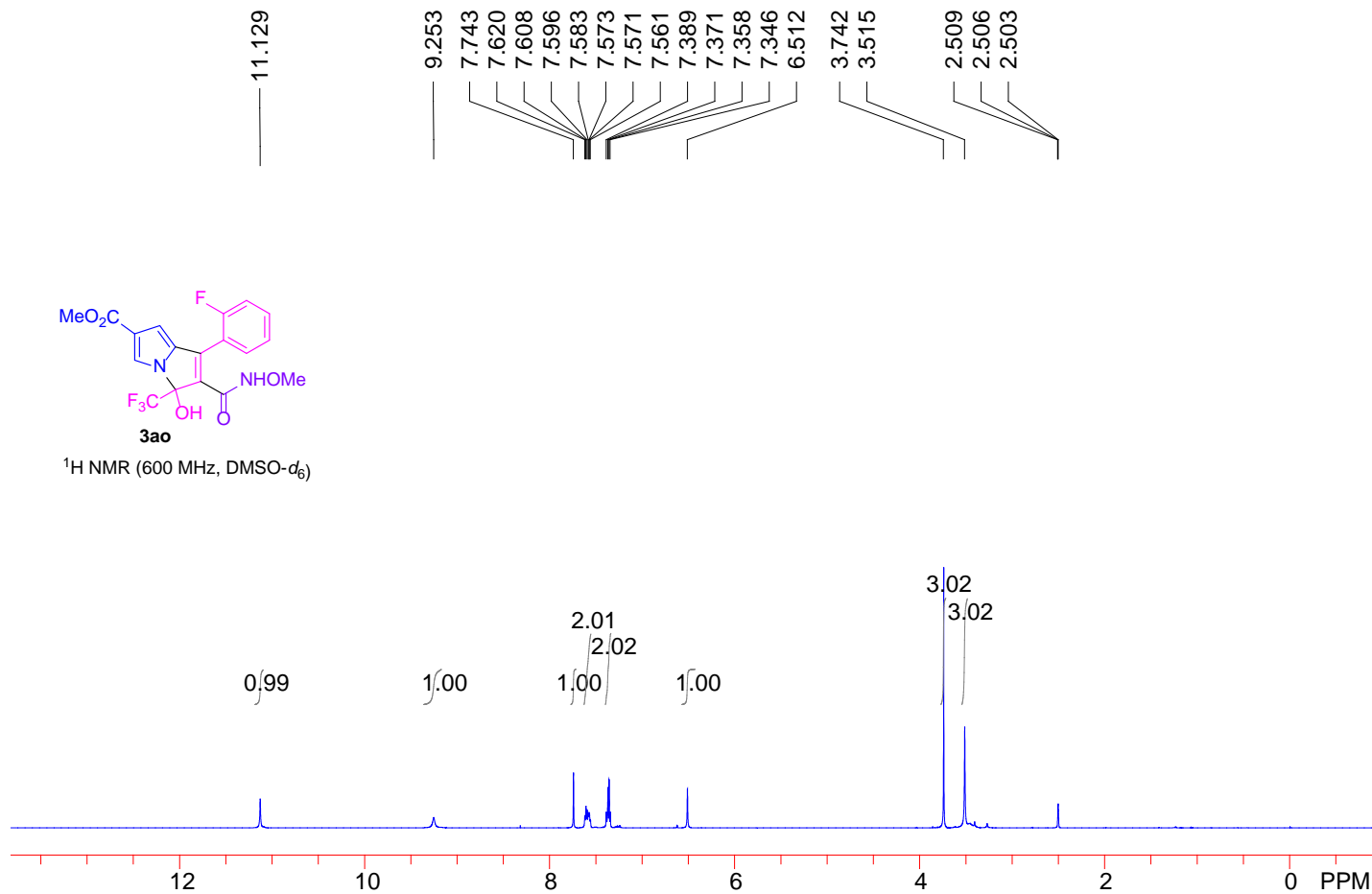


<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

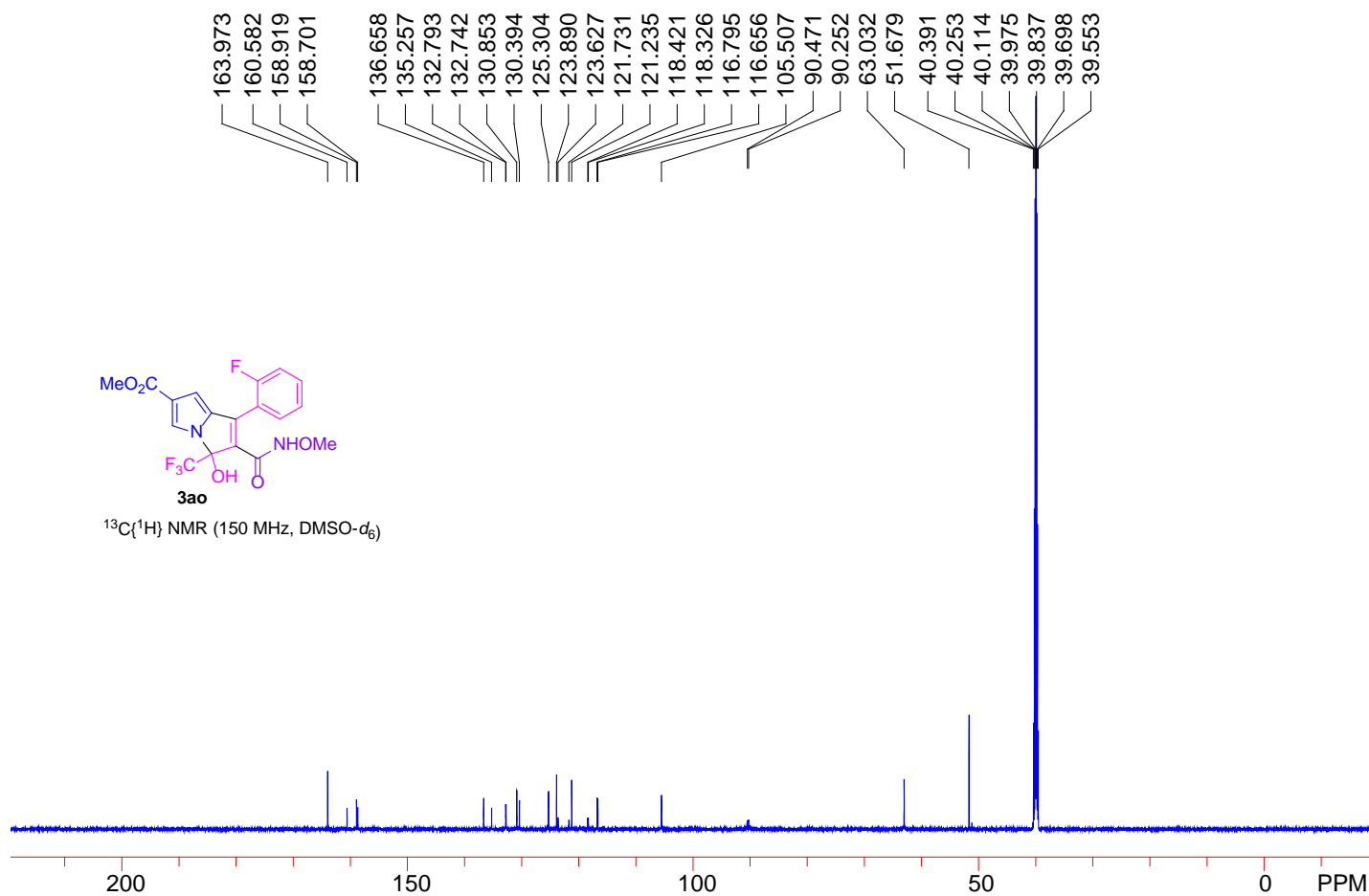




$^1\text{H NMR}$  (600 MHz,  $\text{DMSO-}d_6$ )

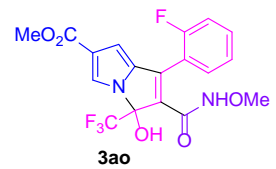


$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ )



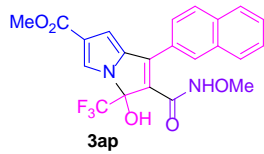
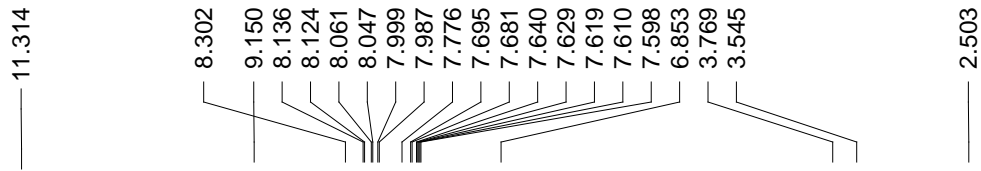


82.872  
-111.512  
-111.530  
-111.541  
-111.552  
-111.571

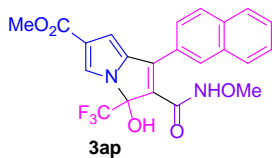
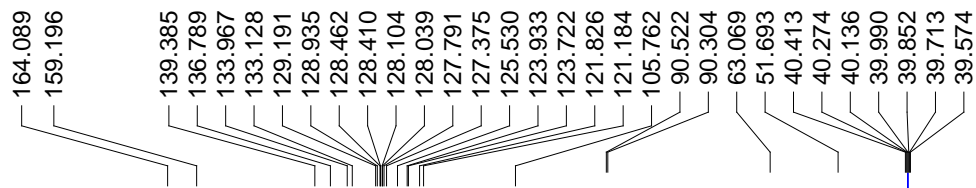
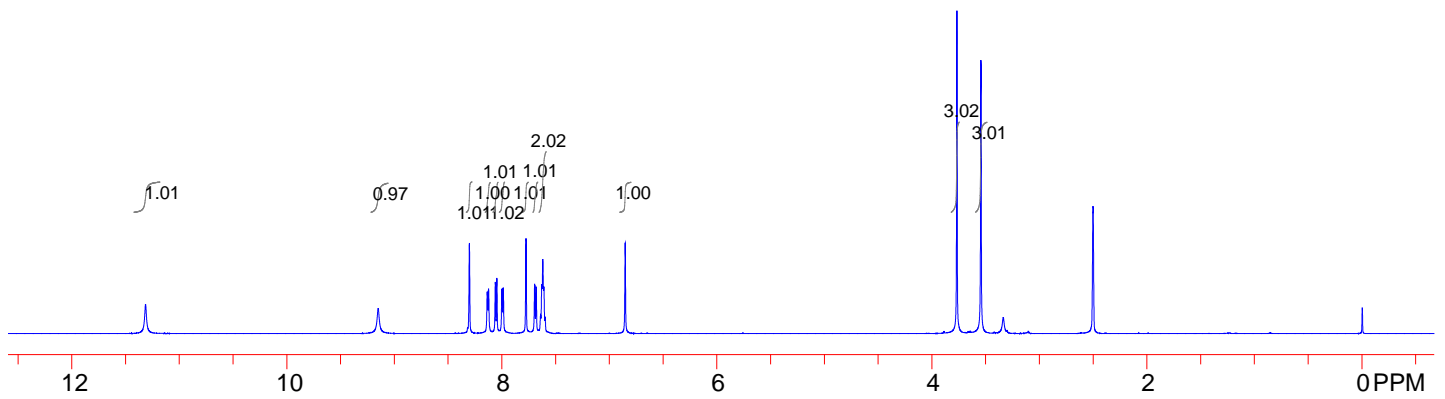


<sup>19</sup>F NMR (376 MHz, CD<sub>3</sub>OD)

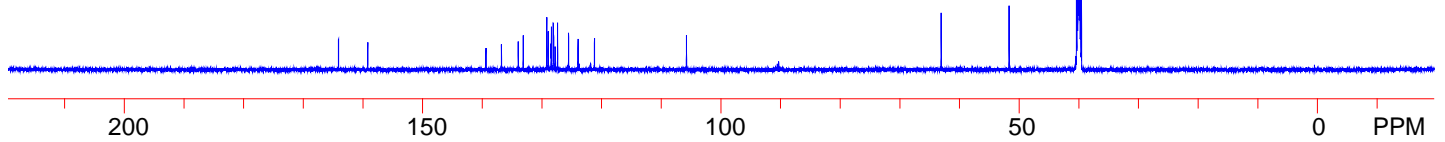
0 -50 -100 -150 -200 PPM



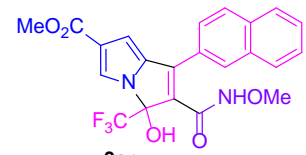
$^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )



$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ )

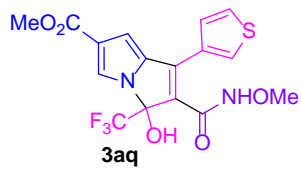


80.237

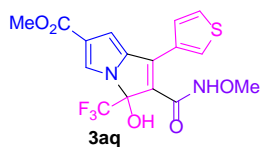
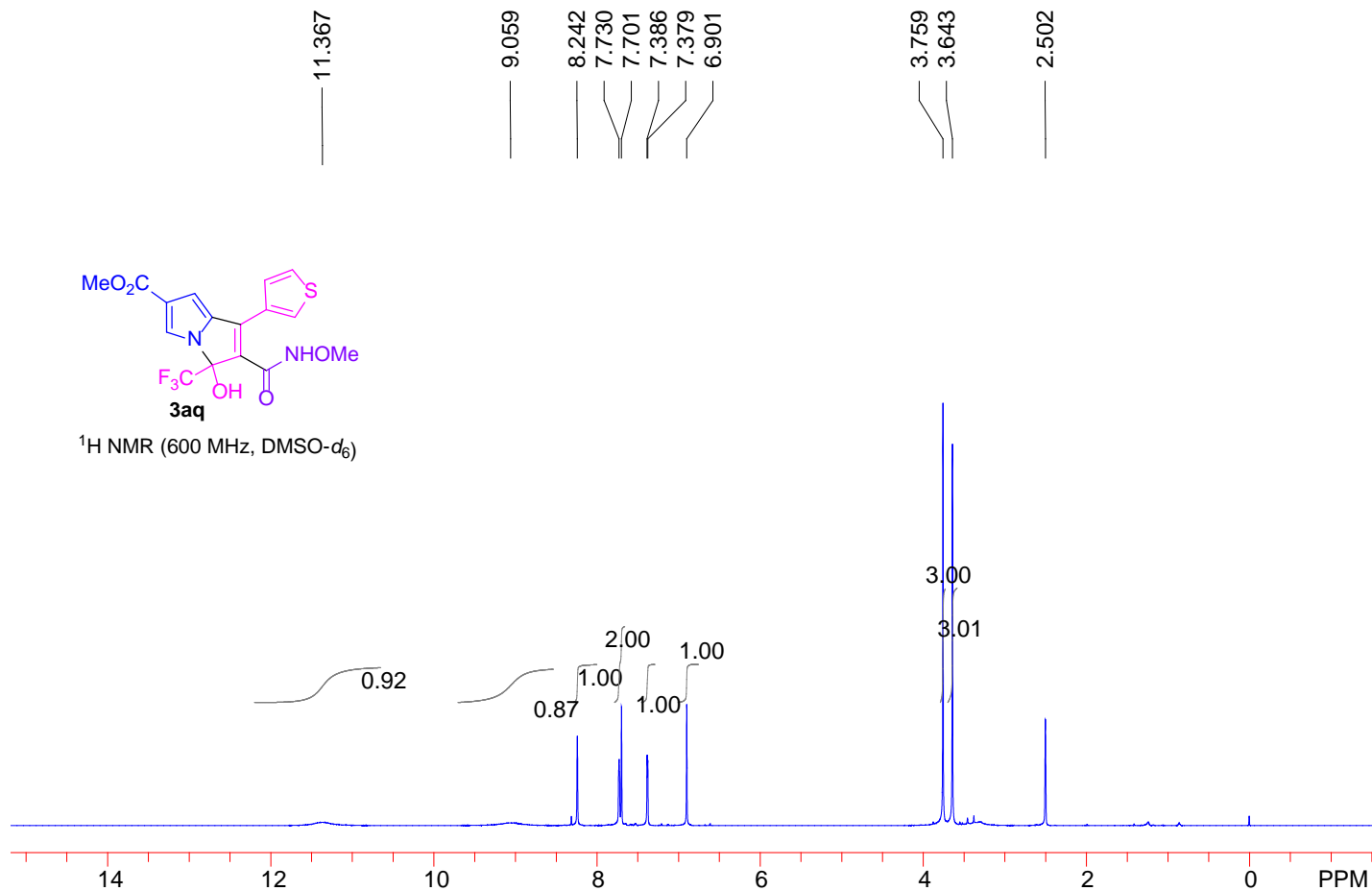


$^{19}\text{F}$  NMR (565 MHz,  $\text{DMSO-}d_6$ )

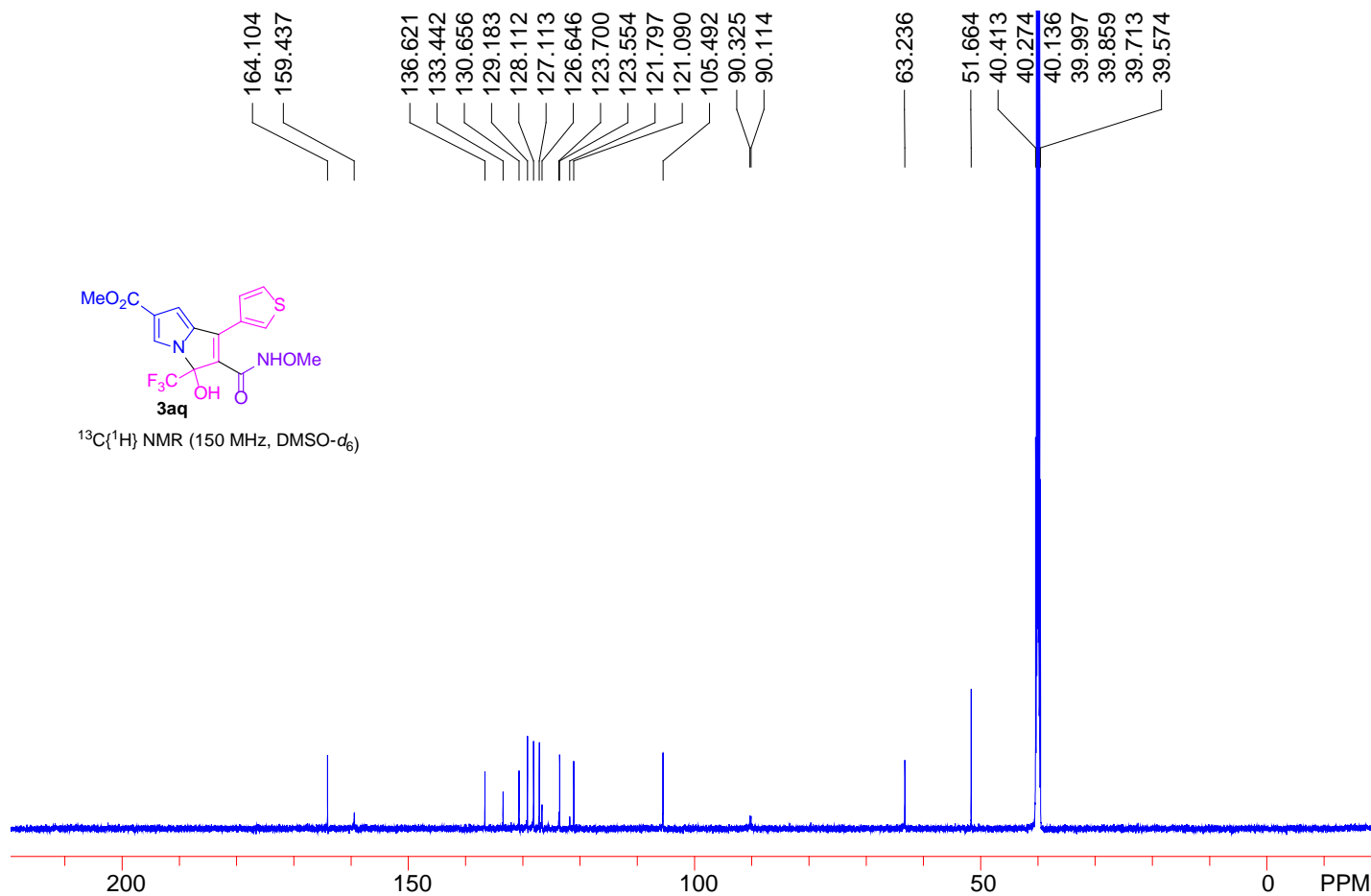
0 -50 -100 -150 -200 PPM



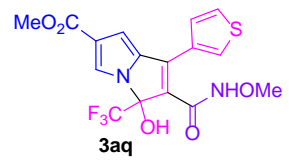
$^1\text{H NMR}$  (600 MHz,  $\text{DMSO-}d_6$ )



$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ )



-80.277



<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

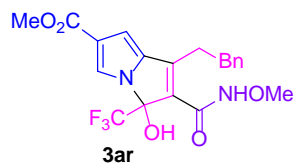
0

-50

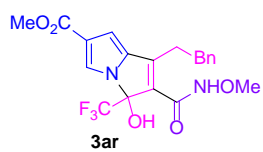
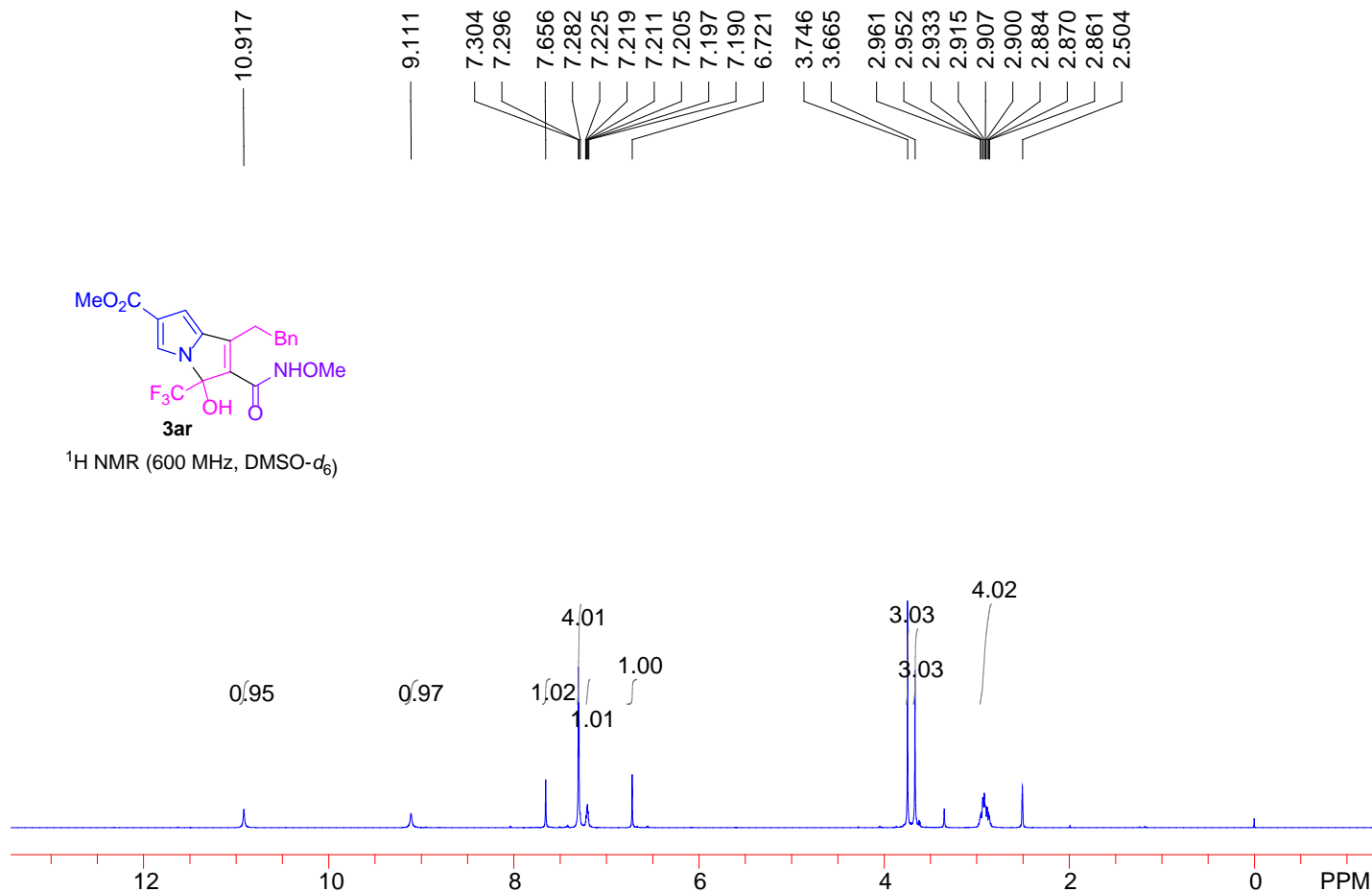
-100

-150

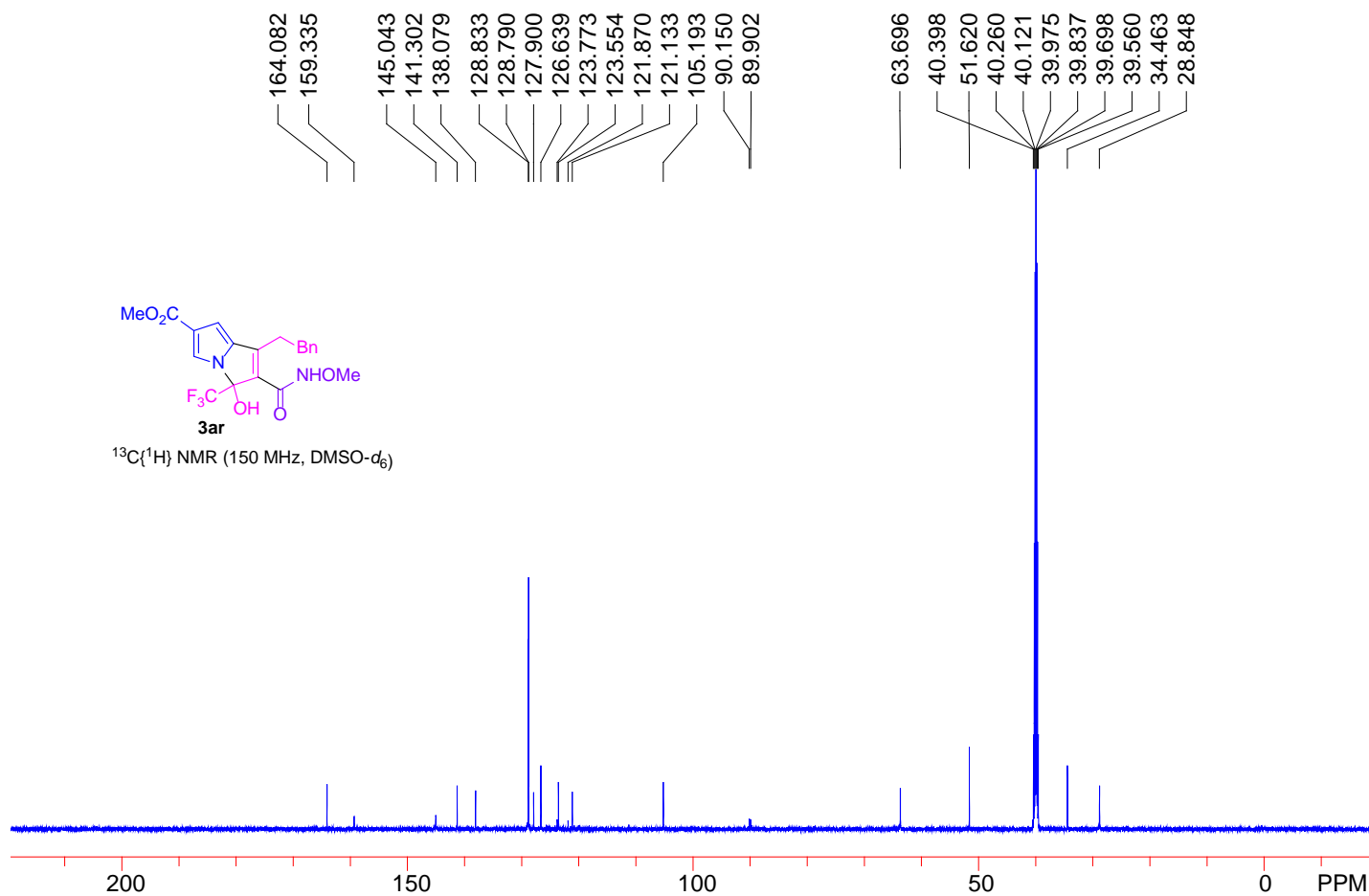
-200 PPM



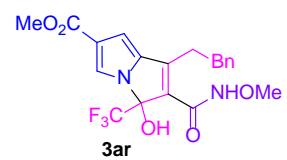
$^1\text{H NMR}$  (600 MHz,  $\text{DMSO-}d_6$ )



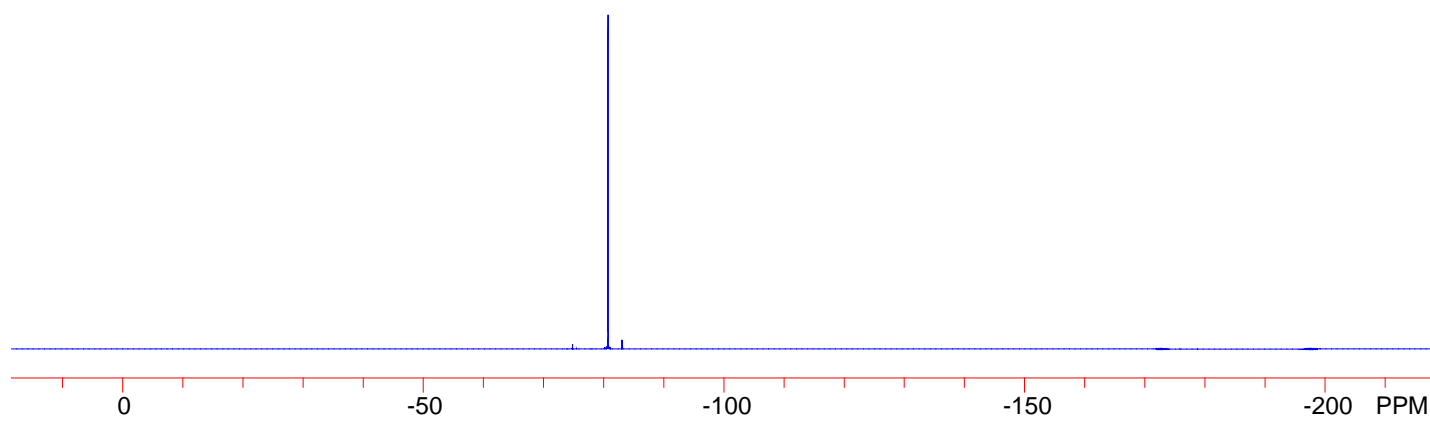
$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ )

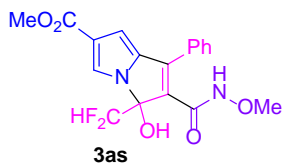


80.700

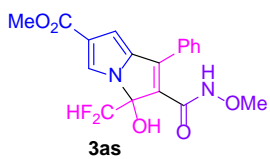
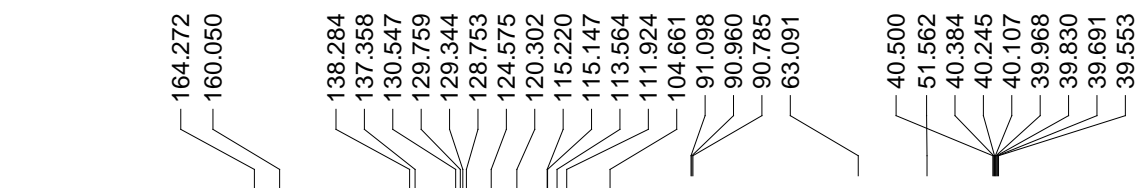
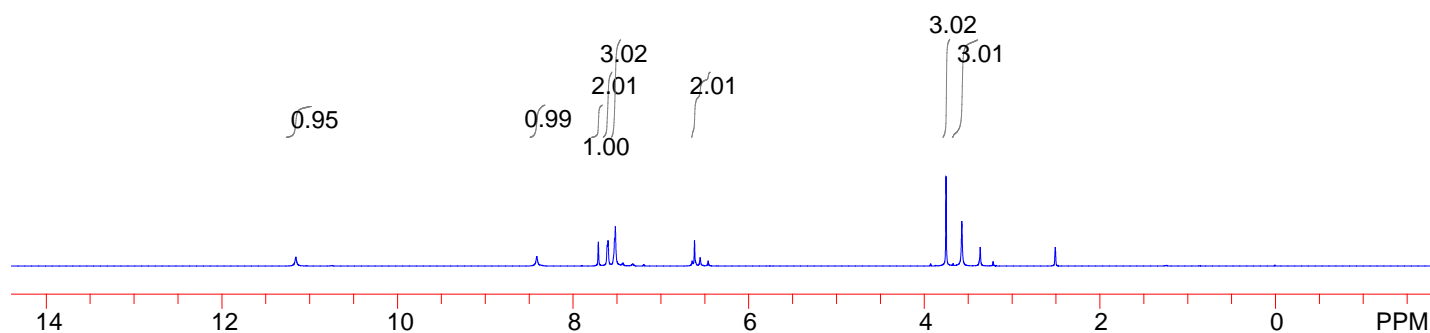
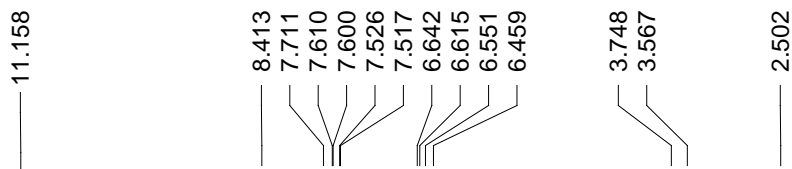


<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

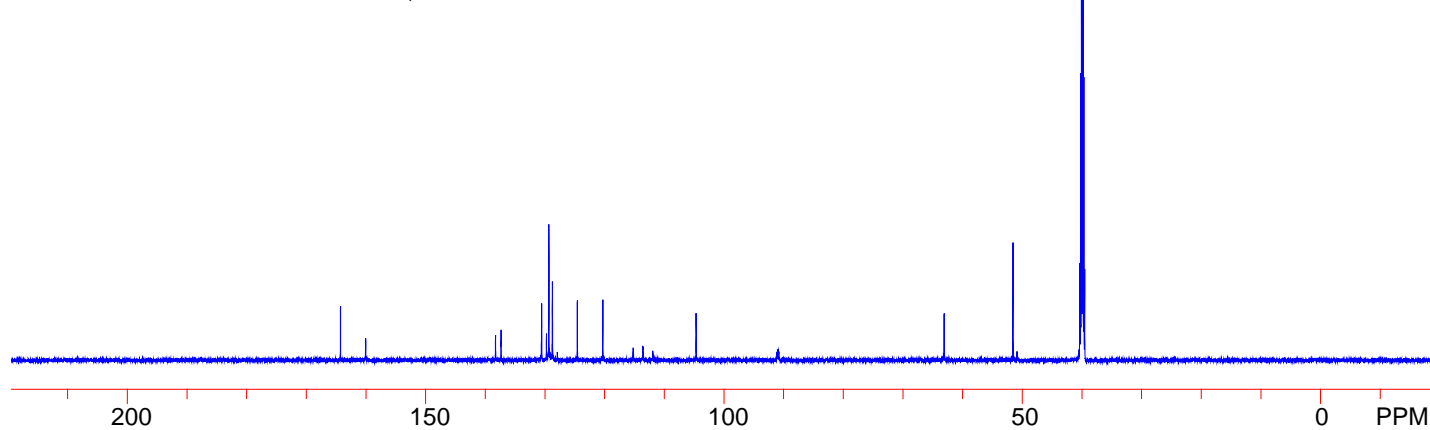




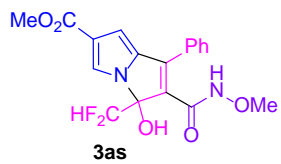
$^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )



$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ )

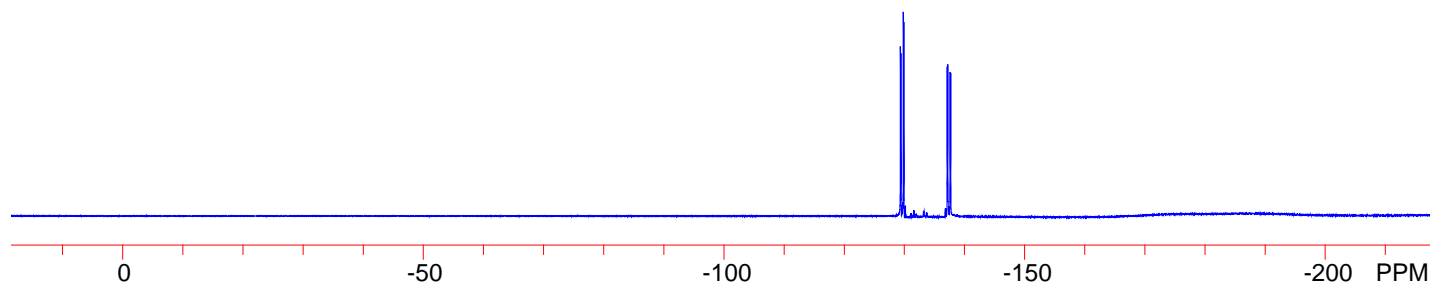


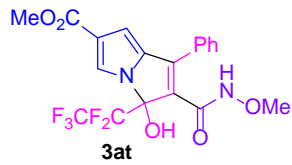
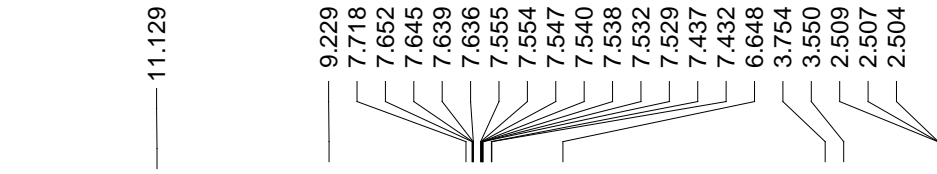




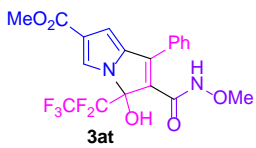
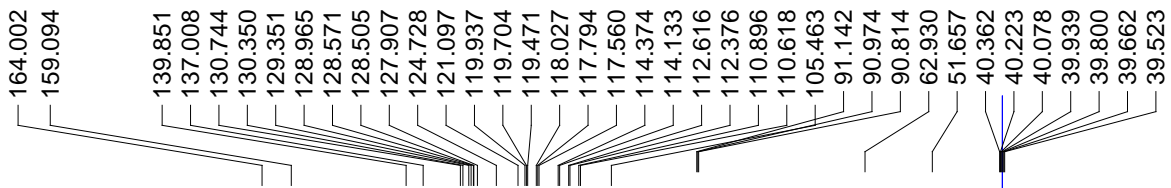
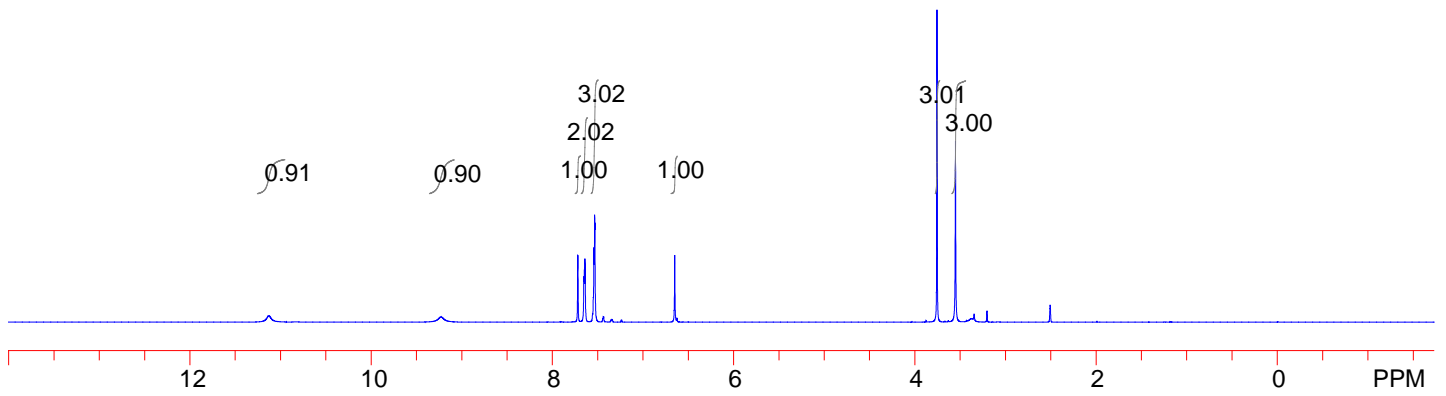
<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

129.280  
129.374  
129.769  
129.863  
137.059  
137.157  
137.547  
137.645

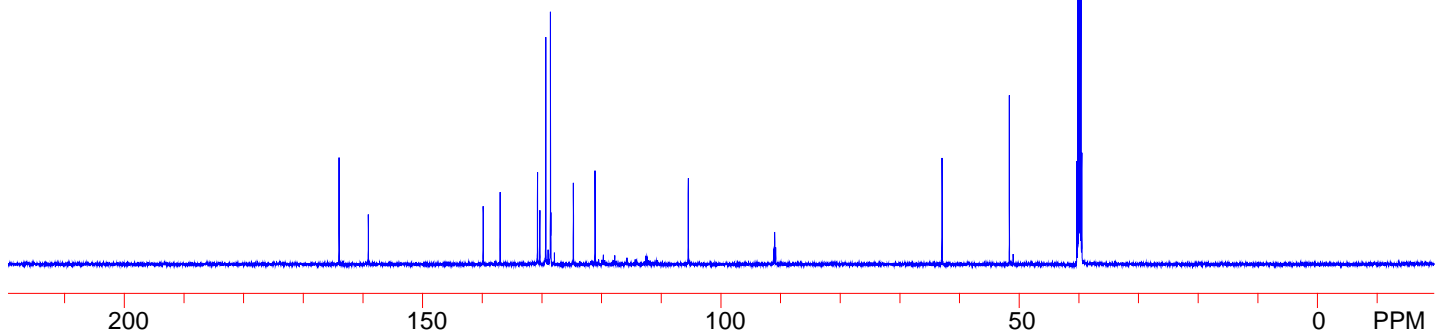


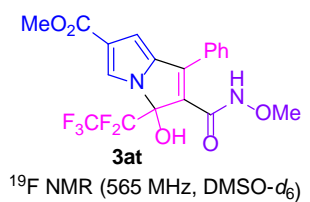


<sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)

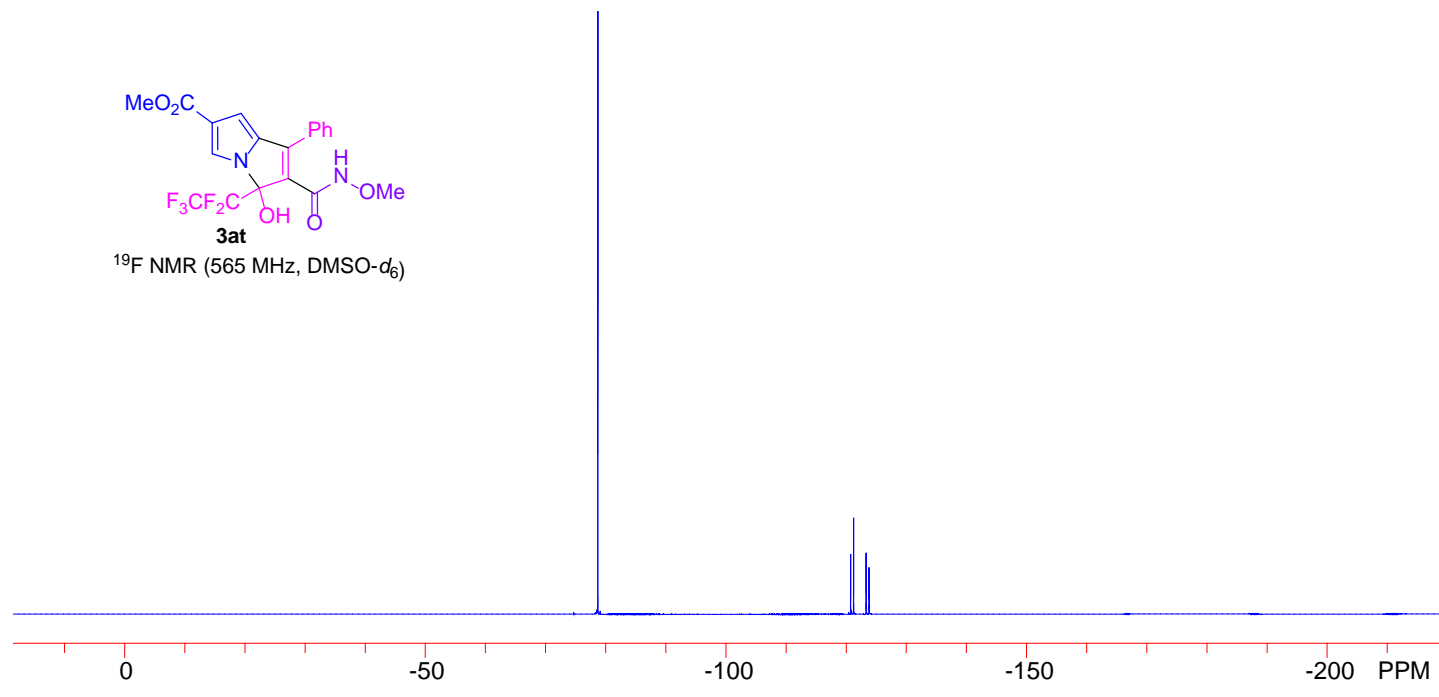


<sup>13</sup>C(<sup>1</sup>H) NMR (150 MHz, DMSO-*d*<sub>6</sub>)

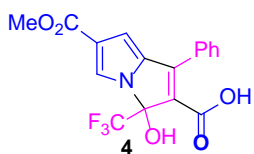




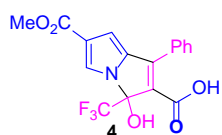
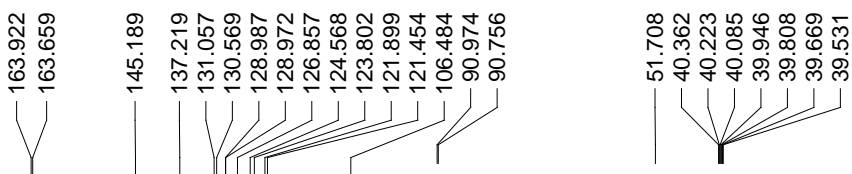
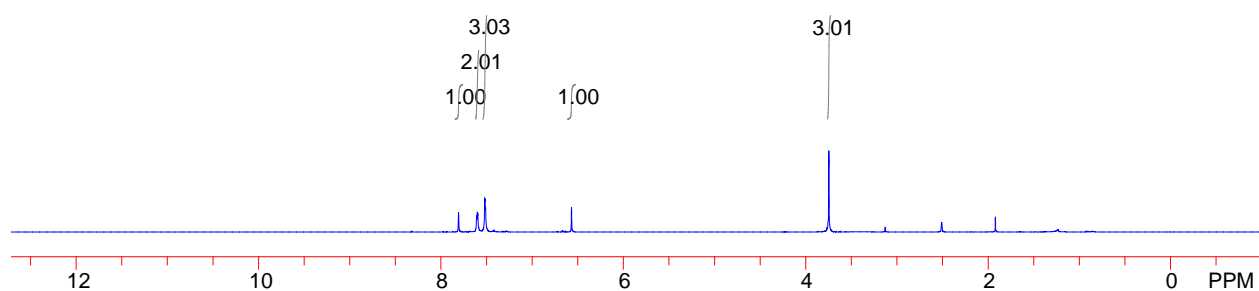
-78.674  
-120.694  
-121.183  
-123.252  
-123.741



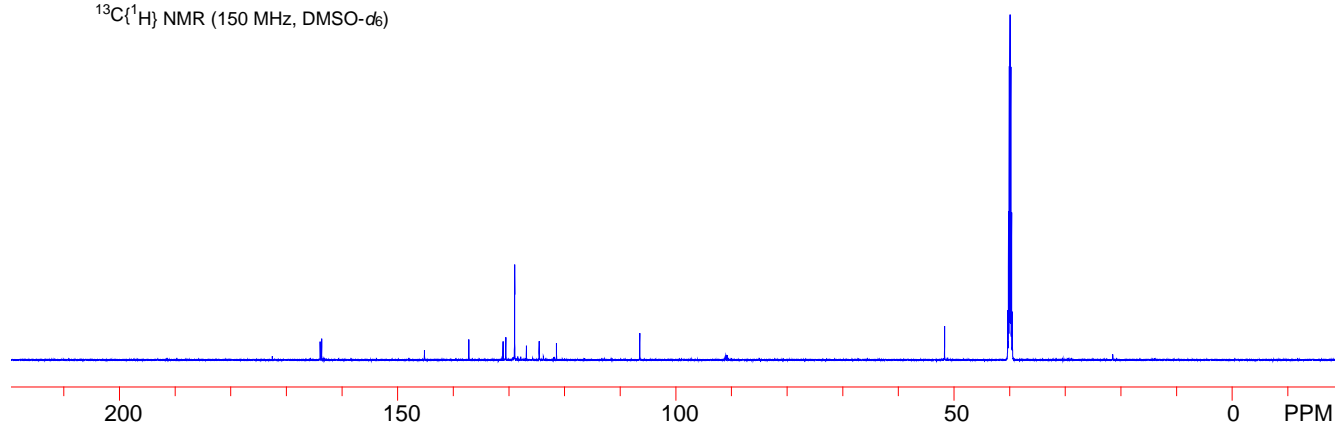
## V. NMR spectra of 4-7



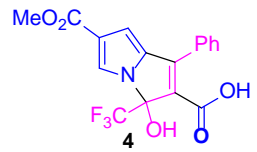
$^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )



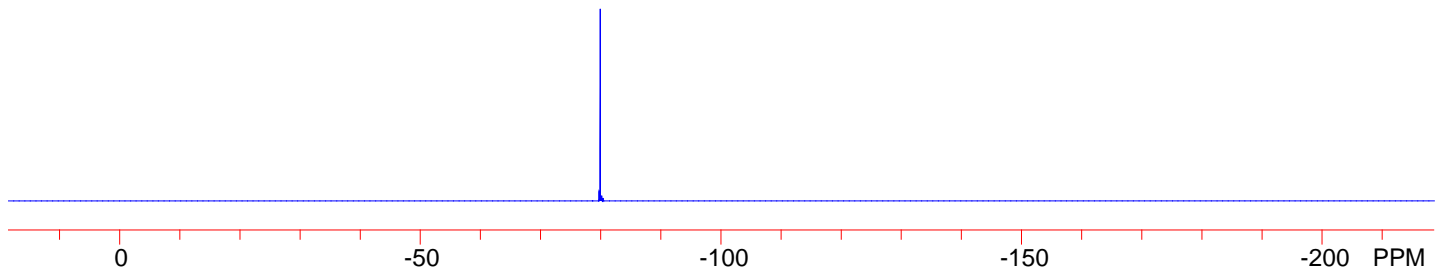
$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz, DMSO- $d_6$ )

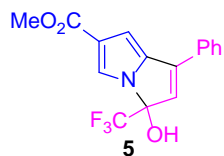
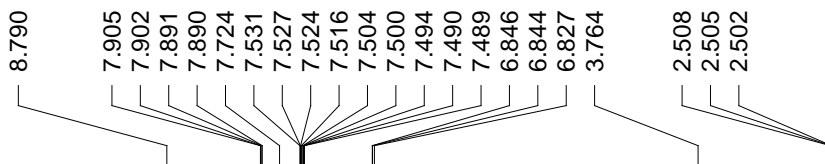


79.897

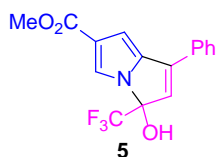
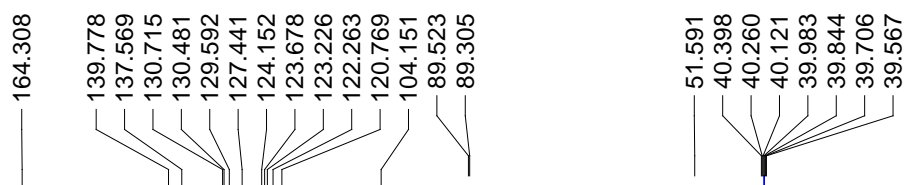
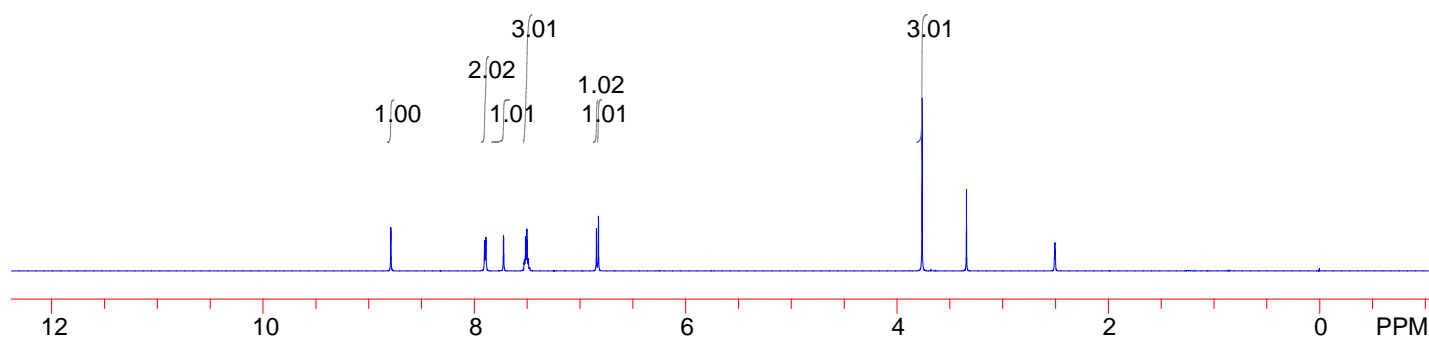


<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

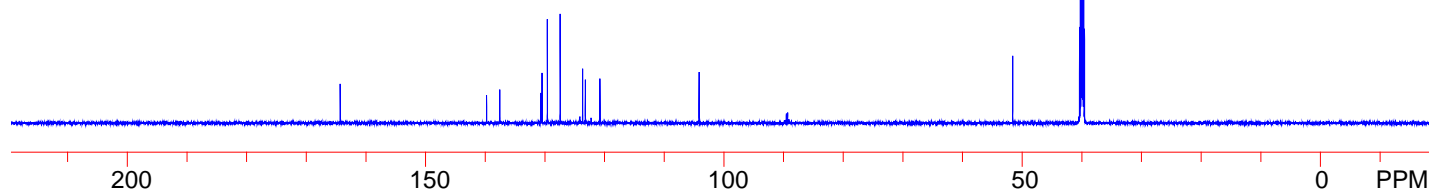




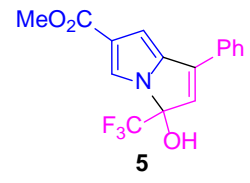
<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>)



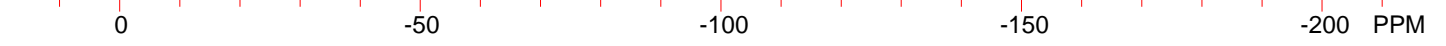
<sup>13</sup>C(<sup>1</sup>H) NMR (150 MHz, DMSO-d<sub>6</sub>)

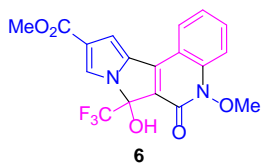
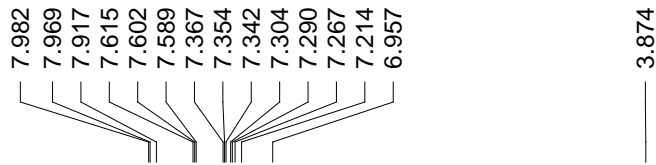


-81.113

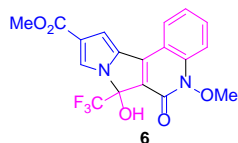
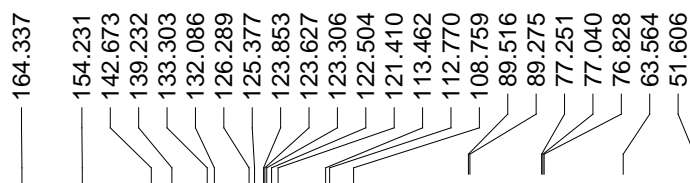
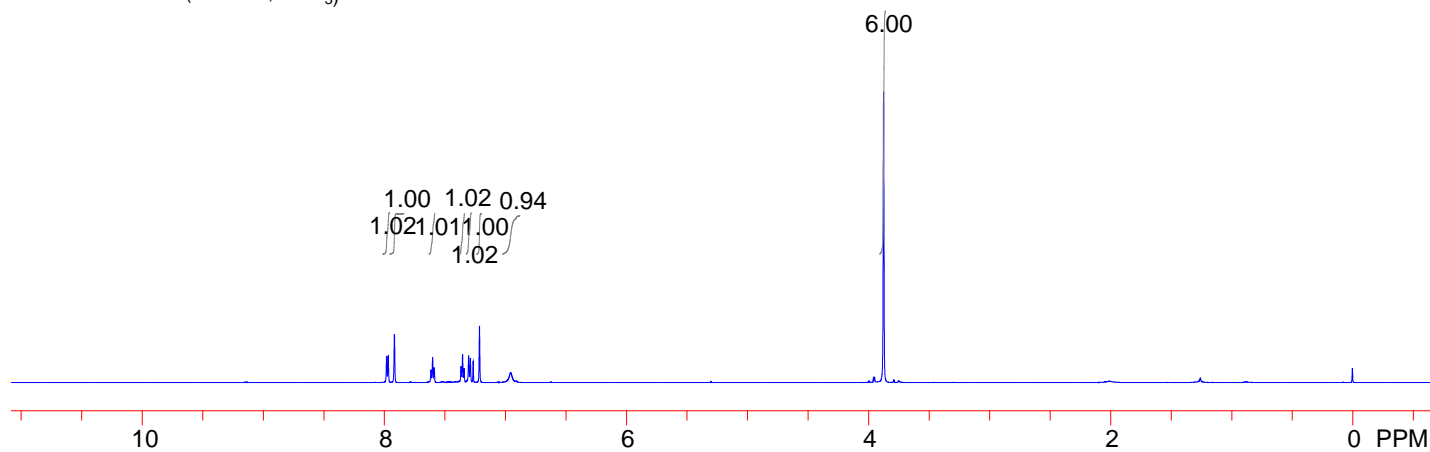


<sup>19</sup>F NMR (565 MHz, DMSO-*d*<sub>6</sub>)

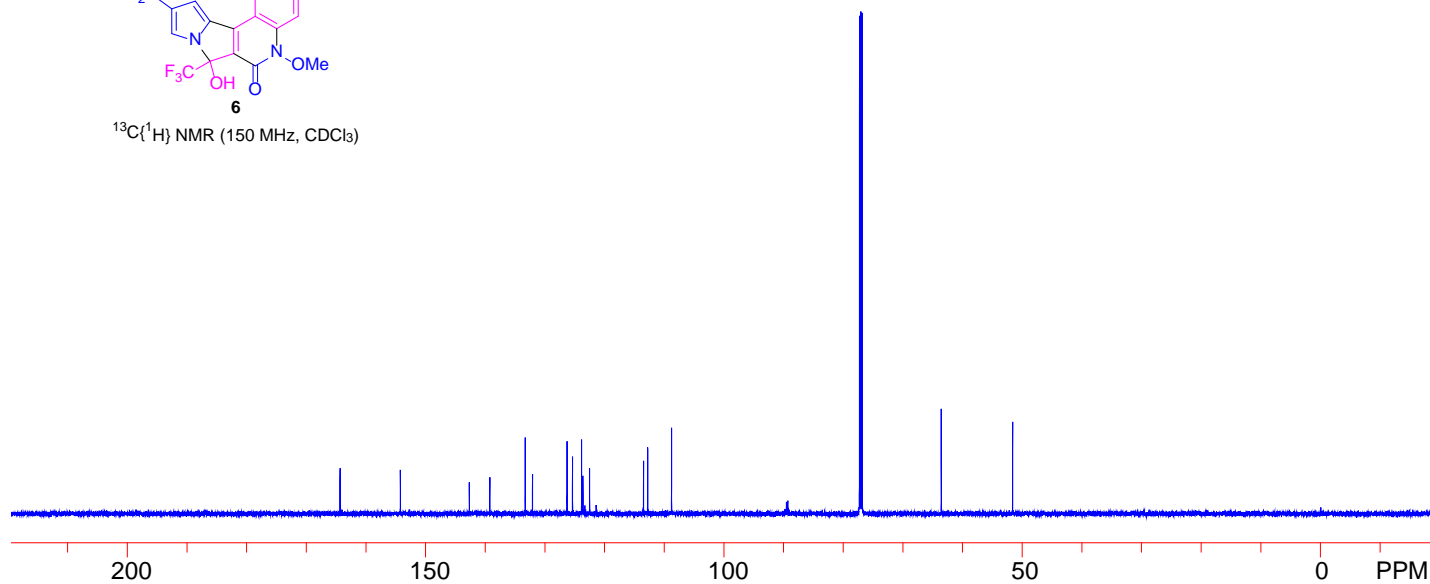




$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )

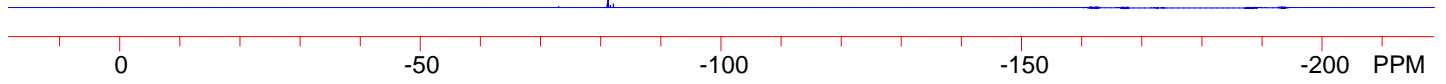
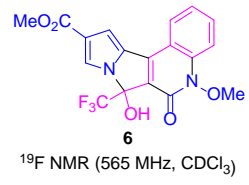


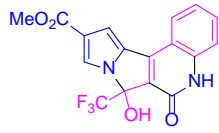
$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{CDCl}_3$ )





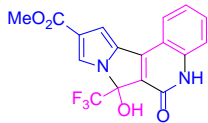
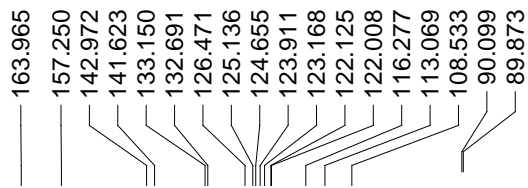
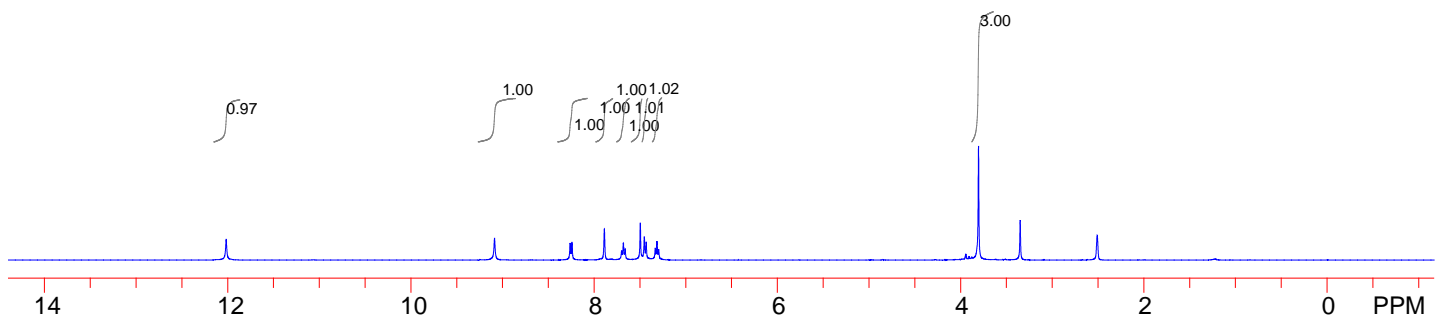
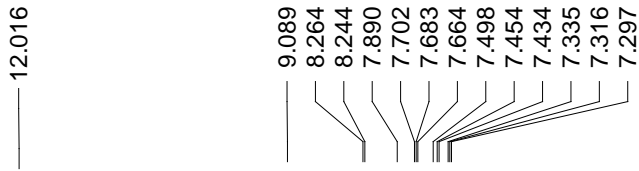
-81.210





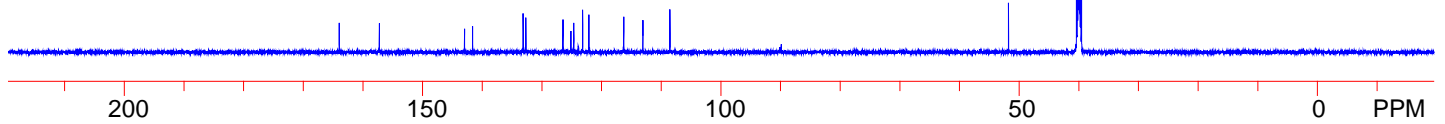
7

$^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )

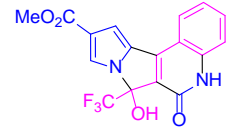


7

$^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{DMSO-}d_6$ )



79.464

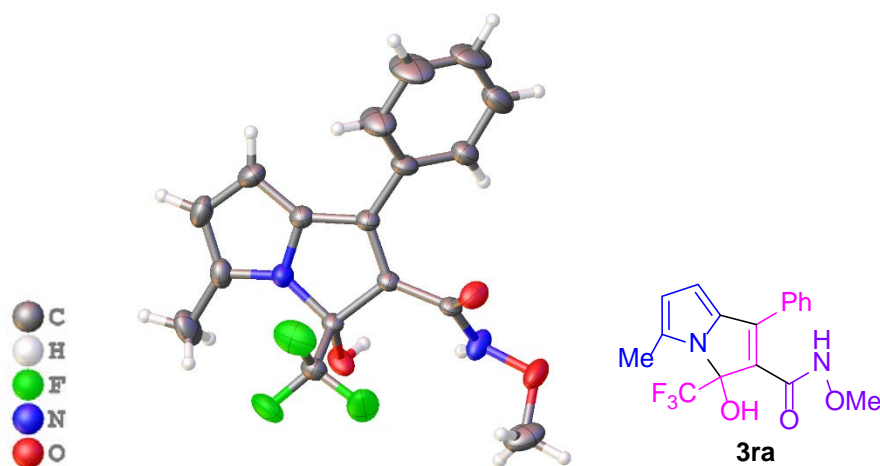


7

<sup>19</sup>F NMR (376 MHz, DMSO-d<sub>6</sub>)

0 -50 -100 -150 -200 PPM

## VI. X-ray crystal structure and data of 3ra



**Fig. S1** X-ray crystal structure of **3ra** with 50% ellipsoid probability

**X-ray structure determination.** Single crystals suitable for X-ray diffraction were obtained by slow evaporation of the solvent from a methanol solution of **3ra**. Crystal data collection and refinement parameters of **3ra** are summarized in Table S1. Intensity data were collected at 293 K on a SuperNova Dual diffractometer using mirror-monochromated Cu K $\alpha$  radiation,  $\lambda = 1.54184 \text{ \AA}$ . The data were corrected for decay, Lorentz, and polarization effects as well as absorption and beam corrections based on the multi-scan technique. Using Olex2, the structure was solved with the SHELXS structure solution program using Direct Methods and refined with the SHELXL refinement package using Least Squares minimisation. Nonhydrogen atoms were refined with anisotropic displacement parameters. The H-atoms were either located or calculated and subsequently treated with a riding model.

**Table S1** Crystallographic data and structure refinement results of **3ra**

Empirical formula	C <sub>17</sub> H <sub>15</sub> F <sub>3</sub> N <sub>2</sub> O <sub>3</sub>
Formula weight	352.31
Temp, K	293(2)
Crystal system	monoclinic
Space group	P2 <sub>1</sub> /c
<i>a</i> , Å	10.9356(7)
<i>b</i> , Å	17.2071(9)
<i>c</i> , Å	9.5578(5)

$\alpha$ (°)	90
$\beta$ (°)	113.916(7)
$\gamma$ (°)	90
Volume, Å <sup>3</sup>	1644.07(18)
$Z$	4
$\rho_{\text{calc}}$ , g cm <sup>-3</sup>	1.423
$\lambda$ , Å	1.54184
$\mu$ , mm <sup>-1</sup>	1.044
No. of data collected	6475
No. of unique data	3142
$R_{\text{int}}$	0.0326
Goodness-of-fit on $F^2$	1.104
$R_1$ , $wR_2$ ( $I > 2\sigma(I)$ )	0.0531, 0.1416
$R_1$ , $wR_2$ (all data)	0.0659, 0.1518

## VII. X-ray crystal structure and data of 7

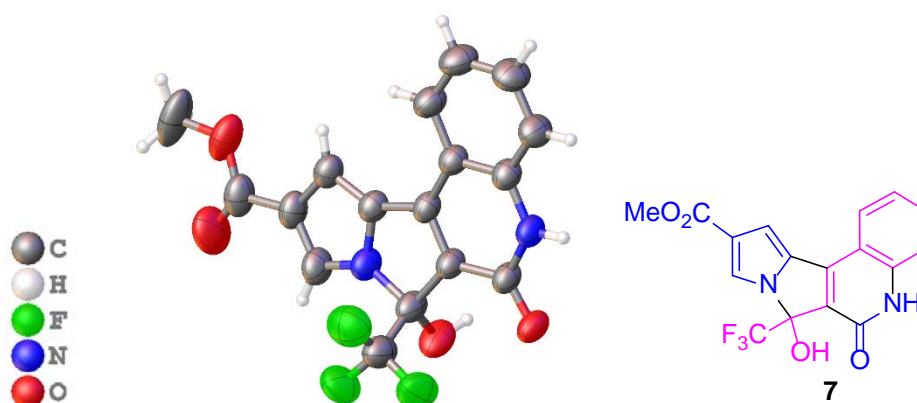


Fig. S2 X-ray crystal structure of 7 with 50% ellipsoid probability

**X-ray structure determination.** Single crystals suitable for X-ray diffraction were obtained by slow evaporation of the solvent from a DMSO solution of compound 7. Crystal data collection and refinement parameters of 7 are summarized in Table S2. Intensity data were collected at 293 K on a SuperNova Dual diffractometer using mirror-monochromated Cu K $\alpha$  radiation,  $\lambda = 1.54184 \text{ \AA}$ . The data were corrected for decay, Lorentz, and polarization effects as well as absorption and beam corrections based on the multi-scan technique. Using Olex2, the structure was solved with the SHELXS structure solution program using Direct Methods and refined with the SHELXL refinement package using Least Squares minimisation. Nonhydrogen atoms were refined with anisotropic displacement parameters. The H-atoms were either located or calculated and subsequently treated with a riding model.

**Table S2** Crystallographic data and structure refinement results of 7

Empirical formula	C <sub>17</sub> H <sub>11</sub> F <sub>3</sub> N <sub>2</sub> O <sub>4</sub>
Formula weight	364.28
Temp, K	293(2)
Crystal system	triclinic
Space group	P-1
<i>a</i> , Å	9.7758(4)
<i>b</i> , Å	10.5130(5)
<i>c</i> , Å	11.2193(5)
$\alpha$ (°)	90.001(4)

$\beta$ (°)	112.552(4)
$\gamma$ (°)	105.120(4)
Volume, Å <sup>3</sup>	1021.51(9)
Z	2
$\rho_{\text{calc}}$ , g cm <sup>-3</sup>	1.184
$\lambda$ , Å	1.54184
$\mu$ , mm <sup>-1</sup>	0.899
No. of data collected	7312
No. of unique data	3851
$R_{\text{int}}$	0.0171
Goodness-of-fit on $F^2$	1.059
$R_1$ , $wR_2$ ( $I > 2\sigma(I)$ )	0.0680, 0.2064
$R_1$ , $wR_2$ (all data)	0.0803, 0.2177

## VIII. References

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