

*Supporting Information*

**I<sub>2</sub>-Promoted Site-Selective C-C Bond Cleavage of Aryl Methyl Ketones as C1 Synthons to Construct 5-Acyl-1*H*-pyrazolo[3,4-*b*]pyridine**

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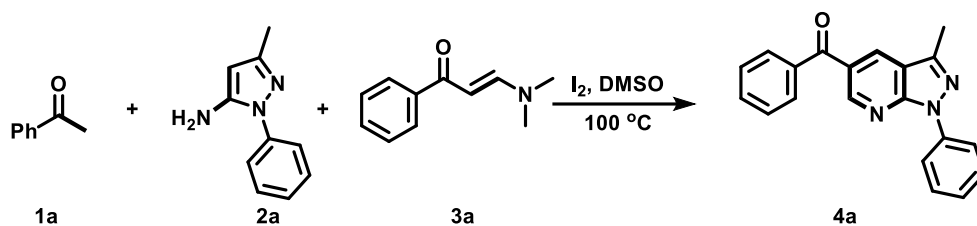
<sup>§</sup>Y. Z. and L.-S. W. contributed equally.

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## 1. General

All substrates and reagents were commercially available and used without further purification. TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200–300 mesh).  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{19}\text{F}$  spectra were recorded in  $\text{CDCl}_3$  on Bruker 400 MHz NMR (AVANCE III HD 400) spectrometers and chemical shifts of  $^1\text{H}$  NMR are reported in ppm, relative to the internal standard of tetramethylsilane (TMS,  $\delta = 0.00$  ppm). Chemical shifts of  $^{13}\text{C}$  NMR were reported in ppm with the solvent as the internal standard ( $\text{CDCl}_3$ ,  $\delta = 77.0$  ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration.  $^{13}\text{C}$  spectra were recorded in  $\text{CDCl}_3$  on 100 MHz NMR spectrometers and resonances ( $\delta$ ) are given in ppm.  $^{19}\text{F}$  spectra were recorded in  $\text{CDCl}_3$  on 376 MHz NMR spectrometers and resonances ( $\delta$ ) are given in ppm. HRMS were obtained on an Agilent LC1290-TOF 6224 equipped with an electrospray source. The *X-ray* crystal-structure determinations of **4a** and **5x** were obtained on a Bruker APEX DUO CCD system. Melting points were determined using XT-4 apparatus and not corrected.

## 2. Screening of the reaction conditions<sup>a</sup>

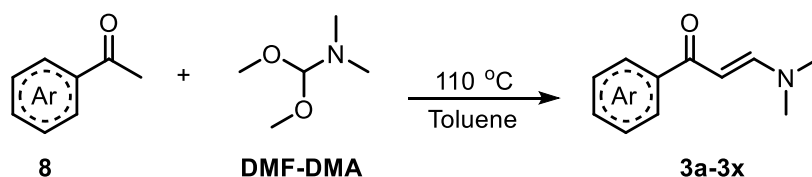


Entry	I <sub>2</sub> (equiv)	Additives	Temp (°C)	Yield (%) <sup>b</sup>
1	0.5	-	100	68
2	1.0	-	100	74
3	<b>1.5</b>	-	<b>100</b>	<b>82</b>
4	2.0	-	100	78
5	1.5	-	80	70
6	1.5	-	120	76
7	1.0	CF <sub>3</sub> COOH	100	65
8	1.0	AcOH	100	70
9	1.0	TfOH	100	55
10	1.0	HCl	100	58
11	1.0	HI	100	54
12	1.0	FeCl <sub>3</sub>	100	63
13	1.0	CuCl <sub>2</sub>	100	56
14	1.0	Cu(OTf) <sub>2</sub>	100	60
15	1.0	ZnCl <sub>2</sub>	100	68
16	1.0	NiCl <sub>2</sub>	100	70
17	1.0	Na <sub>2</sub> CO <sub>3</sub>	100	56
18	1.0	K <sub>2</sub> CO <sub>3</sub>	100	53
19	1.0	NaHCO <sub>3</sub>	100	60
20	1.0	DABCO	100	57
21	1.0	Py	100	63
22	1.0	DIPEA	100	59
23	1.0	Ar ambience	100	75
24	1.0	O <sub>2</sub> ambience	100	73

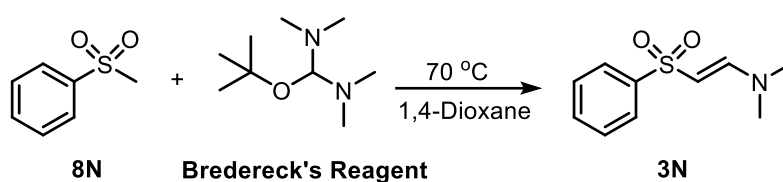
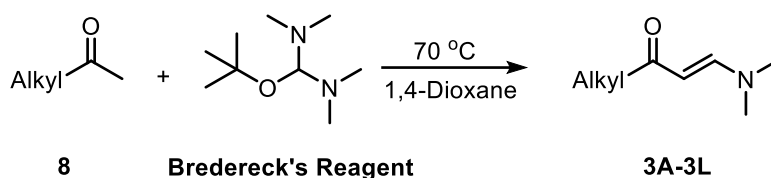
<sup>a</sup>Reaction conditions: **1a** (0.60 mmol), **2a** (0.50 mmol), **3a** (0.50 mmol) and additives (0.5 mmol) at T °C for 4 h under air. <sup>b</sup>Isolated yields.

### 3. Operation methods for synthesis and derivation of target products

#### Synthetic method of ketene amine

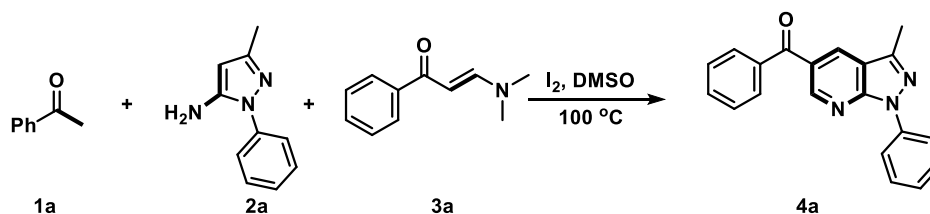


To a stirred solution of aryl methyl ketone (5.0 mmol, 1.0 eq.) in toluene (5.0 mL), 1,1-dimethoxy-*N,N*-dimethylmethanamine (7.0 mmol, 1.4 eq.) was added and stirred at 110 °C. After completion of the reaction (monitored by TLC), use ethyl acetate to transfer the reaction solution to the eggplant shaped bottle, rotate and evaporate under vacuum and pressure at 60 °C to obtain the yellow oil, which turns into yellow solid after cooling. Wash the solid with petroleum ether with the aid of ultrasound and discard the supernatant. In this way, pure yellow solid **3** can be obtained after three times of washing.<sup>1</sup>



To a stirred solution of alkyl methyl ketone (5.0 mmol, 1.0 eq.) in 1,4-dioxane (5.0 mL), Brederick's Reagent (6.0 mmol, 1.2 eq.) was added and stirred at 70 °C. After 5 hours of reaction, ethyl acetate can be used to transfer the reaction solution to the flask, and then the target product can be obtained by vacuum decomposition rotary evaporation. It can be used for standby without column chromatography separation and purification.<sup>2</sup>

#### General procedure for the synthesis of **4** and **5** (**4a** as example)

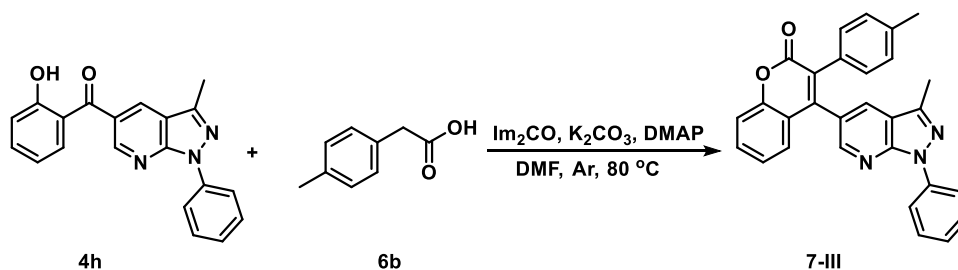


**1.0 mmol scale:** The reactions did not require the protection of inert gases. In a 35 mL sealed tube were added acetophenone (**1a**) (144 mg, 1.2 mmol), iodine (381 mg, 1.5 mmol) and dimethyl sulfoxide (4 mL) and the resulting mixture was stirred at 100 °C (heating block), the reaction tube was removed after about 1 hour. Then additional **2a** (173 mg, 1.0 mmol), **3a** (175 mg, 1.0 mmol) were added at room

temperature, followed by reaction at 100 °C for 4 hours until substrate conversion was almost complete by TLC analysis. The reaction mixture was quenched with saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (50 mL) and NaCl solution (150 mL), then the mixture was extracted with EtOAc (150 mL x 2), the organic layers were separated and combined, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 30:1) to afford the product **4a** (256 mg, 82% yield).

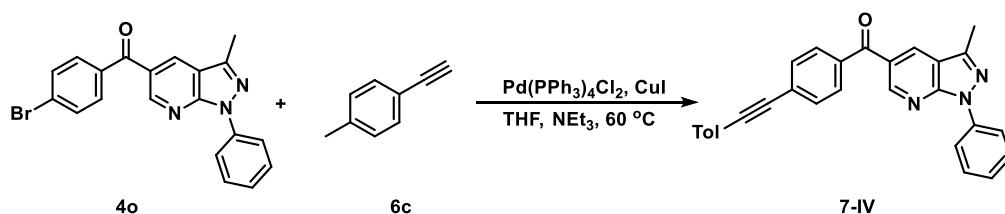
**5.0 mmol scale:** The reactions did not require the protection of inert gases. In a 100 mL round flask were added acetophenone (**1a**) (720 mg, 6.0 mmol), iodine (1905 mg, 7.5 mmol) and dimethyl sulfoxide (30 mL) and the resulting mixture was stirred in oil bath heating at 100 °C, the round flask was removed after about 1 hour. Then additional **2a** (865 mg, 5.0 mmol), **3a** (875 mg, 5.0 mmol) were added at room temperature, followed by reaction at 100 °C for 4 hours until substrate conversion was almost complete by TLC analysis. The reaction mixture was quenched with saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (150 mL) and NaCl solution (300 mL), then the mixture was extracted with EtOAc (300 mL x 2), the organic layers were separated and combined, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 25:1) to afford the product **4a** (1173 mg, 75% yield).

### Synthesis of derivative 7-III<sup>3</sup>



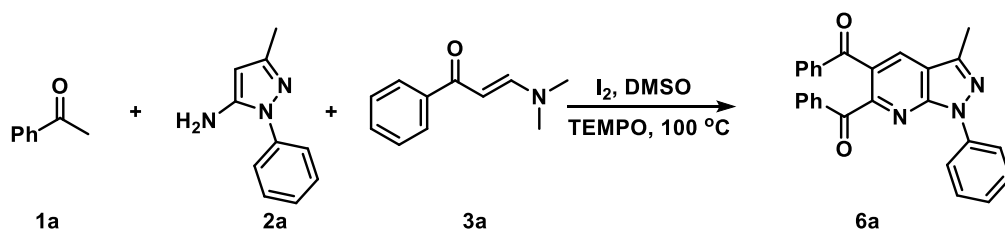
Product of *ortho*-hydroxyl **4h** (165 mg, 0.5 mmol), carbonyl diimidazole (162 mg, 1.0 mmol), K<sub>2</sub>CO<sub>3</sub> (69 mg, 0.5 mmol), DMAP (7 mg, 0.05 mmol), and 4-methylphenylacetic acid (150 mg, 1.0 mmol) were dissolved in DMF (3 ml) and heated under an argon atmosphere for 6h at 80 °C. After addition of EtOAc and brine, the biphasic mixture was several times extracted with brine. The combined organic phases were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated to give crude phenol. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 15:1) to afford the product **7-III** (204 mg, 92% yield).

### Synthesis of derivative 7-IV<sup>4</sup>



Product of *para*-bromine **4o** (196 mg, 0.5 mmol), *p*-methylphenylacetylene (70 mg, 0.6 mmol),  $\text{Pd(PPh}_3)_2\text{Cl}_2$  (18 mg, 0.025 mmol),  $\text{CuI}$  (9.5 mg, 0.05 mmol), and  $\text{NEt}_3$  (14 mL). The vial was then purged with argon and sealed. The reaction mixture was stirred at  $80\text{ }^\circ\text{C}$  for 18 h, until the disappearance of starting material was observed, as monitored by thin layer chromatography. The reaction mixture was diluted with  $\text{EtOAc}$  (40 mL) and washed with brine (40 mL), and the aqueous phase was then extracted with  $\text{EtOAc}$  (40 mL x 2). The combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated using a rotary evaporator under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/ $\text{EtOAc}$  = 30:1) to afford the product **7-IV** (177 mg, 83% yield).

### Synthesis of derivative 6a



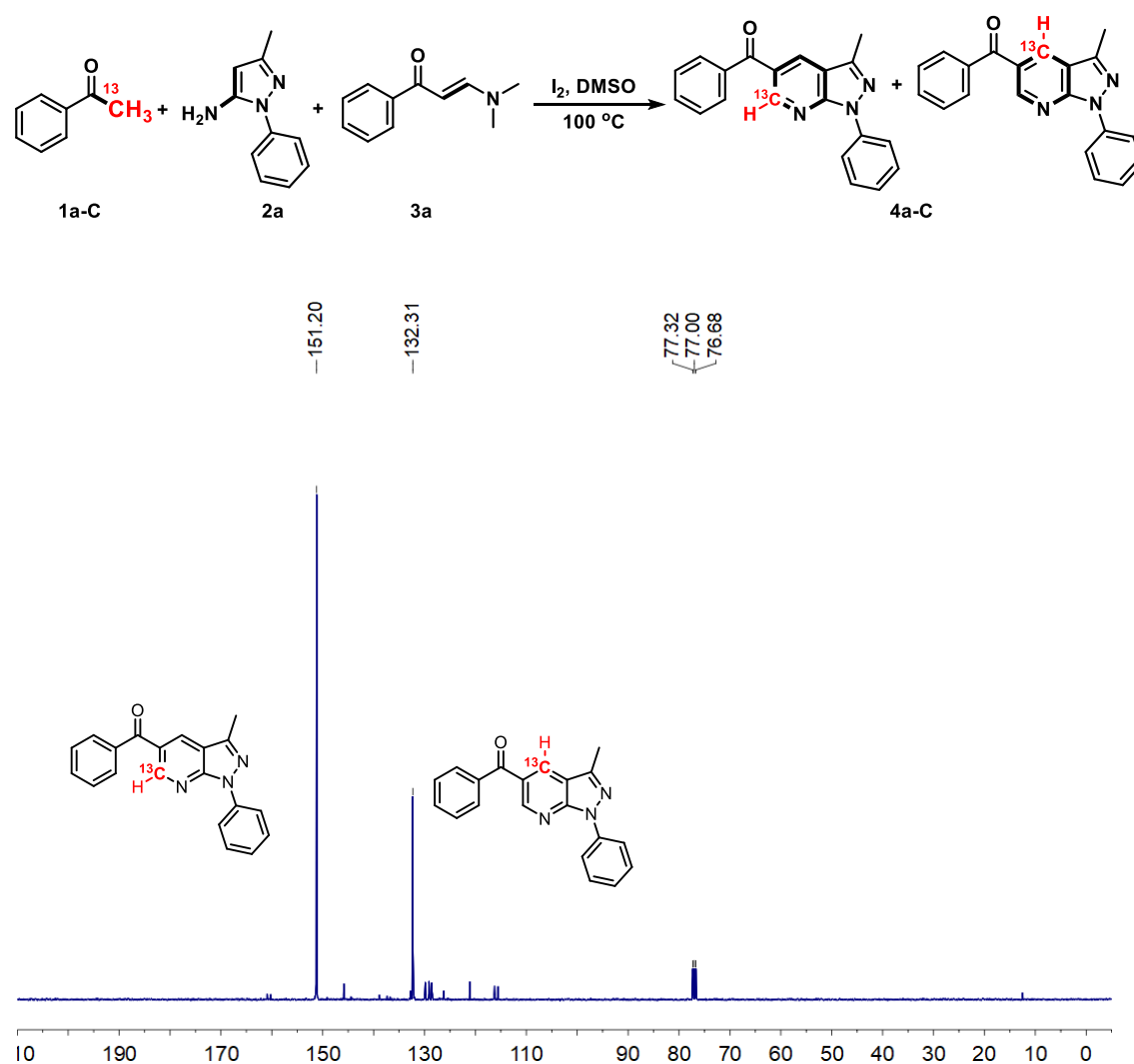
In a 35 mL sealed tube were added acetophenone (**1a**) (144 mg, 1.2 mmol), iodine (381 mg, 1.5 mmol) and dimethyl sulfoxide (4 mL) and the resulting mixture was stirred at  $100\text{ }^\circ\text{C}$  (heating block), the reaction tube was removed after about 1 hour. Then additional **2a** (173 mg, 1.0 mmol), **3a** (175 mg, 1.0 mmol) and TEMPO (312 mg, 2.0 mmol) were added at room temperature, followed by reaction at  $100\text{ }^\circ\text{C}$  for 4 hours until substrate conversion was almost complete by TLC analysis. The reaction mixture was quenched with saturated  $\text{Na}_2\text{S}_2\text{O}_3$  solution (50 mL) and  $\text{NaCl}$  solution (150 mL), then the mixture was extracted with  $\text{EtOAc}$  (150 mL x 2), the organic layers were separated and combined, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/ $\text{EtOAc}$  = 15:1) to afford the product **6a** (250 mg, 60% yield).

1. (a) Wang, F.; Sun, W.; Wang, Y.; Jiang, Y.; Loh, T. P. *Org. Lett.* **2018**, *20*, 1256-1260. (b) Ni, M.; Zhang, J.; Liang, X.; Jiang, Y.; Loh, T. P. *Chem. Commun.* **2017**, *53*, 12286-12289.
2. (a) Bredereck, H.; Simchen, G.; Rebsdatt, S.; Kantlehner, W.; Horn, P.; Wahl, R.; Hoffmann, H.; Grieshaber, P. *Chem. Ber.* **1968**, *101*, 41. (b) Schuda, P. F.; Ebner, C. B.; Morgan, T. M. *Tetrahedron Lett.* **1986**, *27*, 2567. (c) Morera, E.; Pinnen, F.; Lucente, G. *Org. Lett.* **2002**, *4*, 1139-1142
3. Waldmann, H.; Kühn, M.; Liu, W.; Kumar, K. *Chem. Commun.* **2008**, 1211-1213.
4. Domaradzki, M. E.; Long, Y.; She, Z.; Liu, X.; Zhang, G.; Chen, Y. *J. Org. Chem.* **2015**, *80*, 11360-11368.

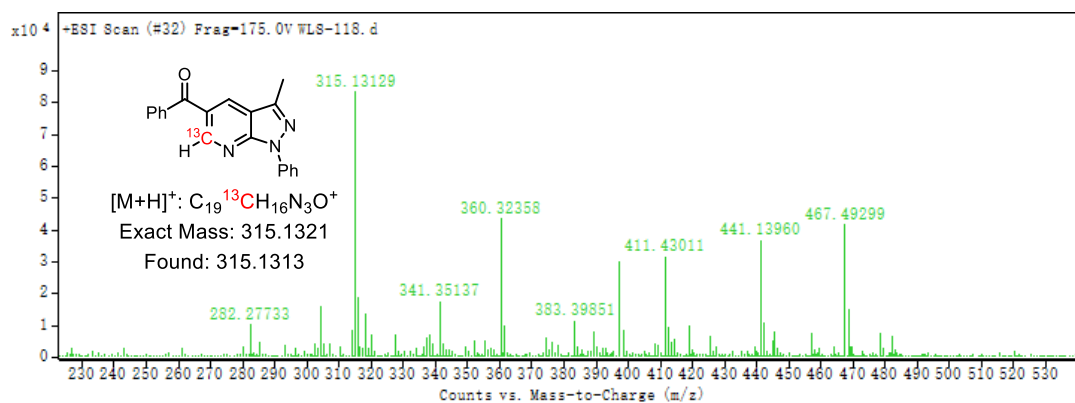
## 4. Mechanistic studies

### Isotope labeling experiment

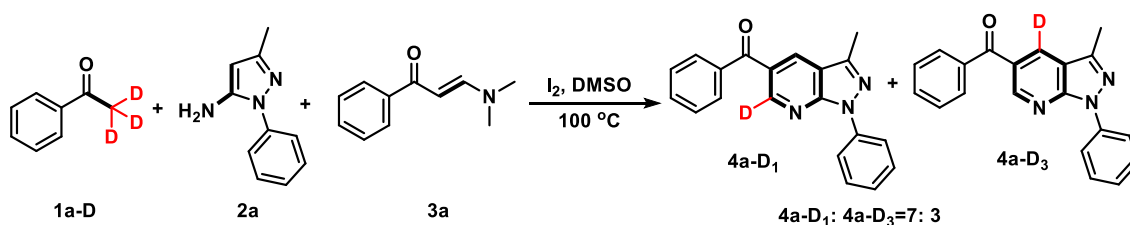
In a 35 mL sealed tube were added  $^{13}\text{C}$ -labeled acetophenone (**1a-C**) (73 mg, 0.6 mmol), iodine (190 mg, 0.75 mmol) and dimethyl sulfoxide (3 mL) and the resulting mixture was stirred at 100 °C (heating block), the reaction tube was removed after about 1 hour. Then additional **2a** (87 mg, 0.5 mmol), **3a** (88 mg, 0.5 mmol) were added at room temperature, followed by reaction at 100 °C for 4 hours until substrate conversion was almost complete by TLC analysis. The reaction mixture was quenched with saturated  $\text{Na}_2\text{S}_2\text{O}_3$  solution (50 mL) and NaCl solution (150 mL), then the mixture was extracted with EtOAc (150 mL x 2), the organic layers were separated and combined, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 30:1) to afford the product **4a-C** (122 mg, 78% yield). the compound **4a-C** was confirmed by  $^{13}\text{C}$  NMR and HRMS.

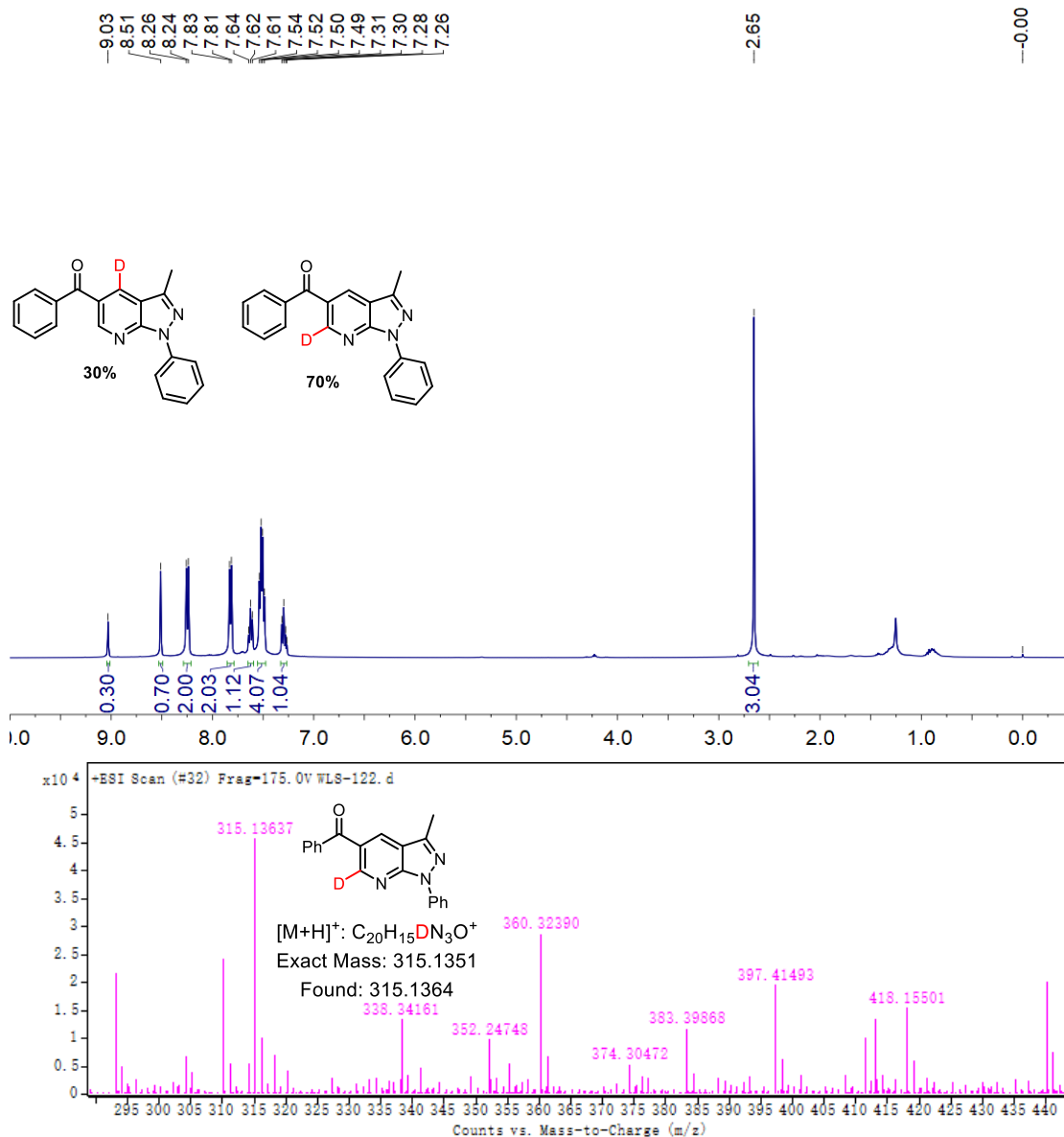




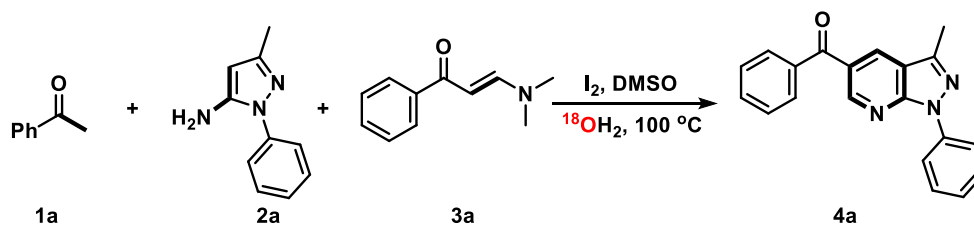


In a 35 mL sealed tube were added CD<sub>3</sub>-labeled acetophenone (**1a-D**) (74 mg, 0.6 mmol), iodine (190 mg, 0.75 mmol) and dimethyl sulfoxide (3 mL) and the resulting mixture was stirred at 100 °C (heating block), the reaction tube was removed after about 1 hour. Then additional **2a** (87 mg, 0.5 mmol), **3a** (88 mg, 0.5 mmol) were added at room temperature, followed by reaction at 100 °C for 4 hours until substrate conversion was almost complete by TLC analysis. The reaction mixture was quenched with saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (50 mL) and NaCl solution (150 mL), then the mixture was extracted with EtOAc (150 mL x 2), the organic layers were separated and combined, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 30:1) to afford the product **4a-D** (125 mg, 80% yield). the compound **4a-D** was confirmed by <sup>1</sup>H NMR and HRMS.



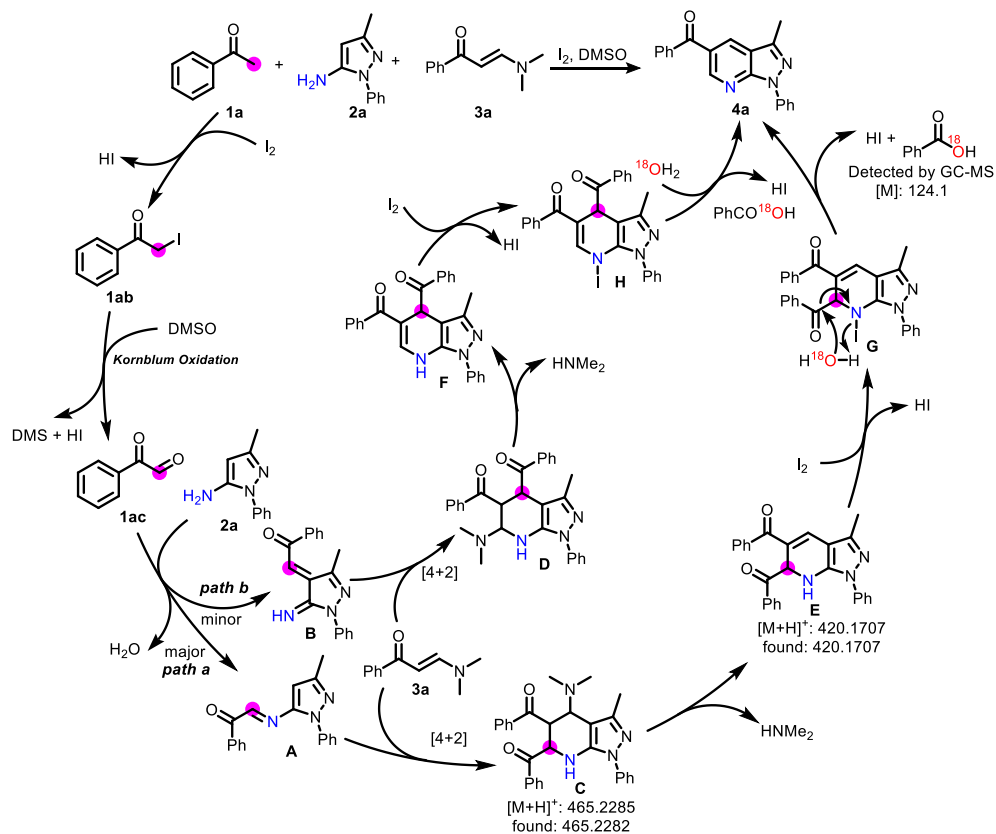


### The mechanism of HPLC-MS and GC-MS

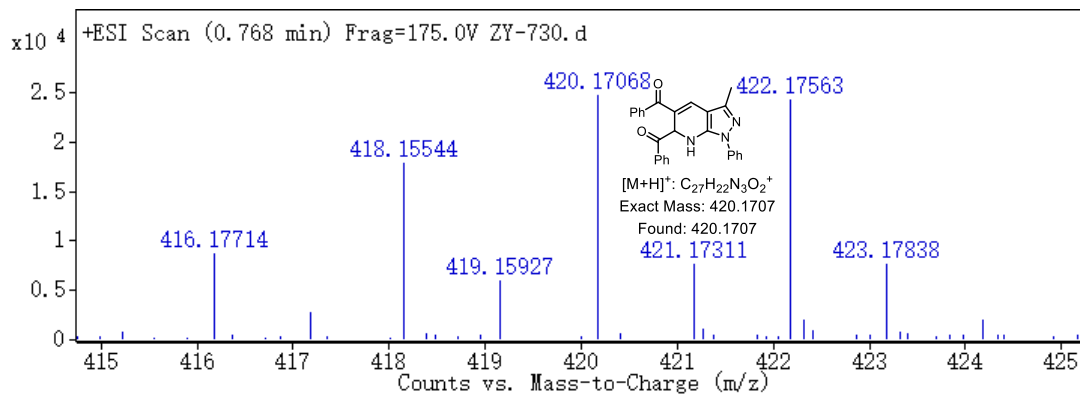
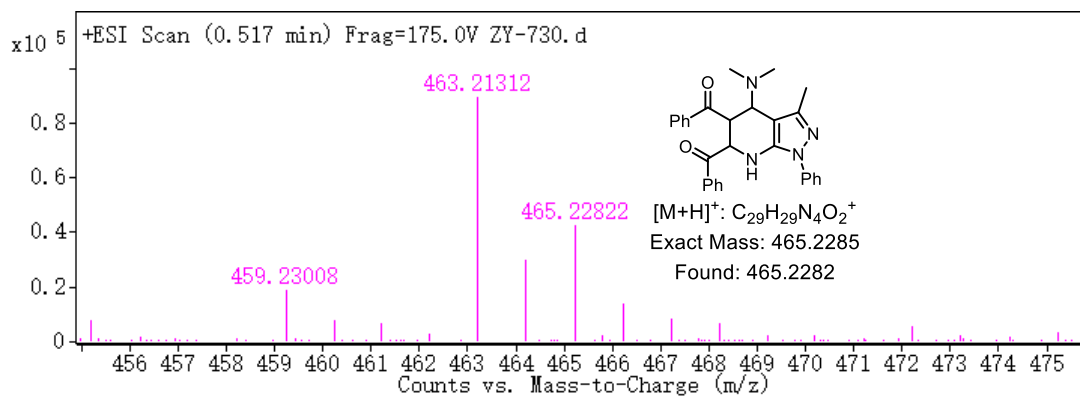


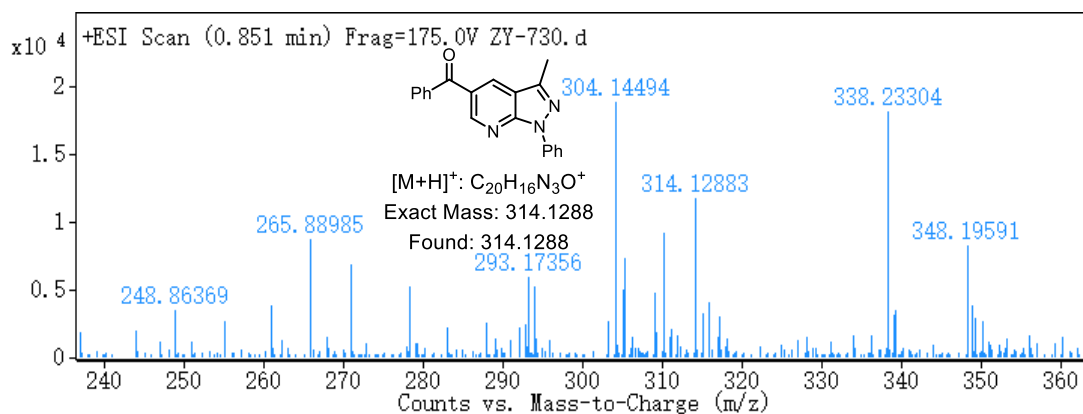
In a sealed tube were added acetophenone (**1a**) (72 mg, 0.6 mmol), iodine (190 mg, 0.75 mmol) and dimethyl sulfoxide (2 mL) and the resulting mixture was stirred at  $100\text{ }^\circ\text{C}$  (heating block), the reaction tube was removed after about 1 hour. Then additional **2a** (87 mg, 0.5 mmol), **3a** (88 mg, 0.5 mmol) and  $^{18}O$ -labeled water ( $^{18}OH_2$ ) (100 mg, 5.0 mmol) were added at room temperature. Then, the 1 mL of the reaction solution was quenched with 4 mL of saturation  $Na_2S_2O_3$  solution, and then extracted with 3 mL of EtOAc. Then 1.0 mL of the extraction solution was added into the test bottle and

diluted with 0.5 mL of EtOAc. The samples were immediately monitored by HPLC-MS or GC-MS.

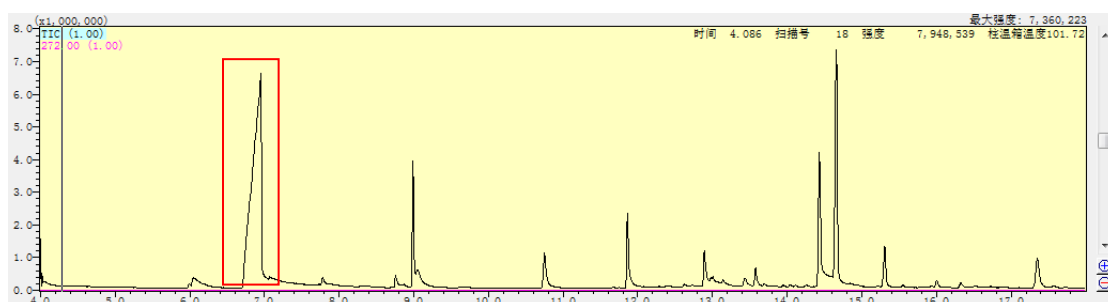


HPLC-MS:

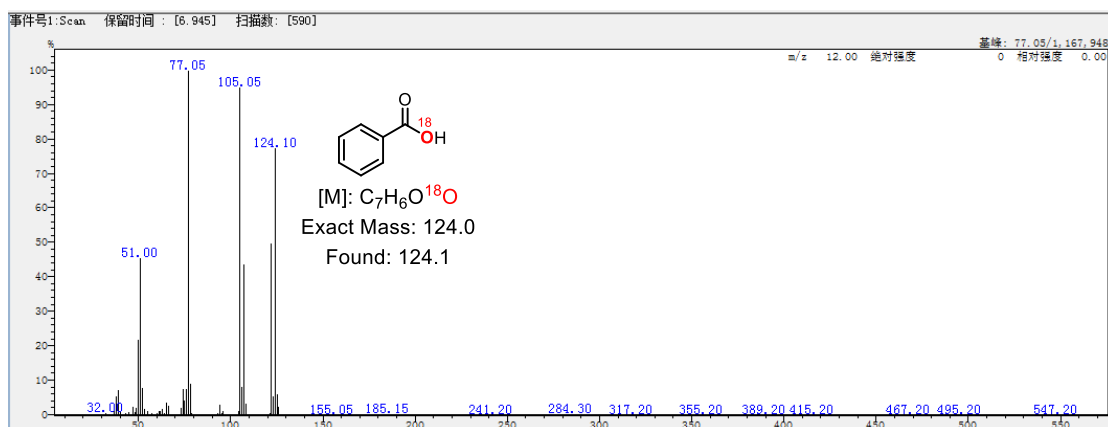




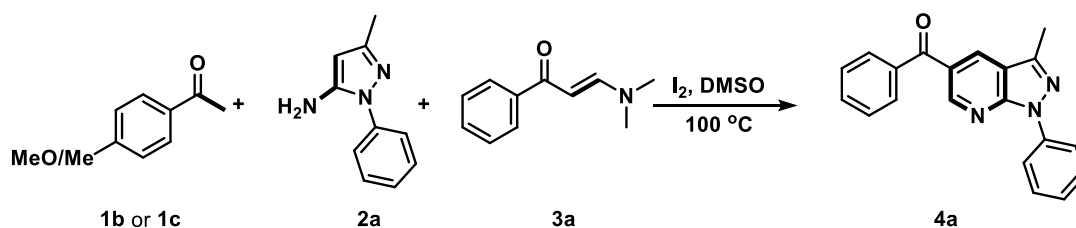
GC-MS:



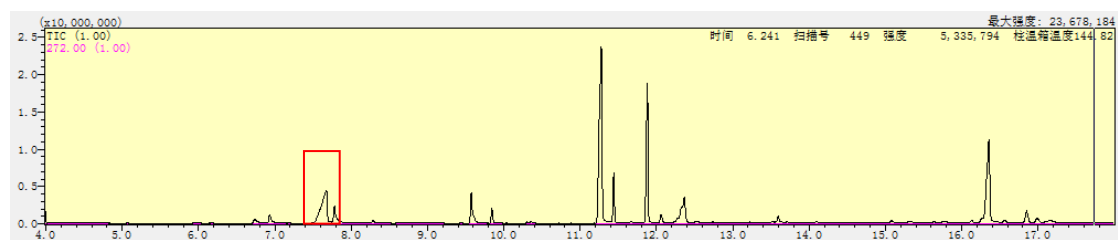
Retention time = 6.95 min



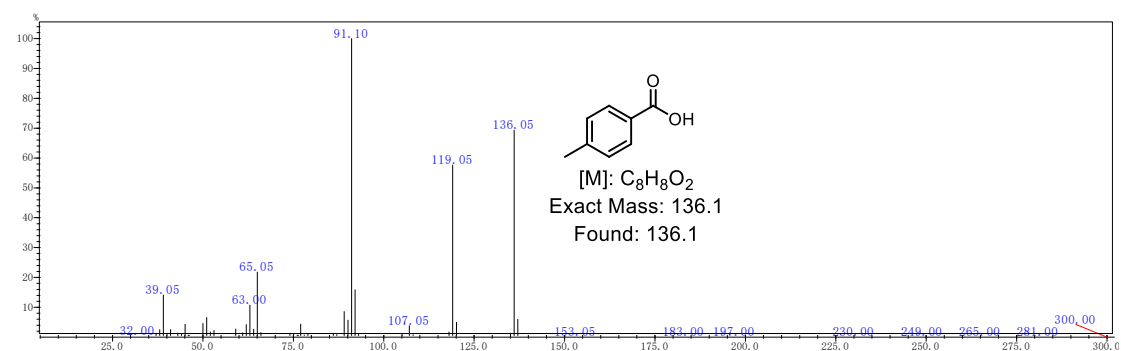
When we use *p*-methylacetophenone (**1b**) or *p*-methoxyacetophenone (**1c**) instead of acetophenone to participate in the reaction, the formation of corresponding aryl carboxylic acids can be detected by GC-MS under the same reaction conditions and operation.



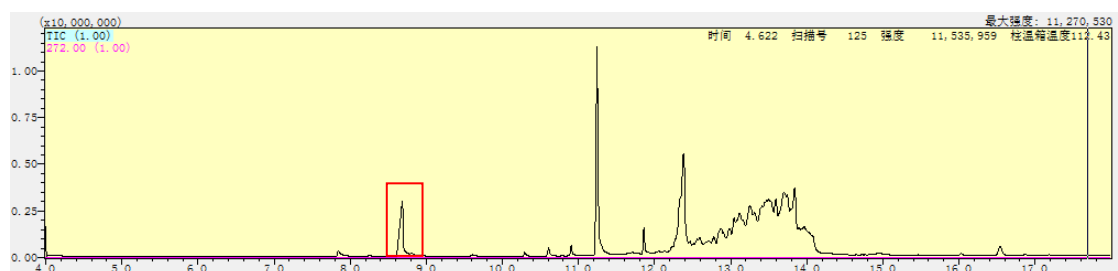
*p*-methylacetophenone (**1b**):



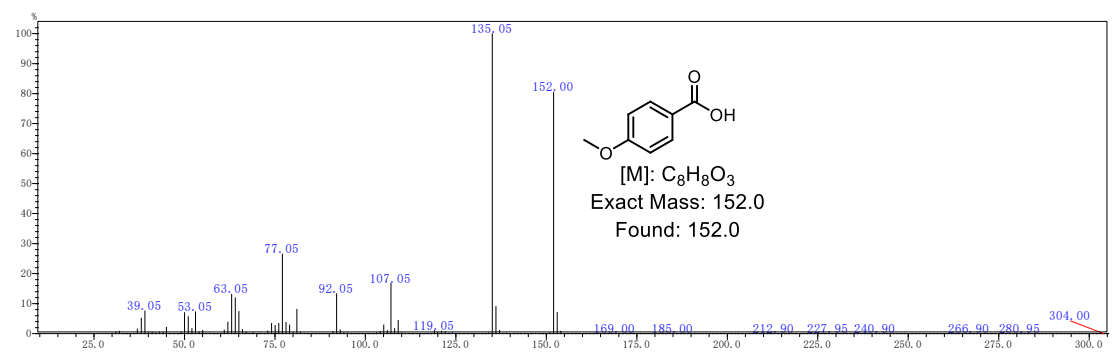
Retention time = 7.67 min



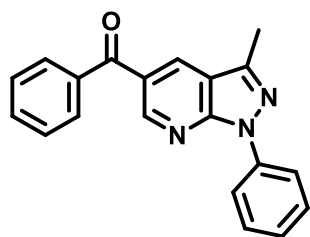
*p*-methoxyacetophenone (**1c**):



Retention time = 8.68 min

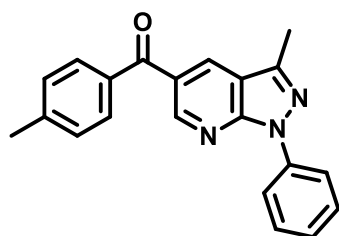


## 5. Characterization data for compounds



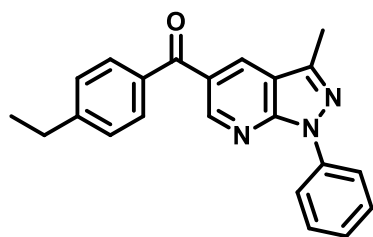
### (3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridin-5-yl)(phenyl)methanone (4a):

Yield 82%; 256 mg; yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 118–120 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.02 (s, 1H), 8.49 (s, 1H), 8.24 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.53–7.48 (m, 4H), 7.29 (t, *J* = 7.2 Hz, 1H), 2.64 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 194.3, 151.2, 151.0, 144.3, 138.8, 137.3, 132.6, 132.2, 129.7, 128.9, 128.4, 126.6, 126.0, 120.8, 116.2, 12.3. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>16</sub>N<sub>3</sub>O<sup>+</sup>: 314.1288; found: 314.1286.



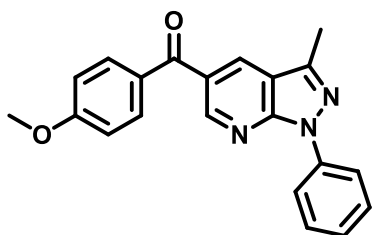
### (3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridin-5-yl)(p-tolyl)methanone (4b):

Yield 84%; 274 mg; white solid; column chromatography, silica gel (PE:EA, 30:1); mp 113–115 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.03 (d, *J* = 1.6 Hz, 1H), 8.50 (d, *J* = 1.6 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 8.0 Hz, 2H), 7.33–7.29 (m, 3H), 2.66 (s, 3H), 2.46 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 194.2, 151.3, 151.0, 144.3, 143.6, 138.9, 134.7, 132.1, 130.1, 129.2, 129.1, 127.1, 126.1, 121.0, 116.3, 21.6, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>21</sub>H<sub>18</sub>N<sub>3</sub>O<sup>+</sup>: 328.1444; found: 328.1440.



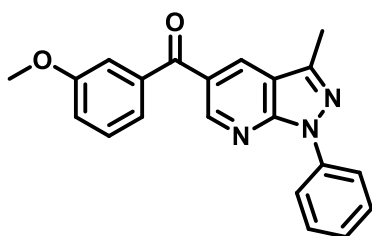
### (4-ethylphenyl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridin-5-yl)methanone (4c):

Yield 85%; 289 mg; yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 99–101 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.01 (s, 1H), 8.47 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.33 (d, *J* = 7.6 Hz, 2H), 7.27 (t, *J* = 7.2 Hz, 1H), 2.73 (q, *J* = 7.6 Hz, 2H), 2.63 (s, 3H), 1.28 (t, *J* = 7.6 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 194.0, 151.1, 150.9, 149.6, 144.2, 138.8, 134.8, 132.0, 130.1, 128.9, 127.9, 127.0, 125.9, 120.8, 116.2, 28.8, 15.1, 12.3. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>22</sub>H<sub>20</sub>N<sub>3</sub>O<sup>+</sup>: 342.1601; found: 342.1606.



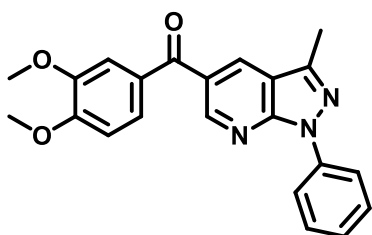
**(4-methoxyphenyl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4d):**

Yield 87%; 298 mg; light yellow solid; column chromatography, silica gel (PE:EA, 15:1); mp 100–102 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.99 (d, *J* = 1.6 Hz, 1H), 8.47 (d, *J* = 1.6 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 2H), 7.84 (d, *J* = 8.8 Hz, 2H), 7.51 (t, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 3H), 2.66 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 193.1, 163.3, 151.2, 150.8, 144.2, 138.9, 132.3, 131.8, 129.8, 129.0, 127.4, 126.0, 120.9, 116.3, 113.7, 55.4, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>21</sub>H<sub>18</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup>: 344.1394; found: 344.1395.



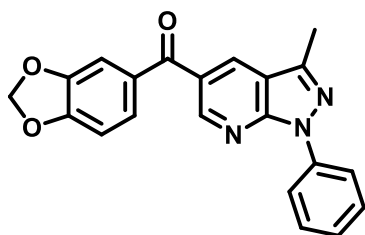
**(3-methoxyphenyl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4e):**

Yield 85%; 291 mg; light yellow solid; column chromatography, silica gel (PE:EA, 15:1); mp 92–94 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.05 (s, 1H), 8.53 (s, 1H), 8.25 (d, *J* = 8.4 Hz, 2H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.44–7.29 (m, 4H), 7.17 (d, *J* = 8.0 Hz, 1H), 3.87 (s, 3H), 2.67 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 194.3, 159.7, 151.3, 151.1, 144.4, 138.9, 138.7, 132.3, 129.4, 129.1, 126.9, 126.2, 122.5, 121.0, 119.0, 116.3, 114.2, 55.4, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>21</sub>H<sub>18</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup>: 344.1394; found: 344.1395.



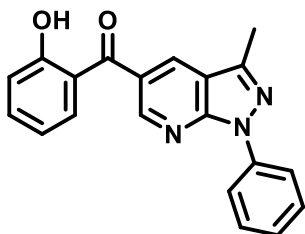
**(3,4-dimethoxyphenyl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4f):**

Yield 81%; 302 mg; yellow solid; column chromatography, silica gel (PE:EA, 8:1); mp 148–150 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.01 (s, 1H), 8.50 (s, 1H), 8.26 (d, *J* = 8.0 Hz, 2H), 7.54–7.50 (m, 3H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 6.8 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 3.97 (s, 3H), 3.96 (s, 3H), 2.67 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 193.1, 153.2, 151.2, 150.7, 149.1, 144.2, 138.9, 131.8, 130.0, 129.0, 127.4, 126.0, 125.1, 120.9, 116.2, 111.8, 109.8, 56.01, 55.95, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>22</sub>H<sub>20</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup>: 374.1499; found: 374.1500.



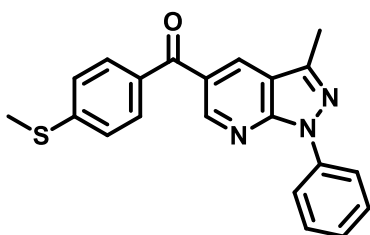
**benzo[d][1,3]dioxol-5-yl(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4g):**

Yield 83%; 296 mg; light yellow solid; column chromatography, silica gel (PE:EA, 15:1); mp 127–129 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.01 (s, 1H), 8.51 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 2H), 7.54 (t, *J* = 8.0 Hz, 2H), 7.41–7.38 (m, 2H), 7.33 (t, *J* = 7.2 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.11 (s, 2H), 2.70 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 192.9, 151.8, 151.3, 150.8, 148.2, 144.4, 138.9, 132.0, 131.8, 129.1, 127.4, 126.7, 126.2, 121.1, 116.4, 109.7, 107.9, 102.0, 12.5. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>21</sub>H<sub>16</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup>: 358.1186; found: 358.1188.



**(2-hydroxyphenyl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4h):**

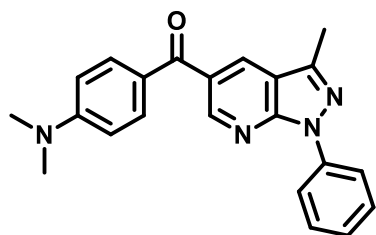
Yield 65%; 213 mg; light yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 115–117 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 11.83 (s, 1H), 8.91 (d, *J* = 1.6 Hz, 1H), 8.39 (d, *J* = 1.6 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.54–7.48 (m, 3H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 1H), 6.91 (t, *J* = 7.6 Hz, 1H), 2.66 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 198.7, 163.0, 151.1, 149.9, 144.2, 138.8, 136.5, 132.9, 131.6, 129.0, 127.1, 126.1, 121.0, 119.1, 118.9, 118.6, 116.2, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>16</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup>: 330.1237; found: 330.1236.



**(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(4-(methylthio)phenyl)methanone (4i):**

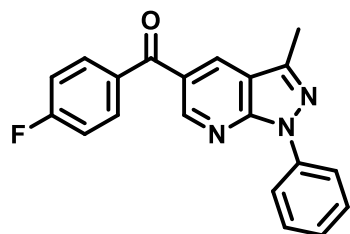
Yield 87%; 312 mg; light yellow solid; column chromatography, silica gel (PE:EA, 20:1); mp 106–108 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.98 (s, 1H), 8.44 (s, 1H), 8.24 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 3H), 2.63 (s, 3H), 2.51 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 193.2, 151.1, 150.7, 145.7, 144.2, 138.8, 133.2, 131.8, 130.3, 128.9, 126.8, 125.9, 124.7, 120.7, 116.2, 14.6, 12.3. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>21</sub>H<sub>18</sub>N<sub>3</sub>OS<sup>+</sup>: 360.1165; found: 360.1168.





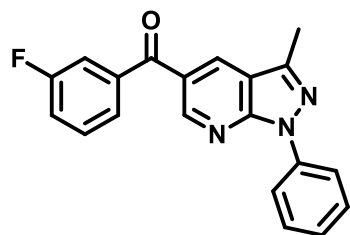
**(4-(dimethylamino)phenyl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4j):**

Yield 77%; 274 mg; yellow solid; column chromatography, silica gel (PE:EA, 10:1); mp 128–130 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.99 (s, 1H), 8.45 (s, 1H), 8.28 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 2H), 3.07 (s, 6H), 2.66 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 192.4, 153.3, 151.1, 150.6, 144.0, 139.1, 132.5, 131.4, 129.0, 128.4, 125.9, 124.5, 120.9, 116.3, 110.7, 39.9, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>22</sub>H<sub>21</sub>N<sub>4</sub>O<sup>+</sup>: 357.1710; found: 357.1713.



**(4-fluorophenyl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4k):**

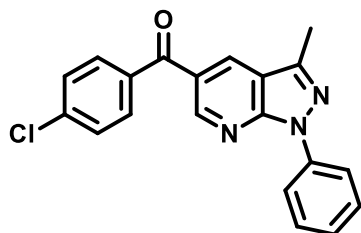
Yield 76%; 251 mg; yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 127–129 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.99 (d, *J* = 2.0 Hz, 1H), 8.48 (d, *J* = 2.0 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 2H), 7.86 (dd, *J* = 8.4 Hz, 5.6 Hz, 2H), 7.51 (t, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 8.4 Hz, 2H), 2.66 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 192.9, 165.4 (d, *J* = 254.0 Hz, <sup>1</sup>*J*<sub>CF</sub>), 151.3, 150.8, 144.4, 138.8, 133.6 (d, *J* = 3.0 Hz, <sup>4</sup>*J*<sub>CF</sub>), 132.4 (d, *J* = 9.0 Hz, <sup>3</sup>*J*<sub>CF</sub>), 132.1, 129.1, 126.7, 126.2, 121.0, 116.3, 115.7 (d, *J* = 22.0 Hz, <sup>2</sup>*J*<sub>CF</sub>), 12.4. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -105.03. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>15</sub>N<sub>3</sub>OF<sup>+</sup>: 332.1194; found: 332.1195.



**(3-fluorophenyl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4l):**

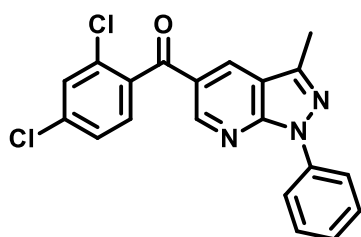
Yield 78%; 258 mg; light yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 107–109 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.02 (s, 1H), 8.52 (s, 1H), 8.24 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.55–7.48 (m, 4H), 7.36–7.30 (m, 2H), 2.68 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 193.1, 162.6 (d, *J* = 248.0 Hz, <sup>1</sup>*J*<sub>CF</sub>), 151.4, 151.0, 144.5, 139.5 (d, *J* = 7.0 Hz, <sup>3</sup>*J*<sub>CF</sub>), 138.8, 132.3, 130.2 (d, *J* = 8.0 Hz, <sup>3</sup>*J*<sub>CF</sub>), 129.1, 126.3, 126.2, 125.6 (d, *J* = 2.0 Hz, <sup>4</sup>*J*<sub>CF</sub>), 121.1, 119.7 (d, *J* = 21.0 Hz, <sup>2</sup>*J*<sub>CF</sub>), 116.6 (d, *J* = 22.0 Hz, <sup>2</sup>*J*<sub>CF</sub>), 116.4, 12.4. <sup>19</sup>F

NMR (376 MHz, CDCl<sub>3</sub>)  $\delta$  -111.15. HRMS (ESI):  $m/z$  [M+H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>15</sub>N<sub>3</sub>OF<sup>+</sup>: 332.1194; found: 332.1196.



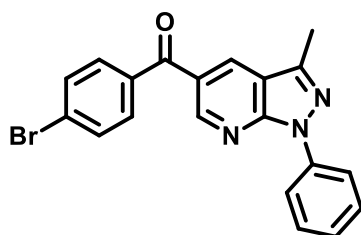
**(4-chlorophenyl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4m):**

Yield 75%; 260 mg; light yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 102–104 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  9.00 (s, 1H), 8.48 (s, 1H), 8.24 (d,  $J$  = 8.0 Hz, 2H), 7.77 (d,  $J$  = 8.4 Hz, 2H), 7.53–7.49 (m, 4H), 7.31 (t,  $J$  = 7.2 Hz, 1H), 2.66 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  193.2, 151.3, 150.9, 144.4, 139.2, 138.8, 135.6, 132.2, 131.2, 129.1, 128.9, 126.4, 126.2, 121.0, 116.3, 12.4. HRMS (ESI):  $m/z$  [M+H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>15</sub>N<sub>3</sub>OCl<sup>+</sup>: 348.0898; found: 348.0905.



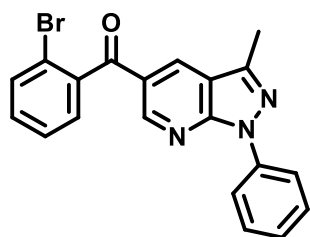
**(2,4-dichlorophenyl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4n):**

Yield 73%; 278 mg; light yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 134–136 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.94 (s, 1H), 8.46 (s, 1H), 8.23 (d,  $J$  = 8.0 Hz, 2H), 7.53–7.46 (m, 3H), 7.40 (s, 2H), 7.30 (t,  $J$  = 7.2 Hz, 1H), 2.64 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  192.1, 151.5, 151.2, 144.8, 138.7, 137.1, 136.3, 132.3, 132.1, 130.2, 130.1, 129.0, 127.4, 126.3, 125.8, 121.0, 116.7, 12.4. HRMS (ESI):  $m/z$  [M+H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>14</sub>N<sub>3</sub>OCl<sub>2</sub><sup>+</sup>: 382.0508; found: 382.0506.



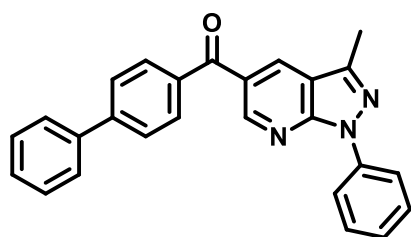
**(4-bromophenyl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4o):**

Yield 71%; 278 mg; light yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 123–125 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  9.01 (s, 1H), 8.49 (s, 1H), 8.24 (d,  $J$  = 6.8 Hz, 2H), 7.77–7.65 (m, 4H), 7.56–7.49 (m, 2H), 7.35–7.29 (m, 1H), 2.68 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  193.4, 151.3, 150.9, 144.5, 138.8, 136.1, 132.2, 131.9, 131.3, 129.1, 127.8, 126.4, 126.3, 121.1, 116.4, 12.5. HRMS (ESI):  $m/z$  [M+H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>15</sub>N<sub>3</sub>OBr<sup>+</sup>: 392.0392; found: 392.0392.



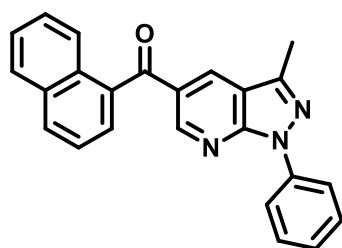
**(2-bromophenyl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4p):**

Yield 69%; 270 mg; light yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 127–129 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.94 (d, *J* = 2.0 Hz, 1H), 8.49 (d, *J* = 2.0 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.49–7.34 (m, 5H), 7.27 (t, *J* = 7.6 Hz, 1H), 2.61 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 193.6, 151.41, 151.36, 144.7, 139.8, 138.6, 133.1, 132.1, 131.4, 128.9, 127.4, 126.0, 125.5, 120.8, 119.3, 116.6, 12.3. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>15</sub>N<sub>3</sub>OBr<sup>+</sup>: 392.0392; found: 392.0391.



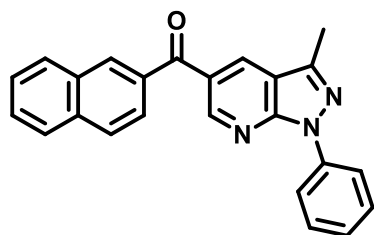
**[1,1'-biphenyl]-4-yl(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4q):**

Yield 82%; 318 mg; light yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 147–149 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.05 (s, 1H), 8.50 (s, 1H), 8.26 (d, *J* = 8.4 Hz, 2H), 7.88 (d, *J* = 7.6 Hz, 2H), 7.71 (d, *J* = 7.6 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.52–7.42 (m, 4H), 7.38 (t, *J* = 6.8 Hz, 1H), 7.28 (t, *J* = 7.2 Hz, 1H), 2.64 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 193.8, 151.2, 150.9, 145.3, 144.3, 139.5, 138.8, 135.9, 132.1, 130.4, 129.0, 128.9, 128.2, 127.1, 127.0, 126.8, 126.0, 120.8, 116.3, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>26</sub>H<sub>20</sub>N<sub>3</sub>O<sup>+</sup>: 390.1601; found: 390.1603.



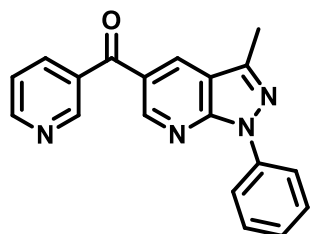
**(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(naphthalen-1-yl)methanone (4r):**

Yield 76%; 275 mg; white solid; column chromatography, silica gel (PE:EA, 30:1); mp 175–177 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.03 (d, *J* = 2.0 Hz, 1H), 8.54 (d, *J* = 2.0 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 2H), 8.11 (d, *J* = 9.2 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.92–7.90 (m, 1H), 7.61 (d, *J* = 6.4 Hz, 1H), 7.54–7.45 (m, 5H), 7.27 (t, *J* = 7.6 Hz, 1H), 2.59 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 195.7, 151.6, 151.4, 144.7, 138.8, 135.7, 133.7, 132.4, 131.6, 130.7, 129.0, 128.4, 127.7, 127.6, 127.4, 126.5, 126.1, 125.3, 124.3, 120.9, 116.5, 12.3. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>18</sub>N<sub>3</sub>O<sup>+</sup>: 364.1444; found: 364.1443.



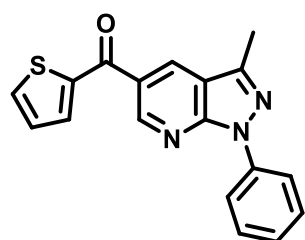
**(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(naphthalen-2-yl)methanone (4s):**

Yield 78%; 283 mg; light yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 128–130 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.10 (d, *J* = 2.0 Hz, 1H), 8.58 (d, *J* = 2.0 Hz, 1H), 8.29–8.25 (m, 3H), 7.99–7.91 (m, 4H), 7.65–7.51 (m, 4H), 7.32 (t, *J* = 7.6 Hz, 1H), 2.67 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 194.4, 151.3, 151.1, 144.4, 138.9, 135.3, 134.6, 132.3, 132.2, 131.6, 129.3, 129.1, 128.6, 128.5, 127.8, 127.1, 127.0, 126.1, 125.5, 121.0, 116.4, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>18</sub>N<sub>3</sub>O<sup>+</sup>: 364.1444; found: 364.1446.



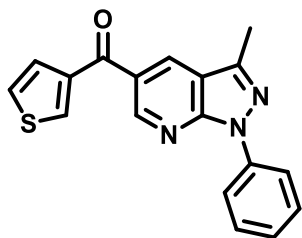
**(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(pyridin-3-yl)methanone (4t):**

Yield 65%; 204 mg; white solid; column chromatography, silica gel (PE:EA, 4:1); mp 144–146 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.05–9.01 (m, 2H), 8.86 (dd, *J* = 4.8 Hz, 1.6 Hz, 1H), 8.50 (d, *J* = 2.0 Hz, 1H), 8.23 (d, *J* = 7.6 Hz, 2H), 8.16–8.13 (m, 1H), 7.53–7.48 (m, 3H), 7.31 (t, *J* = 7.6 Hz, 1H), 2.66 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 192.5, 153.0, 151.3, 150.8, 150.5, 144.5, 138.6, 136.9, 132.9, 132.2, 129.0, 126.2, 125.9, 123.5, 120.9, 116.3, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>19</sub>H<sub>15</sub>N<sub>4</sub>O<sup>+</sup>: 315.1240; found: 315.1244.



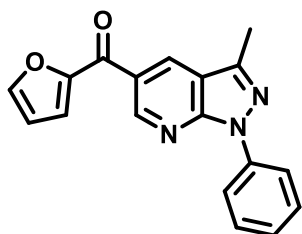
**(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(thiophen-2-yl)methanone (4u):**

Yield 75%; 239 mg; light yellow solid; column chromatography, silica gel (PE:EA, 20:1); mp 122–124 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.12 (s, 1H), 8.58 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 4.8 Hz, 1H), 7.70 (d, *J* = 3.2 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 4.0 Hz, 1H), 2.69 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 185.7, 151.3, 150.1, 144.3, 143.3, 138.9, 134.61, 134.56, 131.4, 129.1, 128.1, 127.4, 126.2, 121.1, 116.4, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>14</sub>N<sub>3</sub>OS<sup>+</sup>: 320.0852; found: 320.0854.



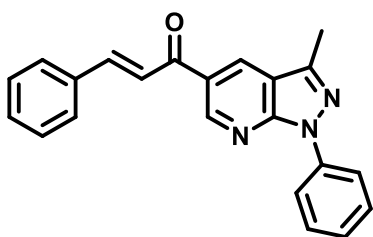
**(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(thiophen-3-yl)methanone (4v):**

Yield 78%; 248 mg; light yellow solid; column chromatography, silica gel (PE:EA, 20:1); mp 105–107 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.11 (s, 1H), 8.58 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 2H), 7.99 (d, *J* = 1.2 Hz, 1H), 7.63 (d, *J* = 5.2 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 2H), 7.47-7.42 (m, 1H), 7.32 (t, *J* = 7.2 Hz, 1H), 2.69 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 187.7, 151.4, 150.5, 144.4, 141.1, 138.9, 133.7, 131.6, 129.1, 128.5, 127.9, 126.7, 126.2, 121.1, 116.5, 12.5. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>14</sub>N<sub>3</sub>OS<sup>+</sup>: 320.0852; found: 320.0852.



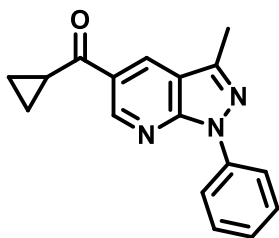
**furan-2-yl(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (4w):**

Yield 71%; 215 mg; yellow solid; column chromatography, silica gel (PE:EA, 15:1); mp 116–118 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.28 (s, 1H), 8.75 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 2H), 7.75 (s, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 3.2 Hz, 1H), 7.32 (t, *J* = 7.2 Hz, 1H), 6.66 (s, 1H), 2.70 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 179.9, 152.4, 151.3, 150.5, 147.1, 144.5, 138.8, 131.9, 129.1, 126.4, 126.2, 121.0, 120.3, 116.5, 112.5, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>14</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup>: 304.1081; found: 304.1083.



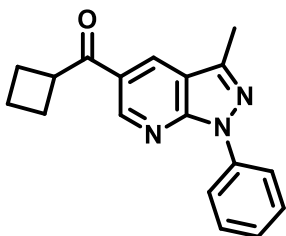
**(*E*)-1-(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)-3-phenylprop-2-en-1-one (4x):**

Yield 76%; 257 mg; yellow solid; column chromatography, silica gel (PE:EA, 20:1); mp 115–117 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.19 (s, 1H), 8.59 (s, 1H), 8.23 (d, *J* = 8.0 Hz, 2H), 7.83 (d, *J* = 15.6 Hz, 1H), 7.64-7.59 (s, 2H), 7.54-7.46 (m, 3H), 7.42-7.37 (s, 3H), 7.27 (t, *J* = 7.2 Hz, 1H), 2.63 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 187.8, 151.3, 149.8, 145.2, 144.4, 138.8, 134.4, 130.7, 130.5, 128.94, 128.86, 128.4, 127.2, 126.0, 121.0, 120.7, 116.5, 12.3. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>22</sub>H<sub>18</sub>N<sub>3</sub>O<sup>+</sup>: 340.1444; found: 340.1455.



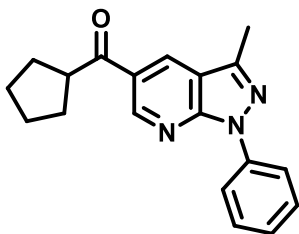
**cyclopropyl(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (5a):**

Yield 70%; 193 mg; white solid; column chromatography, silica gel (PE:EA, 20:1); mp 152–154 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.25 (d, *J* = 2.0 Hz, 1H), 8.66 (d, *J* = 2.0 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 2H), 7.52 (t, *J* = 8.0 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 2.75-2.70 (m, 1H), 2.68 (s, 3H), 1.35-1.31 (m, 2H), 1.15-1.10 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 198.4, 151.5, 149.6, 144.5, 138.9, 130.1, 129.1, 127.3, 126.1, 121.0, 116.5, 17.4, 12.4, 11.9. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>16</sub>N<sub>3</sub>O<sup>+</sup>: 278.1288; found: 278.1288.



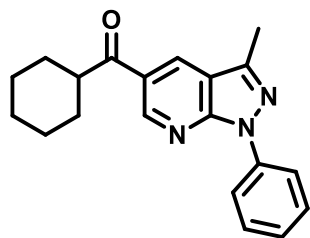
**cyclobutyl(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (5b):**

Yield 74%; 215 mg; white solid; column chromatography, silica gel (PE:EA, 30:1); mp 132–134 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.07 (s, 1H), 8.57 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 4.09-4.00 (m, 1H), 2.66 (s, 3H), 2.52-2.43 (m, 2H), 2.40-2.33 (m, 2H), 2.17-2.10 (m, 1H), 1.99-1.92 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 198.8, 151.4, 149.8, 144.5, 138.9, 130.4, 129.0, 126.0, 124.9, 120.9, 116.7, 42.3, 24.9, 18.1, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>18</sub>N<sub>3</sub>O<sup>+</sup>: 292.1444; found: 292.1439.



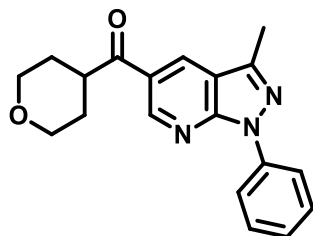
**cyclopentyl(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (5c):**

Yield 77%; 234 mg; yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 92–94 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.19 (d, *J* = 2.0 Hz, 1H), 8.63 (d, *J* = 2.0 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 3.80-3.72 (m, 1H), 2.67 (s, 3H), 2.01-1.96 (m, 4H), 1.78-1.68 (m, 4H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 200.6, 151.4, 150.0, 144.5, 138.9, 130.6, 129.0, 126.1, 126.0, 120.9, 116.6, 46.6, 29.8, 26.3, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>19</sub>H<sub>20</sub>N<sub>3</sub>O<sup>+</sup>: 306.1601; found: 306.1602.



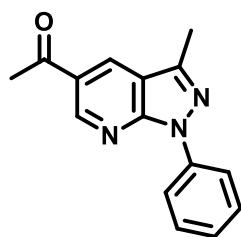
**cyclohexyl(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (5d):**

Yield 75%; 239 mg; yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 94–96 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.05 (s, 1H), 8.47 (s, 1H), 8.20 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 1H), 3.22 (t, *J* = 11.2 Hz, 1H), 2.56 (s, 3H), 1.92–1.83 (m, 4H), 1.74–1.68 (m, 1H), 1.57–1.22 (m, 5H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 201.0, 150.9, 149.3, 144.1, 138.6, 129.9, 128.6, 125.5, 125.0, 120.2, 116.3, 45.5, 29.0, 25.6, 25.4, 12.0. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>22</sub>N<sub>3</sub>O<sup>+</sup>: 320.1757; found: 320.1754.



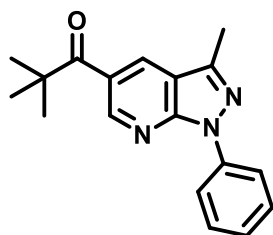
**(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(tetrahydro-2H-pyran-4-yl)methanone (5e):**

Yield 78%; 250 mg; yellow solid; column chromatography, silica gel (PE:EA, 6:1); mp 112–114 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.17 (s, 1H), 8.63 (s, 1H), 8.23 (d, *J* = 8.0 Hz, 2H), 7.53 (t, *J* = 8.0 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 1H), 4.12–4.06 (m, 2H), 3.63–3.53 (m, 3H), 2.69 (s, 3H), 2.01–1.90 (m, 2H), 1.88–1.81 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 199.7, 151.5, 149.7, 144.6, 138.8, 130.7, 129.1, 126.2, 125.0, 121.0, 116.8, 67.1, 43.0, 29.0, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>19</sub>H<sub>20</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup>: 322.1550; found: 322.1548.



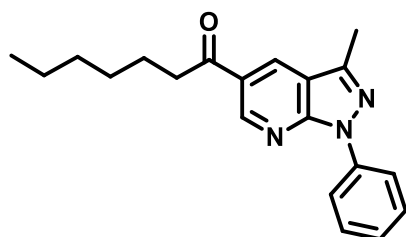
**1-(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)ethan-1-one (5f):**

Yield 72%; 180 mg; light yellow solid; column chromatography, silica gel (PE:EA, 20:1); mp 121–123 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.19 (d, *J* = 1.6 Hz, 1H), 8.65 (d, *J* = 1.6 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 2H), 7.53 (t, *J* = 8.0 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 1H), 2.72 (s, 3H), 2.69 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 196.0, 151.6, 150.0, 144.7, 138.9, 130.5, 129.1, 126.6, 126.3, 121.1, 116.6, 26.8, 12.5. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>15</sub>H<sub>14</sub>N<sub>3</sub>O<sup>+</sup>: 252.1131; found: 252.1134.



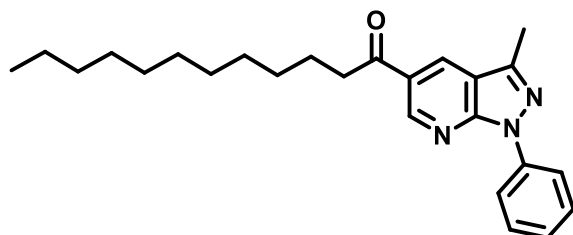
**2,2-dimethyl-1-(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)propan-1-one (5g):**

Yield 75%; 219 mg; yellow solid; column chromatography, silica gel (PE:EA, 40:1); mp 76–78 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.13 (d, *J* = 2.0 Hz, 1H), 8.53 (d, *J* = 2.0 Hz, 1H), 8.23 (dd, *J* = 8.8, 1.2 Hz, 2H), 7.54-7.50 (m, 2H), 7.32-7.27 (m, 1H), 2.67 (s, 3H), 1.45 (s, 9H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 205.7, 150.6, 149.5, 144.1, 138.9, 130.9, 129.1, 126.9, 126.0, 120.9, 116.3, 44.2, 28.1, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>20</sub>N<sub>3</sub>O<sup>+</sup>: 294.1601; found: 294.1603.



**1-(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)heptan-1-one (5h):**

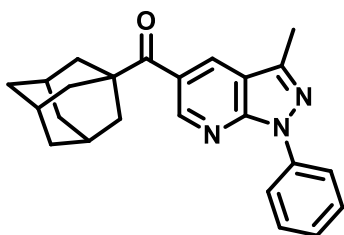
Yield 80%; 256 mg; yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 77–79 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.16 (s, 1H), 8.60 (s, 1H), 8.23 (d, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.30 (t, *J* = 7.2, 1H), 3.03 (t, *J* = 7.2 Hz, 2H), 2.67 (s, 3H), 1.85-1.73 (m, 2H), 1.46-1.28 (m, 6H), 0.99-0.83 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 198.2, 151.3, 149.5, 144.4, 138.8, 130.0, 128.9, 126.2, 125.9, 120.7, 116.5, 38.8, 31.6, 28.9, 24.1, 22.4, 13.9, 12.3. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>24</sub>N<sub>3</sub>O<sup>+</sup>: 322.1914; found: 322.1915.



**1-(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)dodecan-1-one (5i):**

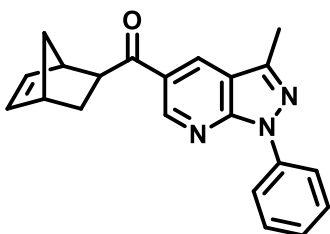
Yield 75%; 293 mg; light yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 75–77 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.14 (d, *J* = 2.0 Hz, 1H), 8.58 (d, *J* = 2.0 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 1H), 3.01 (t, *J* = 7.6 Hz, 2H), 2.65 (s, 3H), 1.84-1.71 (m, 2H), 1.43-1.23 (m, 16H), 0.88 (t, *J* = 6.8 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 198.3, 151.4, 149.6, 144.4, 138.9, 130.1, 129.0, 126.3, 126.0, 120.8, 116.5, 38.8, 31.8, 29.5, 29.42, 29.41, 29.27, 29.25, 24.2, 22.6, 14.0, 12.3. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>25</sub>H<sub>34</sub>N<sub>3</sub>O<sup>+</sup>: 392.2696; found: 392.2701.





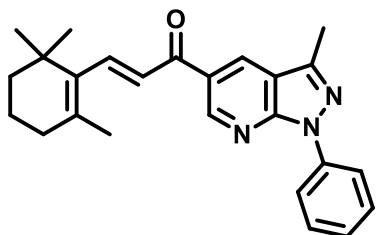
**adamantan-1-yl(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (5j):**

Yield 73%; 270 mg; light yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 107–109 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.07 (s, 1H), 8.42 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.2 Hz, 1H), 2.68 (s, 3H), 2.18-2.04 (m, 9H), 1.83-1.75 (m, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 206.6, 150.5, 148.7, 144.0, 139.0, 130.4, 129.1, 128.1, 126.0, 121.0, 116.3, 47.2, 39.3, 36.5, 28.1, 12.5. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>26</sub>N<sub>3</sub>O<sup>+</sup>: 372.2070; found: 372.2078.



**(bicyclo[2.2.1]hept-5-en-2-yl)(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (5k):**

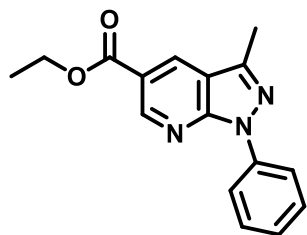
Yield 67%; 220 mg; light yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 134–136 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.21 (d, *J* = 2.0 Hz, 1H), 8.64 (d, *J* = 2.0 Hz, 1H), 8.23 (d, *J* = 7.6 Hz, 2H), 7.52 (t, *J* = 8.0 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 6.28 (s, 2H), 3.21-3.17 (m, 1H), 3.15 (s, 1H), 3.02 (s, 1H), 2.68 (s, 3H), 2.07-2.02 (m, 1H), 1.58-1.53 (m, 2H), 1.45 (d, *J* = 8.4 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 200.2, 151.4, 149.9, 144.5, 138.9, 138.7, 135.7, 130.4, 129.0, 126.3, 126.1, 120.9, 116.6, 46.9, 46.4, 46.0, 42.0, 30.7, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>21</sub>H<sub>20</sub>N<sub>3</sub>O<sup>+</sup>: 330.1601; found: 330.1600.



**(E)-1-(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)-3-(2,6,6-trimethylcyclohex-1-en-1-yl)prop-2-en-1-one (5l):**

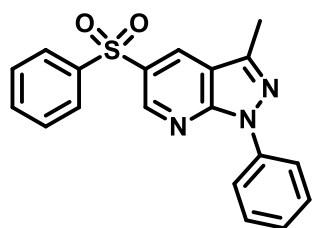
Yield 77%; 296 mg; yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 96–98 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.19 (d, *J* = 1.6 Hz, 1H), 8.63 (d, *J* = 1.6 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 15.6 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 16.0 Hz, 1H), 2.67 (s, 3H), 2.16-2.12 (m, 2H), 1.90 (s, 3H), 1.69-1.63 (m, 2H), 1.54-1.51 (m, 2H), 1.17 (s, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 188.2, 151.3, 149.8, 144.9, 144.4, 138.9, 137.9, 136.6, 130.5, 128.9, 127.7, 125.9, 125.2, 120.8, 116.6, 39.7, 34.1,

33.8, 28.8, 21.9, 18.7, 12.4. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $C_{25}H_{28}N_3O^+$ : 386.2227; found: 386.2228.



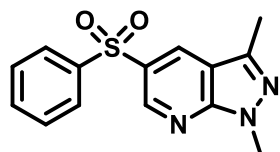
**ethyl 3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carboxylate (5m):**

Yield 74%; 207 mg; white solid; column chromatography, silica gel (PE:EA, 30:1); mp 110–112 °C.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  9.22 (s, 1H), 8.70 (s, 1H), 8.23 (d,  $J$  = 8.0 Hz, 2H), 7.52 (t,  $J$  = 8.0 Hz, 2H), 7.31 (t,  $J$  = 7.6 Hz, 1H), 4.46 (q,  $J$  = 7.2 Hz, 2H), 2.68 (s, 3H), 1.45 (t,  $J$  = 7.2 Hz, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  165.5, 151.7, 150.6, 144.2, 138.9, 131.9, 129.1, 126.1, 121.1, 119.8, 116.4, 61.3, 14.3, 12.4. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $C_{16}H_{16}N_3O_2^+$ : 282.1237; found: 282.1237.



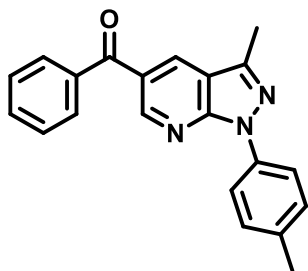
**3-methyl-1-phenyl-5-(phenylsulfonyl)-1H-pyrazolo[3,4-*b*]pyridine (5n):**

Yield 64%; 223 mg; light yellow solid; column chromatography, silica gel (PE:EA, 10:1); mp 179–181 °C.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  9.07 (s, 1H), 8.68 (s, 1H), 8.16 (d,  $J$  = 7.9 Hz, 2H), 8.01 (d,  $J$  = 7.5 Hz, 2H), 7.61-7.49 (m, 5H), 7.33 (t,  $J$  = 7.4 Hz, 1H), 2.70 (s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  151.0, 148.1, 144.4, 141.6, 138.5, 133.5, 131.3, 130.4, 129.6, 129.2, 127.5, 126.6, 121.3, 116.2, 12.5. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $C_{19}H_{16}N_3O_2S^+$ : 350.0958; found: 350.0954.



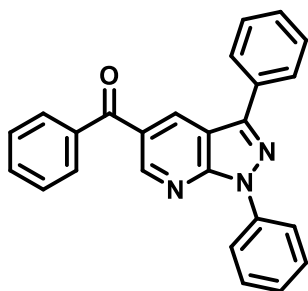
**1,3-dimethyl-5-(phenylsulfonyl)-1H-pyrazolo[3,4-*b*]pyridine (5o):**

Yield 60%; 172 mg; white solid; column chromatography, silica gel (PE:EA, 6:1); mp 138–140 °C.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.99 (s, 1H), 8.62 (s, 1H), 7.99 (d,  $J$  = 7.6 Hz, 2H), 7.59-7.51 (m, 3H), 4.08 (s, 3H), 2.60 (s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  151.4, 147.6, 142.7, 141.8, 133.3, 130.5, 130.1, 129.4, 127.3, 114.2, 33.8, 12.3. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $C_{14}H_{14}N_3O_2S^+$ : 288.0801; found: 288.0806.



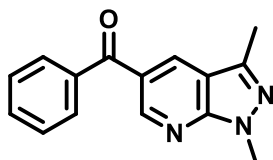
**(3-methyl-1-(p-tolyl)-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(phenyl)methanone (5p):**

Yield 84%; 274 mg; yellow solid; column chromatography, silica gel (PE:EA, 30:1); mp 127–129 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.00 (d, *J* = 2.0 Hz, 1H), 8.47 (d, *J* = 2.0 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 2H), 7.80 (d, *J* = 7.2 Hz, 2H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 2.63 (s, 3H), 2.38 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 194.3, 151.01, 150.97, 144.0, 137.3, 136.3, 135.8, 132.5, 132.1, 129.7, 129.5, 128.4, 126.5, 120.9, 116.0, 20.9, 12.3. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>21</sub>H<sub>18</sub>N<sub>3</sub>O<sup>+</sup>: 328.1444; found: 328.1447.



**(1,3-diphenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(phenyl)methanone (5q):**

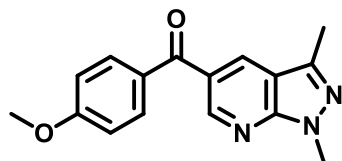
Yield 79%; 296 mg; white solid; column chromatography, silica gel (PE:EA, 40:1); mp 125–127 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.01 (s, 1H), 8.81 (s, 1H), 8.33 (d, *J* = 7.8 Hz, 2H), 7.98 (d, *J* = 7.3 Hz, 2H), 7.82 (d, *J* = 7.4 Hz, 2H), 7.59 (t, *J* = 7.1 Hz, 1H), 7.54–7.45 (m, 6H), 7.44–7.40 (m, 1H), 7.30 (t, *J* = 7.2 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 194.1, 151.6, 150.9, 145.6, 138.8, 137.1, 133.2, 132.7, 131.8, 129.8, 129.1, 129.0, 128.9, 128.5, 127.6, 127.3, 126.4, 121.3, 114.6. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>25</sub>H<sub>18</sub>N<sub>3</sub>O<sup>+</sup>: 376.1444; found: 376.1450.



**(1,3-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(phenyl)methanone (5r):**

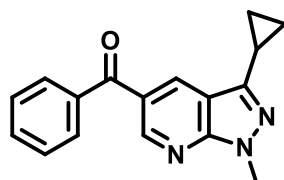
Yield 74%; 185 mg; white solid; column chromatography, silica gel (PE:EA, 8:1); mp 118–120 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.99 (s, 1H), 8.47 (s, 1H), 7.81 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 4.13 (s, 3H), 2.59 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 194.7, 151.7, 150.8, 142.6, 137.5, 132.5, 132.3, 129.7, 128.4, 125.8,

114.2, 33.6, 12.3. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $C_{15}H_{14}N_3O^+$ : 252.1131; found: 252.1133.



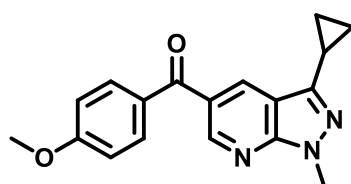
**(1,3-dimethyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(4-methoxyphenyl)methanone (5s):**

Yield 78%; 219 mg; white solid; column chromatography, silica gel (PE:EA, 6:1); mp 130–132 °C.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.94 (d,  $J = 1.2$  Hz, 1H), 8.42 (d,  $J = 1.2$  Hz, 1H), 7.82 (d,  $J = 8.8$  Hz, 2H), 7.00 (d,  $J = 8.8$  Hz, 2H), 4.12 (s, 3H), 3.90 (s, 3H), 2.59 (s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  193.3, 163.2, 151.5, 150.4, 142.3, 132.1, 131.9, 130.0, 126.3, 114.1, 113.6, 55.3, 33.5, 12.2. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $C_{16}H_{16}N_3O_2^+$ : 282.1237; found: 282.1238.



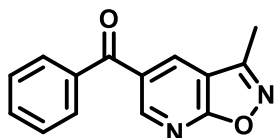
**(3-cyclopropyl-1-methyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(phenyl)methanone (5t):**

Yield 73%; 202 mg; yellow solid; column chromatography, silica gel (PE:EA, 10:1); mp 106–108 °C.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.96 (d,  $J = 2.0$  Hz, 1H), 8.53 (d,  $J = 2.0$  Hz, 1H), 7.81 (d,  $J = 7.2$  Hz, 2H), 7.62 (t,  $J = 7.6$  Hz, 1H), 7.52 (t,  $J = 7.6$  Hz, 2H), 4.08 (s, 3H), 2.25–2.18 (m, 1H), 1.12–1.04 (m, 4H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  194.5, 151.6, 150.7, 147.9, 137.4, 132.3, 132.2, 129.6, 128.3, 125.5, 113.6, 33.5, 8.3, 7.8. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $C_{17}H_{16}N_3O$ : 278.1288<sup>+</sup>; found: 278.1290.



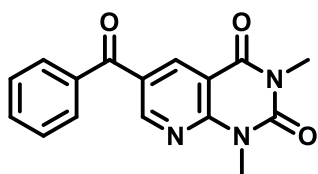
**(3-cyclopropyl-1-methyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(4-methoxyphenyl)methanone (5u):**

Yield 75%; 230 mg; yellow solid; column chromatography, silica gel (PE:EA, 8:1); mp 99–100 °C.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.92 (d,  $J = 2.0$  Hz, 1H), 8.49 (d,  $J = 2.0$  Hz, 1H), 7.82 (d,  $J = 8.8$  Hz, 2H), 6.99 (d,  $J = 8.8$  Hz, 2H), 4.08 (s, 3H), 3.89 (s, 3H), 2.26–2.19 (m, 1H), 1.12–1.04 (m, 4H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  193.1, 163.0, 151.4, 150.4, 147.6, 132.0, 131.7, 129.9, 126.0, 113.5, 113.4, 55.2, 33.4, 8.3, 7.7. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $C_{18}H_{18}N_3O_2^+$ : 308.1394; found: 308.1392.



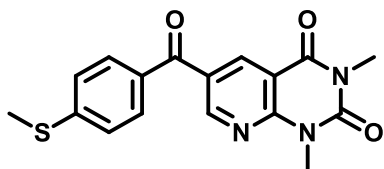
**(3-methylisoxazolo[5,4-*b*]pyridin-5-yl)(phenyl)methanone (5v):**

Yield 58%; 138 mg; light yellow solid; column chromatography, silica gel (PE:EA, 10:1); mp 117–119 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.03 (d, *J* = 1.6 Hz, 1H), 8.53 (d, *J* = 1.6 Hz, 1H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 2H), 2.66 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 193.6, 170.8, 156.3, 152.8, 136.7, 133.6, 133.3, 129.9, 129.8, 128.8, 113.7, 10.8. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>11</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup>: 239.0815; found: 239.0820.



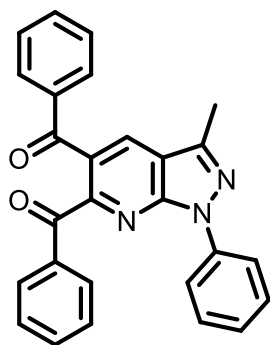
**(3-cyclopropyl-1-methyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(4-methoxyphenyl)methanone (5w):**

Yield 73%; 215 mg; light yellow solid; column chromatography, silica gel (PE:EA, 8:1); mp 160–162 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.10 (d, *J* = 2.0 Hz, 1H), 8.79 (d, *J* = 2.0 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 2H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 3.77 (s, 3H), 3.48 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 192.6, 160.5, 155.5, 152.6, 151.0, 139.1, 136.3, 133.1, 129.6, 128.6, 128.1, 109.5, 29.7, 28.5. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>16</sub>H<sub>14</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup>: 296.1030; found: 296.1035.



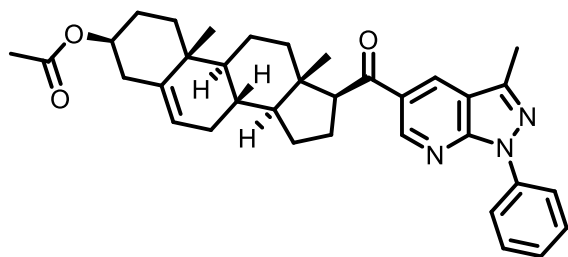
**(3-cyclopropyl-1-methyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(4-methoxyphenyl)methanone (5x):**

Yield 76%; 259 mg; light yellow solid; column chromatography, silica gel (PE:EA, 6:1); mp 176–178 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.06 (d, *J* = 2.0 Hz, 1H), 8.76 (d, *J* = 2.0 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 3.77 (s, 3H), 3.49 (s, 3H), 2.55 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.5, 160.6, 155.3, 152.5, 151.0, 146.5, 138.8, 132.3, 130.1, 128.4, 124.9, 109.4, 29.7, 28.5, 14.6. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>16</sub>N<sub>3</sub>O<sub>3</sub>S<sup>+</sup>: 342.0907; found: 342.0905.



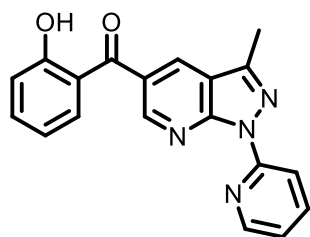
**(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5,6-diyl)bis(phenylmethanone) (6a)**

Yield 60%; 250 mg; yellow solid; column chromatography, silica gel (PE:EA, 15:1); mp 209–211 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.32 (s, 1H), 8.27 (d, *J* = 8.0 Hz, 2H), 8.03 (d, *J* = 7.6 Hz, 2H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.62–7.55 (m, 2H), 7.48–7.42 (m, 6H), 7.28–7.24 (m, 1H), 2.70 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 194.9, 193.2, 156.3, 148.8, 143.9, 138.9, 137.1, 135.7, 133.4, 133.2, 131.8, 130.7, 129.8, 129.4, 129.1, 128.6, 128.2, 126.0, 120.4, 116.1, 12.5. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>27</sub>H<sub>20</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup>: 418.1550; found: 418.1552.



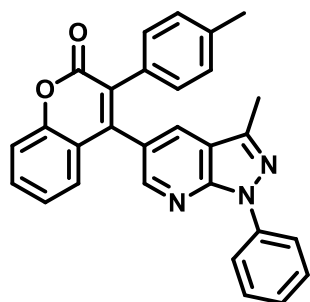
**(3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-10,13-dimethyl-17-(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carbonyl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[*a*]phenanthren-3-yl acetate (7-I)**

Yield 63%; 347 mg; yellow solid; column chromatography, silica gel (PE:EA, 15:1); mp 119–121 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.14 (d, *J* = 1.6 Hz, 1H), 8.58 (d, *J* = 1.6 Hz, 1H), 8.28 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 8.0 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 1H), 5.36 (d, *J* = 4.0 Hz, 1H), 4.62–4.56 (m, 1H), 3.51 (t, *J* = 8.4 Hz, 1H), 2.67 (s, 3H), 2.53–2.46 (m, 1H), 2.35–2.28 (m, 2H), 2.02 (s, 3H), 1.80–1.77 (m, 4H), 1.62–1.41 (m, 6H), 1.34–1.24 (m, 4H), 1.13–1.04 (m, 2H), 0.94 (s, 3H), 0.63 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 199.2, 170.2, 151.3, 149.8, 144.3, 139.3, 138.8, 130.2, 128.8, 128.2, 125.8, 122.0, 120.5, 116.3, 73.5, 57.4, 57.0, 49.6, 44.9, 39.0, 37.8, 36.6, 36.3, 31.8, 31.5, 27.4, 24.6, 23.6, 21.2, 20.7, 19.0, 13.3, 12.3. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>35</sub>H<sub>42</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup>: 552.3221; found: 552.3224.



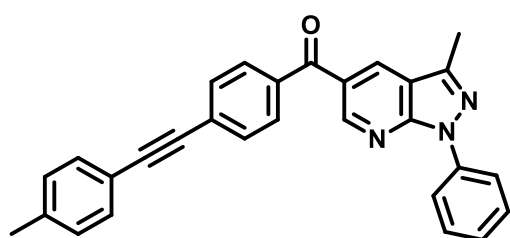
**(2-hydroxyphenyl)(3-methyl-1-(pyridin-2-yl)-1H-pyrazolo[3,4-*b*]pyridin-5-yl)methanone (7-II)**

Yield 45%; 148 mg; yellow solid; column chromatography, silica gel (PE:EA, 3:1); mp 170–172 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 11.83 (s, 1H), 9.00 (s, 1H), 8.69 (d, *J* = 4.0 Hz, 1H), 8.45–8.41 (m, 2H), 7.90 (t, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.28–7.25 (m, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 6.92 (t, *J* = 7.6 Hz, 1H), 2.73 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 198.4, 162.8, 151.3, 150.8, 150.2, 148.8, 145.4, 138.2, 136.5, 132.8, 131.4, 127.6, 121.3, 118.9, 118.8, 118.4, 116.8, 115.4, 12.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>19</sub>H<sub>15</sub>N<sub>4</sub>O<sub>2</sub><sup>+</sup>: 331.1190; found: 331.1189.



**4-(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)-3-(*p*-tolyl)-2H-chromen-2-one (7-III)**

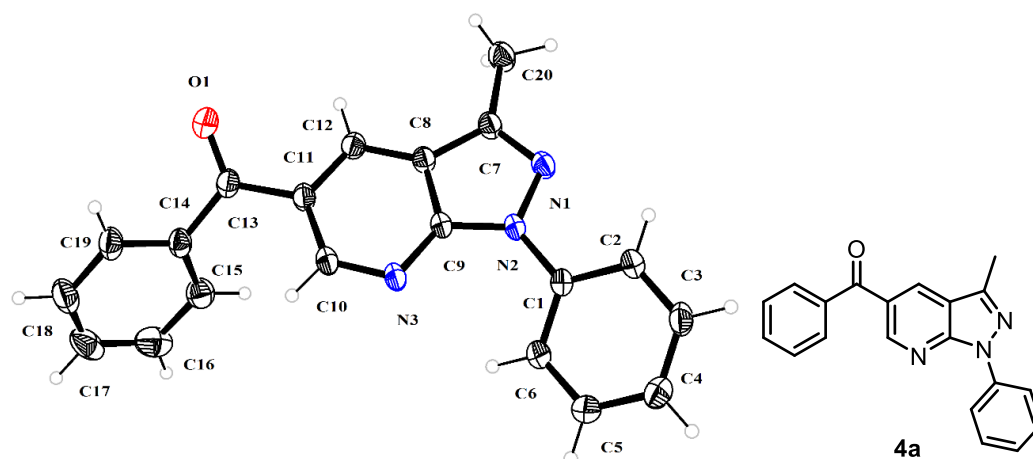
Yield 92%; 204 mg; yellow solid; column chromatography, silica gel (PE:EA, 15:1); mp 251–253 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.36 (d, *J* = 1.6 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 2H), 7.85 (d, *J* = 1.6 Hz, 1H), 7.58–7.45 (m, 4H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.24–7.18 (m, 2H), 7.02 (q, *J* = 8.0 Hz, 4H), 2.59 (s, 3H), 2.22 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 160.8, 153.0, 149.7, 149.2, 147.9, 142.8, 139.0, 137.7, 131.6, 130.3, 130.2, 129.0, 128.8, 128.5, 127.0, 125.8, 124.2, 123.7, 120.6, 120.4, 116.9, 116.1, 21.1, 12.3. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>29</sub>H<sub>22</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup>: 444.1707; found: 444.1703.



**(3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridin-5-yl)(4-(*p*-tolylethynyl)phenyl)methanone (7-IV):**

Yield 83%; 177 mg; white solid; column chromatography, silica gel (PE:EA, 30:1); mp 177–179 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.05 (s, 1H), 8.53 (s, 1H), 8.26 (d, *J* = 8.0 Hz, 2H), 7.83 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.54 (t, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.35–7.30 (m, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 2.69 (s, 3H), 2.38 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 193.8, 151.4, 151.1, 144.5, 139.1, 138.9, 136.3, 132.3, 131.7, 131.6, 129.9, 129.22, 129.15, 128.3, 126.8, 126.3, 121.2, 119.5, 116.4, 93.2, 87.9, 21.6, 12.5. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>29</sub>H<sub>22</sub>N<sub>3</sub>O<sup>+</sup>: 428.1757; found: 428.1755.

## 6. Crystallographic data and molecular structure of 4a and 5x



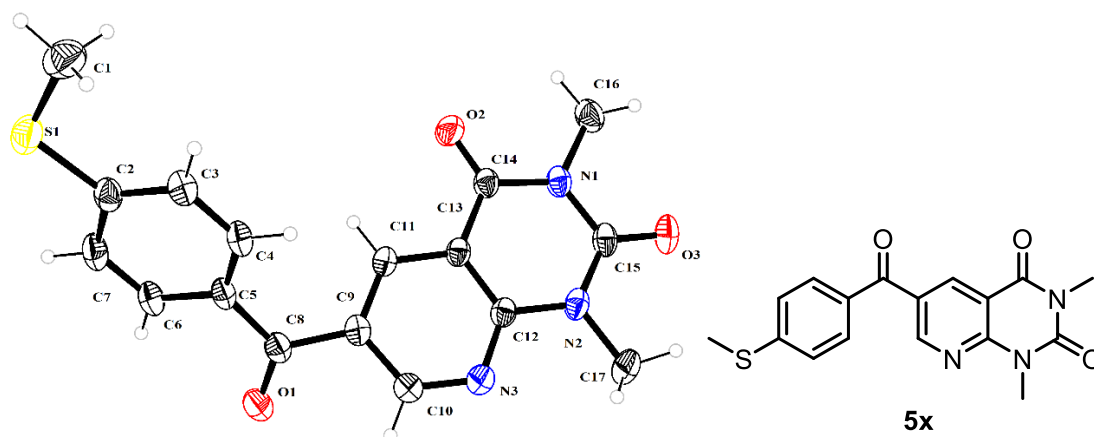
**Figure 1.** Molecular structure of **4a** with 30% probability ellipsoids  
 Crystal Data for Compound **4a**: CCDC 2158056 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic.

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Bond precision:	C-C = 0.0032 Å	Wavelength=0.71073	
Cell:	a=9.726 (3)	b=16.029 (4)	c=10.295 (3)
	alpha=90	beta=101.005 (4)	gamma=90
Temperature:	296 K		
	Calculated	Reported	
Volume	1575.5 (8)	1575.5 (7)	
Space group	P 21/n	P 1 21/n 1	
Hall group	-P 2yn	-P 2yn	
Moiety formula	C20 H15 N3 O	C20 H15 N3 O	
Sum formula	C20 H15 N3 O	C20 H15 N3 O	
Mr	313.35	313.35	
Dx, g cm <sup>-3</sup>	1.321	1.321	
Z	4	4	
Mu (mm <sup>-1</sup> )	0.084	0.084	
F000	656.0	656.0	
F000'	656.25		
h, k, lmax	12, 20, 12	12, 20, 12	
Nref	3223	3198	
Tmin, Tmax	0.992, 0.995	0.638, 0.745	
Tmin'	0.992		
Correction method=	# Reported T Limits: Tmin=0.638 Tmax=0.745		
AbsCorr =	MULTI-SCAN		
Data completeness=	0.992	Theta (max)= 26.365	
R(reflections)=	0.0485 ( 2268)	wR2(reflections)= 0.1492 ( 3198)	
S =	1.036	Npar= 218	

---





**Figure 1.** Molecular structure of **5x** with 30% probability ellipsoids  
Crystal Data for Compound **5x**: CCDC 2165134 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic.

---

Bond precision: C-C = 0.0023 Å Wavelength=0.71073  
 Cell: a=11.285 (2) b=10.0877 (19) c=14.445 (3)  
 alpha=90 beta=105.695 (3) gamma=90  
 Temperature: 296 K

	Calculated	Reported
Volume	1583.1 (5)	1583.1 (5)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C17 H15 N3 O3 S	C17 H15 N3 O3 S
Sum formula	C17 H15 N3 O3 S	C17 H15 N3 O3 S
Mr	341.38	341.38
Dx, g cm <sup>-3</sup>	1.432	1.432
Z	4	4
Mu (mm <sup>-1</sup> )	0.226	0.226
F <sub>000</sub>	712.0	712.0
F <sub>000</sub> '	712.79	
h, k, lmax	15, 13, 19	15, 13, 19
Nref	4342	4312
Tmin, Tmax	0.958, 0.973	0.682, 0.746
Tmin'	0.947	

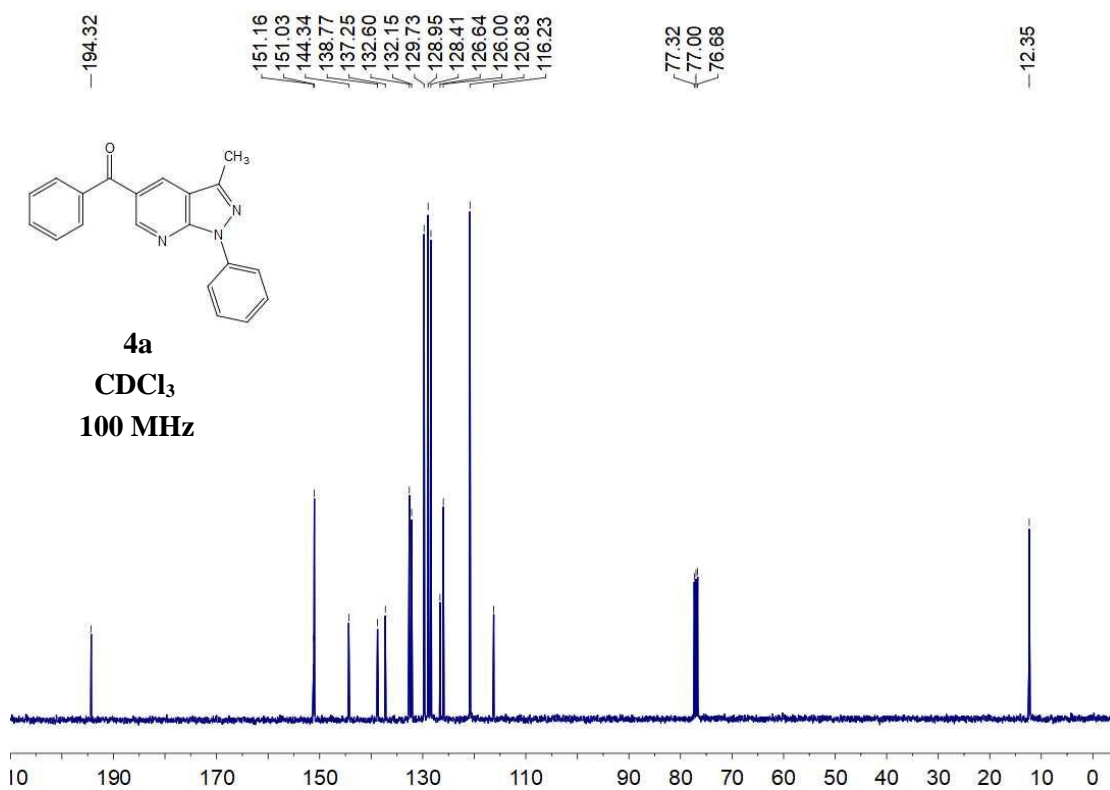
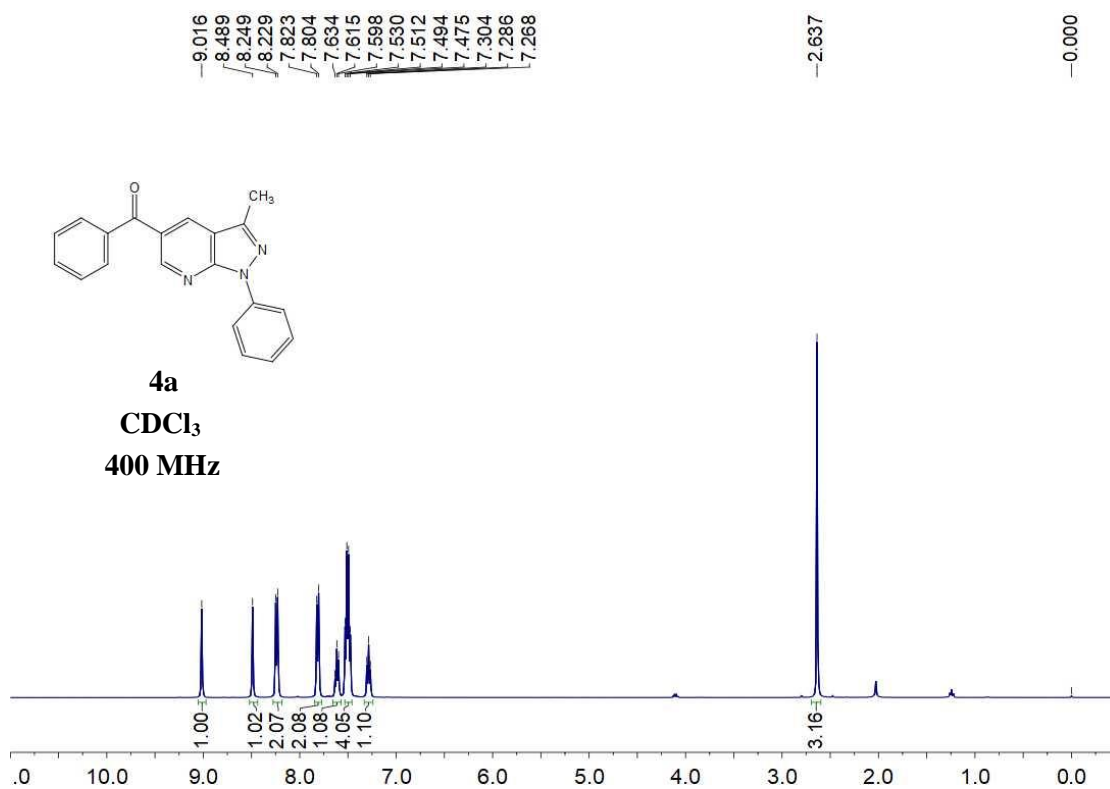
Correction method= # Reported T Limits: Tmin=0.682 Tmax=0.746  
 AbsCorr = MULTI-SCAN

Data completeness= 0.993 Theta (max)= 29.327

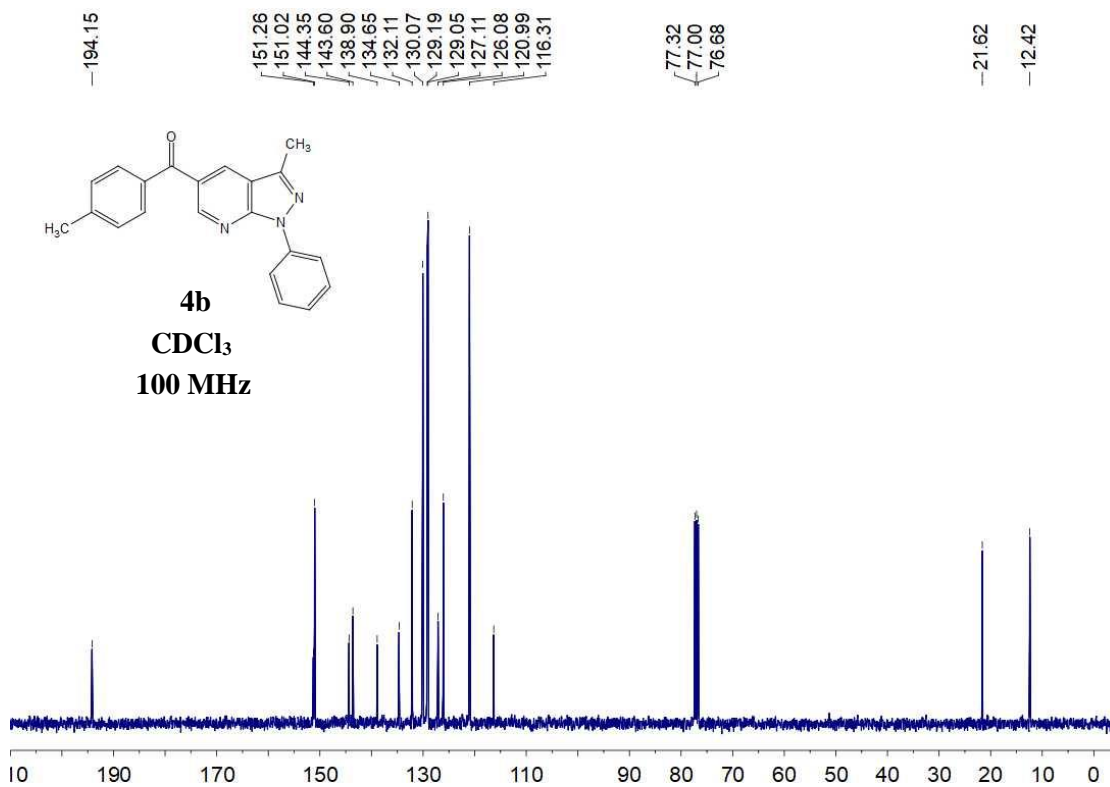
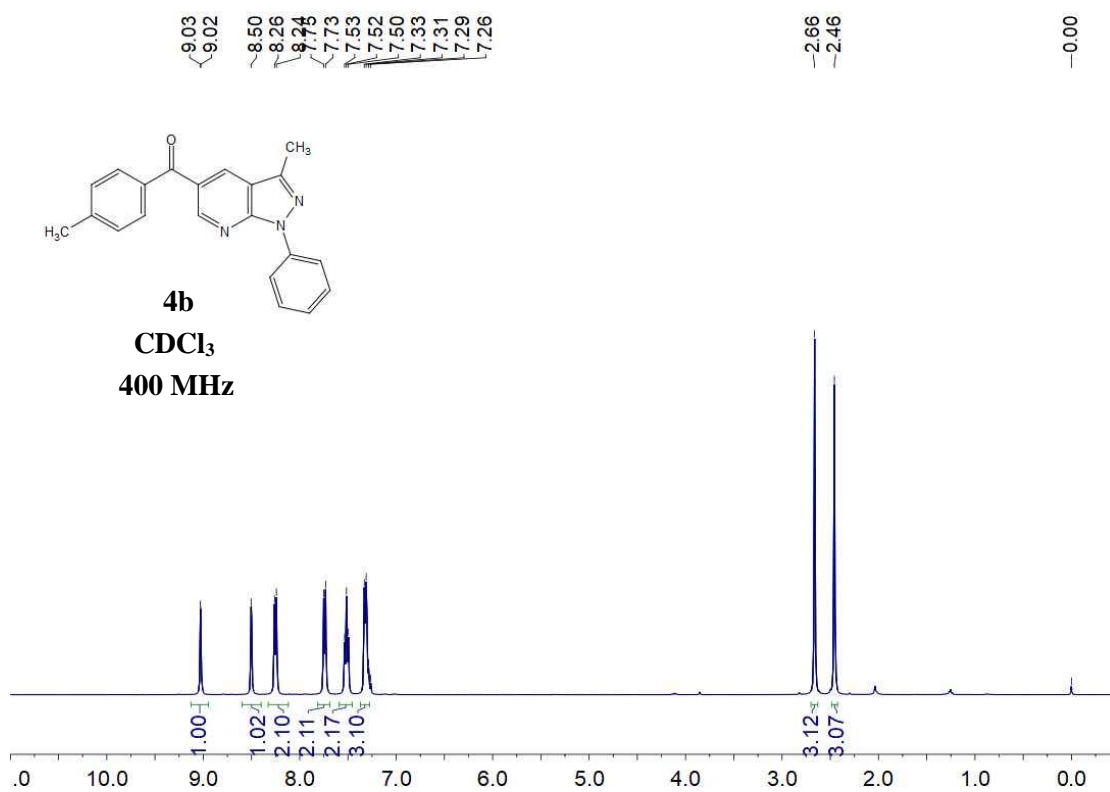
R(reflections)= 0.0479( 3103) wR2(reflections)=  
 0.1565( 4312)  
 S = 1.040 Npar= 220

# 7.<sup>1</sup>H, <sup>13</sup>C and <sup>19</sup>F NMR spectra of compounds

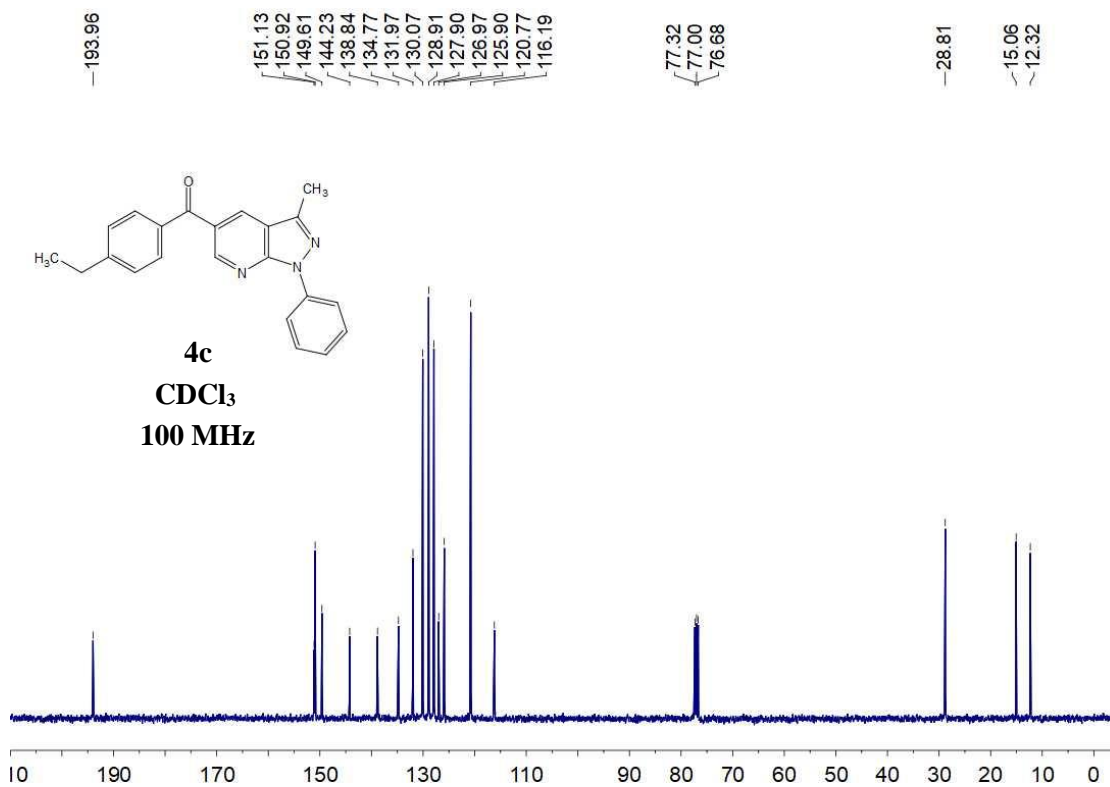
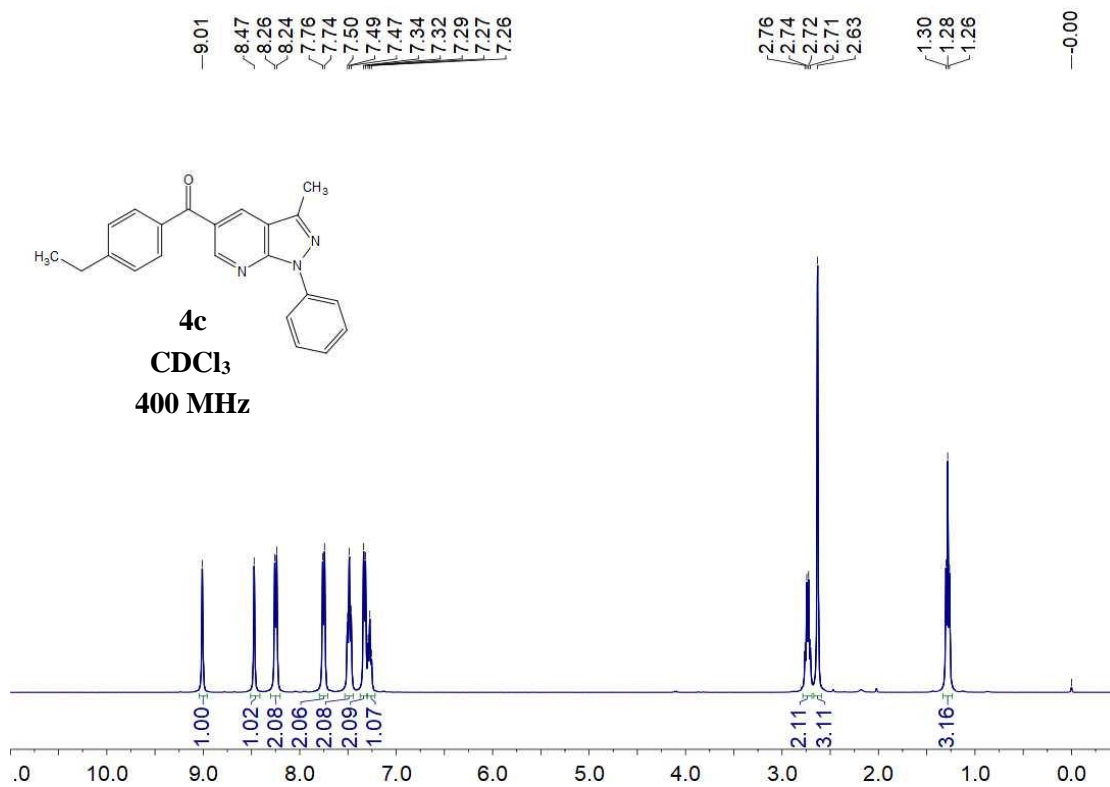
4a



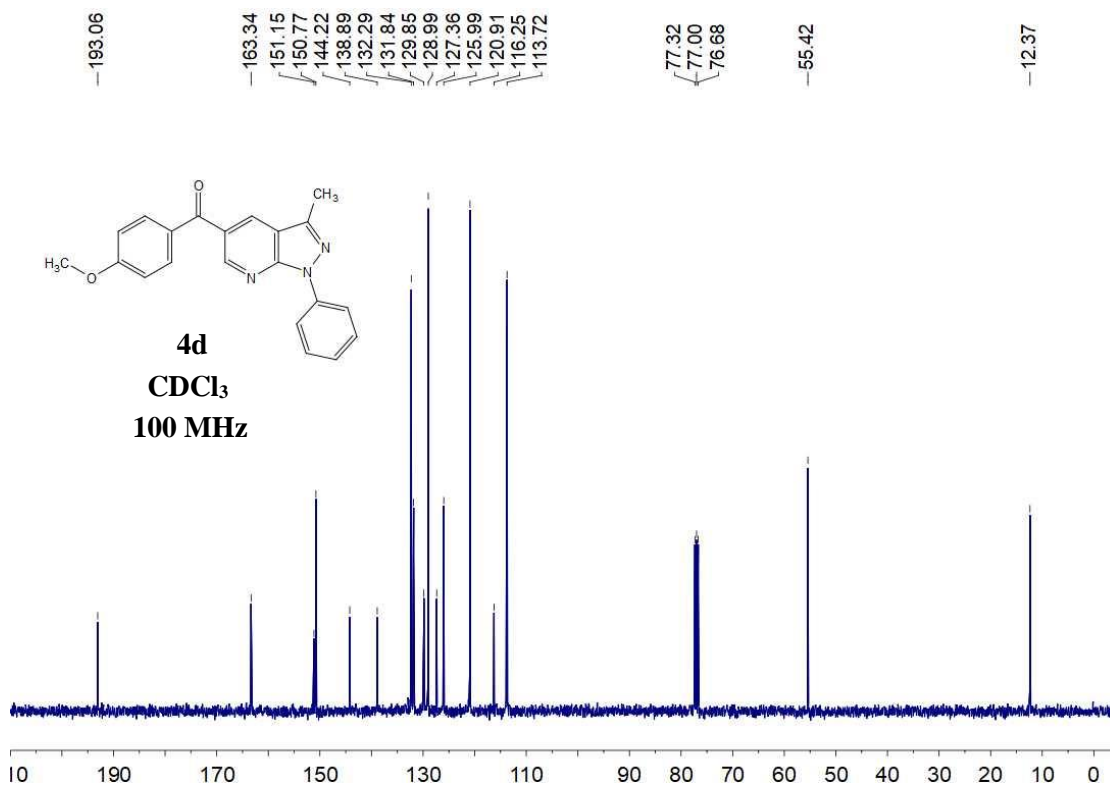
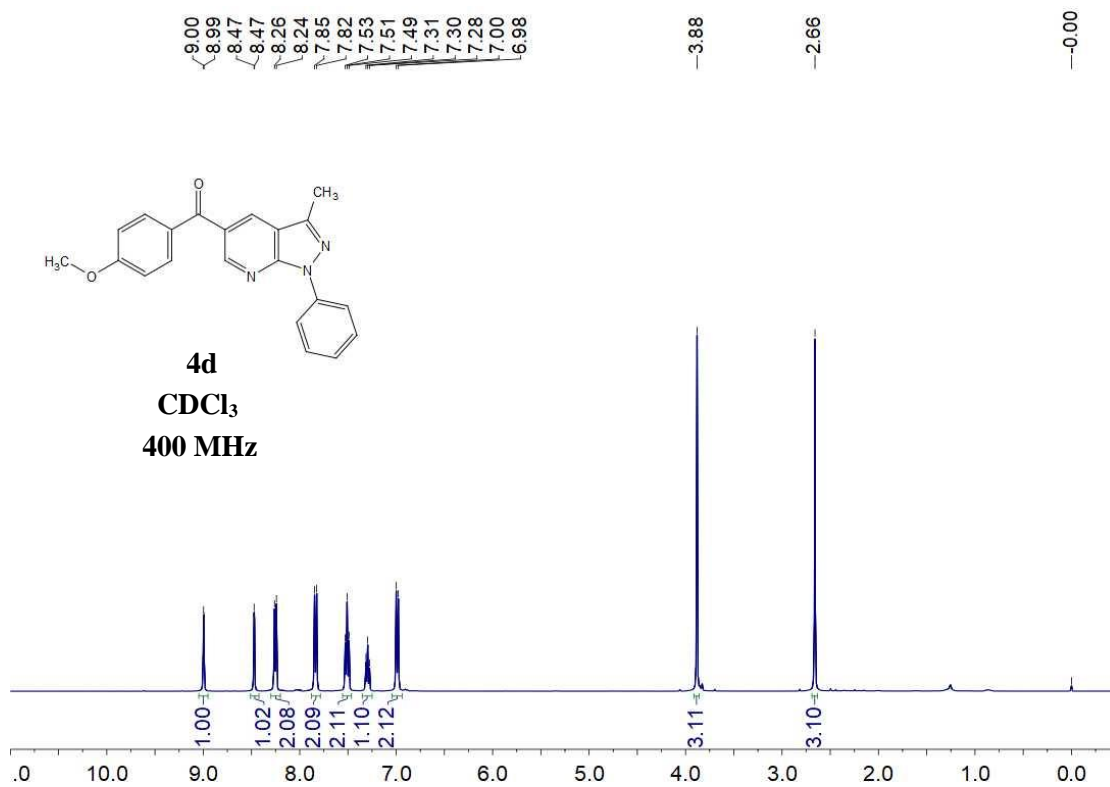
4b



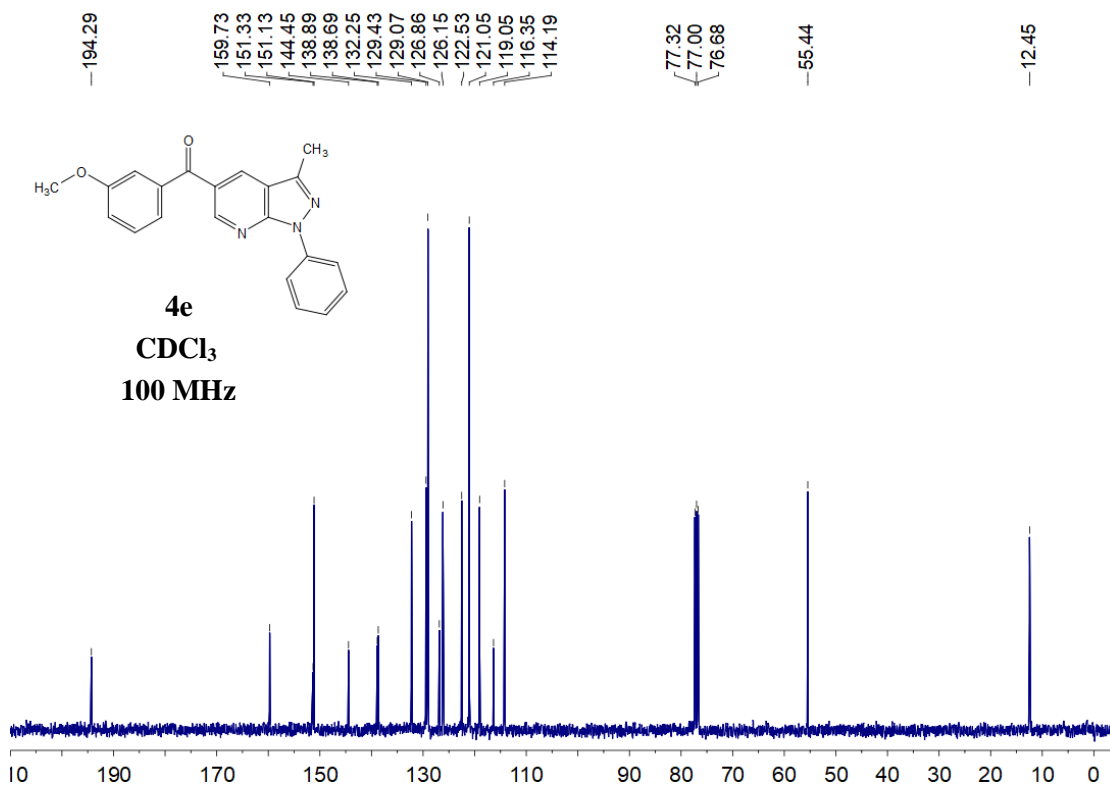
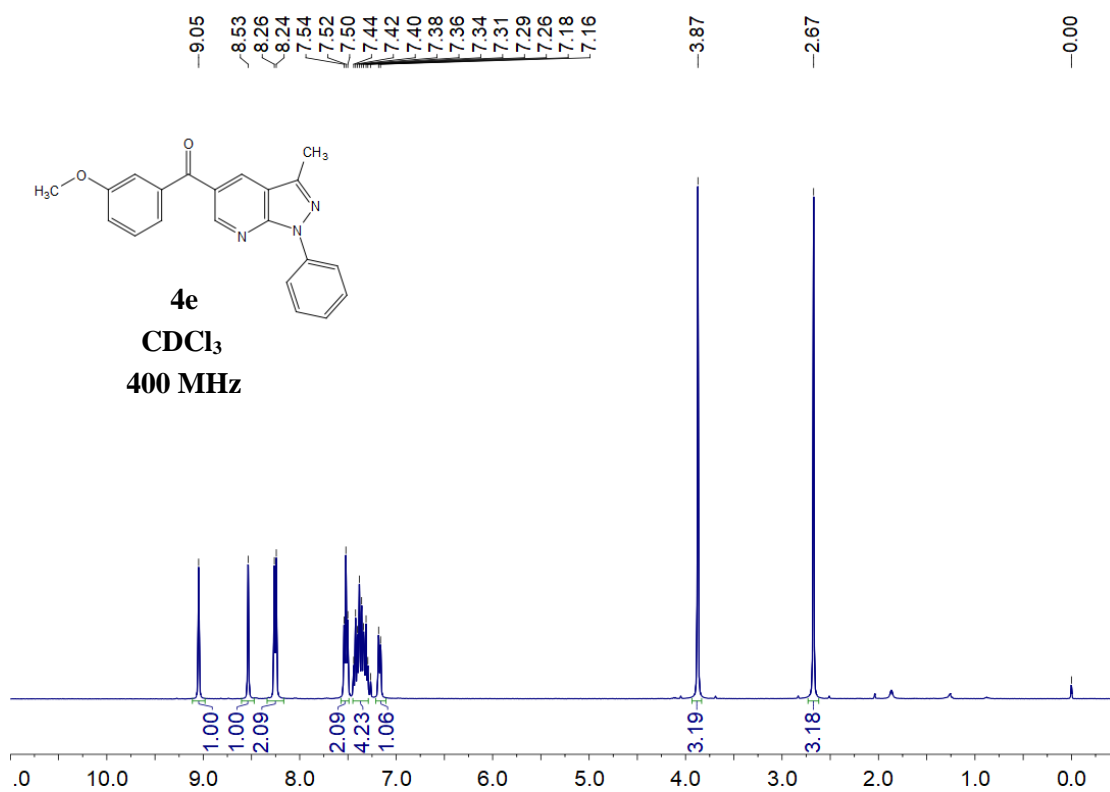
4c



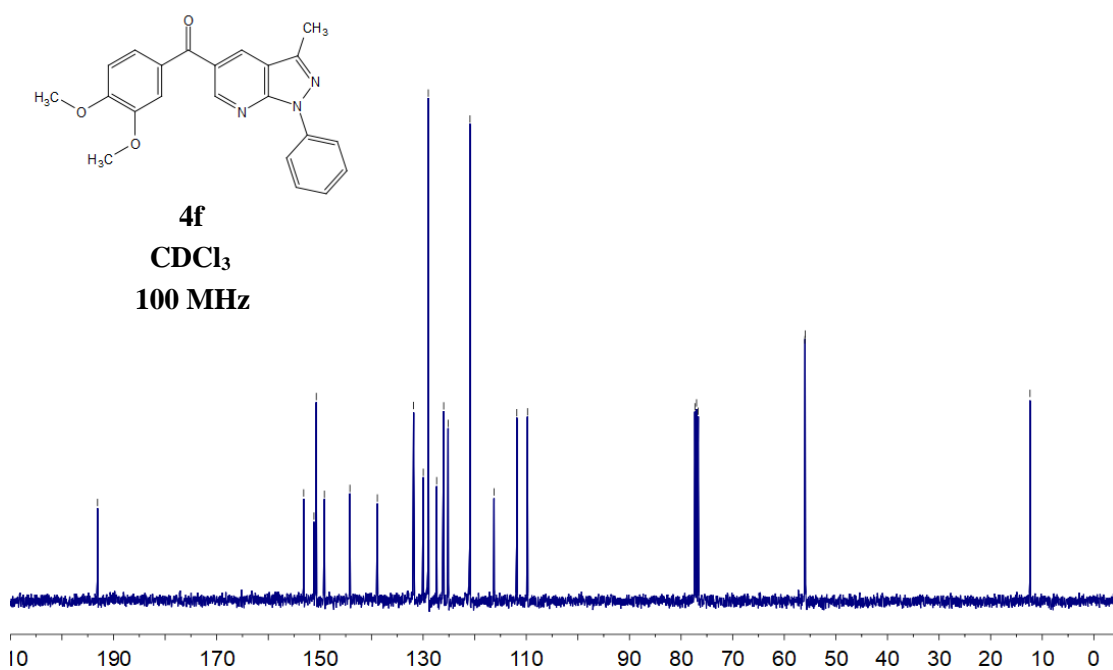
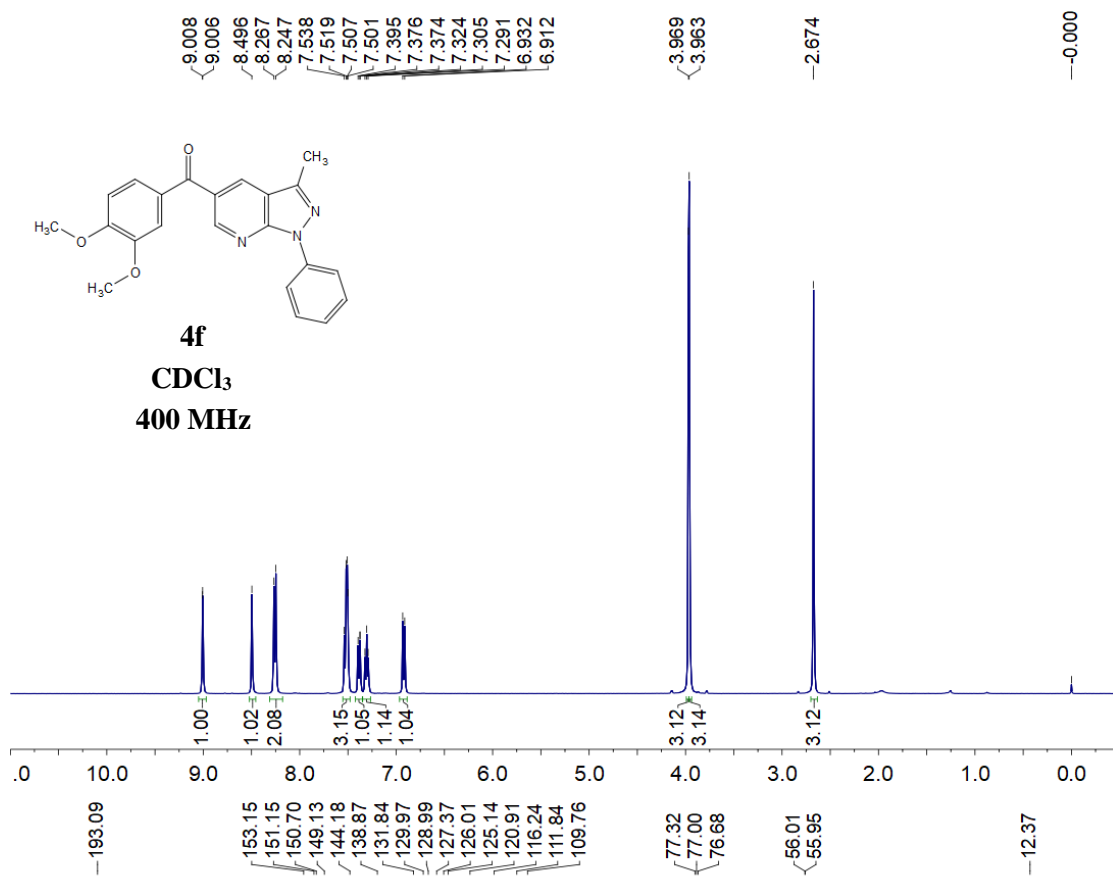
**4d**



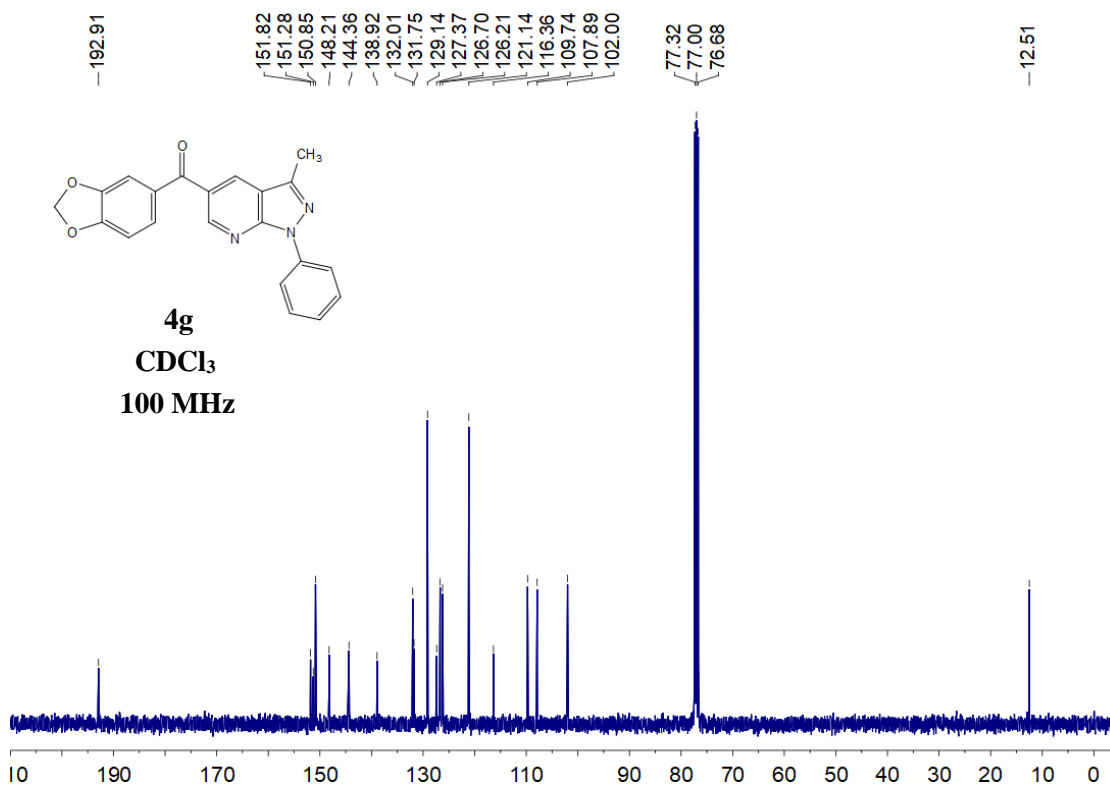
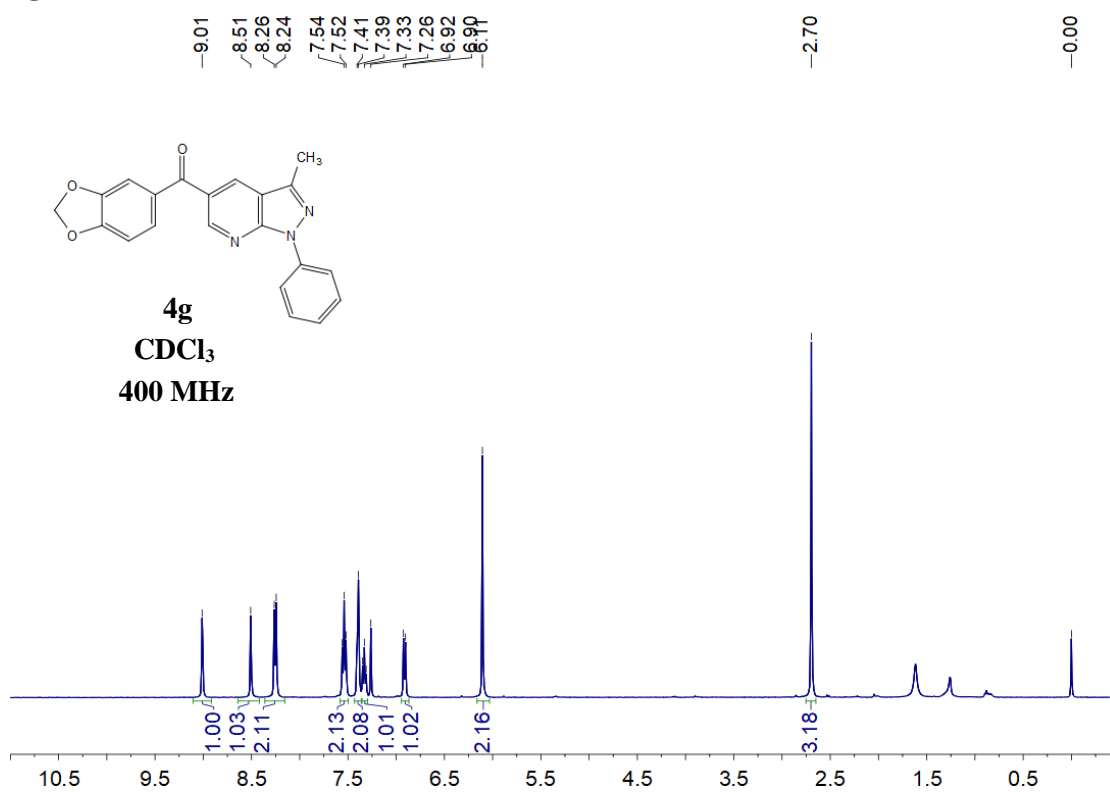
4e



4f

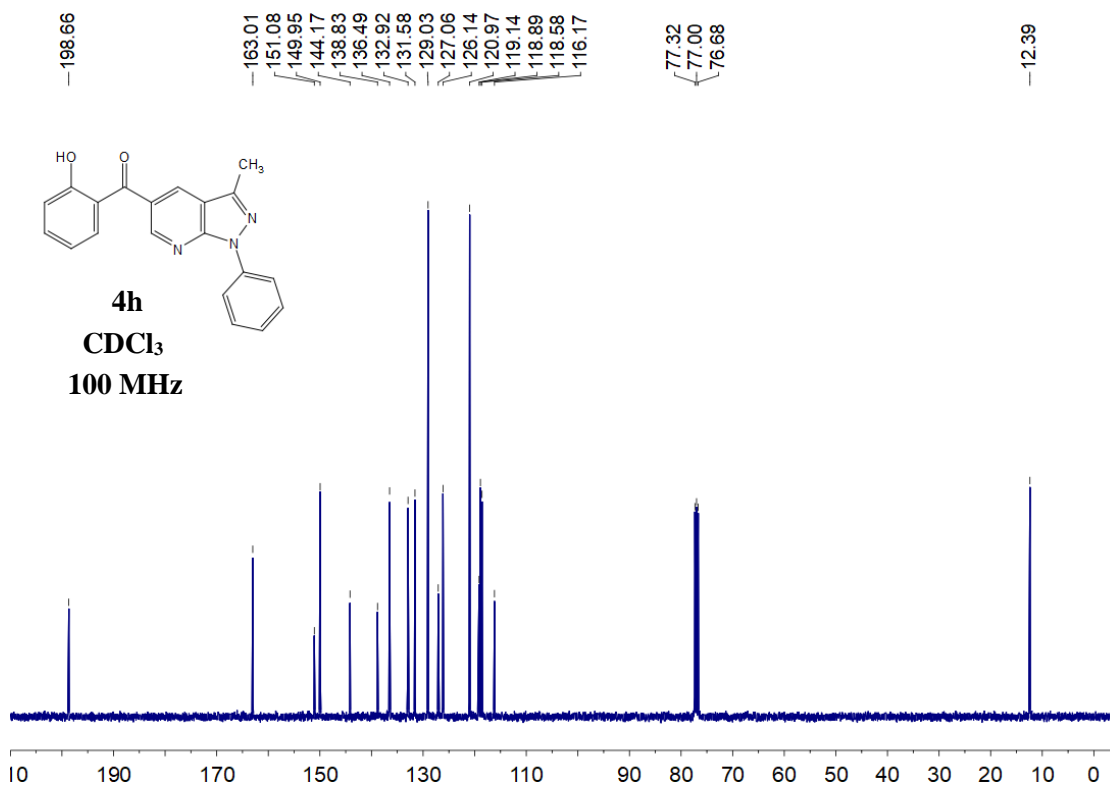
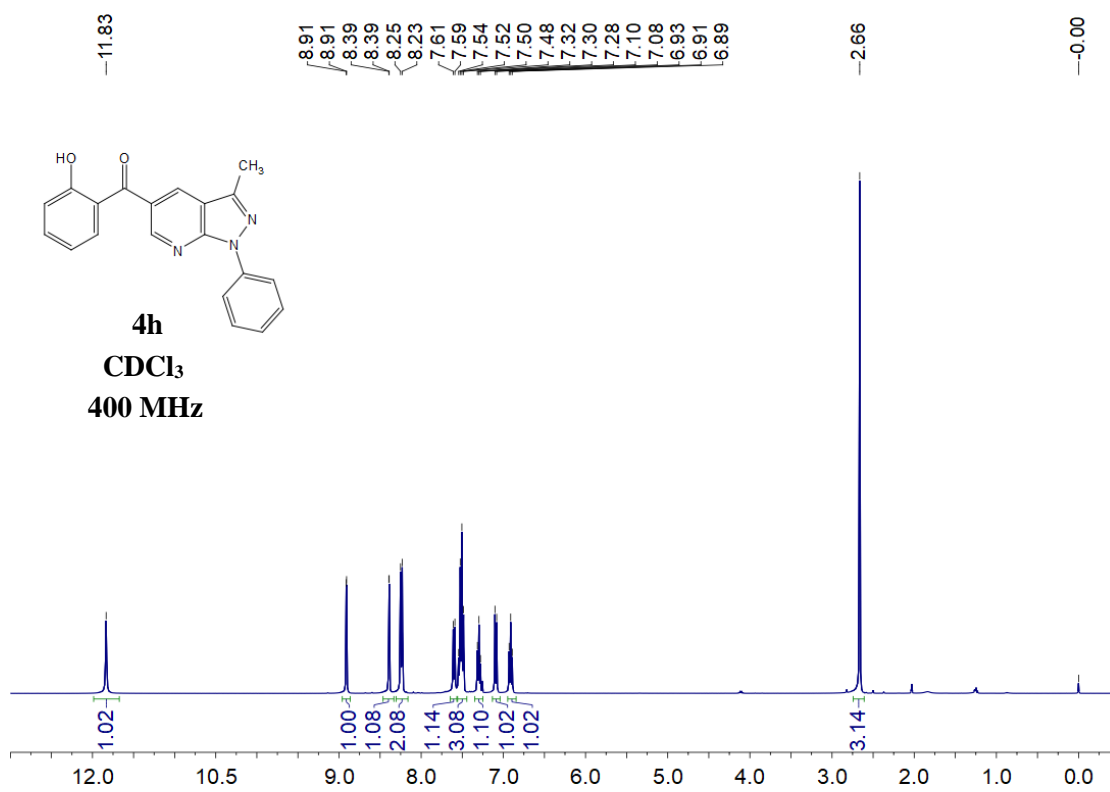


4g

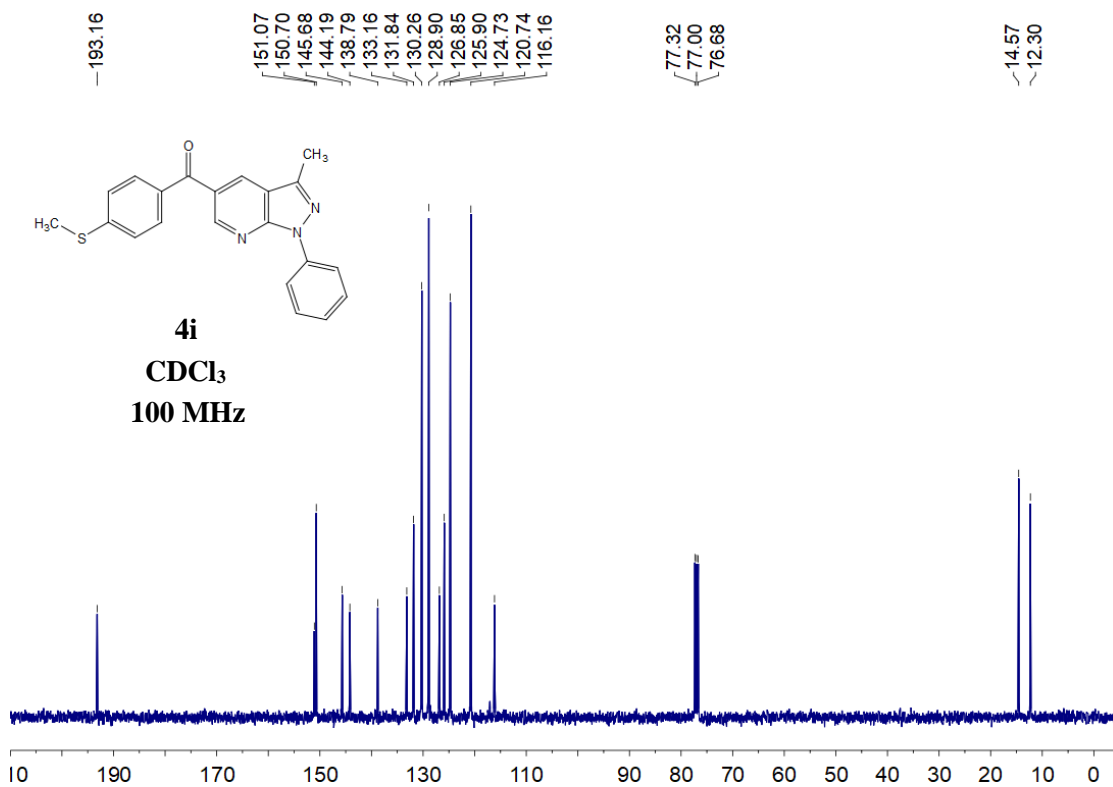
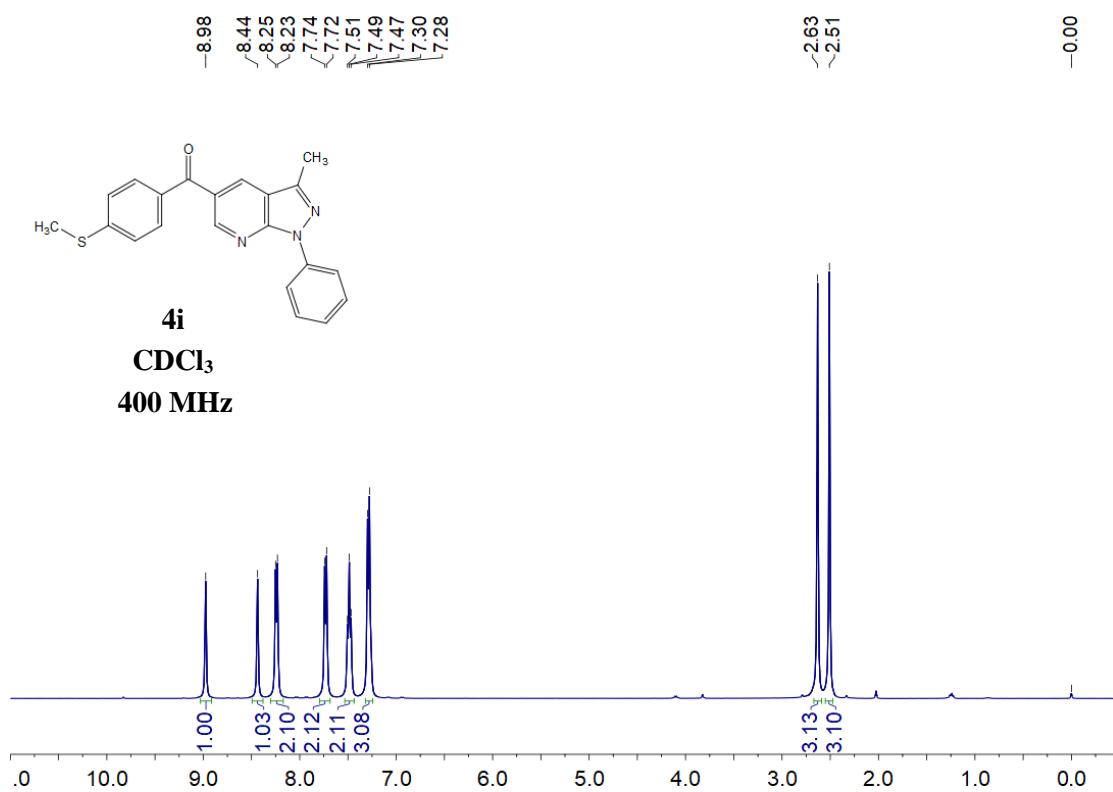




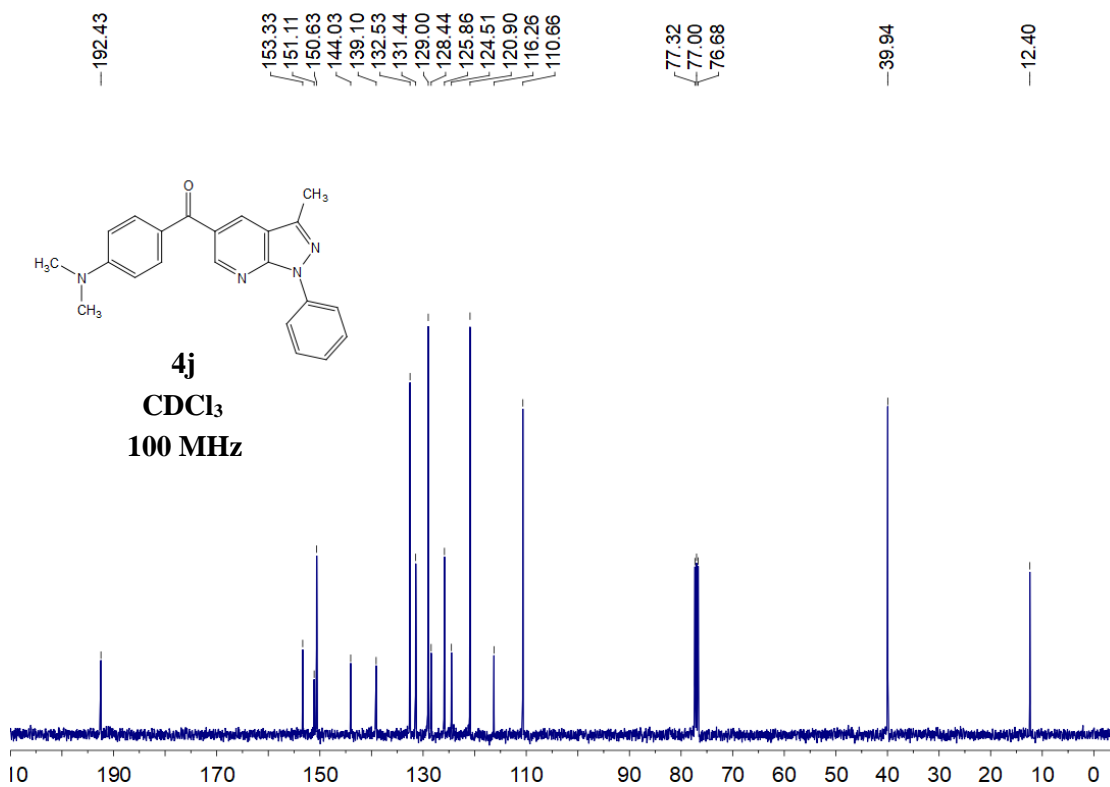
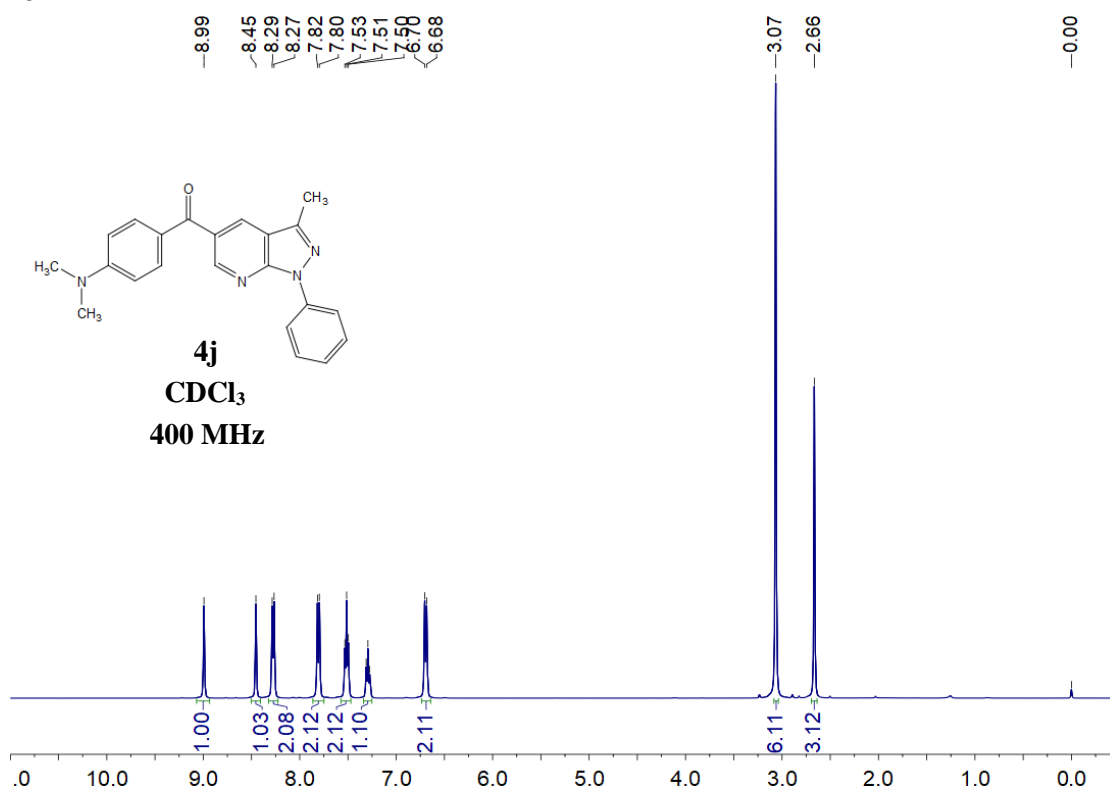
**4h**



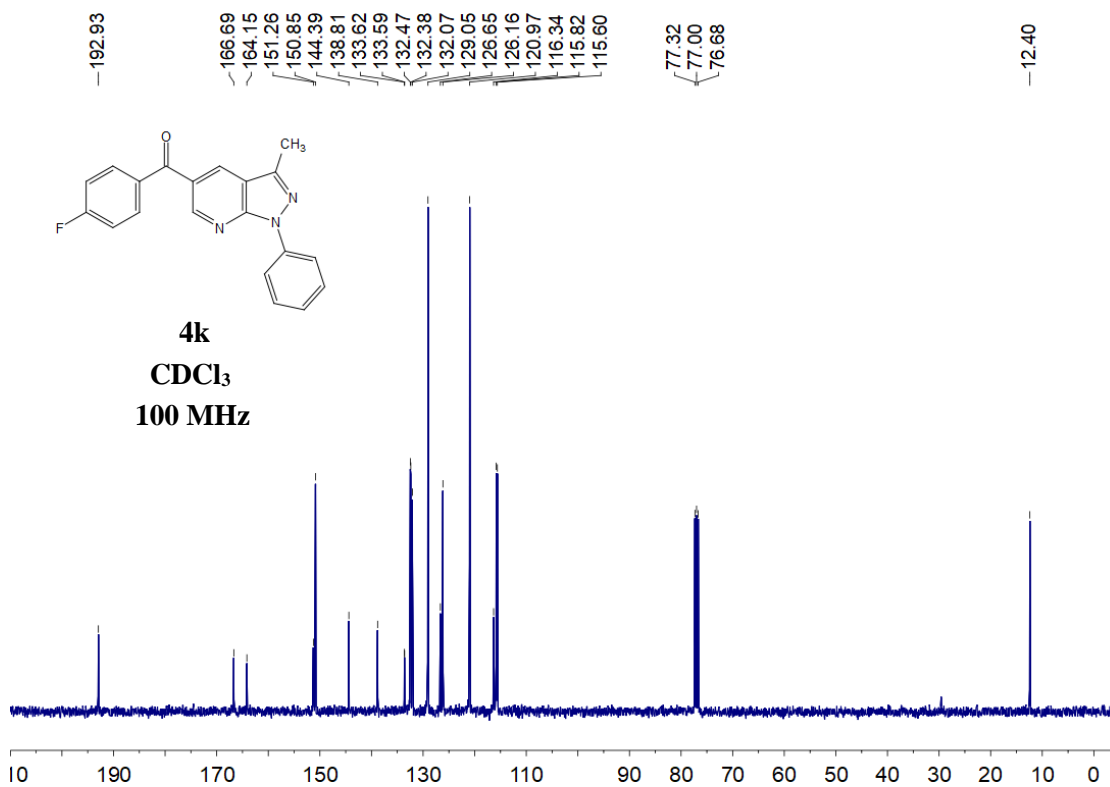
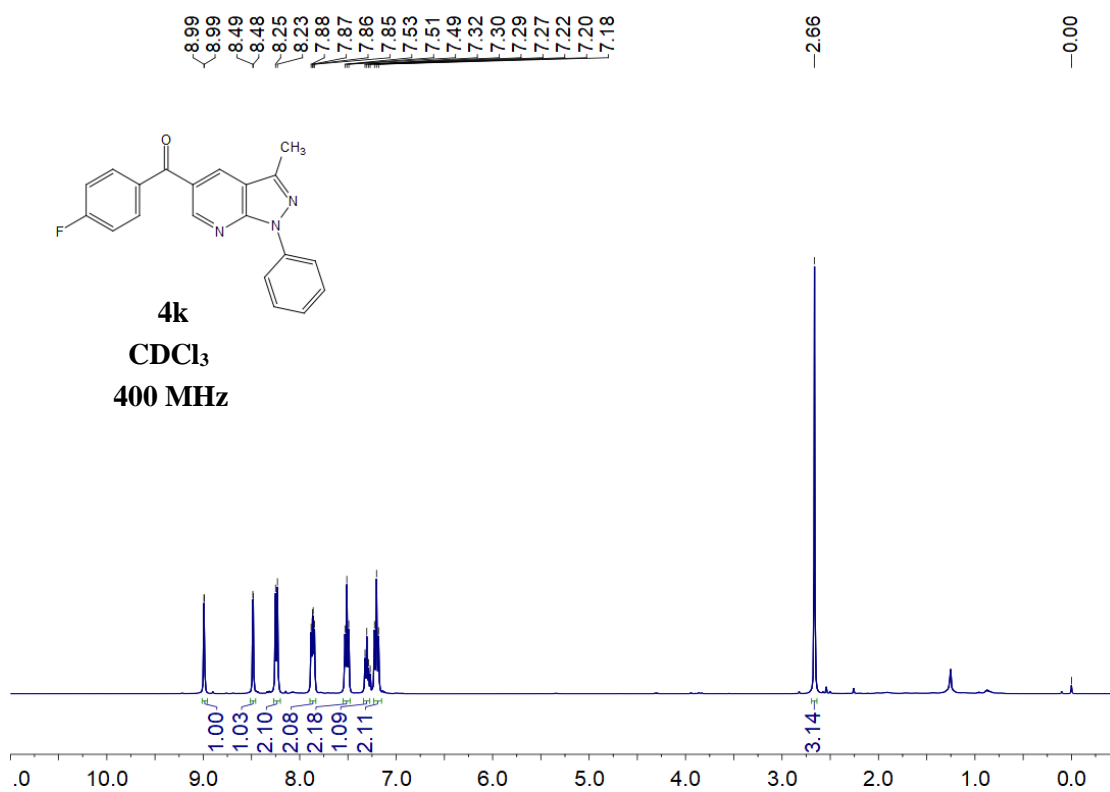
**4i**

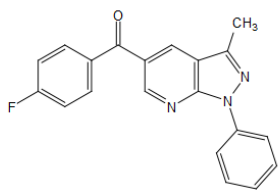


4j

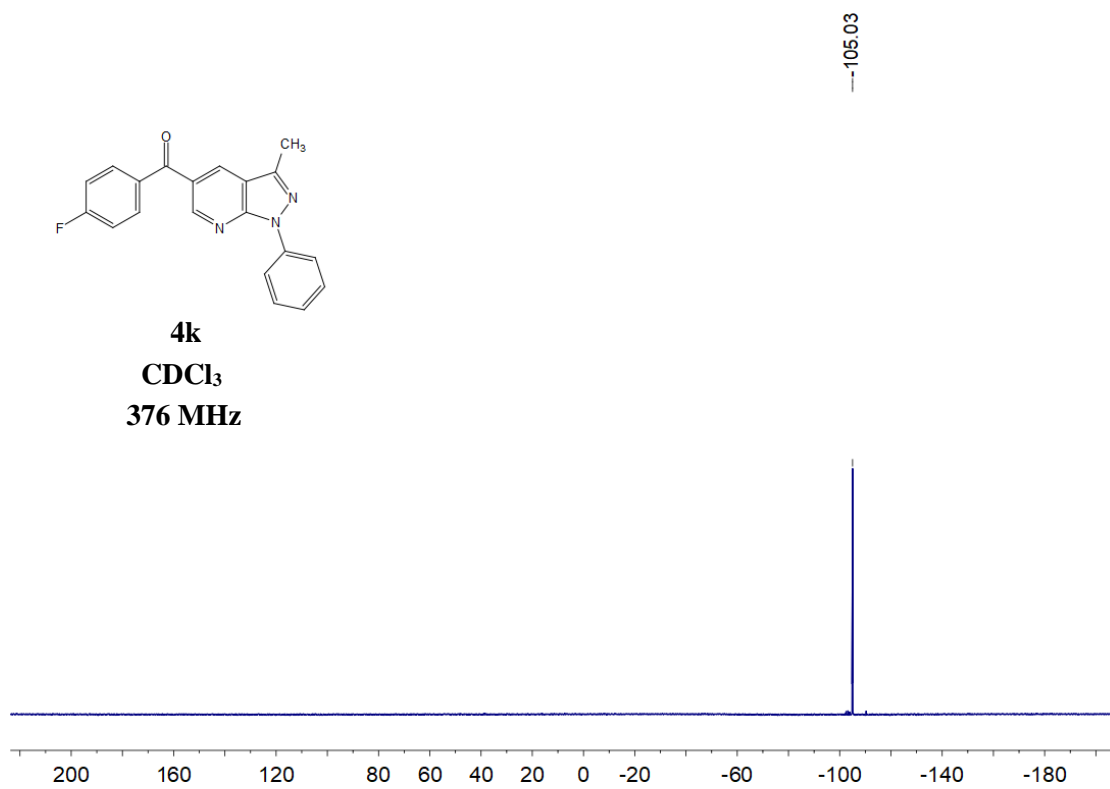


4k

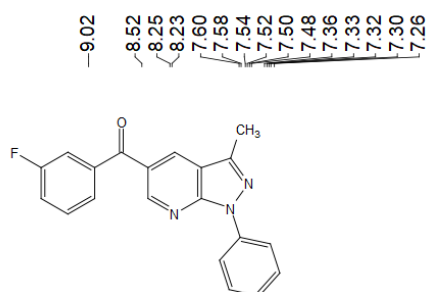




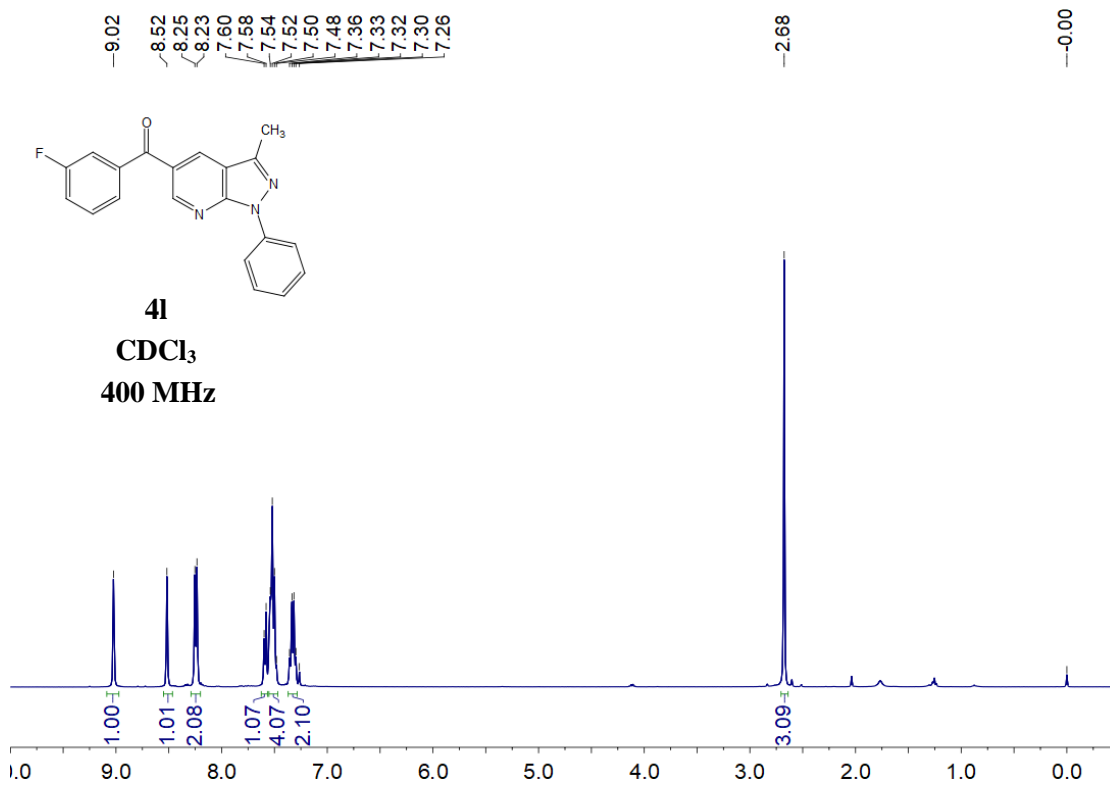
**4k**  
CDCl<sub>3</sub>  
376 MHz

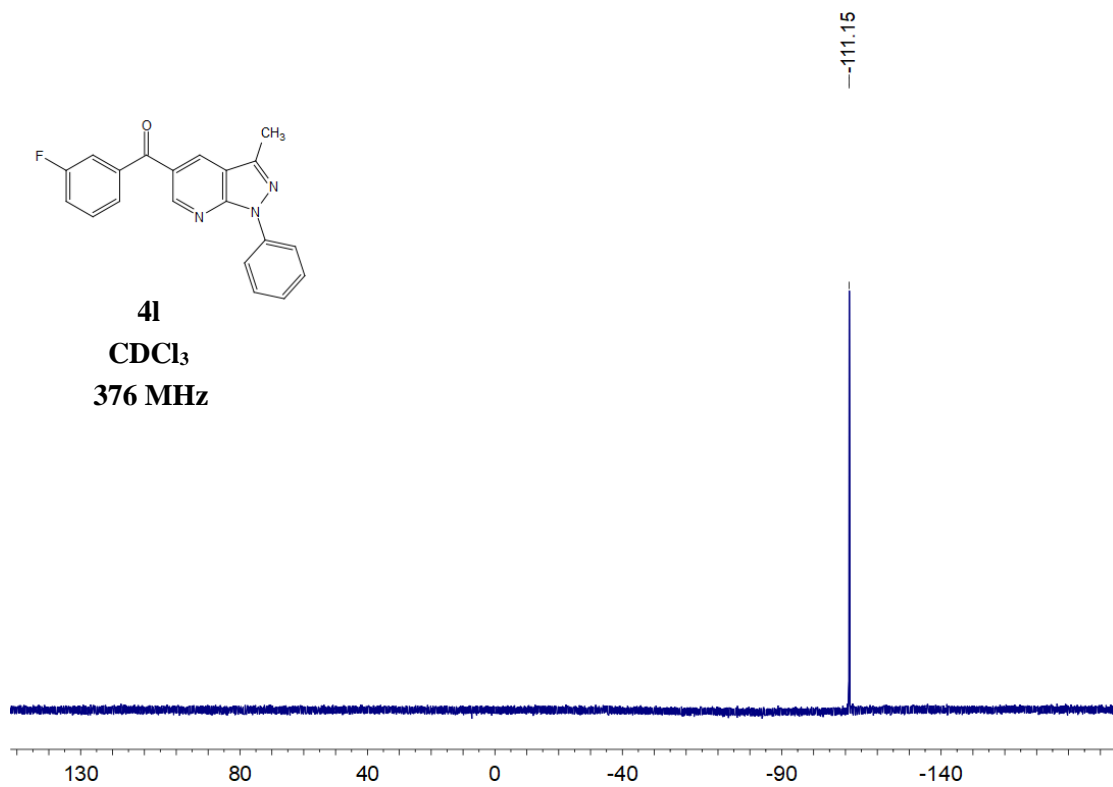
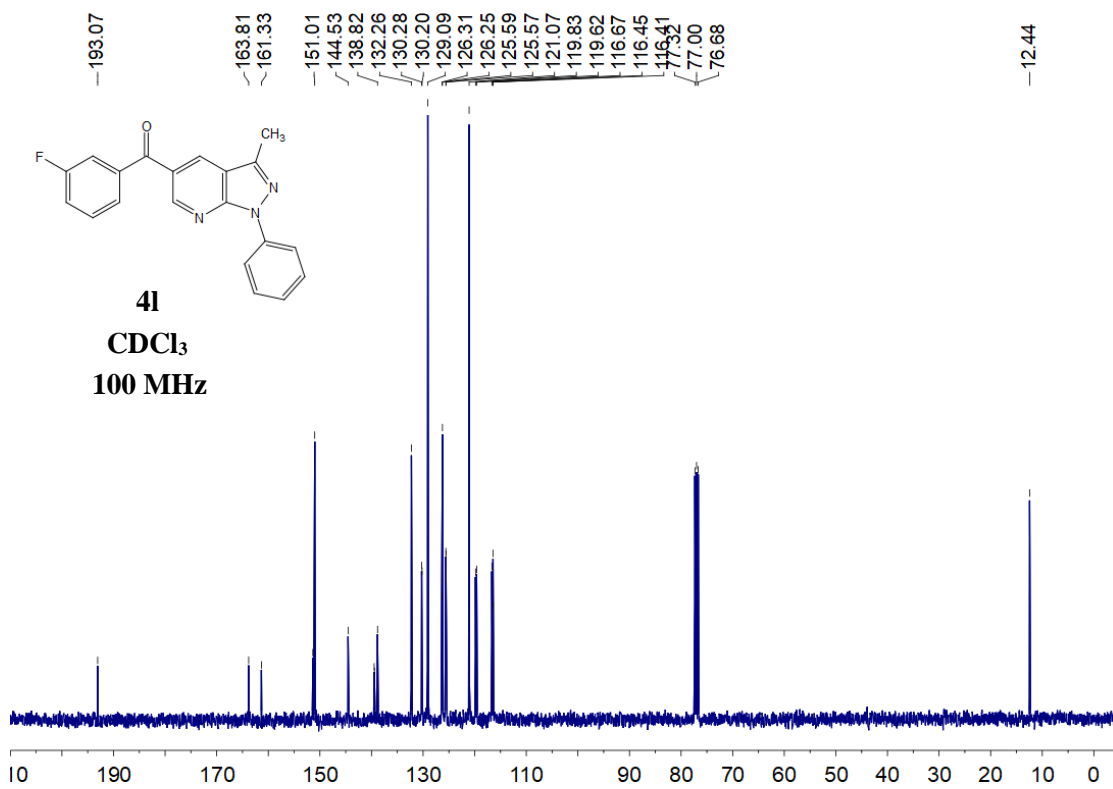


**4l**

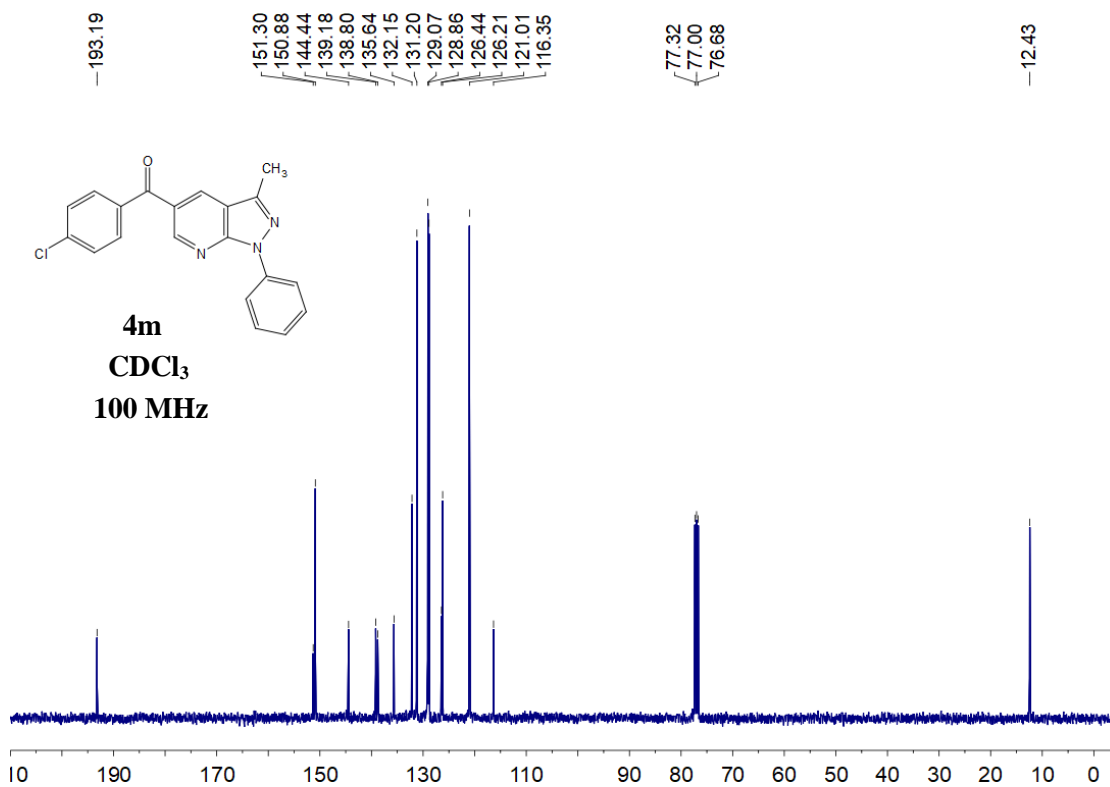
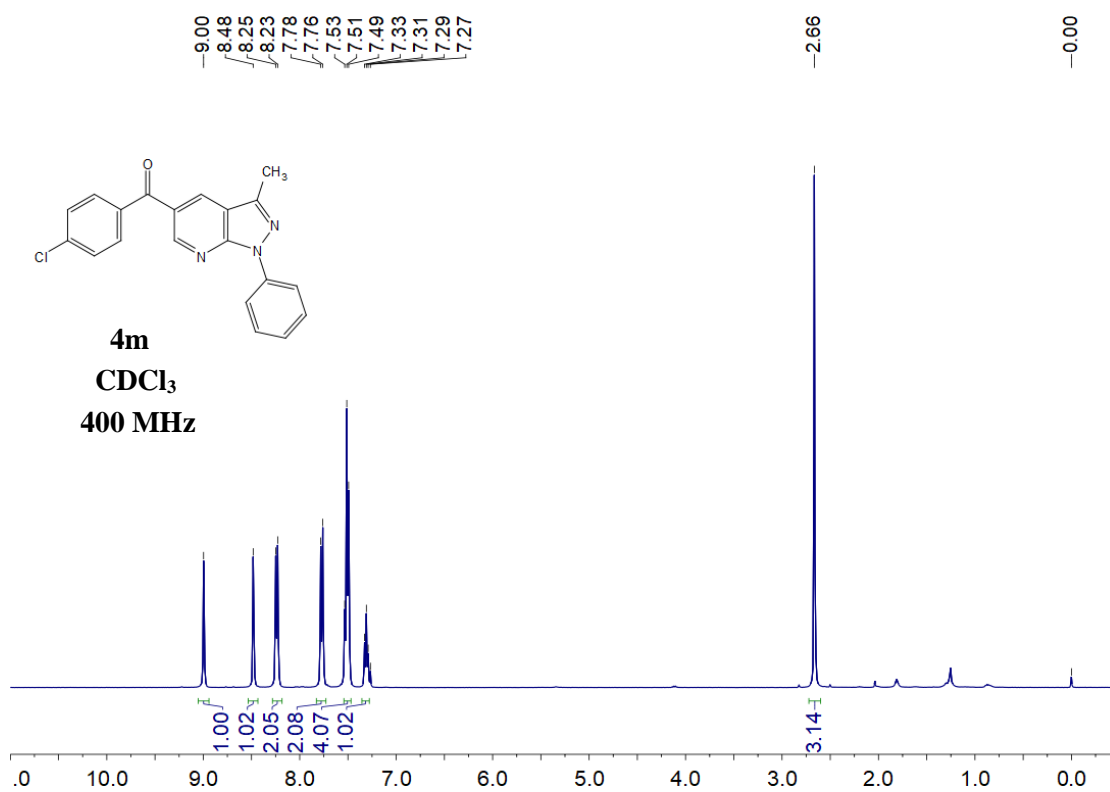


**4l**  
CDCl<sub>3</sub>  
400 MHz

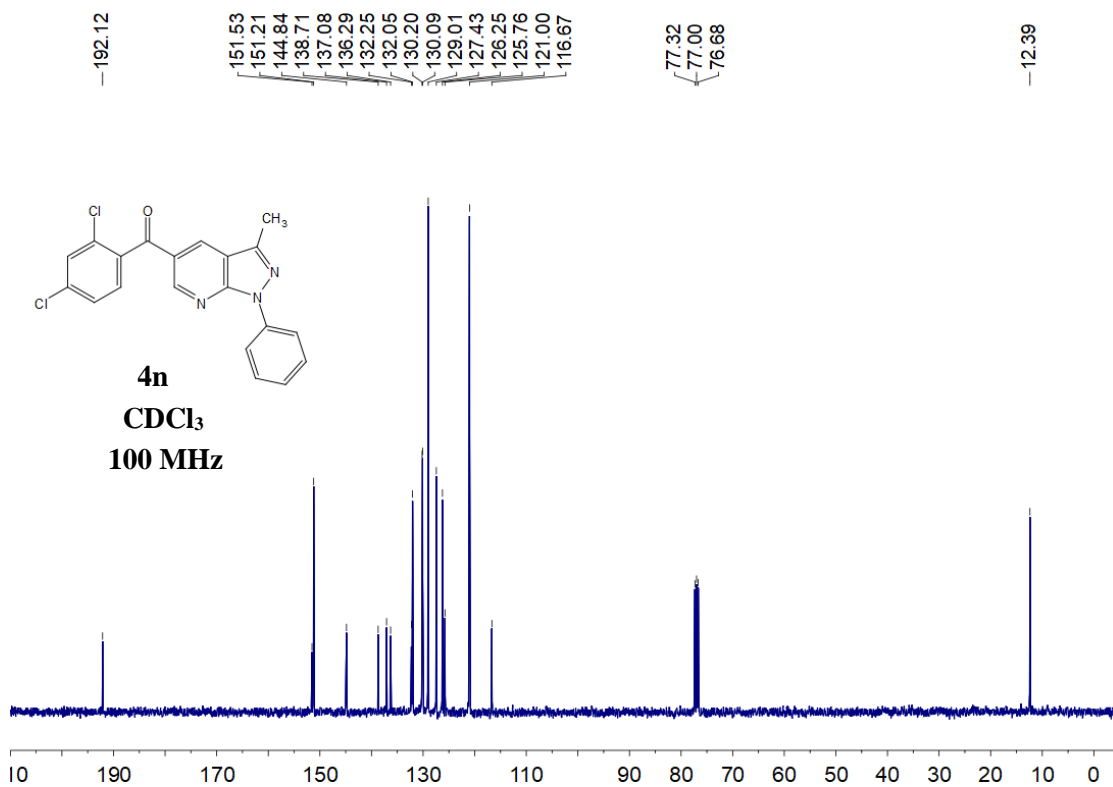
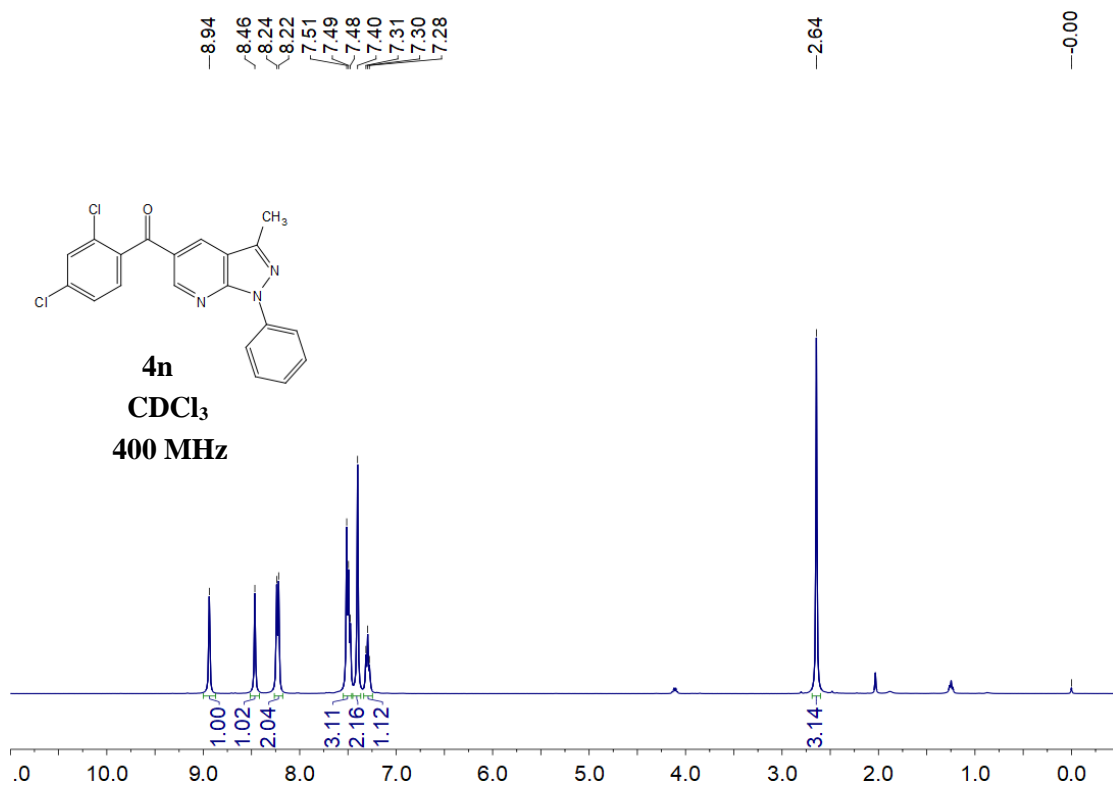




4m

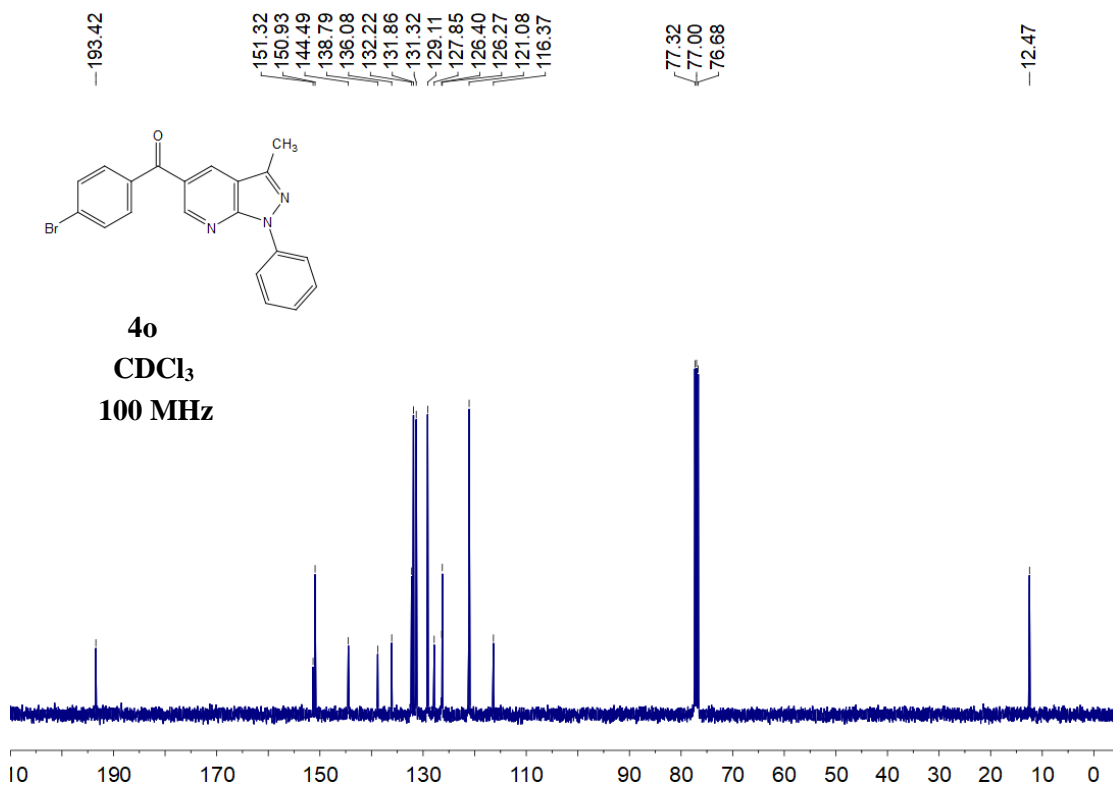
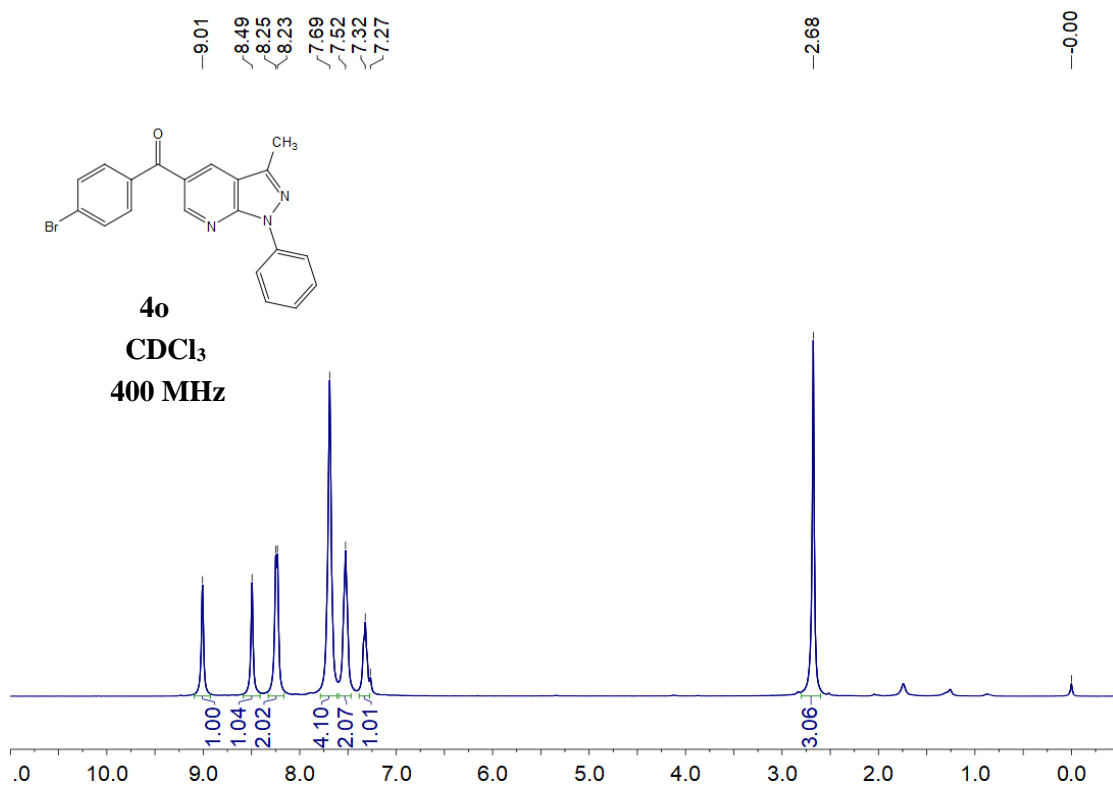


**4n**

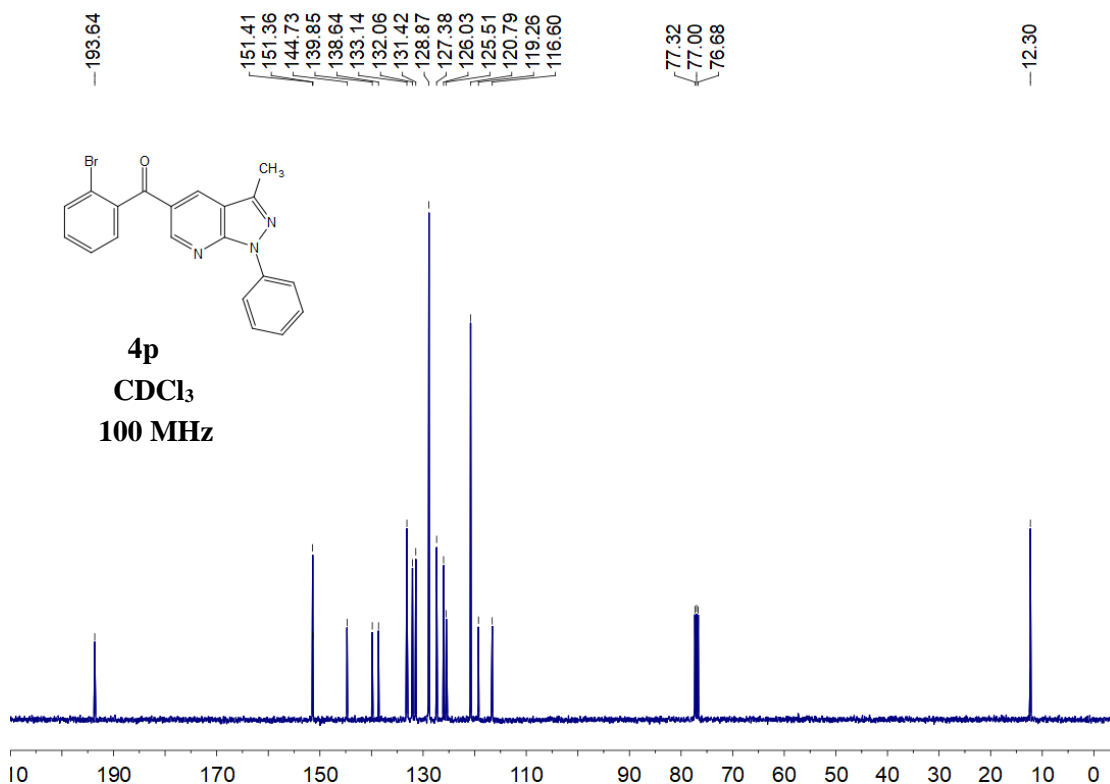
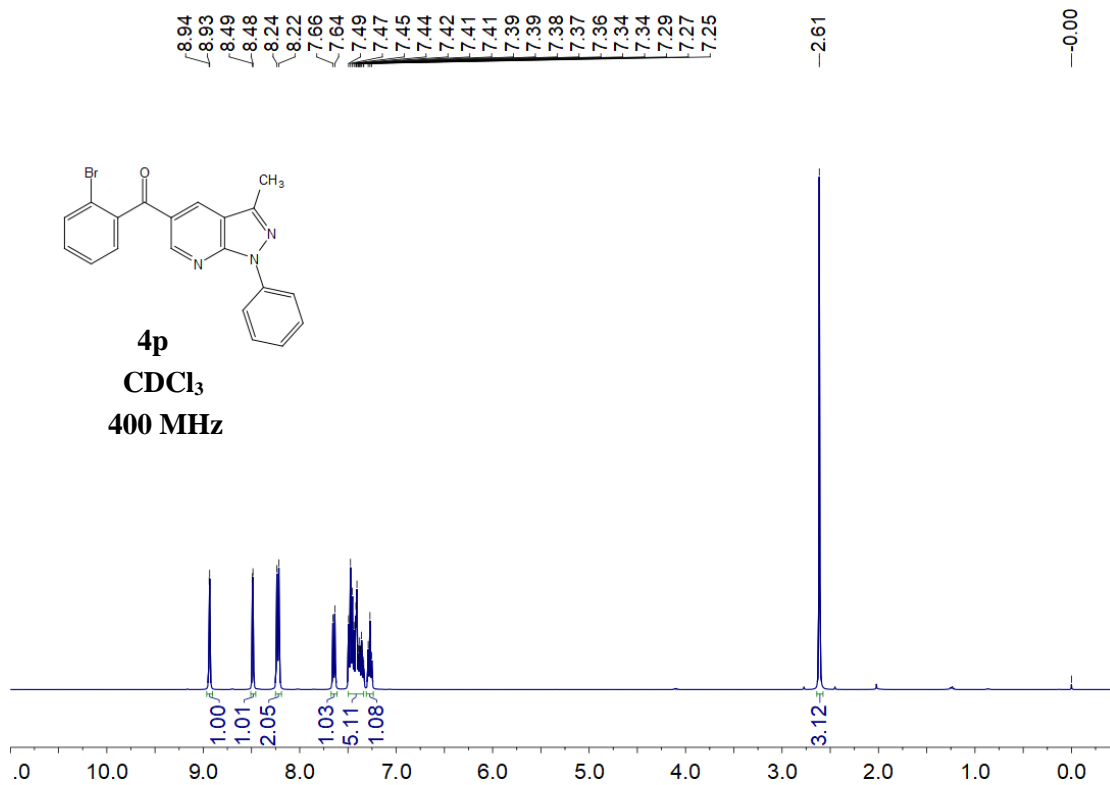




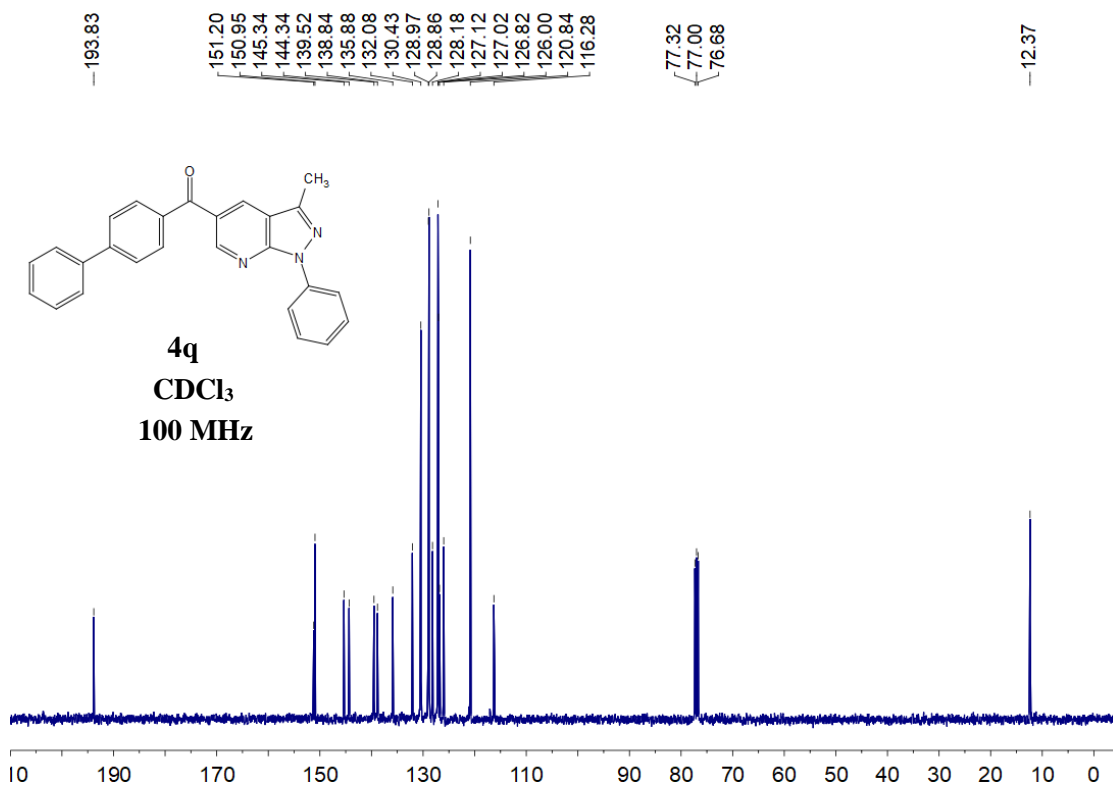
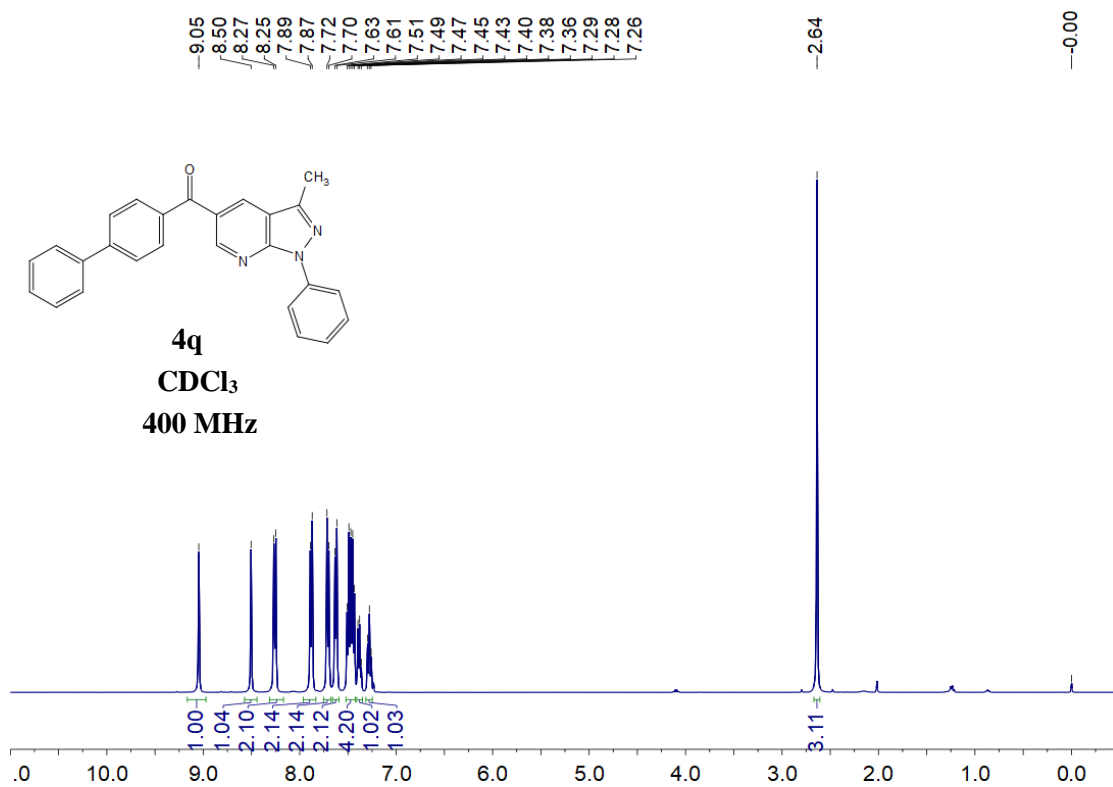
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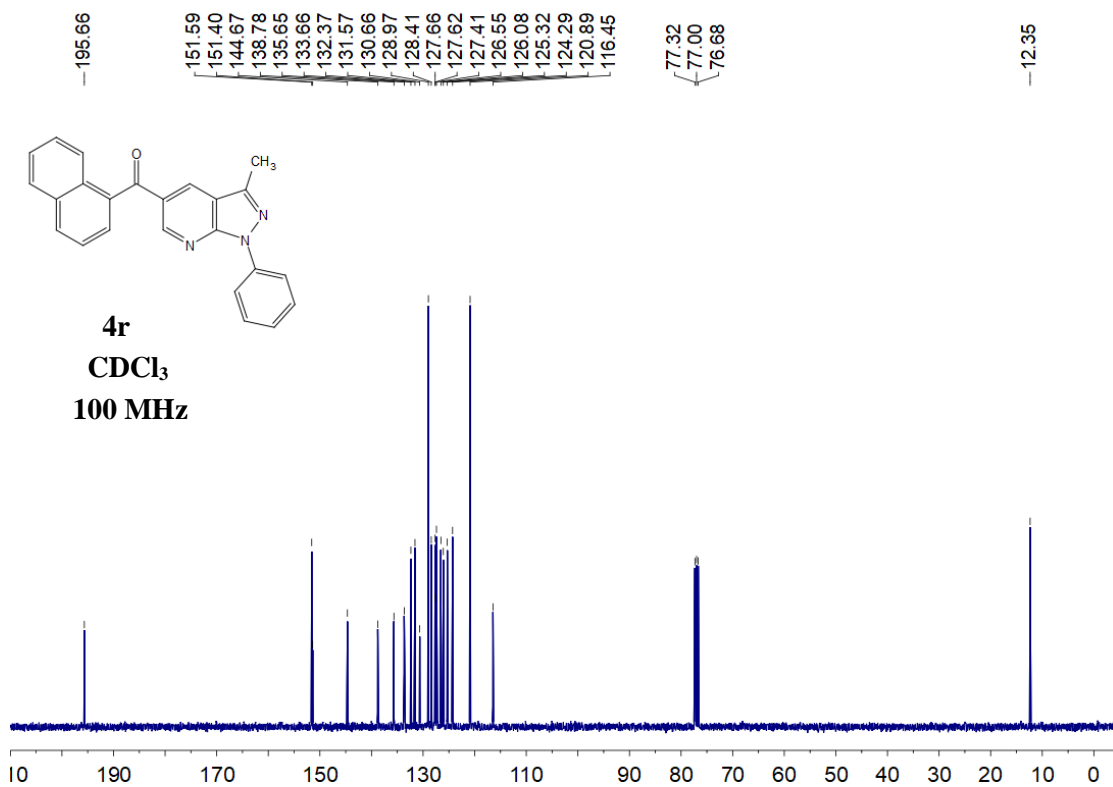
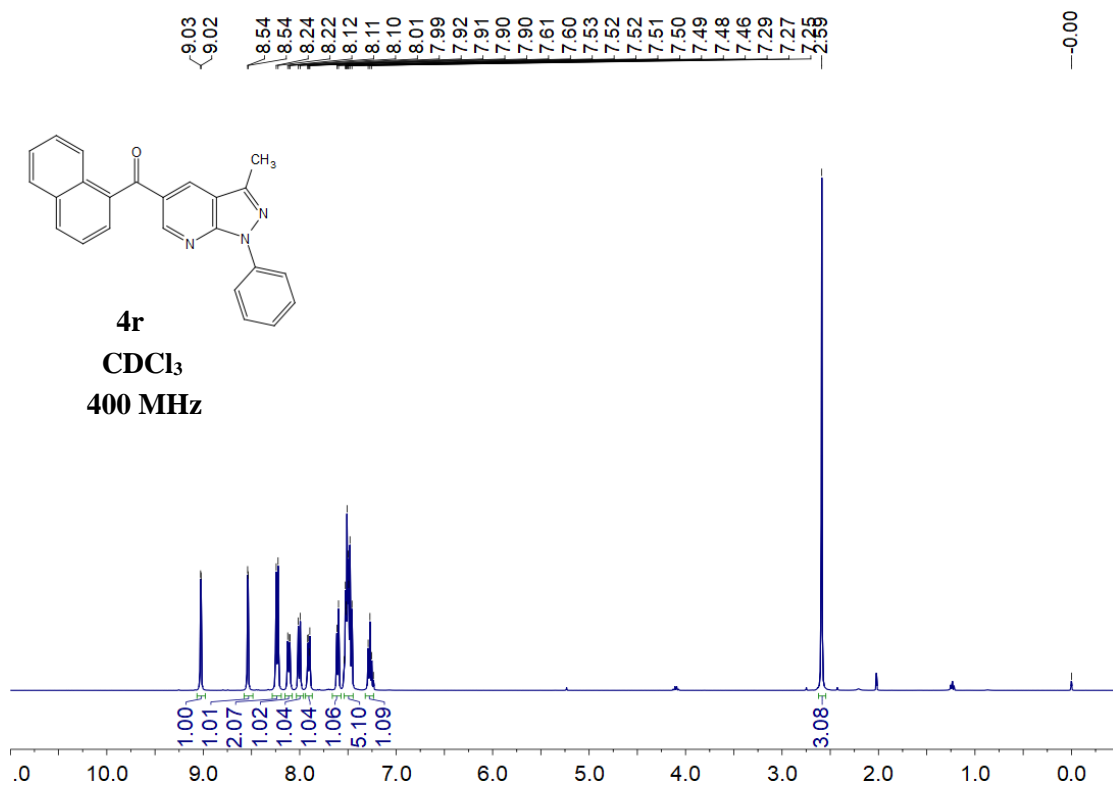
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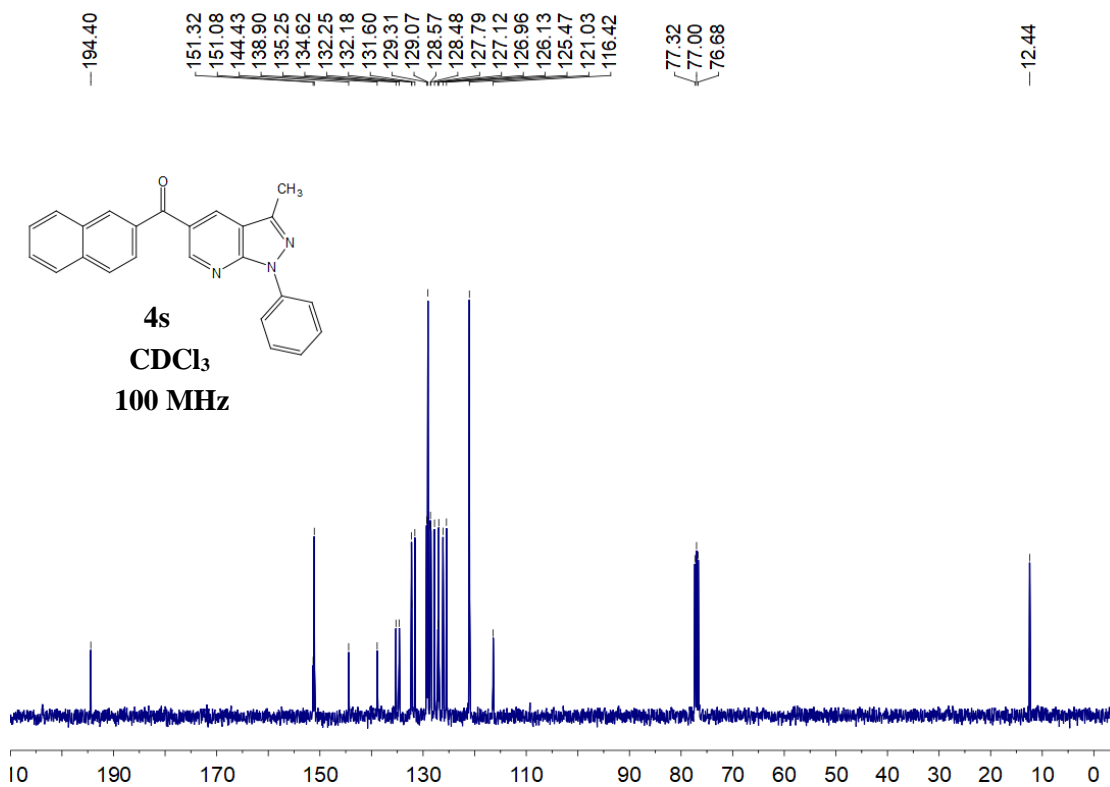
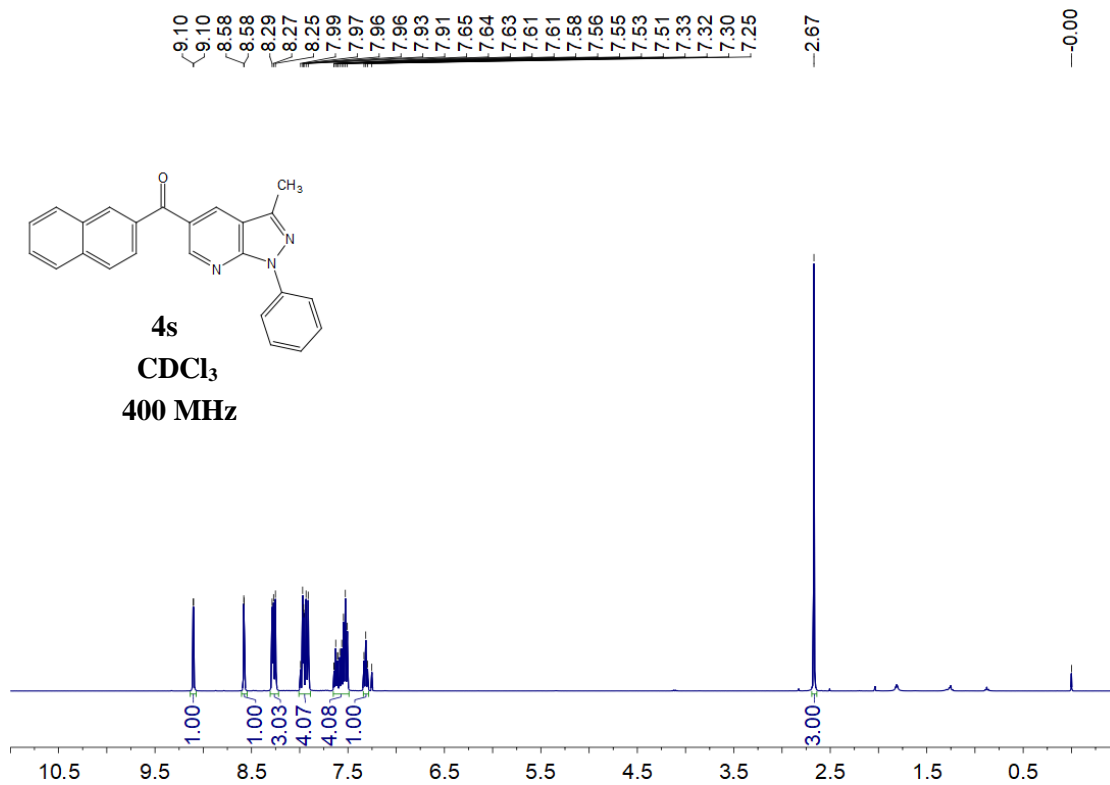
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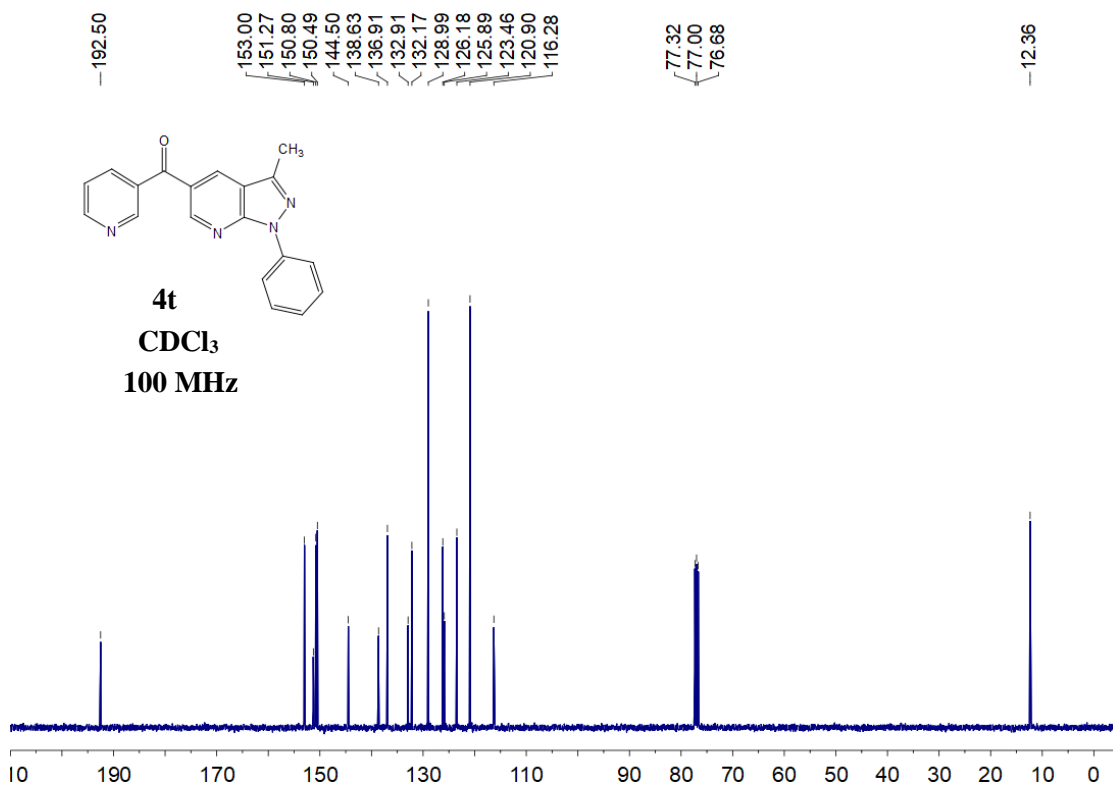
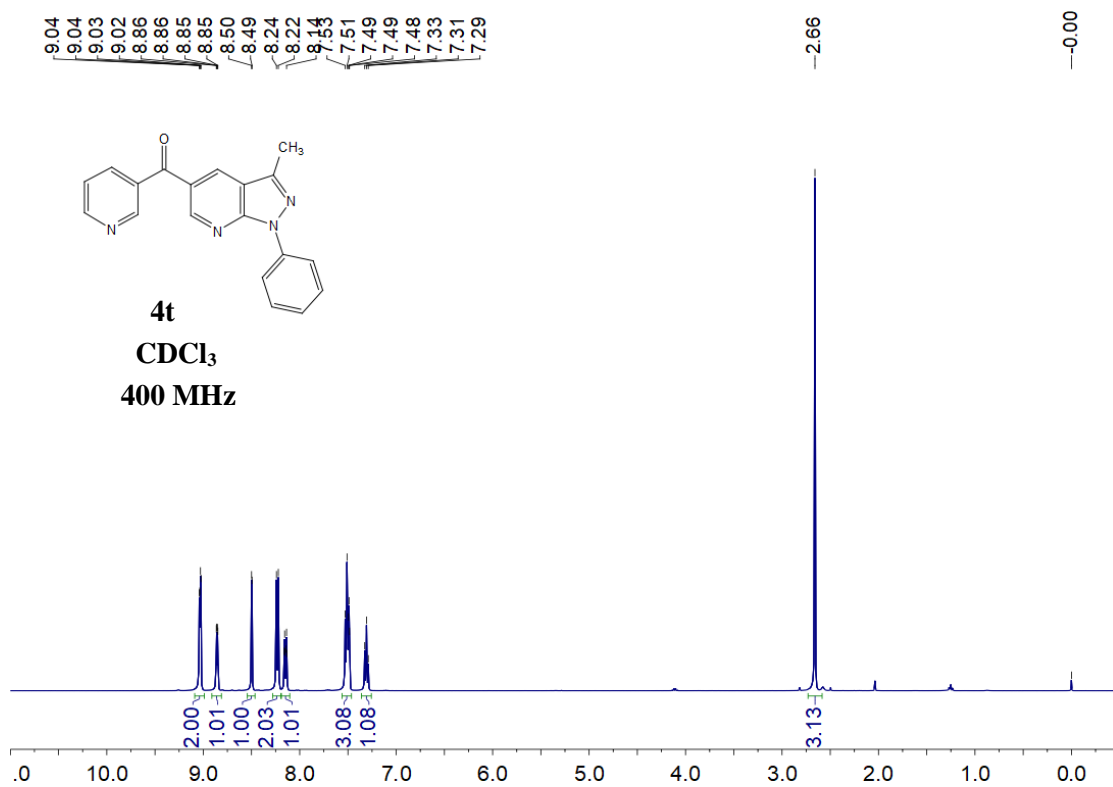
**4r**



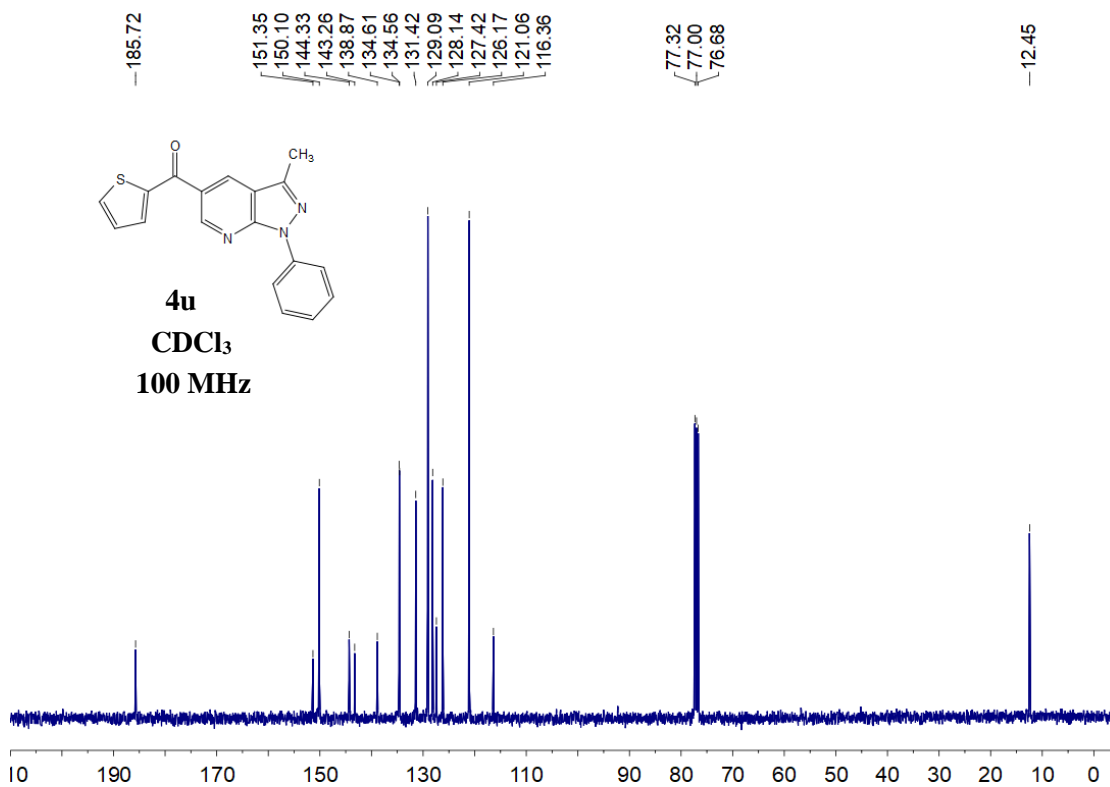
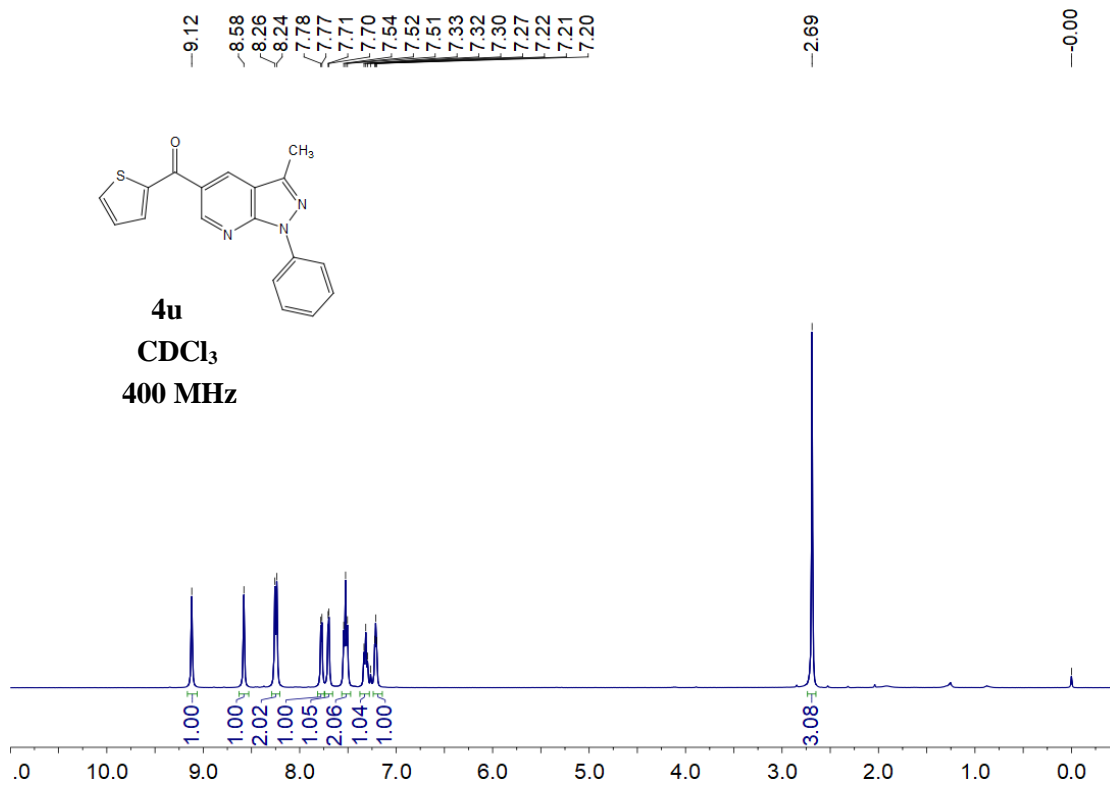
4s



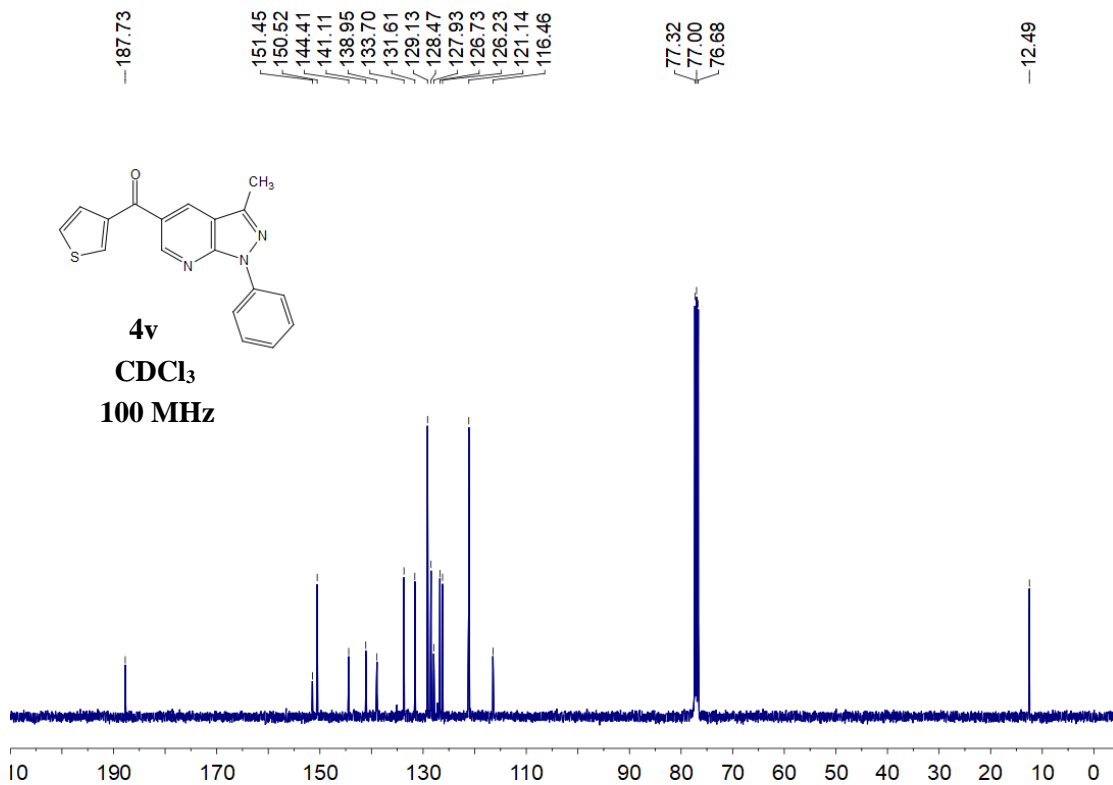
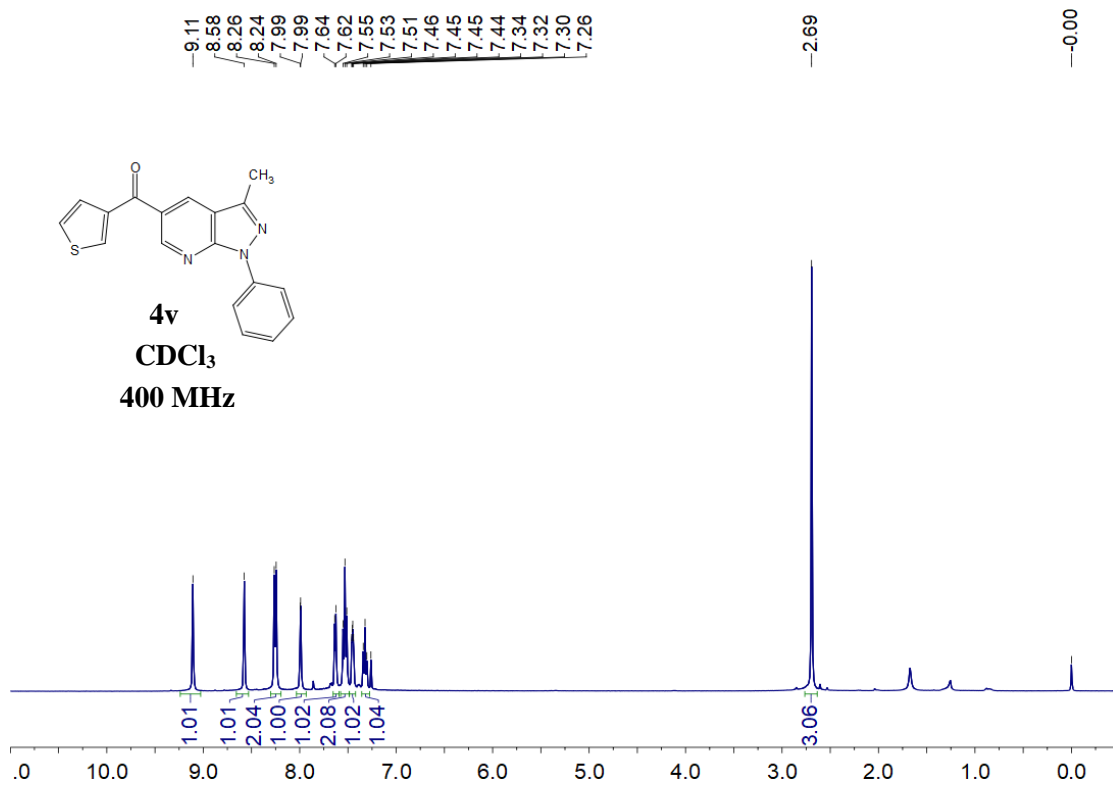
4t



**4u**

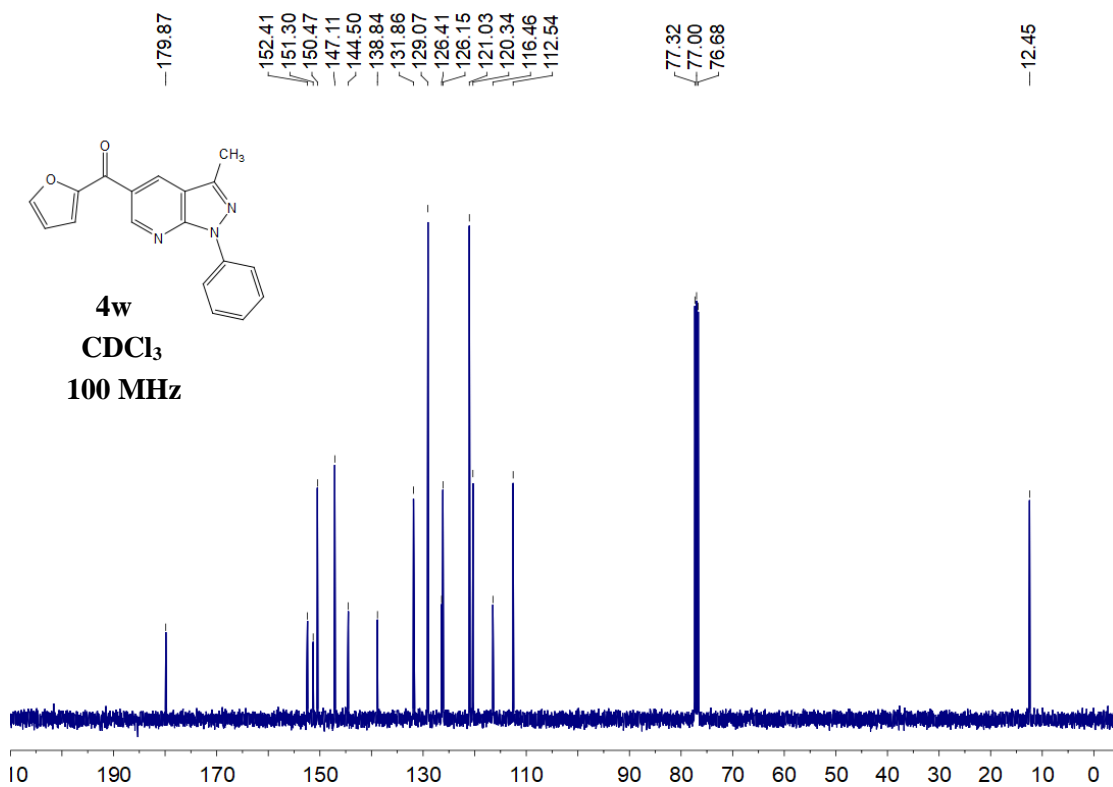
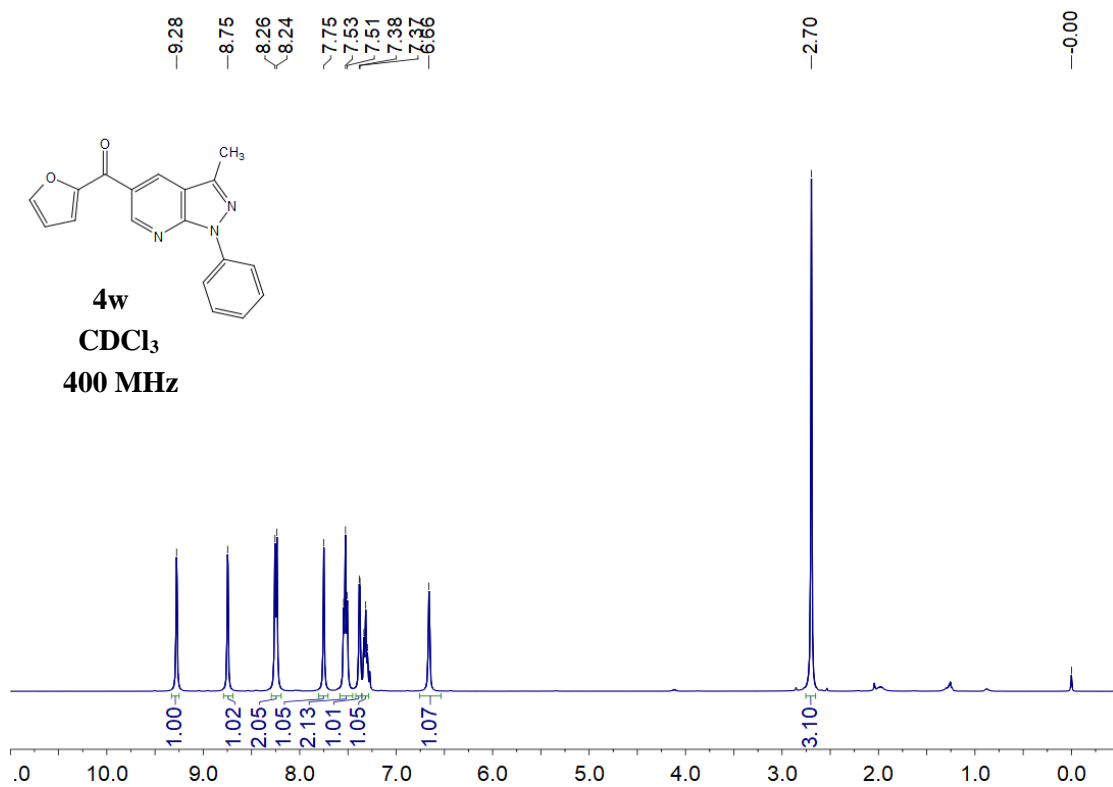


**4v**

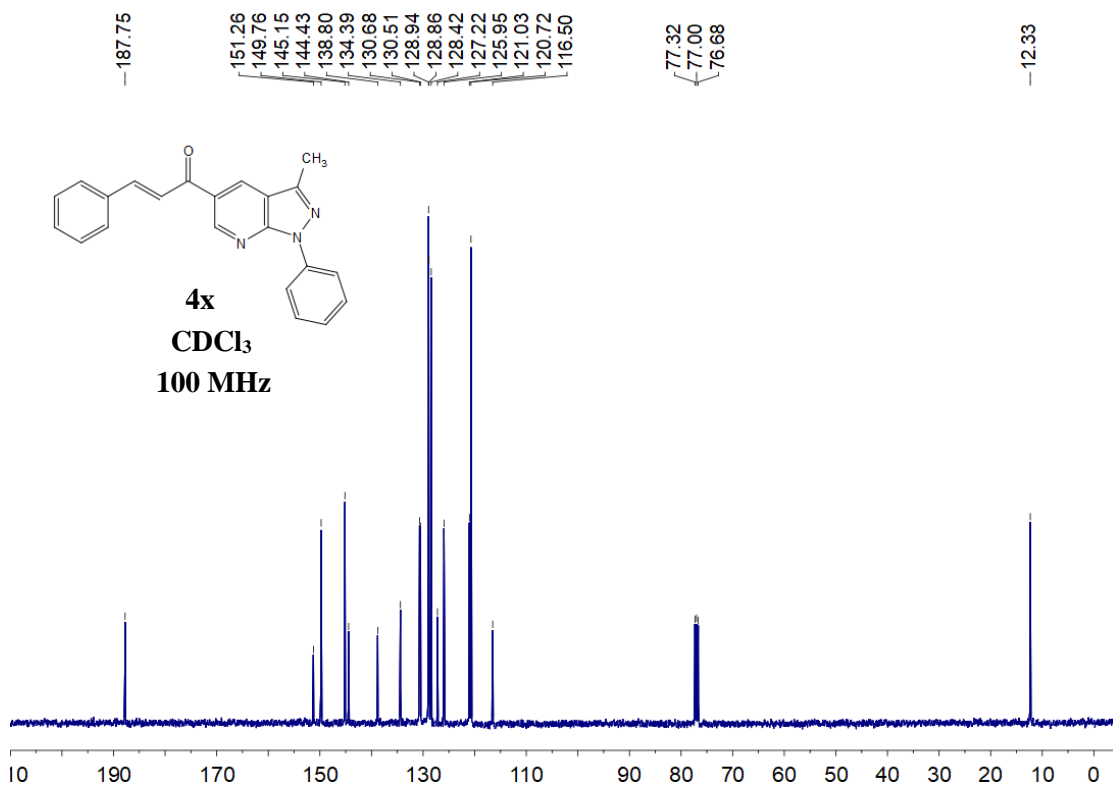
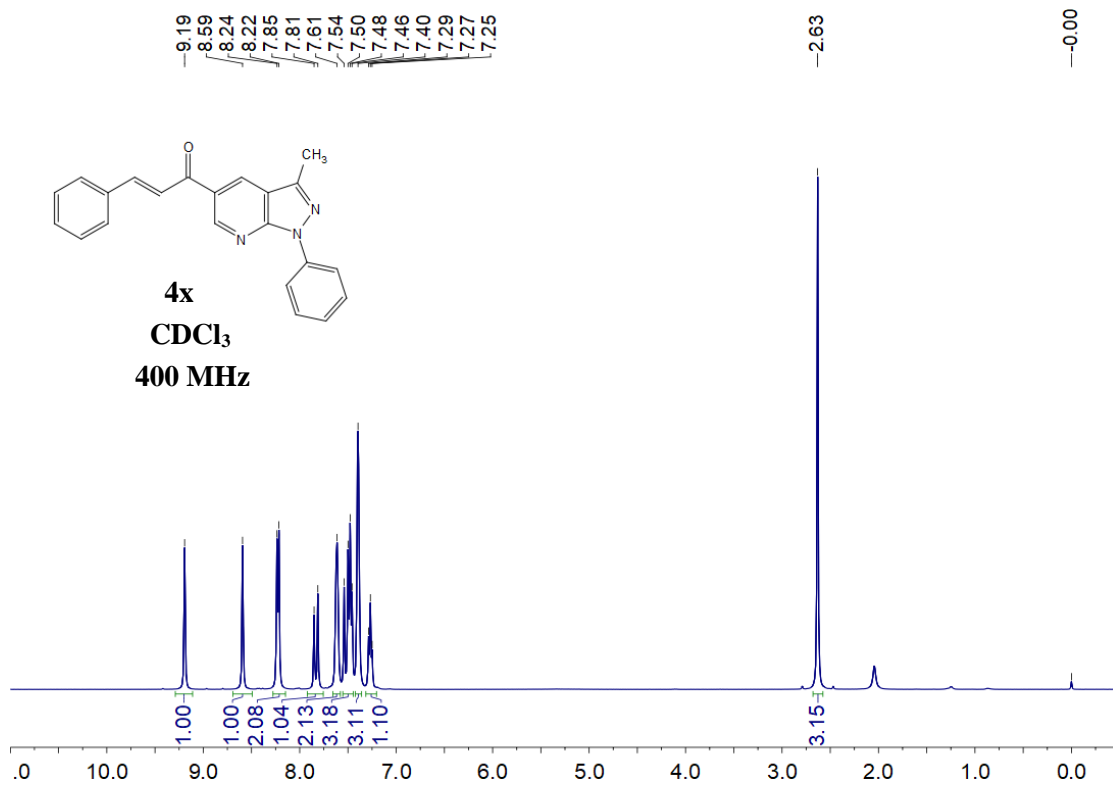




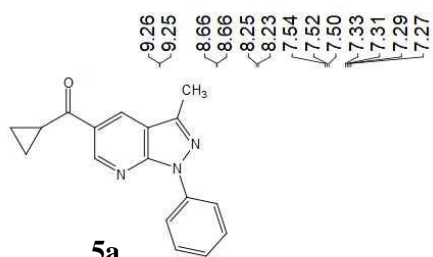
4w



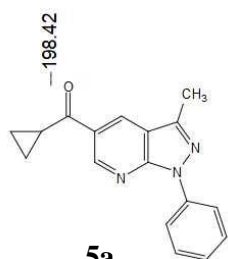
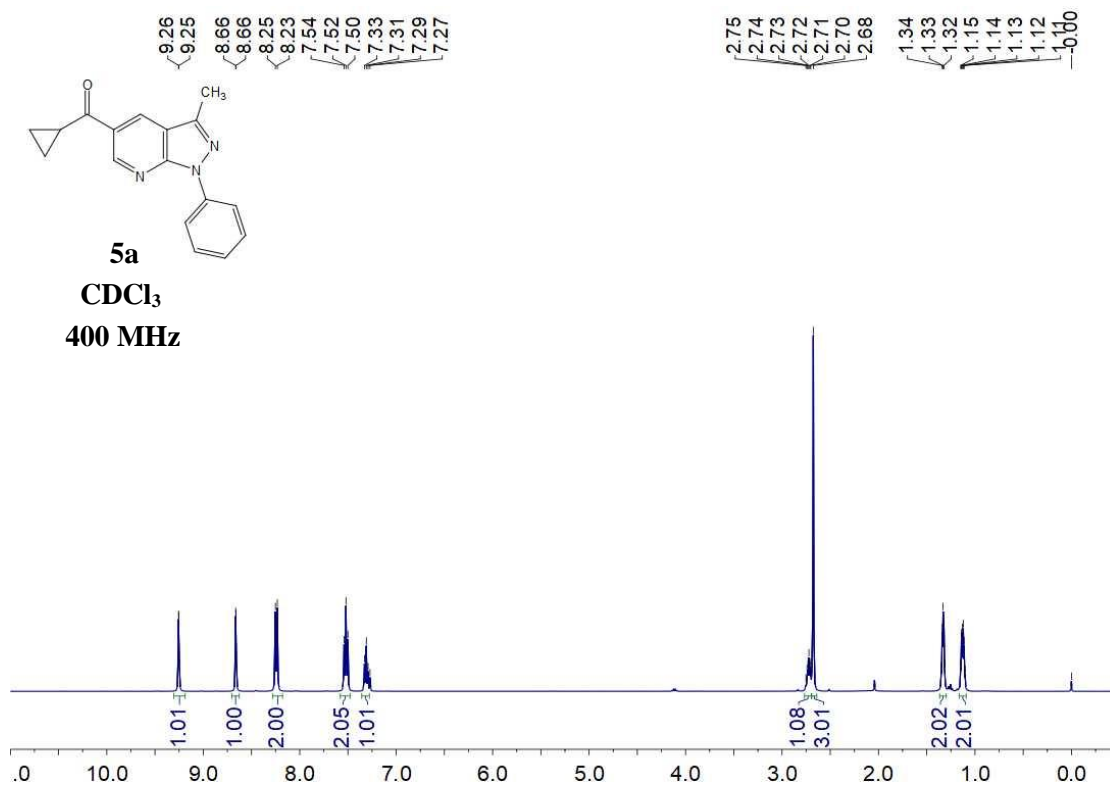
4x



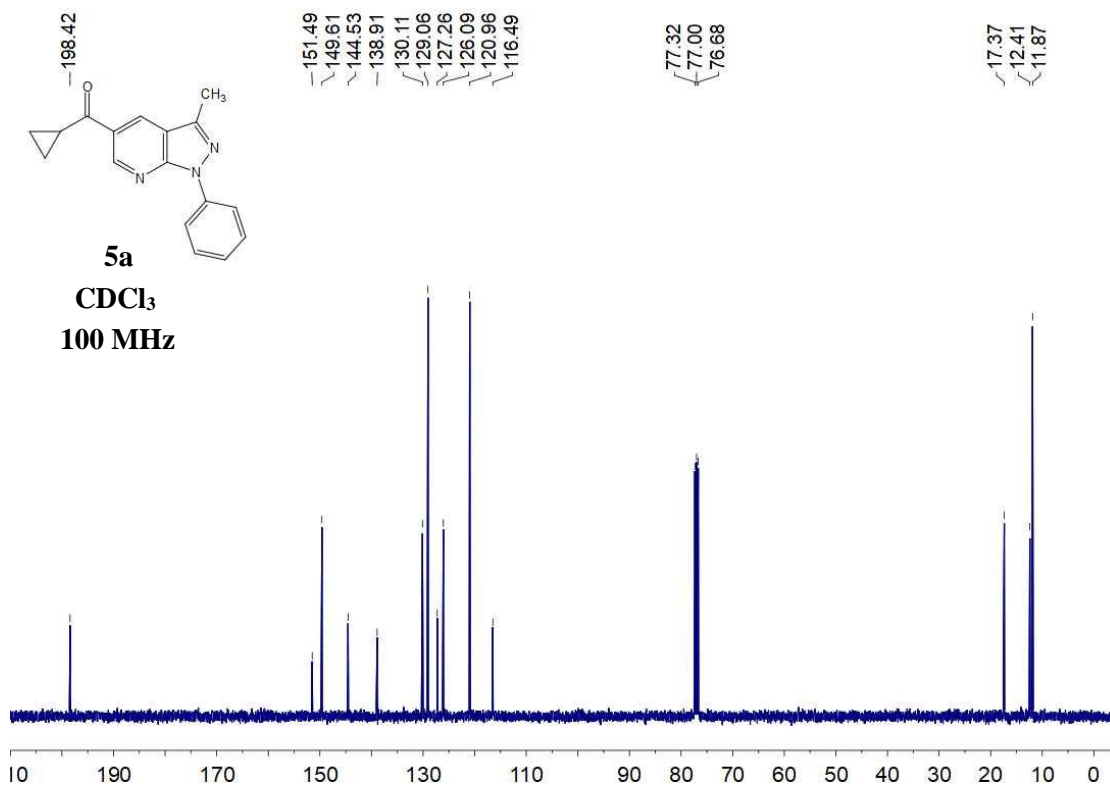
**5a**



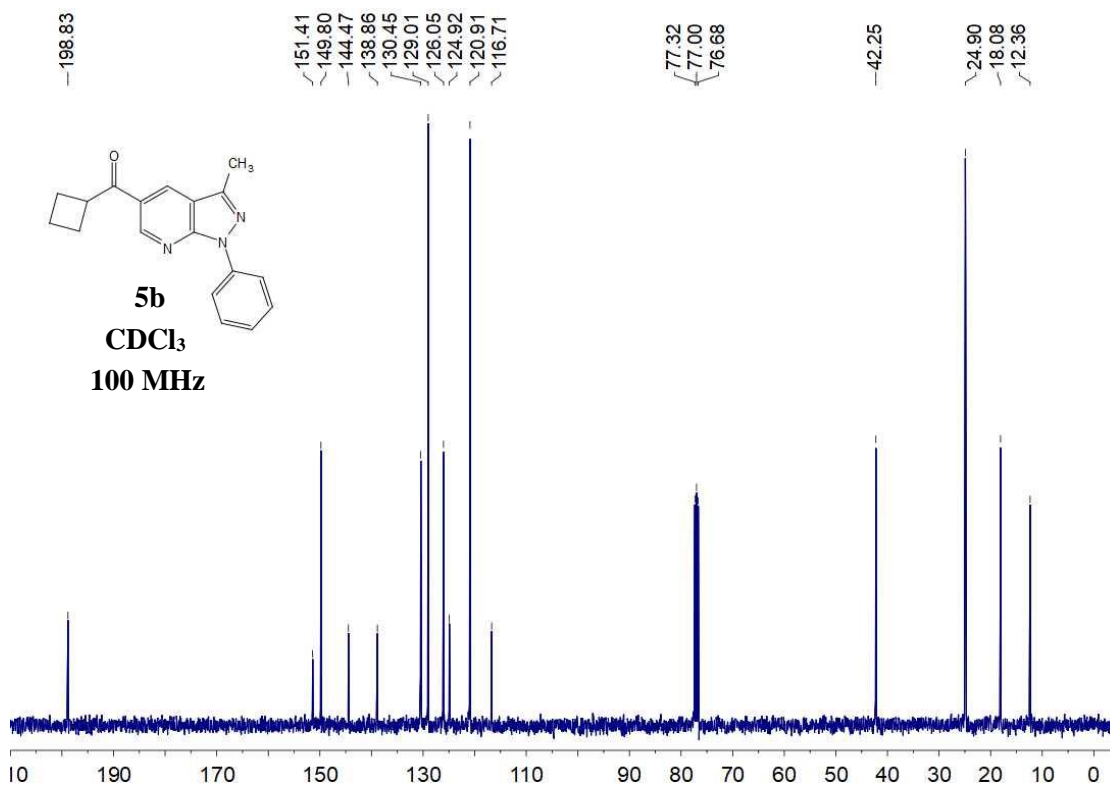
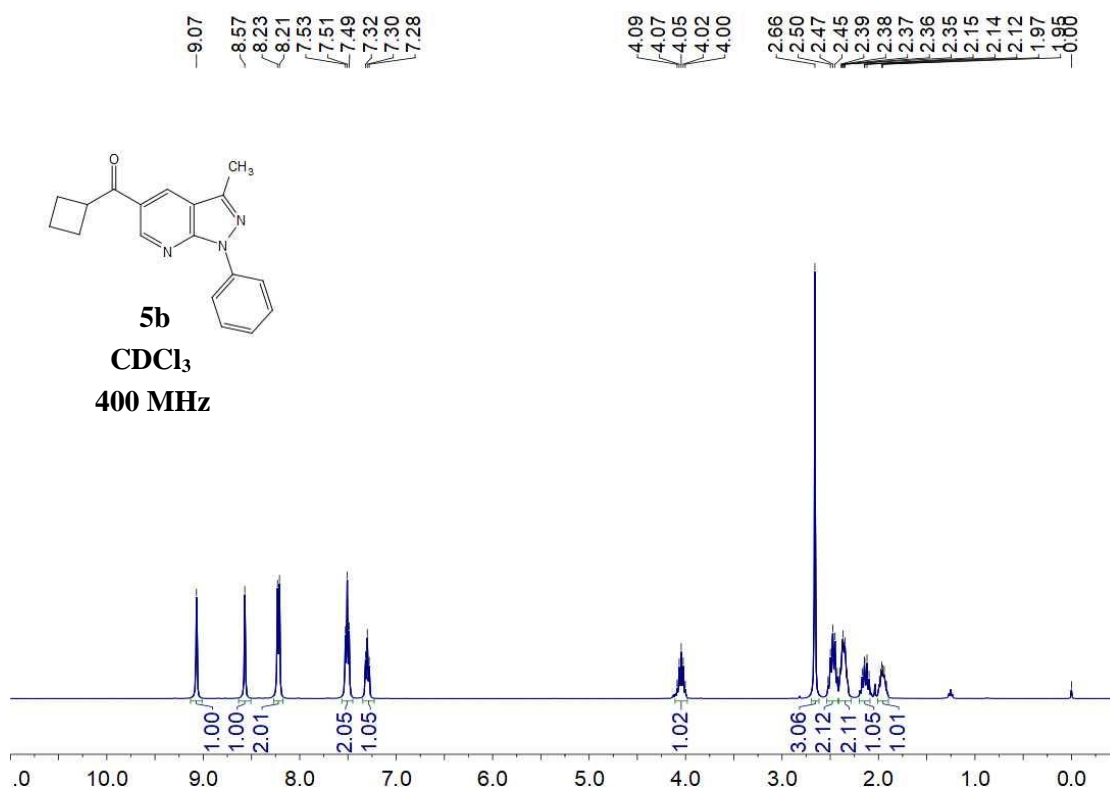
**5a**  
**CDCl<sub>3</sub>**  
**400 MHz**



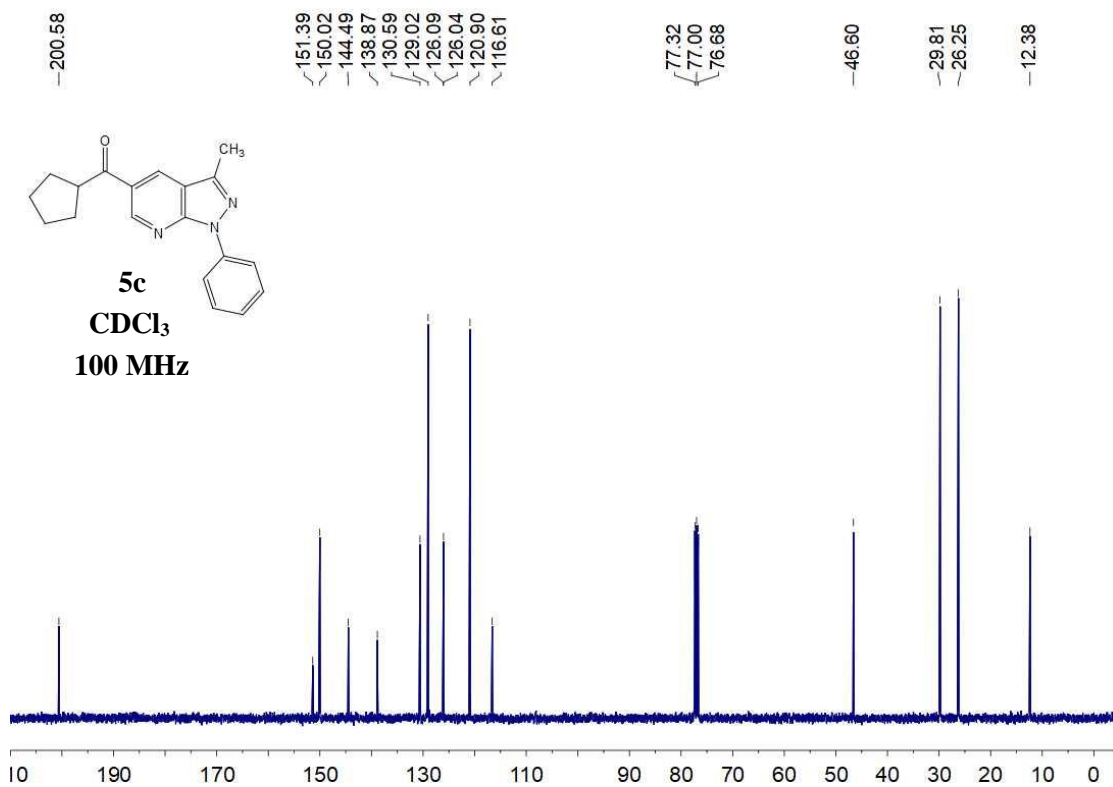
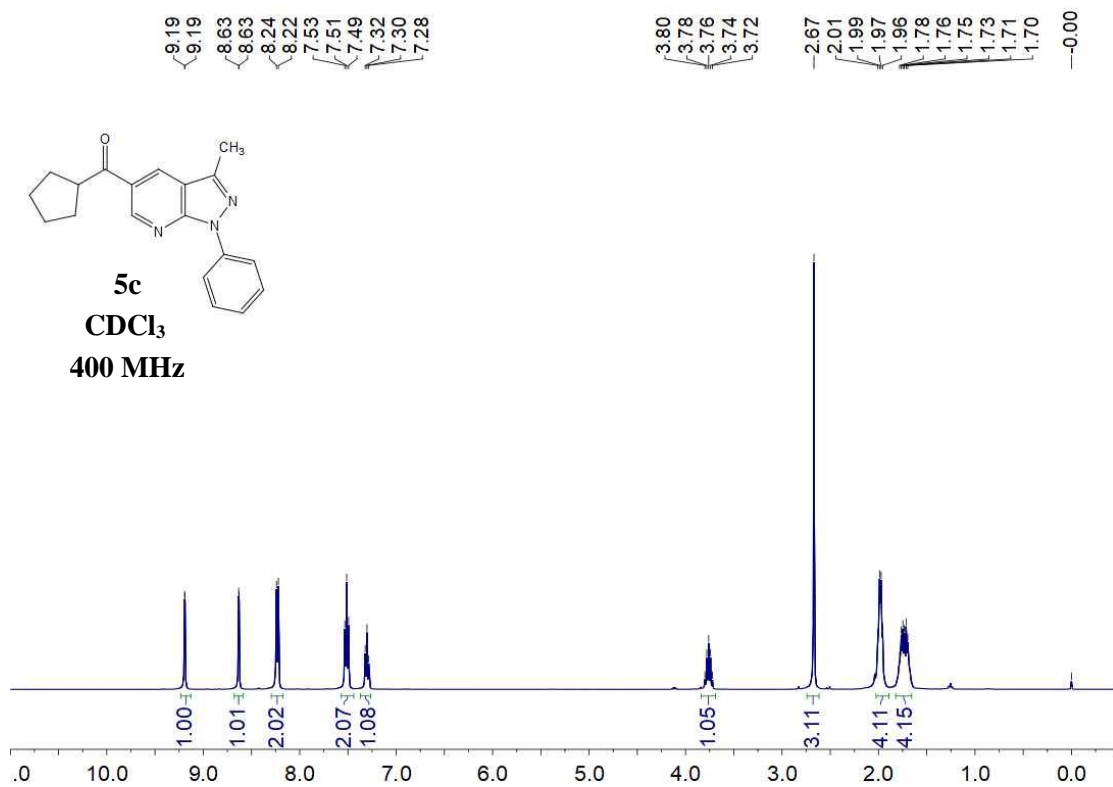
**5a**  
**CDCl<sub>3</sub>**  
**100 MHz**



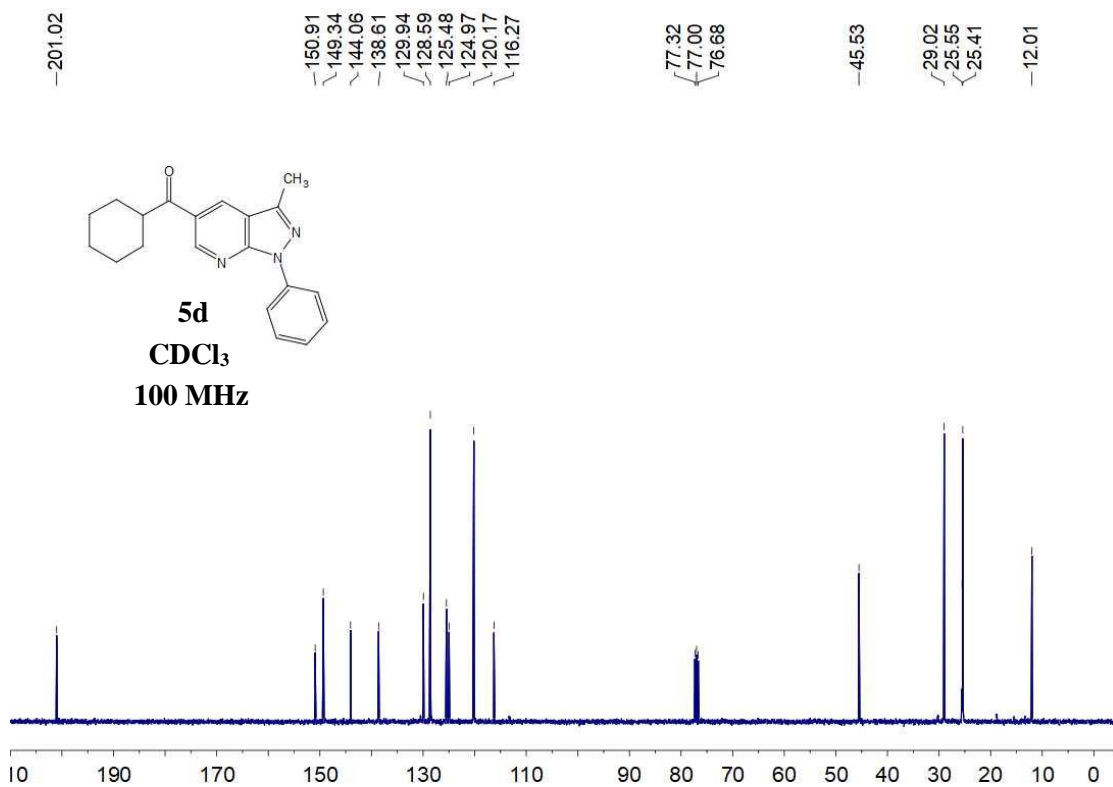
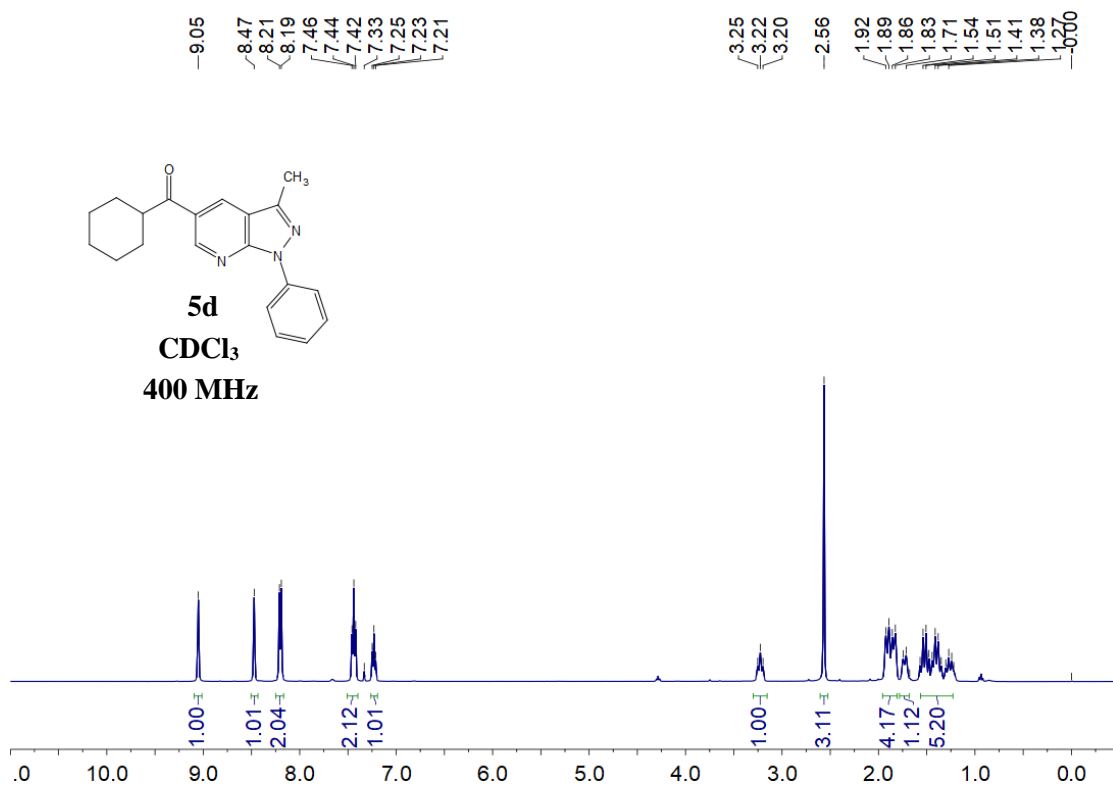
5b



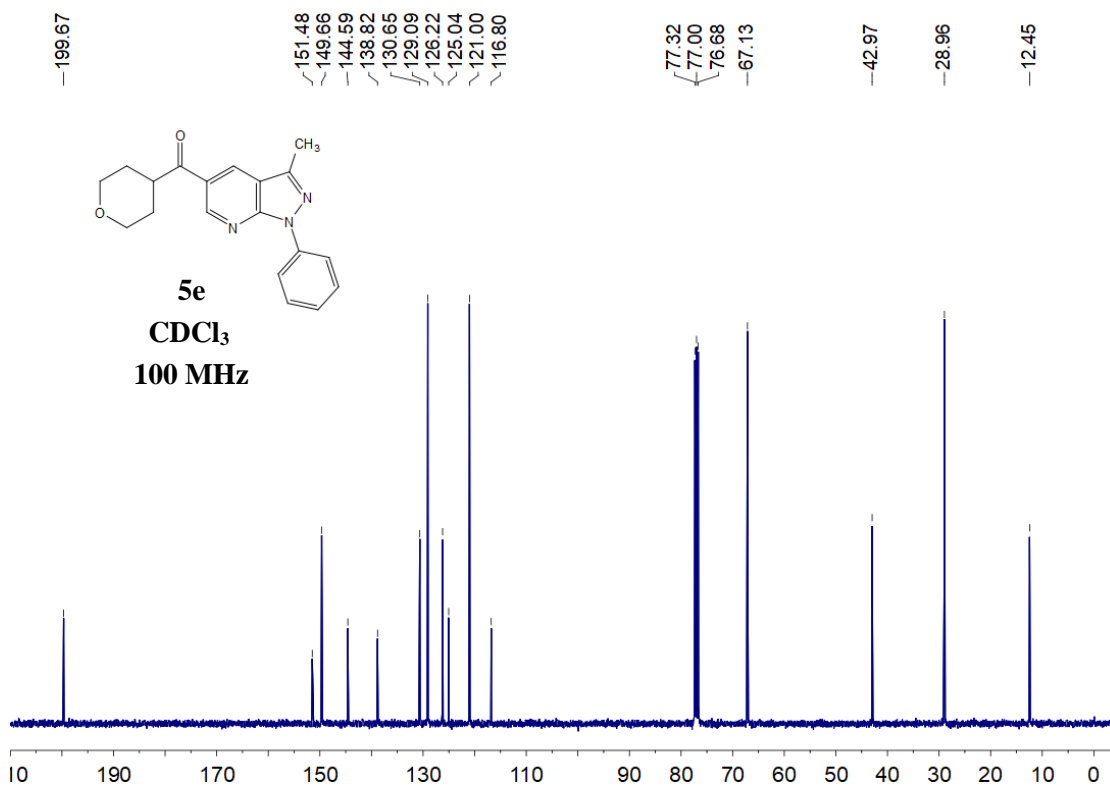
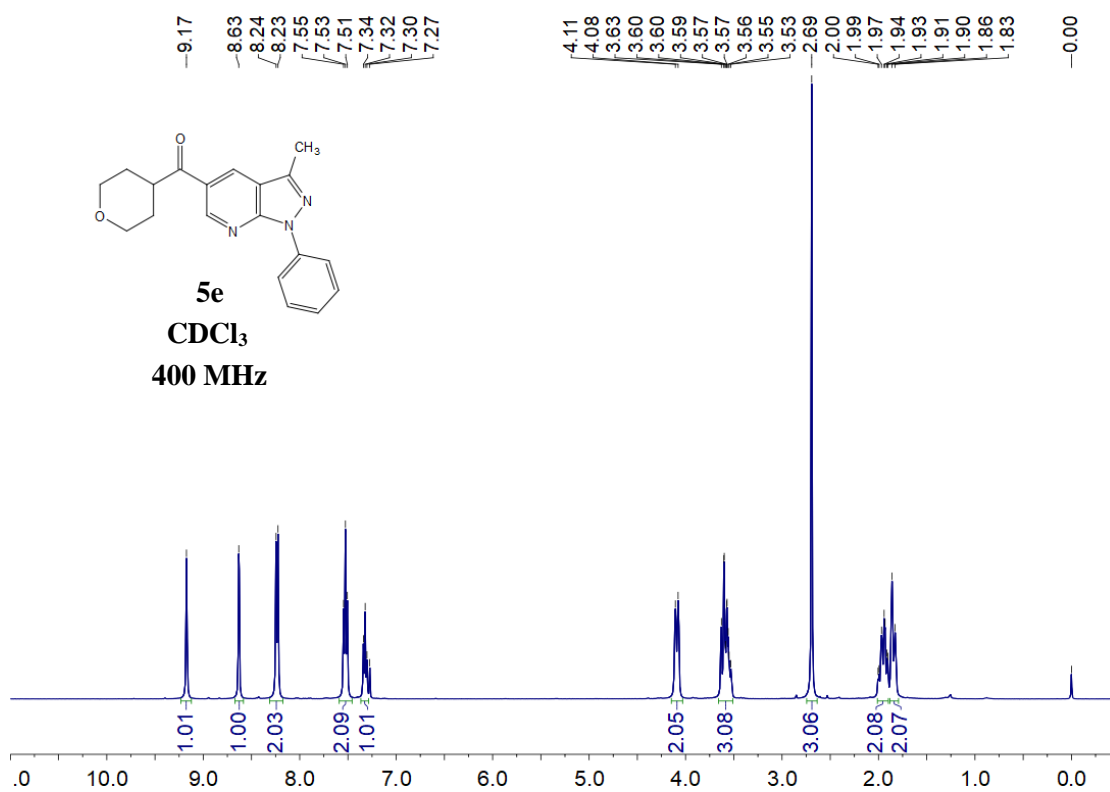
5c



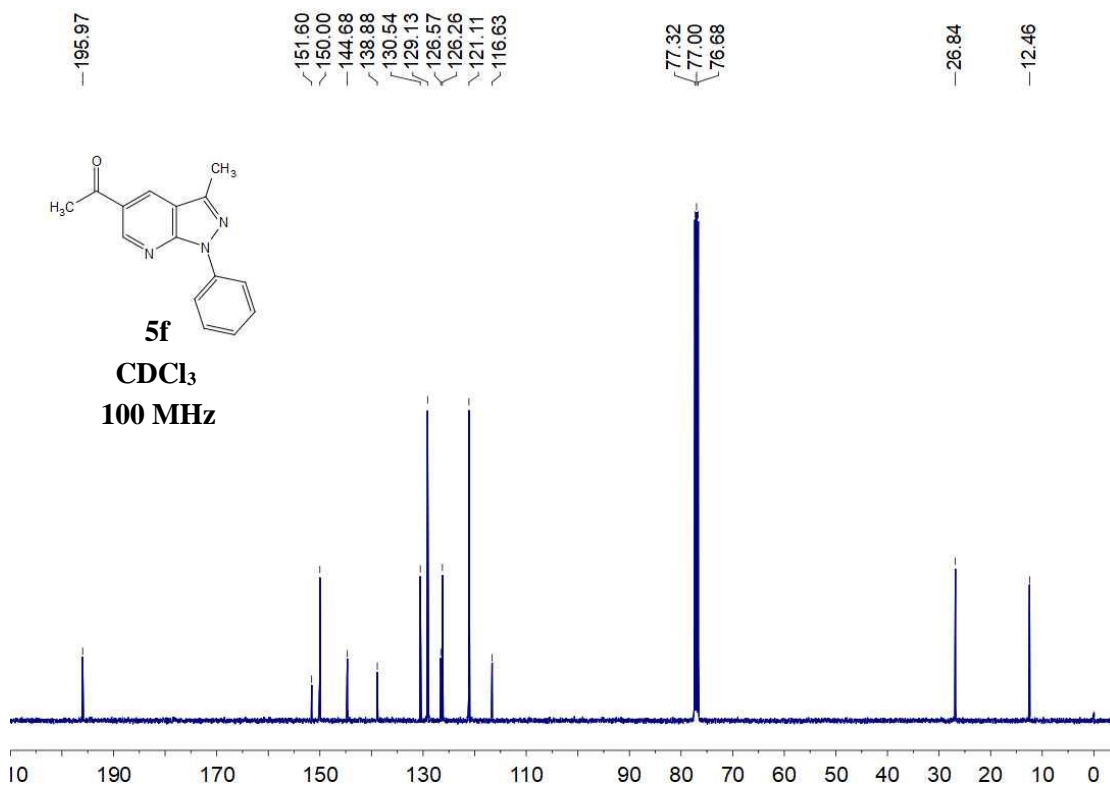
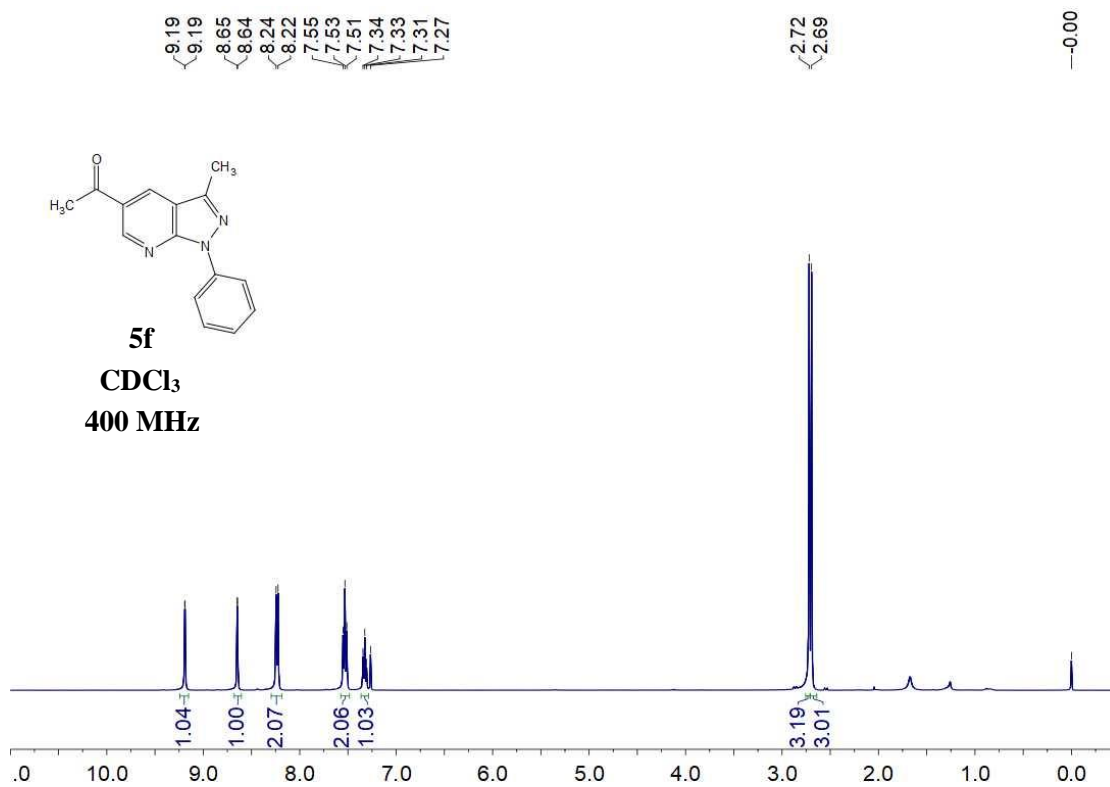
5d



5e

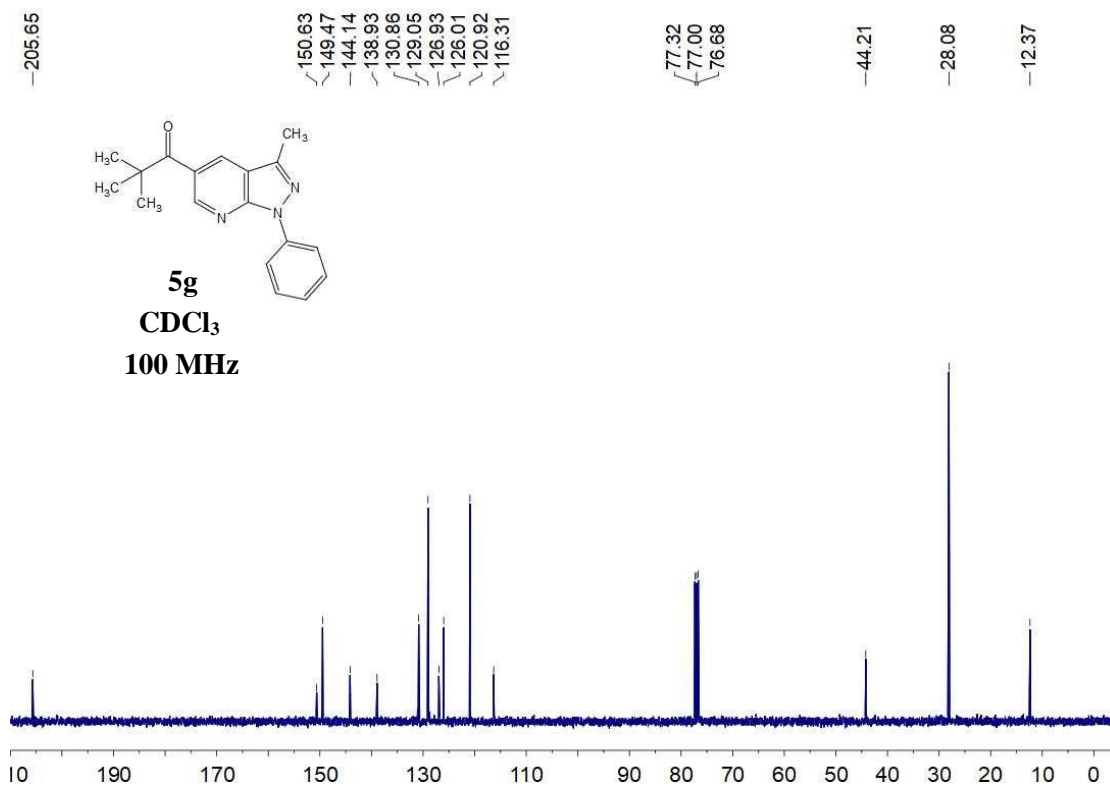
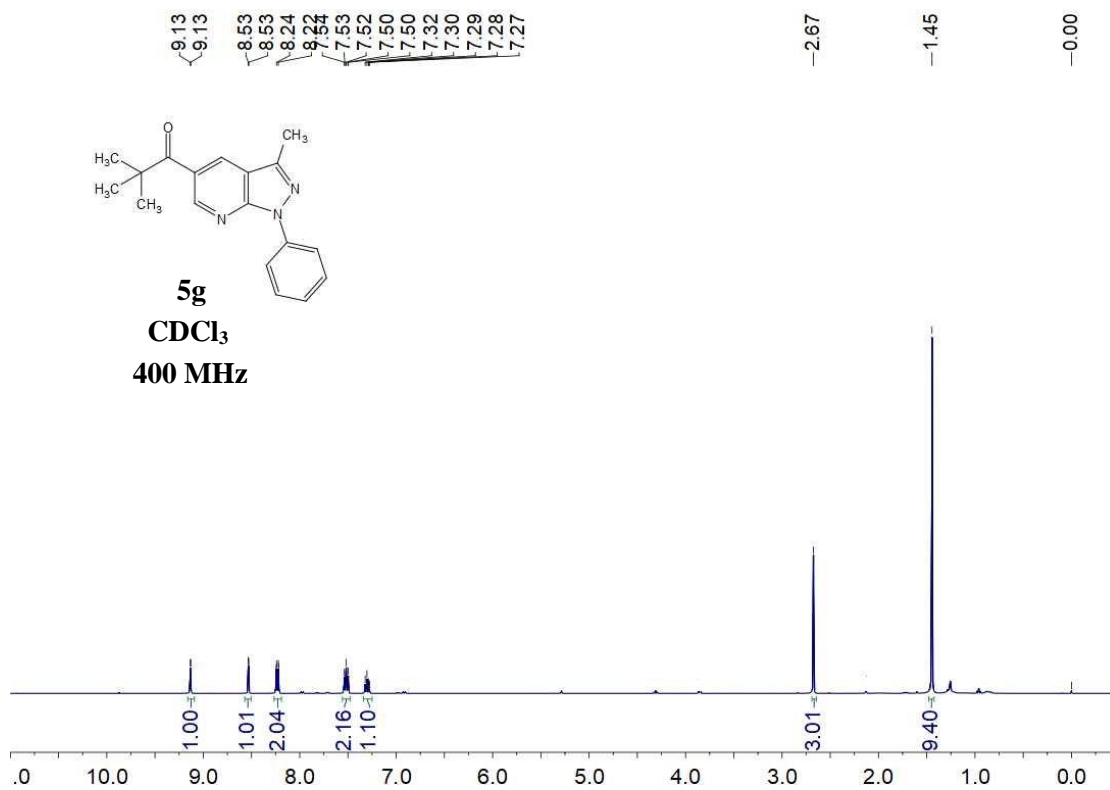


5f

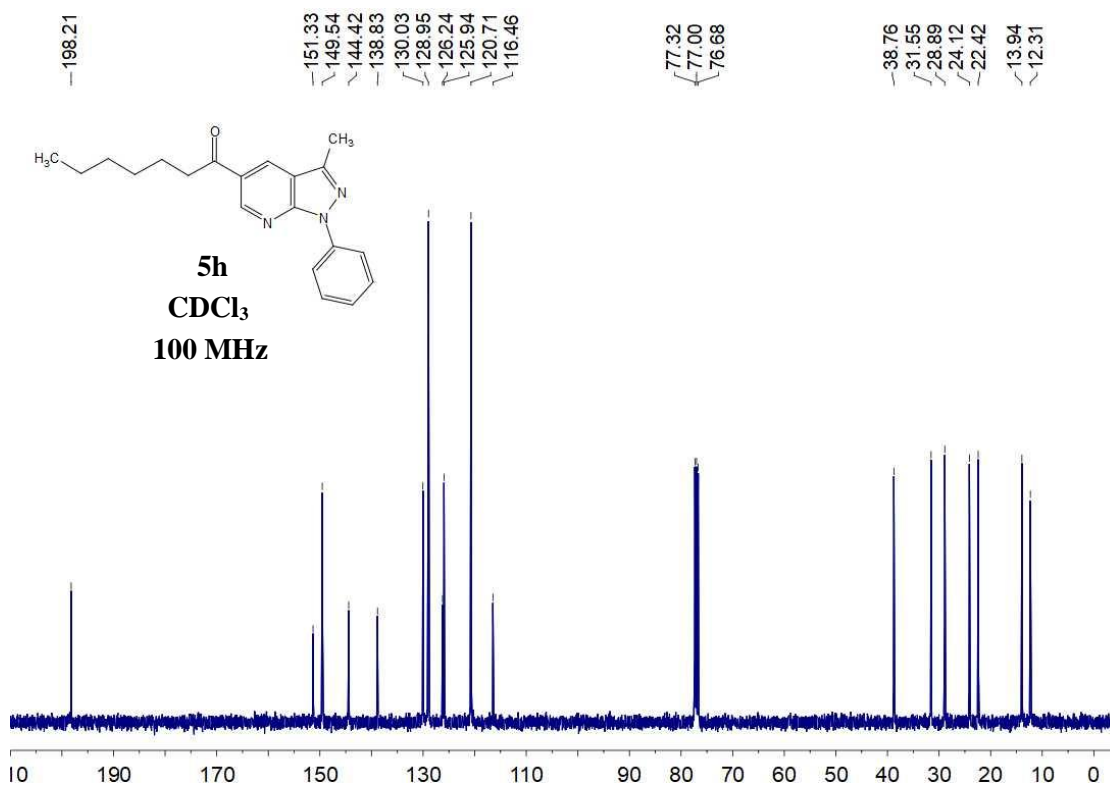
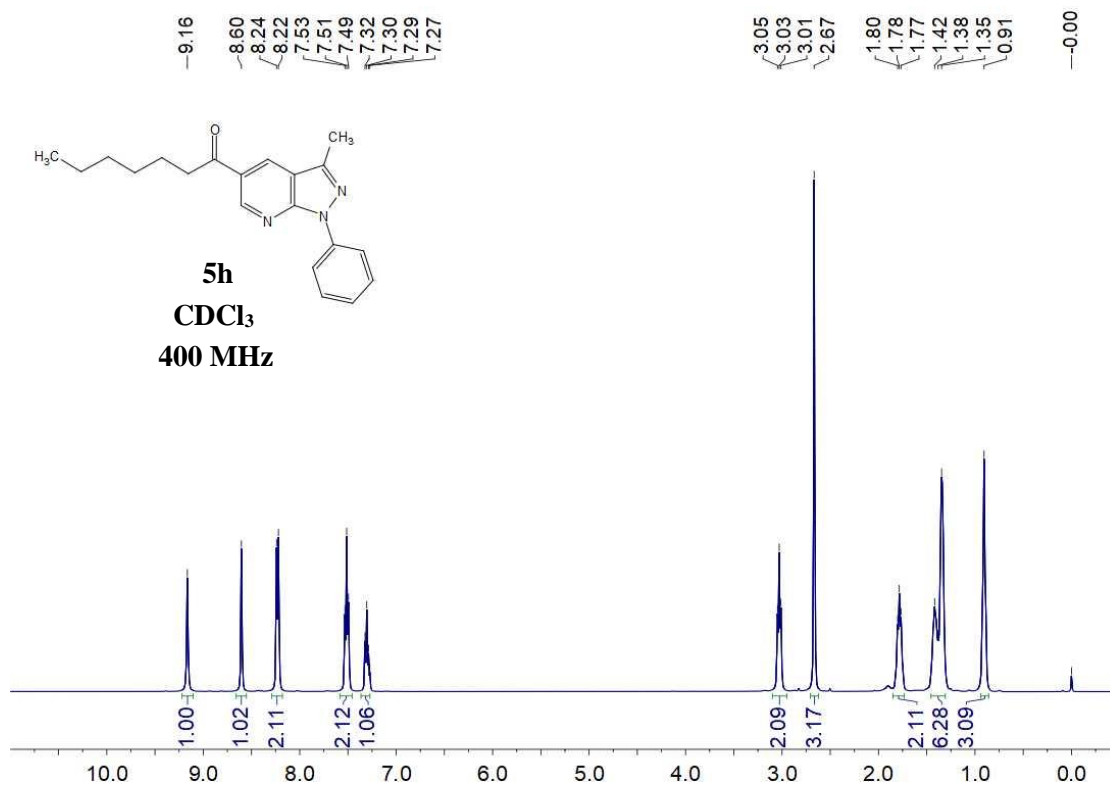




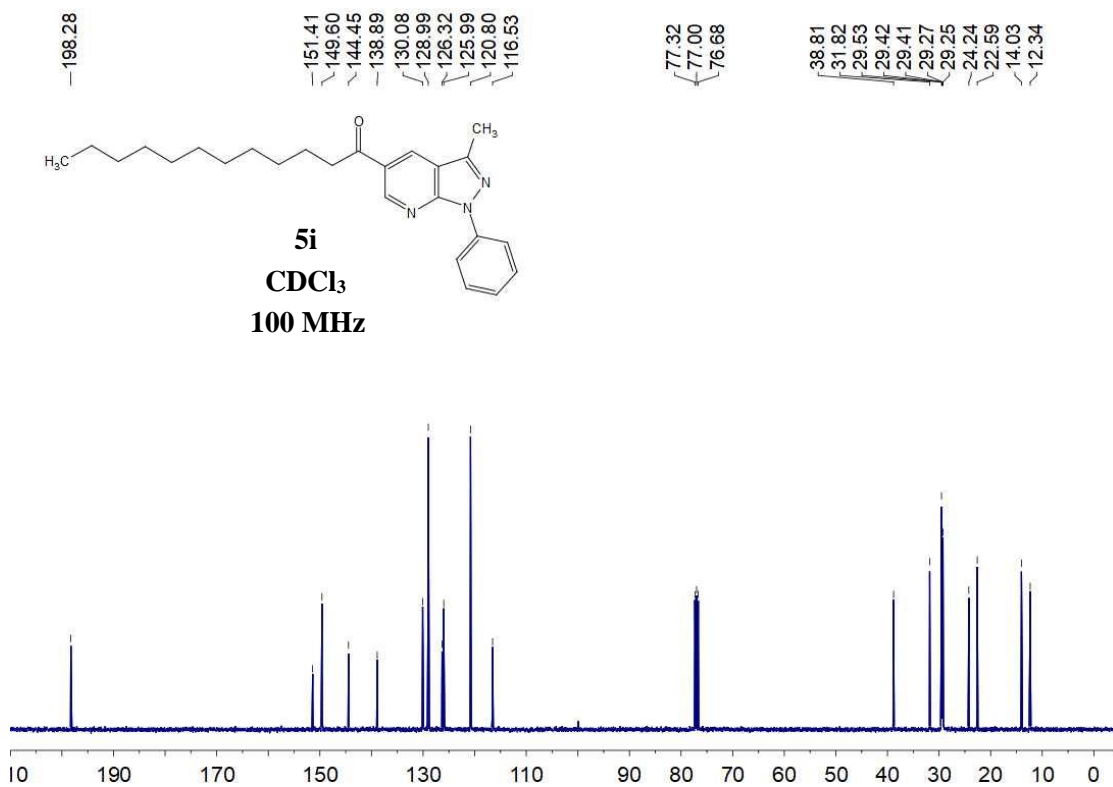
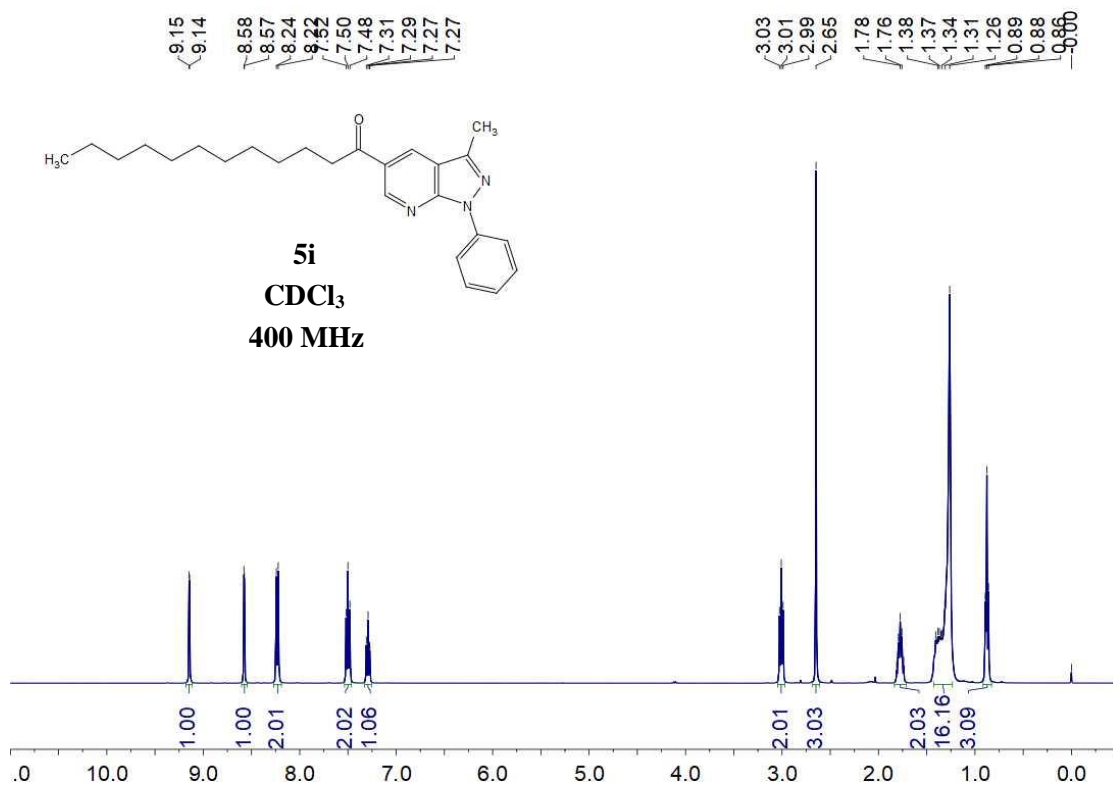
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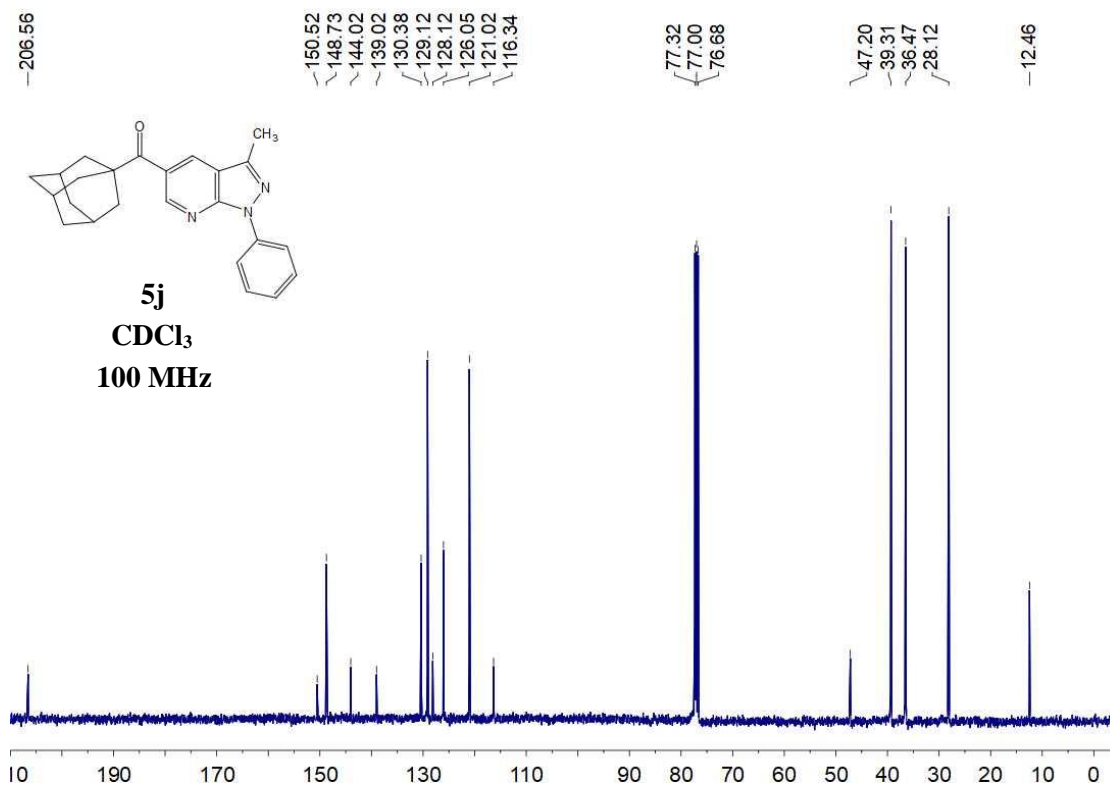
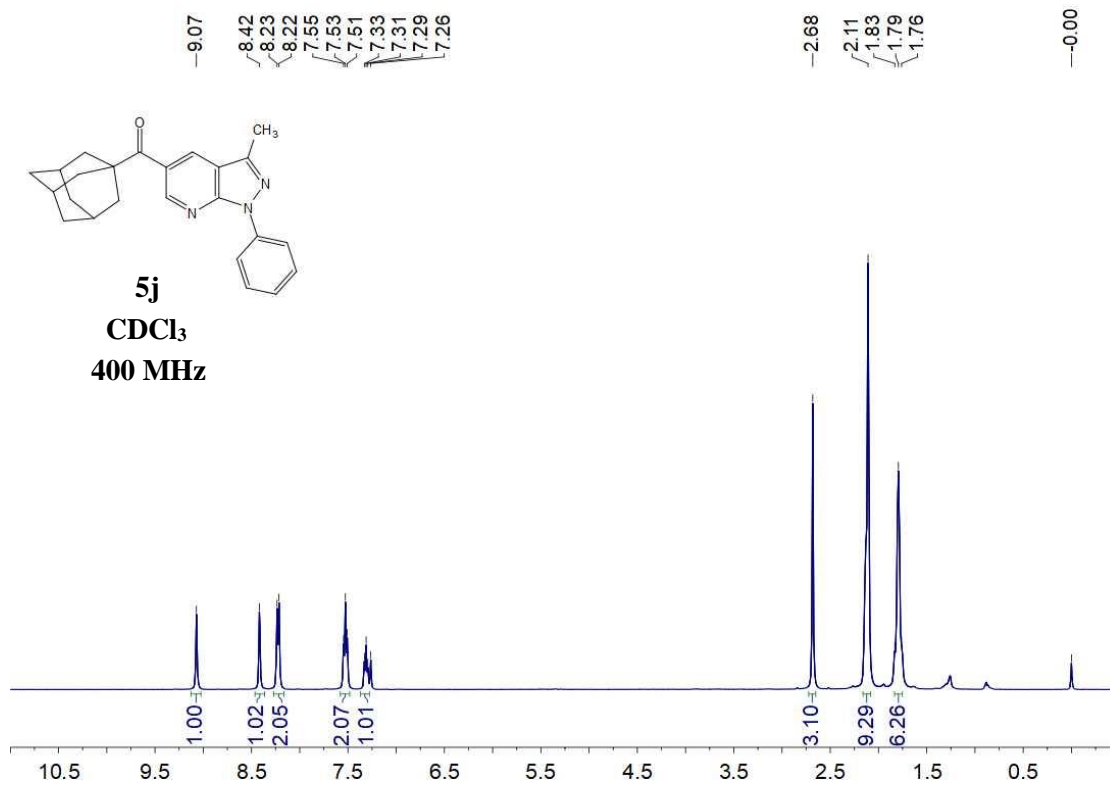
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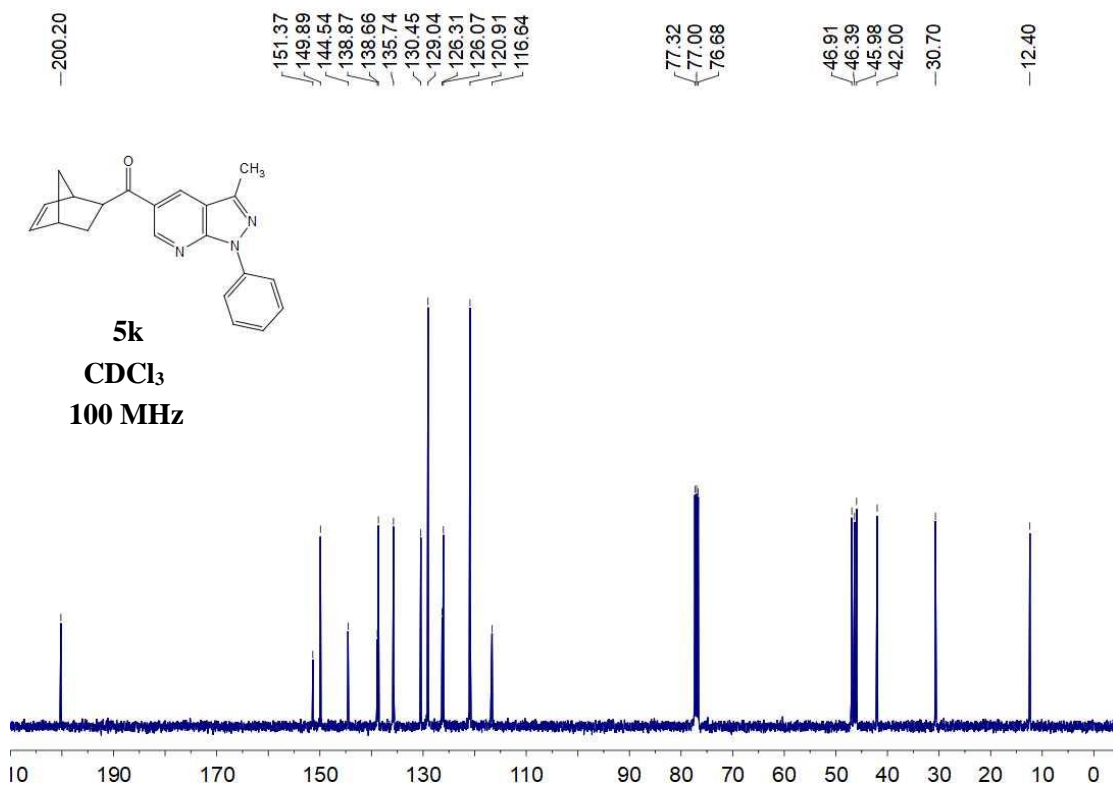
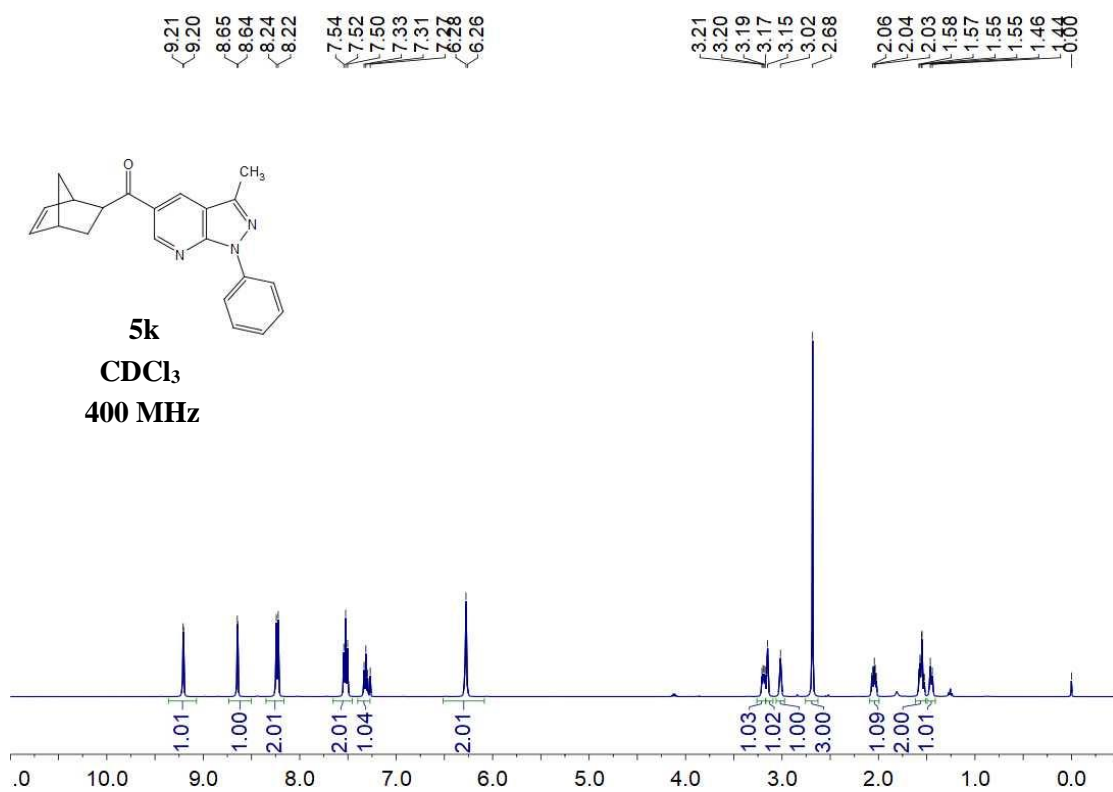
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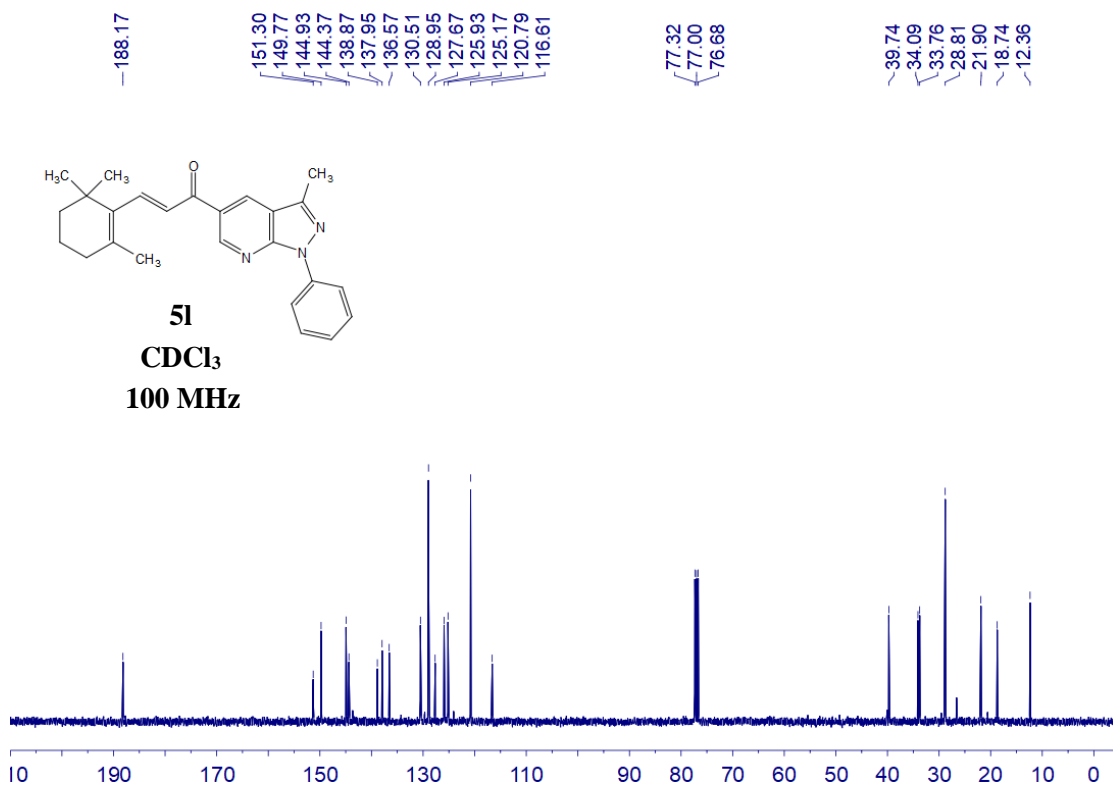
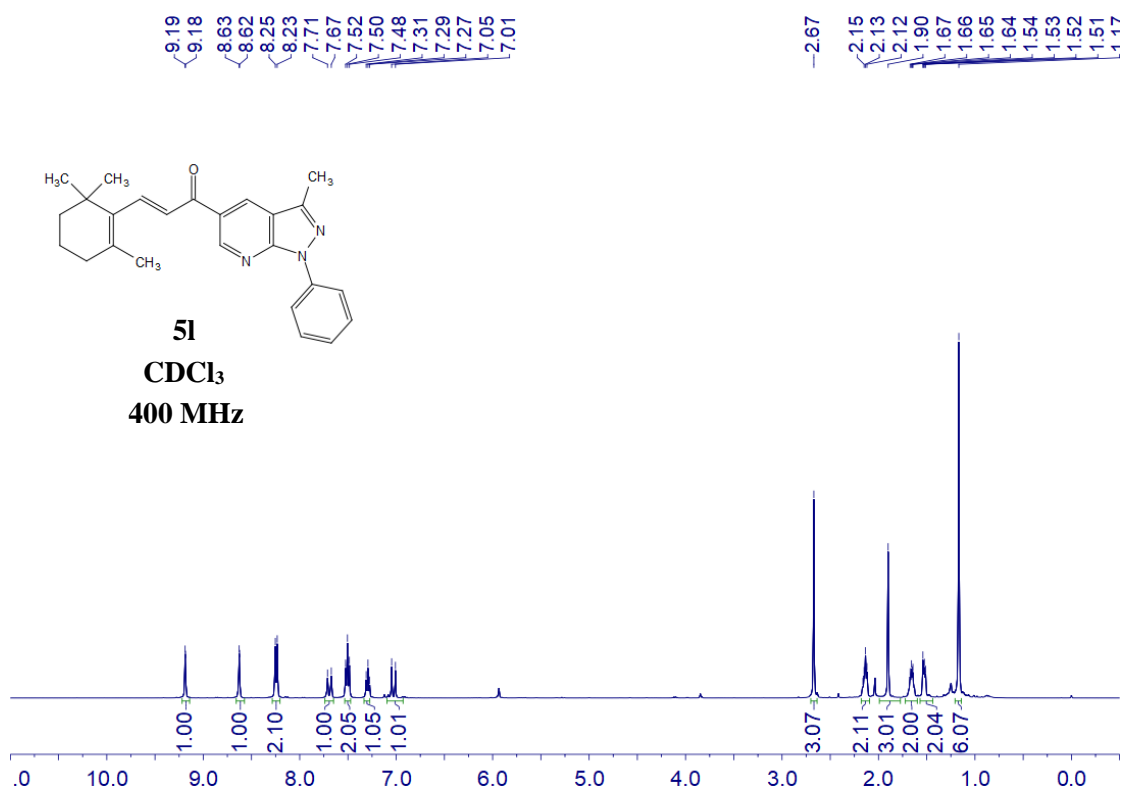
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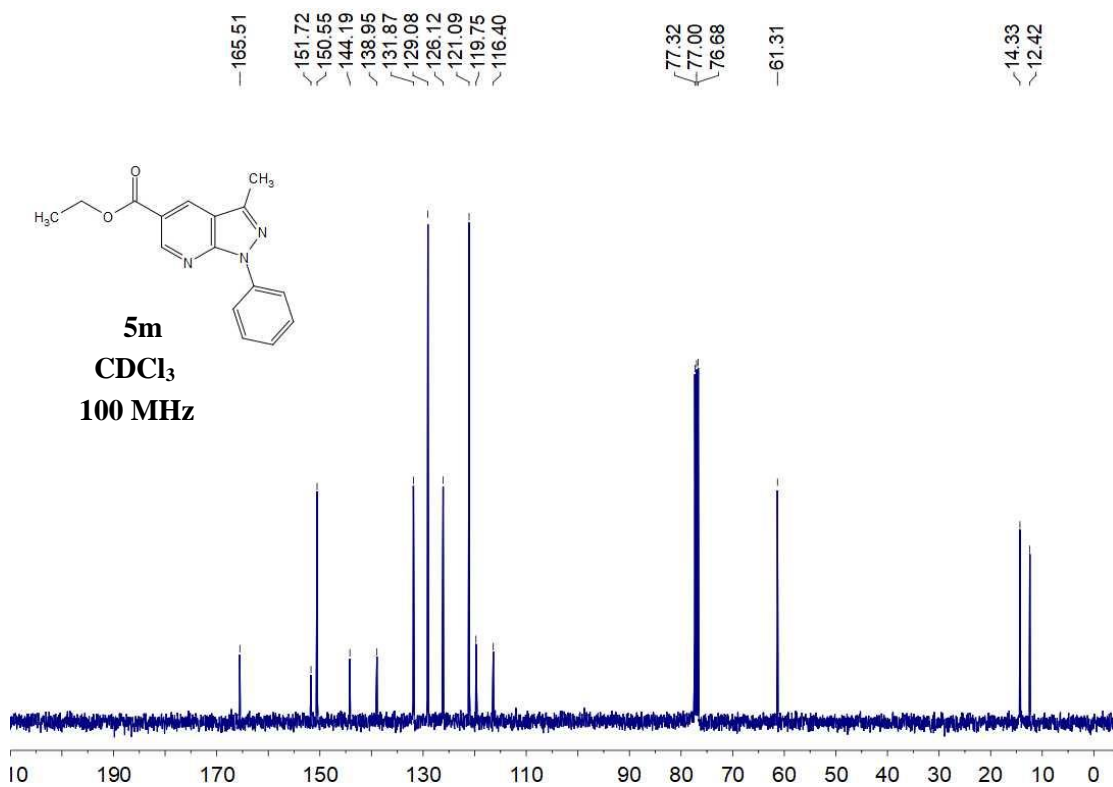
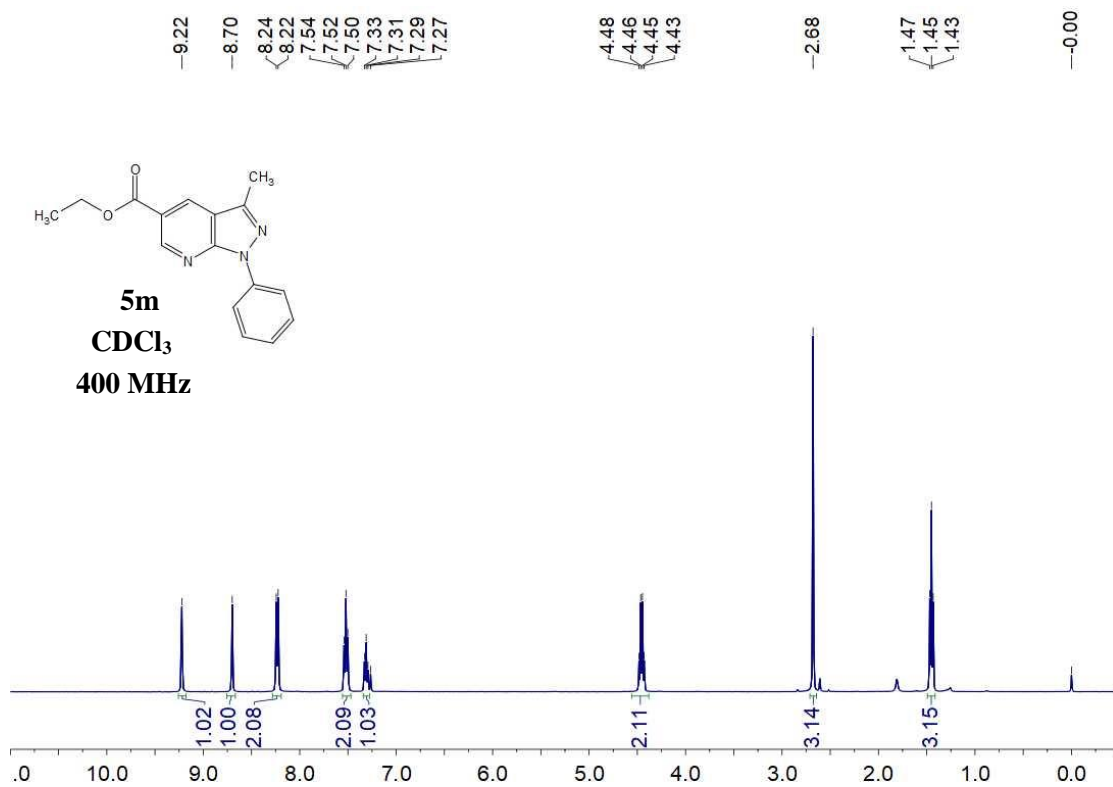
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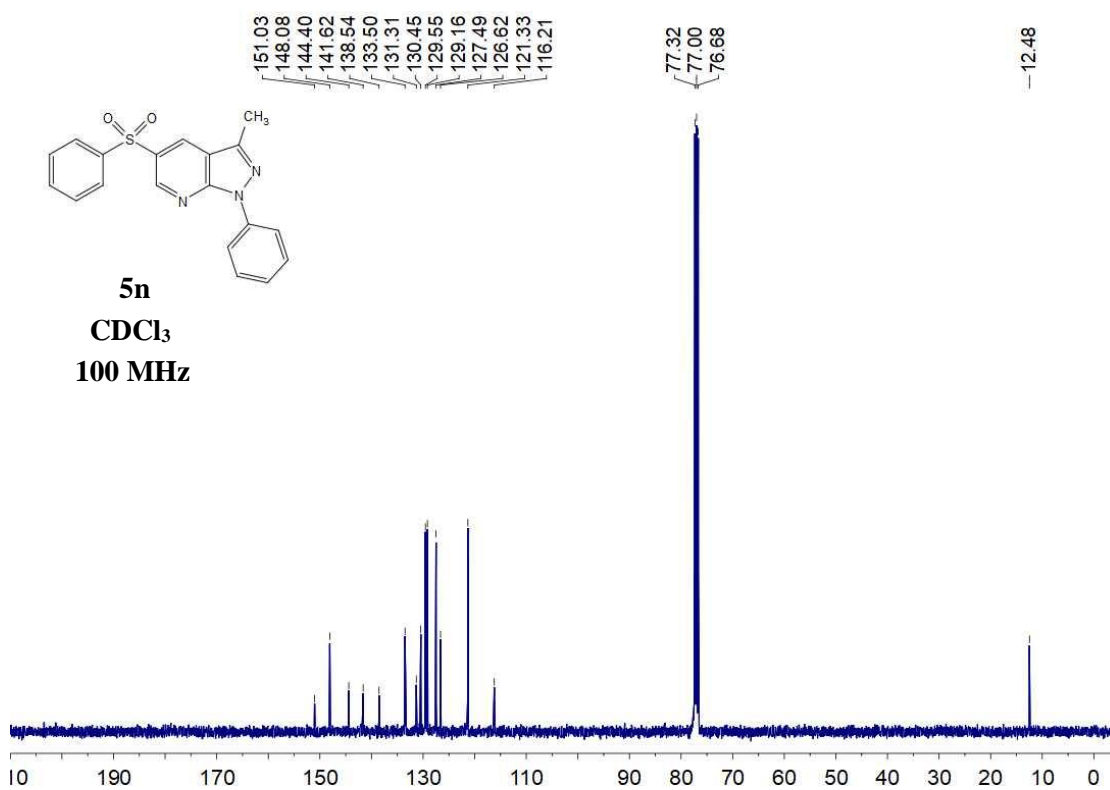
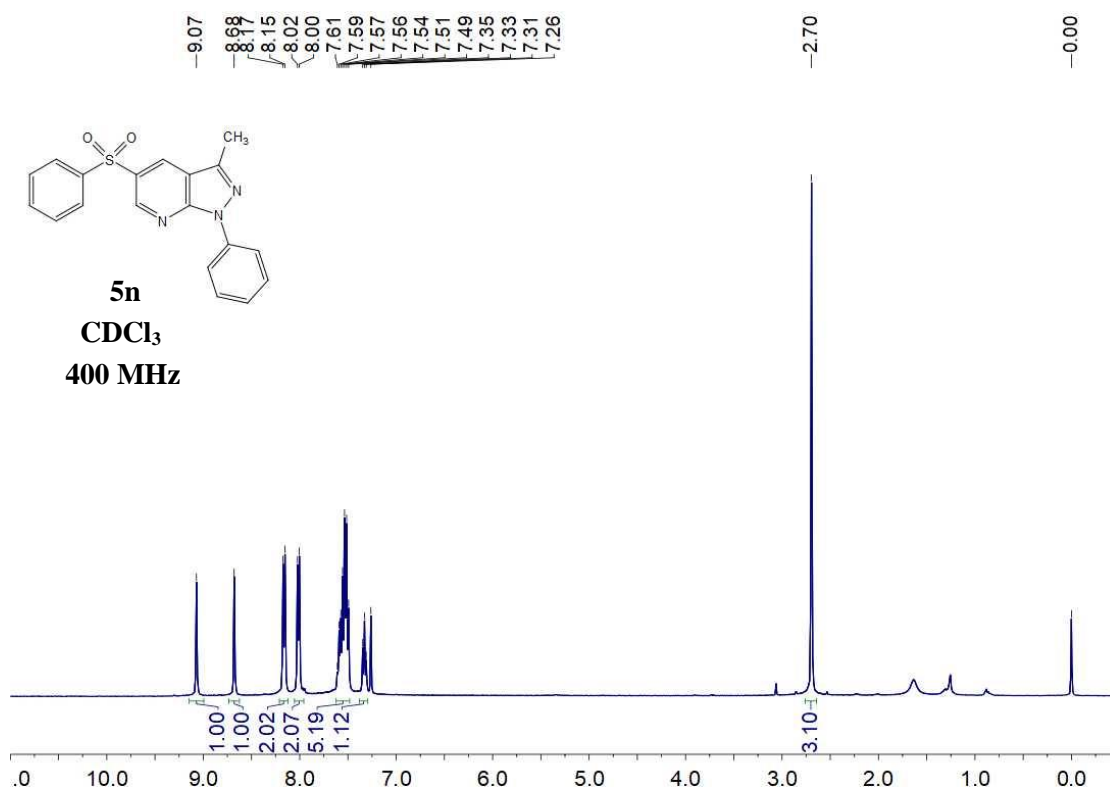
51



**5m**

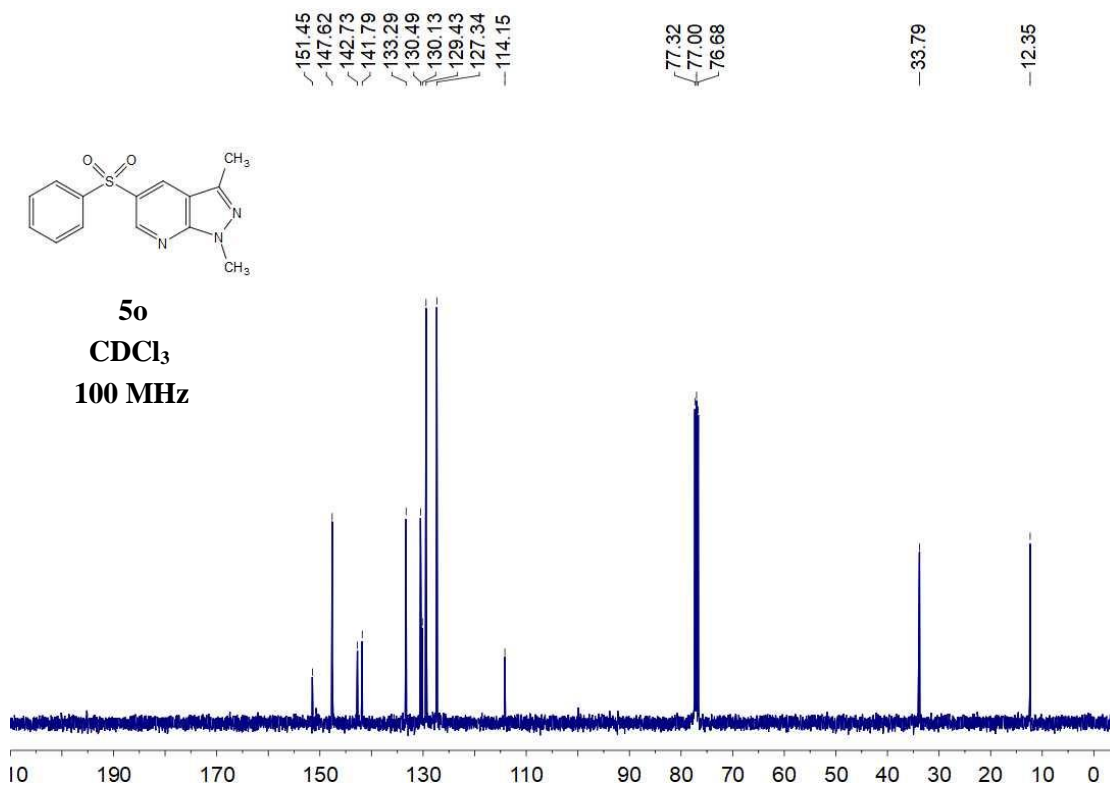
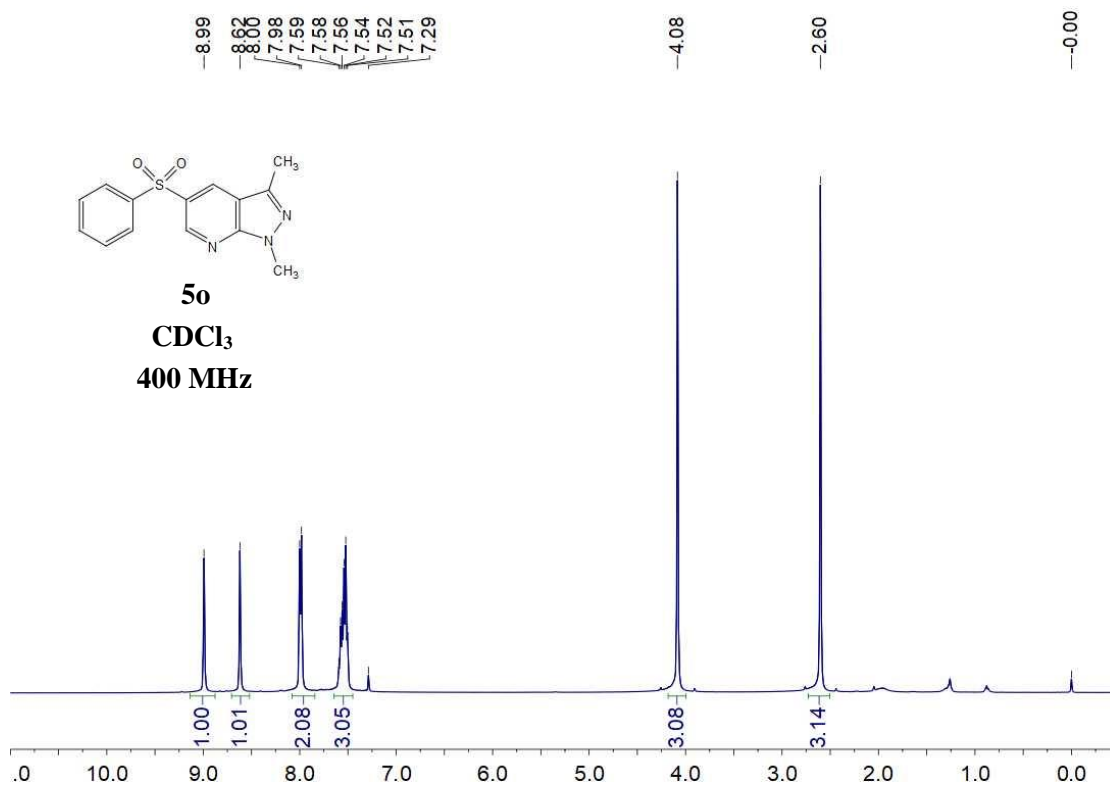


5n

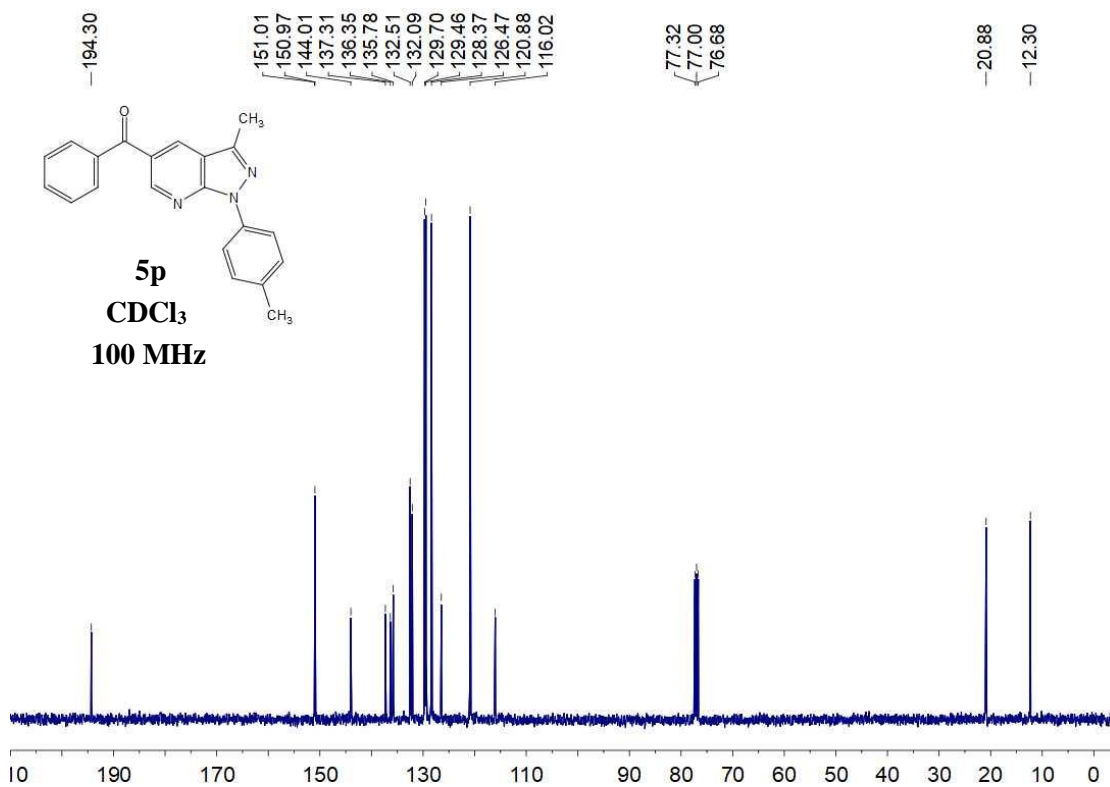
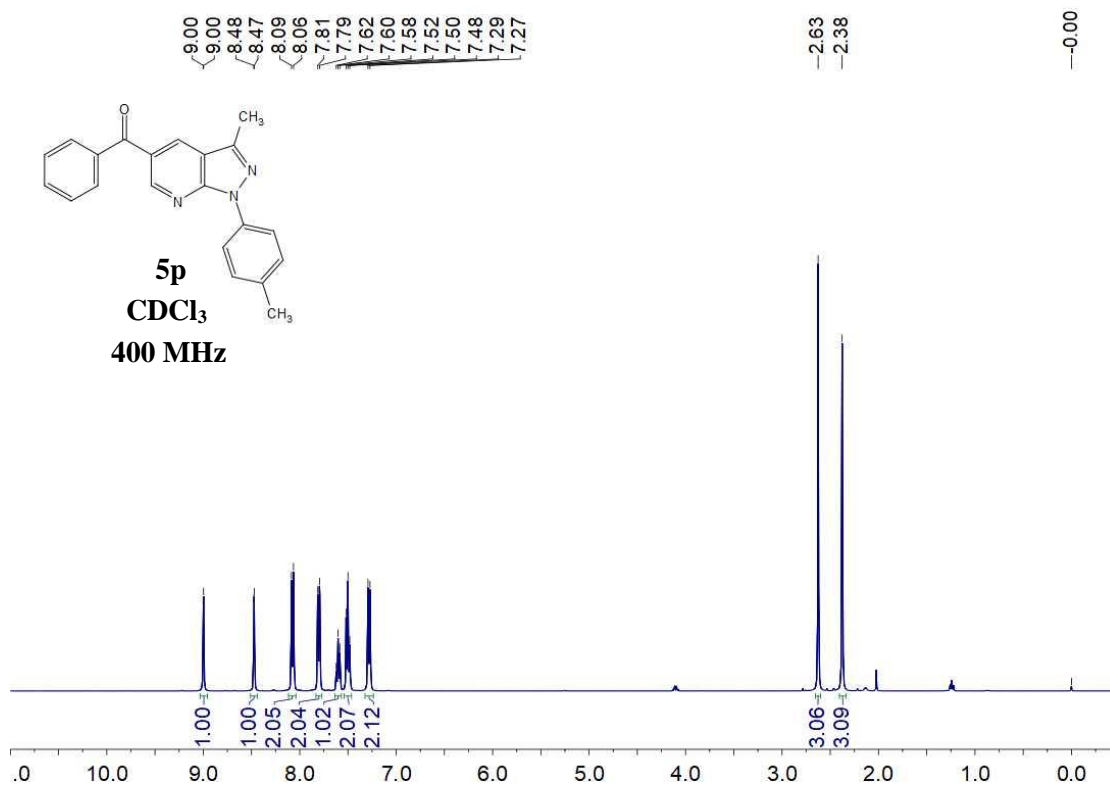




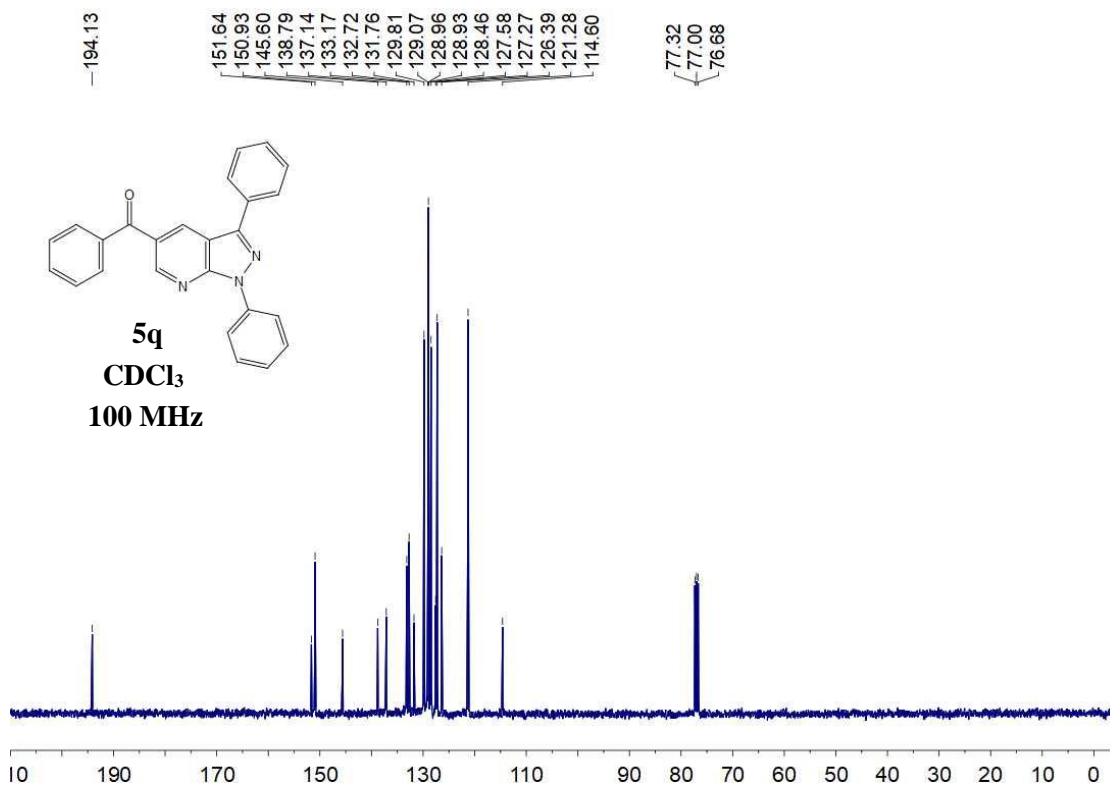
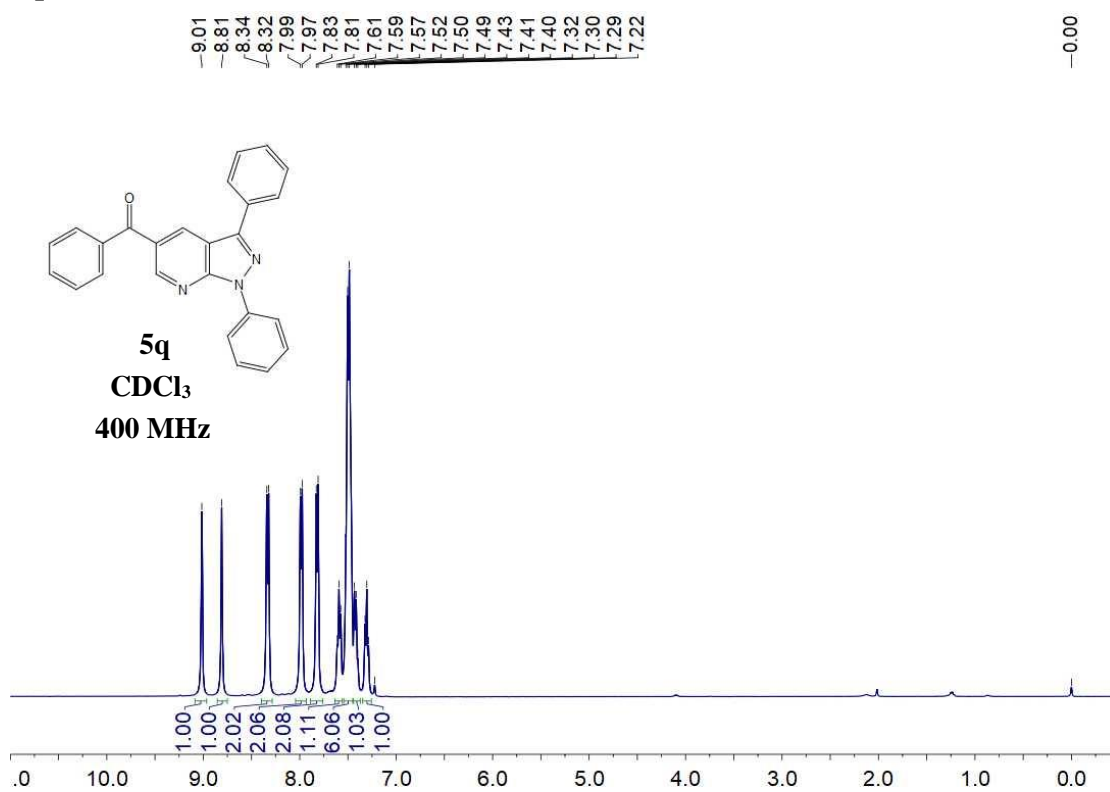
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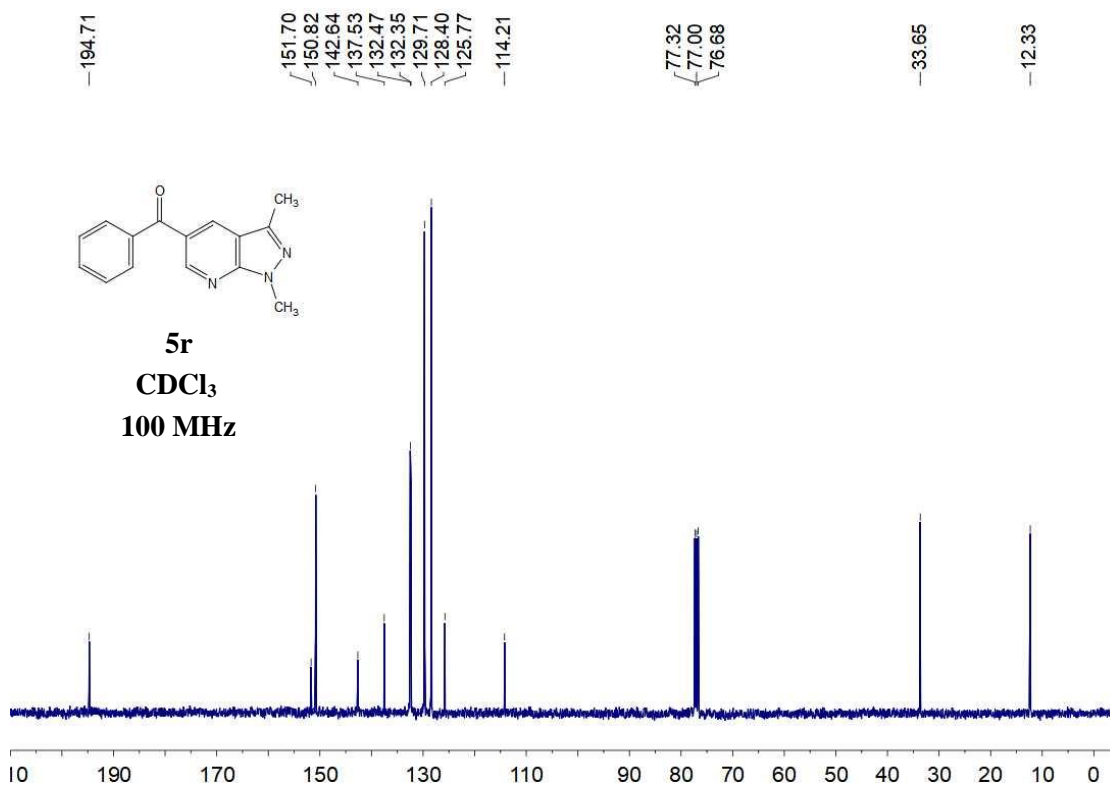
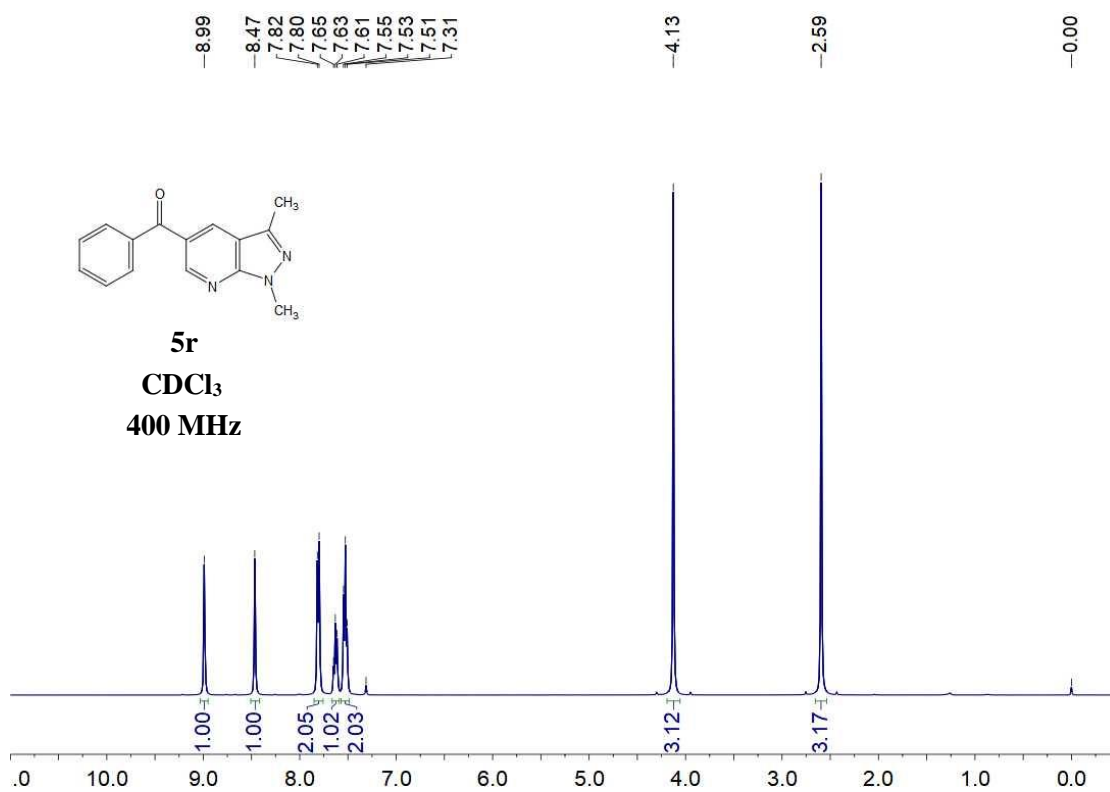
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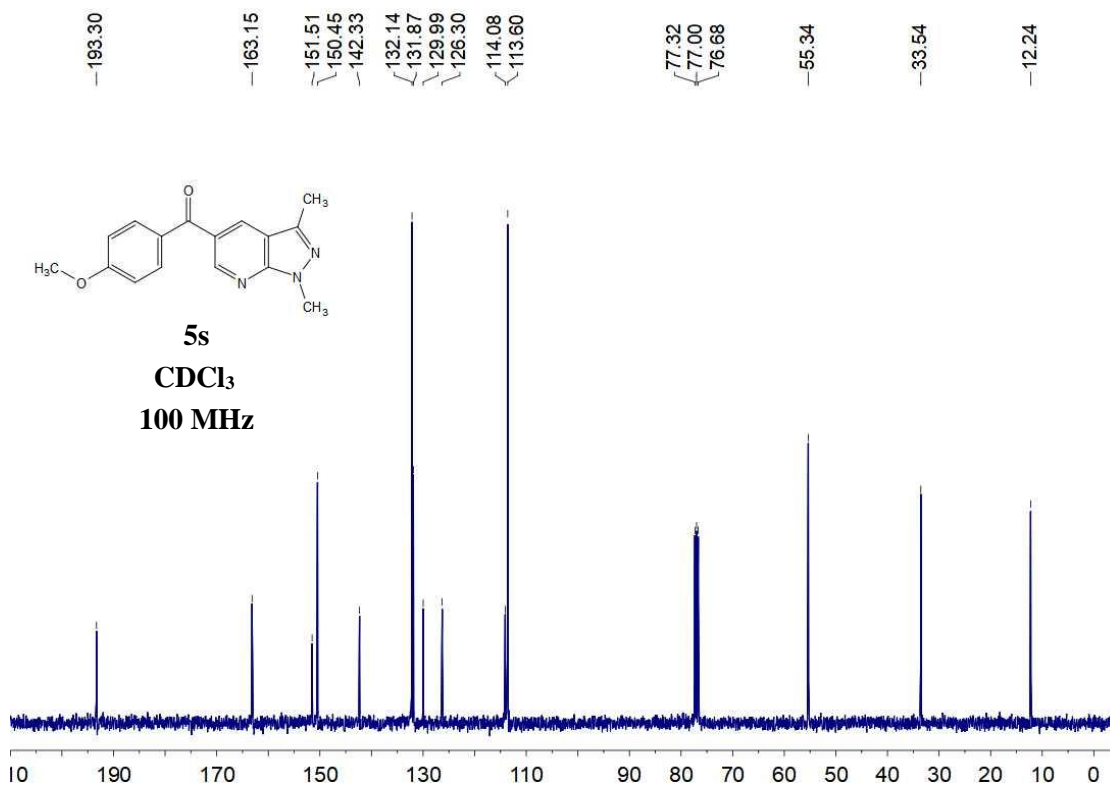
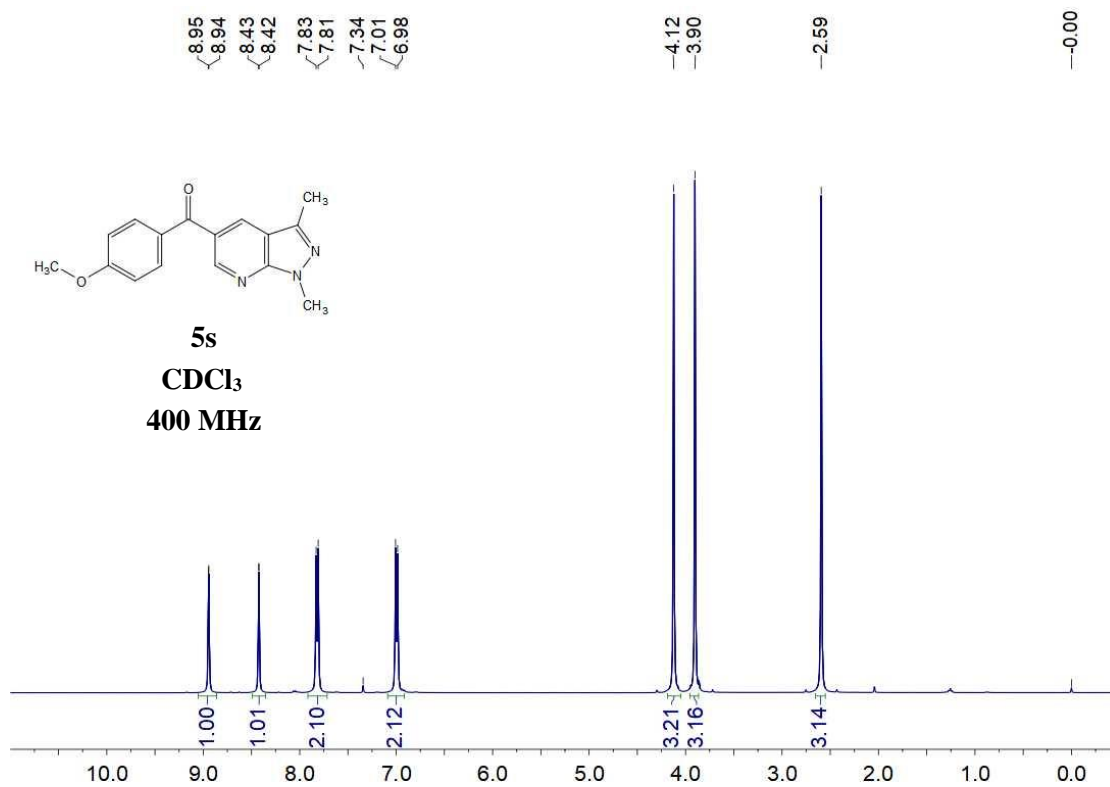
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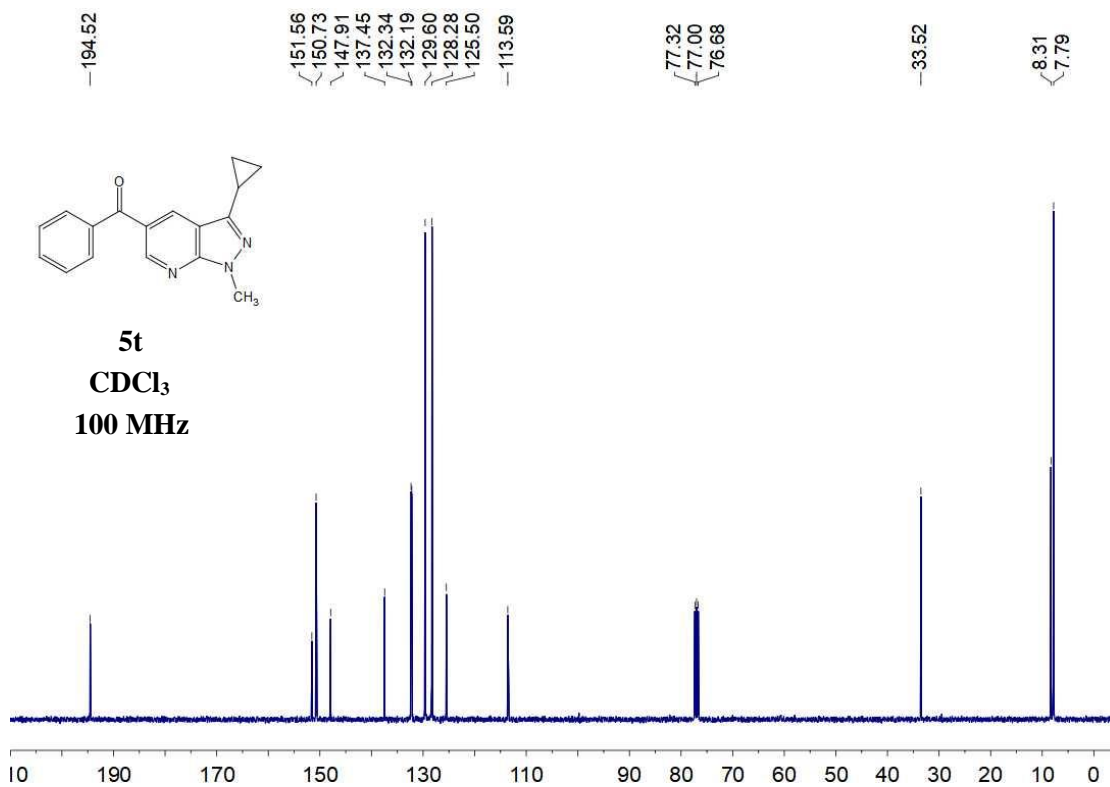
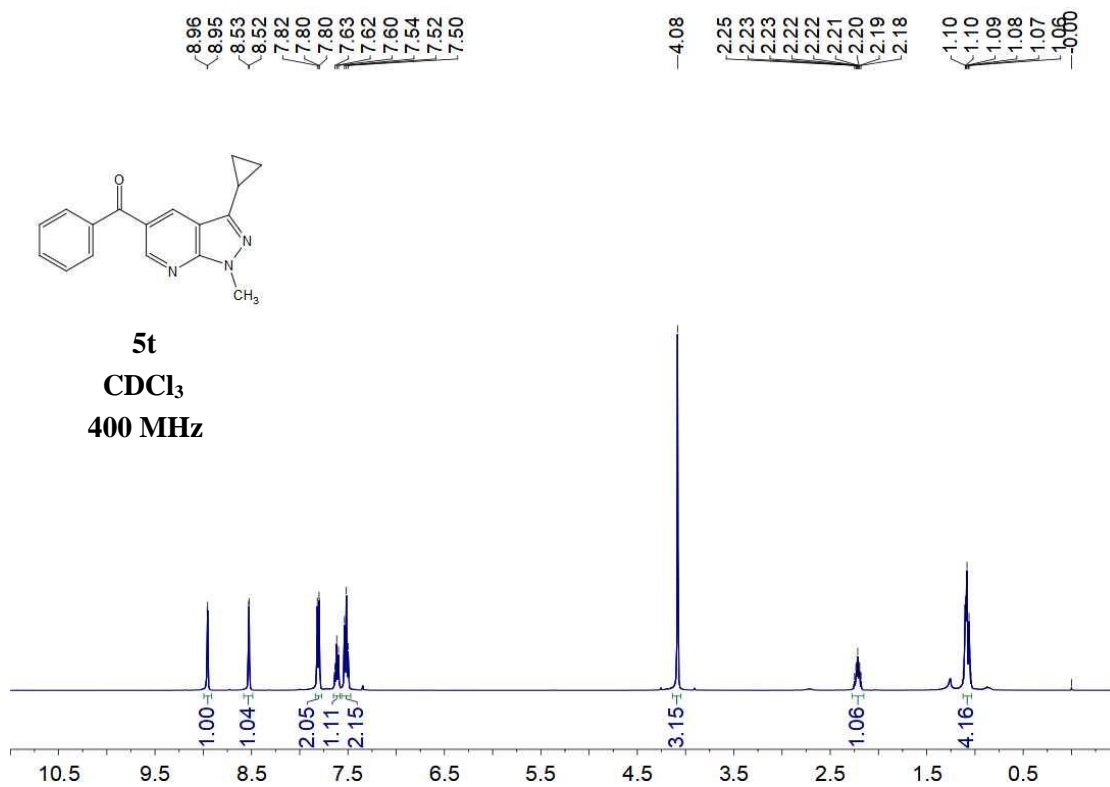
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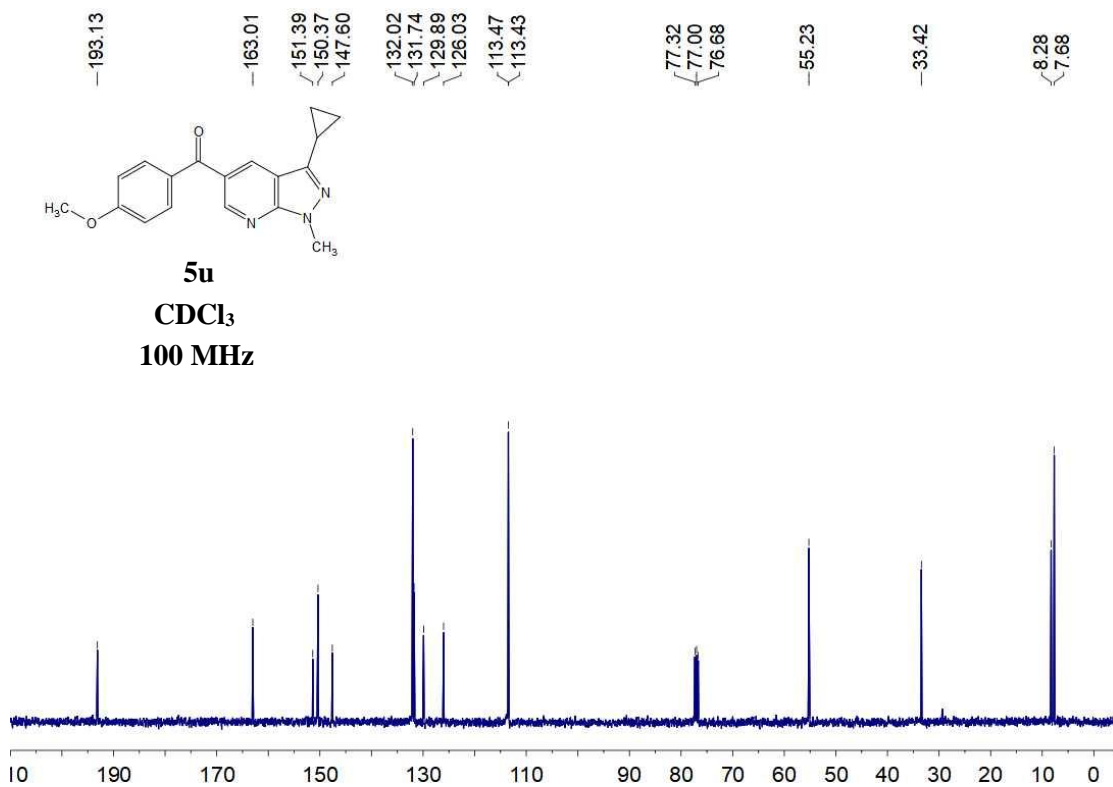
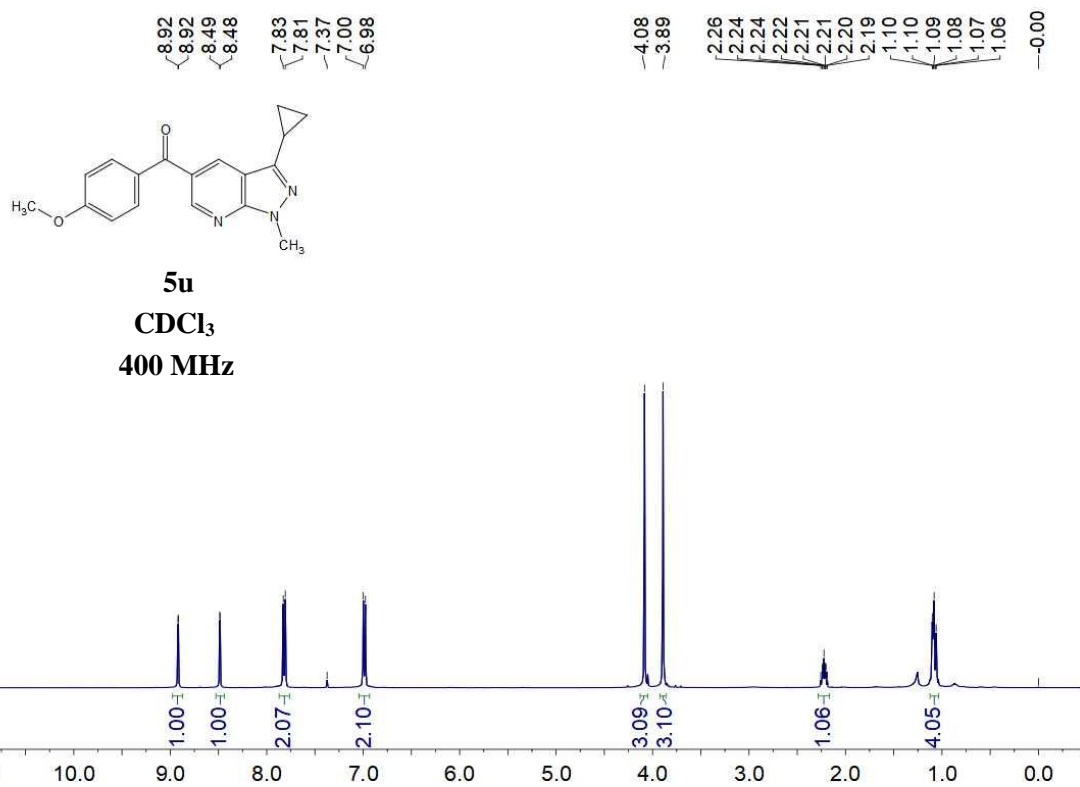
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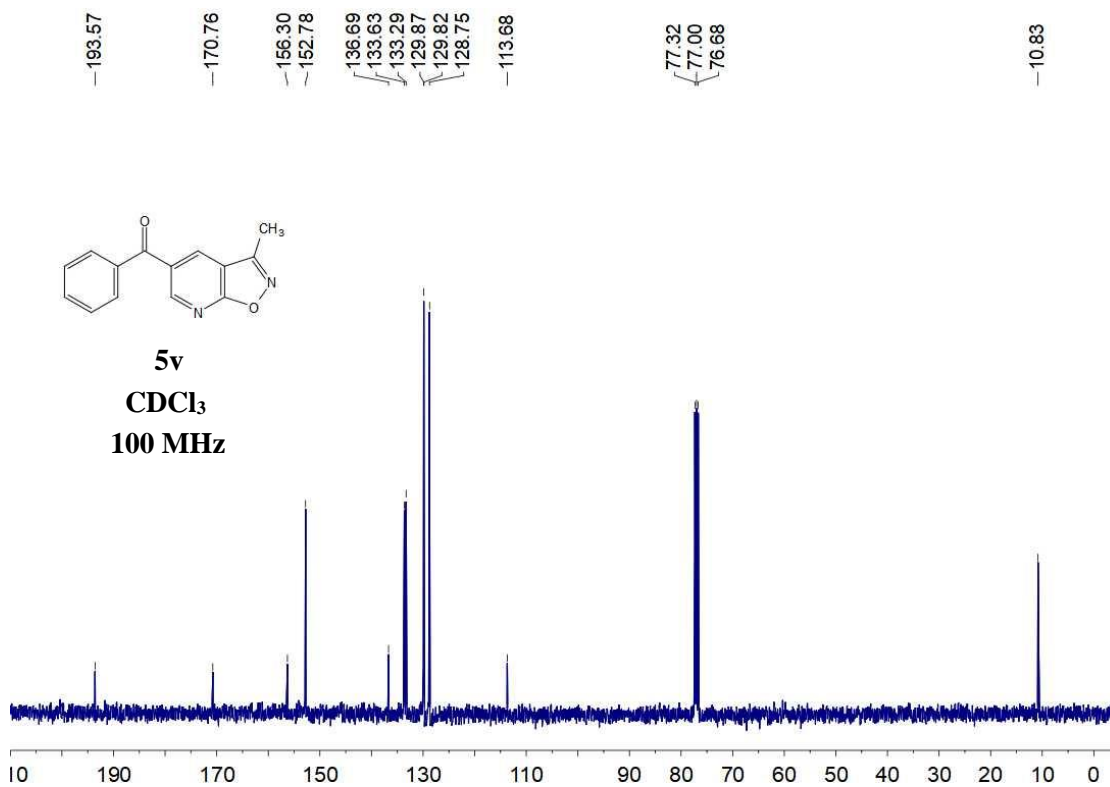
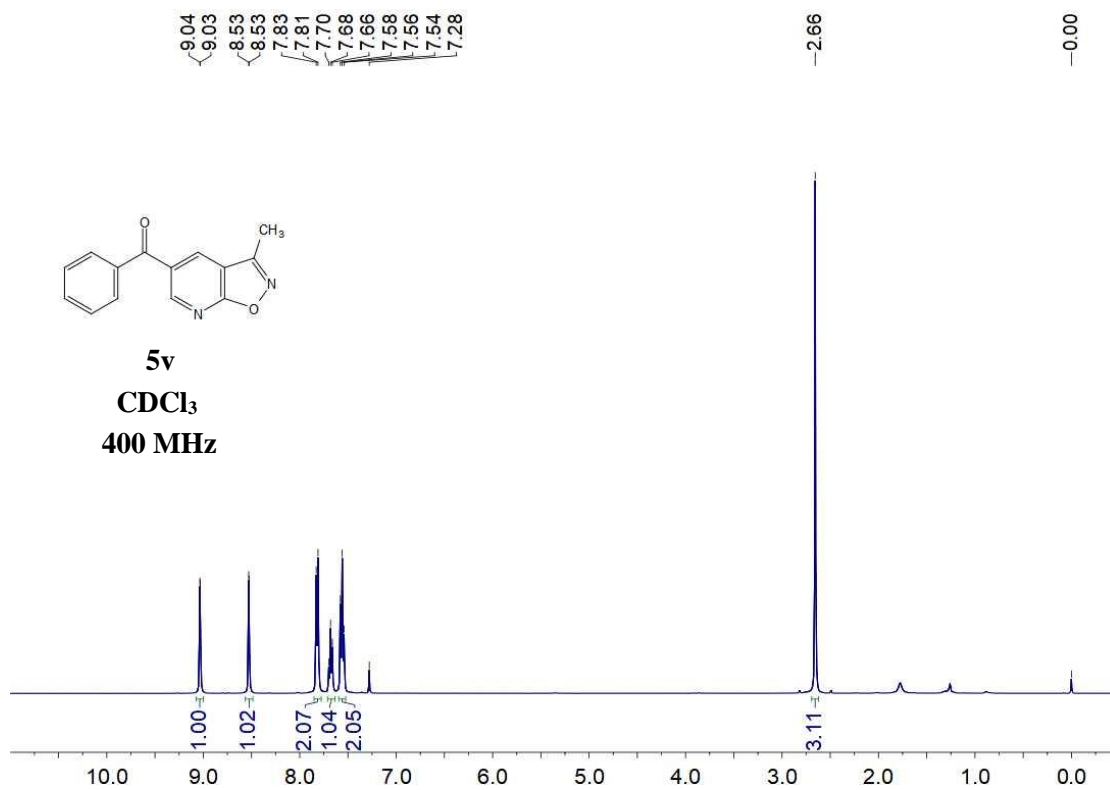
5t



**5u**

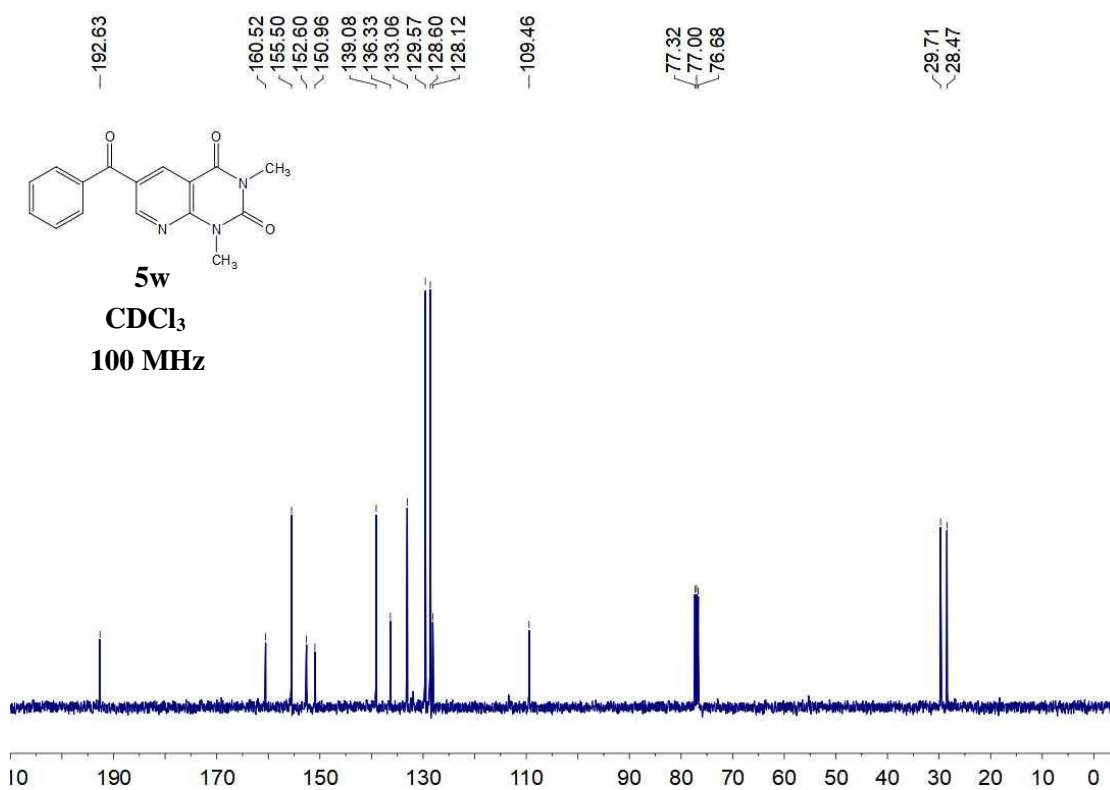
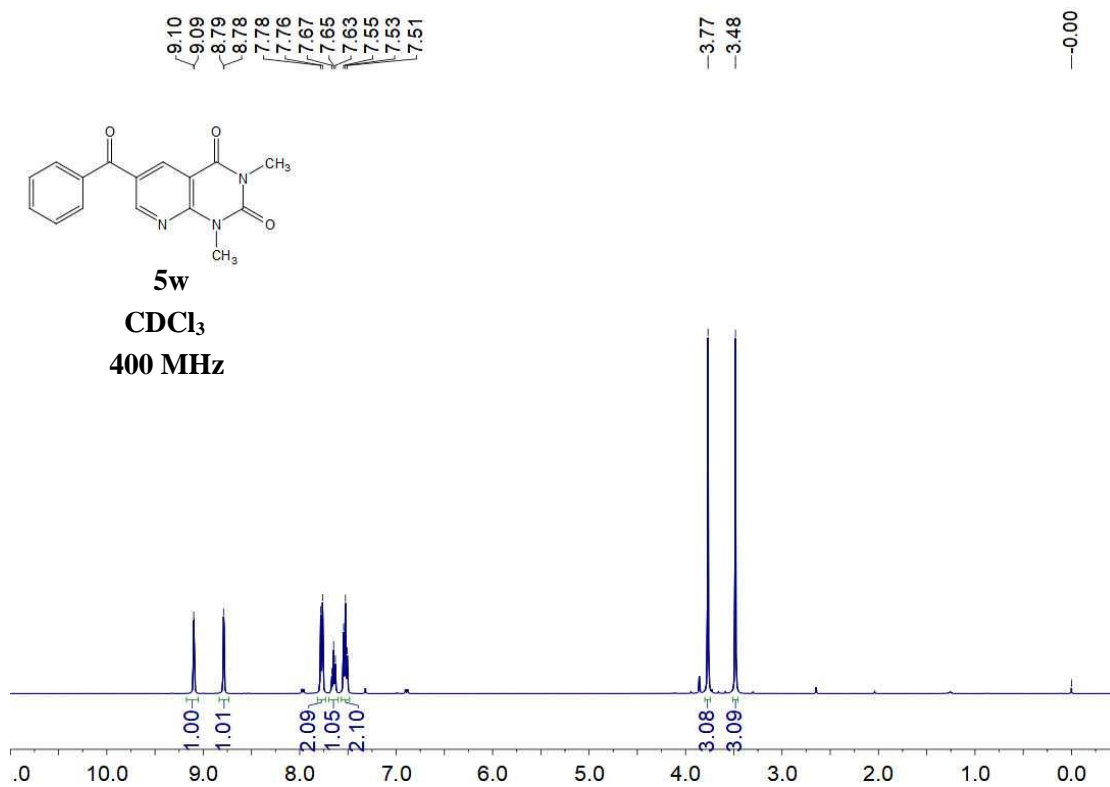


5v

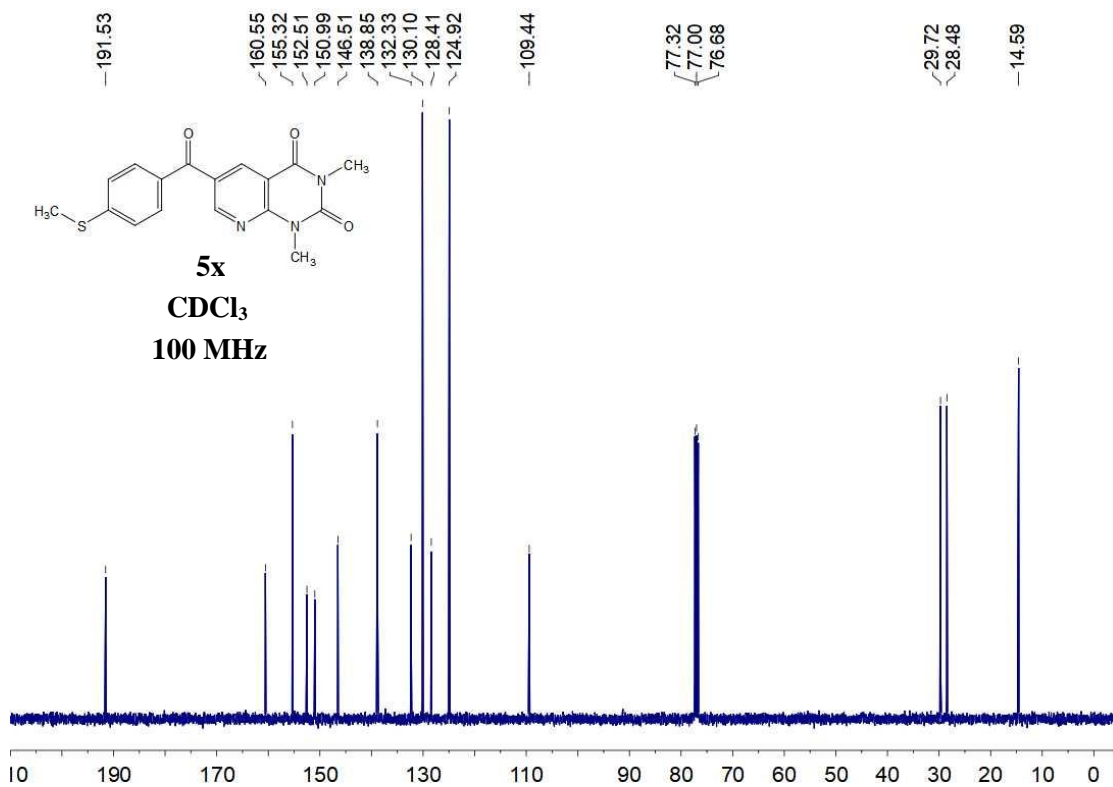
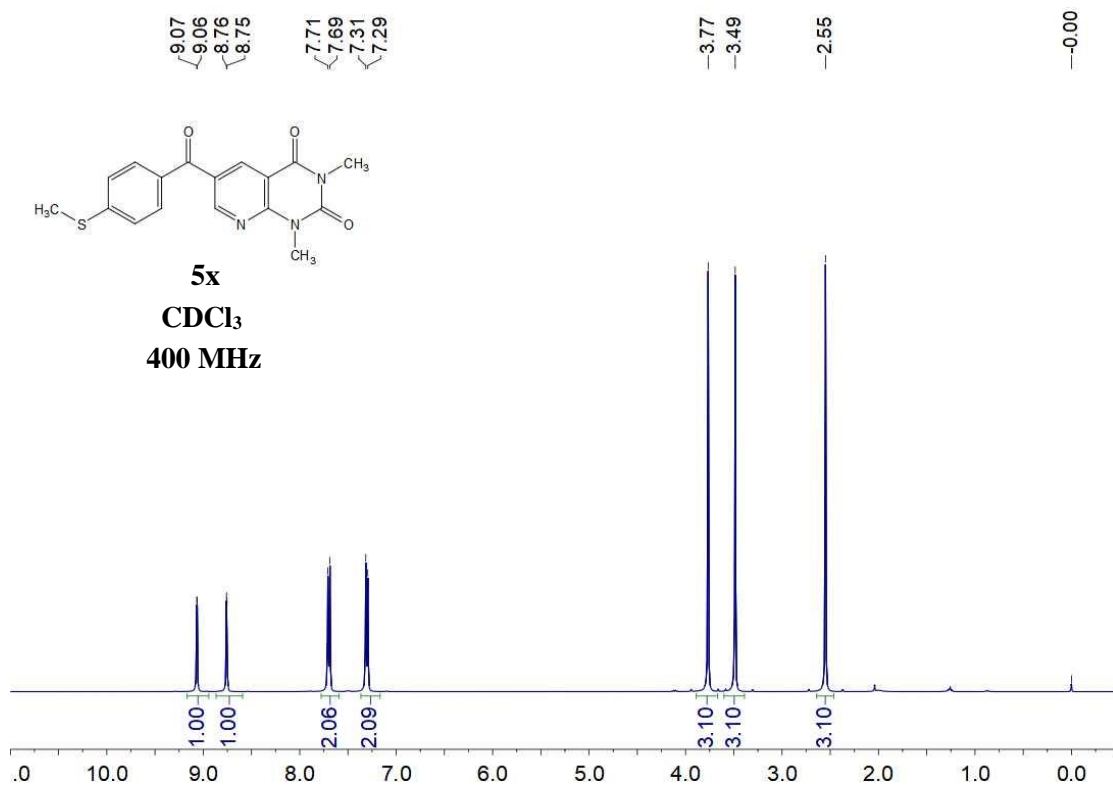




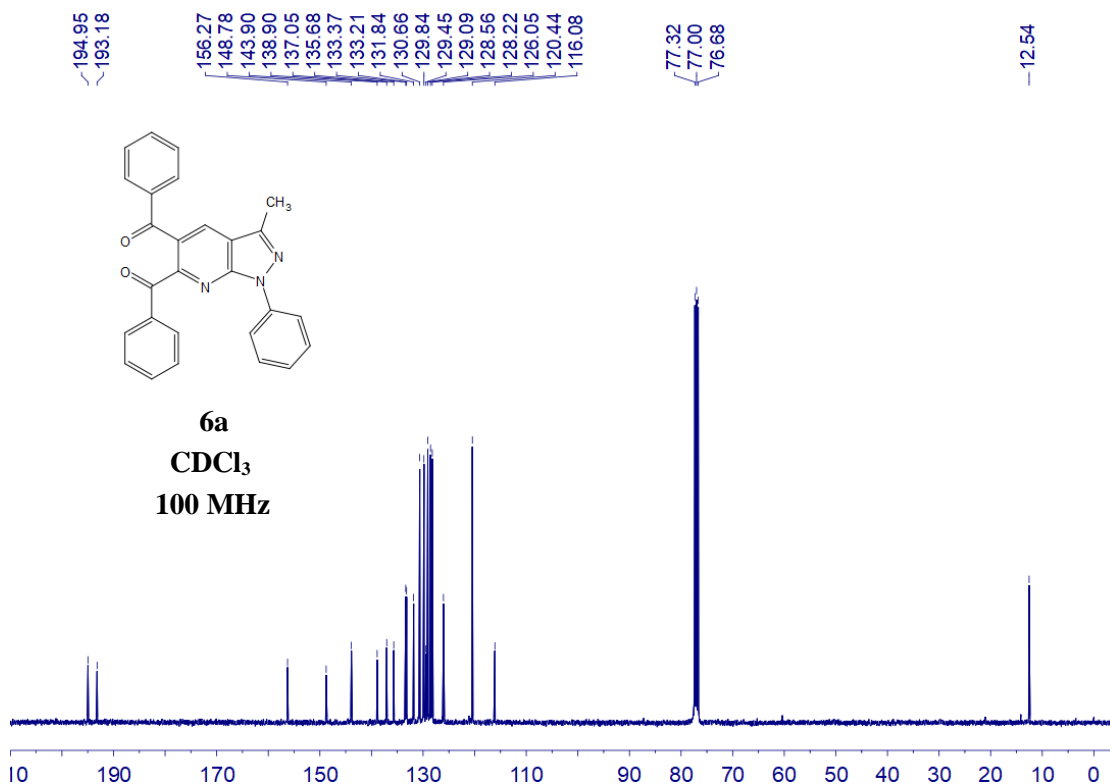
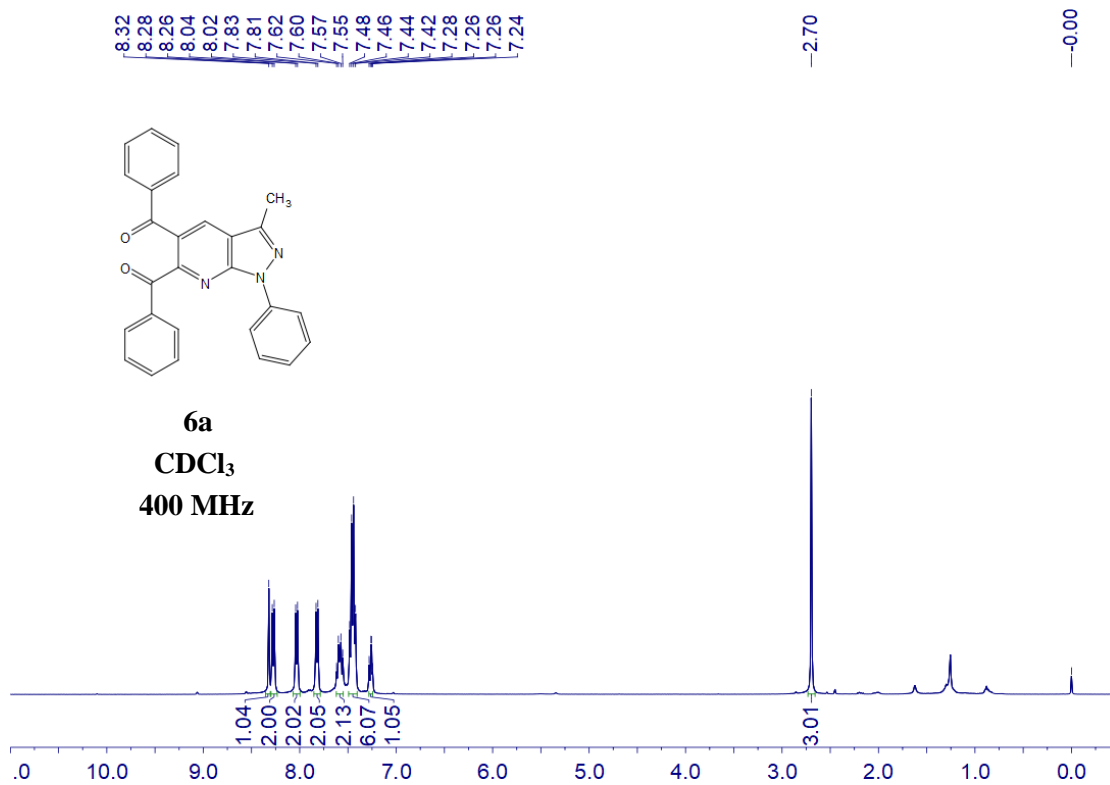
5w



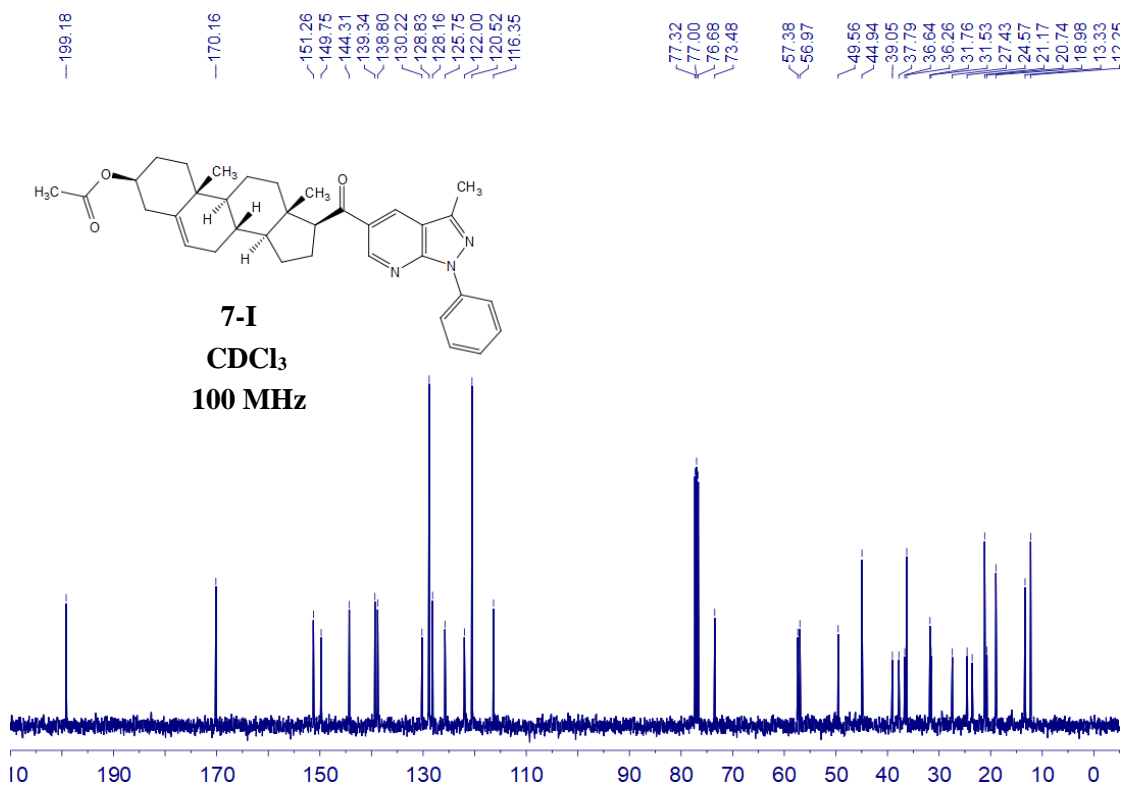
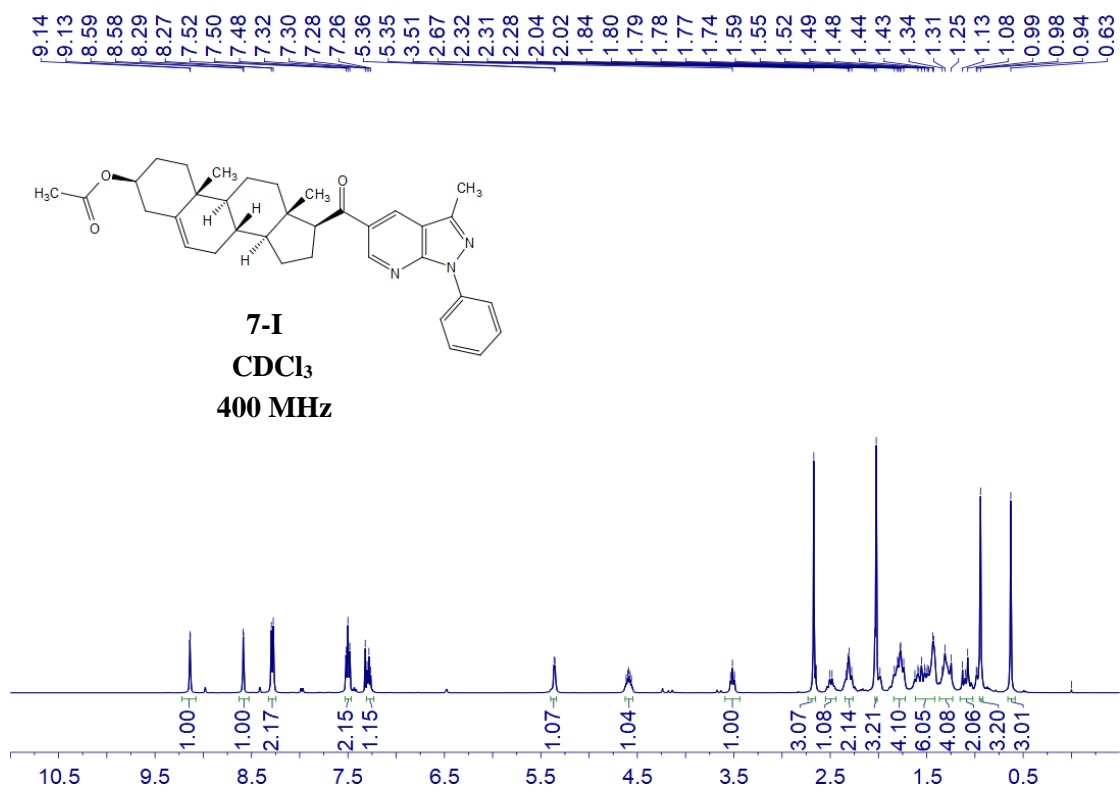
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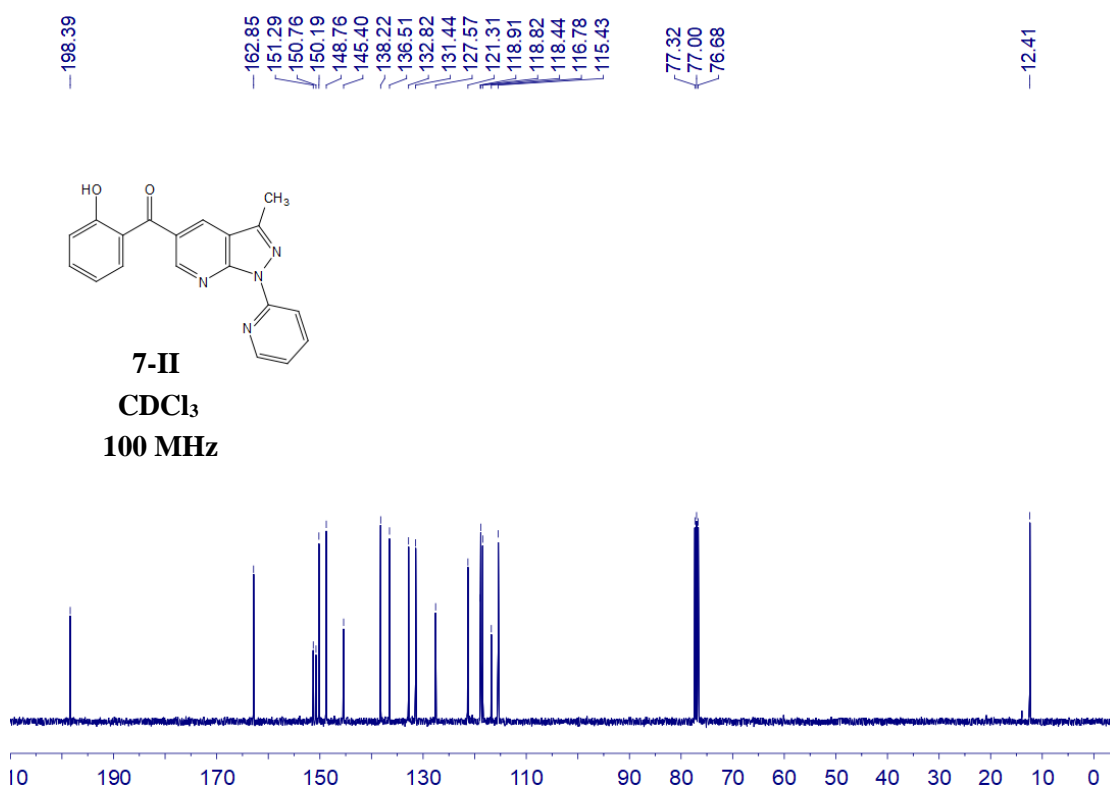
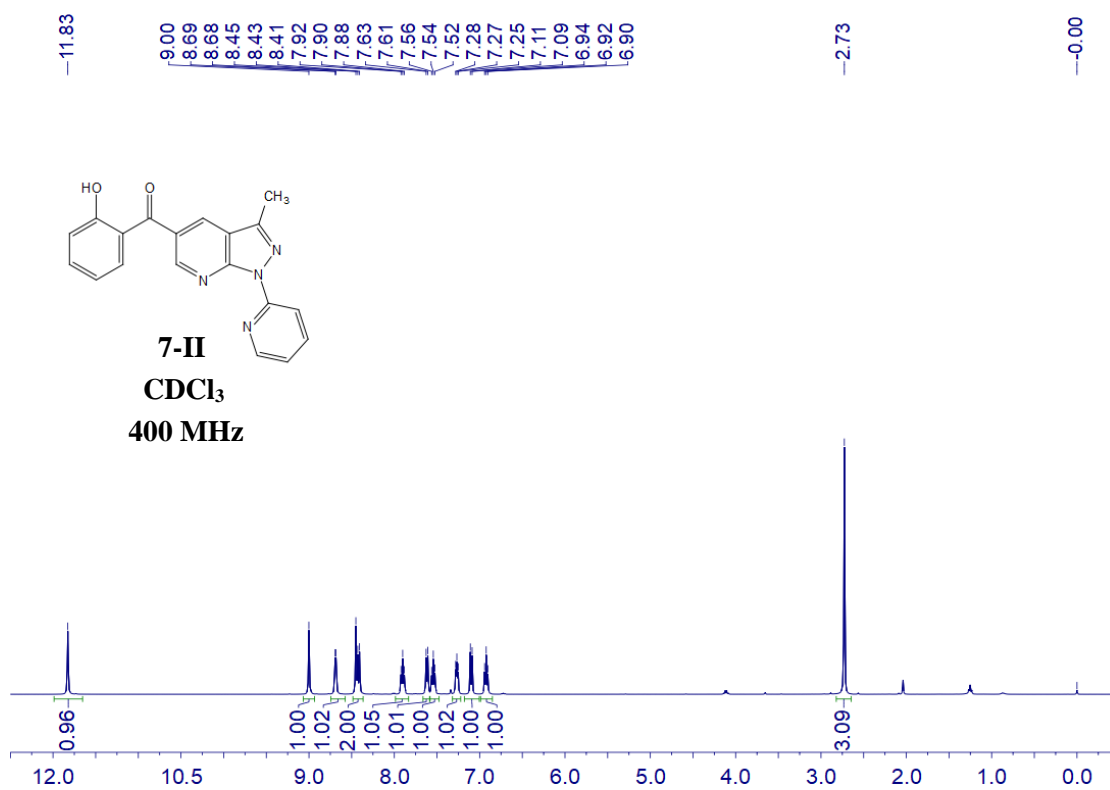
**6a**



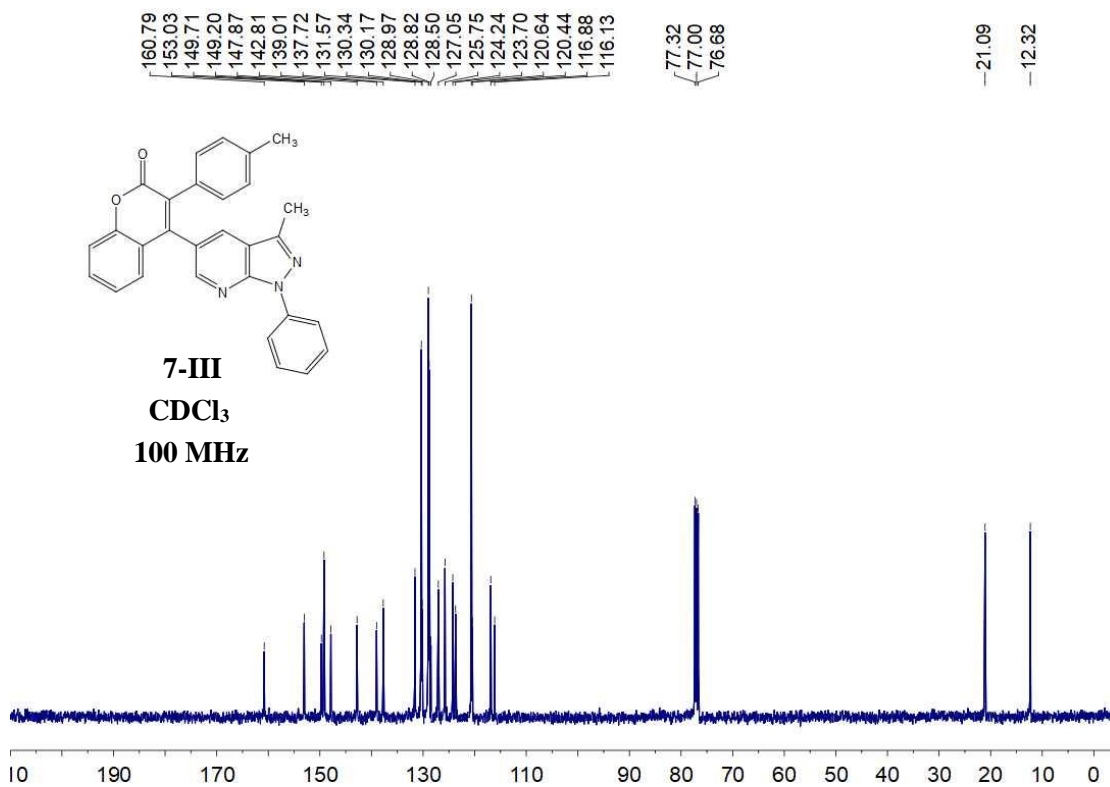
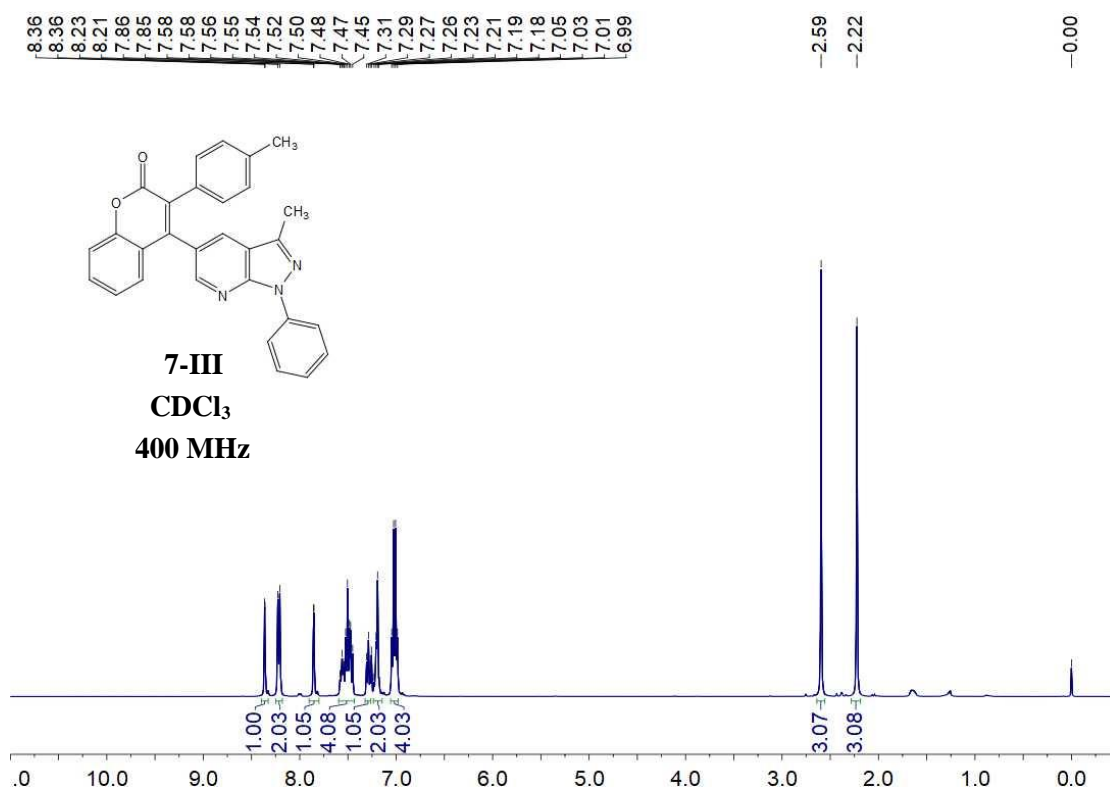
**7-I**



### 7-II



**7-III**



**7-IV**

