

Electronic Supplementary Material (ESI)

This journal is © The Royal Society of Chemistry 2022

Supporting Information for Synthesis of Imidazo[1,2-a]pyridinones via a visible light- photocatalyzed functionalization of alkynes/nitrile insertion/ cyclization tandem sequences using micro-flow technology†

Minghui Wei^a, Jiankun Chen^a, Chengkou Liu^a, Zhao Yang^b, Hong Qin^a, Yujing Hu^a,
Jindian Duan^a, Yuguang Li^d, Zheng Fang^{a,c*}, Kai Guo^{a,c*}

a. College of Biotechnology and Pharmaceutical Engineering Nanjing Tech University ,30 Puzhu Rd S., Nanjing, 211816, China.
E-mail: guok@njtech.edu.cn, fzcpcu@163.com; Fax: +8625 5813 9935; Tel: +8625 5813 9926

b. College of Engineering, China Pharmaceutical University, 24 Tongjiaxiang, Nanjing, 210003, China. E-mail: yzcpu@163.com

c. State Key Laboratory of Materials-Oriented Chemical Engineering, 30 Puzhu Rd S., Nanjing, 211816, China

d. Institute of Nanjing Advanced Biomaterials & Processing Equipment, Liyuguang@njibp.com

Contents

1. General Information	2
2. Batch and Microfluidic Reactor Device	3
3. Select Optimization Results.....	3
4. Preparation of Substrates.....	9
5. Experiments for Mechanistic Studies.....	10
6. Analytical data for isolated compounds.....	11
7. Crystal Data and Structure Refinements.....	39
8. ¹ H NMR and ¹³ C NMR spectra.....	41
9. References	107

1. General Information

$^1\text{H}/^{13}\text{C}$ NMR spectra were recorded on magnet system 400'54 ascend instrument purchased from Bruker Biospin AG. All chemical shifts are given in parts per million and are measured relative to DMSO as an internal standard. ESI-MS spectra were recorded on Agilent Q-TOF 6520. Products were purified by flash chromatography on 200-300 mesh silica gel and visualized using a UV lamp (254 nm or 365 nm). All the solvents were used without further purification, unless otherwise state. the other commercial chemicals were used without further purification. All reactions were performed under an inert atmosphere of nitrogend.

2. Batch and Microfluidic Reactor Device

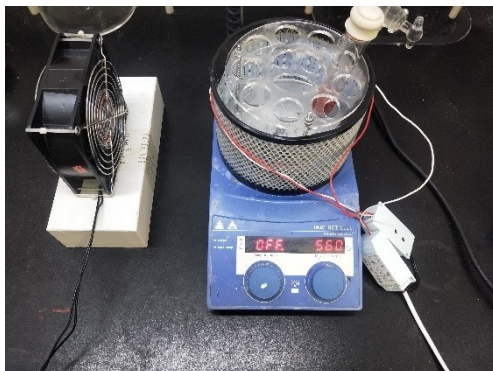


Figure 1 Batch reactor device



Figure 2 Microfluidic reactor device

Note: The light source is a simulated solar lamp (10W, 220V, wavelength 420nm-430nm).

3. Select Optimization Results

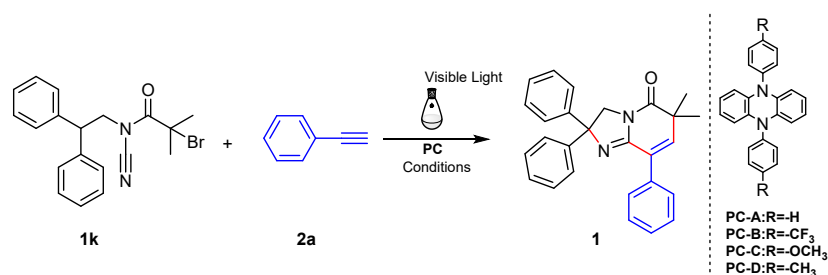
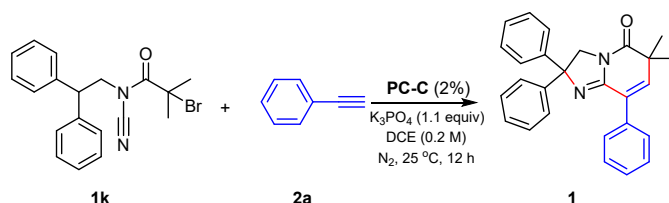


Figure 3 Optimization of reaction conditions

3.1 Table 1. Varying the wavelength of light^a

Table 1 Optimizing the wavelength of light



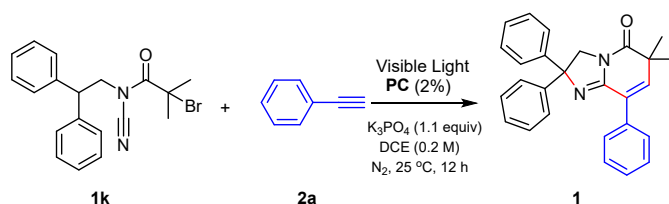
Entry	Wavelength of Light	yield 1 ^b (%)
1	360-370 nm	55
2	380-385 nm	48
3	390-398 nm	53
4	420-430 nm	67
5	435-445 nm	35

[a] Reaction conditions: **1k** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC-C** (2 mmol%, 2 equiv%), K₃PO₄ (1.1 mmol, 1.1 equiv), solvent: DCE (5 mL), N₂, 25°C, 12 h; The models of lamps used are 10 W, 220 V, LED.

[b] Isolated yield.

3.2 Table 2. Varying the Catalyst^a

Table 2 Explore the effects of different catalysts on the reaction



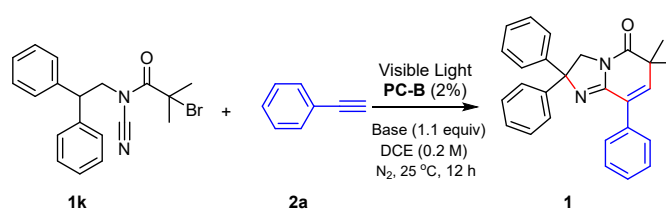
Entry	PC	yield 1 ^b (%)
1	PC-A	58
2	PC-B	69

3	PC-C	67
4	PC-D	46
5	None	None
6 ^c	PC-B	None

[a] Reaction conditions: **1k** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC** (2 mmol%, 2 equiv%), K₃PO₄ (1.1 mmol, 1.1 equiv), solvent: DCE (5 mL), N₂, 25°C, 12 h, bluelight (10 W、220 V、LED、wavelength 420 nm-430 nm). [b] Isolated yield. [c] no light.

3.3 Table 3. Varying the Base^a

Table 3 Explore the effect of different Bases on the reaction

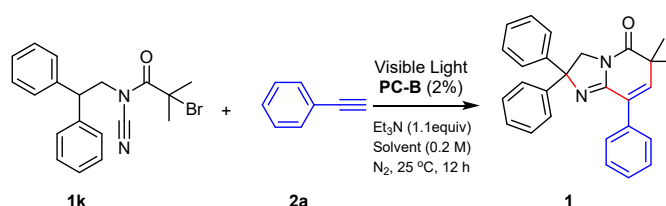


Entry	Base	yield 1 ^b (%)
1	K ₃ PO ₄	69
2	K ₂ CO ₃	53
3	NaHCO ₃	49
4	LiOtBu	42
5	Et₃N	71
6	DMAP	48
7	DBU	36
8	Pyridine	44
9	None	37

[a] Reaction conditions: **1k** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC-B** (2 mmol%, 2 equiv%), Base (1.1 mmol, 1.1 equiv), solvent: DCE (5 mL), N₂, 25°C, 12 h, bluelight (10 W、220 V、LED、wavelength 420 nm-430 nm). [b] Isolated yield.

3.4 Table 4. Varying the Solvent^a

Table 4 Explore the effect of different Solvents on the reaction

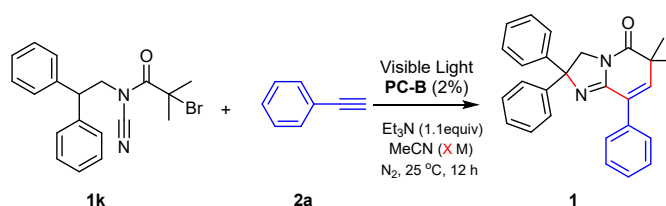


Entry	solvent	yield 1 ^b (%)
1	DCE	71
2	MeCN	82
3	THF	55
4	DMA	43
5	DMF	41
6	Cyclohexane	50
7	1,4-Dioxane	78

[a] Reaction conditions: **1k** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC-B** (2 mmol%, 2 equiv%), Et₃N (1.1 mmol, 1.1 equiv), solvent: (5 mL), N₂, 25°C, 12 h, bluelight (10 W, 220 V, LED, wavelength 420 nm-430 nm). [b] Isolated yield.

3.5 Table 5. Concentration^a

Table 5 Explore the effect of substrate concentration on the reaction

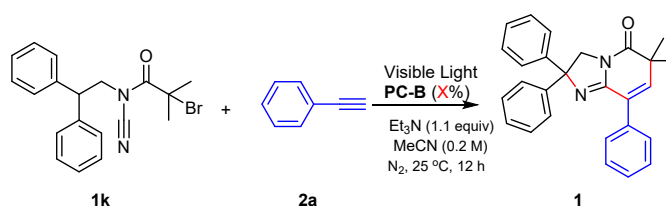


Entry	Concentration	yield 1 ^b (%)
1	1M	80
2	0.5M	81
3	0.2M	82
4	0.1M	64
5	0.05M	43

[a] Reaction conditions : **1k** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC-B** (2 mmol%, 2 equiv%), Et₃N (1.1 mmol, 1.1 equiv), solvent: MeCN (X mL), N₂, 25°C, 12 h, bluelight (10 W, 220 V, LED, wavelength 420 nm-430 nm). [b] Isolated yield.

3.6 Table 6. Catalyst concentration^a

Table 6 Explore the effect of the amount of catalyst on the reaction



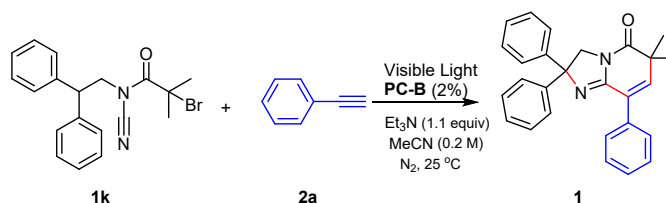
Entry	PC (X mol%)	yield 1 ^b (%)
-------	-------------	---------------------------------

1	4	83
2	2	82
3	1	64
4	0.5	58
5	None	None

[a] Reaction conditions: **1k** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC-B** (X% mmol, X% equiv), Et₃N (1.1 mmol, 1.1 equiv), solvent: MeCN (5 mL), N₂, 25°C, 12 h, bluelight (10 W、220 V、LED、wavelength 420 nm-430 nm). [b] Isolated yield.

3.7 Table 7. Residence time^a

Table 7 Explore the effect of reaction time on the reaction

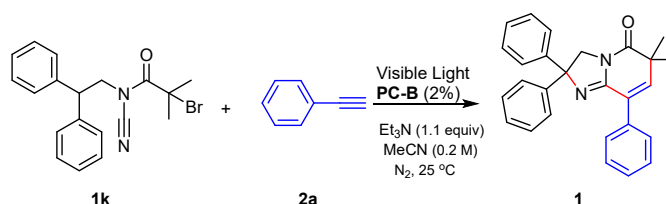


Entry	Time (h)	yield 1 ^b (%)
1	1	24
2	2	31
3	3	57
4	4	81
5	6	83
6	12	82

[a] Reaction conditions: **1k** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC-B** (2 mmol%, 2 equiv%), Et₃N (1.1 mmol, 1.1 equiv), solvent: MeCN (5 mL), N₂, 25°C, bluelight (10 W、220 V、LED、wavelength 420 nm-430 nm). [b] Isolated yield.

3.8 Table 8. Reagent Loading^a

Table 8 Explore the effect of substrate ratio on the reaction



Entry	Phenylacetylene	yield 1 ^b (%)
1	1	73
2	2	81

3	3	84
4	4	82

[a] Reaction conditions: **1k** (1 mmol, 1 equiv), **PC-B** (2 mmol%, 2 equiv%), Et₃N (1.1 mmol, 1.1 equiv), solvent: MeCN (5 mL), N₂, 25°C, 4 h, bluelight (10 W, 220 V, LED, wavelength 420 nm-430 nm). [b] Isolated yield.

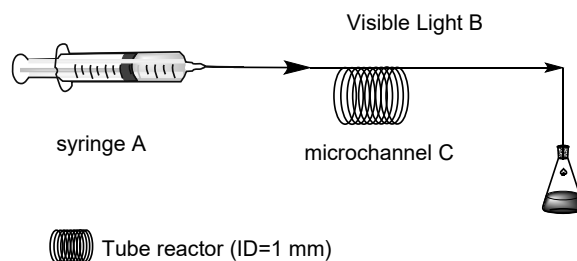
3.9 Table 9. Reagent Loadings^a

Table 9 Optimization of microchannel reaction conditions

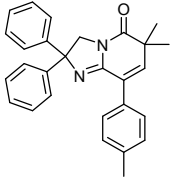
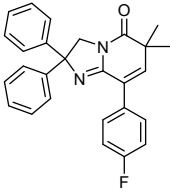
Entry	PC-B (equiv)	Tube diameter (mm)	Tube length (m)	Residence time (minute)	yield 1 ^b (%)
1	2%	1	2	30	85
2	1%	1	2	30	93
3	0.5%	1	2	30	53
4	0.1%	1	2	30	34
5	1%	1	3	30	84
6	1%	1	1	30	81
7	1%	1	0.5	30	68
8	1%	1	2	5	37
9	1%	1	2	10	45
10	1%	1	2	20	91
11	1%	1	2	40	92

[a] Reaction conditions: **1k** (1.0 mmol, 1.0 equiv), **2a** (1.0 mmol, 1.0 equiv), Et₃N (1.1 mmol, 1.1 equiv), 5 mL MeCN (0.2 M) solution, N₂, 25°C; bluelight (10 W, 220 V, LED, wavelength 420 nm-430 nm). [b] Isolated yield.

3.10 A Scale-up Continuous Flow Reaction^a



Entry	Structure	yield (%)
1		89

2		81
3		72

^a Reaction conditions: **1k** (10 mmol), **2a** (1 equiv), MeCN (20 mL), Et₃N (1.1 equiv), and **PC-B** (1 % equiv.) at room temperature for 20 minutes. Isolated yield.

4. Preparation of Substrates

4.1 Method for synthesizing phenazine catalysts

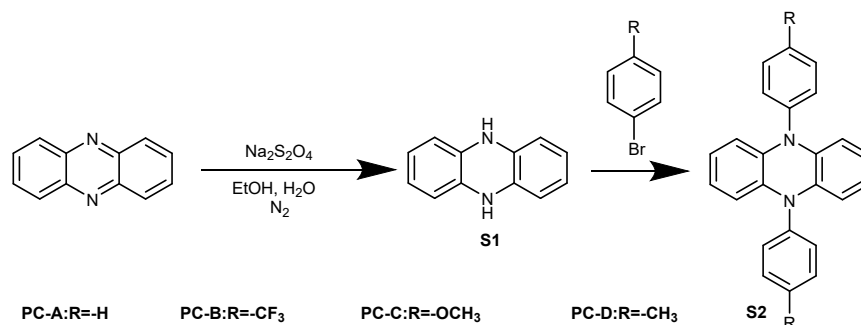


Figure 4 Synthetic method of phenazine catalyst

As shown in Figure 4, S1 and S2 are synthesized according to the literature¹.

4.2 Method for synthesizing phenethylamine-derived bromide substrates

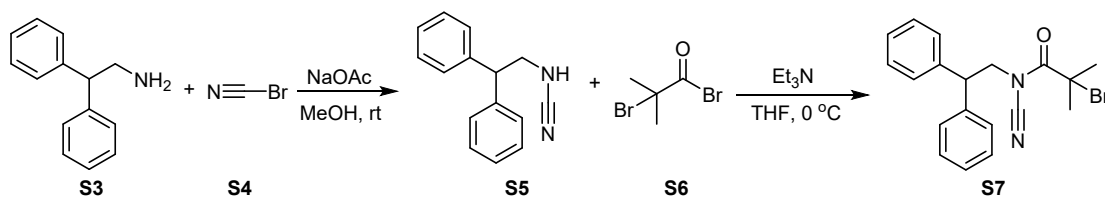


Figure 5 Synthesis method of indole substrates

As shown in Figure 5: 1)² To a stirring solution of S3 (12 mmol, 1.0 equiv.) and NaOAc (3.0 equiv.) in MeOH (100 ml, 0.12 M) at 0 °C, BrCN S4 (1.2 equiv.) was added. Then the reaction was warmed to room temperature and stirred for 12 h. Upon completion, the solvent was removed in vacuo. To the residue was added water and extracted with ethyl acetate, and the combined organic layers were washed by brine and dried over Na₂SO₄, then filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel or recrystallization to give compound S5. 2)² To a stirring solution of S5 (12 mmol, 1.0 equiv.) and Et₃N (2.4 equiv.) in THF (100 ml, 0.12 M) at 0 °C, 2-Bromo-2-methylpropionyl bromide S6 (1.2 equiv) was slowly added. Then the reaction was warmed to room temperature and stirred for 12 h. Upon completion, the solvent was removed in vacuo. To the residue was added water and extracted with ethyl acetate, and the combined organic layers were washed by brine and dried over Na₂SO₄, then filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel or recrystallization to give compound S7.

4.3 Method for synthesizing products (**1** as an example)



Figure 6 Microfluidic reactor device

An oven-dried 10 mL reaction syringe was charged with 2-bromo-N-cyano-N-(2,2-diphenylethyl)-2-methylpropanamide (1 mmol, 1 equiv), phenylacetylene (1 mmol, 1 equiv), PC-B (1 mol %) and Et₃N (1.1 mmol, 1.1 equiv). And add 5 mL MeCN (0.2 M) solution. Pass the solutions through a Quartz tubing (id = 1 mm, length = 2.0 m) to building the **1** during 20 minutes of residence time under blue light (10 W, 220 V, LED, wavelength 420nm-430nm). The reaction mixture was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate or dichloromethane/methanol to afford the desired product **1** (91% yield).

5. Experiments for Mechanistic Studies

5.1 Free radical capture experiment

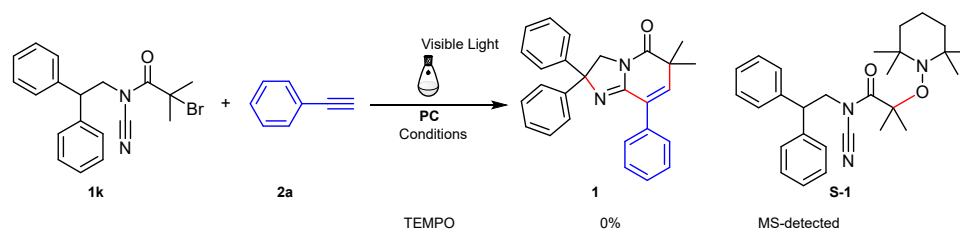


Figure 7 Radical trapping experiment with TEMPO

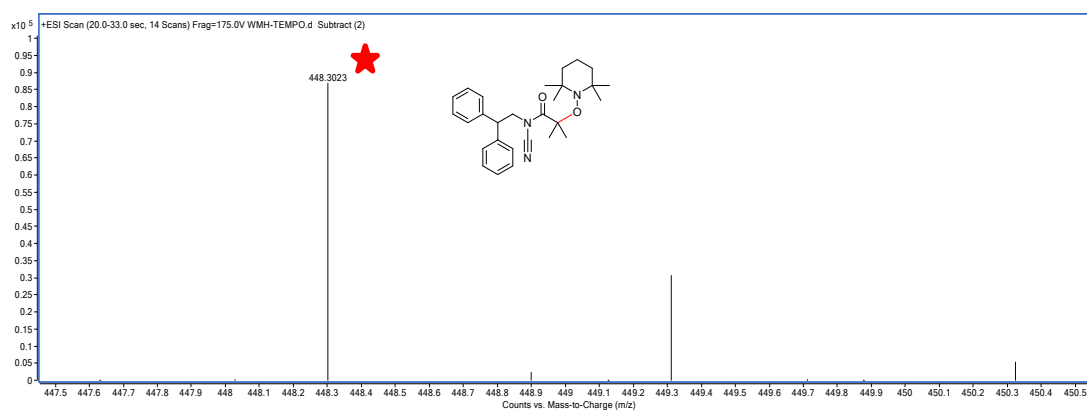


Figure 8 HR-MS (EI) analysis of **S-1**

5.2 Variable control experiment

Table 10 Variable Control Experiment

Entry	Changes to "standard conditions"	yield 1 ^b (%)
1	No organic photocatalyst	0
2	No light	0

[a] Reaction conditions: **1k** (1 mmol, 1 equiv), **2a** (3 mmol, 3 equiv), Et₃N (1.1 mmol, 1.1 equiv), solvent: MeCN (5 mL), N₂, 25°C, 20 minutes, bluelight (10 W, 220 V, LED, wavelength 420 nm-430 nm). [b] Isolated yield.

5.3 Discussion on theoretical reaction mechanism

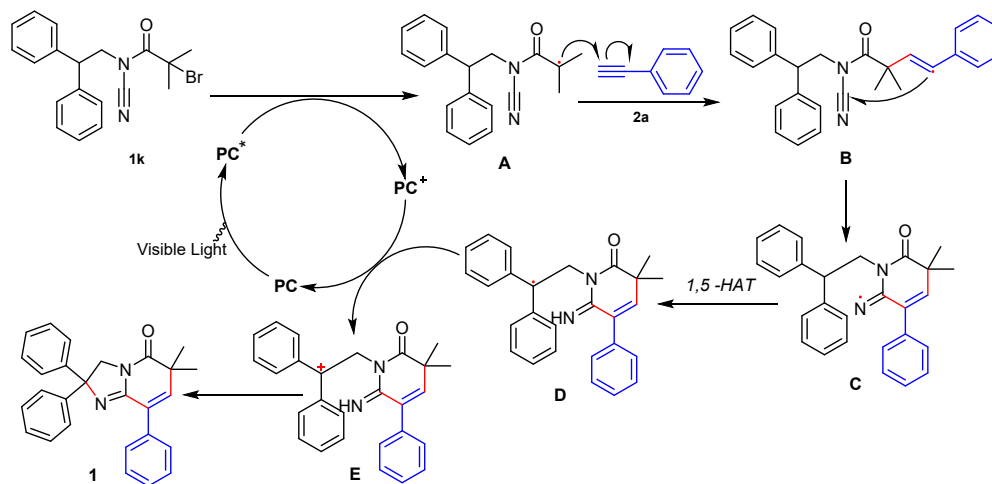
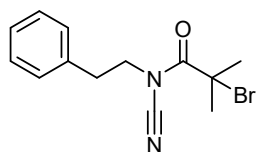


Figure 9 Reaction mechanism

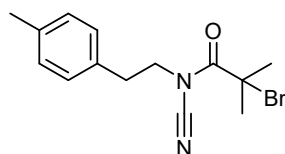
6. Analytical data for isolated compounds

6.1 Characterization data for phenethylamine-derived bromides substrates



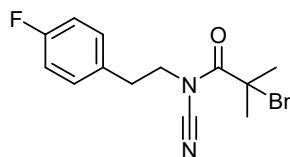
2-bromo-N-cyano-2-methyl-N-phenethylpropanamide:(1a)

Brown oil (3.15 g, 89% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.35 – 7.24 (m, 5H), 3.93 (t, $J = 7.0$ Hz, 2H), 2.94 (t, $J = 7.0$ Hz, 2H), 1.96 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 169.74, 137.32, 129.47, 128.97, 127.28, 110.03, 56.51, 50.48, 33.07, 30.80. **HRMS** (EI) calcd for $\text{C}_{13}\text{H}_{15}\text{N}_2\text{OBr}$ [M+H]: 295.0441; found: 295.0445.



2-bromo-N-cyano-2-methyl-N-(4-methylphenethyl)propanamide:(1b)

Brown oil (3.01 g, 81% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.14 (q, $J = 8.1$ Hz, 4H), 3.89 (t, $J = 7.2$ Hz, 2H), 2.91 (t, $J = 7.1$ Hz, 2H), 2.28 (s, 3H), 1.99 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 169.68, 136.25, 134.12, 129.52, 129.26, 109.97, 56.36, 50.57, 32.74, 30.84, 21.15. **HRMS** (EI) calcd for $\text{C}_{14}\text{H}_{17}\text{N}_2\text{OBr}$ [M+H]: 309.0597; found: 309.0592.

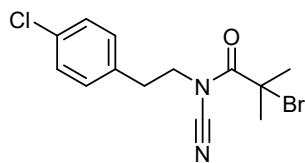


2-bromo-N-cyano-N-(4-fluorophenethyl)-2-methylpropanamide:(1c)

Yellow oil (2.85 g, 76% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.37 – 7.27 (m, 2H), 7.19 – 7.09 (m, 2H), 3.93 (t, $J = 6.9$ Hz, 2H), 2.94 (t, $J = 6.9$ Hz, 2H), 1.97 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 169.74, 161.73 (d, $J = 242.7$ Hz), 133.51 (d, $J = 3.4$ Hz), 131.38 (d, $J = 8.0$ Hz), 115.67 (d, $J = 21.1$ Hz), 110.00, 56.44, 50.52, 32.26, 30.80.

^{19}F NMR (376 MHz, DMSO- d_6) δ -116.11. HRMS (EI) calcd for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{OBrF}$ [M+H]:

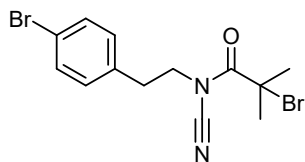
313.0346; found: 313.0348.



2-bromo-N-(4-chlorophenethyl)-N-cyano-2-methylpropanamide:(1d)

Yellow oil (2.84 g, 72% yield); ^1H NMR (400 MHz, DMSO- d_6) δ 7.28 – 7.22 (m, 2H), 7.22 – 7.16 (m, 2H), 3.84 (t, J = 7.0 Hz, 2H), 2.86 (t, J = 6.9 Hz, 2H), 1.89 (s, 6H).

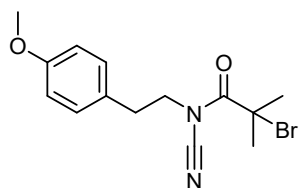
^{13}C NMR (101 MHz, DMSO- d_6) δ 169.69, 136.27, 132.13, 131.27, 128.87, 109.91, 56.26, 50.32, 32.49, 30.84. HRMS (EI) calcd for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{OBrCl}$ [M+H]: 329.0051; found: 329.0056.



2-bromo-N-(4-bromophenethyl)-N-cyano-2-methylpropanamide:(1e)

Yellow oil (3.40 g, 76% yield); ^1H NMR (400 MHz, DMSO- d_6) δ 7.41 – 7.32 (m, 2H), 7.24 – 7.15 (m, 2H), 3.98 (t, J = 6.9 Hz, 2H), 2.99 (t, J = 6.9 Hz, 2H), 2.02 (s, 6H).

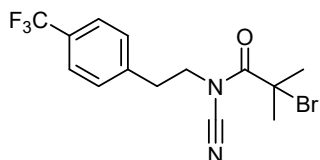
^{13}C NMR (101 MHz, DMSO- d_6) δ 169.87, 136.45, 132.31, 131.45, 129.05, 110.09, 56.43, 50.49, 32.67, 31.02. HRMS (EI) calcd for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{OBr}_2$ [M+H]: 372.9546; found: 372.9546.



2-bromo-N-cyano-N-(4-methoxyphenethyl)-2-methylpropanamide:(1f)

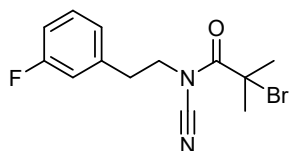
Brown oil (3.08 g, 79% yield); ^1H NMR (400 MHz, DMSO- d_6) δ 7.35 – 7.08 (m, 2H), 6.95 – 6.81 (m, 2H), 3.88 (t, J = 7.0 Hz, 2H), 3.73 (s, 3H), 2.88 (t, J = 7.0 Hz, 2H), 1.98 (s, 6H).

^{13}C NMR (101 MHz, DMSO- d_6) δ 169.73, 158.64, 130.45, 129.06, 114.34, 110.03, 56.44, 55.43, 50.71, 32.25, 30.82. HRMS (EI) calcd for $\text{C}_{14}\text{H}_{17}\text{N}_2\text{O}_2\text{Br}$ [M+H]: 325.0546; found: 325.0548.



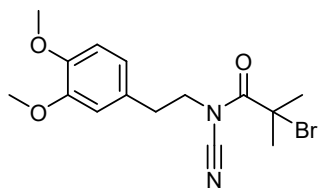
2-bromo-N-cyano-2-methyl-N-(4-(trifluoromethyl)phenethyl)propanamide:(1g)

Brown oil (2.96 g, 68% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.68 (d, $J = 8.0$ Hz, 2H), 7.53 (d, $J = 7.9$ Hz, 2H), 3.99 (t, $J = 6.9$ Hz, 2H), 3.05 (t, $J = 6.9$ Hz, 2H), 1.96 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 169.73, 142.39, 130.41, 125.74 (q, $J = 3.8$ Hz), 124.80 (d, $J = 271.9$ Hz), 109.96, 56.45, 50.07, 46.20, 32.89, 30.77. $^{19}\text{F NMR}$ (376 MHz, $\text{DMSO-}d_6$) δ -60.89. **HRMS** (EI) calcd for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{OBrF}_3$ [M+H]: 363.0314; found: 363.0318.



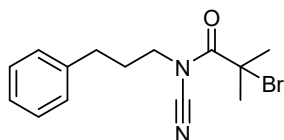
2-bromo-N-cyano-N-(3-fluorophenethyl)-2-methylpropanamide:(1h)

Yellow oil (2.93 g, 78% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.35 (td, $J = 8.1$, 6.3 Hz, 1H), 7.26 – 7.09 (m, 2H), 7.09 – 7.00 (m, 1H), 3.95 (t, $J = 6.9$ Hz, 2H), 2.97 (t, $J = 6.9$ Hz, 2H), 1.97 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 169.68, 162.68 (d, $J = 243.5$ Hz), 140.21 (d, $J = 7.4$ Hz), 130.77 (d, $J = 8.5$ Hz), 125.63 (d, $J = 2.5$ Hz), 116.27 (d, $J = 21.2$ Hz), 114.08 (d, $J = 20.9$ Hz), 109.94, 56.35, 50.24, 32.78, 30.78. $^{19}\text{F NMR}$ (376 MHz, $\text{DMSO-}d_6$) δ -113.34. **HRMS** (EI) calcd for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{OBrF}$ [M+H]: 313.0346; found: 313.0349.



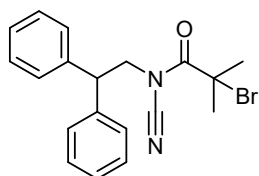
2-bromo-N-cyano-N-(3,4-dimethoxyphenethyl)-2-methylpropanamide:(1i)

Yellow oil (3.66 g, 86% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 6.92 – 6.84 (m, 2H), 6.77 (dd, $J = 8.2$, 2.0 Hz, 1H), 3.91 (t, $J = 7.0$ Hz, 2H), 3.75 (s, 3H), 3.73 (s, 3H), 2.88 (t, $J = 6.9$ Hz, 2H), 1.98 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 169.69, 149.18, 148.21, 129.57, 121.41, 113.09, 112.19, 109.99, 56.34, 55.86, 55.84, 50.69, 32.69, 30.76. **HRMS** (EI) calcd for $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}_3\text{Br}$ [M+H]: 355.0652; found: 355.0655.



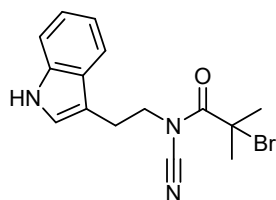
2-bromo-N-cyano-2-methyl-N-(3-phenylpropyl)propanamide:(1j)

Yellow oil (3.30 g, 89% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.33 – 7.28 (m, 2H), 7.24 – 7.18 (m, 3H), 3.70 (t, $J = 7.1$ Hz, 2H), 2.69 – 2.63 (m, 2H), 2.05 (s, 6H), 1.99 – 1.93 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 169.85, 141.03, 128.87, 128.71, 126.53, 110.18, 56.79, 48.87, 32.12, 30.86, 28.99. **HRMS** (EI) calcd for $\text{C}_{14}\text{H}_{17}\text{N}_2\text{OBr}$ $[\text{M}+\text{H}]^+$: 309.0597; found: 309.0595.



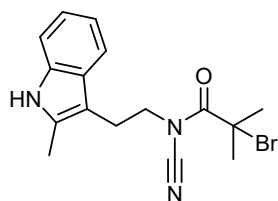
2-bromo-N-cyano-N-(2,2-diphenylethyl)-2-methylpropanamide:(1k)

White solid (3.16 g, 71% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.33 (ddt, $J = 33.1$, 25.9, 7.4 Hz, 10H), 4.37 (d, $J = 6.8$ Hz, 2H), 3.11 (tt, $J = 7.4$, 3.7 Hz, 1H), 1.86 (d, $J = 6.6$ Hz, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 169.85, 140.99, 129.10, 128.48, 127.58, 109.79, 56.14, 52.65, 48.82, 30.93, 30.66. **HRMS** (EI) calcd for $\text{C}_{19}\text{H}_{19}\text{N}_2\text{OBr}$ $[\text{M}+\text{H}]^+$: 371.0754; found: 371.0757.



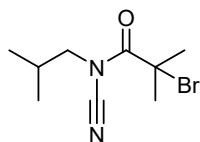
N-(2-(1H-indol-3-yl)ethyl)-2-bromo-N-cyano-2-methylpropanamide:(1l)

Yellow oil (3.85 g, 96% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 10.96 (s, 1H), 7.59 (d, $J = 7.9$ Hz, 1H), 7.39 (d, $J = 8.1$ Hz, 1H), 7.26 (d, $J = 2.4$ Hz, 1H), 7.17 – 7.08 (m, 1H), 7.03 (td, $J = 7.5$, 7.0, 1.1 Hz, 1H), 3.94 (t, $J = 7.3$ Hz, 2H), 3.09 (t, $J = 7.2$ Hz, 2H), 1.99 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 169.85, 136.74, 127.41, 124.18, 121.62, 119.00, 118.48, 112.02, 110.23, 109.50, 56.67, 50.12, 30.82, 23.17. **HRMS** (EI) calcd for $\text{C}_{15}\text{H}_{16}\text{N}_3\text{OBr}$ $[\text{M}+\text{H}]^+$: 334.0551; found: 334.0553.



2-bromo-N-cyano-2-methyl-N-(2-(2-methyl-1H-indol-3-yl)ethyl)propanamide:(1m)

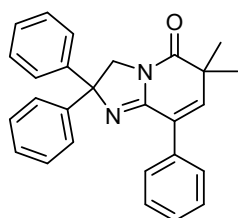
Yellow oil (3.88 g, 93% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 10.82 (s, 1H), 7.42 (d, $J = 7.6$ Hz, 1H), 7.24 (d, $J = 7.7$ Hz, 1H), 7.03 – 6.90 (m, 2H), 3.84 (t, $J = 7.3$ Hz, 2H), 2.99 (t, $J = 7.3$ Hz, 2H), 2.35 (s, 3H), 1.91 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 169.83, 135.68, 133.49, 128.55, 120.65, 118.81, 117.51, 110.97, 110.31, 105.22, 56.60, 50.08, 30.76, 22.12, 11.71. **HRMS** (EI) calcd for $\text{C}_{16}\text{H}_{18}\text{N}_3\text{OBr}$ $[\text{M}+\text{H}]$: 348.0706; found: 348.0709.



2-bromo-N-cyano-N-isobutyl-2-methylpropanamide:(1n)

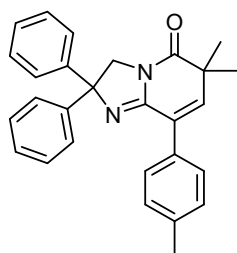
Yellow oil (2.46 g, 83% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 3.52 (d, $J = 7.3$ Hz, 2H), 2.05 (s, 6H), 1.99 (dd, $J = 13.7, 7.0$ Hz, 1H), 0.94 (d, $J = 6.8$ Hz, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 169.97, 110.58, 56.88, 55.94, 30.89, 27.26, 19.64. **HRMS** (EI) calcd for $\text{C}_9\text{H}_{15}\text{N}_2\text{OBr}$ $[\text{M}+\text{H}]$: 247.0441; found: 247.0446

6.2 Product Characterization Data



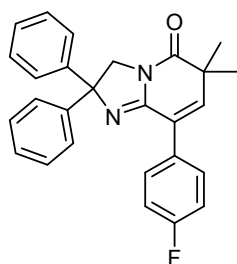
6,6-dimethyl-2,2,8-triphenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(1)

White solid (357.81 mg, 91% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.78 (d, $J = 7.5$ Hz, 2H), 7.53 – 7.40 (m, 7H), 7.35 (t, $J = 7.7$ Hz, 4H), 7.26 – 7.22 (m, 2H), 6.75 (s, 1H), 4.50 (s, 2H), 1.39 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 171.60, 152.69, 147.46, 147.34, 135.72, 129.05, 128.92, 128.61, 128.57, 127.34, 126.58, 125.97, 77.82, 56.43, 42.80, 26.93. **HRMS** (EI) calcd for $\text{C}_{27}\text{H}_{24}\text{N}_2\text{O}$ [$\text{M}+\text{H}$]: 393.1961; found: 393.1965.



6,6-dimethyl-2,2-diphenyl-8-(p-tolyl)-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(2)

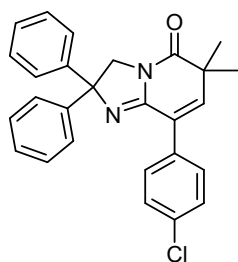
White solid (358.35 mg, 88% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.65 (d, $J = 8.0$ Hz, 2H), 7.45 (d, $J = 7.0$ Hz, 4H), 7.32 (t, $J = 7.7$ Hz, 4H), 7.26 (d, $J = 7.9$ Hz, 2H), 7.21 (t, $J = 7.4$ Hz, 2H), 6.68 (s, 1H), 4.47 (s, 2H), 2.35 (s, 3H), 1.35 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 171.63, 152.77, 147.38, 146.70, 137.95, 132.83, 129.13, 128.91, 127.32, 126.56, 125.82, 77.78, 56.38, 42.73, 26.97, 21.26. **HRMS** (EI) calcd for $\text{C}_{28}\text{H}_{26}\text{N}_2\text{O}$ [$\text{M}+\text{H}$]: 407.2118; found: 407.2113.



8-(4-fluorophenyl)-6,6-dimethyl-2,2-diphenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(3)

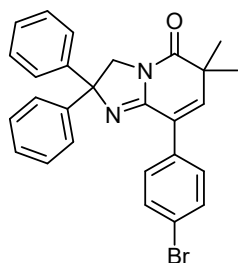
Yellow solid (324.84 mg, 79% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.90 – 7.74 (m, 2H), 7.45 (dd, $J = 8.4, 1.3$ Hz, 4H), 7.30 (q, $J = 8.9, 8.2$ Hz, 6H), 7.23 – 7.17 (m, 2H), 6.72 (s, 1H), 4.49 (s, 2H), 1.35 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 171.54, 162.52 (d, $J = 245.1$ Hz), 152.70, 147.38, 147.30, 132.03 (d, $J = 3.5$ Hz), 131.10 (d, $J = 8.1$ Hz), 128.89, 127.33, 126.58, 124.95, 115.42 (d, $J = 21.4$ Hz), 77.85, 56.47, 42.82, 26.89. ^{19}F

NMR (376 MHz, DMSO- d_6) δ -113.77. **HRMS** (EI) calcd for $C_{27}H_{23}N_2OF$ [M+H]: 411.1867; found: 411.1863.



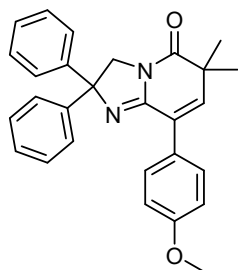
8-(4-chlorophenyl)-6,6-dimethyl-2,2-diphenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(4)

Yellow solid (303.28 mg, 71% yield); **1H NMR** (400 MHz, DMSO- d_6) δ 7.88 – 7.79 (m, 2H), 7.59 – 7.55 (m, 2H), 7.51 – 7.45 (m, 4H), 7.36 (dd, J = 8.4, 7.0 Hz, 4H), 7.28 – 7.22 (m, 2H), 6.83 (s, 1H), 4.51 (s, 2H), 1.40 (s, 6H). **^{13}C NMR** (101 MHz, DMSO- d_6) δ 171.50, 152.54, 147.87, 147.27, 134.47, 133.38, 130.84, 128.92, 128.61, 127.36, 126.58, 124.81, 77.85, 56.44, 42.88, 26.85. **HRMS** (EI) calcd for $C_{27}H_{23}N_2OCl$ [M+H]: 427.1572; found: 427.1577.



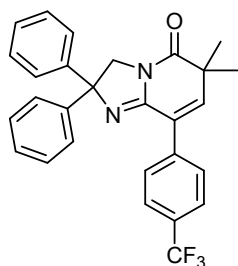
8-(4-bromophenyl)-6,6-dimethyl-2,2-diphenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(5)

Light yellow oily (315.64 mg, 67% yield); **1H NMR** (400 MHz, DMSO- d_6) δ 7.73 (d, J = 8.6 Hz, 2H), 7.65 (d, J = 8.6 Hz, 2H), 7.45 (d, J = 7.0 Hz, 4H), 7.31 (t, J = 7.7 Hz, 4H), 7.20 (t, J = 7.3 Hz, 2H), 6.77 (s, 1H), 4.48 (s, 2H), 1.35 (s, 6H). **^{13}C NMR** (101 MHz, DMSO- d_6) δ 171.47, 152.49, 147.80, 147.28, 134.84, 131.52, 131.15, 128.91, 127.34, 126.58, 124.94, 122.04, 77.87, 56.45, 42.88, 26.84. **HRMS** (EI) calcd for $C_{27}H_{23}N_2OBr$ [M+H]: 471.1067; found: 471.1065.



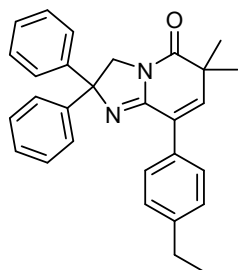
8-(4-methoxyphenyl)-6,6-dimethyl-2,2-diphenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(6)

Yellow solid (258.16 mg, 61% yield); ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.83 – 7.67 (m, 2H), 7.47 (d, *J* = 7.8 Hz, 4H), 7.33 (t, *J* = 7.7 Hz, 4H), 7.24 – 7.20 (m, 2H), 7.06 – 7.02 (m, 2H), 6.66 (s, 1H), 4.48 (s, 2H), 3.81 (s, 3H), 1.36 (s, 6H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.68, 159.70, 152.88, 147.39, 145.95, 130.23, 128.90, 127.94, 127.32, 126.58, 125.37, 113.97, 77.78, 56.39, 55.62, 42.70, 27.02. HRMS (EI) calcd for C₂₈H₂₆N₂O₂ [M+H]: 423.2067; found: 423.2069.



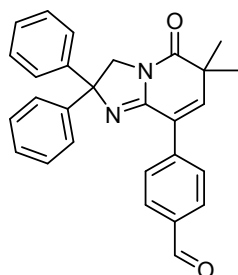
6,6-dimethyl-2,2-diphenyl-8-(4-(trifluoromethyl)phenyl)-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(7)

Yellow oil (285.93 mg, 62% yield); ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.95 – 7.81 (m, 2H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.29 (m, 4H), 7.19 (t, *J* = 7.8 Hz, 4H), 7.09 – 7.05 (m, 2H), 6.74 (s, 1H), 4.38 (s, 2H), 1.25 (s, 6H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.37, 152.40, 148.98, 147.25, 139.73, 129.84, 128.88, 127.32, 126.57, 125.43 (q, *J* = 3.8 Hz), 124.97, 77.95, 56.47, 42.97, 26.74. ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ -61.11. HRMS (EI) calcd for C₂₈H₂₃N₂OF₃ [M+H]: 461.1835; found: 461.1837.



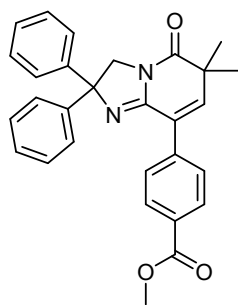
8-(4-ethylphenyl)-6,6-dimethyl-2,2-diphenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(8)

Yellow solid (341.19 mg, 81% yield); ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.73 – 7.60 (m, 2H), 7.50 – 7.40 (m, 4H), 7.32 (q, *J* = 7.7 Hz, 6H), 7.26 – 7.18 (m, 2H), 6.70 (s, 1H), 4.46 (s, 2H), 2.66 (q, *J* = 7.5 Hz, 2H), 1.35 (s, 6H), 1.22 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.64, 152.76, 147.35, 146.86, 144.24, 133.10, 128.96, 128.92, 127.96, 127.34, 126.58, 125.80, 77.79, 56.38, 42.74, 28.37, 26.98, 15.98. HRMS (EI) calcd for C₂₉H₂₈N₂O [M+H]: 421.2274; found: 421.2278.



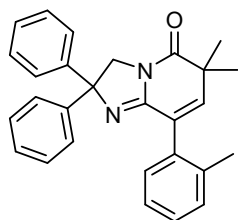
4-(6,6-dimethyl-5-oxo-2,2-diphenyl-2,3,5,6-tetrahydroimidazo[1,2-a]pyridin-8-yl)benzaldehyde:(9)

Yellow oil (219.02 mg, 52% yield); ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.81 – 7.68 (m, 2H), 7.35 – 7.27 (m, 6H), 7.17 (t, *J* = 7.7 Hz, 5H), 7.09 – 7.04 (m, 2H), 6.66 (s, 1H), 4.33 (s, 2H), 1.21 (s, 6H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.48, 152.54, 148.63, 148.29, 147.25, 134.90, 130.95, 128.92, 127.36, 126.60, 124.66, 121.08, 77.89, 56.48, 42.89, 26.84. HRMS (EI) calcd for C₂₈H₂₄N₂O₂ [M+H]: 421.1911; found: 421.1913.



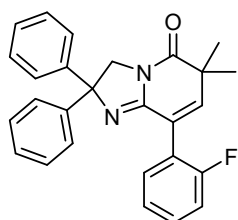
methyl 4-(6,6-dimethyl-5-oxo-2,2-diphenyl-2,3,5,6-tetrahydroimidazo[1,2-a]pyridin-8-yl)benzoate:(10)

Yellow oil (212.06 mg, 47% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 8.06 (d, $J = 8.2$ Hz, 2H), 7.92 (d, $J = 8.2$ Hz, 2H), 7.45 (d, $J = 7.5$ Hz, 2H), 7.35 – 7.28 (m, 6H), 7.23 – 7.19 (m, 2H), 6.89 (s, 1H), 4.48 (s, 2H), 3.89 (d, $J = 1.2$ Hz, 3H), 1.37 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 171.41, 166.47, 152.40, 148.85, 147.28, 142.91, 140.34, 129.41, 128.92, 128.82, 128.43, 127.35, 126.58, 77.91, 56.44, 52.67, 42.98, 26.81. **HRMS** (EI) calcd for $\text{C}_{29}\text{H}_{26}\text{N}_2\text{O}_3$ [M+H]: 451.2016; found: 451.2017.



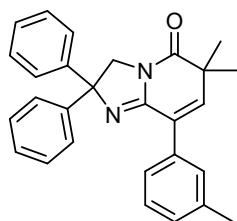
6,6-dimethyl-2,2-diphenyl-8-(o-tolyl)-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(11)

Yellow solid (346.13 mg, 85% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.37 – 7.30 (m, 6H), 7.30 – 7.27 (m, 4H), 7.25 (ddd, $J = 5.4, 3.0, 1.2$ Hz, 2H), 7.22 – 7.18 (m, 2H), 6.43 (s, 1H), 4.47 (s, 2H), 2.18 (s, 3H), 1.36 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 171.78, 153.04, 148.33, 147.20, 136.74, 136.18, 130.30, 130.20, 128.82, 128.52, 127.33, 126.77, 126.60, 126.04, 77.66, 56.73, 42.68, 26.89, 20.10. **HRMS** (EI) calcd for $\text{C}_{28}\text{H}_{26}\text{N}_2\text{O}$ [M+H]: 407.2118; found: 407.2112.



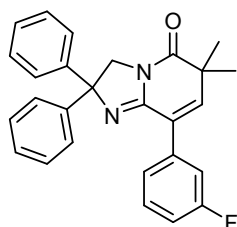
8-(2-fluorophenyl)-6,6-dimethyl-2,2-diphenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(12)

Yellow oil (320.73 mg, 78% yield); ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.31 (td, *J* = 7.6, 2.0 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.21 – 7.19 (m, 3H), 7.09 (t, *J* = 7.7 Hz, 7H), 7.01 – 6.96 (m, 2H), 6.46 (s, 1H), 4.27 (s, 2H), 1.15 (s, 6H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.44, 161.32, 158.87, 152.38, 149.70, 147.30, 132.17, 132.14, 130.88, 130.80, 128.82, 127.30, 126.60, 124.73, 124.69, 123.83, 123.68, 121.60, 116.21, 116.00, 77.73, 56.89, 42.87, 26.82. ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ -113.32. HRMS (EI) calcd for C₂₇H₂₃N₂O [M+H]: 411.1867; found: 411.1869.



6,6-dimethyl-2,2-diphenyl-8-(m-tolyl)-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(13)

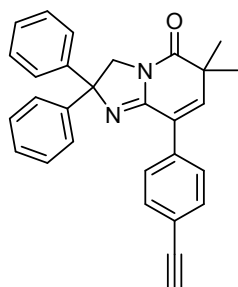
Yellow solid (354.27 mg, 87% yield); ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.63 (d, *J* = 7.9 Hz, 1H), 7.55 (d, *J* = 1.9 Hz, 1H), 7.49 (dd, *J* = 8.3, 1.3 Hz, 4H), 7.38 (t, *J* = 7.9 Hz, 5H), 7.29 – 7.25 (m, 3H), 6.76 (s, 1H), 4.51 (s, 2H), 2.43 (s, 3H), 1.41 (s, 6H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.61, 152.72, 147.35, 147.25, 137.65, 135.68, 129.55, 129.20, 129.13, 128.92, 128.39, 127.34, 126.57, 126.30, 126.03, 77.79, 56.42, 42.77, 26.96, 21.59. HRMS (EI) calcd for C₂₈H₂₆N₂O [M+H]: 407.2118; found: 407.2113.



8-(3-fluorophenyl)-6,6-dimethyl-2,2-diphenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(14)

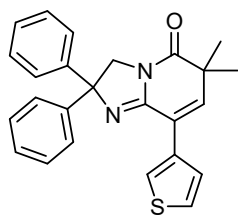
Yellow oil (312.51 mg, 76% yield); ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.68 – 7.59 (m, 2H), 7.54 – 7.48 (m, 1H), 7.44 (d, *J* = 8.2 Hz, 4H), 7.33 (t, *J* = 7.6 Hz, 4H), 7.23 (q, *J* =

7.2, 6.8 Hz, 3H), 6.86 (s, 1H), 4.47 (s, 2H), 1.36 (s, 6H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 171.46, 162.25 (d, $J = 242.5$ Hz), 152.46, 148.42, 147.25, 137.90 (d, $J = 8.0$ Hz), 130.51 (d, $J = 8.4$ Hz), 128.94, 127.37, 126.55, 125.09 (d, $J = 2.8$ Hz), 124.65, 115.85 (d, $J = 22.6$ Hz), 115.40 (d, $J = 20.9$ Hz), 77.87, 56.36, 42.88, 26.82. ^{19}F NMR (376 MHz, DMSO- d_6) δ -113.39. HRMS (EI) calcd for $\text{C}_{27}\text{H}_{23}\text{N}_2\text{OF}$ [M+H]: 411.1867; found: 411.1863.



8-(4-ethynylphenyl)-6,6-dimethyl-2,2-diphenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(15)

Yellow solid (2.28 g, 76% yield); ^1H NMR (400 MHz, DMSO- d_6) δ 7.56 (d, $J = 8.1$ Hz, 2H), 7.34 (d, $J = 8.1$ Hz, 2H), 7.21 (d, $J = 7.5$ Hz, 4H), 7.07 (t, $J = 7.7$ Hz, 4H), 6.96 (t, $J = 7.3$ Hz, 2H), 6.55 (s, 1H), 4.24 (s, 2H), 4.03 (s, 1H), 1.11 (s, 6H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 171.46, 152.49, 148.04, 147.27, 136.14, 132.42, 131.94, 129.30, 128.91, 127.34, 126.58, 125.26, 121.96, 83.75, 82.04, 77.89, 56.42, 42.88, 26.85. HRMS (EI) calcd for $\text{C}_{29}\text{H}_{24}\text{N}_2\text{O}$ [M+H]: 417.1961; found: 417.1964.

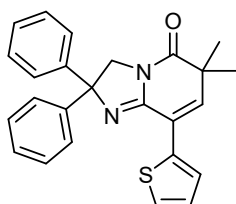


6,6-dimethyl-2,2-diphenyl-8-(thiophen-3-yl)-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(16)

Yellow oil (287.39 mg, 72% yield); ^1H NMR (400 MHz, DMSO- d_6) δ 8.44 (d, $J = 1.6$ Hz, 1H), 7.70 – 7.60 (m, 2H), 7.52 (d, $J = 7.5$ Hz, 4H), 7.33 (t, $J = 7.6$ Hz, 4H), 7.22 (t, $J = 7.4$ Hz, 2H), 7.02 (s, 1H), 4.47 (s, 2H), 1.35 (s, 6H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 171.52, 152.53, 147.37, 145.58, 135.48, 131.08, 128.93, 127.32, 126.58, 126.29, 125.16,

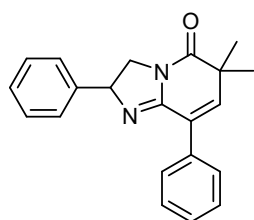
120.42, 77.80, 56.16, 42.47, 26.98. **HRMS** (EI) calcd for C₂₅H₂₂N₂OS [M+H]: 399.1526;

found: 399.1529.



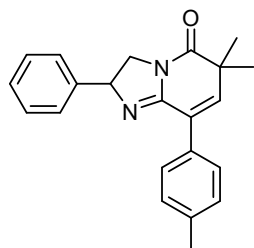
6,6-dimethyl-2,2-diphenyl-8-(thiophen-2-yl)-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(17)

Yellow oil (243.48 mg, 61% yield); **¹H NMR** (400 MHz, DMSO-*d*₆) δ 7.81 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.64 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.56 (dd, *J* = 8.4, 1.3 Hz, 4H), 7.34 (t, *J* = 7.8 Hz, 4H), 7.25 – 7.20 (m, 3H), 7.16 (dd, *J* = 5.2, 3.7 Hz, 1H), 7.05 (s, 1H), 4.50 (s, 2H), 1.35 (s, 6H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 171.41, 151.99, 147.50, 143.96, 136.42, 135.36, 134.42, 128.96, 128.16, 127.42, 127.35, 126.49, 126.37, 119.62, 78.01, 56.54, 42.75, 26.93. **HRMS** (EI) calcd for C₂₅H₂₂N₂OS [M+H]: 399.1526; found: 399.1523.



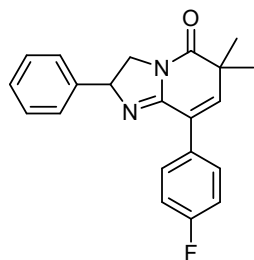
6,6-dimethyl-2,8-diphenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(18)

White solid (225.2 mg, 71% yield); **¹H NMR** (400 MHz, DMSO-*d*₆) δ 7.64 (dd, *J* = 8.1, 1.6 Hz, 2H), 7.43 – 7.33 (m, 5H), 7.32 – 7.27 (m, 3H), 6.70 (s, 1H), 5.35 (dd, *J* = 10.3, 7.4 Hz, 1H), 4.28 (dd, *J* = 11.4, 10.3 Hz, 1H), 3.56 (dd, *J* = 11.4, 7.5 Hz, 1H), 1.39 (s, 6H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 171.50, 154.20, 146.86, 143.37, 135.81, 129.12, 129.08, 128.47, 128.40, 127.78, 127.20, 126.14, 68.48, 50.96, 42.77, 27.17, 26.84. **HRMS** (EI) calcd for C₂₁H₂₀N₂O [M]: 317.1648; found: 317.1642.



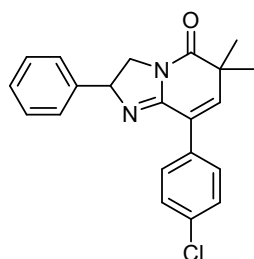
6,6-dimethyl-2-phenyl-8-(p-tolyl)-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(19)

White solid (215.27 mg, 65% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.57 (d, $J = 8.2$ Hz, 2H), 7.42 – 7.35 (m, 2H), 7.34 – 7.27 (m, 3H), 7.21 (d, $J = 7.9$ Hz, 2H), 6.67 (s, 1H), 5.37 (dd, $J = 10.3, 7.5$ Hz, 1H), 4.30 (dd, $J = 11.4, 10.4$ Hz, 1H), 3.57 (dd, $J = 11.4, 7.5$ Hz, 1H), 2.33 (s, 3H), 1.40 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 171.53, 154.28, 146.13, 143.39, 137.80, 132.92, 129.05, 128.99, 128.94, 127.75, 127.16, 126.00, 68.45, 50.93, 42.70, 27.21, 26.87, 21.23. **HRMS** (EI) calcd for $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}$ [$\text{M}+\text{H}$]: 331.1805; found: 331.1803.



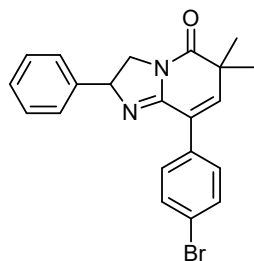
8-(4-fluorophenyl)-6,6-dimethyl-2-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(20)

Yellow solid (191.04 mg, 57% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.74 (ddd, $J = 8.9, 5.5, 3.0$ Hz, 2H), 7.43 – 7.37 (m, 2H), 7.36 – 7.32 (m, 3H), 7.26 (s, 2H), 6.76 (s, 1H), 5.39 (dd, $J = 10.3, 7.5$ Hz, 1H), 4.32 (t, $J = 10.9$ Hz, 1H), 3.64 – 3.56 (m, 1H), 1.42 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 171.47, 162.40 (d, $J = 245.0$ Hz), 154.19, 146.84, 143.32, 135.47 (d, $J = 8.8$ Hz), 131.16 (d, $J = 8.2$ Hz), 129.07, 127.79, 127.21, 125.06, 115.24 (d, $J = 21.3$ Hz), 68.49, 50.99, 42.79, 27.14, 26.79. $^{19}\text{F NMR}$ (376 MHz, $\text{DMSO-}d_6$) δ -114.08. **HRMS** (EI) calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{OF}$ [$\text{M}+\text{H}$]: 335.1554; found: 335.1557.



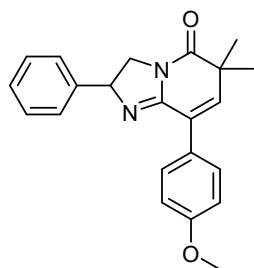
8-(4-chlorophenyl)-6,6-dimethyl-2-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(21)

Light yellow oil (175.56 mg, 50% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.69 (d, $J = 8.5$ Hz, 2H), 7.50 – 7.43 (m, 2H), 7.41 – 7.34 (m, 2H), 7.33 – 7.26 (m, 3H), 6.76 (s, 1H), 5.36 (dd, $J = 10.4, 7.5$ Hz, 1H), 4.29 (t, $J = 10.9$ Hz, 1H), 3.56 (dd, $J = 11.4, 7.5$ Hz, 1H), 1.39 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 171.40, 154.03, 147.27, 143.27, 134.56, 133.24, 130.89, 129.07, 128.42, 127.80, 127.22, 124.97, 68.51, 50.97, 42.85, 27.10, 26.74. **HRMS** (EI) calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{OCl}$ $[\text{M}+\text{H}]$: 351.1259; found: 351.1253.



8-(4-bromophenyl)-6,6-dimethyl-2-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(22)

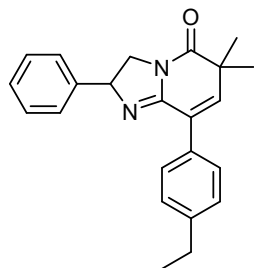
Light yellow oil (168.54 mg, 48% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.45 – 7.33 (m, 4H), 7.10 (dq, $J = 16.3, 8.7, 8.1$ Hz, 5H), 6.53 (s, 1H), 5.13 (dd, $J = 10.3, 7.5$ Hz, 1H), 4.06 (t, $J = 10.9$ Hz, 1H), 3.34 (dd, $J = 11.4, 7.6$ Hz, 1H), 1.16 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 171.36, 153.98, 147.23, 143.27, 134.92, 131.34, 131.20, 129.05, 127.78, 127.21, 125.08, 121.90, 68.53, 50.98, 42.86, 27.10, 26.74. **HRMS** (EI) calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{OBr}$ $[\text{M}+\text{H}]$: 395.0754; found: 395.0758.



8-(4-methoxyphenyl)-6,6-dimethyl-2-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(23)

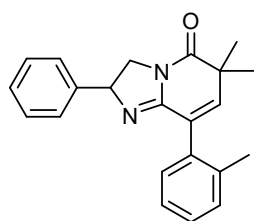
Yellow solid (177.06 mg, 51% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.70 – 7.55 (m, 2H), 7.44 – 7.33 (m, 2H), 7.33 – 7.23 (m, 3H), 7.01 – 6.88 (m, 2H), 6.70 – 6.56 (m, 1H), 5.35 (dd, $J = 10.3, 7.5$ Hz, 1H), 4.28 (dd, $J = 11.4, 10.4$ Hz, 1H), 3.76 (s, 3H), 3.56 (dd, $J = 11.4, 7.5$ Hz, 1H), 1.38 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 171.58, 159.60,

154.39, 145.41, 143.41, 130.30, 129.05, 128.06, 127.75, 127.18, 125.55, 113.79, 68.45, 55.59, 50.93, 42.67, 27.26, 26.92. **HRMS** (EI) calcd for C₂₂H₂₂N₂O₂ [M+H]: 347.1754; found: 347.1755.



8-(4-ethylphenyl)-6,6-dimethyl-2-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(24)

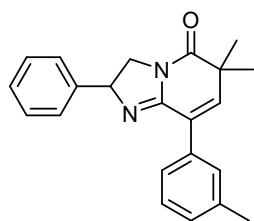
Yellow solid (214.02 mg, 62% yield); **¹H NMR** (400 MHz, DMSO-*d*₆) δ 7.56 (d, *J* = 7.8 Hz, 2H), 7.41 – 7.33 (m, 2H), 7.33 – 7.26 (m, 3H), 7.22 (d, *J* = 7.9 Hz, 2H), 6.65 (s, 1H), 5.35 (dd, *J* = 10.4, 7.5 Hz, 1H), 4.28 (t, *J* = 10.9 Hz, 1H), 3.56 (dd, *J* = 11.4, 7.5 Hz, 1H), 2.60 (q, *J* = 7.5 Hz, 2H), 1.38 (s, 6H), 1.18 (t, *J* = 7.6 Hz, 3H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 171.53, 154.29, 146.21, 144.13, 143.38, 133.20, 129.06, 127.77, 127.18, 126.03, 68.46, 50.94, 42.71, 28.38, 27.22, 26.88, 16.08. **HRMS** (EI) calcd for C₂₃H₂₄N₂O [M+H]: 345.1961; found: 345.1961.



6,6-dimethyl-2-phenyl-8-(o-tolyl)-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(25)

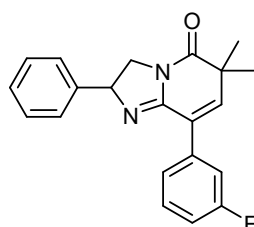
White solid (228.51 mg, 69% yield); **¹H NMR** (400 MHz, DMSO-*d*₆) δ 7.34 (ddd, *J* = 7.4, 6.3, 1.3 Hz, 2H), 7.27 – 7.21 (m, 5H), 7.19 (dd, *J* = 4.7, 1.3 Hz, 2H), 6.47 – 6.39 (m, 1H), 5.25 (dd, *J* = 10.3, 7.4 Hz, 1H), 4.28 (dd, *J* = 11.4, 10.3 Hz, 1H), 3.57 (dd, *J* = 11.4, 7.5 Hz, 1H), 2.23 (s, 3H), 1.39 (d, *J* = 2.1 Hz, 6H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 171.66, 154.46, 147.69, 143.33, 136.65, 136.22, 130.24, 130.17, 129.01, 128.39, 127.77,

127.19, 126.78, 125.88, 68.45, 51.09, 42.67, 27.07, 26.84, 20.18. **HRMS** (EI) calcd for $C_{22}H_{22}N_2O$ [M+H]: 331.1805; found: 331.1807.



6,6-dimethyl-2-phenyl-8-(m-tolyl)-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(26)

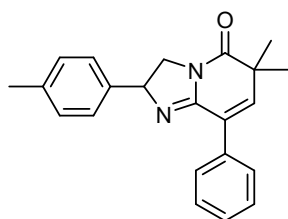
White solid (225.21 mg, 68% yield); 1H NMR (400 MHz, DMSO- d_6) δ 7.52 – 7.44 (m, 2H), 7.42 – 7.36 (m, 2H), 7.33 – 7.26 (m, 4H), 7.18 (d, J = 7.5 Hz, 1H), 6.69 (s, 1H), 5.38 (dd, J = 10.3, 7.4 Hz, 1H), 4.30 (dd, J = 11.4, 10.4 Hz, 1H), 3.58 (dd, J = 11.4, 7.4 Hz, 1H), 2.35 (s, 3H), 1.41 (s, 6H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 171.52, 154.25, 146.70, 143.39, 137.47, 135.80, 129.55, 129.06, 128.24, 127.77, 127.16, 126.43, 126.27, 68.45, 50.98, 42.73, 27.17, 26.86, 21.52. **HRMS** (EI) calcd for $C_{22}H_{22}N_2O$ [M+H]: 331.1805; found: 331.1802.



8-(3-fluorophenyl)-6,6-dimethyl-2-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(27)

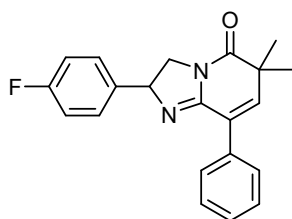
Yellow oil (194.39 mg, 58% yield); 1H NMR (400 MHz, DMSO- d_6) δ 7.58 – 7.50 (m, 2H), 7.43 (td, J = 8.2, 6.2 Hz, 1H), 7.40 – 7.34 (m, 2H), 7.33 – 7.28 (m, 3H), 7.19 (td, J = 6.6, 1.1 Hz, 1H), 6.82 (s, 1H), 5.37 (dd, J = 10.3, 7.5 Hz, 1H), 4.29 (dd, J = 11.4, 10.4 Hz, 1H), 3.57 (dd, J = 11.4, 7.5 Hz, 1H), 1.40 (s, 6H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 171.39, 162.15 (d, J = 242.6 Hz), 153.94, 147.72, 143.25, 137.98 (d, J = 8.6 Hz), 130.33 (d, J = 8.4 Hz), 129.07, 127.80, 127.18, 125.10 (d, J = 2.7 Hz), 124.87 (d, J = 2.8 Hz), 115.97 (d, J = 22.7 Hz), 115.24 (d, J = 20.9 Hz), 68.52, 50.95, 42.84, 27.04, 26.69. ^{19}F

NMR (376 MHz, DMSO-*d*₆) δ -113.64. **HRMS** (EI) calcd for C₂₁H₁₉N₂OF [M+H]: 335.1554; found: 335.1559.



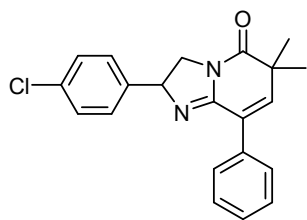
6,6-dimethyl-8-phenyl-2-(p-tolyl)-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(28)

Yellow oil (228.51 mg, 69% yield); **¹H NMR** (400 MHz, DMSO-*d*₆) δ 7.69 – 7.59 (m, 2H), 7.42 – 7.33 (m, 3H), 7.21 – 7.12 (m, 4H), 6.69 (s, 1H), 5.30 (dd, *J* = 10.3, 7.4 Hz, 1H), 4.25 (dd, *J* = 11.4, 10.4 Hz, 1H), 3.54 (dd, *J* = 11.4, 7.5 Hz, 1H), 2.28 (s, 3H), 1.39 (s, 6H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 171.49, 154.02, 146.74, 140.41, 136.89, 135.82, 129.60, 129.12, 128.46, 128.38, 127.10, 126.18, 68.29, 50.98, 42.74, 27.18, 26.84, 21.17. **HRMS** (EI) calcd for C₂₂H₂₂N₂O [M+H]: 331.1805; found: 331.1808.



2-(4-fluorophenyl)-6,6-dimethyl-8-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(29)

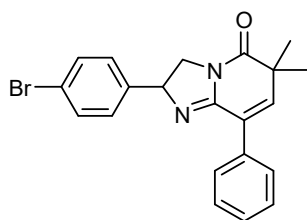
Yellow oil (204.44 mg, 61% yield); **¹H NMR** (400 MHz, DMSO-*d*₆) δ 7.55 (dd, *J* = 8.1, 1.6 Hz, 2H), 7.33 – 7.22 (m, 5H), 7.09 (t, *J* = 8.9 Hz, 2H), 6.60 (s, 1H), 5.27 (dd, *J* = 10.4, 7.6 Hz, 1H), 4.19 (dd, *J* = 11.4, 10.4 Hz, 1H), 3.45 (dd, *J* = 11.5, 7.7 Hz, 1H), 1.30 (s, 6H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 171.53, 161.88 (d, *J* = 242.8 Hz), 154.36, 146.92, 139.56 (d, *J* = 3.2 Hz), 135.81, 129.22 (d, *J* = 8.1 Hz), 129.13, 128.47, 128.39, 126.17, 115.77 (d, *J* = 21.1 Hz), 67.78, 50.96, 42.77, 27.17, 26.77. **¹⁹F NMR** (376 MHz, DMSO-*d*₆) δ -115.37. **HRMS** (EI) calcd for C₂₁H₁₉N₂OF [M+H]: 335.1554; found: 335.1557.



2-(4-chlorophenyl)-6,6-dimethyl-8-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(30)

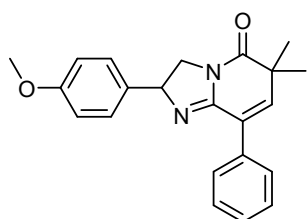
Yellow oil (193.12 mg, 55% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.70 (d, $J = 8.5$ Hz, 2H), 7.47 (d, $J = 8.6$ Hz, 2H), 7.40 – 7.35 (m, 2H), 7.34 – 7.28 (m, 3H), 6.77 (s, 1H), 5.36 (dd, $J = 10.4, 7.5$ Hz, 1H), 4.30 (t, $J = 10.9$ Hz, 1H), 3.57 (dd, $J = 11.4, 7.5$ Hz, 1H), 1.40 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 171.37, 154.00, 147.24, 143.24, 134.53, 133.21, 130.86, 129.04, 128.39, 127.77, 127.19, 124.94, 68.48, 50.94, 42.81, 27.07, 26.71.

HRMS (EI) calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{OCl}$ [M+H]: 351.1259; found: 351.1259.



2-(4-bromophenyl)-6,6-dimethyl-8-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(31)

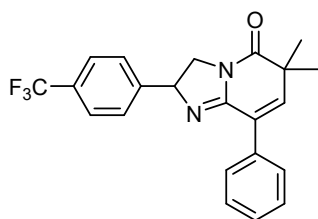
Yellow oil (213.34 mg, 54% yield); $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 7.44 – 7.32 (m, 4H), 7.10 (dq, $J = 16.3, 8.7, 8.1$ Hz, 5H), 6.53 (s, 1H), 5.13 (dd, $J = 10.3, 7.5$ Hz, 1H), 4.06 (t, $J = 10.9$ Hz, 1H), 3.34 (dd, $J = 11.4, 7.6$ Hz, 1H), 1.16 (s, 6H). $^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 171.38, 154.00, 147.26, 143.29, 134.95, 131.37, 131.22, 129.08, 127.81, 127.23, 125.11, 121.92, 68.55, 51.00, 42.88, 27.13, 26.76. **HRMS** (EI) calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{OBr}$ [M+H]: 395.0754; found: 395.0759.



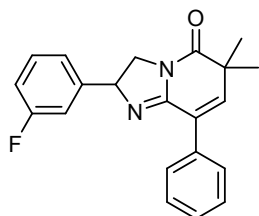
2-(4-methoxyphenyl)-6,6-dimethyl-8-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-

5(3H)-one:(32)

Light yellow oily (177.06 mg, 51% yield); ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.66 (dd, *J* = 8.1, 1.6 Hz, 2H), 7.41 – 7.31 (m, 3H), 7.26 – 7.20 (m, 2H), 6.94 – 6.87 (m, 2H), 6.68 (s, 1H), 5.30 (dd, *J* = 10.2, 7.4 Hz, 1H), 4.25 (dd, *J* = 11.4, 10.3 Hz, 1H), 3.72 (s, 3H), 3.56 (dd, *J* = 11.4, 7.5 Hz, 1H), 1.40 (s, 6H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.47, 158.98, 153.90, 146.66, 135.85, 135.38, 129.13, 128.45, 128.36, 128.34, 126.26, 114.41, 68.06, 55.50, 51.05, 42.74, 27.18, 26.85. HRMS (EI) calcd for C₂₂H₂₂N₂O₂ [M+H]: 347.1754; found: 347.1757.

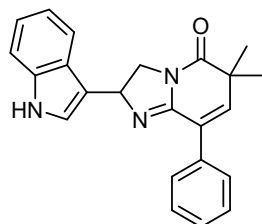
**6,6-dimethyl-8-phenyl-2-(4-(trifluoromethyl)phenyl)-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(33)**

Yellow oil (215.69 mg, 56% yield); ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.73 (d, *J* = 7.7 Hz, 2H), 7.66 – 7.63 (m, 2H), 7.56 (d, *J* = 8.1 Hz, 2H), 7.42 – 7.36 (m, 3H), 6.72 (d, *J* = 0.6 Hz, 1H), 5.47 (dd, *J* = 10.4, 7.6 Hz, 1H), 4.33 (dd, *J* = 11.4, 10.5 Hz, 1H), 3.58 (dd, *J* = 11.5, 7.7 Hz, 1H), 1.39 (d, *J* = 3.0 Hz, 6H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.55, 154.85, 147.94, 147.17, 135.75, 129.13, 128.51, 128.42, 128.14, 126.17 – 125.88 (m), 67.96, 50.69, 42.82, 27.17, 26.75. ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ -60.85. HRMS (EI) calcd for C₂₂H₁₉N₂OF₃ [M+H]: 385.1522; found: 385.1525.

**2-(3-fluorophenyl)-6,6-dimethyl-8-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(34)**

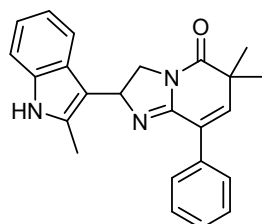
Yellow oil (194.39 mg, 58% yield); ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.51 – 7.38 (m, 2H), 7.23 – 7.13 (m, 4H), 7.01 – 6.96 (m, 2H), 6.92 (td, *J* = 7.5, 2.1 Hz, 1H), 6.51 (s, 1H),

5.18 (dd, $J = 10.4, 7.7$ Hz, 1H), 4.10 (dd, $J = 11.4, 10.4$ Hz, 1H), 3.36 (dd, $J = 11.4, 7.7$ Hz, 1H), 1.19 (s, 6H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 171.53, 162.76 (d, $J = 243.5$ Hz), 154.66, 147.04, 146.20 (d, $J = 7.3$ Hz), 135.79, 131.04 (d, $J = 8.1$ Hz), 129.12, 128.48, 128.40, 126.11, 123.32 (d, $J = 2.8$ Hz), 114.57 (d, $J = 21.0$ Hz), 114.10 (d, $J = 21.7$ Hz), 67.92, 50.78, 42.78, 27.21, 26.71. ^{19}F NMR (376 MHz, DMSO- d_6) δ -112.84. HRMS (EI) calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{OF}$ [M+H]: 335.1554; found: 335.1558.



2-(1H-indol-3-yl)-6,6-dimethyl-8-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(35)

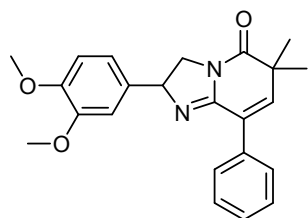
White solid (227.95 mg, 64% yield); ^1H NMR (400 MHz, DMSO- d_6) δ 11.03 (s, 1H), 7.62 (dd, $J = 7.9, 1.7$ Hz, 2H), 7.44 – 7.31 (m, 6H), 7.14 – 7.06 (m, 1H), 7.02 – 6.95 (m, 1H), 6.70 (s, 1H), 5.59 (dd, $J = 10.2, 7.2$ Hz, 1H), 4.42 – 4.22 (m, 1H), 3.79 (dd, $J = 11.3, 7.2$ Hz, 1H), 1.43 (d, $J = 4.9$ Hz, 6H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 171.53, 153.17, 146.41, 137.24, 135.87, 129.09, 128.44, 128.35, 126.32, 125.92, 123.32, 121.75, 119.23, 118.83, 116.21, 112.30, 62.49, 49.52, 42.70, 27.23, 27.11. HRMS (EI) calcd for $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}$ [M+H]: 356.1757; found: 356.1753.



6,6-dimethyl-2-(2-methyl-1H-indol-3-yl)-8-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(36)

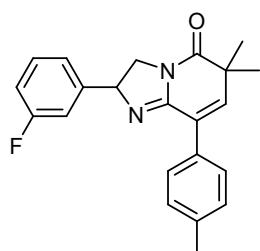
White solid (229.52 mg, 62% yield); ^1H NMR (400 MHz, DMSO- d_6) δ 11.02 (s, 1H), 7.51 (d, $J = 8.1$ Hz, 2H), 7.39 (d, $J = 8.1$ Hz, 2H), 7.32 (d, $J = 2.4$ Hz, 1H), 7.15 (d, $J = 8.0$ Hz, 2H), 7.12 – 7.06 (m, 1H), 7.00 – 6.94 (m, 1H), 6.65 (s, 1H), 5.57 (dd, $J = 10.2, 7.2$ Hz, 1H), 4.32 – 4.18 (m, 1H), 3.77 (dd, $J = 11.3, 7.2$ Hz, 1H), 2.28 (s, 3H), 1.41 (d, $J = 4.5$ Hz,

6H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 171.57, 153.24, 145.70, 137.75, 137.23, 132.97, 128.95, 128.90, 126.13, 125.92, 123.26, 121.74, 119.21, 118.85, 116.24, 112.28, 62.46, 49.47, 42.64, 27.25, 27.15, 21.21. HRMS (EI) calcd for $\text{C}_{24}\text{H}_{23}\text{N}_3\text{O}$ [M+H]: 370.1914; found: 370.1918.



2-(3,4-dimethoxyphenyl)-6,6-dimethyl-8-phenyl-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(37)

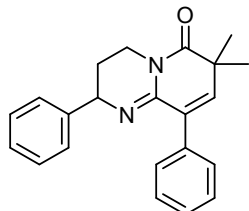
Light yellow oily (203.68 mg, 54% yield); ^1H NMR (400 MHz, DMSO- d_6) δ 7.71 – 7.61 (m, 2H), 7.42 – 7.34 (m, 3H), 6.95 – 6.90 (m, 2H), 6.82 (dd, J = 8.3, 2.0 Hz, 1H), 6.68 (s, 1H), 5.29 (dd, J = 10.2, 7.5 Hz, 1H), 4.25 (t, J = 10.8 Hz, 1H), 3.75 (d, J = 9.4 Hz, 6H), 3.59 (dd, J = 11.4, 7.6 Hz, 1H), 1.39 (d, J = 2.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 171.50, 153.93, 149.27, 148.56, 146.67, 135.87, 135.82, 129.12, 128.46, 128.38, 126.27, 119.10, 112.40, 111.22, 68.28, 56.01, 55.95, 50.96, 42.74, 27.18, 26.85. HRMS (EI) calcd for $\text{C}_{23}\text{H}_{24}\text{N}_2\text{O}_3$ [M+H]: 377.1860; found: 377.1866.



2-(3-fluorophenyl)-6,6-dimethyl-8-(p-tolyl)-2,6-dihydroimidazo[1,2-a]pyridin-5(3H)-one:(38)

Yellow oil (195.54 mg, 56% yield); ^1H NMR (400 MHz, DMSO- d_6) δ 7.51 – 7.42 (m, 2H), 7.34 (td, J = 7.9, 6.0 Hz, 1H), 7.15 – 7.00 (m, 6H), 6.58 (s, 1H), 5.30 (dd, J = 10.4, 7.7 Hz, 1H), 4.21 (dd, J = 11.4, 10.4 Hz, 1H), 3.47 (dd, J = 11.4, 7.7 Hz, 1H), 2.24 (s, 3H), 1.30 (s, 6H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 171.59, 162.77 (d, J = 243.4 Hz), 154.74, 146.36, 146.24 (d, J = 6.7 Hz), 137.83, 132.91, 131.05 (d, J = 8.1 Hz), 128.98, 125.94,

123.30 (d, $J=2.8$ Hz), 114.55 (d, $J=21.0$ Hz), 114.07 (d, $J=21.8$ Hz), 67.88, 50.73, 42.72, 27.24, 26.75, 21.22. ^{19}F NMR (376 MHz, $\text{DMSO-}d_6$) δ -112.87. HRMS (EI) calcd for $\text{C}_{22}\text{H}_{21}\text{N}_2\text{OF}$ [M+H]: 349.1711; found: 349.1718.



7,7-dimethyl-2,9-diphenyl-2,3,4,7-tetrahydro-6H-pyrido[1,2-a]pyrimidin-6-one:(39)

Light yellow oily (135.78 mg, 41% yield); ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 7.47 – 7.41 (m, 2H), 7.35 – 7.25 (m, 7H), 7.23 – 7.17 (m, 1H), 6.39 (s, 1H), 4.60 (dd, $J=9.4, 4.1$ Hz, 1H), 3.93 (dt, $J=13.2, 4.5$ Hz, 1H), 3.58 (ddd, $J=13.2, 11.1, 4.3$ Hz, 1H), 2.26 (dq, $J=13.0, 4.3$ Hz, 1H), 1.63 (dddd, $J=13.8, 11.0, 9.4, 4.7$ Hz, 1H), 1.37 (d, $J=2.9$ Hz, 6H). ^{13}C NMR (101 MHz, $\text{DMSO-}d_6$) δ 174.12, 147.07, 144.88, 141.89, 138.15, 132.27, 130.10, 128.59, 127.81, 127.68, 126.89, 56.97, 40.58, 39.67, 29.13, 27.77, 27.58. HRMS (EI) calcd for $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}$ [M+H]: 331.1805; found: 331.1809.

7. Crystal Data and Structure Refinements

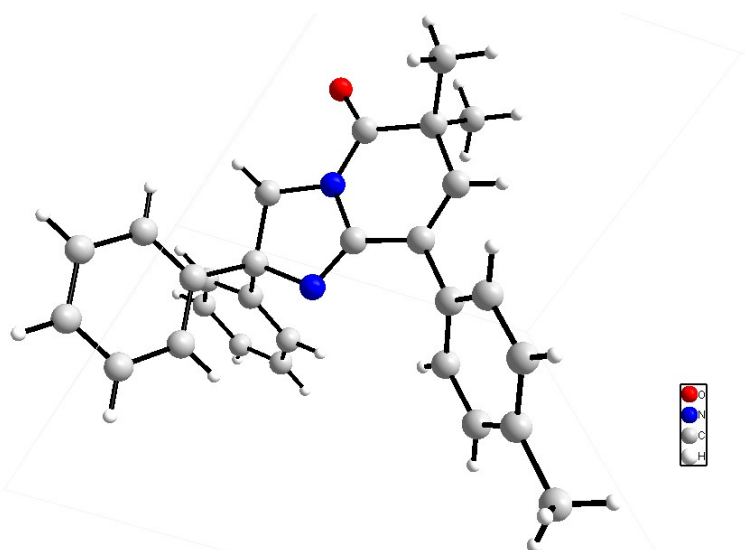


Figure 9 Structure of **3a** by X-Ray crystallographic (CCDC = 2263771)

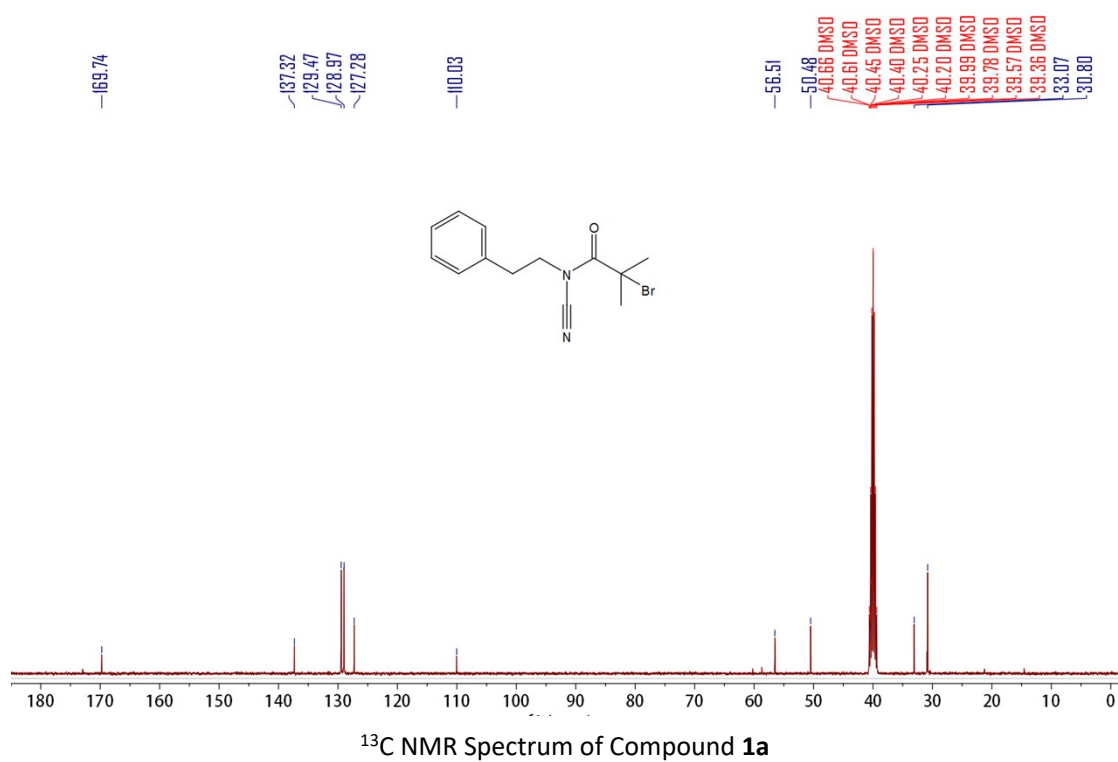
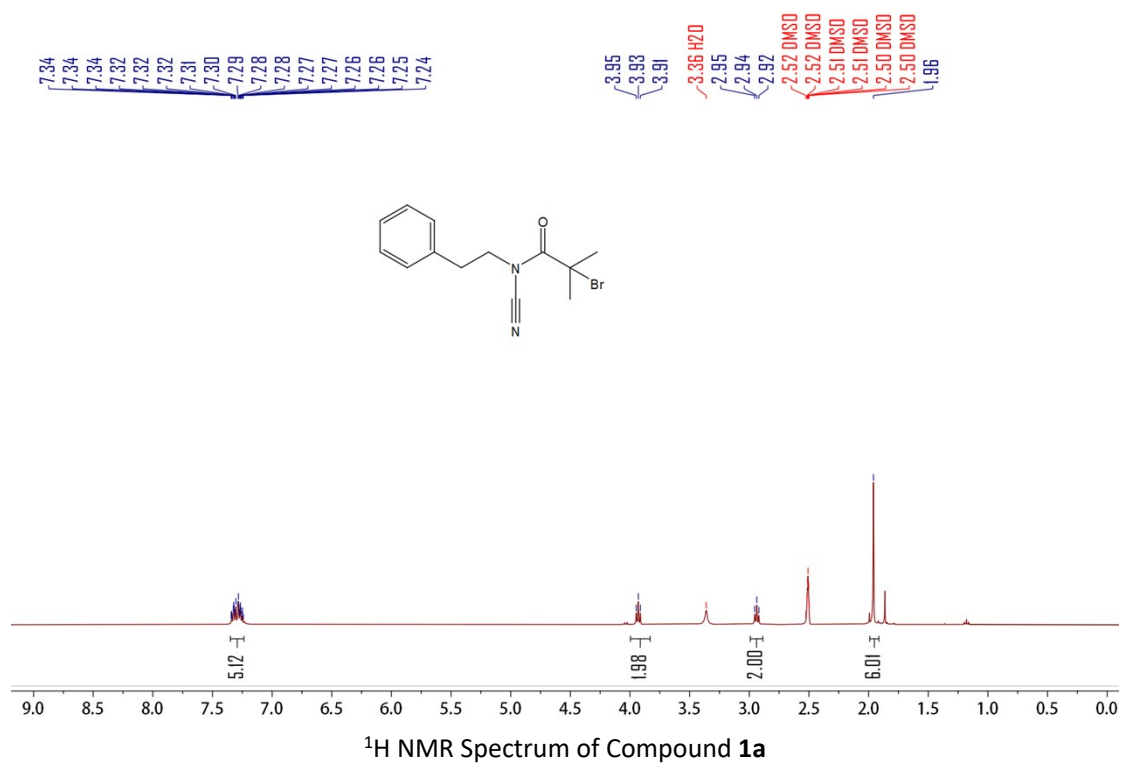
Single crystal suitable for X-ray diffraction was obtained by slow evaporation of a saturated solution of compound **3a** (cyclohexane/CH₂Cl₂) in a loosely capped vial.

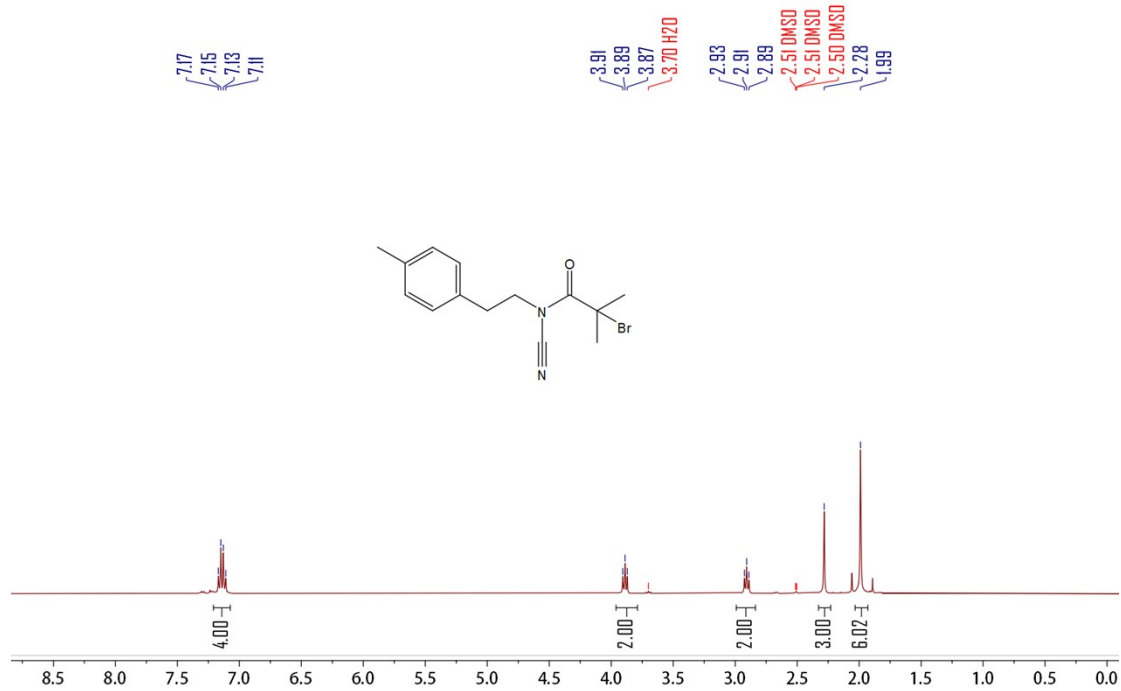
Table 11 Crystal data and structure refinement for **3a**

Empirical formula	C ₂₀ H ₁₉ NO
Formula weight	406.51
Temperature/K	193
Crystal system	monoclinic
Space group	P21/c
a/Å	11.9263(8)
b/Å	17.9508(11)
c/Å	10.8524(8)
α/°	90
β/°	106.642(2)
γ/°	90
Volume/Å ³	2226.0(3)
Z	4
ρ _{calc} /cm ³	1.213
μ/mm ⁻¹	0.074
F(000)	864.0
Crystal size/mm ³	0.13 × 0.12 × 0.1
Radiation	MoKα (λ = 0.71073)
2θ range for data collection/°	4.528 to 55.03
Index ranges	-15 ≤ h ≤ 13, -23 ≤ k ≤ 23, -13 ≤ l ≤ 14

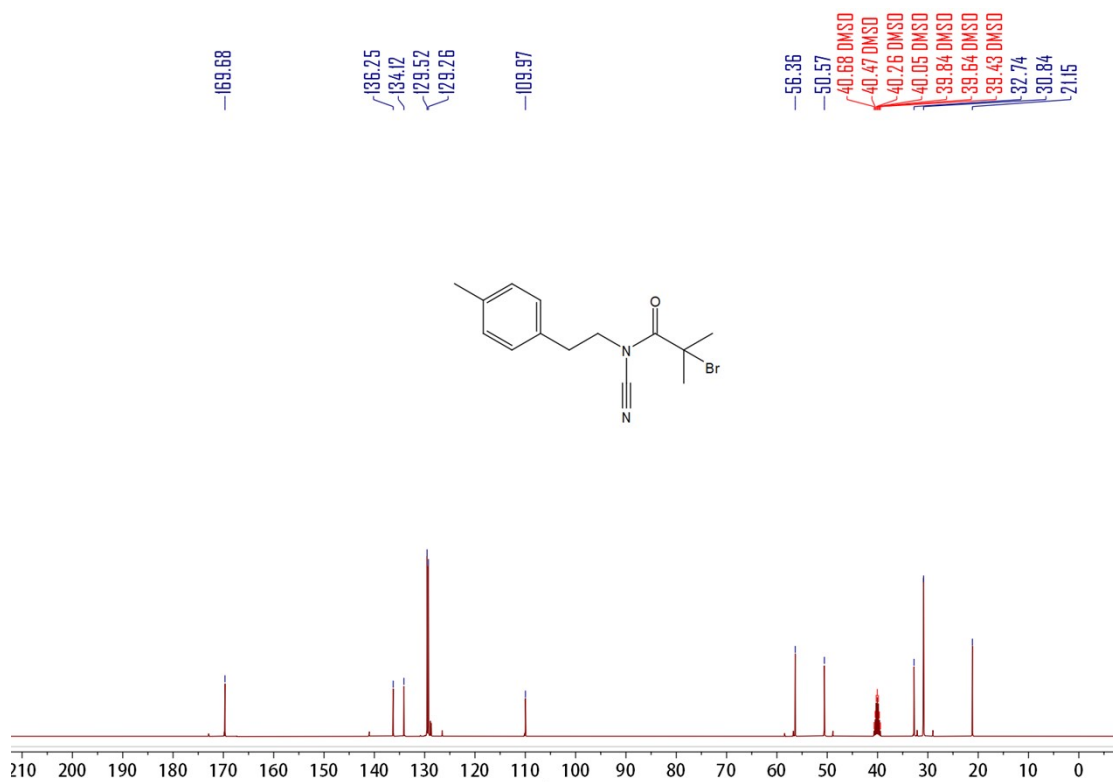
Reflections collected	21000
Independent reflections	5107 [Rint = 0.0597, Rsigma = 0.0564]
Data/restraints/parameters	5107/0/283
Final R indexes [I>2σ (I)]	R1 = 0.0573, wR2 = 0.1164
Final R indexes [all data]	R1 = 0.0998, wR2 = 0.1354
Largest diff. peak/hole / e Å ⁻³	0.23/-0.20

8. ^1H NMR and ^{13}C NMR spectra

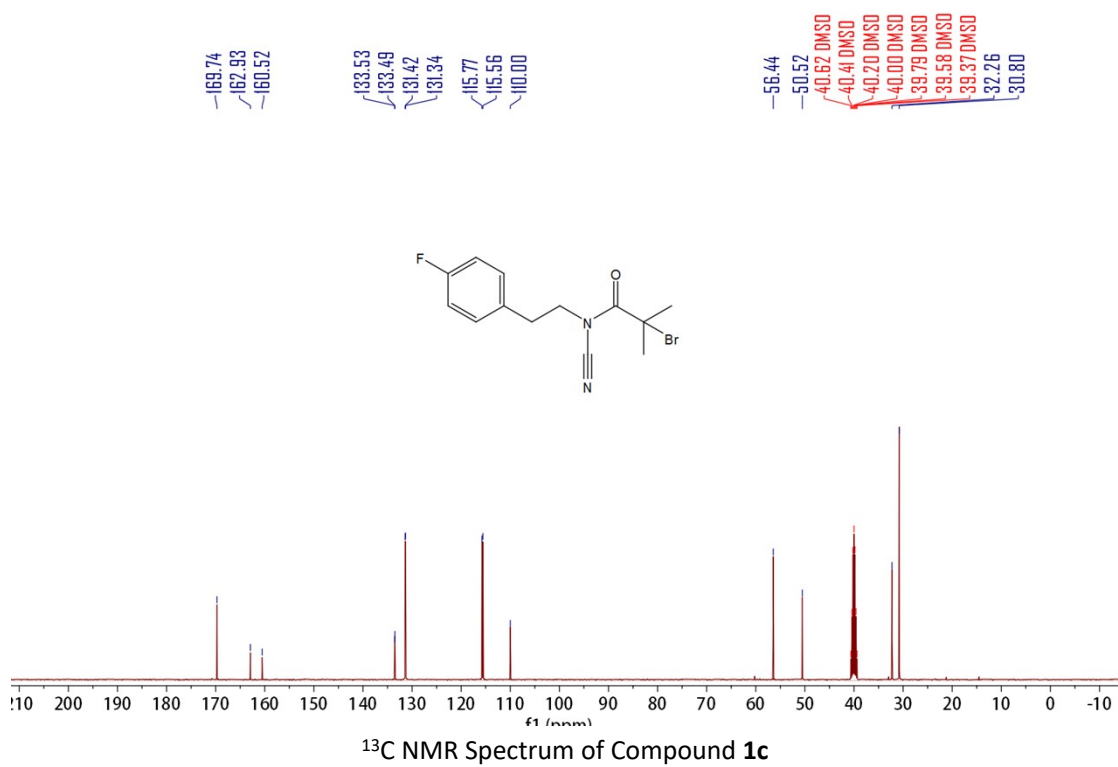
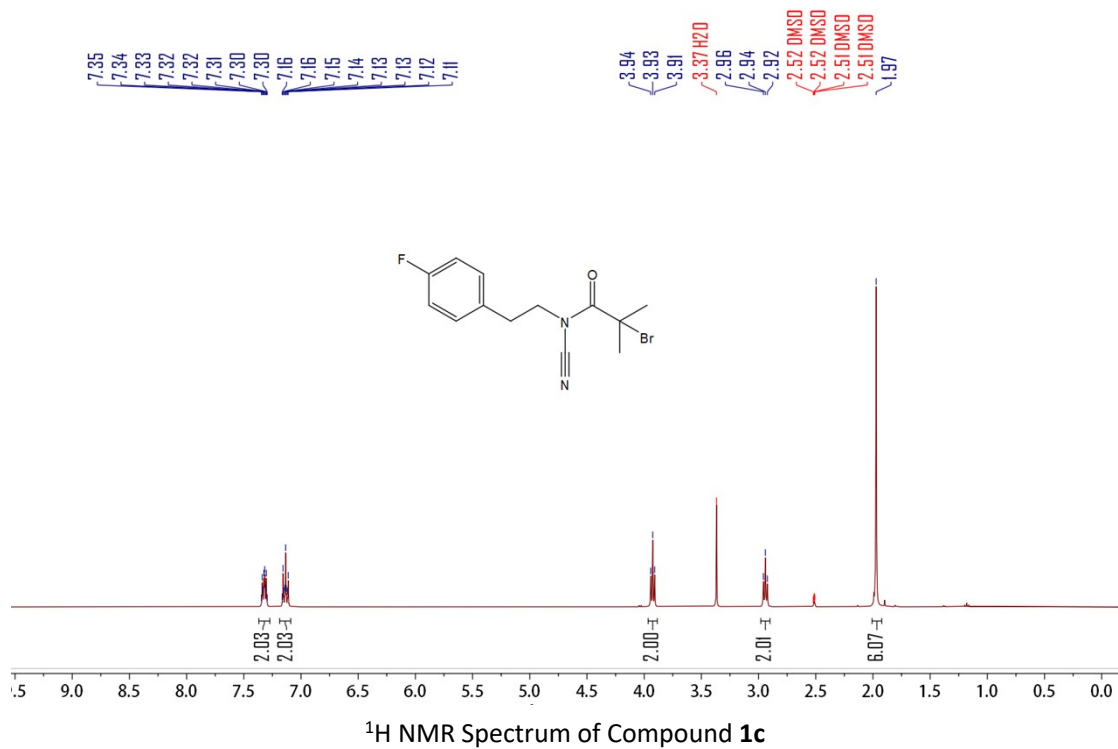


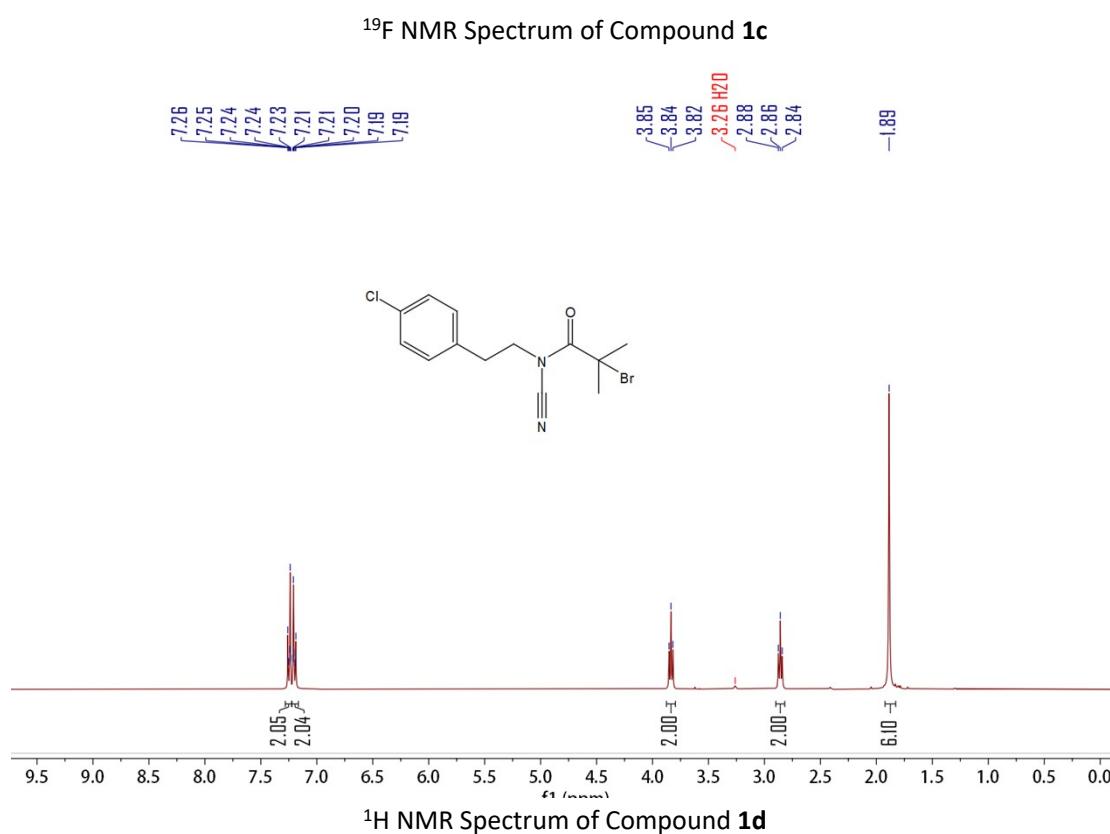
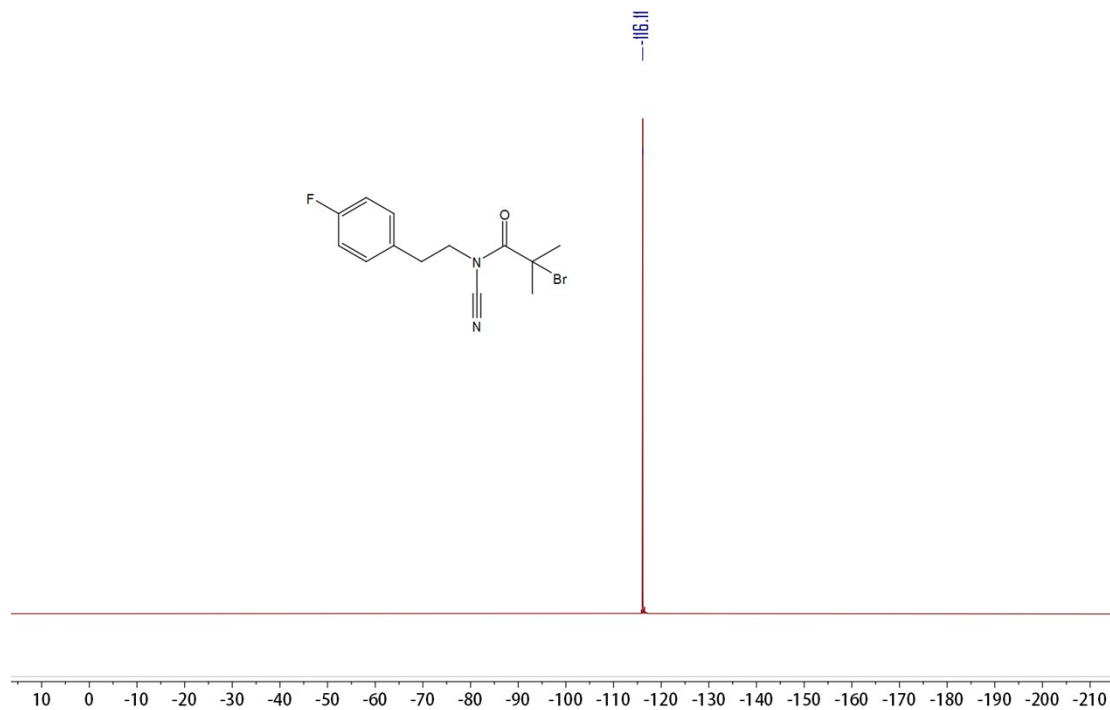


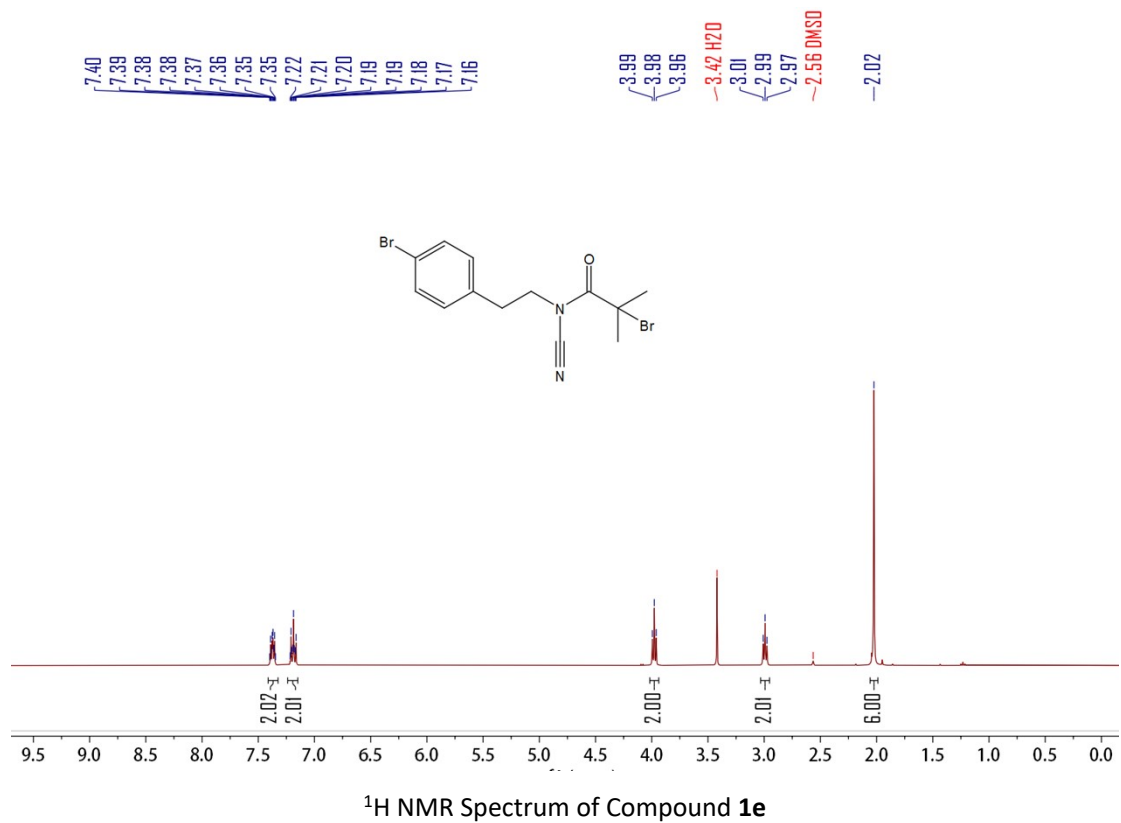
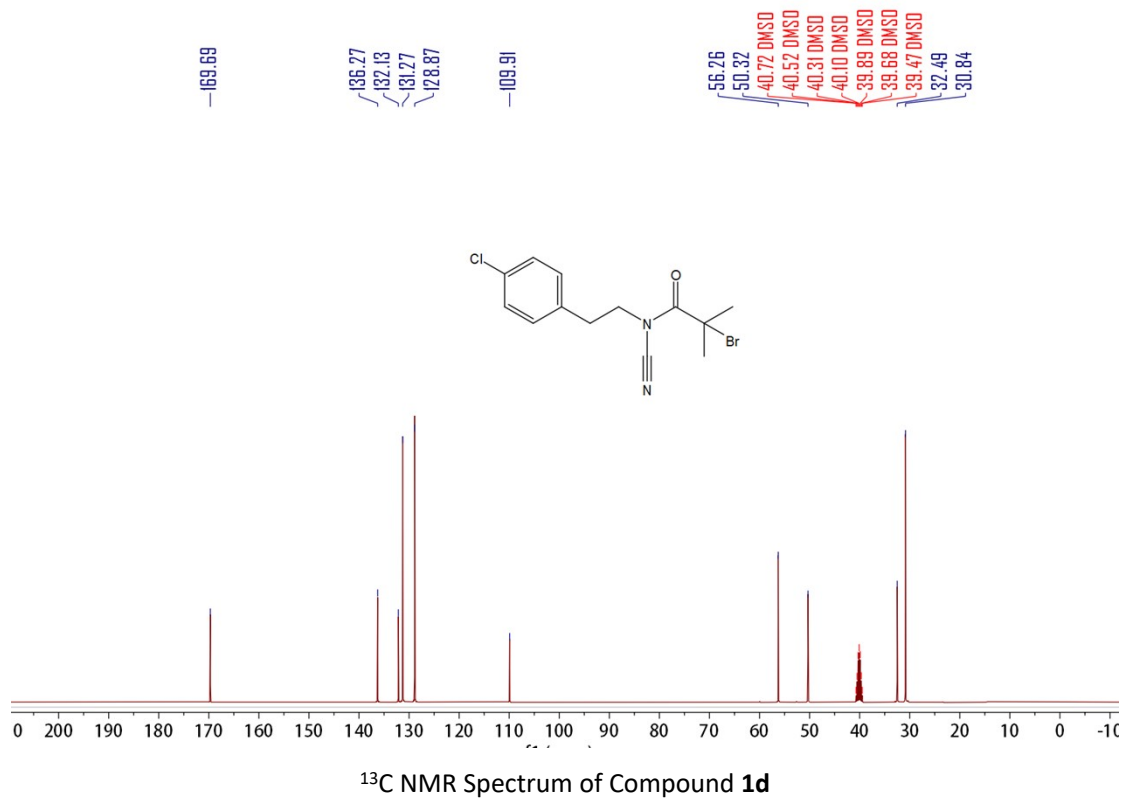
¹H NMR Spectrum of Compound 1b

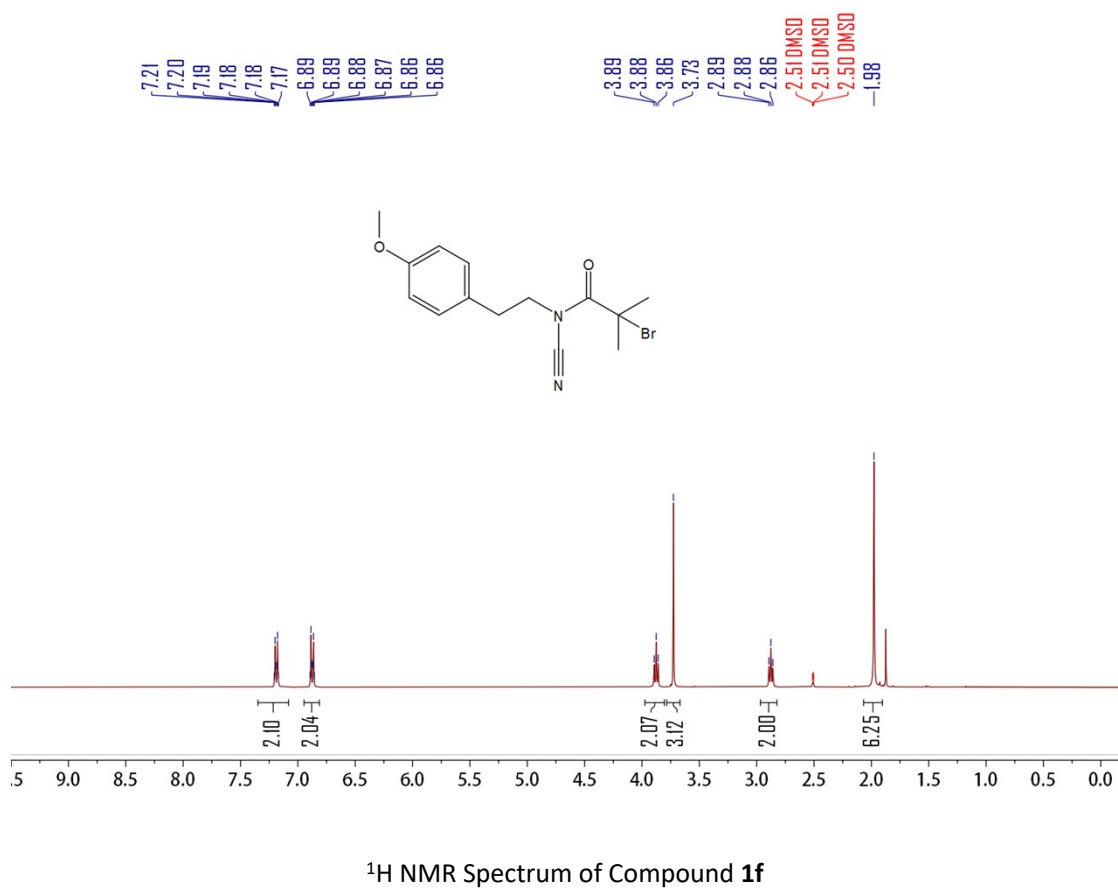
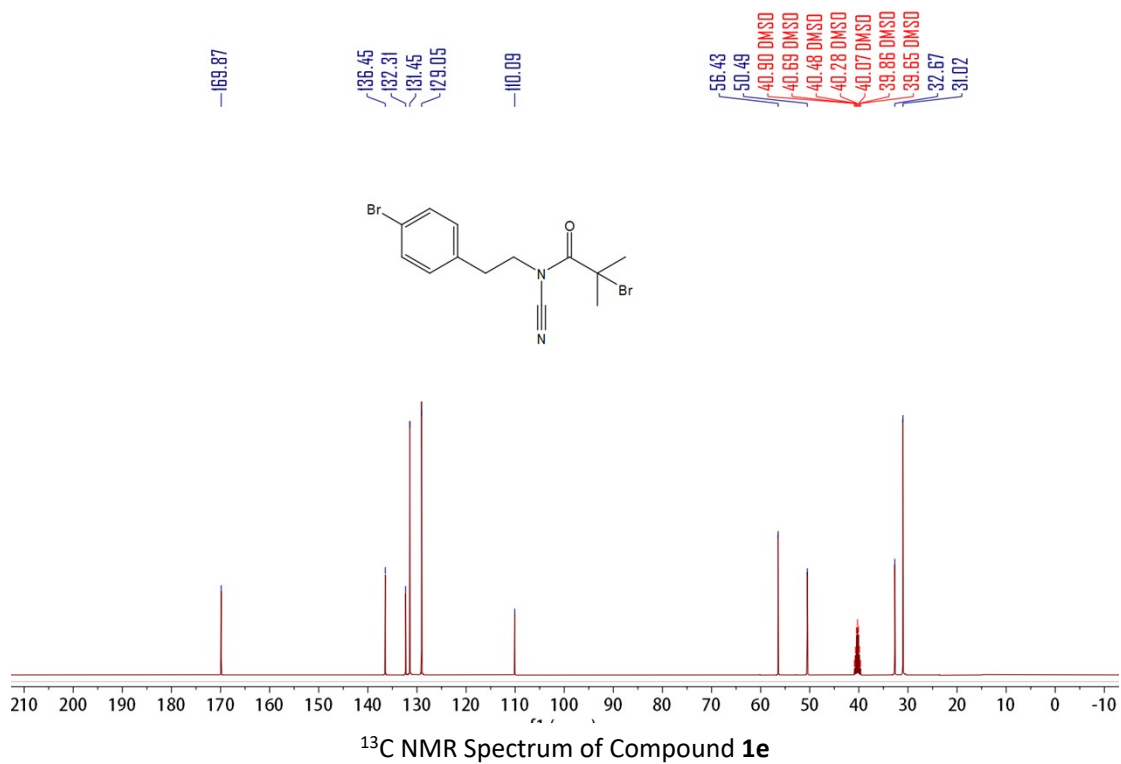


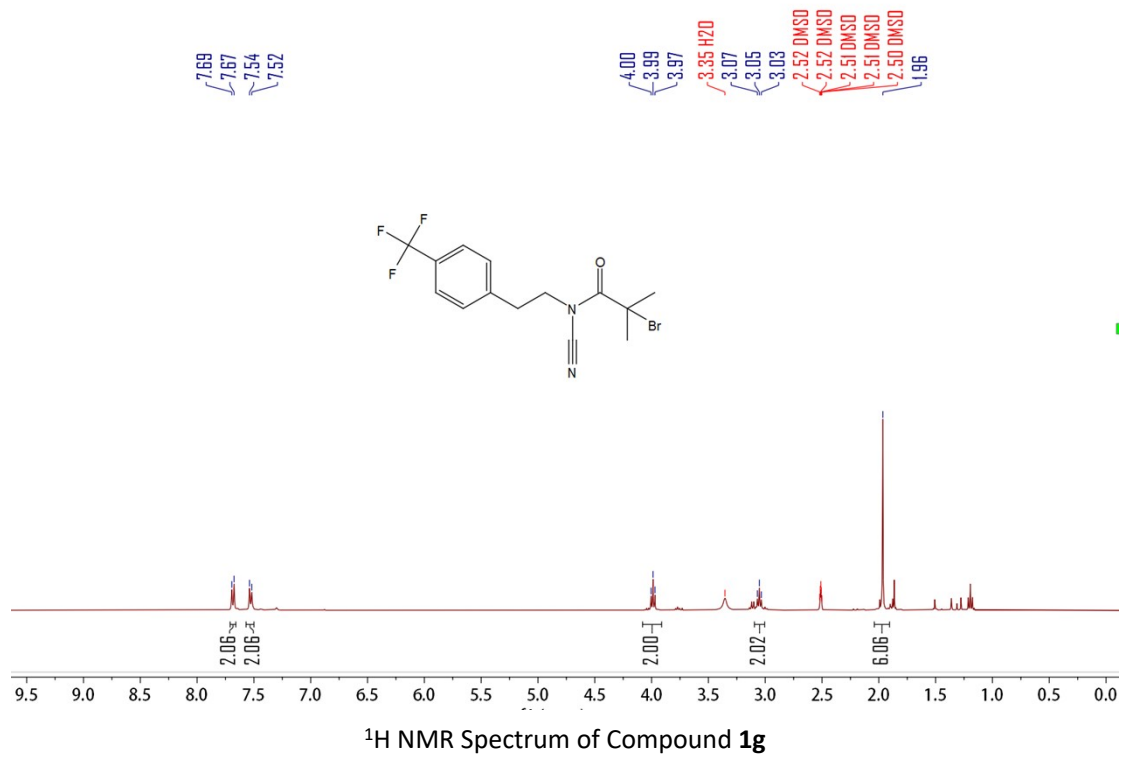
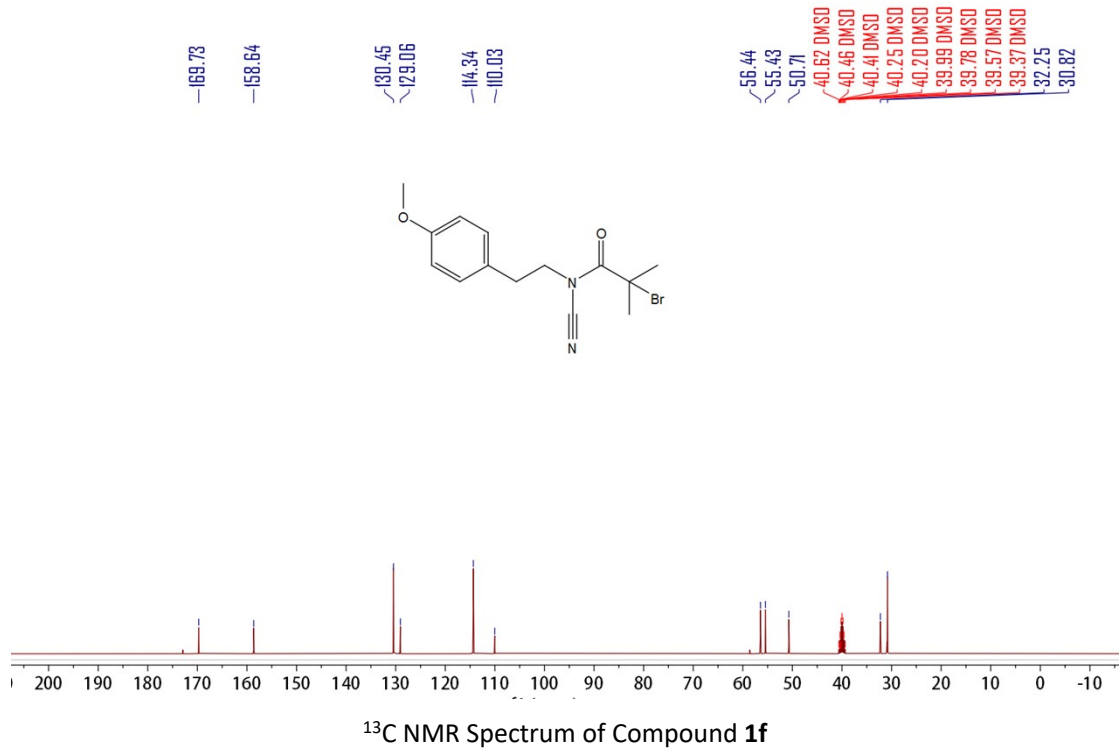
¹³C NMR Spectrum of Compound 1b

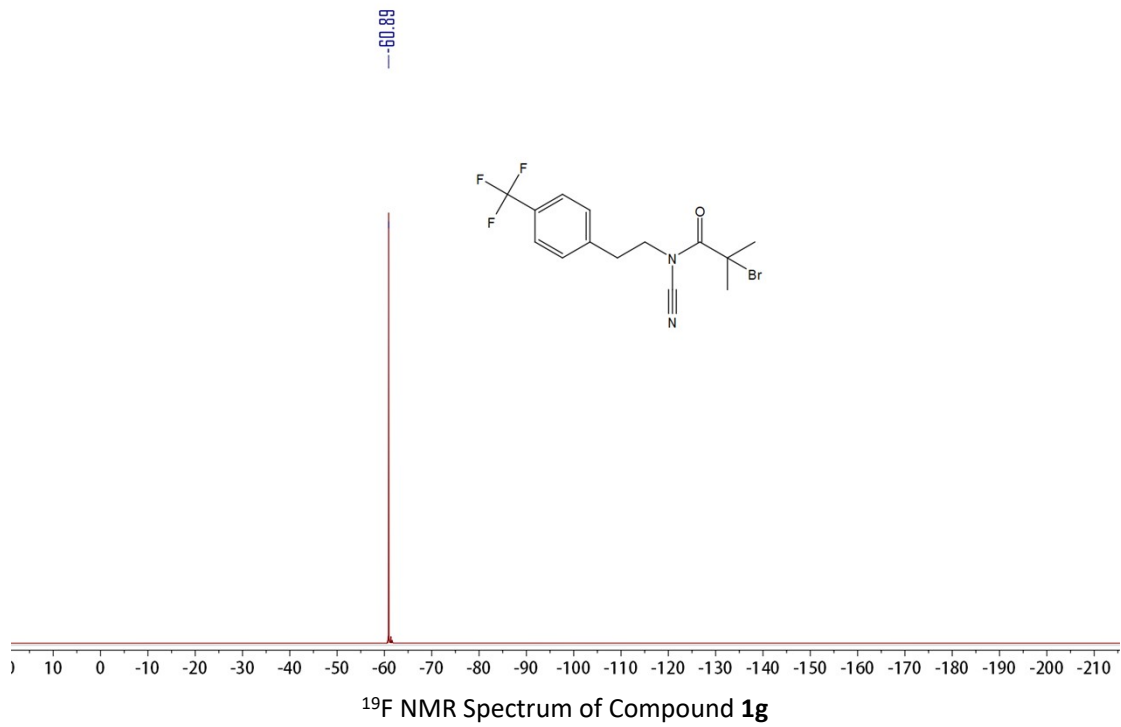
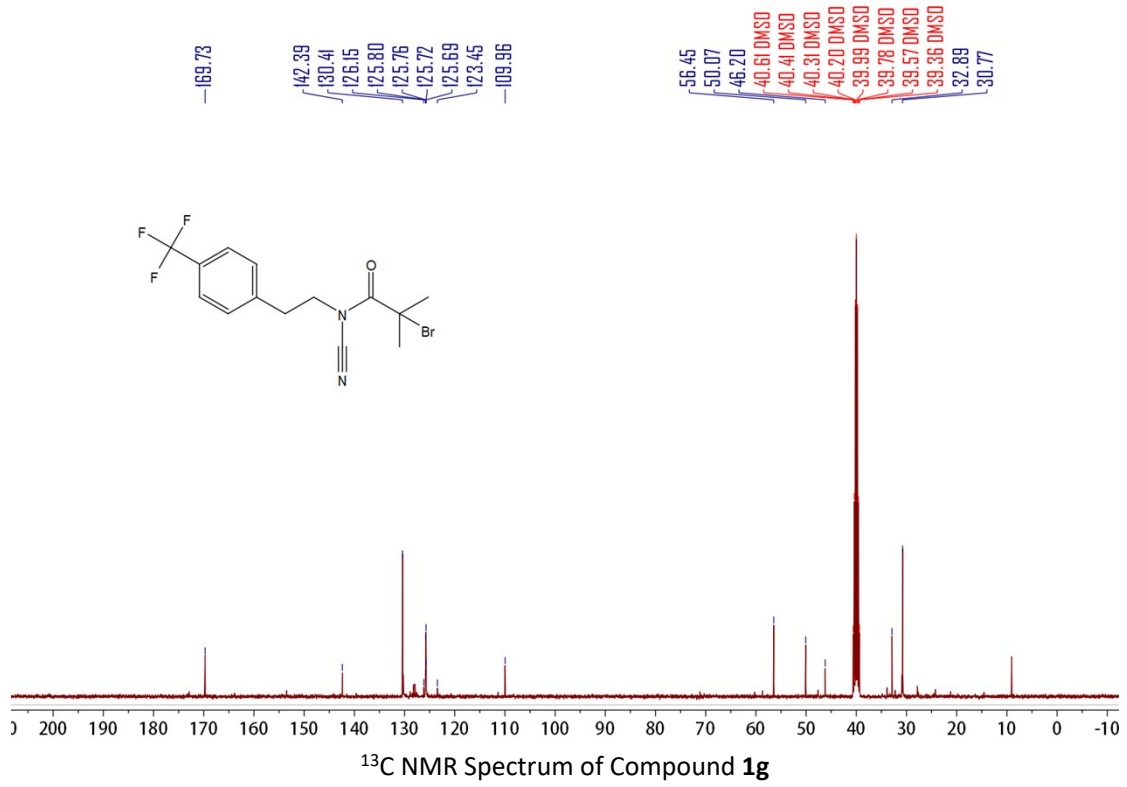


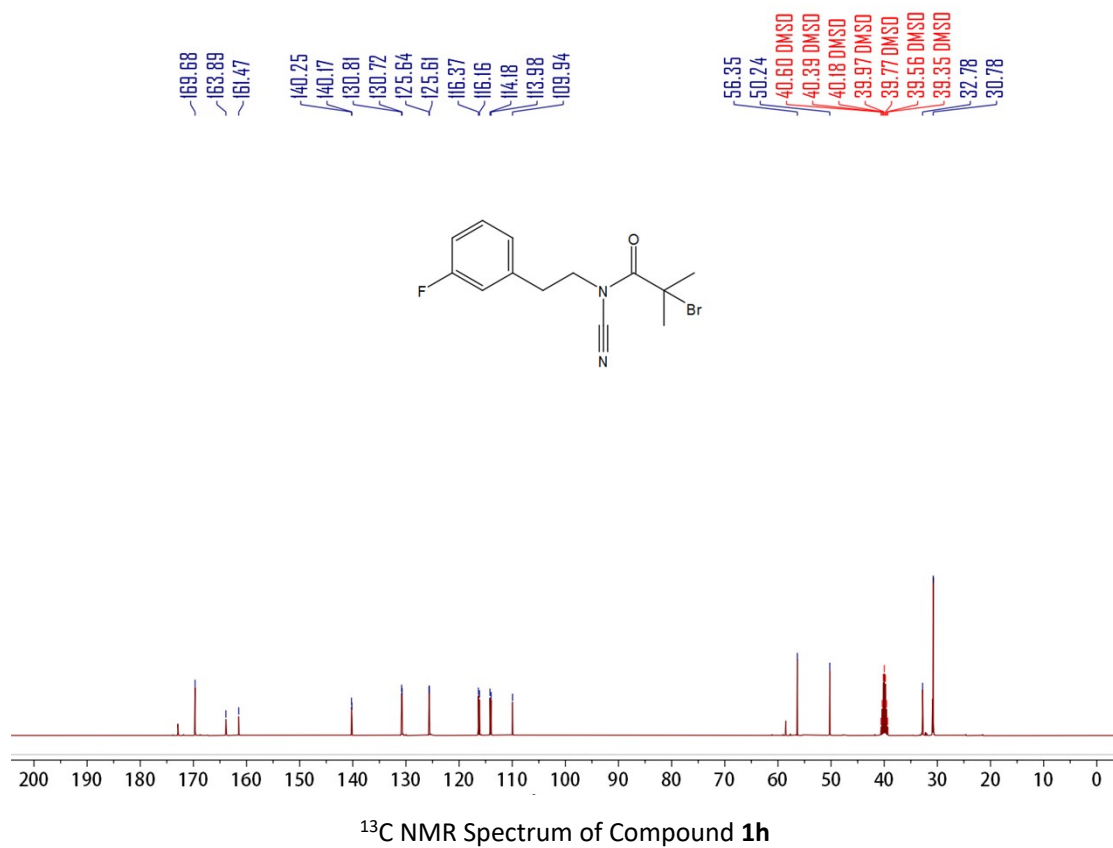
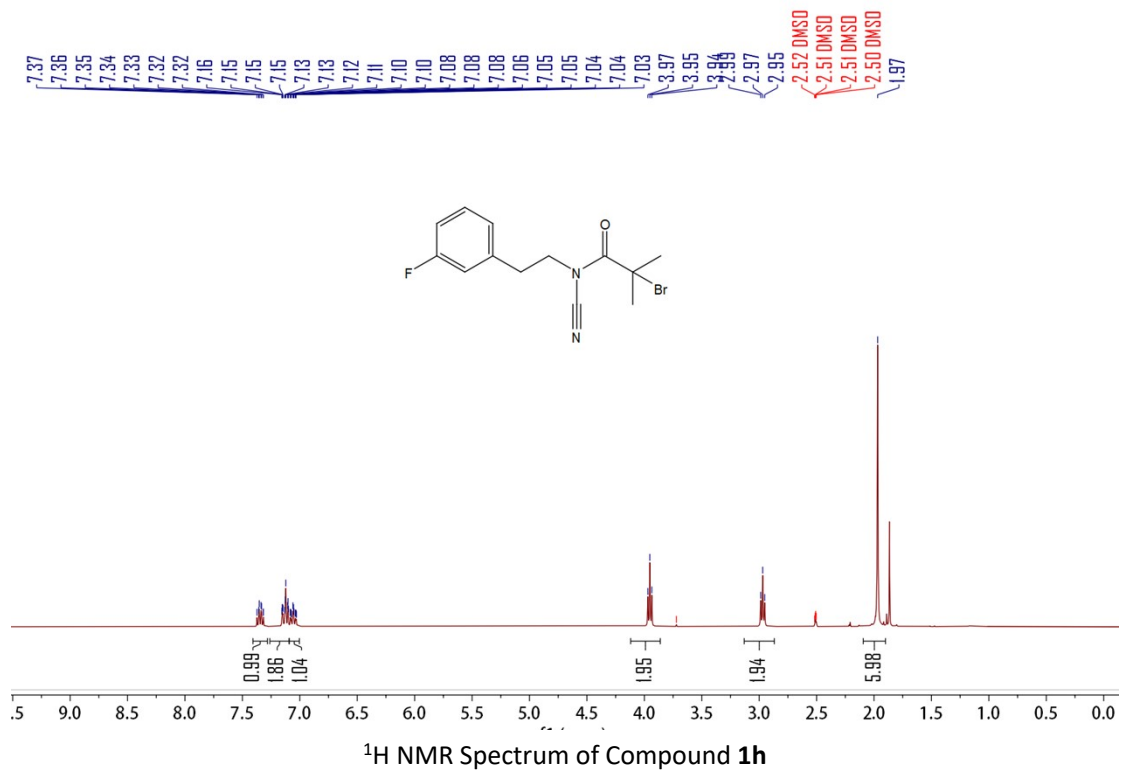


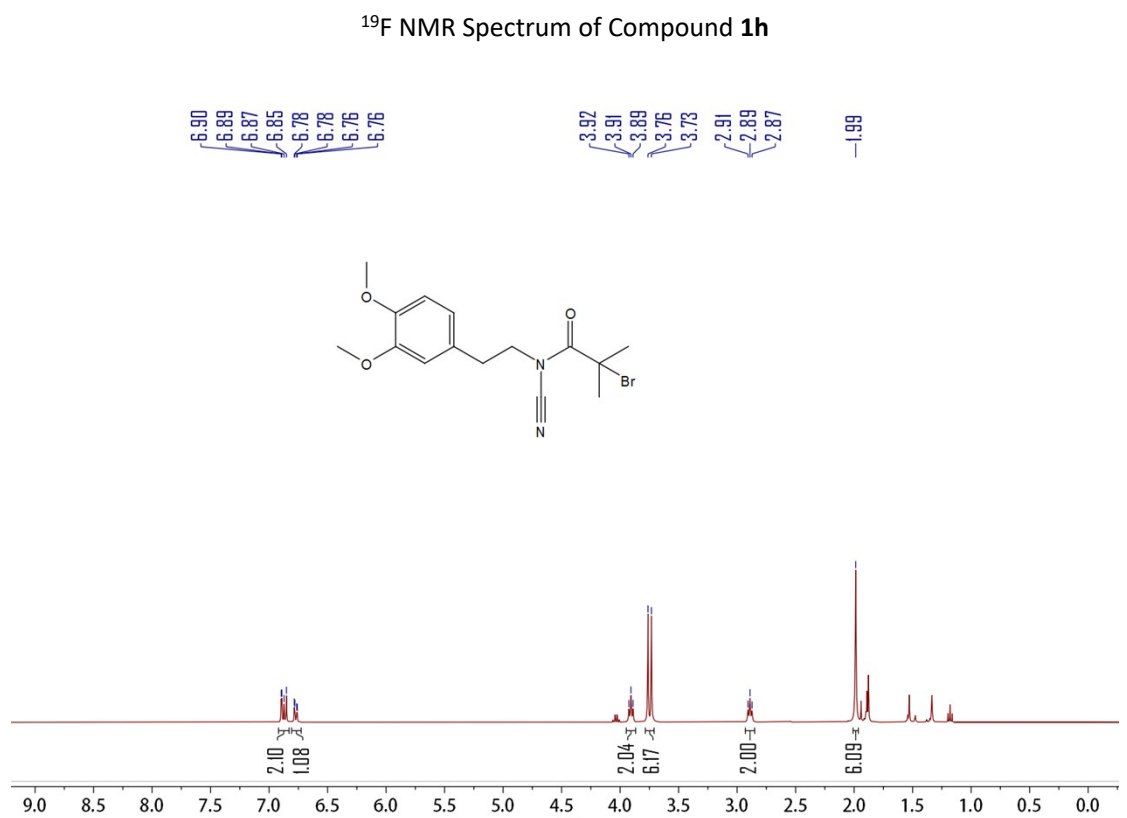
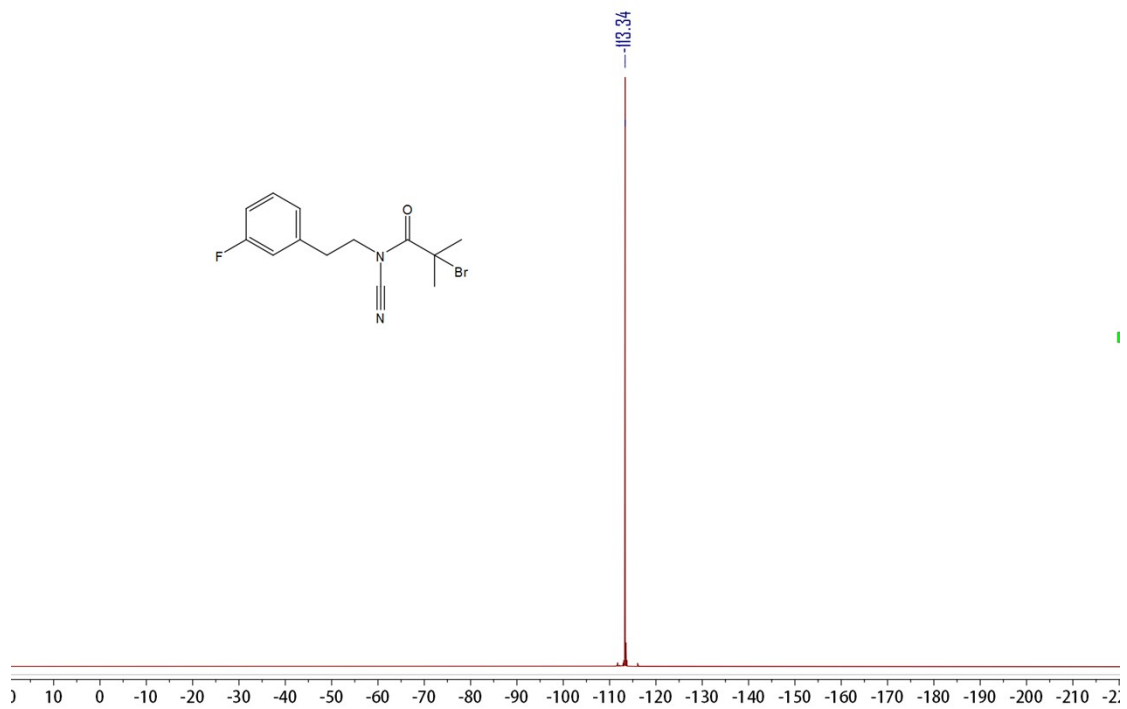


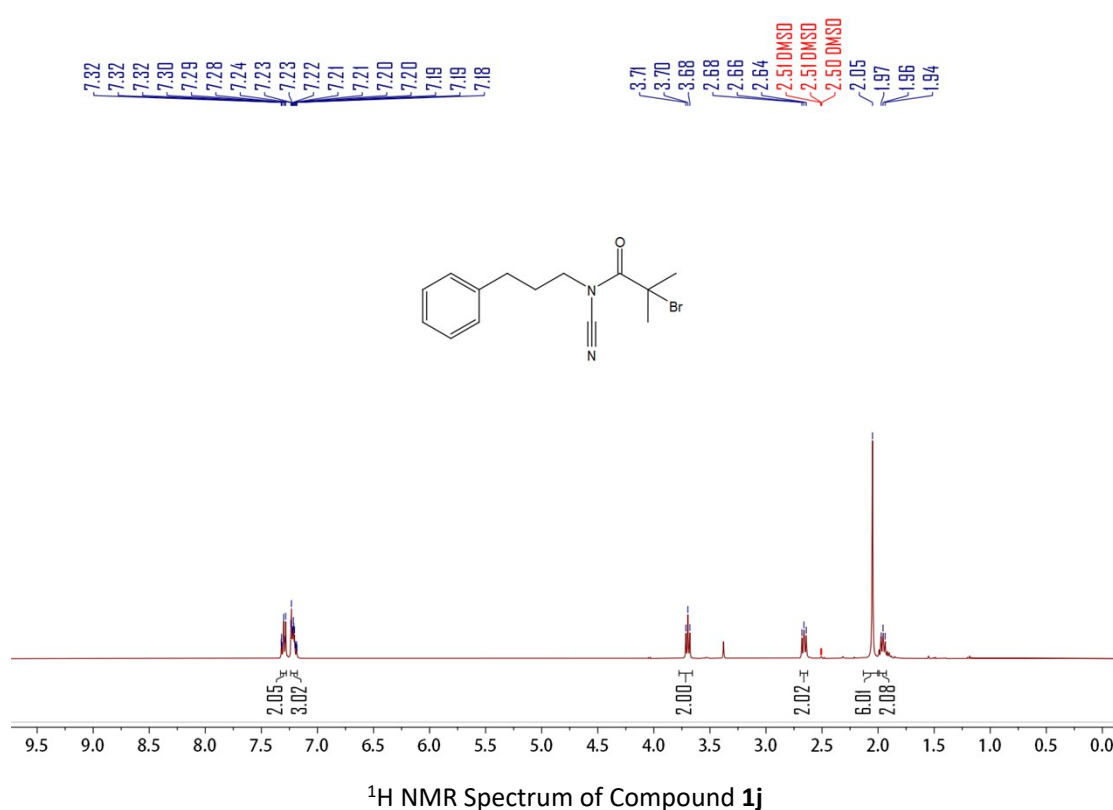
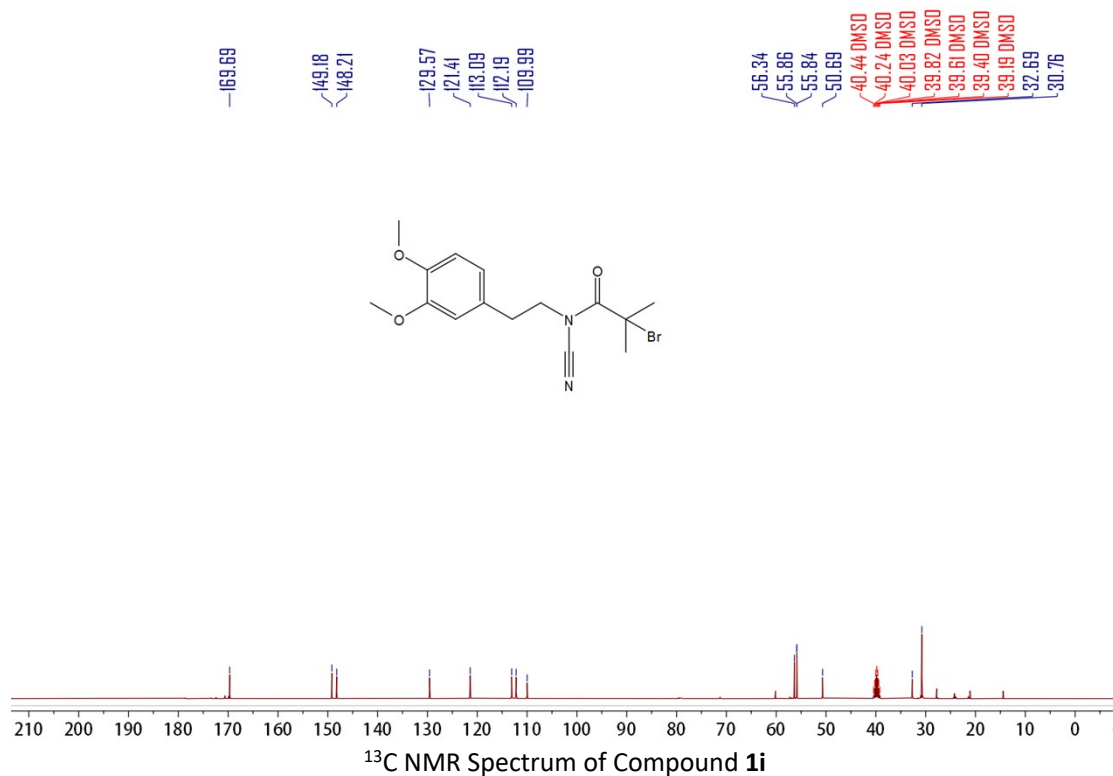


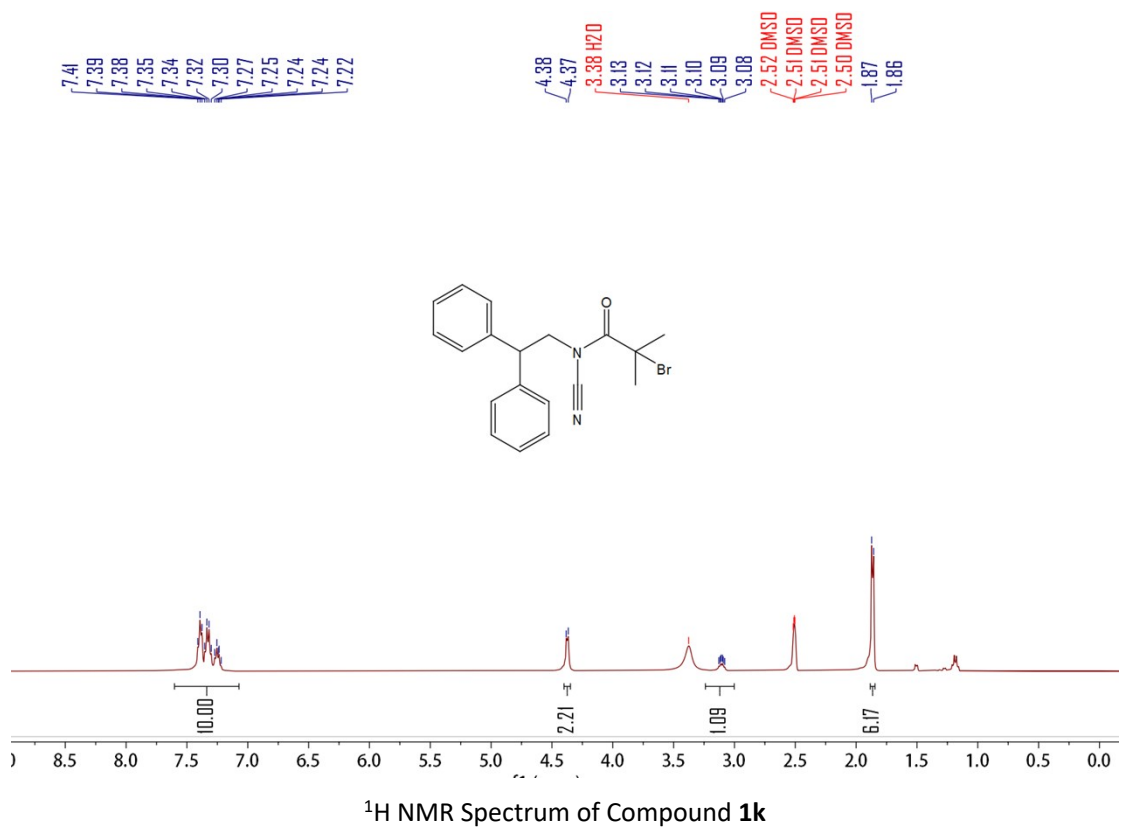
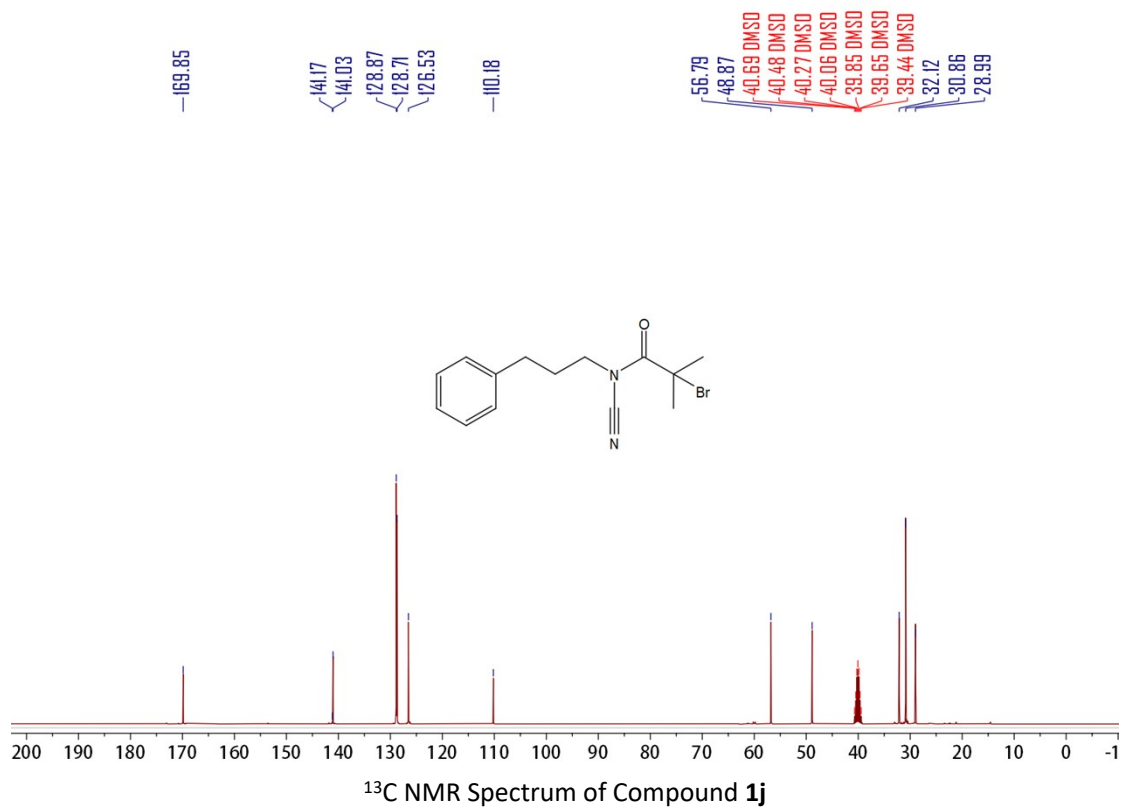


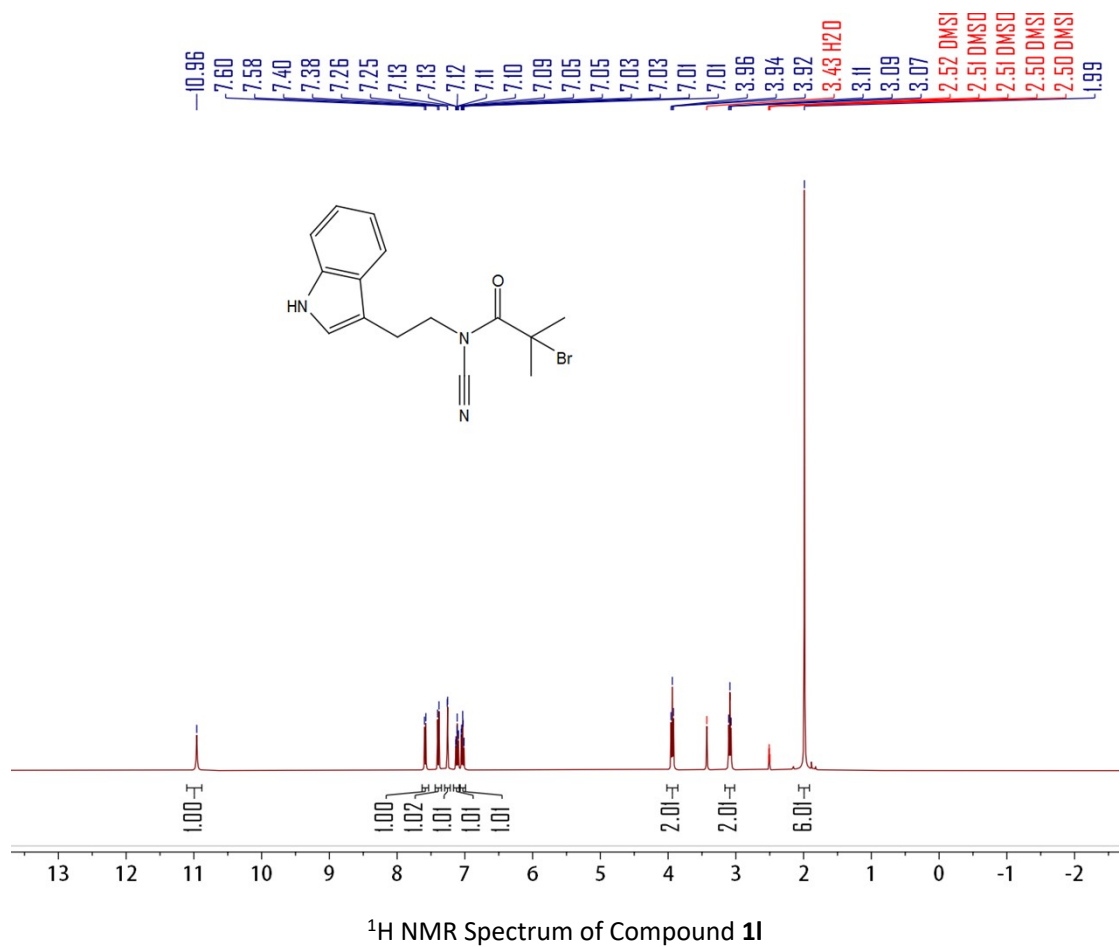
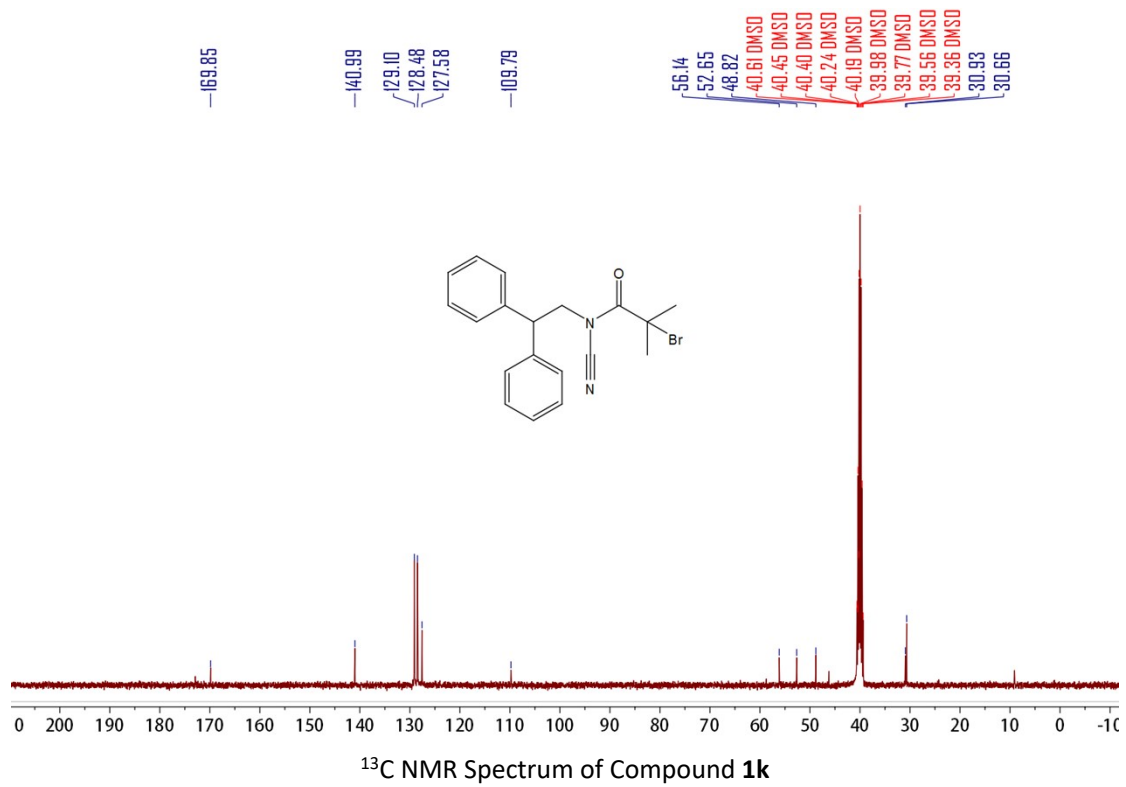


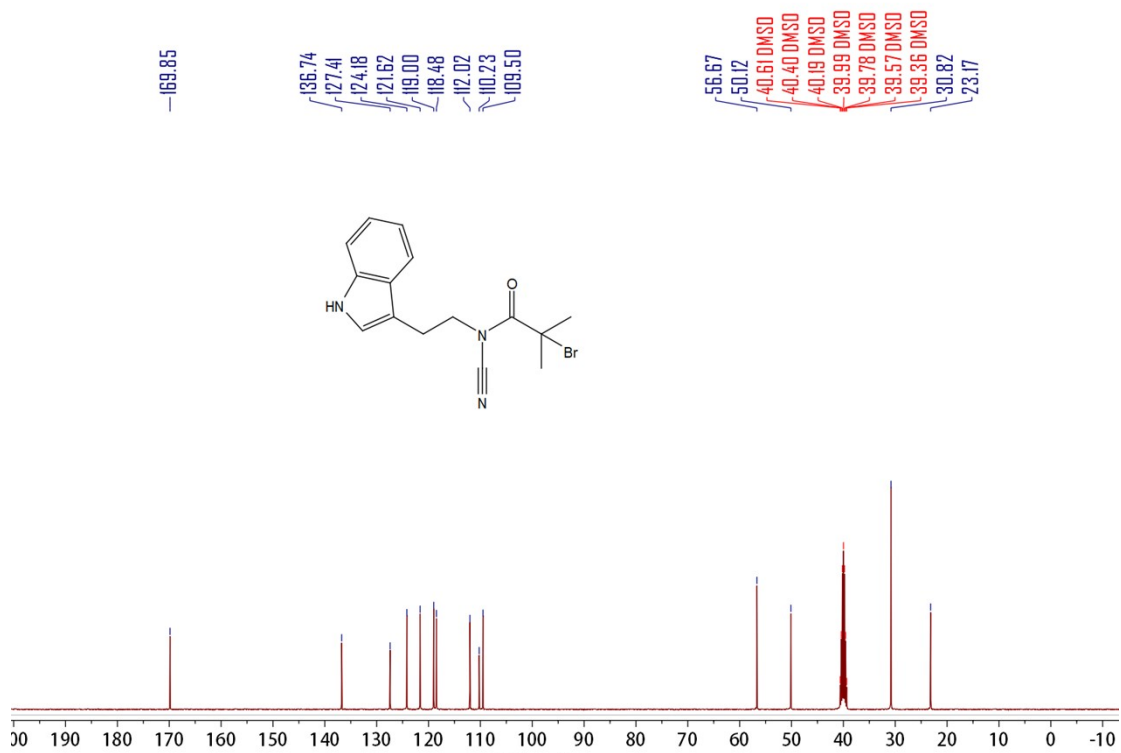




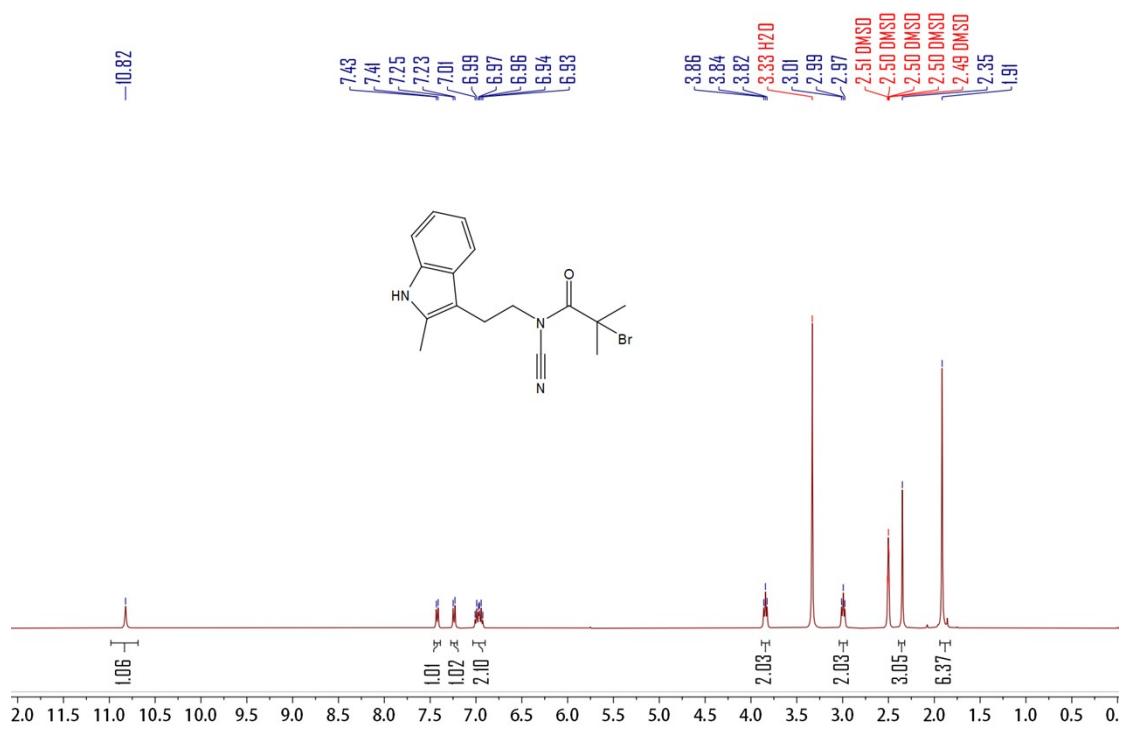




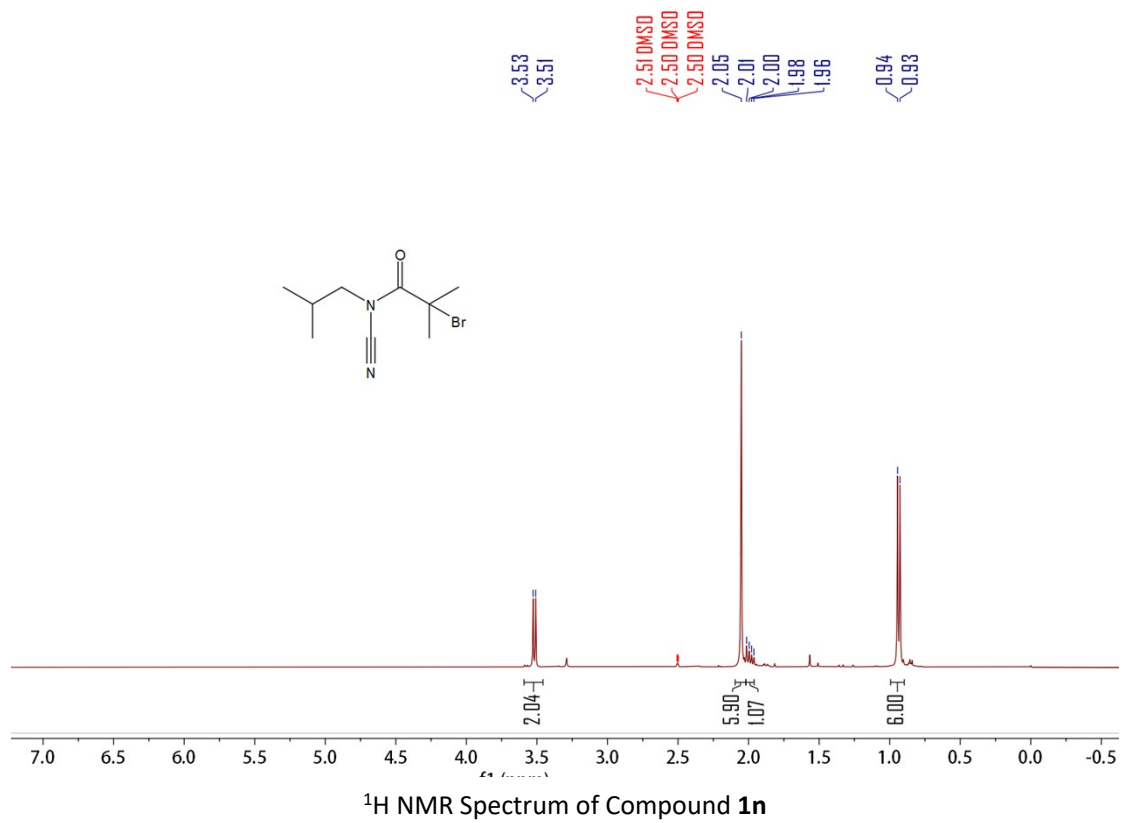
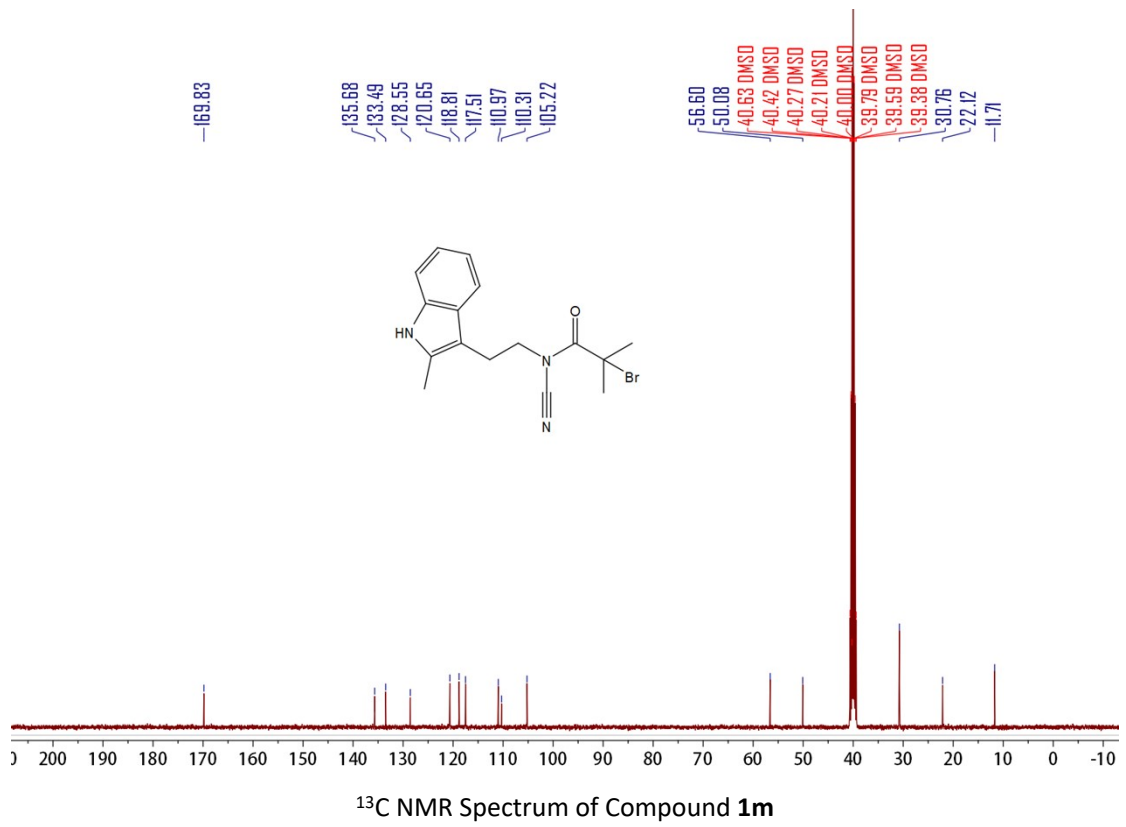


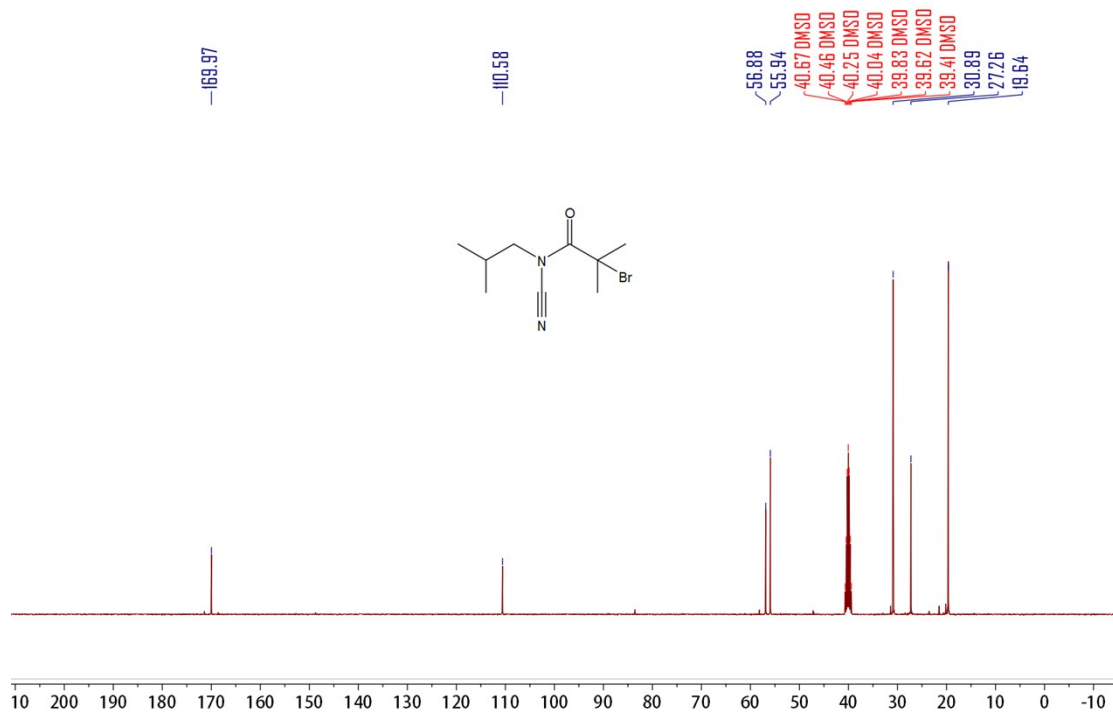


¹³C NMR Spectrum of Compound **1l**

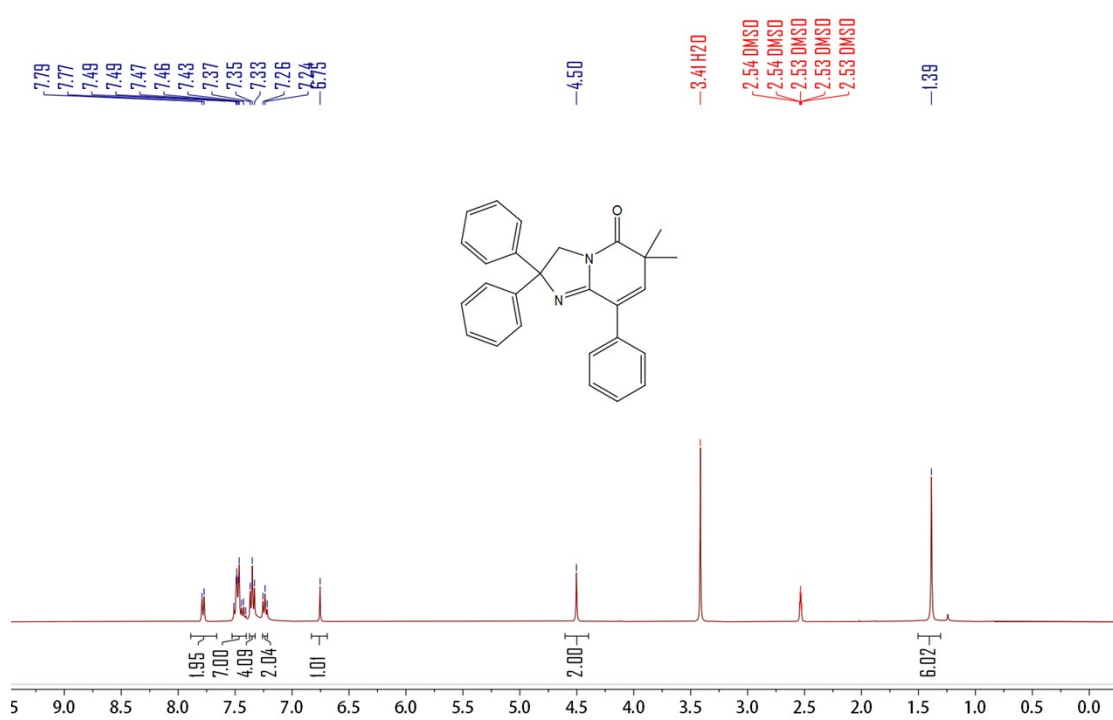


¹H NMR Spectrum of Compound **1m**

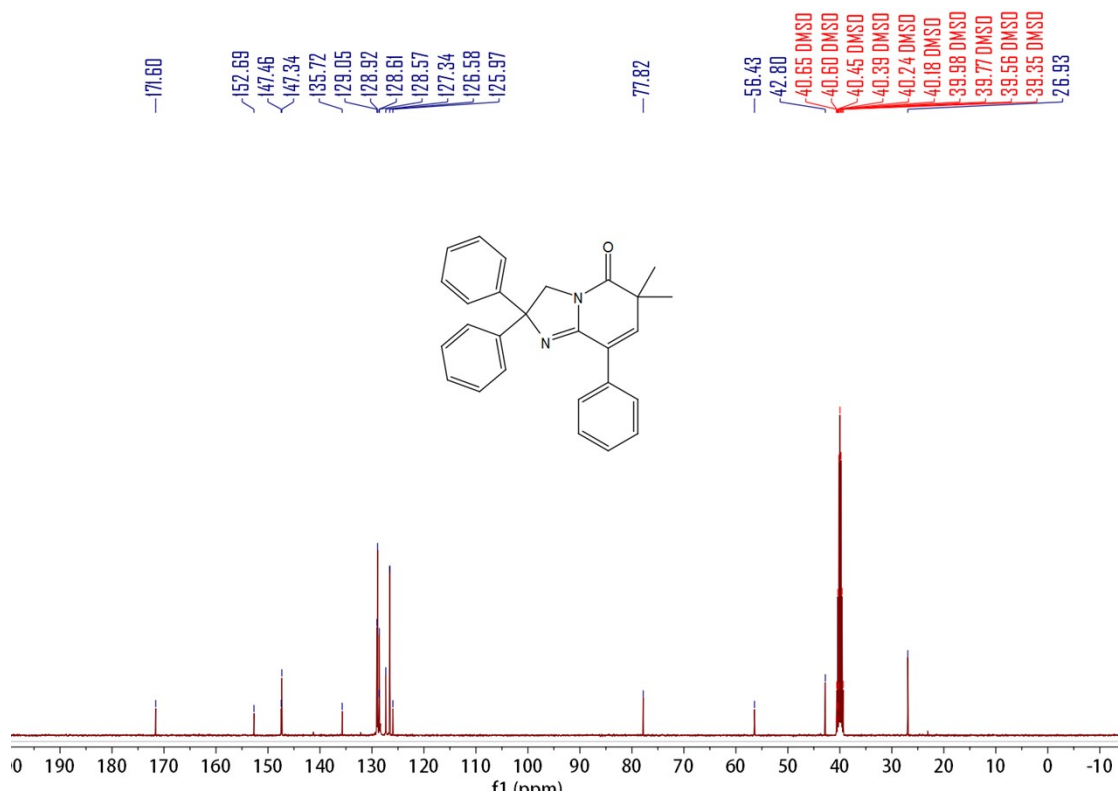




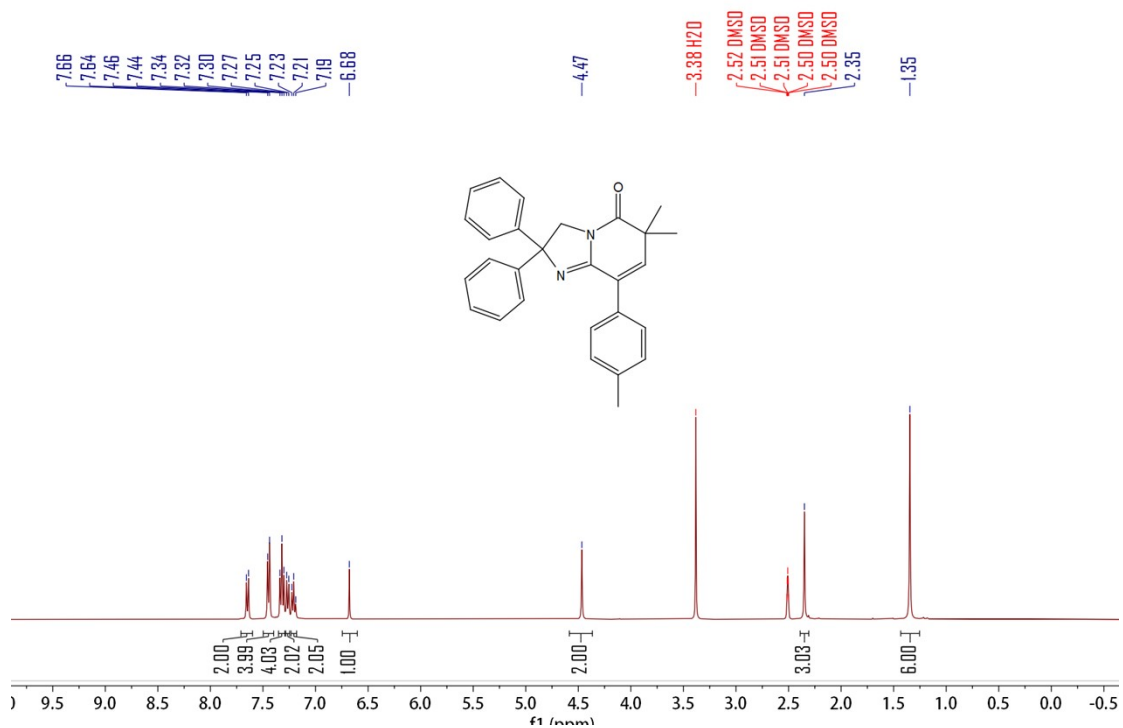
¹³C NMR Spectrum of Compound 1n



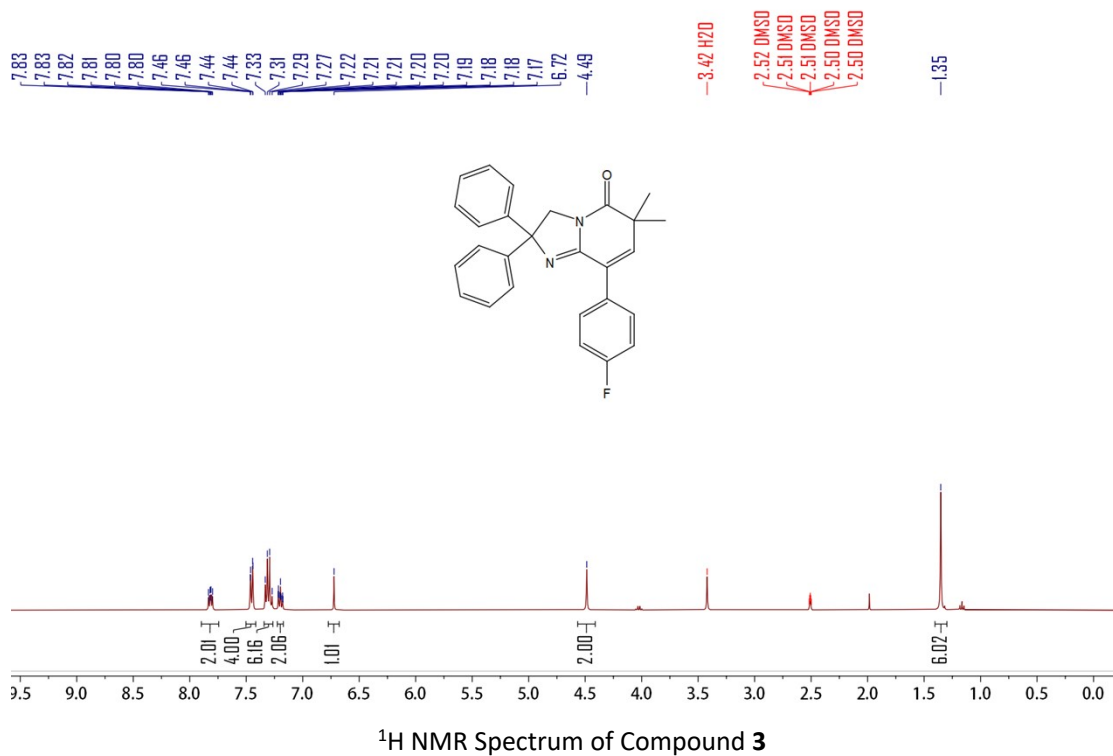
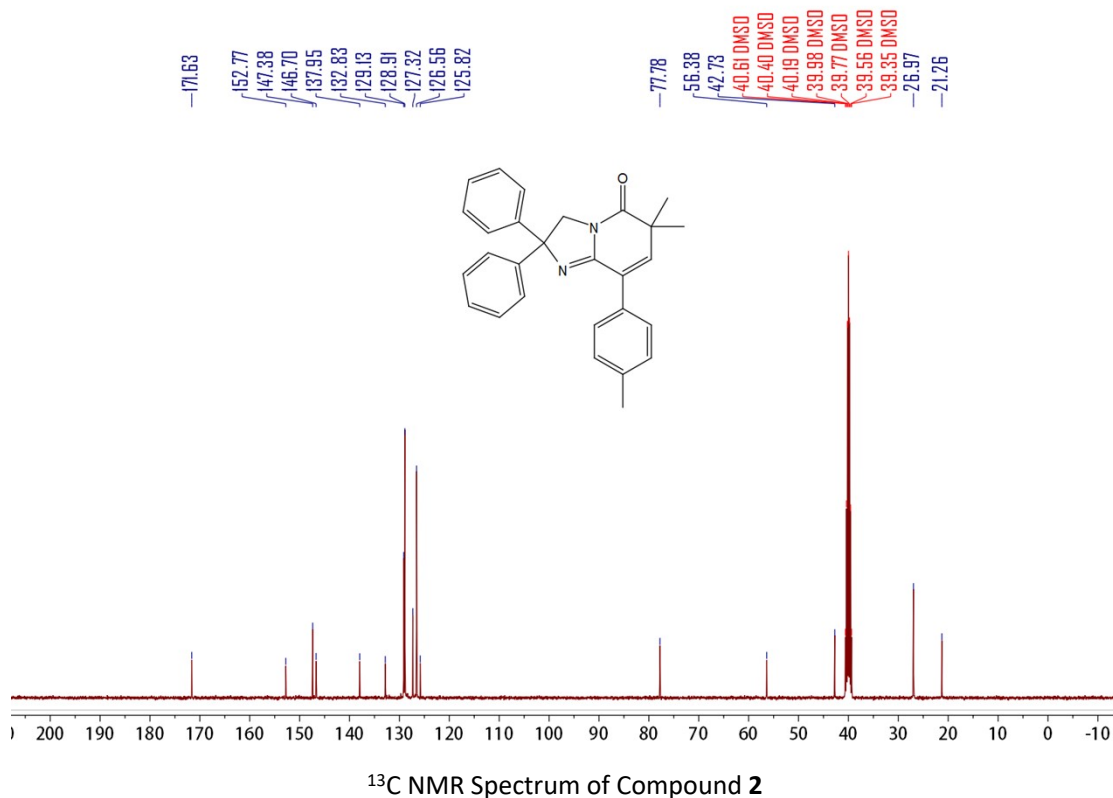
¹H NMR Spectrum of Compound 1

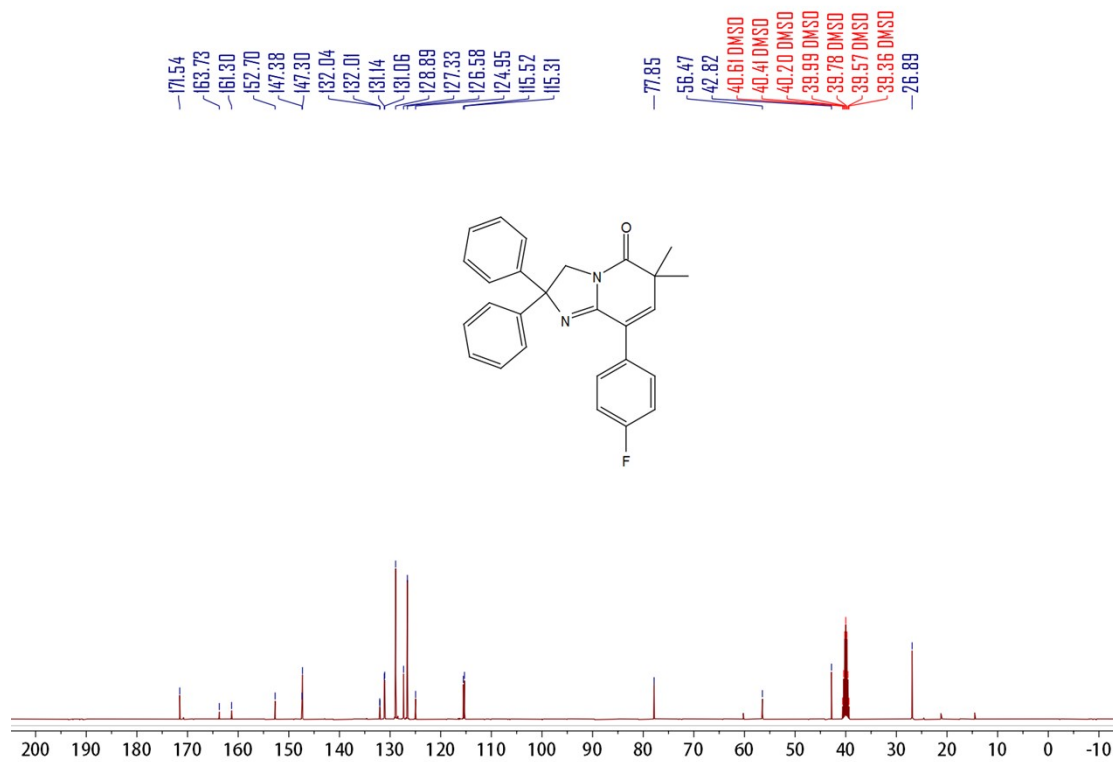


¹³C NMR Spectrum of Compound 1

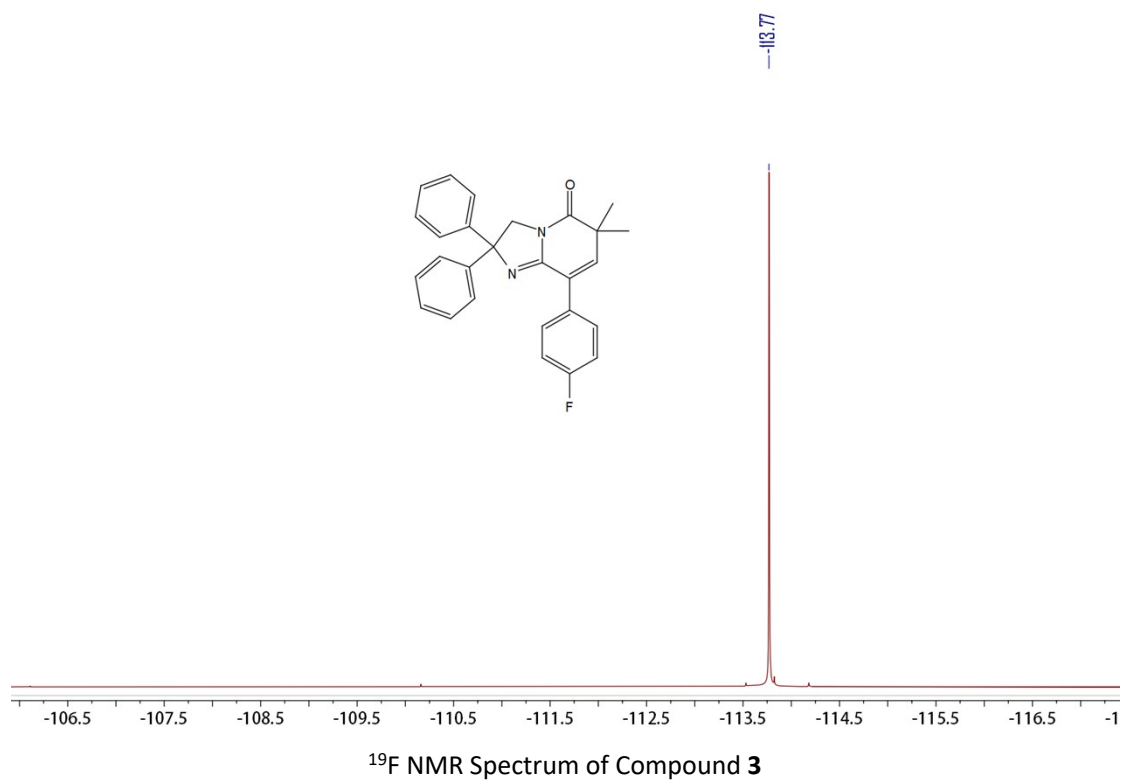


¹H NMR Spectrum of Compound 2

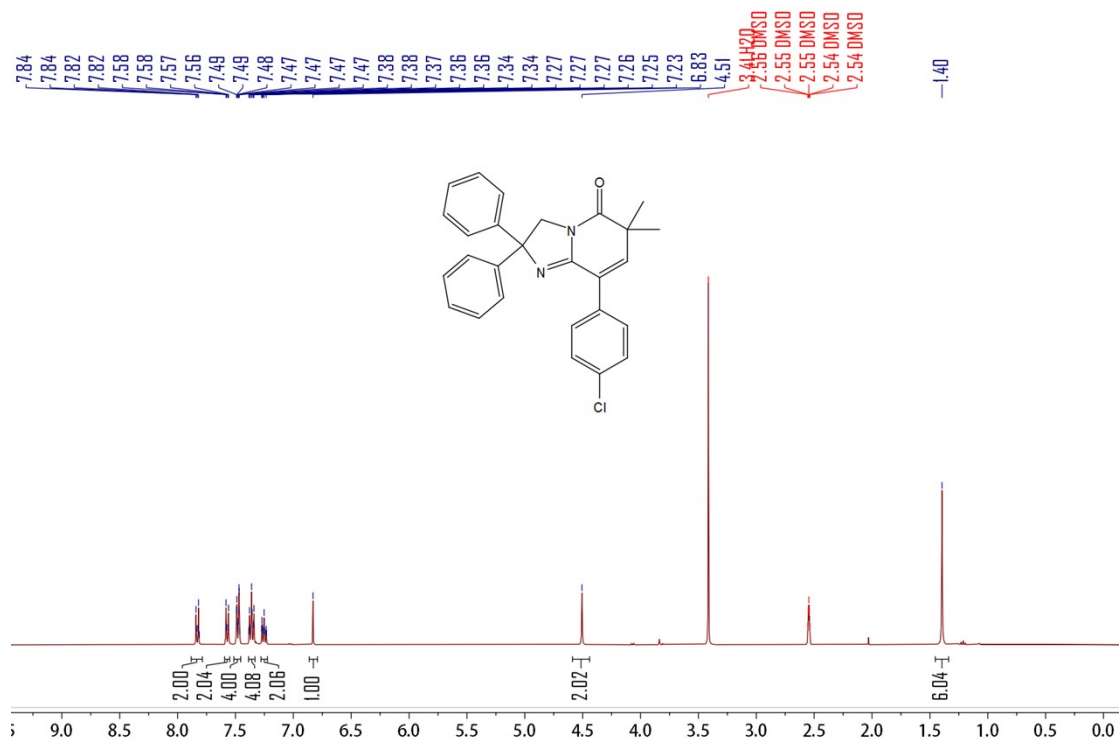




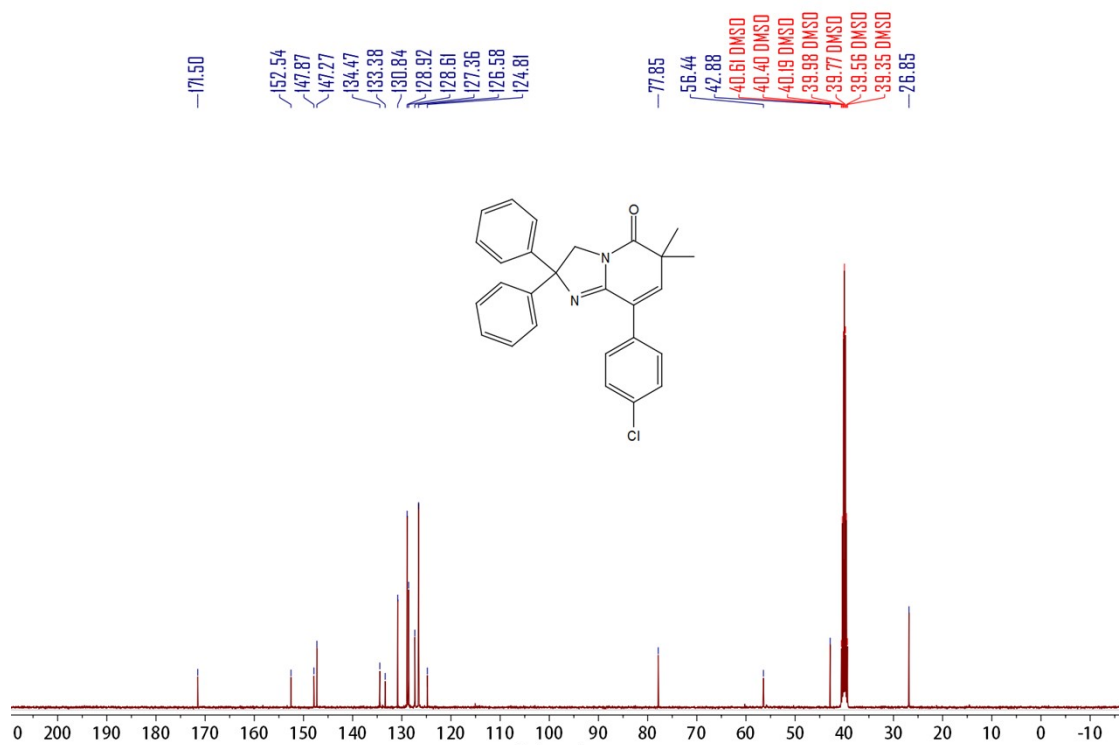
¹³C NMR Spectrum of Compound **3**



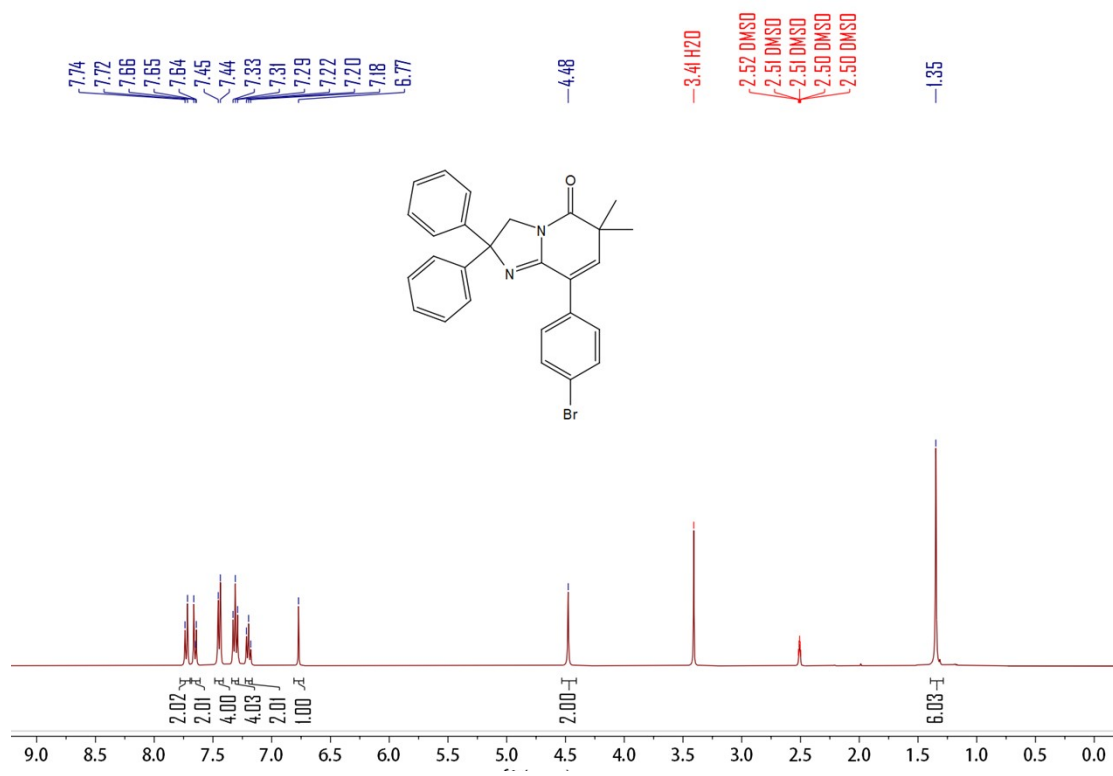
¹⁹F NMR Spectrum of Compound **3**



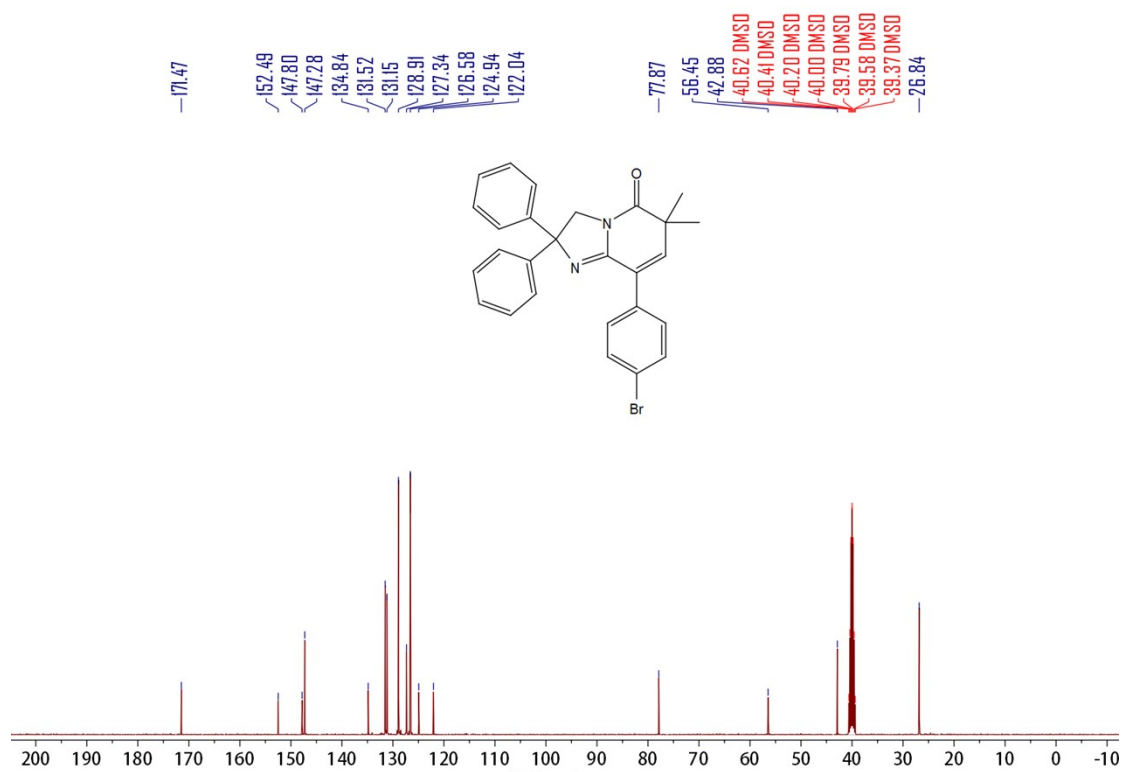
¹H NMR Spectrum of Compound 4



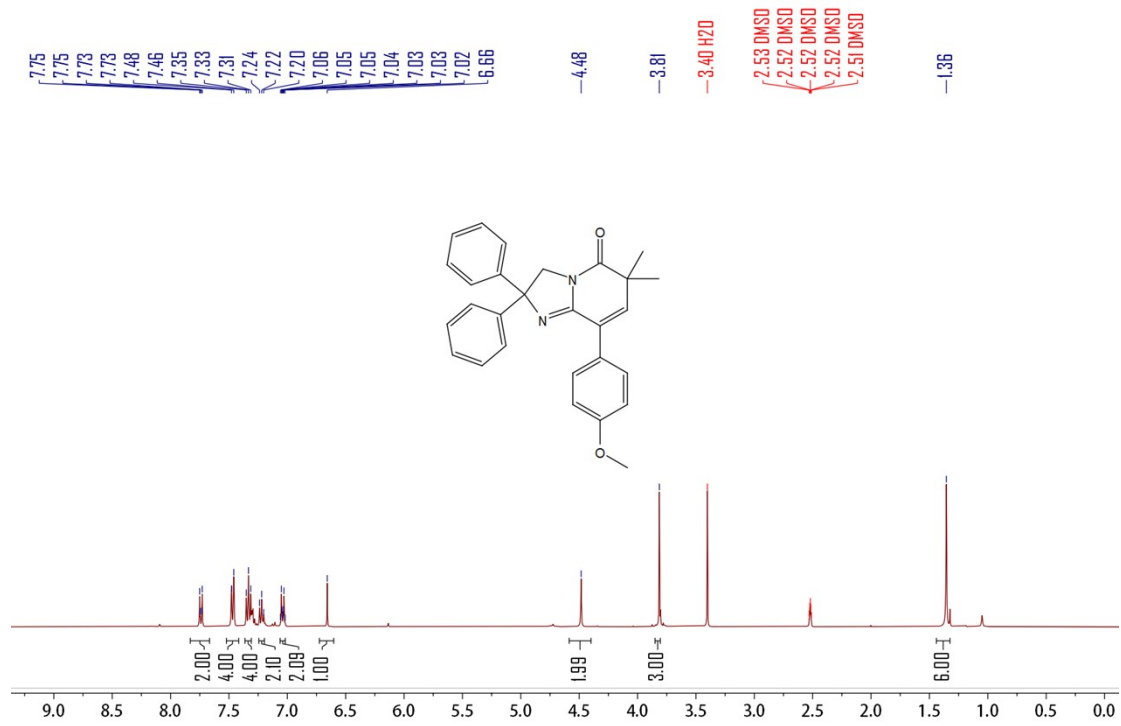
¹³C NMR Spectrum of Compound 4



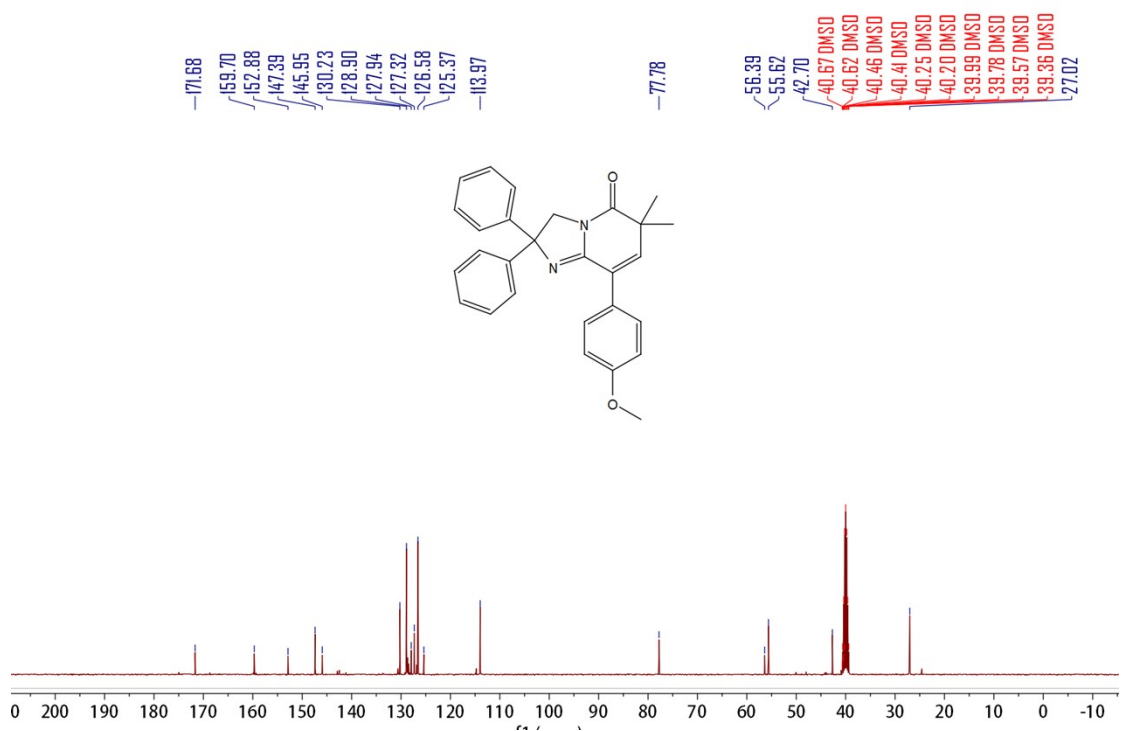
¹H NMR Spectrum of Compound 5



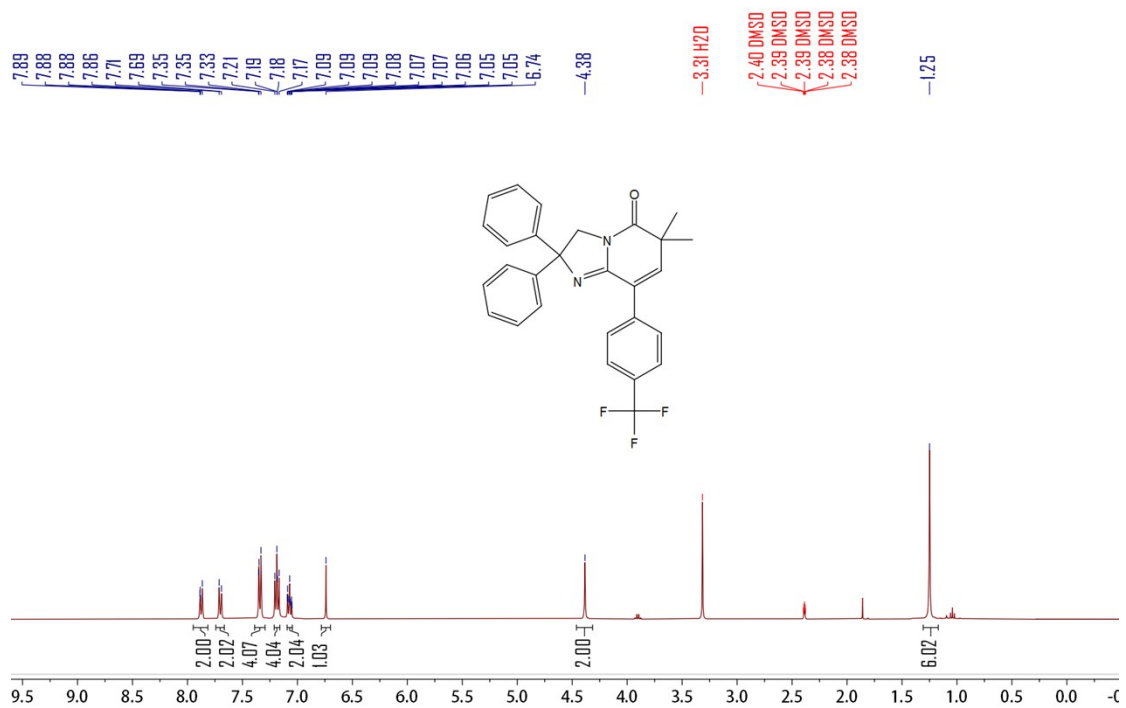
¹³C NMR Spectrum of Compound 5



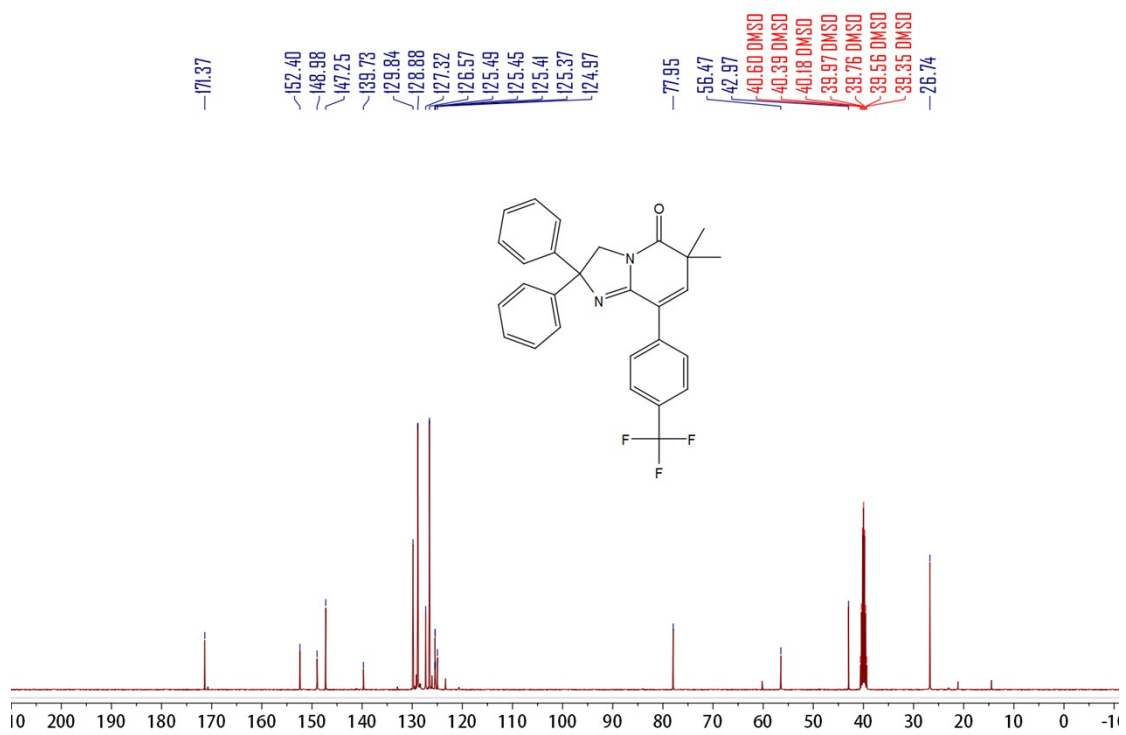
¹H NMR Spectrum of Compound 6



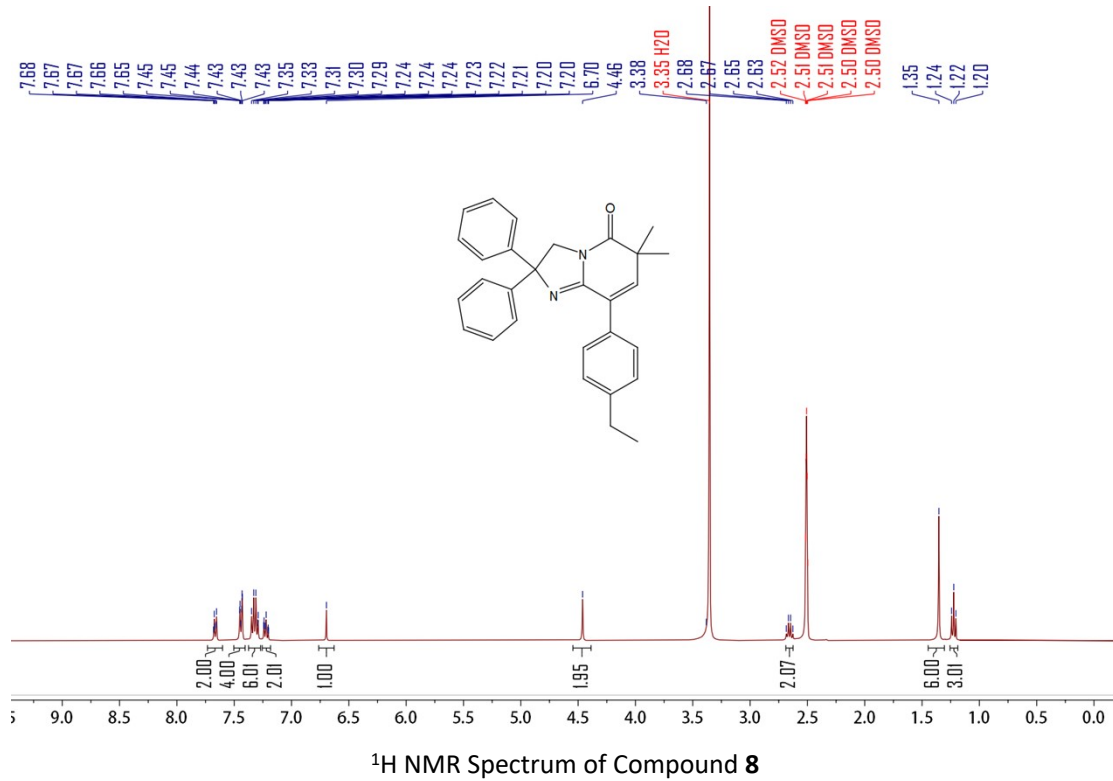
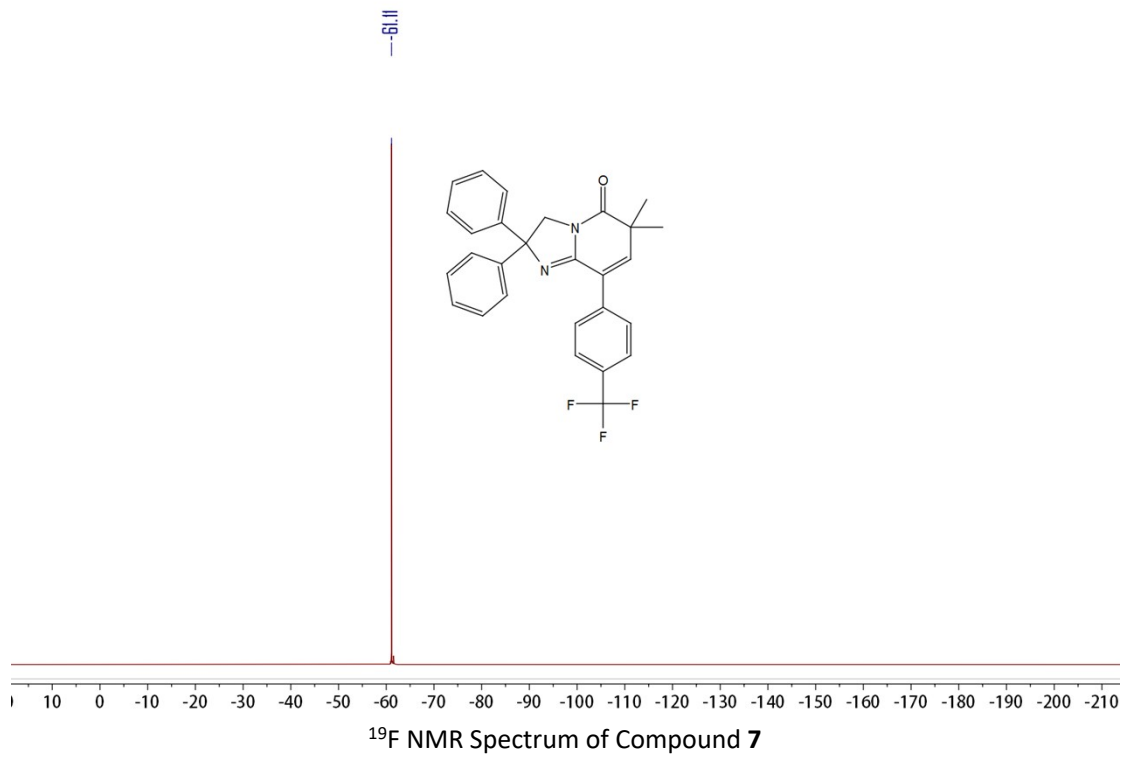
¹³C NMR Spectrum of Compound 6

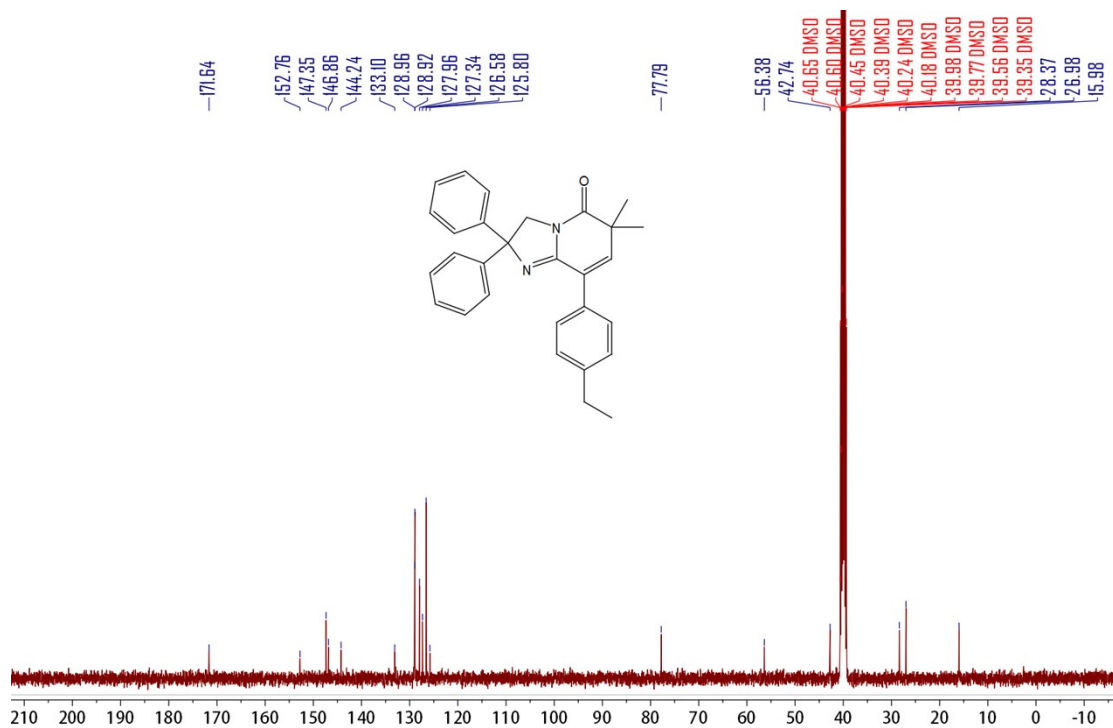


¹H NMR Spectrum of Compound 7

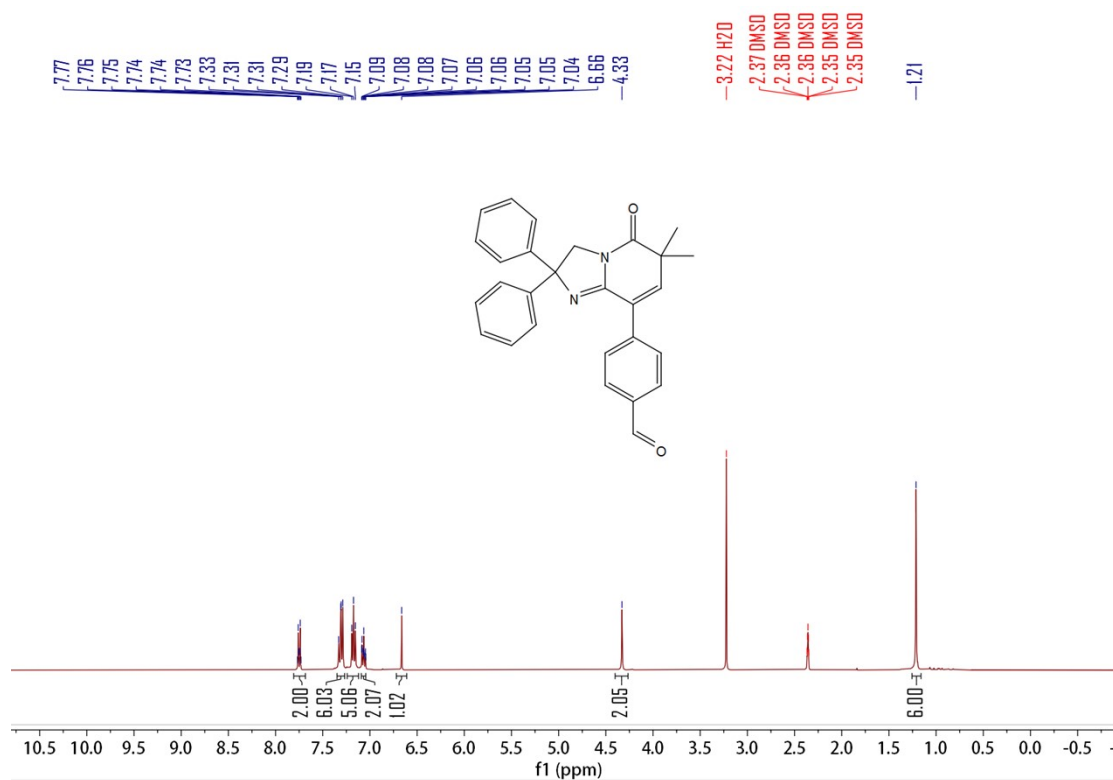


¹³C NMR Spectrum of Compound 7

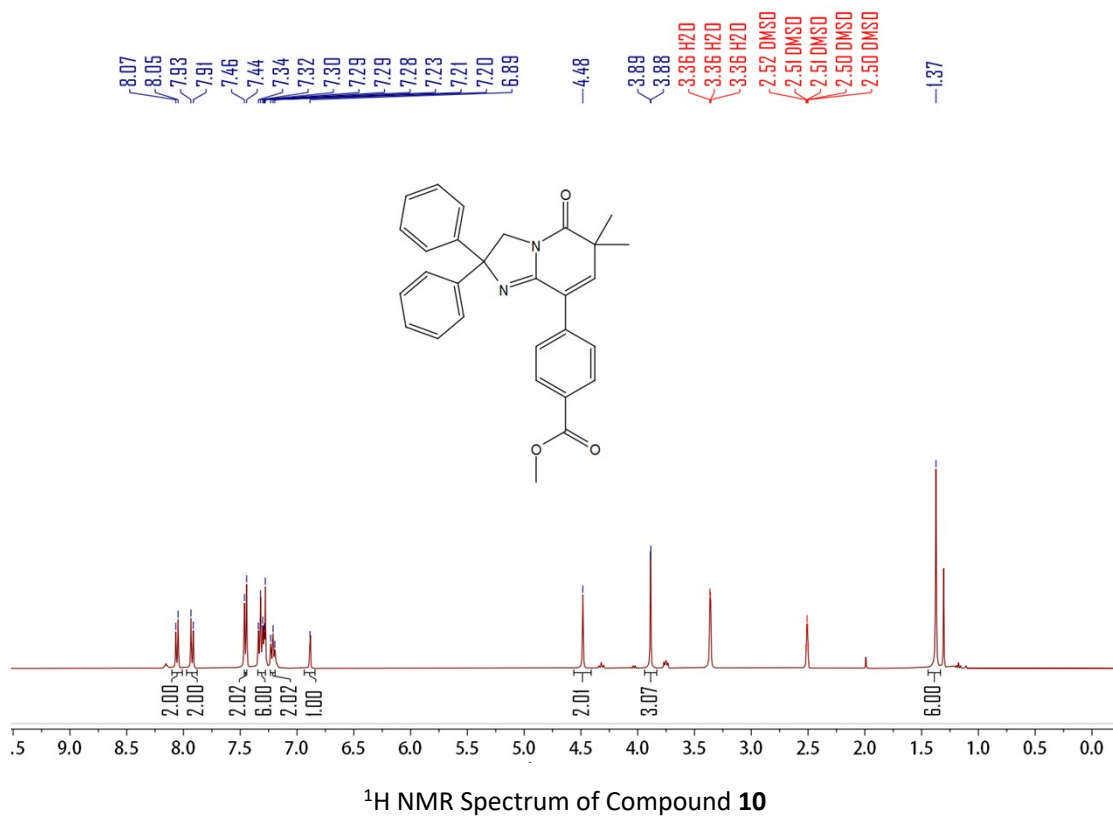
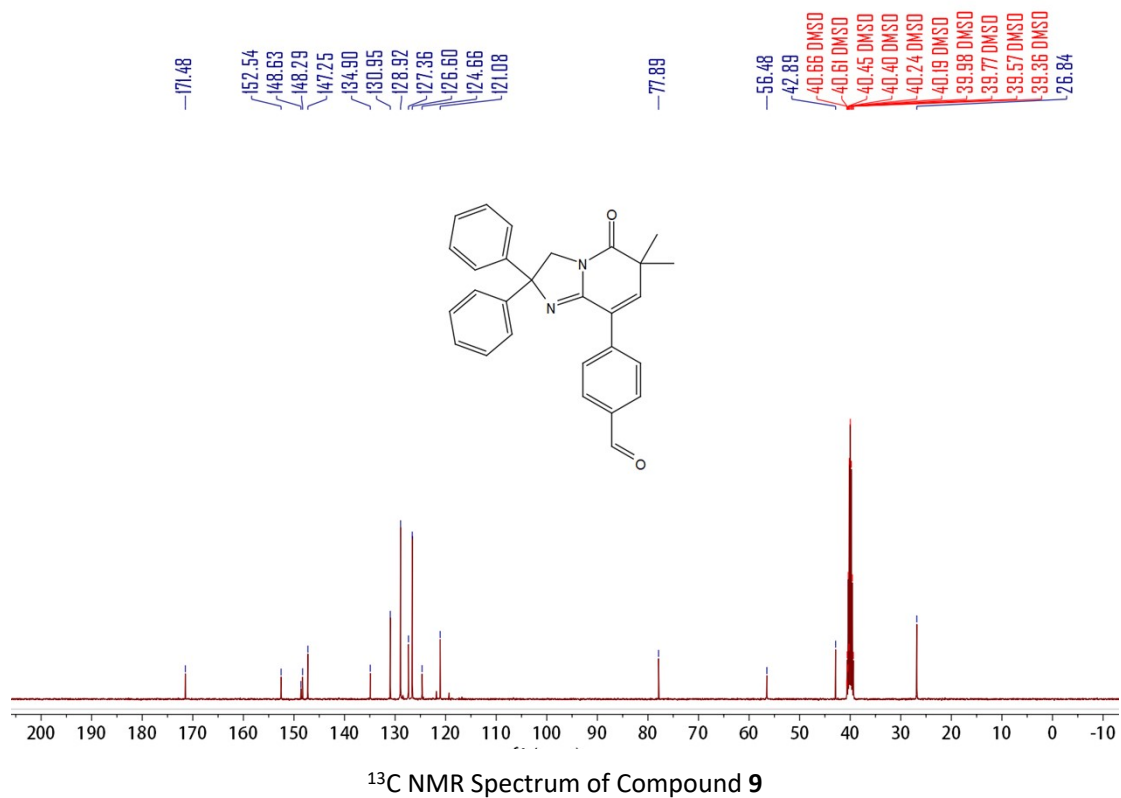


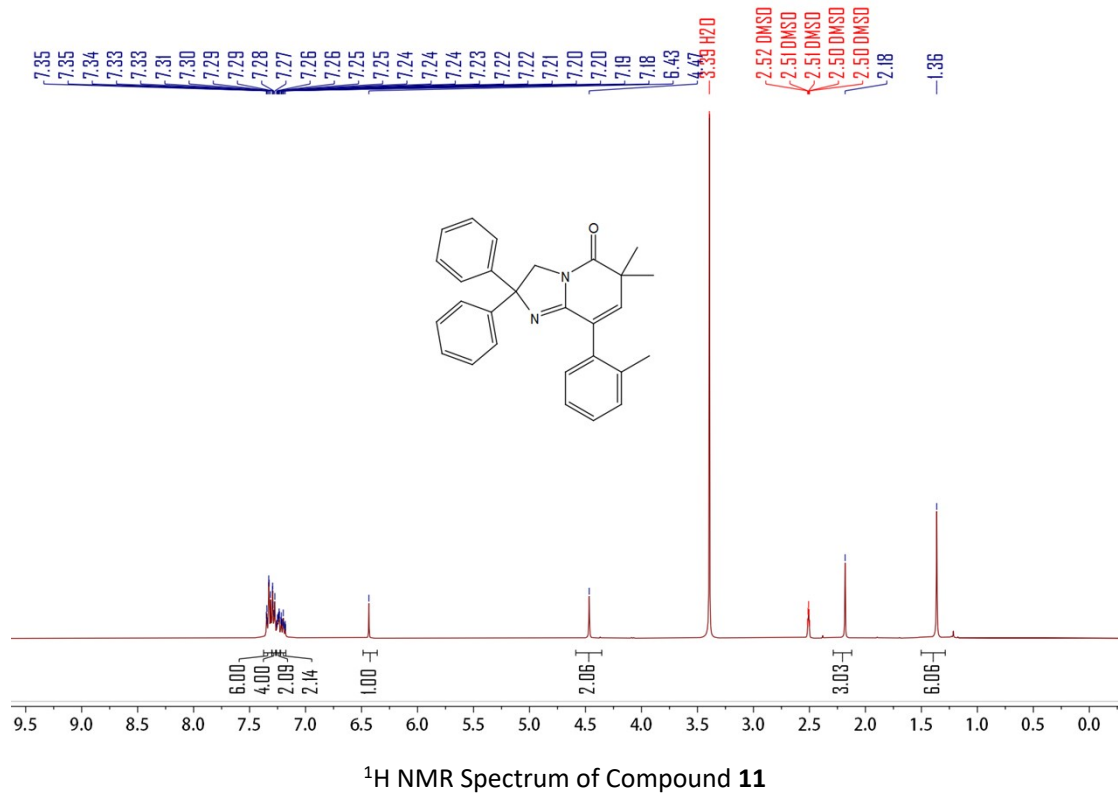
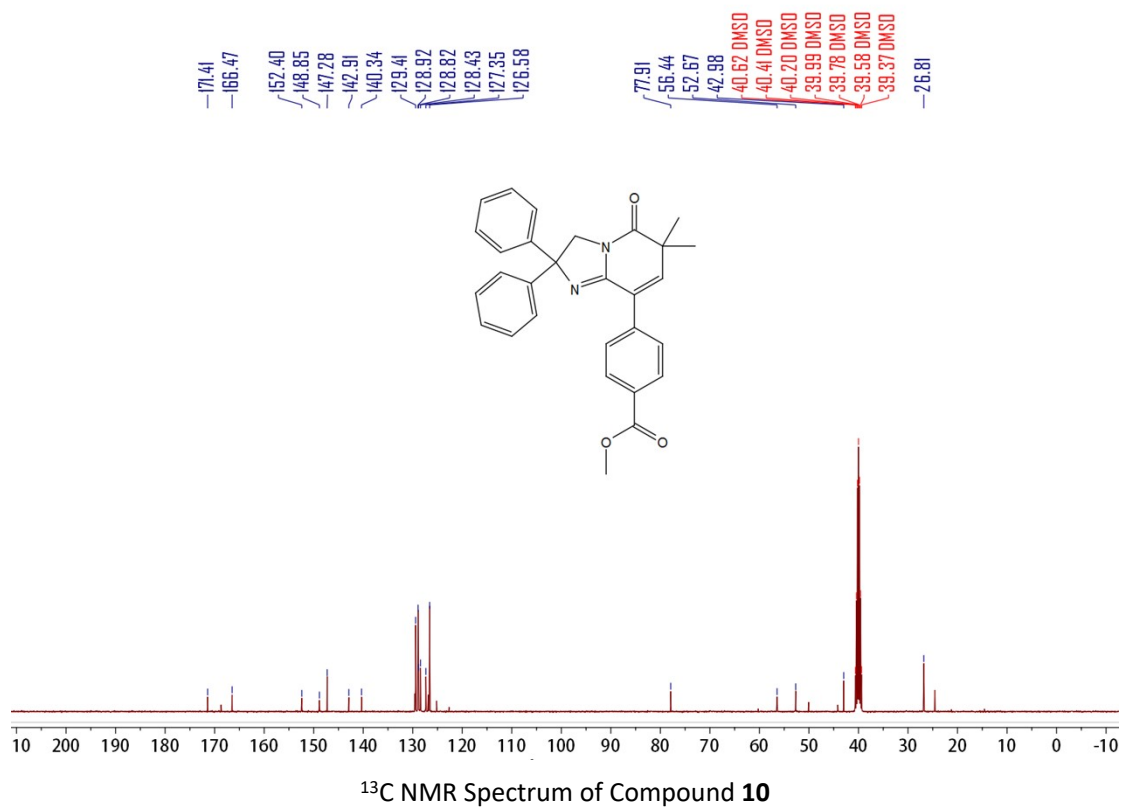


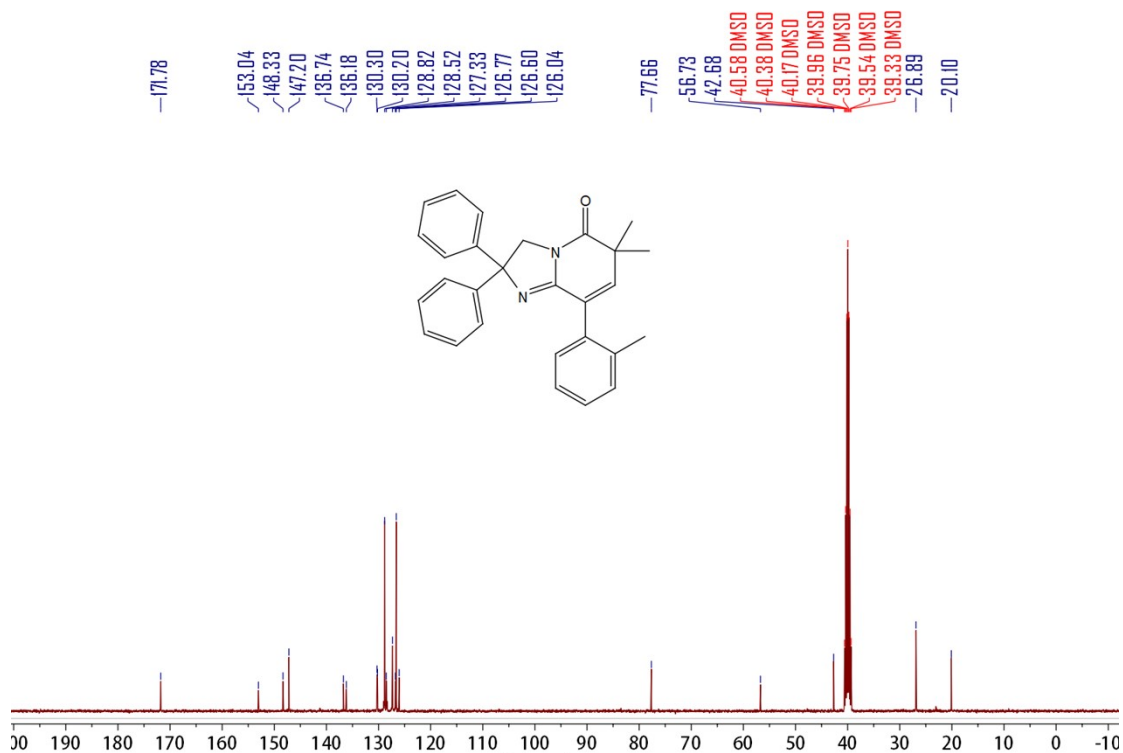
¹³C NMR Spectrum of Compound 8



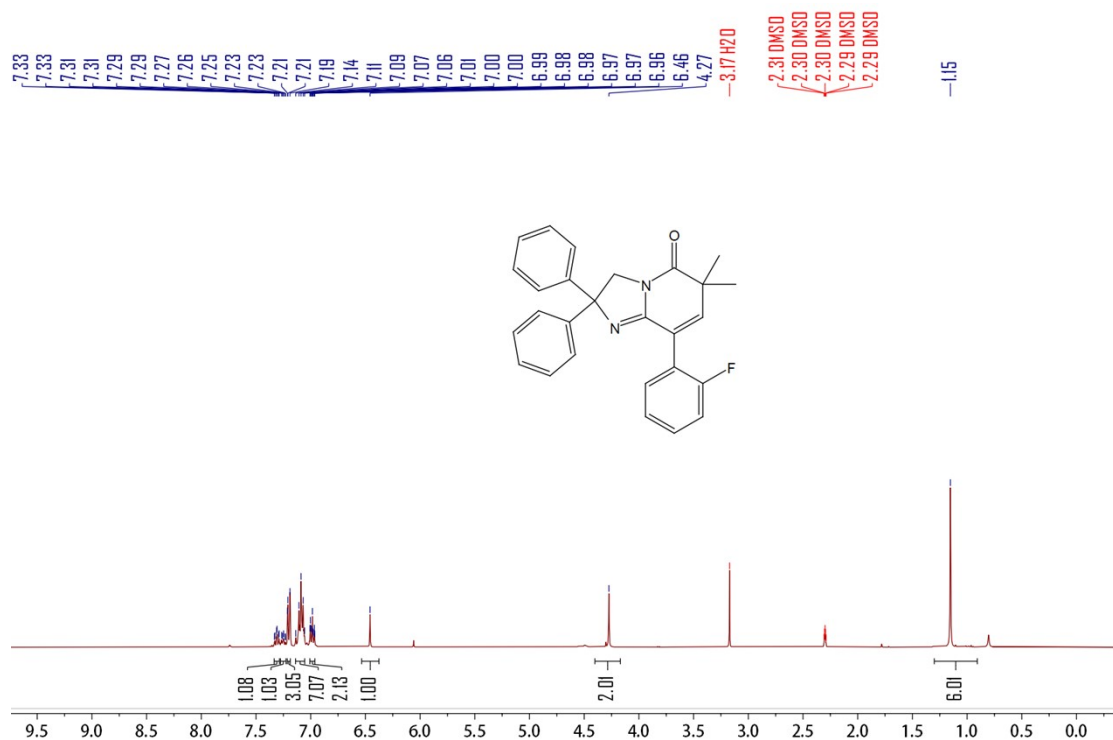
¹H NMR Spectrum of Compound 9



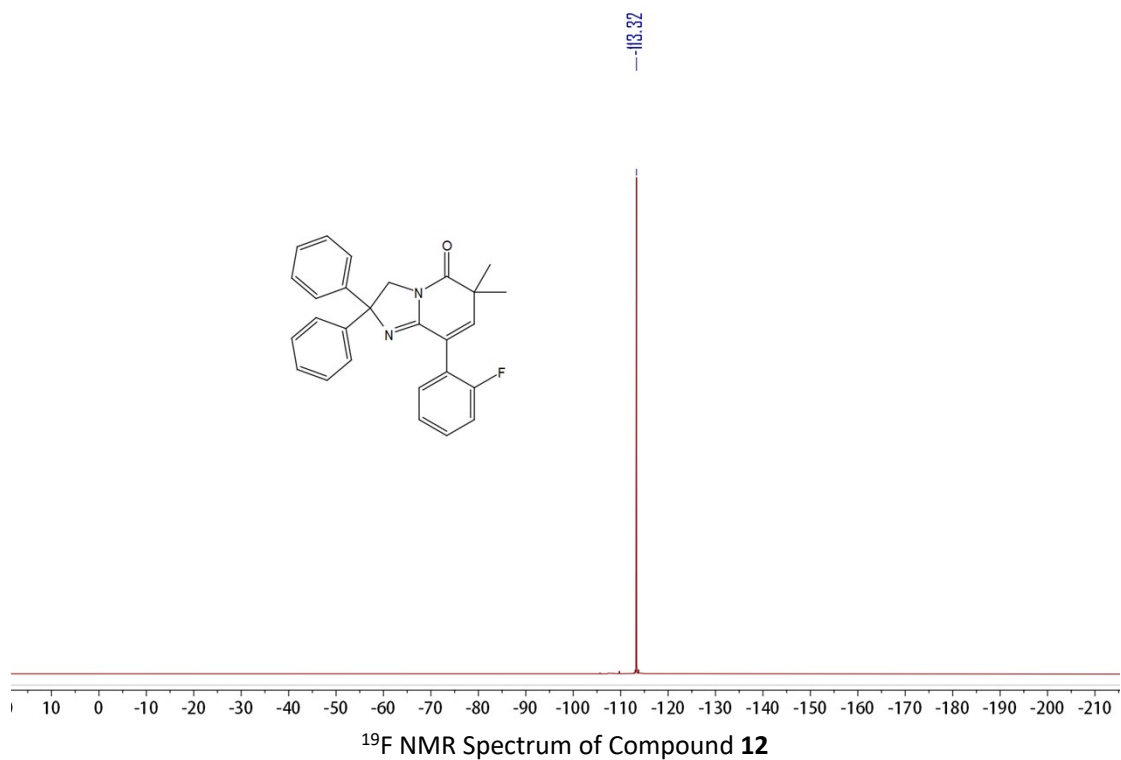
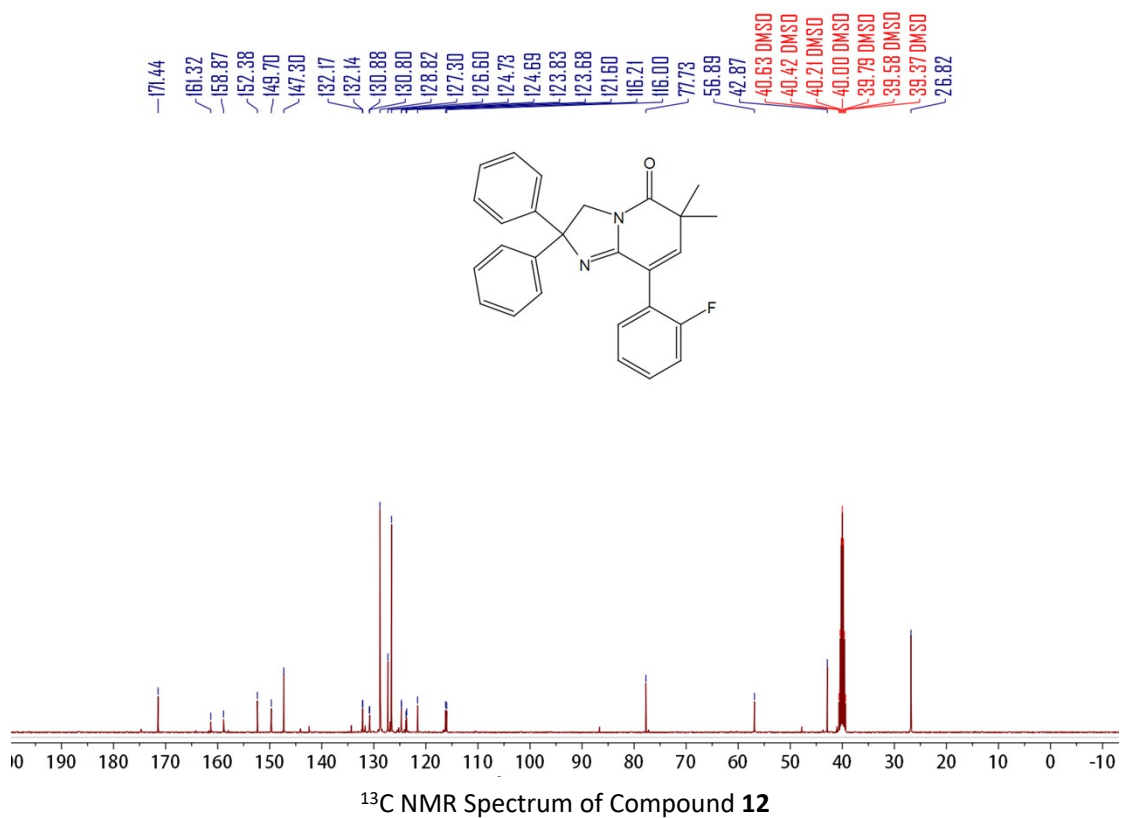


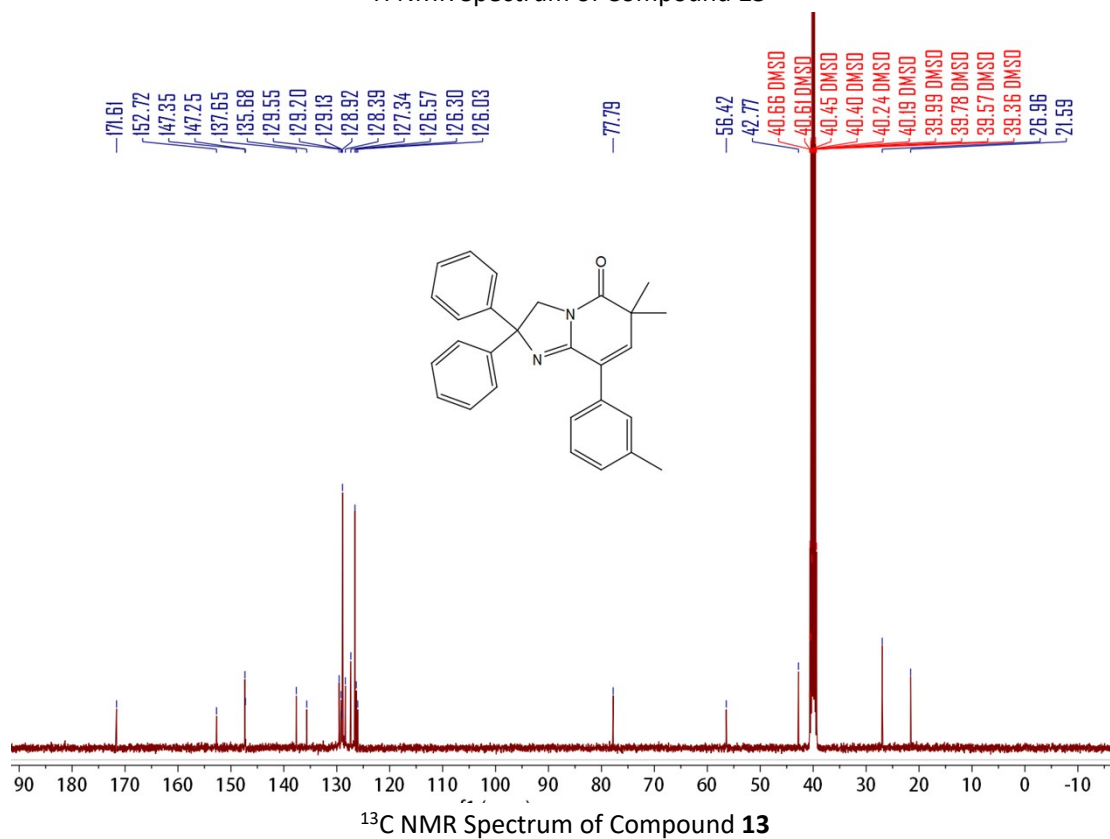
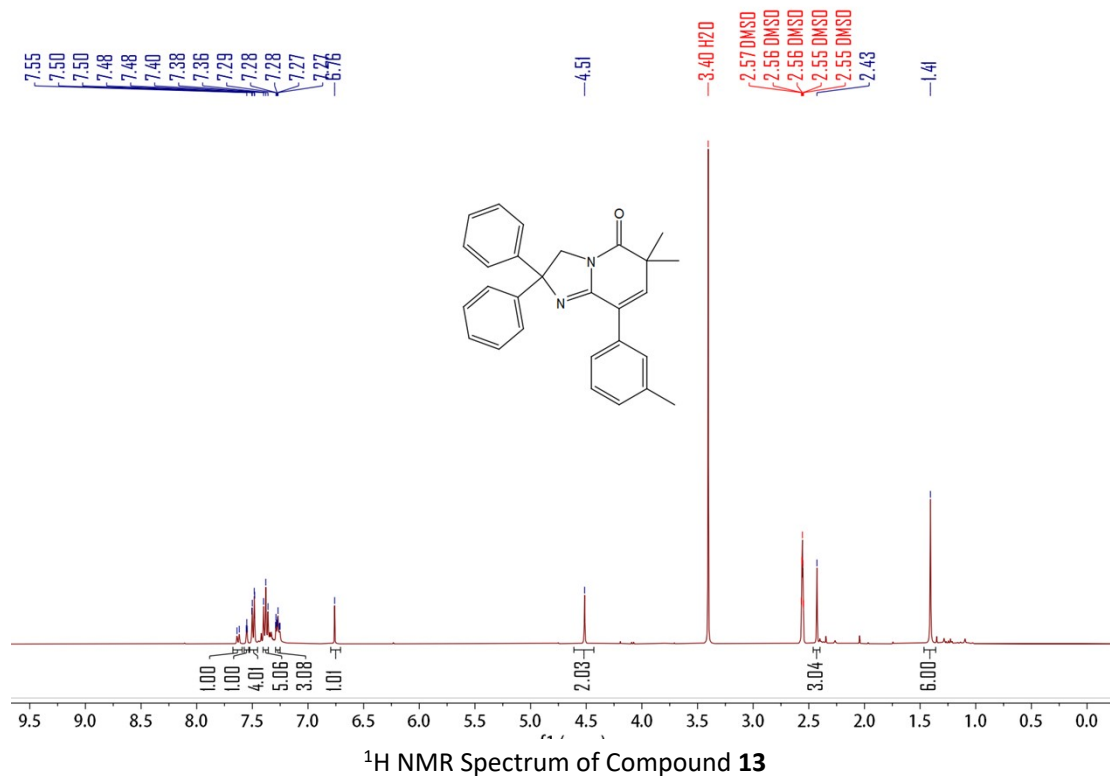


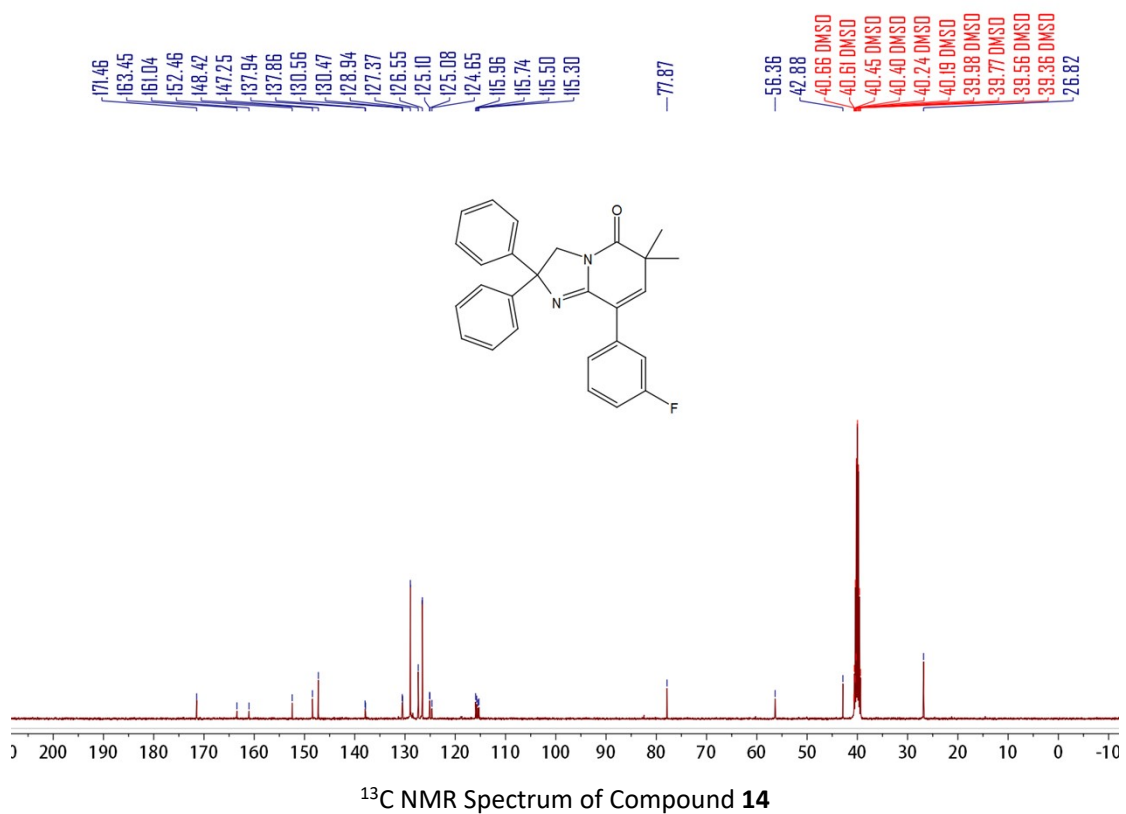
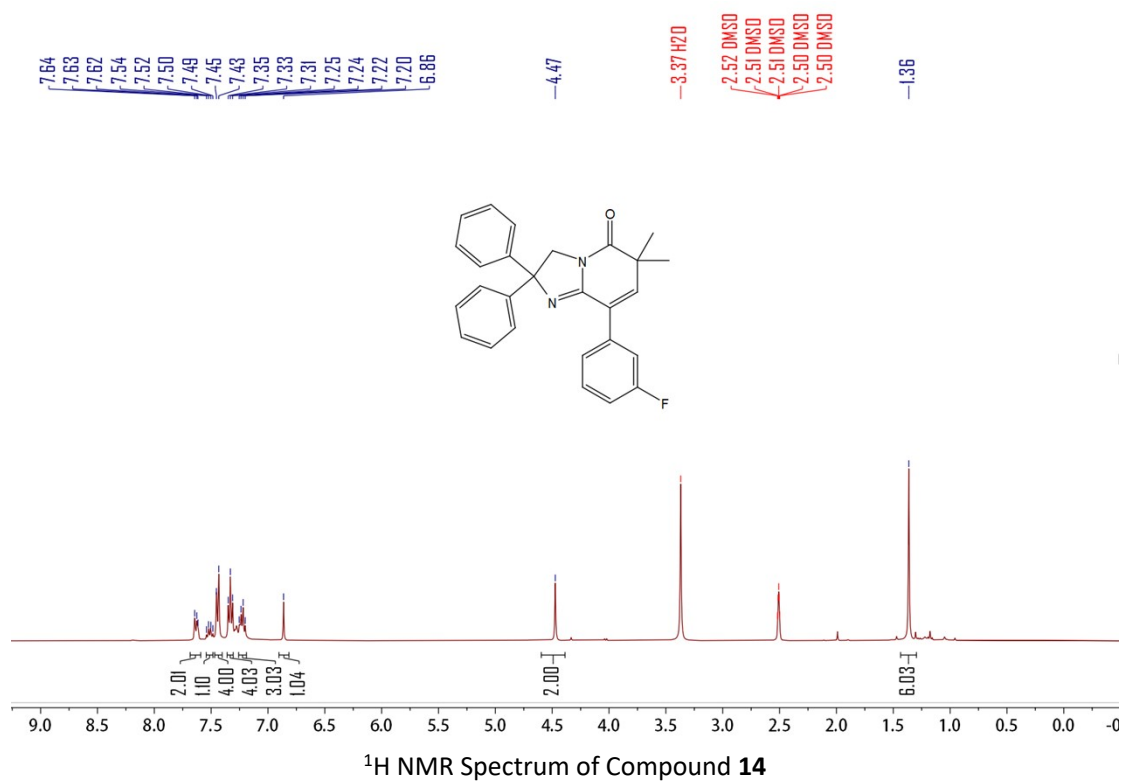
¹³C NMR Spectrum of Compound 11

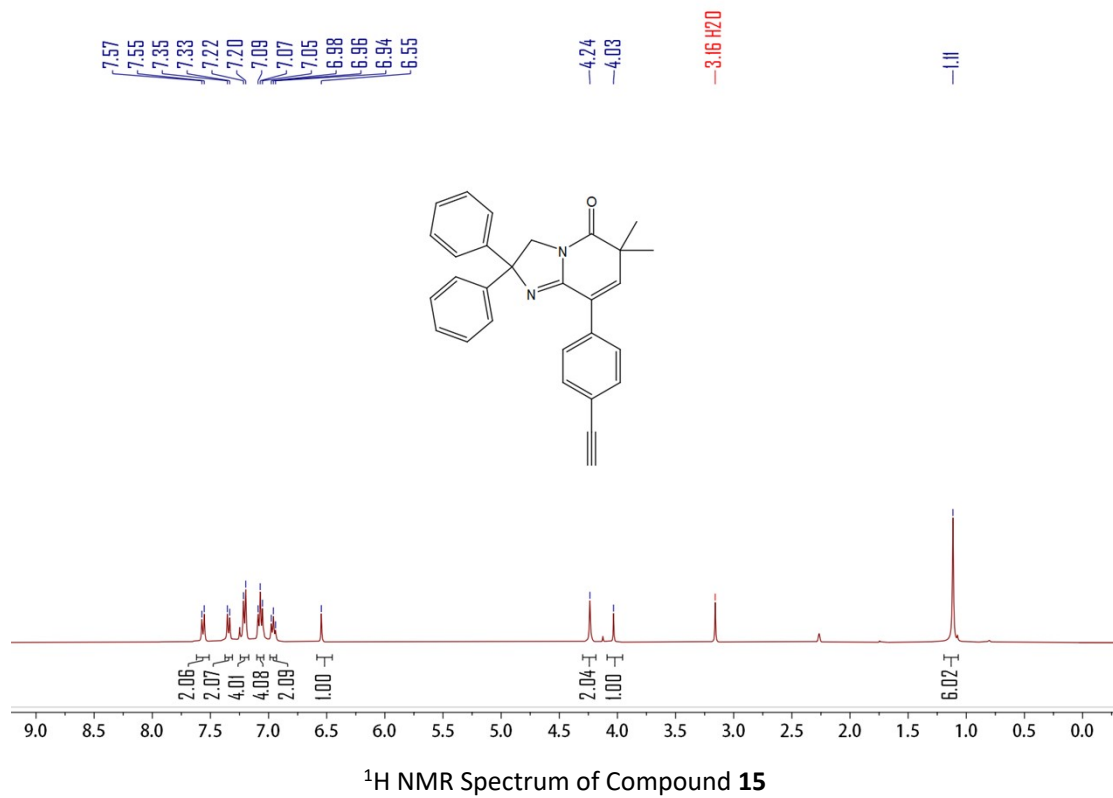
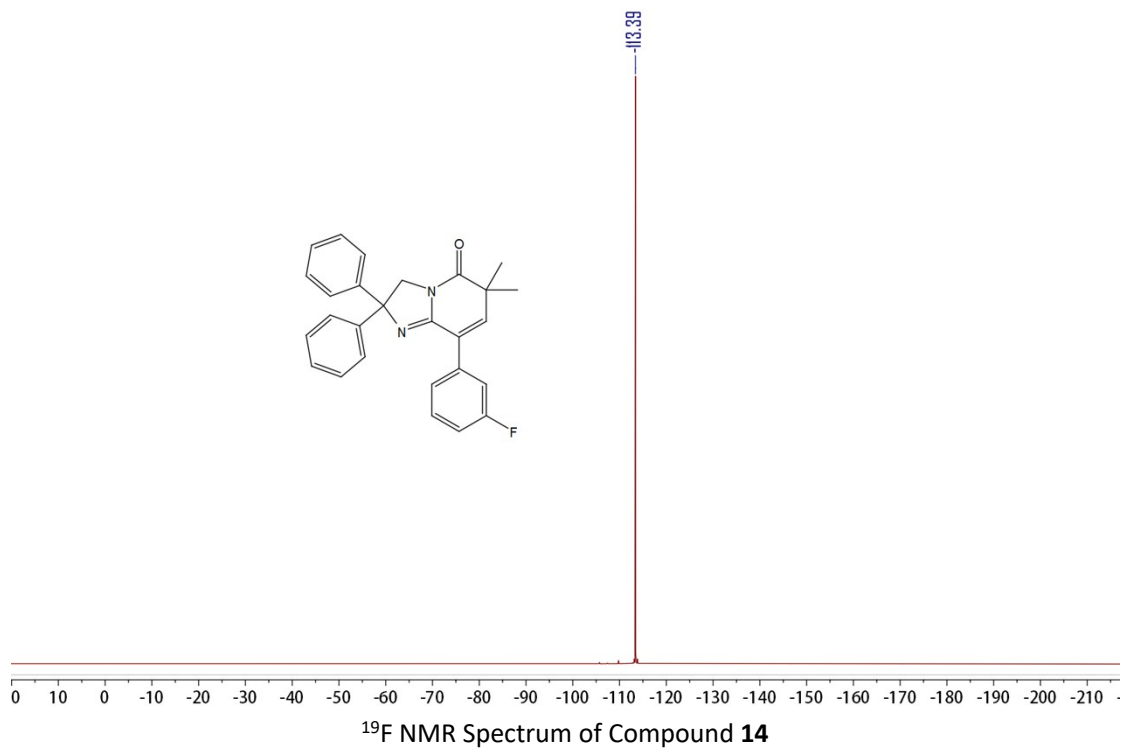


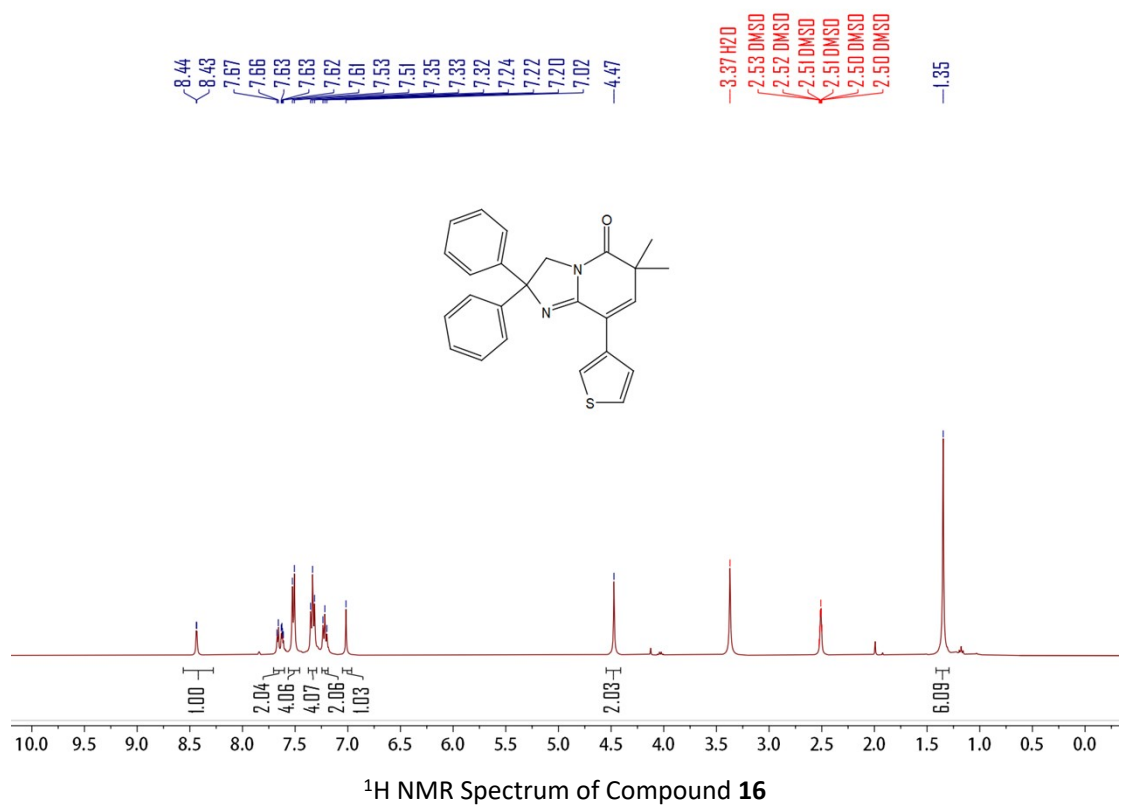
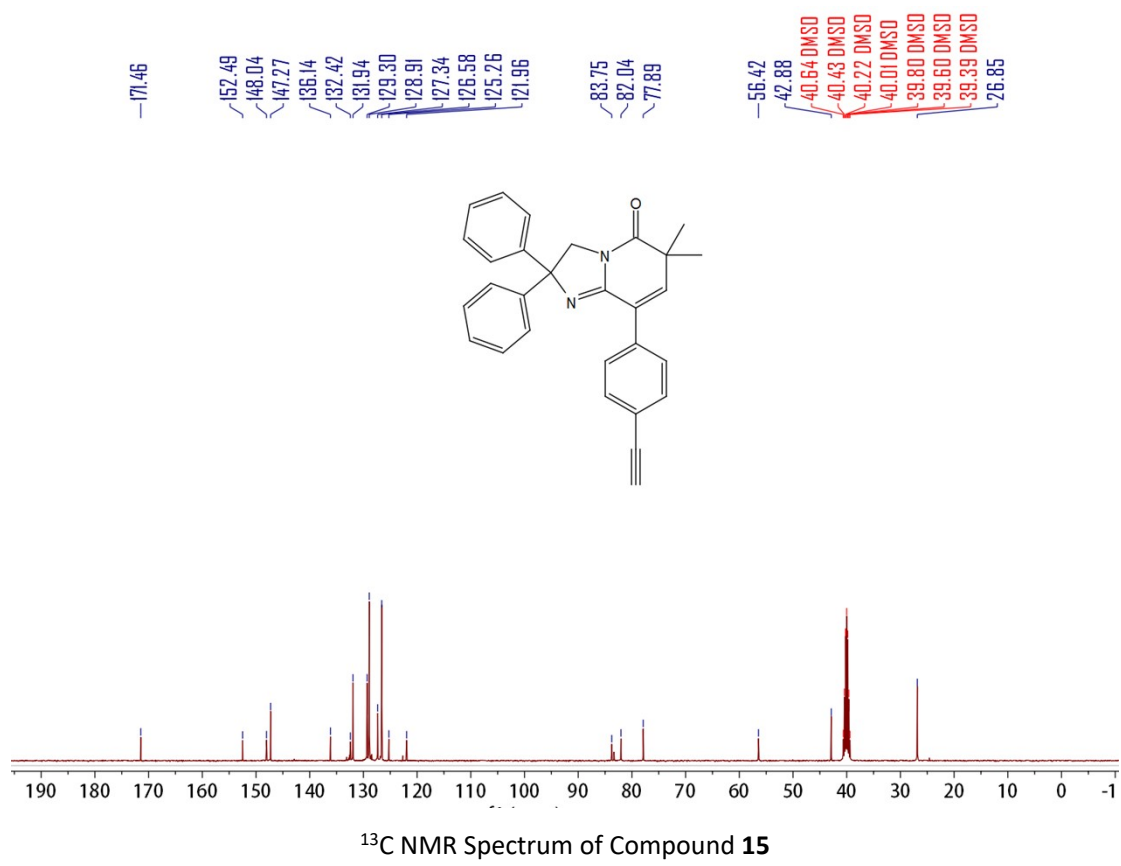
¹H NMR Spectrum of Compound 12

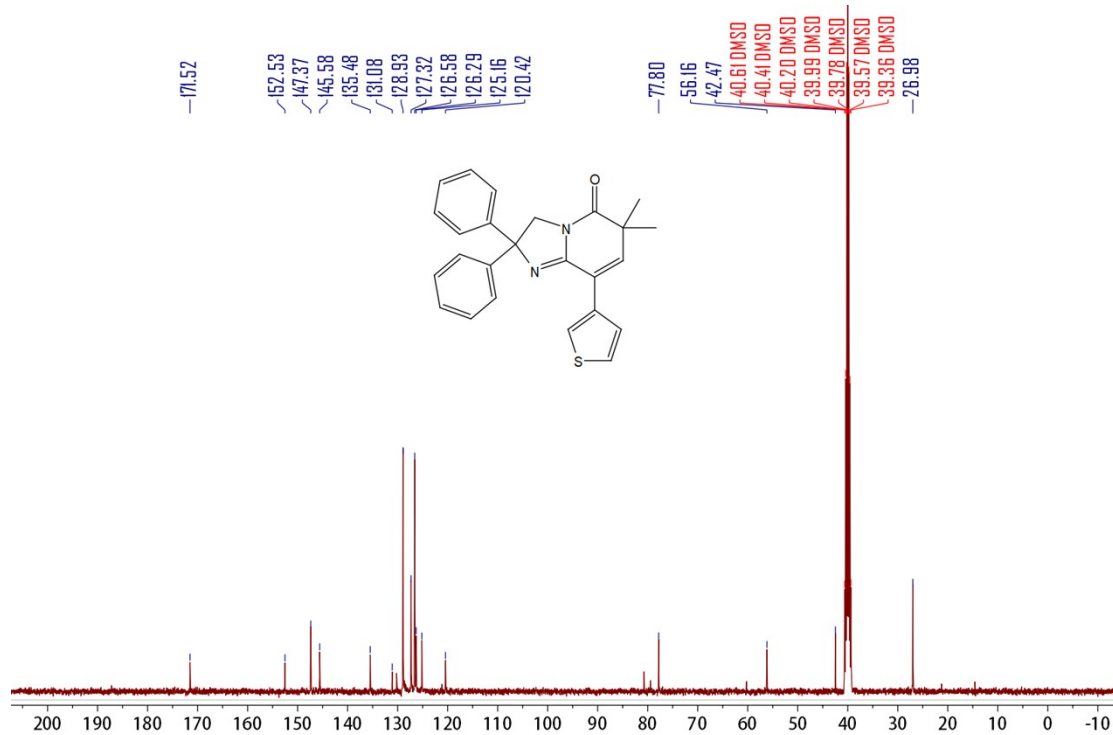




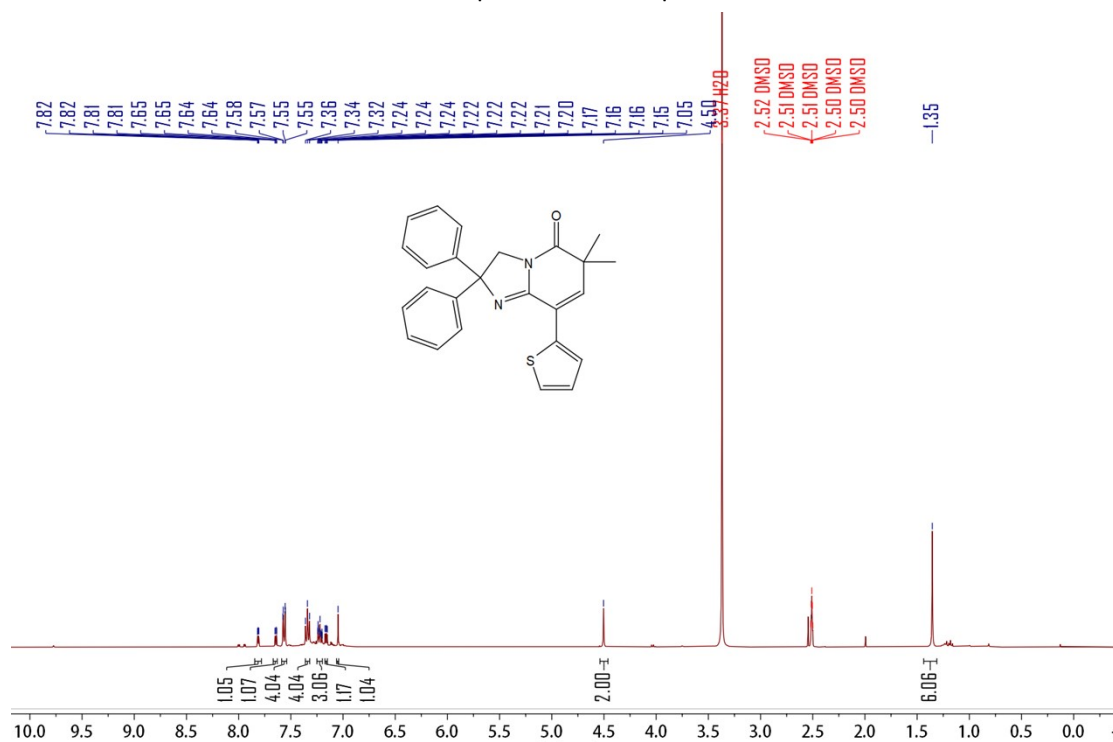




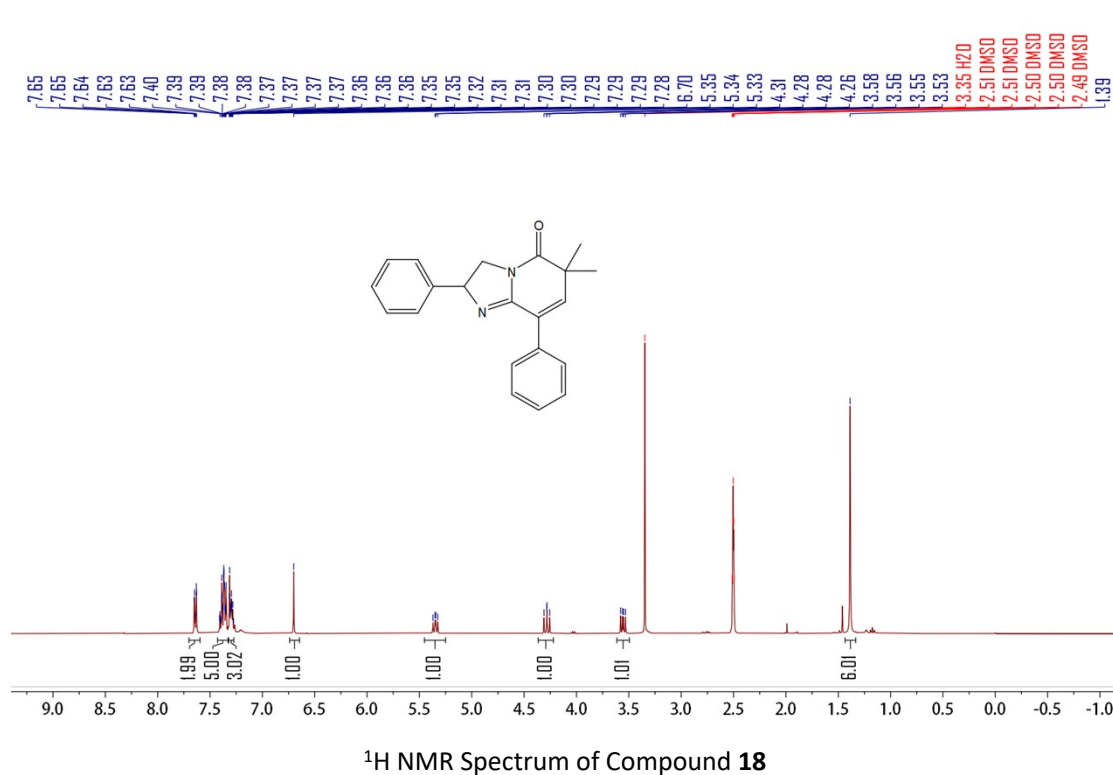
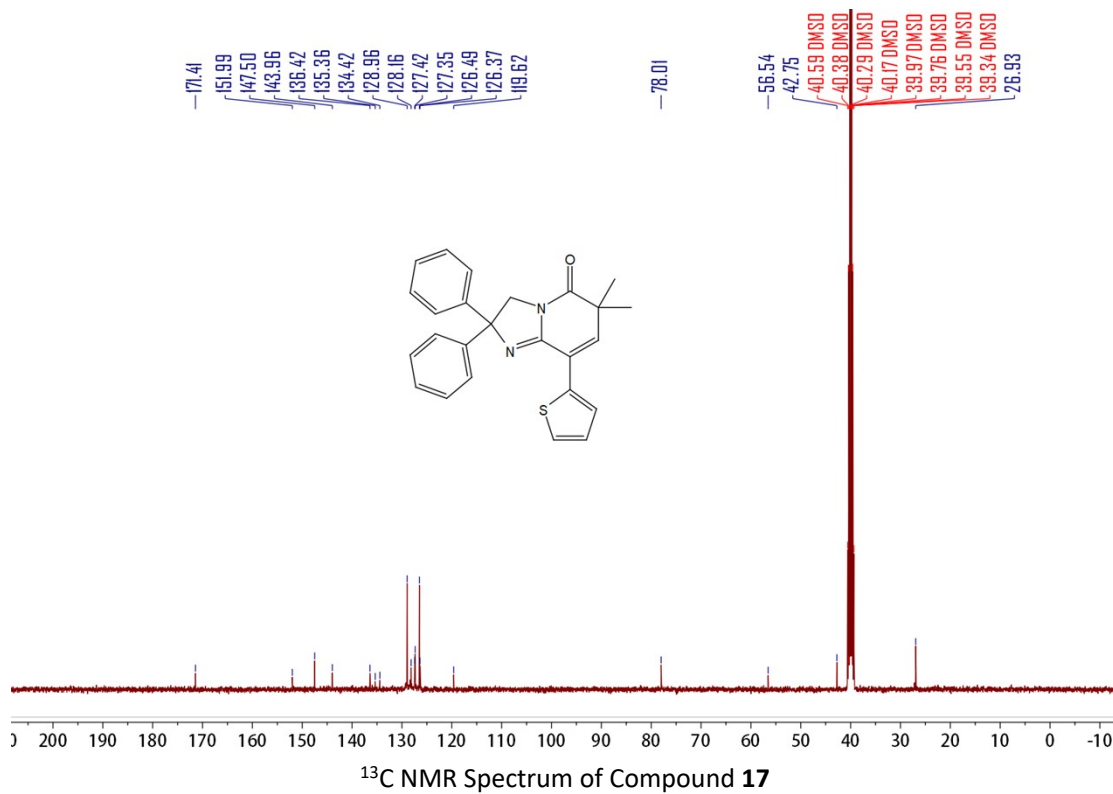


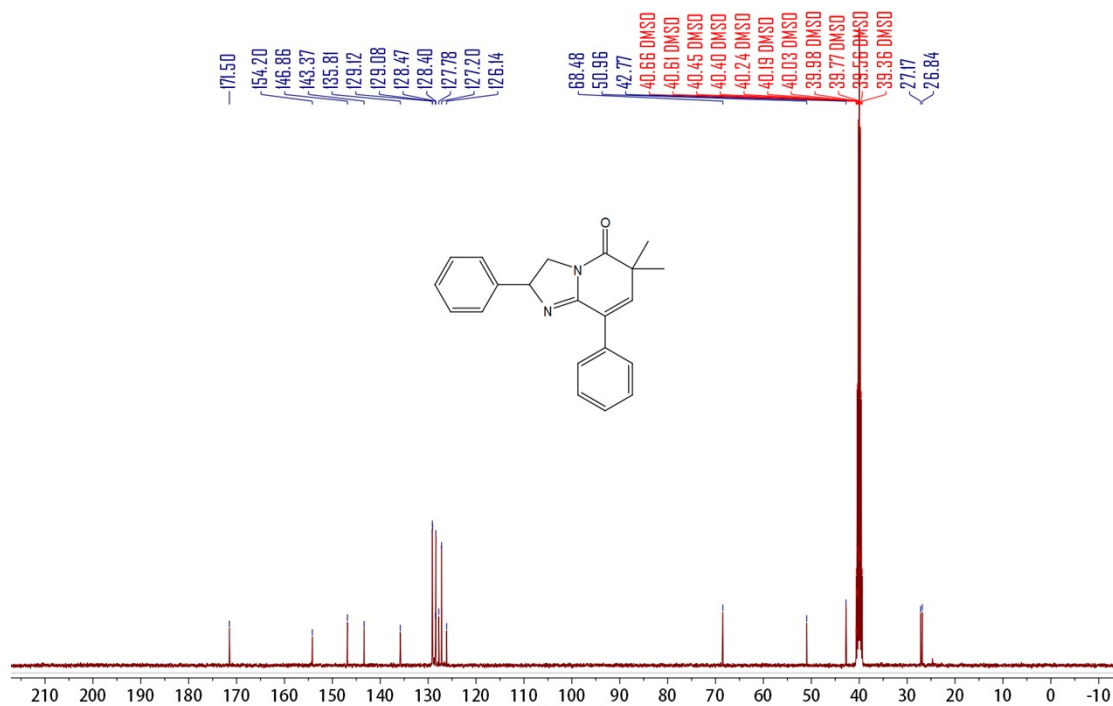


¹³C NMR Spectrum of Compound 16

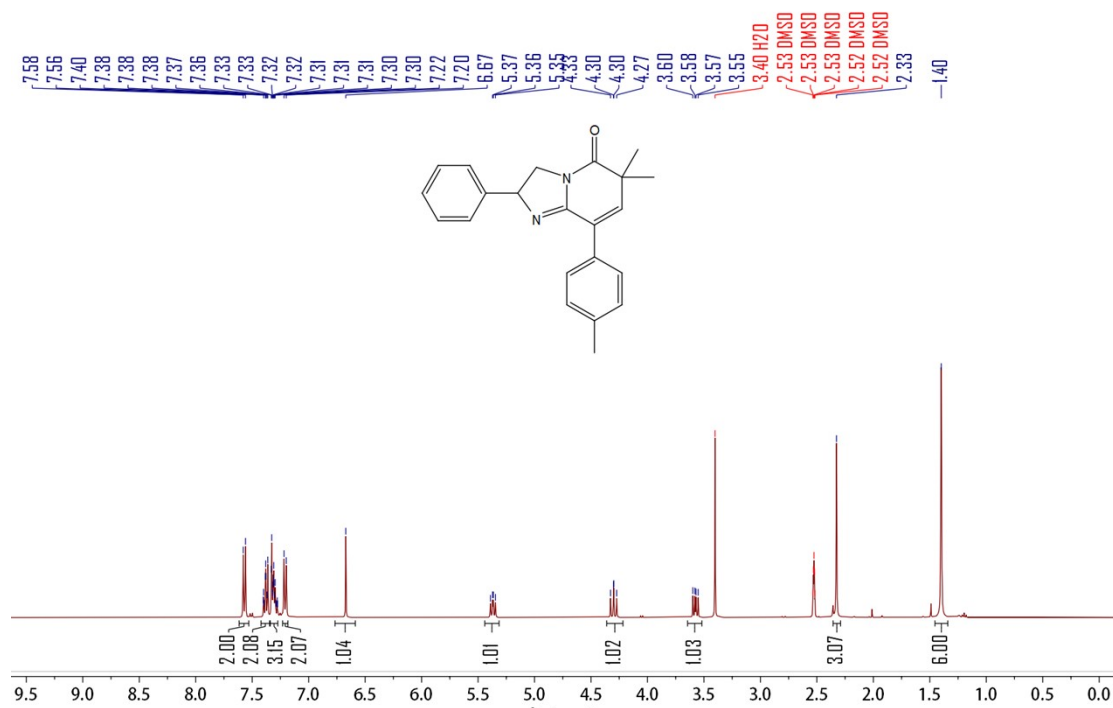


¹H NMR Spectrum of Compound 17

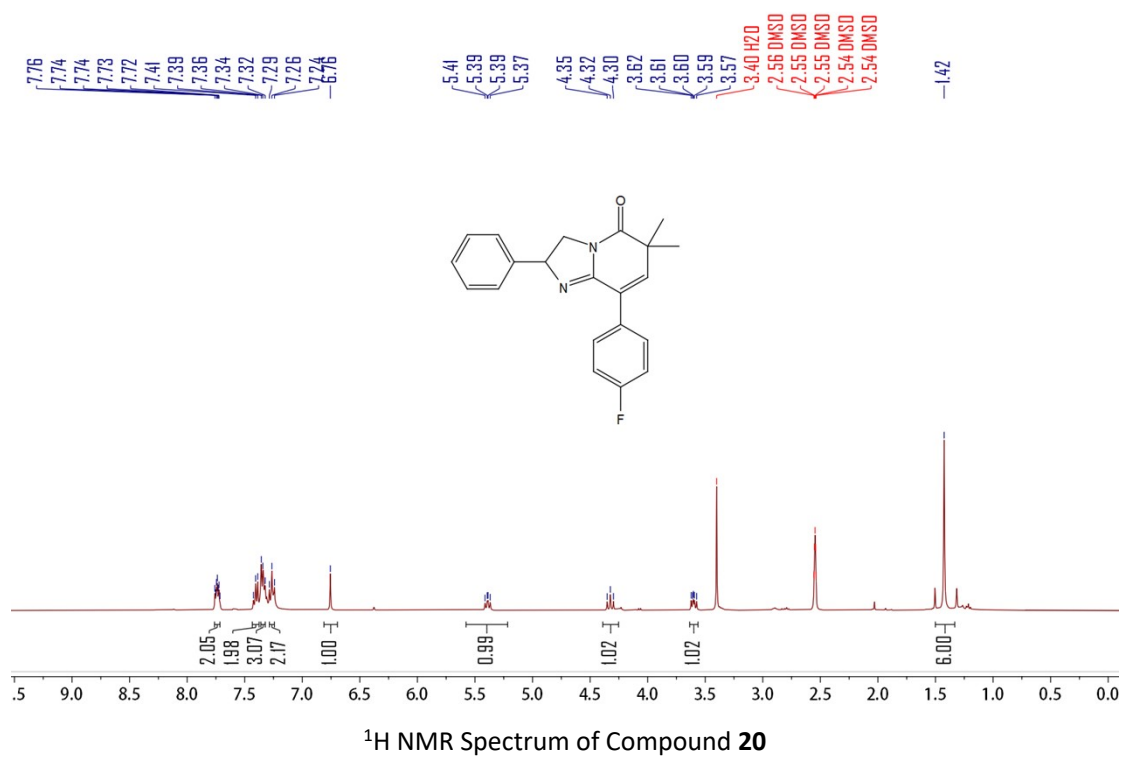
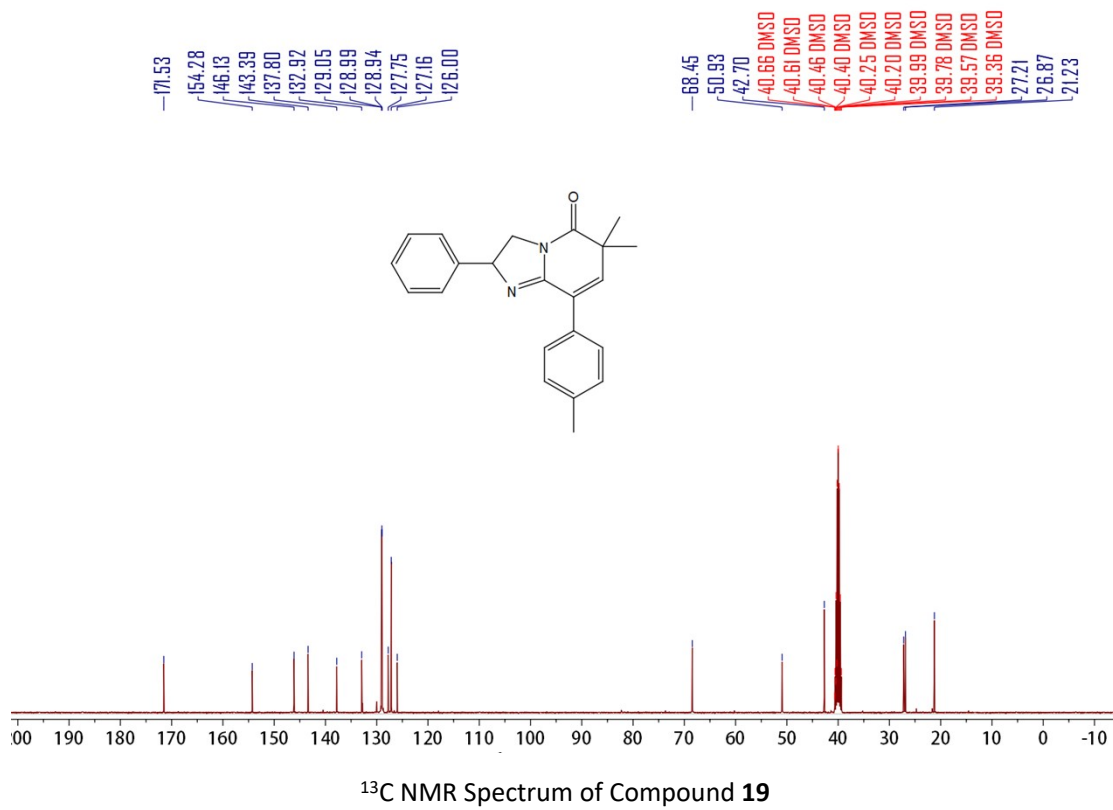


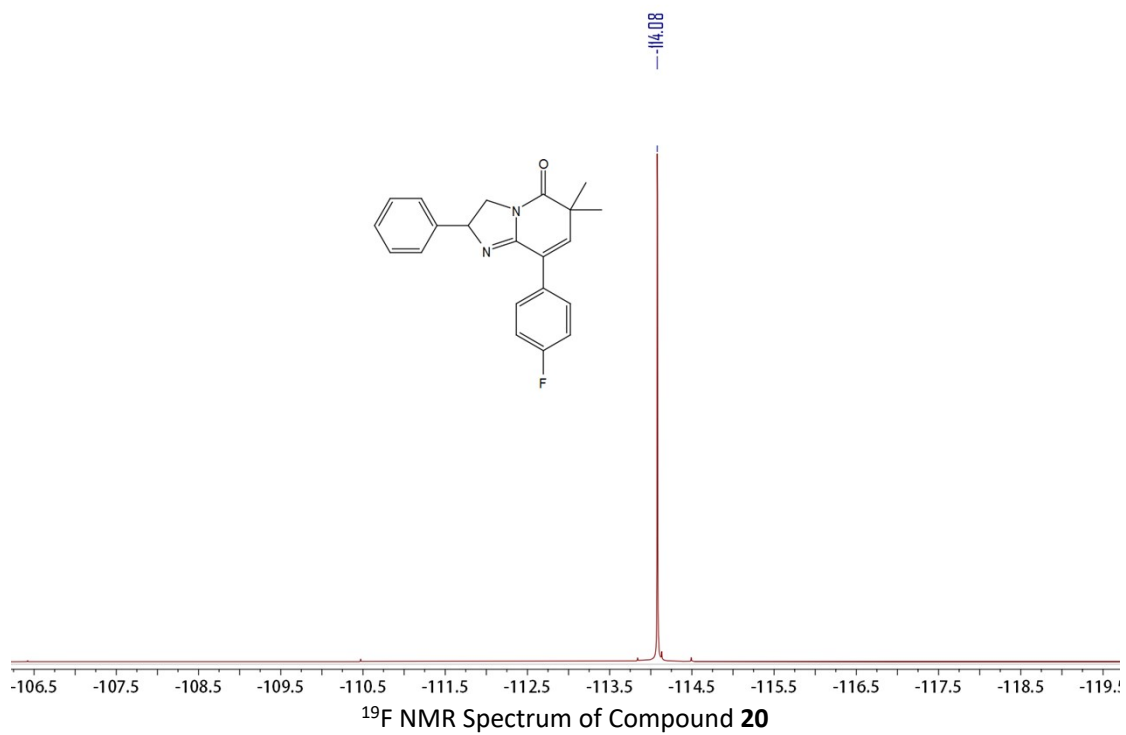
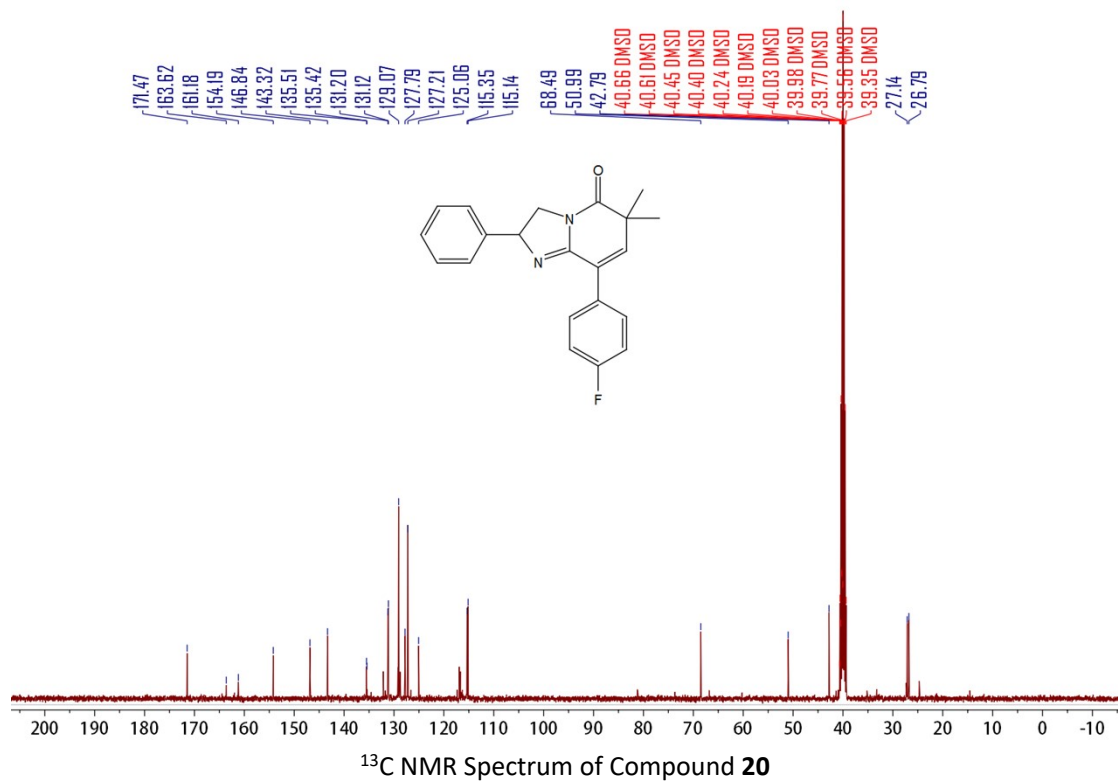


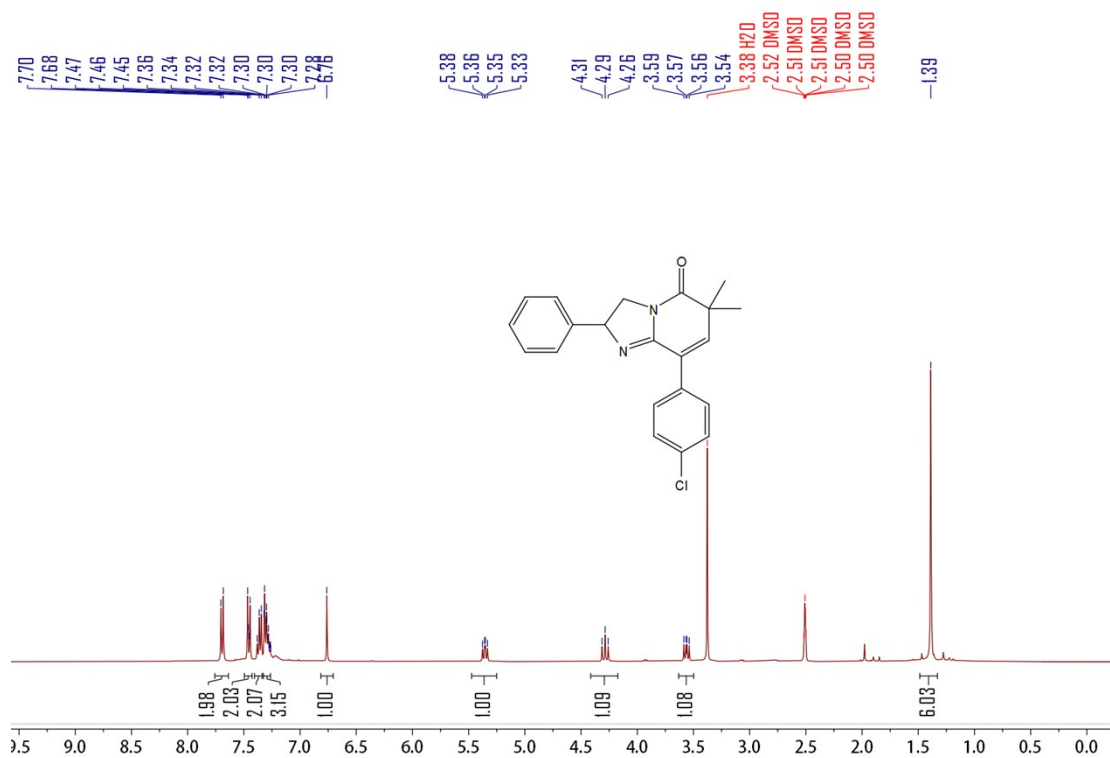
¹³C NMR Spectrum of Compound 18



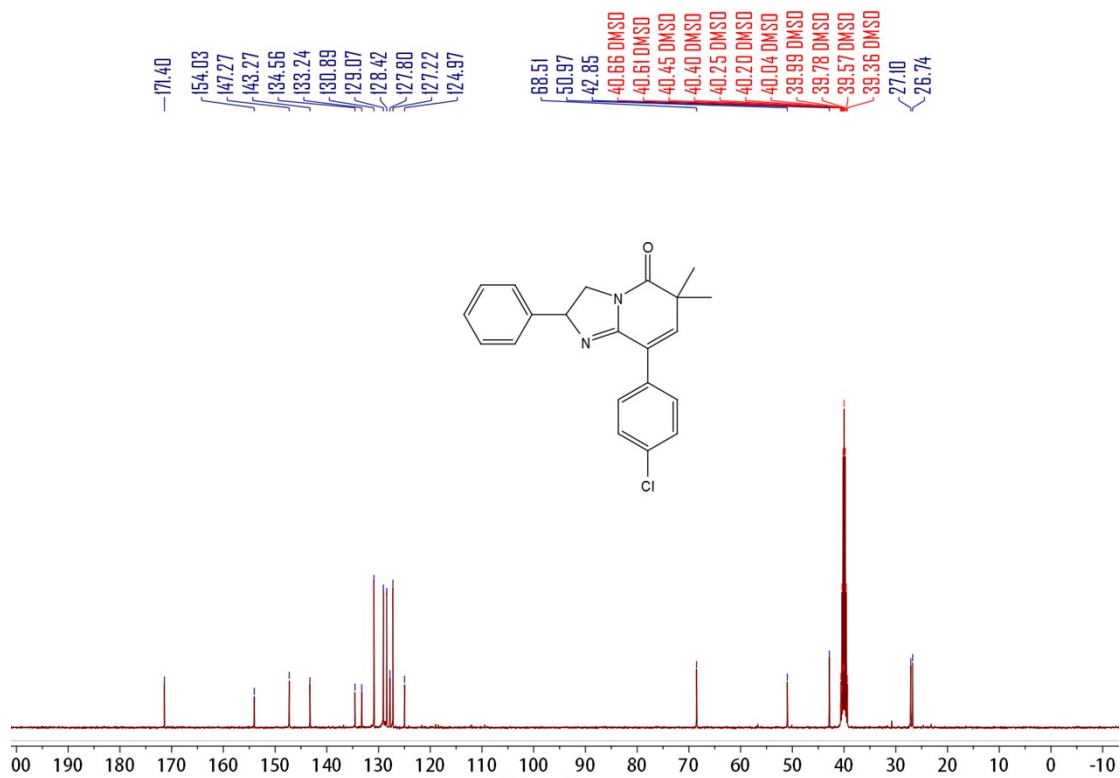
¹H NMR Spectrum of Compound 19



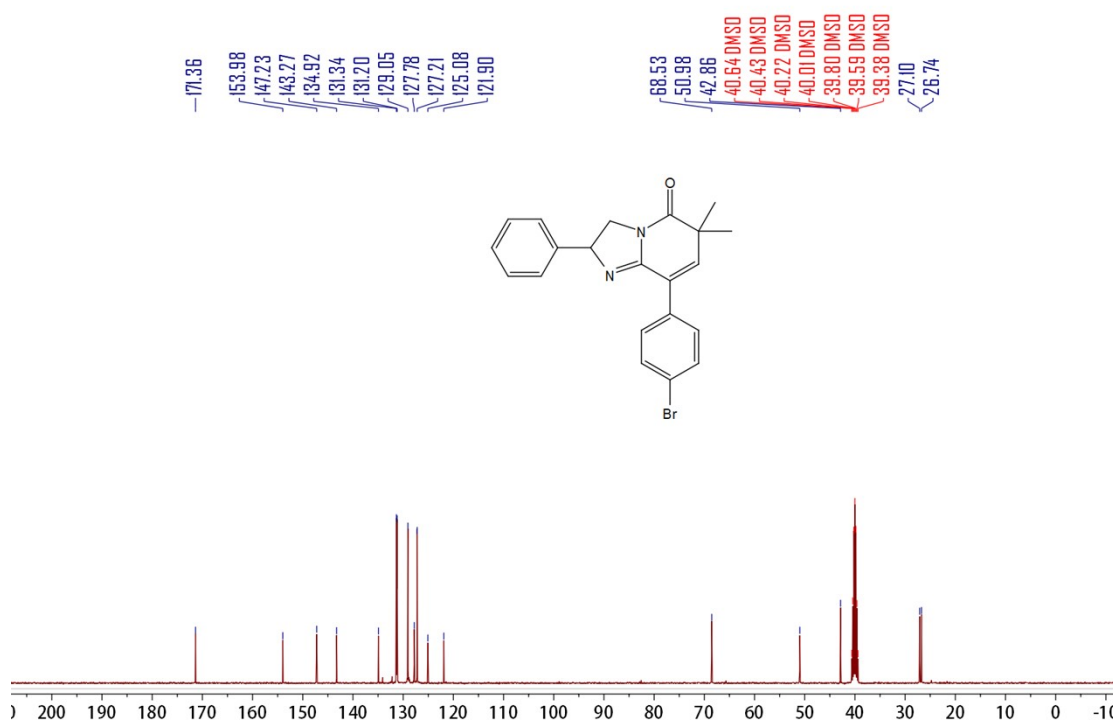
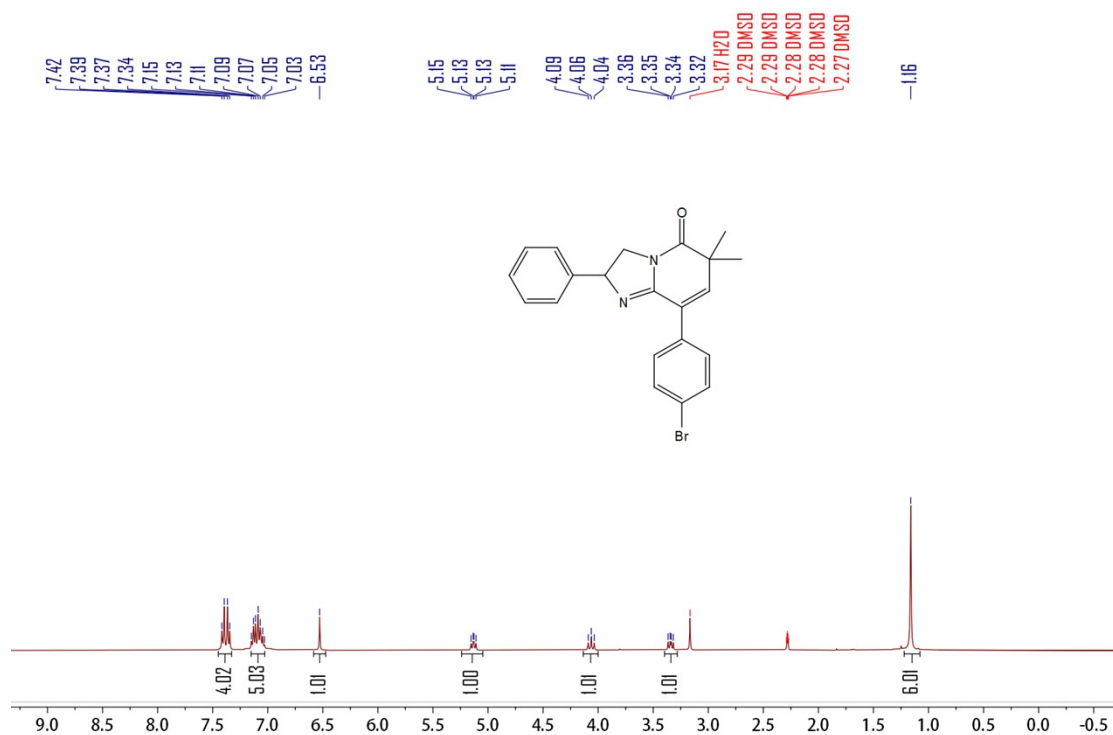


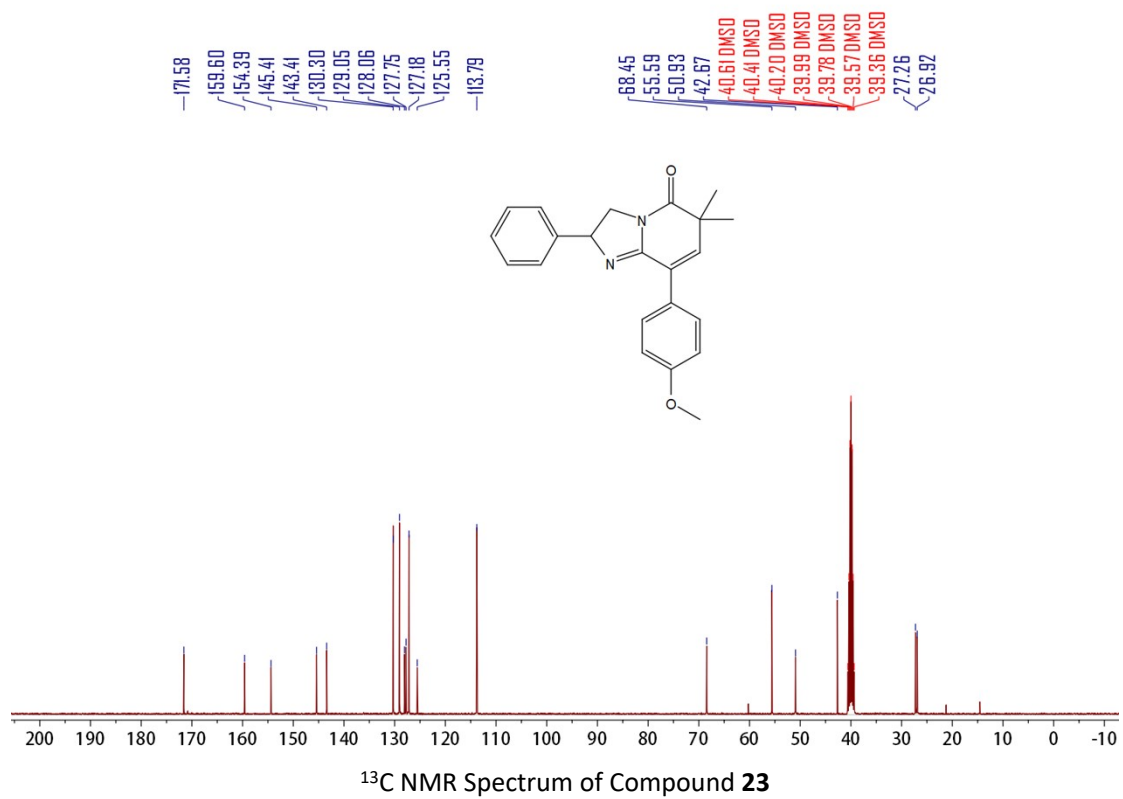
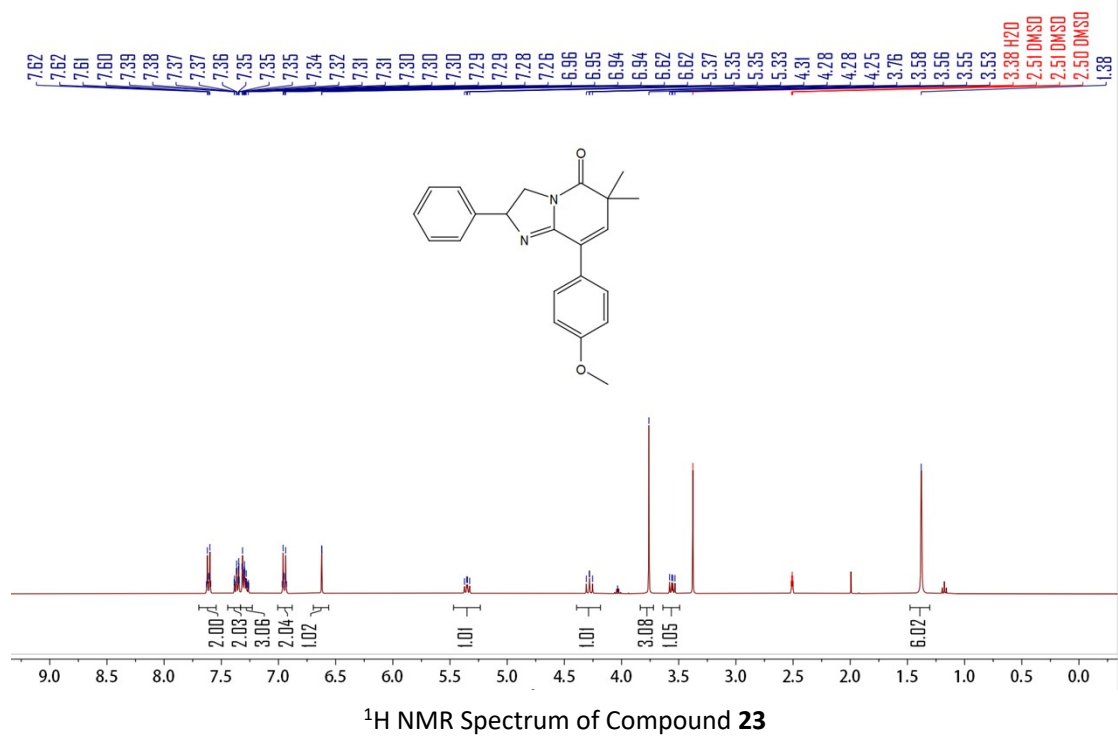


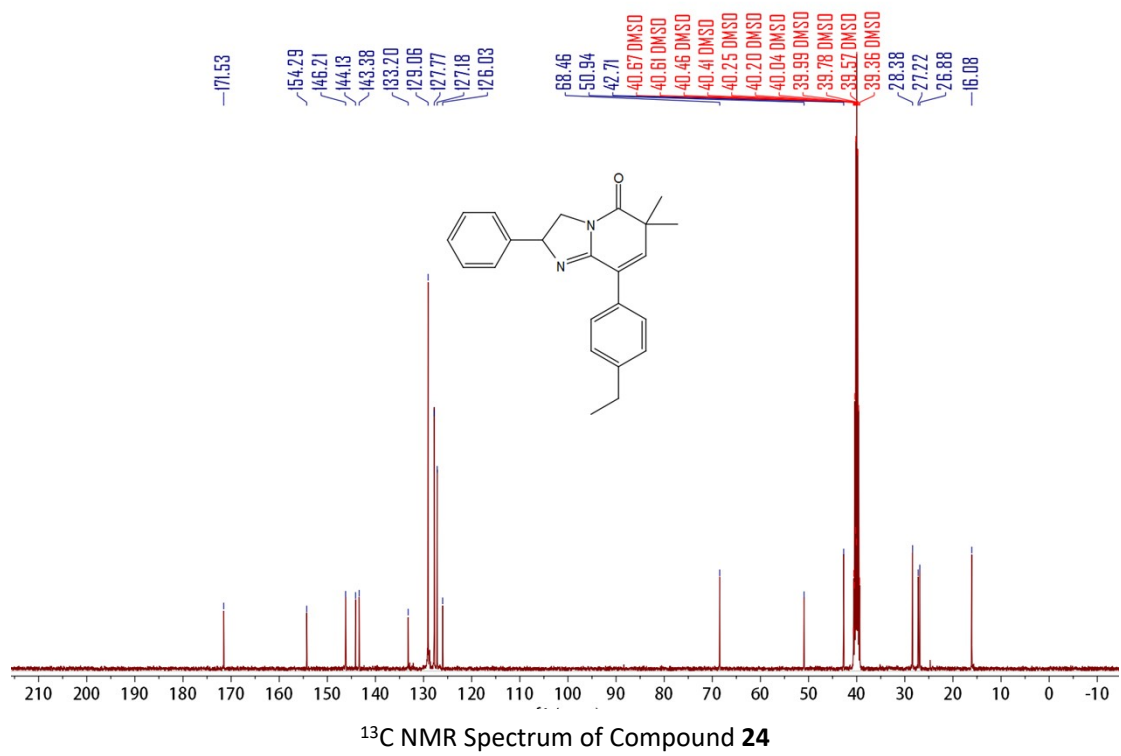
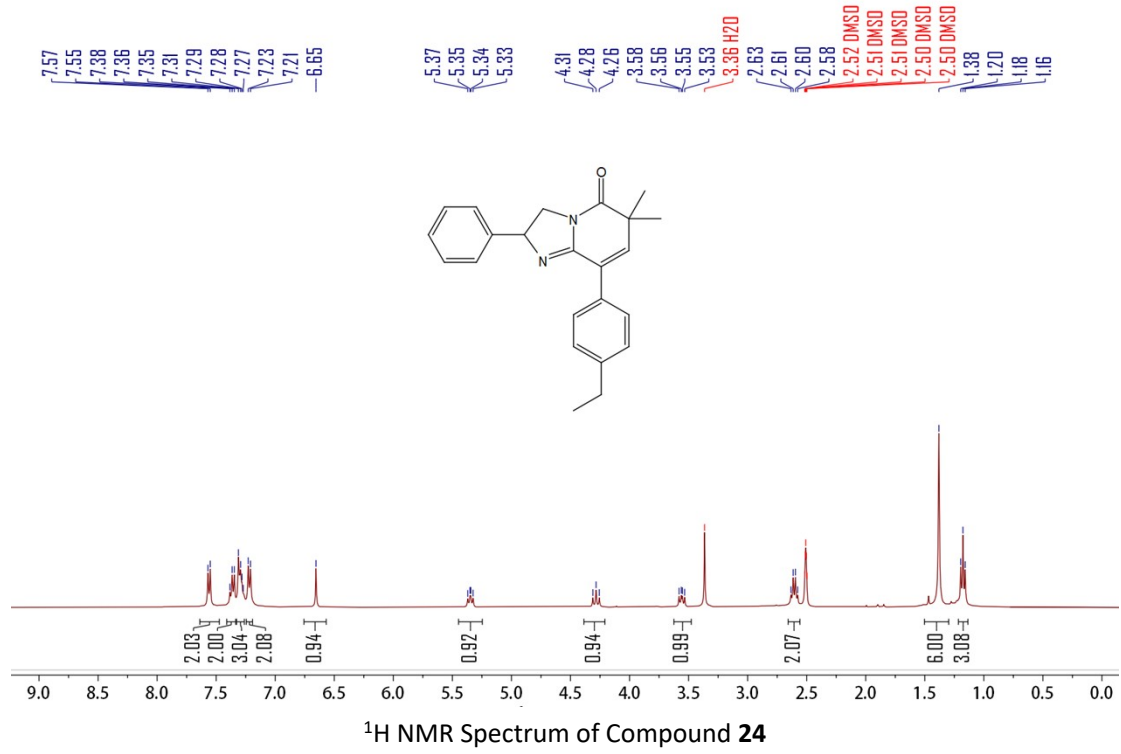
¹H NMR Spectrum of Compound 21

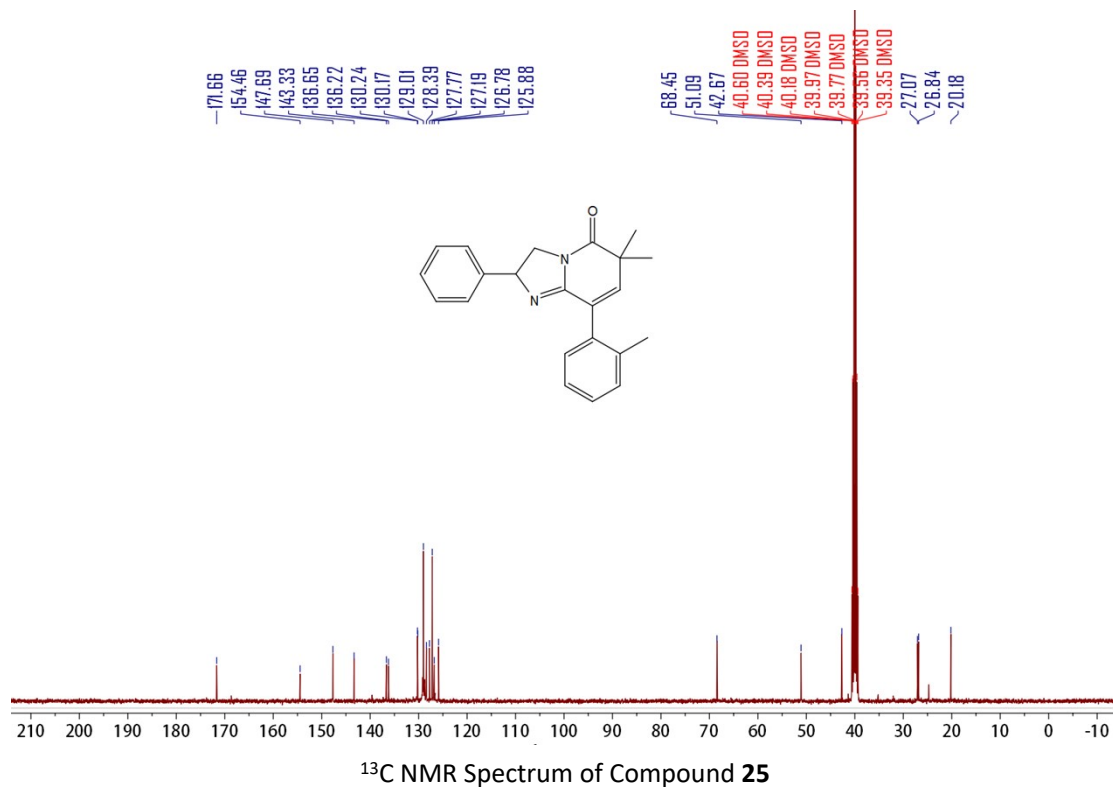
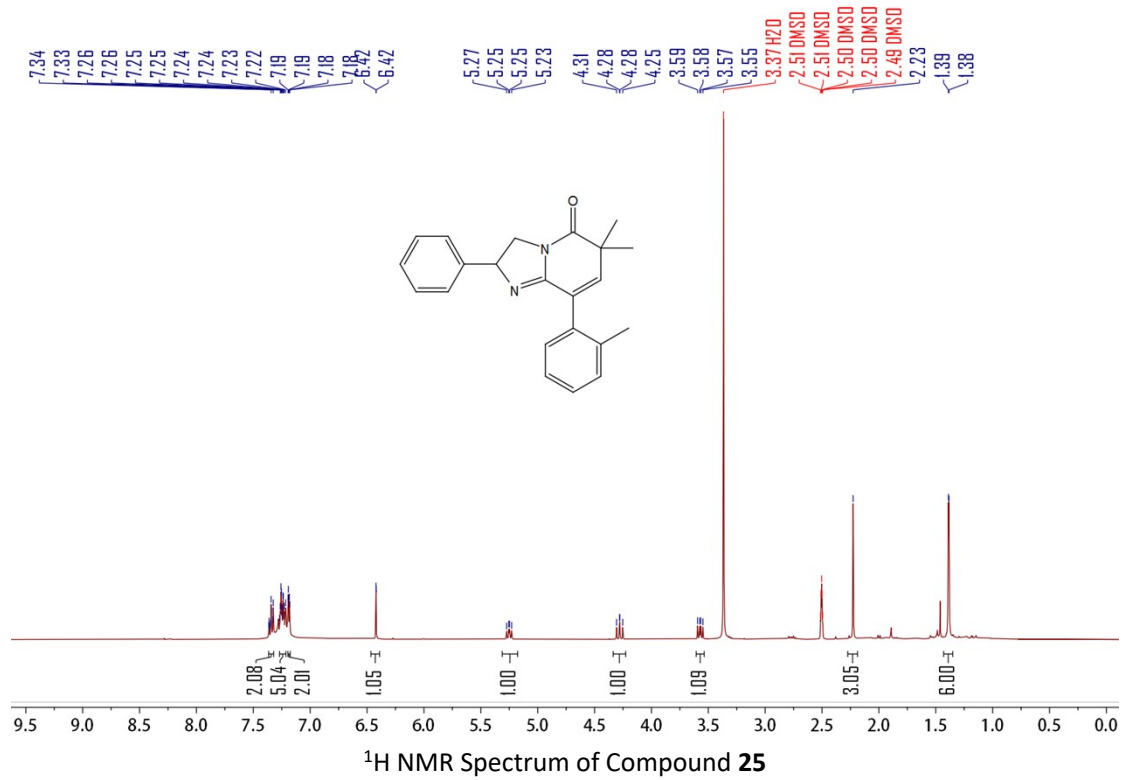


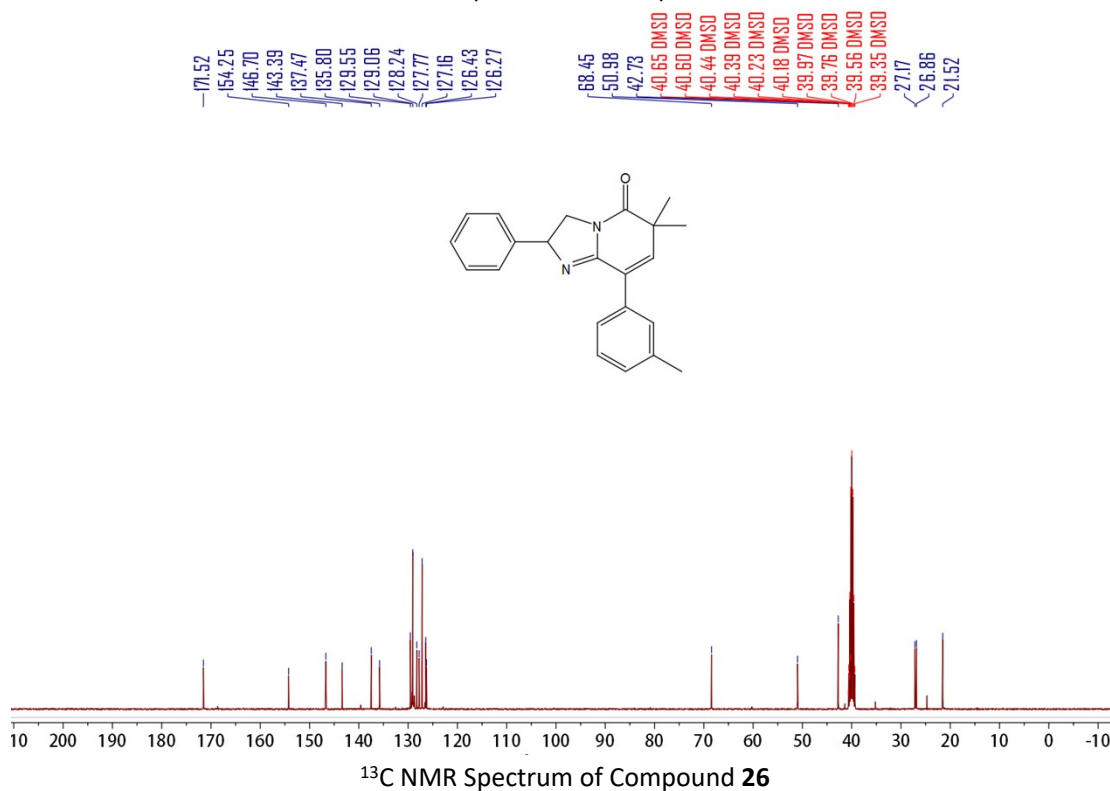
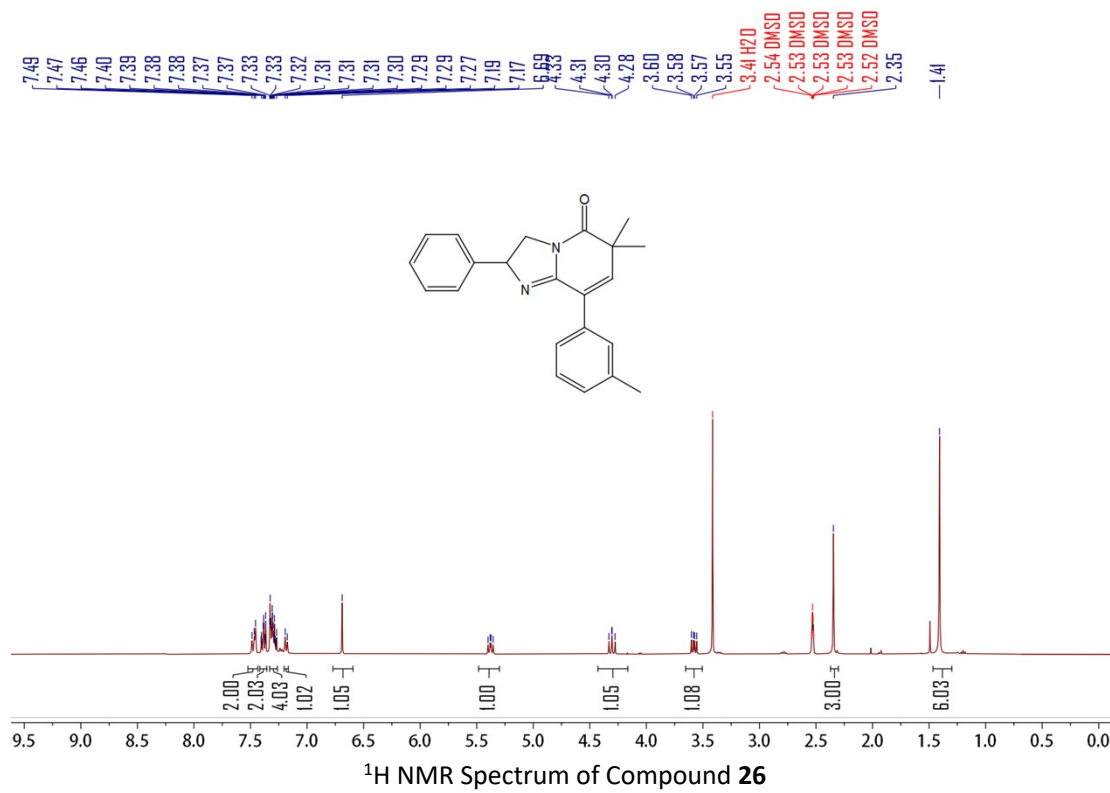
¹³C NMR Spectrum of Compound 21

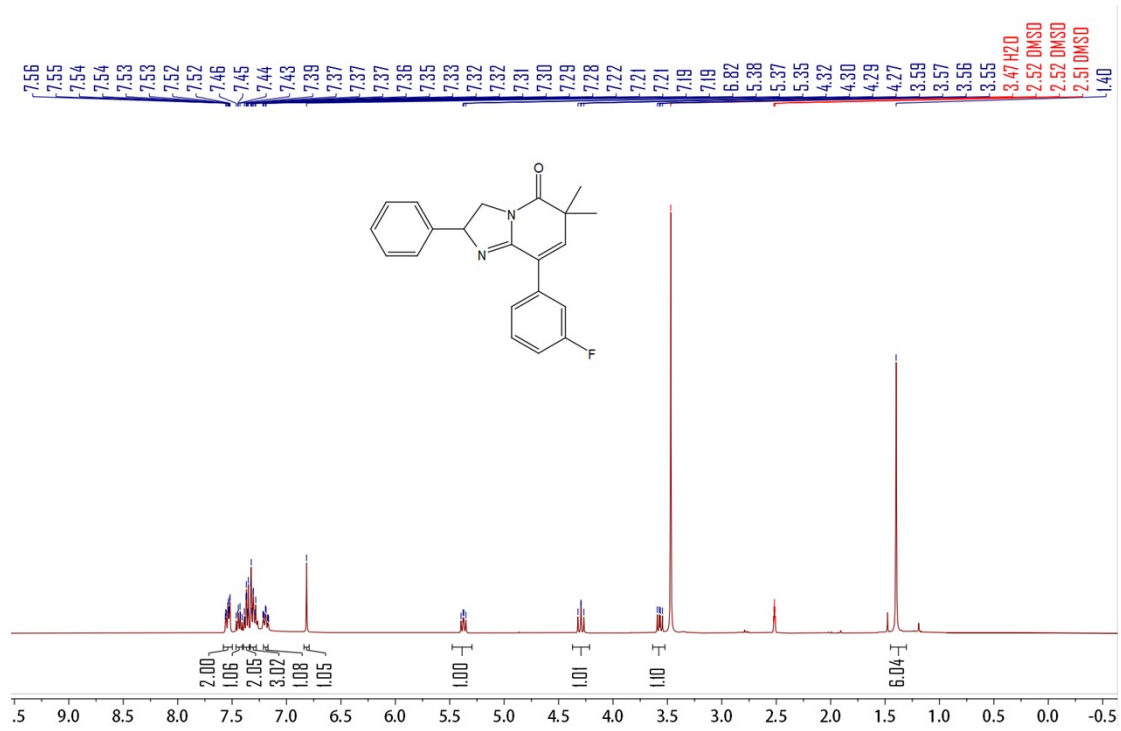




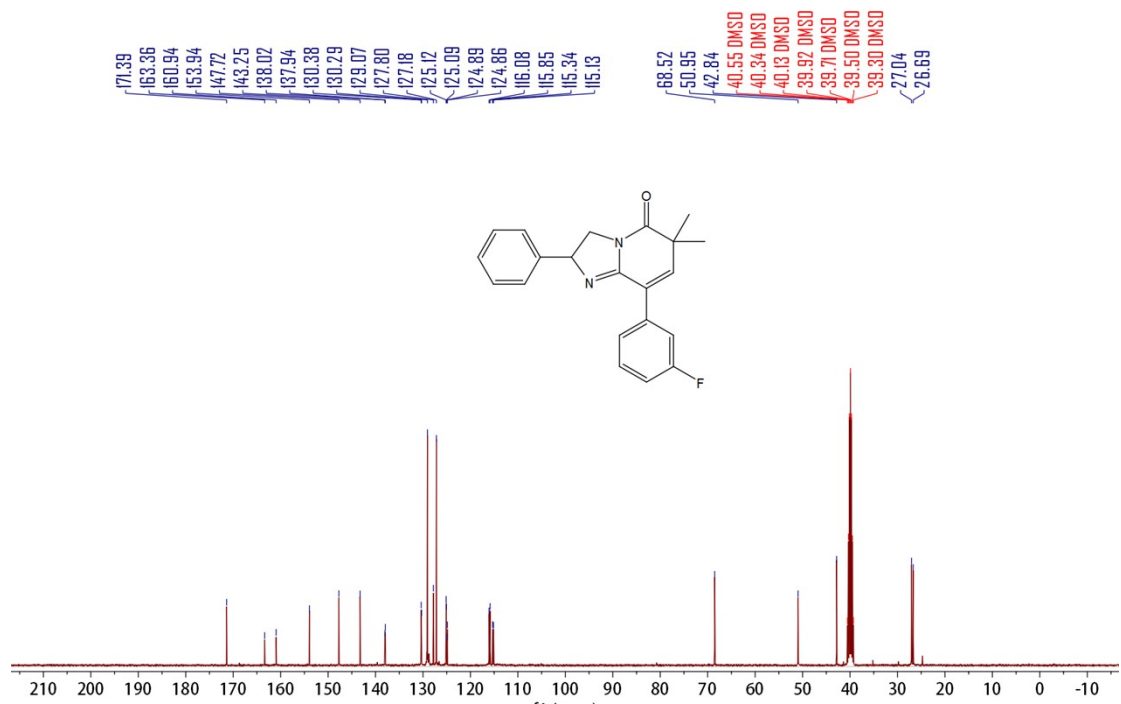




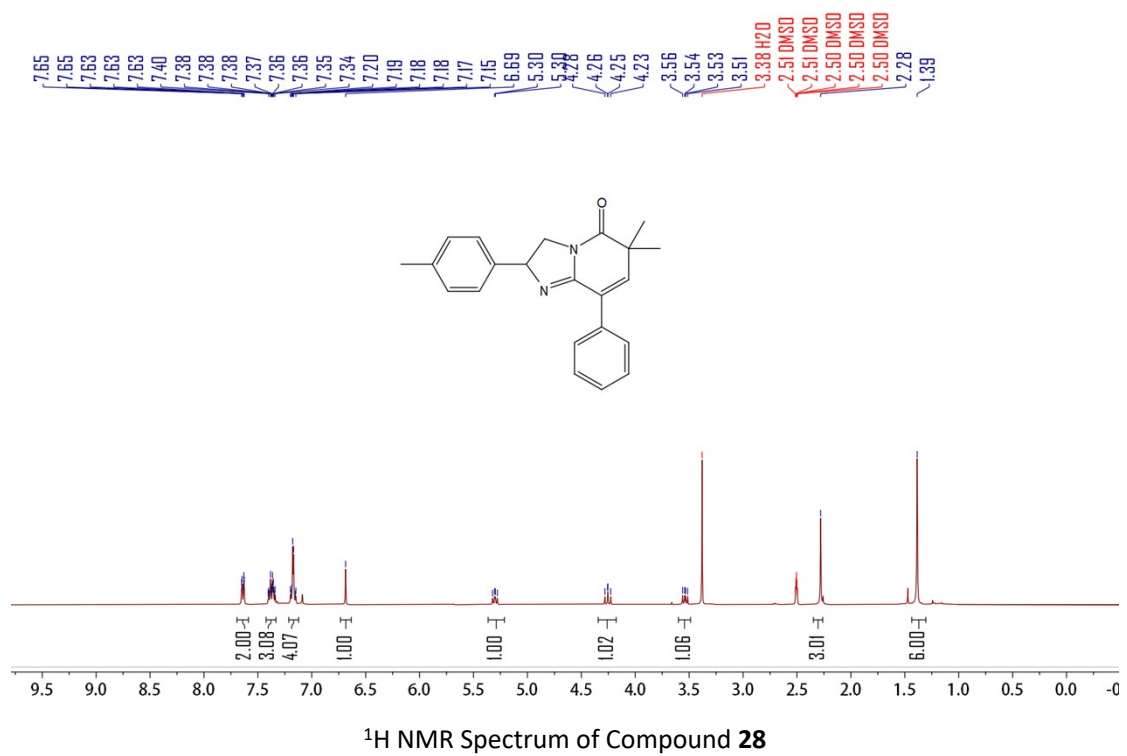
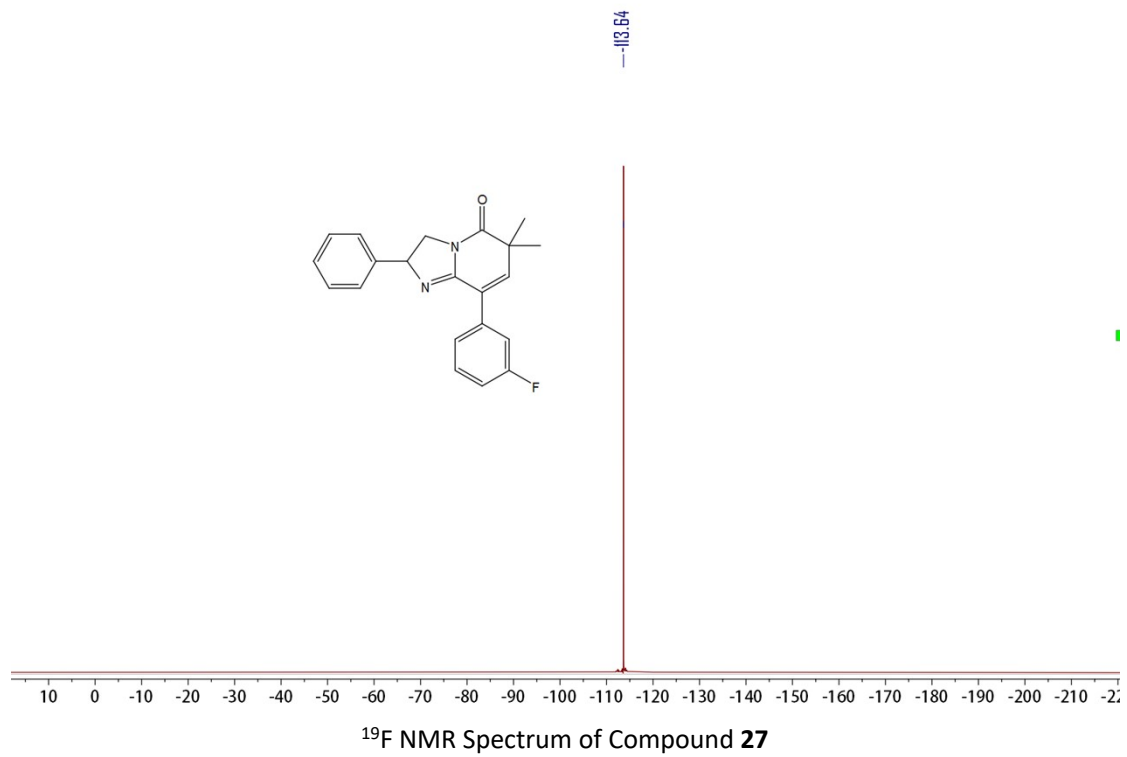


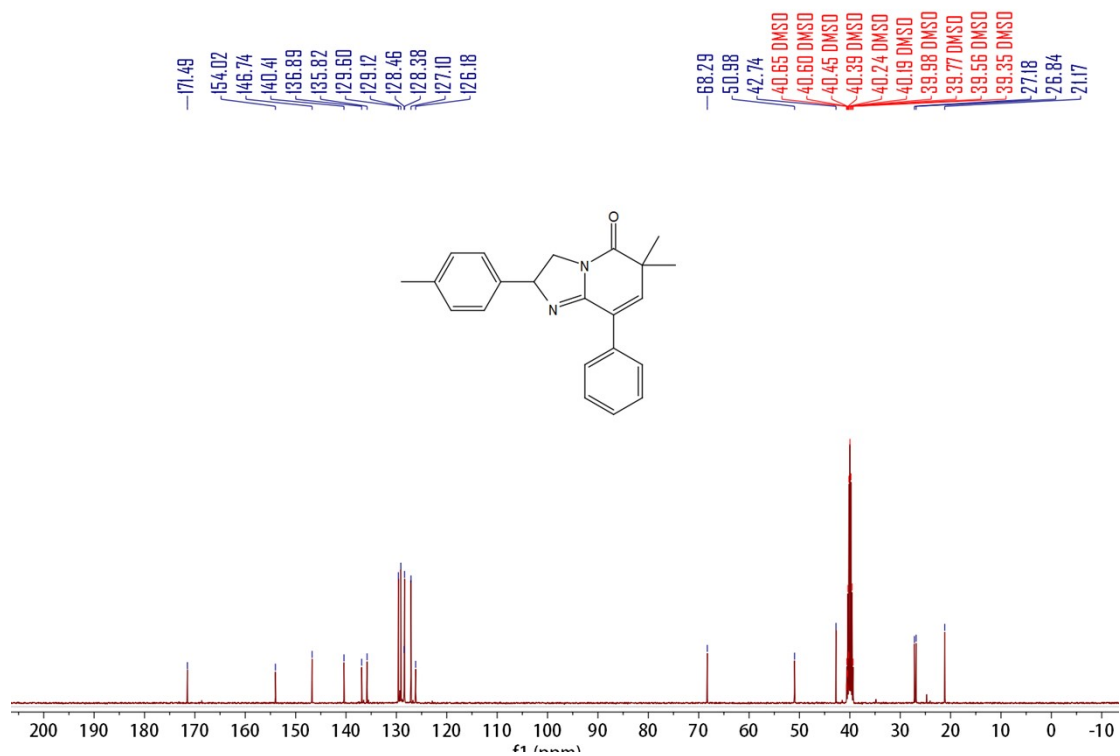


¹H NMR Spectrum of Compound 27

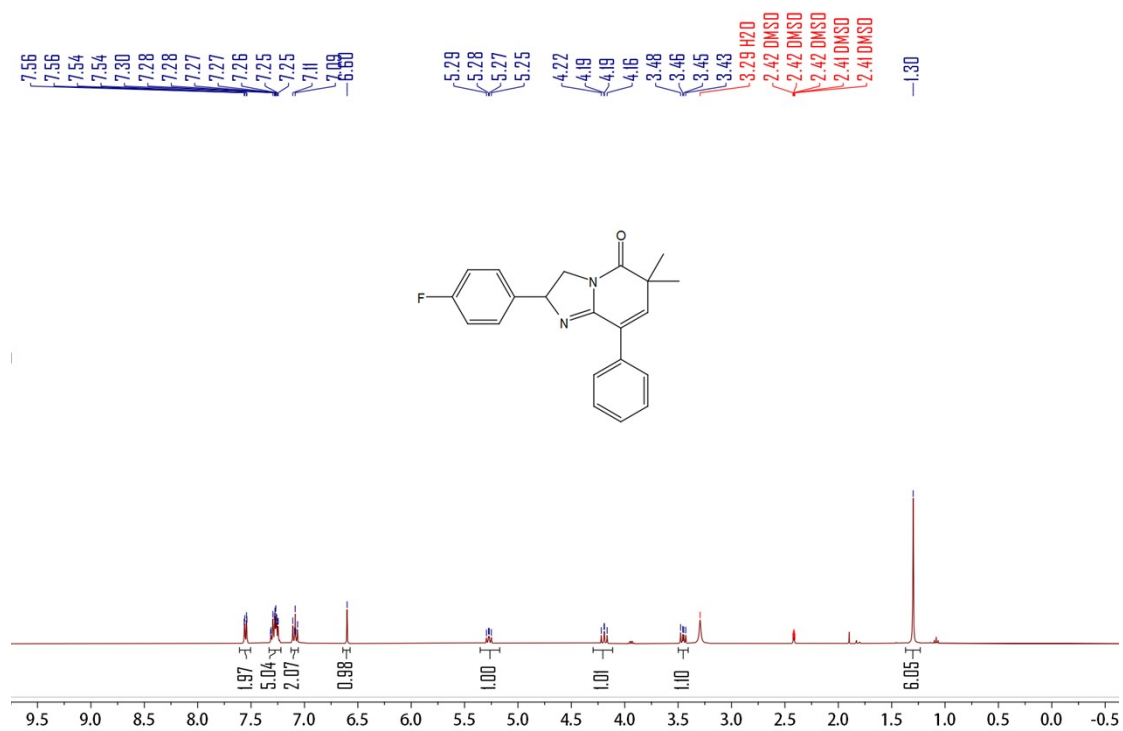


¹³C NMR Spectrum of Compound 27

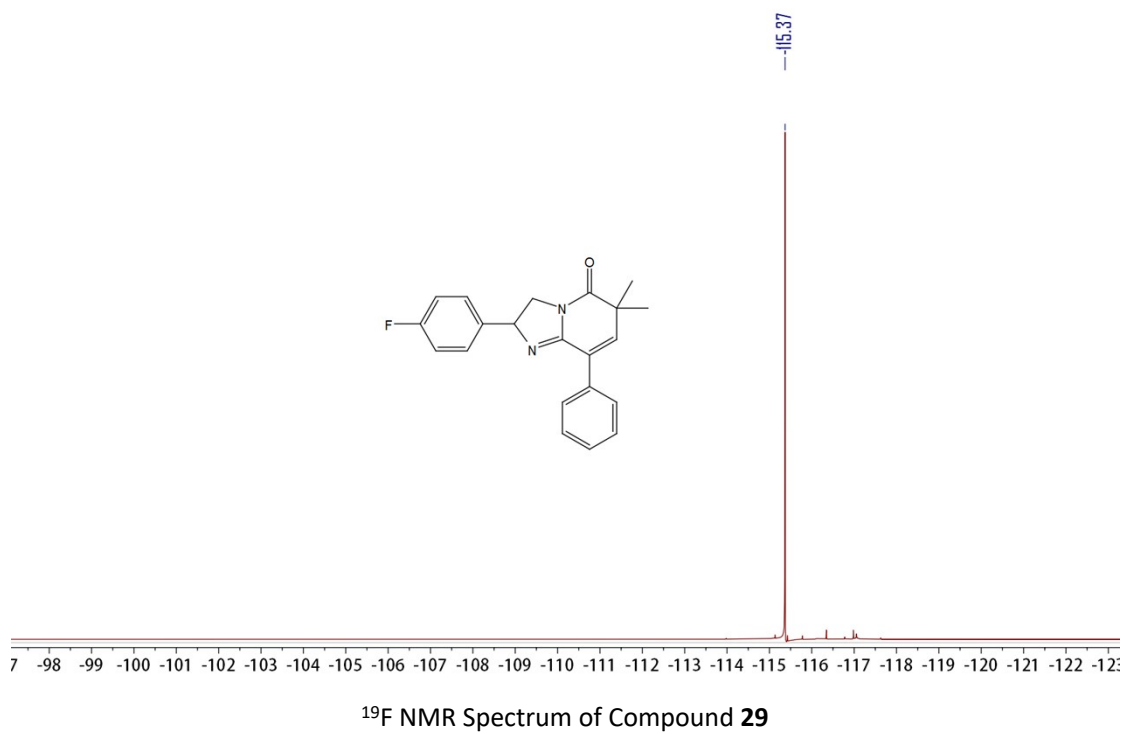
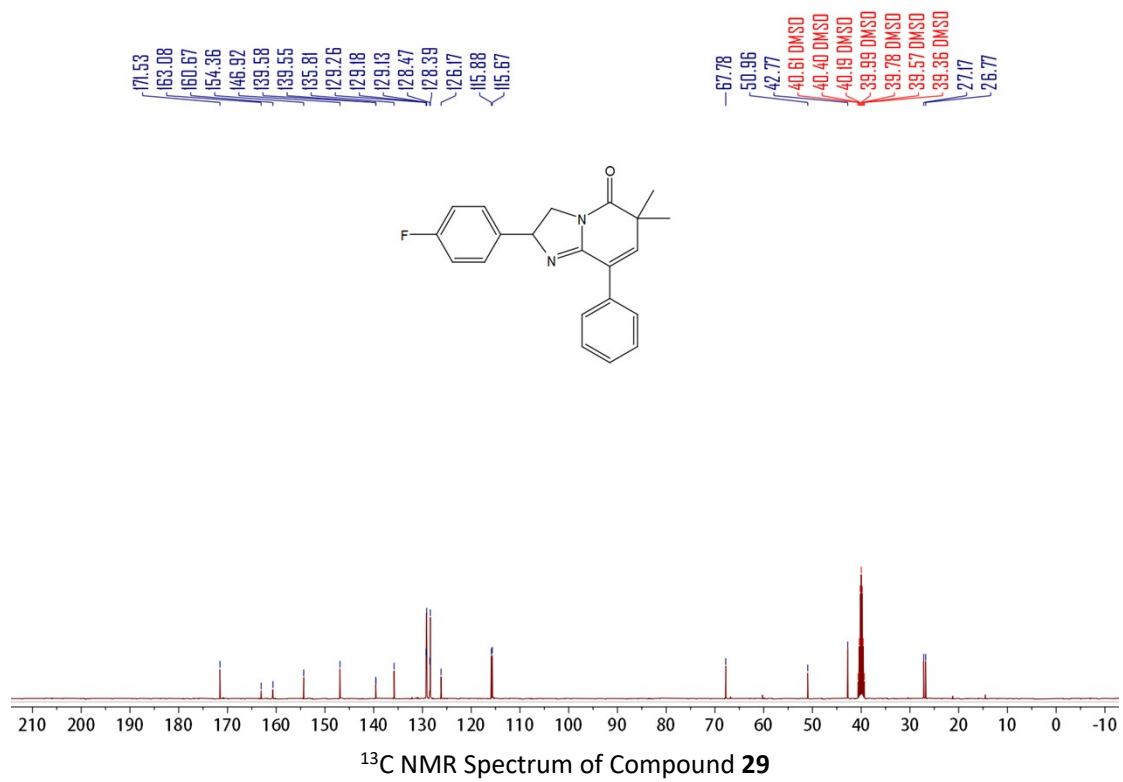


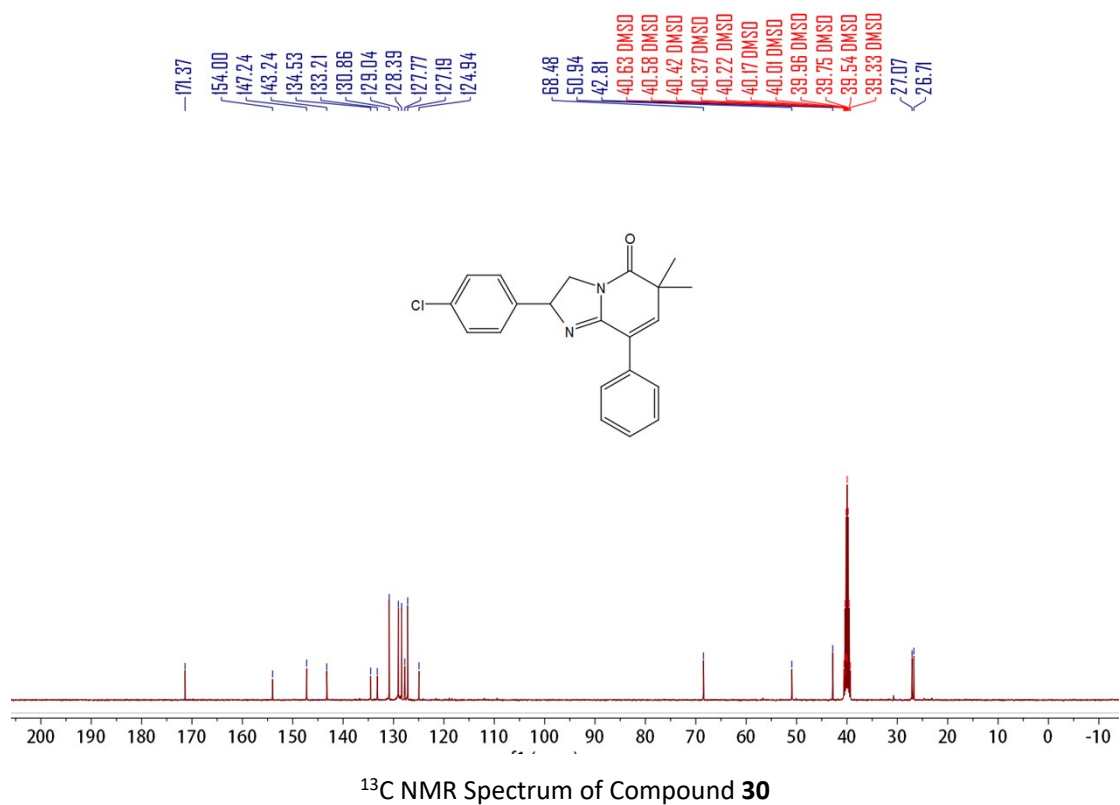
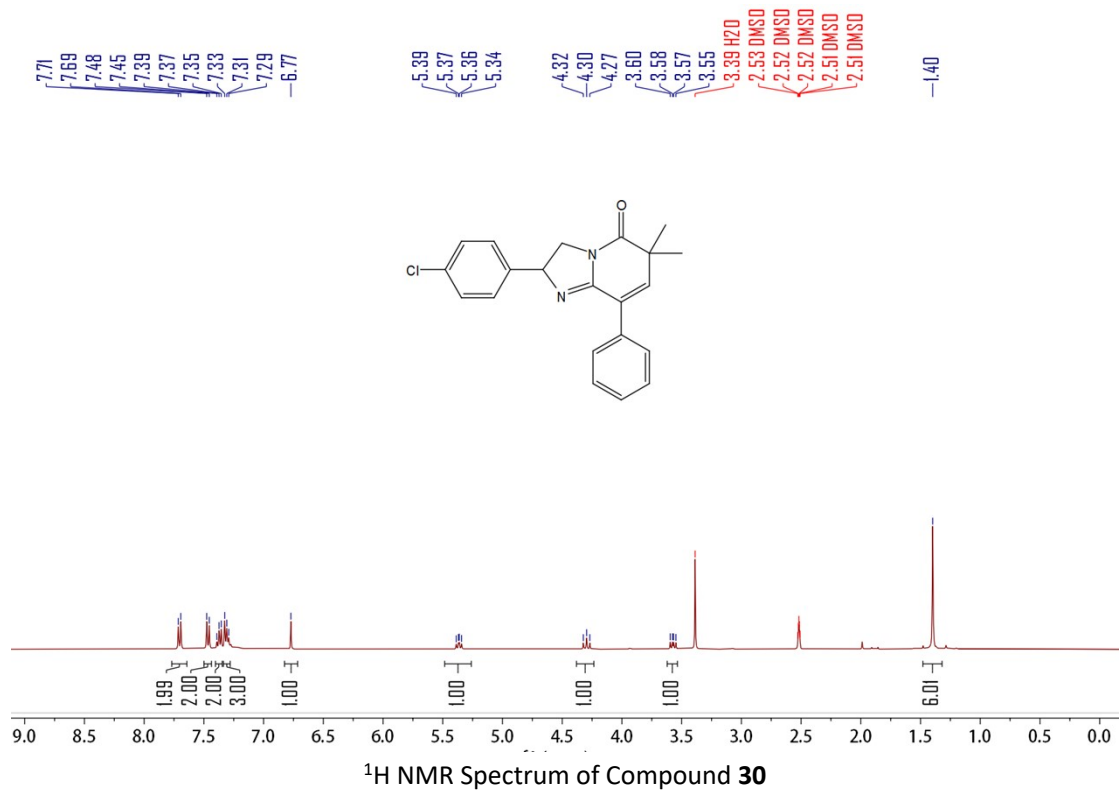


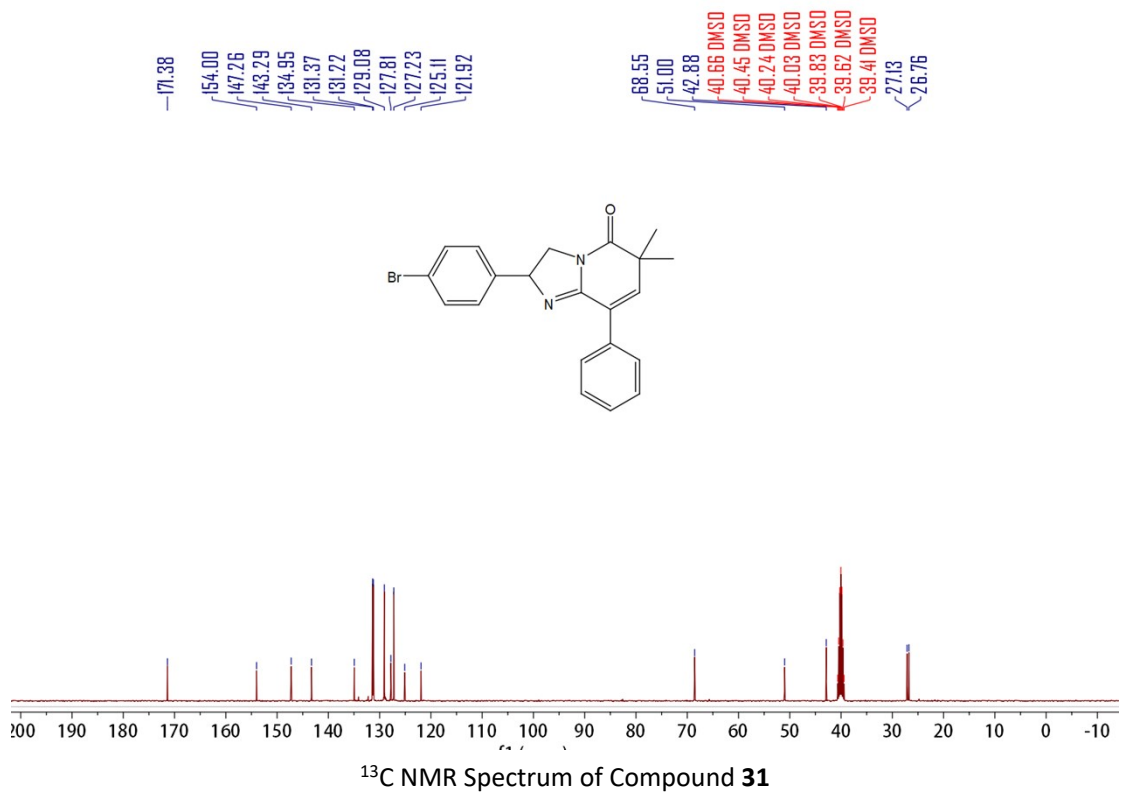
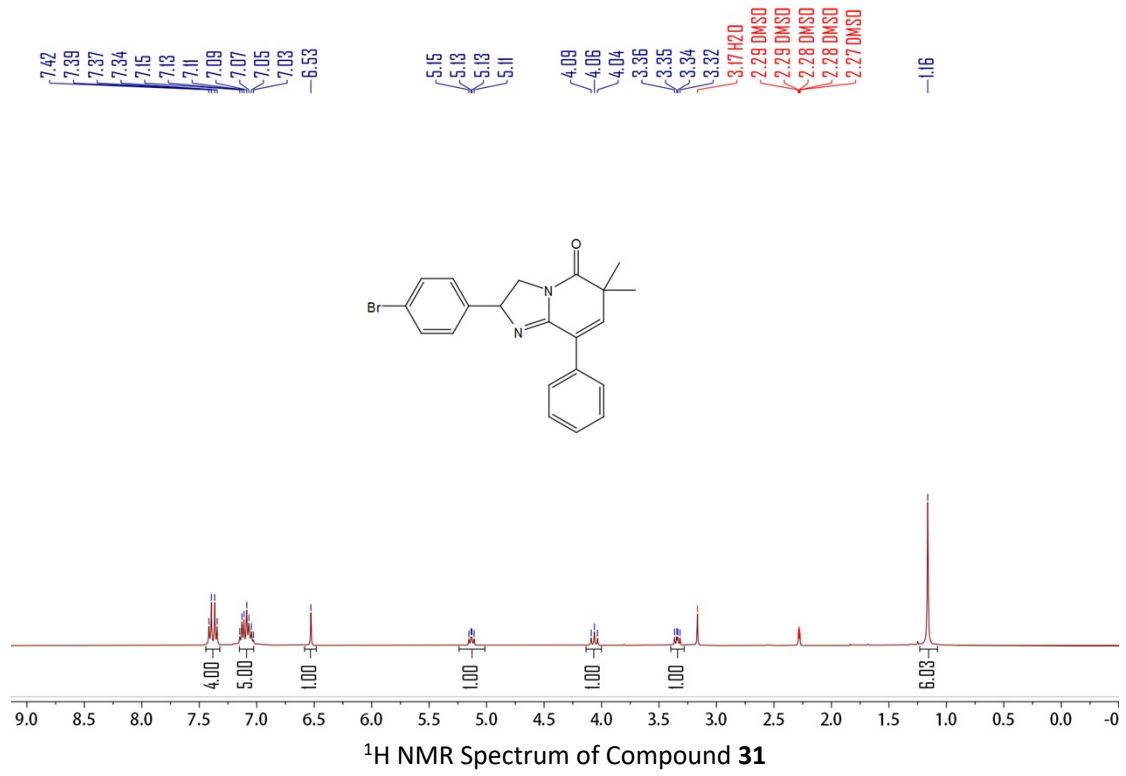
¹³C NMR Spectrum of Compound 28

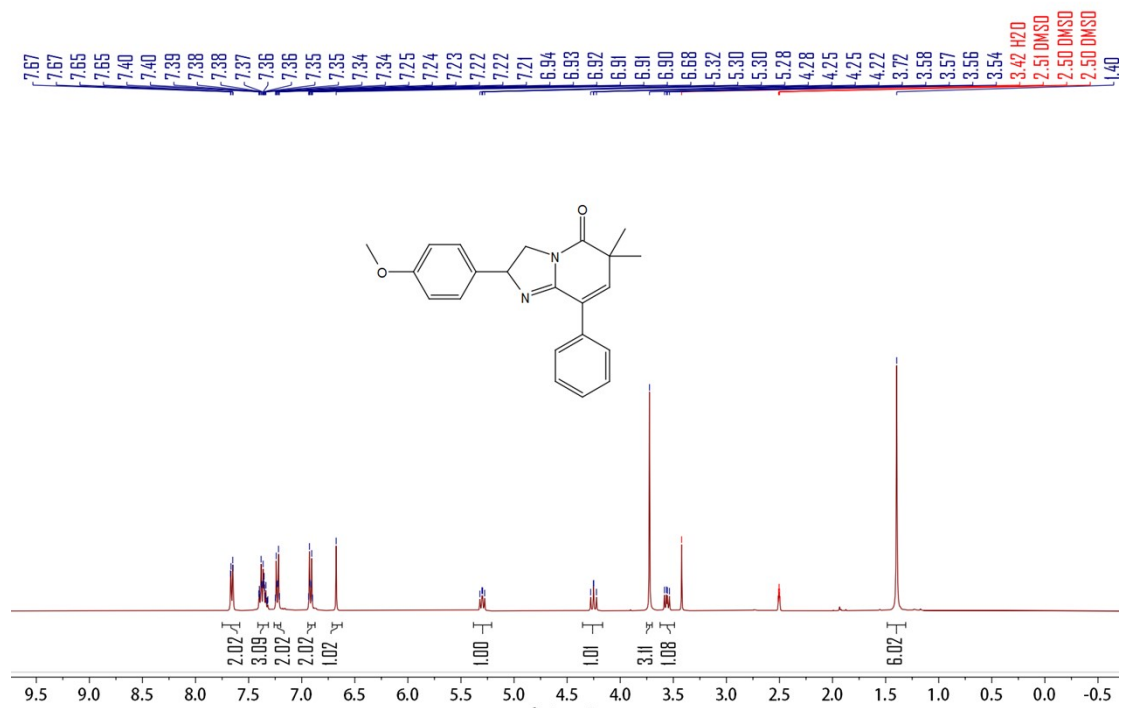


¹H NMR Spectrum of Compound 29

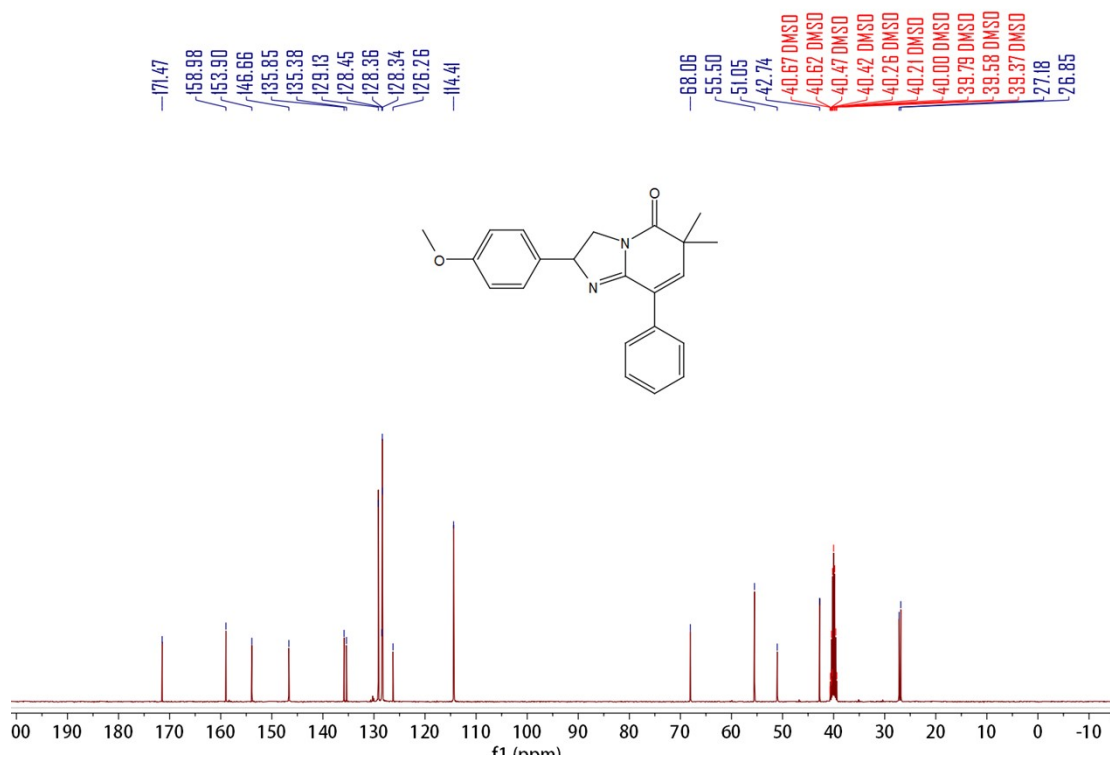




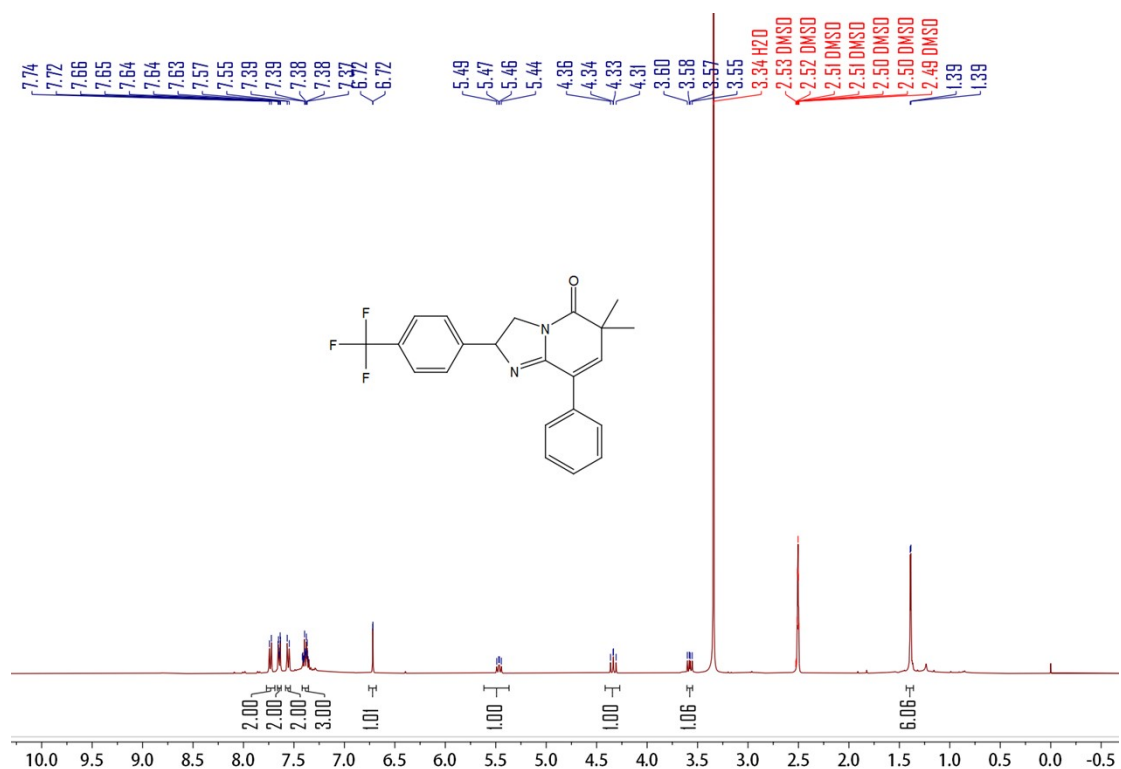




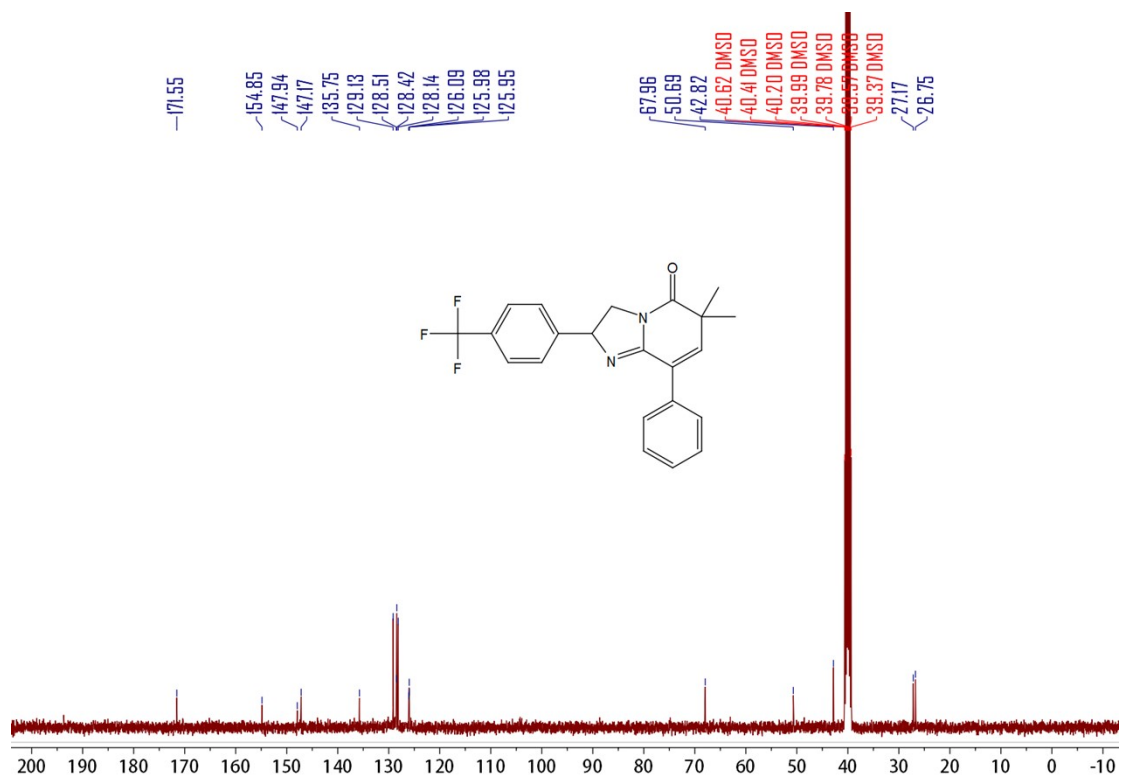
¹H NMR Spectrum of Compound 32



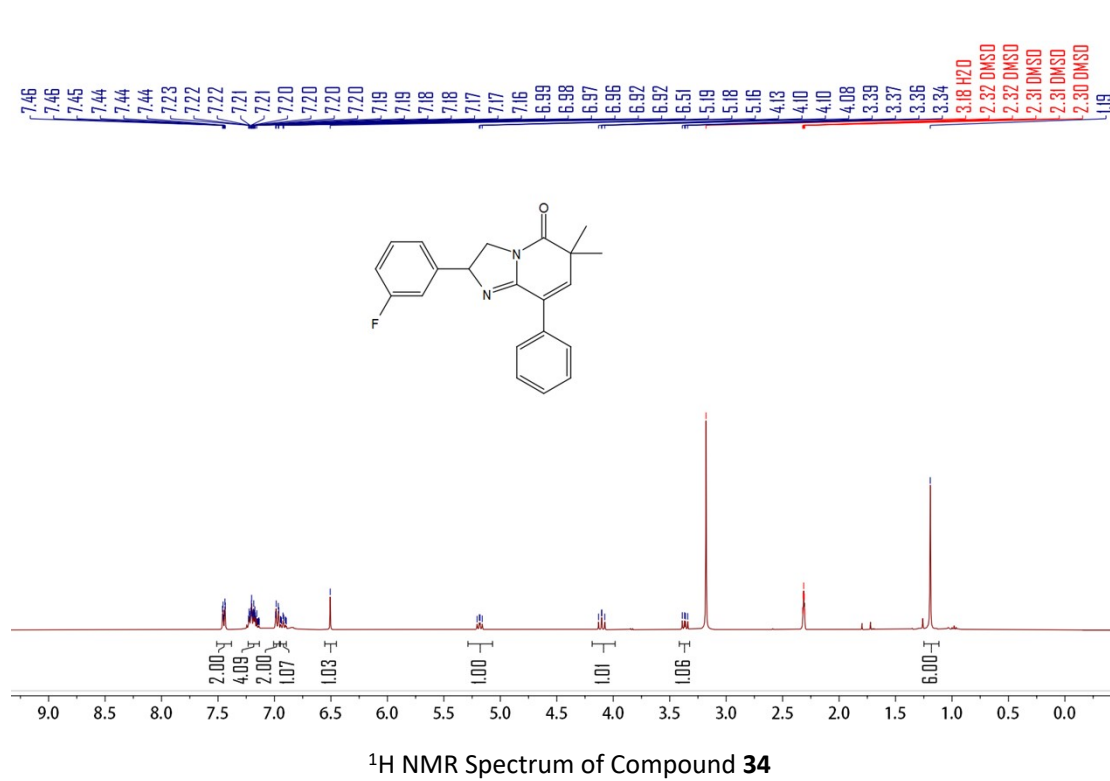
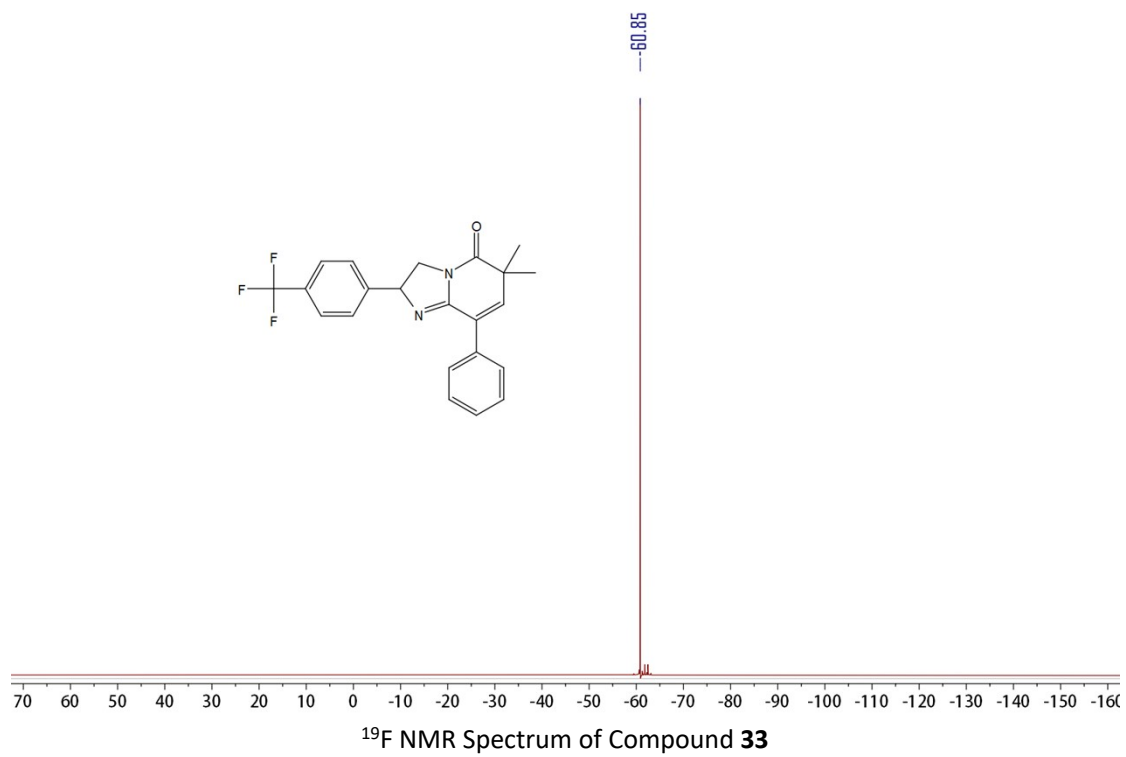
¹³C NMR Spectrum of Compound 32

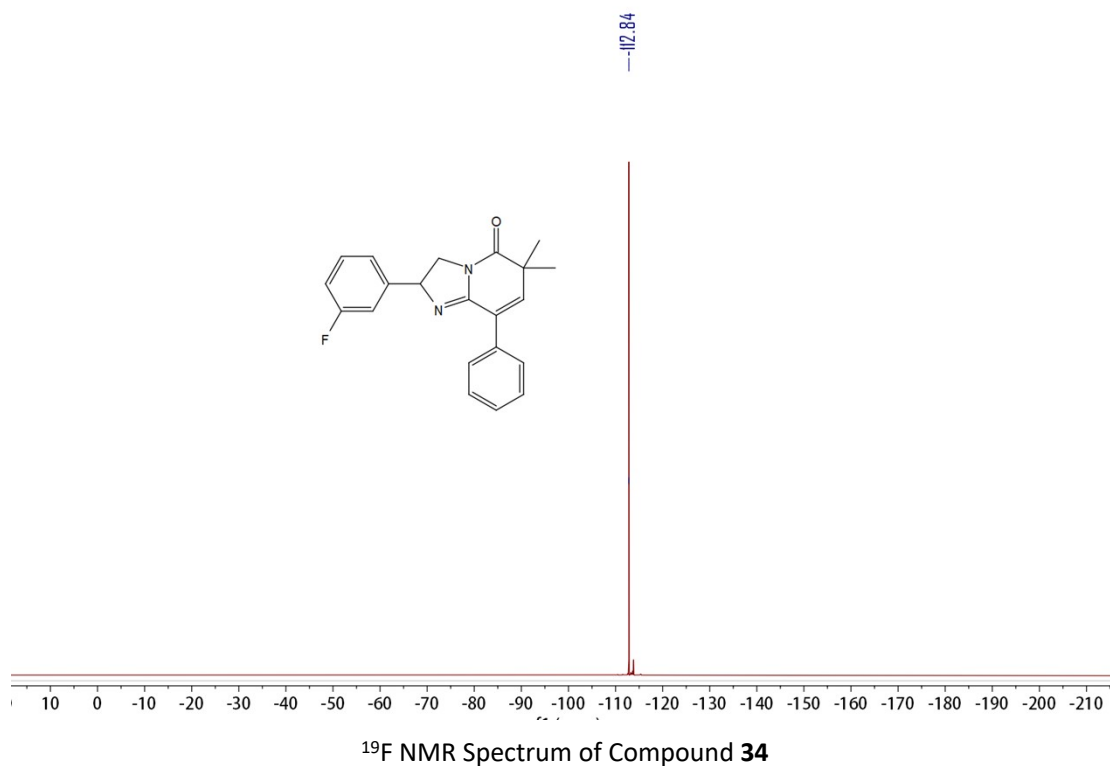
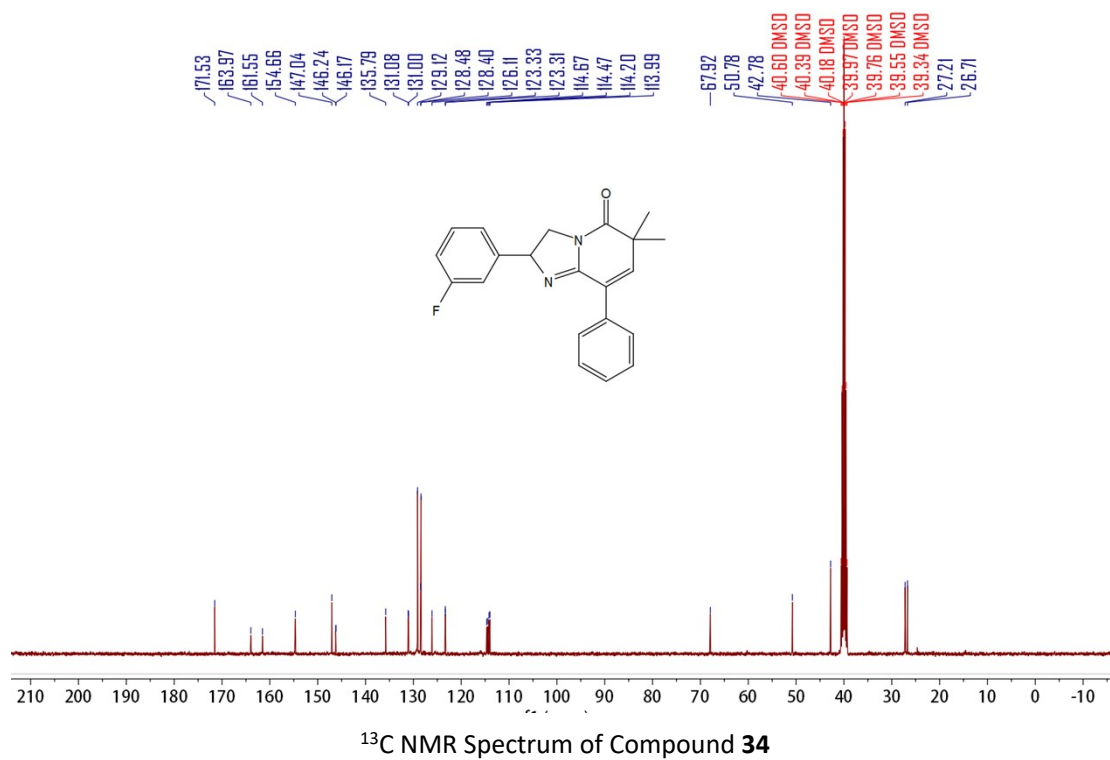


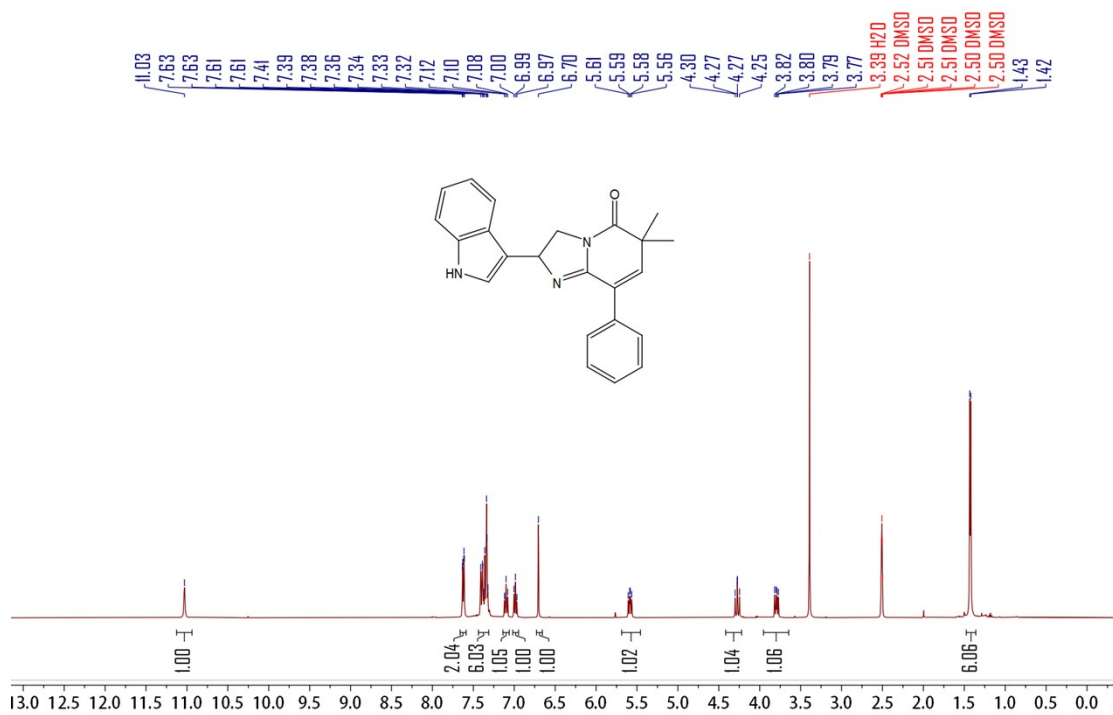
¹H NMR Spectrum of Compound 33



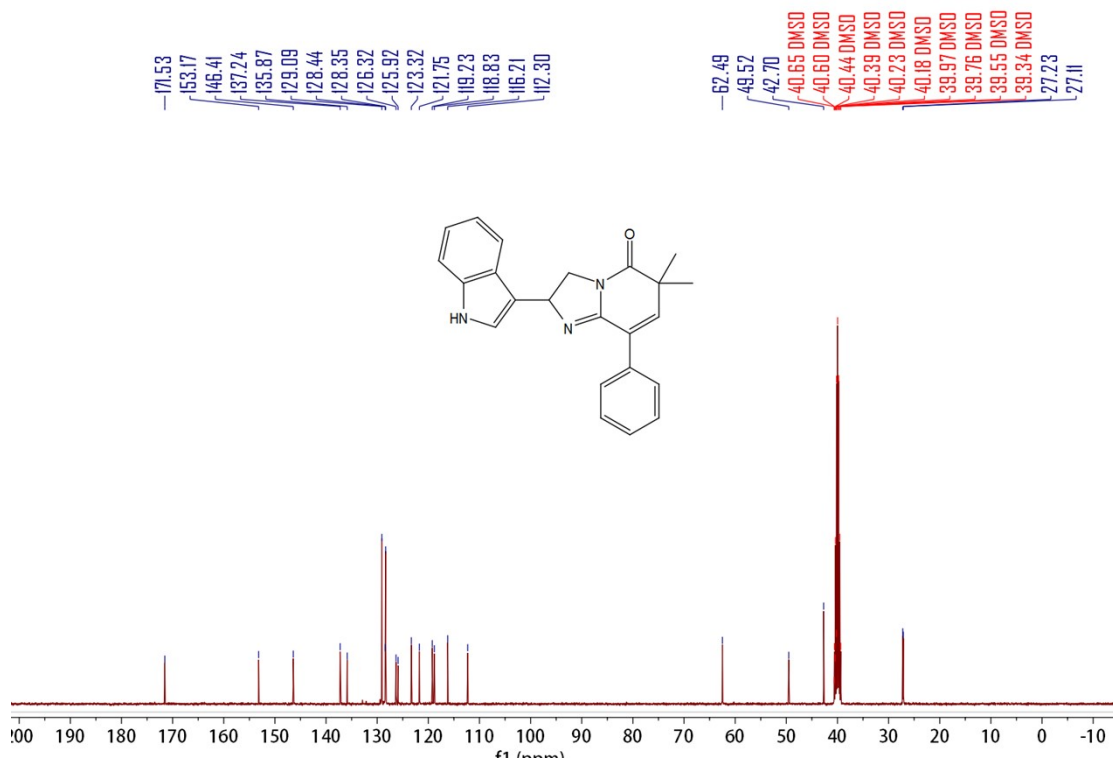
¹³C NMR Spectrum of Compound 33



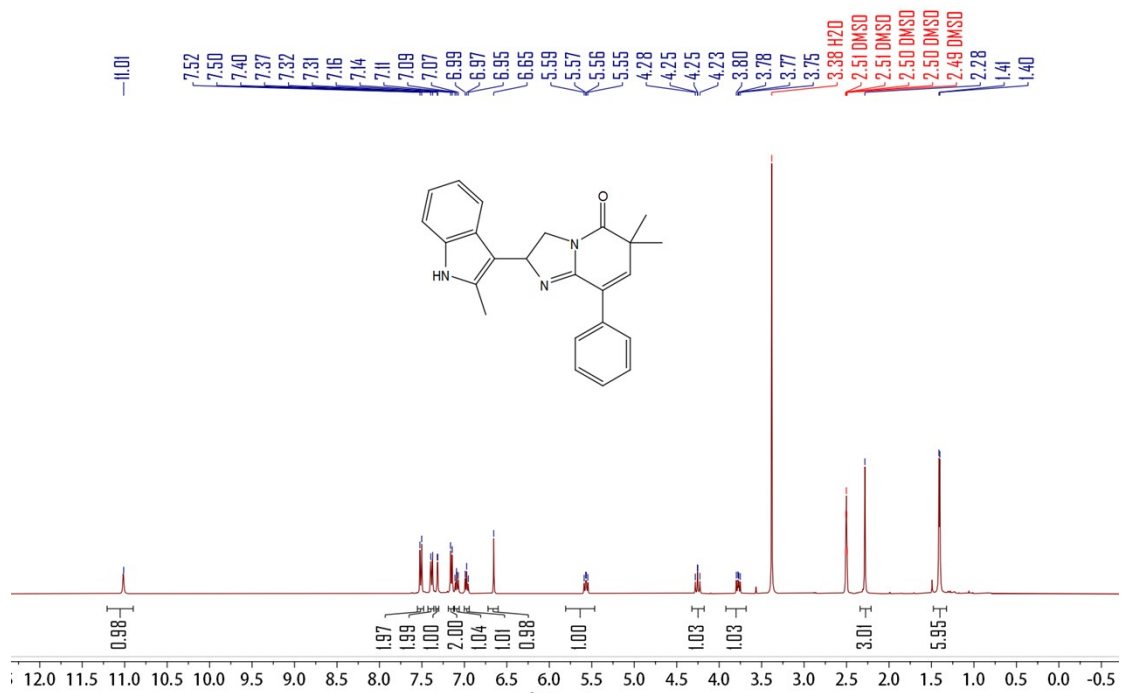




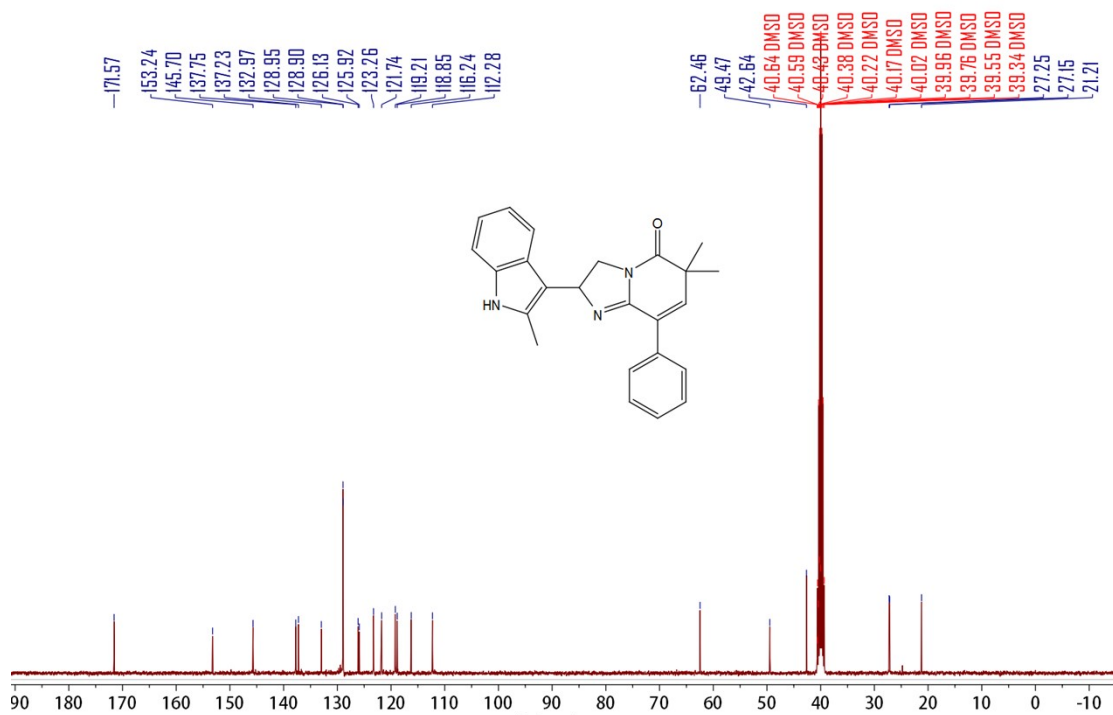
¹H NMR Spectrum of Compound 35



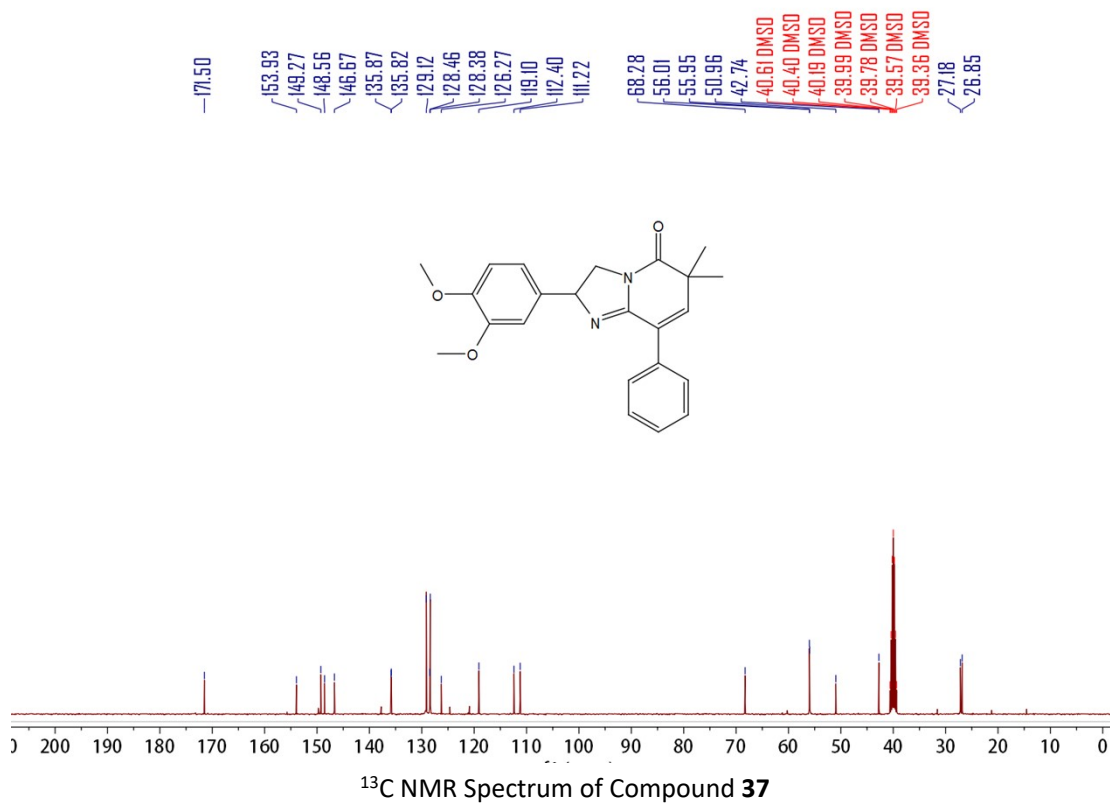
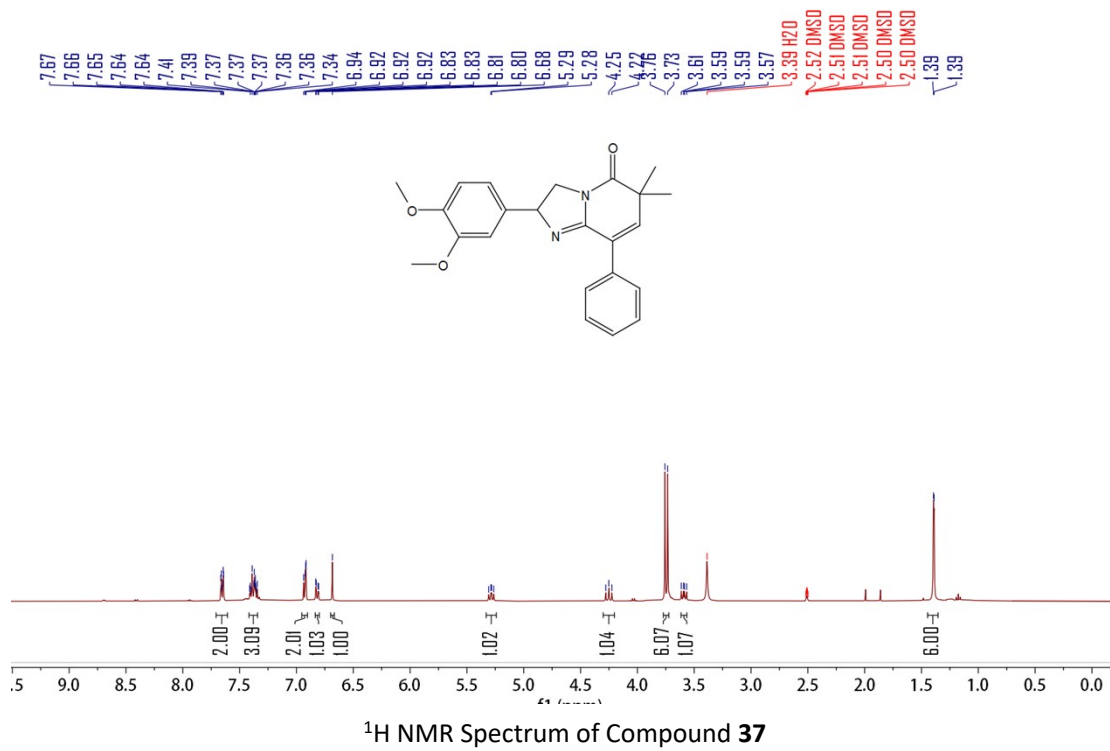
¹³C NMR Spectrum of Compound 35

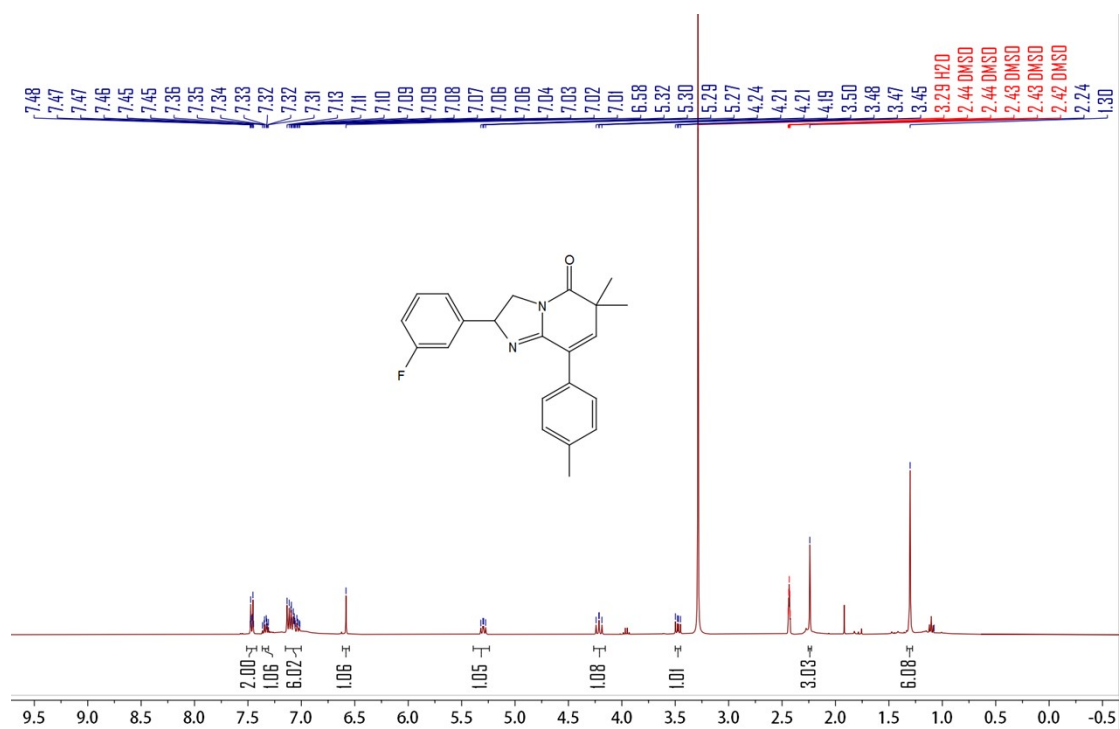


¹H NMR Spectrum of Compound 36

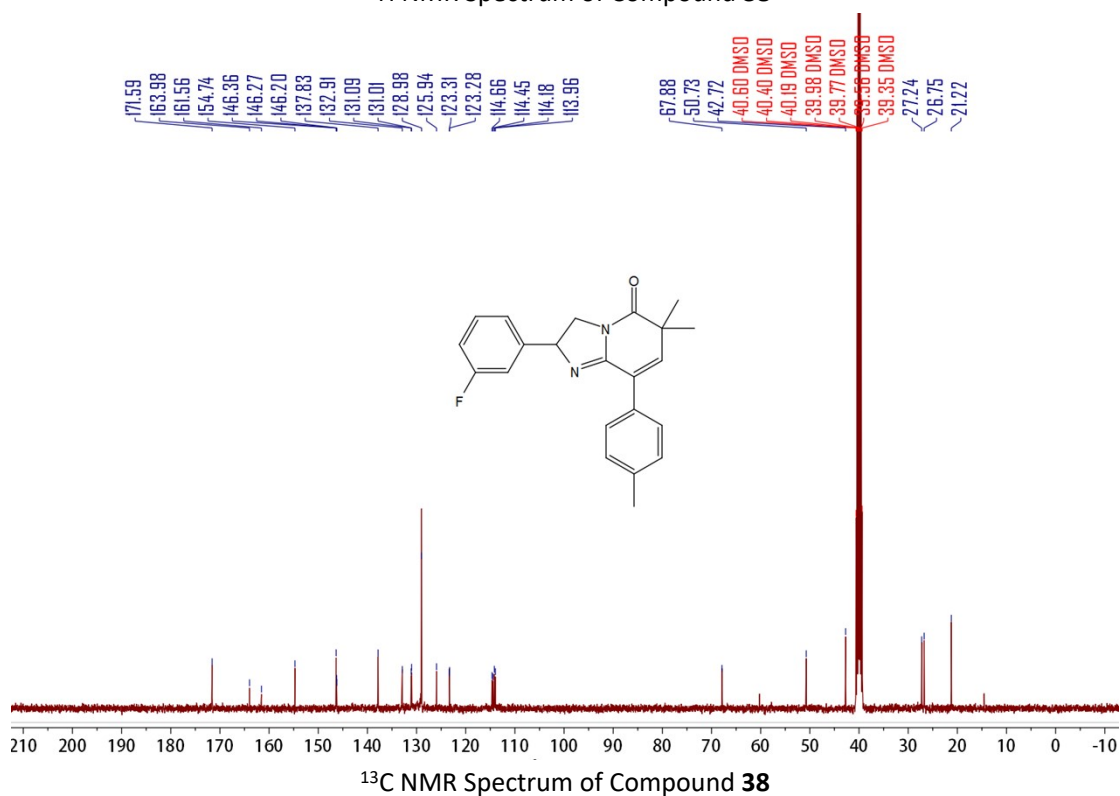


¹³C NMR Spectrum of Compound 36

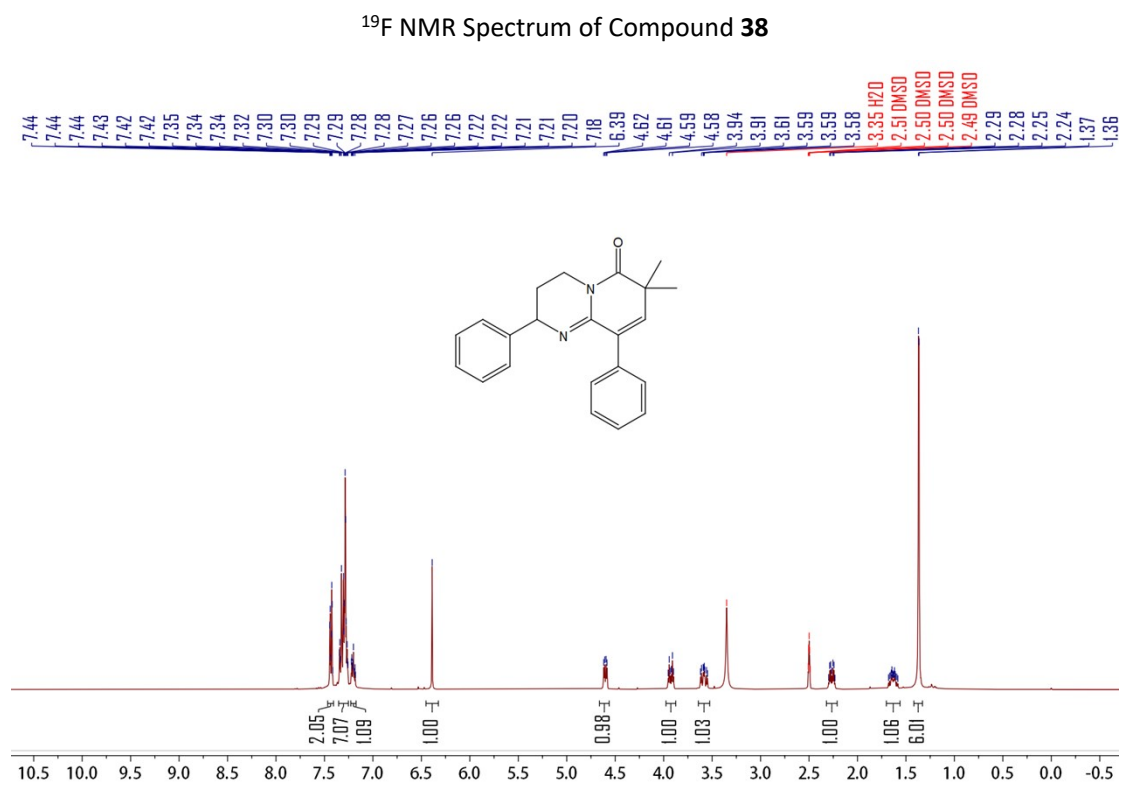
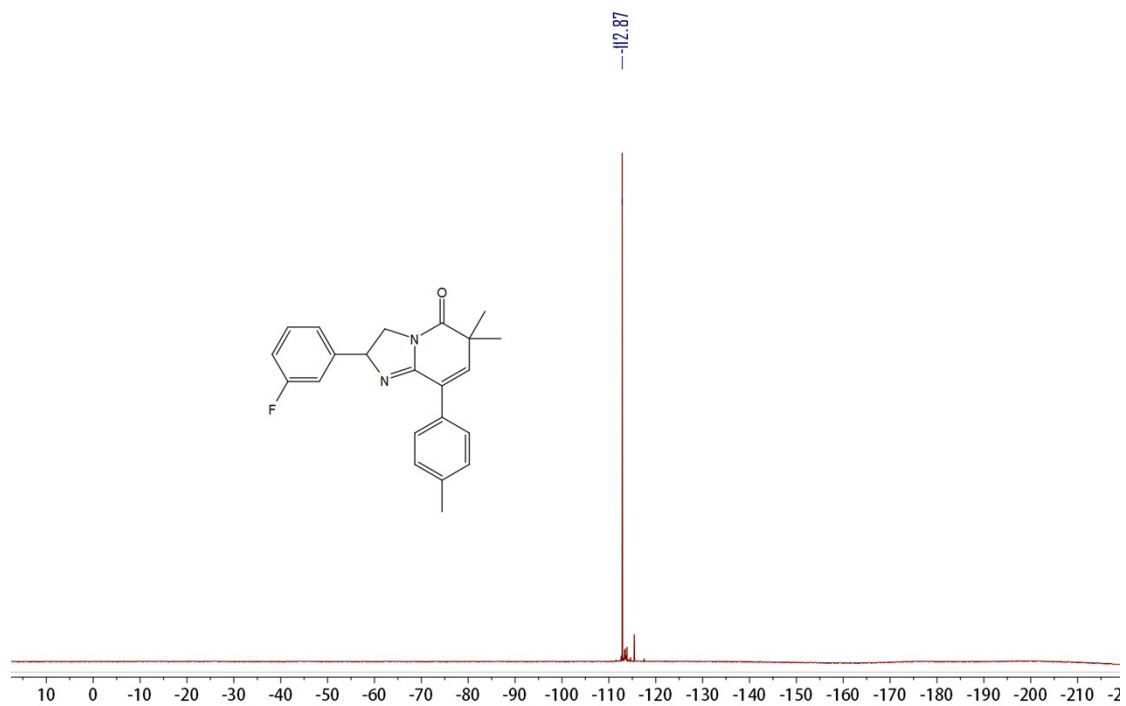


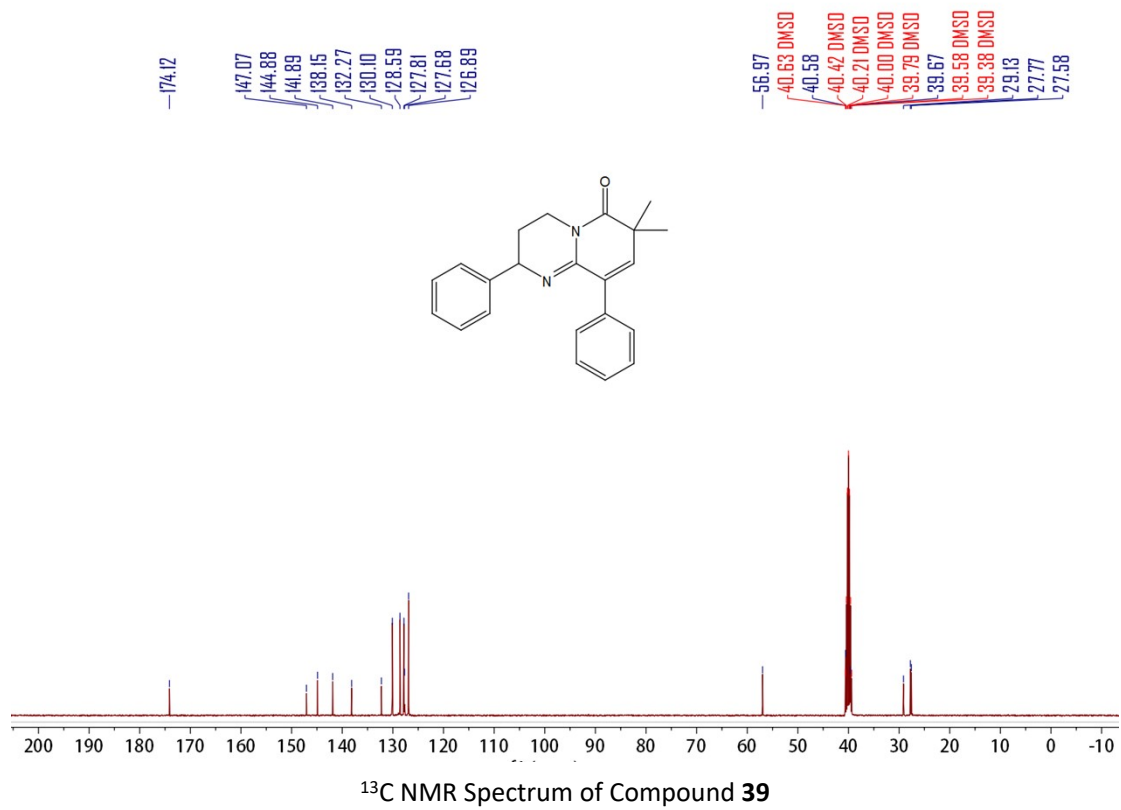


¹H NMR Spectrum of Compound 38



¹³C NMR Spectrum of Compound 38





9. References

1. J. C. Theriot, C. H. Lim, H. Yang, M. D. Ryan, C. B. Musgrave and G. M. Miyake, *Science*, 2016, **352**, 1082-1086.
2. Z. Pan, S. Wang, J. T. Brethorst and C. J. Douglas, *Journal of the American Chemical Society*, 2018, **140**, 3331-3338.