Synthesis of Pyridino [2,1-b] quinazolinones via a visible light-Induced functionalization of alkynes/nitrile insertion/ cyclization tandem sequences in Continuous-Flow technology†

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Contents

1. General Information 2

2. Batch and Microfluidic Reactor Device 3

3. Select Optimization Results 4

4. Preparation of Substrates 10

5. Experiments for Mechanistic Studies 12

6. Analytical data for isolated compounds 14

7. Crystal Data and Structure Refinements 28

8. ^{1}H NMR and ^{13}C NMR spectra 30

9. References 60

1. General Information

$^{1}H/^{13}C$ 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 chromatogrgraphy 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, All the lamps are all purchased online, unless otherwise state. the other commercial chemicals were used without further purification.

2. Batch and Microfluidic Reactor Device

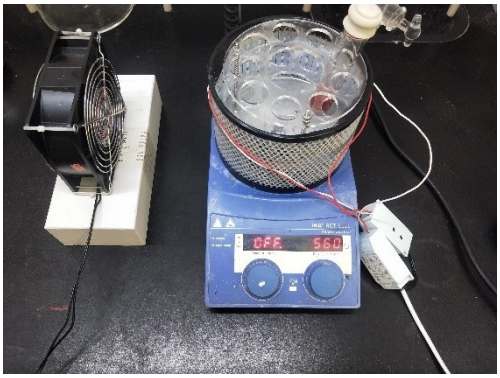
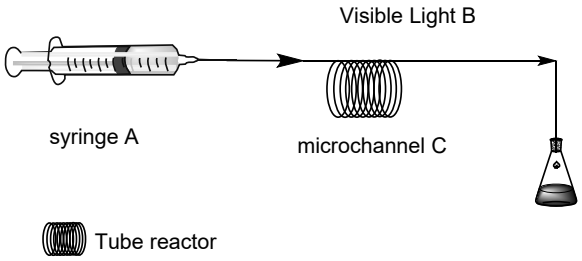


Figure 1 Batch reactor device



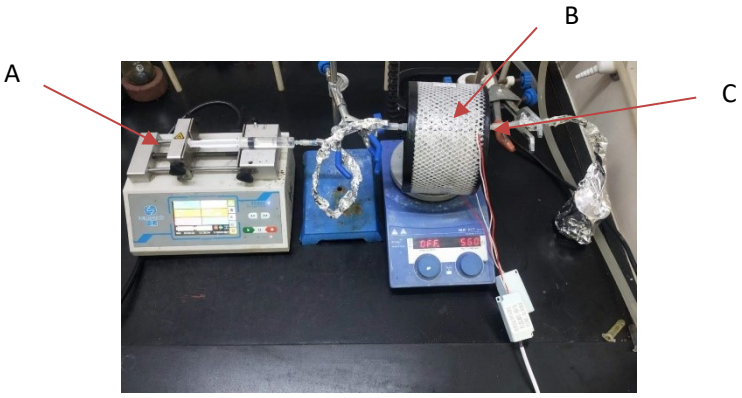


Figure 2 Microfluidic reactor device

Note: The light source is a simulated solar lamp (30 W, 220 V, wavelength 420 nm-430 nm).

3. Select Optimization Results

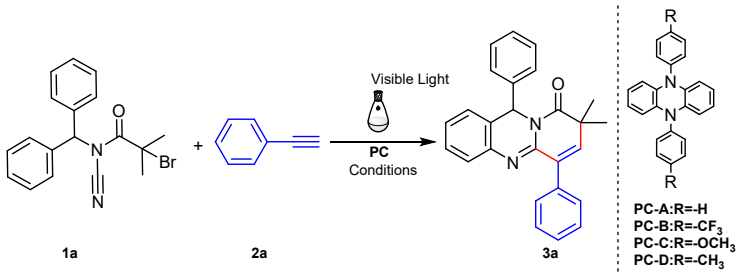
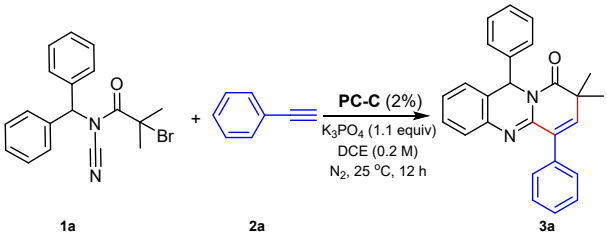


Figure 3 Optimization of reaction conditions

3.1 Table 1. Varying the wavelength of light[a]

Table 1 Optimizing the wavelength of light

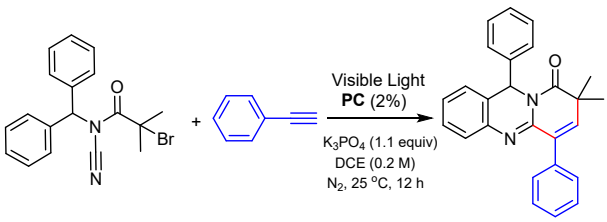


Entry	Wavelength of Light	yield **3a**[b] (%)
1	360-375 nm	37
2	380-390 nm	33
3	390-400 nm	45
4	420-430 nm	59
5	430-440nm	43

[a] Reaction conditions: **1a** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC-C** (2 mmol%, 2 equiv%), K_3PO_4 (1.1 mmol, 1.1 equiv), solvent: DCE (5 mL), N_2, 25°C, 12 h；The models of lamps used are 30 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



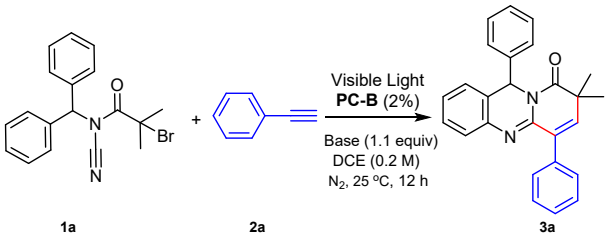
Entry	PC	yield **3a**[b] (%)

1	PC-A	43
2	PC-B	72
3	PC-C	59
4	PC-D	47
5	None	None
6[c]	PC-B	None
7[d]	PC-B	None
8[e]	PC-B	None

[a] Reaction conditions: **1a** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC** (2 mmol%, 2 equiv%), K_3PO_4 (1.1 mmol, 1.1 equiv), solvent: DCE (5 mL), N_2, 25°C, 12 h, bluelight (30 W、220 V、LED、wavelenght 420 nm-430 nm). [b] Isolated yield. [c] In the dark. [d] Under air. [e] Under O_2.

3.3 Table 3. Varying the Base[a]

Table 3 Explore the effect of different Bases on the reaction

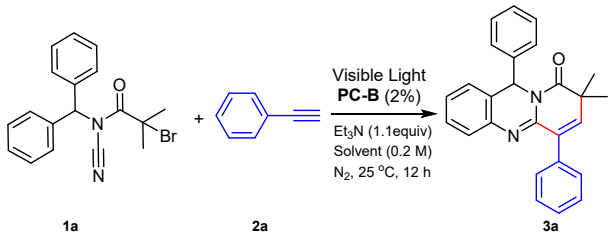


Entry	Base	yield **3a**[b] (%)
1	K_3PO_4	72
2	Na_2CO_3	77
3	$NaHCO_3$	59
4	KO*t*Bu	32
5	Et_3N	78
6	DMAP	38
7	DBU	36
8	Pyridine	34
9	None	47

[a] Reaction conditions: **1a** (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), N_2, 25°C, 12 h, bluelight (30 W、220 V、LED、wavelenght 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

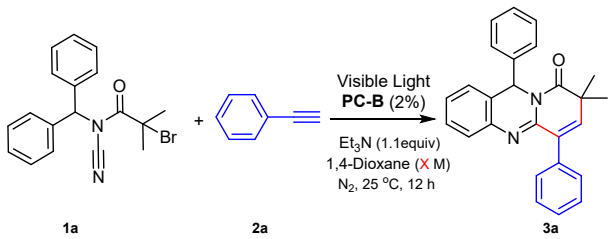


Entry	solvent	yield **3a**[b] (%)
1	DCE	77
2	MeCN	33
3	THF	36
4	DMA	None
5	DMF	None
6	Cyclohexane	72
7	1,4-Dioxane	80

[a] Reaction conditions: **1a** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC-B** (2 mmol%, 2 equiv%), Et_3N (1.1 mmol, 1.1 equiv), solvent: (5 mL), N_2, 25°C, 12 h, bluelight (30 W、220 V、LED、wavelenght 420 nm-430 nm). [b] Isolated yield.

3.5 Table 5. Concentration[a]

Table 5 Explore the effect of substrate concentration on the reaction

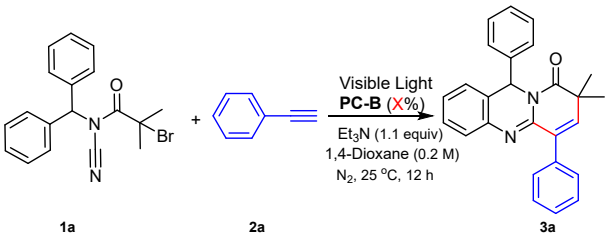


Entry	Concentration	yield **3a**[b] (%)
1	1M	72
2	0.5M	74
3	0.2M	80
4	0.1M	75
5	0.05M	44

[a] Reaction conditions : **1a** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC-B** (2 mmol%, 2 equiv%), Et_3N (1.1 mmol, 1.1 equiv), solvent: 1,4-Dioxane (X mL), N_2, 25°C, 12 h, bluelight (30 W、220 V、LED、wavelenght 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

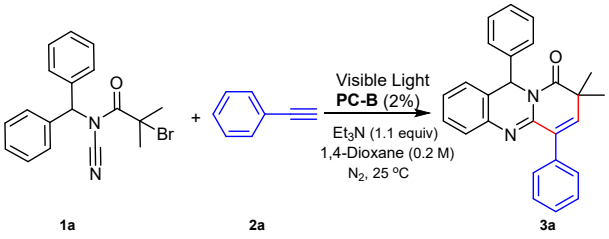


Entry	PC (X mol%)	yield **3a**[b] (%)
1	4	75
2	2	80
3	1	64
4	0.5	42
5	None	None

[a] Reaction conditions: **1a** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC-B** (X% mmol, X% equiv), Et_3N (1.1 mmol, 1.1 equiv), solvent: 1,4-Dioxane (5 mL), N_2, 25°C, 12 h, bluelight (30 W、220 V、LED、wavelenght 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

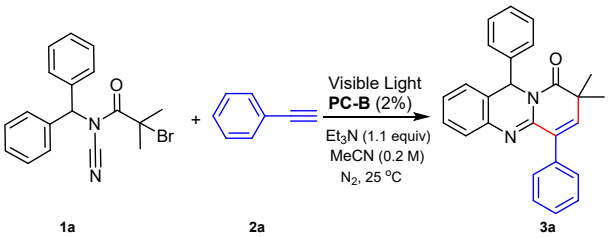


Entry	Time (h)	yield **3a**[b] (%)
1	1	32
2	2	68
3	3	75
4	4	81
5	6	82
6	12	80

[a] Reaction conditions: **1a** (1 mmol, 1 equiv), **2a** (2 mmol, 2 equiv), **PC-B** (2 mmol%, 2 equiv%), Et_3N (1.1 mmol, 1.1 equiv), solvent: 1,4-Dioxane (5 mL), N_2, 25°C, bluelight (30 W、220 V、LED、wavelenght 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



1a 2a 3a

Entry	Phenylacetylene	yield **3a**[b] (%)
1	1	62
2	2	81
3	3	72
4	4	65

[a] Reaction conditions: **1a** (1 mmol, 1 equiv), **PC-B** (2 mmol%, 2 equiv%), Et_3N (1.1 mmol, 1.1 equiv), solvent: 1,4-Dioxane (5 mL), N_2, 25°C, 4 h, bluelight (30 W、220 V、LED、wavelenght 420 nm-430 nm). [b] Isolated yield.

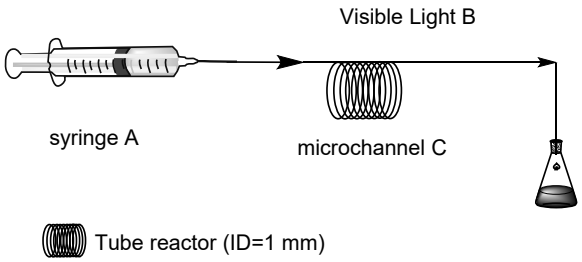
3.9 Table 9. Reagent Loadings[a]

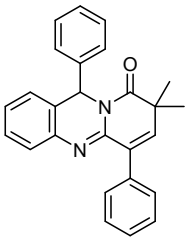
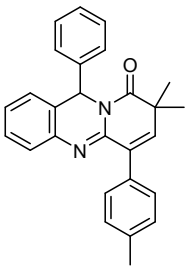
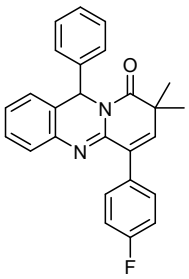
Table 9 Optimization of microchannel reaction conditions

Entry	PC-B (equiv)	Tube diameter (mm)	Tube length (m)	Residence time (minute)	yield **3a**[b] (%)
1	2%	1	2	30	85
2	1%	1	2	30	87
3	0.5%	1	2	30	53
4	0.1%	1	2	30	34
5	1%	1	3	30	78
6	1%	1	1	30	64
7	1%	1	0.5	30	75
8	1%	0.8	2	30	67
9	1%	1.5	2	30	59
10	1%	1	2	5	38
11	1%	1	2	10	91
12	1%	1	2	40	84

[a] Reaction conditions: **1a** (1 mmol, 1 equiv), **2a** (1 mmol, 1 equiv), Et_3N (1.1 mmol, 1.1 equiv), solvent: 1,4-Dioxane (5 mL), 25°C, blue light (30 W、220 V、LED、wavelenght 420 nm-430 nm). [b] Isolated yield.

3.10 A Scale-up Continuous Flow Reaction[a]



Entry	Structure	yield (%)
1		88
2		83
3		75

[a] Reaction conditions: **1a** (10 mmol), **2a** (1 equiv), 1,4-Dioxane (50 mL), Et_3N (1.1 equiv), and **PC-B** (1 % equiv.) at room temperature for 10 minutes. Isolated yield.

4. Preparation of Substrates

4.1 Method for synthesizing phenazine catalysts

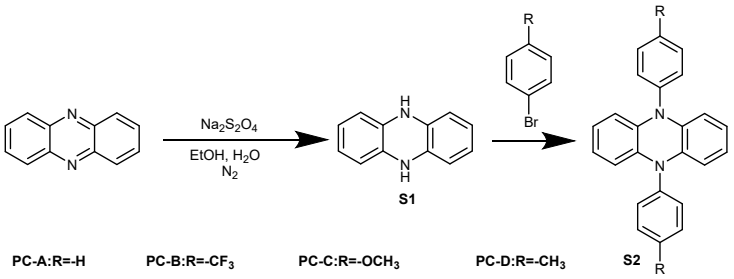


Figure 4 Syntheticmethod of phenazine catalyst

As shown in **Figure 4**, **S1** and **S2** are synthesized according to the literature[1].

4.2 Method for synthesizing phenethylamine-derived bromide substrates

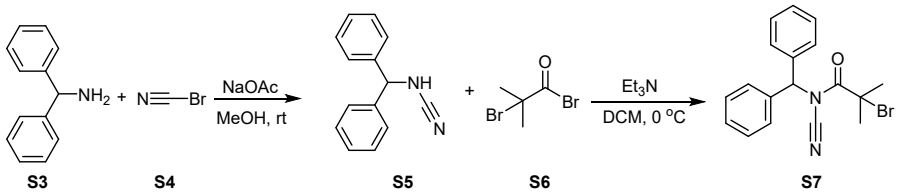


Figure 5 Synthesis method of indole substrates

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 Na_2SO_4, 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 Et_3N (2.4 equiv.) in DCM (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 Na_2SO_4, 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 (3a 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 equiv %) and Et_3N (1.1 mmol, 1.1 equiv). And add 5 mL 1,4-Dioxane (0.2 M) solution. Pass the solutions through a Quartz tubing (id = 1 mm, length =2.0 m) to building the **1** during 10 minutes of residence time under blue light (30 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 **3a** (91% yield).

5. Experiments for Mechanistic Studies

5.1 Free radical capture experiment in batch reaction

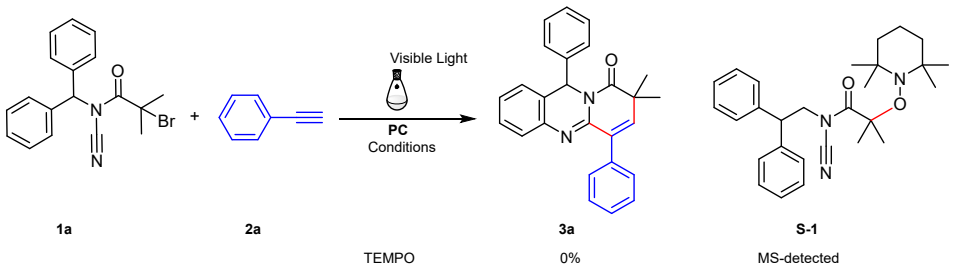


Figure 7 Radical trapping experiment with TEMPO

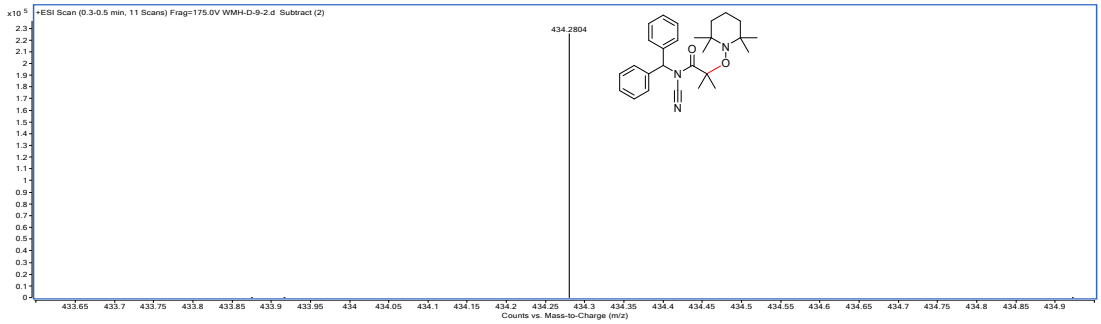


Figure 8 HR-MS (ESI) analysis of **S-1**

5.2. Light on/off experiments in batch reaction

The results showed that when the light was turned off, the yield of the reaction still increased obviously.

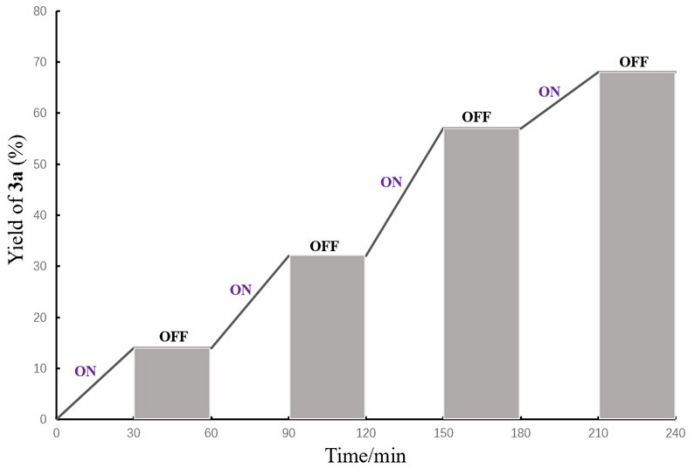


Figure 9. The light on/off experiments: Reaction conditions: **1a** (1.0 mmol, 1.0 equiv), **2a** (2.0 mmol, 2.0 equiv), 1,4-Dioxane (5 mL), Et_3N (1.1 equiv), and **PC-B** (2 % equiv.), N_2, 25°C; blue light (30 W, 220 V, LED, wavelength 420 nm-430 nm). [b] Isolated yield.

5.3 Discussion on theoretical reaction mechanism

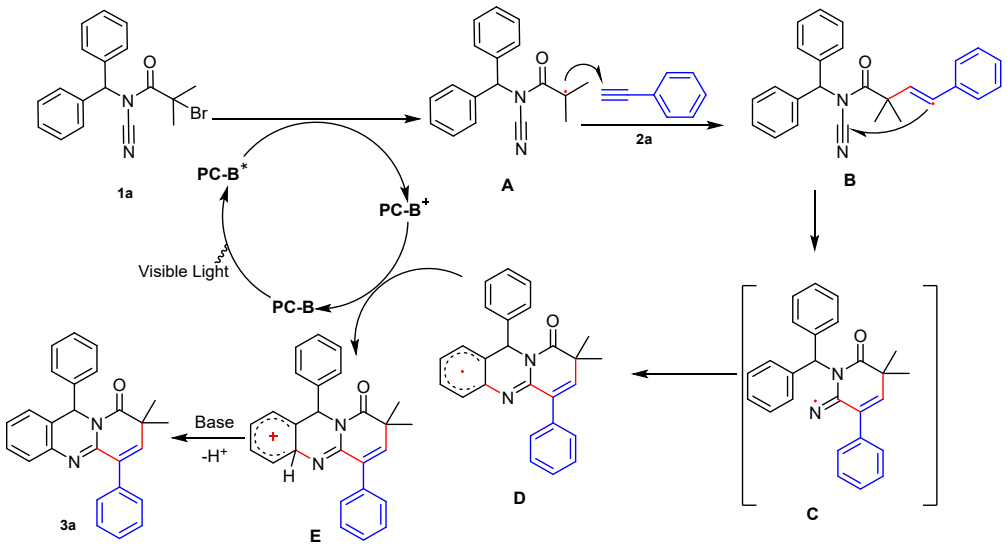
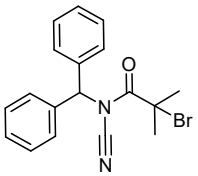


Figure 10 Reaction mechanism

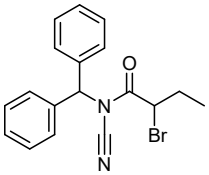
6. Analytical data for isolated compounds

6.1 Characterization data for Phenylmethylamine-derived bromides substrates



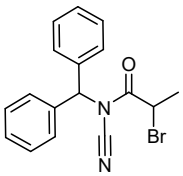
N-benzhydryl-2-bromo-N-cyano-2-methylpropanamide:(1a)

Light yellow solid; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.48 – 7.38 (m, 6H), 7.32 – 7.28 (m, 4H), 6.66 (s, 1H), 2.07 (s, 6H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 169.26, 137.08, 129.34, 129.16, 128.66, 109.30, 63.92, 57.05, 30.72. **HRMS** (ESI) calcd for $C_{18}H_{17}BrN_2O$ [M+H]: 357.0597; found: 357.0593.



N-benzhydryl-2-bromo-N-cyanobutanamide:(1b)

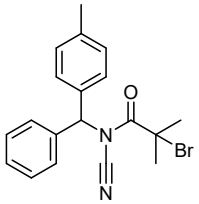
Yellow solid;**^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.47 – 7.40 (m, 6H), 7.30 (dt, J = 7.8, 2.0 Hz, 4H), 6.63 (s, 1H), 4.94 (dd, J = 8.8, 4.9 Hz, 1H), 2.16 – 2.07 (m, 1H), 1.94 – 1.88 (m, 1H), 1.00 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 168.51, 137.36, 136.96, 129.35, 129.25, 129.21, 129.17, 129.03, 128.07, 109.06, 62.18, 47.63, 27.21, 11.76. **HRMS** (ESI) calcd for $C_{18}H_{17}BrN_2O$ [M+H]: 357.0597; found: 357.0596.



N-benzhydryl-2-bromo-N-cyanopropanamide:(1c)

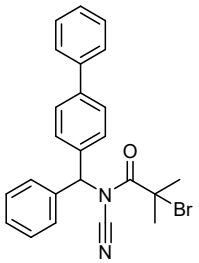
Yellow solid; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.47 – 7.40 (m, 6H), 7.31 (dd, J = 7.5, 1.8 Hz, 4H), 6.61 (s, 1H), 5.13 (q, J = 6.4 Hz, 1H), 1.78 (d, J = 6.5 Hz, 3H). **^{13}C NMR**

(101 MHz, DMSO-d_6) δ 168.96, 137.47, 136.93, 129.34, 129.31, 129.25, 129.17, 128.99, 127.97, 109.12, 62.12, 21.04. **HRMS** (ESI) calcd for $C_{17}H_{15}BrN_2O$ [M+H]: 343.0441; found：343.0444.



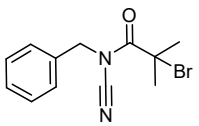
2-bromo-N-cyano-2-methyl-N-(phenyl(p-tolyl)methyl)propanamide:(1d)

Light yellow solid; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.43 (ddd, J = 13.4, 7.9, 6.1 Hz, 3H), 7.31 – 7.24 (m, 4H), 7.18 (d, J = 8.1 Hz, 2H), 6.61 (s, 1H), 2.32 (s, 3H), 2.07 (s, 6H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 172.92, 138.65, 137.26, 134.06, 129.87, 129.29, 129.04, 128.75, 128.44, 109.31, 63.81, 57.06, 30.94, 21.17. **HRMS** (ESI) calcd for $C_{19}H_{19}BrN_2O$ [M+H]: 371.0754; found：371.0757.



N-([1,1'-biphenyl]-4-yl(phenyl)methyl)-2-bromo-N-cyano-2-methylpropanamide:(1e)

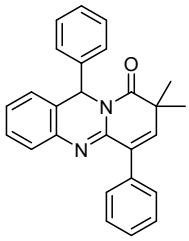
Light yellow solid; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.80 – 7.74 (m, 2H), 7.74 – 7.69 (m, 2H), 7.48 (ddd, J = 7.8, 6.6, 1.9 Hz, 4H), 7.45 – 7.43 (m, 1H), 7.42 – 7.38 (m, 3H), 7.37 – 7.34 (m, 2H), 6.71 (s, 1H), 2.09 (d, J = 2.9 Hz, 6H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 169.29, 140.89, 139.74, 137.05, 136.18, 129.50, 129.40, 129.36, 129.21, 128.83, 128.61, 127.57, 127.24, 109.37, 63.73, 57.09, 30.75, 30.71. **HRMS** (ESI) calcd for $C_{24}H_{21}BrN_2O$ [M+H]: 433.091; found：433.0915.



N-benzyl-2-bromo-N-cyano-2-methylpropanamide:(1f)

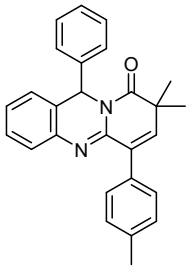
Light yellow solid; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.46 – 7.40 (m, 2H), 7.40 – 7.33 (m, 3H), 4.88 (s, 2H), 2.06 (s, 6H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 169.73, 134.61, 129.34, 129.06, 128.65, 110.24, 56.71, 52.28, 30.84. **HRMS** (ESI) calcd for $C_{12}H_{13}BrN_2O$ [M+H]: 281.0284; found: 281.0287.

6.2 Product Characterization Data



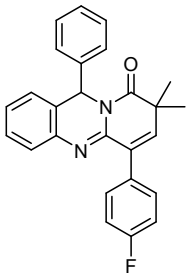
8,8-dimethyl-6,11-diphenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3a)

Light yellow solid (345.05 mg, 91% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.48 (td, J = 7.8, 7.3, 1.8 Hz, 2H), 7.45 – 7.41 (m, 2H), 7.40 (d, J = 3.9 Hz, 1H), 7.32 (dt, J = 14.3, 7.4 Hz, 5H), 7.23 (ddd, J = 11.9, 7.2, 1.7 Hz, 3H), 7.13 (dd, J = 7.5, 1.7 Hz, 1H), 6.78 (s, 1H), 6.63 (s, 1H), 1.40 (s, 3H), 1.31 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.71, 147.26, 143.30, 142.81, 139.28, 137.02, 132.39, 129.90, 129.37, 129.07, 128.30, 128.25, 128.19, 127.77, 127.47, 127.37, 126.34, 126.13, 54.27, 41.94, 28.64, 26.58. **HRMS** (ESI) calcd for $C_{26}H_{22}N_2O$ [M+H]: 379.1805; found: 379.1803.



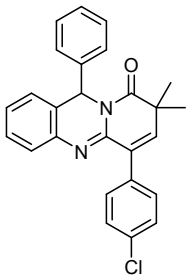
8,8-dimethyl-11-phenyl-6-(p-tolyl)-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3b)

Light yellow solid (334.22 mg, 85% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.45 (dd, J = 7.4, 1.7 Hz, 1H), 7.39 – 7.35 (m, 2H), 7.34 – 7.31 (m, 2H), 7.29 – 7.25 (m, 3H), 7.24 – 7.20 (m, 4H), 7.13 (dd, J = 7.6, 1.6 Hz, 1H), 6.77 (s, 1H), 6.59 (s, 1H), 2.35 (s, 3H), 1.39 (s, 3H), 1.30 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.75, 147.34, 142.80, 142.69, 139.33, 137.52, 134.10, 132.28, 129.77, 129.36, 129.06, 128.87, 128.77, 128.17, 127.73, 127.48, 126.32, 126.13, 54.21, 41.90, 28.72, 26.59, 21.28. **HRMS** (ESI) calcd for $C_{27}H_{24}N_2O$ [M+H]: 393.1961; found: 393.1965.



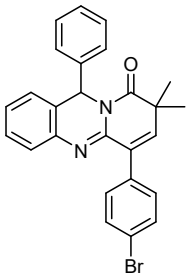
6-(4-fluorophenyl)-8,8-dimethyl-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3c)

Light yellow oily (309.79 mg, 78% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.59 (dd, J = 8.6, 5.7 Hz, 2H), 7.50 (d, J = 7.5 Hz, 1H), 7.37 (d, J = 7.3 Hz, 3H), 7.34 – 7.31 (m, 4H), 7.30 – 7.28 (m, 2H), 7.19 (d, J = 7.6 Hz, 1H), 6.83 (s, 1H), 6.70 (s, 1H), 1.45 (s, 3H), 1.36 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.64, 162.30 (d, J = 244.2 Hz), 147.15, 143.47, 142.87, 139.18, 131.97 (d, J = 8.2 Hz), 131.25, 129.36, 129.07, 128.73, 128.18, 127.81, 127.47, 127.43, 126.36, 126.13, 115.12 (d, J = 21.3 Hz), 54.34, 41.94, 28.56, 26.62. **^{19}F NMR** (376 MHz, DMSO-d_6) δ -114.51. **HRMS** (ESI) calcd for $C_{26}H_{21}FN_2O$ [M+H]: 397.1711; found: 397.1714.



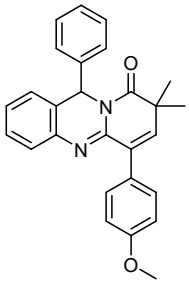
6-(4-chlorophenyl)-8,8-dimethyl-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3d)

Light yellow oily (285.07 mg, 69% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.51 (ddd, J = 18.1, 7.1, 1.8 Hz, 4H), 7.46 – 7.38 (m, 7H), 7.37 – 7.31 (m, 5H), 7.30 – 7.22 (m, 4H), 7.19 – 7.12 (m, 3H), 6.82 (s, 1H), 6.66 (s, 1H), 1.43 (s, 3H), 1.34 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.70, 147.26, 143.28, 142.82, 139.30, 137.33, 137.04, 132.41, 129.90, 129.35, 129.25, 128.48, 128.28, 128.18, 127.76, 127.47, 126.35, 126.15, 54.28, 41.94, 28.63, 26.59. **HRMS** (ESI) calcd for $C_{26}H_{21}ClN_2O$ [M+H]: 413.1415; found: 413.1419.



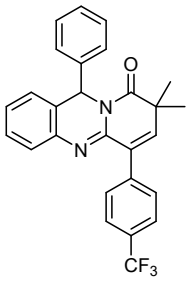
6-(4-bromophenyl)-8,8-dimethyl-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3e)

Light yellow oily (242.26 mg, 53% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.62 (d, J = 8.5 Hz, 2H), 7.46 (d, J = 8.5 Hz, 2H), 7.35 – 7.27 (m, 5H), 7.26 – 7.19 (m, 3H), 7.14 (dd, J = 7.6, 1.6 Hz, 1H), 6.78 (s, 1H), 6.68 (s, 1H), 1.40 (s, 3H), 1.30 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.55, 146.90, 143.77, 142.89, 139.12, 136.21, 132.12, 131.22, 129.36, 129.32, 129.06, 128.18, 127.85, 127.48, 127.41, 126.39, 126.14, 121.62, 54.40, 41.98, 28.46, 26.63. **HRMS** (ESI) calcd for $C_{26}H_{21}BrN_2O$ [M+H]: 457.091; found: 457.0914.



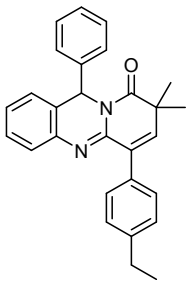
6-(4-methoxyphenyl)-8,8-dimethyl-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3f)

Light yellow oily (261.88 mg, 64% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.42 (dt, J = 13.5, 7.6 Hz, 7H), 7.35 – 7.18 (m, 9H), 7.13 (dd, J = 13.1, 7.2 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H), 6.78 (s, 1H), 6.57 (s, 1H), 3.80 (s, 3H), 1.38 (s, 3H), 1.31 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.78, 159.45, 147.43, 142.76, 142.11, 139.39, 131.94, 131.06, 129.33, 129.06, 128.49, 128.17, 127.71, 127.49, 127.45, 126.32, 126.15, 113.72, 55.61, 54.20, 41.88, 28.78, 26.59. **HRMS** (ESI) calcd for $C_{27}H_{24}N_2O_2$ [M+H]: 409.1911; found: 409.1915.



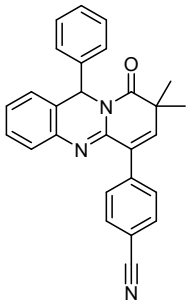
8,8-dimethyl-11-phenyl-6-(4-(trifluoromethyl)phenyl)-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3g)

Light yellow solid (344.32 mg, 77% yield); **^{1}H NMR** 1H NMR (400 MHz, DMSO-d_6) δ 7.80 (d, J = 8.3 Hz, 2H), 7.73 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 7.3 Hz, 1H), 7.34 – 7.29 (m, 4H), 7.27 – 7.19 (m, 3H), 7.16 – 7.13 (m, 1H), 6.78 (d, J = 8.5 Hz, 2H), 1.42 (s, 3H), 1.31 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.47, 146.81, 144.79, 142.95, 141.21, 139.02, 131.11, 130.84, 129.37, 129.06, 128.55 (d, J = 10.9 Hz), 128.19, 127.91, 127.50, 127.40, 126.42, 126.14, 125.16 (q, J = 3.9 Hz), 54.47, 42.06, 28.36, 26.64. **^{19}F NMR** (376 MHz, DMSO-d_6) δ -60.90. **HRMS** (ESI) calcd for $C_{27}H_{21}F_3N_2O$ [M+H]: 447.1679; found: 447.1674.



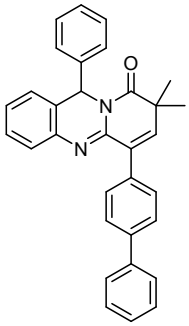
6-(4-ethylphenyl)-8,8-dimethyl-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3h)

Light yellow oily (329.84 mg, 81% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.46 (dd, J = 7.4, 1.7 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.36 – 7.31 (m, 2H), 7.26 (ddt, J = 12.8, 5.3, 1.7 Hz, 6H), 7.23 – 7.19 (m, 1H), 7.14 (dd, J = 7.6, 1.6 Hz, 1H), 6.77 (s, 1H), 6.60 (s, 1H), 2.65 (q, J = 7.5 Hz, 2H), 1.39 (s, 3H), 1.30 (s, 3H), 1.22 (t, J = 7.6 Hz, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.76, 147.34, 143.84, 142.80, 142.78, 139.33, 134.37, 132.28, 129.82, 129.35, 129.07, 128.18, 127.74, 127.70, 127.49, 127.48, 126.32, 126.12, 54.20, 41.91, 28.72, 28.38, 26.58, 16.07. **HRMS** (ESI) calcd for $C_{28}H_{26}N_2O$ [M+H]: 407.2118; found: 407.2117.



4-(8,8-dimethyl-9-oxo-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-6-yl)benzonitrile:(3i)

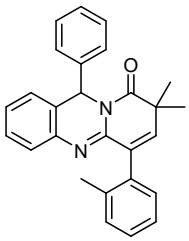
Yellow solid (169.75 mg, 42% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.90 (d, J = 8.3 Hz, 2H), 7.71 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 7.7 Hz, 1H), 7.41 – 7.17 (m, 11H), 7.13 (d, J = 7.5 Hz, 1H), 6.78 (d, J = 2.1 Hz, 2H), 1.41 (s, 3H), 1.31 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.39, 146.63, 145.10, 142.93, 141.83, 138.95, 132.22, 131.00, 129.38, 129.08, 128.84, 128.68, 128.20, 127.95, 127.51, 126.41, 126.16, 119.32, 110.91, 54.49, 42.09, 28.31, 26.60. **HRMS** (ESI) calcd for $C_{27}H_{21}N_3O$ [M+H]: 404.1757; found: 404.1755.



6-([1,1'-biphenyl]-4-yl)-8,8-dimethyl-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3j)

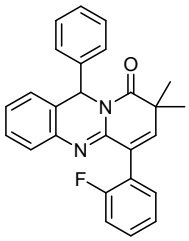
Yellow solid (386.93 mg, 85% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.73 (d, J = 8.5 Hz, 4H), 7.60 (d, J = 8.3 Hz, 2H), 7.51 – 7.44 (m, 3H), 7.41 – 7.38 (m, 1H), 7.35 – 7.30 (m, 4H), 7.25 (dddd, J = 11.4, 7.3, 6.1, 1.6 Hz, 3H), 7.17 (dd, J = 7.5, 1.6 Hz, 1H), 6.81 (s, 1H), 6.69 (s, 1H), 1.41 (s, 3H), 1.32 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.69, 147.26, 143.26, 142.82, 140.22, 140.01, 139.33, 136.13, 132.00, 130.49, 129.48, 129.37, 129.08, 128.60, 128.20, 128.04, 127.79, 127.49, 127.14, 126.58, 126.38, 126.18, 54.31,

41.99, 28.65, 26.61. **HRMS** (ESI) calcd for $C_{32}H_{26}N_2O$ [M+H]: 455.2118; found: 455.2116.



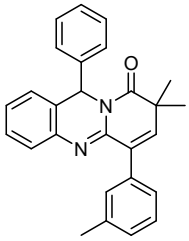
8,8-dimethyl-11-phenyl-6-(o-tolyl)-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3k)

Yellow solid (318.49 mg, 81% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.48 (dd, J = 7.2, 1.9 Hz, 1H), 7.41 – 7.34 (m, 3H), 7.33 – 7.26 (m, 7H), 7.24 (d, J = 7.4 Hz, 1H), 7.10 (dd, J = 7.3, 1.8 Hz, 1H), 6.84 (s, 1H), 6.49 (s, 1H), 2.19 (s, 3H), 1.48 (s, 3H), 1.36 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.89, 147.25, 144.17, 142.88, 139.51, 137.47, 136.77, 132.62, 130.53, 130.05, 129.22, 129.05, 128.23, 128.17, 127.63, 127.51, 127.15, 126.29, 126.25, 125.92, 54.16, 41.87, 28.38, 26.78, 20.15. **HRMS** (ESI) calcd for $C_{27}H_{24}N_2O$ [M+H]: 393.1961; found: 393.1967.



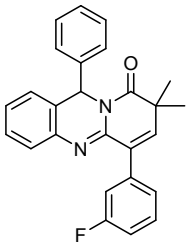
6-(2-fluorophenyl)-8,8-dimethyl-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3l)

Light yellow oily (285.96 mg, 72% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.50 – 7.44 (m, 1H), 7.43 – 7.40 (m, 2H), 7.34 – 7.27 (m, 5H), 7.26 – 7.17 (m, 4H), 7.05 (dd, J = 7.4, 1.7 Hz, 1H), 6.74 (s, 1H), 6.65 (s, 1H), 1.41 (s, 3H), 1.29 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.51, 160.19 (d, J = 246.2 Hz), 146.80, 145.12, 143.20, 139.08, 132.20 (d, J = 3.5 Hz), 130.67 (d, J = 8.5 Hz), 129.24, 128.97, 128.15 (d, J = 3.0 Hz), 127.72, 127.55, 127.45, 126.35, 126.08, 125.34, 125.19, 124.70 (d, J = 3.0 Hz), 115.71 (d, J = 21.8 Hz), 54.57, 42.08, 28.50, 26.52. **^{19}F NMR** (376 MHz, DMSO-d_6) δ -112.40. **HRMS** (ESI) calcd for $C_{26}H_{21}FN_2O$ [M+H]: 397.1711; found: 397.1717.



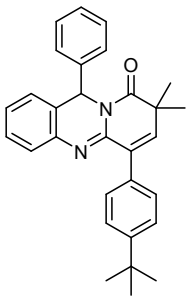
8,8-dimethyl-11-phenyl-6-(m-tolyl)-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3m)

Yellow solid (342.08 mg, 87% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.51 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.34 (dp, *J* = 5.3, 2.0 Hz, 5H), 7.31 (d, *J* = 1.8 Hz, 1H), 7.30 – 7.23 (m, 3H), 7.18 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.83 (s, 1H), 6.66 (s, 1H), 2.41 (s, 3H), 1.45 (s, 3H), 1.36 (s, 3H).**^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.72, 147.32, 143.14, 142.81, 139.31, 137.41, 137.03, 132.50, 130.31, 129.36, 129.06, 128.84, 128.18, 128.10, 127.74, 127.47, 127.20, 126.34, 126.12, 54.24, 41.91, 28.66, 26.59, 21.52. **HRMS** (ESI) calcd for $C_{27}H_{24}N_2O$ [M+H]: 393.1961; found: 393.1964.



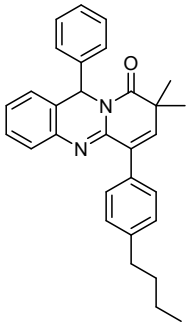
6-(3-fluorophenyl)-8,8-dimethyl-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3n)

Light yellow oily (301.85 mg, 76% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.48 – 7.43 (m, 2H), 7.34 (dt, *J* = 8.6, 1.2 Hz, 3H), 7.32 – 7.29 (m, 2H), 7.29 – 7.18 (m, 5H), 7.15 (dd, *J* = 7.5, 1.6 Hz, 1H), 6.77 (s, 1H), 6.72 (s, 1H), 1.40 (s, 3H), 1.30 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d6) δ 174.52, 162.10 (d, *J* = 242.4 Hz), 146.85, 144.22, 142.88, 139.28 (d, *J* = 8.5 Hz), 139.09, 131.18 – 130.93 (m), 130.16 (d, *J* = 8.4 Hz), 129.37, 129.08, 128.60, 128.18, 127.86, 127.49, 127.42, 126.40, 126.15, 116.80 (d, *J* = 22.3 Hz), 115.04 (d, *J* = 20.5 Hz), 54.39, 41.97, 28.45, 26.58. **^{19}F NMR** (376 MHz, DMSO-d6) δ -114.04. **HRMS** (ESI) calcd for $C_{26}H_{21}FN_2O$ [M+H]: 397.1711; found: 397.1715.



6-(4-(tert-butyl)phenyl)-8,8-dimethyl-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3o)

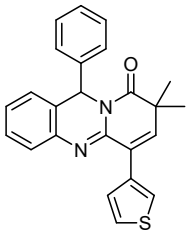
Yellow solid (356.90 mg, 82% yield); **^{1}H NMR** 1H NMR (400 MHz, DMSO-d_6) δ 7.43 (s, 5H), 7.30 (dd, J = 16.1, 7.7 Hz, 5H), 7.23 (dd, J = 7.9, 5.7 Hz, 2H), 7.16 (d, J = 7.6 Hz, 1H), 6.78 (s, 1H), 6.60 (s, 1H), 1.38 (s, 3H), 1.32 (s, 9H), 1.30 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.75, 150.67, 147.35, 142.88, 142.74, 139.37, 134.12, 132.21, 129.51, 129.34, 129.07, 128.18, 127.74, 127.50, 127.46, 126.32, 126.13, 125.09, 54.19, 41.91, 34.78, 31.59, 28.73, 26.56. **HRMS** (ESI) calcd for $C_{30}H_{30}N_2O$ [M+H]: 435.2431; found：435.2437.



6-(4-butylphenyl)-8,8-dimethyl-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3p)

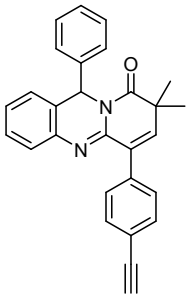
Light yellow oily (300.32 mg, 69% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.45 (dd, J = 7.5, 1.8 Hz, 1H), 7.42 – 7.39 (m, 2H), 7.36 – 7.26 (m, 5H), 7.26 – 7.21 (m, 4H), 7.14 (dd, J = 7.5, 1.5 Hz, 1H), 6.78 (s, 1H), 6.60 (s, 1H), 2.62 (t, J = 7.7 Hz, 2H), 1.63 – 1.54 (m, 2H), 1.39 (s, 3H), 1.37 – 1.32 (m, 2H), 1.30 (s, 3H), 0.92 (t, J = 7.3 Hz, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.74, 147.32, 142.77, 142.43, 139.34, 134.32, 132.28, 130.10, 129.75, 129.34, 129.06, 128.21, 128.17, 127.73, 127.49, 127.47, 126.33, 126.13,

54.21, 41.91, 35.04, 33.59, 28.71, 26.57, 22.29, 14.27. **HRMS** (ESI) calcd for $C_{30}H_{30}N_2O$ [M+H]: 435.2431; found: 435.2438.



8,8-dimethyl-11-phenyl-6-(thiophen-3-yl)-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3q)

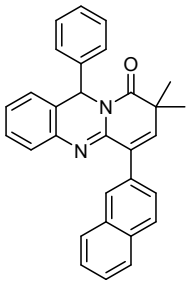
Light yellow oily (273.45 mg, 71% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.97 (dd, J = 3.0, 1.3 Hz, 1H), 7.56 (dd, J = 5.0, 3.0 Hz, 1H), 7.47 – 7.43 (m, 2H), 7.32 – 7.27 (m, 4H), 7.26 – 7.21 (m, 4H), 6.83 (s, 1H), 6.77 (s, 1H), 1.38 (s, 3H), 1.30 (s, 3H).**^{13}C NMR** 13C NMR (101 MHz, DMSO-d_6) δ 174.57, 146.73, 142.82, 142.22, 139.21, 136.63, 129.32, 129.11, 129.00, 128.17, 127.82, 127.47, 127.42, 126.72, 126.45, 126.16, 125.49, 125.24, 54.21, 41.78, 28.70, 26.61. **HRMS** (ESI) calcd for $C_{24}H_{20}N_2OS$ [M+H]: 385.1369; found: 385.1366.



6-(4-ethynylphenyl)-8,8-dimethyl-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3r)

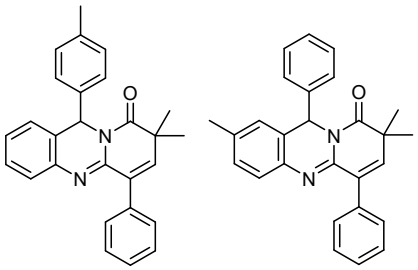
Light yellow oily (254.01 mg, 63% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.55 – 7.50 (m, 4H), 7.45 (d, J = 7.5 Hz, 1H), 7.34 – 7.27 (m, 4H), 7.24 (ddt, J = 10.7, 7.3, 1.8 Hz, 3H), 7.14 (d, J = 7.5 Hz, 1H), 6.78 (s, 1H), 6.69 (s, 1H), 4.27 (s, 1H), 1.40 (s, 3H), 1.31 (s, 3H).**^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.55, 146.93, 143.88, 142.86, 139.13, 137.54, 131.64, 131.57, 130.24, 129.37, 129.07, 128.18, 127.84, 127.49, 127.42, 126.38, 126.14,

121.55, 83.84, 81.87, 54.35, 42.00, 28.51, 26.59. **HRMS** (ESI) calcd for $C_{28}H_{22}N_2O$ [M+H]: 403.1805; found: 403.1808.



8,8-dimethyl-6-(naphthalen-2-yl)-11-phenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3s)

Yellow solid (287.56 mg, 67% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.04 (s, 1H), 8.00 – 7.92 (m, 3H), 7.64 (dd, J = 8.5, 1.8 Hz, 1H), 7.55 (dt, J = 6.2, 3.5 Hz, 2H), 7.46 (dd, J = 7.1, 2.0 Hz, 1H), 7.36 (d, J = 4.4 Hz, 4H), 7.23 (dtd, J = 14.9, 8.0, 7.4, 5.0 Hz, 3H), 7.11 (dd, J = 7.2, 1.9 Hz, 2H), 6.82 (s, 1H), 6.77 (s, 1H), 1.45 (s, 3H), 1.34 (s, 4H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.72, 147.39, 143.84, 142.95, 139.27, 134.97, 133.23, 132.91, 132.44, 129.40, 129.25, 129.04, 128.48, 128.35, 128.20, 127.94, 127.79, 127.50, 127.47, 127.24, 126.77, 126.69, 126.38, 126.19, 54.43, 42.08, 28.63, 26.70. **HRMS** (ESI) calcd for $C_{30}H_{24}N_2O$ [M+H]: 429.1961; found: 429.1969.

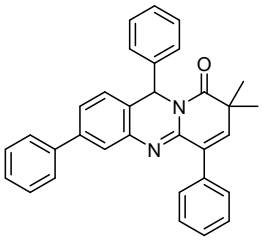


8,8-dimethyl-6-phenyl-11-(p-tolyl)-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3t)

2,8,8-trimethyl-6,11-diphenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3t')

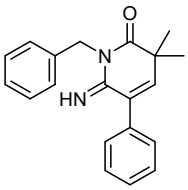
Yellow solid (330.29 mg, 84% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.51 – 7.45 (m, 2H), 7.44 – 7.34 (m, 4H), 7.34 – 7.19 (m, 5H), 7.18 – 7.10 (m, 2H), 7.05 (d, J = 6.8 Hz, 1H), 6.72 (d, J = 11.6 Hz, 1H), 6.60 (d, J = 10.8 Hz, 1H), 2.24 (d, J = 15.6 Hz, 3H), 1.39 (d, J = 2.6 Hz, 3H), 1.30 (d, J = 3.9 Hz, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.67,

174.64, 147.21, 146.50, 143.21, 142.89, 142.77, 139.93, 139.33, 137.46, 137.39, 137.10, 137.02, 132.48, 132.43, 129.88, 129.84, 129.66, 129.34, 128.27, 128.20, 128.16, 127.79, 127.21, 126.25, 126.19, 54.41, 54.01, 41.91, 41.87, 28.67, 28.63, 26.60, 26.58, 21.22, 21.03. **HRMS** (ESI) calcd for $C_{27}H_{24}N_2O$ [M+H]: 393.1961; found: 393.1969.



8,8-dimethyl-3,6,11-triphenyl-8,11-dihydro-9H-pyrido[2,1-b]quinazolin-9-one:(3u)

Yellow solid (432.45 mg, 95% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.84 (d, J = 2.0 Hz, 1H), 7.67 (d, J = 7.9 Hz, 2H), 7.61 – 7.55 (m, 1H), 7.52 (d, J = 6.6 Hz, 2H), 7.47 – 7.40 (m, 6H), 7.39 – 7.32 (m, 7H), 7.23 (dd, J = 10.2, 7.4 Hz, 2H), 6.89 (s, 1H), 6.65 (s, 1H), 1.41 (s, 3H), 1.33 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.74, 147.37, 143.37, 142.83, 139.54, 139.36, 138.76, 137.04, 132.44, 129.94, 129.45, 129.41, 128.32, 128.26, 128.21, 128.11, 127.14, 126.94, 126.87, 126.81, 126.15, 125.66, 54.40, 42.01, 28.69, 26.57. **HRMS** (ESI) calcd for $C_{32}H_{26}N_2O$ [M+H]: 455.2118; found: 455.2113.



1-benzyl-6-imino-3,3-dimethyl-5-phenyl-3,6-dihydropyridin-2(1H)-one:(3x)

Yellow solid (285.91 mg, 94% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.08 (s, 1H), 7.51 – 7.43 (m, 3H), 7.35 – 7.18 (m, 8H), 6.42 (s, 1H), 5.21 (s, 2H), 1.37 (s, 6H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 175.25, 159.12, 142.33, 138.44, 136.07, 129.46, 129.41, 129.15, 128.69, 127.37, 127.07, 43.84, 41.20, 27.41. **HRMS** (ESI) calcd for $C_{20}H_{20}N_2O$ [M+H]: 305.1648; found: 305.1645.

7. Crystal Data and Structure Refinements

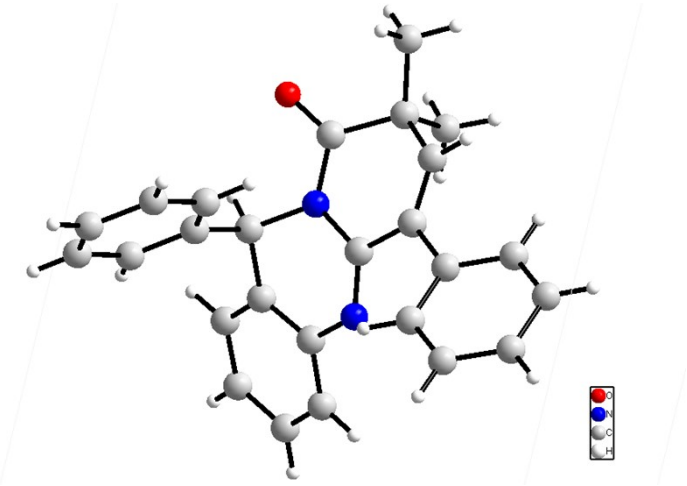


Figure 9 Structure of **3a** by X-Ray crystallographic (CCDC = 2327662)

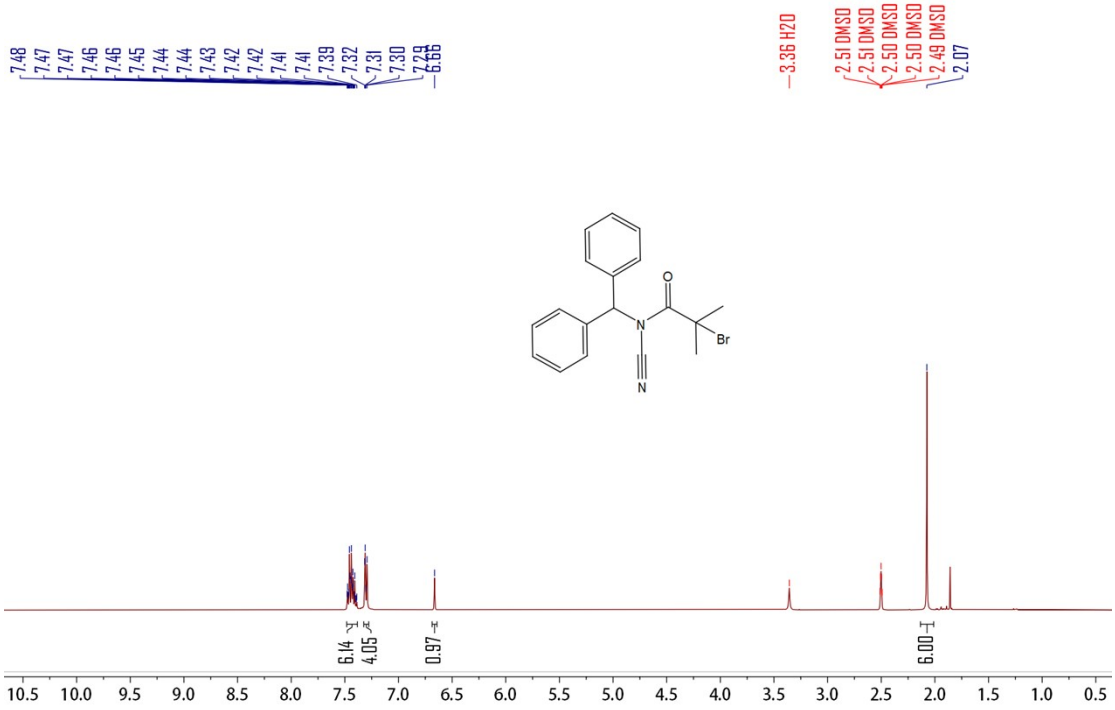
Single crystal suitable for X-ray diffraction was obtained by slow evaporation of a saturated solution of compound **3a** (cyclohexane/CH_2Cl_2) in a loosely capped vial.

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

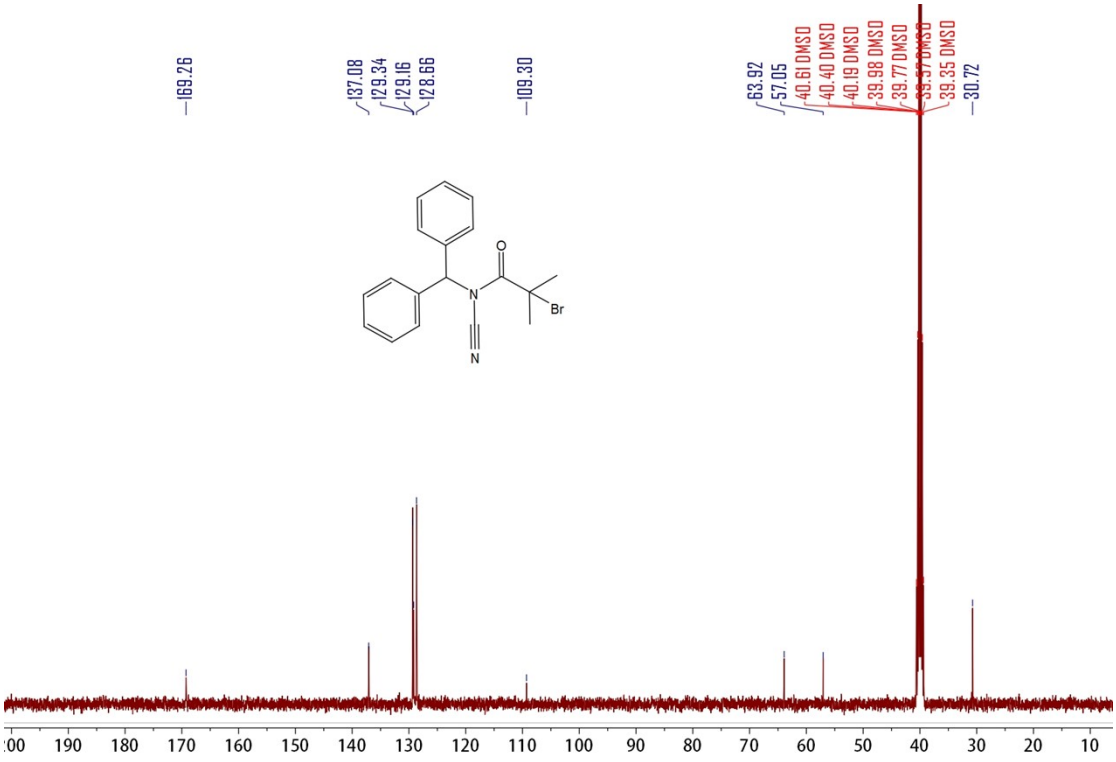
Empirical formula	$C_{26}H_{22}N_2O$
Formula weight	378.45
Temperature/K	150.00
Crystal system	orthorhombic
Space group	Aea2
a/Å	12.6782(8)
b/Å	24.5075(17)
c/Å	12.7134(6)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	3950.2(4)
Z	8
ρcalcg/cm^3	1.273

μ/mm^{-1}	0.078
F(000)	1600.0
Crystal size/mm^3	0.2 × 0.15 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.832 to 52.84
Index ranges	-15 ⩽ h ⩽ 15, -30 ⩽ k ⩽ 30, -15 ⩽ l ⩽ 15
Reflections collected	36824
Independent reflections	4048 [Rint = 0.0822, Rsigma = 0.0410]
Data/restraints/parameters	4048/1/265
Final R indexes [I>=2σ (I)]	R1 = 0.0429, wR2 = 0.0911
Final R indexes [all data]	R1 = 0.0563, wR2 = 0.0987
Largest diff. peak/hole / e Å-3	0.17/-0.15
Flack parameter	0(3)

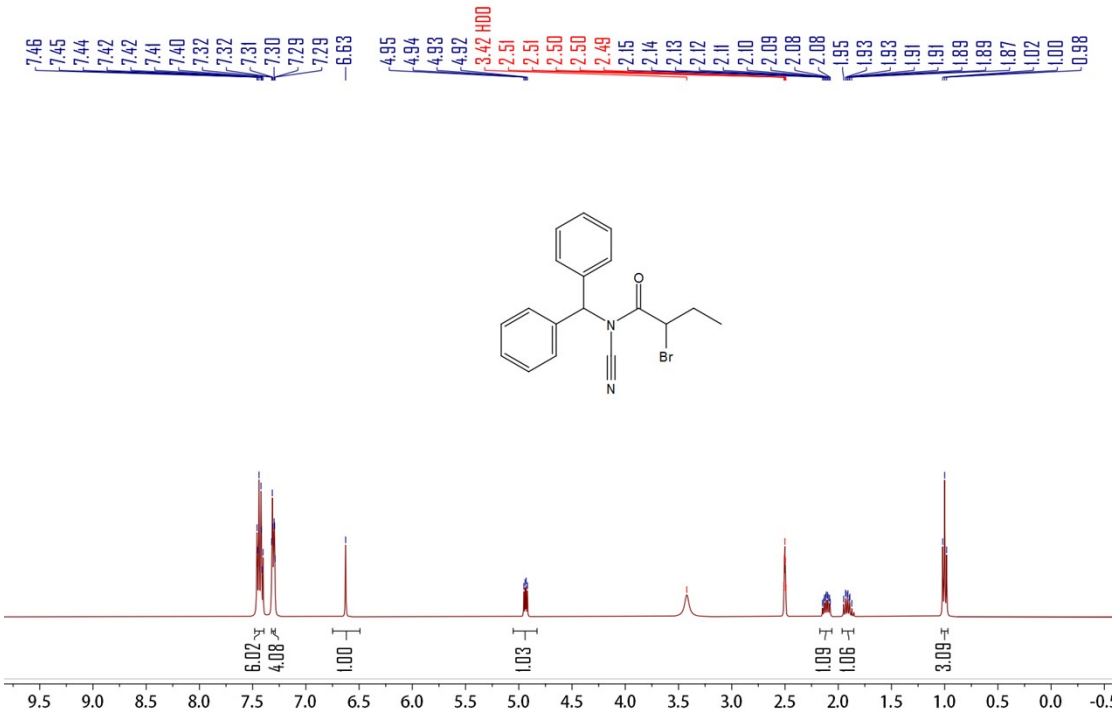
8. ^{1}H NMR and ^{13}C NMR spectra



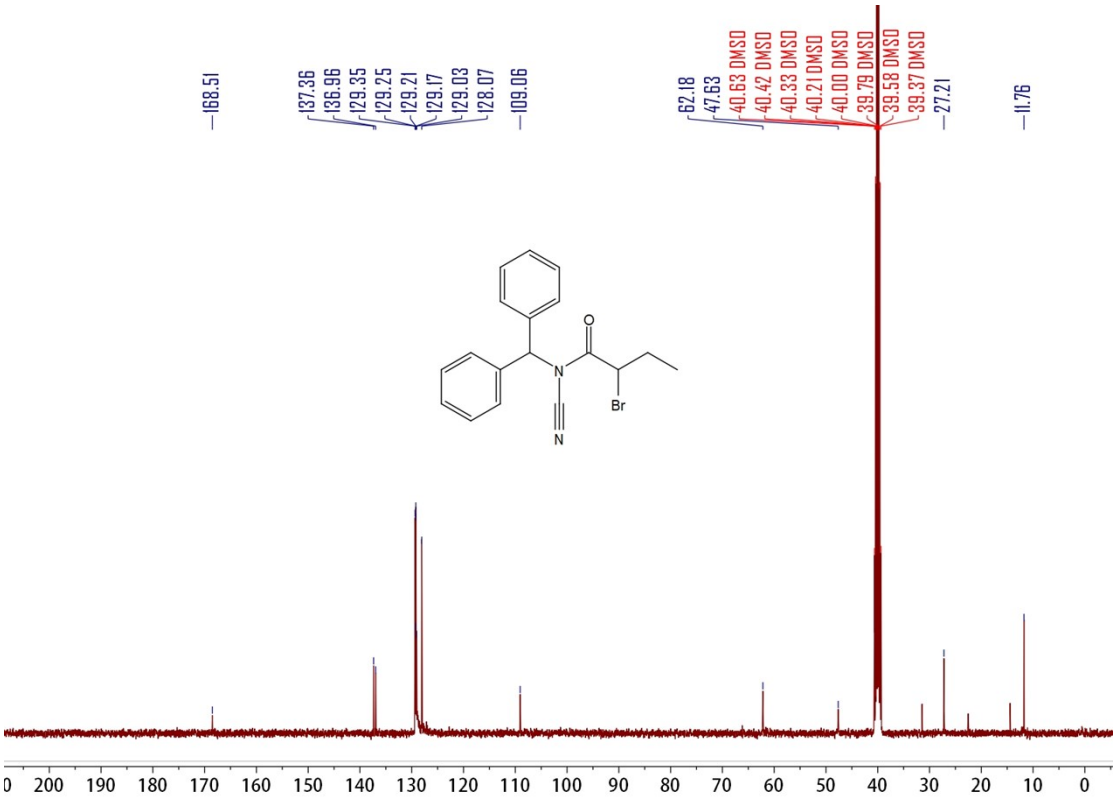
^{1}H NMR Spectrum of Compound **1a**



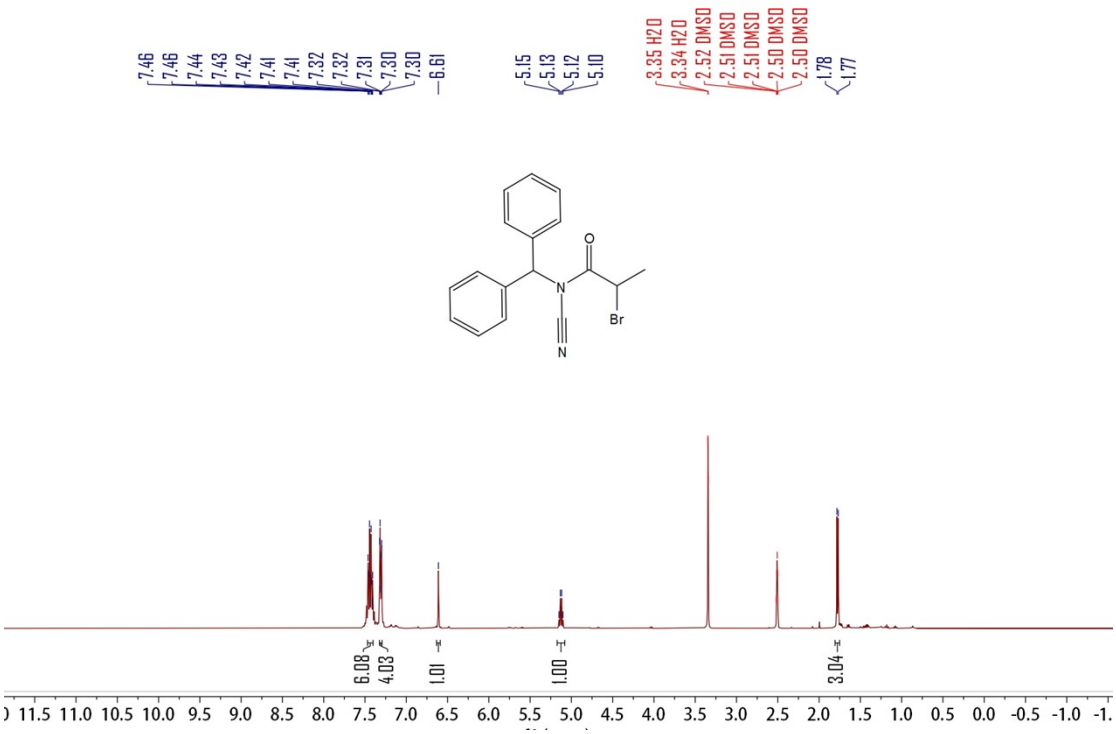
^{13}C NMR Spectrum of Compound **1a**



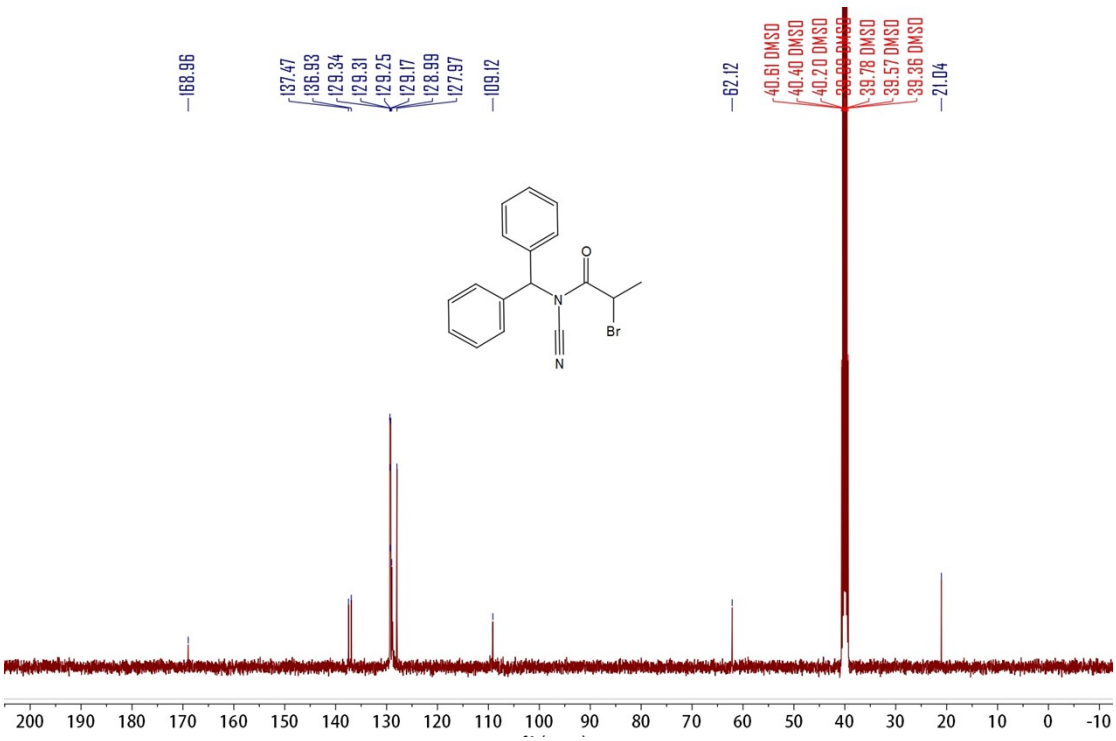
^{1}H NMR Spectrum of Compound **1b**



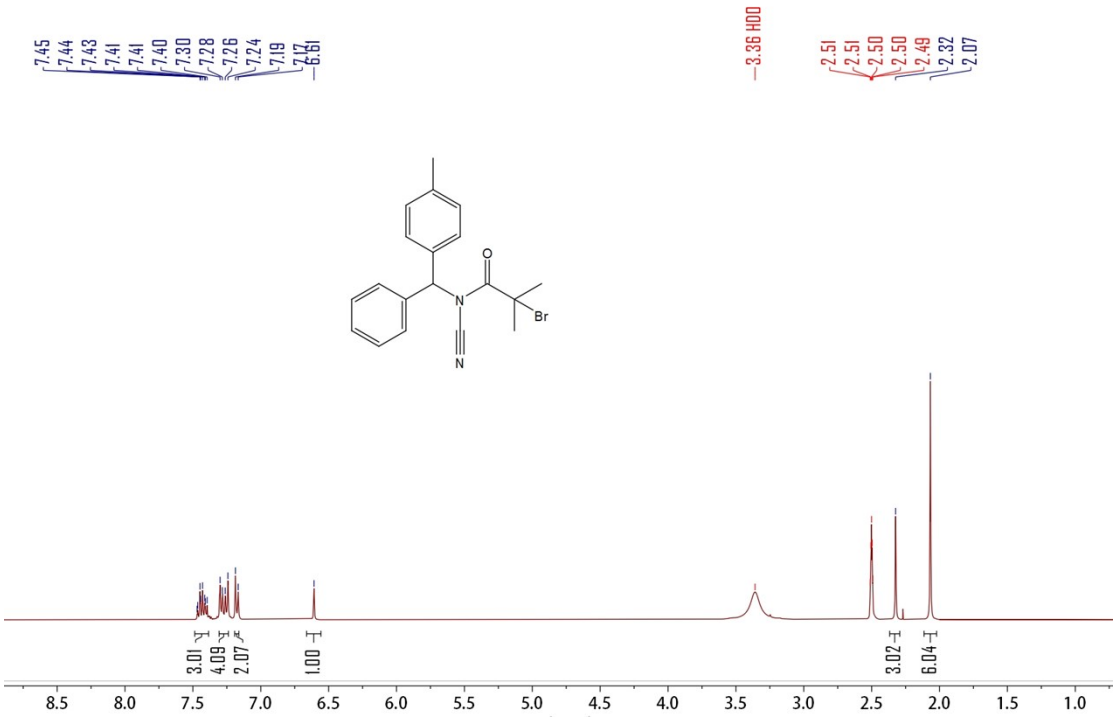
^{13}C NMR Spectrum of Compound **1b**



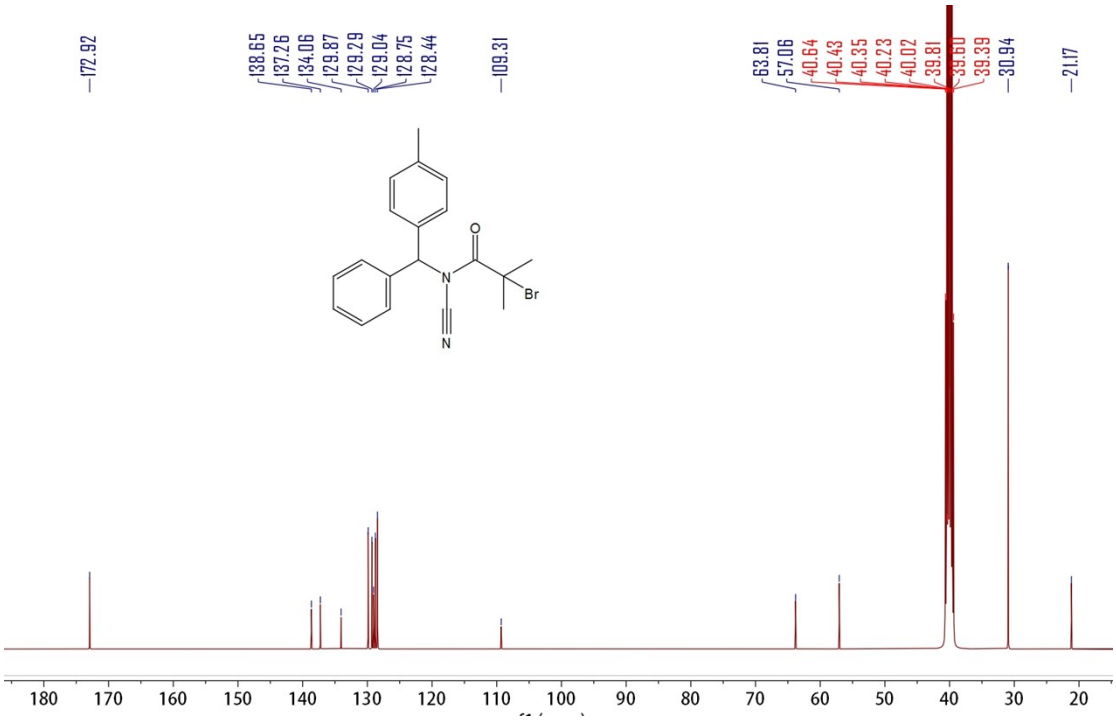
^{1}H NMR Spectrum of Compound **1c**



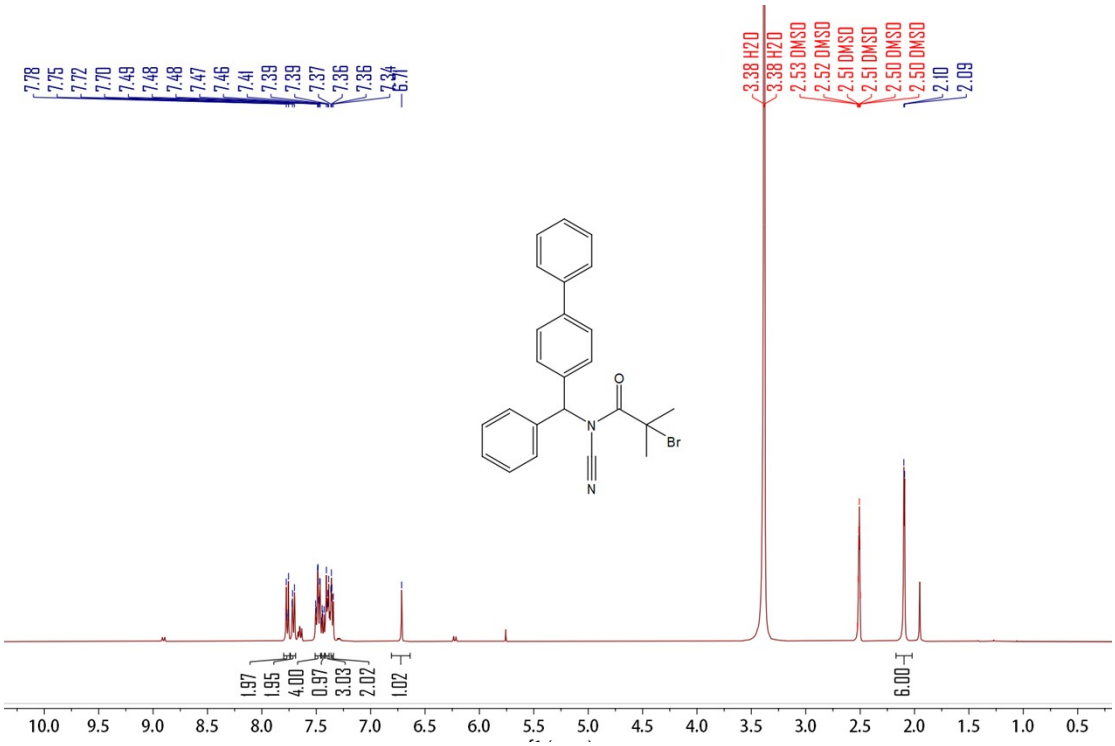
^{13}C NMR Spectrum of Compound **1c**



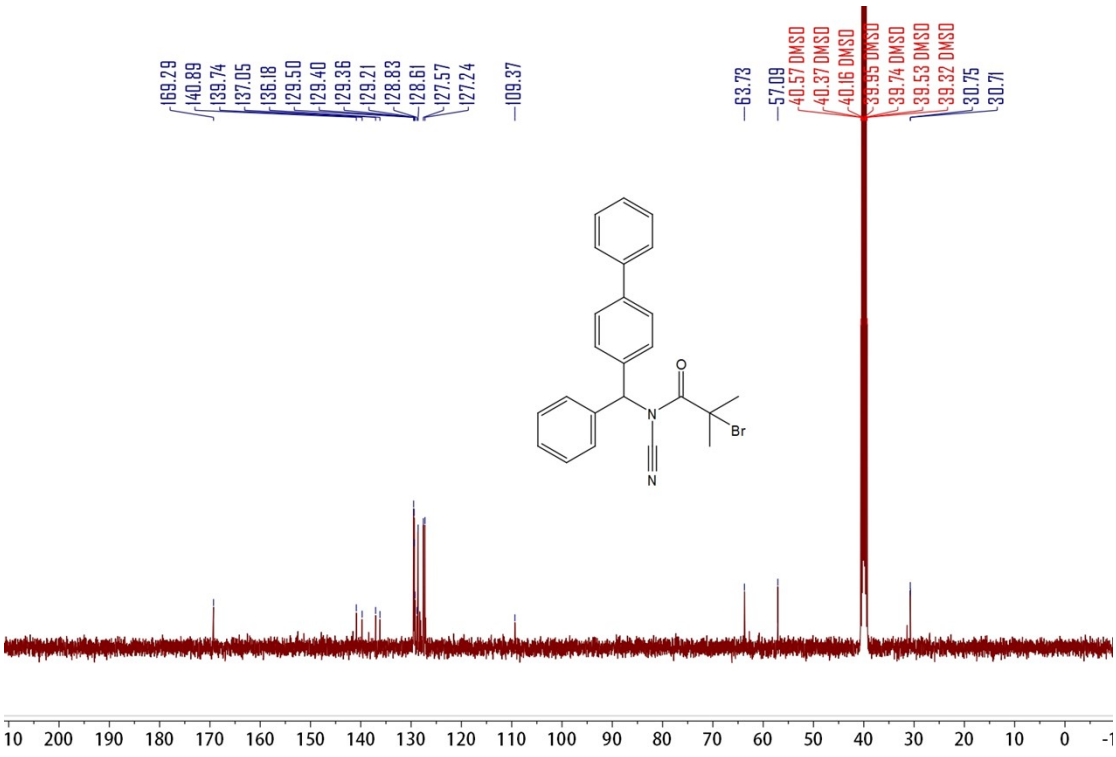
^{1}H NMR Spectrum of Compound **1d**



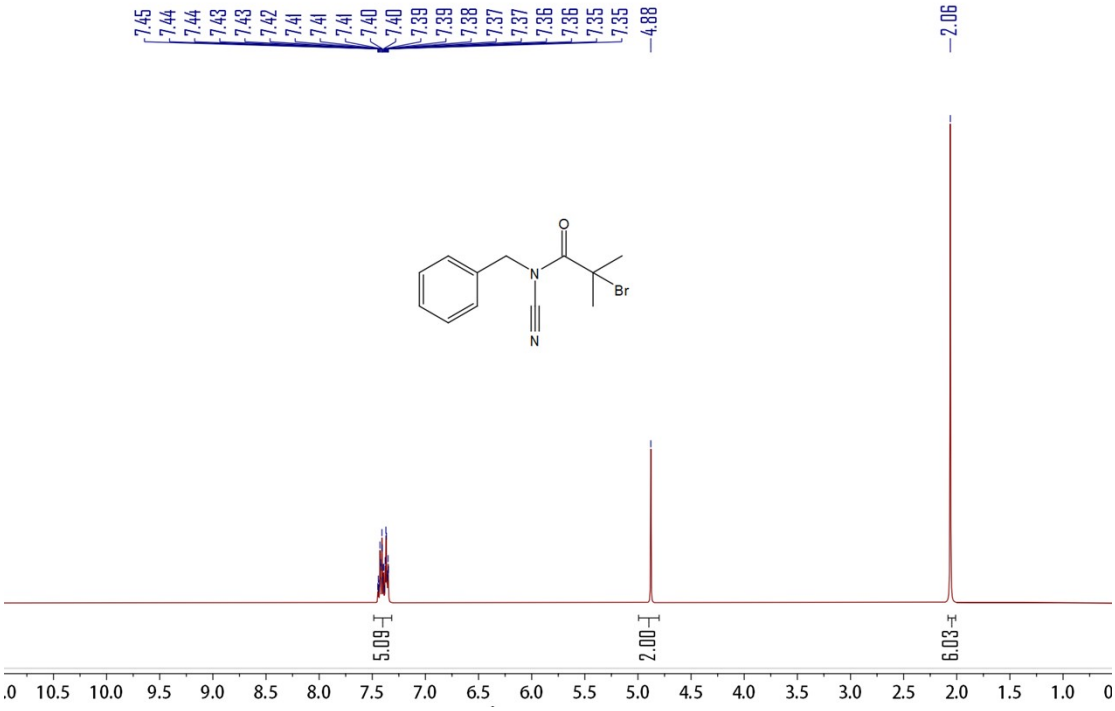
^{13}C NMR Spectrum of Compound **1d**



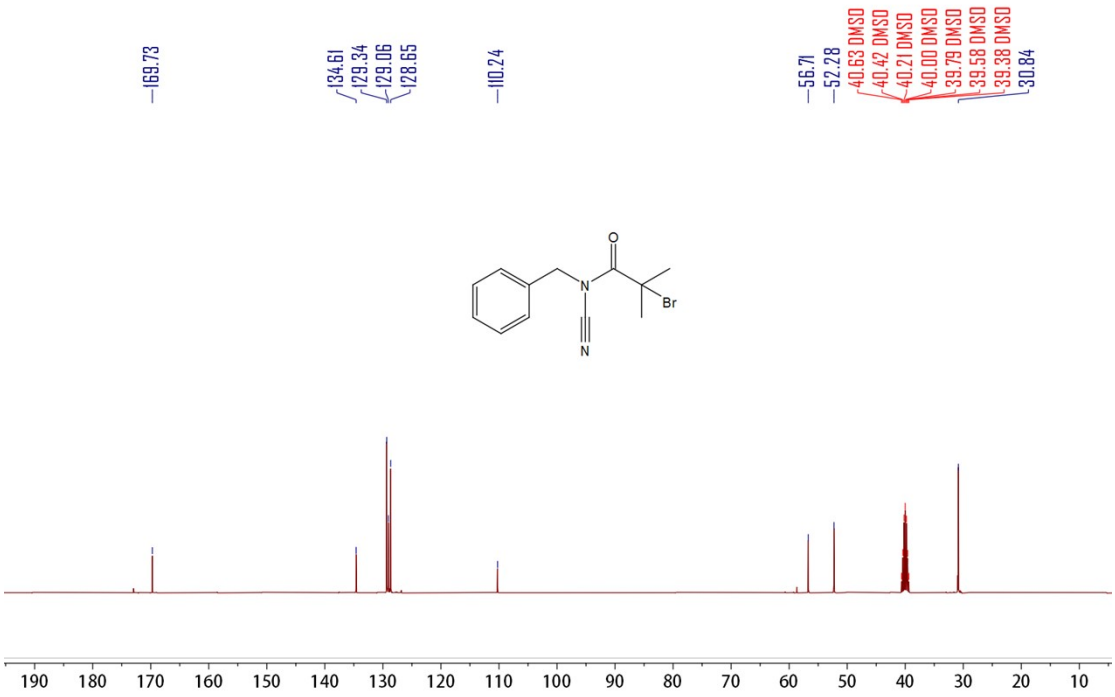
^{1}H NMR Spectrum of Compound **1e**



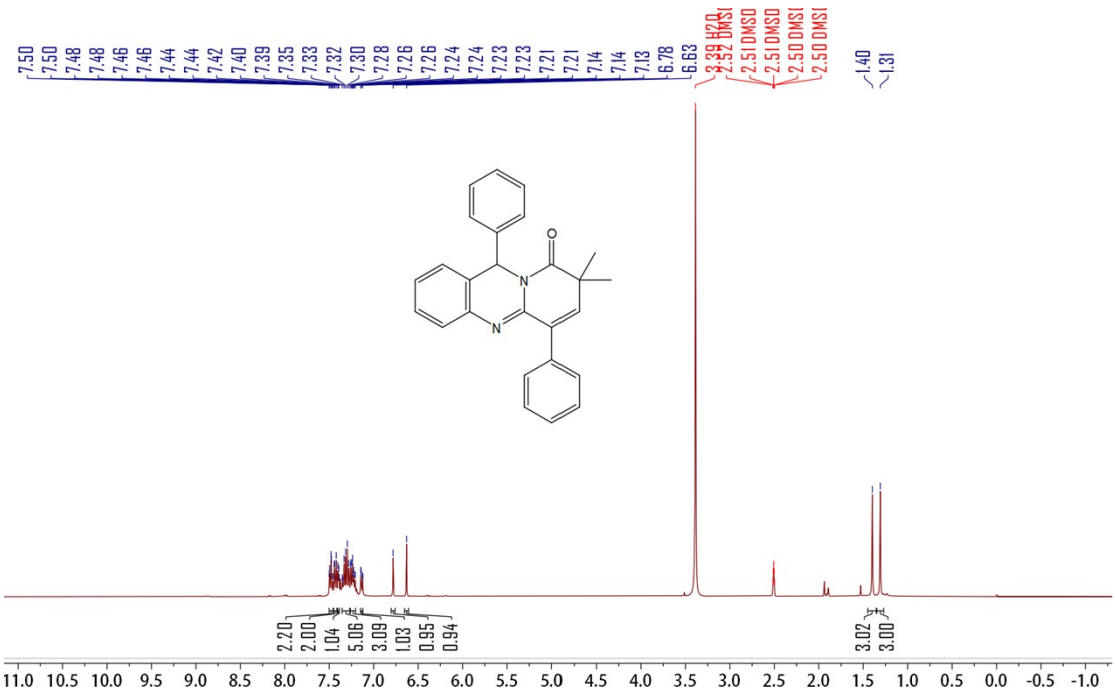
^{13}C NMR Spectrum of Compound **1e**



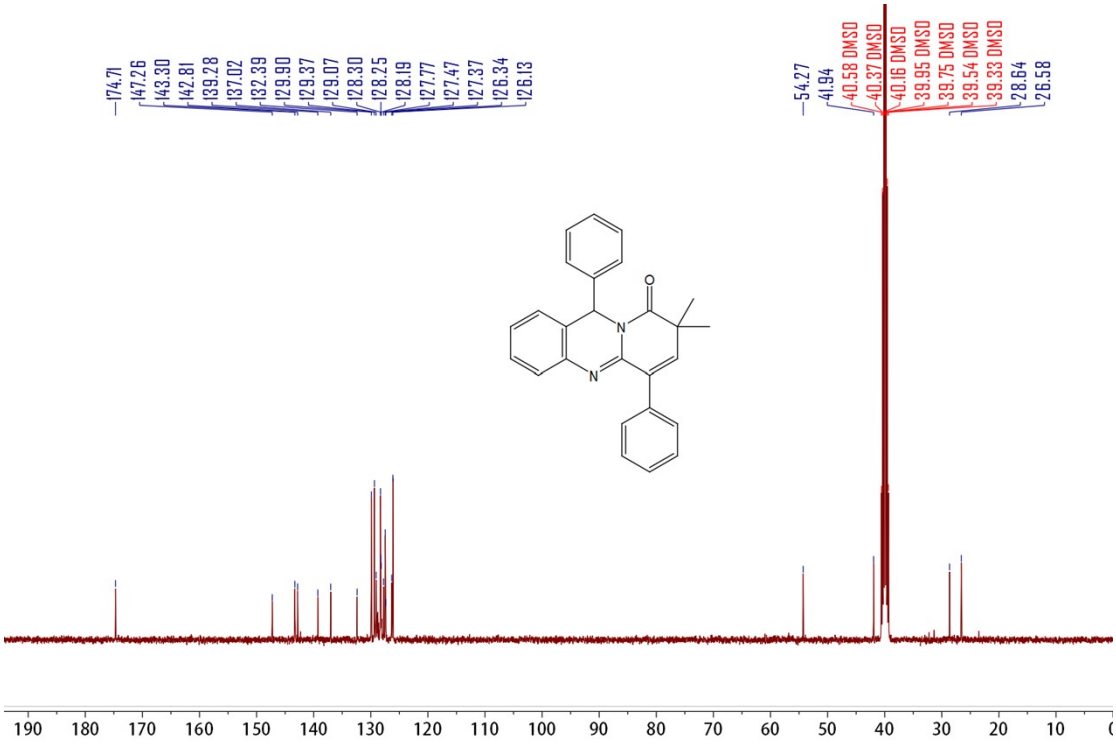
^{1}H NMR Spectrum of Compound **1f**



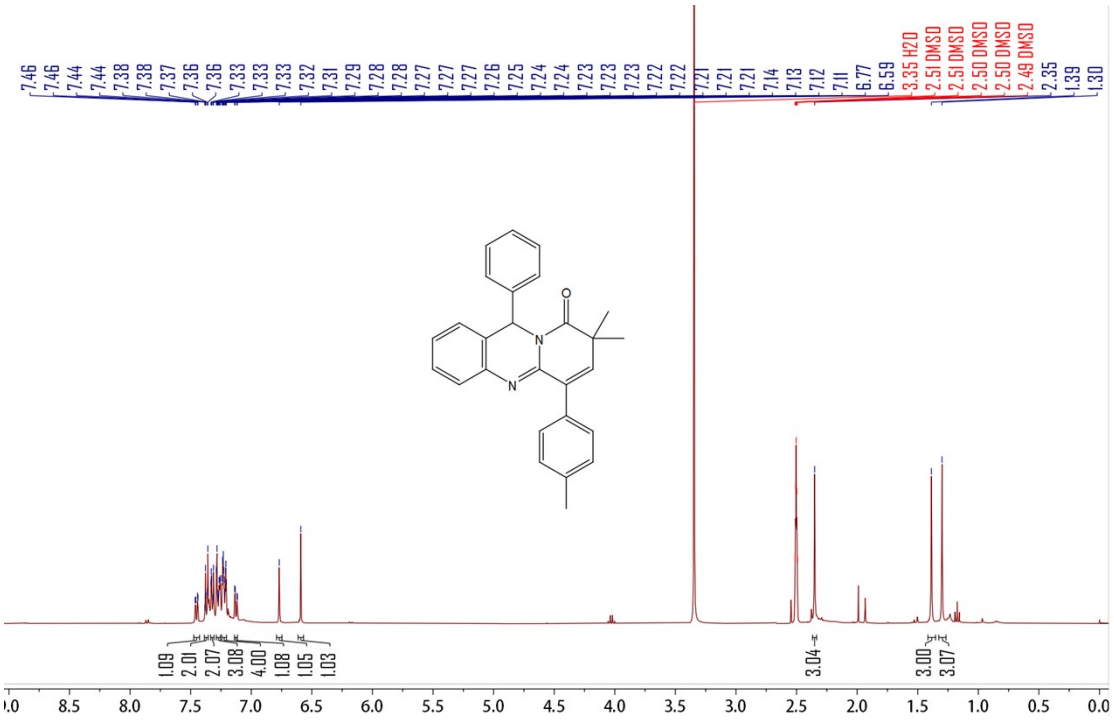
^{13}C NMR Spectrum of Compound **1f**



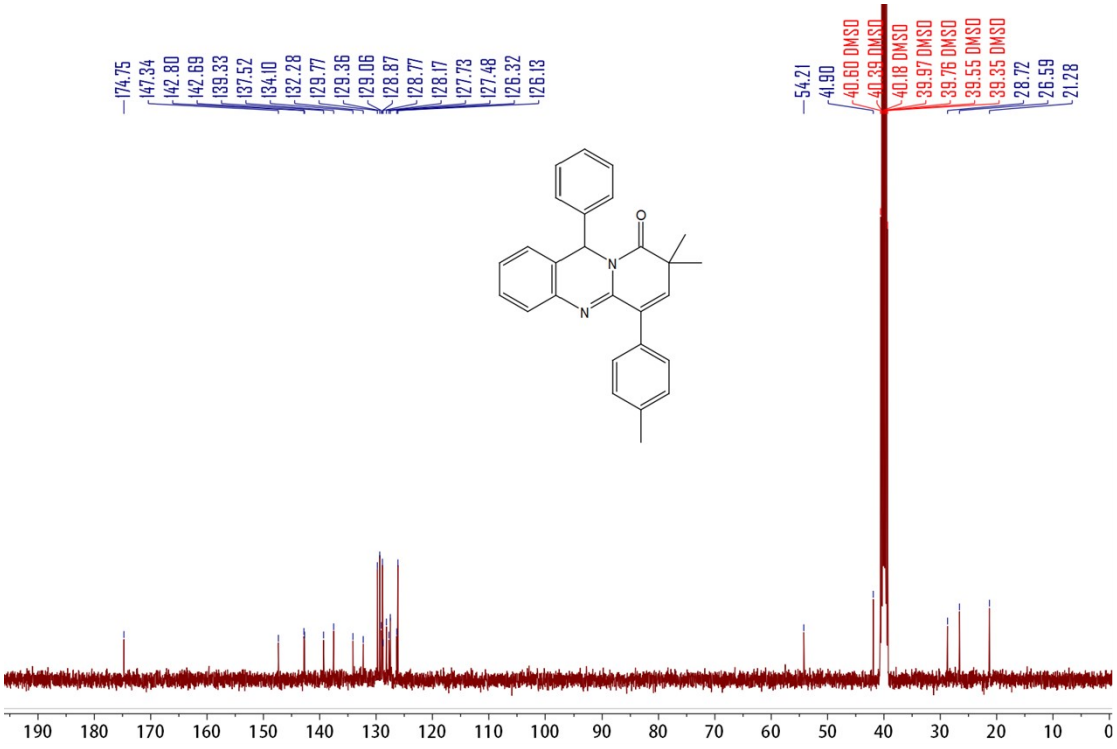
^{1}H NMR Spectrum of Compound **3a**



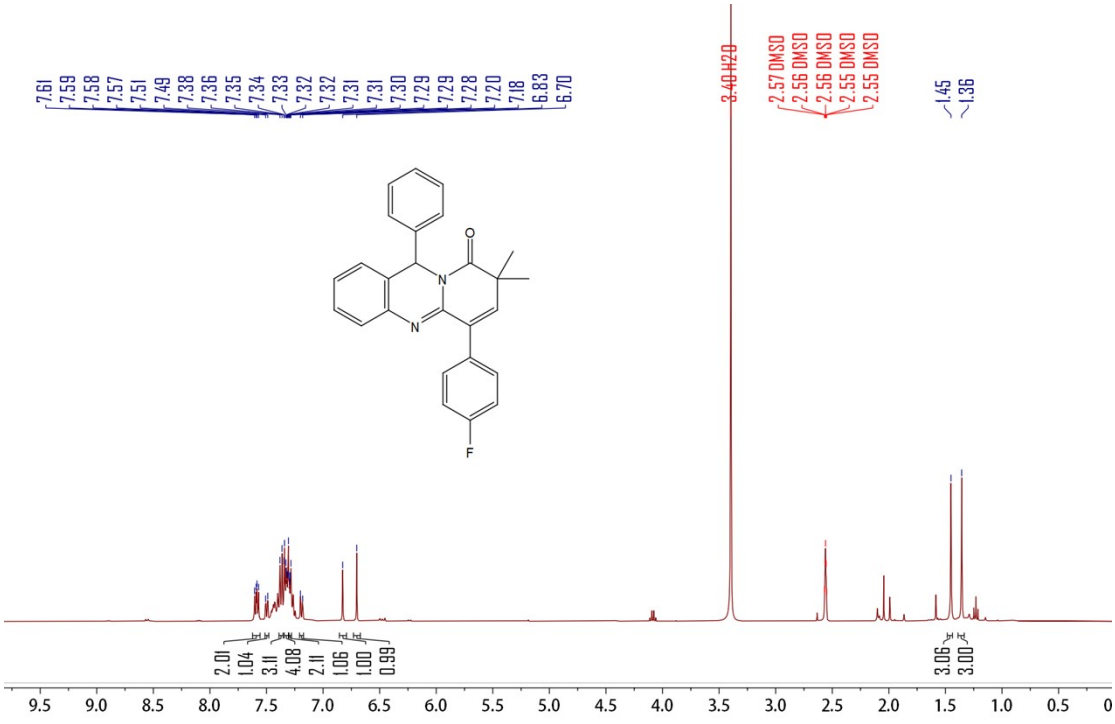
^{13}C NMR Spectrum of Compound **3a**



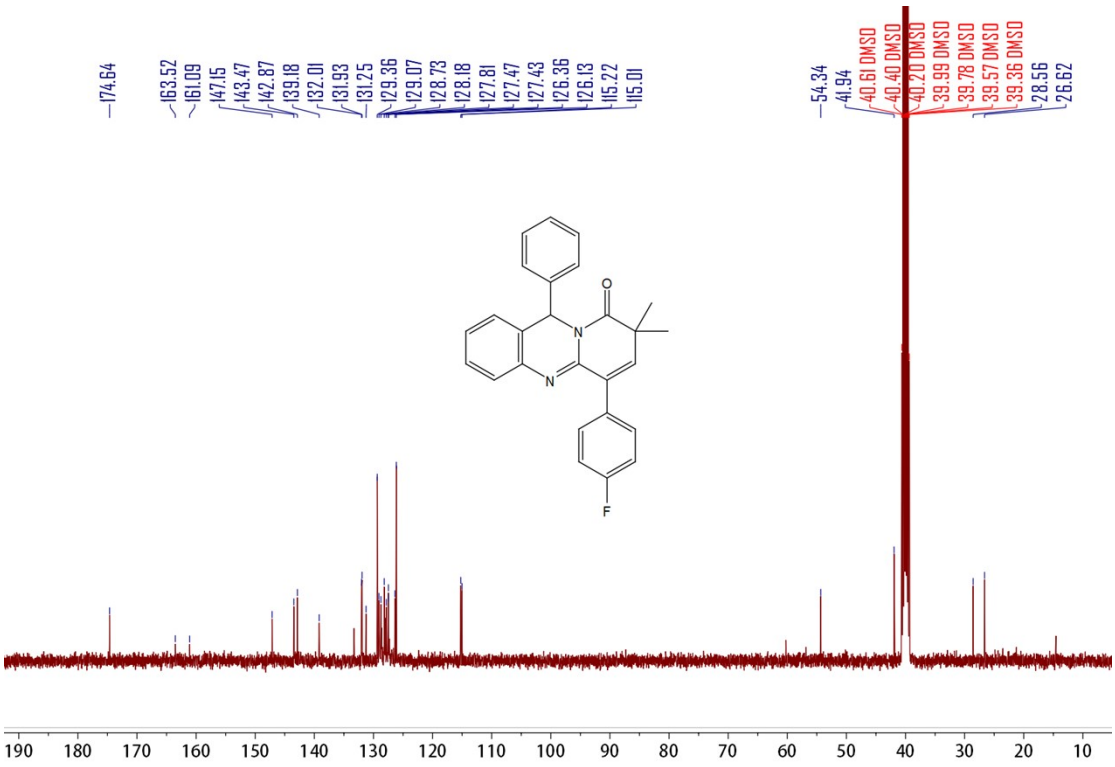
^{1}H NMR Spectrum of Compound **3b**



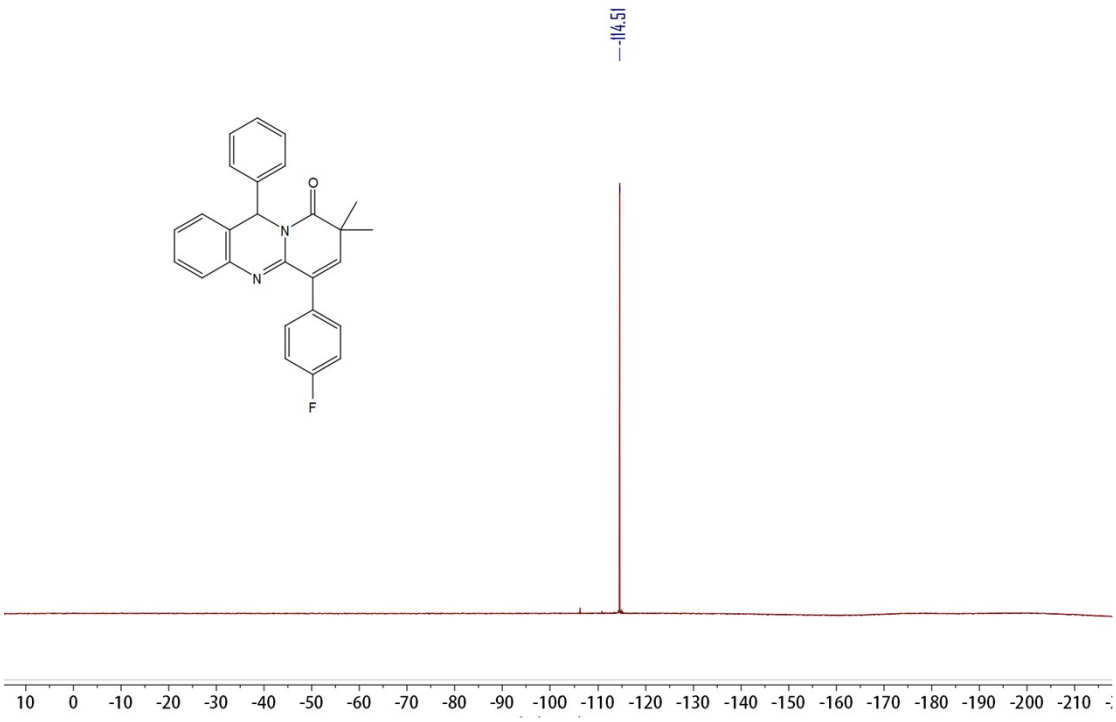
^{13}C NMR Spectrum of Compound **3b**



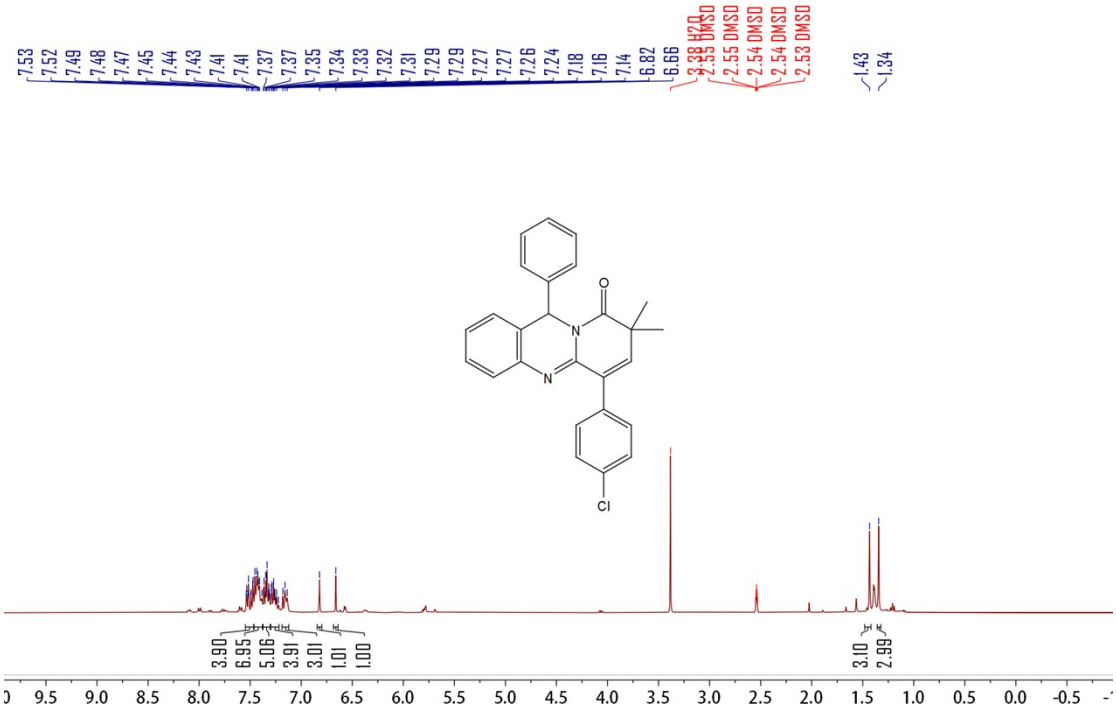
^{1}H NMR Spectrum of Compound **3c**



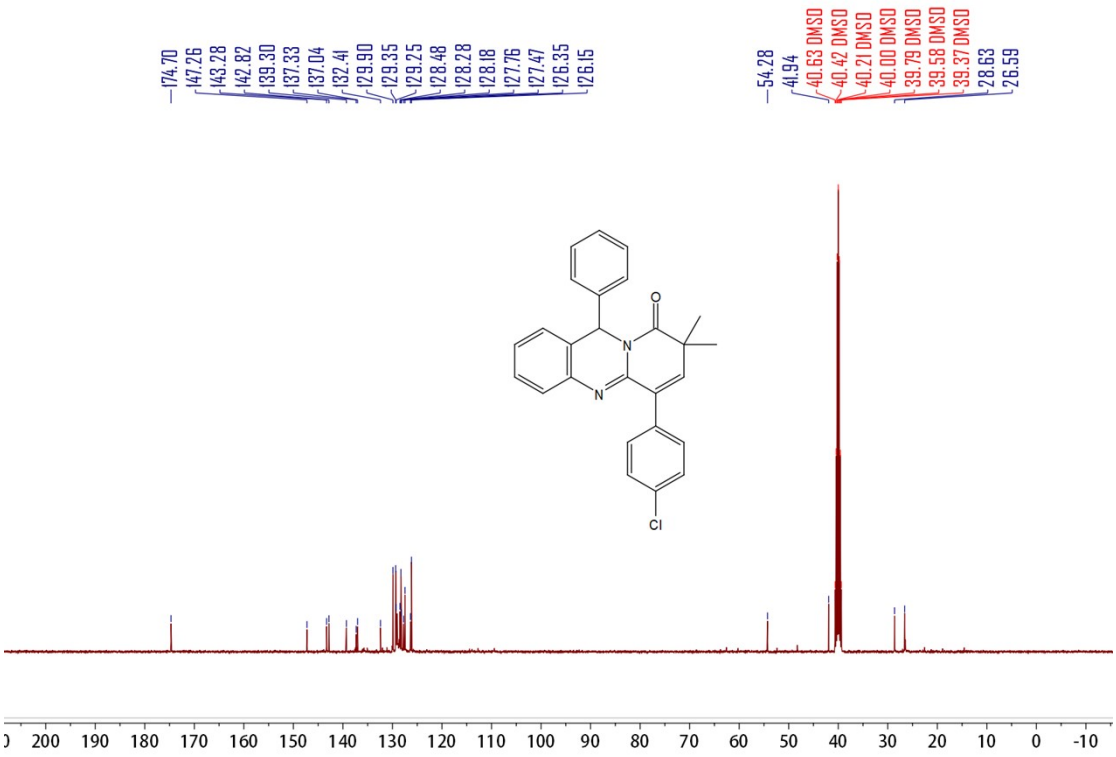
^{13}C NMR Spectrum {Wei, 2023 #20}of Compound **3c**



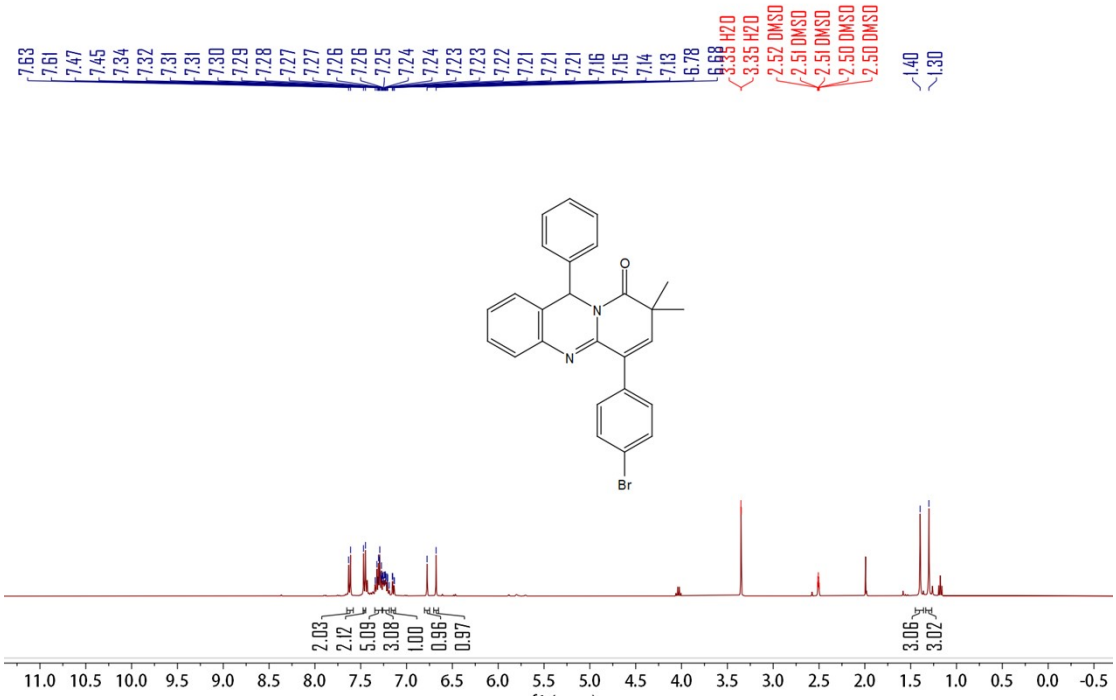
^{19}F NMR Spectrum of Compound **3c**



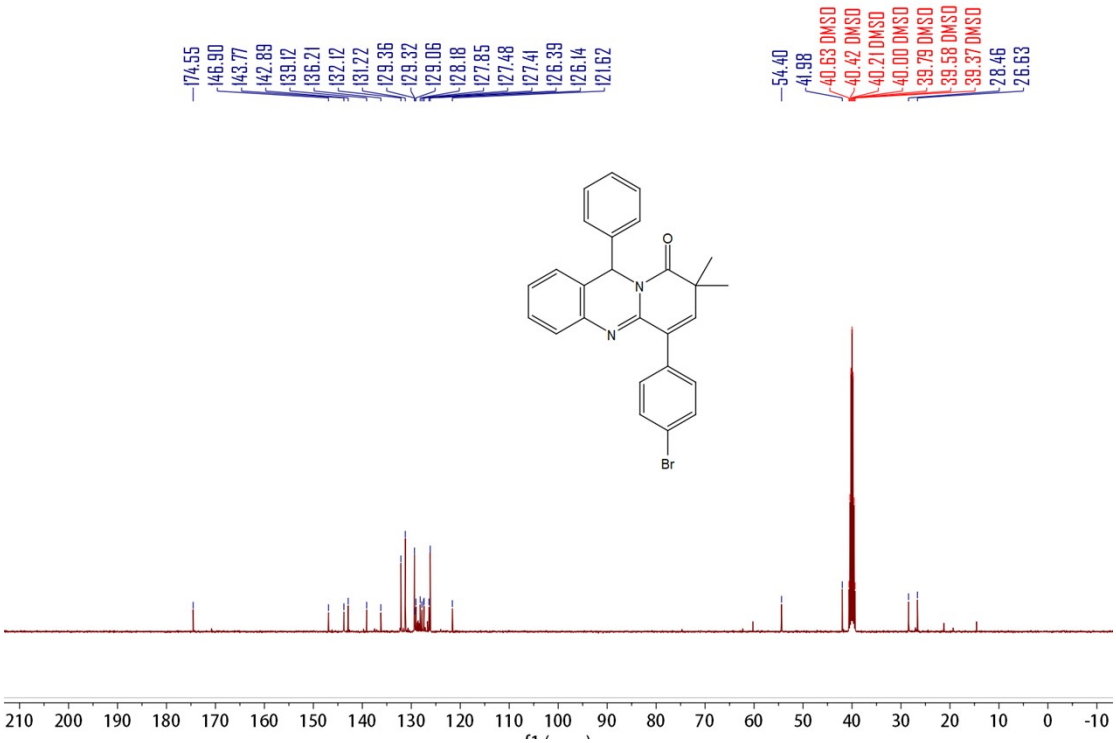
^{1}H NMR Spectrum of Compound **3d**



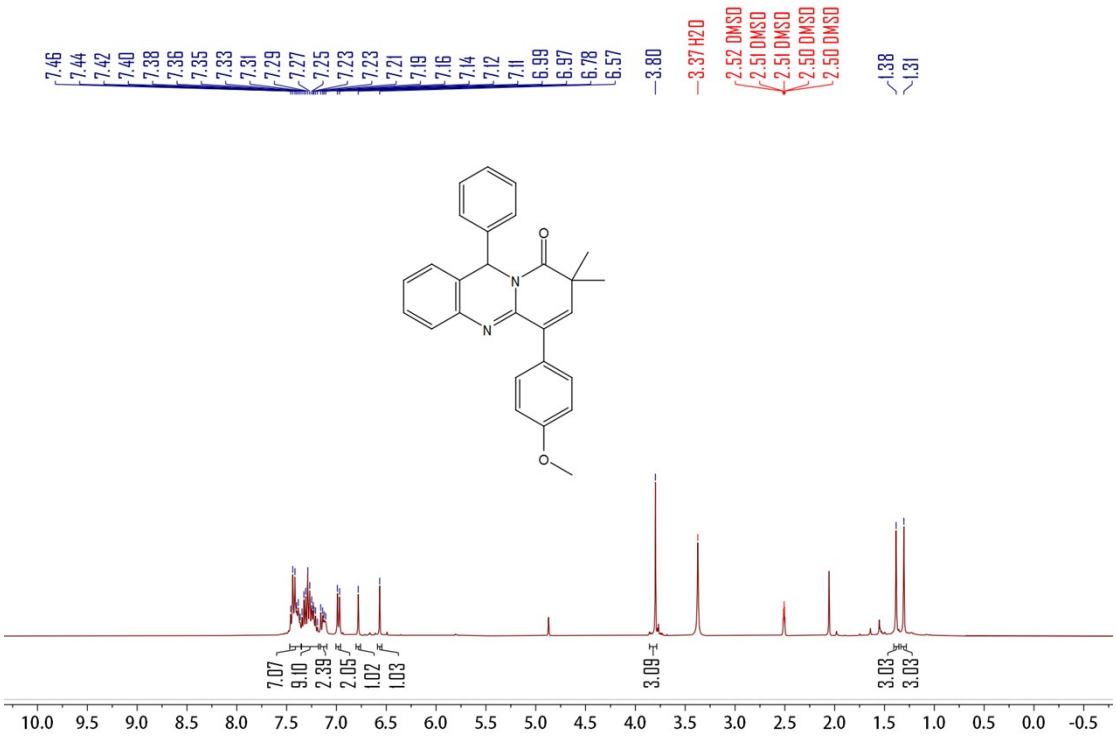
^{13}C NMR Spectrum of Compound **3d**



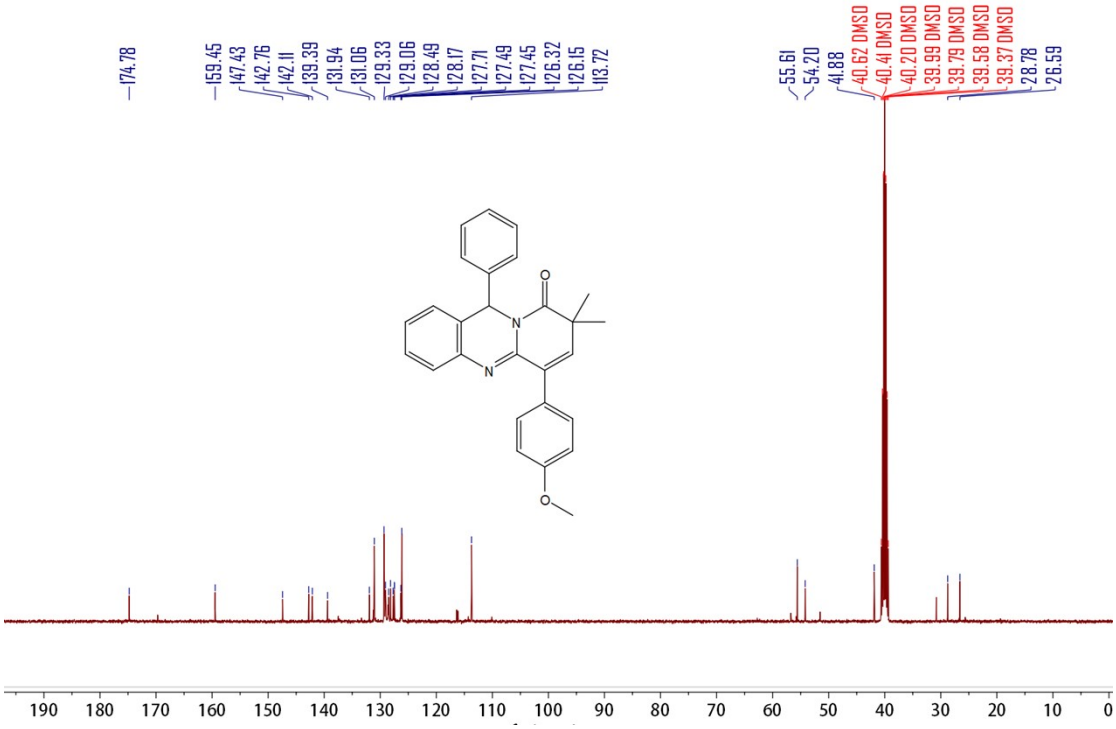
^{1}H NMR Spectrum of Compound **3e**



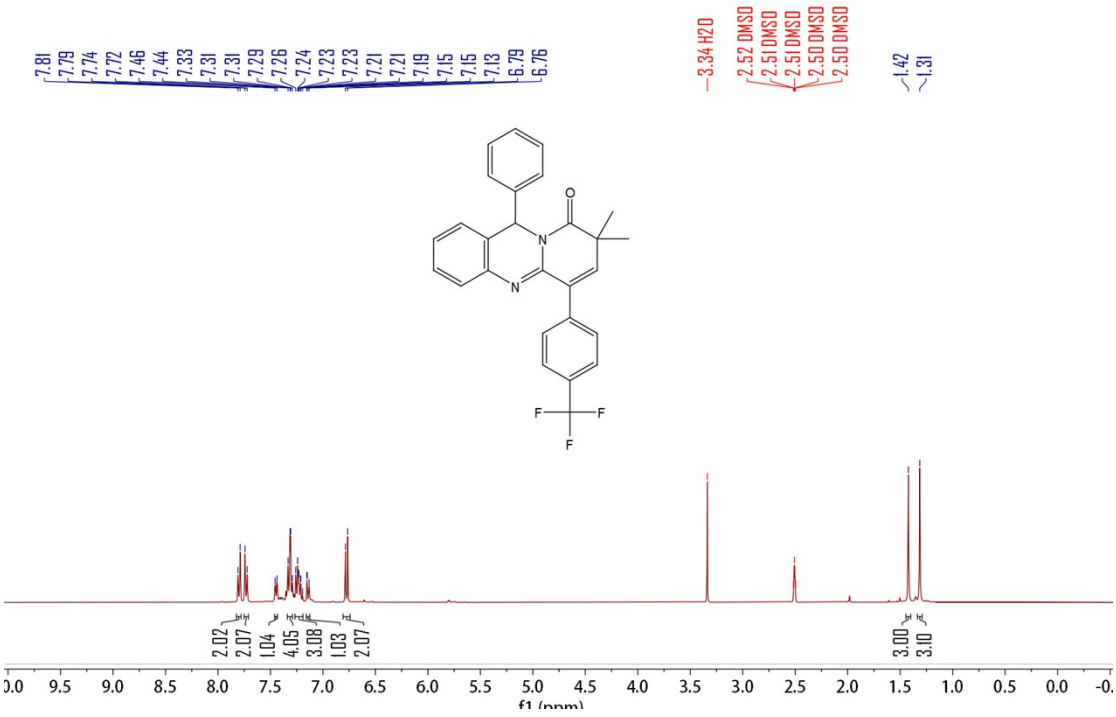
^{13}C NMR Spectrum of Compound **3e**



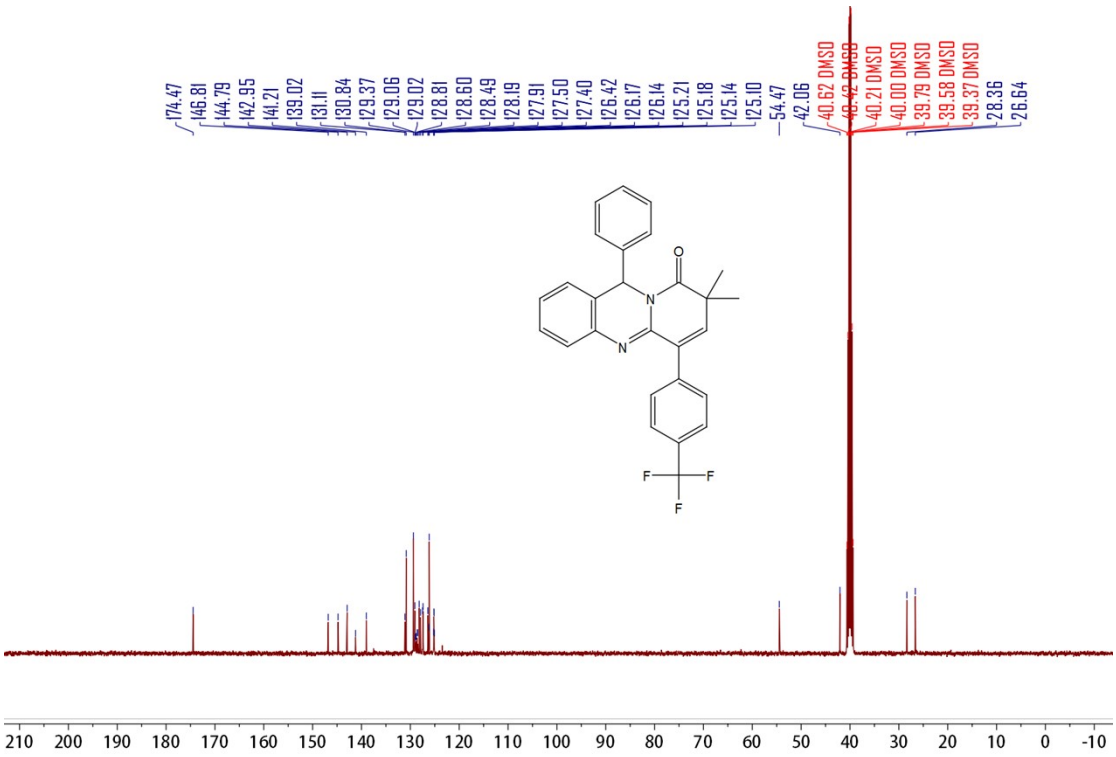
^{1}H NMR Spectrum of Compound **3f**



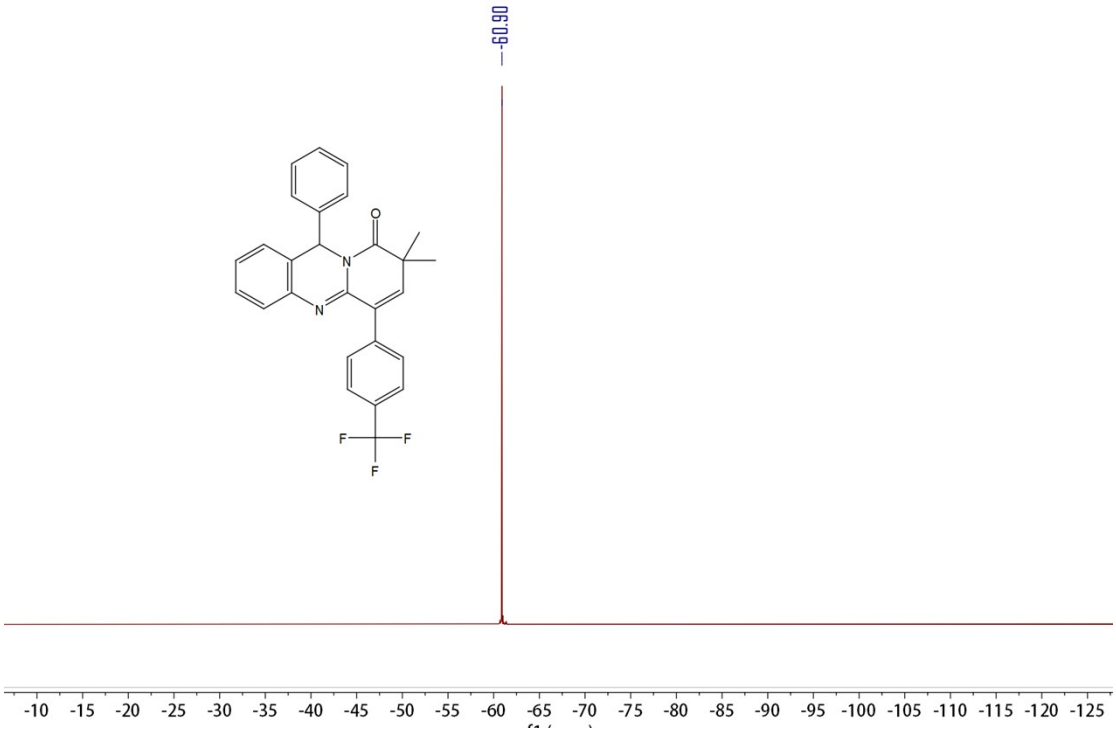
^{13}C NMR Spectrum of Compound **3f**



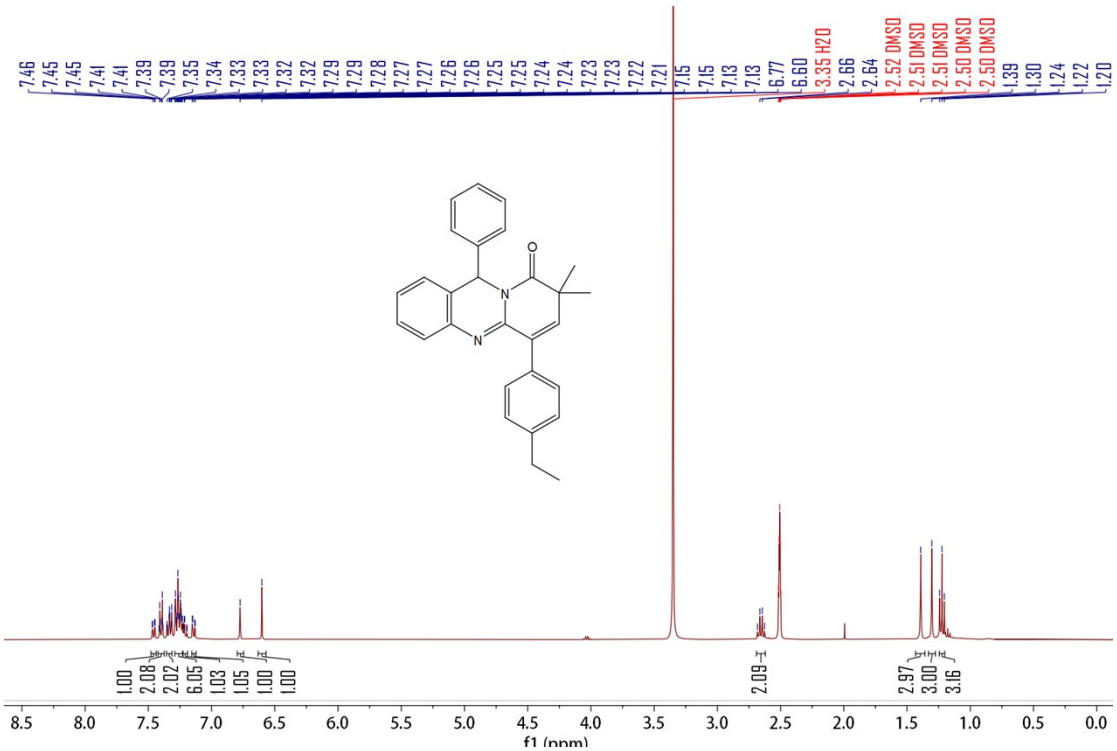
^{1}H NMR Spectrum of Compound **3g**



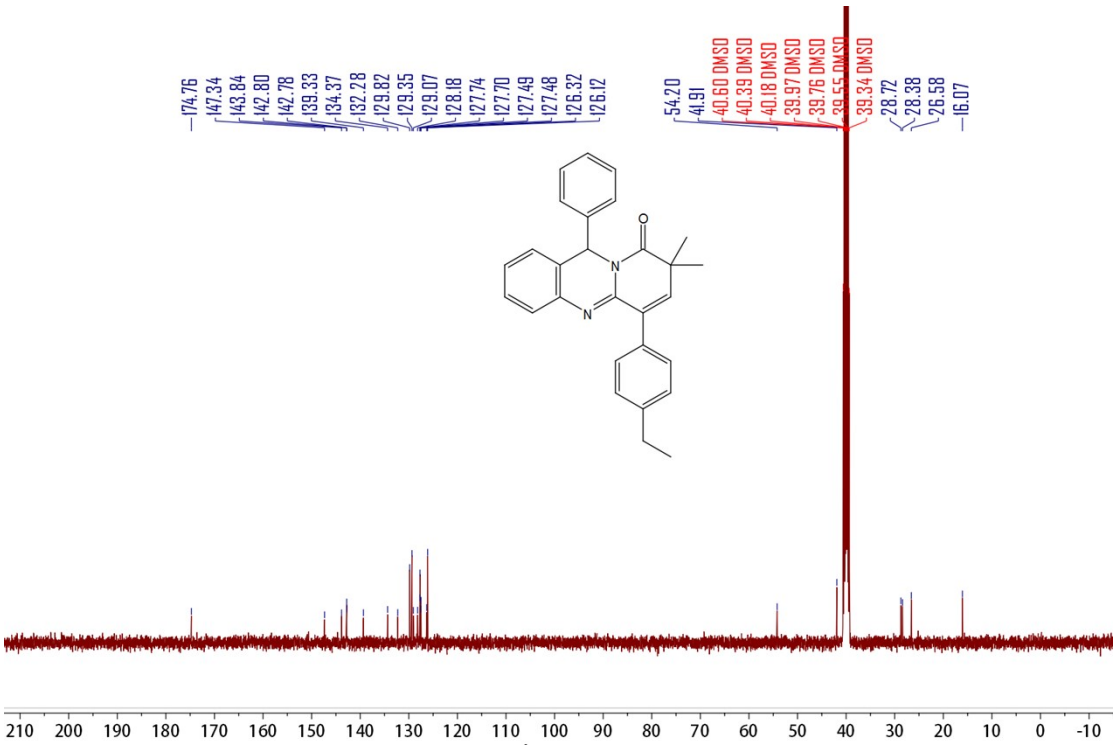
^{13}C NMR Spectrum of Compound **3g**



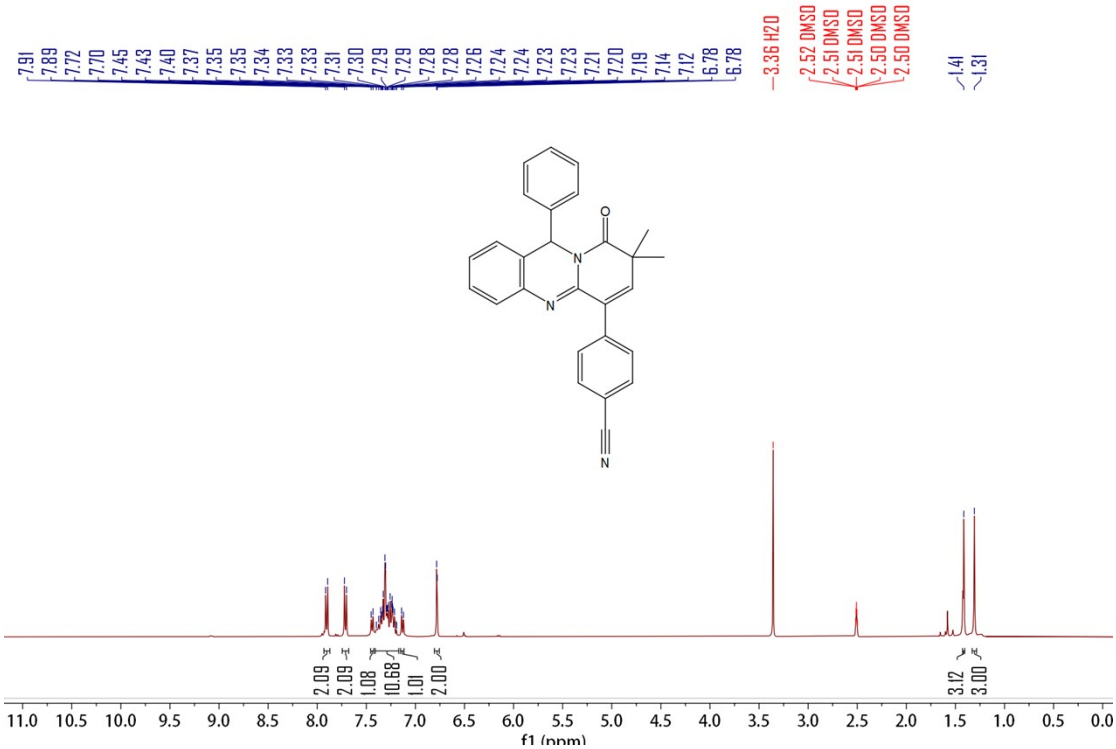
^{19}F NMR Spectrum of Compound **3g**



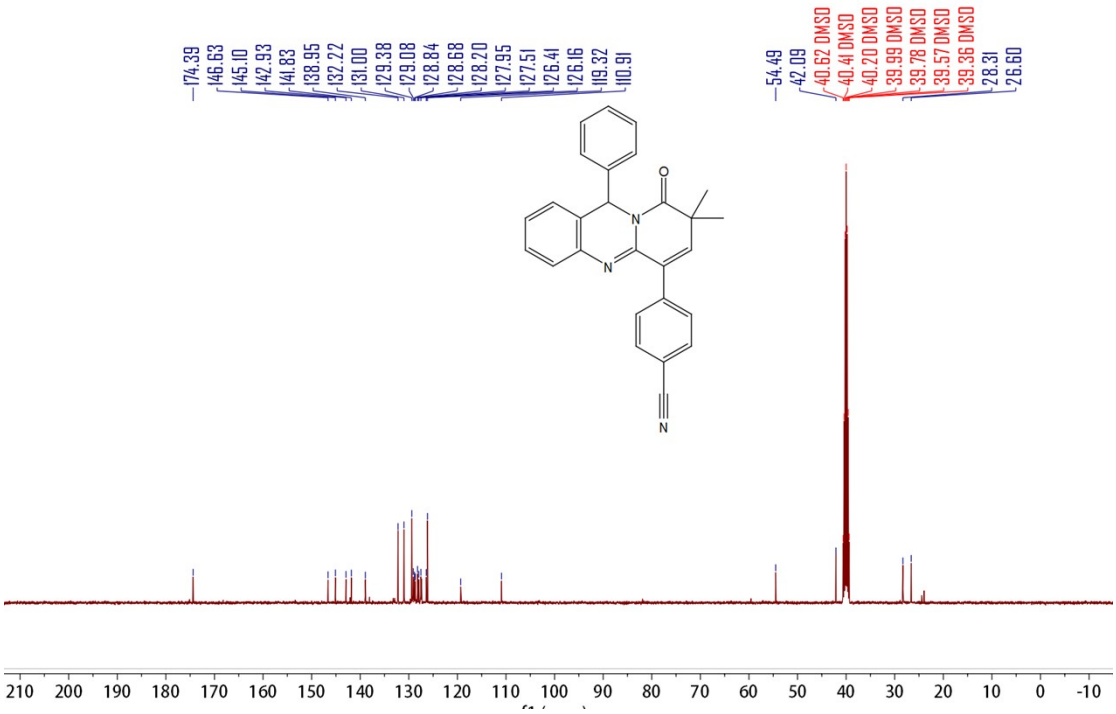
^{1}H NMR Spectrum of Compound **3h**



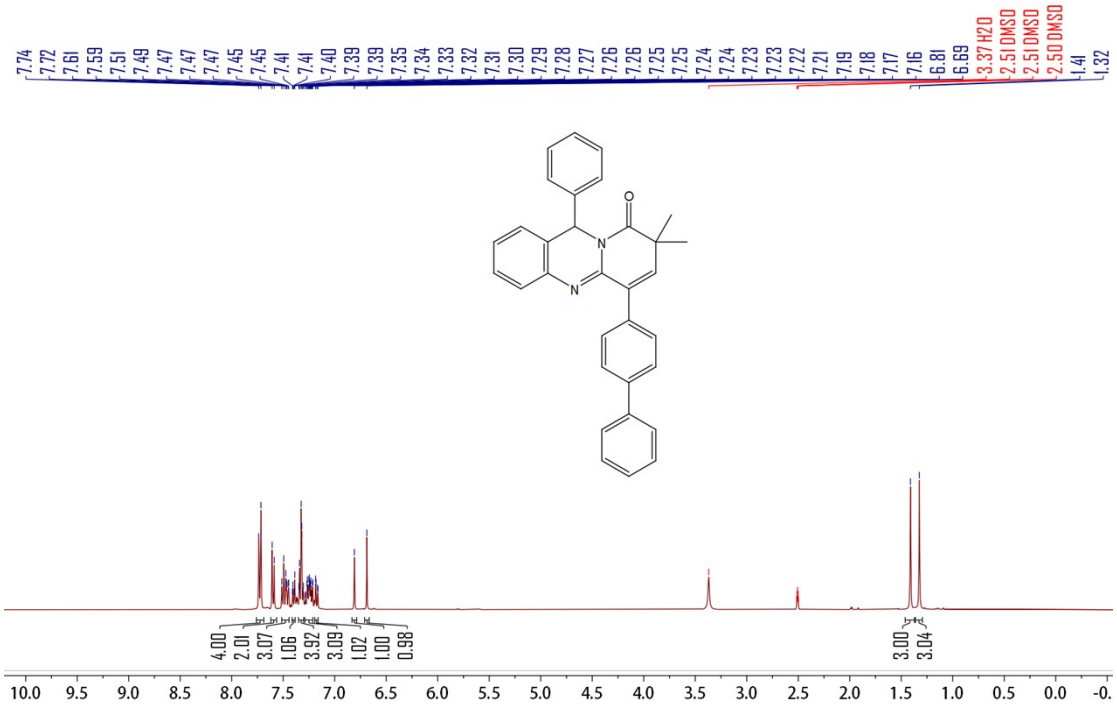
^{13}C NMR Spectrum of Compound **3h**



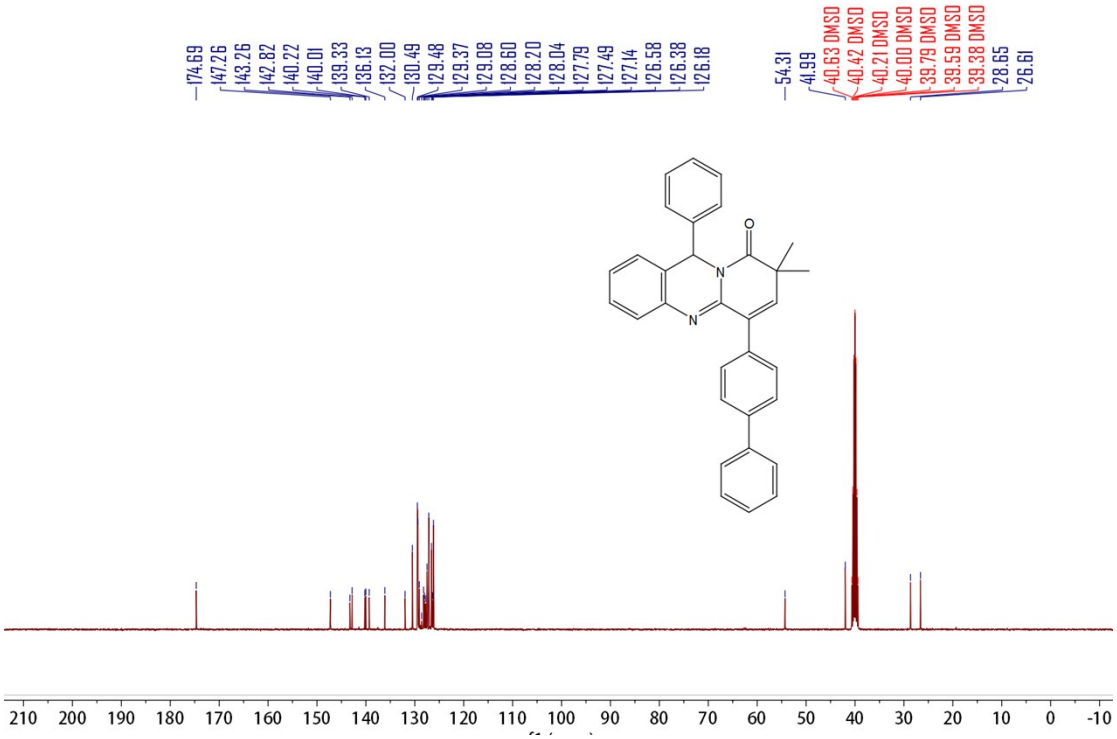
^{1}H NMR Spectrum of Compound **3i**



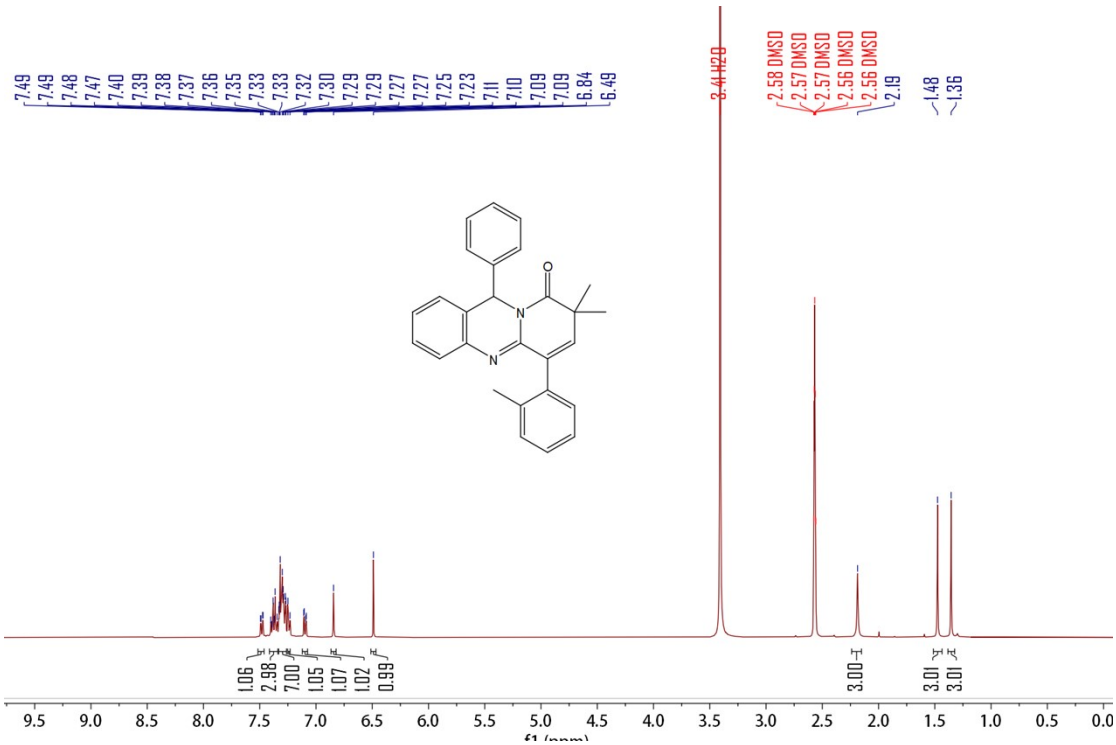
^{13}C NMR Spectrum of Compound **3i**



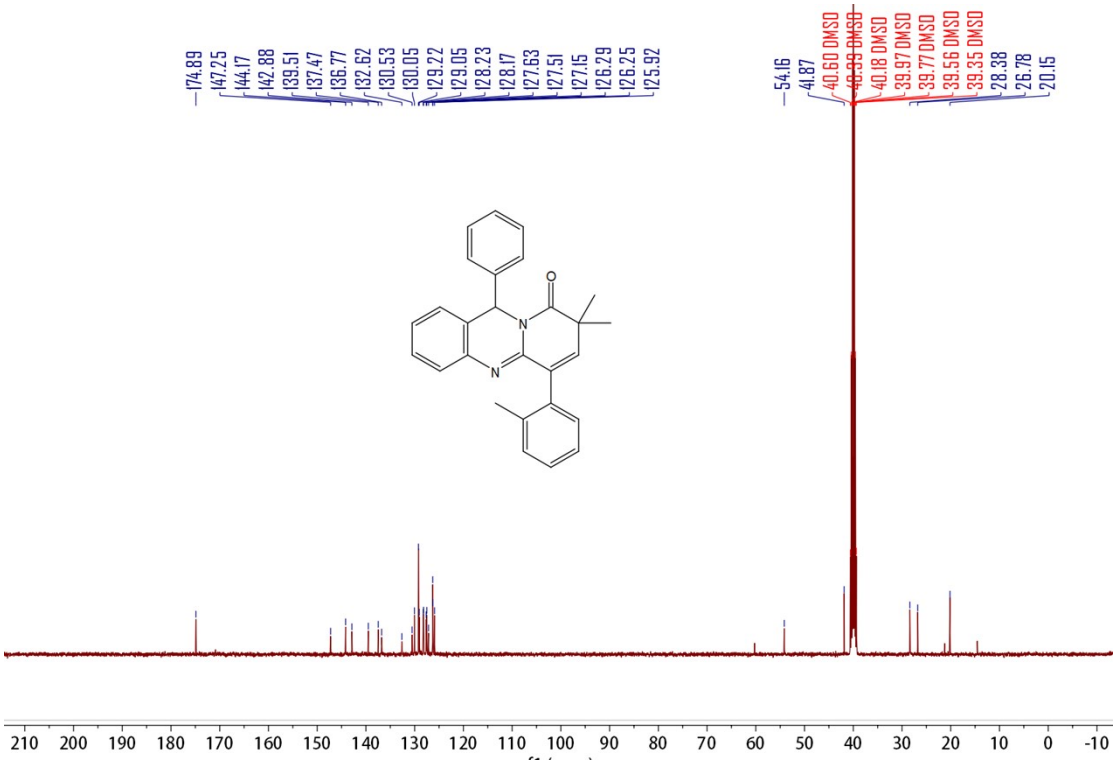
^{1}H NMR Spectrum of Compound **3j**



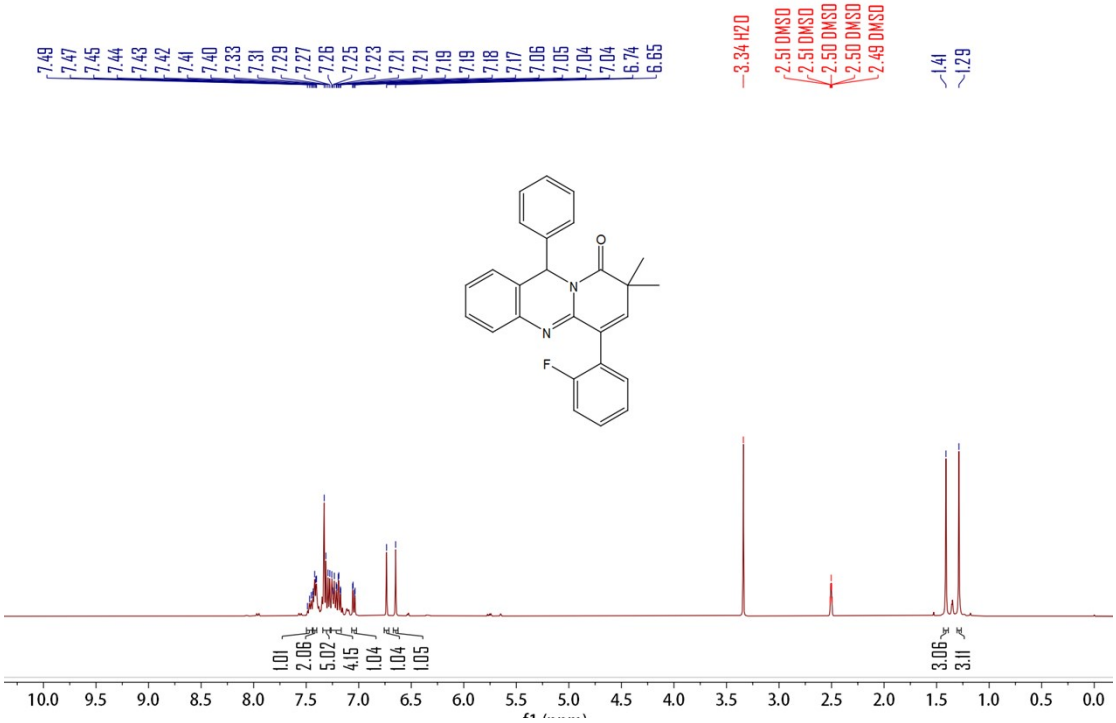
^{13}C NMR Spectrum of Compound **3j**



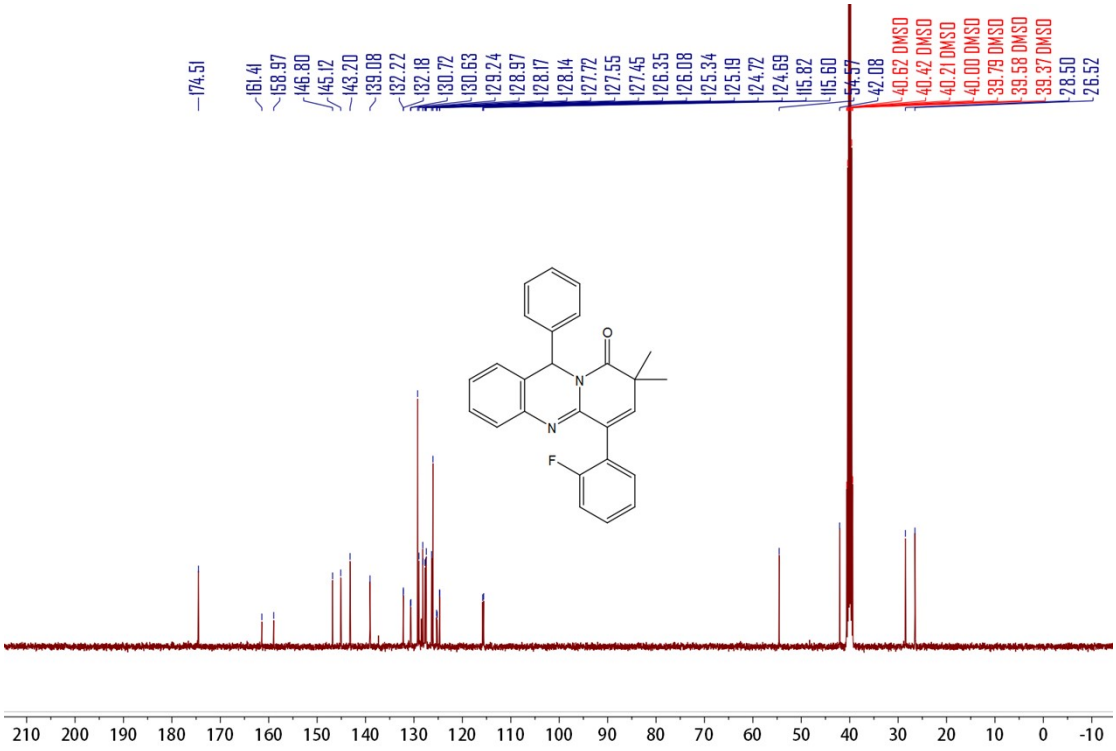
^{1}H NMR Spectrum of Compound **3k**



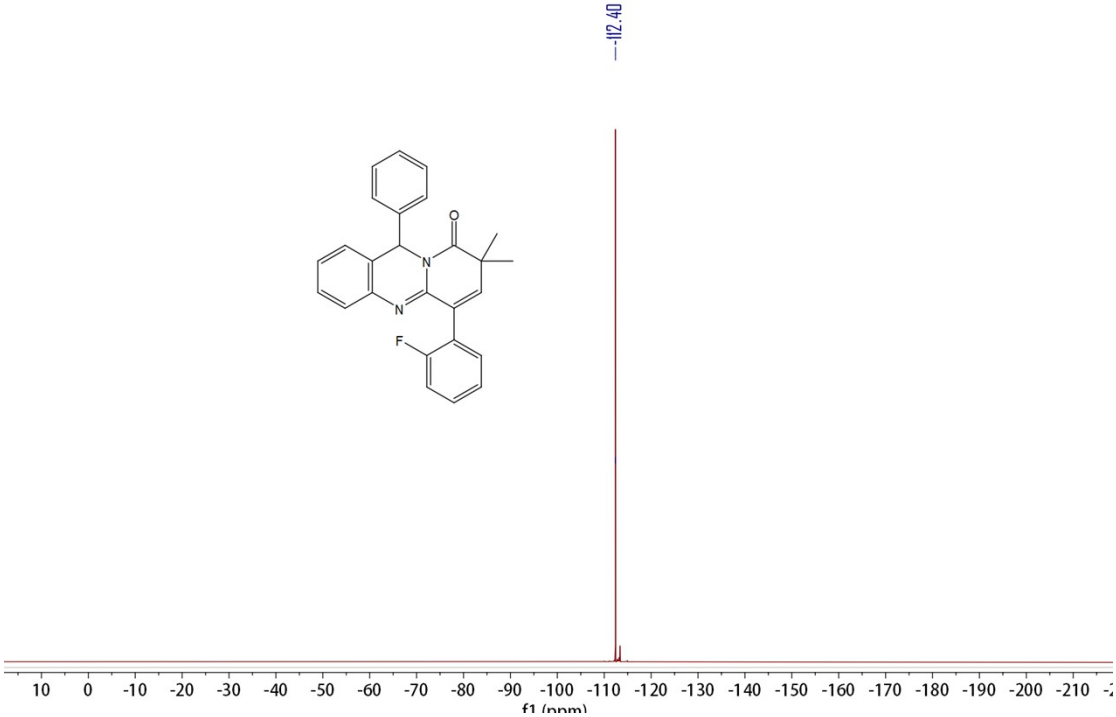
^{13}C NMR Spectrum of Compound **3k**



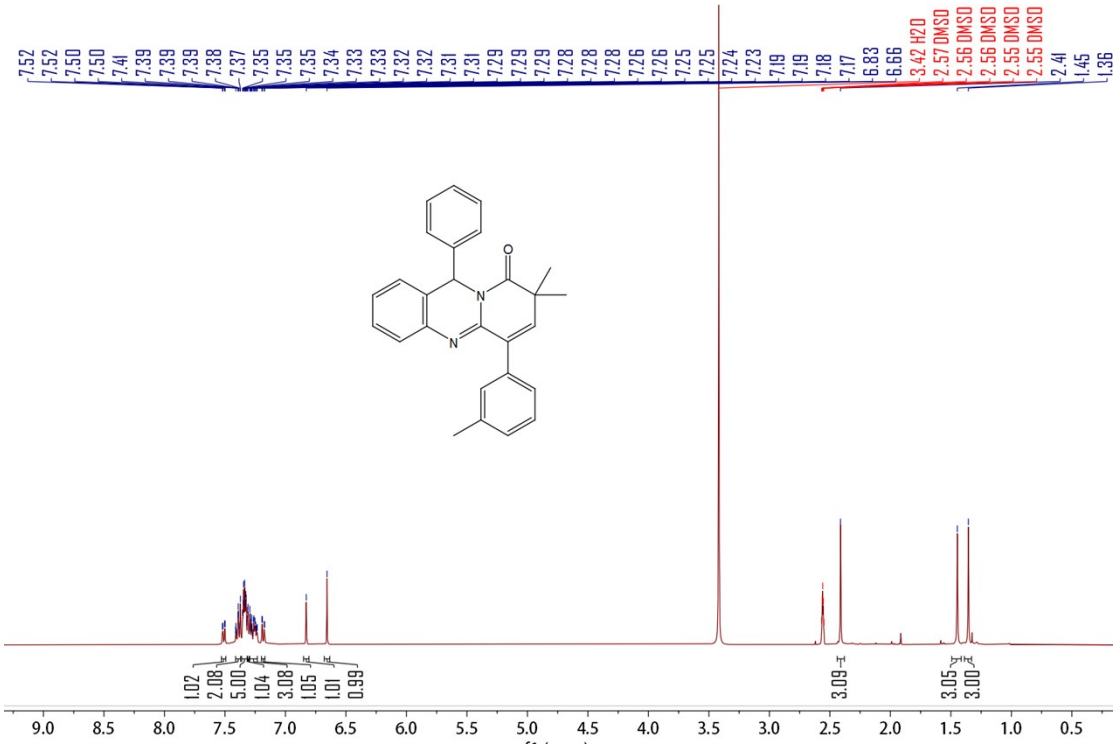
^{1}H NMR Spectrum of Compound **3l**



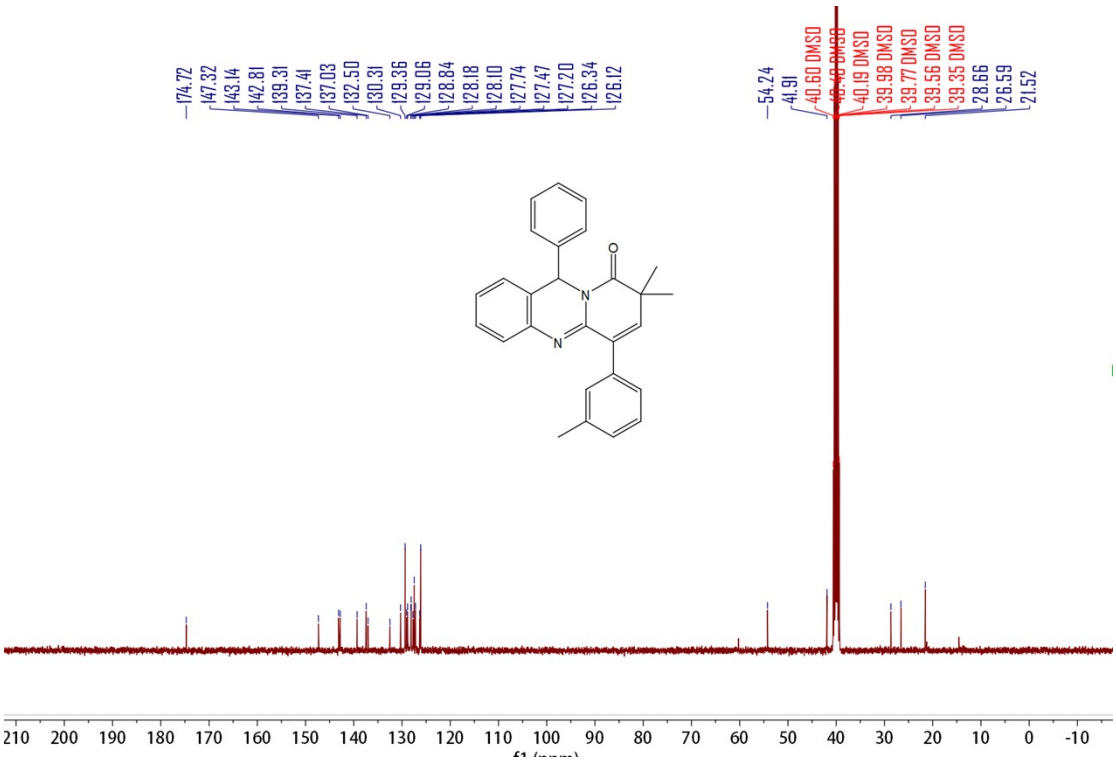
^{13}C NMR Spectrum of Compound **3l**



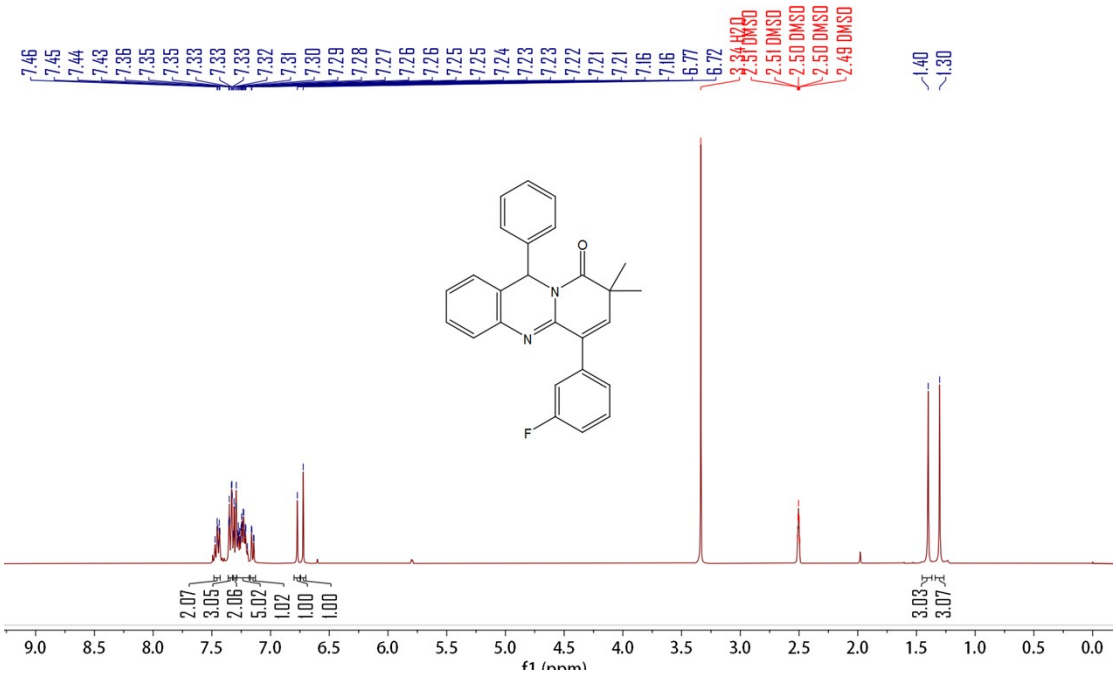
^{19}F NMR Spectrum of Compound **3l**



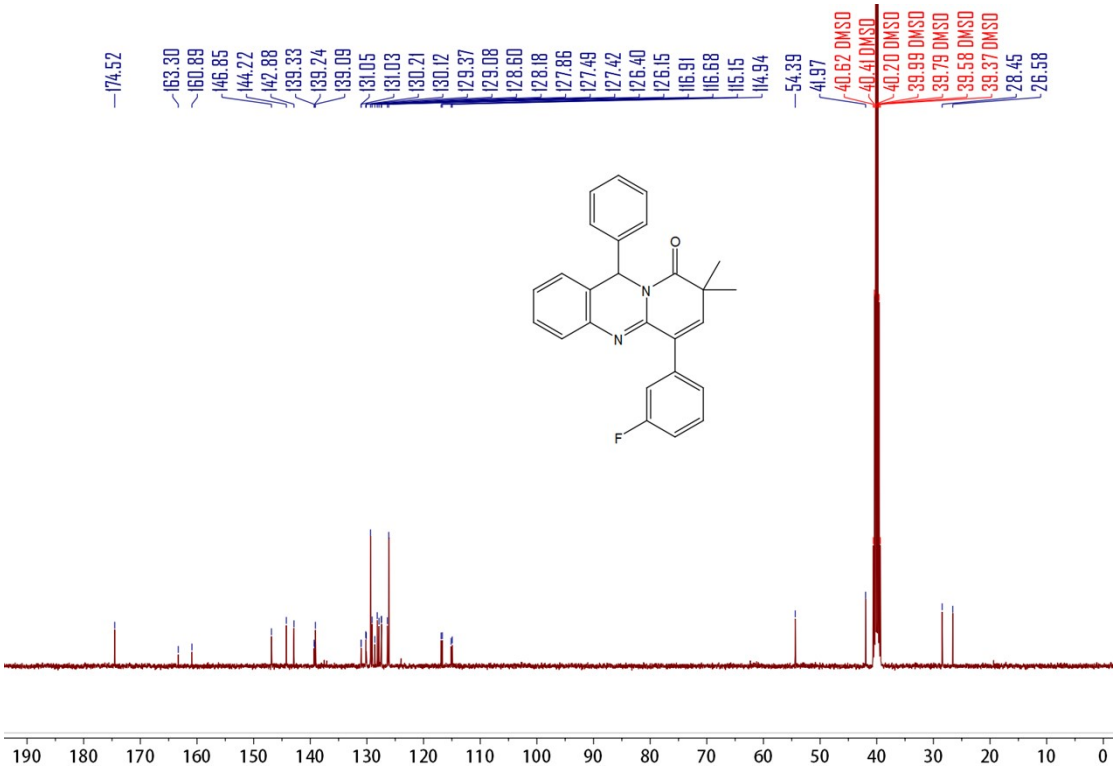
^{1}H NMR Spectrum of Compound **3m**



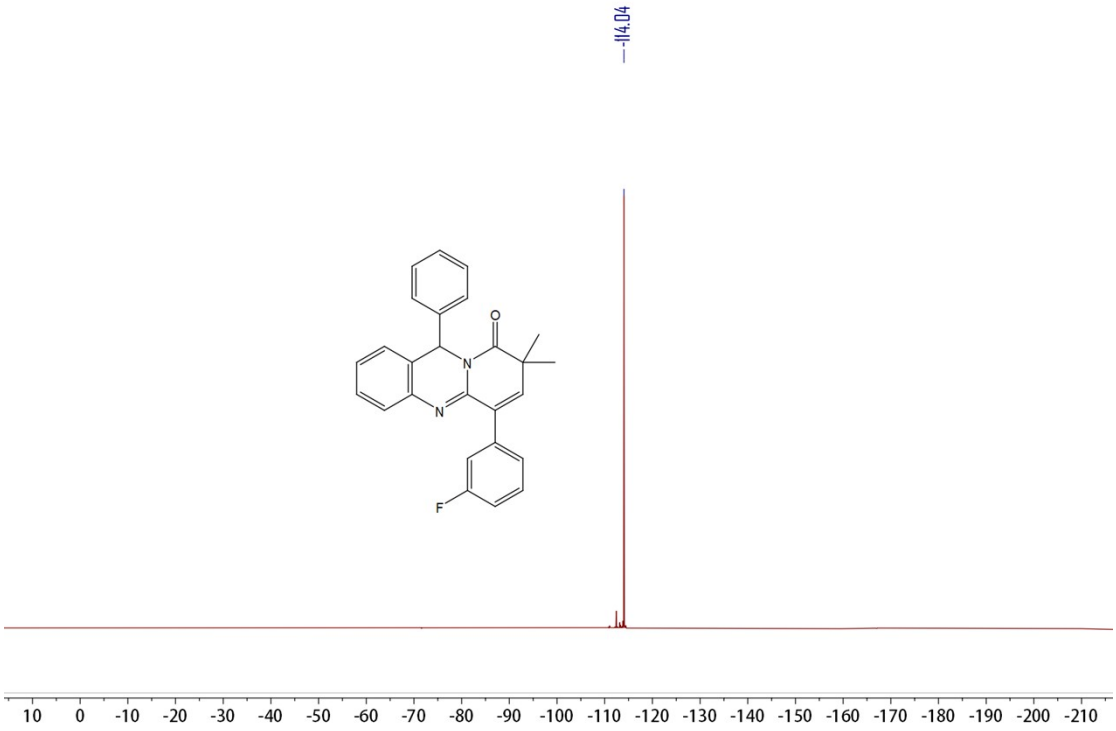
^{13}C NMR Spectrum of Compound **3m**



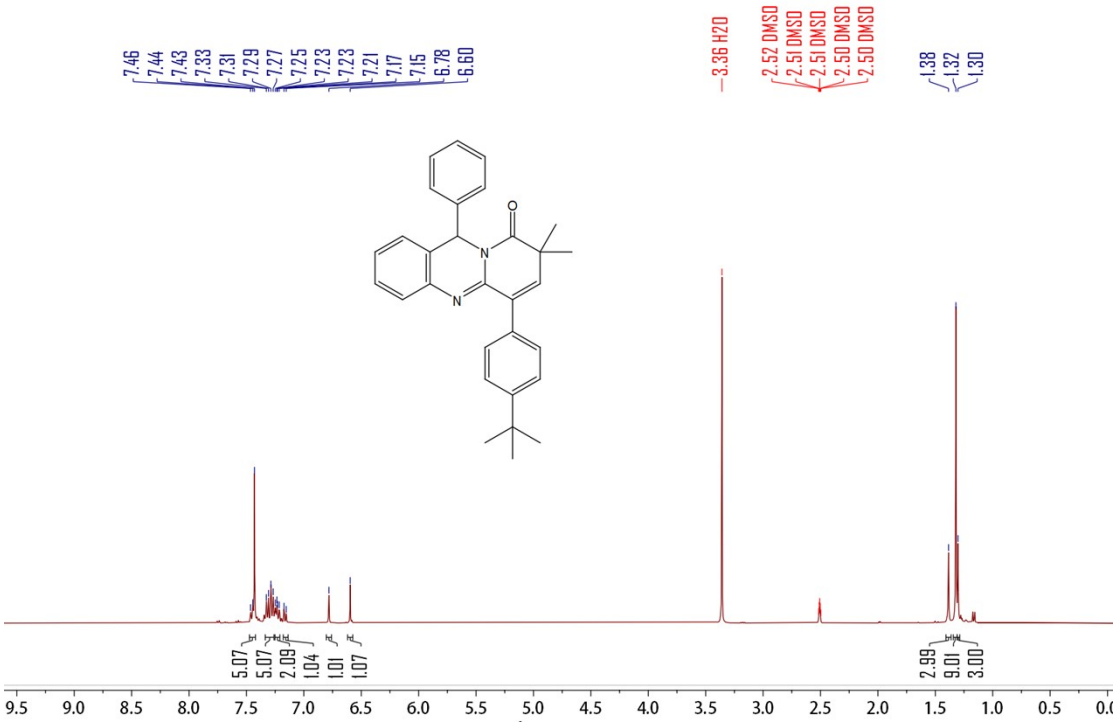
^{1}H NMR Spectrum of Compound **3n**



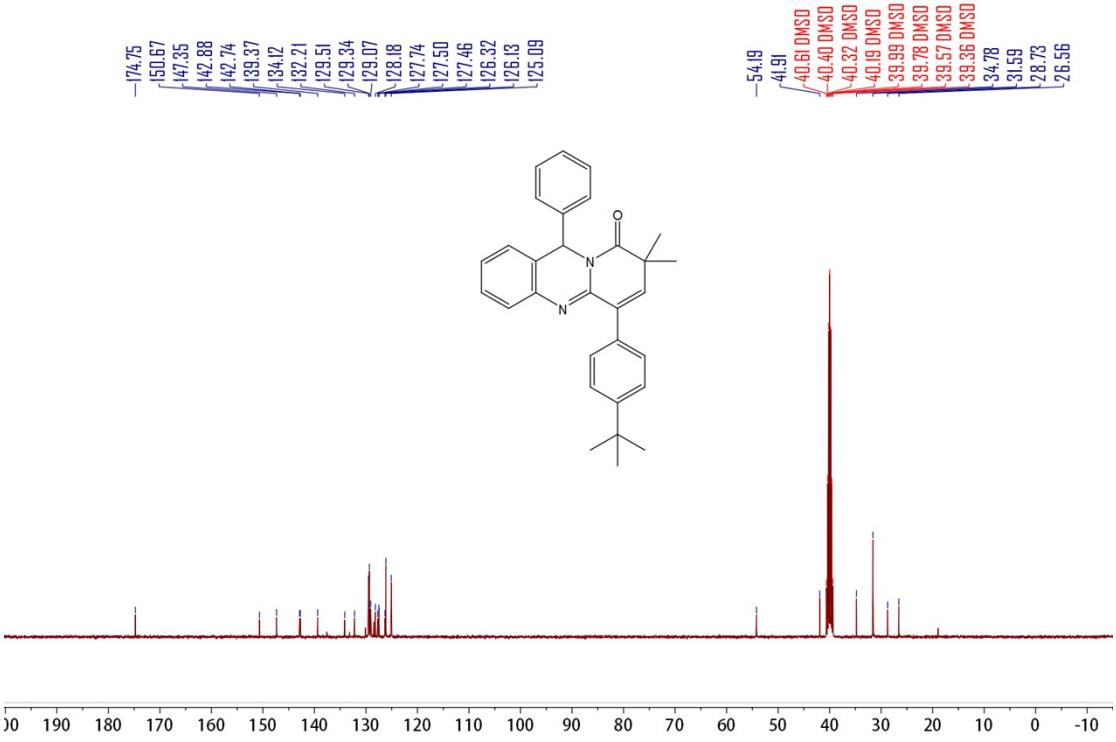
^{13}C NMR Spectrum of Compound **3n**



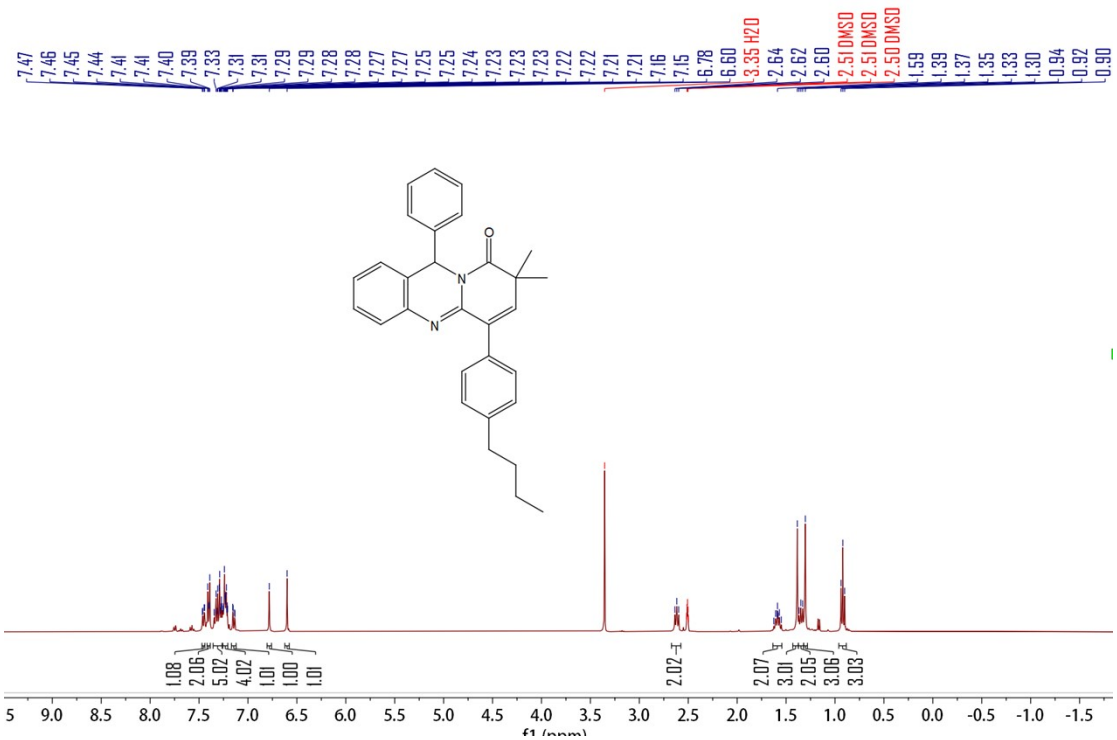
^{19}F NMR Spectrum of Compound **3n**



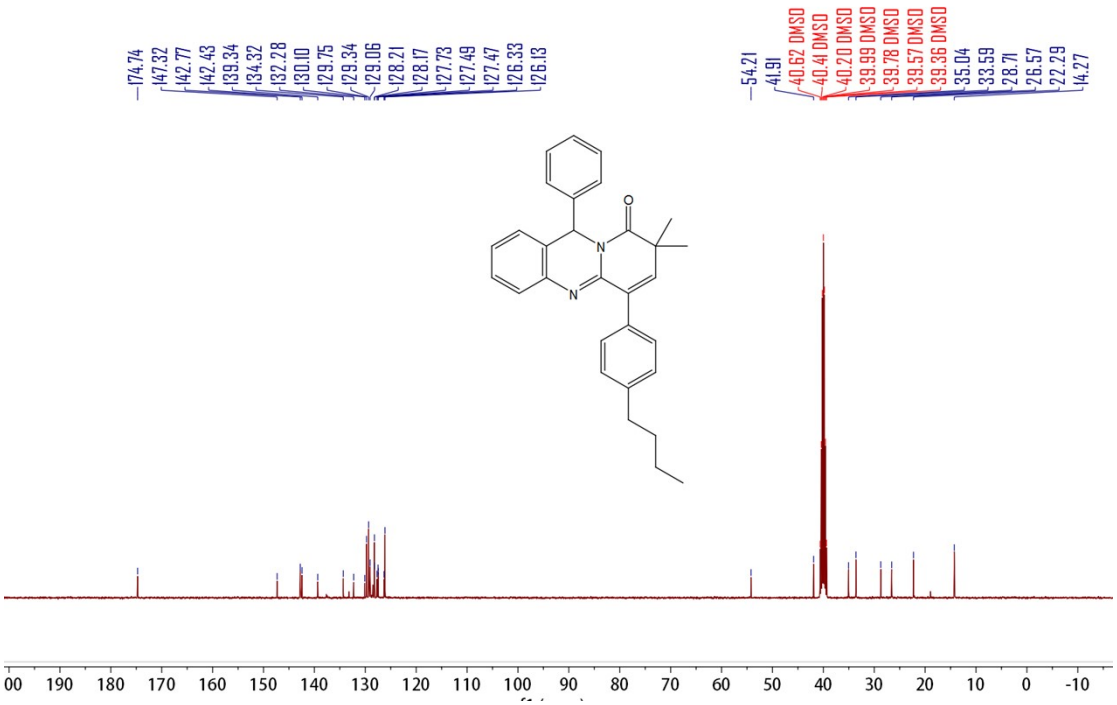
^{1}H NMR Spectrum of Compound **3o**



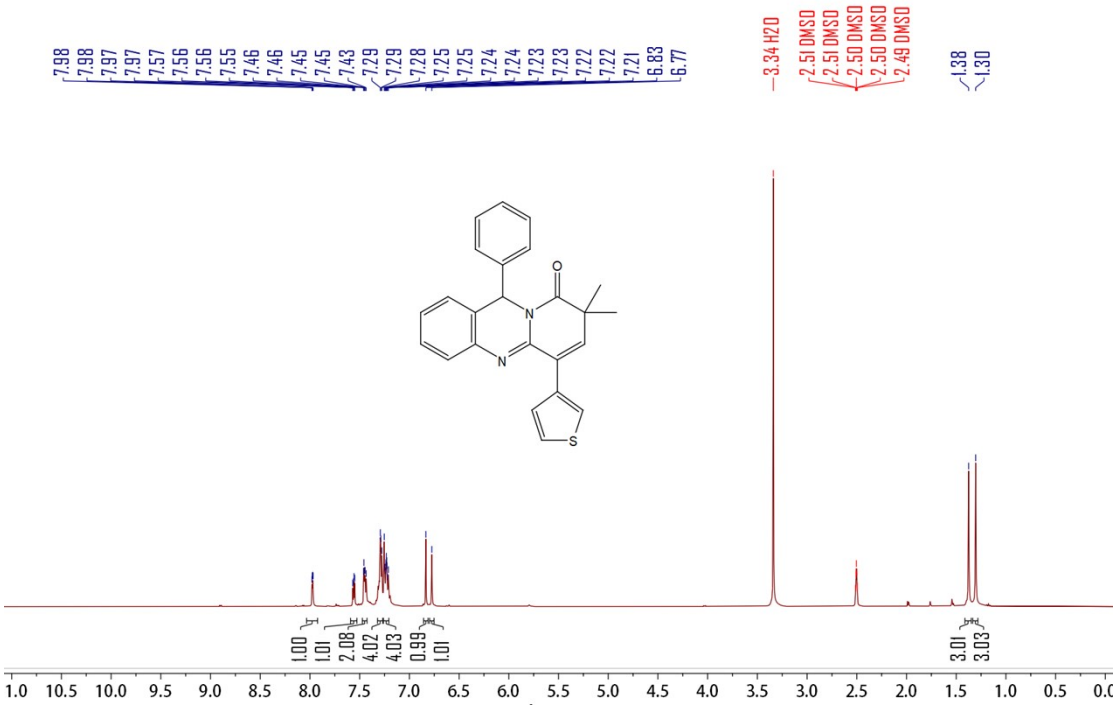
^{13}C NMR Spectrum of Compound **3o**



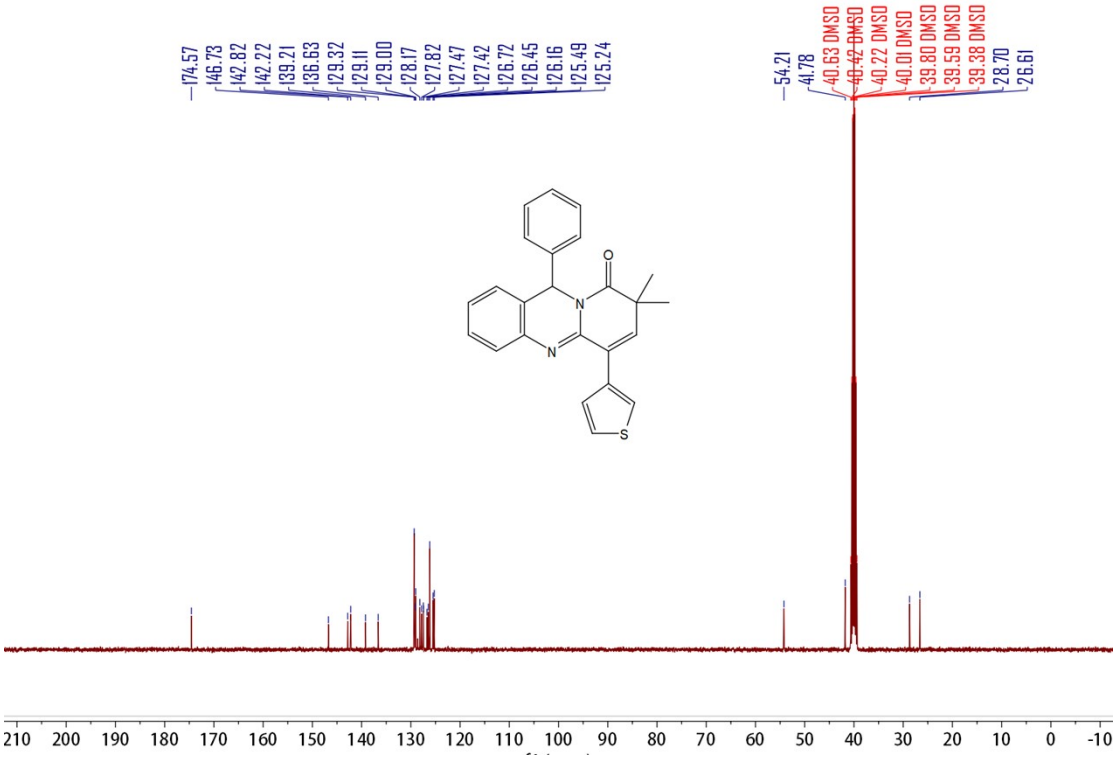
^{1}H NMR Spectrum of Compound **3p**



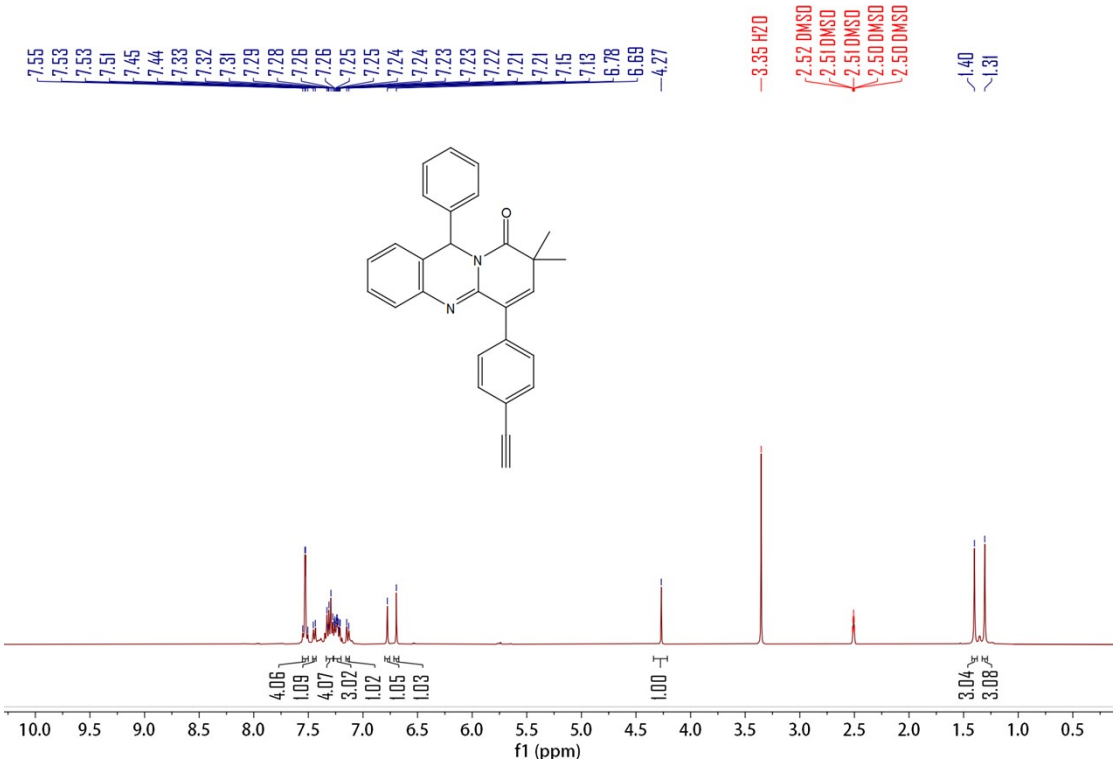
^{13}C NMR Spectrum of Compound **3p**



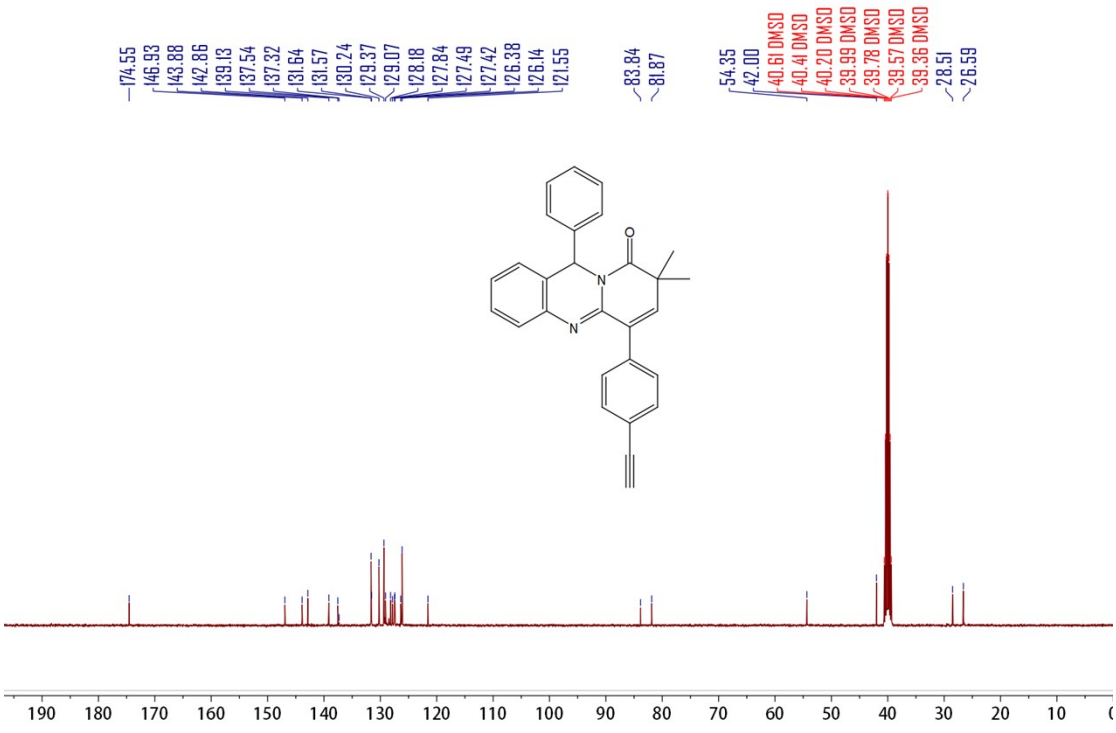
^{1}H NMR Spectrum of Compound **3q**



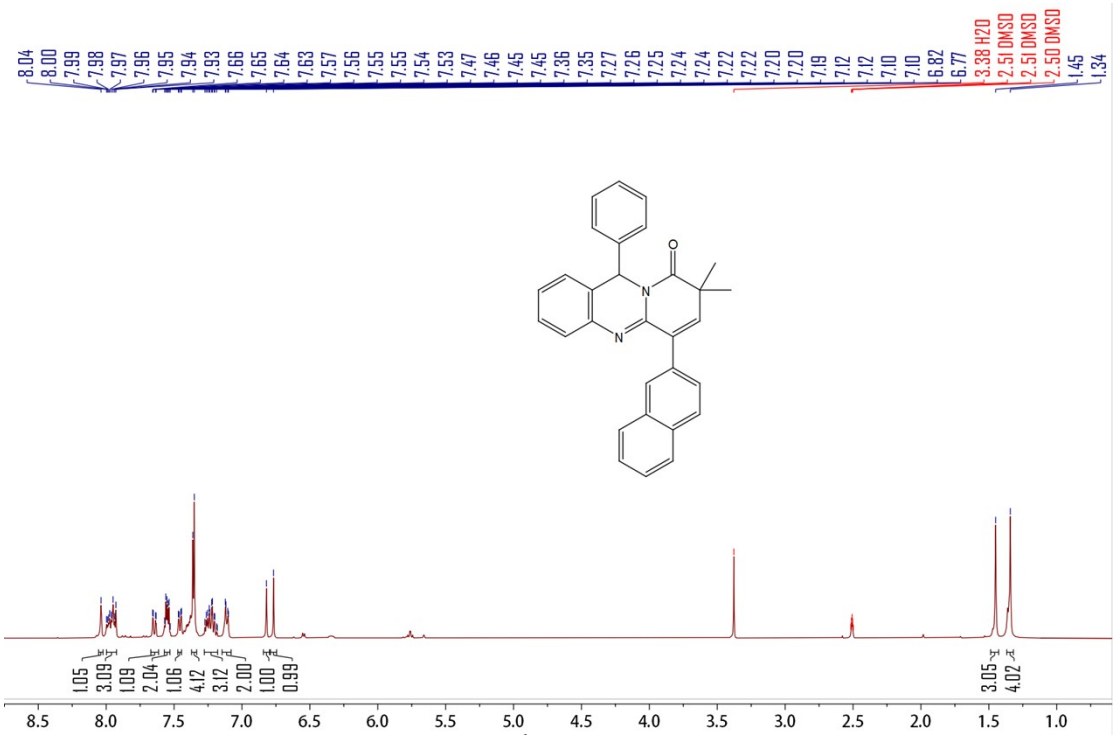
^{13}C NMR Spectrum of Compound **3q**



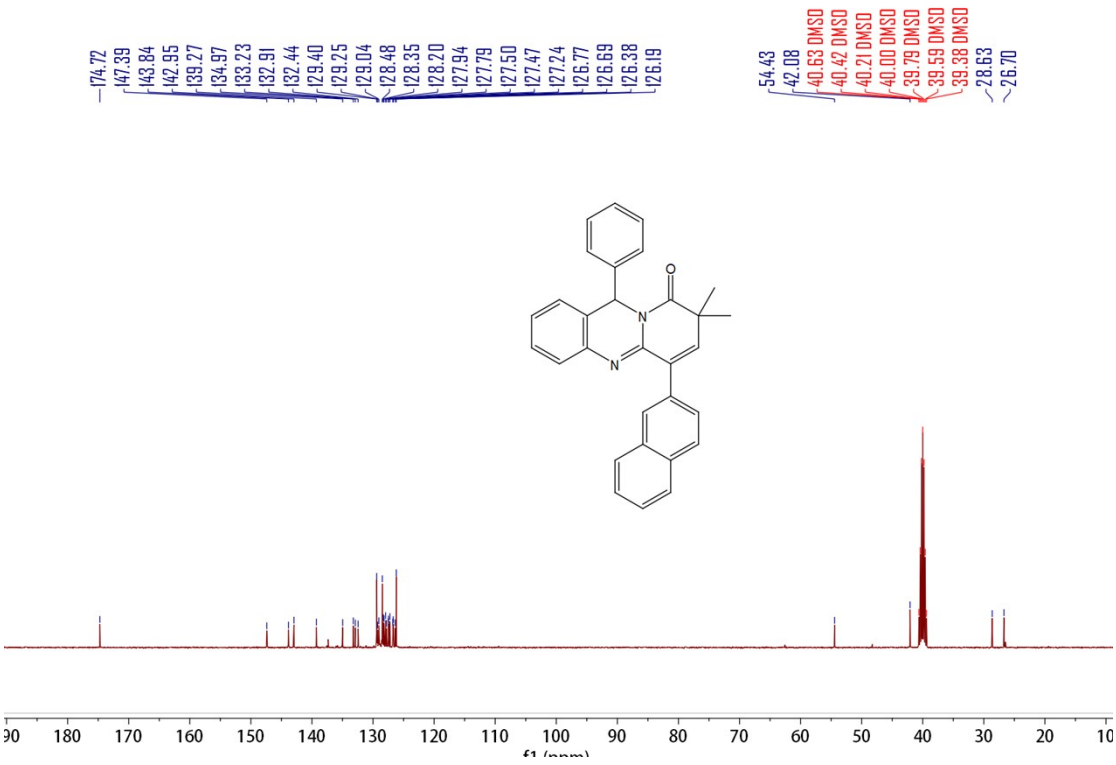
^{1}H NMR Spectrum of Compound **3r**



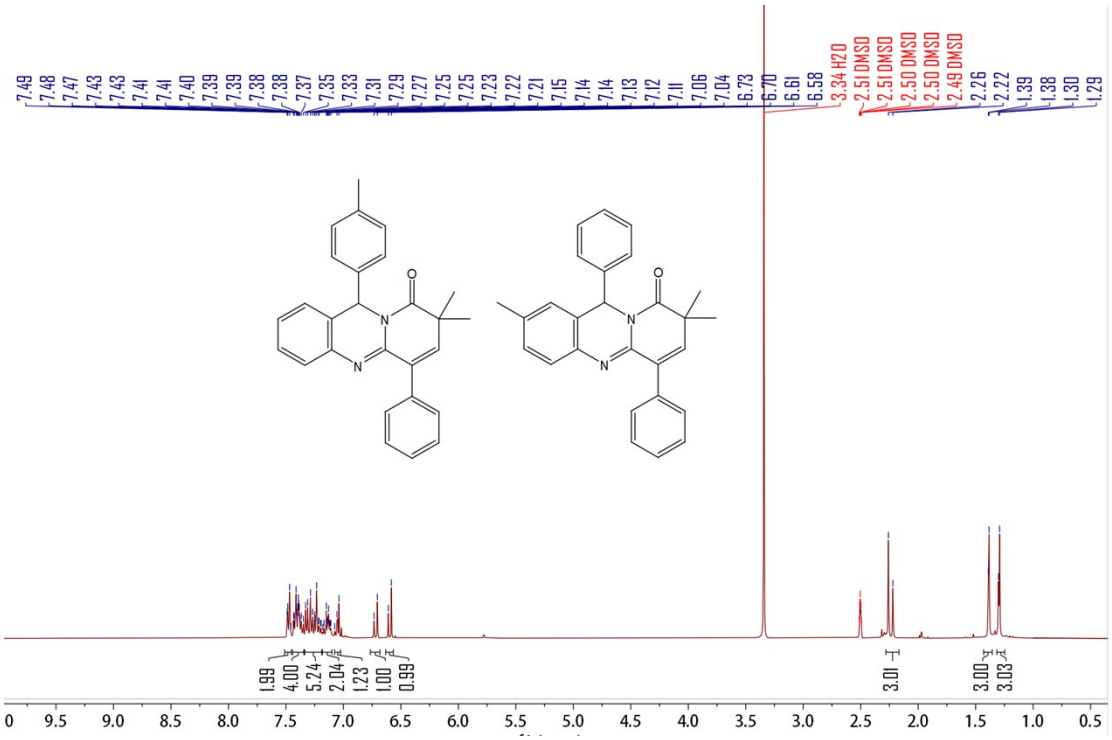
^{13}C NMR Spectrum of Compound **3r**



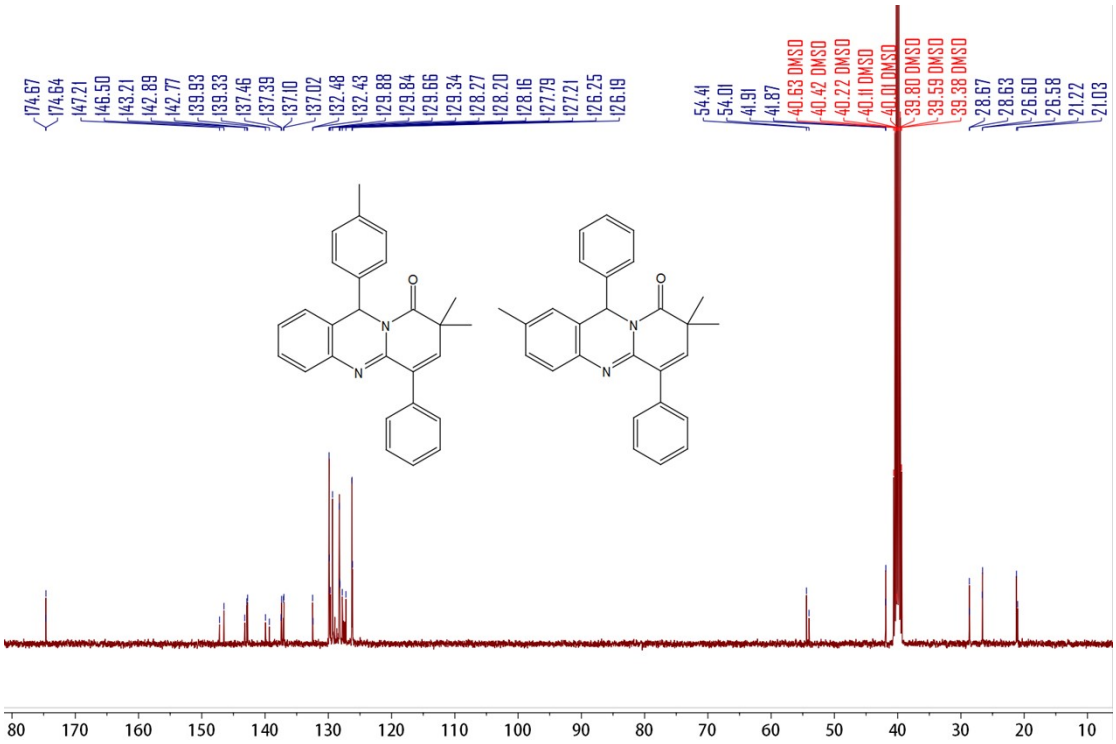
^{1}H NMR Spectrum of Compound **3s**



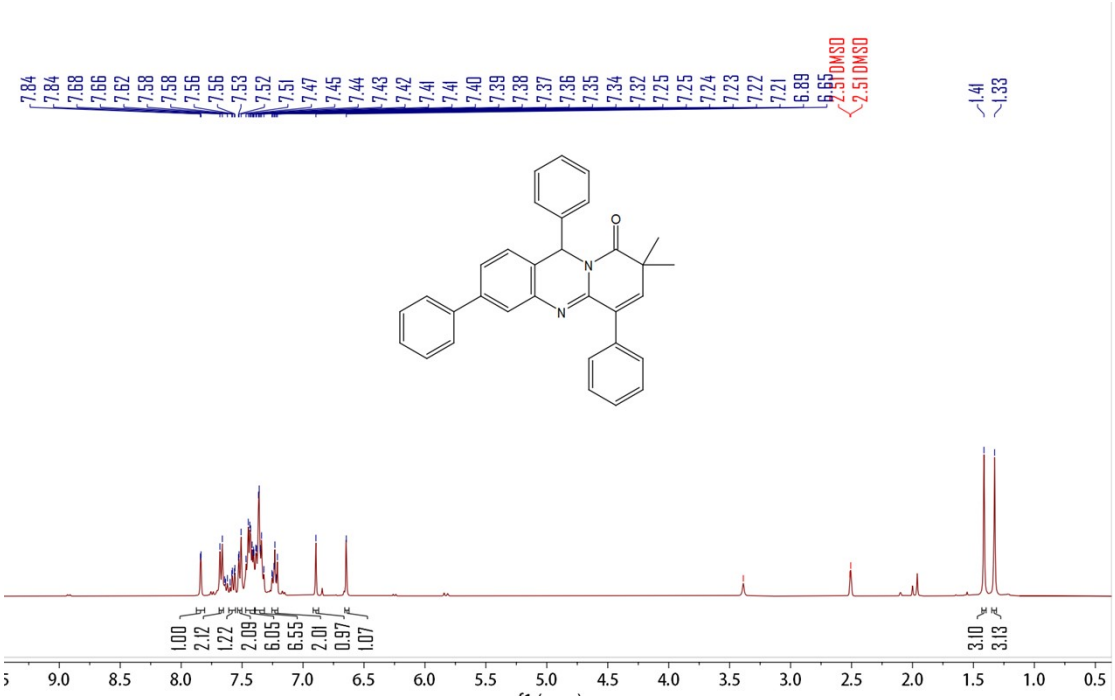
^{13}C NMR Spectrum of Compound **3s**



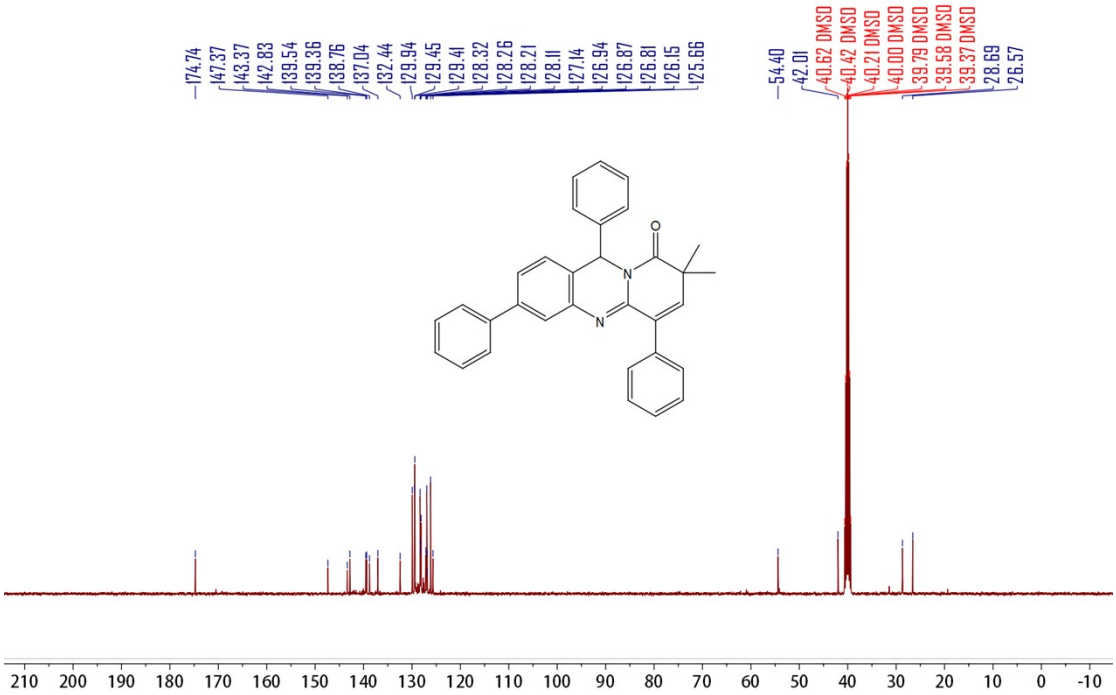
^{1}H NMR Spectrum of Compound **3t**



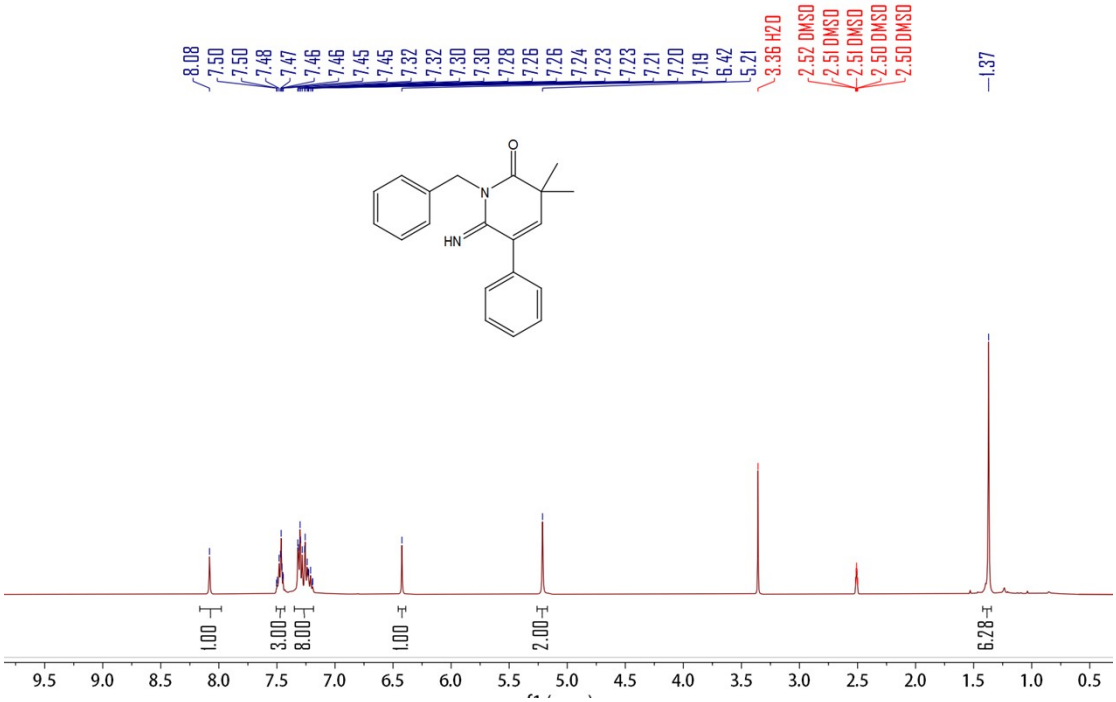
^{13}C NMR Spectrum of Compound **3t**



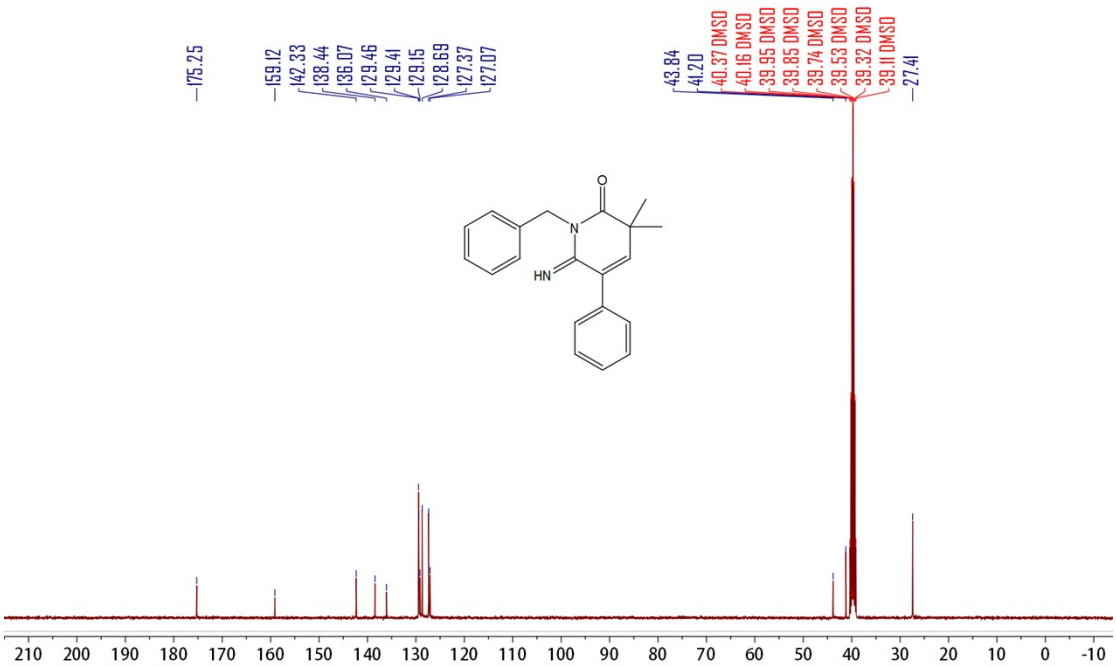
^{1}H NMR Spectrum of Compound **3u**



^{13}C NMR Spectrum of Compound **3u**



^{1}H NMR Spectrum of Compound **3x**



^{13}C NMR Spectrum of Compound **3x**

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.