Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Ni-Catalyzed Cascade Coupling Reactions: Synthesis and thermally-activated delayed fluorescence characterization of quinazolinone derivatives

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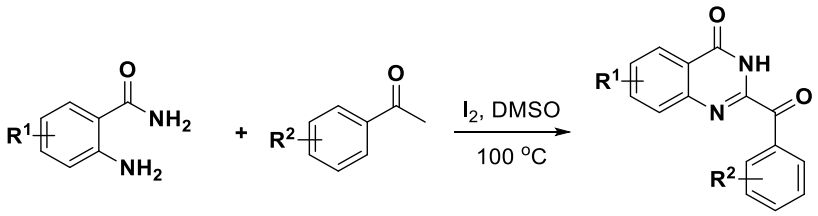
Contents

1 Genral Information

All reagents were commercially available and used without further purification unless otherwise noted. Column chromatography purifications were carried out using 300-400 mesh silica gel with hexanes/ethyl acetate mixture as eluent. Melting points are uncorrected and recorded on Digital Melting Point Apparatus WRS-1B. 1H NMR and 13C NMR spectra were recorded on a 500 MHz spectrometer in solvents as indicated with tetramethylsilane (TMS) as an internal standard at room temperature. Chemical shifts are given in δ relative to TMS, the coupling constants J are given in Hz. Fluorescence spectra were determined by a HITACHI F-7000 fluorometer. Absorption spectra were recorded using a Perkin Elmer Lambda 35 spectrophotometer (USA). The transient photoluminescence decay curves were measured by Edinburgh Instruments.

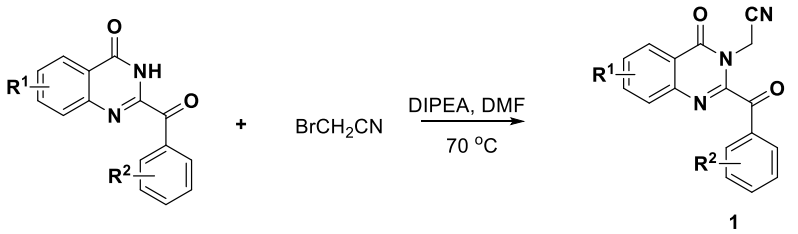
2. Preparation and Characterization of Reaction Substrates



Scheme S1 General procedure for preparation of 2-benzoylquinazolin-4(3H)-one substrates. [1]

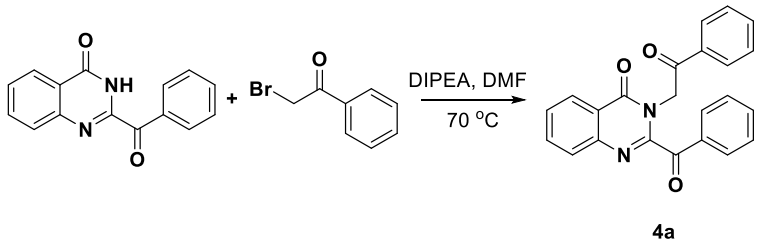
To an oven dried 100 mL Schlenk bottle containing corresponding acetophenone (4 mmol) and I_2 (4.4 mmol) at room temperature, and then DMSO (10 mL) was added. The mixture was stirred at 100 °C. Subsequently, corresponding 2-aminobenzamide (4 mmol) in 6 mL DMSO was added dropwise to the above solution during 2 h. The reaction mixture was kept stirring at 100 °C for 12 h. After disappearance of the reactant (monitored by TLC), the reaction was quenched with saturated aqueous $Na_2S_2O_3$ and the resulting mixture was extracted with CH_2Cl_2 3 times (100 mL ×3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. 2-benzoylquinazolin-4(3H)-one substrates were obtained by column chromatography (silica gel, with a mixture of hexane/ethyl acetate as eluent).

1. L. Long, Y-H. Wang, J-X. Zhuo, Z-C. Tu, R. Wu, M. Yan, Q. Liu, G. Lu. *Eur. J. Med. Chem*. 2018, **157**, 1361-1375.



Scheme S2 General procedure for preparation of 2-benzoylquinazolin-4(3H)-one substrates. [2]

To an oven dried 10 mL Schlenk-tube, 2-benzoylquinazolin-4(3H)-one substrates (3 mmol), bromoacetonitrile (9 mmol), and DIPEA (7.5 mmol) were dissolved in 3 mL DMF. The mixture was heated at 70 °C for 12 h. After disappearance of the reactant (monitored by TLC), the reaction was quenched with water and the resulting mixture was extracted with ethyl acetate 3 times (30 mL ×3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. Corresponding products **1** were obtained by column chromatography (silica gel, with a mixture of hexane/ethyl acetate as eluent).

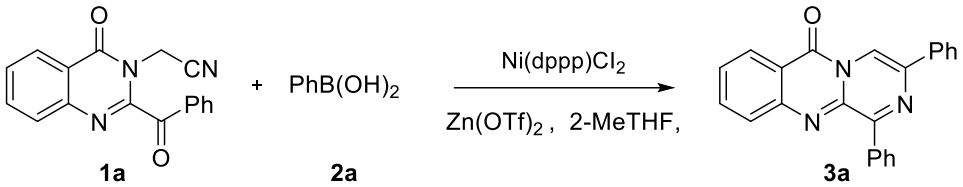


Scheme S3 preparation of 2-benzoyl-3-(2-oxo-2-phenylethyl)quinazolin-4(3H)-one

3. Optimization of Reaction Conditions

Table S1 Optimization of Reaction Conditions[a]:

2. S. N. Kulik, A. S. Kobko, A. A. Tolmachev, A. V. Tverdokhlebov, O. V. Shishkin, A. N. Chernega. *Synthesis* 2007, **10**, 1503-1508.

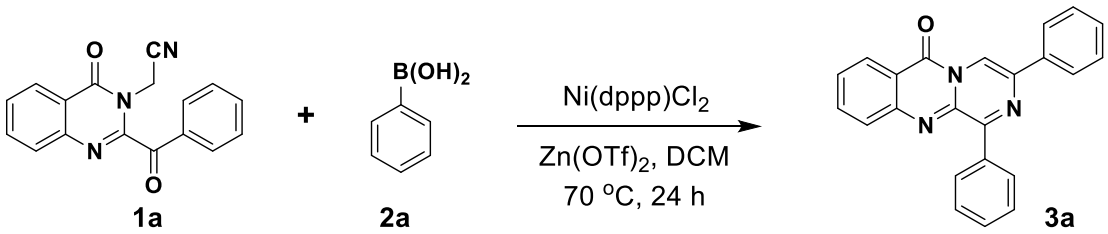


1a 2a 3a

Entry	Atmosphere	Yeild (%)[b]
1	Air	70
2	N_2	72
3	O_2	13

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), Ni catalyst (10 mmol%), $Zn(OTf)_2$ (2.0 equiv.), 2-MeTHF (1 mL), 90 °C, 24 h.
[b] Isolated yield.

4. Preparation and Characterization of 3 (3a as an example)

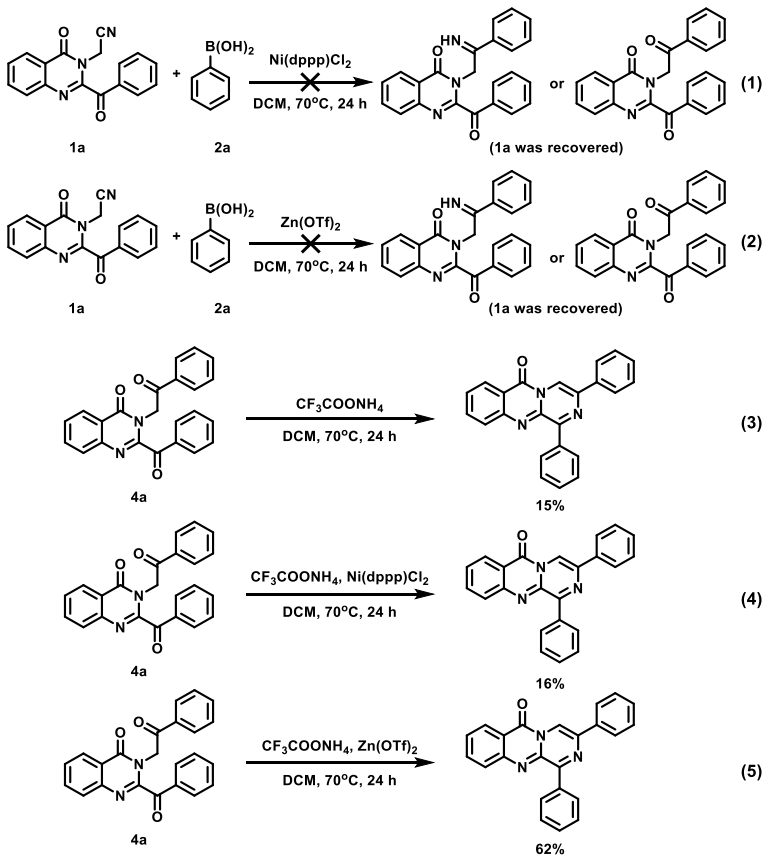


1a 2a 3a

Scheme S4 Synthesis of **3a**.

To a 10 mL Schlenk-tube, 2-(2-benzoyl-4-oxoquinazolin-3(4H)-yl) acetonitrile **1a** (0.2 mmol), phenylboronic acid **2a** (0.4 mmol) in the presence of $Ni(dppp)Cl_2$ (5 mol%), $Zn(OTf)_2$ (3 eq) in CH_2Cl_2 (1 mL) at room temperature or 70 °C for 24 h. The reaction was quenched with saturated aqueous $NaHCO_3$ and the resulting mixture was extracted with CH_2Cl_2 3 times (10 mL ×3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. Corresponding products **3a** were obtained by column chromatography (silica gel, with a mixture of hexane/CH_2Cl_2 as eluent).

5. Mechanistic studies



Scheme S5 Control experiments

6. Photophysical propeties

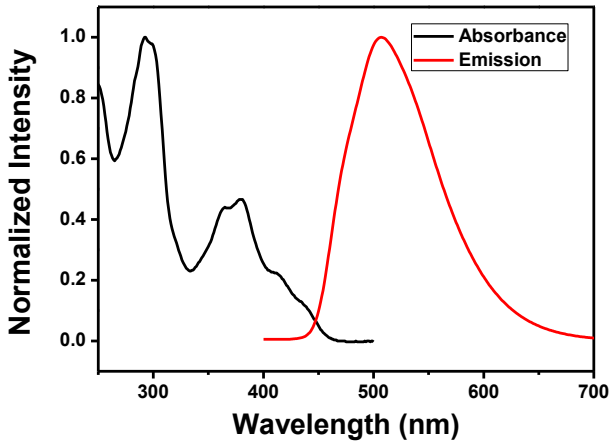


Fig. S1 Normalized absorption (black) and fluorescence emission spectra (red) of **3a** in THF. Concentration: 10 μM, Excitation= 380 nm.

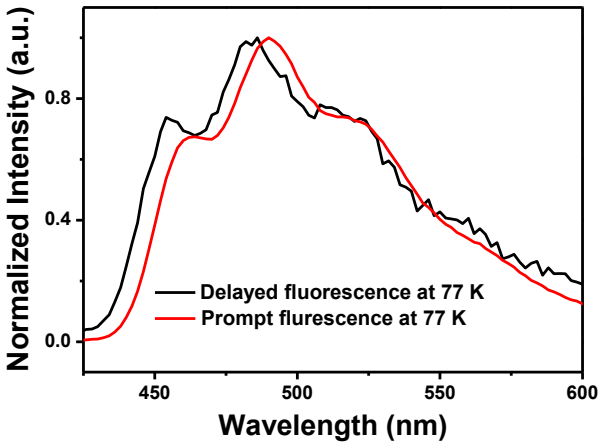


Fig. S2 Normalized delayed fluorescence (10 μs delay) and prompt fluorescence spectra of **3a** in 2-MeTHF at 77 K. Concentration: 10 μM, Excitation= 380 nm.

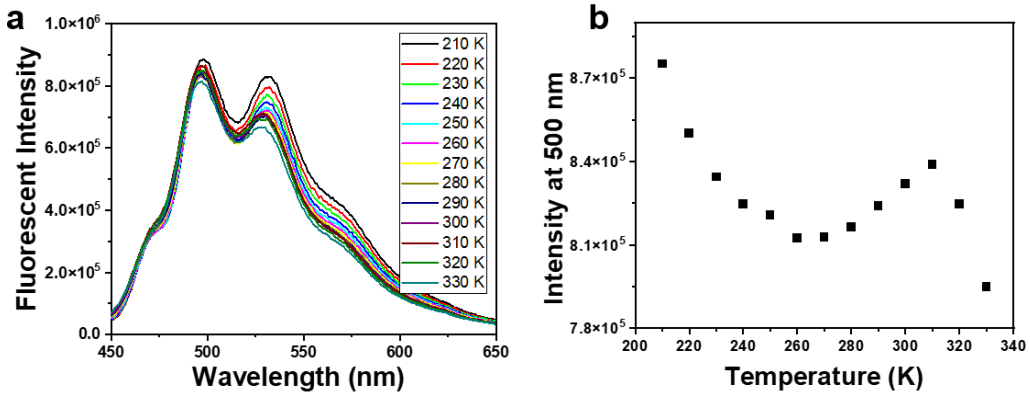


Fig. S3 (a)Temperature-responsive emission spectra of **3a** from 210 K to 330 K, Excitation= 380 nm; A correlation between the temperature and intensity of emission at 500 nm.

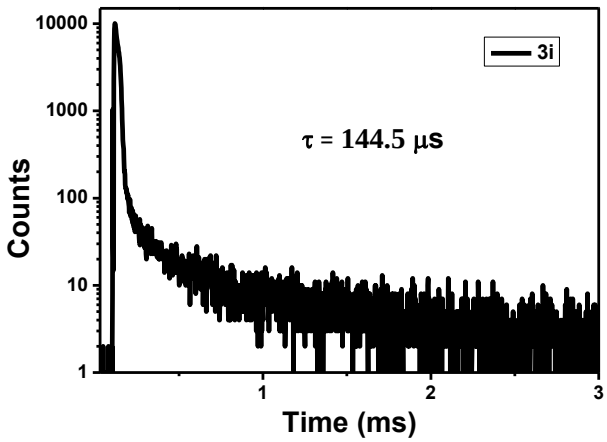
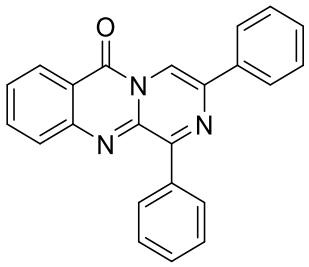
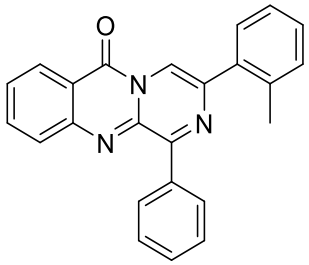


Fig. S4 Transient fluorescence decay of **3i** at room temperature. Excited at 380 nm and monitored at 500 nm.

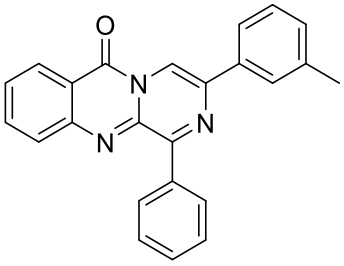
7. NMR Spectra of Compounds



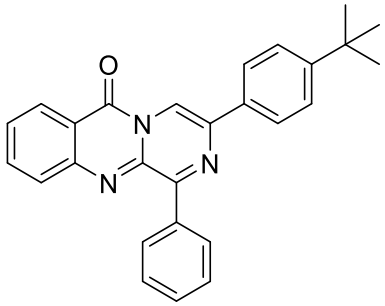
1,3-diphenyl-6H-pyrazino[2,1-b]quinazolin-6-one (3a): Yellow solid (61.4 mg, 88%), mp:248-249 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.02 (s, 1H), 8.52-8.49 (m, 1H), 8.45-8.43 (m, 2H), 8.13-8.11 (m, 2H), 7.91-7.86 (m, 2H), 7.62-7.50 (m, 6H), 7.43 (t, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.4, 158.3, 147.3, 139.0, 137.1, 136.4, 135.5, 135.1, 131.0, 130.6, 129.1, 129.0, 128.7, 127.9, 127.3, 126.0, 117.4, 111.2. HRMS calcd for $C_{23}H_{16}N_3O$ $[M + H]^+$: 350.1288, found 350.1292.



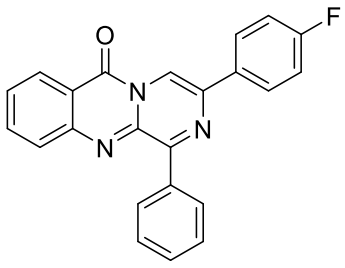
1-phenyl-3-(o-tolyl)-6H-pyrazino[2,1-b]quinazolin-6-one (3b): Yellow solid (62.4 mg, 86%), mp:137-138 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.73 (s, 1H), 8.52-8.50 (m, 1H), 8.39-8.38 (m, 2H), 7.96-7.89 (m, 2H), 7.64-7.59 (m, 2H), 7.55-7.53 (m, 3H), 7.39-7.32 (m, 3H), 2.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.4, 158.0, 147.5, 139.4, 138.8, 136.8, 136.3, 136.0, 135.1, 131.2, 130.9, 130.5, 129.8, 129.0, 128.7, 127.9, 127.3, 127.2, 126.2, 117.6, 114.3, 20.9. HRMS calcd for $C_{24}H_{18}N_3O$ $[M+H]^+$: 364.1444, found 364.1441.



1-phenyl-3-(m-tolyl)-6H-pyrazino[2,1-b]quinazolin-6-one (3c): Yellow solid (62.4 mg, 86%), mp:246-247 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.01 (s, 1H), 8.52-8.50 (m, 1H), 8.44-8.42 (m, 2H), 7.90-7.86 (m, 4H), 7.62-7.57 (m, 4H), 7.40 (t, J = 7.5 Hz, 1H), 7.24 (d, J = 7.5 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.4, 158.3, 147.4, 139.0, 138.7, 137.3, 136.4, 135.4, 135.1, 131.0, 130.5, 129.9, 128.9, 128.7, 127.9, 127.3, 126.7, 123.2, 117.4, 111.1, 21.6. HRMS calcd for $C_{24}H_{18}N_3O$ $[M+H]^+$: 364.1444, found 364.1447.

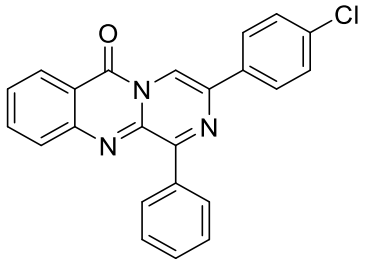


3-(4-(tert-butyl)phenyl)-1-phenyl-6H-pyrazino[2,1-b]quinazolin-6-one (3d): Yellow solid (62.4 mg, 77%), mp:232-233 ºC.^{1}H NMR (400 MHz, $CDCl_3$): δ 9.01 (d, J = 1.6 Hz, 1H), 8.51 (d, J = 8.0 Hz, 1H), 8.45-8.43 (m, 2H), 8.06 (d, J = 6.8 Hz, 2H), 7.94-7.86 (m, 2H), 7.62-7.54 (m, 6H), 1.39 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.4, 158.2, 152.4, 147.4, 139.0, 137.3, 136.5, 135.0, 132.8, 131.0, 130.5, 128. 7, 127.9, 127.2, 126.0, 125.9, 117.4, 110.7, 34.8, 31.3. HRMS calcd for $C_{27}H_{24}N_3O$ $[M+H]^+$: 406.1914, found 406.1907.

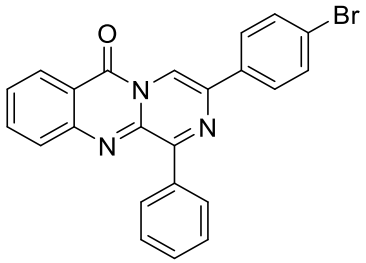


3-(4-fluorophenyl)-1-phenyl-6H-pyrazino[2,1-b]quinazolin-6-one (3e): Yellow solid (61.7 mg, 84%), mp:260-261 ºC.^{1}H NMR (400 MHz, $CDCl_3$): δ 8.98 (s, 1H), 8.51 (d, J = 7.6 Hz, 1H), 8.42-8.41 (m, 2H), 8.12-8.10 (m, 2H), 7.95-7.89 (m, 2H), 7.64-7.58 (m, 4H), 7.22-7.19 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6 (d, $J_{c\text{-}f}$=248.8 Hz), 158.7, 158.5, 147.5, 139.1, 136.5, 135.3, 131.9, 131.8, 131.1, 130.8, 128.9, 128.1, 128.0, 127.5, 127.4, 117.6, 116.1 (d, $J_{c\text{-}f}$=21.3 Hz), 111.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ -

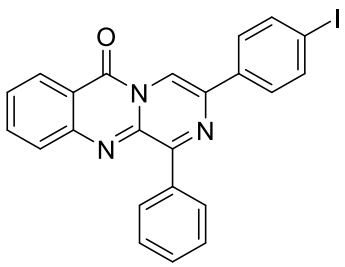
112.36- -112.44 (m, 1F). HRMS calcd for $C_{23}H_{14}FN_3NaO$ $[M+Na]^+$: 390.1013, found 390.1023.



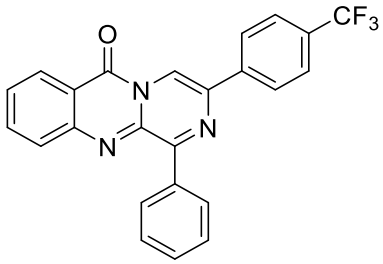
3-(4-chlorophenyl)-1-phenyl-6H-pyrazino[2,1-b]quinazolin-6-one (3f): Yellow solid (69.7 mg, 91%), mp:284-285 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.03 (s, 1H), 8.52 (d, J = 8.0 Hz, 1H), 8.42 (d, J = 5.5 Hz, 2H), 8.08 (d, J = 8.5 Hz, 2H), 7.95-7.91 (m, 2H), 7.61-7.55 (m, 4H), 7.49 (d, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.8, 158.5, 147.5, 139.1, 136.4, 136.2, 135.4, 135.3, 134.2, 131.1, 130.8, 129.3, 128.9, 128.1, 127.6, 127.4, 117.6, 111.4. HRMS calcd for $C_{23}H_{15}ClN_3O$ $[M+H]^+$: 384.0898, found 384.0886.



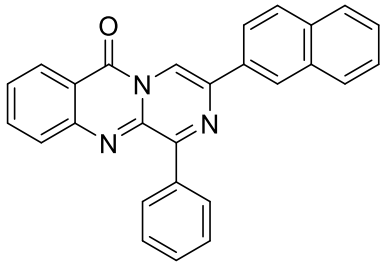
3-(4-bromophenyl)-1-phenyl-6H-pyrazino[2,1-b]quinazolin-6-one (3g): Yellow solid (77.7 mg, 91%), mp:257-258 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.02 (s, 1H), 8.51 (d, J = 8.2 Hz, 1H), 8.42-8.40 (m, 2H), 8.00 (d, J = 8.2 Hz, 2H), 7.95-7.88 (m, 2H), 7.65-7.63 (m, 3H), 7.58-7.57 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.8, 158.5, 147.5, 139.1, 136.4, 136.2, 135.4, 134.7, 132.3, 131.1, 130.8, 128.9, 128.1, 127.7, 127.6, 127.5, 123.5, 117.6, 111.4. HRMS calcd for $C_{23}H_{15}BrN_3O$ $[M+H]^+$: 428.0393, found 428.0386.



3-(4-iodophenyl)-1-phenyl-6H-pyrazino[2,1-b]quinazolin-6-one (3h): Yellow solid (87.4 mg, 92%), mp:256-257 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.04 (s, 1H), 8.51 (d, J = 7.6 Hz, 1H), 8.42-8.40 (m, 2H), 7.95-7.83 (m, 6H), 7.65-7.57 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.6, 158.3, 147.3, 138.9, 138.1, 136.2, 136.1, 135.3, 135.1, 131.0, 130.7, 128.8, 128.0, 127.7, 127.5, 127.3, 117.4, 111.3, 95.2. HRMS calcd for $C_{23}H_{15}IN_3O$ $[M+H]^+$: 476.0254, found 476.0258.

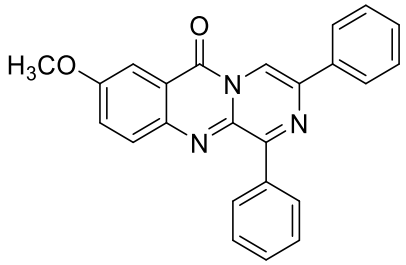


1-phenyl-3-(4-(trifluoromethyl)phenyl)-6H-pyrazino[2,1-b]quinazolin-6-one (3i): Yellow solid (61.7 mg 74%), mp:184-185 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.07 (s, 1H), 8.50 (d, J = 8.0 Hz, 1H), 8.44-8.41 (m, 2H), 8.23 (d, J = 8.0 Hz, 2H), 7.95-7.88 (m, 2H), 7.76 (d, J = 8.4 Hz, 2H), 7.64-7.57 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.7, 158.3, 147.2, 139.0, 138.9, 136.1, 135.5, 135.3, 131.0, 130.8, 128. 8, 128.0, 127.5 (d, $J_{C\text{-}F}$ = 35.0 Hz), 126.2, 125.9(q, $J_{C\text{-}F}$ = 3.8 Hz), 124.1(d, $J_{C\text{-}F}$ = 270.0 Hz), 117.5, 112.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.59 (s, 3F). HRMS calcd for $C_{24}H_{15}F_3N_3O$ $[M+H]^+$: 418.1162, found 418.1163.

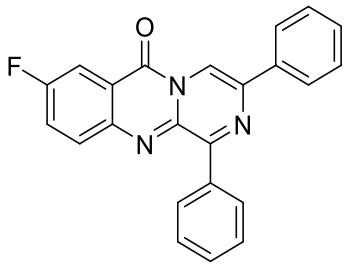


3-(naphthalen-2-yl)-1-phenyl-6H-pyrazino[2,1-b]quinazolin-6-one (3j): Yellow solid (59.9 mg, 75%), mp:266-267 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.11 (s, 1H), 8.64 (s, 1H), 8.52(d, J = 8.4 Hz, 1H), 8.48-8.47 (m, 2H), 8.16-8.14 (m, 1H), 7.95-7.84 (m, 5H), 7.63-7.60 (m, 4H), 7.53-7.46 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.4, 158.3, 147.3, 139.0, 136.9, 136.4, 135.1, 133.6, 133.5, 132.7, 131.1, 130.6, 128.7, 128.7,

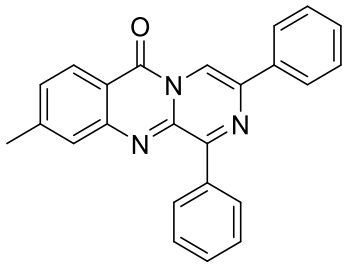
128.0, 127.7, 127.3, 126.7, 126.6, 125.6, 123.2, 117.5, 111.4. HRMS calcd for $C_{27}H_{18}N_3O[M+H]^+$: 400.1444, found 400.1445.



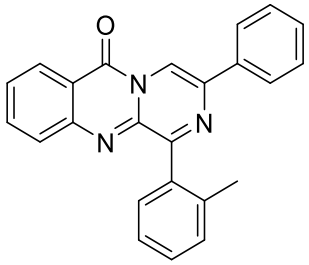
8-methoxy-1,3-diphenyl-6H-pyrazino[2,1-b]quinazolin-6-one (3k): Yellow solid (67.5 mg, 89%), mp: 256-257°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.02 (s, 1H), 8.43-8.42 (m, 2H), 8.13 (d, J = 7.5 Hz, 2H), 7.86 (d, J = 9.0 Hz, 1H), 7.80 (s, 1H), 7.56 (m, 3H), 7.51 (m, 3H), 7.44 (m, 1H), 3.99 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 158.4, 158.0, 142.3, 137.4, 137.1, 136.5, 135.7, 131.0, 130.5, 130.4, 129.0, 128.9, 127.9, 126.7, 126.1, 118.3, 111.1, 105.3, 56.0. HRMS calcd for $C_{24}H_{18}N_3O_2$ $[M+H]^+$: 380.1394, found 380.1404.



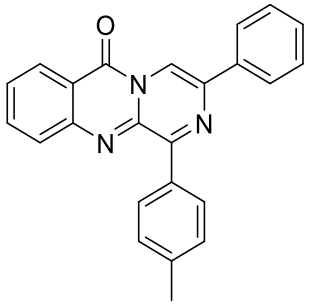
8-fluoro-1,3-diphenyl-6H-pyrazino[2,1-b]quinazolin-6-one (3l): Yellow solid (55.8 mg, 76%), mp:255-256 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.00 (s, 1H), 8.41 (d, J = 6.0 Hz, 2H), 8.12 (d, J = 7.5 Hz, 3H), 7.96-7.94 (m, 1H), 7.65-7.62 (m, 1H), 7.57-7.51 (m, 5H), 7.46-7.43 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2 (d, $J_{C\text{-}F}$ = 248.8 Hz), 158.6, 157.9, 144.3, 138.6, 137.7, 136. 5, 135.6, 131.5 (d, $J_{C\text{-}F}$ = 8.8 Hz), 131.1, 130.8, 129.4, 129.2, 128.1, 126.3, 124.6 (d, $J_{C\text{-}F}$ = 25.0 Hz), 118.6, 111.6 (d, $J_{C\text{-}F}$ = 25.0 Hz), 111.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ -110.63 (td, J = 8.25, 4.95 Hz, 1F). HRMS calcd for $C_{24}H_{15}FN_3O$ $[M+H]^+$: 390.1013, found 390.1009.



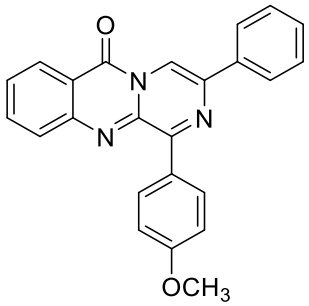
9-methyl-1,3-diphenyl-6H-pyrazino[2,1-b]quinazolin-6-one (3m): Yellow solid (60.3 mg, 83%), mp:227-228 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.00 (s, 1H), 8.44-8.42 (m, 2H), 8.38 (d, J = 8.0 Hz, 1H), 8.11 (d, J = 7.5 Hz, 2H), 7.71 (s, 1H), 7.57-7.56 (d, J = 4.9 Hz, 3H), 7.52-7.49 (m, 2H), 7.44-7.40 (m, 2H), 2.55 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.3, 147.6, 146.5, 139.3, 137.0, 136.6, 135.7, 131.9, 131.1, 130.6, 129.3, 129.1, 129.1, 128.2, 128.0, 127.1, 126.1, 115.3, 111.4, 22.2. HRMS calcd for $C_{24}H_{18}N_3O$ $[M+H]^+$: 364.1444, found 364.1449.



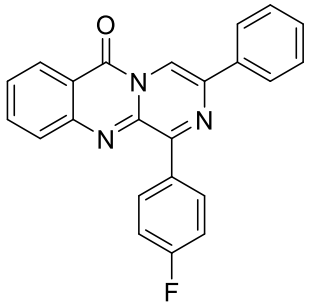
3-phenyl-1-(o-tolyl)-6H-pyrazino[2,1-b]quinazolin-6-one (3n): Yellow solid (56.6 mg, 78%), mp 214-215 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.07 (s, 1H), 8.51 (d, J = 7.5 Hz, 1H), 8.09 (d, J = 7.5 Hz, 2H), 7.87-7.81 (m, 2H), 7.62-7.58 (m, 2H), 7.52-7.43 (m, 4H), 7.40-7.36 (m, 2H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 161.8, 158.4, 147.6, 139.3, 137.2, 137.1, 136.6, 135.4, 135.1, 130. 6, 130. 2, 129.4, 129.1, 129.0, 128.8, 127.3, 127.2, 126.1, 125.4, 117. 5, 111.4, 20.5. HRMS calcd for $C_{24}H_{18}N_3O$ $[M+H]^+$: 364.1444, found 364.1446.



3-phenyl-1-(p-tolyl)-6H-pyrazino[2,1-b]quinazolin-6-one (3o): Yellow solid (59.5 mg, 82%), mp 245-246 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.01 (s, 1H), 8.50 (d, J = 8.0 Hz, 1H), 8.37 (d, J = 8.0 Hz, 2H), 8.12 (d, J = 7.5 Hz, 2H), 7.94-7.86 (m, 2H), 7.60 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.5 Hz, 2H), 7.43 (t, J = 7.5 Hz, 1H), 7.37 (d, J = 8.0 Hz, 2H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.4, 158.2, 147.4, 140.9, 139.0, 137.1, 135.7, 135.0, 133.7, 131.0, 129.0, 128.9, 128.7, 127.2, 127.18, 126.1, 117.4, 110.9, 21.6. HRMS calcd for $C_{24}H_{18}N_3O$ $[M+H]^+$: 364.1444, found 364.1435.

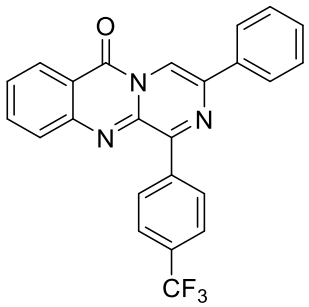


1-(4-methoxyphenyl)-3-phenyl-6H-pyrazino[2,1-b]quinazolin-6-one (3p): Yellow solid (61.4 mg, 81%), mp 235-236 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.97 (s, 1H), 8.54 (d, J = 9.0 Hz, 2H), 8.49 (d, J = 8.0 Hz, 1H), 8.11 (d, J = 8.0 Hz, 2H), 7.93 (d, J = 8.0 Hz, 1H), 7.87 (t, J = 8.0 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.50 (t, J = 7.5 Hz, 2H), 7.42 (t, J = 7.5 Hz, 1H), 7.07 (d, J = 9.0 Hz, 2H), 3.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.7, 158.4, 157.2, 147.3, 139.0, 137.0, 135.7, 135.0, 132.8, 129.0, 128.97, 128.9, 128.6, 127.2, 127.1, 126.0, 117.4, 113.4, 110.5, 55.4. HRMS calcd for $C_{24}H_{18}N_3O_2$ $[M+H]^+$: 380.1394, found 380.1395.

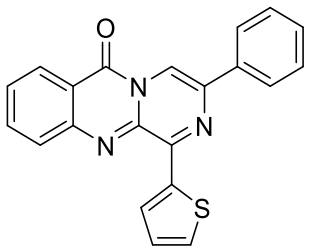


1-(4-fluorophenyl)-3-phenyl-6H-pyrazino[2,1-b]quinazolin-6-one (3q): Yellow solid (69.8 mg, 95%), mp 238-239 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.01 (s, 1H), 8.54-8.49 (m, 3H), 8.10 (d, J = 7.5 Hz, 2H), 7.93-7.88 (m, 2H), 7.61 (t, J = 6.5 Hz, 1H), 7.51 (t, J = 7.5 Hz, 2H), 7.43 (t, J = 6.5 Hz, 1H), 7.23 (d, J = 8.5 Hz, 2H); ^{13}C NMR

(125 MHz, $CDCl_3$): δ 164.5 (d, $J_{C\text{-}F}$ = 250.0 Hz), 158.4, 157.1, 147.4, 139.0, 137.2, 135.6, 135.3, 133.4 (d, $J_{C\text{-}F}$ = 7.5 Hz), 132.6 (d, $J_{C\text{-}F}$ = 3.8 Hz), 129.3, 129.1, 128.7, 127.5, 127.4, 126.1, 117.6, 115.1(d, $J_{C\text{-}F}$ = 21.3 Hz), 111.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ -109.66- -109.74 (m, 1F). HRMS calcd for $C_{23}H_{14}FN_3NaO$ $[M+Na]^+$: 390.1013, found 390.1024.

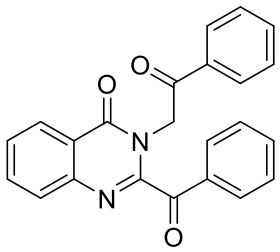


3-phenyl-1-(4-(trifluoromethyl)phenyl)-6H-pyrazino[2,1-b]quinazolin-6-one (3r): Yellow solid (35.9 mg, 43%), mp 313-314 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.06 (s, 1H), 8.57-8.51 (m, 3H), 8.10 (d, J = 7.6 Hz, 2H), 7.92 (s, 2H), 7.82 (d, J = 8.0 Hz, 2H), 7.65-7.62 (m, 1H), 7.53 (t, J = 7.2 Hz, 2H), 7.46 (d, J = 7.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.2, 157.1, 147.2, 139.6, 138.8, 137.2, 135.4, 135.2, 132.1 (d, $J_{C\text{-}F}$ = 30.0 Hz), 131.3, 129.1, 128.6, 128.3 (d, $J_{C\text{-}F}$ =241.3 Hz), 127.6, 126.0, 124.8 (q, $J_{C\text{-}F}$ = 3.8 Hz), 117.5, 111.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.78 (s, 3F). HRMS calcd for $C_{24}H_{15}F_3N_3O$ $[M+H]^+$: 418.1162, found 418.1151.



3-phenyl-1-(thiophen-2-yl)-6H-pyrazino[2,1-b]quinazolin-6-one (3s): Yellow solid (46.9 mg, 66%), mp 246-247 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.87 (s, 1H), 8.80 (d, J = 4.0 Hz, 1H), 8.44 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 7.5 Hz, 2H), 7.95 (d, J = 8.0 Hz, 1H), 7.87 (t, J = 7.5 Hz, 1H), 7.61 (d, J = 5.0 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 7.50 (t, J = 7.5 Hz, 2H), 7.42 (t, J = 7.5 Hz, 1H), 7.19 (t, J = 4.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.1, 151.4, 147.0, 139.3, 137.3, 136.9, 135.4, 135.1, 133.2, 133.0, 129.0,

128.9, 128.2, 127.7, 127.3, 127.1, 126.0, 117.6, 110.0. HRMS calcd for $C_{21}H_{14}N_3OS$ $[M+H]^+$: 356.0852, found 356.0851.



2-**benzoyl-3-(2-oxo-2-phenylethyl)quinazolin-4(3H)-one (4a):**White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 7.6 Hz, 2H), 7.93 (d, J = 7.6 Hz, 2H), 7.84-7.78 (m, 2H), 7.67-7.58 (m, 3H), 7.53-7.45 (m, 4H), 5.97 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.6, 188.5, 161.5, 150.0, 146.0, 134.8, 134.5, 134.4, 134.2, 131.5, 128.9, 128.5, 128.4, 128.3, 128.1, 127.3, 121.8, 48.9.

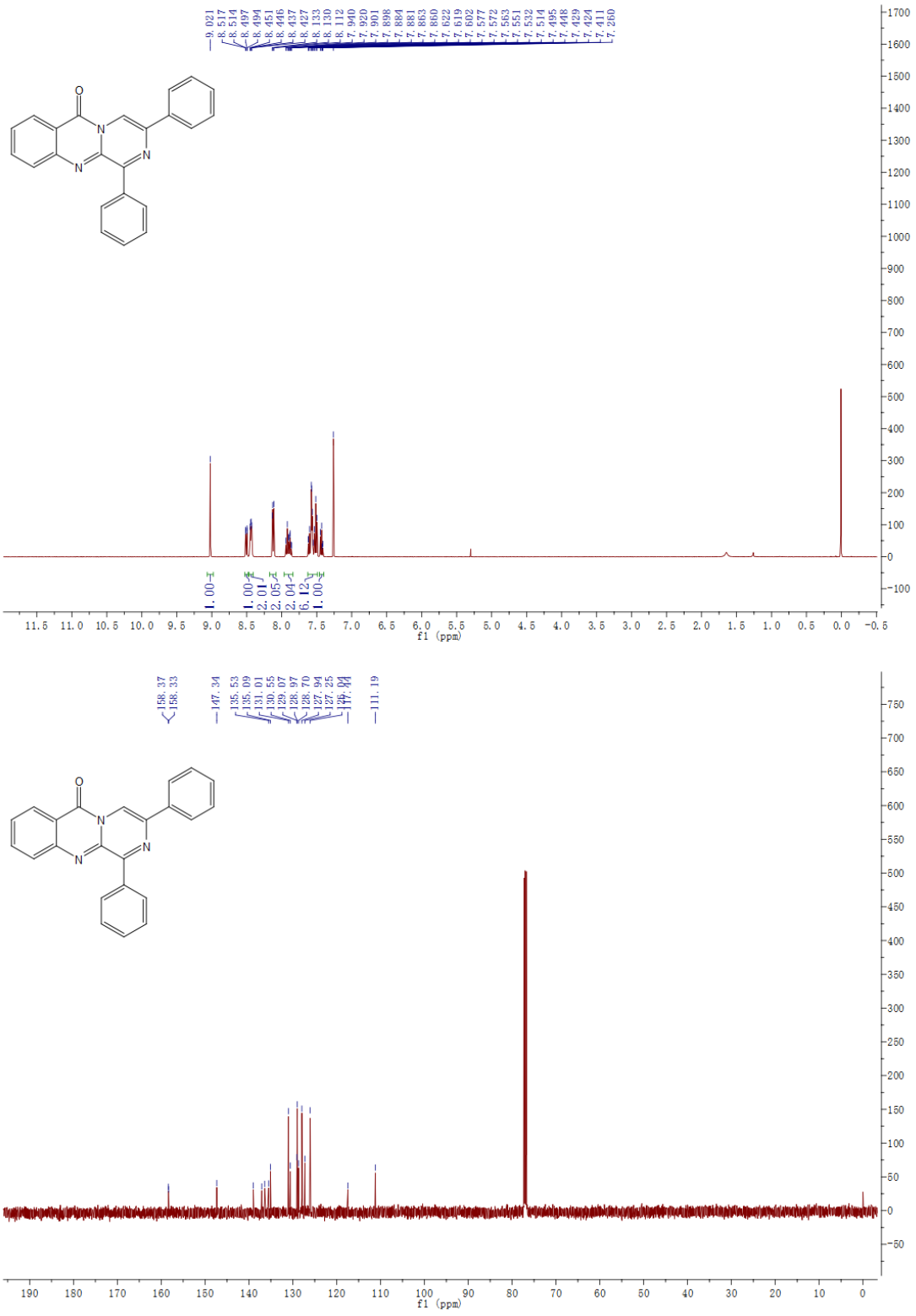


Fig. S5 ^{1}H and ^{13}C NMR spectra of **3a** in $CDCl_3$.

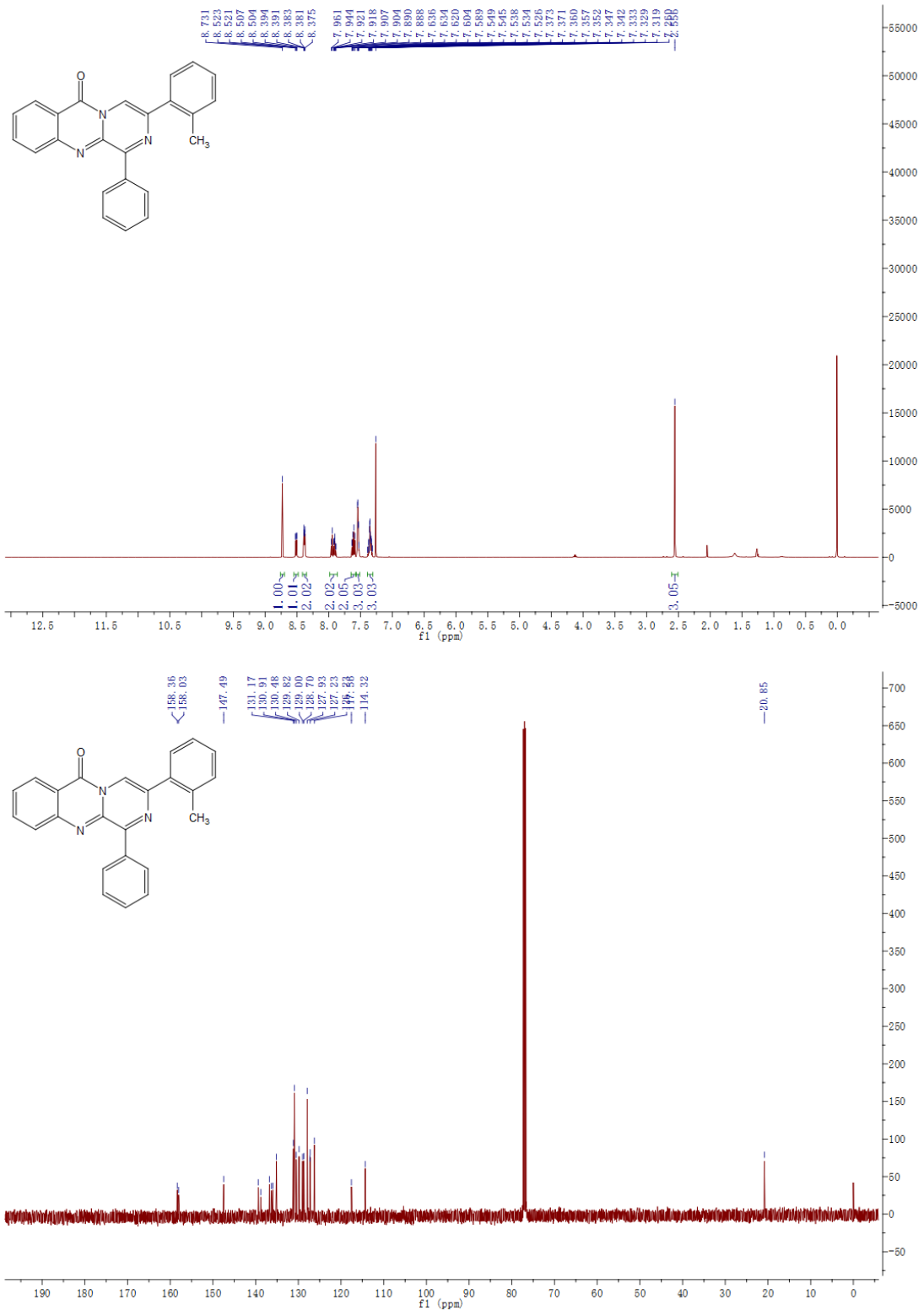


Fig. S6 ^{1}H and ^{13}C NMR spectra of **3b** in $CDCl_3$.

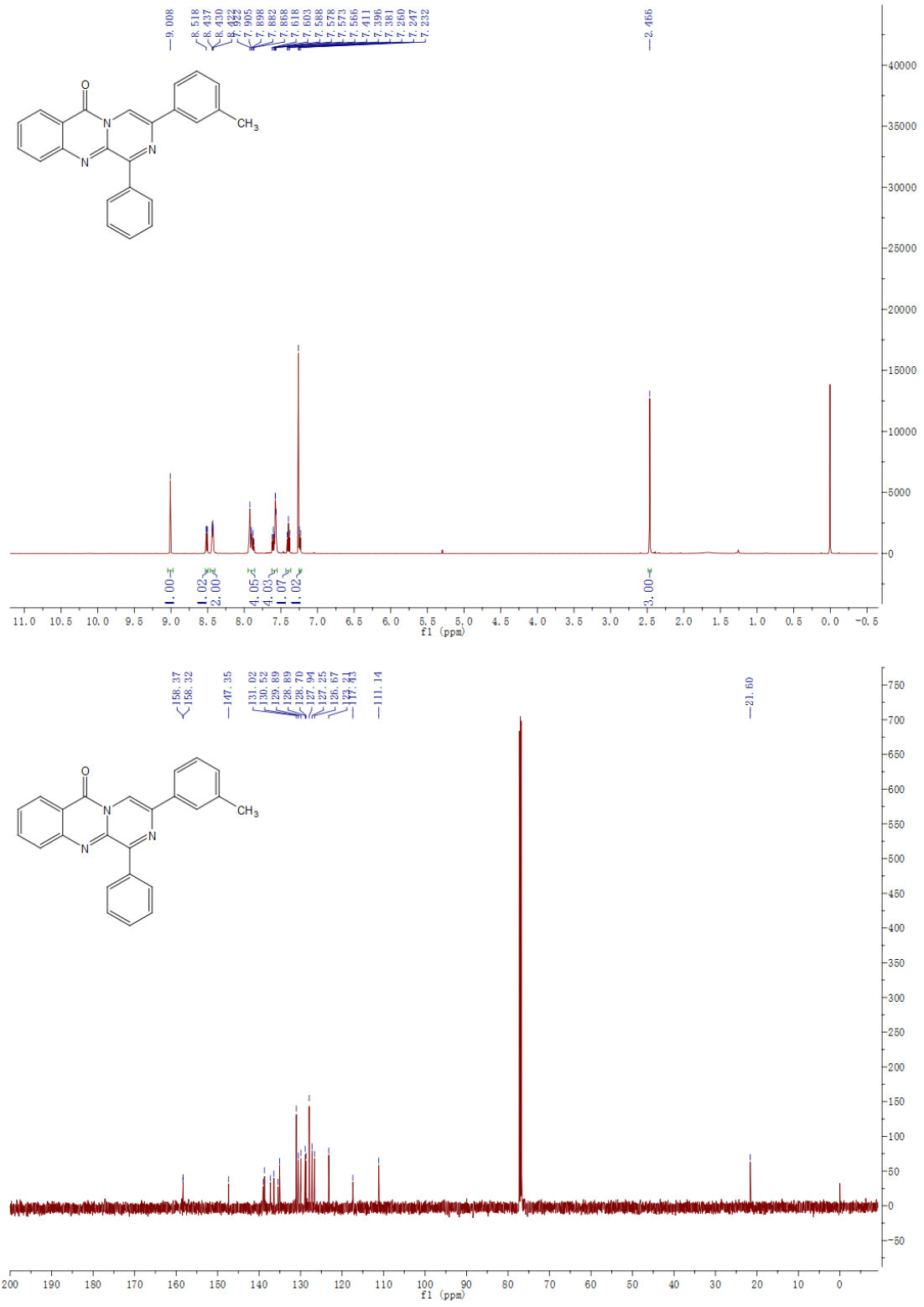


Fig. S7 ^{1}H and ^{13}C NMR spectra of **3c** in $CDCl_3$.

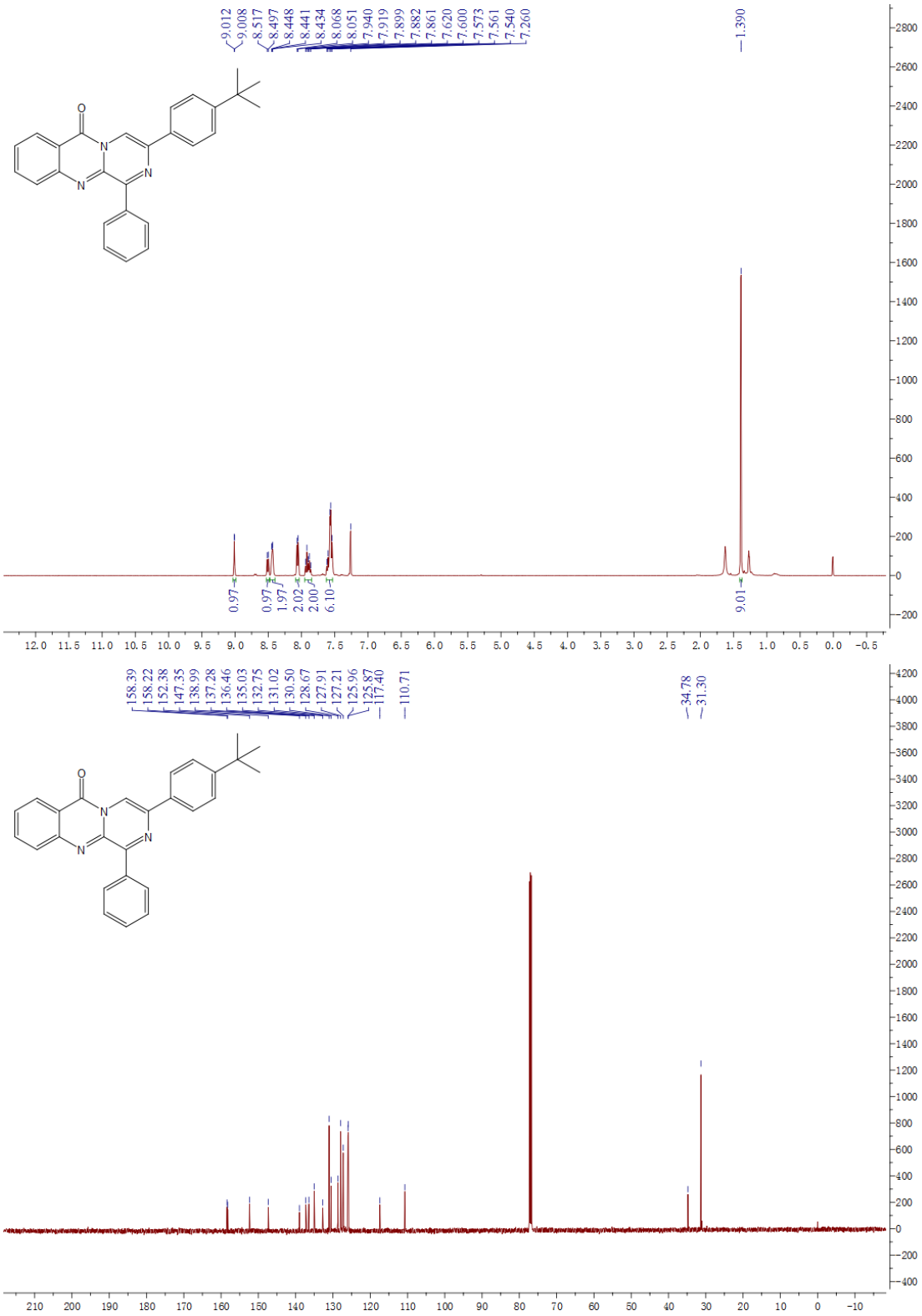
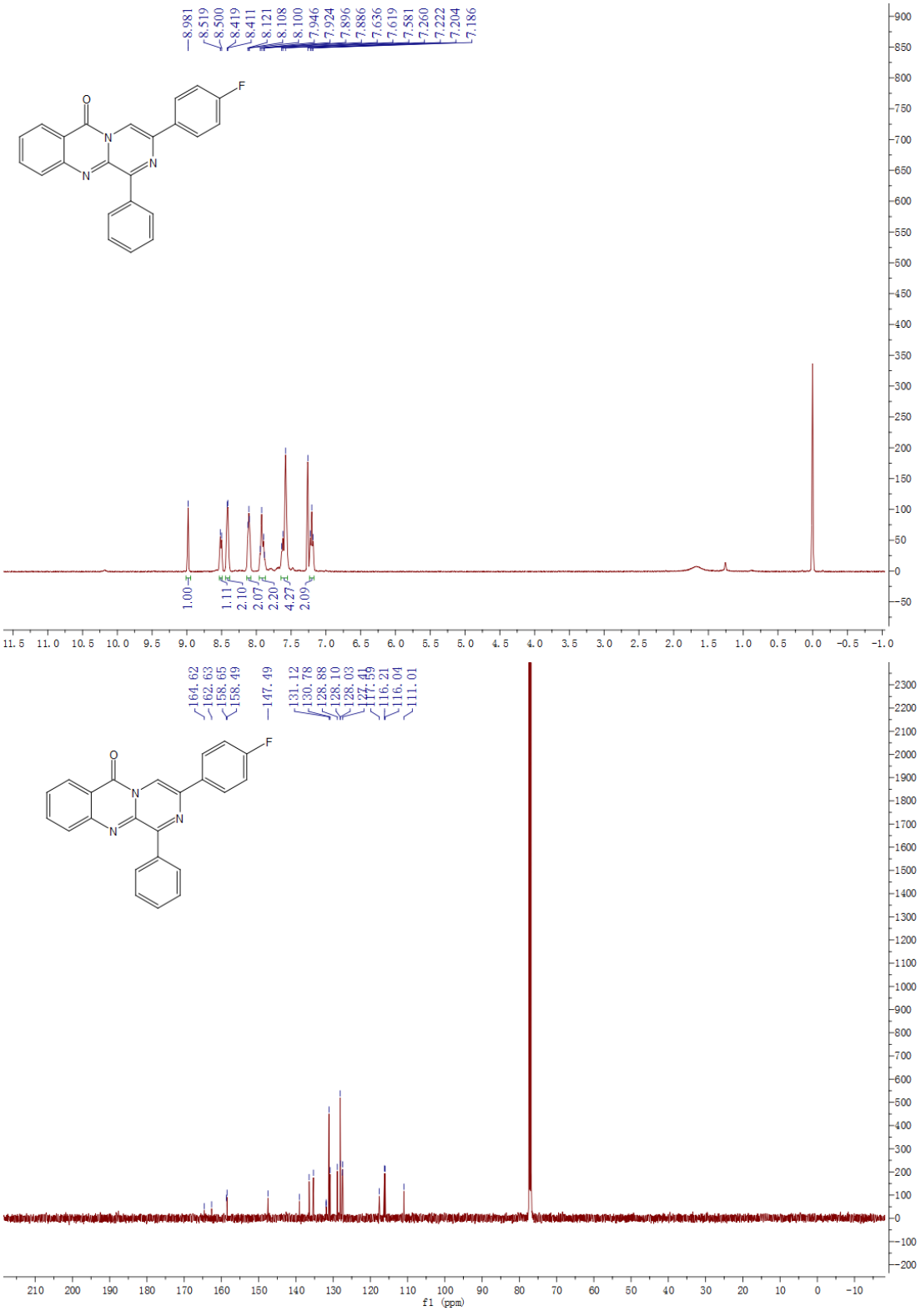


Fig. S8 ^{1}H and ^{13}C NMR spectra of **3d** in $CDCl_3$.


8.981
8.519
8.500
8.419
8.411
8.121
8.108
8.100
7.946
7.924
7.896
7.886
7.636
7.619
7.581
7.260
7.222
7.204
7.186
O
N
N
F
1.00
1.11
2.10
2.07
2.20
4.27
2.09
164.62
162.63
158.65
158.49
147.49
131.12
130.78
128.88
128.10
128.03
127.41
117.59
116.21
116.04
111.01
f1 (ppm)

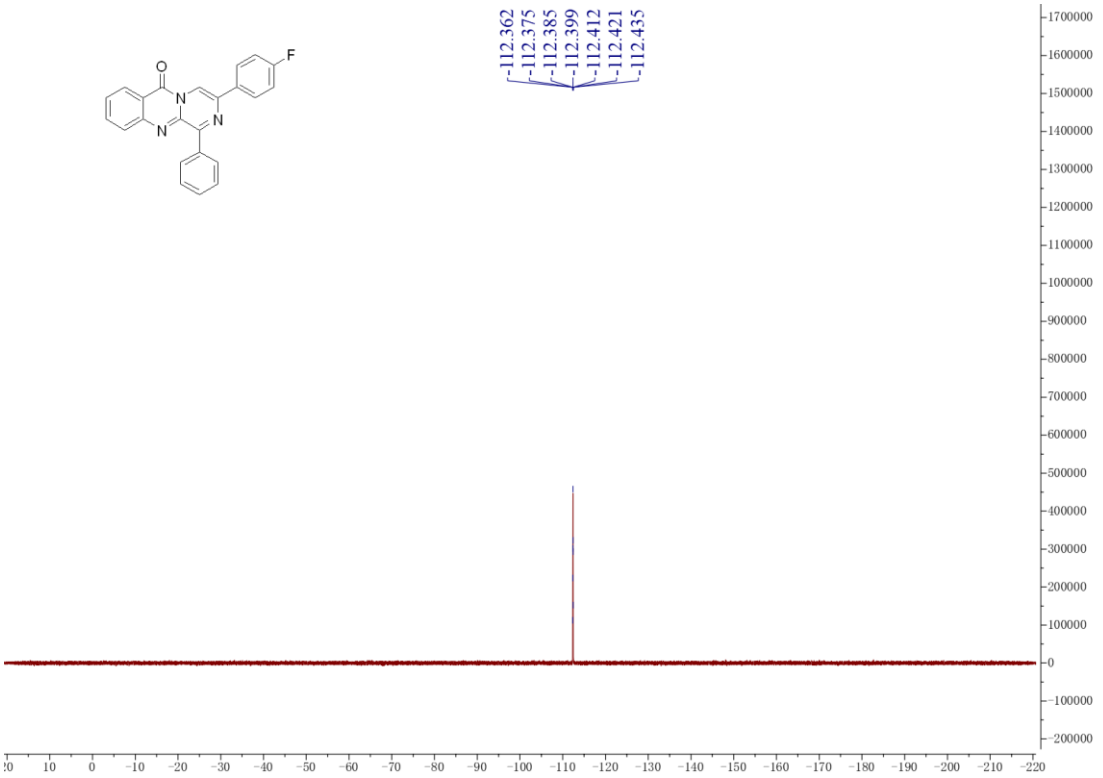
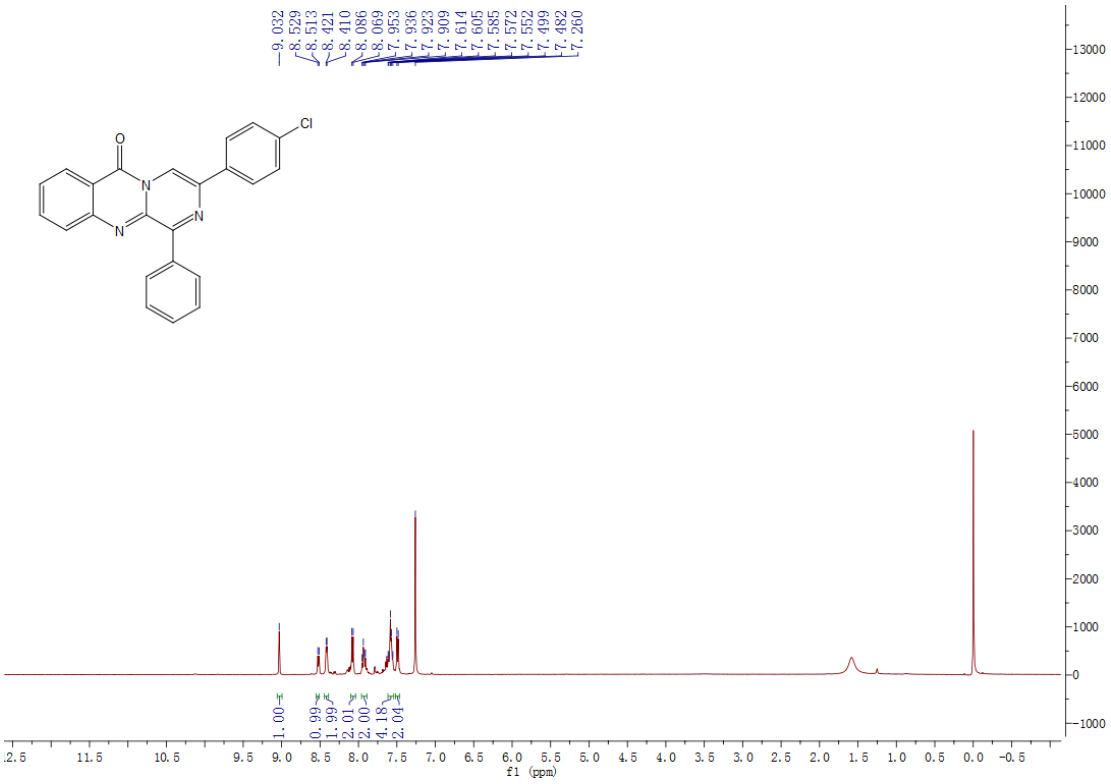


Fig. S9 ^{1}H, ^{13}C and ^{19}F NMR spectra of **3e** in $CDCl_3$.



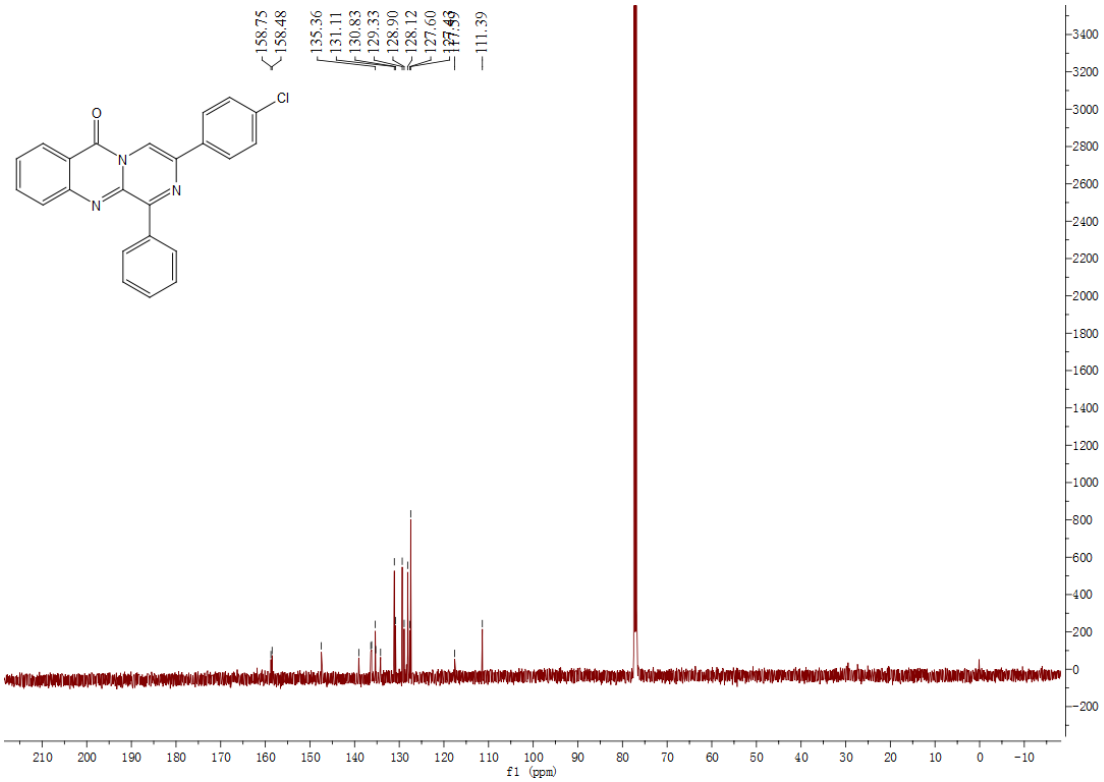
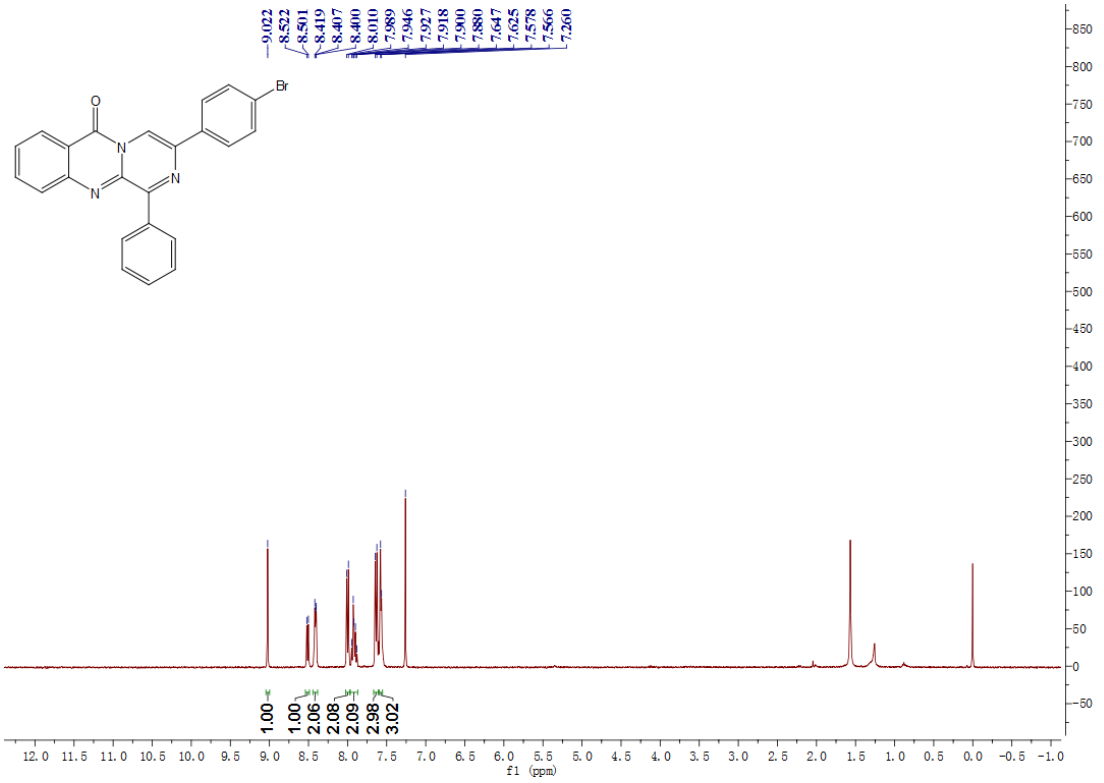


Fig. S10 ^{1}H and ^{13}C NMR spectra of **3f** in $CDCl_3$.



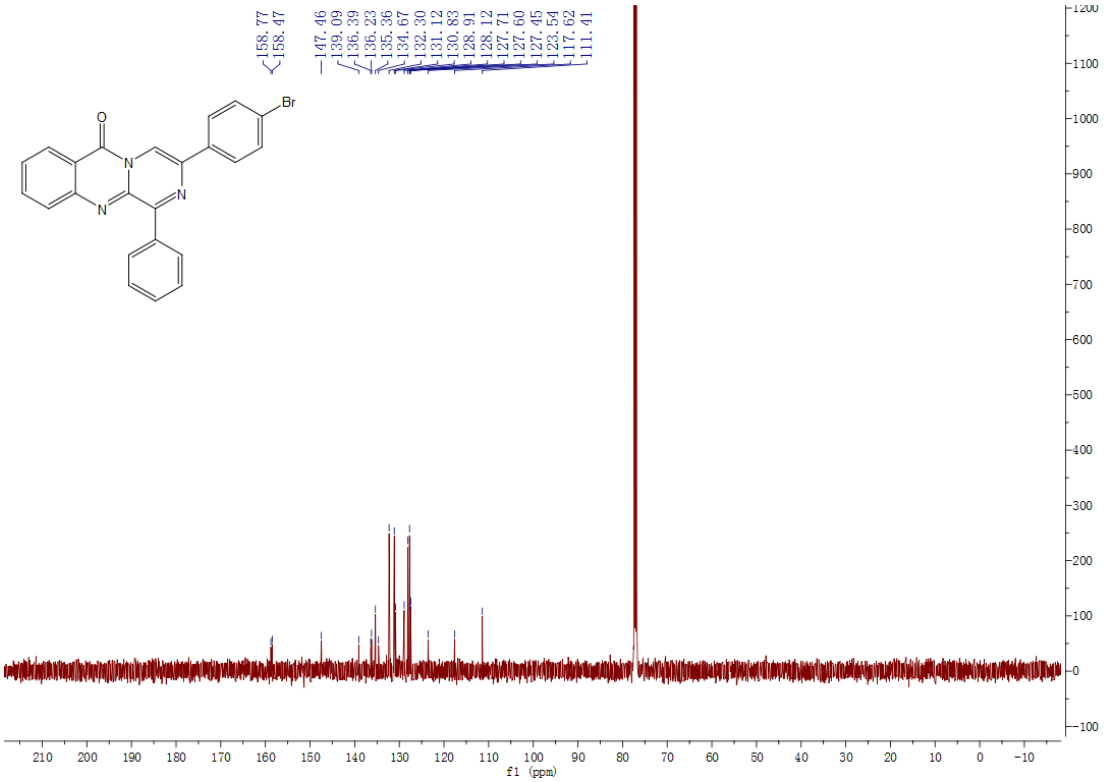
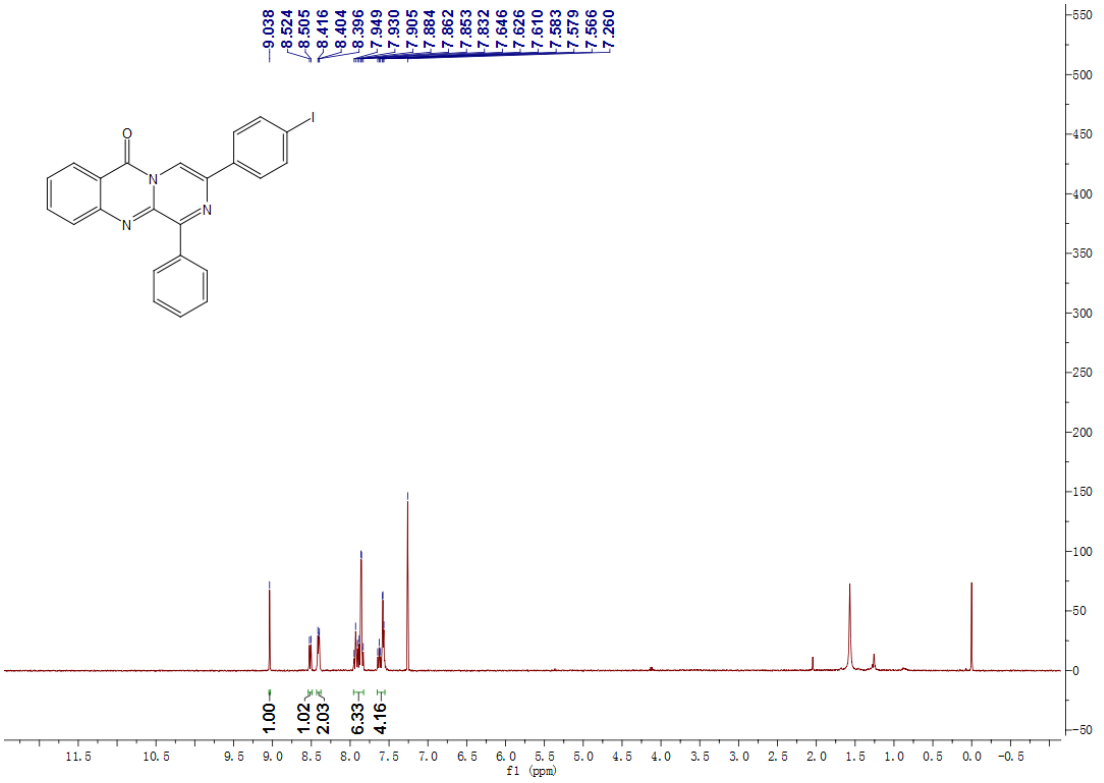


Fig. S11 ^{1}H and ^{13}C NMR spectra of **3g** in $CDCl_3$.



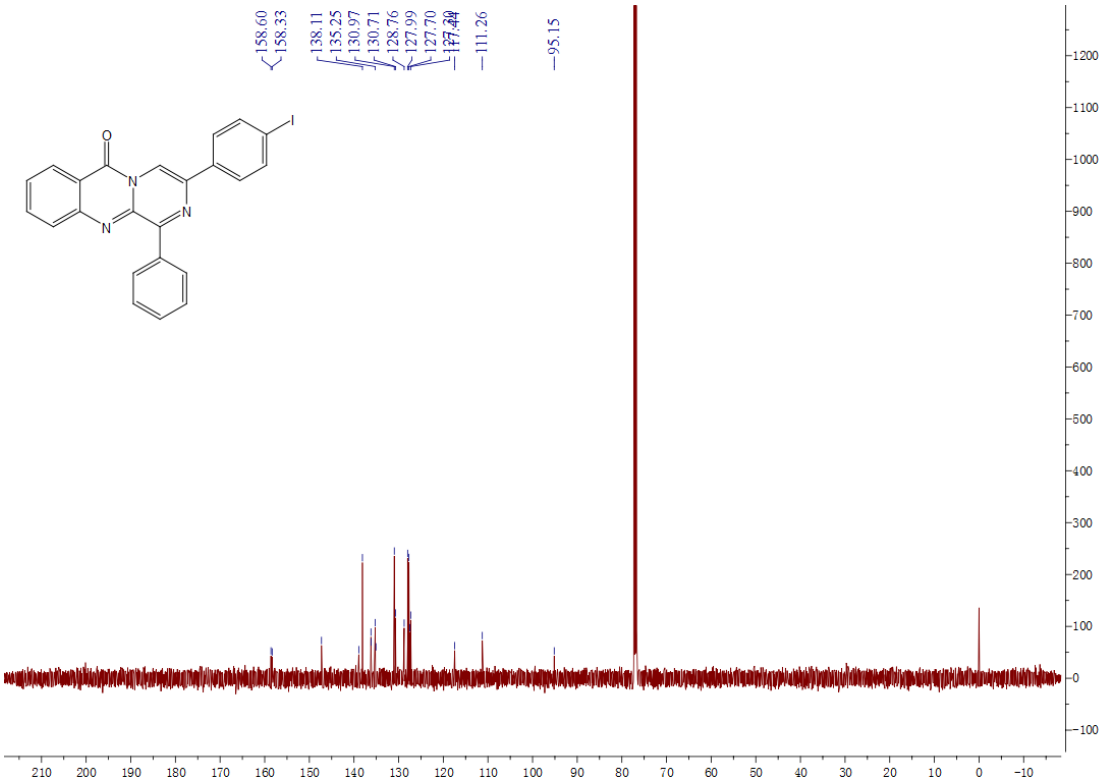
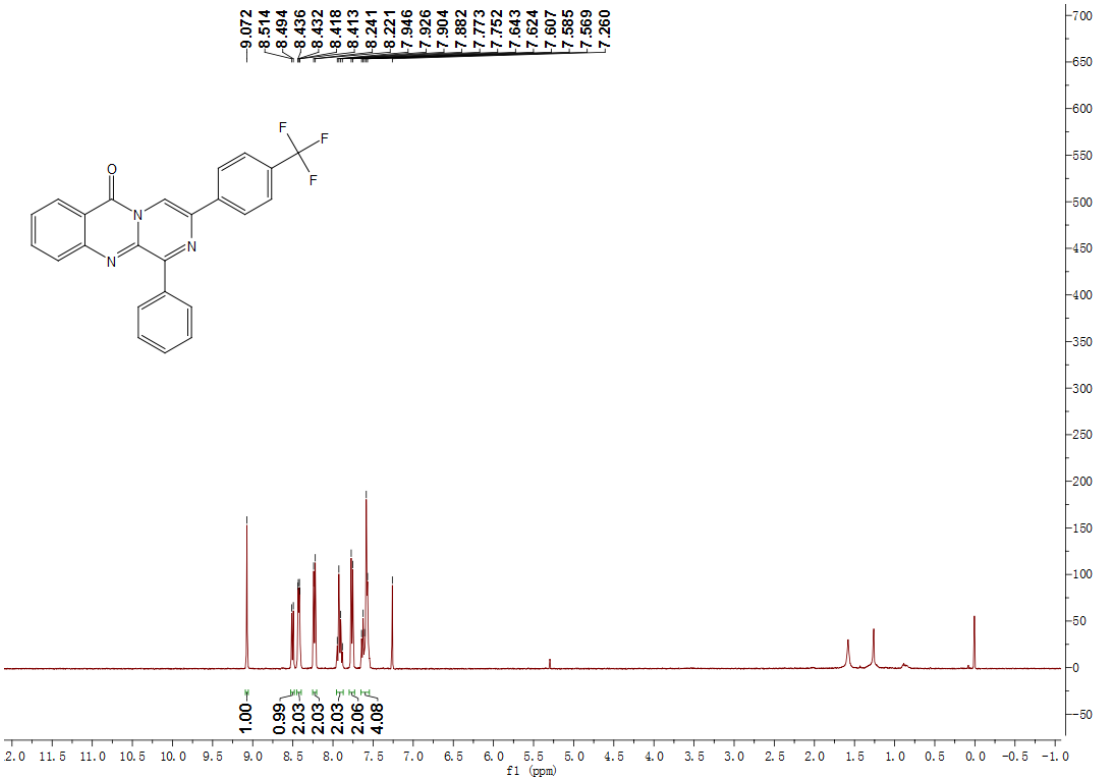


Fig. S12 ^{1}H and ^{13}C NMR spectra of **3h** in $CDCl_3$.



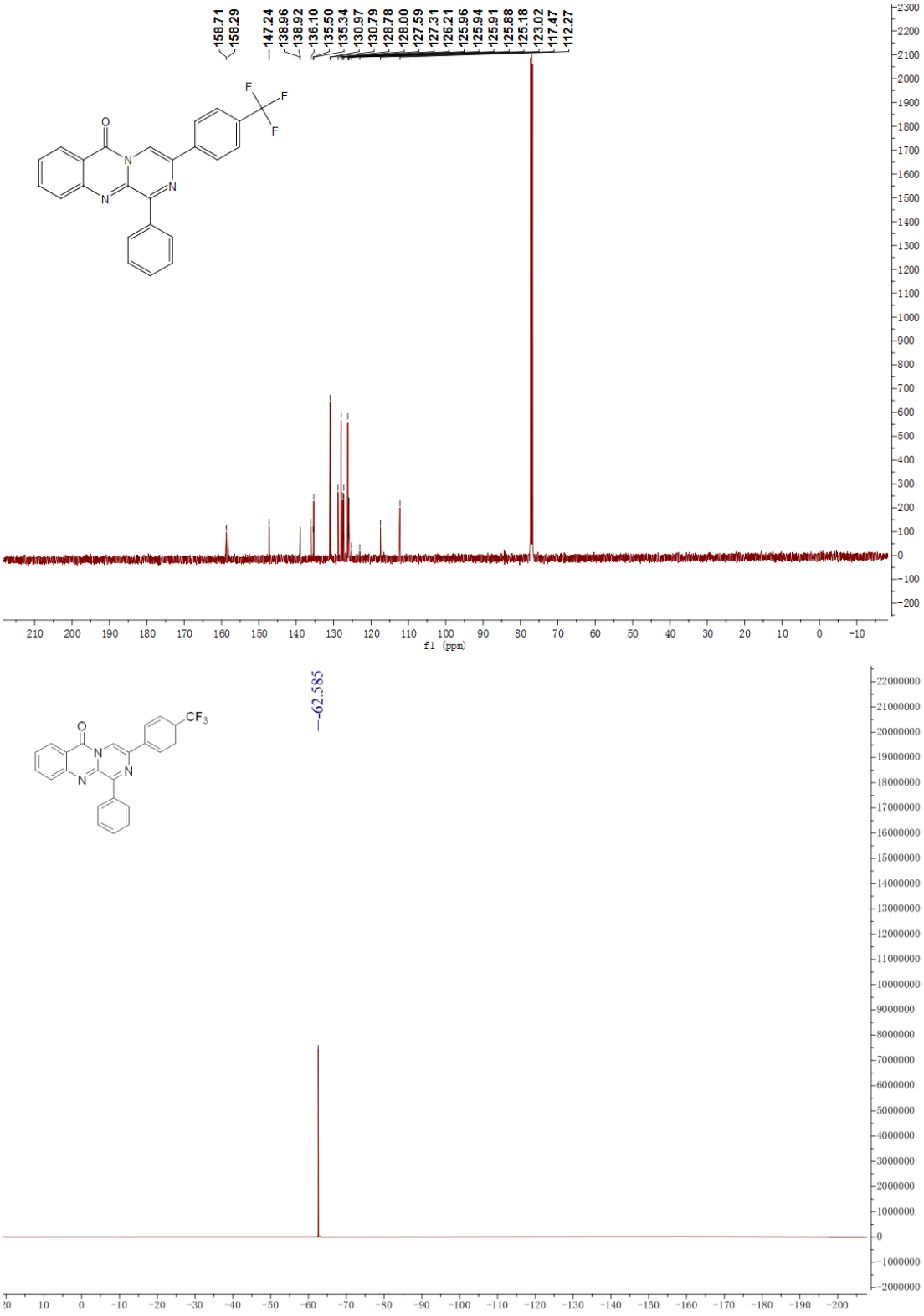


Fig. S13 ^{1}H, ^{13}C and ^{19}F NMR spectra of **3i** in $CDCl_3$.

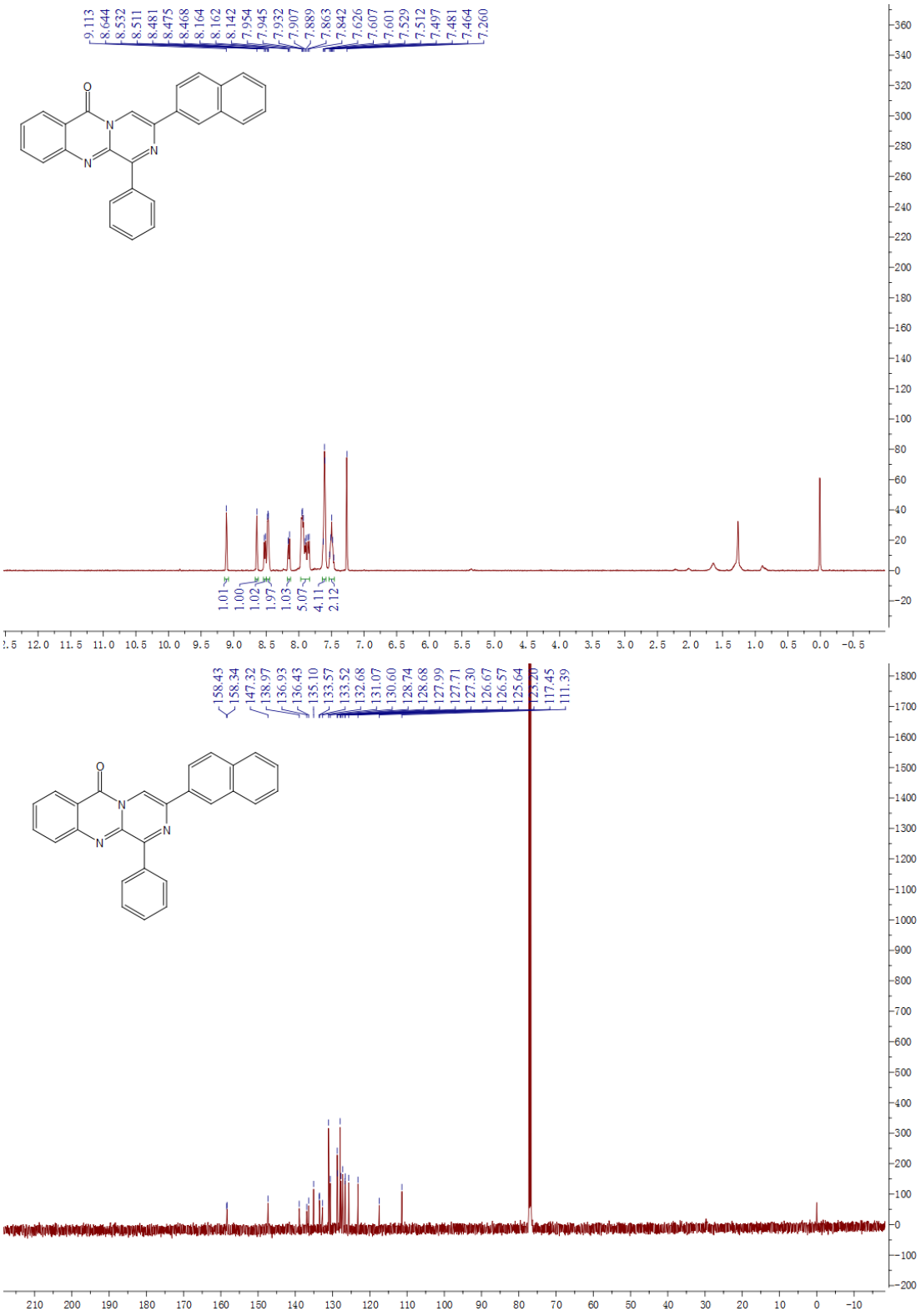


Fig. S14 ^{1}H and ^{13}C NMR spectra of **3j** in $CDCl_3$.

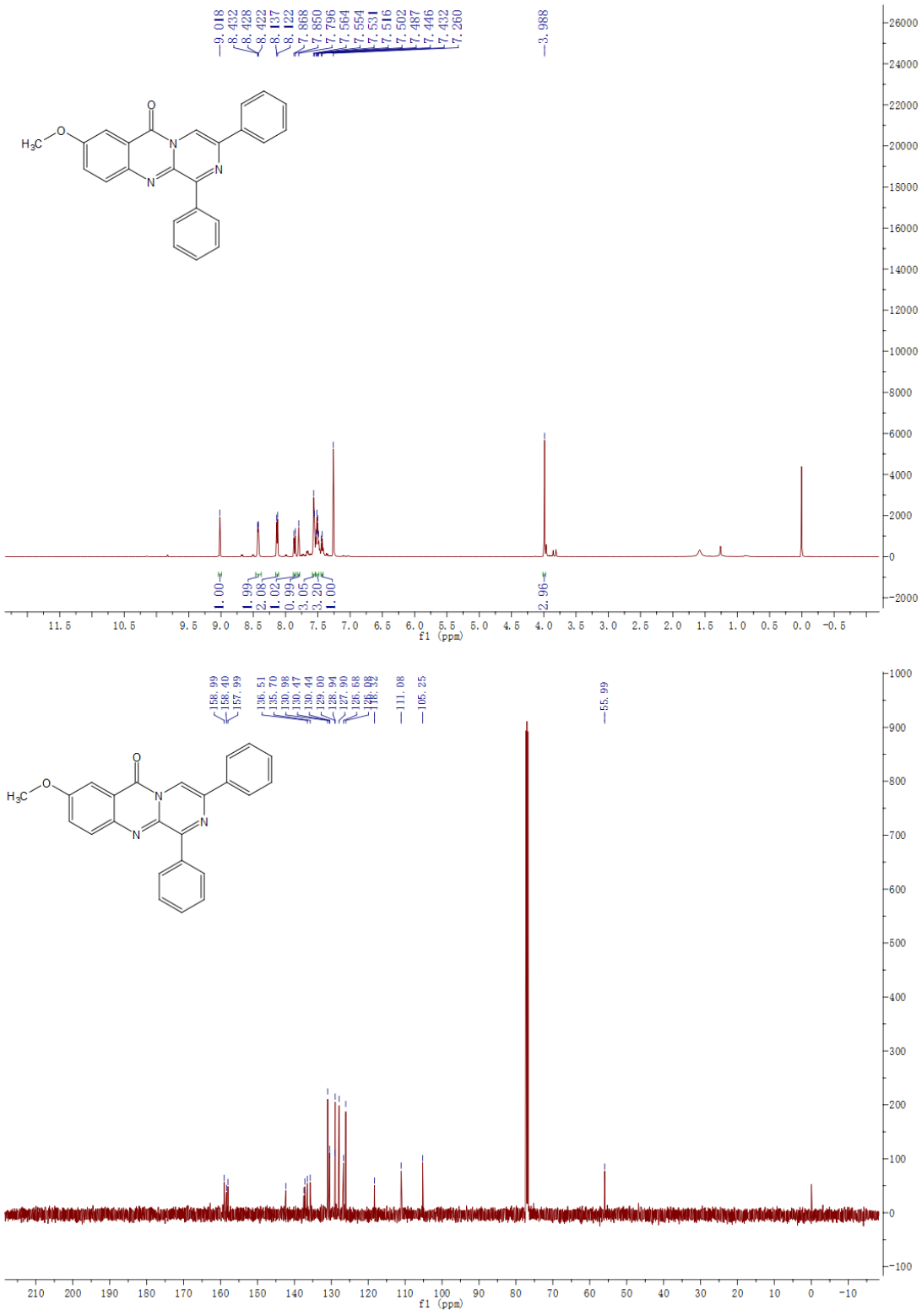
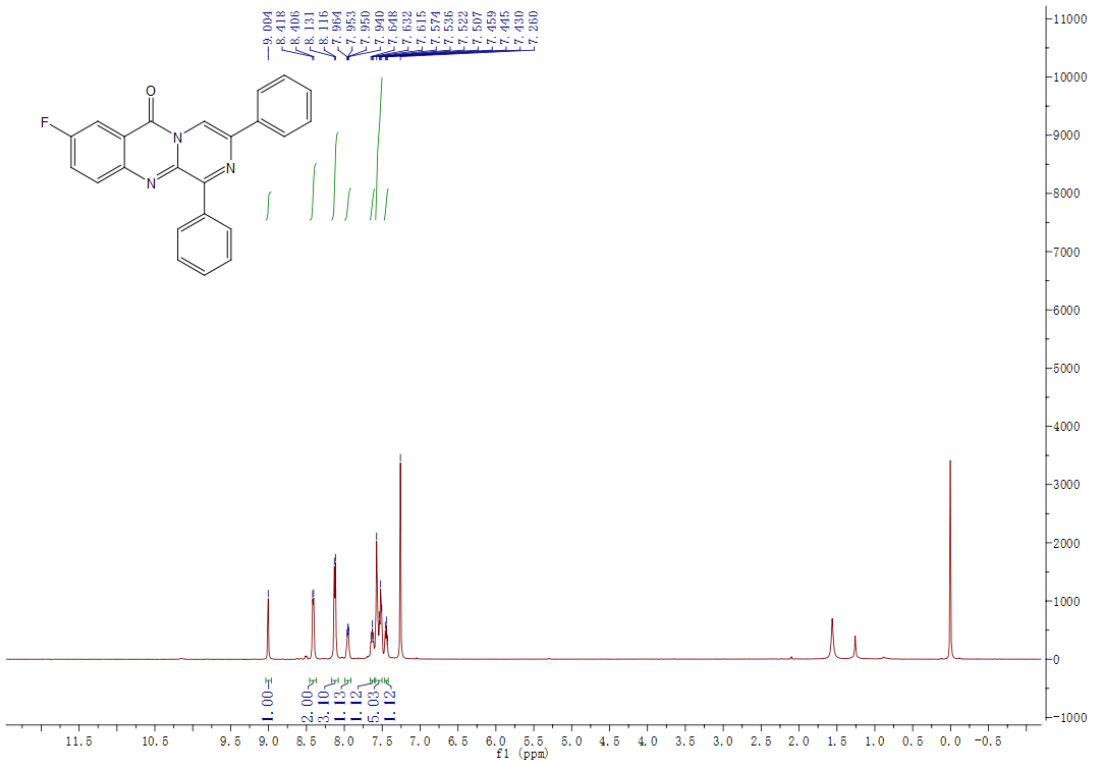
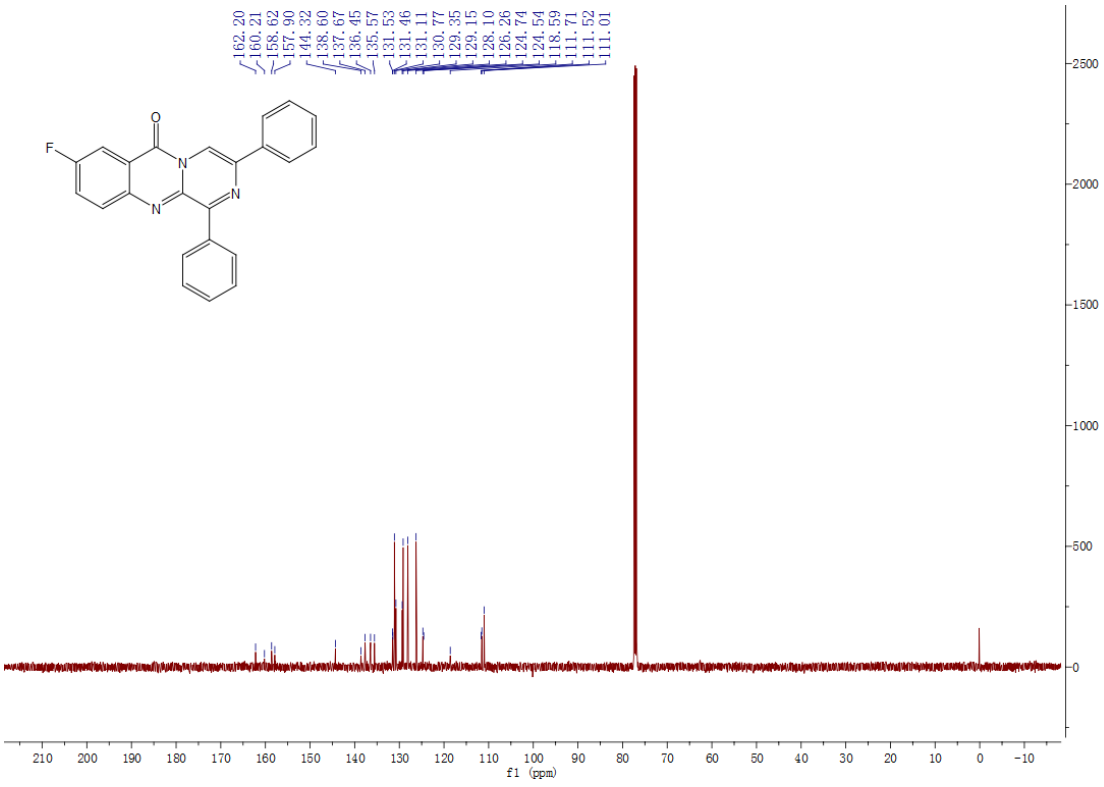


Fig. S15 ^{1}H and ^{13}C NMR spectra of **3k** in $CDCl_3$.


9.004
8.418
8.406
8.131
8.116
7.964
7.953
7.950
7.940
7.648
7.632
7.615
7.574
7.536
7.522
7.507
7.459
7.445
7.430
7.280
F
O
N
N
N
1.00
2.00
3.10
1.13
1.12
5.03
1.12
f1 (ppm)


162.20
160.21
158.62
157.90
144.32
138.60
137.67
136.45
135.57
131.53
131.46
131.11
130.77
129.35
129.15
128.10
126.26
124.74
124.54
118.59
111.71
111.52
111.01
F
O
N
N
N
f1 (ppm)

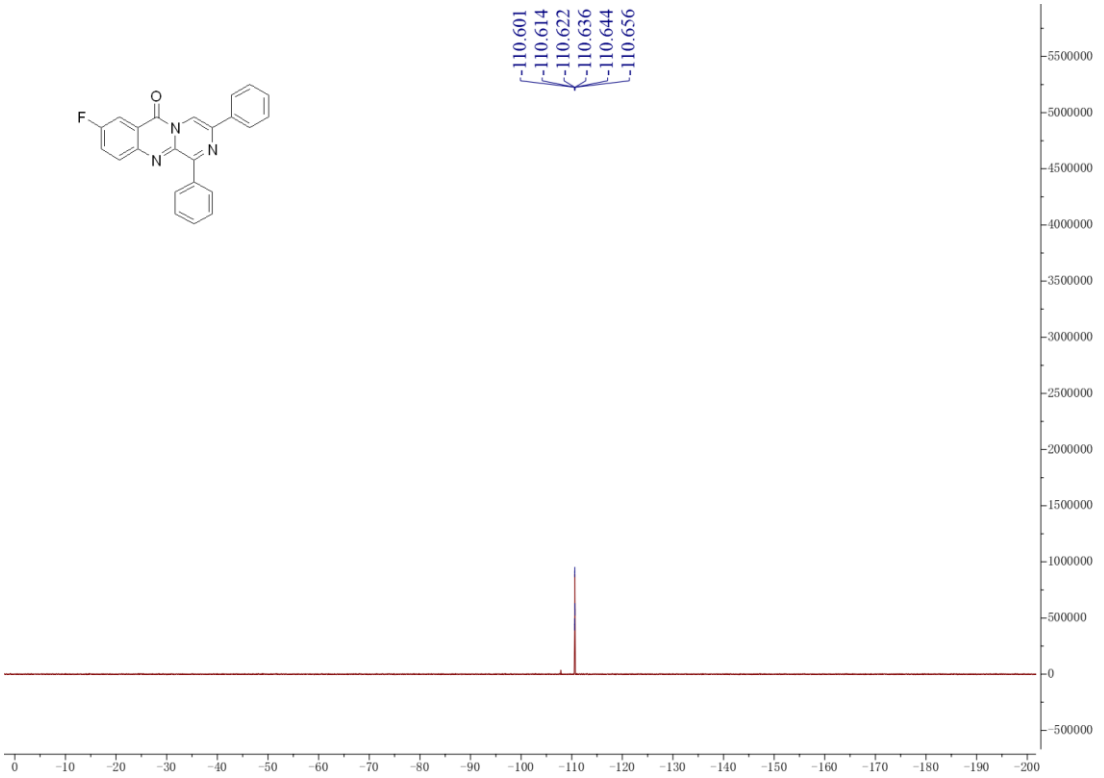
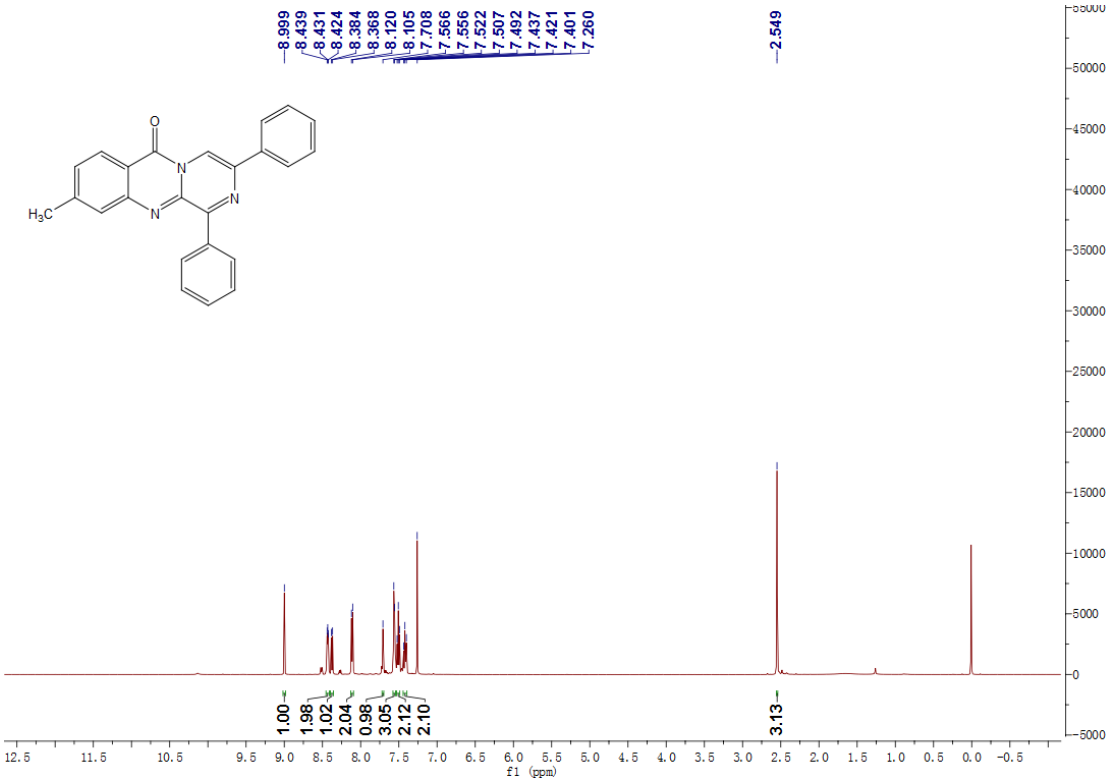


Fig. S16 ^{1}H, ^{13}C and ^{19}F NMR spectra of **3l** in $CDCl_3$.



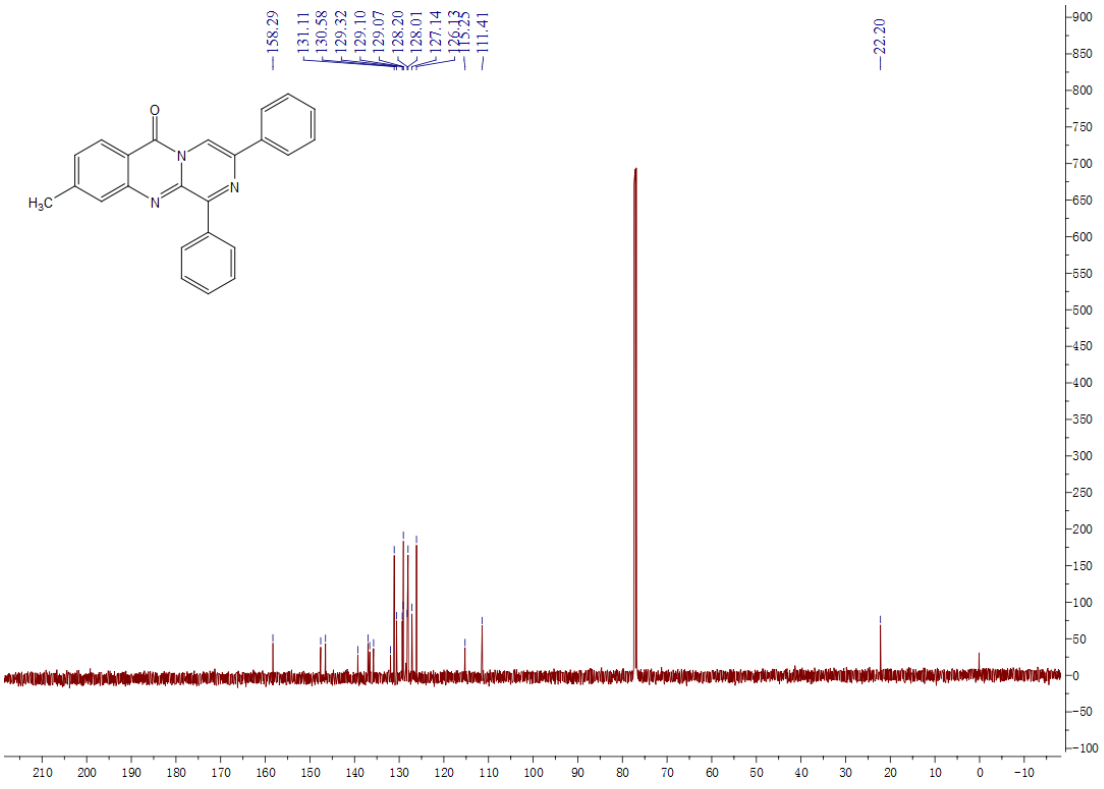
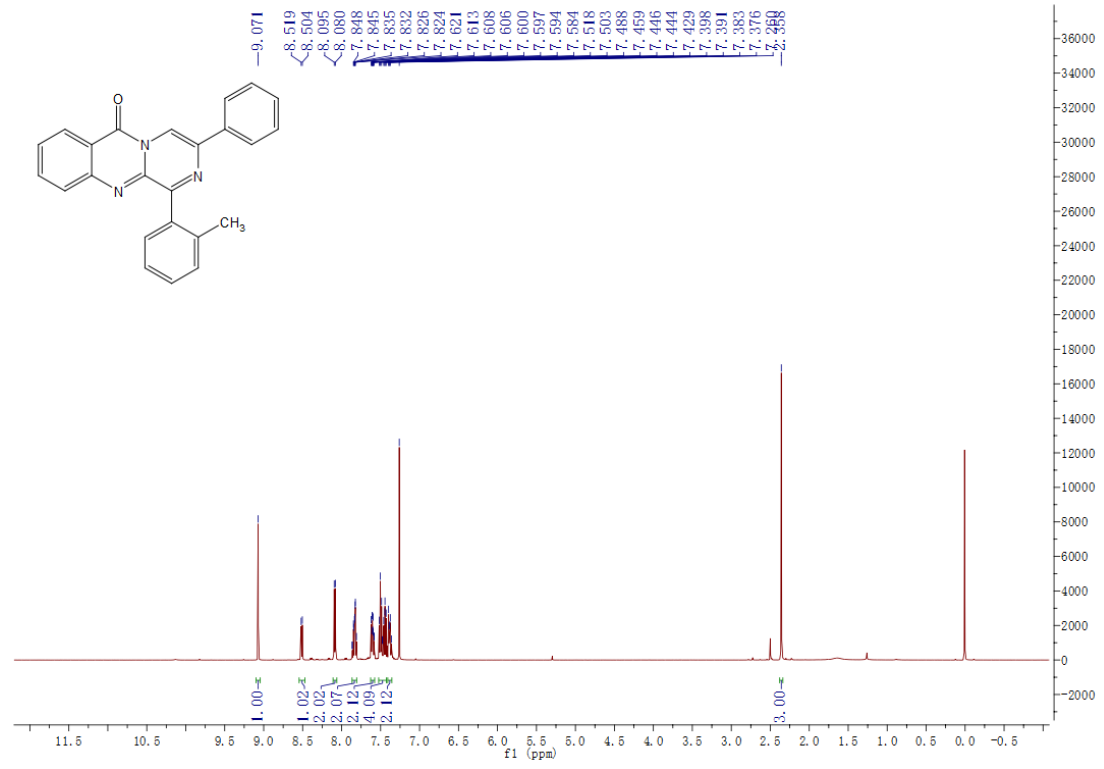


Fig. S17 ^{1}H and ^{13}C NMR spectra of **3m** in $CDCl_3$.



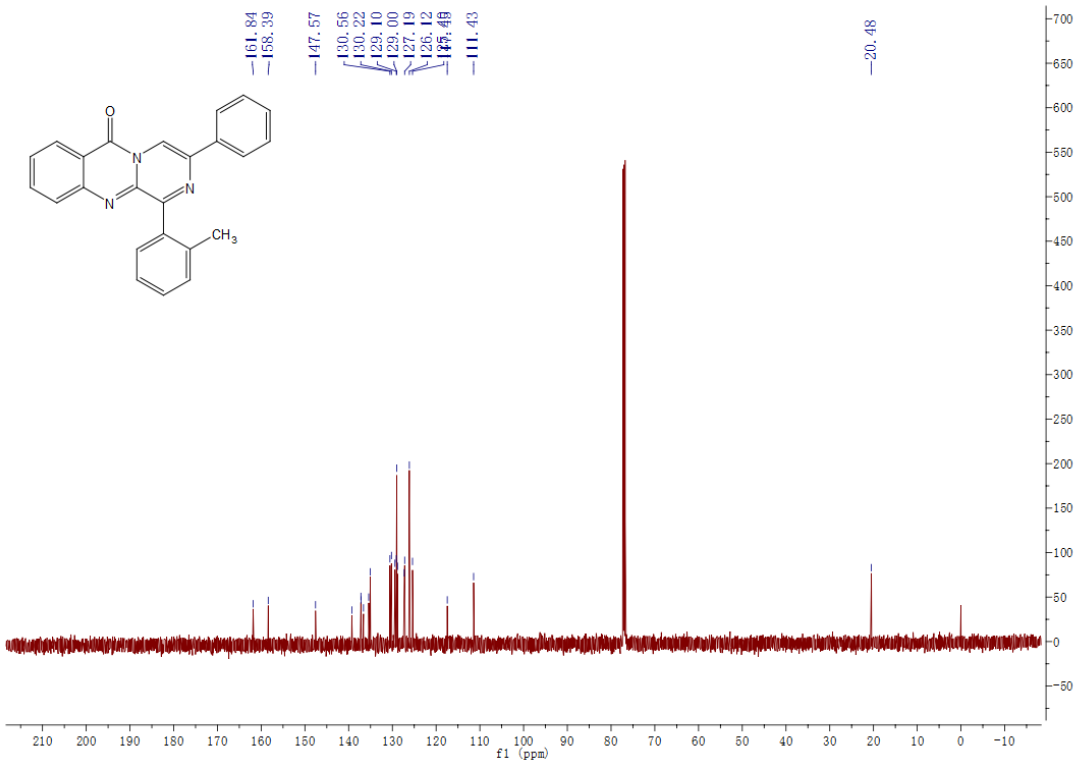
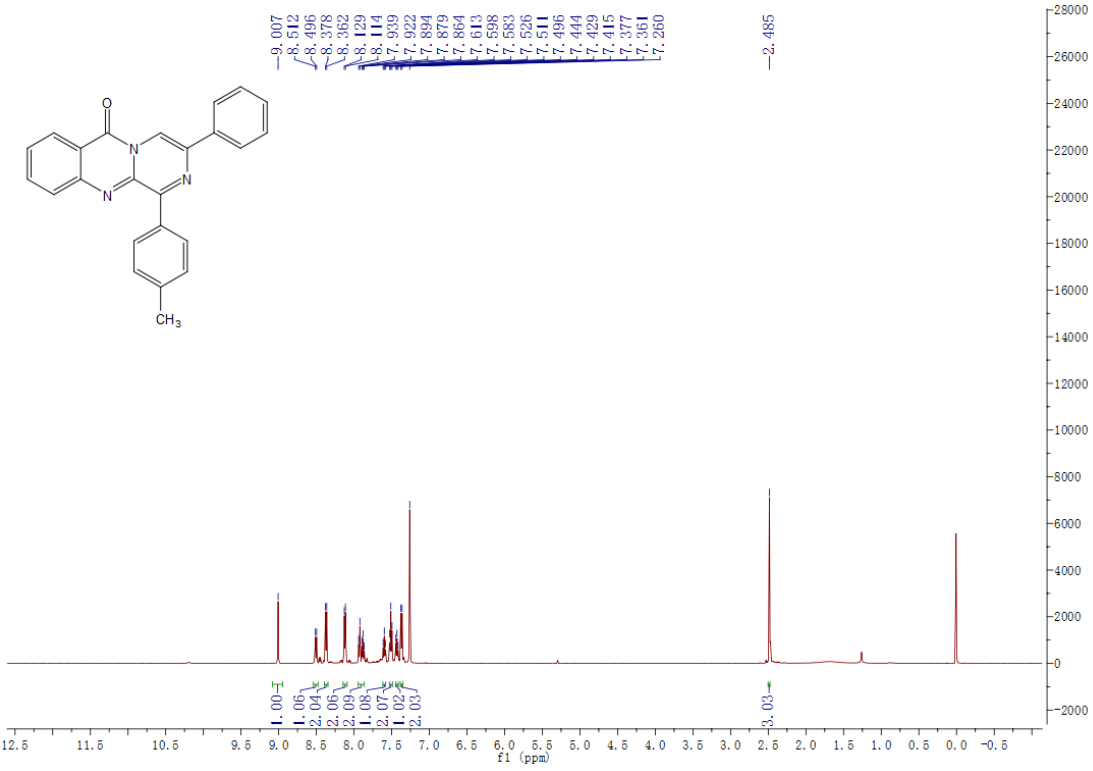


Fig. S18 ^{1}H and ^{13}C NMR spectra of **3n** in $CDCl_3$.



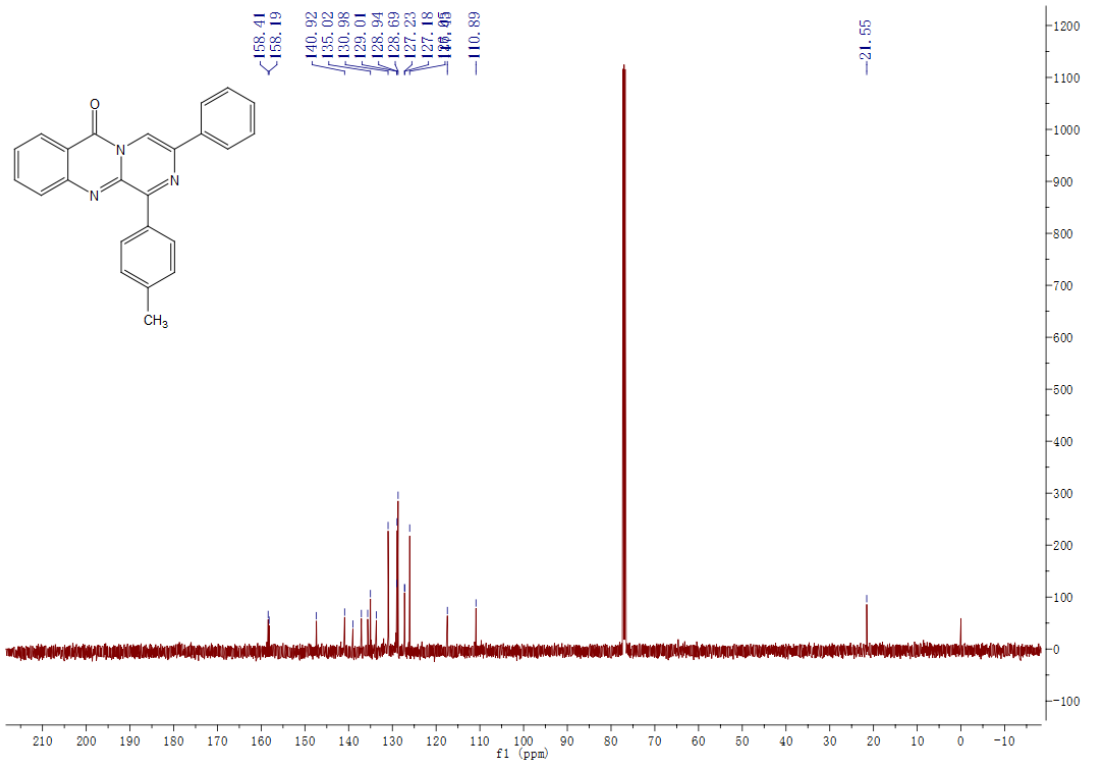
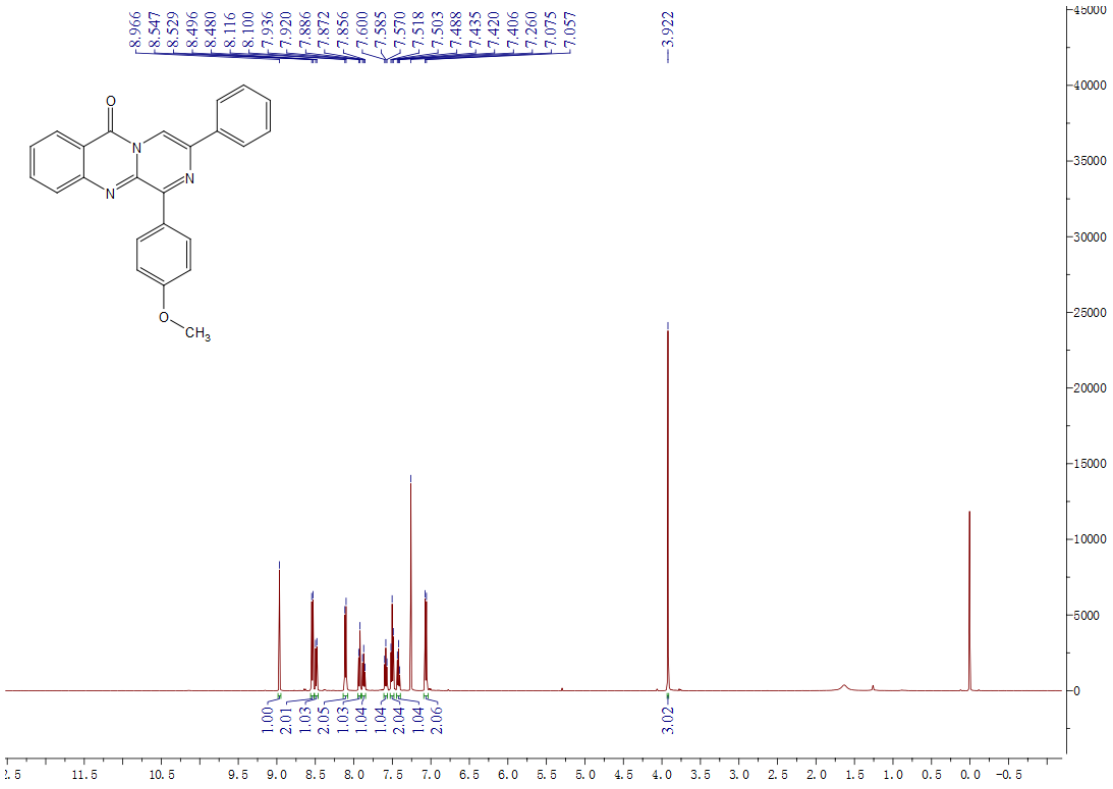


Fig. S19 ^{1}H and ^{13}C NMR spectra of **3o** in $CDCl_3$.



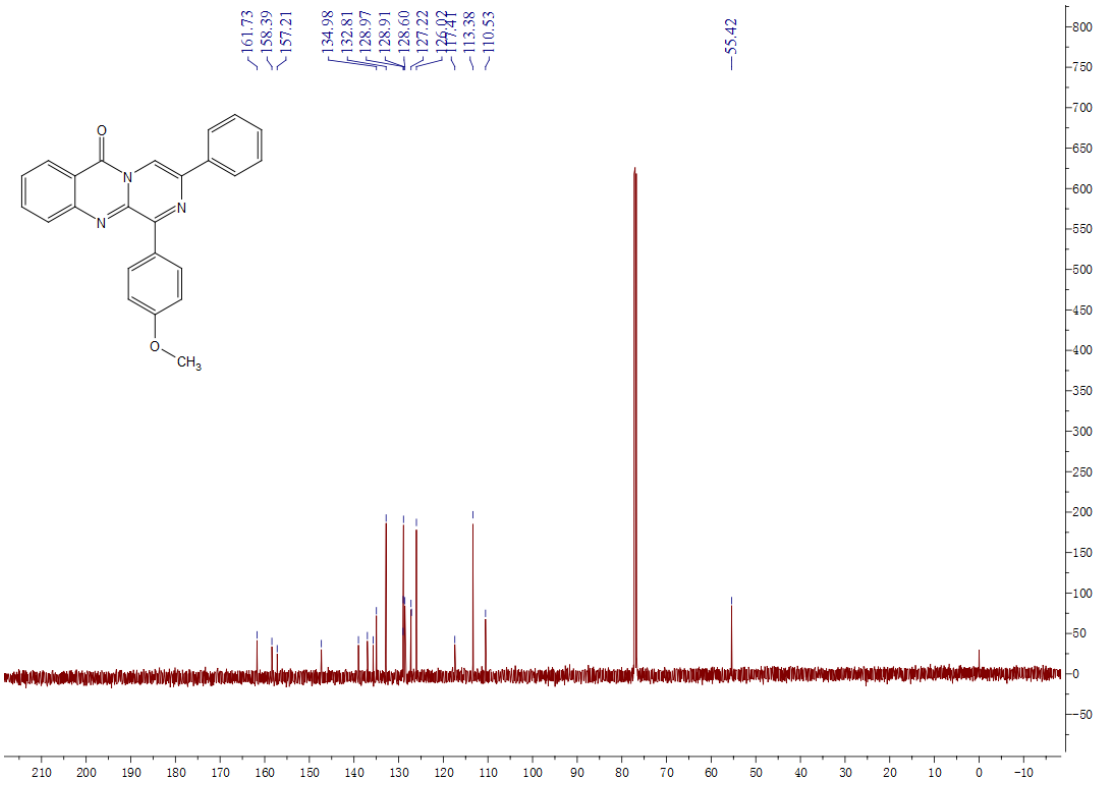
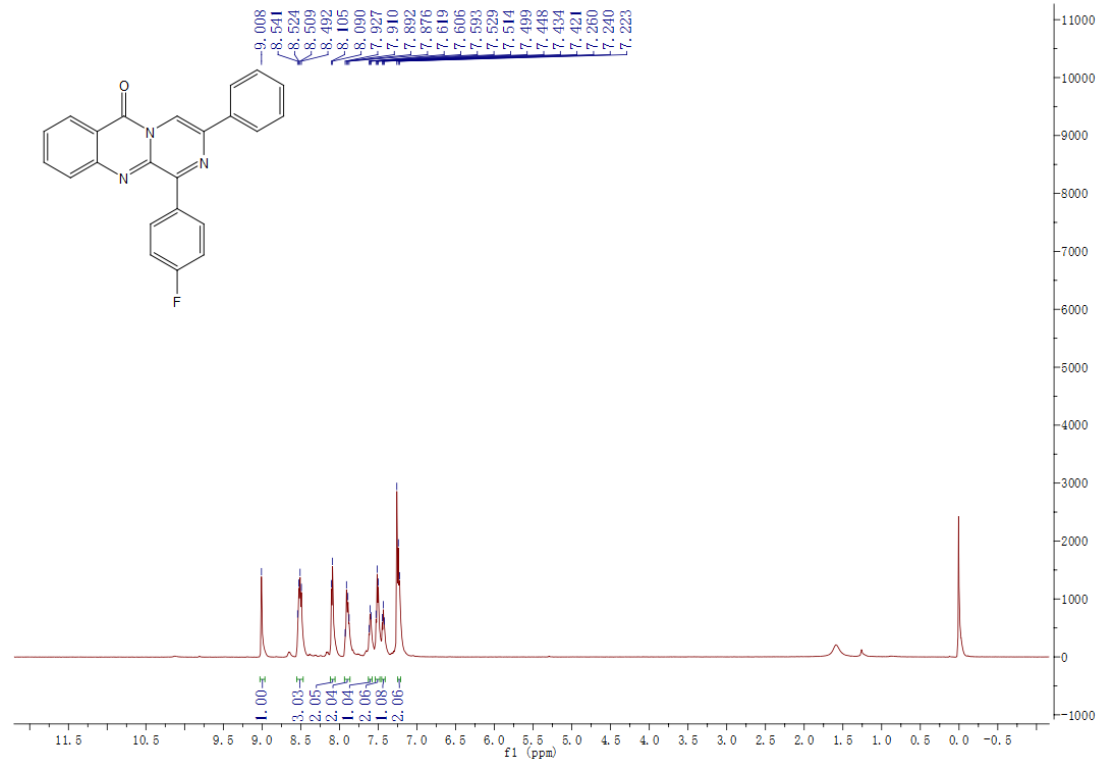


Fig. S20 ^{1}H and ^{13}C NMR spectra of **3p** in $CDCl_3$.



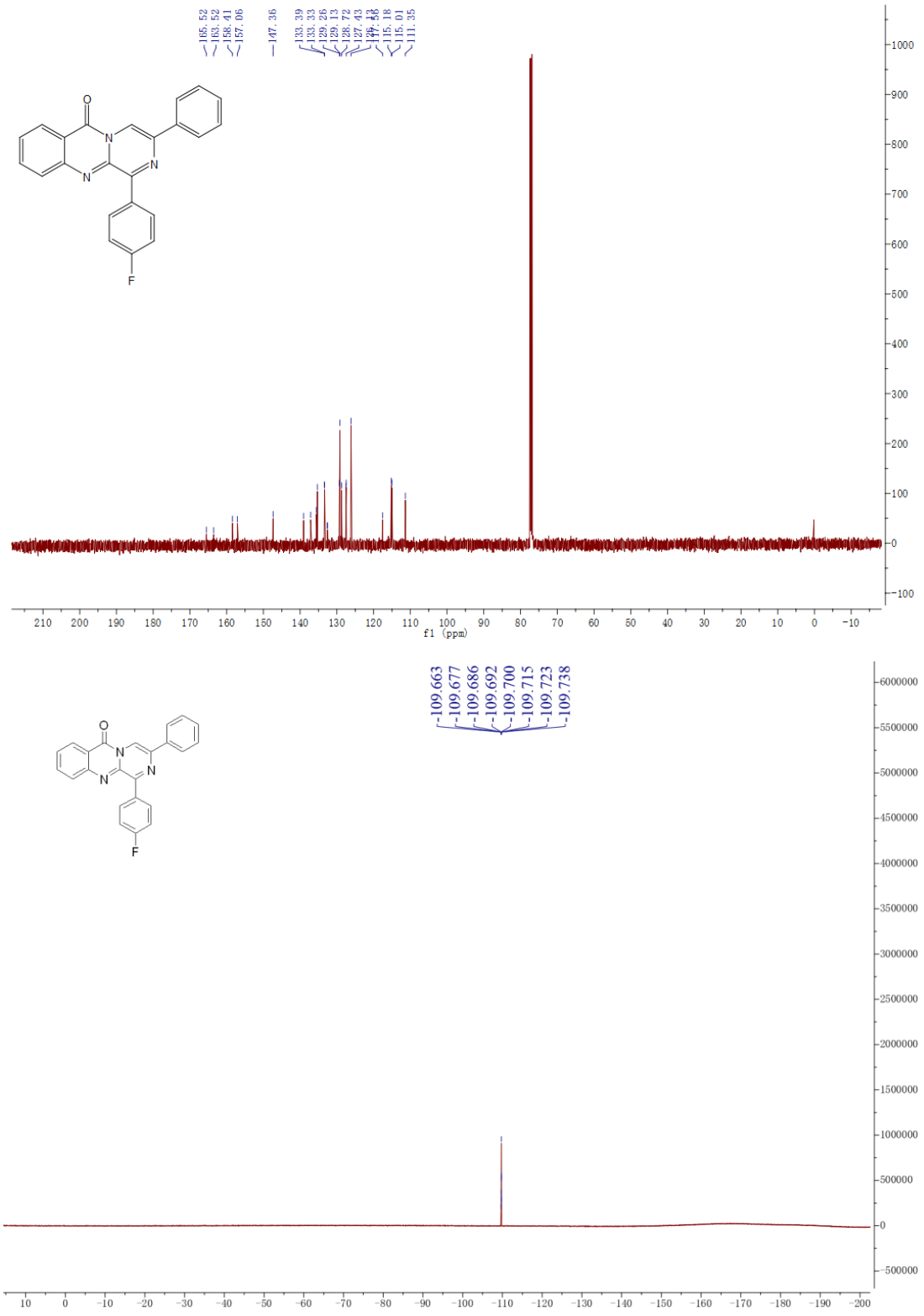
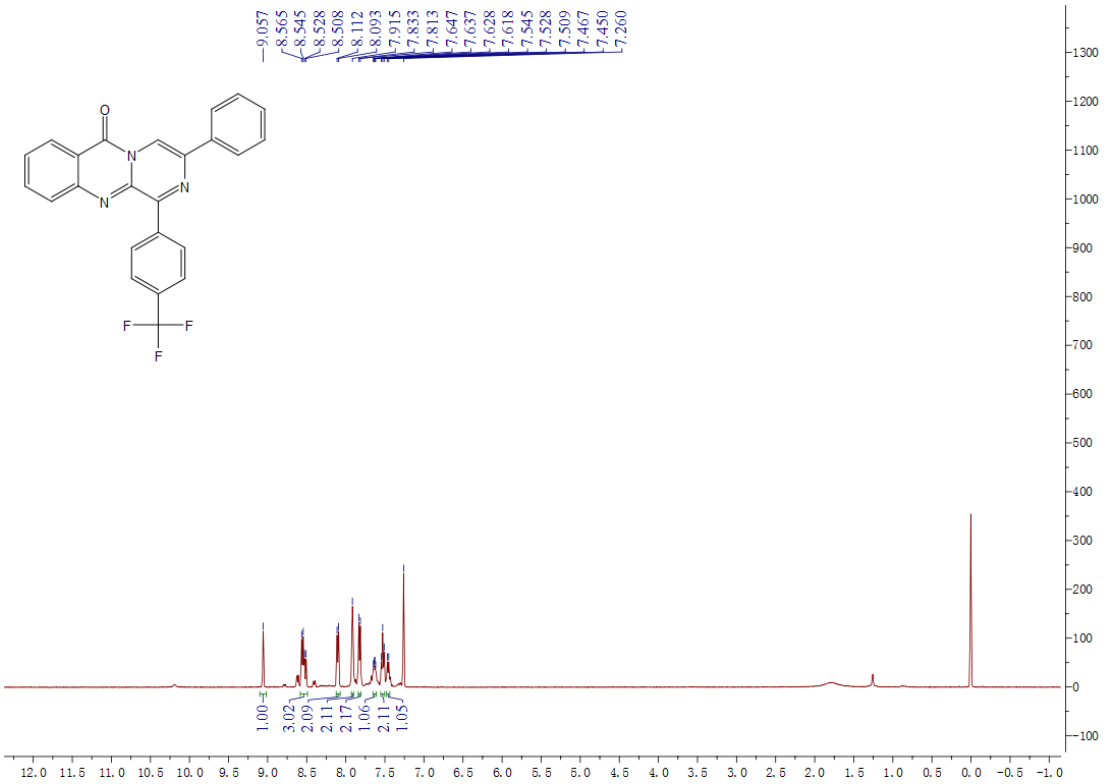
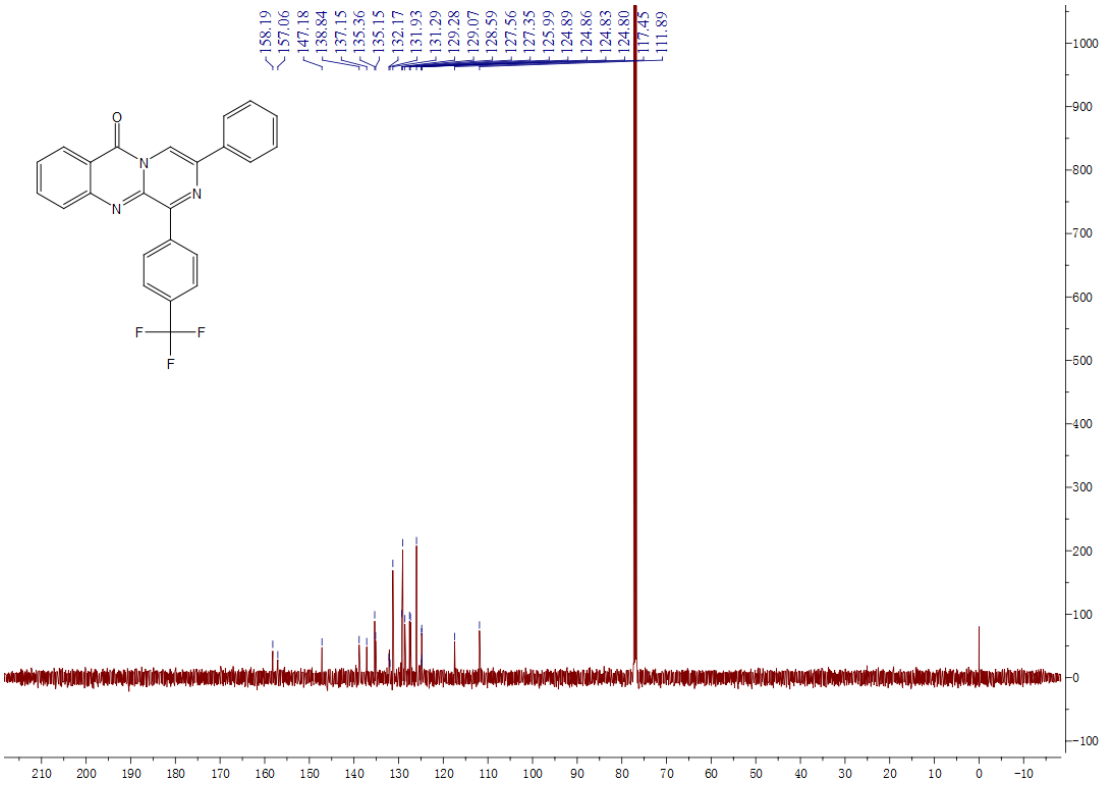


Fig. S21 ^{1}H, ^{13}C and ^{19}F NMR spectra of **3q** in $CDCl_3$.


9.057
8.565
8.545
8.528
8.508
8.112
8.093
7.915
7.833
7.813
7.647
7.637
7.628
7.618
7.545
7.528
7.509
7.467
7.450
7.260
1.00
3.02
2.09
2.11
2.17
1.06
2.11
1.05


158.19
157.06
147.18
138.84
137.15
135.36
135.15
132.17
131.93
131.29
129.28
129.07
128.59
127.56
127.35
125.99
124.89
124.86
124.83
124.80
117.45
111.89

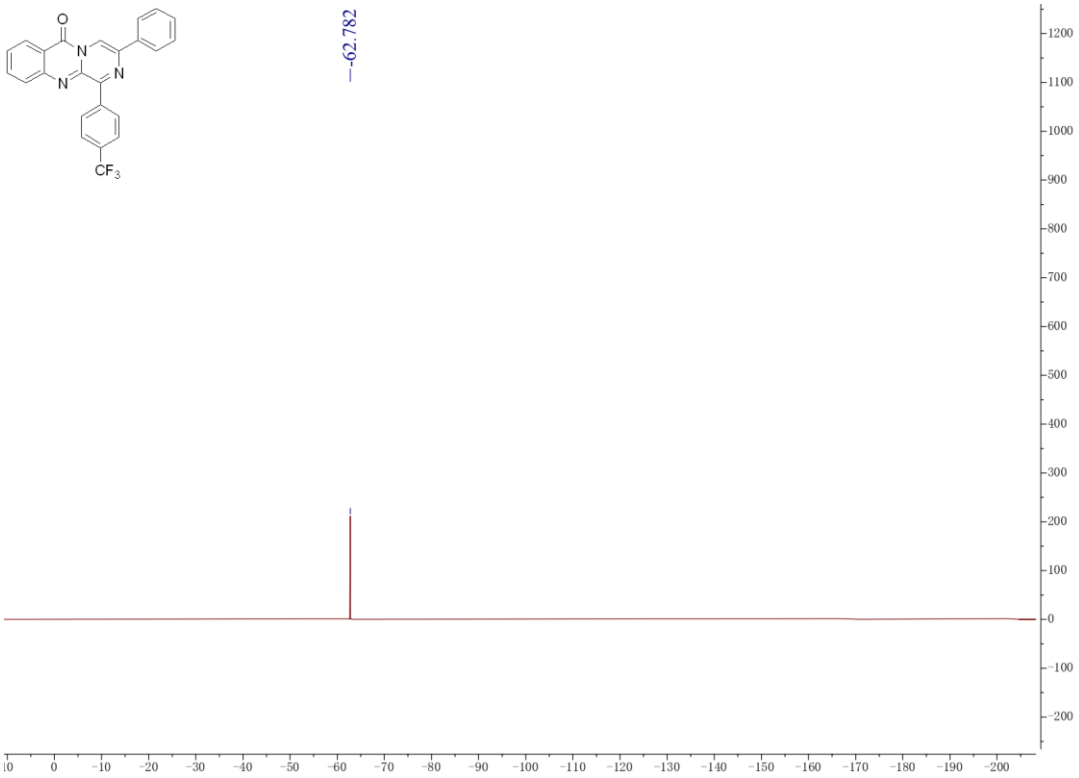
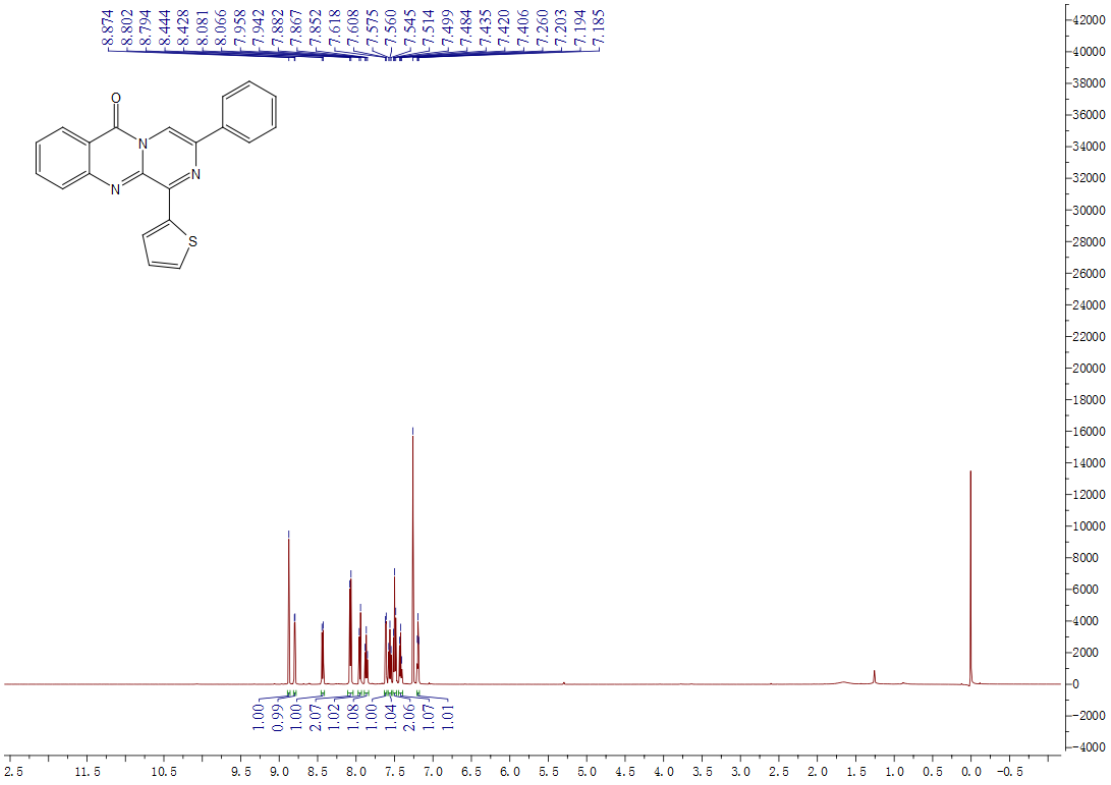


Fig. S22 ^{1}H, ^{13}C and ^{19}F NMR spectra of **3r** in $CDCl_3$.



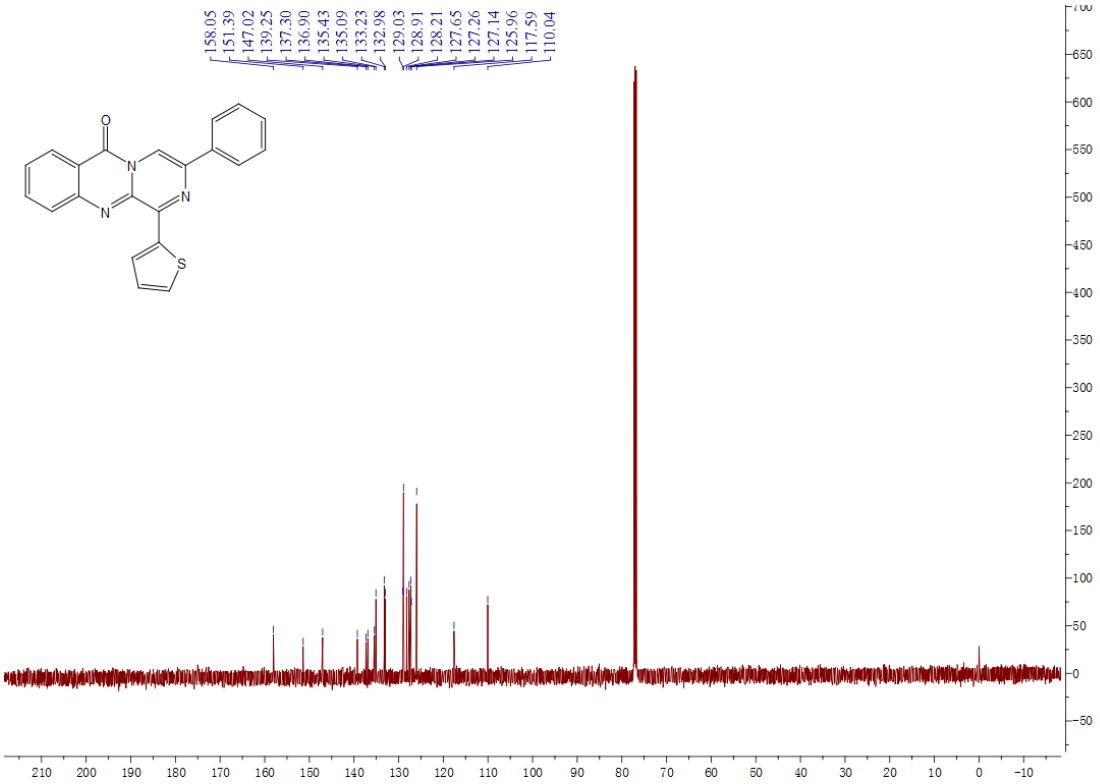
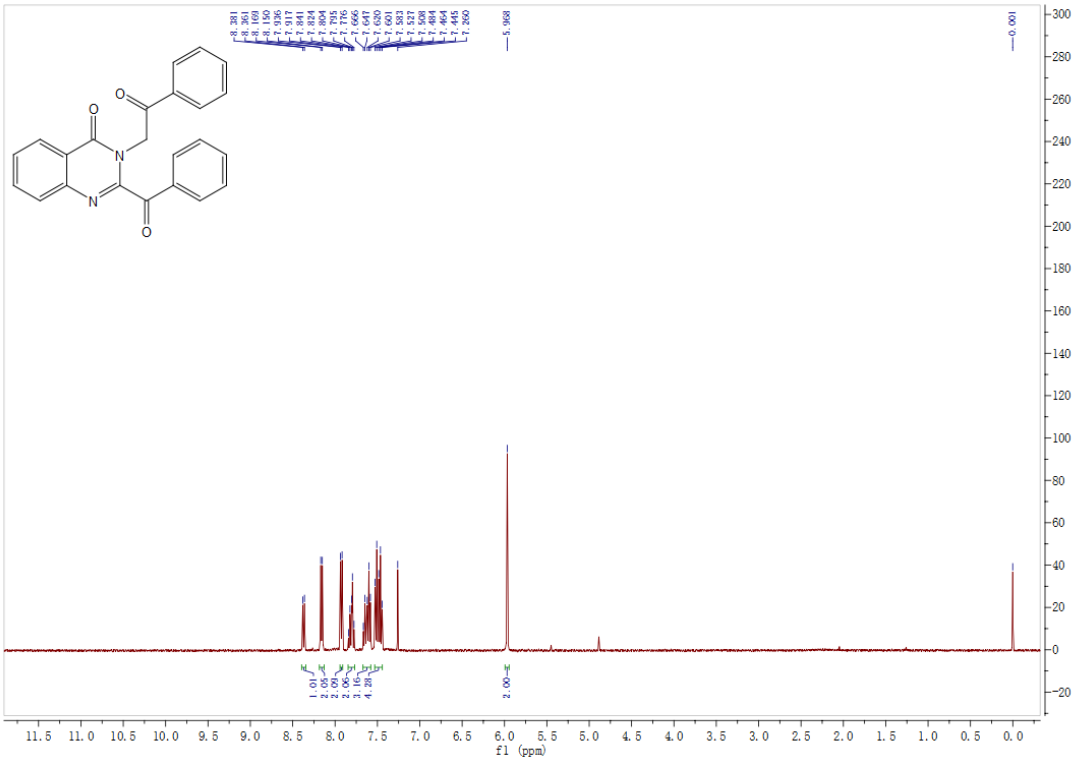


Fig. S23 ^{1}H and ^{13}C NMR spectra of **3s** in $CDCl_3$.



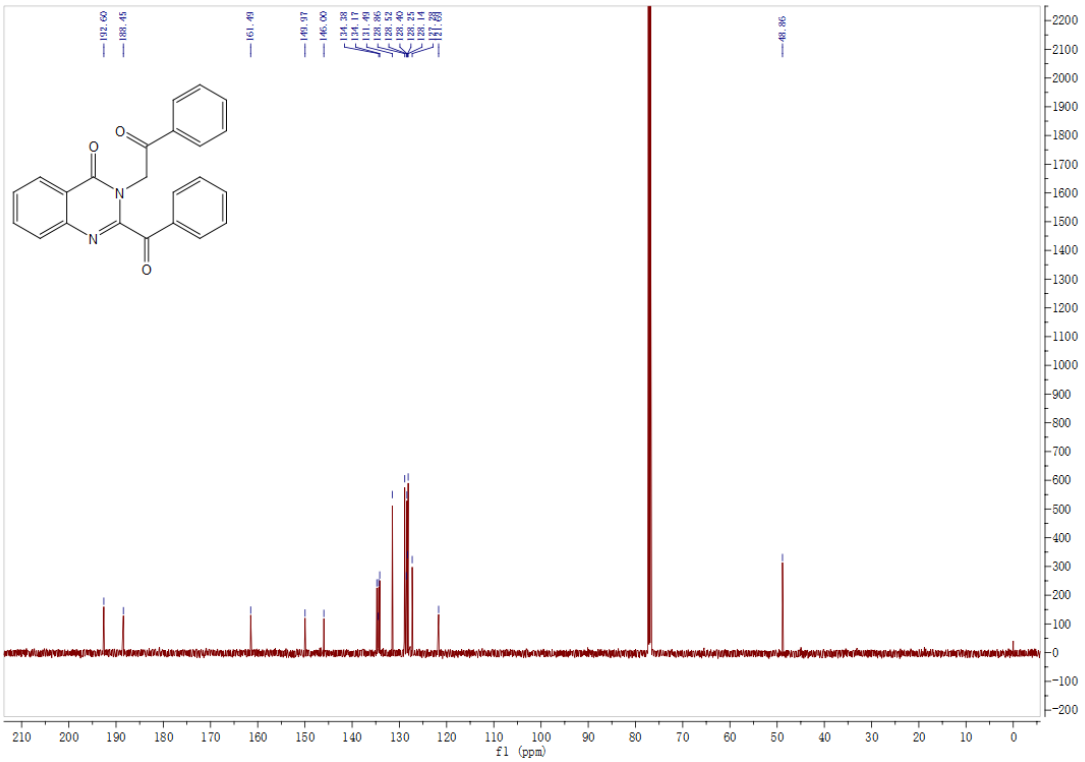
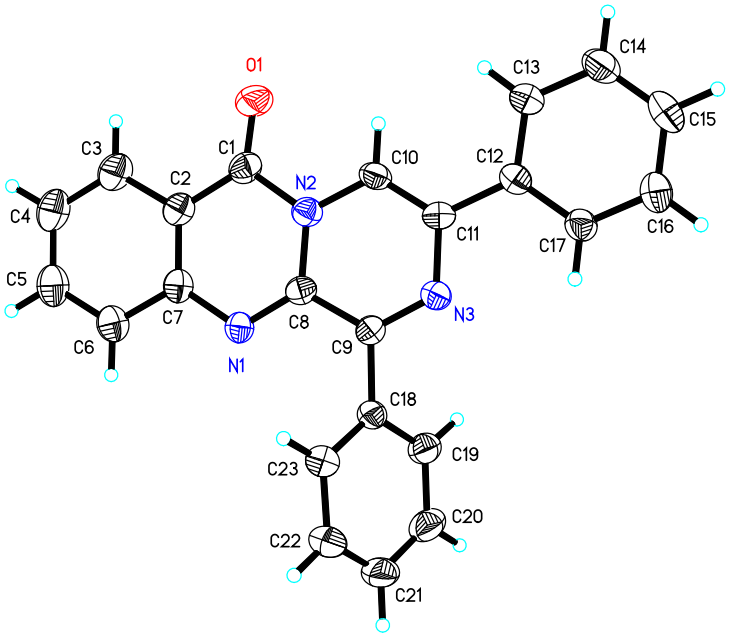


Fig. S24 ^{1}H and ^{13}C NMR spectra of **4a** in $CDCl_3$.

8. X-ray crystallographic data for product 3a



X-ray crystal structure **3a**

X-ray diffraction data for **3a** (CCDC 2034501) were collected on a SMART APEX CCD diffractometer (graphite-monochromated MoKα radiation, ϕ-ω scan technique, λ = 0.71073 Å). The intensity data were integrated by means of the SAINT program. SADABS was used to perform area-detector scaling and absorption corrections. The structure was solved by direct methods and was refined against F^2 using all reflections with the aid of the SHELXTL package. All non-hydrogen atoms were found from the difference Fourier syntheses and refined anisotropically. The H atoms were included in calculated positions with isotropic thermal parameters related to those of the supporting carbon atoms but were not included in the refinement. All calculations were performed using the Bruker Smart program.