Visible-Light-Mediated Minisci C–H Alkylation of Heteroarenes with 4-Alkyl-1,4-dihydropyridines Using O_2 as an Oxidant

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Supporting Information

1. General Information

Reagents were purchased from commercial sources and were used as received. ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were recorded on Bruker Avance 400 Ultrashield NMR spectrometers. Chemical shifts (δ) were given in parts per million (ppm) and were measured downfield from internal tetramethylsilane. High-resolution mass spectrometry (HRMS) data were obtained on an FTICR-MS instrument (Ionspec 7.0 T). The melting points were determined on an X-4 microscope melting point apparatus and are uncorrected. Conversion was monitored by thin layer chromatography (TLC). Flash column chromatography was performed over silica gel (100-200 mesh). Blue LED (36 W, λ_{max} = 470 nm) purchased from JIADENG (LS) was used for blue light irradiation. A fan attached to the apparatus was used to maintain the reaction temperature at room temperature.

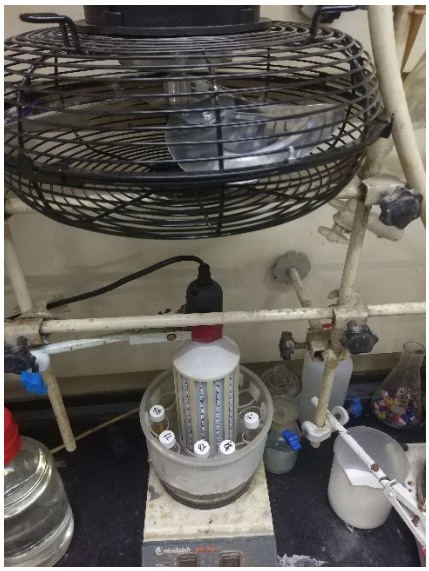


Figure S1 Photograph of the Photocatalytic reactor used for reactions conducted under blue LED irradiation.

2. Preparation of Photocatalyst

The photocatalyst was synthesized according to literature report.[1] The spectral data of the photocatalyst is consistent with the literature data. The other photocatalysts (Eosin Y, Fluorescein, $[Ru(bpy)_3]Cl_2{\cdot}6H_2O$, $Ru(bpy)_3(PF_6)_2$, $Ir(ppy)_3$ and Mes-Acr) are commercially available.

3. Preparation of 4-alkyl-1,4-dihydropyridines

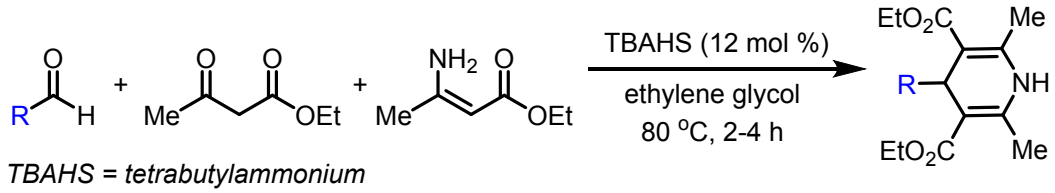
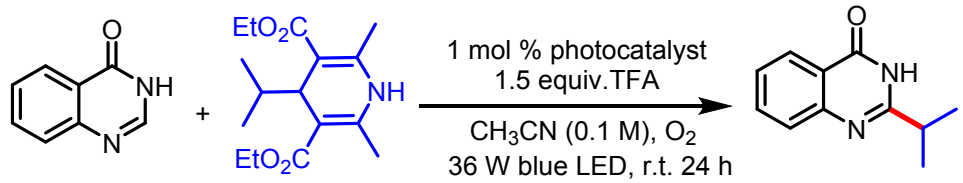


Figure S2

4-alkyl-1,4-dihydropyridines were synthesized according to literature report.[2] The spectral data is consistent with the literature data.

4. Investigation of the Key Reaction Parameters

Table S1: Screening of photocatalysts[a]

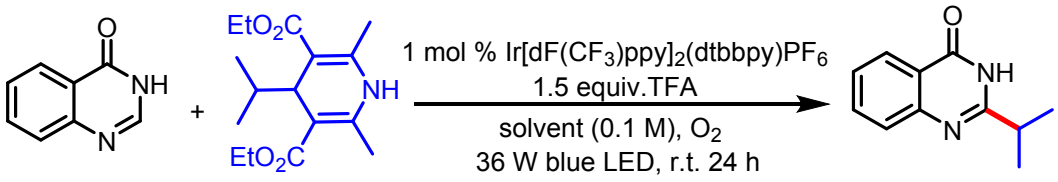


1, 1.0 equiv. **2**, 1.5 equiv. **3**

entry	photocatalyst	yield (%)[b]
1	$[Ir(dtbbpy)(ppy)_2][PF_6]$	15
2	$[Ru(bpy)_3](PF_6)_2$	12
3	$[Ru(bpy)_3]\ 6H_2O$	14
4[c]	4CzIPN	NR
5[c]	Eosin-Y	NR
6	$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$	23

[a]General conditions: **1** (0.3 mmol), **2** (0.45 mmol), photocatalyst (0.003 mmol), TFA (0.45 mmol), CH_3CN (3.0 mL), r.t, O_2 atmosphere, 24 h. [b]Yields were determined by ^1H NMR spectroscopy with dibromomethane as an internal standard. [c]Photocatalyst (0.015 mmol). NR = no reaction.

Table S2: Screening of different solvents[a]

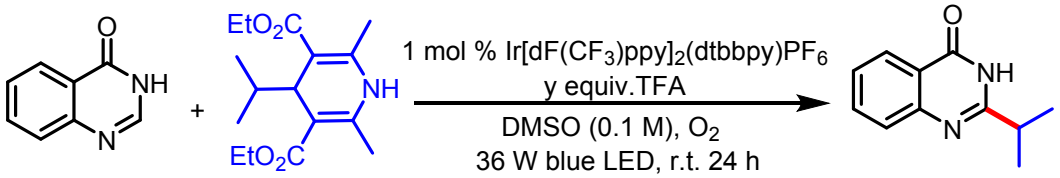


1, 1.0 equiv. **2**, 1.5 equiv. **3**

entry	solvent	yield (%)[b]
1	CH_3CN	23
2	DMSO	89 (85)[c]
3	acetone	NR
4	DCM	NR
5	CH_3CN/H_2O = 1:1	35

[a]General conditions: **1** (0.3 mmol), **2** (0.45 mmol), Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (0.003 mmol), TFA (0.45 mmol), solvent (3.0 mL), r.t, O_2 atmosphere, 24 h. [b]Yields were determined by ^{1}H NMR spectroscopy with dibromomethane as an internal standard. [c]Isolated yield.

Table S3: Screening of the amount of *i*-Pr-DHP (2) and TFA[a]



1, 1.0 equiv. **2**, x equiv. **3**

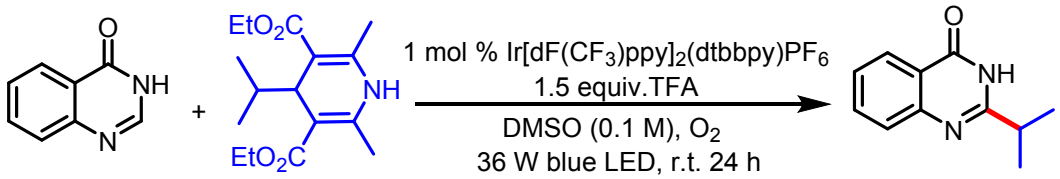
entry	x equiv. **2**	y equiv. TFA	yield (%)[b]
1	2	1.5	90
2	1.5	1.5	89
3	1.2	1.5	72
4	1.5	2.0	90
5	1.5	1.2	64

[a]General conditions: **1** (0.3 mmol), **2** (0.3x mmol), Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (0.003 mmol), TFA (0.3y mmol), DMSO (3.0 mL), r.t, O_2 atmosphere, 24 h. [b]Yields were determined by ^{1}H NMR spectroscopy with dibromomethane as an internal standard.

5. Investigation of the Mechamism

5.1 Control experiments

Table S4

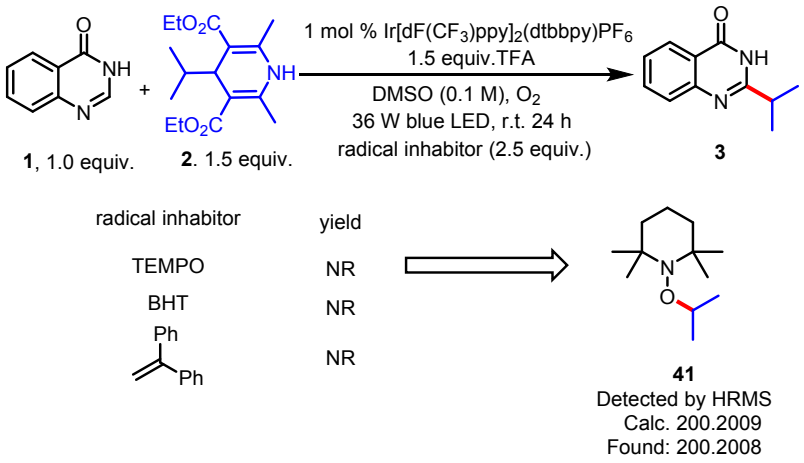


1, 1.0 equiv. **2**, 1.5 equiv. **3**

entry	control conditions	yield (%)[b]
1	w/o photocatalyst	<5
2	w/o light	NR
3	w/o TFA	NR
4	Ar	<5
5	standard conditions, w/all	89

Yields were determined by ^{1}H NMR spectroscopy with dibromomethane as an internal standard.

5.2 TEMPO, BHT and 1,1-diphenylethylene were used as radical scavengers



Scheme S1

To a 10 mL glass vial was added Ir[dF(CF_3)ppy)]$_2$(dtbbpy)PF_6 (3.36mg, 0.003 mmol, 1 mol %), **1** (0.3 mmol, 1.0 equiv), **2** (0.45 mmol, 1.5 equiv), TEMPO (117 mg, 0.75 mmol, 2.5 equiv) or BHT (165mg, 0.75 mmol, 2.5 equiv) or 1,1-diphenylethylene (135 mg, 0.75 mmol, 2.5 equiv), TFA (34 μL, 0.45 mmol, 1.5 equiv) and 3.0 mL of DMSO. The reaction mixture was degassed by bubbling with O_2 for 15 s with an outlet needle and the vial was sealed with PTFE cap. The mixture was then stirred rapidly and irradiated with a 36 W Blue LED (approximately 2 cm away from the light source) at room temperature for 24 h. The corresponding alkylated product **3** was not observed based on ^{1}H NMR analysis, and instead the corresponding product of radical trapping, 1-isopropoxy-2,2,6,6-tetramethylpiperidine (**36**), was detected by HR-MS (positive mode ESI).

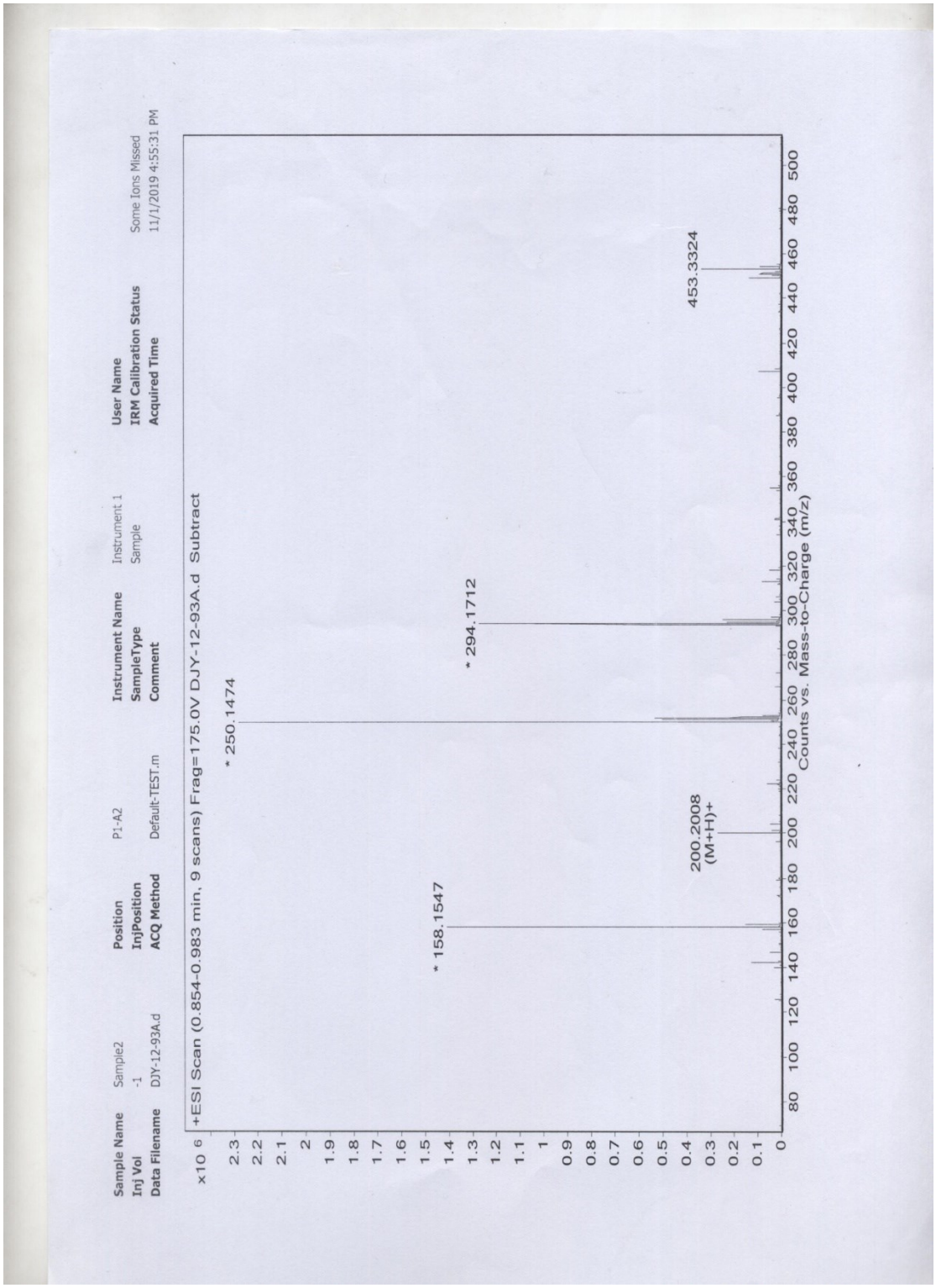


Figure S3 HR-ESI mass spectra of 1-isopropoxy-2,2,6,6-tetramethylpiperidine (**36)**

5.3 Light/dark experiment

Eight standard reaction mixtures in 10 mL glass vials were charged with $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (3.36mg, 0.003 mmol, 1 mol %), **1** (0.3 mmol, 1.0 equiv), **2** (0.45 mmol, 1.5 equiv), TFA (34 μL, 0.45 mmol, 1.5 equiv) and 3.0 mL of DMSO. The reaction

mixtures were degassed by bubbling with O_2 for 15 s with an outlet needle and the vials were sealed with PTFE caps. The mixtures were then stirred rapidly and irradiated with a 36 W Blue LED (approximately 2 cm away from the light source) at room temperature. After 2 h, the Blue LED was turned off, and one vial was removed from the irradiation setup for analysis. The remaining seven vials were stirred in the absence of light for an additional 2 h. Then, one vial was removed for analysis, and the Blue LED was turned back on to irradiate the remaining six reaction mixtures. After an additional 2 h of irradiation, the Blue LED was turned off, and one vial was removed for analysis. The remaining five vials were stirred in the absence of light for an additional 2 h. Then, a vial was removed for analysis, and the Blue LED was turned back on to irradiate the remaining four reaction mixtures. After 2 h, the Blue LED was turned off, and one vial was removed for analysis. The remaining three vials were stirred in the absence of light for an additional 2 h, then, a vial was removed for analysis and the Blue LED was turned back on to irradiate the remaining two reaction mixtures. After 2 h, the Blue LED was turned off, and one vial was removed for analysis. The last vial was stirred in the absence of light for an additional 2 h, and then it was analyzed. The yield was determined by ^{1}H NMR spectroscopy using dibromomethane as the internal standard.

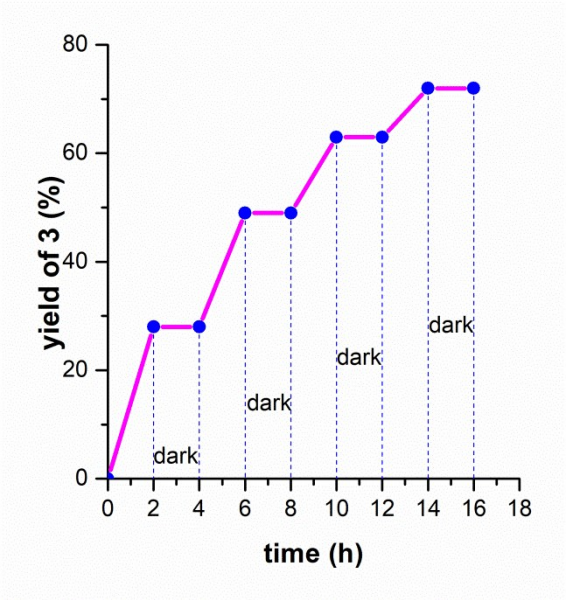


Figure S4 Light/dark experiment.

6. Experimental Procedures and Product Characterization

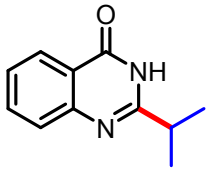
6.1 General Procedure for the alkylation of N-heteroarenes.

To a 10 mL glass vial was added Ir[dF(CF_3)ppy)]$_2$(dtbbpy)PF_6 (3.36mg, 0.003 mmol, 1 mol %), *N*-heteroarene (0.3 mmol, 1.0 equiv), 4-alkyl-1,4-dihydropyridines (0.45 mmol, 1.5 equiv), TFA (34 μL, 0.45 mmol, 1.5 equiv) and 3.0 mL of DMSO. The reaction mixture was degassed by bubbling with O_2 for 15 s with an outlet needle and the vial was sealed with PTFE cap. The mixture was then stirred rapidly and irradiated with a 36 W Blue LED (approximately 2 cm away from the light source) at room temperature for 24 h. The reaction mixture was diluted with 10 mL of aqueous 1 M $NaHCO_3$ solution, and extracted with DCM (3 × 20 mL). The combined organic extracts were washed with brine (40 mL), dried over Na_2SO_4, and concentrated in vacuo.

Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.

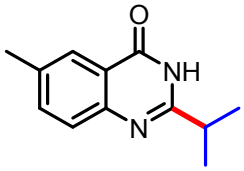
6.2. Product Characterization

2-isopropylquinazolin-4(3*H*)-one (3).



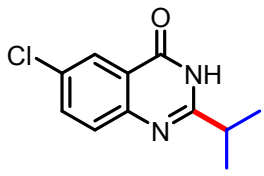
According to the *general procedure*. The spectral data is consistent with the literature data.[3]
White solid (47.9 mg, 85%). M.p. = 190 – 191 °C.
R_f 0.60 (Petroleum ether/EtOAc, 2/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.40 (s, 1H), 8.30 (dd, J = 8.0, 1.2 Hz, 1H), 7.86 – 7.67 (m, 2H), 7.56 – 7.42 (m, 1H), 3.05 (hept, J = 7.2 Hz, 1H), 1.45 (d, J = 7.2 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.4, 161.0, 149.6, 134.8, 127.5, 126.4, 126.4, 120.9, 35.1, 20.6.
HRMS (ESI) calcd for $C_{11}H_{13}N_2O$ $[M + H]^+$ 189.1022, found 189.1024.

2-isopropyl-6-methylquinazolin-4(3*H*)-one (4).



According to the *general procedure*. The spectral data is consistent with the literature data.[3a]
White solid (50.9 mg, 84%). M.p. = 220 – 221 °C.
R_f 0.50 (Petroleum ether/EtOAc, 2/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.99 (s, 1H), 8.06 (s, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 3.29 – 3.11 (m, 1H), 2.51 (s, 3H), 1.50 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.9, 161.3, 145.4, 137.5, 136.9, 126.1, 125.9, 120.1, 34.5, 21.4, 20.4.
HRMS (ESI) calcd for $C_{12}H_{15}N_2O$ $[M + H]^+$ 203.1179, found 203.1181.

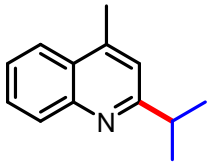
6-chloro-2-isopropylquinazolin-4(3*H*)-one (5).



According to the *general procedure*. The spectral data is consistent with the literature data.[3a]
White solid (53.9 mg, 81%). M.p. = 198 – 199 °C.
R_f 0.50 (Petroleum ether/EtOAc, 2/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.34 (s, 1H), 8.24 (d, J = 2.0 Hz, 1H), 7.75 – 7.62 (m, 2H), 3.14 – 2.95 (m, 1H), 1.44 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.8, 159.4, 148.2, 136.2, 135.3, 125.8, 123.9, 120.7, 34.9, 20.7.

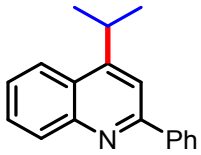
HRMS (ESI) calcd for $C_{11}H_{12}ClN_2O$ $[M + H]^+$ 223.0633, found 223.0633.

2-isopropyl-4-methylquinoline (6).



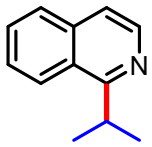
According to the *general procedure*. The spectral data is consistent with the literature data.[2a]
Yellow oil (42.2 mg, 76%).
R_f 0.70 (Petroleum ether/EtOAc, 10/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.72 – 7.61 (m, 1H), 7.53 – 7.44 (m, 1H), 7.17 (s, 1H), 3.29 – 3.13 (m, 1H), 2.67 (s, 3H), 1.38 (d, J = 7.2 Hz, 6H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 147.6, 144.5, 129.6, 129.0, 127.1, 125.5, 123.6, 119.8, 37.3, 22.6, 18.9.
HRMS (ESI) calcd for $C_{13}H_{16}N$ $[M + H]^+$ 186.1277, found 186.1279.

4-isopropyl-2-phenylquinoline (7).



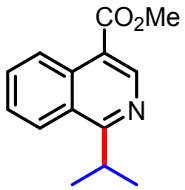
According to the *general procedure*. The spectral data is consistent with the literature data.[2d]
Yellow oil (37.8 mg, 51%).
R_f 0.40 (Petroleum ether/EtOAc, 20/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, J = 21.6, 7.6 Hz, 3H), 8.08 (d, J = 8.4 Hz, 1H), 7.77 (s, 1H), 7.69 (t, J = 7.2 Hz, 1H), 7.52 (t, J = 7.6 Hz, 3H), 7.45 (t, J = 7.2 Hz, 1H), 3.85 – 3.68 (m, 1H), 1.45 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.5, 155.0, 148.7, 140.4, 130.8, 129.3, 129.1, 128.9, 127.7, 126.1, 123.0, 115.0, 28.6, 23.1.
HRMS (ESI) calcd for $C_{18}H_{18}N$ $[M + H]^+$ 248.1434, found 248.1436.

1-isopropylisoquinoline (8).



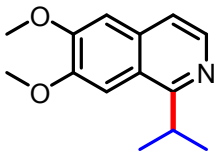
According to the *general procedure*. The spectral data is consistent with the literature data.[4]
Colorless oil (32.3 mg, 63%).
R_f 0.50 (Petroleum ether/EtOAc, 10/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 5.6 Hz, 1H), 8.22 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.70 – 7.61 (m, 1H), 7.61 – 7.54 (m, 1H), 7.48 (d, J = 5.6 Hz, 1H), 4.09 – 3.83 (m, 1H), 1.45 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.3, 141.9, 136.4, 129.6, 127.6, 126.9, 126.2, 124.8, 119.0, 30.9, 22.2.
HRMS (ESI) calcd for $C_{12}H_{14}N$ $[M + H]^+$ 172.1121, found 172.1123.

methyl 1-isopropylisoquinoline-4-carboxylate (9).



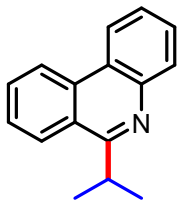
According to the *general procedure*. The spectral data is consistent with the literature data.[3b]
Colorless oil (37.8 mg, 55%).
R_f 0.50 (Petroleum ether/EtOAc, 10/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.98 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 8.4 Hz, 1H), 7.85 – 7.73 (m, 1H), 7.64 (dd, J = 11.2, 4.0 Hz, 1H), 4.07 – 3.94 (m, 4H), 1.45 (d, J = 6.8 Hz, 6H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 167.4, 145.9, 134.4, 131.3, 127.3, 125.9, 125.8, 125.1, 118.8, 52.3, 31.6, 22.2.
HRMS (ESI) calcd for $C_{14}H_{16}NO_2$ $[M + H]^+$ 230.1176, found 230.1179.

1-isopropyl-6,7-dimethoxyisoquinoline (10).



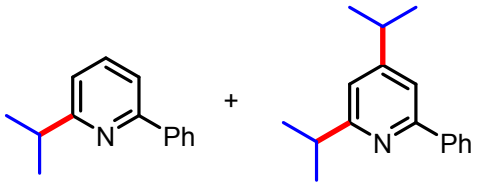
According to the *general procedure*. The spectral data is consistent with the literature data.[3c]
Yellow oil (33.3 mg, 48%).
R_f 0.30 (Petroleum ether/EtOAc, 7/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 5.6 Hz, 1H), 7.41 (s, 1H), 7.36 (d, J = 5.6 Hz, 1H), 7.06 (s, 1H), 4.04 (s, 3H), 4.02 (s, 3H), 3.90 – 3.73 (m, 1H), 1.44 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.8, 152.3, 149.9, 141.1, 133.2, 121.9, 117.9, 105.6, 103.2, 56.1, 56.0, 31.2, 22.1.
HRMS (ESI) calcd for $C_{14}H_{18}NO_2$ $[M + H]^+$ 232.1332, found 232.1334.

6-isopropylphenanthridine (11).



According to the *general procedure*. The spectral data is consistent with the literature data.[4]
Colorless oil (47.7 mg, 72%).
R_f 0.50 (Petroleum ether/EtOAc, 20/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, J = 8.4 Hz, 1H), 8.54 (d, J = 8.0 Hz, 1H), 8.33 (d, J = 8.4Hz, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.81 (t, J = 7.6 Hz, 1H), 7.71 (dt, J = 15.2, 7.6 Hz, 2H), 7.62 (dd, J = 8.0, 7.2 Hz, 1H), 4.12 – 3.90 (m, 1H), 1.55 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.9, 143.9, 133.1, 130.0, 128.5, 127.2, 126.3, 125.8, 124.8, 123.5, 122.7, 121.9, 31.6, 22.1.
HRMS (ESI) calcd for $C_{16}H_{16}N$ $[M + H]^+$ 222.1277, found 222.1281.

4-isopropyl-2-phenylpyridine (12).



(2:1 mixture)

According to the *general procedure*. A 2:1 mixture of mono- and di-substituted compound was obtained. The spectral data is consistent with the literature data.[2a]

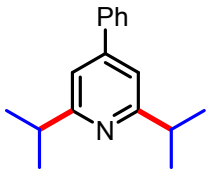
Colorless oil (31.4 mg, 48%).

R_f 0.50 (Petroleum ether/EtOAc, 10/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (t, J = 7.6 Hz, 3H), 7.65 (t, J = 7.6 Hz, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.49 – 7.42 (m, 3H), 7.41 – 7.34 (m, 2H), 7.10 (d, J = 7.6 Hz, 1H), 6.96 (s, 1H), 3.22 – 3.04 (m, 2H), 2.98 – 2.85 (m, 1H), 1.36 (dd, J = 6.8, 1.6 Hz, 10H), 1.30 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.3, 158.5, 156.6, 156.5, 140.5, 140.1, 137.1, 128.8, 128.7, 128.6, 127.2, 127.1, 119.0, 117.8, 117.4, 116.3, 36.6, 34.1, 23.4, 22.9, 22.8.

HRMS (ESI) calcd for $C_{14}H_{16}N$ $[M + H]^+$ 198.1277, found 198.1279. And $C_{17}H_{22}N$ $[M + H]^+$ 240.1747, found 240.1751.

2,6-diisopropyl-4-phenylpyridine (13).



According to the *general procedure*. The spectral data is consistent with the literature data.[3c]

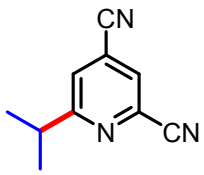
Colorless oil (25.8 mg, 36%).

R_f 0.60 (Petroleum ether/EtOAc, 10/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 7.6 Hz, 2H), 7.53 (t, J = 7.6 Hz, 2H), 7.50 – 7.43 (m, 1H), 7.24 (s, 2H), 3.27 – 3.05 (m, 2H), 1.40 (d, J = 6.8 Hz, 12H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.2, 149.3, 139.8, 129.0, 128.6, 127.3, 115.8, 36.7, 22.9.

HRMS (ESI) calcd for $C_{17}H_{22}N$ $[M + H]^+$ 240.1747, found 240.1748.

6-isopropylpyridine-2,4-dicarbonitrile (14).



According to the *general procedure*.

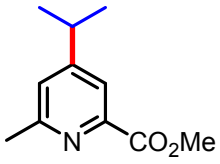
Colorless oil (16.9 mg, 33%).

R_f 0.70 (Petroleum ether/EtOAc, 7/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 7.86 (s, 1H), 3.57 – 3.27 (m, 1H), 1.44 (d, J = 7.2 Hz,

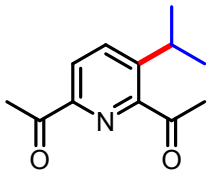
6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.7, 149.6, 132.4, 129.9, 121.0 115.9, 114.1, 31.7, 22.6.
HRMS (ESI) calcd for $C_{10}H_{10}N_3$ $[M + H]^+$ 172.0869, found 172.0870.
IR (neat) υ_{max} = 2971, 2295, 1473, 1370, 1054 cm^{-1}.

methyl 4-isopropyl-6-methylpicolinate (15).



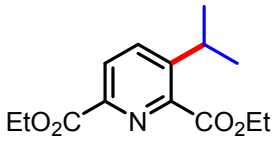
According to the *general procedure*.
Colorless oil (30.2 mg, 54%).
R_f 0.65 (Petroleum ether/EtOAc, 7/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 7.17 (s, 1H), 3.91 (s, 3H), 3.83 (dp, J = 13.6, 6.8 Hz, 1H), 2.58 (s, 3H), 1.25 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.0, 161.8, 159.4, 150.9, 122.7, 120.5, 52.1, 29.0, 24.7, 23.1.
HRMS (ESI) calcd for $C_{11}H_{16}NO_2$ $[M + H]^+$ 194.1176, found 194.1180.
IR (neat) υ_{max} = 2953, 1721, 1596, 1276, 1071 cm^{-1}.

1,1'-(3-isopropylpyridine-2,6-diyl)bis(ethan-1-one) (16).



According to the *general procedure*.
Colorless oil (30.0 mg, 49%).
R_f 0.65 (Petroleum ether/EtOAc, 7/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 3.98 – 3.75 (m, 1H), 2.75 (d, J = 10.8 Hz, 6H), 1.27 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 202.1, 199.5, 151.2, 150.0, 148.5, 136.1, 123.9, 28.9, 28.3, 25.6, 23.6.
HRMS (ESI) calcd for $C_{12}H_{16}NO_2$ $[M + H]^+$ 206.1176, found 206.1178.
IR (neat) υ_{max} = 2957, 2003, 1698, 1357, 1055 cm^{-1}.

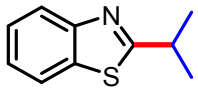
diethyl 3-isopropylpyridine-2,6-dicarboxylate (17).



According to the *general procedure*.
Colorless oil (42.1 mg, 53%).
R_f 0.65 (Petroleum ether/EtOAc, 7/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 4.47 (q, J = 7.2 Hz, 4H), 3.54 – 3.37 (m, 1H), 1.43 (t, J = 7.2 Hz, 6H), 1.29 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.5, 164.8, 149.6, 146.8, 145.7, 135.6, 126.7, 62.1, 29.4, 23.5, 14.4, 14.3.

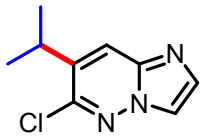
HRMS (ESI) calcd for $C_{14}H_{20}NO_4$ $[M + H]^+$ 266.1387, found 266.1388.
IR (neat) υ_{max} = 2965, 1719, 1313, 1018, 670 cm^{-1}.

2-isopropylbenzo[*d*]thiazole (18).



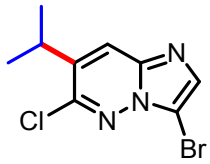
According to the *general procedure*. The spectral data is consistent with the literature data.[3a]
Colorless oil (19.1 mg, 36%).
R_f 0.60 (Petroleum ether/EtOAc, 15/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 7.6 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 3.54 – 3.34 (m, 1H), 1.49 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.7, 153.3, 134.8, 125.9, 124.7, 122.7, 121.7, 34.2, 23.0.
HRMS (ESI) calcd for $C_{10}H_{12}NS$ $[M + H]^+$ 178.0685, found 178.0688.

6-chloro-7-isopropylimidazo[1,2-*b*]pyridazine (19).



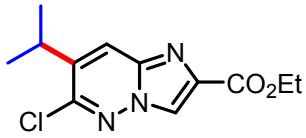
According to the *general procedure*. The spectral data is consistent with the literature data.[3a]
Colorless oil (50.9 mg, 87%).
R_f 0.75 (Petroleum ether/EtOAc, 5/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.73 (s, 1H), 6.88 (s, 1H), 3.75 – 3.62 (m, 1H), 1.42 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.1, 147.4, 137.9, 133.3, 117.3, 114.3, 29.2, 21.6.
HRMS (ESI) calcd for $C_9H_{11}ClN_3$ $[M + H]^+$ 196.0636, found 196.0637.

3-bromo-6-chloro-7-isopropylimidazo[1,2-*b*]pyridazine (20).



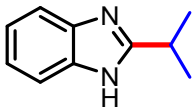
According to the *general procedure*. The spectral data is consistent with the literature data.[3a]
Colorless oil (67.1mg, 82%).
R_f 0.80 (Petroleum ether/EtOAc, 5/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 6.94 (s, 1H), 3.68 (hept, J = 6.8 Hz, 1H), 1.42 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.4, 148.5, 138.6, 133.7, 114.7, 101.3, 28.9, 21.7.
HRMS (ESI) calcd for $C_9H_{10}BrClN_3$ $[M + H]^+$ 273.9741, found 273.9742.

ethyl 6-chloro-7-isopropylimidazo[1,2-*b*]pyridazine-2-carboxylate (21).



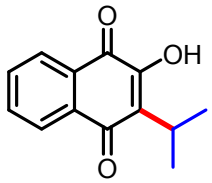
According to the *general procedure*. The spectral data is consistent with the literature data.[3a]
Colorless oil (48.9 mg, 61%).
R_f 0.50 (Petroleum ether/EtOAc, 7/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.07 (s, 1H), 4.46 (q, J = 7.2 Hz, 2H), 3.78 – 3.62 (m, 1H), 1.43 (dt, J = 7.2, 3.6 Hz, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.5, 149.4, 148.9, 141.1, 139.9, 120.60, 116.9, 61.1, 29.3, 21.6, 14.5.
HRMS (ESI) calcd for $C_{12}H_{15}ClN_3O_2$ $[M + H]^+$ 268.0847, found 268.0848.

2-isopropyl-1*H*-benzo[*d*]imidazole (22).



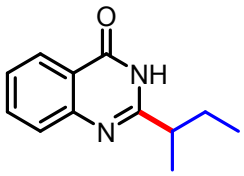
According to the *general procedure*. The spectral data is consistent with the literature data.[3d]
Colorless oil (23.5 mg, 49%).
R_f 0.40 (DCM/MeOH, 20/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, J = 6.0, 3.2 Hz, 2H), 7.20 (dd, J = 6.0, 3.2 Hz, 2H), 3.41 – 3.20 (m, 1H), 1.47 (d, J = 7.2 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.2, 138.5, 122.2, 114.8, 29.2, 21.7.
HRMS (ESI) calcd for $C_{10}H_{13}N_2$ $[M + H]^+$ 161.1073, found 161.1076.

2-hydroxy-3-isopropylnaphthalene-1,4-dione (23).



According to the *general procedure*.
Yellow solid (46.6 mg, 72%). M.p. = 84 – 85 °C.
R_f 0.50 (Petroleum ether/EtOAc, 10/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 6.0 Hz, 1H), 8.06 (d, J = 6.0 Hz, 1H), 7.75 (t, J = 6.0 Hz, 1H), 7.68 (d, J = 6.0 Hz, 1H), 7.47 (s, 1H), 3.43 (dd, J = 6.8, 4.4 Hz, 1H), 1.32 (dd, J = 6.8, 2.0 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 184.6, 182.0, 152.9, 135.0, 133.3, 132.8, 129.3, 128.9, 127.0, 126.1, 24.8, 19.9.
HRMS (ESI) calcd for $C_{13}H_{13}O_3$ $[M + H]^+$ 217.0859, found 217.0860.
IR (neat) υ_{max} = 3373, 2962, 1658, 1273, 725 cm^{-1}.

(*R*)-2-(*sec*-butyl)quinazolin-4(3*H*)-one (24).



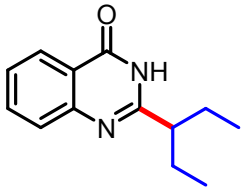
According to the *general procedure*. The spectral data is consistent with the literature data.[2a]
White solid (49.1 mg, 81%). M.p. = 173 – 174 °C.

R_f 0.50 (Petroleum ether/EtOAc, 2/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.01 (s, 1H), 8.31 (d, J = 7.6 Hz, 1H), 7.76 (ddd, J = 15.2, 11.2, 4.4 Hz, 2H), 7.54 – 7.42 (m, 1H), 2.95 – 2.74 (m, 1H), 1.98 (dt, J = 14.8, 7.6 Hz, 1H), 1.84 – 1.67 (m, 1H), 1.45 (d, J = 7.2 Hz, 3H), 0.99 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.5, 160.6, 149.6, 134.8, 127.5, 126.3, 120.8, 42.3, 28.2, 18.3, 12.1.

HRMS (ESI) calcd for $C_{12}H_{15}N_2O$ $[M + H]^+$ 203.1179, found 203.1181.

2-(pentan-3-yl)quinazolin-4(3*H*)-one (25).



According to the *general procedure*. The spectral data is consistent with the literature data.[2a]

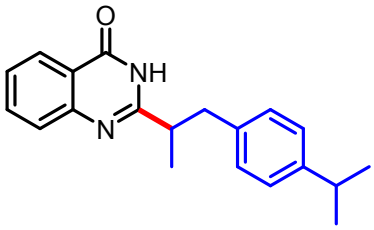
White solid (57.7 mg, 89%). M.p. = 141 – 142 °C.

R_f 0.50 (Petroleum ether/EtOAc, 3/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.46 (s, 1H), 8.30 (d, J = 7.6 Hz, 1H), 7.76 (ddd, J = 14.4, 10.8, 4.3 Hz, 2H), 7.58 – 7.41 (m, 1H), 2.60 (tt, J = 9.2, 5.6 Hz, 1H), 1.97 – 1.77 (m, 4H), 0.95 (t, J = 7.2 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.1, 159.5, 149.6, 134.8, 127.6, 126.4, 120.9, 50.2, 26.6, 12.2.

HRMS (ESI) calcd for $C_{13}H_{17}N_2O$ $[M + H]^+$ 217.1335, found 217.1338.

(*R*)-2-(1-(4-isopropylphenyl)propan-2-yl)quinazolin-4(3*H*)-one (26).



According to the *general procedure*. The spectral data is consistent with the literature data.[2a]

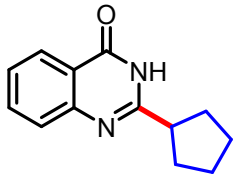
Pale oil (67.0 mg, 73%).

R_f 0.50 (Petroleum ether/EtOAc, 2/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.90 (s, 1H), 8.33 (d, J = 7.6 Hz, 1H), 7.78 (ddd, J = 12.4, 9.6, 4.4 Hz, 2H), 7.59 – 7.45 (m, 1H), 7.22 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 3.25 (dd, J = 13.2, 6.4 Hz, 1H), 3.17 (dd, J = 14.8, 6.8 Hz, 1H), 2.87 (ddd, J = 20.8, 13.6, 7.6 Hz, 2H), 1.41 (d, J = 6.8 Hz, 3H), 1.20 (dd, J = 6.8, 2.0 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.4, 160.0, 149.7, 147.0, 136.7, 134.8, 129.3, 127.6, 126.6, 126.5, 126.4, 120.9, 42.4, 40.9, 33.8, 24.2, 24.1, 17.9.

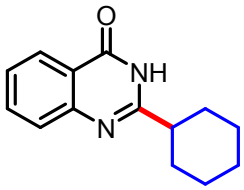
HRMS (ESI) calcd for $C_{20}H_{23}N_2O$ $[M + H]^+$ 307.1805, found 307.1807.

2-cyclopentylquinazolin-4(3*H*)-one (27).



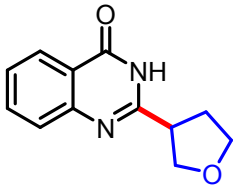
According to the *general procedure*. The spectral data is consistent with the literature data.[3a]
White solid (47.5 mg, 74%). M.p. = 188 – 189 °C.
R_f 0.50 (Petroleum ether/EtOAc, 2/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.35 (s, 1H), 8.27 (d, J = 7.6 Hz, 1H), 7.83 – 7.66 (m, 2H), 7.46 (t, J = 7.6 Hz, 1H), 3.16 (p, J = 8.4 Hz, 1H), 2.25 – 2.11 (m, 2H), 2.09 – 1.98 (m, 2H), 1.96 – 1.85 (m, 2H), 1.77 – 1.70 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.3, 159.8, 149.6, 134.8, 127.5, 126.3, 120.8, 45.7, 31.5, 26.0.
HRMS (ESI) calcd for $C_{13}H_{15}N_2O$ $[M + H]^+$ 215.1179, found 215.1181.

2-cyclohexylquinazolin-4(3*H*)-one (28).



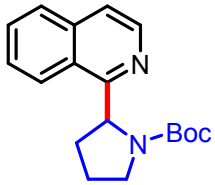
According to the *general procedure*. The spectral data is consistent with the literature data.[3a]
White solid (53.4 mg, 78%). M.p. = 189 – 190 °C.
R_f 0.40 (Petroleum ether/EtOAc, 2/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.78 (s, 1H), 8.29 (d, J = 7.6 Hz, 1H), 7.86 – 7.68 (m, 2H), 7.47 (t, J = 7.2 Hz, 1H), 2.74 (dd, J = 16.4, 7.6 Hz, 1H), 2.06 (d, J = 11.6 Hz, 2H), 1.93 (d, J = 11.6 Hz, 2H), 1.78 (dd, J = 23.6, 11.2 Hz, 3H), 1.44 (dd, J = 23.2, 16.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.4, 160.4, 149.7, 134.8, 127.5, 126.4, 126.3, 120.9, 44.9, 30.6, 26.2, 25.8.
HRMS (ESI) calcd for $C_{14}H_{17}N_2O$ $[M + H]^+$ 229.1335, found 229.1338.

(*R*)-2-(tetrahydrofuran-3-yl)quinazolin-4(3*H*)-one (29).



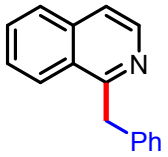
According to the *general procedure*. The spectral data is consistent with the literature data.[3a]
White solid (29.8 mg, 46%). M.p. = 192 – 193 °C.
R_f 0.40 (EtOAc).
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.26 (s, 1H), 8.27 (d, J = 7.2 Hz, 1H), 7.77 (t, J = 7.2 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.48 (t, J = 7.2 Hz, 1H), 4.24 – 4.05 (m, 3H), 3.98 – 3.84 (m, 1H), 3.62 – 3.45 (m, 1H), 2.59 – 2.26 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.0, 156.9, 149.1, 134.9, 127.6, 126.8, 126.4, 120.9, 71.5, 68.4, 44.6, 31.2.
HRMS (ESI) calcd for $C_{12}H_{13}N_2O_2$ $[M + H]^+$ 217.0972, found 217.0967.

***tert*-butyl (*S*)-2-(isoquinolin-1-yl)pyrrolidine-1-carboxylate (30).**



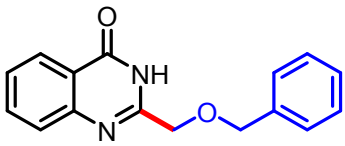
According to the *general procedure*. The spectral data is consistent with the literature data.[5]
Yellow solid (79.6 mg, 89%); M.p. = 70 – 71 °C.
R_f 0.35 (Petroleum ether/EtOAc, 4/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 5.3 Hz, 1H), 8.28 – 8.13 (m, 1H), 7.90 – 7.76 (m, 1H), 7.74 – 7.44 (m, 3H), 5.97 – 5.52 (m, 1H), 3.89 – 3.60 (m, 2H), 2.54 – 2.41 (m, 1H), 2.13 – 1.87 (m, 3H), 1.45 (s, 3H), 0.92 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.2 and 161.1, 154.7 and 154.4, 141.9, 136.5 and 136.3, 129.7, 127.6 and 127.0, 124.4 and 124.1, 119.8 and 119.6, 79.2 and 78.8, 59.6 and 58.7, 47.4 and 47.2, 34.0 and 33.1, 28.1 and 28.0, 24.1 and 23.9.
HRMS (ESI) calcd for $C_{18}H_{23}N_2O_2$ $[M + H]^+$ 299.1754, found 299.1757.

1-benzylisoquinoline (31).



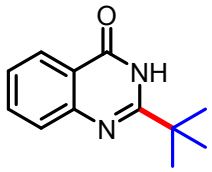
According to the *general procedure*. The spectral data is consistent with the literature data.[6]
Yellow oil (30.4 mg, 51%).
R_f 0.30 (Petroleum ether/EtOAc, 5/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 5.6 Hz, 1H), 8.11 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.53 – 7.43 (m, 2H), 7.30 – 7.19 (m, 4H), 7.13 (t, J = 7.2 Hz, 1H), 4.65 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.2, 142.1, 139.5, 136.6, 129.9, 128.6, 128.5, 127.4, 127.2, 126.3, 125.8, 119.8, 42.1.
HRMS (ESI) calcd for $C_{16}H_{14}N$ $[M + H]^+$ 200.1121, found 200.1124.

2-((benzyloxy)methyl)quinazolin-4(3*H*)-one (32).



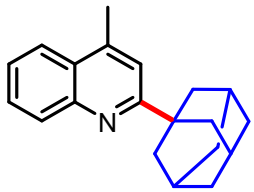
According to the *general procedure*. The spectral data is consistent with the literature data.[2a]
White solid (41.5 mg, 52%). M.p. = 159 – 160 °C.
R_f 0.60 (Petroleum ether/EtOAc, 2/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.27 (dd, J = 8.0, 1.0 Hz, 1H), 7.82 – 7.71 (m, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.41 – 7.29 (m, 5H), 4.70 (s, 2H), 4.56 (s, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 152.8, 148.7, 136.4, 134.9, 128.8, 128.6, 128.3, 127.1, 126.9, 126.8, 121.7, 73.9, 68.7.
HRMS (ESI) calcd for $C_{16}H_{15}N_2O_2$ $[M + H]^+$ 267.1128, found 267.1128.

2-(*tert*-butyl)quinazolin-4(3*H*)-one (33).



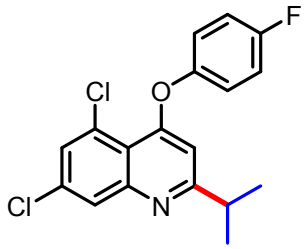
According to the *general procedure*. The spectral data is consistent with the literature data.[3a]
White solid (48.5 mg, 80%). M.p. = 150– 151 °C.
R_f 0.70 (Petroleum ether/EtOAc, 2/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.37 (s, 1H), 8.29 (d, J = 8.0 Hz, 1H), 7.75 (dt, J = 14.8, 4.8 Hz, 2H), 7.51 – 7.40 (m, 1H), 1.51 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.1, 162.3, 149.3, 134.6, 127.8, 126.4, 126.3, 120.7, 37.6, 28.4.
HRMS (ESI) calcd for $C_{12}H_{15}N_2O$ $[M + H]^+$ 203.1179, found 203.1182.

2-(adamantan-1-yl)-4-methylquinoline (34).



According to the *general procedure*. The spectral data is consistent with the literature data.[7]
White solid (69.0 mg, 83%). M.p. = 105 – 106 °C.
R_f 0.65 (Petroleum ether/EtOAc, 40/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.33 (s, 1H), 2.69 (s, 3H), 2.20 – 2.08 (m, 9H), 1.84 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.8, 147.6, 143.6, 130.1, 128.7, 126.8, 125.4, 123.5, 118.6, 41.93, 39.6, 37.0, 28.9, 19.1.
HRMS (ESI) calcd for $C_{20}H_{24}N$ $[M + H]^+$ 278.1903, found 278.1900.

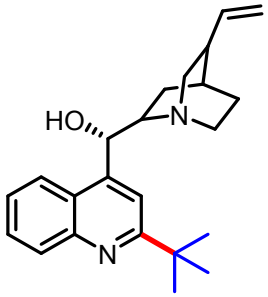
5,7-dichloro-4-(4-fluorophenoxy)-2-isopropylquinoline (35).



According to the *general procedure*.
Red solid (63.9 mg, 61%). M.p. = 54 – 55 °C.
R_f 0.70 (Petroleum ether/EtOAc, 7/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 2.0 Hz, 1H), 7.52 (d, J = 2.0 Hz, 1H), 7.16 (qd, J = 9.2, 3.7 Hz, 4H), 6.56 (s, 1H), 3.12 – 2.97 (m, 1H), 1.27 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.5, 162.5, 159.9 (d, J = 244.2 Hz), 151.5, 150.4, 134.9, 130.0, 128.8, 127.7, 122.1 (d, J = 8.5 Hz), 117.2, 117.0, 105.5, 37.2, 22.2.
HRMS (ESI) calcd for $C_{18}H_{15}Cl_2FNO$ $[M + H]^+$ 350.0509, found 350.0512.

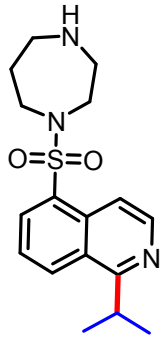
IR (neat) υ_{max} = 2964, 1599, 1551, 1196, 741 cm^{-1}.

(1S)-(2-(*tert*-butyl)quinolin-4-yl)((1*S*,4S)-5-vinylquinuclidin-2-yl)methanol (36).



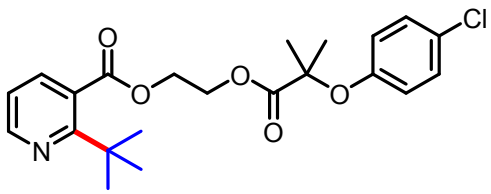
According to the *general procedure*. The spectral data is consistent with the literature data.[2a]
White solid (42.0 mg, 40%). M.p. = 172 – 173 °C.
R_f 0.50 (CH_2Cl_2/MeOH, 20/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, J = 8.4, 0.8 Hz, 1H), 8.04 – 7.99 (m, 1H), 7.65 (ddd, J = 8.4, 6.8, 1.2 Hz, 1H), 7.49 (ddd, J = 8.4, 6.8, 1.2 Hz, 1H), 7.36 (s, 1H), 6.07 – 5.90 (m, 1H), 5.18 – 5.06 (m, 2H), 3.44 (dd, J = 13.2, 4.8 Hz, 1H), 3.20 – 3.10 (m, 1H), 3.08 – 2.88 (m, 5H), 2.36 – 2.22 (m, 1H), 1.60 – 1.49 (m, 3H), 1.46 (s, 9H), 1.37 – 1.29 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.7, 147.8, 144.7, 140.6, 130.3, 128.7, 126.1, 125.6, 123.3, 118.8, 114.7, 56.0, 49.4, 47.7, 40.0, 38.0, 37.8, 30.2, 28.0, 27.9, 26.5.
HRMS (ESI) calcd for $C_{23}H_{31}N_2O$ $[M + H]^+$ 351.2431, found 351.2432.
$[\alpha]^{25}_D$ = -102.976 (c = 0.506, $CHCl_3$).

5-((1,4-diazepan-1-yl)sulfonyl)-1-isopropylisoquinoline (37).



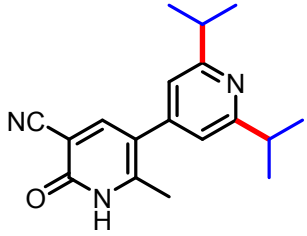
According to the *general procedure*. The spectral data is consistent with the literature data.[2d]
Yellow oil (72.9 mg, 73%).
R_f 0.30 (CH_2Cl_2/MeOH, 10/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 6.0 Hz, 1H), 8.49 (d, J = 8.4 Hz, 1H), 8.30 (dd, J = 10.8, 6.8 Hz, 2H), 7.66 (t, J = 8.0 Hz, 1H), 3.97 (dt, J = 13.2, 6.8 Hz, 1H), 3.56 – 3.39 (m, 4H), 3.09 – 2.92 (m, 4H), 2.48 (s, 1H), 1.93 – 1.76 (m, 2H), 1.45 (d, J = 6.4 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.3, 143.9, 135.3, 132.4, 130.4, 126.9, 125.3, 115.7, 51.0, 50.3, 47.7, 47.5, 31.6, 31.2, 22.4.
HRMS (ESI) calcd for $C_{17}H_{24}N_3O_2S$ $[M + H]^+$ 334.1584, found 334.1585.

2-((2-(4-chlorophenoxy)-2-methylpropanoyl)oxy)ethyl 6-(tert-butyl)nicotinate (38).



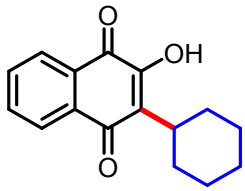
According to the *general procedure*. The spectral data is consistent with the literature data.[8]
Colorless oil (72.9 mg, 58%).
R_f 0.65 (Petroleum ether/EtOAc, 5/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (d, J = 2.0 Hz, 1H), 8.01 (dd, J = 8.4, 2.0 Hz, 1H), 7.37 (d, J = 8.4 Hz, 1H), 7.12 – 7.03 (m, 2H), 6.80 – 6.70 (m, 2H), 4.50 (q, J = 5.6 Hz, 4H), 1.57 (s, 6H), 1.37 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.3, 173.9, 165.2, 153.9, 150.0, 137.3, 129.1, 127.26, 122.5, 120.2, 118.8, 79.3, 63.1, 62.5, 38.0, 30.0, 25.3.
HRMS (ESI) calcd for $C_{22}H_{27}ClNO_5$ $[M + H]^+$ 420.1572, found 420.1575.

2',6'-diisopropyl-2-methyl-6-oxo-1,6-dihydro-[3,4'-bipyridine]-5-carbonitrile (39).



According to the *general procedure*.
Yellow solid (37.2 mg, 42%). M.p. = 143 – 144 °C.
R_f 0.50 (CH_2Cl_2/MeOH, 20/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 6.85 (s, 2H), 3.09 (dt, J = 13.6, 6.8 Hz, 2H), 2.51 (s, 3H), 1.33 (d, J = 6.8 Hz, 12H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.7, 162.7, 150.6, 149.7, 143.9, 119.7, 117.7, 115.4, 101.9, 36.6, 22.8, 18.9.
HRMS (ESI) calcd for $C_{18}H_{22}N_3O$ $[M + H]^+$ 296.1757, found 296.1760.
IR (neat) υ_{max} = 3470, 1643, 1265, 745 cm^{-1}.

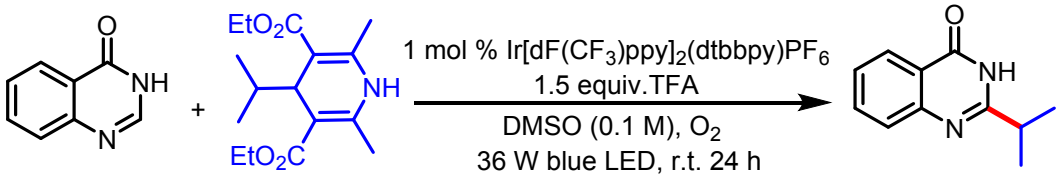
2-cyclohexyl-3-hydroxynaphthalene-1,4-dione (40)



According to the *general procedure*. The spectral data is consistent with the literature data.[2a]
Yellow solid (57.6 mg, 75%). M.p. =128 – 129 °C.
R_f 0.60 (Petroleum ether/EtOAc, 7/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 7.6 Hz, 1H), 8.04 (d, J = 7.6 Hz, 1H), 7.74 (t, J = 7.6 Hz, 1H), 7.65 (t, J = 7.6 Hz, 1H), 7.51 (s, 1H), 3.08 (t, J = 12.4 Hz, 1H), 1.98 (dd, J = 24.4, 12.4 Hz, 2H), 1.81 (d, J = 11.6 Hz, 2H), 1.72 (d, J = 8.8 Hz, 1H), 1.61 (d, J = 12.4 Hz, 2H), 1.40 – 1.24 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 184.7, 182.0, 153.0, 134.9, 133.3, 132.8, 129.3, 128.0, 127.0, 126.0, 35.3, 29.3, 26.8, 26.1.

HRMS (ESI) calcd for $C_{16}H_{17}O_3$ $[M + H]^+$ 257.1172, found 257.1174.

7. Gram-scale Reaction



1, 1.0 equiv. **2**, 1.5 equiv. **3** (73%,1.1 g)

Scheme S2

To an oven dried Schlenk tube was added $Ir[dF(CF_3)ppy)]_2(dtbbpy)PF_6$ (90 mg, 0.08 mmol, 1 mol %), **1** (1.17 g, 8.0 mmol, 1.0 equiv), 2 (3.54 g, 12 mmol, 1.5 equiv), TFA (0.9 mL, 12 mmol, 1.5 equiv) and 80 mL of DMSO. The tube was evacuated and backfilled with O_2 (this process was repeated three times). The mixture was then stirred rapidly and irradiated with two 36 W Blue LEDs (approximately 2 cm away from the light source) at room temperature for 48 h. The reaction mixture was diluted with 60 mL of aqueous 1 M $NaHCO_3$ solution, and extracted with DCM (3 × 100 mL). The combined organic extracts were washed with brine (200 mL), dried over Na_2SO_4, and concentrated in vacuo. After purification by flash column chromatography on silica gel, the product was obtained in 73% yield.

References

[1] M. S. Lowry, J. I. Goldsmith, J. D. Slinker, R. Rohl, R. A. Pascal, G. G. Malliaras, S. Bernhard, *Chem. Mater.***2005**, *17*, 5712.

[2] (a) A. Gutierrez-Bonet, C. Remeur, J. K. Matsui, G. A. Molander, *J. Am. Chem. Soc.* **2017**, *139*, 12251; (b) N. Tewari, N. Dwivedi, R. Tripathi, *Tetrahedron Lett.* **2004**, *45*, 9011; (c) Á. Gutiérrez-Bonet, J. C. Tellis, J. K. Matsui, B. A. Vara, G. A. Molander, *ACS Catal.* **2016**, *6*, 8004; (d) H. Yan, Z.-W. Hou, H.-C. Xu, *Angew. Chem. Int. Ed.* **2019**, *58*, 4592.

[3] (a) J. Dong, Z. Wang, X. Wang, H. Song, Y. Liu, Q. Wang, *Sci. adv.* **2019**, *5* : eaax9955; (b) Z. Li, X. Wang, S. Xia, J. Jin, *Org. Lett.* **2019**, *21*, 4259; (c) Z. Wang, J. Y. Dong, Y. N. Hao, Y. Q. Li, Y. X. Liu, H. J. Song and Q. M. Wang, *J. Org. Chem.* **2019**, *84*, 16245; (d) J. Genovino, Y. Lian, Y. Zhang, T. O. Hope, A. Juneau, Y. Gagné, G. Ingle, M. Frenette, *Org. Lett.* **2018**, *20*, 3229.

[4] L. Zhang, Z. Liu, *Org. Lett.* **2017**, *19*, 6594.

[5] J. Dong, Q. Xia, X. Lyu, C. Yan, H. Song, Y. Liu, Q. Wang, *Org. Lett.* **2018**, *20*, 5661;

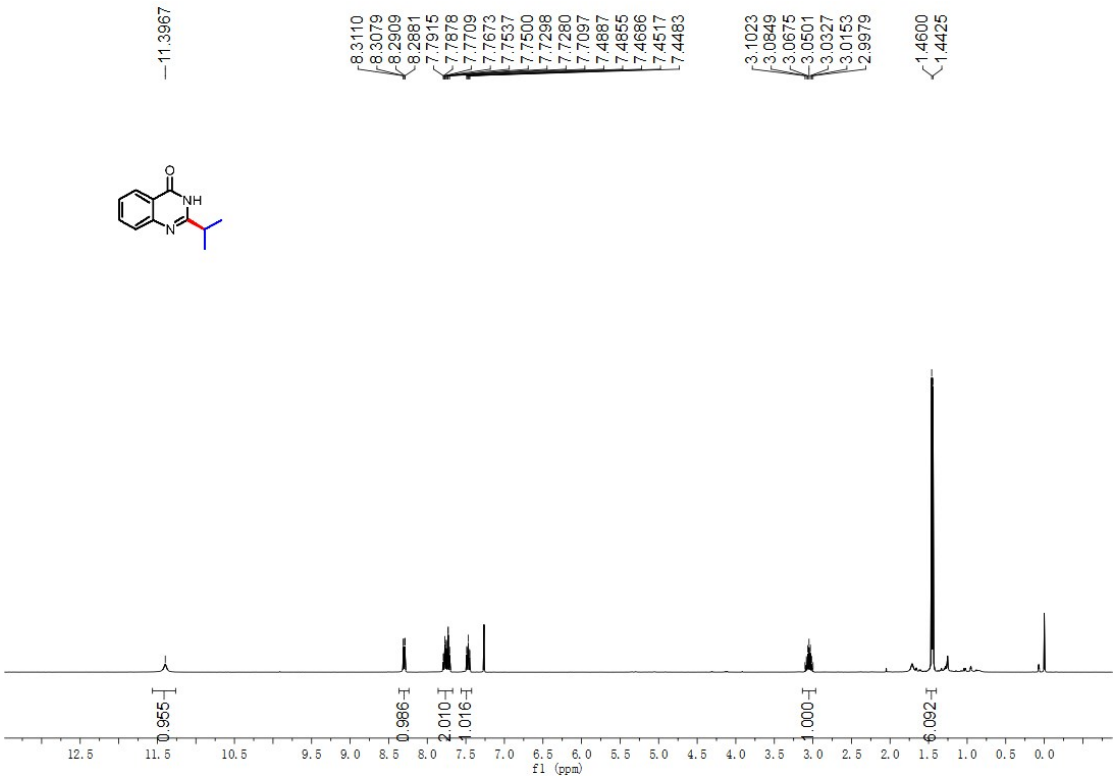
[6] J. Dong, X. Wang, Z. Wang, H. Song, Y. Liu, Q. Wang, *Org. Chem. Front.*, **2019**, *6*, 2902;

[7] T. McCallum, L. Barriault, *Chem. Sci.* **2016**, *7*, 4754–4758.

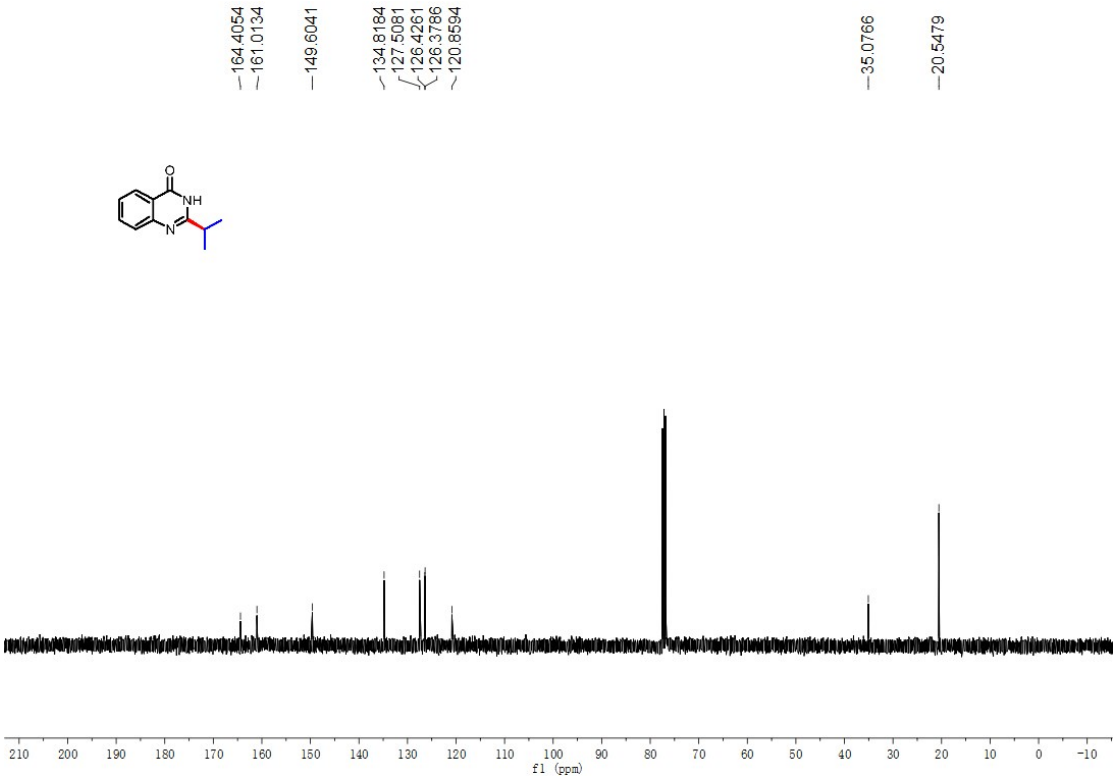
[8] J. Dong, X. Lyu, Z. Wang, X. Wang, H. Song, Y. Liu, Q. Wang, *Chem. Sci.*, **2019**, *10*, 976;

NMR Spectra

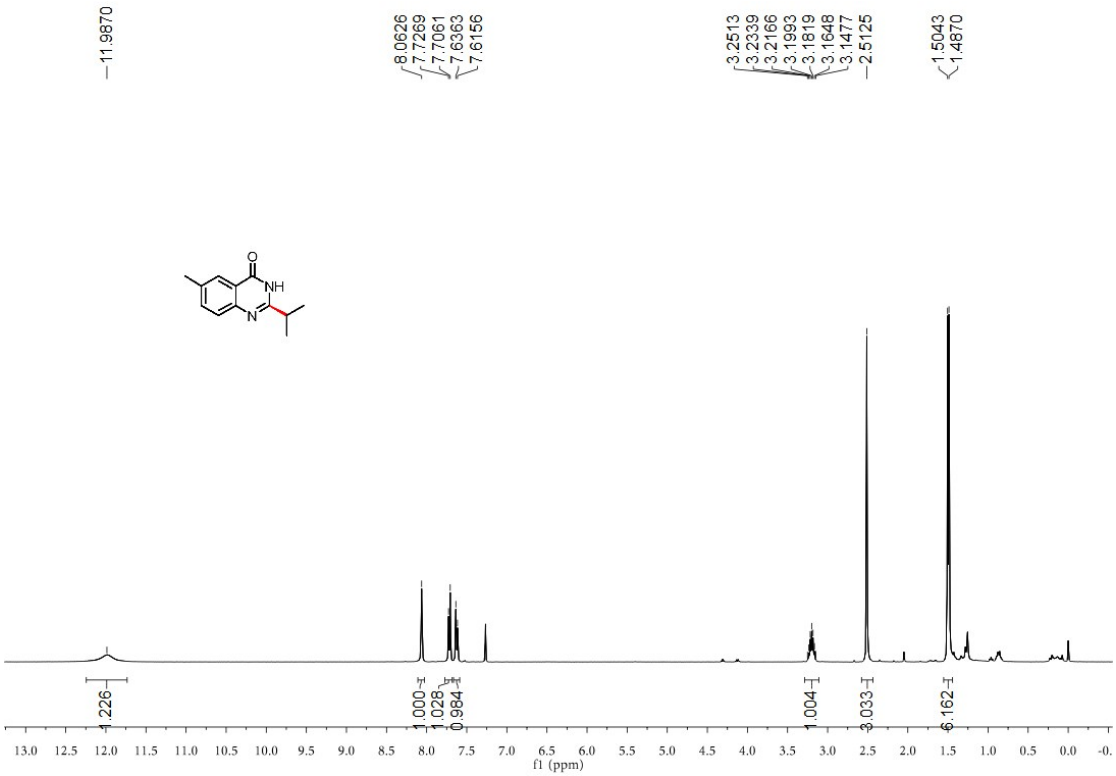
^{1}H NMR spectrum of compound **3**



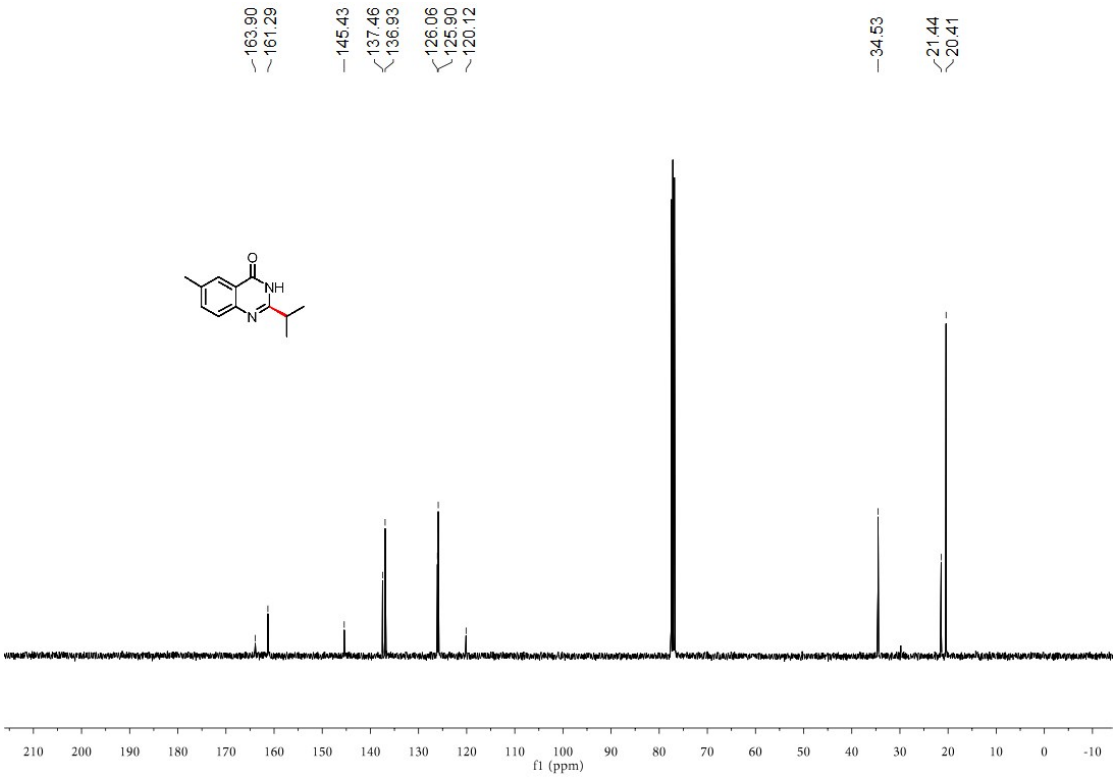
^{13}C NMR spectrum of compound **3**



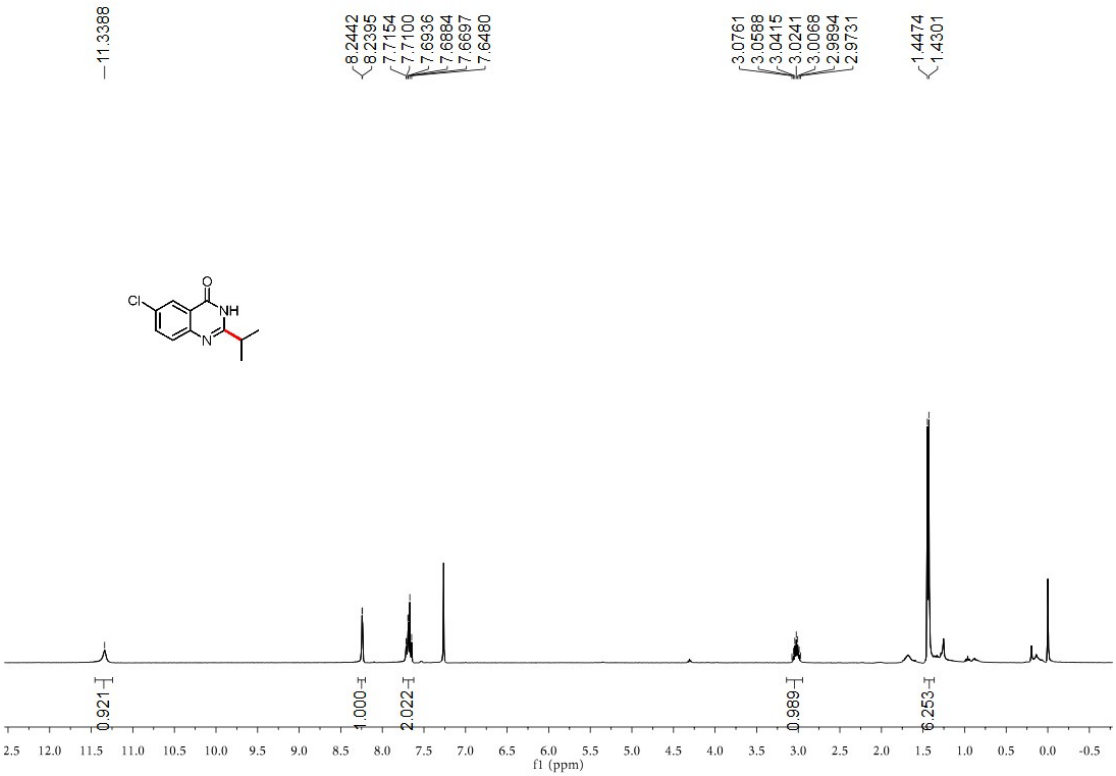
^{1}H NMR spectrum of compound **4**



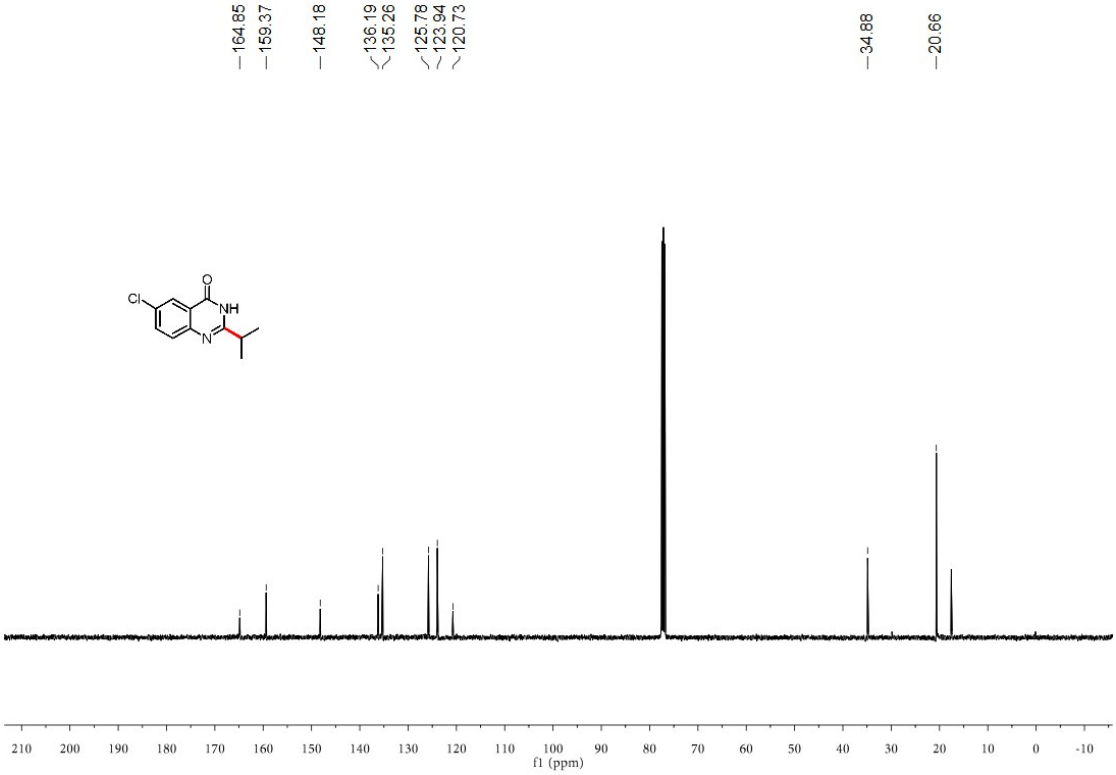
^{13}C NMR spectrum of compound **4**



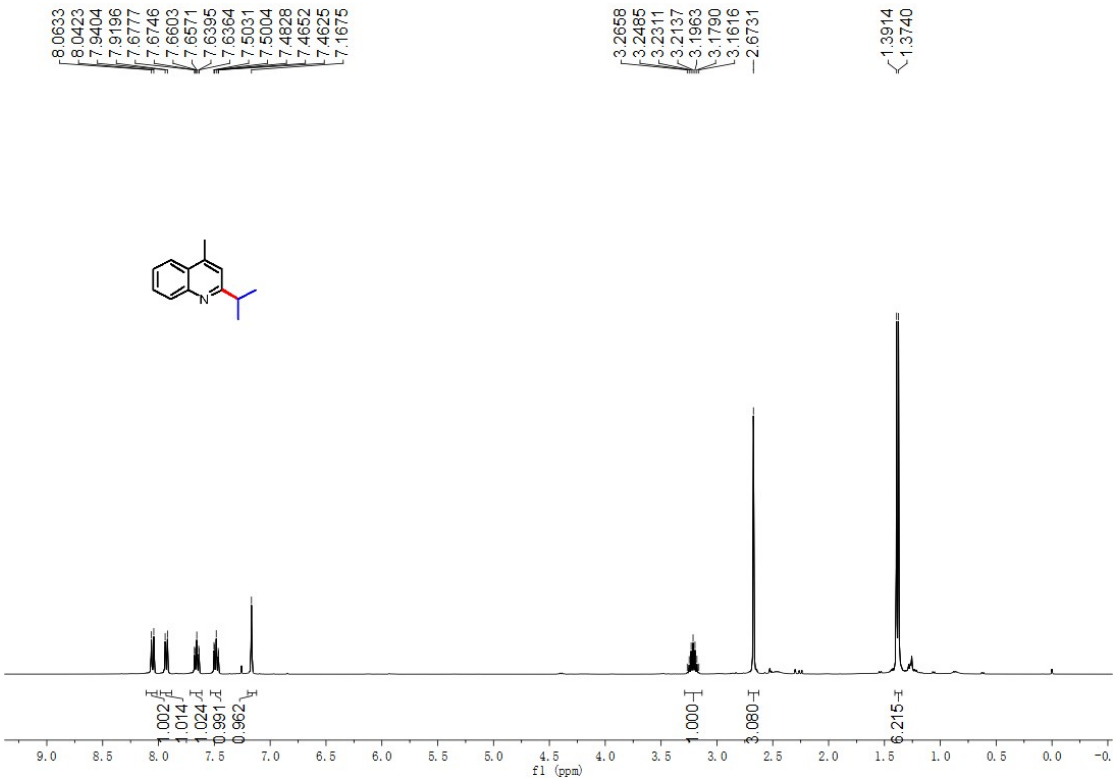
^{1}H NMR spectrum of compound **5**



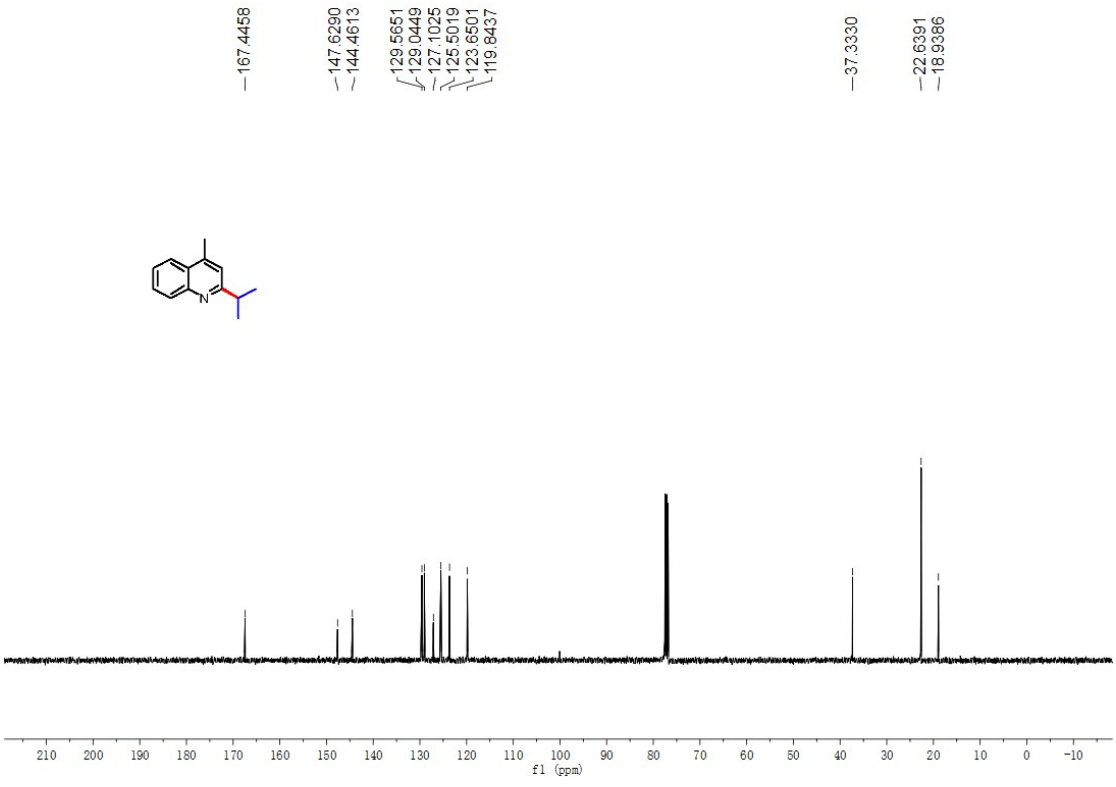
^{13}C NMR spectrum of compound **5**



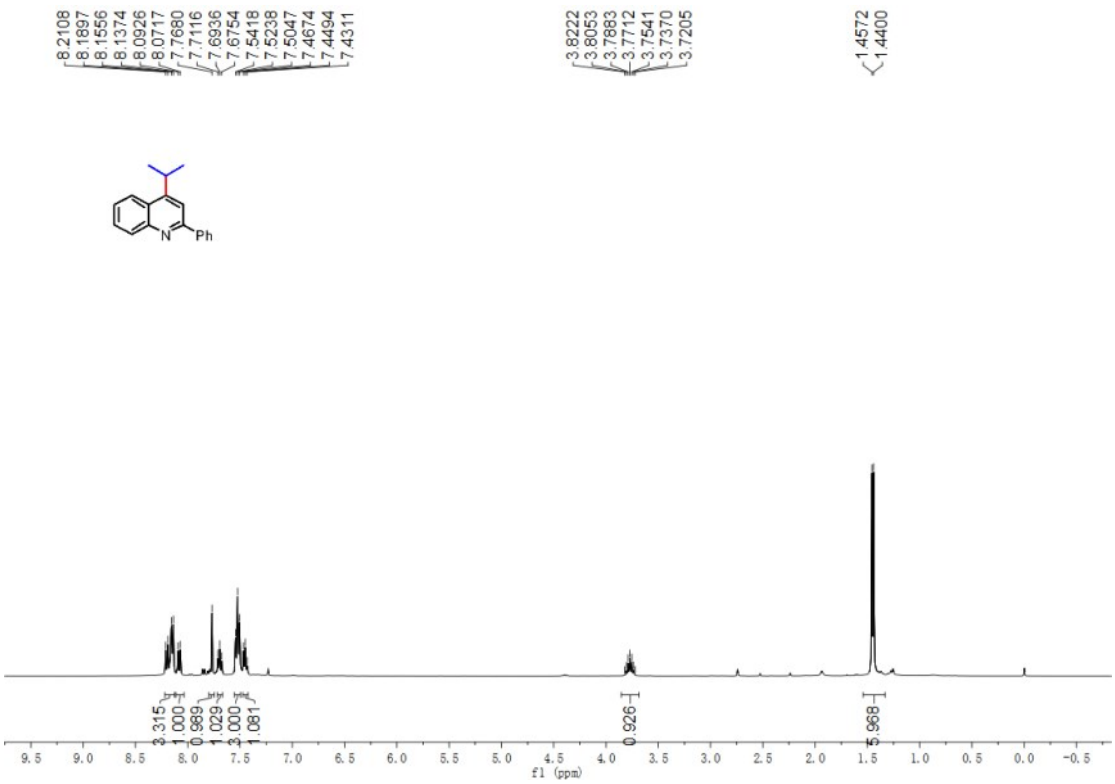
^{1}H NMR spectrum of compound **6**



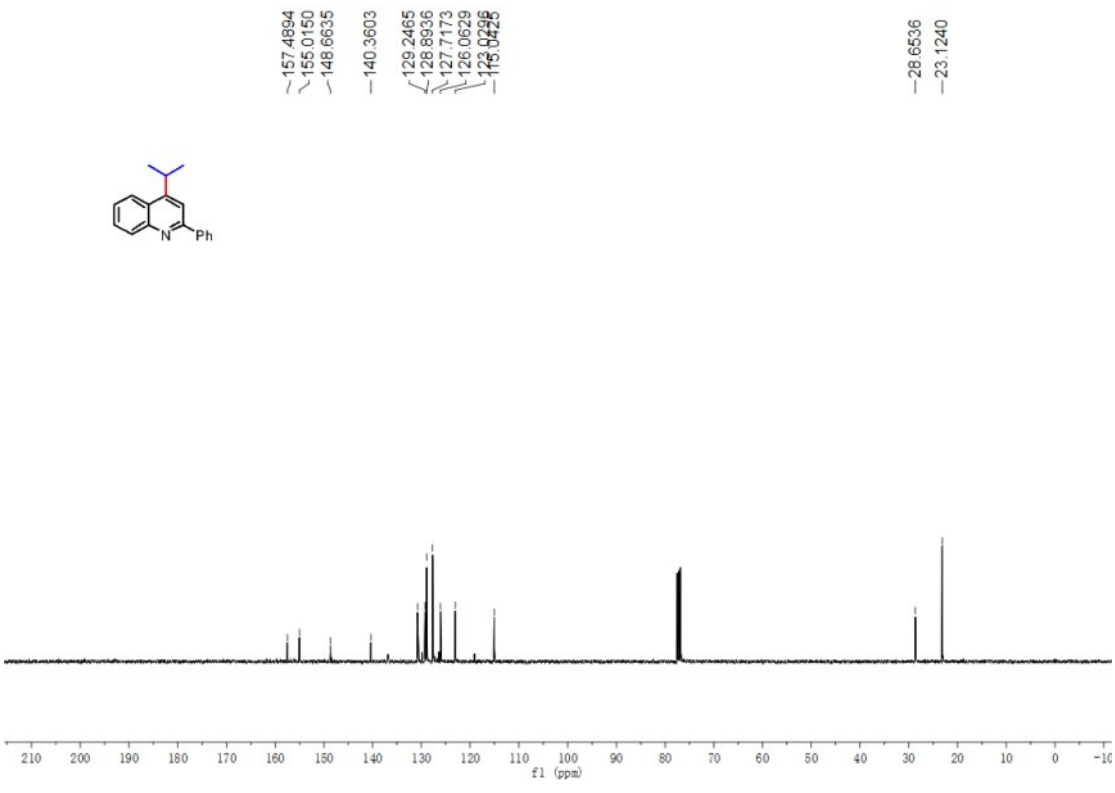
^{13}C NMR spectrum of compound **6**



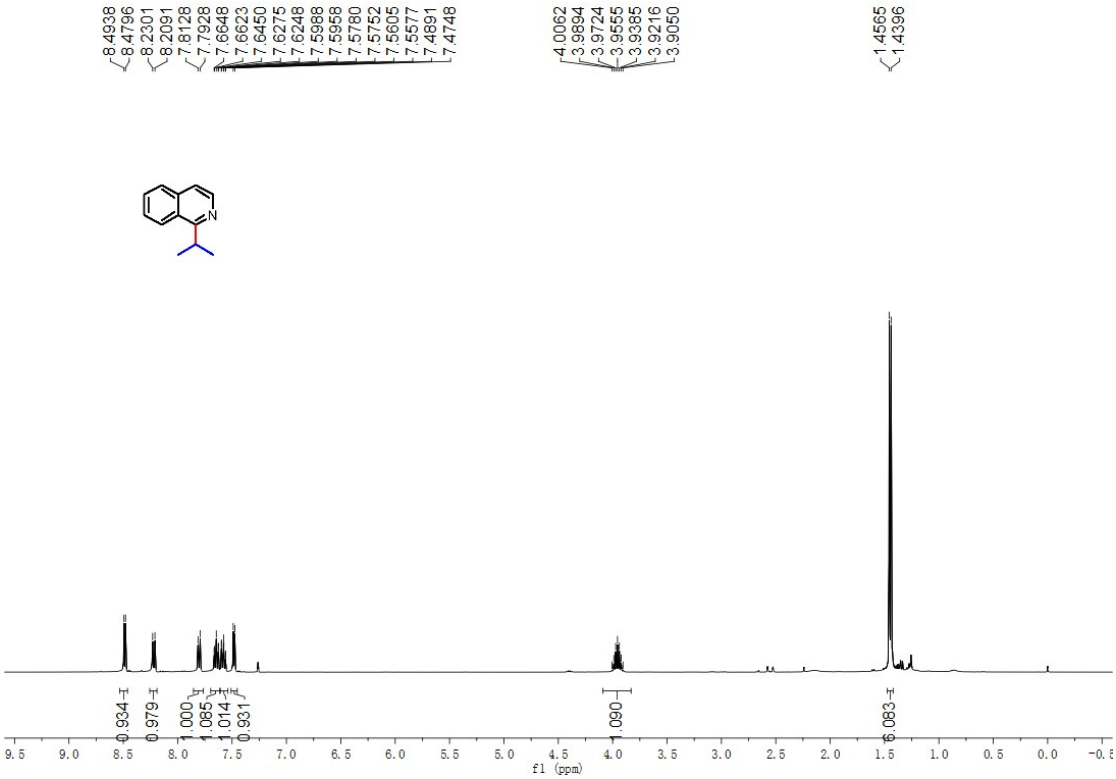
^{1}H NMR spectrum of compound **7**



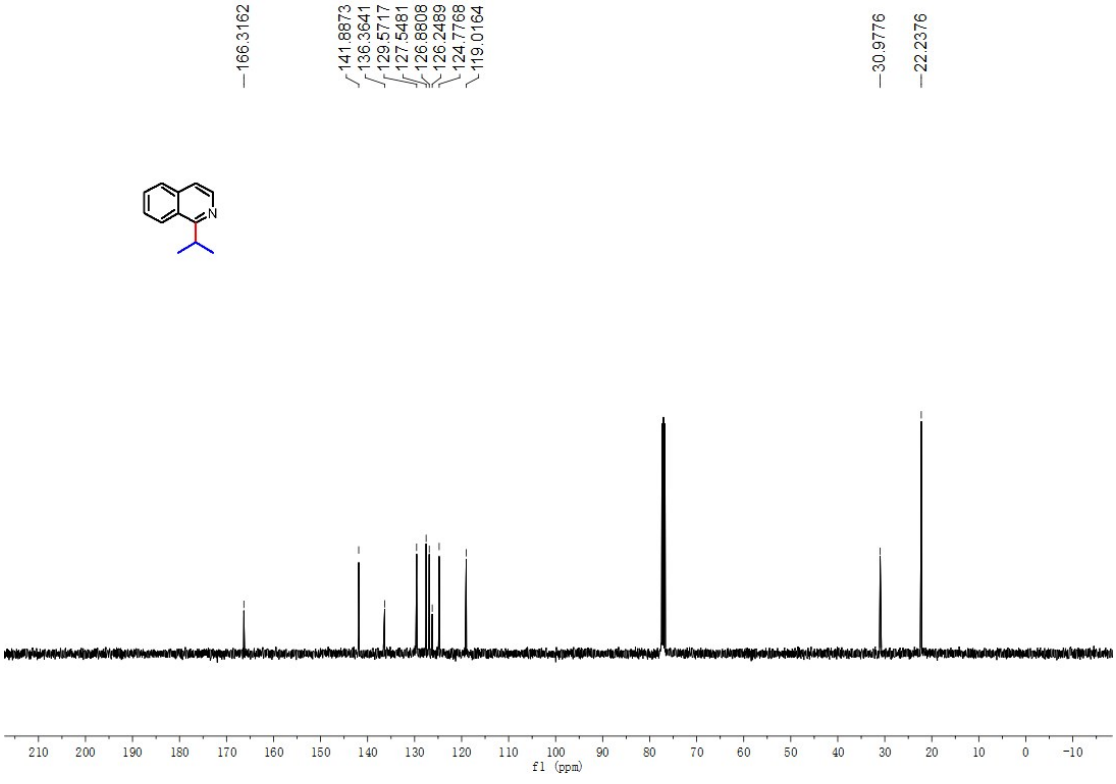
^{13}C NMR spectrum of compound **7**



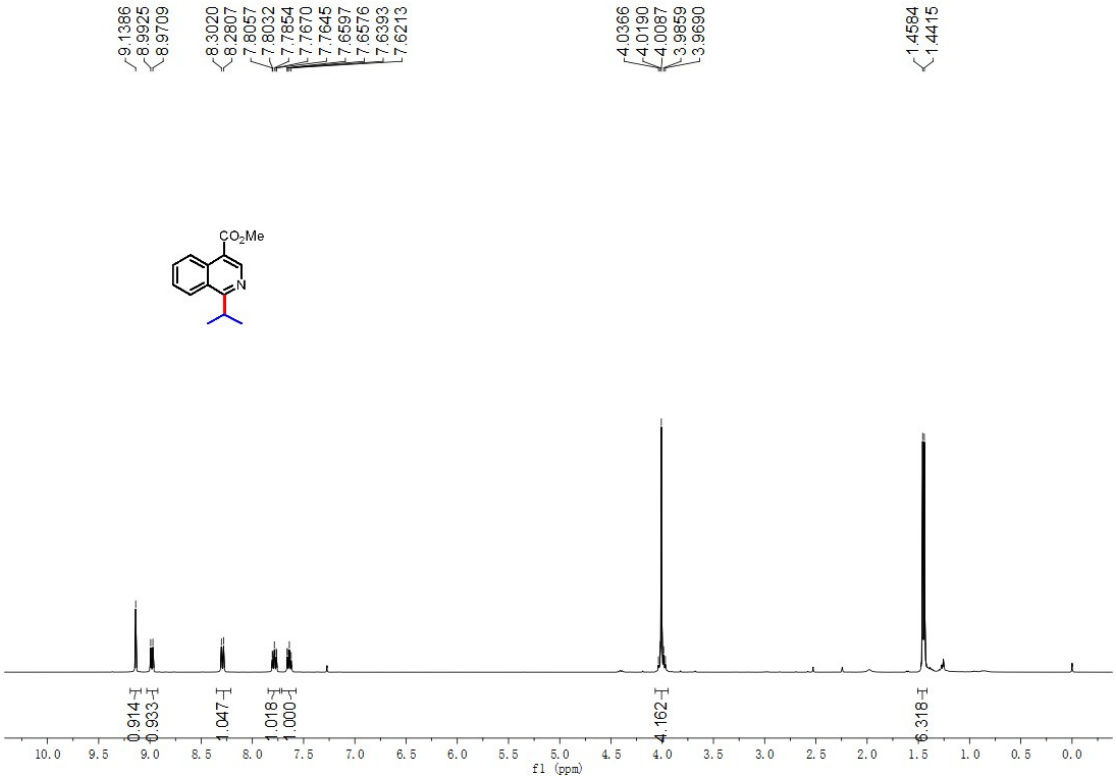
^{1}H NMR spectrum of compound **8**



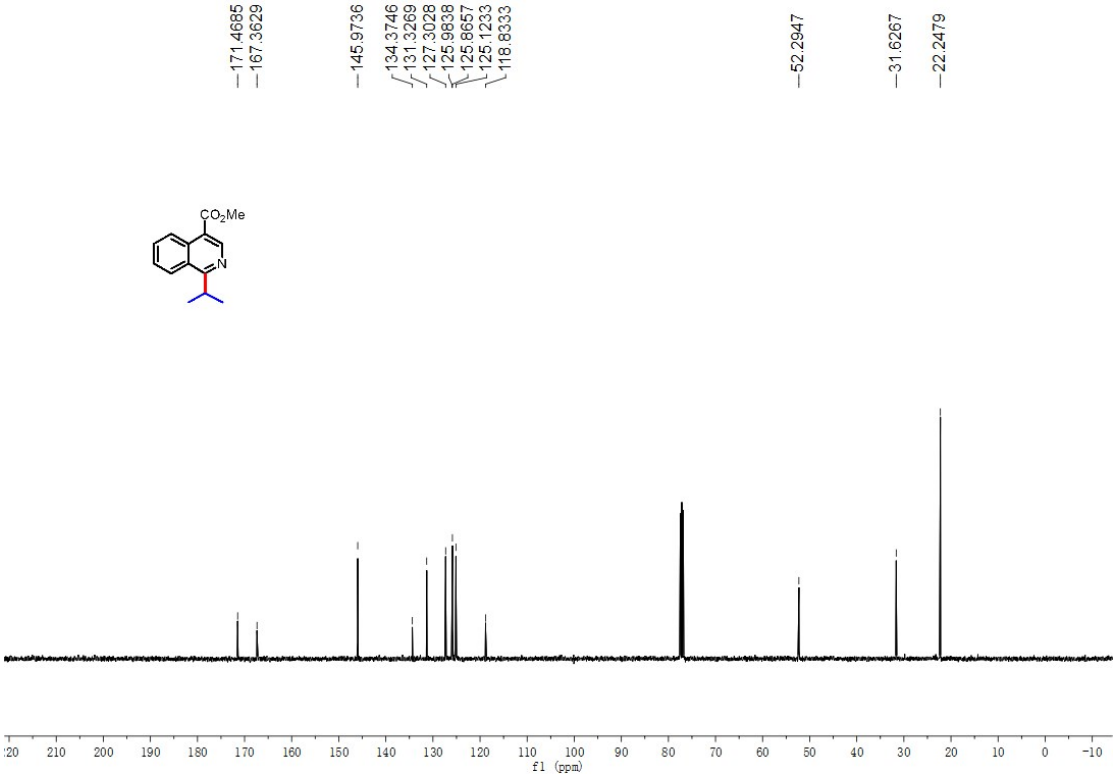
^{13}C NMR spectrum of compound **8**



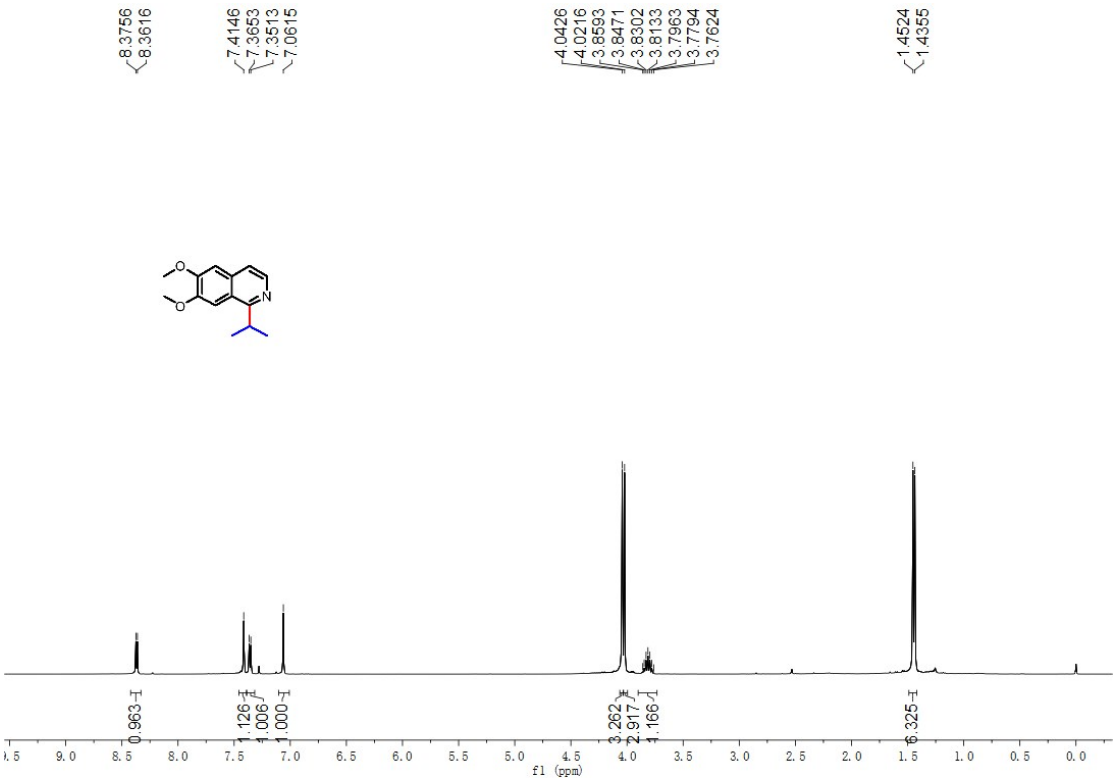
^{1}H NMR spectrum of compound **9**



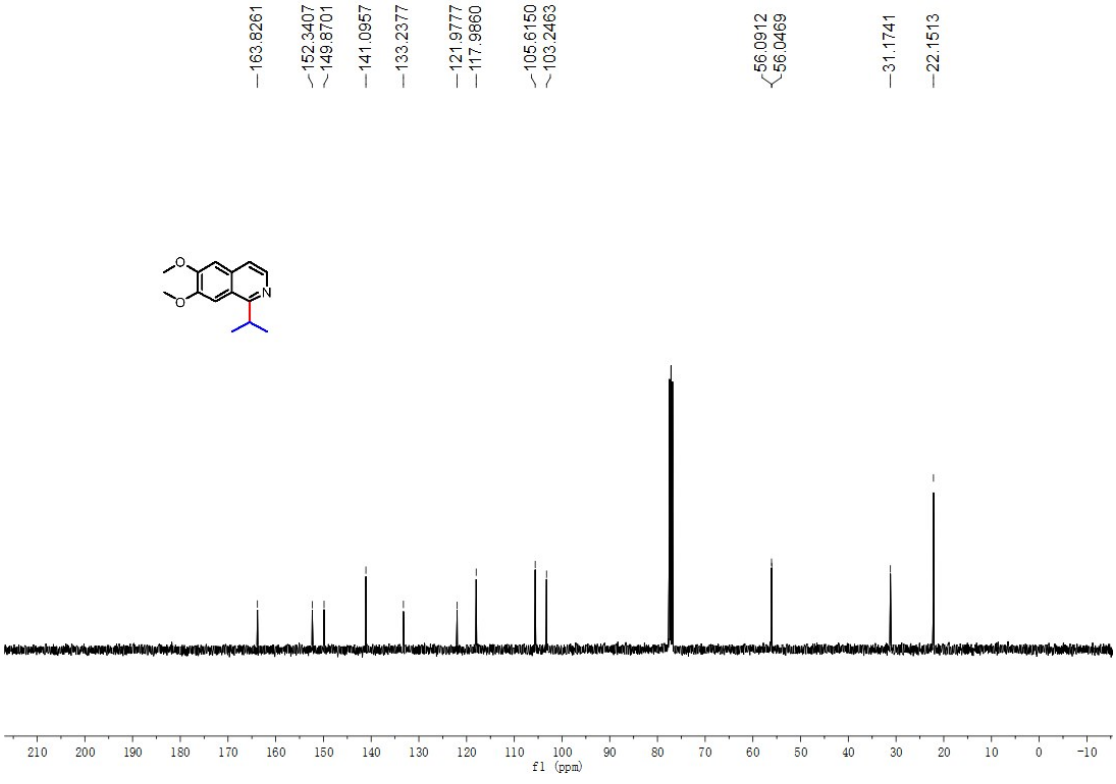
^{13}C NMR spectrum of compound **9**



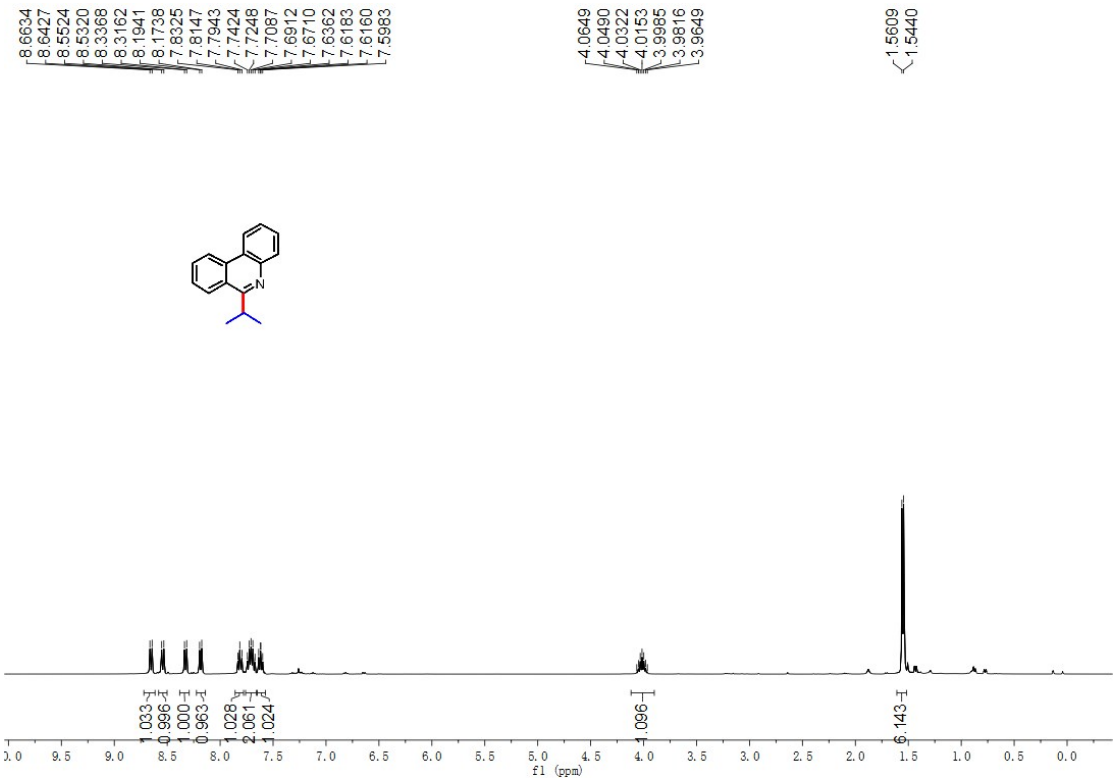
^{1}H NMR spectrum of compound **10**



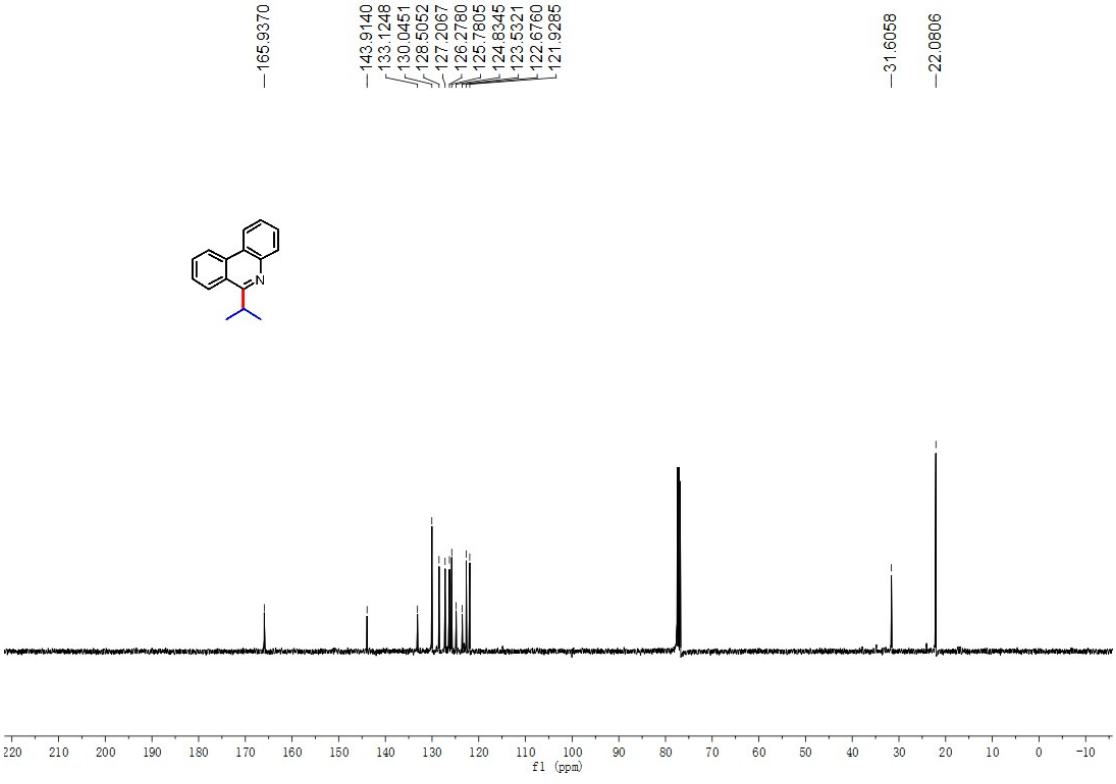
^{13}C NMR spectrum of compound **10**



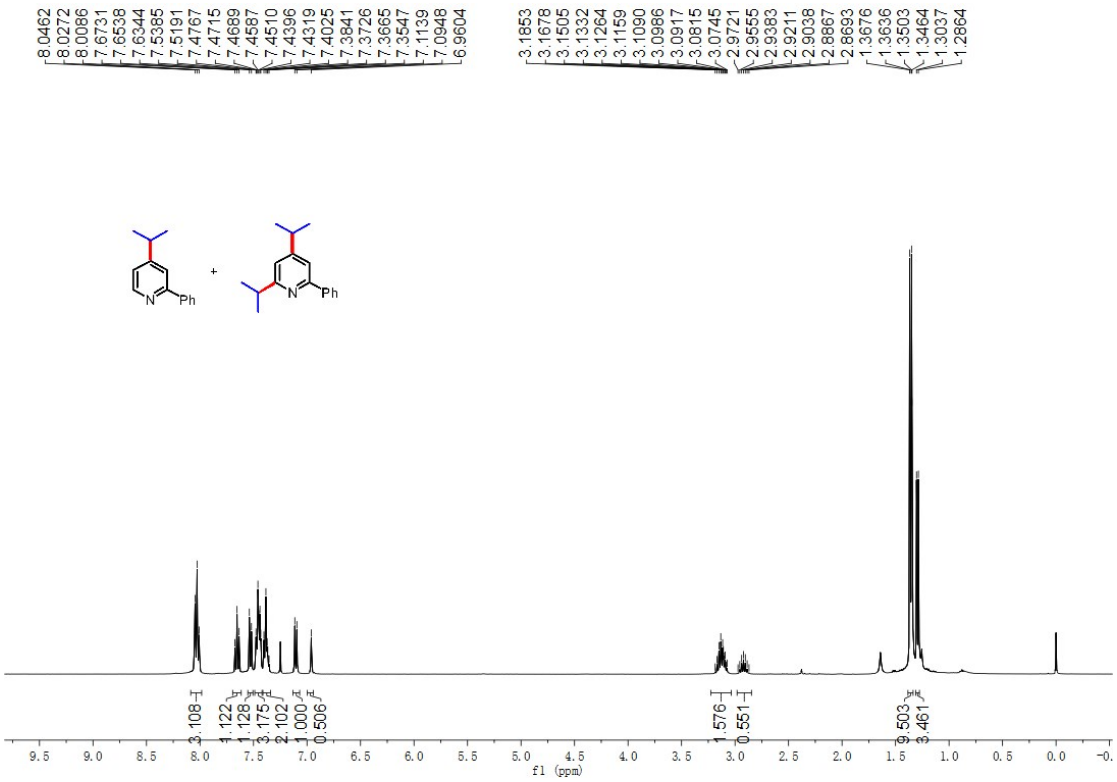
^{1}H NMR spectrum of compound **11**



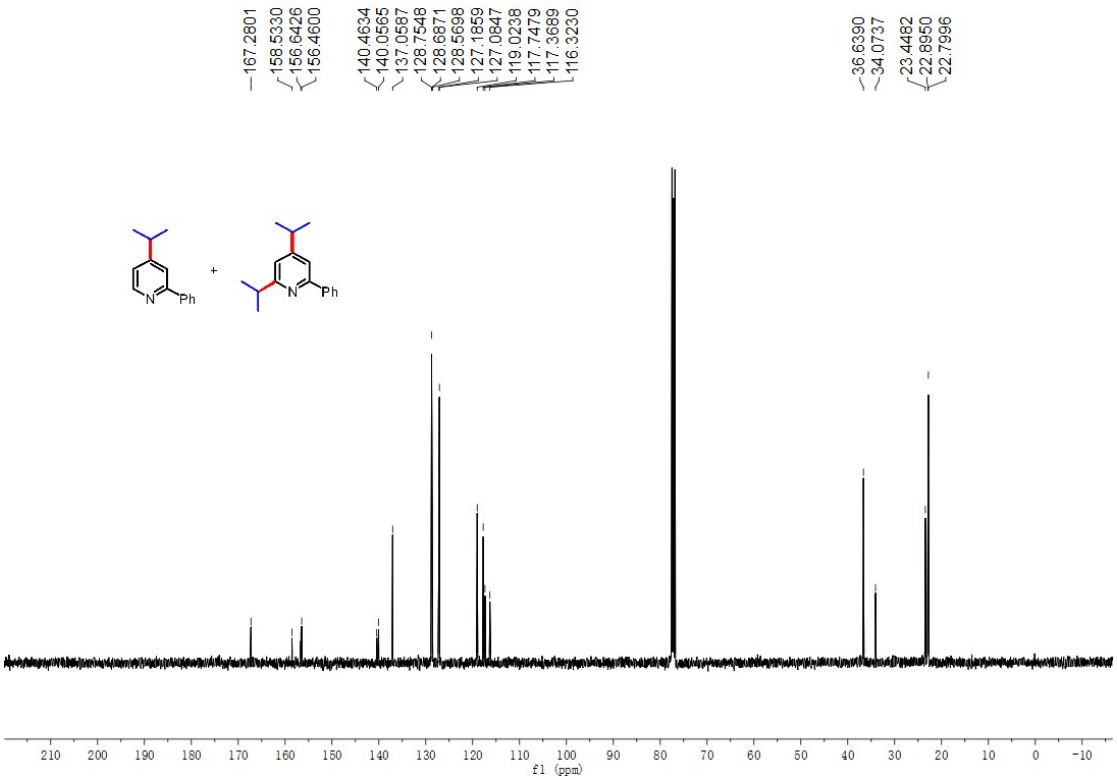
^{13}C NMR spectrum of compound **11**



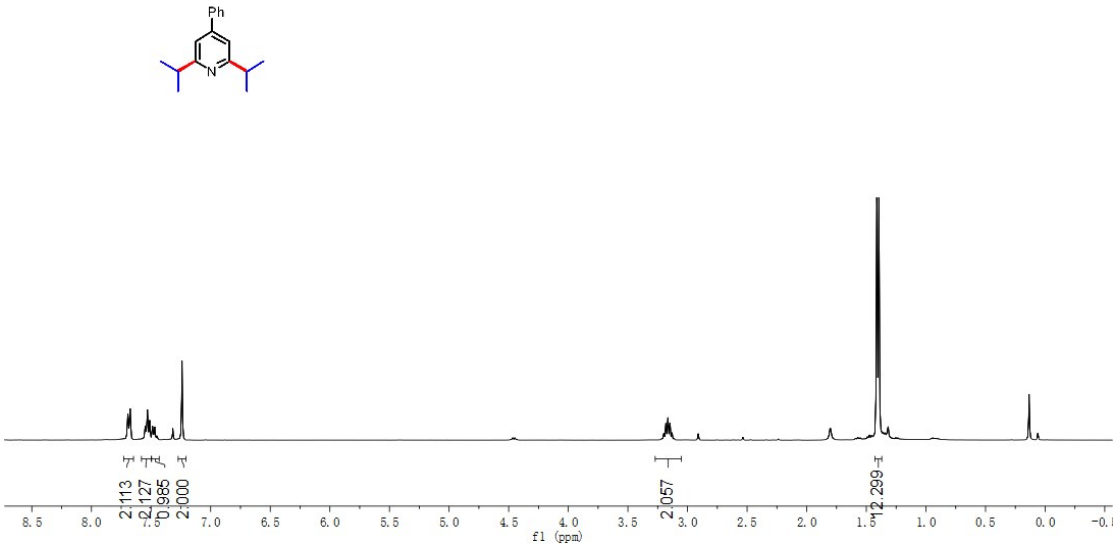
^{1}H NMR spectrum of compound **12**



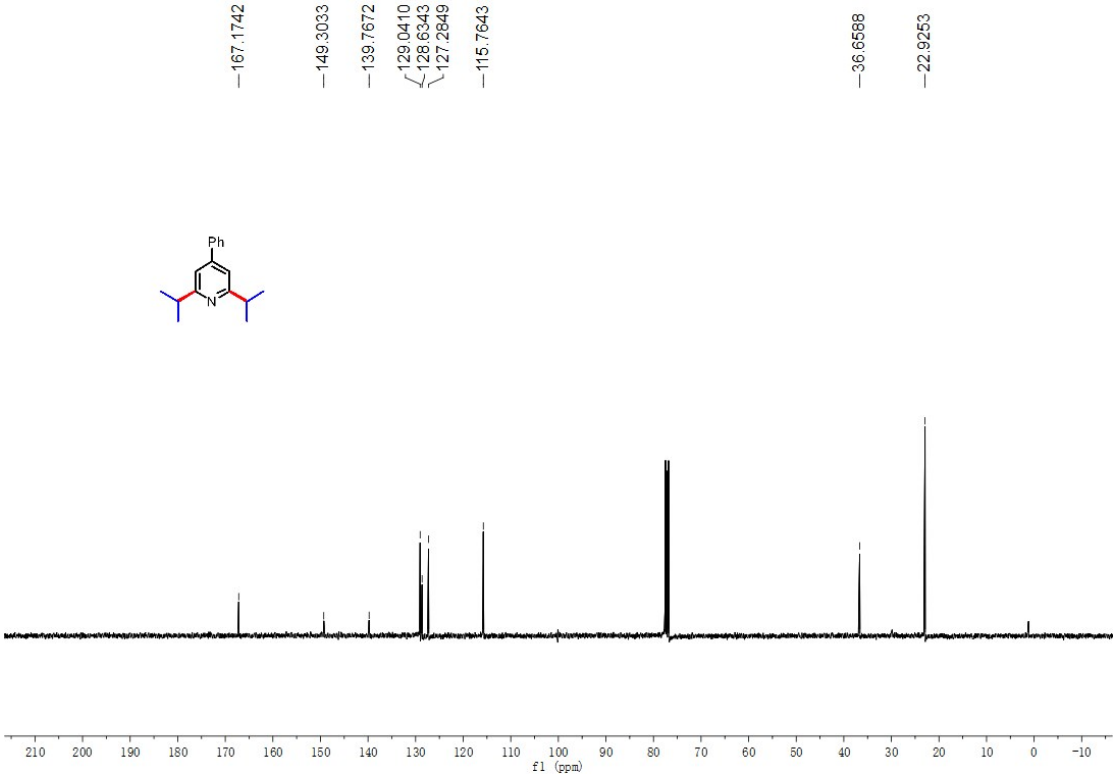
^{13}C NMR spectrum of compound **12**



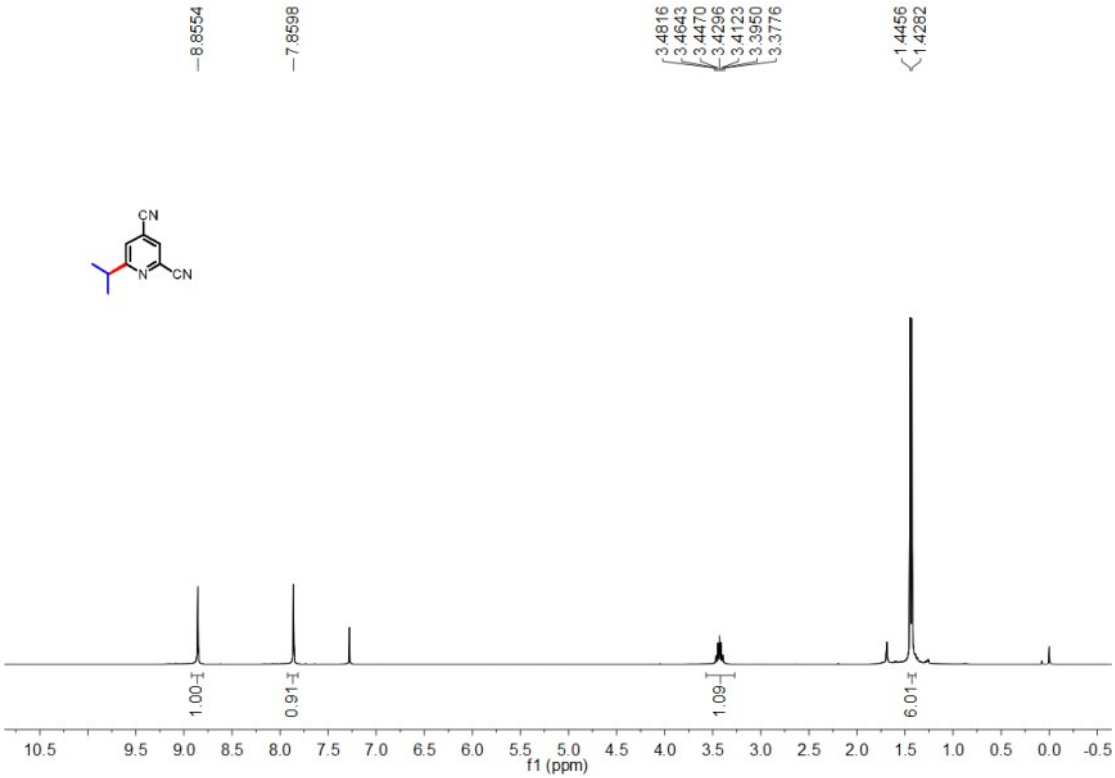
^{1}H NMR spectrum of compound **13**



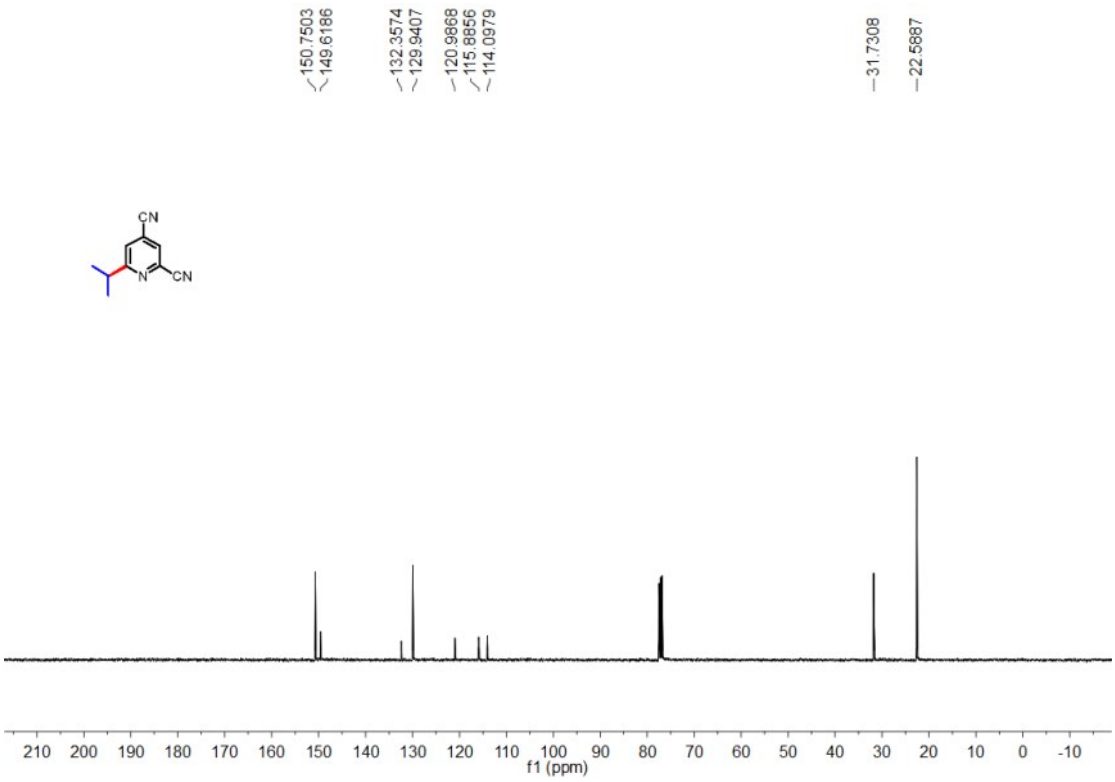
^{13}C NMR spectrum of compound **13**



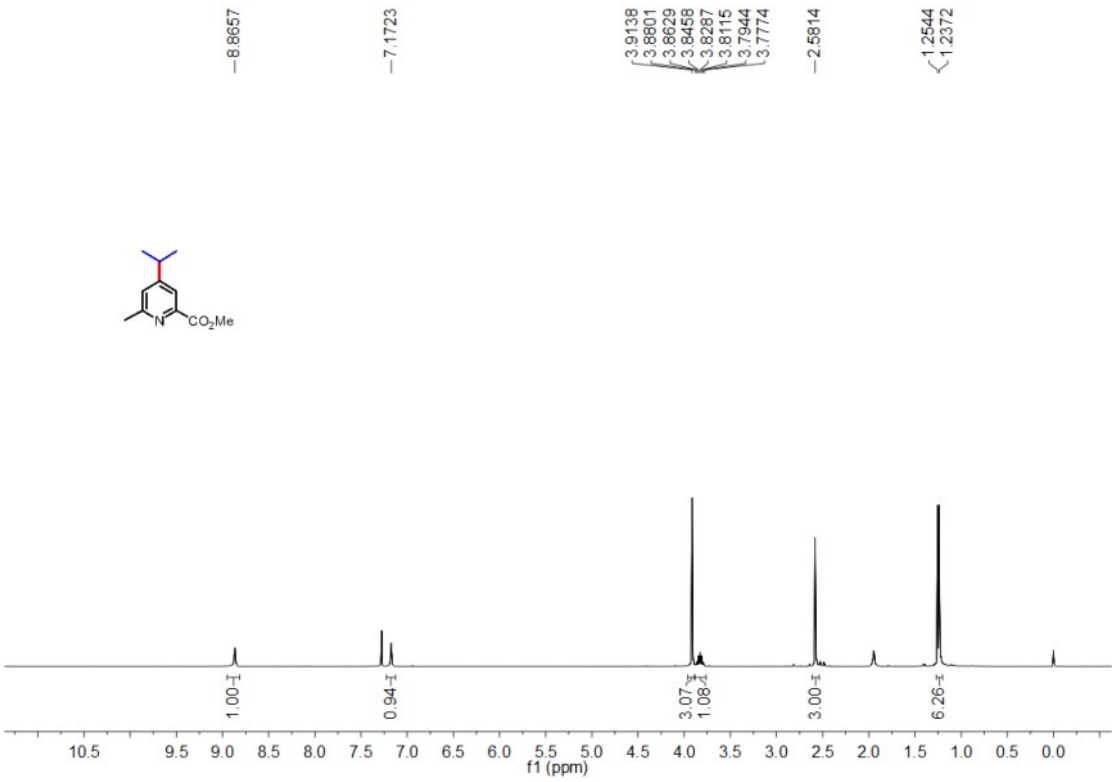
^{1}H NMR spectrum of compound **14**



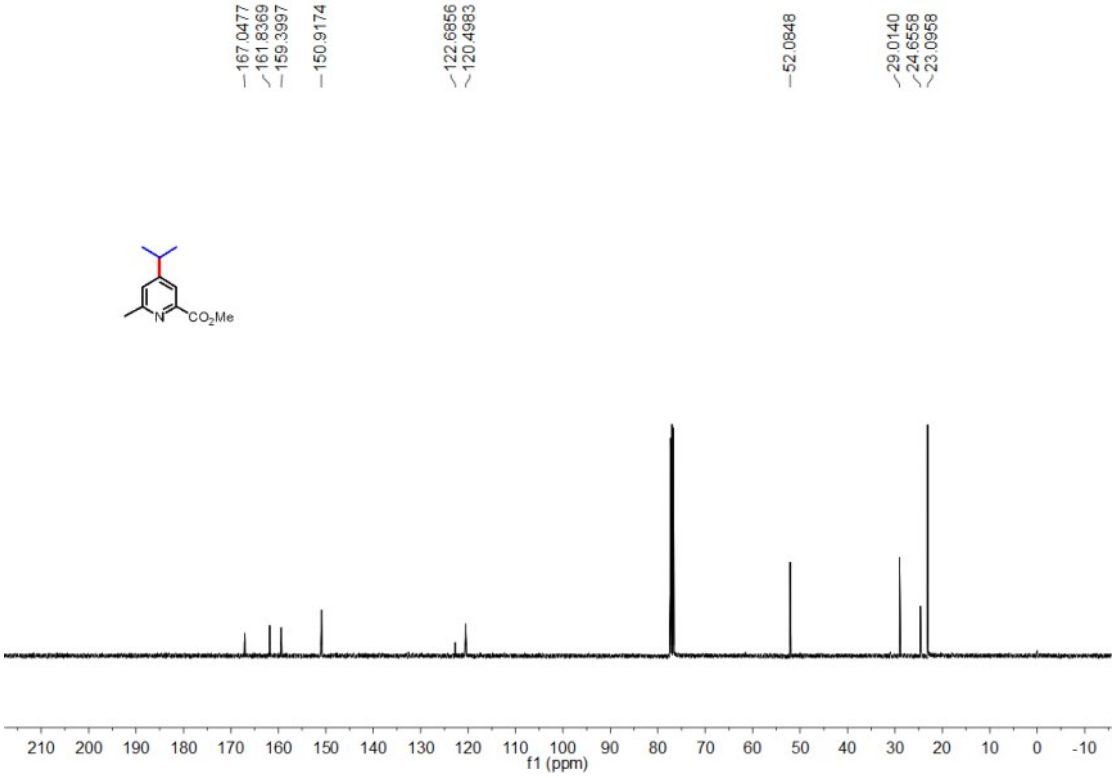
^{13}C NMR spectrum of compound **14**



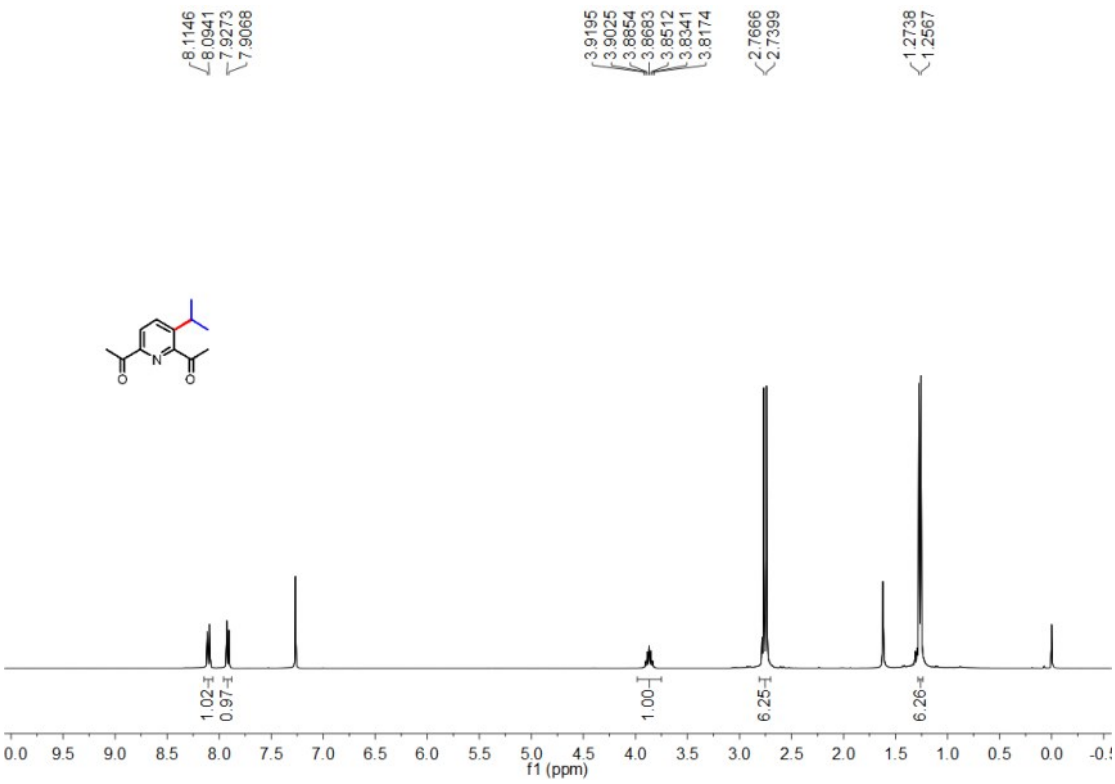
^{1}H NMR spectrum of compound **15**



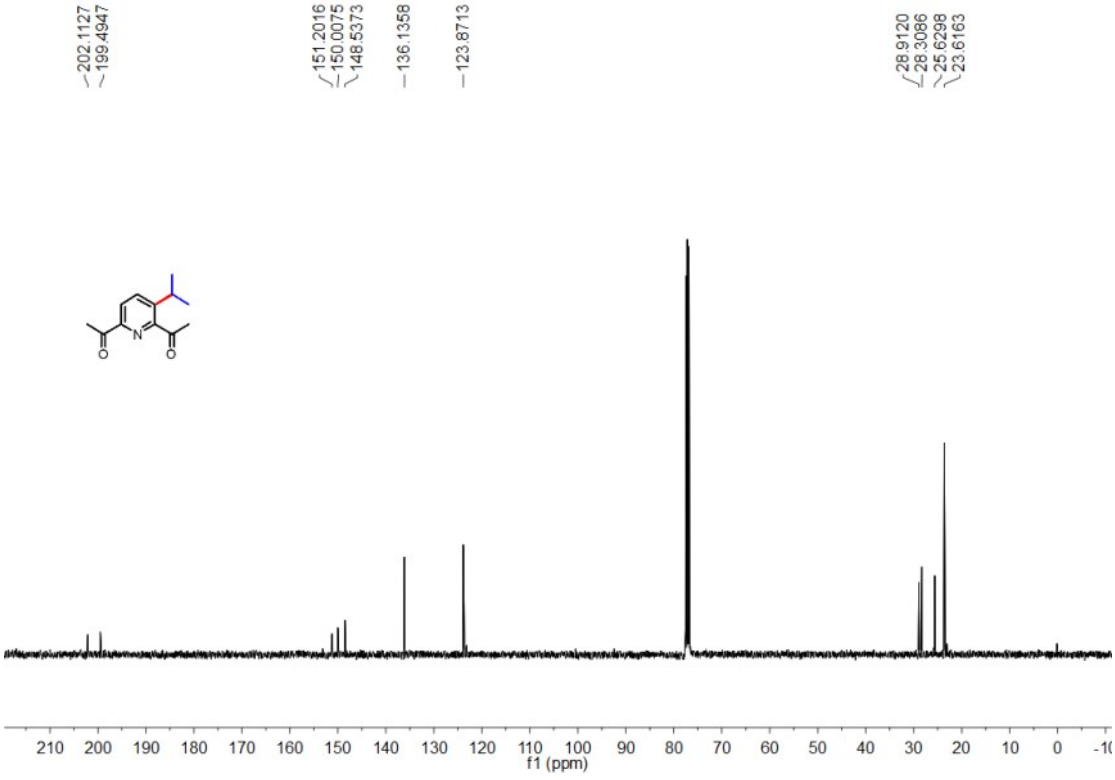
^{13}C NMR spectrum of compound **15**



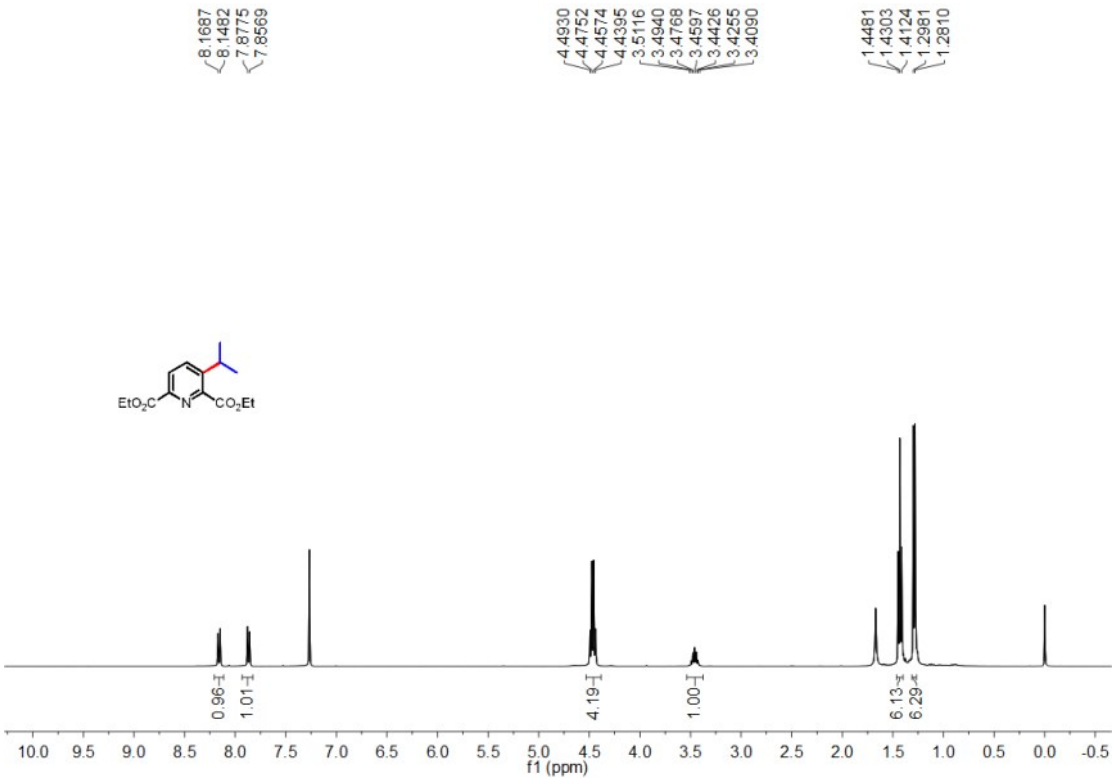
^{1}H NMR spectrum of compound **16**



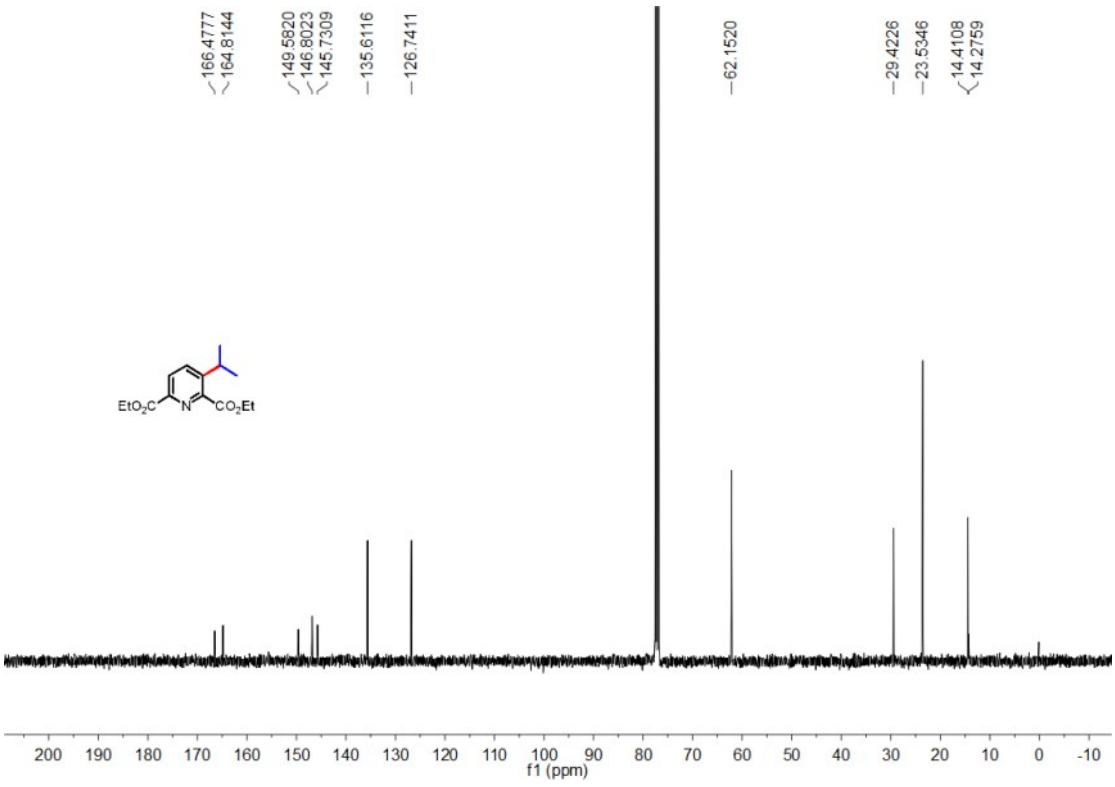
^{13}C NMR spectrum of compound **16**



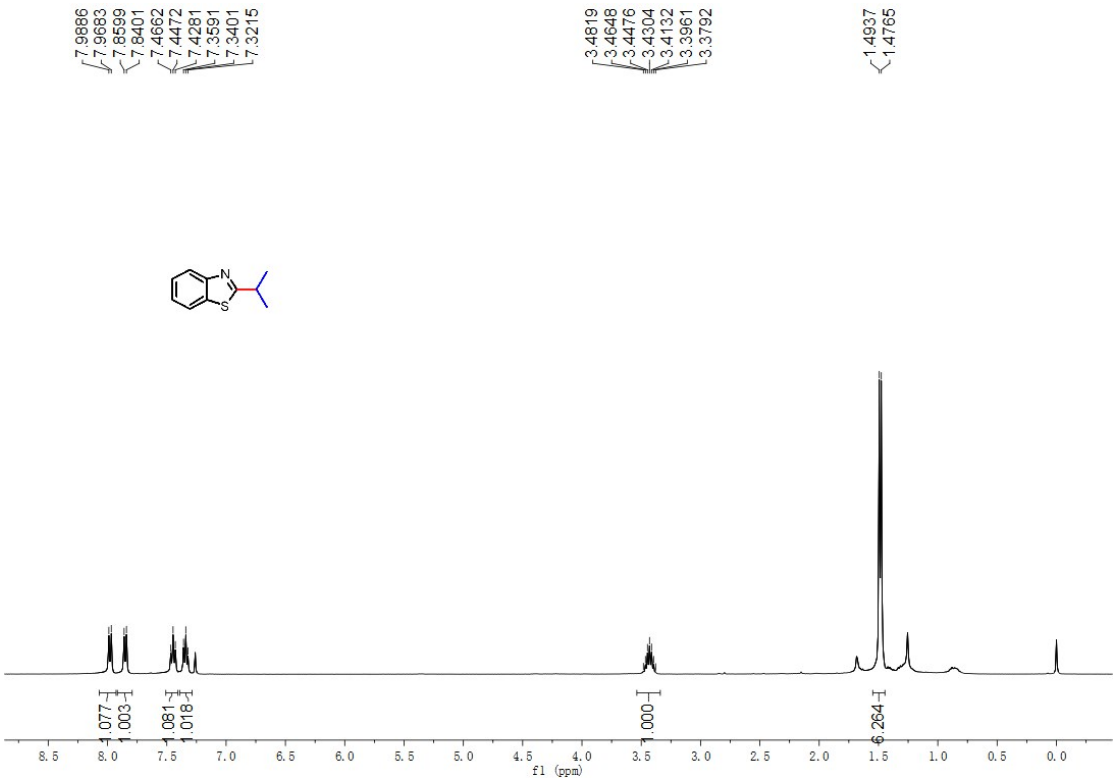
^{1}H NMR spectrum of compound **17**



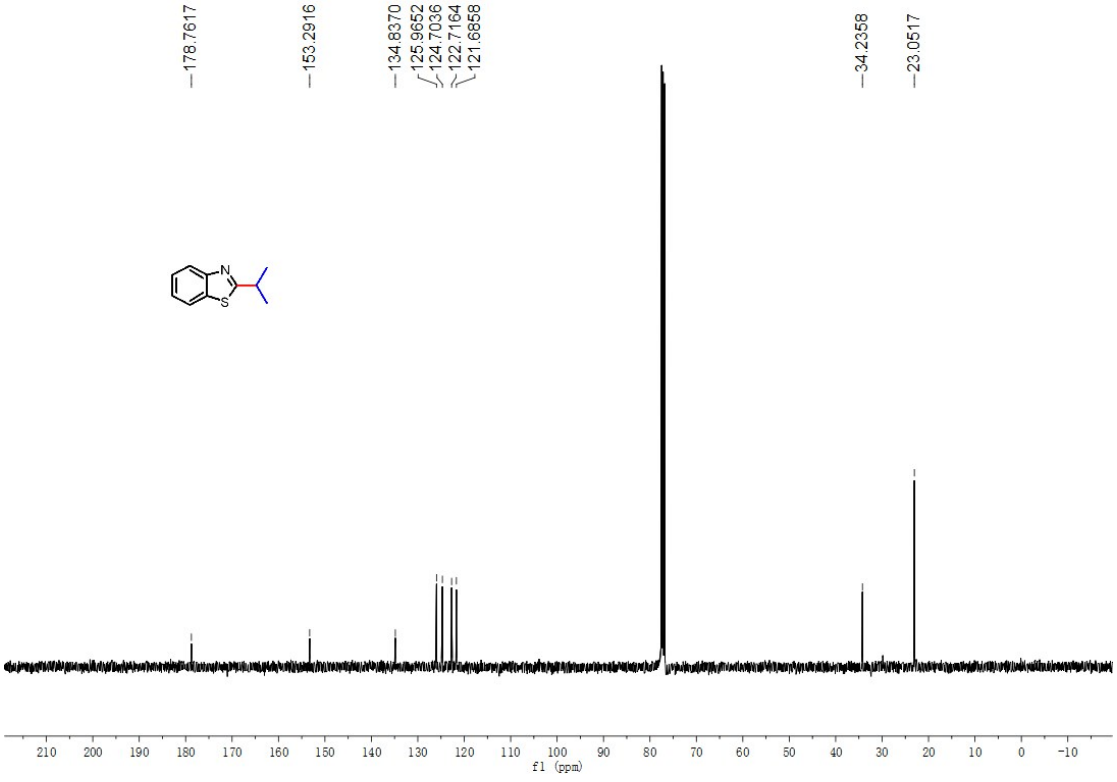
^{13}C NMR spectrum of compound **17**



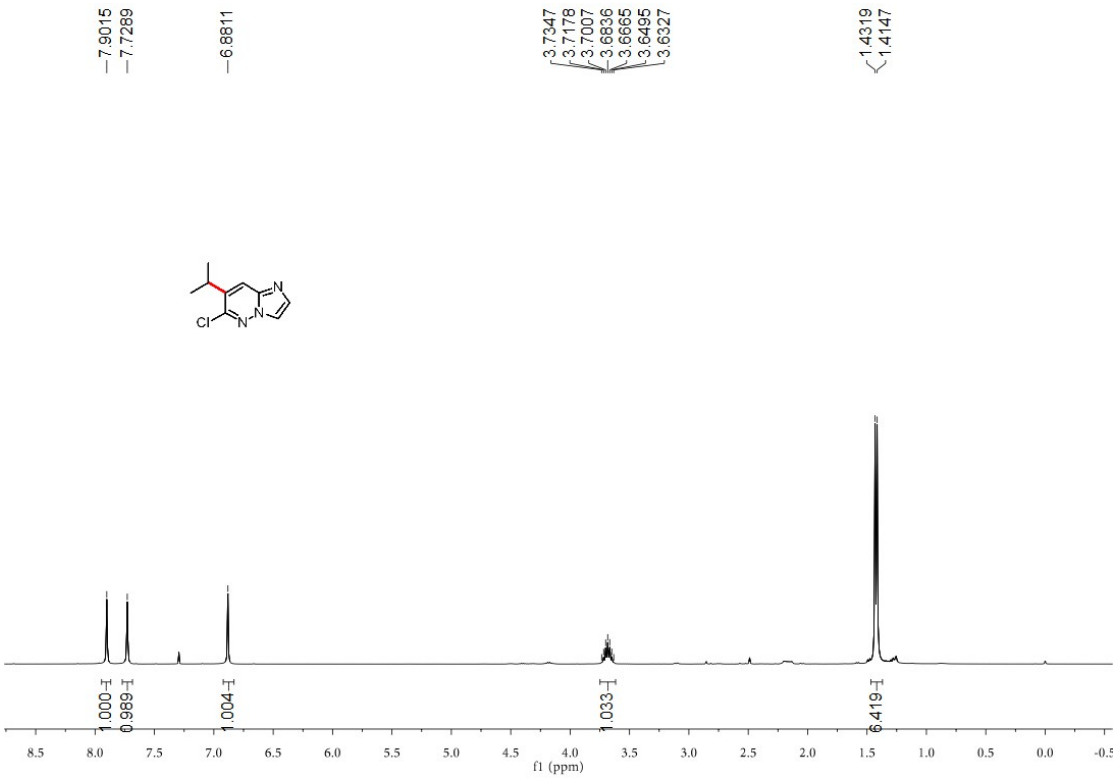
^{1}H NMR spectrum of compound **18**



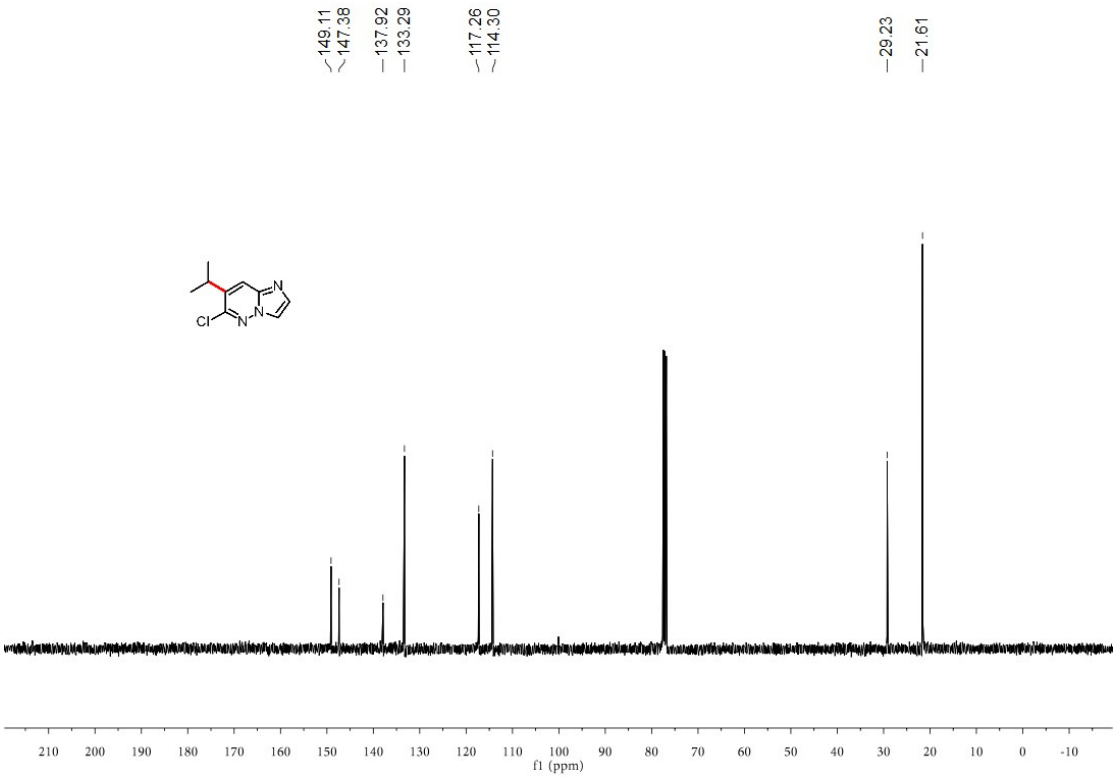
^{13}C NMR spectrum of compound **18**



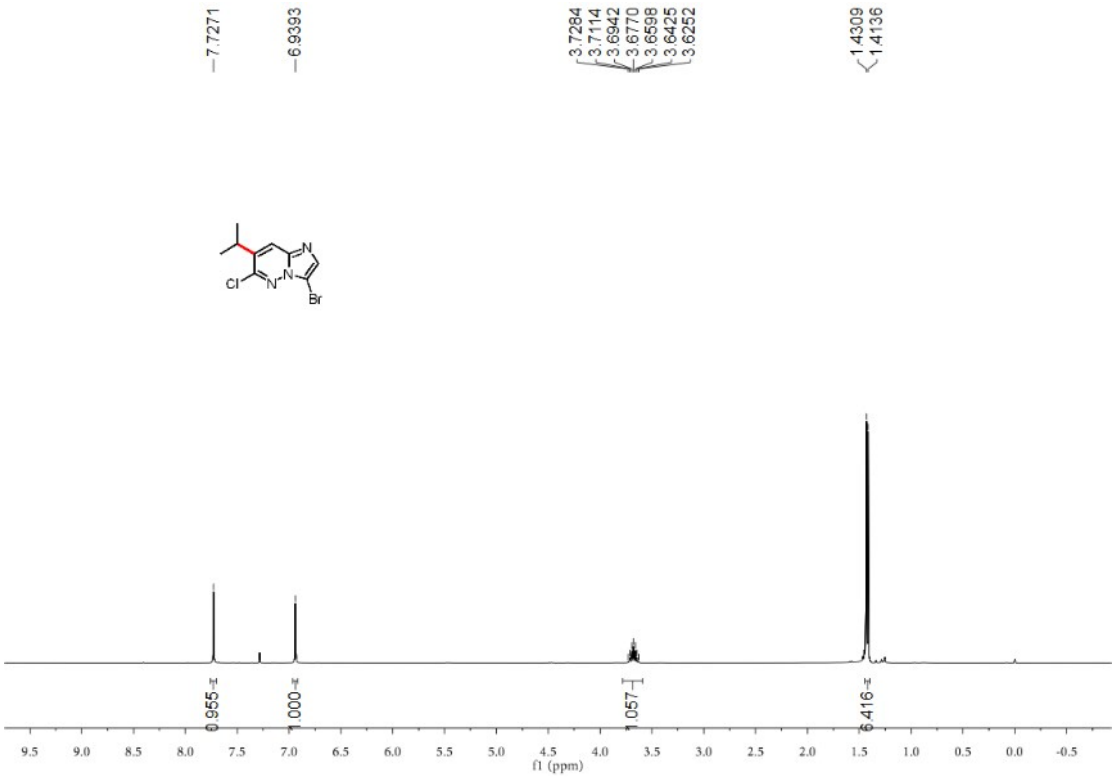
^{1}H NMR spectrum of compound **19**



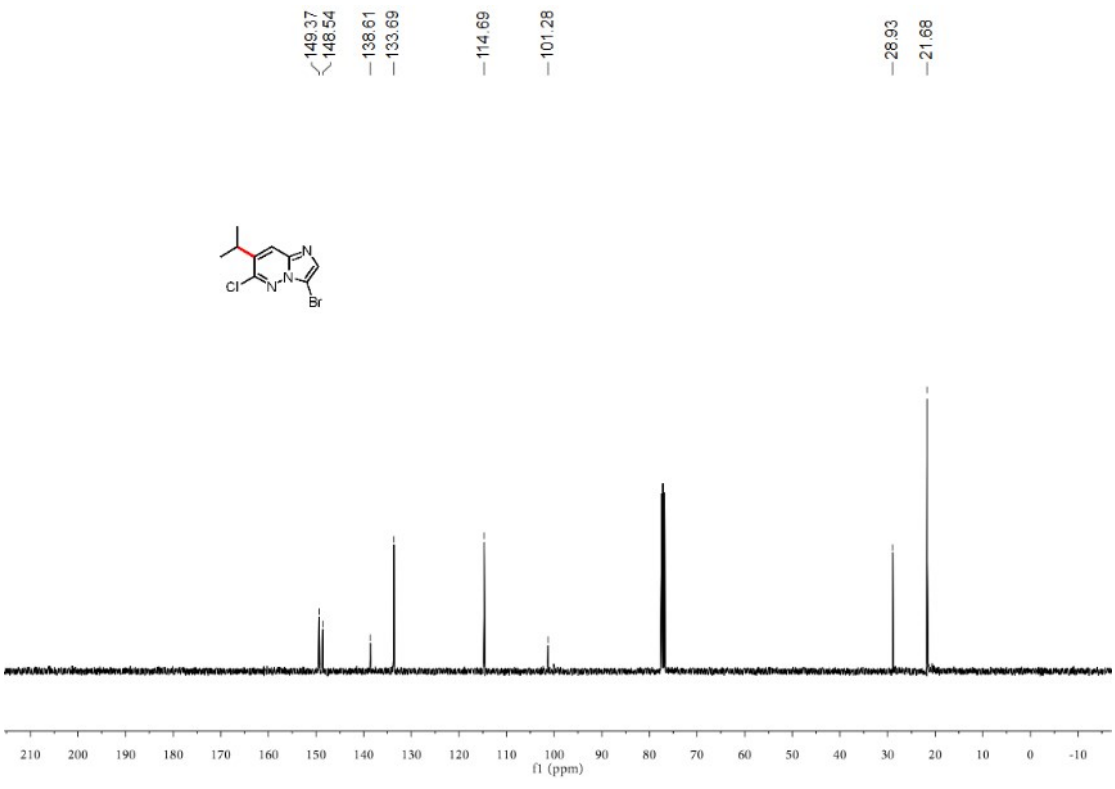
^{13}C NMR spectrum of compound **19**



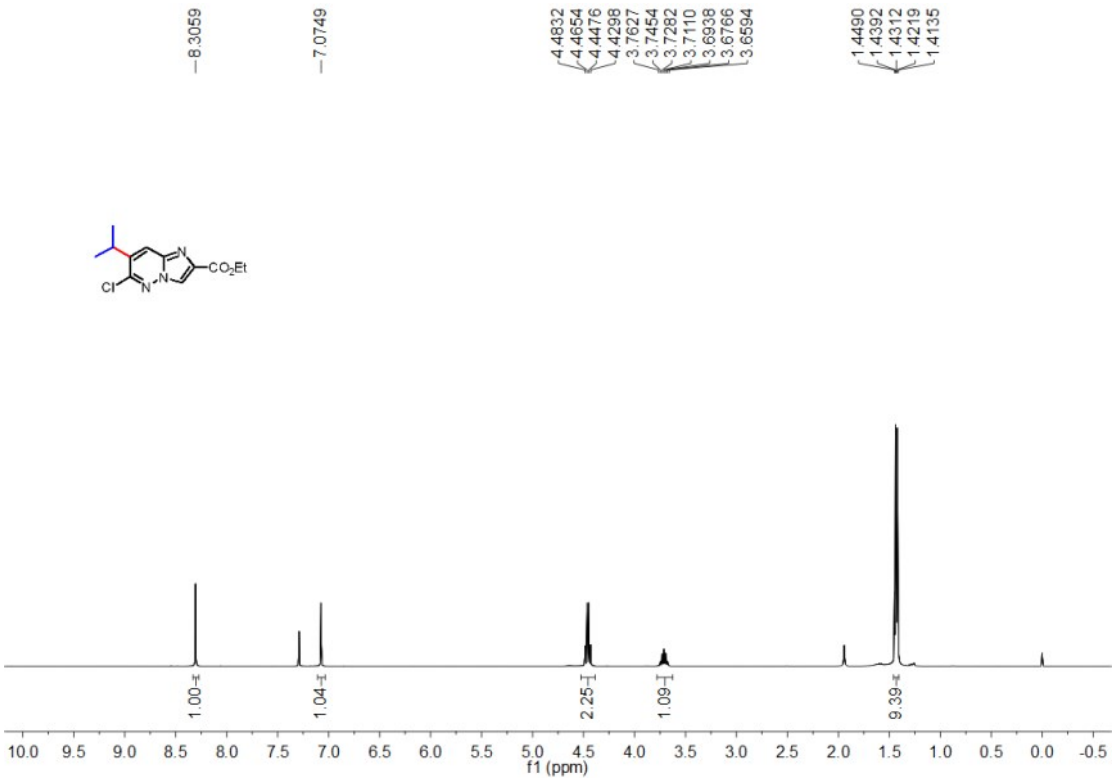
^{1}H NMR spectrum of compound **20**



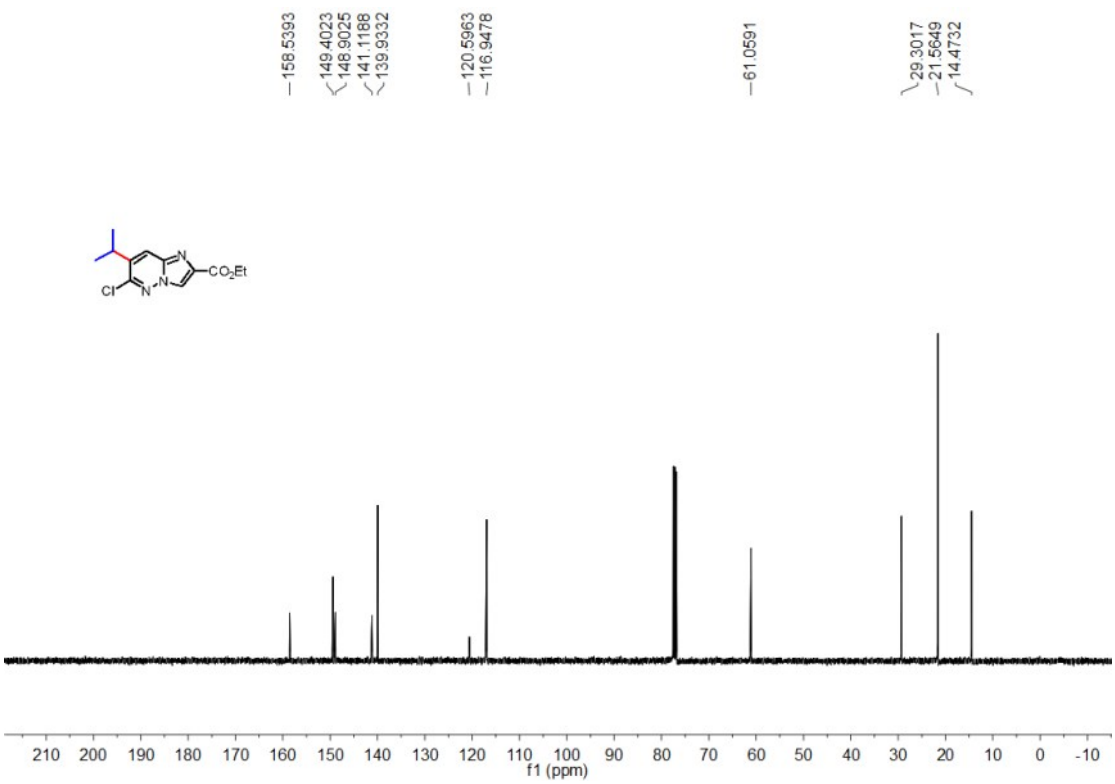
^{13}C NMR spectrum of compound **20**



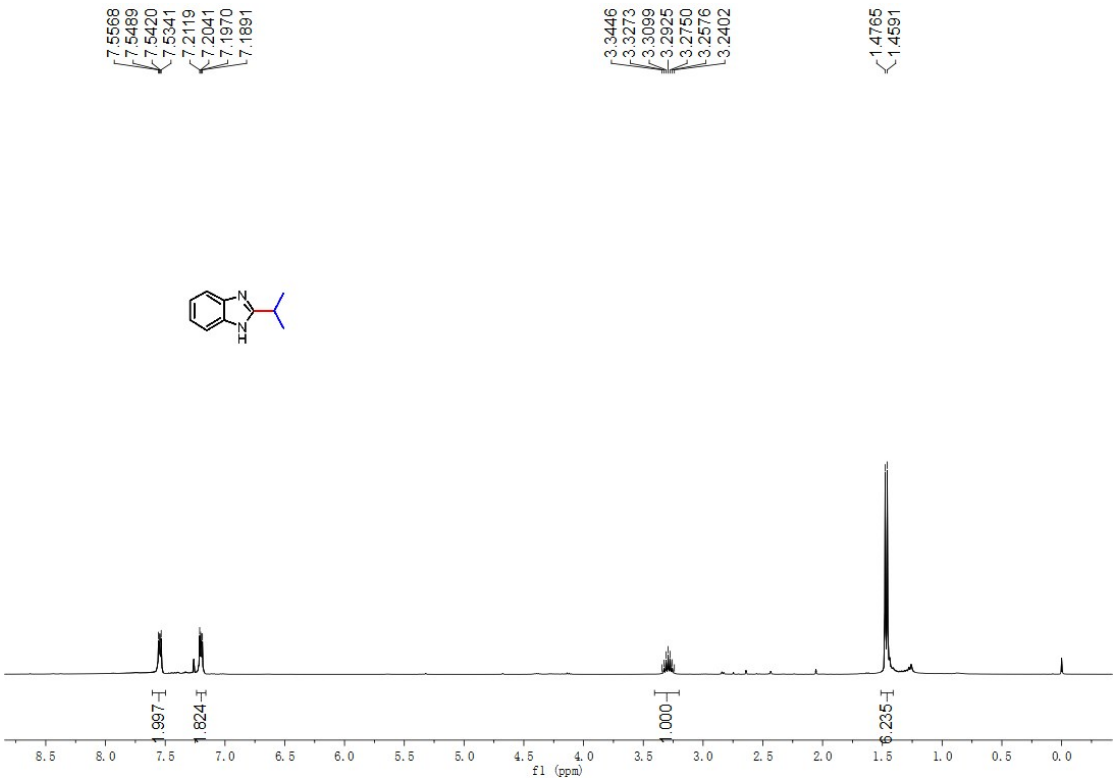
^{1}H NMR spectrum of compound **21**



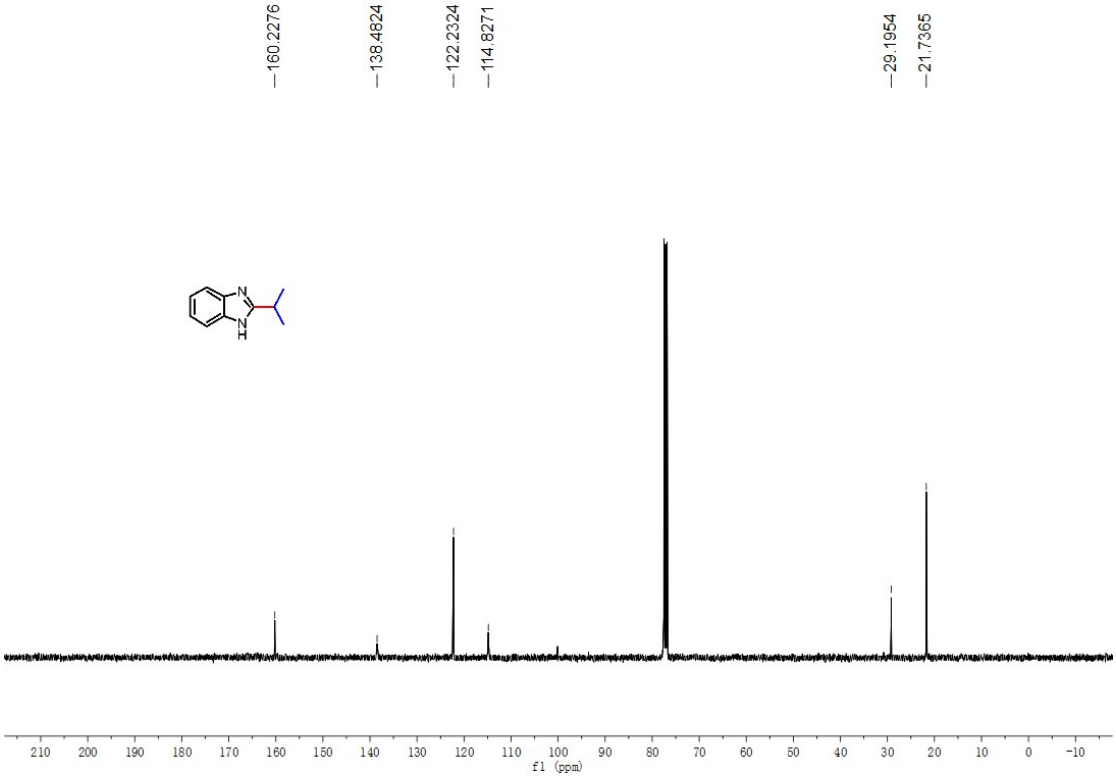
^{13}C NMR spectrum of compound **21**



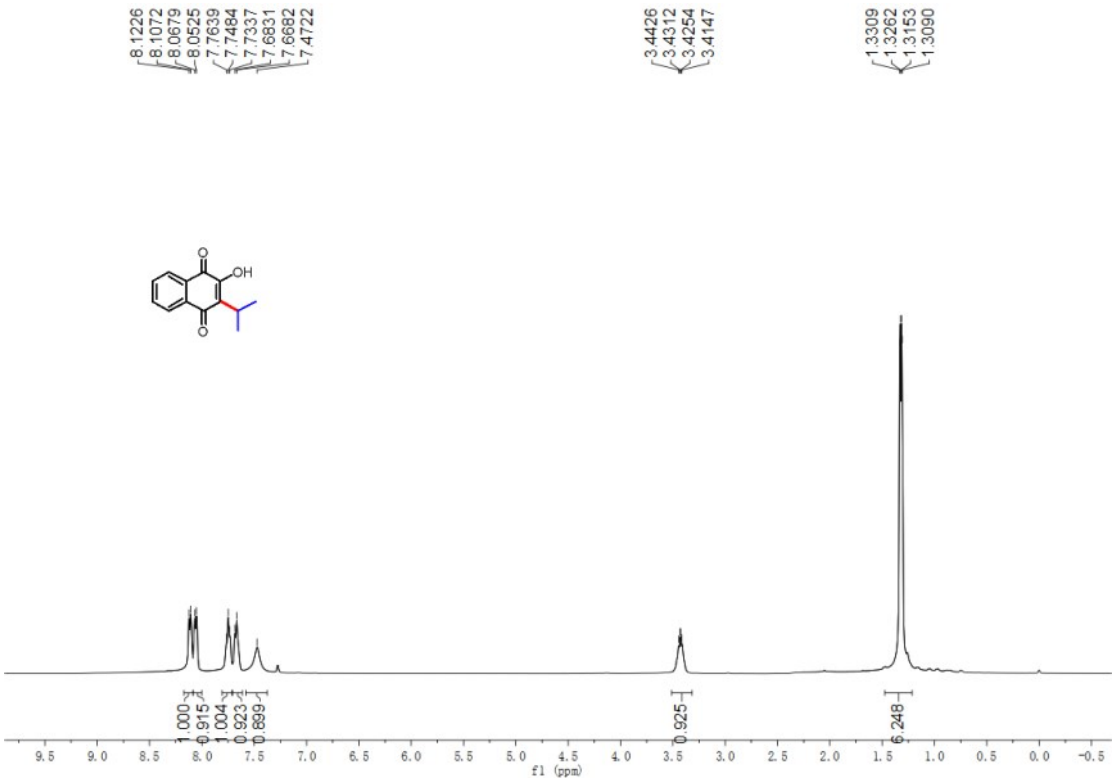
^{1}H NMR spectrum of compound **22**



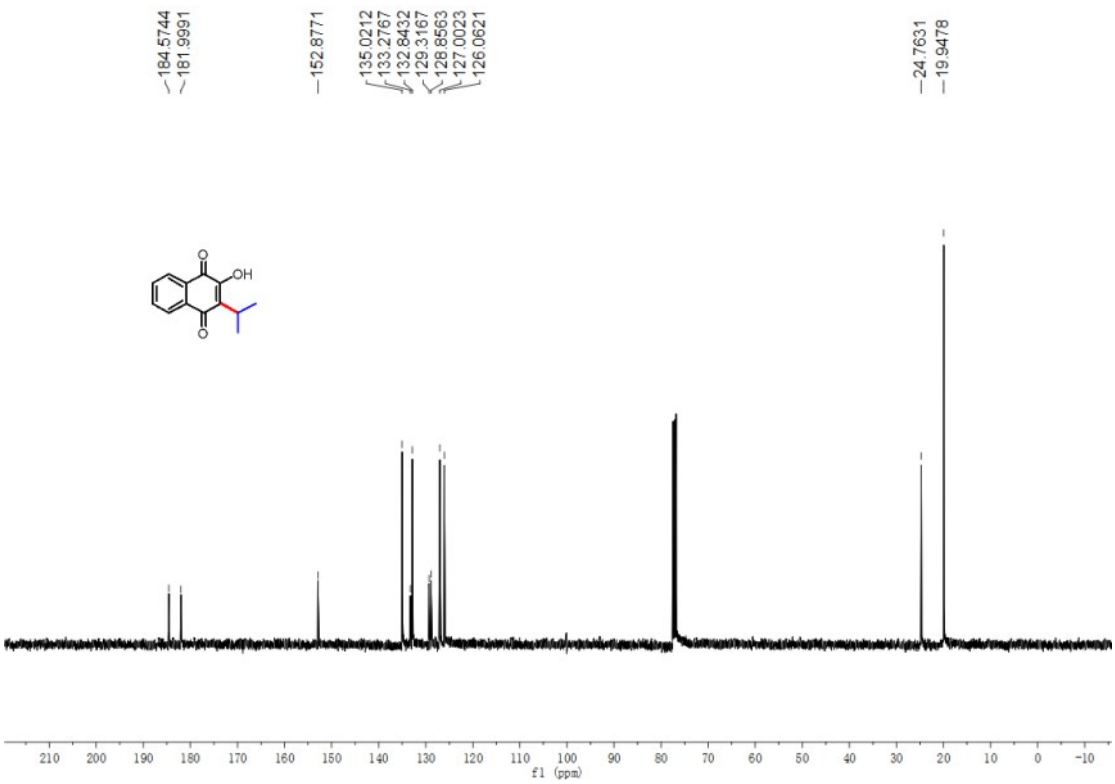
^{13}C NMR spectrum of compound **22**



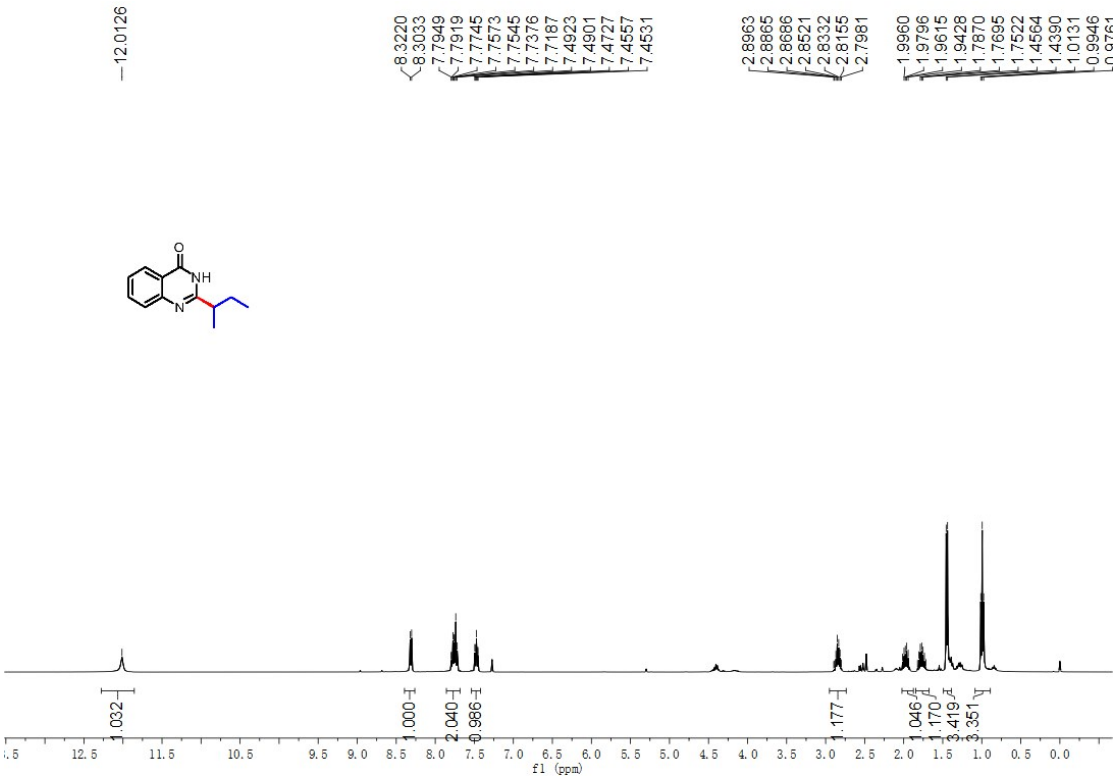
^{1}H NMR spectrum of compound **23**



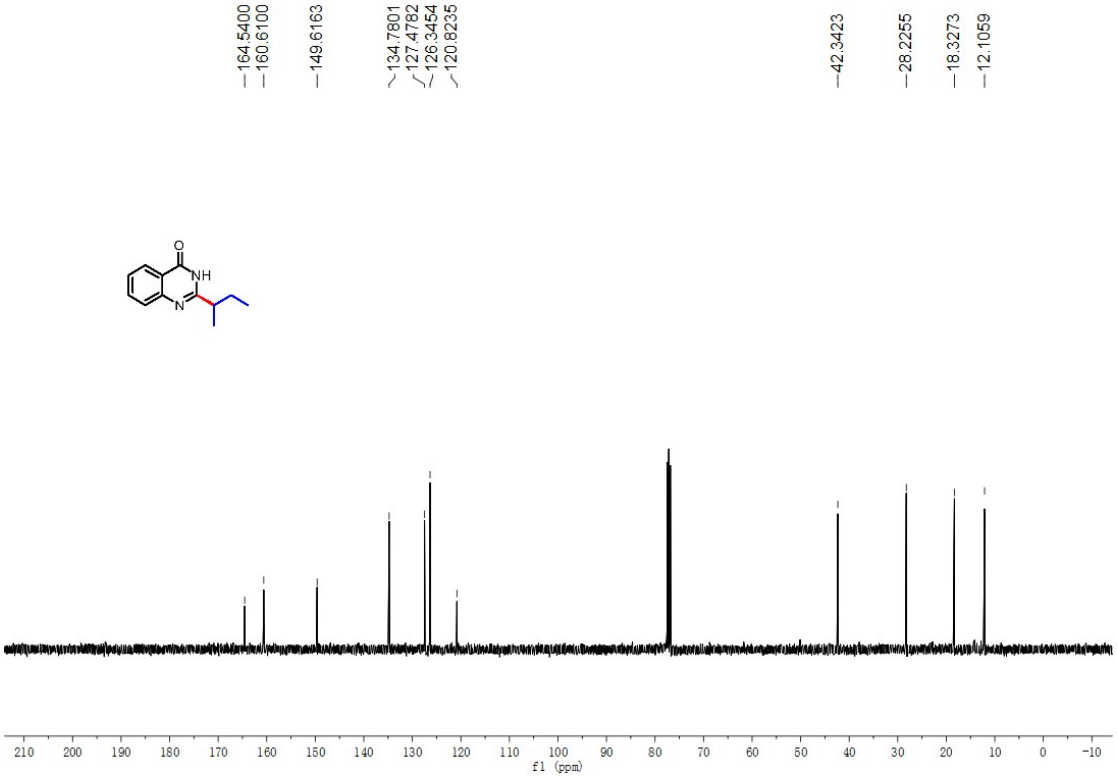
^{13}C NMR spectrum of compound **23**



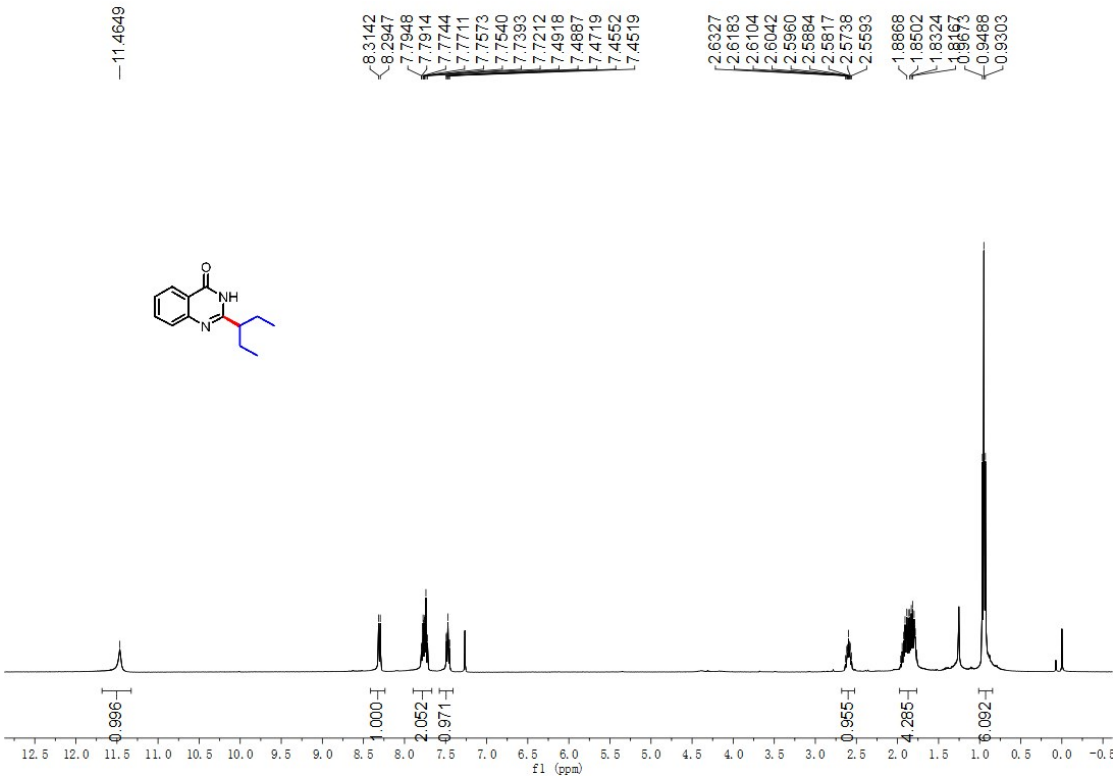
^{1}H NMR spectrum of compound **24**



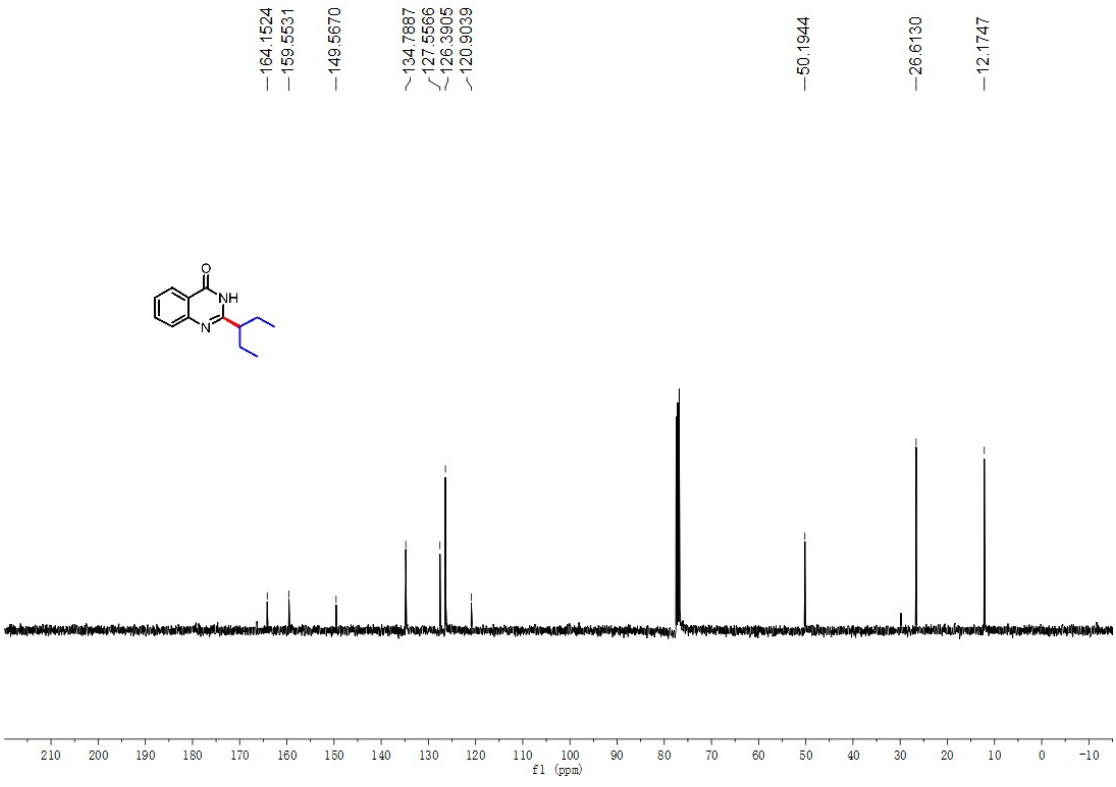
^{13}C NMR spectrum of compound **24**



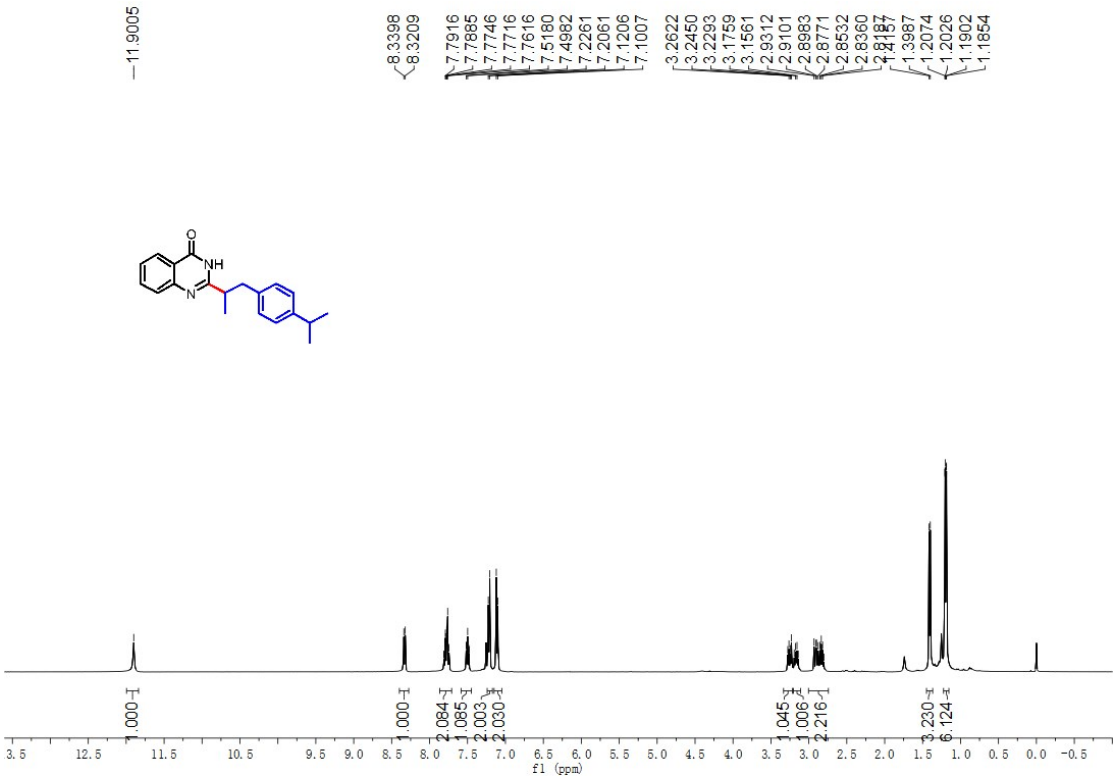
^{1}H NMR spectrum of compound **25**



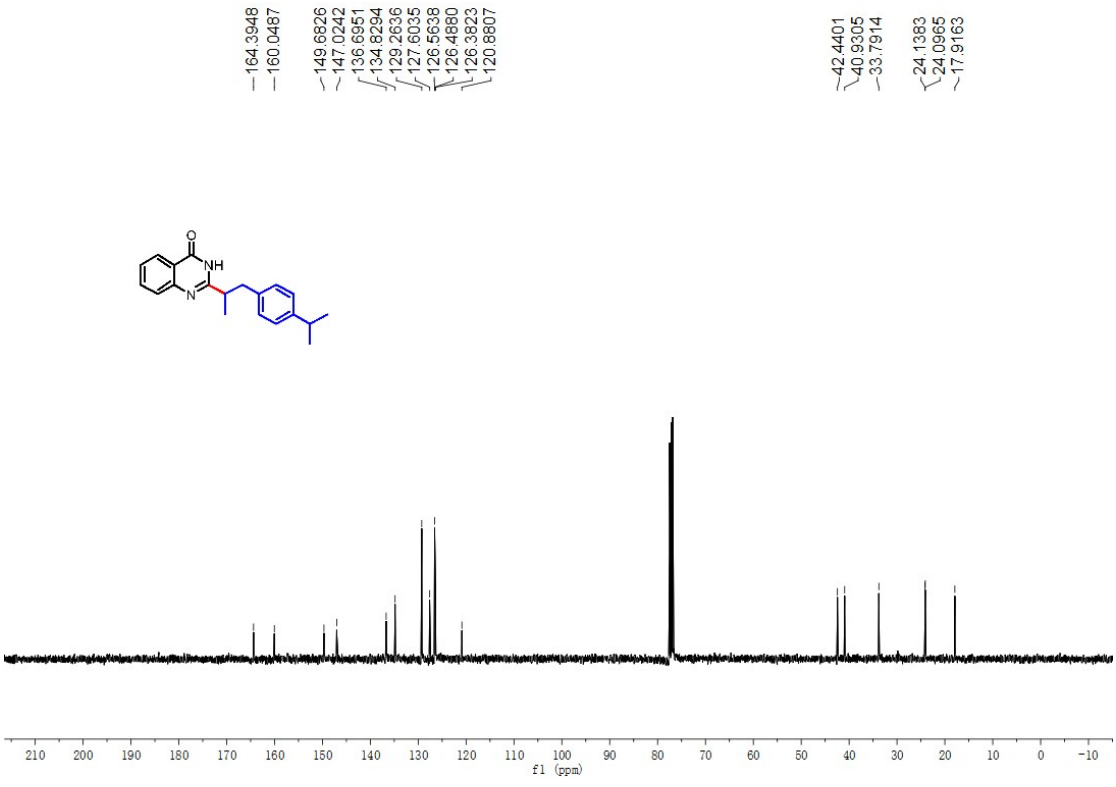
^{13}C NMR spectrum of compound **25**



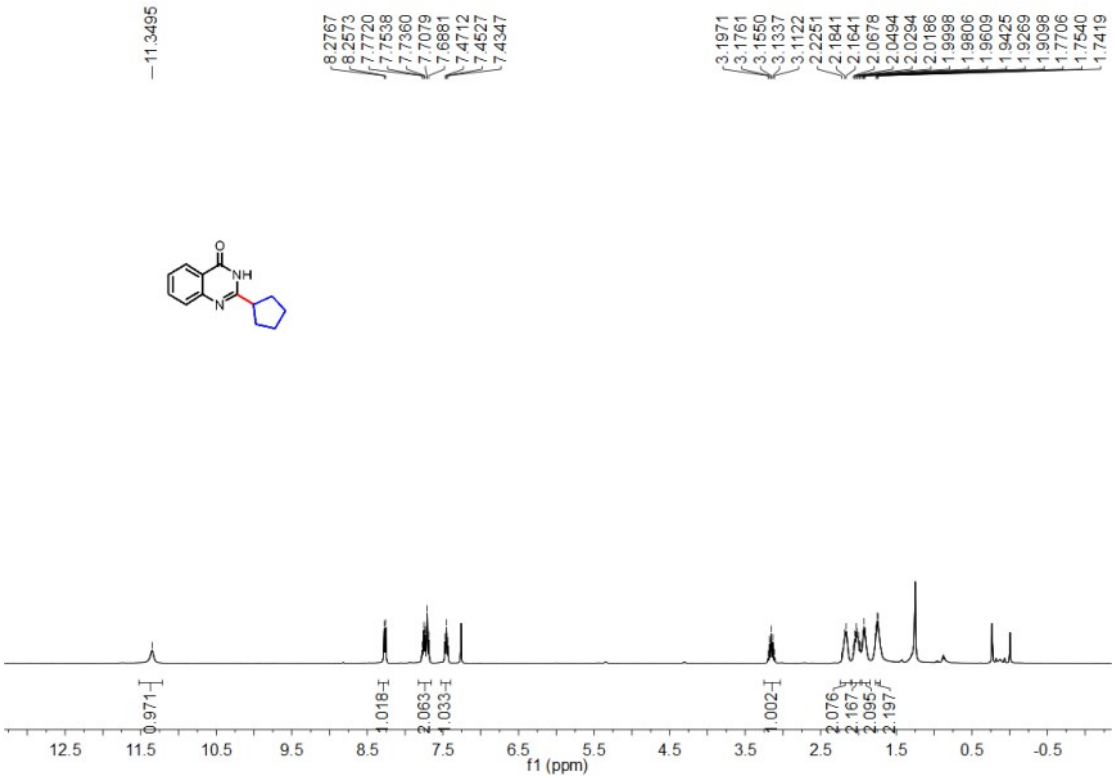
^{1}H NMR spectrum of compound **26**



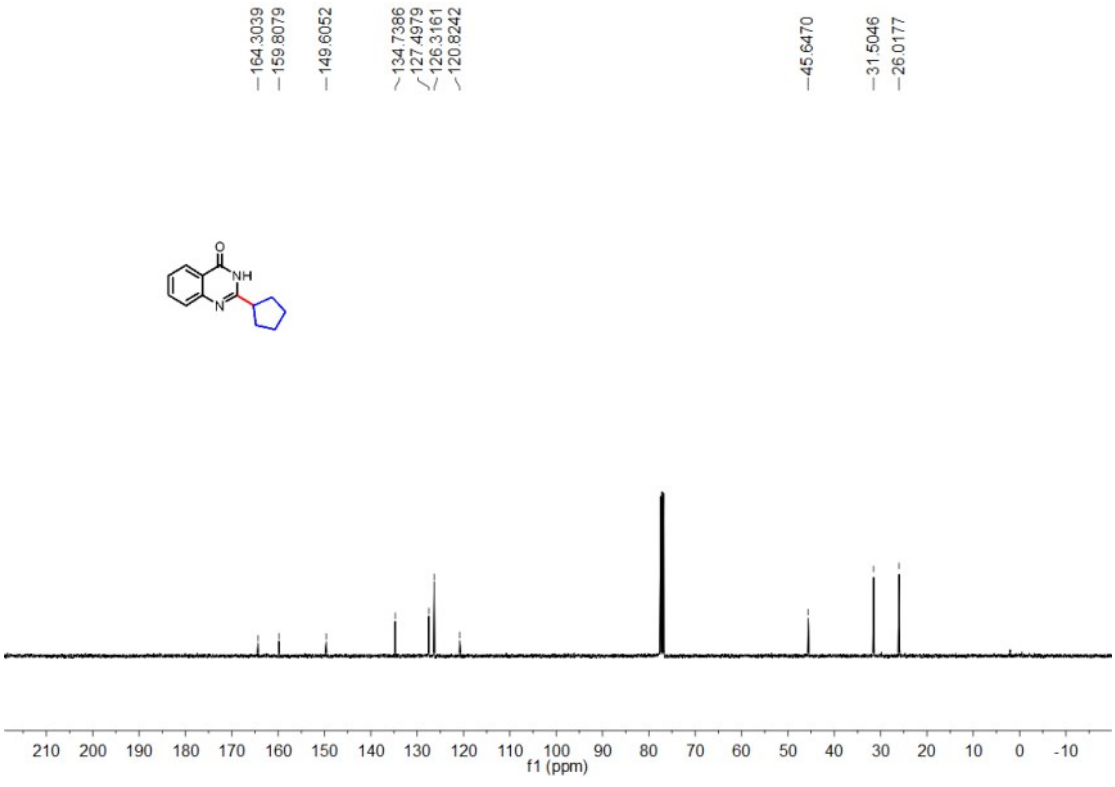
^{13}C NMR spectrum of compound **26**



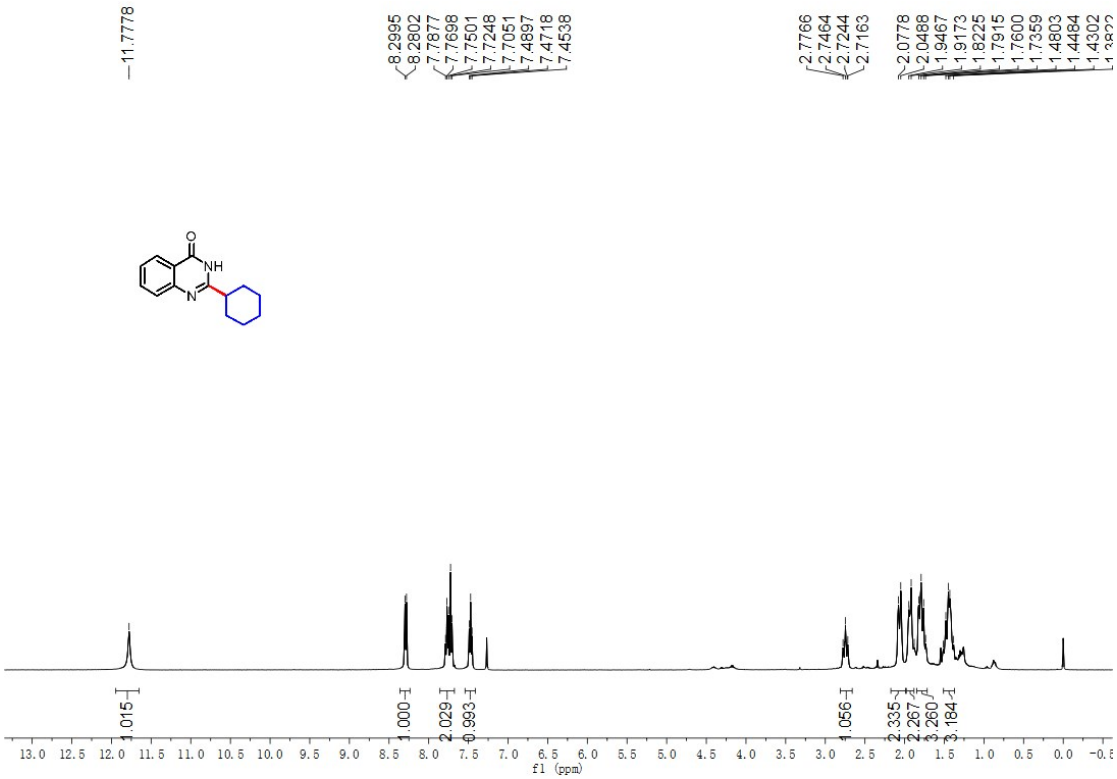
^{1}H NMR spectrum of compound **27**



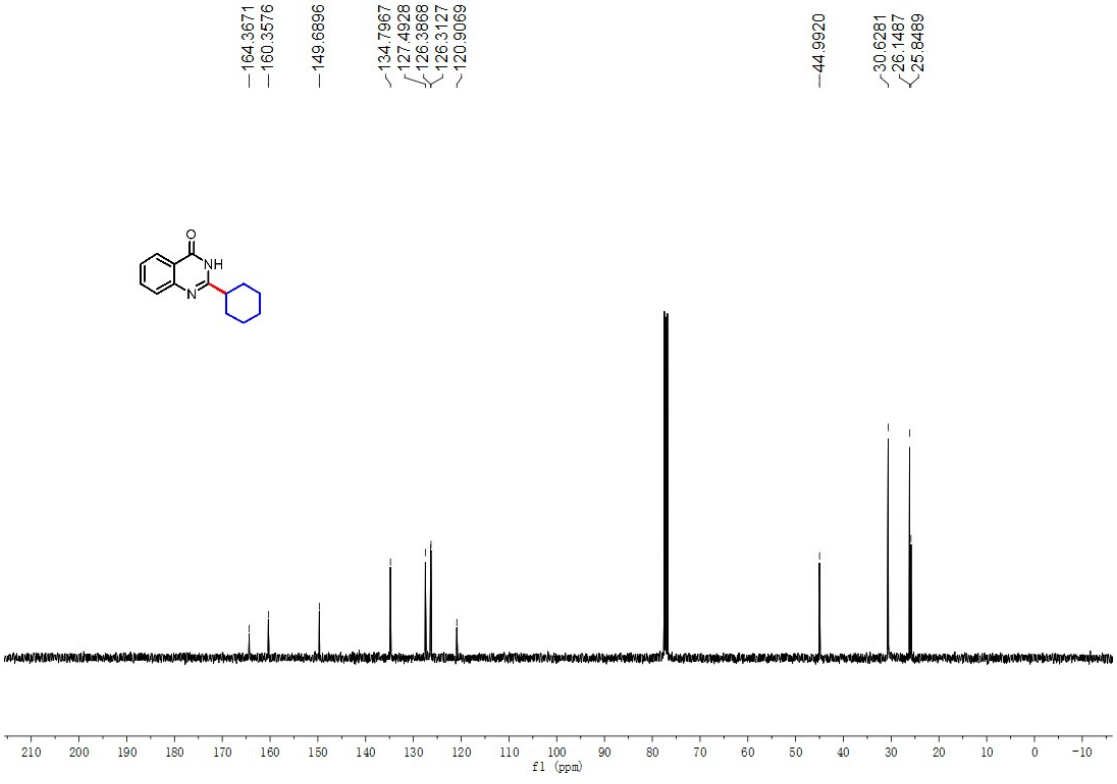
^{13}C NMR spectrum of compound **27**



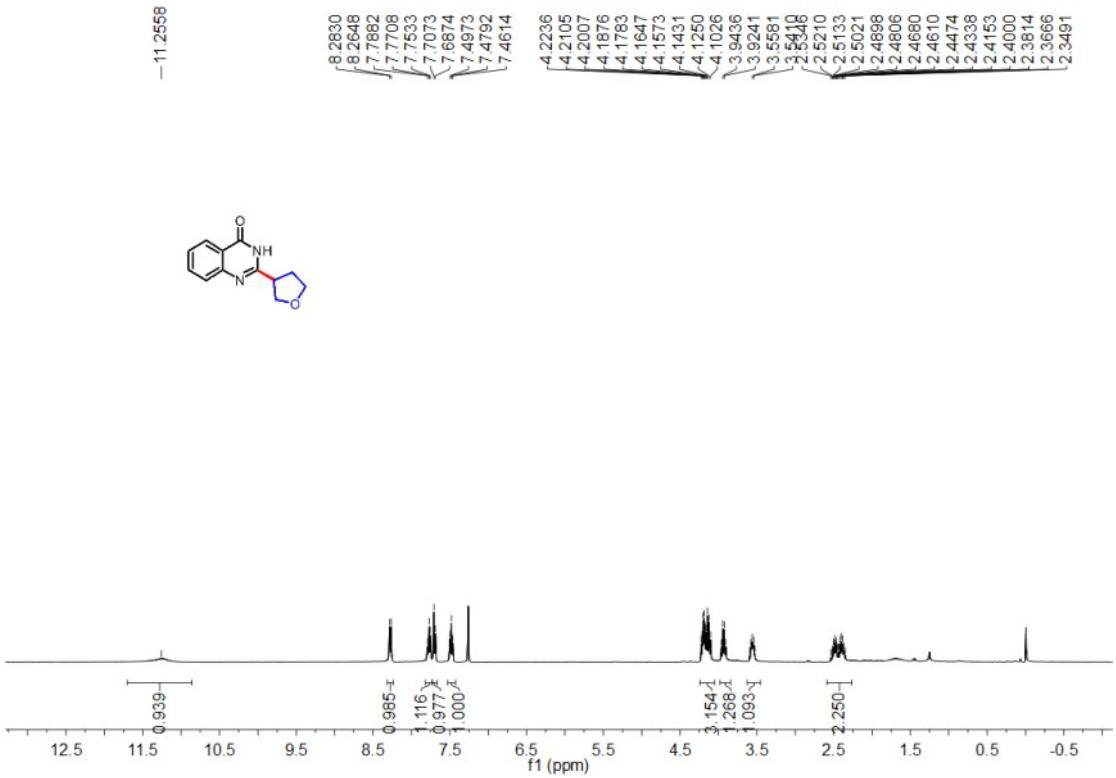
^{1}H NMR spectrum of compound **28**



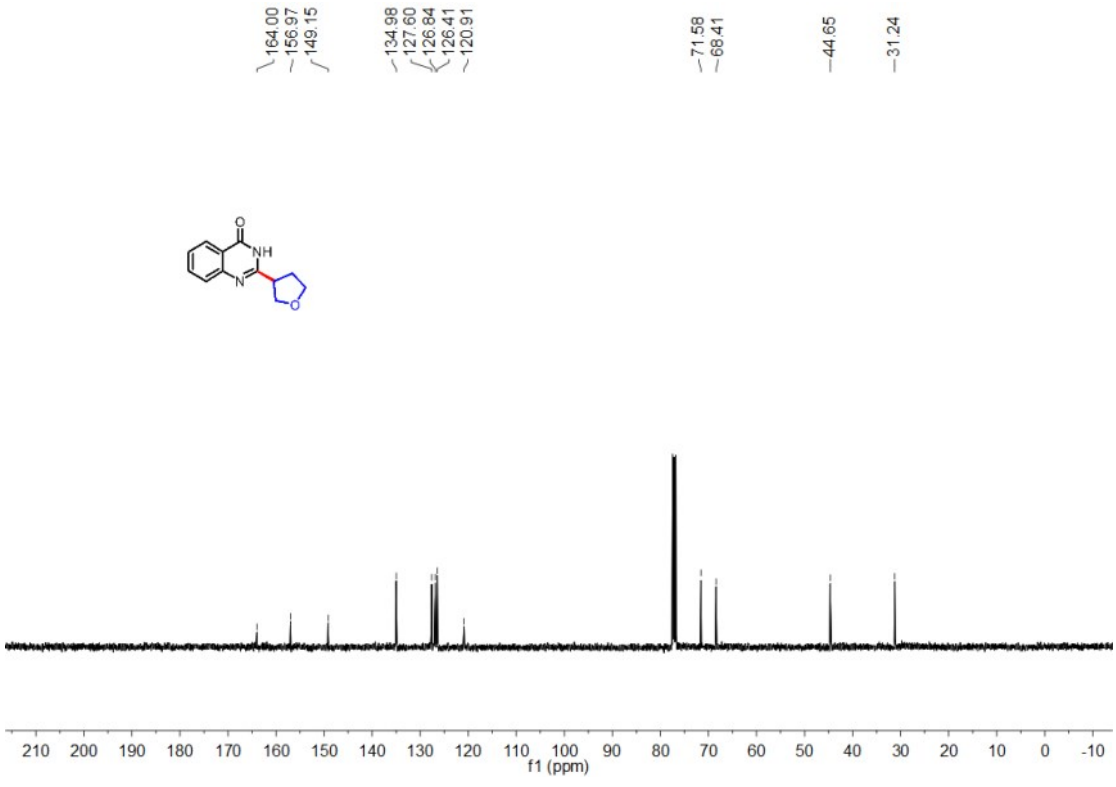
^{13}C NMR spectrum of compound **28**



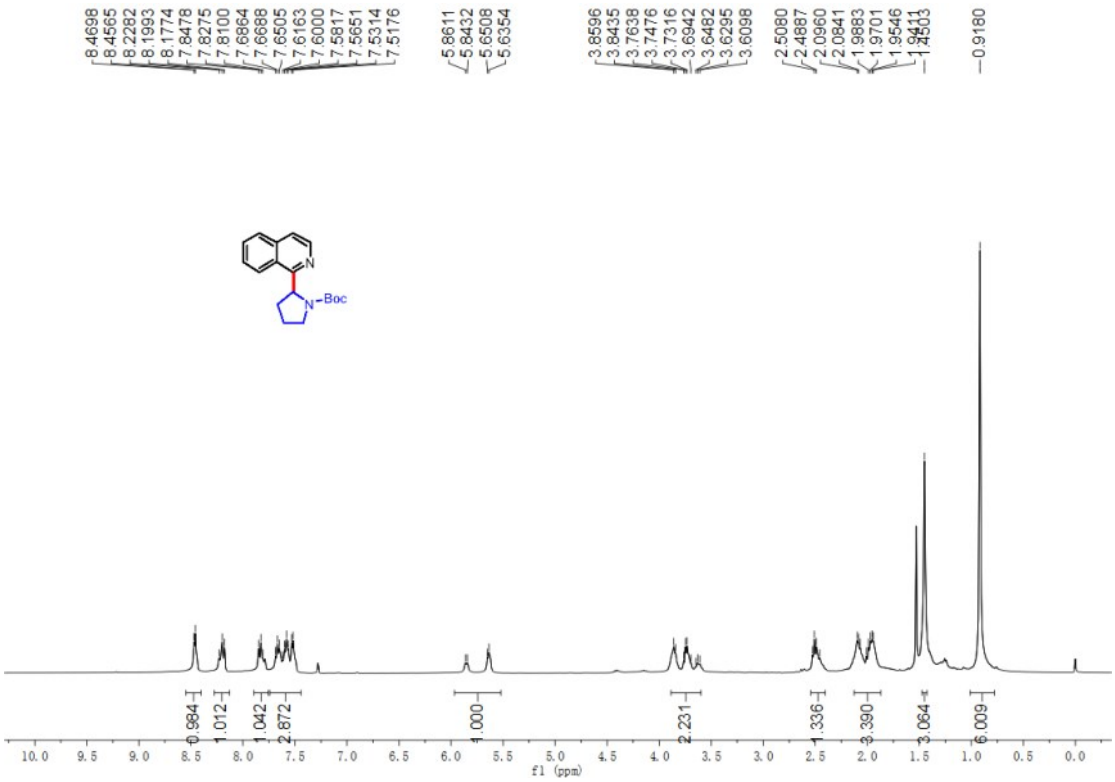
^{1}H NMR spectrum of compound **29**



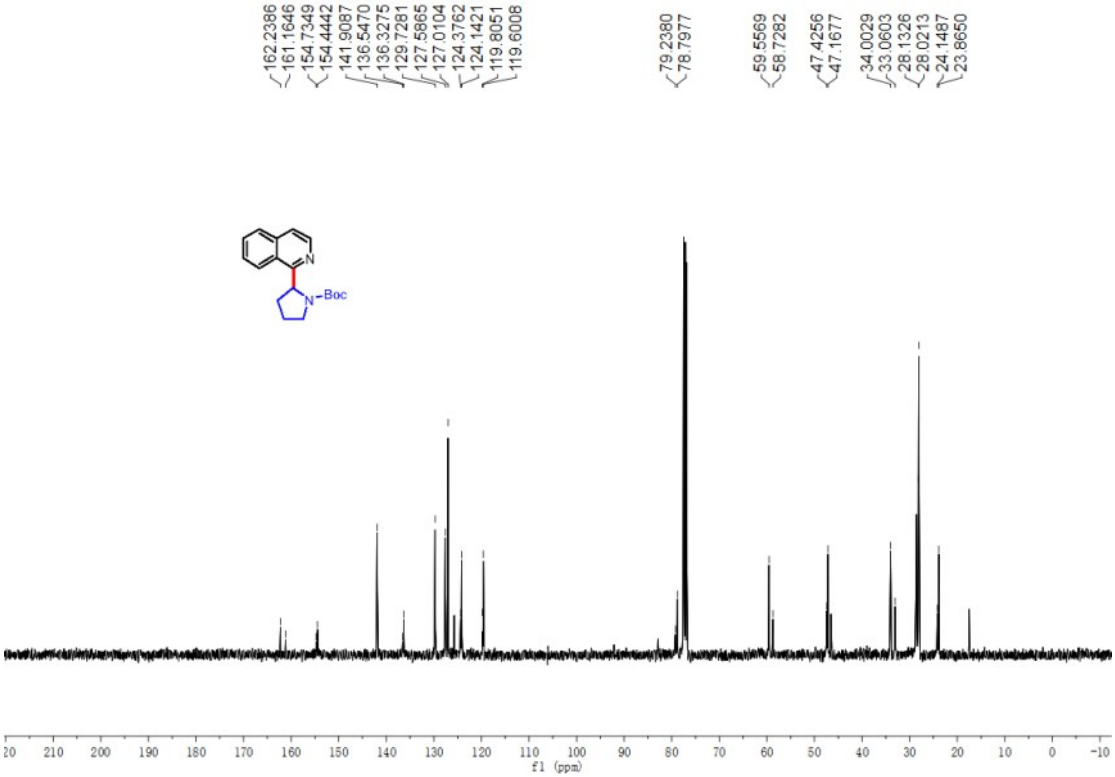
^{13}C NMR spectrum of compound **29**



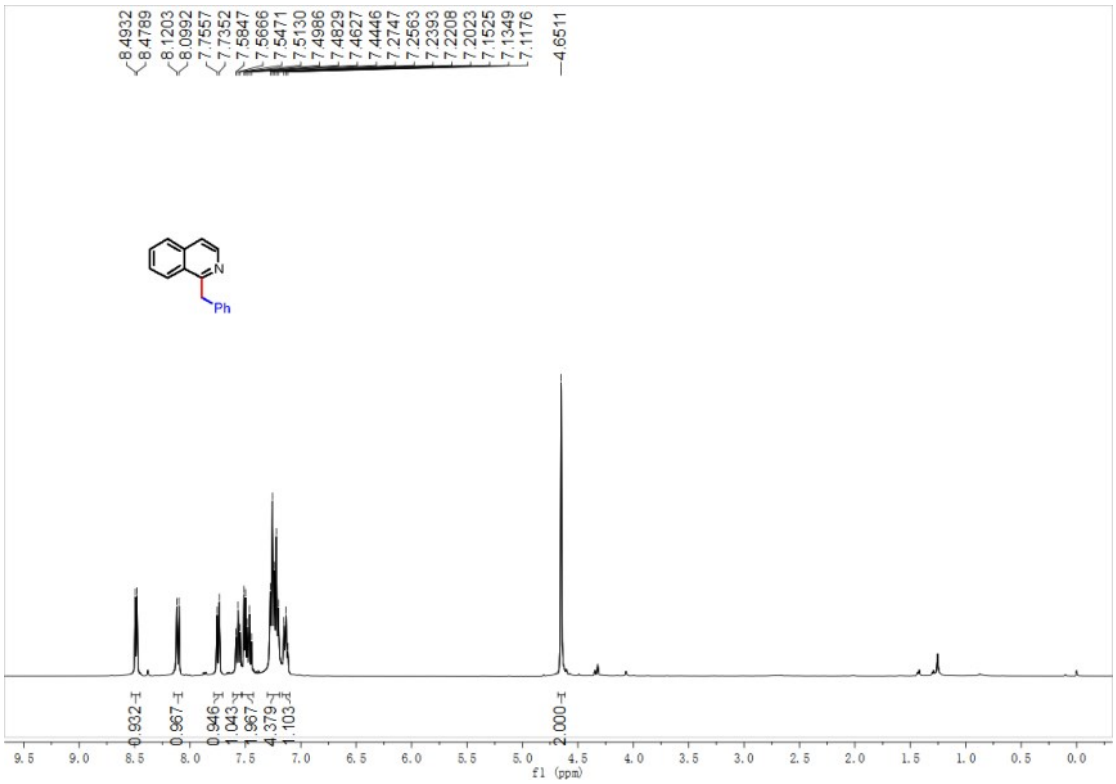
^{1}H NMR spectrum of compound **30**



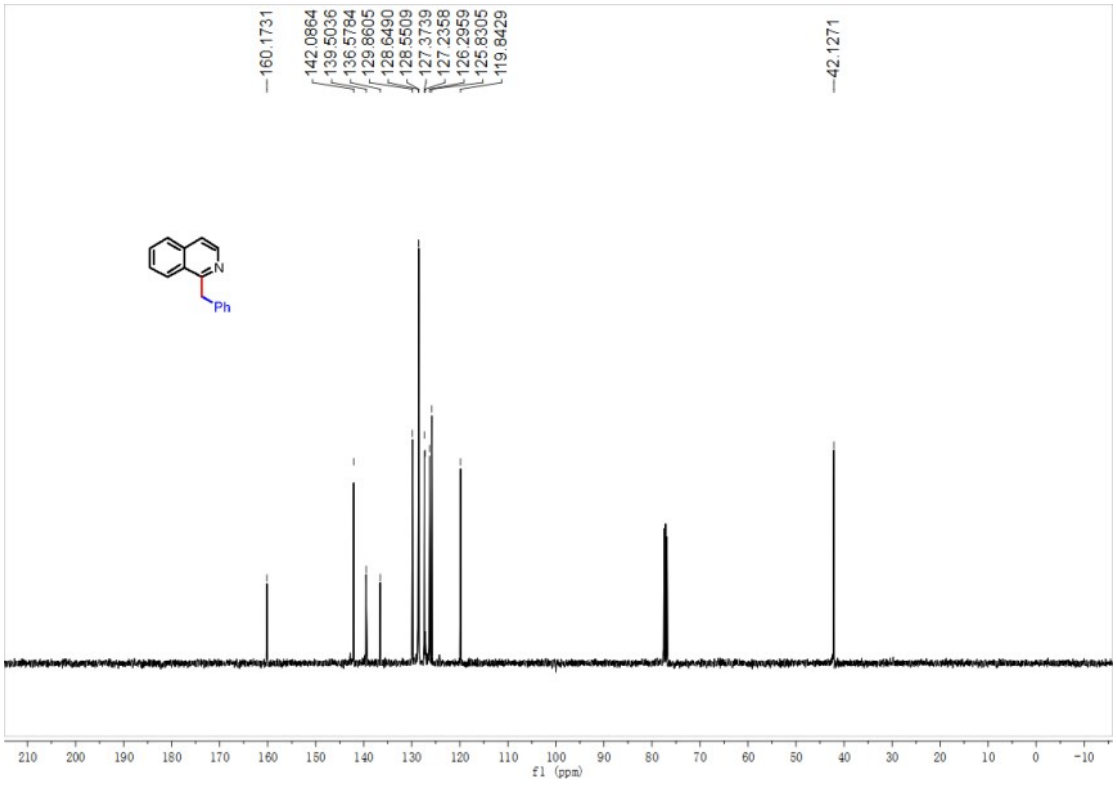
^{13}C NMR spectrum of compound **30**



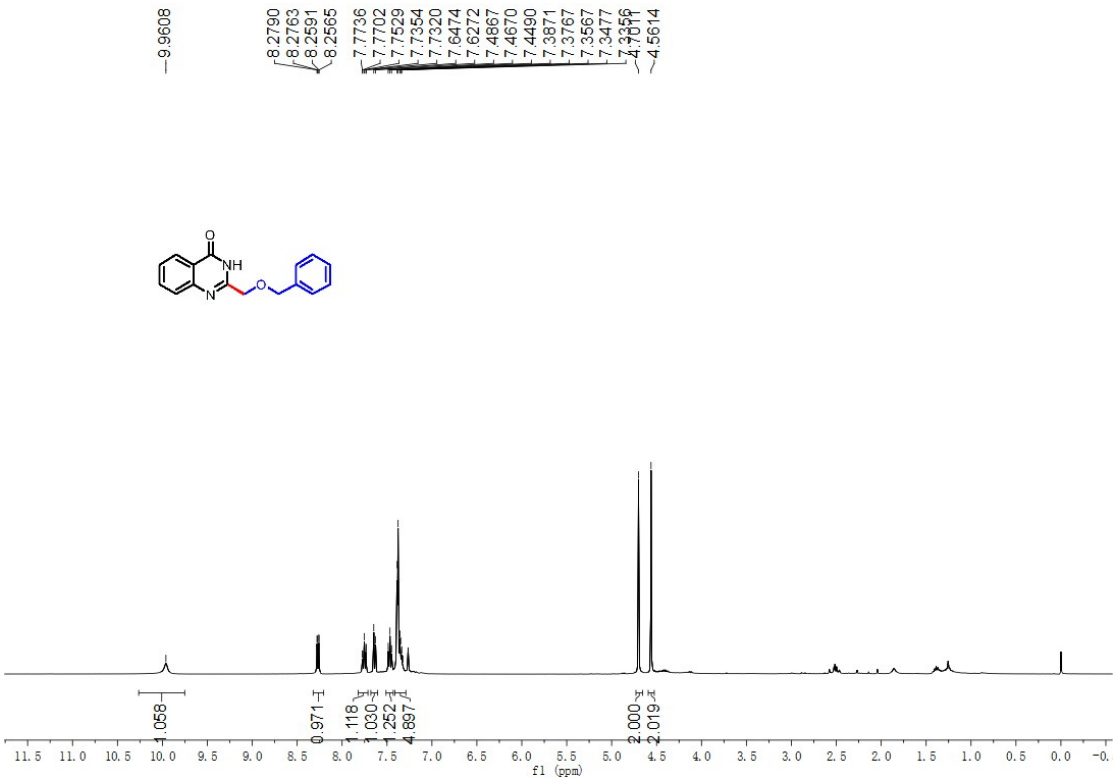
^{1}H NMR spectrum of compound **31**



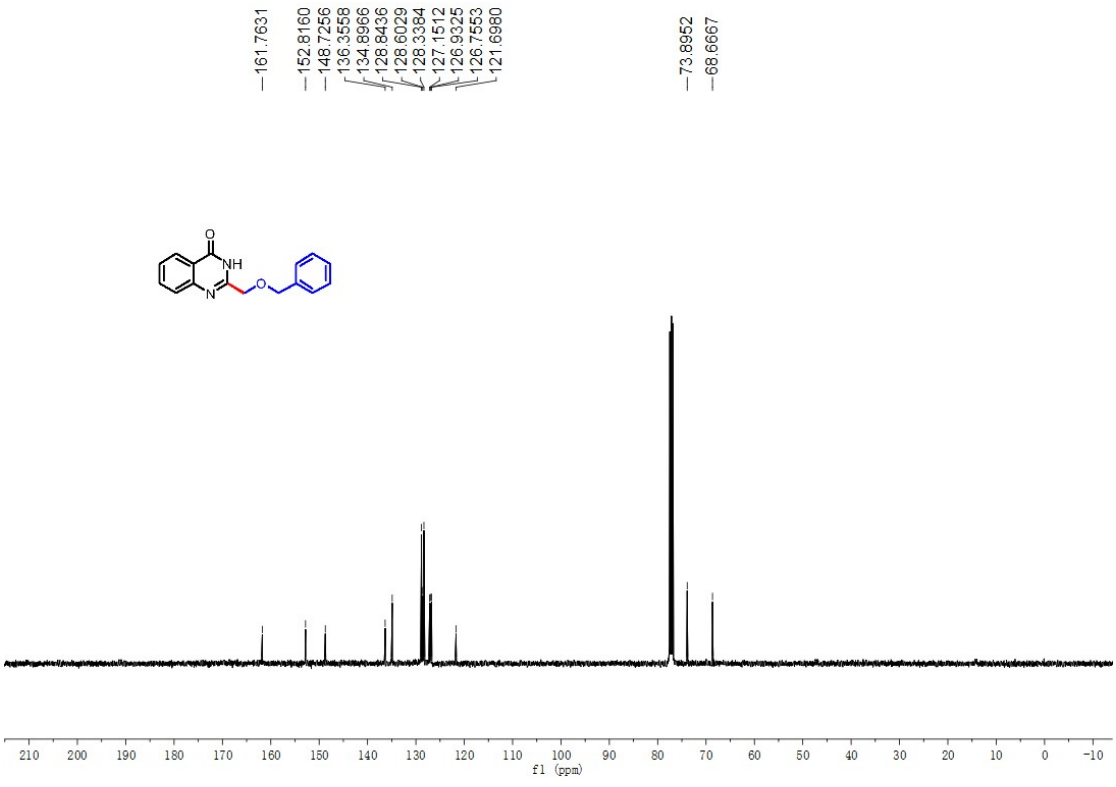
^{13}C NMR spectrum of compound **31**



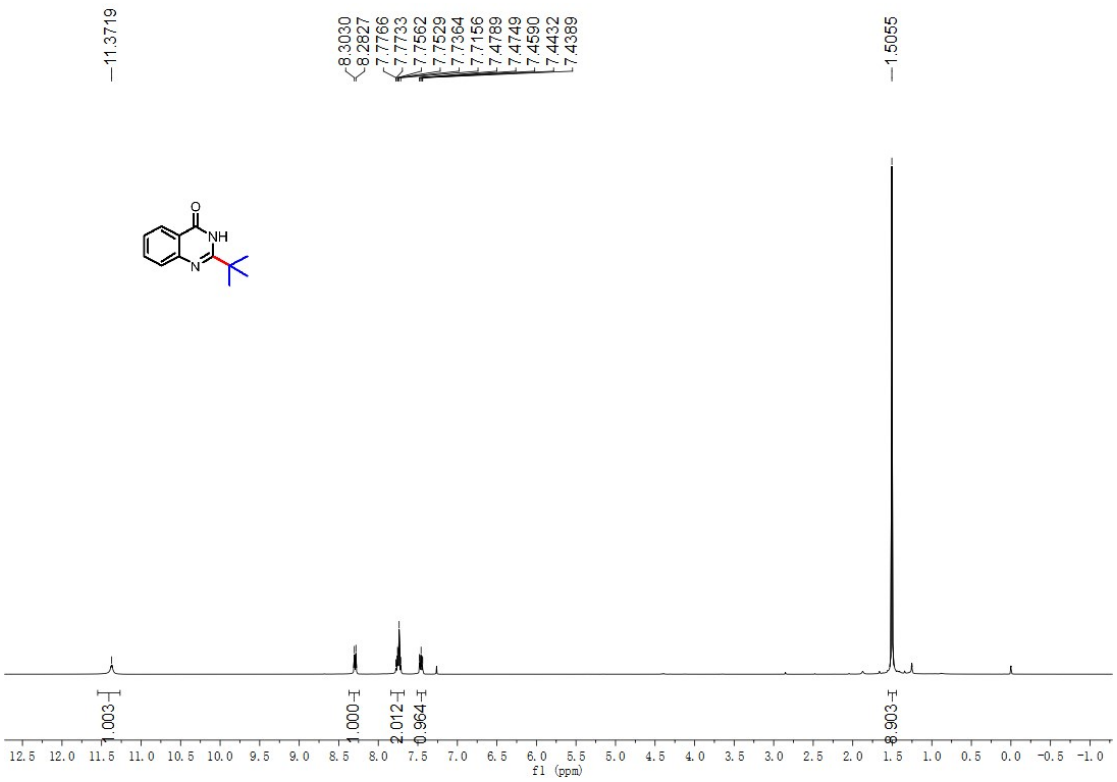
^{1}H NMR spectrum of compound **32**



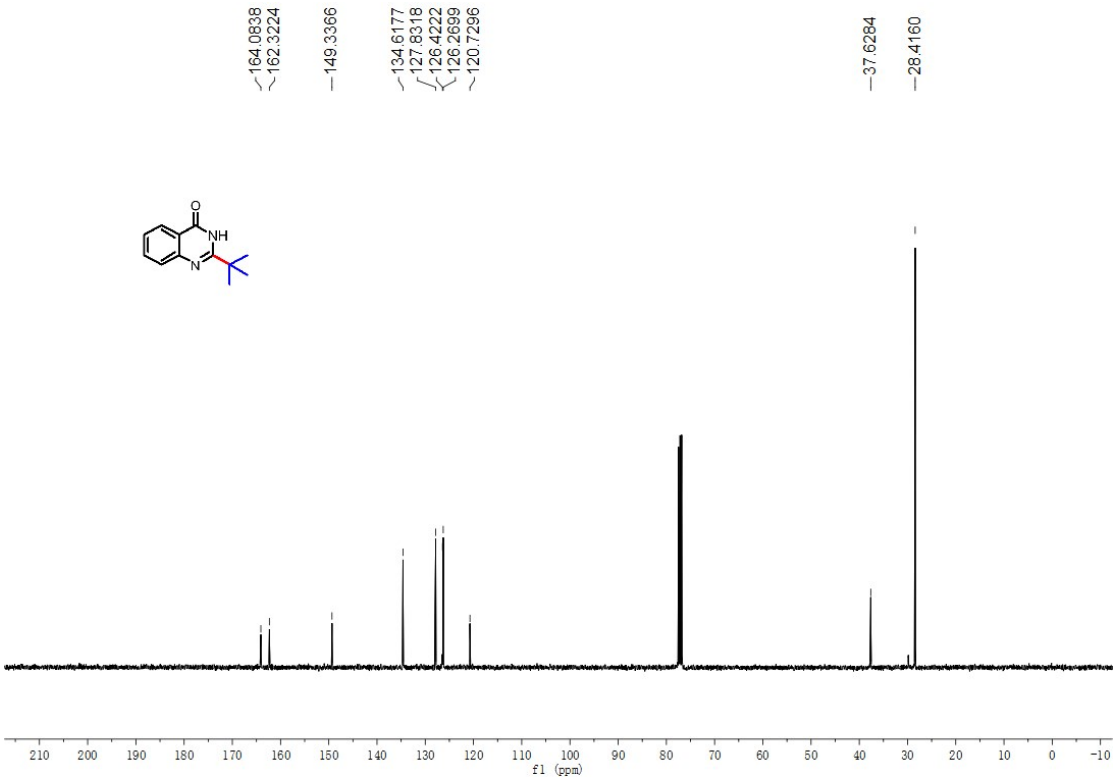
^{13}C NMR spectrum of compound **32**



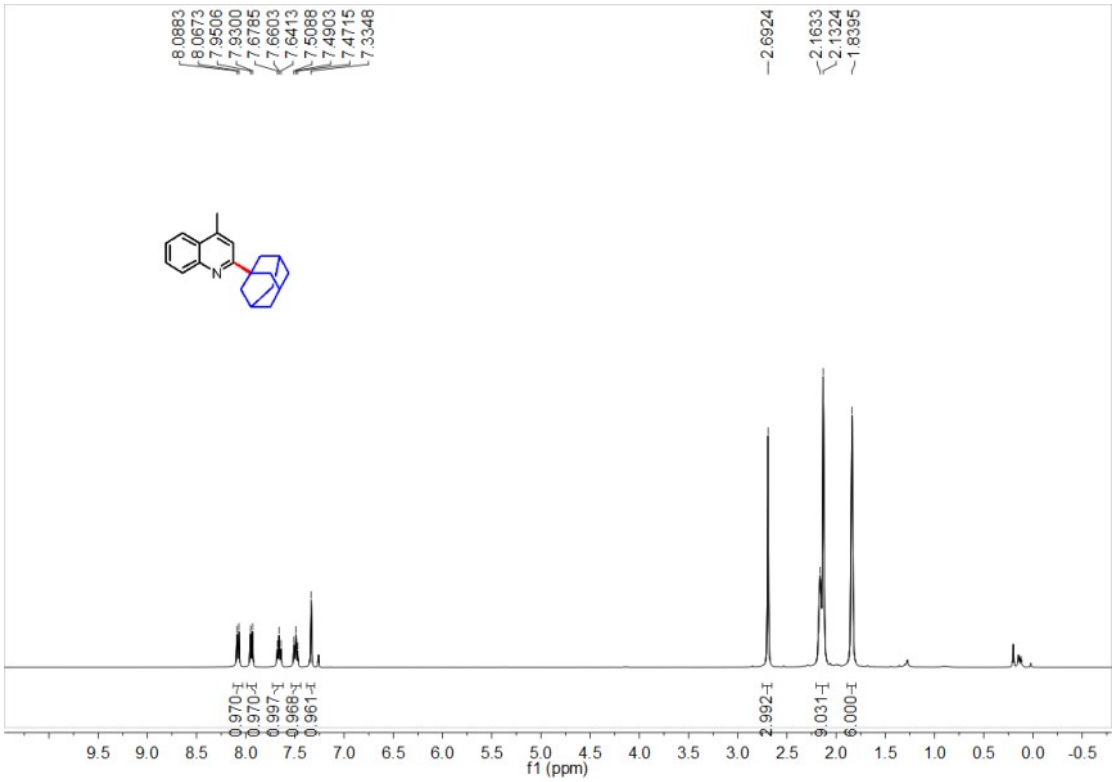
^{1}H NMR spectrum of compound **33**



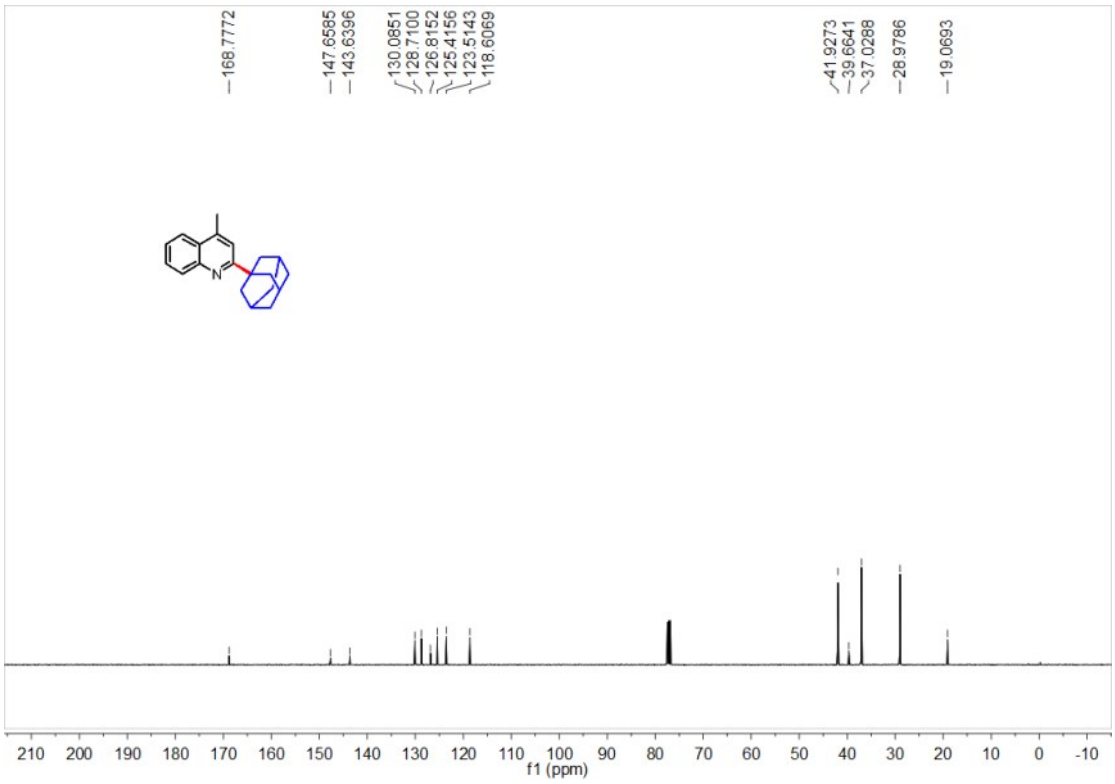
^{13}C NMR spectrum of compound **33**



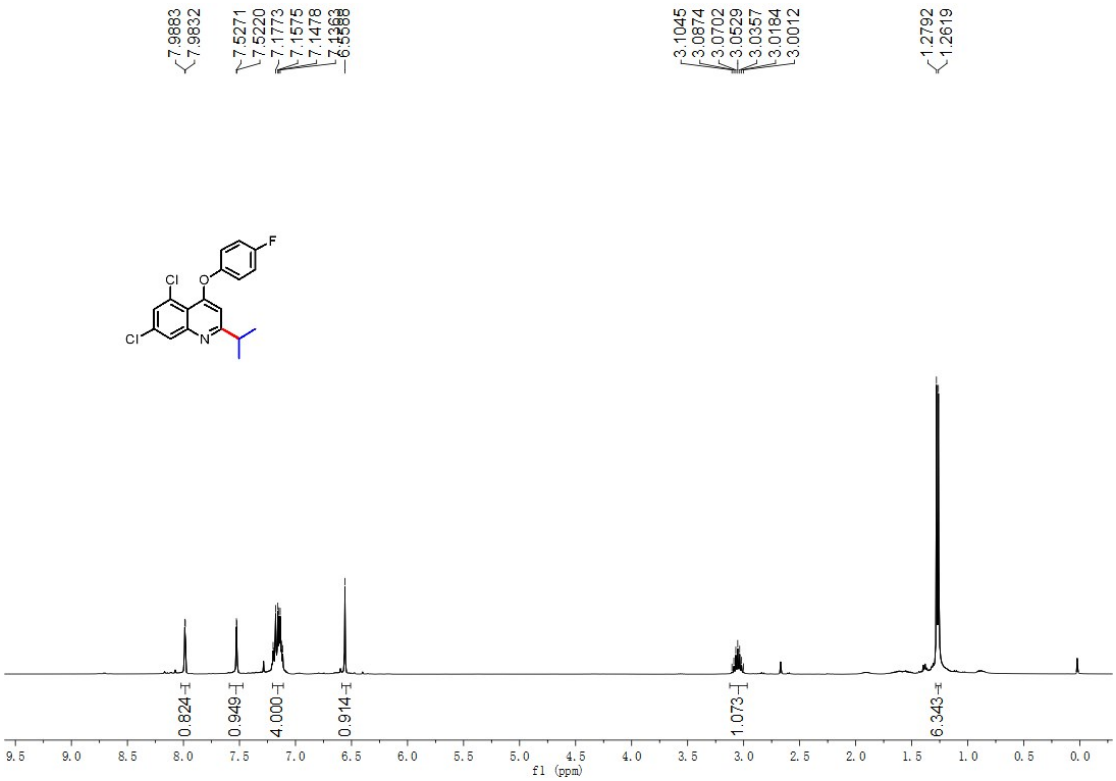
^{1}H NMR spectrum of compound **34**



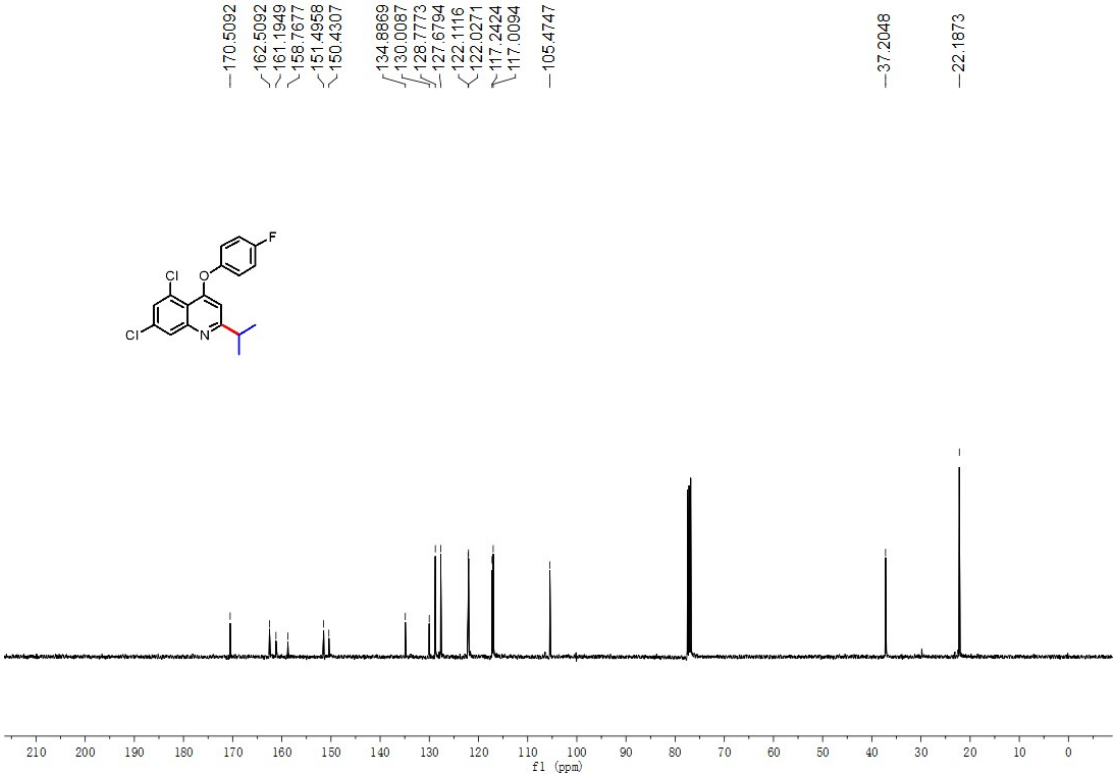
^{13}C NMR spectrum of compound **34**



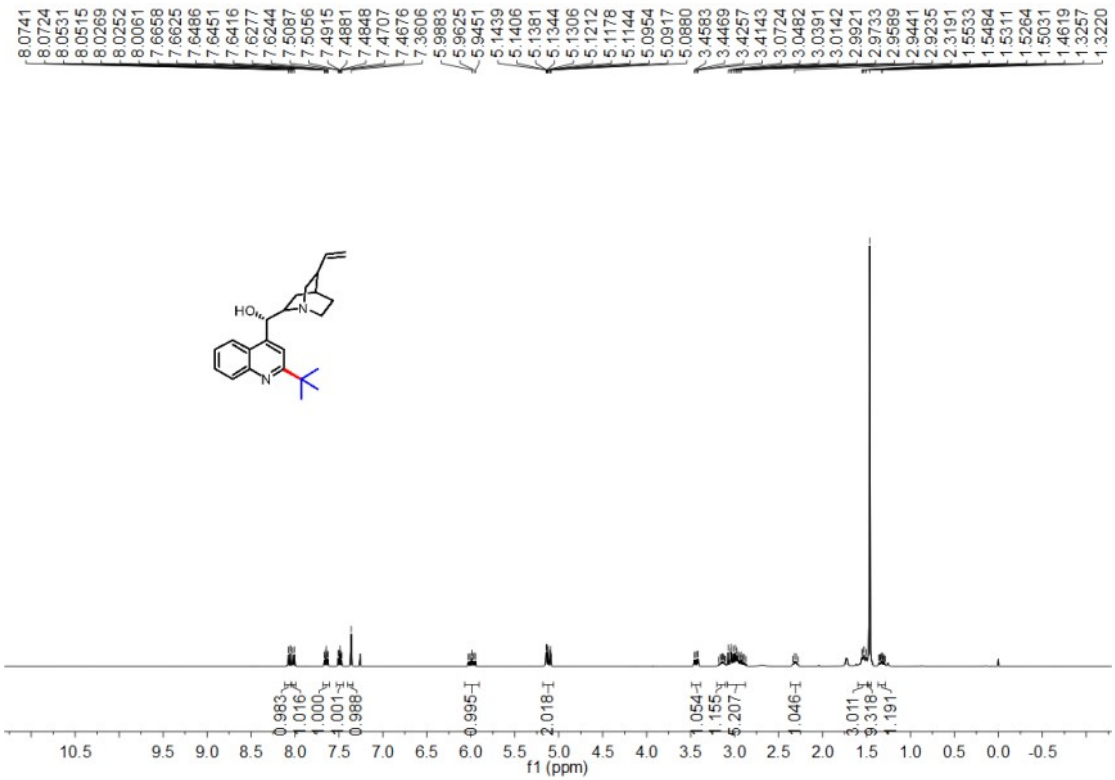
^{1}H NMR spectrum of compound **35**



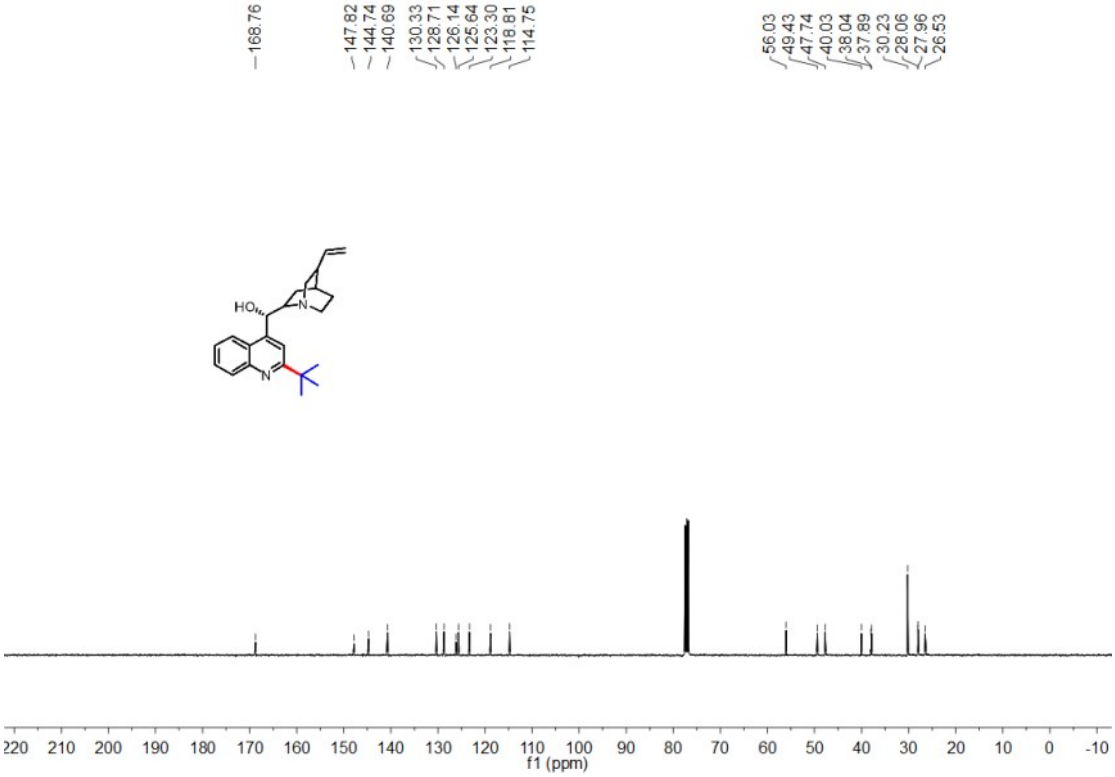
^{13}C NMR spectrum of compound **35**



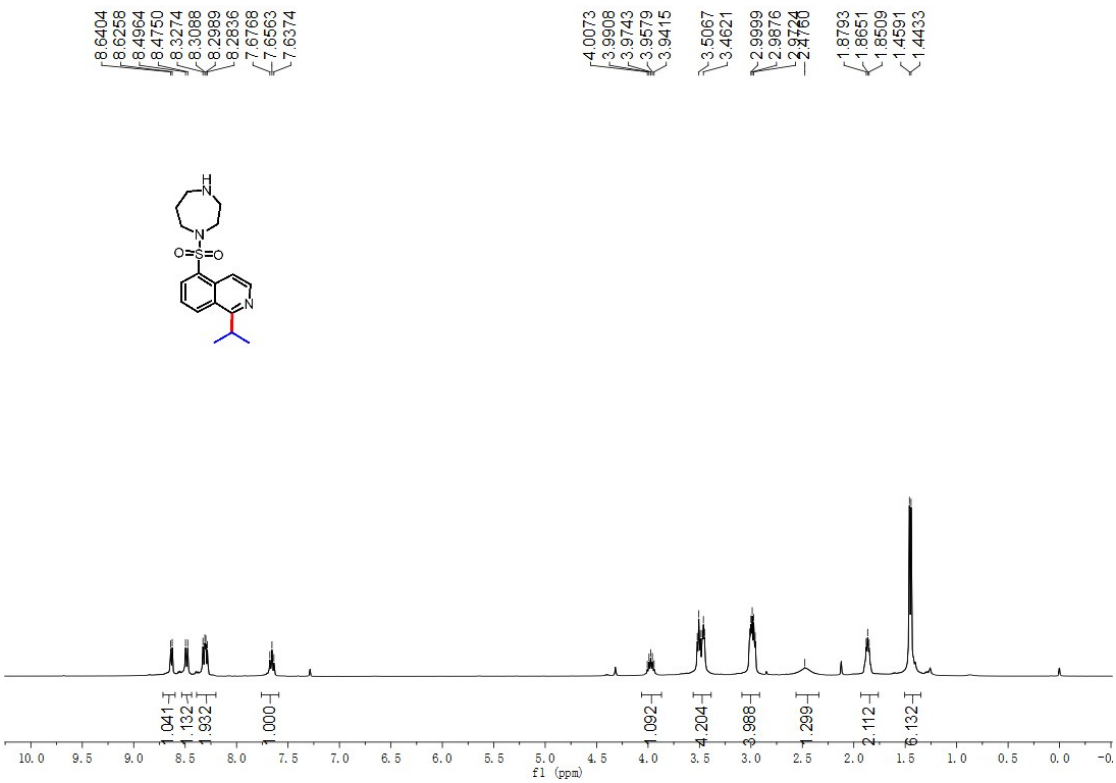
^{1}H NMR spectrum of compound **36**



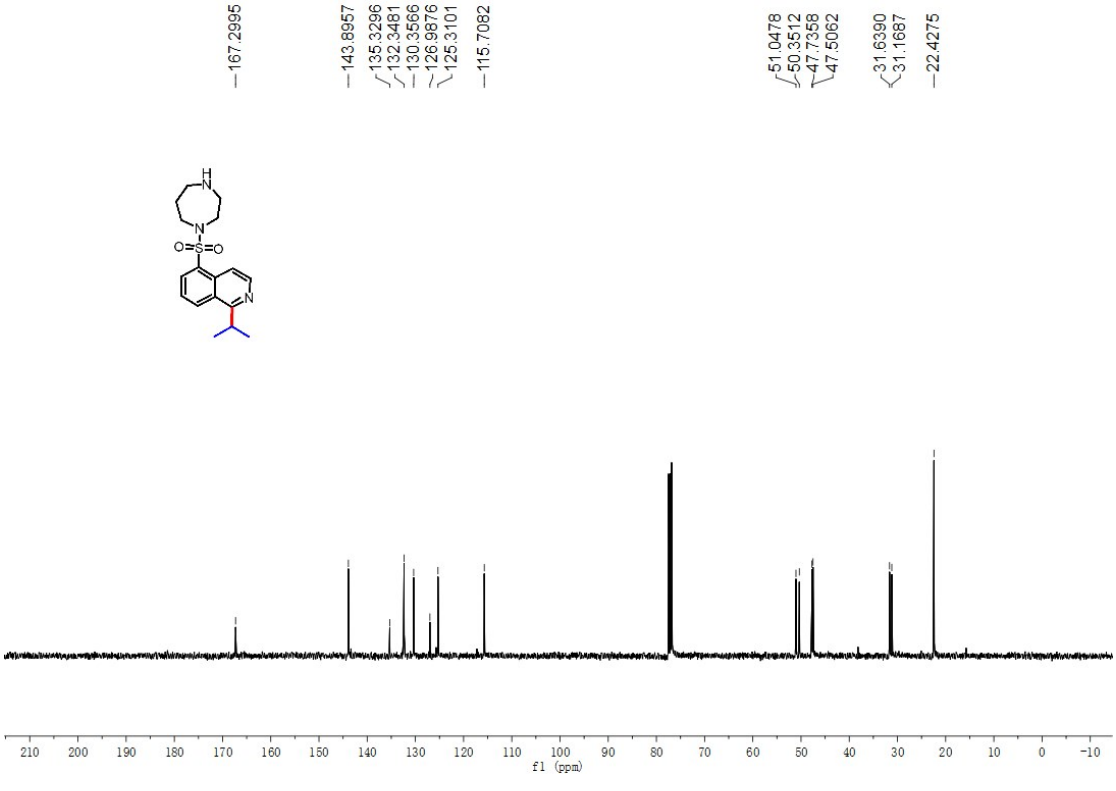
^{13}C NMR spectrum of compound **36**



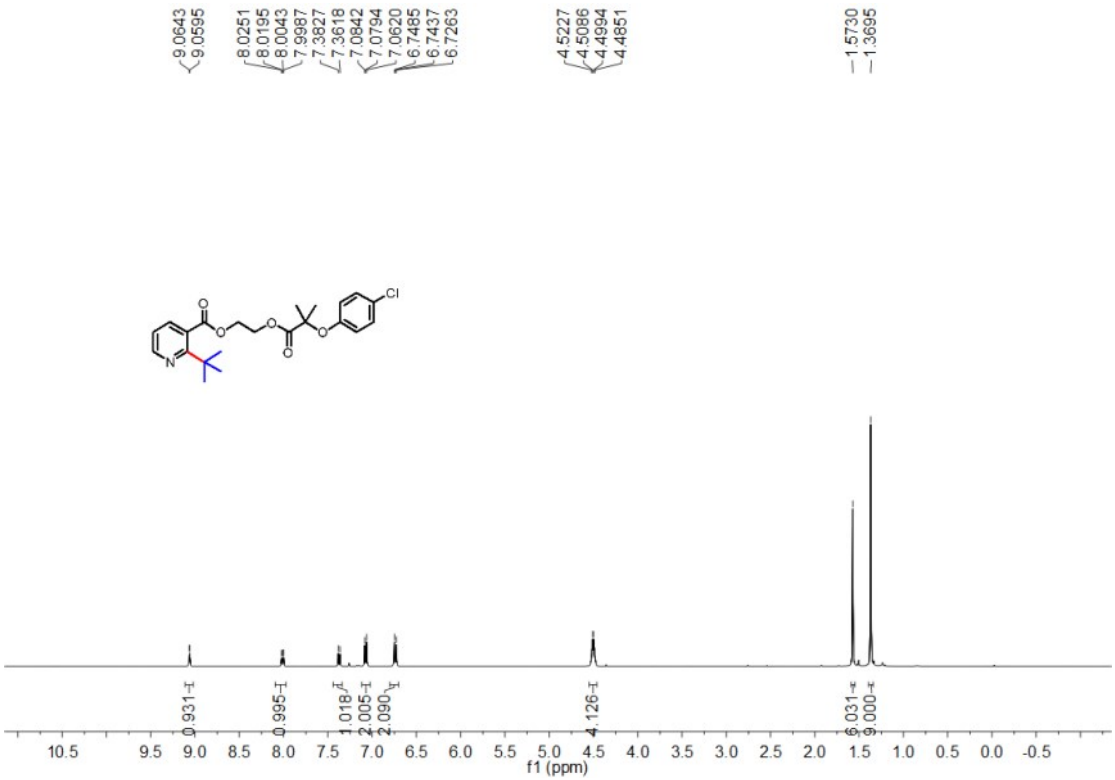
^{1}H NMR spectrum of compound **37**



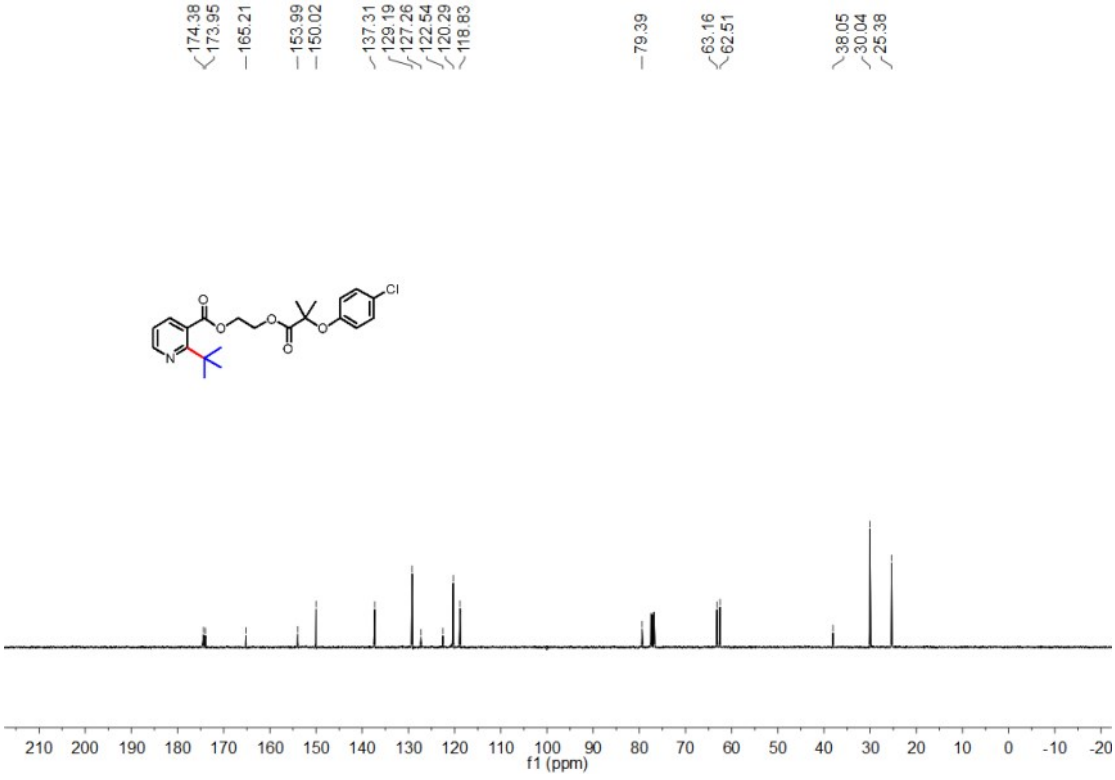
^{13}C NMR spectrum of compound **37**



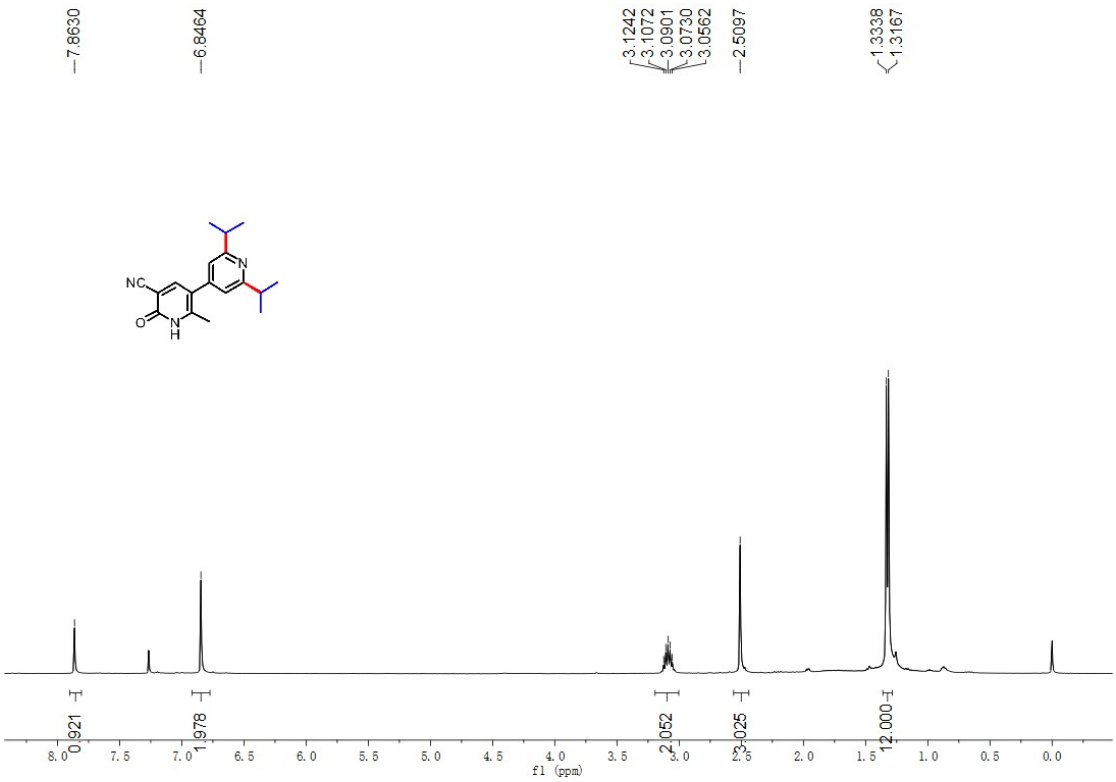
^{1}H NMR spectrum of compound **38**



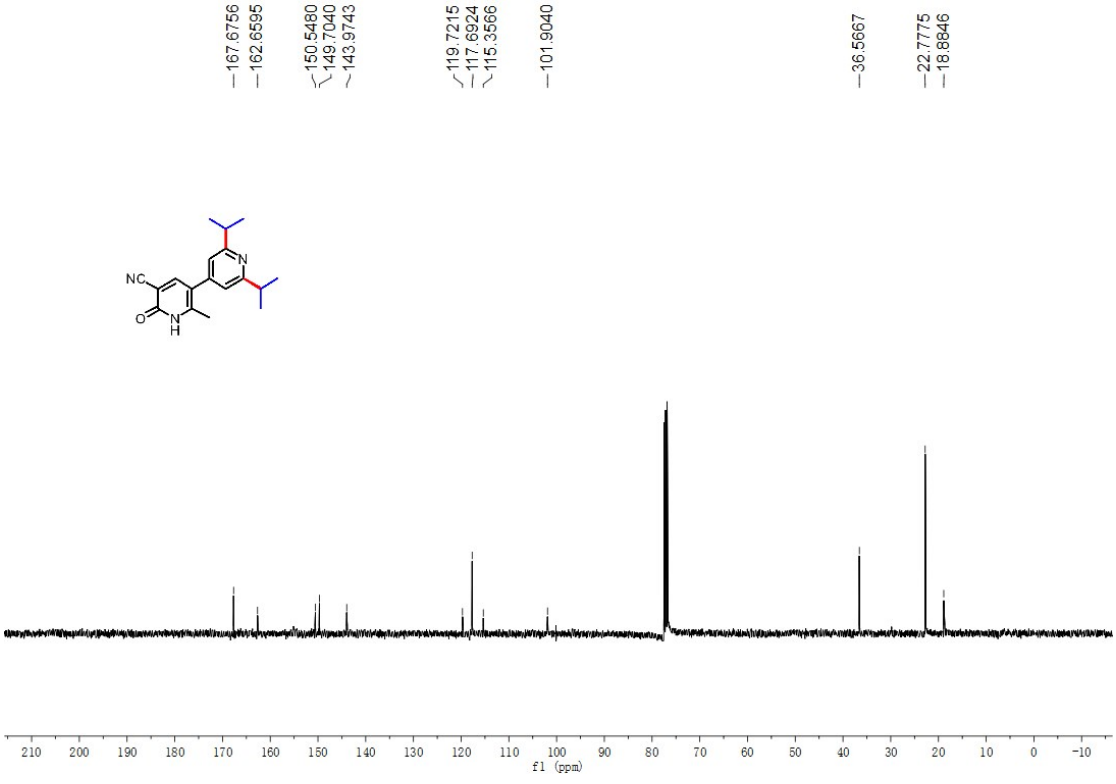
^{13}C NMR spectrum of compound **38**



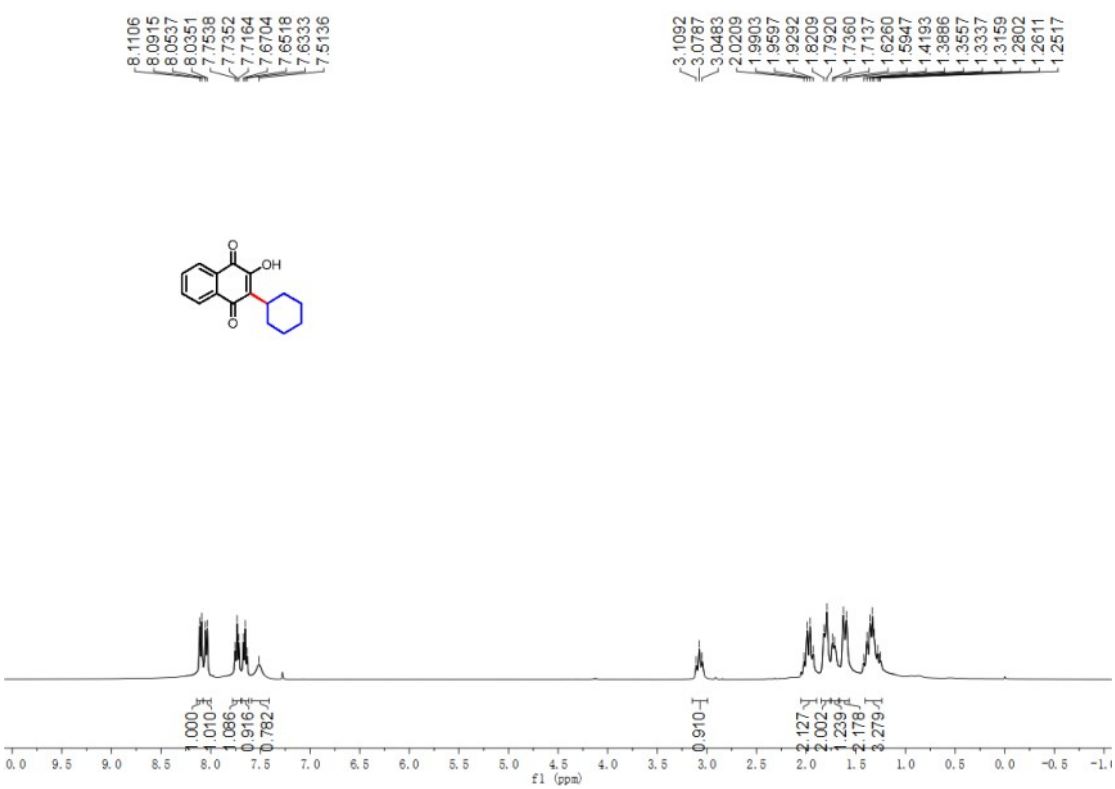
^{1}H NMR spectrum of compound **39**



^{13}C NMR spectrum of compound **39**



^{1}H NMR spectrum of compound **40**



^{13}C NMR spectrum of compound **40**