

Catalyst- and Oxidant-Free Electrochemical *para*-Selective Hydroxylation of *N*-Arylamides in Batch and Continuous-Flow

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1 General Remarks

Reagents: Commercially available reagents and solvents were of reagent grade quality without any further purification.

N-Arylamides were prepared according to a previous method.

Chromatography: Flash column chromatography was performed using silicycle silica gel (200-300 mesh).

Analytical thin-layer chromatography (TLC) was performed on 0.2 mm coated silica gel plates (HSGF 254) and visualized using a UV lamp (254 nm or 365 nm).

Nuclear Magnetic Resonance Spectroscopy:

¹H NMR and ¹³C NMR were recorded on magnet system 400'54 ascend purchased from Bruker Biospin AG.

¹H NMR spectra chemical shifts (δ) were reported in parts per million (ppm) referenced to hydrogen resonances in the NMR solvent (CDCl₃ or DMSO-*d*₆).

¹³C NMR spectra chemical shifts (δ) were reported in parts per million (ppm) referenced to carbon resonances in the NMR solvent.

ESI-MS spectra were recorded on Agilent Q-TOF 6520.

All electrochemical *para*-selective hydroxylation of *N*-arylamides were carried out in an undivided electrochemical cell equipped with two C rod electrodes (ø 6 mm), which were purchased from Shanghai Jing Chong Electronic Technology Development Co., Ltd Contract. And, electrolysis was conducted under an AXIOMET AX3003P potentiostat in constant current mode. Cyclic voltammogram experiments were investigated using a Metrohm Autolab PGSTAT204 workstation and Nova 2.0 software.

2 General Material Information for Batch Setup and Continuous-Flow Electrochemical Reactor

2.1 General Material Information for Batch setup

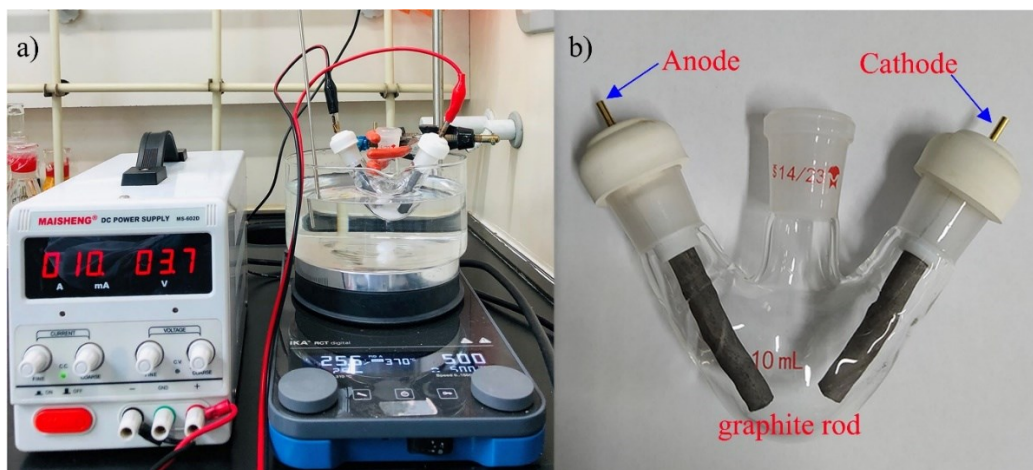


Figure S1 pictures of batch setup

The batch electrolysis setup used is shown in figure S1.

2.2 General Material Information for Continuous-Flow Electrochemical Reactor

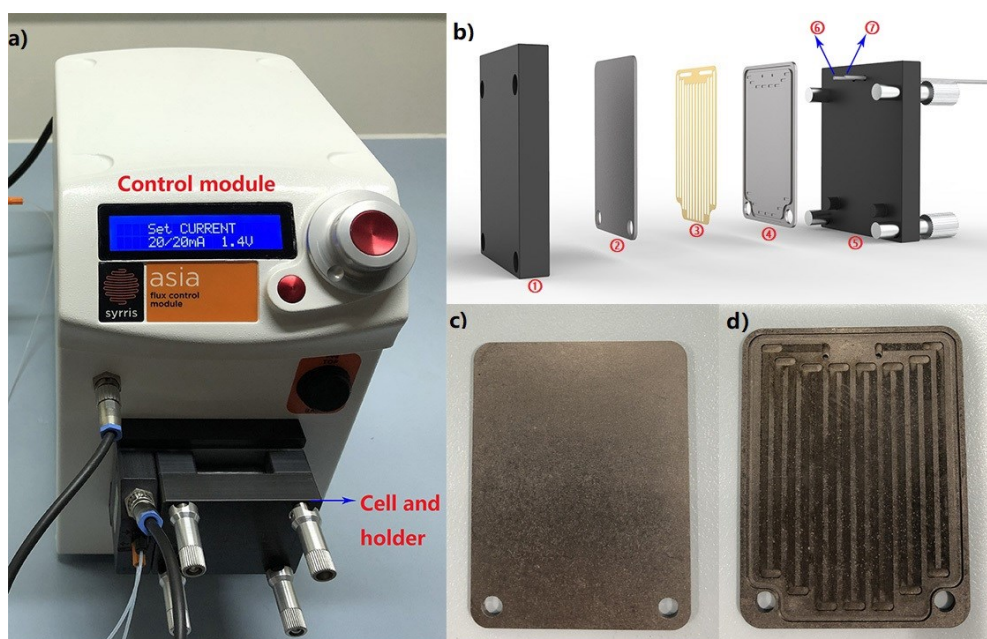
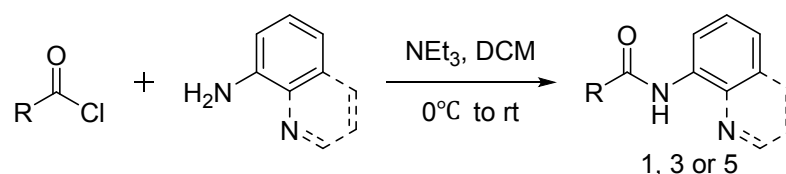


Figure S2 pictures of continuous-flow electrochemical reactor

a) the outside views of control module and cell; b) the diagram of reactor. ① and ⑤: electrode holder; ②: cathode; ③ channel reactor; ④: Anode; ⑥ and ⑦: inlet and outlet. c) C flat electrode (carbon filled PPS, 5.0×4.0 cm). d) C gasket electrode (carbon filled PPS, 5.0×4.0 cm).

The continuous-flow electrochemical reactor used was the Asia Flux Module purchased from Syrris as shown in Fig. S2.

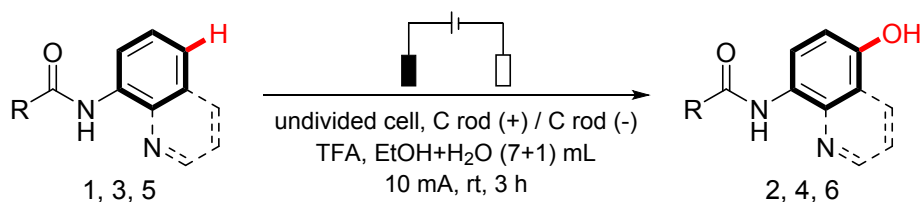
3 Synthesis of the Starting Materials 1, 3, 5^[1]



The corresponding amine (10 mmol) and triethylamine (20 mmol, 2.023 g) were dissolved in anhydrous CH_2Cl_2 (30 mL). the specific acyl chloride (10.5 mmol) in CH_2Cl_2 (10 mL) was added dropwise to the solution at 0 °C. The reaction mixture was stirred for another 2h at ambient temperature. The reaction mixture was diluted with CH_2Cl_2 (110 mL). The crude product was washed with HCl solution (3%, 150 mL), saturated NaHCO_3 solution (150 mL) and water (150 mL). The separated organic layer was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to give the crude product 1, 3, or 5, which was purified by recrystallization from ethyl acetate or column chromatographic separation (petroleum ether /ethyl acetate).

4 General Procedure for the Electrochemical *para*-Selective

Hydroxylation of *N*-Arylamides in Batch



In an undivided cell equipped with a carbon rod ($\varnothing$ 6 mm) anode and a carbon rod ($\varnothing$ 6 mm) cathode, amide **1**, **3** or **5** (0.2 mmol) and TFA (1.4 mmol, 159.6 mg, 7 eq) were dissolved in a mixed solvent of EtOH/H₂O [(7:1) mL]. At ambient temperature, the reaction was started at a constant current of 10 mA for 3 h. The mixtures were concentrated under reduced pressure. The residue was diluted with CH₂Cl₂ (50 mL) and washed with brine (50 mL) and H₂O (50 mL). The separated organic layer was dried over anhydrous Na₂SO₄ and filtered. The filtrate was concentrated under reduced pressure to give the crude product, which was purified by column chromatographic separation (petroleum ether/ethyl acetate).

5 Optimization of Amount of TFA in Continuous-Flow Reactor

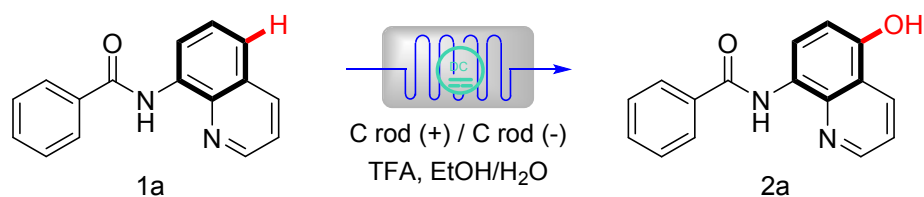


Table S1 Screening equiv. of TFA in continuous-flow reactor^a

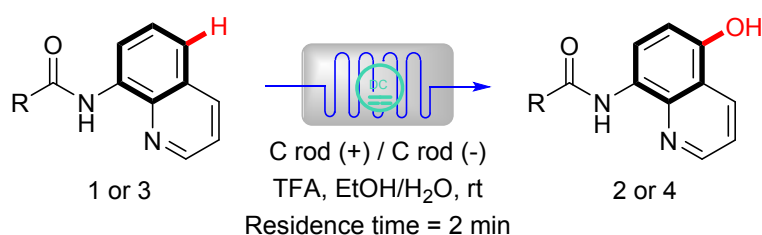
Entry	Equiv. of TFA	Yield (%)
1	2	78
2	3	89
3	4	88

^aReaction conditions: 1a (0.2 mmol), TFA (X mmol), EtOH/H₂O (7 mL/1 mL), C (carbon filled PPS, 5.0 × 4.0 cm) anode, C (carbon filled PPS, 5.0 × 4.0 cm) cathode, volume (0.12 mL), flow rate: 0.06 mL/min, residence time: 2 min, I = 10 mA, rt, isolated yield.

This reaction was investigated using less amount of TFA in continuous-flow reactor (Table S1). To our delight, reducing the amount of TFA from 7 equivalents to 3 equivalents could also give excellent yield (Table S1, entry 2).

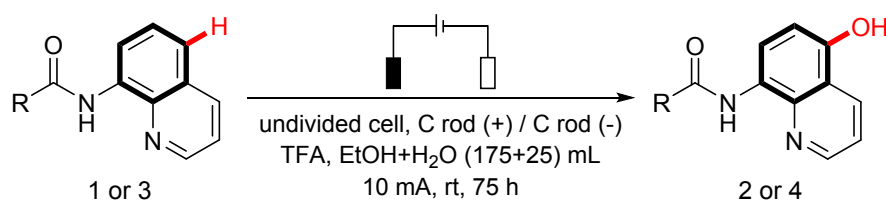
6 Gram-Scale Synthesis of 2a, 2w and 4b in Batch and Continuous-Flow Reactor

6.1 In continuous-flow reactor



1 or **3** (5 mmol) and TFA (15 mmol, 1.71 g) were dissolved in a mixed solvent of EtOH/H₂O [(175:25) mL]. At ambient temperature, the reaction mixtures were introduced into the reactor at 0.06 mL/min at a constant current of 10 mA. The reaction solution was concentrated under reduced pressure. The residue was diluted with CH₂Cl₂ (250 mL) and washed with brine (250 mL) and H₂O (250 mL). The separated organic layer was dried over anhydrous Na₂SO₄ and filtered. The filtrate was concentrated under reduced pressure to give the crude product, which was purified by column chromatographic separation (petroleum ether/ethyl acetate).

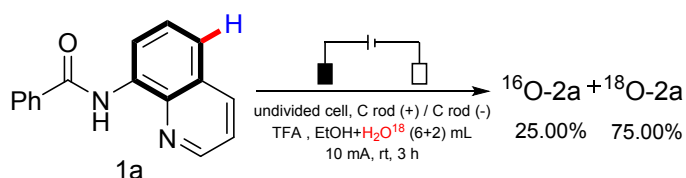
6.2 In batch



In an undivided cell equipped with a carbon rod ($\varnothing$ 6 mm) anode and a carbon rod ($\varnothing$ 6 mm) cathode, amide **1** or **3** (5 mmol) and TFA (35 mmol, 3.99 g, 7 eq) were dissolved in a mixed solvent of EtOH/H₂O [(175:25) mL]. At ambient temperature, the reaction was started at a constant current of 10 mA for 75 h. The reaction solution was concentrated under reduced pressure. The residue was diluted with CH₂Cl₂ (250 mL) and washed with brine (250 mL) and H₂O (250 mL). The separated organic layer was dried over anhydrous Na₂SO₄ and filtered. The filtrate was concentrated under reduced pressure to give the crude product, which was purified by column chromatographic separation (petroleum ether/ethyl acetate).

7 Mechanistic Studies

7.1 ¹⁸O-labeled experiments



In an undivided cell equipped with a carbon rod ($\varnothing$ 6 mm) anode and a carbon rod ($\varnothing$ 6 mm) cathode, *N*-(quinolin-8-yl)benzamide **1a** (0.2 mmol, 49.6 mg) and TFA (1.4 mmol, 159.6 mg, 7 eq) were dissolved in a mixed solvent of anhydrous EtOH/ H_2O^{18} [(6:2) mL]. At ambient temperature, the reaction was started at a constant current of 10 mA under N_2 for 3 h. The crude mixture was analyzed by HRMS (ESI), which revealed that the ratio between ^{16}O -2a and ^{18}O -2a was 25.00:75.00 (Fig. S3).

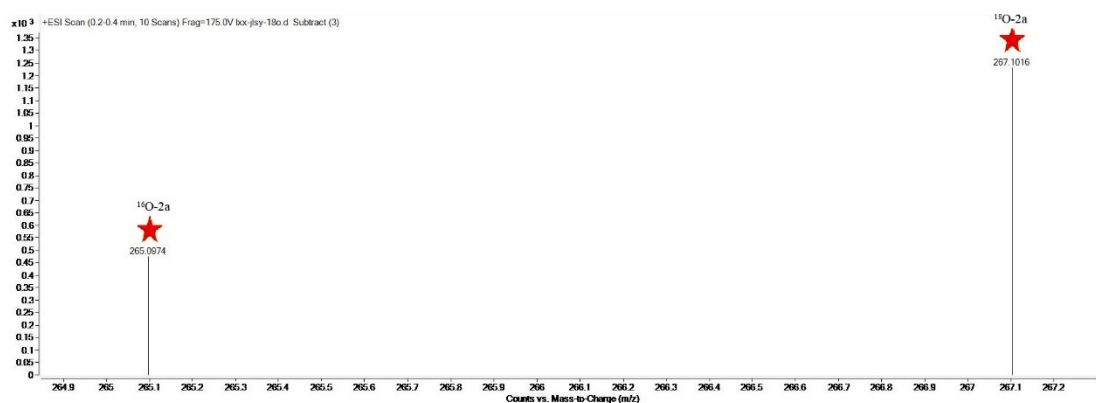
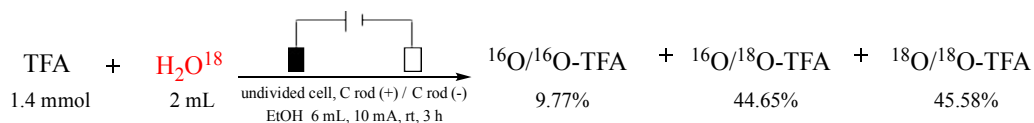


Figure S3 HRMS (ESI) analysis of electrochemically generated ^{16}O -2a and ^{18}O -2a using the mixed solvent of EtOH/ H_2O^{18}



In an undivided cell equipped with a carbon rod ($\varnothing$ 6 mm) anode and a carbon rod ($\varnothing$ 6 mm) cathode, TFA (1.4 mmol, 159.6 mg, 7 eq) was dissolved in a mixed solvent of anhydrous EtOH/ H_2O^{18} [(6:2) mL]. At ambient temperature, the reaction was started at a constant current of 10 mA under N_2 for 3 h. The crude mixture was analyzed by MS-ESI, which revealed that the ratio between $^{16}\text{O}/^{16}\text{O}$ -TFA, $^{16}\text{O}/^{18}\text{O}$ -TFA and $^{18}\text{O}/^{18}\text{O}$ -TFA was 9.77:44.65:45.58 (Fig. S4).

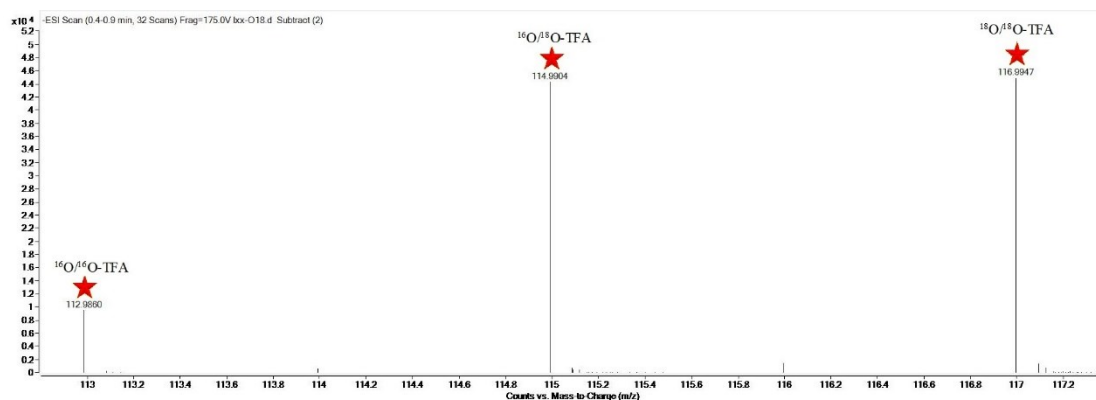
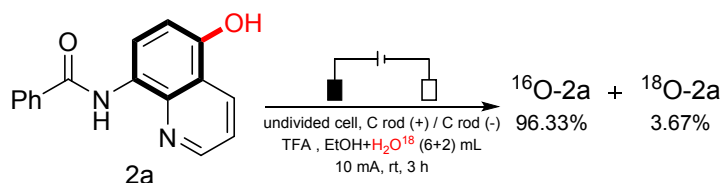


Figure S4 HRMS (ESI) analysis of electrochemically generated $^{16}\text{O}/^{16}\text{O}$ -TFA, $^{16}\text{O}/^{18}\text{O}$ -TFA and $^{18}\text{O}/^{18}\text{O}$ -TFA using the mixed solvent of EtOH/ H_2O^{18}



In an undivided cell equipped with a carbon rod ($\varnothing$ 6 mm) anode and a carbon rod ($\varnothing$ 6 mm) cathode, *N*-(5-hydroxyquinolin-8-yl)benzamide (2a, 0.2 mmol, 52.8 mg) TFA (1.4 mmol, 159.6 mg, 7 eq) was dissolved in a mixed solvent of anhydrous EtOH/ H_2O^{18} [(6:2) mL]. At ambient temperature, the reaction was started at a constant current of 10 mA under N_2 for 3 h. The crude mixture was analyzed by MS-ESI, which revealed that the ratio between ^{16}O -2a and ^{18}O -2a was 96.33:3.67 (Fig. S5).

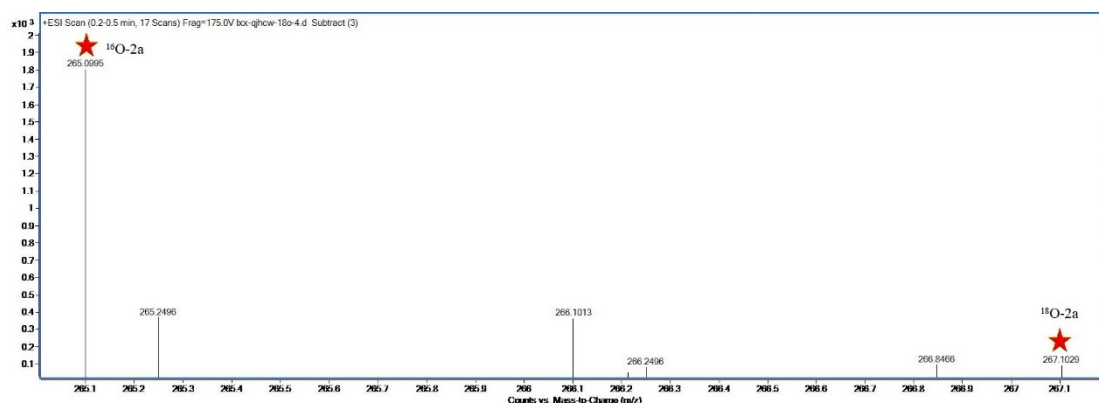
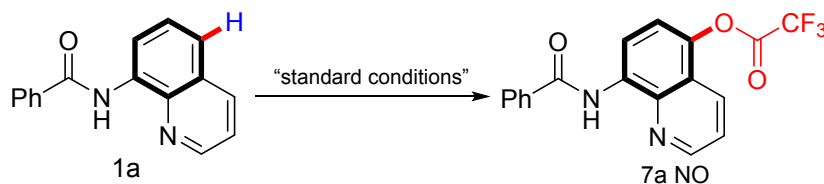
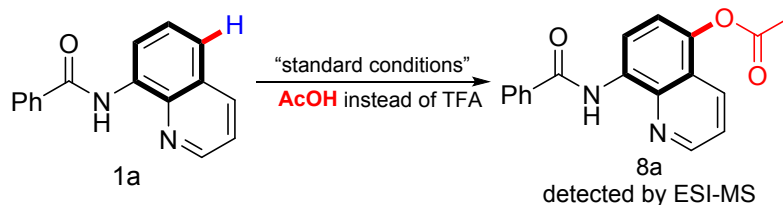


Figure S5 HRMS (ESI) analysis of electrochemically generated ^{18}O -2a from ^{16}O -2a using the mixed solvent of EtOH/ H_2O^{18}

7.2 Intermediate-monitoring experiments



In an undivided cell equipped with a carbon rod ($\varnothing$ 6 mm) anode and a carbon rod ($\varnothing$ 6 mm) cathode, *N*-(quinolin-8-yl)benzamide **1a** (0.2 mmol, 49.6 mg) and TFA (1.4 mmol, 159.6 mg, 7 eq) were dissolved in a mixed solvent of EtOH/H₂O [(7:1) mL]. At ambient temperature, the reaction was started at a constant current of 10 mA. The mixture was monitored by TLC and MS-ESI. The corresponding esterification product **7a** was not detected.



In an undivided cell equipped with a carbon rod ($\varnothing$ 6 mm) anode and a carbon rod ($\varnothing$ 6 mm) cathode, *N*-(quinolin-8-yl)benzamide **1a** (0.2 mmol, 49.6 mg) and AcOH (1.4 mmol, 84.1 mg, 7 eq) were dissolved in a mixed solvent of EtOH/H₂O [(7:1) mL]. At ambient temperature, the reaction was started at a constant current of 10 mA. The mixture was monitored by TLC and MS-ESI. And, the corresponding esterification product **8a** was detected (Calcd for C₁₈H₁₅N₂O₃ [M+H]⁺: 307.1077; found: 307.1051, Fig. **S6**).

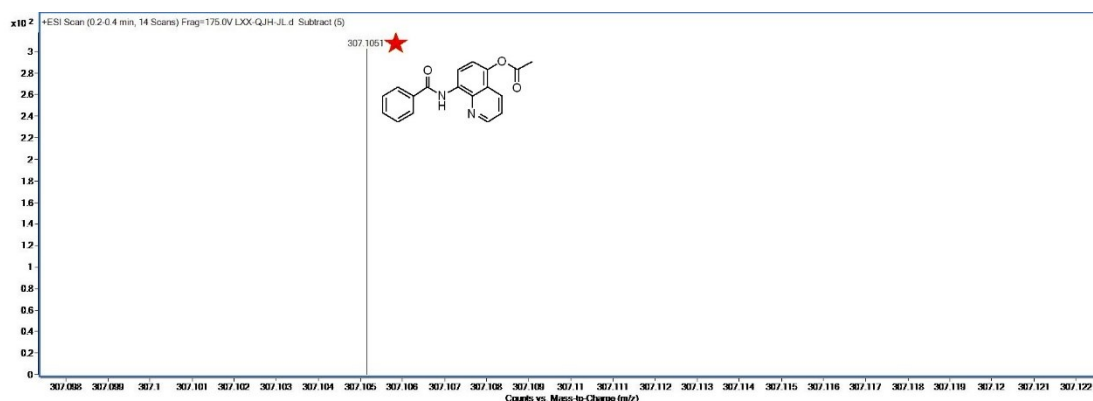
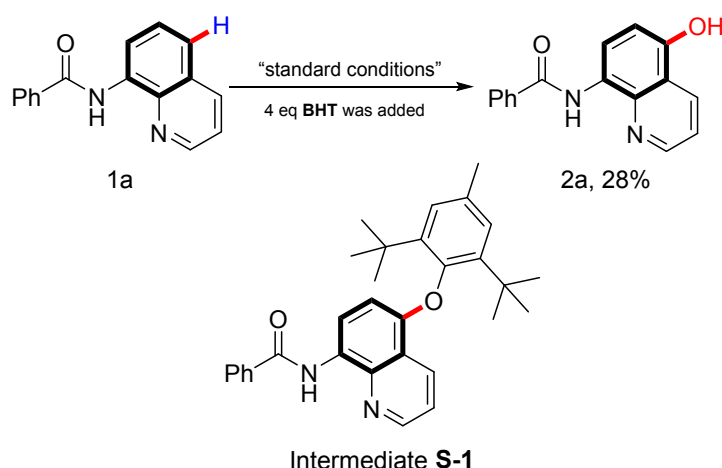


Figure **S6** HRMS (ESI) analysis of esterification product **8a**

7.3 Radical-trapping experiments



In an undivided cell equipped with a carbon rod ($\varnothing$ 6 mm) anode and a carbon rod ($\varnothing$ 6 mm) cathode, *N*-(quinolin-8-yl)benzamide **1a** (0.2 mmol, 49.6 mg), TFA (1.4 mmol, 159.6 mg, 7 eq) and BHT (0.8 mmol, 176.3 mg, 4 eq) were dissolved in a mixed solvent of EtOH/H₂O [(7:1) mL]. At ambient temperature, the reaction was started at a constant current of 10 mA for 3 h. The mixtures were concentrated under reduced pressure. The residue was diluted with CH₂Cl₂ (50 mL) and washed with brine (50 mL) and H₂O (50 mL). The separated organic layer was dried over anhydrous Na₂SO₄ and filtered. The filtrate was concentrated under reduced pressure to give the crude product, which was purified by column chromatographic separation (petroleum ether/ethyl acetate 12/1) to give the desired product **2a** (14.8 mg, 28%). And, the corresponding radical-trapping intermediate **S-1** was detected by MS-ESI (Calcd for C₃₁H₃₅N₂O₂ [M+H]⁺: 467.2693; found: 467.2674, Fig. S7).

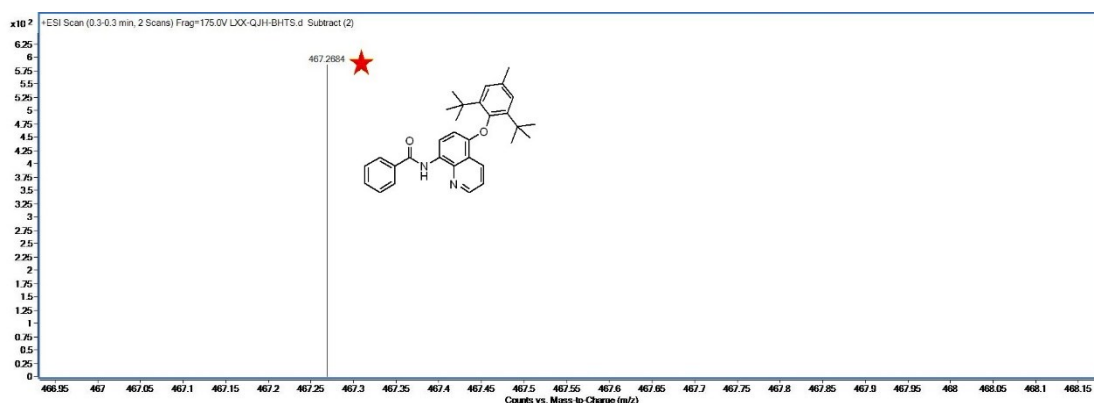
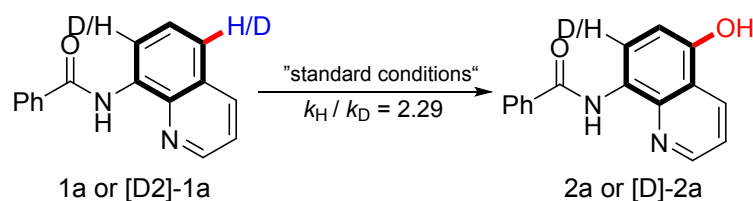


Figure S7 HRMS (ESI) analysis of corresponding radical-trapping intermediate **S-1**

7.4 KIE studies



In an undivided cell equipped with a carbon rod ($\varnothing$ 6 mm) anode and a carbon rod ($\varnothing$ 6 mm) cathode, *N*-(quinolin-8-yl)benzamide **1a** or **[D2]-1a** (0.2 mmol, 49.6 mg or 50.0 mg) and TFA (1.4 mmol, 159.6 mg, 7 eq) were dissolved in a mixed solvent of EtOH/H₂O [(7:1) mL]. At ambient temperature, the reaction was started at a constant current of 10 mA. Aliquots of 0.2 mL were removed from the cell every 15 minutes and analyzed by ¹H-NMR using CH₂Br₂ (5 μ L) as the internal standard (Fig. S8 and Fig. S9).

Time [min]	30	45	60	75	90
2a [%]	12.18	20.65	27.94	34.76	40.71
[D]-2a [%]	11.09	14.25	17.38	20.35	23.55

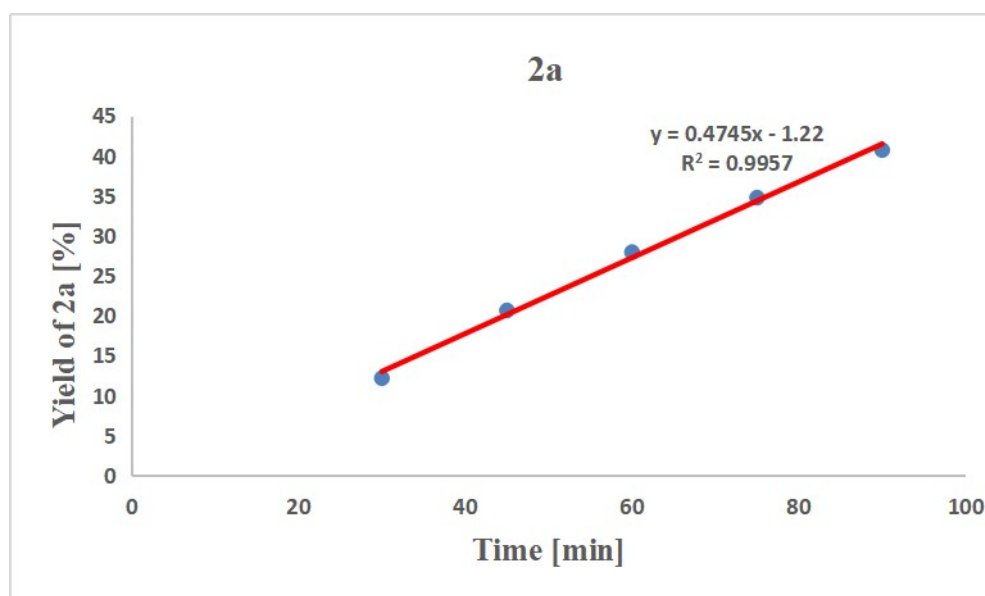


Figure S8 Parallel experiment of 1a

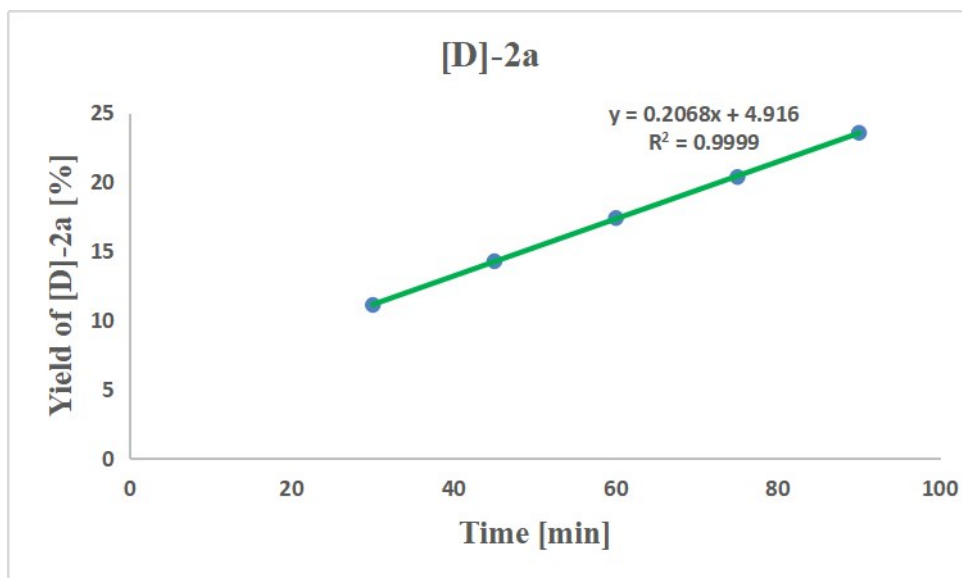


Figure S9 Parallel experiment of [D2]-1a

7.5 Cyclic voltammetry

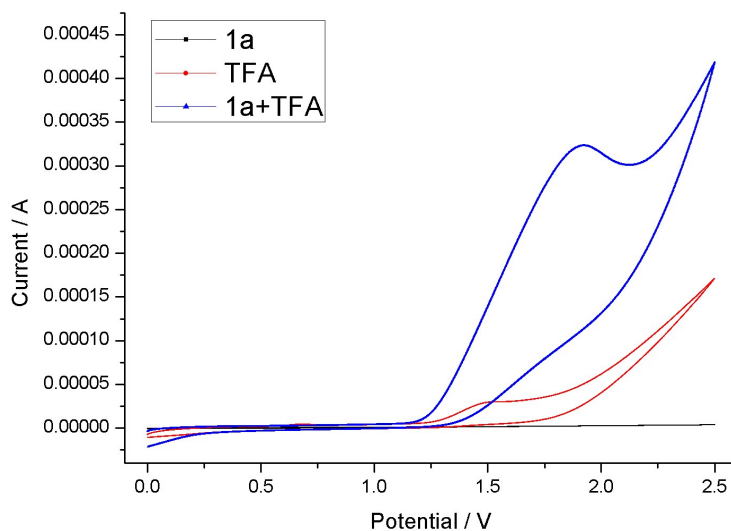


Figure S10 Cyclic Voltammetry

100 mVs⁻¹: Solvent: EtOH (8 mL). (black) substrate 1a (0.1 mmol); (red) TFA (0.7 mmol); (blue) 1a (0.1 mmol) and TFA (0.7 mmol).

The undivided cell was equipped with glassy-carbon disk working electrode (diameter, 3.0 mm) and Pt wire auxiliary electrode. The Ag/AgCl was used as reference electrode. The scan range was 0.0 V to 2.5 V. The scan rate was 100 mVs⁻¹ (Fig. S10).

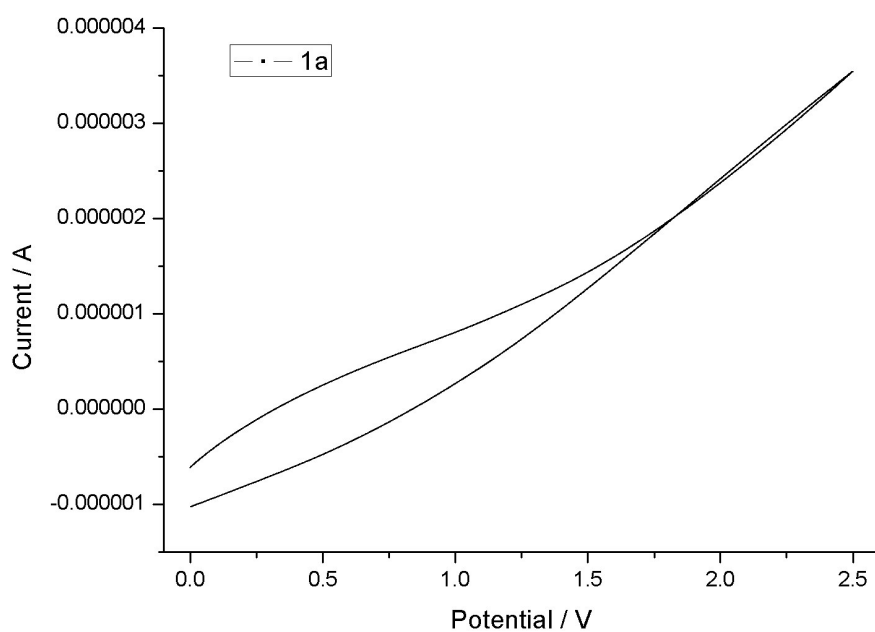


Figure **S11**: Cyclic Voltammetry of 1a

100 mVs-1: Solvent: EtOH (8 mL). (black) substrate 1a (0.1 mmol).

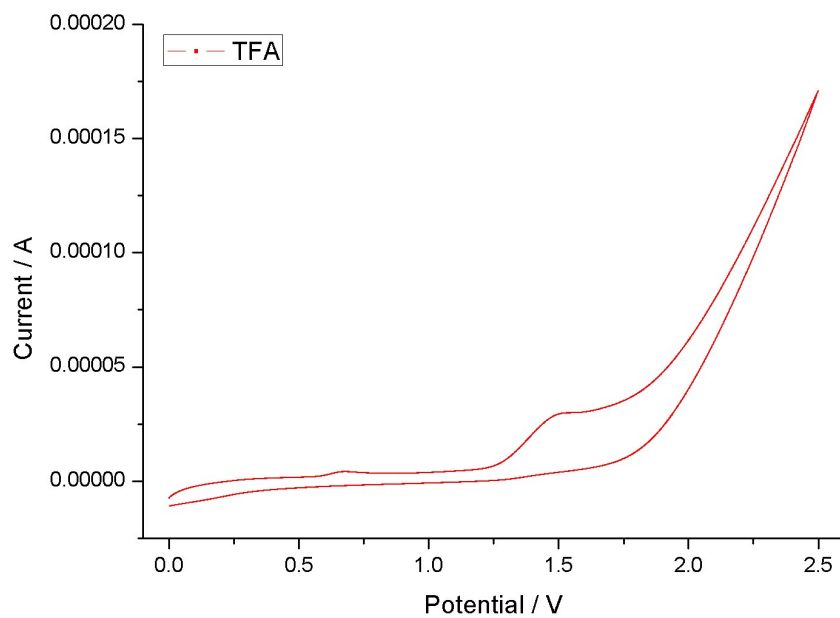


Figure **S12**: Cyclic Voltammetry of TFA

100 mVs-1: Solvent: EtOH (8 mL). (red) TFA (0.7 mmol).

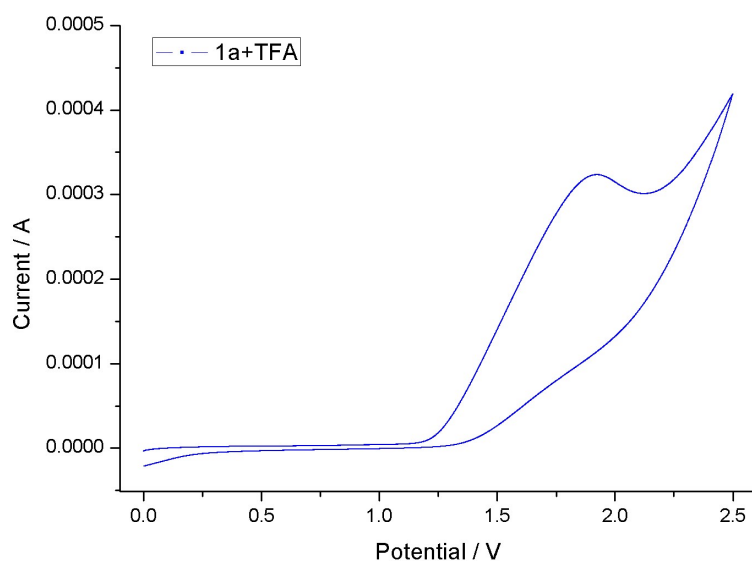
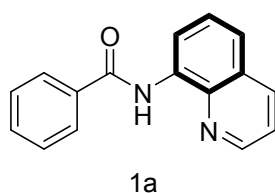


Figure S13: Cyclic Voltammetry of the mixture of 1a and TFA

100 mVs-1: Solvent: EtOH (8 mL). (blue) 1a (0.1 mmol) and TFA (0.7 mmol).

8 Characterization Data of 1, 3, 5 and 2, 4, 6

8.1 Characterization Data of 1



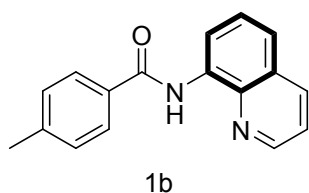
N-(Quinolin-8-yl)benzamide (1a):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 15/1). **¹H**

NMR (400 MHz, CDCl₃) δ 10.74 (s, 1H), 8.94 (t, *J* = 6.5 Hz, 1H), 8.83 (brs, 1H), 8.20 - 8.05 (m, 3H), 7.68 – 7.36 (m, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.52, 148.28, 138.68, 136.56,

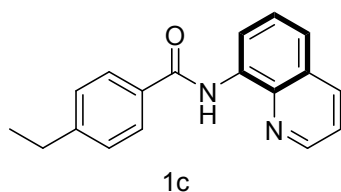
135.13, 134.55, 131.93, 128.86, 128.04, 127.52, 127.36, 121.80, 121.75, 116.69. **HRMS** (ESI)

Calcd for C₁₆H₁₃N₂O [M+H]⁺: 249.1022; found: 249.1044.



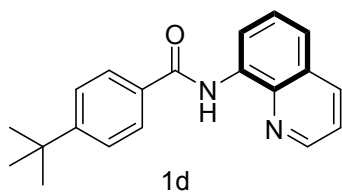
4-Methyl-N-(quinolin-8-yl)benzamide (1b):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 15/1). **¹H NMR** (400 MHz, CDCl₃) δ 10.45 (s, 1H), 8.73 (d, *J* = 7.6, 1H), 8.59 – 8.48 (m, 1H), 7.86 – 7.78 (m, 1H), 7.78 - 7.70 (m, 2H), 7.36 – 7.25 (m, 1H), 7.25 – 6.99 (m, 4H), 2.18 (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.04, 148.00, 142.13, 138.41, 136.07, 134.39, 131.99, 129.25, 127.69, 127.13, 127.06, 121.44, 121.37, 116.13, 21.36. **HRMS** (ESI) Calcd for C₁₇H₁₅N₂O [M+H]⁺: 263.1179; found: 263.1191.



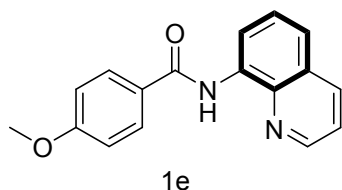
4-Ethyl-N-(quinolin-8-yl)benzamide (1c):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 15/1). **¹H NMR** (400 MHz, CDCl₃) δ 10.69 (s, 1H), 8.93 (dd, *J* = 7.7, 1.3 Hz, 1H), 8.80 - 8.75 (m, 1H), 8.12 - 8.04 (m, 1H), 8.00 (d, *J* = 7.9 Hz, 2H), 7.59 - 7.49 (m, 1H), 7.48 - 7.42 (m, 1H), 7.41 - 7.35 (m, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 2.70 (q, *J* = 7.6 Hz, 2H), 1.26 (t, *J* = 6.1 Hz, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.34, 148.49, 148.13, 138.56, 136.30, 134.55, 132.42, 128.22, 127.87, 127.33, 121.59, 121.51, 116.36, 28.79, 15.32. **HRMS** (ESI) Calcd for C₁₈H₁₇N₂O [M+H]⁺: 277.1335; found: 277.1356.



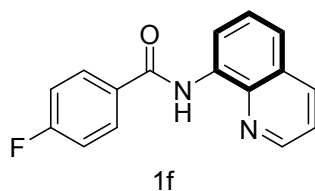
4-(*tert*-butyl)-*N*-(quinolin-8-yl)benzamide (1d):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 15/1). **¹H NMR** (400 MHz, CDCl₃) δ 10.74 (s, 1H), 8.94 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.84 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.07 – 8.02 (m, 2H), 7.62 – 7.53 (m, 4H), 7.48 (dd, *J* = 8.3, 4.2 Hz, 1H), 1.38 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.66, 155.50, 148.26, 138.75, 136.69, 134.76, 132.41, 128.15, 127.68, 127.31, 125.87, 121.77, 121.70, 116.82, 35.15, 31.32. **HRMS** (ESI) Calcd for C₂₀H₂₁N₂O [M+H]⁺: 305.1648; found: 305.1661.



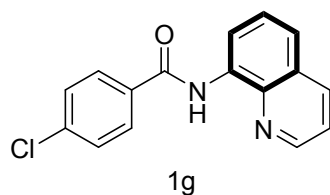
4-methoxy-*N*-(quinolin-8-yl)benzamide (1e):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). **¹H NMR** (400 MHz, CDCl₃) δ 10.62 (s, 1H), 8.90 (dd, *J* = 7.7, 1.2 Hz, 1H), 8.78 (dd, *J* = 4.2, 1.9 Hz, 1H), 8.08 (dq, *J* = 8.5, 1.7 Hz, 1H), 8.05 – 7.99 (m, 2H), 7.52 (td, *J* = 8.0, 1.4 Hz, 1H), 7.44 (dq, *J* = 8.3, 1.3 Hz, 1H), 7.41 - 7.35 (m, 1H), 7.01 – 6.95 (m, 2H), 3.84 – 3.80 (m, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 164.86, 162.47, 148.15, 138.64, 136.30, 134.69, 129.10, 127.92, 127.38, 127.32, 121.60, 121.38, 116.26, 113.93, 55.40. **HRMS** (ESI) Calcd for C₁₇H₁₅N₂O₂ [M+H]⁺: 279.1128; found: 279.1112.



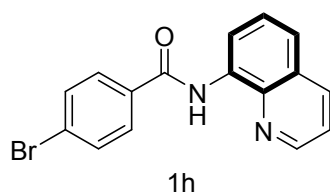
4-fluoro-*N*-(quinolin-8-yl)benzamide (1f):

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.70 (s, 1H), 8.90 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.85 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.15 – 8.07 (m, 2H), 7.63 – 7.54 (m, 2H), 7.49 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.25 – 7.19 (m, 2H). **¹³C NMR** (101 MHz, CDCl₃) δ 166.37, 164.53, 163.86, 148.31, 138.64, 136.82, 134.45, 131.38 (d, *J* = 3.0 Hz), 129.89, 129.79, 128.15, 127.66, 121.99, 121.85, 116.96, 116.08, 115.86. **HRMS** (ESI) Calcd for C₁₆H₁₂FN₂O [M+H]⁺: 267.0928; found: 267.0937.



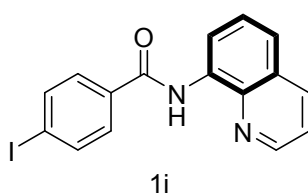
4-chloro-*N*-(quinolin-8-yl)benzamide (1g):

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.61 (s, 1H), 8.84 (t, *J* = 7.7 Hz, 1H), 8.76 (brs, 1H), 8.07 (t, *J* = 7.2 Hz, 1H), 7.93 (7, *J* = 7.8 Hz, 2H), 7.59 - 7.34 (m, 5H). **¹³C NMR** (101 MHz, CDCl₃) δ 164.07, 148.25, 138.51, 138.00, 136.32, 134.19, 133.31, 128.93, 128.62, 127.85, 127.31, 121.85, 121.69, 116.47. **HRMS** (ESI) Calcd for C₁₆H₁₂ClN₂O [M+H]⁺: 283.0633; found: 283.0653.



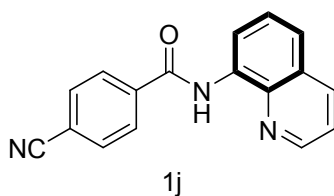
4-bromo-*N*-(quinolin-8-yl)benzamide (1h):

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.70 (s, 1H), 8.89 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.83 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.96 – 7.91 (m, 2H), 7.70 – 7.63 (m, 2H), 7.61 – 7.51 (m, 2H), 7.47 (dd, *J* = 8.3, 4.3 Hz, 1H). **¹³C NMR** (101 MHz, CDCl₃) δ 164.43, 148.32, 138.62, 136.55, 134.27, 133.94, 132.04, 128.92, 128.00, 127.48, 126.64, 121.98, 121.79, 116.72. **HRMS** (ESI) Calcd for C₁₆H₁₂BrN₂O [M+H]⁺: 327.0128; found: 327.0141.



4-iodo-*N*-(quinolin-8-yl)benzamide (1i):

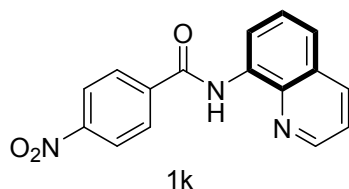
Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.70 (s, 1H), 8.89 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.84 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.92 – 7.86 (m, 2H), 7.82 – 7.77 (m, 2H), 7.61 – 7.53 (m, 2H), 7.48 (dd, *J* = 8.3, 4.3 Hz, 1H). **¹³C NMR** (101 MHz, CDCl₃) δ 164.75, 148.40, 138.73, 138.13, 136.67, 134.66, 134.38, 128.99, 128.12, 127.60, 122.06, 121.86, 116.89, 99.08. **HRMS** (ESI) Calcd for C₁₆H₁₂IN₂O [M+H]⁺: 374.9989; found: 374.9998.



4-cyano-*N*-(quinolin-8-yl)benzamide (1j):

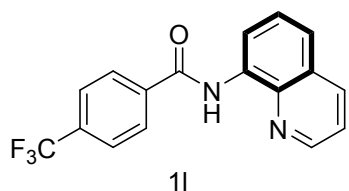
Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.80 (s, 1H), 8.90 (dd, *J* = 6.3, 2.7 Hz, 1H), 8.86 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.23 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.19 – 8.15 (m, 2H), 7.86 – 7.82 (m, 2H), 7.65 – 7.57 (m, 2H), 7.52 (dd, *J* = 8.3, 4.3 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ 163.50, 148.39, 138.94, 138.50, 136.80, 133.88, 133.02, 132.67, 128.06, 128.02, 127.54, 127.51, 122.48, 121.91, 118.10, 117.13, 115.37. **HRMS** (ESI) Calcd for C₁₇H₁₂N₃O [M+H]⁺: 274.0975; found: 274.0953.



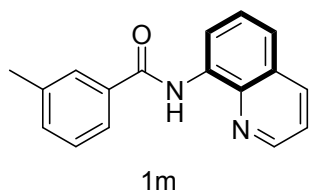
4-nitro-*N*-(quinolin-8-yl)benzamide (1k):

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.83 (s, 1H), 8.91 (dd, *J* = 6.1, 2.8 Hz, 1H), 8.87 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.43 – 8.36 (m, 2H), 8.28 – 8.20 (m, 3H), 7.66 – 7.59 (m, 2H), 7.53 (dd, *J* = 8.3, 4.3 Hz, 1H). **¹³C NMR** (101 MHz, CDCl₃) δ 163.36, 149.90, 148.56, 140.70, 138.64, 136.88, 133.98, 128.62, 128.18, 127.61, 124.17, 122.67, 122.06, 117.23. **HRMS** (ESI) Calcd for C₁₆H₁₂N₃O₃ [M+H]⁺: 294.0873; found: 294.0861.



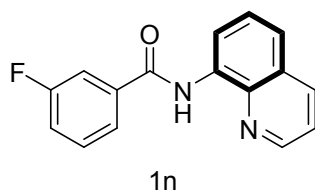
***N*-(quinolin-8-yl)-4-(trifluoromethyl)benzamide (1l):**

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.79 (s, 1H), 8.97 – 8.80 (m, 2H), 8.18 (t, *J* = 7.5 Hz, 3H), 7.80 (t, *J* = 8.0 Hz, 2H), 7.66 - 7.44 (m, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 164.19, 148.49, 138.67, 138.45, 136.73, 134.18, 133.70, 133.39, 128.11, 127.89, 127.57, 125.97 (q, *J* = 3.1 Hz), 125.18, 122.47, 122.34, 121.95, 116.99. **¹⁹F NMR** (376 MHz, CDCl₃) δ -62.87. **HRMS** (ESI) Calcd for C₁₇H₁₂F₃N₂O [M+H]⁺: 317.0896; found: 317.0912.



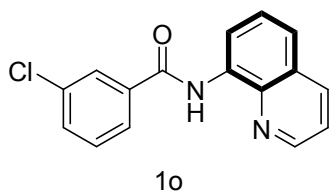
3-Methyl-N-(quinolin-8-yl)benzamide (1m):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 15/1). **¹H NMR** (400 MHz, CDCl₃) δ 10.70 (s, 1H), 8.94 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.83 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.91 – 7.84 (m, 2H), 7.61 – 7.49 (m, 2H), 7.47 – 7.35 (m, 3H), 2.47 (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.72, 148.33, 138.79, 138.72, 136.42, 135.16, 134.66, 132.68, 128.70, 128.10, 128.02, 127.49, 124.27, 121.73, 121.70, 116.56, 21.56. **HRMS** (ESI) Calcd for C₁₇H₁₅N₂O [M+H]⁺: 263.1179; found: 263.1188.



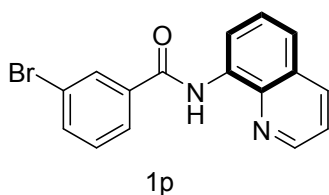
3-Fluoro-N-(quinolin-8-yl)benzamide (1n):

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.71 (s, 1H), 8.90 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.84 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.85 (dt, *J* = 7.7, 1.2 Hz, 1H), 7.78 (ddd, *J* = 9.4, 2.6, 1.7 Hz, 1H), 7.61 – 7.50 (m, 3H), 7.49 – 7.44 (m, 1H), 7.31 – 7.23 (m, 1H). **¹³C NMR** (101 MHz, CDCl₃) δ 164.18, 164.06 (d, *J* = 2.7 Hz), 148.39, 138.63, 137.41, 137.34, 136.52, 134.22, 130.53, 130.46, 127.99, 127.45, 122.75 (d, *J* = 2.9 Hz), 122.05, 121.82, 119.01, 118.80, 116.72, 114.85, 114.62. **¹⁹F NMR** (376 MHz, CDCl₃) δ -111.50. **HRMS** (ESI) Calcd for C₁₆H₁₂FN₂O [M+H]⁺: 267.0928; found: 267.0942.



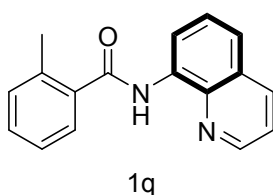
3-Chloro-*N*-(quinolin-8-yl)benzamide (1o):

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.64 (s, 1H), 8.87 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.03 (t, *J* = 1.9 Hz, 1H), 7.90 (dt, *J* = 7.6, 1.5 Hz, 1H), 7.59 – 7.47 (m, 3H), 7.47 – 7.38 (m, 2H). **¹³C NMR** (101 MHz, CDCl₃) δ 163.88, 148.40, 138.63, 136.84, 136.41, 135.00, 134.20, 131.87, 130.08, 127.93, 127.72, 127.37, 125.23, 122.04, 121.80, 116.65. **HRMS** (ESI) Calcd for C₁₆H₁₂ClN₂O [M+H]⁺: 283.0633; found: 283.0629.



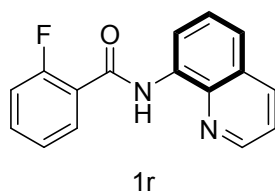
3-Bromo-*N*-(quinolin-8-yl)benzamide (1p):

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.69 (s, 1H), 8.90 (dd, *J* = 7.2, 1.8 Hz, 1H), 8.86 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.23 – 8.18 (m, 2H), 7.99 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.70 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.50 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.42 (t, *J* = 7.9 Hz, 1H). **¹³C NMR** (101 MHz, CDCl₃) δ 164.07, 148.42, 138.64, 137.17, 136.77, 134.94, 134.25, 130.77, 130.44, 128.12, 127.60, 125.86, 123.16, 122.21, 121.90, 117.07. **HRMS** (ESI) Calcd for C₁₆H₁₂BrN₂O [M+H]⁺: 327.0128; found: 327.0138.

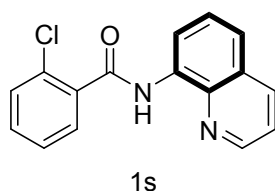


2-Methyl-*N*-(quinolin-8-yl)benzamide (1q):

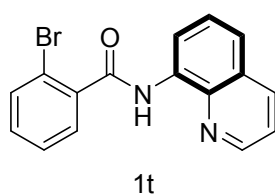
Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.27 (s, 1H), 9.01 (t, *J* = 6.9 Hz, 1H), 8.75 (brs, 1H), 8.10 (t, *J* = 7.3 Hz, 1H), 7.71 (t, *J* = 7.0 Hz, 1H), 7.64 - 7.47 (m, 2H), 7.40 (t, *J* = 7.1 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 2H), 2.65 (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 167.99, 148.09, 138.30, 136.54, 136.38, 136.24, 134.51, 131.28, 130.25, 127.80, 127.20, 127.10, 125.91, 121.72, 121.54, 116.34, 20.17. **HRMS** (ESI) Calcd for C₁₇H₁₅N₂O [M+H]⁺: 263.1179; found: 263.1181.

**2-Fluoro-*N*-(quinolin-8-yl)benzamide (1r):**

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 11.03 (d, *J* = 12.5 Hz, 1H), 8.86 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.73 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.11 (td, *J* = 7.8, 1.9 Hz, 1H), 8.02 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.49 – 7.38 (m, 3H), 7.32 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.21 (td, *J* = 7.6, 1.1 Hz, 1H), 7.16 – 7.08 (m, 1H). **¹³C NMR** (101 MHz, CDCl₃) δ 161.81, 161.65, 161.62, 159.33, 148.50, 138.75, 136.30, 134.81, 133.68, 133.59, 132.03 (d, *J* = 2.0 Hz), 127.98, 127.38, 124.89 (d, *J* = 3.4 Hz), 122.11, 121.98, 121.71, 117.25, 116.49, 116.25. **HRMS** (ESI) Calcd for C₁₆H₁₂FN₂O [M+H]⁺: 267.0928; found: 267.0938.

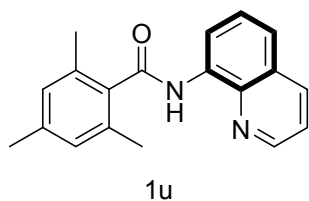
**2-Chloro-*N*-(quinolin-8-yl)benzamide (1s):**

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.49 (s, 1H), 8.96 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.83 – 7.79 (m, 1H), 7.63 – 7.55 (m, 2H), 7.52 – 7.48 (m, 1H), 7.47 – 7.37 (m, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.05, 148.43, 138.62, 136.56, 135.91, 134.46, 131.63, 131.27, 130.62, 130.14, 128.10, 127.53, 127.27, 122.29, 121.83, 117.11. **HRMS** (ESI) Calcd for C₁₆H₁₂ClN₂O [M+H]⁺: 283.0633; found: 283.0624.



2-Bromo-*N*-(quinolin-8-yl)benzamide (1t):

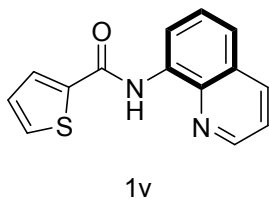
Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.30 (s, 1H), 8.95 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.77 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.71 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.67 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.62 – 7.57 (m, 1H), 7.57 - 7.53 (m, 1H), 7.47 – 7.40 (m, 2H), 7.33 (td, *J* = 7.8, 1.8 Hz, 1H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.94, 148.36, 138.54, 138.33, 136.44, 134.32, 133.70, 131.52, 129.55, 128.02, 127.68, 127.42, 122.24, 121.76, 119.73, 116.96. **HRMS** (ESI) Calcd for C₁₆H₁₂BrN₂O [M+H]⁺: 327.0128; found: 327.0125.



2,4,6-Trimethyl-*N*-(quinolin-8-yl)benzamide (1u):

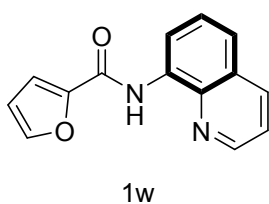
Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 9.94 (s, 1H), 9.00 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.73 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H),

7.64 – 7.54 (m, 2H), 7.44 (dd, $J = 8.3, 4.2$ Hz, 1H), 6.94 (s, 2H), 2.41 (s, 6H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 169.16, 148.20, 138.78, 138.48, 136.44, 135.40, 134.56, 134.51, 128.45, 128.05, 127.49, 121.85, 121.64, 116.82, 21.17, 19.44. HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 291.1492; found: 291.1505.



***N*-(quinolin-8-yl)thiophene-2-carboxamide (1v):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). ^1H NMR (400 MHz, CDCl_3) δ 10.45 (s, 1H), 8.77 (dd, $J = 7.6, 1.5$ Hz, 1H), 8.71 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.00 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.72 (dd, $J = 3.8, 1.2$ Hz, 1H), 7.51 (dd, $J = 5.0, 1.2$ Hz, 1H), 7.45 (t, $J = 7.9$ Hz, 1H), 7.41 - 7.36 (m, 1H), 7.31 (dd, $J = 8.2, 4.2$ Hz, 1H), 7.09 (dd, $J = 5.0, 3.7$ Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.70, 148.12, 139.87, 138.13, 136.11, 134.00, 130.87, 128.21, 127.80, 127.69, 127.11, 121.55, 116.15. HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{11}\text{N}_2\text{OS}$ $[\text{M}+\text{H}]^+$: 255.0587; found: 255.0587.

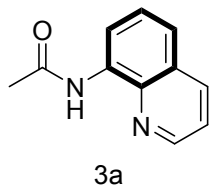


***N*-(quinolin-8-yl)furan-2-carboxamide (1w):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). ^1H NMR (400 MHz, CDCl_3) δ 10.73 (s, 1H), 8.88 – 8.81 (m, 2H), 8.12 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.59 (d, $J = 2.1$ Hz, 1H), 7.57 – 7.46 (m, 2H), 7.42 (dd, $J = 8.3, 4.2$ Hz, 1H), 7.29 (dd, $J = 3.5, 0.9$ Hz, 1H), 6.56 (dd, $J = 3.5, 1.8$ Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 156.37, 148.39,

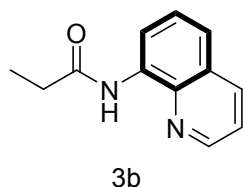
148.36, 144.56, 138.57, 136.35, 134.15, 127.99, 127.36, 121.84, 121.71, 116.66, 115.12, 112.45. **HRMS** (ESI) Calcd for $C_{14}H_{11}N_2O_2$ $[M+H]^+$: 239.0815; found: 239.0823.

8.2 Characterization Data of **3**



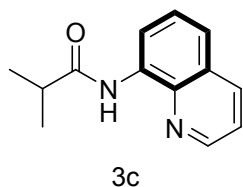
***N*-(quinolin-8-yl)acetamide (3a):**

Purified by recrystallization from ethyl acetate. **1H NMR** (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.83 – 8.72 (m, 2H), 8.14 (dd, J = 8.3, 1.7 Hz, 1H), 7.55 – 7.46 (m, 2H), 7.46 - 7.41 (m, 1H), 2.34 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.88, 148.16, 138.26, 136.53, 134.58, 128.01, 127.51, 121.68, 121.55, 116.55, 25.23. **HRMS** (ESI) Calcd for $C_{11}H_{11}N_2O$ $[M+H]^+$: 187.0866; found: 187.0863.



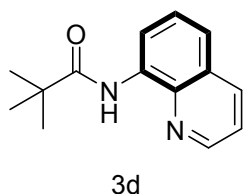
***N*-(quinolin-8-yl)propionamide (3b):**

Purified by recrystallization from ethyl acetate. **1H NMR** (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.83 – 8.76 (m, 2H), 8.16 (dd, J = 8.3, 1.7 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.45 (dd, J = 8.3, 4.3 Hz, 1H), 2.60 (q, J = 7.6 Hz, 2H), 1.34 (t, J = 7.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.67, 148.12, 138.32, 136.68, 134.63, 128.09, 127.64, 121.67, 121.47, 116.68, 31.37, 9.88. **HRMS** (ESI) Calcd for $C_{12}H_{13}N_2O$ $[M+H]^+$: 201.1022; found: 201.1036.



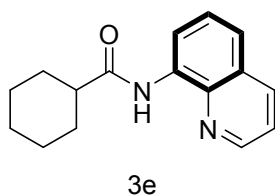
***N*-(quinolin-8-yl)isobutyramide (3c):**

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 9.92 (s, 1H), 8.81 (d, *J* = 1.6 Hz, 1H), 8.80 (dd, *J* = 3.3, 1.6 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 2.78 (hept, *J* = 6.9 Hz, 1H), 1.36 (s, 3H), 1.34 (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 175.92, 148.17, 138.49, 136.63, 134.72, 128.08, 127.63, 121.67, 121.44, 116.64, 37.26, 19.86. **HRMS** (ESI) Calcd for C₁₃H₁₅N₂O [M+H]⁺: 215.1179; found: 215.1190.



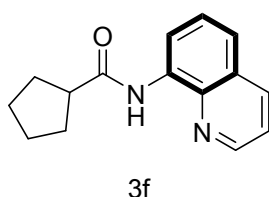
***N*-(quinolin-8-yl)pivalamide (3d):**

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 10.28 (s, 1H), 8.81 (dd, *J* = 3.4, 1.6 Hz, 1H), 8.79 (d, *J* = 1.6 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.54 – 7.44 (m, 2H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 1.43 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 177.34, 148.26, 138.77, 136.42, 134.71, 127.97, 127.49, 121.60, 121.33, 116.29, 40.42, 27.81. **HRMS** (ESI) Calcd for C₁₄H₁₇N₂O [M+H]⁺: 229.1335; found: 229.1332.



***N*-(quinolin-8-yl)cyclohexanecarboxamide (3e):**

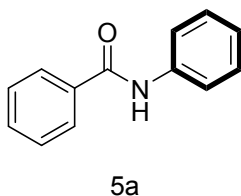
Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 9.91 (s, 1H), 8.83 – 8.78 (m, 2H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.56 – 7.43 (m, 3H), 2.49 (tt, *J* = 11.7, 3.5 Hz, 1H), 2.12 – 2.05 (m, 2H), 1.91 - 1.83 (m, 2H), 1.76 – 1.71 (m, 1H), 1.69 - 1.57 (m, 2H), 1.45 - 1.27 (m, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 175.01, 148.01, 138.33, 136.60, 134.59, 127.99, 127.56, 121.56, 121.32, 116.62, 46.91, 29.78, 25.77. **HRMS** (ESI) Calcd for C₁₆H₁₉N₂O [M+H]⁺: 255.1492; found: 255.1495.



***N*-(quinolin-8-yl)cyclopentanecarboxamide (3f):**

Purified by recrystallization from ethyl acetate. **¹H NMR** (400 MHz, CDCl₃) δ 9.87 (s, 1H), 8.82 – 8.76 (m, 2H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.54 – 7.49 (m, 1H), 7.48 - 7.44 (m, 1H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 2.94 (p, *J* = 8.1 Hz, 1H), 2.08 – 1.94 (m, 4H), 1.89 – 1.77 (m, 2H), 1.73 – 1.61 (m, 2H). **¹³C NMR** (101 MHz, CDCl₃) δ 175.20, 148.12, 138.38, 136.48, 134.76, 128.00, 127.53, 121.61, 121.30, 116.44, 47.45, 30.69, 26.09. **HRMS** (ESI) Calcd for C₁₅H₁₇N₂O [M+H]⁺: 241.1335; found: 241.1345.

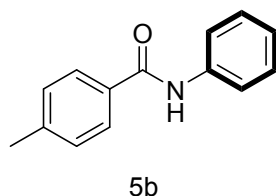
8.3 Characterization Data of 5



***N*-phenylbenzamide (5a):**

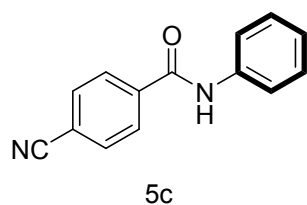
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 16/1). **¹H NMR** (400 MHz, CDCl₃) δ 7.95 (s, 1H), 7.88 – 7.84 (m, 2H), 7.67 – 7.62 (m, 2H), 7.56 – 7.51

(m, 1H), 7.49 – 7.43 (m, 2H), 7.39 – 7.33 (m, 2H), 7.18 – 7.13 (m, 1H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.96, 138.07, 135.13, 131.95, 129.21, 128.90, 127.17, 124.71, 120.40. **HRMS** (ESI) Calcd for C₁₃H₁₂NO [M+H]⁺: 198.0913; found: 198.0922.



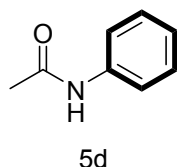
4-Methyl-N-phenylbenzamide (5b):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 16/1). **¹H NMR** (400 MHz, CDCl₃) δ 7.87 (s, 1H), 7.79 – 7.74 (m, 2H), 7.66 – 7.61 (m, 2H), 7.39 – 7.33 (m, 2H), 7.29 – 7.27 (m, 1H), 7.17 – 7.11 (m, 1H), 2.42 (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.73, 142.38, 138.07, 132.14, 129.44, 129.08, 127.06, 124.45, 120.21, 21.51. **HRMS** (ESI) Calcd for C₁₄H₁₄NO [M+H]⁺: 212.1070; found: 212.1072.



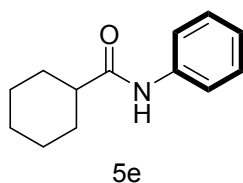
4-Cyano-N-phenylbenzamide (5c):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). **¹H NMR** (400 MHz, CDCl₃) δ 7.99 – 7.94 (m, 2H), 7.89 (s, 1H), 7.80 – 7.75 (m, 2H), 7.62 (d, *J* = 7.8 Hz, 2H), 7.42 – 7.36 (m, 2H), 7.20 (tt, *J* = 7.6, 1.2 Hz, 1H). **¹³C NMR** (101 MHz, CDCl₃) δ 163.94, 138.90, 137.28, 132.65, 129.26, 127.80, 125.29, 120.43, 117.90, 115.43. **HRMS** (ESI) Calcd for C₁₄H₁₁N₂O [M+H]⁺: 223.0866; found: 223.0879.



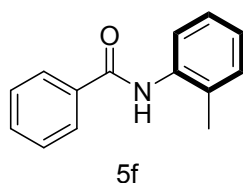
***N*-phenylacetamide (5d):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 15/1). **¹H NMR** (400 MHz, CDCl₃) δ 7.64 (s, 1H), 7.54 – 7.46 (m, 2H), 7.30 (t, *J* = 8.0 Hz, 2H), 7.14 – 7.06 (m, 1H), 2.16 (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 168.74, 138.04, 129.08, 124.44, 120.12, 24.63. **HRMS** (ESI) Calcd for C₈H₁₀NO [M+H]⁺: 135.0684; found: 135.0691.



***N*-phenylcyclohexanecarboxamide (5e):**

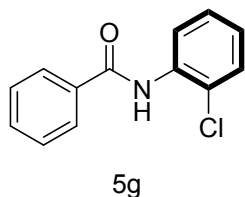
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 15/1). **¹H NMR** (400 MHz, CDCl₃) δ 7.53 (d, *J* = 7.8 Hz, 2H), 7.33 – 7.27 (m, 3H), 7.12 – 7.05 (m, 1H), 2.23 (tt, *J* = 11.8, 3.5 Hz, 1H), 1.99 – 1.92 (m, 2H), 1.86 - 1.80 (m, 2H), 1.73 – 1.66 (m, 1H), 1.60 - 1.48 (m, 2H), 1.35 – 1.23 (m, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 174.55, 138.24, 129.08, 124.20, 119.91, 46.68, 29.80, 25.80. **HRMS** (ESI) Calcd for C₁₃H₁₈NO [M+H]⁺: 204.1383; found: 204.1371.



***N*-(*o*-tolyl)benzamide (5f):**

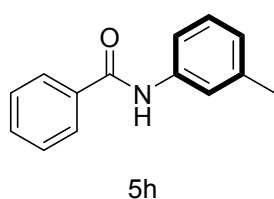
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 16/1). **¹H NMR** (400 MHz, CDCl₃) δ 7.95 (d, *J* = 8.1 Hz, 1H), 7.91 – 7.87 (m, 2H), 7.70 (s, 1H), 7.60 –

7.54 (m, 1H), 7.53 – 7.47 (m, 2H), 7.29 – 7.22 (m, 2H), 7.13 (td, $J = 7.5, 1.3$ Hz, 1H), 2.34 (s, 3H). **^{13}C NMR** (101 MHz, CDCl_3) δ 165.68, 135.79, 135.04, 131.88, 130.59, 129.24, 128.87, 127.07, 126.94, 125.39, 123.14, 17.86. **HRMS** (ESI) Calcd for $\text{C}_{14}\text{H}_{14}\text{NO}$ $[\text{M}+\text{H}]^+$: 212.1070; found: 212.1079.



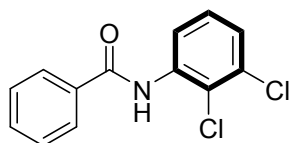
***N*-(2-chlorophenyl)benzamide (5g):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 16/1). **^1H NMR** (400 MHz, CDCl_3) δ 8.56 (dd, $J = 8.3, 1.6$ Hz, 1H), 8.46 (s, 1H), 7.94 – 7.90 (m, 2H), 7.60 – 7.55 (m, 1H), 7.51 (tt, $J = 6.6, 1.8$ Hz, 2H), 7.41 (dd, $J = 8.0, 1.5$ Hz, 1H), 7.36 – 7.30 (m, 1H), 7.08 (td, $J = 7.7, 1.6$ Hz, 1H). **^{13}C NMR** (101 MHz, CDCl_3) δ 165.29, 134.77, 134.63, 132.21, 129.05, 128.96, 127.90, 127.12, 124.79, 123.11, 121.58. **HRMS** (ESI) Calcd for $\text{C}_{13}\text{H}_{11}\text{NOCl}$ $[\text{M}+\text{H}]^+$: 232.0524; found: 232.0532.



***N*-(*m*-tolyl)benzamide (5h):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 16/1). **^1H NMR** (400 MHz, CDCl_3) δ 7.89 – 7.80 (m, 4H), 7.56 – 7.51 (m, 1H), 7.48 – 7.42 (m, 2H), 7.24 – 7.18 (m, 2H), 7.10 (td, $J = 7.3, 6.9, 1.3$ Hz, 1H), 2.29 (s, 3H). **^{13}C NMR** (101 MHz, CDCl_3) δ 165.84, 135.79, 134.93, 131.86, 130.60, 129.80, 128.82, 127.15, 126.84, 125.51, 123.51, 17.90. **HRMS** (ESI) Calcd for $\text{C}_{14}\text{H}_{14}\text{NO}$ $[\text{M}+\text{H}]^+$: 212.1070; found: 212.1074.

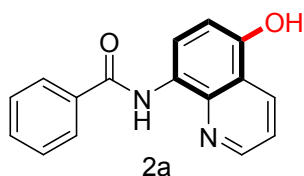


5i

***N*-(2,3-dichlorophenyl)benzamide (5i):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 15/1). **¹H NMR** (400 MHz, CDCl₃) δ 8.58 – 8.46 (m, 2H), 7.95 – 7.89 (m, 2H), 7.63 – 7.57 (m, 1H), 7.56 – 7.50 (m, 2H), 7.31 – 7.23 (m, 2H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.34, 136.40, 134.37, 132.77, 132.43, 129.05, 127.99, 127.14, 125.37, 121.61, 119.43. **HRMS** (ESI) Calcd for C₁₃H₁₀NOCl₂ [M+H]⁺: 266.0134; found: 266.0142.

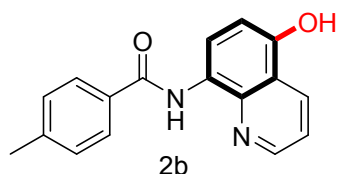
8.4 Characterization Data of 2



2a

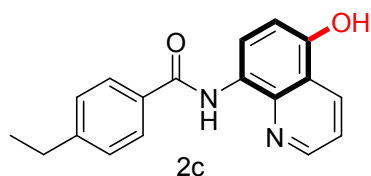
***N*-(5-hydroxyquinolin-8-yl)benzamide (2a)^[2]:**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). White solid, 45.9 mg, 87%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.40 (s, 1H), 10.35 (s, 1H), 8.94 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.58 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.50 (d, *J* = 8.4 Hz, 1H), 8.06 – 7.98 (m, 2H), 7.65 – 7.57 (m, 4H), 6.98 (d, *J* = 8.4 Hz, 1H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 164.52, 149.85, 149.45, 140.05, 135.29, 132.24, 131.93, 129.40, 127.39, 126.53, 121.34, 120.09, 118.91, 108.52. **HRMS** (ESI) Calcd for C₁₆H₁₃N₂O₂ [M+H]⁺: 265.0972; found: 265.0953.



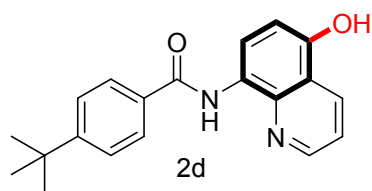
***N*-(5-hydroxyquinolin-8-yl)-4-methylbenzamide (2b)^[2]:**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). White solid, 49.5 mg, 89%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.39 (s, 1H), 10.31 (s, 1H), 8.95 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.58 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.50 (d, *J* = 8.4 Hz, 1H), 7.93 - 7.89 (m, 2H), 7.60 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 1H), 2.41 (s, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 164.37, 149.84, 149.30, 142.30, 139.96, 132.45, 131.93, 129.93, 127.40, 126.59, 121.35, 120.07, 118.73, 108.52, 21.51. HRMS (ESI) Calcd for C₁₇H₁₅N₂O₂ [M+H]⁺: 279.1128; found: 279.1103.



4-Ethyl-*N*-(5-hydroxyquinolin-8-yl)benzamide (2c):

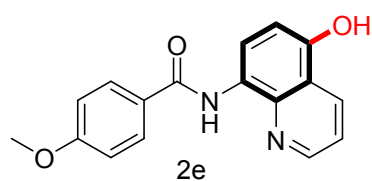
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). White solid, 51.4 mg, 88%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.40 (s, 1H), 10.31 (s, 1H), 8.95 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.58 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.50 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 2H), 7.60 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 1H), 2.71 (q, *J* = 7.6 Hz, 2H), 1.23 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 164.42, 149.83, 149.29, 148.42, 139.94, 132.76, 131.93, 128.77, 127.49, 126.61, 121.35, 120.07, 118.68, 108.52, 28.55, 15.82. HRMS (ESI) Calcd for C₁₈H₁₇N₂O₂ [M+H]⁺: 293.1285; found: 293.1245.



4-(*tert*-butyl)-*N*-(5-hydroxyquinolin-8-yl)benzamide (2d):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1).

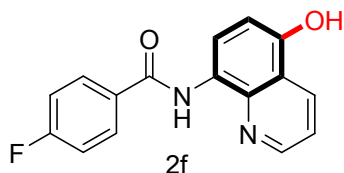
White solid, 51.9 mg, 81%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.40 (s, 1H), 10.32 (s, 1H), 8.94 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.58 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 7.94 (dt, *J* = 8.8, 2.0 Hz, 2H), 7.63 - 7.56 (m, 3H), 6.97 (d, *J* = 8.4 Hz, 1H), 1.33 (s, 9H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 164.41, 155.12, 149.81, 149.27, 139.89, 132.58, 131.94, 127.22, 126.62, 126.20, 121.35, 120.07, 118.54, 108.52, 35.19, 31.39. **HRMS** (ESI) Calcd for C₂₀H₂₁N₂O₂ [M+H]⁺: 321.1598; found: 321.1587.



***N*-(5-hydroxyquinolin-8-yl)-4-methoxybenzamide (2e)^[2]:**

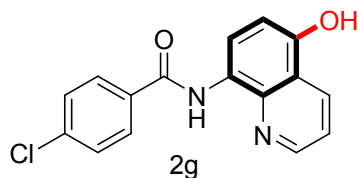
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 15/1).

White solid, 46.5 mg, 79%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.38 (s, 1H), 10.27 (s, 1H), 8.95 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.58 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.48 (d, *J* = 8.4 Hz, 1H), 8.01 – 7.96 (m, 2H), 7.61 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.17 – 7.10 (m, 2H), 6.97 (d, *J* = 8.4 Hz, 1H), 3.86 (s, 3H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 164.03, 162.47, 149.79, 149.18, 139.97, 131.92, 129.28, 127.41, 126.71, 121.32, 120.07, 118.66, 114.62, 108.54, 55.95. **HRMS** (ESI) Calcd for C₁₇H₁₅N₂O₃ [M+H]⁺: 295.1077; found: 295.1067.



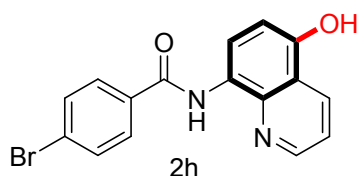
4-Fluoro-N-(5-hydroxyquinolin-8-yl)benzamide (2f)^[2]:

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). White solid, 44.0 mg, 78%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.44 (s, 1H), 10.32 (s, 1H), 8.94 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.58 (dd, *J* = 8.4, 1.5 Hz, 1H), 8.43 (d, *J* = 8.4 Hz, 1H), 8.13 - 8.05 (m, 2H), 7.60 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.42 (t, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 165.84, 163.63, 163.37, 149.89, 149.62, 140.28, 131.90, 131.80, 131.77, 130.25, 130.16, 126.43, 121.33, 120.08, 119.49, 116.42, 116.21, 108.47. ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ -108.64. HRMS (ESI) Calcd for C₁₆H₁₂FN₂O₂ [M+H]⁺: 283.0877; found: 283.0883.



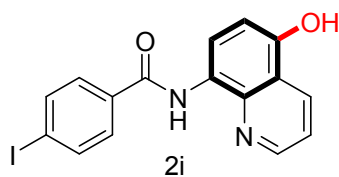
4-Chloro-N-(5-hydroxyquinolin-8-yl)benzamide (2g)^[2]:

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). White solid, 50.1 mg, 84%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.45 (s, 1H), 10.36 (s, 1H), 8.95 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.58 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.44 (d, *J* = 8.3 Hz, 1H), 8.04 (d, *J* = 8.6 Hz, 2H), 7.67 (d, *J* = 8.6 Hz, 2H), 7.61 (dd, *J* = 8.4, 4.2 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 163.61, 149.93, 149.73, 140.31, 137.01, 134.01, 131.91, 129.46, 129.42, 126.33, 121.35, 120.08, 119.63, 108.47. HRMS (ESI) Calcd for C₁₆H₁₂ClN₂O₂ [M+H]⁺: 299.0582; found: 299.0588.



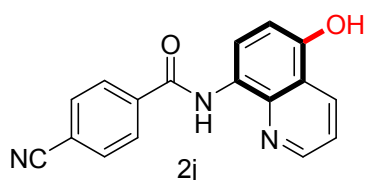
4-Bromo-N-(5-hydroxyquinolin-8-yl)benzamide (2h)^[2]:

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). White solid, 52.9 mg, 76%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.44 (s, 1H), 10.36 (s, 1H), 8.95 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.59 (dd, *J* = 8.5, 1.7 Hz, 1H), 8.44 (d, *J* = 8.4 Hz, 1H), 7.99 – 7.92 (m, 2H), 7.84 – 7.78 (m, 2H), 7.61 (dd, *J* = 8.4, 4.2 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 163.72, 149.92, 149.73, 140.29, 134.37, 132.35, 131.91, 129.62, 126.32, 125.95, 121.35, 120.08, 119.59, 108.48. HRMS (ESI) Calcd for C₁₆H₁₂BrN₂O₂ [M+H]⁺: 343.0077; found: 343.0082.



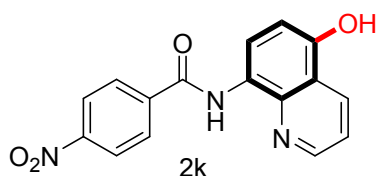
N-(5-hydroxyquinolin-8-yl)-4-iodobenzamide (2i)^[2]:

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). White solid, 58.5 mg, 75%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.47 (s, 1H), 10.39 (s, 1H), 8.98 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.62 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.48 (d, *J* = 8.4 Hz, 1H), 8.02 (dt, *J* = 8.4, 1.6 Hz, 2H), 7.83 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.64 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 163.96, 149.91, 149.68, 140.23, 138.22, 134.66, 131.91, 129.41, 126.33, 121.35, 120.08, 119.47, 108.49, 99.94. HRMS (ESI) Calcd for C₁₆H₁₂IN₂O₂ [M+H]⁺: 390.9938; found: 390.9935.

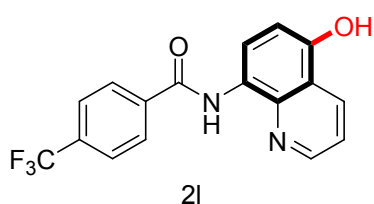


4-Cyano-*N*-(5-hydroxyquinolin-8-yl)benzamide (2j)^[2]:

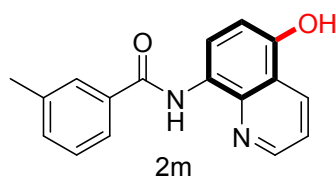
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). Light yellow solid, 41.0 mg, 71%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.50 (s, 1H), 10.46 (s, 1H), 8.94 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.58 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.17 (d, *J* = 8.4 Hz, 2H), 8.06 (dt, *J* = 8.5, 2.0 Hz, 2H), 7.60 (dd, *J* = 8.4, 4.2 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 163.34, 150.08, 150.00, 140.51, 139.25, 133.35, 131.90, 128.45, 126.10, 121.36, 120.18, 120.09, 118.79, 114.42, 108.42. **HRMS** (ESI) Calcd for C₁₇H₁₂N₃O₂ [M+H]⁺: 290.0924; found: 290.0903.

***N*-(5-hydroxyquinolin-8-yl)-4-nitrobenzamide (2k):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 8/1). Light yellow solid, 40.8 mg, 66%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.51 - 10.49 (m, 2H), 8.95 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.59 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.46 – 8.38 (m, 3H), 8.28 – 8.22 (m, 2H), 7.61 (dd, *J* = 8.5, 4.2 Hz, 1H), 6.99 (d, *J* = 8.3 Hz, 1H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 163.15, 150.17, 150.03, 149.71, 140.89, 140.56, 131.91, 129.16, 126.10, 124.46, 121.38, 120.31, 120.11, 108.44. **HRMS** (ESI) Calcd for C₁₆H₁₂N₃O₄ [M+H]⁺: 310.0822; found: 310.0836.

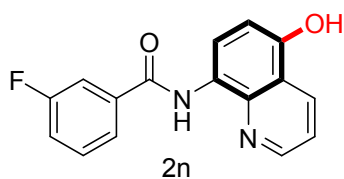
***N*-(5-hydroxyquinolin-8-yl)-4-(trifluoromethyl)benzamide (2l):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). White solid, 50.5 mg, 76%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.49 (s, 1H), 10.46 (s, 1H), 8.94 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.58 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.44 (d, *J* = 8.4 Hz, 1H), 8.21 (d, *J* = 8.1 Hz, 2H), 7.97 (d, *J* = 8.3 Hz, 2H), 7.60 (dd, *J* = 8.4, 4.2 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 163.54, 149.96, 140.43, 139.05, 132.09, 131.91, 131.78, 128.51, 126.39, 126.36, 126.32, 126.28, 126.19, 125.75, 123.04, 121.37, 120.10, 119.96, 108.44. **¹⁹F NMR** (376 MHz, DMSO-*d*₆) δ -61.32. **HRMS** (ESI) Calcd for C₁₇H₁₂F₃N₂O₂ [M+H]⁺: 333.0845; found: 333.0846.



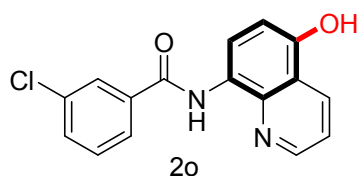
***N*-(5-hydroxyquinolin-8-yl)-3-methylbenzamide (2m)^[2]:**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). White solid, 48.4 mg, 87%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.41 (s, 1H), 10.31 (s, 1H), 8.95 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.59 (dd, *J* = 8.5, 1.7 Hz, 1H), 8.50 (d, *J* = 8.4 Hz, 1H), 7.84 – 7.78 (m, 2H), 7.61 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.53 – 7.42 (m, 2H), 6.98 (d, *J* = 8.4 Hz, 1H), 2.44 (s, 3H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 164.66, 149.88, 149.40, 140.02, 138.79, 135.32, 132.87, 131.93, 129.29, 127.97, 126.55, 124.43, 121.35, 120.07, 118.90, 108.50, 21.49. **HRMS** (ESI) Calcd for C₁₇H₁₅N₂O₂ [M+H]⁺: 279.1128; found: 279.1138.



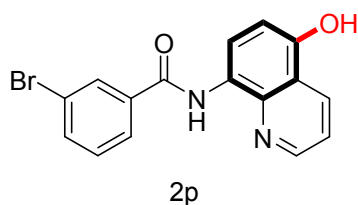
3-Fluoro-*N*-(5-hydroxyquinolin-8-yl)benzamide (2n):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). White solid, 44.6 mg, 79%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.43 (s, 1H), 10.35 (s, 1H), 8.94 (s, 1H), 8.58 (d, *J* = 7.8 Hz, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 7.1 Hz, 1H), 7.79 (d, *J* = 9.2 Hz, 1H), 7.70 – 7.55 (m, 2H), 7.49 (t, *J* = 6.9 Hz, 1H), 6.98 (d, *J* = 8.1 Hz, 1H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 163.93, 163.41, 161.49, 149.96, 149.85, 140.41, 137.78, 137.71, 131.88, 131.60, 131.52, 126.25, 123.48, 123.46, 121.33, 120.09, 119.86, 119.22, 119.01, 114.66, 114.44, 108.45. **¹⁹F NMR** (376 MHz, DMSO-*d*₆) δ -112.02. **HRMS** (ESI) Calcd for C₁₆H₁₂FN₂O₂ [M+H]⁺: 283.0877; found: 283.0878.



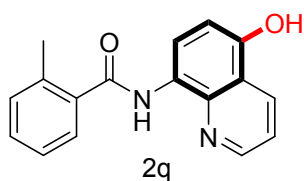
3-Chloro-*N*-(5-hydroxyquinolin-8-yl)benzamide (2o)^[2]:

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). White solid, 52.4 mg, 88%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.44 (s, 1H), 10.35 (s, 1H), 8.94 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.58 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 8.02 (t, *J* = 2.0 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.65 – 7.57 (m, 2H), 6.98 (d, *J* = 8.4 Hz, 1H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 163.35, 149.96, 149.91, 140.51, 137.37, 134.12, 132.00, 131.87, 131.29, 127.52, 126.25, 126.10, 121.30, 120.10, 120.08, 108.45. **HRMS** (ESI) Calcd for C₁₆H₁₂ClN₂O₂ [M+H]⁺: 299.0582; found: 299.0599.



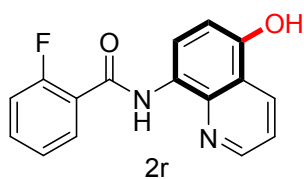
3-Bromo-*N*-(5-hydroxyquinolin-8-yl)benzamide (2p):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). White solid, 51.3 mg, 75%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.47 (s, 1H), 10.36 (s, 1H), 8.95 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.58 (dd, *J* = 8.5, 1.7 Hz, 1H), 8.39 (d, *J* = 8.3 Hz, 1H), 8.17 (t, *J* = 1.9 Hz, 1H), 8.04 – 8.00 (m, 1H), 7.84 (ddd, *J* = 8.1, 2.1, 1.0 Hz, 1H), 7.62 – 7.53 (m, 2H), 6.98 (d, *J* = 8.4 Hz, 1H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 163.28, 149.97, 149.93, 140.54, 137.53, 134.90, 131.87, 131.52, 130.40, 126.48, 126.24, 122.58, 121.30, 120.15, 120.10, 108.44. **HRMS** (ESI) Calcd for C₁₆H₁₂BrN₂O₂ [M+H]⁺: 343.0077; found: 343.0085.



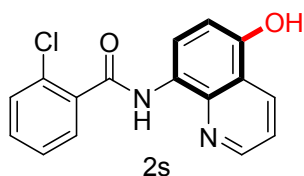
***N*-(5-hydroxyquinolin-8-yl)-2-methylbenzamide (2q):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). White solid, 47.3 mg, 85%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.39 (s, 1H), 9.88 (s, 1H), 8.88 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.57 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.51 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 7.1 Hz, 1H), 7.58 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.44 (td, *J* = 7.5, 1.5 Hz, 1H), 7.38 - 7.33 (m, 2H), 6.98 (d, *J* = 8.4 Hz, 1H), 2.48 (s, 3H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 167.22, 149.80, 149.38, 139.79, 137.18, 136.15, 131.88, 131.53, 130.56, 127.33, 126.69, 126.55, 121.31, 120.05, 118.59, 108.45, 20.11. **HRMS** (ESI) Calcd for C₁₇H₁₅N₂O₂ [M+H]⁺: 279.1128; found: 279.1133.



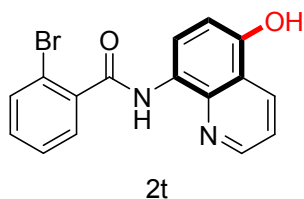
2-Fluoro-*N*-(5-hydroxyquinolin-8-yl)benzamide (2r)^[2]:

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). White solid, 34.4 mg, 61%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.72 (d, *J* = 11.0 Hz, 1H), 10.45 (s, 1H), 8.93 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.65 (d, *J* = 8.4 Hz, 1H), 8.58 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.06 (td, *J* = 7.9, 1.9 Hz, 1H), 7.72 – 7.65 (m, 1H), 7.61 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.50 – 7.39 (m, 2H), 6.97 (d, *J* = 8.4 Hz, 1H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 161.3, 160.66 (d, *J* = 2.6 Hz), 158.94, 149.91, 149.44, 139.40, 134.44 (d, *J* = 9.2 Hz), 131.95, 131.70 (d, *J* = 1.6 Hz), 126.65, 125.75 (d, *J* = 3.0 Hz), 122.40, 122.28, 121.48, 120.02, 118.39, 117.15, 116.91, 108.54. **¹⁹F NMR** (376 MHz, DMSO-*d*₆) δ -112.95. **HRMS** (ESI) Calcd for C₁₆H₁₂FN₂O₂ [M+H]⁺: 283.0877; found: 283.0872.



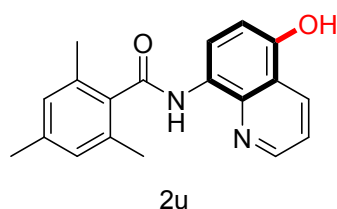
2-Chloro-*N*-(5-hydroxyquinolin-8-yl)benzamide (2s)^[2]:

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). White solid, 50.1 mg, 84%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.44 (s, 1H), 10.13 (s, 1H), 8.88 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.57 (dd, *J* = 8.5, 1.7 Hz, 1H), 8.51 (d, *J* = 8.4 Hz, 1H), 7.76 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.64 – 7.55 (m, 3H), 7.55 – 7.48 (m, 1H), 6.98 (d, *J* = 8.4 Hz, 1H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 164.28, 149.87, 149.64, 139.80, 136.61, 132.12, 131.87, 130.56, 130.30, 129.96, 128.06, 126.40, 121.37, 120.03, 118.93, 108.44. **HRMS** (ESI) Calcd for C₁₆H₁₂ClN₂O₂ [M+H]⁺: 299.0582; found: 299.0584.

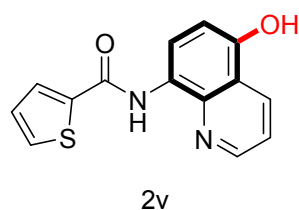


2-Bromo-N-(5-hydroxyquinolin-8-yl)benzamide (2t)^[2]:

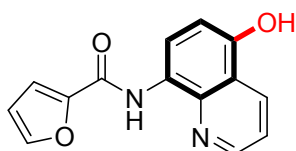
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). White solid, 52.7 mg, 77%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.44 (s, 1H), 10.00 (s, 1H), 8.87 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.57 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.50 (d, *J* = 8.4 Hz, 1H), 7.76 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.70 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.60 – 7.52 (m, 2H), 7.47 (td, *J* = 7.7, 1.8 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 165.35, 149.86, 149.65, 139.80, 139.02, 133.60, 132.11, 131.87, 129.68, 128.49, 126.36, 121.37, 120.03, 119.31, 118.94, 108.42. HRMS (ESI) Calcd for C₁₆H₁₂BrN₂O₂ [M+H]⁺: 343.0077; found: 343.0081.

**N-(5-hydroxyquinolin-8-yl)-2,4,6-trimethylbenzamide (2u):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). White solid, 48.4 mg, 79%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.45 (s, 1H), 9.66 (s, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.55 (dd, *J* = 8.5, 1.7 Hz, 1H), 8.45 (d, *J* = 8.4 Hz, 1H), 7.55 (dd, *J* = 8.5, 4.2 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 6.93 (s, 2H), 2.30-2.26 (m, 9H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 167.64, 149.47, 149.15, 139.63, 138.03, 135.64, 133.79, 131.44, 128.13, 126.03, 120.90, 119.68, 118.82, 108.06, 20.79, 19.02. HRMS (ESI) Calcd for C₁₉H₁₉N₂O₂ [M+H]⁺: 307.1441; found: 307.1447.

**N-(5-hydroxyquinolin-8-yl)thiophene-2-carboxamide (2v):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). Light yellow solid, 36.6 mg, 68%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.44 (s, 1H), 10.25 (s, 1H), 8.95 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.58 (dd, *J* = 8.5, 1.7 Hz, 1H), 8.31 (d, *J* = 8.4 Hz, 1H), 7.96 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.89 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.60 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.26 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 159.55, 149.98, 149.77, 140.36, 140.18, 132.13, 131.88, 129.15, 128.85, 126.11, 121.33, 120.09, 120.02, 108.50. **HRMS** (ESI) Calcd for C₁₄H₁₁N₂O₂S [M+H]⁺: 271.0536; found: 271.0542.

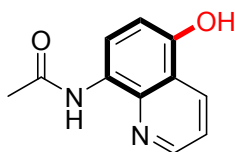


2w

***N*-(5-hydroxyquinolin-8-yl)furan-2-carboxamide (2w)^[2]:**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). Light yellow solid, 33.0 mg, 65%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.43 (s, 1H), 10.38 (s, 1H), 8.97 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.58 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 8.02 (dd, *J* = 1.6, 0.7 Hz, 1H), 7.62 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.30 (d, *J* = 4.1 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.76 (dd, *J* = 3.5, 1.7 Hz, 1H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 155.46, 149.90, 149.33, 148.15, 146.26, 139.32, 132.01, 126.00, 121.49, 120.06, 117.90, 115.32, 113.16, 108.57. **HRMS** (ESI) Calcd for C₁₄H₁₁N₂O₃ [M+H]⁺: 255.0746; found: 255.0742.

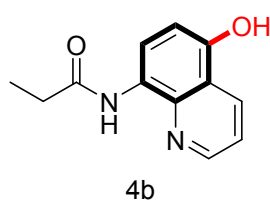
8.5 Characterization Data of 4



4a

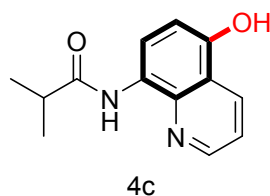
***N*-(5-hydroxyquinolin-8-yl)acetamide (4a)^[2]:**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). Colorless oil, 31.1 mg, 77%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.24 (s, 1H), 9.79 (s, 1H), 8.90 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.53 (dd, *J* = 8.4, 1.8 Hz, 1H), 8.36 (d, *J* = 8.4 Hz, 1H), 7.56 (dd, *J* = 8.4, 4.2 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 2.21 (s, 3H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 168.57, 149.43, 148.79, 139.76, 131.65, 127.19, 121.05, 119.93, 118.81, 108.46, 24.74. **HRMS** (ESI) Calcd for C₁₁H₁₁N₂O₂ [M+H]⁺: 203.0815; found: 203.0819.



***N*-(5-hydroxyquinolin-8-yl)propionamide (4b)^[2]:**

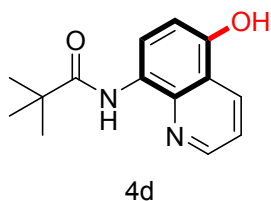
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). Colorless oil, 35.0 mg, 81%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.24 (s, 1H), 9.72 (s, 1H), 8.89 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.53 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.39 (d, *J* = 8.4 Hz, 1H), 7.55 (dd, *J* = 8.5, 4.2 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 2.57 – 2.50 (m, 2H), 1.13 (t, *J* = 7.5 Hz, 3H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 172.05, 149.43, 148.68, 139.66, 127.12, 121.08, 119.94, 118.53, 108.48, 30.18, 10.29. **HRMS** (ESI) Calcd for C₁₂H₁₃N₂O₂ [M+H]⁺: 217.0972; found: 217.0981.



***N*-(5-hydroxyquinolin-8-yl)isobutyramide (4c)^[2]:**

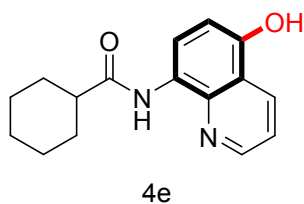
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). Colorless oil, 36.4 mg, 79%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.24 (s, 1H), 9.71 (s, 1H), 8.90 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.54 (dd, *J* = 8.5, 1.7 Hz, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 7.56 (dd, *J* =

8.4, 4.2 Hz, 1H), 6.89 (d, $J = 8.4$ Hz, 1H), 2.92 – 2.79 (m, 1H), 1.17 (d, $J = 6.8$ Hz, 6H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 175.51, 149.92, 149.13, 140.12, 132.15, 127.46, 121.53, 120.37, 118.88, 108.88, 36.11, 20.59. HRMS (ESI) Calcd for $\text{C}_{13}\text{H}_{15}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 231.1128; found: 231.1131.



***N*-(5-hydroxyquinolin-8-yl)pivalamide (4d)^[2]:**

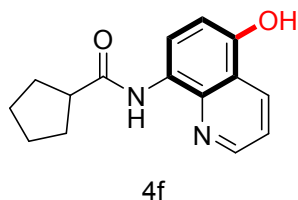
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). Colorless oil, 36.1 mg, 74%. ^1H NMR (400 MHz, DMSO- d_6) δ 10.26 (s, 1H), 9.83 (s, 1H), 8.91 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.55 (dd, $J = 8.5, 1.7$ Hz, 1H), 8.45 (d, $J = 8.4$ Hz, 1H), 7.58 (dd, $J = 8.4, 4.2$ Hz, 1H), 6.90 (d, $J = 8.4$ Hz, 1H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 175.81, 149.68, 148.62, 139.42, 131.91, 126.75, 121.26, 119.98, 117.29, 108.49, 40.64, 28.81, 27.88. HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{17}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 245.1285; found: 245.1256.



***N*-(5-hydroxyquinolin-8-yl)cyclohexanecarboxamide (4e)^[2]:**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). Colorless oil, 41.1 mg, 76%. ^1H NMR (400 MHz, DMSO- d_6) δ 10.25 (s, 1H), 9.68 (s, 1H), 8.90 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.53 (dd, $J = 8.4, 1.7$ Hz, 1H), 8.40 (d, $J = 8.4$ Hz, 1H), 7.56 (dd, $J = 8.4, 4.2$ Hz, 1H), 6.88 (d, $J = 8.4$ Hz, 1H), 2.57 (tt, $J = 11.4, 3.4$ Hz, 1H), 1.89 (d, $J = 10.8$ Hz, 2H), 1.76 (dt, $J = 12.4, 3.2$ Hz, 2H), 1.69 - 1.61 (m, 1H), 1.52 – 1.26 (m, 5H). ^{13}C NMR (101

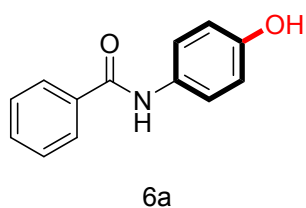
MHz, DMSO-*d*₆) δ 174.08, 149.48, 148.64, 139.60, 131.74, 127.02, 121.12, 119.94, 118.25, 108.45, 45.46, 29.91, 25.92, 25.65. **HRMS** (ESI) Calcd for C₁₆H₁₉N₂O₂ [M+H]⁺: 271.1441; found: 271.1444.



***N*-(5-hydroxyquinolin-8-yl)cyclopentanecarboxamide (4f):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). Colorless oil, 36.9 mg, 72%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.22 (s, 1H), 9.69 (s, 1H), 8.90 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.54 (dd, *J* = 8.4, 1.8 Hz, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 7.56 (dd, *J* = 8.4, 4.2 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 3.12 – 2.96 (m, 1H), 1.97 – 1.86 (m, 2H), 1.84 – 1.64 (m, 4H), 1.59 (dt, *J* = 8.2, 4.2 Hz, 2H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 174.35, 149.47, 148.66, 139.59, 131.72, 127.13, 121.10, 119.94, 118.36, 108.48, 46.09, 30.67, 26.14. **HRMS** (ESI) Calcd for C₁₅H₁₇N₂O₂ [M+H]⁺: 257.1285; found: 257.1288.

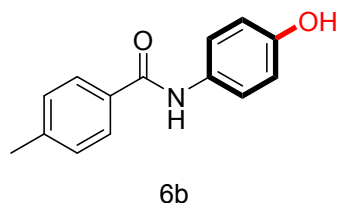
8.6 Characterization Data of 6



***N*-(4-hydroxyphenyl)benzamide (6a)^[3]:**

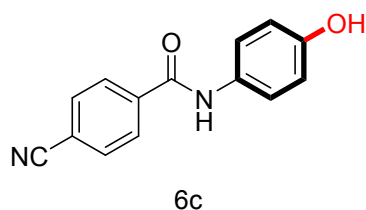
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). Light red solid, 25.1 mg, 59%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.02 (s, 1H), 9.26 (s, 1H), 7.96 – 7.91 (m, 2H), 7.58 – 7.48 (m, 5H), 6.78 – 6.73 (m, 2H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ

165.44, 154.19, 135.65, 131.73, 131.17, 128.78, 127.97, 122.76, 115.45. **HRMS** (ESI) Calcd for $C_{13}H_{12}NO_2$ $[M+H]^+$: 214.0863; found: 214.0862.



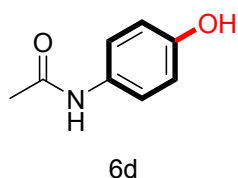
***N*-(4-hydroxyphenyl)-4-methylbenzamide (6b)^[4]:**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). Light red solid, 27.2 mg, 60%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 9.92 (s, 1H), 9.23 (s, 1H), 7.89 – 7.81 (m, 2H), 7.57 – 7.48 (m, 2H), 7.31 (d, J = 8.0 Hz, 2H), 6.78 – 6.69 (m, 2H), 2.37 (s, 3H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 164.78, 153.63, 141.19, 132.29, 130.76, 128.83, 127.52, 122.28, 114.95, 20.98. **HRMS** (ESI) Calcd for $C_{14}H_{14}NO_2$ $[M+H]^+$: 228.1019; found: 228.1015.



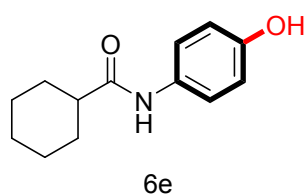
4-Cyano-*N*-(4-hydroxyphenyl)benzamide (6c):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). Light red solid, 24.3 mg, 51%. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 10.25 (s, 1H), 9.31 (s, 1H), 8.10 – 8.06 (m, 2H), 8.01 – 7.98 (m, 2H), 7.56 – 7.50 (m, 2H), 6.78 – 6.73 (m, 2H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ 163.48, 154.04, 139.18, 132.41, 130.25, 128.38, 122.32, 118.37, 115.06, 113.59. **HRMS** (ESI) Calcd for $C_{14}H_{11}N_2O_2$ $[M+H]^+$: 239.0815; found: 239.0808.



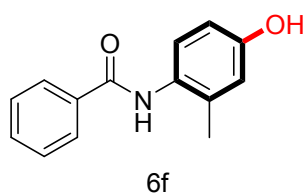
N-(4-hydroxyphenyl)acetamide (6d)^[3]:

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). Colorless oil, 9.7 mg, 32%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.64 (s, 1H), 9.12 (s, 1H), 7.35 – 7.31 (m, 2H), 6.69 – 6.64 (m, 2H), 1.97 (s, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 167.49, 153.10, 131.03, 120.79, 114.98, 23.73. HRMS (ESI) Calcd for C₈H₁₀NO₂ [M+H]⁺: 152.0706; found: 152.0698.



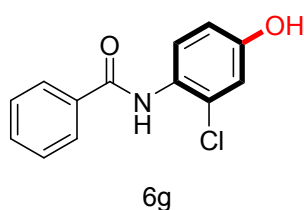
N-(4-hydroxyphenyl)cyclohexanecarboxamide (6e)^[5]:

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 10/1). Colorless oil, 22.4 mg, 51%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.49 (s, 1H), 9.10 (s, 1H), 7.38 – 7.33 (m, 2H), 6.68 – 6.63 (m, 2H), 2.25 (tt, *J* = 11.5, 3.3 Hz, 1H), 1.79 – 1.70 (m, 4H), 1.67 – 1.60 (m, 1H), 1.45 – 1.33 (m, 2H), 1.31 – 1.16 (m, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 173.55, 152.98, 131.18, 120.80, 114.92, 44.73, 29.21, 25.43, 25.28. HRMS (ESI) Calcd for C₁₃H₁₈NO₂ [M+H]⁺: 220.1332; found: 220.1321.



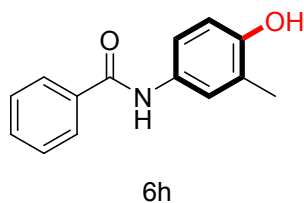
N-(4-hydroxy-2-methylphenyl)benzamide (6f):

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). Light red solid, 18.6 mg, 41%. ^1H NMR (400 MHz, DMSO- d_6) δ 9.70 (s, 1H), 9.32 (s, 1H), 7.99 – 7.93 (m, 2H), 7.58 – 7.47 (m, 3H), 7.05 (d, J = 8.5 Hz, 1H), 6.67 (d, J = 2.7 Hz, 1H), 6.60 (dd, J = 8.4, 2.8 Hz, 1H), 2.13 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.68, 135.79, 135.04, 131.88, 130.59, 129.24, 128.87, 127.07, 126.94, 125.39, 123.14, 17.86. HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{14}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 228.1019; found: 228.1024.



***N*-(2-chloro-4-hydroxyphenyl)benzamide (6g):**

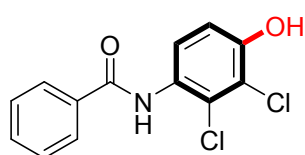
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). Light red solid, 19.3 mg, 39%. ^1H NMR (400 MHz, DMSO- d_6) δ 9.92 (s, 1H), 9.88 (s, 1H), 7.97 (d, J = 7.5 Hz, 2H), 7.62 – 7.56 (m, 1H), 7.55 - 7.49 (m, 2H), 7.27 (d, J = 8.6 Hz, 1H), 7.08 (d, J = 2.6 Hz, 1H), 6.82 (dd, J = 8.6, 2.7 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 165.97, 157.07, 134.61, 132.10, 130.67, 128.90, 128.15, 128.04, 122.16, 119.14, 115.47. HRMS (ESI) Calcd for $\text{C}_{13}\text{H}_{11}\text{NO}_2\text{Cl}$ $[\text{M}+\text{H}]^+$: 248.0473; found: 248.0490.



***N*-(4-hydroxy-3-methylphenyl)benzamide (6h):**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). Light red solid, 18.2 mg, 40%. ^1H NMR (400 MHz, DMSO- d_6) δ 9.96 (s, 1H), 9.16 (s, 1H), 7.95 –

7.89 (m, 2H), 7.56 – 7.48 (m, 3H), 7.44 (d, $J = 2.6$ Hz, 1H), 7.36 (dd, $J = 8.6, 2.6$ Hz, 1H), 6.73 (d, $J = 8.6$ Hz, 1H), 2.12 (s, 3H). **^{13}C NMR** (101 MHz, DMSO- d_6) δ 165.31, 152.26, 135.65, 131.70, 130.92, 128.78, 127.94, 124.03, 124.00, 119.95, 114.70, 16.68. **HRMS** (ESI) Calcd for $\text{C}_{14}\text{H}_{14}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 228.1019; found: 228.1032.



6i

***N*-(2,3-dichloro-4-hydroxyphenyl)benzamide (6i):**

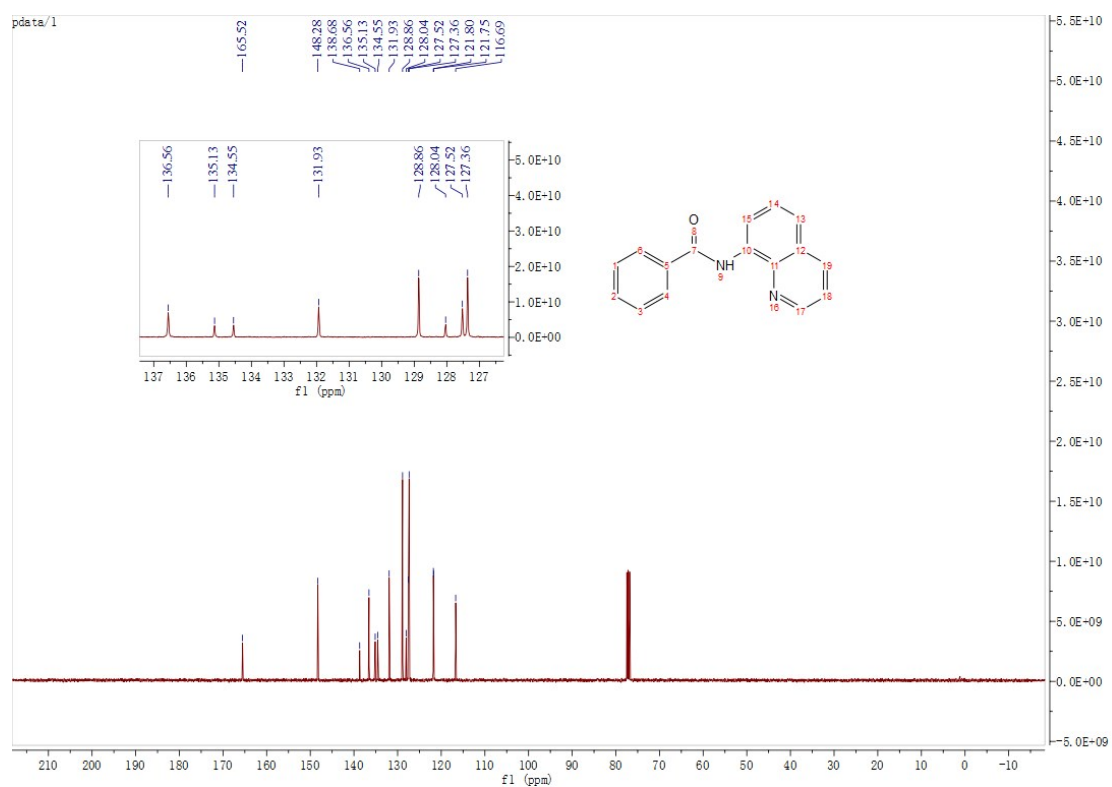
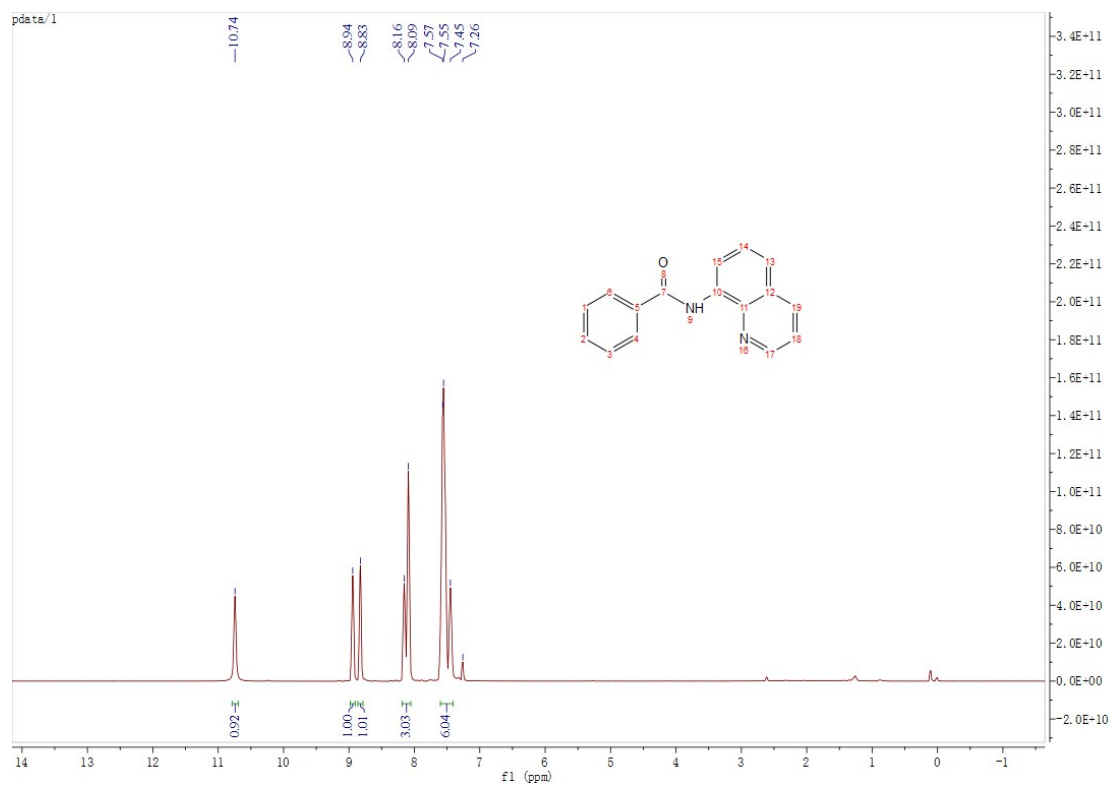
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate 12/1). Light red solid, 18.0 mg, 32%. **^1H NMR** (400 MHz, DMSO- d_6) δ 10.72 (s, 1H), 10.06 (s, 1H), 8.00 - 7.95 (m, 2H), 7.63 – 7.57 (m, 1H), 7.56 - 7.50 (m, 2H), 7.29 (d, $J = 8.8$ Hz, 1H), 7.00 (d, $J = 8.8$ Hz, 1H). **^{13}C NMR** (101 MHz, DMSO) δ 166.04, 153.43, 134.33, 132.26, 130.64, 128.95, 128.26, 128.10, 128.07, 119.25, 114.75. **HRMS** (ESI) Calcd for $\text{C}_{13}\text{H}_9\text{NO}_2\text{Cl}_2$ $[\text{M}+\text{H}]^+$: 282.0083; found: 282.0099.

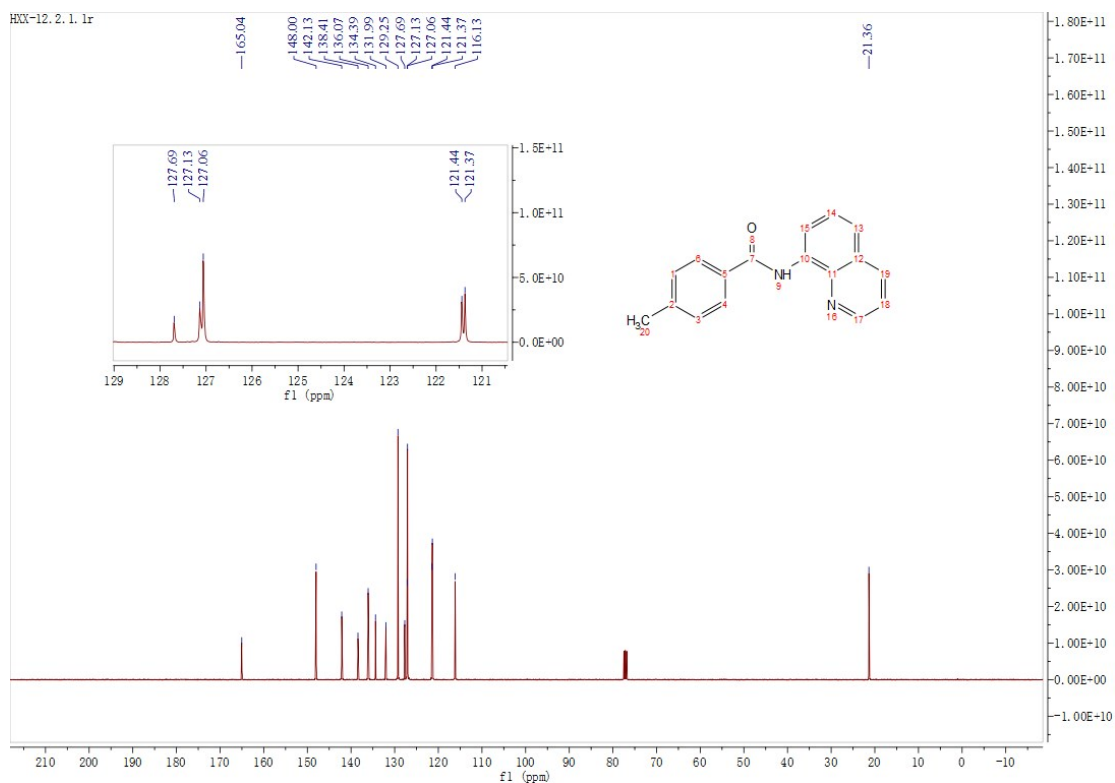
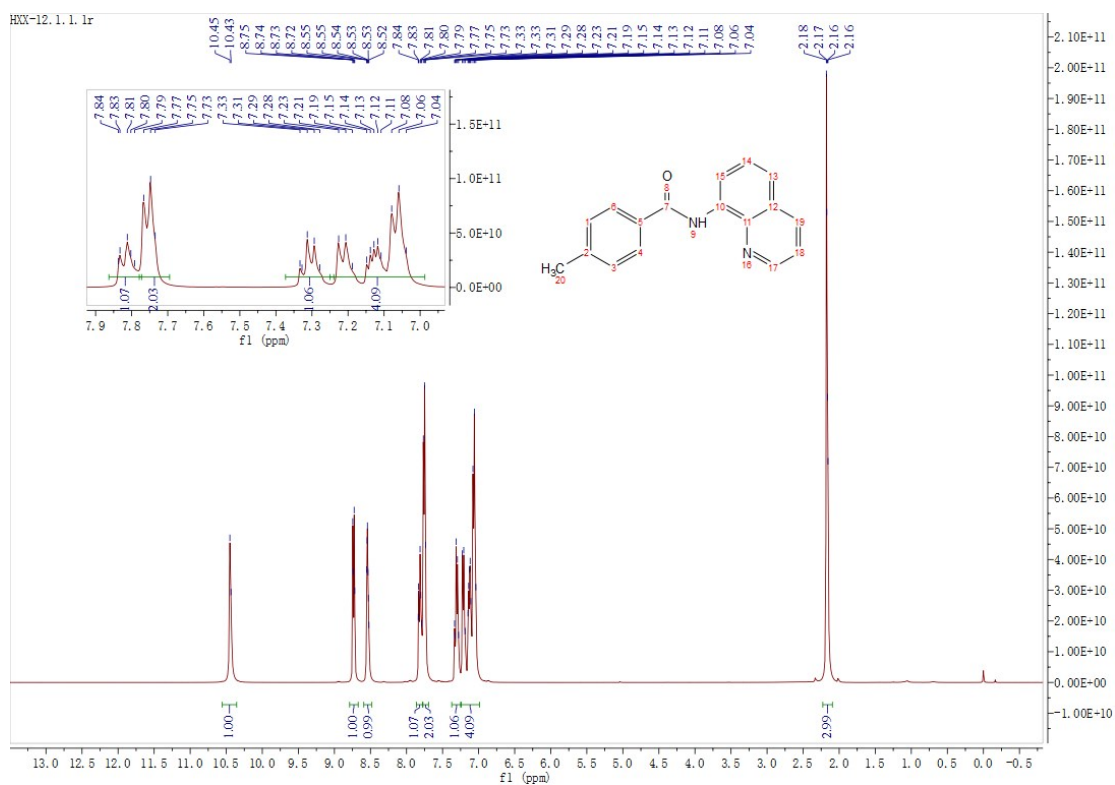
9 References

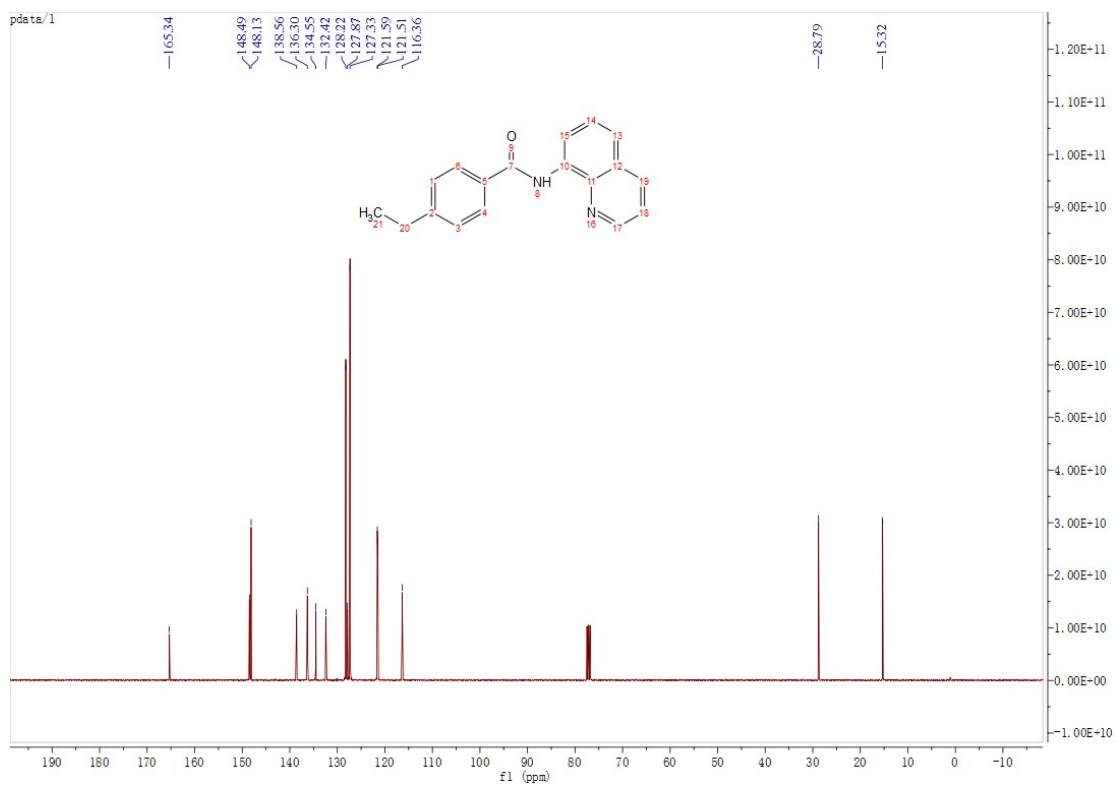
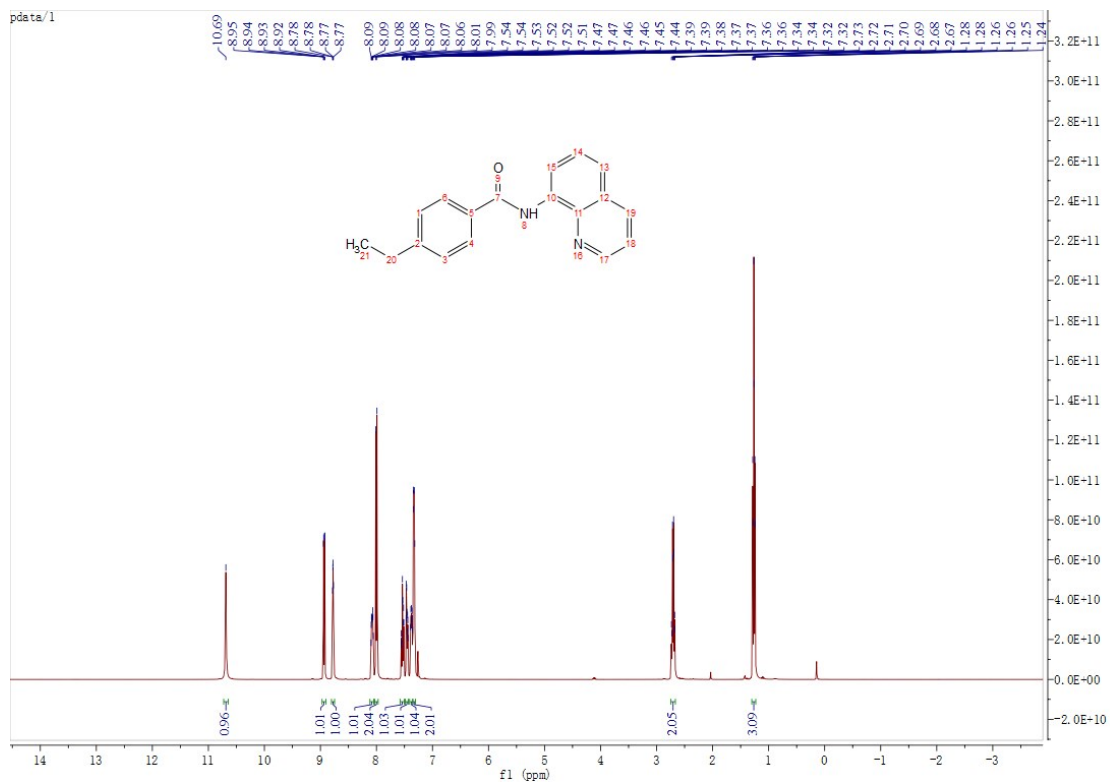
- [1] Gou, F.-R., Wang, X.-C., Huo, P.-F., Bi, H.-P., Guan, Z.-H. & Liang, Y.-M. Palladium-catalyzed aryl C-H bonds activation/acetoxylation utilizing a bidentate System. *Org. Lett.* **11**, 5726-5729 (2009).
- [2] Mondal, S. & Hajra, A. Metal-Free C-5 hydroxylation of 8-aminoquinoline amide. *J. Org. Chem.* **83**, 11392-11398 (2018).
- [3] Yan, D.-Y., Wang, G.-Q., Xiong, F., Sun, W.-Y., Shi, Z.-., Lu, Y.; Li, S.-H. & Zhao, J. A selenium-catalysed para-amination of phenols. *Nat. Commun.* **9**, 1-9 (2018).
- [4] Xu, T.-Y. & Alper, H. Pd-catalyzed chemoselective carbonylation of aminophenols with iodoarenes: Alkoxy carbonylation vs aminocarbonylation. *J. Am. Chem. Soc.* **136**, 16970-16973 (2014).
- [5] Ben Halima, T., Vandavasi, J. K., Shkoor, M. & Newman, S. G. A cross-coupling approach to amide bond formation from esters. *ACS Catal.* **7**, 2176-2180 (2017).

10 NMR-Spectra of 1, 3, 5 and 2, 4, 6

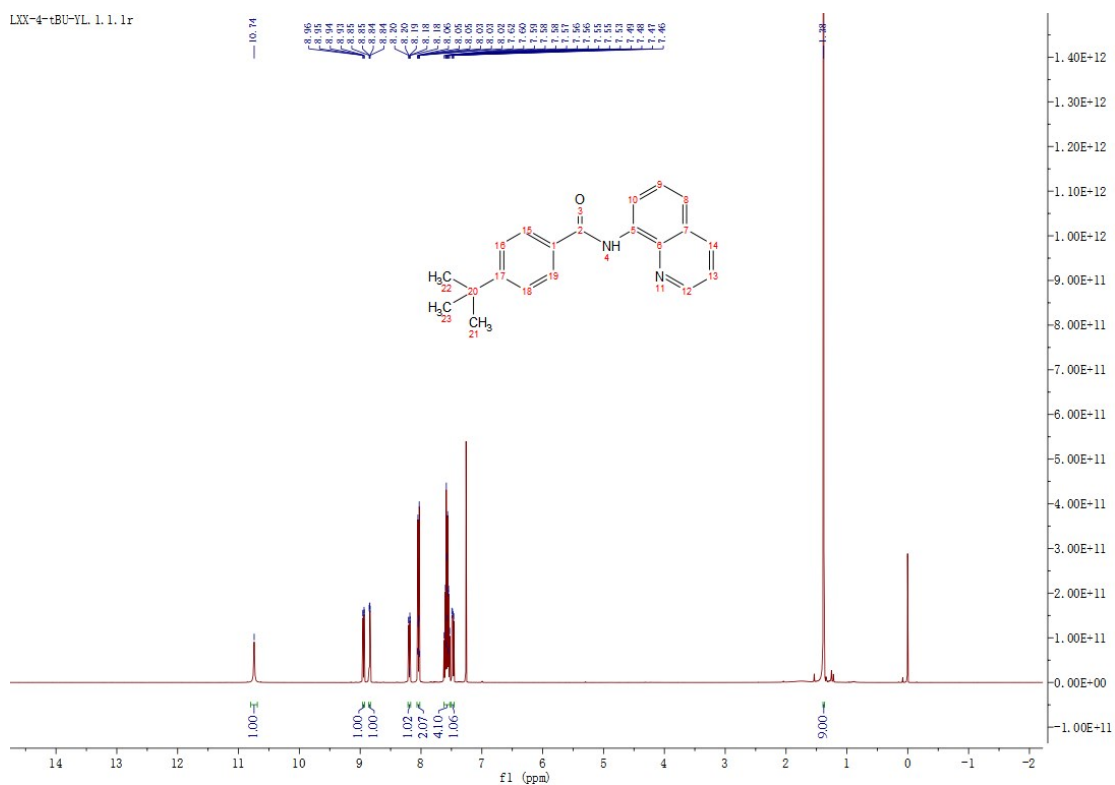
10.1 NMR-Spectra of 1



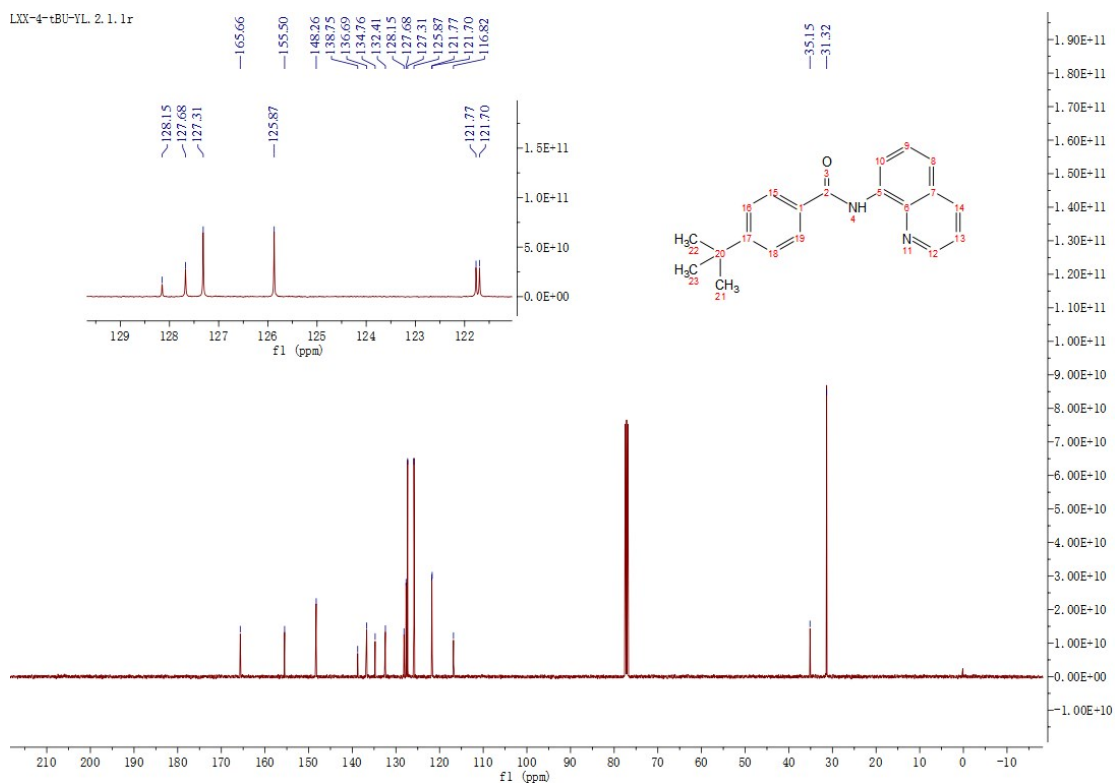


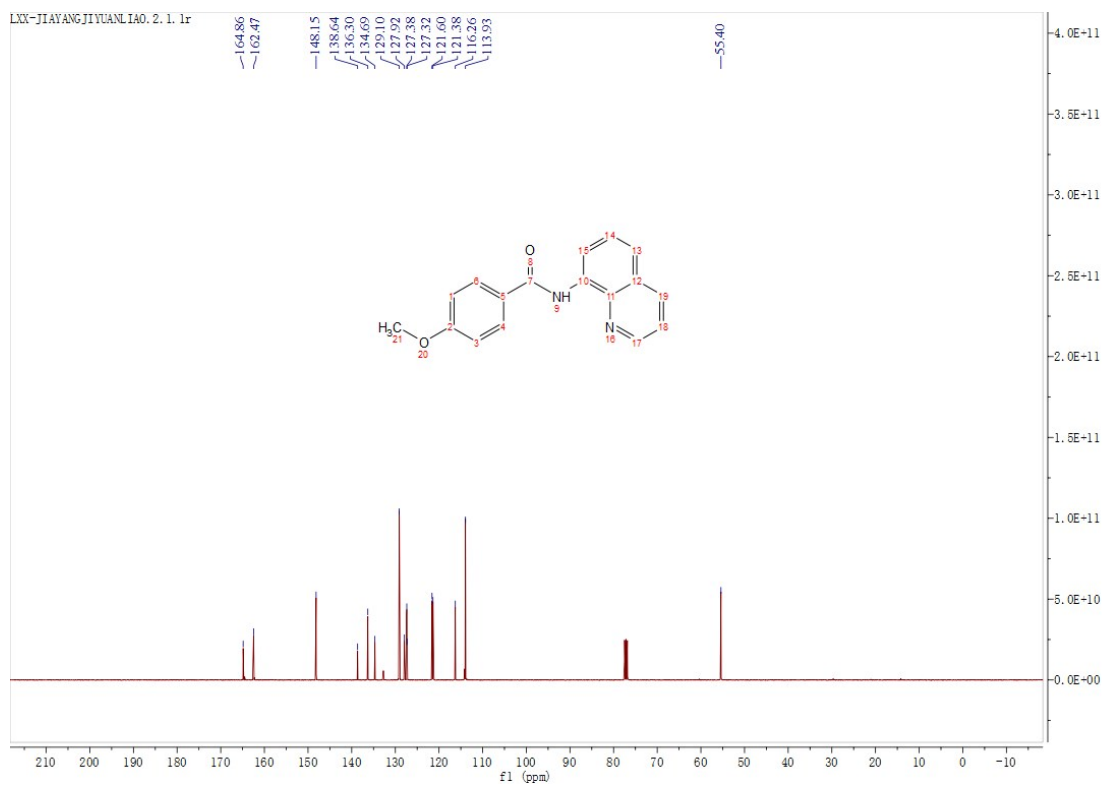
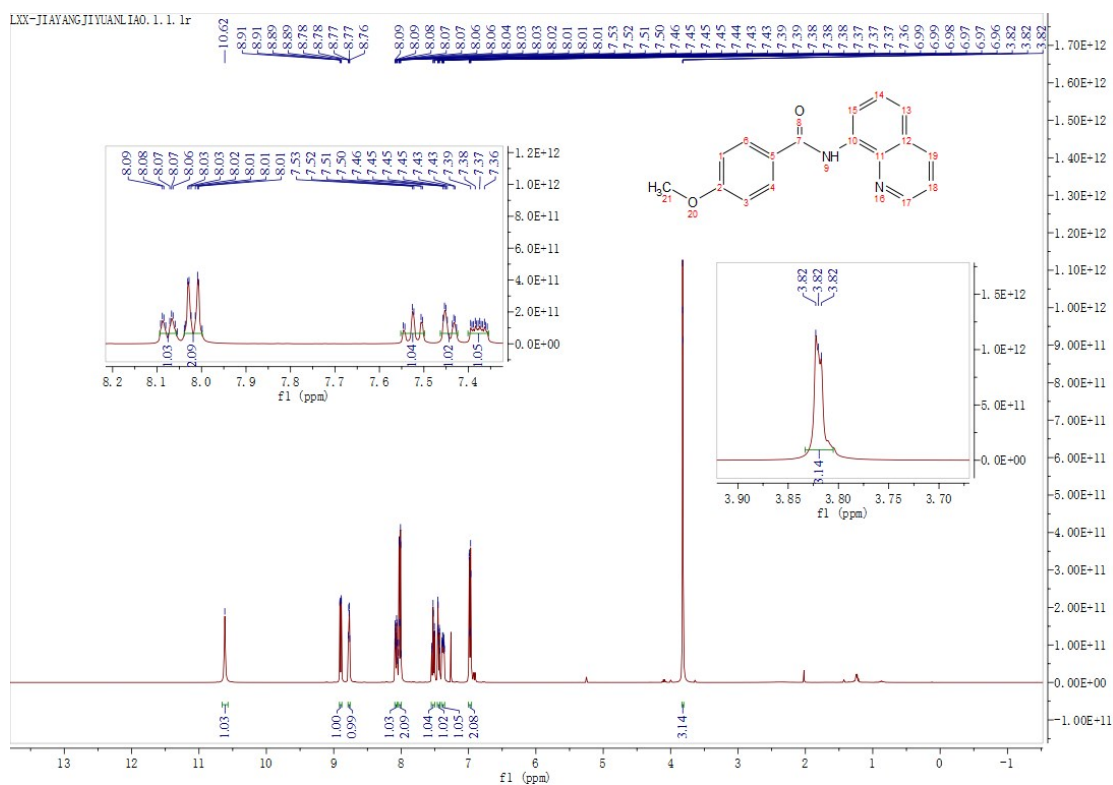


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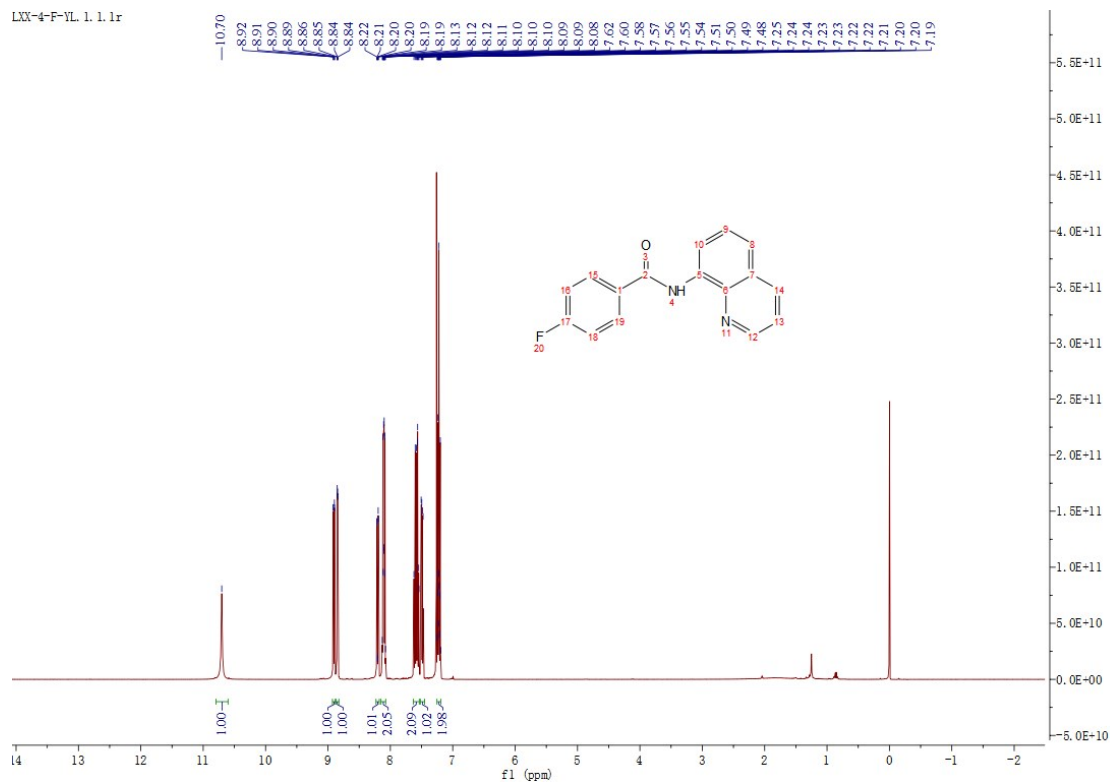


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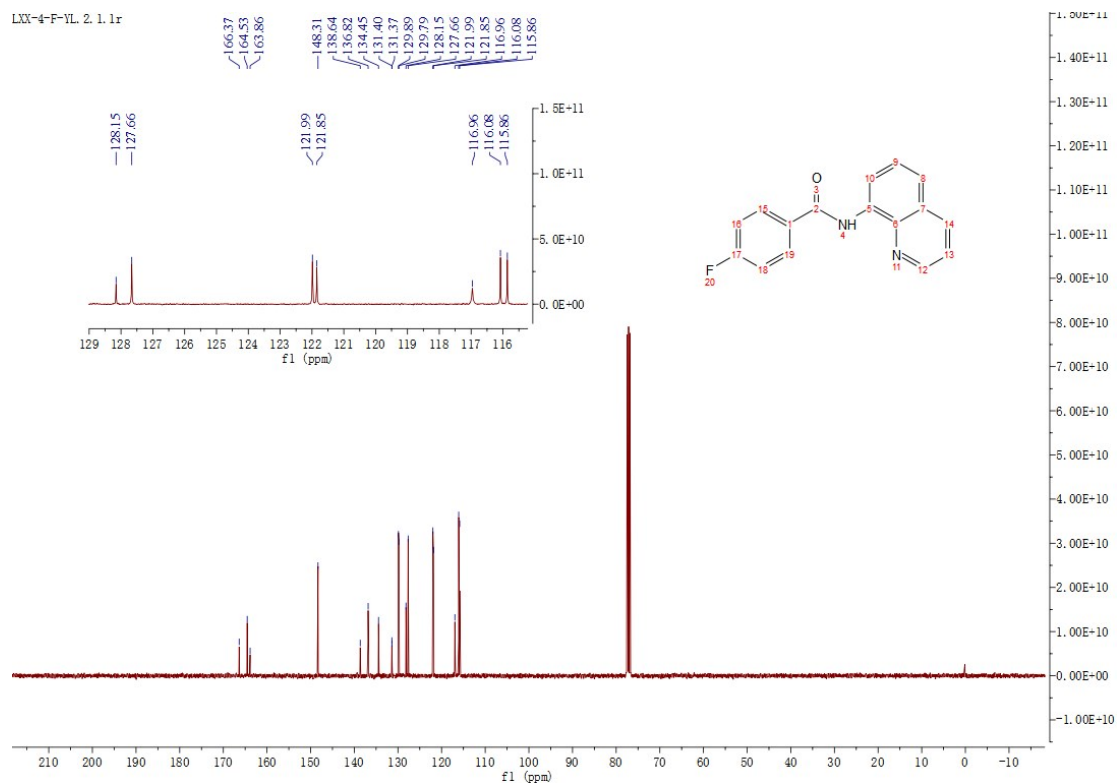


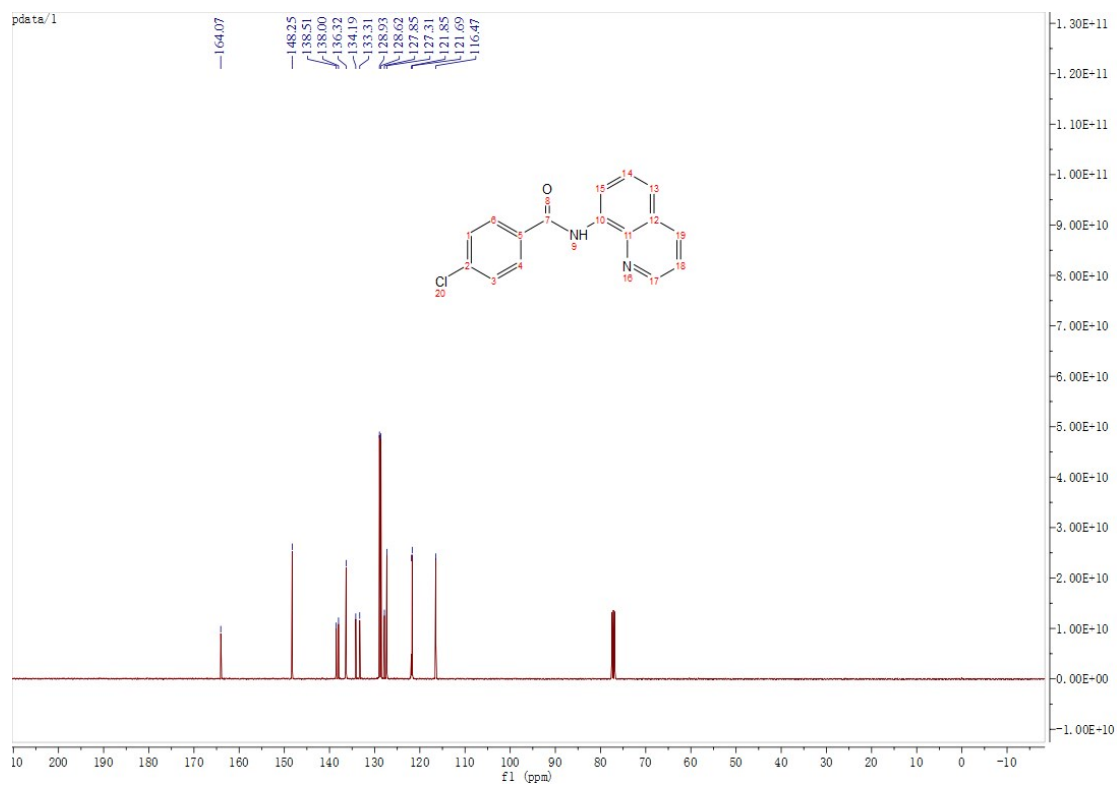
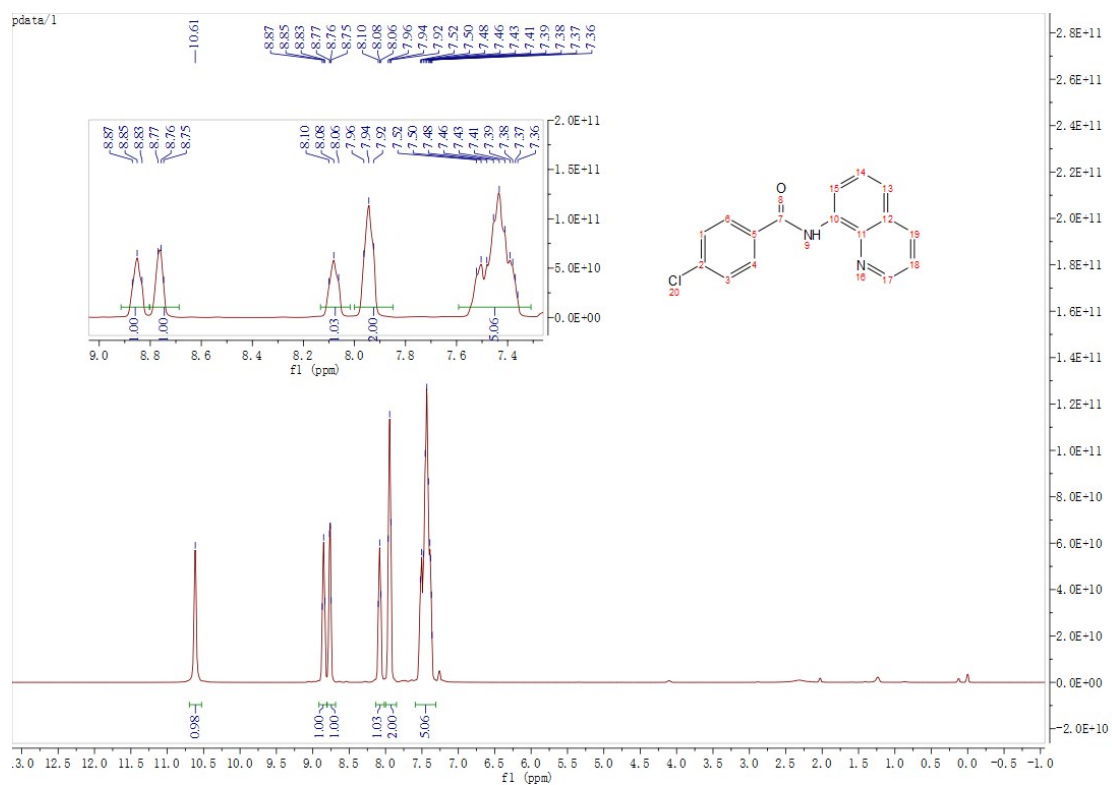


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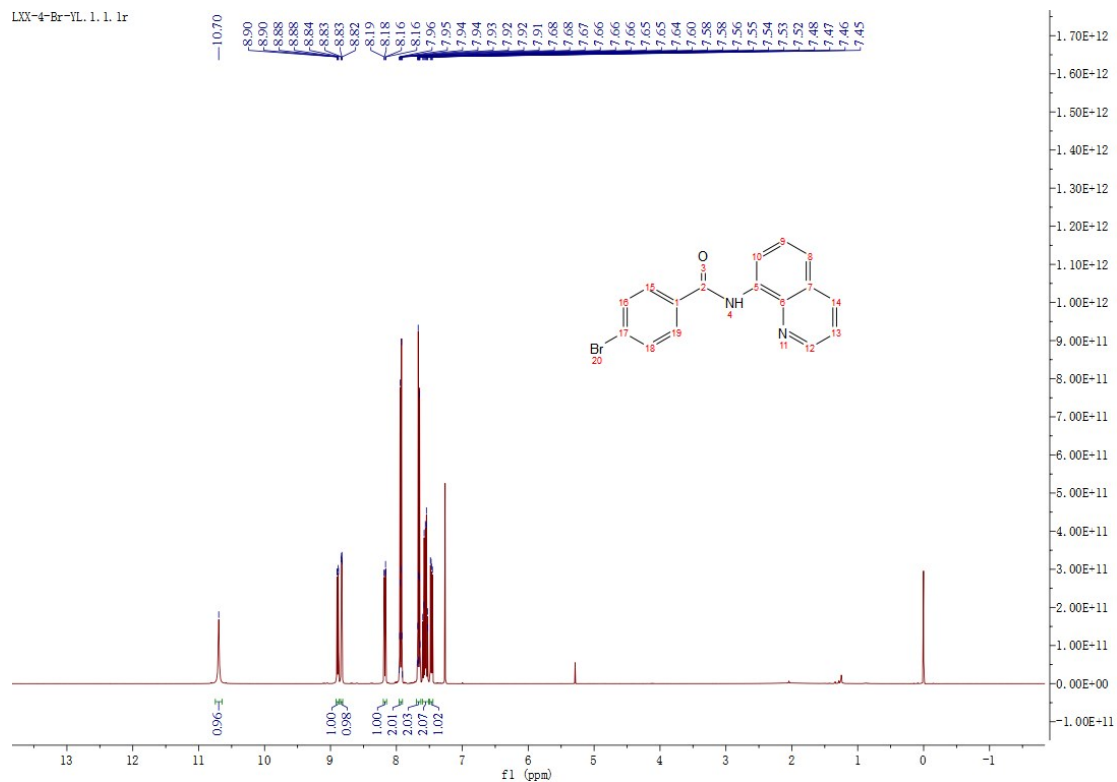


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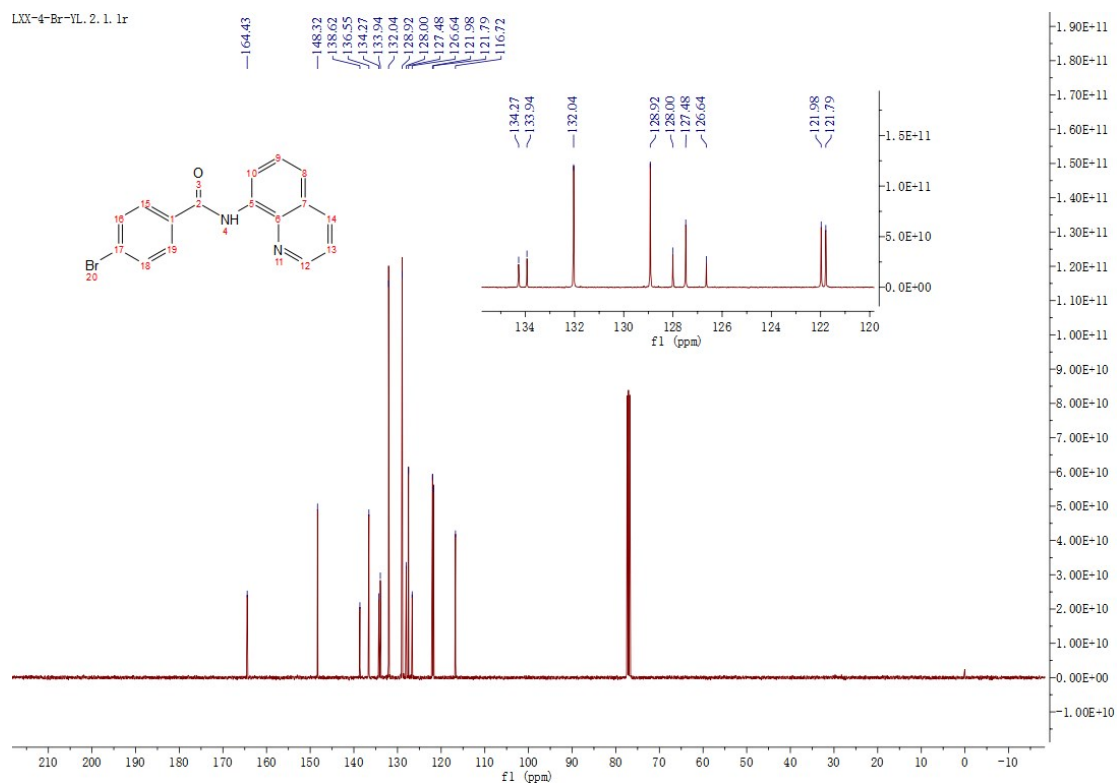


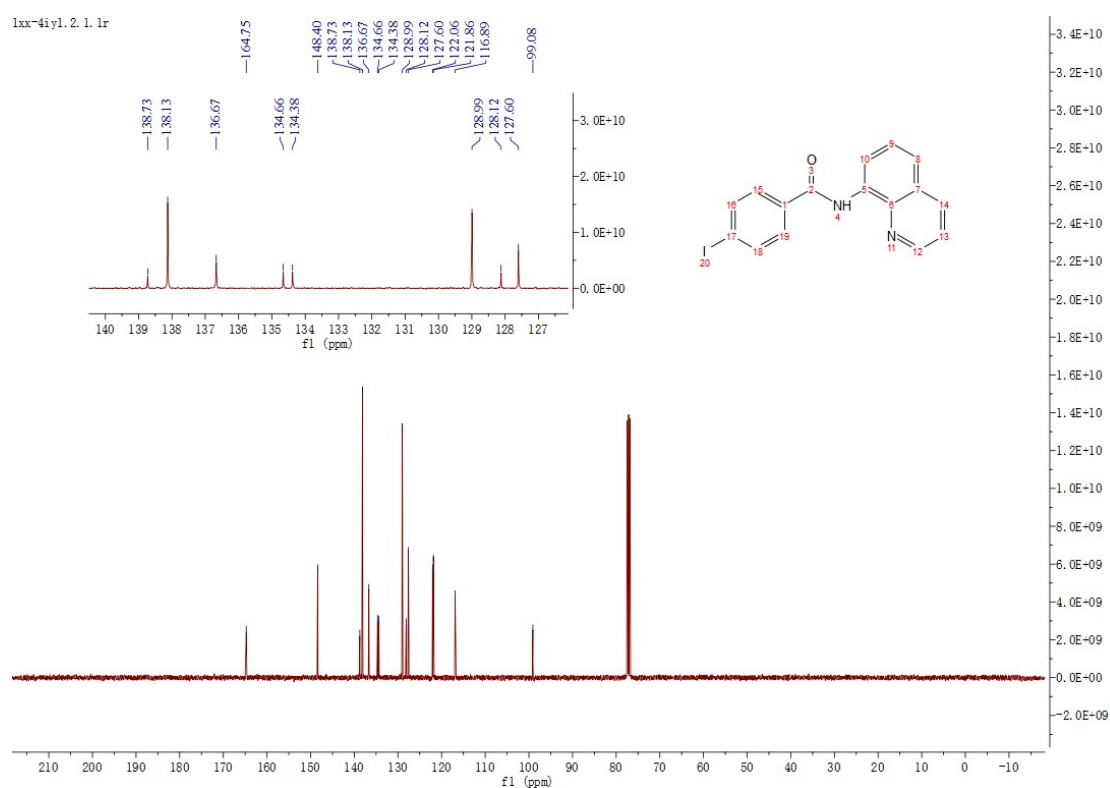
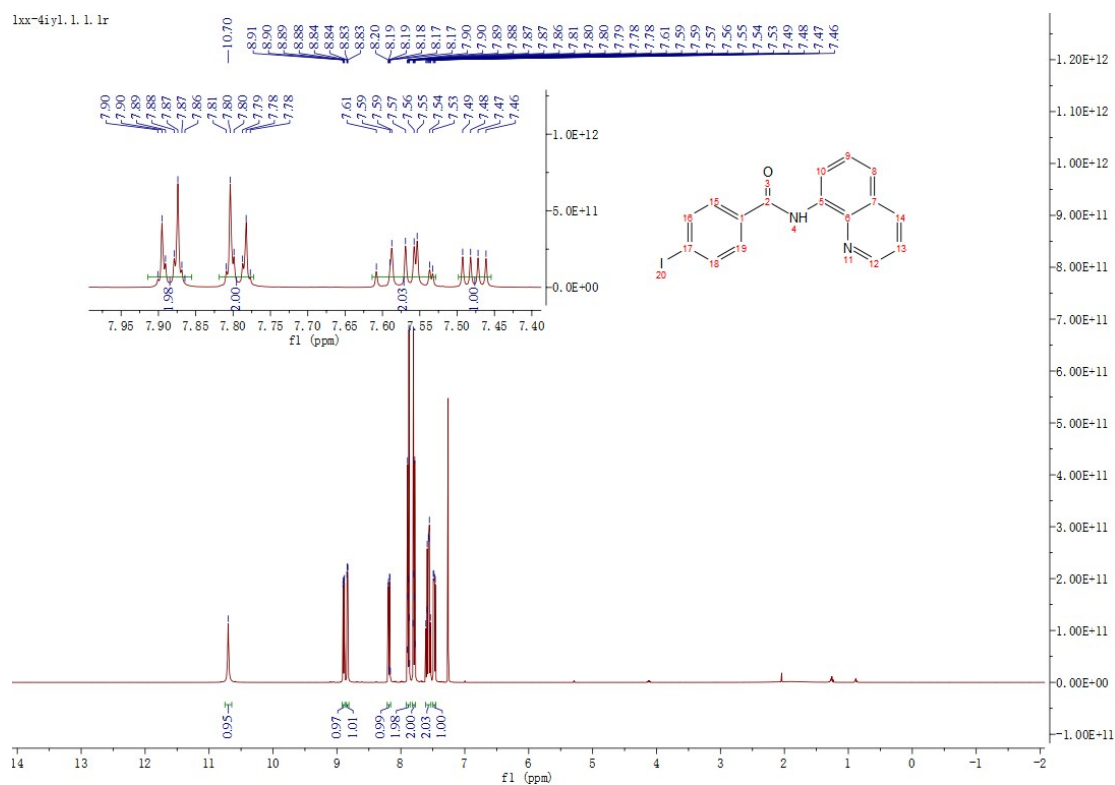


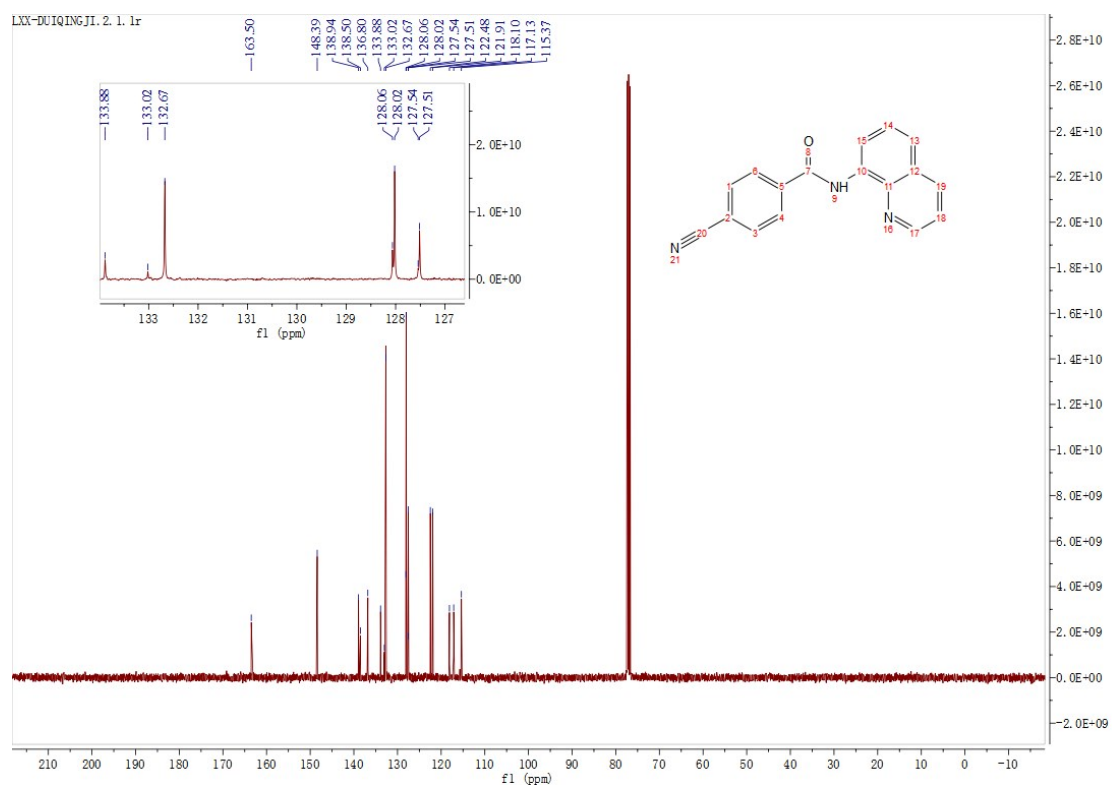
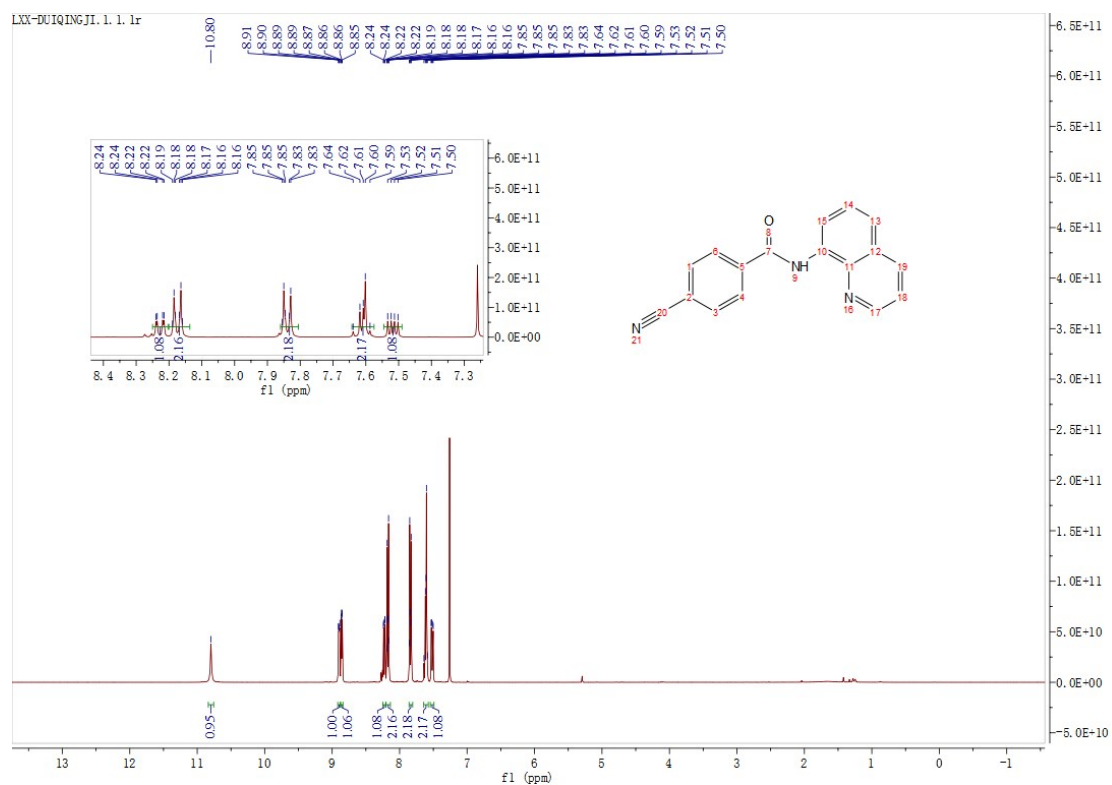
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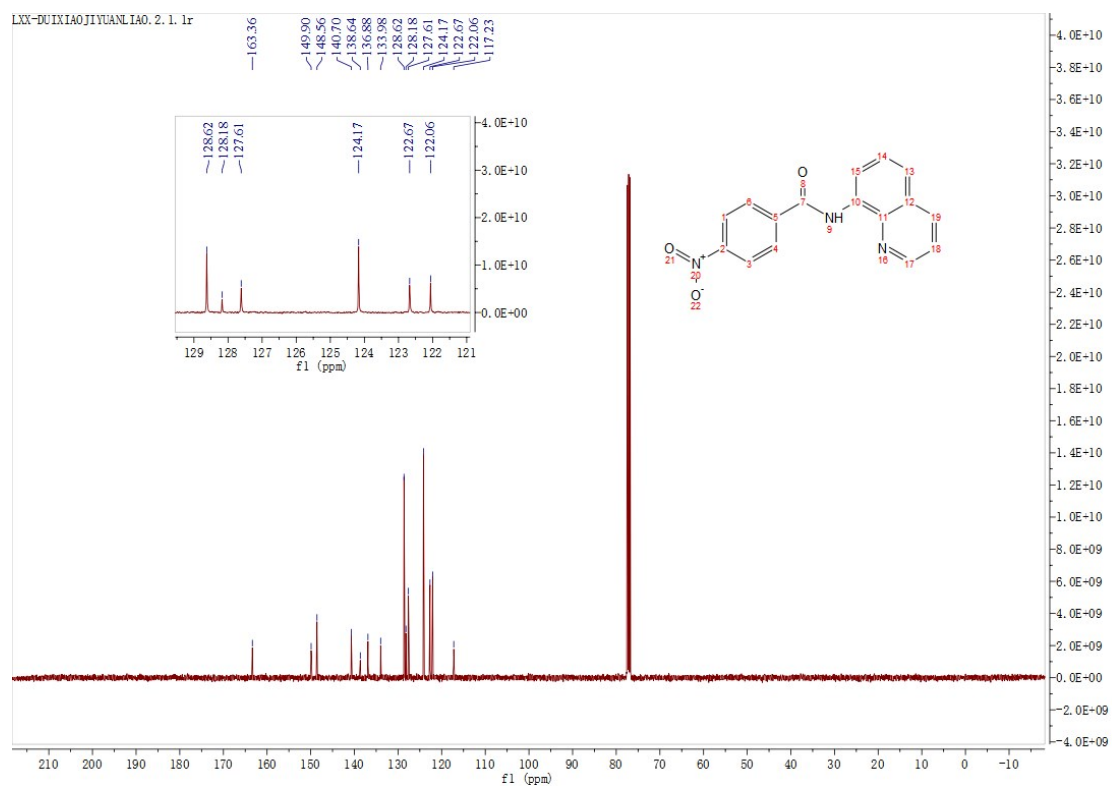
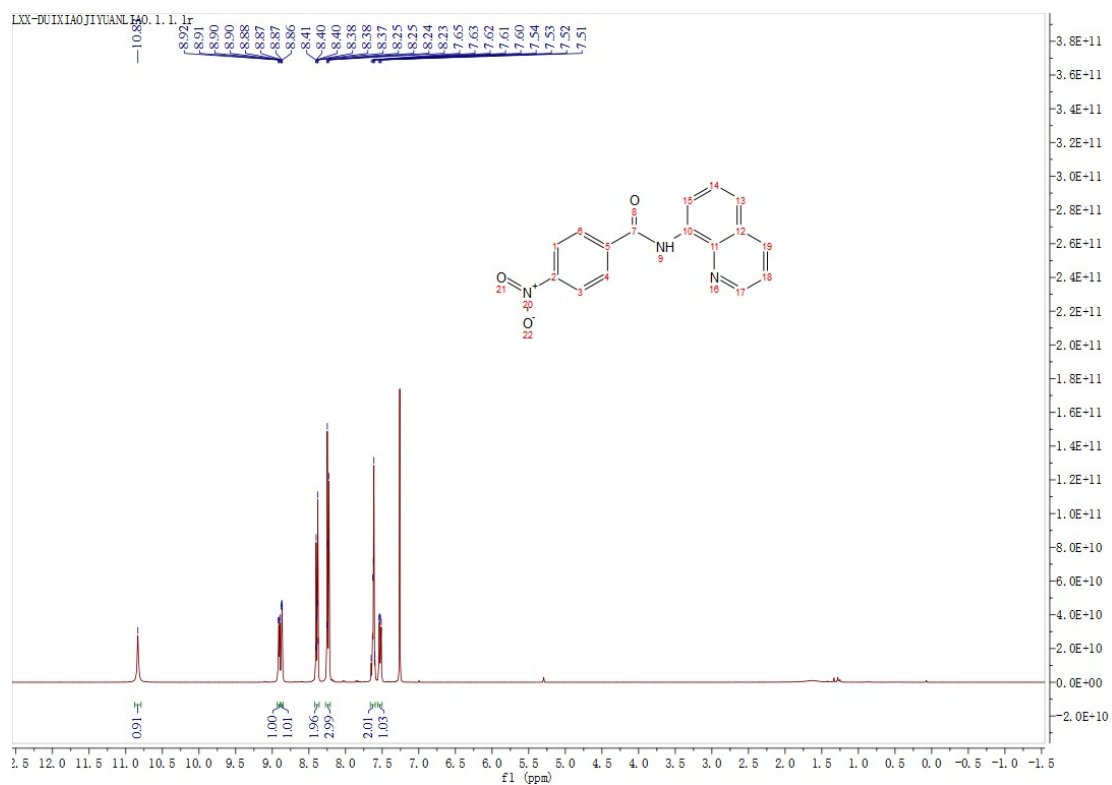


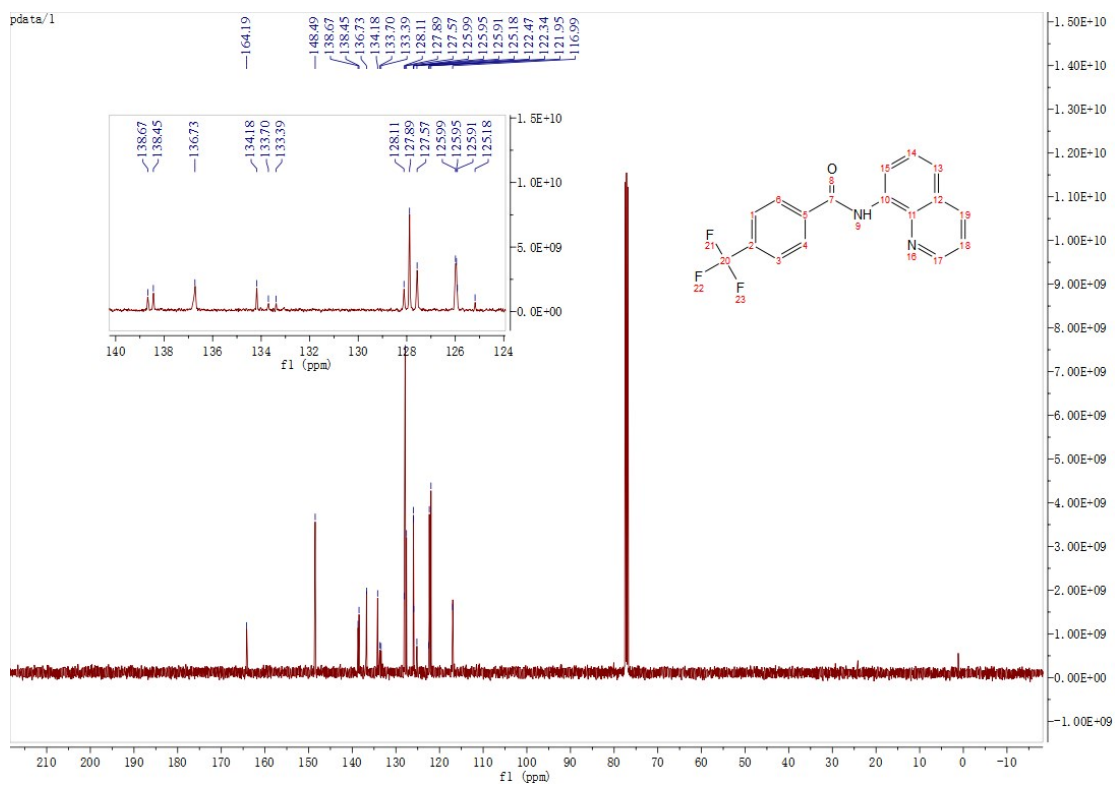
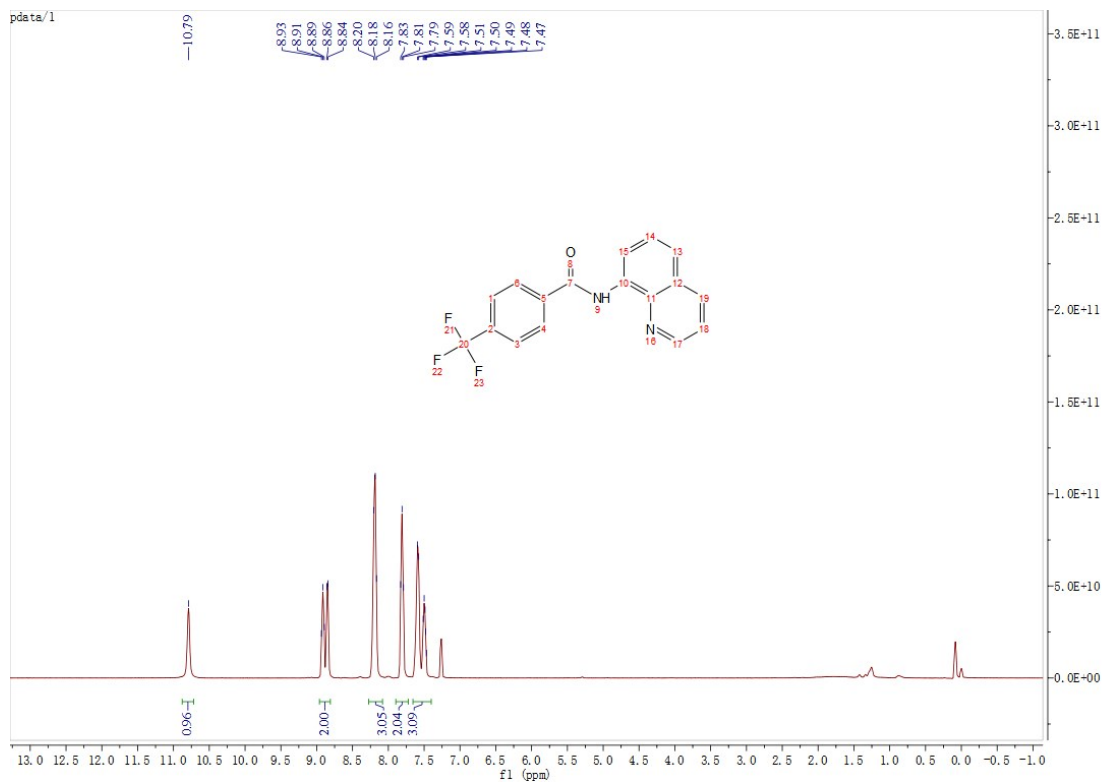
LXX-4-Br-1L, 2. 1. 1r

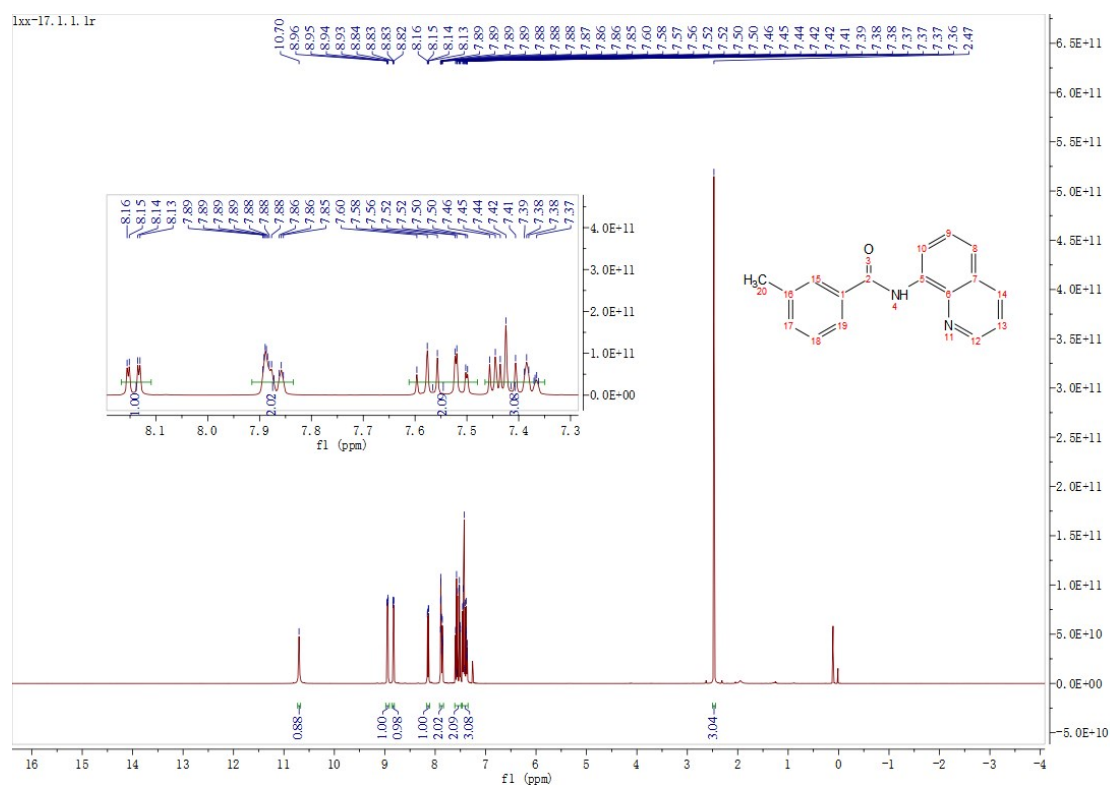


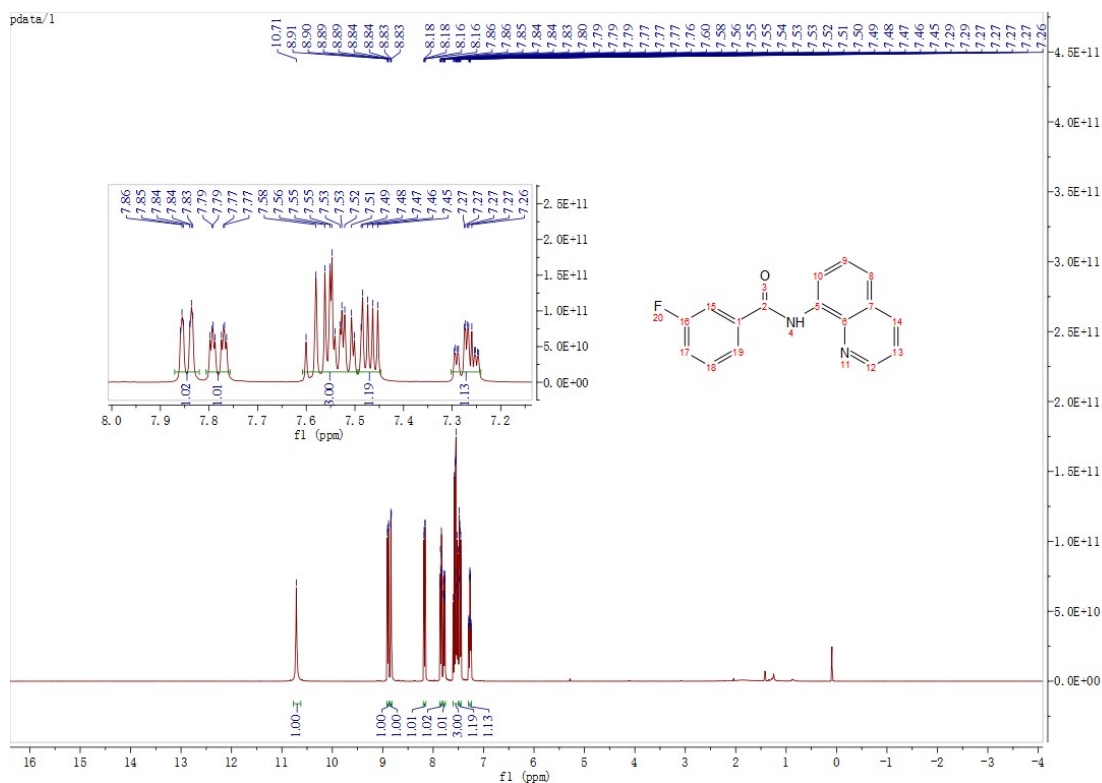
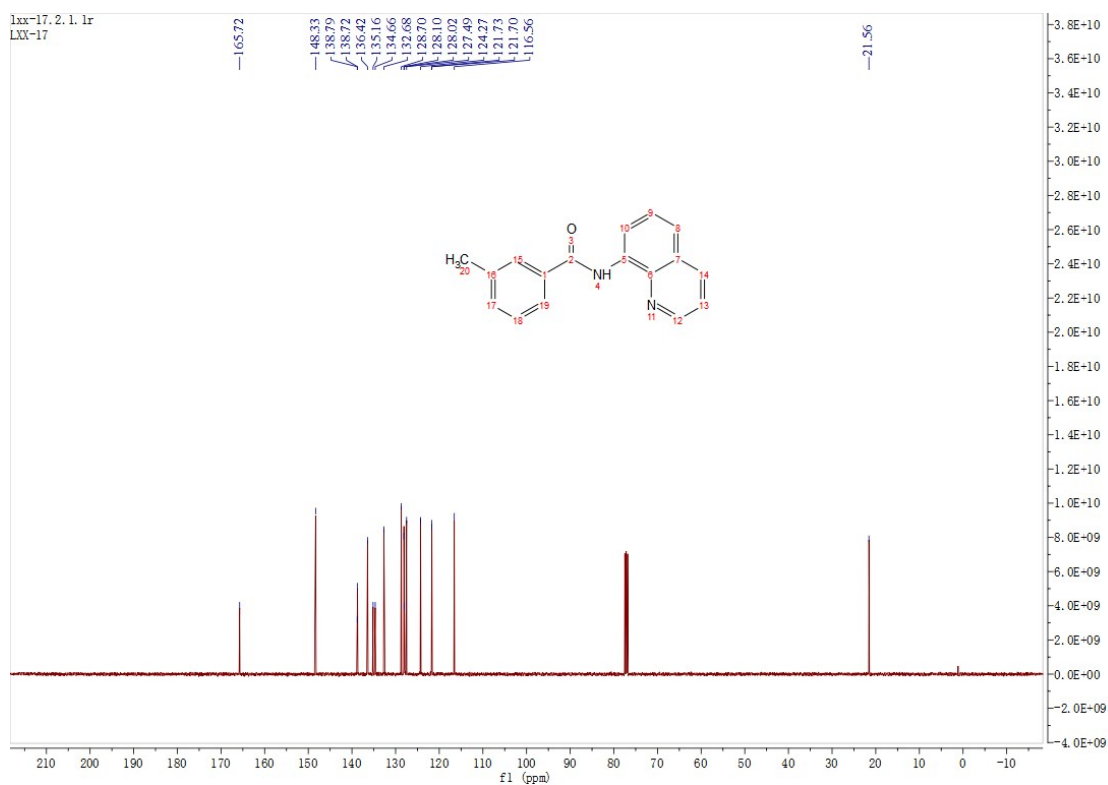


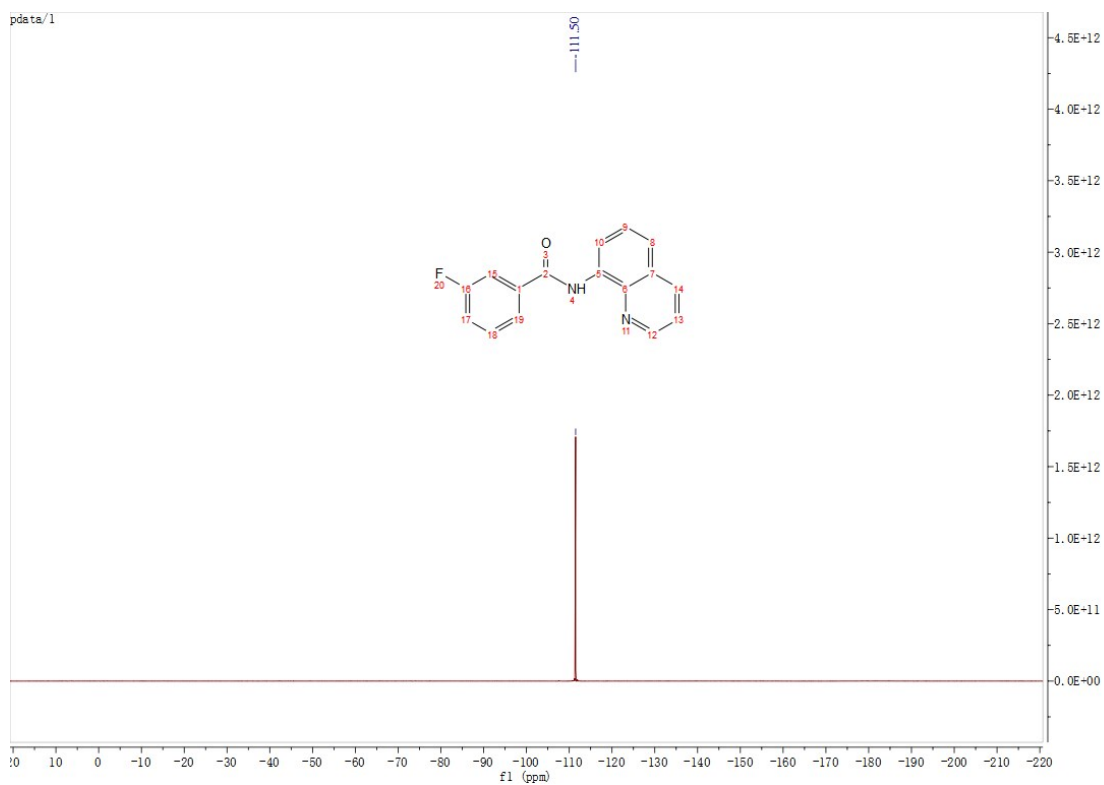
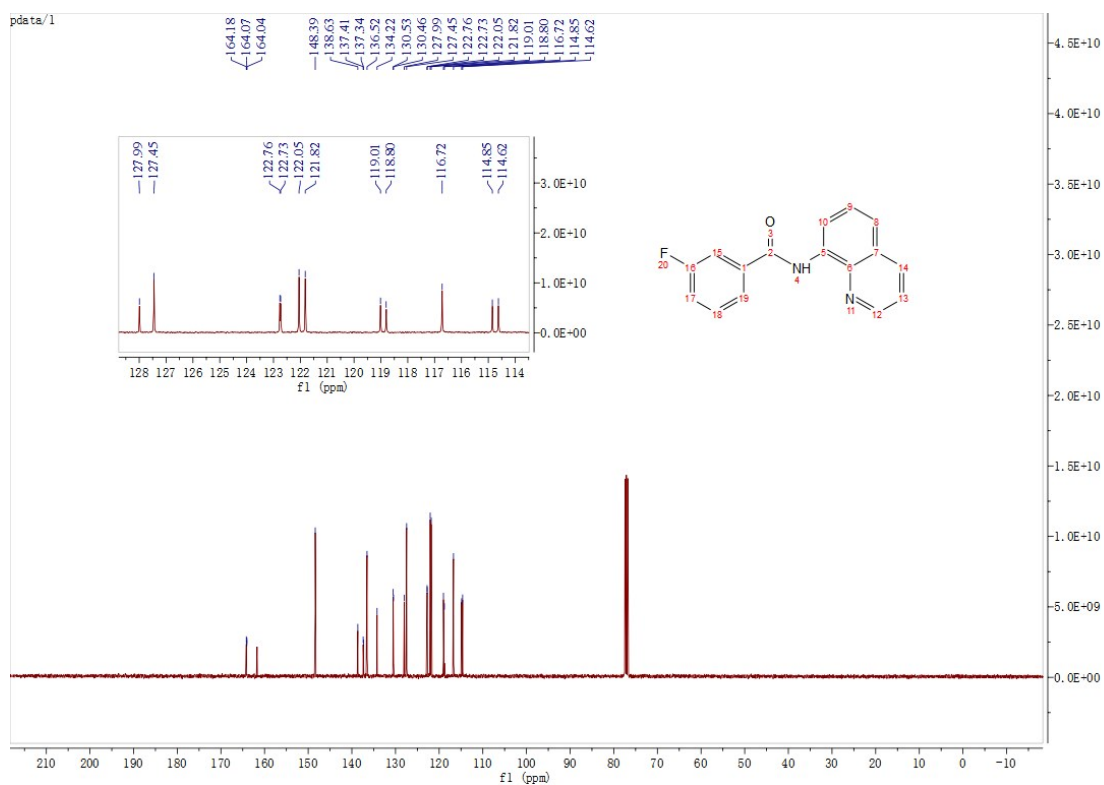


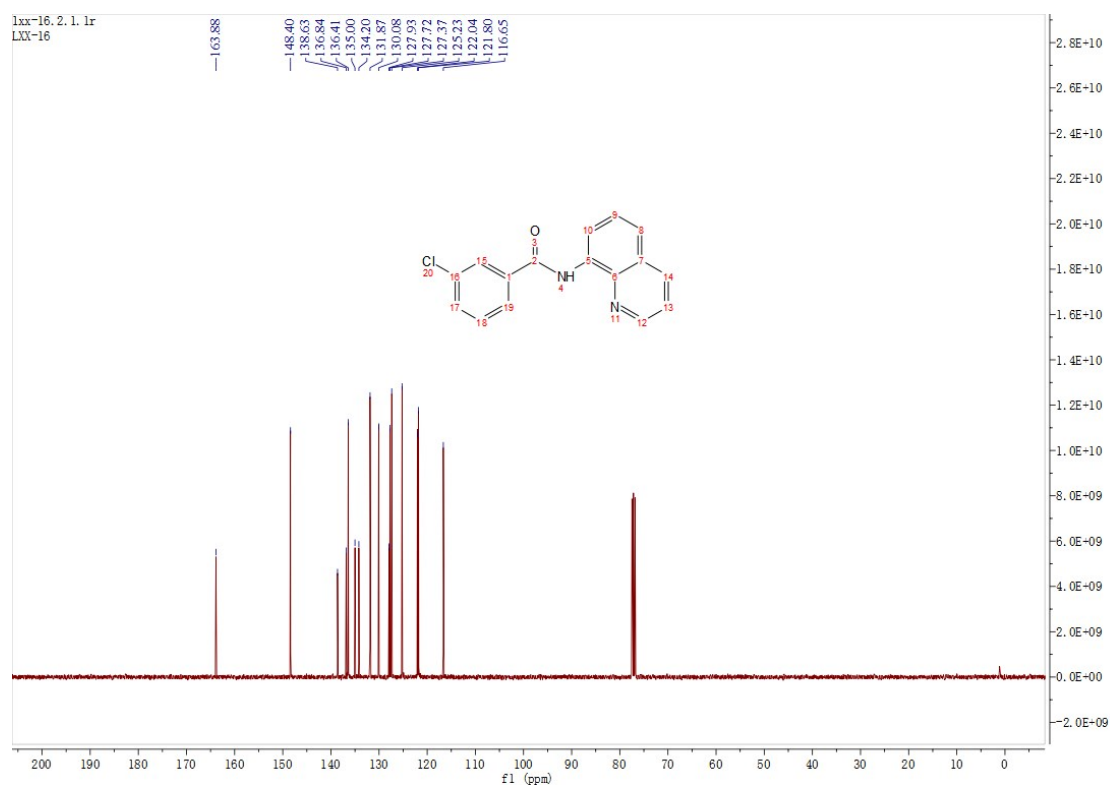
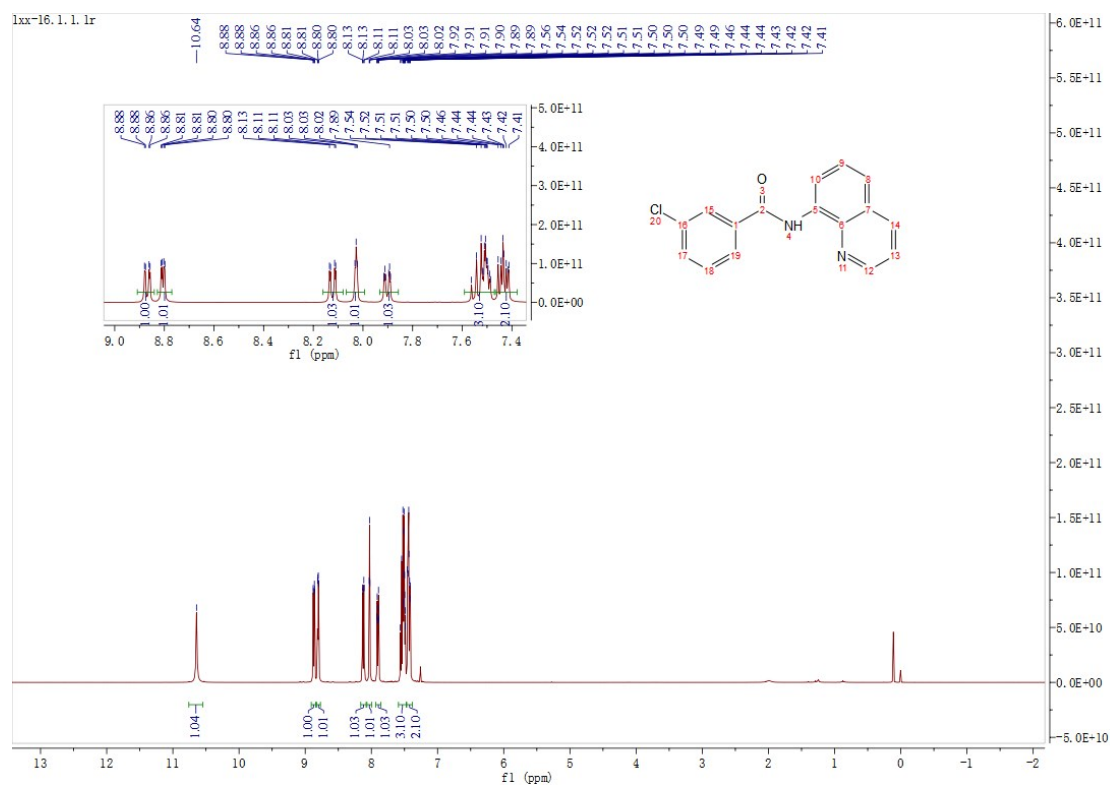


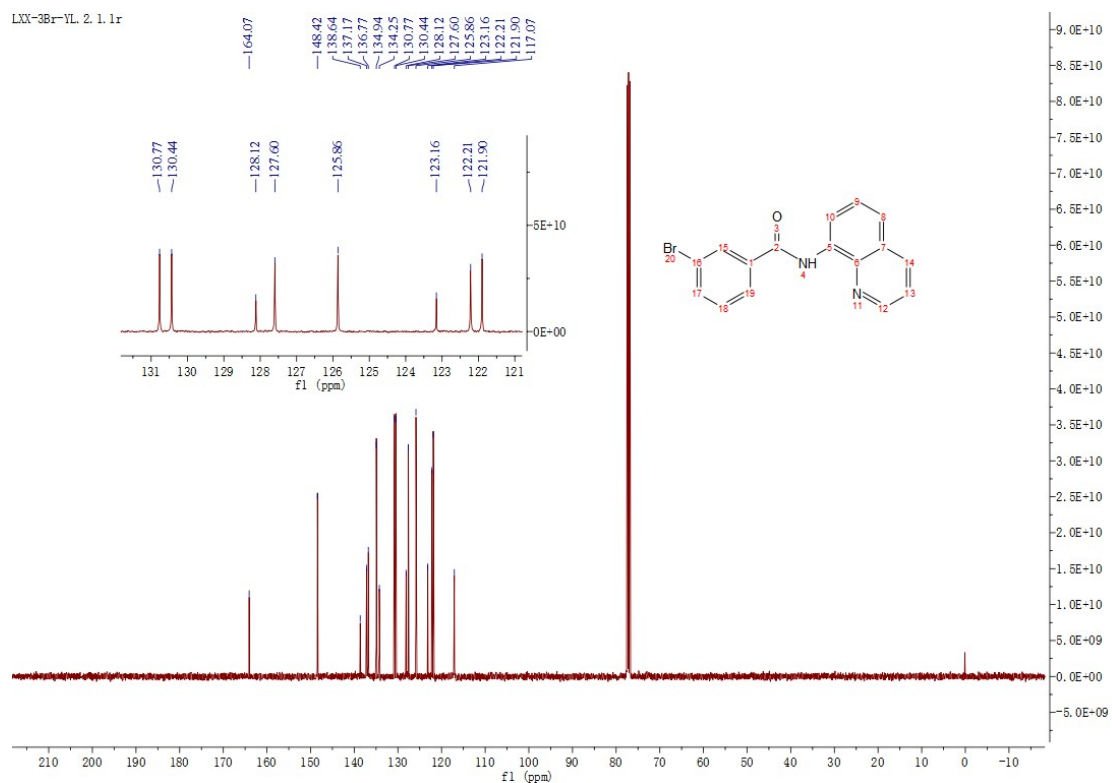
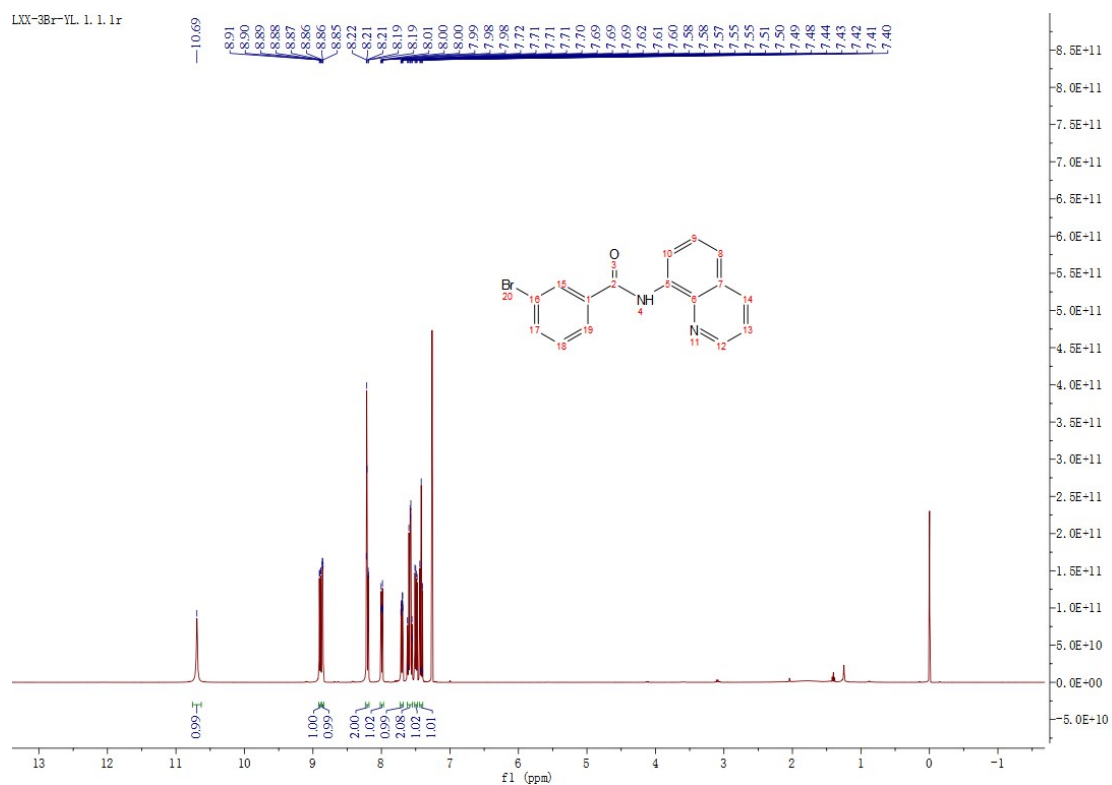


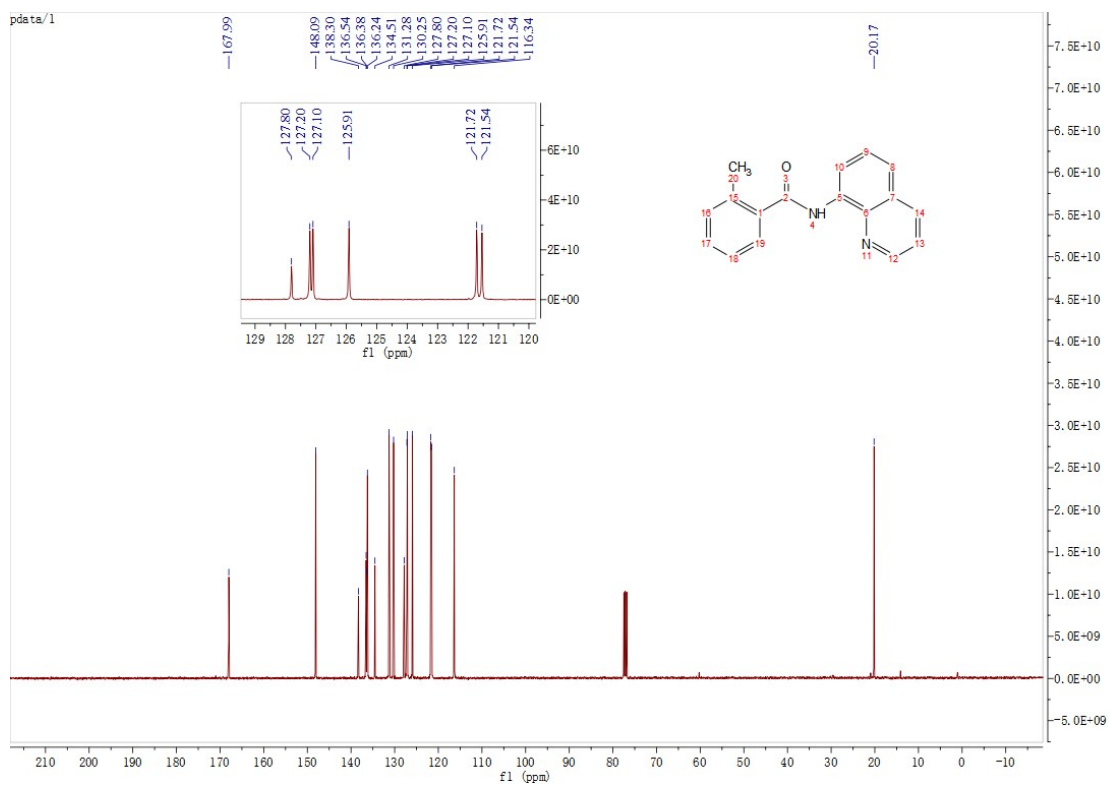
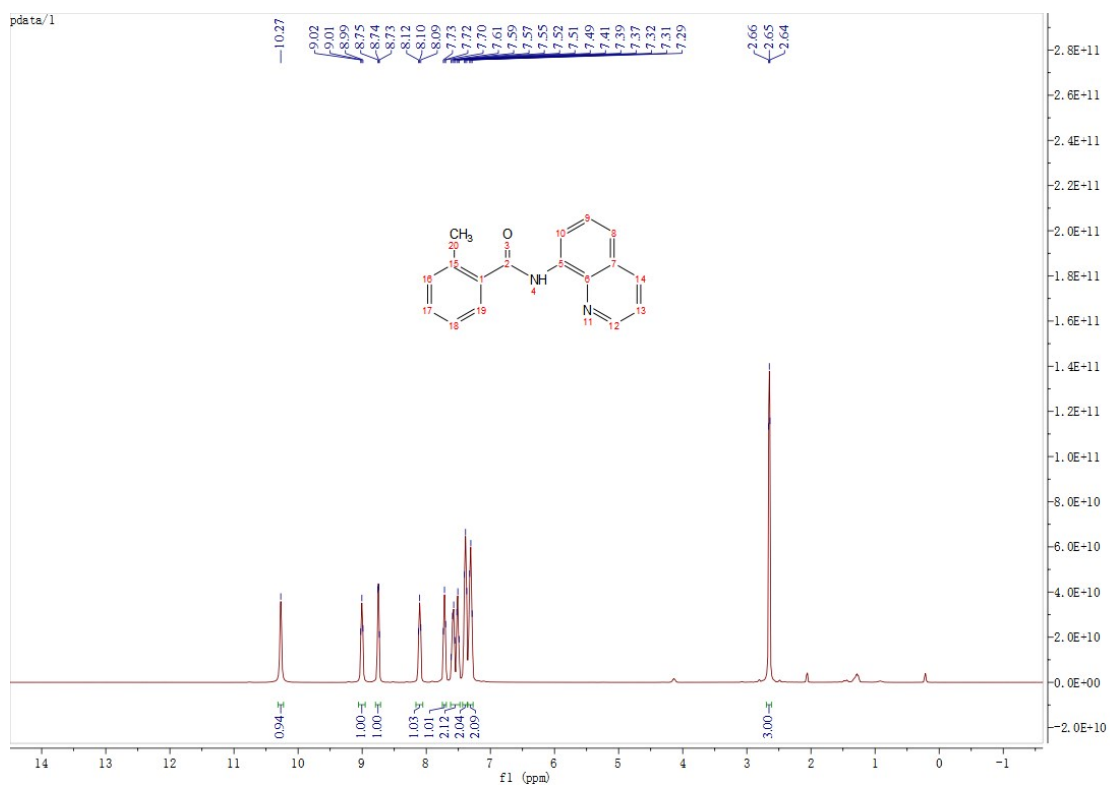


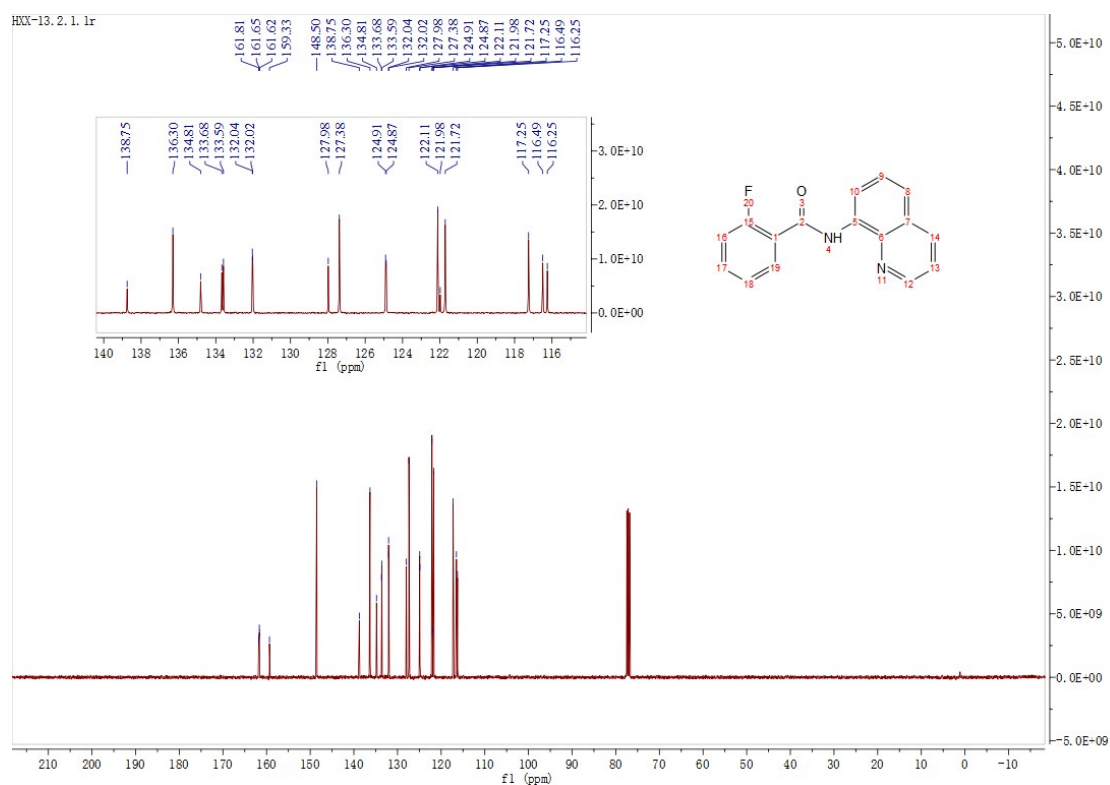
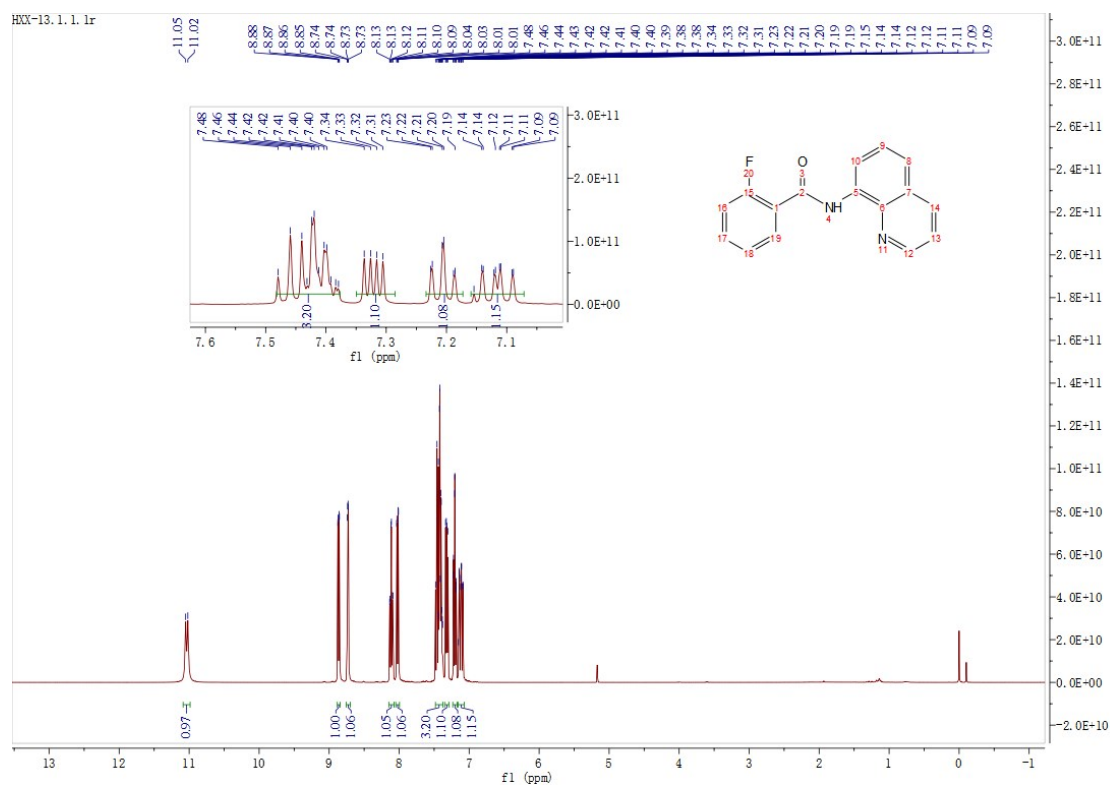












Chemical structure of compound 1r is shown, which is 2-chloro-N-(1,2,3,4,5,6-hexafluorophenyl)benzamide. The structure is labeled with numbers 1-20 for atom assignment.

The ^1H NMR spectrum (CDCl₃) shows peaks in the aromatic region (7.3-7.7 ppm). The inset provides a detailed view of this region with peak labels and integrations.

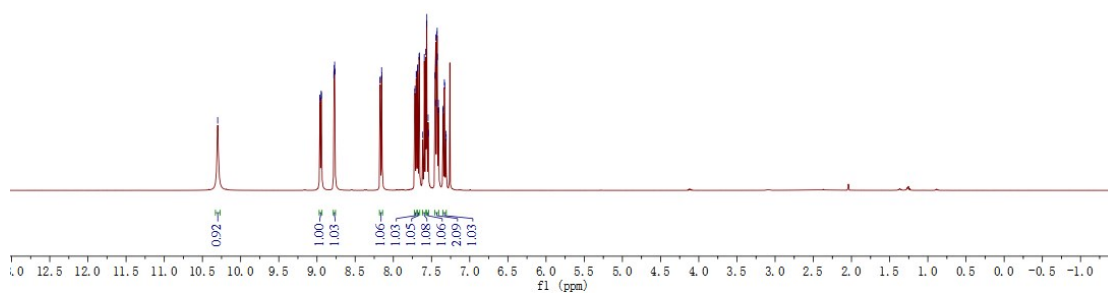
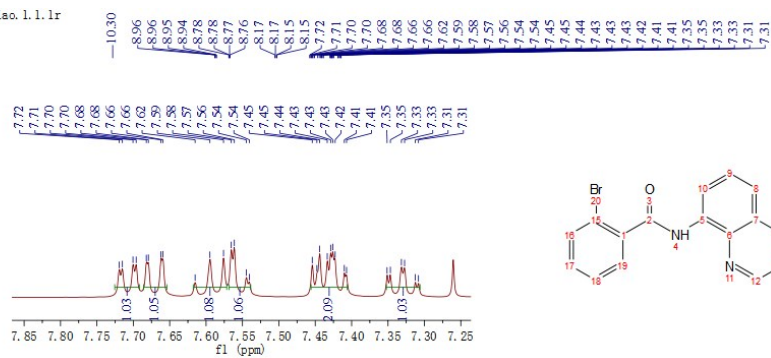
Peak labels (ppm): 7.62, 7.61, 7.60, 7.58, 7.57, 7.55, 7.51, 7.50, 7.49, 7.48, 7.47, 7.46, 7.45, 7.44, 7.43, 7.42, 7.41, 7.40, 7.38.

Integrations: 1.06, 1.02, 3.04.

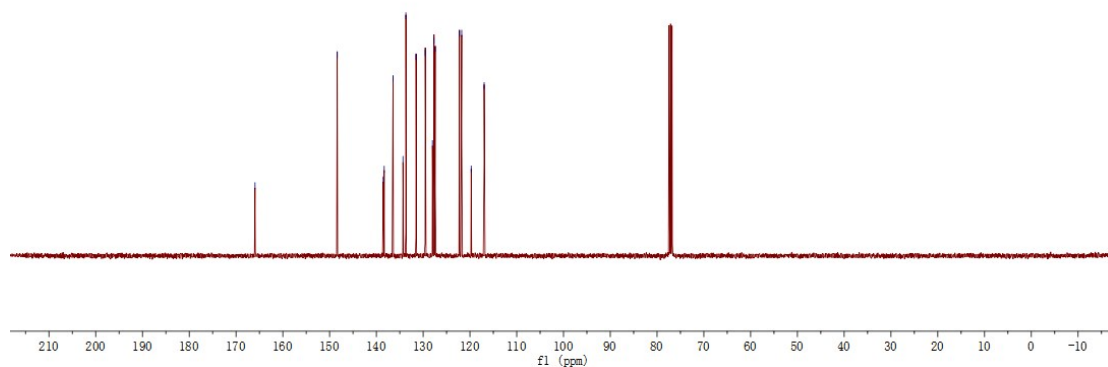
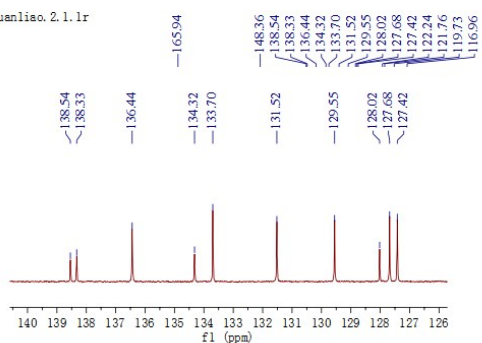
Chemical structure labels: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20.

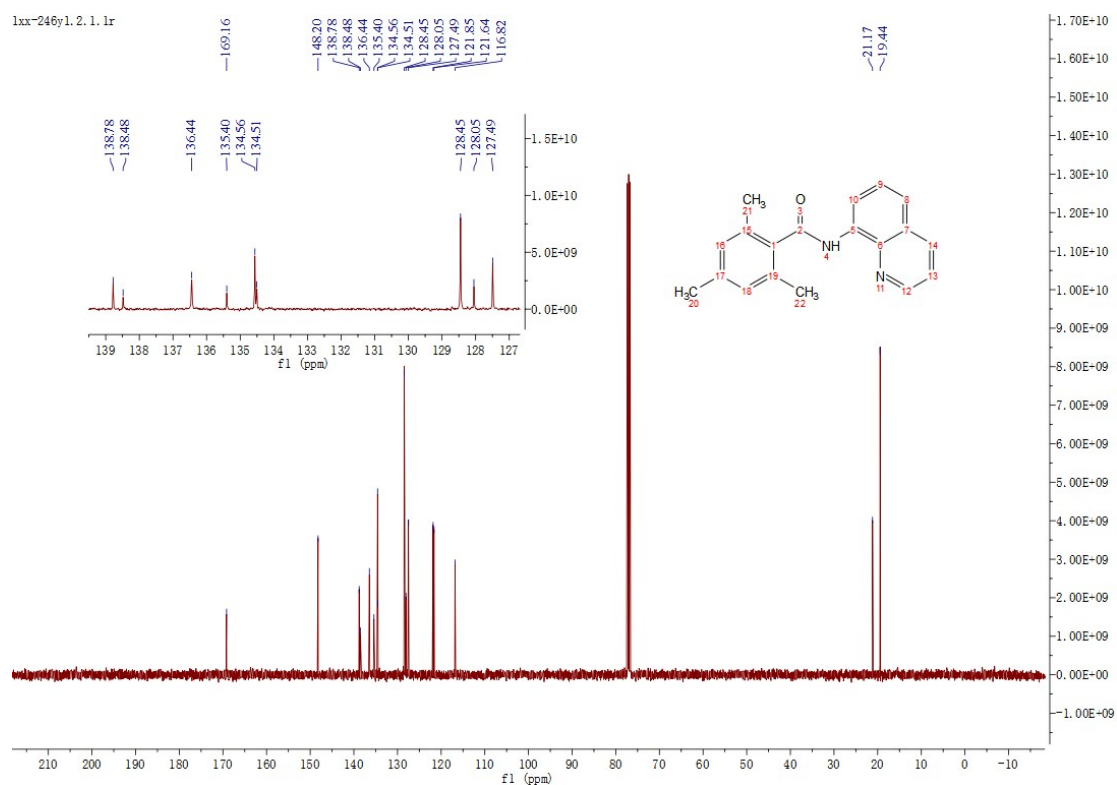
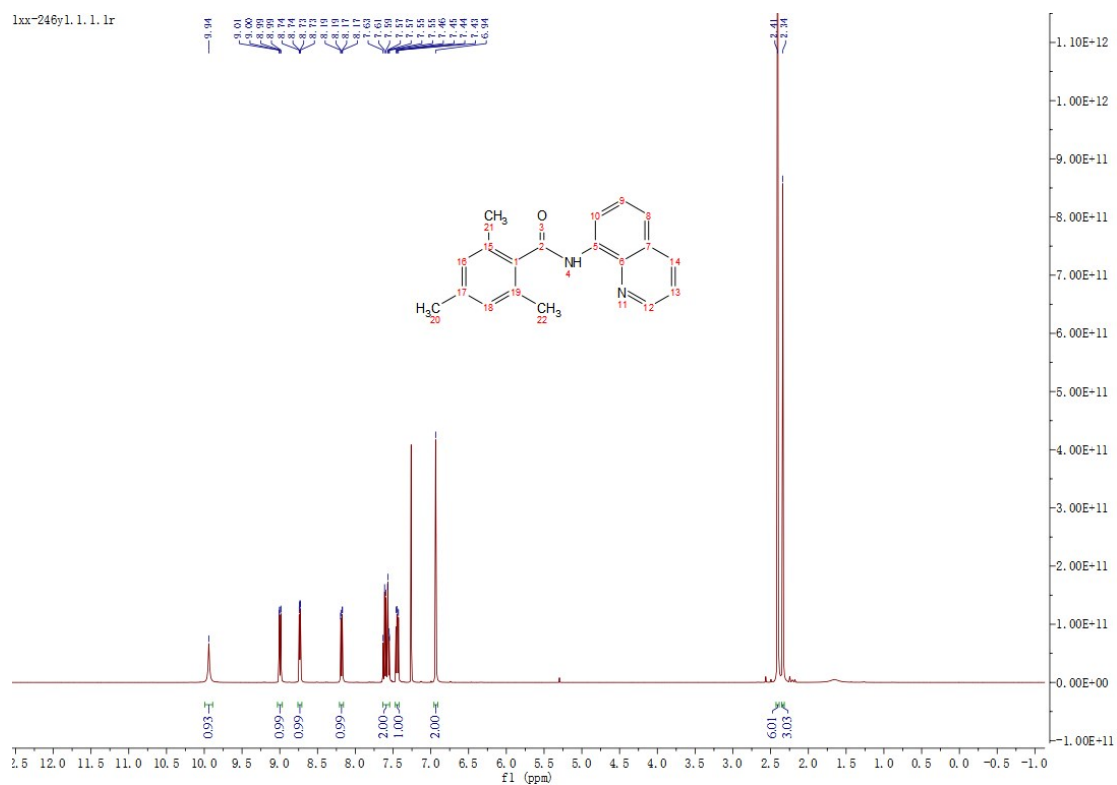
Chemical structure of compound 1r is shown, which is 2-chloro-N-(1,2,3,4,5,6-hexafluorophenyl)benzamide. The structure is labeled with numbers 1-20 for atom assignment.

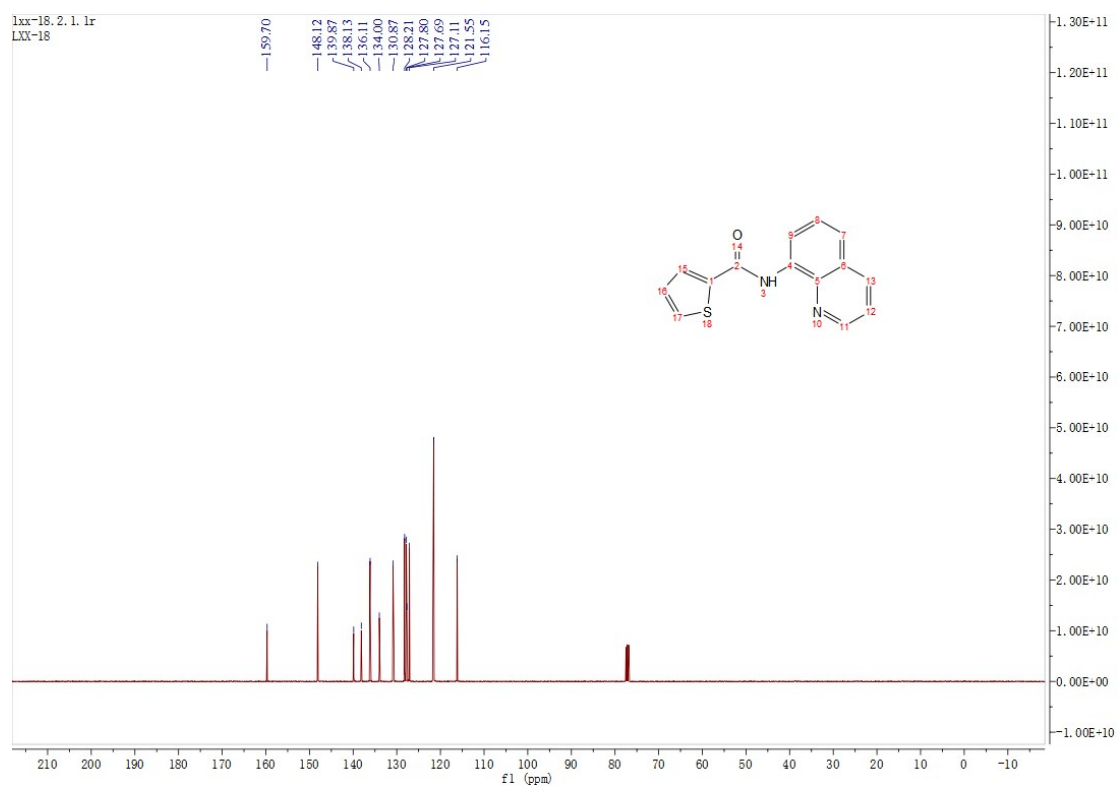
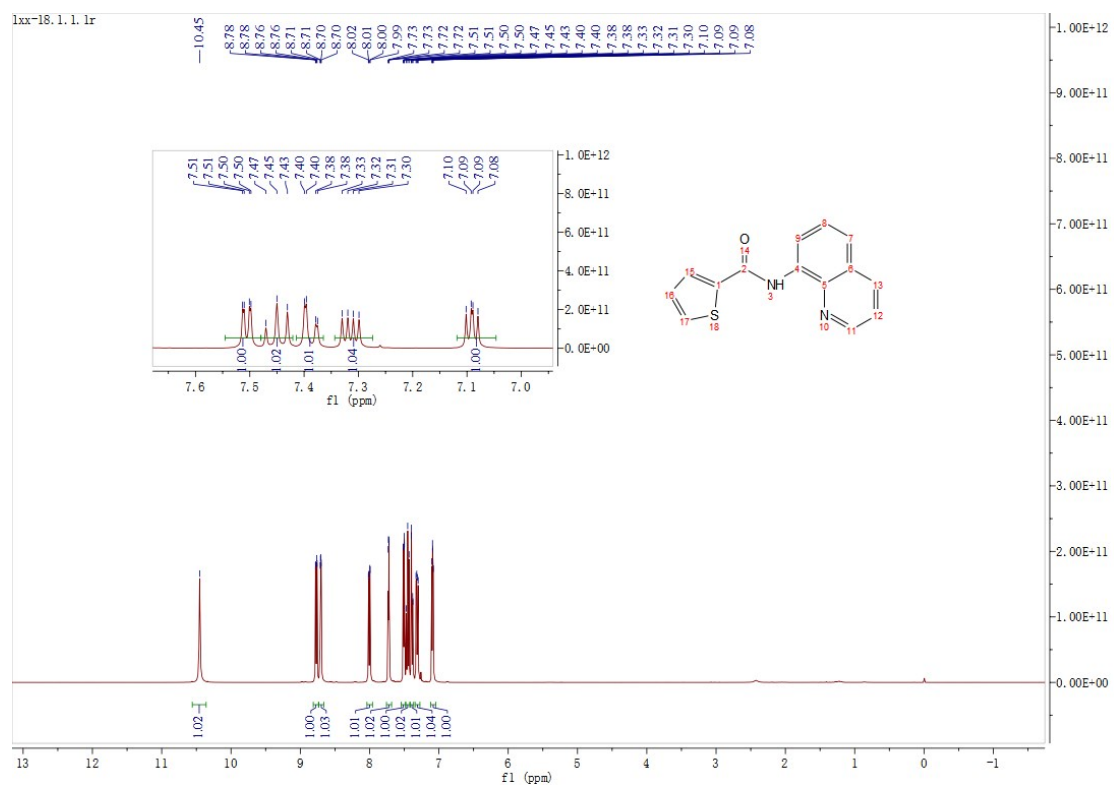
lxx-linbryuanliao. 1.1.1r

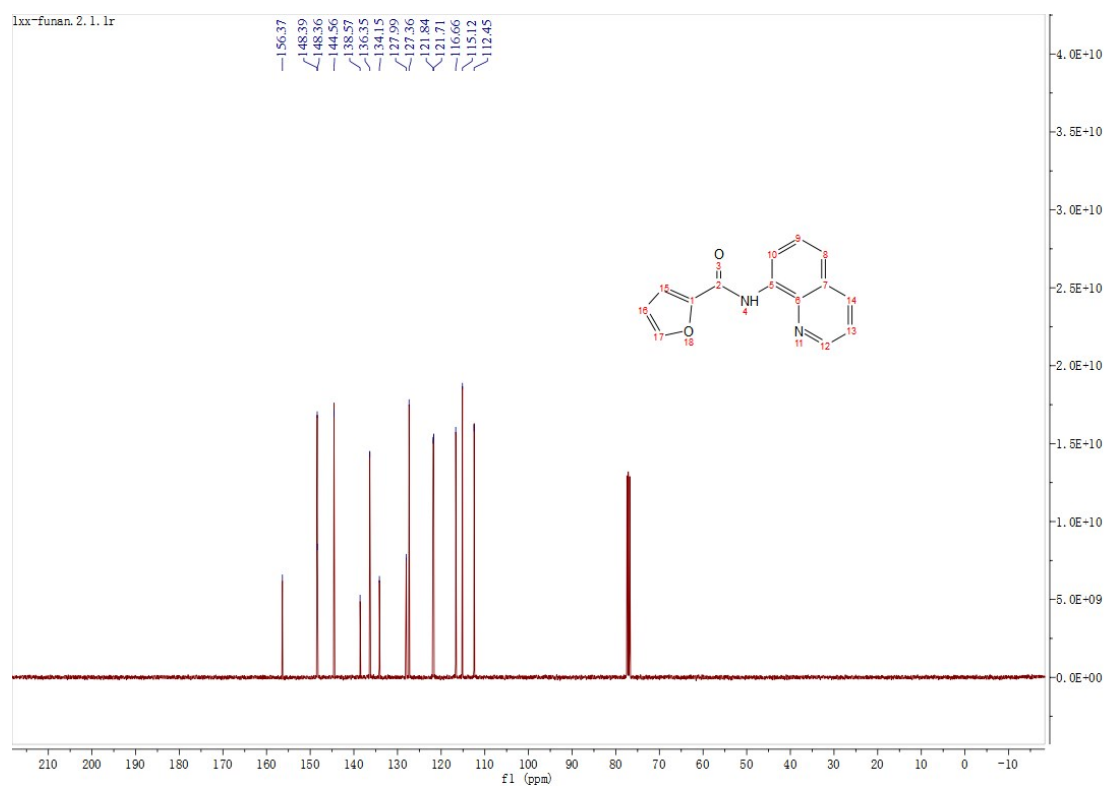
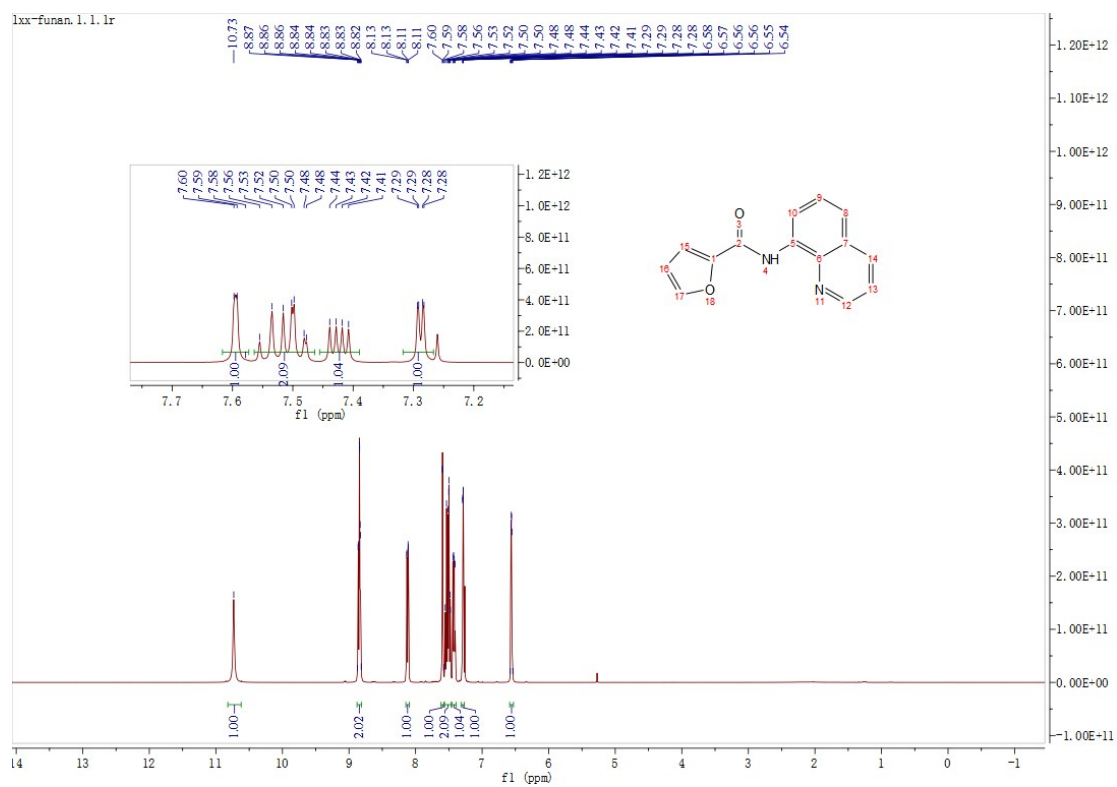


lxx-linbryuanliao. 2.1.1r

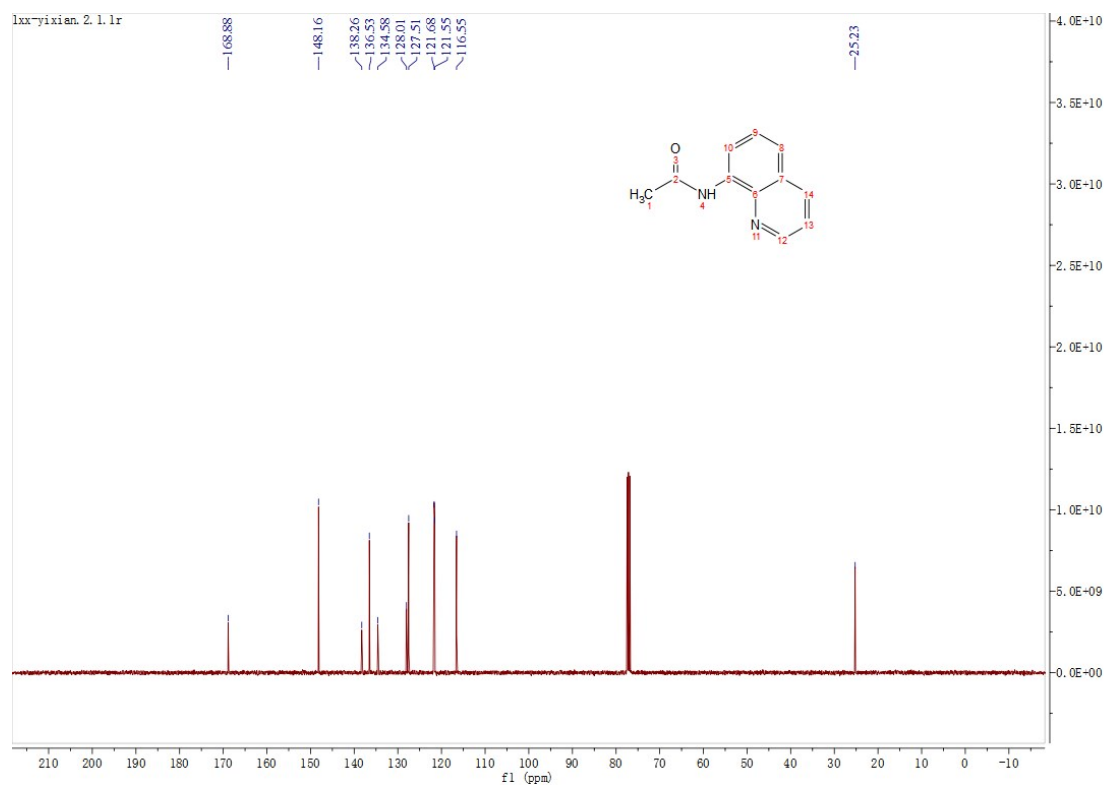
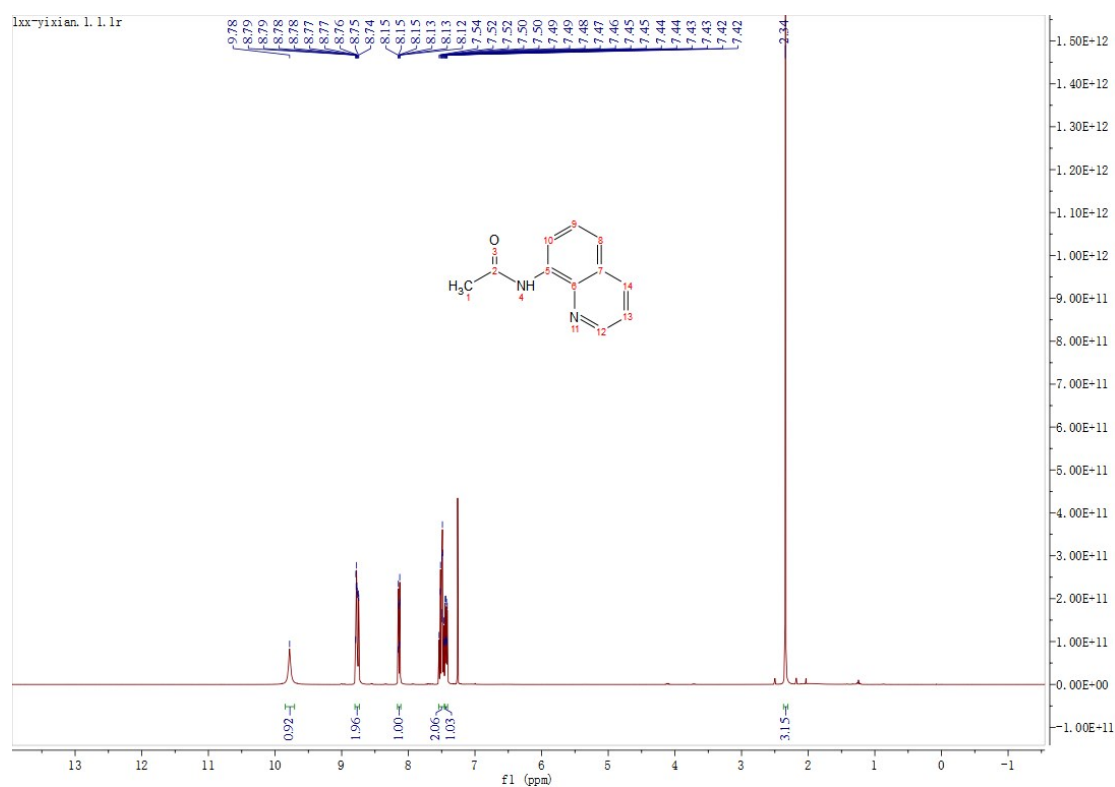


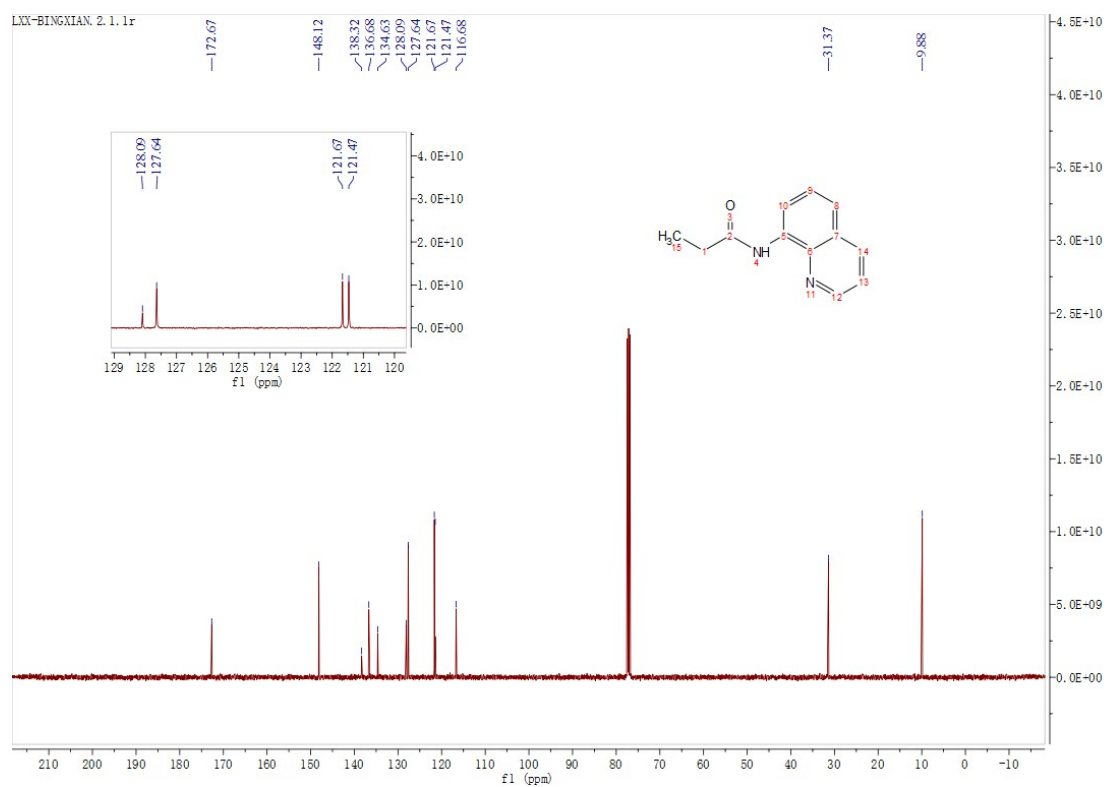
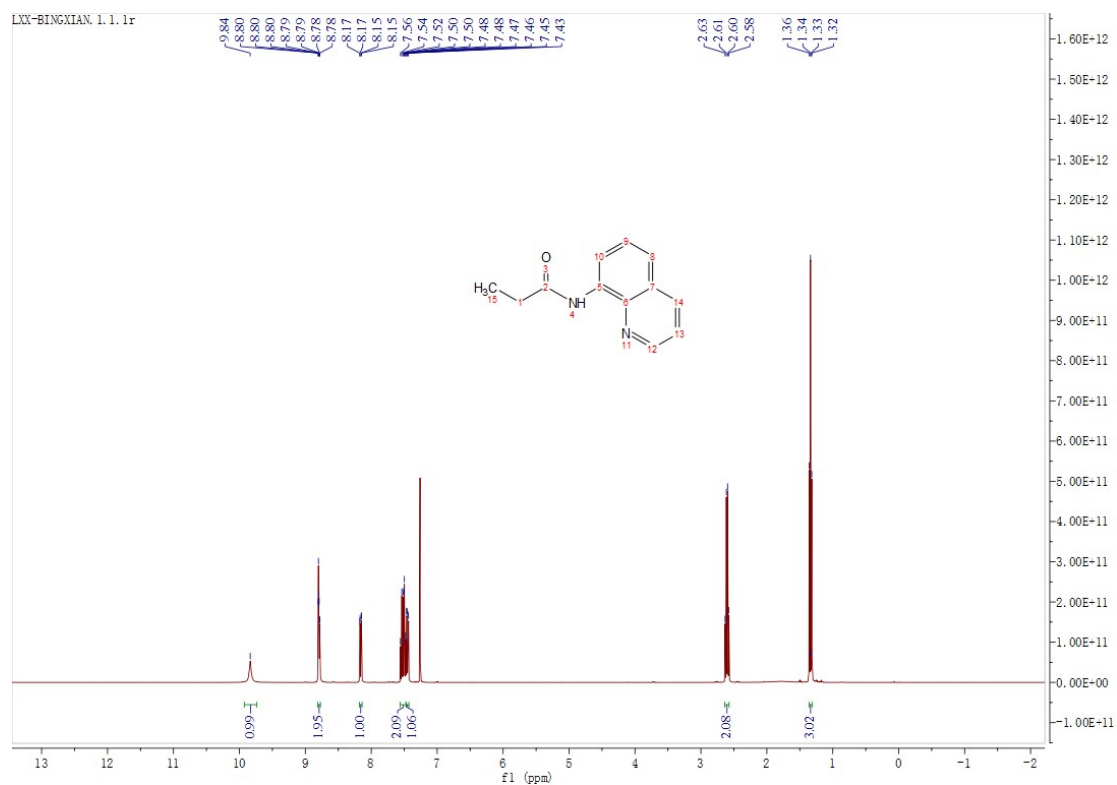


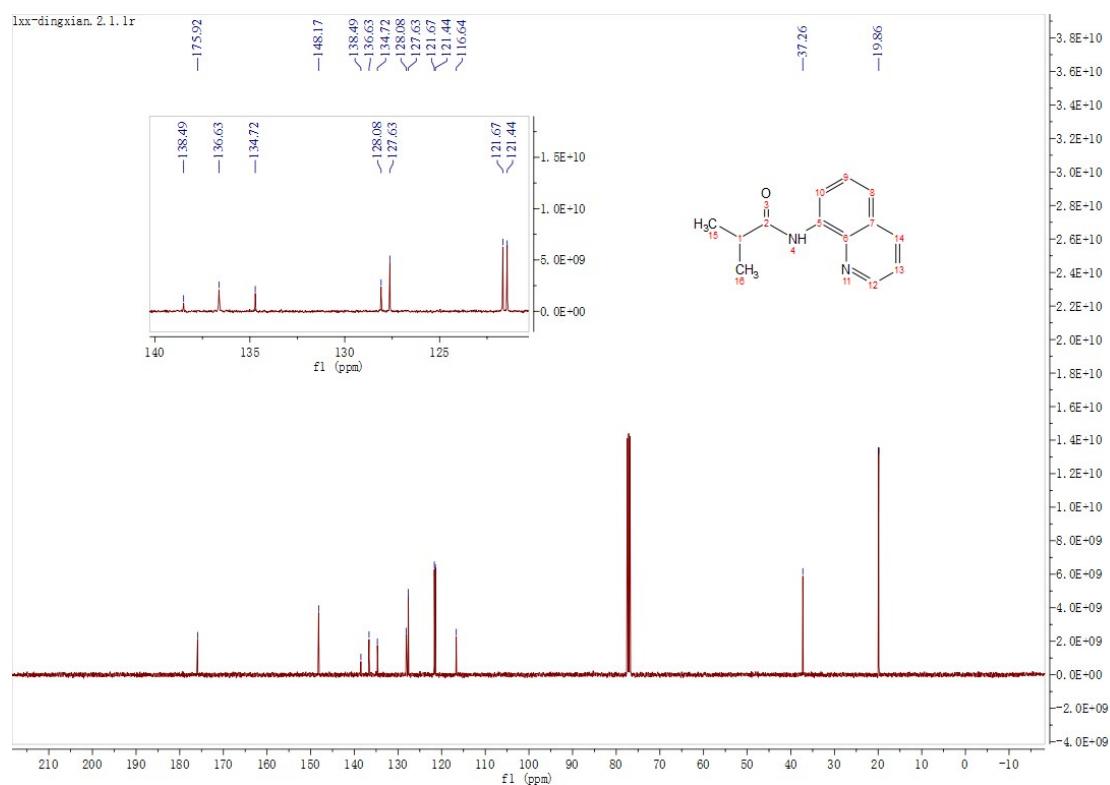
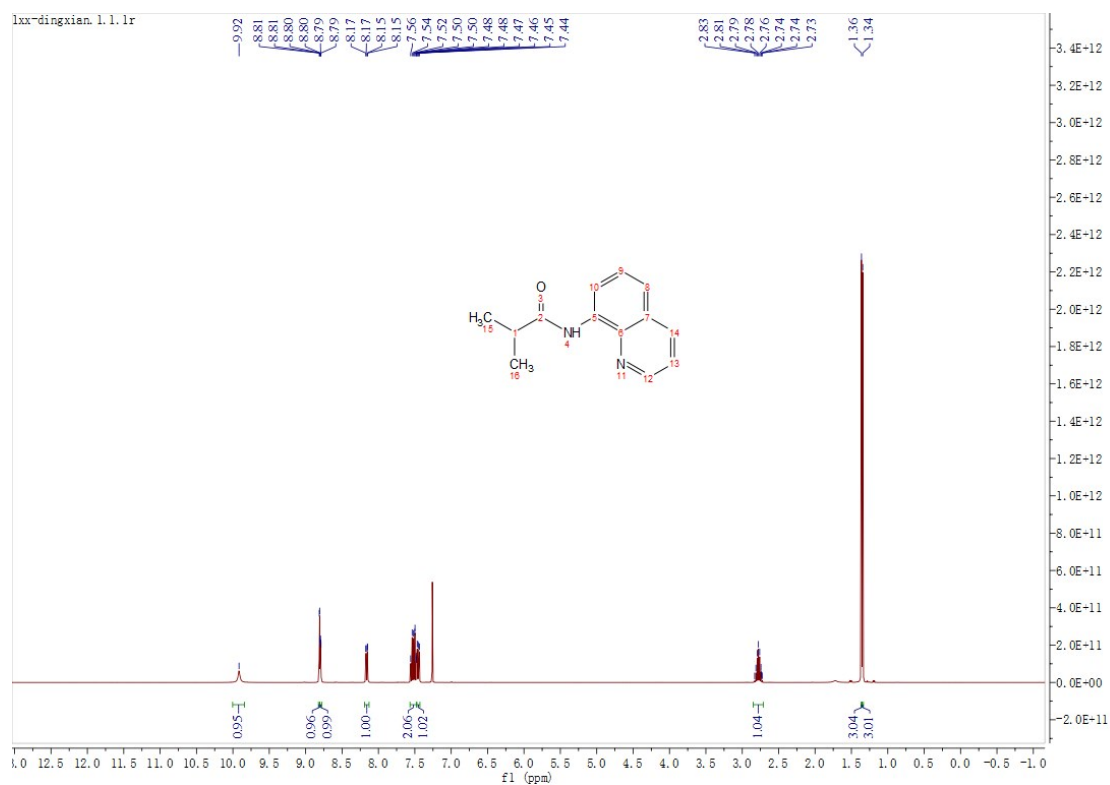




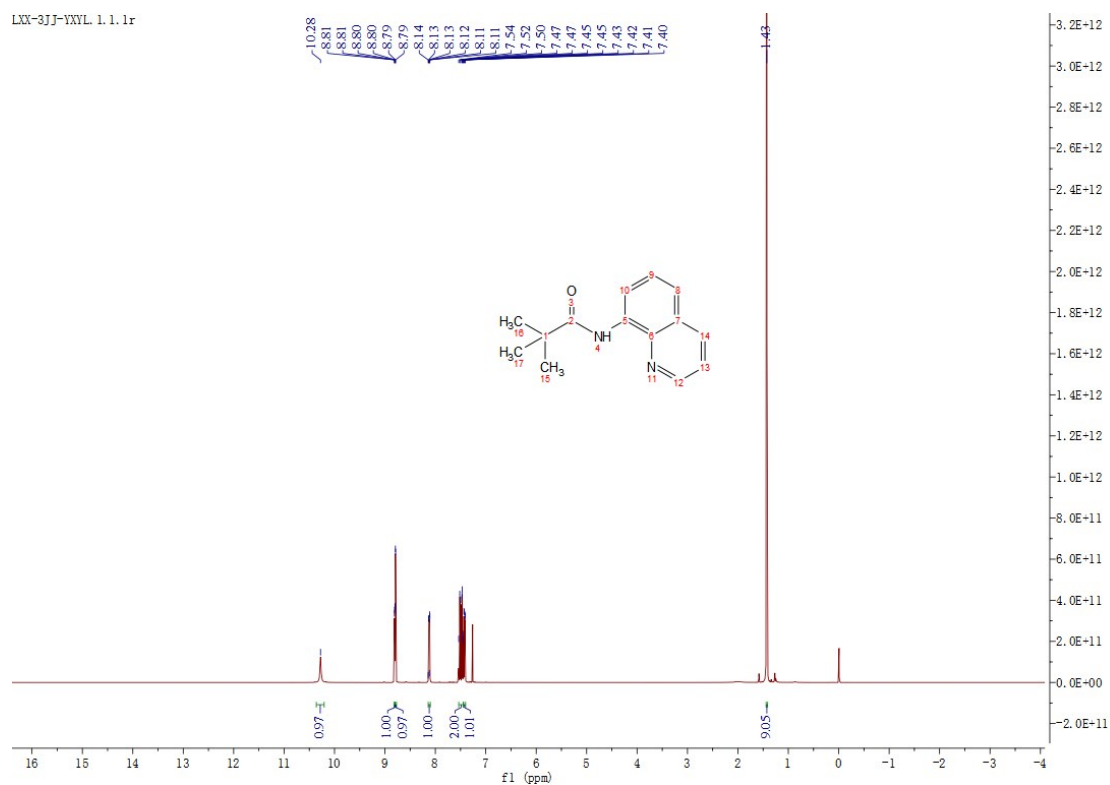
10.2 NMR-Spectra of **3**



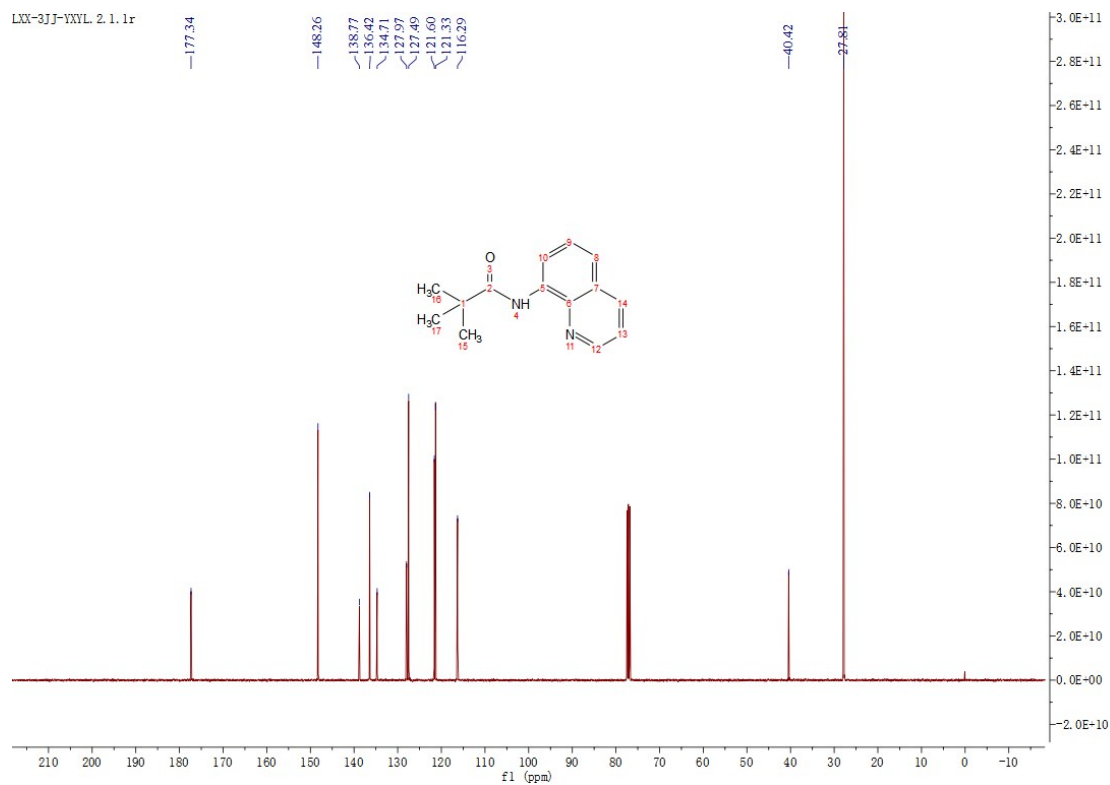


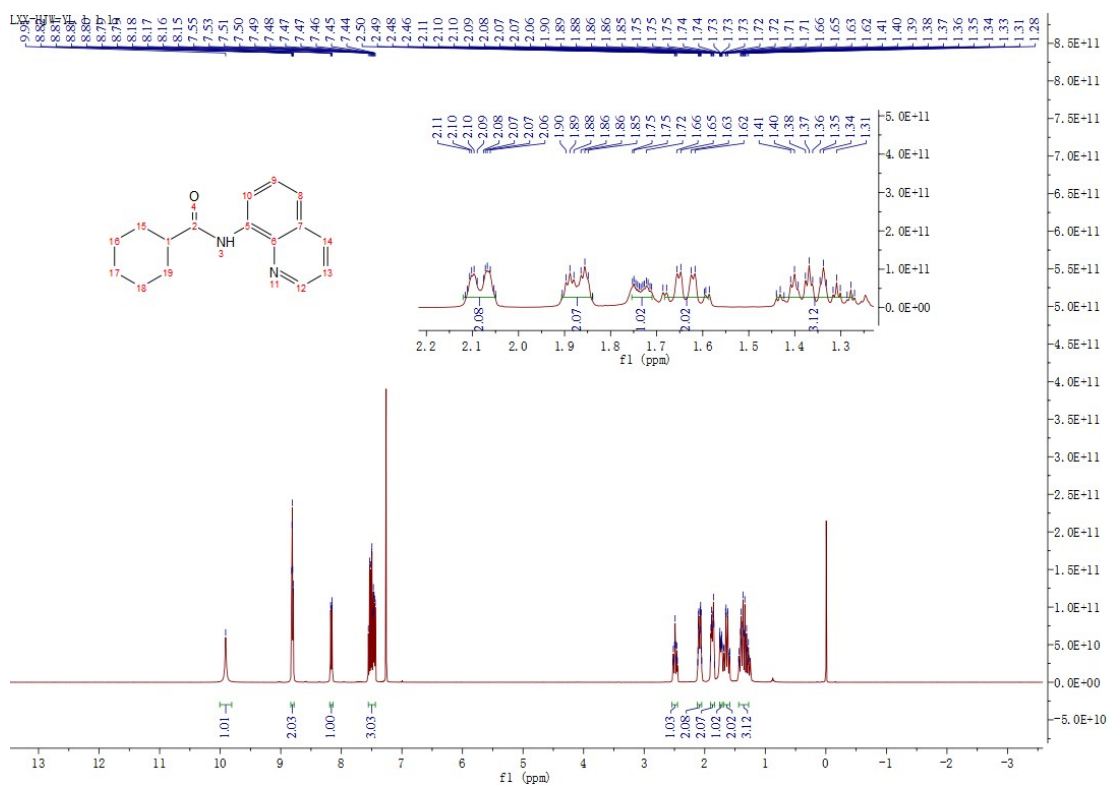


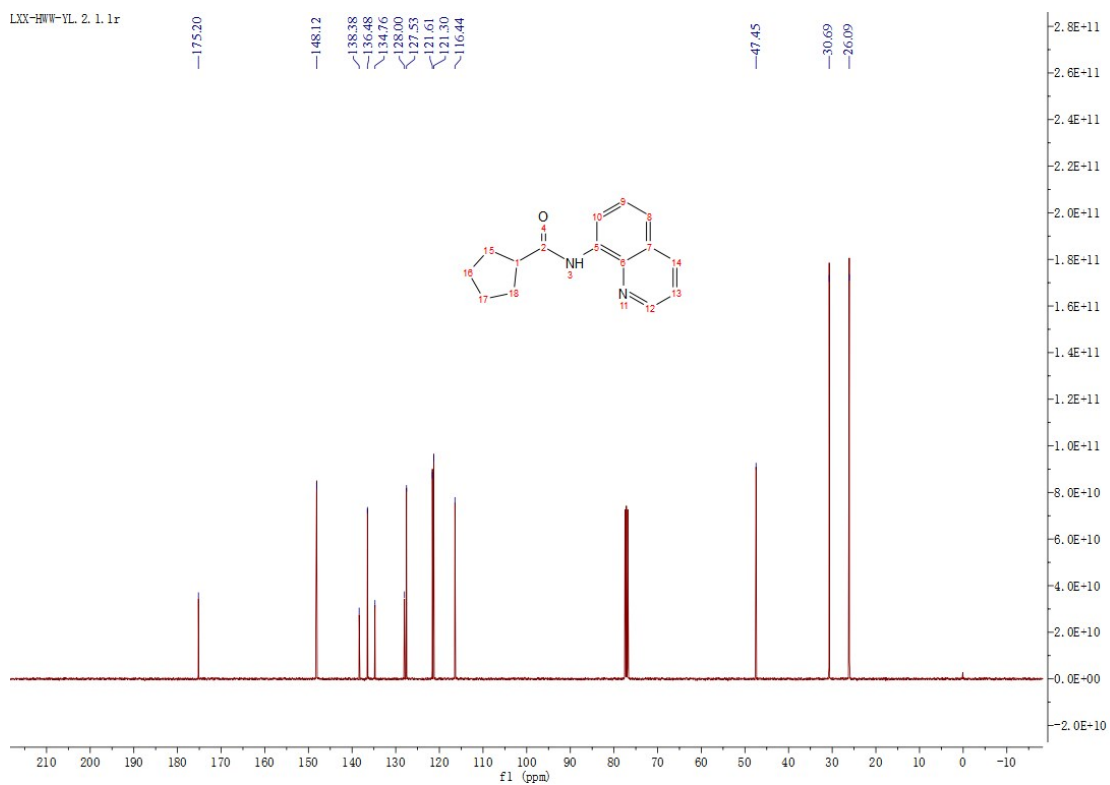
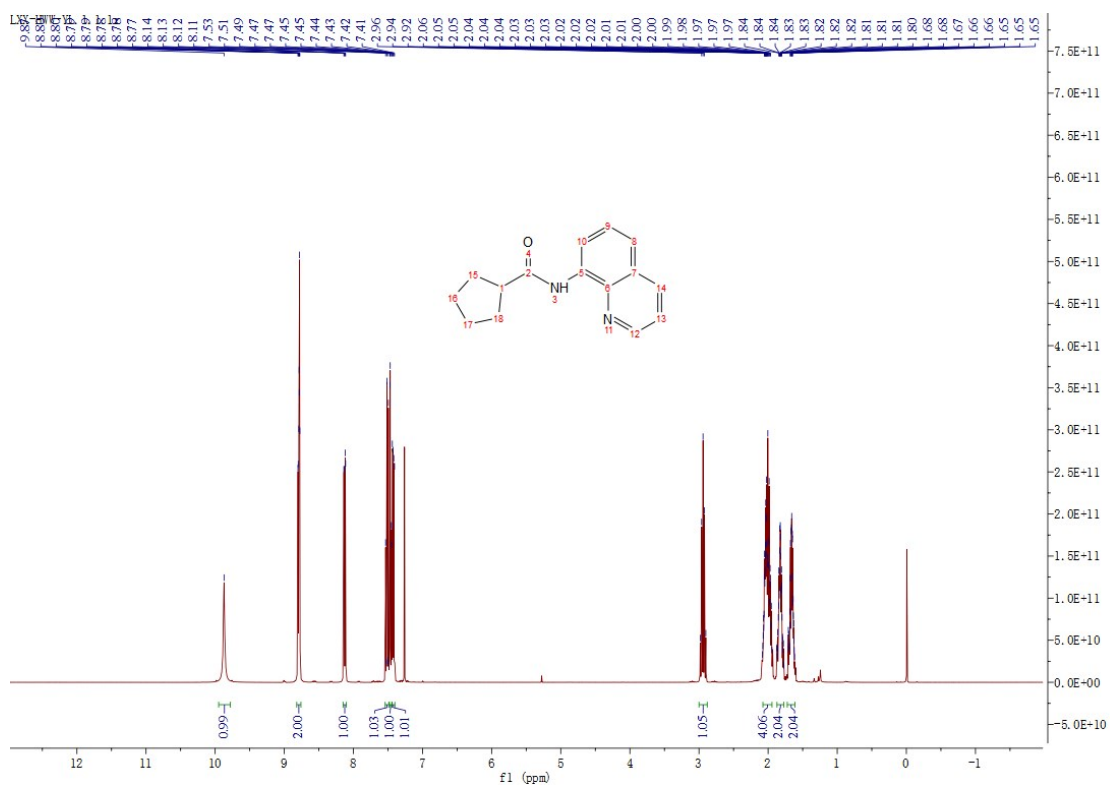
LXX-3JJ-YXYL 1.1.1r



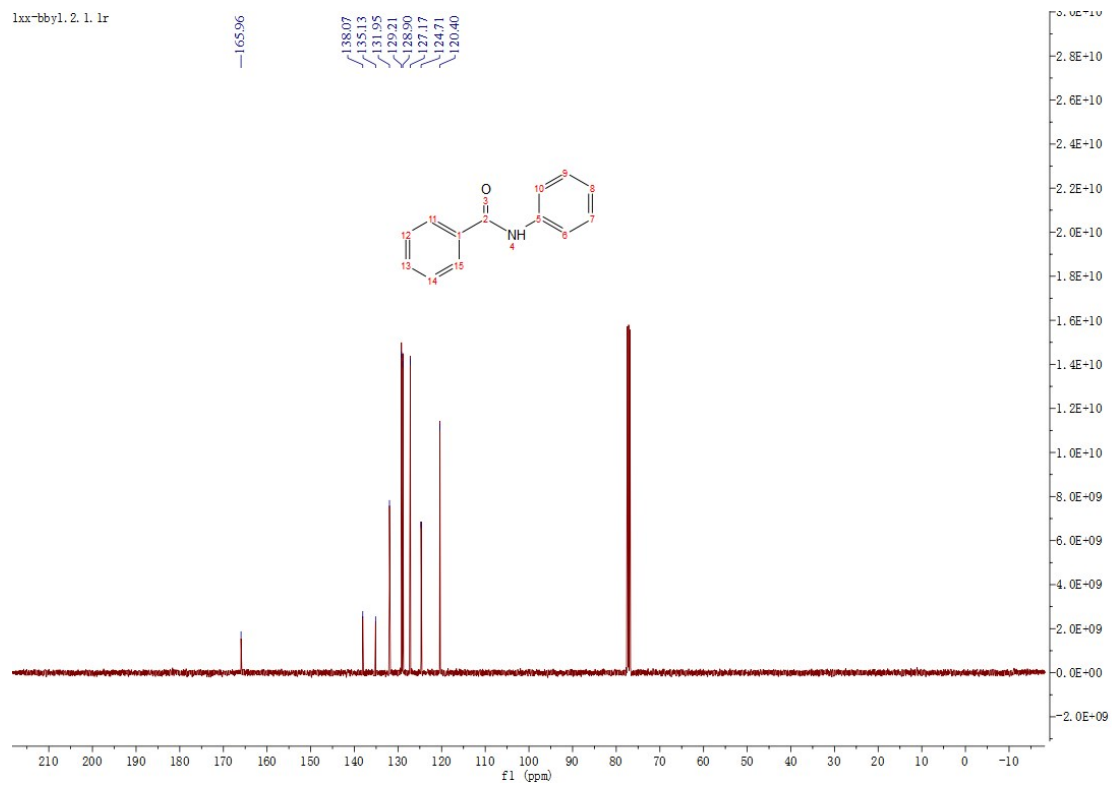
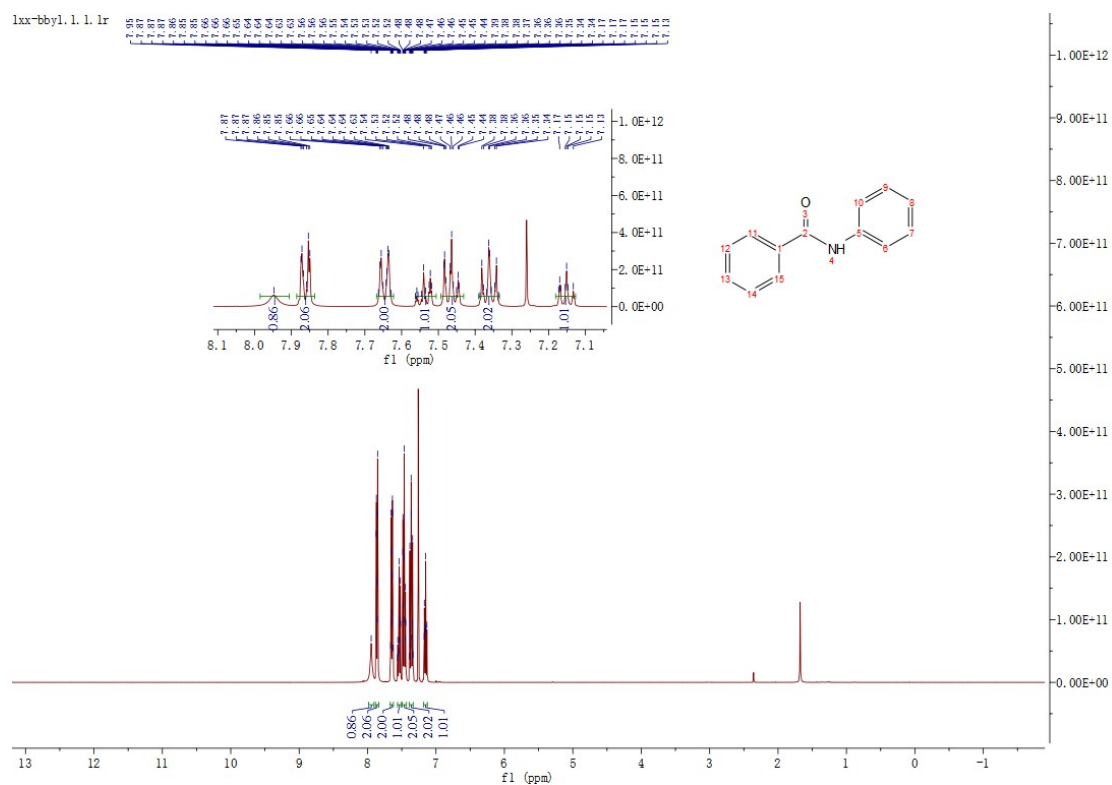
LXX-3JJ-YXYL 2.1.1r

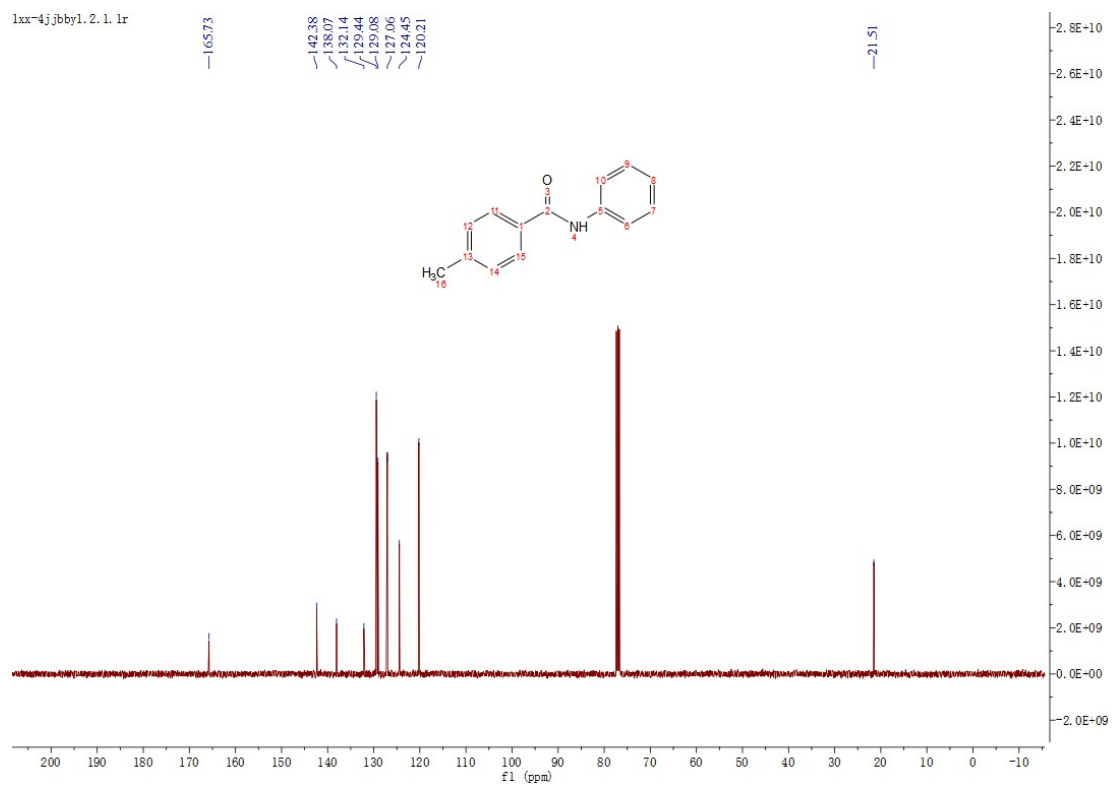
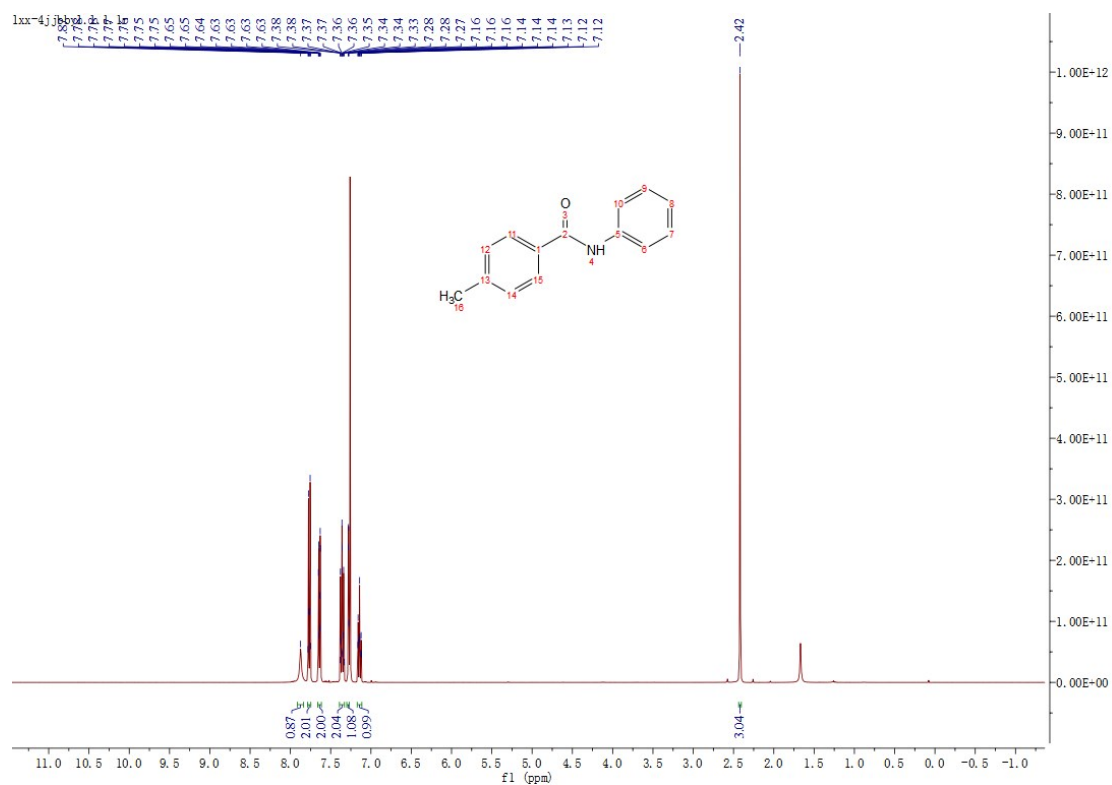


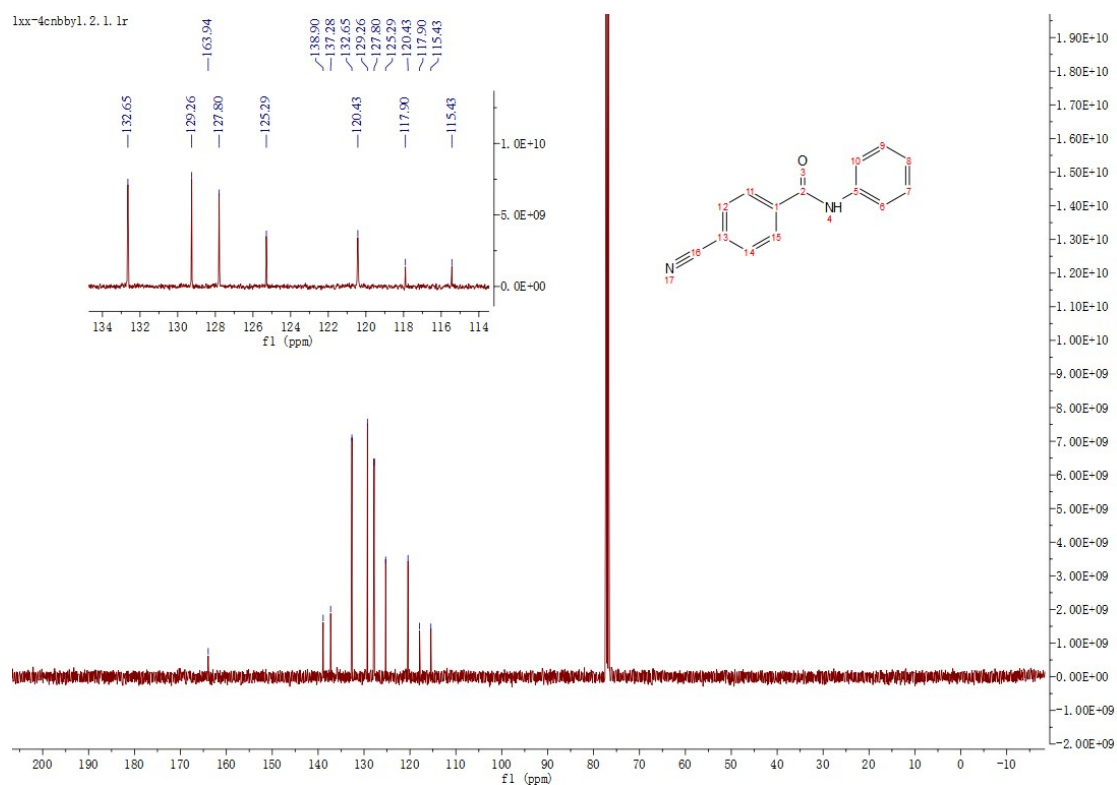
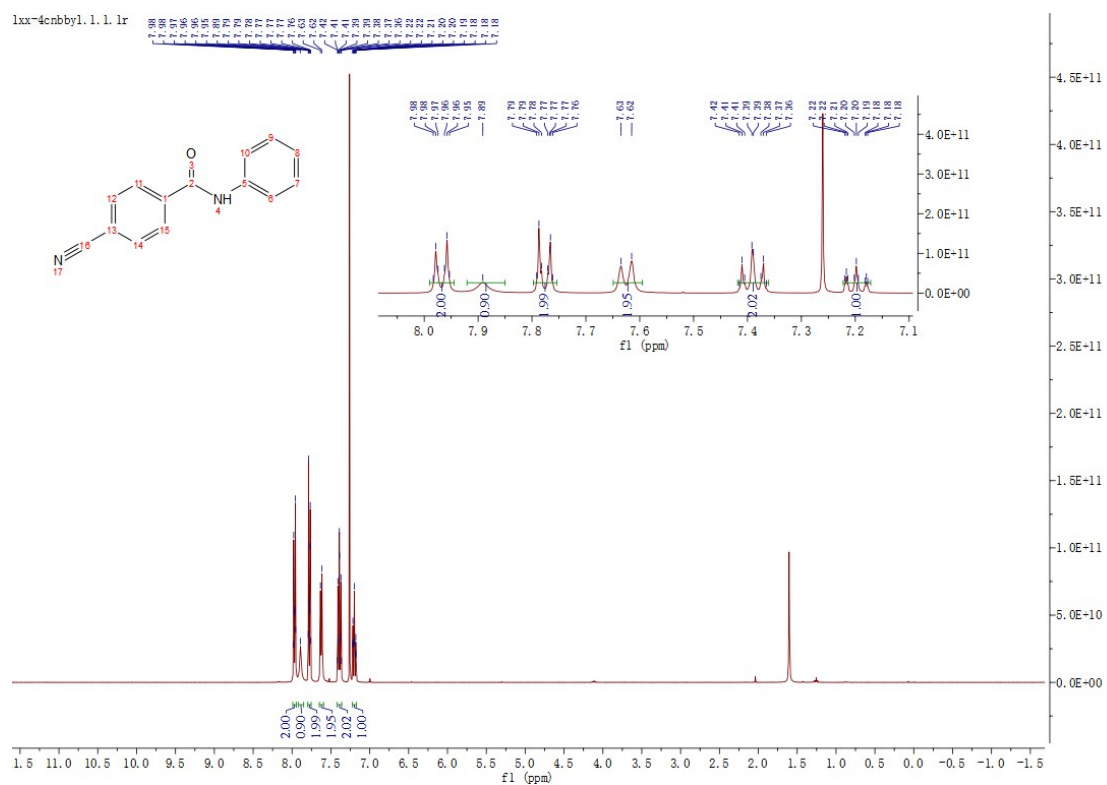


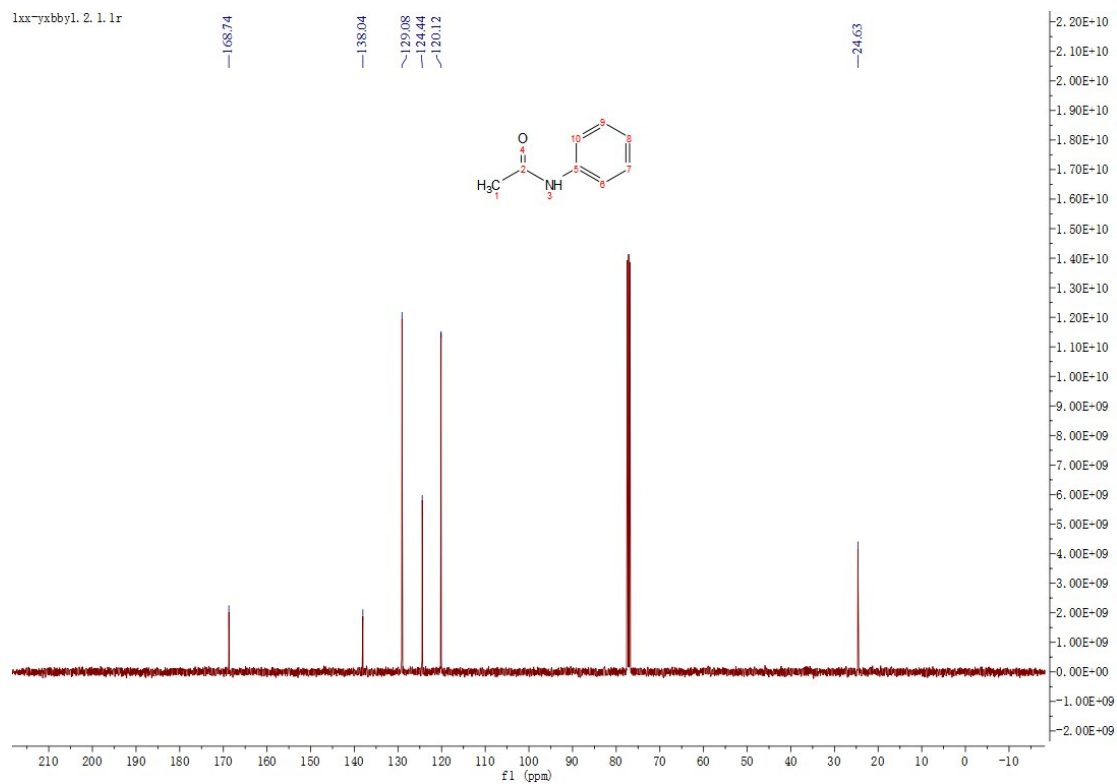
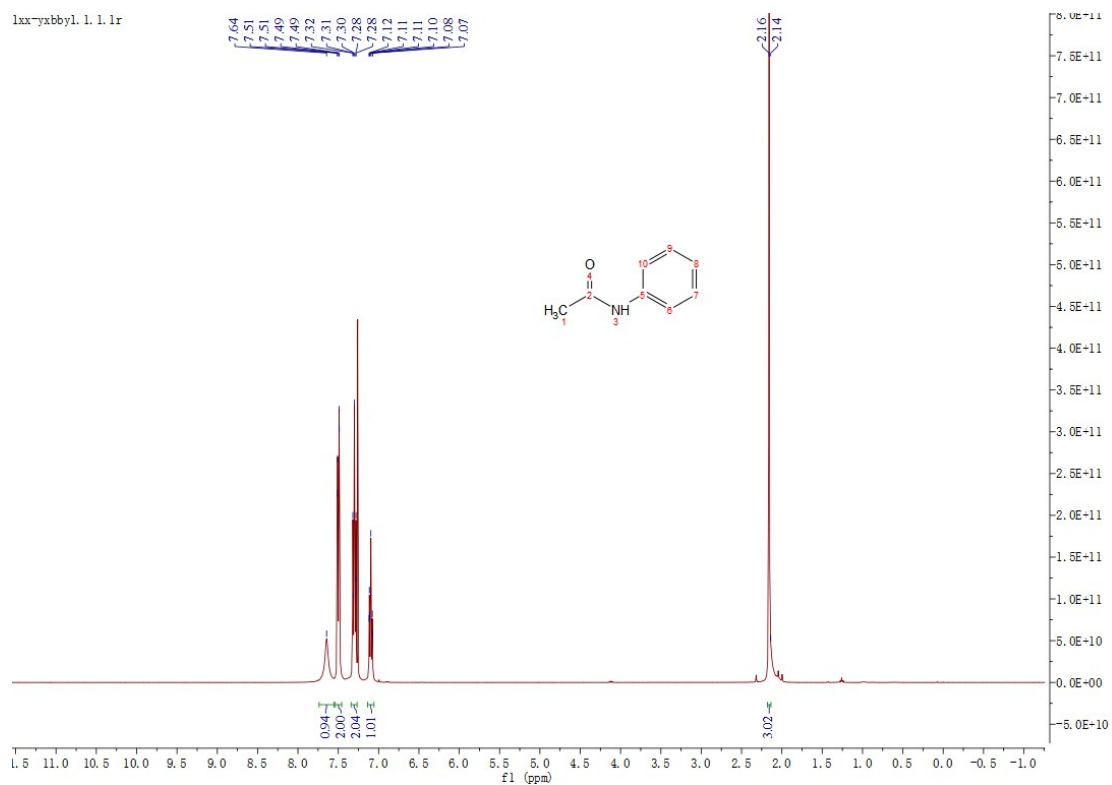


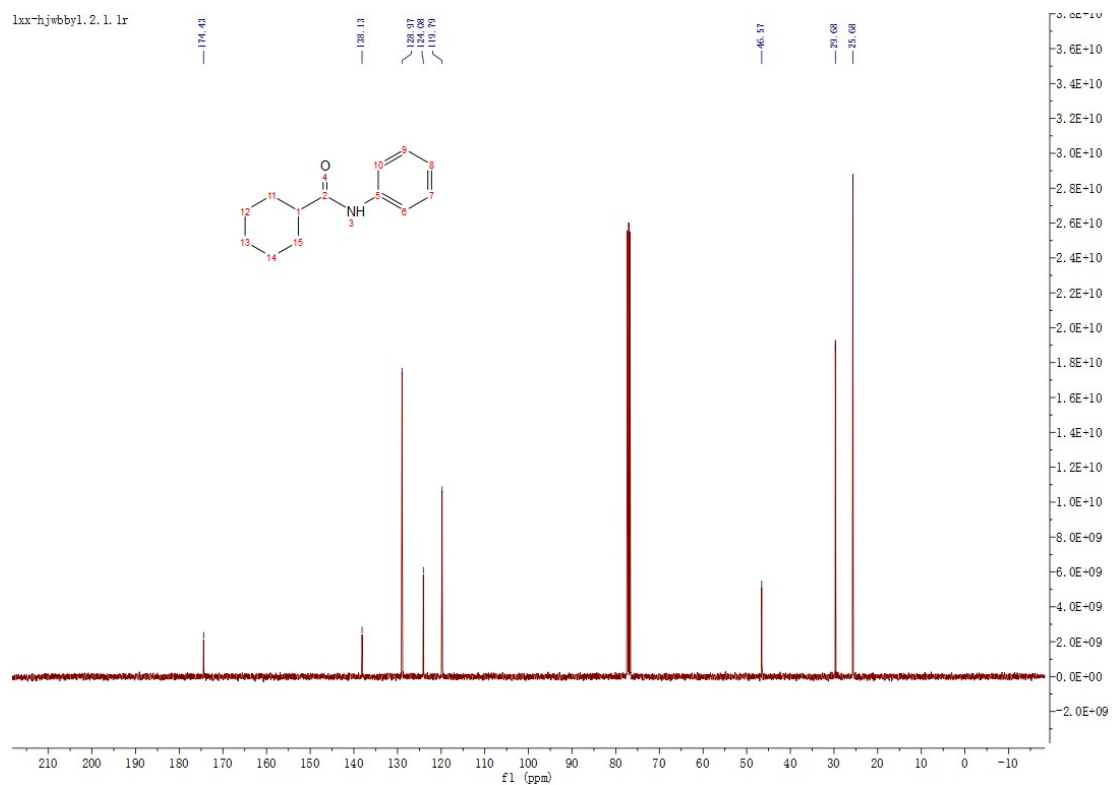
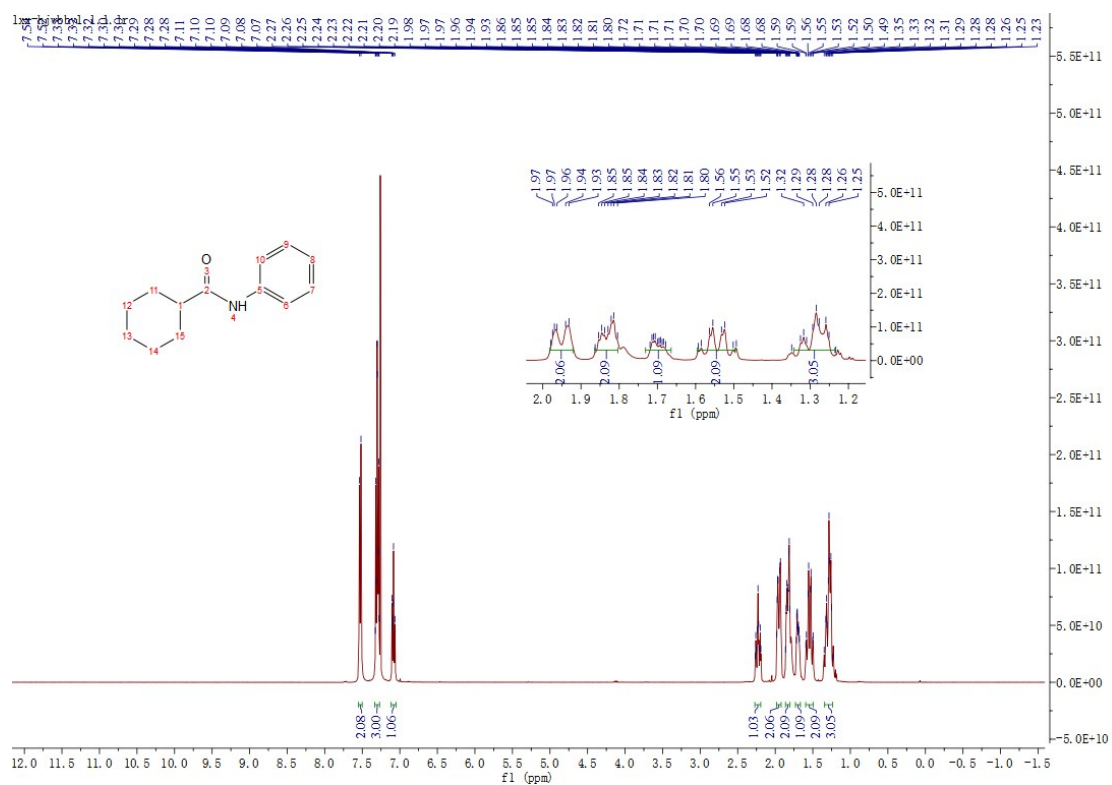
10.3 NMR-Spectra of **5**

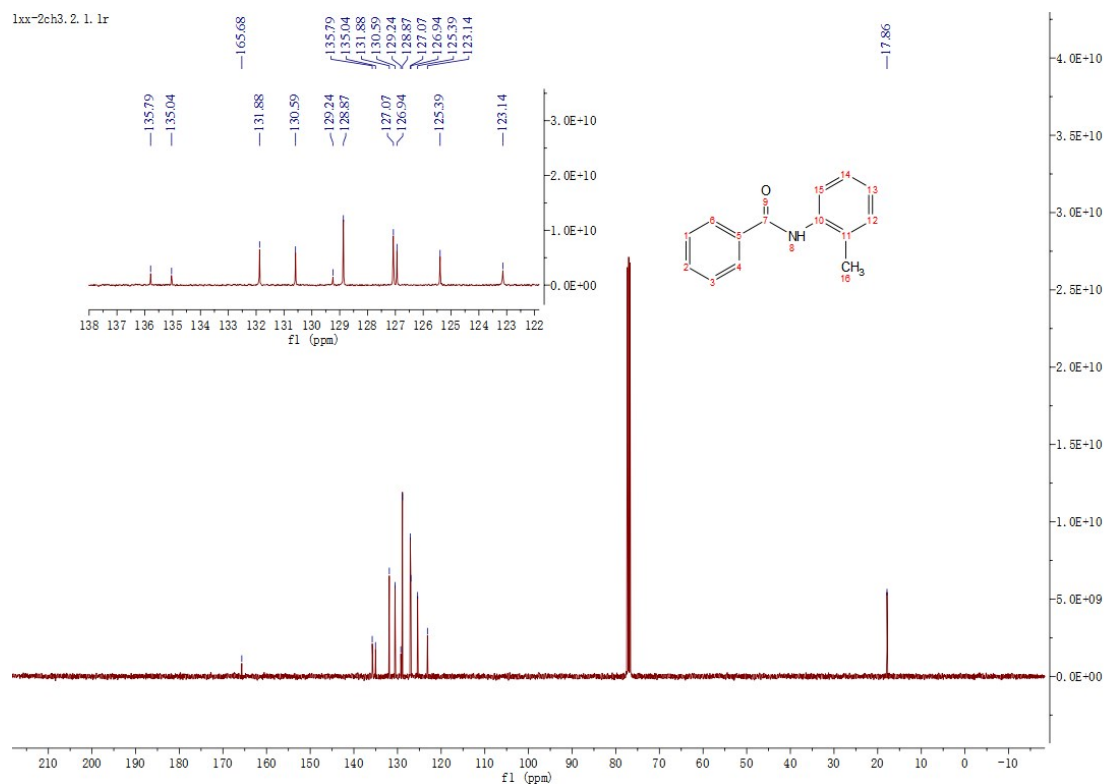
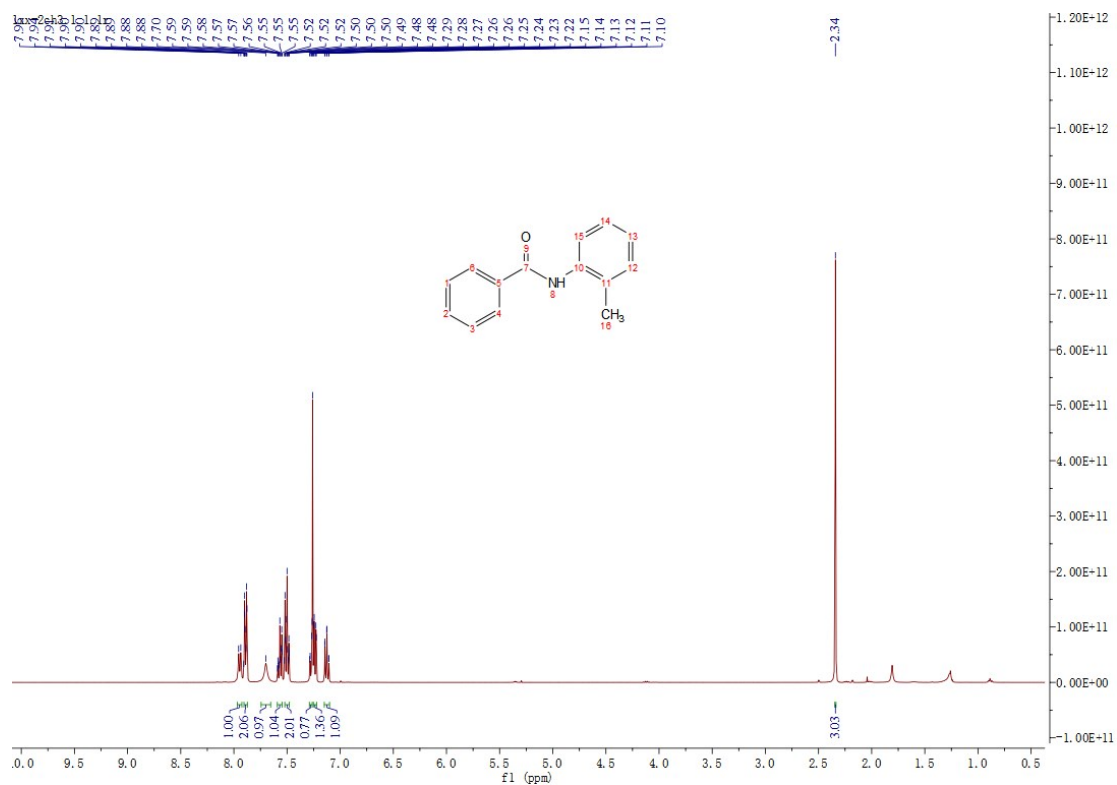


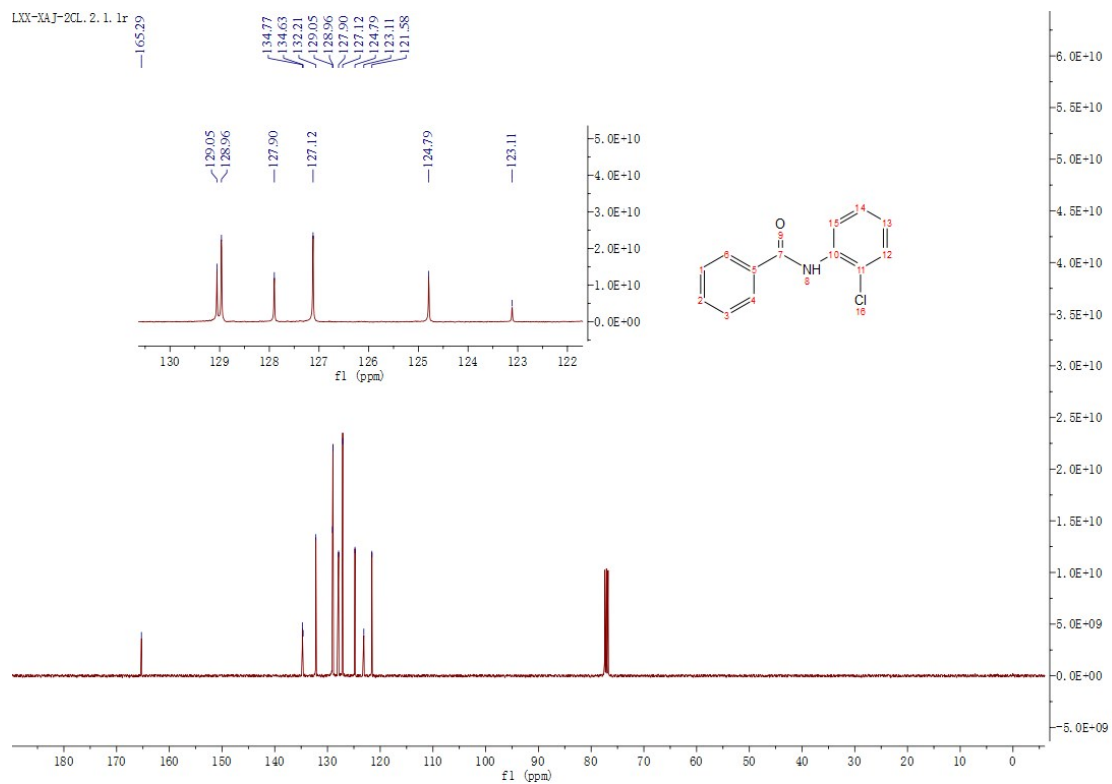
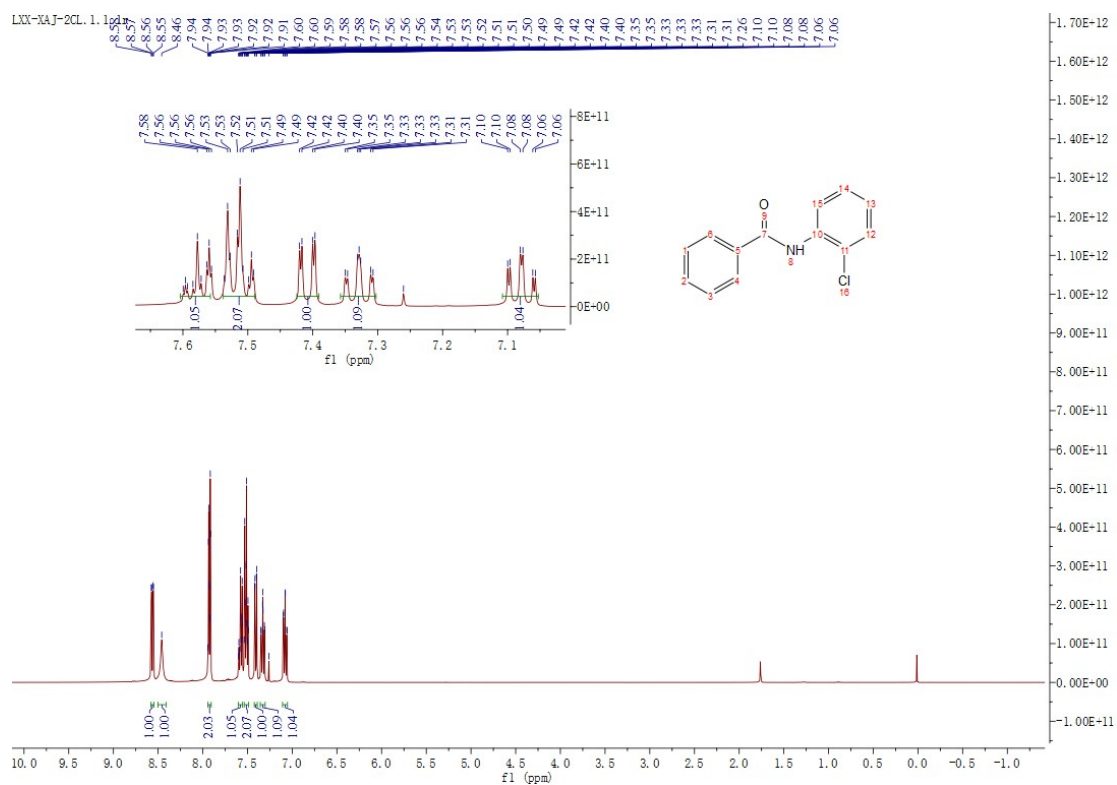


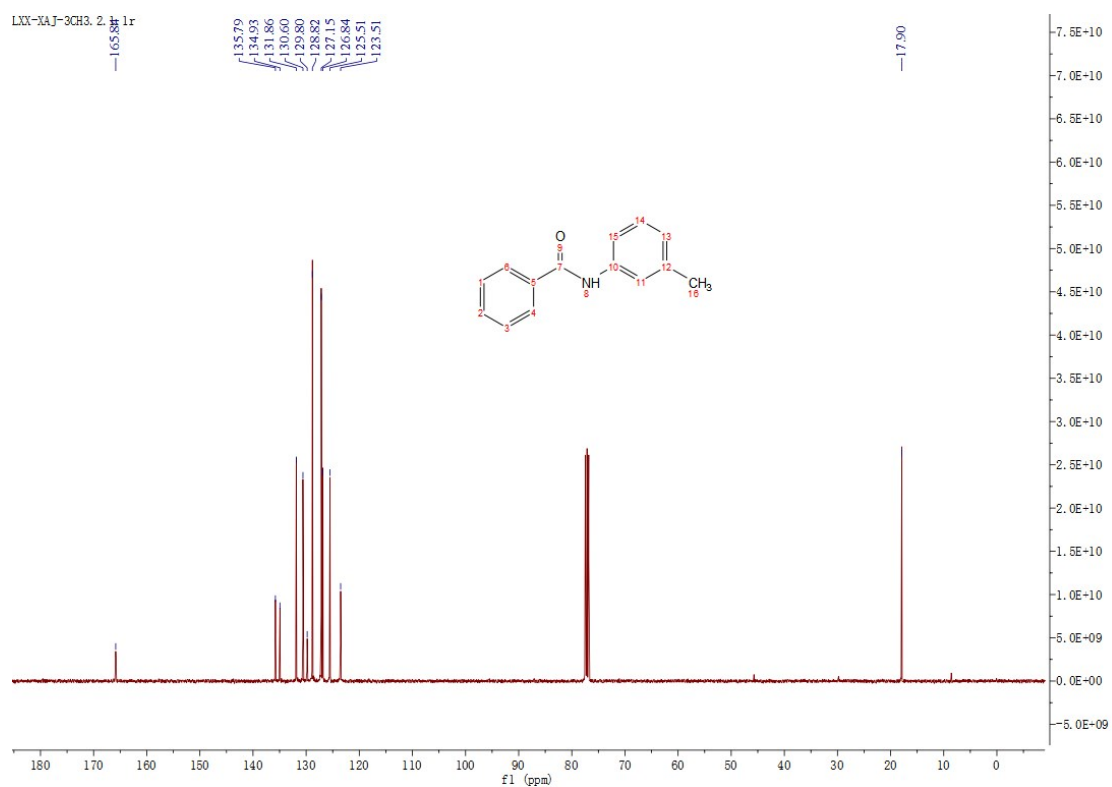
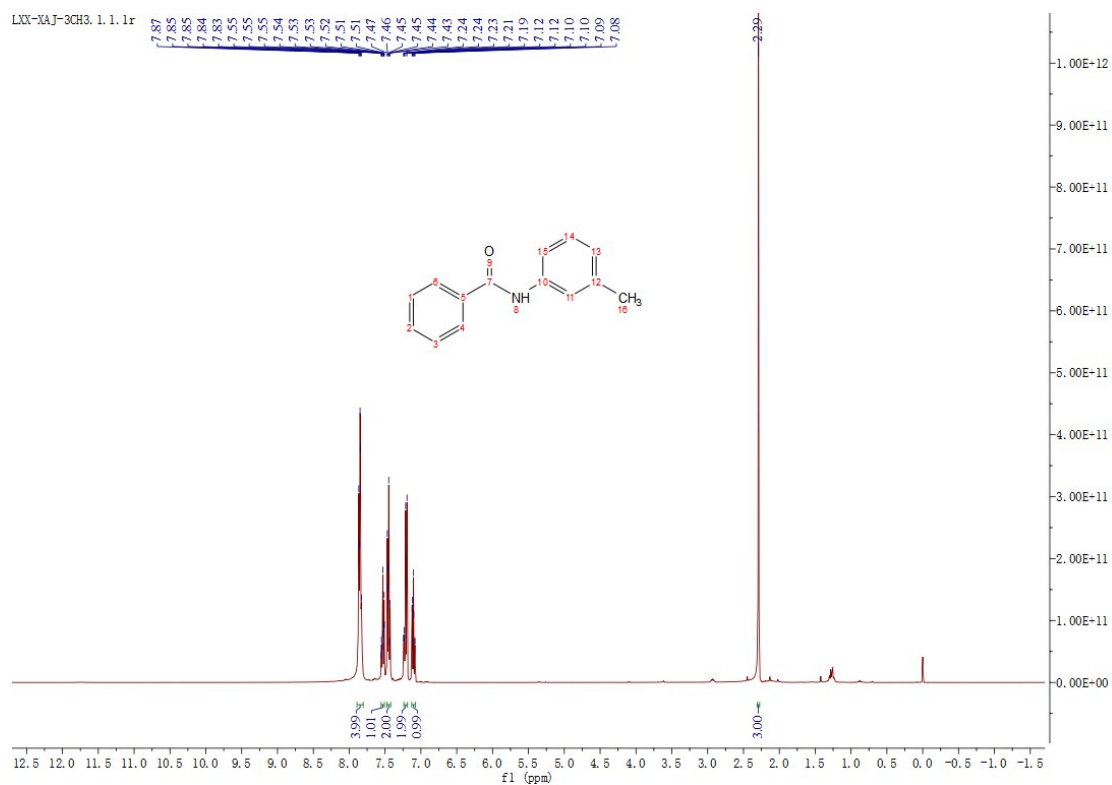


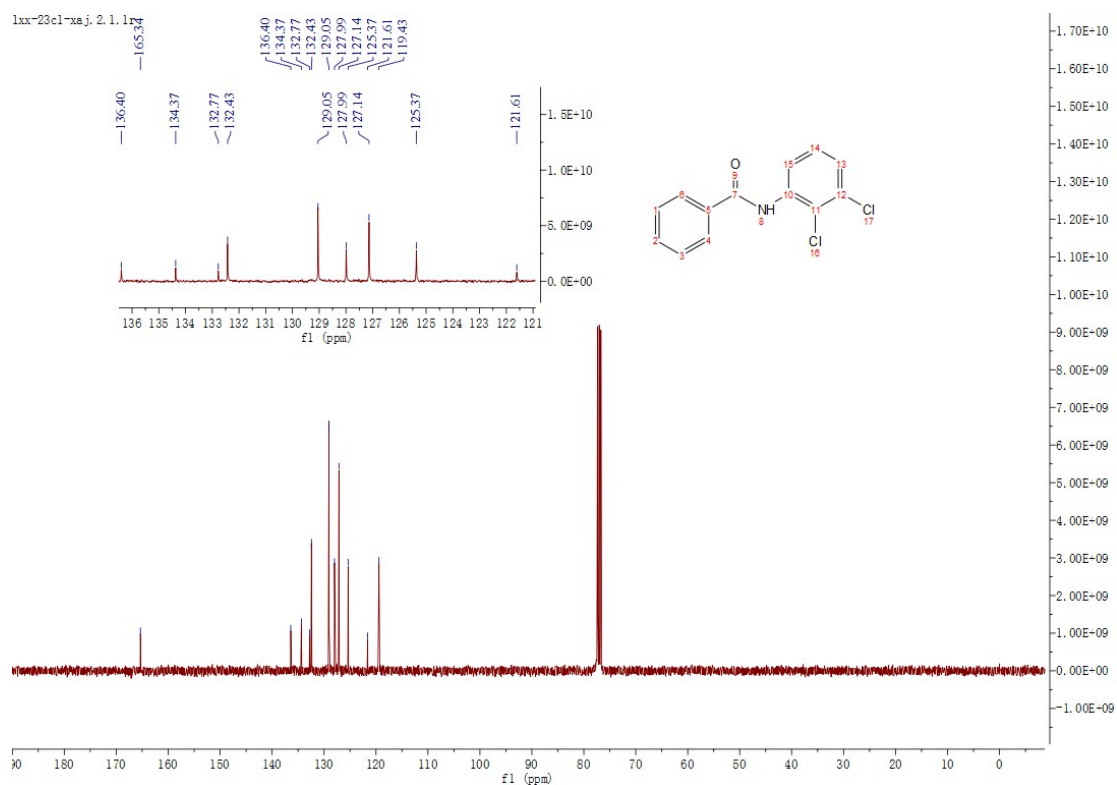
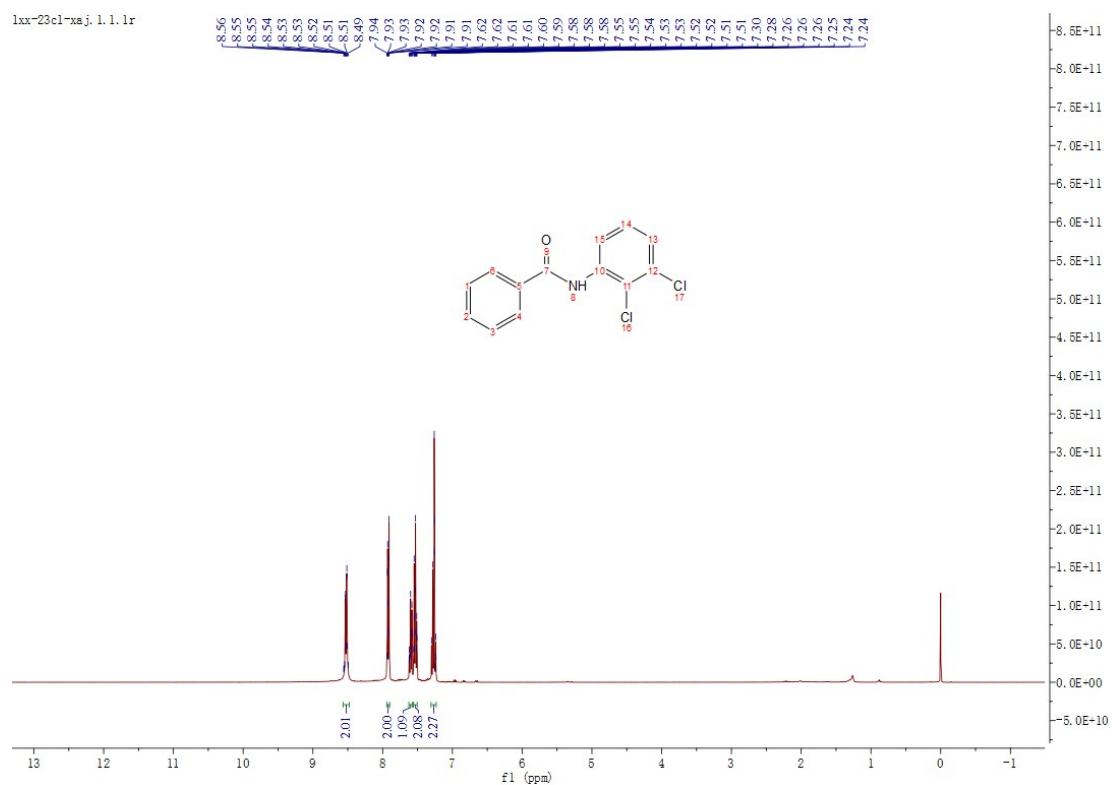




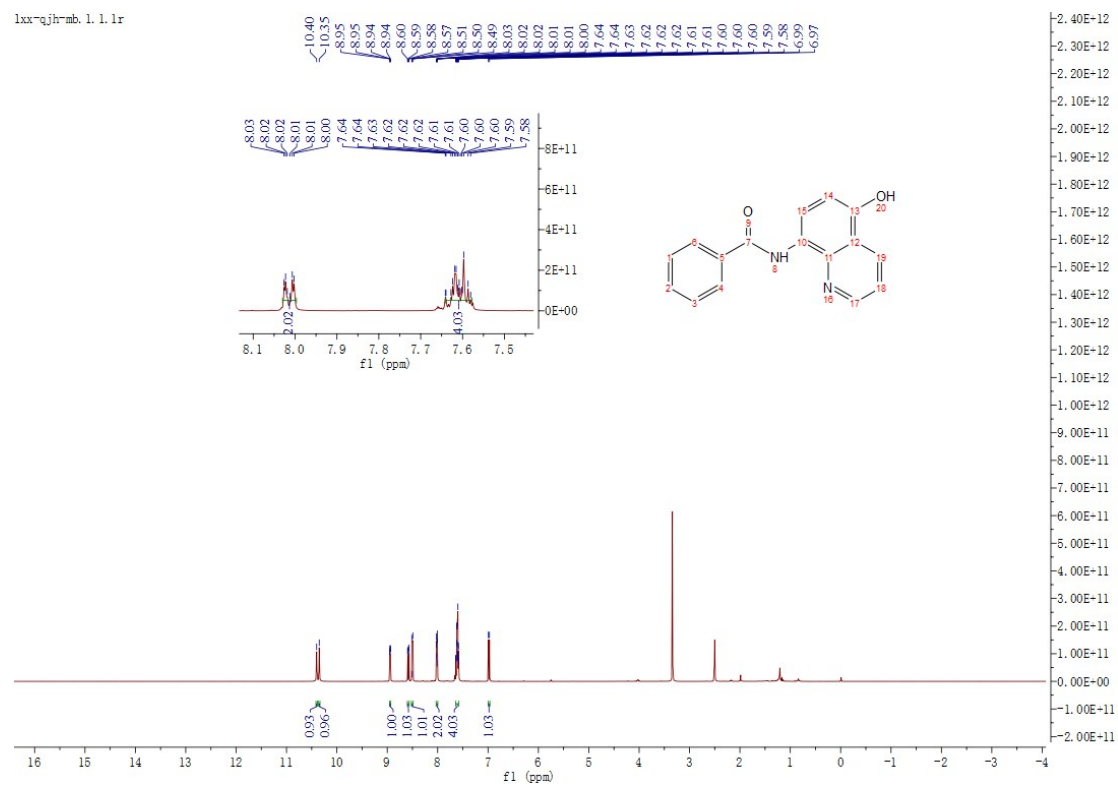


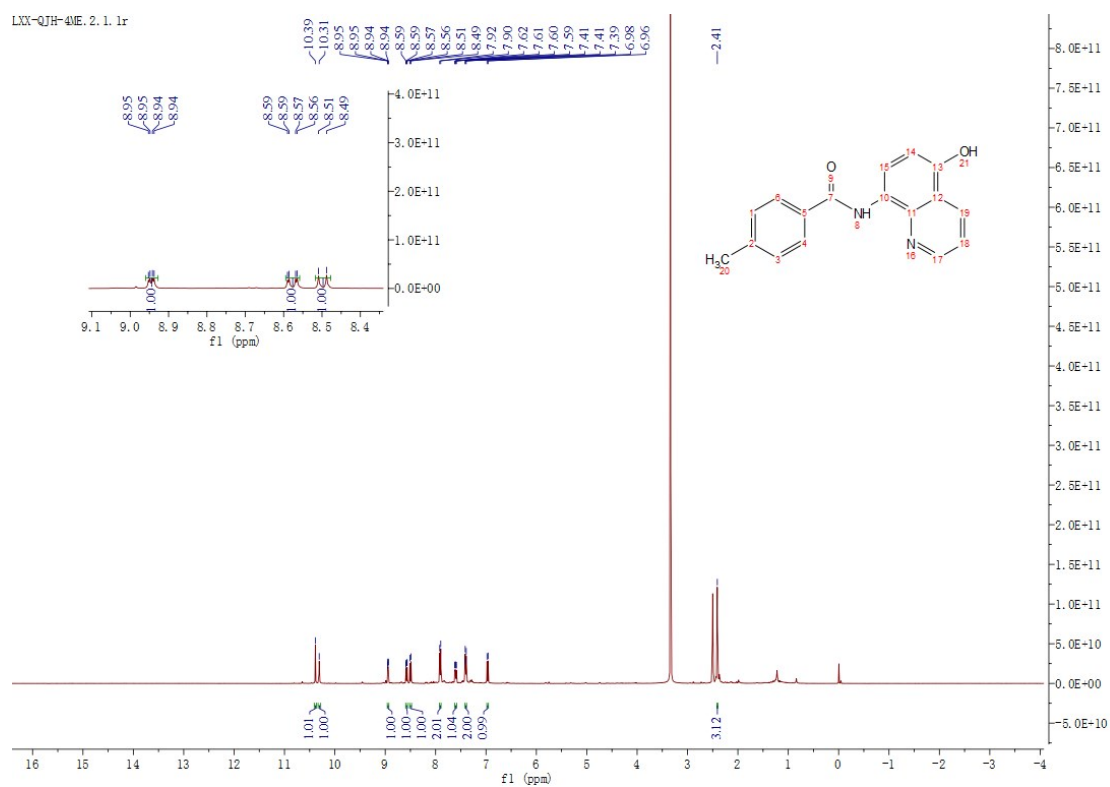
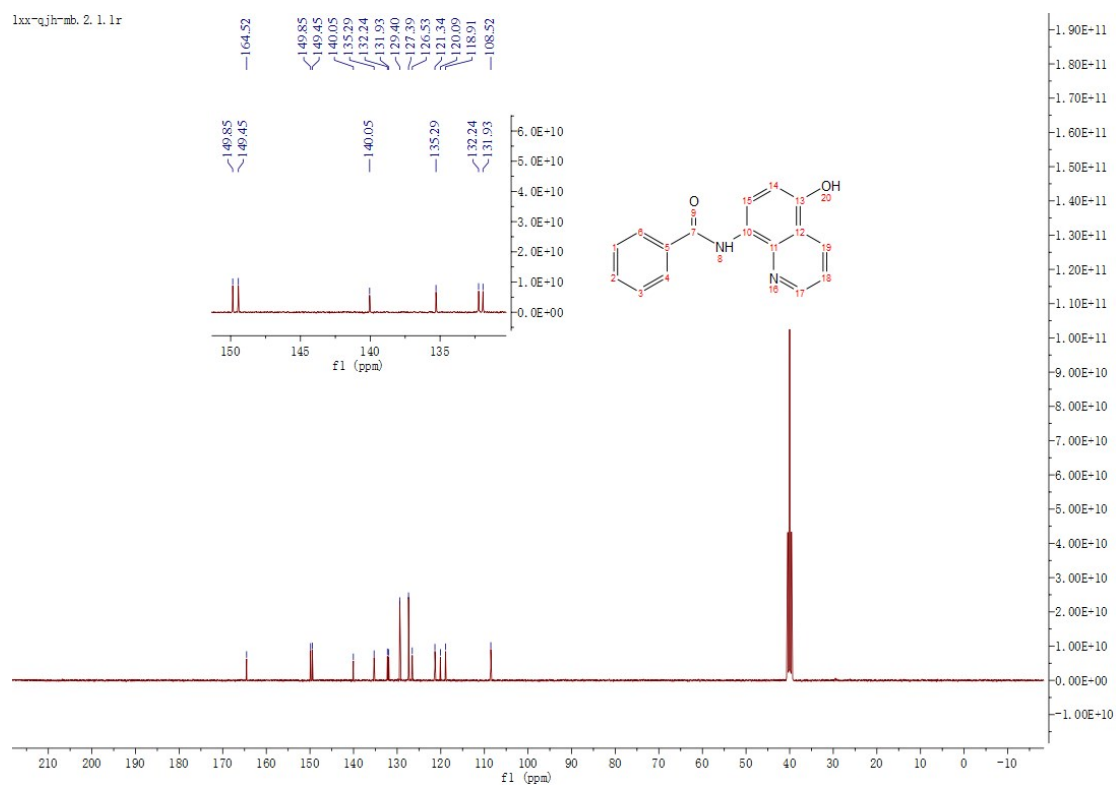




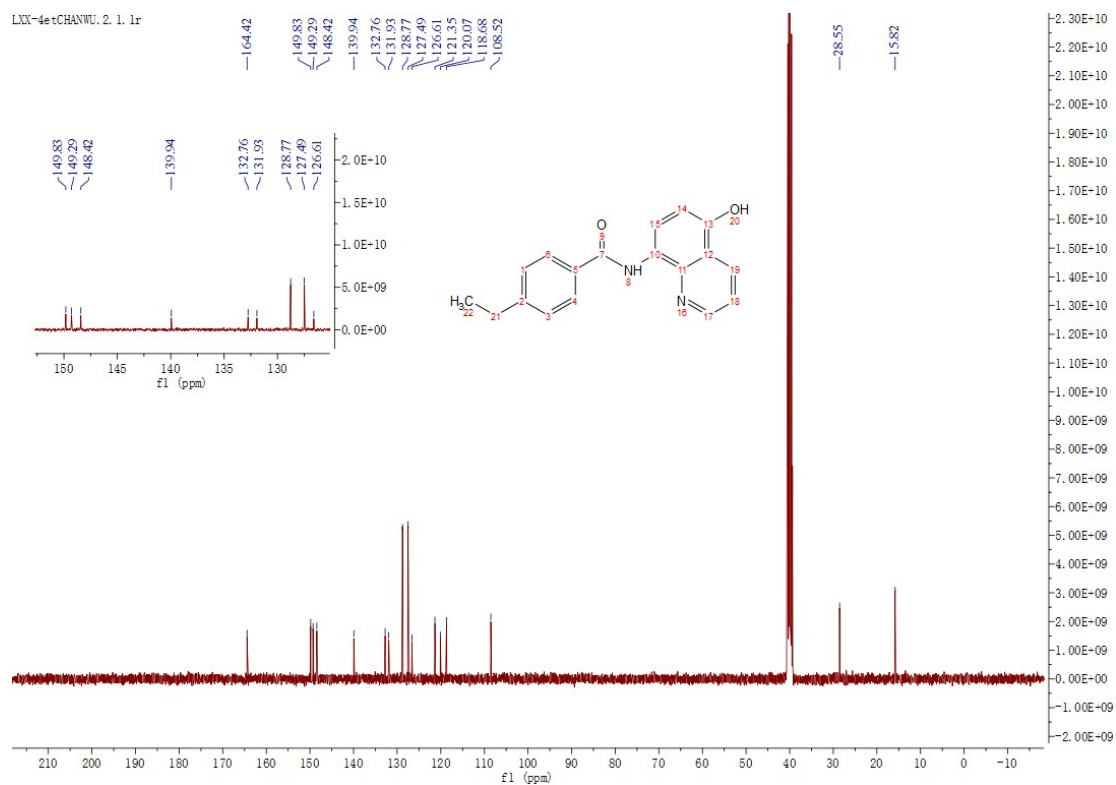


10.4 NMR-Spectra of 2

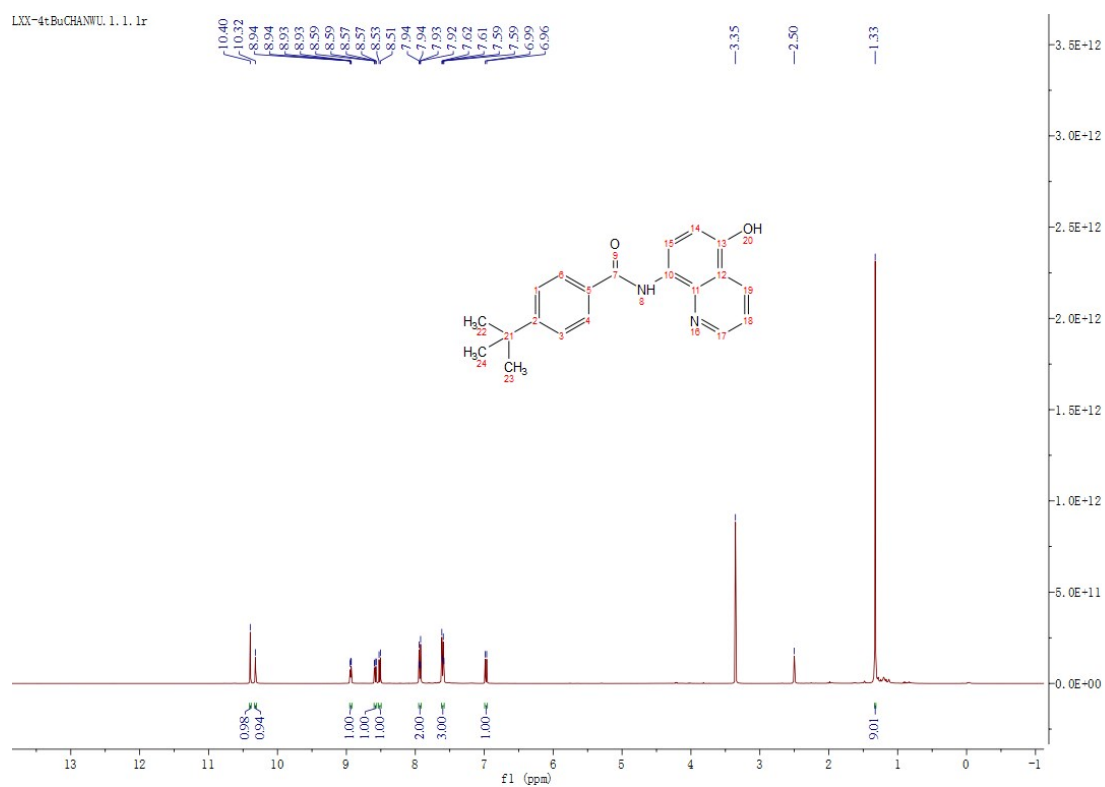




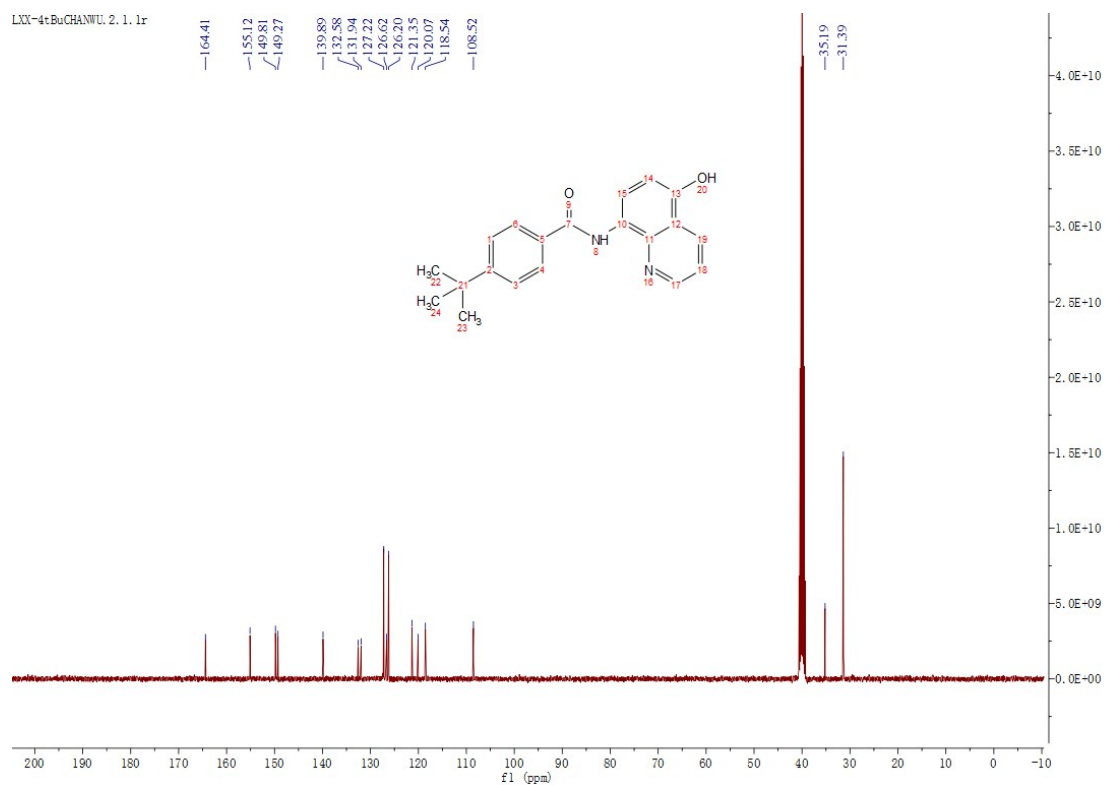
LXX-4etCHANWU. 2. 1. 1r



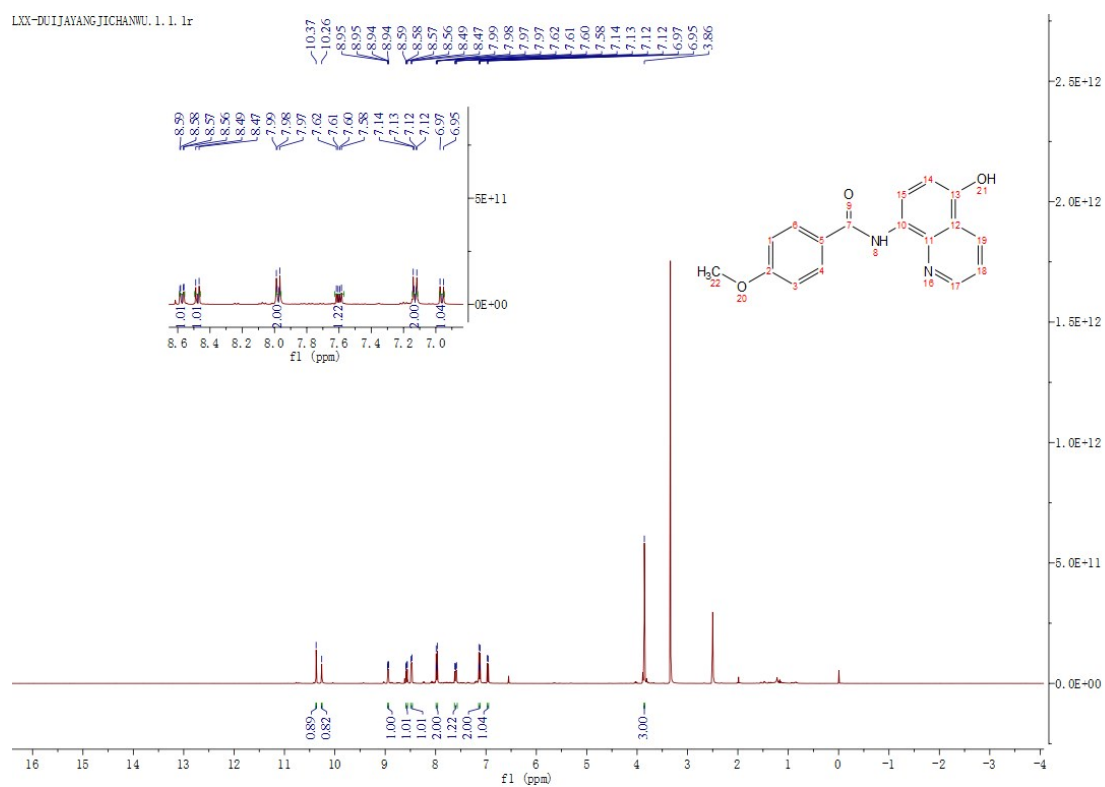
LXX-4tBuCHANWU. 1. 1. 1r



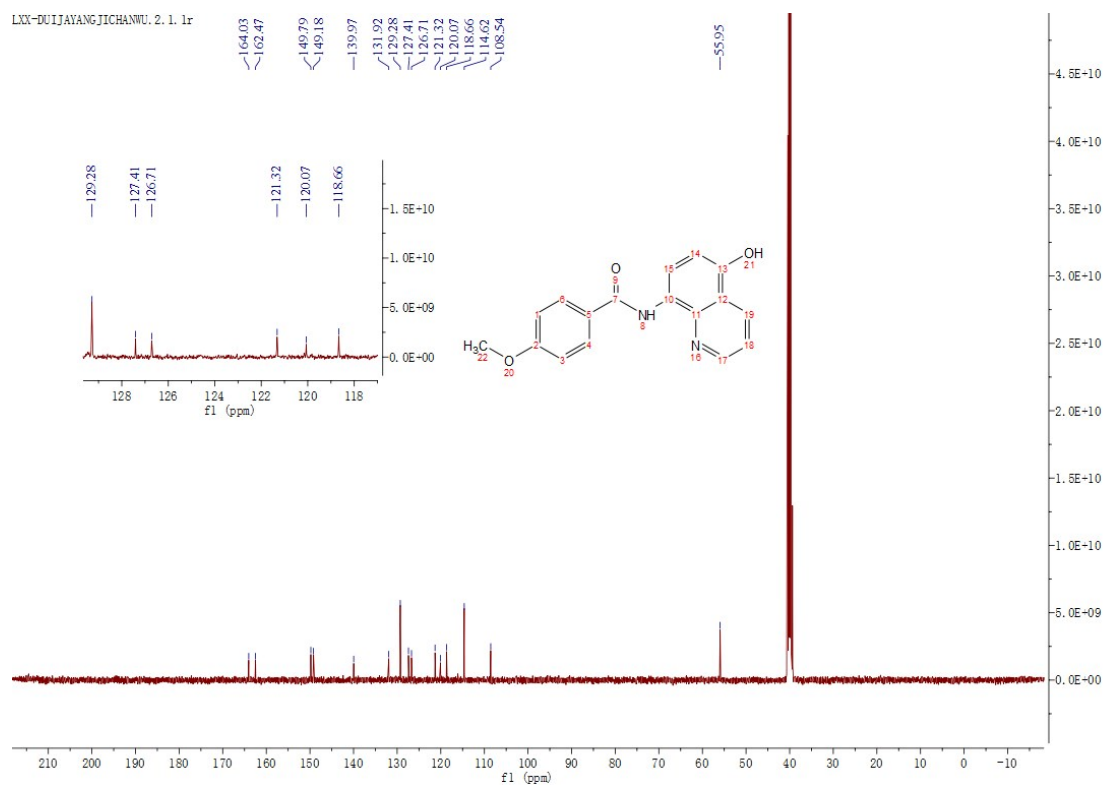
LXX-4tBuCHANWU, 2. 1. 1r



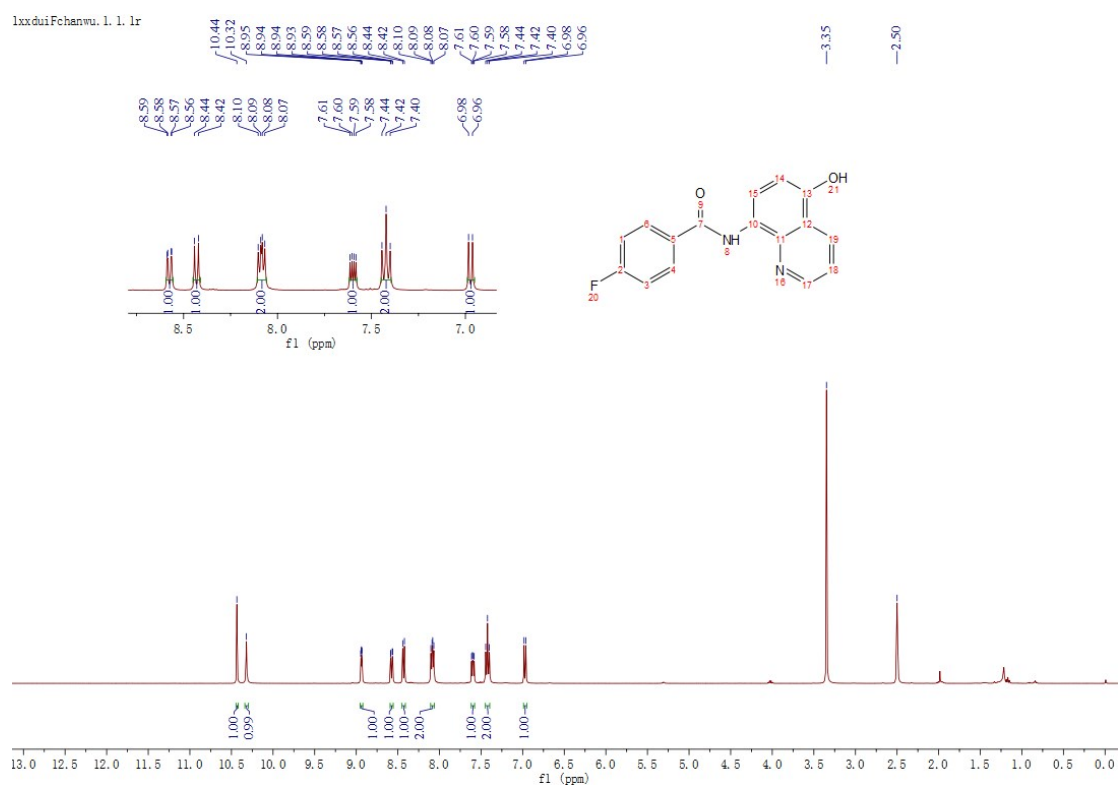
LXX-DUIJAYANGJICHANWU, 1. 1. 1r



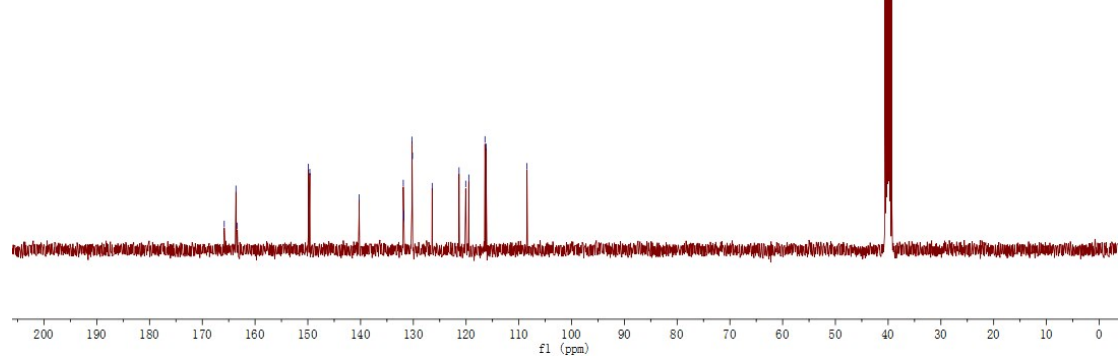
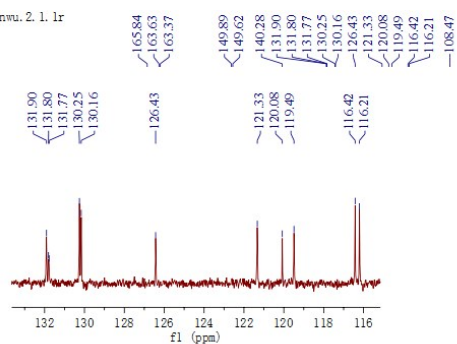
LXX-DUIJAYANGJICHANWU, 2. 1. 1r



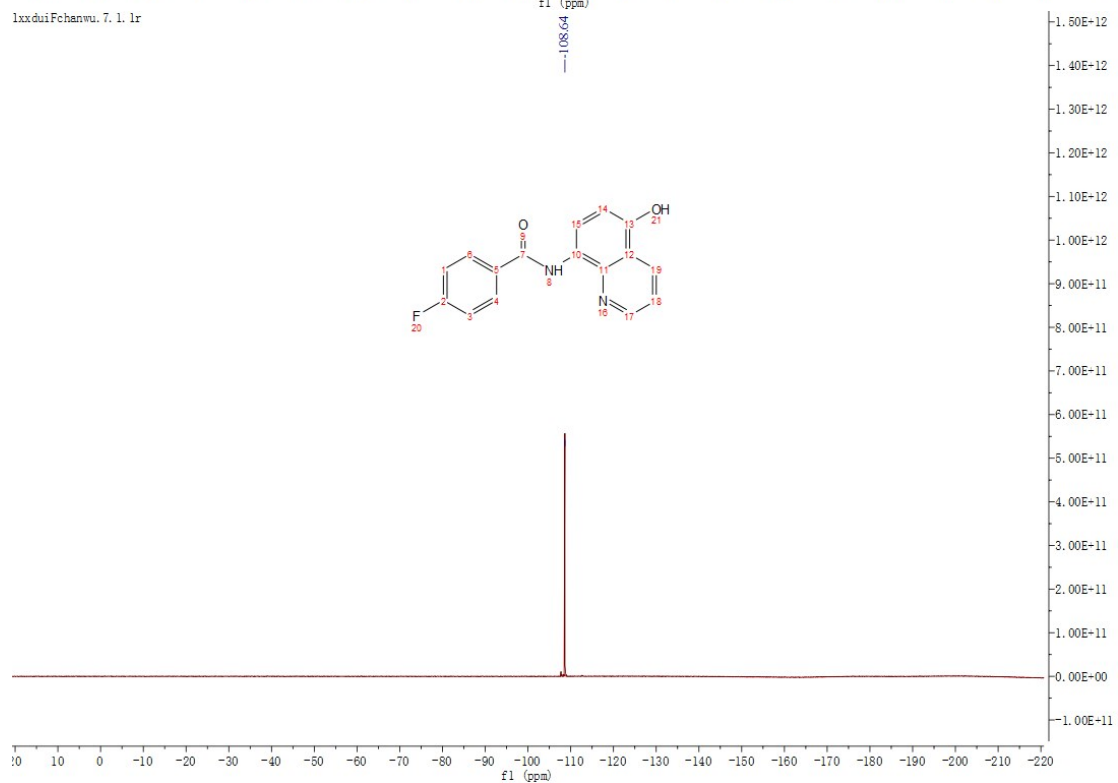
lxxduiFchanwu, 1. 1. 1r

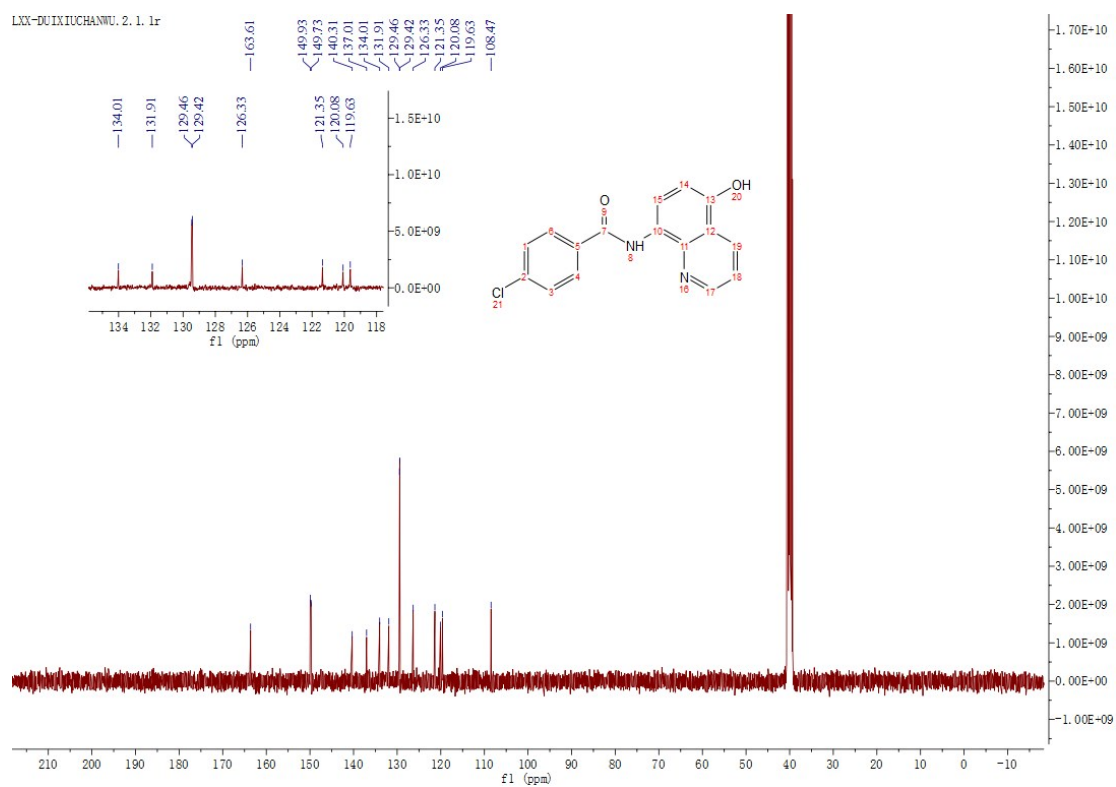
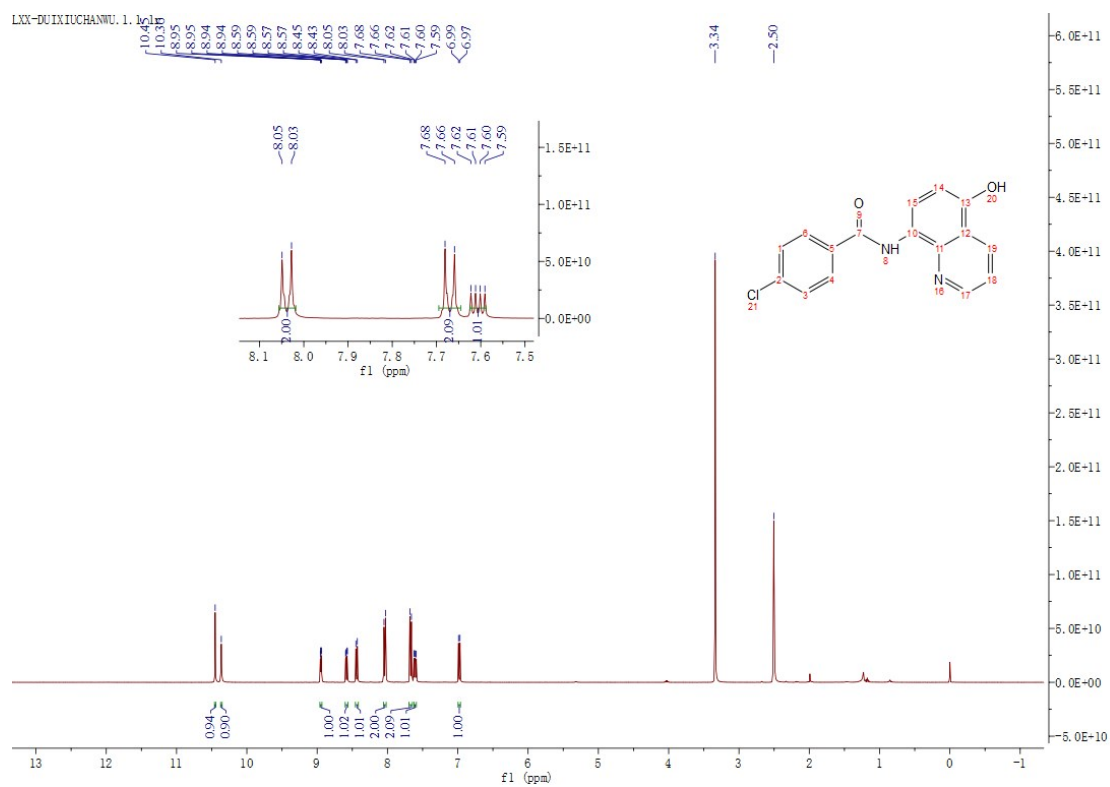


lxdduiFchanwu. 2. 1. 1r

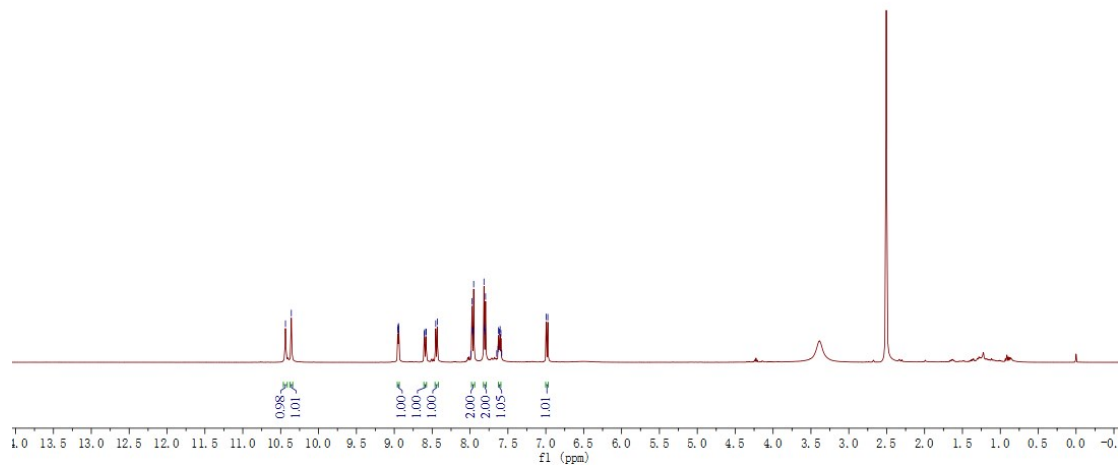
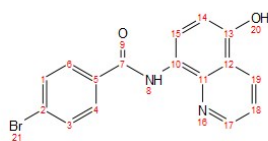


lxdduiFchanwu. 7. 1. 1r

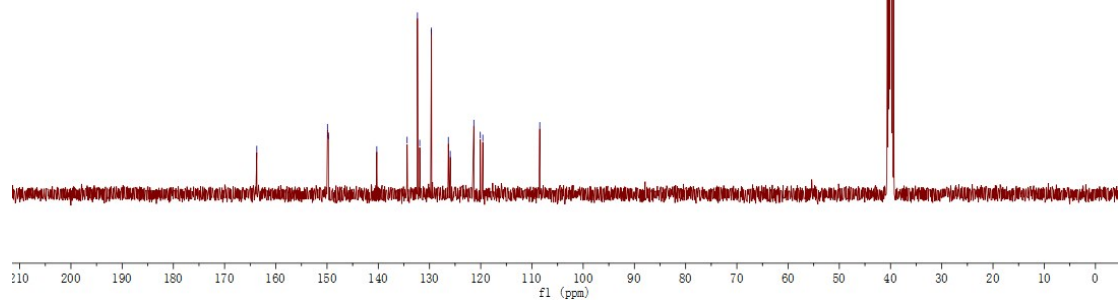
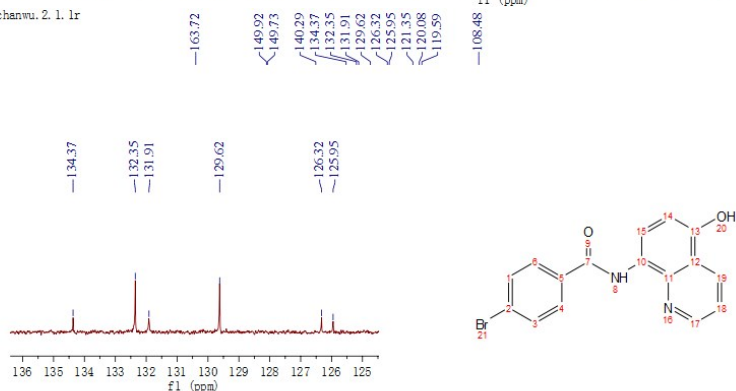


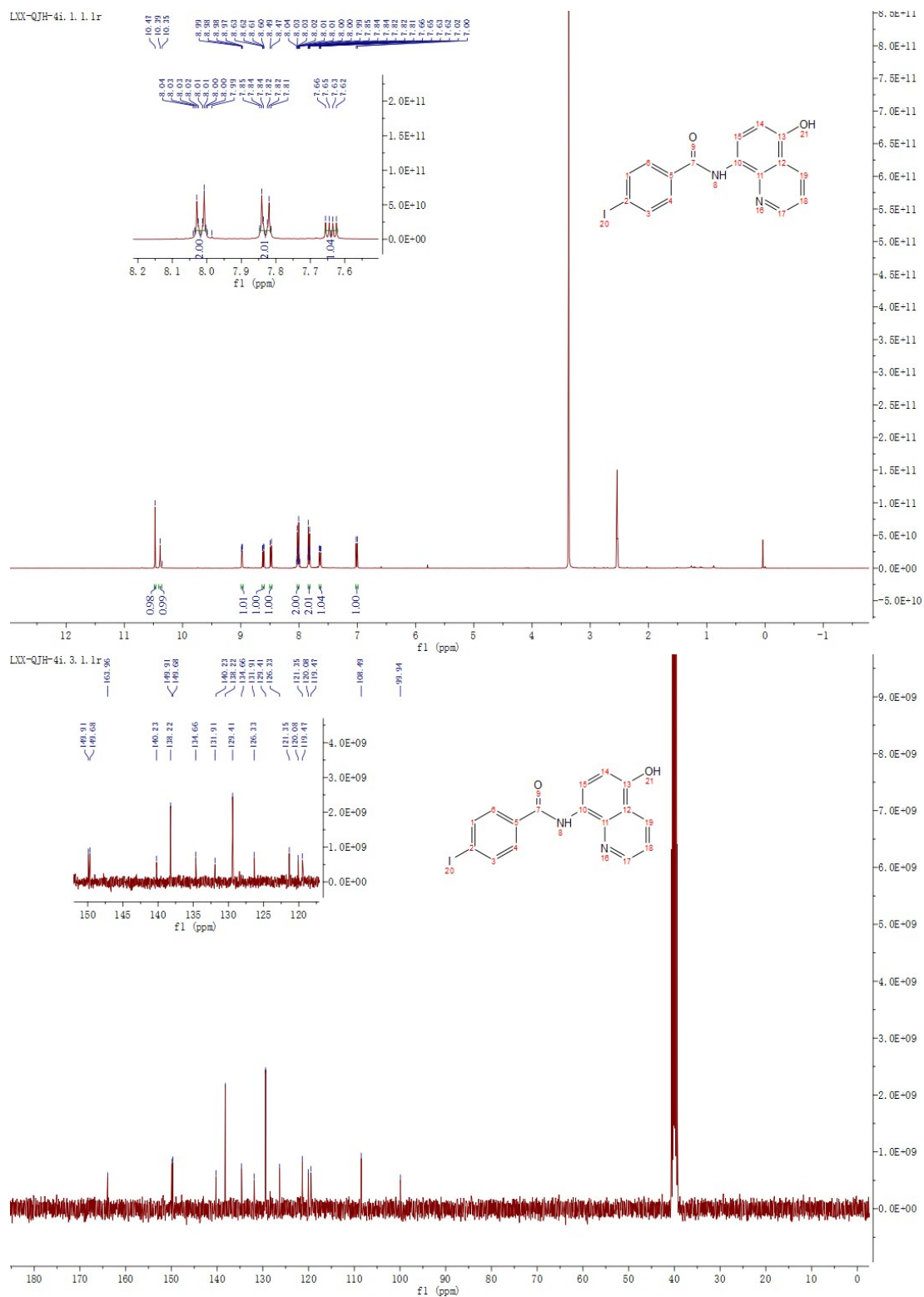


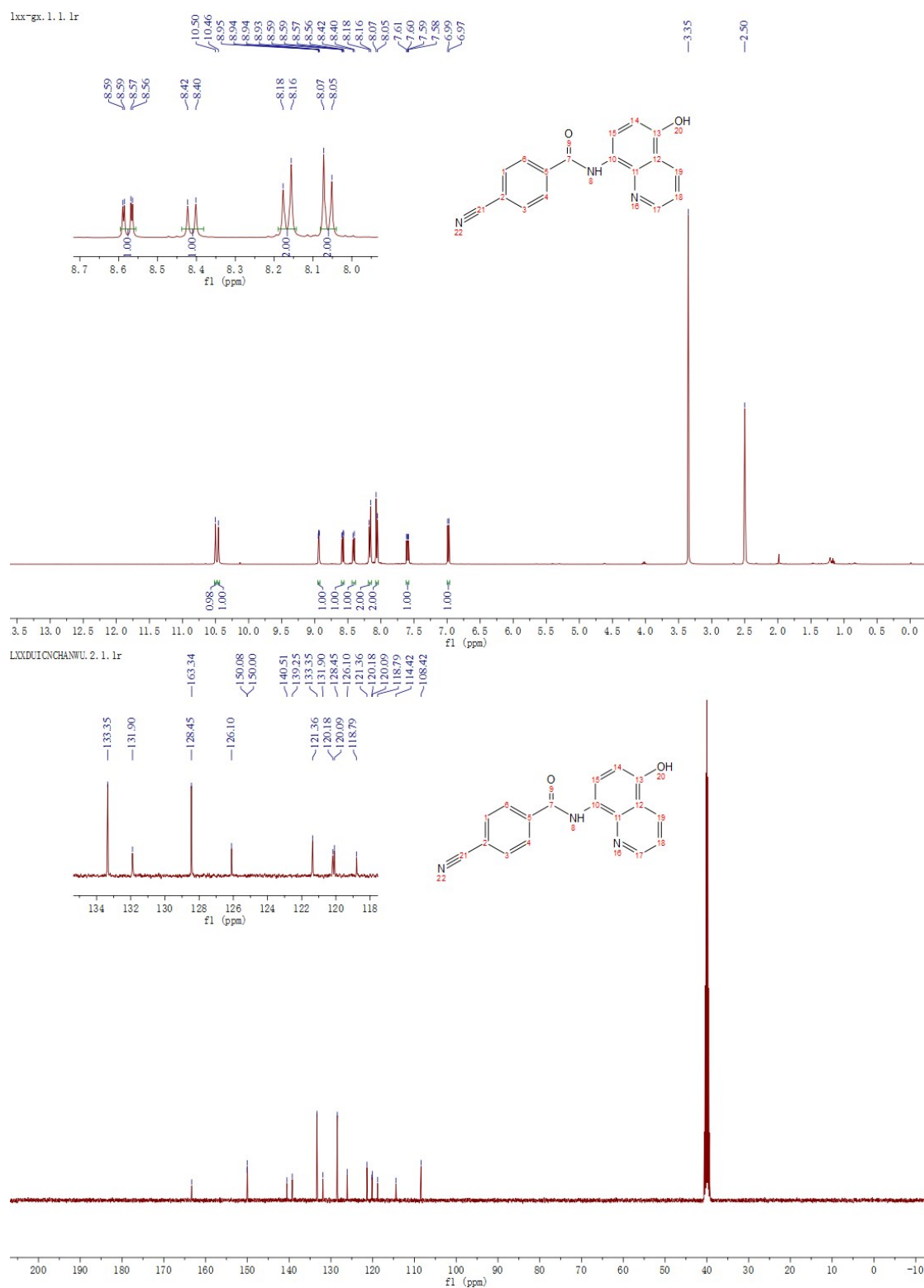
LXX-DUIXIUCHANWU.3.1.1r

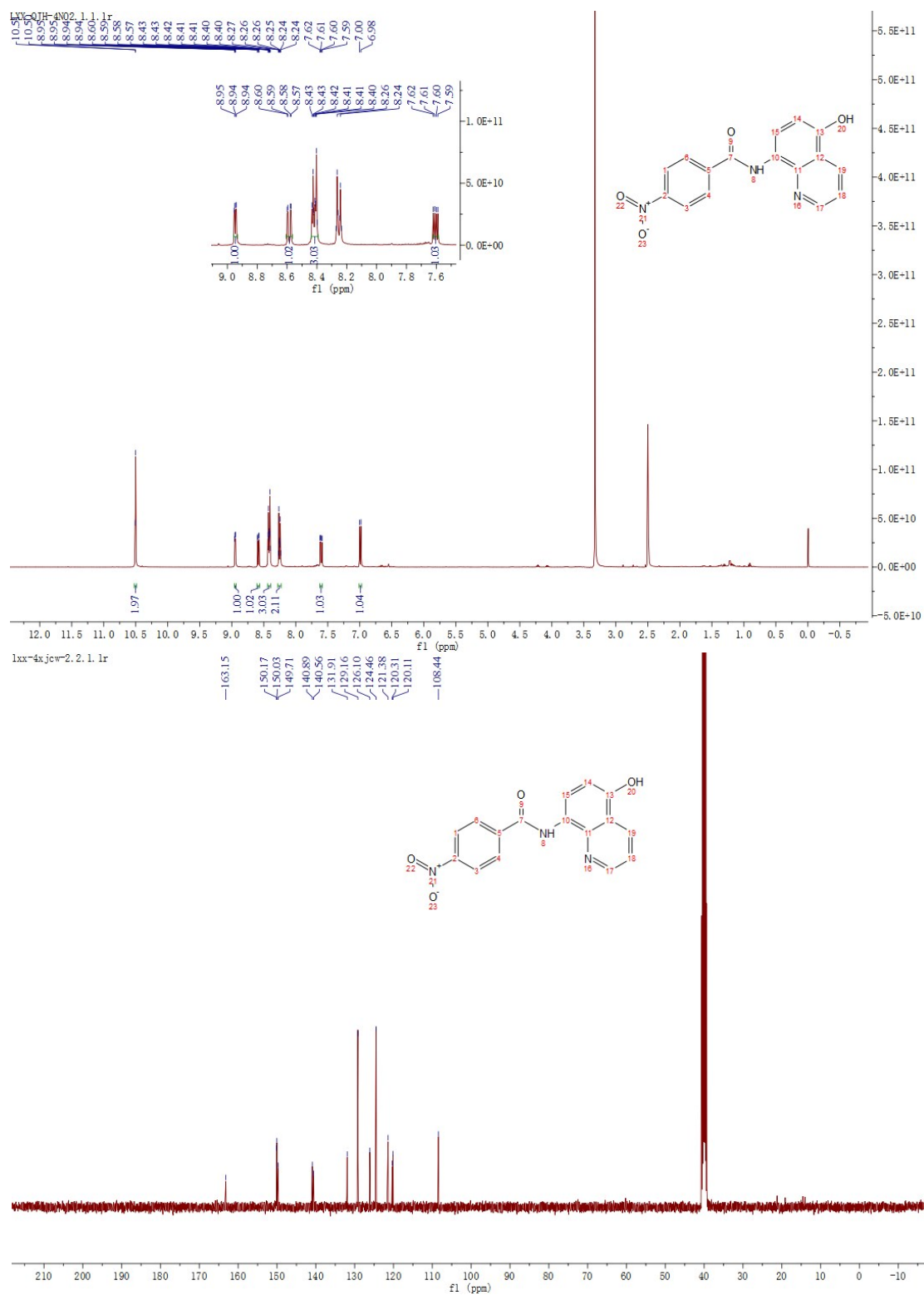


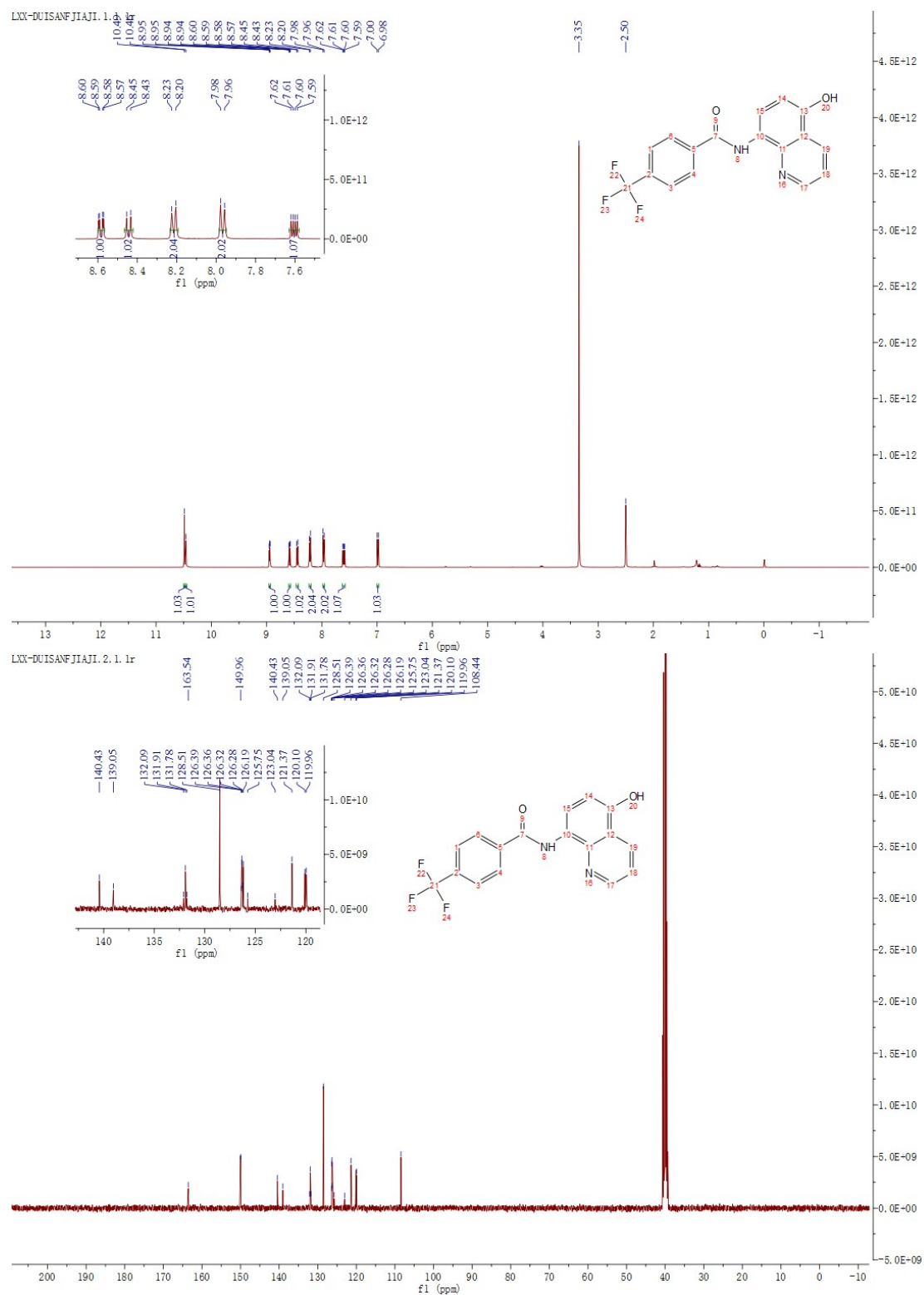
1xx-dbrchanwu.2.1.1r

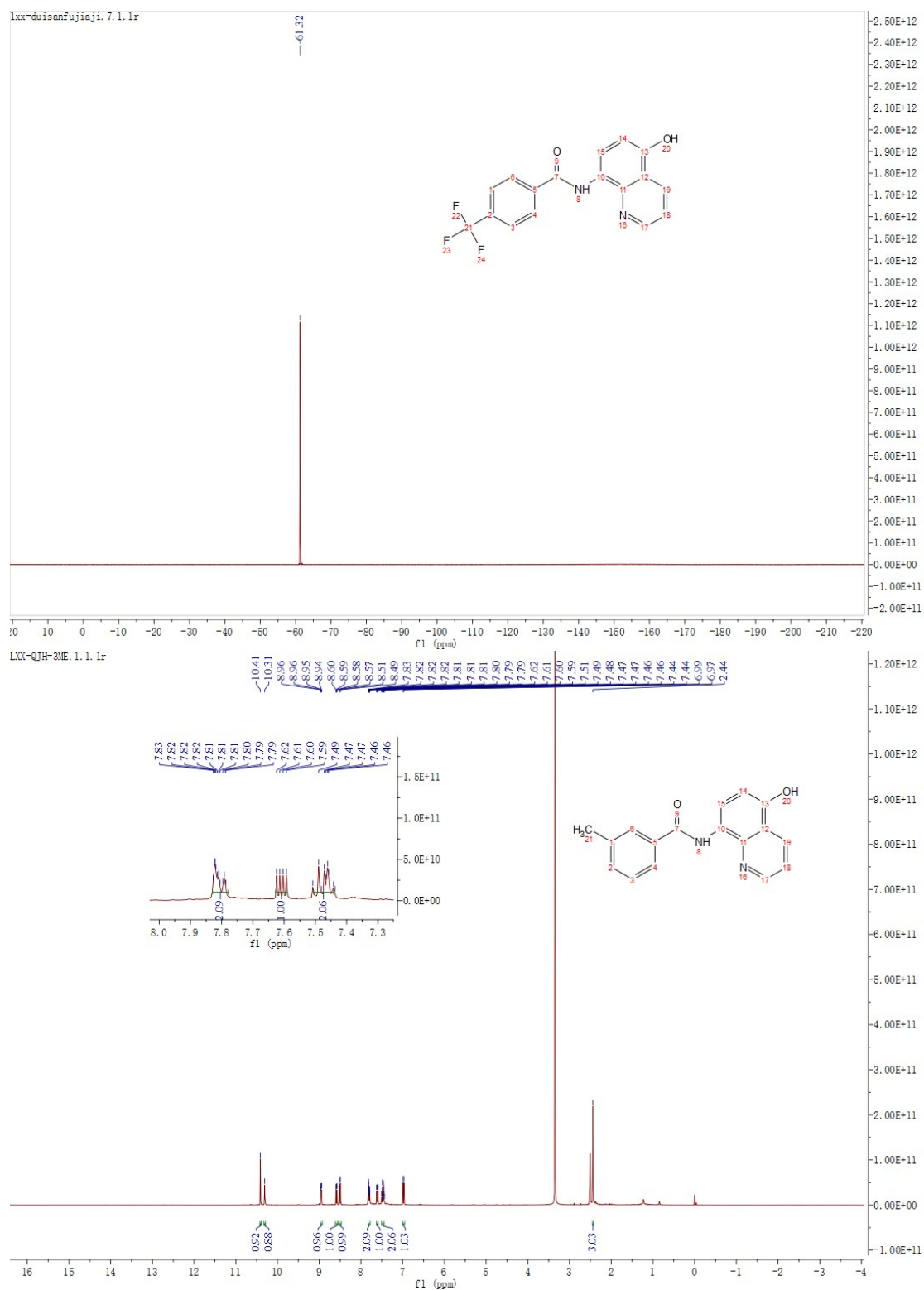


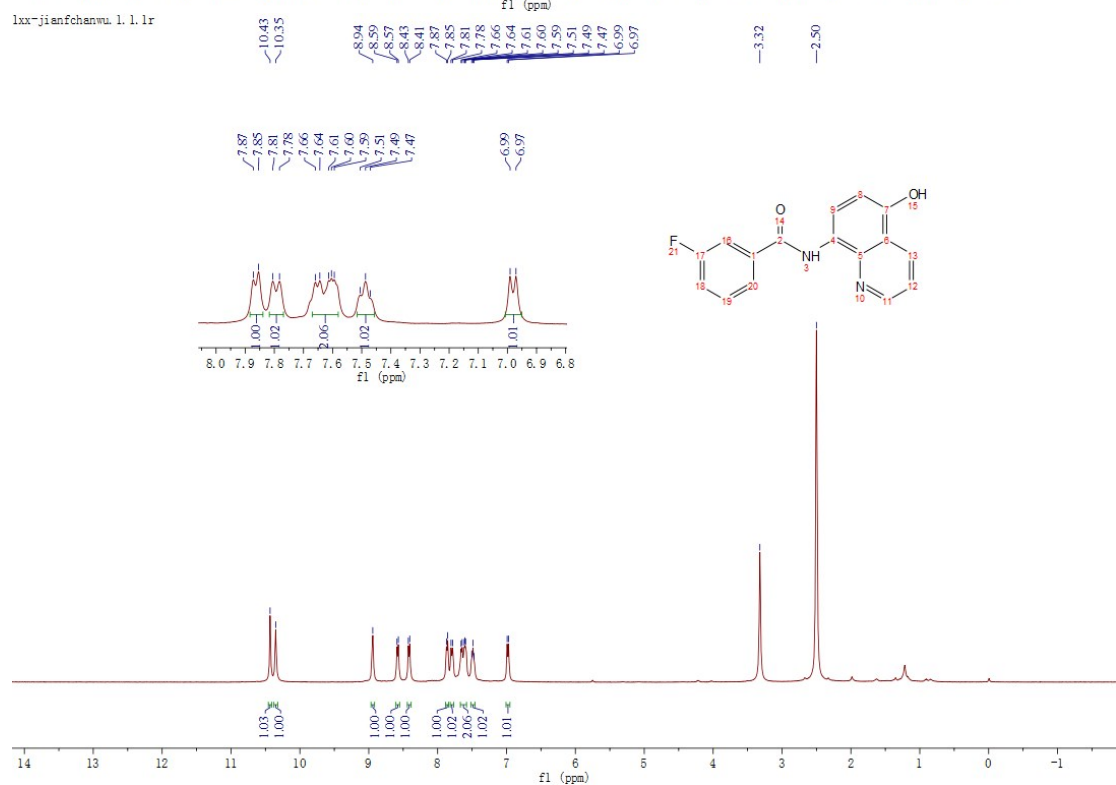
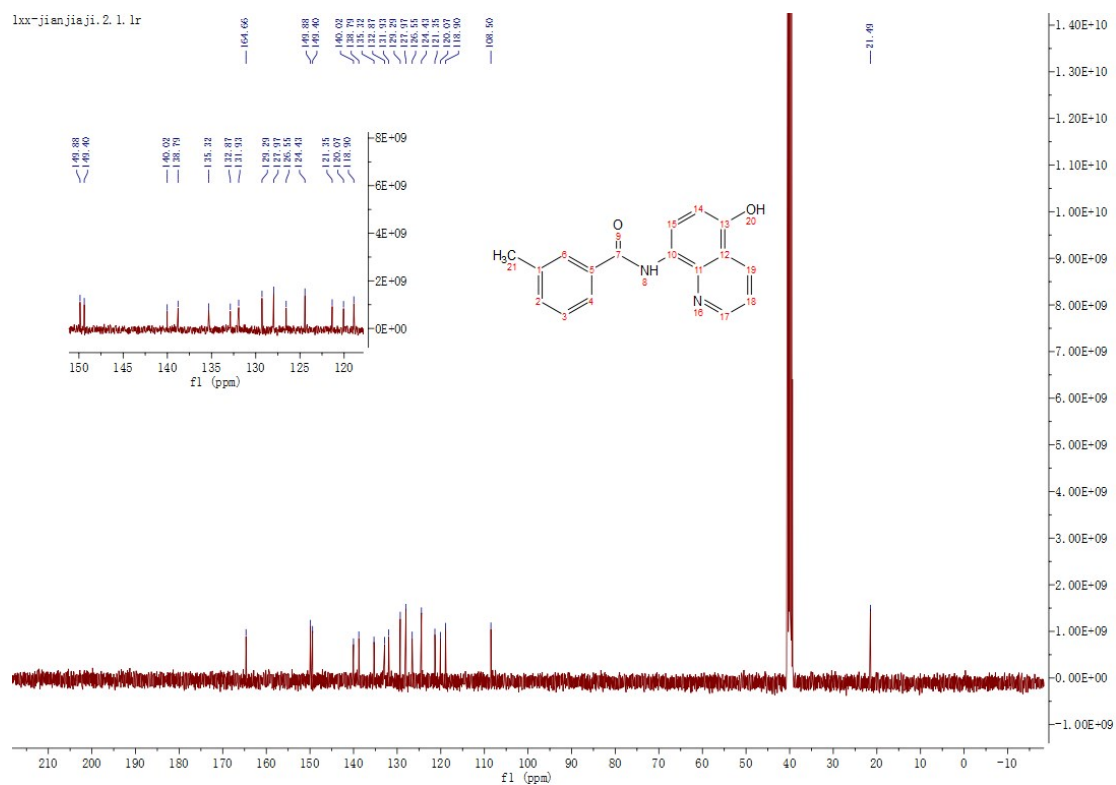




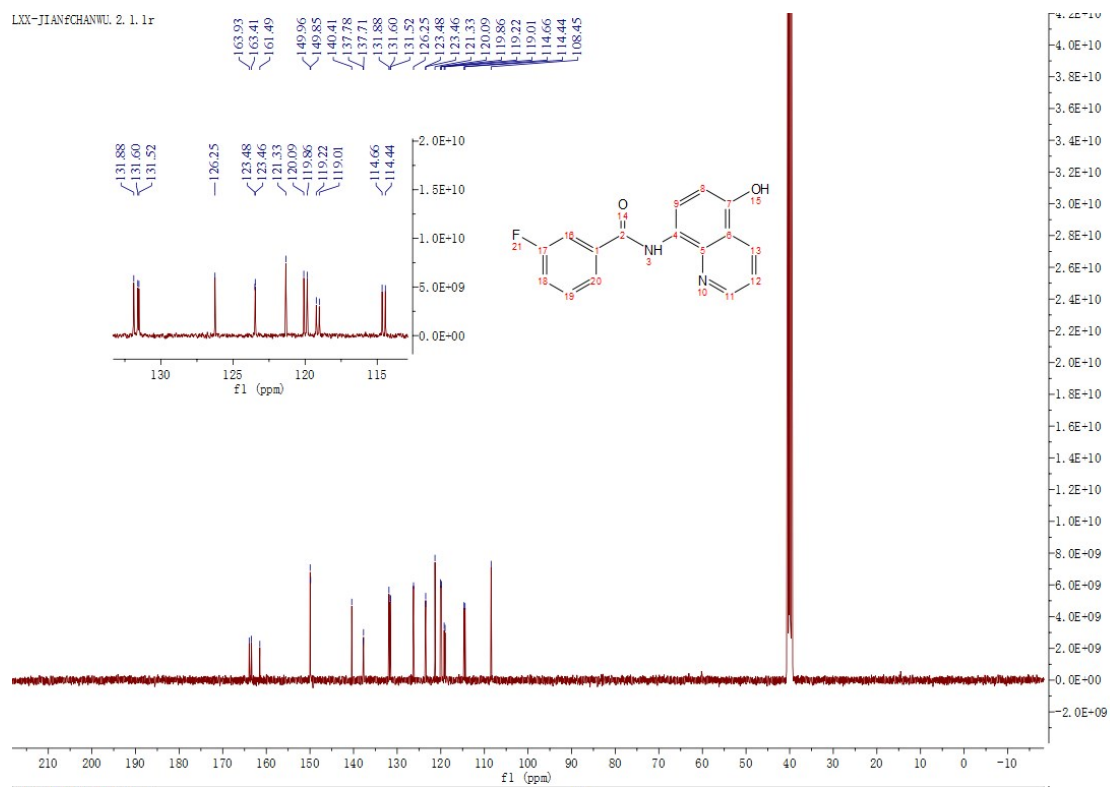




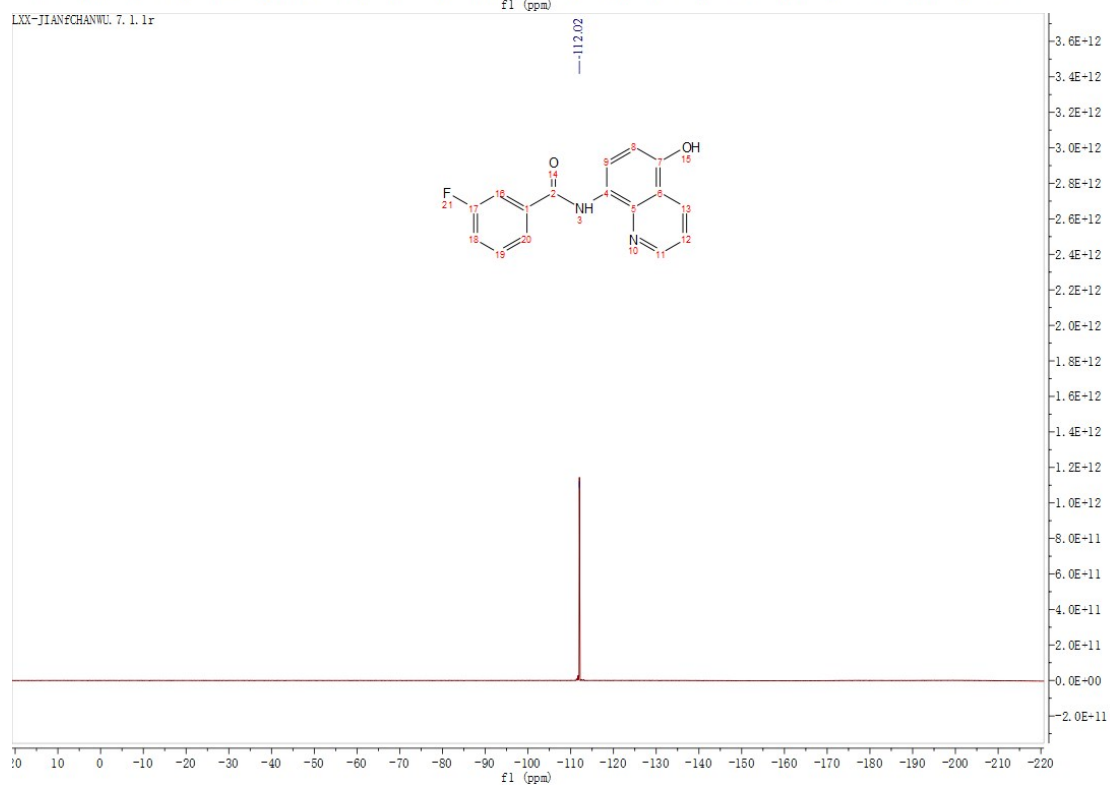


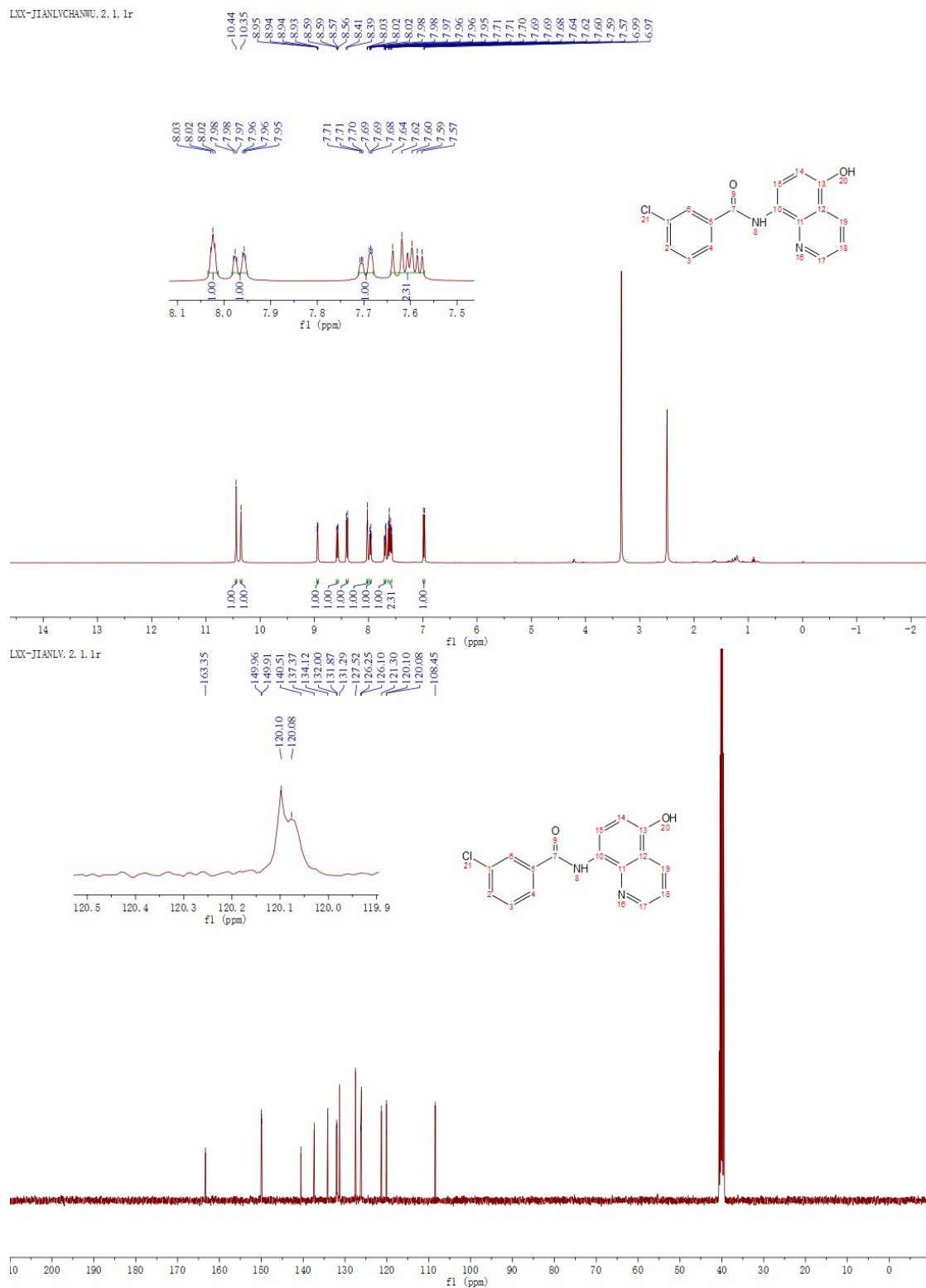


LXX-JIANFCHANWU. 2. 1. 1r

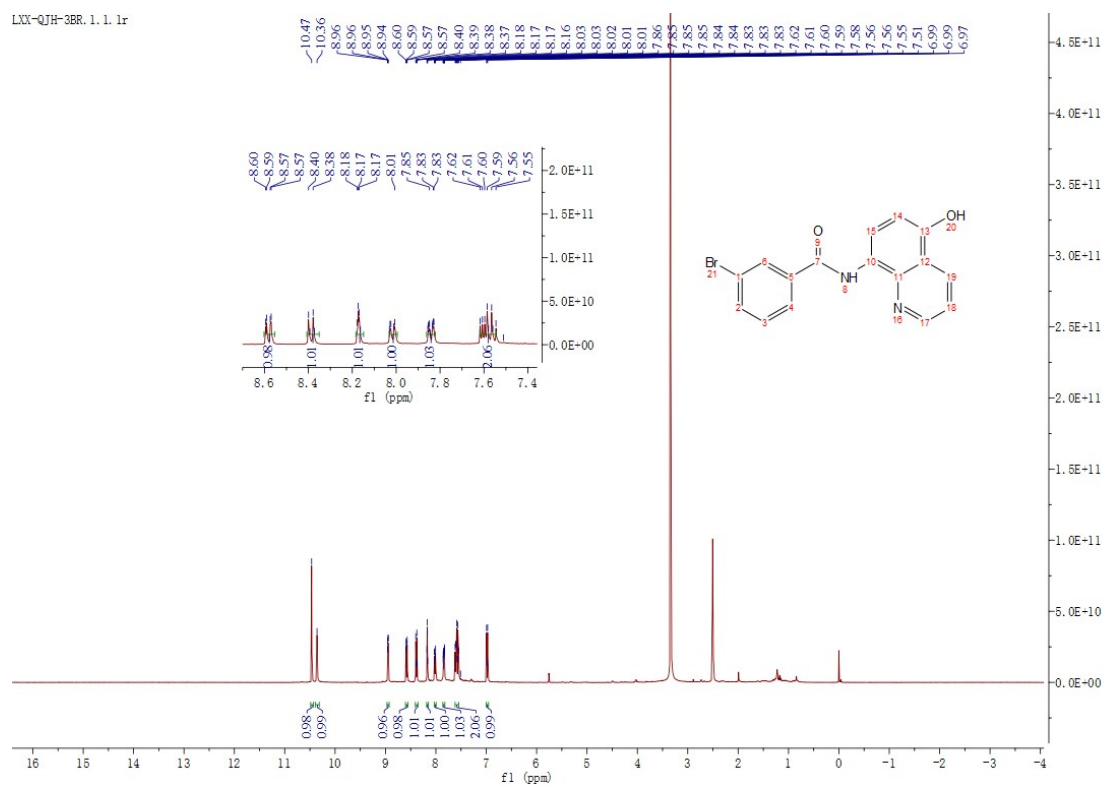


LXX-JIANFCHANWU. 7. 1. 1r

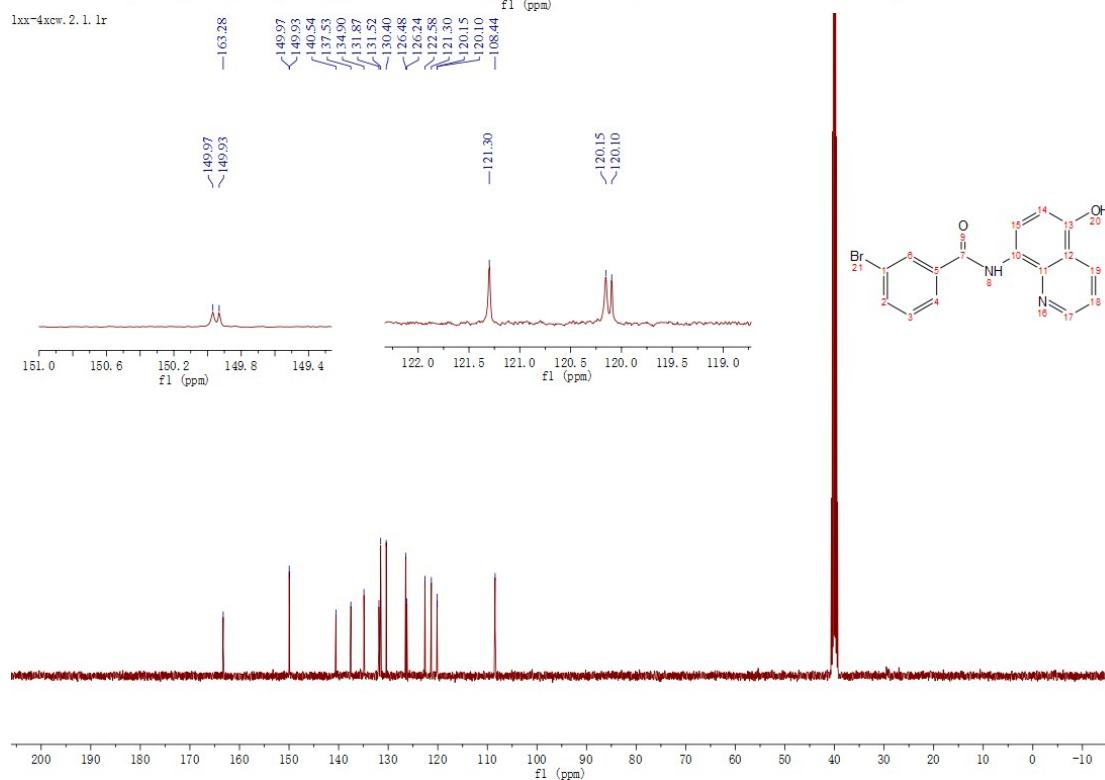




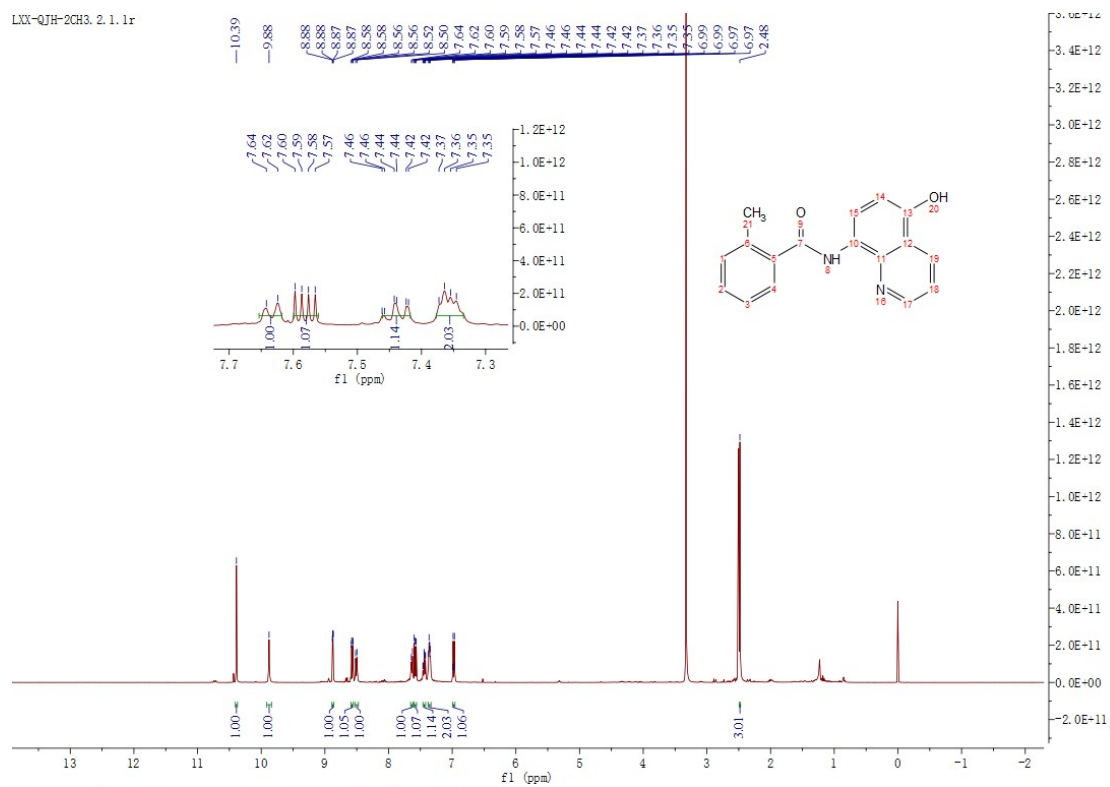
LXX-QJH-3BR. 1. 1. 1r



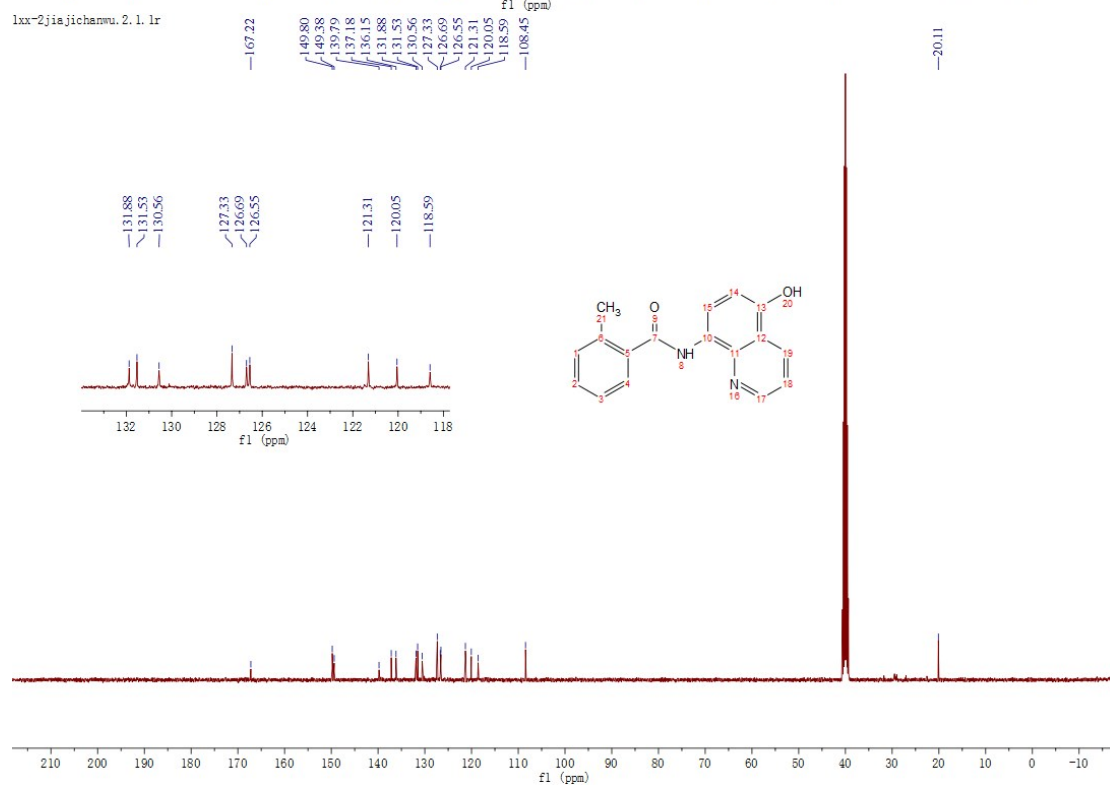
lxx-4xcv. 2. 1. 1r



LXX-QJH-2CH3. 2. 1. 1r



lxx-2jiajichanmu. 2. 1. 1r



1H NMR spectrum of compound 11 in CDCl₃.

Chemical structure of 11: O=C1NC2=CC=CC=C2N1c3ccccc3F

Peak list (ppm): 10.73, 10.71, 10.45, 8.94, 8.93, 8.93, 8.92, 8.66, 8.64, 8.59, 8.57, 8.57, 8.08, 8.06, 8.04, 8.04, 7.77, 7.77, 7.69, 7.68, 7.67, 7.67, 7.67, 7.66, 7.65, 7.65, 7.62, 7.61, 7.60, 7.59, 7.49, 7.49, 7.48, 7.47, 7.46, 7.46, 7.45, 7.44, 7.44, 7.43, 7.43, 7.41, 7.41, 6.98, 6.96.

Integration values: 0.97, 1.00, 1.00, 1.00, 1.00, 1.00, 1.00, 2.04, 0.97.

Chemical structure numbering: The structure is numbered 1-21. The benzotriazinone ring is numbered 1-10, and the phenyl ring is numbered 11-21. The fluorine atom is at position 20.

13C NMR spectrum of compound 1r in CDCl₃. The spectrum shows peaks from 150 to 40 ppm. An inset shows the aromatic region from 150 to 116 ppm. The chemical structure of 1r is shown with atom numbering 1-21. The main spectrum has a list of peak values on the right: 161.39, 160.68, 158.94, 149.91, 149.44, 139.40, 134.88, 134.39, 131.95, 131.71, 131.69, 126.65, 125.76, 125.73, 122.40, 121.48, 120.02, 118.39, 117.15, 116.91, 108.54. The inset has a list of peak values on the left: 149.91, 149.44, 139.40, 134.88, 134.39, 131.95, 131.71, 131.69, 126.65, 125.76, 125.73, 122.40, 121.48, 120.02, 118.39, 117.15, 116.91.

1xx-2f.2.1.1r

-112.95

Chemical structure: 2-(2-fluorophenyl)-2H-1,2,3-triazol-3-ol. The structure is shown with atom numbering: 1-6 for the phenyl ring, 7-8 for the triazole ring, and 9-10 for the hydroxyl group. The peak is labeled with its chemical shift, -112.95.

10.44
10.13
8.89
8.88
8.87
8.87
8.58
8.58
8.56
8.56
8.52
8.50
7.77
7.77
7.76
7.75
7.62
7.60
7.60
7.58
7.58
7.57
7.57
7.56
7.56
7.54
7.53
7.52
7.51
7.51
7.49
7.49
6.99
6.97

6.0E-11
5.0E-11
4.0E-11
3.0E-11
2.0E-11
1.0E-11
0.0E+00

7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9

f1 (ppm)

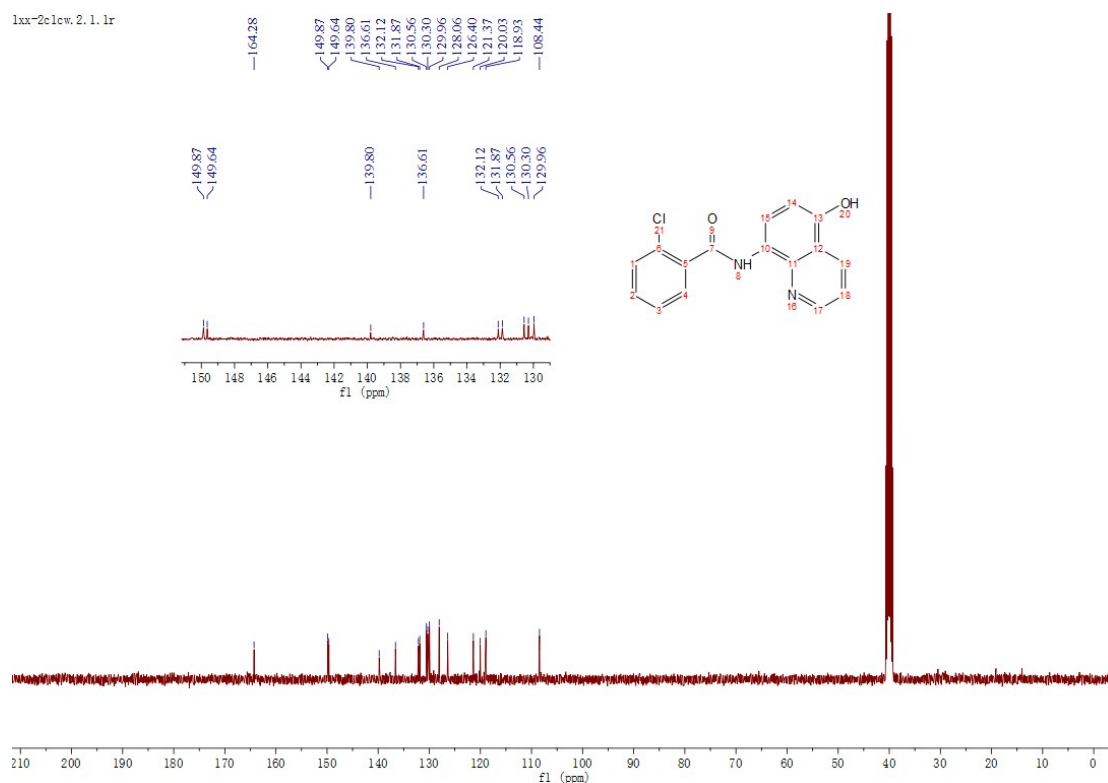
1.00
1.01
1.00
1.00
1.01
1.00
3.03
1.09
1.05

13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2

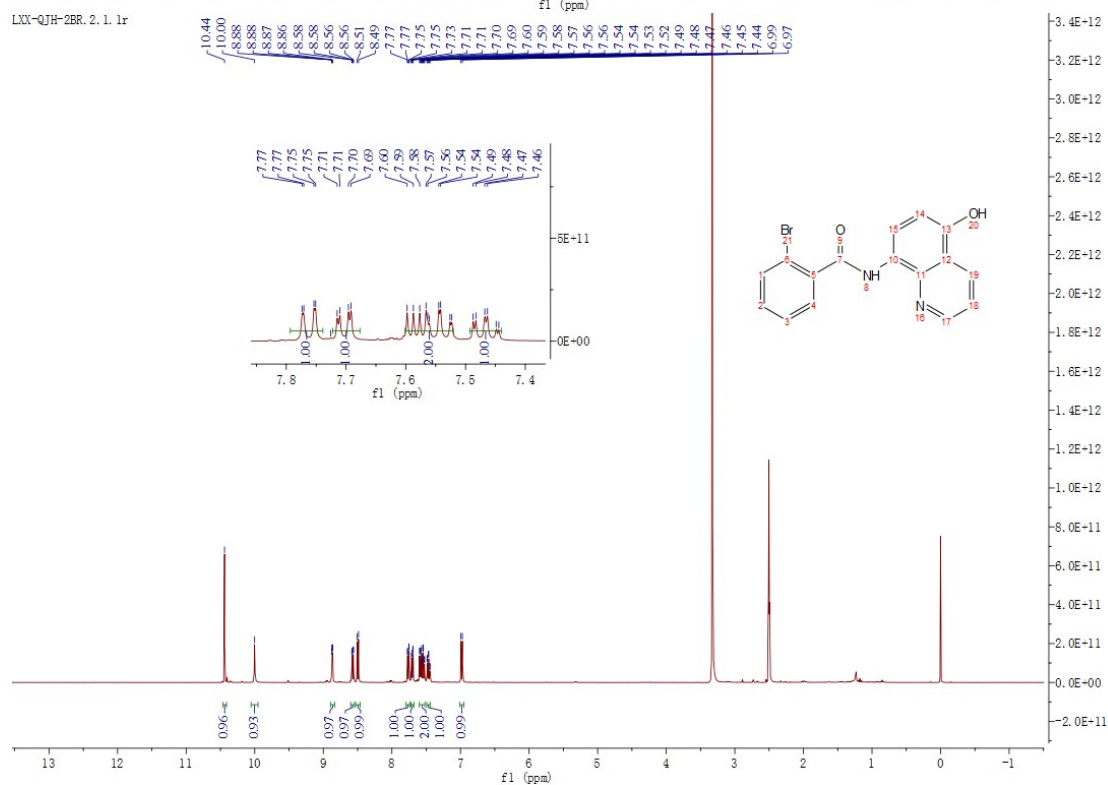
f1 (ppm)

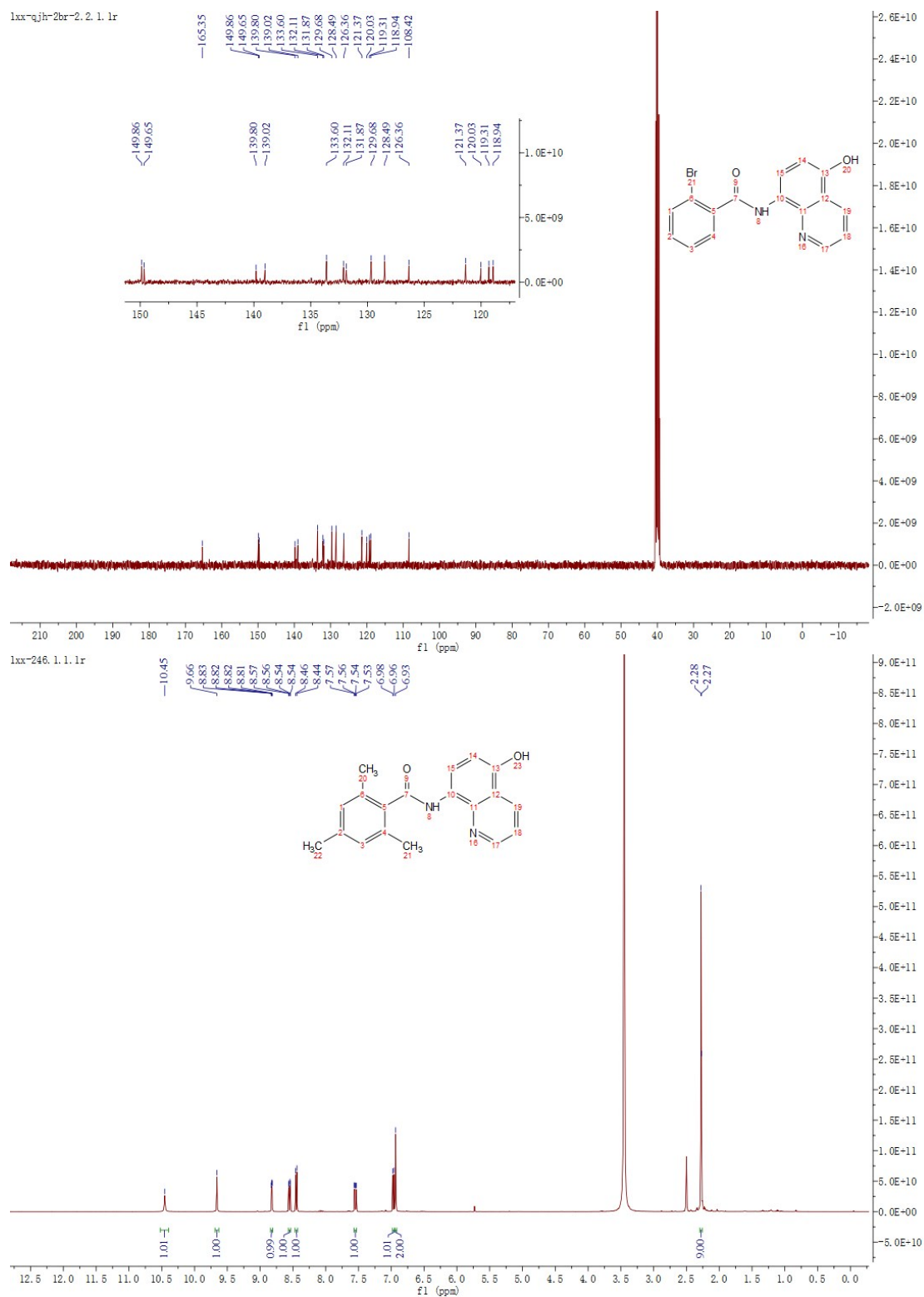
Chemical structure of 2c: Oc1ccccc1NC(=O)c2ccccc2Cl

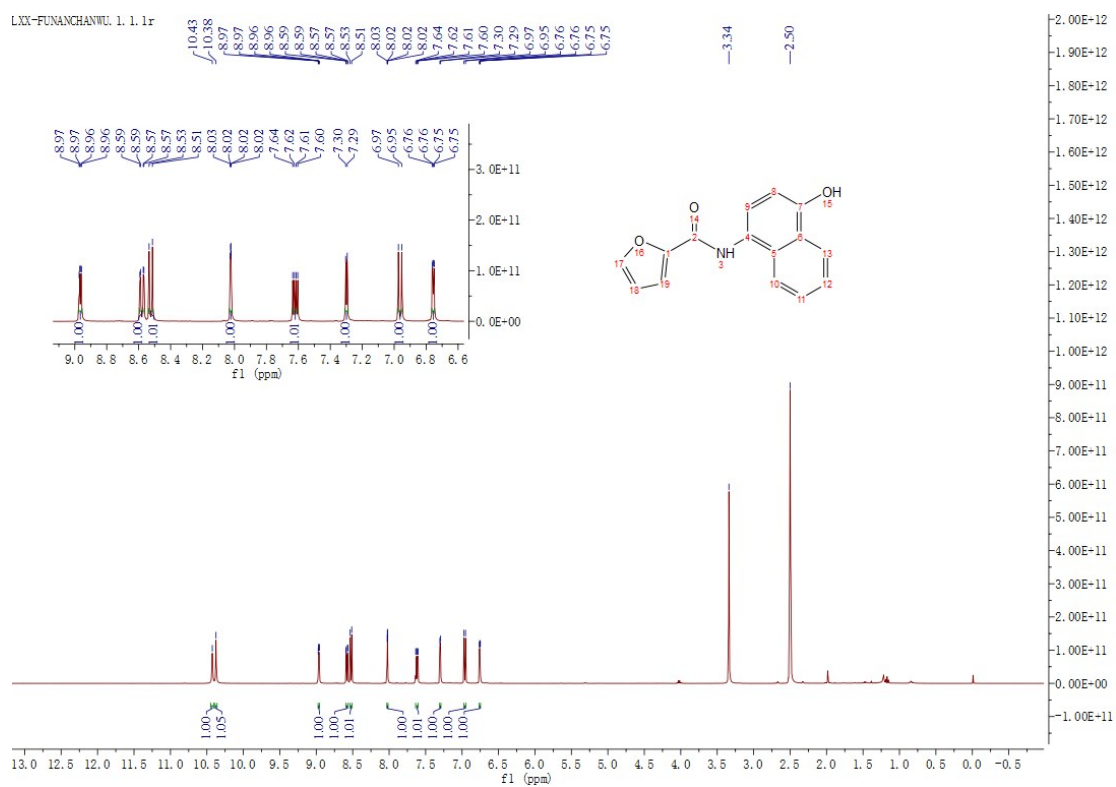
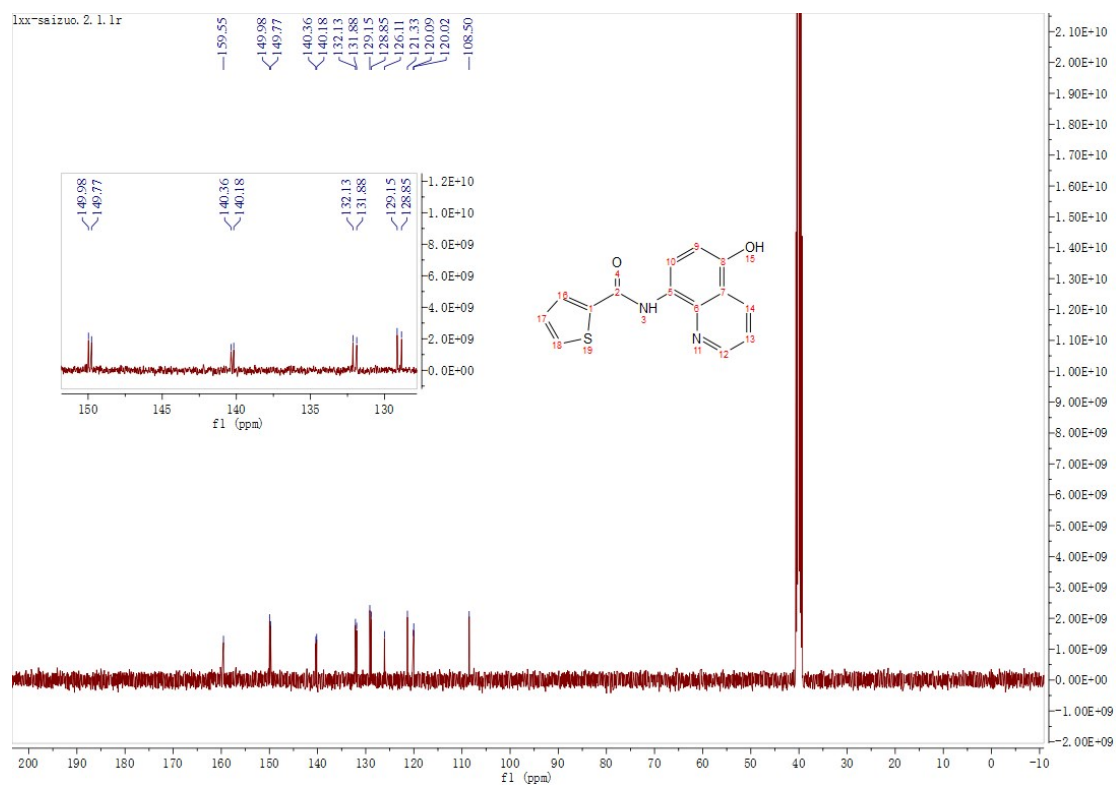
lxx-2c1cw.2.1.1r



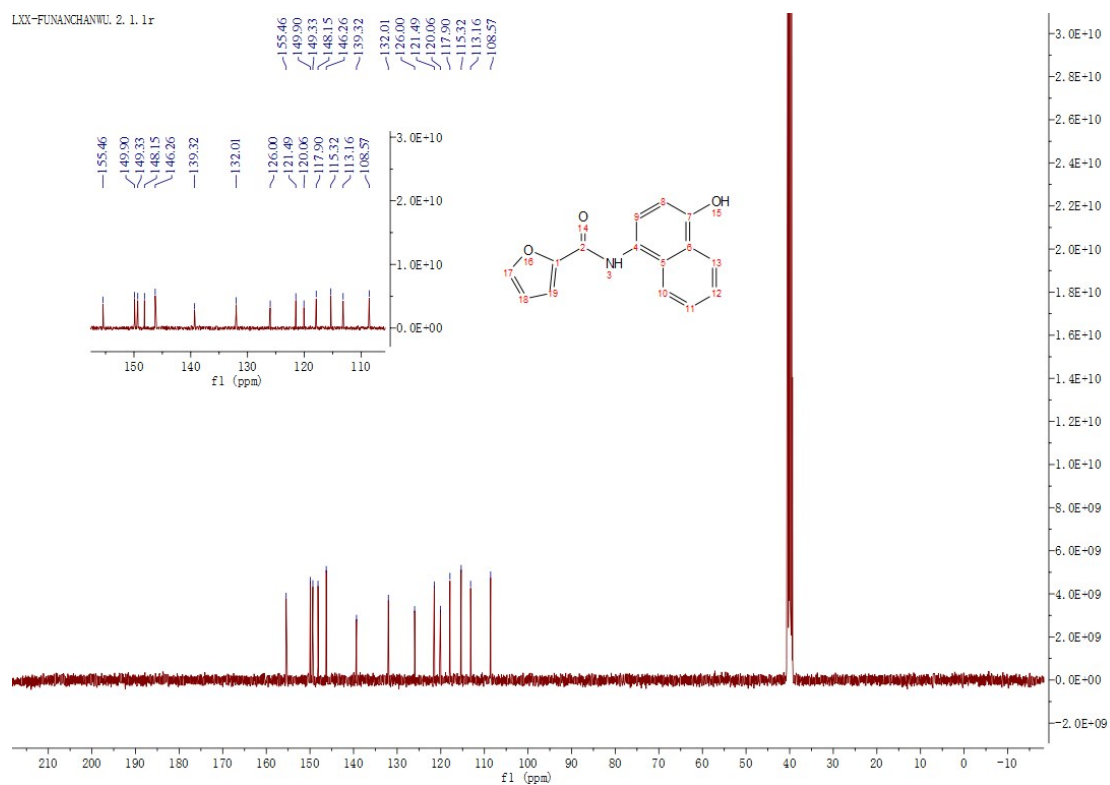
LXV-QJH-2BR.2.1.1r





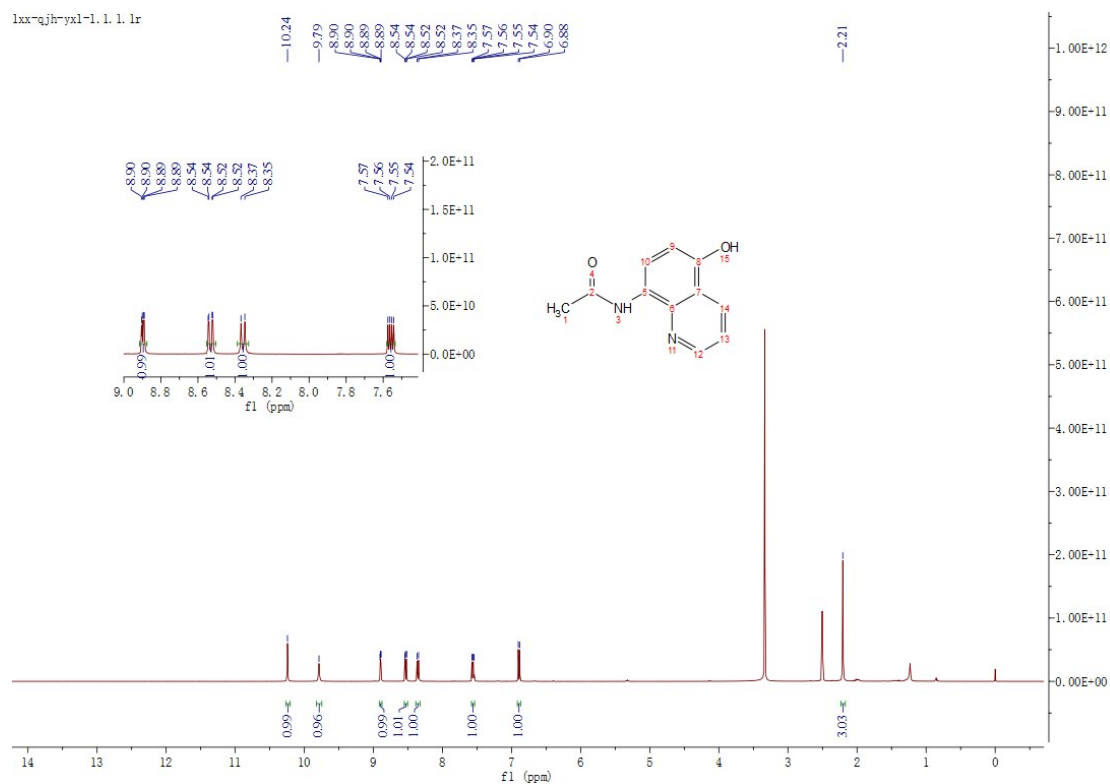


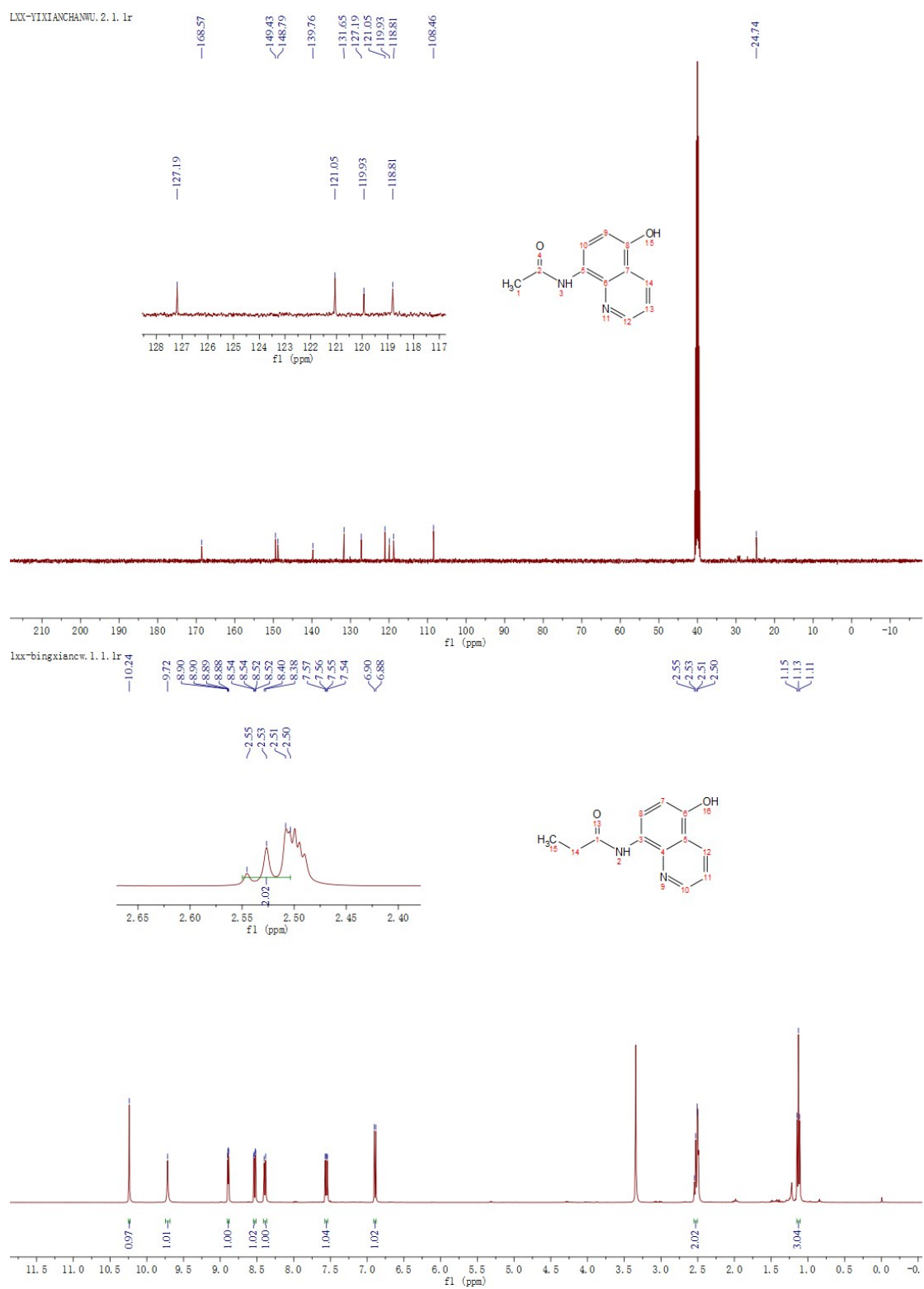
LXX-FUNANCHANWU. 2. 1. 1r



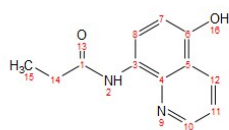
10.5 NMR-Spectra of 4

lxx-qjhr-yxl-1. 1. 1. 1r

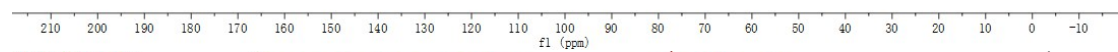




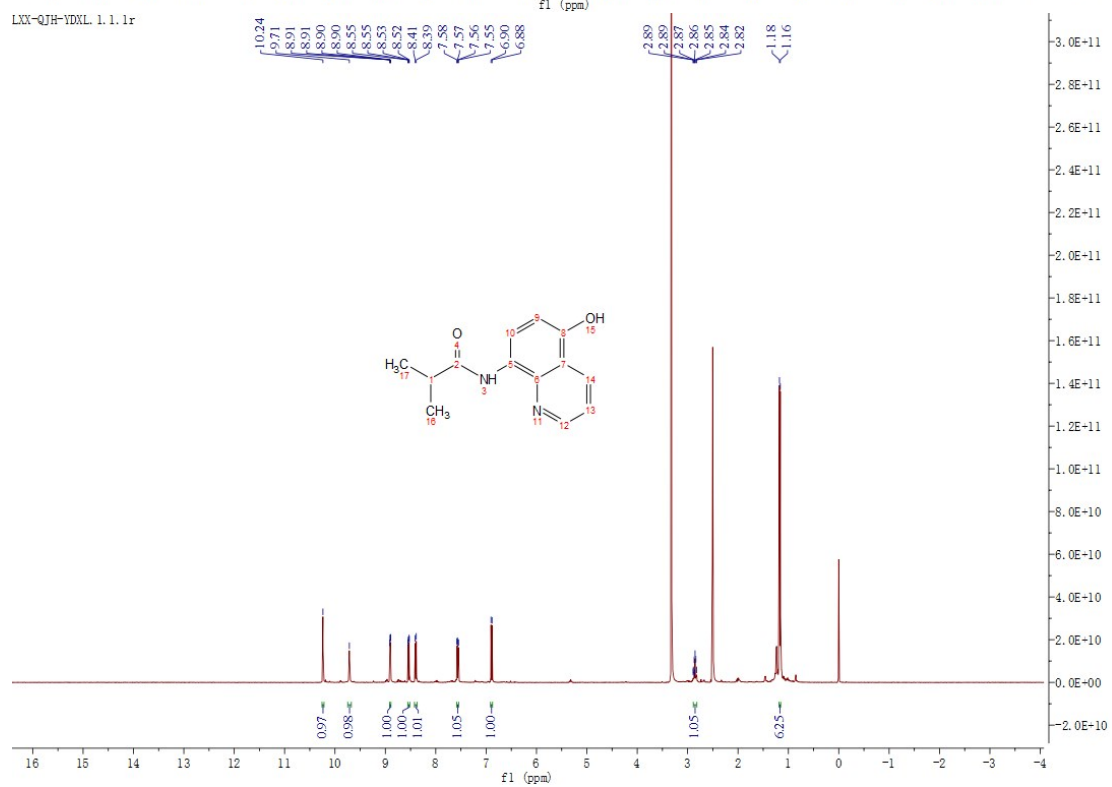
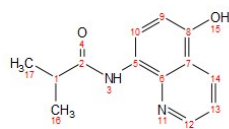
—108.48



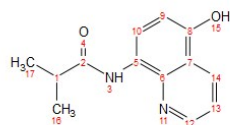
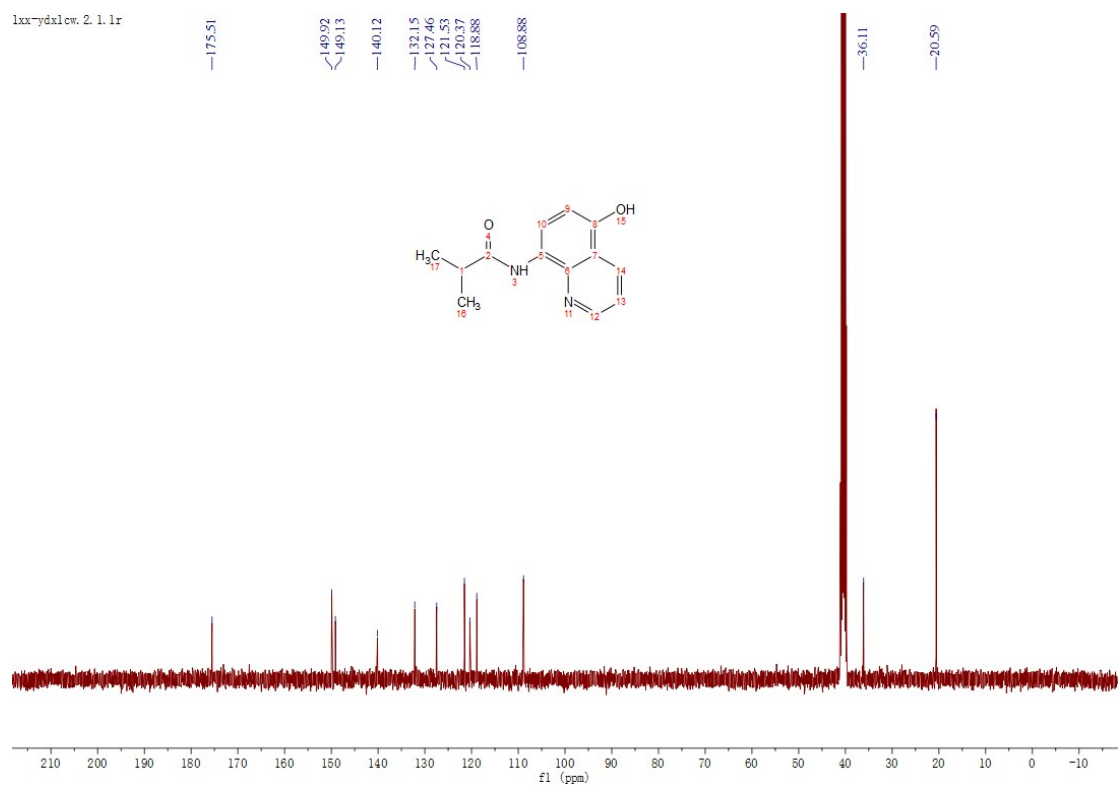
—10.29



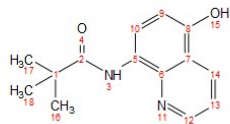
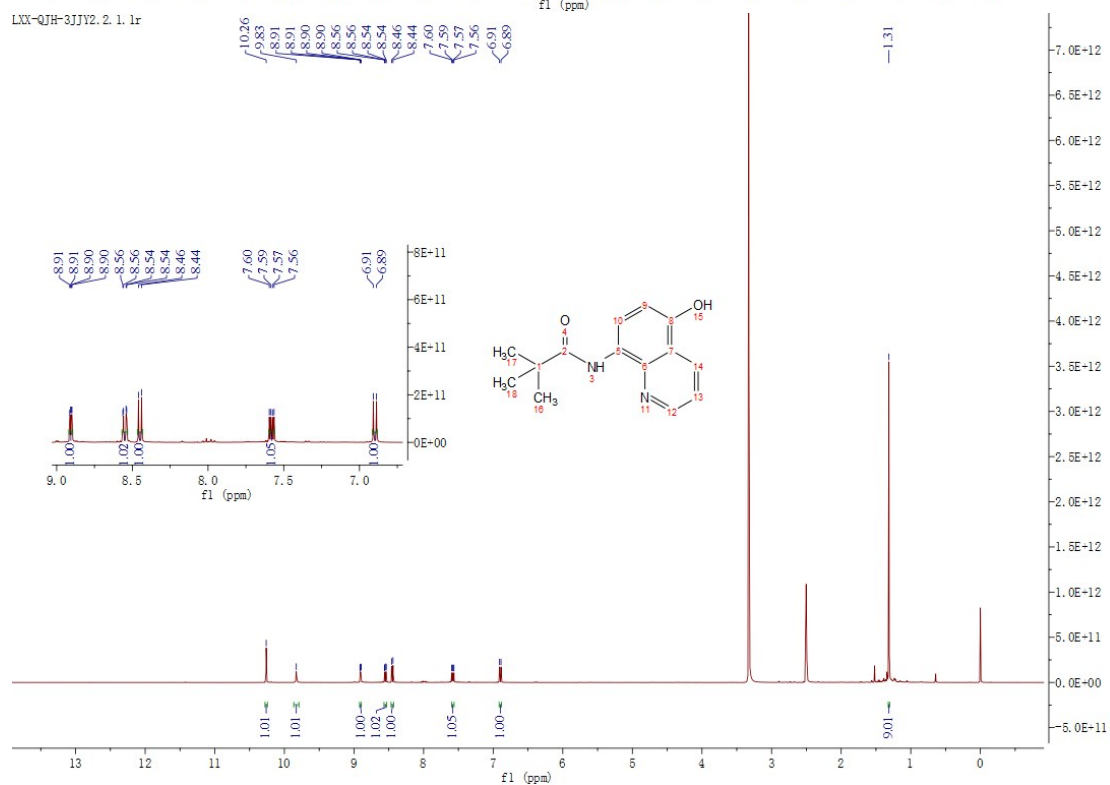
LXX-QJH-YDXL. 1.1.1r



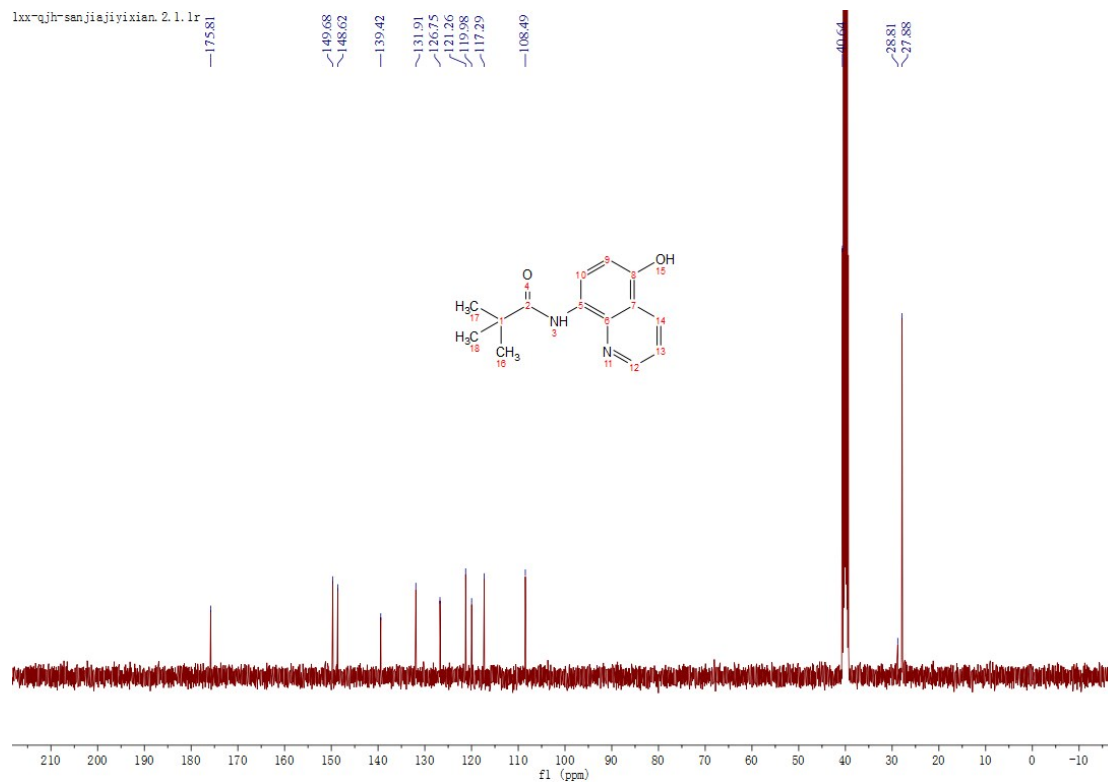
lxx-ydxlcw. 2. 1. 1r



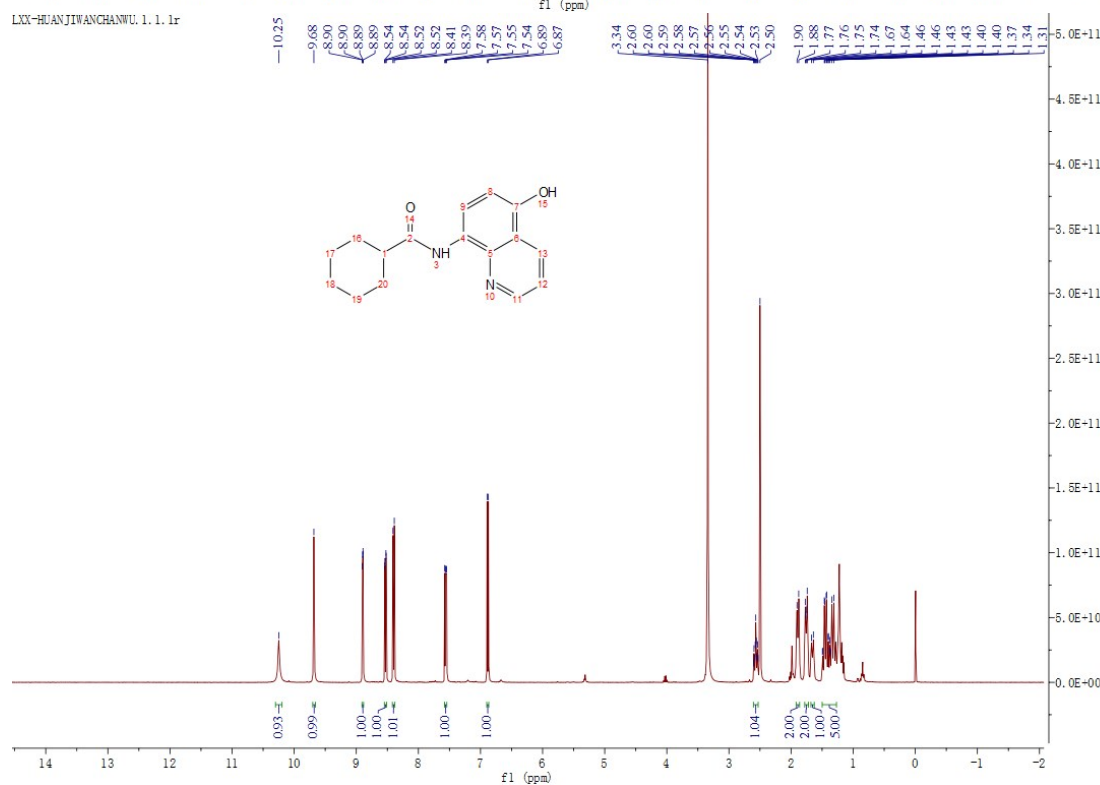
LXX-QJH-3JJY2.2.1.1r

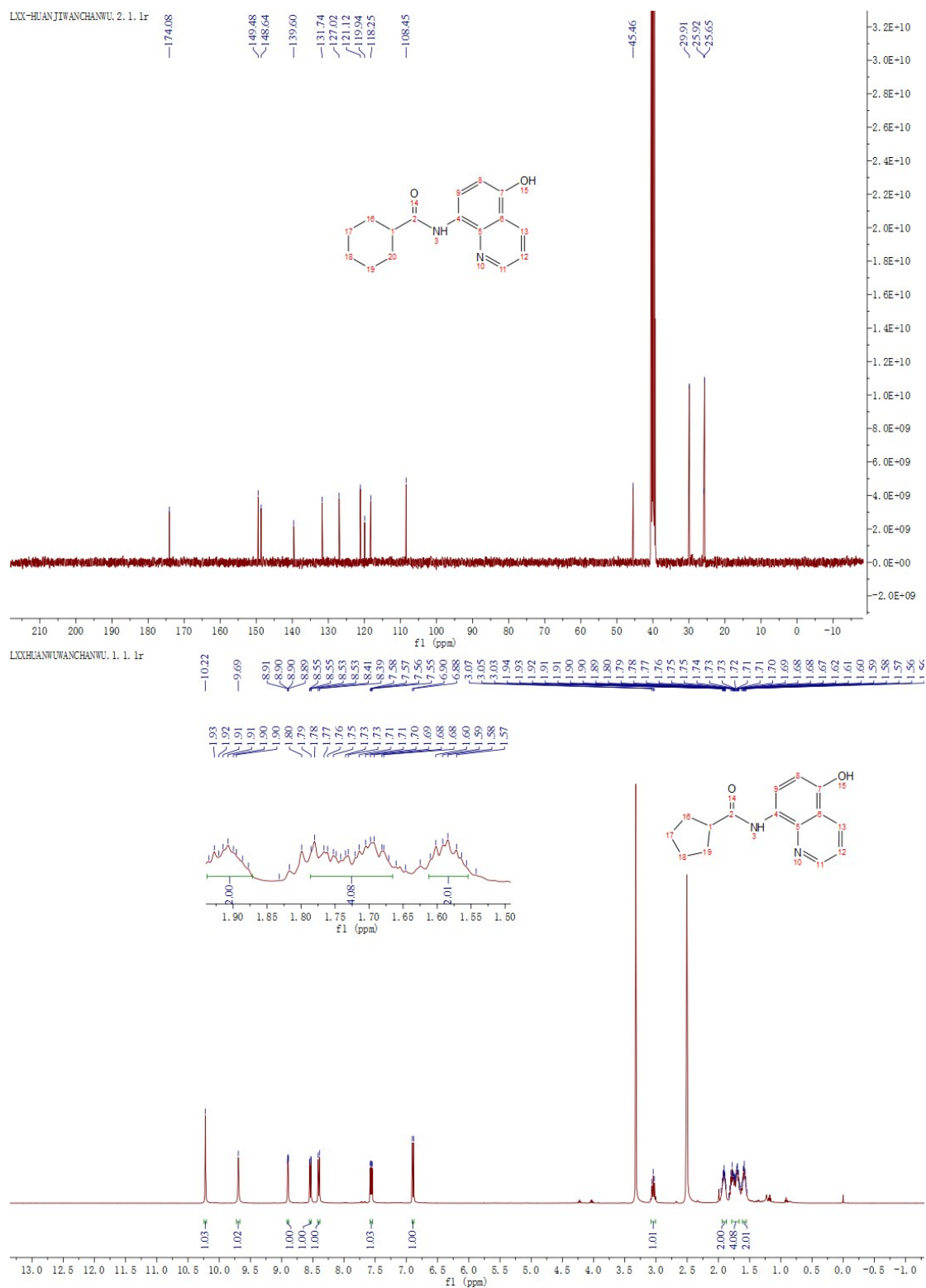


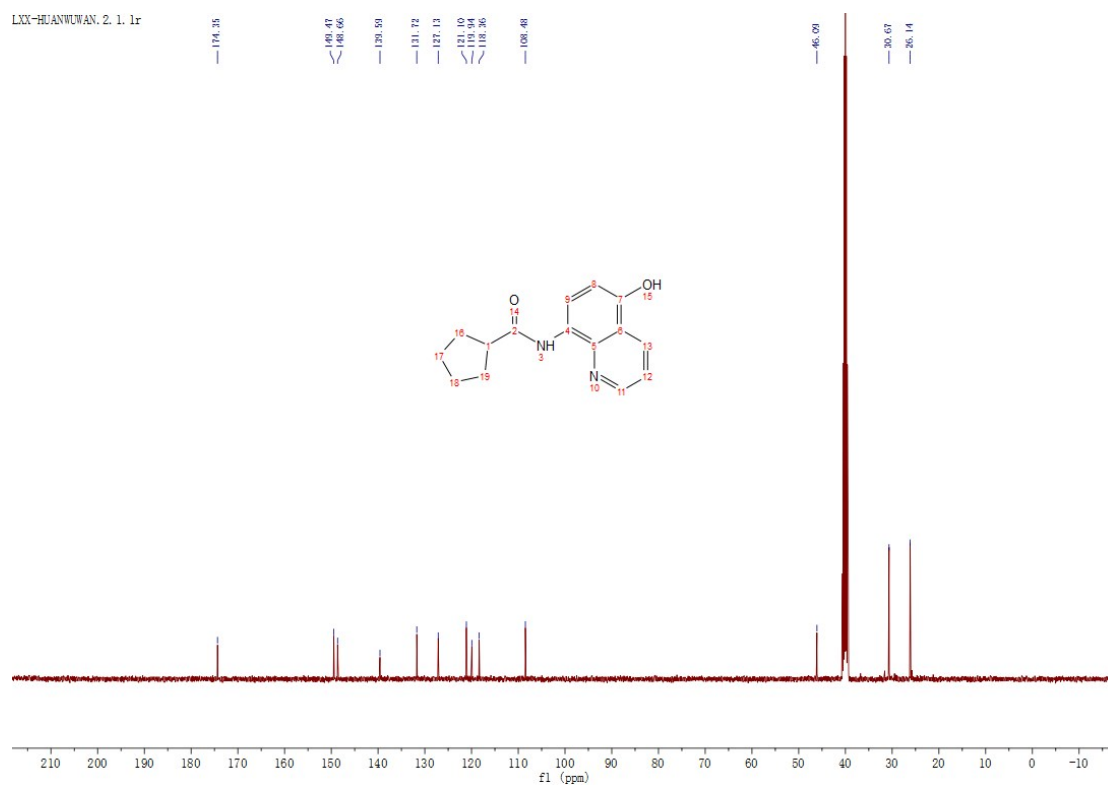
lxx-qjh-sanjiajiyixian. 2.1.1r



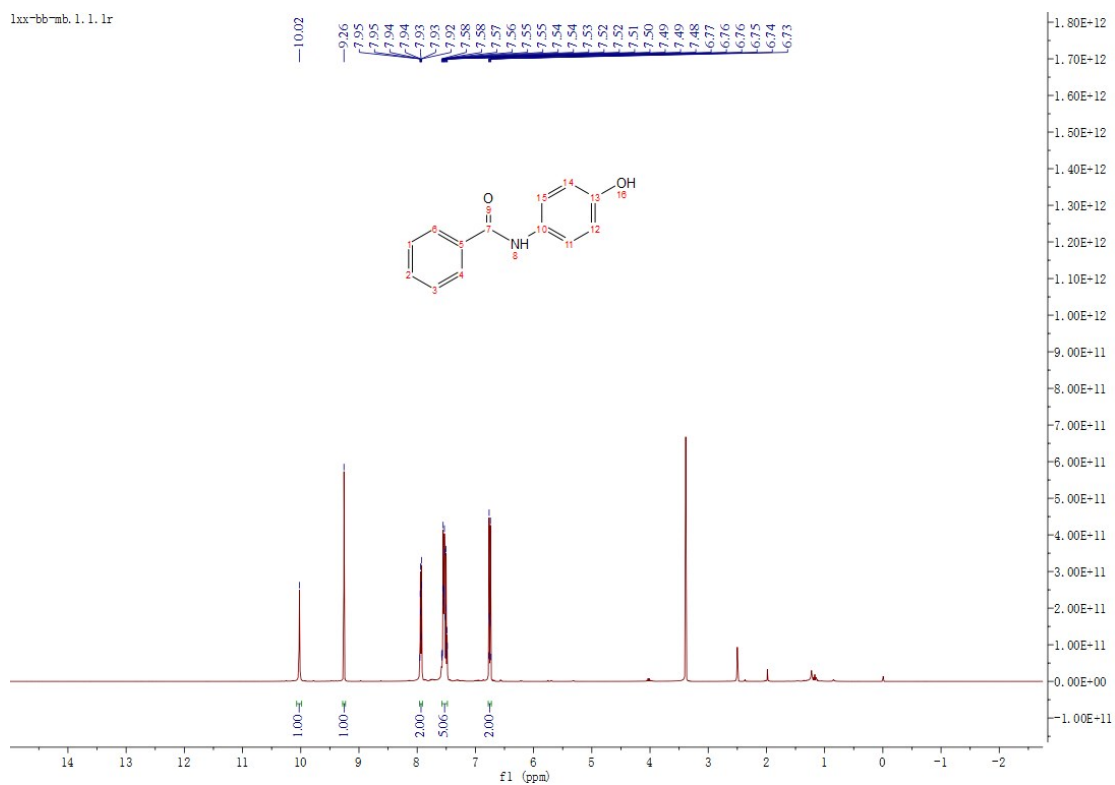
LXX-HUANJIWANCHANWU. 1.1.1r

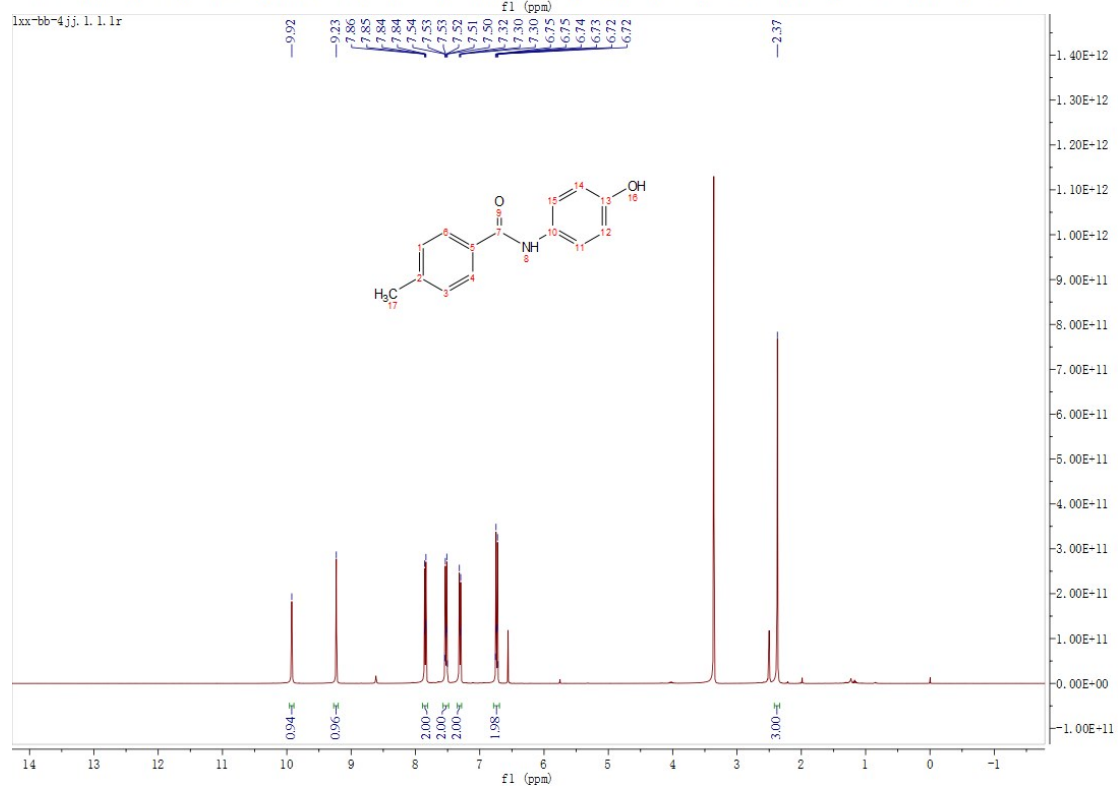
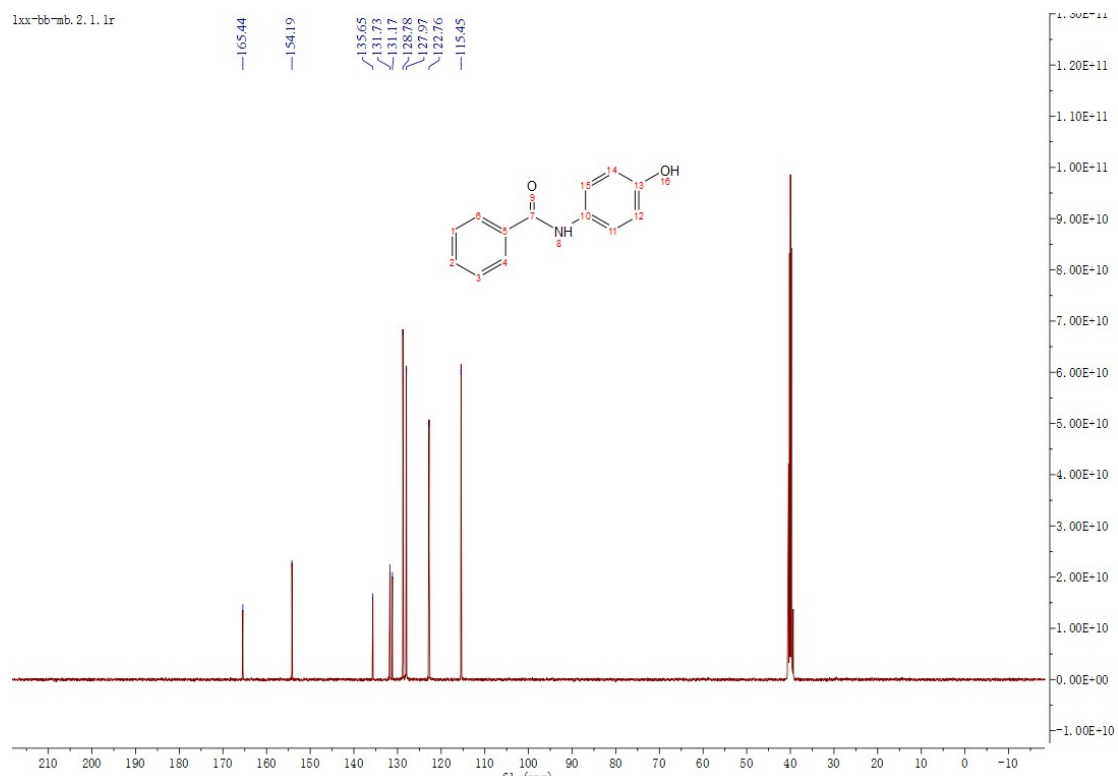


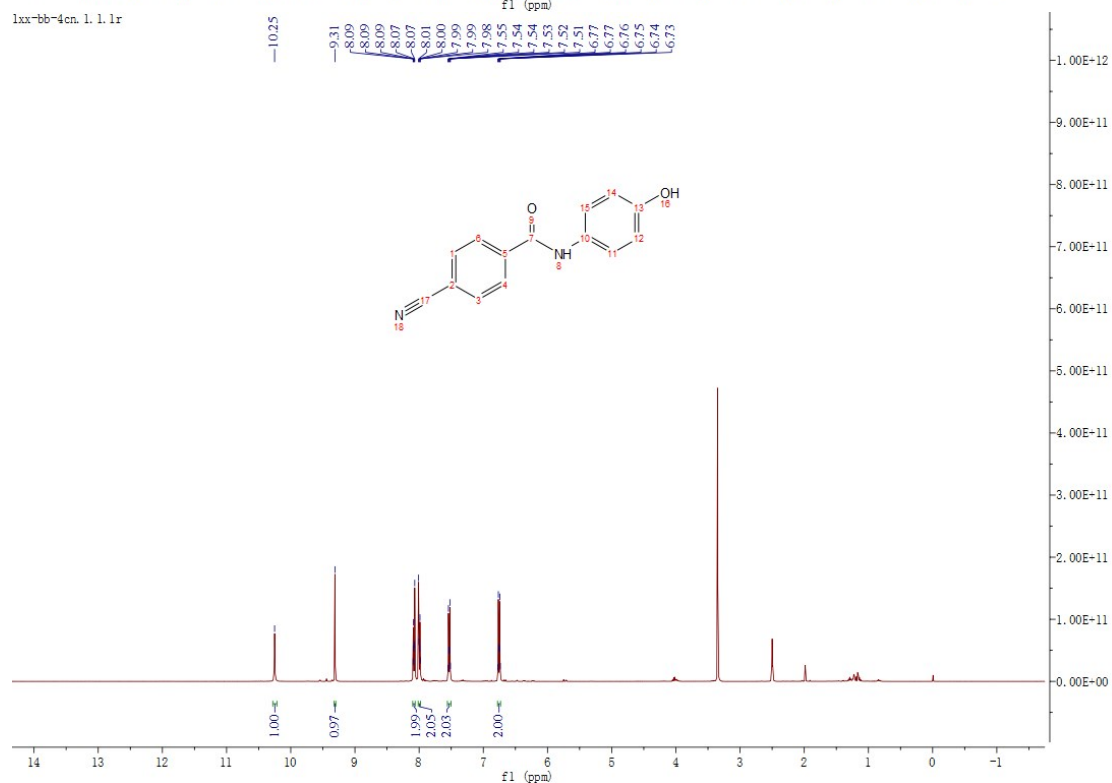
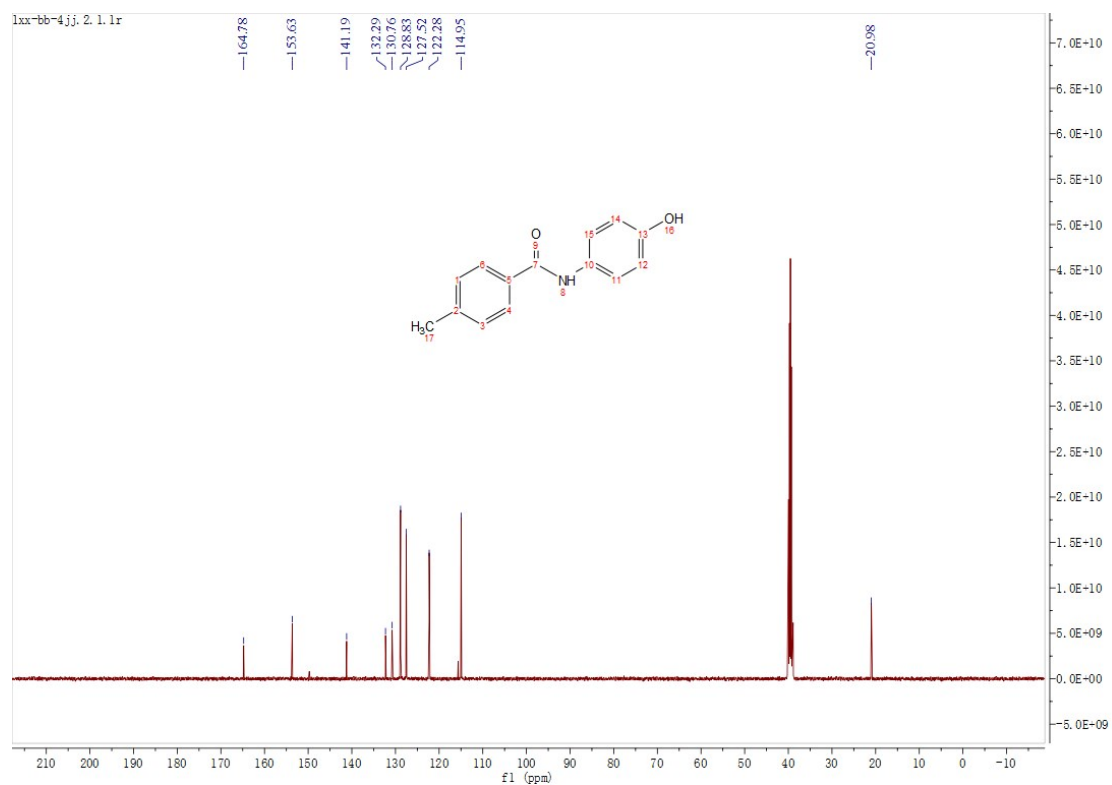


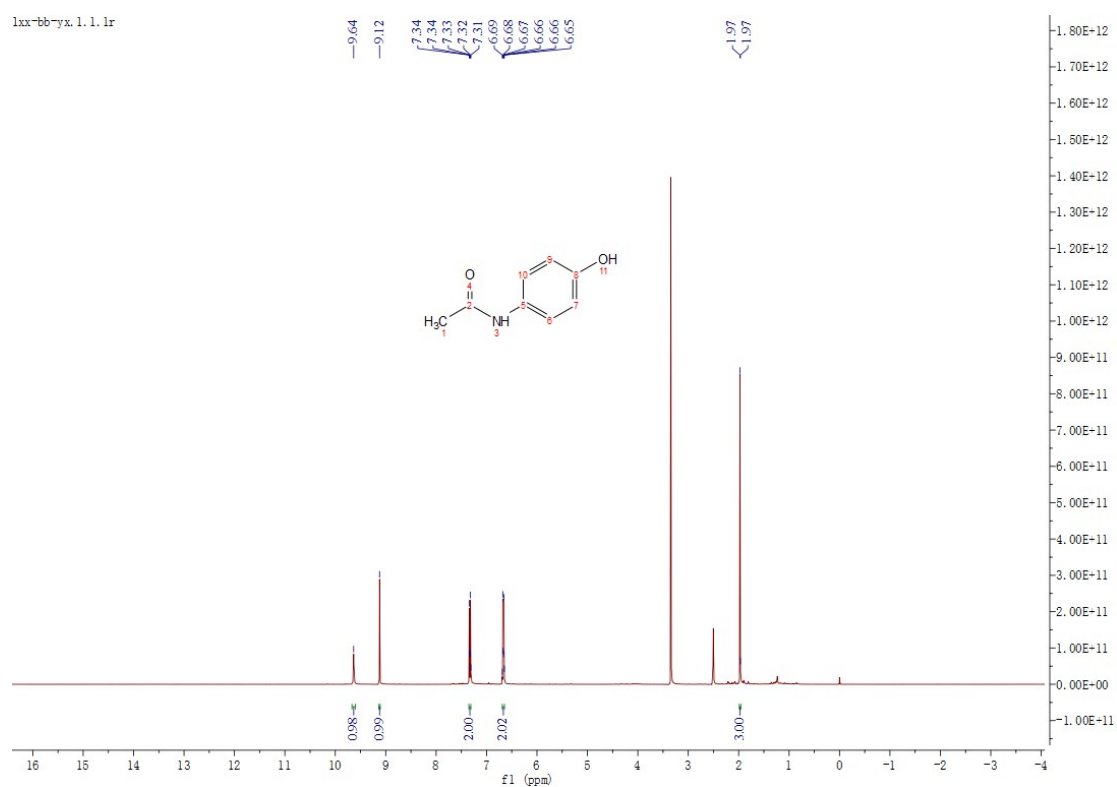
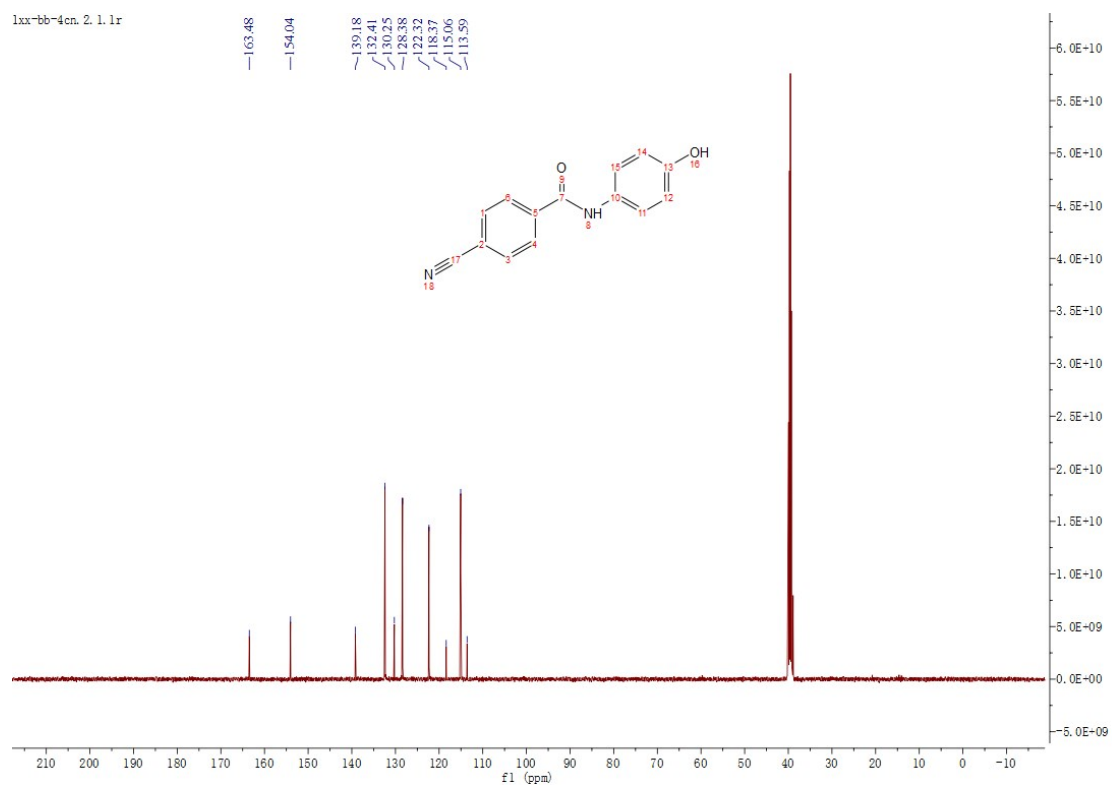


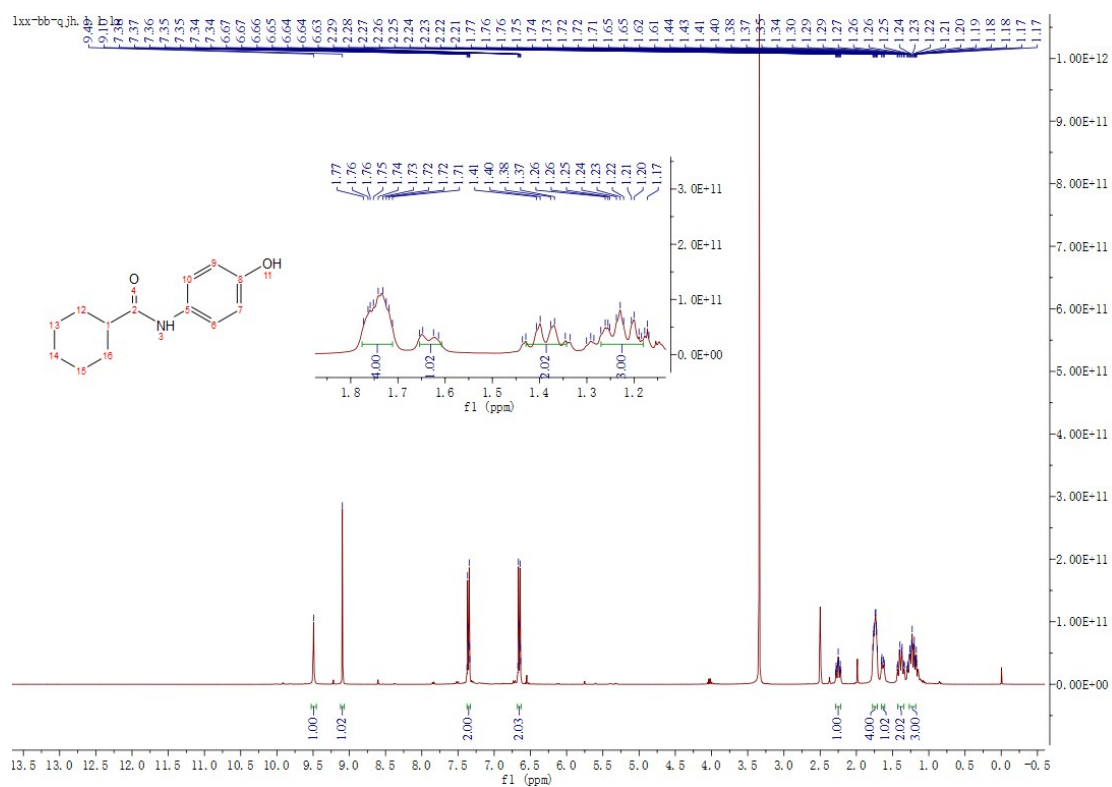
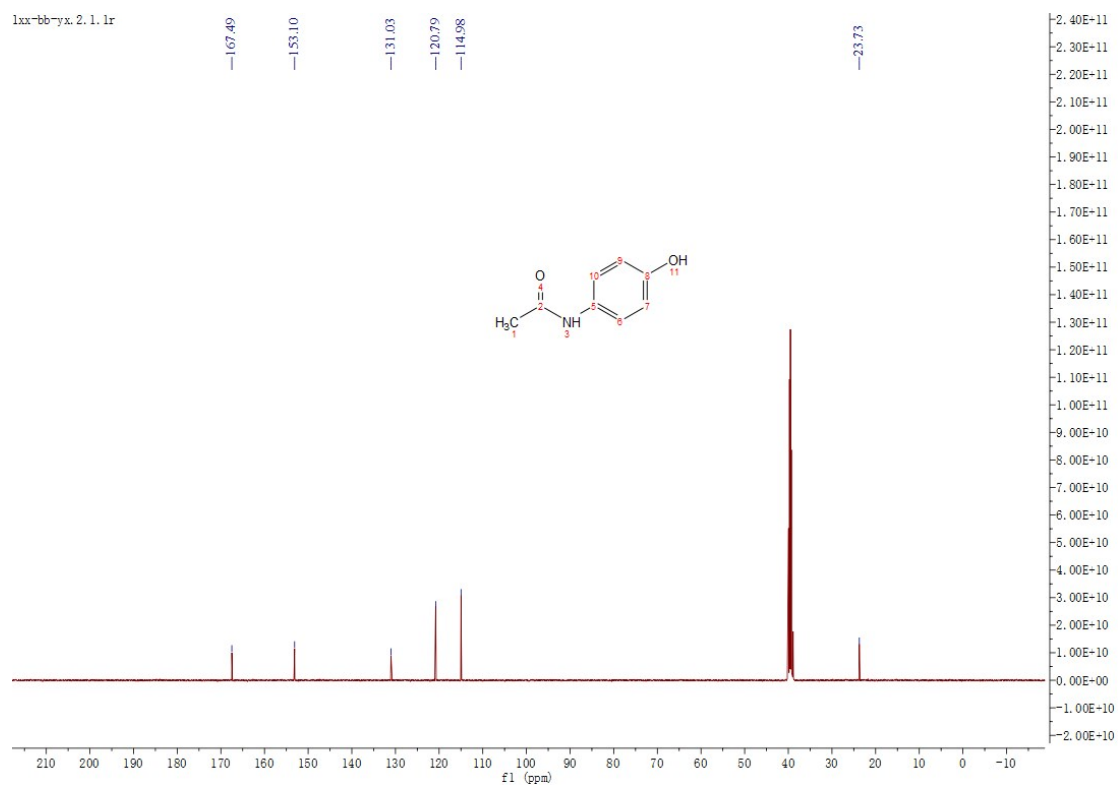
10.6 NMR-Spectra of 6

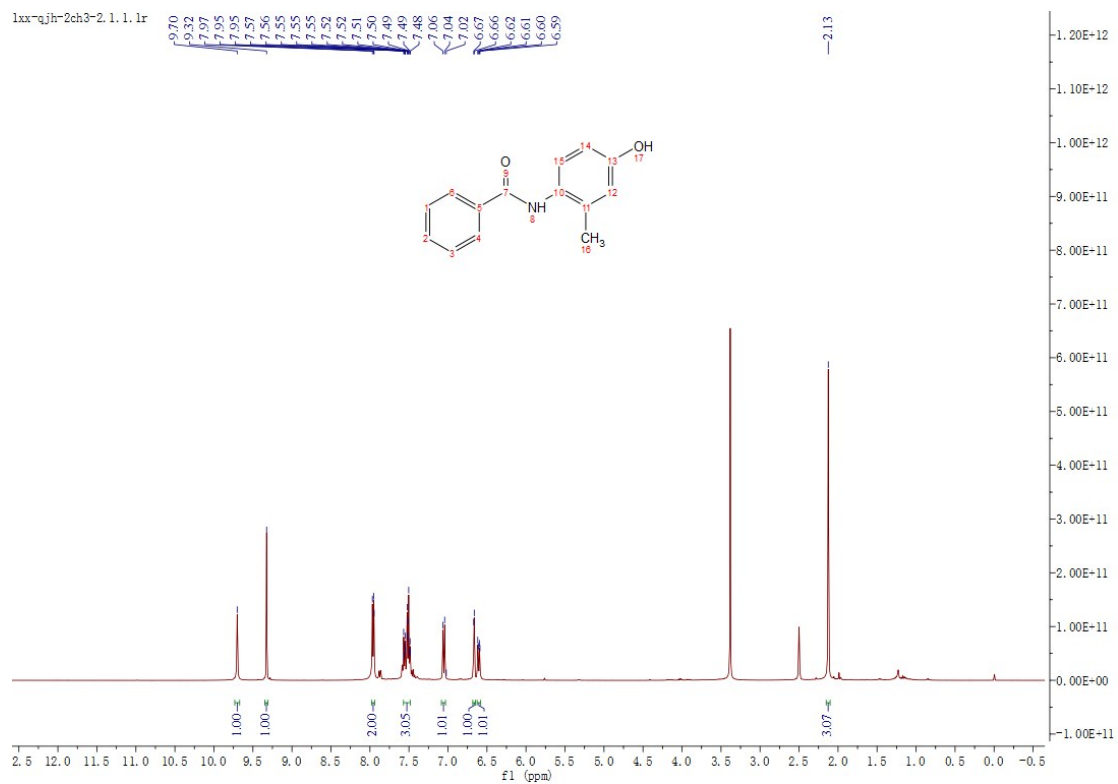
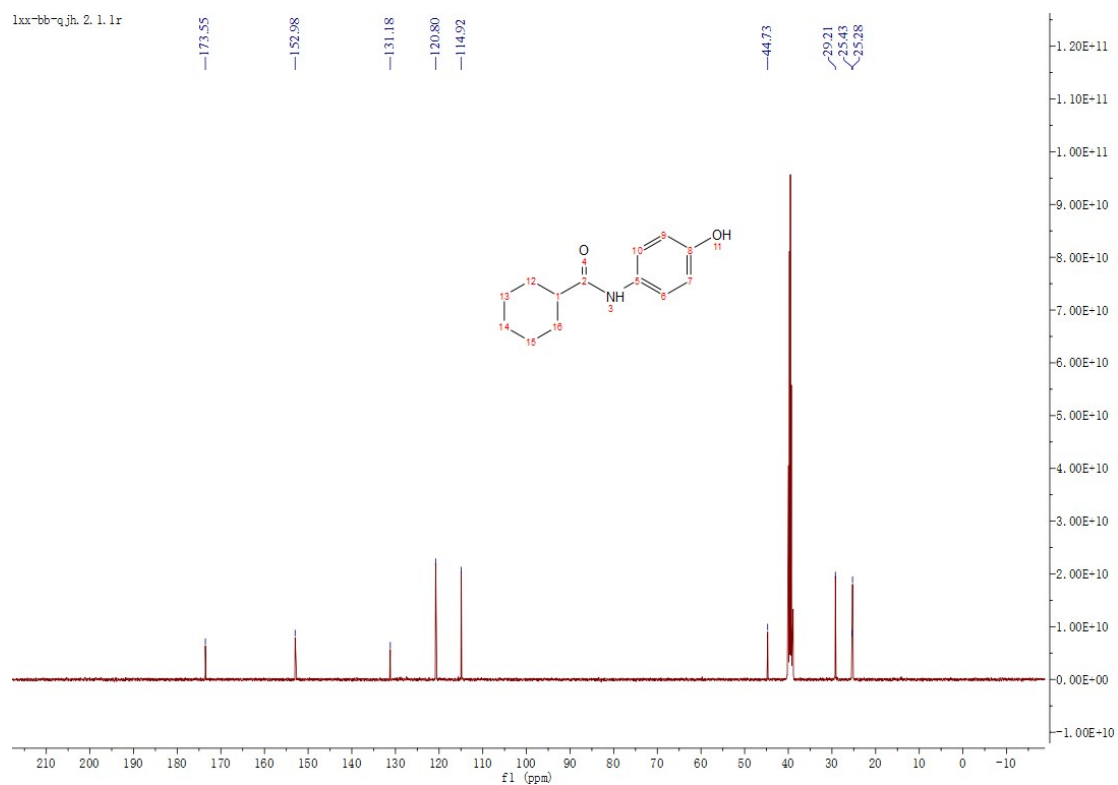


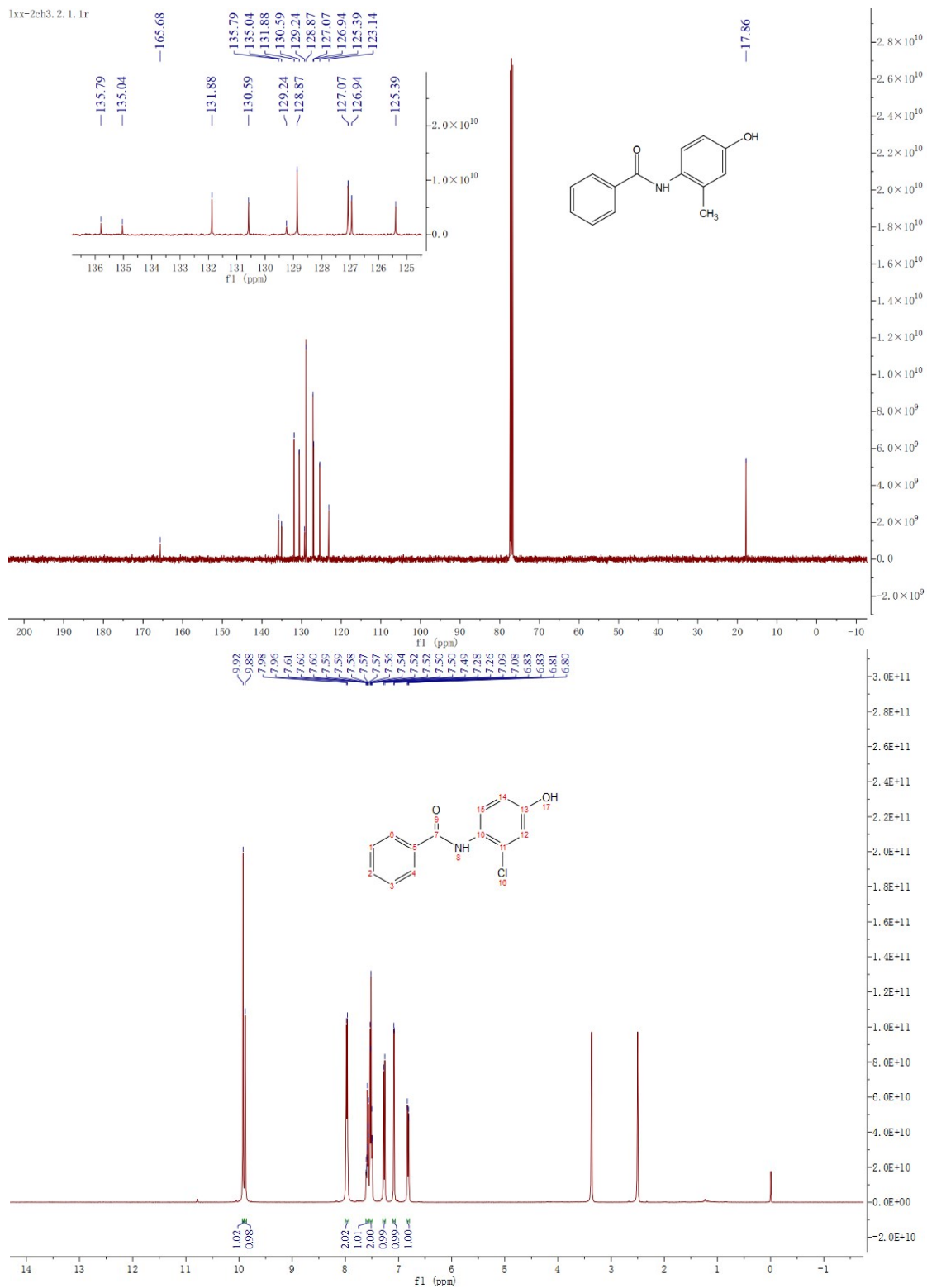


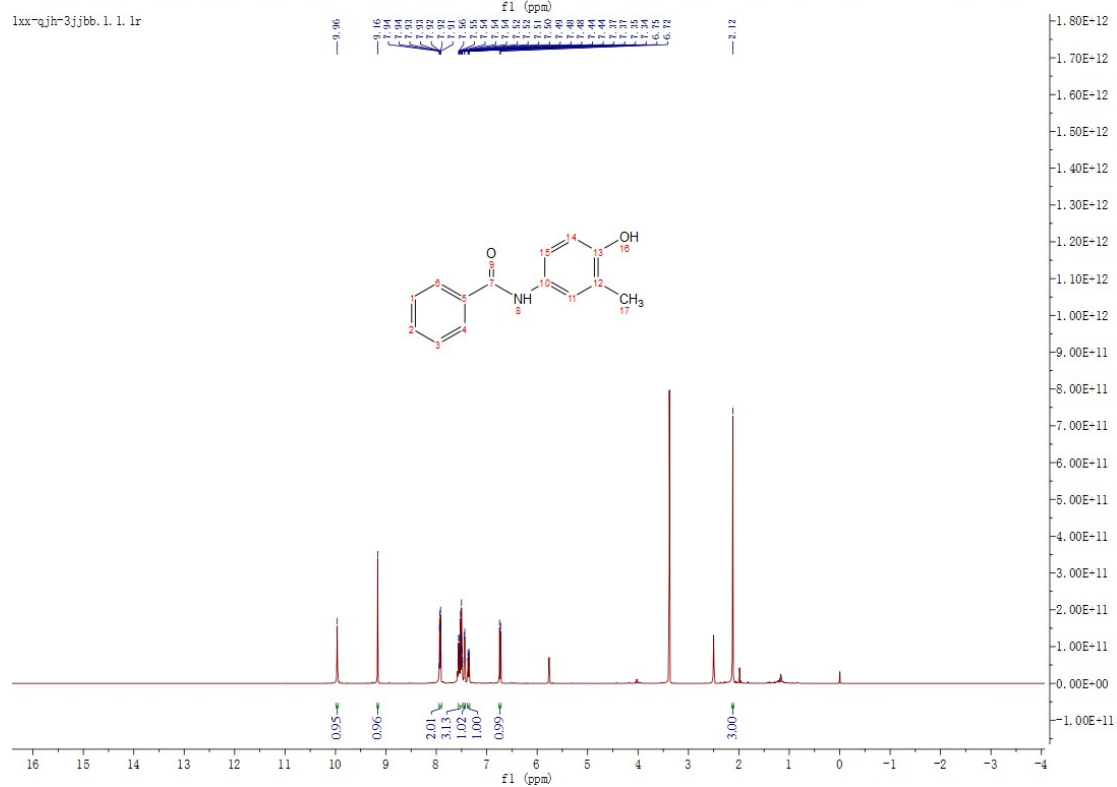
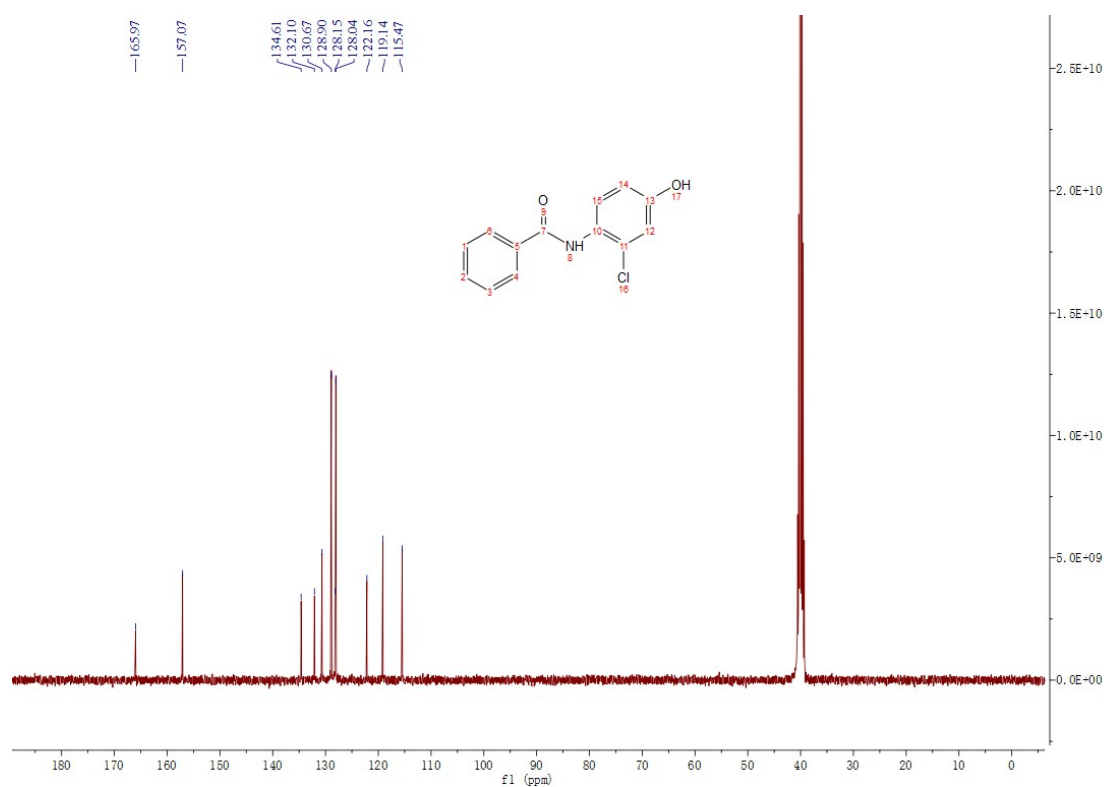




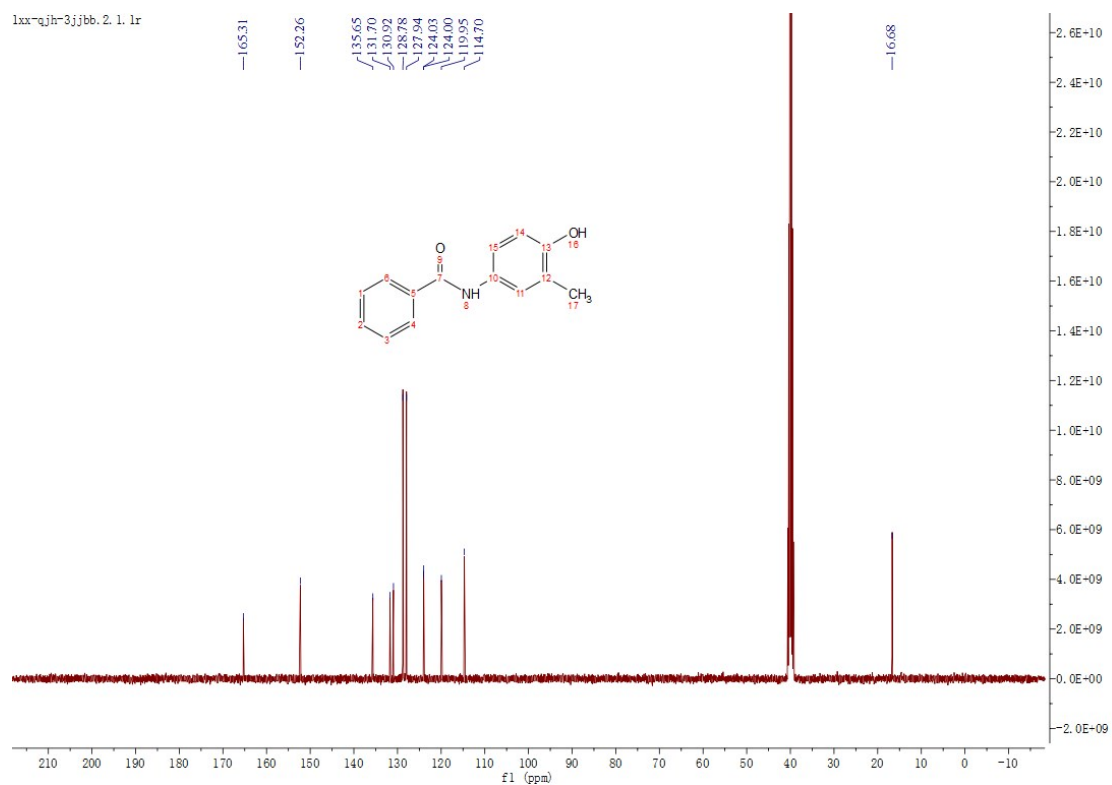








lxx-qjh-3jjbb.2.1.1r



LXX-9-th-2,3-cl-bb.1.1.1r

