

## Copper-Catalyzed C–H Alkylation of 8-Aminoquinolines via 8-Amide Chelation Assistance

Xiao-Feng Xia, \*<sup>†</sup> Su-Li Zhu, <sup>†</sup> Zhen Gu, <sup>†</sup> Haijun Wang, <sup>†</sup>

<sup>†</sup> The Key Laboratory of Food Colloids and Biotechnology, Ministry of Education, School of Chemical and Material Engineering, Jiangnan University, Wuxi, Jiangsu, 214122, China.

E-mail: [xiaxf@jiangnan.edu.cn](mailto:xiaxf@jiangnan.edu.cn)

### Table of Contents

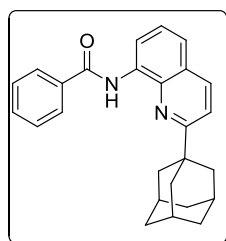
1	<b>General Remarks</b>	S2
2	<b>Typical procedure for the synthesis of product 3</b>	S2
3	<b>Characterization data of compounds 3</b>	S2-13
4	<b>General Procedure for Removal of the protecting group benzoyl</b>	S13-14
5	<b>Crystal Data and Structure Refinement for 3f.</b>	S14-15
6	<b><sup>1</sup>H NMR and <sup>13</sup>C NMR spectra for compounds 3 and 4</b>	S16-36

**General Remarks:** Column chromatography was carried out on silica gel. Unless noted  $^1\text{H}$  NMR spectra were recorded on 400 MHz in  $\text{CDCl}_3$ ,  $^{13}\text{C}$  NMR spectra were recorded on 100 MHz in  $\text{CDCl}_3$ . IR spectra were recorded on an FT-IR spectrometer and only major peaks are reported in  $\text{cm}^{-1}$ . Melting points were determined on a microscopic apparatus and were uncorrected. All new products were further characterized by HRMS (high resolution mass spectra), high resolution mass spectrometry (HRMS) spectra was obtained on a micrOTOF-Q instrument equipped with an ESI source; copies of their  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra are provided. Commercially available reagents and solvents were used without further purification.

**Typical procedure for the synthesis of product 3.**

A mixture of **1** (0.3 mmol), **2a** (0.6 mmol),  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (10% mmol),  $\text{AgNO}_3$  (30% mmol),  $\text{K}_2\text{S}_2\text{O}_8$  (0.6 mmol),  $\text{CH}_3\text{CN}/\text{H}_2\text{O}$  (1:1, 2.0 mL) was stirred at  $80^\circ\text{C}$  for 12h. Afterwards, the mixture was extracted by ethyl acetate ( $2 \times 10$  mL). The crude product was purified by flash column chromatography on silica gel (ethyl acetate/hexane= 10:1) to give the product **3**.

**Characterization data of compounds 3.**



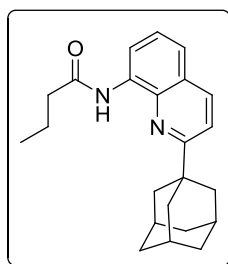
m.p. = 126-128  $^\circ\text{C}$

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 11.1 (s, 1 H), 8.85-8.87 (m, 1 H), 8.11-8.16 (m, 3 H), 7.48-7.59 (m, 6 H), 2.16-2.19 (m, 9 H), 1.82-1.89 (m, 6 H);

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 167.1, 164.8, 137.5, 136.5, 135.3, 134.4, 131.8, 128.8, 127.2, 126.6, 126.1, 121.1, 118.5, 116.0, 42.1, 39.8, 36.8, 28.8;

HRMS (ESI) m/z: calcd for  $\text{C}_{26}\text{H}_{27}\text{N}_2\text{O}$ :  $\text{M}+\text{H} = 383.2123$ ; found: 383.2109.

IR ( $\text{cm}^{-1}$ ): 3344, 2903, 1737, 1674, 1533, 756, 697;

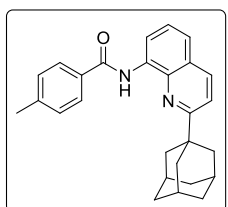


m.p. =72-74 °C

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 10.0 (s, 1 H, NH), 8.71-8.73 (m, 1 H), 8.05-8.08 (m, 1 H), 7.42-7.50 (m, 3 H), 2.54-2.57 (m, 2 H), 2.11-2.17 (m, 9 H), 1.80-1.90 (m, 8 H), 1.10 (t,  $J = 8.0$  Hz, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 171.3, 166.9, 137.0, 136.3, 134.3, 126.4, 126.0, 120.8, 118.3, 115.9, 41.9, 40.2, 39.7, 36.8, 28.7, 19.0, 13.8;

HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{23}\text{H}_{28}\text{N}_2\text{ONa}$ :  $\text{M}+\text{Na} = 371.2099$ ; found: 371.2121.

IR ( $\text{cm}^{-1}$ ): 3346, 2960, 2903, 2848, 1688, 1525, 839, 801;



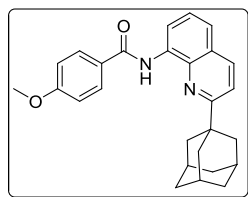
m.p.= 113-115°C

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 11.1 (s, 1 H), 8.85-8.87 (m, 1 H), 8.08-8.11 (m, 1 H), 8.03-8.05 (m, 2 H), 7.45-7.55 (m, 3 H), 7.33-7.35 (m, 2 H), 2.45 (s, 3 H), 2.16-2.19 (m, 9 H), 1.82-1.89 (m, 6 H);

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 166.9, 164.8, 142.2, 137.5, 136.5, 134.5, 132.5, 129.5, 127.2, 126.5, 126.1, 120.9, 118.4, 115.9, 42.1, 39.8, 36.8, 28.8, 21.5;

HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{27}\text{H}_{29}\text{N}_2\text{O}$ :  $\text{M}+\text{H} = 397.2280$ ; found: 397.2263.

IR (cm<sup>-1</sup>): 3341, 2904, 1734, 1675, 1534, 840, 757, 697;



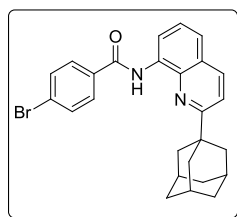
m.p. = 146-148 °C

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 11.0 (s, 1 H, NH), 8.85-8.87 (m, 1 H), 8.11-8.13 (m, 3 H), 7.49-7.55 (m, 3 H), 7.04-7.07 (m, 2 H), 3.92 (s, 3 H), 2.18-2.21 (m, 9 H), 1.84-1.92 (m, 6 H);

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 166.9, 164.4, 162.4, 137.4, 136.4, 134.5, 128.9, 127.6, 126.5, 126.1, 120.8, 118.4, 115.8, 113.9, 55.5, 42.0, 39.8, 36.8, 28.8;

HRMS (ESI) m/z: calcd for C<sub>27</sub>H<sub>29</sub>N<sub>2</sub>O<sub>2</sub>: M+H = 413.2229; found: 413.2216.

IR (cm<sup>-1</sup>): 3341, 2902, 2847, 1670, 1605, 1535, 1508, 1488, 1248, 1170, 839, 761.



m.p. >200 °C

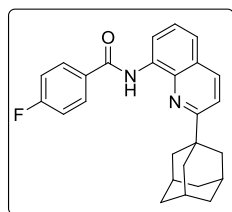
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 11.0 (s, 1 H), 8.81-8.83 (m, 1 H), 8.09-8.11 (m, 1 H), 7.97-7.99 (m, 2 H), 7.66-7.68 (m, 2 H), 7.47-7.56 (m, 3 H), 2.14-2.19 (m, 9 H), 1.81-1.89 (m, 6 H);

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 167.1, 163.7, 137.3, 136.5, 134.0, 132.0, 128.7, 126.5, 126.1, 121.3, 118.6, 116.0, 42.0, 39.8, 36.8, 28.7;

HRMS (ESI) m/z: calcd for C<sub>26</sub>H<sub>26</sub>N<sub>2</sub>BrO: M+H = 461.1228; found:

461.1201

IR (cm<sup>-1</sup>): 3351, 2898, 2843, 1673, 1528, 1480, 1339, 897, 841, 743;



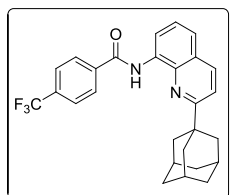
m.p. = 187-188 °C

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 11.0 (s, 1 H), 8.81-8.83 (m, 1 H), 8.09-8.15 (m, 3 H), 7.47-7.56 (m, 3 H), 7.19-7.24 (m, 2 H), 2.15-2.19 (m, 9 H), 1.81-1.89 (m, 6 H);

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 167.1, 166.2, 163.7, 137.4, 136.5, 134.2, 131.5, 129.5, 129.4, 126.5, 126.1, 121.2, 118.5, 115.9, 115.7, 42.1, 39.8, 36.8, 28.8;

HRMS (ESI) m/z: calcd for C<sub>26</sub>H<sub>26</sub>N<sub>2</sub>FO: M+H = 401.2029; found: 401.2021.

IR (cm<sup>-1</sup>): 3328, 2902, 1670, 1599, 1226, 837, 757, 637;



m.p. = 204-206 °C

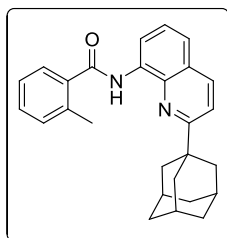
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 11.1 (s, 1 H, NH), 8.84-8.86 (m, 1 H), 8.23-8.25 (m, 2 H), 8.13-8.15 (m, 1 H), 7.81-7.83 (m, 2 H), 7.53 (m, 3 H), 2.16-2.21 (m, 9 H), 1.82-1.91 (m, 6 H);

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 167.3, 163.3, 138.4, 137.4, 136.5, 133.9, 127.6, 125.9, 125.8, 121.7, 118.7, 116.2, 42.1, 39.8, 36.8, 28.7;

HRMS (ESI) m/z: calcd for C<sub>27</sub>H<sub>26</sub>N<sub>2</sub>F<sub>3</sub>O: M+H = 451.1997; found:

451.1998.

IR (cm<sup>-1</sup>): 3353, 2973, 2903, 1672, 1598, 1430, 1322, 1124, 1049, 880, 859, 840, 767;



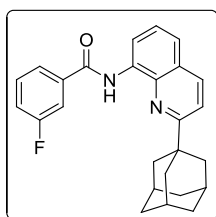
m.p. = 113-115 °C

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 10.5 (s, 1 H), 8.87-8.89 (m, 1 H), 8.09-8.12 (m, 1 H), 7.77-7.79 (m, 1 H), 7.48-7.55 (m, 3 H), 7.39-7.43 (m, 1 H), 7.31-7.34 (m, 2 H), 2.68 (s, 3 H), 2.07-2.13 (m, 9 H), 1.76-1.84 (m, 6 H);

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 167.6, 167.2, 137.4, 137.3, 136.5, 136.4, 134.6, 131.6, 130.4, 127.3, 126.5, 126.2, 125.9, 121.2, 118.4, 116.0, 41.9, 39.8, 36.8, 28.7, 20.5;

HRMS (ESI) m/z: calcd for C<sub>27</sub>H<sub>29</sub>N<sub>2</sub>O: M+H = 397.2280; found: 397.2264.

IR (cm<sup>-1</sup>): 3339, 2904, 2848, 1676, 1525, 840, 801;



m.p. = 138-140 °C

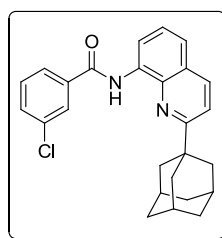
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 11.1 (s, 1 H, NH), 8.81-8.83 (m, 1 H), 8.10-8.13 (m, 1 H), 7.90-7.92 (m, 1 H), 7.82-7.85 (m, 1 H), 7.50-7.53 (m, 4 H), 7.25-7.31 (m, 1 H), 2.16-2.19 (m, 9 H), 1.82-1.90 (m, 6 H);

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 167.2, 164.2, 163.3, 161.7, 137.5, 137.4,

136.5, 133.9, 130.4, 126.1, 121.4, 118.6, 116.0, 114.6, 114.4, 42.1, 39.8, 36.8, 28.7;

HRMS (ESI)  $m/z$ : calcd for  $C_{26}H_{26}N_2FO$ :  $M+H = 401.2029$ ; found: 401.2022.

IR ( $cm^{-1}$ ): 3336, 2903, 2848, 1678, 1536, 1268, 1228, 850, 839, 800;



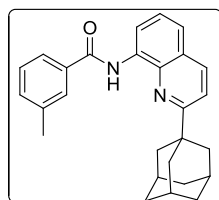
m.p. = 145-146 °C

$^1H$  NMR (400 MHz,  $CDCl_3$ ): 11.1 (s, 1 H), 8.79-8.82 (m, 1 H), 8.11-8.13 (m, 2 H), 8.02-8.05 (m, 1 H), 7.47-7.57 (m, 5 H), 2.16-2.21 (m, 9 H), 1.86-1.87 (m, 6 H);

$^{13}C$  NMR (100 MHz,  $CDCl_3$ ): 167.3, 163.1, 137.4, 136.9, 136.5, 134.9, 133.9, 131.7, 130.2, 127.3, 126.5, 126.1, 125.6, 121.4, 118.6, 116.0, 42.1, 39.9, 36.8, 28.7;

HRMS (ESI)  $m/z$ : calcd for  $C_{26}H_{26}N_2ClO$ :  $M+H = 417.1734$ ; found: 417.1733.

IR ( $cm^{-1}$ ): 3323, 2904, 2848, 1675, 1536, 752, 682;



m.p. = 134-135 °C

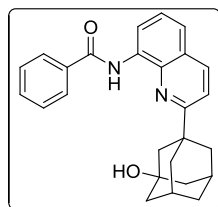
$^1H$  NMR (400 MHz,  $CDCl_3$ ): 11.1 (s, 1 H, NH), 8.85-8.87 (m, 1 H), 8.09 (m, 1 H), 7.96-7.97 (m, 2 H), 7.38-7.56 (m, 5 H), 2.48 (s, 3 H), 2.17-2.19

(m, 9 H), 1.81-1.89 (m, 6 H);

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 166.9, 164.8, 138.4, 137.4, 136.4, 135.1, 134.3, 132.5, 128.8, 124.6, 121.0, 118.4, 115.9, 42.0, 39.8, 36.8, 28.8, 21.4;

HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{27}\text{H}_{29}\text{N}_2\text{O}$ :  $M+H = 397.2280$ ; found: 397.2264.

IR ( $\text{cm}^{-1}$ ): 3341, 3048, 2903, 2847, 1674, 1536, 1269, 839, 733;



m.p. = 166-168 °C

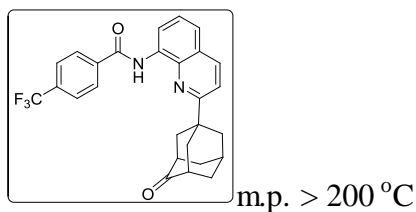
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 11.0 (s, 1 H, NH), 8.85-8.87 (m, 1 H), 8.11-8.13 (m, 3 H), 7.49-7.56 (m, 6 H), 2.42 (s, 2 H), 2.13 (s, 2 H), 2.06-2.09 (m, 2 H), 1.98-2.01 (m, 2 H), 1.80-1.87 (m, 4 H), 1.72 (m, 2 H);

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 165.3, 164.8, 137.4, 136.7, 135.1, 134.3, 131.8, 127.1, 126.7, 126.2, 121.1, 118.4, 116.1, 69.0, 49.4, 44.5, 43.5, 40.9, 35.3, 30.9;

HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{26}\text{H}_{27}\text{N}_2\text{O}_2$ :  $M+H = 399.2072$ ; found: 399.2058.

IR ( $\text{cm}^{-1}$ ): 3340, 2919, 2851, 1671, 1535, 1339, 697;



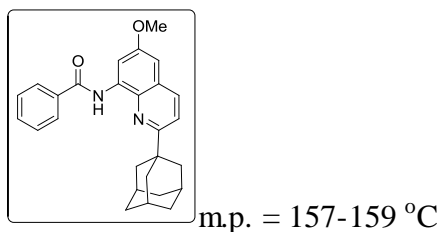


$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 10.9 (s, 1 H), 8.86-8.87 (m, 1 H), 8.16-8.18 (m, 3 H), 7.79-7.81 (m, 2 H), 7.53-7.59 (m, 3 H), 2.78 (m, 2 H), 2.39-2.54 (m, 6 H), 2.14-2.21 (m, 4 H), 1.25 (m, 1 H);

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 216.9, 164.3, 163.3, 138.2, 137.2, 137.1, 133.8, 127.4, 125.8, 121.6, 118.2, 116.6, 46.4, 43.2, 40.9, 39.5, 38.4, 27.9;

HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{27}\text{H}_{23}\text{F}_3\text{N}_2\text{O}_2\text{Na}$ :  $M+\text{Na} = 487.1609$ ; found: 487.1610.

IR( $\text{cm}^{-1}$ ): 3331, 2913, 2858, 1723, 1669, 1328, 1114, 1063, 828;



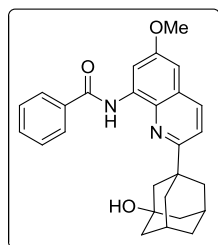
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 11.06 (s, 1 H, NH), 8.60 (m, 1 H), 8.12-8.14 (m, 2 H), 7.97-7.99 (m, 1 H), 7.47-7.57 (m, 4 H), 6.78 (m, 1 H), 3.93 (s, 3 H), 2.13-2.17 (m, 9 H), 1.80-1.85 (m, 6 H);

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 164.7, 164.4, 157.9, 135.2, 135.1, 135.0, 133.8, 131.8, 128.8, 127.1, 126.9, 118.8, 108.2, 99.8, 55.5, 42.1, 39.4, 36.8, 28.8;

HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{27}\text{H}_{28}\text{N}_2\text{O}_2\text{Na}$ :  $M+\text{Na} = 435.2048$ ; found:

435.2056.

IR (cm<sup>-1</sup>): 3333, 2903, 2848, 1675, 1534, 1457, 1264, 1159, 1059, 876, 795, 696;



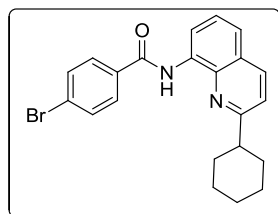
m.p. > 200 °C

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 10.9 (s, 1 H, NH), 8.58 (s, 1 H), 8.07-8.09 (m, 2 H), 7.96-7.97 (m, 1 H), 7.51-7.54 (m, 3 H), 7.43-7.44 (m, 1 H), 6.76 (s, 1 H), 3.89 (s, 3 H), 2.04 (s, 2 H), 2.11 (s, 2 H), 1.95-2.05 (m, 5 H), 1.83 (m, 4 H), 1.71 (m, 2 H);

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 164.7, 162.7, 158.1, 135.4, 135.1, 134.9, 133.8, 131.8, 128.8, 127.1, 127.0, 118.8, 108.4, 99.7, 68.9, 55.5, 49.5, 44.5, 43.1, 40.9, 35.3, 30.9;

HRMS (ESI) m/z: calcd for C<sub>27</sub>H<sub>28</sub>N<sub>2</sub>O<sub>3</sub>Na: M+Na = 451.1998; found: 451.2037.

IR (cm<sup>-1</sup>): 3334, 2921, 2851, 1673, 1534, 1457, 1159, 849;



r.r.(C2:C4)= 3:5, m.p. = 129-131 °C

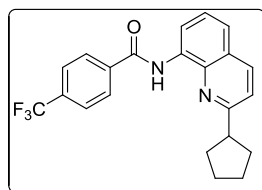
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 10.9 (s, 0.76 H), 10.8 (s, 0.51 H), 8.81-8.88 (m, 1.6 H), 8.73-8.74 (m, 0.6 H), 7.91-7.93 (m, 1 H), 7.77-7.80 (m, 3 H),

7.63-7.69 (m, 0.8 H), 7.55-7.59 (m, 3.2 H), 7.46-7.51 (m, 2.8 H),  
7.32-7.36 (m, 1.5 H), 3.31 (m, 0.67 H), 2.87-2.90 (m, 1 H), 2.07-2.10 (m,  
1.76 H), 2.00-2.02 (m, 1.5 H), 1.91-1.94 (m, 3 H), 1.81-1.84 (m, 1.65 H),  
1.66-1.72 (m, 2.3 H), 1.47-1.56 (m, 4.6 H), 1.25-1.38 (m, 1.6 H);

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 164.7, 163.9, 154.1, 148.1, 136.5, 134.1,  
134.0, 133.8, 131.9, 126.6, 126.3, 121.5, 120.9, 118.0, 117.3, 116.2,  
115.9, 46.5, 39.0, 33.5, 32.7, 26.8, 26.4, 26.2;

HRMS (ESI)  $m/z$ : calcd for  $\text{C}_{22}\text{H}_{21}\text{BrN}_2\text{ONa}$ :  $M+\text{Na} = 431.0735$ ; found:  
431.0739.

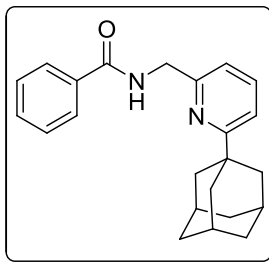
IR ( $\text{cm}^{-1}$ ): 3338, 2926, 2851, 1675, 1532, 1482, 1009, 838, 757;



r.r.(C2:C4) = 5:3, oil

$^1\text{H}$  NMR (400 M Hz,  $\text{CDCl}_3$ ): 11.0 (s, 1 H), 8.90-8.92 (m, 0.7 H),  
8.86-8.88 (m, 0.5 H), 8.76-8.77 (m, 0.6 H), 8.19-8.21 (m, 2.6 H), 8.09 (m,  
0.4 H), 7.81 (m, 3.3 H), 7.59-7.63 (m, 0.7 H), 7.53-7.54 (m, 1 H),  
7.40-7.42 (m, 1 H), 3.79-3.85 (m, 1.0 H), 3.41-3.49 (m, 0.6 H), 2.21-2.26  
(m, 1 H), 1.79-1.86 (m, 7 H);  $^{13}\text{C}$  NMR (100 MHz,  
 $\text{CDCl}_3$ ): 164.6, 163.9, 153.2, 148.2, 138.7, 137.8, 136.5, 134.6, 133.7,  
127.7, 126.3, 125.8, 121.6, 118.3, 117.8, 116.5, 116.2, 47.9, 40.7, 33.4,  
31.4, 26.1, 25.5; MS ( $\text{C}_{22}\text{H}_{19}\text{F}_3\text{N}_2\text{O}$ ): 384( $M^+$ ).

IR( $\text{cm}^{-1}$ ): 3340, 2961, 2870, 1679, 1534, 1326, 1260, 1129, 1068, 1017,  
856, 800, 767;



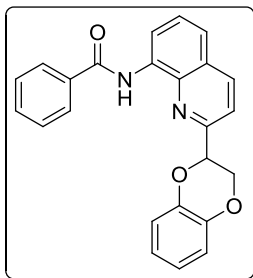
m.p. = 157-159 °C

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 8.47 (s, 1 H, NH), 7.88-7.90 (m, 2 H), 7.83-7.85 (m, 1 H), 7.42-7.50 (m, 3 H), 7.31 (m, 1 H), 7.20-7.21 (m, 1 H), 4.74-4.75 (m, 2 H), 2.10-2.12 (m, 3 H), 1.89 (m, 6 H), 1.74-1.83 (m, 6 H);

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 167.3, 161.3, 155.9, 148.5, 134.4, 131.3, 128.4, 127.3, 127.1, 119.4, 119.1, 44.8, 42.3, 36.4, 36.3, 28.5;

IR(cm<sup>-1</sup>): 3310, 3062, 2905, 2849, 1645, 1603, 1578, 1549, 1308, 806, 696;

HRMS (ESI) m/z: calcd for C<sub>23</sub>H<sub>27</sub>N<sub>2</sub>O: M+H=347.2123; found: 347.2118.

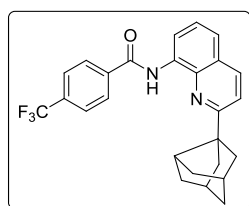


oil, r.r. (C2:C4)= 5:3

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 10.84 (s, 1 H), 10.55 (s, 0.6 H), 8.94-8.97 (m, 1.6 H), 8.87-8.89 (d, *J* = 8.0 Hz, 1 H), 8.22-8.24 (d, *J* = 8.0 Hz, 0.6 H), 8.03-8.08 (m, 3.0 H), 7.73-7.75 (d, *J* = 8.0 Hz, 0.6 H), 7.70-7.71 (d, *J* = 4.0 Hz, 1.0 H), 7.64-7.66 (m, 2.0 H), 7.51-7.60 (m, 6.0 H), 7.05-7.08 (m, 1.6 H), 6.97-7.00 (m, 1 H), 6.89-6.96 (m, 3.8 H), 5.85-5.87 (m, 1 H), 5.48-5.51 (m, 0.6 H), 4.70-4.73 (m, 0.6 H), 4.59-4.62 (m, 1.0 H),

4.35-4.39 (m, 0.6 H), 4.00-4.05 (m, 1.0 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 165.4, 165.2, 154.8, 148.1, 142.0, 137.7, 134.9, 131.9, 127.8, 124.9, 121.9, 119.0, 117.6, 117.4, 117.3, 117.0, 116.5, 115.9, 75.6, 71.3, 68.5, 67.6; MS ( $\text{C}_{24}\text{H}_{19}\text{N}_2\text{O}_3^+$ ): 383.1 (M+H).

IR: 3354, 3049, 2923, 1673, 1533, 1493, 1264, 1075, 752, 697;



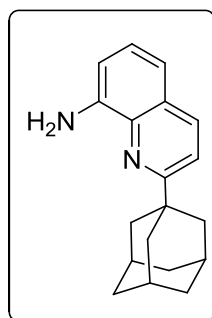
r.r. = 2:3 (C2:C4), Solid, m.p.= 178-180 °C

$^1\text{H}$  NMR (400 M Hz,  $\text{CDCl}_3$ ): 11.1 (m, 1 H), 8.84-8.87 (m, 1 H), 8.72-8.73 (m, 0.4 H), 8.21 (m, 2 H), 8.10 (m, 0.6 H), 7.99 (m, 0.4 H), 7.80 (m, 2 H), 7.43-7.51 (m, 2.8 H), 2.98-3.01 (m, 0.4 H), 2.84-2.87 (m, 0.6 H), 2.48 (s, 2 H), 2.34-2.37 (m, 0.9 H), 2.26-2.29 (m, 1.6 H), 2.08-2.11 (m, 1.3 H), 2.01-2.04 (m, 2.4 H), 1.71-1.90 (m, 4.8 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 166.7, 163.8, 163.2, 155.8, 147.8, 139.4, 137.4, 136.4, 134.9, 133.7, 126.0, 125.7, 119.8, 116.3, 115.8, 56.1, 53.5, 51.1, 50.1, 45.3, 43.7, 37.9, 35.1, 34.8; MS ( $\text{C}_{26}\text{H}_{24}\text{F}_3\text{N}_2\text{O}$ ): 437.2 (M+H). IR ( $\text{cm}^{-1}$ ): 3345, 2966, 1675, 1535, 1325, 1265, 1130, 1070, 1015, 860, 801.

### General Procedure for Removal of the protecting group benzoly

A mixture of **3h** (178.7 mg, 0.3969 mmol) and NaOH (238 mg) in EtOH (5 mL) was stirred at 80 °C for 8 h. After completion of the reaction, the resulting dark red solution was cooled to room temperature. The mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (3 × 15 mL). The organic layers were

combined, dried over  $\text{MgSO}_4$ , and filtered, and the solvent was evaporated under a vacuum. Purification by silica gel column chromatography (PE/EA=20:1) afforded 2-adamantyl-8-amino-quinoline **4** as a light yellow solid (70.6 mg, 64%).

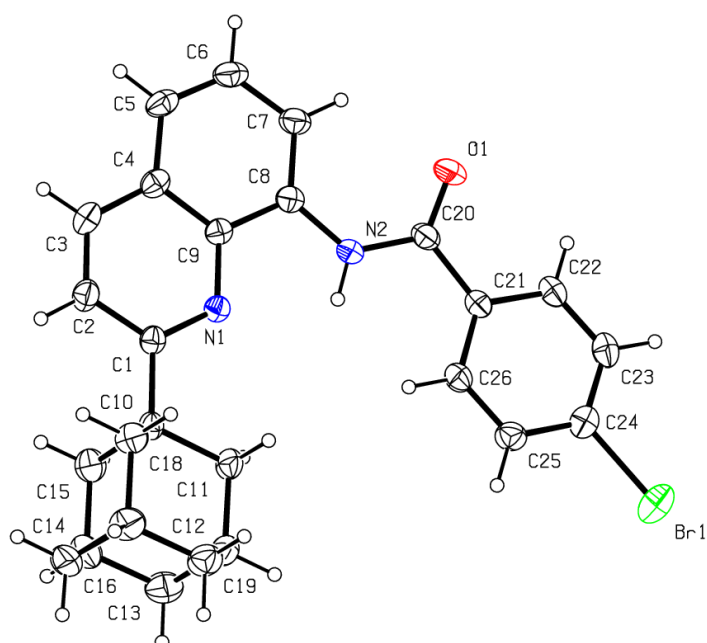


m.p. = 145-147 °C

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 7.85 (d,  $J = 8.0$  Hz, 1 H), 7.31 (d,  $J = 8.0$  Hz, 1 H), 7.13 (t,  $J = 6.0$  Hz, 1 H), 6.97-6.99 (m, 1 H), 6.75-6.77 (m, 1 H), 4.89 (s, 2 H,  $\text{NH}_2$ ), 1.96-2.03 (m, 9 H), 1.67-1.74 (m, 6 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 165.9, 143.8, 137.1, 135.8, 126.8, 126.2, 117.9, 115.5, 109.6, 41.9, 39.6, 36.8, 28.8;

IR( $\text{cm}^{-1}$ ): 3469, 3372, 2899, 2848, 1616, 1587, 1447, 1433, 836, 744;

### Crystal Data and Structure Refinement for **3f**.



## Datablock: xiaxf0628

---

Bond precision: C-C = 0.0034 Å                      Wavelength=1.54180

Cell:                      a=30.6160(15)              b=6.6330(2)              c=20.9653(10)  
                            alpha=90                      beta=93.234(4)              gamma=90

Temperature:              295 K

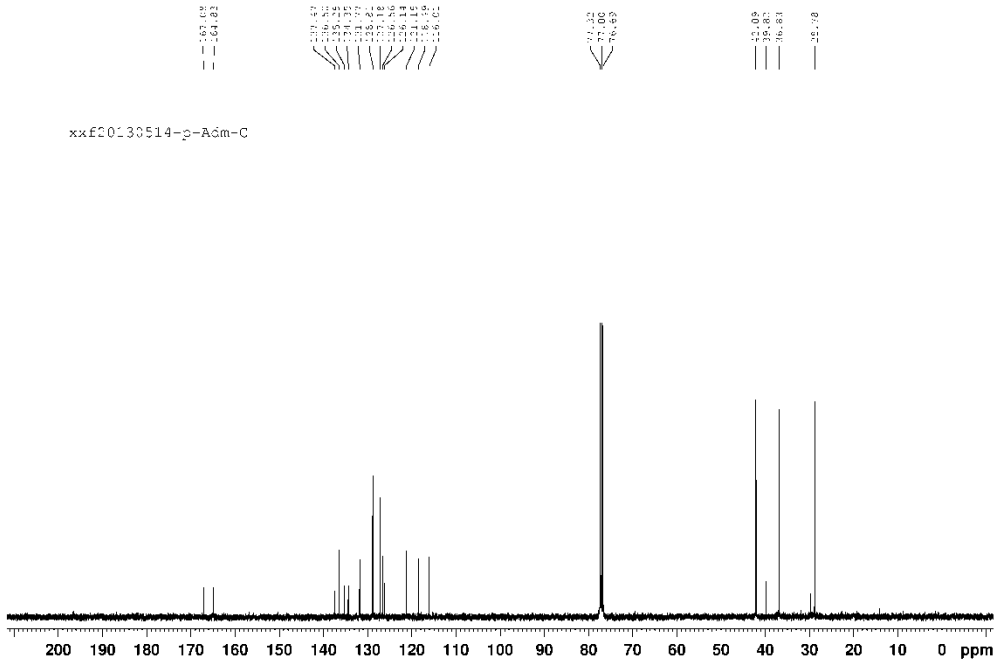
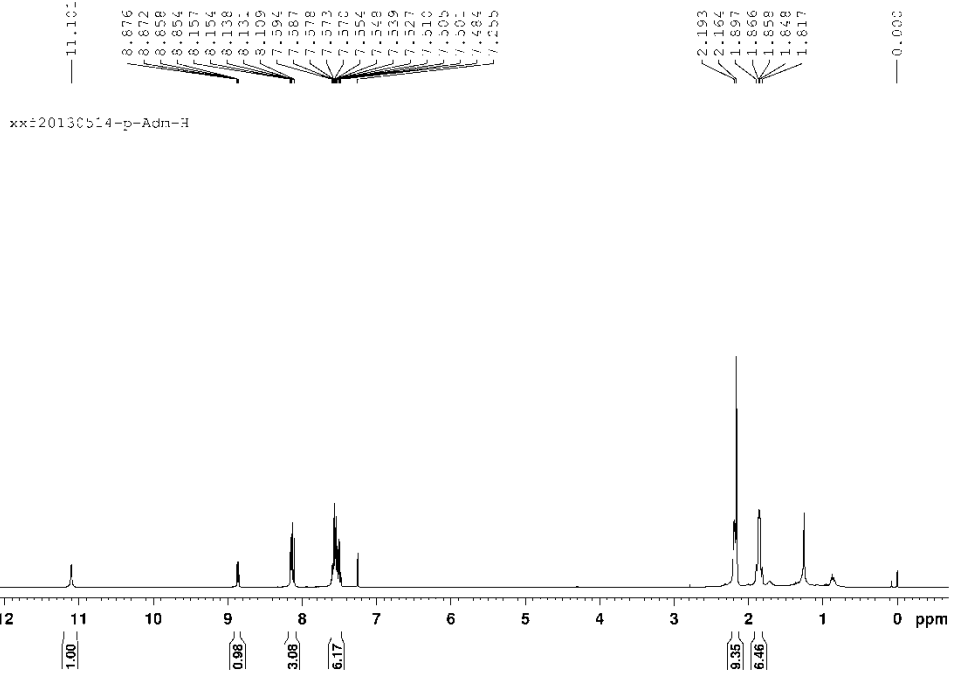
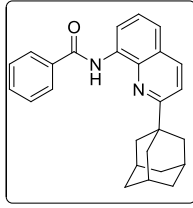
	Calculated	Reported
Volume	4250.8(3)	4250.8(3)
Space group	I 2/c	I 1 2/c 1
Hall group	-I 2yc	-I 2yc
Moiety formula	C26 H25 Br N2 O	C26 H25 Br N2 O
Sum formula	C26 H25 Br N2 O	C26 H25 Br N2 O
Mr	461.38	461.39
Dx, g cm-3	1.442	1.442
Z	8	8
Mu (mm-1)	2.786	2.786
F000	1904.0	1904.0
F000'	1902.97	
h,k,lmax	37,8,25	37,8,25
Nref	4036	4034
Tmin,Tmax	0.658,0.736	0.667,1.000
Tmin'	0.340	

Correction method= MULTI-SCAN

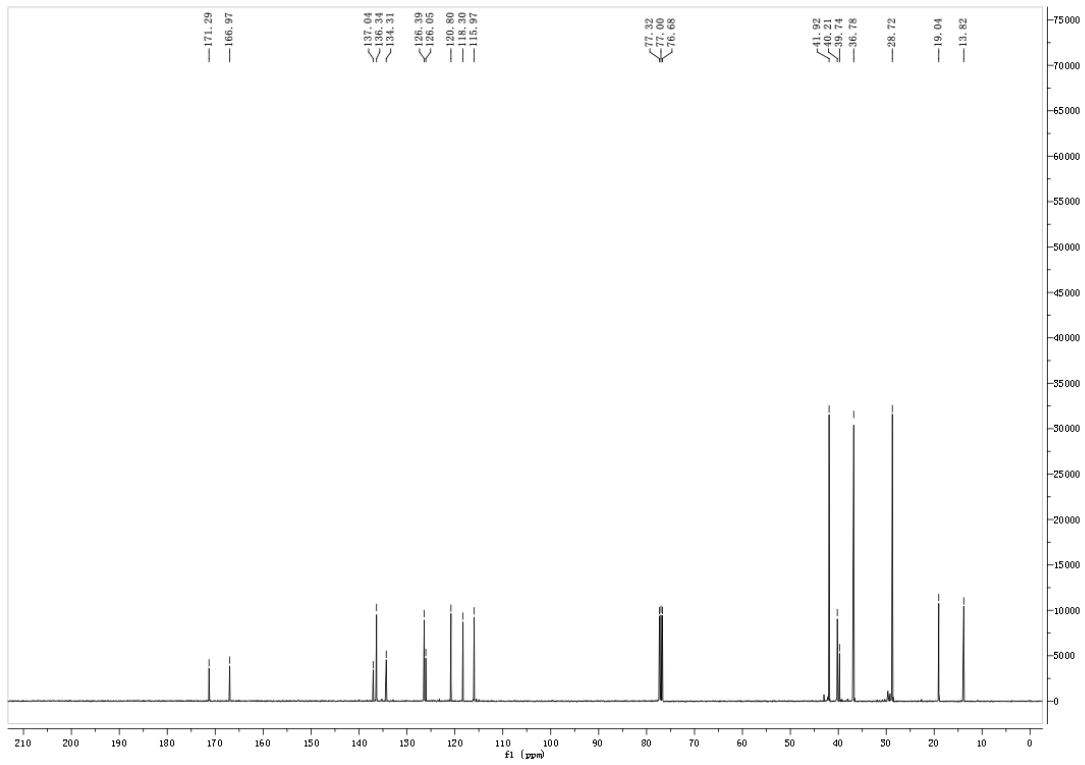
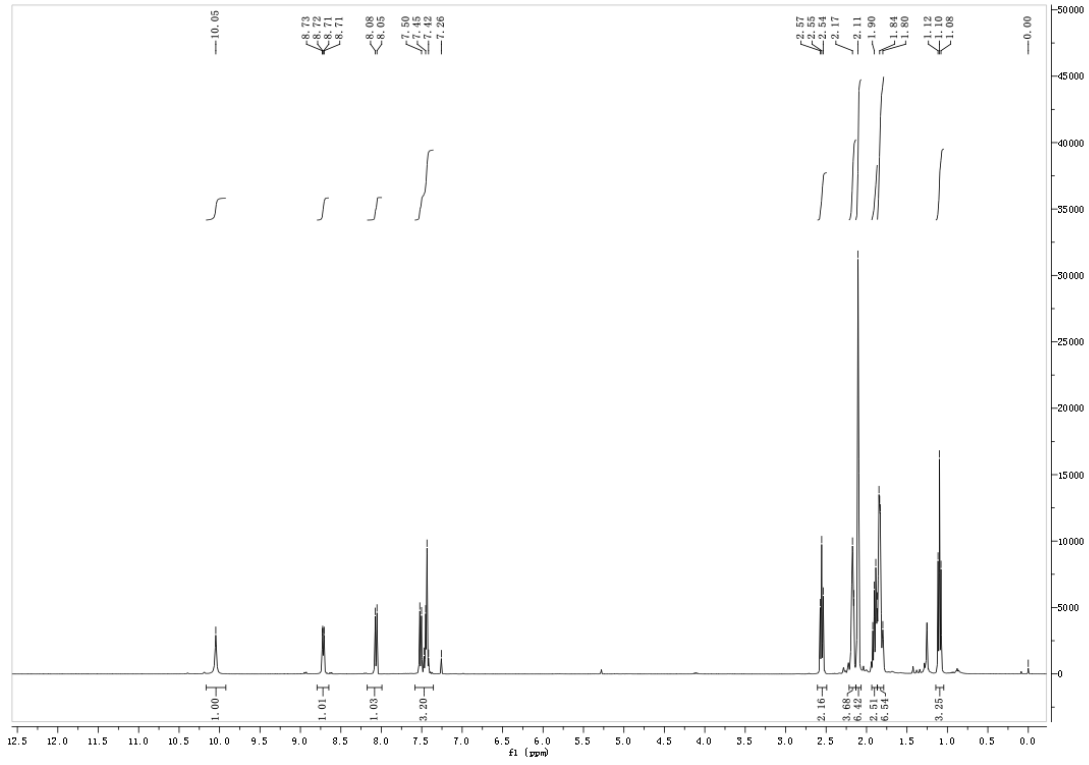
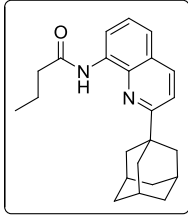
Data completeness= 1.000                      Theta (max)= 70.076

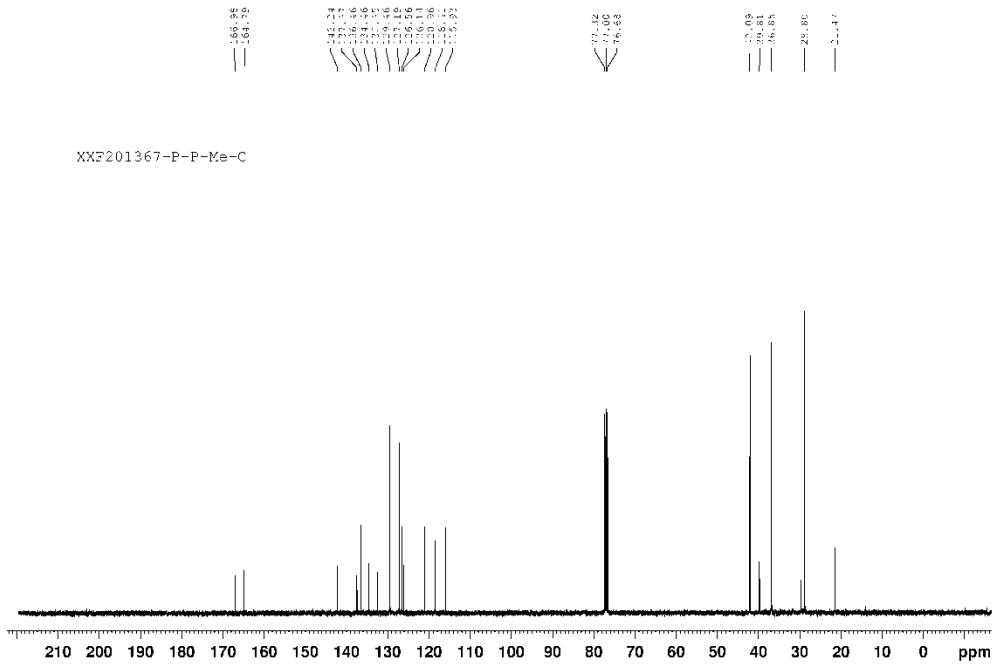
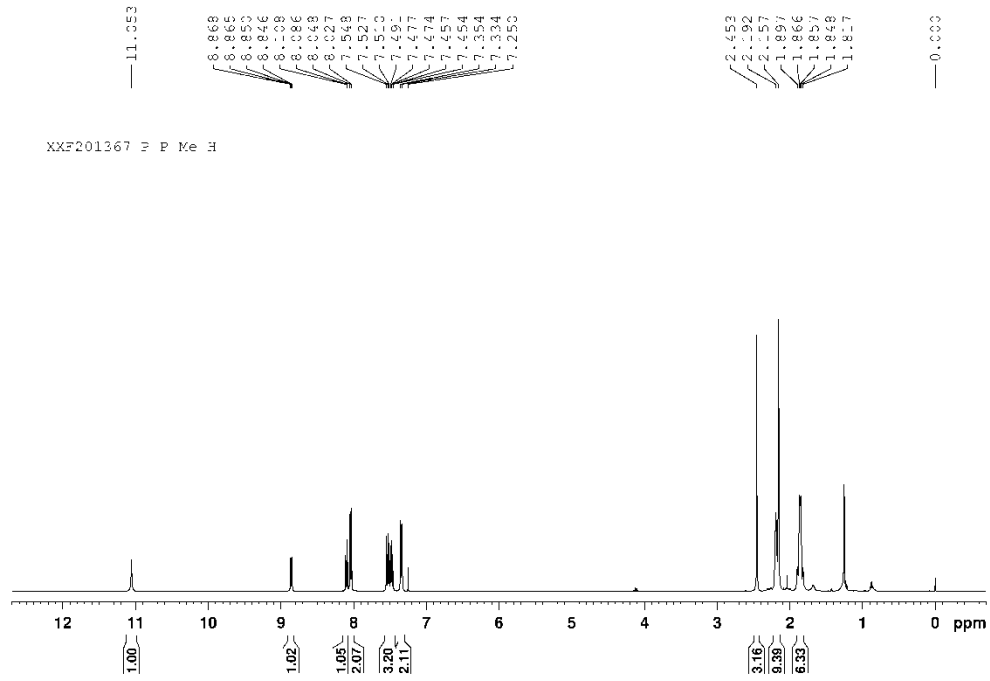
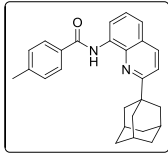
R(reflections)= 0.0388( 3541)                      wR2(reflections)= 0.1107( 4034)

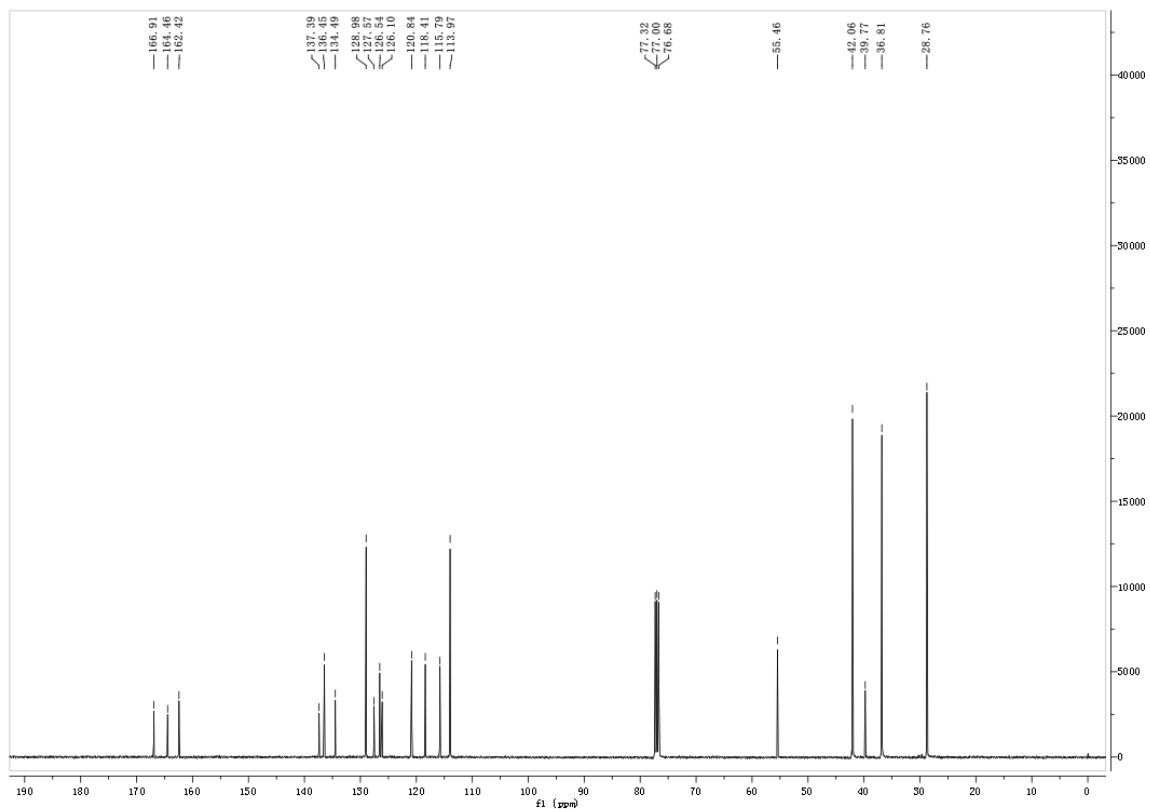
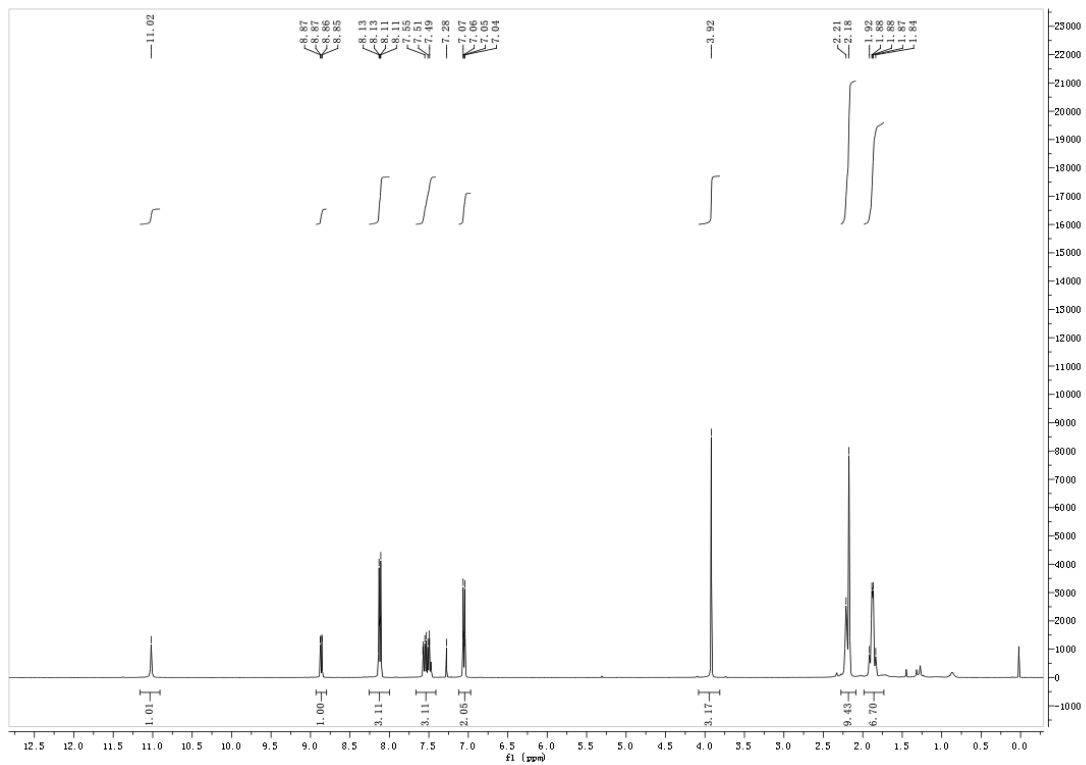
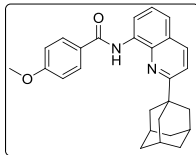
S = 1.034    Npar= 271

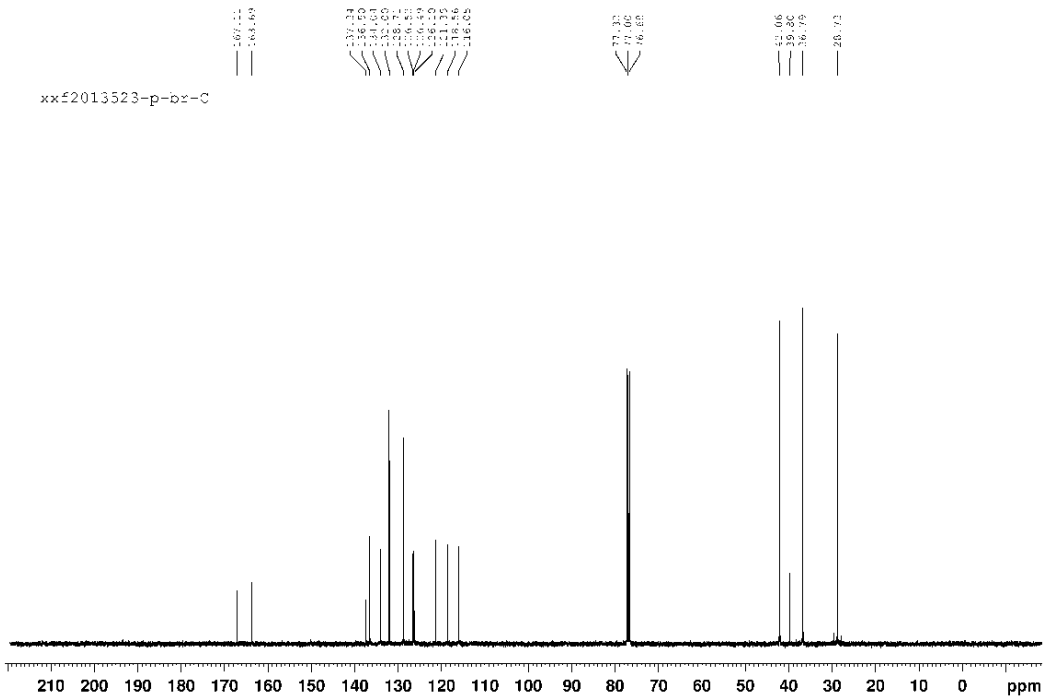
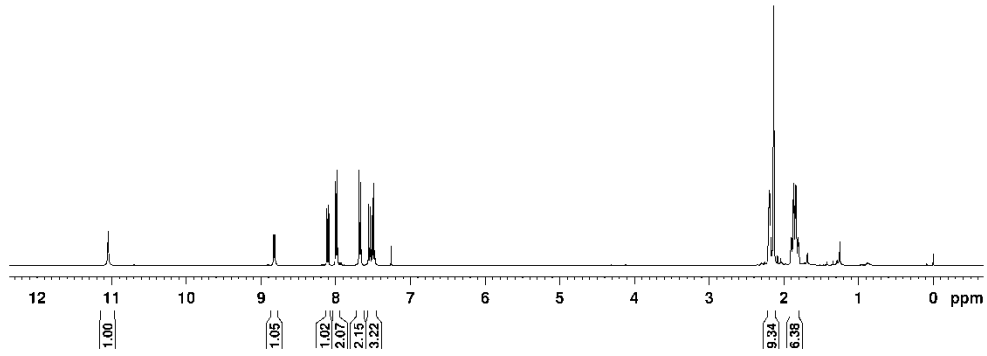
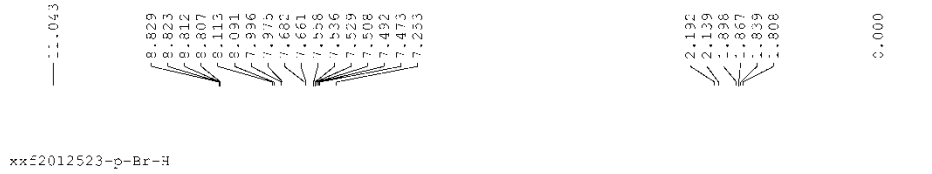
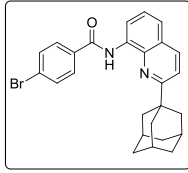


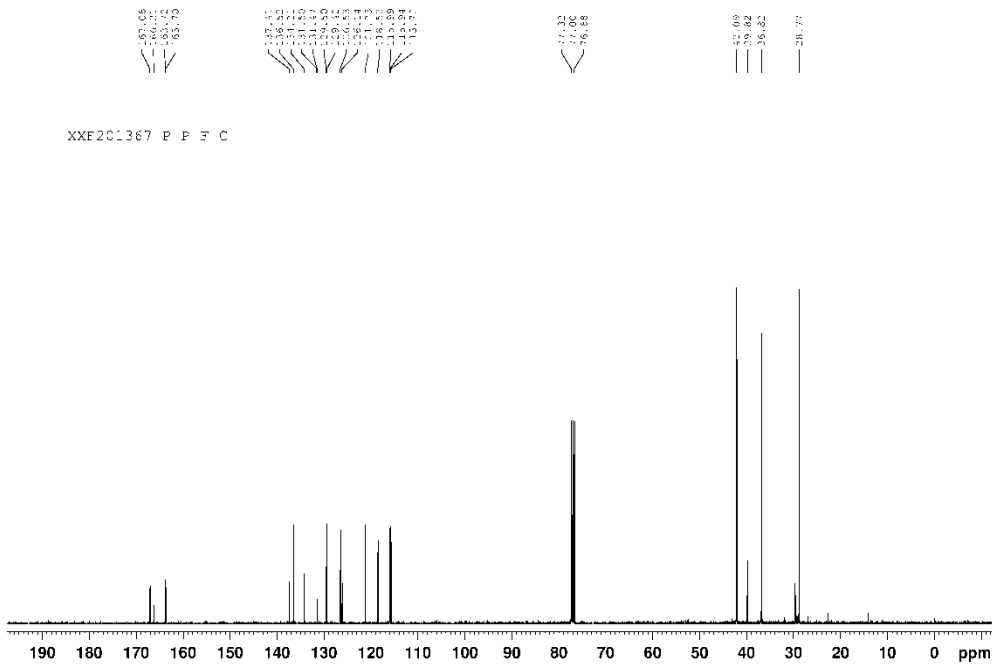
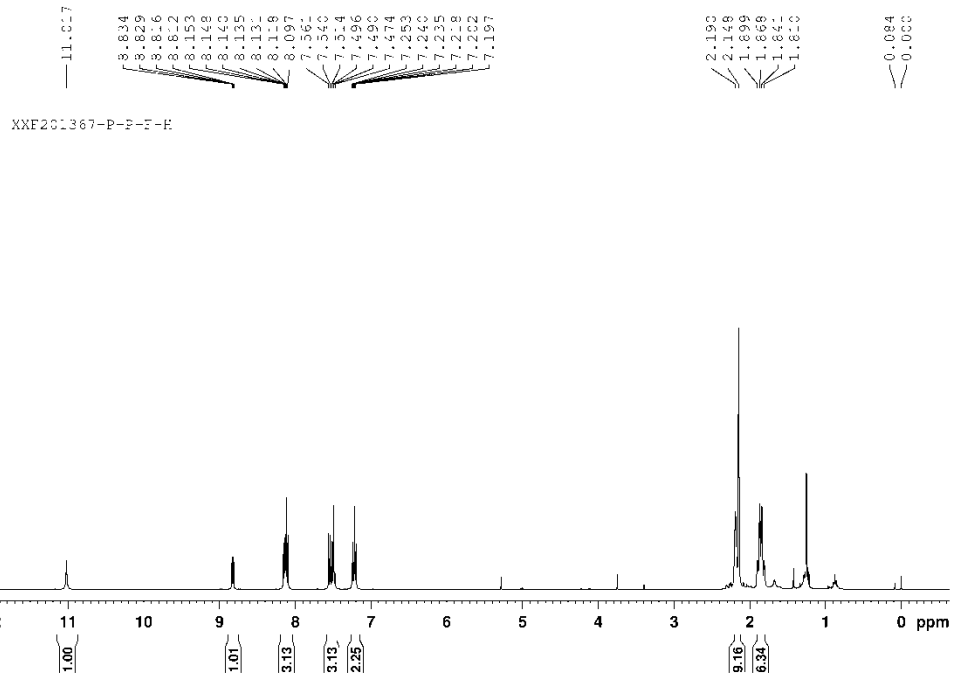
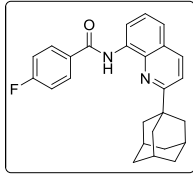


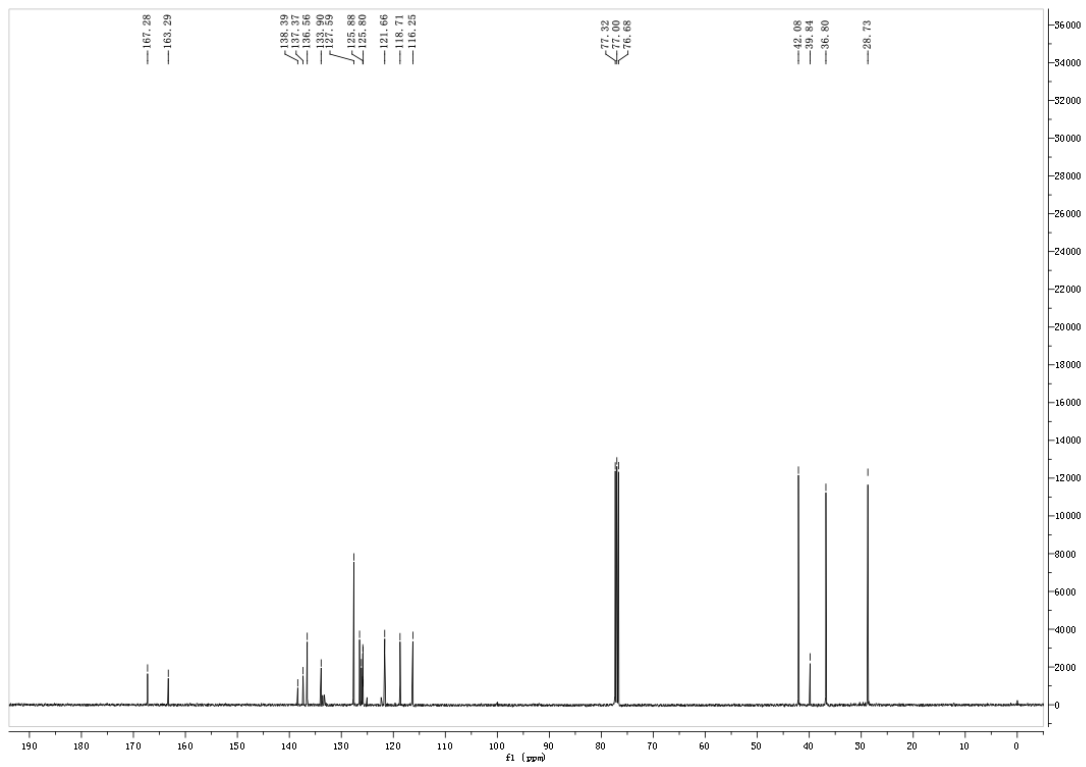
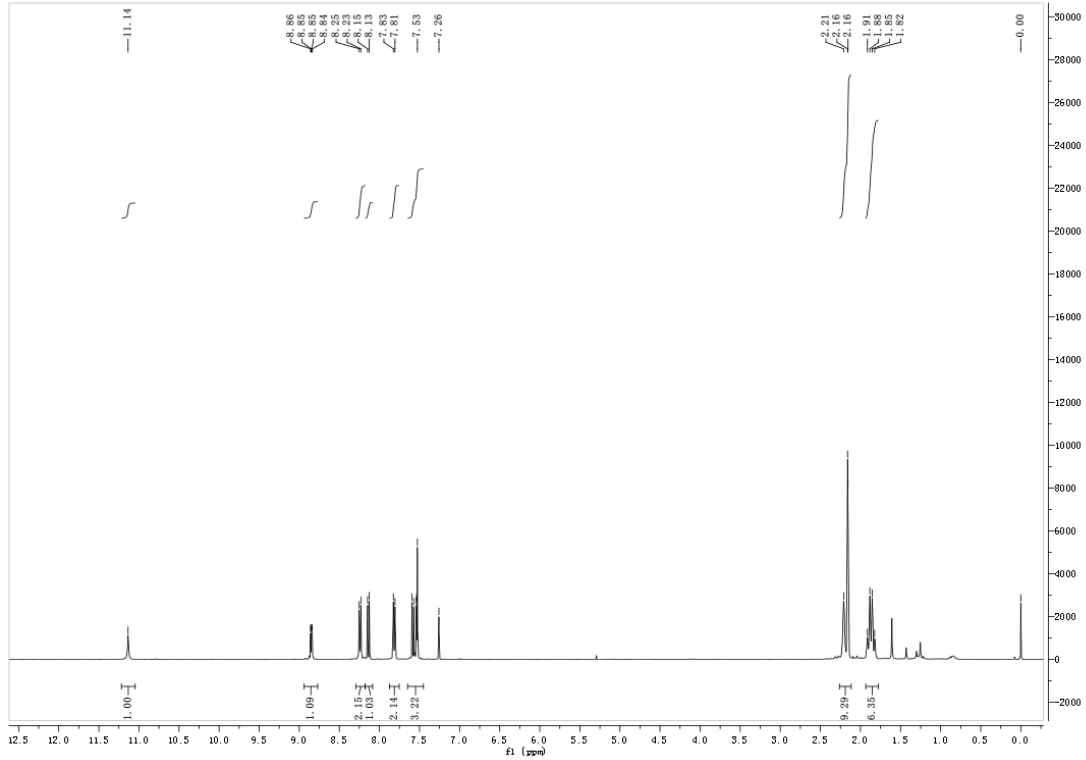
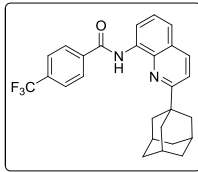


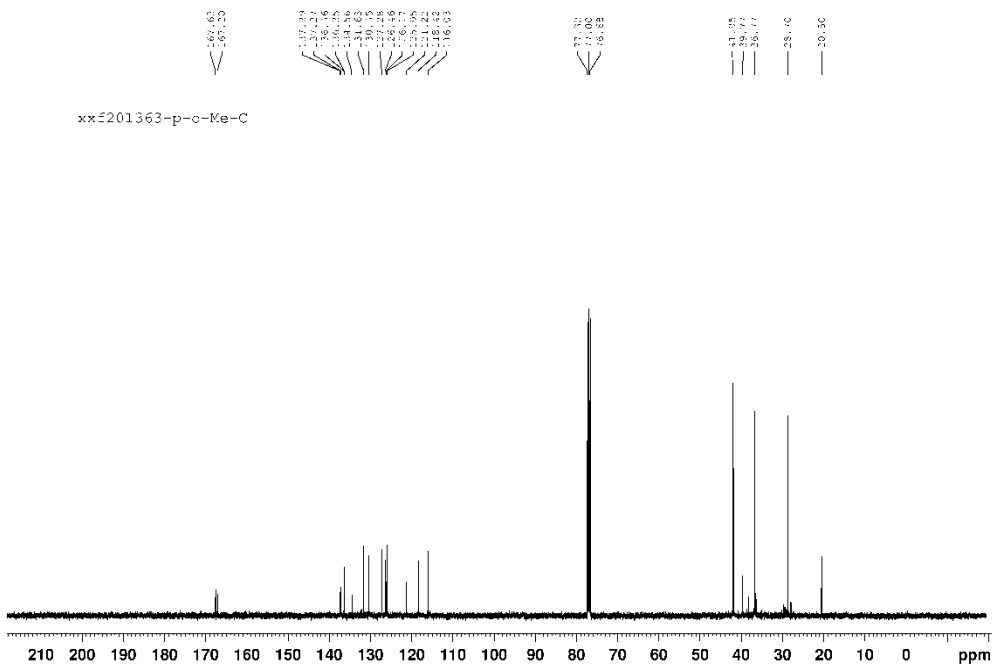
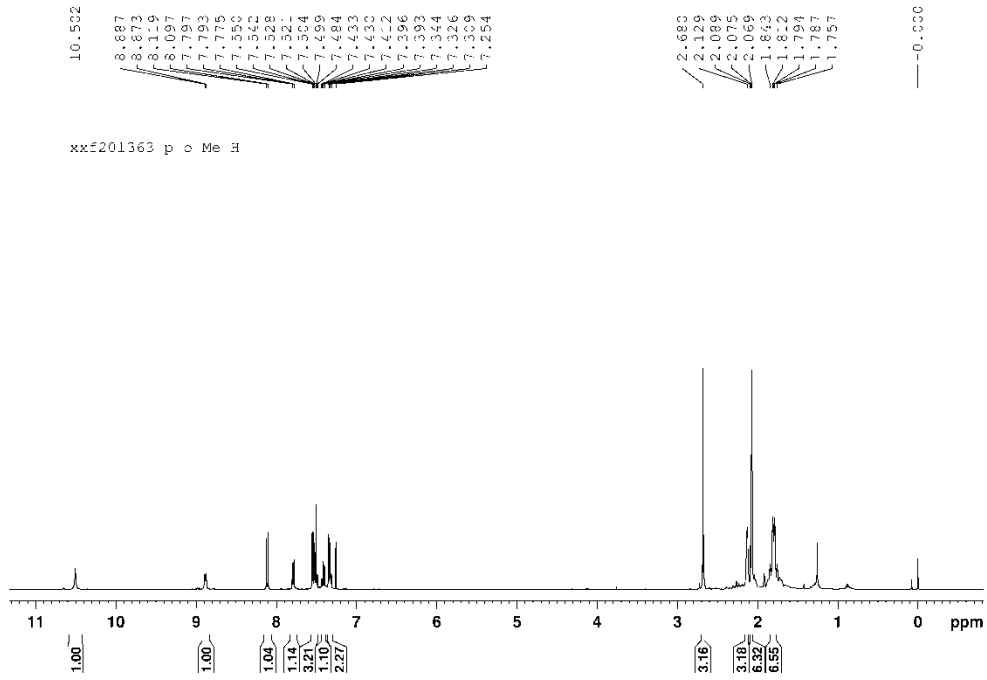
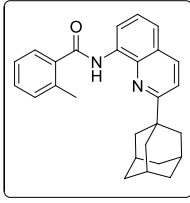


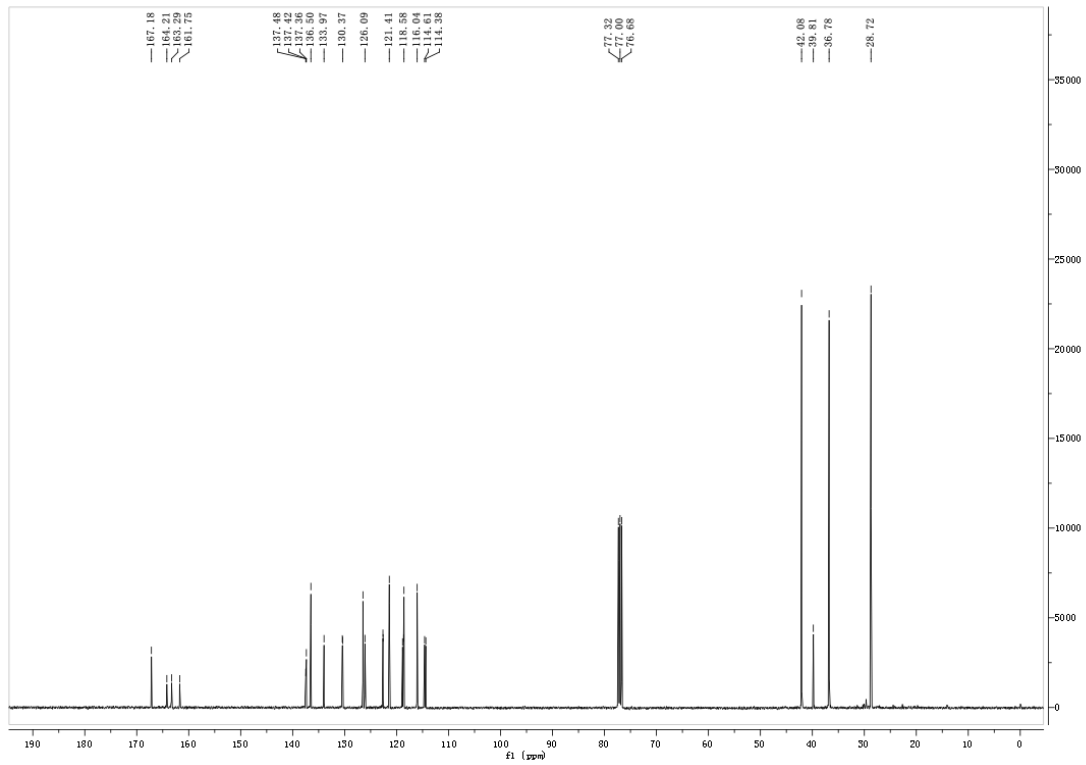
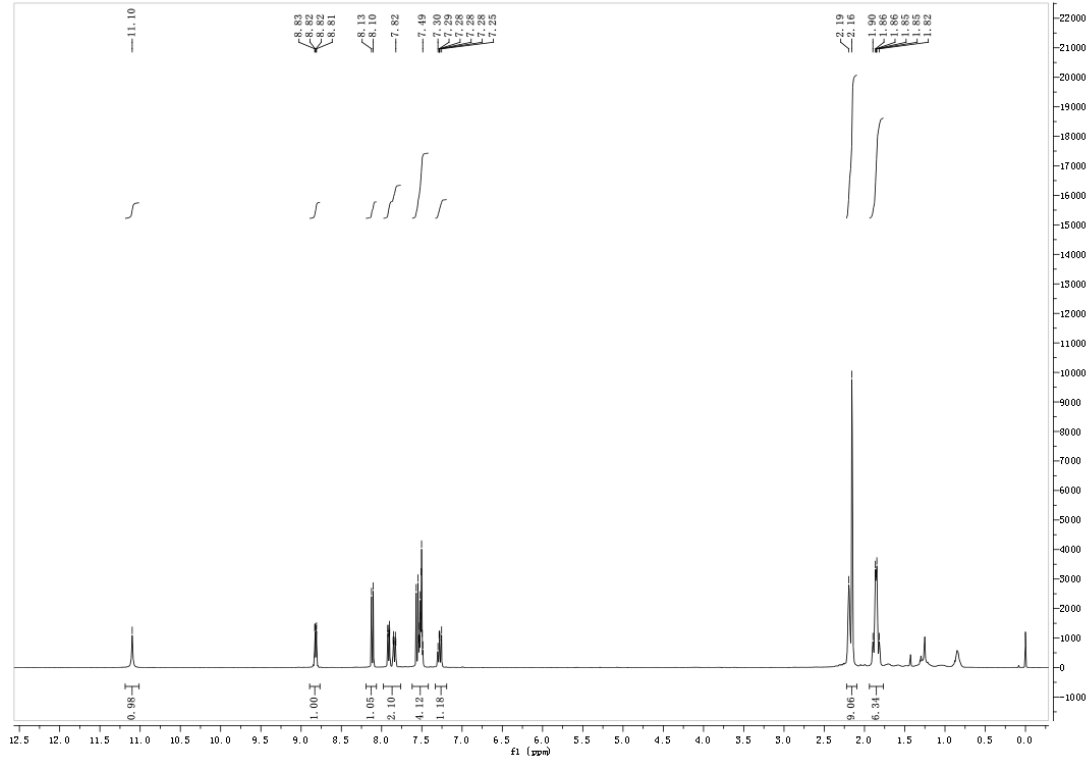
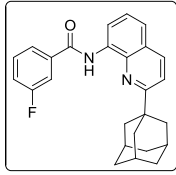




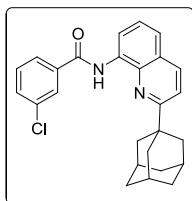










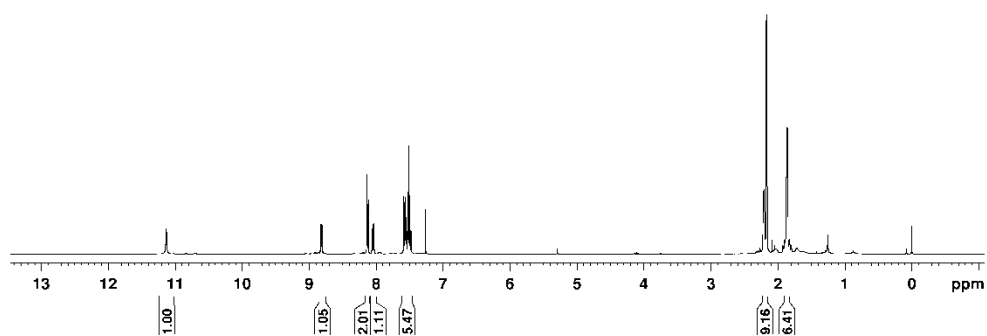


1.128  
 8.821  
 8.814  
 8.806  
 8.799  
 8.131  
 8.124  
 8.110  
 8.049  
 8.046  
 8.045  
 8.030  
 8.027  
 8.023  
 7.580  
 7.572  
 7.569  
 7.567  
 7.564  
 7.559  
 7.552  
 7.548  
 7.547  
 7.544  
 7.522  
 7.512  
 7.506  
 7.491  
 7.471  
 7.256

2.206  
 2.169  
 2.163  
 1.865  
 1.860

0.000

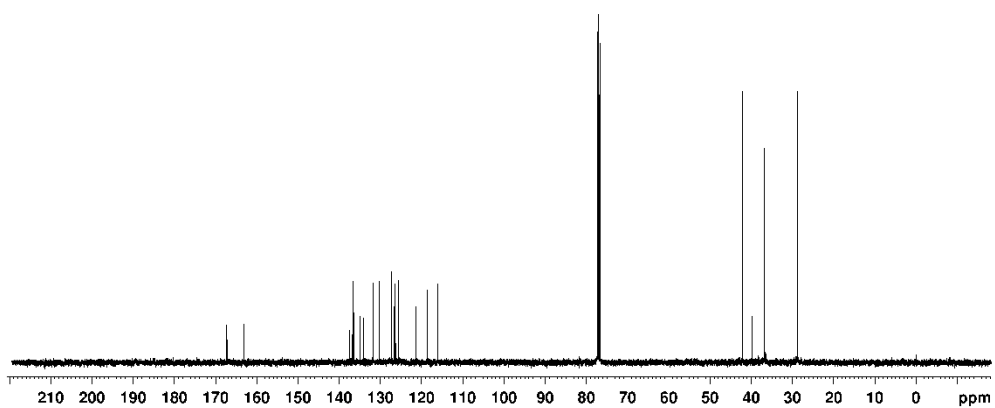
xxf2013531-p-m-cl-h

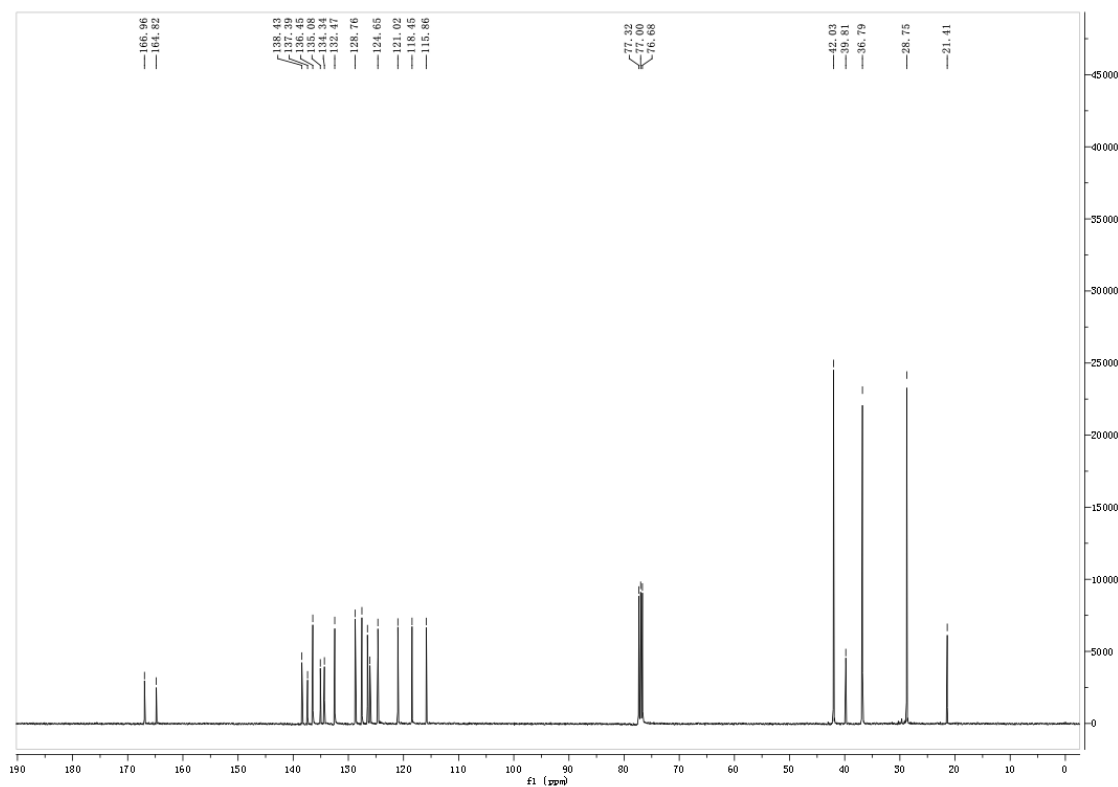
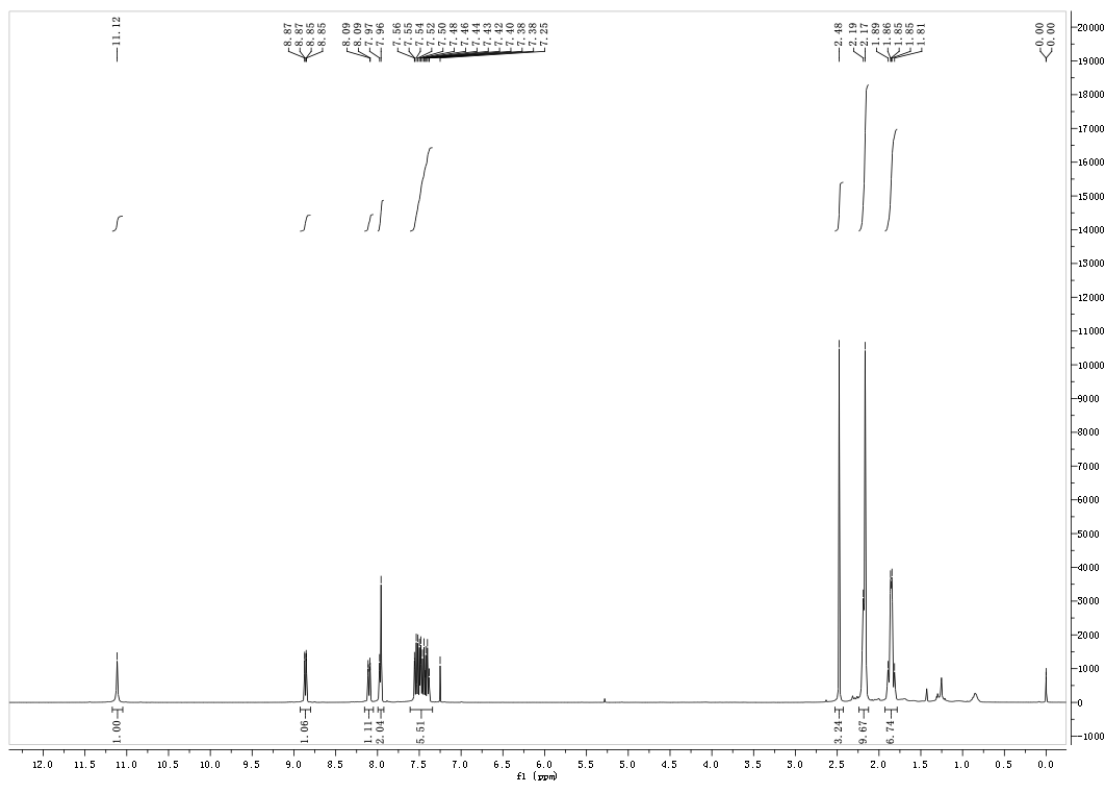
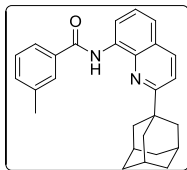


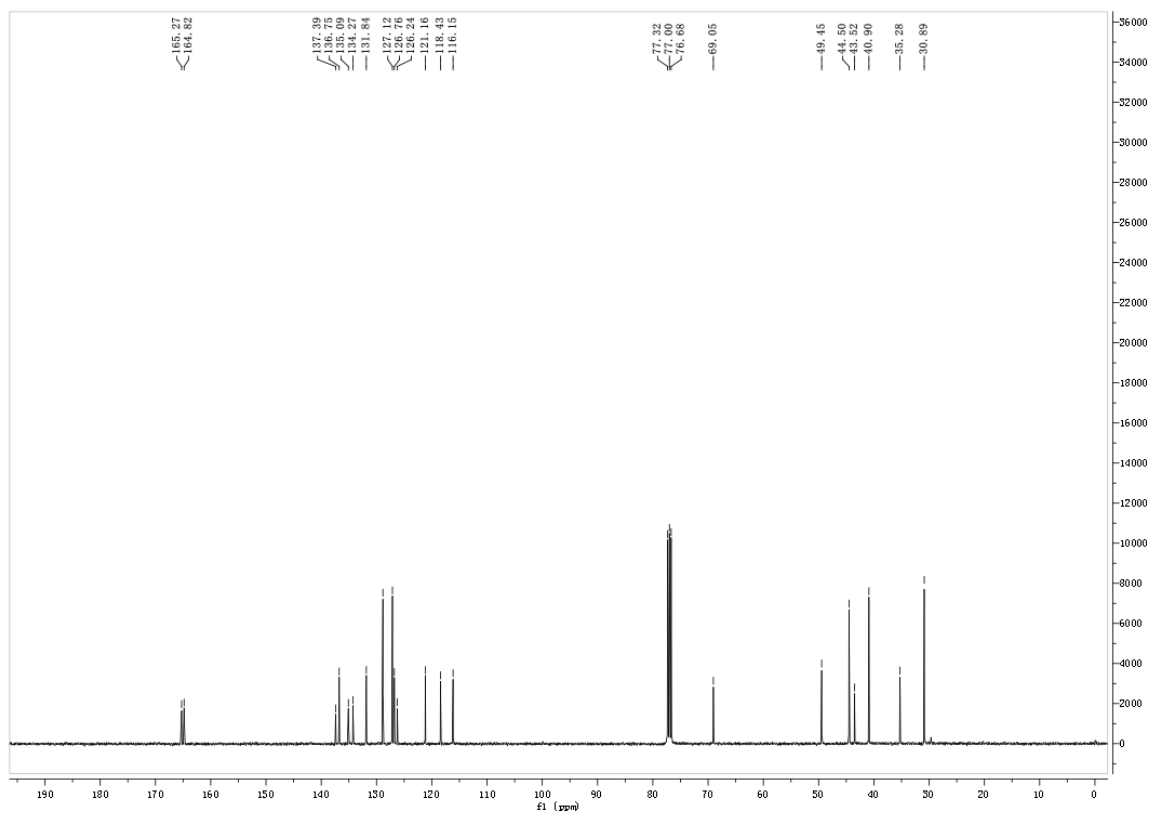
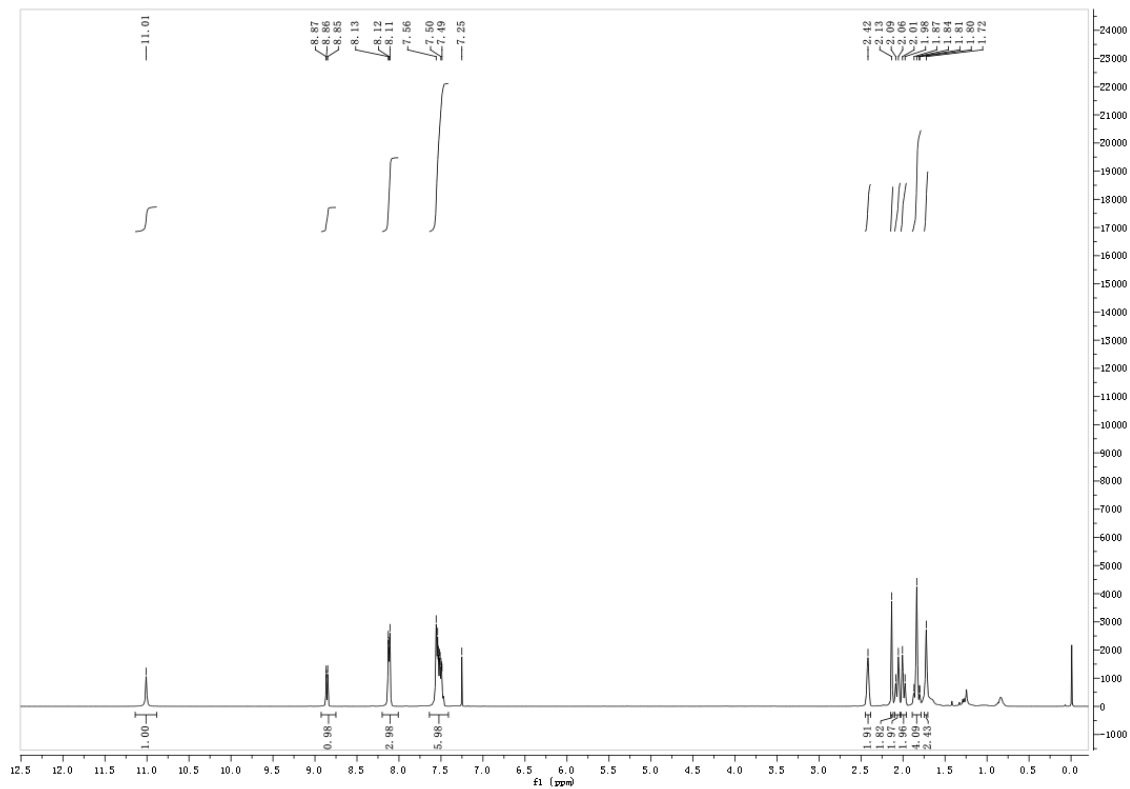
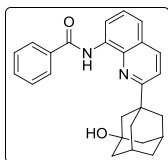
167.26  
 163.25  
 136.88  
 136.71  
 134.93  
 131.75  
 130.16  
 128.56  
 126.51  
 125.93  
 123.93  
 119.64  
 116.07

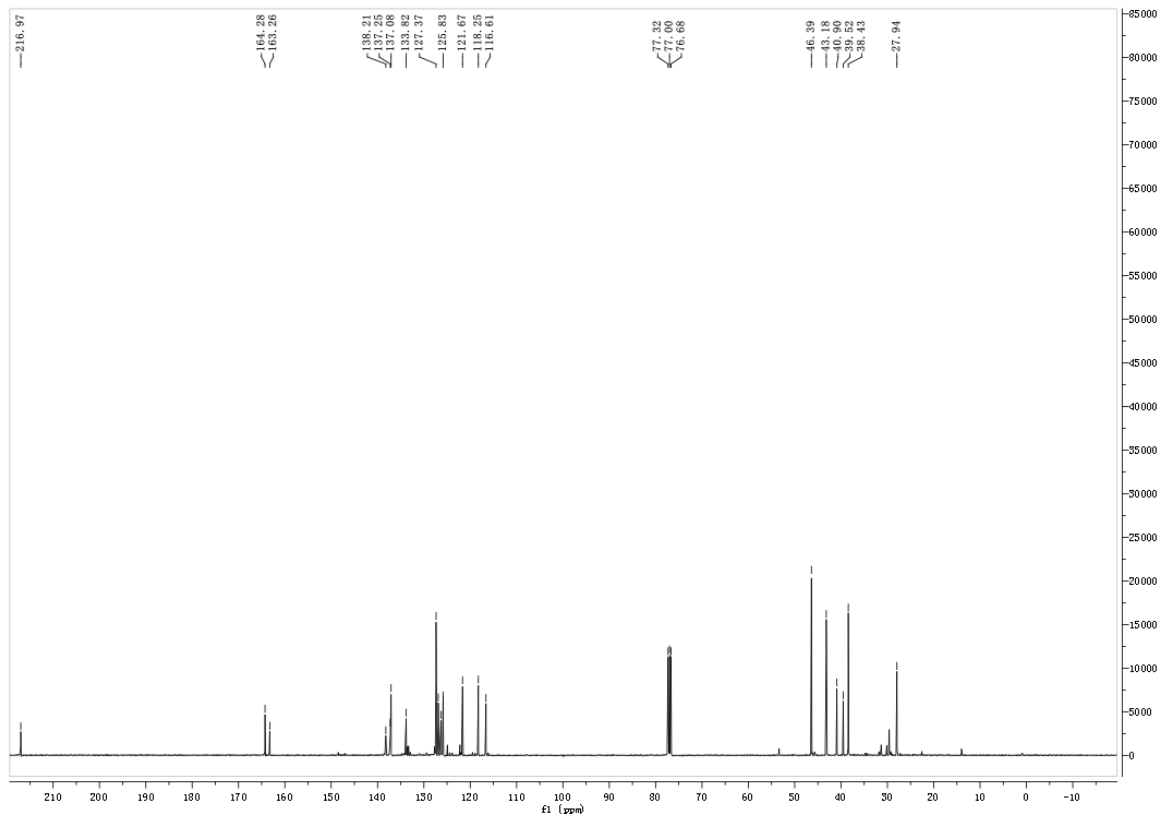
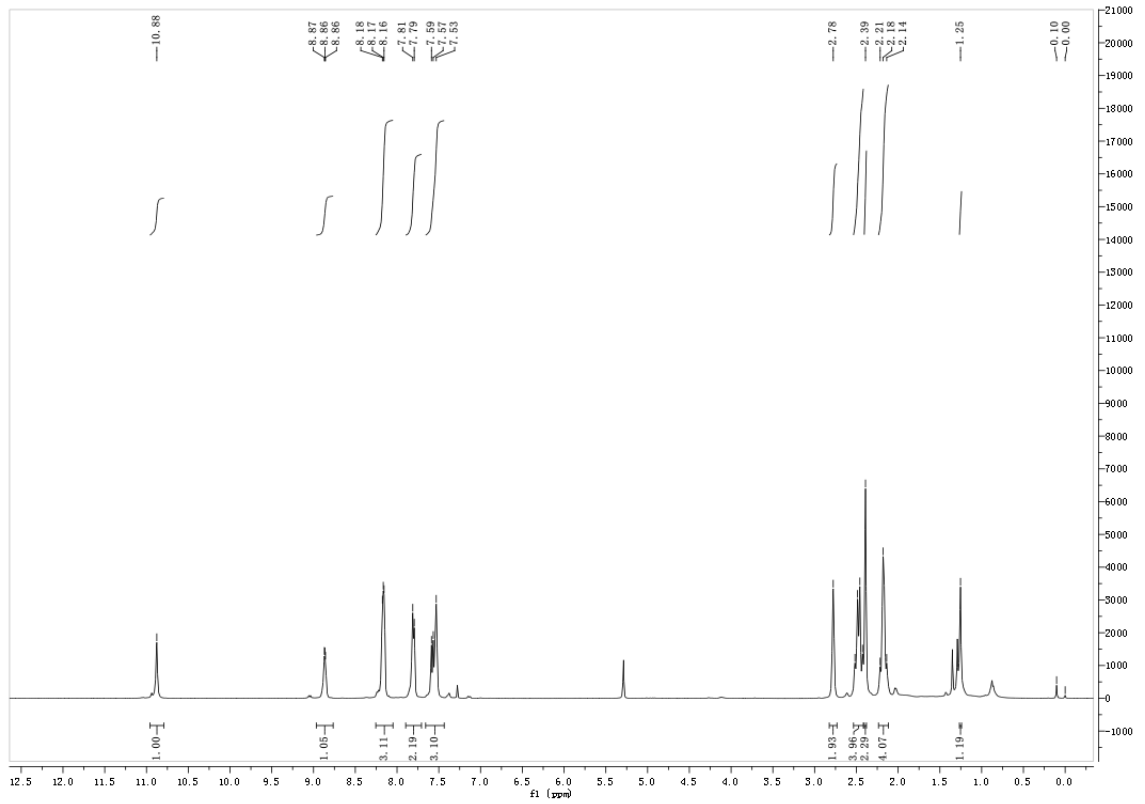
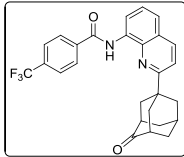
77.32  
 76.85  
 39.36  
 36.66  
 20.74

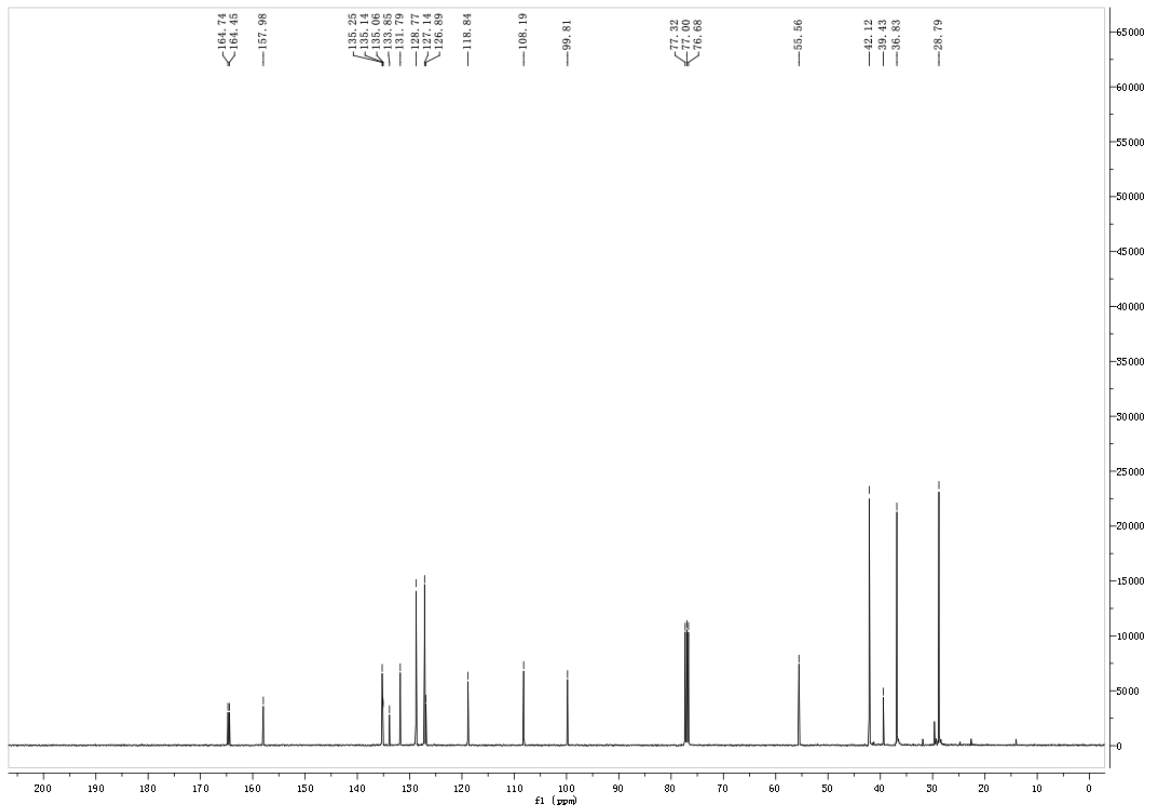
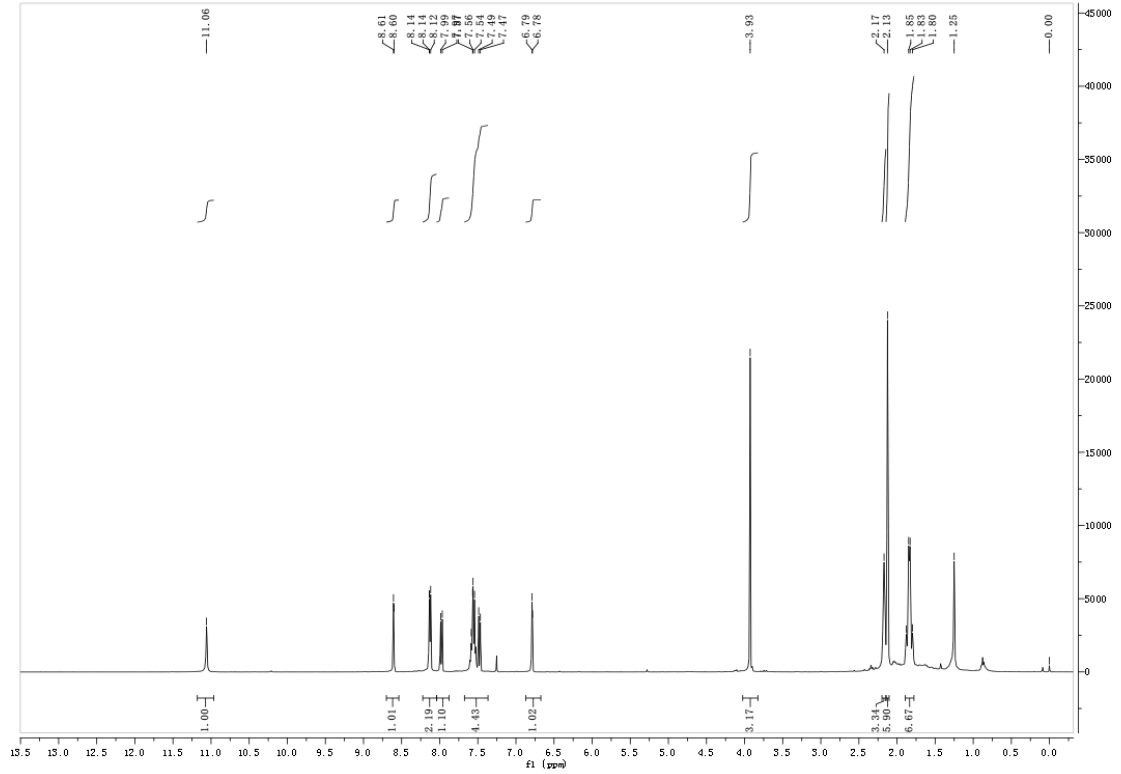
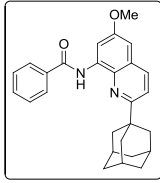
xxf2013531-p-m-cl-c

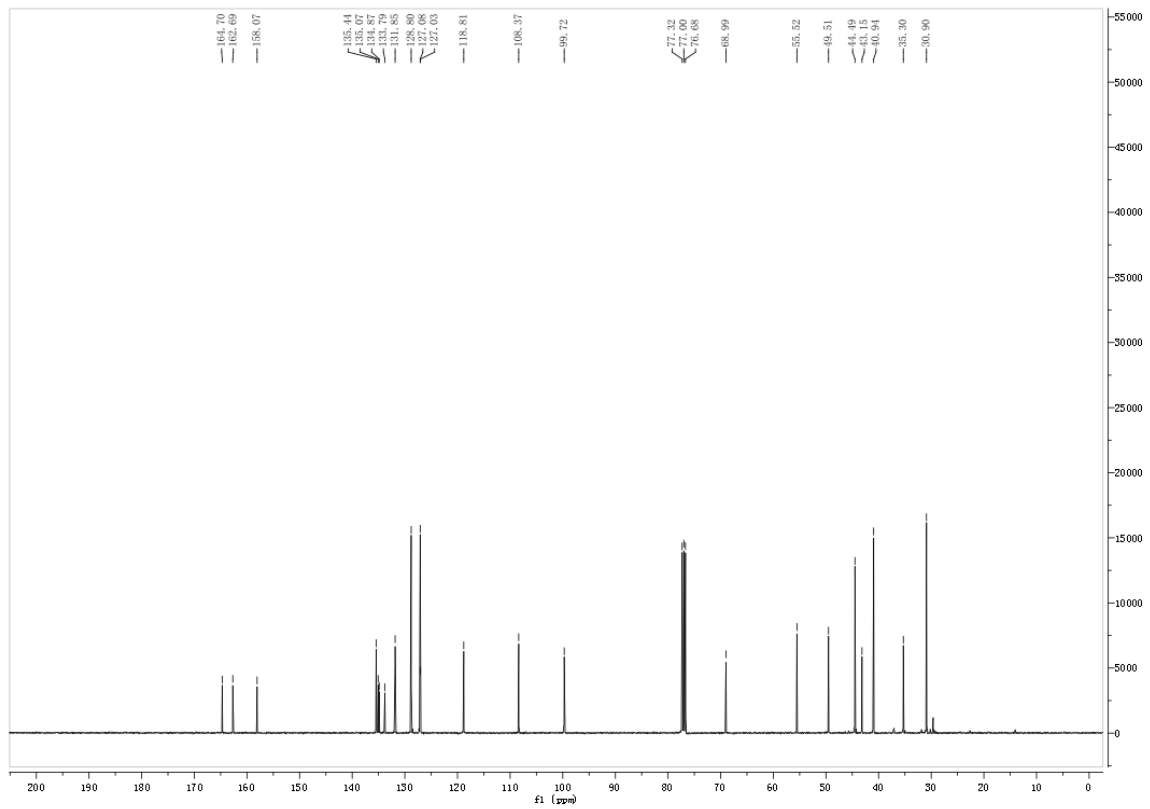
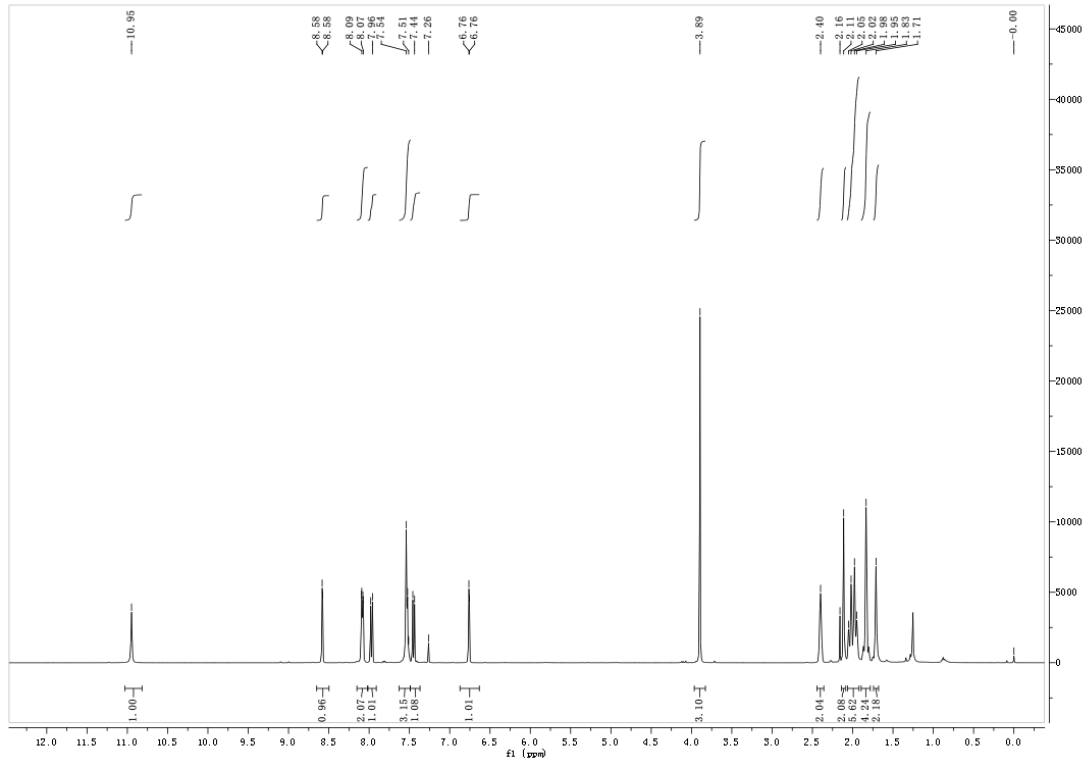
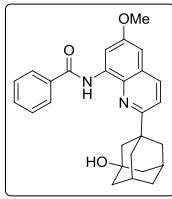


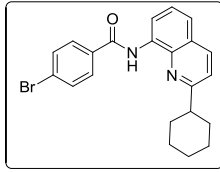




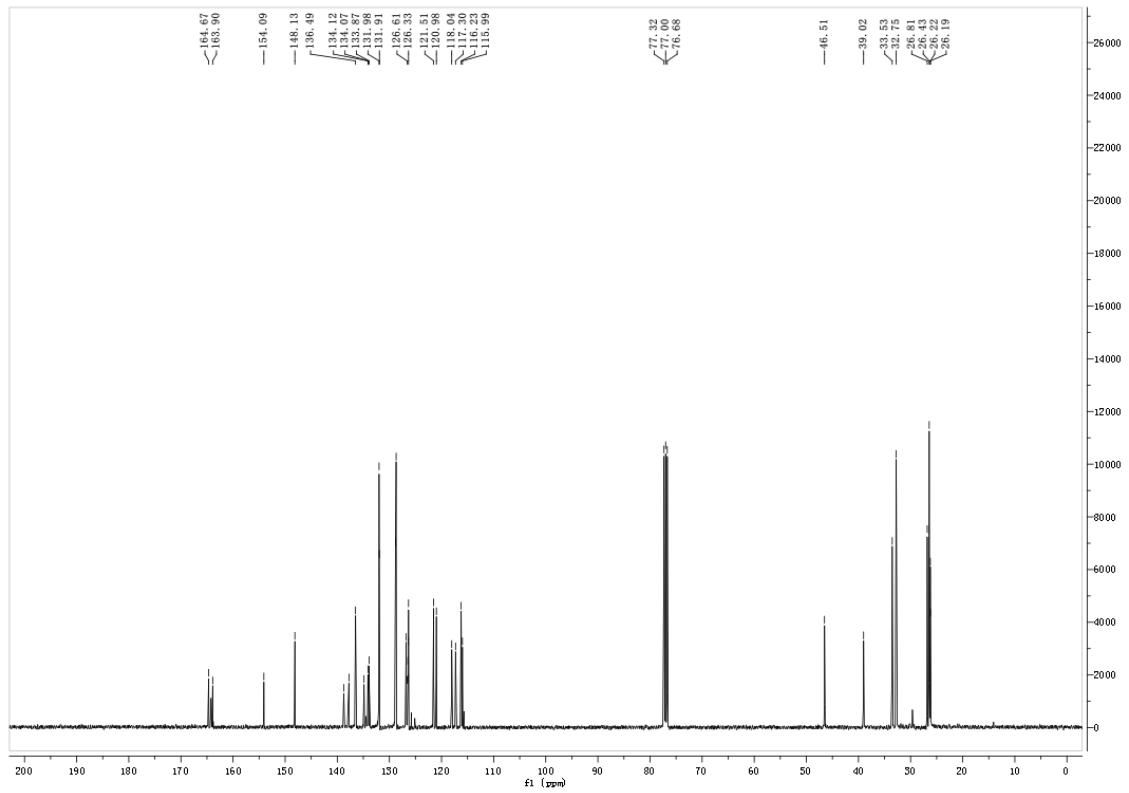
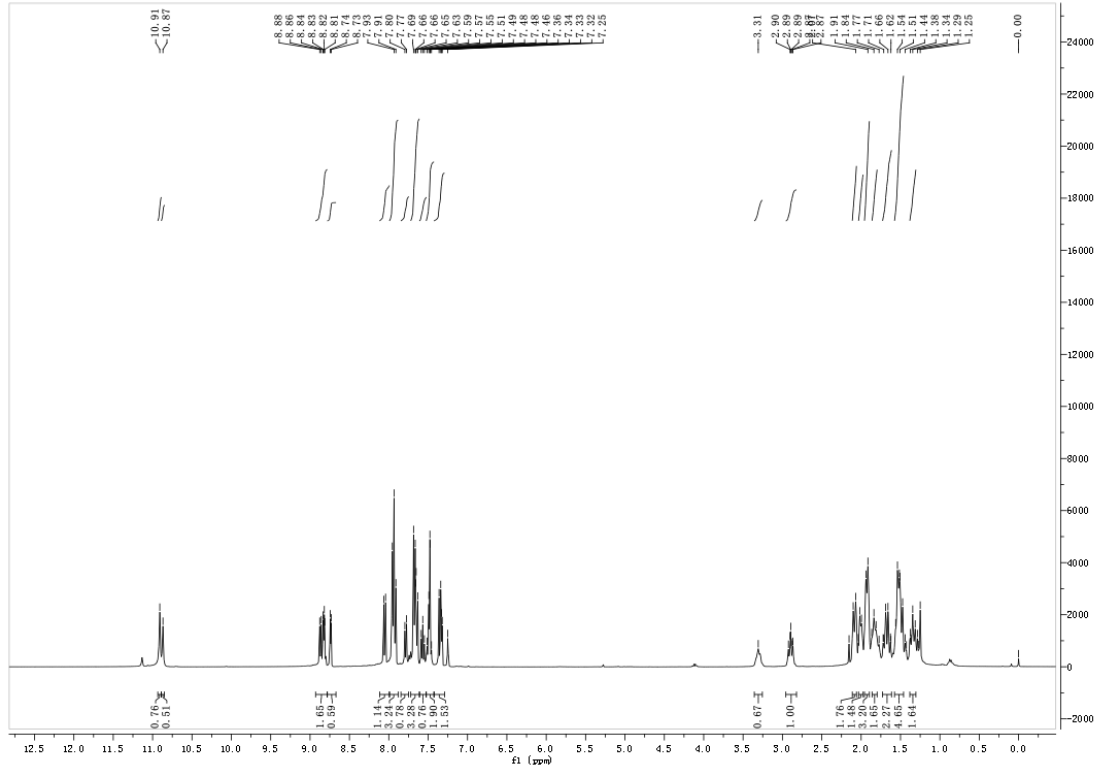


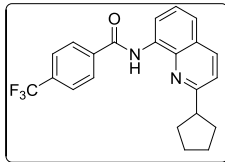




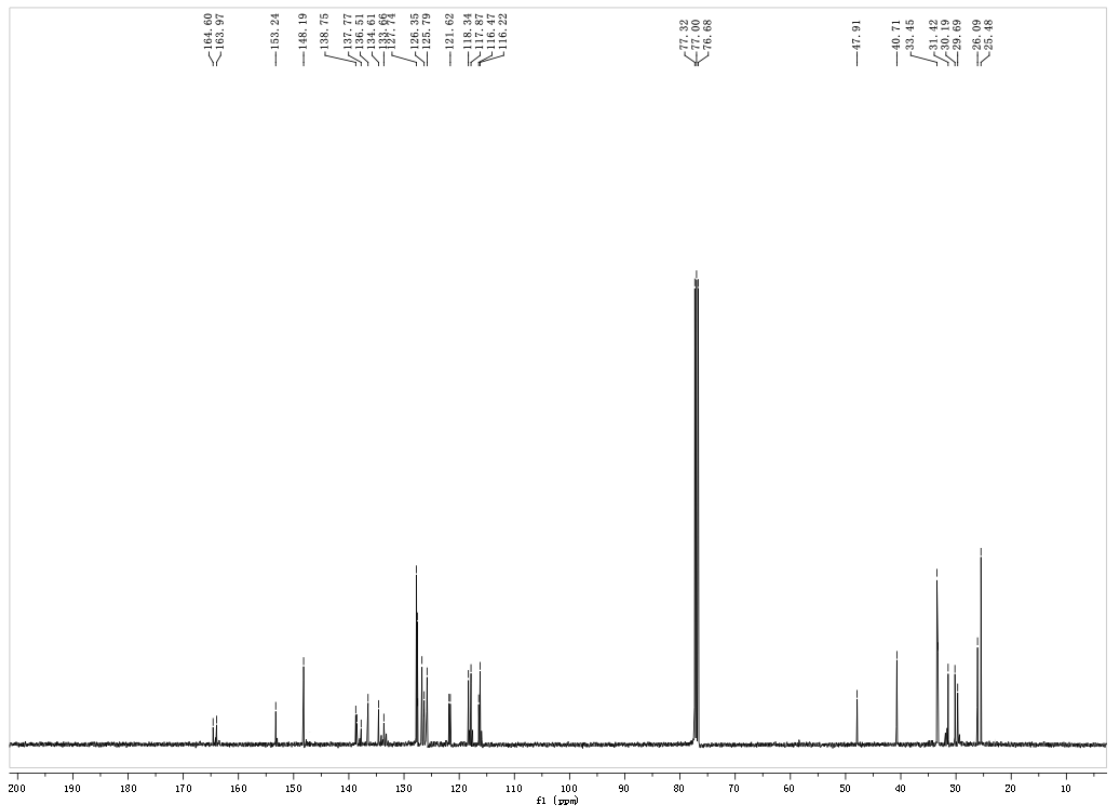
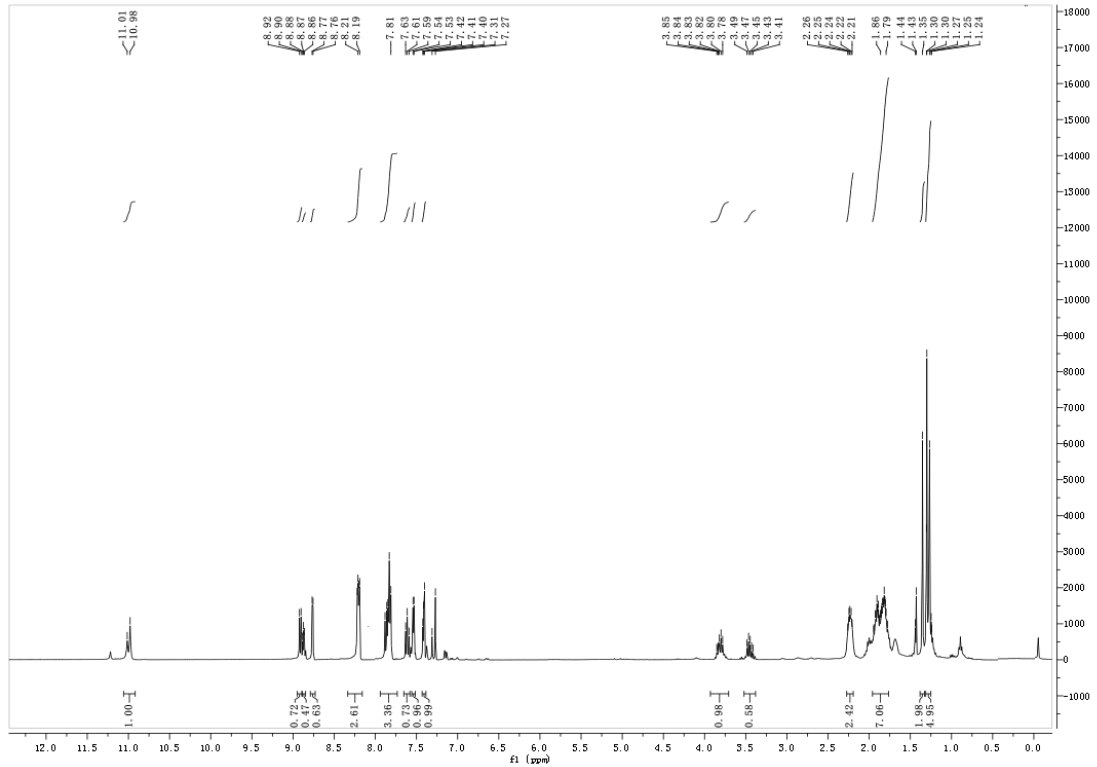


r.r.=3:5 (C2:C4)

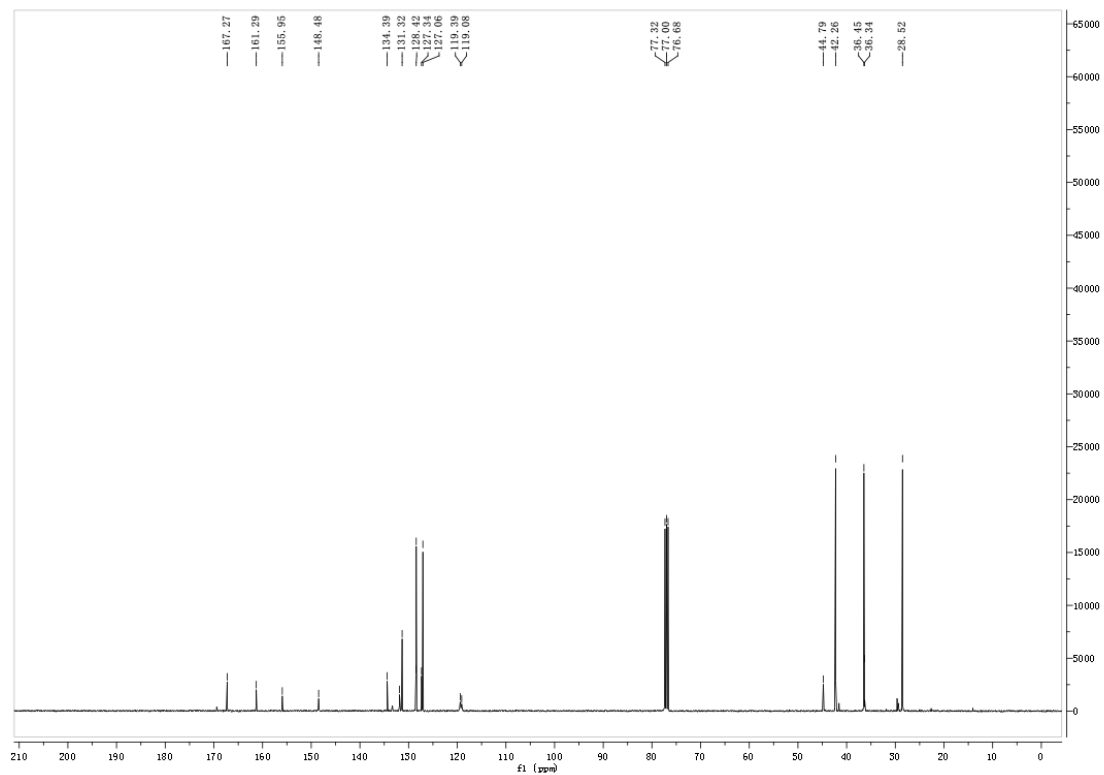
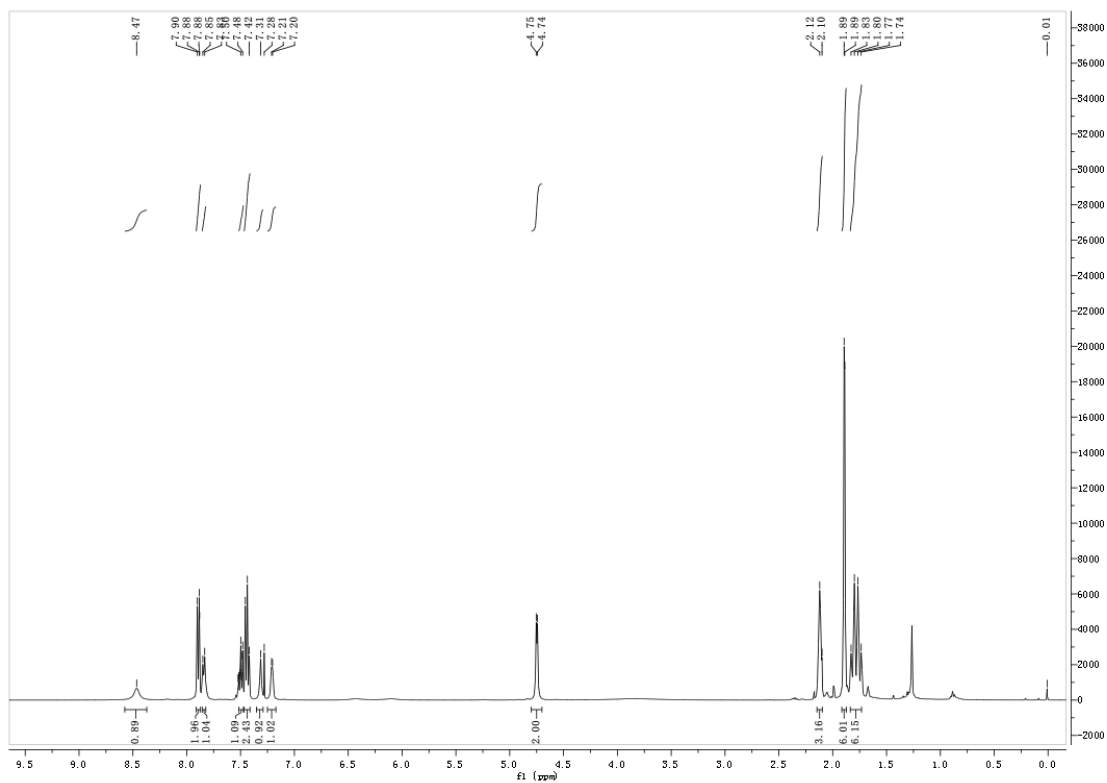
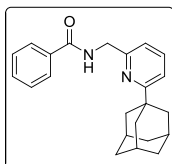


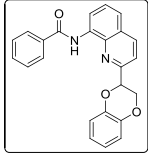


r.r. = 5:3 (C2:C4)

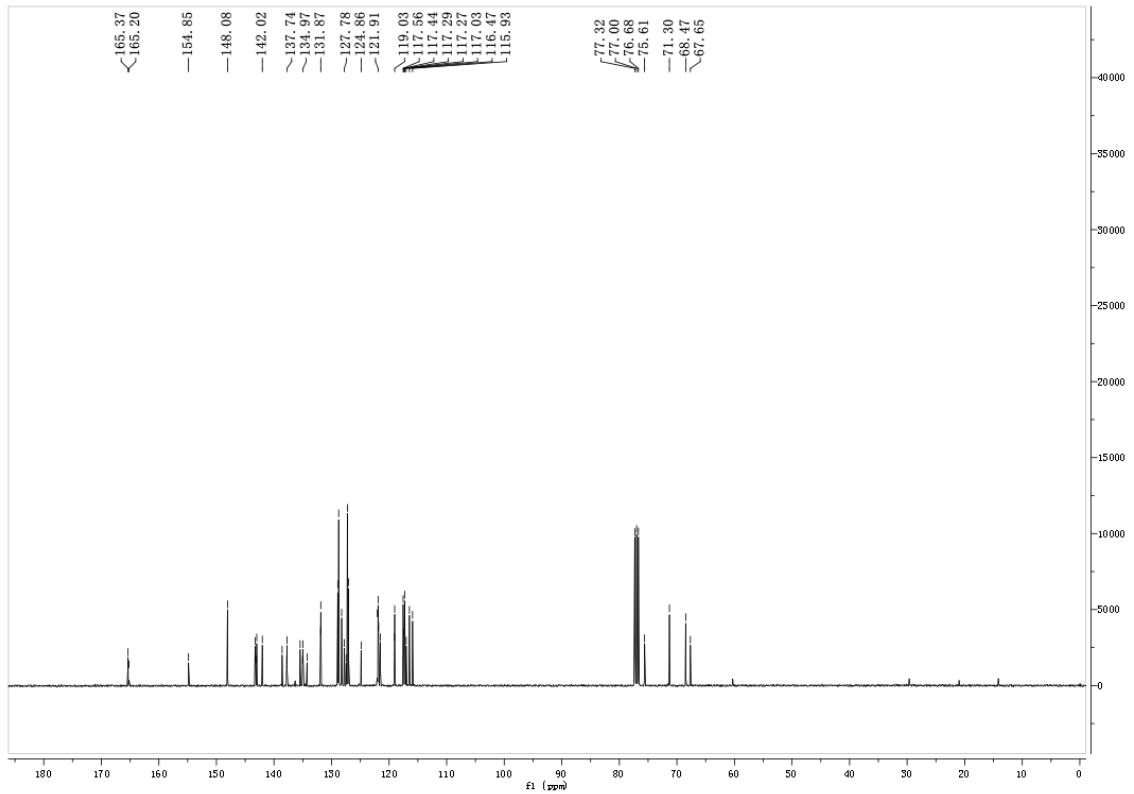
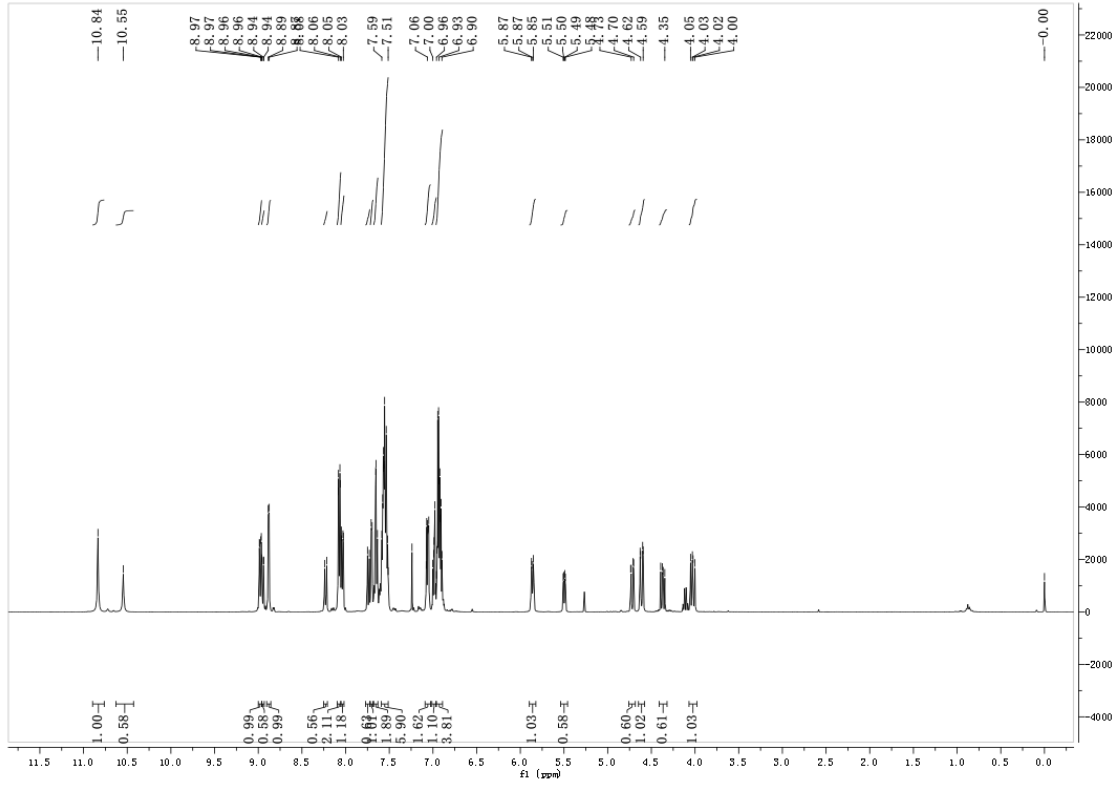


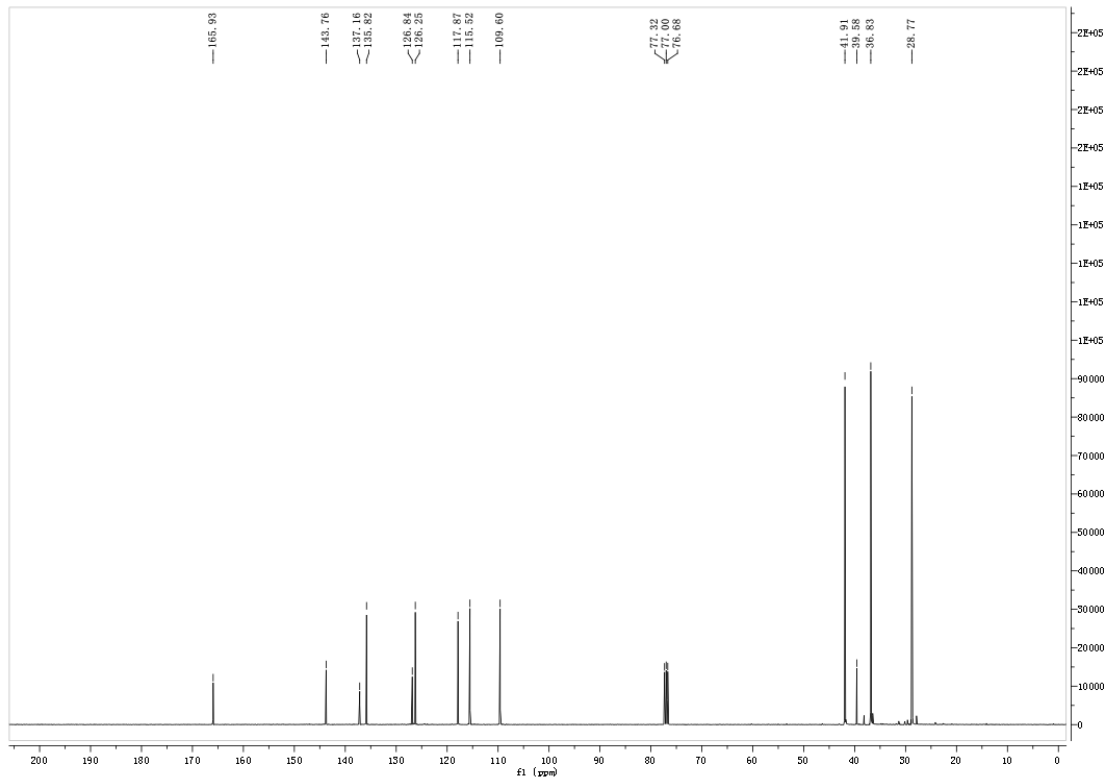
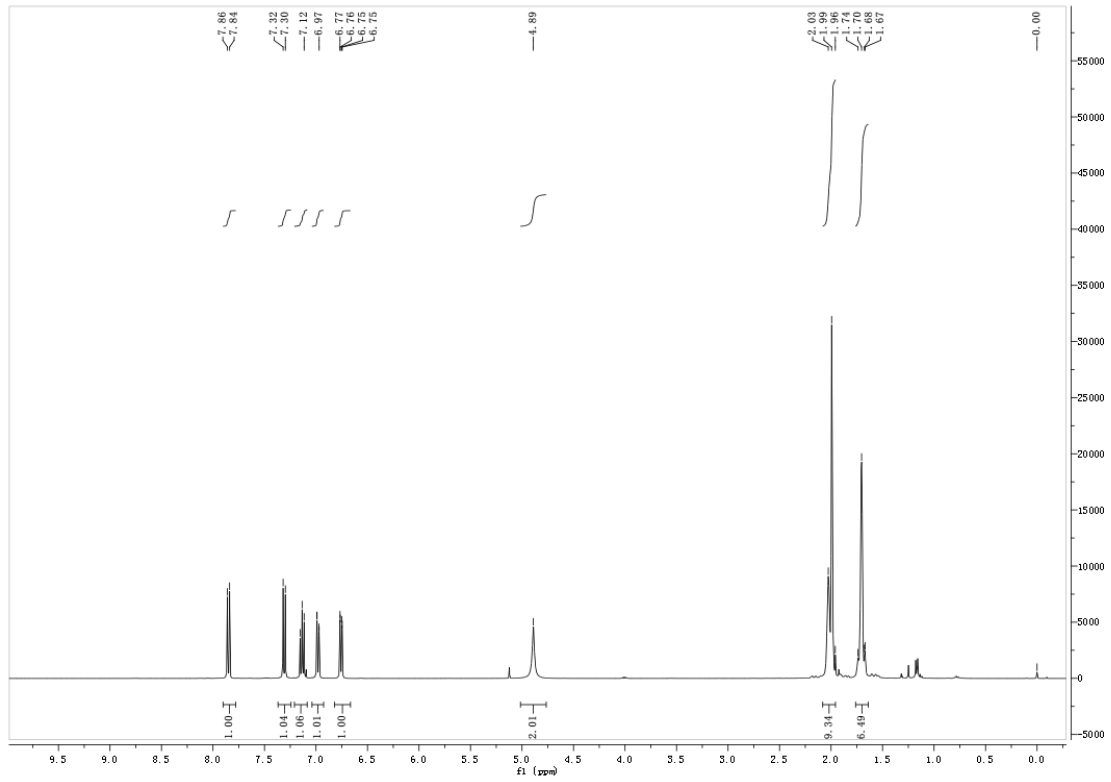
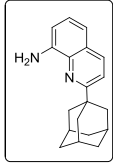


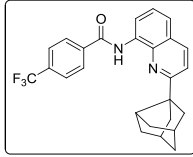




r.r (C2/C4= 5:3)







r.r. = 2:3 (C2:C4)

