Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Cleavage of the C-C Triple Bond of the Ketoalkynes: Synthesis of 4(3*H*)-quinazolinones

Xifa Yang, Guolin Cheng*, Jinhai Shen, Changsheng Kuai, Xiuling Cui*

Engineering Research Center of Molecular Medicine, Ministry of Education, Key Laboratory of Xiamen Marine and Gene Drugs, Institutes of Molecular Medicine and School of Biomedical Sciences, Huaqiao University, Xiamen 361021, China

Contents:

General information:

General Methods: Unless otherwise noted, all solvents were purchased from commercial suppliers and used without further purification. The ketoalkynes **2** were prepared according to the literatures.[1] Silica gel was purchased from Qing Dao Hai Yang Chemical Industry Co. ^{1}H and ^{13}C NMR spectra were measured on 400 MHz spectrometers (^{1}H 400 MHz, ^{13}C100 MHz), using dimethylsulfoxide (DMSO-d6) or $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature.

General Methods: Unless otherwise noted, all solvents were purchased from commercial suppliers and used

General Procedure for Synthesis of 4(3*H*)-quinazolines.

For 4(3*H*)-quinazoline, entry 1, 3, 4, 7, 9, 10-16, 3a, 3b-3f, 3l-3p.

The mixture of ketoalkynes **1** (0.65 mmol) and **2a** (0.5 mmol) in dry toluene (2 mL) was stirred at 90 °C under nitrogen atmosphere. After 16h, the reaction solution was cooled to room temperature and solvent was evaporated via vacuum. To this residue, water was added and reaction mixture was neutralized with sodium bicarbonate and extracted with dichloromethane (5 × 60 mL). The organic solvent was evaporated via vacuum. The resulting crude was crystallized using ethanol to get the pure product as a white solid.

For 2-phenylquinazolin-4(3*H*)-one, entry 2, 5, 6, 8.

The mixture of ketoalkynes **1** (0.65 mmol) and **2a** (0.5 mmol) in dry toluene (2 mL) was stirred under nitrogen atmosphere. After 16h, the reaction solution was cooled to room temperature and then added 30 mL saturated solution of $NaHCO_3$, and extracted with dichloromethane 5 times (5 × 40 mL). The combined organic layers were washed with brine (30 mL). The organic solvent was evaporated via vacuum. The resulting crude was crystallized using ethanol to get the pure products as white solid.

For 4(3*H*)-quinazoline 3g-3k, 3q.

The mixture of Ketoalkynes **1** (0.65 mmol) and **2a** (0.5 mmol) in dry toluene (2 mL) was stirred at 90 °C under nitrogen atmosphere for 16 h. The reaction was cooled to room temperature and solvent was evaporated via vacuum. The residue was purified by silica gel column chromatography with DCM/ethyl acetate (8:1) to provide the desired 4(3*H*)-quinazolines.

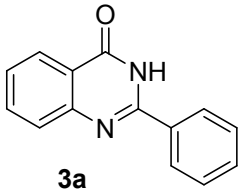
For 4(3*H*)-quinazoline 3r.

The key intermediate (E)-2-{(4-oxo-4-phenylbutan-2-ylidene}amino benzamide **4b** (0.5 mmol) in dry toluene (2 mL) was stirred at 90 °C with 3eq of TFA under nitrogen atmosphere for 16 h. The reaction was cooled to room temperature and solvent was evaporated via vacuum. The residue was purified by silica gel column chromatography with petroleum ether /ethyl acetate (2:1) to provide the desired 4(3*H*)-quinazolines.

For (E)-2-{(4-oxo-4-phenylbutan-2-ylidene)amino}benzamide 4b.

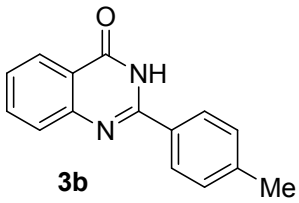
The mixture of 1,3-diphenylpropane-1,3-dione (2 mmol) and 2-aminobenzenesulfonamide (2 mmol) in dry toluene was stirred at 120 °C and the water was removed by water separator for 24 h. The reaction was cooled to room temperature and solvent was evaporated via vacuum. The residue was purified by silica gel column chromatography with petroleum ether /ethyl acetate/ Et_3N (6:1:0.1) to provide the desired (E)-2-{(4-oxo-4-phenylbutan-2-ylidene)amino}benzamide **4b**.

Product characterizations



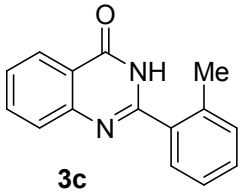
3a

2-phenylquinazolin-4(3H)-one (3a). White solid. Mp: 235 – 236 °C (lit[2]. 235 – 237 °C). ^{1}H NMR (400 MHz, DMSO) δ 12.50 (s, 1H), 8.15 (dd, *J* = 9.5, 7.8 Hz, 3H), 7.86 – 7.77 (m, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.63 – 7.46 (m, 4H). ^{13}C NMR (101 MHz, DMSO) δ 162.69, 152.78, 149.22, 135.06, 133.20, 131.85, 129.06, 128.23, 127.98, 127.05, 126.32, 121.46.



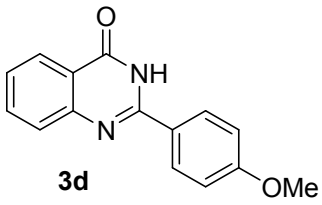
3b

2-(p-tolyl)quinazolin-4(3H)-one (3b). White solid. Mp: 245 – 246 °C(lit[2]. 241 – 243 °C). ^{1}H NMR (400 MHz, DMSO) δ 12.42 (s, 1H), 8.15 – 8.05 (m, 3H), 7.83 – 7.77 (m, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.48 (ddd, *J* = 8.0, 7.2, 1.1 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 162.72, 152.69, 149.30, 141.91, 135.01, 130.37, 129.65, 128.15, 127.88, 126.84, 126.31, 121.37, 21.45.



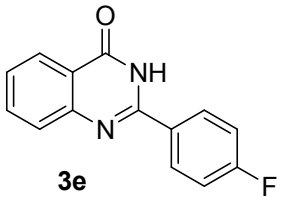
3c

2-(o-tolyl)quinazolin-4(3H)-one (3c). White solid. Mp: 223 – 224 °C(lit[2]. 216 – 218 °C). ^{1}H NMR (400 MHz, DMSO) δ 12.41 (s, 1H), 8.15 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.84 – 7.78 (m, 1H), 7.67 (d, *J* = 7.9 Hz, 1H), 7.51 (td, *J* = 7.7, 1.1 Hz, 2H), 7.41 (td, *J* = 7.6, 1.3 Hz, 1H), 7.35 – 7.28 (m, 2H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 162.28, 154.88, 149.17, 136.59, 134.90, 134.71, 130.99, 130.34, 129.59, 127.77, 127.08, 126.26, 126.15, 121.45. 20.02.



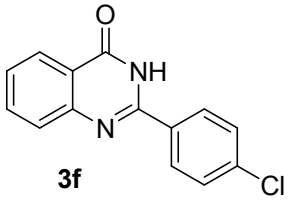
3d

2-(4-methoxyphenyl)quinazolin-4(3H)-one **(*3d*).** White solid. Mp: 240 – 241°C (lit[3]. 245 – 246°C). ^{1}H NMR (400 MHz, DMSO) δ 12.38 (s, 1H), 8.22 – 8.08 (m, 3H), 7.83 – 7.76 (m, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.49 – 7.43 (m, 1H), 7.07 (dd, *J* = 6.8, 5.0 Hz, 2H), 3.83 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 162.84, 162.35, 152.41, 149.34, 134.99, 129.93, 127.67, 126.58, 126.30, 125.31, 121.15, 114.47, 55.94.



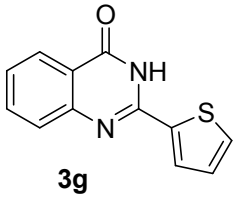
3e

2-(4-fluorophenyl)quinazolin-4(3H)-one (3e). White solid. Mp: 257 – 259 °C (lit[2].284 – 287 °C). ^{1}H NMR (400 MHz, DMSO) δ 12.53 (s, 1H), 8.26 – 8.20 (m, 2H), 8.13 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.82 (ddd, *J* = 8.5, 7.2, 1.5 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.50 (ddd, *J* = 8.1, 7.2, 1.1 Hz, 1H), 7.40 – 7.33 (m, 2H). ^{13}C NMR (101 MHz, DMSO) δ 165.76, 162.97 (d, *J* = 62.1 Hz), 151.84, 149.13, 135.10, 130.84 (d, *J* = 9.0 Hz), 129.70, 127.93, 127.08, 126.32, 121.37, 116.09 (d, *J* = 21.9 Hz).



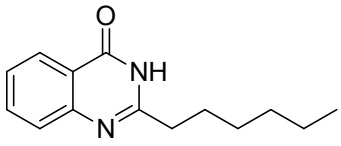
3f

2-(4-chlorophenyl)quinazolin-4(3H)-one (3f). White solid. Mp: 298 – 299 °C. (lit[2]. 298 – 300 °C) ^{1}H NMR (400 MHz, DMSO) δ 12.57 (s, 1H), 8.21 – 8.16 (m, 2H), 8.13 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.82 (ddd, *J* = 8.5, 7.1, 1.6 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.64 – 7.57 (m, 2H), 7.54 – 7.49 (m, 1H). ^{13}C NMR (101 MHz, DMSO) δ 162.78, 151.96, 149.02, 136.74, 135.10, 132.13, 130.10, 129.15, 127.91, 127.21, 126.35, 121.47.



3g

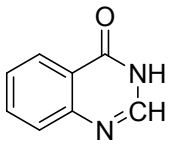
2-(thiophen-2-yl)quinazolin-4(3H)-one (3g). Yellow solid. Mp: 271 – 272 °C.(lit[4]. 275 – 276 °C) ^{1}H NMR (400 MHz, DMSO) δ 12.63 (s, 1H), 8.23 (d, *J* = 3.6 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.85 (d, *J* = 5.0 Hz, 1H), 7.79 (t, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 4.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 162.25, 149.12, 148.30, 137.85, 135.13, 132.59, 129.86, 128.95, 127.42, 126.78, 126.45, 121.36.



3h

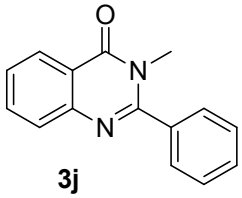
2-hexylquinazolin-4(3H)-one (3h). White solid. Mp: 145 – 146 °C. (lit[5]. 149 – 151 °C). ^{1}H NMR (400 MHz, DMSO) δ 12.11 (s, 1H), 8.05 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.77 – 7.69 (m, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.45 – 7.38 (m, 1H), 2.61 – 2.51 (m, 2H), 1.75

– 1.63 (m, 2H), 1.27 (d, *J* = 15.2 Hz, 6H), 0.81 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 162.28, 157.97, 149.43, 134.69, 127.24, 126.32, 126.12, 121.24, 34.96, 31.38, 28.64, 27.19, 22.40, 14.34.



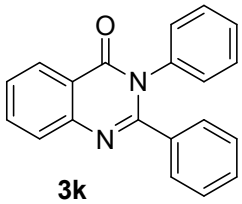
3i

quinazolin-4(3H)-one (3i). White solid. Mp: 200 – 202 °C (lit[6]. 209 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.56 (s, 1H), 8.31 (dd, *J* = 8.0, 1.0 Hz, 1H), 8.14 (s, 1H), 7.91 – 7.70 (m, 2H), 7.55 (ddd, *J* = 8.1, 6.9, 1.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.08, 148.93, 143.42, 135.00, 132.75, 127.80, 127.50, 126.40, 122.46.



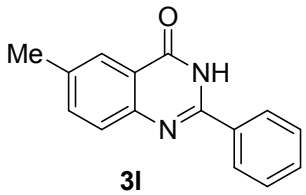
3j

3-methyl-2-phenylquinazolin-4(3H)-one (3j) White solid. Mp: 133°C. (lit[7]. 131 – 132 °C). ^{H}NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.7 Hz, 1H), 7.81 – 7.70 (m, 2H), 7.66 – 7.41 (m, 6H), 7.27 (s, 1H), 3.50 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.74 (s), 156.14 (s), 147.35 (s), 135.44 (s), 134.32 (s), 130.08 (s), 128.90 (s), 128.01 (s), 127.53 (s), 127.00 (s), 126.70 (s), 120.56 (s), 34.26 (s).



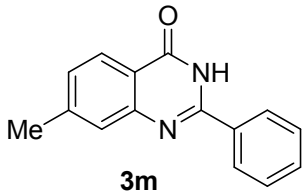
3k

2,3-diphenylquinazolin-4(3H)-one (3k). White solid. Mp: 161 – 162°C. (lit[8] 158 – 159 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 – 8.30 (m, 1H), 7.90 – 7.72 (m, 2H), 7.66 – 7.48 (m, 1H), 7.38 – 7.11 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.29, 155.22, 147.53, 137.70, 135.48, 134.74, 129.30, 129.14, 128.99, 128.42, 127.99, 127.77, 127.29, 127.23, 121.00.



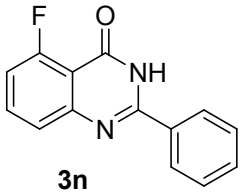
3l

6-methyl-2-phenylquinazolin-4(3H)-one (3l). White solid. Mp: 268–269 °C. (lit[9]. 238 – 240 °C) ^{1}H NMR (400 MHz, DMSO) δ 12.42 (s, 1H), 8.17 – 8.13 (m, 2H), 7.95 – 7.92 (m, 1H), 7.63 (d, *J* = 1.5 Hz, 2H), 7.57 – 7.49 (m, 3H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 162.61, 151.93, 147.22, 136.77, 136.34, 133.26, 131.69, 129.05, 128.10, 127.85, 125.71, 121.20, 21.32.



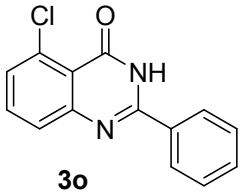
3m

7-methyl-2-phenylquinazolin-4(3H)-one (3m). White solid. Mp: 240–241 °C. (lit[3]. 240 – 241 °C). ^{1}H NMR (400 MHz, DMSO) δ 12.41 (s, 1H), 8.15 (dd, *J* = 5.4, 2.8 Hz, 2H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.62 – 7.48 (m, 4H), 7.32 (d, *J* = 8.0 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 162.57, 152.80, 149.34, 145.53, 133.27, 131.79, 129.06, 128.48, 128.17, 127.63, 126.18, 119.07, 21.83.



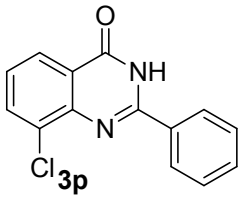
3n

5-fluoro-2-phenylquinazolin-4(3H)-one (3n). White solid. Mp: 257 – 258 °C. (lit[9]. 308 – 310 °C) ^{1}H NMR (400 MHz, DMSO) δ 12.51 (s, 1H), 8.20 – 8.12 (m, 2H), 7.78 (td, *J* = 8.2, 5.7 Hz, 1H), 7.62 – 7.49 (m, 4H), 7.23 (ddd, *J* = 10.9, 8.2, 0.8 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 162.32, 159.87 (d, *J* = 31.7 Hz), 153.79, 151.35, 135.61 (d, *J* = 10.5 Hz), 132.71, 132.13, 129.08, 128.33, 124.03, 113.34 (d, *J* = 20.5 Hz), 110.87.



3o

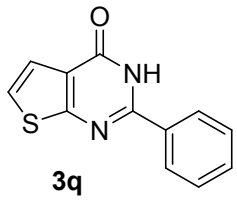
5-chloro-2-phenylquinazolin-4(3H)-one (3o). White solid. Mp: 282 – 284 °C. (no literature give the mp) ^{1}H NMR (400 MHz, DMSO) δ 12.51 (s, 1H), 8.16 (d, *J* = 7.3 Hz, 2H), 7.76 – 7.63 (m, 2H), 7.54 (dq, *J* = 12.3, 7.4 Hz, 4H). ^{13}C NMR (101 MHz, DMSO) δ 160.86, 153.47, 151.76, 134.82, 132.97, 132.60, 132.16, 129.36, 129.09, 128.31, 127.57, 118.41.



3p

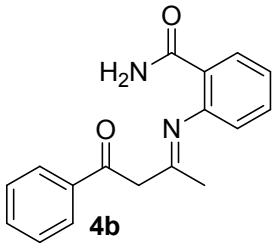
8-chloro-2-phenylquinazolin-4(3H)-one (3p). White solid. Mp: 287 – 288 °C. (no literature give the mp) ^{1}H NMR (400 MHz, DMSO) δ 12.74 (s, 1H), 8.27 – 8.18 (m, 2H), 8.09 (d, *J* = 7.9 Hz, 1H), 7.96 (dd, *J* = 6.9, 2.2 Hz, 1H), 7.63 – 7.52 (m, 3H), 7.47

(t, *J* = 7.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 162.33, 153.44, 145.66, 135.13, 132.95, 132.24, 131.48, 129.14, 128.45, 127.28, 125.49, 123.23.



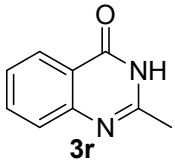
3q

2-phenylthieno[2,3-d]pyrimidin-4(3H)-one (3q). Yellow solid. Mp: 226 – 227 °C (lit[10]. 233 °C). ^{1}H NMR (400 MHz, DMSO) δ 12.68 (s, 1H), 8.12 (d, *J* = 7.5 Hz, 2H), 7.61 – 7.50 (m, 4H), 7.41 (d, *J* = 5.8 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 165.24, 159.09, 153.43, 132.44, 132.01, 129.18, 128.29, 124.46, 123.28, 122.12.



4b

(E)-2-(4-oxo-4-phenylbutan-2-ylideneamino) benzamide **(*4b*)**. Yellow solid. Mp: 158 °C (lit[11]. 160 °C). ^{1}H NMR (400 MHz, DMSO) δ 12.88 (s, 1H), 7.91 (dd, J = 8.0, 1.5 Hz, 1H), 7.55 – 7.42 (m, 2H), 7.37 (d, J = 7.5 Hz, 1H), 7.27 (td, J = 7.5, 1.0 Hz, 1H), 6.05 (s, 1H), 2.08 (s, 1H).^{13}C NMR (101 MHz, DMSO) δ 186.75, 169.03, 161.16, 139.62, 136.26, 131.73, 131.08, 130.18, 128.44, 128.15, 126.97, 126.36, 125.33, 94.65, 20.26.



3r

2-methylquinazolin-4(3*H*)-one (3*r*). White solid. Mp: 242 – 244 °C (lit[12]. 238 – 240 °C)._1H NMR (400 MHz, DMSO) δ 12.18 (s, 1H), 8.08 (d, J = 7.7 Hz, 1H), 7.77 (dd, J = 11.1, 4.1 Hz, 1H), 7.57 (d, J = 8.1 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 2.35 (s, 3H)..^{13}C NMR (101 MHz, DMSO) δ 162.17 (s), 154.71 (s), 149.45 (s), 134.71 (s), 127.04 (s), 126.30 (s), 126.13 (s), 121.11 (s), 21.90 (s).

References

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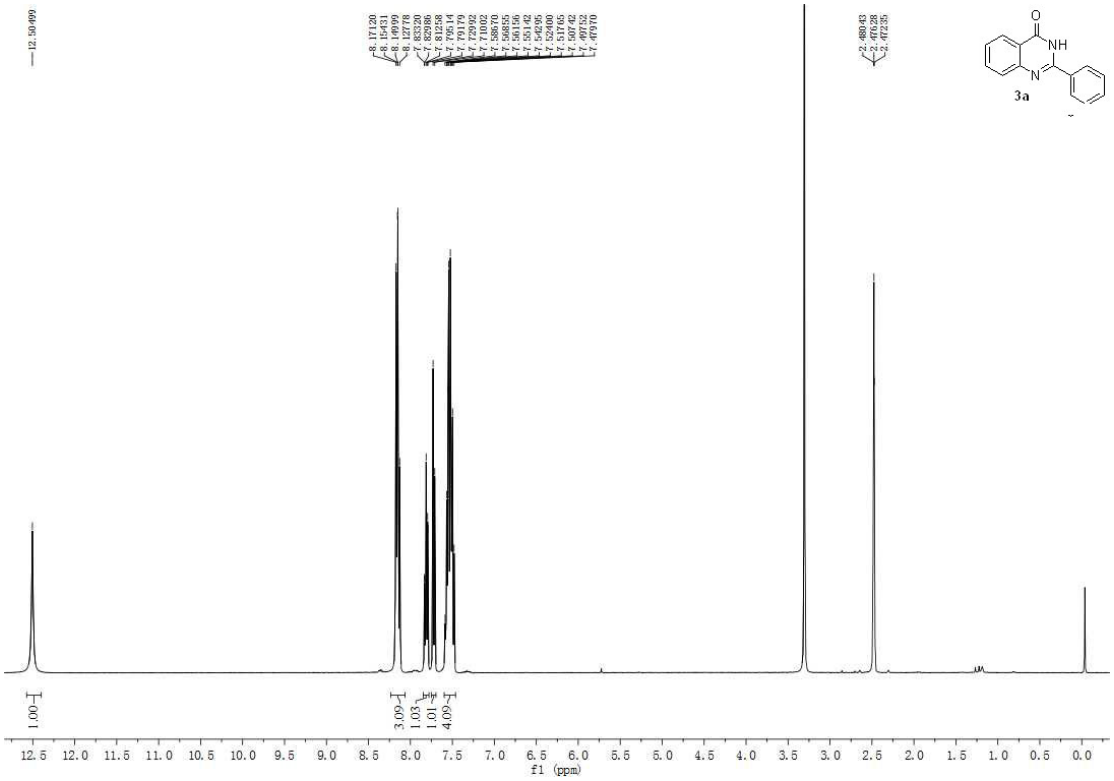
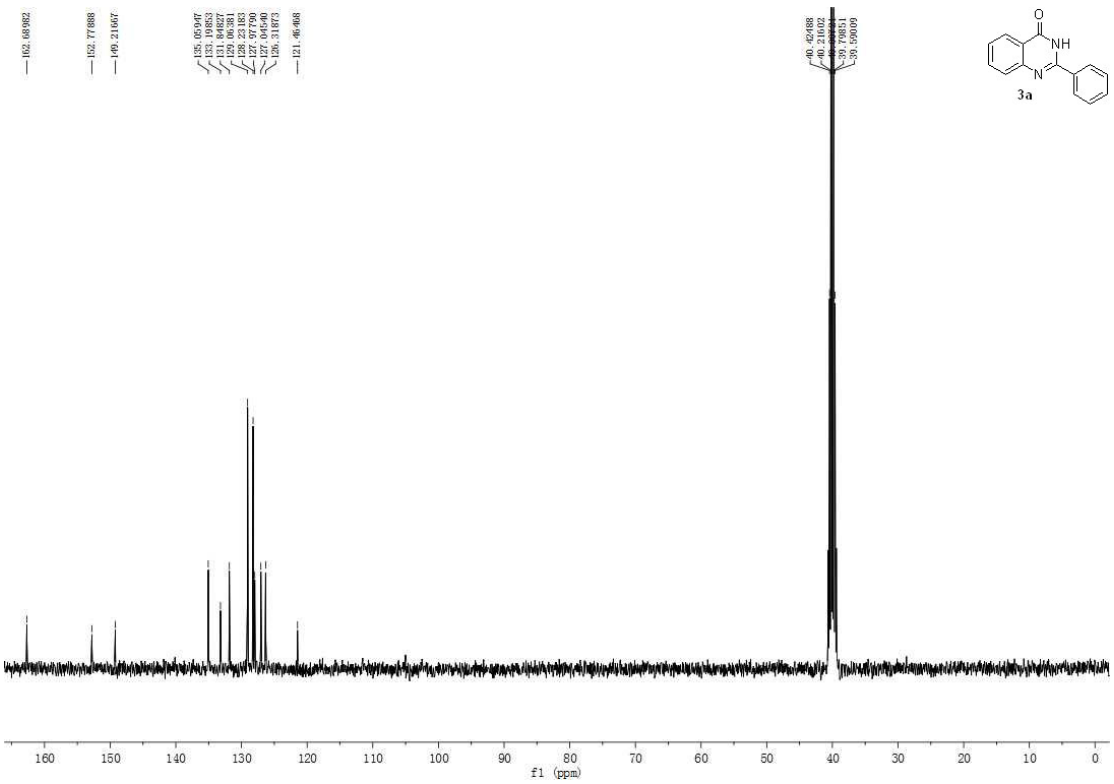
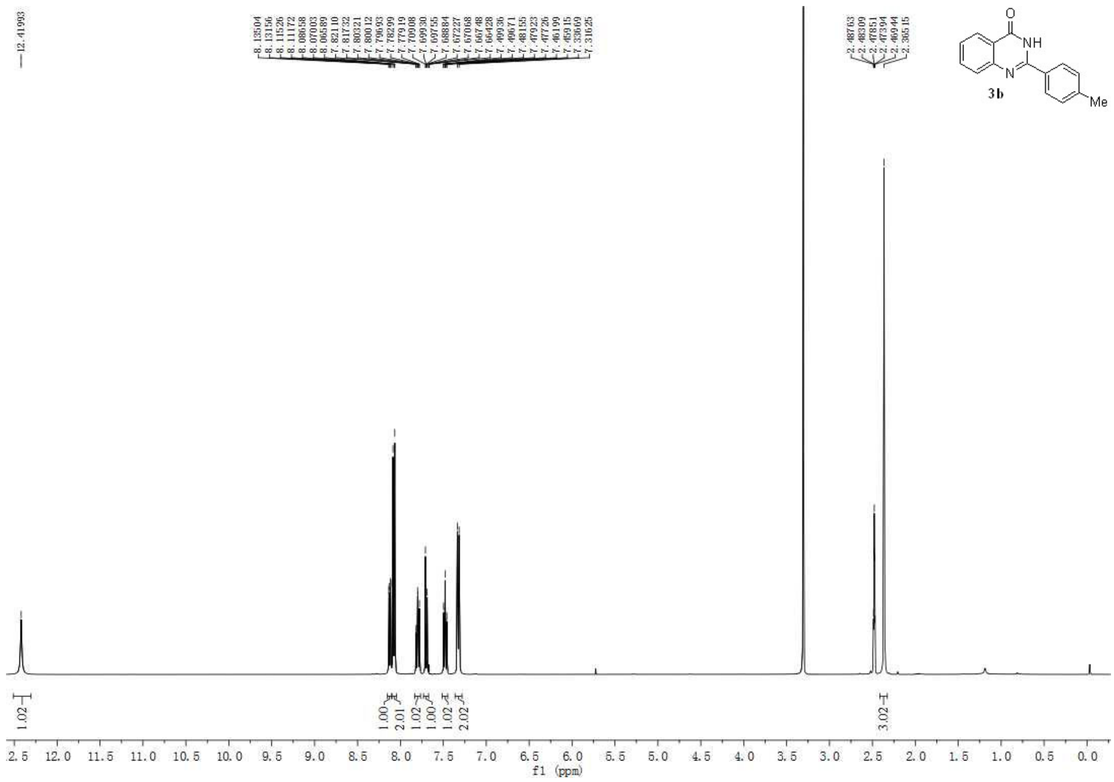
^{1}H NMR, ^{13}C NMR spectra of products







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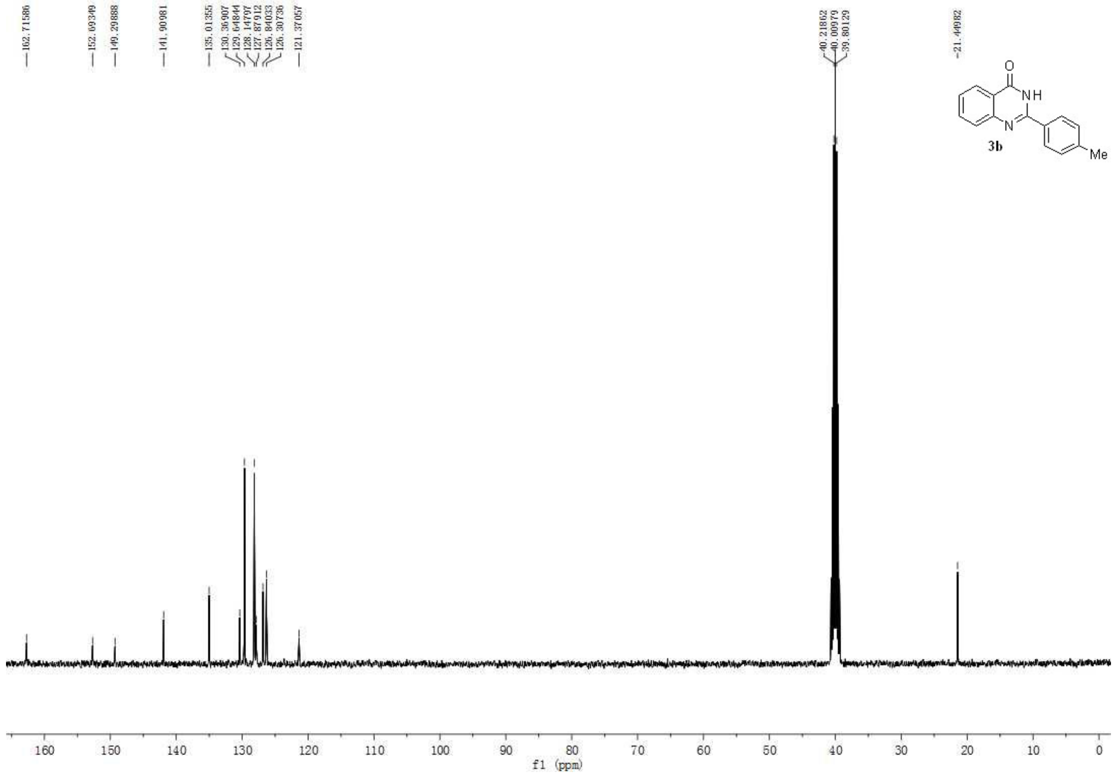

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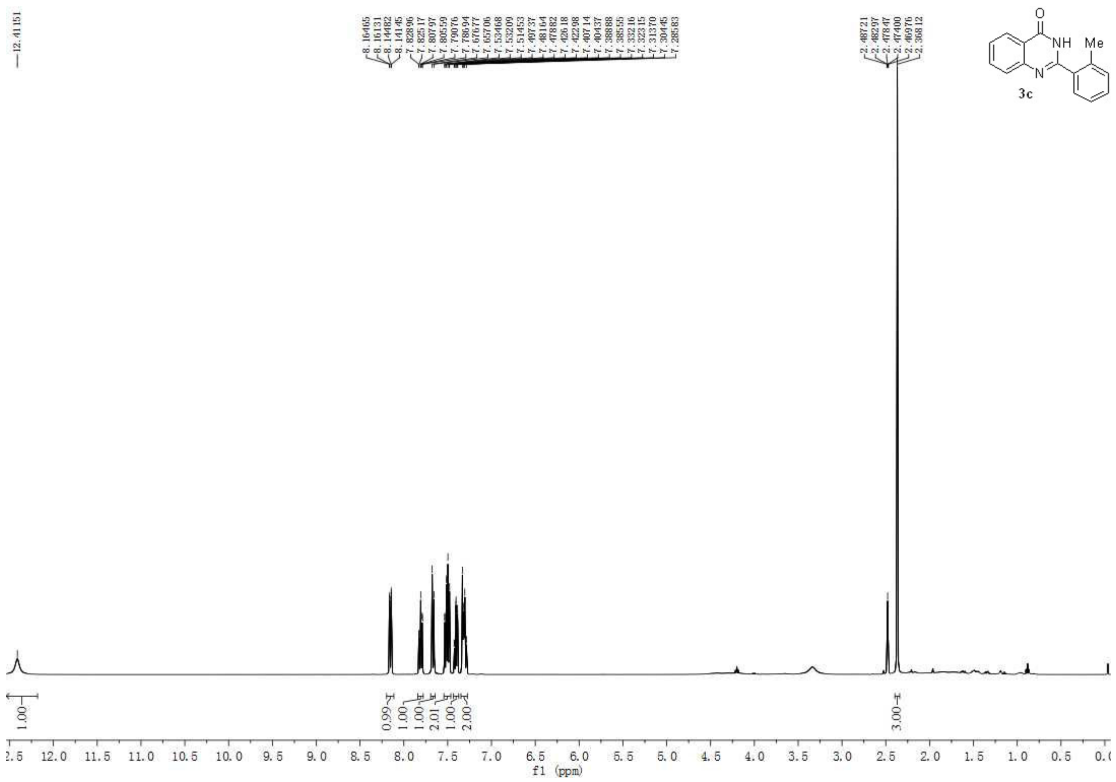

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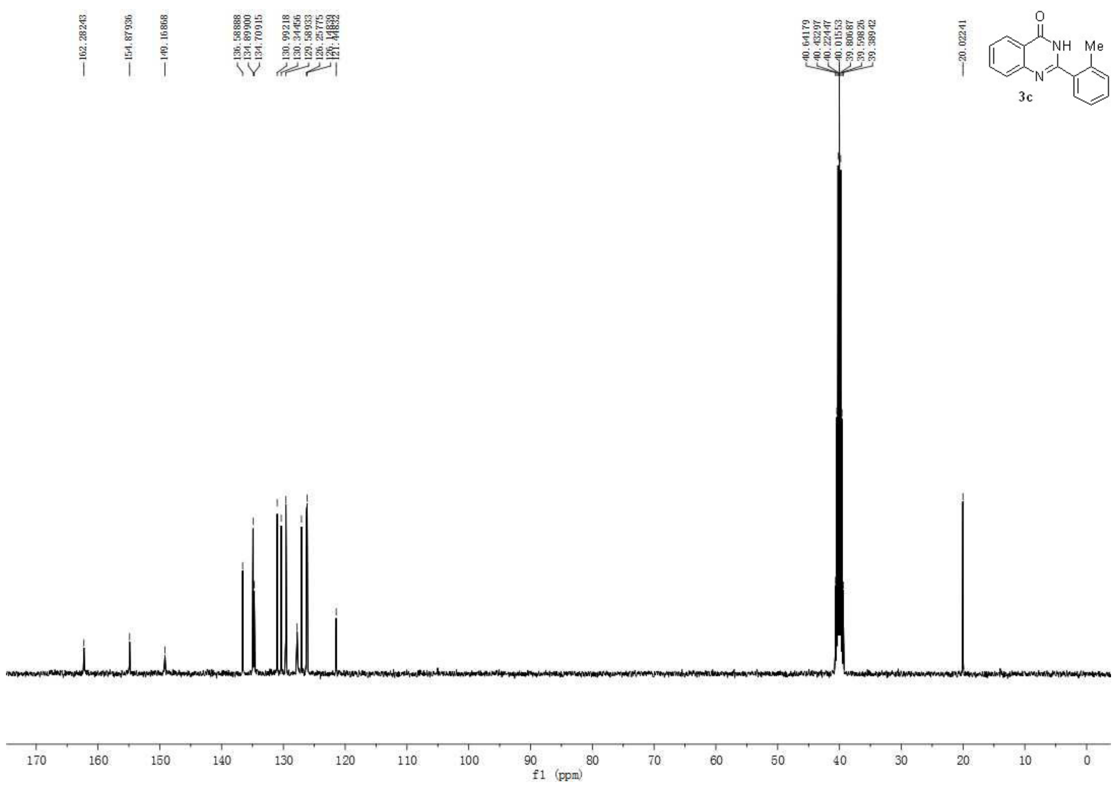

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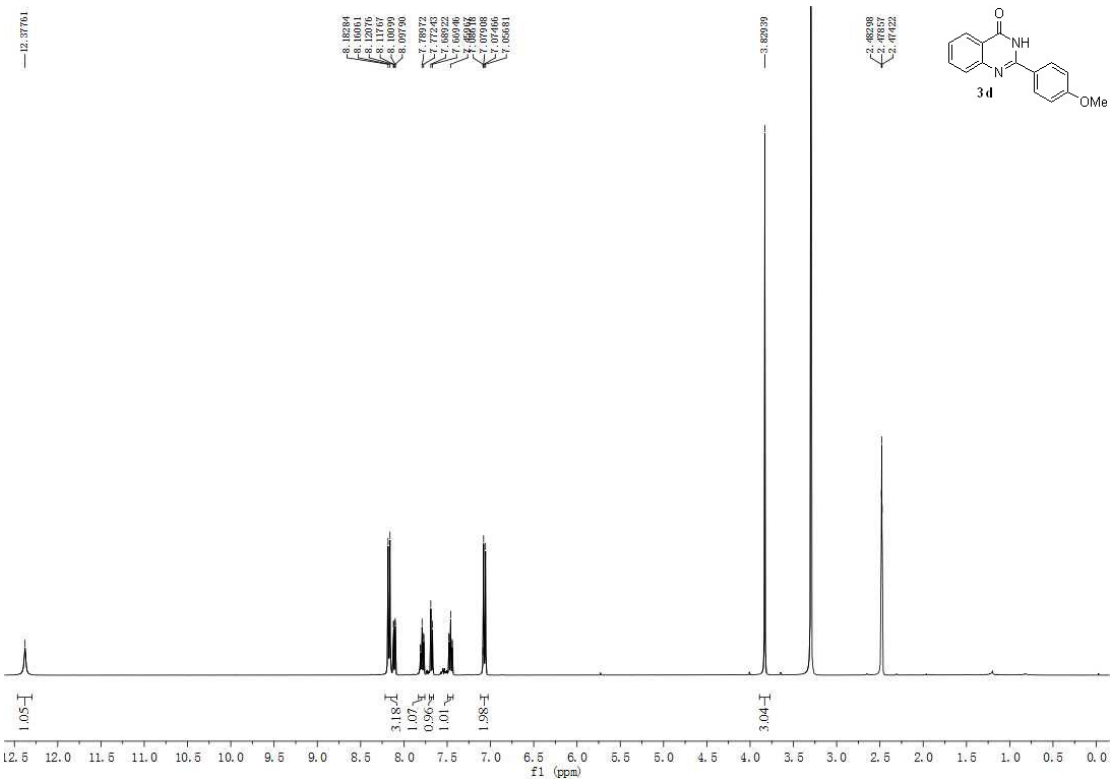
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3d
OMe
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3.18
1.07
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1.01
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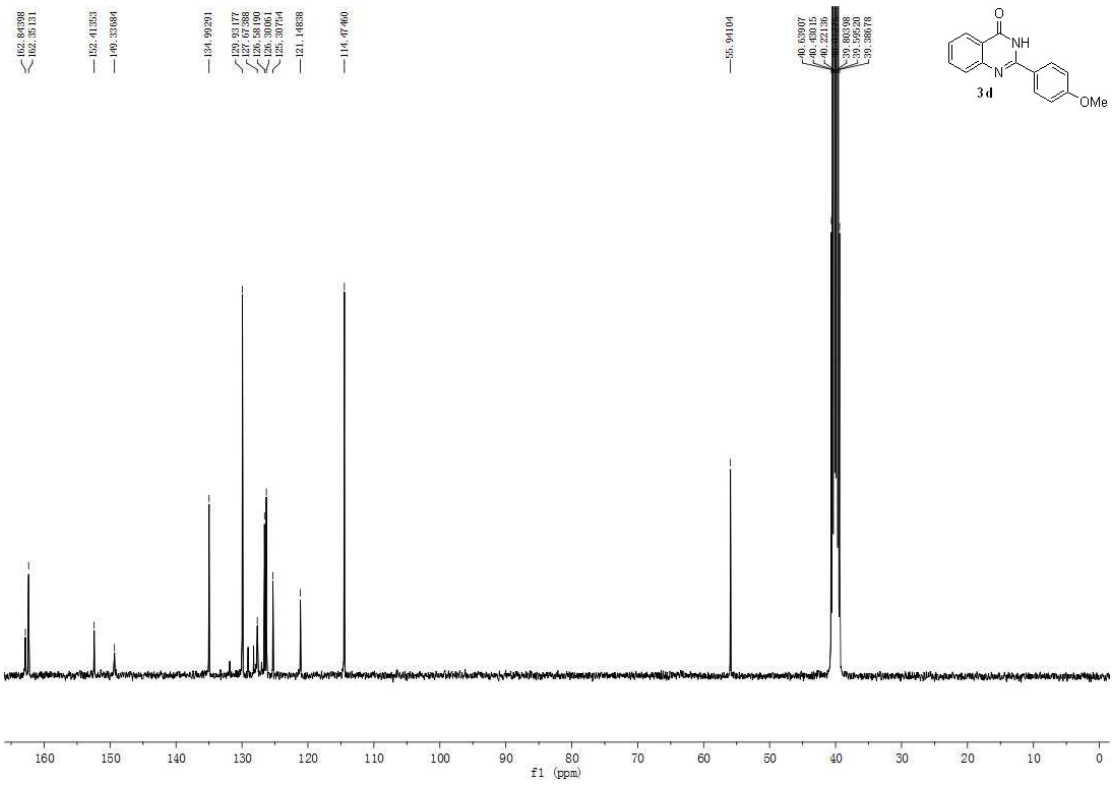
3.04
f1 (ppm)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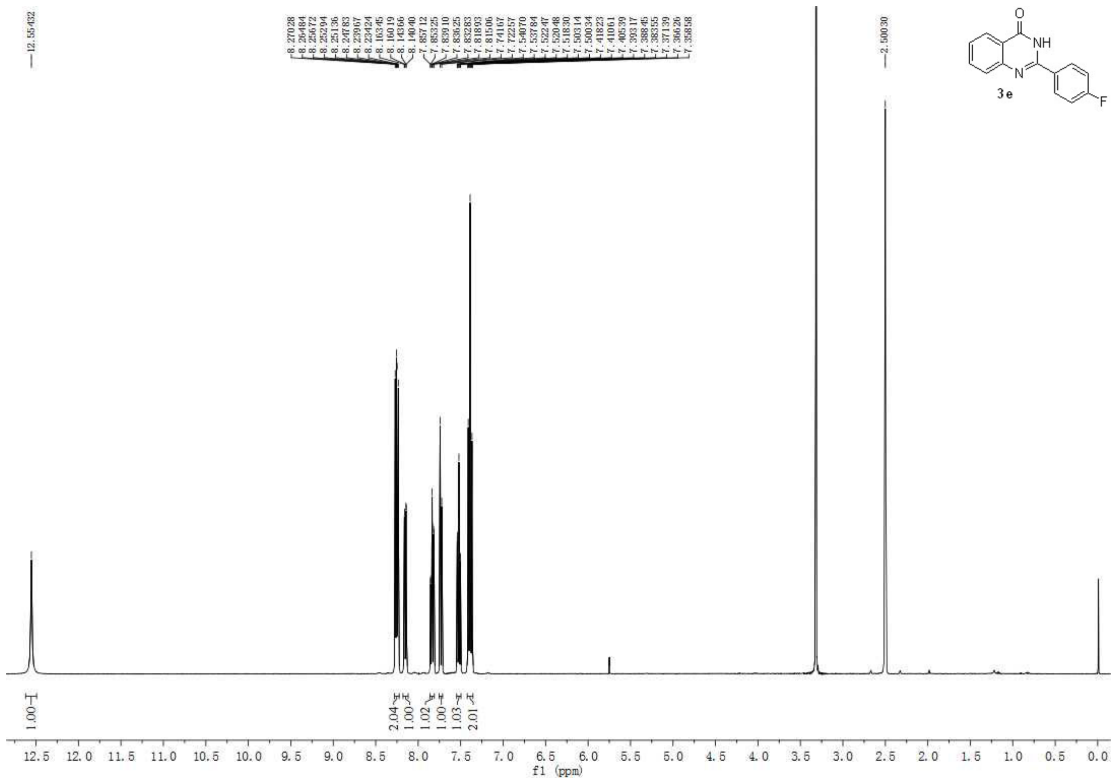
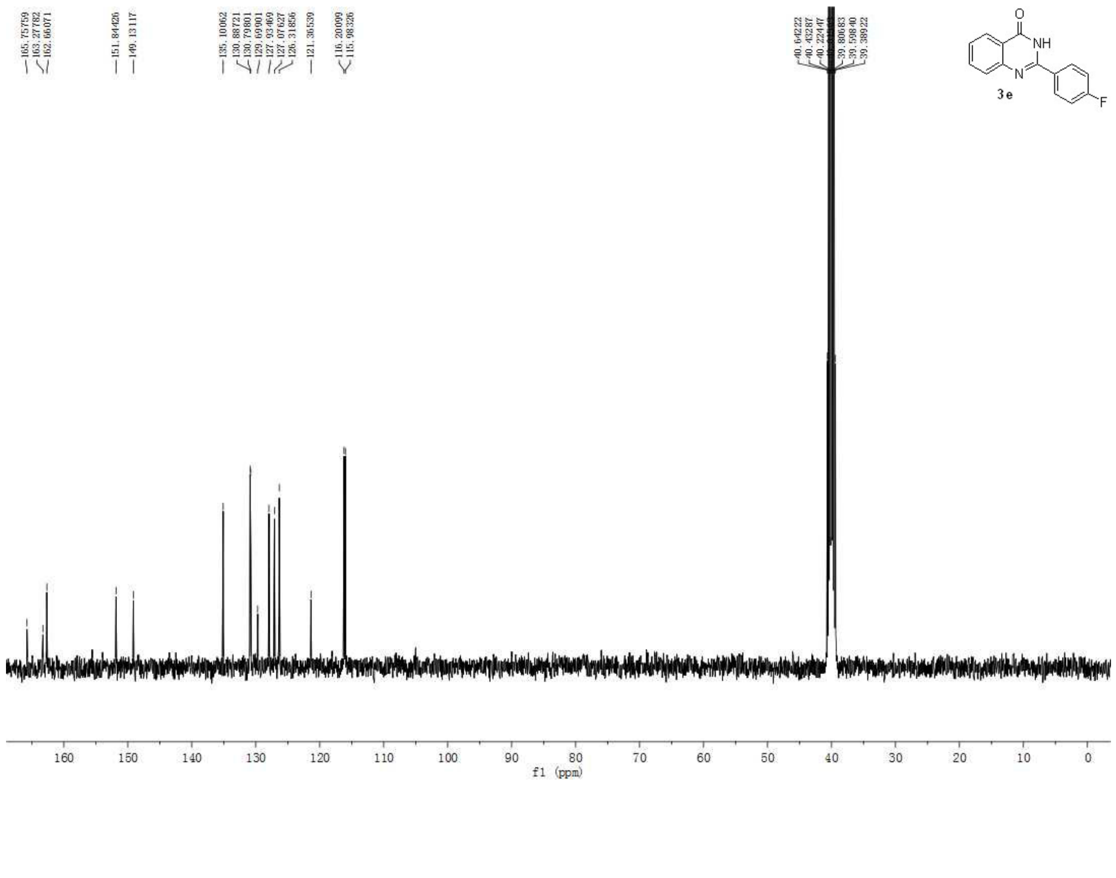
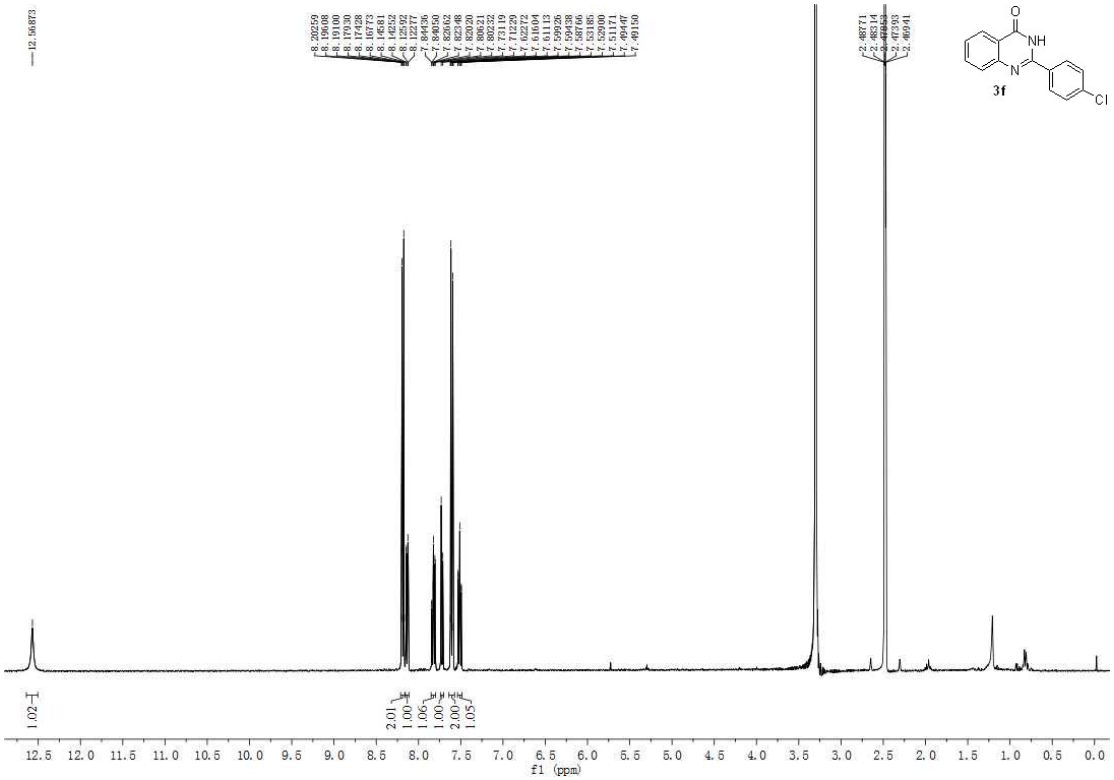
OMe
f1 (ppm)



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N
Cl
3f
1.02
2.01
1.00
1.06
1.00
2.00
1.05
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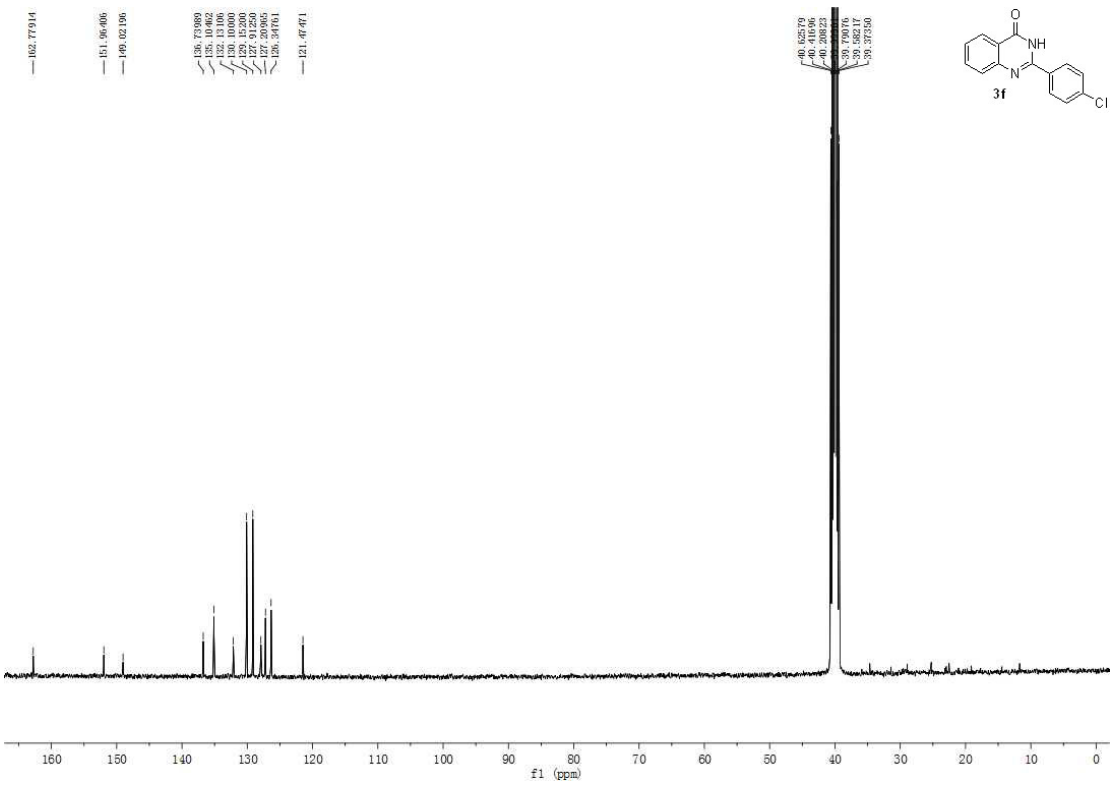
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NH
N
Cl
3f
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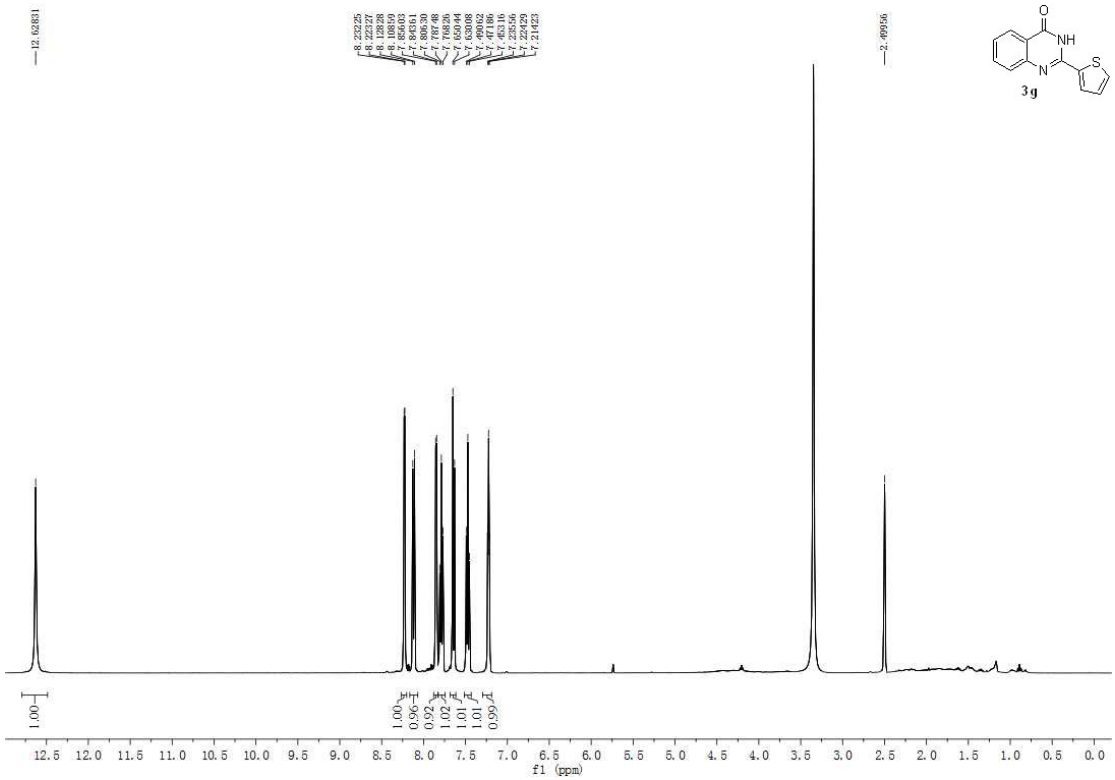
f1 (ppm)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1.01
1.01
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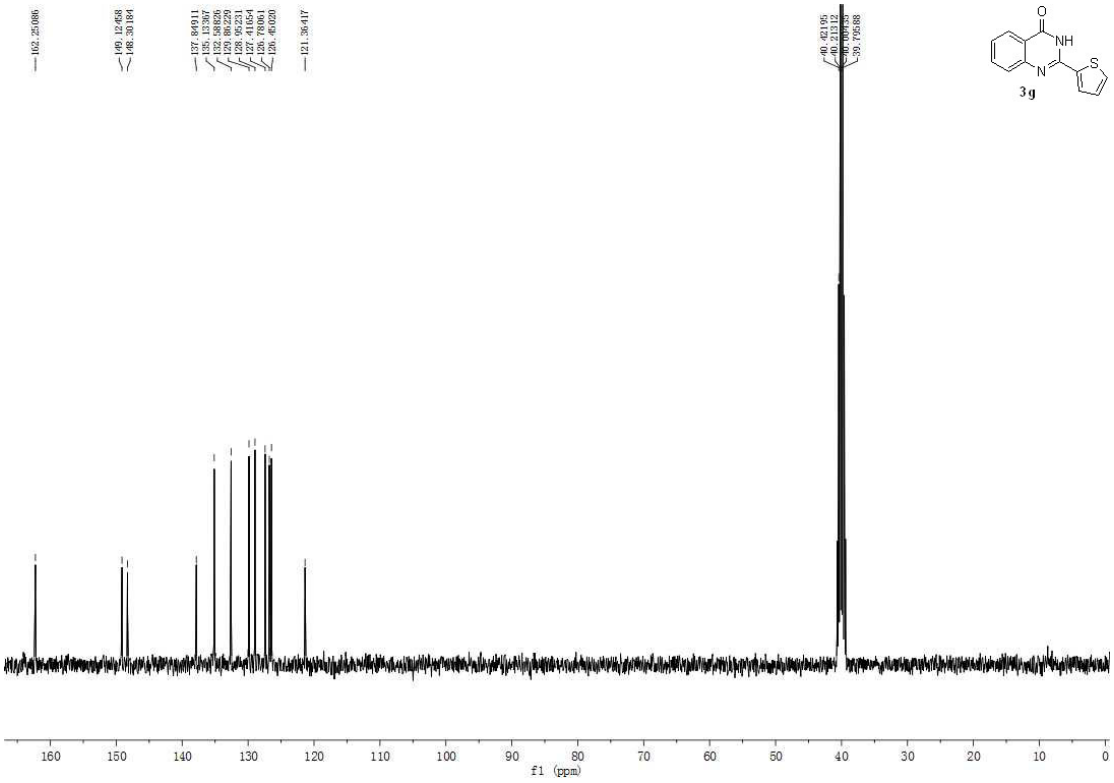
f1 (ppm)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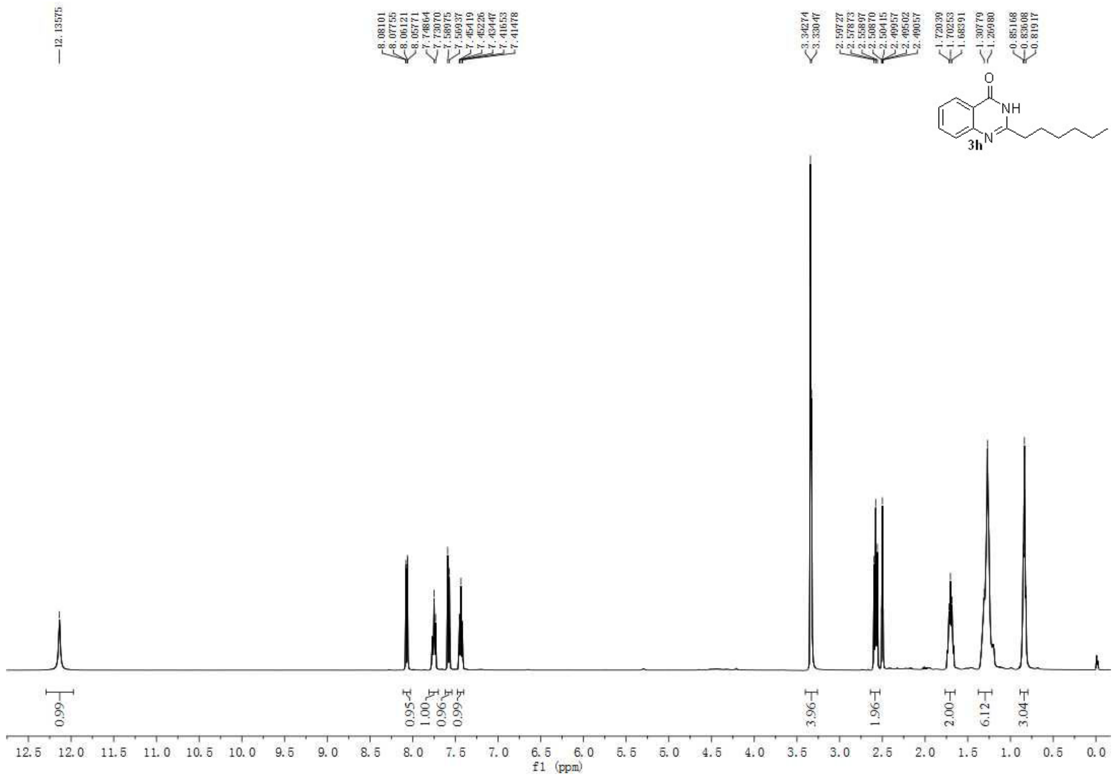
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0.83608
0.81917
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N
3h
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0.95
1.00
0.96
0.99
3.96
1.96
2.00
6.12
3.04
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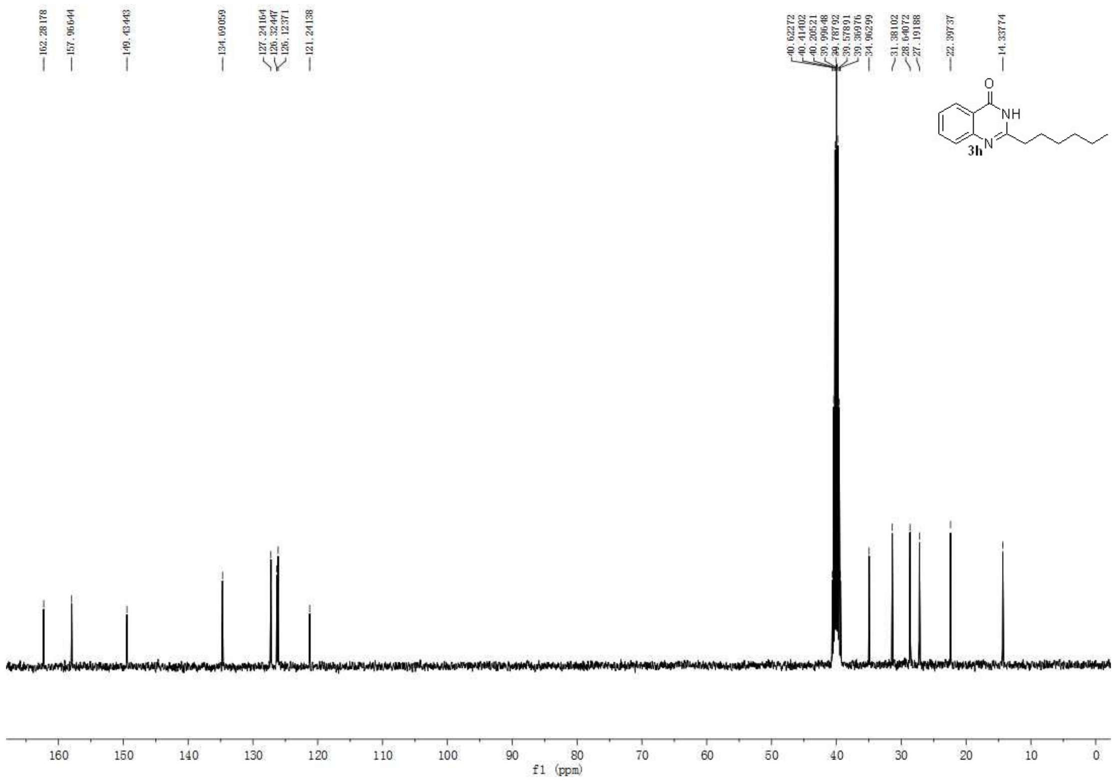
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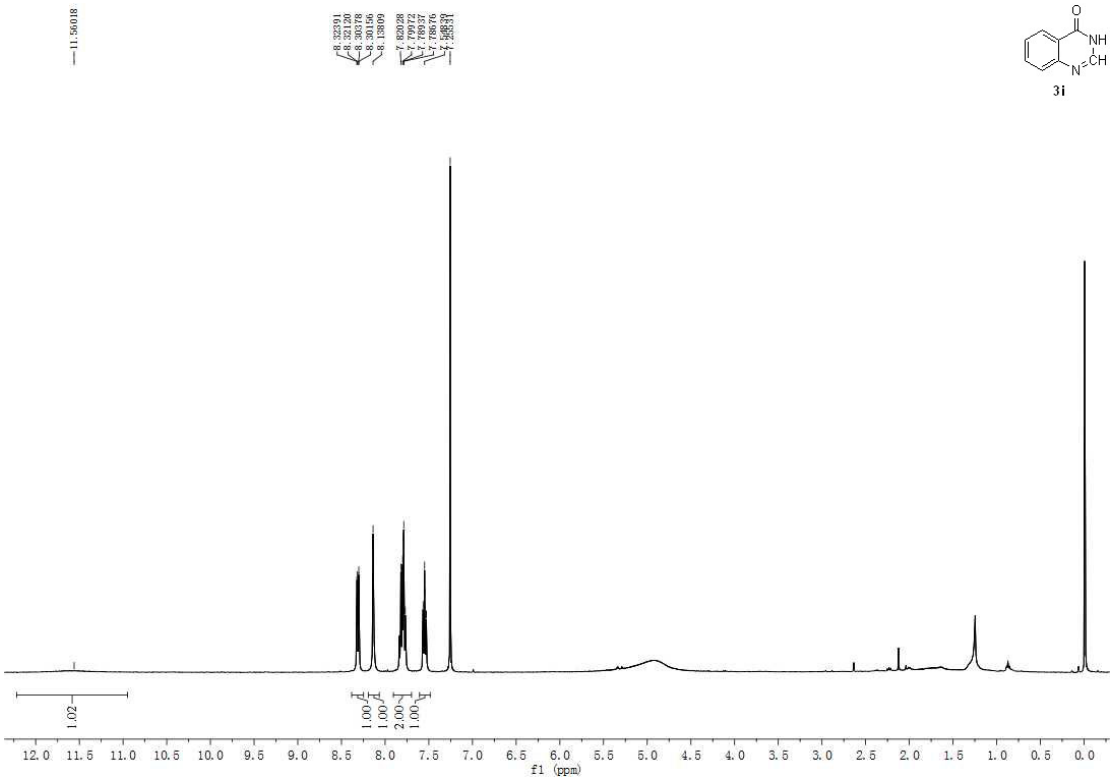
f1 (ppm)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f1 (ppm)
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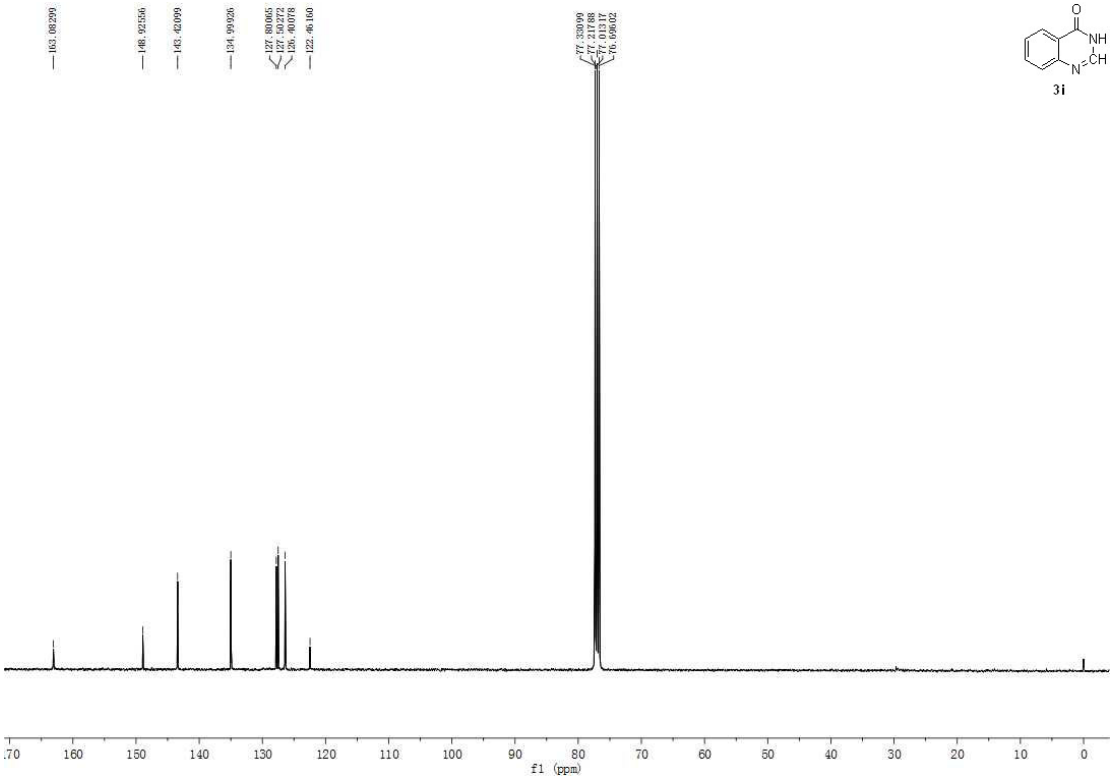
NH
CH
N
3i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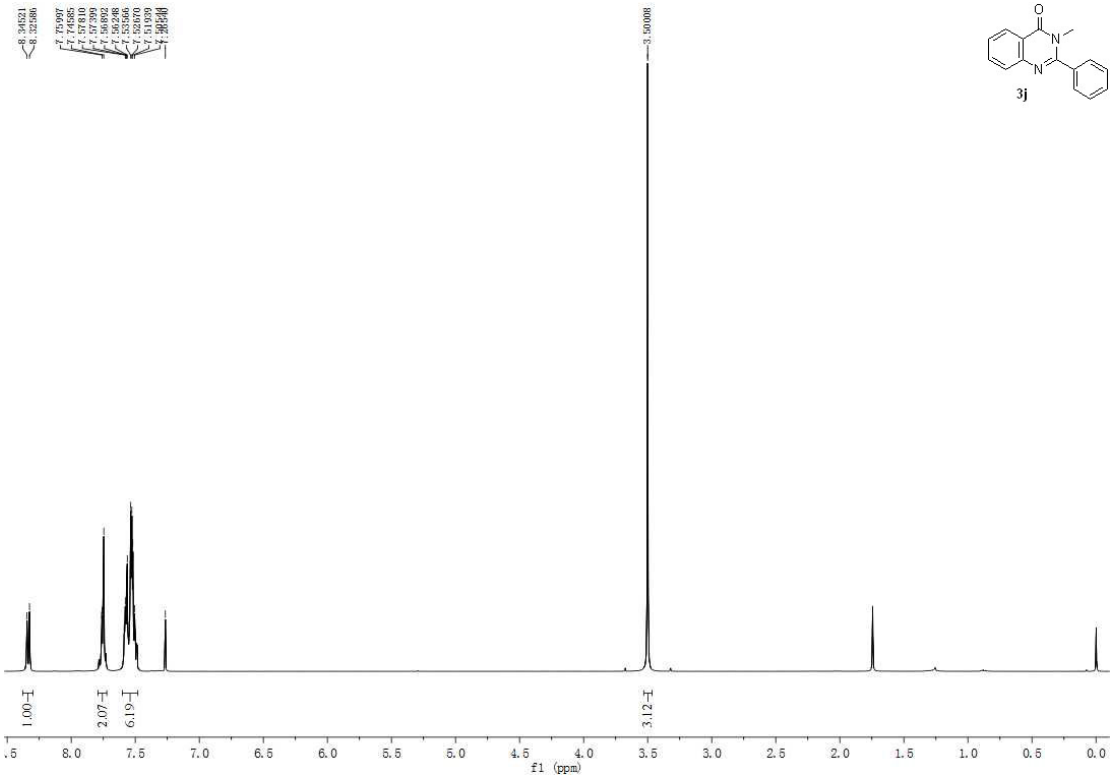
CH
N
3i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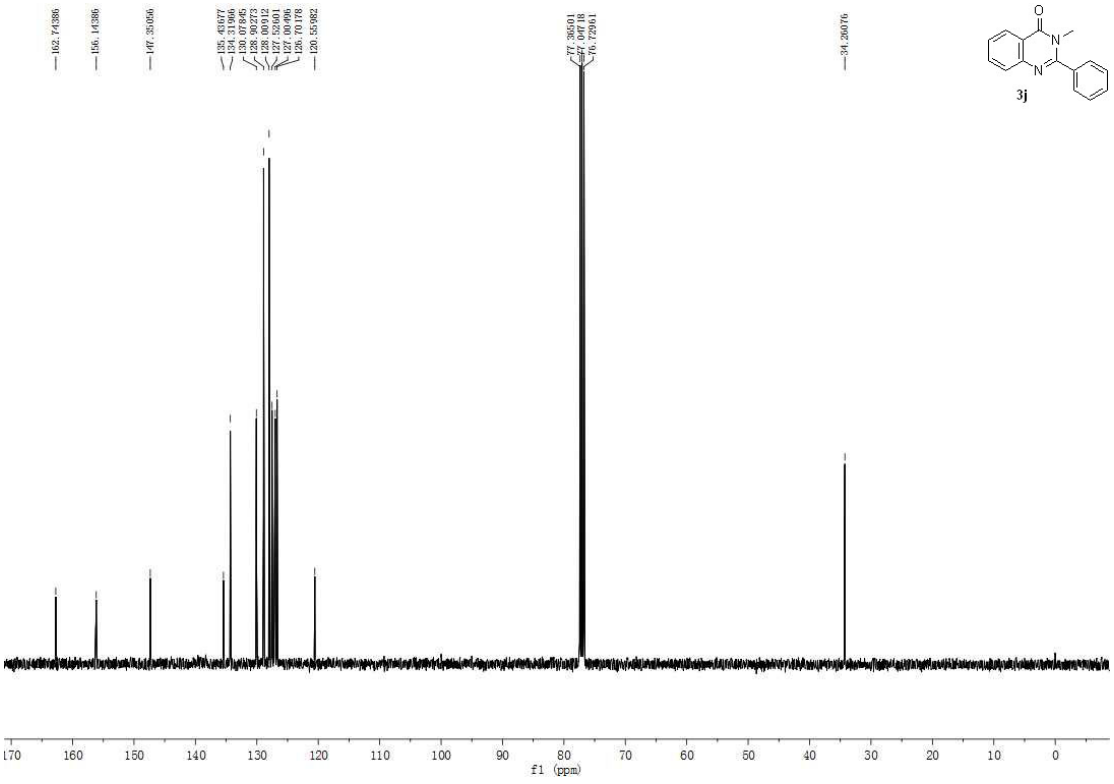
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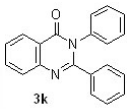
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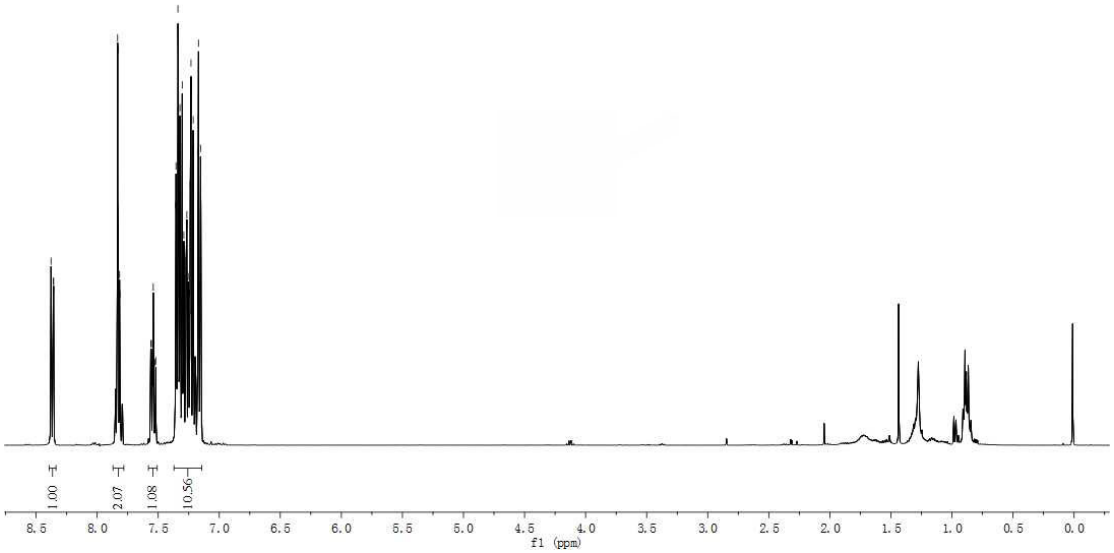
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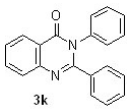
f1 (ppm)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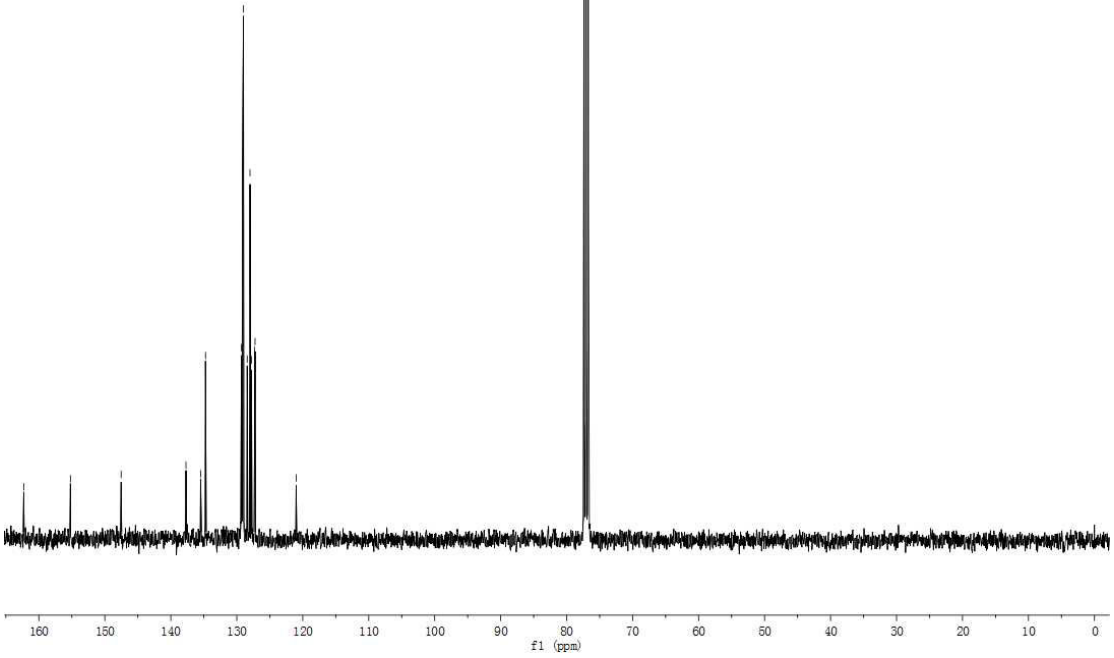
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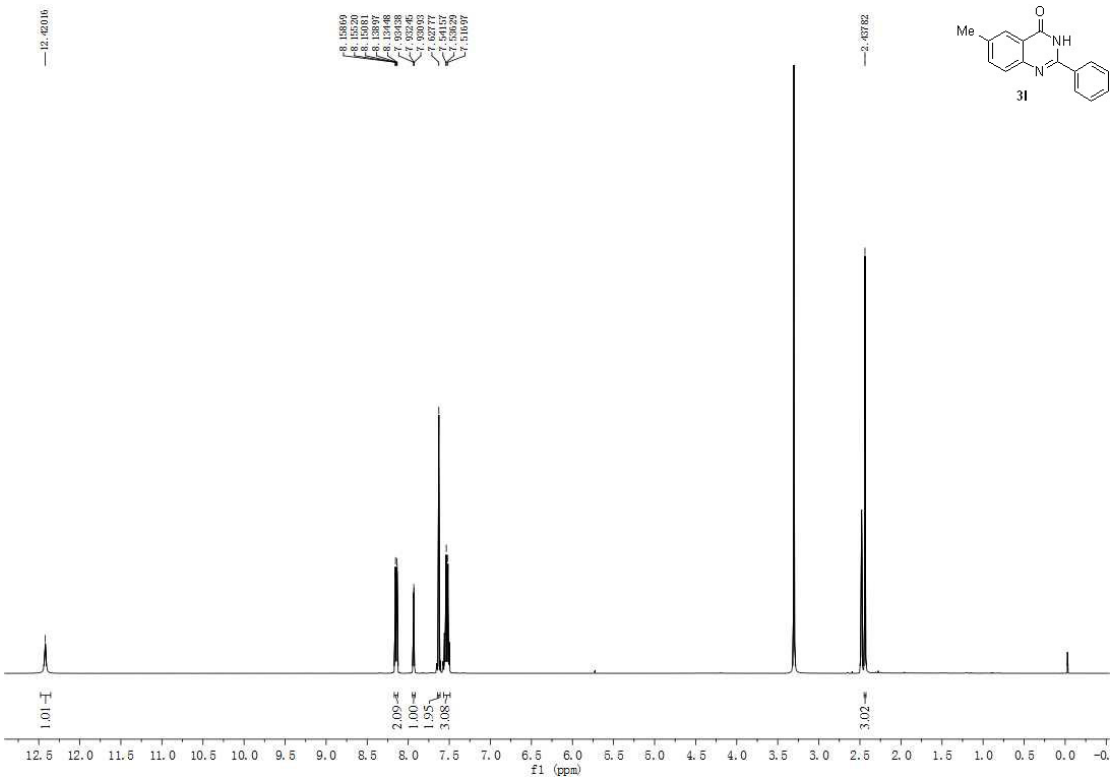
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1.00
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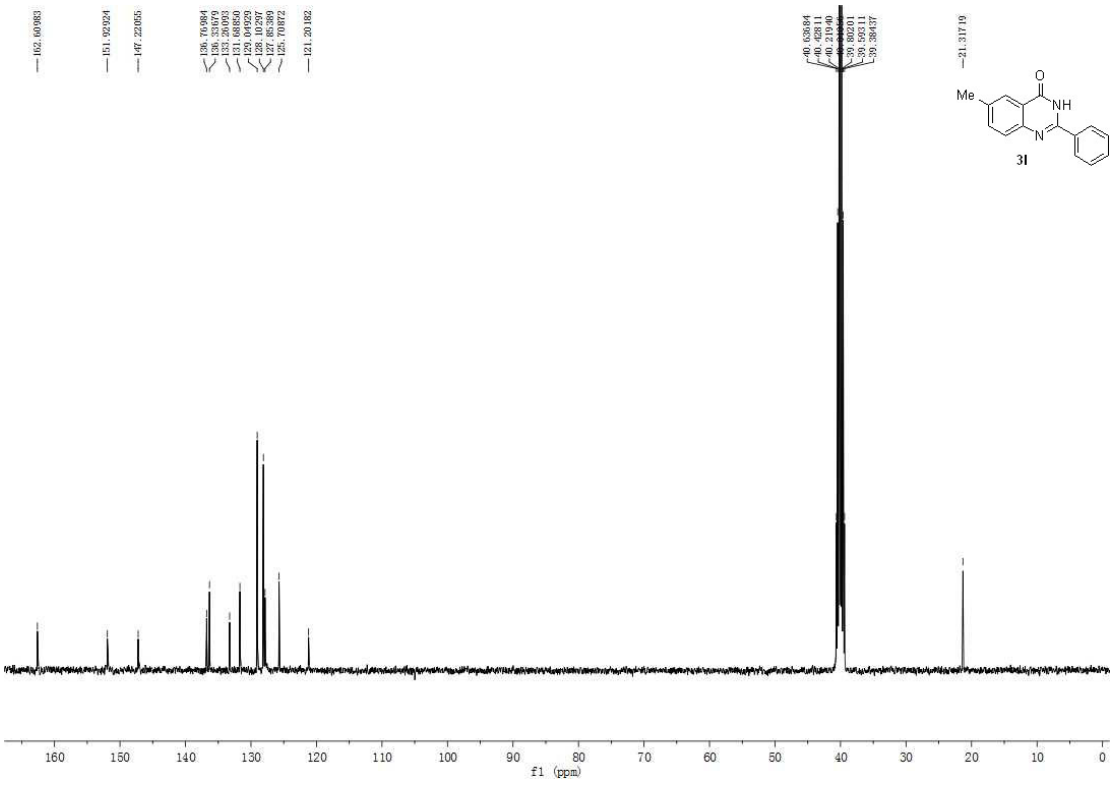
f1 (ppm)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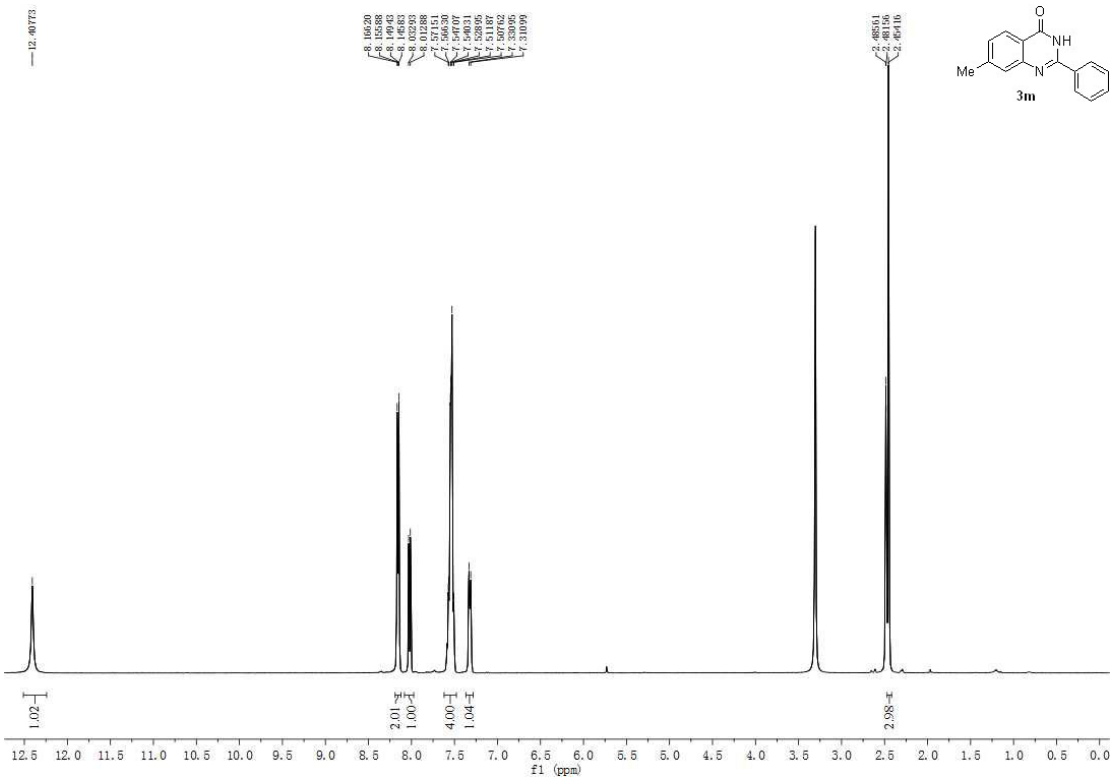
f1 (ppm)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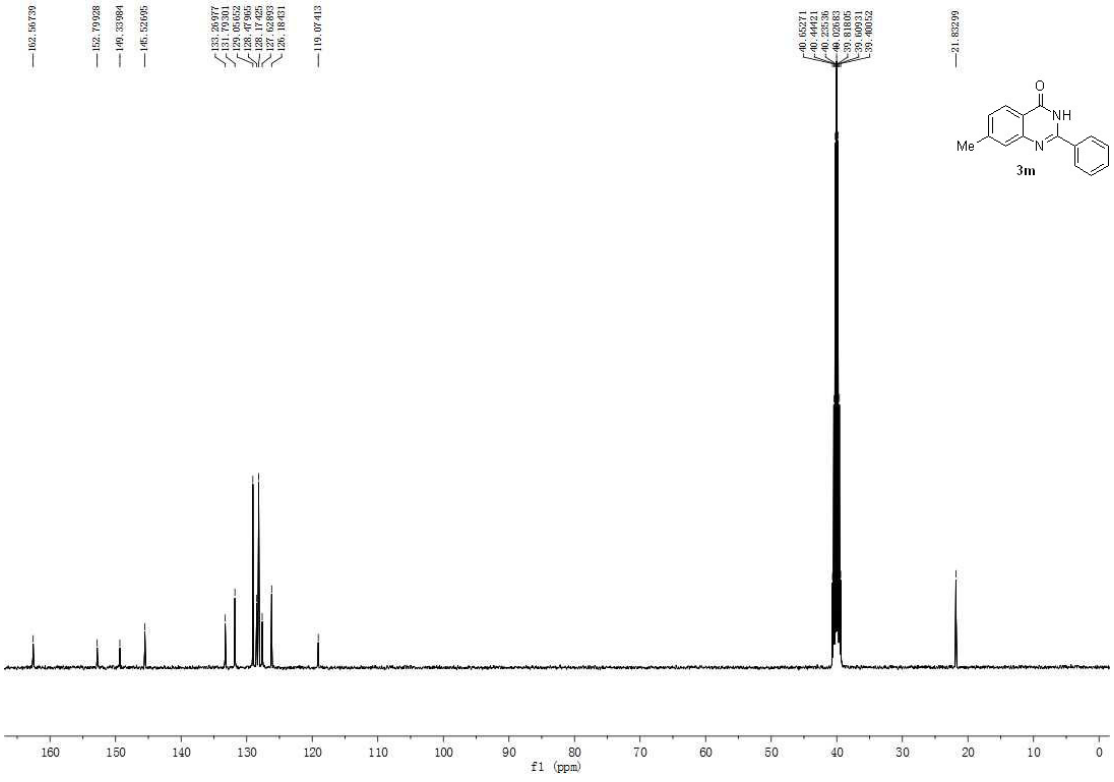
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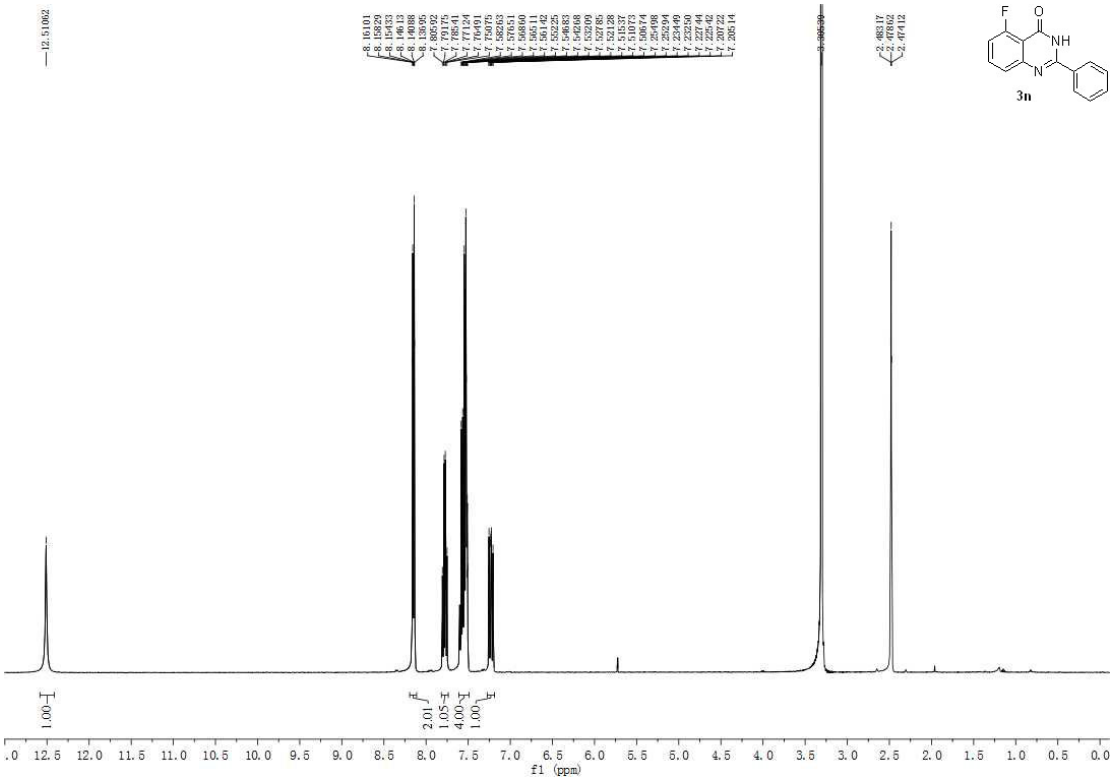
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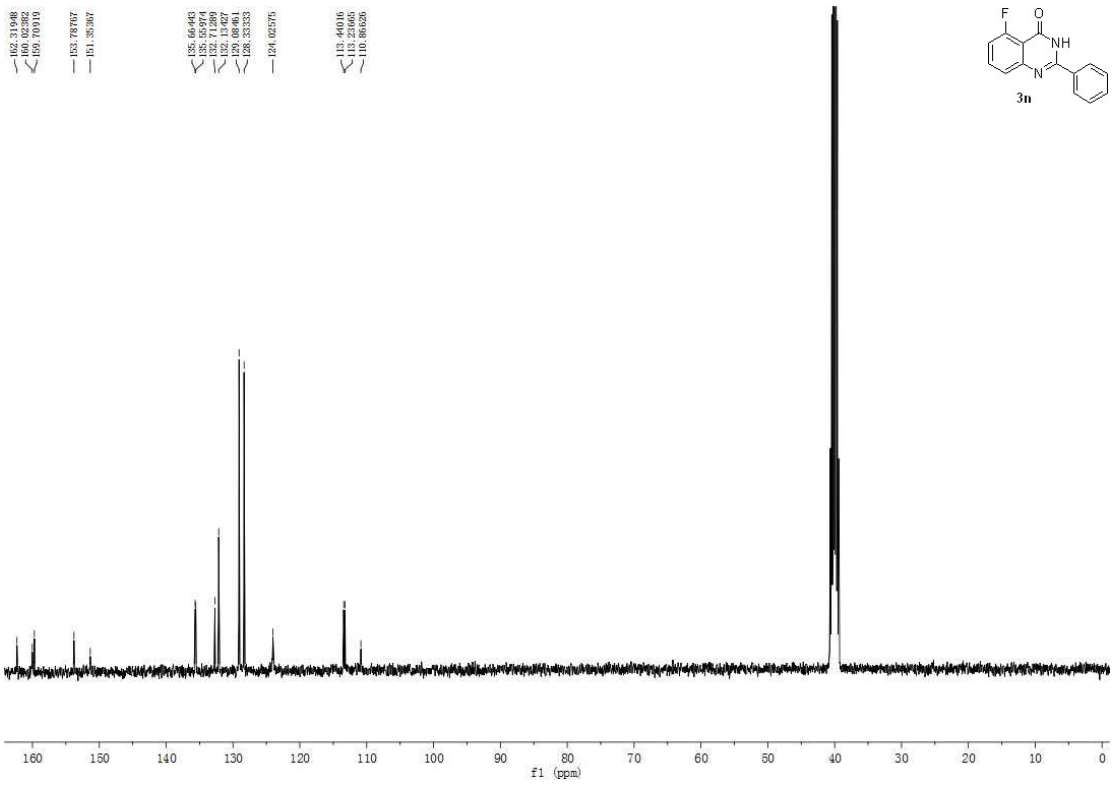
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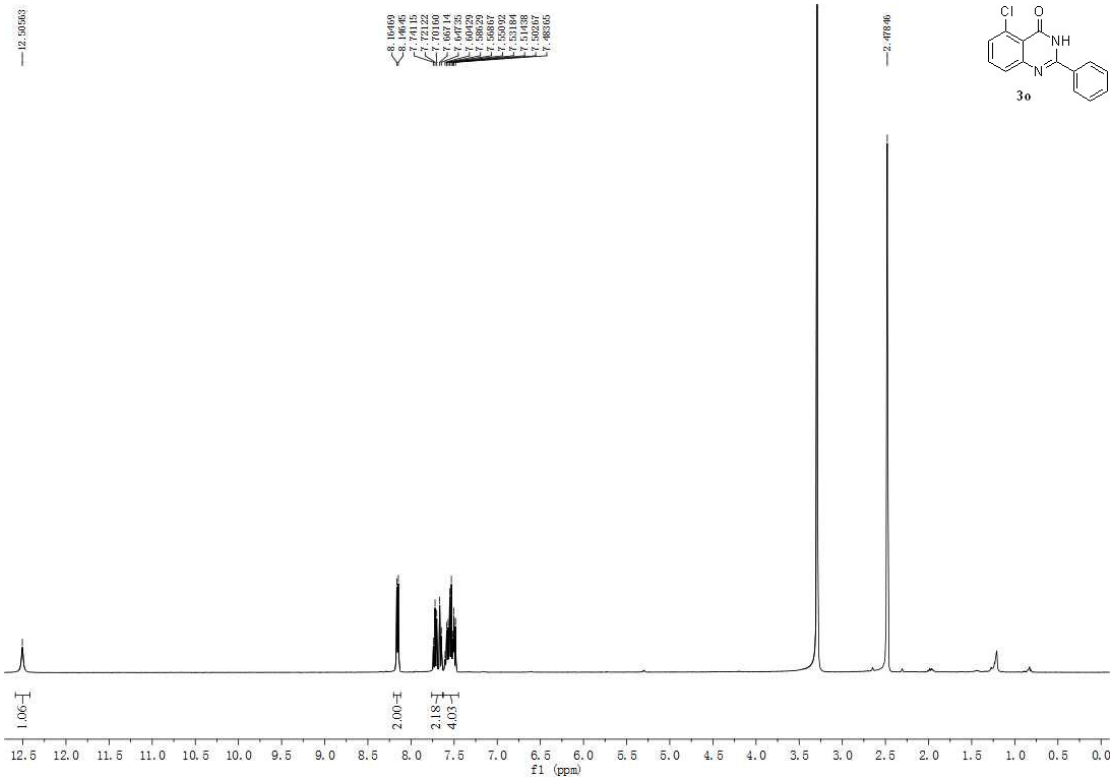
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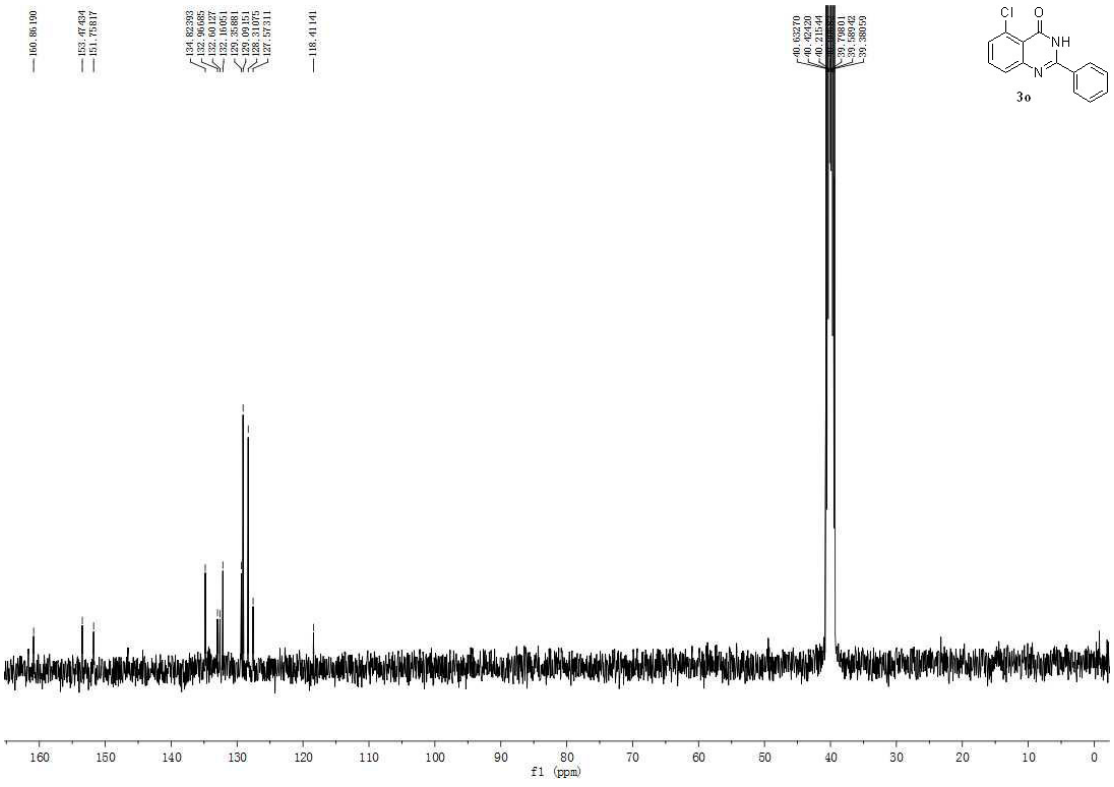
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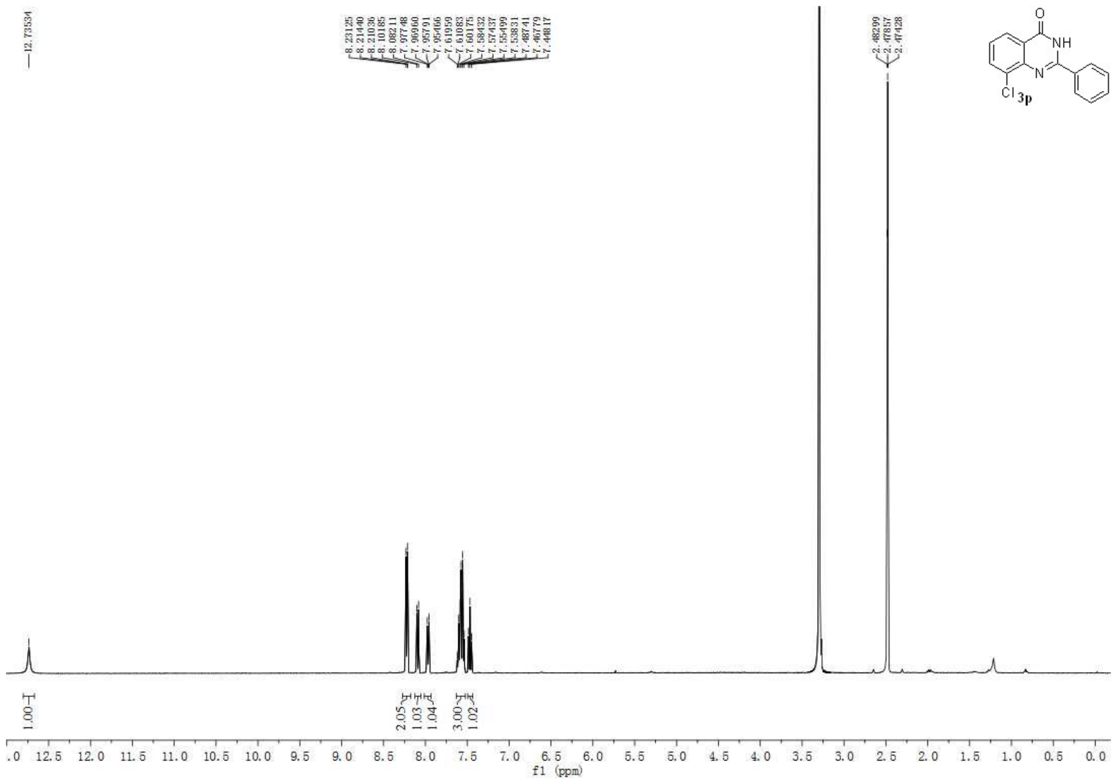

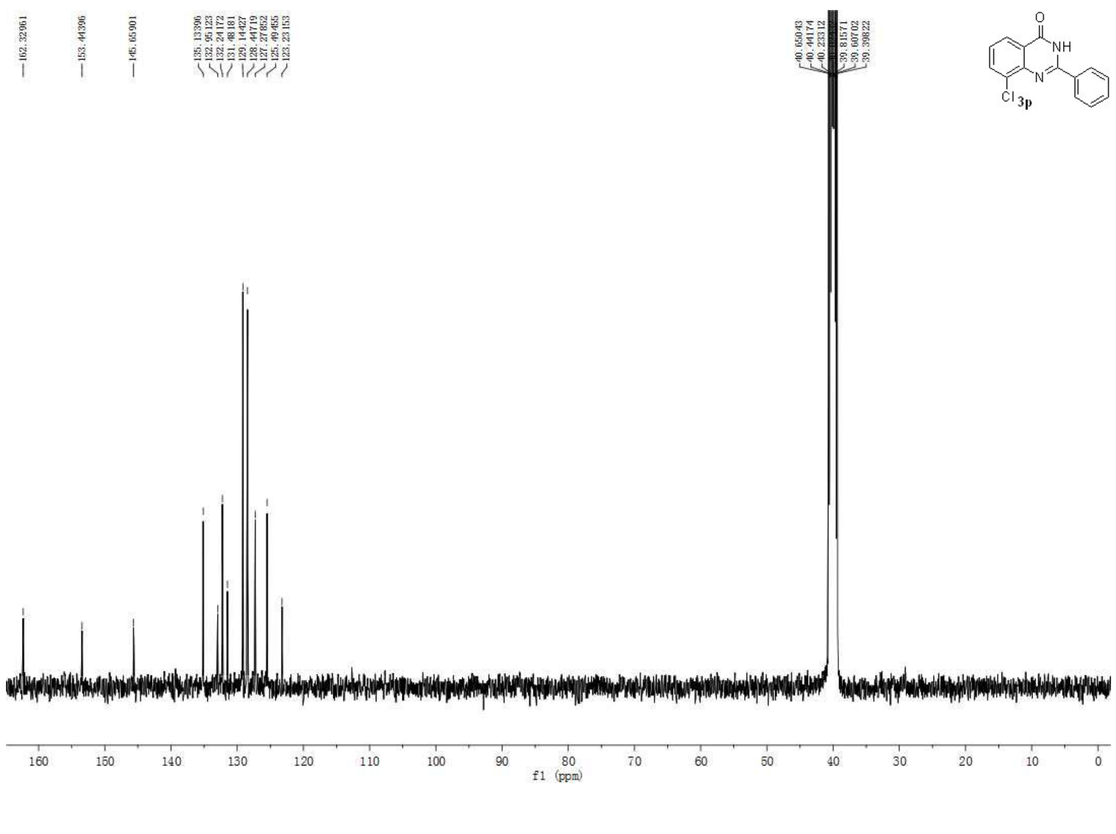

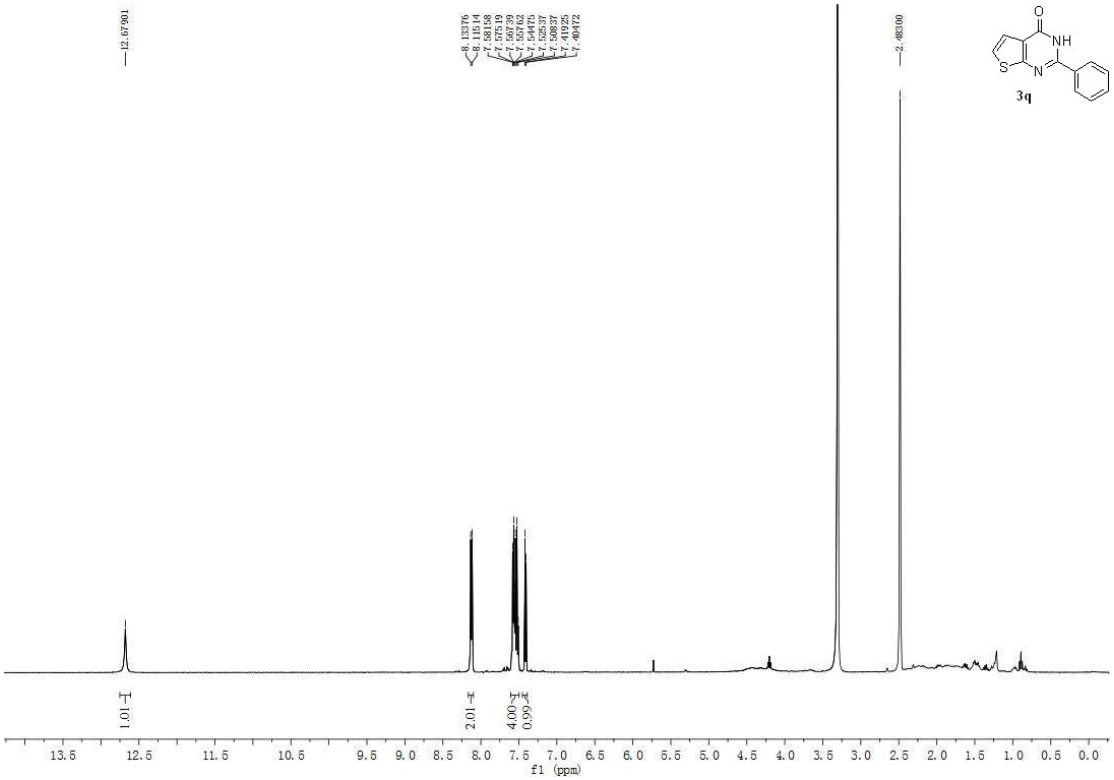
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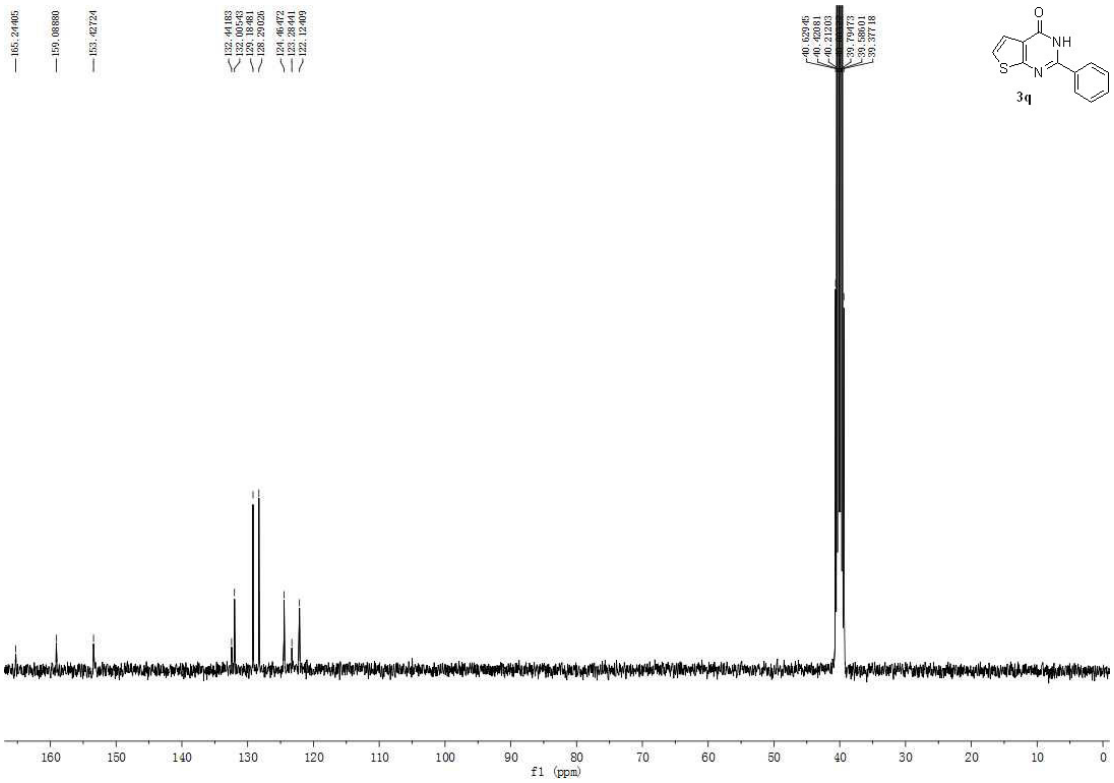
7.41925
7.40472
2.48100
1.01
2.01
4.00
0.99
f1 (ppm)
3q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153.42724
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132.00645
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128.29026
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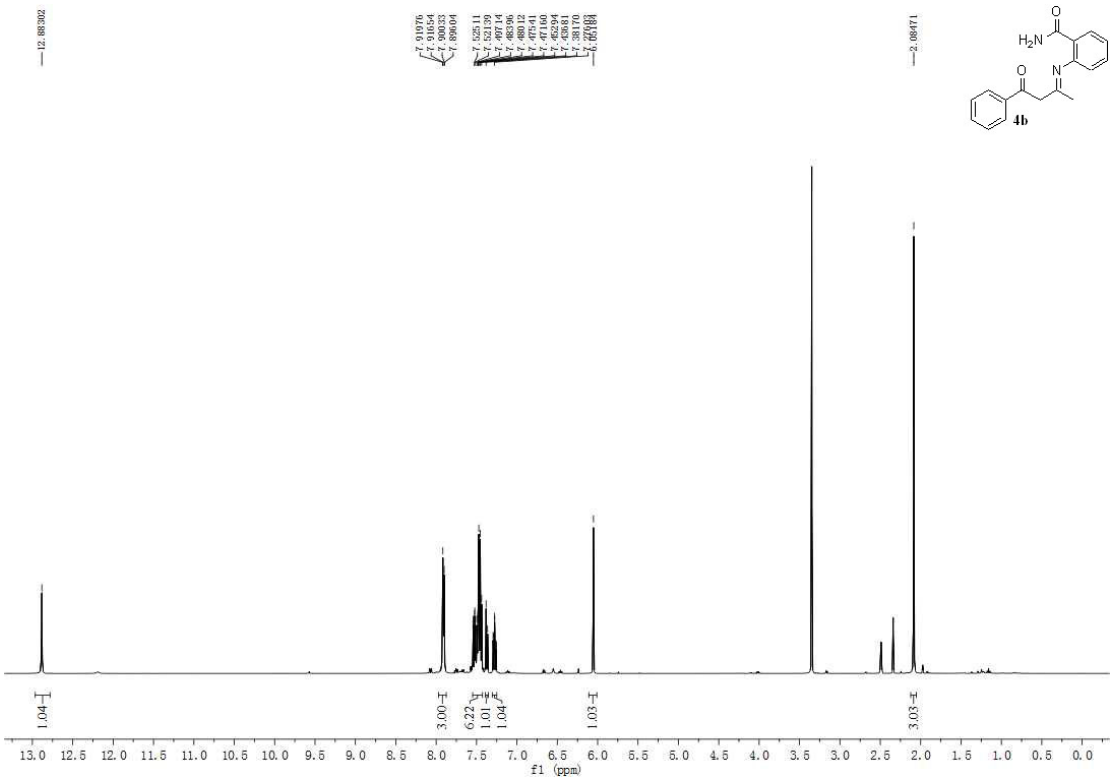
40.42081
40.21403
39.79473
39.58601
39.37718
f1 (ppm)
3q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7.91654
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7.89604
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7.49714
7.48396
7.48012
7.47644
7.47160
7.45294
7.43681
7.39170
7.27049
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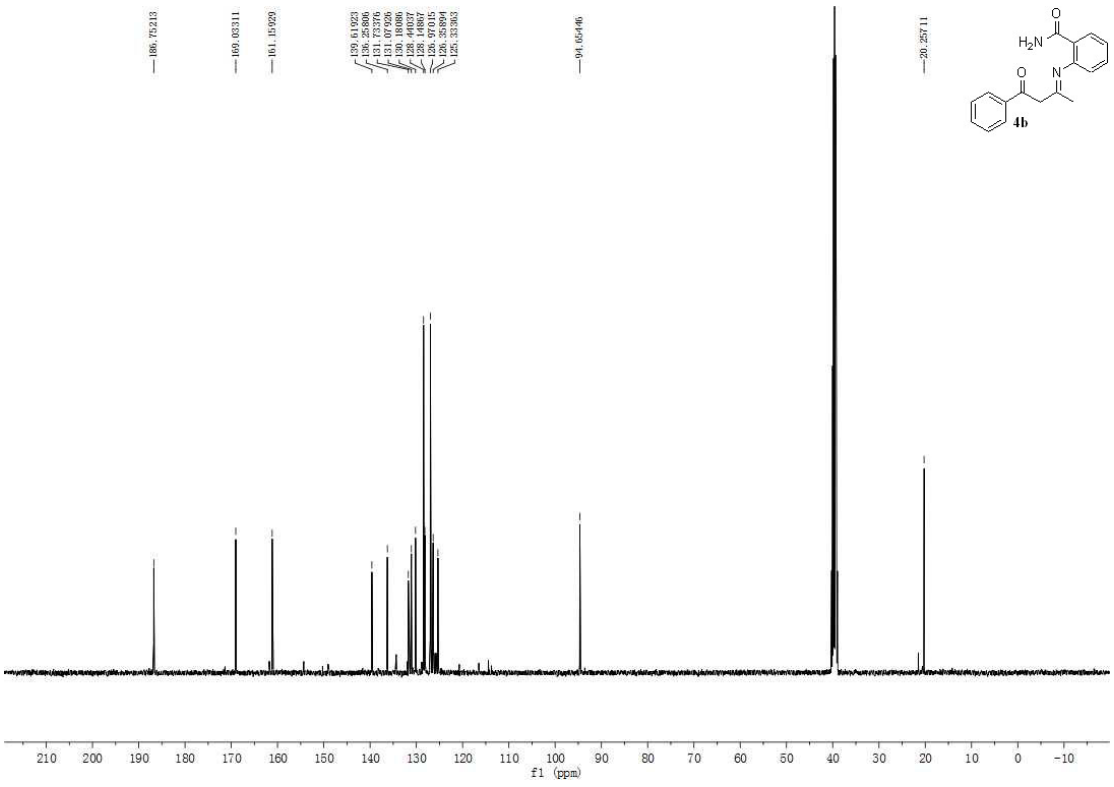
2.08471
1.04
3.00
6.22
1.01
1.04
1.03
3.03
f1 (ppm)
4b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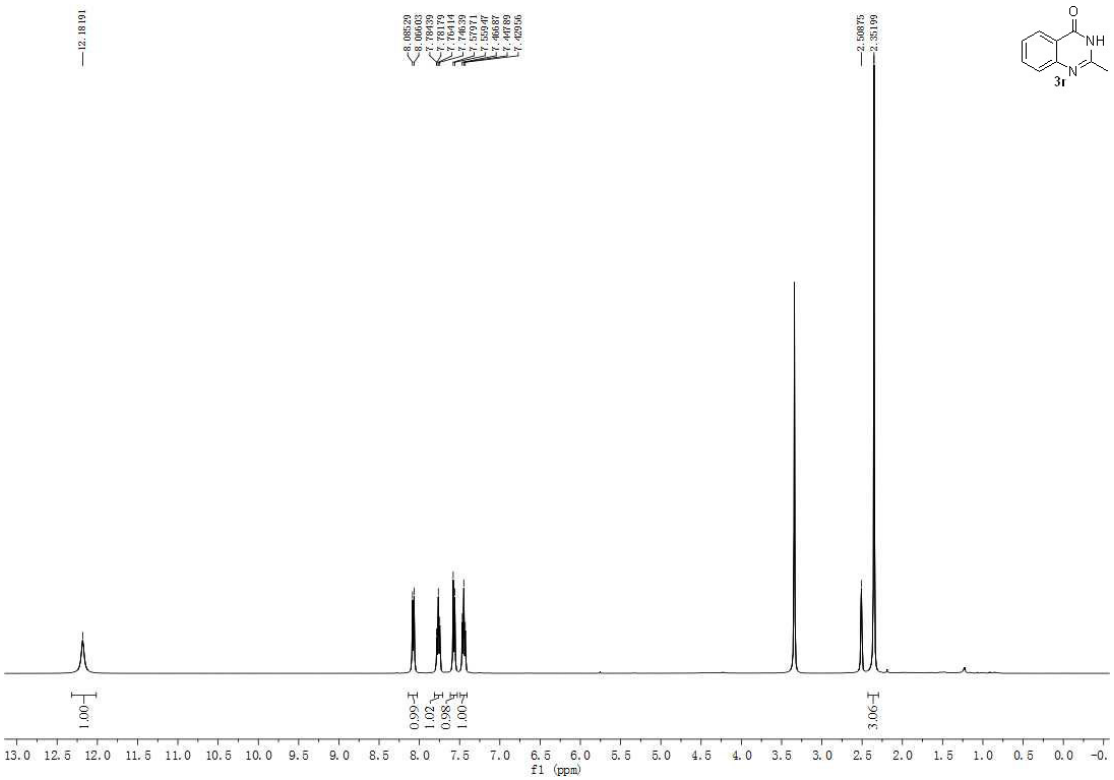
169.03311
161.15929
139.61923
136.58986
131.73376
131.07926
130.18686
128.44037
128.14697
126.97035
126.35894
125.33363
91.65446
20.25711
f1 (ppm)
4b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8.06603
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7.78179
7.77914
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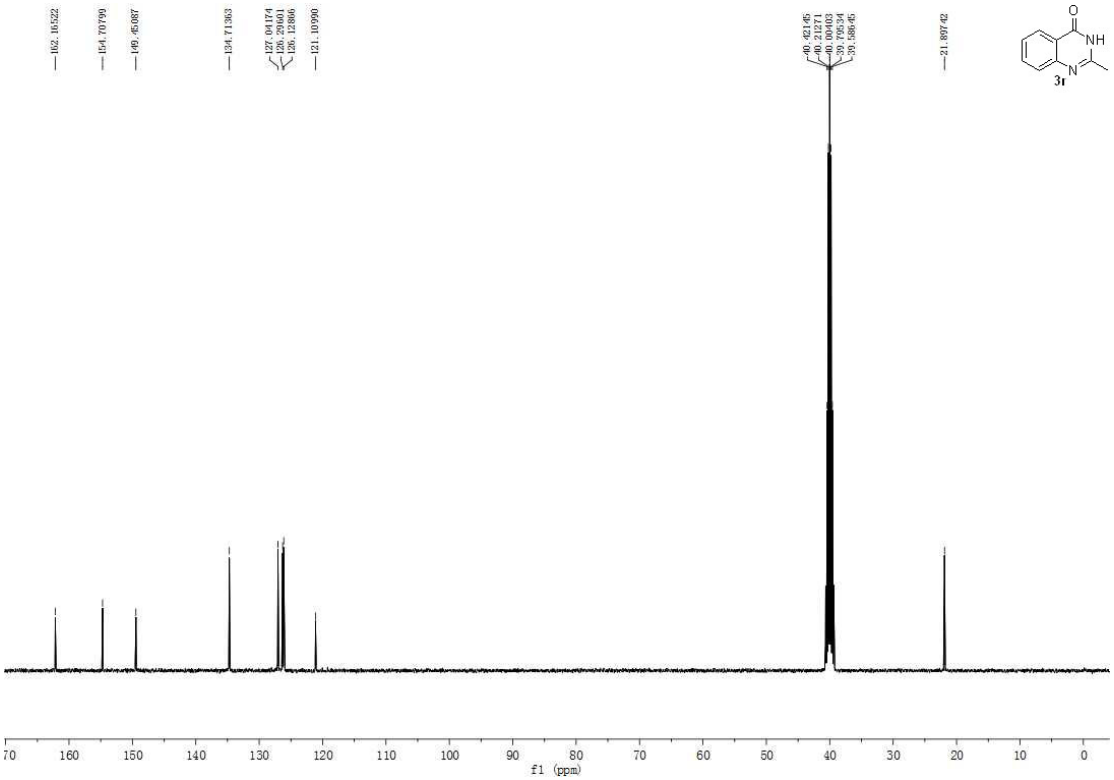
7.59947
7.57971
7.46687
7.46489
7.45956
2.58875
2.35199
1.00
0.99
1.02
0.98
1.00
3.06
f1 (ppm)
3r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40.00403
39.79534
39.58645
21.89742
f1 (ppm)
3r