Transition-Metal-Free Oxidative C5 C−H-Halogenation of 8-Aminoquinoline Amides using Sodium Halides

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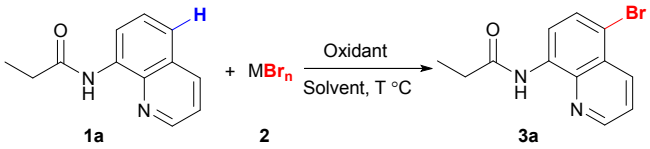
Supplementary Information

Contents

Optimization process data in detail

Table 1. Optimization of the reaction conditions for bromination[a]

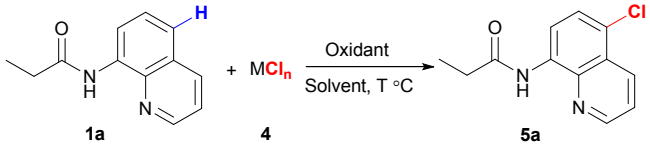


1a 2 3a

Entry	MBr_n	equivalent	oxidant	Solvent	T (ºC)	Yield[b](%)
1	NaBr	2	oxone	CH_3CN	85	<5
2	NaBr	2	oxone	DCE	85	51
3	NaBr	2	oxone	DME	85	43
4	NaBr	2	oxone	DMF	130	49
5	NaBr	2	oxone	PhCl	130	38
6	NaBr	2	oxone	THF	67	36
7	NaBr	2	oxone	PhMe	110	23
8	NaBr	2	oxone	1-4 dioxane	100	32
9	NaBr	2	oxone	CH_2Cl_2	40	<5
10	NaBr	2	$K_2S_2O_8$	DCE	85	NR
11	NaBr	2	$PhI(OAc)_2$	DCE	85	NR
12	NaBr	2	TBHP	DCE	85	NR
13	NaBr	2	PhIO	DCE	85	NR
14	NaBr	2	BQ	DCE	85	NR
14	NaBr	2	BP	DCE	85	NR
16	NaBr	2	oxone	DCE	65	51
17	NaBr	2	oxone	DCE	45	51
18	NaBr	2	oxone	DCE	rt	51
19	KBr	2	oxone	DCE	rt	43
20	$CaBr_2$	1	oxone	DCE	rt	<5
21	NaBr	2.5	oxone	DCE	rt	54
22	NaBr	3	oxone	DCE	rt	73
23	**NaBr**	**4**	**oxone**	**DCE**	**rt**	**92**

[a]Reaction conditions: **1a** (0.2 mmol), MBr_n (**2**), oxidant (0.3 mmol) in solvent (2.0 mL) stirring for 10 h under air. [b] Isolated yield.

Table 2. Optimization of the reaction conditions for chlorination[a]



1a 4 5a

Entry	MCl_n	equivalent	oxidant	Solvent	T (ºC)	Yield[b](%)
1	NaCl	2	oxone	CH_3CN	85	30[c]
2	NaCl	2	oxone	DCE	85	30[c]
3	NaCl	2	oxone	DME	85	29[c]
4	NaCl	2	oxone	DMF	130	84[c] (75)
5	NaCl	2	oxone	PhCl	130	19[c]
6	NaCl	2	oxone	THF	67	NR
7	NaCl	2	oxone	PhMe	110	16[c]
8	NaCl	2	oxone	1-4 dioxane	100	NR
9	NaCl	2	oxone	CH_2Cl_2	40	NR
10	NaCl	3	oxone	DMF	130	82
11	**NaCl**	**4**	**oxone**	**DMF**	**130**	**86**
12	NaCl	4	oxone	DMF	105	66
13	NaCl	4	oxone	DMF	85	37
14	KCl	4	oxone	DMF	130	75
15	$CaCl_2$	2	oxone	DMF	130	45

[a]Reaction conditions: **1a** (0.2 mmol), MBr_n (**2**), oxidant (0.3 mmol) in solvent (2.0 mL) stirring for 10 h under air. [b] Isolated yield. [c] GC yield.

Experimental Section

Instrumentation and chemicals

^{1}H NMR, ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer with $CDCl_3$ as the solvent and TMS as an internal standard, operating at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR. Melting points were measured by SGW X-4A microscopic apparatus. GC analysis was performed on Thermo Trace 1300 gas chromatograph. The X-ray crystallography was measured on Bruker D8 VENTURE PHOTON instrument. Dichloromethane, ethyl acetate and hexane were used for column chromatography without further purification. All solvents and chemicals were obtained from commercial sources and used as-received unless otherwise noted.

General procedures

General procedure for the C5 C−H-bromination. A mixture of N-(8-quinolinyl)amide (0.2 mmol), oxone (0.3 mmol) and NaBr (0.8 mmol) were added into a vial containing a stirring bar and sealed with a Teflon-lined cap. Then DCE (2 mL) was introduced. The resulting mixture was stirred at 25 ºC for 10 h. After the reaction was complete, the mixture was added into H_2O (25 mL) and extracted with ethyl acetate (10 mL) for three times. The combined organic layer was dried over anhydrous Na_2SO_4 and filtered. After removal of the solvent *in vacuo*, the residue was purified by column chromatography (ethyl acetate/hexane) to afford the pure product.

General procedure for the C5 C−H-chlorination. A mixture of N-(8-quinolinyl)amide (0.2 mmol),

oxone (0.3 mmol) and NaCl (0.8 mmol) were added into a vial containing a stirring bar and sealed with a Teflon-lined cap. Then DMF (2 mL) was introduced. The resulting mixture was stirred at 130 °C for 10 h. After the reaction was complete, the mixture was added into H_2O (15 mL) and extracted with ethyl acetate (10 mL) for three times. The combined organic layer was dried over anhydrous $MgSO_4$ and filtered. After removal of the solvent *in* vacuo, the residue was purified by silica gel column (hexane/EtOAc) to afford the pure product.

Synthesis of substrates 1

The aminoquinoline (2.0 mmol) and triethylamine (2.2 mmol) were dissolved in dry CH_2Cl_2 (5 mL) and stirred at room temperature for 10 min, then stirred for a further 10 min while the reaction solution was cooled in an ice bath. The acid chloride (2.0 mmol) was added dropwise. The reaction solution was left in the cooling bath for 1 hour and then allowed to warm to room temperature. Stirring was continued at room temperature for 2 h. The reaction mixture was dissolved in CH_2Cl_2 (20 mL) and 1M NaOH aqueous solution (3×15 mL). The organic layer was dried with anhydrous MgSO4, filtered. After removal of the solvent in vacuo, the residue was purified by silica gel column with hexane/EtOAc to afford the pure product.

Synthesis of 8a

A mixture of N-(5-bromoquinolin-8-yl)propanamide (0.2 mmol), $Pd(OAc)_2$ (5 mol%), Xphos (10 mol%), 4-methoxyphenylboronic acid (0.3 mmol) and K_2CO_3 (0.4 mmol) were added into a vial containing a stirring bar and sealed with a Teflon-lined cap. Then EtOH (2 mL) was introduced. The resulting mixture was stirred at 80 °C for 6 h. After the reaction was complete, the mixture was added into H_2O (15 mL) and extracted with ethyl acetate (10 mL) for three times. The combined organic layer was dried over anhydrous $MgSO_4$ and filtered. After removal of the solvent *in* vacuo, the residue was purified by silica gel column (hexane/EtOAc) to afford the pure product.

Synthesis of 8b

A mixture of N-(5-bromoquinolin-8-yl)propanamide (0.2 mmol), $Pd(OAc)_2$ (5 mol%), Xphos (10 mol%), B_2pin_2 (0.4 mmol) and KOAc (0.4 mmol) were added into a vial containing a stirring bar and sealed with a Teflon-lined cap. Then 1,4-dioxane (2 mL) was introduced. The resulting mixture was stirred at 110 °C for 5 h. After the reaction was complete, the mixture was added into H_2O (15 mL) and extracted with ethyl acetate (10 mL) for three times. The combined organic layer was dried over anhydrous $MgSO_4$ and filtered. After removal of the solvent *in* vacuo, the residue was purified by silica gel column (hexane/EtOAc) to afford the pure product.

Characterization Data

N-(5-bromoquinolin-8-yl)propanamide(**3a**)

Yellow solid, mp 103–105 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (t, *J* = 7.56 Hz, 3H), 2.60 (q, *J* = 7.56 Hz, 2H), 7.56 (q, *J* = 4.20 Hz, 1H), 7.78 (d, *J* = 8.40 Hz, 1H), 8.50–8.53 (m, 1H), 8.68 (d, *J* = 8.40 Hz, 1H), 8.80–

8.82 (m, 1H), 9.79 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.7, 31.3, 114.0, 116.9, 122.6, 127.2, 131.0, 134.5, 136.0, 139.1, 148.6, 172.5.

N-(5-bromoquinolin-8-yl)acetamide(**3b**)

Light yellow solid, mp 139–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3H), 7.53–7.57 (m, 1H), 7.77 (d, *J* = 8.36 Hz, 1H), 8.51 (d, *J* = 8.52 Hz, 1H), 8.65 (d, *J* = 8.40 Hz, 1H), 8.80 (d, *J* = 4.08 Hz, 1H), 9.75 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.1, 114.1, 116.9, 122.6, 127.2, 130.9, 134.5, 136.0, 138.9, 148.6, 168.7.

N-(5-bromoquinolin-8-yl)butyrylamide(**3c**)

Light yellow solid, mp 79–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.06 (t, *J* = 7.36 Hz, 3H), 1.85 (q, *J* = 7.44 Hz, 2H), 2.54 (t, *J* = 7.40 Hz, 2H), 7.54–7.58 (m, 1H), 7.78 (d, *J* = 8.36 Hz, 1H), 8.52 (d, *J* = 8.52 Hz, 1H), 8.69 (d, *J* = 8.40 Hz, 1H), 8.80–8.82 (m, 1H), 9.78 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 19.1, 40.2, 114.0, 116.9, 122.6, 127.2, 131.0, 134.5, 136.0, 139.0, 148.6, 171.8.

N-(5-bromoquinolin-8-yl)-3-phenylpropanamide(**3d**)

Light yellow solid, mp 107–108 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.87 (t, *J* = 8.12 Hz, 2H), 3.14 (t, *J* = 7.52 Hz, 2H), 7.19 (q, *J* = 44.08 Hz, 1H), 7.28–7.30 (m, 4H), 7.52 (q, *J* = 4.20 Hz, 1H), 7.77 (d, *J* = 8.40 Hz, 1H), 8.50 (d, *J* = 8.52 Hz, 1H), 8.67 (d, *J* = 8.40 Hz, 1H), 8.76 (d, *J* = 4.12 Hz, 1H), 9.74 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.4, 39.7, 114.1, 117.0, 122.6, 126.3, 127.2, 128.4, 128.6, 130.9, 134.4, 136.0, 139.0, 140.6, 148.6, 170.8.

N-(5-bromoquinolin-8-yl)isobutyramide(**3e**)

Light yellow solid, mp 77–78 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34–1.37 (m, 6H), 2.72–2.80 (m, 1H), 7.54–7.58 (m, 1H), 7.79 (d, *J* = 8.04 Hz, 1H), 8.51 (d, *J* = 8.44 Hz, 1H), 8.69 (d, *J* = 8.40 Hz, 1H), 8.81–8.83 (m, 1H), 9.88 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.7, 37.2, 114.0, 116.9, 122.6, 127.2, 131.0, 134.6, 136.0, 139.2, 148.6, 175.8.

N-(5-bromoquinolin-8-yl)-t-butyl carboxamide(**3f**)

Yellow solid, mp 90–92 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 9H), 7.53–7.57 (m, 1H), 7.78 (d, *J* = 8.40 Hz, 1H), 8.51 (d, *J* = 8.52 Hz, 1H), 8.69 (d, *J* = 8.40 Hz, 1H), 8.82–8.84 (m, 1H), 10.23 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.7, 40.4, 113.9, 116.8, 122.6, 127.2, 131.0, 134.7, 135.9, 139.5, 148.7, 177.3.

N-(5-bromoquinolin-8-yl)cyclohexane carboxamide(**3g**)

Light yellow solid, mp 92–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.25–1.44 (m, 4H), 1.58–1.65 (m, 2H), 1.86–1.90 (m, 2H), 2.06–2.10 (m, 2H), 2.43–2.51 (m, 1H), 7.54–7.58 (m, 1H), 7.77–7.80 (m, 1H), 8.52 (d, *J* = 8.48 Hz, 1H), 8.69 (d, *J* = 8.40 Hz, 1H), 8.82 (d, *J* = 4.12 Hz, 1H), 9.86 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.7, 29.7, 46.9, 113.9, 116.9, 122.6, 127.2, 131.0, 134.6, 136.0, 139.2, 148.6, 174.9.

N-(5-bromoquinolin-8-yl)benzamide(**3h**)

White solid, mp 120–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.59 (m, 4H), 7.83 (d, *J* = 8.36 Hz, 1H), 8.06 (d, *J* = 7.32 Hz, 2H), 8.53 (d, *J* = 8.48 Hz, 1H), 8.81–8.86 (m, 2H), 10.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 114.4, 117.0, 121.6, 122.7, 127.3, 128.8, 131.0, 132.0, 134.5, 134.9, 136.0, 139.5, 148.7, 165.4.

4-methyl-N-(5-bromoquinolin-8-yl)benzamide(**3i**)

Yellow solid, mp 156–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H), 7.35 (d, *J* = 7.64 Hz, 2H), 7.56–7.61 (m, 1H), 7.84 (dd, *J* = 8.32 Hz, *J* = 2.88 Hz, 1H), 7.96 (d, *J* = 7.84 Hz, 2H), 8.53–8.57 (m, 1H), 8.81–8.87 (m, 2H), 10.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 114.2, 117.0, 122.7, 127.3, 129.5, 131.0, 132.1, 134.7, 136.0, 139.5, 142.6, 148.7, 165.4.

4-fluoro-N-(5-bromoquinolin-8-yl)benzamide(**3j**)

White solid, mp 169–171 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20–7.26 (m, 2H), 7.60 (q, *J* = 41.60 Hz, 1H), 7.85 (d, *J* = 8.40 Hz, 1H), 8.08 (q, *J* = 5.40 Hz, 2H), 8.55 (d, *J* = 8.44 Hz, 1H), 8.83 (dd, *J* = 24.20 Hz, *J* = 3.92 Hz, 2H), 10.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 114.6, 115.9 (d, *J* = 21.84 Hz), 117.0, 122.8, 127.3, 129.7 (d, *J* = 9.00 Hz), 131.0, 131.1 (d, *J* = 3.04 Hz), 134.4, 136.1, 139.4, 148.9, 164.3, 165.1 (d, *J* = 251.30 Hz).

4-chloro-N-(5-bromoquinolin-8-yl)benzamide(**3k**)

White solid, mp 145–146 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 8.36 Hz, 2H), 7.59 (q, *J* = 4.20 Hz, 1H), 7.84 (d, *J* = 8.40 Hz, 1H), 8.00 (d, *J* = 8.36 Hz, 2H), 8.55 (d, *J* = 8.52 Hz, 1H), 8.79 (d, *J* = 8.40 Hz, 1H), 8.86 (d, *J* = 4.20 Hz, 1H), 10.66 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 114.7, 117.1, 122.8, 127.3, 128.7, 129.1, 131.0, 133.3, 134.3, 136.1, 138.4, 139.4, 148.8, 164.3.

4-trifluoromethyl-N-(5-bromoquinolin-8-yl)benzamide(**3l**)

Yellow solid, mp 135–137 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (dd, *J* = 8.44 Hz, *J* = 4.20 Hz, 1H), 7.84 (dd, *J* = 16.48 Hz, *J* = 8.36 Hz, 3H), 8.17 (d, *J* = 8.00 Hz, 2H), 8.57 (d, *J* = 8.52 Hz, 1H), 8.81 (d, *J* = 8.36 Hz, 1H), 8.87 (d, *J* = 4.08 Hz, 1H), 10.74 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 115.0, 117.2, 122.3, 122.9, 125.9 (q, *J* = 3.73 Hz), 127.3, 127.8, 131.0, 133.7 (q, *J* = 32.52 Hz), 134.1, 136.2, 138.1, 139.4, 148.9, 164.0.

N-(5-bromo-2-methylquinolin-8-yl)propanamide(**3m**)

Light yellow solid, mp 118–119 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (t, *J* = 7.52 Hz, 3H), 2.60 (q, *J* = 7.52 Hz, 2H), 2.76 (s, 3H), 7.38–7.41 (m, 1H), 7.67–7.71 (m, 1H), 8.36 (d, *J* = 8.60Hz, 1H), 8.63 (d, *J* = 8.36Hz, 1H), 9.83 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.6, 25.0, 31.3, 113.9, 116.9, 123.4, 125.4, 129.9, 133.9, 136.0, 138.5, 157.9, 172.4.

N-(5-bromo-2-methylquinolin-8-yl)acetamide(**3n**)

Light yellow solid, mp 127–129 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34 (s, 3H), 2.77 (s, 3H), 7.37–7.42 (m, 1H), 7.67–7.71 (m, 1H), 8.36 (t, *J* = 7.80 Hz, 1H), 8.59–8.63 (m, 1H), 9.78 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.0, 25.1, 114.1, 116.9, 123.5, 125.4, 129.8, 133.8, 136.0, 138.4, 157.9, 168.6.

N-(5-chloroquinolin-8-yl)propanamide(**5a**)

Yellow solid, mp 68–71 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (t, *J* = 7.56 Hz, 3H), 2.60 (q, *J* = 7.56 Hz, 2H), 7.54–7.61(m, 2H), 8.56 (d, *J* = 8.48 Hz, 1H), 8.73 (d, *J* = 8.44 Hz, 1H), 8.83–8.85 (m, 1H), 9.77 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.7, 31.2, 116.3, 122.3, 124.1, 125.9, 127.3, 133.4, 133.9, 138.9, 148.6, 172.5.

N-(5-chloroquinolin-8-yl)acetamide(**5b**)

Yellow solid, mp 135–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3H), 7.53–7.59 (m, 2H), 8.55 (d, *J* = 8.52 Hz, 1H), 8.69 (d, *J* = 8.40 Hz, 1H), 8.82 (d, *J* = 3.96 Hz, 1H), 9.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.1, 116.4, 122.3, 124.2, 125.9, 127.3, 133.4, 133.8, 138.8, 148.6, 168.7.

N-(5-chloroquinolin-8-yl)butyrylamide(**5c**)

Light yellow solid, mp 46–48 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.06 (t, *J* = 7.40 Hz, 3H), 1.85 (q, *J* = 7.40 Hz, 2H), 2.54 (t, *J* = 7.44 Hz, 2H), 7.55–7.61 (m, 2H), 8.56 (d, *J* = 8.52 Hz, 1H), 8.73 (d, *J* = 8.40 Hz, 1H), 8.83–8.85 (m, 1H), 9.76 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 19.1, 40.1, 116.3, 122.3, 124.1, 125.9, 127.3, 133.4, 133.8, 138.9, 148.6, 171.8.

N-(5-chloroquinolin-8-yl)-3-phenylpropanamide(**5d**)

Yellow solid, mp 109–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.88 (t, *J* = 8.16 Hz, 2H), 3.14 (t, *J* = 7.52 Hz, 2H), 7.21 (q, *J* = 4.16 Hz, 1H), 7.28–7.30 (m, 4H), 7.52–7.60 (m, 2H), 8.54 (d, *J* = 8.48 Hz, 1H), 8.72 (d, *J* = 8.20 Hz, 1H), 8.79 (d, *J* = 4.04 Hz, 1H), 9.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.4, 39.7, 116.4, 122.3, 124.2, 125.9, 126.3, 127.2, 128.4, 128.6, 133.4, 133.7, 138.8, 140.7, 148.6, 170.7.

N-(5-chloroquinolin-8-yl)isobutyramide(**5e**)

Light yellow solid, mp 70–72 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (d, *J* = 6.88 Hz, 6H), 2.72–2.80 (m, 1H), 7.55–7.61 (m, 2H), 8.56 (d, *J* = 8.48 Hz, 1H), 8.74 (d, *J* = 8.40 Hz, 1H), 8.85 (d, *J* = 4.08 Hz, 1H), 9.85 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.7, 37.1, 116.3, 122.3, 124.1, 126.0, 127.3, 133.4, 133.9, 139.1, 148.6, 175.7.

N-(5-chloroquinolin-8-yl)-t-butyl carboxamide(**5f**)

Light yellow solid, mp 80–82 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 9H), 7.54–7.60 (m, 2H), 8.55 (d, *J* = 8.48 Hz, 1H), 8.74 (d, *J* = 8.40 Hz, 1H), 8.85 (d, *J* = 4.08 Hz, 1H), 10.21 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.7, 40.4, 116.2, 122.2, 124.0, 125.9, 127.3, 133.4, 134.1, 139.4, 148.7, 177.3.

N-(5-chloroquinolin-8-yl)cyclopropane carboxamide(**5g**)

Yellow solid, mp 69–72 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90–0.96 (m, 2H), 1.14–1.18 (m, 2H), 1.76–1.83 (m, 1H), 7.55–7.59 (m, 2H), 8.56 (d, *J* = 8.52 Hz, 1H), 8.68 (d, *J* = 8.40 Hz, 1H), 8.84–8.86 (m, 1H), 9.97 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 8.3, 16.3, 116.3, 122.3, 123.9, 125.9, 127.3, 133.4, 134.0, 138.8, 148.5, 172.3.

N-(5-chloroquinolin-8-yl)benzamide(**5h**)

Yellow solid, mp 128–130 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.66 (m, 5H), 8.07 (d, *J* = 7.32 Hz, 2H), 8.58 (d, *J* = 8.48 Hz, 1H), 8.87–8.90 (m, 2H), 10.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.5, 122.4, 124.5, 126.0, 127.2, 127.3, 128.9, 132.0, 133.5, 133.9, 134.9, 139.3, 148.8, 165.4.

4-methyl-N-(5-chloroquinolin-8-yl)benzamide(**5i**)

Yellow solid, mp 120–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H), 7.34 (d, *J* = 7.84 Hz, 2H), 7.58 (q, *J* = 4.20 Hz, 1H), 7.64 (d, *J* = 8.40 Hz, 1H), 7.96 (d, *J* = 7.92 Hz, 2H), 8.57 (d, *J* = 8.48 Hz, 1H), 8.86–8.89 (m, 2H), 10.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 116.4, 122.4, 124.3, 126.0, 127.3, 127.4, 129.5, 132.1, 133.4, 134.0, 139.3, 142.6, 148.7, 165.4.

4-fluoro-N-(5-chloroquinolin-8-yl)benzamide(**5j**)

White solid, mp 149–151 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20–7.26 (m, 2H), 7.58–7.66 (m, 2H), 8.08 (dd, *J* = 8.08 Hz, *J* = 5.48 Hz, 2H), 8.59 (d, *J* = 8.88 Hz, 1H), 8.85 (d, *J* = 8.36 Hz, 1H), 8.89 (d, *J* = 4.12 Hz, 1H), 10.63 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 115.9 (d, *J* = 21.85 Hz), 116.5, 122.5, 124.6, 126.0, 127.3, 129.7 (d, *J* = 8.98 Hz), 131.1 (d, *J* = 3.14 Hz), 133.5, 133.7, 139.3, 148.8, 164.3, 165.1 (d, *J* = 251.34 Hz).

4-chloro-N-(5-chloroquinolin-8-yl)benzamide(**5k**)

Yellow solid, mp 129–132 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59–7.68 (m, 2H), 7.80–7.83 (m, 2H), 8.17 (d, *J* = 8.28 Hz, 2H), 8.60 (d, *J* = 8.48 Hz, 1H), 8.84–8.91 (m, 2H), 10.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.5, 122.5, 124.8, 126.0, 127.3, 128.7, 129.1, 133.2, 133.5, 133.6, 138.3, 139.3, 148.8, 164.3.

4-trifluoromethyl-N-(5-chloroquinolin-8-yl)benzamide(**5l**)

White solid, mp 142–145 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59–7.68 (m, 2H), 7.80–7.83 (m, 2H), 7.16–7.19 (m, 2H), 7.60 (d, *J* = 8.48 Hz, 1H), 8.84–8.91 (m, 2H), 10.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.7, 122.6, 125.1, 125.9 (q, *J* = 3.62 Hz), 126.0, 127.3, 127.7, 133.4, 133.5, 133.6, 133.8, 138.1, 139.2, 148.9, 164.0.

N-(5-chloro-2-methylquinolin-8-yl)propanamide(**5m**)

Yellow solid, mp 88–90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (t, *J* = 7.56 Hz, 3H), 2.60 (q, *J* = 7.56 Hz, 2H), 2.76 (s, 3H), 7.39–7.42 (m, 1H), 7.49–7.52 (m, 1H), 8.39–8.42 (m, 1H), 8.68 (d, *J* = 8.40 Hz, 1H), 9.81 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.7, 25.1, 31.2, 116.3, 123.1, 124.0, 124.1, 126.2, 133.2, 133.4, 138.3, 157.8, 172.4.

N-(5-chloro-2-methylquinolin-8-yl)acetamide(**5n**)

Yellow solid, mp 134–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3H), 2.76 (s, 3H), 7.39–7.42 (m, 1H), 7.48–7.51 (m, 1H), 8.40 (d, *J* = 8.60 Hz, 1H), 8.65 (d, *J* = 8.40 Hz, 1H), 9.76 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.1, 25.2, 116.3, 123.2, 124.1, 124.2, 126.2, 133.1, 133.4, 138.2, 157.9, 168.7.

N-[5-(4-methoxy-phenyle)quinolin-8-yl]propanamide(**8a**)

White solid, mp 175–176 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (t, *J* = 7.52 Hz, 3H), 2.62 (q, *J* = 7.56 Hz, 2H), 3.89 (s, 3H), 7.01–7.04 (m, 2H), 7.35–7.42 (m, 3H), 7.48 (d, *J* = 7.96 Hz, 1H), 8.29 (d, *J* = 8.52 Hz, 1H), 8.80–8.83 (m, 2H), 9.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.8, 31.3, 55.4, 114.0, 116.1, 121.4, 126.5, 127.8, 131.2, 131.6, 133.7, 133.9, 134.9, 138.5, 147.8, 159.1, 172.6.

N-(5-borane-quinolin-8-yl]propanamide(**8b**)

Yellow solid, mp 165–167 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16–1.18 (m, 2H), 1.33 (s, 12H), 2.52–2.56 (m, 3H), 7.43–7.47 (m, 2H), 8.08 (t, *J* = 7.64 Hz, 2H), 9.10 (d, *J* = 8.40 Hz, 1H), 10.00 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.7, 25.0, 31.3, 83.8, 116.5, 121.4, 121.6, 121.8, 127.5, 128.0, 134.5, 137.8, 148.1, 172.6.

X-ray Crystal Data for 3a

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 3a

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 3a

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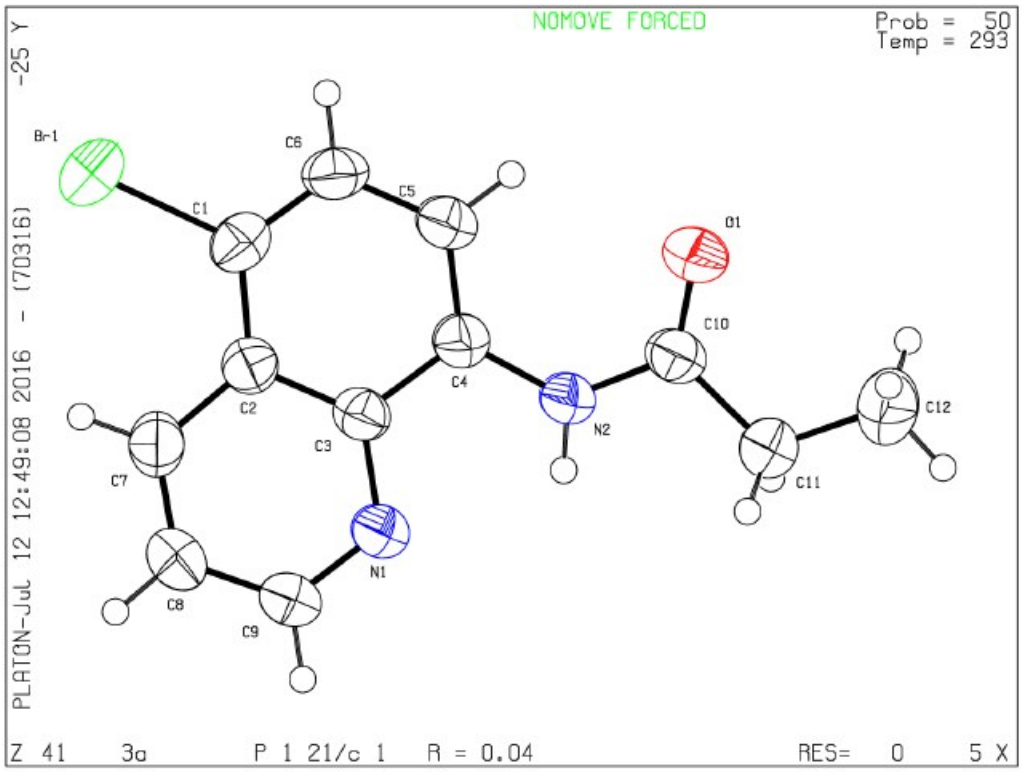
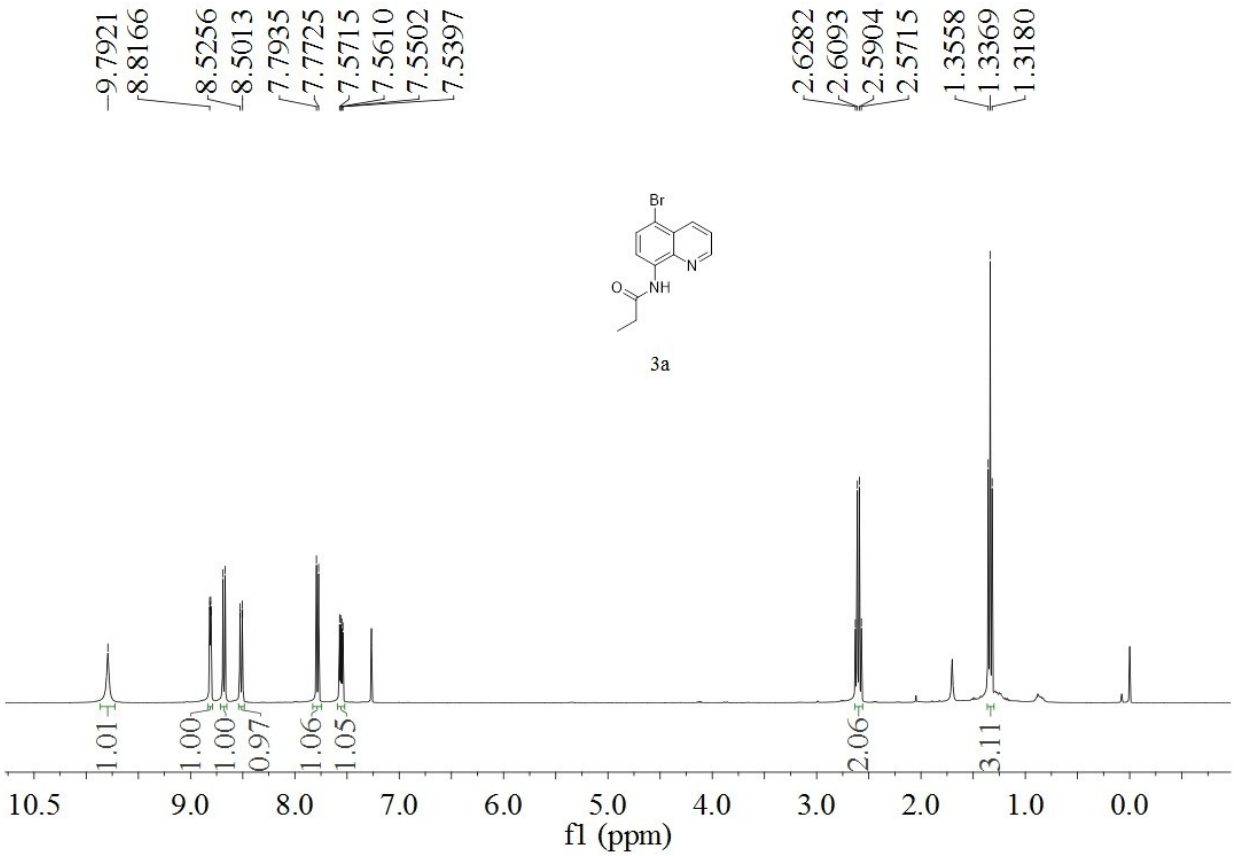
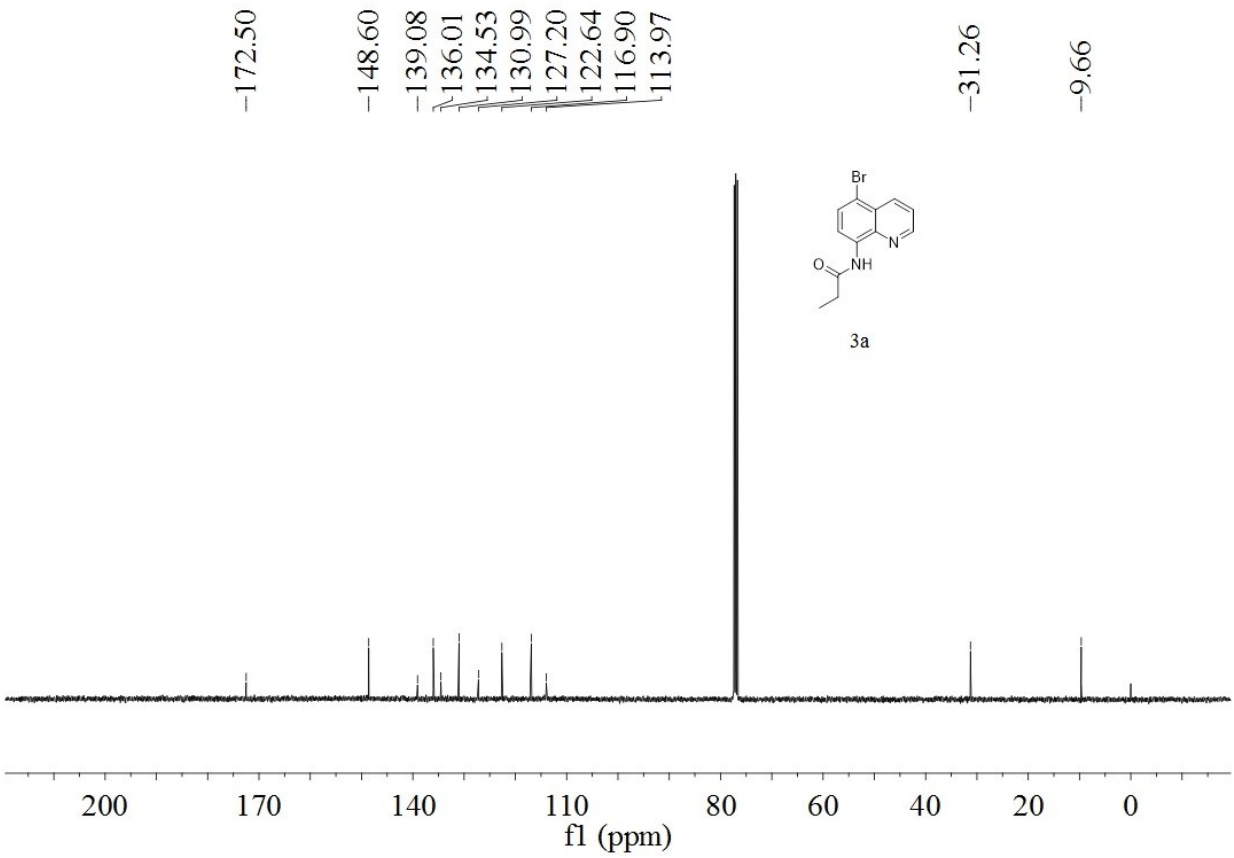
PLATON version of 06/05/2016; check.def file version of 05/05/2016

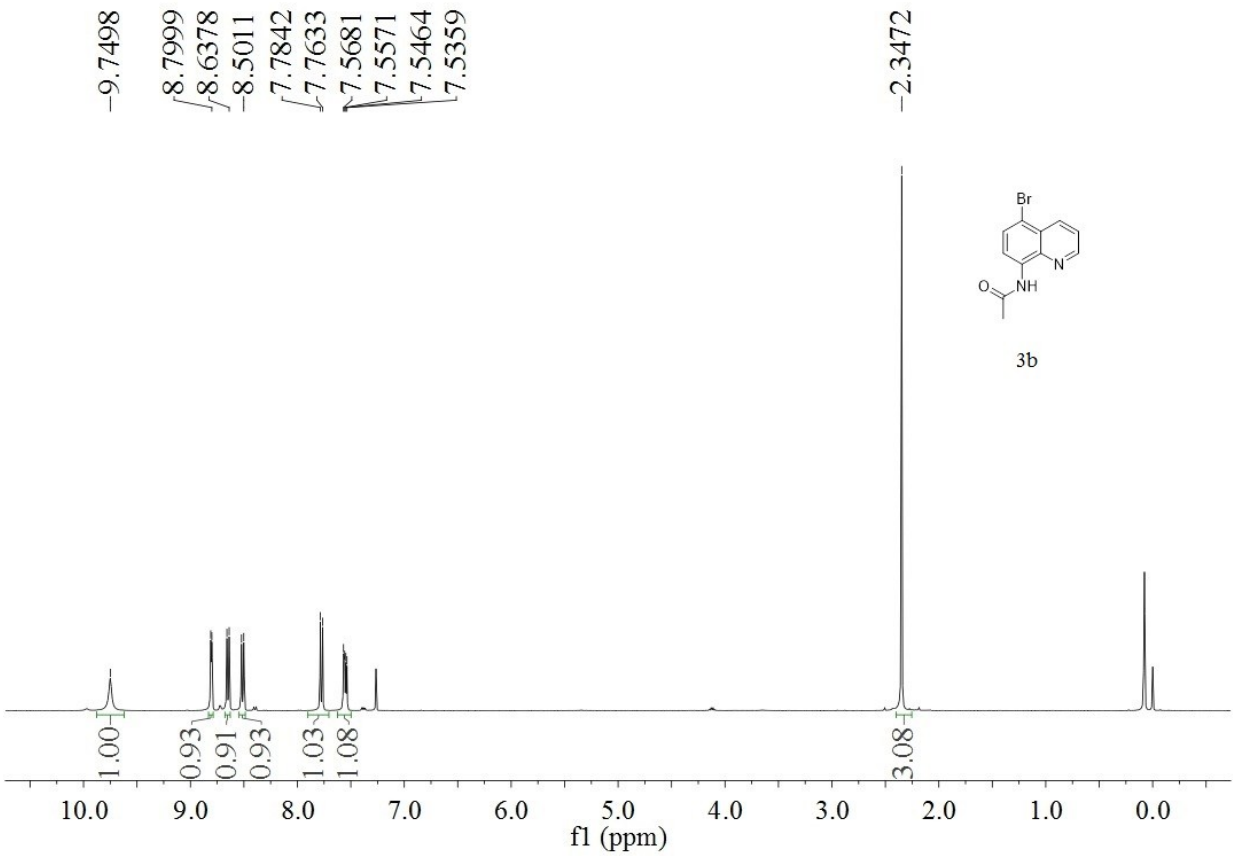
Datablock: 3a - ellipsoid plot



Copies of ^{1}H and ^{13}C NMR spectra



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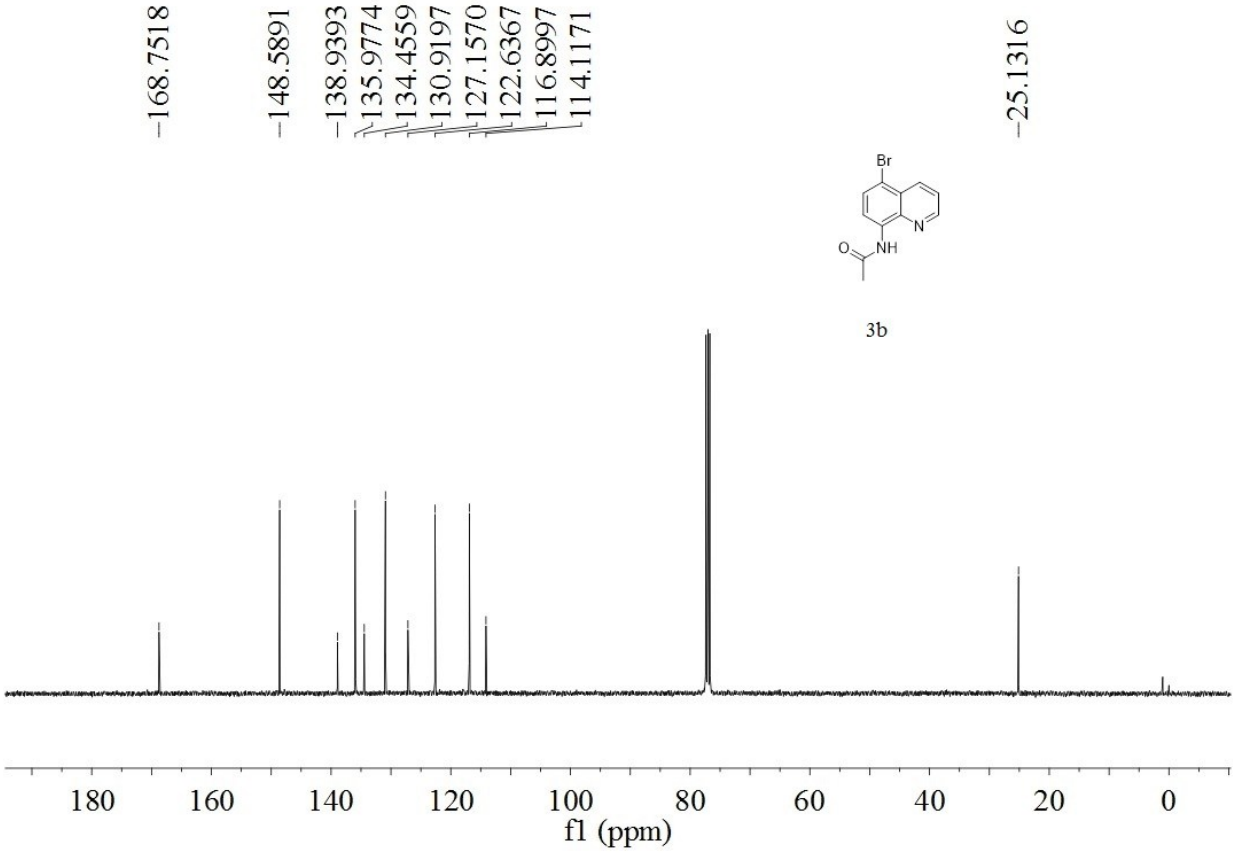
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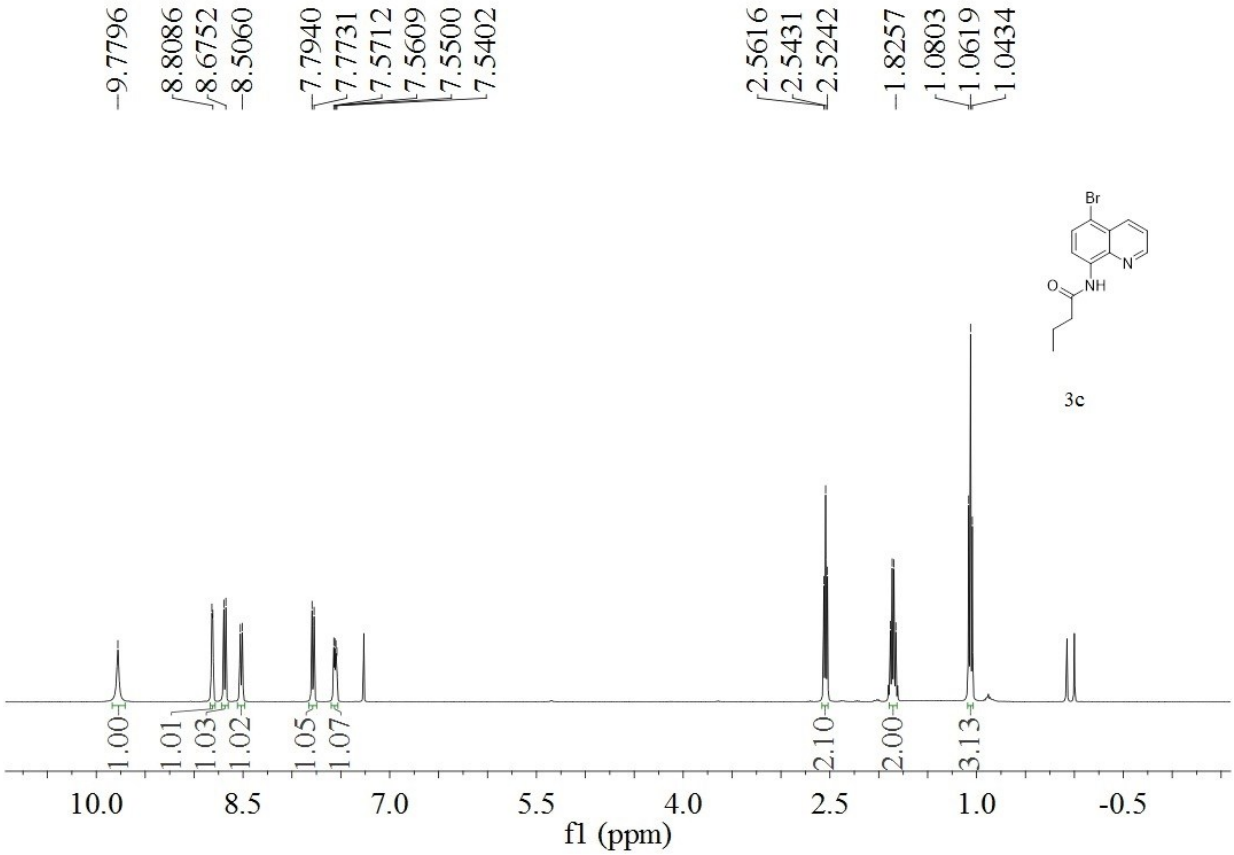
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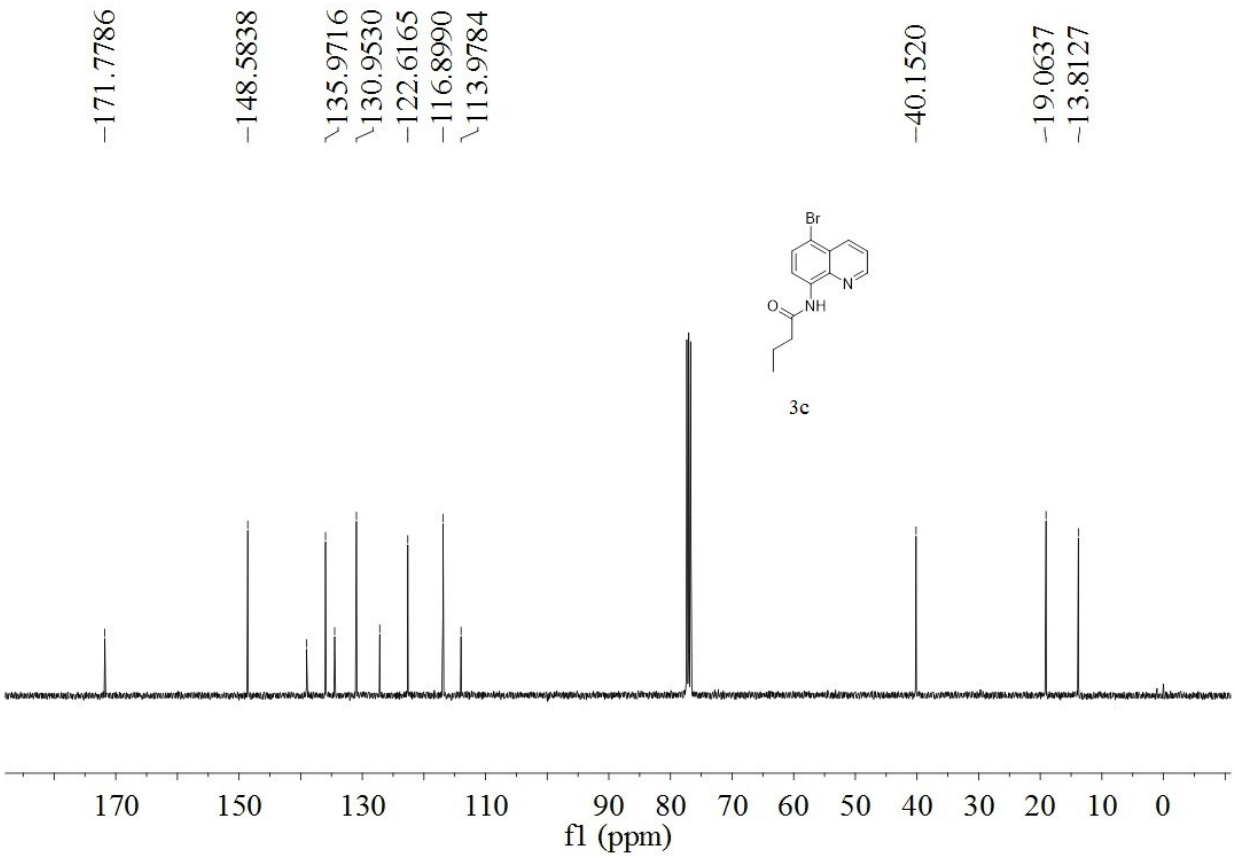
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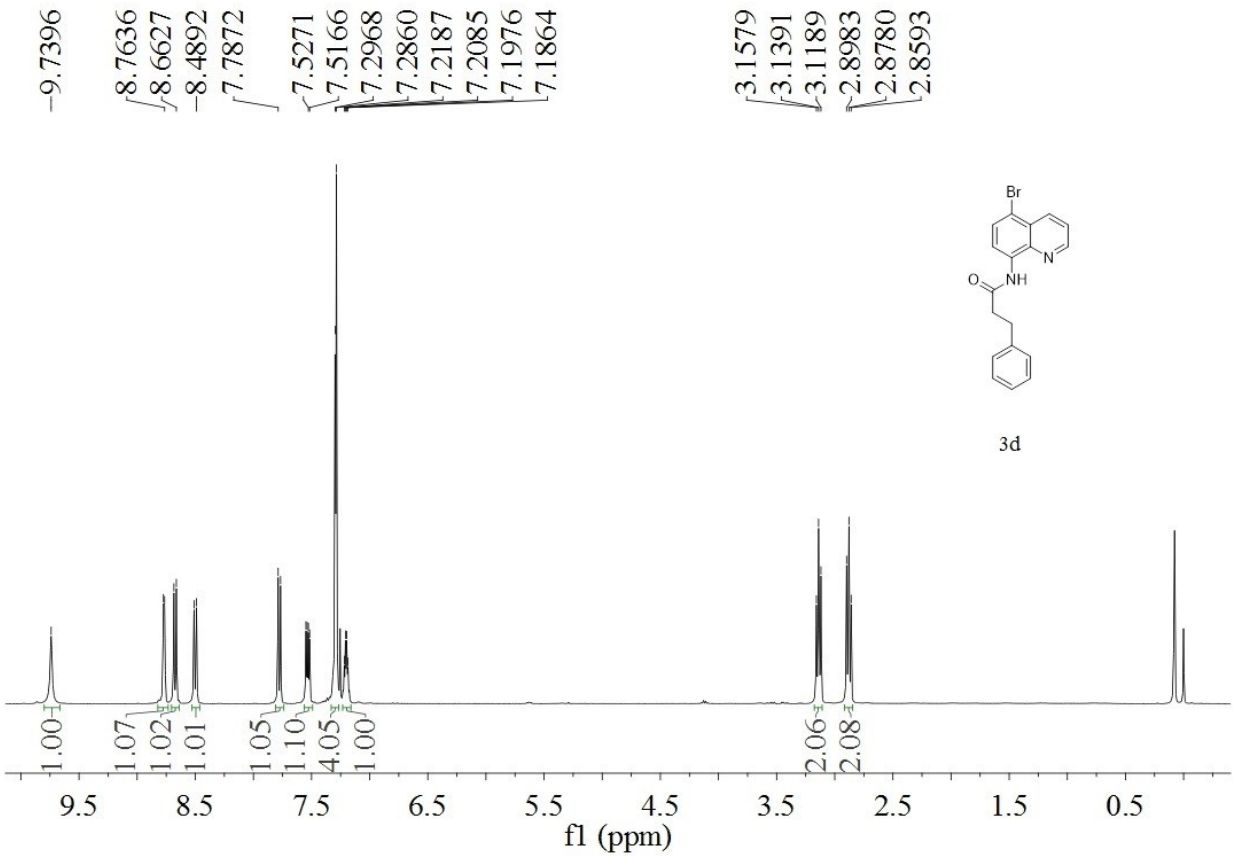
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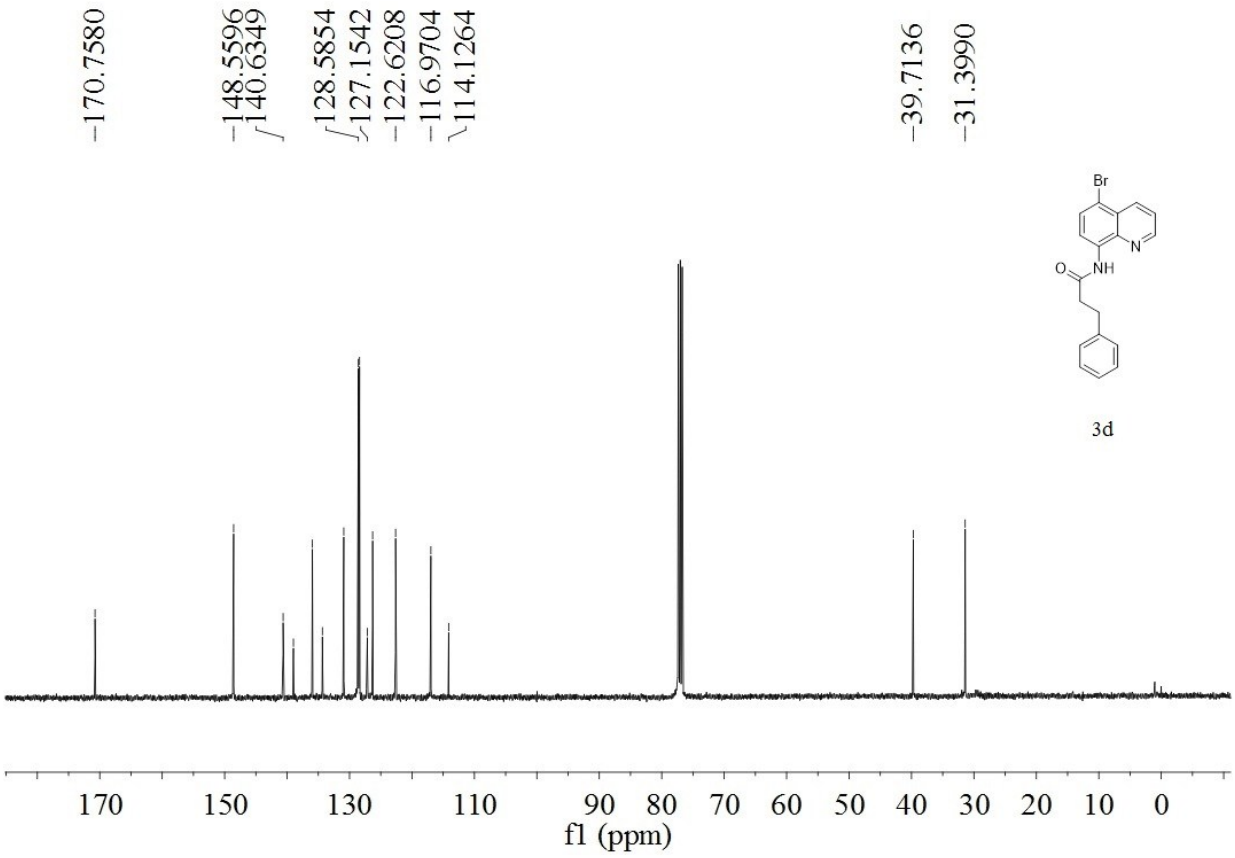
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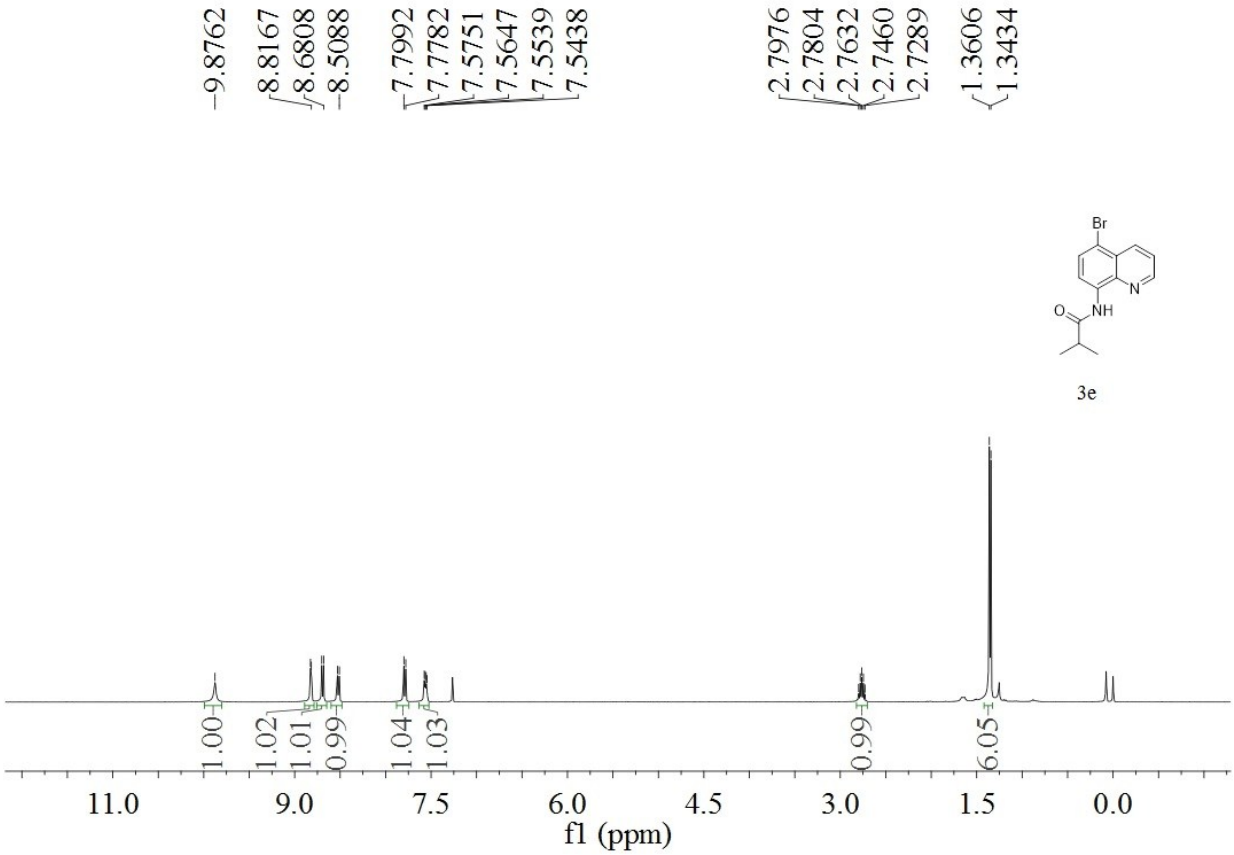
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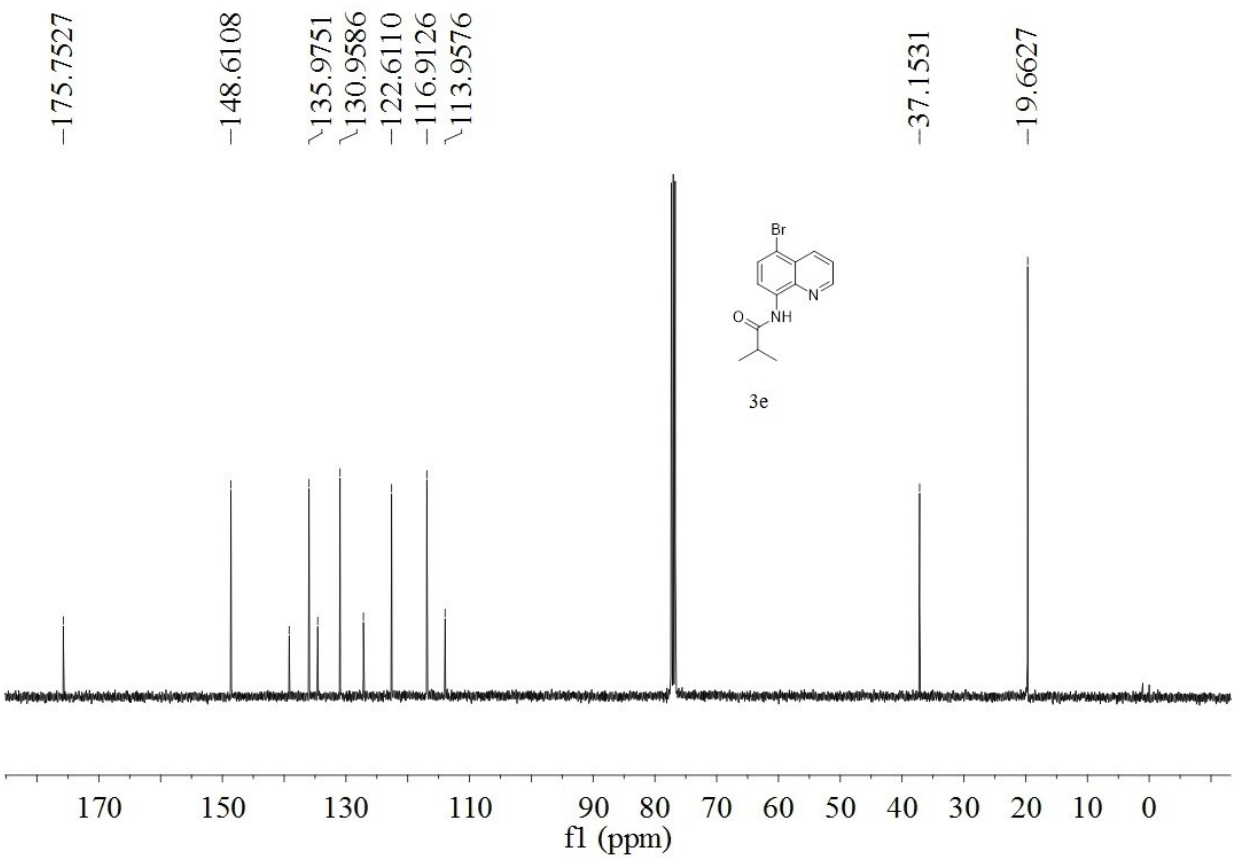
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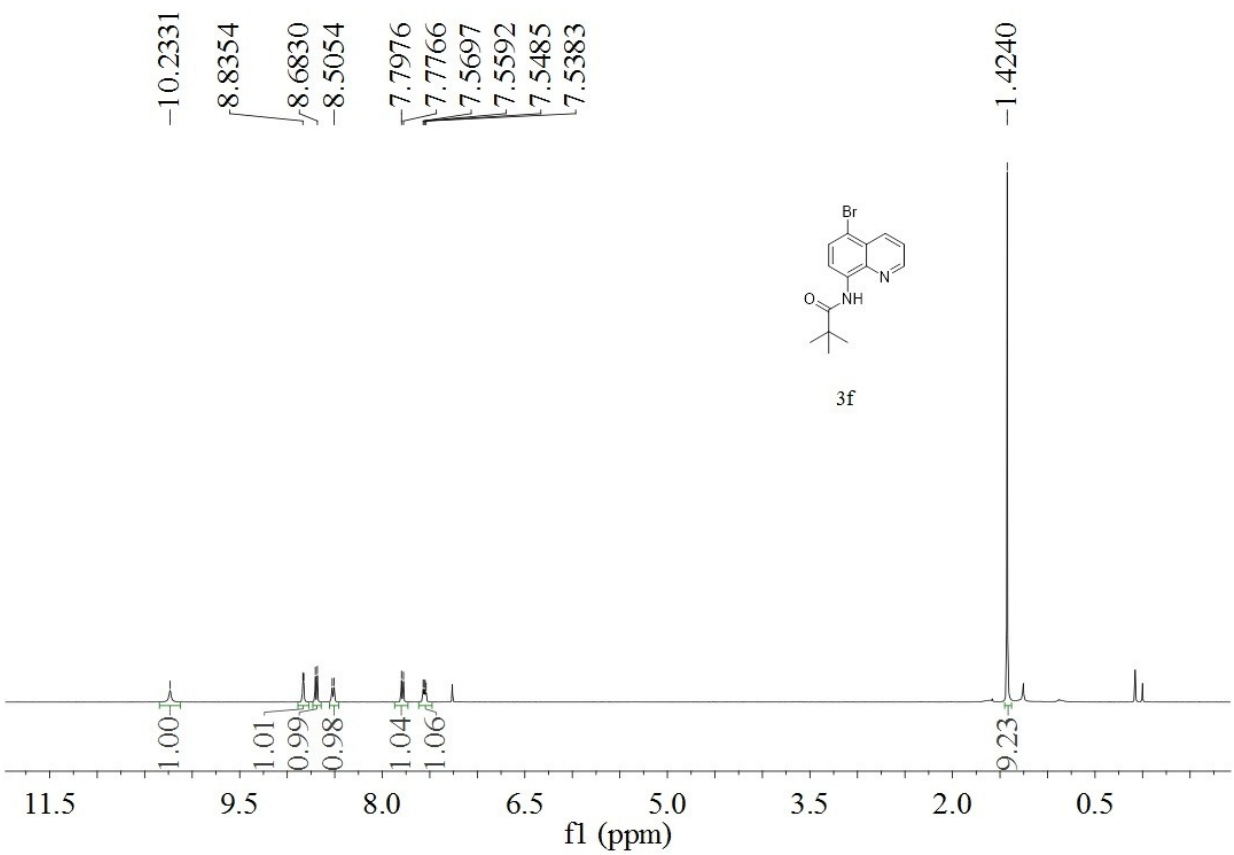
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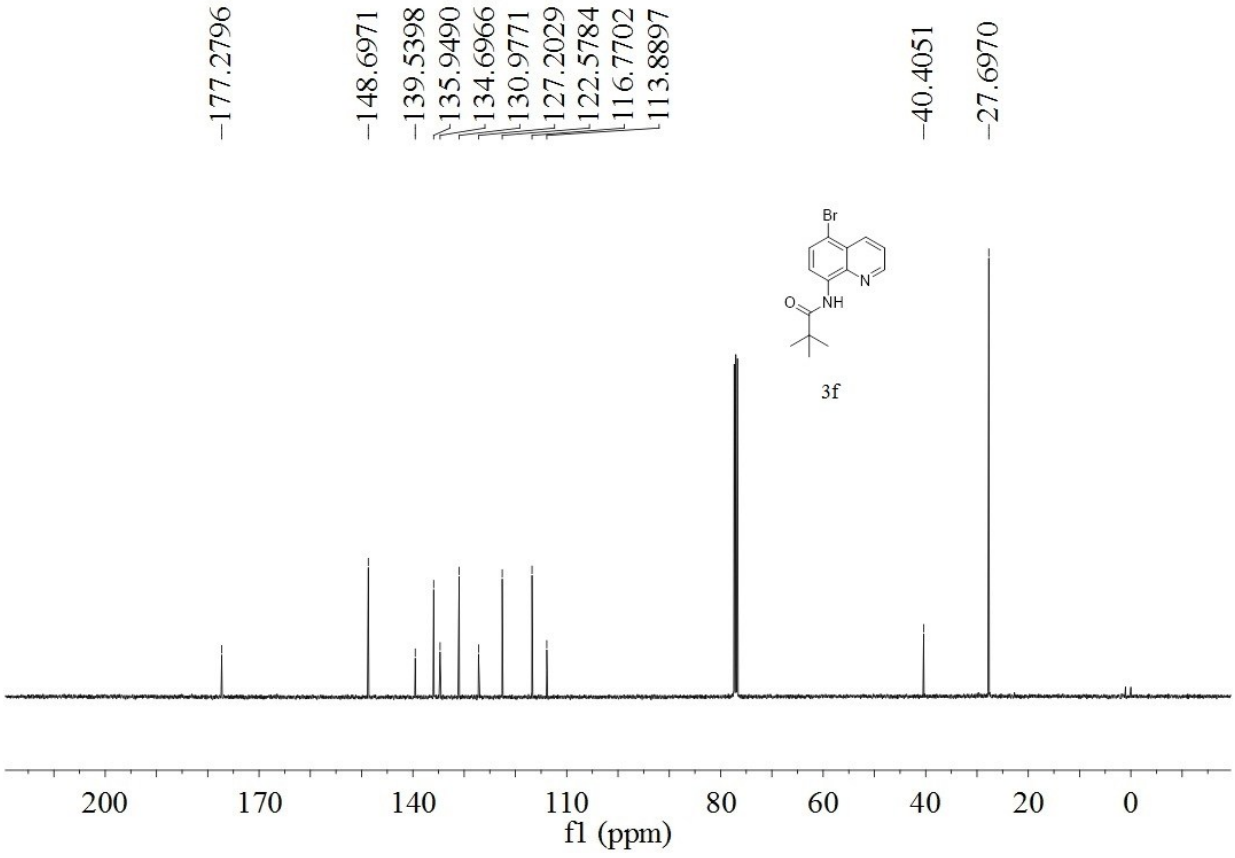
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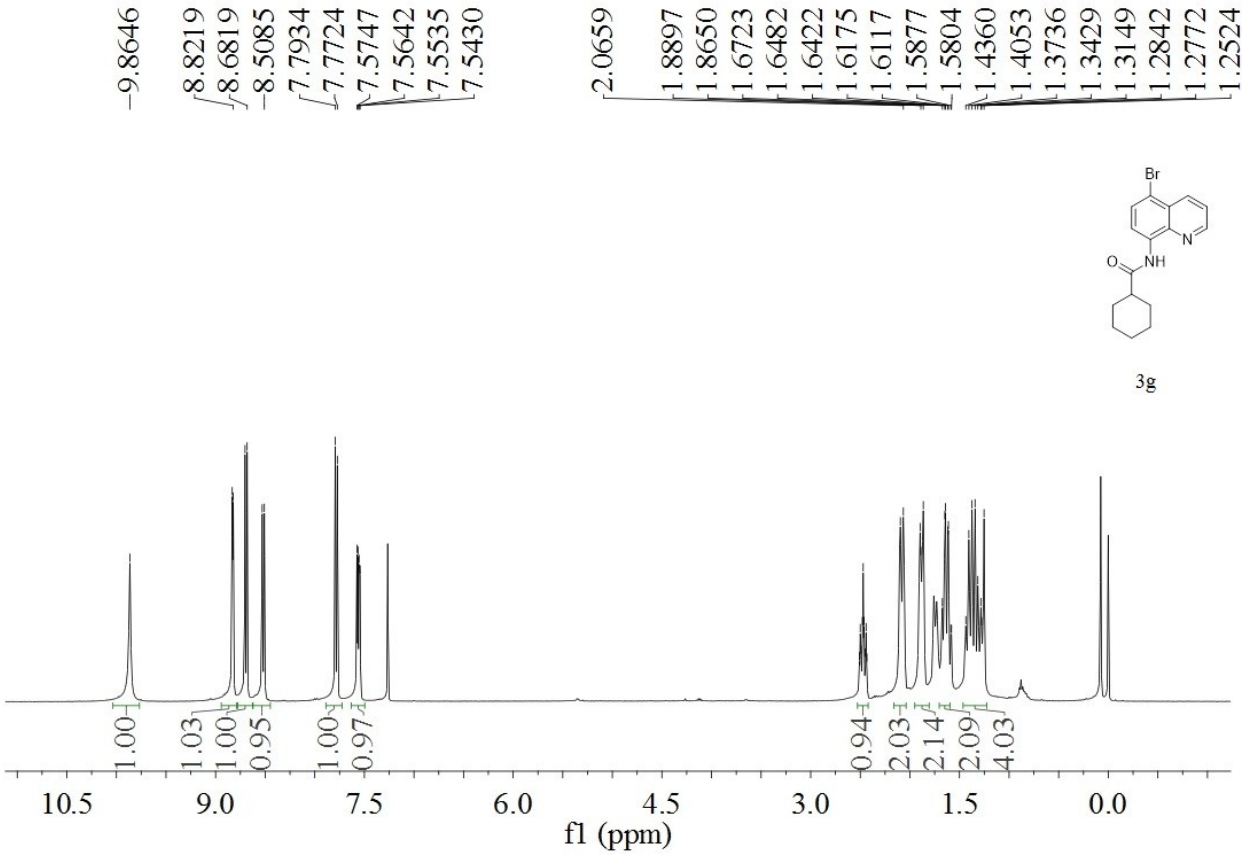
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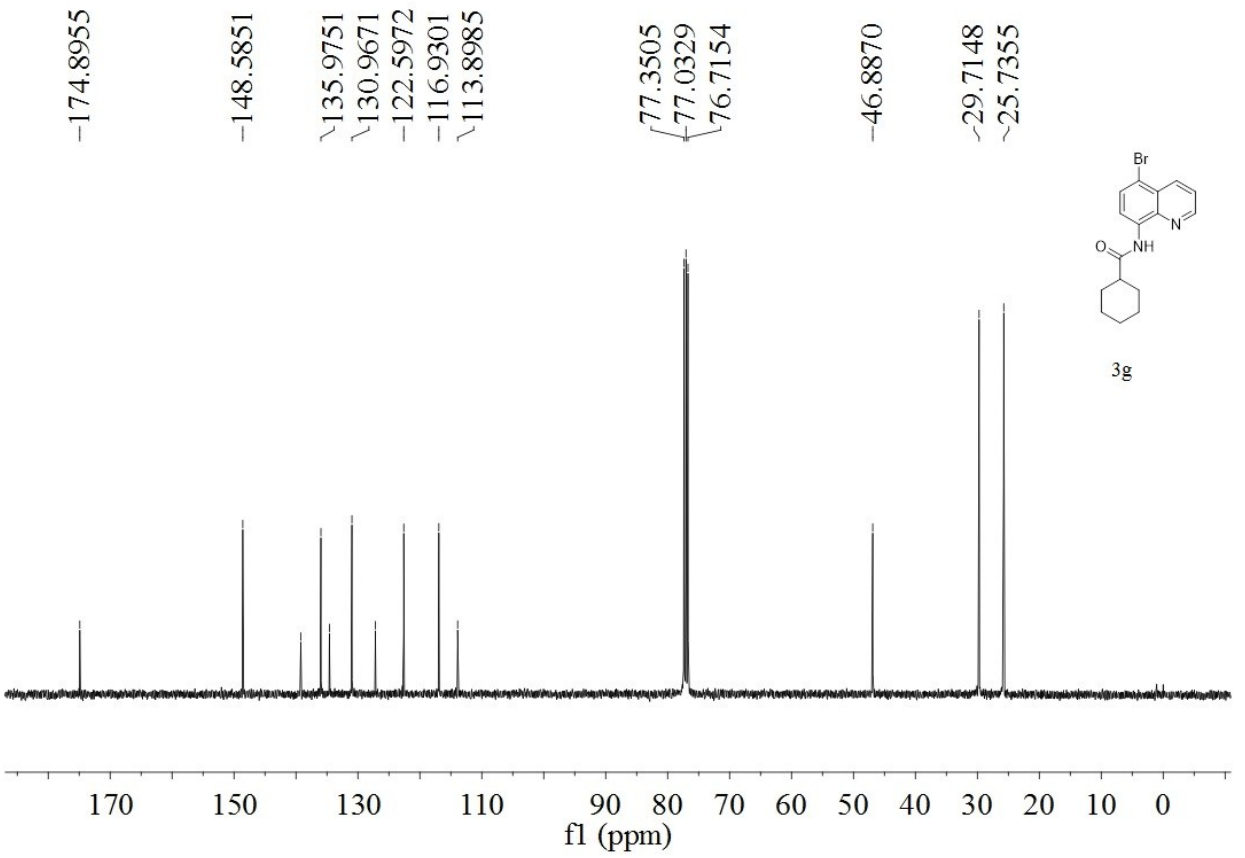
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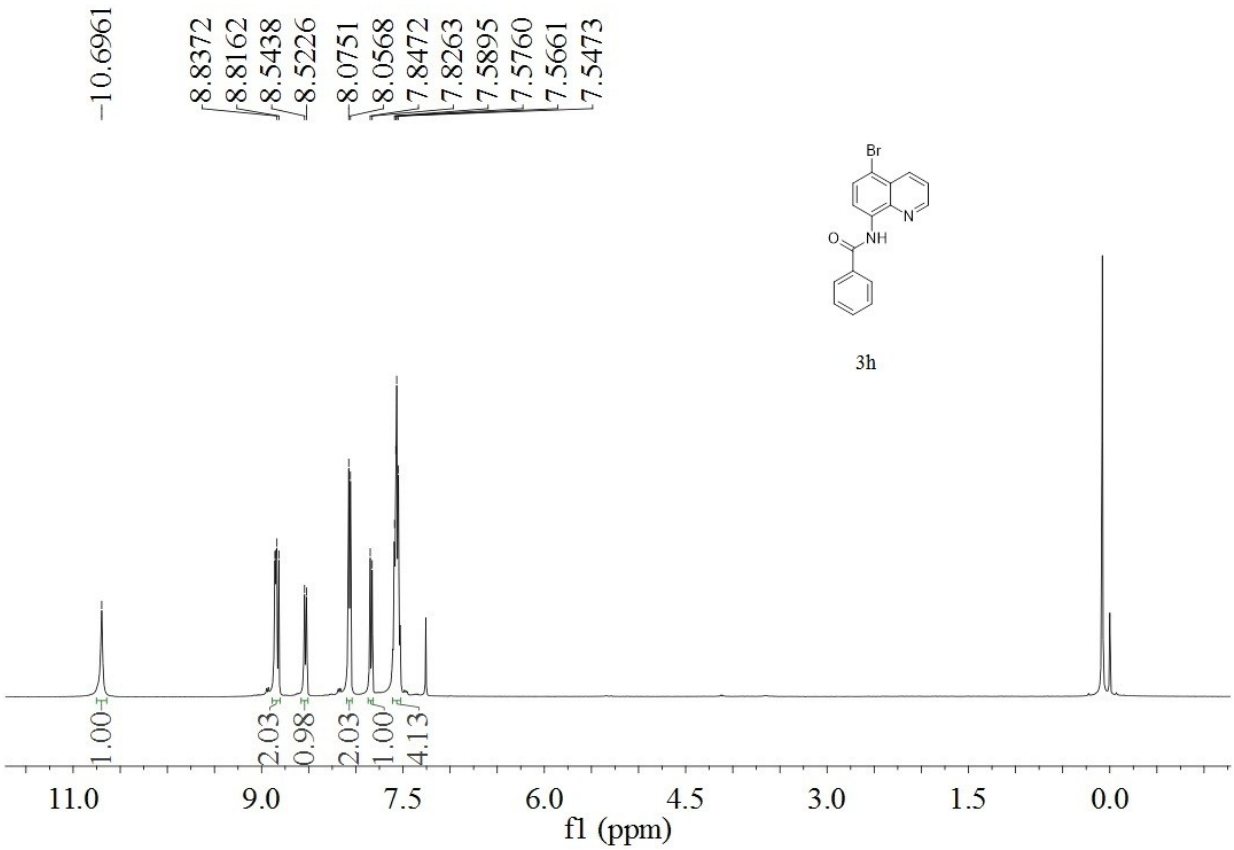
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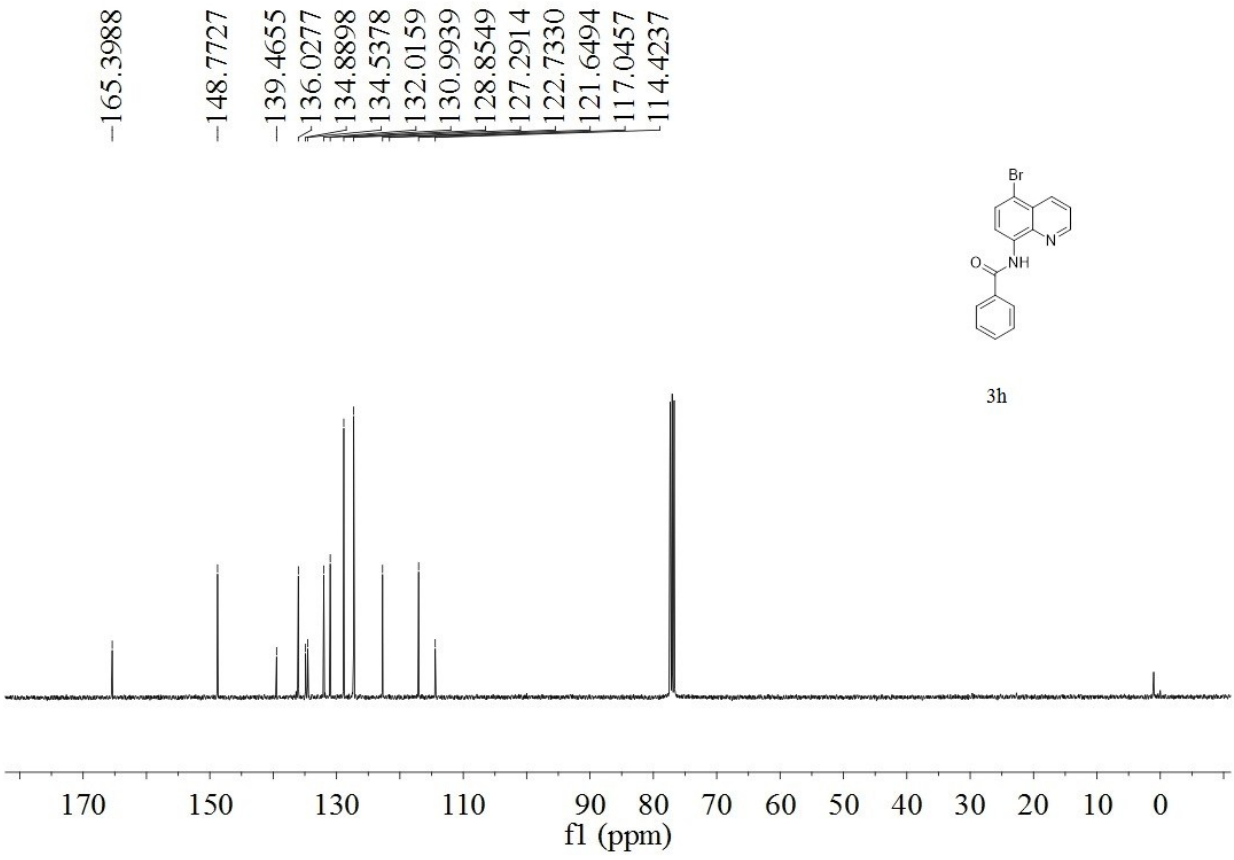
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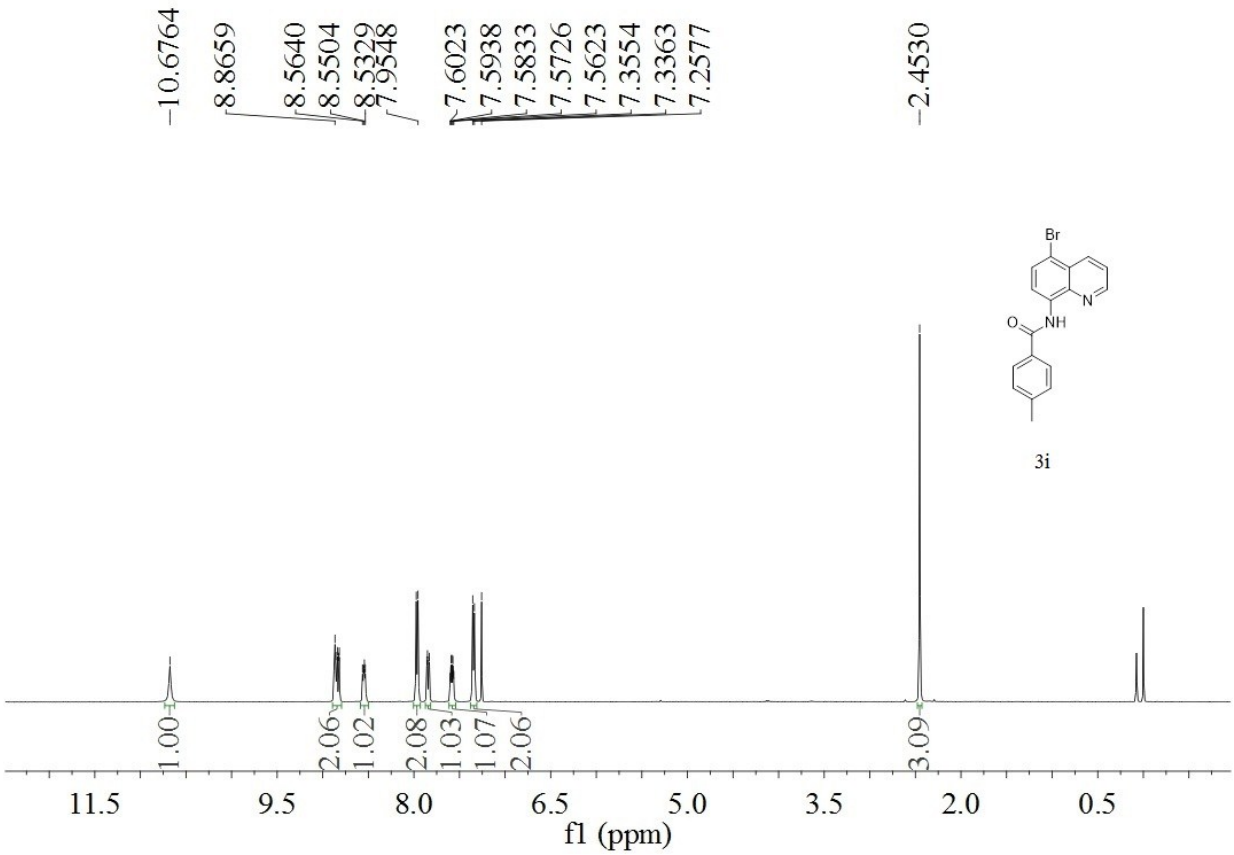
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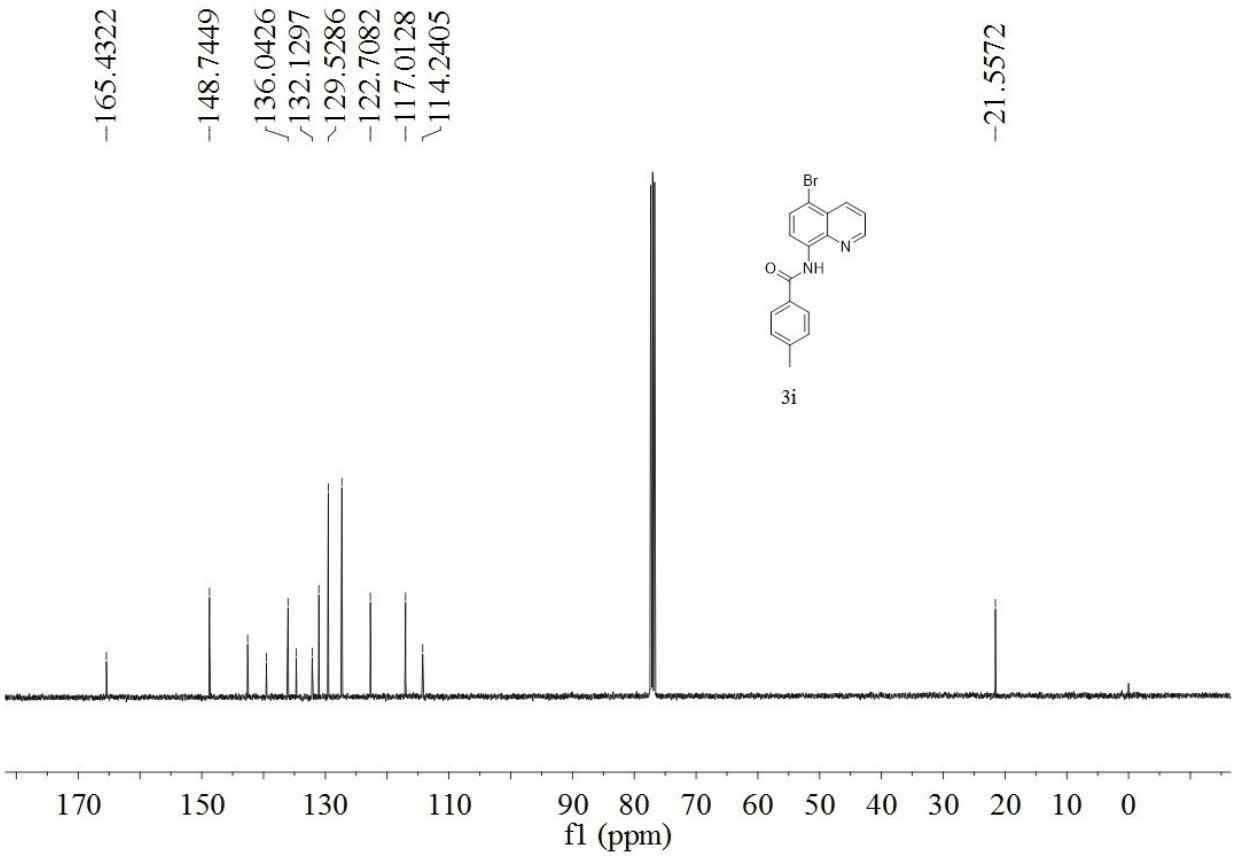
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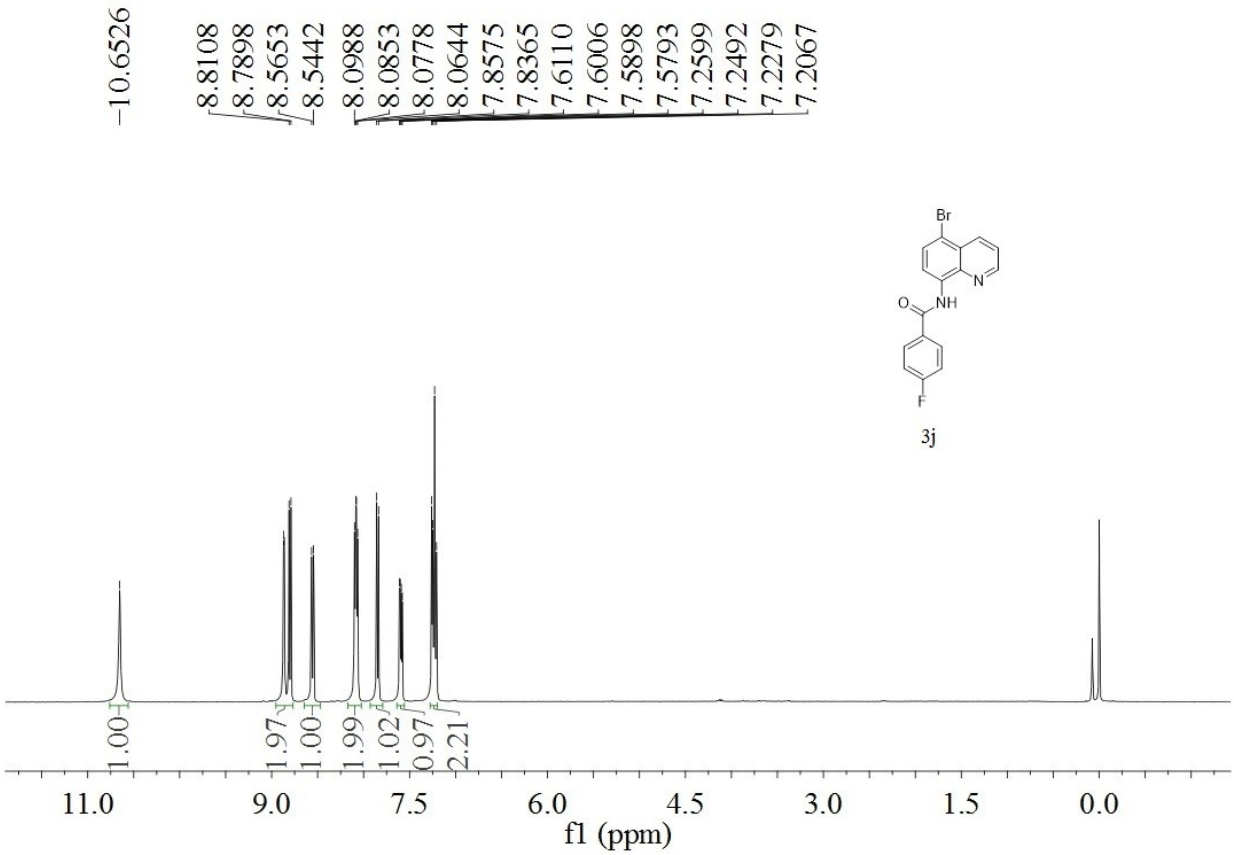
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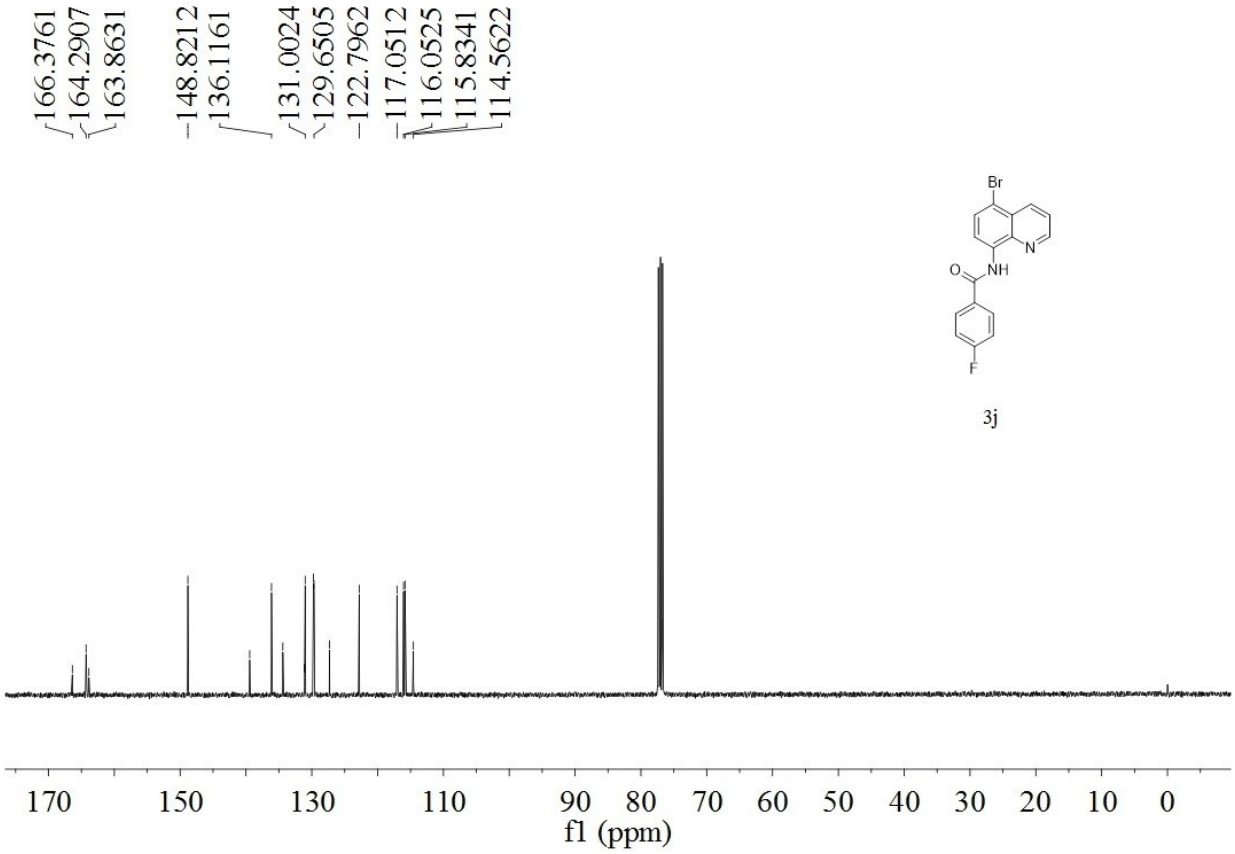
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136.1161
131.0024
129.6505
122.7962
117.0512
116.0525
115.8341
114.5622
Br
N
NH
O
F
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130
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90
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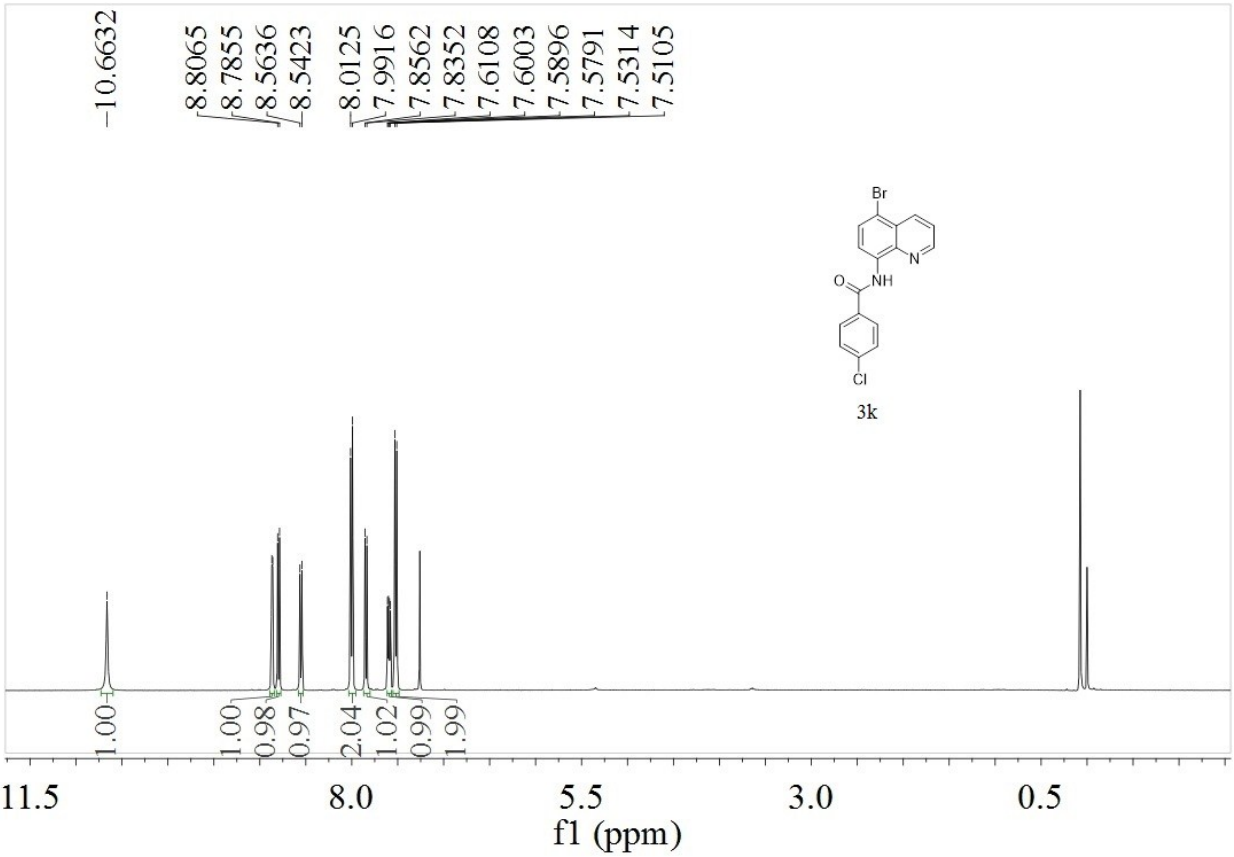
50
40
30
20
10
0
f1 (ppm)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8.7855
8.5636
8.5423
8.0125
7.9916
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7.6108
7.6003
7.5896
7.5791
7.5314
7.5105
Br
N
NH
O
Cl
3k
1.00
1.00
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1.02
0.99
1.99
11.5
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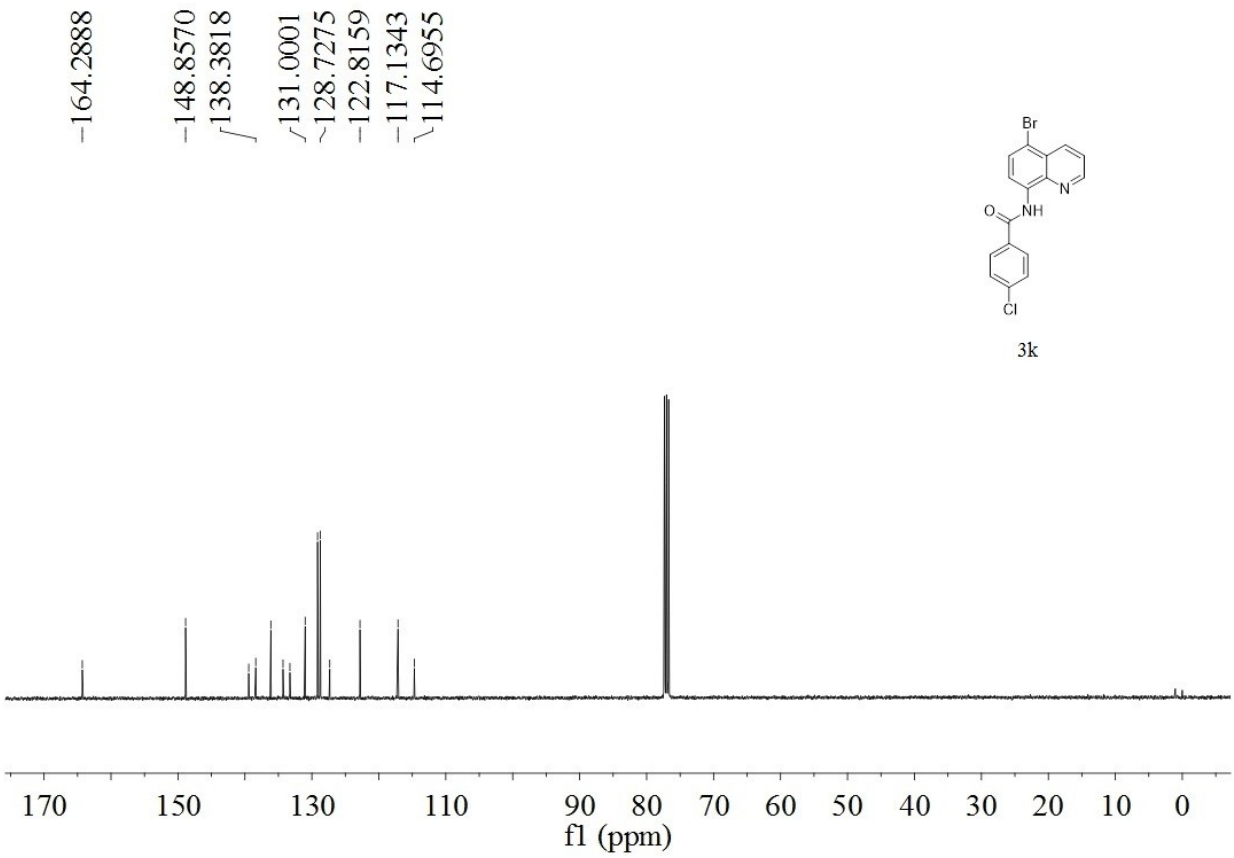
5.5
3.0
0.5
f1 (ppm)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117.1343
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Br
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150
130
110
90
80
70
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50
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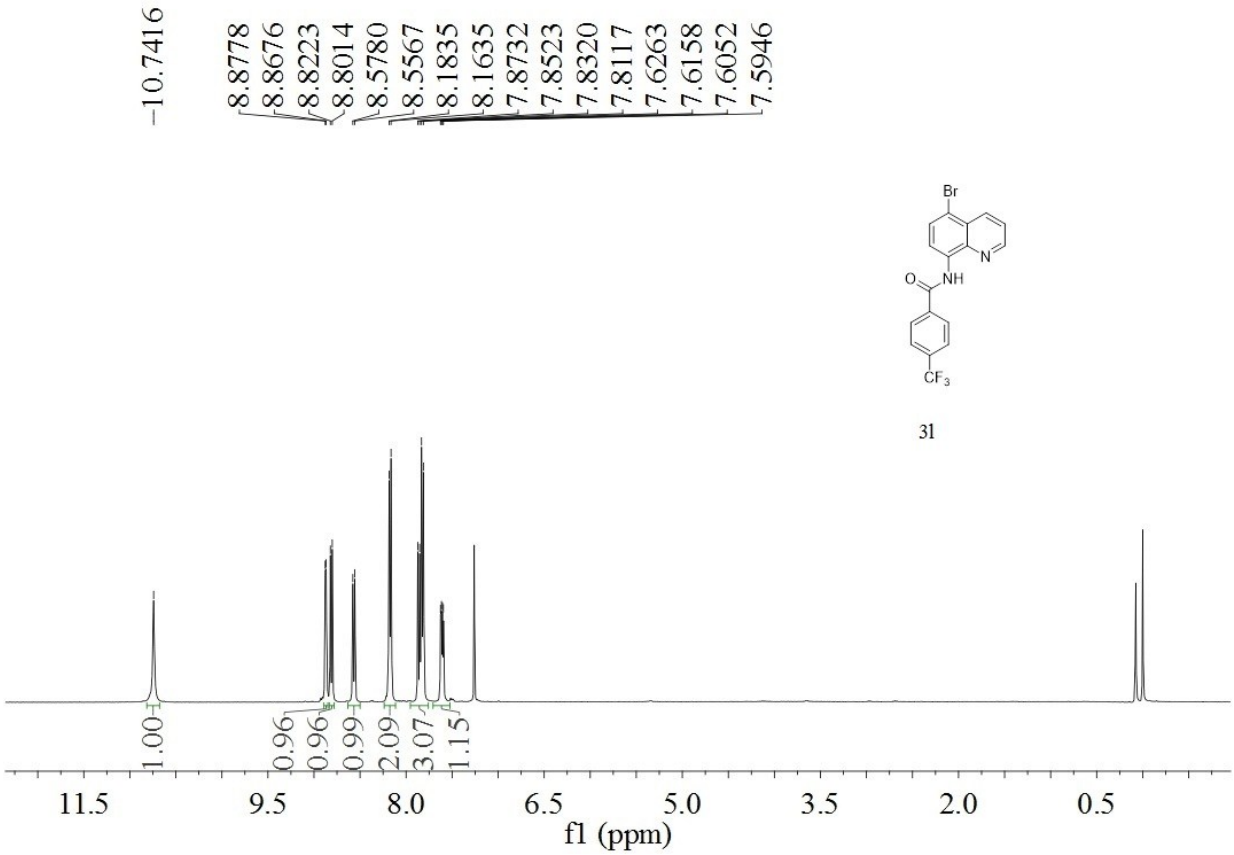
f1 (ppm)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8.5567
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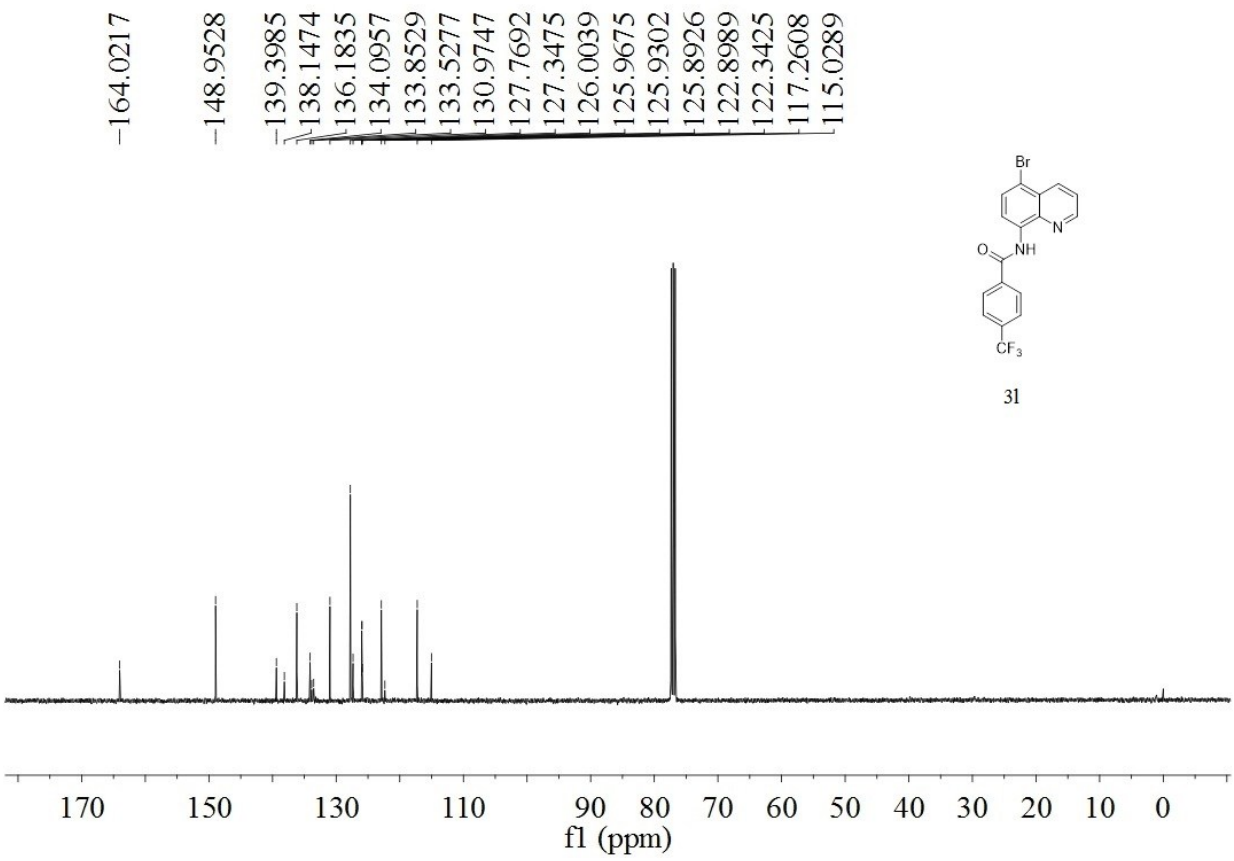
7.8523
7.8320
7.8117
7.6263
7.6158
7.6052
7.5946
Br
N
O
NH
CF3
31
1.00
0.96
0.96
0.99
2.09
3.07
1.15
11.5
9.5
8.0
6.5
5.0
3.5
2.0
0.5
f1 (ppm)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127.7692
127.3475
126.0039
125.9675
125.9302
125.8926
122.8989
122.3425
117.2608
115.0289
Br
N
O
NH
CF3
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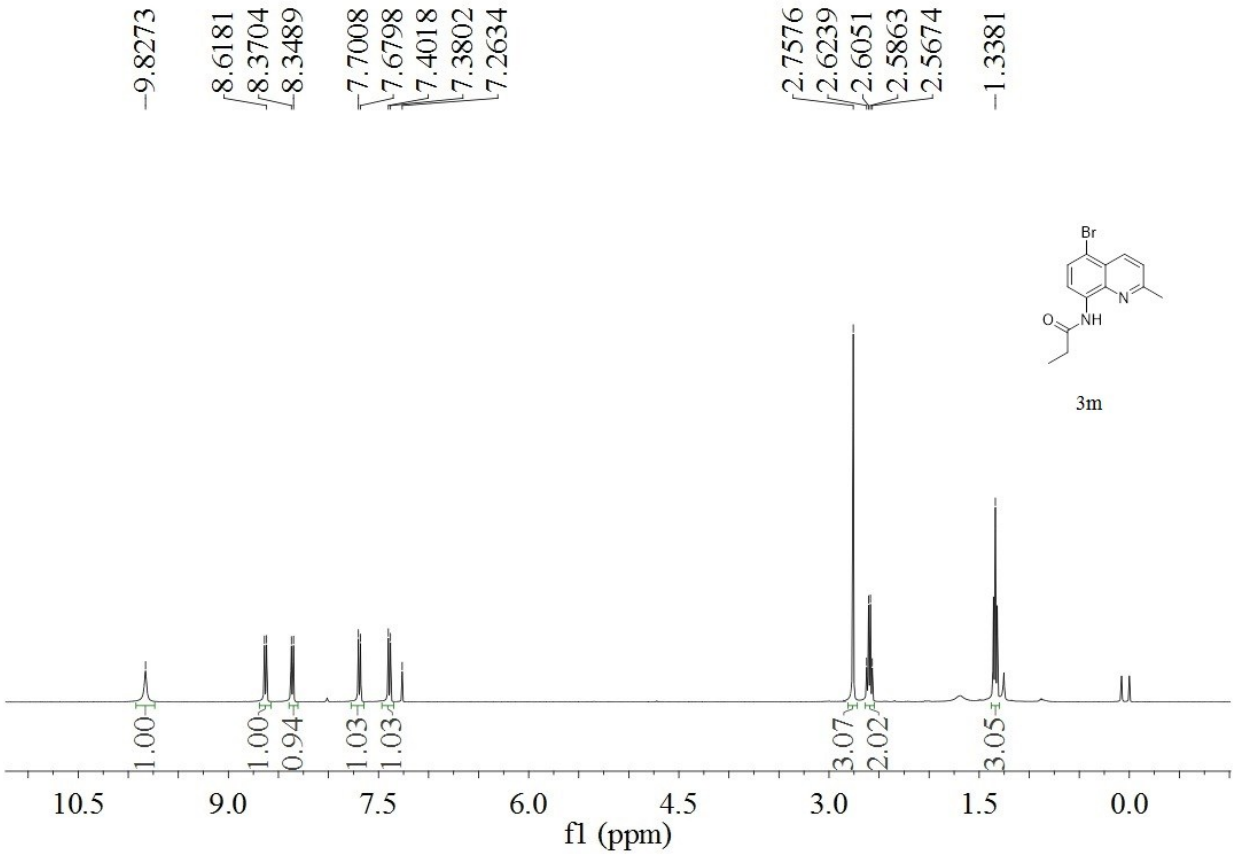
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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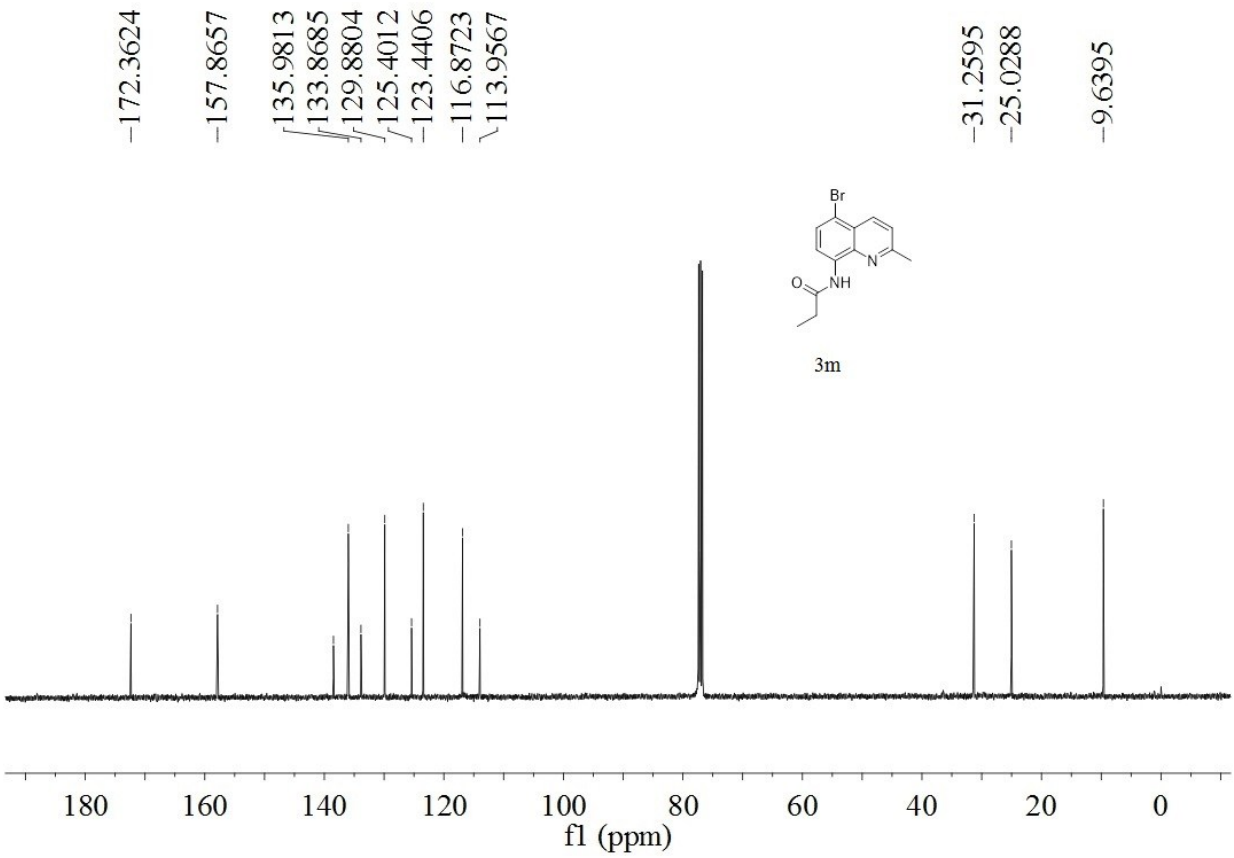
7.7008
7.6798
7.4018
7.3802
7.2634
2.7576
2.6239
2.6051
2.5863
2.5674
1.3381
Br
N
O
NH
3m
1.00
1.00
0.94
1.03
1.03
3.07
2.02
3.05
10.5
9.0
7.5
6.0
4.5
3.0
1.5
0.0
f1 (ppm)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129.8804
125.4012
123.4406
116.8723
113.9567
31.2595
25.0288
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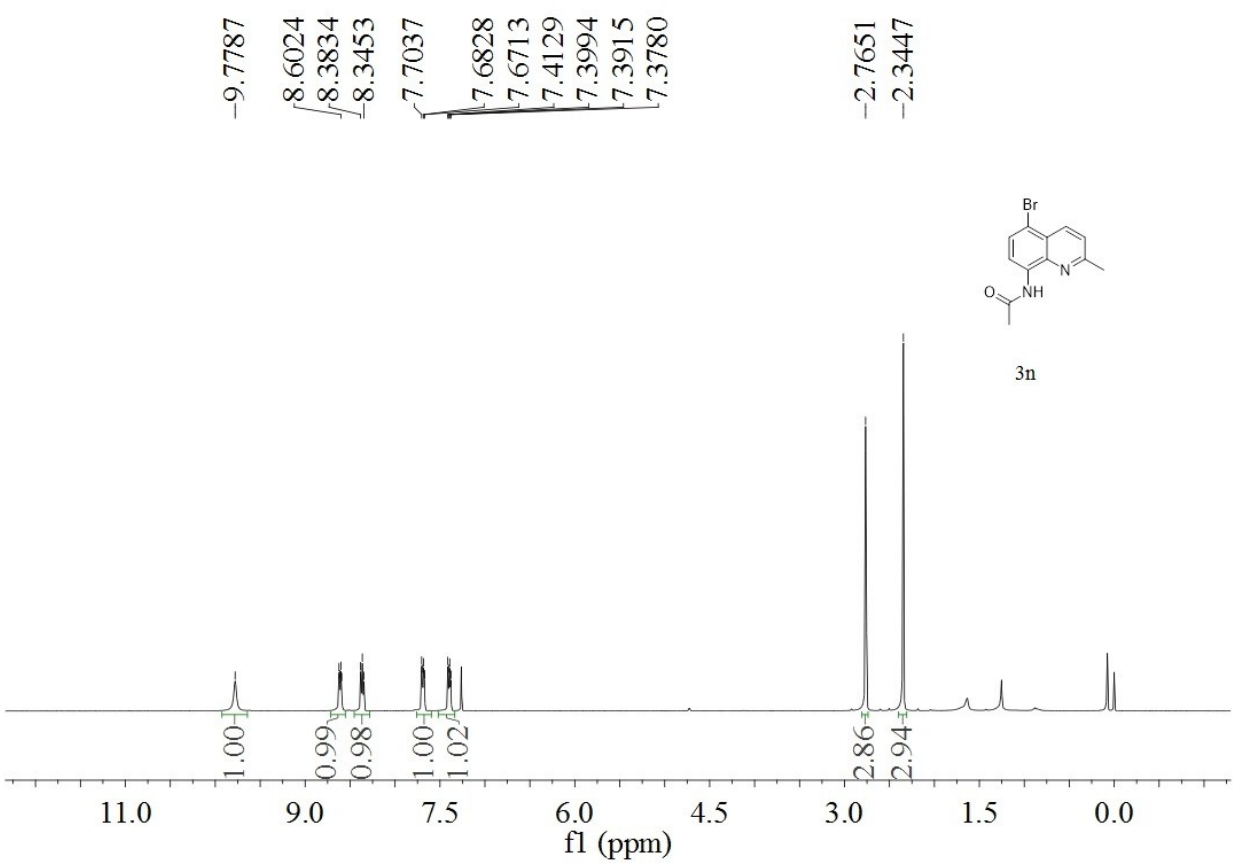
O
NH
3m
180
160
140
120
100
80
60
40
20
0
f1 (ppm)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8.3834
8.3453
7.7037
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7.6713
7.4129
7.3994
7.3915
7.3780
2.7651
2.3447
Br
N
O
NH
3n
1.00
0.99
0.98
1.00
1.02
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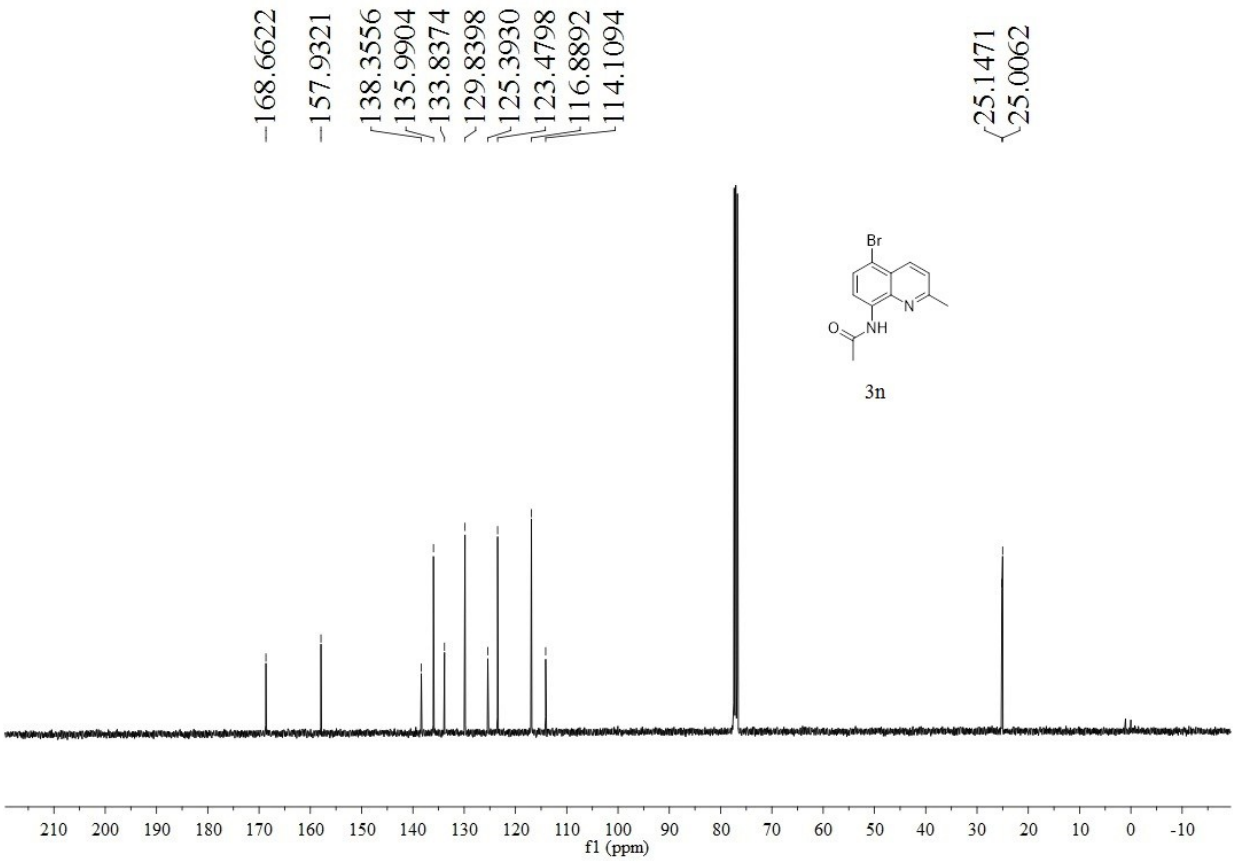
11.0
9.0
7.5
6.0
4.5
3.0
1.5
0.0
f1 (ppm)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138.3556
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133.8374
129.8398
125.3930
123.4798
116.8892
114.1094
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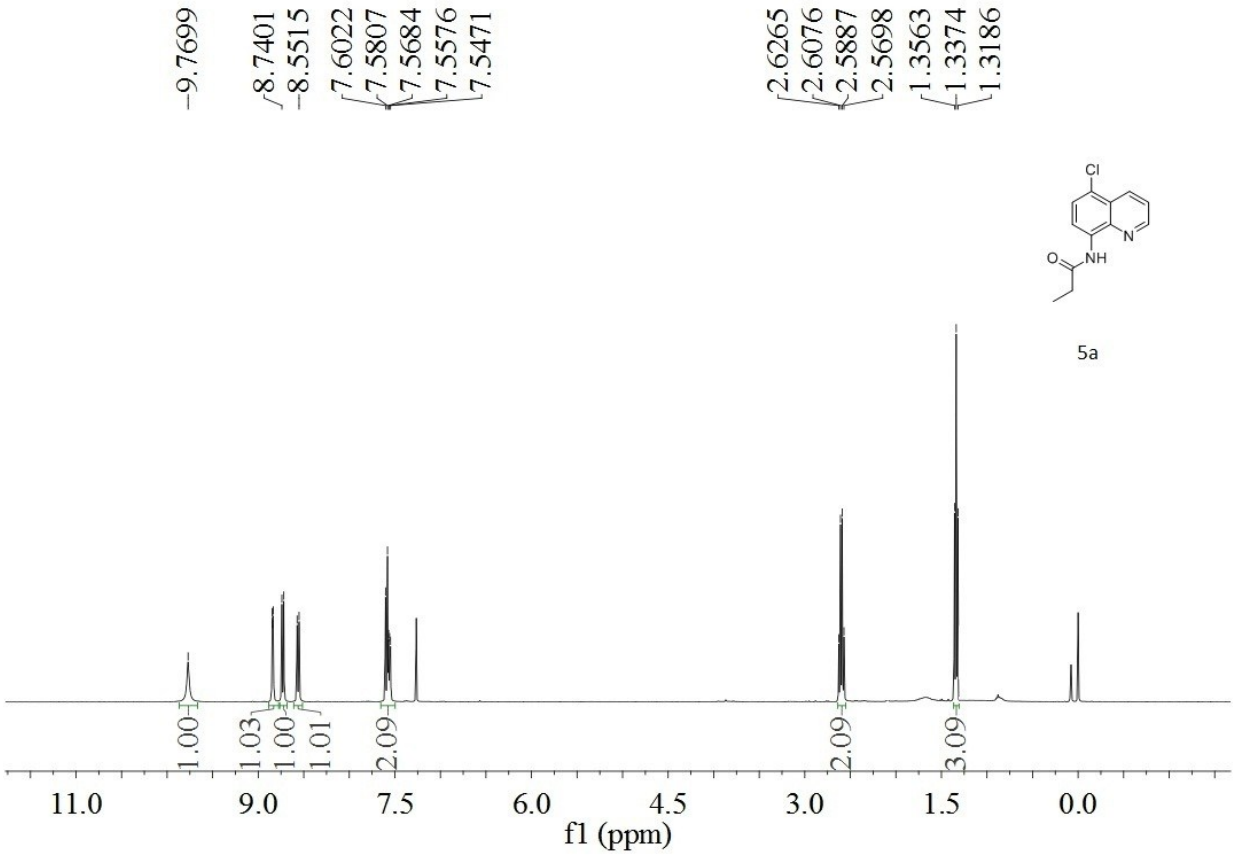
25.0062
Br
N
O
NH
3n
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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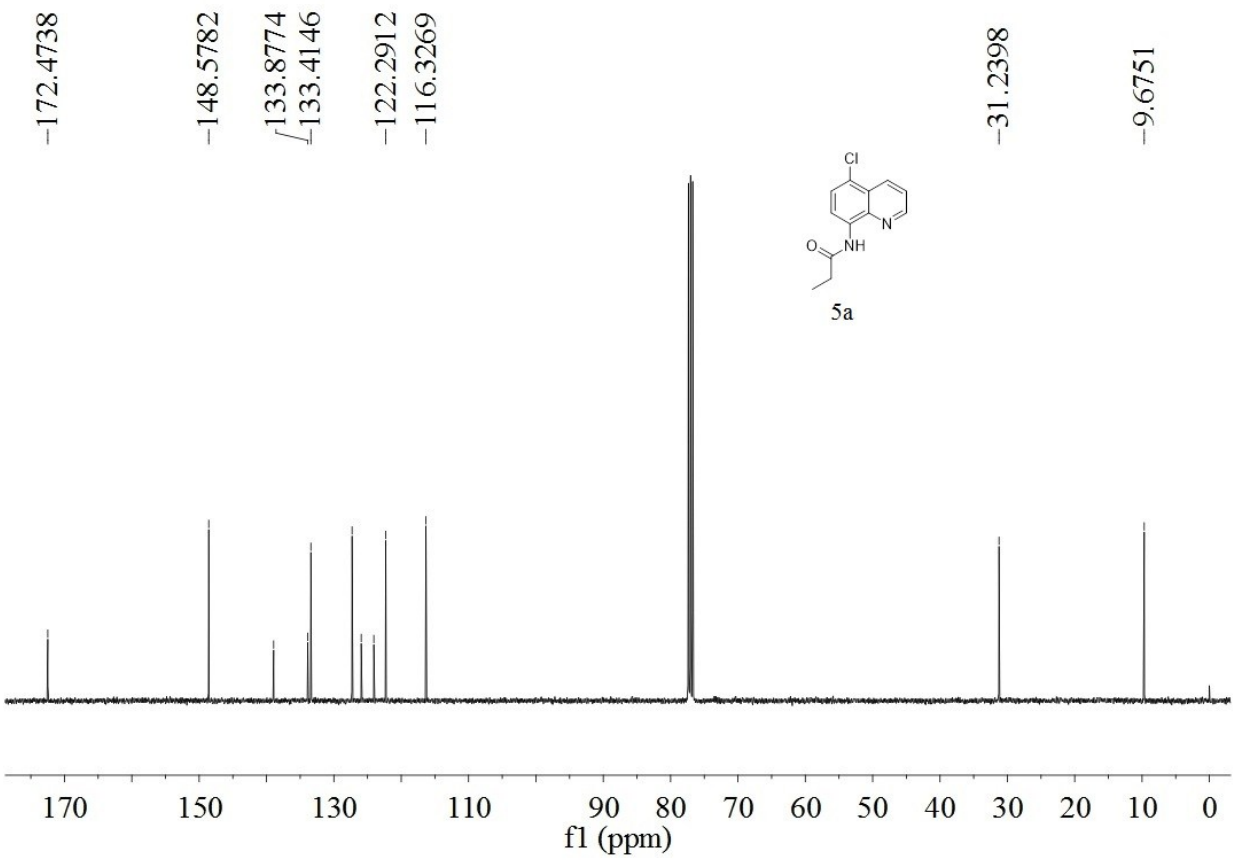
8.5515
7.6022
7.5807
7.5684
7.5576
7.5471
2.6265
2.6076
2.5887
2.5698
1.3563
1.3374
1.3186
Cl
N
O
NH
5a
1.00
1.03
1.00
1.01
2.09
2.09
3.09
11.0
9.0
7.5
6.0
4.5
3.0
1.5
0.0
f1 (ppm)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148.5782
133.8774
133.4146
122.2912
116.3269
31.2398
9.6751
Cl
N
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NH
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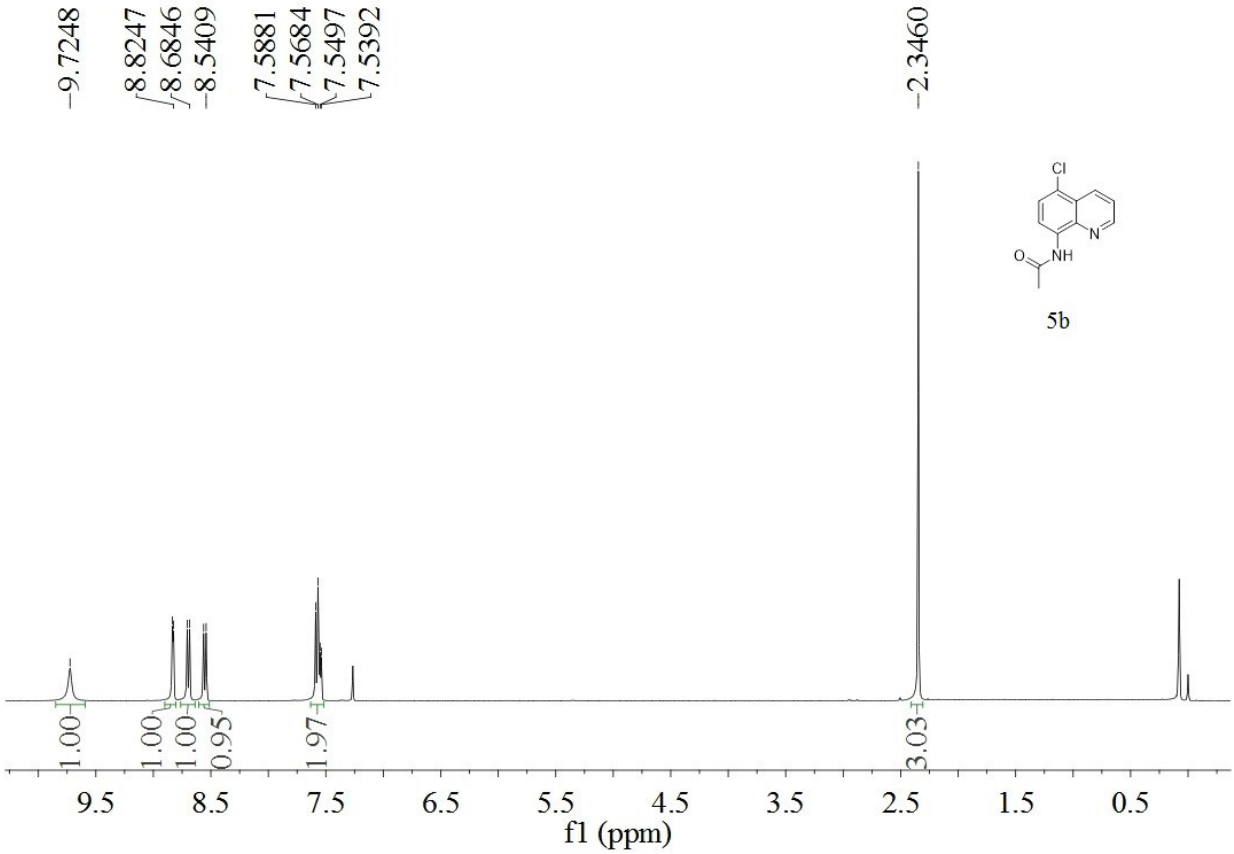
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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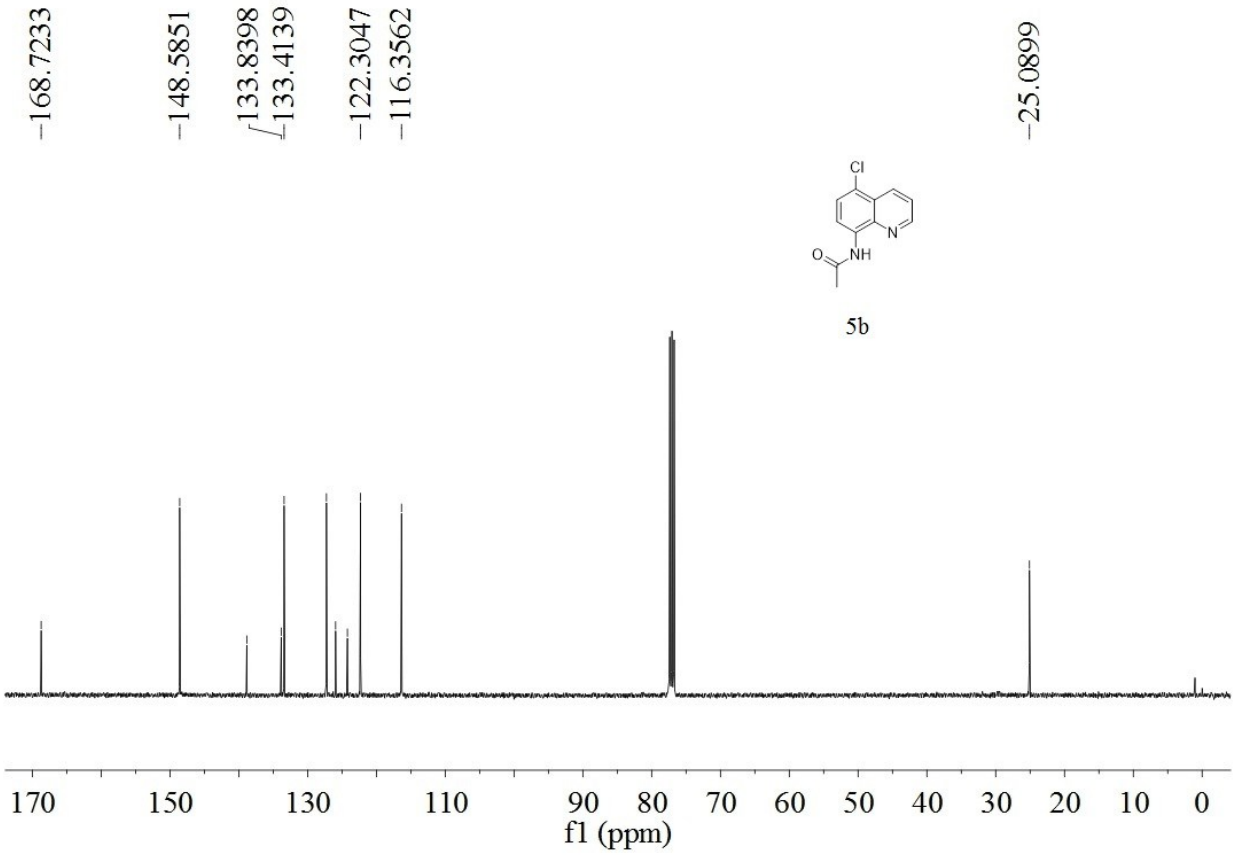
8.6846
8.5409
7.5881
7.5684
7.5497
7.5392
2.3460
Cl
N
NH
O
5b
1.00
1.00
1.00
0.95
1.97
3.03
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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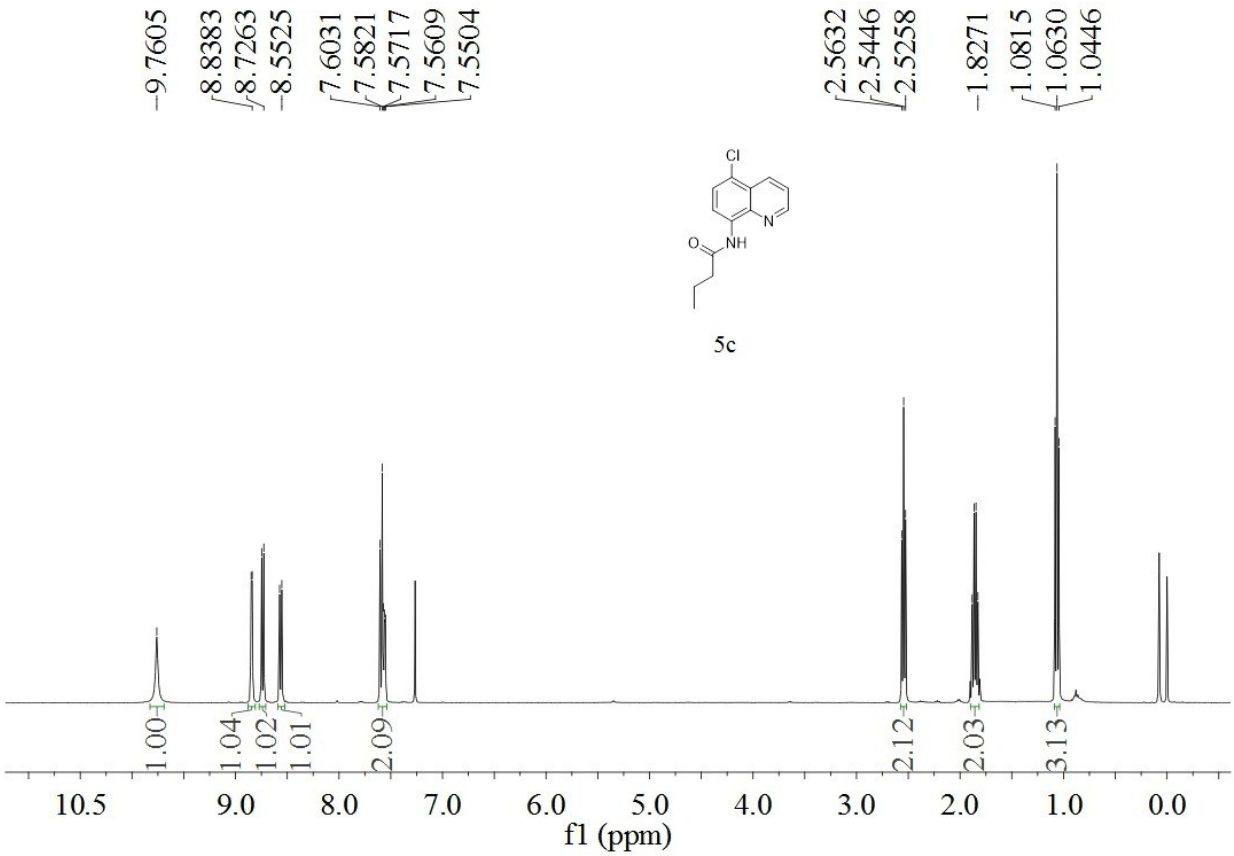
148.5851
133.8398
133.4139
122.3047
116.3562
25.0899
Cl
N
NH
O
5b
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.7263
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7.6031
7.5821
7.5717
7.5609
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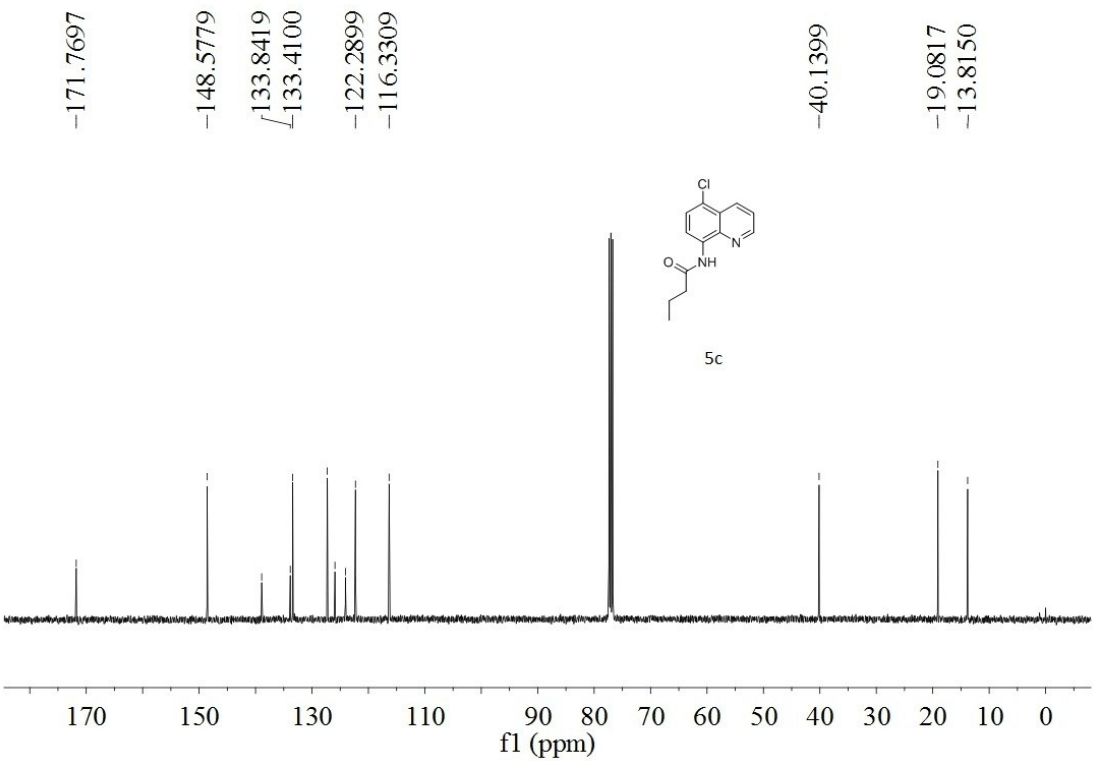
2.5632
2.5446
2.5258
1.8271
1.0815
1.0630
1.0446
Cl
N
O
NH
5c
1.00
1.04
1.02
1.01
2.09
2.12
2.03
3.13
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)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133.4100
122.2899
116.3309
40.1399
19.0817
13.8150
Cl
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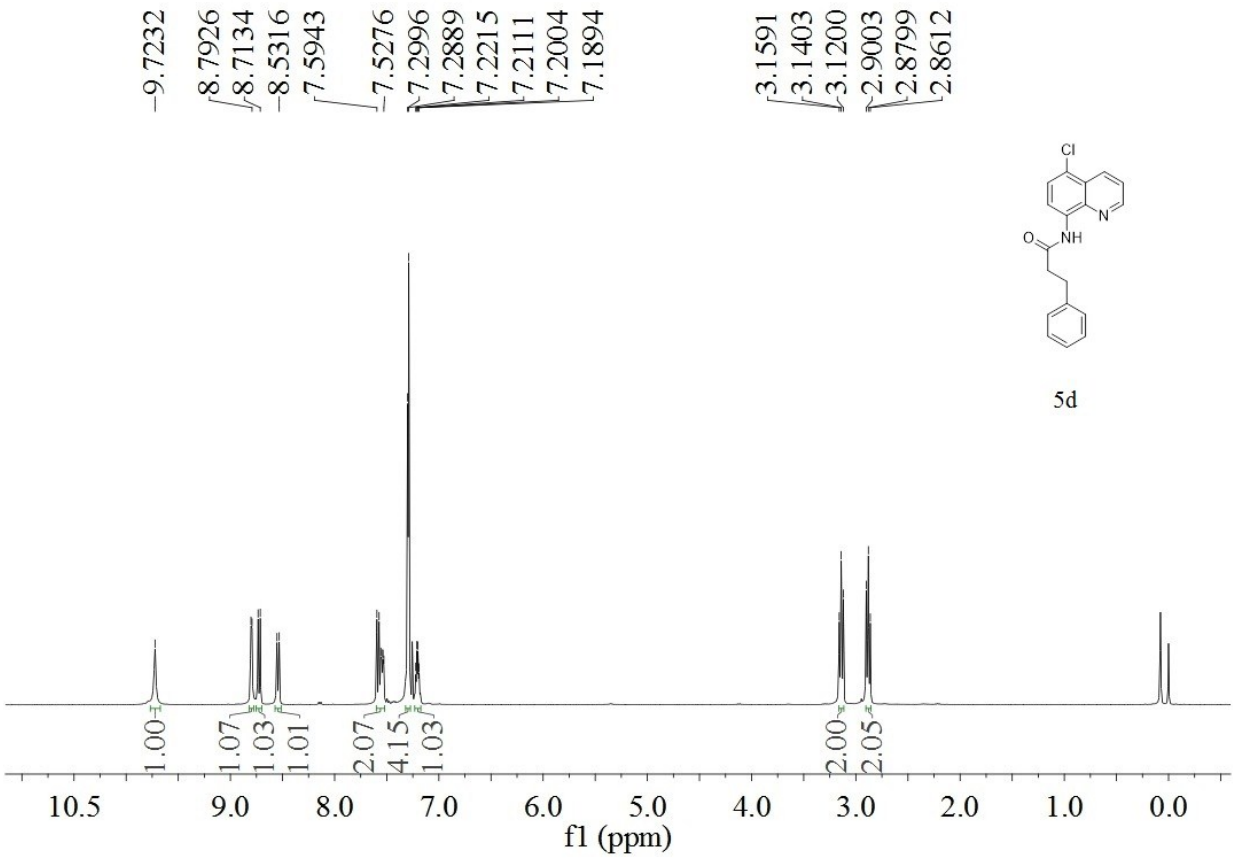
NH
5c
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.5316
7.5943
7.5276
7.2996
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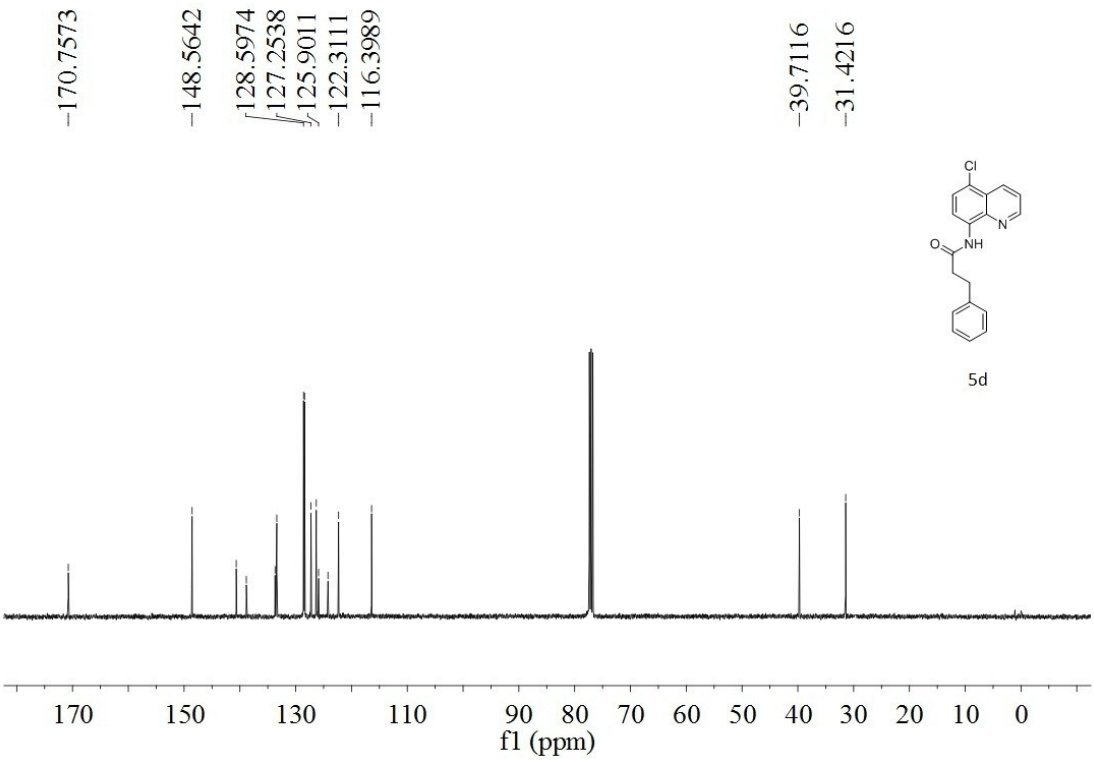
7.2215
7.2111
7.2004
7.1894
3.1591
3.1403
3.1200
2.9003
2.8799
2.8612
Cl
N
O
NH
5d
1.00
1.07
1.03
1.01
2.07
4.15
1.03
2.00
2.05
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)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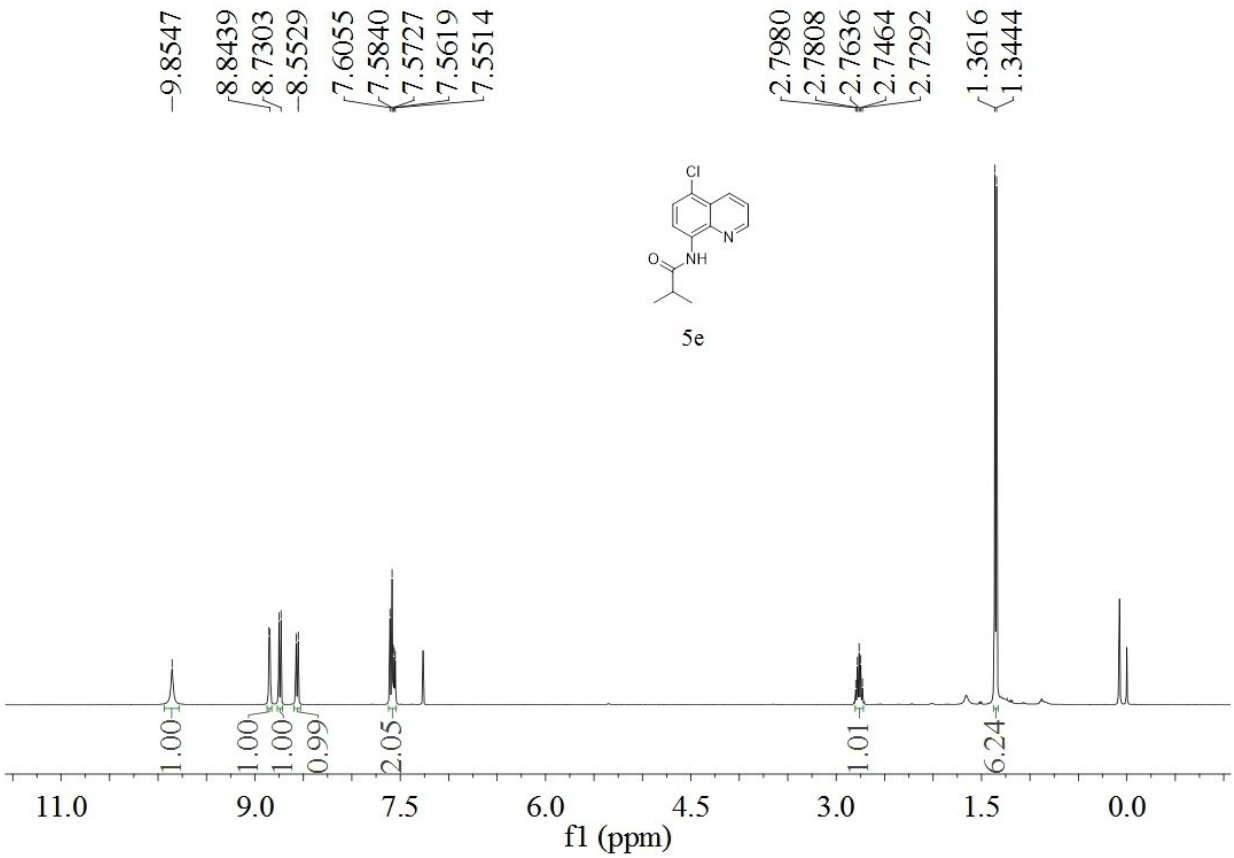
128.5974
127.2538
125.9011
122.3111
116.3989
39.7116
31.4216
Cl
N
O
NH
5d
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.5727
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7.5514
2.7980
2.7808
2.7636
2.7464
2.7292
1.3616
1.3444
Cl
N
O
NH
5e
1.00
1.00
1.00
0.99
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1.01
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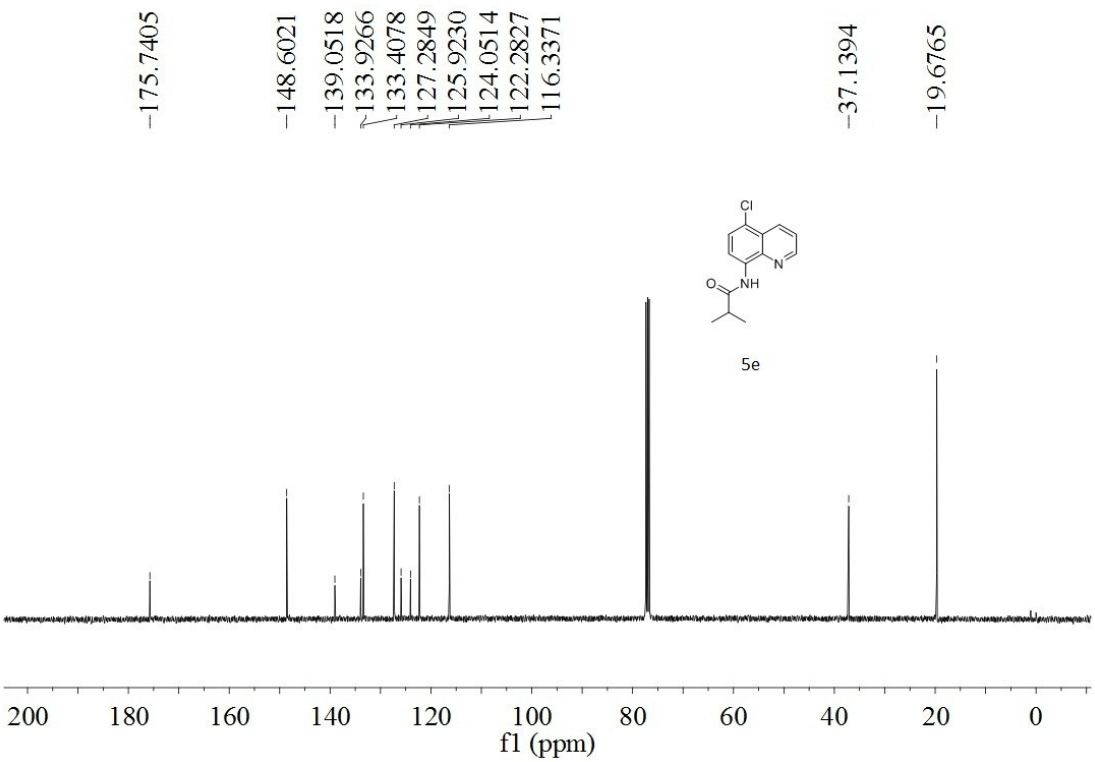
11.0
9.0
7.5
6.0
4.5
3.0
1.5
0.0
f1 (ppm)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125.9230
124.0514
122.2827
116.3371
37.1394
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O
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5e
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180
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140
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100
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20
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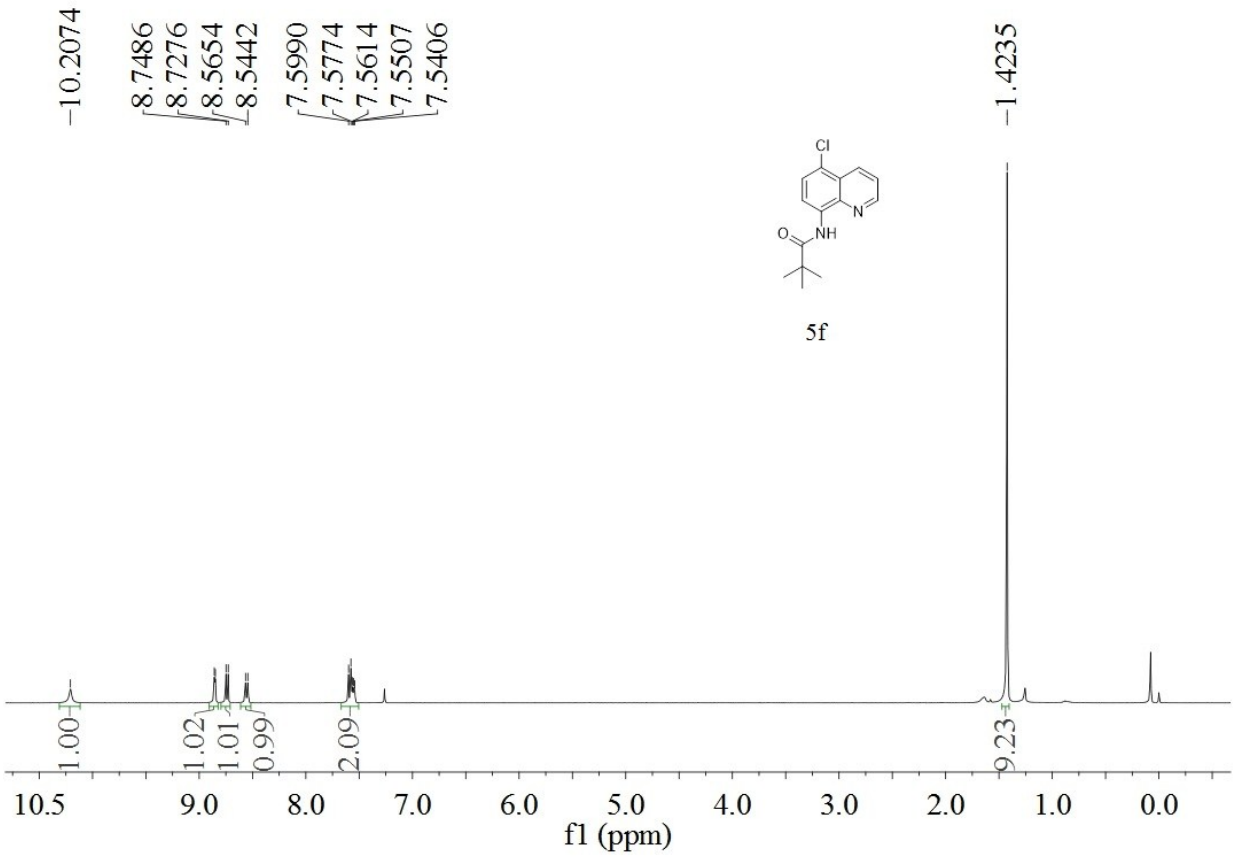
f1 (ppm)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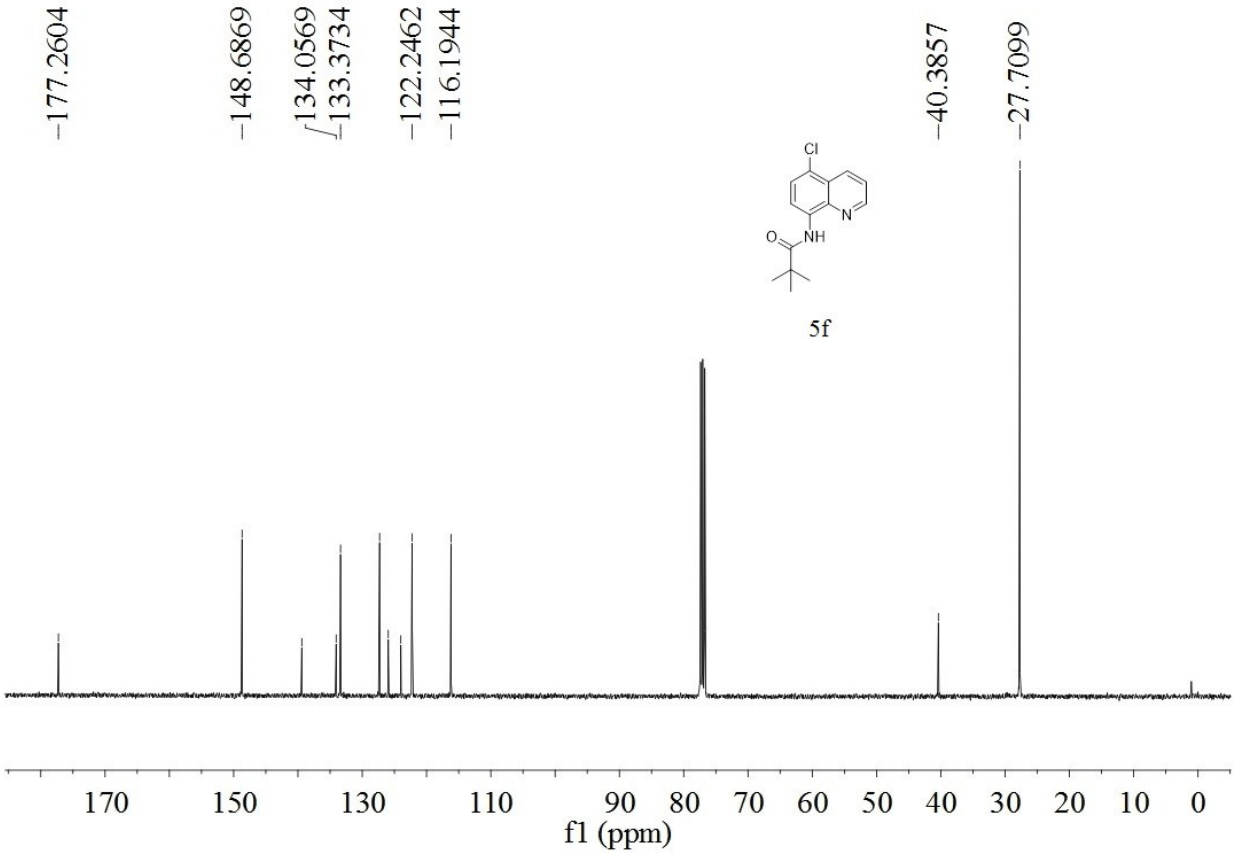
7.5774
7.5614
7.5507
7.5406
1.4235
Cl
N
NH
O
5f
1.00
1.02
1.01
0.99
2.09
9.23
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)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40.3857
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Cl
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150
130
110
90
80
70
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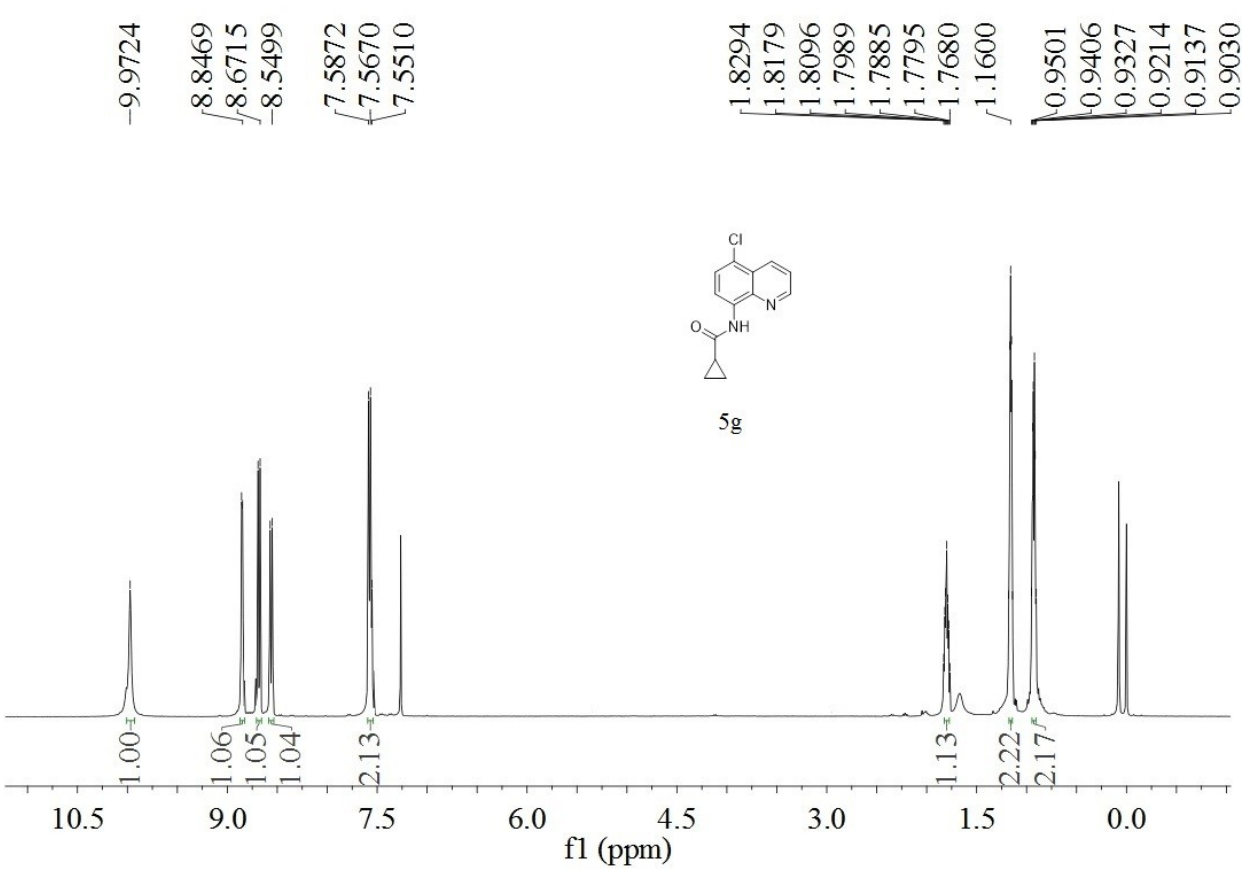
50
40
30
20
10
0
f1 (ppm)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1.7989
1.7885
1.7795
1.7680
1.1600
0.9501
0.9406
0.9327
0.9214
0.9137
0.9030
Cl
N
O
NH
5g
1.00
1.06
1.05
1.04
2.13
1.13
2.22
2.17
10.5
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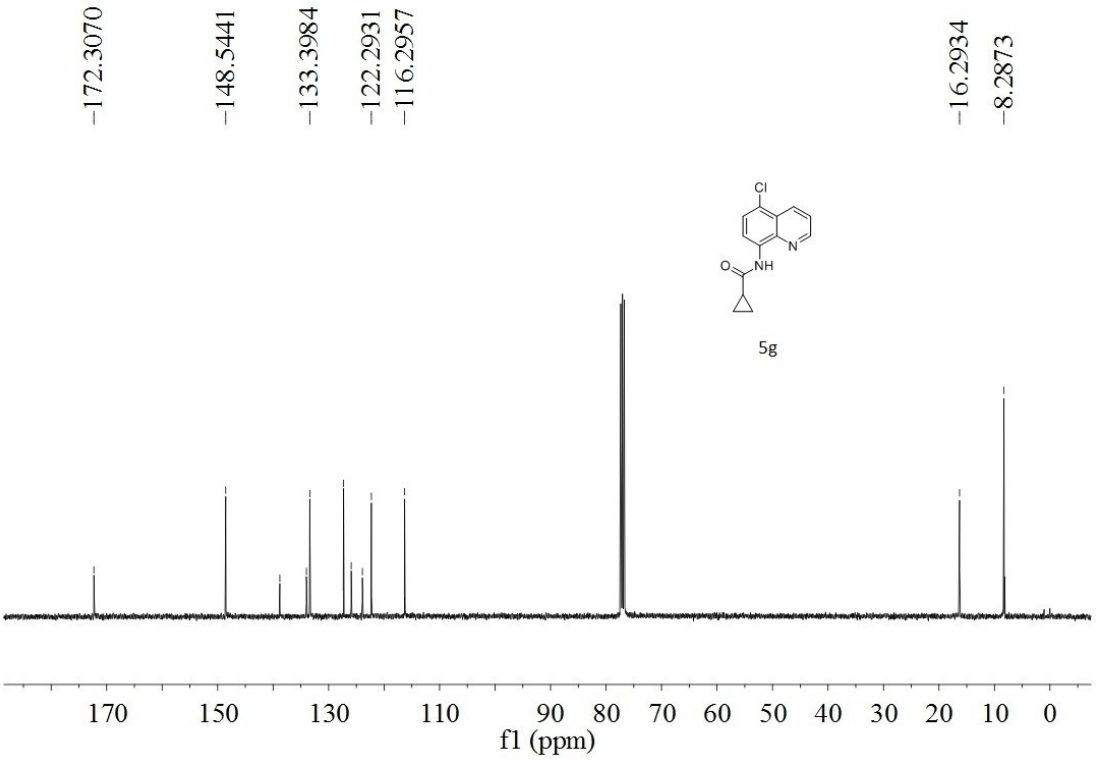
6.0
4.5
3.0
1.5
0.0
f1 (ppm)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122.2931
116.2957
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8.2873
Cl
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NH
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170
150
130
110
90
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70
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50
40
30
20
10
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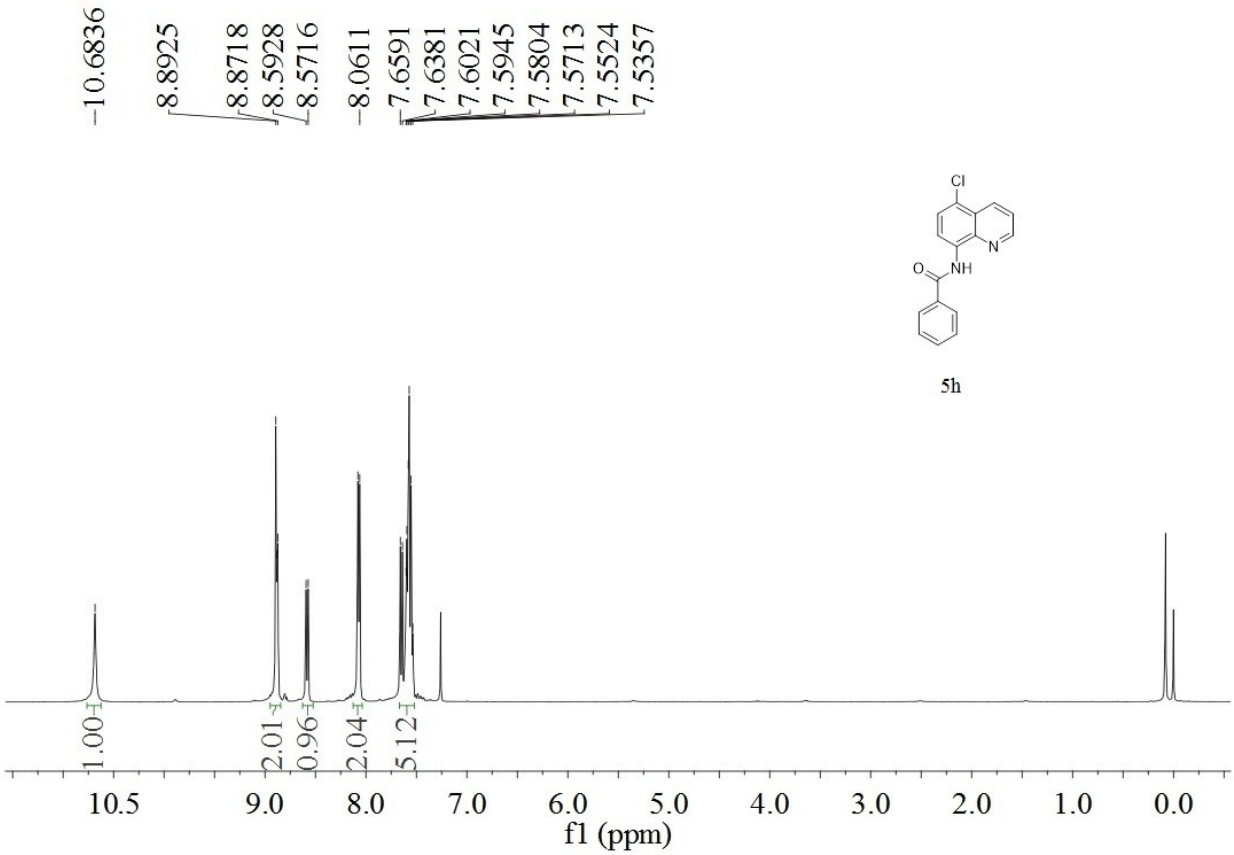
f1 (ppm)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7.5945
7.5804
7.5713
7.5524
7.5357
Cl
N
NH
O
5h
1.00
2.01
0.96
2.04
5.12
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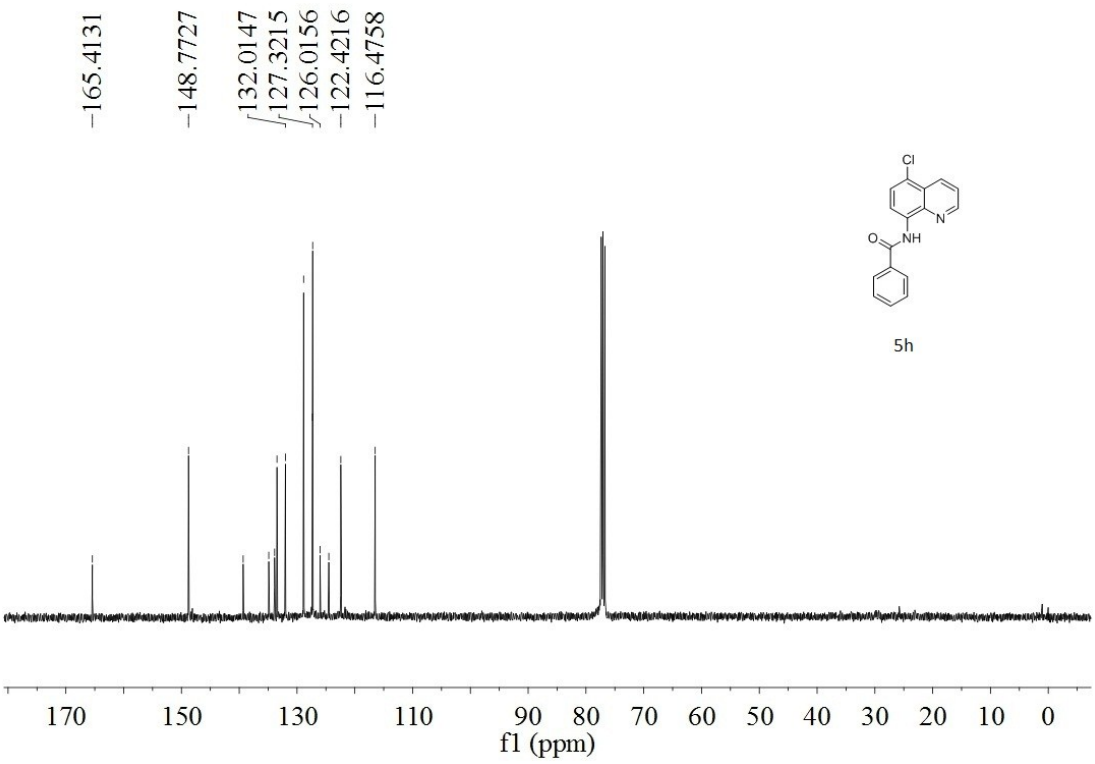
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


165.4131
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132.0147
127.3215
126.0156
122.4216
116.4758
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NH
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170
150
130
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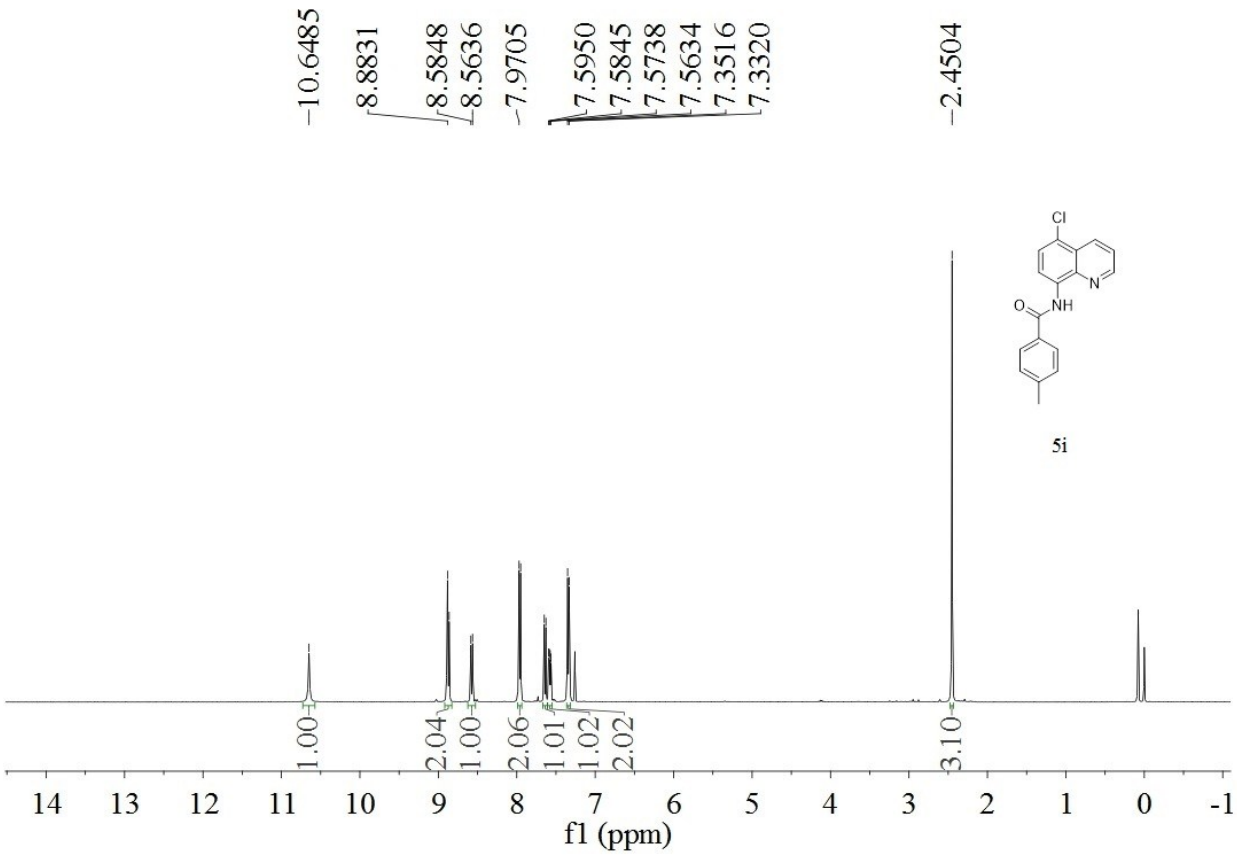
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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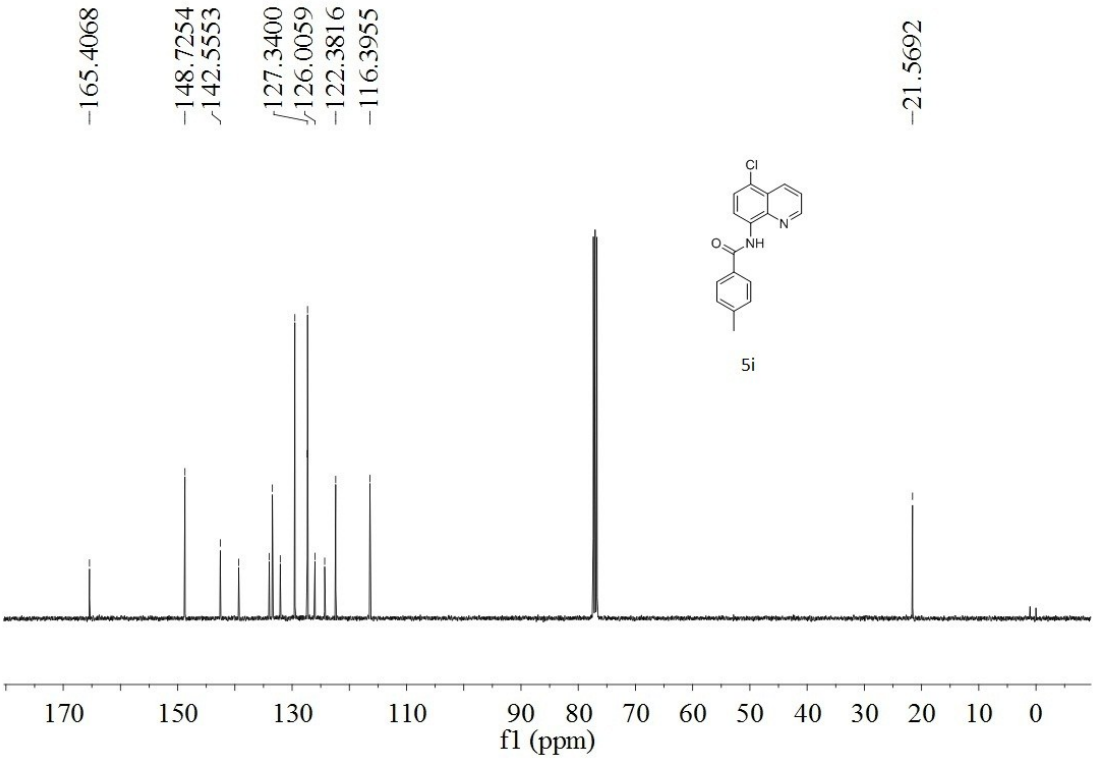
7.3320
2.4504
Cl
N
O
NH
5i
1.00
2.04
1.00
2.06
1.01
1.02
2.02
3.10
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)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142.5553
127.3400
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116.3955
21.5692
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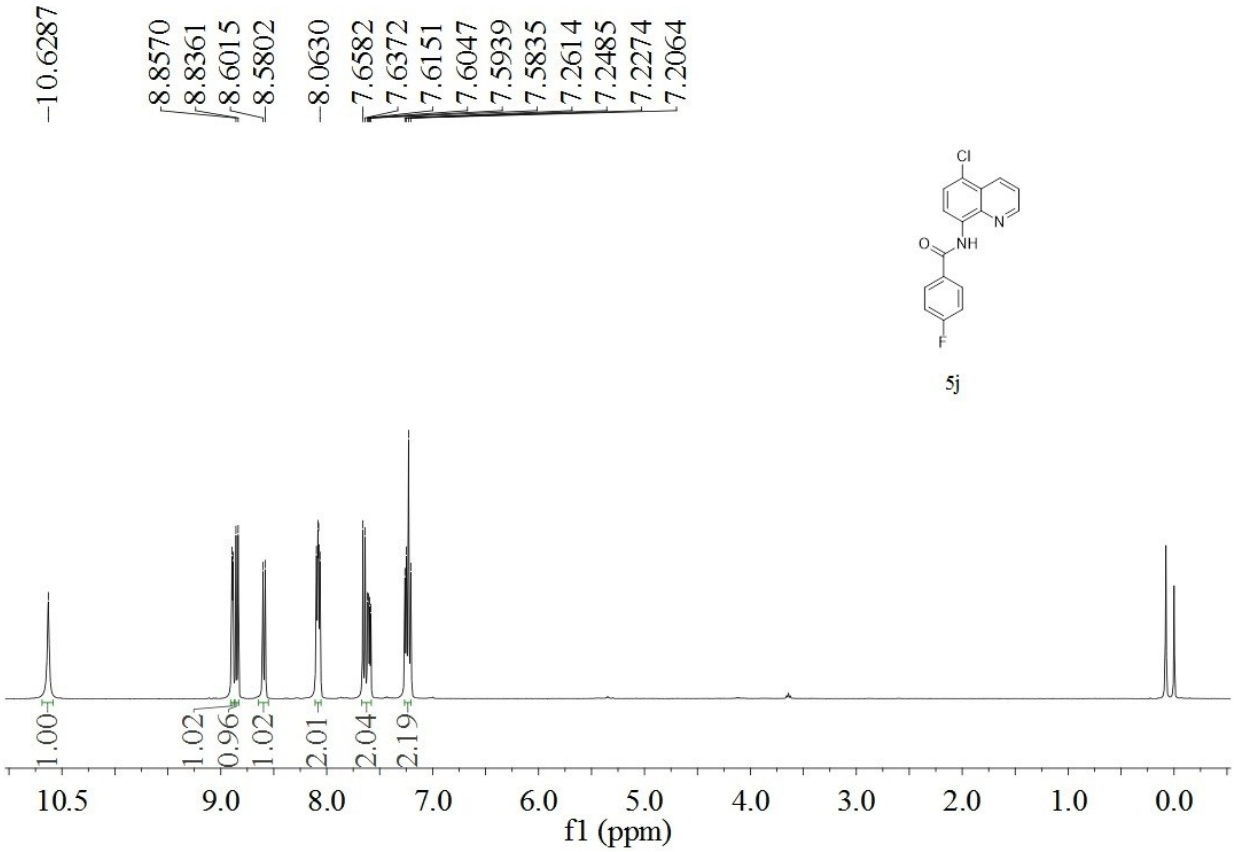
O
NH
5i
170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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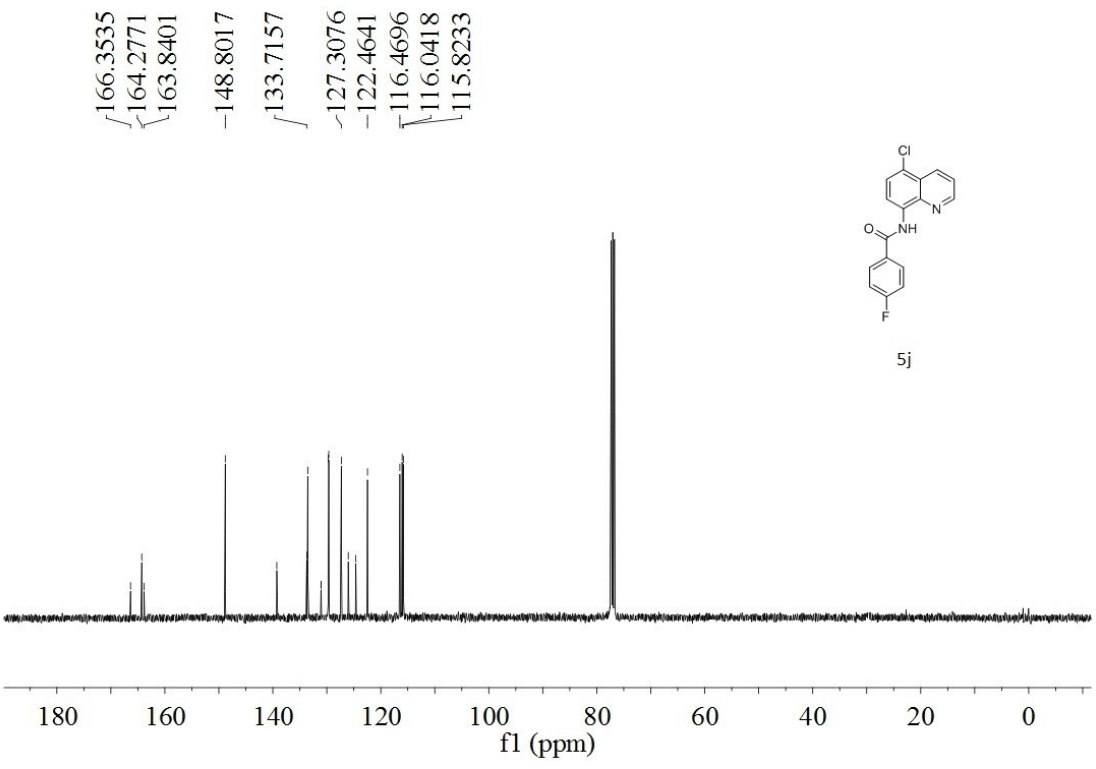
7.5939
7.5835
7.2614
7.2485
7.2274
7.2064
Cl
N
O
NH
F
5j
1.00
1.02
0.96
1.02
2.01
2.04
2.19
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)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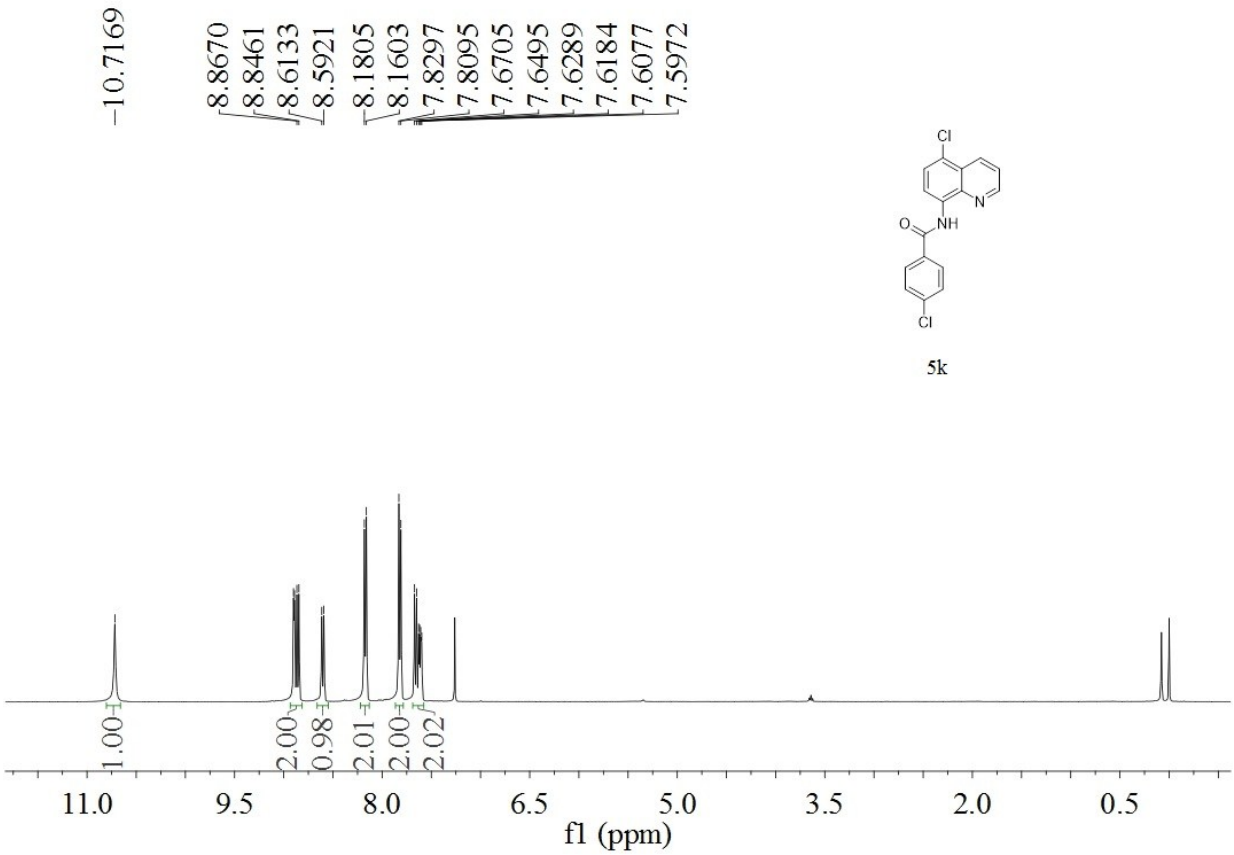
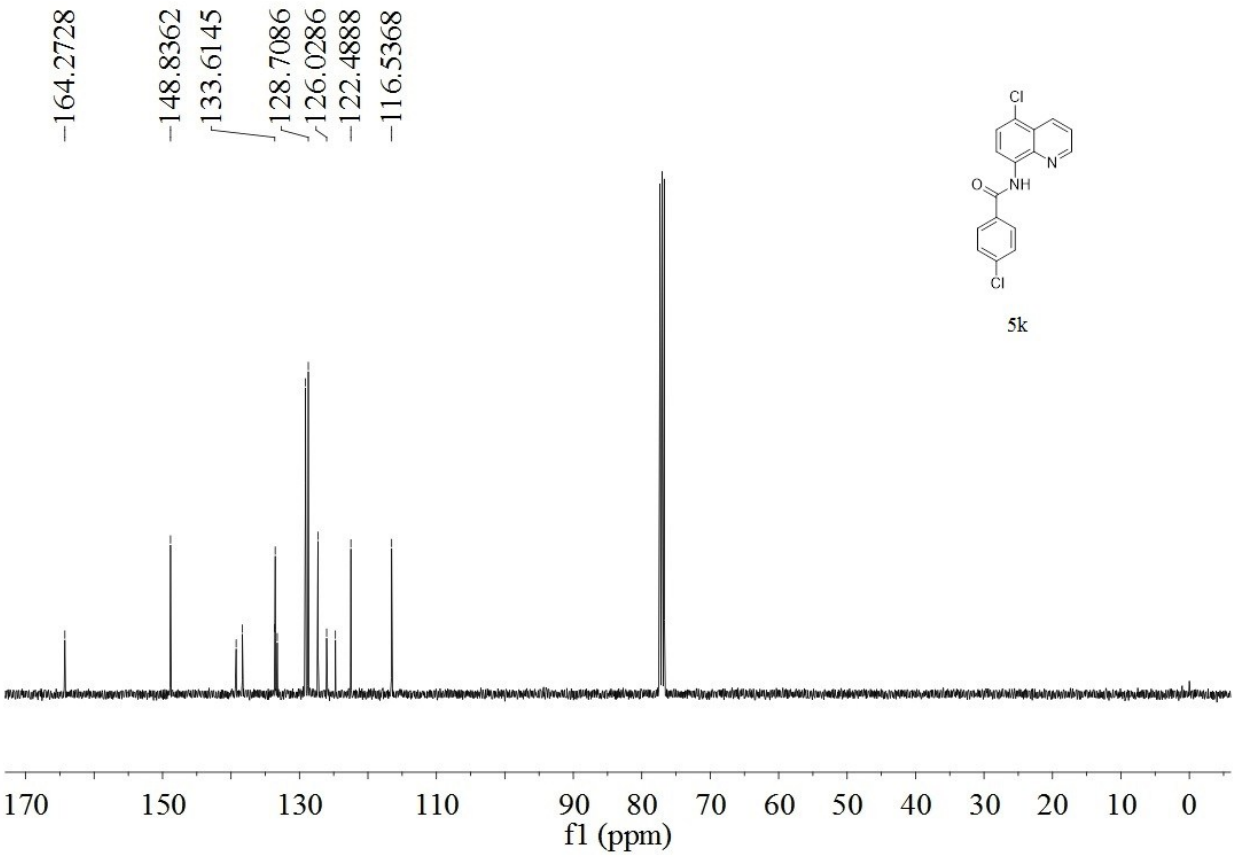
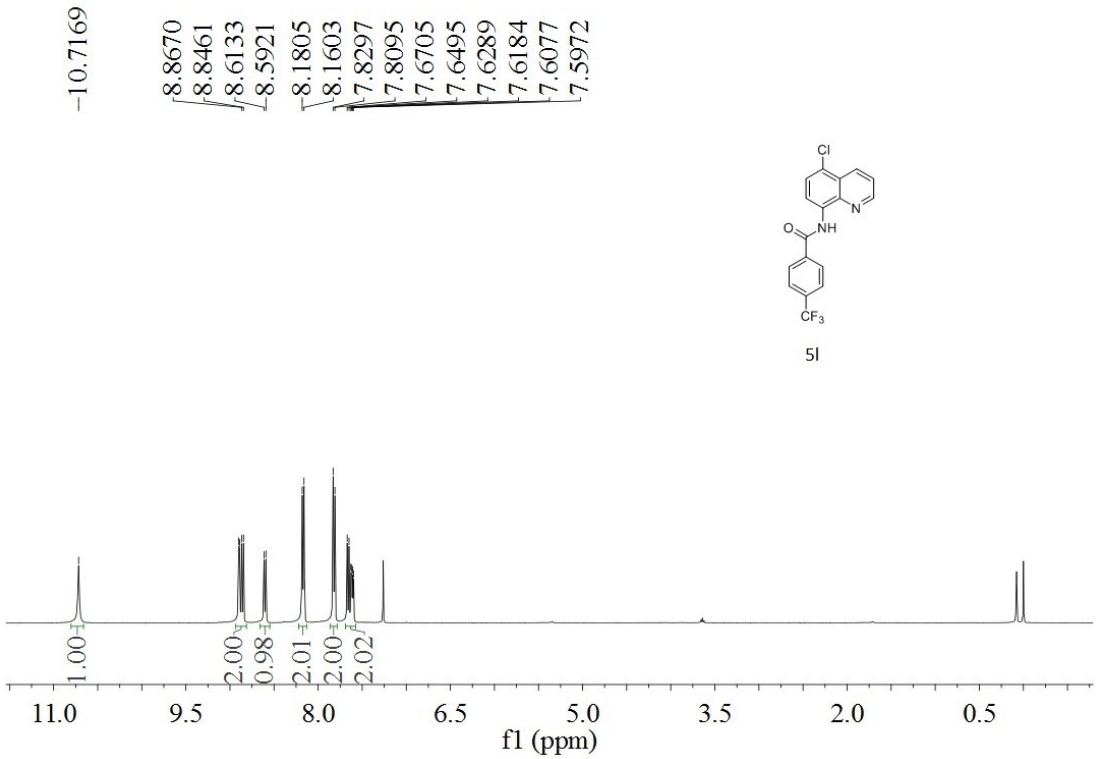
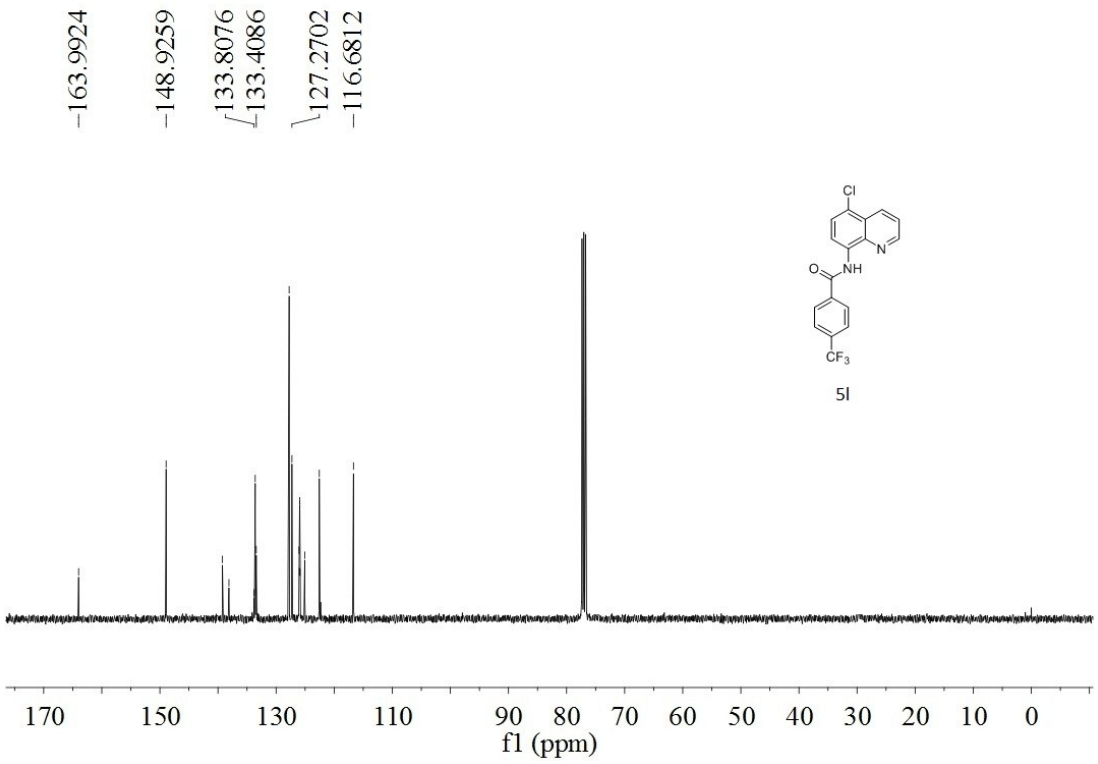
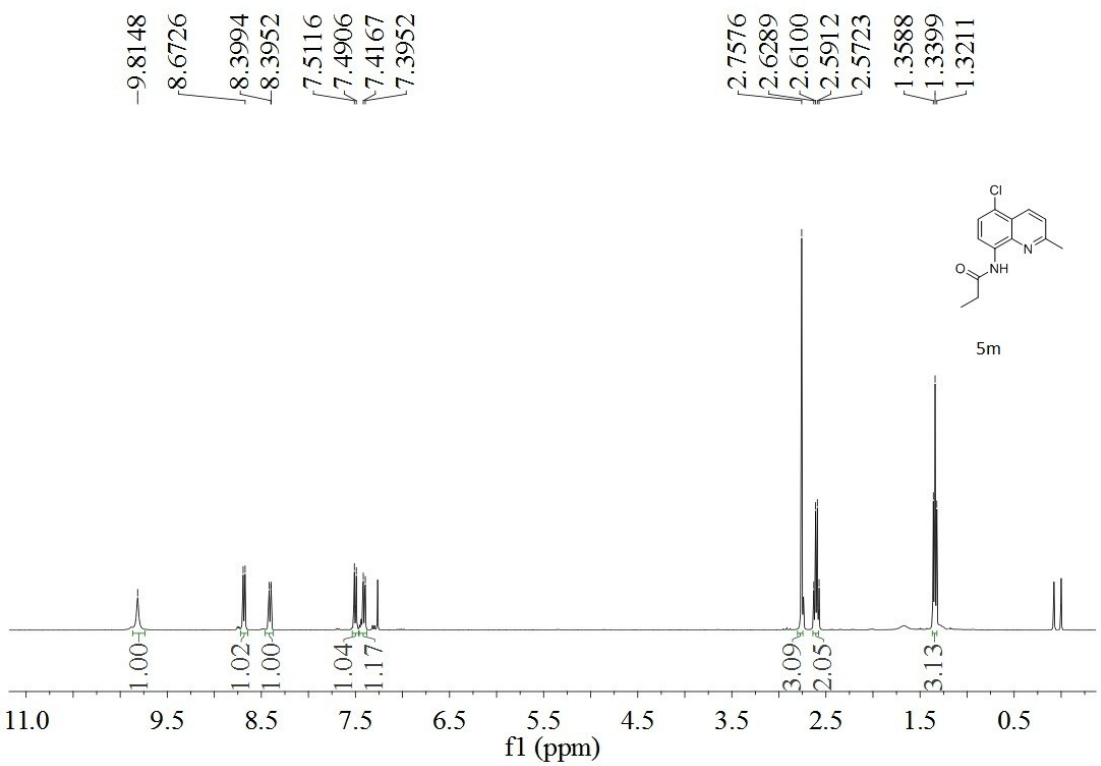
148.8017
133.7157
127.3076
122.4641
116.4696
116.0418
115.8233
Cl
N
O
NH
F
5j
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

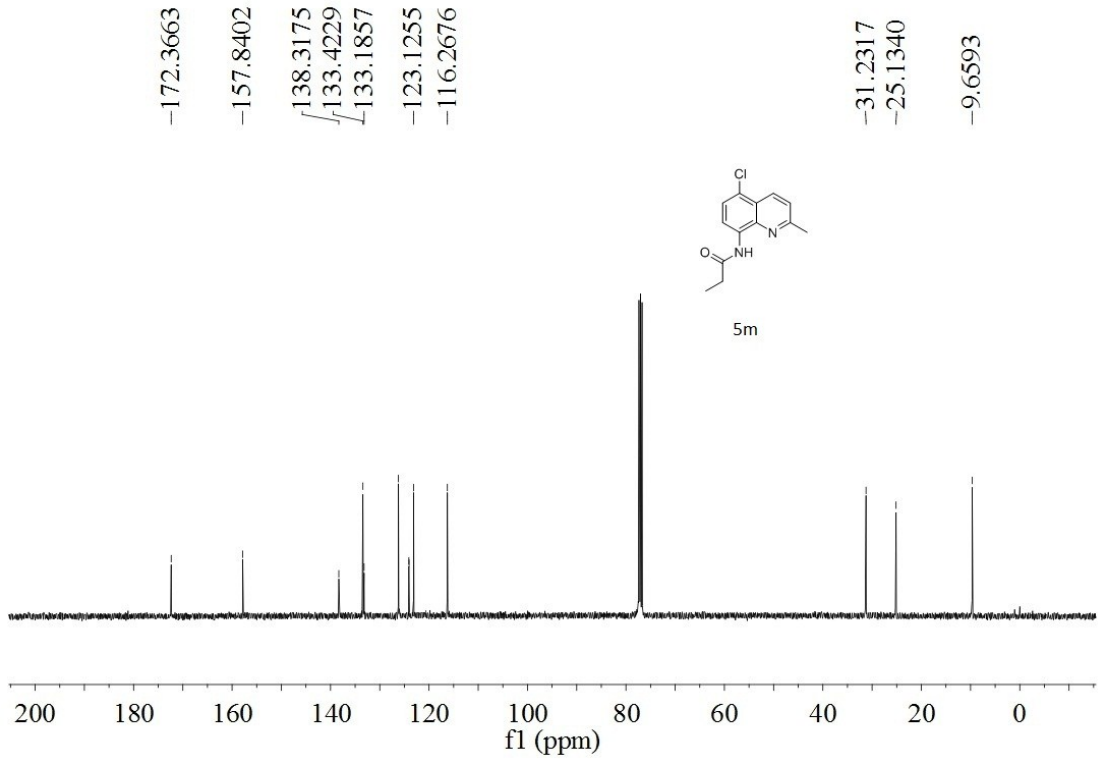

10.7169
8.8670
8.8461
8.6133
8.5921
8.1805
8.1603
7.8297
7.8095
7.6705
7.6495
7.6289
7.6184
7.6077
7.5972
Cl
N
O
NH
Cl
5k
1.00
2.00
0.98
2.01
2.00
2.02
11.0
9.5
8.0
6.5
5.0
3.5
2.0
0.5
f1 (ppm)

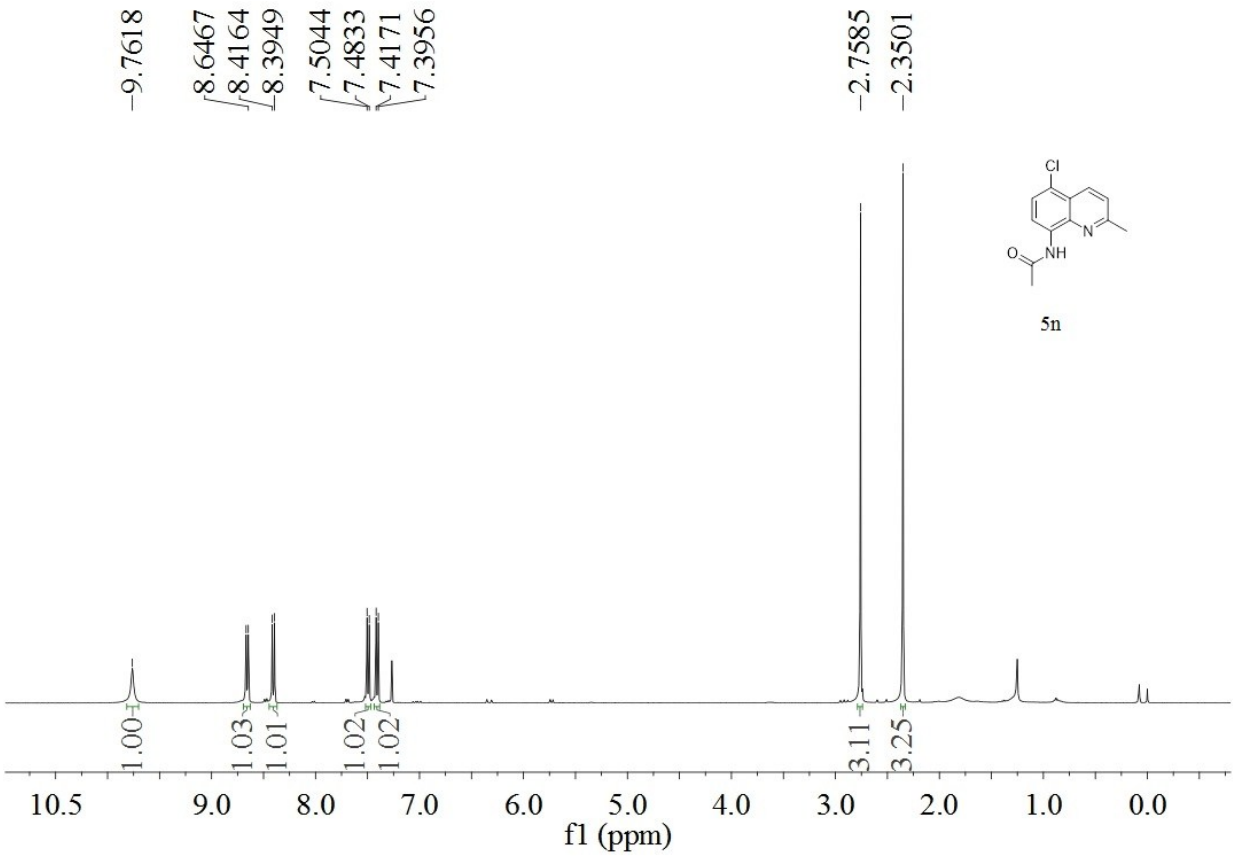

164.2728
148.8362
133.6145
128.7086
126.0286
122.4888
116.5368
Cl
N
O
NH
Cl
5k
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

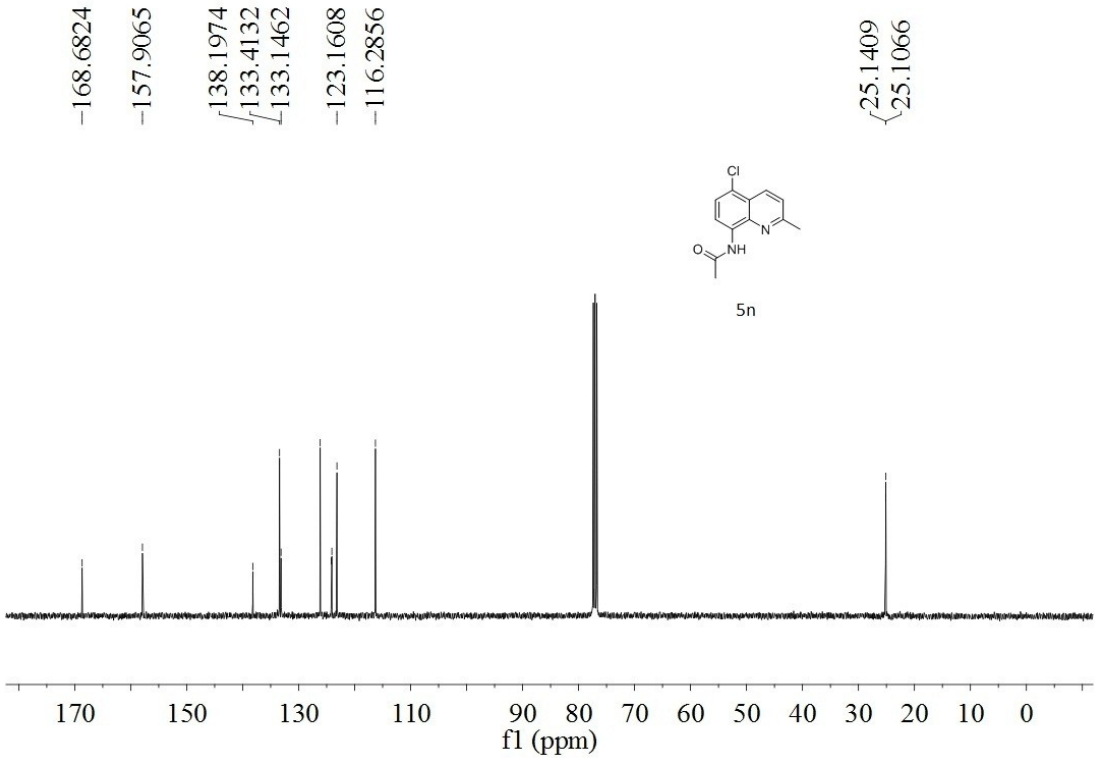

10.7169
8.8670
8.8461
8.6133
8.5921
8.1805
8.1603
7.8297
7.8095
7.6705
7.6495
7.6289
7.6184
7.6077
7.5972
Cl
N
NH
O
CF3
5l
1.00
2.00
0.98
2.01
2.00
2.02
11.0
9.5
8.0
6.5
5.0
3.5
2.0
0.5
f1 (ppm)

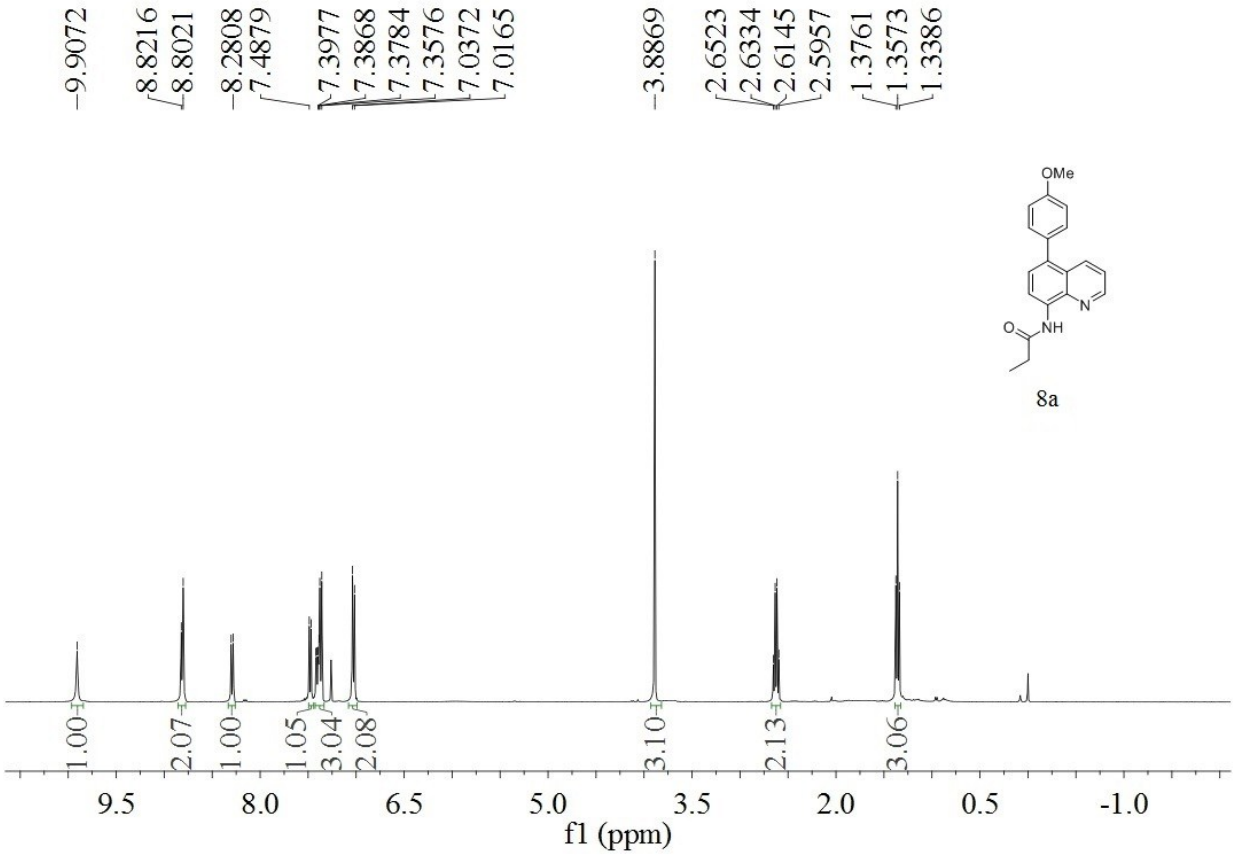

163.9924
148.9259
133.8076
133.4086
127.2702
116.6812
Cl
N
NH
O
CF3
5l
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

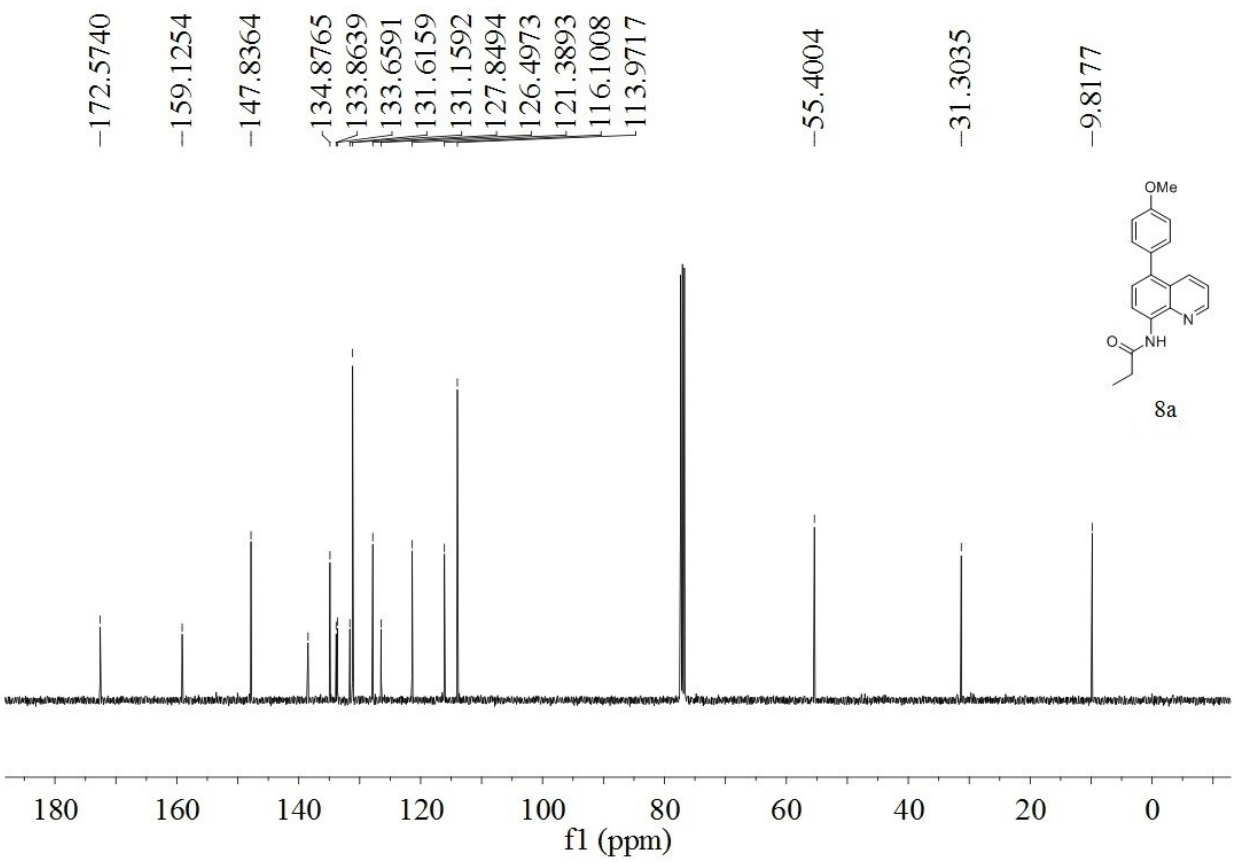

9.8148
8.6726
8.3994
8.3952
7.5116
7.4906
7.4167
7.3952
2.7576
2.6289
2.6100
2.5912
2.5723
1.3588
1.3399
1.3211
Cl
N
O
NH
5m
1.00
1.02
1.00
1.04
1.17
3.09
2.05
3.13
11.0
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

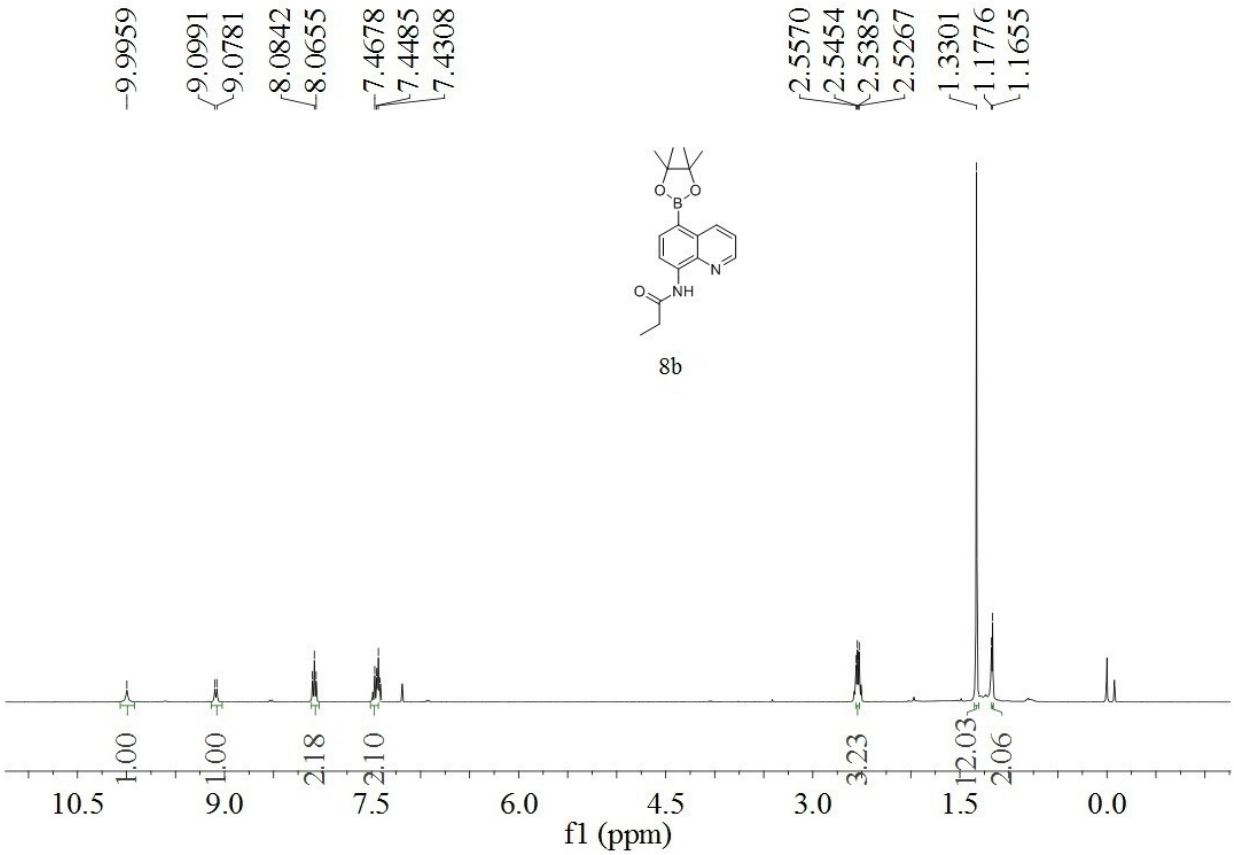

172.3663
157.8402
138.3175
133.4229
133.1857
123.1255
116.2676
31.2317
25.1340
9.6593
Cl
N
O
NH
5m
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

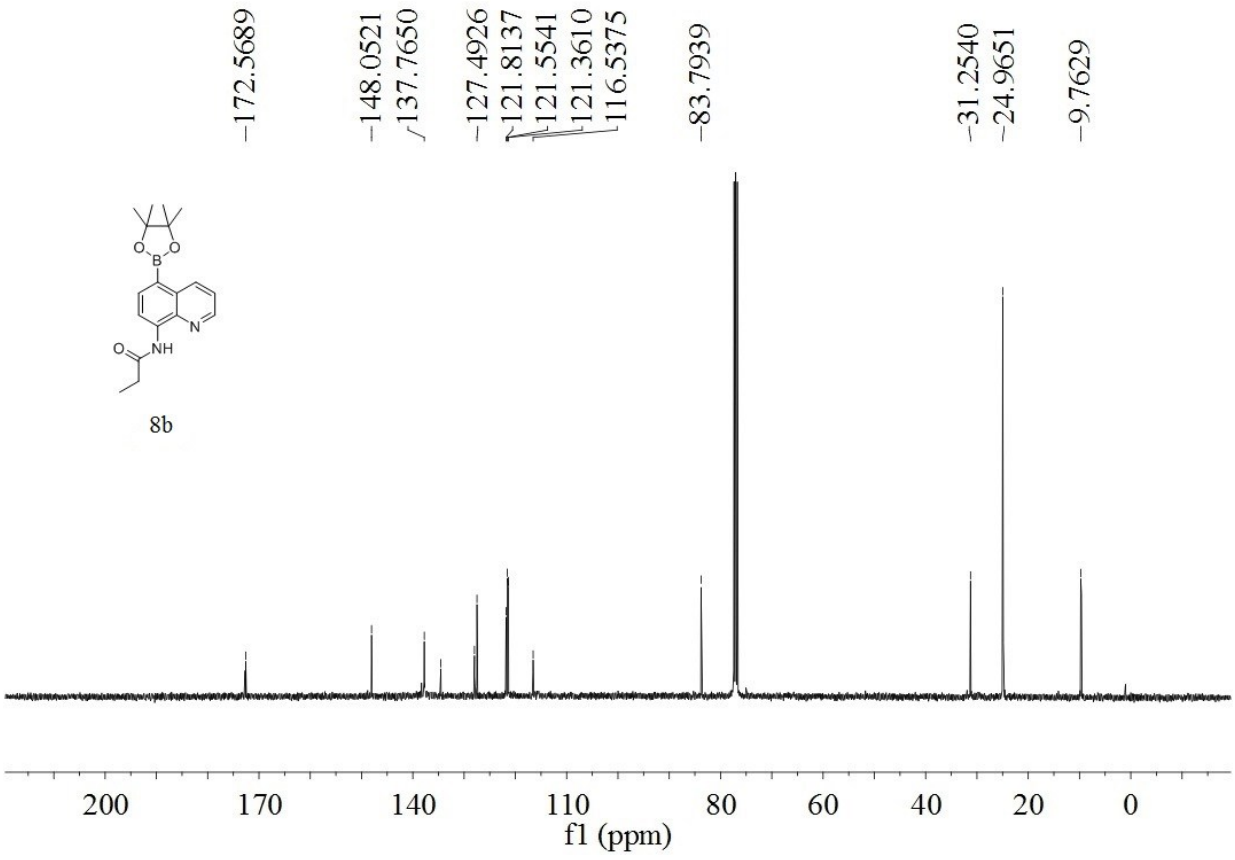

9.7618
8.6467
8.4164
8.3949
7.5044
7.4833
7.4171
7.3956
2.7585
2.3501
Cl
N
O
NH
5n
1.00
1.03
1.01
1.02
1.02
3.11
3.25
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


168.6824
157.9065
138.1974
133.4132
133.1462
123.1608
116.2856
25.1409
25.1066
Cl
N
O
NH
5n
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.9072
8.8216
8.8021
8.2808
7.4879
7.3977
7.3868
7.3784
7.3576
7.0372
7.0165
3.8869
2.6523
2.6334
2.6145
2.5957
1.3761
1.3573
1.3386
OMe
N
NH
O
8a
1.00
2.07
1.00
1.05
3.04
2.08
3.10
2.13
3.06
9.5
8.0
6.5
5.0
3.5
2.0
0.5
-1.0
f1 (ppm)


172.5740
159.1254
147.8364
134.8765
133.8639
133.6591
131.6159
131.1592
127.8494
126.4973
121.3893
116.1008
113.9717
55.4004
31.3035
9.8177
OMe
N
NH
O
8a
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


9.9959
9.0991
9.0781
8.0842
8.0655
7.4678
7.4485
7.4308
2.5570
2.5454
2.5385
2.5267
1.3301
1.1776
1.1655
8b
1.00
1.00
2.18
2.10
3.23
12.03
2.06
10.5
9.0
7.5
6.0
4.5
3.0
1.5
0.0
f1 (ppm)


172.5689
148.0521
137.7650
127.4926
121.8137
121.5541
121.3610
116.5375
83.7939
31.2540
24.9651
9.7629
8b
200
170
140
110
80
60
40
20
0
f1 (ppm)