Supporting Information

Unprecedented Copper-Mediated Oxidative Demethylation of Propionamides via Bidentate-Chelation Assistance

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I. General Information

a). Materials

Unless otherwise noted, all the reactions were carried out in anhydrous solvents under O_2 atmosphere (purity ≥99.995%). $Cu(OAc)_2$(98%) was purchased from Sigma-Aldrich. Anhydrous solvents (DMF, DMSO, NMP) were purchased from Acros and used without further purification. K_2CO_3 and Na_2CO_3 were purchased from Sinopharm Chemical Reagent Co., Ltd and used as received. The following reagents were purchased from commercial sources: Ag_2O(99%, Alfa), Ag_2CO_3(99%, Acros), AgOAc(99%, Stream), $(BOC)_2O$(95%, TCI), TMSOAc(98%, J&K), Cs_2CO_3(99.5%, Acros).

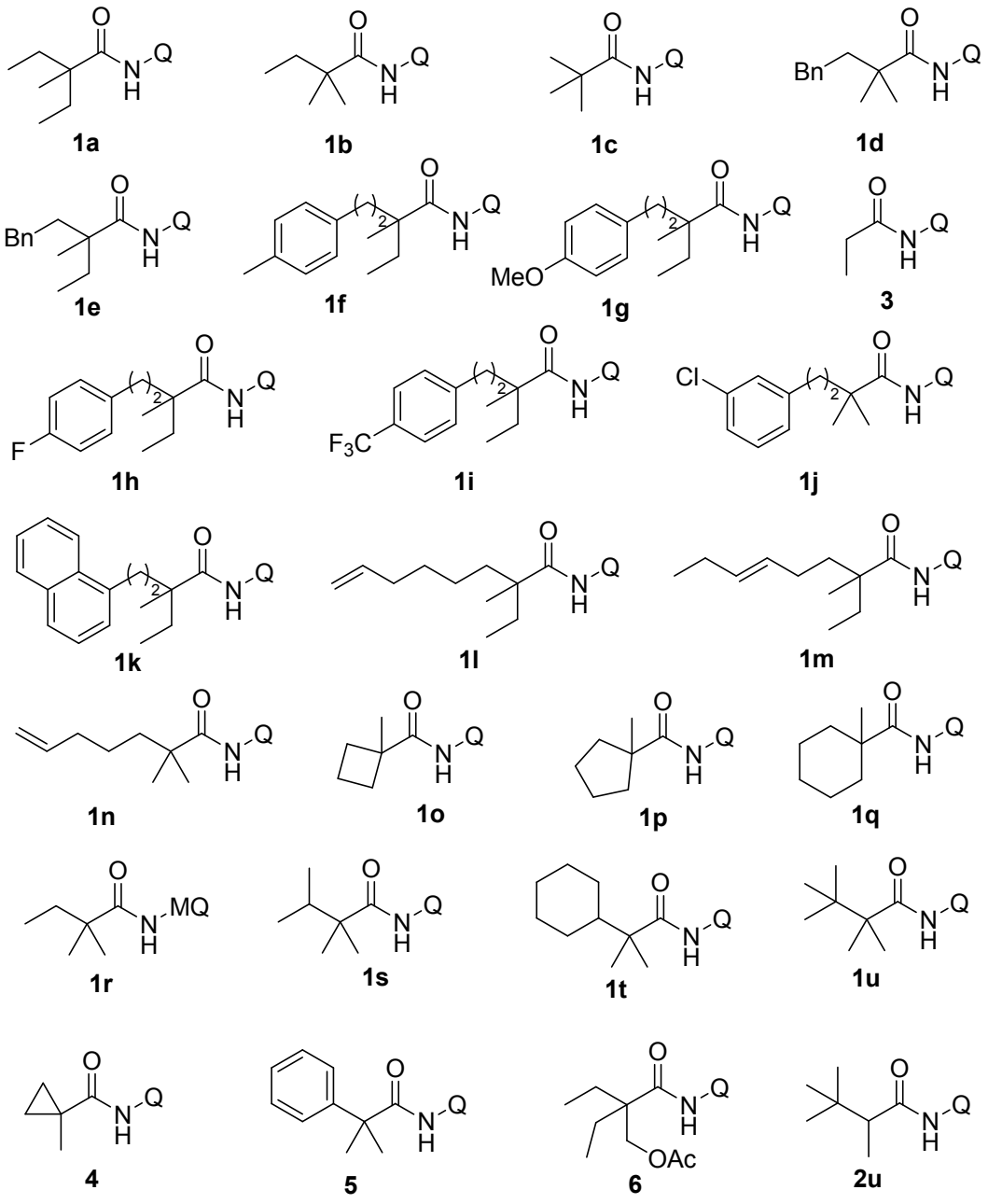
All the other reagents and solvents mentioned in this text were purchased from commercial sources and used without purification.

b). Analytical Methods

^{1}H-NMR, ^{13}C-NMR and ^{19}F-NMR spectra were recorded on a Bruker Avance 400 spectrometer at ambient temperature in $CDCl_3$ unless otherwise noted; Data for ^{1}H-NMR are reported as follows: chemical shift (δ ppm), multiplicity, integration, and coupling constant (Hz). Data for ^{13}C-NMR are reported in terms of chemical shift (δ ppm), multiplicity, and coupling constant (Hz). Gas chromatographic (GC) analysis was acquired on a Shimadzu GC-2014 Series GC System equipped with a flame-ionization detector. GC-MS analysis was performed on Thermo Scientific AS 3000 Series GC-MS System. Organic solutions were concentrated under reduced pressure on a Buchi rotary evaporator. Flash column chromatographic purification of products was accomplished using forced-flow chromatography on Silica Gel (200-300 mesh).

II. Preparation of Propionamides

Strating materials:



a). Starting materials **1a-d, 2u** were prepared according to literature **[1]**. Starting materials **3, 1o, 1p, 1q, 4, 5** were synthesized according to literature **[2]**. Substrate **1s** was synthesized according to literature **[3]**. Substrates **1e** and **1u** were synthesized according to literature **[4]**. Substrate **6** was synthesized according to literature **[5]**.

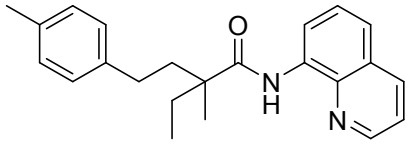
b) General procedure for the synthesis of **1f-1n, 1t** [1].

To a solution of carboxylate ester (20 mmol) in THF (20 mL) at -78 °C, LDA (2.0 M THF solution, 11 mL) was added dropwise and the mixture was stirred at this temperature for 1 h. Alkyl halide (20 mmol) was then added dropwise to the solution at -78 °C. After the addition, the mixture was warmed to room temperature and stirred overnight. Then the mixture was quenched with water, extracted with Et_2O (40 mL x 3). The combined organic layers were washed with brine, dried over $MgSO_4$, and then evaporated in vacuo to give the crude ester.

To the ester was added NaOH (60 mmol) and methanol (50 mL). The mixture was stirred overnight at 80 °C. After removal of methanol in vacuo, the pH of the mixture was adjusted to 2 with 3.0 M HCl. The mixture was then saturated with NaCl and extracted with Et_2O (40 mL x 3). The combined organic layers were washed with brine, dried over $MgSO_4$, and then evaporated in vacuo to give the crude carboxylic acid, which was used directly for the next step without further purification.

Oxalyl chloride (3.5 mL, 40 mmol) was added slowly to a stirred solution of the carboxylic acid in CH_2Cl_2 (40 mL) and DMF (0.2 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C and another 16 h at room temperature, and evaporated in vacuo. The residue was then dissolved in toluene (5 mL), evaporated in vacuo twice, to give the crude acid chloride, which was used directly for the next step without further purification.

The acid chloride was added dropwise to a solution of 8-aminoquinoline (2.0 g, 14 mmol) and NEt_3 (3.8 mL, 28 mmol) in CH_2Cl_2 (50 mL). The mixture was stirred overnight at room temperature. Then the mixture was diluted with CH_2Cl_2 (50 mL), washed successively with water, and brine. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/hexane (1:100, v/v), to afford corresponding 8-aminoquinolinyl amides **1**.



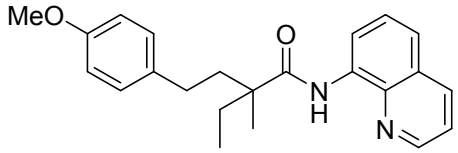
2-ethyl-2-methyl-N-(quinolin-8-yl)-4-(p-tolyl)butanamide

Compound **1f**, yellow oil, was prepared from ethyl 2-methylbutanoate and 1-(2-iodoethyl)-4-methylbenzene.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.29 (s, 1H), 8.88 – 8.79 (m, 2H), 8.18 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.60 – 7.43 (m, 3H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 7.9 Hz, 2H), 2.72 – 2.53 (m, 2H), 2.28 (s, 3H), 2.21 – 2.10 (m, 1H), 2.00 – 1.80 (m, 2H), 1.75-1.66 (m, 1H), 1.46 (s, 3H), 0.97 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.64, 148.13, 139.31, 138.65, 136.51, 135.18, 134.52, 129.00, 128.29, 127.99, 127.53, 121.54, 121.27, 116.52, 47.71, 42.33, 33.05, 30.77, 20.96, 20.81, 8.95.

HRMS calcd for $C_{23}H_{26}N_2O$ (M+ H^+): 347.2118, Found: 347.2116.



2-ethyl-4-(4-methoxyphenyl)-2-methyl-N-(quinolin-8-yl)butanamide.

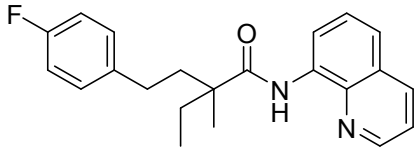
Compound **1g**, yellow oil, was prepared from ethyl 2-methylbutanoate and 1-(2-iodoethyl)-4-

methoxybenzene.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.29 (s, 1H), 8.83 (dd, *J* = 4.9, 3.0 Hz, 2H), 8.18 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.59 – 7.44 (m, 3H), 7.12 (d, *J* = 8.6 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 3.75 (s, 3H), 2.70 – 2.51 (m, 2H), 2.21 – 2.09 (m, 1H), 1.99 - 1.90 (m, 1H), 1.89 – 1.78 (m, 1H), 1.75-1.60 (m, 1H), 1.46 (s, 3H), 0.98 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.65, 157.69, 148.12, 138.62, 136.54, 134.49, 134.45, 129.29, 127.99, 127.54, 121.54, 121.28, 116.53, 113.72, 55.23, 47.69, 42.41, 33.05, 30.29, 20.79, 8.95.

HRMS calcd for $C_{23}H_{26}N_2O_2$ (M+ H^+): 363.2067, Found: 363.2068.



2-ethyl-4-(4-fluorophenyl)-2-methyl-N-(quinolin-8-yl)butanamide

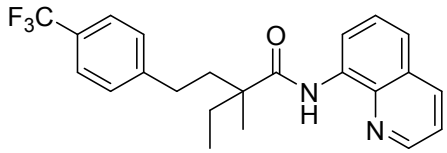
Compound **1h**, yellow oil, was prepared from ethyl 2-methylbutanoate and 1-fluoro-4-(2-iod oethyl)benzene.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.29 (s, 1H), 8.84-8.82 (m, 2H), 8.18 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.60 – 7.43 (m, 3H), 7.18-7.12 (m, 2H), 6.91 (t, *J* = 8.7 Hz, 2H), 2.73 – 2.53 (m, 2H), 2.20 – 2.09 (m, 1H), 2.01 – 1.77 (m, 2H), 1.75-1.65 (m, 1H), 1.46 (s, 3H), 0.98 (t, *J* = 7.5 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -117.89.

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.46, 161.20 (d, *J* = 241 Hz), 148.21, 138.73, 137.95 (d, *J* = 4 Hz), 136.44, 134.47, 129.74(d, *J* = 7 Hz), 127.98, 127.49, 121.59, 121.34, 116.39, 115.01 (d, *J* = 21 Hz), 47.68, 42.24, 33.07, 30.45, 20.79, 8.95.

HRMS calcd for $C_{22}H_{23}FN_2O$ (M+ H^+): 351.1867, Found: 351.1865.



2-ethyl-2-methyl-N-(quinolin-8-yl)-4-(4-(trifluoromethyl)phenyl)butanamide

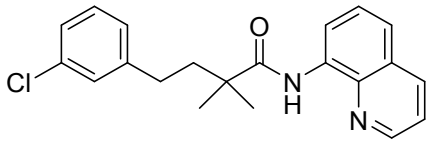
Compound **1i**, yellow oil, was prepared from ethyl 2-methylbutanoate and 1-(2-iodoethyl)-4-(trifluoromethyl)benzene.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.29 (s, 1H), 8.86 – 8.76 (m, 2H), 8.19 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.60 – 7.44 (m, 5H), 7.31 (d, *J* = 8.0 Hz, 2H), 2.81 – 2.62 (m, 2H), 2.24 – 2.12 (m, 1H), 2.02 – 1.80 (m, 2H), 1.71 (dq, *J* = 14.8, 7.5 Hz, 1H), 1.48 (s, 3H), 0.99 (t, *J* = 7.5 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.27.

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.28, 148.23, 146.50, 138.70, 136.49, 134.39, 128.75, 128.12 (q, *J* = 33 Hz), 128.00, 127.50, 125.22 (q, *J* = 4.0 Hz), 124.33 (q, *J* = 270 Hz), 121.62, 121.42, 116.44, 47.68, 41.76, 33.12, 31.20, 20.81, 8.94.

HRMS calcd for $C_{23}H_{23}F_3N_2O$ (M+ H^+): 401.1835, Found: 401.1837.



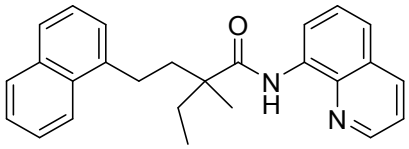
4-(3-chlorophenyl)-2,2-dimethyl-N-(quinolin-8-yl)butanamide

Compound **1j**, colourless oil, was prepared from methyl isobutyrate and 1-chloro-3-(2-iodoet hyl)benzene.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (s, 1H), 8.86-8.80 (m, 2H), 8.17 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.59 – 7.43 (m, 3H), 7.24-7.22 (m, 1H), 7.19 – 7.06 (m, 3H), 2.70 – 2.61 (m, 2H), 2.06 – 1.98 (m, 2H), 1.48 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.89, 148.31, 144.27, 138.77, 136.39, 134.48, 134.03, 129.56, 128.56, 127.96, 127.44, 126.65, 125.95, 121.62, 121.40, 116.36, 43.85, 43.43, 31.30, 25.81.

HRMS calcd for $C_{21}H_{21}ClN_2O$ (M+ H^+): 353.1415, Found: 353.1413.



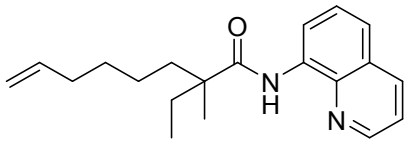
2-ethyl-2-methyl-4-(naphthalen-1-yl)-N-(quinolin-8-yl)butanamide

Compound **1k**, yellow oil, was prepared from ethyl 2-methylbutanoate and 1-(2-iodoethyl)na phthalene.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.37 (s, 1H), 8.91 (dd, *J* = 7.5, 1.1 Hz, 1H), 8.82 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.4 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.67 (dd, *J* = 7.0, 2.1 Hz, 1H), 7.62 – 7.28 (m, 7H), 3.25 – 2.99 (m, 2H), 2.40 – 2.23 (m, 1H), 2.06 – 1.87 (m, 2H), 1.74 (dq, *J* = 14.7, 7.4 Hz, 1H), 1.57 (s, 3H), 1.01 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.57, 148.25, 138.76, 138.56, 136.39, 134.57, 133.84, 131.76, 128.65, 127.99, 127.54, 126.59, 126.05, 125.79, 125.58, 125.38, 123.83, 121.57, 121.31, 116.37, 47.92, 41.65, 33.20, 28.49, 20.73, 9.00.

HRMS calcd for $C_{26}H_{26}N_2O$ (M+ H^+): 383.2118, Found: 383.2115.



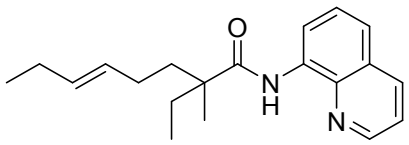
2-ethyl-2-methyl-N-(quinolin-8-yl)oct-7-enamide

Compound **1l**, yellow oil, was prepared from ethyl 2-methylbutanoate and 6-iodohex-1-ene.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.84 – 8.79 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57 – 7.40 (m, 3H), 5.76 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 4.98 – 4.84 (m, 2H), 2.07 – 1.99 (m, 2H), 1.92-1.81 (m, 2H), 1.70 – 1.53 (m, 2H), 1.47 – 1.29 (m, 7H), 0.94 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.03, 148.20, 138.89, 138.80, 136.30, 134.64, 127.95, 127.48, 121.51, 121.14, 116.20, 114.28, 47.62, 39.80, 33.59, 32.91, 29.51, 24.11, 20.75, 8.99.

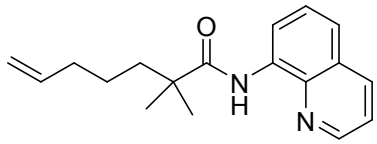
HRMS calcd for $C_{20}H_{26}N_2O$ (M+ H^+): 311.2118, Found: 311.2114.



(E)-2-ethyl-2-methyl-N-(quinolin-8-yl)oct-5-enamide

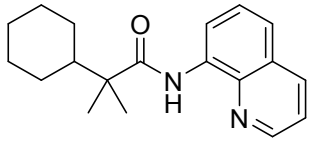
Compound **1m**, yellow oil, was prepared from ethyl 2-methylbutanoate and (E)-1-iodohex-3-ene.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 8.82 (dt, *J* = 5.5, 1.5 Hz, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57 – 7.41 (m, 3H), 5.51 – 5.29 (m, 2H), 2.13 – 1.97 (m, 2H), 1.96 – 1.86 (m, 4H), 1.68-1.60 (m, 2H), 1.38 (s, 3H), 0.97-0.88 (m, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 175.82, 148.21, 138.82, 136.27, 134.63, 132.25, 128.73, 127.94, 127.46, 121.51, 121.15, 116.20, 47.50, 39.94, 32.92, 27.82, 25.52, 20.65, 13.80, 8.97.
HRMS calcd for $C_{20}H_{26}N_2O$ (M+ H^+): 311.2118, Found: 311.2115.



2,2-dimethyl-N-(quinolin-8-yl)hept-6-enamide

Compound **1n**, yellow oil, was prepared from methyl isobutyrate and 5-iodopent-1-ene.
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.25 (s, 1H), 8.83 – 8.78 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.56 – 7.41 (m, 3H), 5.78 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.03 – 4.88 (m, 2H), 2.12 – 2.03 (m, 2H), 1.76 – 1.69 (m, 2H), 1.51 – 1.42 (m, 2H), 1.41 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.56, 148.19, 138.80, 138.58, 136.32, 134.65, 127.95, 127.46, 121.53, 121.21, 116.25, 114.63, 43.72, 41.03, 34.19, 25.65, 24.25.
HRMS calcd for $C_{18}H_{22}N_2O$ (M+H^+): 283.1805, Found: 283.1801.



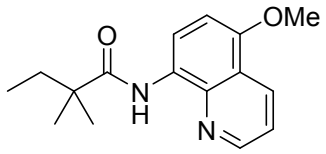
2-cyclohexyl-2-methyl-N-(quinolin-8-yl)propanamide

Compound **1t**, yellow oil, was prepared from methyl 2-cyclohexylacetate and iodomethane.
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 8.86 – 8.79 (m, 2H), 8.17 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.58 – 7.42 (m, 3H), 1.82 – 1.65 (m, 6H), 1.36 – 1.26 (m, 8H), 1.17 – 1.10 (m, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 177.25, 148.09, 138.64, 136.55, 134.55, 128.00, 127.56, 121.49, 121.21, 116.52, 47.05, 46.24, 27.85, 26.86, 26.57, 22.22.
HRMS calcd for $C_{19}H_{24}N_2O$ (M+ H^+): 297.1961, Found: 297.1963.

c) General procedure for the synthesis of **1r** and **5-(2,5-dimethylphenoxy)-2,2-dimethyl-N-(quinolin-8-yl)pentanamide (9)**[2].

Oxalyl chloride (3.5 mL, 40 mmol) was added slowly to a stirred solution of 2,2-dimethylbutanoic acid(20 mmol) in CH_2Cl_2 (40 mL) and DMF (0.2 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C and another 16 h at room temperature, and evaporated in vacuo to give the crude acid chloride, which was used directly for the next step without further purification.

The acid chloride was added dropwise to a solution of 5-methoxyquinolin-8-amine (2.0 g, 14 mmol) and NEt_3 (3.8 mL, 28 mmol) in CH_2Cl_2 (50 mL). The mixture was stirred overnight at room temperature. Then the mixture was diluted with CH_2Cl_2 (50 mL), washed successively with water, and brine. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/hexane (1:100, v/v), to afford corresponding 8-aminoquinolinyl amides **1r** (yellow oil).

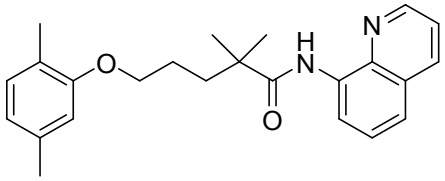


N-(5-methoxyquinolin-8-yl)-2,2-dimethylbutanamide

Compound **1r**, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.73 (d, *J* = 8.5 Hz, 1H), 8.56 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.43 (dd, *J* = 8.4, 4.3 Hz, 1H), 6.83 (d, *J* = 8.6 Hz, 1H), 3.98 (s, 3H), 1.76 (q, *J* = 7.5 Hz, 2H), 1.38 (s, 6H), 0.95 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.21, 150.04, 148.66, 139.45, 131.20, 128.14, 120.62, 120.44, 116.29, 104.38, 55.76, 43.89, 34.15, 25.13, 9.34.

HRMS calcd for $C_{16}H_{20}N_2O_2$ (M+ H^+): 273.1598, Found: 273.1601.



5-(2,5-dimethylphenoxy)-2,2-dimethyl-N-(quinolin-8-yl)pentanamide (9)

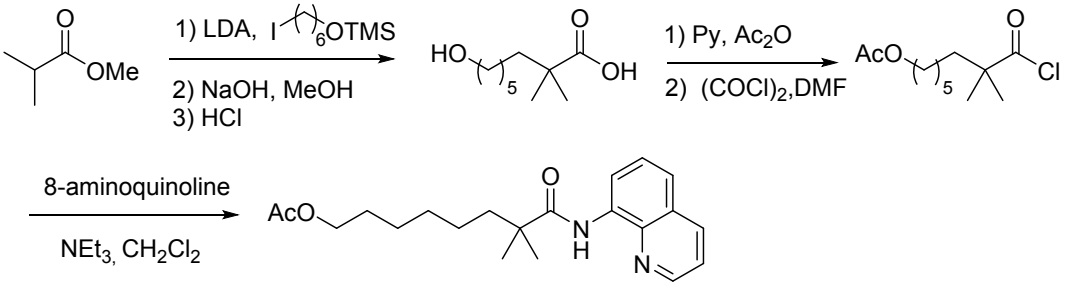
Compound **9** , Colourless oil. It was prepared from Gemfibrozil and 8-aminoquinoline.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.29 (s, 1H), 8.83 – 8.78 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57 – 7.42 (m, 3H), 6.95 (d, *J* = 7.5 Hz, 1H), 6.61 (d, *J* = 7.5 Hz, 1H), 6.57 (s, 1H), 3.94 (t, *J* = 5.9 Hz, 2H), 2.25 (s, 3H), 2.13 (s, 3H), 1.97 – 1.83 (m, 4H), 1.46 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.35, 156.91, 148.15, 138.65, 136.44, 136.39, 134.54, 130.20, 127.96, 127.47, 123.54, 121.52, 121.31, 120.61, 116.40, 111.92, 67.91, 43.58, 37.94, 25.66, 25.18, 21.36, 15.76.

HRMS calcd for $C_{24}H_{28}N_2O_2$ (M+ H^+): 377.2224, Found: 377.2221.

d) General procedure for the synthesis of **7,7-dimethyl-8-oxo-8-(quinolin-8-ylamino)octyl acetate (7)**.[1]



To a solution of methyl isobutyrate (20 mmol) in THF (20 mL) at -78 °C, LDA (2.0 M THF solution, 11 mL) was added dropwise and the mixture was stirred at this temperature for 1 h. ((6-iodohexyl)oxy)trimethylsilane (15 mmol) was then added dropwise to the solution at -78 °C. After the addition, the mixture was warmed to room temperature and stirred overnight. Then the mixture was quenched with water, extracted with Et_2O (40 mL x 3). The combined organic layers were washed with brine, dried over $MgSO_4$, and then evaporated in vacuo to give the crude ester.

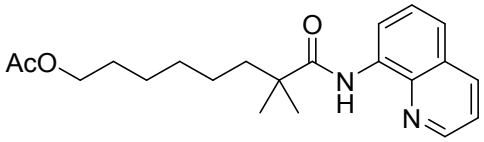
To the ester was added NaOH (60 mmol) and methanol (50 mL). The mixture was stirred overnight at 80 °C. After removal of methanol in vacuo, the pH of the mixture was adjusted to 2 with 3.0 M HCl. The mixture was then extracted with CH_2Cl_2 (40 mL x 3). The combined organic layers were washed with brine, dried over $MgSO_4$, and then evaporated in vacuo to give the crude

carboxylic acid, which was used directly for the next step without further purification.

To a solution of the crude carboxylic acid in 20 mL pyridine, Ac_2O (30 mmol) was added dropwise and the mixture was stirred at room temperature for 10 h. Then the mixture was quenched with 2.0 M HCl, extracted with CH_2Cl_2 (40 mL x 3). The combined organic layers were washed with brine, dried over $MgSO_4$, and then evaporated in vacuo to give the crude carboxylic acid

Oxalyl chloride (3.5 mL, 40 mmol) was added slowly to a stirred solution of the carboxylic acid in CH_2Cl_2 (40 mL) and DMF (0.2 mL) at 0 ^oC. The mixture was stirred for 1 h at 0 ^oC and another 16 h at room temperature, and evaporated in vacuo. The residue was then dissolved in toluene (5 mL), evaporated in vacuo twice, to give the crude acid chloride, which was used directly for the next step without further purification.

The acid chloride was added dropwise to a solution of 8-aminoquinoline (2.0 g, 14 mmol) and NEt_3 (3.8 mL, 28 mmol) in CH_2Cl_2 (50 mL). The mixture was stirred overnight at room temperature. Then the mixture was diluted with CH_2Cl_2 (50 mL), washed successively with water, and brine. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/hexane (1:50, v/v), to afford corresponding 8-aminoquinolinyl amide (yellow oil).



7,7-dimethyl-8-oxo-8-(quinolin-8-ylamino)octyl acetate

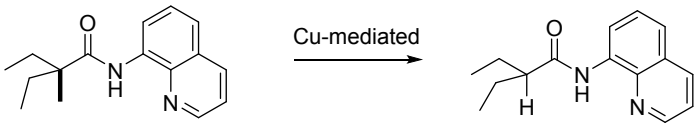
Compound **7** , yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 8.84 – 8.77 (m, 2H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57 – 7.41 (m, 3H), 4.00 (t, *J* = 6.7 Hz, 2H), 2.01 (s, 3H), 1.73-1.69 (m, 2H), 1.62 – 1.53 (m, 2H), 1.40 (s, 6H), 1.38 – 1.30 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.62, 171.19, 148.20, 138.79, 136.35, 134.66, 127.96, 127.48, 121.54, 121.22, 116.24, 64.55, 43.77, 41.51, 29.79, 28.55, 25.77, 25.67, 24.84, 20.99.

HRMS calcd for $C_{21}H_{28}N_2O_3$ (M+ H^+): 357.2173, Found: 357.2169.

III. General Experimental Procedures, Spectral Data

Experimental Procedures for Examples Described in Table 1.



1a **2a**

Entry	Catalyst	Base	Additive	Solvent	Yield[a] (%)
1	$Cu(OAc)_2$	Na_2CO_3	-	DMSO	21
2	$Cu(OAc)_2$	Na_2CO_3	Ag_2O	DMSO	20
3	$Cu(OAc)_2$	Na_2CO_3	Ag_2CO_3	DMSO	16
4	$Cu(OAc)_2$	Na_2CO_3	AgOAc	DMSO	41
5	$Cu(OAc)_2$	Na_2CO_3	Ac_2O	DMSO	24
6	$Cu(OAc)_2$	Na_2CO_3	$(BOC)_2O$	DMSO	22
7	$Cu(OAc)_2$	Na_2CO_3	TMSOAc	DMSO	38
8	$Cu(OAc)_2$	K_2CO_3	TMSOAc	DMSO	45
9	$Cu(OAc)_2$	Cs_2CO_3	TMSOAc	DMSO	40
10	$Cu(OAc)_2$	Li_2CO_3	TMSOAc	DMSO	36
11	$Cu(OAc)_2$	NaOAc	TMSOAc	DMSO	8
12	$Cu(OAc)_2$	KOAc	TMSOAc	DMSO	trace
13	$Cu(OAc)_2$	Na_3PO_4	TMSOAc	DMSO	trace
14	$Cu(OAc)_2$	K_3PO_4	TMSOAc	DMSO	trace
15	$Cu(OAc)_2$	Na_2HPO_4	TMSOAc	DMSO	trace
16	$Cu(OAc)_2$	K_2HPO_4	TMSOAc	DMSO	trace
17	$Cu(OAc)_2$	PhCOOK	TMSOAc	DMSO	trace
18	$Cu(OAc)_2$	PhCOONa	TMSOAc	DMSO	trace
19[c]	$Cu(OAc)_2$	K_2CO_3+Na_2CO_3	TMSOAc	DMSO	48
20[c,e]	$Cu(OAc)_2$	K_2CO_3+Na_2CO_3	TMSOAc	DMSO	56
21[c,e]	$Cu(OAc)_2$	K_2CO_3+Na_2CO_3	TMSOAc	DMF	32
22[c,e]	$Cu(OAc)_2$	K_2CO_3+Na_2CO_3	TMSOAc	NMP	19
23[c,d,e]	$Cu(OAc)_2$	K_2CO_3+Na_2CO_3	TMSOAc	DMSO	72(70[b])
24[c,d,e]	$Cu(OTf)_2$	K_2CO_3+Na_2CO_3	TMSOAc	DMSO	trace
25[c,d,e]	$CuCl_2$	K_2CO_3+Na_2CO_3	TMSOAc	DMSO	trace
26[c,d,e]	$CuBr_2$	K_2CO_3+Na_2CO_3	TMSOAc	DMSO	trace
27[c,e,f]	$Pd(OAc)_2$	K_2CO_3+Na_2CO_3	TMSOAc	DMSO	trace
28[c,d,e,f]	$Cu(OAc)_2$	K_2CO_3+Na_2CO_3	TMSOAc	DMSO	54
29[c,e]	-	K_2CO_3+Na_2CO_3	TMSOAc	DMSO	trace

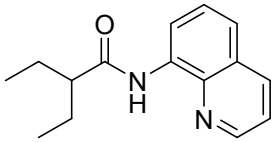
[a] Reaction conditions: **1a** (0.1 mmol), Cu catalyst (0.1 mmol), base (0.3 mmol), additive (0.4 mmol) in 1 mL solvent for at 150°C 16h under O_2. Yields (average of two runs) were determined by GC with triphenylmethane as the internal standard. [b] Isolated yields. [c]

The reaction was conducted with K_2CO_3 (0.2 mmol) and Na_2CO_3 (0.1 mmol). [d] $Cu(OAc)_2$ (0.2 mmol) was added. [e] 4A-MS (30 mg) was added. [f] $Pd(OAc)_2$(10% mmol) was added. $(BOC)_2O$ = di-tert-butyl dicanonate, TMSOAc = trimethylsilyl acetate.

To a 15 mL Schlenk tube Cu catalyst (0.20 mmol), Base (0.3 mmol), **1a** (0.10 mmol), 4A-MS (30 mg) and a stir bar were added. The vessel was then evacuated and filled with O_2 (three cycles). Additive (0.40 mmol, if additive is a solid , it was added along with the Cu catalyst) and solvent (1.0 mL) were added in turn under O_2. The reaction mixture was stirred at the mentioned temperature for the indicated amount of time. After that, the reaction mixture was diluted with EtOAc, filtered through silica gel with copious washings (EtOAc). Triphenylmethane (24.4 mg, 0.10 mmol) was added and the product yield was determined by GC analysis.

General Procedures for Examples Described in Table 2.

To a 15 mL Schlenk tube $Cu(OAc)_2$ (36.2 mg, 0.20 mmol), K_2CO_3 (27.6 mg, 0.2 mmol), Na_2CO_3 (10.6 mg, 0.1 mmol), propionamide (0.10 mmol), 4A-MS (30 mg) and a stir bar were added. The vessel was then evacuated and filled with O_2 (three cycles). TMSOAc (0.40 mmol) and DMSO (1.0 mL) were added in turn under O_2. The reaction mixture was stirred at 150°C for 16h. After that, the reaction mixture was diluted with EtOAc, filtered through silica gel with copious washings (EtOAc), concentrated, and purified by column chromatography (EtOAc/hexane = 1/100 to 1/50, v/v).



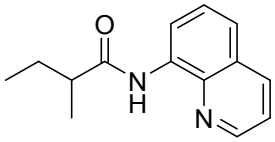
2-ethyl-N-(quinolin-8-yl)butanamide (2a)

Following the general procedure, colourless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.89 – 8.78 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.56 – 7.41 (m, 3H), 2.39 – 2.26 (m, 1H), 1.88 – 1.75 (m, 2H), 1.72 – 1.58 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.77, 148.14, 138.43, 136.35, 134.53, 127.95, 127.45, 121.54, 121.32, 116.47, 52.64, 25.87, 12.12.

HRMS calcd for $C_{15}H_{18}N_2O$ ($M+H^+$): 243.1492, Found: 243.1491.



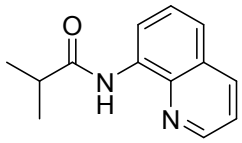
2-methyl-N-(quinolin-8-yl)butanamide (2b)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.84 – 8.79 (m, 2H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58 – 7.40 (m, 3H), 2.61 – 2.49 (m, 1H), 1.94 – 1.80 (m, 1H), 1.67-1.57 (m, 1H), 1.33 (d, *J* = 6.9 Hz, 3H), 1.02 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.40, 148.10, 138.41, 136.43, 134.58, 127.96, 127.48, 121.55, 121.32, 116.50, 44.57, 27.50, 17.57, 11.95.

HRMS calcd for $C_{14}H_{16}N_2O$ ($M+H^+$): 229.1335, Found: 229.1333.



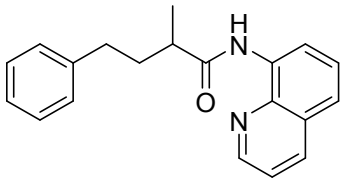
N-(quinolin-8-yl)isobutyramide (2c)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.83 – 8.78 (m, 2H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58 – 7.42 (m, 3H), 2.78 (hept, *J* = 6.9 Hz, 1H), 1.36 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.79, 148.13, 138.48, 136.41, 134.64, 127.96, 127.48, 121.57, 121.32, 116.44, 37.16, 19.75.

HRMS calcd for $C_{13}H_{14}N_2O$ ($M+H^+$): 215.1179, Found: 215.1178.



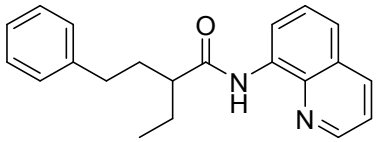
2-methyl-4-phenyl-N-(quinolin-8-yl)butanamide (2d)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.88 – 8.77 (m, 2H), 8.17 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.57-7.45 (m, 3H), 7.30 – 7.17 (m, 5H), 2.83 – 2.56 (m, 3H), 2.24-2.19 (m, 1H), 1.90-1.83 (m, 1H), 1.36 (d, *J* = 8.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.04, 148.11, 141.75, 138.42, 136.43, 134.51, 128.51, 128.40, 127.96, 127.48, 125.88, 121.59, 121.44, 116.58, 42.27, 36.04, 33.63, 18.25.

HRMS calcd for $C_{20}H_{20}N_2O$ ($M+H^+$): 305.1648, Found: 305.1646.



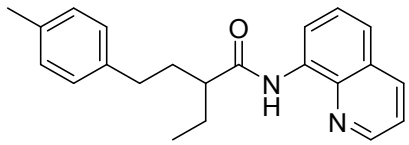
2-ethyl-4-phenyl-N-(quinolin-8-yl)butanamide (2e)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.91 – 8.78 (m, 2H), 8.18 (d, *J* = 8.2 Hz, 1H), 7.58-7.45 (m, 3H), 7.31 – 7.14 (m, 5H), 2.82 – 2.72 (m, 1H), 2.69-2.62 (m, 1H), 2.47-2.40 (m, 1H), 2.24 – 2.11 (m, 1H), 1.91-1.84 (m, 2H), 1.71 – 1.61 (m, 1H), 1.00 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.48, 148.06, 141.84, 138.30, 136.52, 134.38, 128.52, 128.38, 127.99, 127.51, 125.84, 121.58, 121.48, 116.68, 50.12, 34.46, 33.76, 26.41, 12.01.

HRMS calcd for $C_{21}H_{22}N_2O$ ($M+ H^+$): 319.1805, Found: 319.1804.



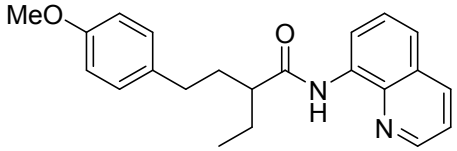
2-ethyl-N-(quinolin-8-yl)-4-(p-tolyl)butanamide (2f)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.90 – 8.77 (m, 2H), 8.19 (d, *J* = 8.2 Hz, 1H), 7.62 – 7.41 (m, 3H), 7.09 (q, *J* = 8.1 Hz, 4H), 2.78 – 2.56 (m, 2H), 2.46-2.39 (m, 1H), 2.30 (s, 3H), 2.21 – 2.10 (m, 1H), 1.92 – 1.77 (m, 2H), 1.70-1.60 (m, 1H), 0.99 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.55, 148.04, 138.73, 138.30, 136.52, 135.27, 134.40, 129.05, 128.40, 127.99, 127.51, 121.56, 121.45, 116.70, 50.11, 34.57, 33.31, 26.42, 21.00, 12.00.

HRMS calcd for $C_{22}H_{24}N_2O$ ($M+H^+$): 333.1961, Found: 333.1960.



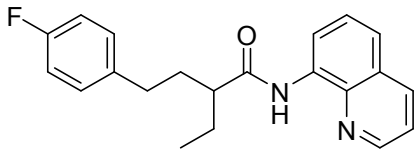
2-ethyl-4-(4-methoxyphenyl)-N-(quinolin-8-yl)butanamide (2g)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.90 – 8.76 (m, 2H), 8.18 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.60 – 7.43 (m, 3H), 7.13 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 3. 77 (s, 3H), 2.77 – 2.66 (m, 1H), 2.65 – 2.54 (m, 1H), 2.43-2.31 (m, 1H), 2.20 – 2.08 (m, 1H), 1.92 – 1.78 (m, 2H), 1.68-1.60 (m, 1H), 0.99 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.53, 157.77, 148.11, 138.39, 136.42, 134.43, 133.87, 129.41, 127.97, 127.48, 121.59, 121.44, 116.58, 113.77, 55.23, 50.08, 34.68, 32.84, 26.43, 12.03.

HRMS calcd for $C_{22}H_{24}N_2O_2$ ($M+H^+$): 349.1911, Found: 349.1909.



2-ethyl-4-(4-fluorophenyl)-N-(quinolin-8-yl)butanamide (2h)

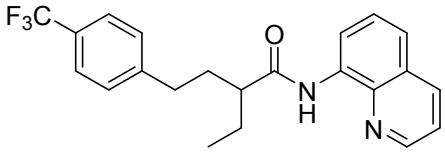
Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.89 – 8.77 (m, 2H), 8.19 (d, *J* = 7.2 Hz, 1H), 7.60-7.45 (m, 3H), 7.20-7.11 (m, 2H), 6.94 (t, *J* = 8.7 Hz, 2H), 2.78 – 2.57 (m, 2H), 2.40 (ddd, *J* = 13.9, 9.4, 4.9 Hz, 1H), 2.22 – 2.09 (m, 1H), 1.92 – 1.79 (m, 2H), 1.71 – 1.63 (m, 1H), 1.00 (t, *J* = 7.4 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -117.73.

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.34, 161.33(d, *J* = 242 Hz), 148.13, 138.35, 137.39(d, *J* = 4 Hz), 136.49, 134.35, 129.83(d, *J* = 8 Hz), 128.00, 127.50, 121.62, 121.53, 116.64, 115.10 (d, *J* = 21 Hz), 50.05, 34.52, 32.95, 26.45, 12.02.

HRMS calcd for $C_{21}H_{21}N_2FO$ ($M+H^+$): 337.1711, Found: 337.1710.



2-ethyl-N-(quinolin-8-yl)-4-(4-(trifluoromethyl)phenyl)butanamide (2i)

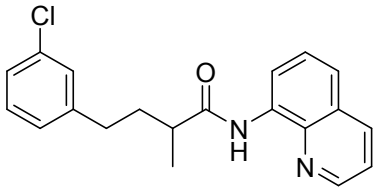
Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.92 – 8.77 (m, 2H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.63 – 7.43 (m, 5H), 7.32 (d, *J* = 7.9 Hz, 2H), 2.88 – 2.65 (m, 2H), 2.50 – 2.37 (m, 1H), 2.26 – 2.11 (m, 1H), 1.95 – 1.80 (m, 2H), 1.70 – 1.59 (m, 1H), 1.01 (t, *J* = 7.4 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.26.

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.09, 148.22, 145.92, 138.42, 136.42, 134.31, 128.84, 128.24 (q, *J* = 32 Hz), 127.99, 127.45, 125.31(q, *J* = 4.0 Hz), 124.36 (q, *J* = 270 Hz), 121.68, 121.61, 116.58, 50.07, 34.03, 33.63, 26.52, 12.00.

HRMS calcd for $C_{22}H_{21}N_2F_3O$ ($M+H^+$): 387.1679, Found: 387.1680.



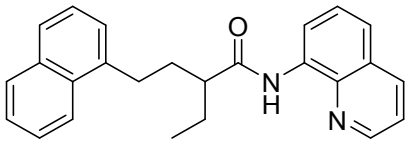
4-(3-chlorophenyl)-2-methyl-N-(quinolin-8-yl)butanamide (2j)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.87-8.812 (m, 2H), 8.19 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.60 – 7.43 (m, 3H), 7.24-7.08 (m, 4H), 2.80 – 2.58 (m, 3H), 2.24-2.15 (m, 1H), 1.89-1.80 (m, 1H), 1.36 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.78, 148.11, 143.79, 138.31, 136.58, 134.36, 134.13, 129.64, 128.63, 127.98, 127.50, 126.71, 126.10, 121.62, 121.55, 116.71, 42.16, 35.78, 33.31, 18.31.

HRMS calcd for $C_{20}H_{19}ClN_2O$ ($M+H^+$): 339.1259, Found: 339.1257.



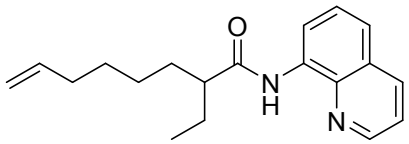
2-ethyl-4-(naphthalen-1-yl)-N-(quinolin-8-yl)butanamide (2k)

Following the general procedure, orange liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 8.91 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.09 – 8.03 (m, 1H), 7.85 – 7.79 (m, 1H), 7.69 (p, *J* = 3.1 Hz, 1H), 7.61 – 7.33 (m, 7H), 3.30-3.23 (m, 1H), 3.12-3.05 (m, 1H), 2.58 – 2.47 (m, 1H), 2.36-2.27 (m, 1H), 2.05-1.96 (m, 1H), 1.92 – 1.81 (m, 1H), 1.70 – 1.63 (m, 1H), 1.01 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.41, 148.16, 138.42, 138.00, 136.41, 134.44, 133.88, 131.80, 128.68, 127.98, 127.48, 126.69, 126.16, 125.83, 125.53, 125.43, 123.88, 121.59, 121.49, 116.63, 50.64, 33.75, 31.11, 26.55, 12.04.

HRMS calcd for $C_{25}H_{24}N_2O$ ($M+H^+$): 369.1961, Found: 369.1959.



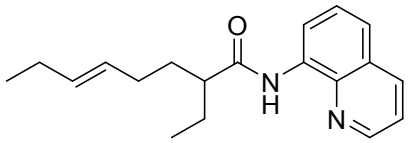
2-ethyl-N-(quinolin-8-yl)oct-7-enamide (2l)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.87 – 8.79 (m, 2H), 8.16 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.57 – 7.43 (m, 3H), 5.77 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.02 – 4.82 (m, 2H), 2.45 – 2.34 (m, 1H), 1.85-1.76 (m, 2H), 1.88 – 1.75 (m, 2H), 1.69 – 1.60 (m, 2H), 1.47 – 1.37 (m, 4H), 1.00 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.85, 148.15, 138.90, 138.44, 136.38, 134.51, 127.96, 127.48, 121.57, 121.35, 116.50, 114.33, 50.97, 33.61, 32.72, 29.02, 27.14, 26.27, 12.13.

HRMS calcd for $C_{19}H_{24}N_2O$ ($M+H^+$): 297.1961, Found: 297.1965.



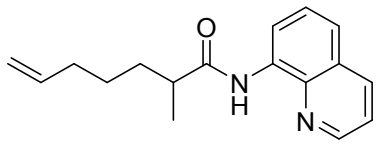
(E)-2-ethyl-N-(quinolin-8-yl)oct-5-enamide (2m)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.89 – 8.77 (m, 2H), 8.16 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.57 – 7.43 (m, 3H), 5.56 – 5.33 (m, 2H), 2.46-2.38 (m, 1H), 2.14-1.79 (m, 6H), 1.67-1.61 (m, 2H), 1.00 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.76, 148.12, 138.43, 136.36, 134.51, 133.08, 128.27, 127.96, 127.48, 121.56, 121.35, 116.49, 50.12, 32.64, 30.56, 26.29, 25.57, 13.88, 12.11.

HRMS calcd for $C_{19}H_{24}N_2O$ ($M+H^+$): 297.1961, Found: 297.1960.



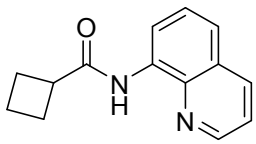
2-methyl-N-(quinolin-8-yl)hept-6-enamide (2n)

Following the general procedure, orange liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.78 – 8.70 (m, 2H), 8.09 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.50 – 7.35 (m, 3H), 5.73 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 4.97 – 4.84 (m, 2H), 2.54 (dt, *J* = 13.7, 6.9 Hz, 1H), 2.07 – 1.99 (m, 2H), 1.85 – 1.74 (m, 1H), 1.55 – 1.42 (m, 3H), 1.26 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.30, 148.10, 138.51, 138.43, 136.38, 134.55, 127.94, 127.45, 121.54, 121.33, 116.48, 114.67, 42.89, 33.94, 33.75, 26.73, 18.00.

HRMS calcd for $C_{17}H_{20}N_2O$ ($M+H^+$): 269.1648, Found: 269.1646.



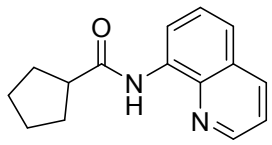
N-(quinolin-8-yl)cyclobutanecarboxamide (2o)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 8.86 – 8.73 (m, 2H), 8.15 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.59 – 7.41 (m, 3H), 3.46 – 3.34 (m, 1H), 2.57 – 2.42 (m, 2H), 2.37-2.29 (m, 2H), 2.11 – 1.94 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.78, 148.10, 138.41, 136.40, 134.58, 127.96, 127.48, 121.56, 121.30, 116.41, 41.40, 25.51, 18.18.

HRMS calcd for $C_{14}H_{14}N_2O$ ($M+H^+$): 227.1179, Found: 227.1178.



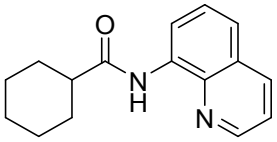
N-(quinolin-8-yl)cyclopentanecarboxamide (2p)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.84 – 8.74 (m, 2H), 8.16 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.57 – 7.40 (m, 3H), 3.02 – 2.88 (m, 1H), 2.11-1.94 (m, 4H), 1.88 – 1.79 (m, 2H), 1.72-1.64 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.11, 148.01, 138.30, 136.41, 134.67, 127.92, 127.46, 121.50, 121.19, 116.38, 47.37, 30.59, 25.99.

HRMS calcd for $C_{15}H_{16}N_2O$ (M+H$^+$): 241.1335, Found: 241.1337.



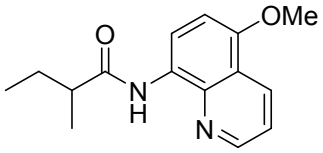
N-(quinolin-8-yl)cyclohexanecarboxamide (2q)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.85 – 8.75 (m, 2H), 8.16 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.61 – 7.39 (m, 3H), 2.53-2.45 (m, 1H), 2.15 – 2.02 (m, 2H), 1.94 – 1.83 (m, 2H), 1.75 – 1.61 (m, 3H), 1.48 – 1.20 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.93, 148.07, 138.45, 136.44, 134.63, 127.96, 127.49, 121.54, 121.26, 116.48, 46.91, 29.77, 25.79, 25.76.

HRMS calcd for $C_{16}H_{18}N_2O$ (M+H$^+$): 255.1492, Found: 255.1495.



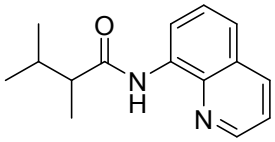
N-(5-methoxyquinolin-8-yl)-2-methylbutanamide (2r)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.73 (d, *J* = 8.5 Hz, 1H), 8.57 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.44 (dd, *J* = 8.4, 4.2 Hz, 1H), 6.84 (d, *J* = 8.6 Hz, 1H), 3.99 (s, 3H), 2.57 – 2.45 (m, 1H), 1.94 – 1.80 (m, 1H), 1.67 – 1.55 (m, 1H), 1.32 (d, *J* = 6.9 Hz, 3H), 1.01 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.92, 150.13, 148.58, 139.17, 131.27, 128.08, 120.65, 120.46, 116.58, 104.43, 55.78, 44.50, 27.55, 17.61, 11.98.

HRMS calcd for $C_{15}H_{18}N_2O_2$ (M+H$^+$): 259.1441, Found: 259.1439.



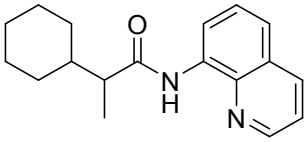
2,3-dimethyl-N-(quinolin-8-yl)butanamide (2s)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.85 – 8.77 (m, 2H), 8.16 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.58 – 7.41 (m, 3H), 2.40 – 2.27 (m, 1H), 2.09-2.01 (m, 1H), 1.31 (d, *J* = 6.9 Hz, 3H), 1.05-1.02 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.23, 148.14, 138.46, 136.40, 134.57, 127.96, 127.49, 121.56, 121.31, 116.45, 49.95, 31.75, 21.18, 19.62, 14.99.

HRMS calcd for $C_{15}H_{18}N_2O$ (M+H$^+$): 243.1492, Found: 243.1490.



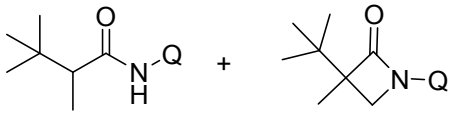
2-cyclohexyl-N-(quinolin-8-yl)propanamide (2t)

Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.87 – 8.77 (m, 2H), 8.16 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.59 – 7.41 (m, 3H), 2.41 – 2.31 (m, 1H), 1.96-1.88 (m, 1H), 1.84 – 1.74 (m, 2H), 1.71-1.64 (m, 3H), 1.34 – 1.24 (m, 6H), 1.13 – 0.97 (m, 2H).

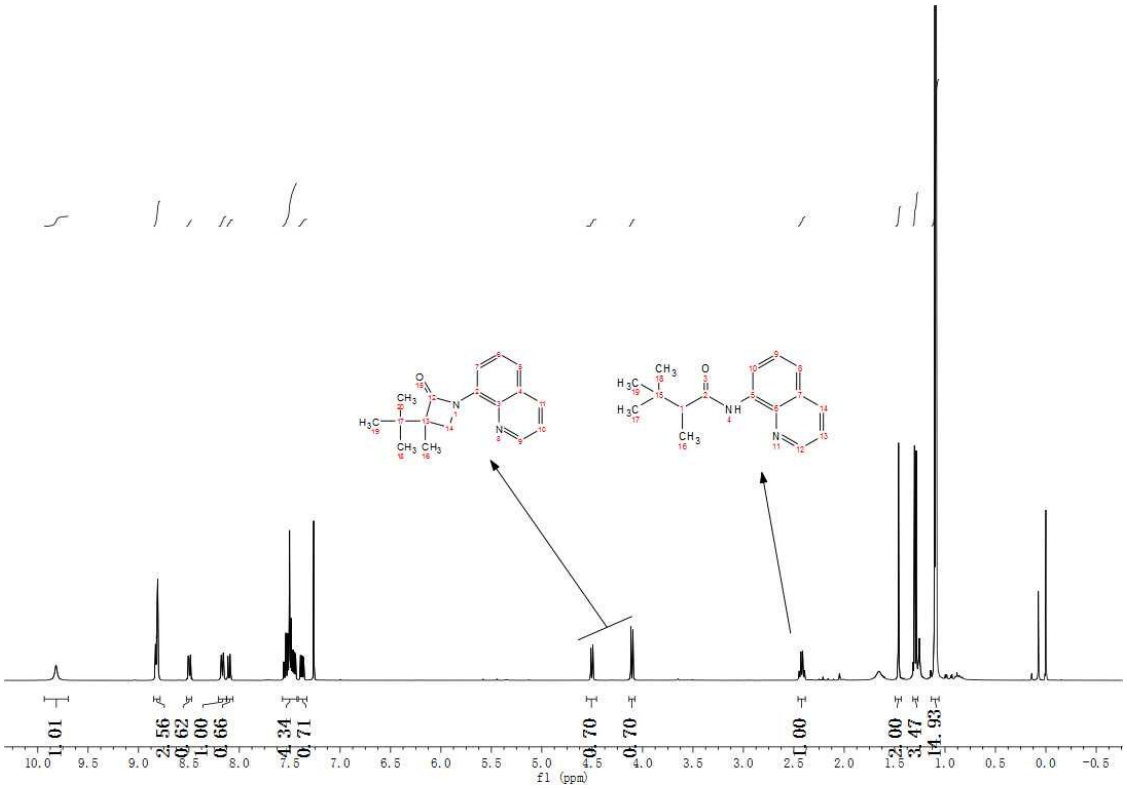
^{13}C NMR (101 MHz, $CDCl_3$) δ 175.33, 148.12, 138.42, 136.43, 134.53, 127.97, 127.50, 121.56, 121.32, 116.47, 49.17, 41.31, 31.52, 30.02, 26.40, 26.34, 26.29, 15.03.

HRMS calcd for $C_{18}H_{22}N_2O$ ($M+H^+$): 283.1805, Found: 283.1804.

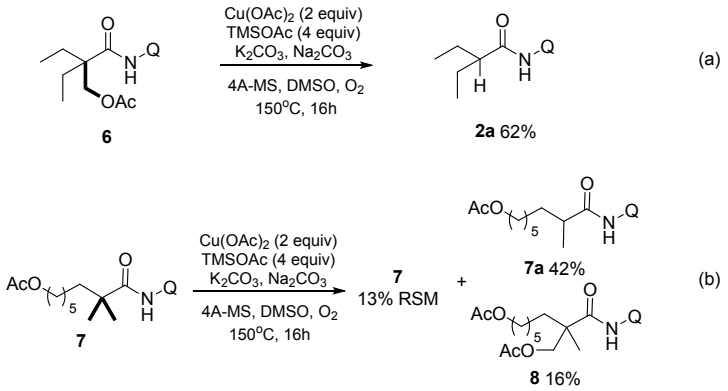


2u 25% **2u'** 17%

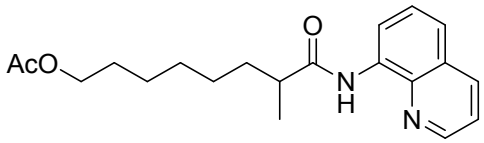
2u and **2u'** were isolated as an inseparable yellow oil (42%). The yields were determined by ^{1}H NMR analysis in comparision with literature reports (**2u**[1] : **2u'**[4] = 1 : 0.7). **2u** ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.85 – 8.79 (m, 2H), 8.17 (d, J = 8.2 Hz, 1H), 7.57 – 7.43 (m, 3H), 2.42 (q, J = 7.0 Hz, 1H), 1.29 (d, J = 7.0 Hz, 3H), 1.09 (s, 9H). **2u'** ^{1}H NMR (400 MHz, CDCl3) δ 8.84 – 8.81 (m, 1H), 8.53 – 8.47 (m, 1H), 8.10 (dd, J = 8.3, 1.8 Hz, 1H), 7.56 – 7.42 (m, 2H), 7.40-7.35 (m, 1H), 4.50 (d, J = 8.0 Hz, 1H), 4.11 (d, J = 8.0 Hz, 1H), 1.46 (s, 3H), 1.10 (s, 9H).



General procedure for examples described in scheme 2



General procedure for example described in **scheme 2a** : To a 15 mL Schlenk tube $Cu(OAc)_2$ (36.2 mg, 0.20 mmol), K_2CO_3 (27.6 mg, 0.2 mmol), Na_2CO_3 (10.6 mg, 0.1 mmol), propionamide **6** (0.10 mmol), 4A-MS (30 mg) and a stir bar were added. The vessel was then evacuated and filled with O_2 (three cycles). TMSOAc (0.40 mmol) and DMSO (1.0 mL) were added in turn under O_2. The reaction mixture was stirred at 150°C for 16h. After that, the reaction mixture was diluted with EtOAc, filtered through silica gel with copious washings (EtOAc), concentrated, and purified by column chromatography (EtOAc/hexane = 1/100 to 1/50, v/v) to give **2a** in 62% yield.
General procedure for example described in **scheme 2b** : To a 15 mL Schlenk tube $Cu(OAc)_2$ (36.2 mg, 0.20 mmol), K_2CO_3 (27.6 mg, 0.2 mmol), Na_2CO_3 (10.6 mg, 0.1 mmol), propionamide **7** (0.10 mmol), 4A-MS (30 mg) and a stir bar were added. The vessel was then evacuated and filled with O_2 (three cycles). TMSOAc (0.40 mmol) and DMSO (1.0 mL) were added in turn under O_2. The reaction mixture was stirred at 150°C for 16h. After that, the reaction mixture was diluted with EtOAc, filtered through silica gel with copious washings (EtOAc), concentrated, and purified by column chromatography (EtOAc/hexane = 1/100 to 1/50, v/v).



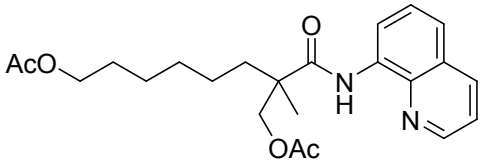
7-methyl-8-oxo-8-(quinolin-8-ylamino)octyl acetate (7a)

Following the general procedure, orange liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.85 – 8.78 (m, 2H), 8.17 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.60 – 7.42 (m, 3H), 4.02 (t, *J* = 6.7 Hz, 2H), 2.67 – 2.54 (m, 1H), 2.02 (s, 3H), 1.90 – 1.80 (m, 1H), 1.65 – 1.53 (m, 3H), 1.42 – 1.30 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.36, 171.20, 148.08, 138.39, 136.42, 134.53, 127.94, 127.46, 121.54, 121.33, 116.50, 64.53, 42.98, 34.38, 29.27, 28.52, 27.33, 25.77, 20.97, 18.04.

HRMS calcd for $C_{20}H_{26}N_2O_3$ ($M+H^+$): 343.2016, found: 343.2014.

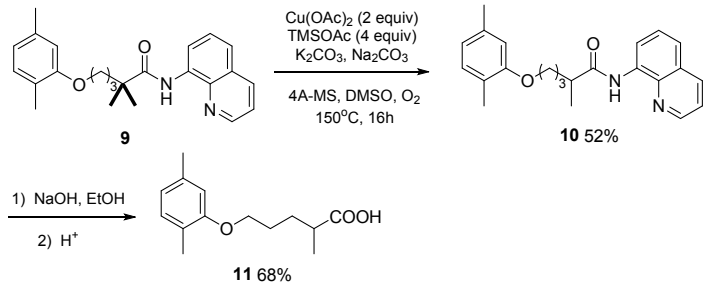


2-methyl-2-(quinolin-8-ylcarbamoyl)octane-1,8-diyl diacetate (8)

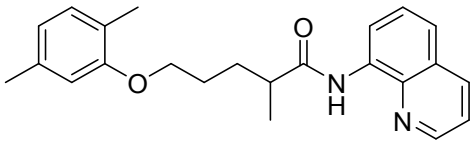
Following the general procedure, yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.44 (s, 1H), 8.84 – 8.77 (m, 2H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58 – 7.44 (m, 3H), 4.37 (d, *J* = 11.1 Hz, 1H), 4.21 (d, *J* = 11.1 Hz, 1H), 4.00 (t, *J* = 6.7 Hz, 2H), 2.15 (s, 3H), 2.01 (s, 3H), 1.92 – 1.80 (m, 1H), 1.70 – 1.51 (m, 3H), 1.44 (s, 3H), 1.42 – 1.29 (m, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.51, 171.17, 170.82, 148.18, 138.77, 136.41, 134.55, 128.00, 127.47, 121.61, 121.54, 116.56, 69.45, 64.46, 47.08, 36.69, 29.72, 28.50, 25.71, 24.05, 20.98, 20.93, 19.85.
HRMS calcd for $C_{23}H_{30}N_2O_5$ ($M+H^+$): 415.2227, found: 415.2234.

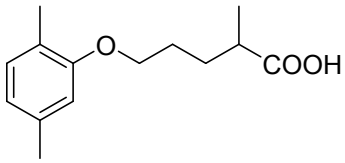
General procedure for examples described in scheme 4



General procedure for examples described in **scheme 4**: To a 15 mL Schlenk tube $Cu(OAc)_2$ (36.2 mg, 0.20 mmol), K_2CO_3 (27.6 mg, 0.2 mmol), Na_2CO_3 (10.6 mg, 0.1 mmol), propionamide **9** (0.10 mmol), 4A-MS (30 mg) and a stir bar were added. The vessel was then evacuated and filled with O_2 (three cycles). TMSOAc (0.40 mmol) and DMSO (1.0 mL) were added in turn under O_2. The reaction mixture was stirred at 150°C for 16h. After that, the reaction mixture was diluted with EtOAc, filtered through silica gel with copious washings (EtOAc), concentrated, and purified by column chromatography (EtOAc/hexane = 1/100 to 1/50, v/v) to give **10** in 52% yield.
Genenral procedure for removal of 8-aminoquinoline [6]: Propionamide **10** (0.3 mmol) and NaOH (1.8 mmol) were heated in 2 mL EtOH for 12h at 100°C. Then the reaction mixture was diluted with water and extracted with ether (20 mL). The aqueous layer was acidified with 3.0 M HCl until pH~2 and extracted with ether (20 mL x 3). The orgaic phases was combined, dried over Na_2SO_4 and evapored to afford the alkyl carboxylic acid **11**.



5-(2,5-dimethylphenoxy)-2-methyl-N-(quinolin-8-yl)pentanamide (10)
Compound **10**, colourless liquid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 8.86 – 8.75 (m, 2H), 8.17 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.58 – 7.42 (m, 3H), 6.98 (d, *J* = 7.4 Hz, 1H), 6.69 – 6.56 (m, 2H), 4.06 – 3.89 (m, 2H), 2.80-2.75 (m, 1H), 2.29 (s, 3H), 2.17 (s, 3H), 2.10 – 1.99 (m, 1H), 1.98 – 1.87 (m, 2H), 1.86 – 1.75 (m, 1H), 1.38 (d, *J* = 6.9 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 175.13, 156.95, 148.05, 138.34, 136.53, 136.45, 134.49, 130.28, 127.98, 127.50, 123.64, 121.56, 121.44, 120.70, 116.66, 112.01, 67.58, 42.64, 31.05, 27.30, 21.38, 18.12, 15.84.
HRMS calcd for $C_{23}H_{26}N_2O_2$ ($M+H^+$): 363.2067, found: 363.2062.



5-(2,5-dimethylphenoxy)-2-methylpentanoic acid (11)

Compound **11**, yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (d, *J* = 7.3 Hz, 1H), 6.66 (d, *J* = 7.5 Hz, 1H), 6.62 (s, 1H), 3.96 (dt, *J* = 5.8, 3.8 Hz, 2H), 2.64 – 2.51 (m, 1H), 2.31 (s, 3H), 2.17 (s, 3H), 1.93 – 1.80 (m, 3H), 1.74 – 1.63 (m, 1H), 1.24 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 181.88, 156.90, 136.48, 130.32, 123.62, 120.75, 111.94, 67.37, 38.93, 30.15, 27.03, 21.40, 16.98, 15.78.

HRMS calcd for $C_{14}H_{20}O_3$ (M - H^+): 235.1328, found: 235.1335.

IV. References

[1] X. Wu, K. Yang, Y. Zhao, H. Sun, G. Li, H. Ge, *Nat. Chem.* **2015**, *6*, 1-10.

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[3] M. Li, Y. Yang, D. Zhou, D. Wan, J. You, *Org. Lett.* **2015**, *17*, 2546-2549.

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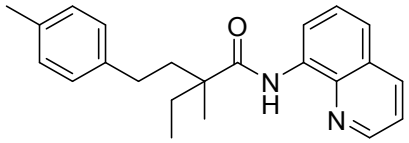
V. NMR Spetra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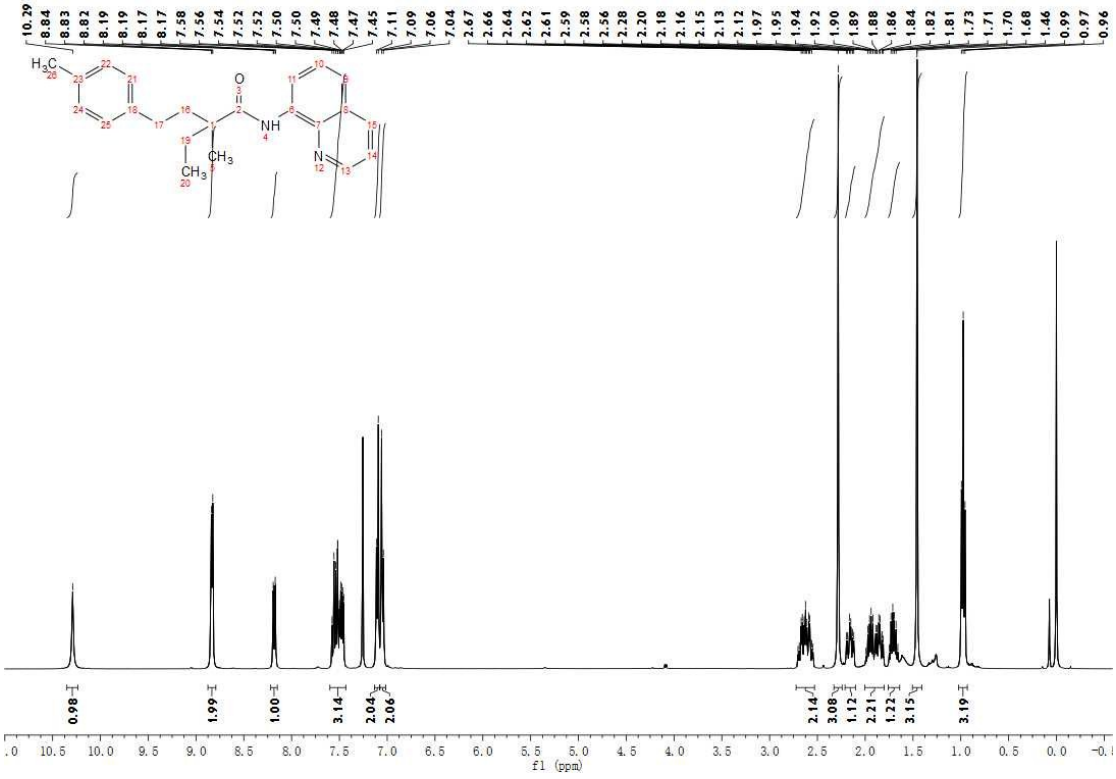
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1.99
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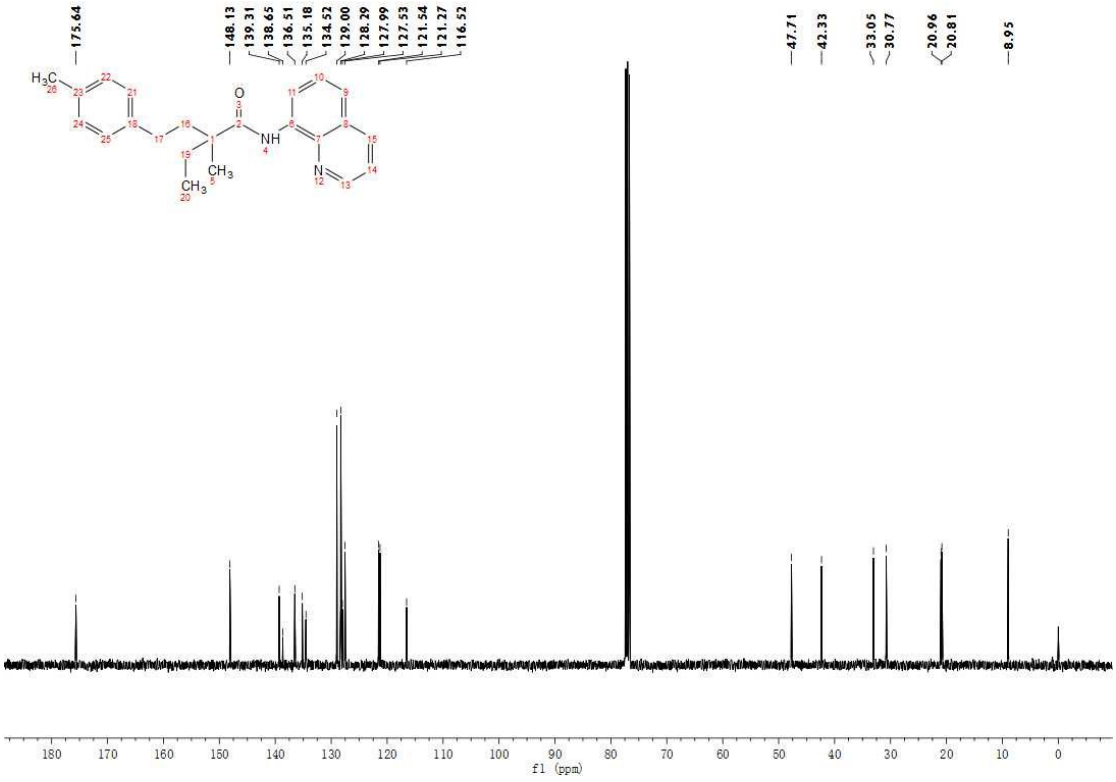
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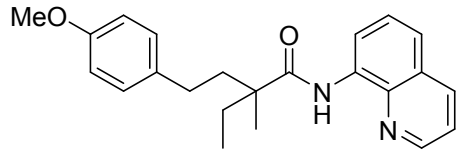
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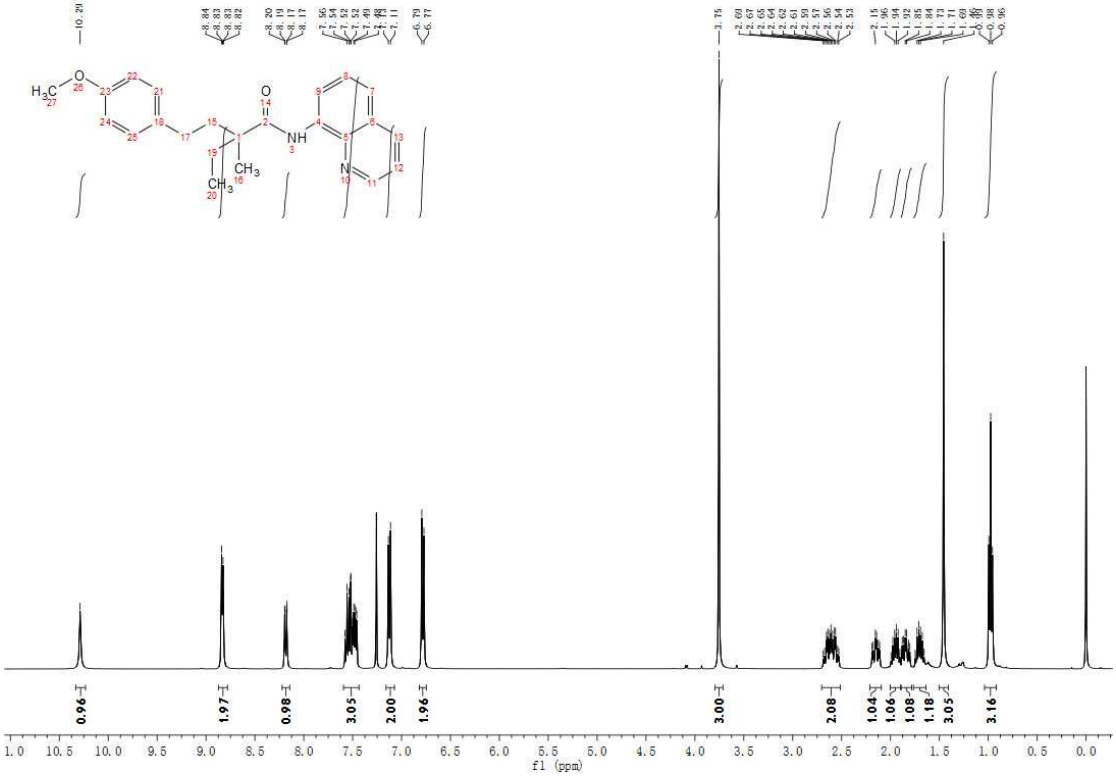
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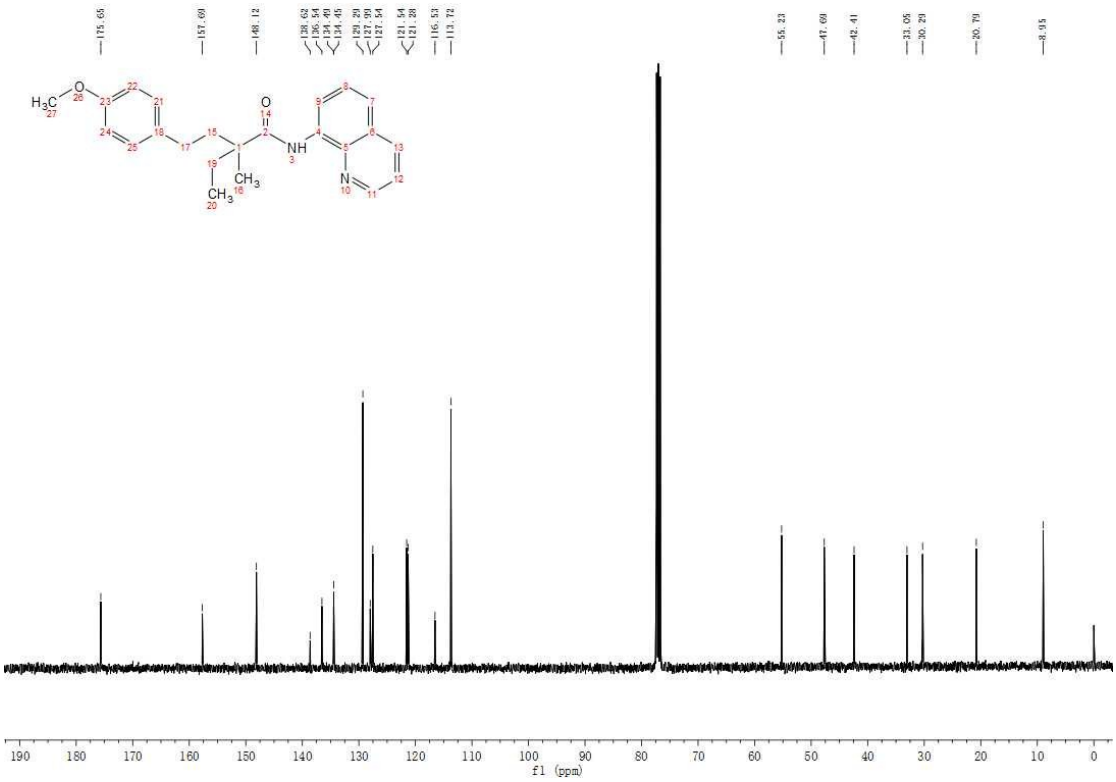
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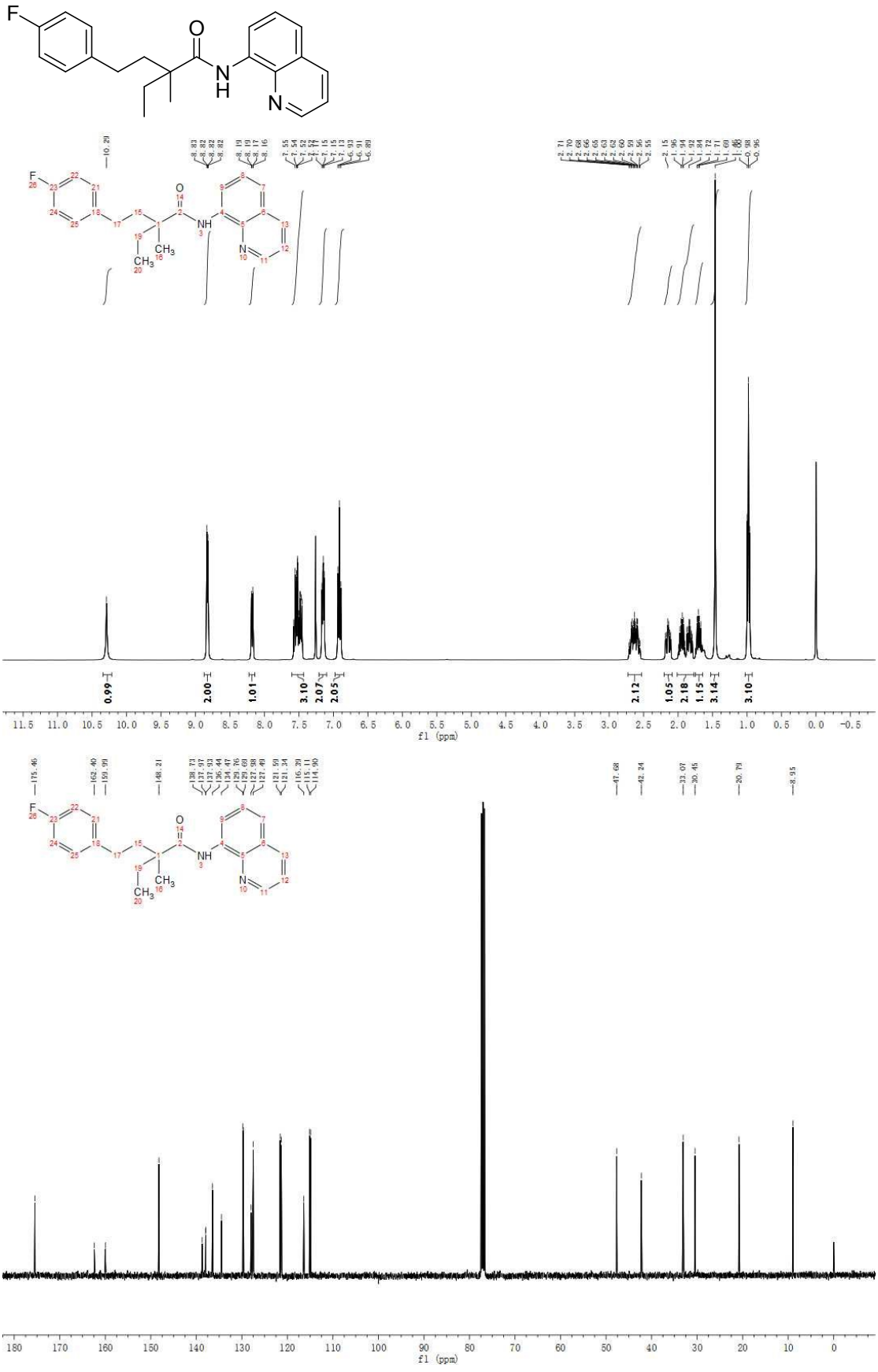
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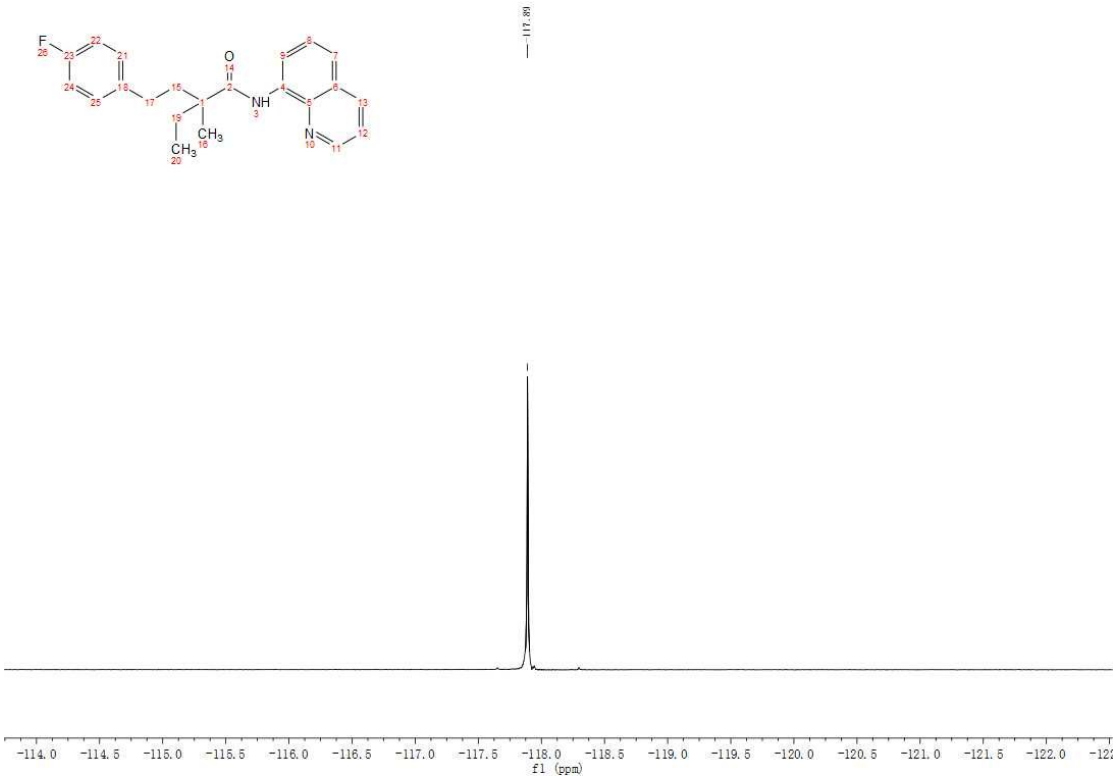
f1 (ppm)
f1 (ppm)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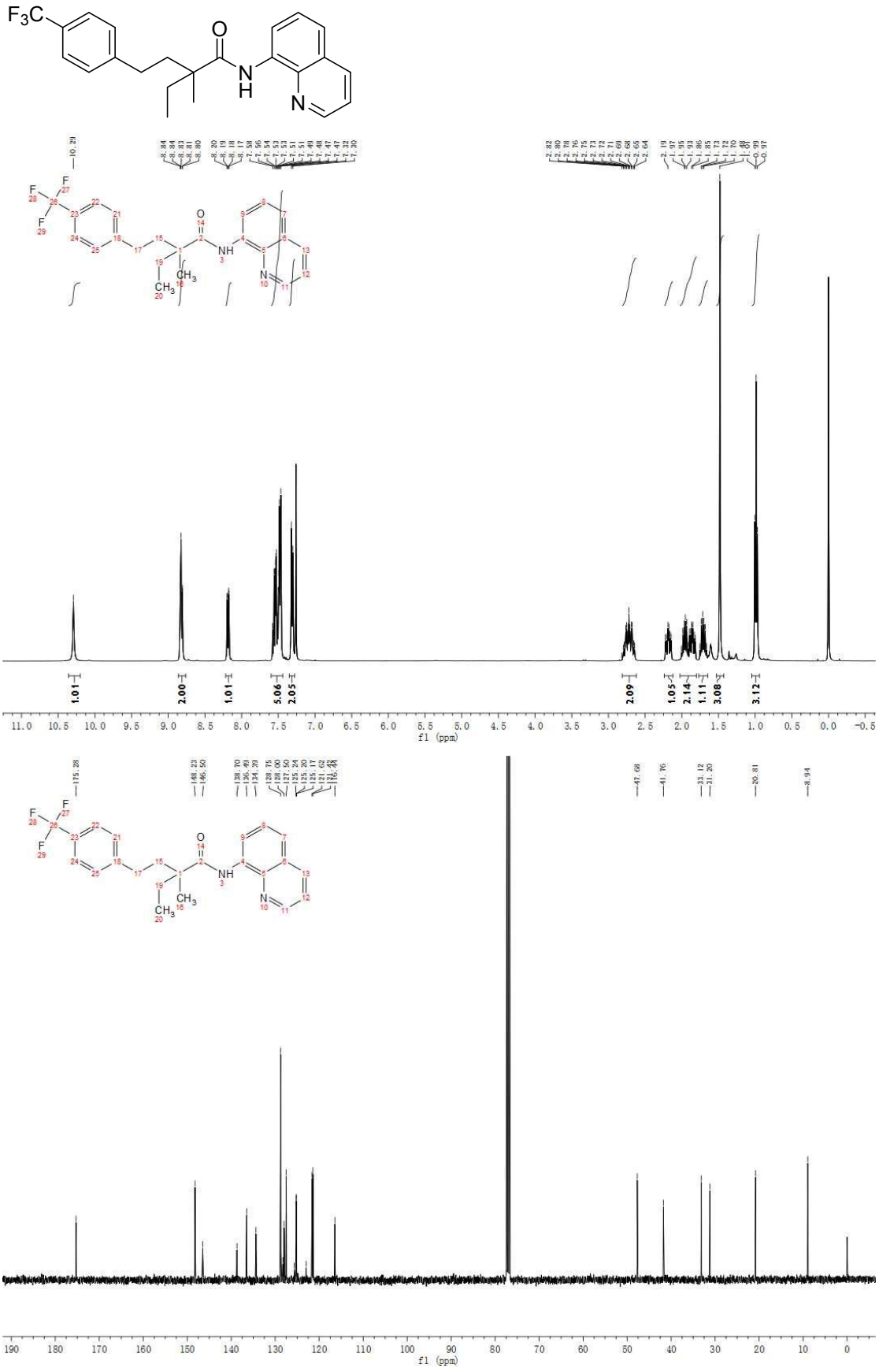

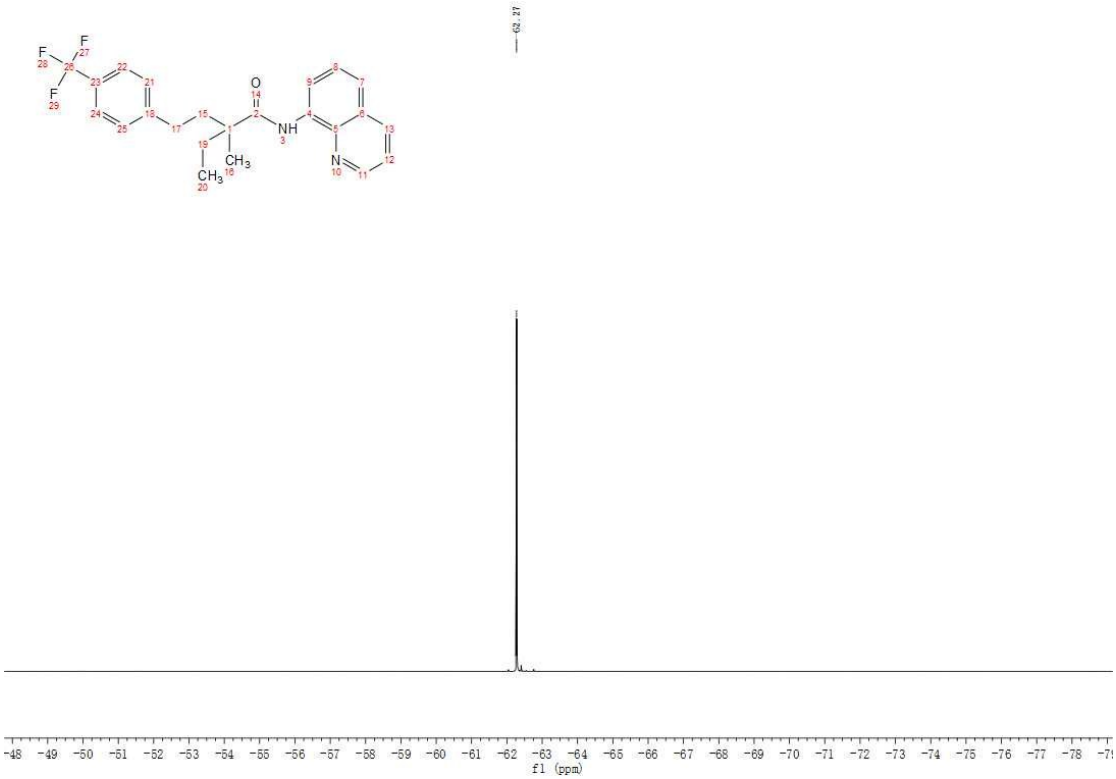
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F
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CH3
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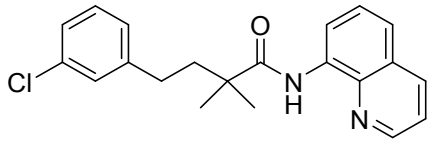
f1 (ppm)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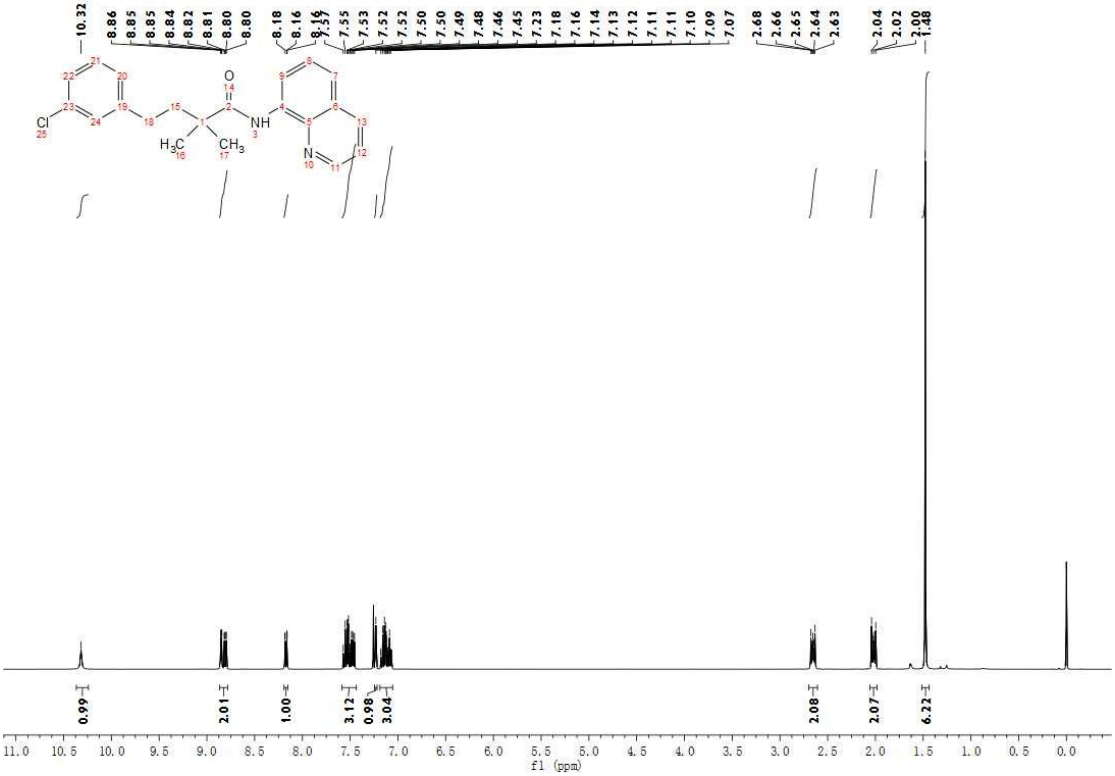
H
N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2.07
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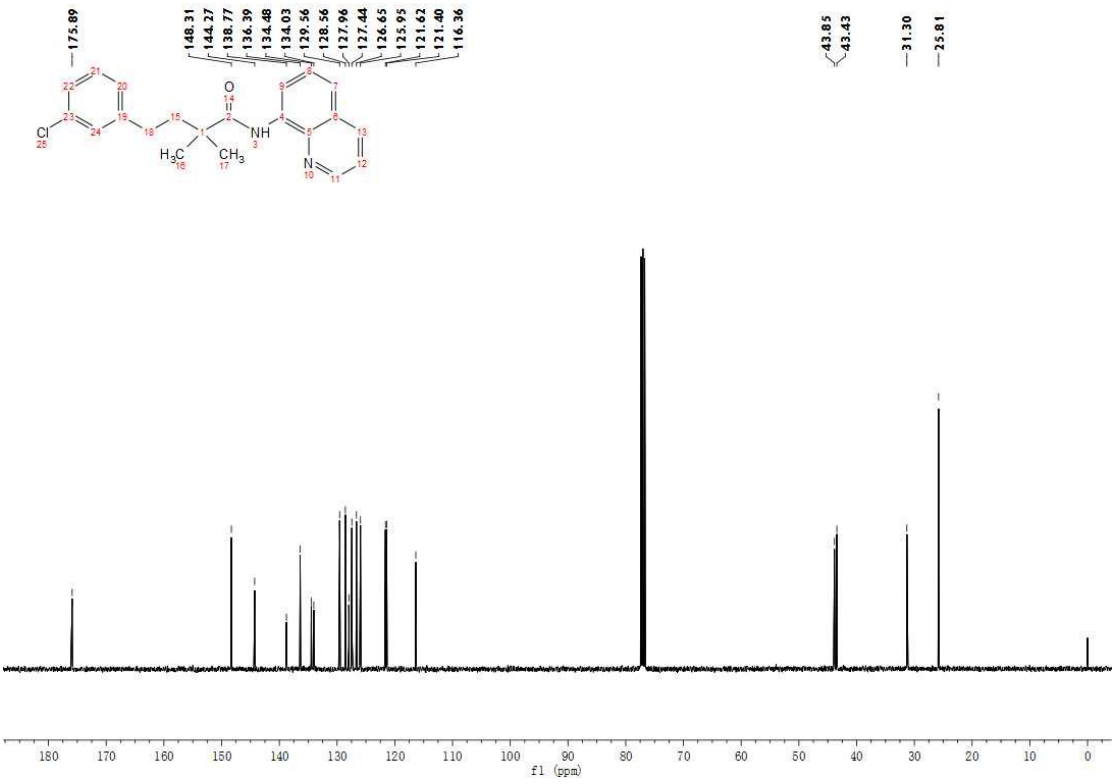
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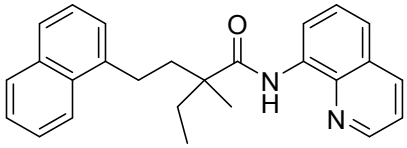
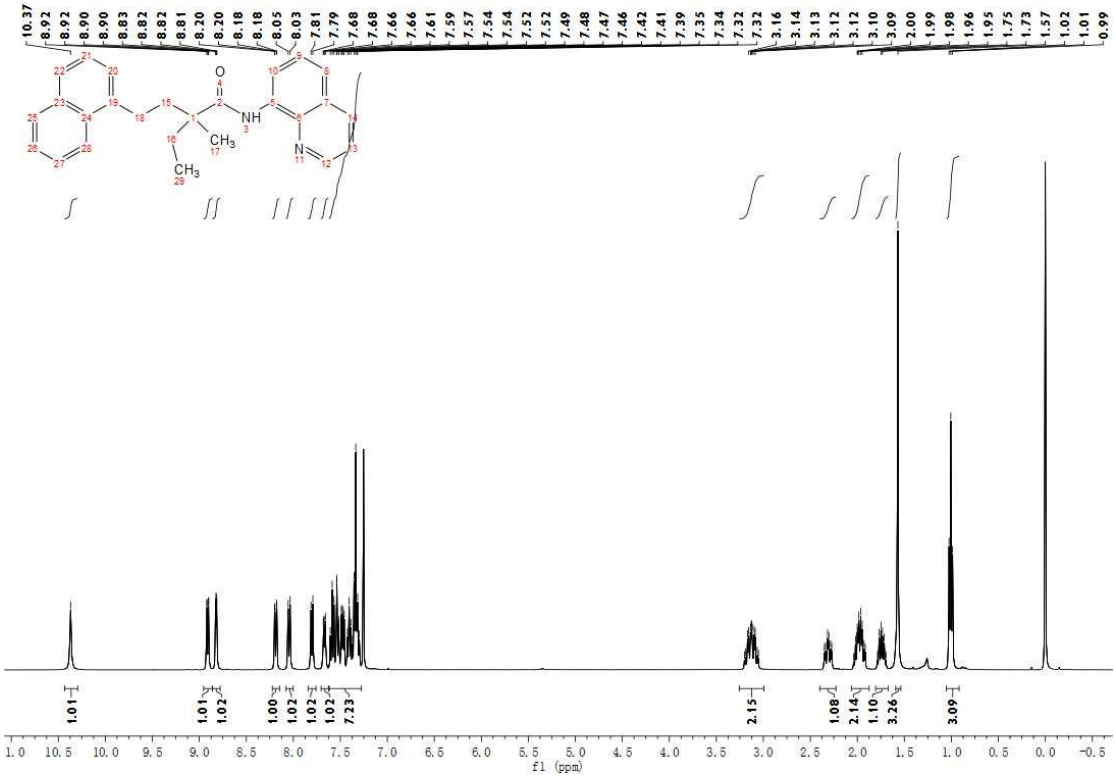
43.43
31.30
25.81
f1 (ppm)


O
N
H
N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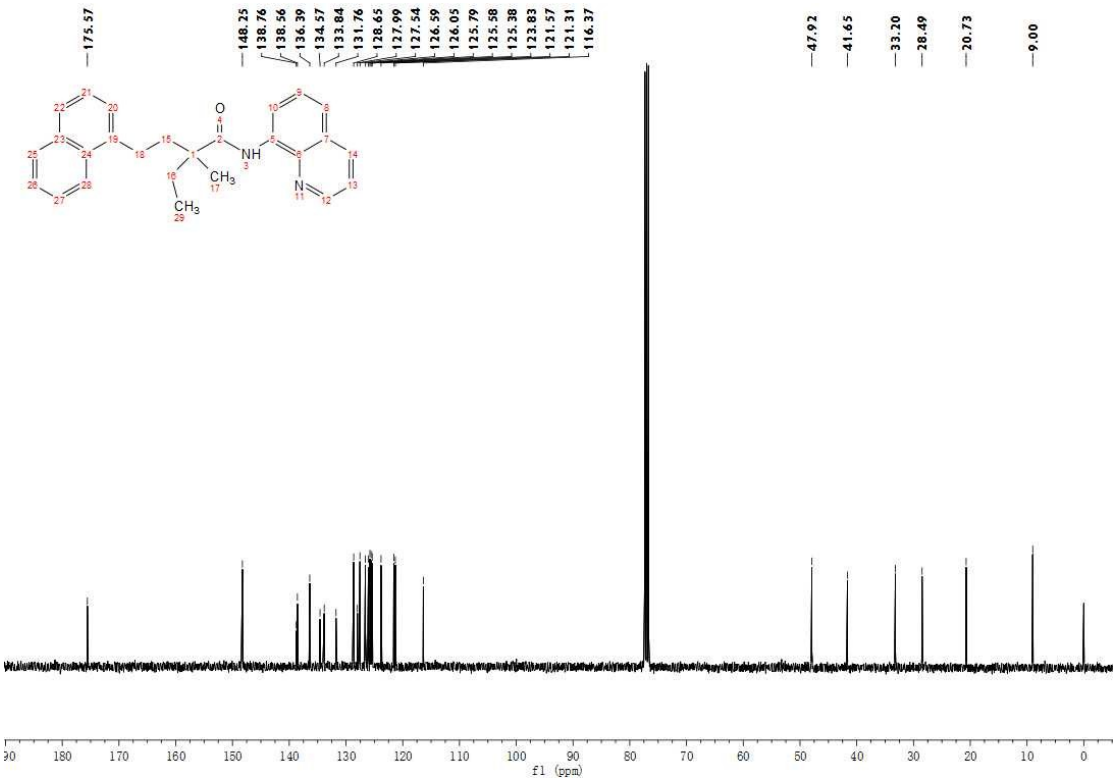
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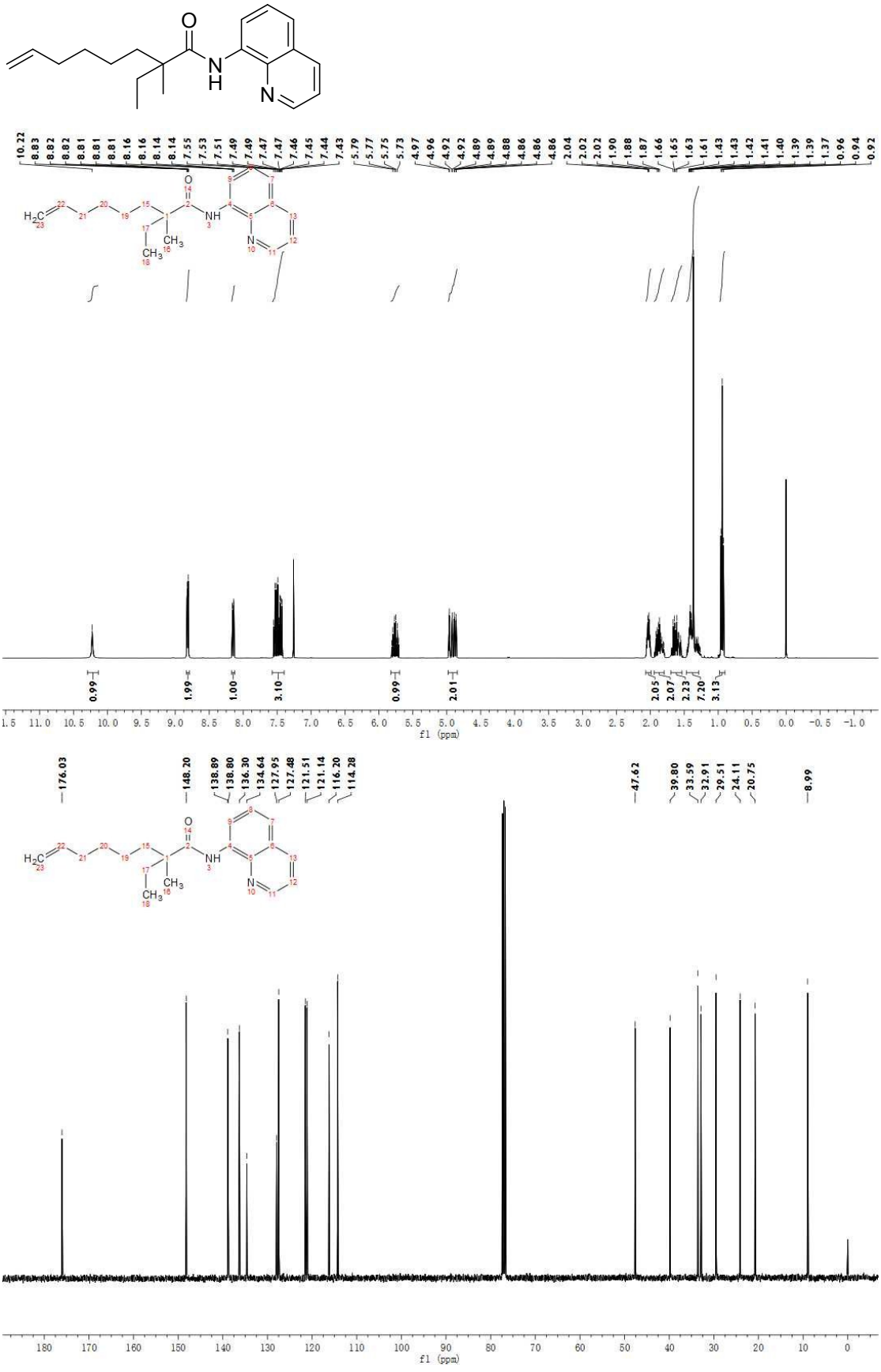

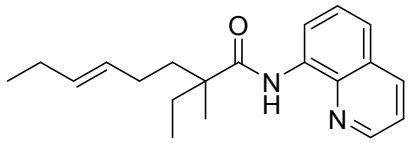

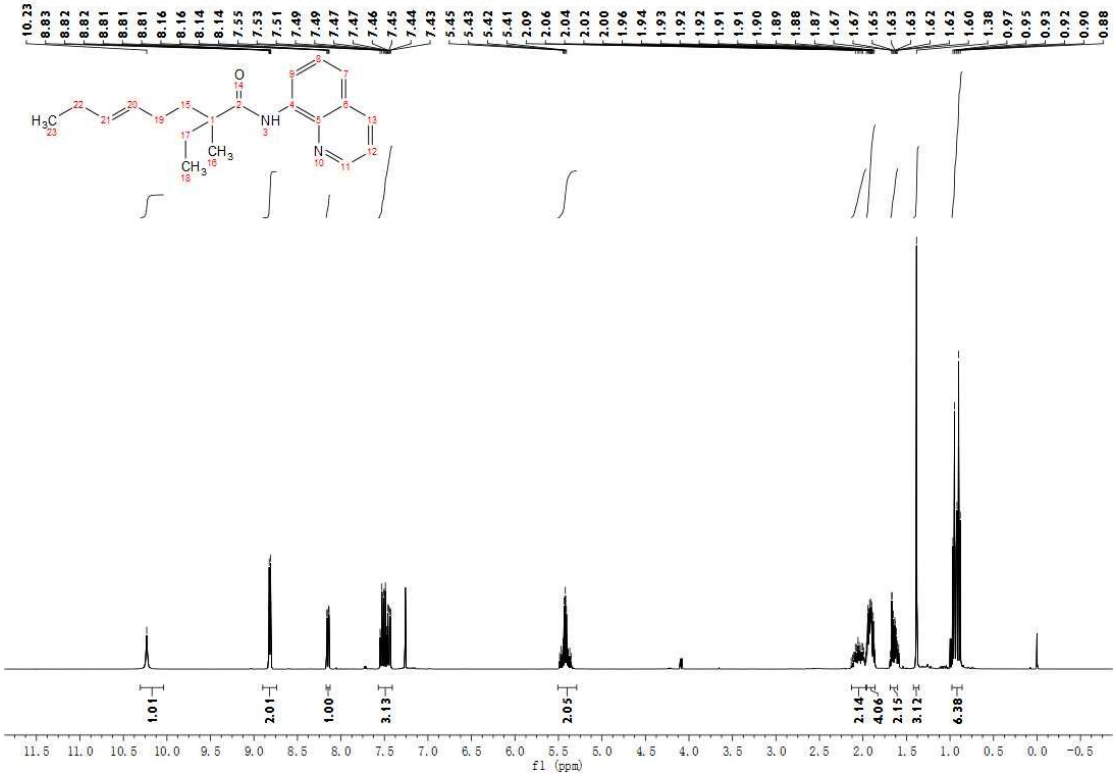
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5.45 5.43 5.42 5.41 2.09 2.06 2.04 2.02 2.00 1.96 1.94 1.93 1.92 1.92 1.91 1.91 1.90 1.89 1.88 1.87 1.67 1.67 1.65 1.63 1.63 1.62 1.62 1.60 1.38 0.97 0.95 0.93 0.92 0.90 0.88
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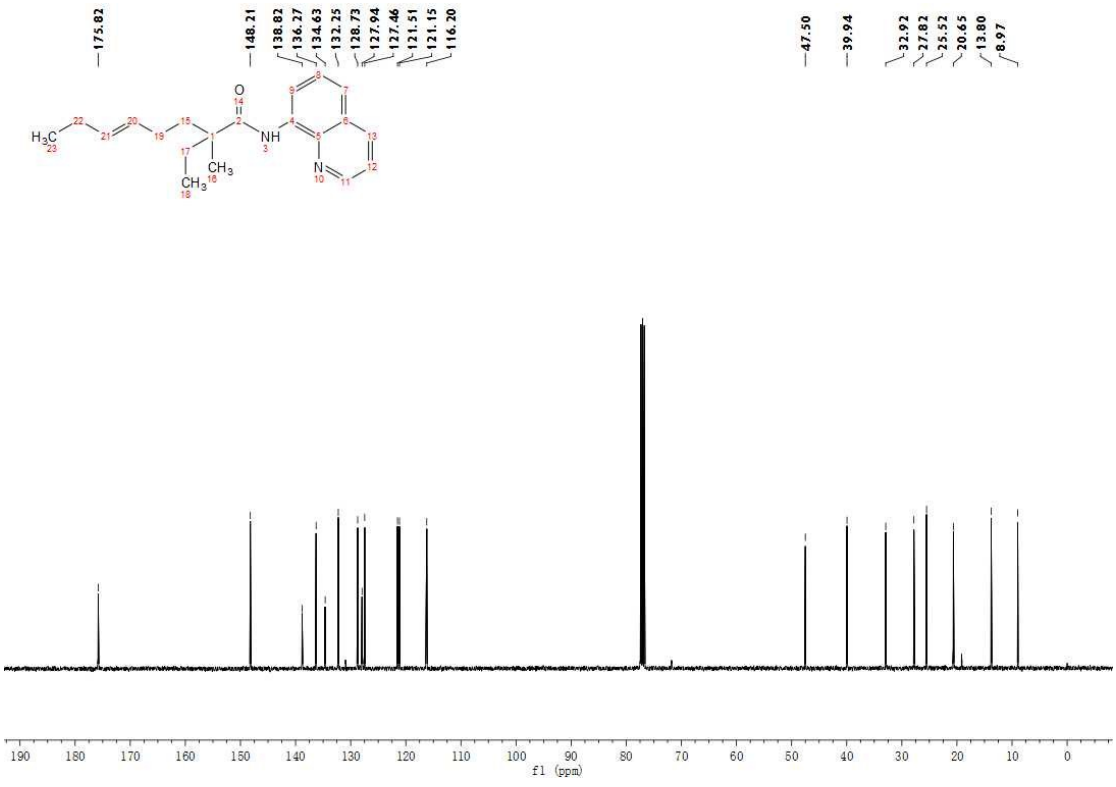
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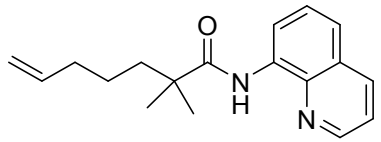

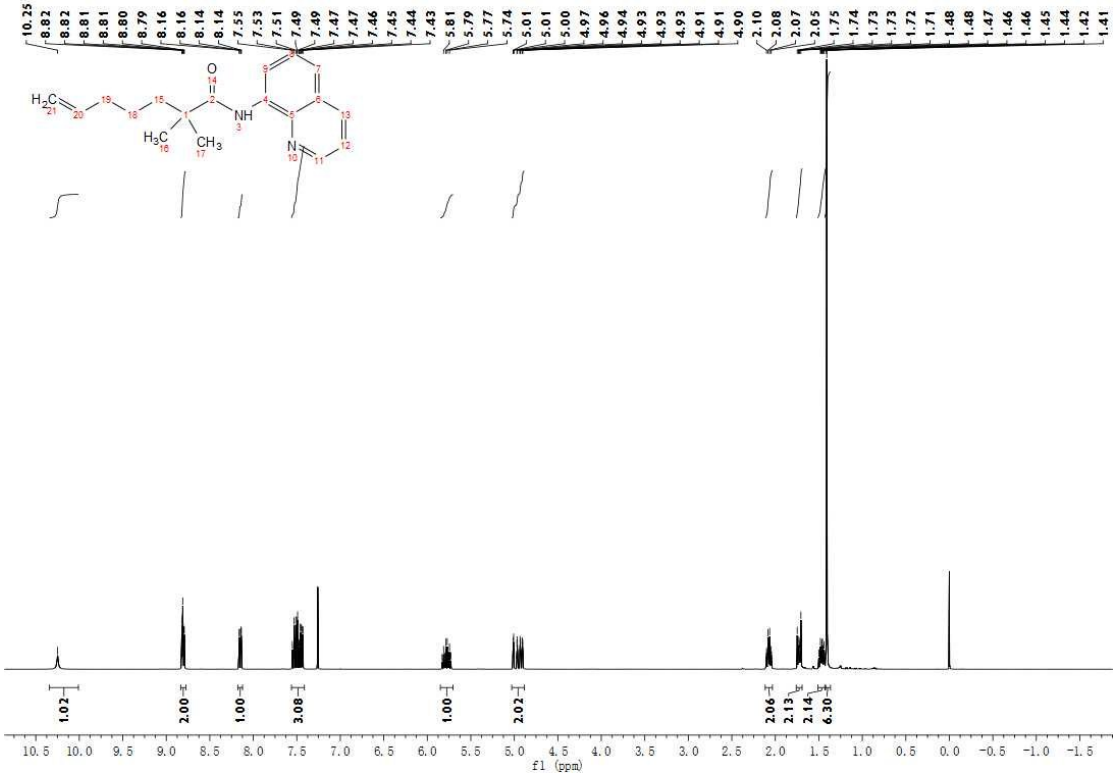
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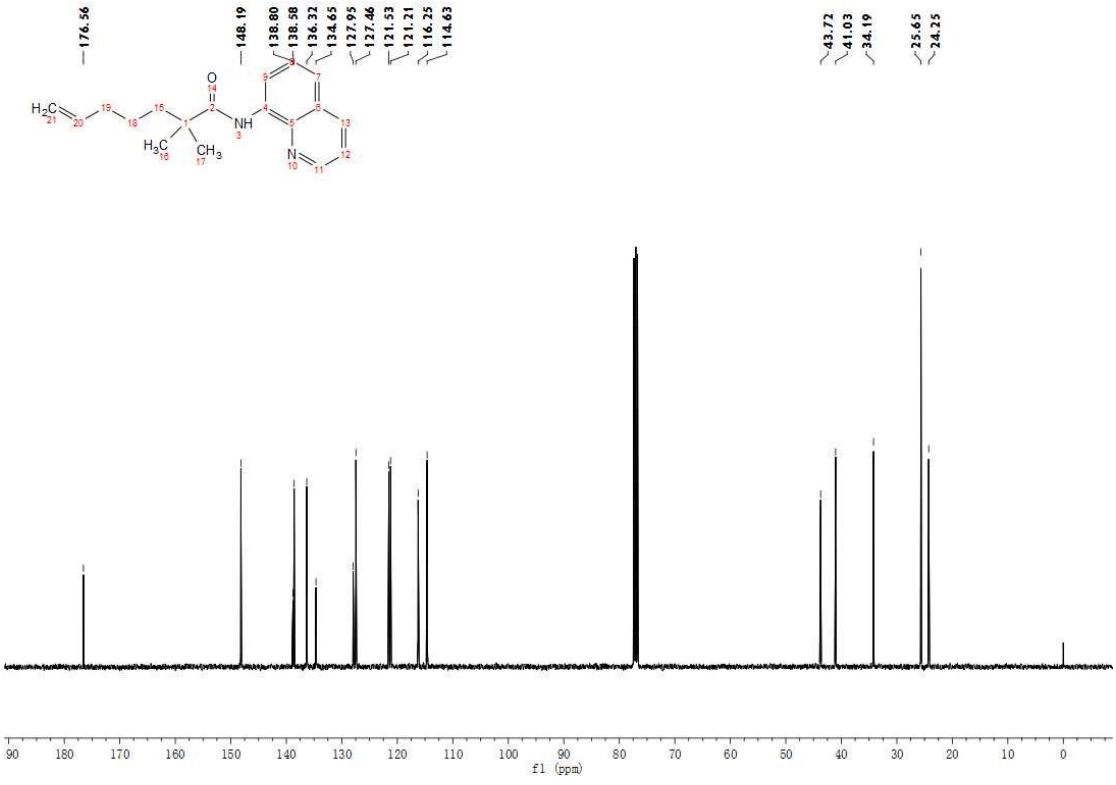
f1 (ppm)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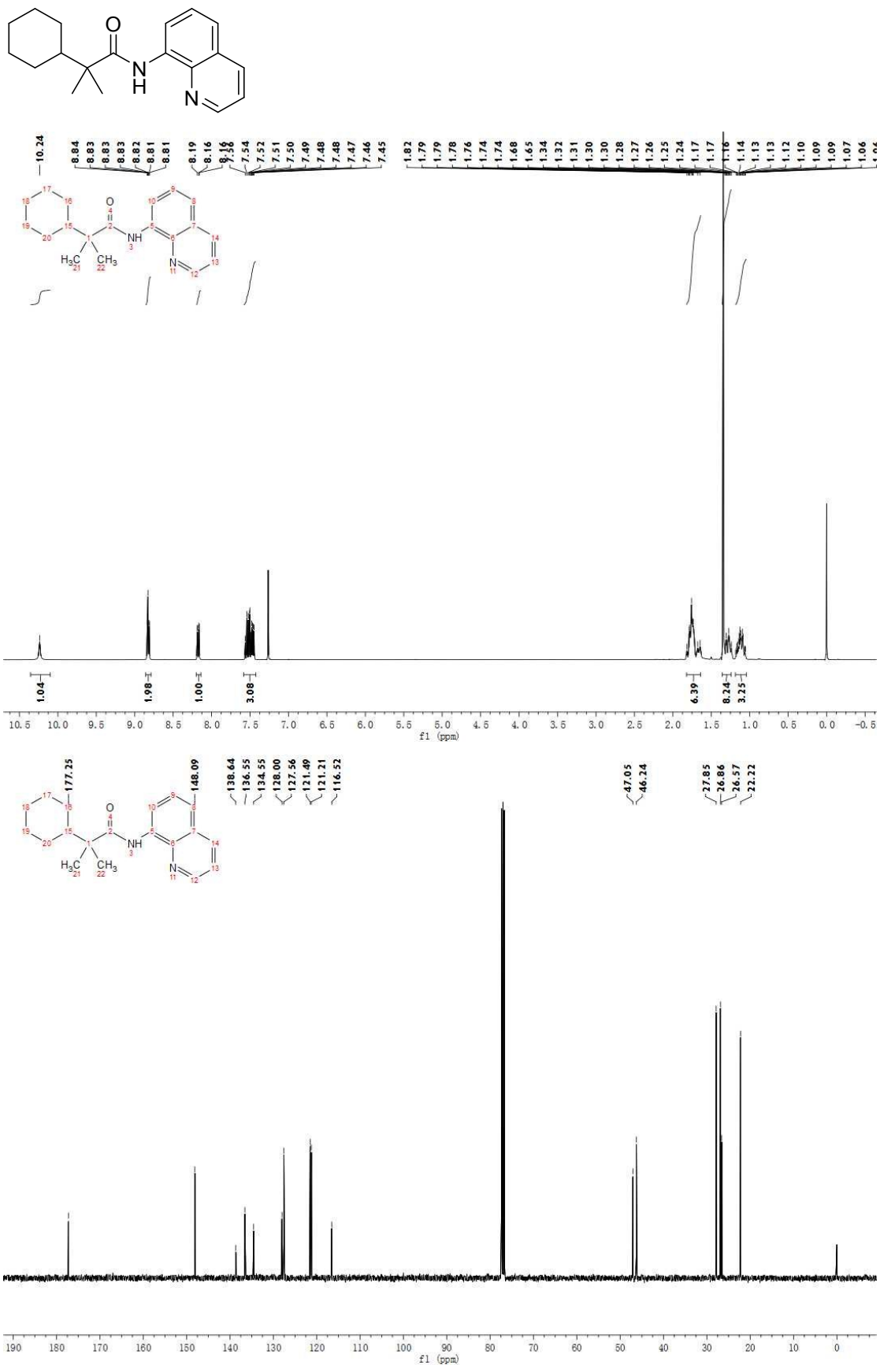

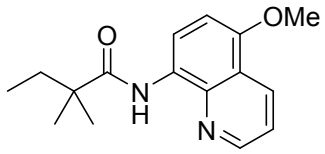
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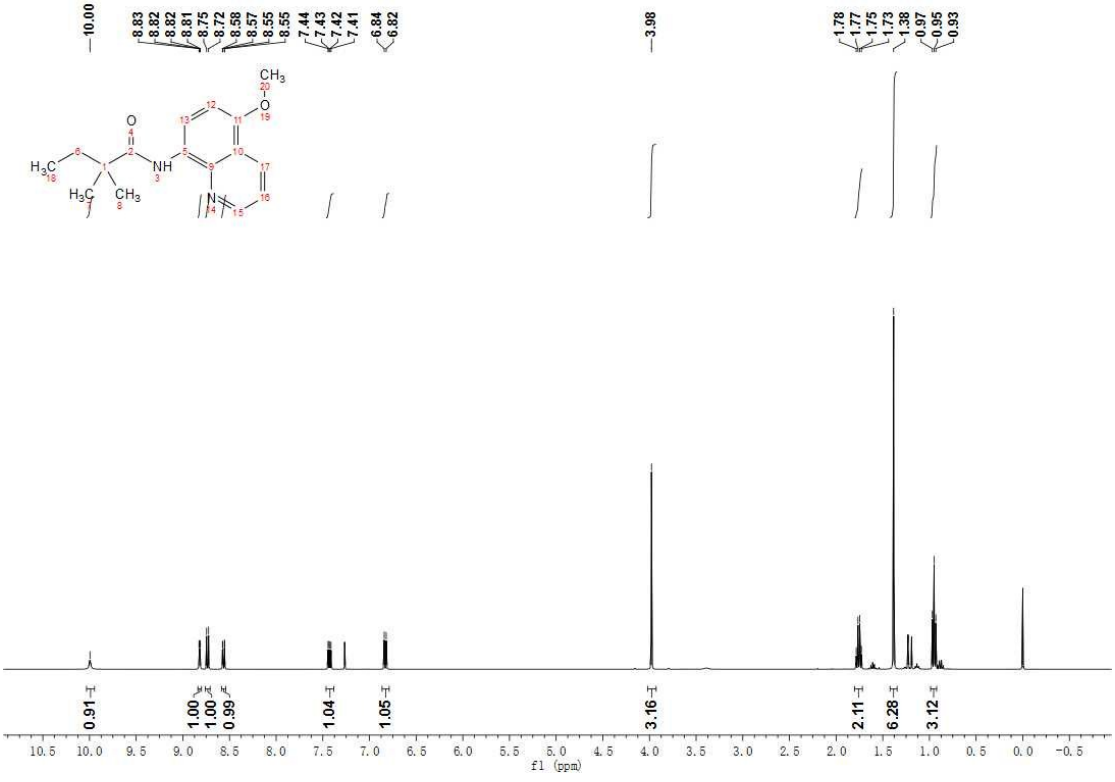
H
N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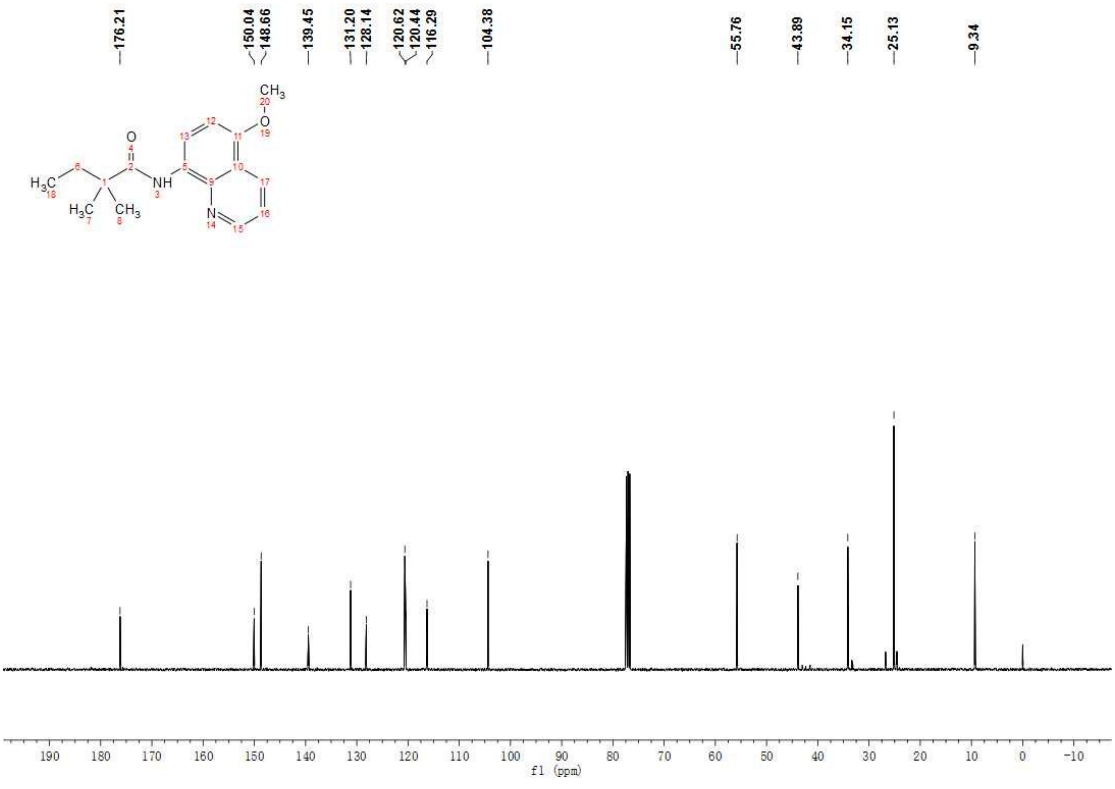
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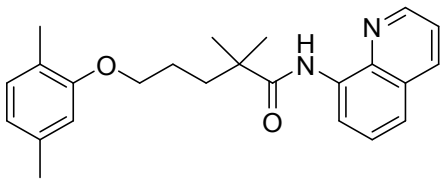
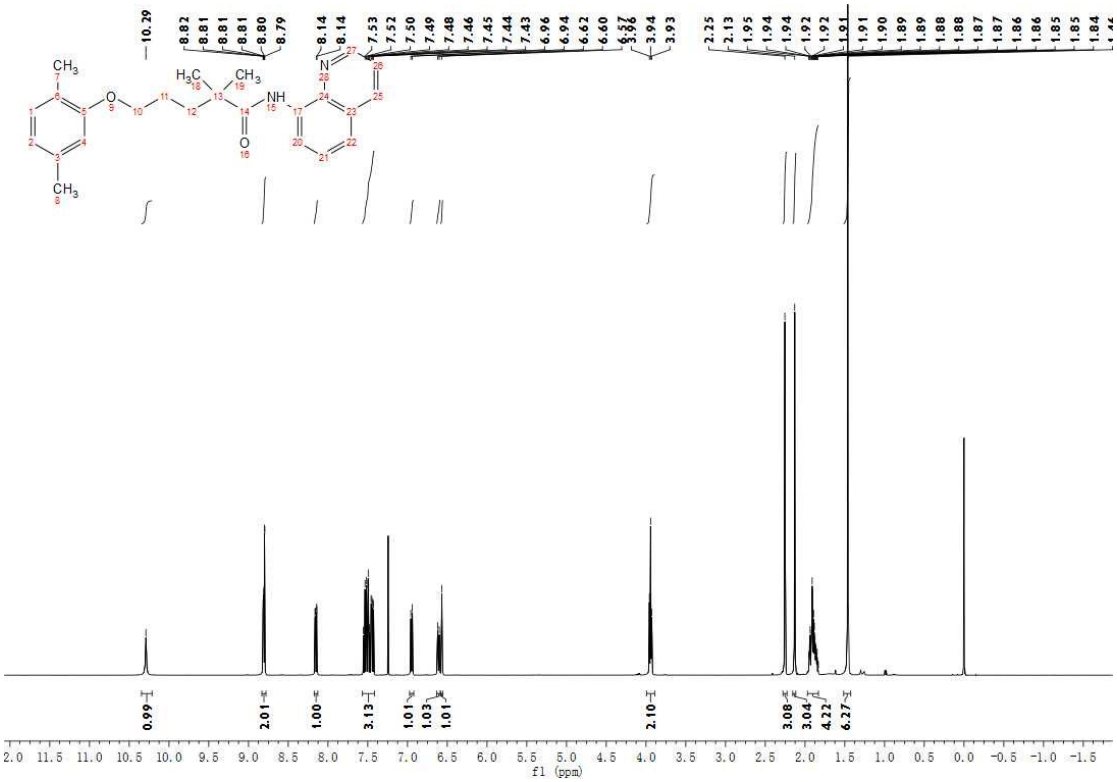
9.34
f1 (ppm)

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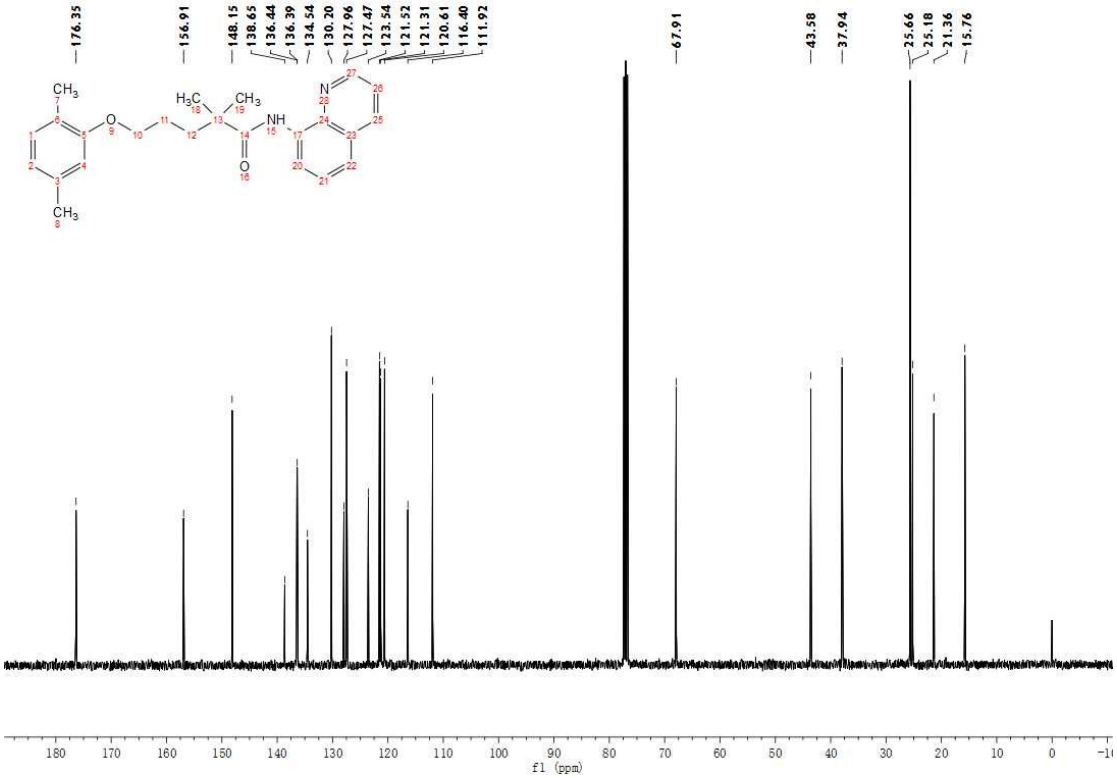
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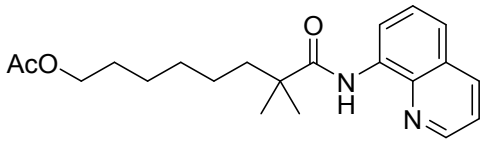
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H
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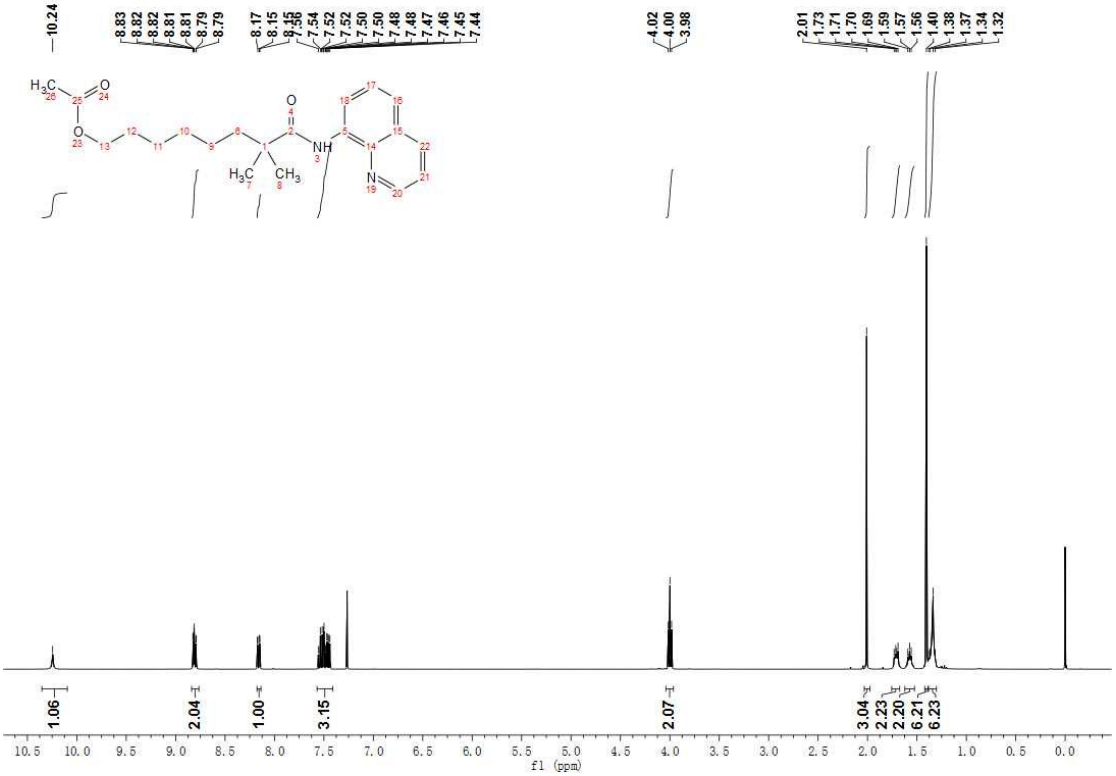
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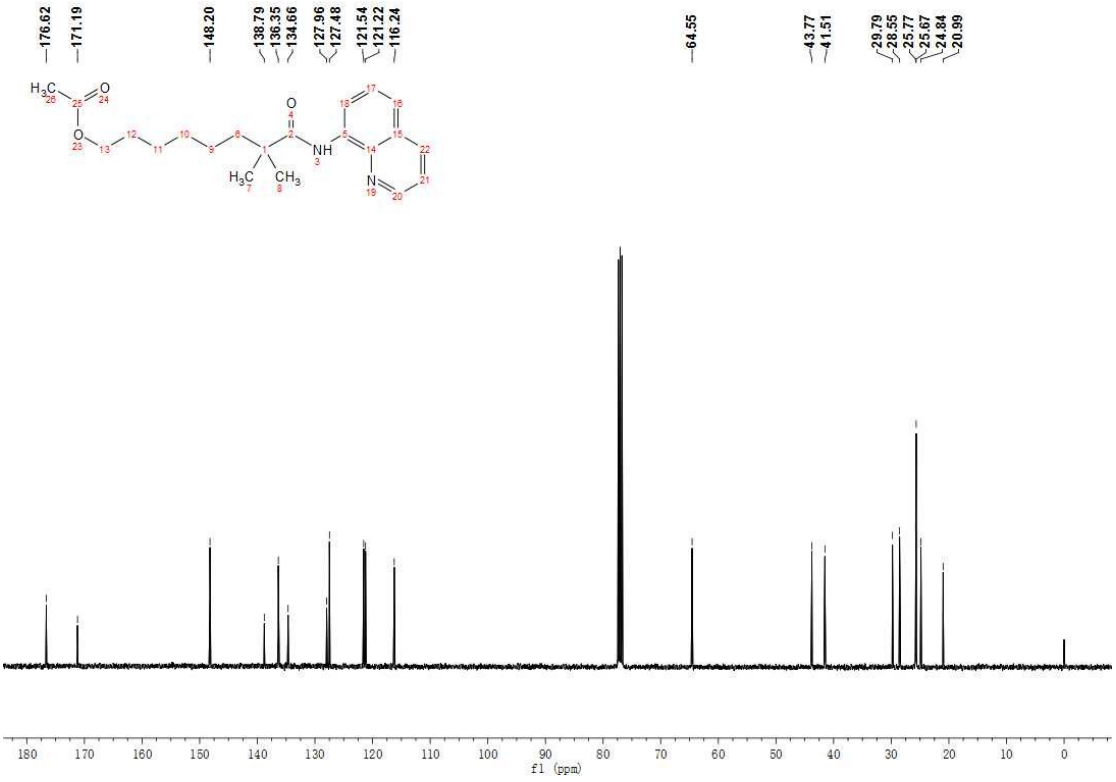
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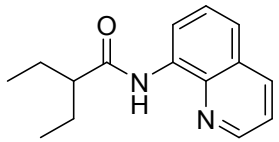

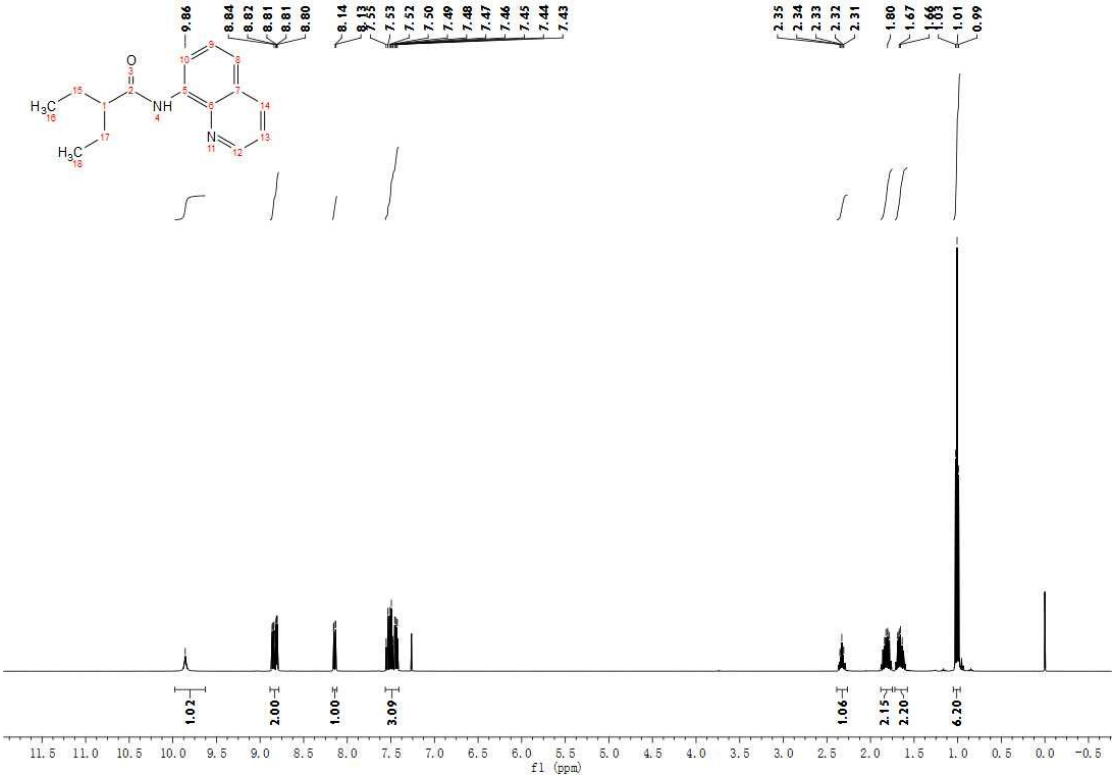
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7.45
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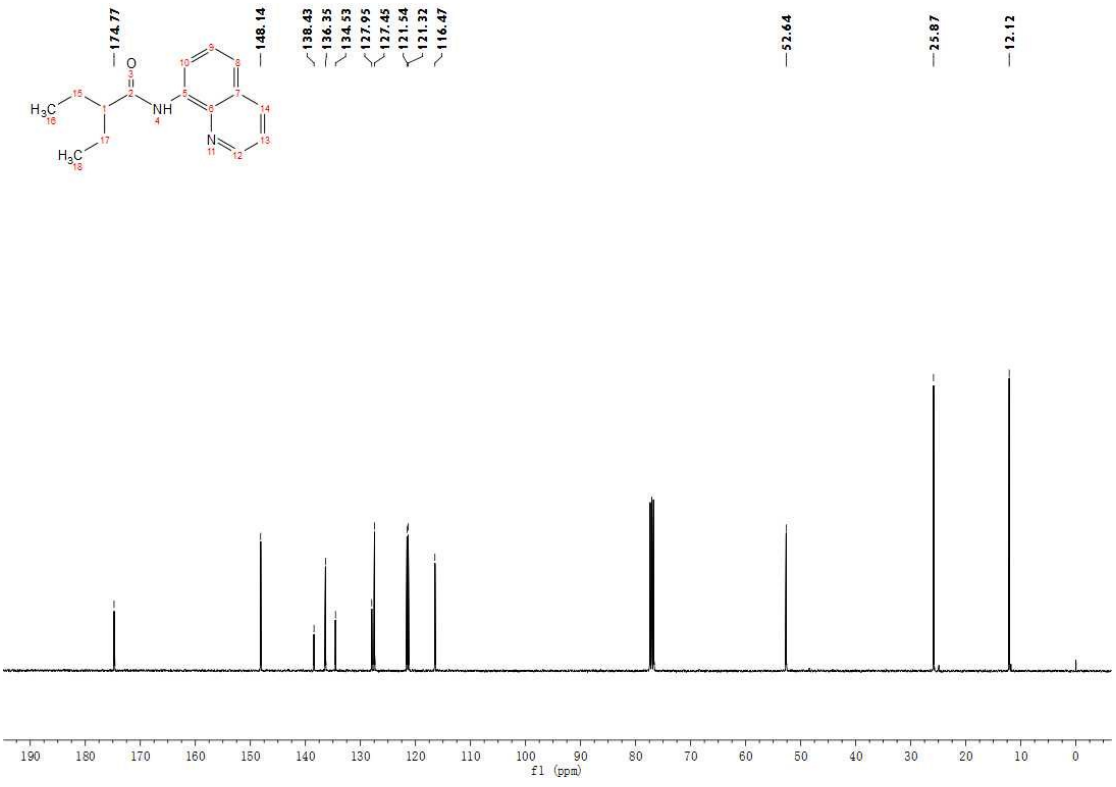
f1 (ppm)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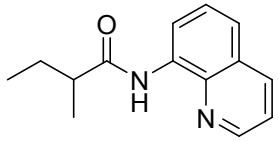
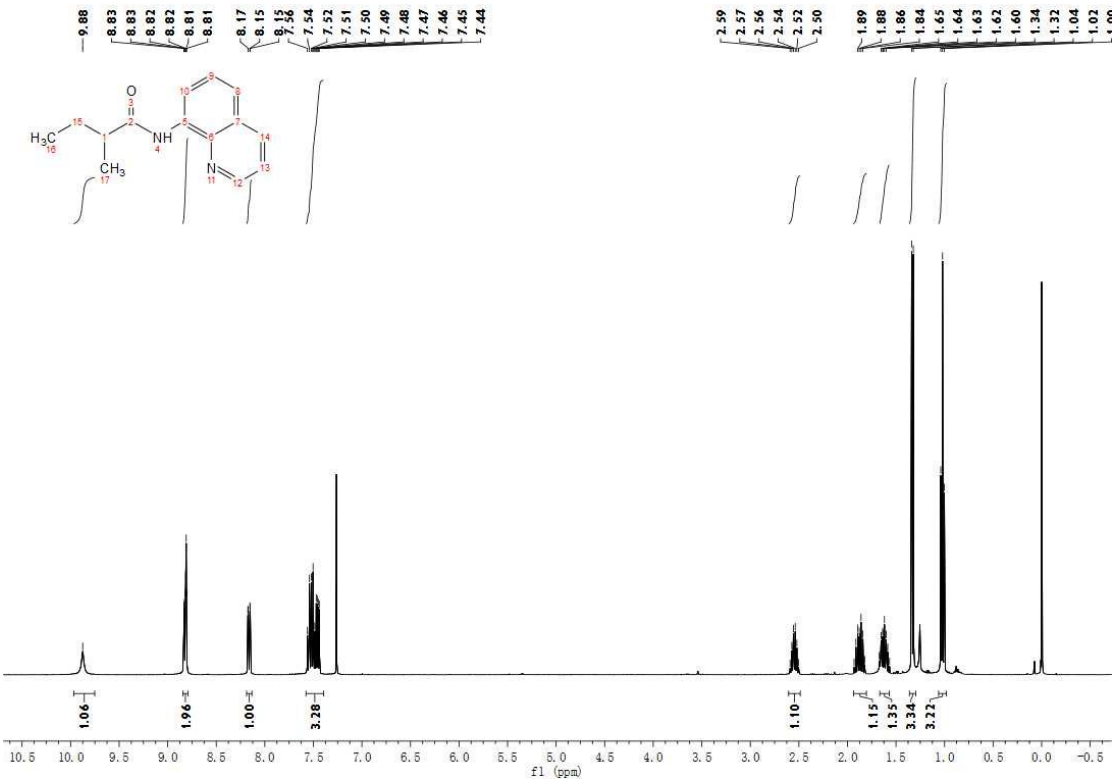
116.47
52.64
25.87
12.12
f1 (ppm)




9.88
8.83
8.83
8.82
8.82
8.81
8.81
8.17
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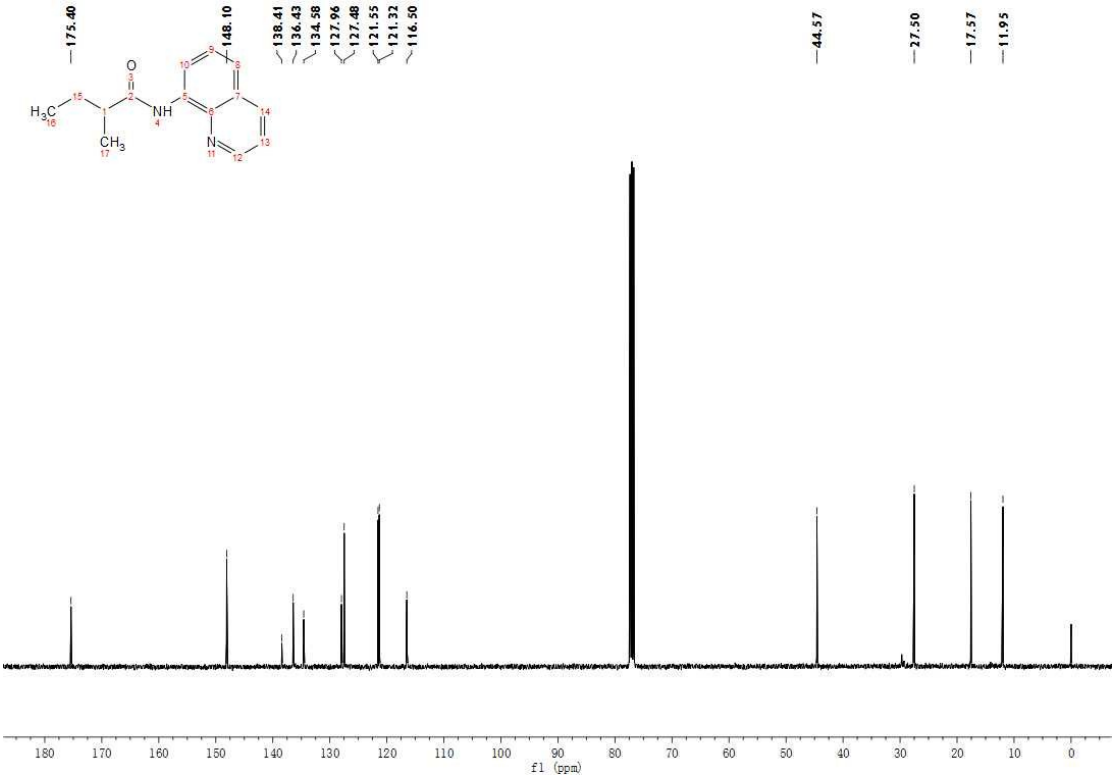
7.54
7.52
7.51
7.50
7.49
7.48
7.47
7.46
7.45
7.44
2.59
2.57
2.56
2.54
2.52
2.50
1.89
1.88
1.86
1.84
1.65
1.64
1.63
1.62
1.60
1.34
1.32
1.04
1.02
1.06
1.96
1.00
3.28
1.10
1.15
1.35
3.34
3.22
f1 (ppm)


175.40
148.10
138.41
136.43
134.58
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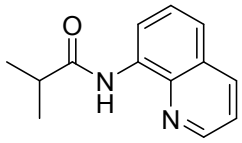
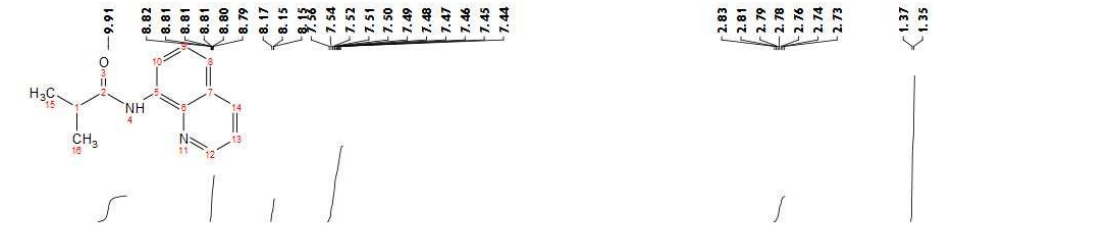
127.48
121.55
121.32
116.50
44.57
27.50
17.57
11.95
f1 (ppm)

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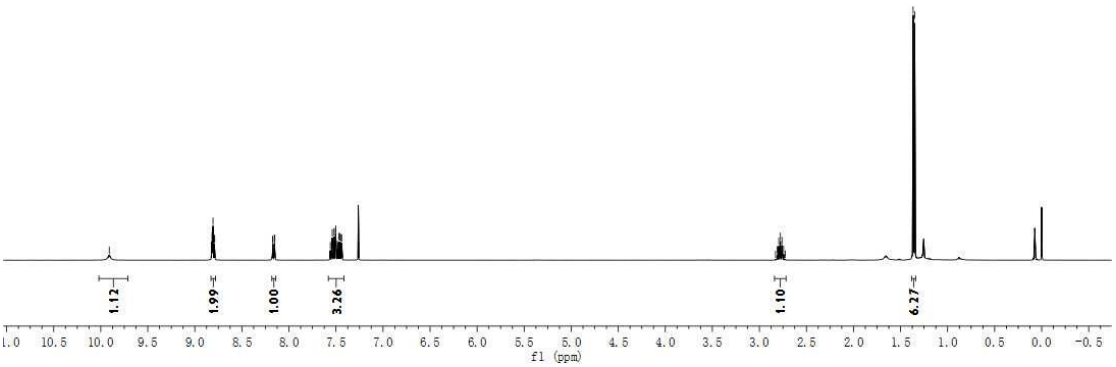
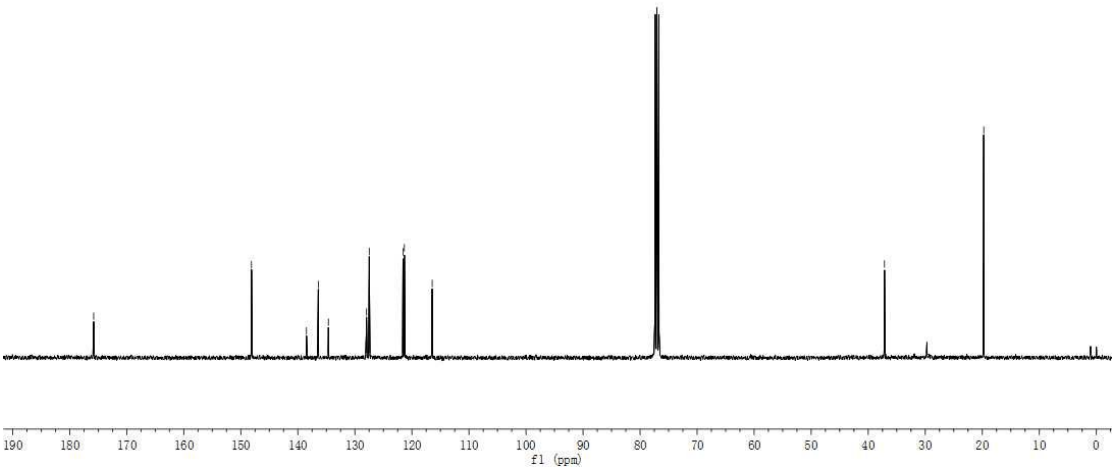
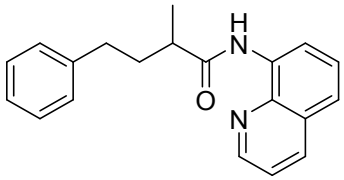
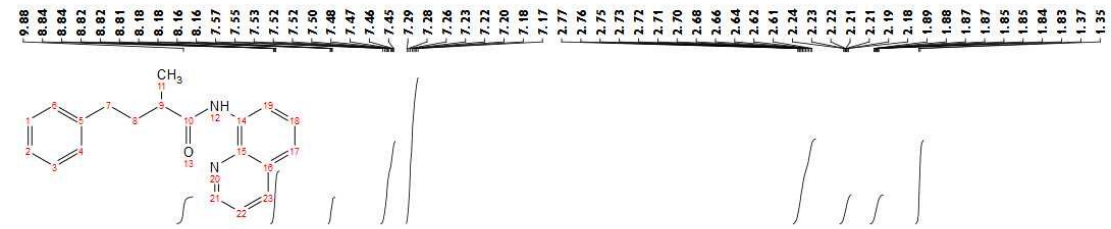
8.82
8.81
8.81
8.81
8.80
8.79
8.17
8.15
7.54
7.52
7.51
7.50
7.49
7.48
7.47
7.46
7.45
7.44
2.83
2.81
2.79
2.78
2.76
2.74
2.73
1.37
1.35

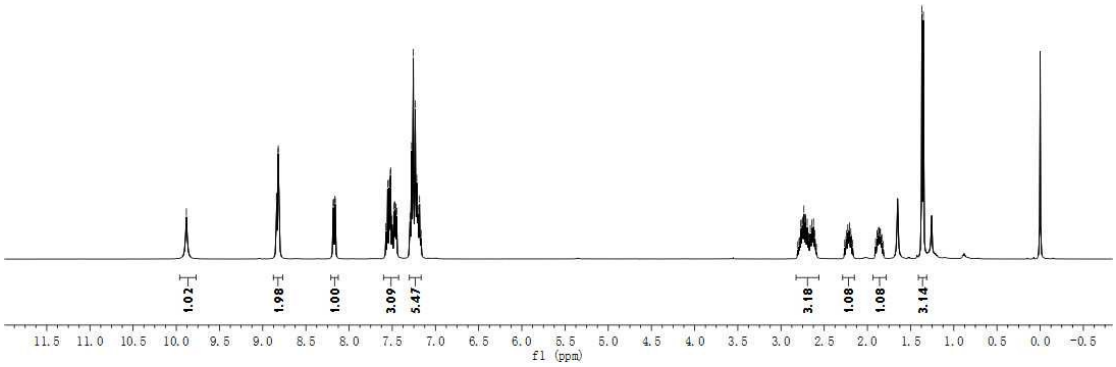

1.12
1.99
1.00
3.26
1.10
6.27
f1 (ppm)

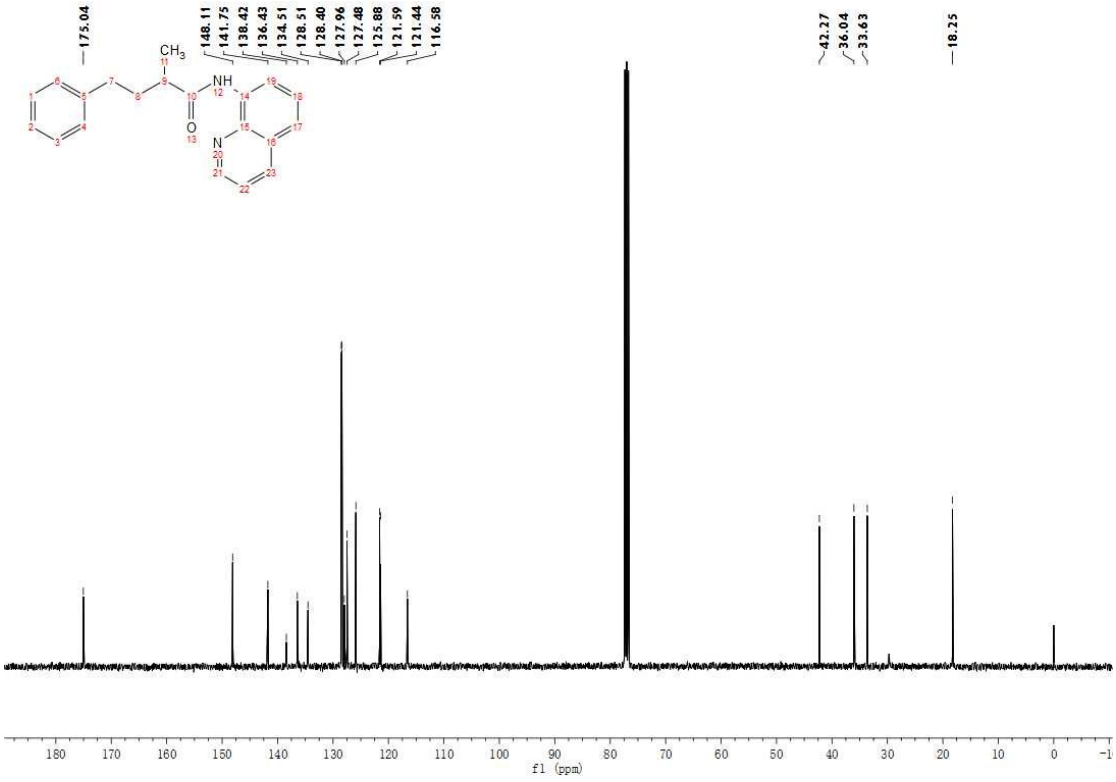

175.79
148.13
138.48
136.41
134.64
127.96
127.48
121.57
121.32
116.44
37.16
19.75

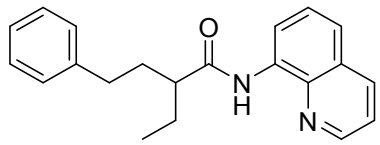

f1 (ppm)

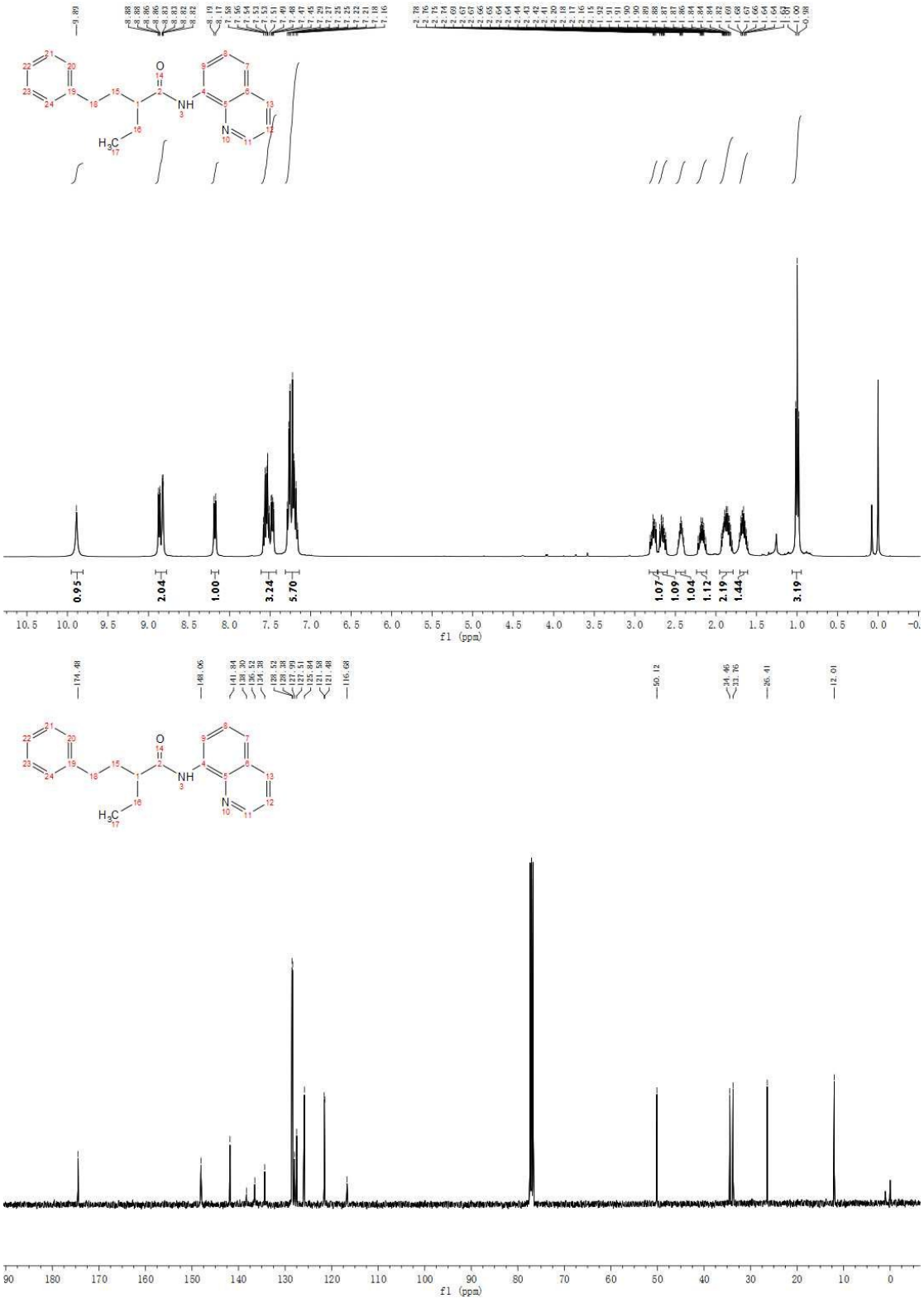

H
N
O
N

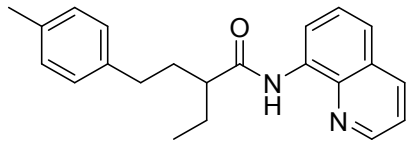

9.88 8.84 8.84 8.82 8.82 8.81 8.18 8.18 8.16 8.16 7.57 7.55 7.53 7.52 7.52 7.50 7.48 7.47 7.46 7.45 7.29 7.28 7.26 7.23 7.22 7.20 7.18 7.17 2.77 2.76 2.75 2.73 2.72 2.71 2.70 2.68 2.66 2.64 2.62 2.61 2.24 2.23 2.22 2.21 2.21 2.19 2.18 1.89 1.88 1.87 1.87 1.85 1.85 1.84 1.83 1.37 1.35
CH3
NH
O
N

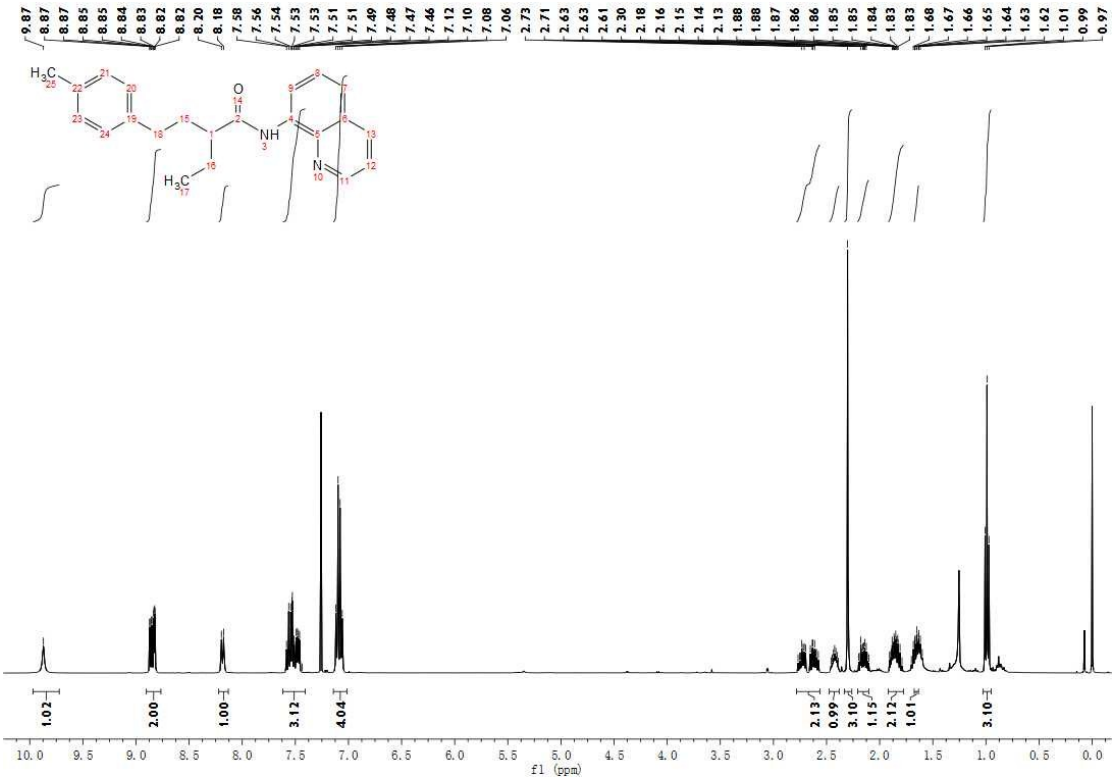

1.02 1.98 1.00 3.09 5.47 3.18 1.08 1.08 3.14
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

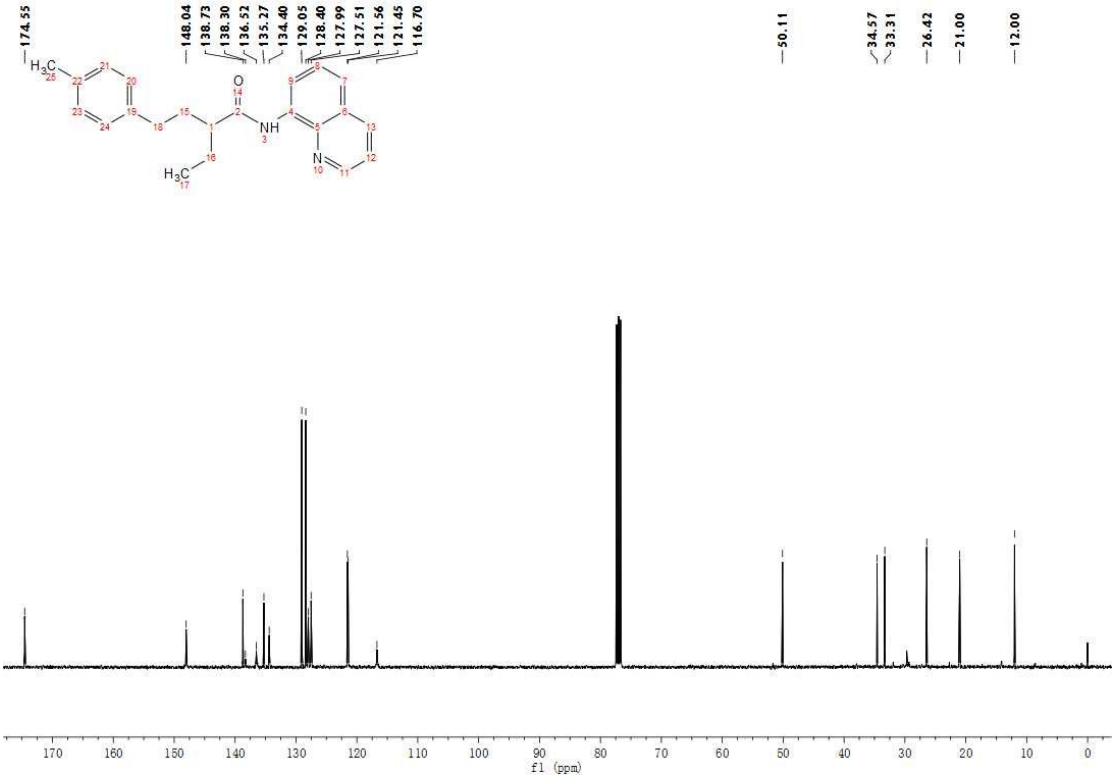

175.04
148.11 141.75 138.42 136.43 134.51 128.51 128.40 127.96 127.48 125.88 121.59 121.44 116.58
42.27 36.04 33.63
18.25
CH3
NH
O
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

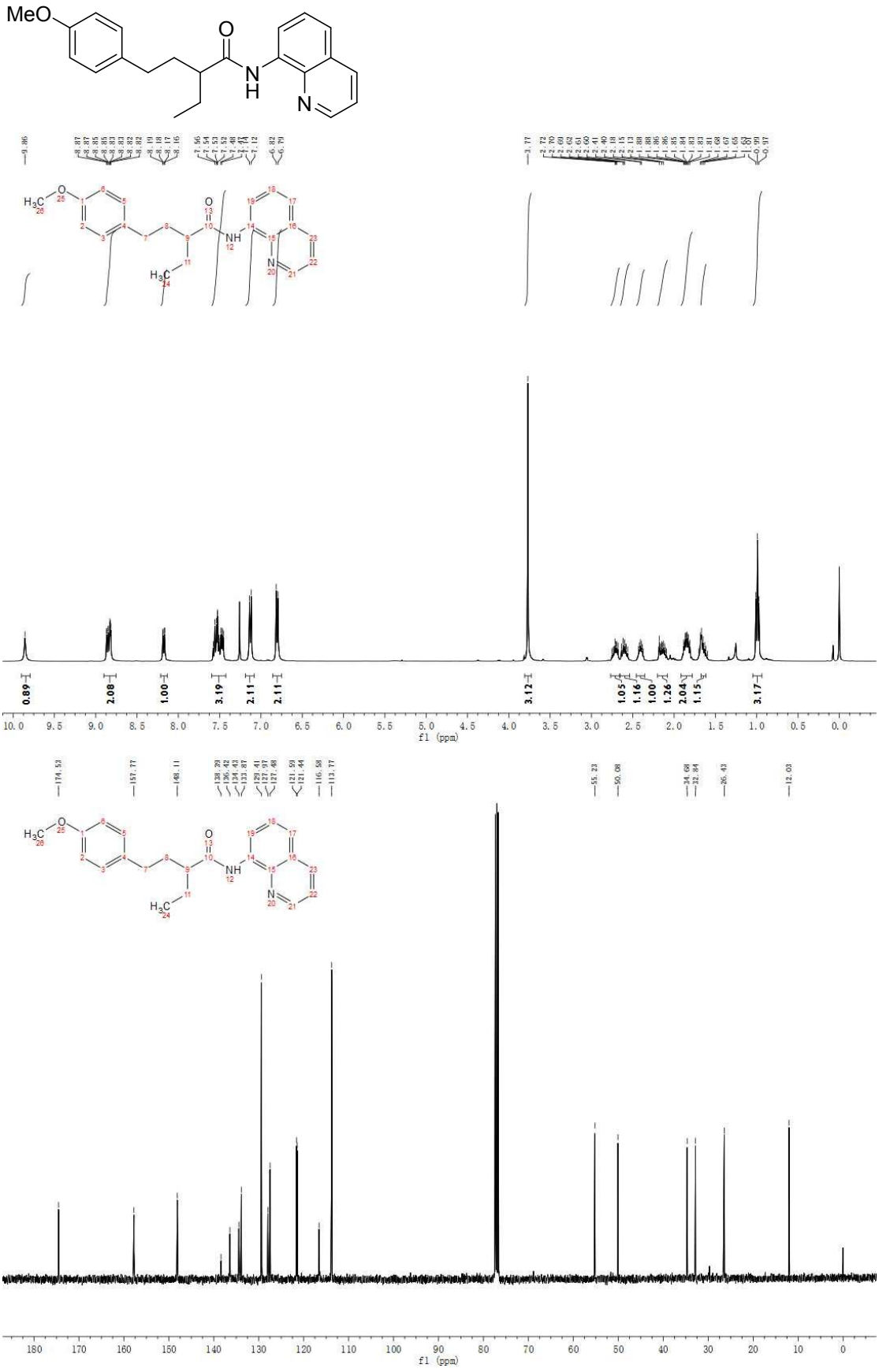


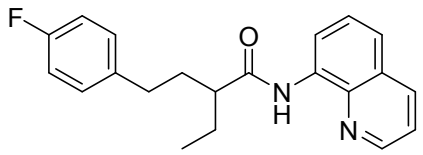

0.95
2.04
1.00
3.24
5.70
1.07
1.09
1.04
1.12
2.19
1.44
3.19
f1 (ppm)
f1 (ppm)

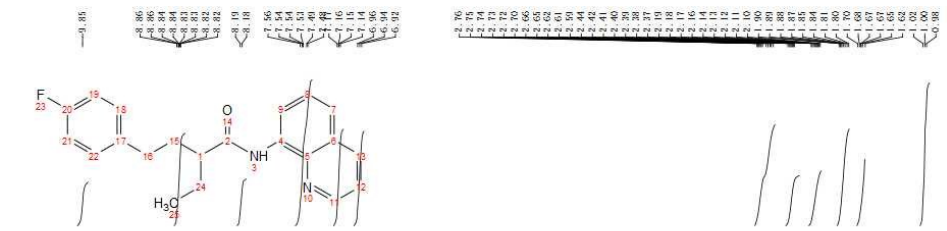


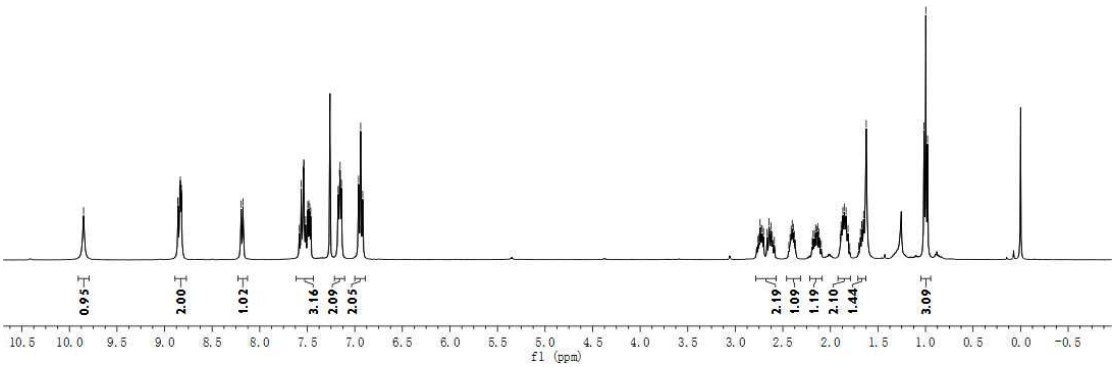


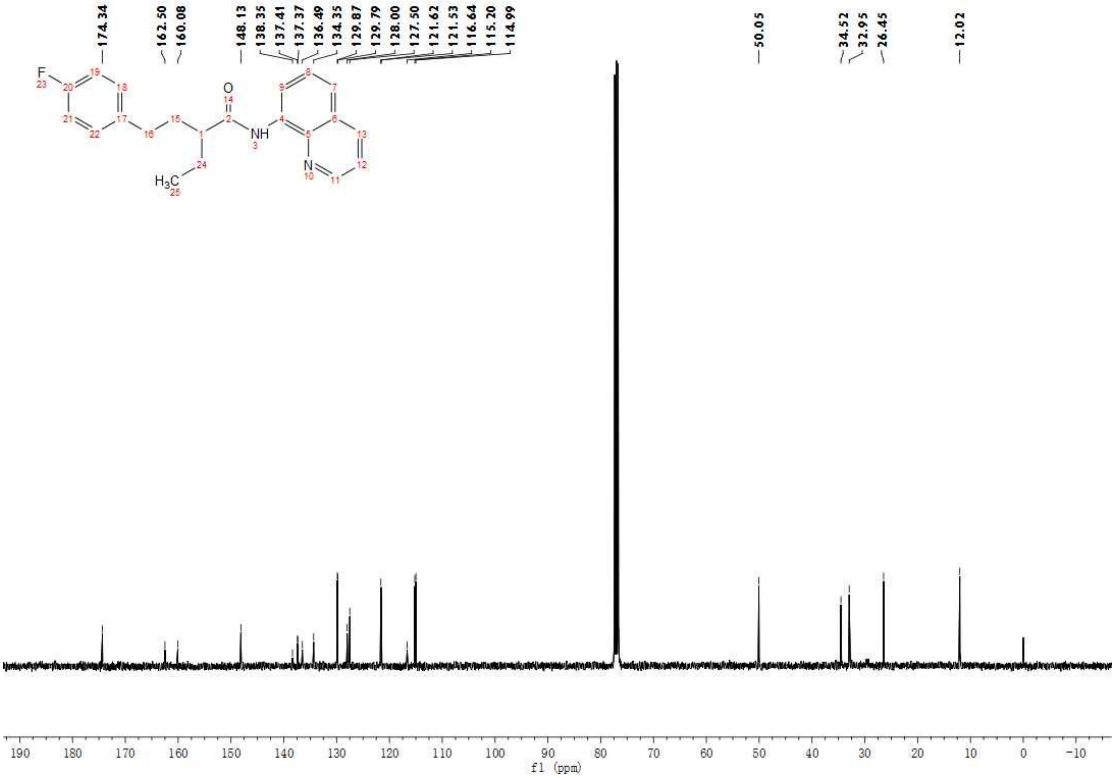


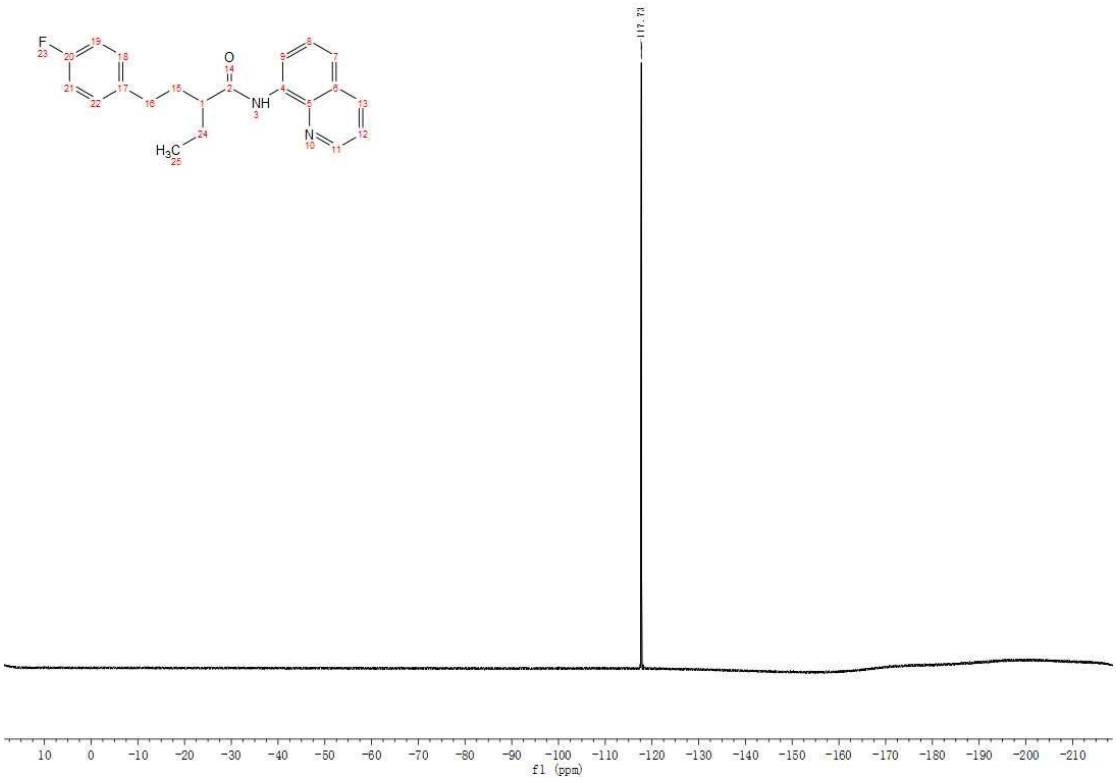

MeO
O
N
H
N
f1 (ppm)
f1 (ppm)

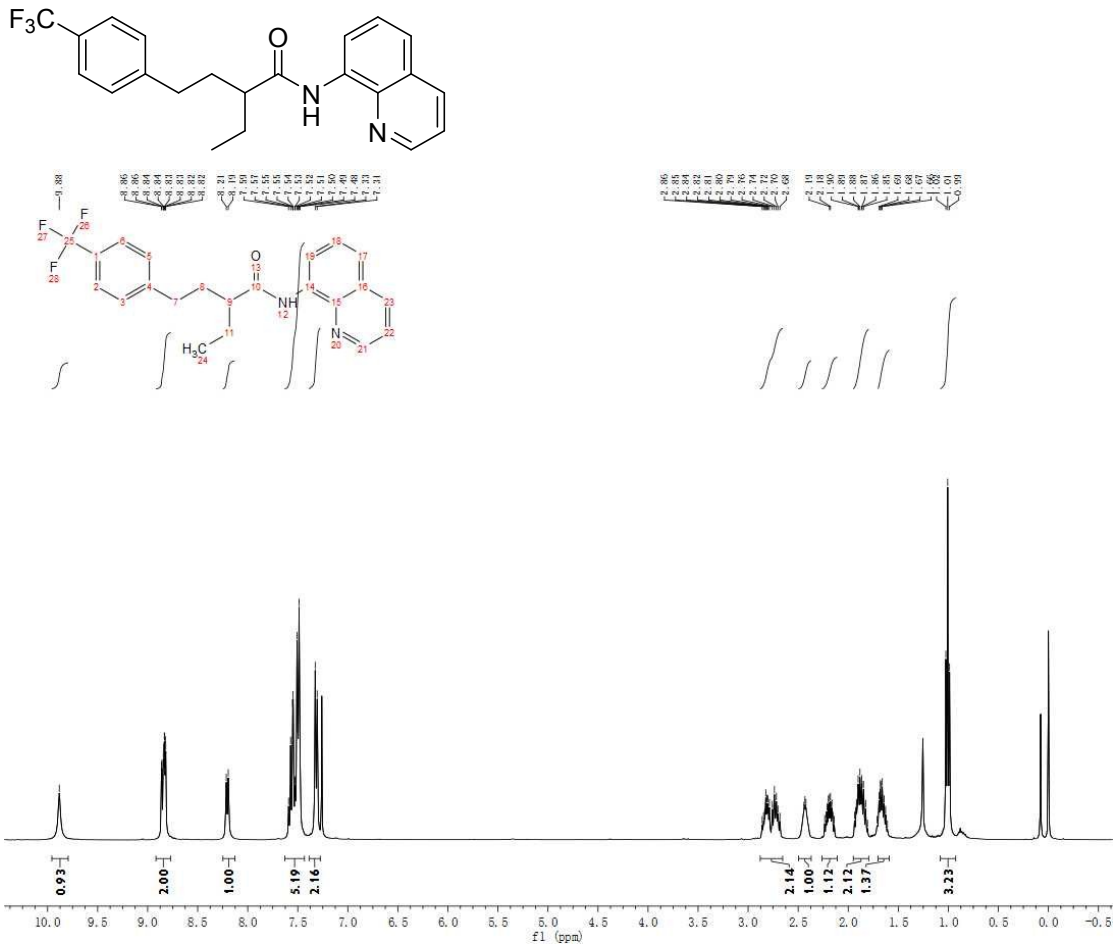

F
O
N
H
N

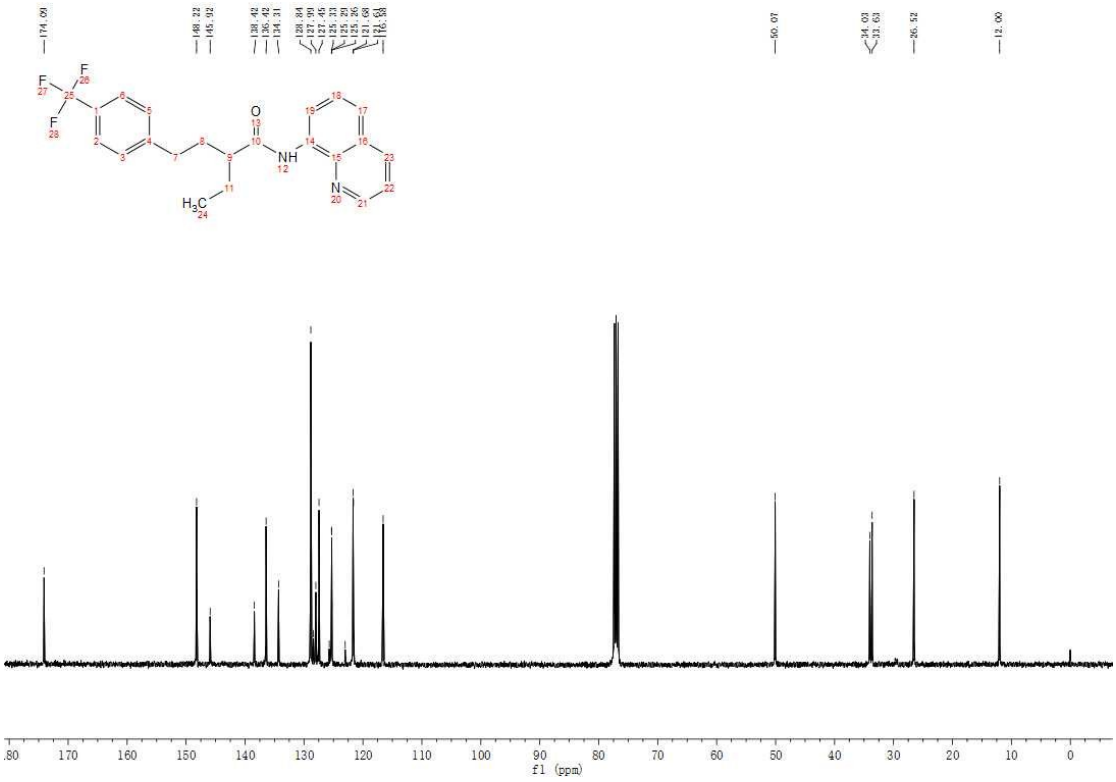



0.95
2.00
1.02
3.16
2.09
2.05
2.19
1.09
1.19
2.10
1.44
3.09
f1 (ppm)


174.34
162.50
160.08
148.13
138.35
137.41
137.37
136.49
134.35
129.87
129.79
128.00
127.50
121.62
121.53
116.64
115.20
114.99
50.05
34.52
32.95
26.45
12.02
f1 (ppm)


F
O
NH
N
H_3C
-117.73
f1 (ppm)


F_3C
O
N
H
N
H_3C
0.93
2.00
1.00
5.19
2.16
2.14
1.00
1.12
2.12
1.37
3.23
f1 (ppm)


174.09
148.22
145.92
138.42
136.42
134.31
120.84
127.09
127.45
125.33
125.29
125.26
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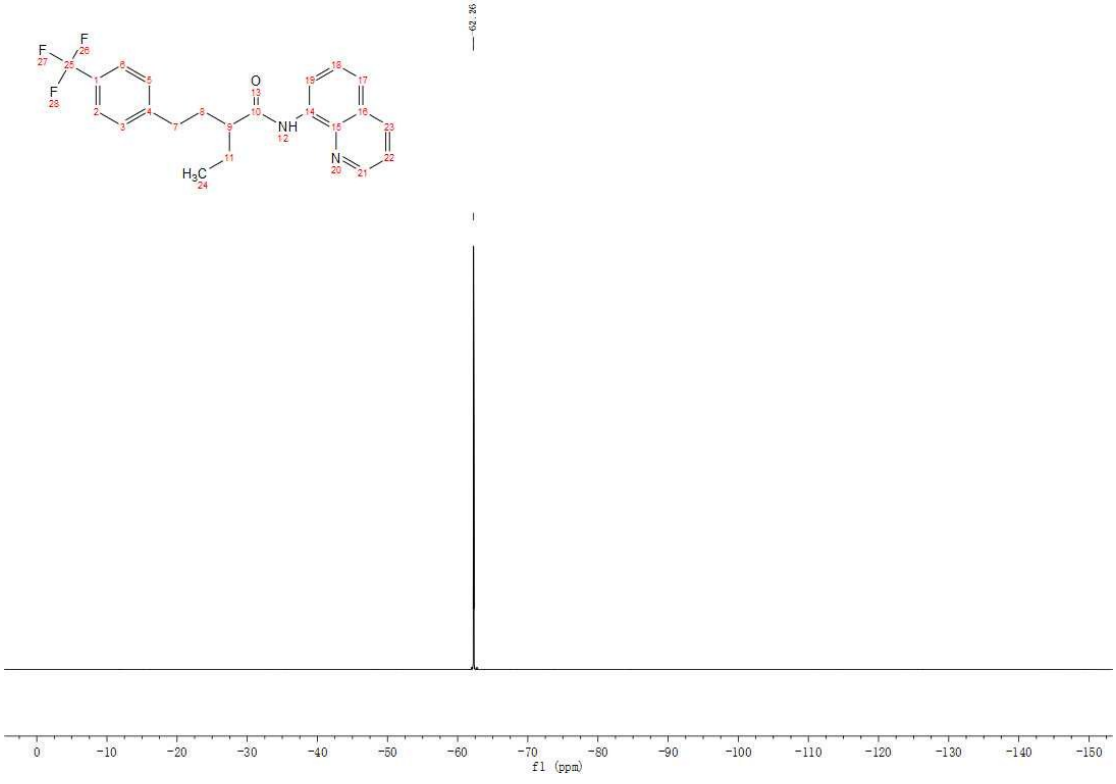
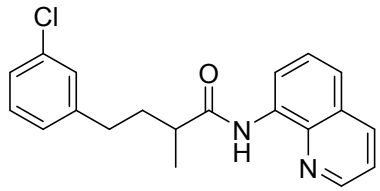
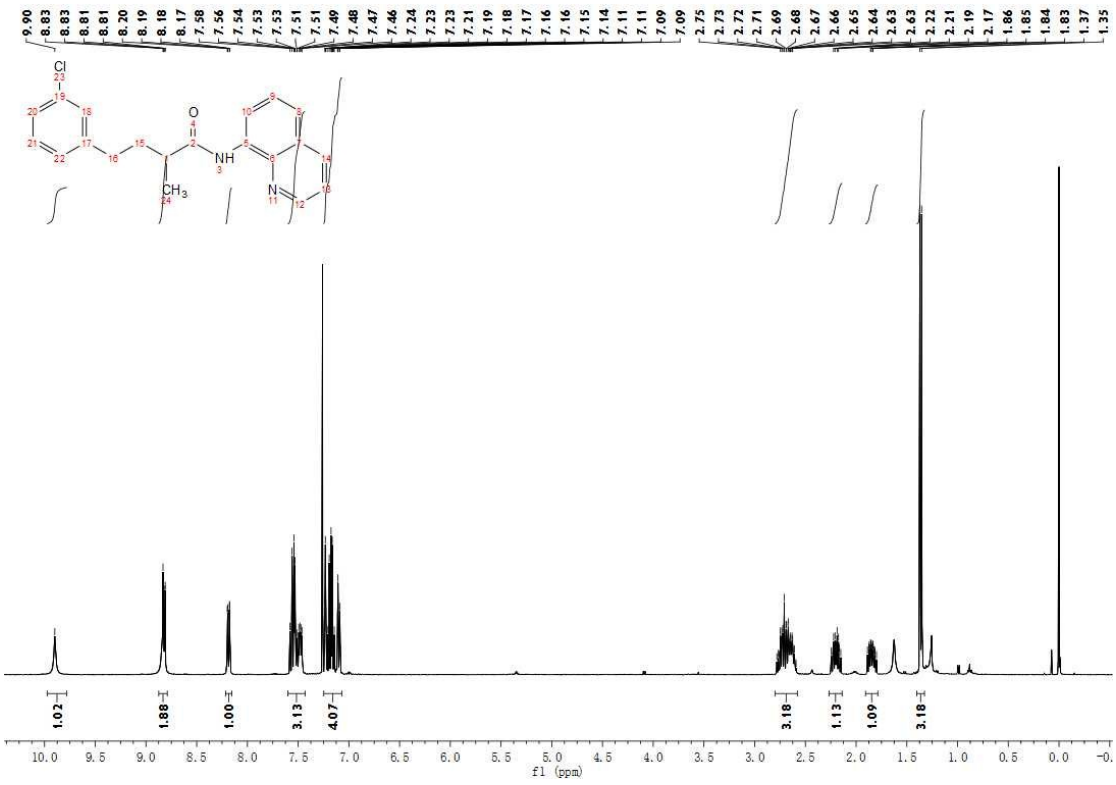
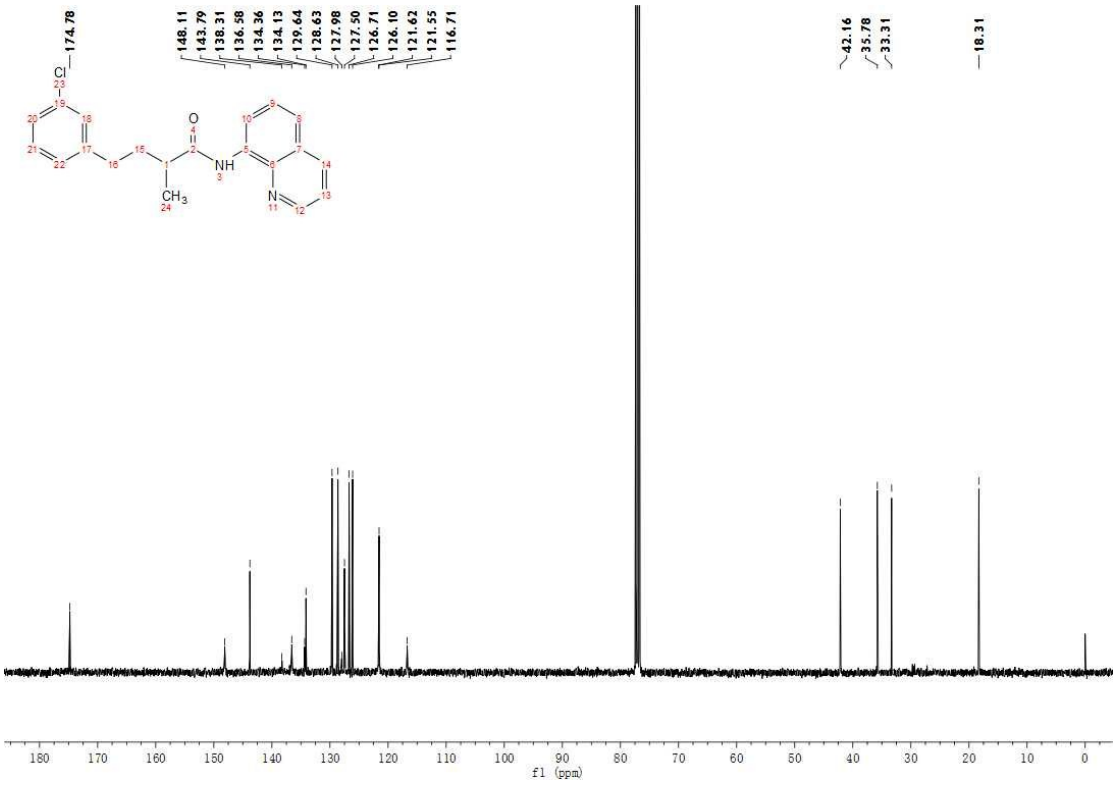
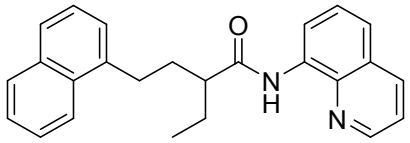
34.03
33.63
26.52
12.00
f1 (ppm)

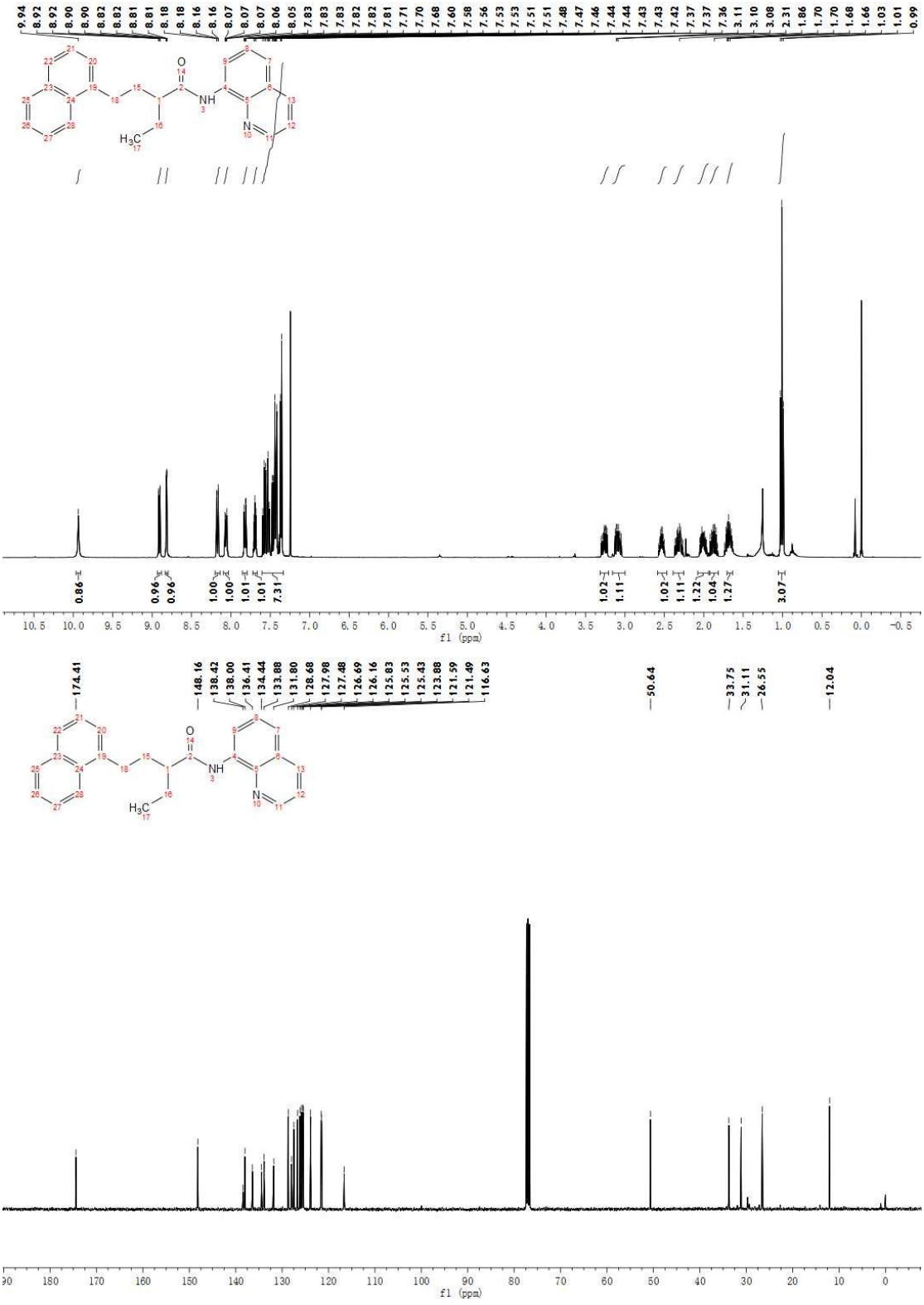

62.26
f1 (ppm)

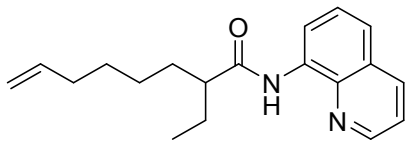

Cl
O
N
H
N

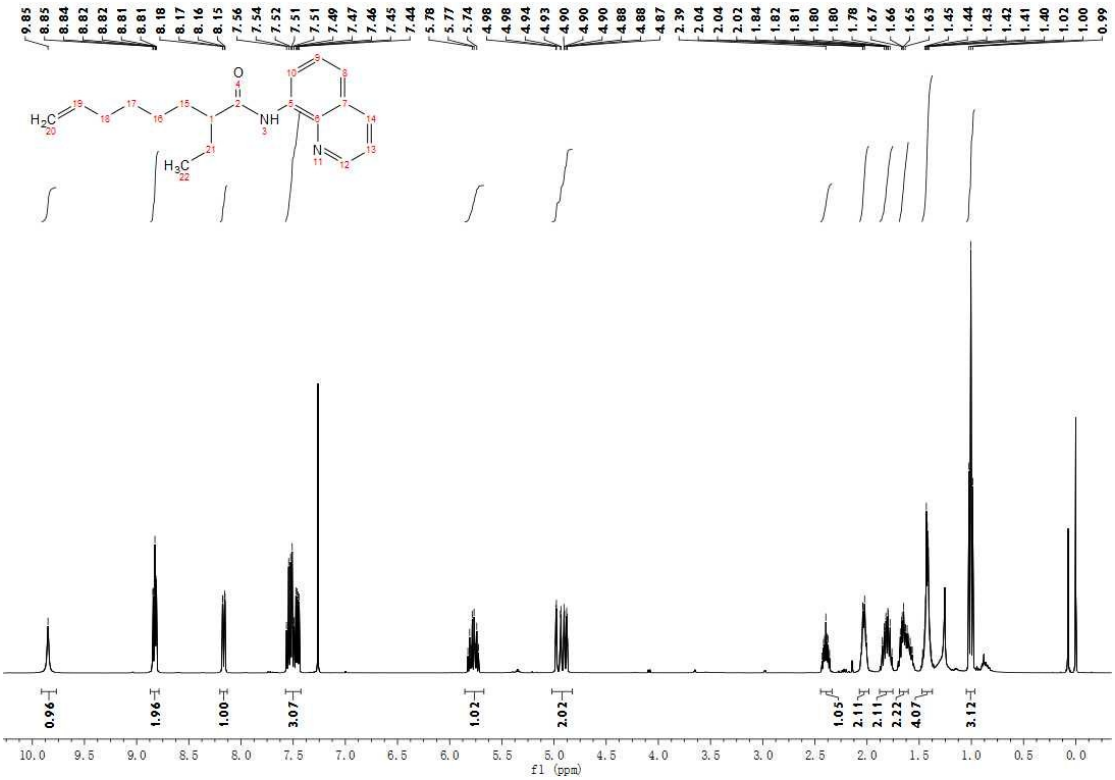

9.90 8.83 8.83 8.81 8.81 8.20 8.19 8.18 8.17 7.58 7.56 7.54 7.53 7.53 7.51 7.51 7.49 7.48 7.47 7.46 7.24 7.23 7.23 7.21 7.19 7.18 7.17 7.16 7.16 7.15 7.14 7.11 7.11 7.09 7.09 2.75 2.73 2.72 2.71 2.69 2.68 2.67 2.66 2.65 2.64 2.63 2.63 2.22 2.21 2.19 2.17 1.86 1.85 1.84 1.83 1.37 1.35
1.02 1.88 1.00 3.13 4.07 3.18 1.13 1.09 3.18
f1 (ppm)

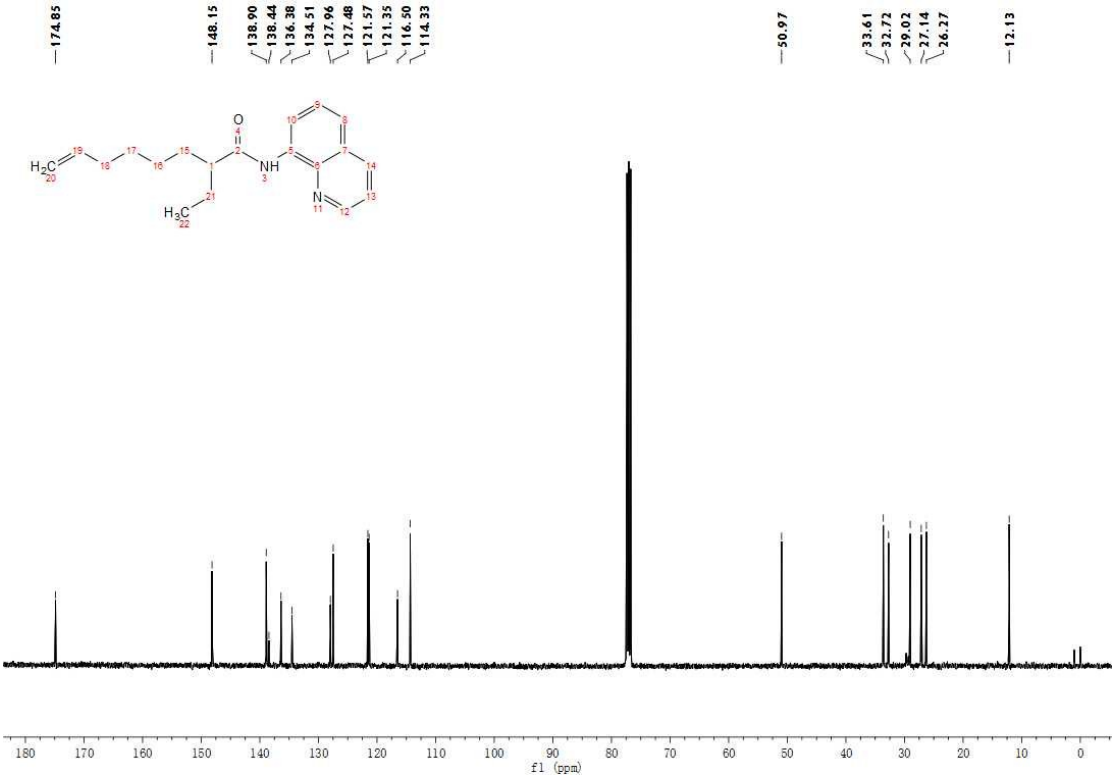

174.78 148.11 143.79 138.31 136.58 134.36 134.13 129.64 128.63 127.98 127.50 126.71 126.10 121.62 121.55 116.71 42.16 35.78 33.31 18.31
f1 (ppm)

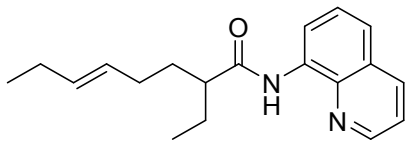


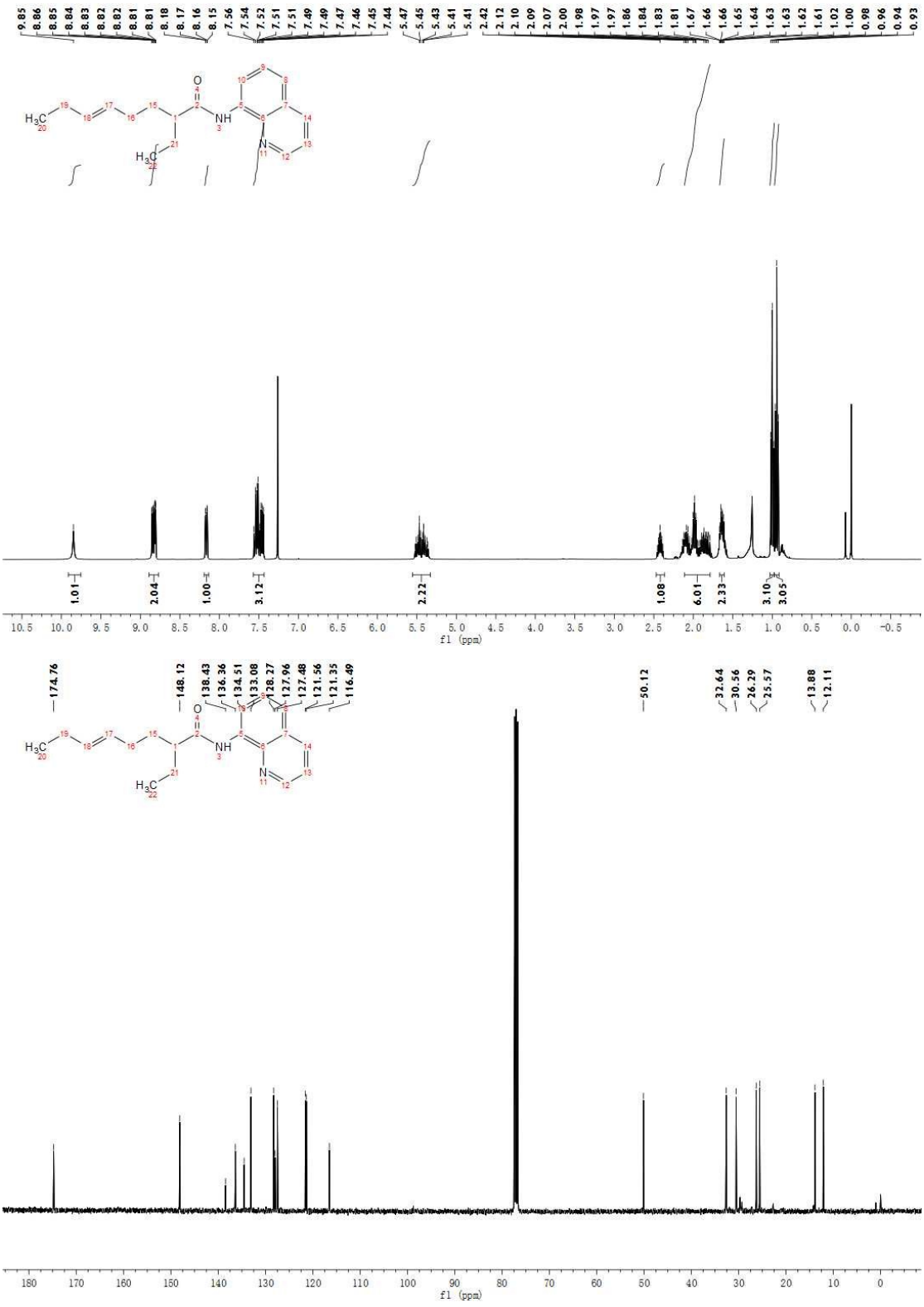


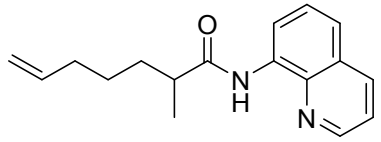

O
N
H
N

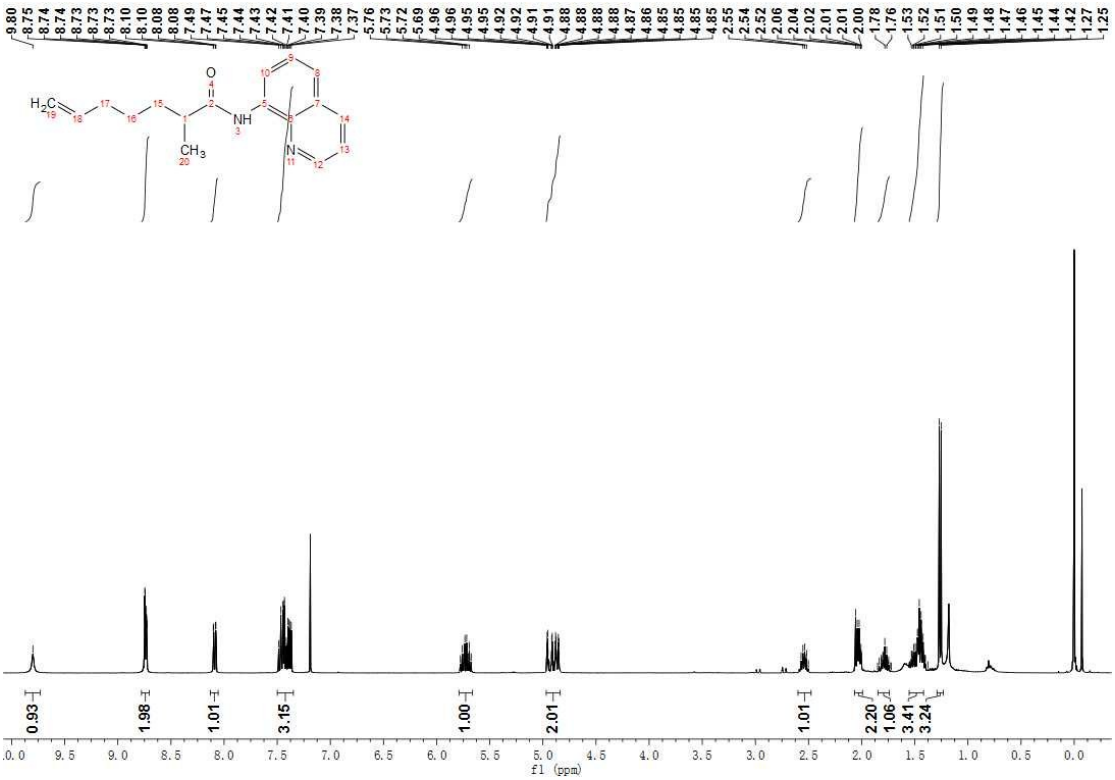

9.85 8.85 8.84 8.82 8.82 8.81 8.81 8.18 8.17 8.16 8.15 7.56 7.54 7.52 7.51 7.51 7.49 7.47 7.46 7.45 7.44 5.78 5.77 5.74 4.98 4.98 4.94 4.93 4.90 4.90 4.90 4.88 4.87 2.39 2.04 2.04 2.02 1.84 1.82 1.81 1.80 1.80 1.78 1.67 1.66 1.65 1.63 1.45 1.44 1.43 1.42 1.41 1.40 1.02 1.00 0.99
0.96 1.96 1.00 3.07 1.02 2.02 1.05 2.11 2.11 2.22 4.07 3.12
f1 (ppm)

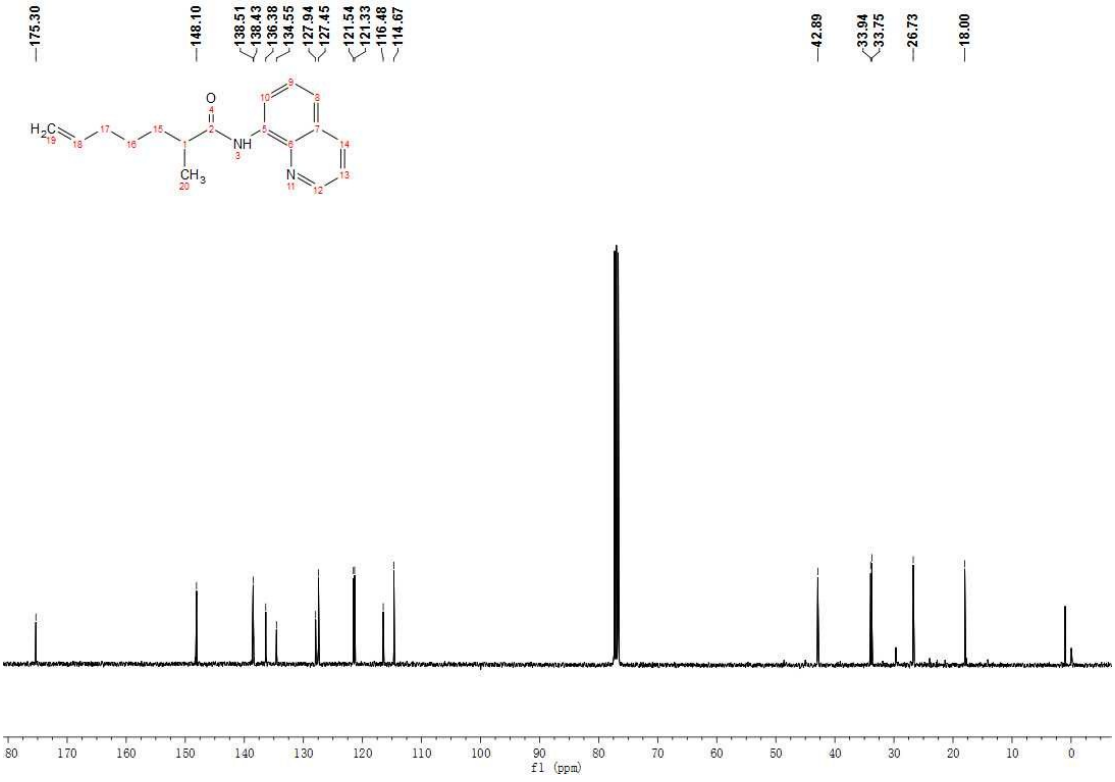

174.85 148.15 138.90 138.44 136.38 134.51 127.96 127.48 121.57 121.35 116.50 114.33 50.97 33.61 32.72 29.02 27.14 26.27 12.13
f1 (ppm)

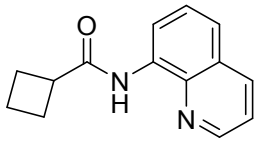


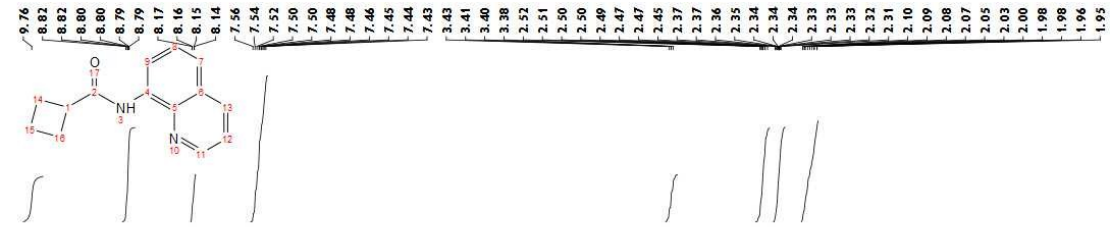

9.85 8.86 8.85 8.84 8.83 8.82 8.82 8.81 8.81 8.18 8.17 8.16 8.15 7.56 7.54 7.52 7.51 7.51 7.49 7.49 7.47 7.46 7.45 7.44 5.47 5.45 5.43 5.41 5.41 2.42 2.12 2.10 2.09 2.07 2.00 1.98 1.97 1.97 1.86 1.84 1.83 1.81 1.67 1.66 1.66 1.65 1.64 1.63 1.63 1.62 1.61 1.02 1.00 0.98 0.96 0.94 0.93
1.01 2.04 1.00 3.12 2.22 1.08 6.01 2.33 3.10 3.05
f1 (ppm)
174.76 148.12 138.43 136.36 134.51 133.08 128.27 127.96 127.48 121.56 121.35 116.49 50.12 32.64 30.56 26.29 25.57 13.88 12.11
f1 (ppm)

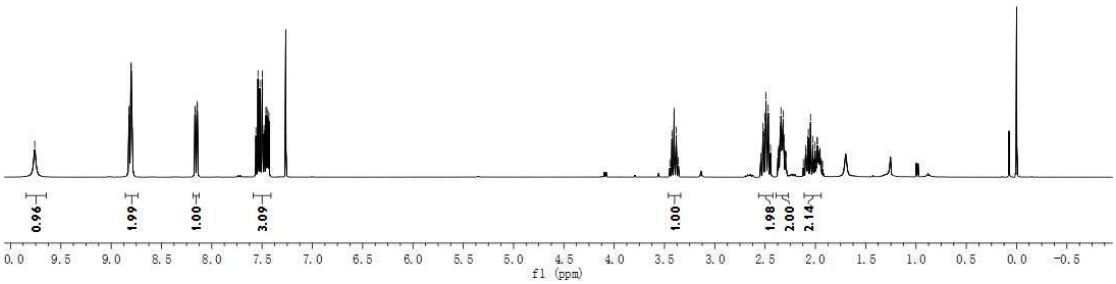


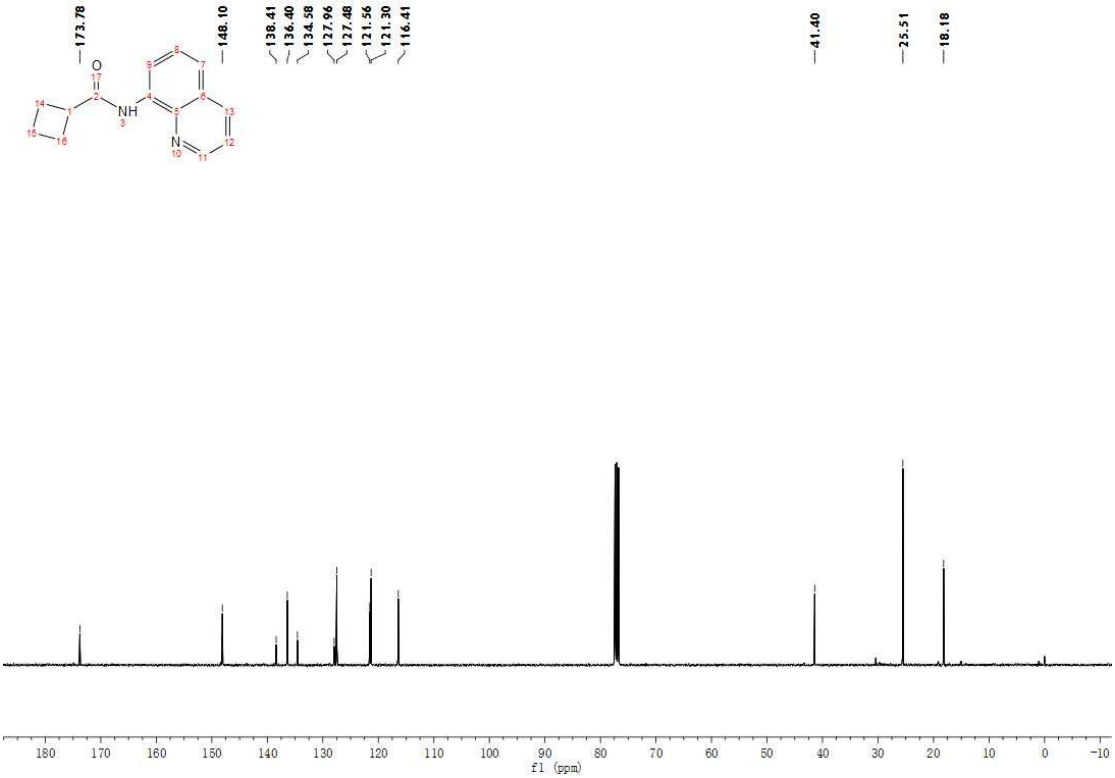


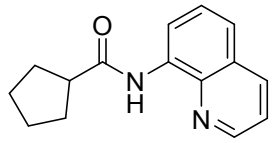


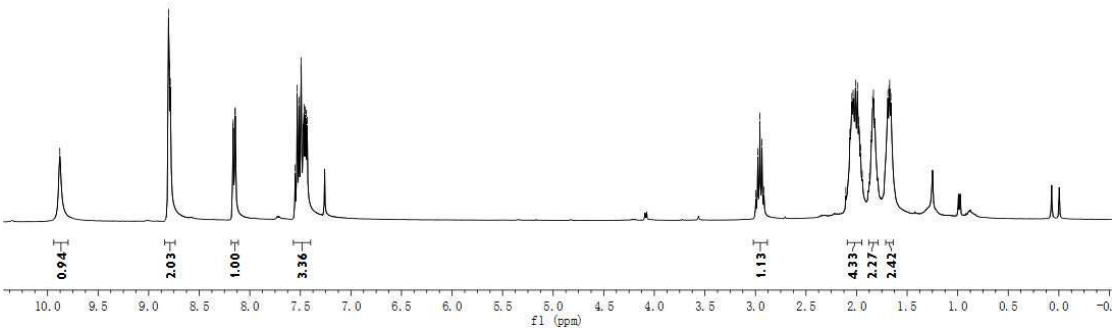

O
N
H
N


9.76 8.82 8.82 8.80 8.80 8.79 8.79 8.17 8.16 8.15 8.14 7.56 7.54 7.52 7.50 7.50 7.48 7.48 7.46 7.45 7.44 7.43 3.43 3.41 3.40 3.38 2.52 2.51 2.50 2.50 2.49 2.47 2.47 2.45 2.37 2.37 2.36 2.35 2.34 2.34 2.33 2.33 2.32 2.31 2.10 2.09 2.08 2.07 2.05 2.03 2.00 1.98 1.98 1.96 1.95
O
17
NH
3
N
10
11
12
13
14
15
16


0.96 1.99 1.00 3.09 1.00 1.98 2.00 2.14
f1 (ppm)


173.78 148.10 138.41 136.40 134.58 127.96 127.48 121.56 121.30 116.41 41.40 25.51 18.18
O
17
NH
3
N
10
11
12
13
14
15
16
f1 (ppm)

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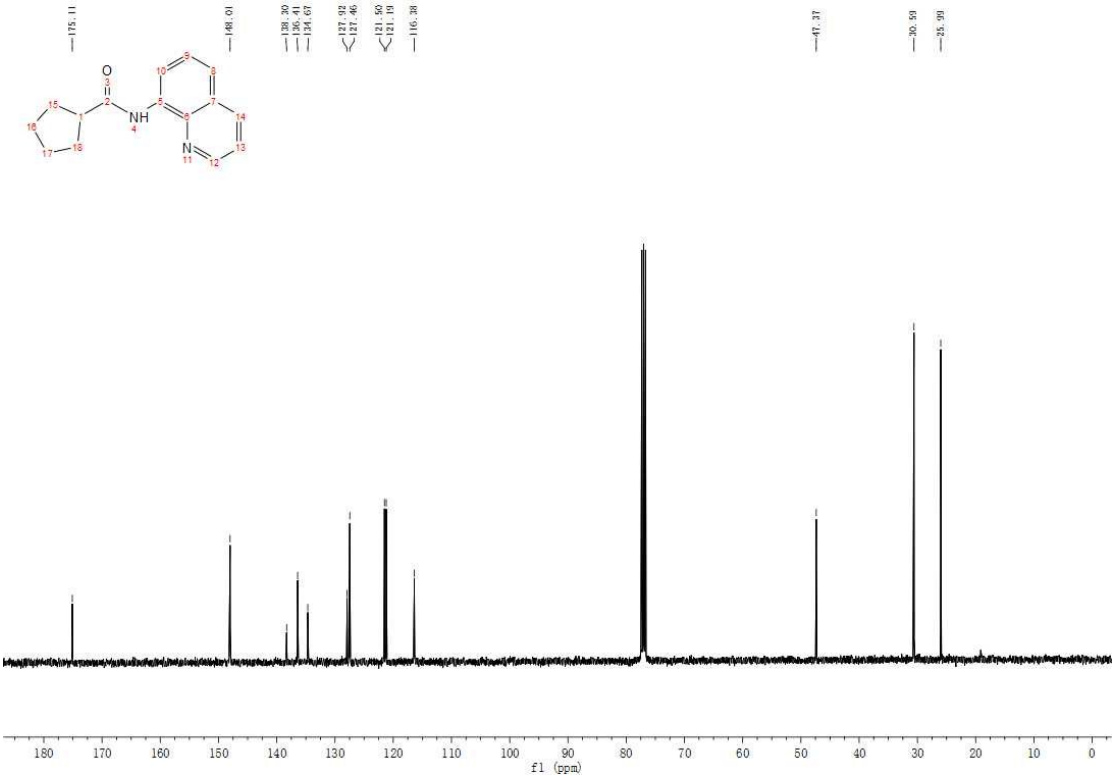
4.33
2.27
2.42
f1 (ppm)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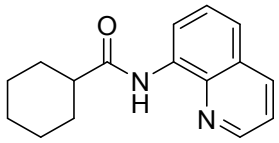

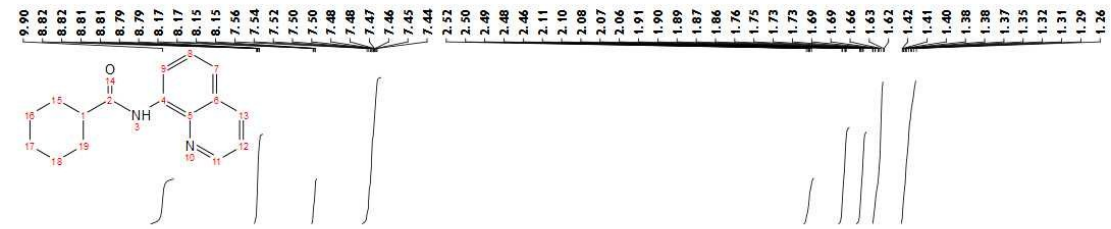
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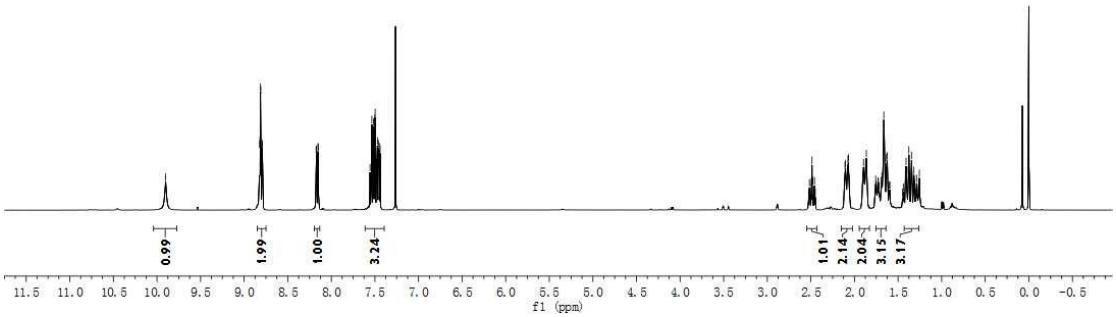
2.52 2.50 2.49 2.48 2.46 2.11 2.10 2.08 2.07 2.06 1.91 1.90 1.89 1.87 1.86 1.76 1.75 1.73 1.73 1.69 1.69 1.66 1.63 1.62 1.42 1.41 1.40 1.38 1.38 1.37 1.35 1.32 1.31 1.29 1.26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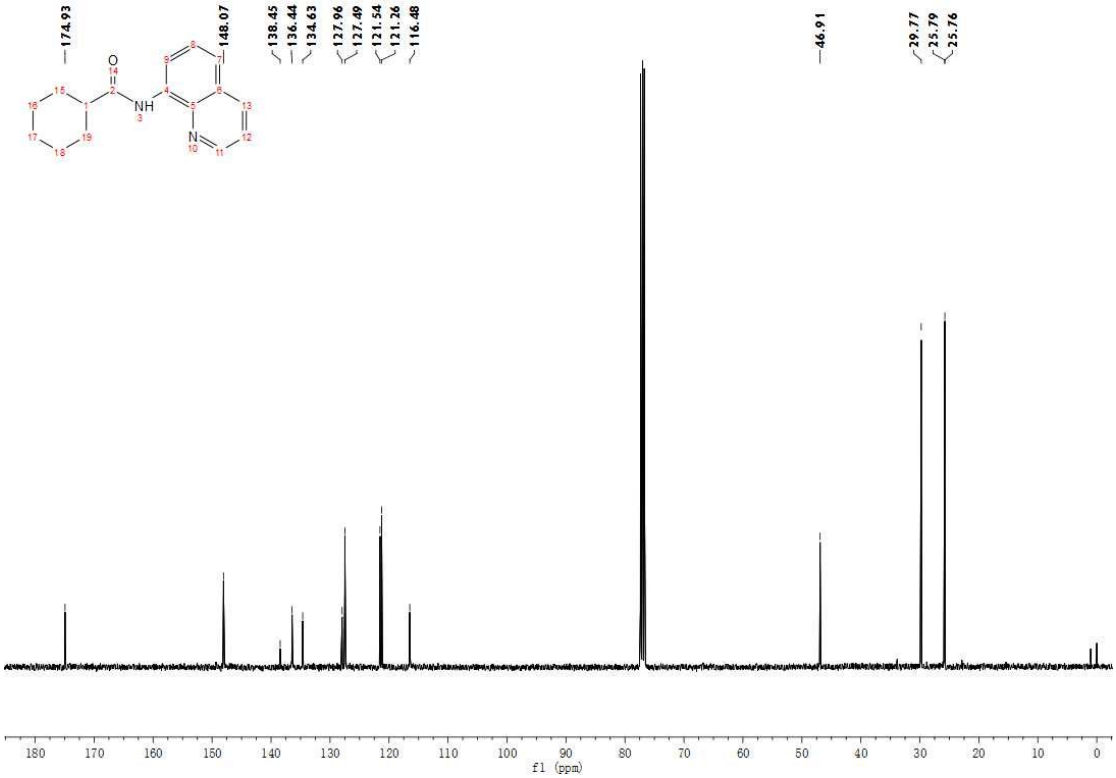
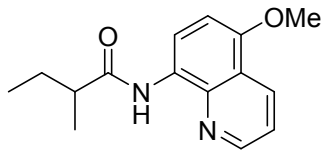
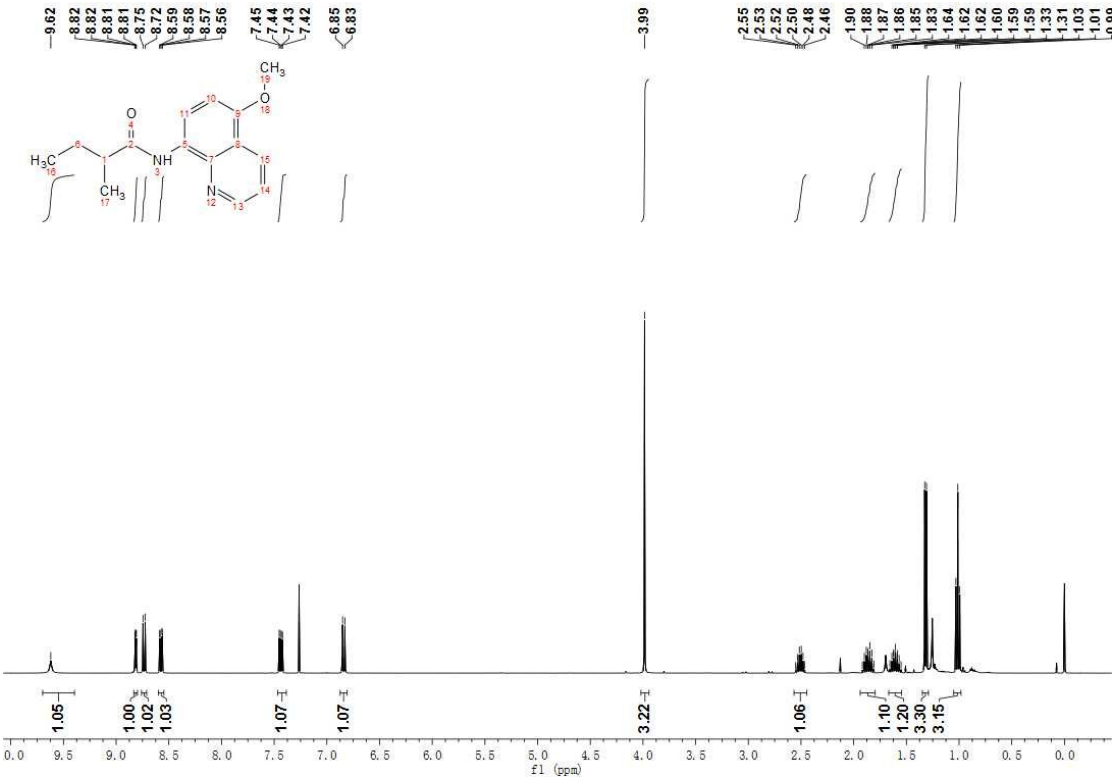
1.01
2.14
2.04
3.15
3.17
f1 (ppm)


174.93
148.07
138.45
136.44
134.63
127.96
127.49
121.54
121.26
116.48
46.91
29.77
25.79
25.76
f1 (ppm)


OMe
O
N
H
N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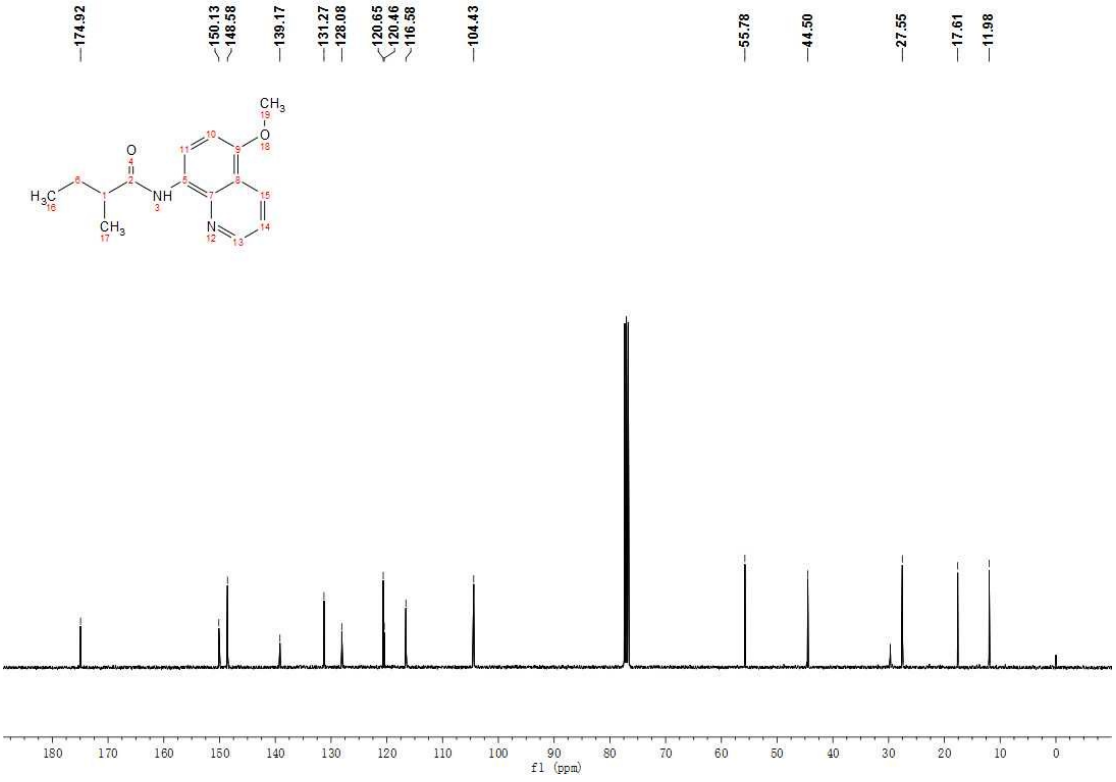
8.82
8.82
8.81
8.81
8.75
8.72
8.59
8.58
8.57
8.56
7.45
7.44
7.43
7.42
6.85
6.83
3.99
2.55
2.53
2.52
2.50
2.48
2.46
1.90
1.88
1.87
1.86
1.85
1.83
1.64
1.62
1.62
1.60
1.59
1.59
1.33
1.31
1.03
1.01
1.05
1.00
1.02
1.03
1.07
1.07
3.22
1.06
1.10
1.20
3.30
3.15
f1 (ppm)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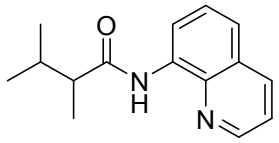
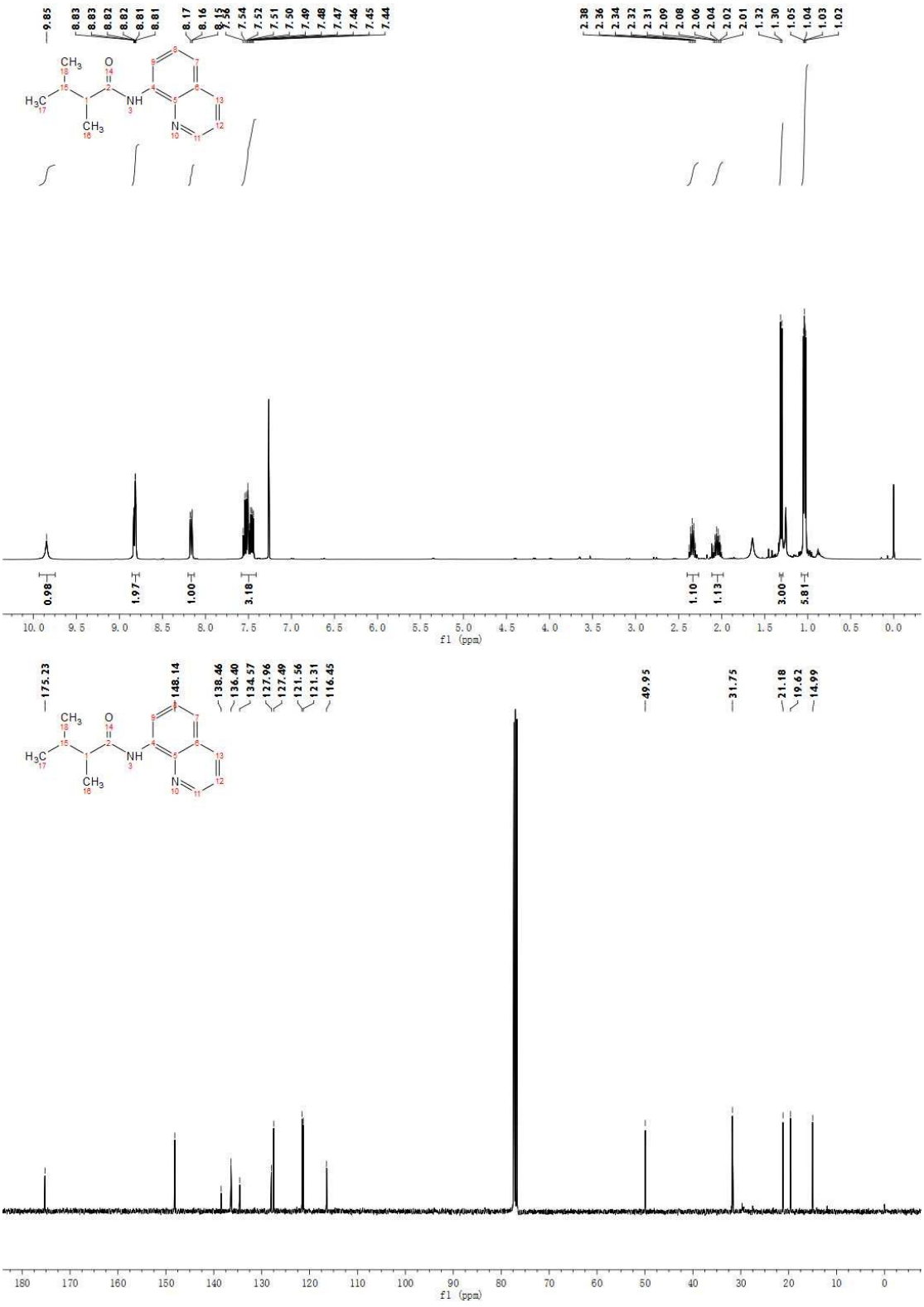
150.13
148.58
139.17
131.27
128.08
120.65
120.46
116.58
104.43
55.78
44.50
27.55
17.61
11.98
f1 (ppm)

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8.83
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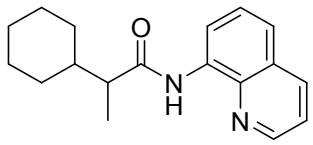
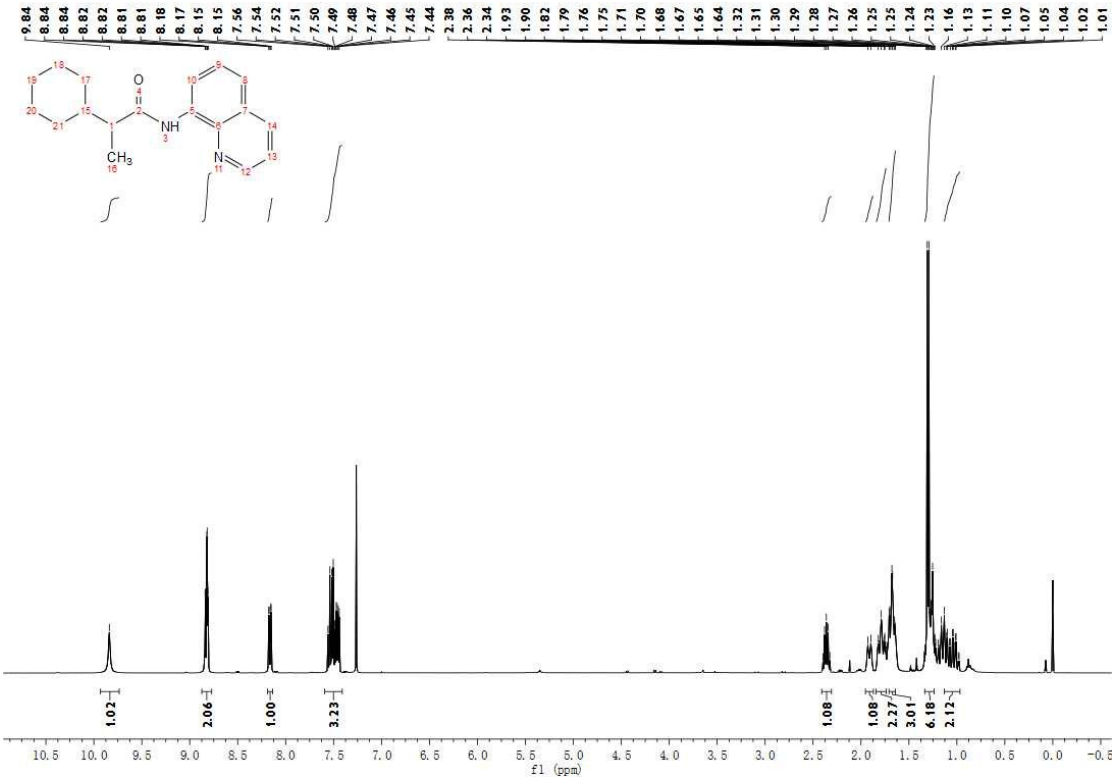
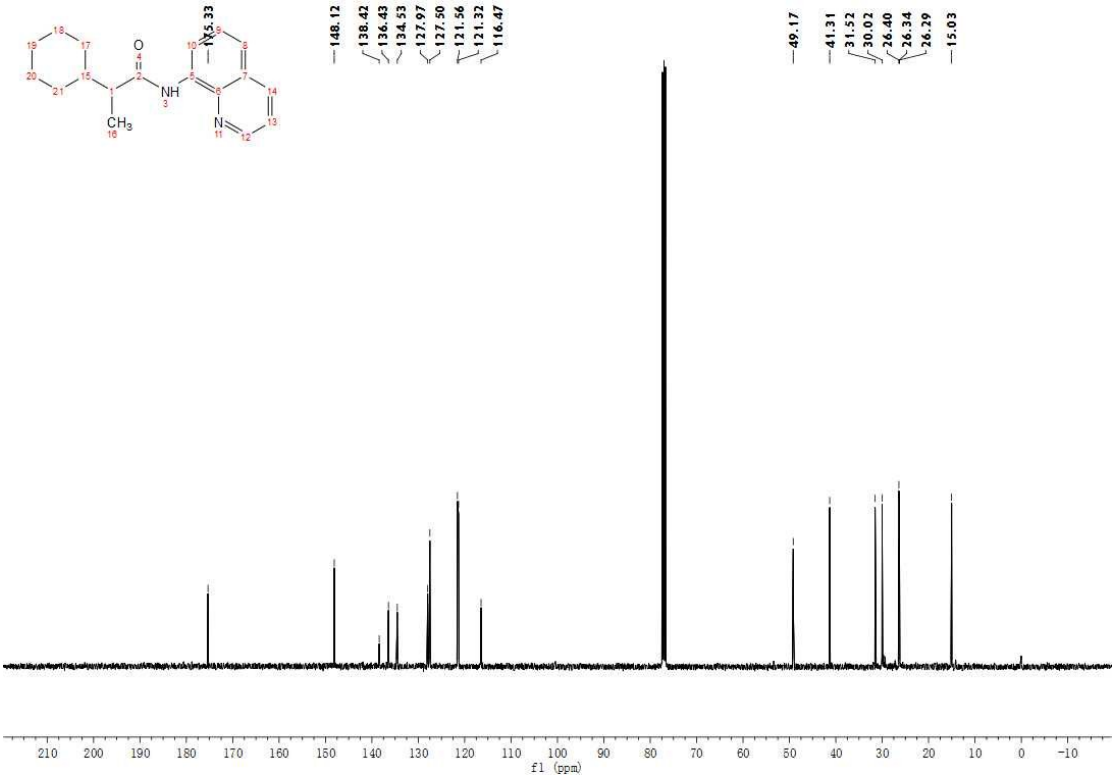
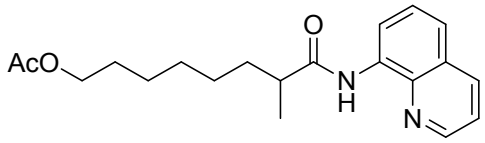
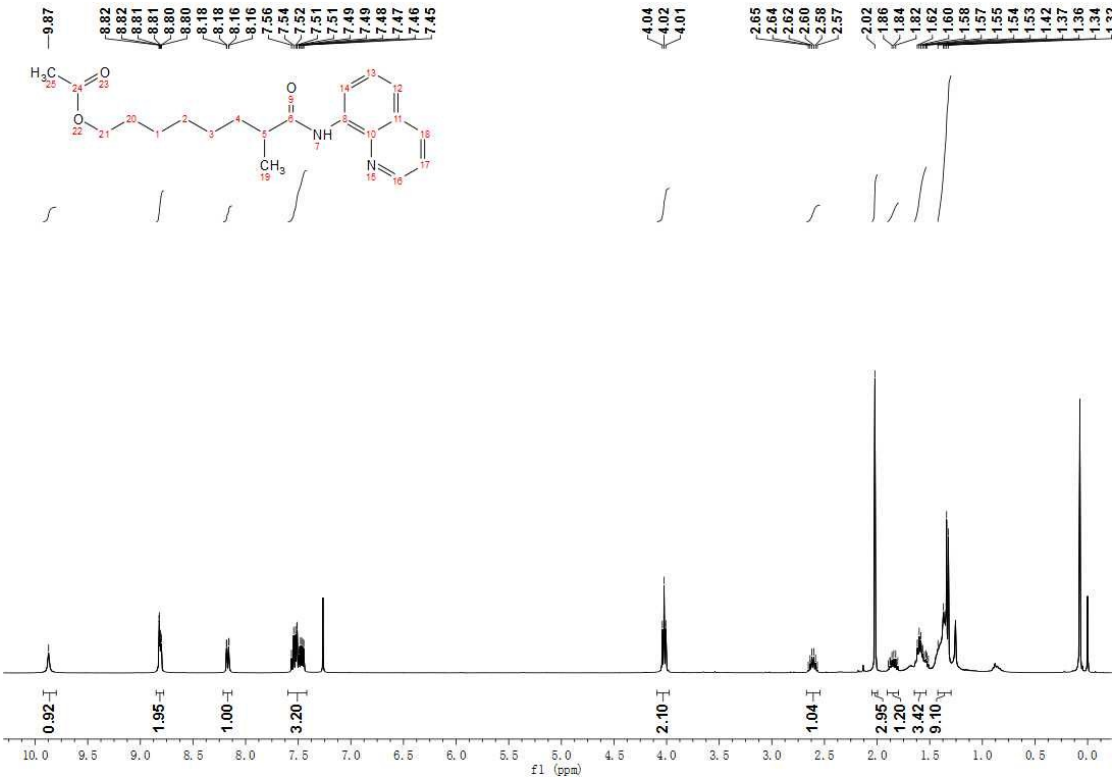
8.82
8.81
8.81
8.17
8.16
7.54
7.52
7.51
7.50
7.49
7.48
7.47
7.46
7.45
7.44
2.38
2.36
2.34
2.32
2.31
2.09
2.08
2.06
2.04
2.02
2.01
1.32
1.30
1.05
1.04
1.03
1.02
0.98
1.97
1.00
3.18
1.10
1.13
3.00
5.81
f1 (ppm)
175.23
148.14
138.46
136.40
134.57
127.96
127.49
121.56
121.31
116.45
49.95
31.75
21.18
19.62
14.99
f1 (ppm)


O
N
H
N


9.84 8.84 8.84 8.82 8.82 8.81 8.81 8.18 8.17 8.15 8.15 7.56 7.54 7.52 7.51 7.50 7.49 7.48 7.47 7.46 7.45 7.44 2.38 2.36 2.34 1.93 1.90 1.82 1.79 1.76 1.75 1.71 1.70 1.68 1.67 1.65 1.64 1.32 1.31 1.30 1.29 1.28 1.27 1.26 1.25 1.25 1.24 1.23 1.16 1.13 1.11 1.10 1.07 1.05 1.04 1.02 1.01
O
NH
CH3
N
1.02 2.06 1.00 3.23 1.08 1.08 2.27 3.01 6.18 2.12
f1 (ppm)


148.12 138.42 136.43 134.53 127.97 127.50 121.56 121.32 116.47
49.17 41.31 31.52 30.02 26.40 26.34 26.29 15.03
O
NH
CH3
N
f1 (ppm)


AcO
O
N
H
N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8.80
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8.18
8.18
8.16
8.16
7.56
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7.52
7.51
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7.49
7.49
7.48
7.47
7.46
7.45
4.04
4.02
4.01
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2.64
2.62
2.60
2.58
2.57
2.02
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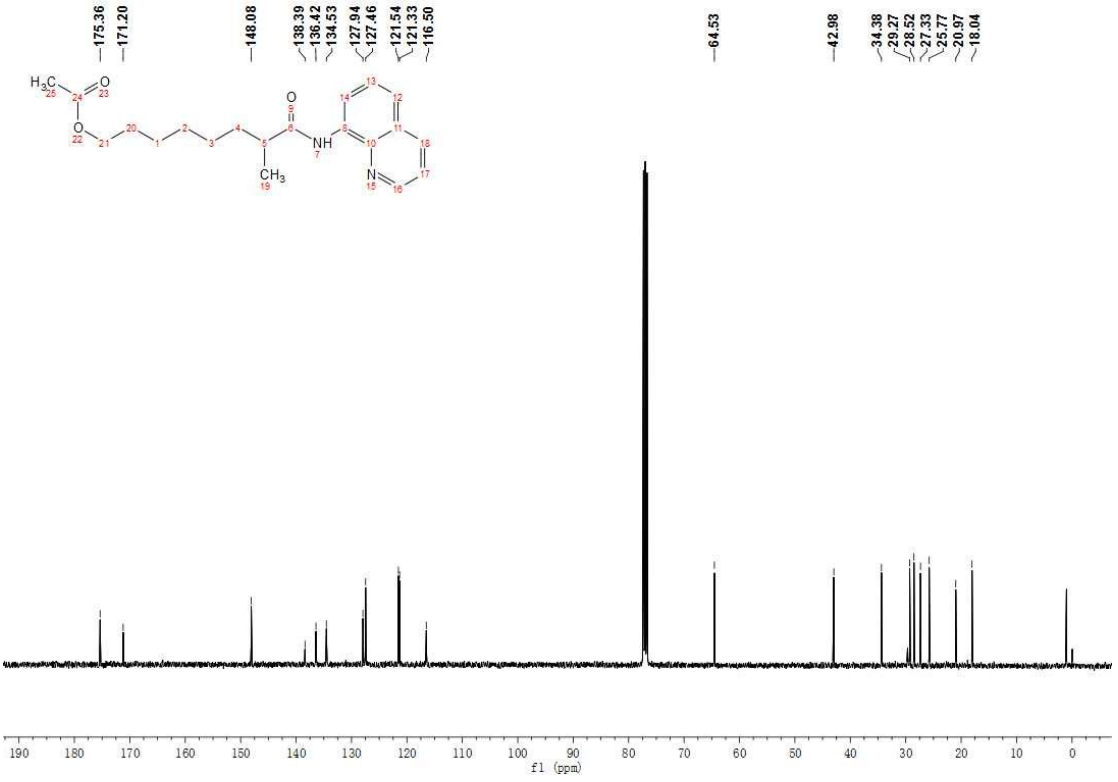
1.84
1.82
1.62
1.60
1.58
1.57
1.55
1.54
1.53
1.42
1.37
1.36
1.34
0.92
1.95
1.00
3.20
2.10
1.04
2.95
1.20
3.42
9.10
f1 (ppm)


175.36
171.20
148.08
138.39
136.42
134.53
127.94
127.46
121.54
121.33
116.50
64.53
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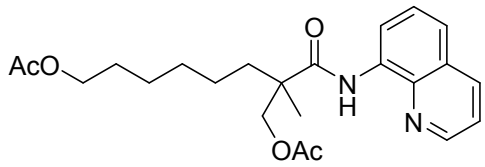
27.33
25.77
20.97
18.04
f1 (ppm)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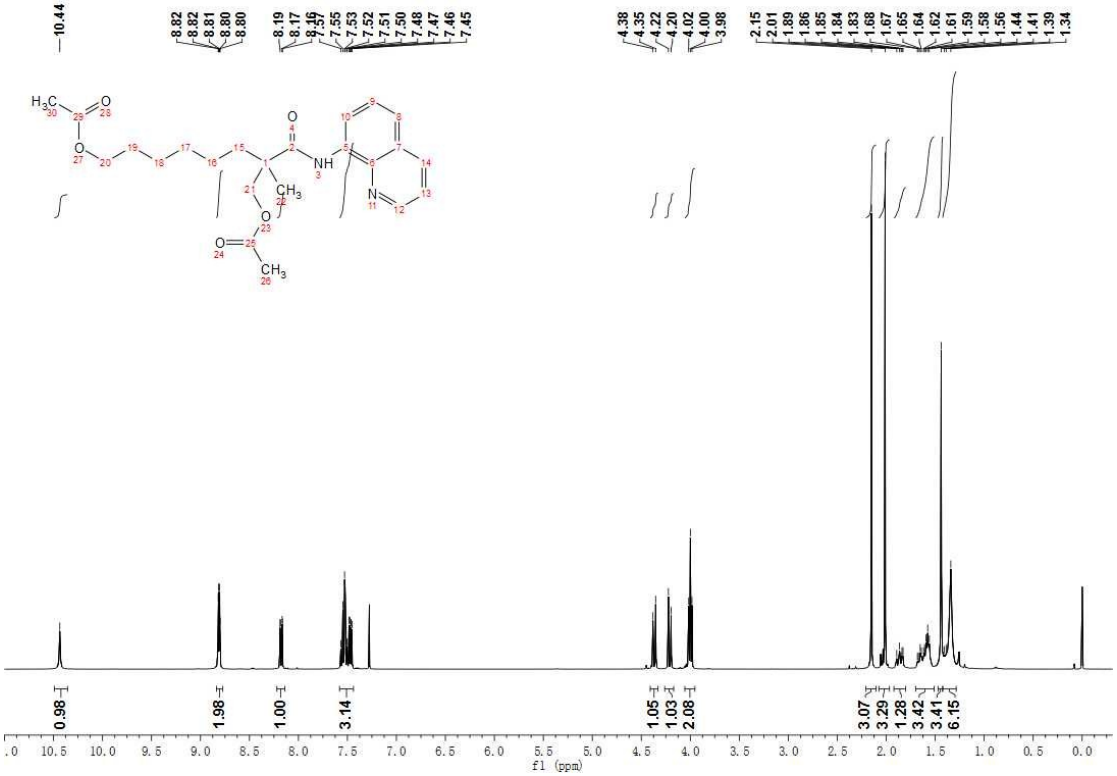
O
N
H
N
OAc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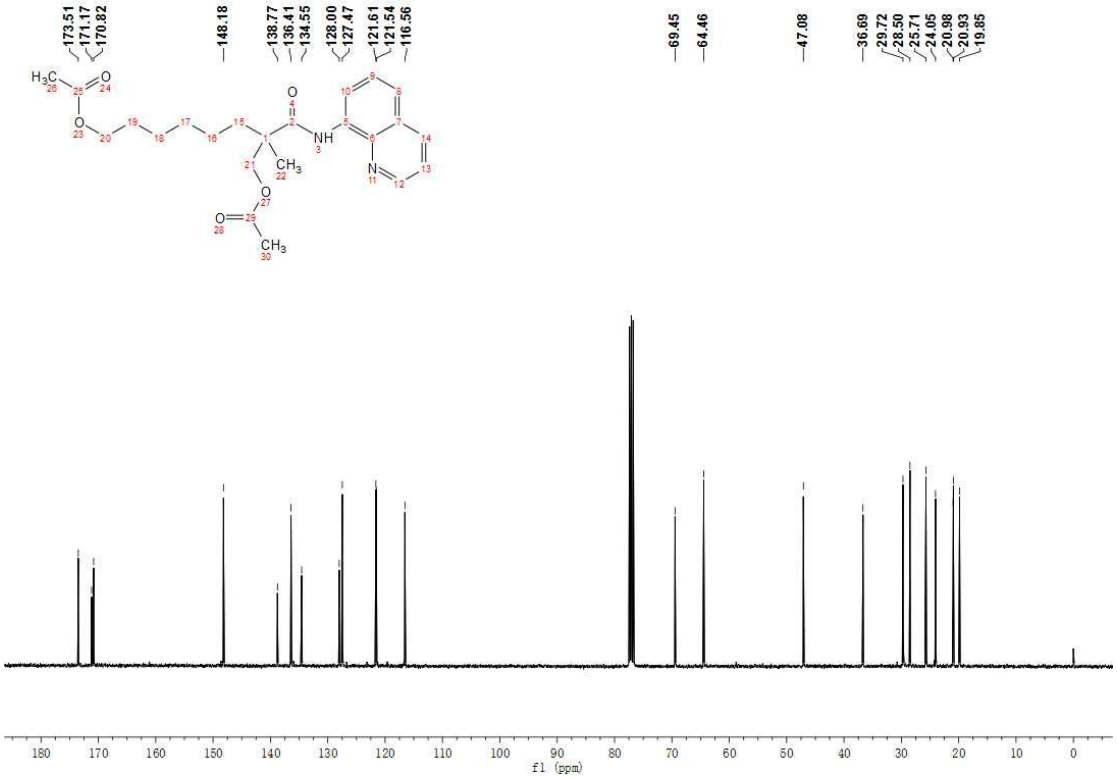
8.82
8.81
8.80
8.80
8.19
8.17
7.55
7.53
7.52
7.51
7.50
7.48
7.47
7.46
7.45
4.38
4.35
4.22
4.20
4.02
4.00
3.98
2.15
2.01
1.89
1.86
1.85
1.84
1.83
1.68
1.67
1.65
1.64
1.62
1.61
1.59
1.58
1.56
1.44
1.41
1.39
1.34
0.98
1.98
1.00
3.14
1.05
1.03
2.08
3.07
3.29
1.28
3.42
3.41
6.15
f1 (ppm)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171.17
170.82
148.18
138.77
136.41
134.55
128.00
127.47
121.61
121.54
116.56
69.45
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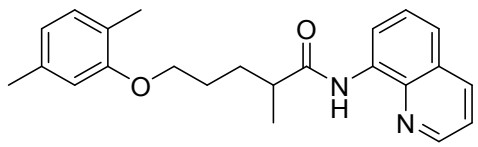
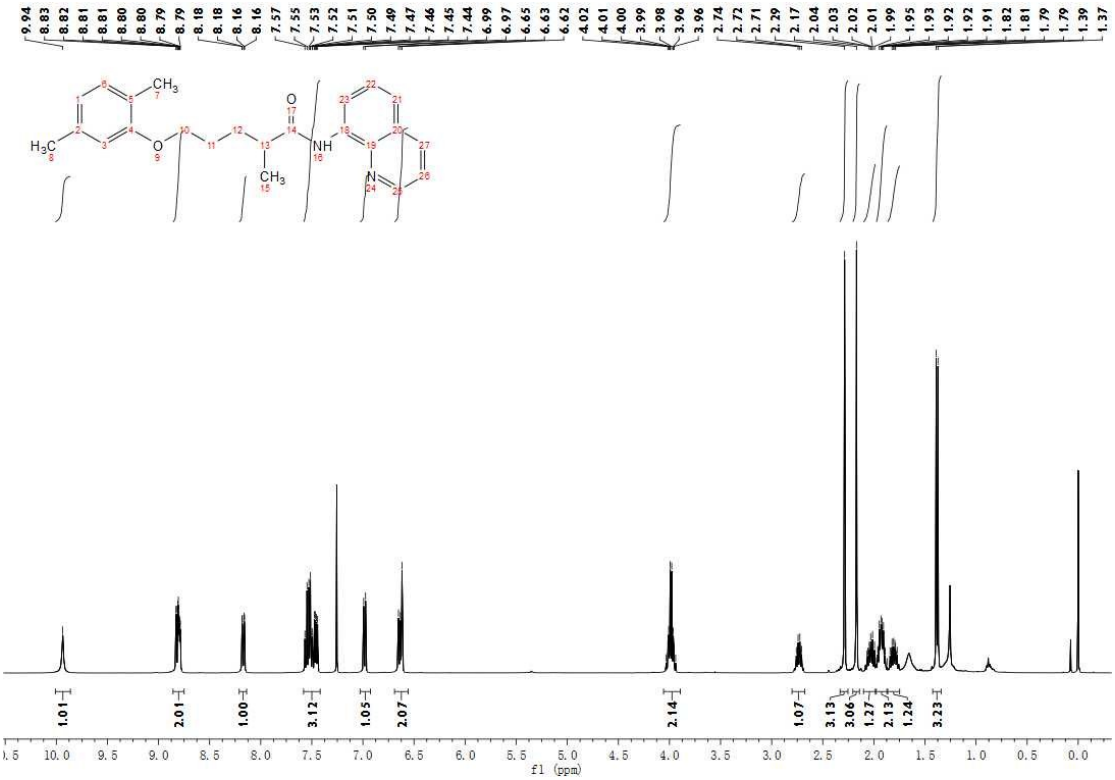
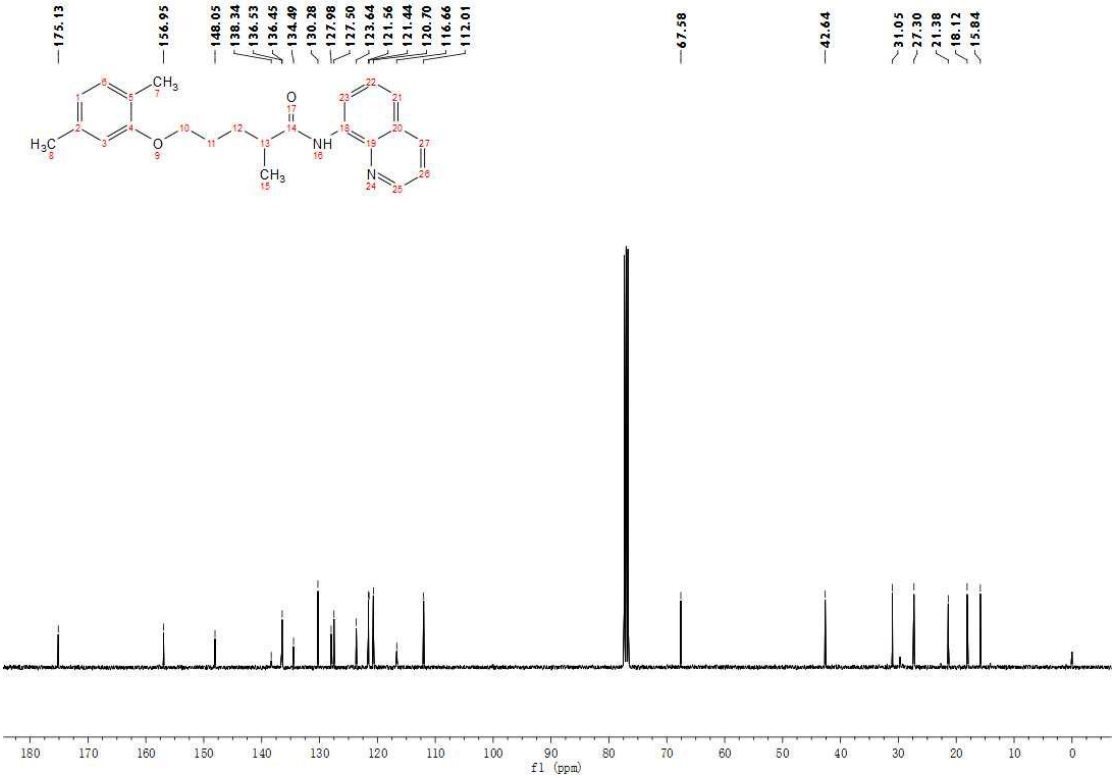
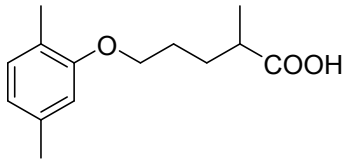
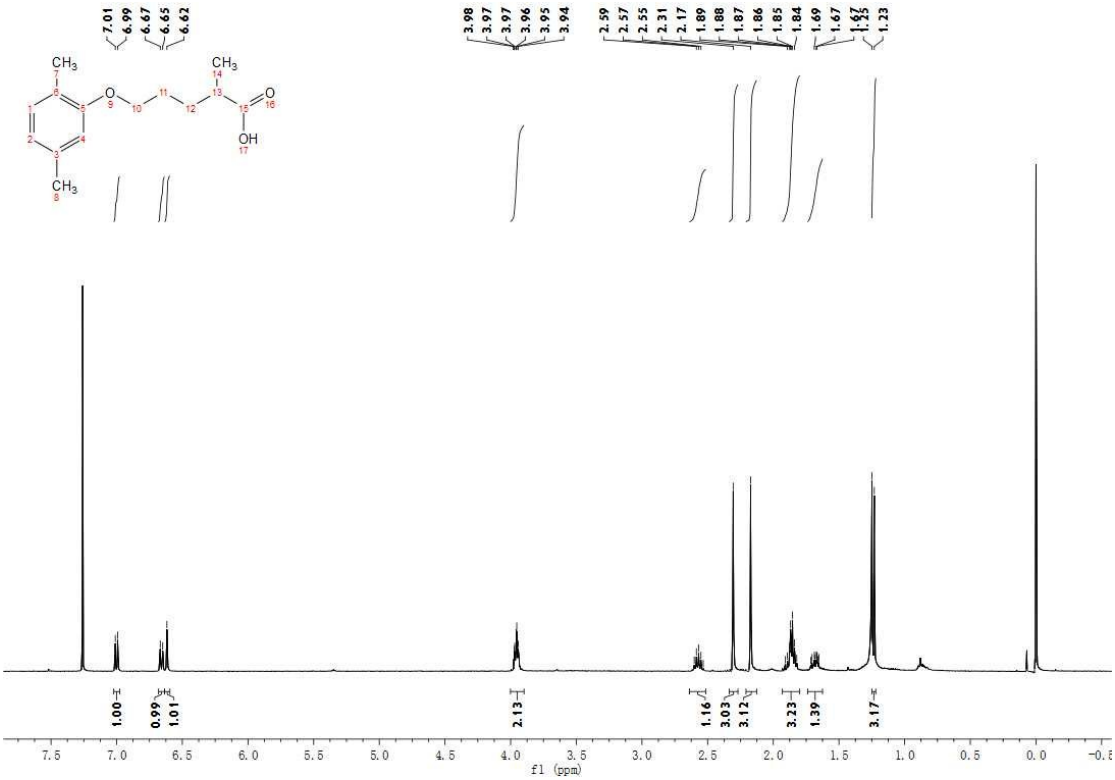
47.08
36.69
29.72
28.50
25.71
24.05
20.98
20.93
19.85
f1 (ppm)


O
O
N
H
N


9.94 8.83 8.82 8.81 8.81 8.80 8.80 8.79 8.79 8.18 8.18 8.16 8.16 7.57 7.55 7.53 7.52 7.51 7.50 7.49 7.47 7.46 7.45 7.44 6.99 6.97 6.65 6.63 6.62 4.02 4.01 4.00 3.99 3.98 3.96 3.96 2.74 2.72 2.71 2.29 2.17 2.04 2.03 2.02 2.01 1.99 1.95 1.93 1.92 1.92 1.91 1.82 1.81 1.79 1.79 1.39 1.37
1.01 2.01 1.00 3.12 1.05 2.07 2.14 1.07 3.13 3.06 1.27 2.13 1.24 3.23
f1 (ppm)


175.13 156.95 148.05 138.34 136.53 136.45 134.49 130.28 127.98 127.50 123.64 121.56 121.44 120.70 116.66 112.01 67.58 42.64 31.05 27.30 21.38 18.12 15.84
f1 (ppm)


O
COOH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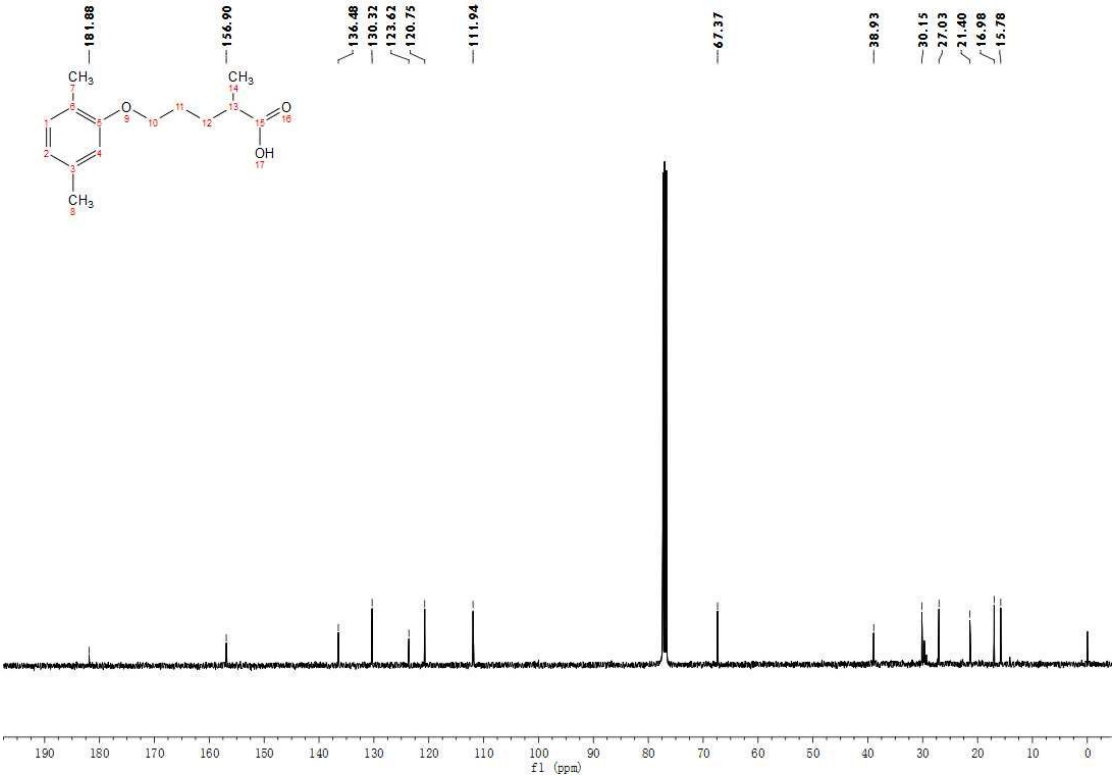
6.65
6.62
3.98
3.97
3.97
3.96
3.95
3.94
2.59
2.57
2.55
2.31
2.17
1.89
1.88
1.87
1.86
1.85
1.84
1.69
1.67
1.23
1.00
0.99
1.01
2.13
1.16
3.03
3.12
3.23
1.39
3.17
f1 (ppm)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156.90
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130.32
123.62
120.75
111.94
67.37
38.93
30.15
27.03
21.40
16.98
15.78
f1 (ppm)