Supporting Information
For

Nickel-Catalyzed Direct C (sp^3)-H Arylation of Aliphatic Amides with Thiophenes

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1. General

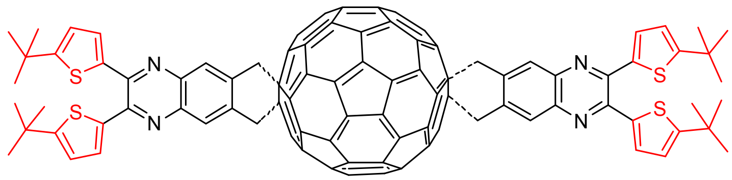
1.1 Instrumentation

All the reactions were carried out under an N_2 atmosphere using standard Schlenk techniques. Glassware was dried in an oven (150 $^{\circ}$C) and heated under reduced pressure before use. For thin layer chromatography (TLC) analyses throughout this work, Flash column chromatography was performed using Qingdao Haiyang silica gel (300-400) with distilled solvents. ^{1}H NMR (400MHz) spectra were recorded on Bruker Avance 400 spectrometers in $CDCl_3$ [using $(CH_3)_4Si$ (for ^{1}H, δ = 0.00) as internal standard]. ^{13}C NMR (100 MHz) spectra on Bruker Avance 400 spectrometers in $CDCl_3$ [using $CDCl_3$ (for ^{13}C, δ = 77.00) as internal standard]. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiple. Chemical shifts (δ) are in parts per million relative to $CDCl_3$ at 7.26 ppm for ^{1}H and at 77.16 ppm for $^{13}C\{^{1}H\}$, respectively. The NMR yields were determined by ^{1}H NMR spectra with dibromomethane as an internal standard.

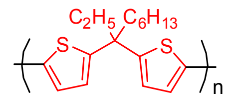
1.2 Chemicals

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. All the solvents and commercially available reagents were purchased from commercial sources and used directly. Starting materials were prepared according to literature procedures.[1]

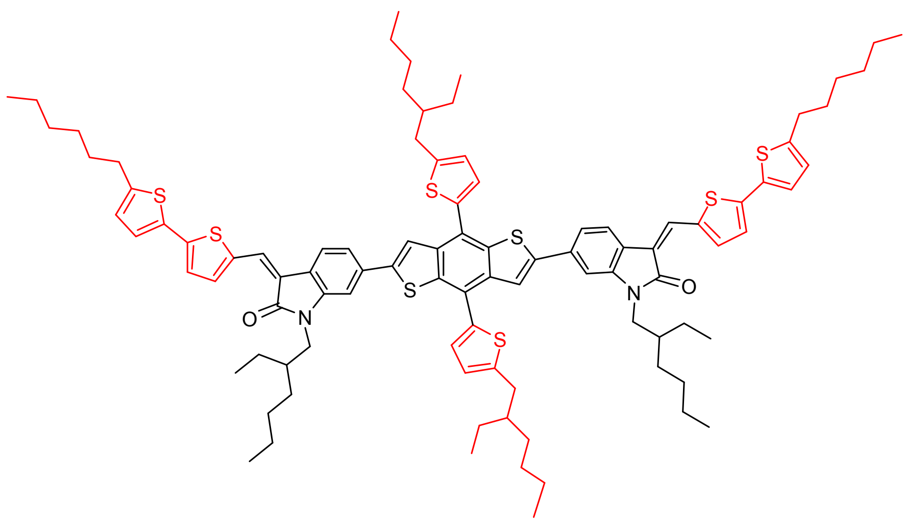
2. The organic semiconductors which contain alkyl-substituted thiophenes



2,3-bis(5-*tert*-butylthiophen-2-yl)-6,7-dimethylquinoxaline-C_{60}-bisadduct



poly(bithienylmethylene)s



TIBDT

3. Synthesis of Starting Materials

3.1 General Procedure for the Preparation of Starting Materials

A solution of LDA (10 mmol) in THF was prepared from diisopropylamine (1.5 mL, 10.7 mmol) and 2.5 M *n*-BuLi in hexane (4.0 mL, 10 mmol) at -78 °C. To this LDA solution, carboxylate ester (10 mmol) was added dropwise at -78 °C and the mixture was stirred at this temperature for 1 h. Alkyl halide (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 at 0 °C, extracted with Et_2O (15 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.

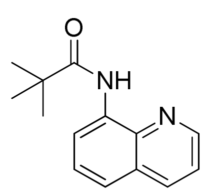
To the ester was added a solution of NaOH (2 M, 8.0 mL) and methanol (10 mL).The mixture was stirred overnight at 60 °C. After removal of methanol in vacuo, the pH of the mixture was adjusted to 2 with 3.0 M HCl. The mixture was then saturated with NaCl and extracted with Et_2O (15 mL x 3). The combined 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 (1.75 mL, 20 mmol) was added slowly to a stirred solution of the carboxylic acid in CH_2Cl_2 (20 mL) and DMF (0.1 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 (1.01 g, 7.0 mmol) and Et_3N (1.7 mL, 12 mmol) in CH_2Cl_2 (12 mL). The mixture was stirred overnight at room temperature. Then the mixture was diluted with CH_2Cl_2 (10 mL), washed successively with water, saturated aqueous $NaHCO_3$, 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 (1:60, v/v), to afford corresponding 8-aminoquinolinyl amides **1**.

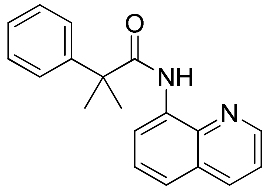
3.2 Analytical Data for Starting Materials

***N*-(quinolin-8-yl)pivalamide (1a)**



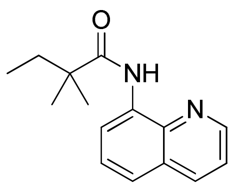
This amide was obtained as colorless oil. δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.43 (s, 9 H), 7.37–7.53 (m, 3 H), 8.07–8.11 (m, 1 H), 8.79–8.81 (m, 2 H), 10.27 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 27.75, 40.36, 116.20, 121.25, 121.53, 127.40, 127.92, 134.70, 136.28, 138.79, 148.21, 177.24; Ms (EI): *m/z* = 228.1 $[M+H]^+$.

2-methyl-2-phenyl-*N*-(quinolin-8-yl)propanamide (1b)



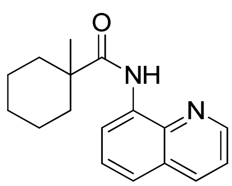
This amide was obtained as white solid. Melting point: 100-101 °C. δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.78 (s, 6 H), 7.28–7.35 (m, 2 H), 7.38–7.44 (m, 3 H), 7.48–7.55 (m, 3 H), 8.05–8.07 (m, 1 H), 8.58–8.59 (m, 1 H), 8.75–8.77 (m, 1 H), 9.87 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 27.02, 48.40, 115.97, 121.26, 121.43, 126.37, 127.02, 127.33, 127.84, 128.79, 134.72, 136.09, 138.68, 144.90, 148.12, 175.82; Ms (EI): m/z = 290.1 $[M+H]^+$.

2,2-dimethyl-*N*-(quinolin-8-yl)butanamide (1c)



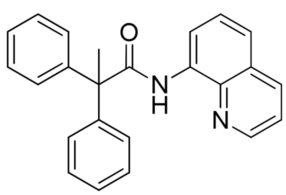
This amide was obtained as yellow oil. δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.96 (t, J = 7.2 Hz, 3 H), 1.39 (s, 6 H), 1.77 (q, J = 7.2 Hz, 2 H), 7.42–7.55 (m, 3 H), 8.13–8.15 (m, 1 H), 8.81–8.83 (m, 2 H), 10.25 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 9.33, 25.11, 34.13, 44.08, 116.17, 121.21, 121.52, 127.36, 127.42, 127.93, 134.67, 136.24, 136.27, 138.79, 148.23, 176.65; Ms (EI): m/z = 242.1 $[M+H]^+$.

1-methyl-*N*-(quinolin-8-yl)cyclohexanecarboxamide (1d)



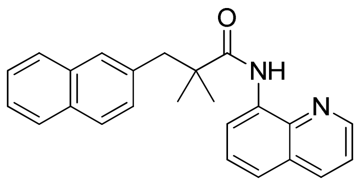
This amide was obtained as yellow oil. δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.36 (s, 3 H), 1.50-1.68 (m, 8 H), 2.18–2.22 (m, 2 H), 7.41–7.55 (m, 3 H), 8.12–8.14 (m, 1 H), 8.80–8.84 (m, 2 H), 10.29 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 22.90, 25.76, 26.54, 35.69, 44.27, 116.09, 121.01, 121.40, 127.34, 127.83, 134.70, 136.18, 138.70, 148.11, 176.51; Ms (EI): m/z = 268.2 $[M+H]^+$.

2,2-diphenyl-*N*-(quinolin-8-yl)propanamide (1e)



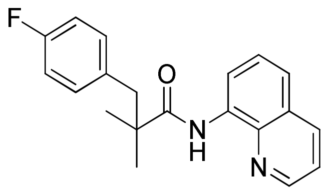
This amide was obtained as white solid. Melting point: 153 °C. δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.17 (s, 3 H), 7.29–7.41 (m, 11 H), 7.45–7.54 (m, 2 H), 8.06–8.08 (m, 1 H), 8.49–8.50 (m, 1 H), 8.84–8.86 (m, 1 H), 10.12 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 27.16. 58.44, 116.02, 121.45, 121.58, 126.99, 127.34, 127.82, 128.34, 128.57, 134.50, 136.02, 138.80, 144.94, 148.06, 173.75; Ms (EI): m/z = 352.1 $[M+H]^+$.

2,2-dimethyl-3-(naphthalen-2-yl)-*N*-(quinolin-8-yl)propanamide (1f)



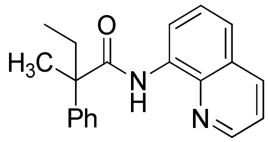
This amide was obtained as brown oil. δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.48 (s, 6 H), 3.22 (s, 2 H), 7.33–7.40 (m, 4 H), 7.47–7.50 (m, 1 H), 7.54–7.58 (m, 1 H), 7.64–7.73 (m, 4 H), 8.08–8.11 (m, 1 H), 8.59–8.60 (m, 1 H), 8.86–8.88 (m, 1 H), 10.15 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.40, 45.20, 47.07, 116.32, 121.40, 121.48, 125.28, 125.74, 127.39, 127.45, 127.47, 127.59, 127.87, 128.79, 128.84, 132.24, 133.33, 134.49, 135.63, 136.15, 138.75, 148.11, 176.07; Ms (EI): m/z = 354.2 $[M+H]^+$.

3-(4-fluorophenyl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (1g)



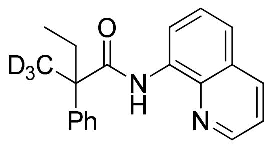
This amide was obtained as white solid. Melting point: 93 °C. δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.41 (s, 6 H), 3.01 (s, 2 H), 6.86 (t, J = 8.4 Hz, 2 H), 7.13–7.16 (m, 2 H), 7.40–7.43 (m, 1 H), 7.48–7.56 (m, 2 H), 8.12–8.14 (m, 1 H), 8.74–8.75 (m, 1 H), 8.81–8.83 (m, 1 H), 10.13 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.26, 45.00 (d, J_{C-F} = 0.8 Hz), 46.12, 114.78 (d, J_{C-F} = 20.9 Hz), 116.30, 121.46, 121.56, 127.40, 127.92, 131.60 (d, J_{C-F} = 7.8 Hz), 133.65 (d, J_{C-F} = 3.3 Hz), 134.39, 136.27, 138.77, 148.22, 161.71 (d, J_{C-F} = 242.7 Hz), 175.77; Ms (EI): m/z = 322.3 $[M+H]^+$.

2-methyl-2-phenyl-*N*-(quinolin-8-yl)butanamide (1h)



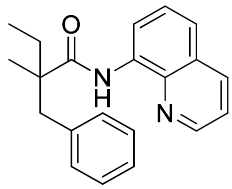
This amide was obtained as yellow oil. δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.83 (t, J = 7.6 Hz, 3 H), 1.66 (s, 3 H), 2.07–2.27 (m, 2 H), 7.17–7.36 (m, 5 H), 7.40–7.44 (m, 3 H), 7.97–7.99 (m, 1 H), 8.51–8.52 (m, 1 H), 8.68–8.70 (m, 1 H), 9.78 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 9.04, 22.98, 31.72, 52.27, 116.00, 121.20, 121.42, 126.04, 126.83, 126.89, 127.34, 127.85, 128.36, 128.70, 134.73, 136.08, 138.68, 143.87, 148.11, 175.45; Ms (EI): m/z = 304.3 $[M+H]^+$.

$[D_3]$-2-methyl-2-phenyl-*N*-(quinolin-8-yl)butanamide ($[D_3]$-1h)



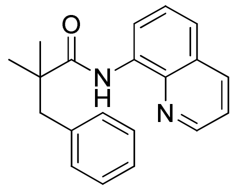
This amide was obtained as yellow oil. δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.82 (t, J = 7.2 Hz, 3 H), 2.09–2.22 (m, 2 H), 7.15–7.24 (m, 2 H), 7.27–7.33 (m, 3 H), 7.38–7.42 (m, 3 H), 7.94–7.96 (m, 1 H), 8.49–8.50 (m, 1 H), 8.68–8.70 (m, 1 H), 9.77 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 9.04, 31.65, 52.07, 116.00, 121.21, 121.42, 126.83, 126.90, 127.33, 127.85, 128.72, 134.73, 136.08, 138.68, 143.86, 148.11, 175.47; Ms (EI): m/z = 307.4 $[M+H]^+$.

2-benzyl-2-methyl-*N*-(quinolin-8-yl)butanamide (1i)



This amide was obtained as pale yellow solid. Melting point: 64-65 °C. δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.87 (t, J = 7.2 Hz, 3 H), 1.23 (s, 3 H), 1.43–1.50 (m, 1 H), 1.91–1.96 (m, 1 H), 2.71, 3.15 (AB, J_{AB} = 13.2 Hz, 2 H), 6.99–7.09 (m, 5 H), 7.22–7.25 (m, 1 H), 7.32–7.34 (m, 1 H), 7.38–7.42 (m, 1 H), 7.94–7.96 (m, 1 H), 8.58–8.59 (m, 1 H), 8.74–8.76 (m, 1 H), 10.02 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 9.22, 20.26, 32.85, 46.04, 49.03, 116.29, 121.38, 121.53, 126.35, 127.43, 127.93, 128.01, 130.34, 134.46, 136.22, 137.91, 138.80, 148.22, 175.31; Ms (EI): m/z = 318.2 $[M+H]^+$.

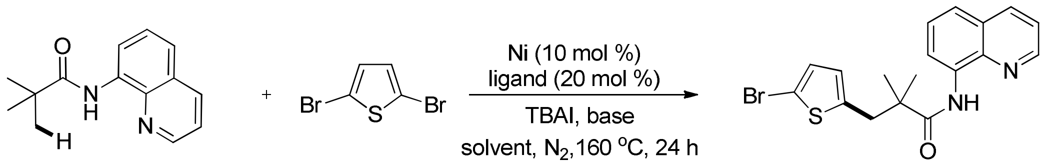
2,2-dimethyl-3-phenyl-*N*-(quinolin-8-yl)propanamide (1j)



This amide was obtained as pale yellow solid. Melting point: 60 °C. δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.42 (s, 6 H), 3.05 (s, 2 H), 7.14–7.20 (m, 5 H), 7.41–7.44 (m, 1 H), 7.48–7.57 (m, 2 H), 8.13–8.15 (m, 1 H), 8.74–8.75 (m, 1 H), 8.83–8.85 (m, 1 H), 10.17 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.27, 44.97, 46.89, 116.30, 121.35, 121.50, 126.36, 127.44, 127.92, 127.98, 130.29, 134.52, 136.24, 137.95, 138.82, 148.17, 176.07; Ms (EI): m/z = 304.2 $[M+H]^+$.

4. Synthesis of Thiophenes products

4.1 General Procedure for Nickel-Catalyzed heteroarylation of amide with bromide thiophene



A 10-mL Schlenk tube was charged with *N*-(quinolin-8-yl)pivalamide **1a** (45.6 mg, 0.2 mmol), 2,5-dibromothiophene (143.8 mg, 0.6 mmol), $NiBr_2$ (4.4 mg, 0.02 mmol), MesCOOH (6.6 mg, 0.04 mmol), Na_2CO_3 (42.4 mg, 0.4 mmol), TBAI (147.6 mg, 0.4 mmol) and DMF (0.5 mL). The vial was evacuated and filled with N_2, and stirred at 160 °C for 24 h. The mixture was then cooled to room temperature, diluted with CH_2Cl_2 (2 mL), filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/Hexane (1:100 ~ 1:60, v/v), to afford the desired product **2a**

4.2 Optimization of solvents and bases for thiophenes products synthesis

A: Solvents

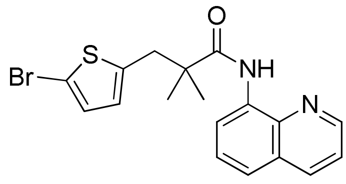
Entry	Solvent	Yield(%)
1	DMSO	60
2	NMP	62
3	Toluene	trace
4	Tert-amyl alcohol	63
5	Dioxane	15

B: Bases：

Entry	Base	Yield(%)
1	K_2CO_3	68
2	Cs_2CO_3	trace
3	K_3PO_4	trace
4	NaOH	trace
5	Li_2CO_3	50
6	$NaHCO_3$	66
7	$Na_2(OAc)$	20
8	Na_2CO_3 (4eq)	79

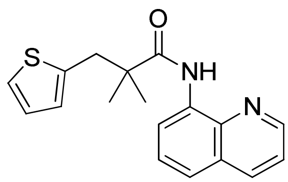
4.3 Analytical Data for Thiophenes Products

3-(5-bromothiophen-2-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (2a)



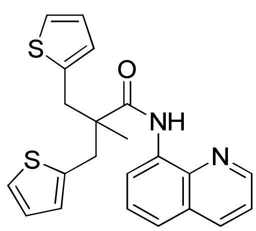
This amide was obtained 55.9 mg (72%) as pale white viscous oil. R_f = 0.36 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.46 (s, 6 H), 3.17 (s, 2 H), 6.59–6.60 (m, 1 H), 6.79–6.80 (m, 1 H), 7.44–7.46 (m, 1 H), 7.51–7.58 (m, 2 H), 8.15–8.17 (m, 1 H), 8.79–8.83 (m, 2 H), 10.23 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.46, 41.25, 44.97, 116.45, 121.55, 121.59, 127.39, 127.44, 127.94, 129.40, 134.36, 136.31, 138.78, 141.86, 148.28, 175.34; HRMS (ESI): $M+H^+$ found 388.0239; $C_{18}H_{17}Br_1N_2S_1O_1$ requires 388.0245.

2,2-dimethyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)propanamide (2ba)



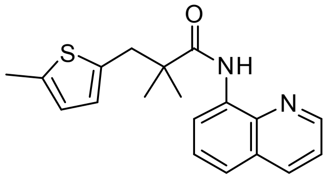
This amide was obtained 34.5 mg (56%) as yellow viscous oil. R_f = 0.29 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.46 (s, 6 H), 3.26 (s, 2 H), 6.84–6.87 (m, 2 H), 7.06–7.07 (m, 1 H), 7.41–7.45 (m, 1 H), 7.49–7.57 (m, 2 H), 8.13–8.15 (m, 1 H), 8.77–8.78 (m, 1 H), 8.84–8.85 (m, 1 H), 10.23 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.39, 40.86, 45.09, 116.40, 121.43, 121.55, 124.09, 126.61, 126.96, 127.46, 127.93, 134.50, 136.28, 138.81, 139.87, 148.23, 175.68; HRMS (ESI): $M+H^+$ found 310.1134; $C_{18}H_{18}N_2S_1O_1$ requires 310.1140.

2-methyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)-2-(thiophen-2-ylmethyl)propanamide (2bb)



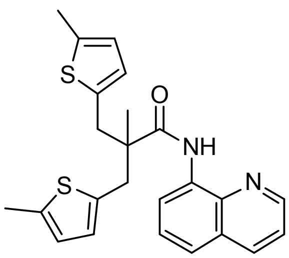
This amide was obtained 19.9 mg (25%) as brown viscous oil. R_f = 0.24 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.46 (s, 3 H), 3.08, 3.59 (AB, J_{AB} = 14.4 Hz, 4 H), 6.84–6.86 (m, 4 H), 7.06–7.07 (m, 2 H), 7.39–7.42 (m, 1 H), 7.49–7.58 (m, 2 H), 8.12–8.14 (m, 1 H), 8.70–8.71 (m, 1 H), 8.86–8.88 (m, 1 H), 10.11 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 20.47, 39.91, 49.87, 116.52, 121.50, 121.54, 124.31, 126.67, 127.29, 127.44, 127.88, 134.25, 136.17, 139.09, 148.18, 174.05; HRMS (ESI): $M+H^+$ found 392.1011; $C_{22}H_{20}N_2S_2O_1$ requires 392.1017.

2,2-dimethyl-3-(5-methylthiophen-2-yl)-*N*-(quinolin-8-yl)propanamide (2ca)



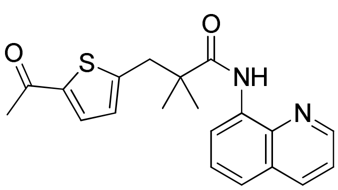
This amide was obtained 32.8 mg (51%) as yellow oil. R_f = 0.31 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.45 (s, 6 H), 2.34 (s, 3 H), 3.16 (s, 2 H), 6.49–6.50 (m, 1 H), 6.60–6.61 (m, 1 H), 7.42–7.45 (m, 1 H), 7.49–7.57 (m, 2 H), 8.14–8.16 (m, 1 H), 8.78–8.79 (m, 1 H), 8.83–8.84 (m, 1 H), 10.23 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 15.18, 25.36, 41.07, 44.98, 116.41, 121.36, 121.52, 124.64, 126.78, 127.47, 127.93, 134.55, 136.27, 137.51, 138.40, 138.83, 148.19, 175.83; HRMS (ESI): M+H$^+$ found 324.1292; $C_{19}H_{20}N_2S_1O_1$ requires 324.1296.

2-methyl-3-(5-methylthiophen-2-yl)-2-((5-methylthiophen-2-yl)methyl)-*N*-(quinolin-8-yl)propanamide (2cb)



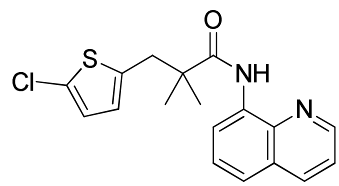
This amide was obtained 21.3 mg (25%) as yellow viscous oil. R_f = 0.28 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.45 (s, 3 H), 2.32 (s, 6 H), 2.99, 3.46 (AB, J_{AB} = 14.4 Hz, 4 H), 6.47–6.48 (m, 2 H), 6.61–6.62 (m, 2 H), 7.40–7.43 (m, 1 H), 7.49–7.58 (m, 2 H), 8.13–8.15 (m, 1 H), 8.72–8.73 (m, 1 H), 8.85–8.87 (m, 1 H), 10.13 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 15.17, 20.66, 39.97, 49.68, 116.55, 121.40, 121.46, 124.70, 127.11, 127.47, 127.88, 134.40, 136.16, 136.84, 138.59, 138.81, 148.12, 174.31; HRMS (ESI): M+H$^+$ found 420.1329; $C_{24}H_{24}N_2S_2O_1$ requires 420.1330.

3-(5-acetylthiophen-2-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (2d)



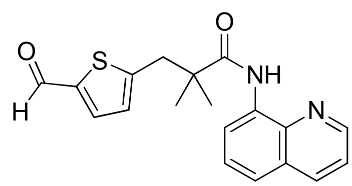
This amide was obtained 28.9 mg (41%) as brown viscous oil. R_f = 0.21 (petroleum ether/ethyl acetate = 10:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.49 (s, 6 H), 2.44 (s, 3 H), 3.26 (s, 2 H), 6.86–6.87 (m, 1 H), 7.43–7.46 (m, 2 H), 7.51–7.58 (m, 2 H), 8.15–8.17 (m, 1 H), 8.76–8.78 (m, 1 H), 8.80–8.83 (m, 1 H), 10.23 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.51, 26.54, 41.37, 45.14, 116.47, 121.61, 121.64, 127.43, 127.92, 128.32, 132.67, 134.26, 136.33, 138.75, 142.98, 148.29, 149.87, 175.00, 190.51; HRMS (ESI): M+H$^+$ found 352.1230; $C_{20}H_{20}N_2S_1O_2$ requires 352.1245.

3-(5-chlorothiophen-2-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide（2e）



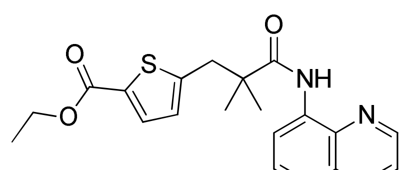
This amide was obtained 42.7 mg (62%) as colorless oil. R_f = 0.33 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.46 (s, 6 H), 3.14 (s, 2 H), 6.59–6.60 (m, 1 H), 6.65–6.66 (m, 1 H), 7.43–7.58 (m, 3 H), 8.15–8.17 (m, 1 H), 8.78–8.83 (m, 2 H), 10.23 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.46, 41.31, 45.00, 116.45, 121.57, 121.59, 125.61, 126.33, 127.44, 127.88, 127.94, 134.36, 136.32, 138.78, 138.93, 148.28, 175.35; HRMS (ESI): $M+H^+$ found 344.0746; $C_{18}H_{17}N_2S_1O_1Cl_1$ requires 344.0750.

3-(5-formylthiophen-2-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (2f)



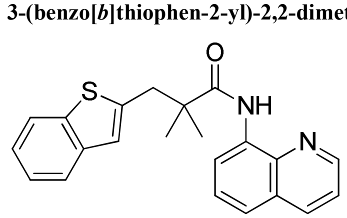
This amide was obtained 33.1 mg (49%) as yellow viscous oil. R_f = 0.24 (petroleum ether/ethyl acetate = 10:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.50 (s, 6 H), 3.30 (s, 2 H), 6.95–6.96 (m, 1 H), 7.43–7.46 (m, 1 H), 7.51–7.58 (m, 3 H), 8.15–8.17 (m, 1 H), 8.76–8.82 (m, 2 H), 9.75 (s, 1 H), 10.23 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.57, 41.52, 45.21, 116.48, 121.63, 121.71, 127.44, 127.93, 128.56, 134.20, 136.35, 136.63, 138.75, 142.57, 148.31, 151.73, 174.83, 182.70; HRMS (ESI): $M+H^+$ found 338.1078; $C_{19}H_{18}N_2S_1O_2$ requires 338.1089.

ethyl 5-(2,2-dimethyl-3-oxo-3-(quinolin-8-ylamino)propyl)thiophene-2-carboxylate (2g)



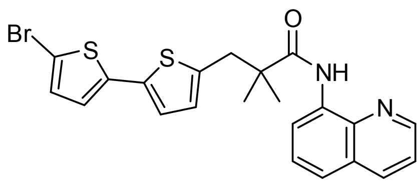
This amide was obtained 32.9 mg (43%) as pale yellow viscous oil. R_f = 0.34 (petroleum ether/ethyl acetate = 10:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.31 (t, *J* = 6.8 Hz, 3 H), 1.48 (s, 6 H), 3.25 (s, 2 H), 4.27 (q, *J* = 7.2 Hz, 2 H), 6.83–6.84 (m, 1 H), 7.42–7.46 (m, 1 H), 7.50–7.58 (m, 3 H), 8.14–8.17 (m, 1 H), 8.76–8.83 (m, 2 H), 10.22 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 14.30, 25.47, 41.15, 45.07, 60.88, 116.48, 121.57, 127.42, 127.89, 127.93, 132.33, 133.30, 134.32, 136.29, 138.79, 147.88, 148.26, 162.24, 175.11; HRMS (ESI): $M+H^+$ found 382.1344; $C_{21}H_{22}N_2S_1O_3$ requires 382.1351.

3-(benzo[*b*]thiophen-2-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (2h)



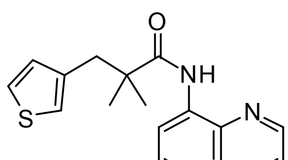
This amide was obtained 39.6 mg (55%) as yellow viscous oil. R_f = 0.58 (petroleum ether/ethyl acetate = 10:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.52 (s, 6 H), 3.34 (s, 2 H), 7.07 (s, 1 H), 7.18–7.26 (m, 2 H), 7.39–7.42 (m, 1 H), 7.50–7.62 (m, 3 H), 7.67–7.69 (m, 1 H), 8.12–8.15 (m, 1 H), 8.68–8.69 (m, 1 H), 8.86–8.87 (m, 1 H), 10.26 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.66, 41.66, 45.06, 116.47, 121.50, 121.53, 121.95, 122.82, 123.53, 123.61, 123.93, 127.43, 127.91, 134.47, 136.23, 138.79, 139.88, 140.00, 141.26, 148.21, 175.54; HRMS (ESI): $M+H^+$ found 360.1288; $C_{22}H_{20}N_2S_1O_1$ requires 360.1296.

3-(5'-bromo-[2,2'-bithiophen]-5-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (2i)



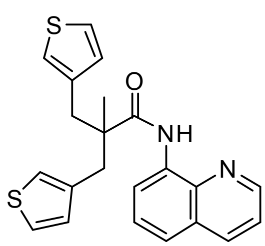
This amide was obtained 39.5 mg (42%) as yellow viscous oil. R_f = 0.59 (petroleum ether/ethyl acetate = 10:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.49 (s, 6 H), 3.20 (s, 2 H), 6.73–6.74 (m, 1 H),6.85–6.88 (m, 1 H), 6.92–6.93 (m, 1 H),7.01–7.12 (m, 1 H), 7.41–7.44 (m, 1 H), 7.49–7.57 (m, 2 H), 8.13–8.15 (m, 1 H), 8.75–8.76 (m, 1 H), 8.82–8.84 (m, 1 H), 10.23 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.47, 41.05, 45.09, 116.44, 121.47, 121.51, 121.53, 121.55, 123.23, 123.39, 123.66, 123.79, 127.43, 127.61, 127.75, 127.82, 127.93, 130.43, 134.42, 135.05, 136.27, 138.80, 139.19, 139.29, 139.93, 148.24, 175.41; HRMS (ESI): $M+H^+$ found 470.0111; $C_{22}H_{19}Br_1N_2S_2O_1$ requires 470.0122.

2,2-dimethyl-*N*-(quinolin-8-yl)-3-(thiophen-3-yl)propanamide (2ja)



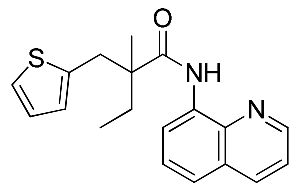
This amide was obtained 28.7 mg (46%) as colorless viscous oil. R_f = 0.34 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.42 (s, 6 H), 3.07 (s, 2 H), 6.92–6.93 (m, 1 H), 7.01 (s, 1 H), 7.12–7.14 (m, 1 H), 7.41–7.45 (m, 1 H), 7.49–7.57 (m, 2 H), 8.13–8.16 (m, 1 H), 8.76–8.77 (m, 1 H), 8.81–8.83 (m, 1 H), 10.19 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.43, 41.32, 44.81, 116.30, 121.40, 121.55, 122.84, 124.80, 127.44, 127.93, 129.58, 134.49, 136.28, 138.23, 138.80, 148.22, 176.09; HRMS (ESI): $M+H^+$ found 310.1138; $C_{18}H_{18}N_2S_1O_1$ requires 310.1140.

2-methyl-*N*-(quinolin-8-yl)-3-(thiophen-3-yl)-2-(thiophen-3-ylmethyl)propanamide (2jb)



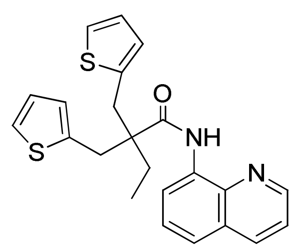
This amide was obtained 13.9 mg (18%) as colorless viscous oil. R_f = 0.31 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.35 (s, 3 H), 2.85, 3.40 (AB, J_{AB} = 13.6 Hz, 4 H), 6.92–6.93 (m, 2 H), 7.01 (s, 2 H), 7.10–7.12 (m, 2 H), 7.38–7.41 (m, 1 H), 7.49–7.58 (m, 2 H), 8.12–8.14 (m, 1 H), 8.68–8.69 (m, 1 H), 8.84–8.86 (m, 1 H), 10.00 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 20.43, 40.69, 49.42, 116.30, 121.48, 121.50, 123.01, 124.88, 127.39, 127.88, 129.58, 134.28, 136.16, 137.76, 138.74, 148.16, 174.76; HRMS (ESI): M+H$^+$ found 392.1014; $C_{22}H_{20}N_2S_2O_1$ requires 392.1017.

2-methyl-*N*-(quinolin-8-yl)-2-(thiophen-2-ylmethyl)butanamide (2ma)



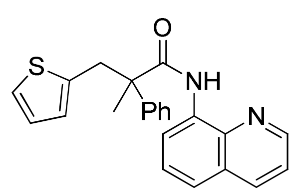
This amide was obtained 31.1 mg (48%) as yellow viscous oil. R_f = 0.34 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.00 (t, J = 7.2 Hz, 3 H), 1.41 (s, 3 H), 1.65–1.69 (m, 1 H), 1.96–2.03 (m, 1 H), 3.05, 3.46 (AB, J_{AB} = 14.4 Hz, 2 H), 6.83–6.86 (m, 2 H), 7.05–7.06 (m, 1 H), 7.42–7.45 (m, 1 H), 7.49–7.57 (m, 2 H), 8.14–8.16 (m, 1 H), 8.77–8.78 (m, 1 H), 8.84–8.86 (m, 1 H), 10.21 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 9.16, 20.63, 32.70, 39.47, 49.00, 116.35, 121.36, 121.52, 124.02, 126.56, 126.94, 127.46, 127.92, 134.42, 136.25, 138.79, 139.78, 148.23, 174.97; HRMS (ESI): M+H$^+$ found 324.1277; $C_{19}H_{20}N_2S_1O_1$ requires 324.1296.

***N*-(quinolin-8-yl)-2,2-bis(thiophen-2-ylmethyl)butanamide (2mb)**



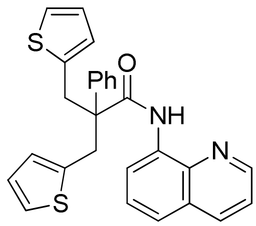
This amide was obtained 19.5 mg (24%) as yellow viscous oil. R_f = 0.31 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.14 (t, J = 7.6 Hz, 3 H), 1.88 (q, J = 7.2 Hz, 2 H), 3.26, 3.47 (AB, J_{AB} = 14.8 Hz, 4 H), 6.85–6.87 (m, 2 H), 6.89–6.90 (m, 2 H), 7.08–7.09 (m, 2 H), 7.40–7.43 (m, 1 H), 7.50–7.59 (m, 2 H), 8.13–8.15 (m, 1 H), 8.72–8.73 (m, 1 H), 8.85–8.87 (m, 1 H), 10.21 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 8.82, 26.48, 34.92, 53.41, 116.55, 121.48, 121.54, 124.22, 126.62, 127.34, 127.48, 127.91, 134.24, 136.21, 138.76, 138.96, 148.22, 173.68; HRMS (ESI): M+H$^+$ found 406.1171; $C_{23}H_{22}N_2S_2O_1$ requires 406.1174.

2-methyl-2-phenyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)propanamide (2na)



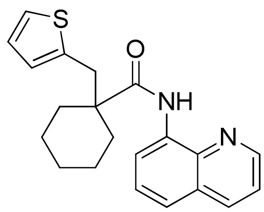
This amide was obtained 19.1 mg (26%) as yellow viscous oil. R_f = 0.39 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.77 (s, 3 H), 3.61, 3.84 (AB, J_{AB} = 14.4 Hz, 2 H), 6.64–6.65 (m, 1 H), 6.81–6.83 (m, 1 H), 7.02–7.04 (m, 1 H), 7.33–7.42 (m, 4 H), 7.45–7.55 (m, 4 H), 8.07–8.09 (m, 1 H), 8.58–8.59 (m, 1 H), 8.79–8.81 (m, 1 H), 9.90 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 22.85, 39.83, 52.73, 116.11, 121.38, 121.45, 124.26, 126.16, 127.22, 127.33, 127.41, 127.46, 127.85, 128.78, 134.58, 136.09, 138.65, 139.53, 142.52, 148.14, 174.67; HRMS (ESI): M+H$^+$ found 372.1273; $C_{23}H_{20}N_2S_1O_1$ requires 372.1296.

2-phenyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)-2-(thiophen-2-ylmethyl)propanamide (2nb)



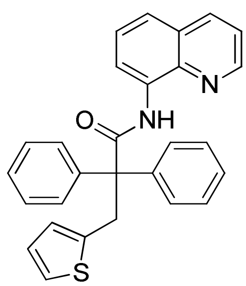
This amide was obtained 46.6 mg (51%) as yellow viscous oil. R_f = 0.35 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 3.76 (q, J = 14.8, 4 H) 6.72–6.73 (m, 2 H), 6.83–6.85 (m, 2 H), 7.06–7.07 (m, 2 H), 7.34–7.41 (m, 4 H), 7.46–7.49 (m, 3 H), 7.51–7.56 (m, 1 H), 8.09–8.11 (m, 1 H), 8.59–8.60 (m, 1 H), 8.72–8.74 (m, 1 H), 9.97 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 35.44, 57.29, 116.35, 121.40, 121.49, 124.54, 126.32, 127.37, 127.60, 127.70, 127.87, 127.98, 128.85, 134.37, 136.10, 138.50, 141.55, 148.22, 172.84; HRMS (ESI): M+H$^+$ found 454.1163; $C_{27}H_{22}N_2S_2O_1$ requires 454.1174.

***N*-(quinolin-8-yl)-1-(thiophen-2-ylmethyl)cyclohexanecarboxamide (2o)**



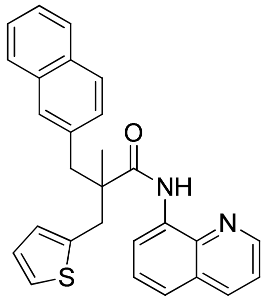
This amide was obtained 46.9 mg (67%) as yellow viscous oil. R_f = 0.31 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.54–1.70 (m, 8 H), 2.19–2.22 (m, 2 H), 3.17 (s, 2 H), 6.71–6.75 (m, 2 H), 6.95–6.97 (m, 1 H), 7.36–7.52 (m, 3 H), 8.08–8.11 (m, 1 H), 8.70–8.71 (m, 1 H), 8.77–8.79 (m, 1 H), 10.13 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 22.92, 25.83, 33.86, 40.05, 49.32, 116.38, 121.25, 121.44, 123.90, 126.59, 126.80, 127.41, 127.85, 134.41, 136.15, 138.78, 138.85, 148.15, 174.52; HRMS (ESI): M+H$^+$ found 350.1450; $C_{21}H_{22}N_2S_1O_1$ requires 350.1453.

2,2-diphenyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)propanamide (2p)



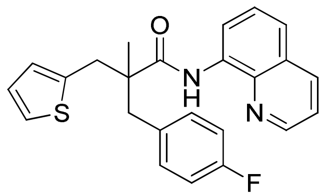
This amide was obtained 67.7 mg (78%) as brown solid. R_f = 0.42 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 4.12 (s, 2 H), 6.42–6.43 (m, 1 H), 6.70–6.72 (m, 1 H), 6.98–6.99 (m, 1 H), 7.28–7.34 (m, 7 H), 7.40–7.46 (m, 5 H), 7.50–7.54 (m, 1 H), 8.06–8.08 (m, 1 H), 8.52–8.53 (m, 1 H), 8.81–8.83 (m, 1 H),10.18 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 39.45, 64.23, 116.10, 121.45, 124.51, 125.87, 126.98, 127.24, 127.29, 127.84, 128.23, 128.27, 128.34, 128.56, 129.41, 134.59, 135.99, 138.73, 139.78, 141.99, 148.10, 172.19; HRMS (ESI): M+H$^+$ found 434.1453; $C_{28}H_{22}N_2S_1O_1$ requires 434.1453.

2-methyl-3-(naphthalen-2-yl)-*N*-(quinolin-8-yl)-2-(thiophen-2-ylmethyl)propanamide (2q)



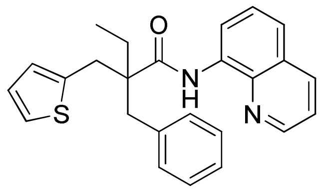
This amide was obtained 60.2 mg (69%) as yellow viscous oil. R_f = 0.38 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.42 (s, 3 H), 3.00–3.07 (m, 2 H), 3.55, 3.72 (AB, J_{AB} = 14.4 Hz, 2 H), 6.85–6.86 (m, 2 H), 7.05–7.06 (m, 1 H), 7.29–7.36 (m, 5 H), 7.47–7.49 (m, 1 H), 7.55–7.59 (m, 1 H), 7.61–7.69 (m, 3 H), 8.06–8.08 (m, 1 H), 8.46–8.47 (m, 1 H), 8.87–8.89 (m, 1 H), 9.96 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 20.13, 40.22, 46.55, 50.10, 116.45, 121.38, 121.50, 124.23, 125.30, 125.71, 126.60, 127.17, 127.31, 127.40, 127.53, 127.76, 128.68, 128.96, 132.24, 133.26, 134.17, 134.92, 135.98, 138.63, 139.49, 148.00, 174.37; HRMS (ESI): $M+H^+$ found 436.1602; $C_{28}H_{24}N_2O_1S_1$ requires 436.1609.

2-(4-fluorobenzyl)-2-methyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)propanamide (2r)



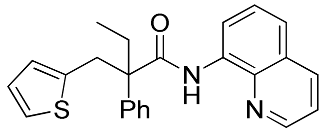
This amide was obtained 59.8 mg (74%) as yellow viscous oil. R_f = 0.34 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.37 (s, 3 H), 2.78, 3.37 (AB, J_{AB} = 13.6 Hz, 2 H), 2.99, 3.65 (AB, J_{AB} = 14.4 Hz, 2 H), 6.81–6.85 (m, 4 H), 7.05–7.06 (m, 1 H), 7.12–7.16 (m, 2 H), .7.38–7.41 (m, 1 H), 7.51–7.56 (m, 2 H), 8.11–8.13 (m, 1 H), 8.65–8.66 (m, 1 H), 8.83–8.85 (m, 1 H), 9.96 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 19.96, 40.27, 45.60, 50.00, 114.86 (d, $J_{C\text{-}F}$ = 21.0 Hz), 116.43, 121.57 (d, $J_{C\text{-}F}$ = 10.1 Hz), 124.28, 126.64, 127.18, 127.36, 127.86, 131.67 (d, $J_{C\text{-}F}$ = 7.8 Hz), 132.98 (d, $J_{C\text{-}F}$ = 3.4 Hz), 134.09, 136.16, 138.70, 139.33, 148.17, 161.76 (d, $J_{C\text{-}F}$ = 242.8 Hz), 174.10; HRMS (ESI): $M+H^+$ found 404.1355; $C_{24}H_{21}F_1N_2O_1S_1$ requires 404.1359.

2-benzyl-*N*-(quinolin-8-yl)-2-(thiophen-2-ylmethyl)butanamide (2s)



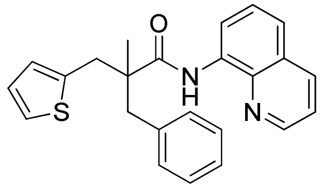
This amide was obtained 45.6 mg (57%) as yellow solid. R_f = 0.31 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.11 (t, J = 7.2 Hz, 3 H), 1.74–1.80 (m, 2 H), 2.97, 3.45 (AB, J_{AB} = 15.2 Hz, 2 H), 3.15–3.23 (m, 2 H), 6.79–6.83 (m, 2 H), 7.02–7.09 (m, 4 H), 7.13–7.15 (m, 2 H), 7.31–7.34 (m, 1 H), 7.43–7.52 (m, 2 H), 8.05–8.07 (m, 1 H), 8.59–8.60 (m, 1 H), 8.79–8.81 (m, 1 H), 10.01 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 8.74, 25.20, 35.16, 41.72, 53.40, 116.44, 121.41, 121.47, 124.08, 126.46, 126.54, 127.15, 127.44, 127.86, 128.09, 130.15, 134.24, 136.12, 137.24, 138.75, 139.51, 148.12, 174.09; HRMS (ESI): $M+H^+$ found 400.1607; $C_{25}H_{24}N_2O_1S_1$ requires 400.1609.

2-phenyl-*N*-(quinolin-8-yl)-2-(thiophen-2-ylmethyl)butanamide (2t)



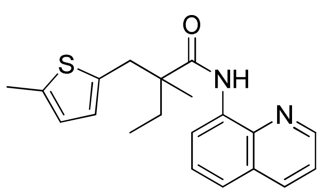
This amide was obtained 47.9 mg (62%) as brown viscous oil. R_f = 0.38 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.99 (t, J = 7.2 Hz, 3 H), 2.05–2.21 (m, 2 H), 3.56, 3.76 (AB, J_{AB} = 14.8 Hz, 2 H), 6.43–6.44 (m, 1 H), 6.71–6.73 (m, 1 H), 6.93–6.94 (m, 1 H), 7.19–7.48 (m, 8 H), 8.00–8.02 (m, 1 H), 8.51–8.52 (m, 1 H), 8.70–8.72 (m, 1 H), 9.75 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 8.96, 27.02, 35.46, 56.65, 116.07, 121.28, 121.47, 124.02, 126.16, 127.08, 127.34, 127.64, 127.89, 128.69, 134.60, 136.09, 138.63, 139.13, 142.27, 148.20, 174.01; HRMS (ESI): M+H$^+$ found 386.1437 ; $C_{24}H_{22}N_2O_1S_1$ requires 386.1453.

2-benzyl-2-methyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)propanamide (2u)



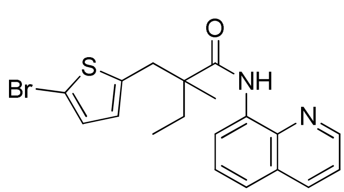
This amide was obtained 45.5 mg (59%) as yellow viscous oil. R_f = 0.27 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.38 (s, 3 H), 2.86, 3.39 (AB, J_{AB} = 13.2 Hz, 2 H), 2.99, 3.67 (AB, J_{AB} = 14.4 Hz, 2 H), 6.83–6.84 (m, 2 H), 7.04–7.05 (m, 1 H), 7.11–7.21 (m, 5 H), 7.37–7.40 (m, 1 H), 7.48–7.56 (m, 2 H), 8.10–8.12 (m, 1 H), 8.65–8.66 (m, 1 H), 8.86–8.88 (m, 1 H), 10.00 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 20.06, 40.21, 46.47, 49.98, 116.42, 121.46, 121.48, 124.21, 126.51, 126.60, 127.14, 127.41, 127.85, 128.06, 130.35, 134.25, 136.13, 137.30, 138.75, 139.53, 148.12, 174.34; HRMS (ESI): M+H$^+$ found 386.1452; $C_{24}H_{22}N_2S_1O_1$ requires 386.1453.

2-methyl-2-((5-methylthiophen-2-yl)methyl)-*N*-(quinolin-8-yl)butanamide (2v)



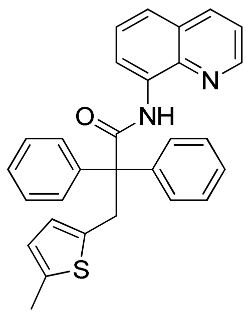
This amide was obtained 46.1 mg (68%) as yellow viscous oil. R_f = 0.36 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.99 (t, J = 7.2 Hz, 3 H), 1.40 (s, 3 H), 1.65–1.70 (m, 1H), 1.96–2.01 (m, 1H), 2.34 (s, 3 H), 2.97, 3.36 (AB, J_{AB} = 14.4 Hz, 2 H), 6.48–6.49 (m, 1 H), 6.59–6.60 (m, 1 H), 7.42–7.57 (m, 3 H), 8.14–8.16 (m, 1 H), 8.77–8.78 (m, 1 H), 8.84–8.86 (m, 1 H), 10.20 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 9.13, 15.16, 20.67, 32.61, 39.64, 48.88, 116.35, 121.28, 121.49, 124.59, 126.75, 127.47, 127.91, 134.48, 136.23, 137.43, 138.32, 138.80, 148.19, 175.09; HRMS (ESI): M+H$^+$ found 338.1453; $C_{20}H_{22}N_2S_1O_1$ requires 338.1453

2-((5-bromothiophen-2-yl)methyl)-2-methyl-*N*-(quinolin-8-yl)butanamide (2w)



This amide was obtained 51.3 mg (64%) as brown viscous oil. R_f = 0.33 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.00 (t, J = 7.6 Hz, 3 H), 1.41 (s, 3 H), 1.64–1.69 (m, 1 H), 1.95–2.01 (m, 1 H), 2.93, 3.41 (AB, J_{AB} = 14.8 Hz, 2 H), 6.59–6.62 (m, 1 H), 6.78–6.79 (m, 1 H), 7.43–7.46 (m, 1 H), 7.50–7.58 (m, 2 H), 8.15–8.17 (m, 1 H), 8.78–8.84 (m, 2 H), 10.20 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 9.09, 20.75, 32.82, 39.78, 48.86, 110.01, 116.42, 121.49, 121.57, 127.39, 127.45, 127.94, 129.38, 134.32, 136.29, 141.82, 148.29, 174.65; HRMS (ESI): $M+H^+$ found 402.0397; $C_{19}H_{19}Br_1N_2S_1O_1$ requires 402.0401.

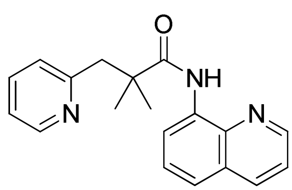
3-(5-methylthiophen-2-yl)-2,2-diphenyl-*N*-(quinolin-8-yl)propanamide (2x)



This amide was obtained 73.4 mg (82%) as yellow solid. R_f = 0.39 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.30 (s, 3 H), 4.03 (s, 2 H), 6.15–6.16 (m, 1 H), 6.33–6.34 (m, 1 H), 7.28–7.47 (m, 12 H), 7.50–7.54 (m, 1 H), 8.05–8.07 (m, 1 H), 8.52–8.53 (m, 1 H), 8.81–8.83 (m, 1 H), 10.17 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 15.21, 39.77, 64.09, 116.11, 121.44, 123.93, 127.20, 127.31, 127.83, 128.13, 128.24, 129.43, 134.61, 135.99, 137.29, 138.79, 142.08, 148.09, 172.31; HRMS (ESI): $M+H^+$ found 448.1596; $C_{29}H_{24}N_2S_1O_1$ requires 448.1609.

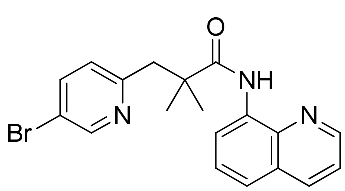
5. Synthesis of *N*-heteroarylated products

2,2-dimethyl-3-(pyridin-2-yl)-*N*-(quinolin-8-yl)propanamide (3a)



This amide was obtained 25.1 mg (41%) as yellow viscous oil. R_f = 0.54 (petroleum ether/ethyl acetate = 10:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.48 (s, 6 H), 3.24 (s, 2 H), 7.03–7.06 (m, 1 H), 7.19 (d, J = 7.6 Hz, 1 H), 7.41–7.56 (m, 4 H), 8.13–8.16 (m, 1 H), 8.48–8.49 (m, 1 H), 8.75–8.76 (m, 1 H), 8.81–8.83 (m, 1 H), 10.25 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.53, 44.99, 48.51, 116.34, 121.38, 121.45, 121.52, 124.55, 127.41, 127.91, 134.54, 136.18, 136.23, 138.83, 148.20, 148.78, 158.55, 175.95; HRMS (ESI): $M+H^+$ found 305.1521; $C_{19}H_{19}N_3O_1$ requires 305.1528.

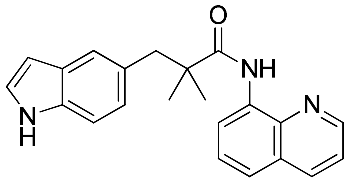
3-(5-bromopyridin-2-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (3b)



This amide was obtained 33.7 mg (44%) as brown viscous oil. R_f = 0.66 (petroleum ether/ethyl acetate = 10:1); δ_H

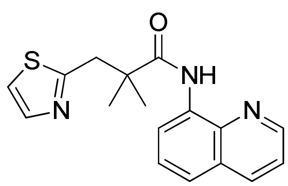
(400 MHz; $CDCl_3$; Me_4Si) 1.40 (s, 6 H), 3.11 (s, 2 H), 7.01–7.03 (m, 1 H), 7.35–7.50 (m, 4 H), 8.06–8.08 (m, 1 H), 8.45 (s, 1 H), 8.68–8.72 (m, 2 H), 10.11 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.58, 44.94, 47.93, 116.36, 118.67, 121.50, 121.57, 125.78, 127.37, 127.92, 134.40, 136.26, 138.66, 138.78, 148.27, 149.91, 157.26, 175.58; HRMS (ESI): M+H$^+$ found 383.0631; $C_{19}H_{18}Br_1N_3O_1$ requires 383.0633.

3-(1*H*-indol-5-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (3c)



This amide was obtained 41.2 mg (60%) as yellow solid. R_f = 0.43 (petroleum ether/ethyl acetate = 10:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.44 (s, 6 H), 3.15 (s, 2 H), 6.42 (s, 1 H), 7.02–7.04 (m, 1 H), 7.11 (s, 1 H), 7.17–7.19 (m, 1 H), 7.37–7.40 (m, 1 H), 7.47–7.49 (m, 2 H), 7.52–7.56 (m, 1 H), 8.10–8.12 (m, 1 H), 8.18 (br, 1 H), 8.67–8.68 (m, 1 H), 8.85–8.87 (m, 1 H), 10.18 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.27, 45.24, 47.05, 102.30, 110.44, 116.31, 121.27, 121.44, 122.12, 124.17, 124.67, 127.42, 127.81, 127.90, 129.06, 134.63, 134.76, 136.16, 138.82, 148.11, 176.73; HRMS (ESI): M+H$^+$ found 343.1676; $C_{22}H_{21}N_3O_1$ requires 343.1685.

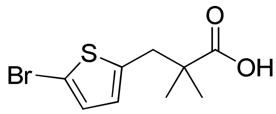
2,2-dimethyl-*N*-(quinolin-8-yl)-3-(thiazol-2-yl)propanamide (3d)



This amide was obtained 32.3 mg (52%) as yellow viscous oil. R_f = 0.24 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.52 (s, 6 H), 3.48 (s, 2 H), 7.14 (d, J = 3.6 Hz, 1 H), 7.43–7.46 (m, 1 H), 7.50–7.57 (m, 2 H), 7.66 (d, J = 3.2 Hz, 1 H), 8.14–8.16 (m, 1 H), 8.77–8.79 (m, 1 H), 8.83–8.85 (m, 1 H), 10.28 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.56, 43.49, 45.09, 116.45, 119.23, 121.56, 121.59, 127.43, 127.92, 134.39, 136.29, 138.79, 142.07, 148.28, 166.78, 175.21; HRMS (ESI): M+H$^+$ found 311.1088; $C_{17}H_{17}N_3O_1S_1$ requires 311.1092.

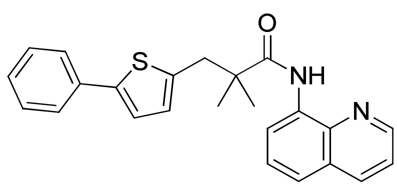
6. Application of Thiophenes Products

3-(5-bromothiophen-2-yl)-2,2-dimethylpropanoic acid (4)



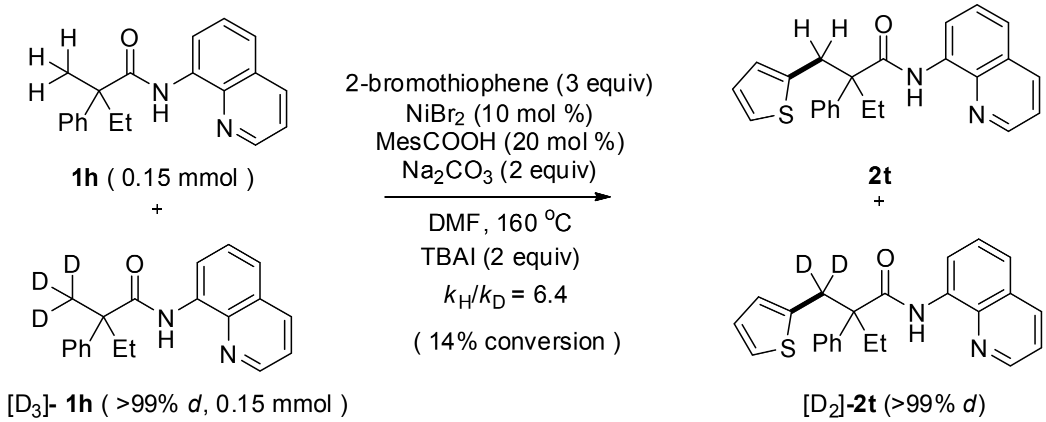
3-(5-bromothiophen-2-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide **2a** (155.2 mg, 0.4 mmol) and NaOH (96 mg, 2.4 mmol) were heated in ethanol (0.7 mL) for 12 h at 100 °C. After completion, water was added to the reaction mixture followed by extraction with ether (3 x 5 mL). These ether extracts were discarded. Aqueous layer was acidified with 1N $NaHSO_4$ until pH~2 followed by extraction with ether (3 x 10 mL). Ether extracts from acidified aqueous layer were combined and dried over $MgSO_4$. Evaporation of solvent gave 96.4 mg (92%) of brown liquid. δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.25 (s, 6 H), 3.01 (s, 2 H), 6.57–6.58 (m, 1 H), 6.87–6.88 (m, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 24.79, 40.40, 43.41, 110.21, 127.55, 129.46, 141.36, 182.86; Ms (EI): *m*/*z* = 264.3 $[M+H]^+$.

2,2-dimethyl-3-(5-phenylthiophen-2-yl)-*N*-(quinolin-8-yl)propanamide (5)



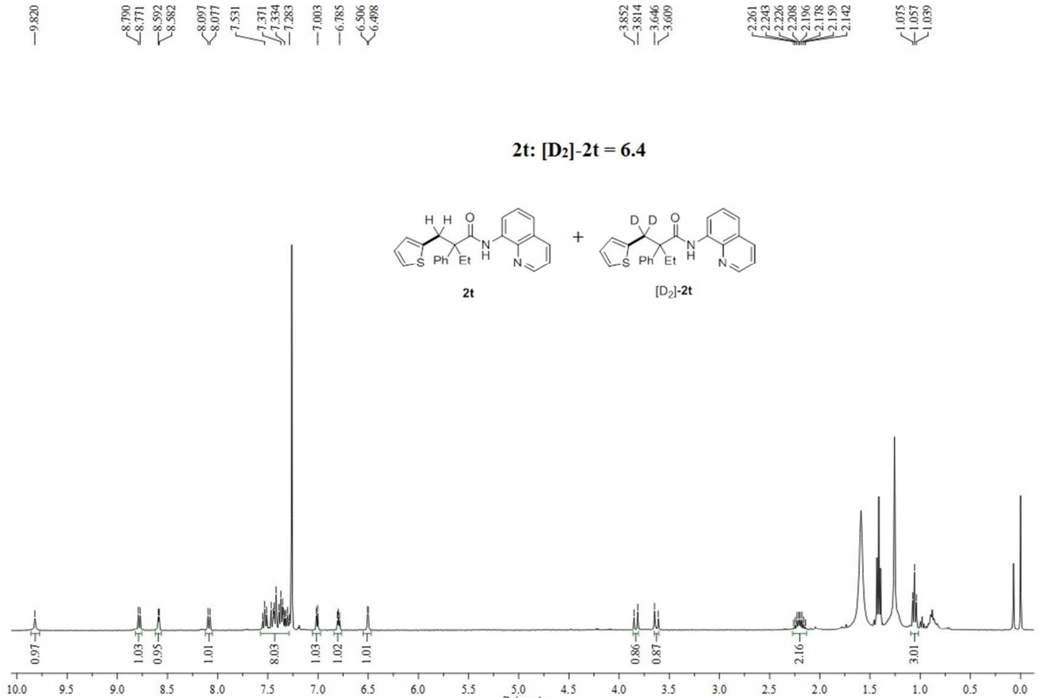
To a solution of 3-(5-bromothiophen-2-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide **2a** (77.6 mg, 0.2 mmol) and phenylboronic acid (28.6 mg, 0.22 mmol, 1.1 equiv) in THF (0.5 mL), 2 M aqueous solution of Na_2CO_3 (42.4 mg, 0.4mmol, 2 equiv) and tetrakis(triphenylphosphine) palladium (0) (11.4 mg) were added. The reaction mixture was heated at 80°C for 12 h. After removing THF, the aqueous layer was extracted with ethyl acetate. The combined organic layer was dried over anhydrous magnesium sulfate and filtered. The solvent was removed, and the crude product was purified by column chromatography (silica gel) using hexane/ EtOAc (20:1, v/v) as eluent to yield 70.3 mg (91%) as pale white oil. R_f = 0.27 (petroleum ether/ethyl acetate = 60:1); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.42 (s, 6 H), 3.17 (s, 2 H), 6.71–6.72 (m, 1 H), 6.99–7.00 (m, 1 H), 7.10–7.23 (m, 3 H), 7.32–7.50 (m, 5 H), 8.04–8.06 (m, 1 H), 8.67–8.68 (m, 1 H), 8.76–8.78 (m, 1 H), 10.18 (s, 1 H); δ_C (100 MHz; $CDCl_3$; Me_4Si) 25.44, 41.16, 45.10, 116.44, 121.47, 121.53, 122.70, 125.53, 127.04, 127.44, 127.93, 128.05, 128.72, 134.49, 134.54, 136.25, 138.82, 139.66, 142.93, 148.24, 175.65; HRMS (ESI): $M+H^+$ found 386.1448; $C_{24}H_{22}N_2S_1O_1$ requires 386.1453.

7. Deuterium Labeling Experiment

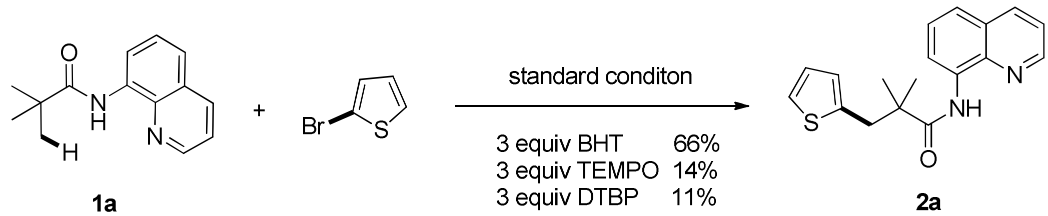


A 10-mL Schlenk tube was charged with **1h** (45.6 mg, 0.15 mmol), **[D$_3$]-1h** (46.1 mg, 0.15 mmol), 2-bromothiophene (146.7 mg, 0.9 mmol), $NiBr_2$ (6.6 mg, 0.03 mmol), MesCOOH (9.8 mg, 0.06 mmol), Na_2CO_3 (63.6 mg, 0.6 mmol), TBAI (147.6 mg, 0.4 mmol) and DMF (0.7 mL). The vial was evacuated and filled with N_2, and stirred at 160 °C for 1 h. The mixture was then cooled to room temperature, diluted with CH_2Cl_2 (2 mL), filtered through a celite pad, analyzed by GC-MS, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/Hexane (1:100 ~ 1:20, v/v), to afford the heteroarylated product. The ratio of **2t** and **[D$_2$]-2t** was determined by ^{1}H NMR.

The mixture of **2t** and **[D$_2$]-2t**: δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.06 (t, J = 7.2 Hz, 3 H), 2.14–2.26 (m, 2 H), **3.63, 3.83 (AB, J_{AB} = 15.2 Hz, 1.7 H),** 6.50–6.51 (m, 1 H), 6.78–6.81 (m, 1 H), 7.00–7.02 (m, 1 H), 7.28–7.53 (m, 8 H), 8.08–8.10 (m, 1 H), 8.58–8.59 (m, 1 H), 8.77–8.79 (m, 1 H), 9.82 (s, 1 H).



Radical Trapping Experiment



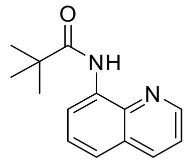
A 10-mL Schlenk tube was charged with **1a** (45.6 mg, 0.2 mmol), TEMPO (93.8 mg, 0.6 mmol, 3.0 equiv) or BHT (132.2 mg, 0.6 mmol, 3.0 equiv) or DTBP (87.7 mg, 0.6 mmol, 3.0 equiv), 2-bromothiophene (146.7 mg, 0.9 mmol), $NiBr_2$ (4.4 mg, 0.02 mmol), MesCOOH (6.6 mg, 0.04 mmol), Na_2CO_3 (42.4 mg, 0.4 mmol), TBAI (147.6 mg, 0.4 mmol) and DMF (0.5 mL). The vial was evacuated and filled with N_2, and stirred at 160 °C for 24 h. The mixture was then cooled to room temperature, diluted with CH_2Cl_2 (2 mL), filtered through a celite pad, analyzed by GC-MS, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/hexane (1:100 ~ 1:20, v/v), to afford the heteroarylated product **2a** (yield = 11% to 66%).

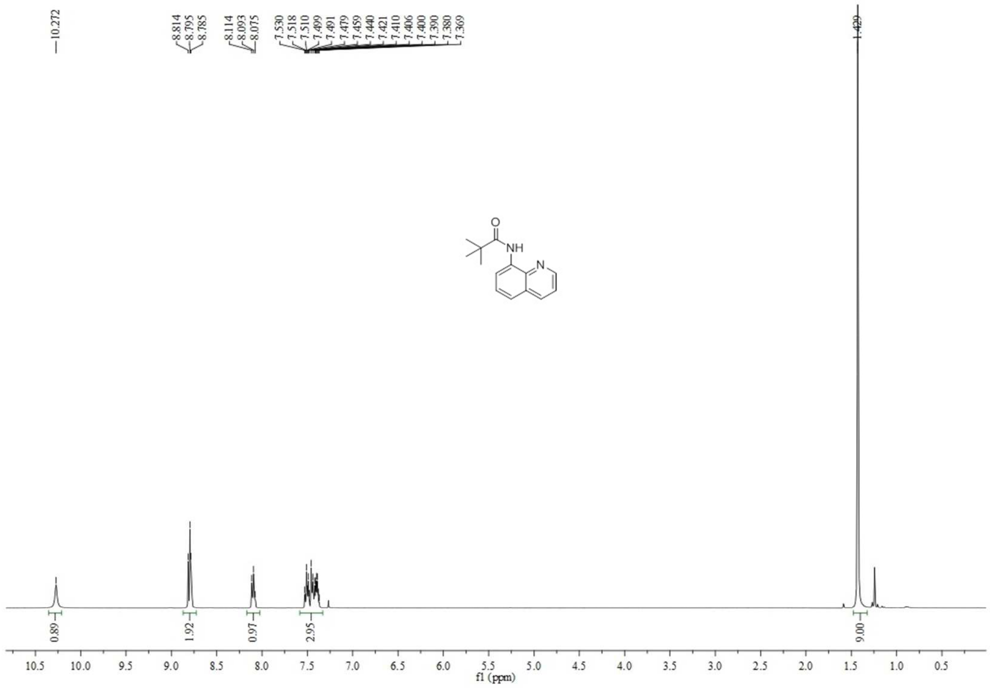
8. Reference

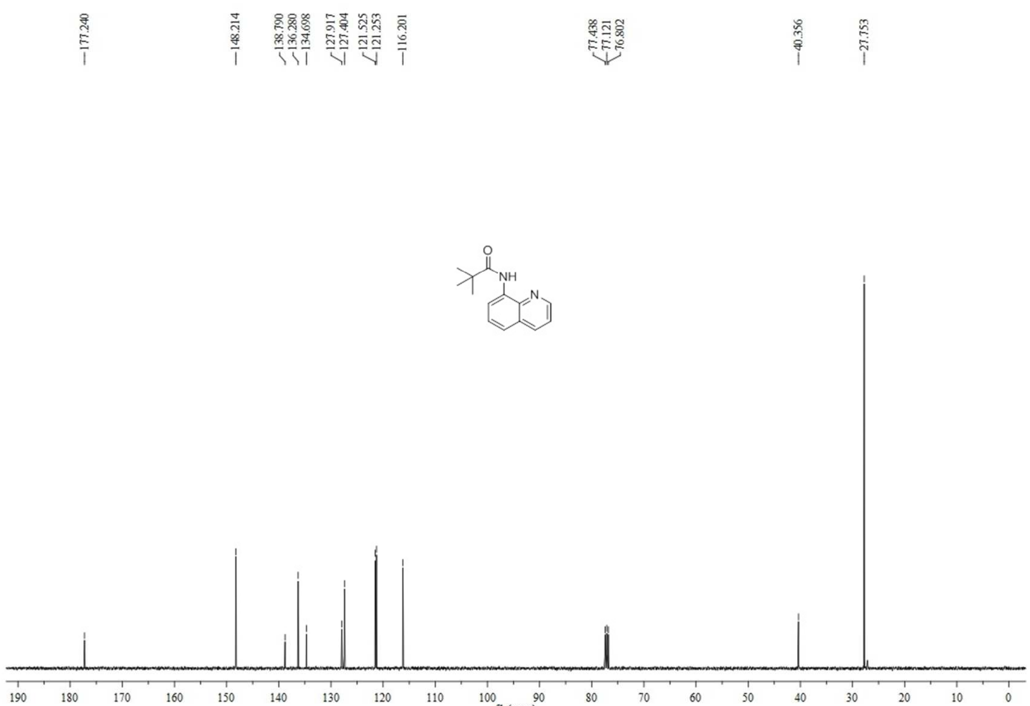
(a) Rui, S.; Laurean, I.; Arimasa, M.; Eiichi N. *J. A. Chem. Soc.* **2013**, *135*, 6030-6032;
(b) Wu, X-S.; Zhao, Y.; Ge, H-B. *J. A. Chem. Soc*. **2014**, *136*, 1789-1792;
(c) Aihara, Y.; Chatani, N. *J. A. Chem. Soc*. **2014**, *136*, 898-901.
(d) Lee, W.; Lee, D.-W.; Lee, M.; Hong, J.-I. *Chem. Commun*. **2014**, *50*, 14851.

9. Copies of ^{1}H, ^{13}C NMR Charts for the Compounds

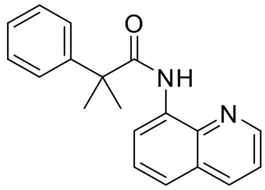
***N*-(quinolin-8-yl)pivalamide (1a)**

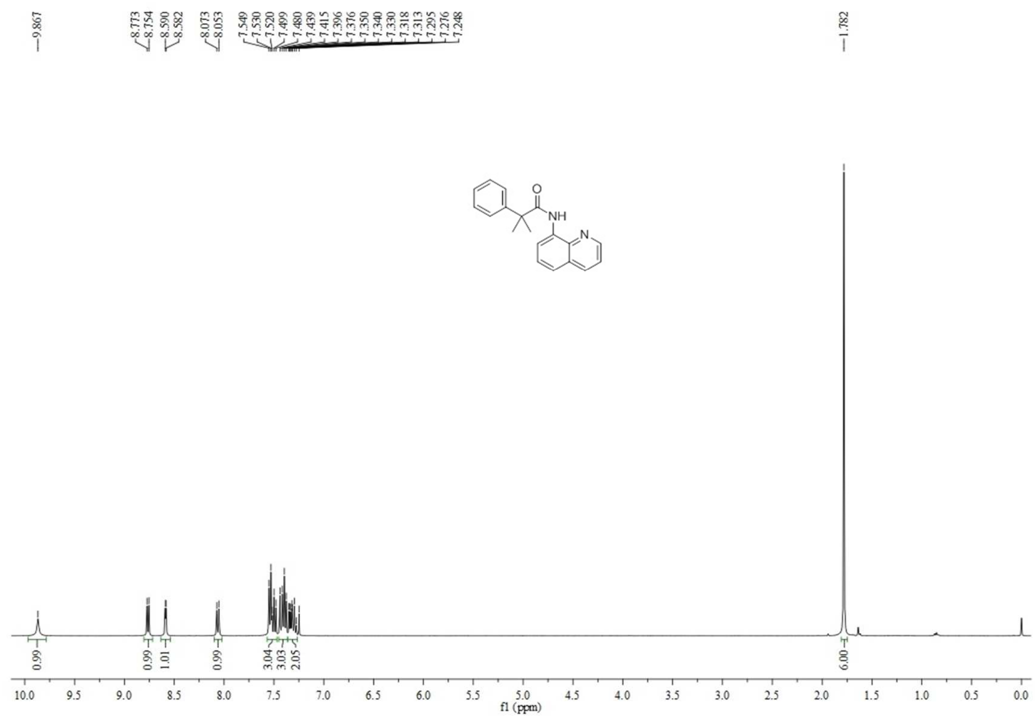


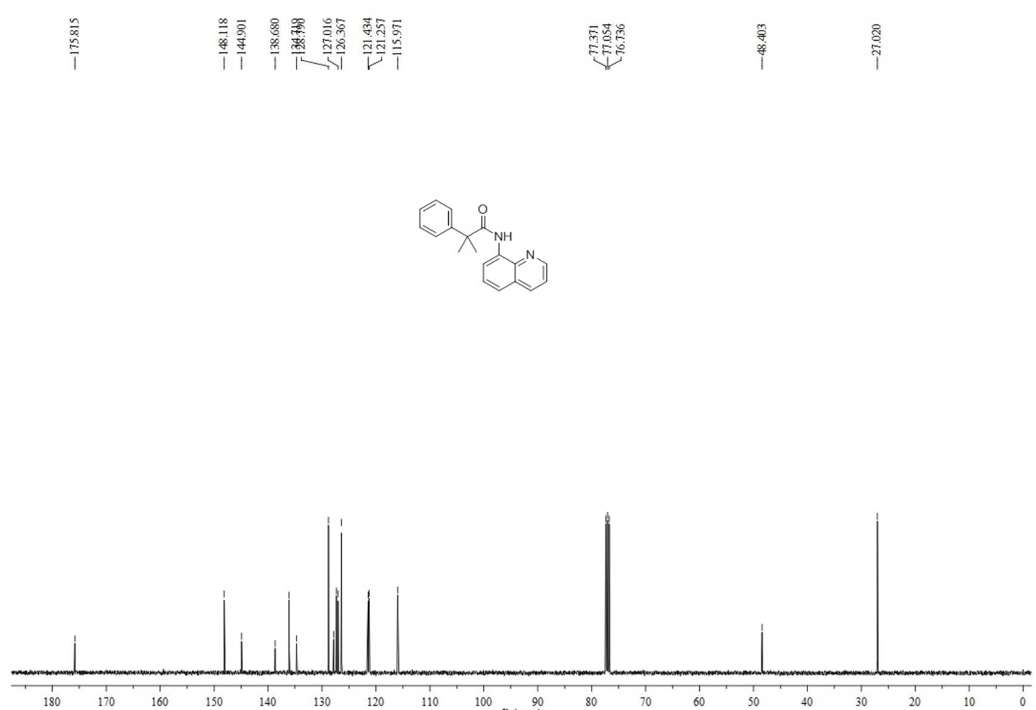




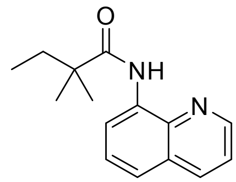
2-methyl-2-phenyl-*N*-(quinolin-8-yl)propanamide (1b)

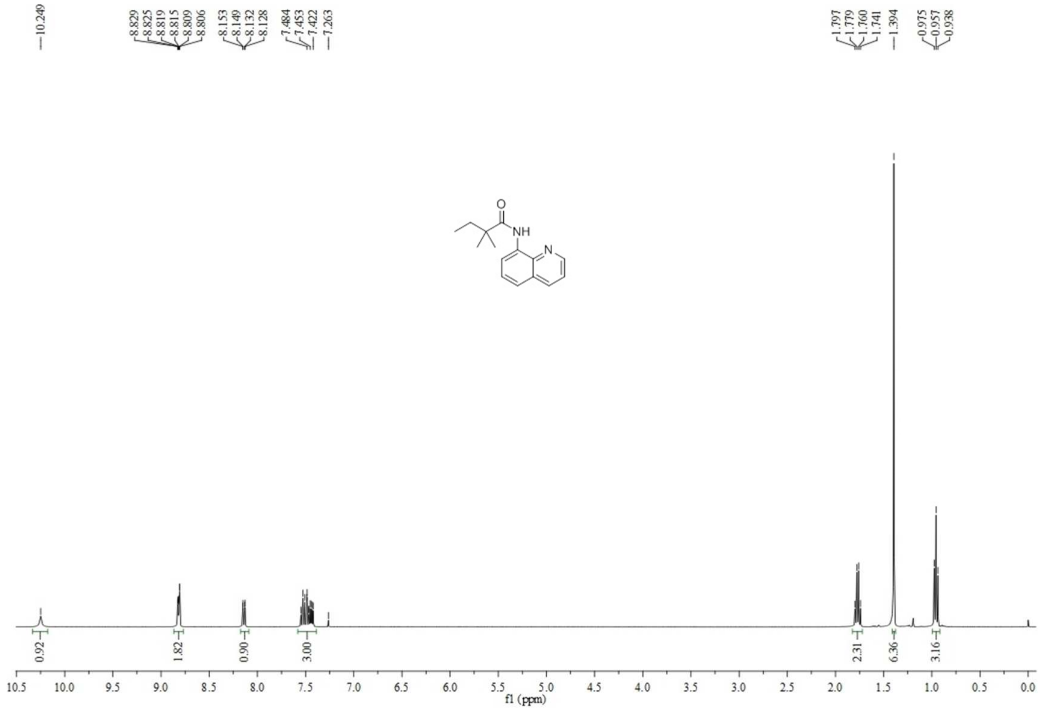


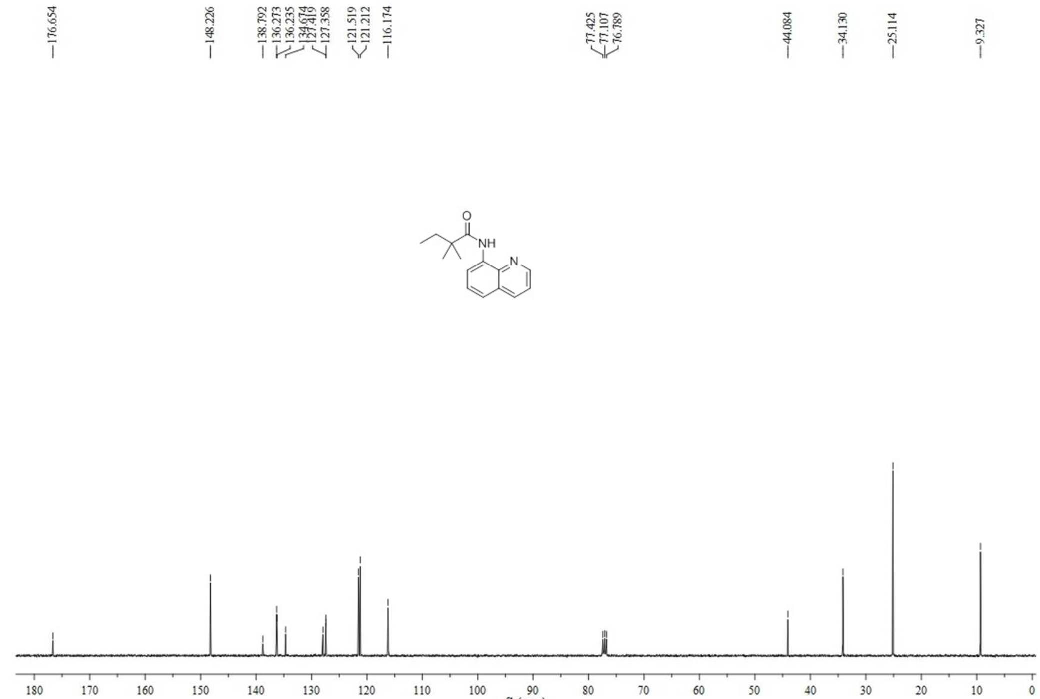




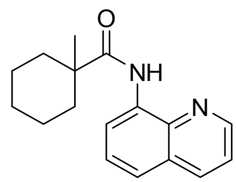
2,2-dimethyl-*N*-(quinolin-8-yl)butanamide (1c)

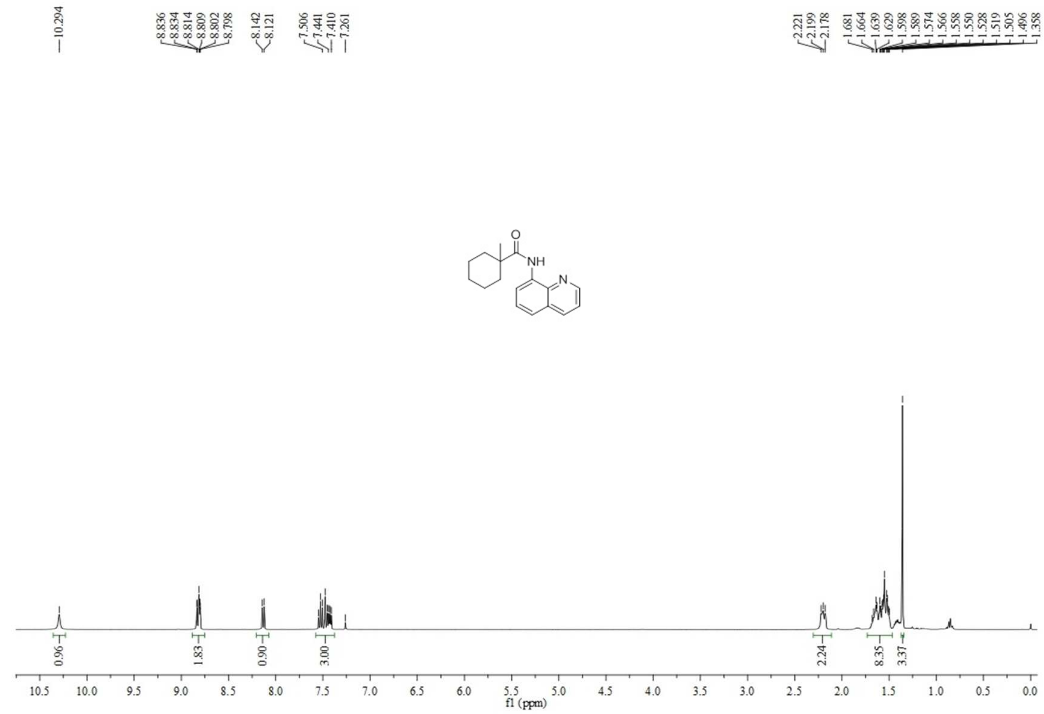


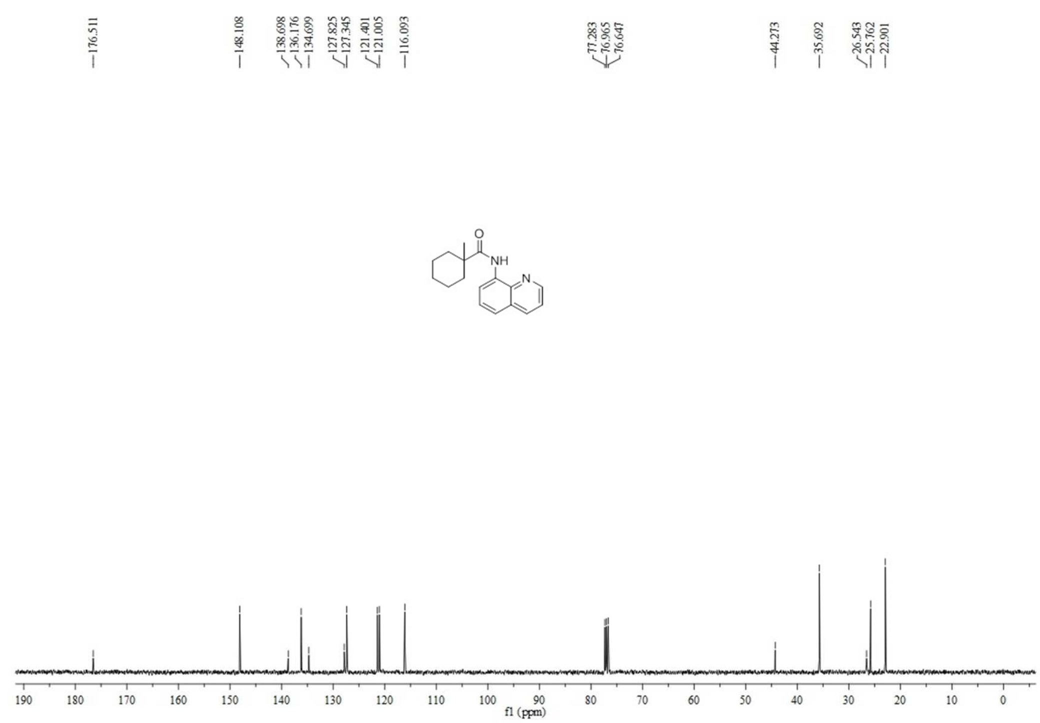




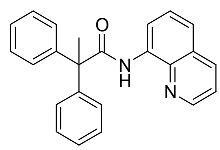
1-methyl-*N*-(quinolin-8-yl)cyclohexanecarboxamide (1d)

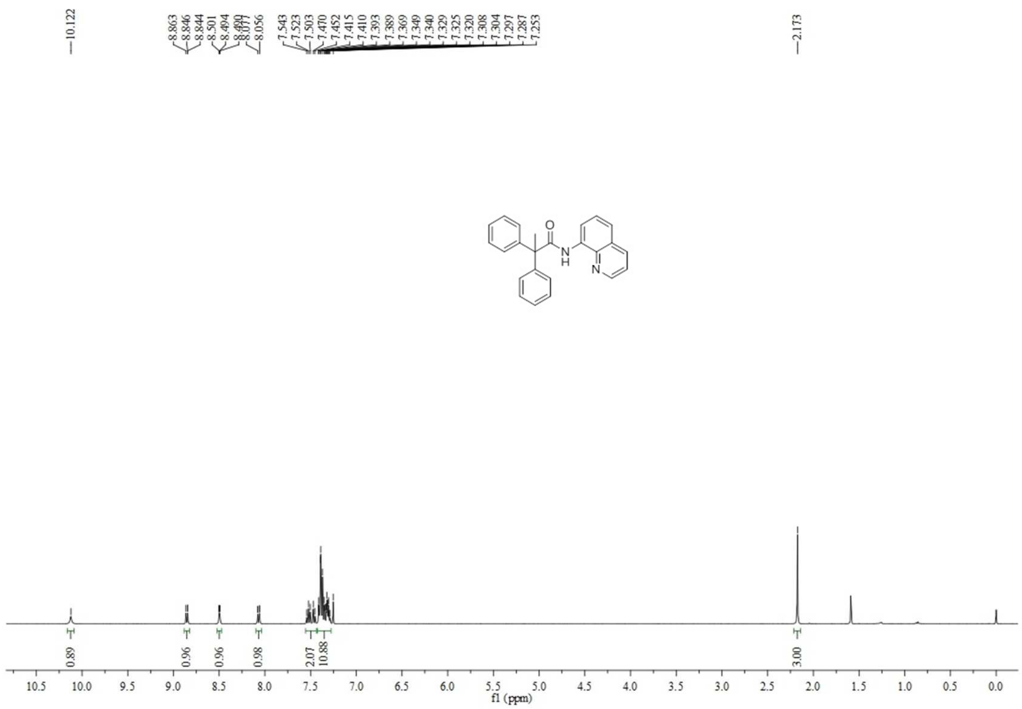


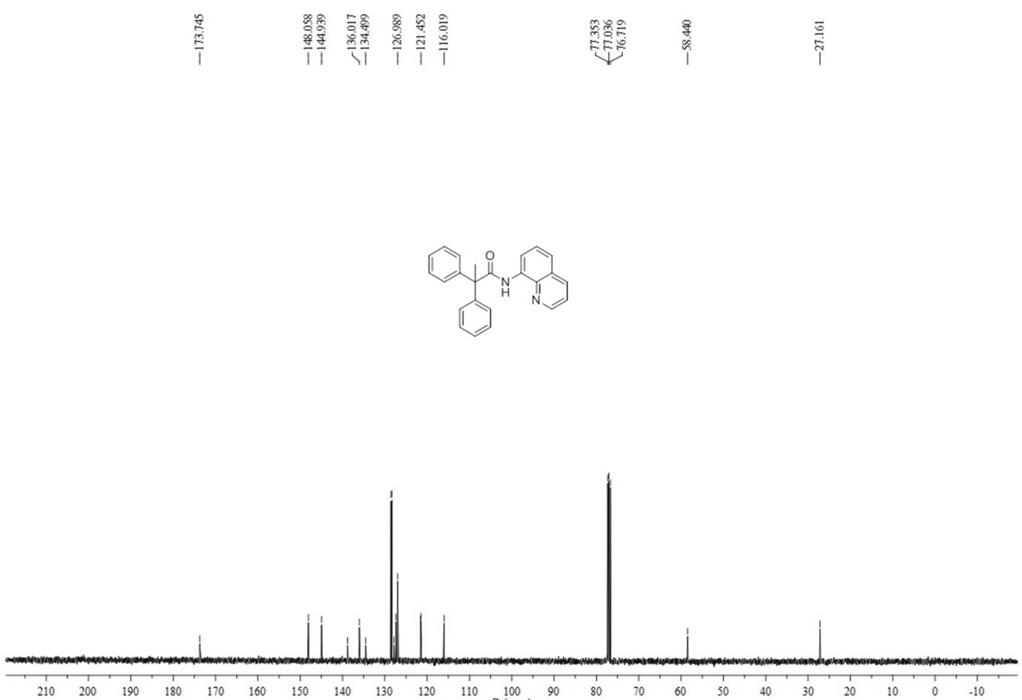




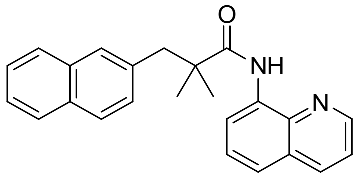
2,2-diphenyl-*N*-(quinolin-8-yl)propanamide (1e)

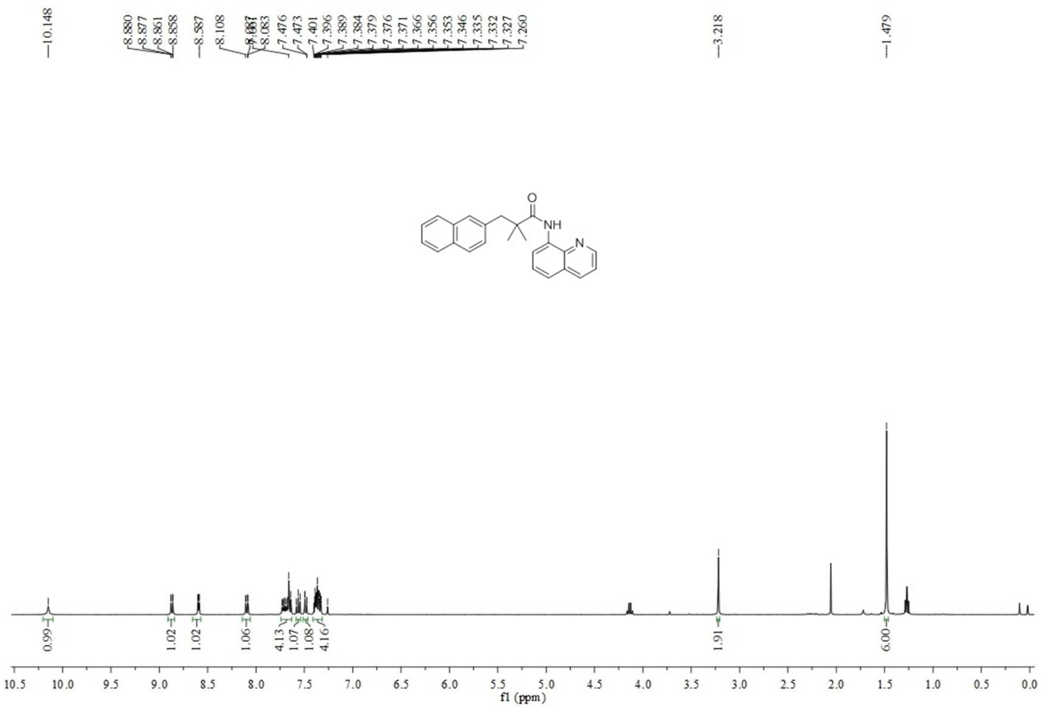


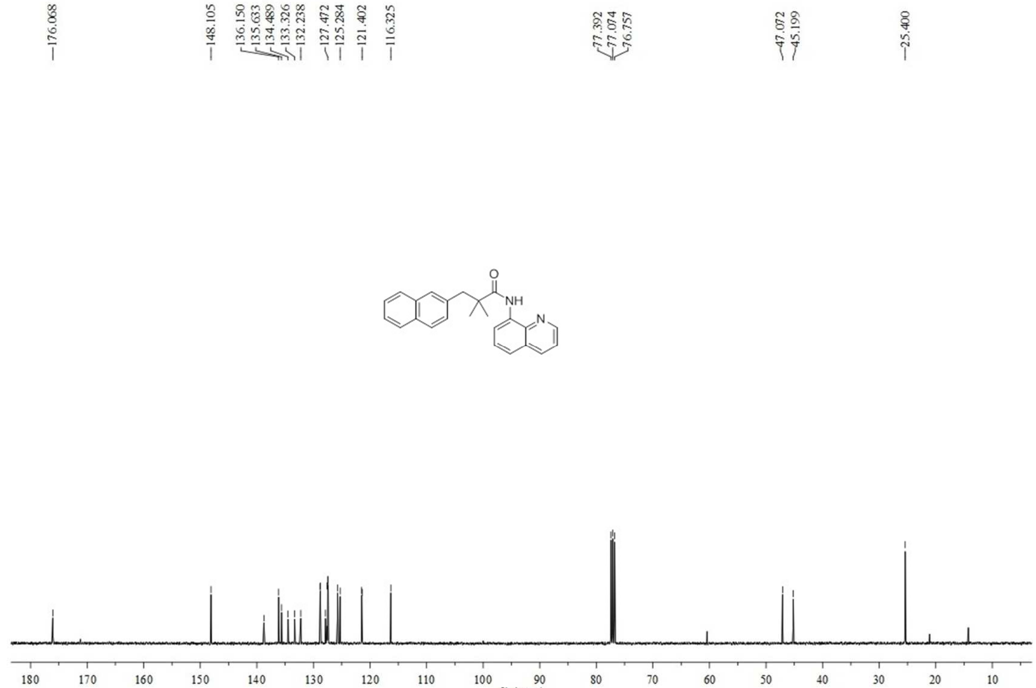




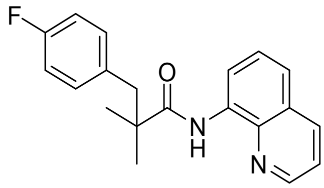
2,2-dimethyl-3-(naphthalen-2-yl)-*N*-(quinolin-8-yl)propanamide (1f)

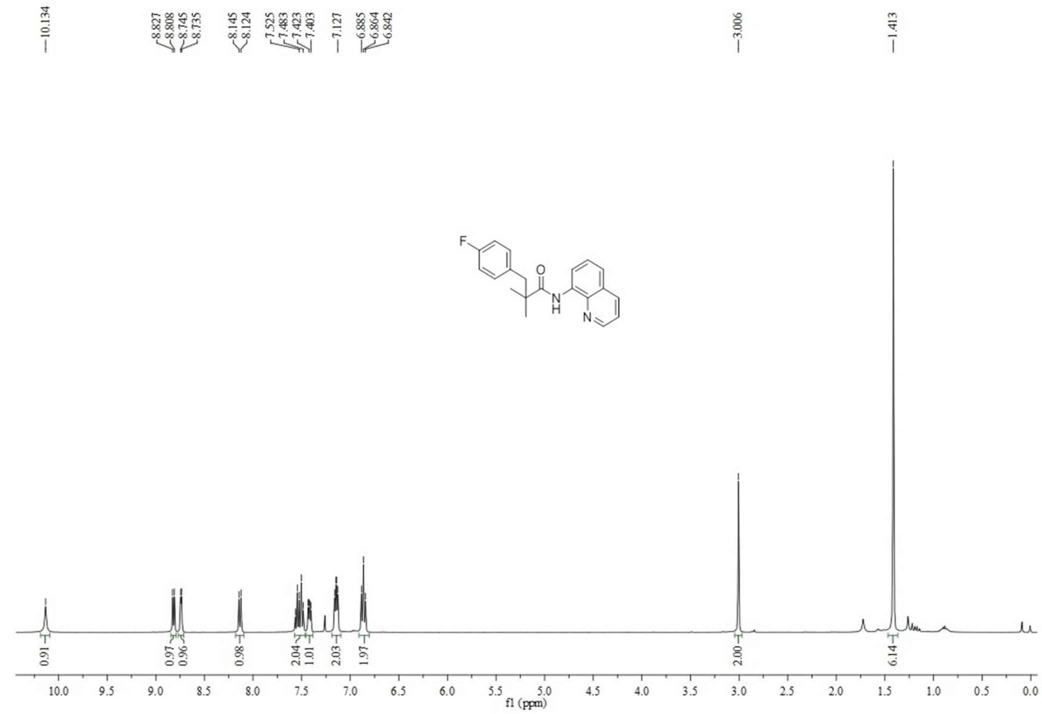


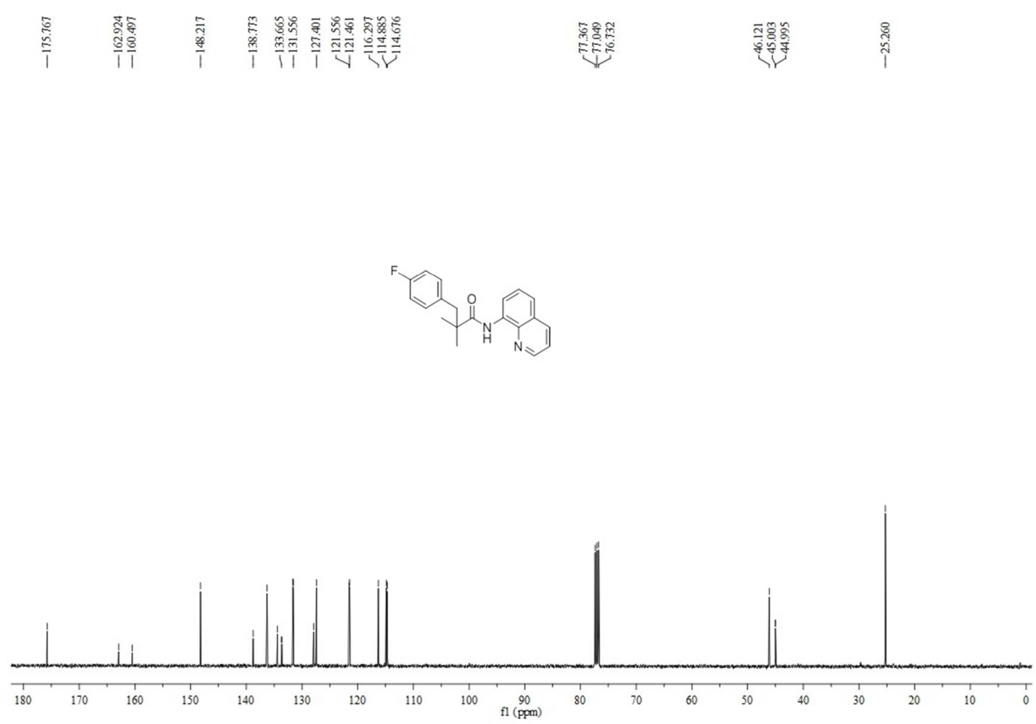




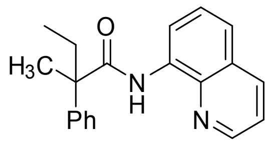
3-(4-fluorophenyl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (1g)

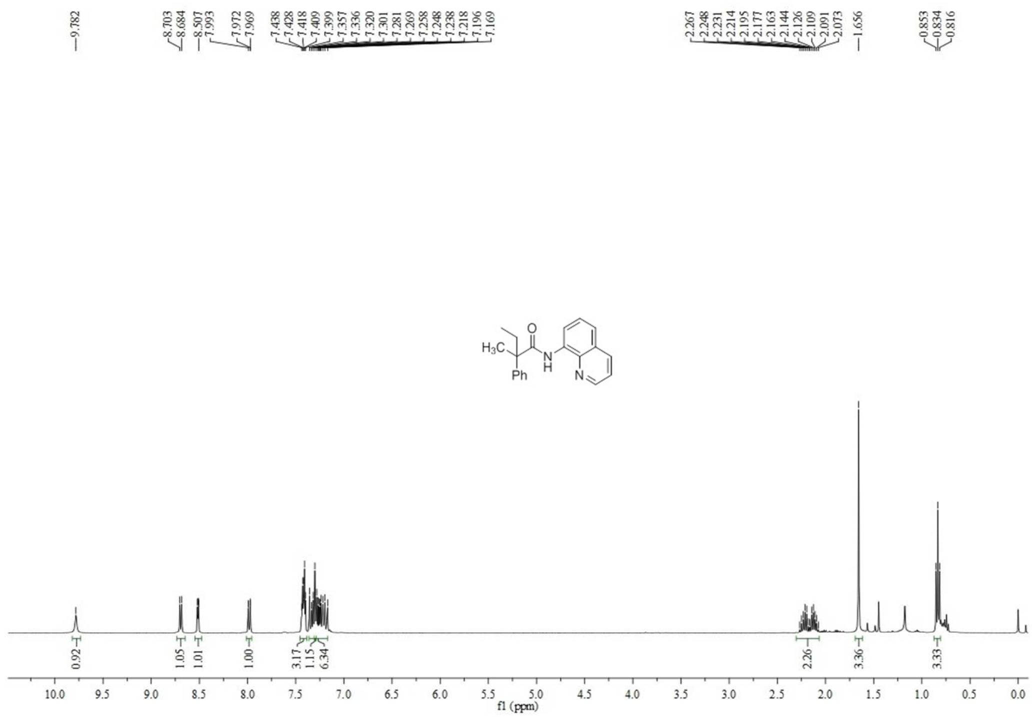


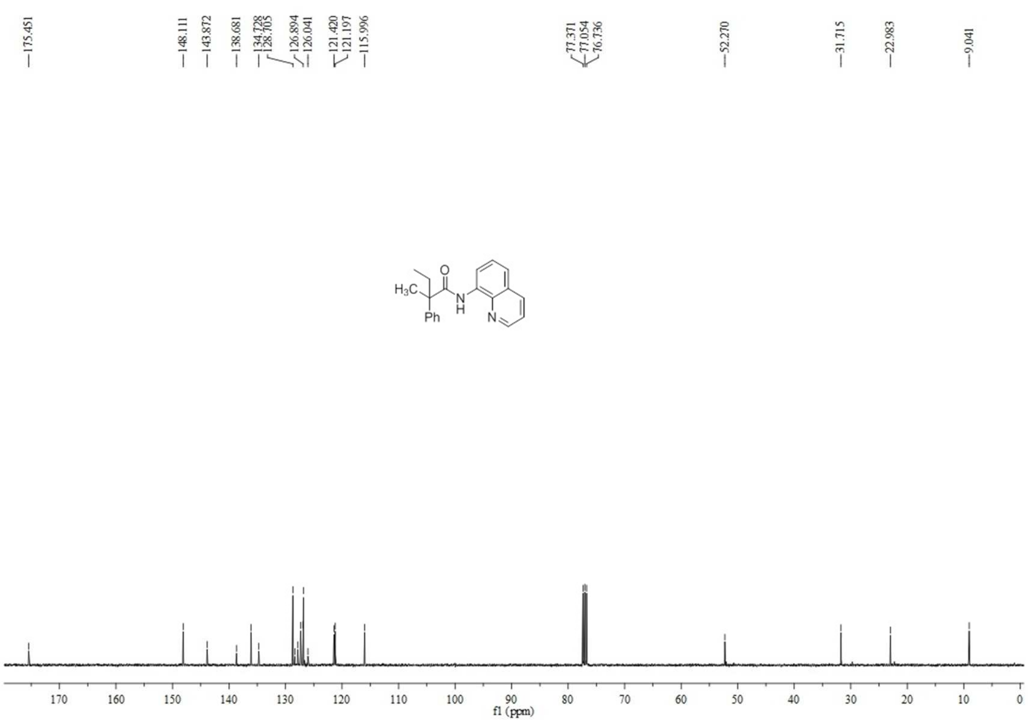




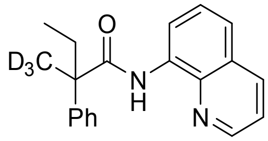
2-methyl-2-phenyl-*N*-(quinolin-8-yl)butanamide (1h)

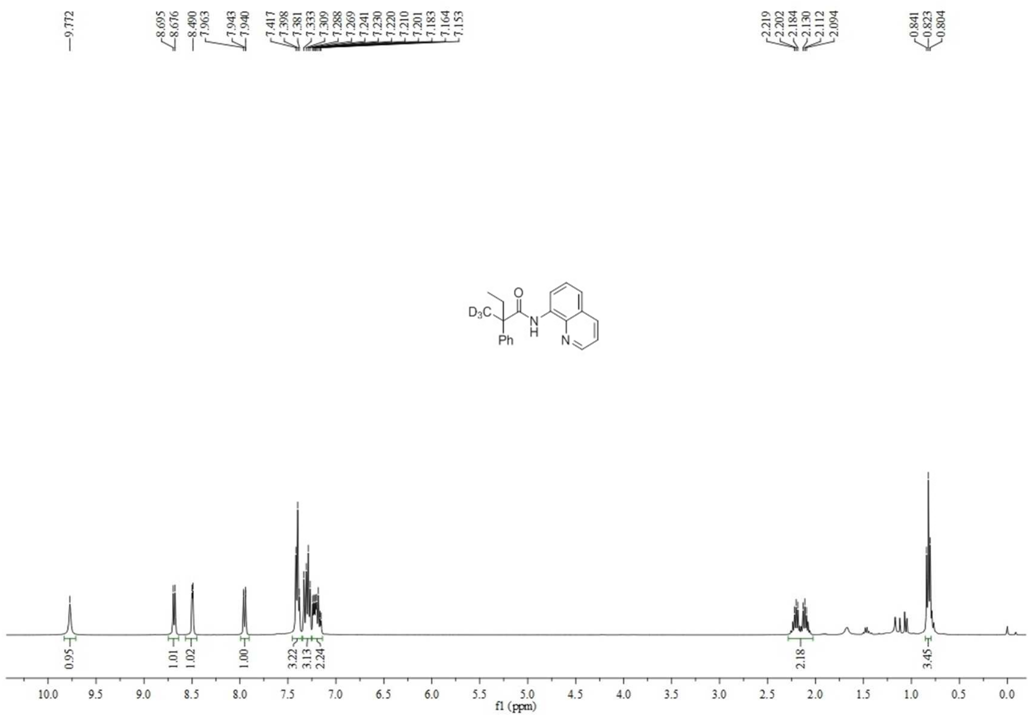


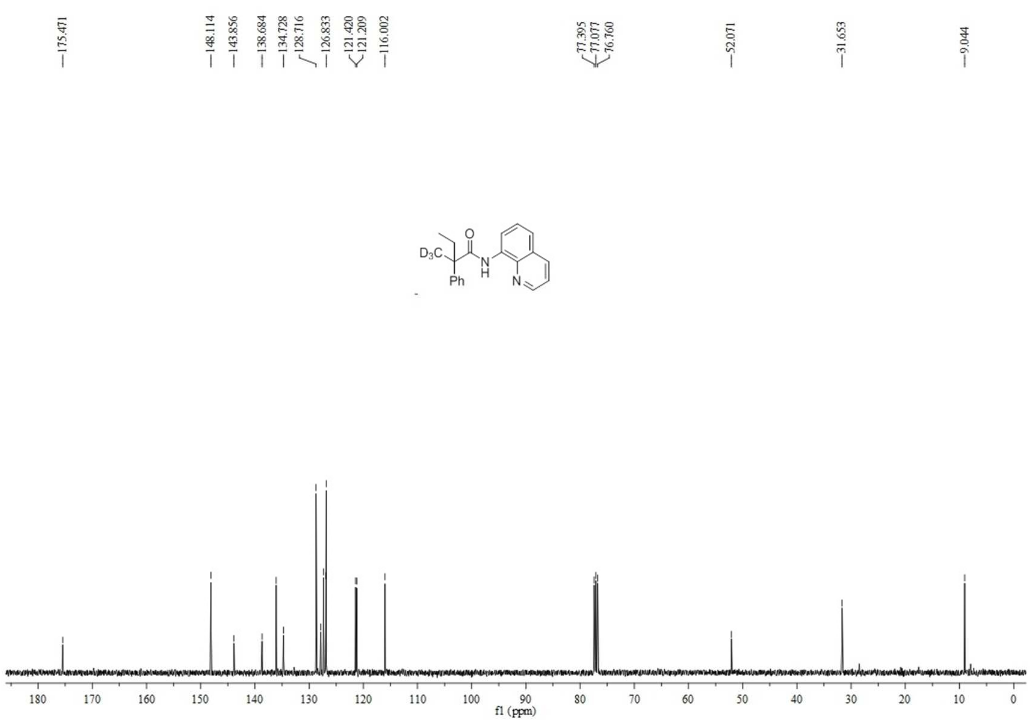




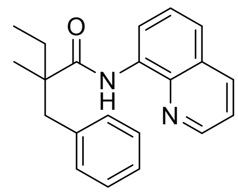
[D_3]-2-methyl-2-phenyl-*N*-(quinolin-8-yl)butanamide ([D_3]-1h)

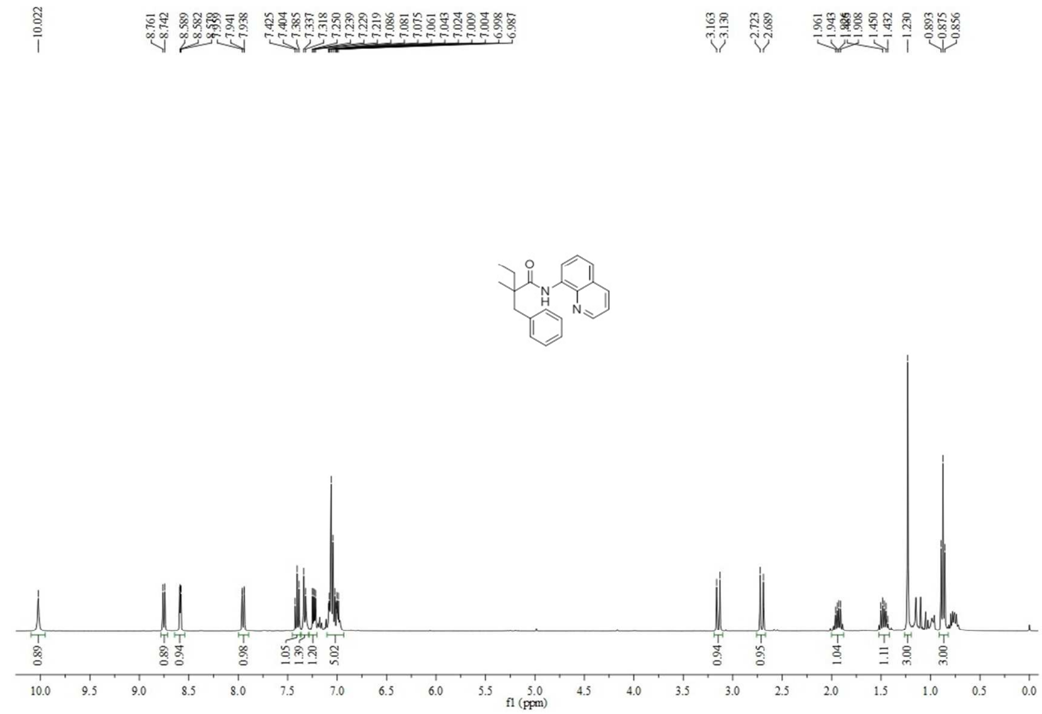


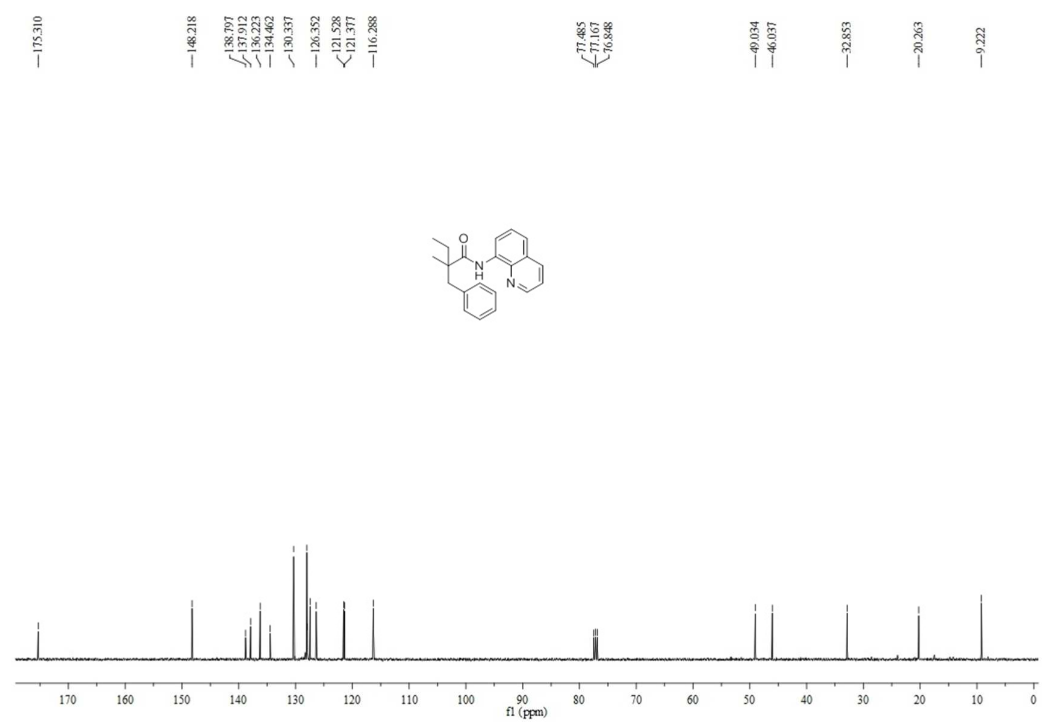




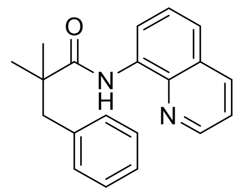
2-benzyl-2-methyl-*N*-(quinolin-8-yl)butanamide (1i)

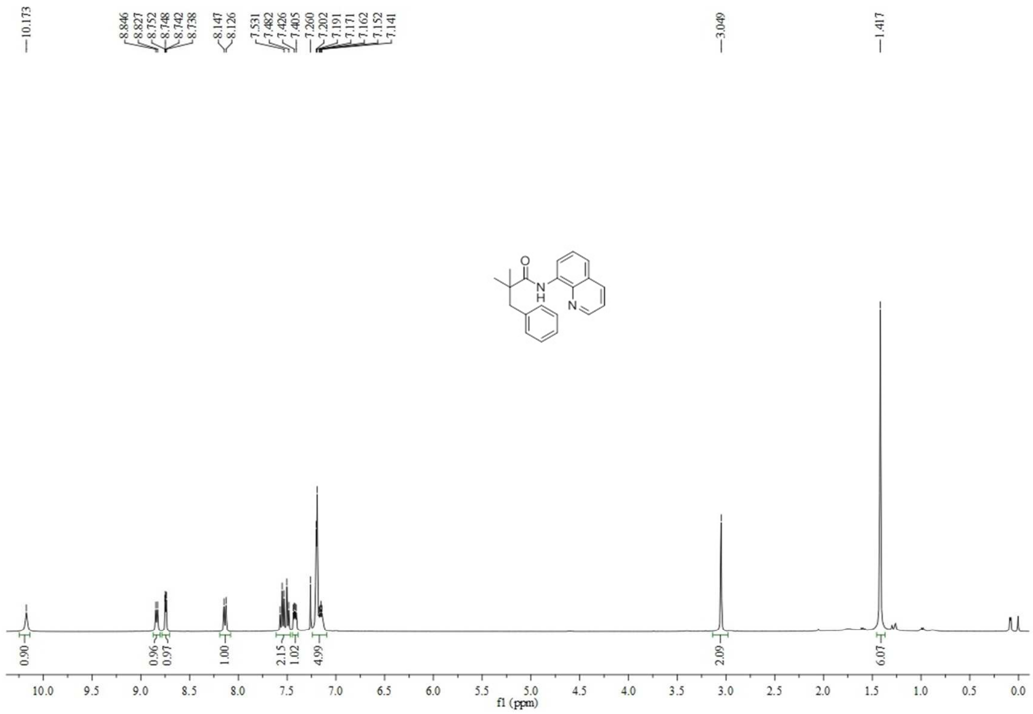


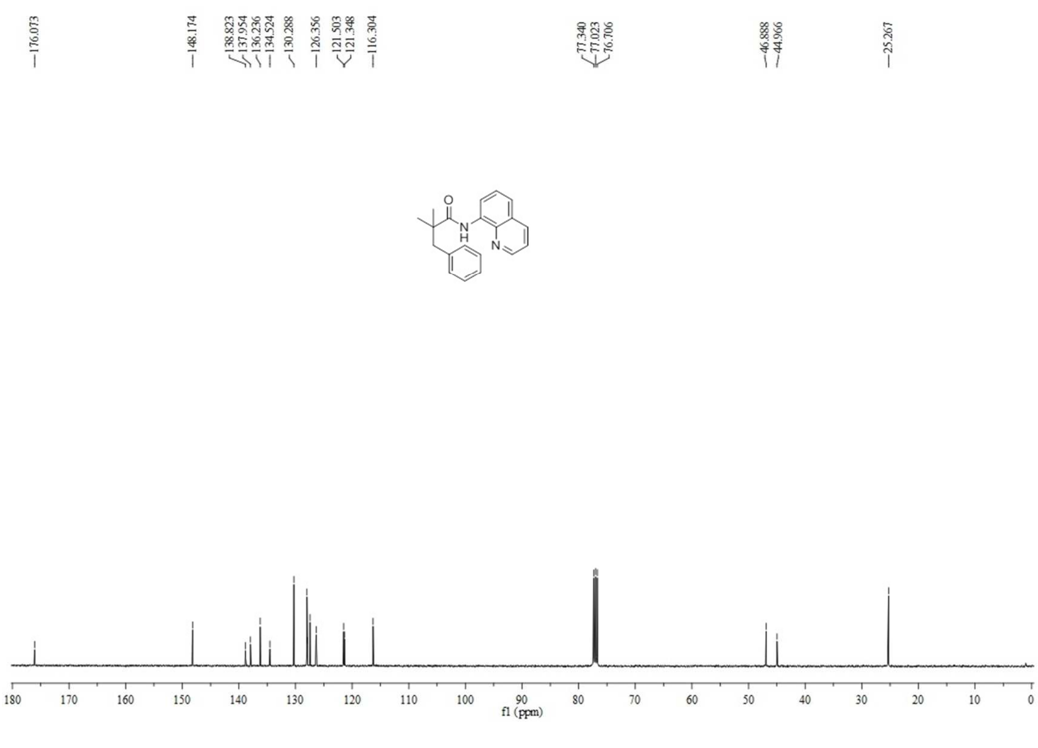




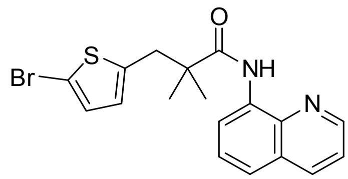
2,2-dimethyl-3-phenyl-*N*-(quinolin-8-yl)propanamide (1j)

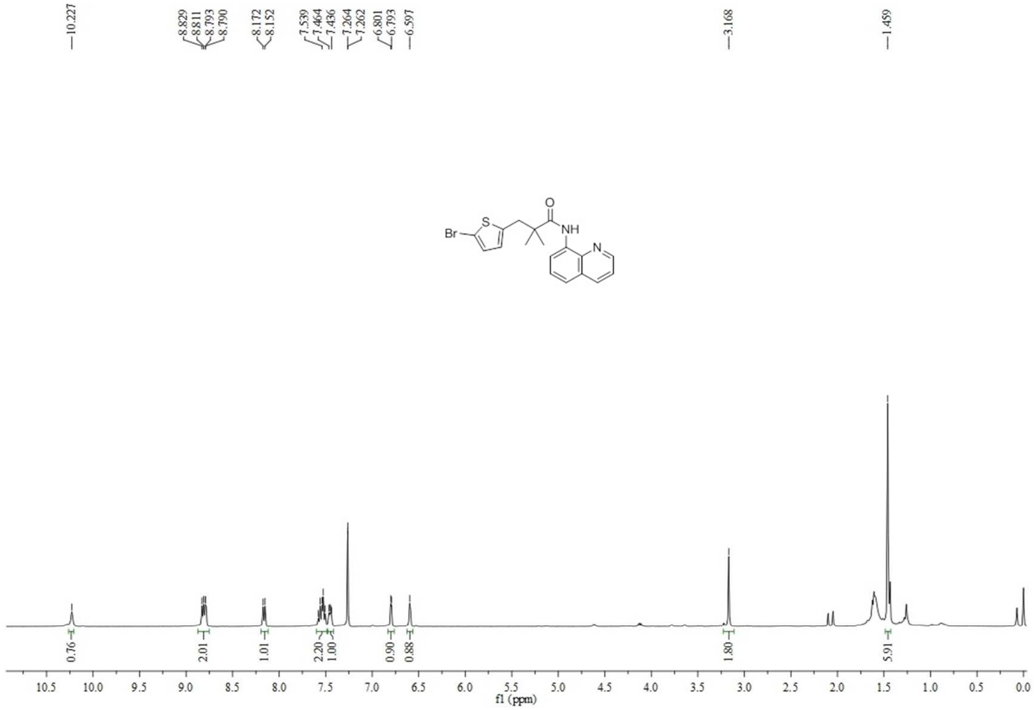


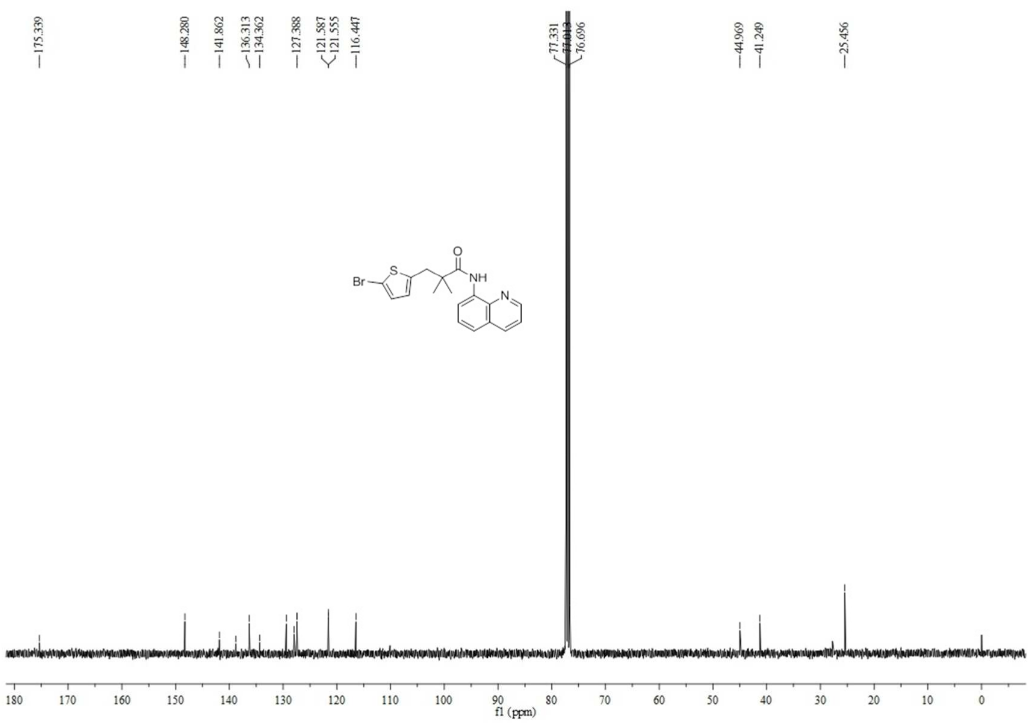




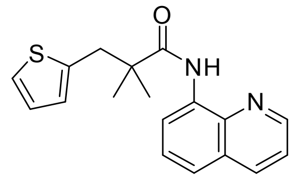
3-(5-bromothiophen-2-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (2a)

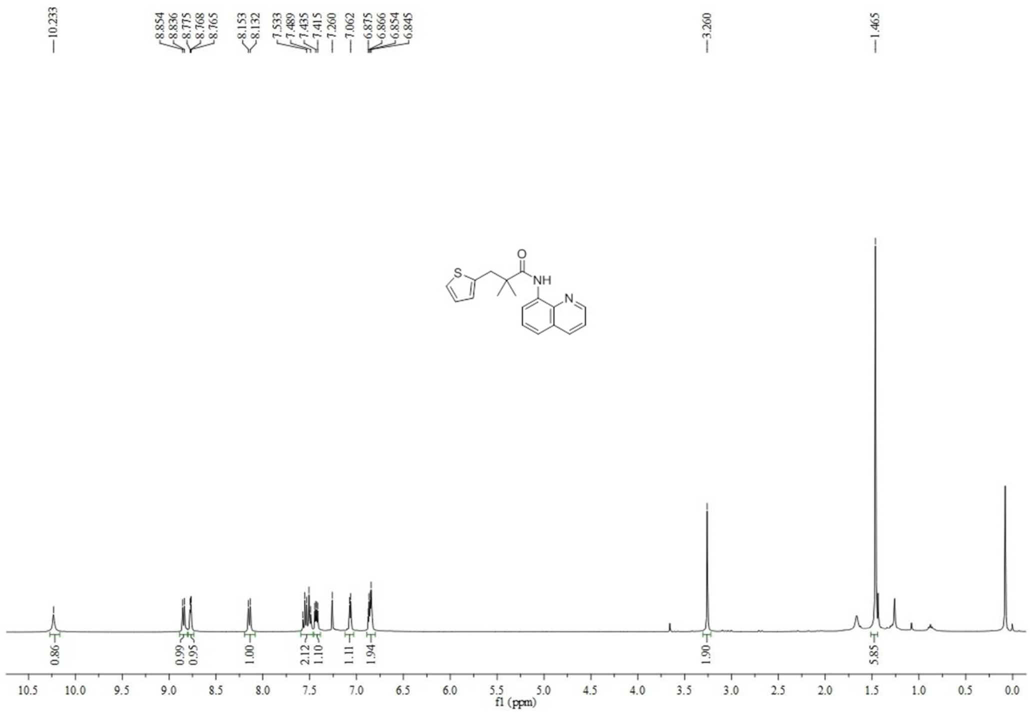


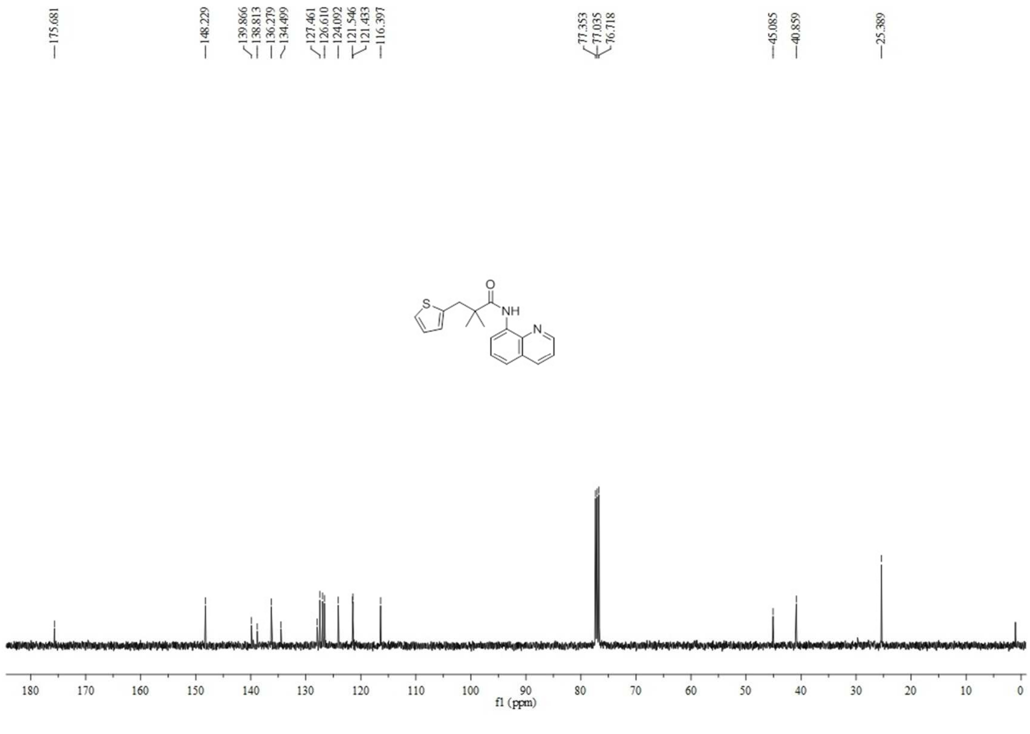




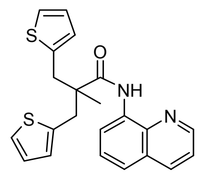
2,2-dimethyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)propanamide (2ba)

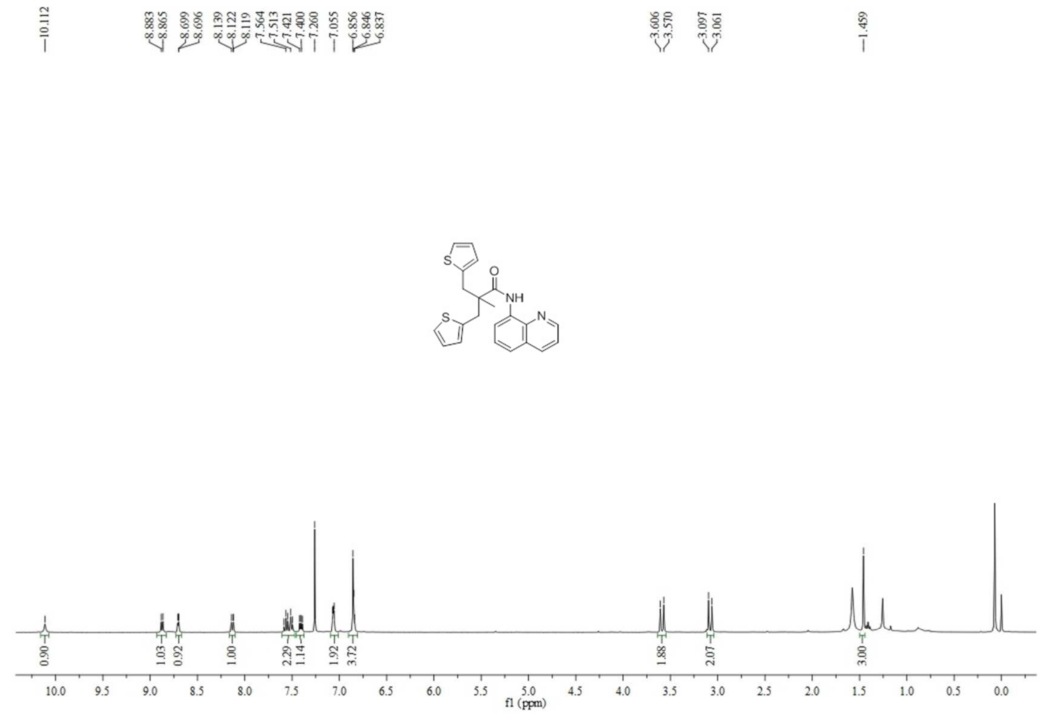


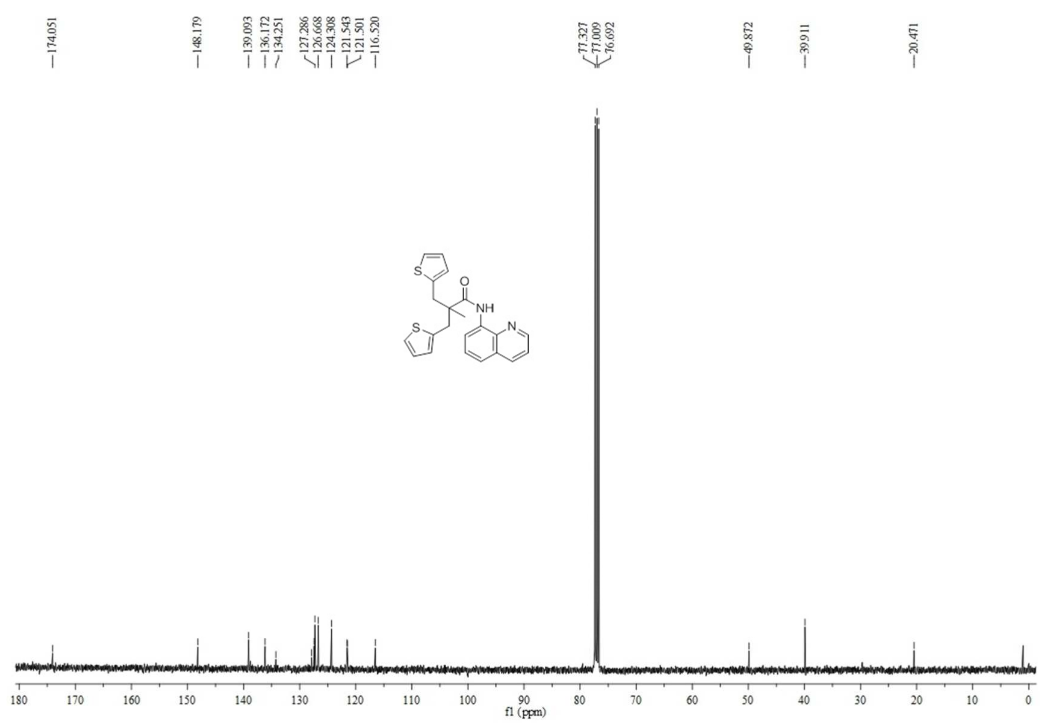




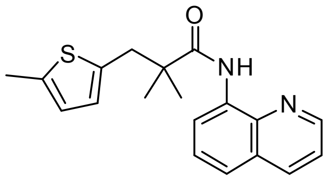
2-methyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)-2-(thiophen-2-ylmethyl)propanamide (2bb)

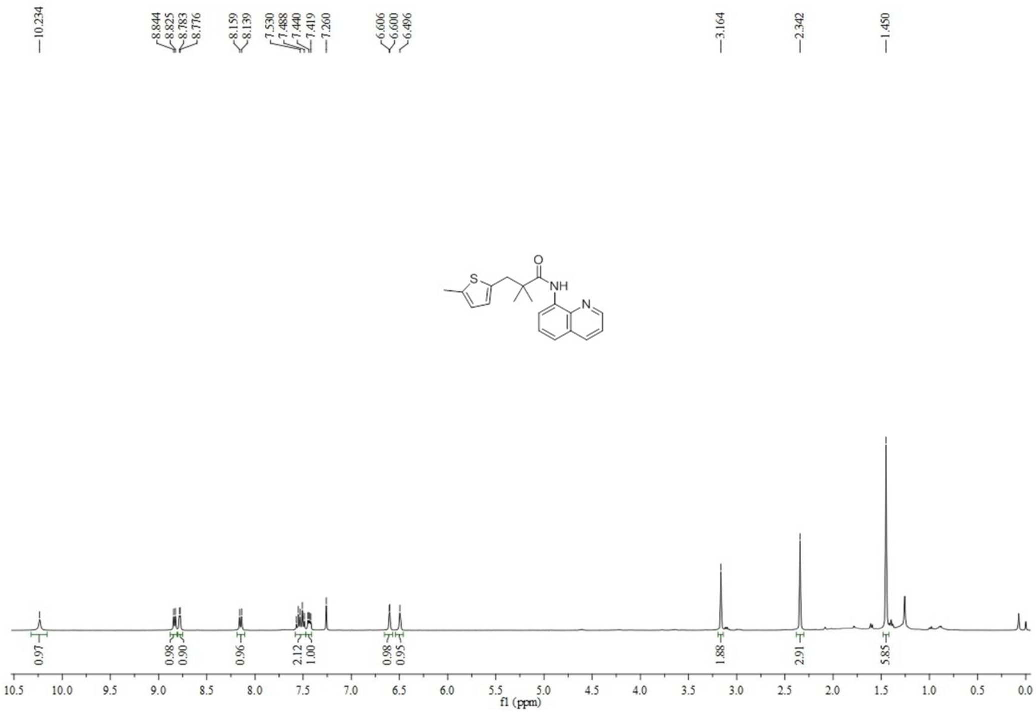


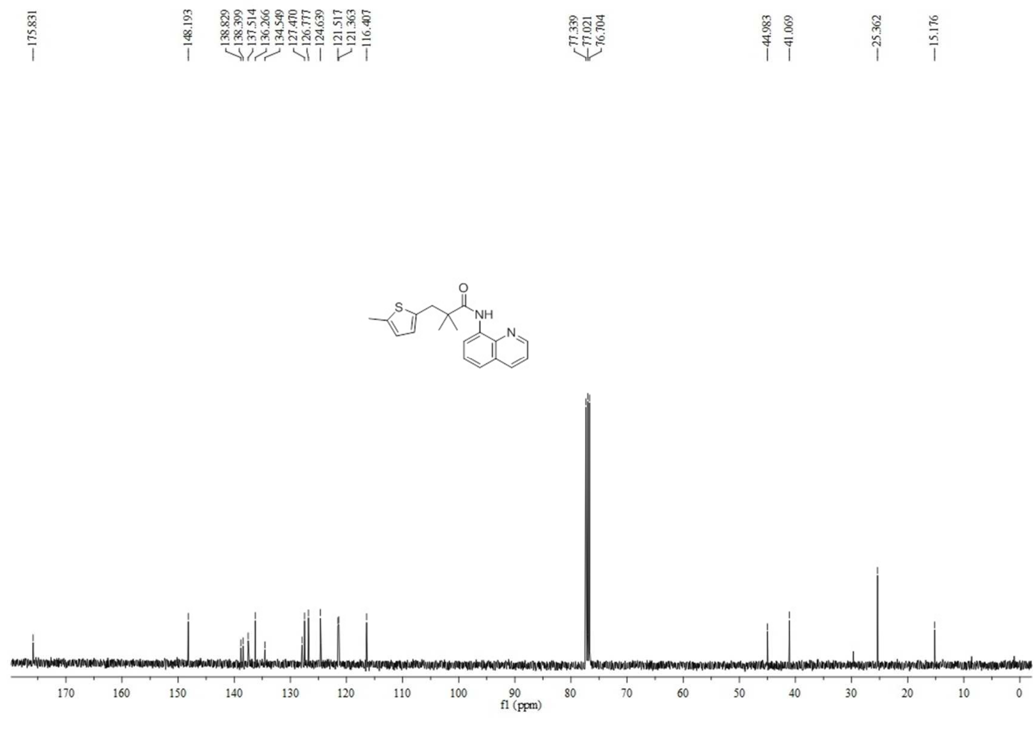




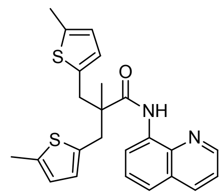
2,2-dimethyl-3-(5-methylthiophen-2-yl)-*N*-(quinolin-8-yl)propanamide (2ca)

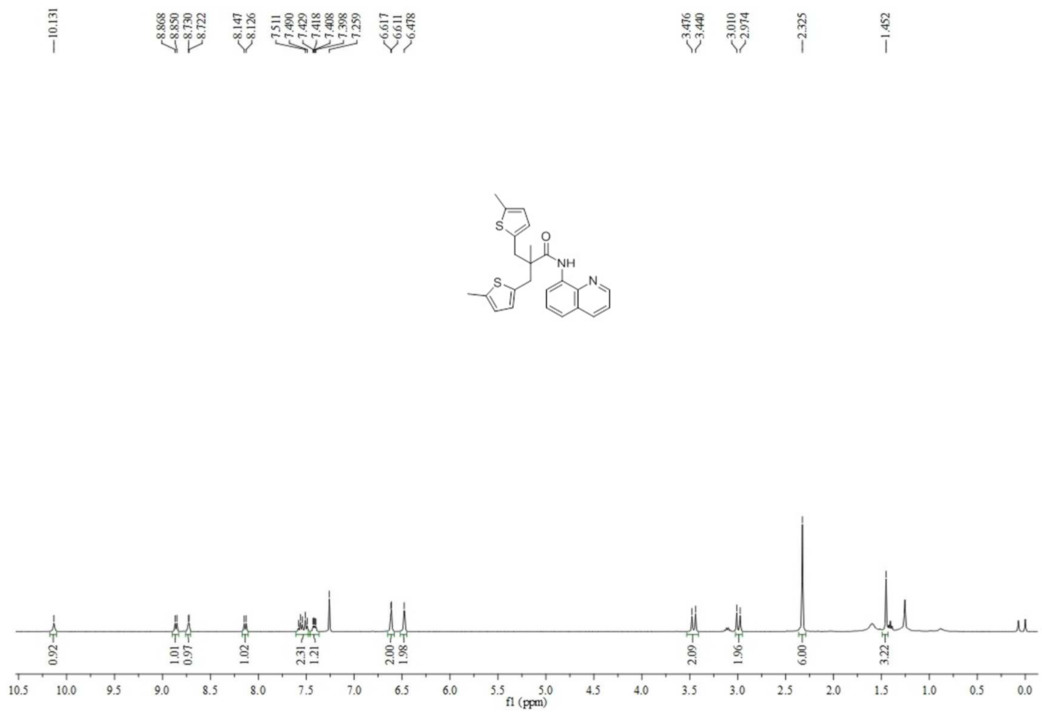


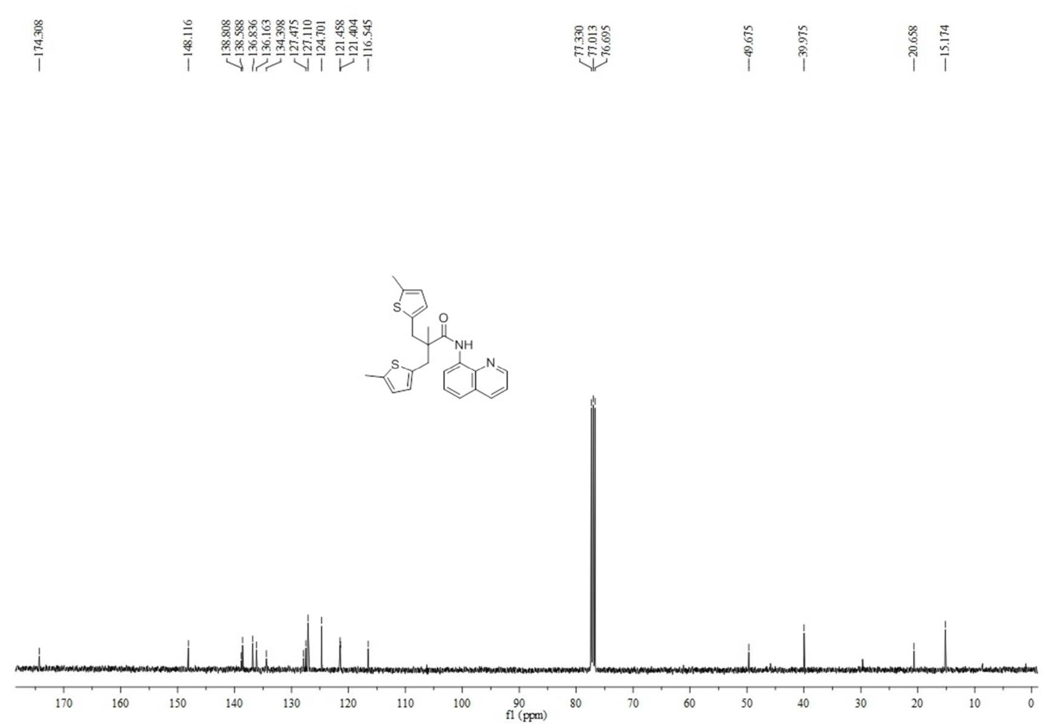




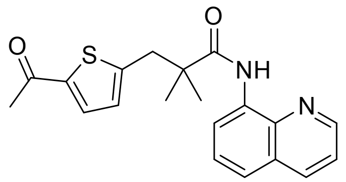
2-methyl-3-(5-methylthiophen-2-yl)-2-((5-methylthiophen-2-yl)methyl)-N-(quinolin-8-yl)propanamide (2cb)

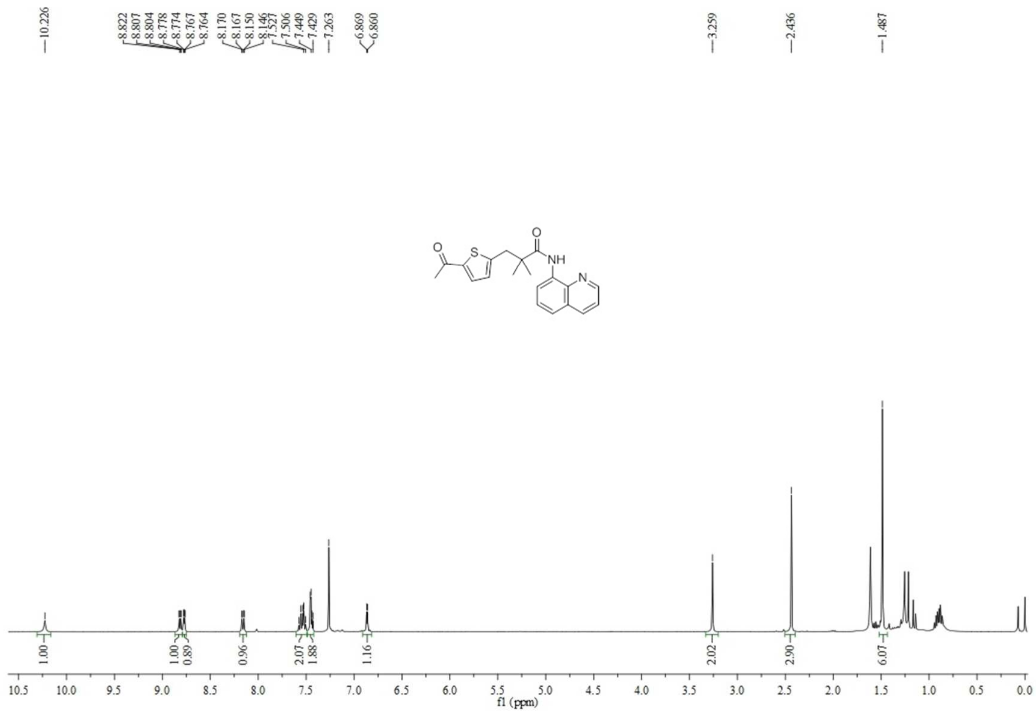


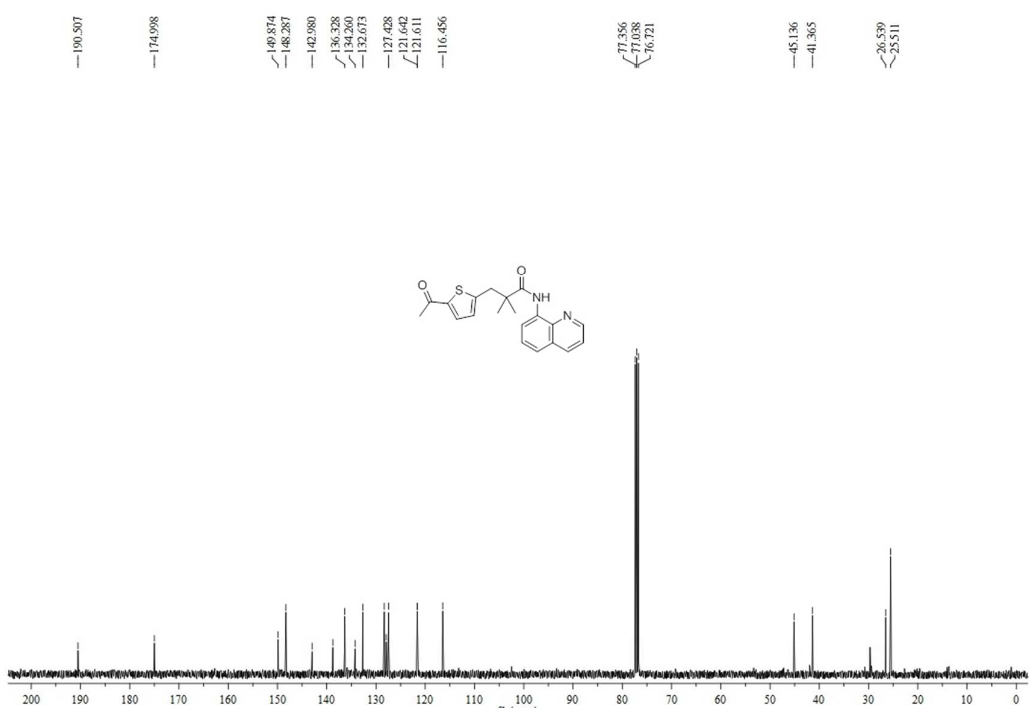




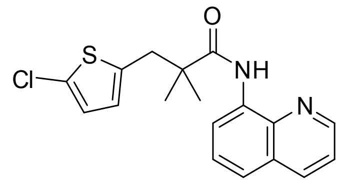
3-(5-acetylthiophen-2-yl)-2,2-dimethyl-N-(quinolin-8-yl)propanamide (2d)

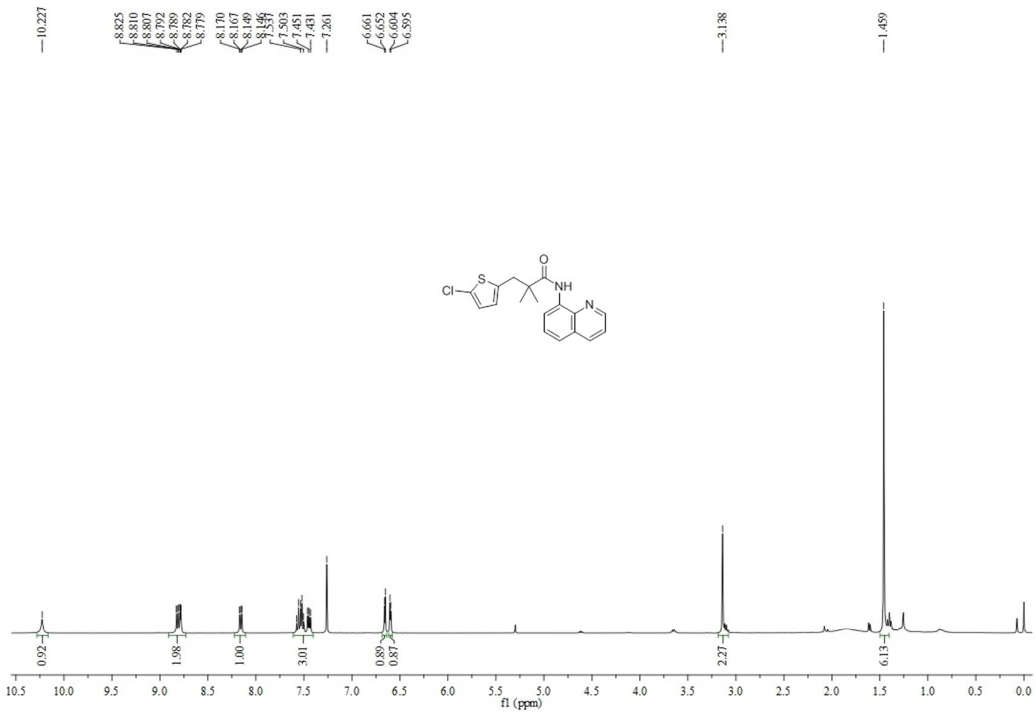


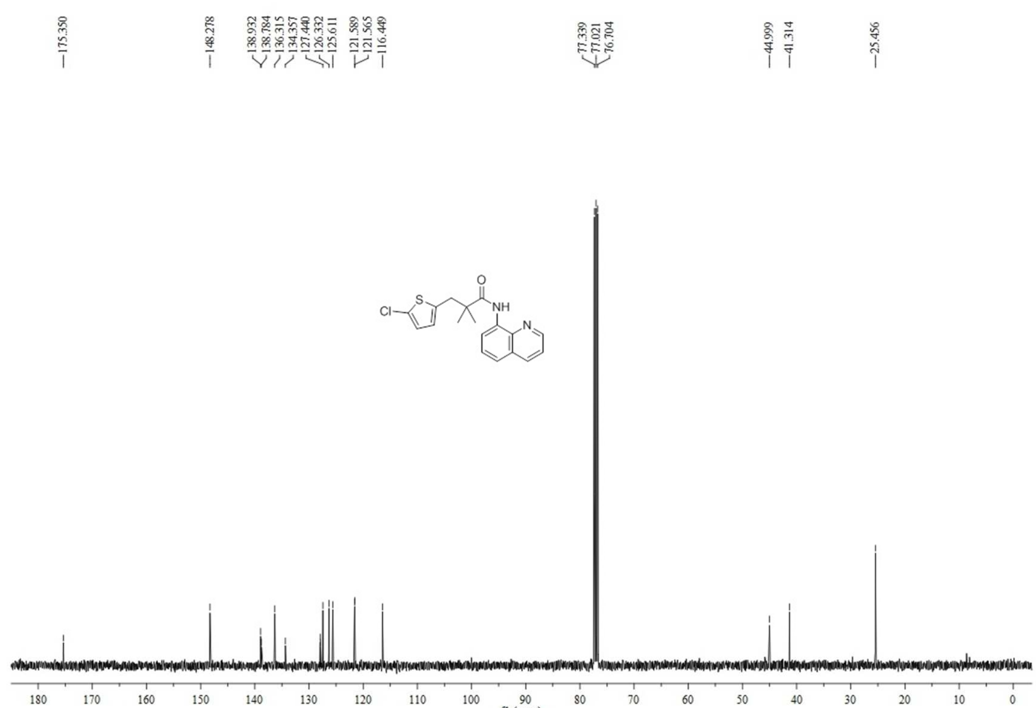




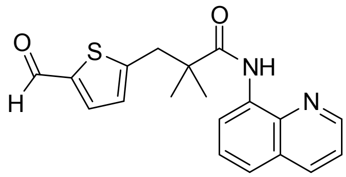
3-(5-chlorothiophen-2-yl)-2,2-dimethyl-N-(quinolin-8-yl)propanamide（2e）

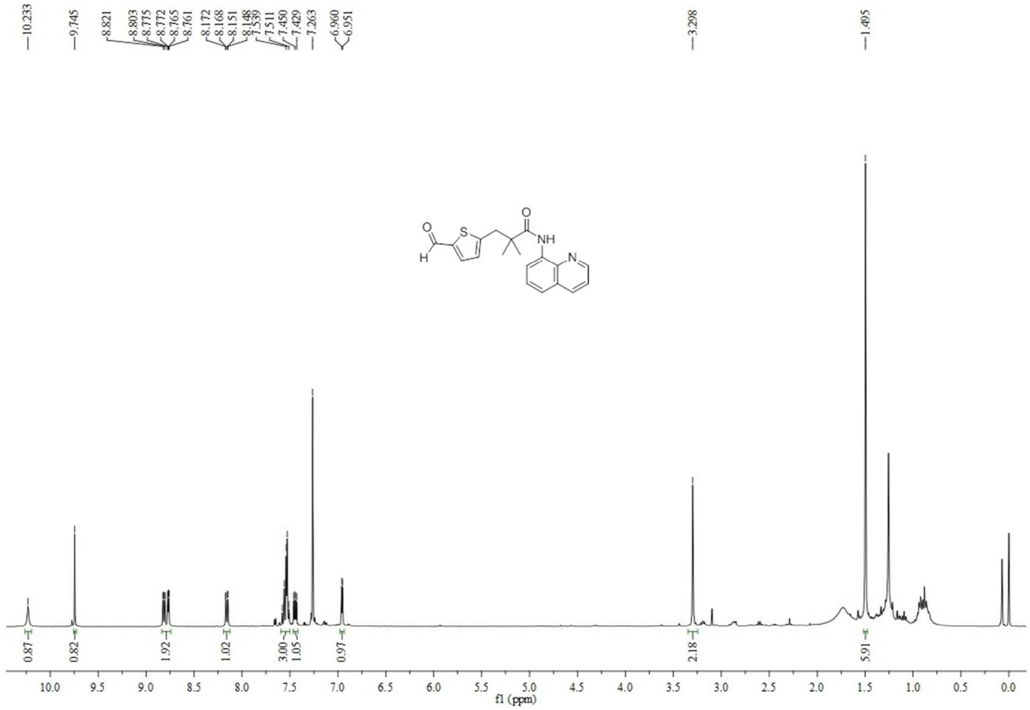


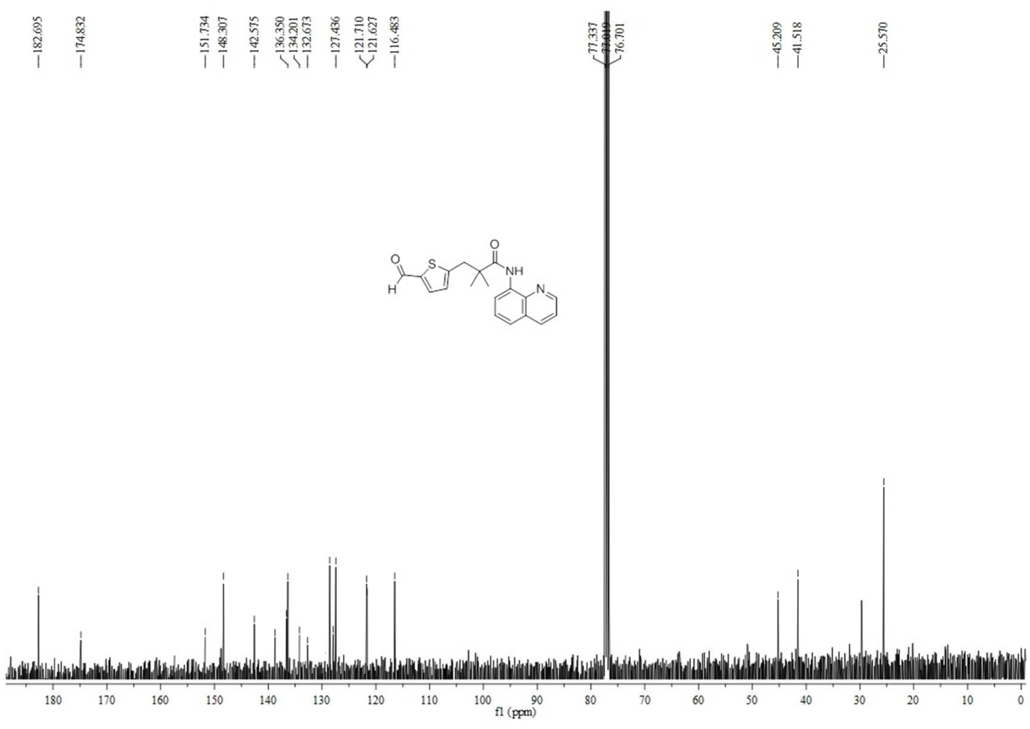




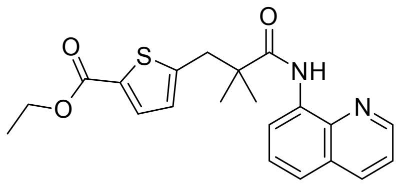
3-(5-formylthiophen-2-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (2f)

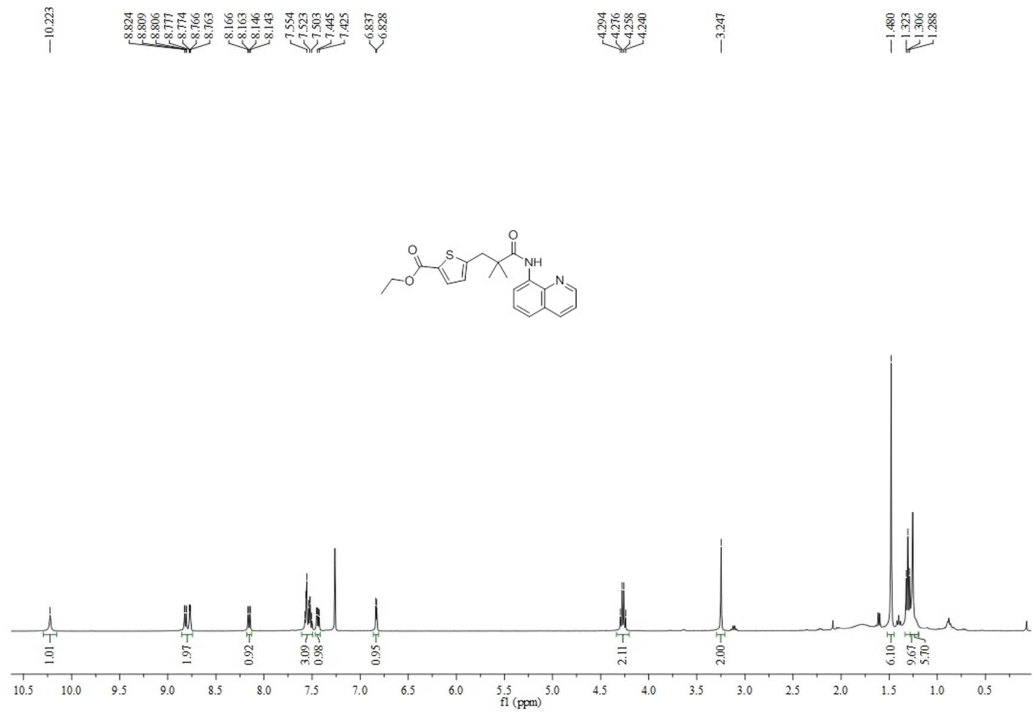


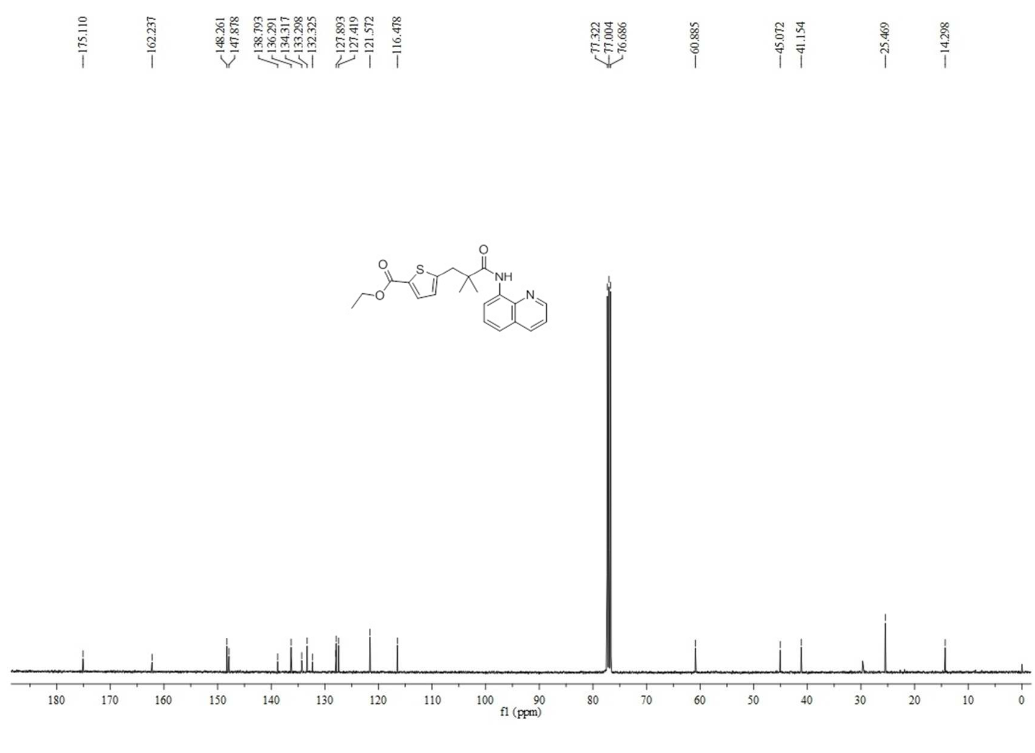




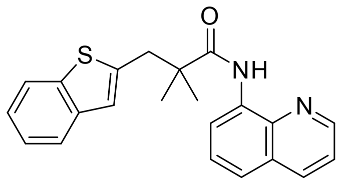
ethyl 5-(2,2-dimethyl-3-oxo-3-(quinolin-8-ylamino)propyl)thiophene-2-carboxylate (2g)

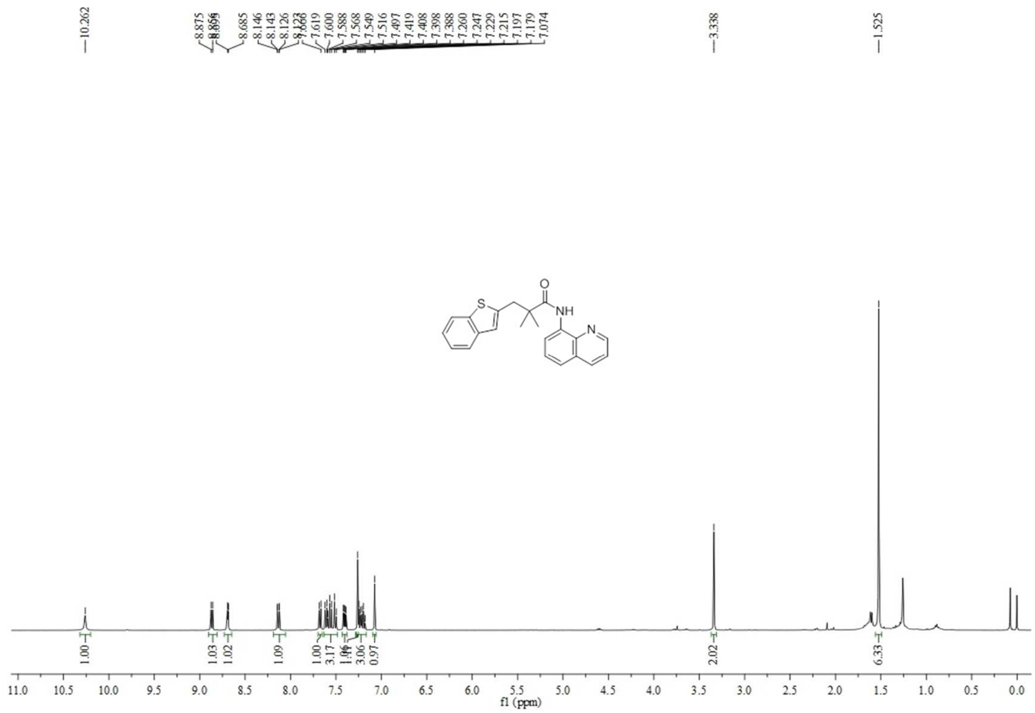


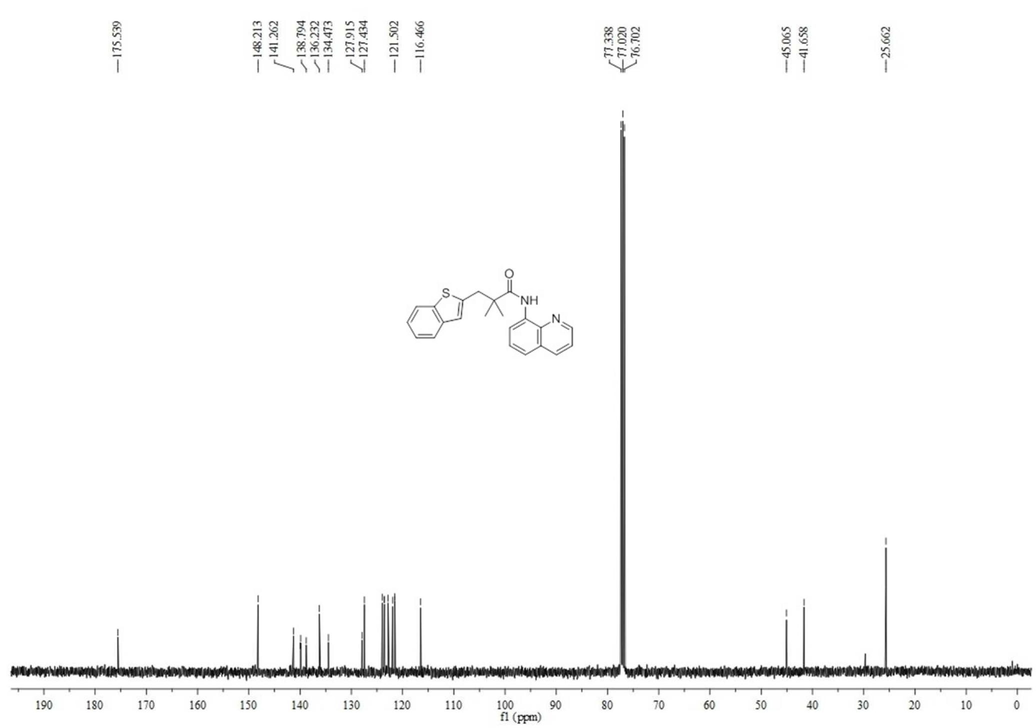




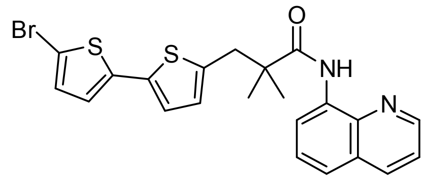
3-(benzo[b]thiophen-2-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (2h)

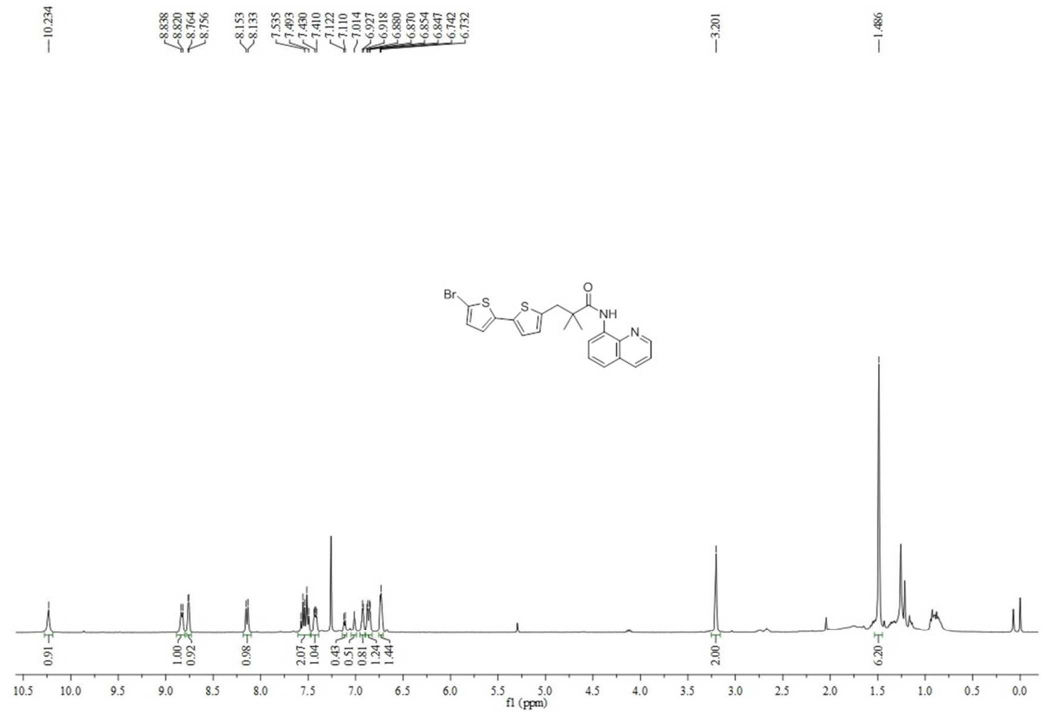


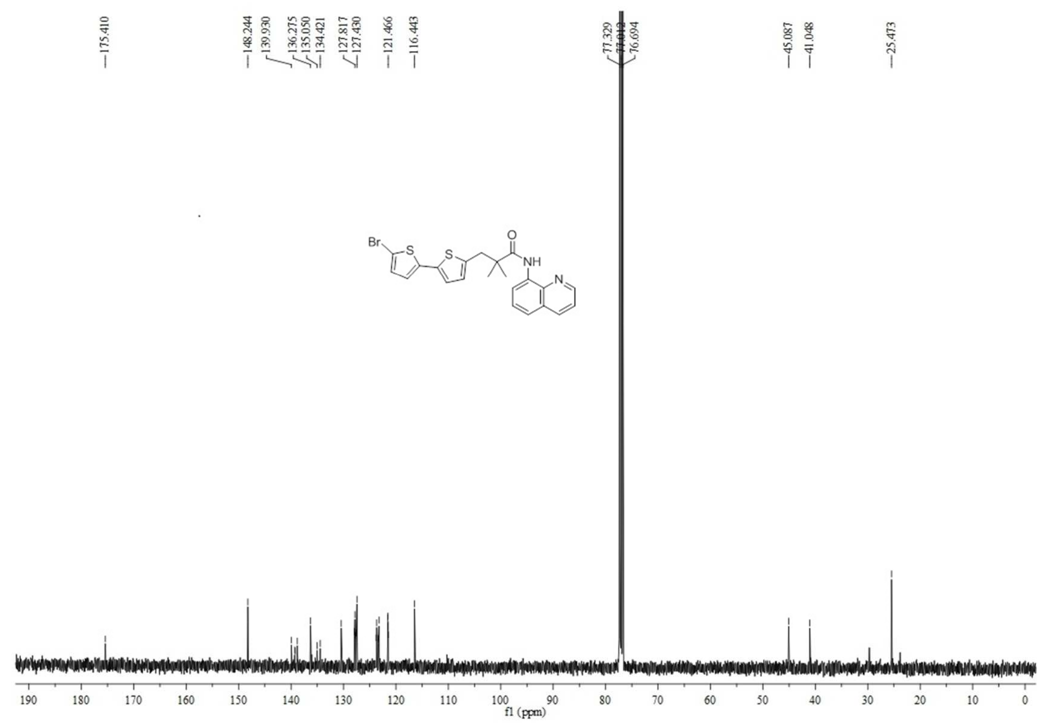




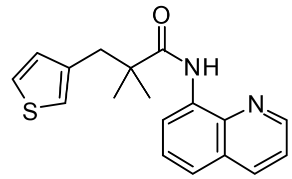
3-(5'-bromo-[2,2'-bithiophen]-5-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (2i)

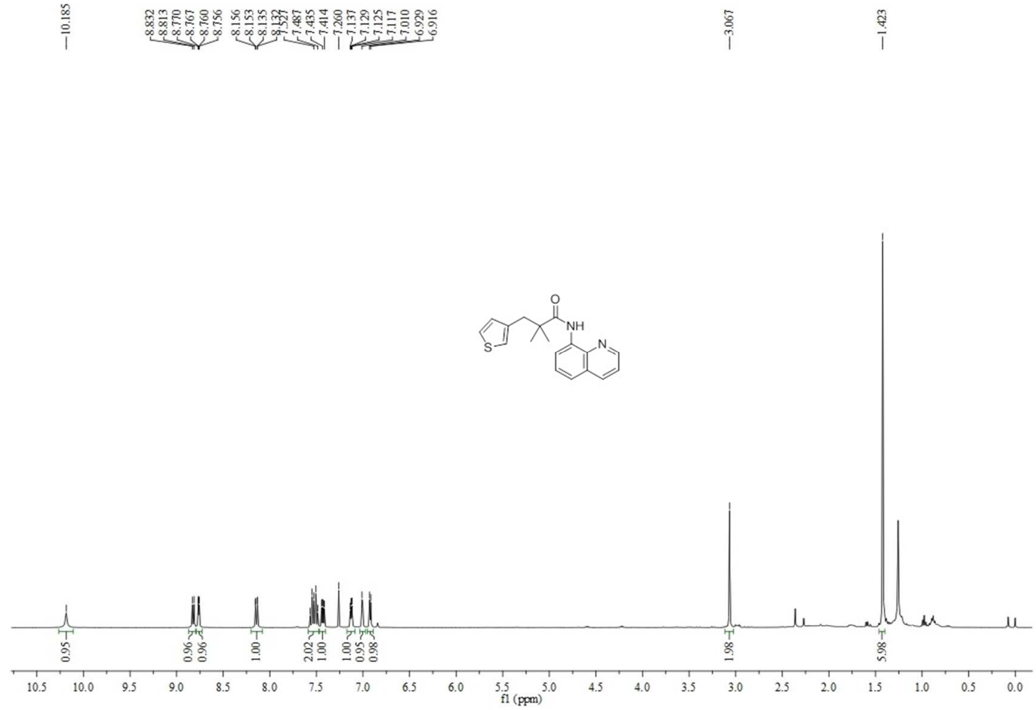


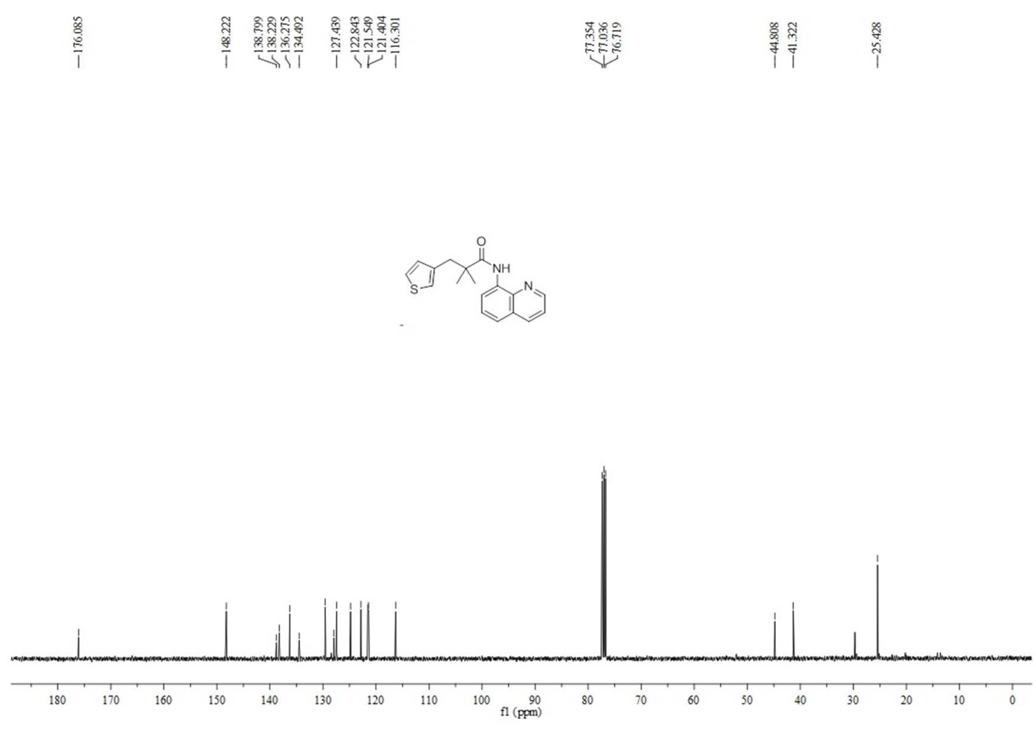




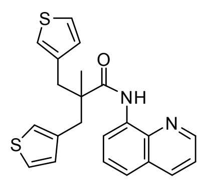
2,2-dimethyl-*N*-(quinolin-8-yl)-3-(thiophen-3-yl)propanamide (2ja)

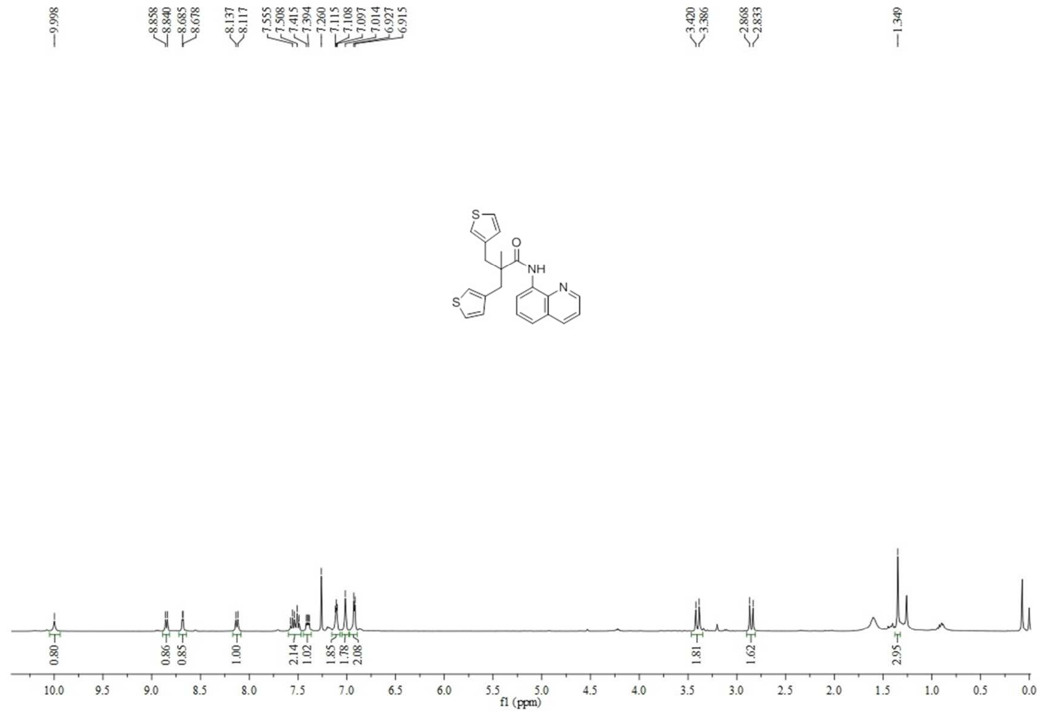


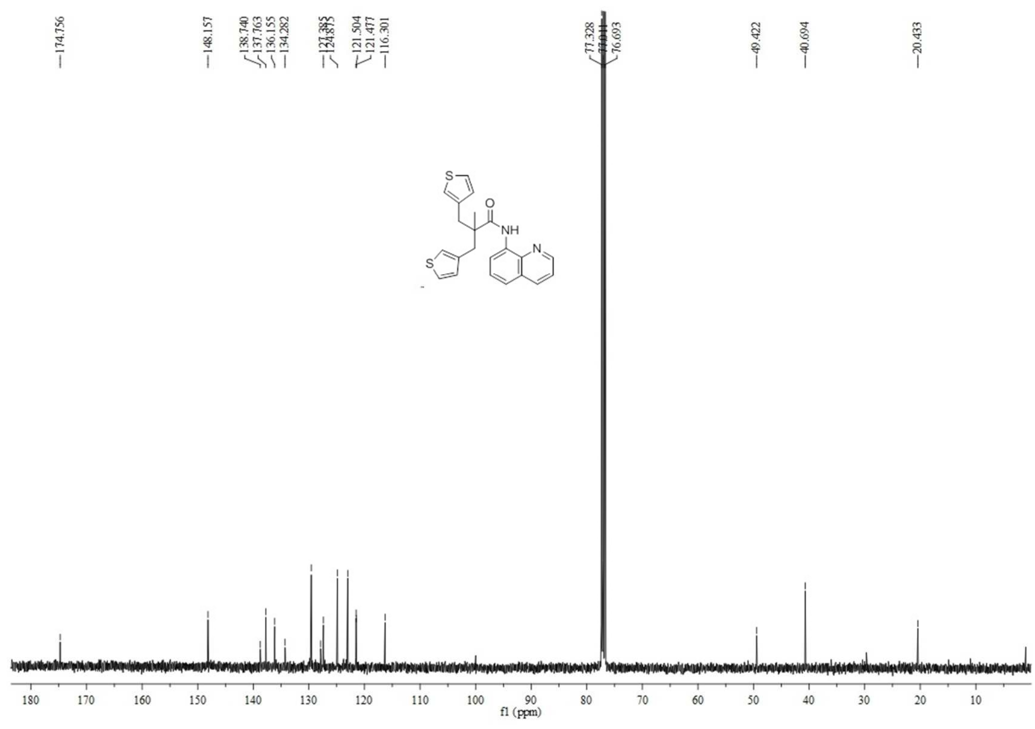




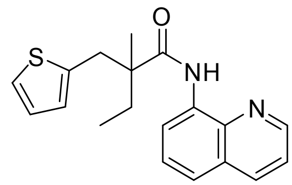
2-methyl-*N*-(quinolin-8-yl)-3-(thiophen-3-yl)-2-(thiophen-3-ylmethyl)propanamide (2jb)

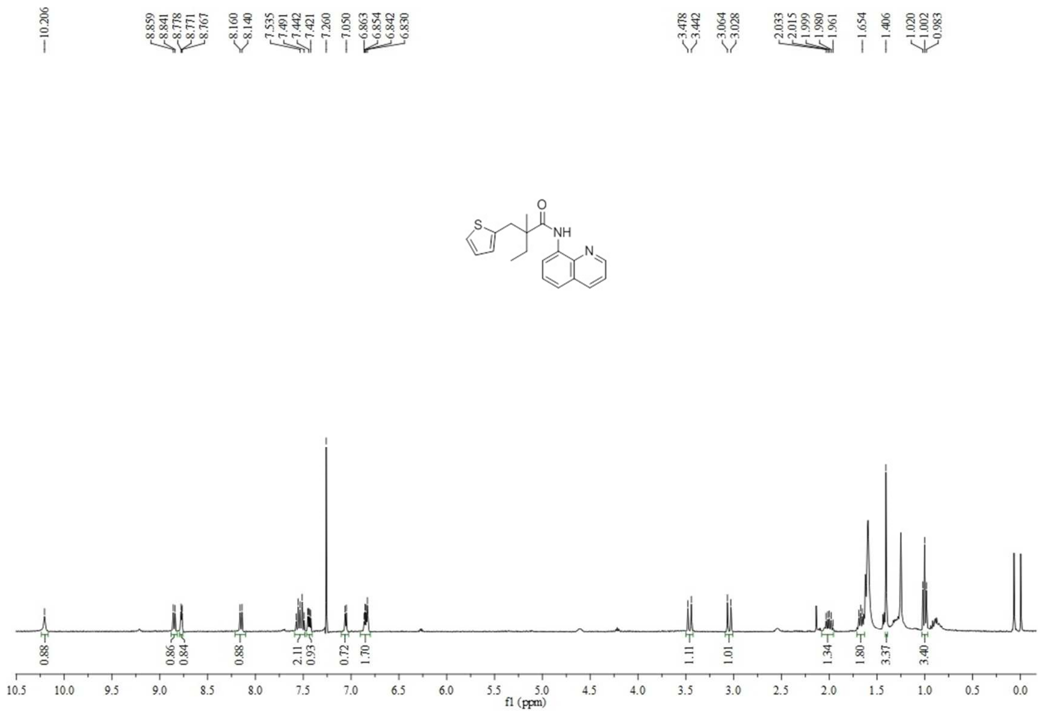


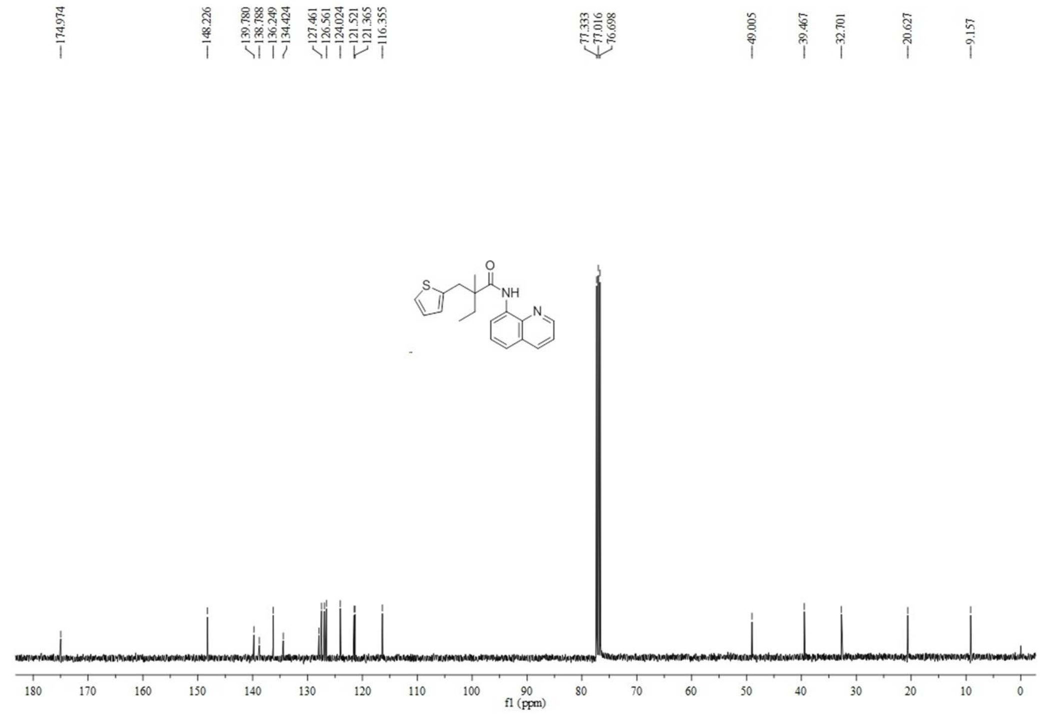




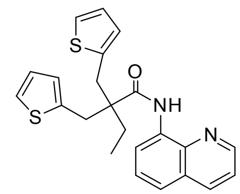
2-methyl-*N*-(quinolin-8-yl)-2-(thiophen-2-ylmethyl)butanamide (2ma)

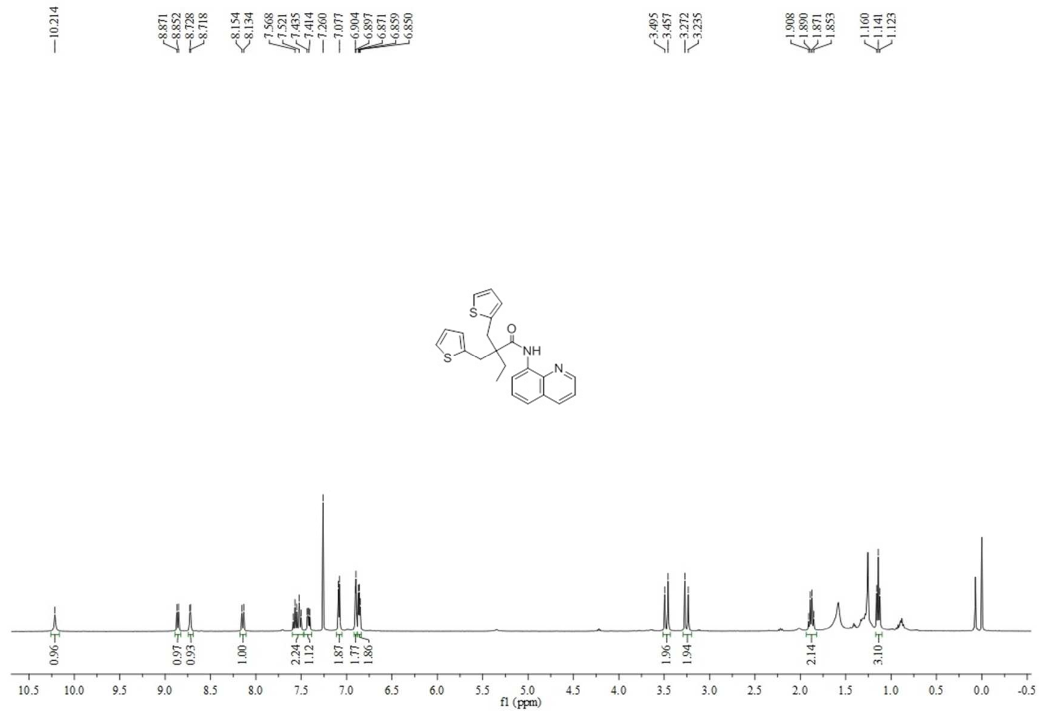


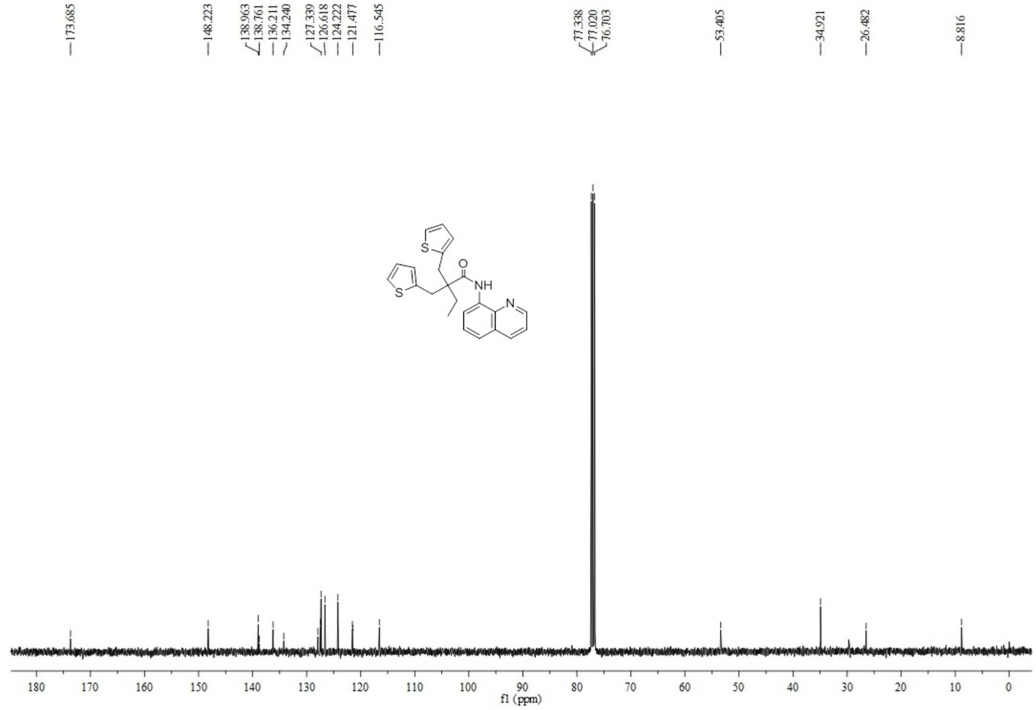




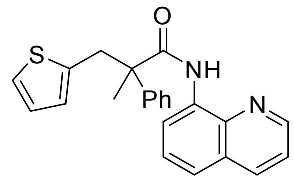
***N*-(quinolin-8-yl)-2,2-bis(thiophen-2-ylmethyl)butanamide (2mb)**

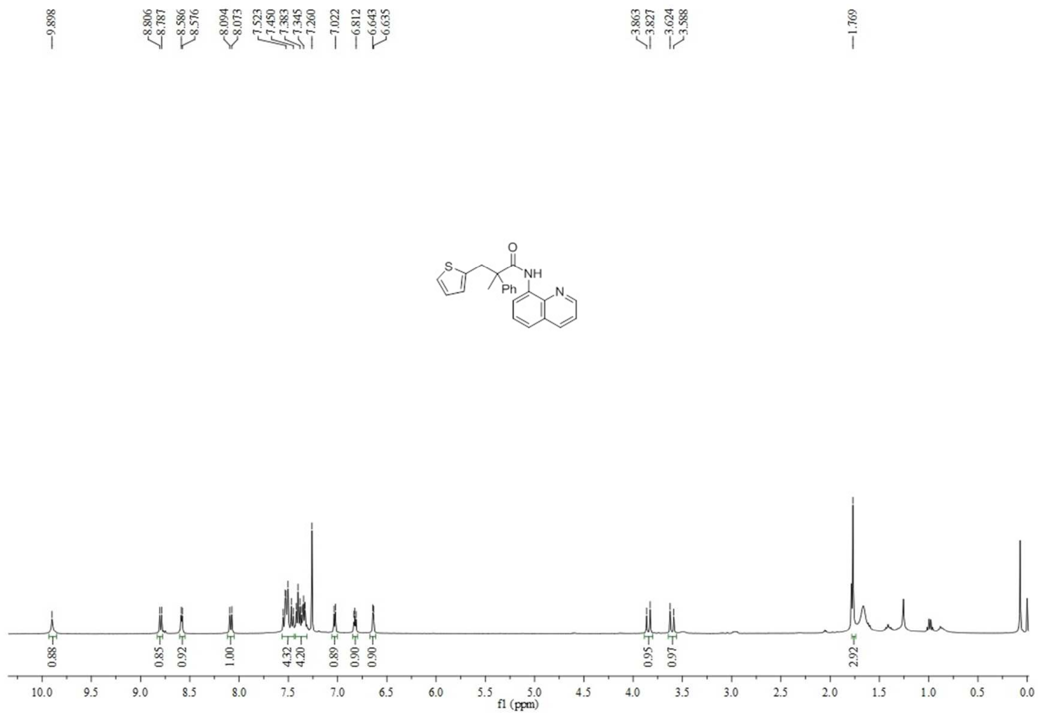


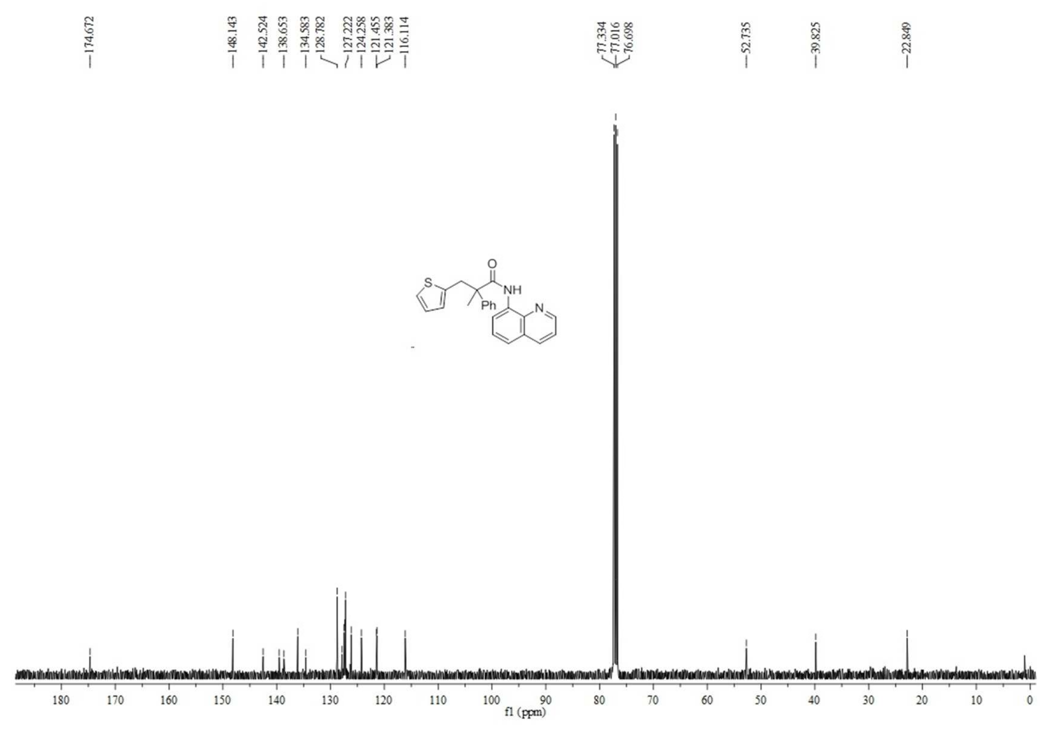




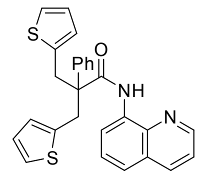
2-methyl-2-phenyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)propanamide (2na)

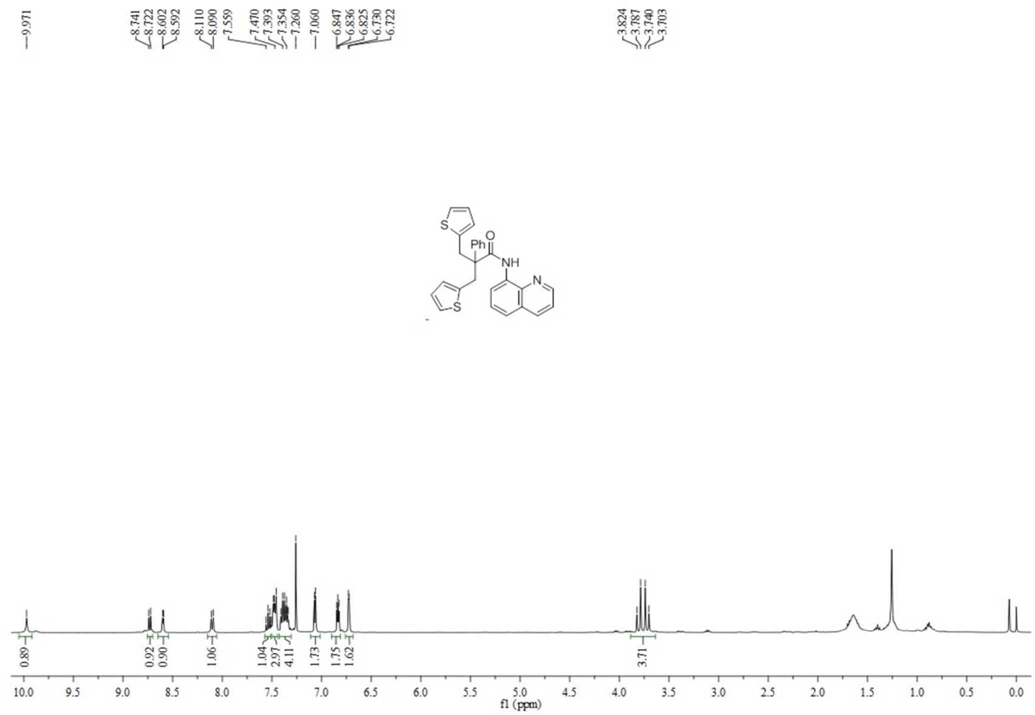


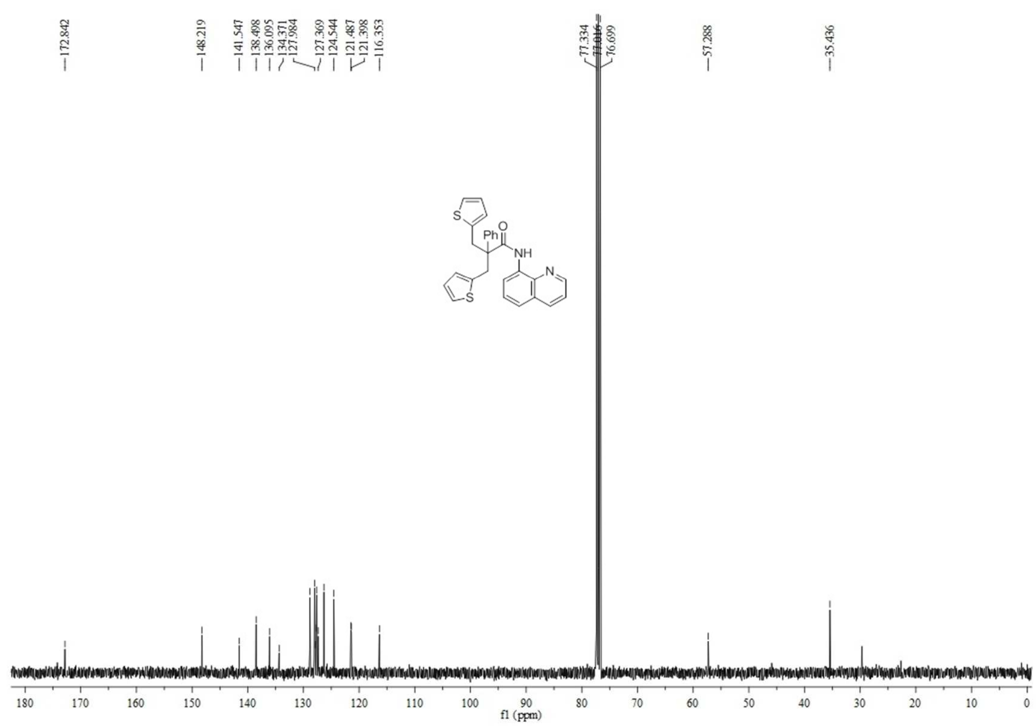




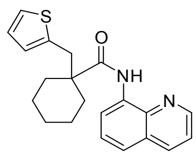
2-phenyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)-2-(thiophen-2-ylmethyl)propanamide (2nb)

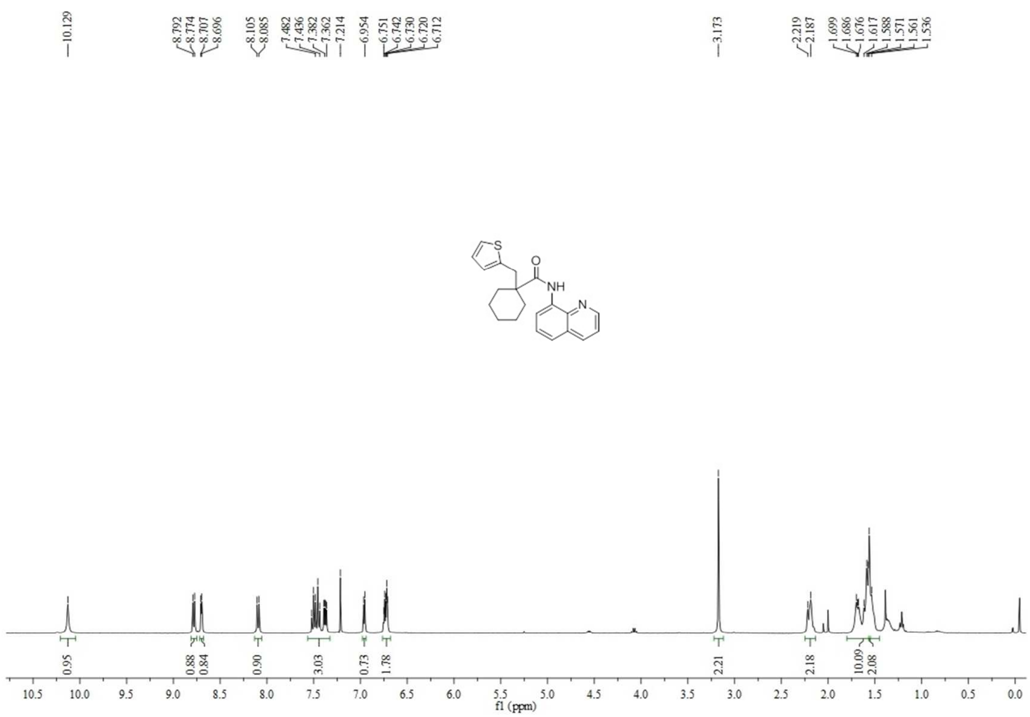


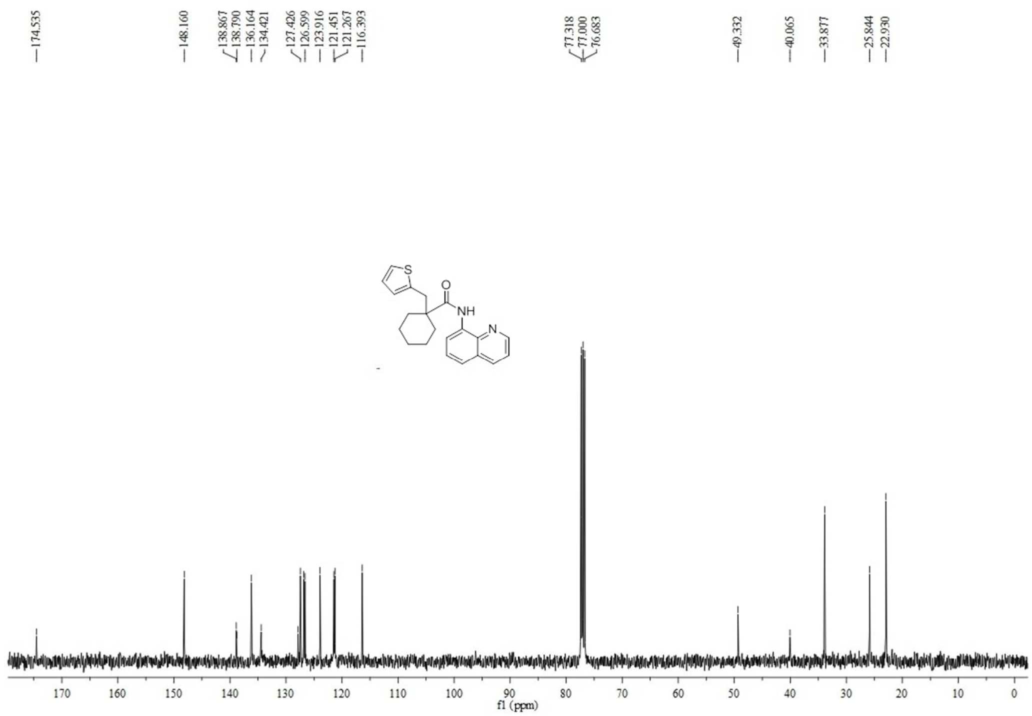




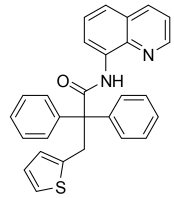
***N*-(quinolin-8-yl)-1-(thiophen-2-ylmethyl)cyclohexanecarboxamide (2o)**

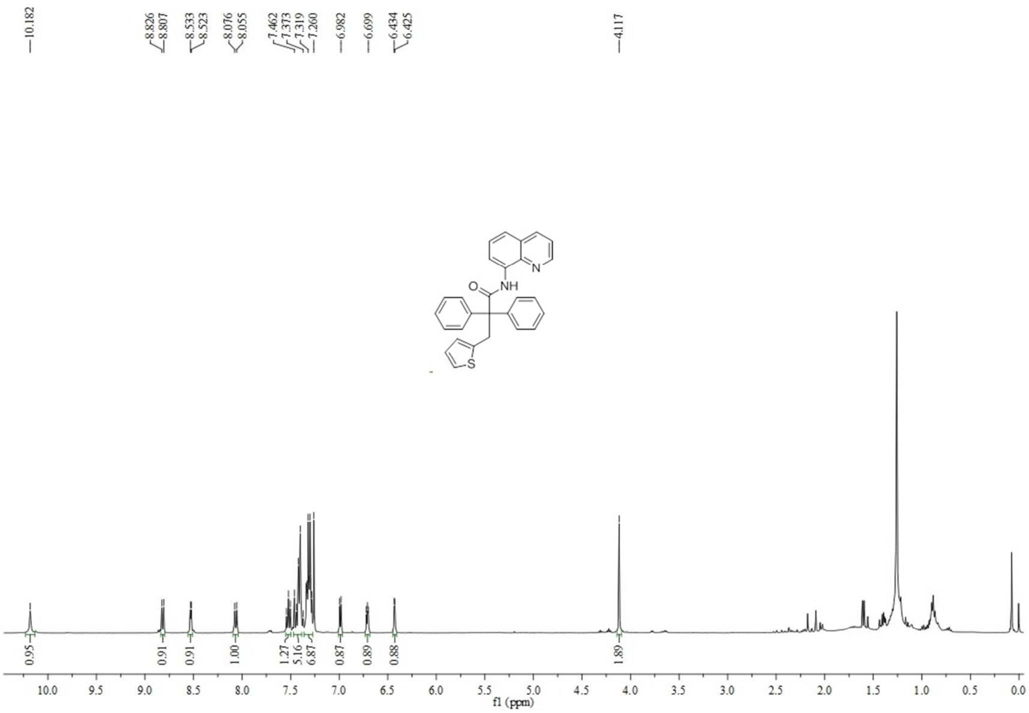


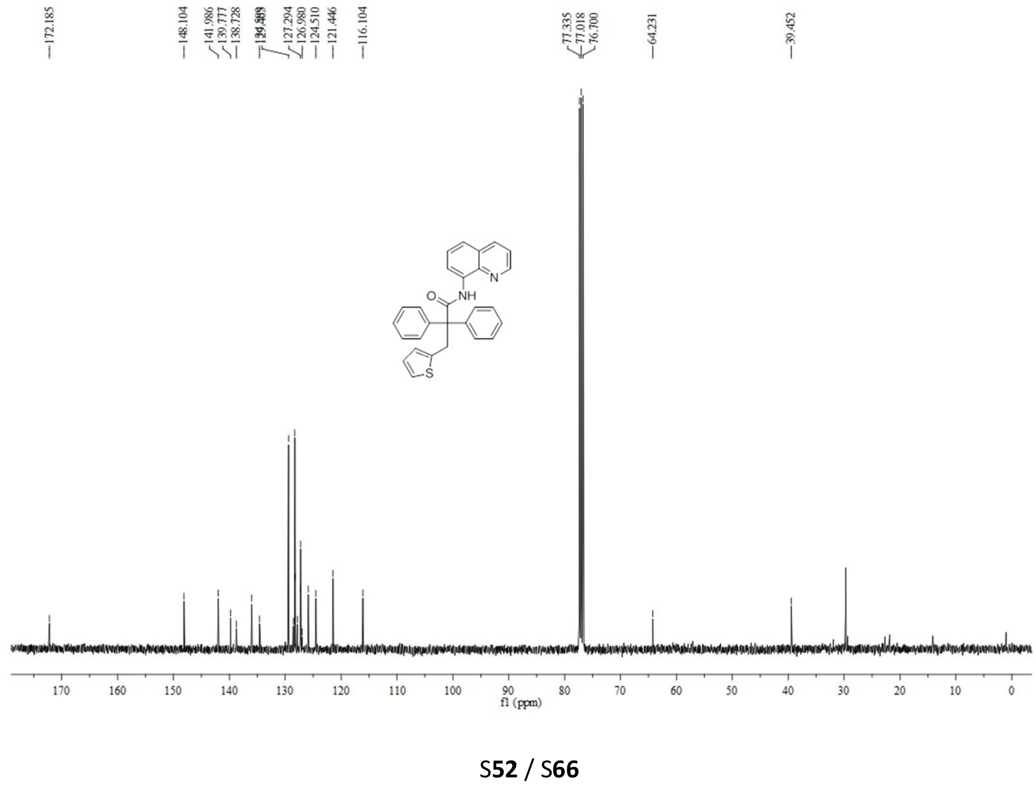




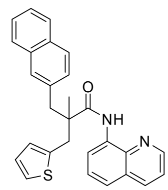
2,2-diphenyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)propanamide (2p)

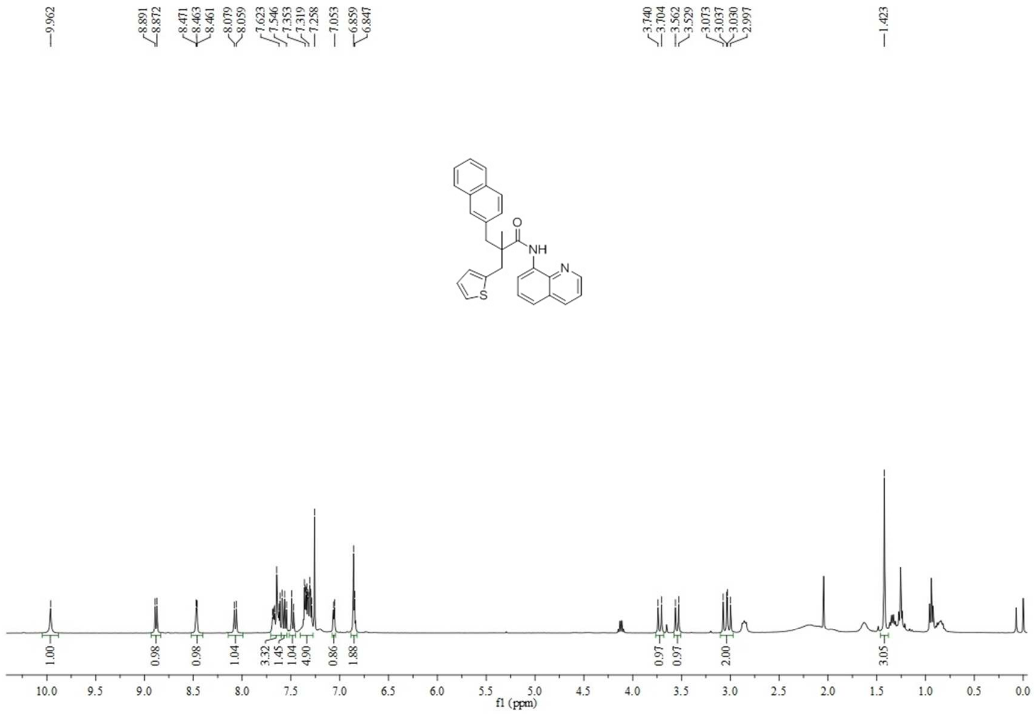


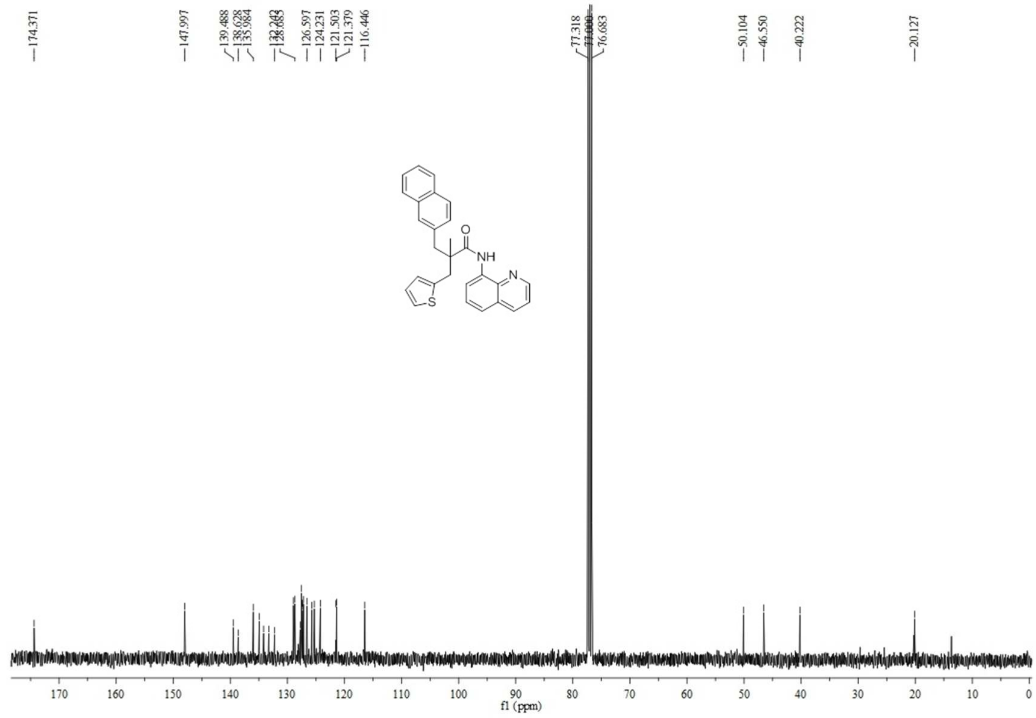




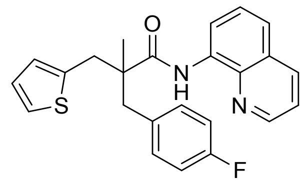
2-methyl-3-(naphthalen-2-yl)-*N*-(quinolin-8-yl)-2-(thiophen-2-ylmethyl)propanamide (2q)

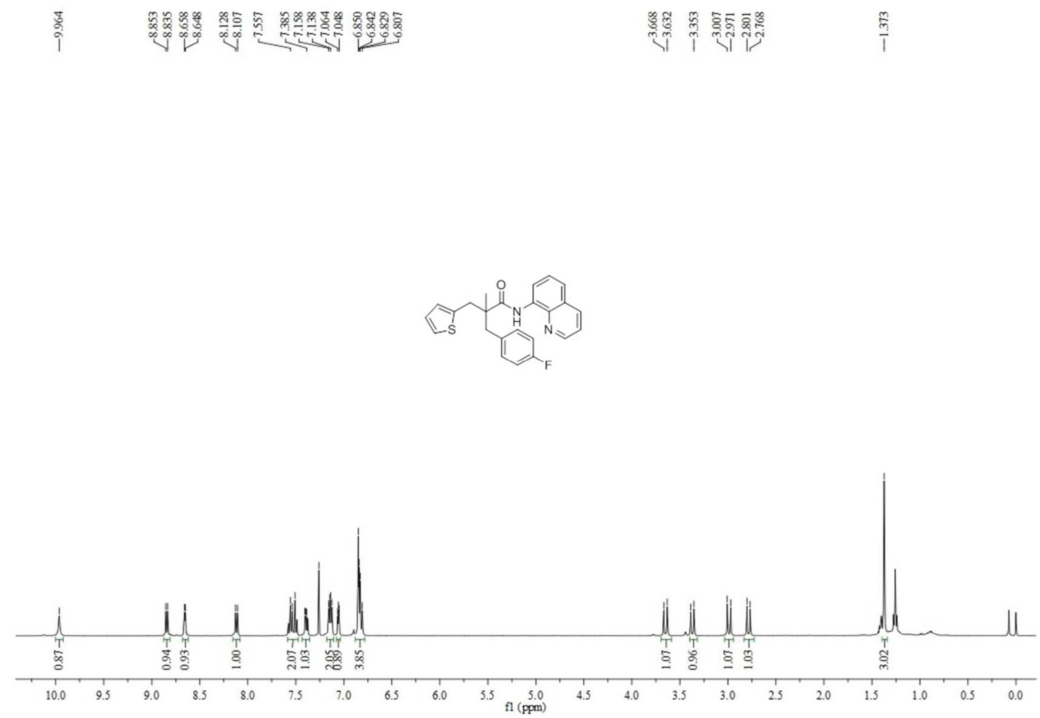


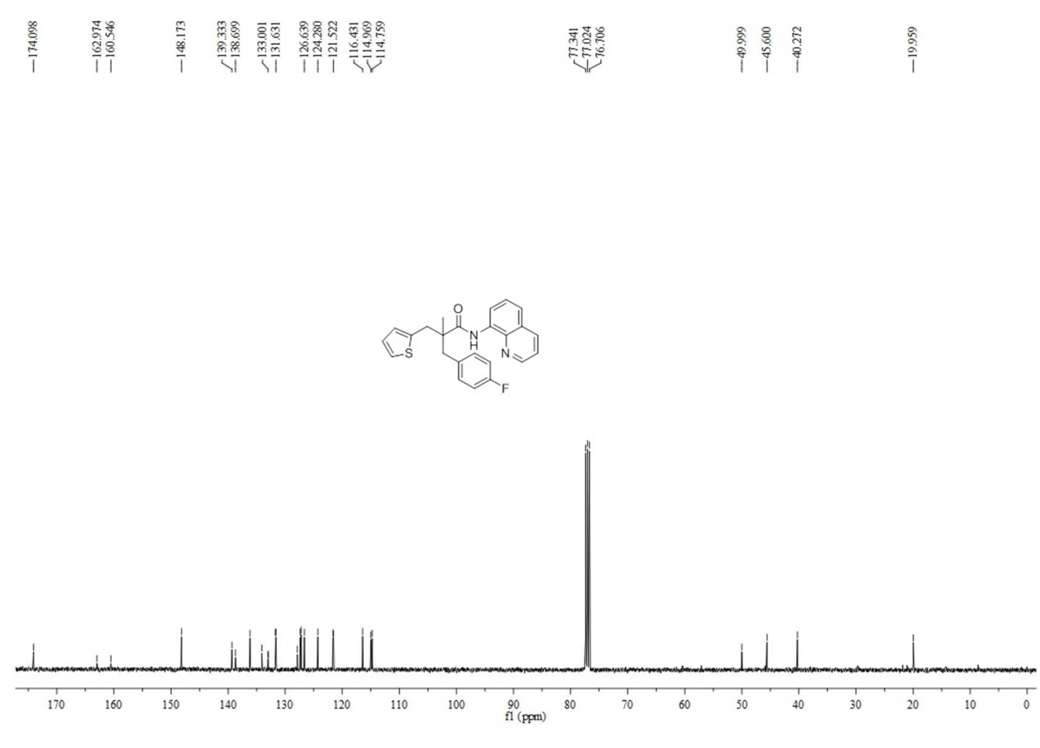




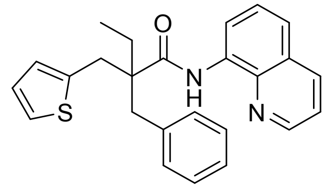
2-(4-fluorobenzyl)-2-methyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)propanamide (2r)

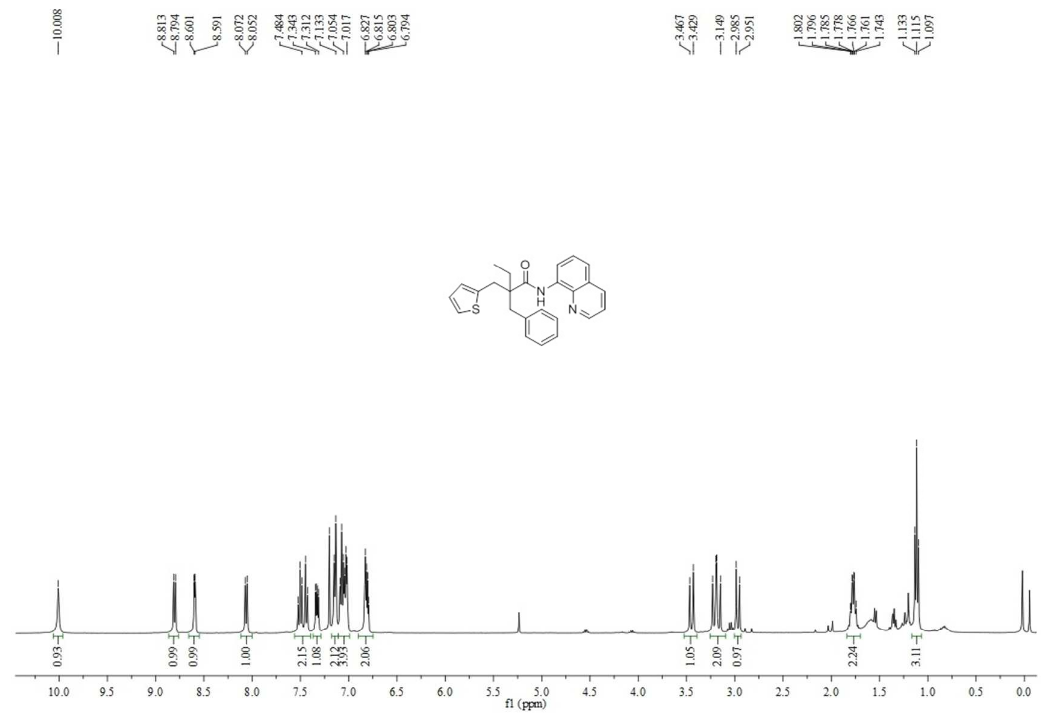


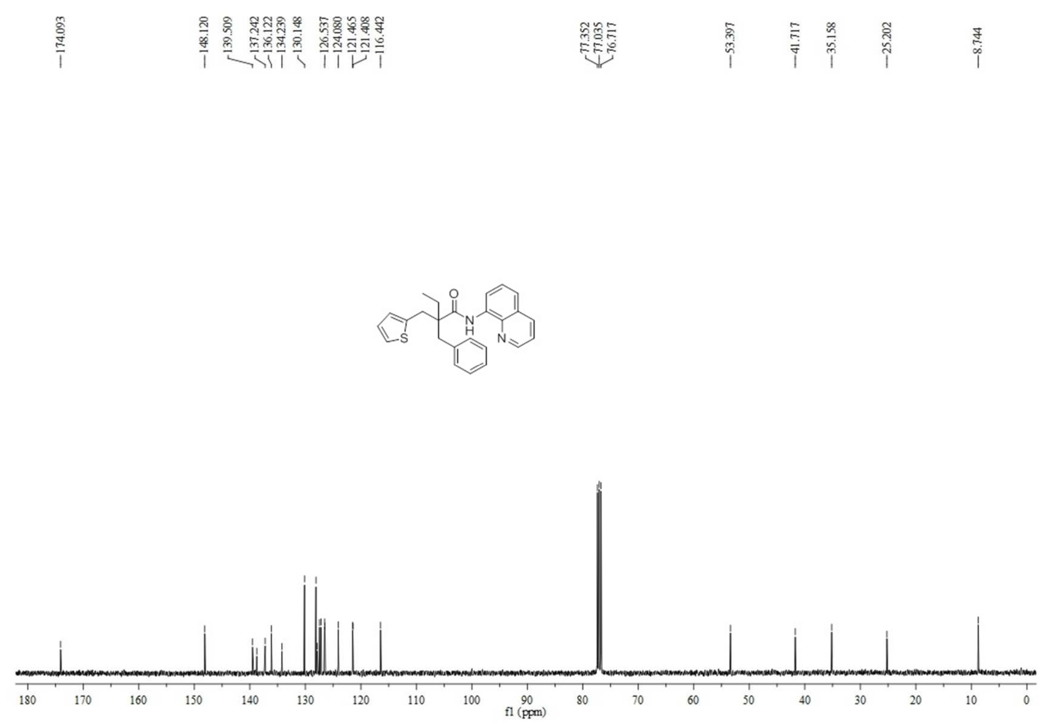




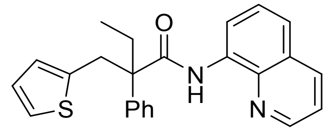
2-benzyl-*N*-(quinolin-8-yl)-2-(thiophen-2-ylmethyl)butanamide (2s)

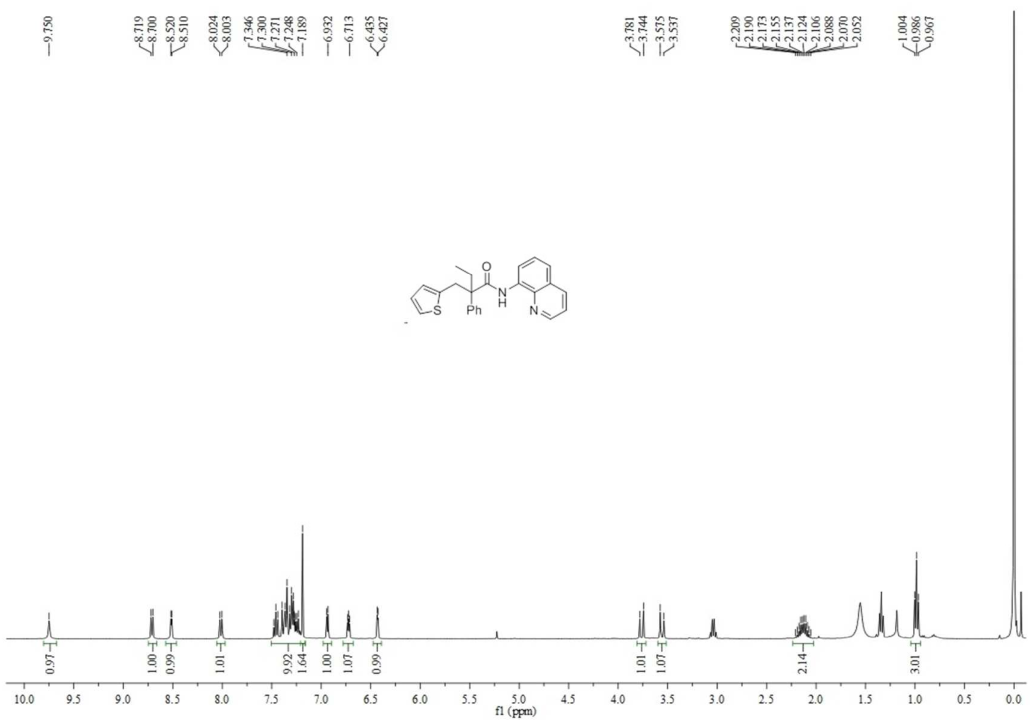


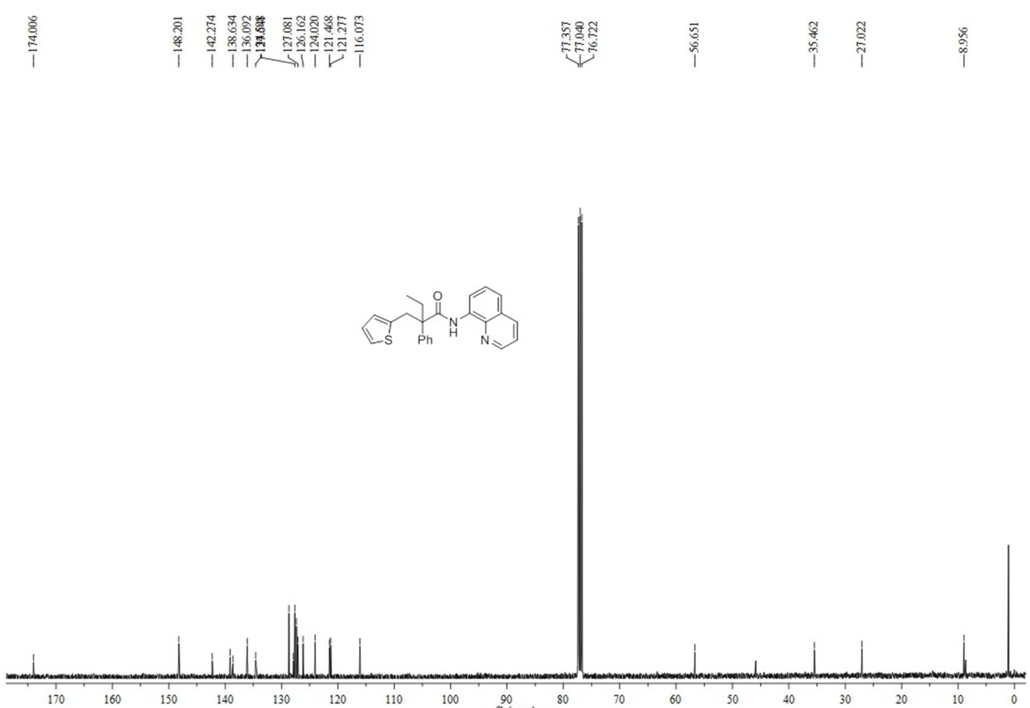




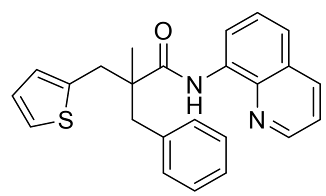
2-phenyl-*N*-(quinolin-8-yl)-2-(thiophen-2-ylmethyl)butanamide (2t)

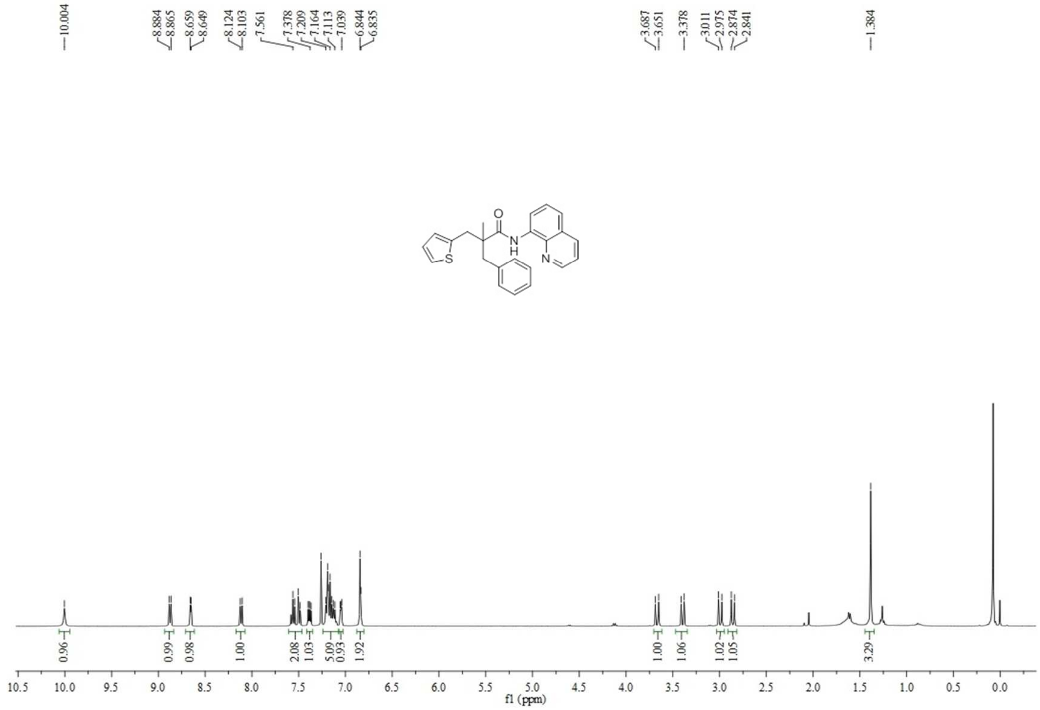


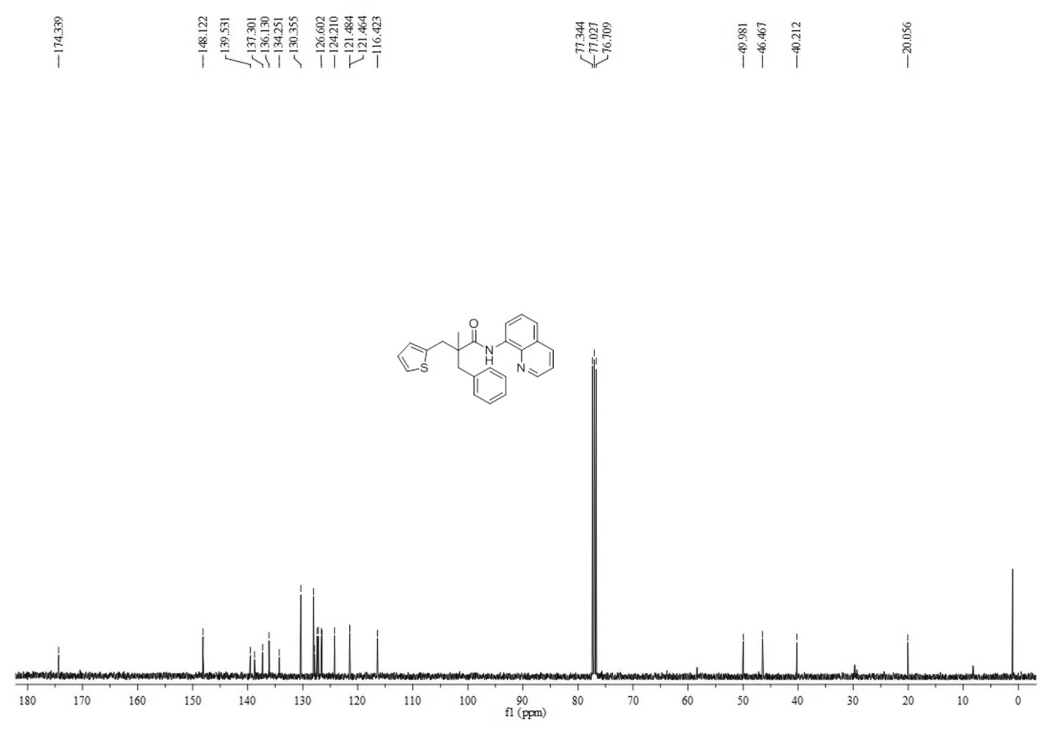




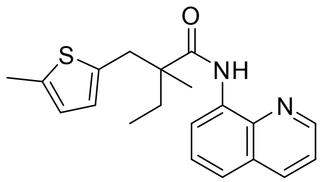
2-benzyl-2-methyl-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)propanamide (2u)

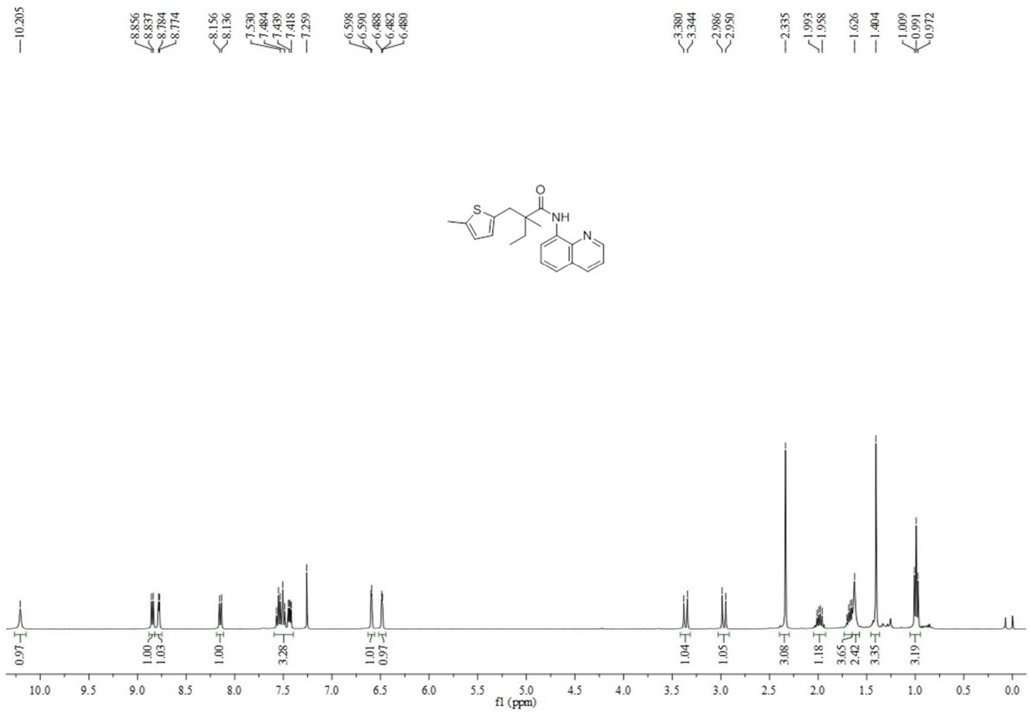


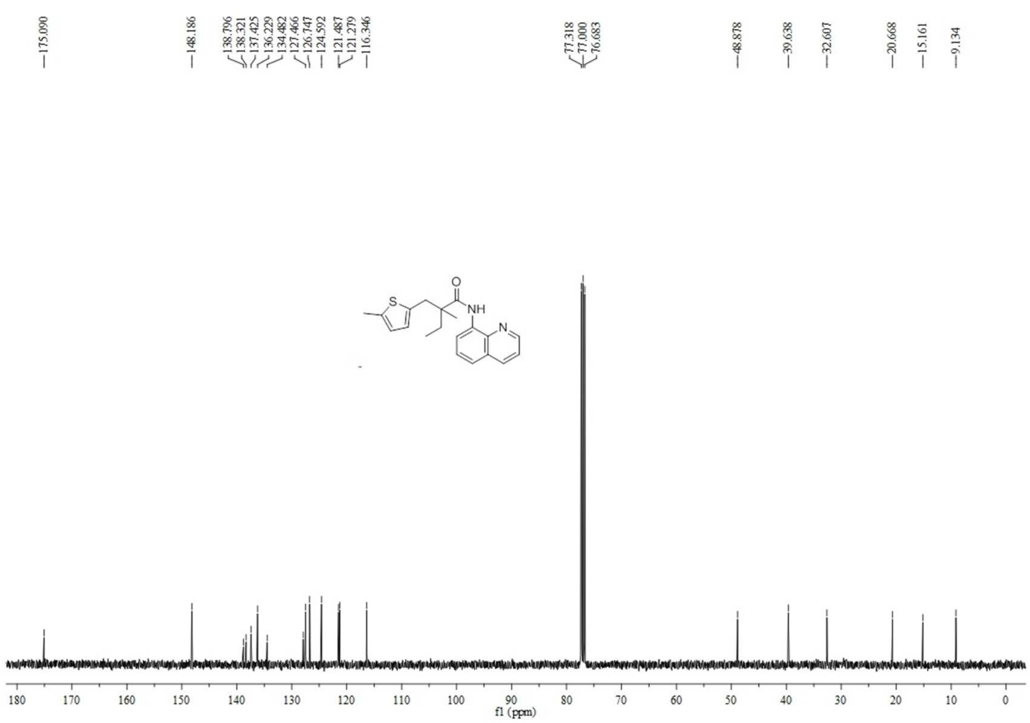




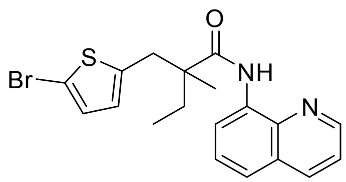
2-methyl-2-((5-methylthiophen-2-yl)methyl)-*N*-(quinolin-8-yl)butanamide (2v)

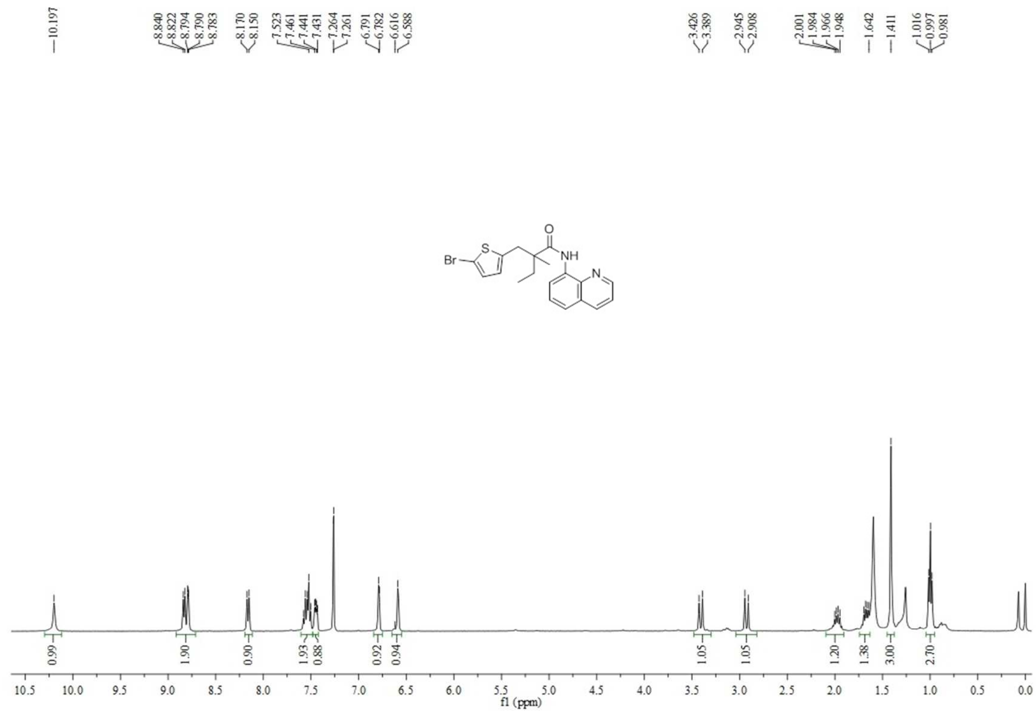


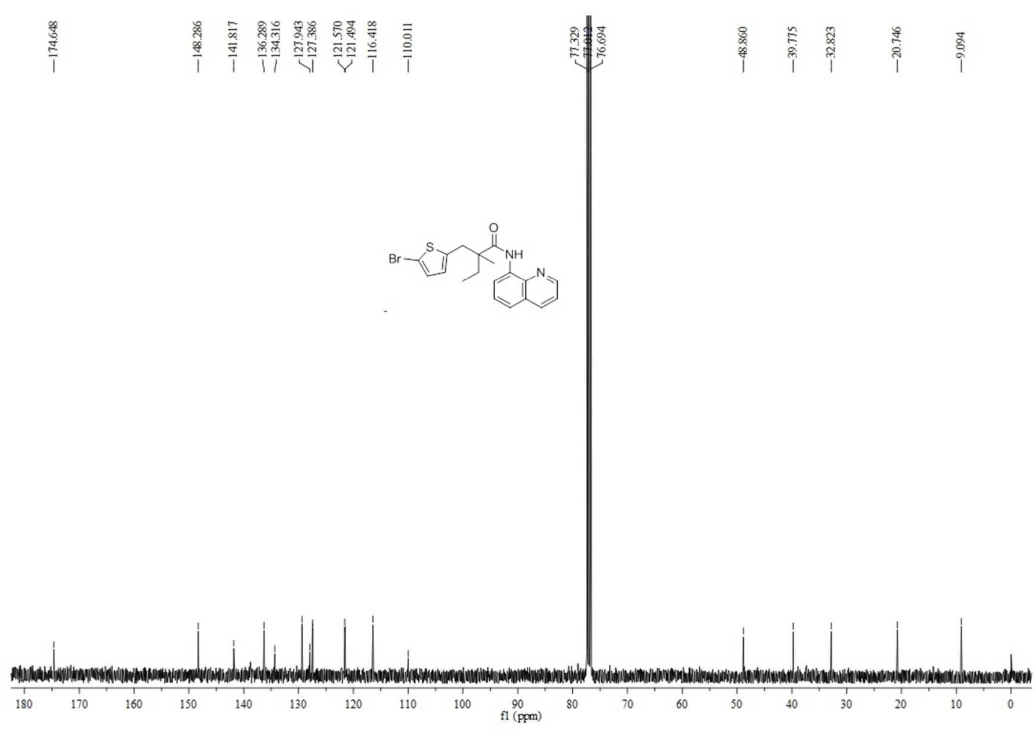




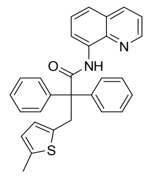
2-((5-bromothiophen-2-yl)methyl)-2-methyl-*N*-(quinolin-8-yl)butanamide (2w)

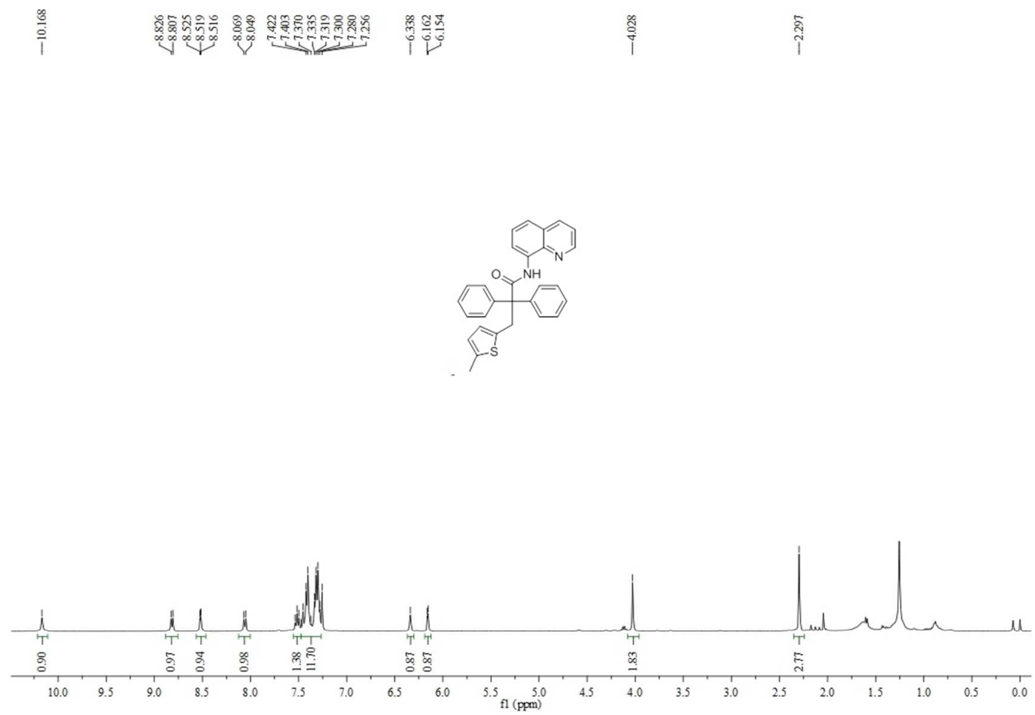


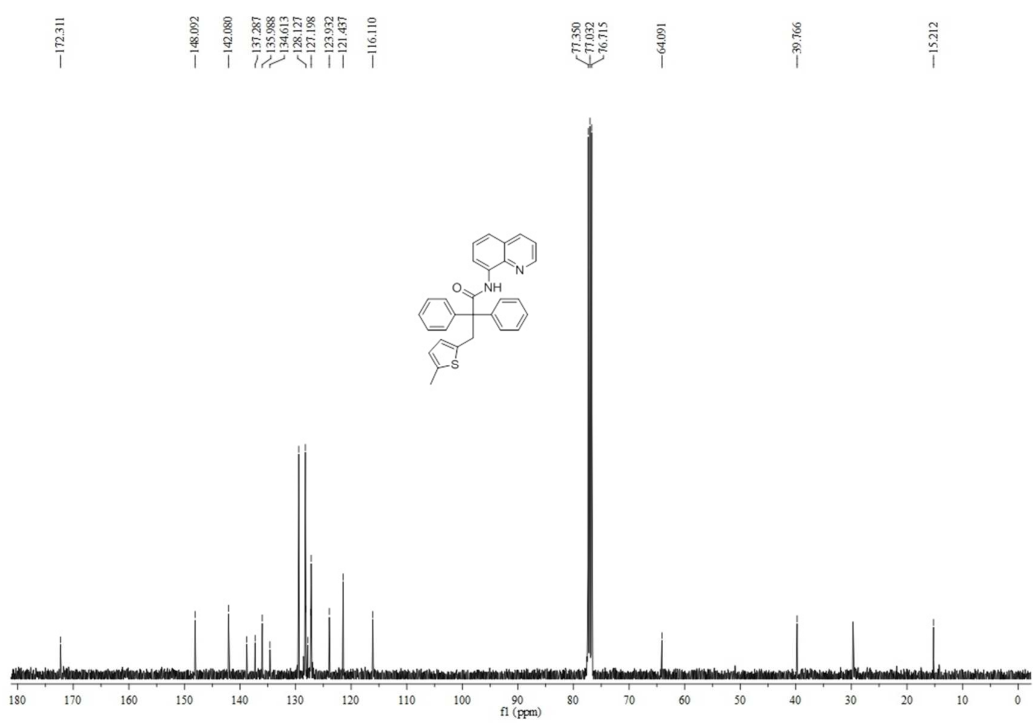




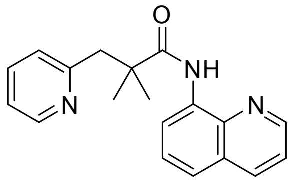
3-(5-methylthiophen-2-yl)-2,2-diphenyl-*N*-(quinolin-8-yl)propanamide (2x)

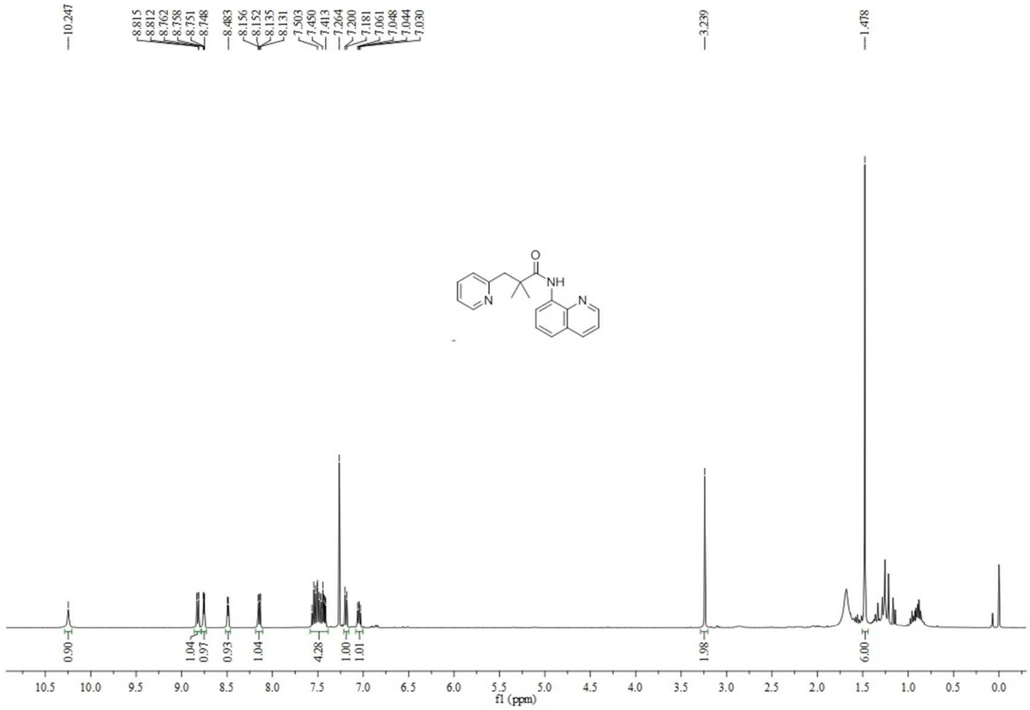


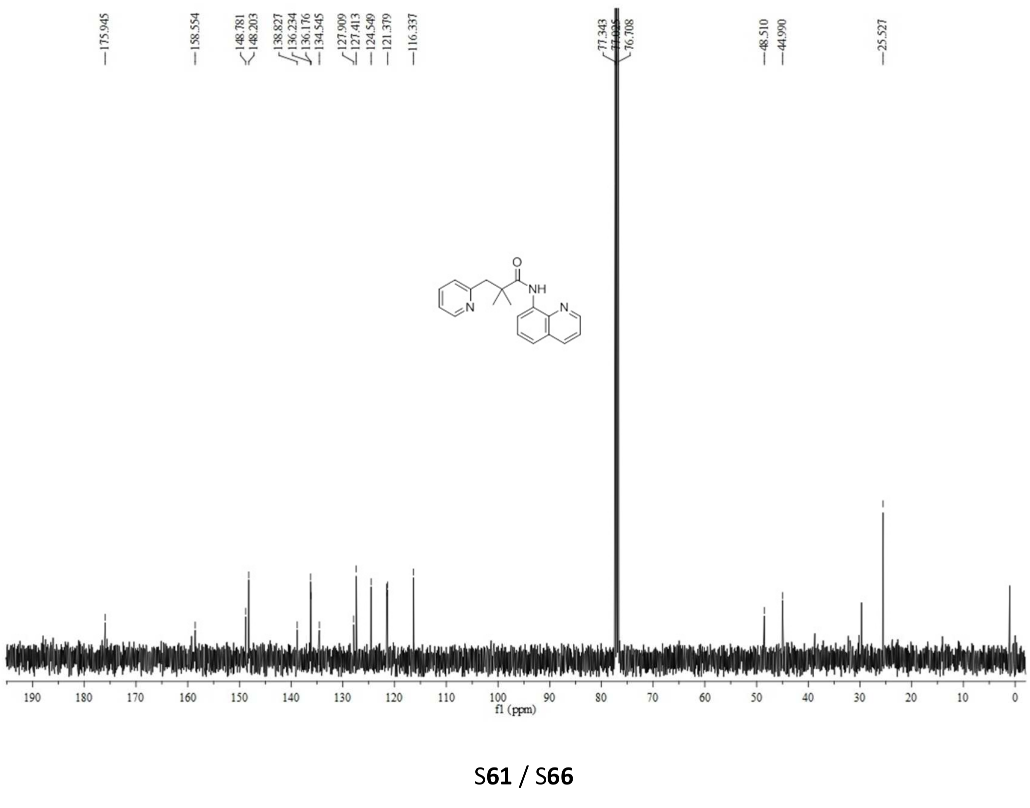




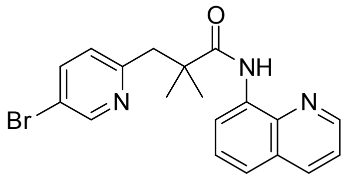
2,2-dimethyl-3-(pyridin-2-yl)-*N*-(quinolin-8-yl)propanamide (3a)

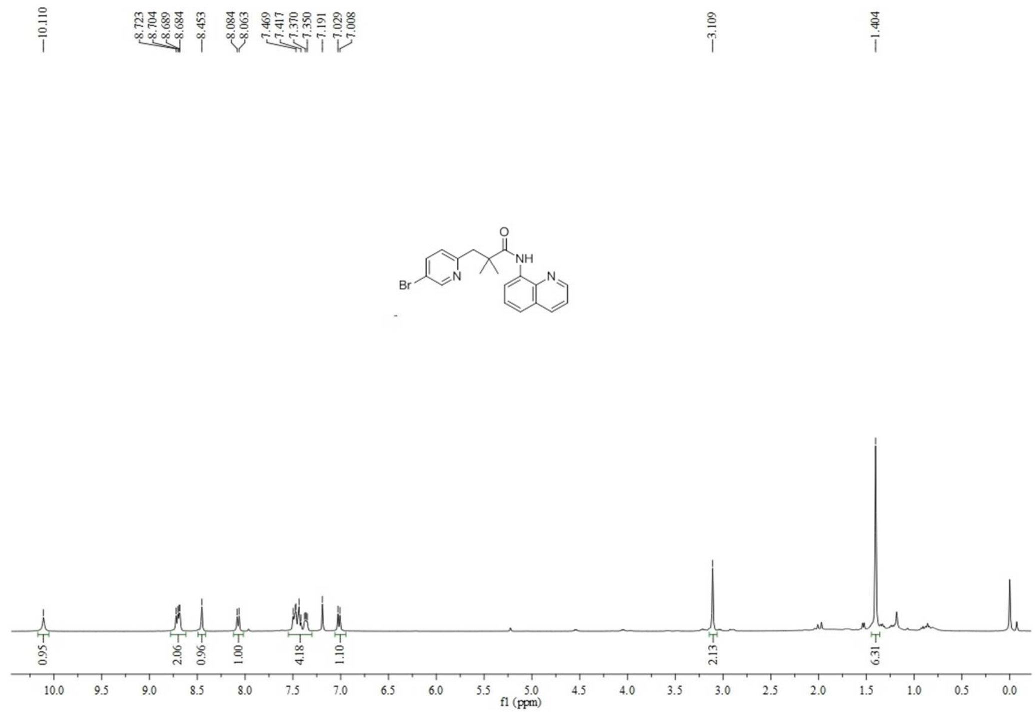


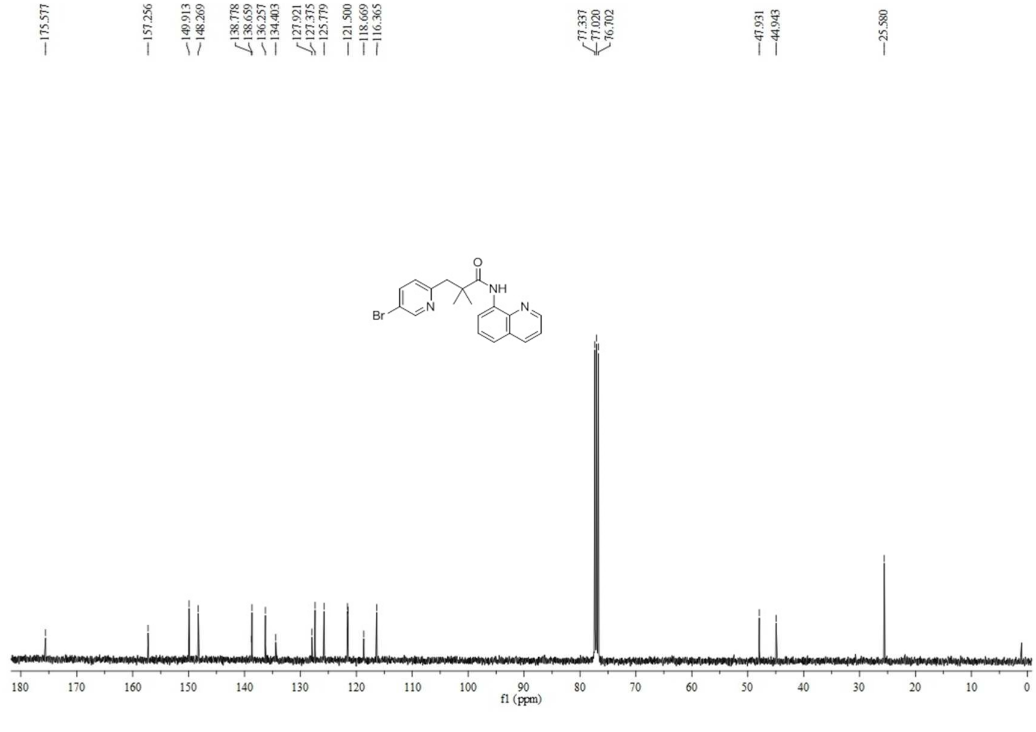




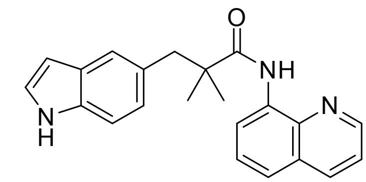
3-(5-bromopyridin-2-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (3b)

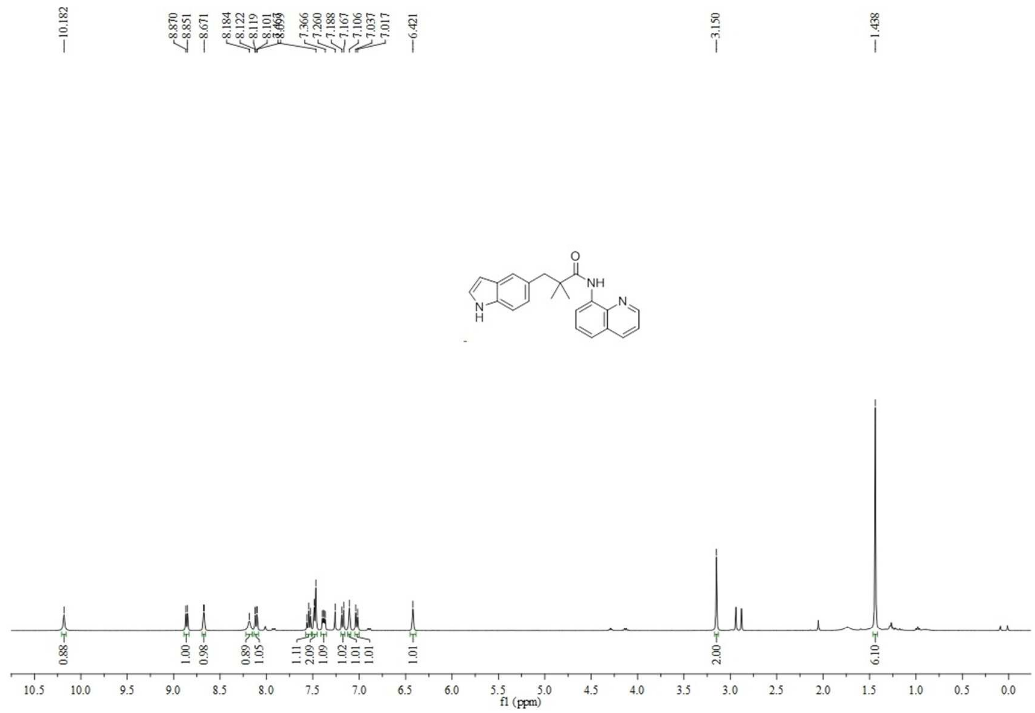


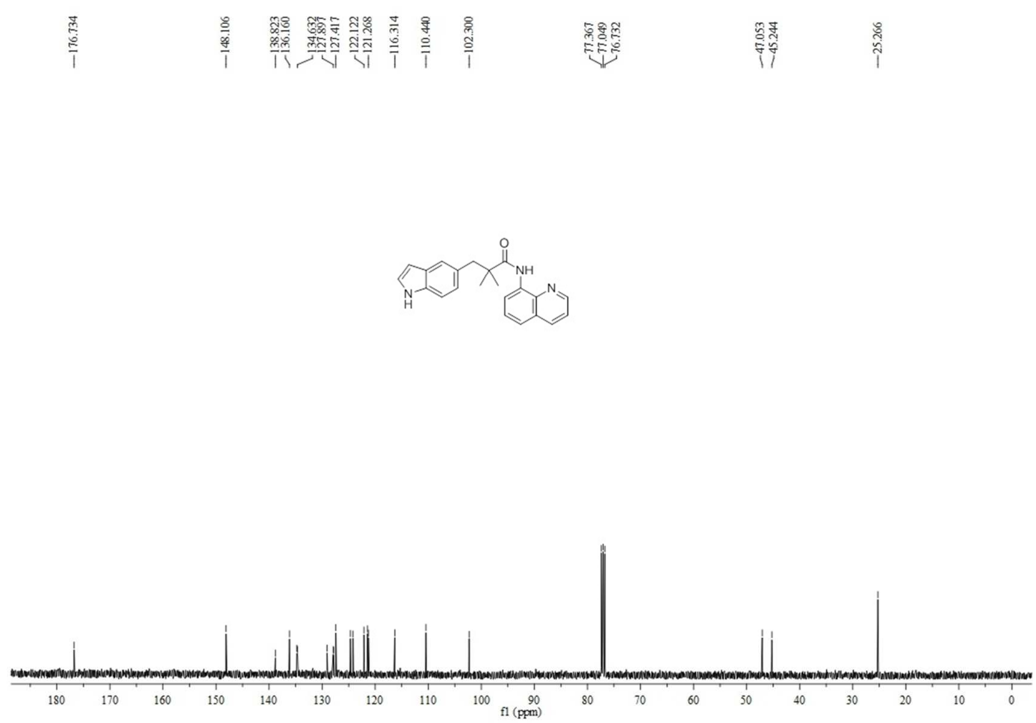




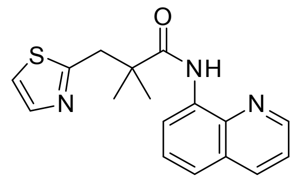
3-(1*H*-indol-5-yl)-2,2-dimethyl-*N*-(quinolin-8-yl)propanamide (3c)

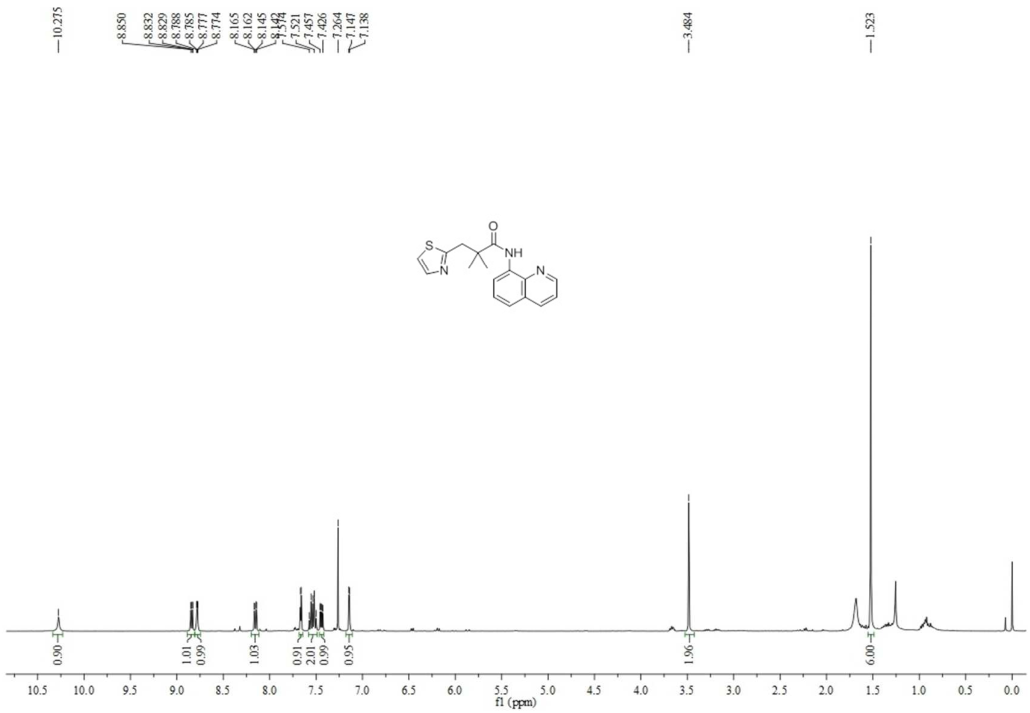


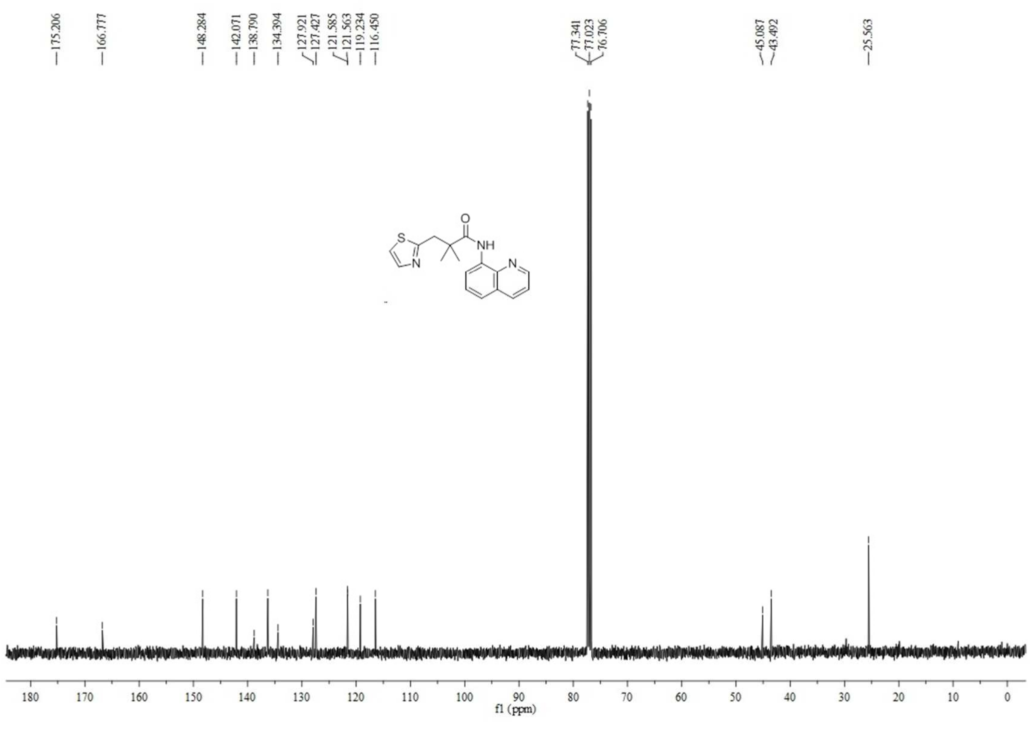




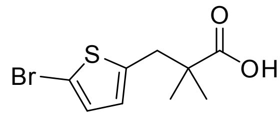
2,2-dimethyl-*N*-(quinolin-8-yl)-3-(thiazol-2-yl)propanamide (3d)

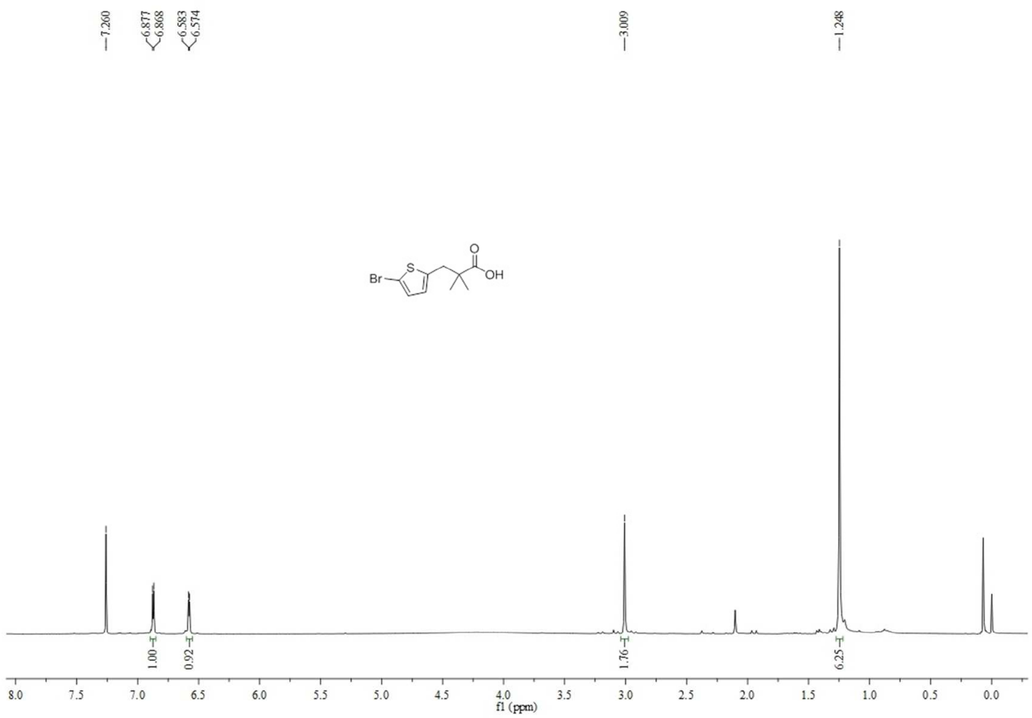


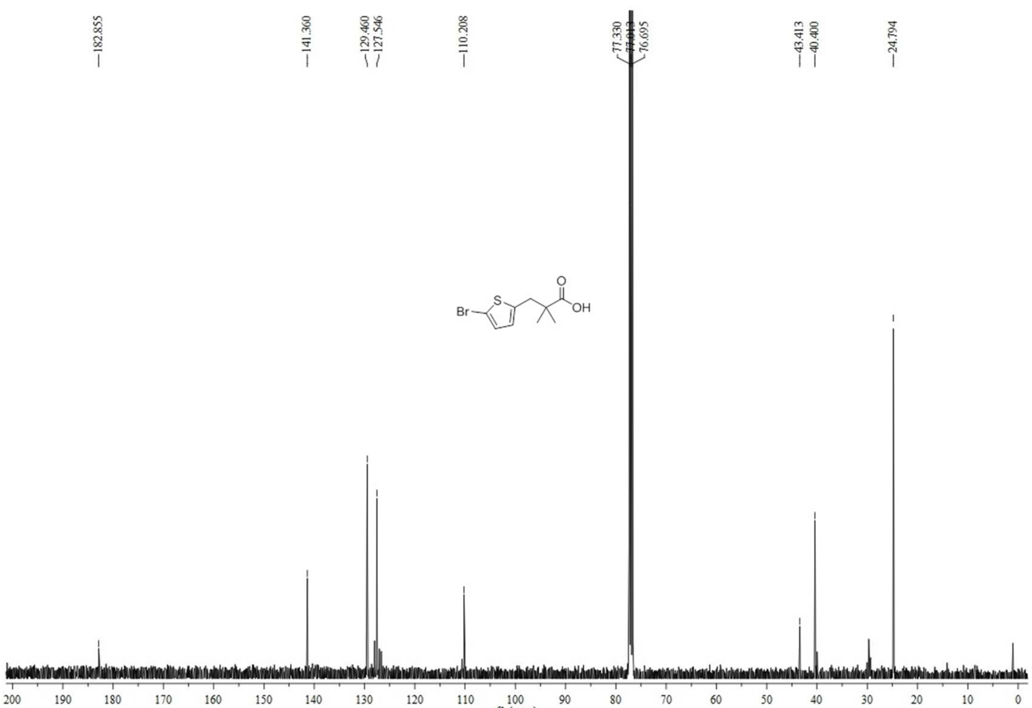




3-(5-bromothiophen-2-yl)-2,2-dimethylpropanoic acid (4)







2,2-dimethyl-3-(5-phenylthiophen-2-yl)-*N*-(quinolin-8-yl)propanamide (5)