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Palladium-catalyzed δ-selective reductive Heck reaction of alkenyl carbonyl compounds with aryl iodides and bromides

Yang Li, Jun-Fang Gong* and Mao-Ping Song*

College of Chemistry, Henan Key Laboratory of Chemical Biology and Organic Chemistry, Green Catalysis Center, Zhengzhou University, Zhengzhou 450001, People's Republic of China

E-mail: *gongjf@zzu.edu.cn (J.-F. Gong) or mpsong@zzu.edu.cn (M.-P. Song).*

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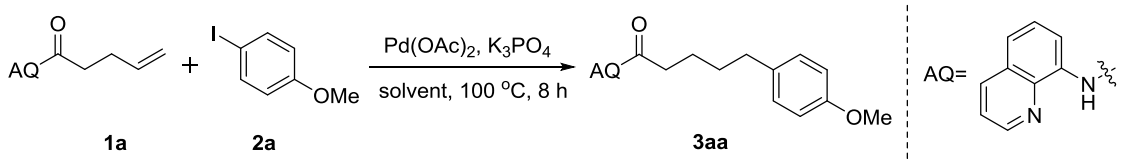
1. General Information

^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a Bruker DPX 400 or Bruker DPX 600 instruments using tetramethylsilane as an internal standard. Signal multiplicities are represented by the following abbreviations: (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, dt = doublet of triplet), coupling constant (*J* values) in Hz and integration. HRMS was determined on a *Waters* Q-Tof Micro MS/MS System ESI spectrometer. Melting points were measured on a WC-1 instrument and are uncorrected. Catalytic reactions were carried out in 35 mL pressure tubes with Teflon screw caps under air. Solvents were dried with standard methods and freshly distilled prior to use if needed. Substrates **1a**-**1k** were synthesized according to relevant literatures. Unless otherwise mentioned, all materials were commercially obtained and used without further purification.

2. Experimental Section

2.1 Optimization of Reaction Conditions

Table S1 Effect of Solvents[a]

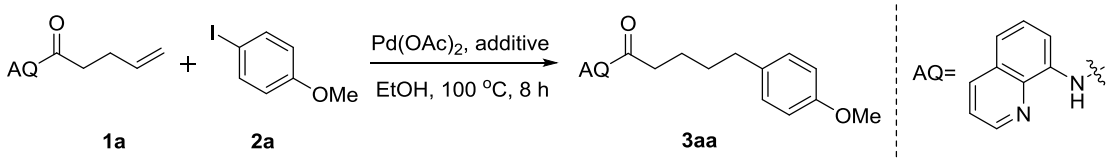


1a 2a 3aa

Entry	Solvent	Yield (%)
1	MeOH	34
2	**EtOH**	**73**
3	*i*-PrOH	31
4	*t*-BuOH	trace
5	*n*-BuOH	31
6	*n*-PrOH	36
7	HOAc	trace
8	DMSO	trace
9	CH_3CN	trace
10	DMF	trace
11	Toluene	trace
12	THF	trace
13	EtOAc	trace
14	1,4-Dioxane	trace
15	DCE	trace
16[b]	EtOH	71
17[c]	EtOH	67
18[d]	EtOH	73
19	EG	32

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (5 mol%), K_3PO_4 (0.3 mmol), solvent (1.0 mL), 100 °C, 8 h, under air. Isolated yields. [b]Under Ar. [c]Dry EtOH. [d]H_2O (5 equiv) was added.

Table S2 Effect of Additives[a]

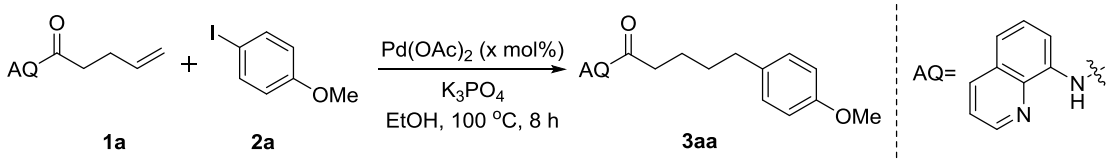


1a 2a 3aa

Entry	Additive	Yield (%)
1	/	trace
2	**K_3PO_4**	**73**
3	K_2CO_3	30
4	*t*-BuOK	60
5	KTFA	ND
6	$KHCO_3$	ND
7	$K_2HPO_4{\cdot}3H_2O$	ND
8	KOAc	trace
9	KOH	65
10	KBr	ND
11	NaF	ND
12	Na_2CO_3	ND
13	PivOK	ND
14	NaOH	67
15	EtONa	29
16	$NaNO_2$	trace
17	PhCOONa	trace
18	$Na_2C_2O_4$	trace
19	HOAc	ND
20	PhCOOH	ND
21	LiOH	37

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (5 mol%), additive (0.3 mmol), EtOH (1.0 mL), 100 °C, 8 h, under air. Isolated yields. ND: not detected.

Table S3 Effect of Catalyst Loading[a]

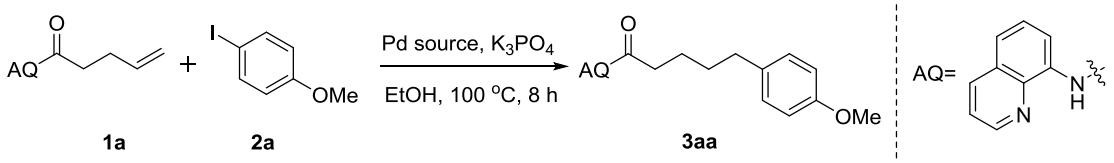


1a 2a 3aa

Entry	Catalyst loading (mol%)	Yield (%)
1	10.0	72
2	**5.0**	**73**
3	2.5	65
4	1.0	43

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (x mol%), K_3PO_4 (0.3 mmol), EtOH (1.0 mL), 100 °C, 8 h, under air. Isolated yields.

Table S4 Effect of Pd Sources[a]

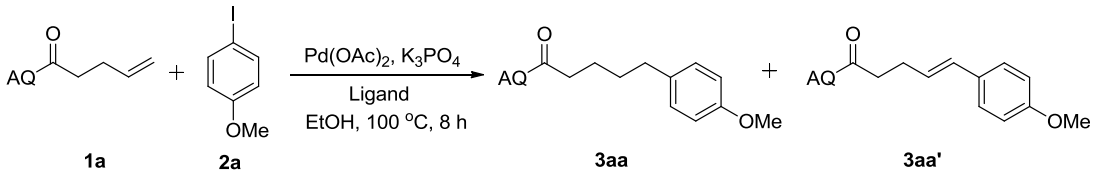


1a 2a 3aa

Entry	Pd source	Yield (%)
1	**$Pd(OAc)_2$**	**73**
2	$PdCl_2$	63
3	**$Pd(CH_3CN)_2Cl_2$**	**73**
4	$Pd(PPh_3)_2Cl_2$	ND
5	$Pd_2(dba)_3$	48
6	$Pd(dba)_2$	46
7	$Pd(PPh_3)_4$	ND

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), Pd source (5 mol%), K_3PO_4 (0.3 mmol), EtOH (1.0 mL), 100 °C, 8 h, under air. Isolated yields. ND: not detected.

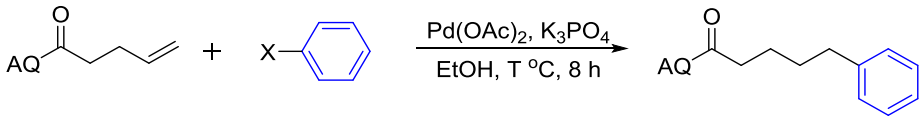
Table S5 Effect of Ligands[a]



Entry	Ligand (10 mol%)	**3aa** (%)	**3aa′** (%)
1	/	73	ND
2	Cy-Johnphos	26	18
3	PCy_3HBF_4	ND	34
4	X-phos	74	ND
5	PCy_3	ND	40
6	Ph_2PCy	ND	26
7	Ph_2PEt	ND	17
8	Cy_2NH	71	ND

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (5 mol%), K_3PO_4 (0.3 mmol), Ligand (10 mol%), EtOH (1.0 mL), 100 °C, 8 h, under Ar. Isolated yields.

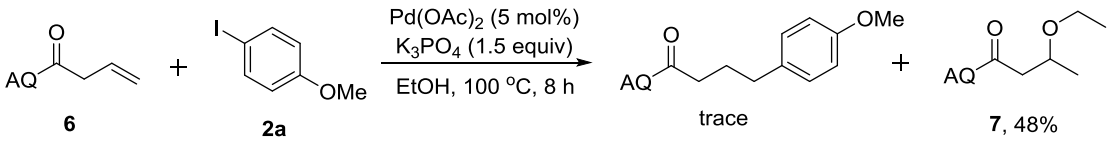
Table S6 Reaction of 1a with phenyl bromide and chloride[a]



Entry	Catalyst loading (mol%)	X	T (°C)	Ligand (mol%)	Yield (%)
1	5	Br	100	/	38
2	5	Cl	100	/	ND
3	5	Br	120	/	ND
4[b,c]	5	Br	100	X-phos (10 mol%)	36
5[b,c]	5	Br	100	Cy-Johnphos (10 mol%)	23
6	10	Br	100	/	44
7[d]	10	Br	100	/	66

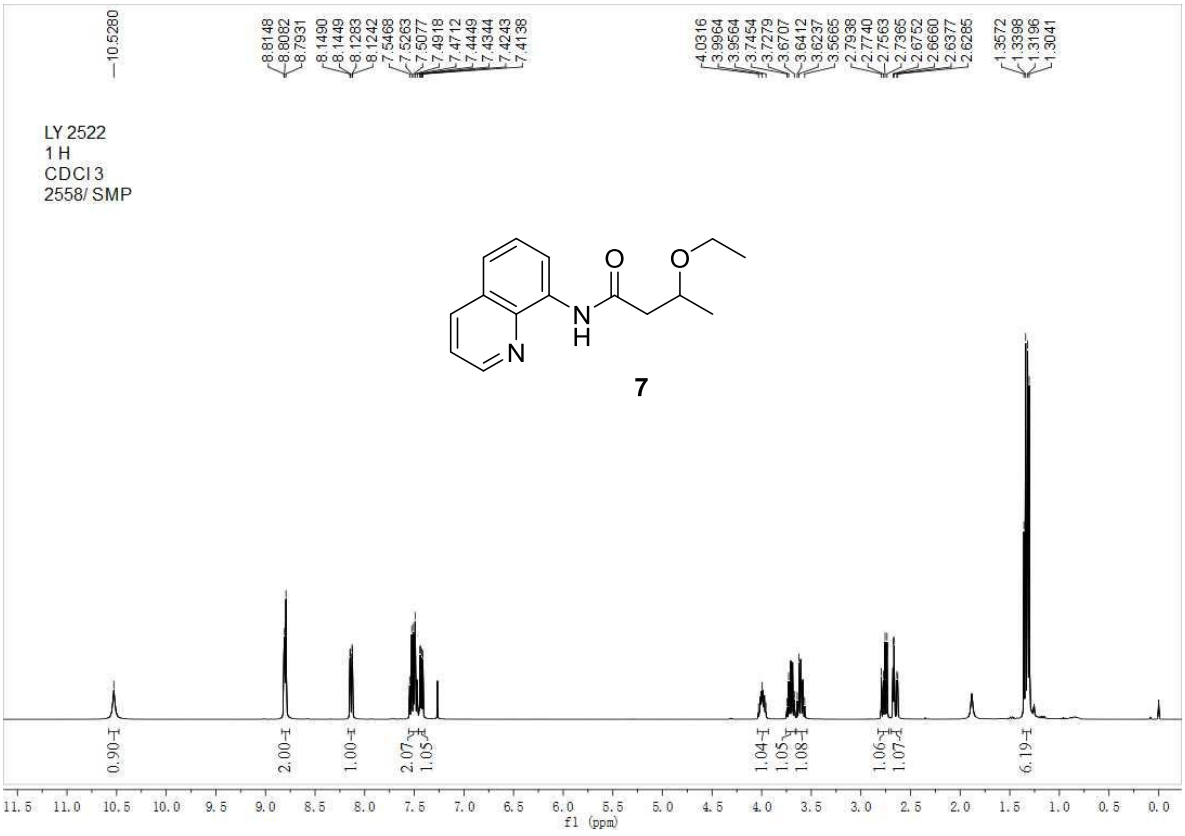
[a]Reaction conditions: **1a** (0.2 mmol), **2b′** or **2b″** (0.3 mmol), $Pd(OAc)_2$, K_3PO_4 (0.3 mmol), EtOH (1.0 mL), 8 h, under air. Isolated yields. ND: not detected. [b]Under Ar. [c]Occurrence of the Heck reaction was observed. [d]**2b′** (0.6 mmol).

Reaction of 3-butenoic acid derivative bearing AQ group (6) with 4-iodoanisole:

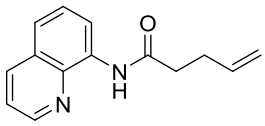


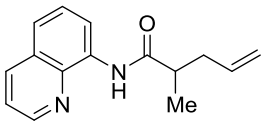
6 **2a** trace **7**, 48%

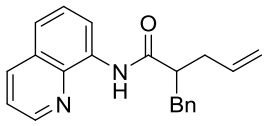
To a 35 mL pressure tube, **6** (0.2 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (5 mol%), K_3PO_4 (0.3 mmol) and EtOH (1.0 mL) were added sequentially. The reaction was stirred in a *pre*-warmed 100 °C oil bath for 8 hours under air. Then the reaction was quenched with ethyl acetate, filtered through a pad of celite, concentrated and purified by preparative TLC on silica gel plates (petroleum ether/ethyl acetate = 7/1) to give **7** in 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.53 (s, 1H), 8.84 – 8.76 (m, 2H), 8.14 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.56 – 7.46 (m, 2H), 7.43 (dd, *J* = 4.2, 8.2 Hz, 1H), 4.04 – 3.93 (m, 1H), 3.76 – 3.66 (m, 1H), 3.65 – 3.54 (m, 1H), 2.77 (dd, *J* = 7.9, 15.0 Hz, 1H), 2.65 (dd, *J* = 3.7, 15.0 Hz, 1H), 1.37 – 1.29 (m, 6H).

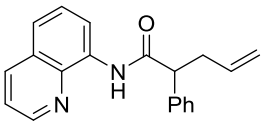


2.2 Synthesis of Alkene Substrates


1a


1b


1c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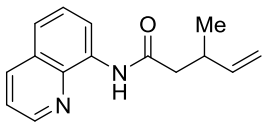
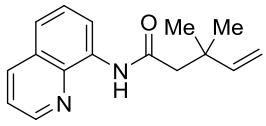
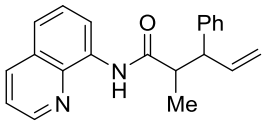
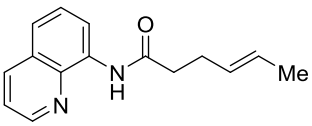
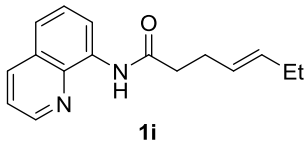
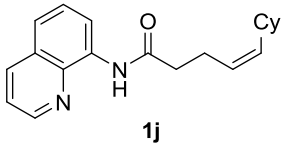

1e

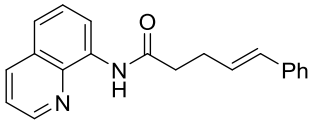

1f


1g

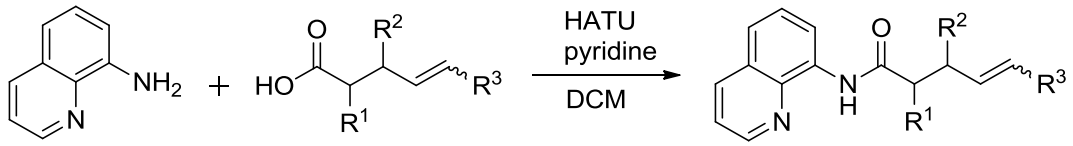

1h


1i


1j

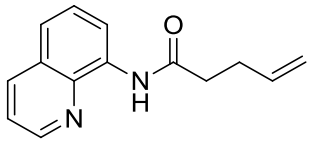

1k

General Procedure A for Installing Directing Group: [1]



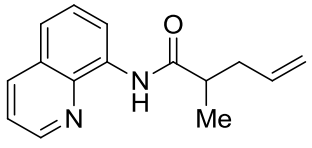
To a 100 mL round bottom flask equipped with a magnetic stir bar were added 8-aminoquinoline (1.0 equiv), pyridine (3.0 equiv), HATU (1.5 equiv), DCM (0.4 M) and corresponding acid (1.0 equiv). The reaction was stirred at 25 ^{o}C for 12 h. The solvent was removed under vacuum, and the residue was diluted with ethyl acetate, washed with sat. $NaHCO_3$ (20 mL, ×2) and brine (20 mL, ×1). The organic layer was then dried, concentrated under vacuum, and purified by column chromatography (petroleum ether/ethyl acetate = 20/1-15/1) to afford corresponding product.

_N_-(quinolin-8-yl)pent-4-enamide (1a)



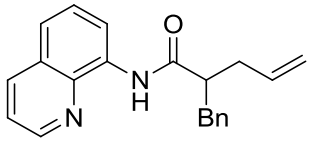
The title compound was prepared from 4-pentenoic acid according to the general procedure A, affording **1a** as a yellow oil in 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.89 – 8.71 (m, 2H), 8.16 (dd, *J* = 1.7, 8.3 Hz, 1H), 7.58 – 7.48 (m, 2H), 7.45 (dd, *J* = 4.2, 8.3 Hz, 1H), 6.01 – 5.87 (m, 1H), 5.16 (qd, *J* = 1.6, 17.1 Hz, 1H), 5.08 – 5.02 (m, 1H), 2.72 –2.63 (m, 2H), 2.62 – 2.54 (m, 2H).

2-methyl-_N_-(quinolin-8-yl)pent-4-enamide (1b)



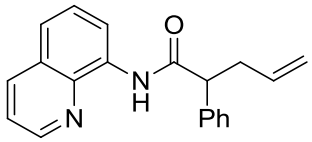
2-methylpent-4-enoic acid was prepared by an adjusted literature procedure.[2] To a 100 mL flask was added diisopropylamine (22 mmol) in THF (0.5 M) and then *n*-BuLi (22 mmol, 2.5 M in THF) was added dropwise at -78 ^{o}C. The mixture was warmed to 0 ^{o}C and stirred for 0.5 h to afford LDA. Allylacetic acid (10 mmol) in THF (1 M) was added at -78 ^{o}C and the mixture was stirred for 0.5 h. Then iodomethane (11 mmol) was added into the mixture. The mixture was heated to room temperature and stirred overnight. After the reaction, the mixture was poured into 20 mL ice water. The organic phase was separated. The aqueous layer was acidified with HCl (2 M) and extracted with ethyl acetate (15 mL, ×9). The combined organic layer was washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, crude 2-methylpent-4-enoic acid was obtained. The crude acid was taken forward to the next step without further purification according to general procedure A to afford **1b** as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.84 – 8.75 (m, 2H), 8.13 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.55 – 7.45 (m, 2H), 7.42 (dd, *J* = 4.2, 8.3 Hz, 1H), 5.93 – 5.80 (m, 1H), 5.19 – 5.09 (m, 1H), 5.08 – 5.00 (m, 1H), 2.75 – 2.53 (m, 2H), 2.38 – 2.27 (m, 1H), 1.34 (d, *J* = 6.8 Hz, 3H).

2-benzyl-N-(quinolin-8-yl)pent-4-enamide (1c)



2-benzylpent-4-enoic acid was prepared by literature procedure.[3] Crude 2-benzylpent-4-enoic acid was taken forward to the next step without further purification according to general procedure A to afford **1c** as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H), 8.78 (dd, *J* = 1.5, 7.4 Hz, 1H), 8.73 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.11 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.54 – 7.44 (m, 2H), 7.40 (dd, *J* = 4.2, 8.2 Hz, 1H), 7.30 – 7.18 (m, 4H), 7.15 – 7.08 (m, 1H), 5.95 – 5.81 (m, 1H), 5.20 – 5.10 (m, 1H), 5.07 – 5.00 (m, 1H), 3.20 – 3.10 (m, 1H), 2.96 – 2.80 (m, 2H), 2.65 – 2.54 (m, 1H), 2.45 – 2.35 (m, 1H).

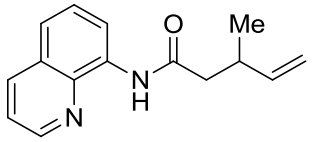
2-phenyl-*N*-(quinolin-8-yl)pent-4-enamide (1d)



2-phenylpent-4-enoic acid was prepared by literature procedure.[4] Crude 2-phenylpent-4-enoic acid was taken forward to the next step without further purification according to general procedure A to afford **1d** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.77 (dd, *J* = 1.6, 7.3 Hz, 1H), 8.73 (dd, *J* = 1.7, 4.2 Hz, 1H), 8.11

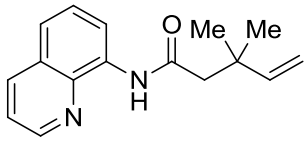
(dd, *J* = 1.6, 8.3 Hz, 1H), 7.53 – 7.44 (m, 4H), 7.42 – 7.34 (m, 3H), 7.31 – 7.26 (m, 1H), 5.89 – 5.76 (m, 1H), 5.18 – 5.10 (m, 1H), 5.04 – 4.98 (m, 1H), 3.81 (t, *J* = 7.6 Hz, 1H), 3.12 – 3.02 (m, 1H), 2.74 – 2.64 (m, 1H).

3-methyl-*N*-(quinolin-8-yl)pent-4-enamide (1e)



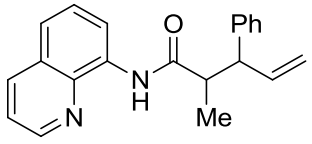
3-methylpent-4-enoic acid was prepared by literature procedure.[5] Crude 3-methylpent-4-enoic acid was taken forward to the next step without further purification according to general procedure A to afford **1e** as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.84 – 8.75 (m, 2H), 8.19 – 8.11 (m, 1H), 7.56 – 7.47 (m, 2H), 7.45 (dd, *J* = 4.2, 8.2 Hz, 1H), 5.96 – 5.84 (m, 1H), 5.17 – 5.08 (m, 1H), 5.04 – 4.97 (m, 1H), 2.96 – 2.84 (m, 1H), 2.66 – 2.57 (m, 1H), 2.55 – 2.46 (m, 1H), 1.17 (d, *J* = 6.8 Hz, 3H).

3,3-dimethyl-*N*-(quinolin-8-yl)pent-4-enamide (1f)



3,3-dimethylpent-4-enoic acid was prepared by literature procedure.[1] Crude 3,3-dimethylpent-4-enoic acid was taken forward to the next step without further purification according to general procedure A to afford **1f** as a yelow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 8.83 – 8.74 (m, 2H), 8.13 (dd, *J* = 1.4, 8.3 Hz, 1H), 7.55 – 7.45 (m, 2H), 7.43 (dd, *J* = 4.2, 8.3 Hz, 1H), 6.06 (dd, *J* = 10.7, 17.4 Hz, 1H), 5.12 – 5.01 (m, 2H), 2.54 (s, 2H), 1.26 (s, 6H).

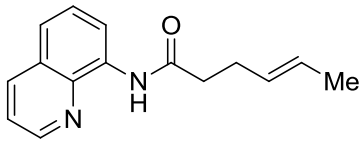
2-methyl-3-phenyl-*N*-(quinolin-8-yl)pent-4-enamide (1g)



2-methyl-3-phenylpent-4-enoic acid was prepared by literature procedure.[5] Crude 2-methyl-3-phenylpent-4-enoic acid was taken forward to the next step without further purification according to general procedure A to afford **1g** as a yelow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 8.67 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.62 (dd, *J* = 1.2, 7.5 Hz, 1H), 7.92 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.37 – 7.22 (m, 5H), 7.19 – 7.11 (m, 2H), 7.02 – 6.94 (m, 1H), 6.06 – 5.94 (m, 1H), 5.22 – 5.14 (m, 1H), 5.12 (dd, *J* = 1.5, 10.1 Hz, 1H), 3.69 (t, *J* =

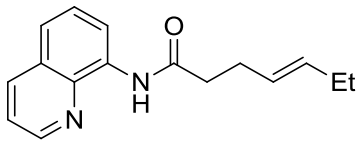
9.6 Hz, 1H), 2.97 – 2.88 (m, 1H), 1.39 (d, *J* = 6.8 Hz, 3H).

(*E*)-*N*-(quinolin-8-yl)hex-4-enamide (1h)



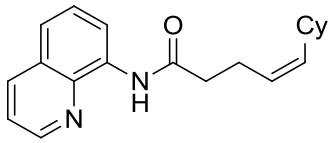
(*E*)-hex-4-enoic acid was prepared by literature procedure.[6] Crude (*E*)-hex-4-enoic acid was taken forward to the next step without further purification according to general procedure A to afford **1h** as a brown oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.83 – 8.76 (m, 2H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.46 – 7.42 (m, 1H), 5.64 – 5.50 (m, 2H), 2.62 (t, *J* = 7.4 Hz, 2H), 2.53 – 2.47 (m, 2H), 1.66 (d, *J* = 5.4 Hz, 3H).

(*E*)-*N*-(quinolin-8-yl)hept-4-enamide (1i)



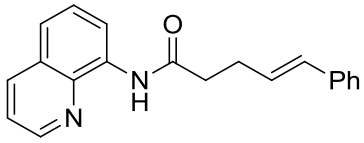
(*E*)-hept-4-enoic acid was prepared by an adjusted literature procedure.[6] Crude (*E*)-hept-4-enoic acid was taken forward to the next step without further purification according to general procedure A to afford **1i** as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.82 – 8.75 (m, 2H), 8.15 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.45 (dd, *J* = 4.2, 8.3 Hz, 1H), 5.66 – 5.57 (m, 1H), 5.56 – 5.47 (m, 1H), 2.67 – 2.60 (m, 2H), 2.55 – 2.47 (m, 2H), 2.06 – 1.95 (m, 2H), 0.95 (t, *J* = 7.5 Hz, 3H).

(*Z*)-5-cyclohexyl-*N*-(quinolin-8-yl)pent-4-enamide (1j)



(*Z*)-5-cyclohexylpent-4-enoic acid was prepared by literature procedure.[7] Crude (*Z*)-5-cyclohexylpent-4-enoic acid was taken forward to the next step without further purification according to general procedure A to afford **1j** as a yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.83 – 8.78 (m, 2H), 8.16 (dd, *J* = 1.1, 8.2 Hz, 1H), 7.56 – 7.48 (m, 2H), 7.45 (dd, *J* = 4.2, 8.2 Hz, 1H), 5.38 – 5.32 (m, 1H), 5.31 – 5.27 (m, 1H), 2.64 – 2.54 (m, 4H), 2.38 – 2.30 (m, 1H), 1.70 – 1.57 (m, 5H), 1.31 – 1.21 (m, 2H), 1.19 – 1.10 (m, 1H), 1.09 – 1.00 (m, 2H).

(*E*)-5-phenyl-*N*-(quinolin-8-yl)pent-4-enamide (1k)



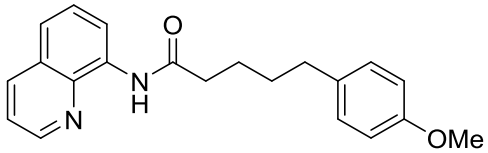
The title compound was prepared by an adjusted literature procedure as a yellow solid.[8] ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.79 (dd, *J* = 1.4, 7.4 Hz, 1H), 8.73 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.13 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.56 – 7.45 (m, 2H), 7.41 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.30 – 7.24 (m, 2H), 7.21 – 7.15 (m, 1H), 6.52 (d, *J* = 15.8 Hz, 1H), 6.38 – 6.26 (m, 1H), 2.77 – 2.69 (m, 4H).

2.3 Pd-catalyzed Intermolecular Reductive Heck Reaction

Typical procedure for reductive Heck reaction of unactivated alkenes with aryl iodides: To a 35 mL pressure tube, alkene substrate (0.2 mmol), aryl iodide (0.3 mmol), $Pd(OAc)_2$ (5 mol%), K_3PO_4 (0.3 mmol) and EtOH (1.0 mL) were added sequentially. The reaction was stirred in a *pre*-warmed 100 ^{o}C oil bath for 8 hours under air. Then the reaction was quenched with ethyl acetate, filtered through a pad of celite, concentrated and purified by preparative TLC on silica gel plates (petroleum ether/ethyl acetate = 5/1-25/1 or dichloromethane/ethyl acetate = 120/1) to give the desired product.

Typical procedure for reductive Heck reaction of unactivated alkenes with aryl bromides: To a 35 mL pressure tube, alkene substrate (0.2 mmol), aryl bromide (0.6 mmol), $Pd(OAc)_2$ (10 mol%), K_3PO_4 (0.3 mmol) and EtOH (1.0 mL) were added sequentially. The reaction was stirred in a *pre*-warmed 100 ^{o}C oil bath for 8 hours under air. Then the reaction was quenched with ethyl acetate, filtered through a pad of celite, concentrated and purified by preparative TLC on silica gel plates (petroleum ether/ethyl acetate = 13/1 or dichloromethane/ethyl acetate = 120/1) to give the desired product.

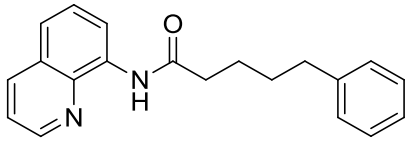
5-(4-methoxyphenyl)-*N*-(quinolin-8-yl)pentanamide (3aa)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3aa** as a yellow solid (48.8 mg, 73%), mp = 62-64 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.83 – 8.75 (m, 2H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.57 – 7.46 (m, 2H), 7.44 (dd, *J* = 4.2, 8.2 Hz, 1H), 7.15 – 7.08 (m, 2H), 6.86 – 6.78 (m, 2H), 3.77 (s, 3H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.58 (t, *J* = 7.4 Hz, 2H), 1.92 – 1.81 (m, 2H), 1.79 – 1.69 (m, 2H). ^{13}C NMR (100

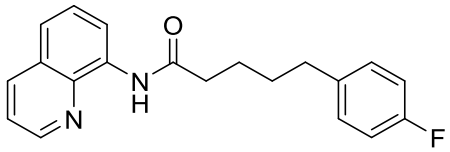
MHz, $CDCl_3$) δ 171.7, 157.8, 148.1, 138.4, 136.4, 134.6, 134.3, 129.3, 128.0, 127.4, 121.6, 121.4, 116.4, 113.8, 55.3, 38.1, 34.8, 31.3, 25.3. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{21}H_{23}N_2O_2$ 335.1754, found 335.1764.

5-phenyl-*N*-(quinolin-8-yl)pentanamide (3ab)



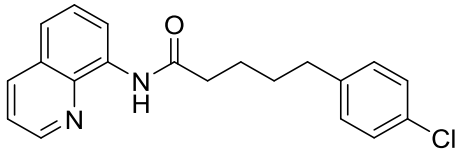
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3ab** as a yellow oil (49.9 mg, 82%). ^1H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.83 – 8.74 (m, 2H), 8.15 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.44 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.30 – 7.24 (m, 2H), 7.22 – 7.13 (m, 3H), 2.69 (t, *J* = 7.6 Hz, 2H), 2.58 (t, *J* = 7.4 Hz, 2H), 1.94 – 1.83 (m, 2H), 1.82 – 1.72 (m, 2H).

5-(4-fluorophenyl)-*N*-(quinolin-8-yl)pentanamide (3ac)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 12/1) to provide **3ac** as a brown oil (43.2 mg, 67%). ^1H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.82 – 8.74 (m, 2H), 8.15 (dd, *J* = 1.5, 8.2 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.44 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.17 – 7.10 (m, 2H), 6.98 – 6.91 (m, 2H), 2.66 (t, *J* = 7.6 Hz, 2H), 2.58 (t, *J* = 7.4 Hz, 2H), 1.92 – 1.81 (m, 2H), 1.80 – 1.69 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 161.2 (d, $^1J_{CF}$ = 241.6 Hz), 148.1, 138.3, 137.8 (d, $^4J_{CF}$ = 3.2 Hz), 136.4, 134.5, 129.7 (d, $^3J_{CF}$ = 7.7 Hz), 128.0, 127.4, 121.6, 121.4, 116.5, 115.0 (d, $^2J_{CF}$ = 21.0 Hz), 38.0, 34.9, 31.2, 25.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.89. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{20}H_{20}FN_2O$ 323.1554, found 323.1560.

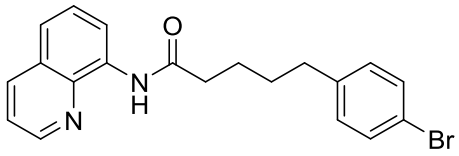
5-(4-chlorophenyl)-*N*-(quinolin-8-yl)pentanamide (3ad)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3ad** as a pale brown solid (46.7 mg, 69%), mp = 67-69 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.83 – 8.74 (m, 2H), 8.16 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.45 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.25 – 7.19 (m, 2H), 7.15 – 7.08 (m, 2H), 2.66 (t, *J* = 7.5 Hz, 2H),

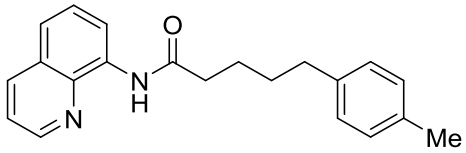
2.58 (t, J = 7.3 Hz, 2H), 1.92 – 1.81 (m, 2H), 1.79 – 1.70 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.1, 140.6, 138.3, 136.4, 134.5, 131.5, 129.8, 128.4, 128.0, 127.5, 121.6, 121.5, 116.4, 38.0, 35.1, 30.9, 25.2. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{20}H_{20}ClN_2O$ 339.1259, found 339.1264.

5-(4-bromophenyl)-*N*-(quinolin-8-yl)pentanamide (3ae)



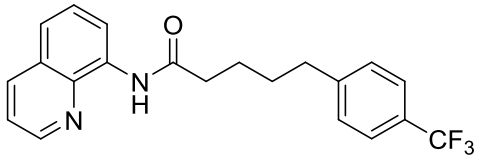
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3ae** as a yellow solid (40.6 mg, 53%), mp = 90-91 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.83 – 8.72 (m, 2H), 8.14 (dd, J = 1.4, 8.2 Hz, 1H), 7.55 – 7.46 (m, 2H), 7.44 (dd, J = 4.2, 8.2 Hz, 1H), 7.40 – 7.33 (m, 2H), 7.08 – 7.02 (m, 2H), 2.63 (t, J = 7.6 Hz, 2H), 2.57 (t, J = 7.3 Hz, 2H), 1.91 – 1.79 (m, 2H), 1.78 – 1.67 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.5, 148.1, 141.3, 138.3, 136.4, 134.5, 131.4, 130.2, 128.0, 127.4, 121.6, 121.4, 119.5, 116.4, 37.9, 35.1, 30.9, 25.2. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{20}H_{20}BrN_2O$ 383.0754, found 383.0759.

5-(*p*-tolyl)-*N*-(quinolin-8-yl)pentanamide (3af)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3af** as a pale yellow solid (43.3 mg, 68%), mp =42-43 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.83 – 8.76 (m, 2H), 8.15 (dd, J = 1.6, 8.3 Hz, 1H), 7.57 – 7.48 (m, 2H), 7.45 (dd, J = 4.2, 8.3 Hz, 1H), 7.13 – 7.06 (m, 4H), 2.67 (t, J = 7.6 Hz, 2H), 2.59 (t, J = 7.5 Hz, 2H), 2.32 (s, 3H), 1.94 – 1.83 (m, 2H), 1.80 – 1.71 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 148.1, 139.1, 138.3, 136.4, 135.2, 134.5, 129.0, 128.3, 128.0, 127.5, 121.6, 121.4, 116.4, 38.1, 35.3, 31.3, 25.4, 21.0. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{21}H_{23}N_2O$ 319.1805, found 319.1812.

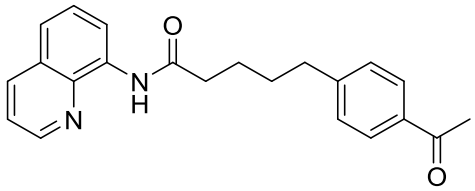
5-(4-(trifluoromethyl)phenyl)-*N*-(quinolin-8-yl)pentanamide (3ag)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide

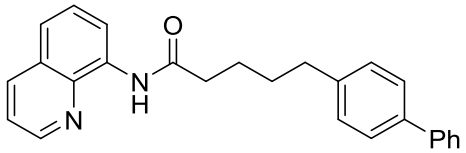
3ag as a brown oil (49.9 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.82 – 8.72 (m, 2H), 8.14 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.56 – 7.46 (m, 4H), 7.44 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 2.74 (t, *J* = 7.5 Hz, 2H), 2.59 (t, *J* = 7.3 Hz, 2H), 1.93 – 1.82 (m,2H), 1.82 – 1.73 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 148.1, 146.3, 138.3, 136.4, 134.5, 128.7, 128.2 (q, $^{2}J_{CF}$ = 32.1 Hz), 128.0, 127.4, 125.3 (q, $^{3}J_{CF}$ = 3.8 Hz), 124.4 (q, $^{1}J_{CF}$ = 270.1 Hz), 121.6, 121.5, 116.4, 37.9, 35.6, 30.7, 25.2. ^{19}F NMR (565 MHz, $CDCl_3$) δ -62.27. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{21}H_{20}F_3N_2O$ 373.1522, found 373.1531.

5-(4-acetylphenyl)-*N*-(quinolin-8-yl)pentanamide (3ah)



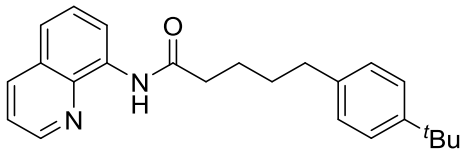
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 6/1) to provide **3ah** as a brown oil (31.9 mg, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.82 – 8.74 (m, 2H), 8.18 – 8.12 (m, 1H), 7.86 (d, *J* = 8.2 Hz, 2H), 7.56 – 7.47 (m, 2H), 7.44 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 2H), 2.75 (t, *J* = 7.4 Hz, 2H), 2.59 (t, *J* = 7.2 Hz, 2H), 2.56 (s, 3H), 1.92 – 1.74 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 171.4, 148.1, 148.0, 138.3, 136.4, 135.1, 134.5, 128.6, 128.5, 128.0, 127.4, 121.6, 121.5, 116.4, 37.9, 35.7, 30.6, 26.5, 25.2. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{22}H_{23}N_2O_2$ 347.1754, found 347.1770.

5-([1,1'-biphenyl]-4-yl)-*N*-(quinolin-8-yl)pentanamide (3ai)



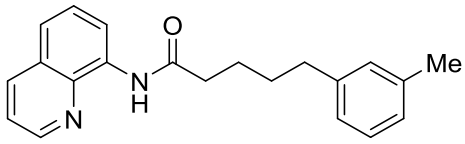
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3ai** as a pale yellow solid (54.8 mg, 72%), mp = 83-85 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.83 – 8.73 (m, 2H), 8.11 (dd, *J* = 1.5, 8.3 Hz, 1H), 7.59 – 7.44 (m, 6H), 7.43 – 7.37 (m, 3H), 7.33 – 7.21 (m, 3H), 2.72 (t, *J* = 7.5 Hz, 2H), 2.59 (t, *J* = 7.4 Hz, 2H), 1.95 – 1.85 (m, 2H), 1.84 – 1.74 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 148.1, 141.4, 141.2, 138.8, 138.4, 136.4, 134.6, 128.9, 128.7, 128.0, 127.5, 127.1, 127.0, 121.6, 121.4, 116.5, 38.1, 35.4, 31.1, 25.4. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{26}H_{25}N_2O$ 381.1961, found 381.1967.

5-(4-(*tert*-butyl)phenyl)-*N*-(quinolin-8-yl)pentanamide (3aj)



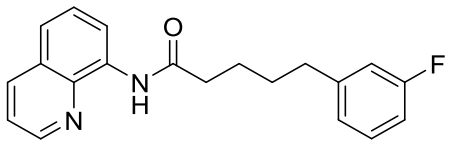
Purified by preparative TLC on silica gel (dichloromethane/ethyl acetate = 120/1) to provide **3aj** as a yellow oil (39.6 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.85 – 8.76 (m, 2H), 8.16 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.58 – 7.48 (m, 2H), 7.45 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.34 – 7.28 (m, 2H), 7.18 – 7.12 (m, 2H), 2.68 (t, *J* = 7.6 Hz, 2H), 2.60 (t, *J* = 7.4 Hz, 2H), 1.95 – 1.85 (m, 2H), 1.83 – 1.73 (m, 2H), 1.31 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 148.5, 148.1, 139.1, 138.4, 136.4, 134.6, 128.1, 128.0, 127.5, 125.2, 121.6, 121.4, 116.5, 38.2, 35.2, 34.4, 31.5, 31.1, 25.5. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{24}H_{29}N_2O$ 361.2274, found 361.2281.

5-(*m*-tolyl)-*N*-(quinolin-8-yl)pentanamide (3ak)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3ak** as a yellow oil (44.6 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.85 – 8.68 (m, 2H), 8.13 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.57 – 7.45 (m, 2H), 7.42 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.04 – 6.89 (m, 3H), 2.65 (t, *J* = 7.6 Hz, 2H), 2.57 (t, *J* = 7.4 Hz, 2H), 2.30 (s, 3H), 1.93 – 1.82 (m, 2H), 1.81 – 1.68 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 148.1, 142.2, 138.3, 137.9, 136.4, 134.6, 129.3, 128.3, 128.0, 127.5, 126.5, 125.5, 121.6, 121.4, 116.4, 38.1, 35.7, 31.2, 25.4, 21.4. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{21}H_{23}N_2O$ 319.1805, found 319.1810.

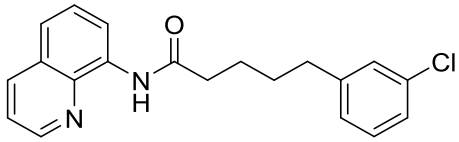
5-(3-fluorophenyl)-*N*-(quinolin-8-yl)pentanamide (3al)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3al** as a yellow oil (39.3 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.81 – 8.74 (m, 2H), 8.14 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.56 – 7.46 (m, 2H), 7.43 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.27 – 7.17 (m, 1H), 6.96 (d, *J* = 7.7 Hz, 1H), 6.92 – 6.82 (m, 2H), 2.68 (t, *J* = 7.5 Hz, 2H), 2.58 (t, *J* = 7.3 Hz, 2H), 1.91 – 1.80 (m, 2H), 1.80 – 1.70 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 162.9 (d, $^{1}J_{CF}$ = 244.0 Hz), 148.1, 144.8 (d, $^{3}J_{CF}$ = 7.0 Hz) 138.3, 136.3,

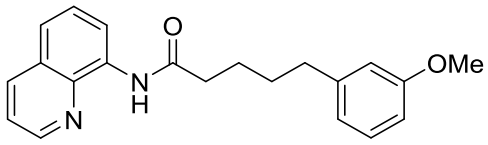
134.5, 129.7 (d, $^{3}J_{CF}$ = 8.0 Hz), 128.0, 127.4, 124.1 (d, $^{4}J_{CF}$ = 2.0 Hz), 121.6, 121.4, 116.4, 115.2 (d, $^{2}J_{CF}$ = 20.0 Hz), 112.6 (d, $^{2}J_{CF}$ = 21.0 Hz), 38.0, 35.5 (d, $^{4}J_{CF}$ = 1.0 Hz), 30.7, 25.2. ^{19}F NMR (565 MHz, $CDCl_3$) δ -113.89. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{20}H_{20}FN_2O$ 323.1554, found 323.1560.

5-(3-chlorophenyl)-*N*-(quinolin-8-yl)pentanamide (3am)



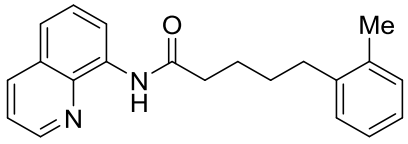
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3am** as a brown solid (37.9 mg, 56%), mp = 42-44 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.82 – 8.75 (m, 2H), 8.14 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.44 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.21 – 7.12 (m, 3H), 7.09 – 7.04 (m, 1H), 2.66 (t, *J* = 7.6 Hz, 2H), 2.58 (t, *J* = 7.3 Hz, 2H), 1.93 – 1.80 (m, 2H), 1.79 – 1.69 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.1, 144.2, 138.3, 136.4, 134.5, 134.1, 129.6, 128.5, 128.0, 127.4, 126.7, 126.0, 121.6, 121.4, 116.4, 37.9, 35.4, 30.8, 25.2. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{20}H_{20}ClN_2O$ 339.1259, found 339.1274.

5-(3-methoxyphenyl)-*N*-(quinolin-8-yl)pentanamide (3an)



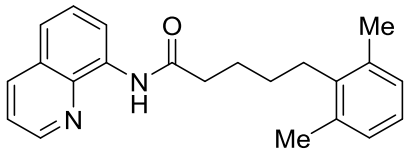
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3an** as a yellow oil (46.1 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.83 – 8.76 (m, 2H), 8.14 (dd, *J* = 1.5, 8.3 Hz, 1H), 7.56 – 7.46 (m, 2H), 7.43 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.78 – 6.69 (m, 2H), 3.78 (s, 3H), 2.68 (t, *J* = 7.6 Hz, 2H), 2.59 (t, *J* = 7.4 Hz, 2H), 1.94 – 1.84 (m, 2H), 1.82 – 1.72 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 159.7, 148.1, 143.9, 138.3, 136.4, 134.5, 129.3, 128.0, 127.4, 121.6, 121.4, 120.9, 116.4, 114.2, 111.1, 55.1, 38.1, 35.8, 31.0, 25.4. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{21}H_{23}N_2O_2$ 335.1754, found 335.1764.

5-(*o*-tolyl)-*N*-(quinolin-8-yl)pentanamide (3ao)



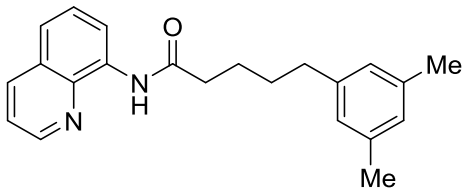
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3ao** as a brown oil (39.5 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.84 – 8.77 (m, 2H), 8.15 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.57 – 7.48 (m, 2H), 7.45 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.19 – 7.07 (m, 4H), 2.69 (t, *J* = 7.8 Hz, 2H), 2.61 (t, *J* = 7.5 Hz, 2H), 2.32 (s, 3H), 1.99 – 1.88 (m, 2H), 1.78 – 1.68 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 148.1, 140.4, 138.4, 136.4, 135.8, 134.6, 130.2, 128.9, 128.0, 127.5, 125.93, 125.92, 121.6, 121.4, 116.5, 38.1, 33.1, 29.9, 25.7, 19.3. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{21}H_{23}N_2O$ 319.1805, found 319.1811.

5-(2,6-dimethylphenyl)-*N*-(quinolin-8-yl)pentanamide (3ap)



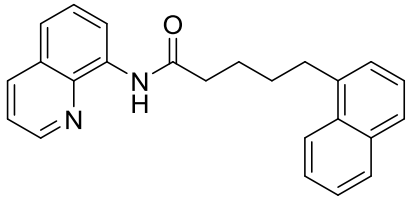
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3ap** as a brown solid (49.2 mg, 74%), mp = 82-84 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.84 – 8.78 (m, 2H), 8.16 (dd, *J* = 1.7, 8.3 Hz, 1H), 7.58 – 7.48 (m, 2H), 7.45 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.02 – 6.97 (m, 3H), 2.75 – 2.68 (m, 2H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.34 (s, 6H), 2.03 – 1.94 (m, 2H), 1.68 – 1.58 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 148.1, 139.1, 138.4, 136.4, 136.0, 134.5, 128.1, 128.0, 127.5, 125.6, 121.6, 121.4, 116.5, 38.1, 29.6, 28.8, 26.2, 19.9. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{22}H_{25}N_2O$ 333.1961, found 333.1971.

5-(3,5-dimethylphenyl)-*N*-(quinolin-8-yl)pentanamide (3aq)



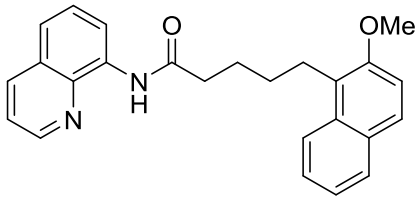
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3aq** as a yellow oil (42.6 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.86 – 8.69 (m, 2H), 8.13 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.55 – 7.45 (m, 2H), 7.42 (dd, *J* = 4.2, 8.3 Hz, 1H), 6.86 – 6.73 (m, 3H), 2.67 – 2.50 (m, 4H), 2.26 (s, 6H), 1.92 – 1.80 (m, 2H), 1.80 – 1.66 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 148.1, 142.2, 138.3, 137.8, 136.4, 134.6, 128.0, 127.5,127.4, 126.3, 121.6, 121.4, 116.4, 38.2, 35.6, 31.2, 25.5, 21.3. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{22}H_{25}N_2O$ 333.1961, found 333.1973.

5-(naphthalen-1-yl)-*N*-(quinolin-8-yl)pentanamide (3ar)



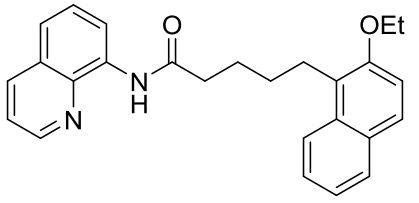
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 20/1) to provide **3ar** as a pale yellow solid (41.1 mg, 58%), mp = 69-72 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.83 – 8.72 (m, 2H), 8.12 (dd, *J* = 1.6, 8.3 Hz, 1H), 8.06 – 7.99 (m, 1H), 7.85 – 7.78 (m, 1H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.52 (t, *J* = 7.9 Hz, 1H), 7.48 – 7.31 (m, 6H), 3.14 (t, *J* = 7.3 Hz, 2H), 2.60 (t, *J* = 7.3 Hz, 2H), 2.03 – 1.83 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 148.1, 138.34, 138.28, 136.4, 134.5, 133.9, 131.8, 128.8, 128.0, 127.5, 126.6, 126.0, 125.8, 125.6, 125.4, 123.8, 121.6, 121.4, 116.5, 38.1, 32.9, 30.4, 25.8. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{24}H_{23}N_2O$ 355.1805, found 355.1810.

5-(2-methoxynaphthalen-1-yl)-*N*-(quinolin-8-yl)pentanamide (3as)



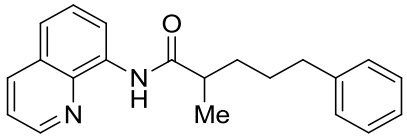
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 20/1) to provide **3as** as a brown solid (48.4 mg, 63%), mp = 85-87 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.79 (dd, *J* = 1.2, 7.5 Hz, 1H), 8.75 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.09 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.95 (d, *J* = 8.6 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.47 – 7.36 (m, 3H), 7.33 – 7.26 (m, 1H), 7.23 (d, *J* = 9.0 Hz, 1H), 3.91 (s, 3H), 3.16 (t, *J* = 7.7 Hz, 2H), 2.61 (t, *J* = 7.7 Hz, 2H), 2.03 – 1.91 (m, 2H), 1.82 – 1.72 (m, 2H). ^{13}C NMR (100 MHz, CDCl3) δ 171.9, 154.4, 148.1, 138.4, 136.4, 134.6, 133.0, 129.3, 128.6, 128.0, 127.6, 127.5, 126.2, 123.6, 123.3, 123.2, 121.6, 121.4, 116.5, 113.4, 56.5, 38.3, 29.7, 25.9, 24.5. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{25}H_{25}N_2O_2$ 385.1911, found 385.1900.

5-(2-ethoxynaphthalen-1-yl)-*N*-(quinolin-8-yl)pentanamide (3at)



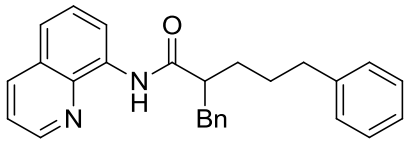
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 20/1) to provide **3at** as a yellow oil (44.6 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.79 (dd, *J* = 1.3, 7.5 Hz, 1H), 8.75 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.09 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.96 (d, *J* = 8.5 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 9.0 Hz, 1H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.46 – 7.37 (m, 3H), 7.32 – 7.26 (m, 1H), 7.21 (d, *J* = 9.0 Hz, 1H), 4.14 (q, *J* = 7.0 Hz, 2H), 3.17 (t, *J* = 7.7 Hz, 2H), 2.62 (t, *J* = 7.7 Hz, 2H), 2.04 – 1.91 (m, 2H), 1.84 – 1.74 (m, 2H), 1.42 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 153.8, 148.1, 138.4, 136.4, 134.6, 133.1, 129.3, 128.5, 128.0, 127.5, 126.2, 124.0, 123.3, 123.1, 121.6, 121.3, 116.5, 114.6, 64.9, 38.3, 29.7, 25.9, 24.6, 15.3. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{26}H_{27}N_2O_2$ 399.2067, found 399.2062.

2-methyl-5-phenyl-*N*-(quinolin-8-yl)pentanamide (3bb)



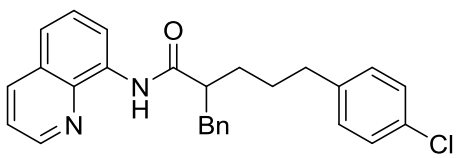
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3bb** as a yellow oil (35.7 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.85 – 8.75 (m, 2H), 8.14 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.56 – 7.46 (m, 2H), 7.43 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.27 – 7.20 (m, 2H), 7.19 – 7.10 (m, 3H), 2.72 – 2.55 (m, 3H), 1.97 – 1.84 (m, 1H), 1.80 – 1.69 (m, 2H), 1.66 – 1.55 (m, 1H), 1.32 (d, *J* = 6.9 Hz, 3H).

2-benzyl-5-phenyl-*N*-(quinolin-8-yl)pentanamide (3cb)



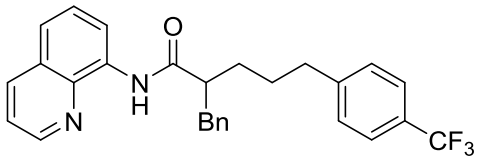
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3cb** as a yellow oil (54.5 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H), 8.81 – 8.75 (m, 1H), 8.70 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.07 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.52 – 7.42 (m, 2H), 7.37 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.25 – 7.16 (m, 6H), 7.14 – 7.08 (m, 4H), 3.19 – 3.08 (m, 1H), 2.89 – 2.81 (m, 1H), 2.79 – 2.70 (m, 1H), 2.62 (t, *J* = 7.5 Hz, 2H), 1.98 – 1.85 (m, 1H), 1.83 – 1.59 (m, 3H).

2-benzyl-5-(4-chlorophenyl)-*N*-(quinolin-8-yl)pentanamide (3cd)



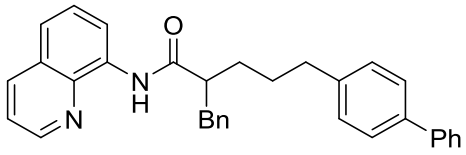
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3cd** as a light yellow oil (34.3 mg, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H), 8.77 (d, *J* = 7.3 Hz, 1H), 8.72 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.11 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.54 – 7.45 (m, 2H), 7.41 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.24 –7.18 (m, 4H), 7.17 – 7.08 (m, 3H), 7.06 – 6.99 (m, 2H), 3.13 (dd, *J* = 8.0, 13.5 Hz, 1H), 2.84 (dd, *J* = 6.6, 13.5 Hz, 1H), 2.78 – 2.69 (m, 1H), 2.58 (t, *J* = 7.4 Hz, 2H), 1.95 – 1.82 (m, 1H), 1.79 – 1.58 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 148.1, 140.5, 139.5, 138.4, 136.3, 134.3, 131.4, 129.8, 129.0, 128.5, 128.4, 127.9, 127.4, 126.3, 121.6, 121.5, 116.5, 51.1, 39.3, 35.2, 32.1, 29.2. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{27}H_{26}ClN_2O$ 429.1728, found 429.1729.

2-benzyl-*N*-(quinolin-8-yl)-5-(4-(trifluoromethyl)phenyl)pentanamide (3cg)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3cg** as a colorless oil (41.6 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 8.78 (d, *J* = 7.3 Hz, 1H), 8.72 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.11 (dd, *J* = 1.5, 8.2 Hz, 1H), 7.54 – 7.43 (m, 4H), 7.41 (dd, *J* = 4.2, 8.2 Hz, 1H), 7.27 – 7.16 (m, 6H), 7.15 – 7.09 (m, 1H), 3.14 (dd, *J* = 7.9, 13.5 Hz, 1H), 2.85 (dd, *J* = 6.7, 13.5 Hz, 1H), 2.80 – 2.71 (m, 1H), 2.67 (t, *J* = 7.5 Hz, 2H), 1.99 – 1.86 (m, 1H), 1.85 – 1.59 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 148.1, 146.2, 139.5, 138.4, 136.3, 134.3, 129.0, 128.7, 128.5, 128.1 (q, $^2J_{CF}$ = 32.1 Hz), 127.9, 127.4, 126.3, 125.2 (q, $^3J_{CF}$ = 3.8 Hz), 124.4 (q, $^1J_{CF}$ = 272.9 Hz), 121.58, 121.56, 116.5, 51.0, 39.3, 35.7, 32.1, 29.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.26. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{28}H_{26}F_3N_2O$ 463.1992, found 463.1993.

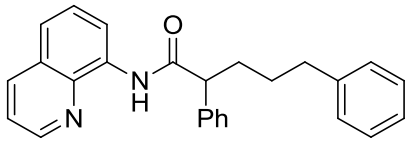
5-([1,1'-biphenyl]-4-yl)-2-benzyl-*N*-(quinolin-8-yl)pentanamide (3ci)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3ci** as a colorless oil (43.3 mg, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1H), 8.85 – 8.76 (m, 1H), 8.70 (d, *J* = 4.1 Hz, 1H), 8.09 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.57 – 7.35 (m, 9H), 7.32 – 7.27 (m, 1H), 7.26 – 7.16 (m, 6H), 7.15 – 7.08 (m, 1H), 3.21 – 3.09 (m, 1H), 2.92 – 2.83 (m, 1H), 2.82 – 2.72 (m, 1H), 2.67 (t, *J* = 7.3 Hz, 2H), 2.02 – 1.89 (m, 1H), 1.88 – 1.65 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 148.1, 141.3, 141.1, 139.7, 138.7, 138.4, 136.3, 134.4, 129.0, 128.9, 128.7, 128.5, 127.9, 127.4, 127.1, 127.0, 126.3, 121.6,

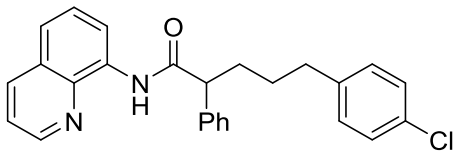
121.5, 116.5, 51.2, 39.3, 35.6, 32.4, 29.3. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{33}H_{31}N_2O$ 471.2431, found 471.2432.

2,5-diphenyl-*N*-(quinolin-8-yl)pentanamide (3db)



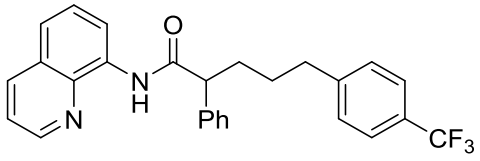
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3db** as a yellow oil (41.1 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.76 (dd, *J* = 1.4, 7.5 Hz, 1H), 8.70 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.06 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.51 – 7.40 (m, 4H), 7.38 – 7.32 (m, 3H), 7.29 – 7.20 (m, 3H), 7.17 – 7.11 (m, 3H), 3.70 (t, *J* = 7.6 Hz, 1H), 2.76 – 2.57 (m, 2H), 2.42 – 2.29 (m, 1H), 2.05 – 1.93 (m, 1H), 1.81 – 1.57 (m, 2H).

5-(4-chlorophenyl)-2-phenyl-*N*-(quinolin-8-yl)pentanamide (3dd)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3dd** as a yellow oil (44.0 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.75 (d, *J* = 7.4 Hz, 1H), 8.71 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.09 (d, *J* = 8.2 Hz, 1H), 7.53 – 7.42 (m, 4H), 7.41 – 7.32 (m, 3H), 7.30 – 7.23 (m, 1H), 7.19 (d, *J* = 8.3 Hz, 2H), 7.06 (d, *J* = 8.3 Hz, 2H), 3.70 (t, *J* = 7.5 Hz, 1H), 2.75 – 2.52 (m, 2H), 2.40 – 2.27 (m, 1H), 2.02 – 1.89 (m, 1H), 1.78 – 1.54 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 148.2, 140.5, 139.7, 138.4, 136.3, 134.5, 131.5, 129.8, 128.9, 128.4, 128.0, 127.9, 127.4, 127.3, 121.6, 121.5, 116.3, 54.9, 35.2, 32.9, 29.5. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{26}H_{24}ClN_2O$ 415.1572, found 415.1574.

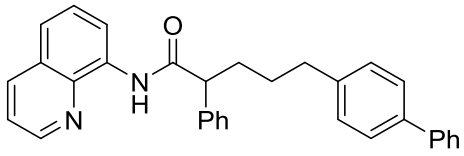
2-phenyl-*N*-(quinolin-8-yl)-5-(4-(trifluoromethyl)phenyl)pentanamide (3dg)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3dg** as a yellow oil (51.9 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.75 (dd, *J* = 1.5, 7.4 Hz, 1H), 8.71 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.08 (dd, *J* = 1.6, 8.2 Hz, 1H), 7.51 – 7.42 (m, 6H), 7.40 – 7.33 (m, 3H), 7.30 – 7.21 (m, 3H), 3.71 (t, *J* = 7.6 Hz, 1H), 2.80 –

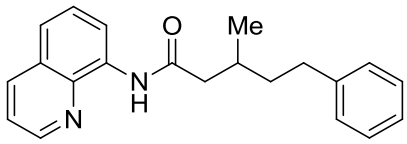
2.62 (m, 2H), 2.42 – 2.83 (m, 1H), 2.03 – 1.91 (m, 1H), 1.82 – 1.56 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 148.2, 146.2, 139.6, 138.4, 136.3, 134.4, 129.0, 128.7, 128.2 (q, $^2J_{CF}$ = 32.4 Hz), 128.0, 127.9, 127.5, 127.3, 125.2 (q, $^3J_{CF}$ = 3.8 Hz), 124.4 (q, $^1J_{CF}$ = 272.8 Hz), 121.6, 116.4, 54.8, 35.7, 32.9, 29.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.24. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{27}H_{24}F_3N_2O$ 449.1835, found 449.1837.

5-([1,1'-biphenyl]-4-yl)-2-phenyl-*N*-(quinolin-8-yl)pentanamide (3di)



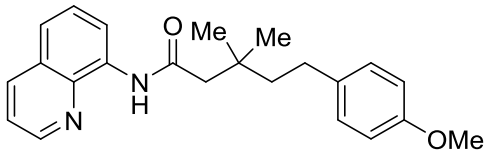
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3di** as a pale yellow oil (42.9 mg, 47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.77 (d, *J* = 7.5 Hz, 1H), 8.70 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.07 (dd, *J* = 1.4, 8.3 Hz, 1H), 7.57 – 7.52 (m, 2H), 7.52 – 7.42 (m, 6H), 7.42 – 7.33 (m, 5H), 7.32 – 7.24 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 3.72 (t, *J* = 7.5 Hz, 1H), 2.80 – 2.62 (m, 2H), 2.46 – 2.32 (m, 1H), 2.09 – 1.95 (m, 1H), 1.85 – 1.60 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 148.2, 141.3, 141.2, 139.8, 138.8, 138.4, 136.3, 134.5, 128.93, 128.89, 128.7, 128.1, 127.9, 127.38, 127.36, 127.1, 127.03, 127.00, 121.6, 121.5, 116.4, 55.0, 35.5, 33.1, 29.6. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{32}H_{29}N_2O$ 457.2274, found 457.2272.

3-methyl-5-phenyl-*N*-(quinolin-8-yl)pentanamide (3eb)



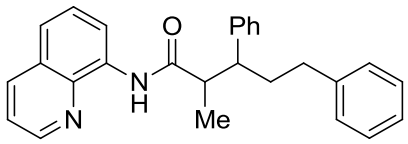
Purified by preparative TLC on silica gel (dichloromethane/ethyl acetate = 120/1) to provide **3eb** as a yellow oil (36.3 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.85 – 8.75 (m, 2H), 8.13 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.57 – 7.46 (m, 2H), 7.43 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.29 – 7.22 (m, 2H), 7.22 – 7.12 (m, 3H), 2.81 – 2.57 (m, 3H), 2.45 – 2.34 (m, 1H), 2.32 – 2.18 (m, 1H), 1.87 – 1.73 (m, 1H), 1.68 – 1.53 (m, 1H), 1.12 (d, *J* = 6.6 Hz, 3H).

5-(4-methoxyphenyl)-3,3-dimethyl-*N*-(quinolin-8-yl)pentanamide (3fa)



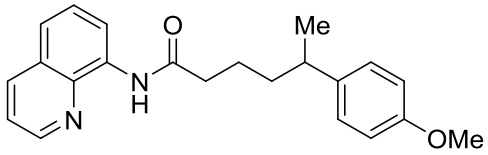
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3fa** as a yellow oil (27.5 mg, 38%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.82 – 8.75 (m, 2H), 8.15 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.44 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.16 – 7.09 (m, 2H), 6.83 – 6.77 (m, 2H), 3.76 (s, 3H), 2.70 – 2.61 (m, 2H), 2.50 (s, 2H), 1.77 – 1.71 (m, 2H), 1.20 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 157.7, 148.2, 138.4, 136.4, 135.0, 134.6, 129.3, 128.0, 127.4, 121.6, 121.4, 116.4, 113.8, 55.3, 50.1, 44.9, 34.0, 30.0, 27.6. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{23}H_{27}N_2O_2$ 363.2067, found 363.2072.

2-methyl-3,5-diphenyl-*N*-(quinolin-8-yl)pentanamide (3gb)



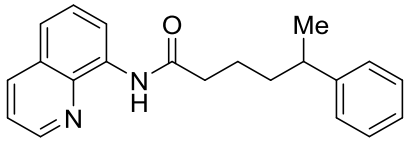
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3gb** as a yellow oil (30.8 mg, 39%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 (s, 1H), 8.65 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.54 (dd, *J* = 2.1, 6.9 Hz, 1H), 8.02 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.41 – 7.29 (m, 3H), 7.25 – 7.19 (m, 2H), 7.19 – 7.10 (m, 4H), 7.10 – 6.95 (m, 4H), 3.04 – 2.93 (m, 1H), 2.81 – 2.71 (m, 1H), 2.44 – 2.27 (m, 2H), 2.23 – 2.12 (m, 1H), 2.01 – 1.87 (m, 1H), 1.32 (d, *J* = 6.8 Hz, 3H).

5-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hexanamide (3ha)



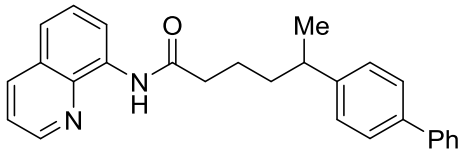
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 12/1) to provide **3ha** as a brown solid (35.5 mg, 51%), mp = 72-74 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.75 (s, 1H), 8.82 – 8.74 (m, 2H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.55 – 7.47 (m, 2H), 7.44 (dd, *J* = 4.1, 8.1 Hz, 1H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.83 (d, *J* = 8.2 Hz, 2H), 3.77 (s, 3H), 2.75 – 2.69 (m, 1H), 2.55 – 2.48 (m, 2H), 1.83 – 1.74 (m, 1H), 1.72 – 1.64 (m, 3H), 1.25 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 157.8, 148.1, 139.4, 138.3, 136.4, 134.6, 128.0, 127.8, 127.5, 121.6, 121.3, 116.4, 113.8, 55.2, 39.1, 38.2, 38.1, 23.9, 22.5. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{22}H_{25}N_2O_2$ 349.1911, found 349.1922.

5-phenyl-*N*-(quinolin-8-yl)hexanamide (3hb)



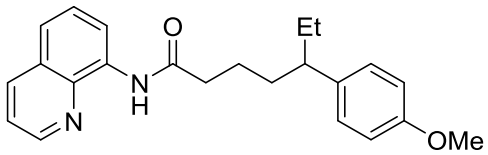
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 12/1) to provide **3hb** as a yellow oil (29.3 mg, 46%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.76 (s, 1H), 8.82 – 8.74 (m, 2H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.55 – 7.46 (m, 2H), 7.44 (dd, *J* = 4.1, 8.0 Hz, 1H), 7.30 – 7.24 (m, 2H), 7.23 – 7.14 (m, 3H), 2.80 – 2.72 (m, 1H), 2.55 – 2.47 (m, 2H), 1.85 – 1.76 (m, 1H), 1.75 – 1.61 (m, 3H), 1.28 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 148.1, 147.3, 138.3, 136.4, 134.5, 128.4, 128.0, 127.5, 127.0, 126.0, 121.6, 121.3, 116.4, 39.9, 38.2, 37.9, 23.9, 22.3. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{21}H_{23}N_2O$ 319.1805, found 319.1807.

5-([1,1'-biphenyl]-4-yl)-*N*-(quinolin-8-yl)hexanamide (3hi)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 12/1) to provide **3hi** as a brown oil (34.7 mg, 44%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.77 (s, 1H), 8.80 – 8.73 (m, 2H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 2H), 7.55 – 7.47 (m, 4H), 7.45 – 7.39 (m, 3H), 7.33 – 7.24 (m, 3H), 2.86 – 2.77 (m, 1H), 2.58 – 2.51 (m, 2H), 1.90 – 1.80 (m, 1H), 1.80 – 1.68 (m, 3H), 1.31 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 148.1, 146.4, 141.2, 138.9, 138.3, 136.4, 134.5, 128.7, 128.0, 127.5, 127.4, 127.2, 127.02, 126.96, 121.6, 121.4, 116.4, 39.6, 38.2, 37.9, 23.9, 22.3. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{27}H_{27}N_2O$ 395.2118, found 395.2131.

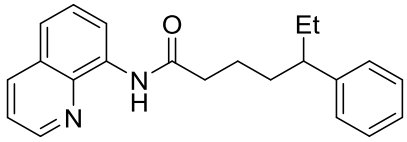
5-(4-methoxyphenyl)-*N*-(quinolin-8-yl)heptanamide (3ia)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 25/1) to provide **3ia** as a yellow oil (47.1 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 8.82 – 8.72 (m, 2H), 8.14 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.56 – 7.46 (m, 2H), 7.44 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.10– 7.02 (m, 2H), 6.87 – 6.78 (m, 2H), 3.77 (s, 3H), 2.52 – 2.38 (m, 3H), 1.83 – 1.57 (m, 5H), 1.57 – 1.46 (m, 1H), 0.76 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.7,

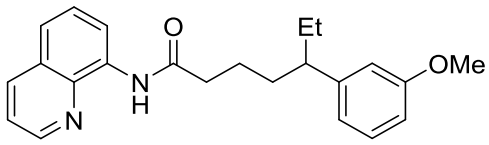
157.8, 148.1, 138.3, 137.4, 136.4, 134.6, 128.6, 127.9, 127.5, 121.6, 121.3, 116.4, 113.7, 55.2, 46.9, 38.3, 36.2, 29.8, 23.9, 12.2. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{23}H_{27}N_2O_2$ 363.2067, found 363.2070.

5-phenyl-*N*-(quinolin-8-yl)heptanamide (3ib)



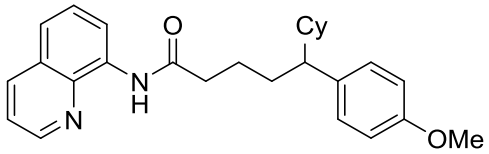
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3ib** as a yellow oil (47.9 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.80 – 8.73 (m, 2H), 8.12 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.54 – 7.44 (m, 2H), 7.41 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.31 – 7.23 (m, 2H), 7.19 – 7.13 (m, 3H), 2.56 – 2.41 (m, 3H), 1.87 – 1.50 (m, 6H), 0.77 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 148.1, 145.4, 138.3, 136.4, 134.5, 128.3, 128.0, 127.4, 127.5, 126.0, 121.6, 121.4, 116.4, 47.8, 38.3, 36.1, 29.7, 23.9, 12.2. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{22}H_{25}N_2O$ 333.1961, found 333.1964.

5-(3-methoxyphenyl)-*N*-(quinolin-8-yl)heptanamide (3in)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3in** as a brown oil (47.1 mg, 65%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.74 (s, 1H), 8.81 – 8.73 (m, 2H), 8.15 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.54 – 7.47 (m, 2H), 7.44 (dd, *J* = 4.2, 8.2 Hz, 1H), 7.22 – 7.17 (m, 2H), 6.77 (d, *J* = 7.5 Hz, 1H), 6.73 – 6.70 (m, 2H), 3.78 (s, 3H), 2.50 (t, *J* = 7.1 Hz, 2H), 2.47 – 2.42 (m, 1H), 1.82 – 1.52 (m, 6H), 0.78 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.7, 159.6, 148.1, 147.2, 138.4, 136.4, 134.6, 129.2, 127.9, 127.4, 121.6, 121.3, 120.3, 116.4, 113.6, 110.9, 55.1, 47.9, 38.3, 36.0, 29.6, 23.9, 12.2. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{23}H_{27}N_2O_2$ 363.2067, found 363.2073.

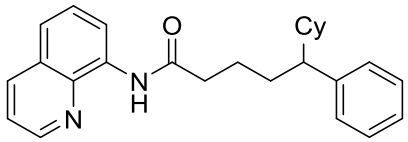
5-cyclohexyl-5-(4-methoxyphenyl)-*N*-(quinolin-8-yl)pentanamide (3ja)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3ja** as a yellow oil (55.8 mg, 67%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.72 (s, 1H), 8.81 – 8.73 (m, 2H), 8.17 – 8.13 (m, 1H), 7.54 – 7.47 (m, 2H), 7.45 (dd, *J* = 4.2, 8.2 Hz, 1H), 7.03 (d, *J*

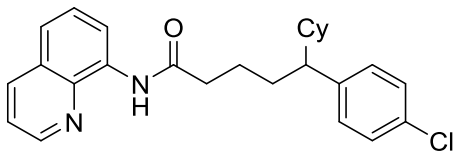
= 8.5 Hz, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 3.77 (s, 3H), 2.53 – 2.42 (m, 2H), 2.35 – 2.29 (m, 1H), 1.94 – 1.83 (m, 2H), 1.71 – 1.56 (m, 6H), 1.47 – 1.37 (m, 2H), 1.24 – 1.14 (m, 1H), 1.14 – 0.99 (m, 2H), 0.94 – 0.84 (m, 1H), 0.80 – 0.71 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.8, 157.7, 148.1, 138.4, 136.4, 136.2, 134.6, 129.3, 128.0, 127.5, 121.6, 121.3, 116.4, 113.4, 55.2, 51.2, 43.3, 38.3, 32.3, 31.5, 30.9, 26.61, 26.55, 24.1. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{27}H_{33}N_2O_2$ 417.2537, found 417.2538.

5-cyclohexyl-5-phenyl-*N*-(quinolin-8-yl)pentanamide (3jb)



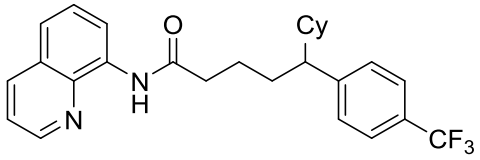
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 20/1) to provide **3jb** as a yellow oil (43.3 mg, 56%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.72 (s, 1H), 8.81 – 8.72 (m, 2H), 8.15 (d, *J* = 8.1 Hz, 1H), 7.54 – 7.47 (m, 2H), 7.46 – 7.43 (m, 1H), 7.29 – 7.23 (m, 2H), 7.19 – 7.10 (m, 3H), 2.53 – 2.42 (m, 2H), 2.39 – 2.33 (m, 1H), 1.97 – 1.87 (m, 2H), 1.74 – 1.65 (m, 2H), 1.62 – 1.55 (m, 4H), 1.50 – 1.39 (m, 2H), 1.24 – 1.15 (m, 1H), 1.14 – 1.00 (m, 2H), 0.96 – 0.86 (m, 1H), 0.82 – 0.73 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.7, 148.1, 144.2, 138.4, 136.4, 134.6, 128.6, 128.0, 127.9, 127.5, 125.8, 121.54, 121.3, 116.4, 52.1, 43.2, 38.3, 32.2, 31.4, 31.0, 26.6, 26.5, 24.1. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{26}H_{31}N_2O$ 387.2431, found 387.2438.

5-(4-chlorophenyl)-5-cyclohexyl-*N*-(quinolin-8-yl)pentanamide (3jd)



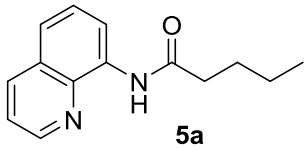
Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3jd** as a pale yellow oil (53.1 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 8.77 (dd, *J* = 1.6, 4.2 Hz, 1H), 8.76 – 8.71 (m, 1H), 8.14 (dd, *J* = 1.2, 8.2 Hz, 1H), 7.56 – 7.46 (m, 2H), 7.43 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.24 – 7.18 (m, 2H), 7.08 – 7.02 (m, 2H), 2.55 – 2.39 (m, 2H), 2.39 – 2.29 (m, 1H), 1.97 – 1.82 (m, 2H), 1.78 – 1.51 (m, 6H), 1.47 – 1.35 (m, 2H), 1.28 – 1.12 (m, 1H), 1.12 – 0.98 (m, 2H), 0.94 – 0.81 (m, 1H), 0.80 – 0.66 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.1, 142.7, 138.3, 136.4, 134.5, 131.5, 129.8, 128.2, 127.9, 127.4, 121.6, 121.4, 116.4, 51.6, 43.2, 38.2, 32.1, 31.4, 30.9, 26.52, 26.46, 24.0. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{26}H_{30}ClN_2O$ 421.2041, found 421.2044.

5-cyclohexyl-*N*-(quinolin-8-yl)-5-(4-(trifluoromethyl)phenyl)pentanamide (3jg)



Purified by preparative TLC on silica gel (petroleum ether/ethyl acetate = 15/1) to provide **3jg** as a pale yellow oil (59.9 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.80 – 8.70 (m, 2H), 8.13 (dd, *J* = 1.1, 8.2 Hz, 1H), 7.54 – 7.45 (m, 4H), 7.43 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 2.56 – 2.39 (m, 3H), 2.00 – 1.85 (m, 2H), 1.76 – 1.65 (m, 2H), 1.64 – 1.42 (m, 5H), 1.41 – 1.34 (m, 1H), 1.28 – 1.14 (m, 1H), 1.13 – 0.98 (m, 2H), 0.97 – 0.84 (m, 1H), 0.81 – 0.68 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 148.5, 148.1, 138.3, 136.4, 134.5, 128.8, 128.2 (q, $^{2}J_{CF}$ = 32.3 Hz), 128.0, 127.4, 125.0 (q, $^{3}J_{CF}$ = 3.8 Hz), 124.4 (q, $^{1}J_{CF}$ = 272.9 Hz), 121.6, 121.4, 116.4, 52.2, 43.1, 38.2, 32.0, 31.3, 31.0, 26.49, 26.47, 26.42, 24.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.15. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{27}H_{30}F_3N_2O$ 455.2305, found 455.2304.

***N*-(quinolin-8-yl)pentanamide (5a)**

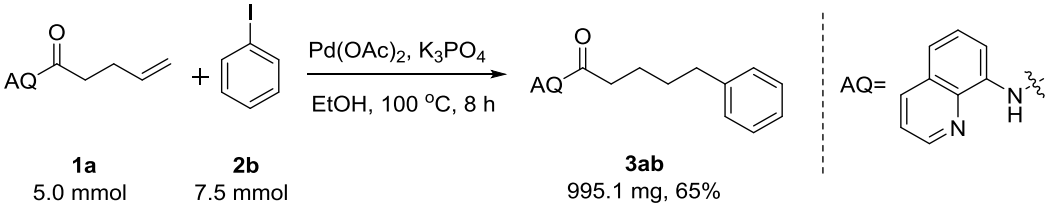


5a

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.84 – 8.75 (m, 2H), 8.16 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 2.57 (t, *J* = 7.5 Hz, 2H), 1.87 – 1.76 (m, 2H), 1.53 – 1.40 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

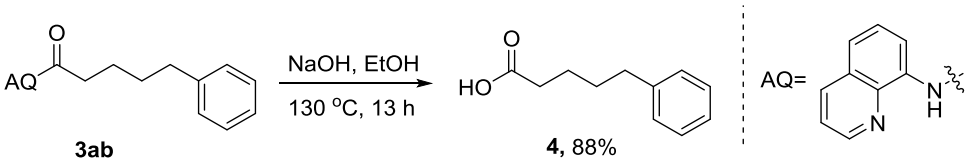
2.4 Scale-up Reaction and Removal of Directing Group

Scale-up reaction:



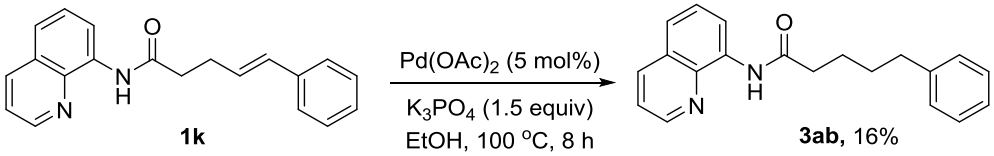
Procedure for scale-up reaction: To a 150 mL pressure tube **1a** (5.0 mmol, 1.31 g), **2b** (7.5 mmol, 1.53 g), $Pd(OAc)_2$ (5 mol%, 56.1 mg), K_3PO_4 (7.5 mmol, 1.59 g) and EtOH (25 mL) were added sequentially. The reaction was stirred in a *pre*-warmed 100 °C oil bath for 8 hours under air. Then the reaction was quenched with ethyl acetate and filtered through a pad of celite. The filtrate was concentrated and purified by preparative TLC on silica gel plates (petroleum ether/ethyl acetate = 20/1) to give the desired product **3ab** (995.1 mg, 65%).

Removal of directing group:



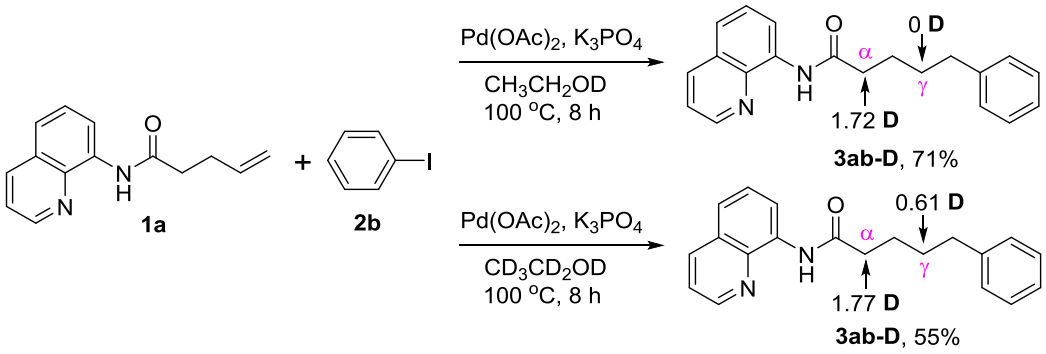
*Procedure for removal of directing group (taking **3ab** as an example):* To a 150 mL pressure tube were added a suitable size magnet, **3ab** (1.0 mmol, 304.4 mg), sodium hydroxide (15.0 mmol, 600 mg), ethanol (20 mL) sequentially. The reaction was stirred vigorously in a *pre*-warmed 130 °C oil bath for 13 hours under air. After completion of the reaction, the reaction mixture was cooled to room temperature. Aqueous sodium hydroxide solution (20 mL, 1M) and dichloromethane (20 mL) were added to the mixture, and then transferred to a separating funnel to carry out liquid separation. The aqueous phase was separated and the organic phase was extracted with sodium hydroxide (1M, 15 mL, ×3). All aqueous phases were combined and then washed with 20 mL of dichloromethane. The aqueous phase was then acidified to pH = 1 with hydrochloric acid (1M). The acidified aqueous phase was extracted with ethyl acetate (20 mL, ×3), and the organic phases were combined and washed once with 20 mL of brine. The organic phase was dried over anhydrous sodium sulfate, concentrated under reduced pressure to afford 5-phenylpentanoic acid **4** (157.1 mg, 88%).

2.5 Studies on Mechanism

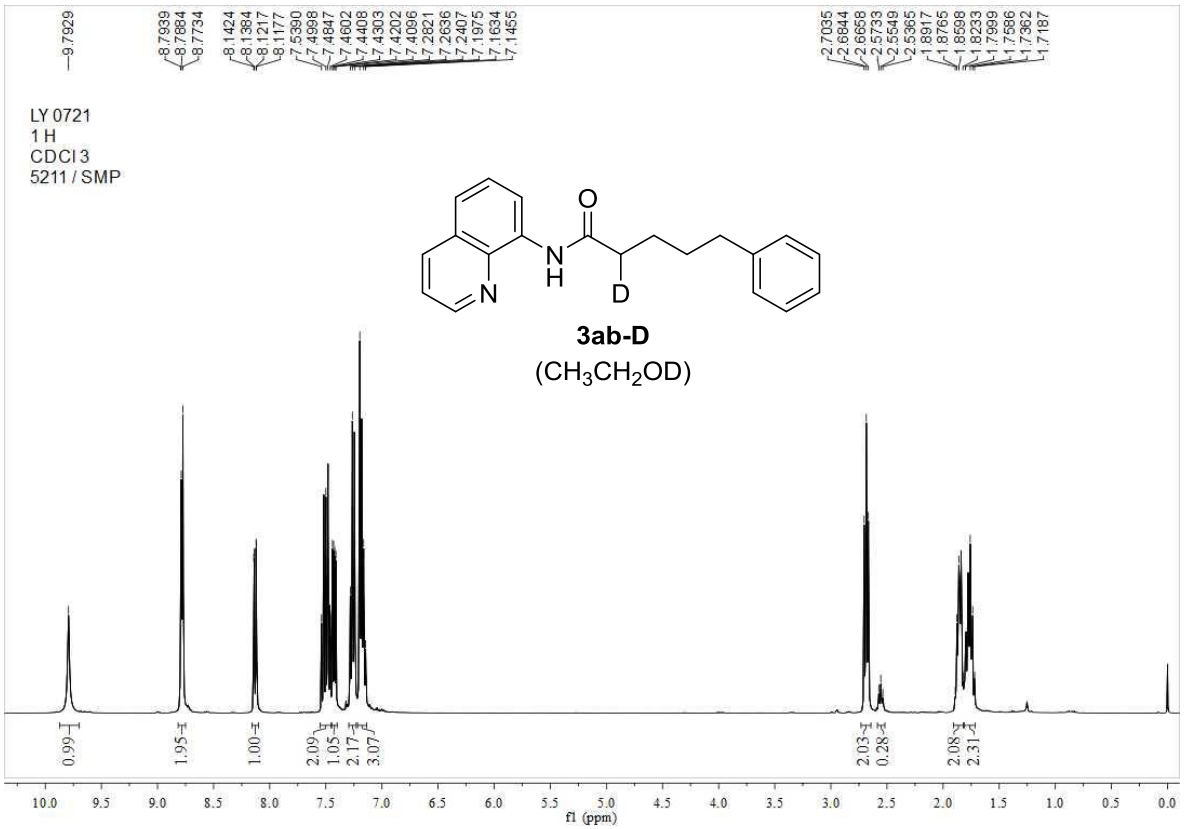


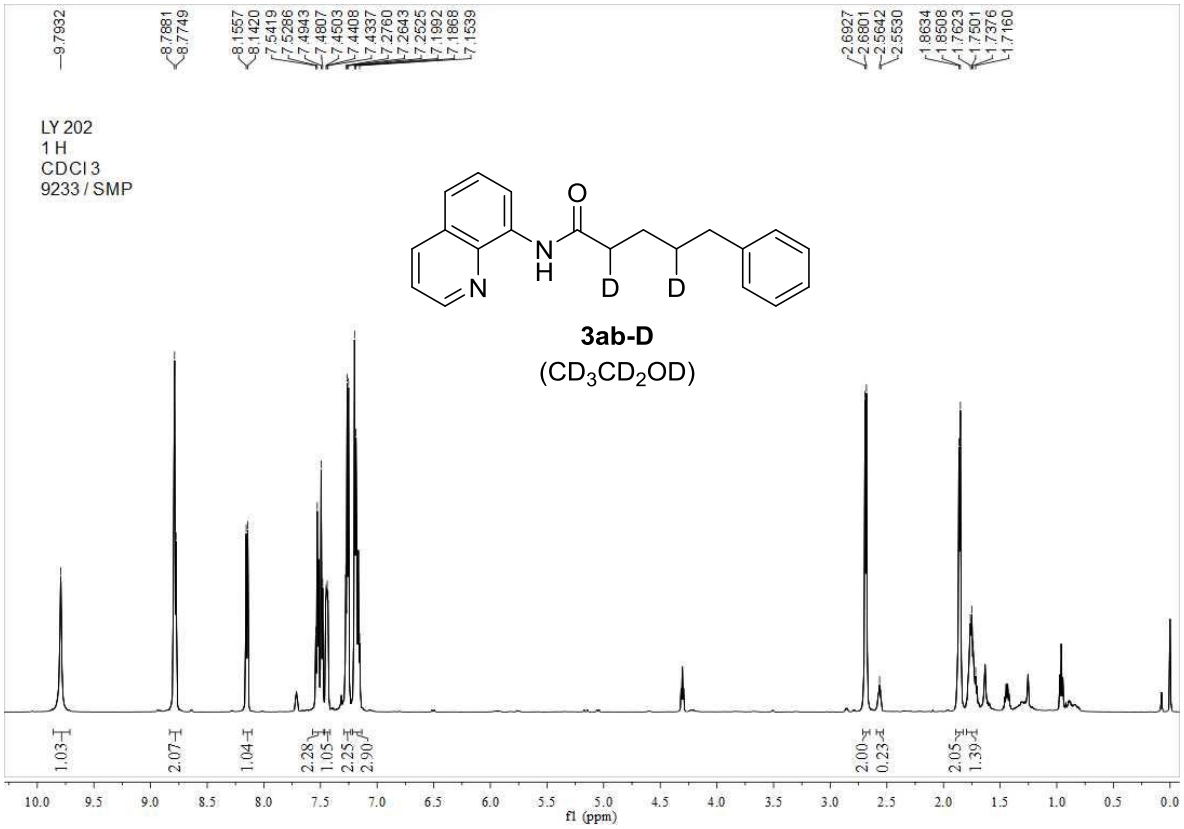
To a 35 mL pressure tube **1k** (0.20 mmol, 60.5 mg), $Pd(OAc)_2$ (5.0 mol%, 2.2 mg), K_3PO_4 (0.30 mmol, 63.7 mg) and EtOH (1.0 mL) were added sequentially. The reaction was stirred in a *pre*-warmed 100 °C oil bath for 8 hours. Then the reaction was quenched with ethyl acetate and filtered through a pad of celite. The filtrate was concentrated and purified by preparative TLC on silica gel plates (petroleum ether/ethyl acetate = 15/1), affording **3ab** (9.7 mg, 16%).

Deuteration experiments:



To a 35 mL pressure tube **1a** (0.2 mmol, 45.3 mg), 2b (0.3 mmol, 61.2 mg), $Pd(OAc)_2$ (5 mol%, 2.2 mg), K_3PO_4 (0.3 mmol, 63.7 mg) and D-labeling solvent (1.0 mL) were added sequentially. The reaction was stirred in a *pre*-warmed 100 °C oil bath for 8 hours. Then the reaction was quenched with ethyl acetate and filtered through a pad of celite. The filtrate was concentrated and purified by preparative TLC on silica gel plates (petroleum ether/ethyl acetate = 15/1), affording compound **3ab-D** (CH_3CH_2OD) which was partially deuterated at the α-position in 71% isolated yield or **3ab-D** (CD_3CD_2OD) which was partially deuterated at both the α- and γ-positions in 55% isolated yield. The products from deuteration experiments were confirmed by ^1H NMR.


LY 0721
1 H
CDCl 3
5211 / SMP
O
N
H
N
D
3ab-D
(CH3CH2OD)
f1 (ppm)


LY 202
1 H
CDCl 3
9233 / SMP
O
N
H
N
D
D
3ab-D
(CD3CD2OD)
f1 (ppm)

2.6 Crystal Reports for 3ai

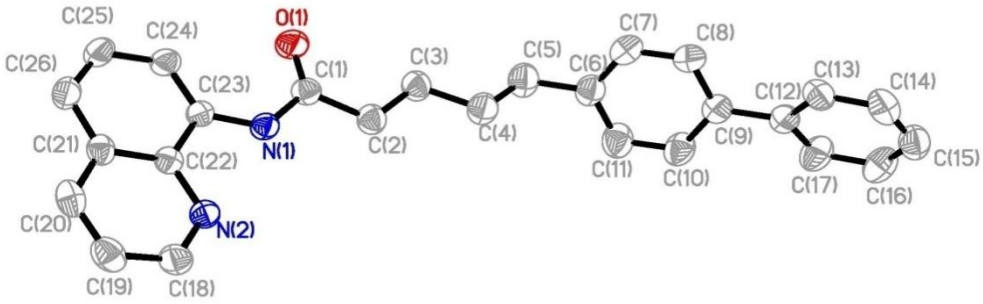


Figure S1. Molecular structure of 3ai. Hydrogen atoms are omitted for clarity.

Crystals of **3ai** (CCDC 1914045) were obtained by recrystallization from petroleum ether/ethyl acetate at ambient temperature. The data were collected on a Xcalibur, Eos, Gemini diffractometer with graphite-monochromated Cu Kα radiation (λ = 1.54184 Å). The structure was solved by direct methods using the SHELXS-97 program, and all non-hydrogen atoms were refined anisotropically on F^2 by the full-matrix least-squares technique, which used the SHELXL-97 crystallographic software package. The hydrogen atoms were included but not refined.

Table S6 Summary of crystal structure determination for 3ai

	3ai
Empirical formula	$C_{26}H_{24}N_2O$
Formula weight	380.47
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	6.05095(10)
b/Å	8.47658(13)
c/Å	40.4530(7)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2074.89(6)
Z	4
ρ_{calc}g/cm^3	1.218
μ/mm^{-1}	0.579

F(000)	808.0
Crystal size/mm^3	0.15 ×0.12 ×0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.744 to 141.778
Index ranges	$-7 \leq h \leq 4$, $-10 \leq k \leq 10$, $-49 \leq l \leq 47$
Reflections collected	15538
Independent reflections	3974 [R_{int} = 0.0287, R_{sigma} = 0.0207]
Data/restraints/parameters	3974/0/262
Goodness-of-fit on F^2	1.035
Final R indexes [I>=2σ (I)]	R_1 = 0.0529, wR_2 = 0.1471
Final R indexes [all data]	R_1 = 0.0596, wR_2 = 0.1565
Largest diff. peak/hole / e $Å^{-3}$	0.17/-0.19

Table S7 Bond lengths (Å) for compound 3ai

	Length/Å		Length/Å
C1-C2	1.518(5)	C13-C14	1.372(6)
C1-N1	1.358(4)	C14-C15	1.347(7)
C1-O1	1.208(4)	C15-C16	1.354(7)
C2-C3	1.489(5)	C16-C17	1.403(6)
C3-C4	1.531(5)	C18-C19	1.392(5)
C4-C5	1.479(6)	C18-N2	1.317(4)
C5-C6	1.509(6)	C19-C20	1.364(5)
C6-C7	1.373(6)	C20-C21	1.404(5)
C6-C11	1.393(6)	C21-C22	1.418(4)
C7-C8	1.380(6)	C21-C26	1.414(5)
C8-C9	1.383(5)	C22-C23	1.436(4)
C9-C10	1.377(6)	C22-N2	1.363(4)
C9-C12	1.477(5)	C23-C24	1.368(4)
C10-C11	1.391(6)	C23-N1	1.393(4)
C12-C13	1.383(5)	C24-C25	1.409(5)
C12-C17	1.370(6)	C25-C26	1.343(6)

Table S8 Bond angles for 3ai

	Angle/^{o}		Angle/^{o}
N1-C1-C2	112.5(3)	C15-C14-C13	121.2(5)
O1-C1C2	123.9(3)	C14-C15-C16	118.8(4)
O1-C1-N1	123.6(3)	C15-C16-C17	120.7(5)
C3-C2-C1	116.2(3)	C12-C17-C16	121.0(5)
C2-C3-C4	113.1(3)	N2-C18-C19	124.0(3)
C5-C4-C3	113.9(3)	C20-C19-C18	118.9(3)
C4-C5-C6	113.9(4)	C19-C20-C21	119.9(3)
C7-C6-C5	120.2(4)	C20-C21-C22	117.0(3)
C7-C6-C11	117.5(4)	C20-C21-C26	124.2(3)
C11-C6-C5	122.1(4)	C26-C21-C22	118.8(3)
C6-C7-C8	121.6(4)	C21-C22-C23	119.5(3)
C7-C8-C9	121.4(4)	N2-C22-C21	122.5(3)
C8-C9-C12	120.6(3)	N2-C22-C23	118.0(2)
C10-C9-C8	117.2(4)	C24-C23-C22	119.4(3)
C10-C9-C12	122.1(3)	C24-C23-N1	125.8(3)
C9-C10-C11	121.7(4)	N1-C23-C22	114.8(2)
C10-C11-C6	120.4(4)	C23-C24-C25	119.7(3)
C13-C12-C9	121.4(3)	C26-C25-C24	122.4(3)
C17-C12-C9	122.1(4)	C25-C26- C21	120.1(3)
C17-C12-C13	116.5(4)	C1-N1-C23	129.1(2)
C14-C13-C12	121.8(4)	C18-N2-C22	117.7(3)

3. References

1. M. Liu, P. Yang, M. K. Karunananda, Y. Wang, P. Liu and K. M. Engle, *J. Am. Chem. Soc.*, 2018, **140**, 5805.
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3. I. I. Strambeanu and M. C. White, *J. Am. Chem. Soc.*, 2013, **135**, 12032.
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5. C. Wang, G. Xiao, T. Guo, Y. Ding, X. Wu and T.-P. Loh, *J. Am. Chem. Soc.*, 2018, **140**, 9332.
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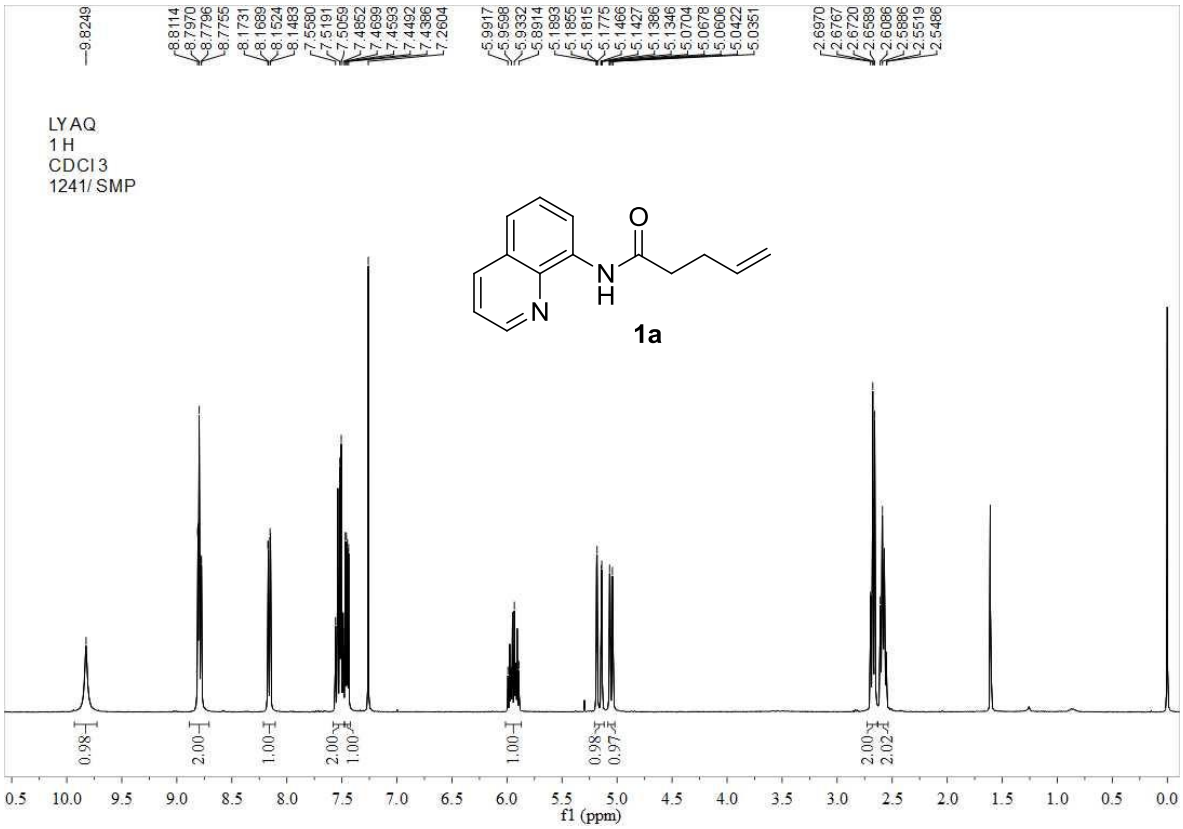
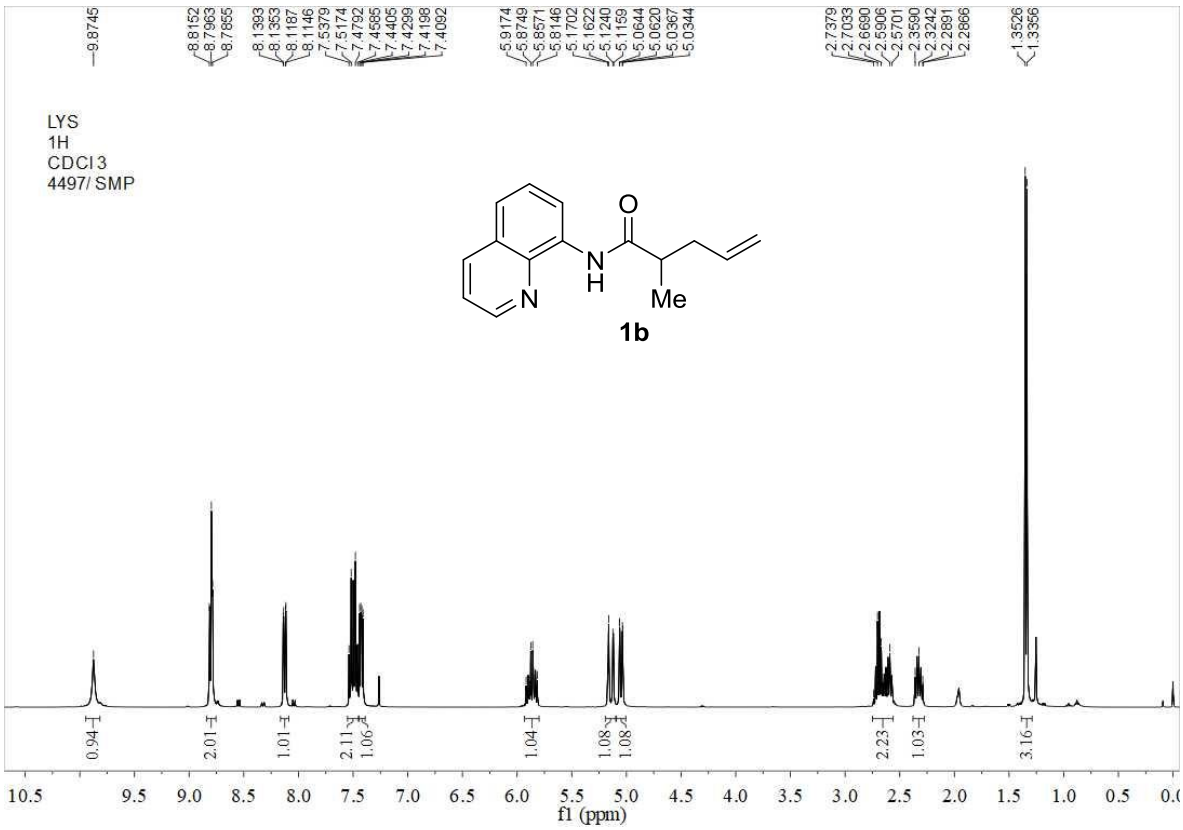
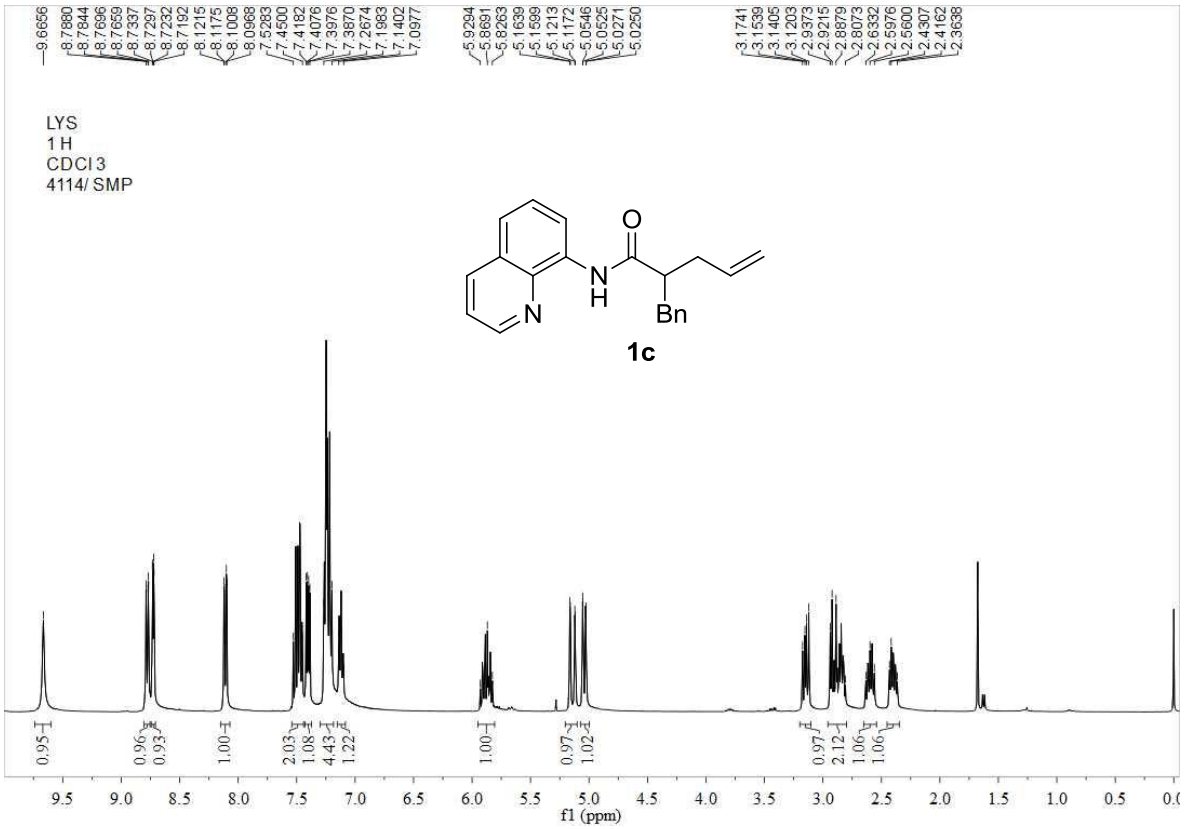
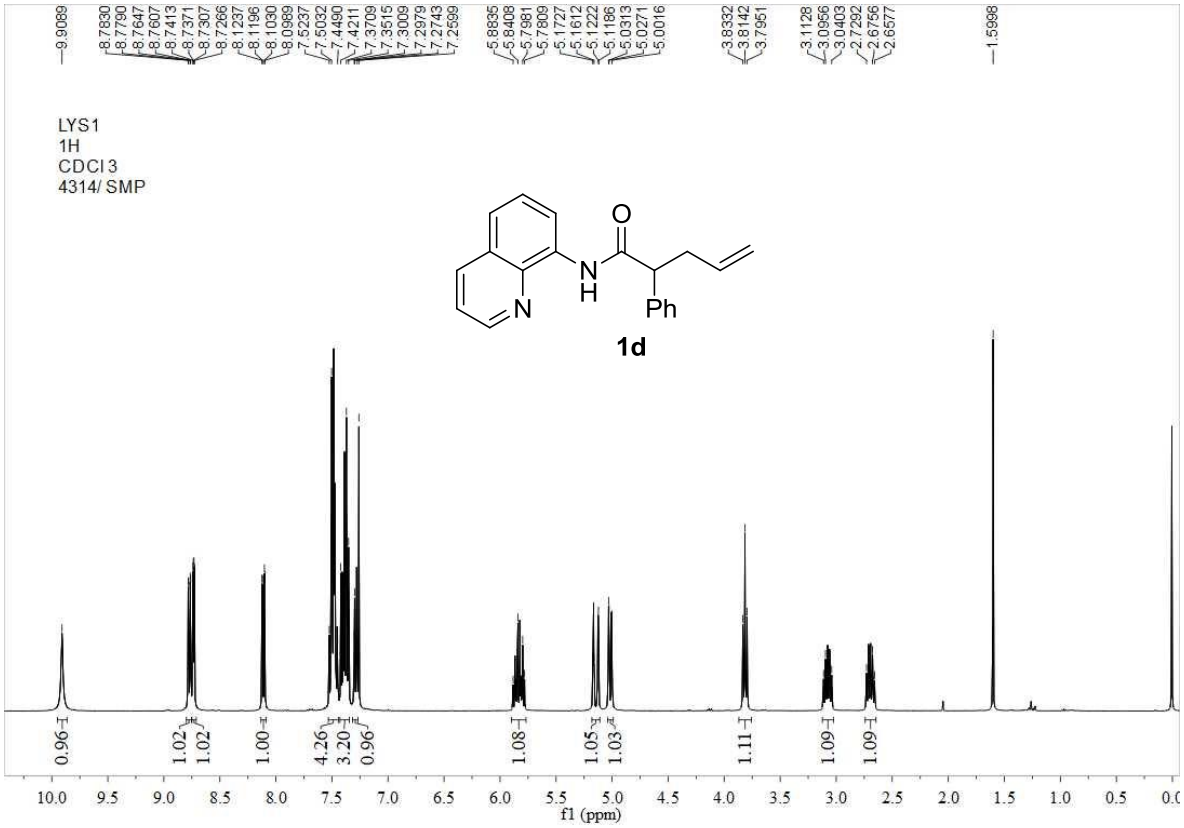
7. K. Rode, M. Palomba, S. Ortgies, R. Rieger and A. Breder, *Synthesis*, 2018, **50**, 3875.
8. F. V. Singh and T. Wirth, *Org. Lett.*, 2011, **13**, 6504.

4. NMR Spectra






LYS
1 H
CDCl 3
4114/ SMP
O
N
H
N
Bn
1c
f1 (ppm)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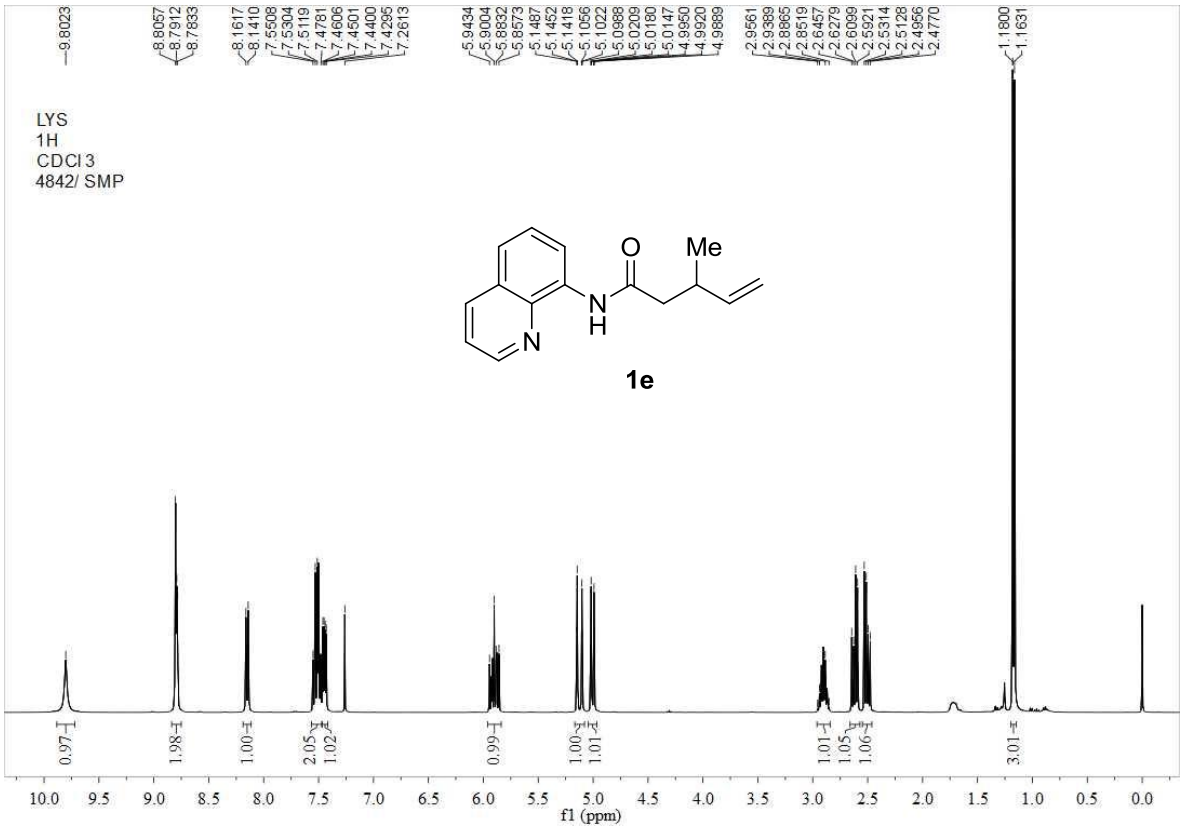
O
N
H
N
Ph
1d
f1 (ppm)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1H
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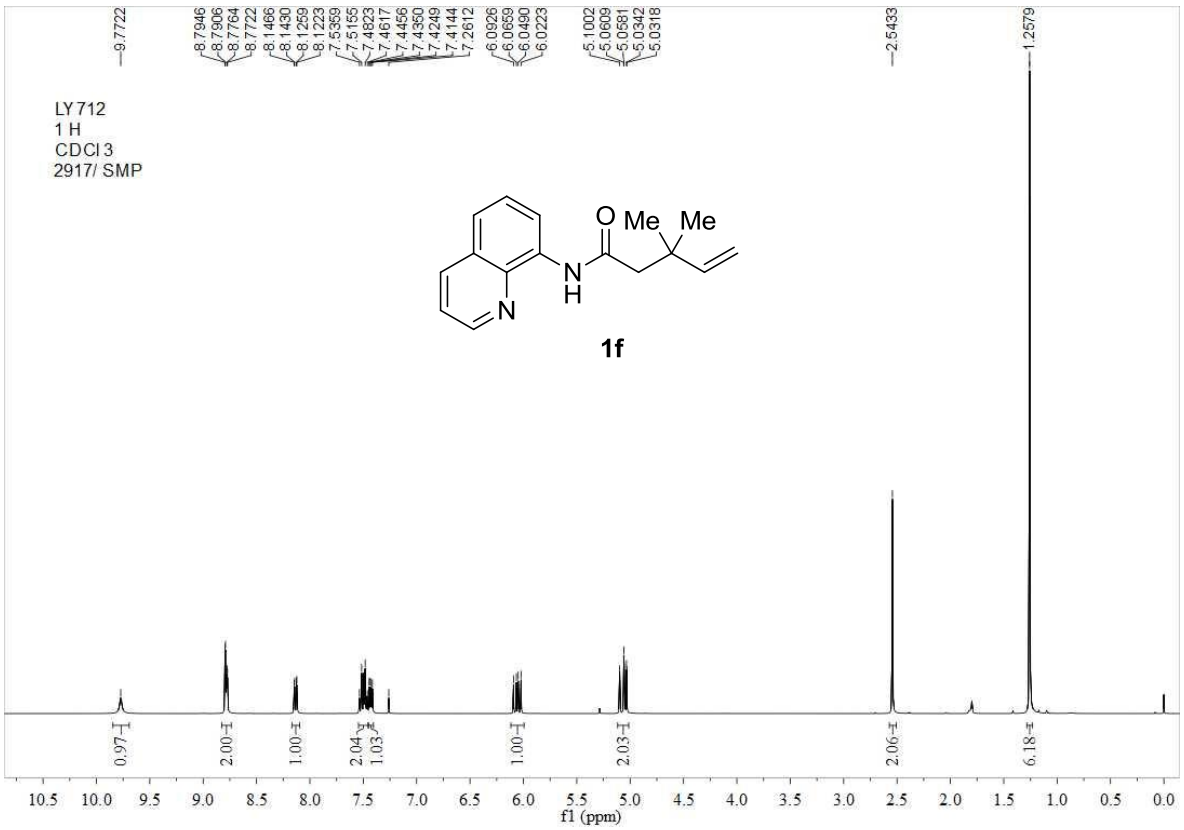
4842/ SMP
O
Me
N
H
N
1e
f1 (ppm)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Me
Me
N
H
N
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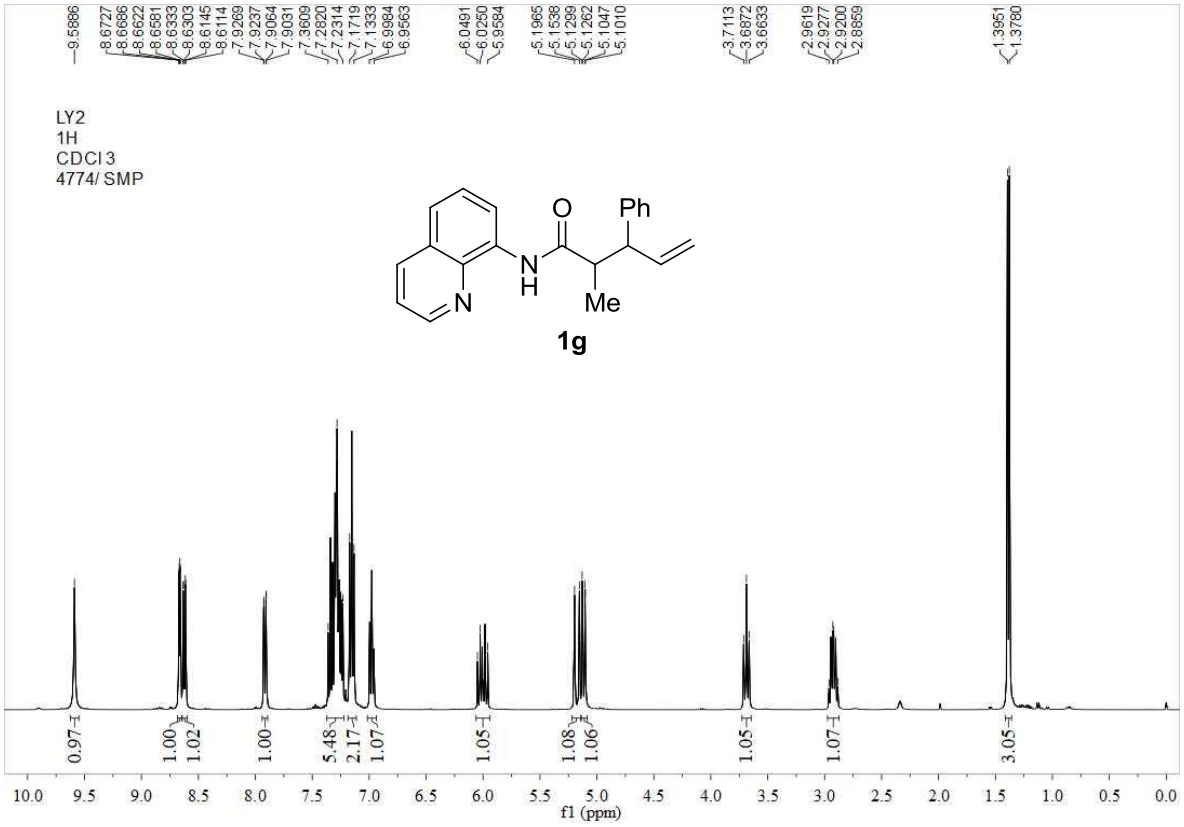
f1 (ppm)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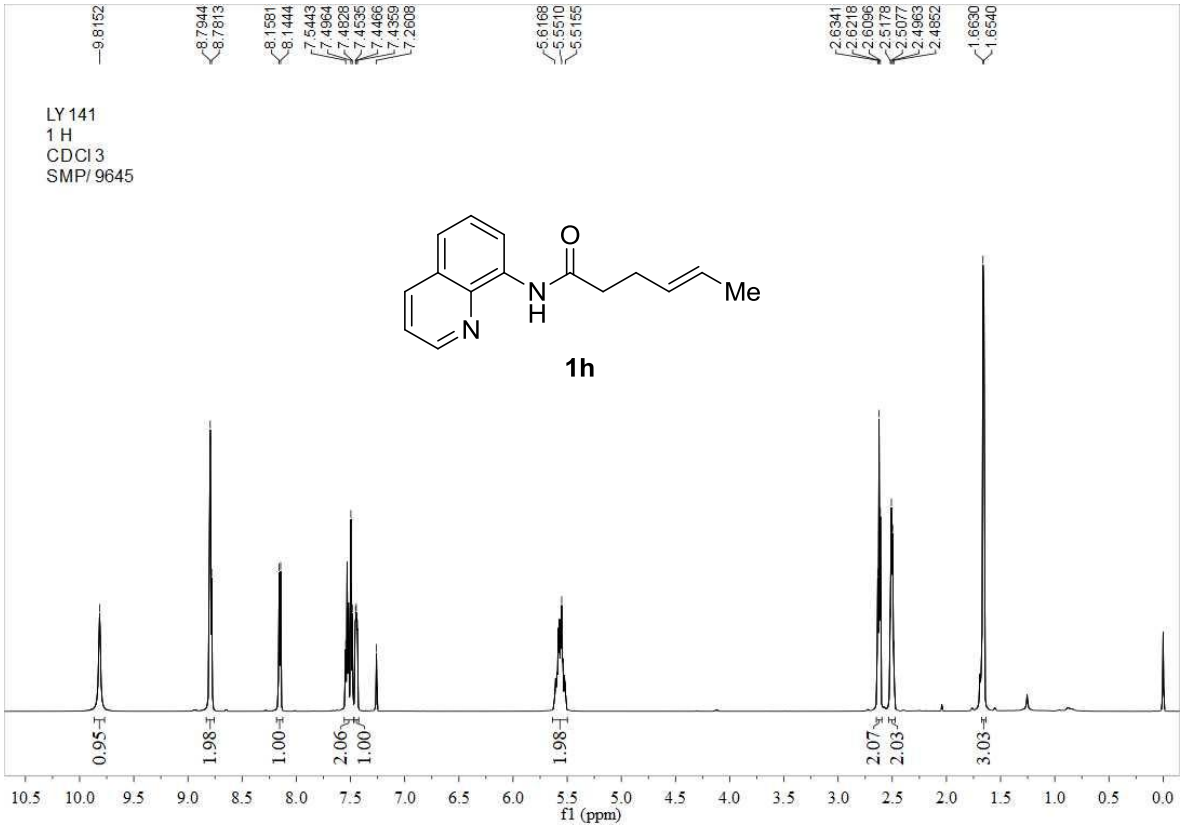
Ph
N
H
N
Me
f1 (ppm)

1g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N
Me
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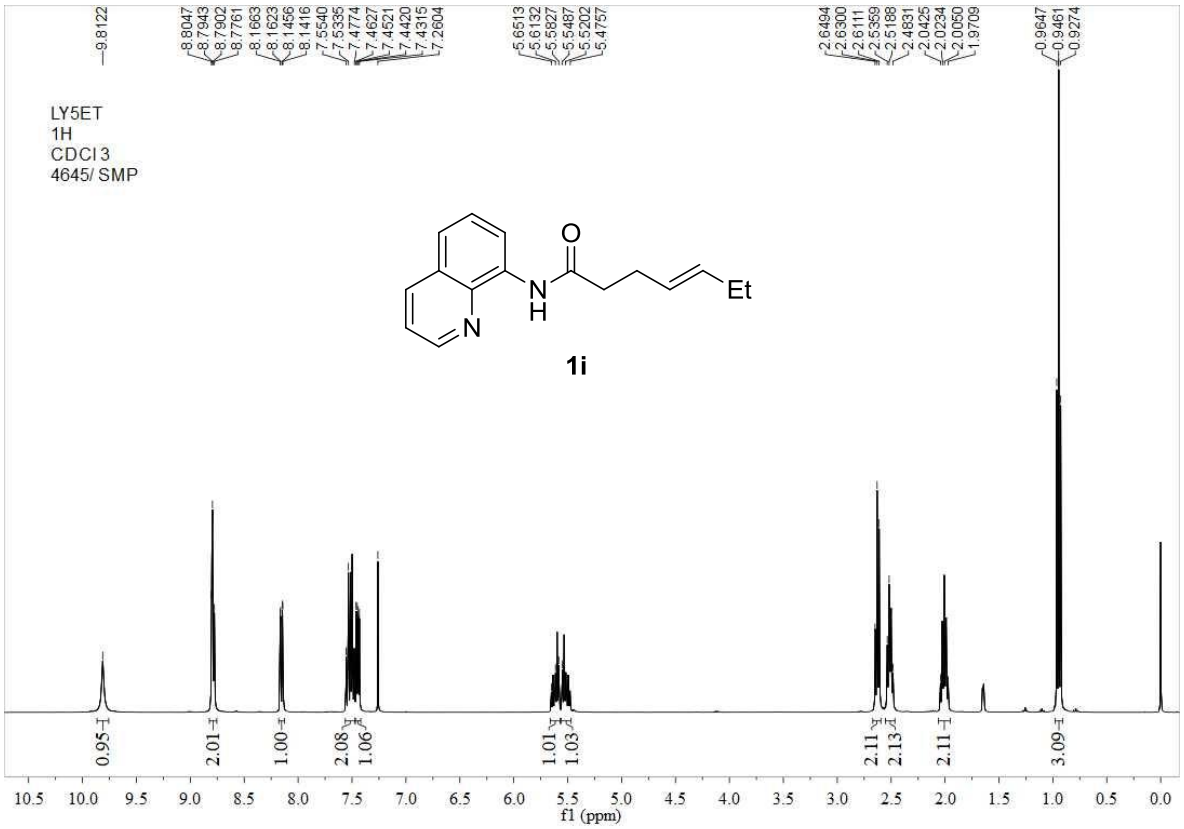
1h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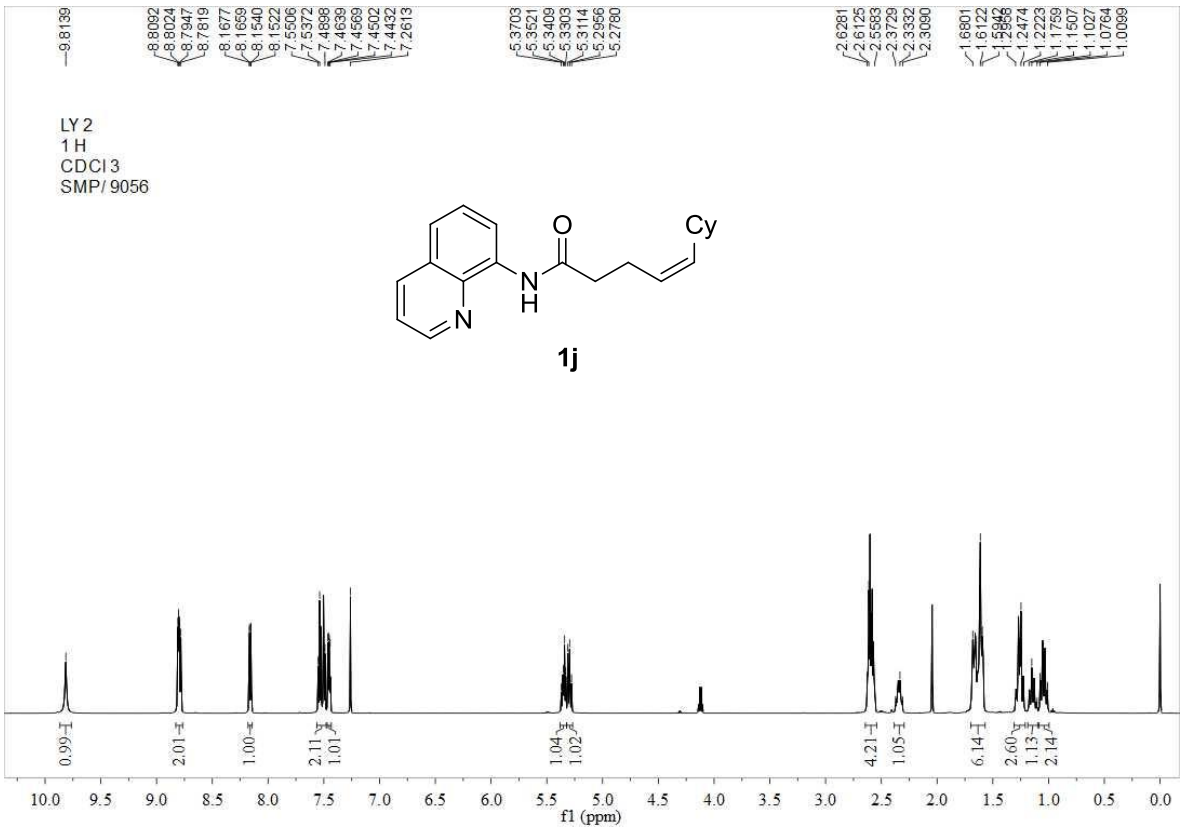
1H
CDCl3
4645/ SMP
O
N
H
N
Et
1i
f1 (ppm)


LY 2
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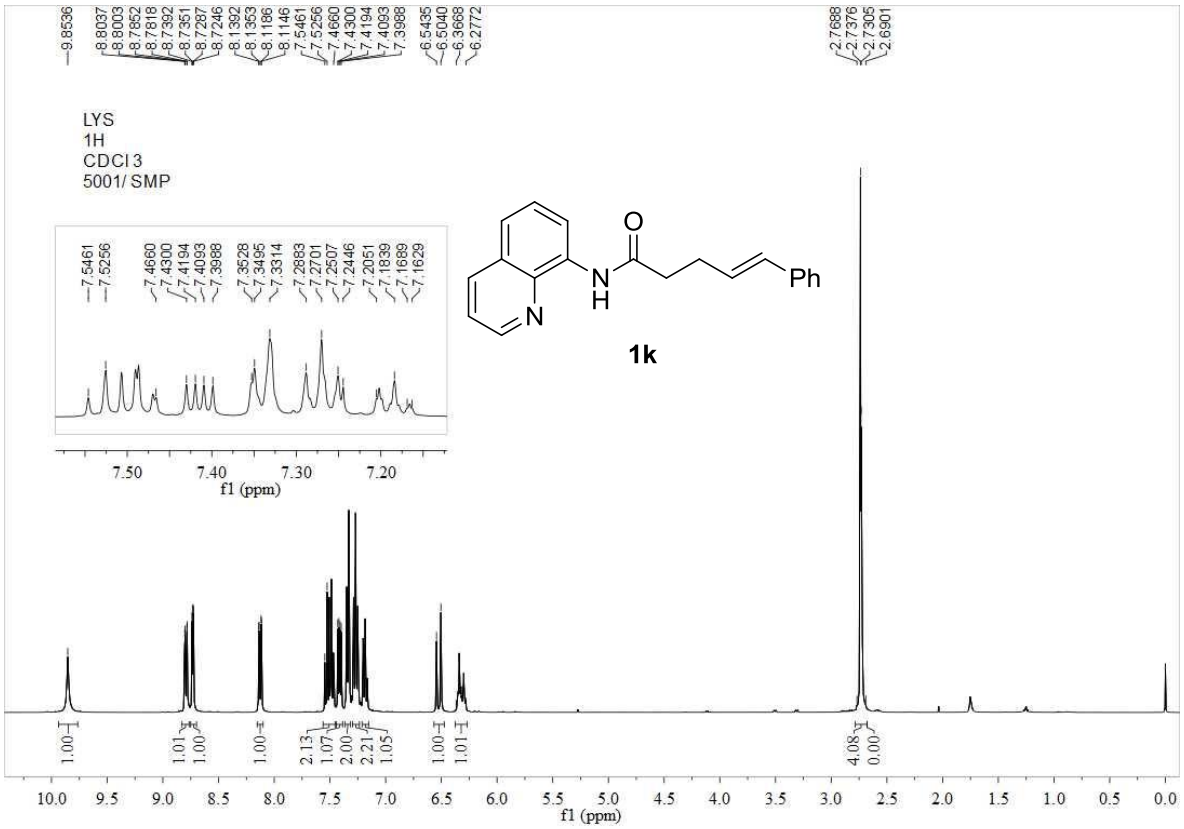
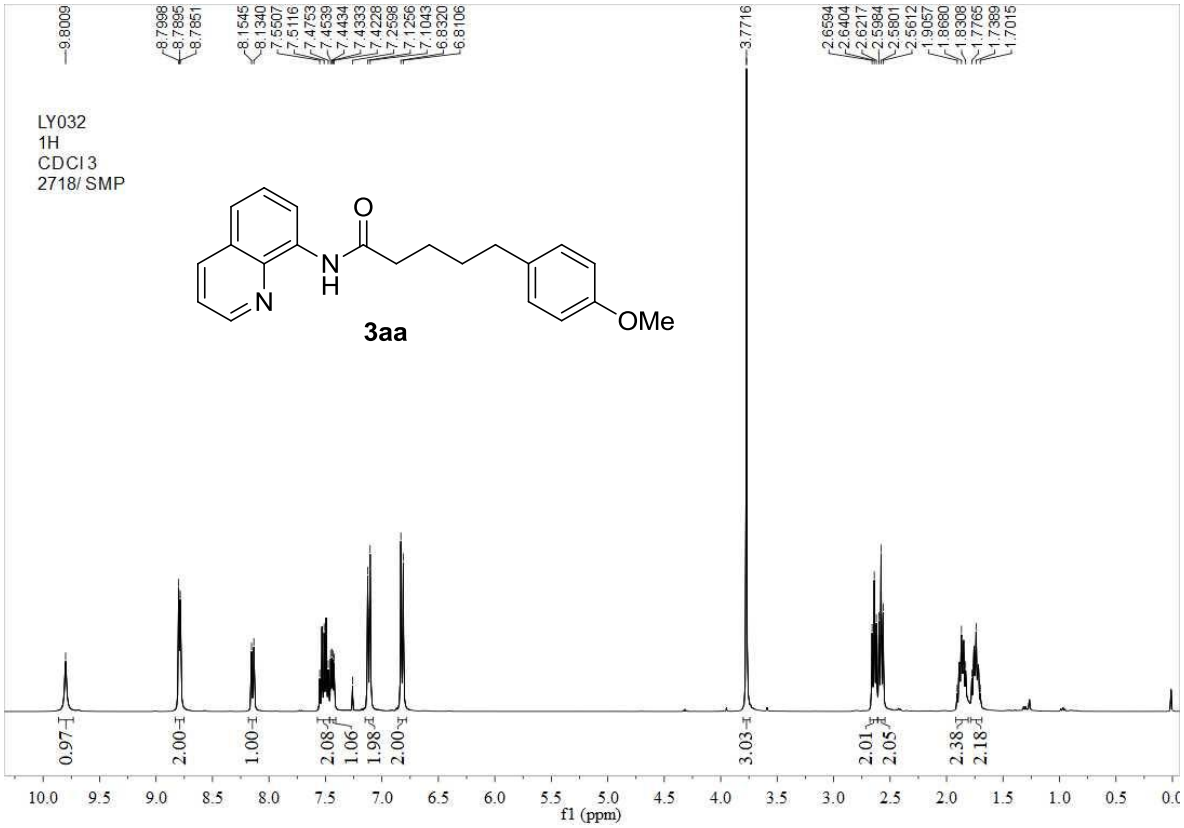
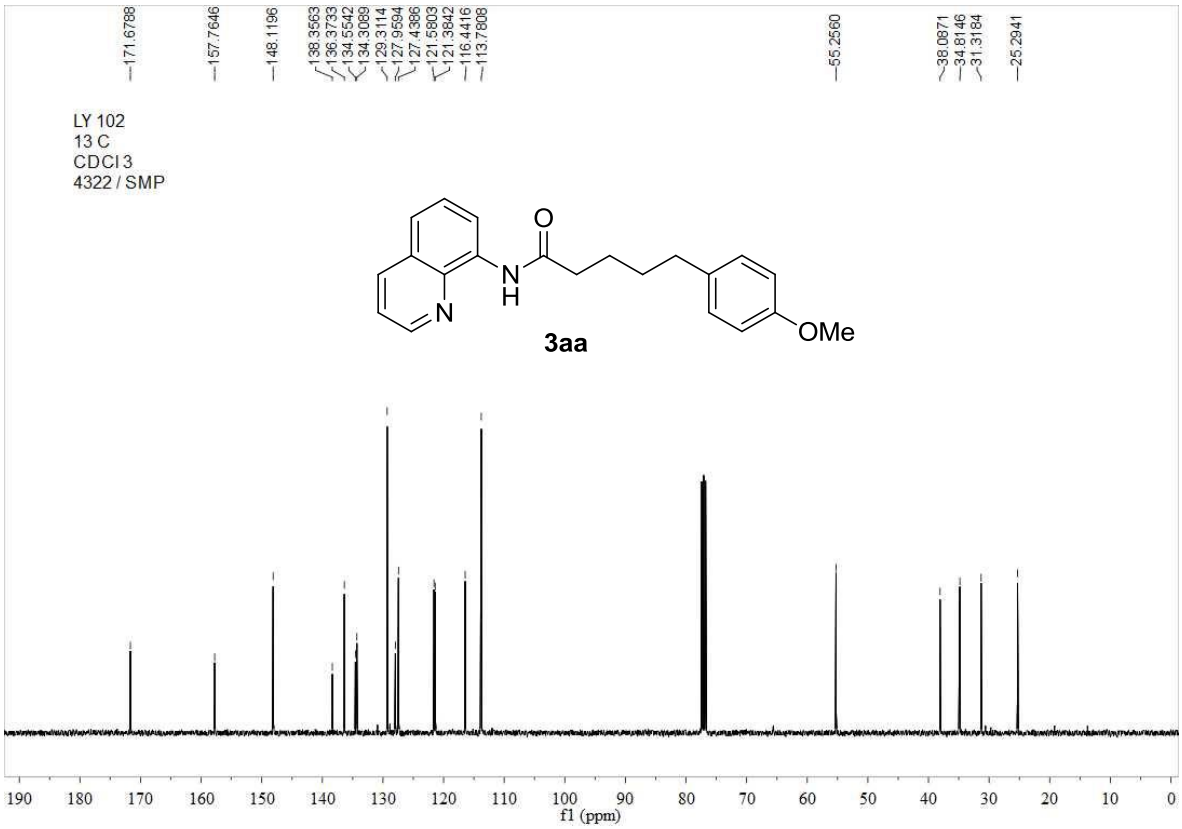
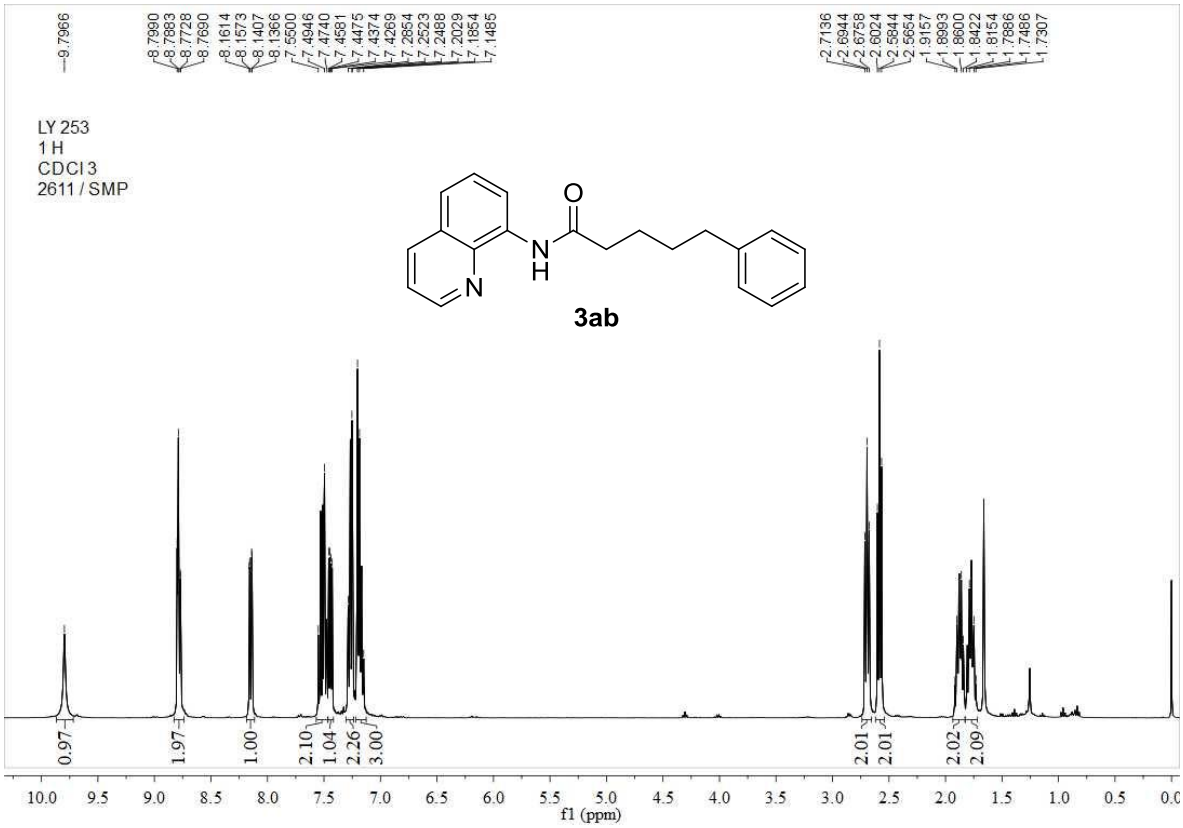
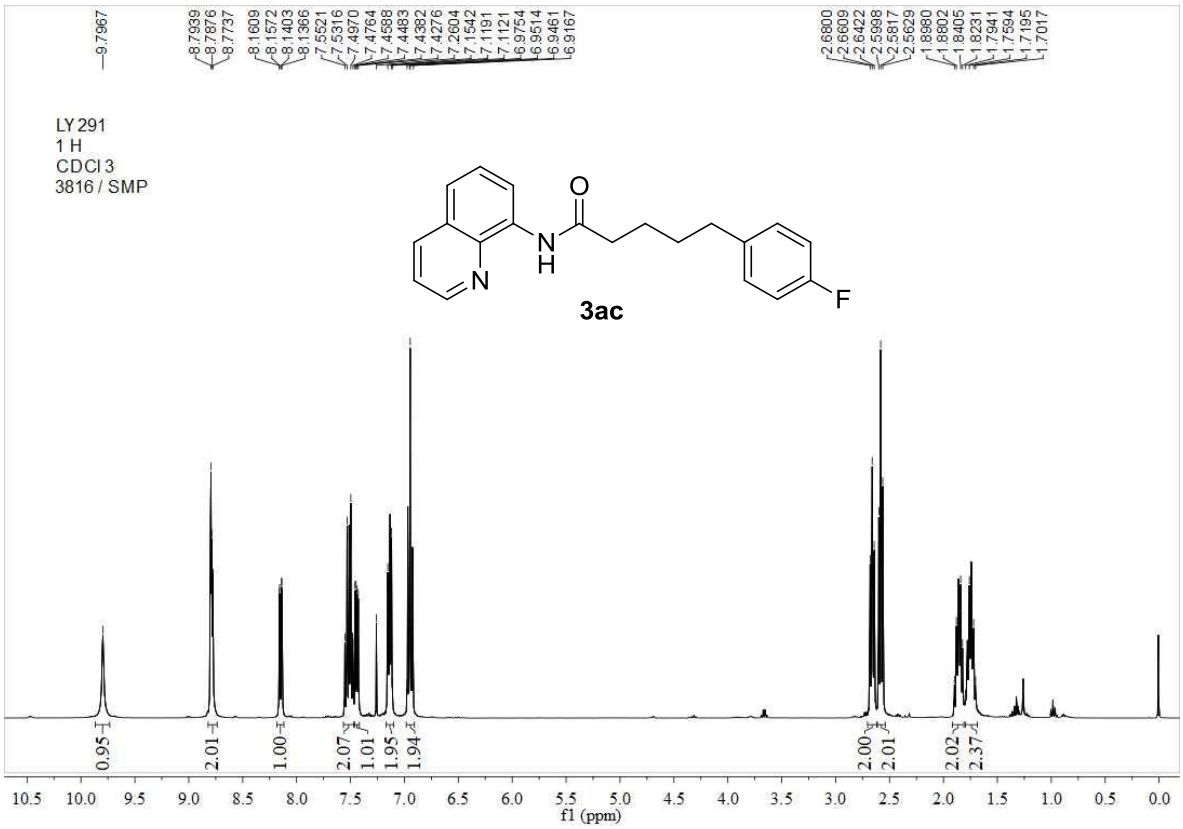
CDCl3
SMP/ 9056
O
N
H
N
Cy
1j
f1 (ppm)

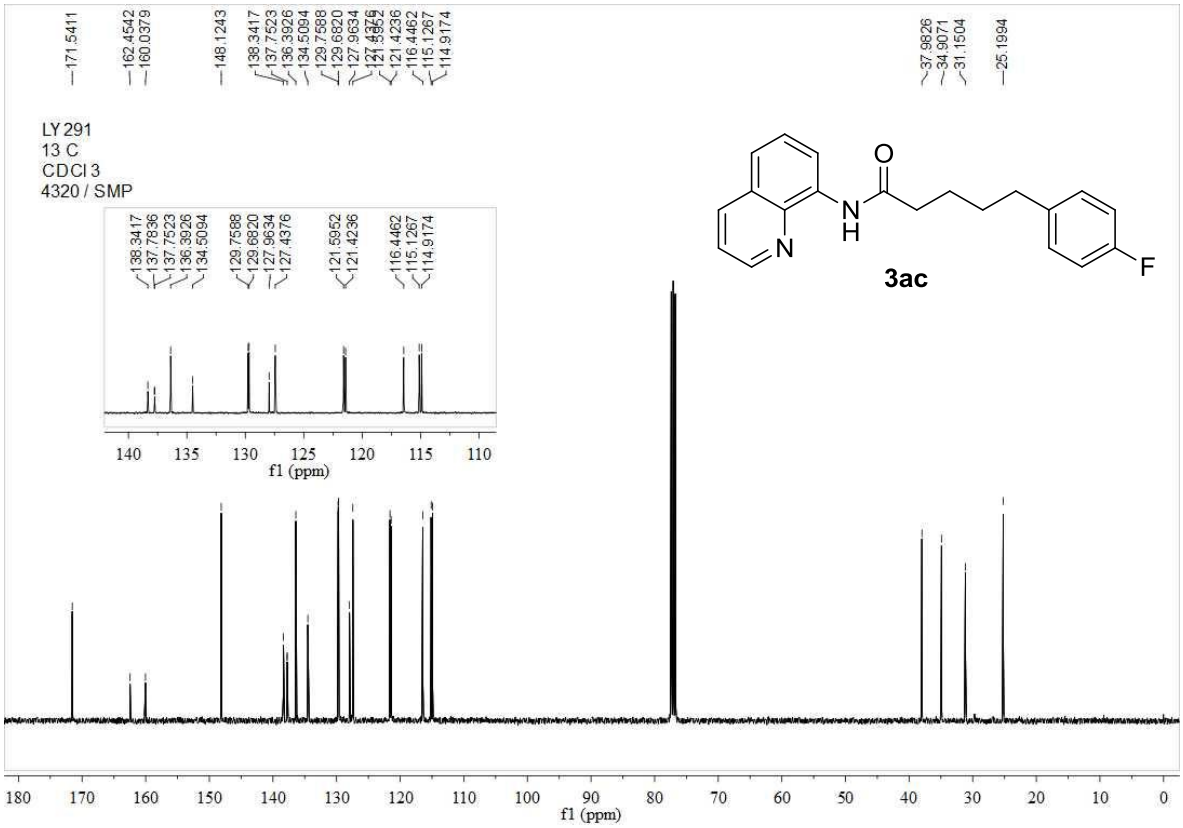

LYS
1H
CDCl3
5001/ SMP
1k
f1 (ppm)

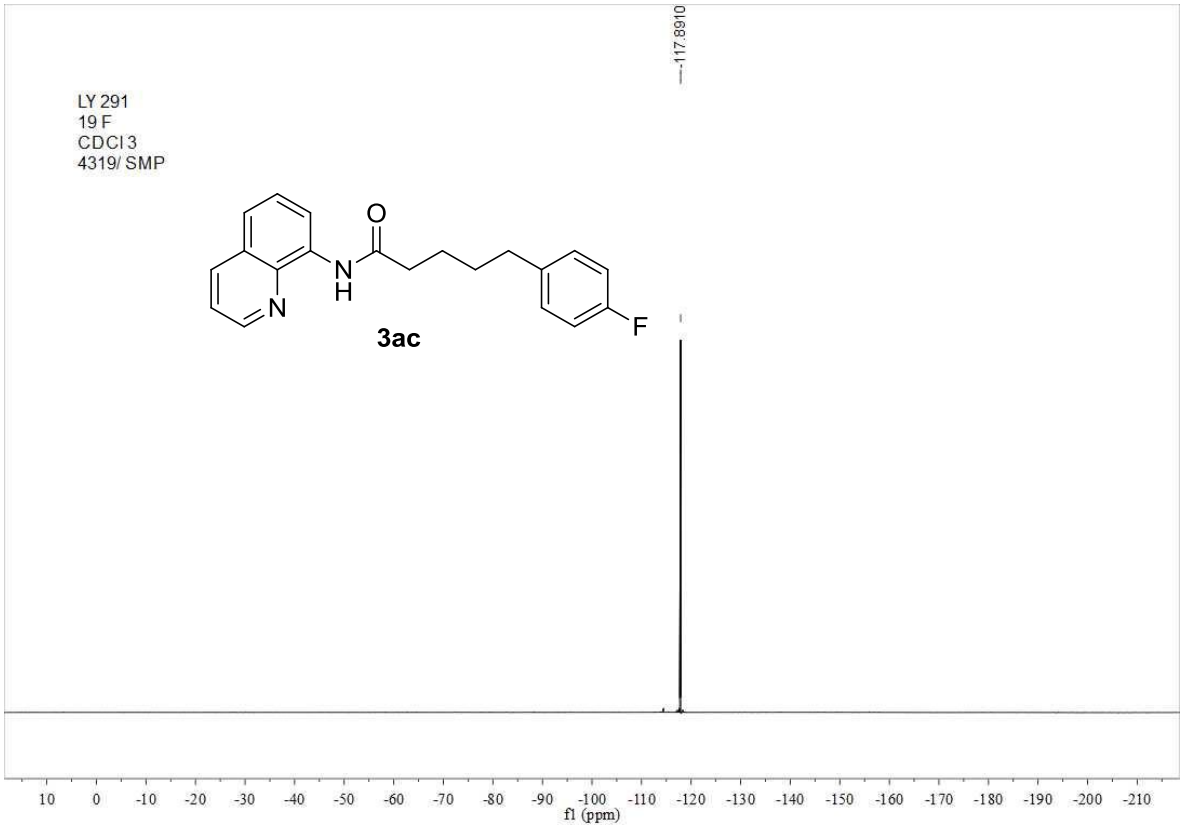

LY032
1H
CDCl3
2718/ SMP
3aa
OMe
f1 (ppm)

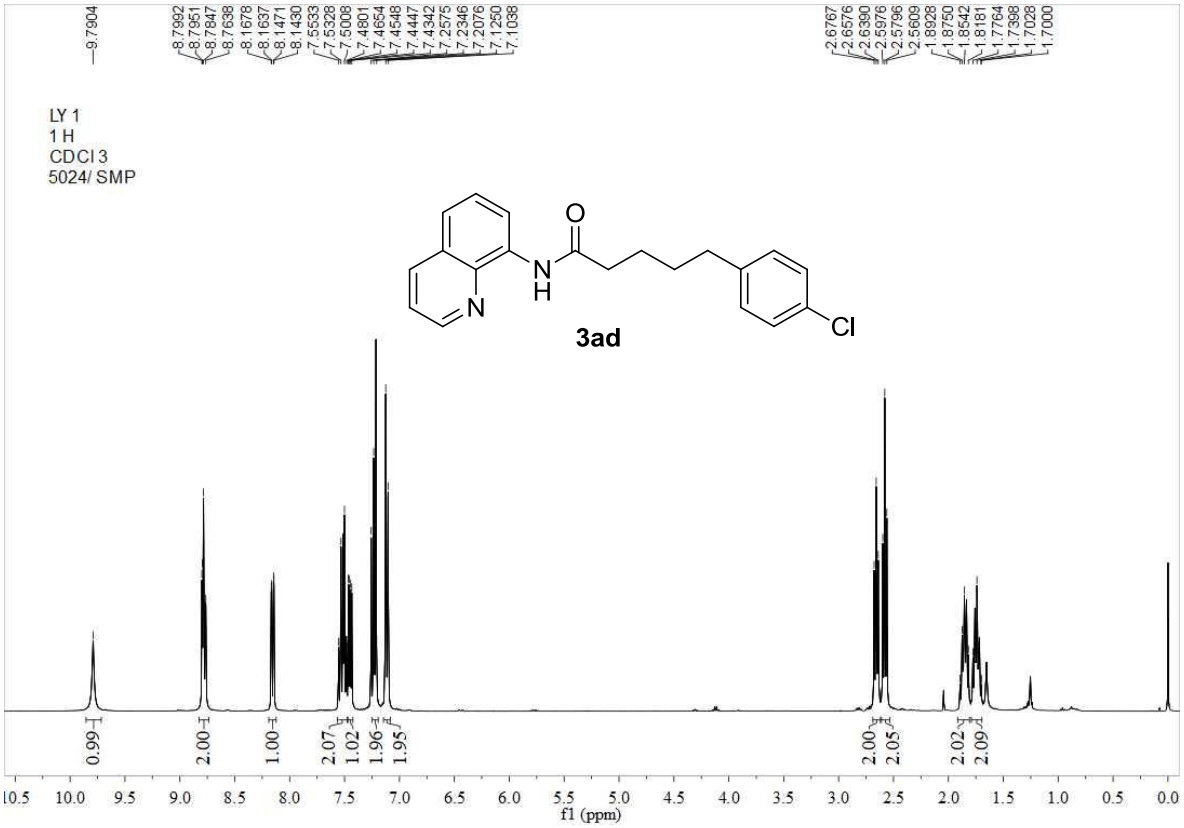

171.6788
157.7646
148.1196
138.3563
136.3733
134.5542
134.3089
129.3114
127.9594
127.4386
121.5803
121.3842
116.4416
113.7808
55.2560
38.0871
34.8146
31.3184
25.2941
LY 102
13 C
CDCl3
4322 / SMP
O
N
H
N
OMe
3aa
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

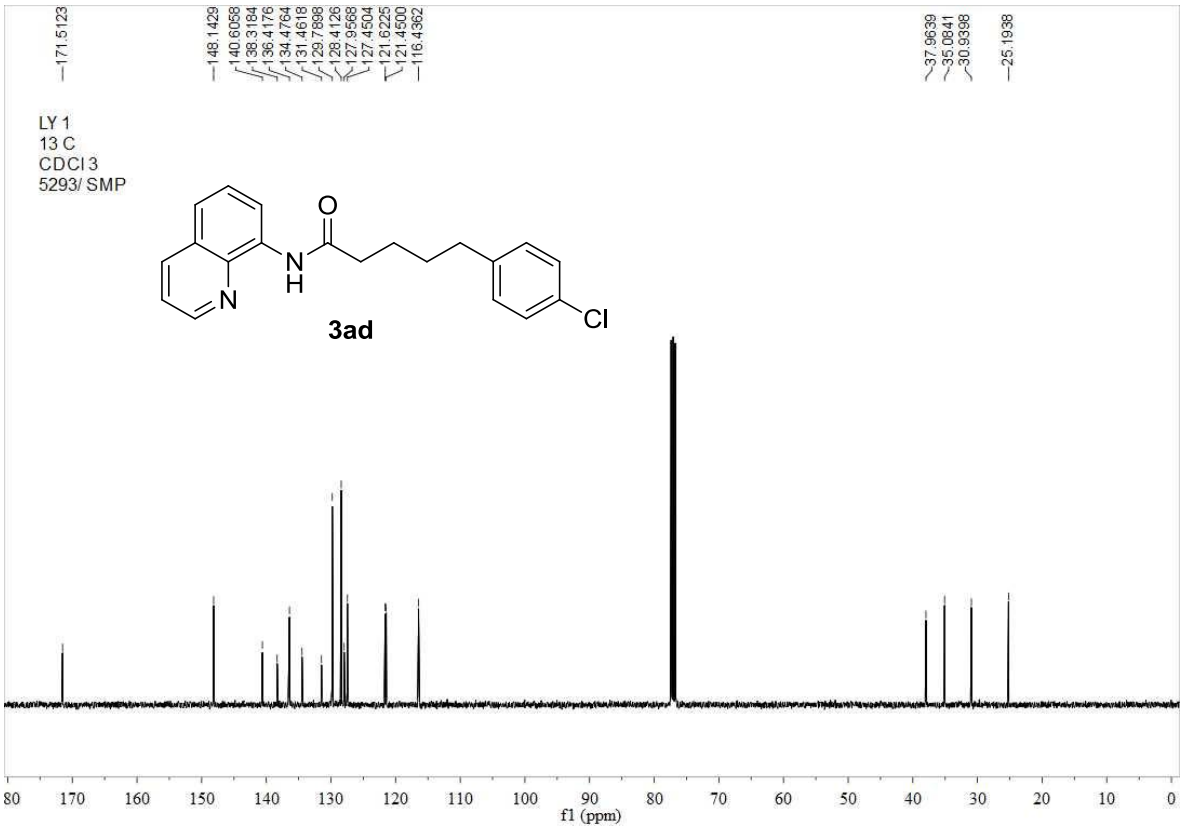

9.7966
8.7990
8.7883
8.7728
8.7690
8.1614
8.1573
8.1407
8.1366
7.5500
7.4946
7.4740
7.4581
7.4475
7.4374
7.4269
7.2854
7.2523
7.2488
7.2029
7.1854
7.1485
2.7136
2.6944
2.6758
2.6024
2.5844
2.5654
1.9157
1.8993
1.8600
1.8422
1.8154
1.7886
1.7486
1.7307
LY 253
1 H
CDCl3
2611 / SMP
O
N
H
N
3ab
0.97
1.97
1.00
2.10
1.04
2.26
3.00
2.01
2.01
2.02
2.09
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
f1 (ppm)

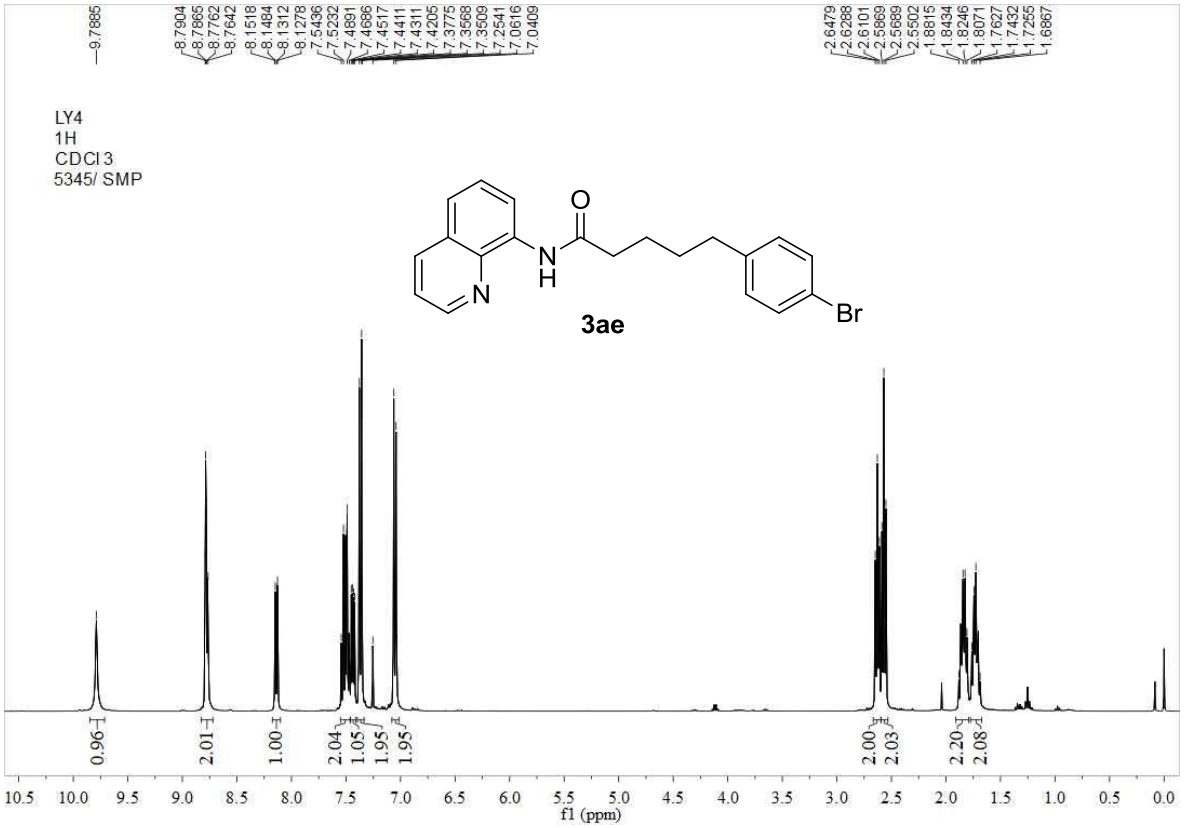

LY 291
1 H
CDCl 3
3816 / SMP
3ac
f1 (ppm)

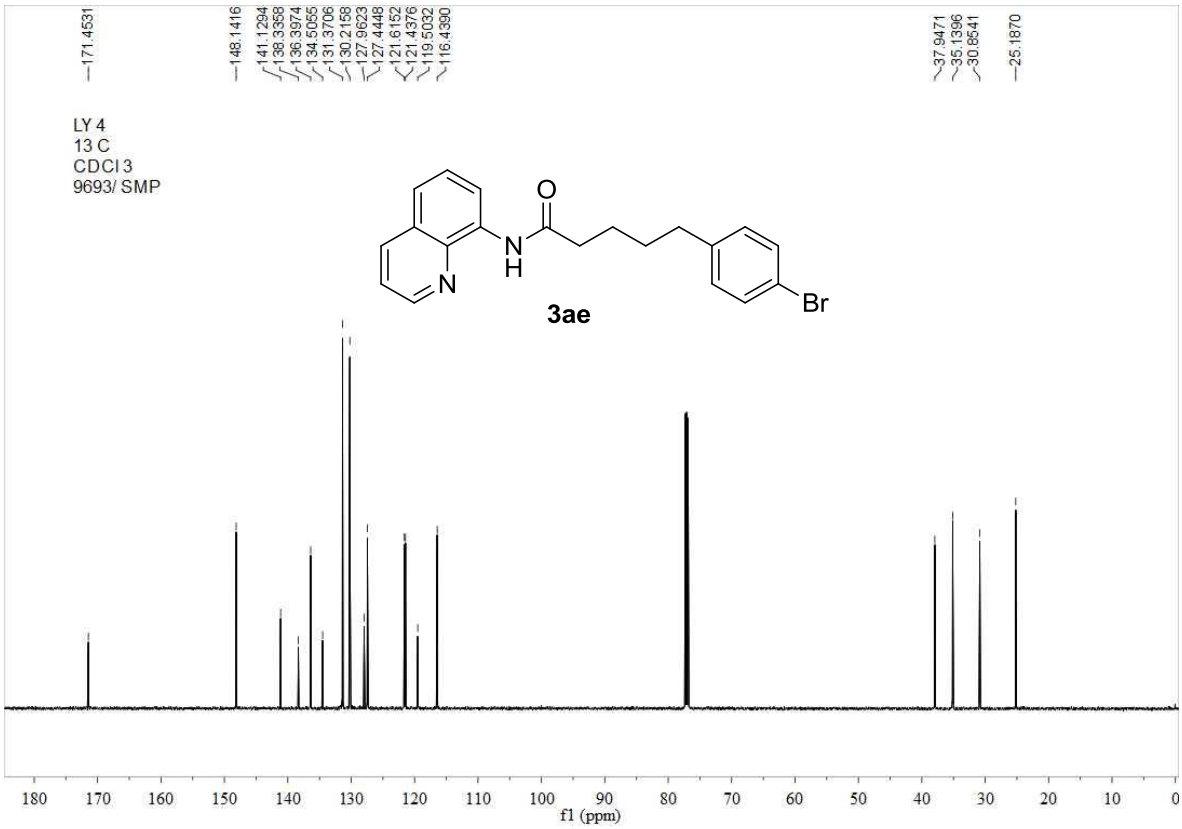

LY 291
13 C
CDCl 3
4320 / SMP
3ac
f1 (ppm)

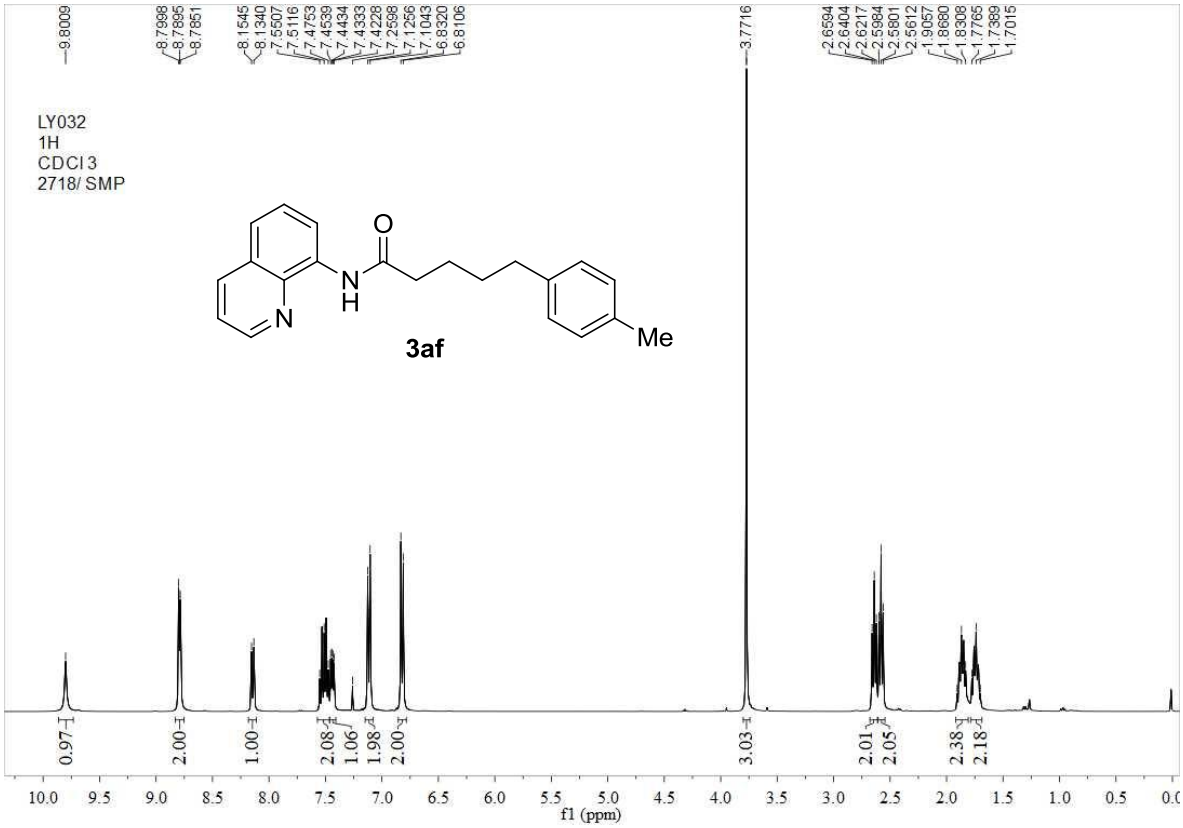

LY 291
19 F
CDCl 3
4319/ SMP
-117.8910
O
N
H
N
F
3ac
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

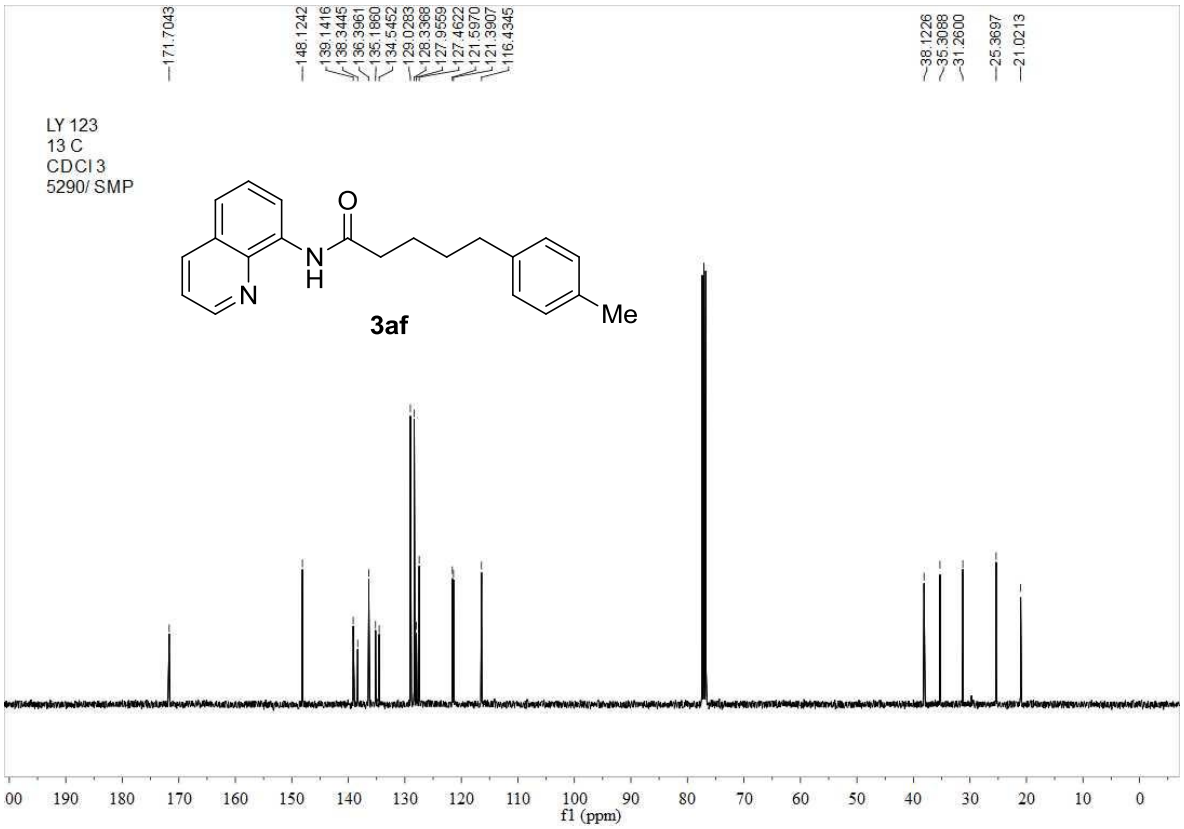

-9.7904
8.7992
8.7951
8.7847
8.7638
8.1678
8.1637
8.1471
8.1430
7.5533
7.5328
7.5008
7.4801
7.4654
7.4548
7.4447
7.4342
7.2575
7.2346
7.2076
7.1250
7.1038
2.6767
2.6576
2.6390
2.5976
2.5796
2.5609
1.8928
1.8750
1.8542
1.8181
1.7764
1.7398
1.7028
1.7000
LY 1
1 H
CDCl 3
5024/ SMP
O
N
H
N
Cl
3ad
0.99
2.00
1.00
2.07
1.02
1.96
1.95
2.00
2.05
2.02
2.09
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
f1 (ppm)

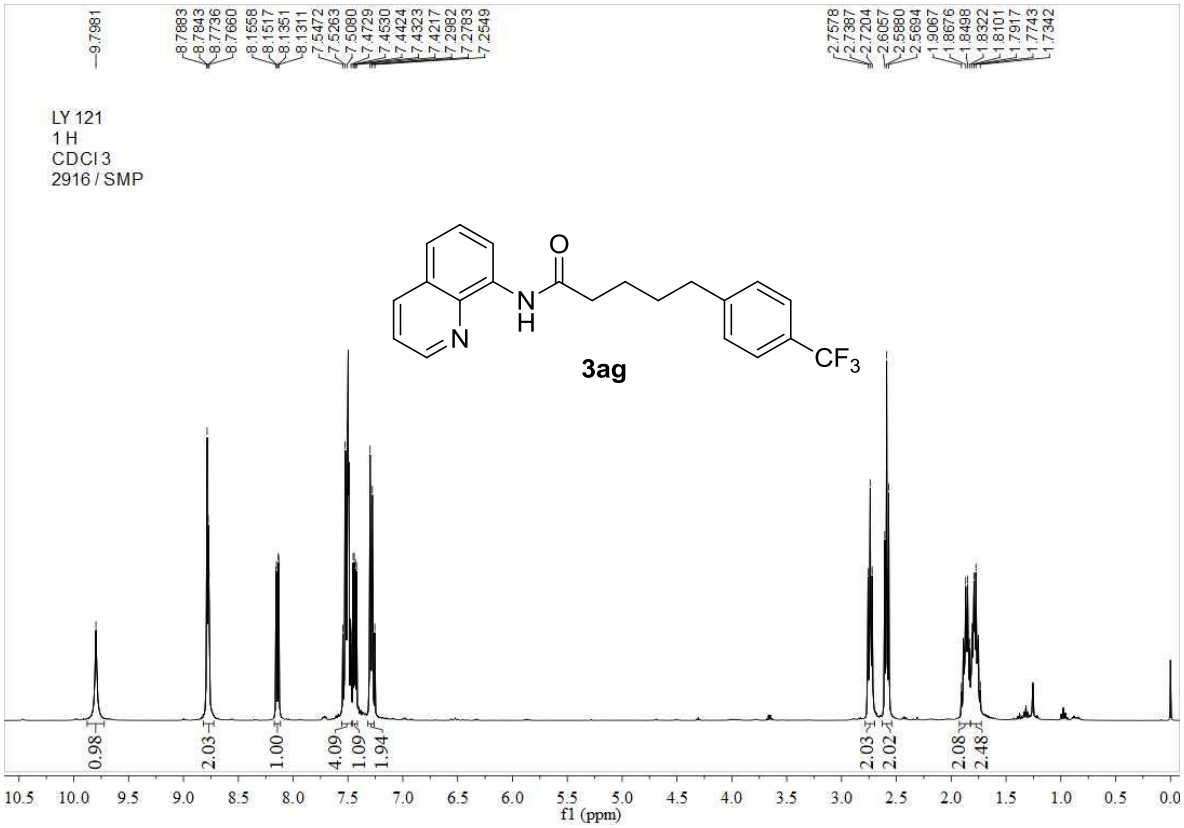

171.5123
148.1429
140.6058
138.3184
136.4176
134.4764
131.4618
129.7898
128.4126
127.9568
127.4504
121.6225
121.4500
116.4362
37.9639
35.0841
30.9398
25.1938
LY 1
13 C
CDCl 3
5293/ SMP
O
N
H
N
Cl
3ad
f1 (ppm)

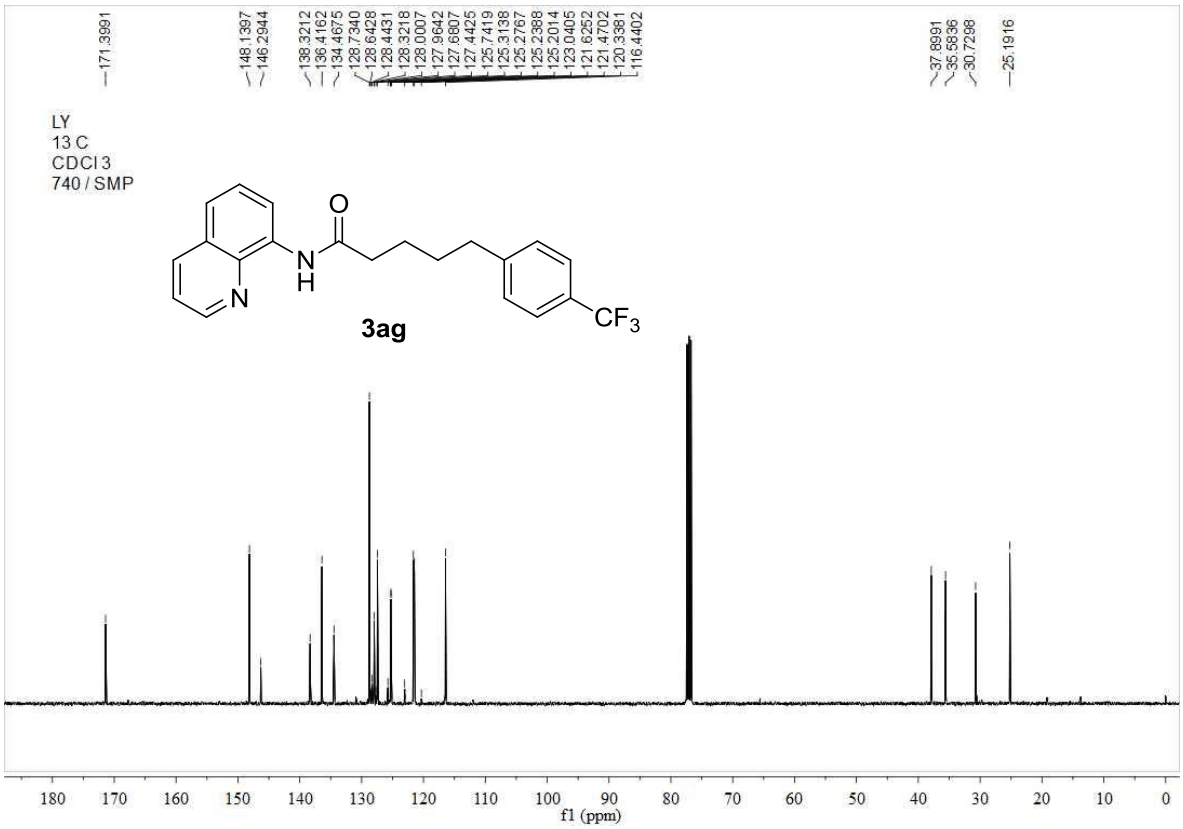

9.7885
8.7904
8.7865
8.7762
8.7642
8.1518
8.1484
8.1312
8.1278
7.5436
7.5232
7.4891
7.4686
7.4517
7.4411
7.4311
7.4205
7.3775
7.3568
7.3509
7.2541
7.0616
7.0409
2.6479
2.6288
2.6101
2.5869
2.5689
2.5502
1.8815
1.8434
1.8246
1.8071
1.7627
1.7432
1.7255
1.6867
LY4
1H
CDCl 3
5345/ SMP
O
N
H
N
Br
3ae
0.96
2.01
1.00
2.04
1.05
1.95
1.95
2.00
2.03
2.20
2.08
f1 (ppm)

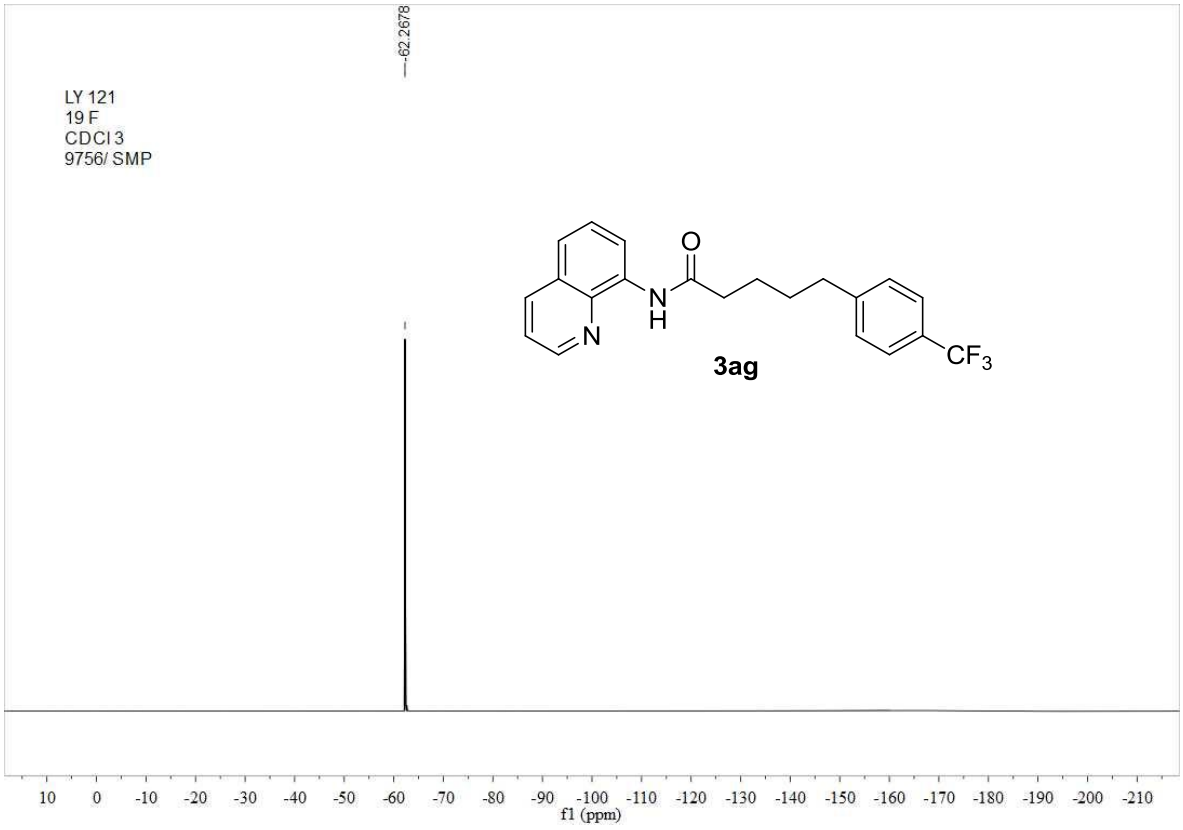

171.4531
148.1416
141.1294
138.3358
136.3974
134.5055
131.3706
130.2158
127.9623
127.4448
121.6152
121.4376
119.5032
116.4390
37.9471
35.1396
30.8541
25.1870
LY 4
13 C
CDCl 3
9693/ SMP
O
N
H
N
Br
3ae
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

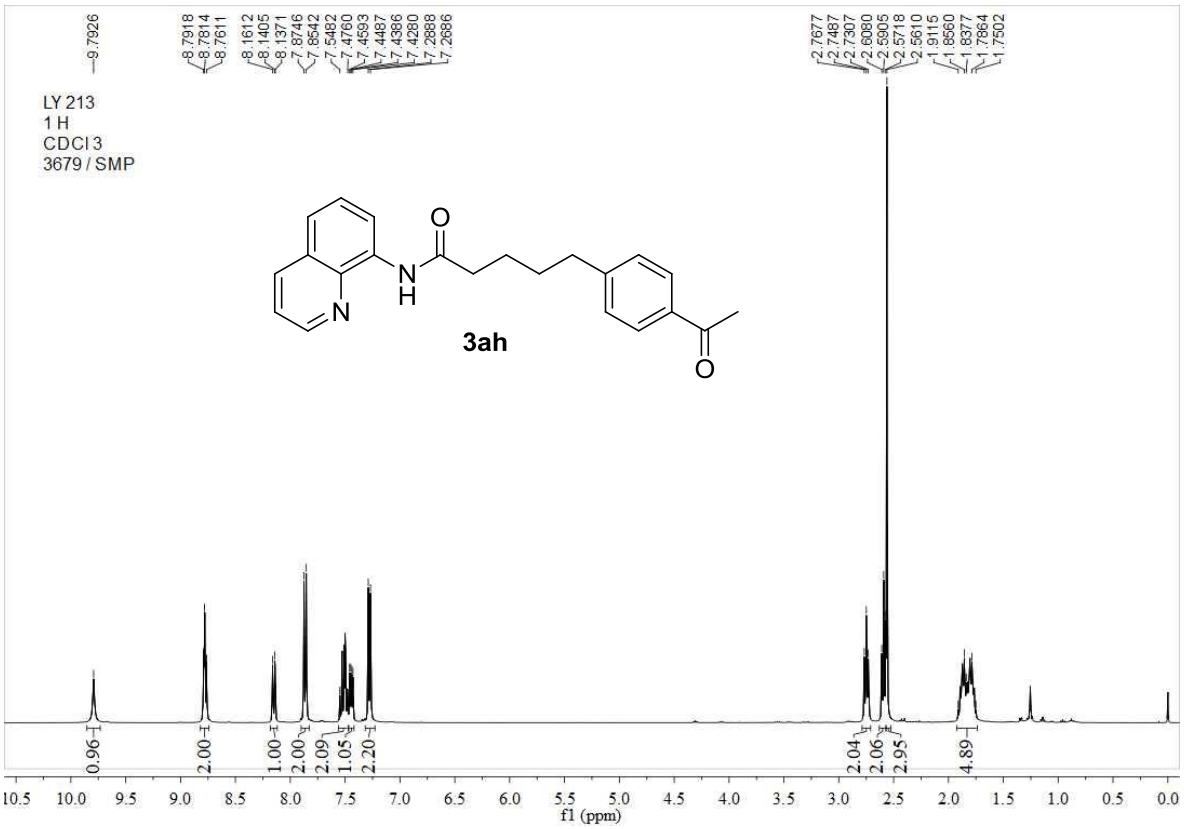

9.8009
8.7998
8.7895
8.7851
8.1545
8.1340
7.5507
7.5116
7.4753
7.4539
7.4434
7.4333
7.4228
7.2598
7.1256
7.1043
6.8320
6.8106
3.7716
2.6594
2.6404
2.6217
2.5984
2.5801
2.5612
1.9057
1.8680
1.8308
1.7765
1.7389
1.7015
LY032
1H
CDCl 3
2718/ SMP
O
N
H
N
Me
3af
0.97
2.00
1.00
2.08
1.06
1.98
2.00
3.03
2.01
2.05
2.38
2.18
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
f1 (ppm)

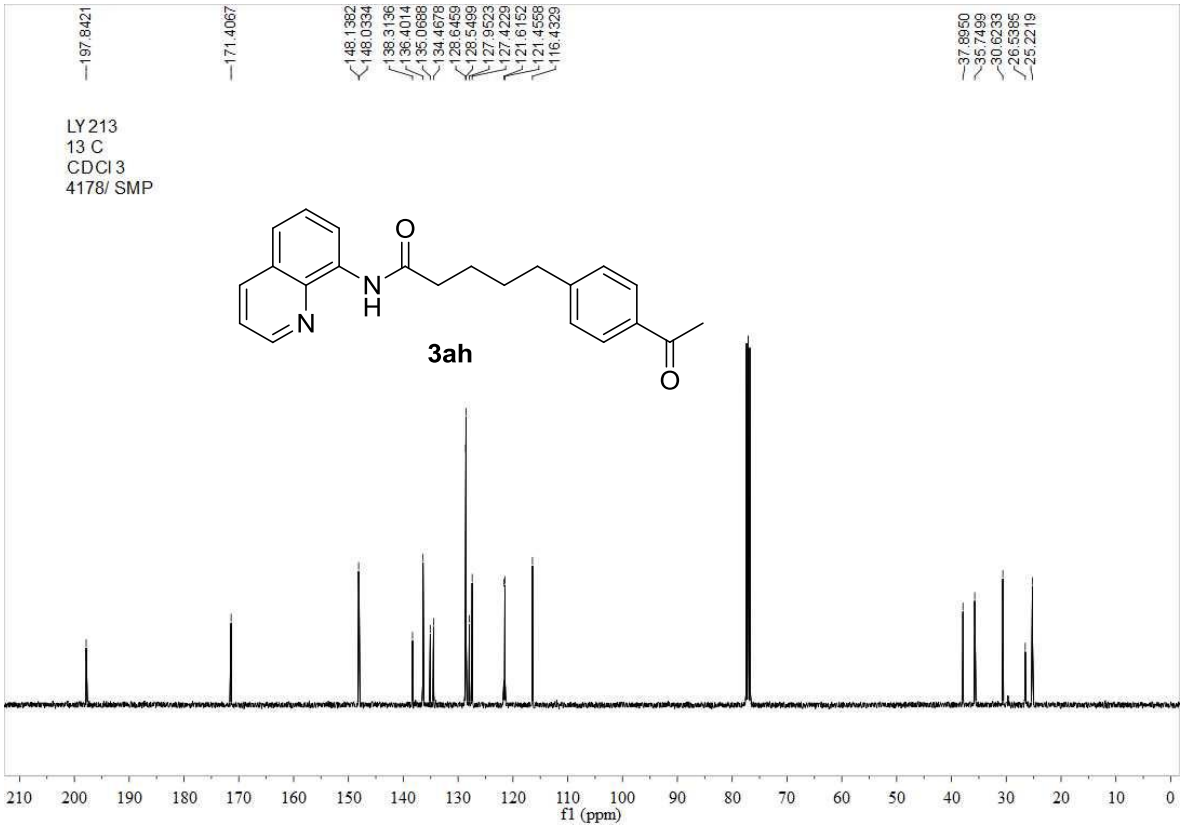

LY 123
13 C
CDCl 3
5290/ SMP
171.7043
148.1242
139.1416
138.3445
136.3961
135.1860
134.5452
129.0283
128.3368
127.9559
127.4622
121.5970
121.3907
116.4345
38.1226
35.3088
31.2600
25.3697
21.0213
O
N
H
N
Me
3af
f1 (ppm)

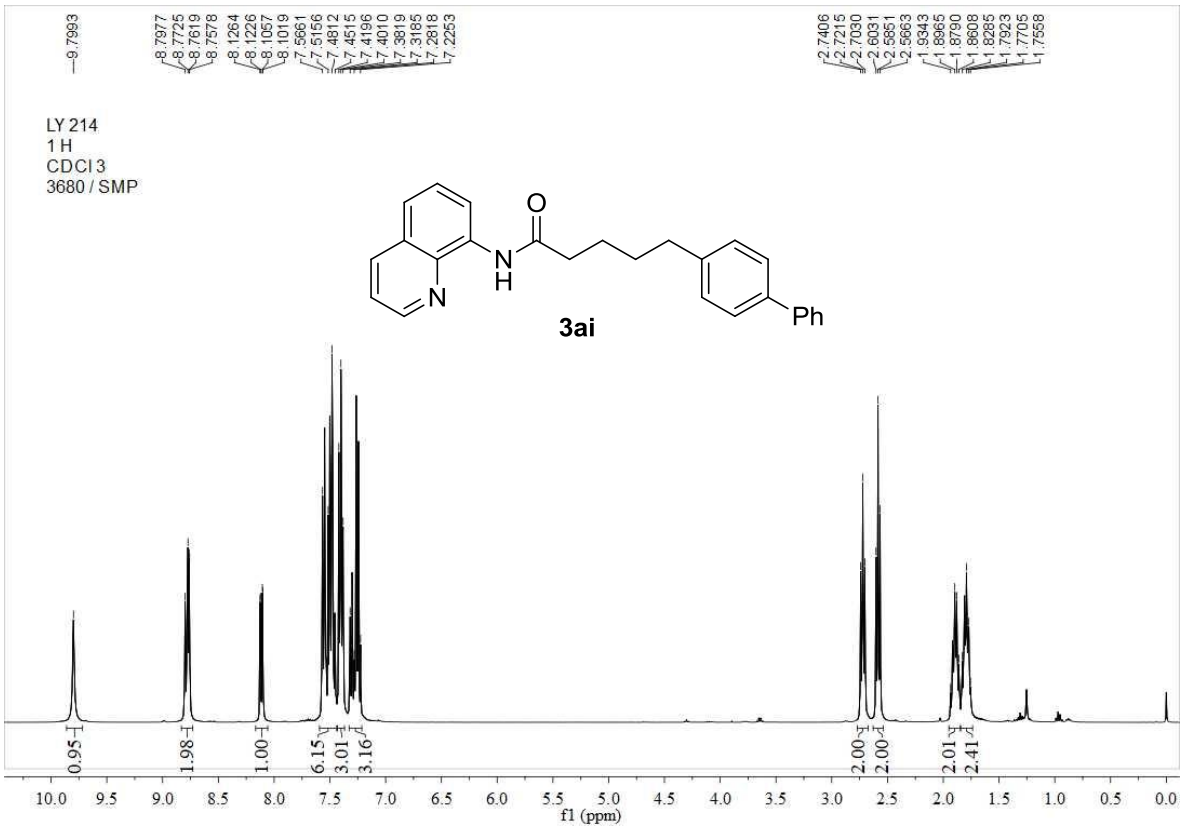

LY 121
1 H
CDCl 3
2916 / SMP
9.7981
8.7883
8.7843
8.7736
8.7660
8.1558
8.1517
8.1351
8.1311
7.5472
7.5263
7.5080
7.4729
7.4530
7.4424
7.4323
7.4217
7.2982
7.2783
7.2549
2.7578
2.7387
2.7204
2.6057
2.5880
2.5694
1.9067
1.8676
1.8498
1.8322
1.8101
1.7917
1.7743
1.7342
O
N
H
N
CF3
3ag
0.98
2.03
1.00
4.09
1.09
1.94
2.03
2.02
2.08
2.48
f1 (ppm)

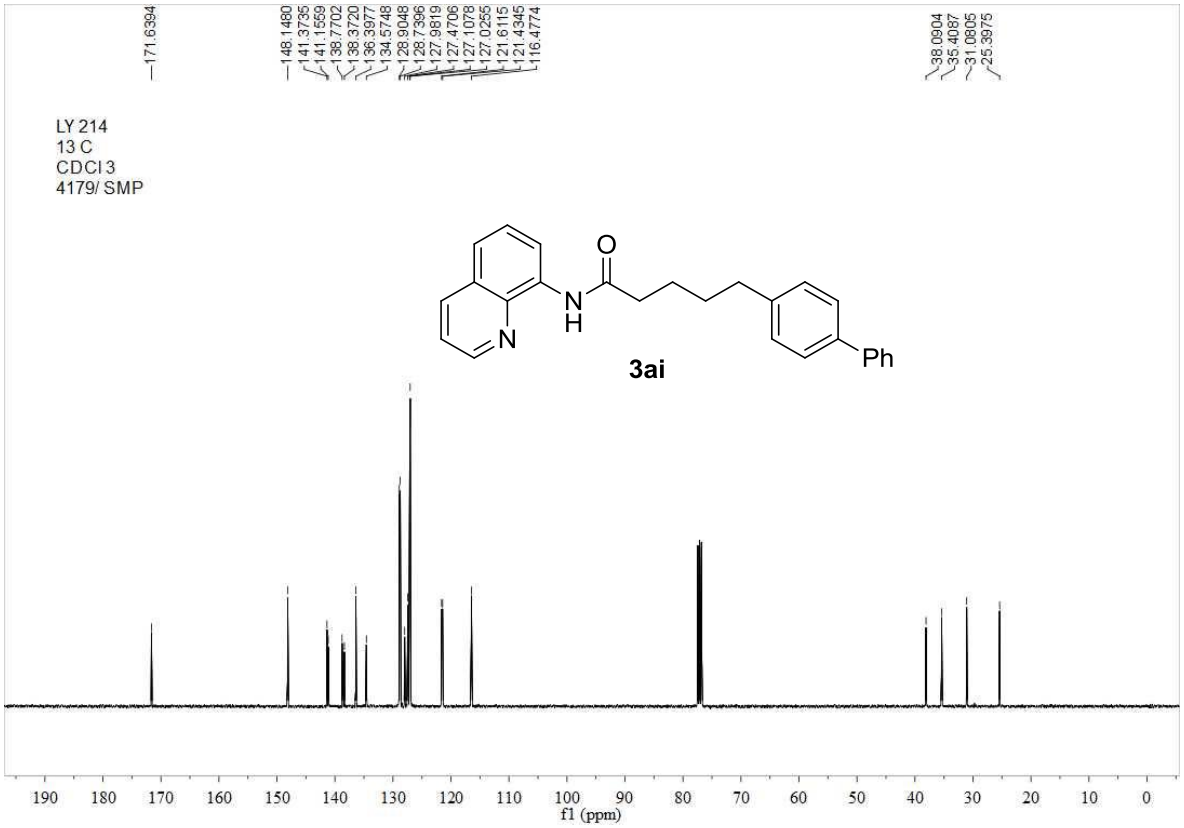

171.3991
148.1397
146.2944
138.3212
136.4162
134.4675
128.7340
128.6428
128.4431
128.3218
128.0007
127.9642
127.6807
127.4425
125.7419
125.3138
125.2767
125.2388
125.2014
123.0405
121.6252
121.4702
120.3381
116.4402
37.8991
35.5836
30.7298
25.1916
LY
13 C
CDCl 3
740 / SMP
O
N
H
N
CF3
3ag
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

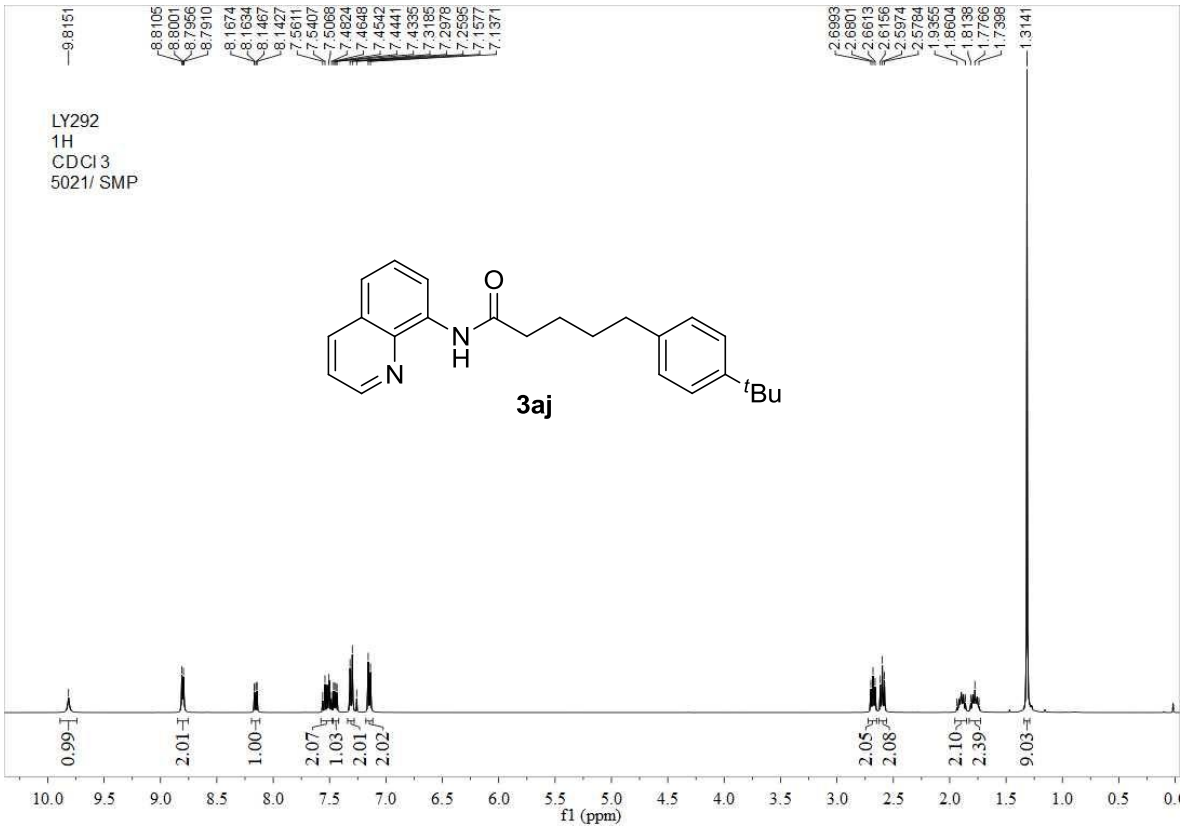

62.2678
LY 121
19 F
CDCl 3
9756/ SMP
O
N
H
N
CF3
3ag
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

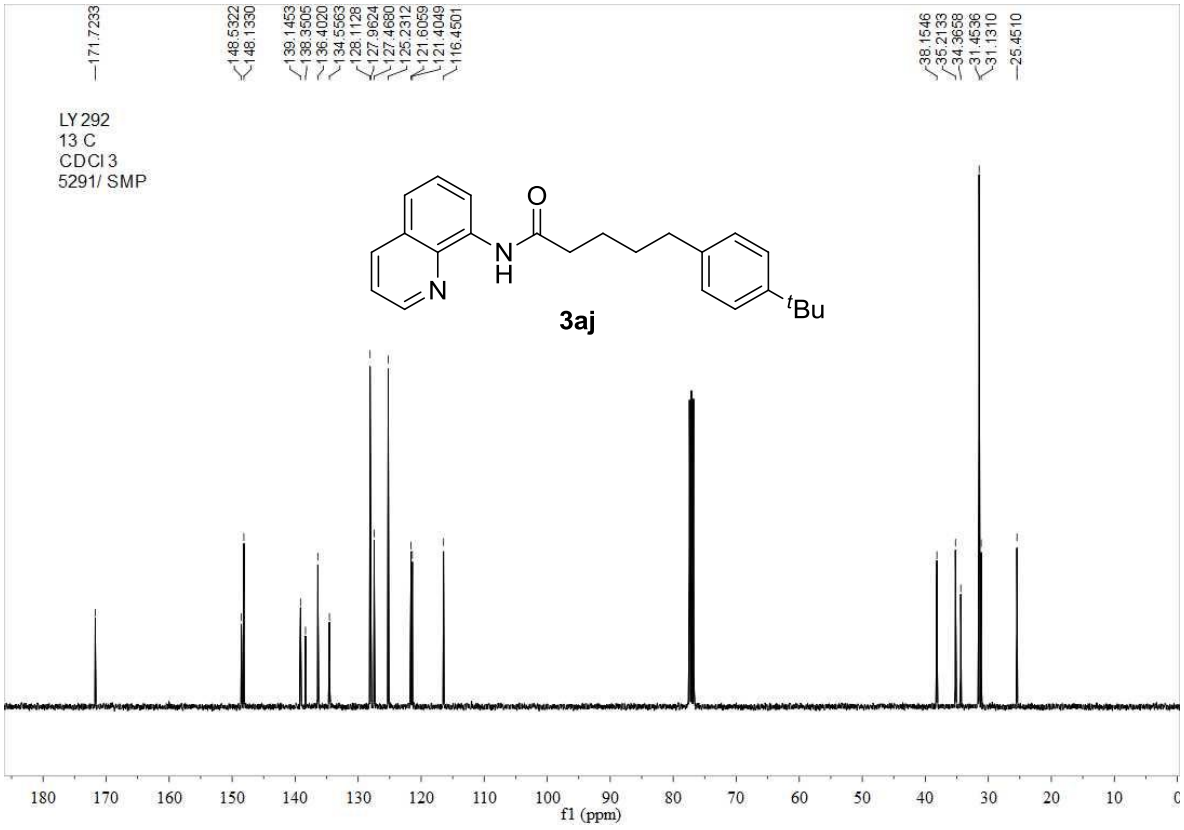

LY 213
1 H
CDCl 3
3679 / SMP
3ah
f1 (ppm)

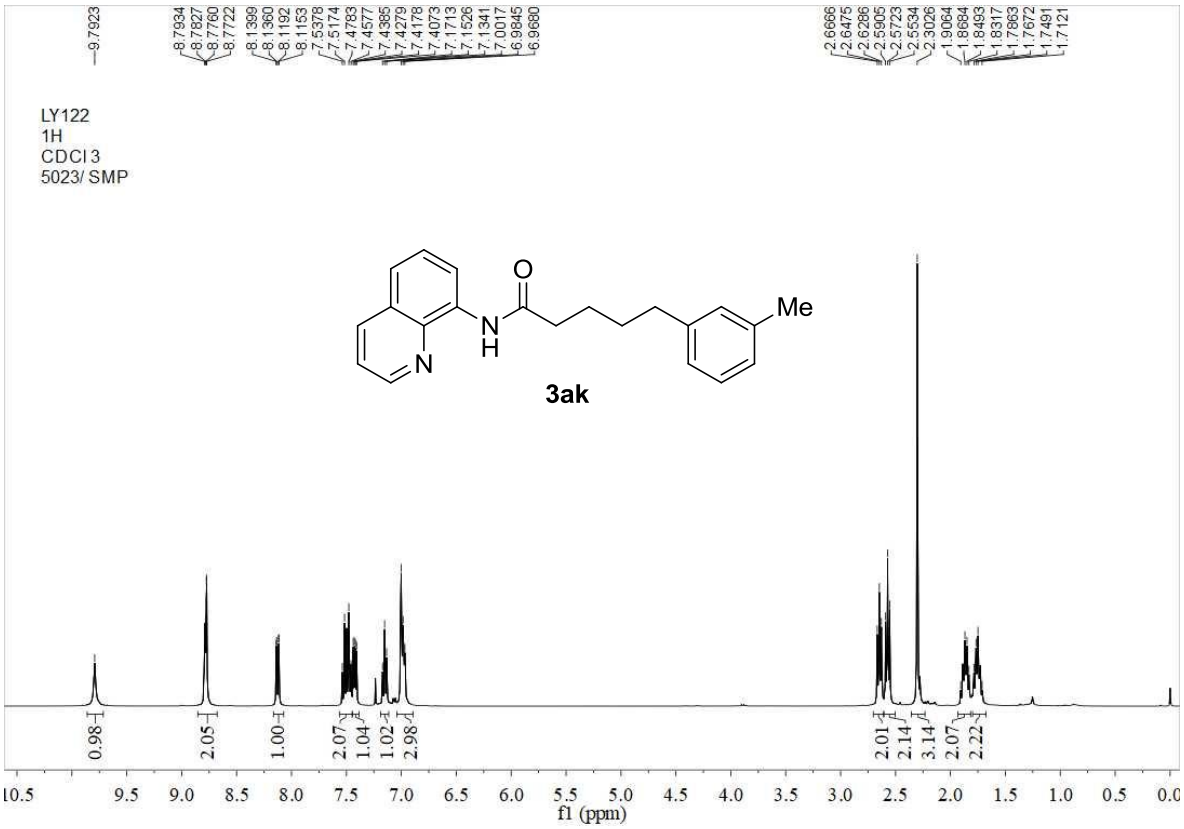

LY 213
13 C
CDCl 3
4178/ SMP
3ah
f1 (ppm)

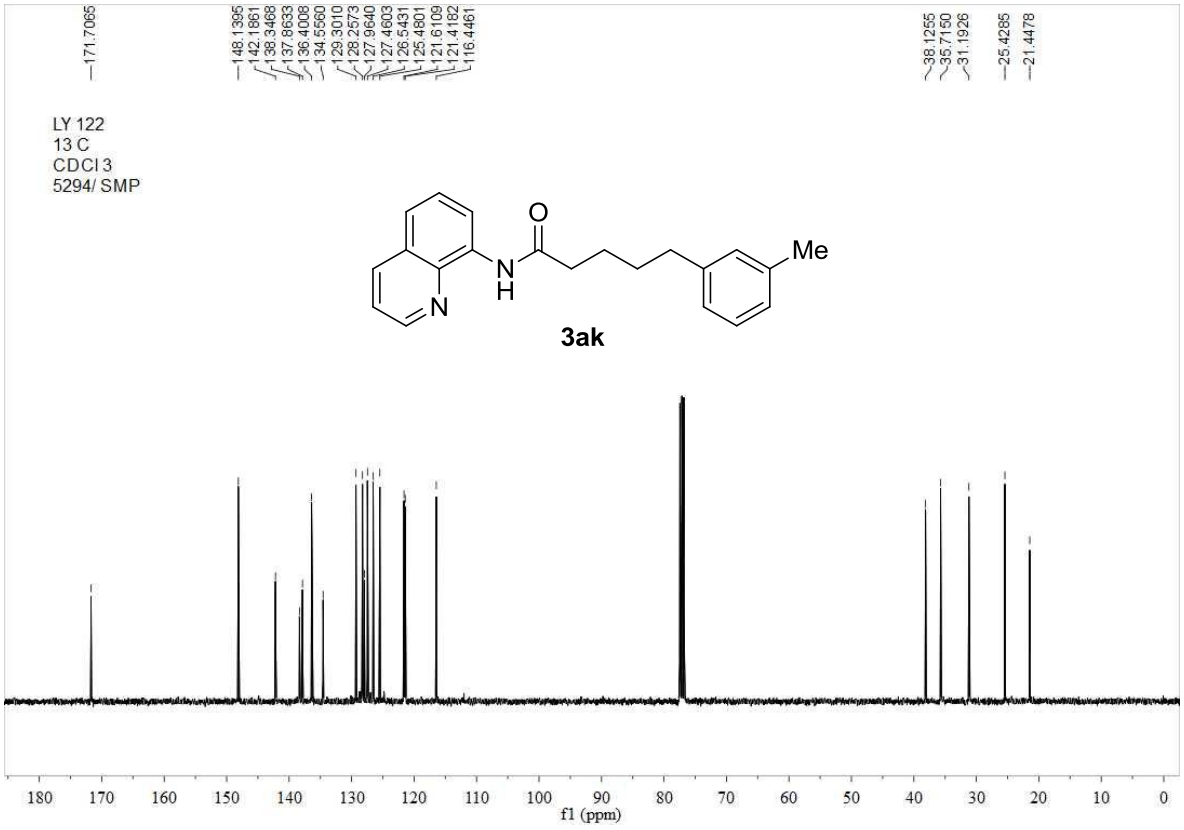

LY 214
1 H
CDCl 3
3680 / SMP
3ai
f1 (ppm)

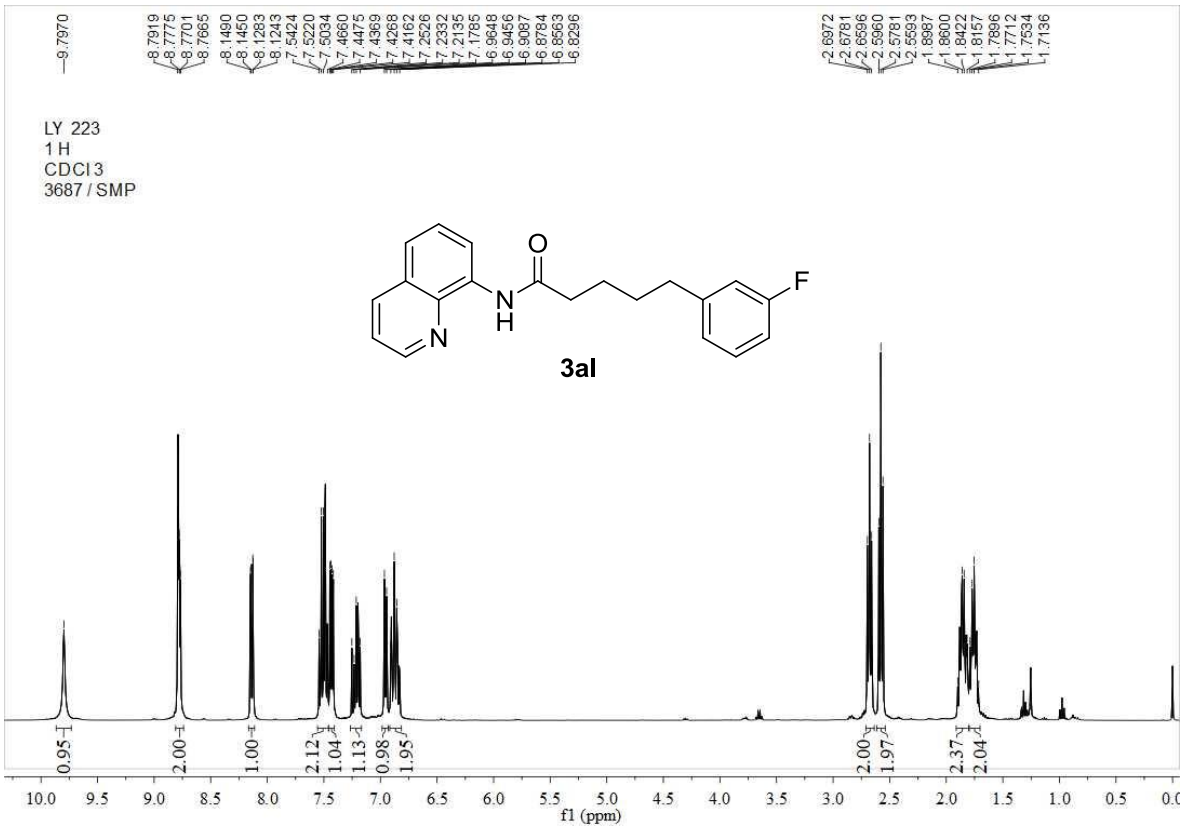

LY 214
13 C
CDCl 3
4179/ SMP
3ai
f1 (ppm)

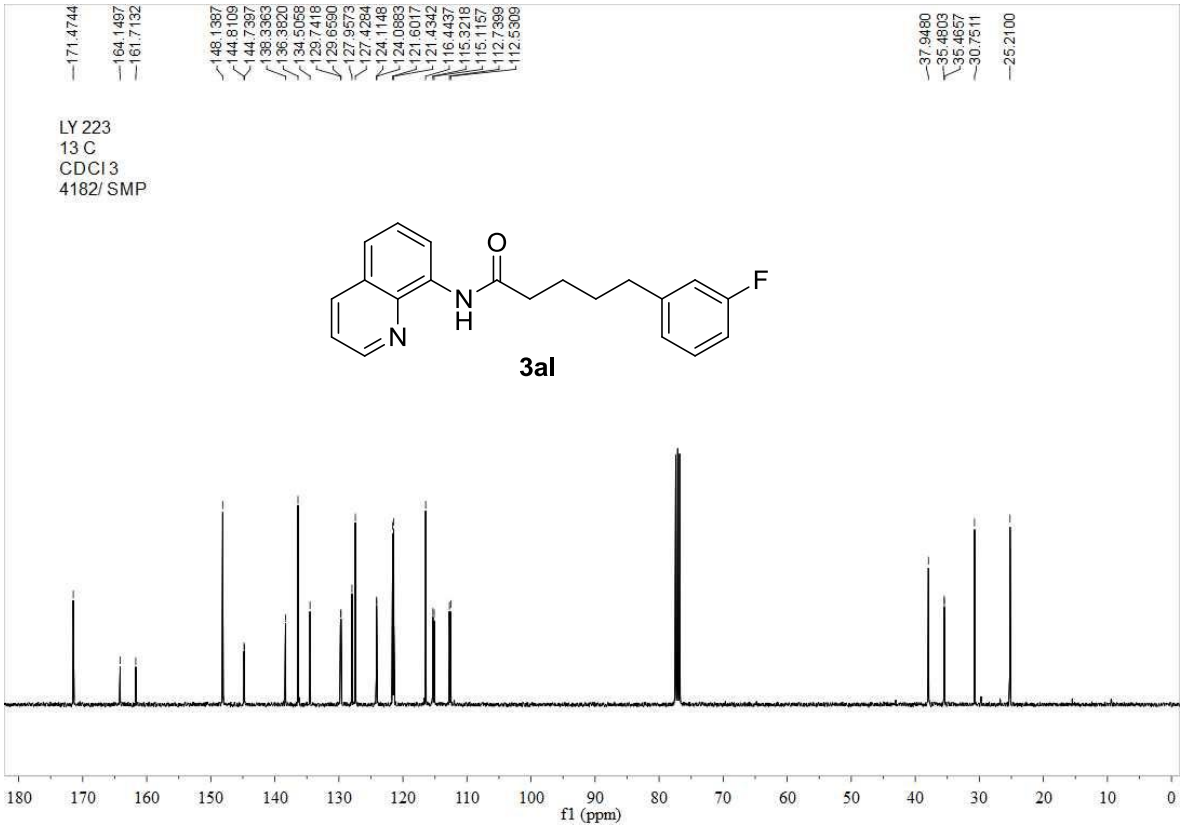

LY292
1H
CDCl3
5021/ SMP
3aj
f1 (ppm)

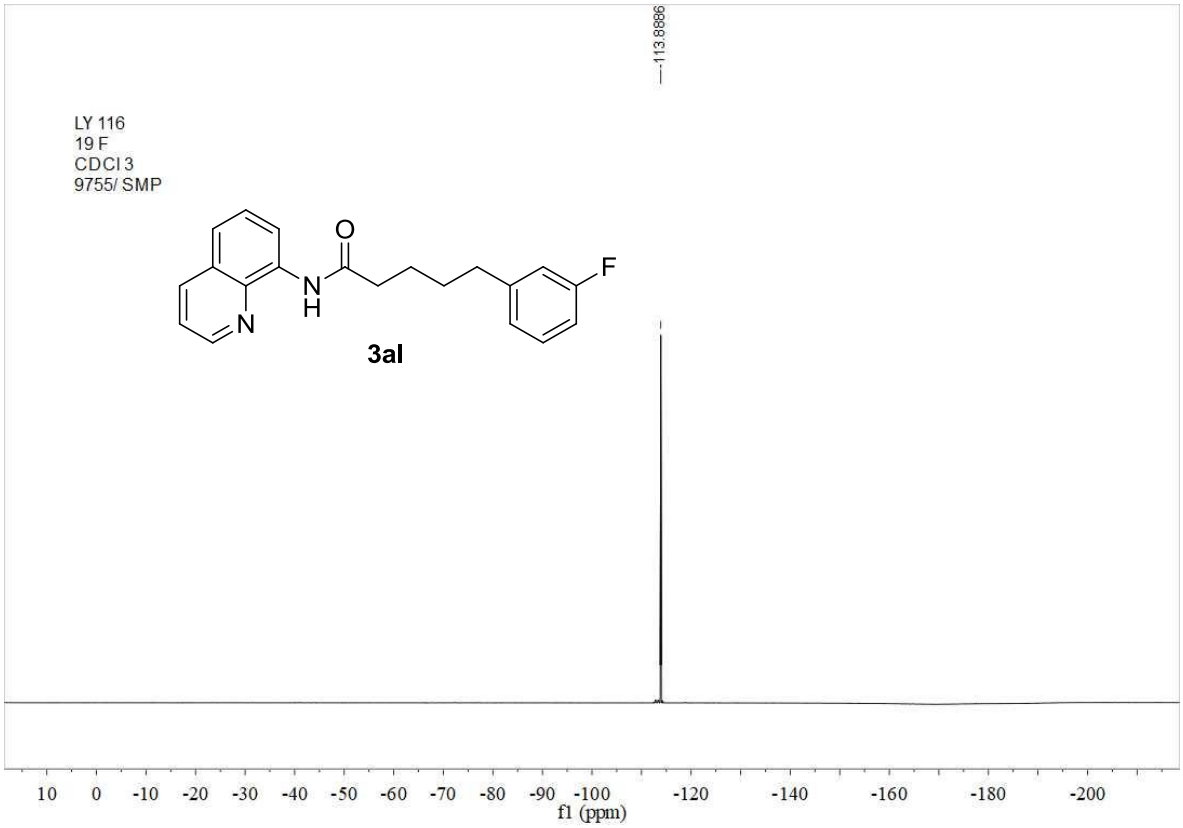

LY292
13 C
CDCl3
5291/ SMP
3aj
f1 (ppm)

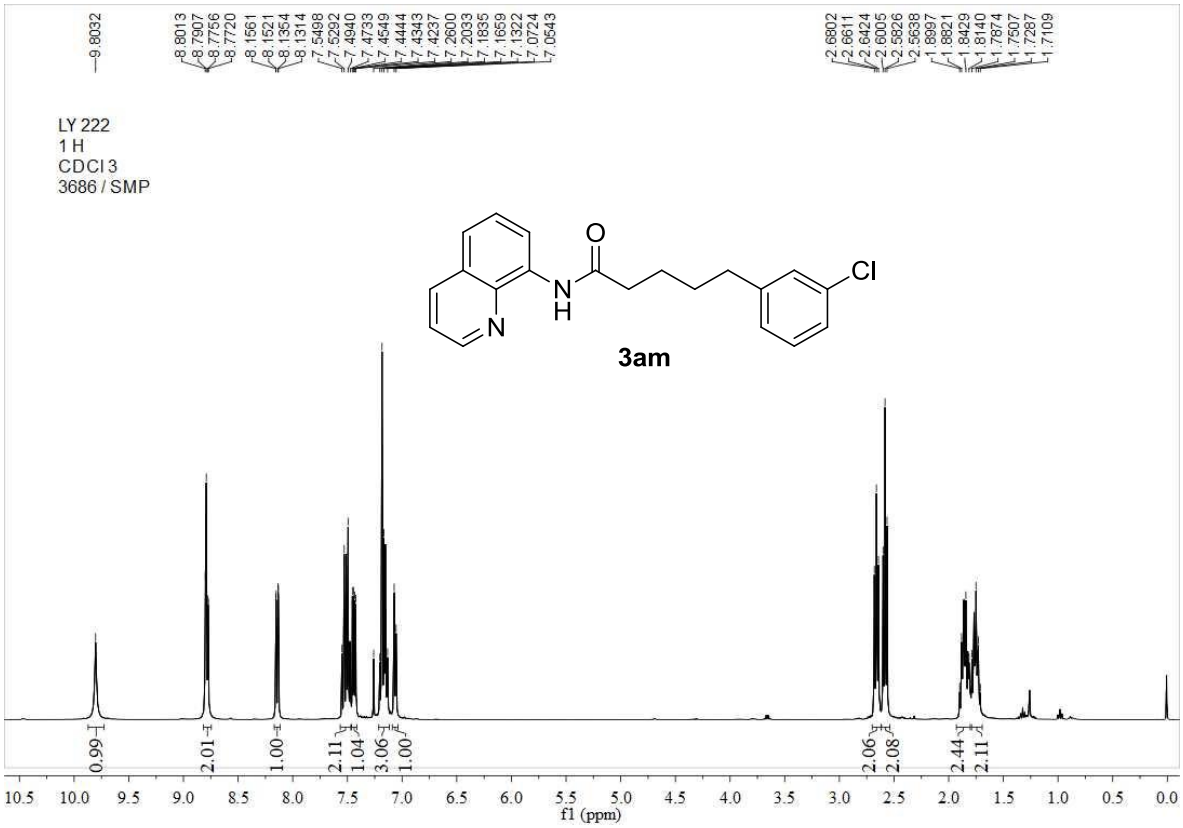

LY122
1H
CDCl3
5023/ SMP
3ak
f1 (ppm)

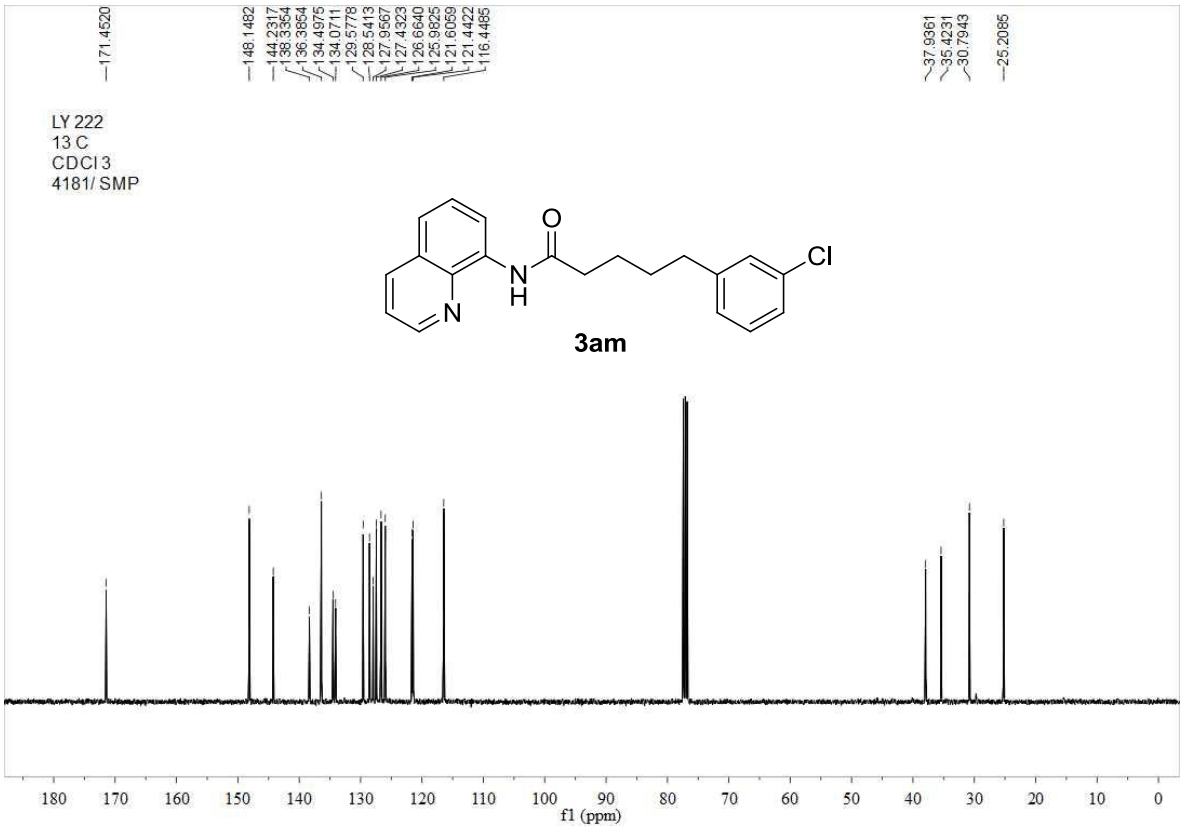

LY 122
13 C
CDCl3
5294/ SMP
3ak
f1 (ppm)

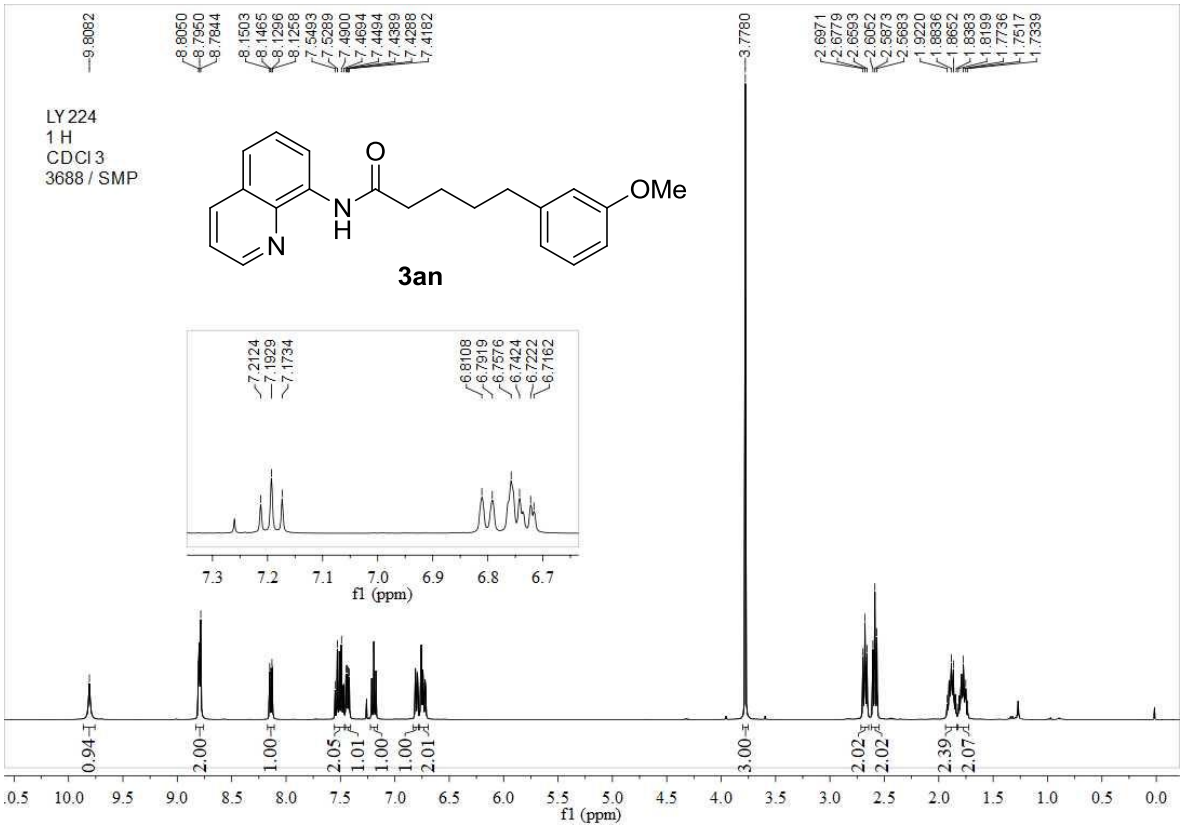

LY 223
1 H
CDCl3
3687 / SMP
3al
f1 (ppm)

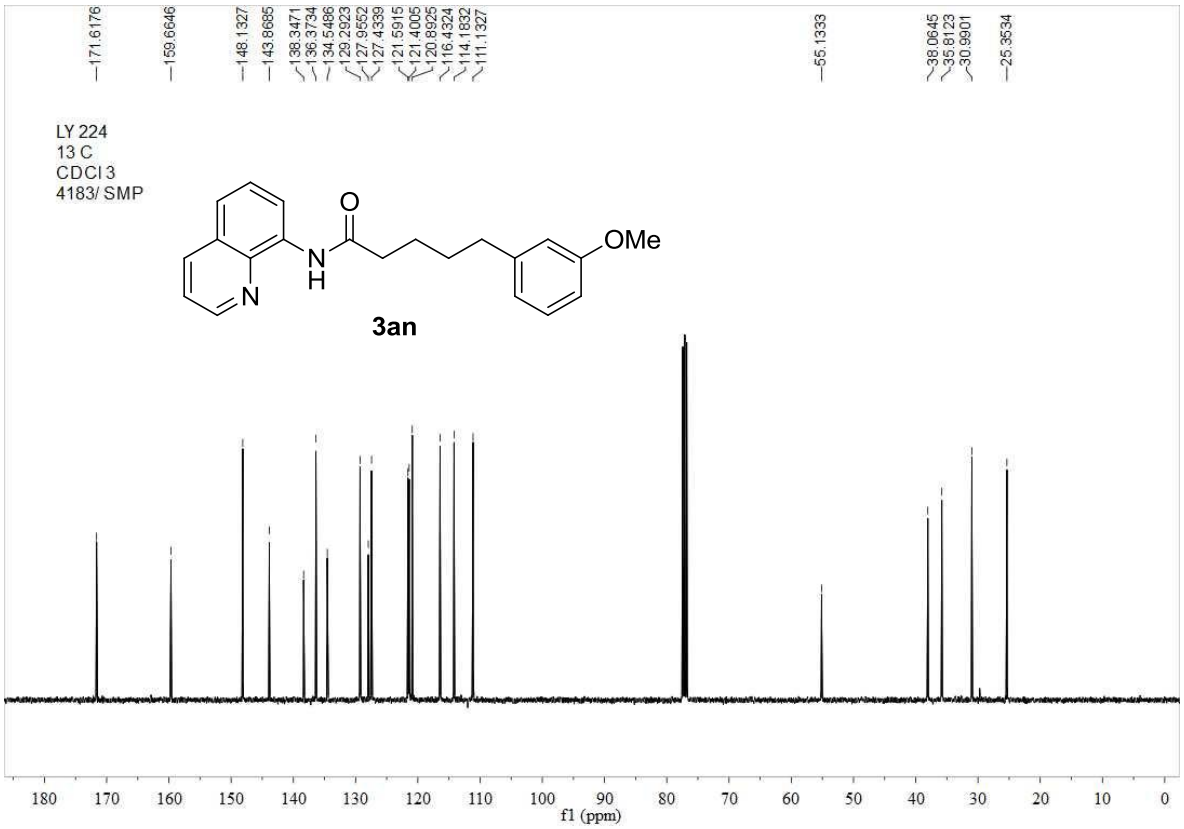

LY 223
13 C
CDCl3
4182/ SMP
3al
f1 (ppm)

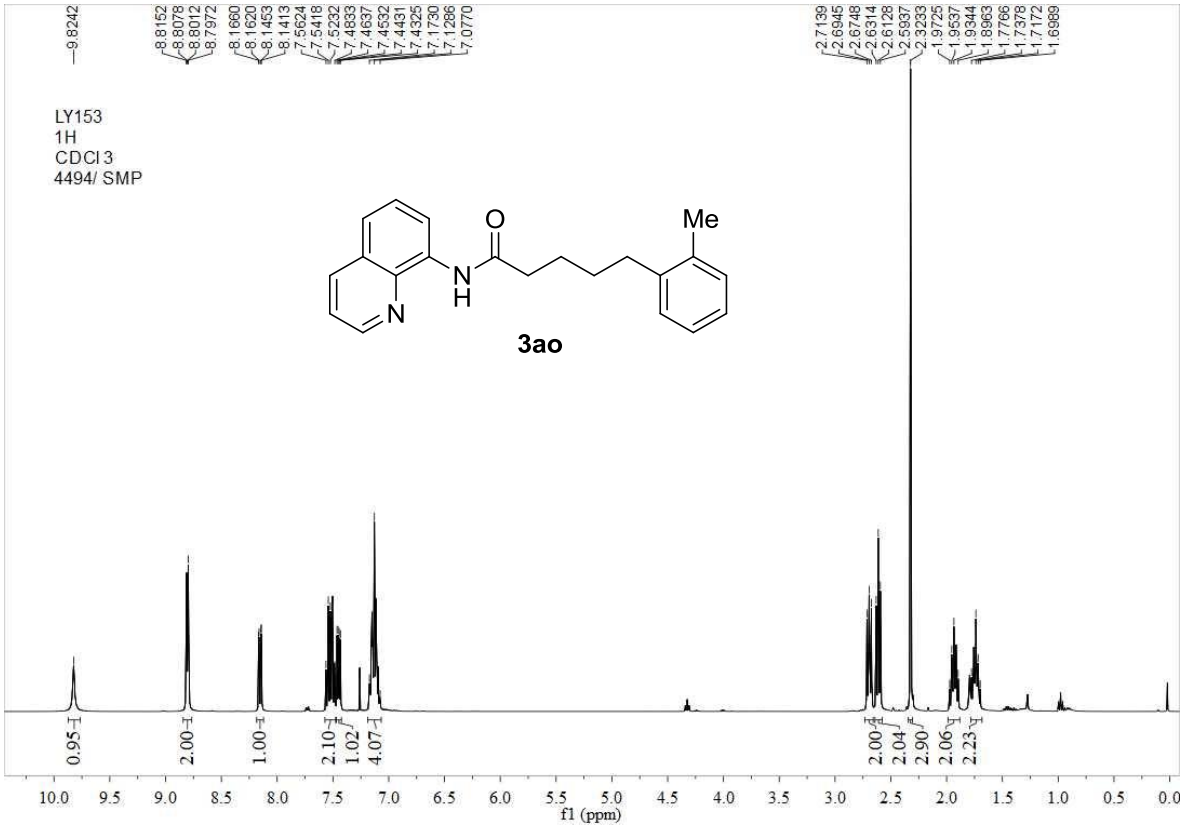

LY 116
19 F
CDCl 3
9755/ SMP
-113.8886
O
N
H
N
F
3al
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

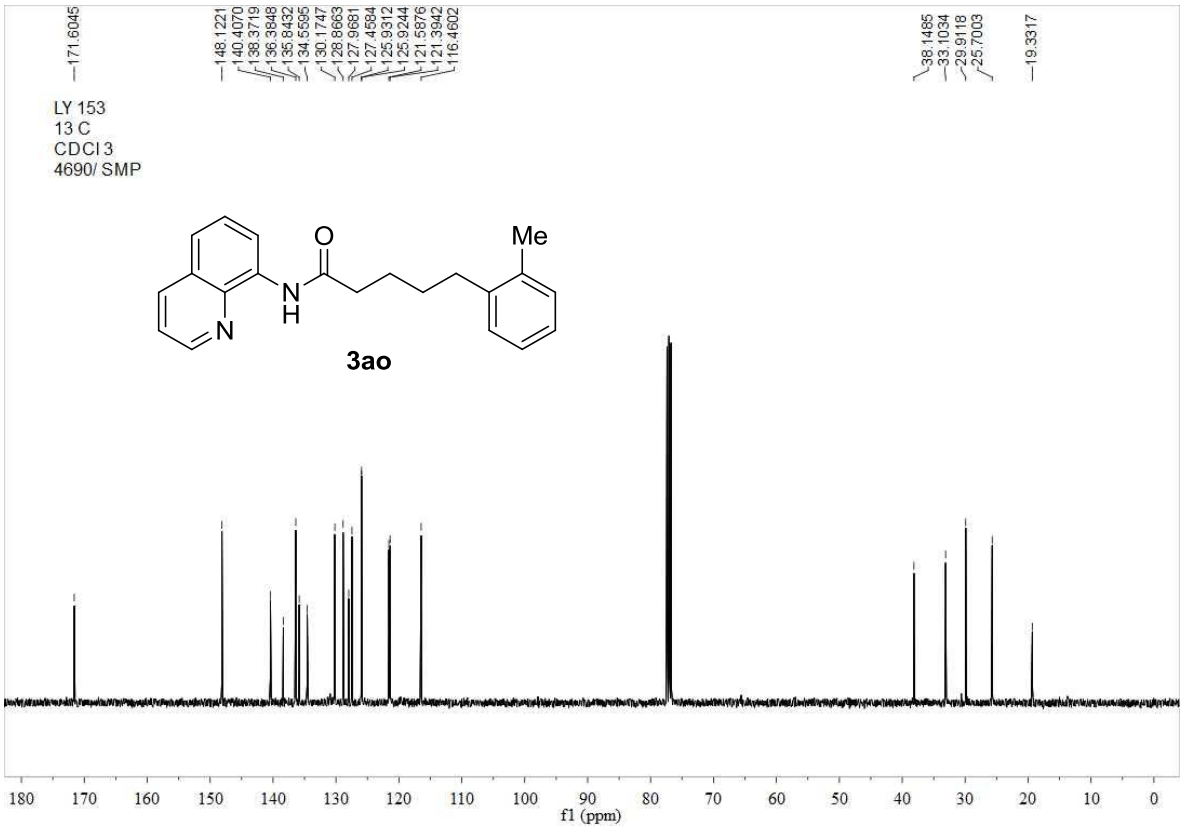

9.8032
8.8013
8.7907
8.7756
8.7720
8.1561
8.1521
8.1354
8.1314
7.5498
7.5292
7.4940
7.4733
7.4549
7.4444
7.4343
7.4237
7.2600
7.2033
7.1635
7.1659
7.1322
7.0724
7.0543
2.6802
2.6611
2.6424
2.6005
2.5826
2.5638
1.8997
1.8821
1.8429
1.8140
1.7874
1.7507
1.7287
1.7109
LY 222
1 H
CDCl 3
3686 / SMP
O
N
H
N
Cl
3am
0.99
2.01
1.00
2.11
1.04
3.06
1.00
2.06
2.08
2.44
2.11
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
f1 (ppm)

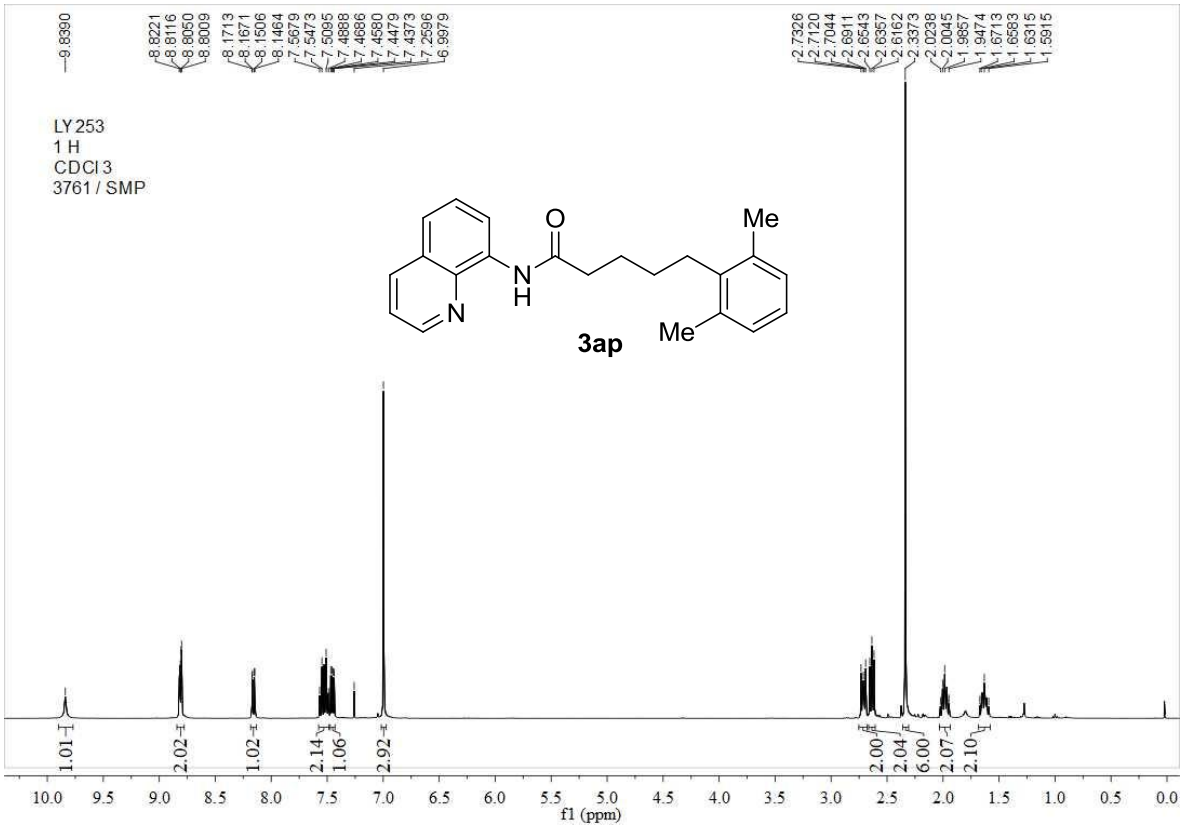

LY 222
13 C
CDCl 3
4181/ SMP
171.4520
148.1482
144.2317
138.3354
136.3654
134.4975
134.0711
129.5778
128.5413
127.9567
127.4323
126.6640
125.9825
121.6059
121.4422
116.4485
37.9361
35.4231
30.7943
25.2085
O
N
H
N
Cl
3am
f1 (ppm)

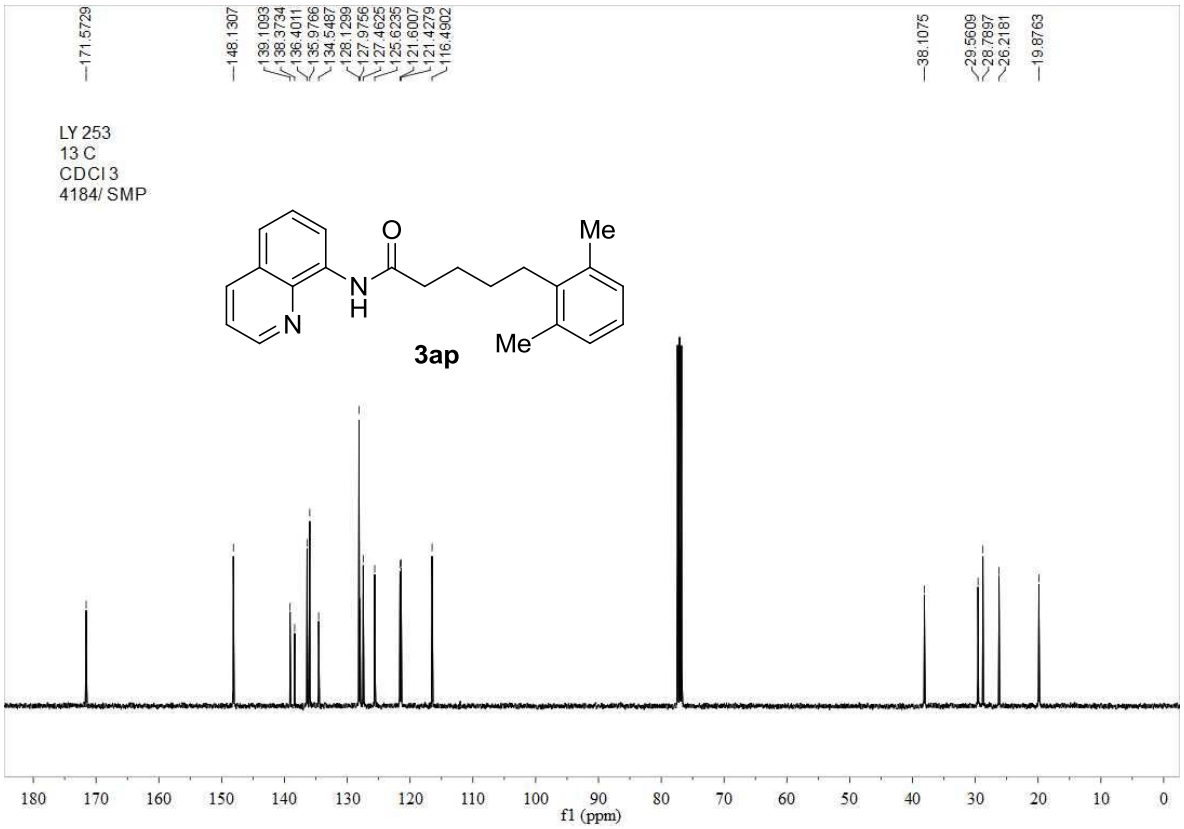

LY 224
1 H
CDCl 3
3688 / SMP
9.8082
8.8050
8.7950
8.7844
8.1503
8.1465
8.1296
8.1258
7.5493
7.5289
7.4900
7.4694
7.4494
7.4389
7.4288
7.4182
3.7780
2.6971
2.6779
2.6593
2.6052
2.5873
2.5683
1.9220
1.8836
1.8652
1.8383
1.8199
1.7736
1.7517
1.7339
O
N
H
N
OMe
3an
7.2124
7.1929
7.1734
6.8108
6.7919
6.7576
6.7424
6.7222
6.7162
f1 (ppm)
0.94
2.00
1.00
2.05
1.01
1.00
1.00
2.01
3.00
2.02
2.02
2.39
2.07
f1 (ppm)


171.6176
159.6646
148.1327
143.8685
138.3471
136.3734
134.5486
129.2923
127.9552
127.4339
121.5915
121.4005
120.8925
116.4324
114.1832
111.1327
55.1333
38.0645
35.8123
30.9901
25.3534
LY 224
13 C
CDCl 3
4183/ SMP
O
N
H
N
OMe
3an
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


9.8242
8.8152
8.8078
8.8012
8.7972
8.1660
8.1620
8.1453
8.1413
7.5624
7.5418
7.5232
7.4833
7.4637
7.4532
7.4431
7.4325
7.1730
7.1286
7.0770
2.7139
2.6945
2.6748
2.6314
2.6128
2.5937
2.3233
1.9725
1.9537
1.9344
1.8963
1.7766
1.7378
1.7172
1.6989
LY153
1H
CDCl 3
4494/ SMP
O
N
H
N
Me
3ao
0.95
2.00
1.00
2.10
1.02
4.07
2.00
2.04
2.90
2.06
2.23
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
f1 (ppm)


LY 153
13 C
CDCl 3
4690/ SMP
O
Me
N
H
N
3ao
f1 (ppm)


LY 253
1 H
CDCl 3
3761 / SMP
O
Me
N
H
N
Me
3ap
f1 (ppm)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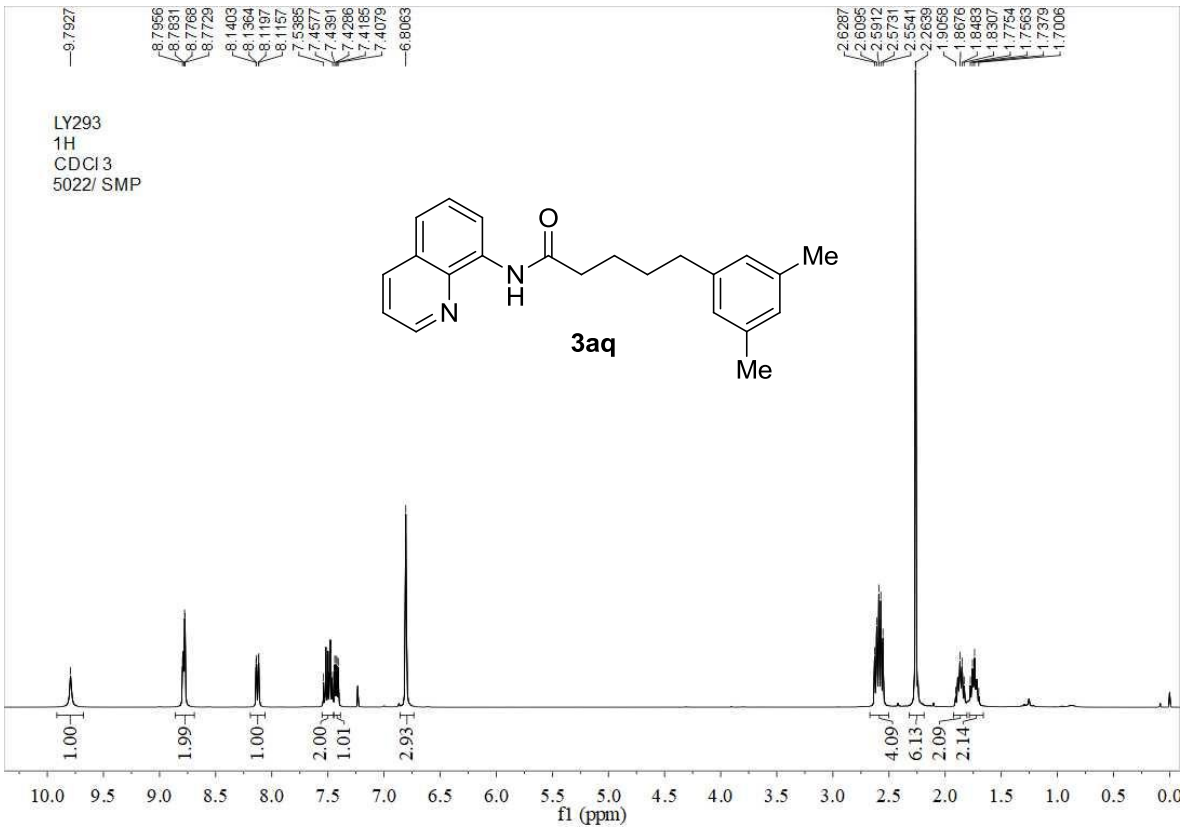
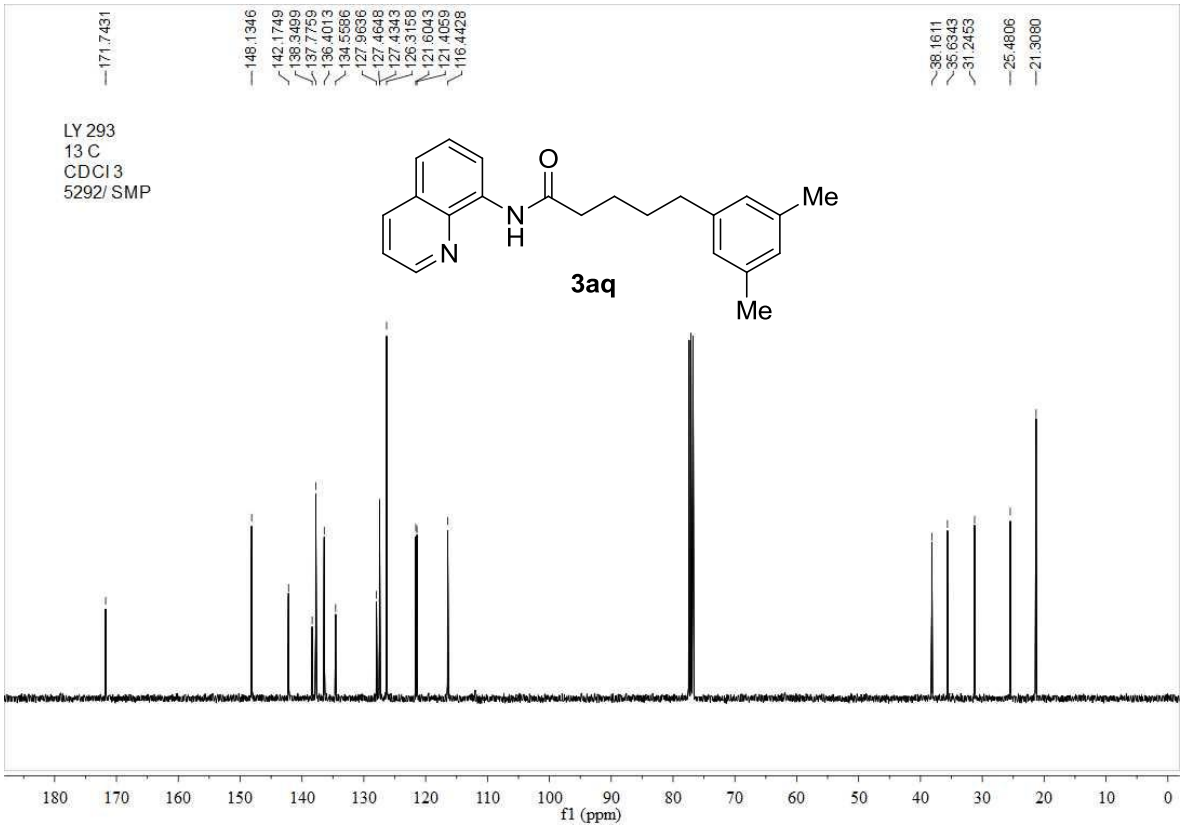
148.1307
139.1093
138.3734
136.4011
135.9766
134.5487
128.1299
127.9756
127.4625
125.6235
121.6007
121.4279
116.4902
38.1075
29.5609
28.7897
26.2181
19.8763
LY 253
13 C
CDCl 3
4184/ SMP
O
N
H
N
Me
Me
3ap
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.7927
8.7956
8.7831
8.7768
8.7729
8.1403
8.1364
8.1197
8.1157
7.5385
7.4577
7.4391
7.4286
7.4185
7.4079
6.8063
2.6287
2.6095
2.5912
2.5731
2.5541
2.2639
1.9058
1.8676
1.8483
1.8307
1.7754
1.7563
1.7379
1.7006
LY293
1H
CDCl 3
5022/ SMP
O
N
H
N
Me
Me
3aq
1.00
1.99
1.00
2.00
1.01
2.93
4.09
6.13
2.09
2.14
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
f1 (ppm)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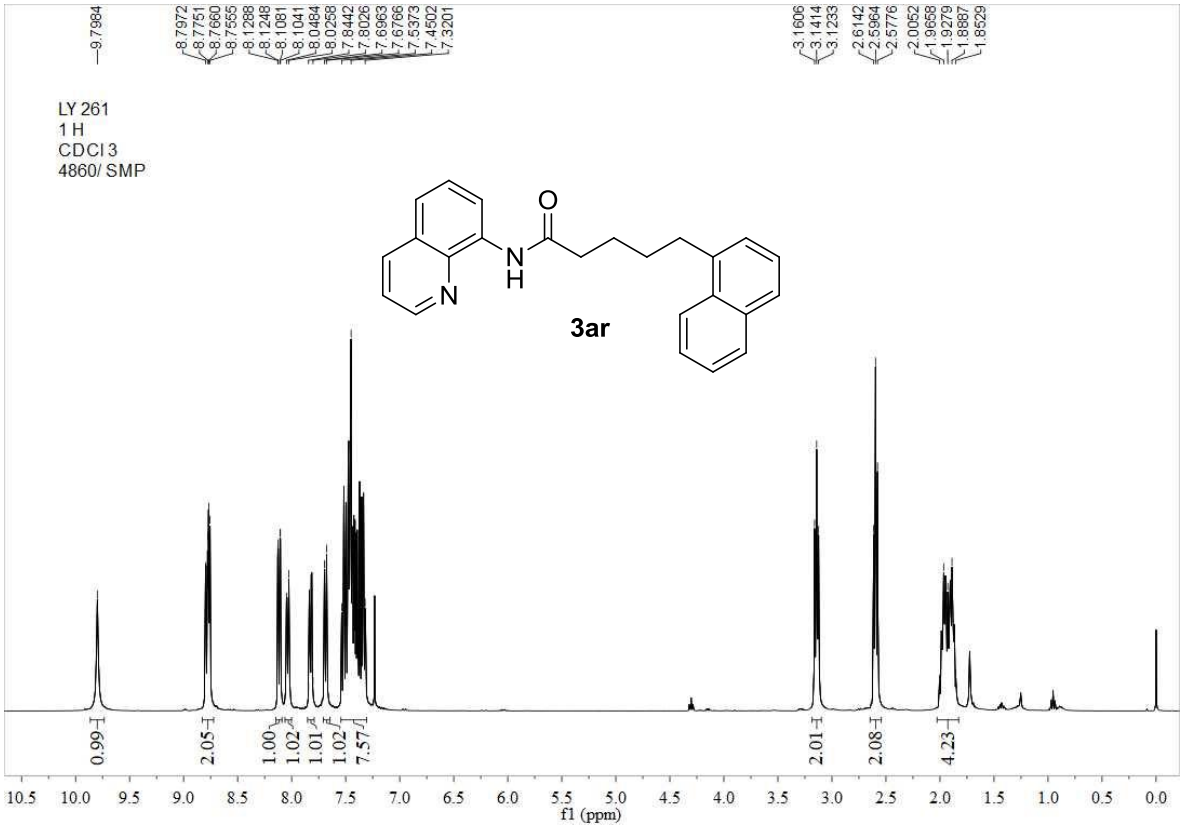
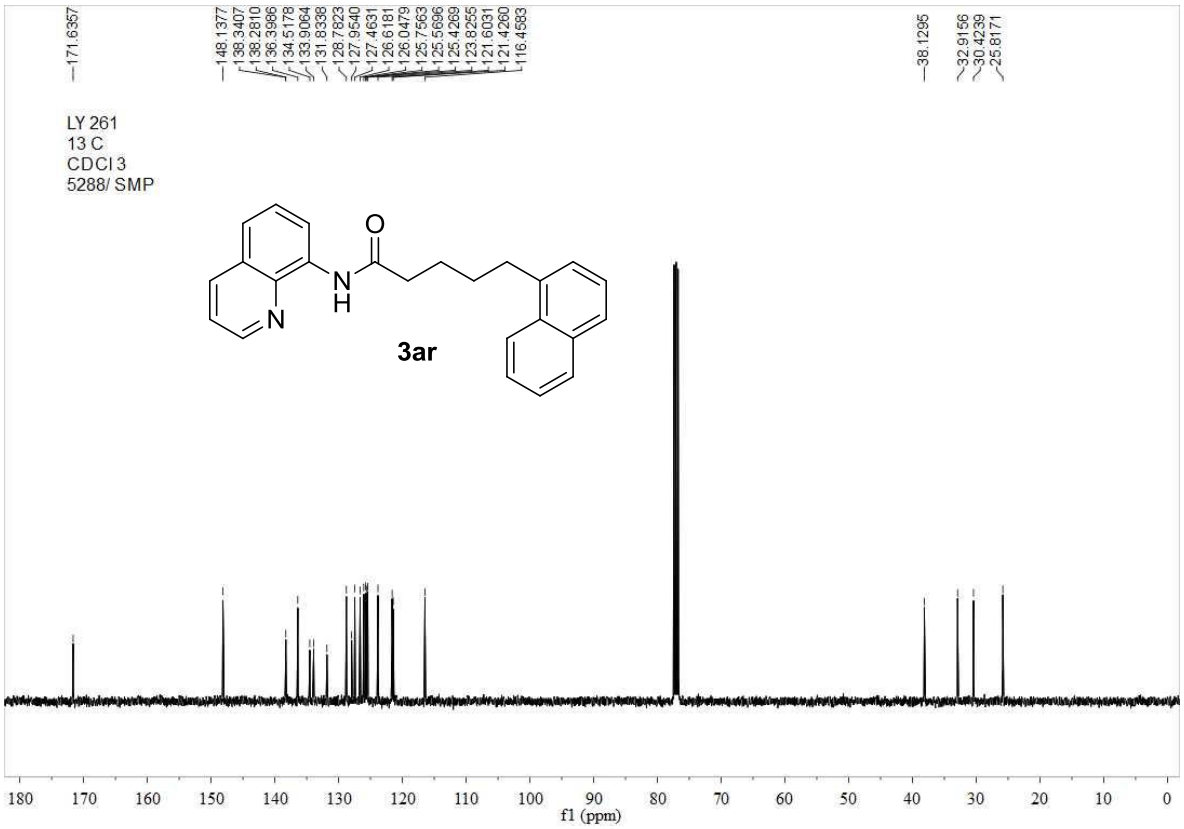
148.1346
142.1749
138.3499
137.7759
136.4013
134.5586
127.9636
127.4648
127.4343
126.3158
121.6043
121.4059
116.4428
38.1611
35.6343
31.2453
25.4806
21.3080
LY 293
13 C
CDCl 3
5292/ SMP
O
N
H
N
Me
Me
3aq
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.7984
8.7972
8.7751
8.7660
8.7555
8.1288
8.1248
8.1081
8.1041
8.0484
8.0258
7.8442
7.8026
7.6963
7.6766
7.5373
7.4502
7.3201
3.1606
3.1414
3.1233
2.6142
2.5964
2.5776
2.0052
1.9658
1.9279
1.8887
1.8529
LY 261
1 H
CDCl 3
4860/ SMP
O
N
H
N
3ar
0.99
2.05
1.00
1.02
1.01
1.02
7.57
2.01
2.08
4.23
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
f1 (ppm)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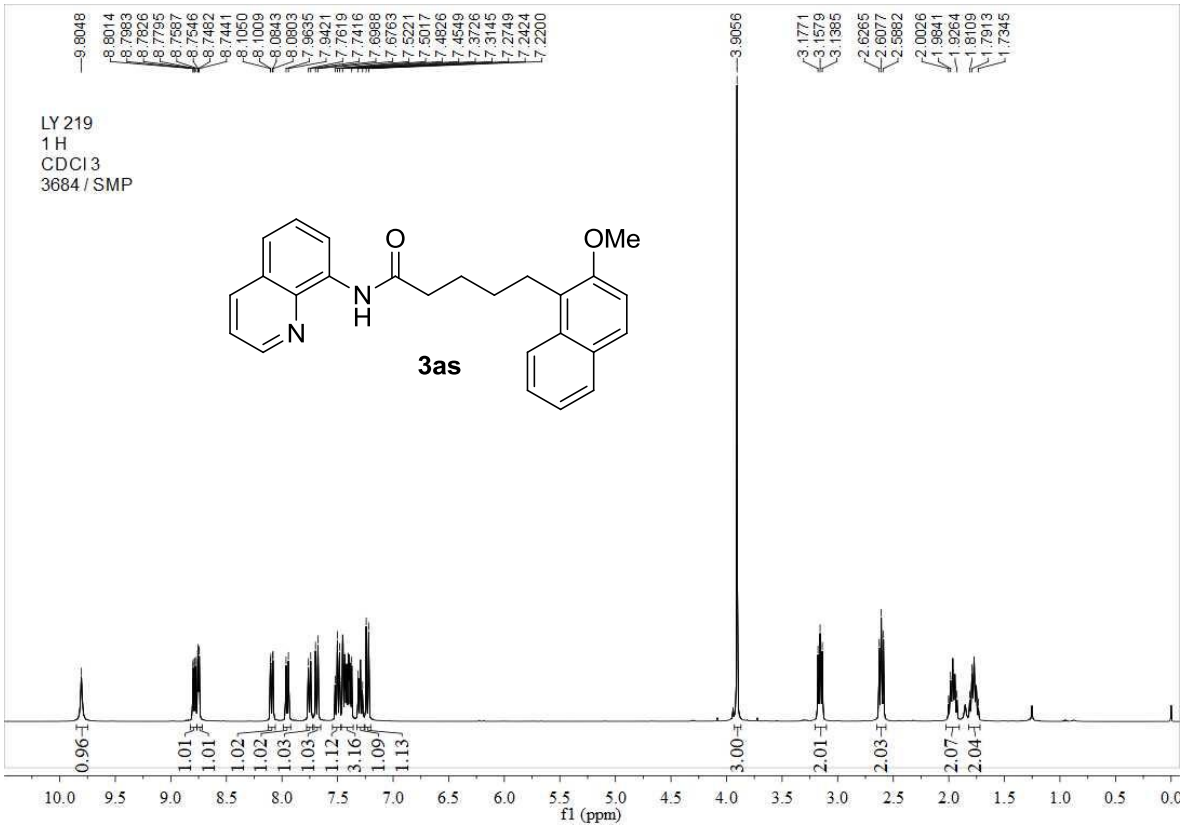
138.3407
138.2810
136.3986
134.5178
133.9064
131.8338
128.7823
127.9540
127.4631
126.6181
126.0479
125.7563
125.5696
125.4269
123.8255
121.6031
121.4260
116.4583
38.1295
32.9156
30.4239
25.8171
LY 261
13 C
CDCl 3
5288/ SMP
O
N
H
N
3ar
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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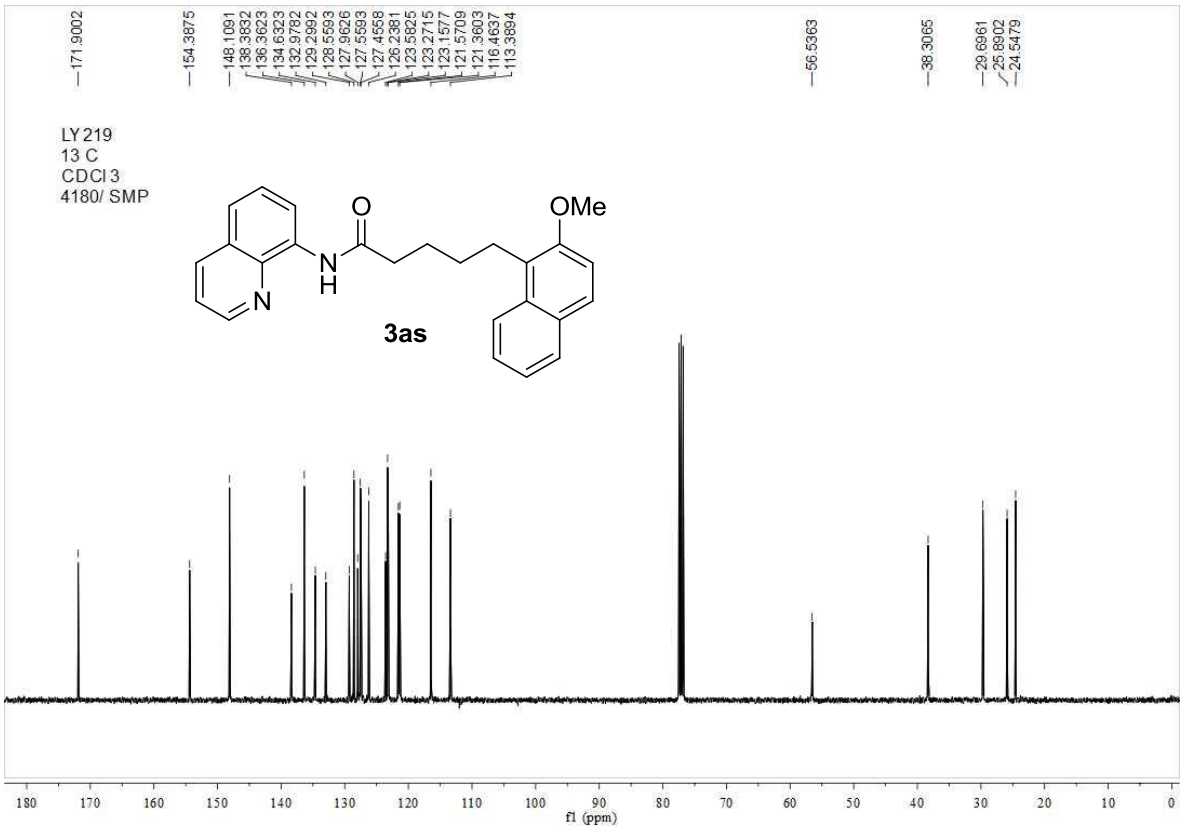
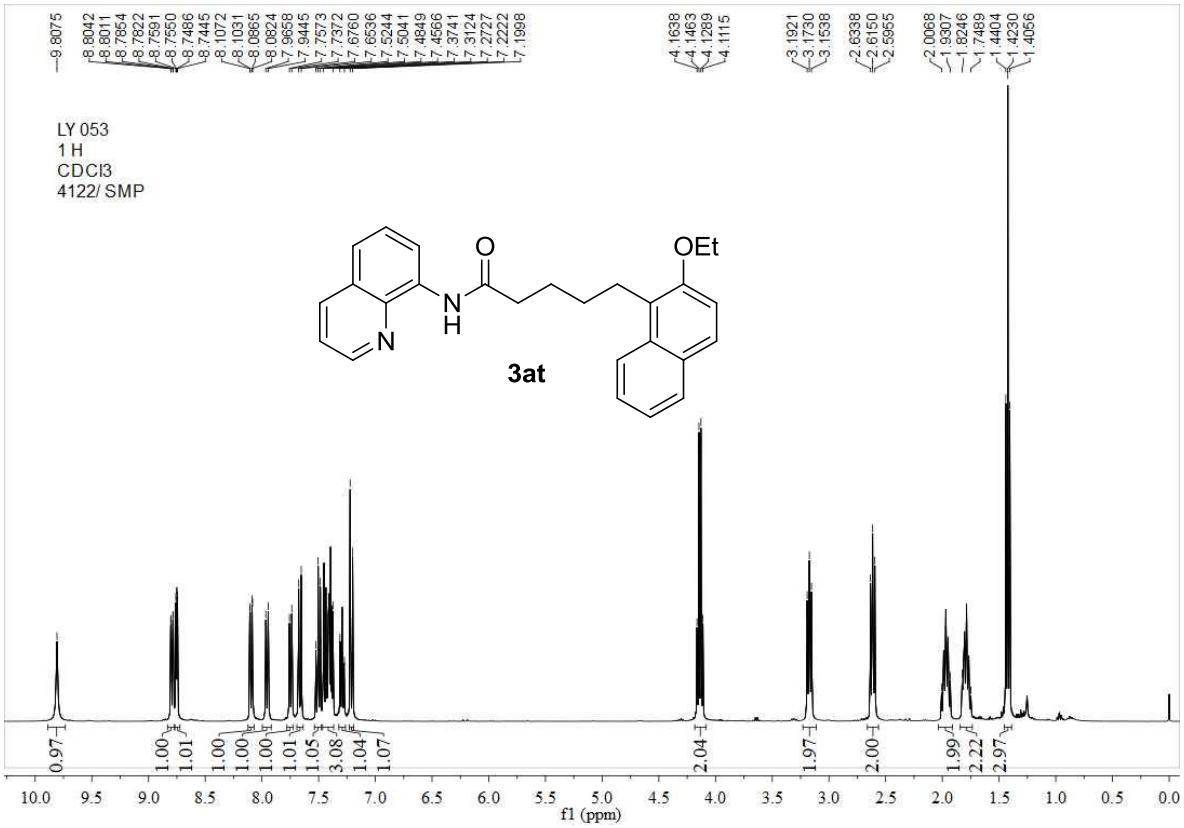
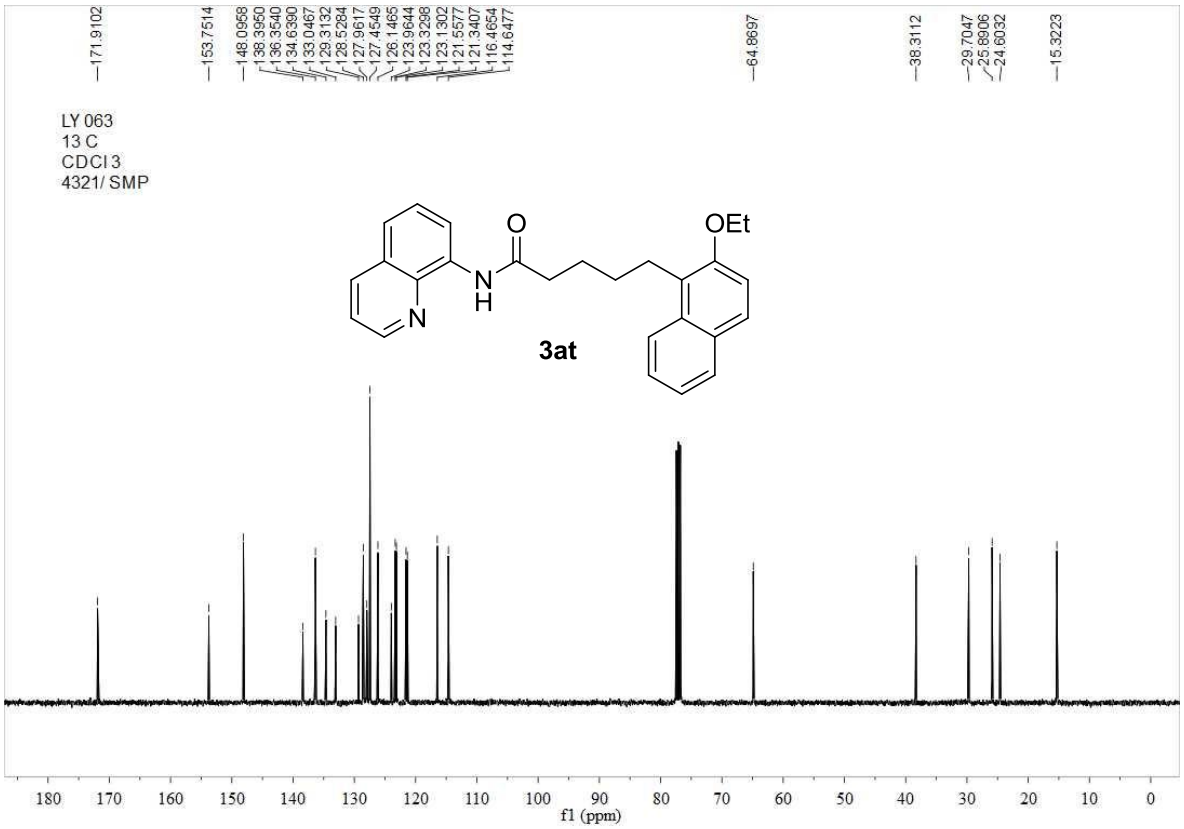
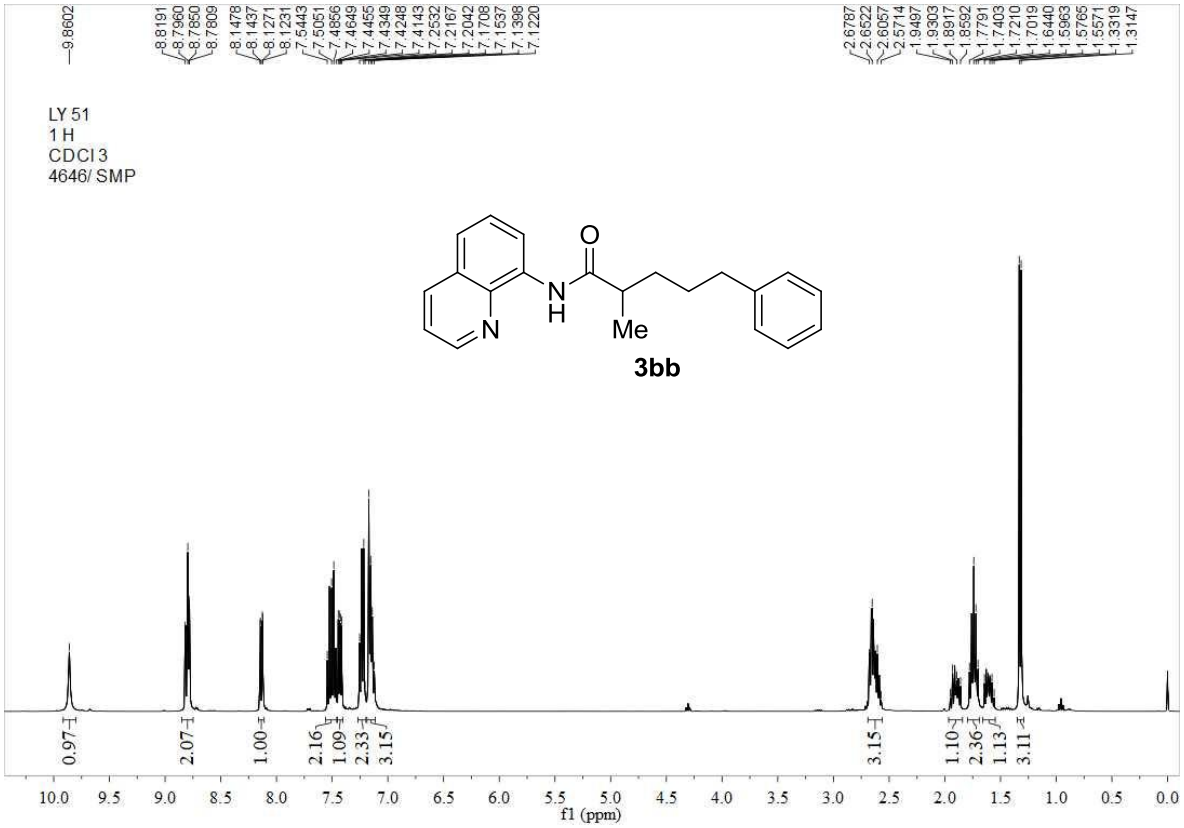
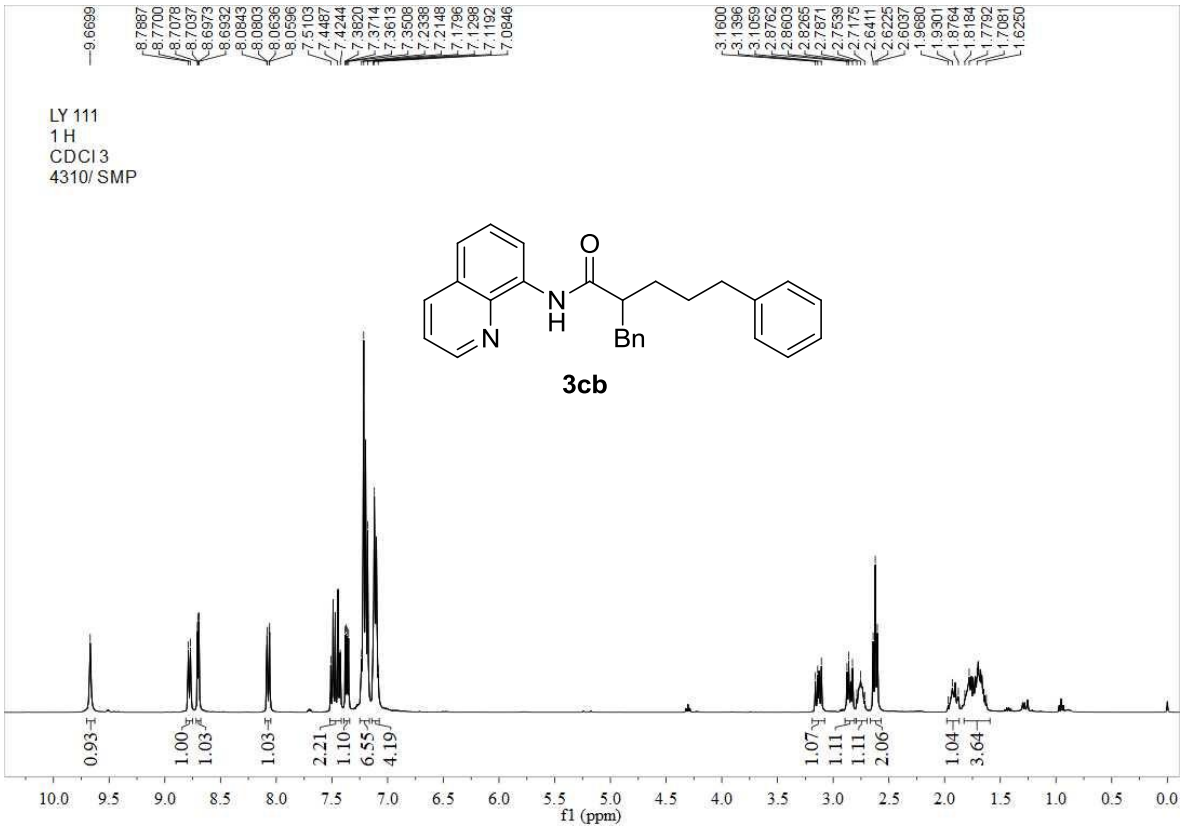
8.8014
8.7983
8.7826
8.7795
8.7587
8.7546
8.7482
8.7441
8.1050
8.1009
8.0843
8.0803
7.9635
7.9421
7.7619
7.7416
7.6968
7.6763
7.5221
7.5017
7.4826
7.4549
7.3726
7.3145
7.2749
7.2424
7.2200
3.9056
3.1771
3.1579
3.1385
2.6265
2.6077
2.5882
2.0026
1.9841
1.9264
1.8109
1.7913
1.7345
LY 219
1 H
CDCl 3
3684 / SMP
O
OMe
N
H
N
3as
0.96
1.01
1.01
1.02
1.02
1.03
1.03
1.12
3.16
1.09
1.13
3.00
2.01
2.03
2.07
2.04
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
f1 (ppm)

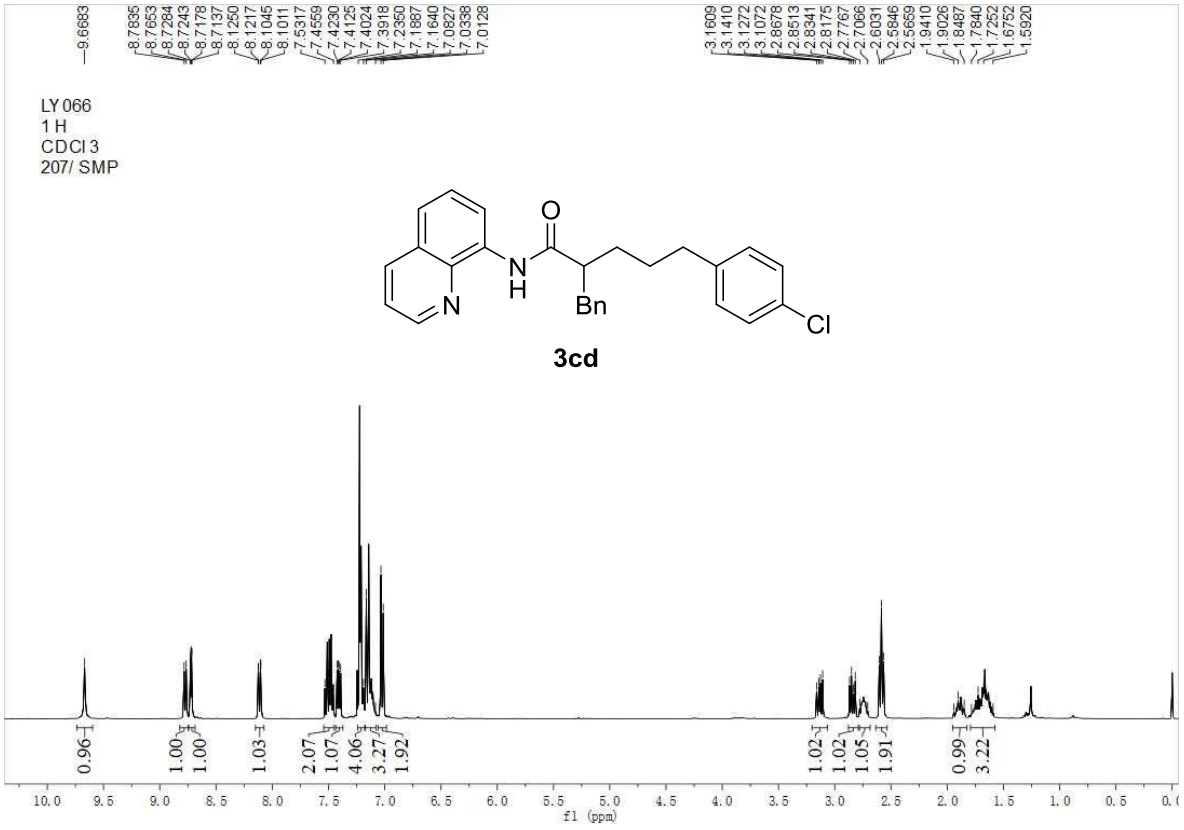

LY 219
13 C
CDCl 3
4180/ SMP
O
OMe
N
H
N
3as
f1 (ppm)

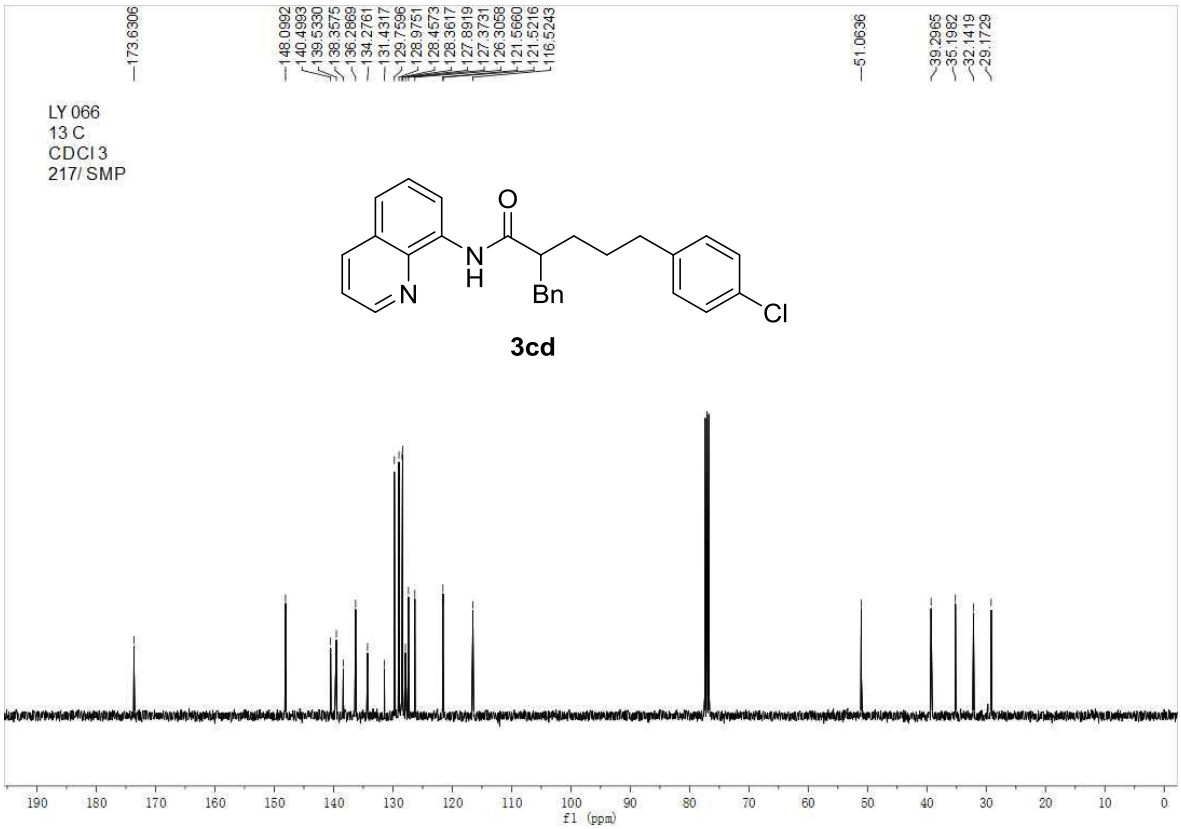

LY 053
1 H
CDCl3
4122/ SMP
O
OEt
N
H
N
3at
f1 (ppm)

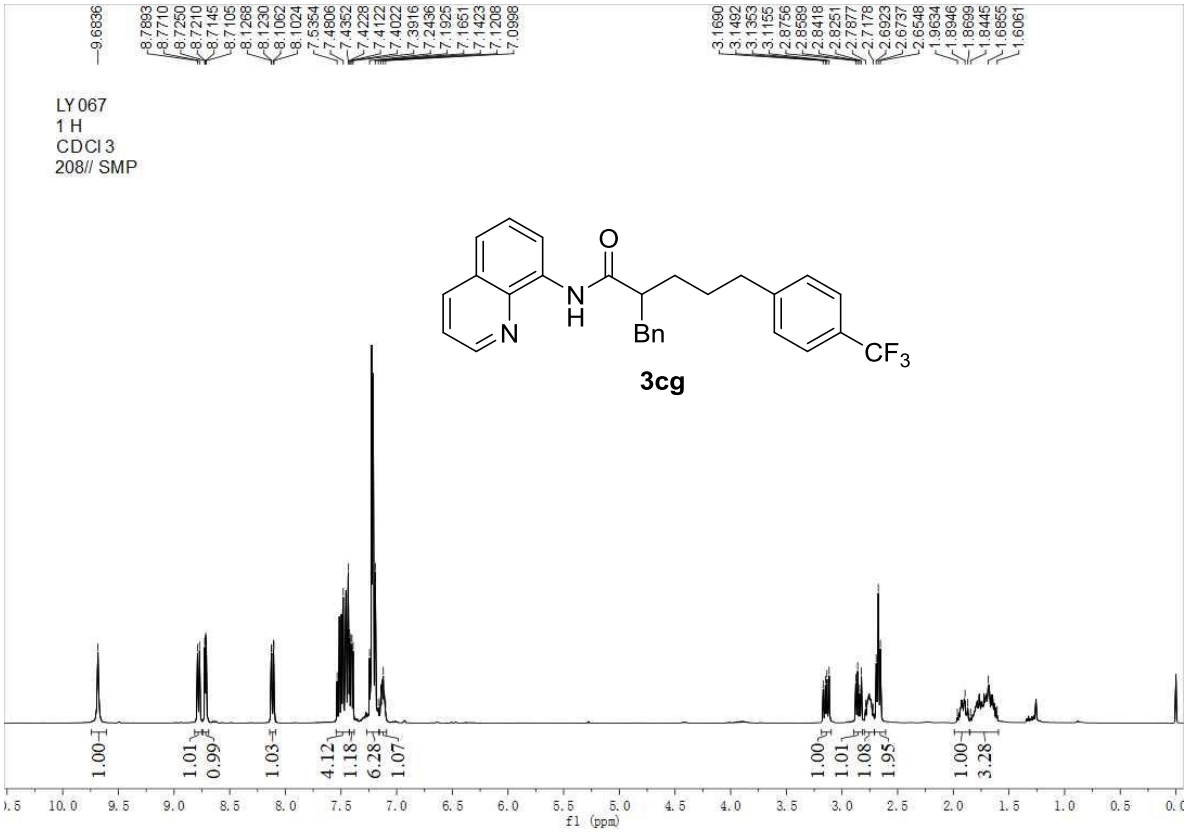

171.9102
153.7514
148.0958
138.3950
136.3540
134.6390
133.0467
129.3132
128.5284
127.9617
127.4549
126.1465
123.9644
123.3298
123.1302
121.5577
121.3407
116.4654
114.6477
64.8697
38.3112
29.7047
25.8906
24.6032
15.3223
LY 063
13 C
CDCl 3
4321/ SMP
O
OEt
N
H
N
3at
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

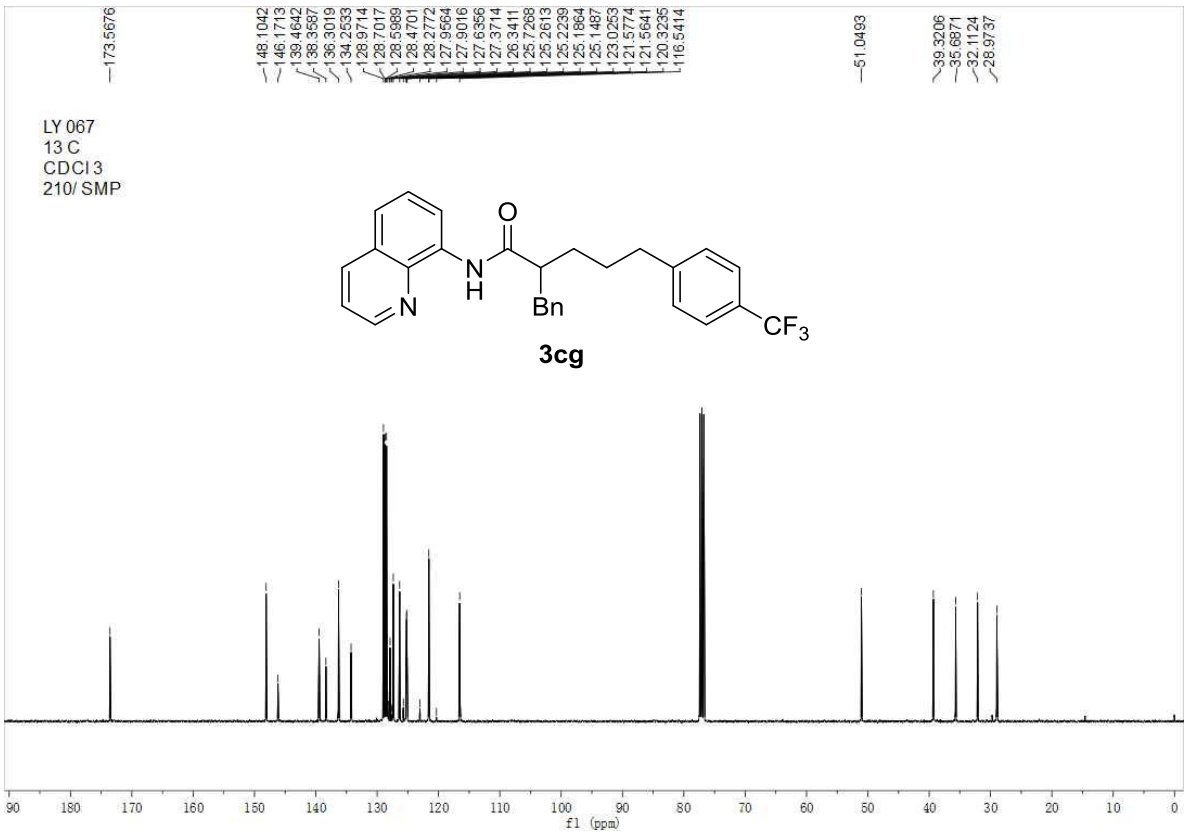

9.8602
8.8191
8.7960
8.7850
8.7809
8.1478
8.1437
8.1271
8.1231
7.5443
7.5051
7.4856
7.4649
7.4455
7.4349
7.4248
7.4143
7.2532
7.2167
7.2042
7.1708
7.1537
7.1398
7.1220
2.6787
2.6522
2.6057
2.5714
1.9497
1.9303
1.8917
1.8592
1.7791
1.7403
1.7210
1.7019
1.6440
1.5963
1.5765
1.5571
1.3319
1.3147
LY 51
1 H
CDCl 3
4646/ SMP
O
N
H
N
Me
3bb
0.97
2.07
1.00
2.16
1.09
2.33
3.15
3.15
1.10
2.36
1.13
3.11
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
f1 (ppm)

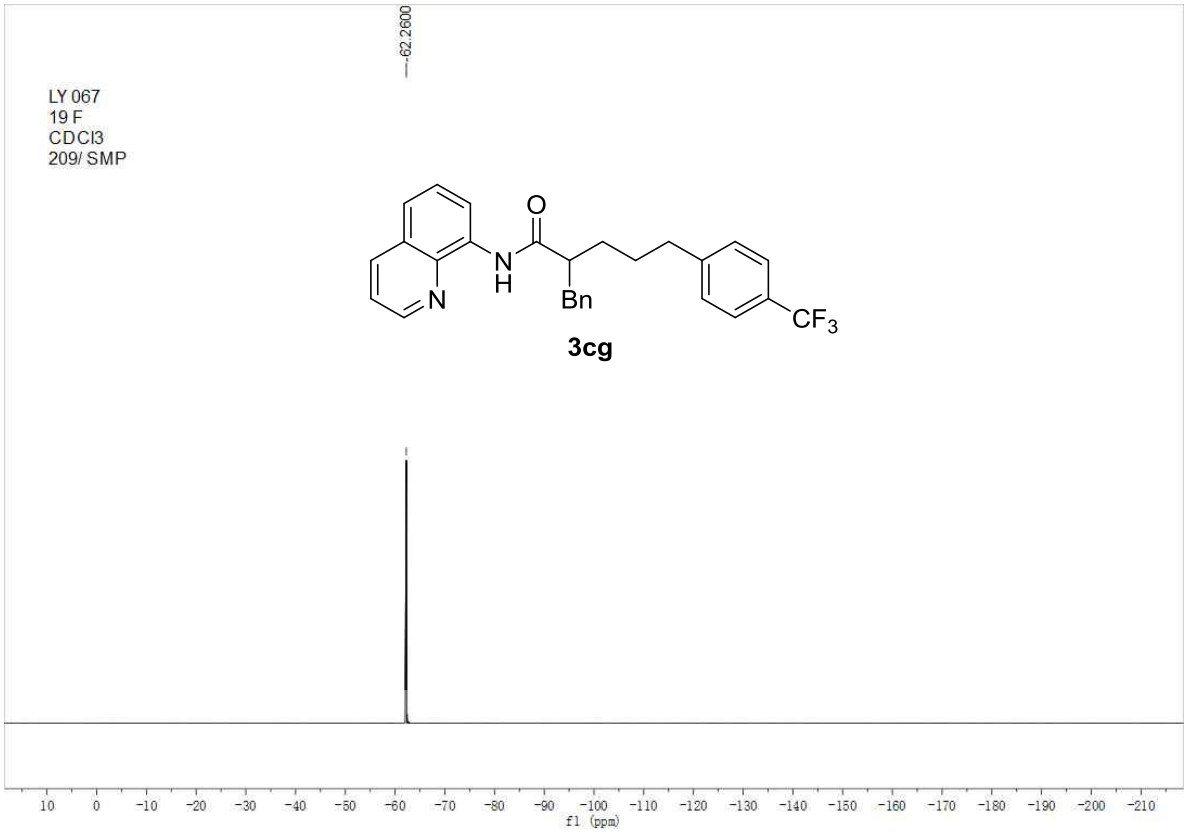

LY 111
1 H
CDCl 3
4310/ SMP
O
N
H
N
Bn
3cb
f1 (ppm)

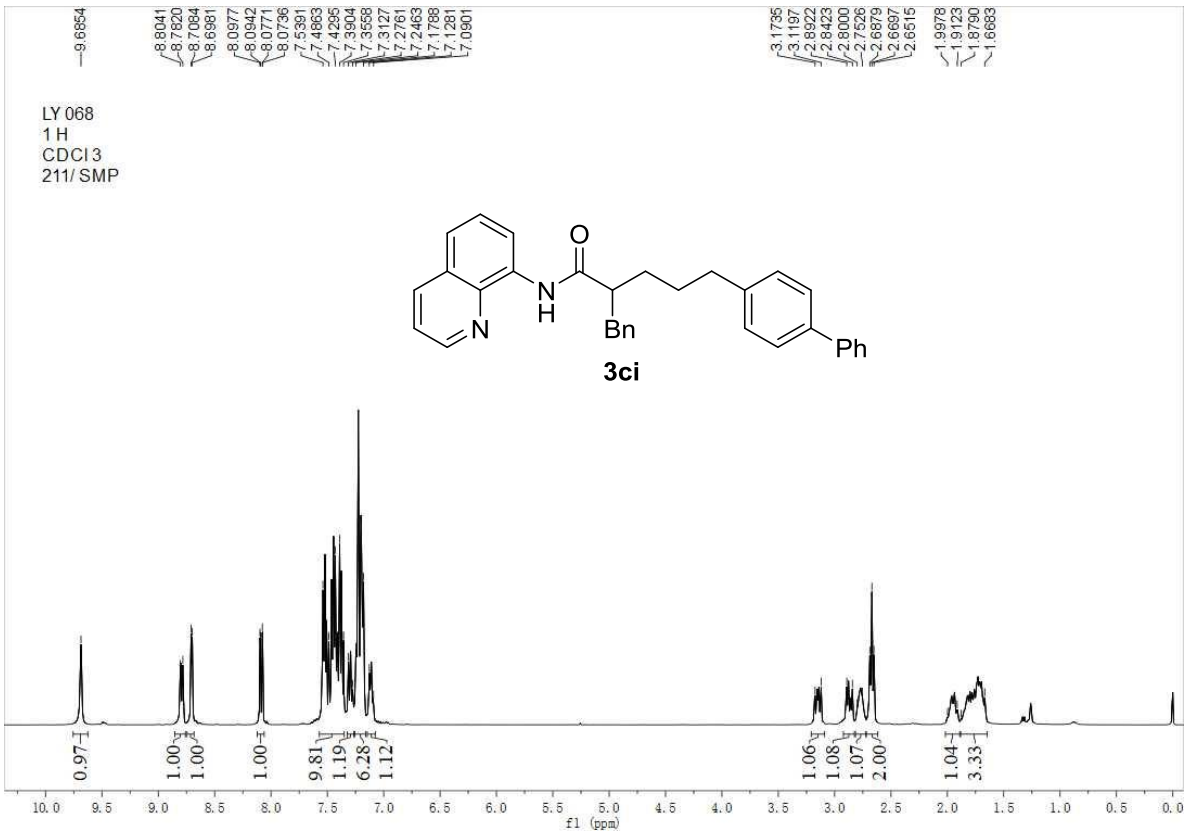

LY 066
1 H
CDCl 3
207/ SMP
O
N
H
N
Bn
Cl
3cd
f1 (ppm)

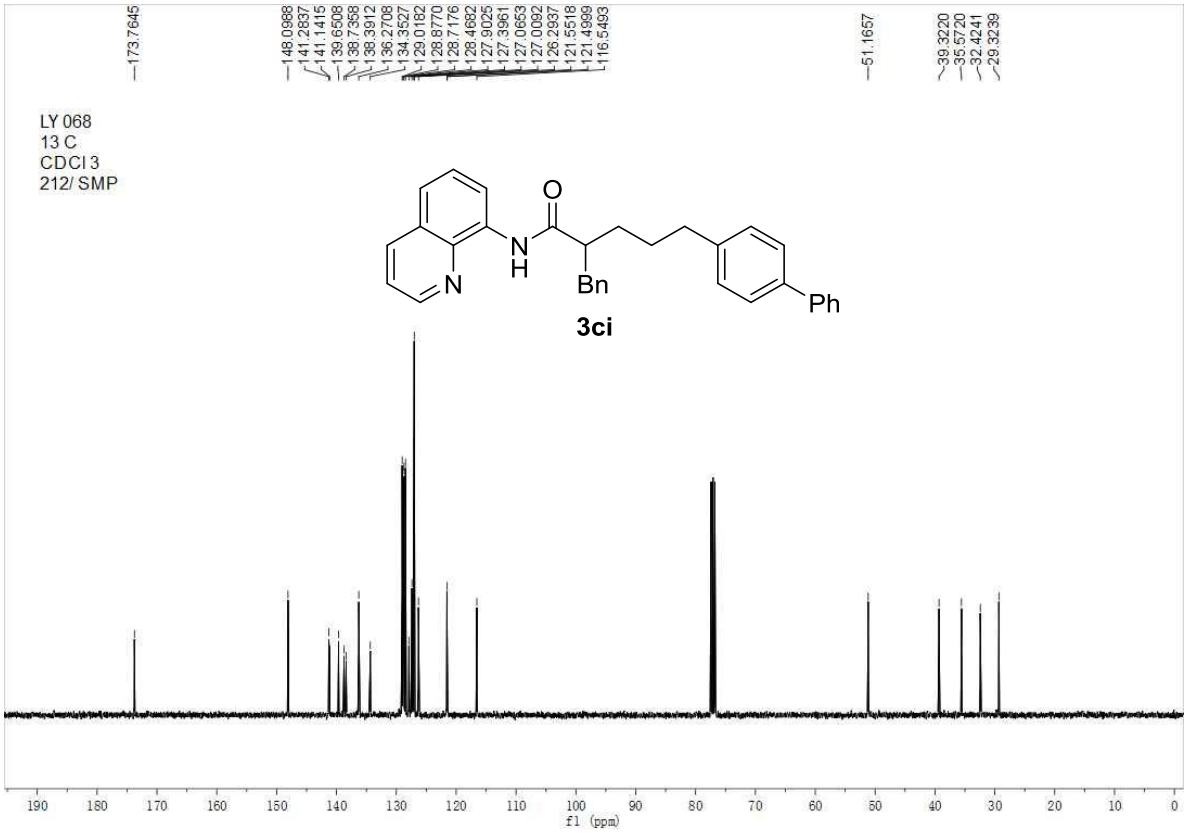

LY 066
13 C
CDCl 3
217/ SMP
O
N
H
N
Bn
Cl
3cd
f1 (ppm)

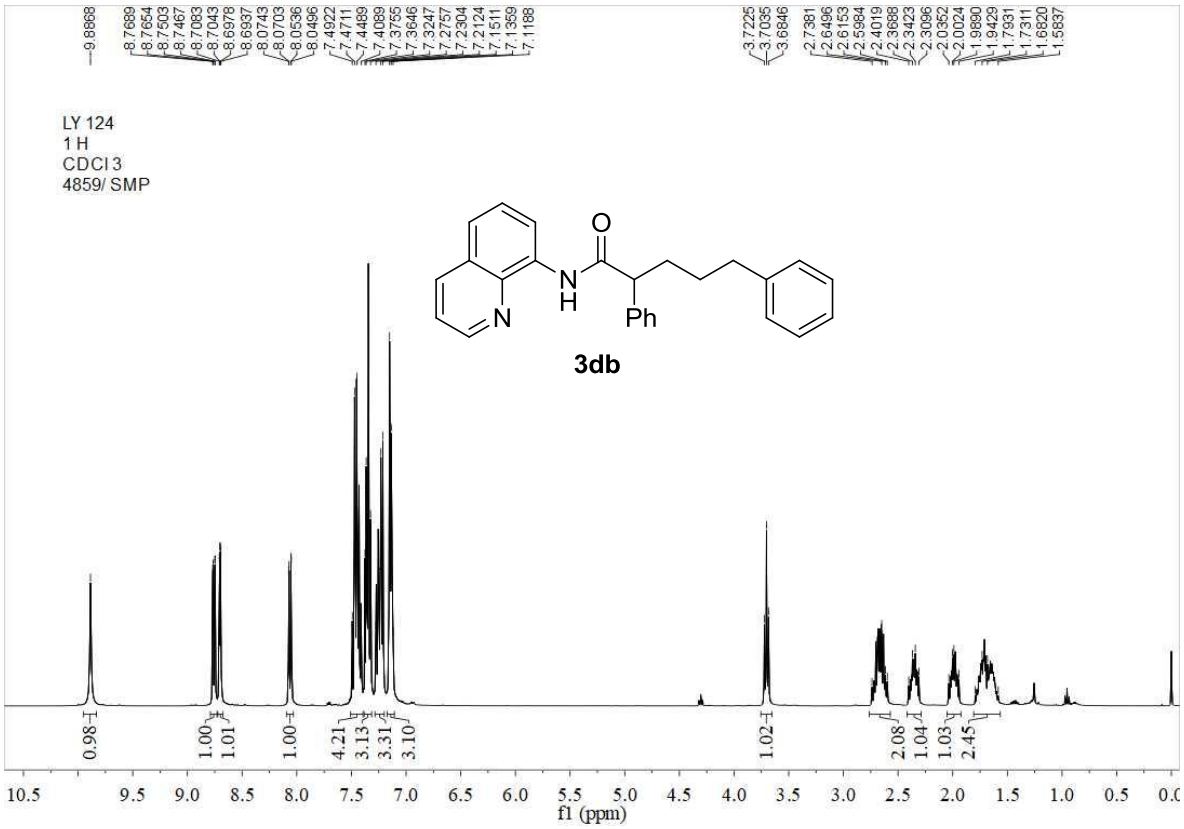

LY 067
1 H
CDCl 3
208// SMP
O
N
H
N
Bn
CF3
3cg
f1 (ppm)

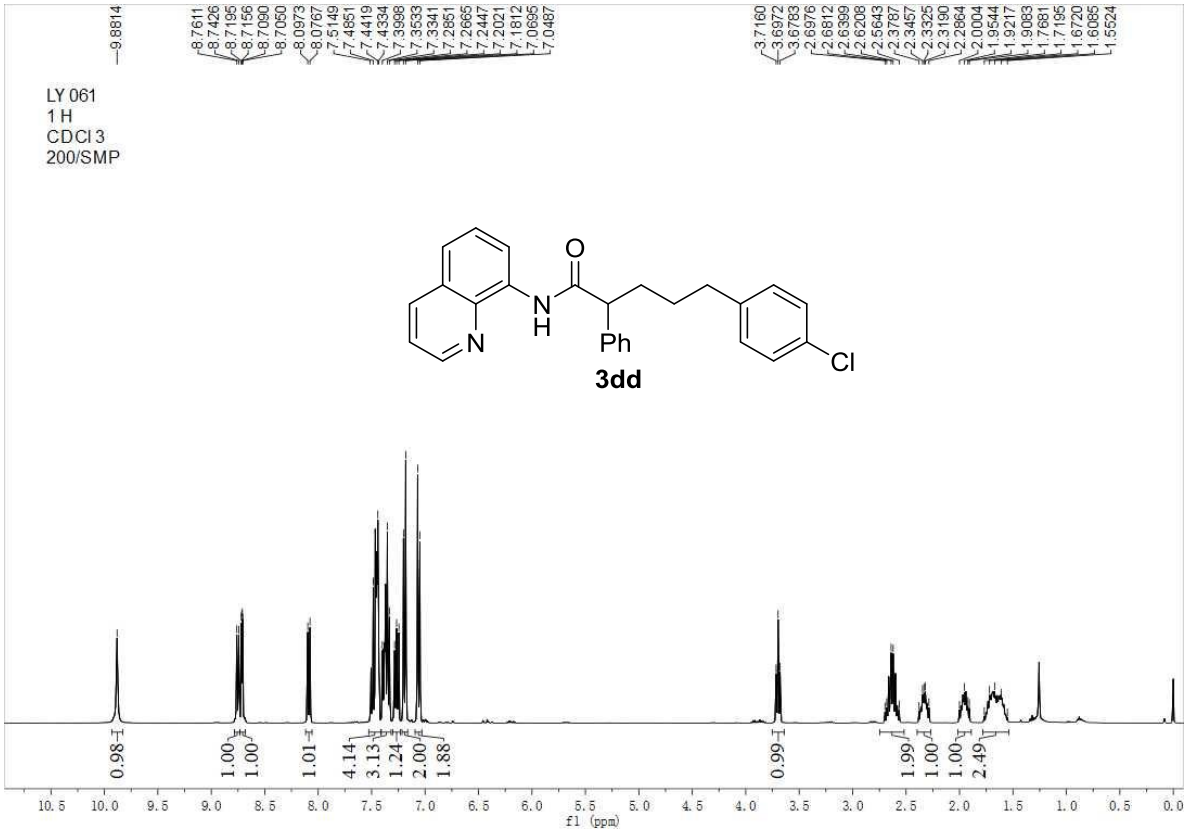

LY 067
13 C
CDCl 3
210/ SMP
O
N
H
N
Bn
CF3
3cg
f1 (ppm)

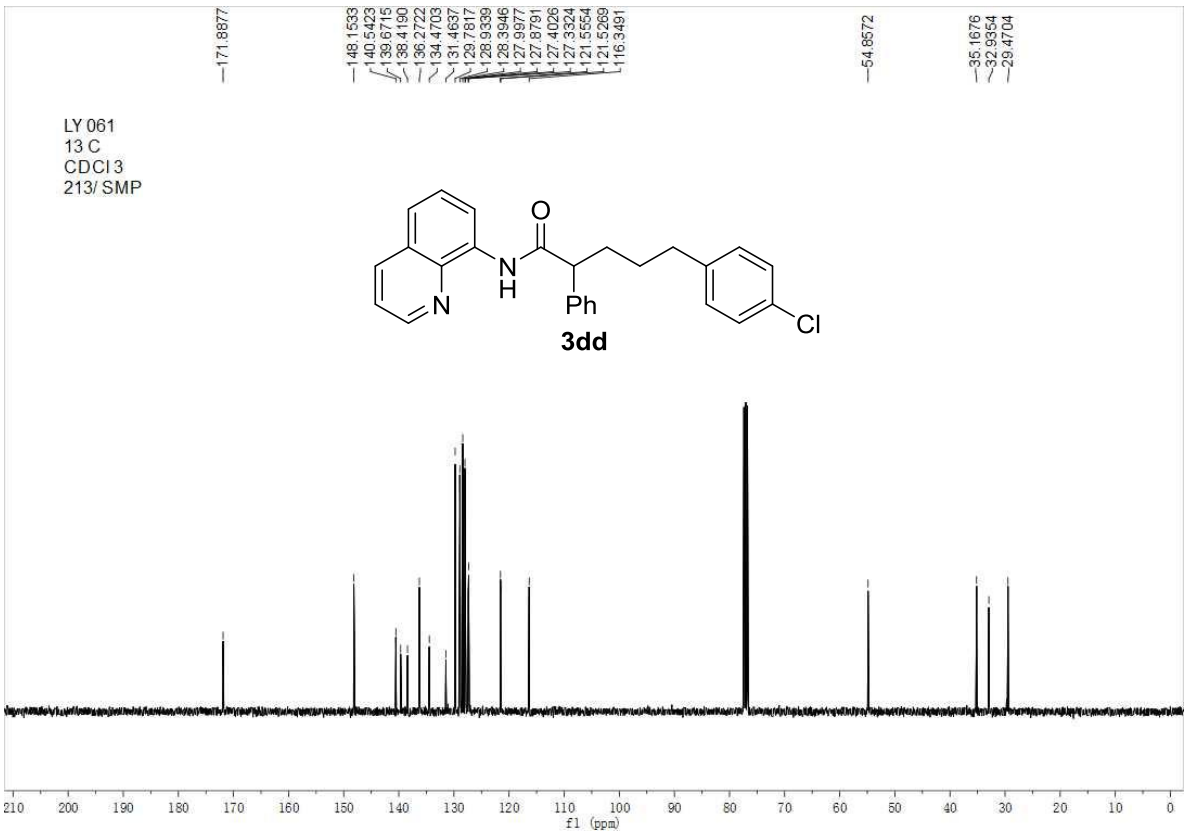

LY 067
19 F
CDCl3
209/ SMP
O
N
H
N
Bn
CF3
3cg
f1 (ppm)

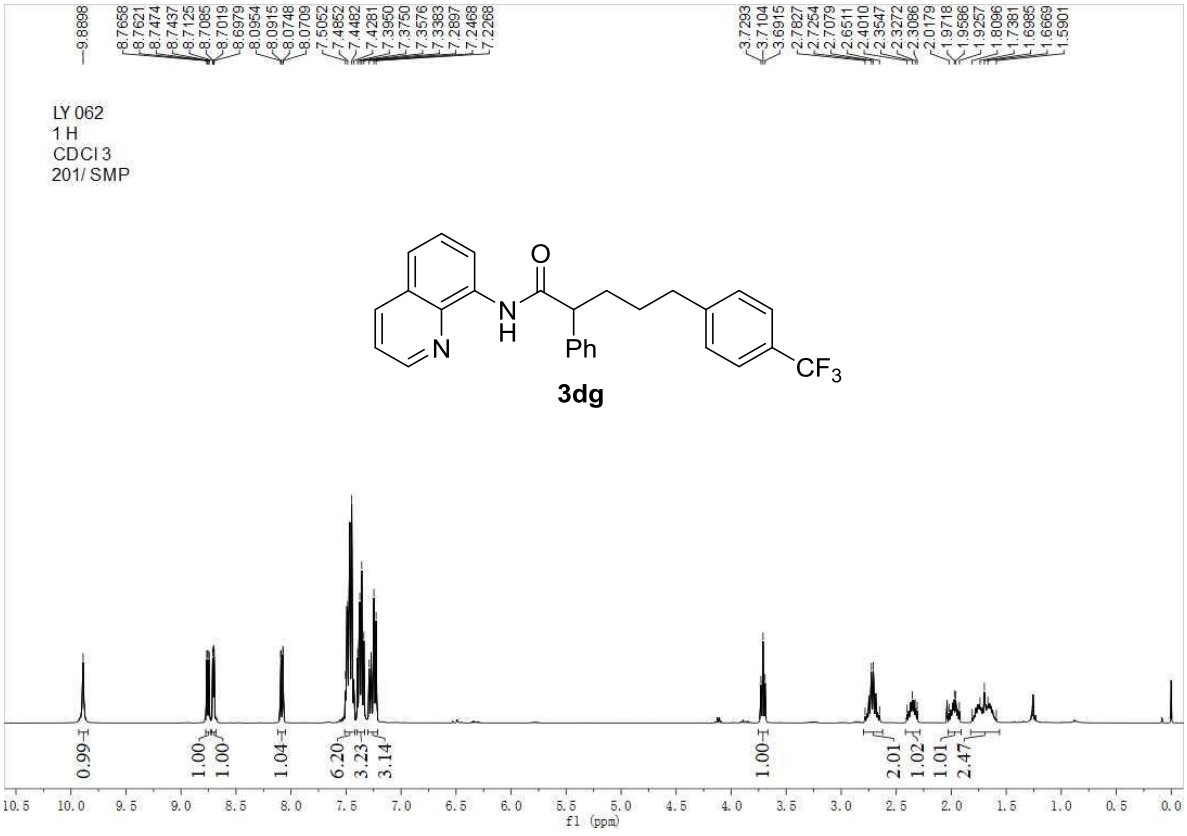

LY 068
1 H
CDCl 3
211/ SMP
3ci


LY 068
13 C
CDCl 3
212/ SMP
3ci


LY 124
1 H
CDCl 3
4859/ SMP
O
N
H
N
Ph
3db
f1 (ppm)


LY 061
1 H
CDCl 3
200/SMP
O
N
H
N
Ph
Cl
3dd
f1 (ppm)


171.8877
148.1533
140.5423
139.6715
138.4190
136.2722
134.4703
131.4637
129.7817
128.9339
128.3946
127.9977
127.8791
127.4026
127.3324
121.5554
121.5269
116.3491
54.8572
35.1676
32.9354
29.4704
LY 061
13 C
CDCl 3
213/ SMP
O
N
H
N
Ph
Cl
3dd
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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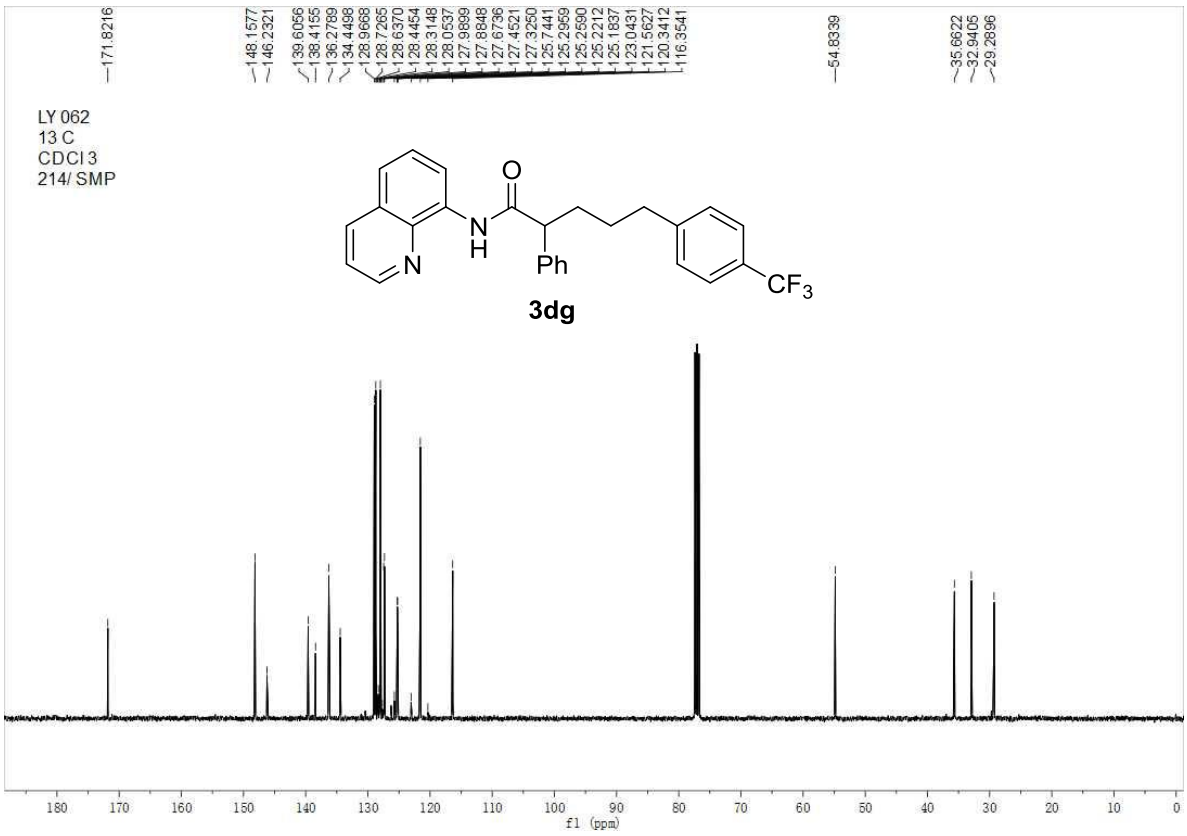
8.7621
8.7474
8.7437
8.7125
8.7085
8.7019
8.6979
8.0954
8.0915
8.0748
8.0709
7.5052
7.4852
7.4482
7.4281
7.3950
7.3750
7.3576
7.3383
7.2897
7.2468
7.2268
3.7293
3.7104
3.6915
2.7827
2.7254
2.7079
2.6511
2.4010
2.3547
2.3272
2.3086
2.0179
1.9718
1.9586
1.9257
1.8096
1.7381
1.6985
1.6669
1.5901
LY 062
1 H
CDCl 3
201/ SMP
O
N
H
N
Ph
CF3
3dg
0.99
1.00
1.00
1.04
6.20
3.23
3.14
1.00
2.01
1.02
1.01
2.47
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
f1 (ppm)


171.8216
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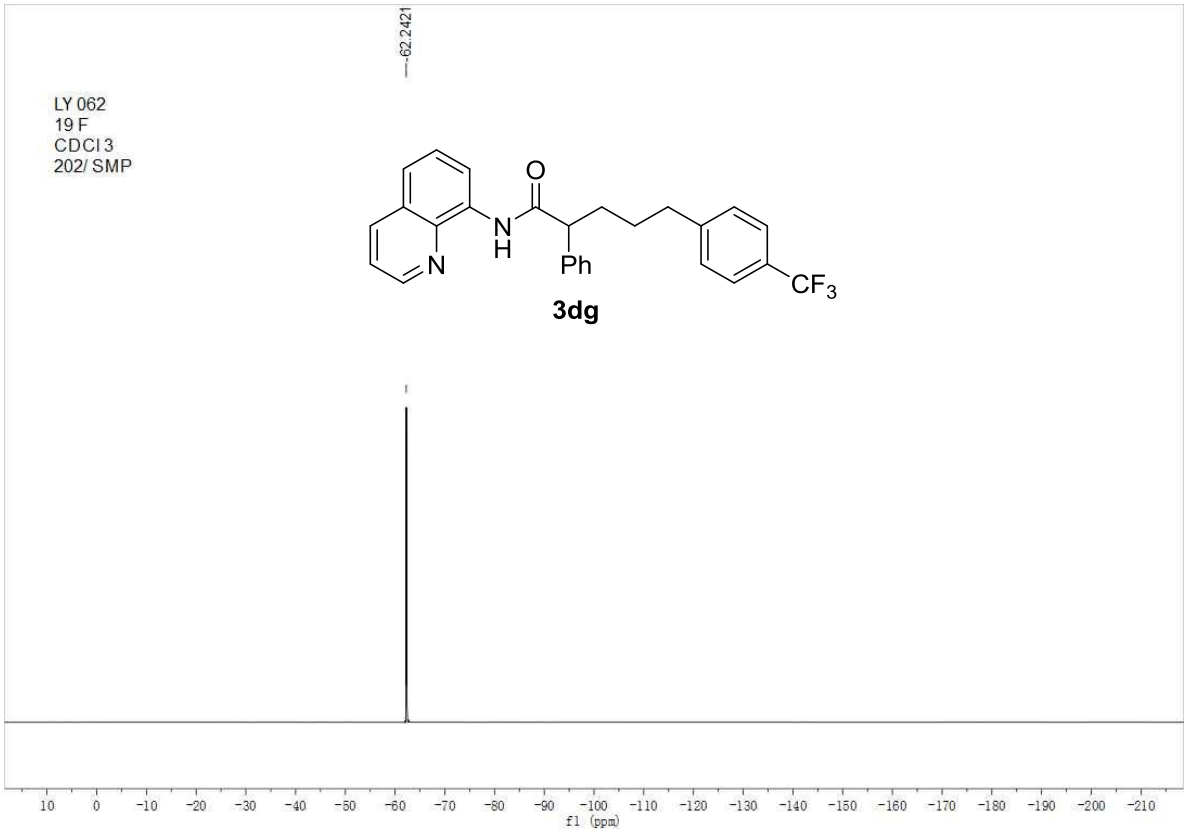
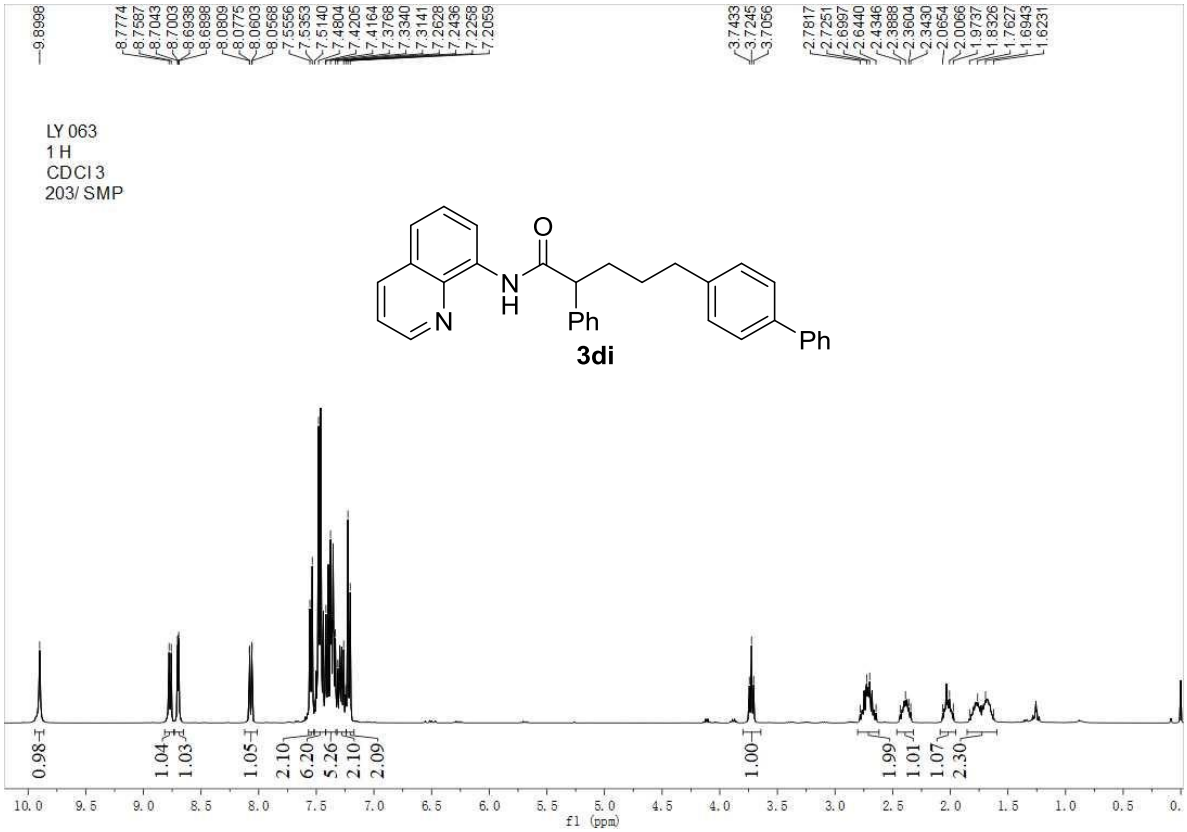
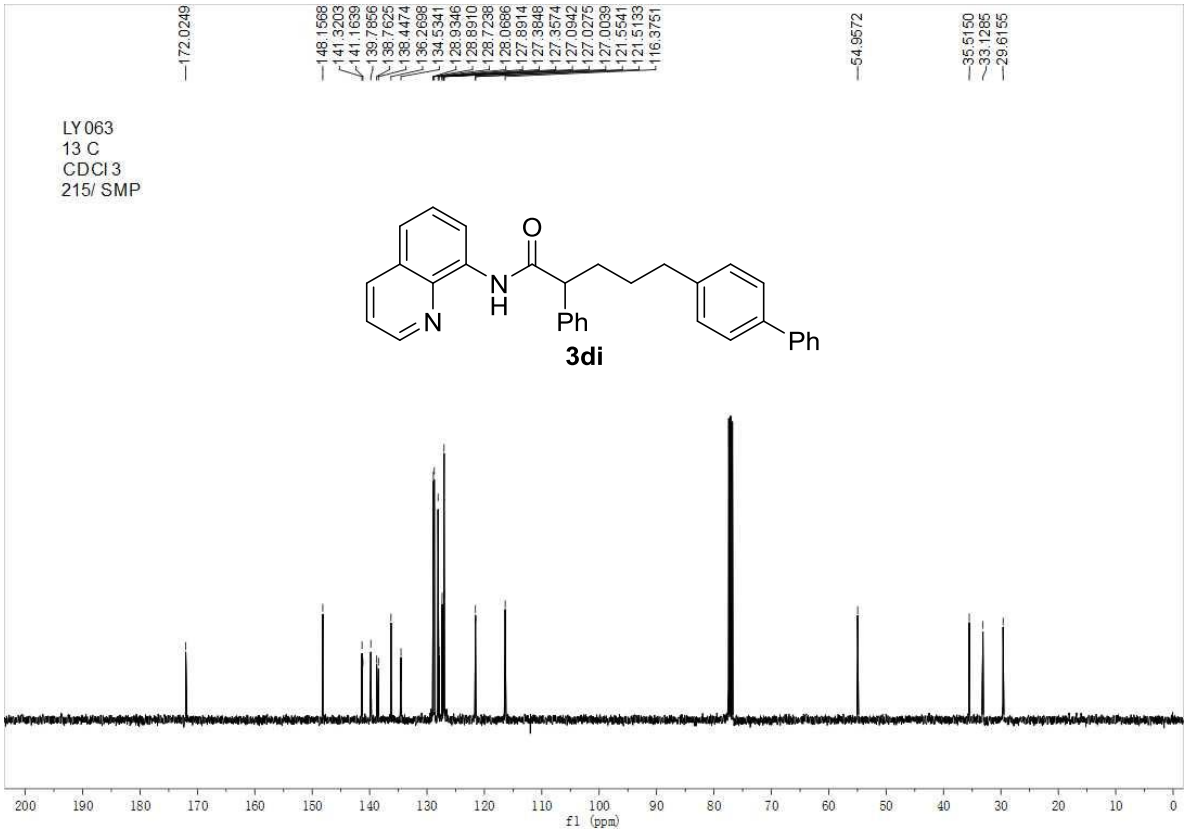
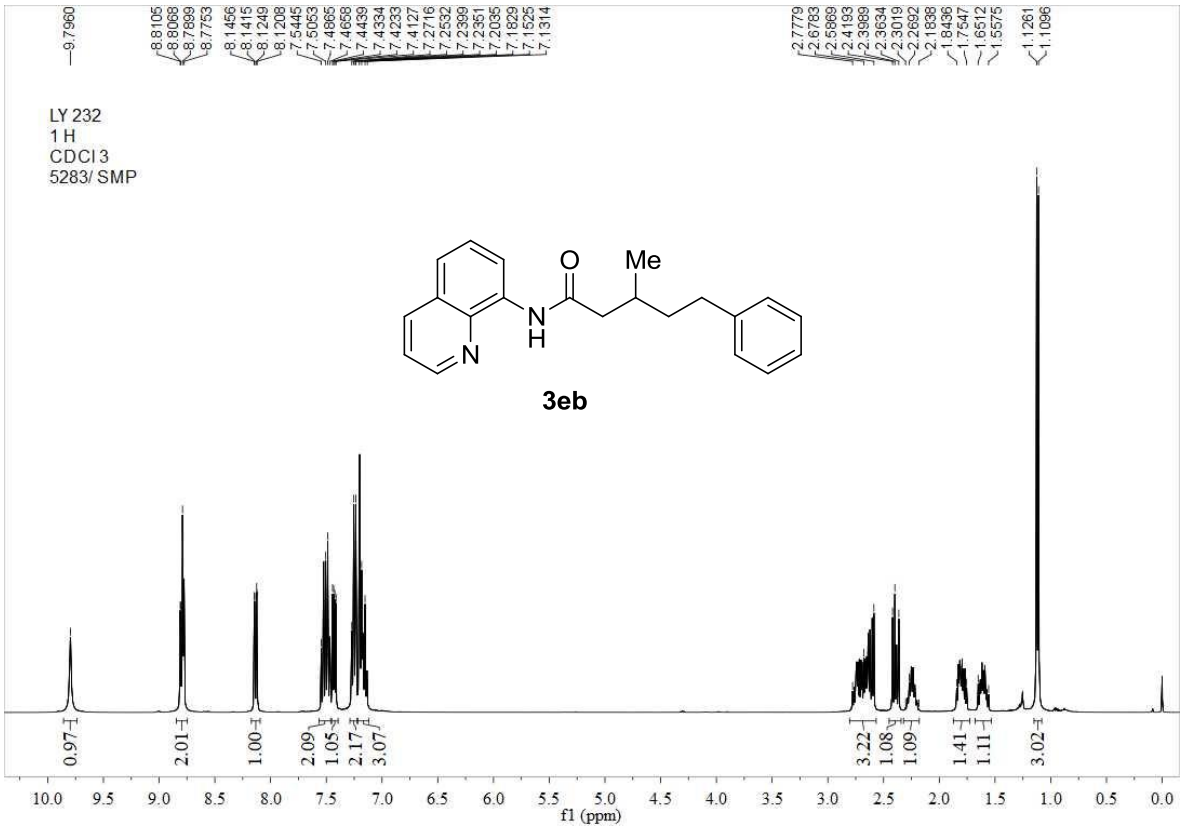
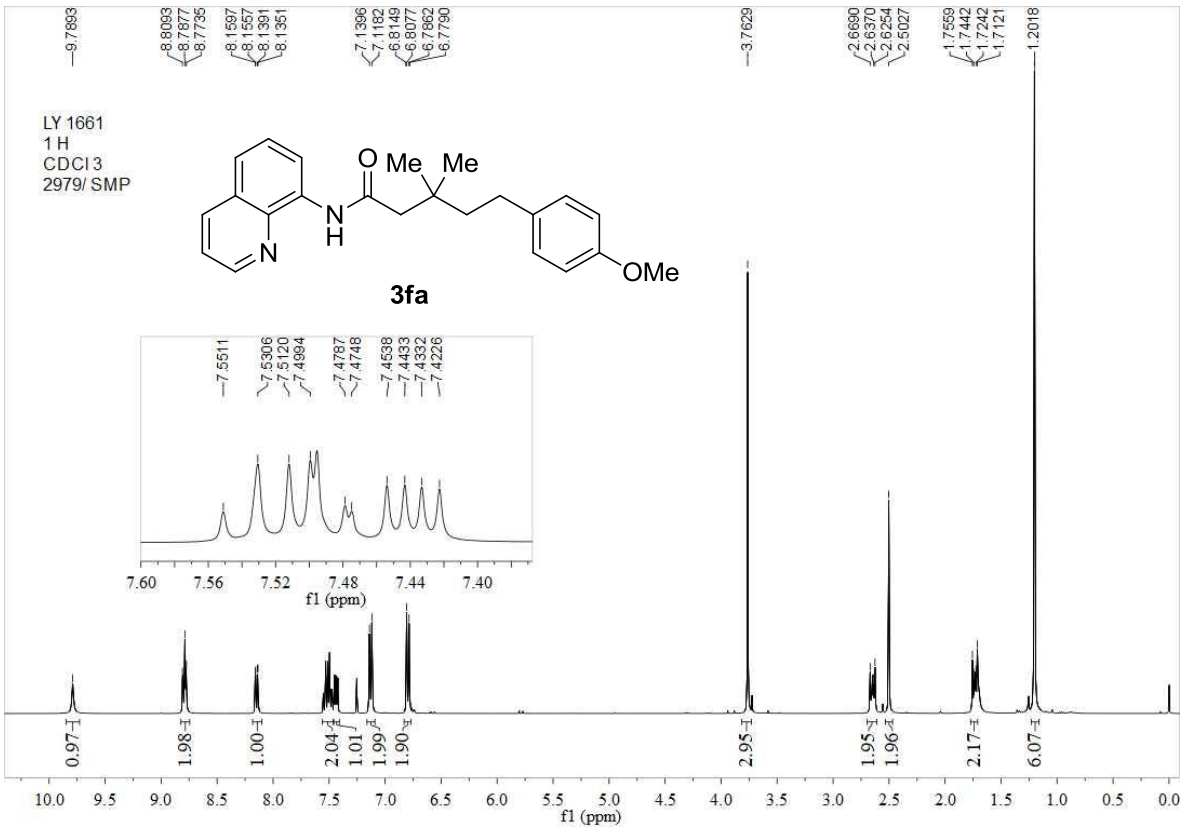
146.2321
139.6056
138.4155
136.2789
134.4498
129.9668
128.7265
128.6370
128.4454
128.3148
128.0537
127.9899
127.8848
127.6736
127.4521
127.3250
125.7441
125.2959
125.2590
125.2212
125.1837
123.0431
121.5627
120.3412
116.3541
54.8339
35.6622
32.9405
29.2896
LY 062
13 C
CDCl 3
214/ SMP
O
N
H
N
Ph
CF3
3dg
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

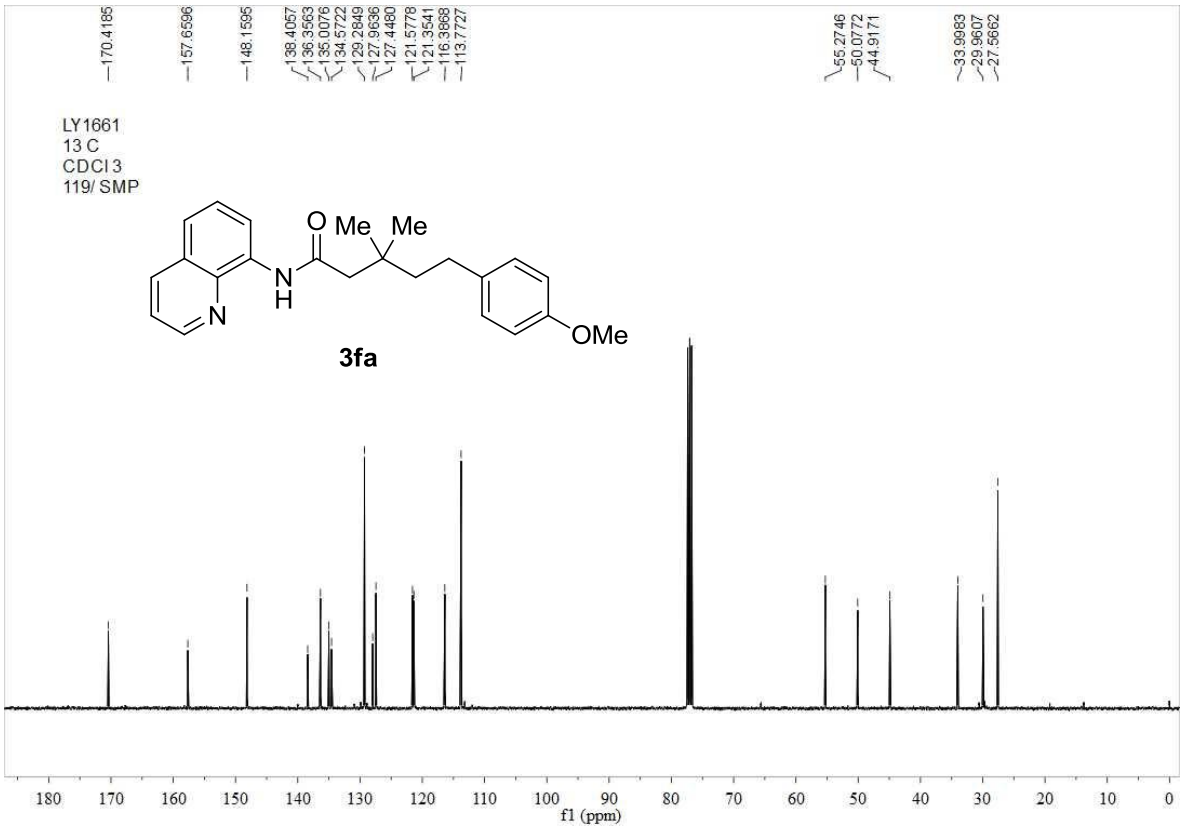

62.2421
LY 062
19 F
CDCl 3
202/ SMP
O
N
H
N
Ph
CF3
3dg
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

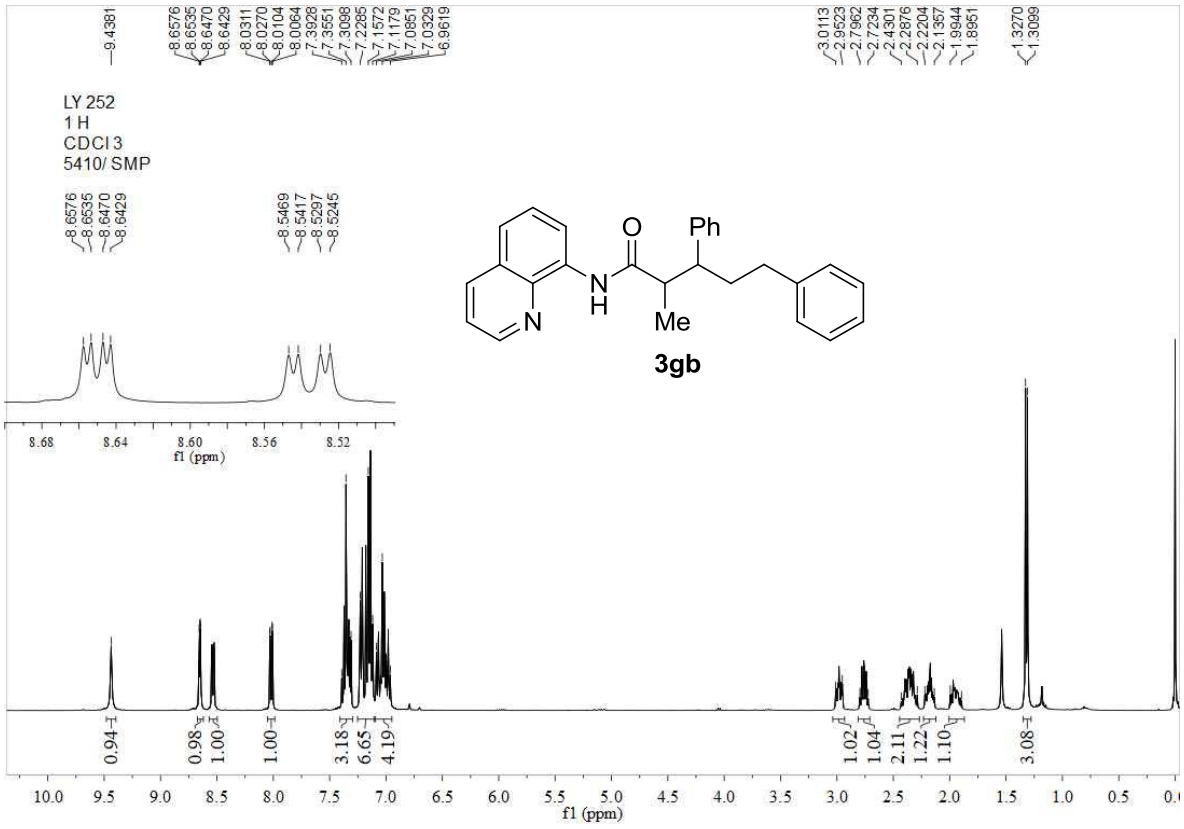

LY 063
1 H
CDCl 3
203/ SMP
O
N
H
N
Ph
Ph
3di
f1 (ppm)

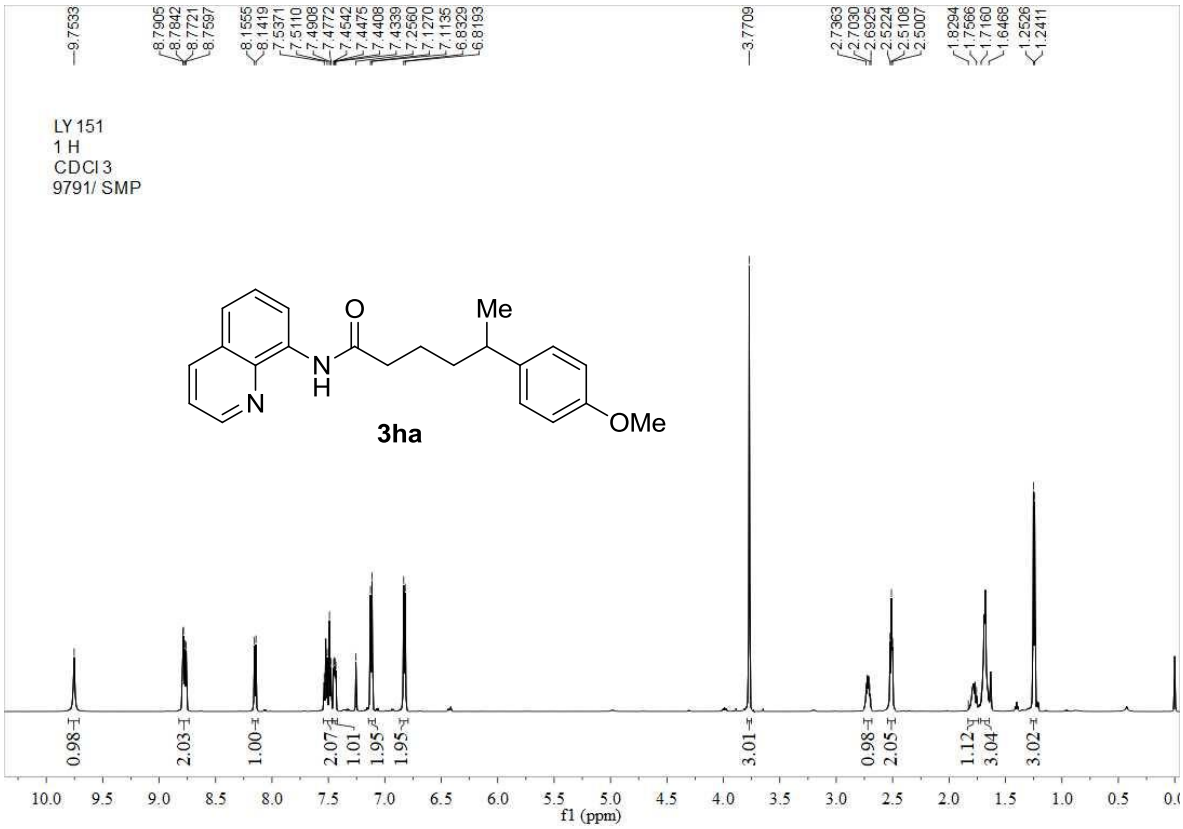

LY 063
13 C
CDCl 3
215/ SMP
O
N
H
N
Ph
Ph
3di
f1 (ppm)

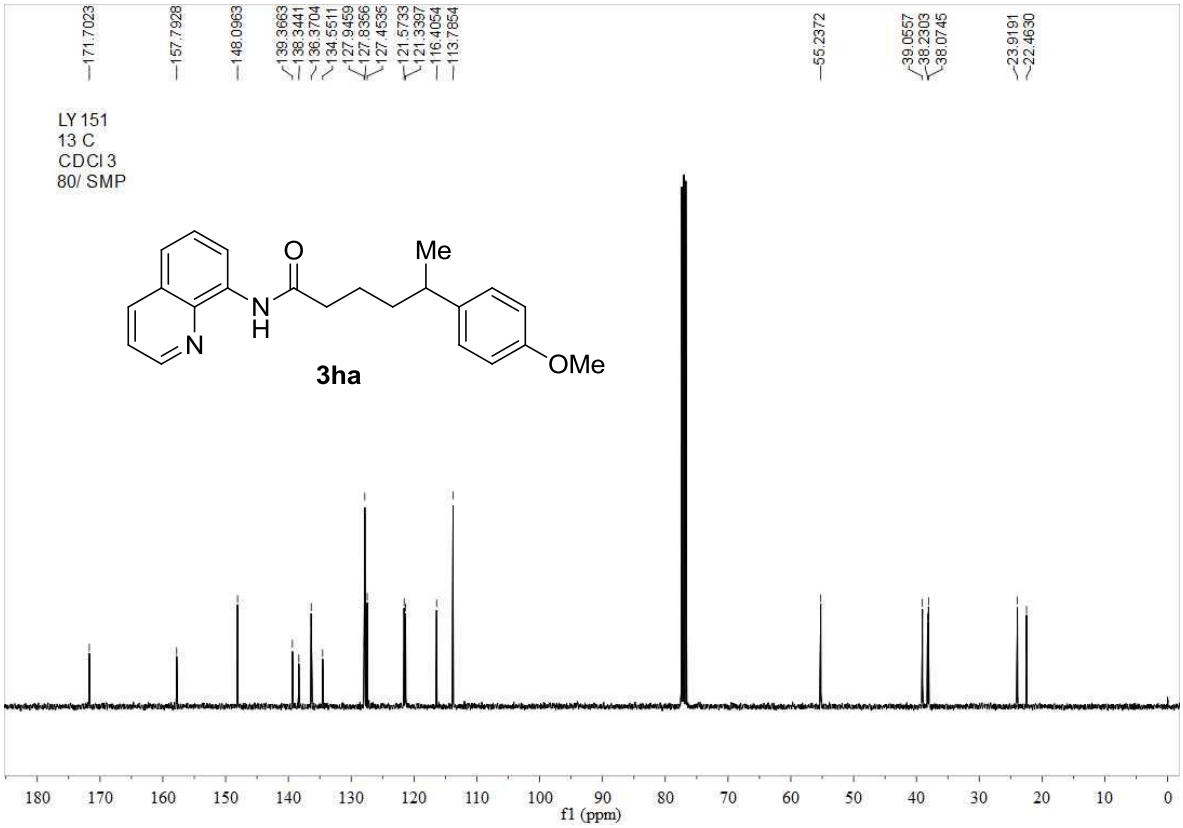

LY 232
1 H
CDCl 3
5283/ SMP
O
Me
N
H
N
3eb
f1 (ppm)

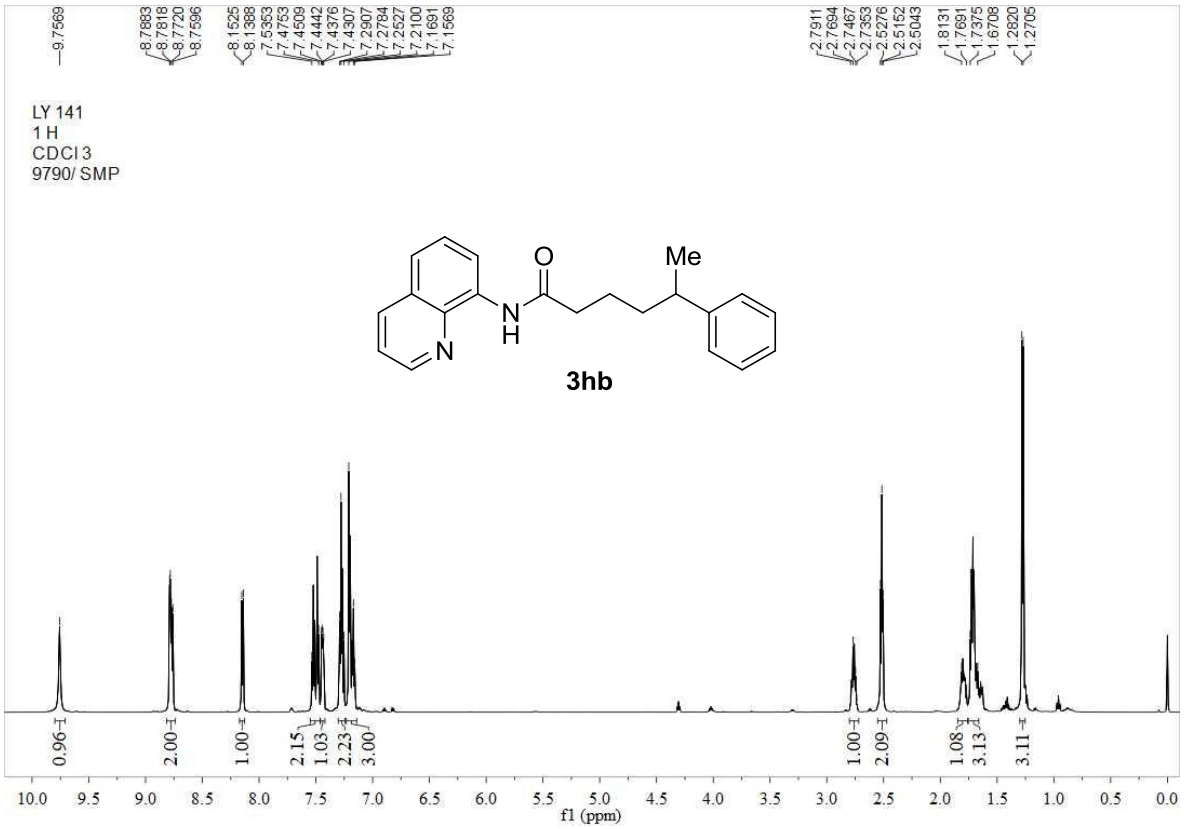

LY 1661
1 H
CDCl 3
2979/ SMP
O
Me
Me
N
H
N
OMe
3fa
f1 (ppm)

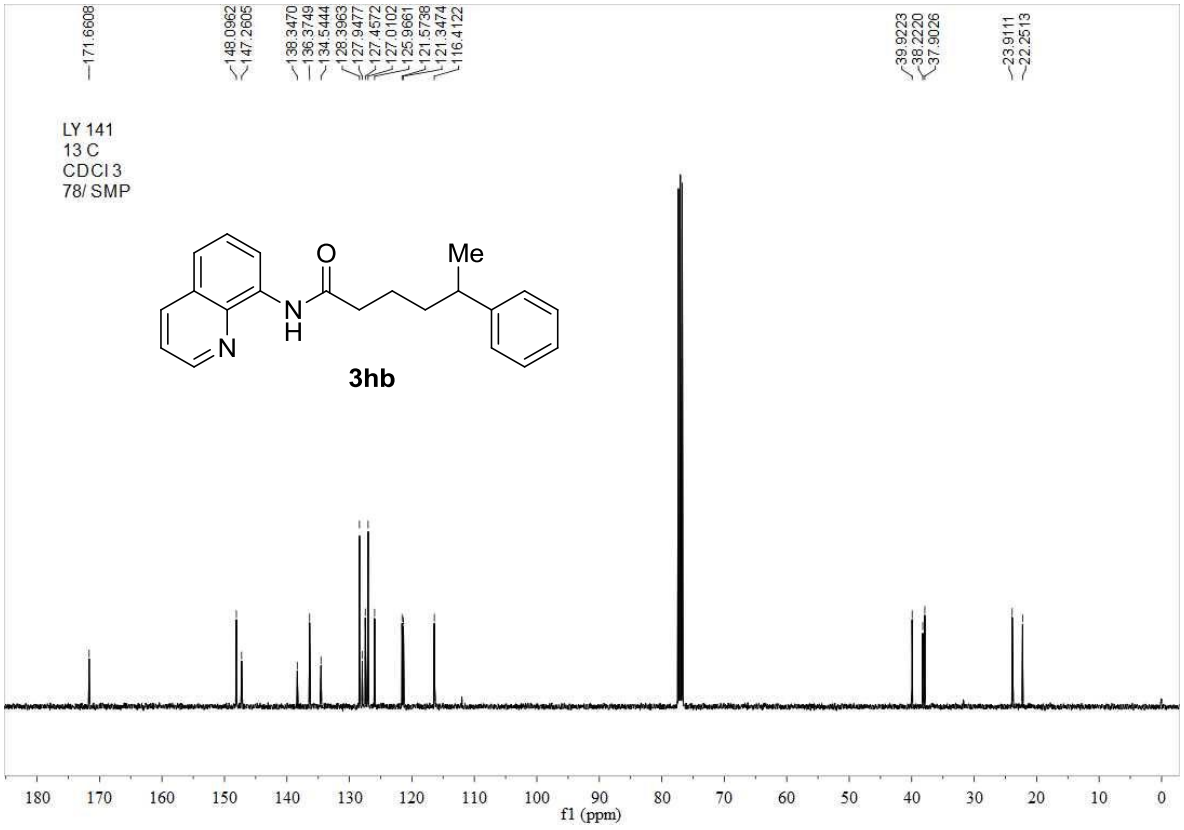

LY1661
13 C
CDCl3
119/ SMP
O
Me
Me
N
H
N
OMe
3fa
f1 (ppm)

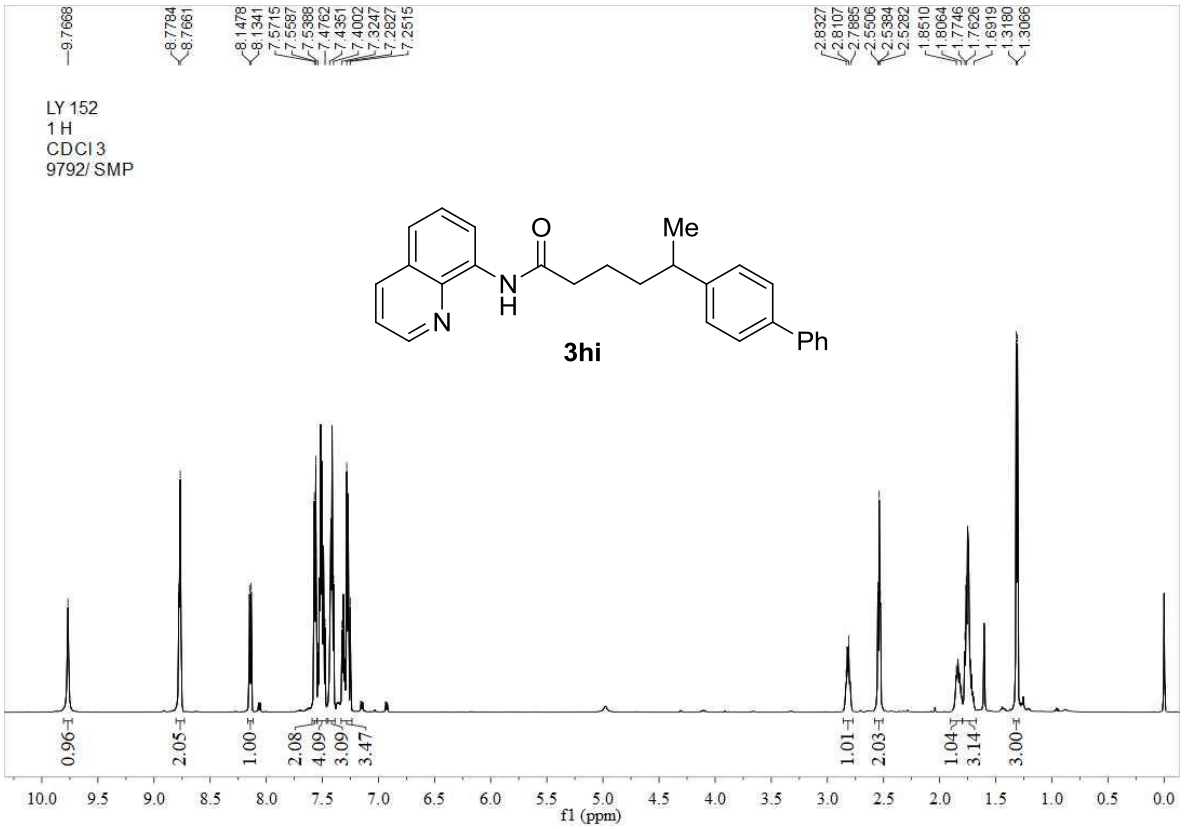

LY 252
1 H
CDCl3
5410/ SMP
O
Ph
N
H
N
Me
3gb
f1 (ppm)

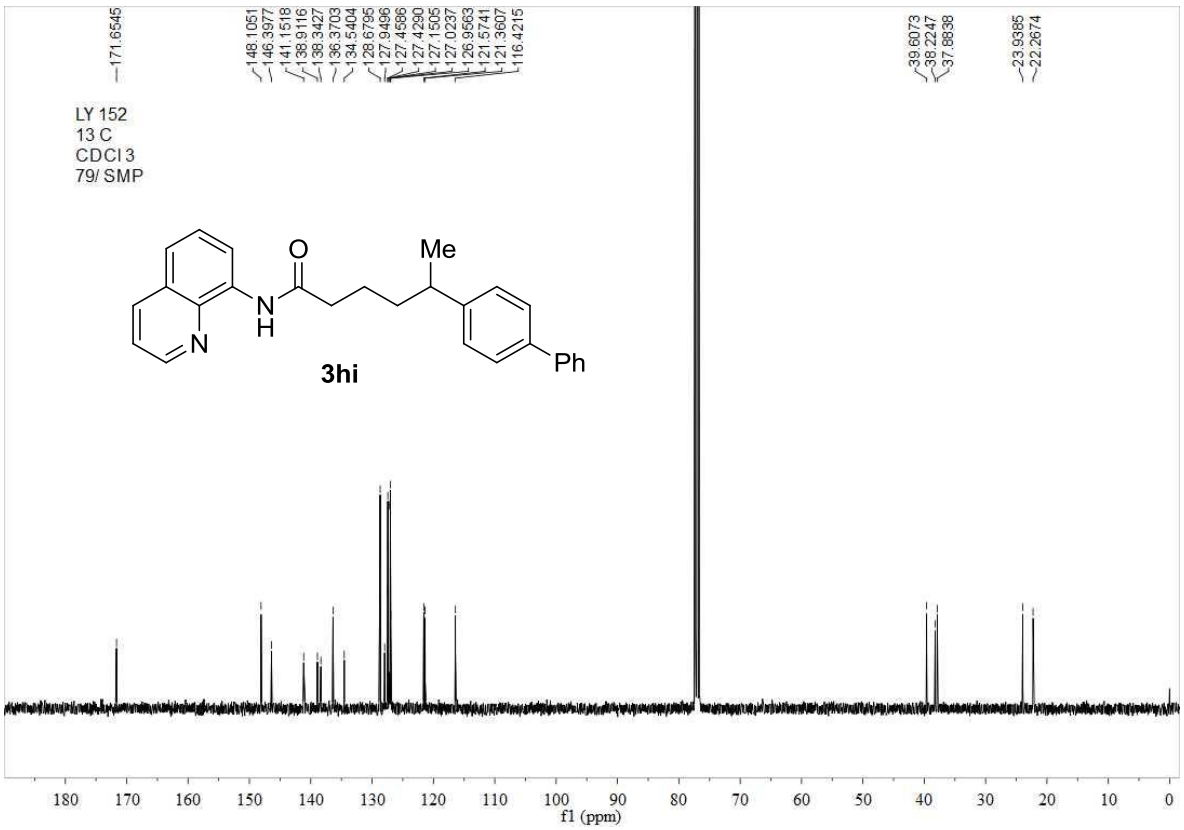

LY 151
1 H
CDCl 3
9791/ SMP
3ha
f1 (ppm)

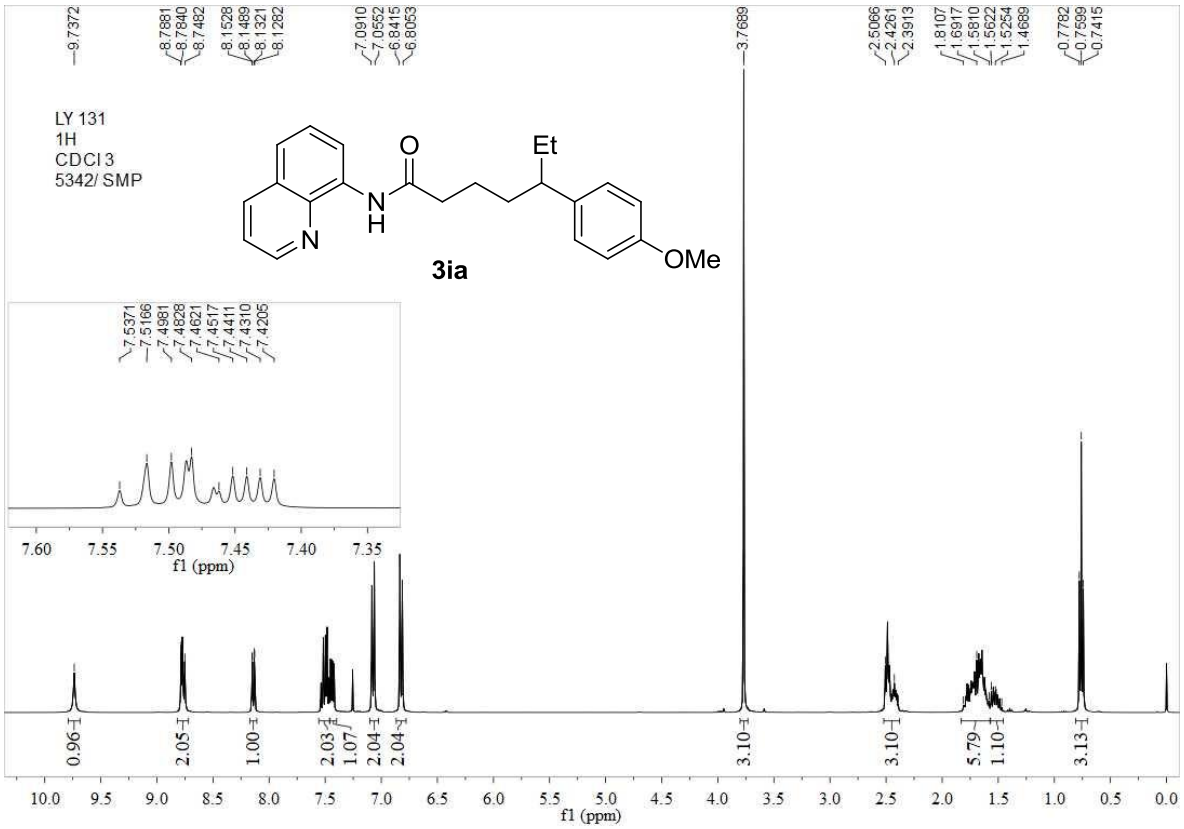

LY 151
13 C
CDCl 3
80/ SMP
3ha
f1 (ppm)

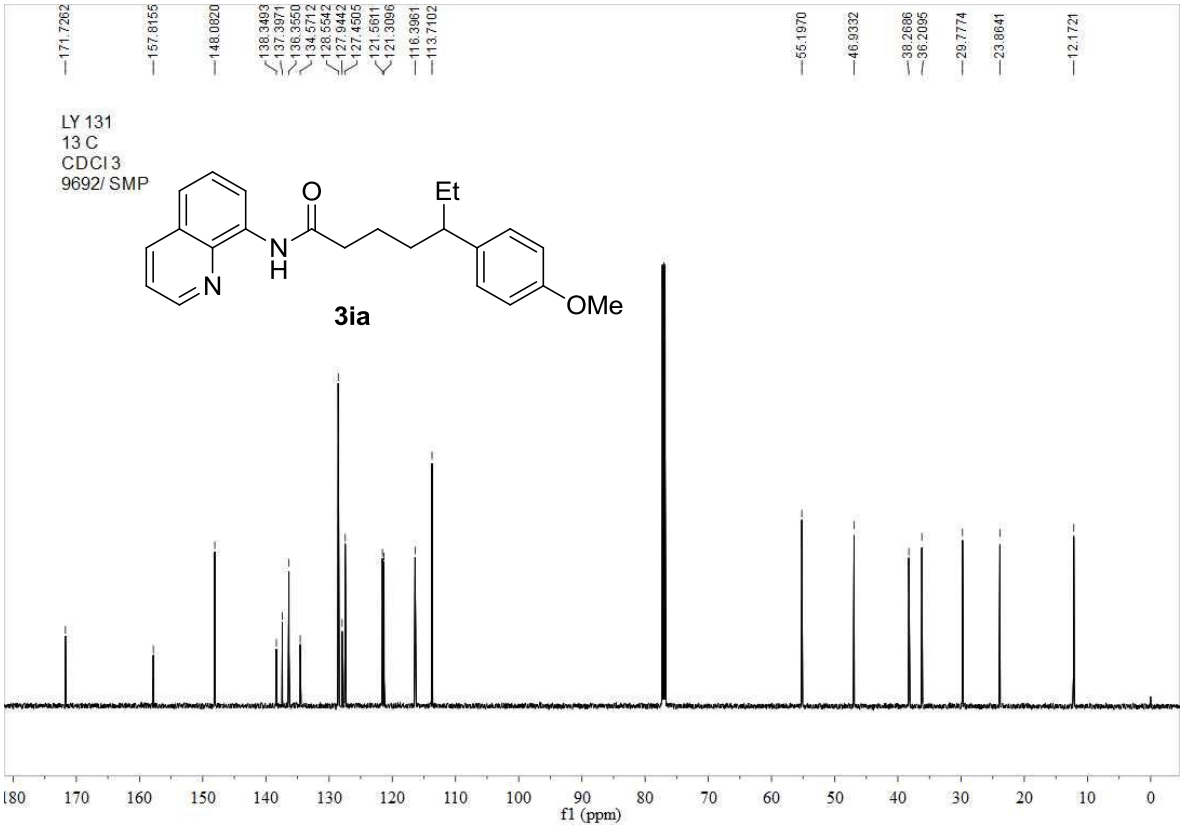

LY 141
1 H
CDCl 3
9790/ SMP
O
Me
N
H
N
3hb
f1 (ppm)

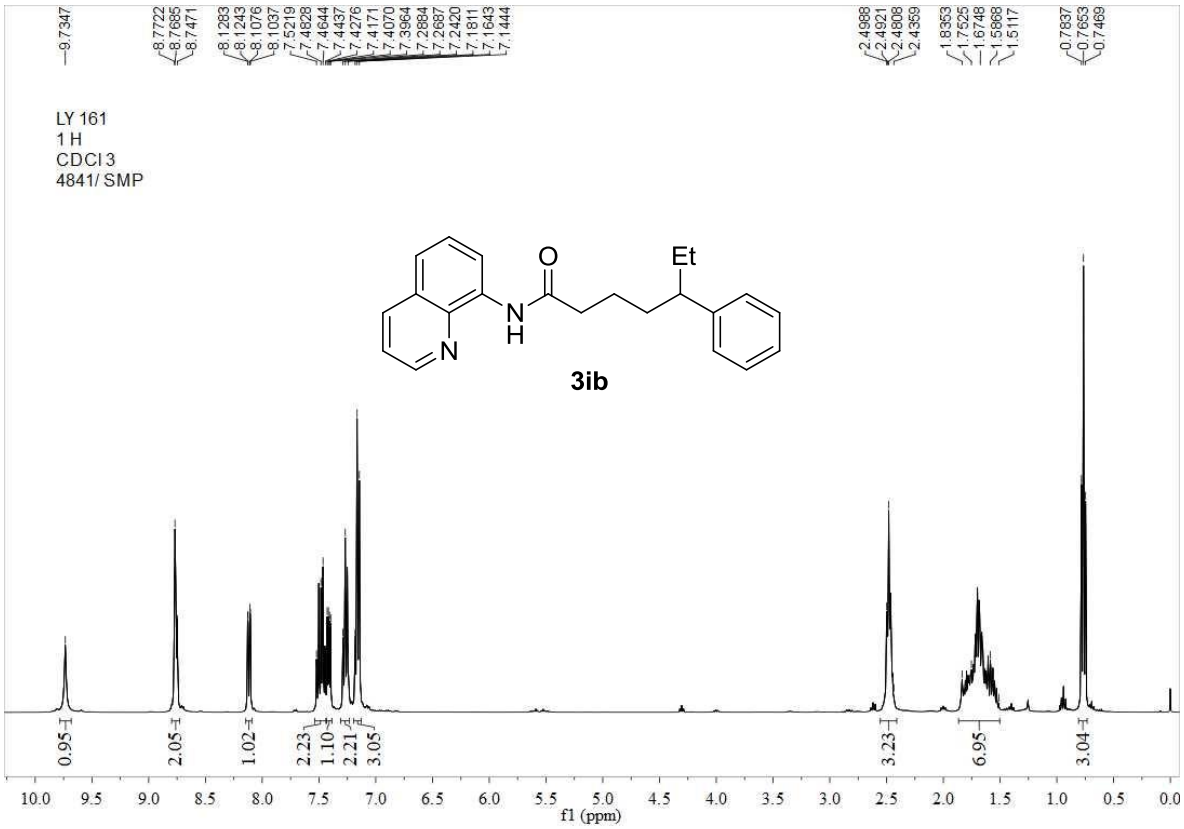

LY 141
13 C
CDCl 3
78/ SMP
O
Me
N
H
N
3hb
f1 (ppm)

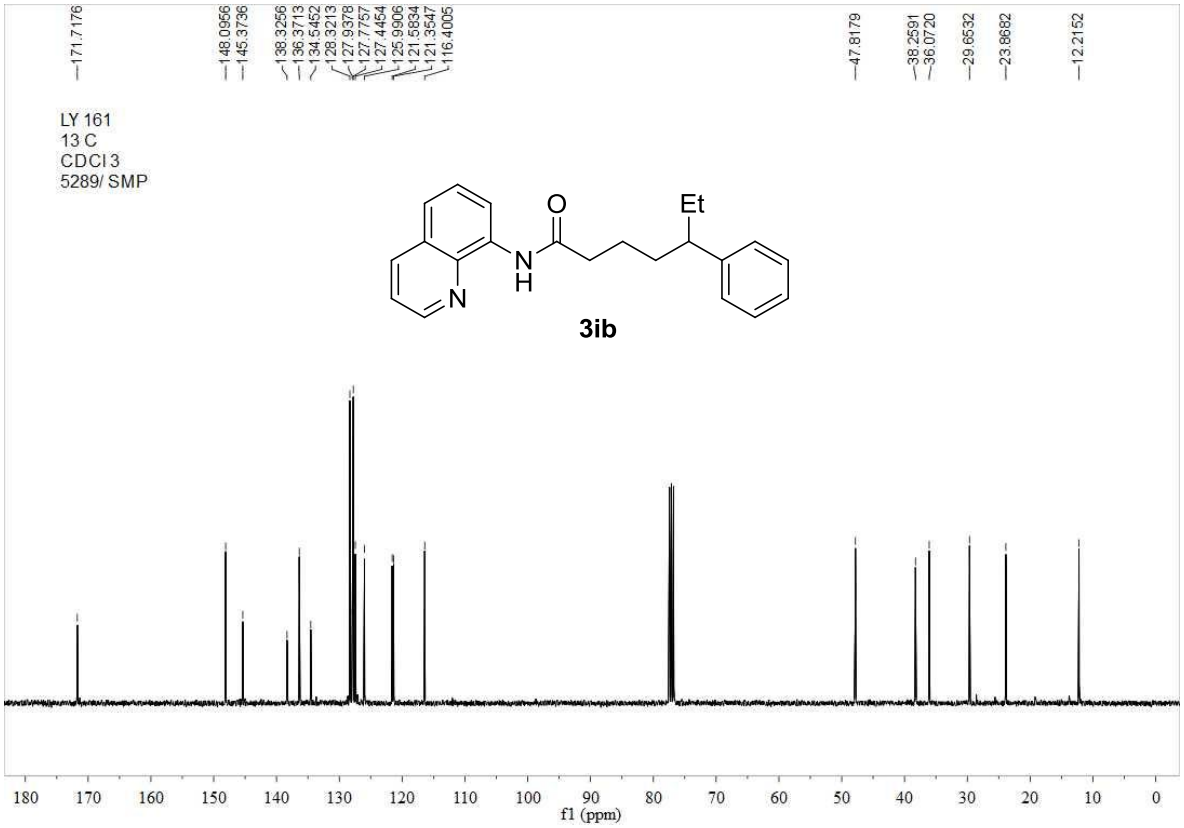

LY 152
1 H
CDCl 3
9792/ SMP
3hi
f1 (ppm)

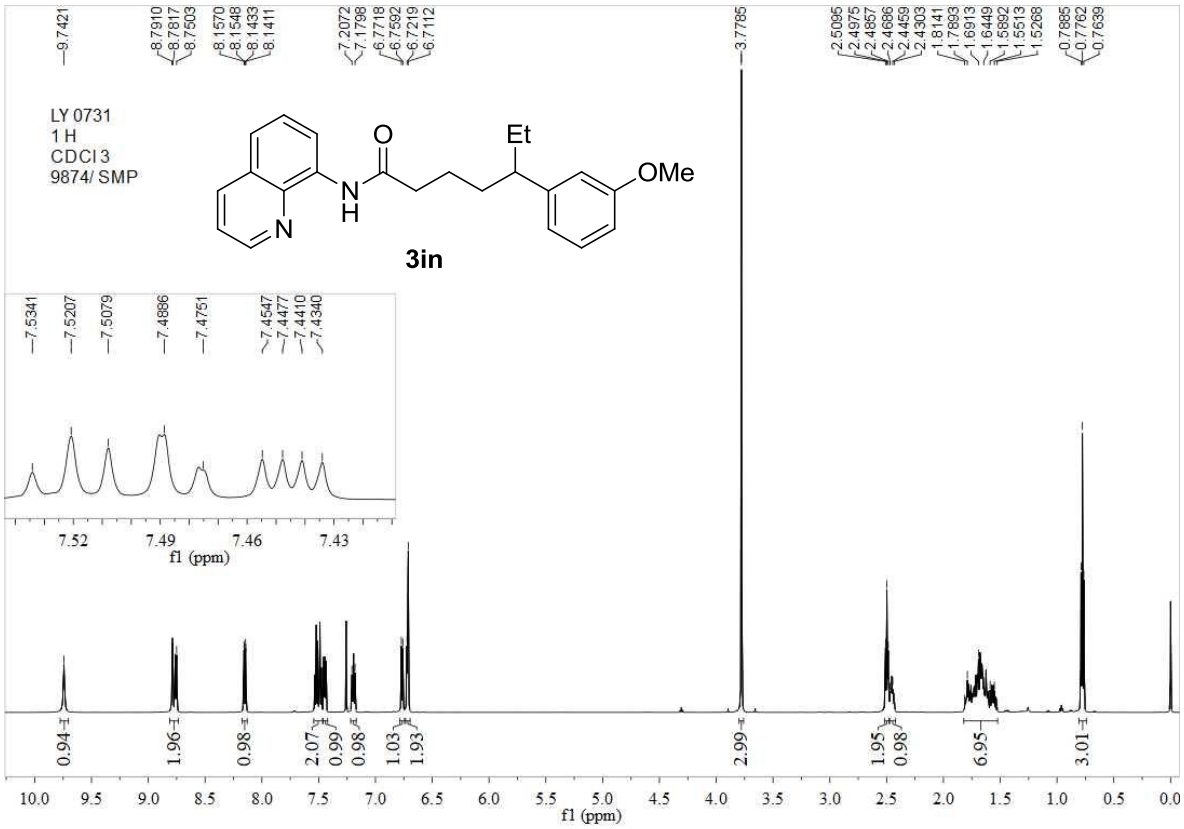

LY 152
13 C
CDCl 3
79/ SMP
3hi
f1 (ppm)

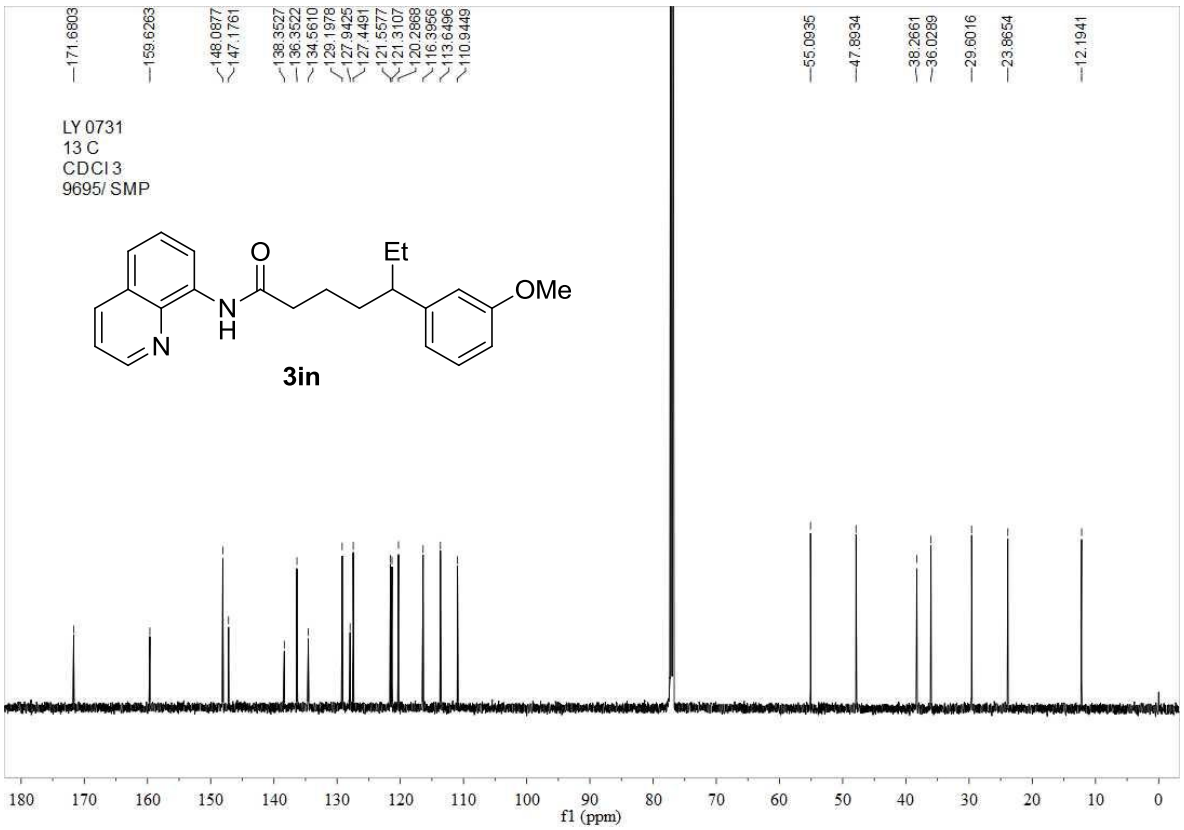

LY 131
1H
CDCl3
5342/ SMP
3ia
f1 (ppm)

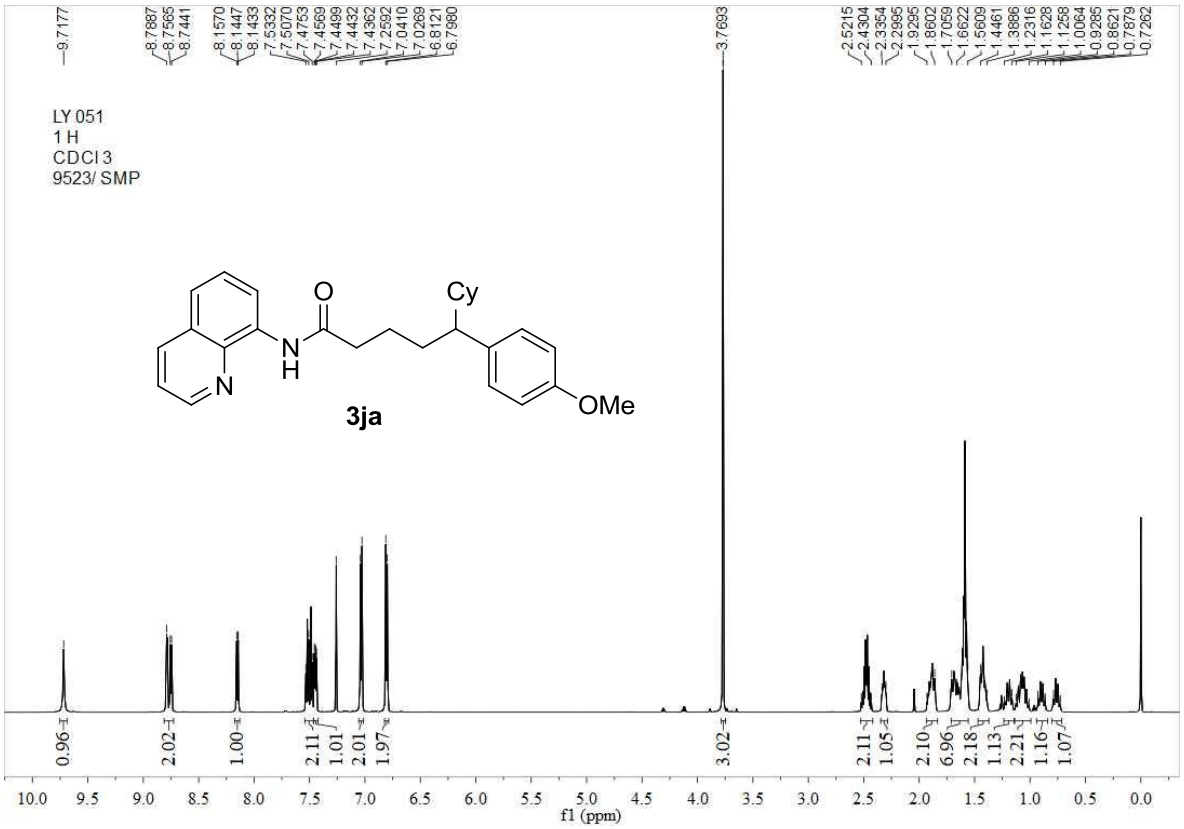

LY 131
13 C
CDCl3
9692/ SMP
3ia
f1 (ppm)

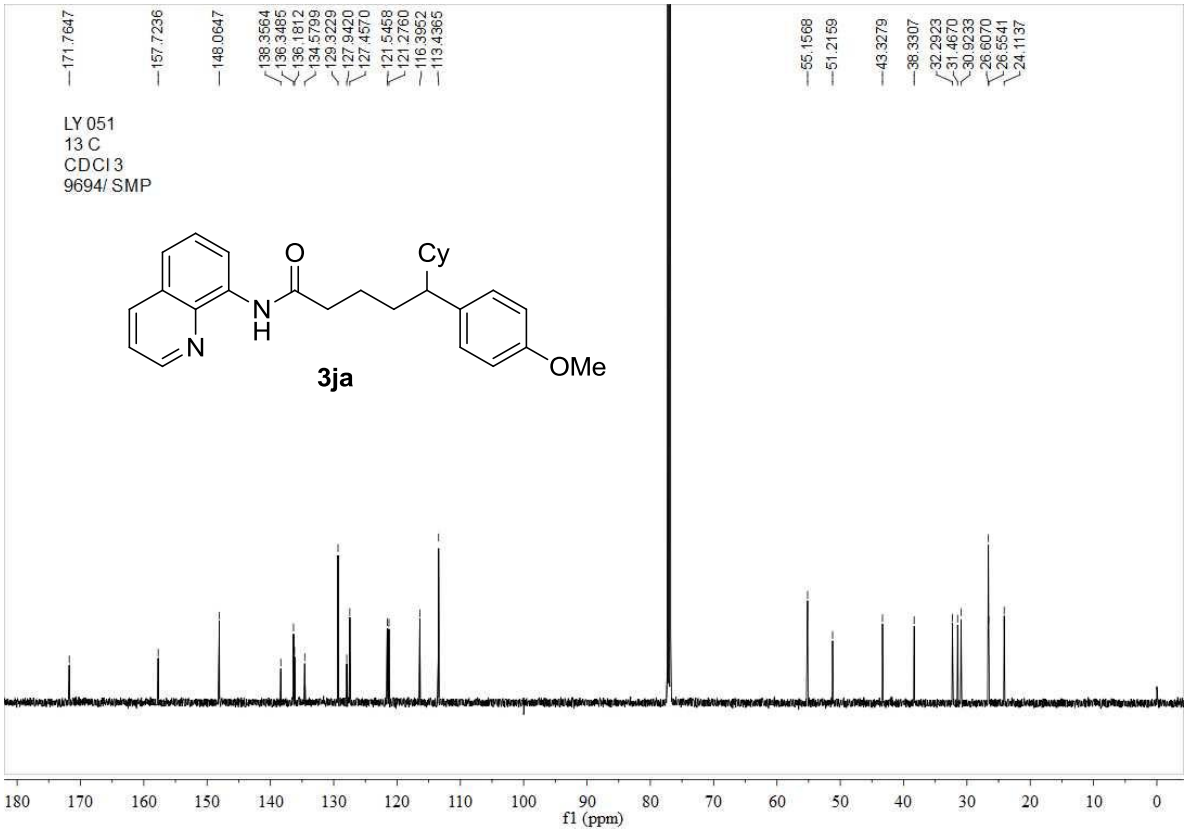

LY 161
1 H
CDCl 3
4841/ SMP
O
Et
N
H
N
3ib
f1 (ppm)

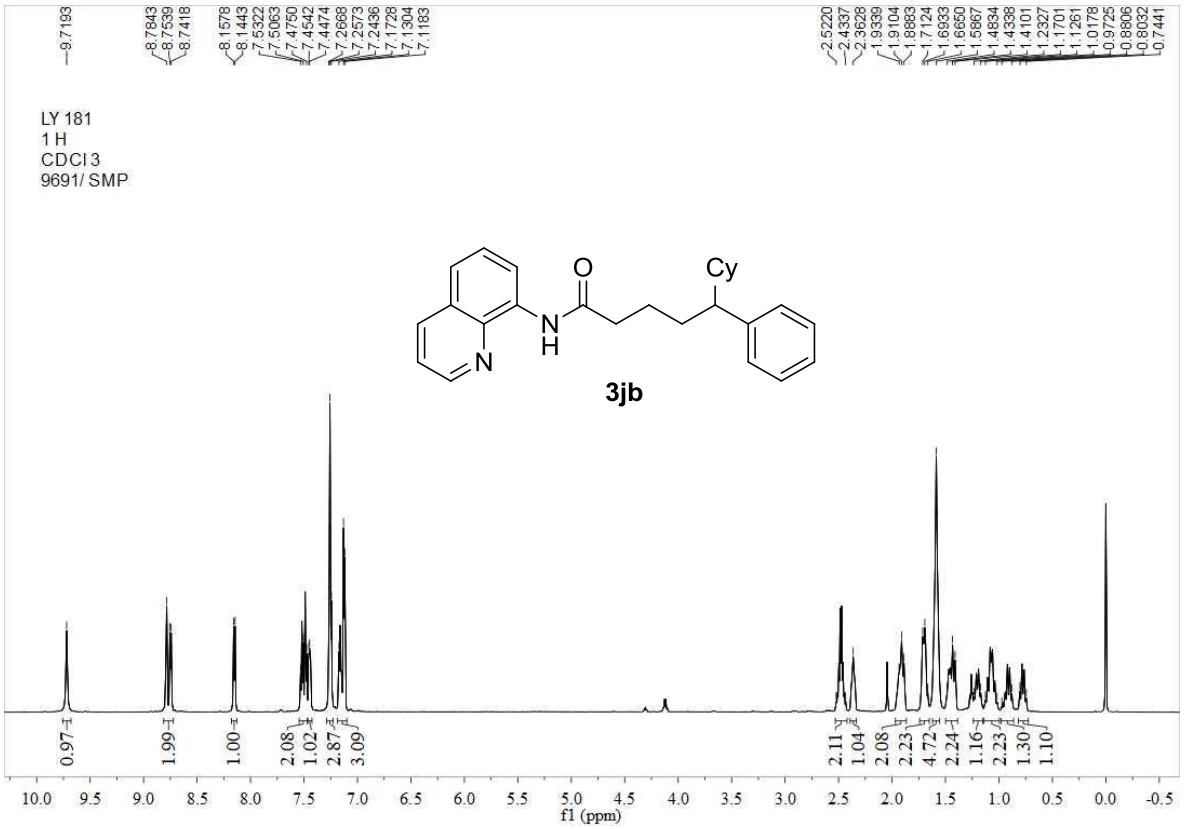

LY 161
13 C
CDCl 3
5289/ SMP
O
Et
N
H
N
3ib
f1 (ppm)

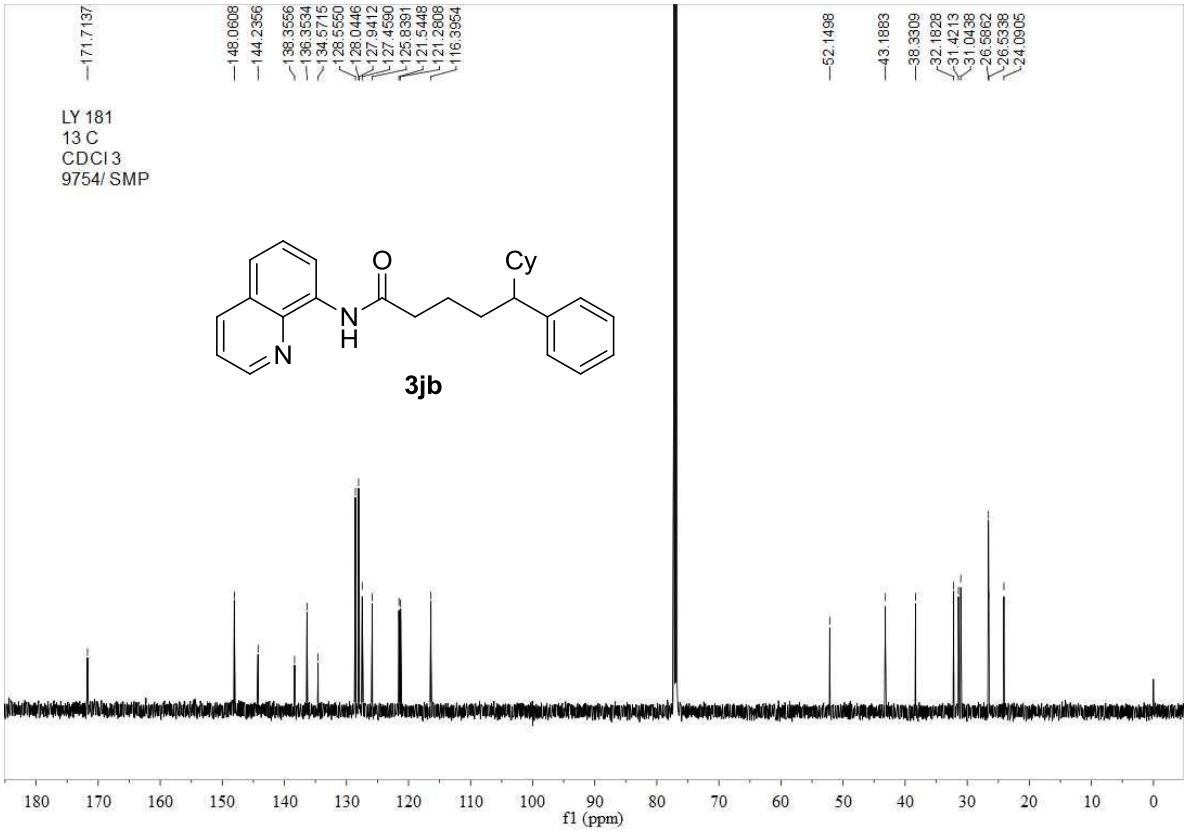

LY 0731
1 H
CDCl 3
9874/ SMP
O
Et
N
H
N
OMe
3in
f1 (ppm)

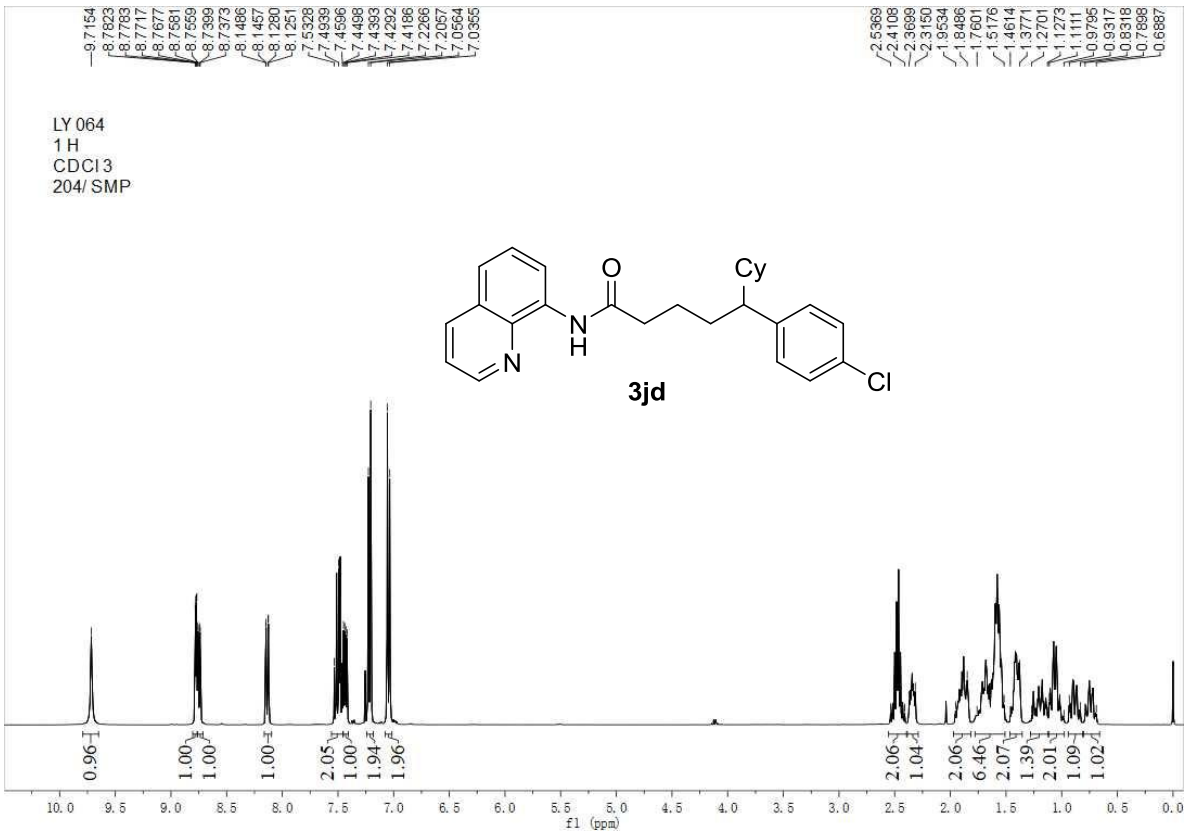

LY 0731
13 C
CDCl 3
9695/ SMP
O
Et
N
H
N
OMe
3in
f1 (ppm)

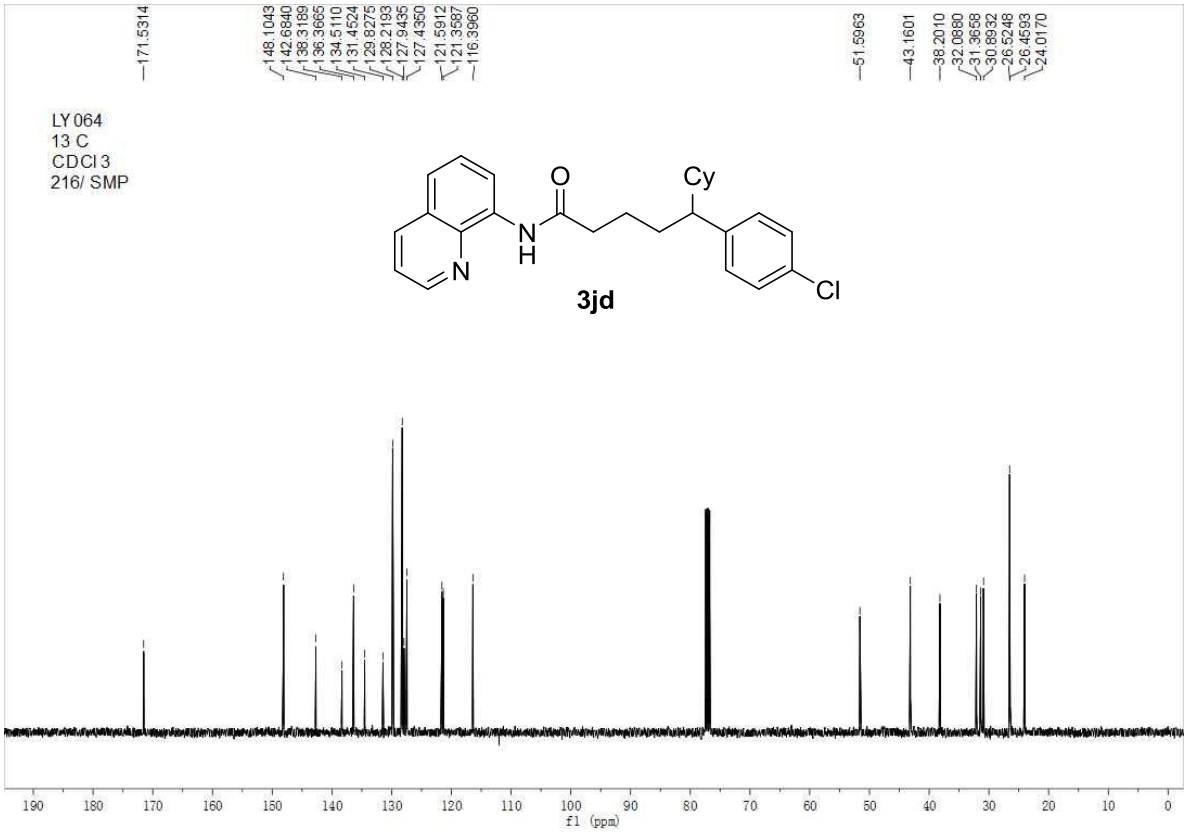

LY 051
1 H
CDCl 3
9523/ SMP
3ja
f1 (ppm)

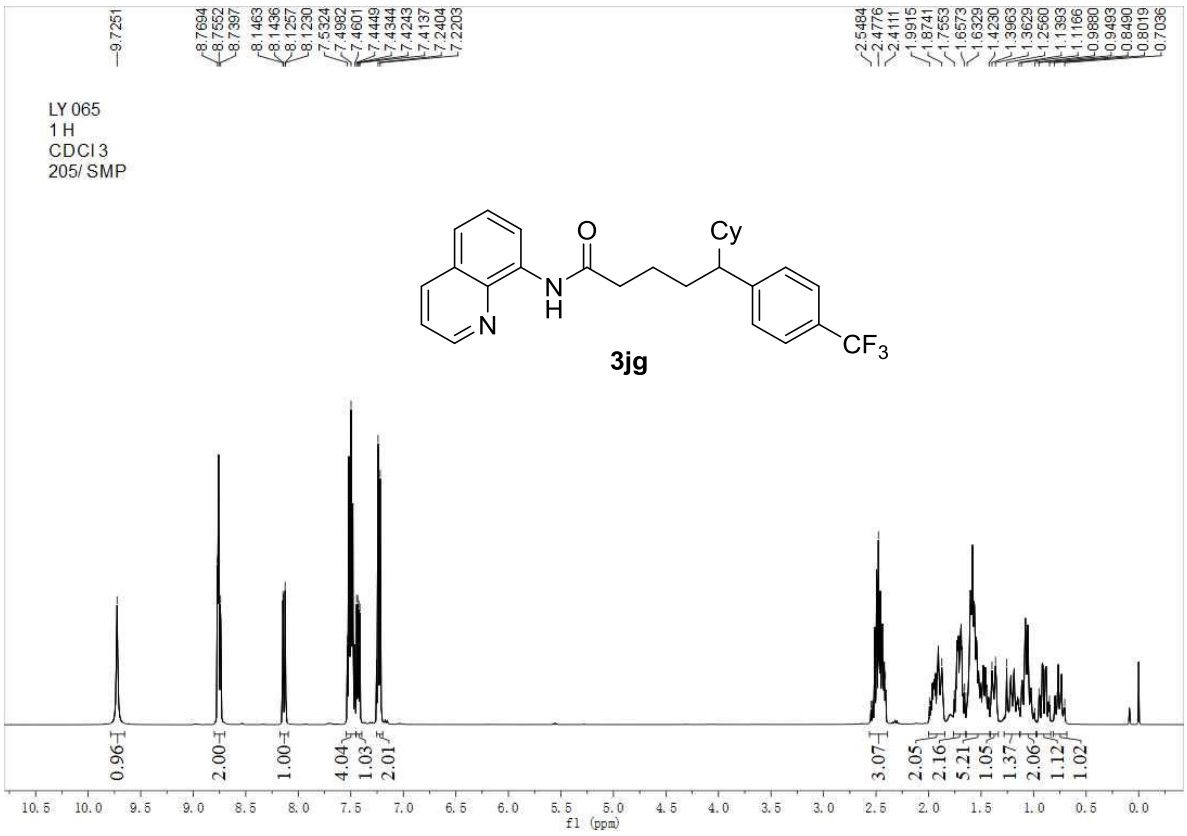

LY 051
13 C
CDCl 3
9694/ SMP
3ja
f1 (ppm)

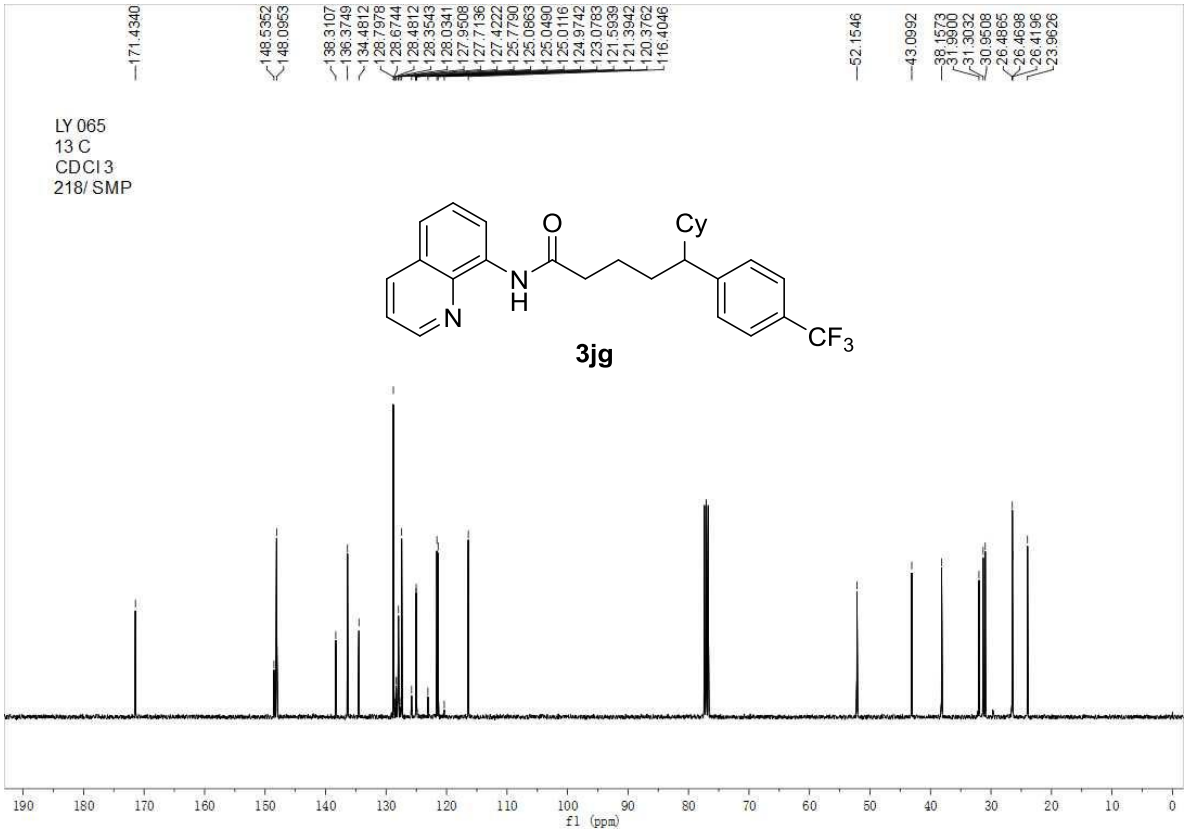

LY 181
1 H
CDCl 3
9691/ SMP
O
Cy
N
H
N
3jb
f1 (ppm)

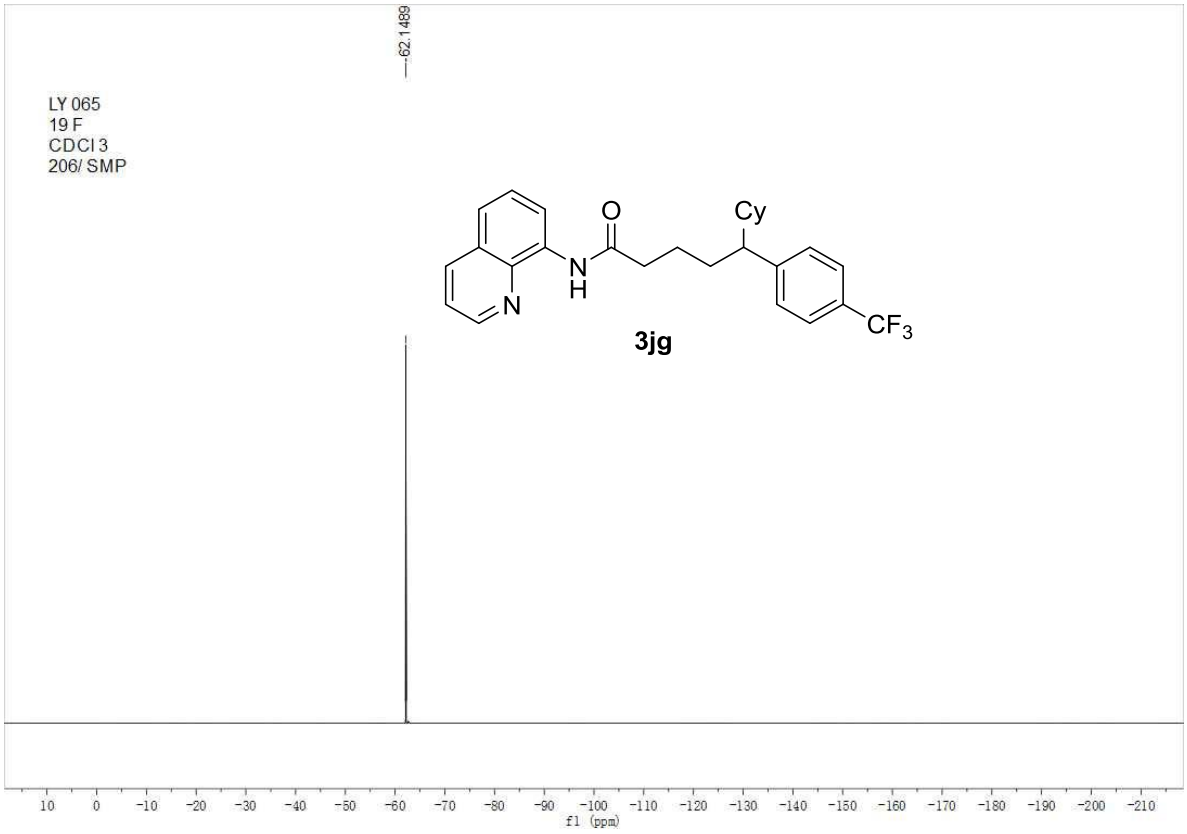

LY 181
13 C
CDCl 3
9754/ SMP
O
Cy
N
H
N
3jb
f1 (ppm)

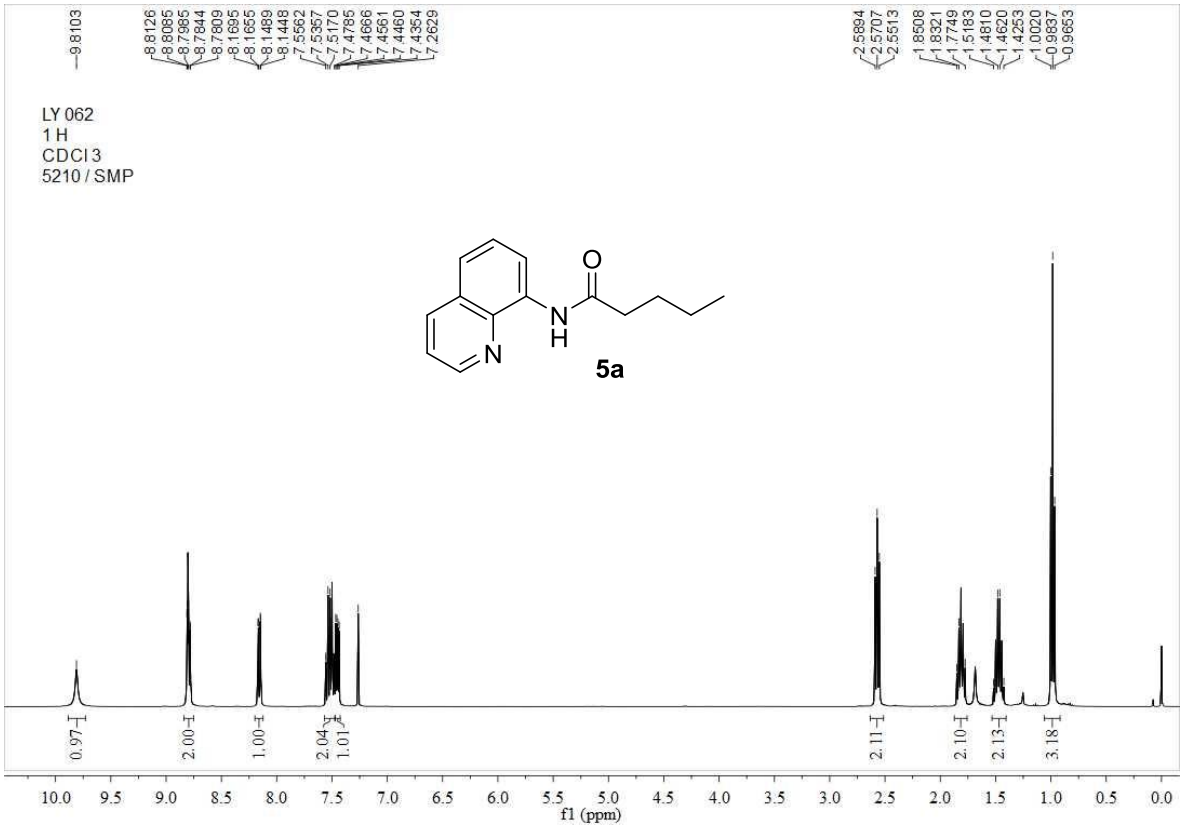

LY 064
1 H
CDCl 3
204/ SMP
O
Cy
N
H
N
Cl
3jd
fl (ppm)


LY 064
13 C
CDCl 3
216/ SMP
O
Cy
N
H
N
Cl
3jd
fl (ppm)


LY 065
1 H
CDCl 3
205/ SMP
O
Cy
N
H
N
CF3
3jg
f1 (ppm)


LY 065
13 C
CDCl 3
218/ SMP
O
Cy
N
H
N
CF3
3jg
f1 (ppm)


LY 065
19 F
CDCl 3
206/ SMP
-62.1489
O
Cy
N
H
N
CF3
3jg
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


9.8103
8.8126
8.8085
8.7985
8.7844
8.7809
8.1695
8.1655
8.1489
8.1448
7.5562
7.5357
7.5170
7.4785
7.4666
7.4561
7.4460
7.4354
7.2629
2.5894
2.5707
2.5513
1.8508
1.8321
1.7749
1.5183
1.4810
1.4620
1.4253
1.0020
0.9837
0.9653
LY 062
1 H
CDCl 3
5210 / SMP
O
N
H
N
5a
0.97
2.00
1.00
2.04
1.01
2.11
2.10
2.13
3.18
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
f1 (ppm)