

Supporting Information

Palladium(II)-Catalyzed Stereospecific Alkenyl C-H Bond Alkylation of Alkenes with Alkyl Iodides

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1. General Information

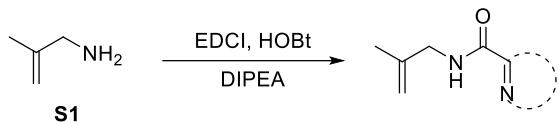
Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. ^1H NMR and ^{13}C NMR spectra were recorded at 25 $^{\circ}\text{C}$ on a Bruker Advance 400M NMR spectrometers (CDCl_3 as solvent). Chemical shifts for ^1H NMR spectra are reported as δ in units of parts per million (ppm) downfield from SiMe_4 (δ 0.00) and relative to the signal of SiMe_4 (δ 0.00 singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublet of doublets); dt (doublet of triplets); m (multiplets), etc. Coupling constants are reported as a J value in Hz. ^{13}C NMR spectra are reported as δ in units of parts per million (ppm) downfield from SiMe_4 (δ 0.00) and relative to the signal of chloroform-*d* (δ 77.16 triplet). Infrared spectra (IR) were recorded using a thin film on a Nicolet 6700 ATR/FT-ATR spectrometer, and ν_{max} are partially reported in cm^{-1} . High resolution mass spectral analysis (HRMS) was performed on Waters XEVO G2 Q-TOF using ESI-QTOF. The enantiomeric excesses were determined by HPLC analysis on Chiral Daicel Chiralpak OD-3 and OB-H columns. Flash chromatography was performed using 200-300 mesh silica gel with the indicated solvent system. Gas chromatography was performed with machines of Agilent Technologies 7890A. Optical rotations were recorded on an Anton Paar MCP 200 polarimeter at 589 nm in CHCl_3 .

2. Experimental Procedures

2.1 Synthesis of Starting Materials

Method A:

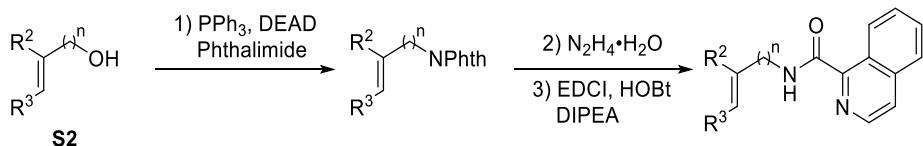
The starting materials **1a**-(**A-N**) and **1b**, were prepared according to the literature procedure¹ with slight modifications.



A mixture of 2-methylallylamine **S1** (0.78g, 10 mmol), acid (11 mmol), *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDCI) (2.11 g, 11 mmol), 1-hydroxybenzotriazole (HOBt) (1.49 g, 11 mmol), and DIPEA (3.3 mL, 20 mmol) in DCM (30 mL) was stirred at room temperature overnight. Water was added and the mixture was extracted with DCM. The combined organic layers were washed with water and brine, dried over anhydrous Na₂SO₄, filtered and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the desired product.

Method B:

The starting materials **[D₂]-1a**, **1c**, **1i** and **1n** were prepared according to the literature procedure^{1,2} with slight modifications. The starting material **[D₂]-1a** was prepared from **[D₂]-N-(2-methylallyl)-phthalimide** which was prepared according to the literature procedure³.



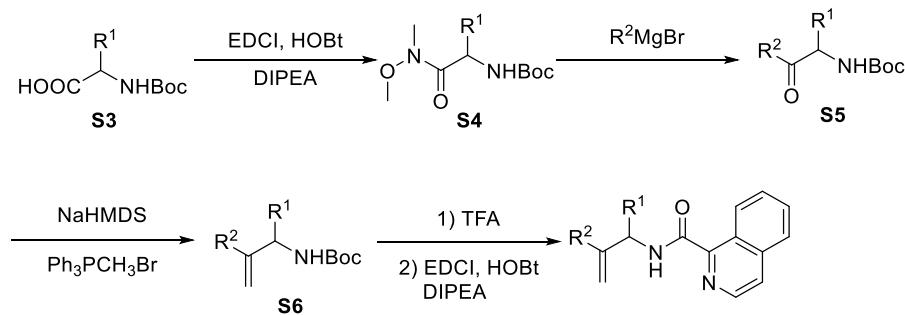
To a mixture of triphenylphosphine (25mmol), phthalimide (25 mmol) and the corresponding allyl alcohol (25mmol) in THF (30 mL) was slowly added diethyl azodicarboxylate (DEAD) (25mmol) at 0 °C under N₂ atmosphere. The mixture was stirred at 0 °C for 3 h. After the completion of the reaction, the reaction mixture was diluted with hexane and filtered. The filtrate was dried over Na₂SO₄ and concentrated *in vacuo* to give the crude product, which was used without further purification.

To the solution of phthalimide product in ethanol (100 mL) was added hydrazine monohydrate (50 mmol) at 50 °C. The mixture was stirred for 1 h and quenched with hydrochloric acid (6.0 M, 20 mL). The precipitates formed were removed by filtration, and the resultant filtrate was dried over Na₂SO₄ and concentrated *in vacuo* to give an unsaturated amine hydrochloride. Aqueous NaOH (6.0 M, 10 mL) was added to the amine salt, and the resulting solution was extracted with DCM (25 mL ×3). The combined organic extracts was then washed again with brine (10 mL), dried over Na₂SO₄, and filtered. The amine solution was used without further purification.

To the solution of amine (10 mmol) was successively added isoquinoline-1-carboxylic acid (11 mmol), EDCI (2.11 g, 11 mmol), HOBr (1.49 g, 11 mmol), and DIPEA (3.3 mL, 20 mmol). The resultant mixture was stirred at room temperature overnight. Water was added and the mixture was extracted with DCM. The combined organic layers were washed with water and brine, dried over anhydrous Na₂SO₄, filtered and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the desired product.

Method C:

The starting materials **1d-h** and **1j-m** were prepared according to the literature procedure^{1,4} with slight modifications.



Stage 1:

To the stirred solution of **S3** (10 mmol) in DCM (30 mL) were added EDCI (2.11 g, 11 mmol) and HOBr (1.49 g, 11 mmol), and the mixture was stirred for 30 min. *N,O*-dimethylhydroxylamine·HCl (1.07 g, 11 mmol) was added to the reaction mixture followed by DIPEA (2.58 g, 3.3 mL, 20 mmol), and the mixture was stirred for another 14 h at rt. The reaction mixture was diluted with H₂O (20 mL), extracted with DCM (2

$\times 20$ mL). The combined organic layers were washed successively with 1 N HCl (10 mL), H₂O (10 mL), and brine (10 mL), dried over Na₂SO₄, filtered and concentrated to afford the desired product as an off white powder.

Stage 2:

S4 (10 mmol, 1.0 equiv.) obtained from stage 1 was added to a 250 mL RBF followed by THF (50 mL) as the solvent. The mixture was cooled to 0 °C and a corresponding Grignard reagent in THF (30.0 mmol, 3.0 equiv.) was added over 8 min. The reaction mixture was stirred for 1.0 h at 0 °C and for an additional 1.0 h at rt. Subsequently, the reaction was again cooled to 0 °C and quenched by slow addition of 1.0 M HCl (50 mL). The mixture was transferred to a separatory funnel with additional 1.0 M HCl (50 mL) and extracted with EtOAc (3 \times 40 mL). The organic phases were combined, washed with water, brine and dried over MgSO₄, filtered and the solvent was removed *in vacuo*. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the desired product **S5**.

Stage 3:

To a suspension of Ph₃PCH₃Br (22 mmol) in toluene (40 mL), was slowly added a solution of NaHMDS in THF (1 M, 21 mL) at 0 °C and the resulting yellow solution was stirred for 15 min at 0 °C. Then a solution of the ketone **S5** (10 mmol) in toluene (10 mL) was added dropwise at 0 °C and continued stirring for 2 h at rt. Water (50 mL) was added and the aqueous layer was extracted with Et₂O (3 \times 20 mL). The organic phases were combined, washed with water, brine and dried over MgSO₄, filtered and the solvent was removed *in vacuo*. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the desired product *N*-Boc protected allylamine **S6**.

Stage 4:

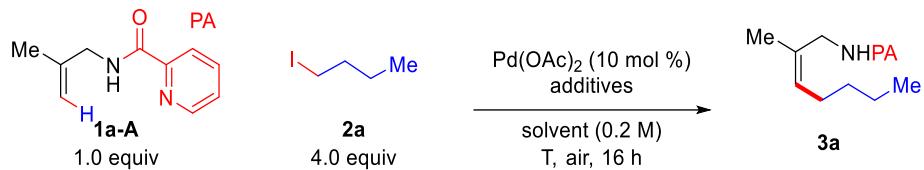
To a solution of *N*-Boc protected allylamine **S6** (10 mmol) in anhydrous DCM (15 ml) at 0 °C, trifluoroacetic acid (15 ml, 19 mmol) was added slowly with stirring at 0 °C. After the starting material had been consumed, the reaction mixture was concentrated *in vacuo*. Aqueous NaOH (2.0 M, 50 mL) was added to the residue, and the resulting solution was extracted with DCM (30 mL \times 2). The combined organic extracts were then washed with brine solution (10 mL), dried over Na₂SO₄, filtered.

The amine solution was used without further purification.

To the solution of amine (10 mmol) was successively added isoquinoline-1-carboxylic acid (11 mmol), EDCI (2.11 g, 11 mmol), HOBt (1.49 g, 11 mmol), and DIPEA (3.3 mL, 20 mmol). The resultant mixture was stirred at room temperature overnight. Water was added and the mixture was extracted with DCM. The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4 , filtered and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the desired product.

2.2 Optimization of Reaction Conditions

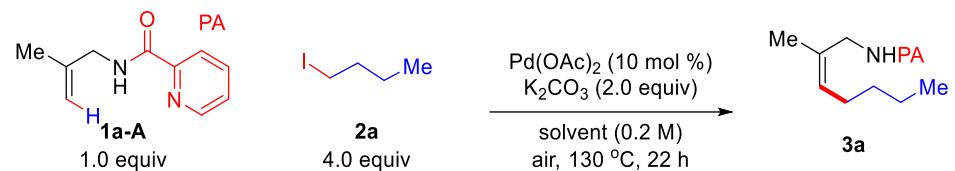
Table S1. Initial Optimization



entry	Additive/equiv	solvent	T/°C	1a-A	3a
1	K ₂ CO ₃ (2.0) NaOTf (3.0)	^t AmylOH	110	80	12
2	Ag ₂ CO ₃ (1.5) NaOCN (2.0) TsNH ₂ (0.3)	1,4-dioxane	80	68	0
3	Ag ₂ CO ₃ (1.0) (BnO) ₂ PO ₂ H (0.2) NaI (0.3)	toluene : ^t AmylOH (1 : 9)	110	76	0
4	Ag ₂ CO ₃ (1.0) (BnO) ₂ PO ₂ H (0.2)	toluene : ^t AmylOH (1 : 9)	110	78	trace
5	Ag ₂ CO ₃ (2.0) (BnO) ₂ PO ₂ H (0.2)	^t AmylOH	110	69	trace
6	Ag ₂ CO ₃ (2.0) (BnO) ₂ PO ₂ H (0.2) CuCl ₂ (0.3)	^t AmylOH	110	48	trace
7	K ₂ CO ₃ (2.0) PivOH (0.2)	^t AmylOH	110	82	15
8	AgOAc (2.0)	^t BuOH	110	83	trace
9	Ag ₂ CO ₃ (1.0) <i>o</i> -PBA (1.0)	^t BuOH	80	88	0
10	Ag ₂ CO ₃ (1.5) BQ (0.1)	^t BuOH	110	89	trace
11	KHCO ₃ (1.0) <i>o</i> -PBA (0.2)	DCE	110	88	0
12	AgOAc (2.0) LiCl (1.0)	toluene	110	93	0
13	Ag ₂ CO ₃ (2.0) Boc- <i>L</i> e-OH (0.2)	MTBE	80	46	trace
14	Ag ₂ CO ₃ (2.0)	ⁿ hexane	80	40	0
15	Ag ₂ CO ₃ (2.0) H ₂ O (5.0)	ⁿ hexane	80	35	0

The reactions were performed at 0.2 mmol scale. The yields were determined by ¹H NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard.

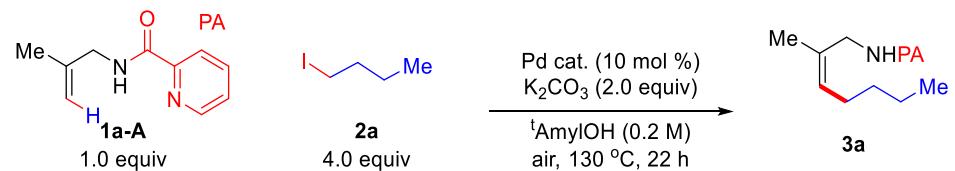
Table S2. Screening of Solvents



entry	solvent	1a-A	3a	entry	solvent	1a-A	3a
1	^t AmylOH	60	29	10	PhCl	86	5
2	toluene	79	5	11	DME	97	0
3	DCE	0	0	12	NMP	69	< 8
4	DMF	40	< 10	13	DEM	34	trace
5	1,4-dioxane	77	2	14	MTBE	76	5
6	MeCN	52	< 8	15	ⁿ hexane	86	3
7	DMSO	55	trace	16	HFIP	80	0
8	PhCF ₃	82	6	17	acetone	63	2
9	^t BuOH	61	12	18	MeNO ₂	78	0

The reactions were performed at 0.2 mmol scale. The yields were determined by ¹H NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard.

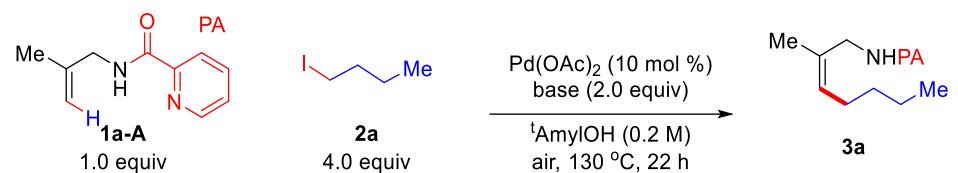
Table S3. Screening of Palladium Catalysts



entry	Pd cat.	1a-A	3a	entry	Pd cat.	1a-A	3a
1	$\text{Pd}(\text{OAc})_2$	60	29	10	PdCl_2	61	30
2	$\text{Pd}(\text{TFA})_2$	73	14	11	PdBr_2	57	30
3	$\text{Pd}(\text{OPiv})_2$	62	24	12	$\text{Pd}(\text{OH})_2/\text{C}$	34	2
4	$\text{Pd}(\text{MeCN})_2\text{Cl}_2$	59	26	13	$\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$	85	4
5	$\text{Pd}(\text{PhCN})_2\text{Cl}_2$	67	12	14	$\text{Pd}(\text{dppf})(\text{CH}_2\text{Cl}_2)\text{Cl}_2$	85	4
6	$\text{Pd}(\text{cod})_2\text{Cl}_2$	62	26	15	$\text{Pd}(\eta^3\text{-C}_3\text{H}_5)\text{Cl} \cdot \text{SIPr}$	85	0
7	$\text{Pd}(\text{MeCN})_4(\text{BF}_4)_2$	74	10	16	Na_2PdCl_4	70	0
8	$\text{Pd}(\text{acac})_2$	76	10	17	$\text{Pd}(\text{OAc})_2 \cdot \text{white ligand}$	63	26
9	$[\text{Pd}(\eta^3\text{-C}_3\text{H}_5)\text{Cl}]_2$	90	0	18	Pd_2dba_3	97	0

The reactions were performed at 0.2 mmol scale. The yields were determined by ¹H NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard.

Table S4. Screening of Bases



entry	base	1a-A	3a	entry	base	1a-A	3a
1	NaHCO ₃	96	0	18	K ₃ PO ₄	72	13
2	KHCO ₃	89	4	19	K ₂ HPO ₄	100	0
3	Li ₂ CO ₃	90	0	20	KH ₂ PO ₄	97	0
4	Na ₂ CO ₃	100	0	21	LiO'Bu	49	-
5	K ₂ CO ₃	60	29	22	NaO'Bu	25	0
6	Cs ₂ CO ₃	54	12	23	KO'Bu	60	1
7	LiOAc	97	0	24	LiOH	75	8
8	NaOAc	100	0	25	NaOH	10	2
9	KOAc	86	0	26	KOH	48	4
10	CsOAc	89	0	27	NaNO ₂	61	0
11	LiF	75	0	28	KOCN	98	0
12	NaF	87	0	29	NaOCN	0	0
13	KF	96	0	30	NBu ₄ OH	0	0
14	CsF	97	0	31	TMSOK	64	2
15	Na ₃ PO ₄	95	5	32	DIPEA	97	0
16	Na ₂ HPO ₄	97	0	33	2,6-di-tert-butylpyridine	65	0
17	NaH ₂ PO ₄	73	0				

The reactions were performed at 0.2 mmol scale. The yields were determined by ¹H NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard.

Table S5. Screening of Additives

entry	additive/equiv	1a-A	3a	entry	additive/quiv	1a-A	3a
1	AgOAc (1.0)	66	16	24	KHCO ₃ (1.0)	53	26
2	Ag ₂ CO ₃ (2.0)	55	0	25	Li ₂ CO ₃ (1.0)	17	24
3	PivOH (0.2)	75	19	26	Na ₂ CO ₃ (1.0)	50	26
4	(BnO) ₂ PO ₂ H (0.2)	70	11	27	Cs ₂ CO ₃ (1.0)	53	12
5	TsNH ₂ (0.2)	56	26	28	LiOAc (1.0)	52	26
6	KOAc (1.0)	62	24	29	NaOAc (1.0)	50	28
7	NaOAc (1.0)	69	22	30	KOAc (1.0)	55	30
8	NaOTf (3.0)	67	14	31	CsOAc (1.0)	58	26
9	O ₂ (1 atm)	56	24	32	TEMPO (0.3)	46	38
10	CF ₃ CH ₂ OH (5.0)	68	12	33	TEMPO (0.15)	48	36
11	DMSO (5.0)	50	10	34	TEMPO (0.5)	39	37
12	DMF (5.0)	57	16	35	TEMPO (1.0)	38	39
13	HFIP (5.0)	74	2	36	TEMPO (1.5)	53	26
14	CuCl ₂ (0.3)	-	2	37	TEMPO (2.0)	51	25
15	TBABF ₄ (0.5)	56	16	38	DDQ (0.3)	85	4
16	NaOTf (1.0)	83	10	39	I ₂ (0.3)	34	24
17	LiOTf (1.0)	81	2	40	PhI(OAc) ₂ (0.3)	43	4
18	NaOCN (1.0)	62	24	41	NHPI (0.3)	89	4
19	KOCN (1.0)	47	32	42	oxone (0.3)	67	20
20	NaNO ₂ (1.0)	67	14	43	m-CPBA (0.3)	65	25
21	KPF ₆ (1.0)	56	24	44	Me ₃ N ⁺ -O ⁻ (0.3)	70	18
22	NaBF ₄ (1.0)	62	26	45	Pyridine N-oxide (0.3)	72	24
23	NaHCO ₃ (1.0)	62	18	46	NMO (0.3)	39	37

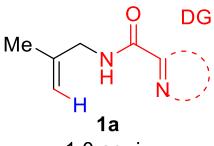
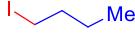
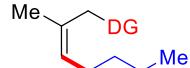
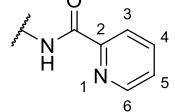
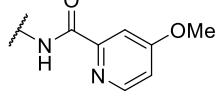
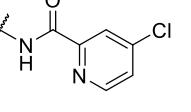
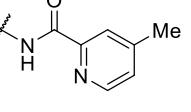
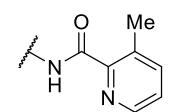
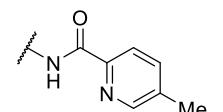
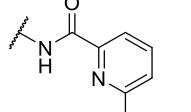
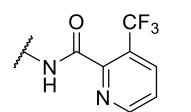
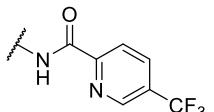
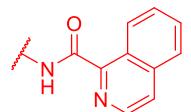
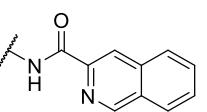
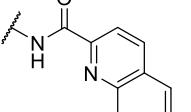
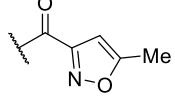
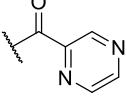
The reactions were performed at 0.2 mmol scale. The yields were determined by ¹H NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard.

Table S6. Screening of Additives in the Presence of TEMPO

entry	additive/equiv	1a-A	3a	entry	additive/quiv	1a-A	3a
1	18-crown-6 (0.5)	58	14	16	NMe ₄ Br (0.5)	42	38
2	ⁿ C ₁₂ H ₂₅ SO ₄ Na (0.5)	44	36	17	NEt ₄ Br (0.5)	41	40
3	NaBPh ₄ (0.5)	63	0	18	NBu ₄ Br (0.5)	39	32
4	(PhO) ₂ PO ₂ H (0.5)	44	34	19	NEt ₄ Cl (0.5)	44	38
5	MePh ₃ PBr (50)	56	8	20	NEt ₄ BF ₄ (0.5)	48	36
6	4 Å MS (50 mg)	58	26	21	NEt ₄ I (0.5)	43	40
7	18-crown-6 (0.05)	36	45	22	H ₂ O (0.5)	44	33
8	18-crown-6 (0.07)	41	39	23	H ₂ O (1.0)	46	33
9	KOAc (1.0)	43	38	24	H ₂ O (2.0)	48	34
10	KHCO ₃ (1.0)	45	36	25	^t BuOH as solvent	54	30
11	Cs ₂ CO ₃ (1.0)	56	18	26	Rb ₂ CO ₃ as base	50	28
12	Na ₃ PO ₄ (1.0)	50	32	27	PdCl ₂ as catalyst	41	40
13	K ₃ PO ₄ (1.0)	52	26	28	PdBr ₂ as catalyst	40	42
14	LiOH (1.0)	60	10	29	PdI ₂ as catalyst	60	24
15	KOCN (1.0)	45	36	30	ⁱ Pr ₂ S (2.0)	48	32

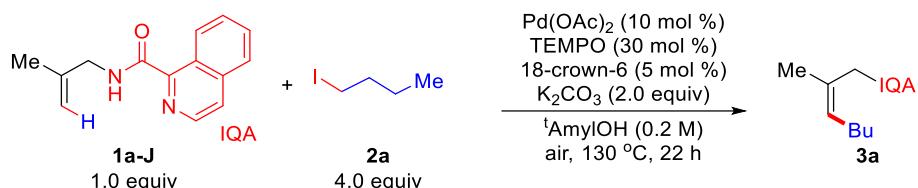
The reactions were performed at 0.2 mmol scale. The yields were determined by ¹H NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard.

Table S7. Optimization of Directed Group

 1a 1.0 equiv	 2a 4.0 equiv	$\xrightarrow[\substack{\text{tAmyLOH (1.5 mL)} \\ \text{air, 130 }^\circ\text{C, 22 h}}]{\substack{\text{Pd(OAc)}_2 (10 \text{ mol\%}) \\ \text{TEMPO (30 mol\%)} \\ 18\text{-crown-6 (5 mol\%)} \\ \text{K}_2\text{CO}_3 (2.0 \text{ equiv})}}$	 3a
 DG^b = A , 43%	 B , 29%	 C , 35%	 D , 38%
 E , 52%	 F , 34%	 G , 8%	 H , 32%
 I , 14%	 J , 62%	 K , 26%	 L , 8%
 M , 0%	 N , 8%		

The reactions were performed at 0.3 mmol scale. The yields were determined by ¹H NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard.

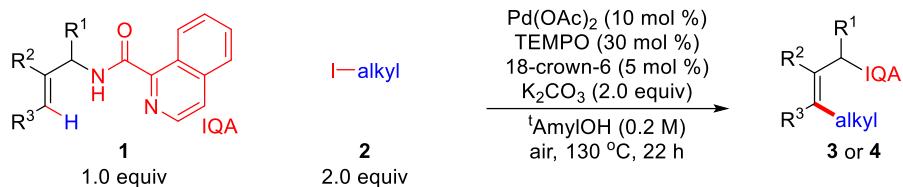
Table S8. Optimization of Reaction Conditions for **1a-J**



entry	conditions	1a-J	3a	entry	conditions	1a-J	3a
1	no 18-c-6, no TEMPO	42	30	13	Pd(MeCN) ₂ Cl ₂ (10 mol %)	17	56
2	no TEMPO	21	54	14	Pd(cod)Cl ₂ (10 mol %)	35	44
3	no 18-crown-6	34	38	15	PdCl ₂ (10 mol %)	14	61
4	18-crown-6 (2 mol %)	20	54	16	PdBr ₂ (10 mol %)	21	56
5	18-crown-6 (4 mol %)	12	60	17	PdI ₂ (10 mol %)	27	48
6	18-crown-6 (6 mol %)	16	57	18	Pd(OAc) ₂ (12.5 mol %)	6	65
7	18-crown-6 (8 mol %)	20	53	19	Pd(OAc) ₂ (7.5 mol %)	22	51
8	18-crown-6 (10 mol %)	16	56	20	Pd(OPiv) ₂ (10 mol %)	10	62
9	ⁿ Bu-I (6.0 equiv)	16	56	21	Ar (1 atm)	15	62
10	ⁿ Bu-I (5.0 equiv)	17	55	22	O ₂ (1 atm)	8	62
11	ⁿ Bu-I (3.0 equiv)	22	54	23	^t AmylOH (0.3 M)	8	56
12	ⁿ Bu-I (2.0 equiv)	23	55	24	140 °C	10	62

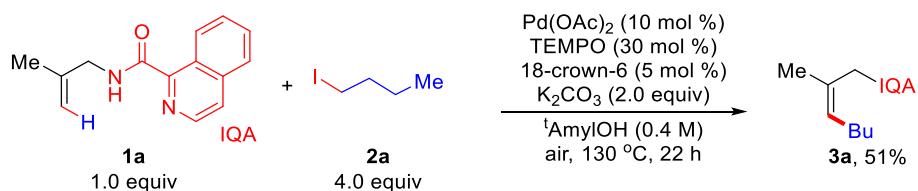
The reactions were performed at 0.3 mmol scale. The yields were determined by ¹H NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard.

2.3 General Procedure for alkylation of alkenes



A 35 mL sealed tube was charged with **1** (0.3 mmol, 1.0 equiv), **2** (0.6 mmol, 2.0 equiv), **Pd(OAc)₂** (6.7 mg, 10 mol %), **TEMPO** (14.1 mg, 30 mol %), **K₂CO₃** (82.9 mg, 2.0 equiv) and **18-crown-6** (4.0 mg, 5 mol %, in 1.5 mL **tAmylOH**). The mixture was first stirred at 25 °C for 5 min and then heated to 130 °C for 22 h under vigorous stirring. Then the mixture was cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the desired product **3** or **4**.

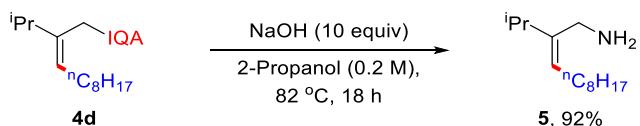
2.4 Large Scale Reaction of **1a** and **2a**



A 35 mL sealed tube was charged with **1a** (452.6 mg, 2.0 mmol), **2a** (1.47 g, 8 mmol), **Pd(OAc)₂** (44.9 mg, 0.2 mmol), **TEMPO** (93.8 mg, 0.6 mmol), **K₂CO₃** (552.8 mg, 4.0 mmol) and **18-crown-6** (26.4 mg, 5 mol %, in 5.0 mL **tAmylOH**). The mixture was first stirred at 25 °C for 5 min and then heated to 130 °C for 24 h under vigorous stirring. Then the mixture was cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the desired product **3a** as yellow oil (288.0 mg, 51% yield).

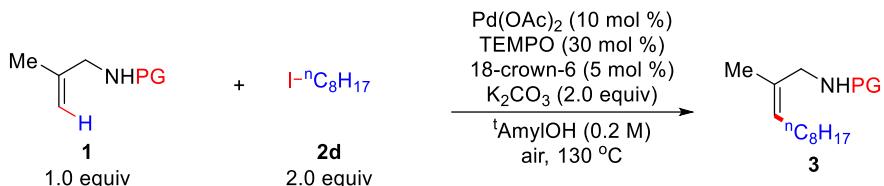
2.5 Deprotection of Isoquinoline-1-carbonyl Protected Amines

The deprotection of IQA-Protected amines were according to the literature procedure⁵ with small modifications.



To a solution of **4d** (101.0 mg, 0.3 mmol) in 2-propanol (1.5 mL) was added NaOH (120 mg, 3.0 mmol) and the reaction mixture was stirred at 82 °C for 18 h. After addition of water (10 mL) and EtOAc (10 mL), the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water and brine, dried over anhydrous Na₂SO₄, filtered and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography (MeOH/DCM) to give the desired product **5** as yellow oil (63.4 mg, 92 % yield).

2.6 Initial Rate Kinetics



General procedure for monitoring the reaction by NMR spectroscopy: A 35 mL sealed tube was charged with **1** (0.2 mmol, 1.0 equiv), **2d** (0.4 mmol, 2.0 equiv), Pd(OAc)₂ (4.4 mg, 10 mol %), TEMPO (9.4 mg, 30 mol %), K₂CO₃ (55.3 mg, 2.0 equiv), 18-crown-6 (2.6 mg, 5 mol %, in 1.0 mL ^tAmylOH). The mixture was first stirred at 25 °C for 5 min and then heated to 130 °C for desired reaction time under vigorous stirring. Then the mixture was quickly cooled to 0 °C, diluted with EtOAc (10 mL). The combined organic layers were washed with water and brine, dried over anhydrous Na₂SO₄, filtered and concentrated *in vacuo*. The crude product was added 1,1,2,2-tetrachloroethane (33.6 mg, 0.2 mmol) as internal standard and was analyzed by ¹H NMR. Yields and concentrations of **3** were used to obtain reaction rate profiles and initial rates.

Initial rate varying from concentrations of alkenes **1a**

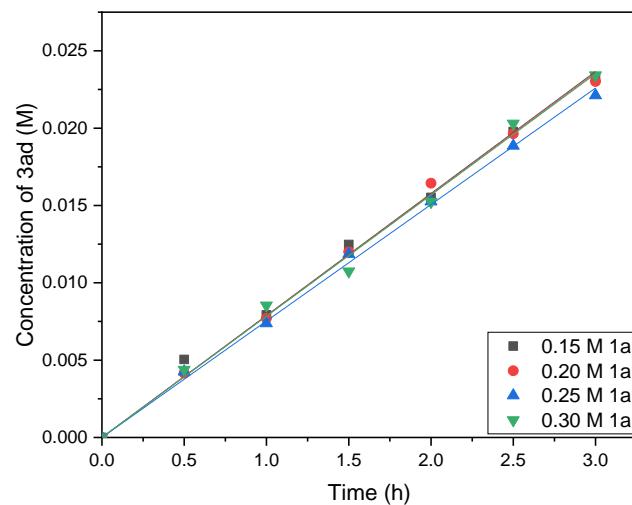
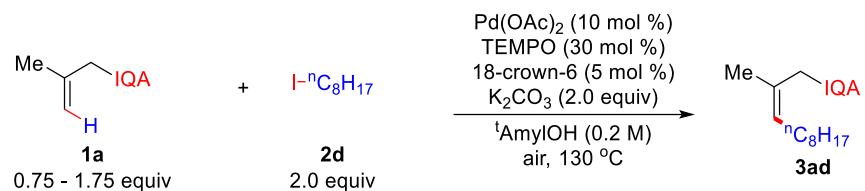


Figure S1. Plot of the concentrations of **3ad** over time with four different initial concentrations of **1a**.

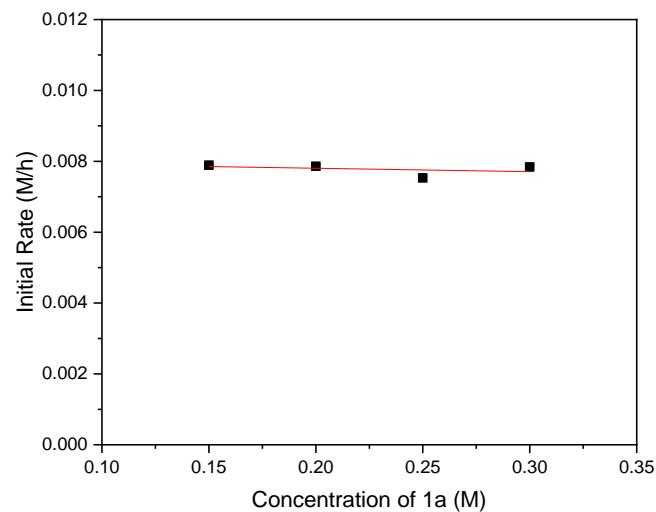


Figure S2. Plot of the initial rates vs concentrations of **1a**.

Initial rate varying from concentrations of alkylation reagent **2d**

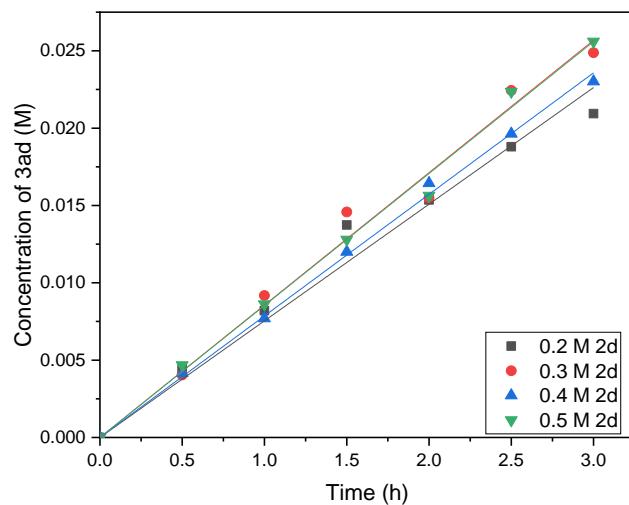
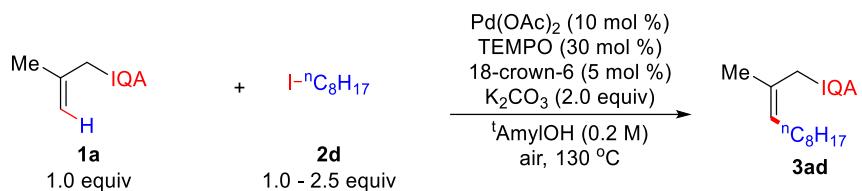


Figure S3. Plot of the concentrations of **3ad** over time with four different initial concentrations of **2d**.

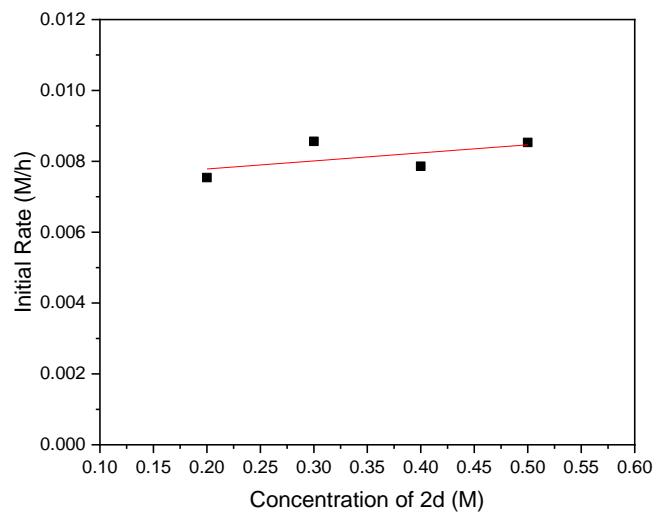


Figure S4. Plot of the initial rates vs concentrations of **2d**.

Initial rate varying from concentrations of $\text{Pd}(\text{OAc})_2$

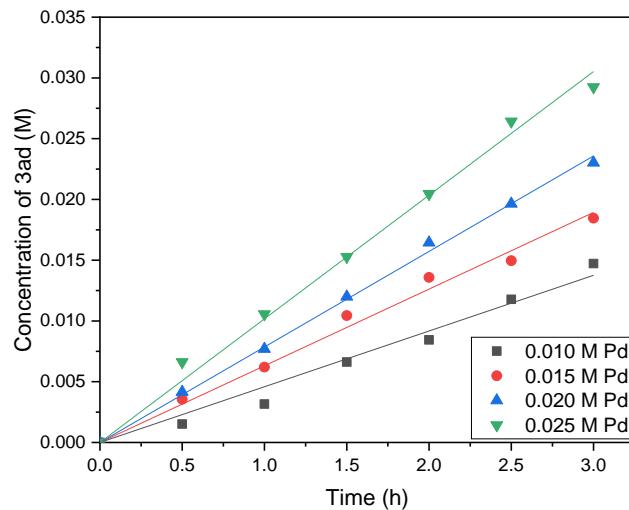
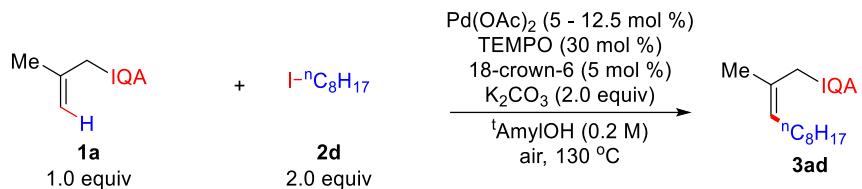


Figure S5. Plot of the concentrations of **3ad** over time with four different initial concentrations of $\text{Pd}(\text{OAc})_2$.

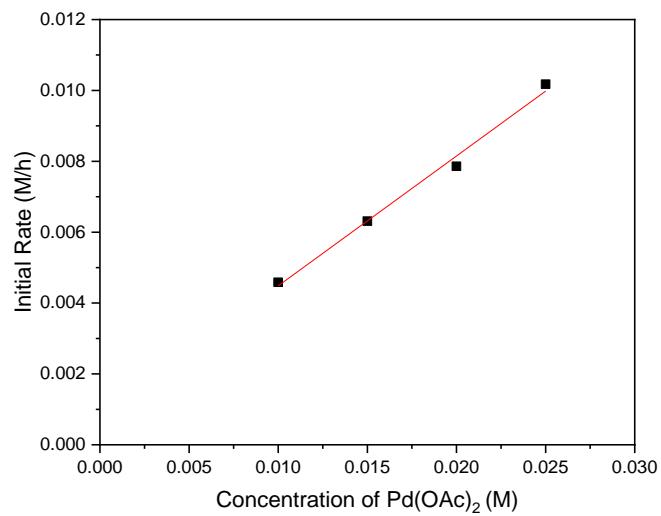


Figure S6. Plot of the initial rates vs concentrations of $\text{Pd}(\text{OAc})_2$.

Initial rate varying from the different additives

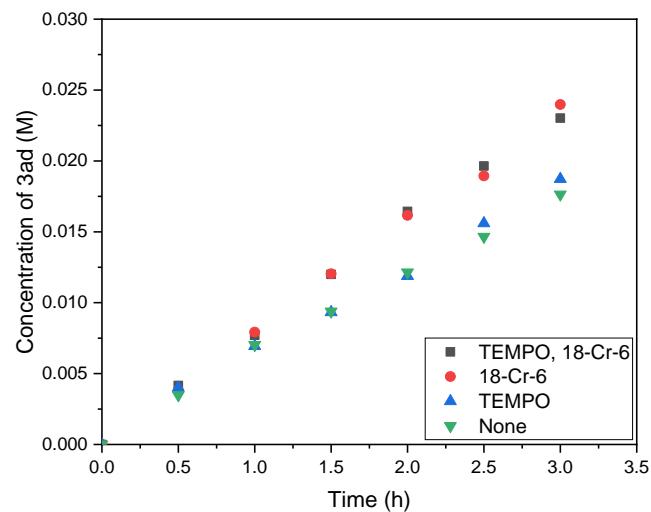
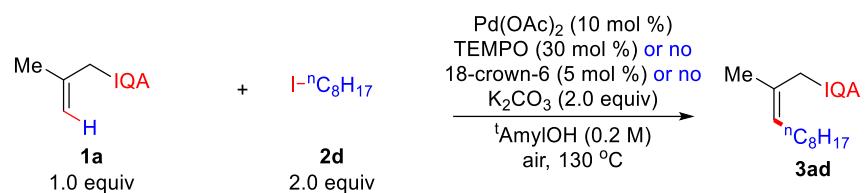


Figure S7. Plot of the concentrations of **3ad** over time with four different additives.

Initial rate varying from the directed groups

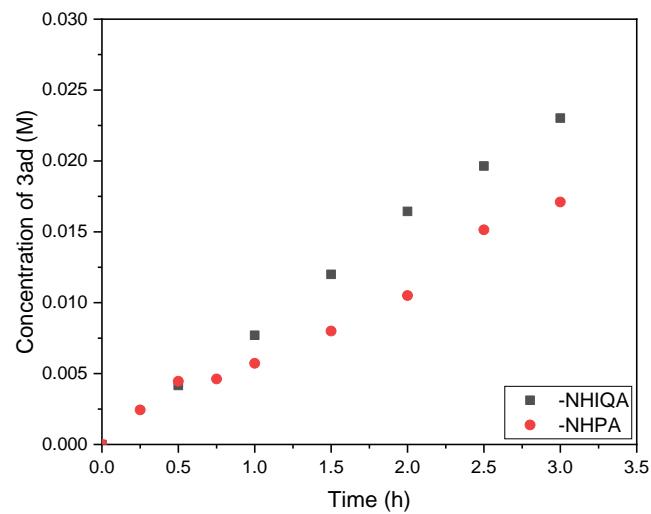
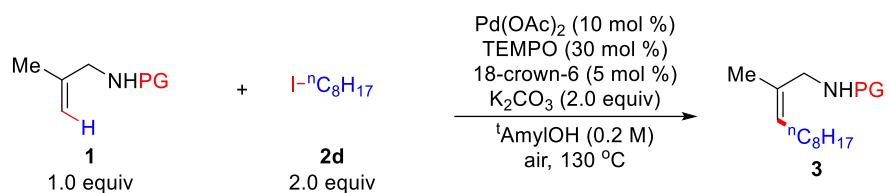


Figure S8. Plot of the concentrations of **3ad** over time with two different directing groups.

Kinetic isotope effect

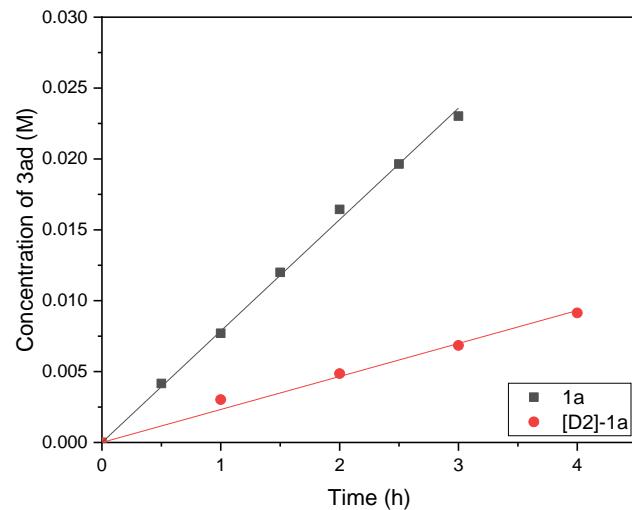
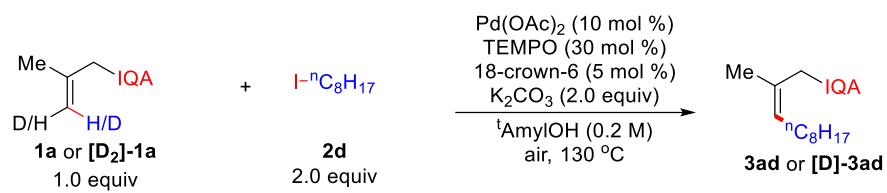
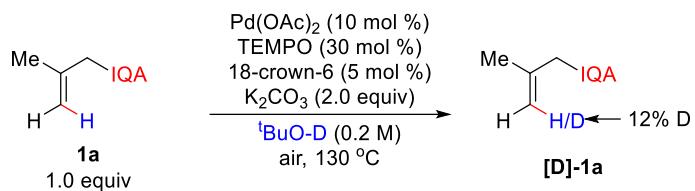


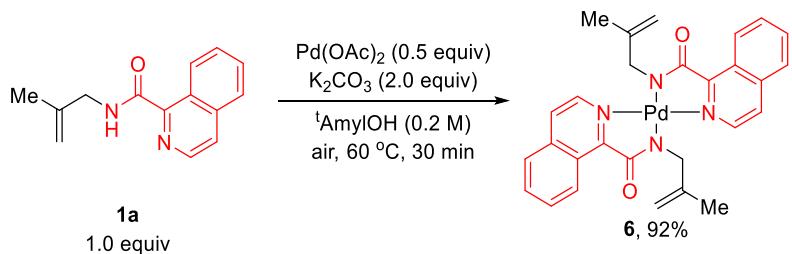
Figure S9. Plot of the concentrations of **3ad** and **[D]-3ad** over time.

2.7 H/D exchange study

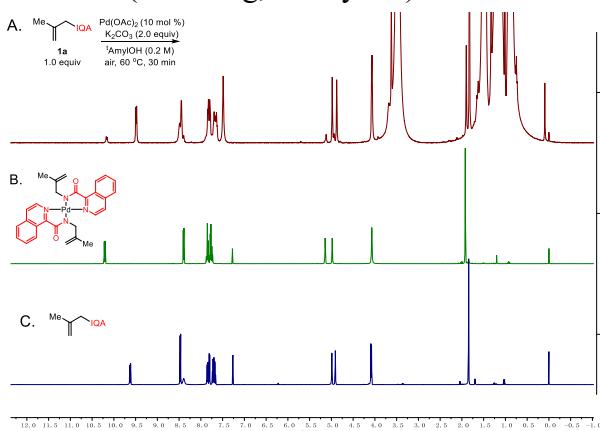


A 35 mL sealed tube was charged with **1a** (0.3 mmol, 1.0 equiv), $Pd(OAc)_2$ (6.7 mg, 10 mol %), TEMPO (14.1 mg, 30 mol %), K_2CO_3 (82.9 mg, 2.0 equiv) and 18-crown-6 (4.0 mg, 5 mol %, in 1.5 mL $'BuO-D$). The mixture was first stirred at 25 °C for 5 min and then heated to 130 °C for 22 h under vigorous stirring. Then the mixture was cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated *in vacuo*. The deuteration ratio was determined by 1H NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard.

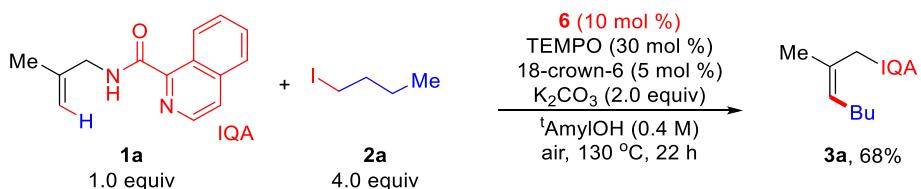
2.8 Synthesis and Application of Palladium(II) Complex 6



A 35 mL sealed tube was charged with **1a** (0.4 mmol, 1.0 equiv), Pd(OAc)₂ (44.9 mg, 50 mol %), K₂CO₃ (110.6 mg, 2.0 equiv) and ^tAmylOH (4.0 mL, 0.1 M). The mixture was stirred at 60 °C for 30 min until the yellow solid are precipitated and brown solid Pd(OAc)₂ completely disappear. Then the mixture was cooled to room temperature, filtered through a celite pad and washed with ^tAmylOH (1.0 mL × 3). The residue was dissolved in DCM (40 mL), washed again with H₂O (20 mL), and brine (10 mL), dried over Na₂SO₄, filtered and concentrated to afford the desired product as a yellow solid without further purification (102.0 mg, 92% yield).



A 35 mL sealed tube was charged with **1a** (0.3 mmol, 1.0 equiv), Pd(OAc)₂ (6.7 mg, 10 mol %), K₂CO₃ (82.9 mg, 2.0 equiv) and ^tAmylOH (1.5 mL, 0.2 M). The mixture was first stirred at 60 °C for 30 min. Then the mixture was cooled to room temperature, diluted with CDCl₃ (1.5 mL) and determined by ¹H NMR analysis.



A 35 mL sealed tube was charged with **1a** (0.3 mmol, 1.0 equiv), **2a** (0.6 mmol, 2.0 equiv), **6** (16.7 mg, 10 mol %), TEMPO (14.1 mg, 30 mol %), K₂CO₃ (82.9 mg, 2.0 equiv) and 18-crown-6 (4.0 mg, 5 mol %, in 1.5 mL ^tAmylOH). The mixture was first

stirred at 25 °C for 5 min and then heated to 130 °C for 22 h under vigorous stirring. Then the mixture was cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the desired product **3a** as yellow oil (57.4 mg, 68% yield).

2.9 X-Ray Crystallographic Data of 6

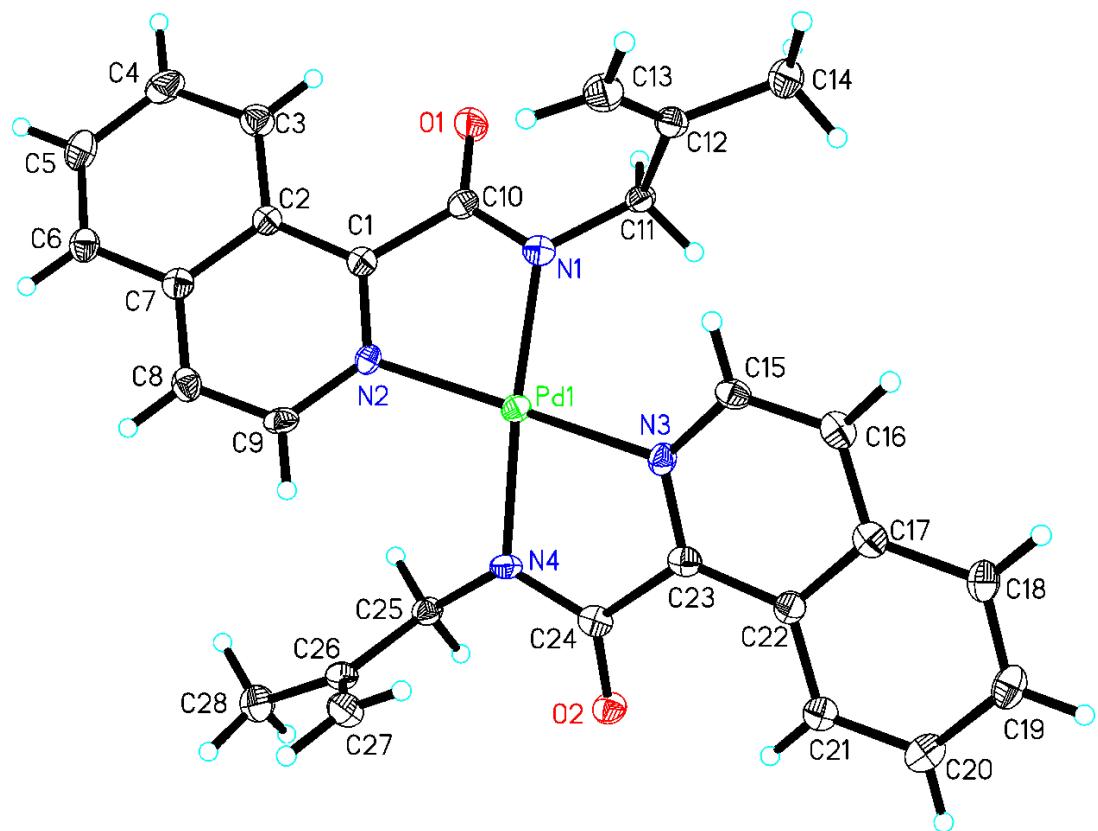
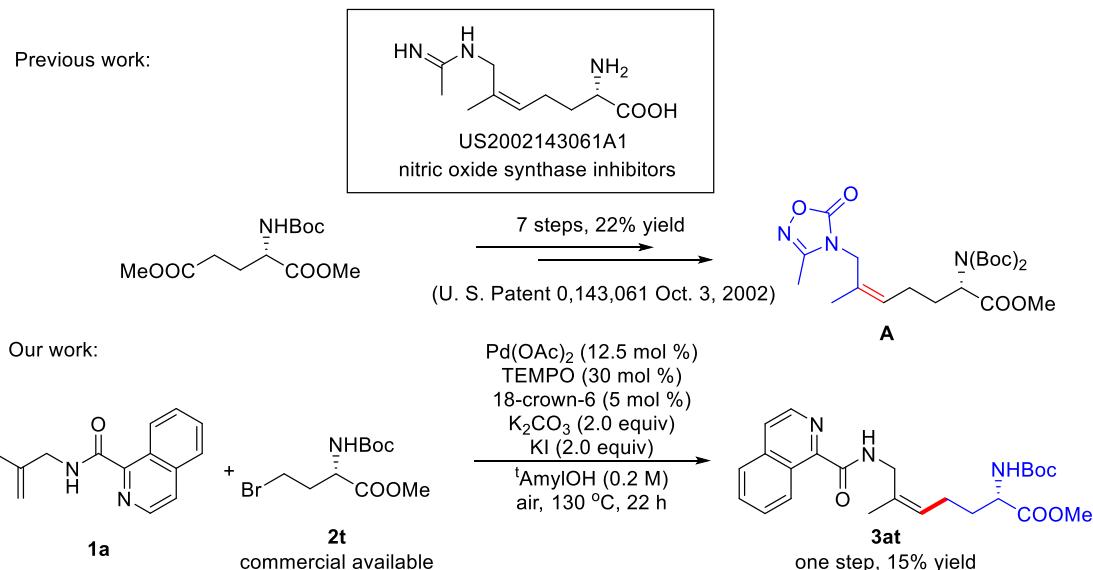


Table S9. Crystal data and structure refinement for **6**

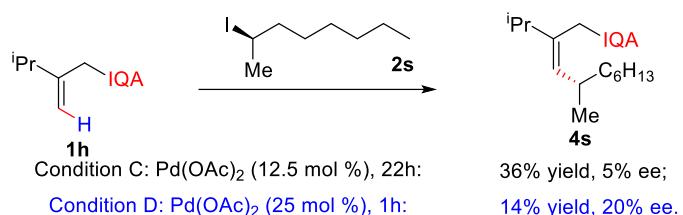
Identification code	6
Empirical formula	C ₂₈ H ₂₆ N ₄ O ₂ Pd
Formula weight	556.93
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	P2 ₁ /n
a/Å	8.3908(2)
b/Å	20.0893(6)
c/Å	14.6398(4)
α/°	90
β/°	100.460(3)
γ/°	90
Volume/Å ³	2426.77(11)
Z	4
ρ _{calcg} /cm ³	1.524
μ/mm ⁻¹	6.434
F(000)	1136.0
Crystal size/mm ³	0.11 × 0.1 × 0.08
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.554 to 146.862
Index ranges	-10 ≤ h ≤ 8, -24 ≤ k ≤ 24, -17 ≤ l ≤ 17
Reflections collected	10871
Independent reflections	4757 [R _{int} = 0.0733, R _{sigma} = 0.0821]
Data/restraints/parameters	4757/12/334
Goodness-of-fit on F ²	1.019
Final R indexes [I>=2σ (I)]	R ₁ = 0.0703, wR ₂ = 0.1842
Final R indexes [all data]	R ₁ = 0.0861, wR ₂ = 0.1918
Largest diff. peak/hole / e Å ⁻³	1.43/-1.47

2.10 Synthesis of methyl (S, Z)-2-((tert-butoxycarbonyl)amino)-7-(isoquinoline-1-carboxamido)-6-methylhept-5-enoate

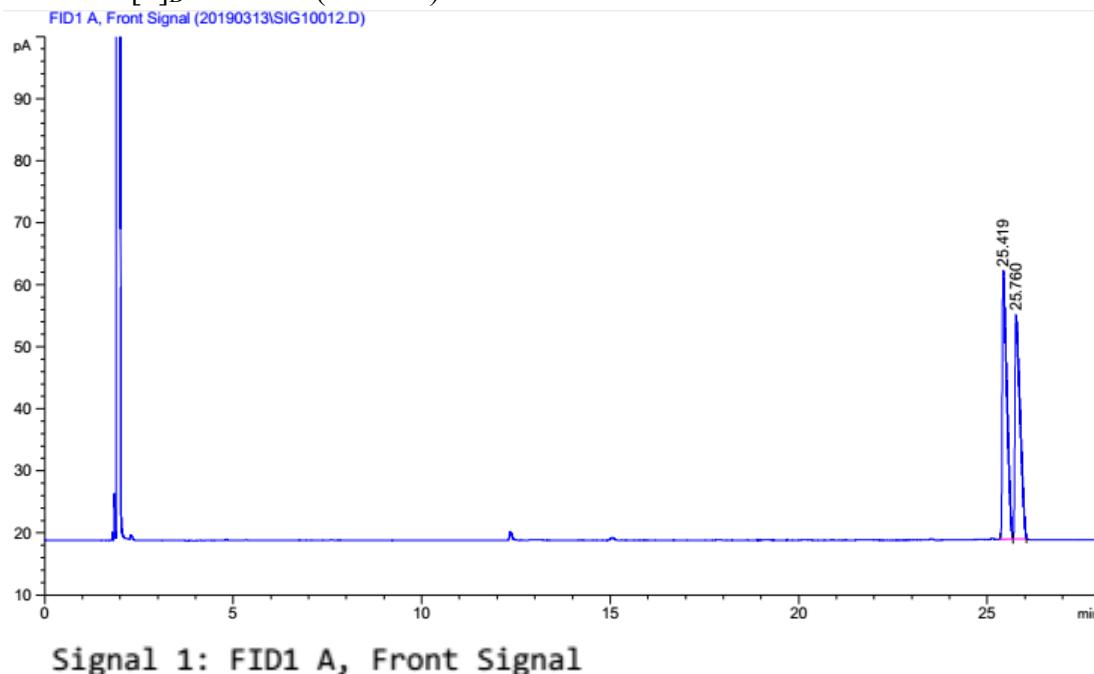


A 35 mL sealed tube was charged with **1a** (0.2 mmol, 1.0 equiv), **2t** (0.4 mmol, 2.0 equiv), $\text{Pd}(\text{OAc})_2$ (5.6 mg, 12.5 mol %), TEMPO (9.4 mg, 30 mol %), K_2CO_3 (55.3 mg, 2.0 equiv), KI (66.4 mg, 2.0 equiv) and 18-crown-6 (2.6 mg, 5 mol %, in 1.0 mL ${}^t\text{AmylOH}$). The mixture was first stirred at 25 °C for 5 min and then heated to 130 °C for 22 h under vigorous stirring. Then the mixture was cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the desired product **3at** (13.2 mg, 15 % yield).

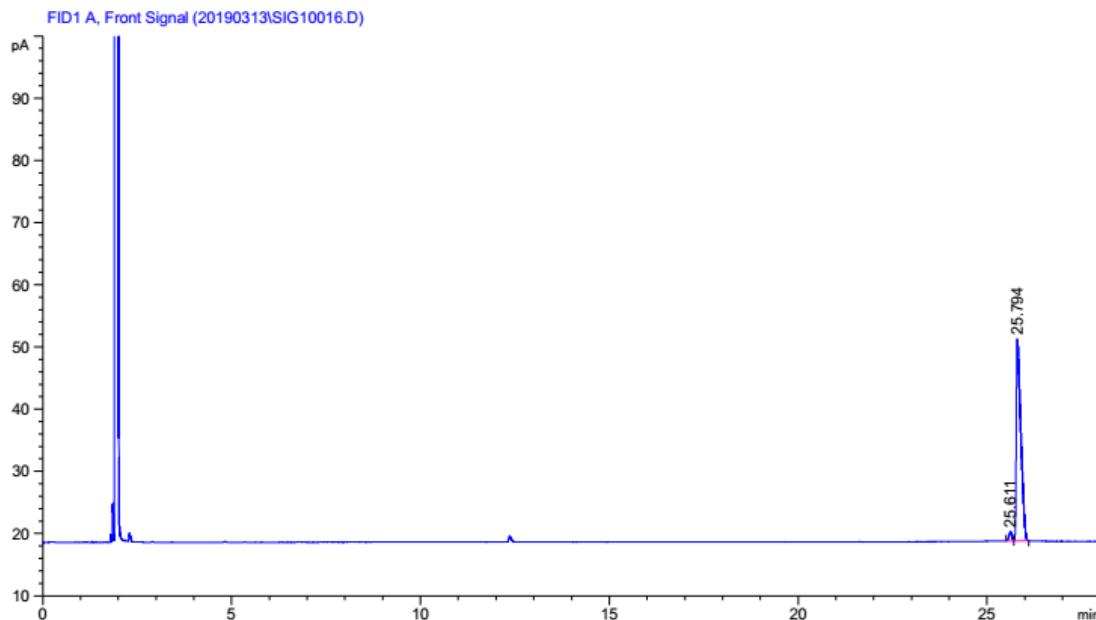
2.11 Alkylation reaction of **1h** with chiral secondary iodine **2u**



The (*R*)-2-iodooctane **2u** was prepared from corresponding (*S*)-octan-2-ol according to the literature procedure⁶. The ee of **2u** was determined using GC with column VARIAN CHIRASIL-DEX CB (25×0.25×0.25); temperature = 65 °C holding time 2 min, then 2.0 °C/min heating rate to 180 °C holding time 10 min; N₂: 10.0 psi; split: 70:1. Retention times: 25.61 min [minor enantiomer], 25.79 min [major enantiomer]. 94.0% ee. $[\alpha]_D^{20} = -47.7$ (c = 0.58).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	25.419	BB	0.1144	361.01880	43.25682	51.47399
2	25.760	BB	0.1250	340.34274	36.10852	48.52601

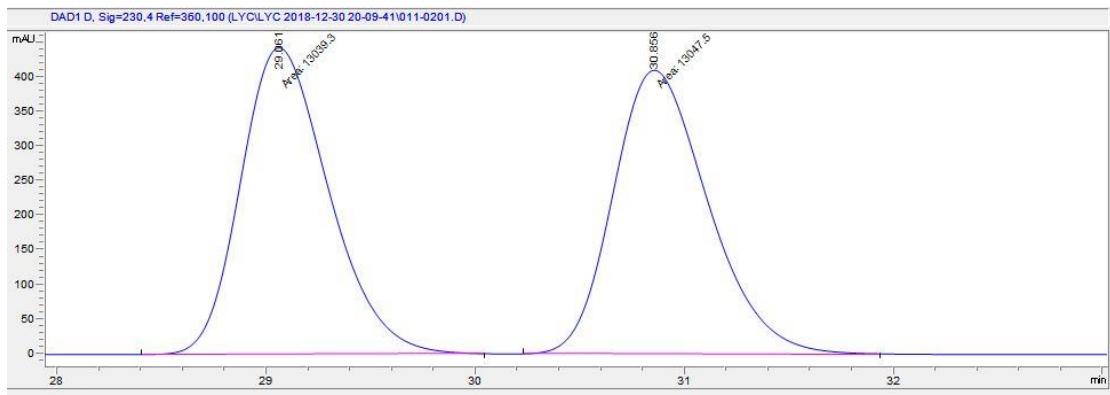


Signal 1: FID1 A, Front Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	25.611	MF R	0.0864	7.73675	1.49300	2.79218
2	25.794	FM R	0.1374	269.34964	32.52897	97.20782

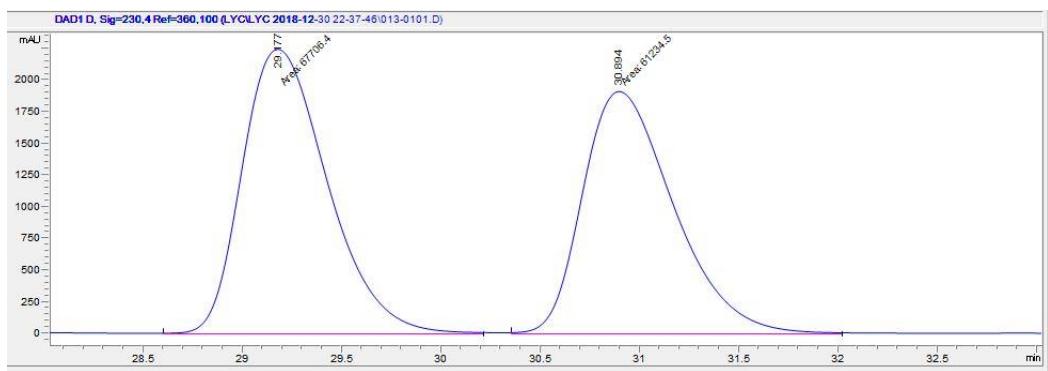
The compound **8** were prepared according to the literature procedure⁶ with slight modifications.

A 35 mL sealed tube was charged with **1h** (0.3 mmol, 1.0 equiv), **2u** (0.6 mmol, 2.0 equiv), Pd(OAc)₂ (8.4 mg, 12.5 mol %), TEMPO (14.1 mg, 30 mol %), K₂CO₃ (82.9 mg, 2.0 equiv) and 18-crown-6 (4.0 mg, 5 mol %, in 1.5 mL 'AmyloOH). The mixture was first stirred at 25 °C for 5 min and then heated to 130 °C for 22 h under vigorous stirring. Then the mixture was cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the desired product **4u** (26.8 mg, 36% yield). The ee was determined on Daicel Chiralcel OD-3 column with 2-propanol/hexane = 1/200, flow rate = 0.30 mL/min, temperature = 20 °C, wave length = 230 nm. Retention times: 29.1 min [major enantiomer], 30.9 min [minor enantiomer]. 5% ee.



Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.061	MM	0.4904	1.30393e4	443.17365	49.9842
2	30.856	MM	0.5299	1.30475e4	410.34009	50.0158
Totals :					2.60868e4	853.51373

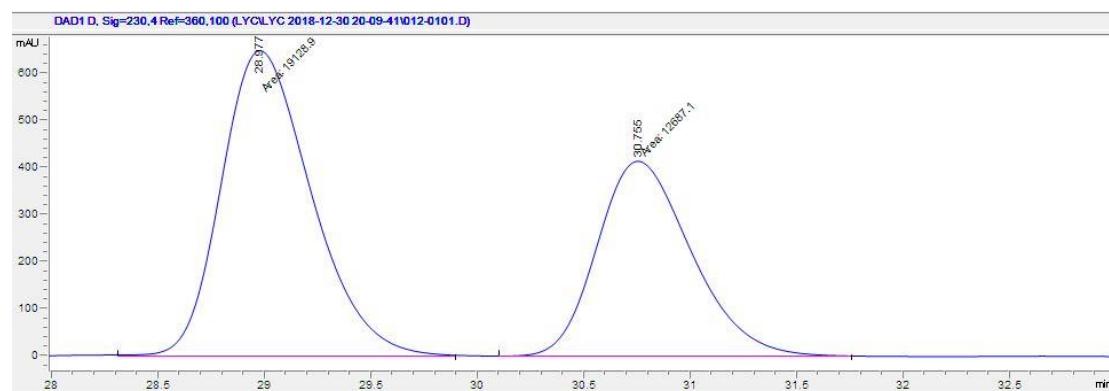


Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.177	MM	0.5000	6.77064e4	2256.75610	52.5097
2	30.894	MM	0.5316	6.12345e4	1919.68286	47.4903
Totals :					1.28941e5	4176.43896

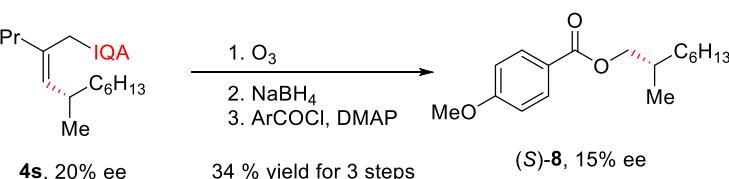
A 35 mL sealed tube was charged with **1h** (0.3 mmol, 1.0 equiv), **2u** (0.6 mmol, 2.0 equiv), Pd(OAc)₂ (16.8 mg, 10 mol %), TEMPO (14.1 mg, 30 mol %), K₂CO₃ (82.9 mg, 2.0 equiv) and 18-crown-6 (4.0 mg, 5 mol %, in 1.5 mL ¹AmylOH). The mixture

was first stirred at 25 °C for 5 min and then heated to 130 °C for 1 h under vigorous stirring. Then the mixture was cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the desired product **4u** (10.4 mg, 14% yield). The ee was determined on Daicel Chiralcel OD-3 column with 2-propanol/hexane = 1/200, flow rate = 0.30 mL/min, temperature = 20 °C, wave length = 230 nm. Retention times: 29.0 min [major enantiomer], 30.8 min [minor enantiomer]. 20% ee.



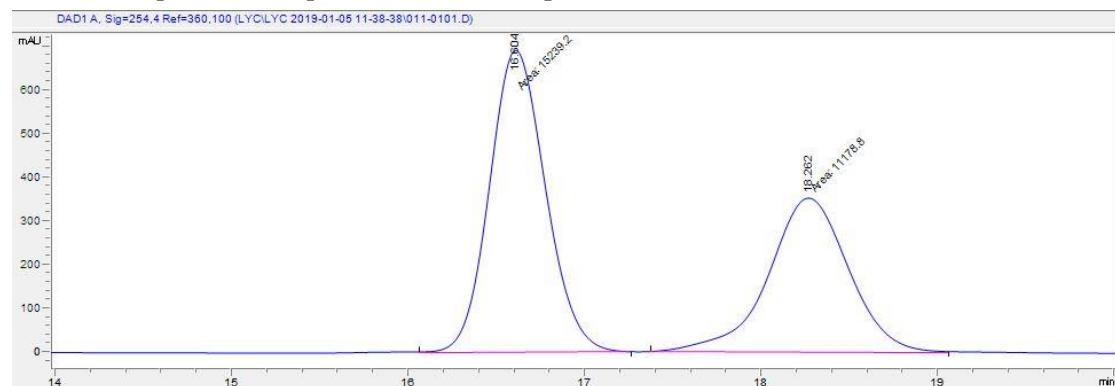
Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.977	MM	0.4930	1.91289e4	646.74377	60.1235
2	30.755	MM	0.5133	1.26871e4	411.91541	39.8765
Totals :					3.18160e4	1058.65918



The solution of compound **4u** (40.0 mg, 0.11 mmol, 20% ee) in MeOH (1.0 mL) and DCM (1.0 mL) was saturated with ozone at -78 °C until a persistent blue color was observed. The reaction mixture was stirred until the blue color disappeared and then sodium borohydride (41.6 mg, 1.10 mmol) was added. After stirring for 1h at room temperature, the reaction mixture was diluted with DCM and Na₂SO₄·10H₂O was

added to quench it. The formed precipitate was filtered off and washed with DCM (3×3 mL). Solvents were evaporated from the filtrate to obtain the crude alcohol. A flame-dried 20 mL flask was charged with the crude alcohol in DCM (1 mL). Et₃N (44 μ L, 0.32 mmol), DMAP (10.0 mg, 0.08 mmol) and 4-methoxybenzoyl chloride (42.0 mg, 0.24 mmol) were added successively, and the reaction mixture was stirred at room temperature for 20 h. The reaction mixture was quenched with the sat. aq. NaHCO₃ solution and extracted with DCM (3×10 mL). The combined organic phases were dried over MgSO₄ and solvents were evaporated. The crude product was purified by column chromatography on silica gel to afford (*S*)-2-methyloctyl 4-methoxybenzoate **8** (10.2 mg, 34% yield over 3 steps) as a colorless oil. The ee was determined on Daicel Chiralcel OB-H column with 2-propanol/hexane = 1/100, flow rate = 0.30 mL/min, temperature = 40 °C, wave length = 254 nm. Retention times: 16.6 min [major enantiomer], 18.3 min [minor enantiomer]. 15% ee.

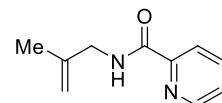


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

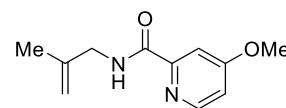
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.604	MM	0.3668	1.52392e4	692.38879	57.6849
2	18.262	MM	0.5274	1.11788e4	353.25800	42.3151
Totals :					2.64180e4	1045.64679

3. Characterization Data and Spectrum of Products

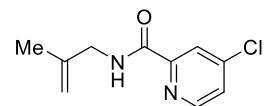
N-(2-methylallyl)picolinamide (**1a-A**)


 Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 8.64 – 8.50 (m, 1H), 8.41 – 8.03 (m, 2H), 7.94 – 7.77 (m, 1H), 7.50 – 7.38 (m, 1H), 4.98 – 4.81 (m, 2H), 4.11 – 3.93 (m, 2H), 1.84 – 1.77 (m, 3H). **13C NMR** (101 MHz, CDCl₃) δ 164.3, 150.0, 148.2, 142.0, 137.5, 126.3, 122.5, 111.2, 45.1, 20.6. **HRMS (ESI)**: m/z calculated for C₁₀H₁₂N₂ONa [M+Na]⁺: 199.0842, found: 199.0851. **IR (KBr)**: 3390, 3058, 1678, 1591, 1525, 1289, 1246, 1164, 998, 894, 820, 751, 690.

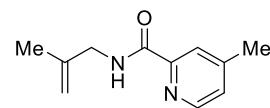
4-methoxy-*N*-(2-methylallyl)picolinamide (**1a-B**)


 Colorless oil. **1H NMR** (400 MHz, CDCl₃) δ 8.35 (dd, *J* = 5.6, 0.5 Hz, 1H), 8.21 (br s, 1H), 7.76 (d, *J* = 2.6 Hz, 1H), 6.96 – 6.85 (m, 1H), 5.03 – 4.74 (m, 2H), 4.07 – 3.98 (ddd, *J* = 6.3, 1.6, 0.8 Hz, 2H), 3.92 (d, *J* = 1.5 Hz, 3H), 1.80 (dd, *J* = 1.6, 0.8 Hz, 3H). **13C NMR** (101 MHz, CDCl₃) δ 167.1, 164.3, 152.0, 149.3, 141.9, 113.1, 111.3, 107.6, 55.7, 45.2, 20.6. **HRMS (ESI)**: m/z calculated for C₁₁H₁₄N₂O₂Na [M+Na]⁺: 229.0947, found: 229.0957. **IR (KBr)**: 3385, 3080, 1674, 1600, 1521, 1310, 1141, 1032, 994, 893, 840, 785.

4-chloro-*N*-(2-methylallyl)picolinamide (**1a-C**)

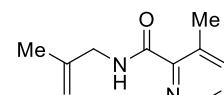

 Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 8.46 (dd, *J* = 5.3, 0.6 Hz, 1H), 8.22 (dd, *J* = 2.2, 0.6 Hz, 1H), 8.12 (br s, 1H), 7.44 (dd, *J* = 5.3, 2.2 Hz, 1H), 4.94 – 4.85 (m, 2H), 4.06 – 3.98 (ddd, *J* = 6.3, 1.5, 0.8 Hz, 2H), 1.80 (dd, *J* = 1.5, 0.8 Hz, 3H). **13C NMR** (101 MHz, CDCl₃) δ 163.1, 151.4, 149.1, 145.9, 141.6, 126.4, 123.0, 111.3, 45.1, 20.5. **HRMS (ESI)**: m/z calculated for C₁₀H₁₁N₂OClNa [M+Na]⁺: 233.0452, found: 233.0461. **IR (KBr)**: 3336, 3058, 1667, 1527, 1295, 1093, 897, 746, 700.

4-methyl-*N*-(2-methylallyl)picolinamide (**1a-D**)

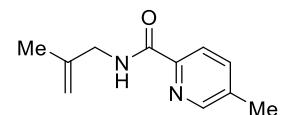

 Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 8.40 (dd, *J* = 5.0, 0.8 Hz, 1H), 8.19 (br s, 1H), 8.05 (dt, *J* = 1.8, 0.8 Hz, 1H), 7.24 (ddd, *J* = 5.0, 1.8, 0.8 Hz, 1H), 4.96 – 4.81 (m, 2H), 4.03 (ddd, *J* = 6.4, 1.5, 0.8 Hz,

2H), 2.43 (d, J = 0.8 Hz, 3H), 1.80 (dd, J = 1.5, 0.8 Hz, 3H). **^{13}C NMR** (101 MHz, CDCl_3) δ 164.6, 149.8, 148.9, 148.0, 142.0, 127.1, 123.3, 111.2, 45.1, 21.3, 20.6. **HRMS (ESI)**: m/z calculated for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{ONa} [\text{M}+\text{Na}]^+$: 213.0998, found: 213.1008. **IR (KBr)**: 3392, 3081, 1678, 1525, 1306, 1029, 894, 783.

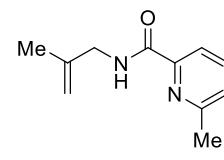
3-methyl-*N*-(2-methylallyl)picolinamide (**1a-E**)

 Colorless oil. **^1H NMR** (400 MHz, CDCl_3) δ 8.43 – 8.35 (ddd, J = 4.6, 1.6, 0.6 Hz, 1H), 8.31 (br s, 1H), 7.62 – 7.56 (m Hz, 1H), 7.31 (dd, J = 7.7, 4.6 Hz, 1H), 5.02 – 4.81 (m, 2H), 3.99 (ddd, J = 6.4, 1.4, 0.7 Hz, 2H), 2.76 (s, 3H), 1.81 (dd, J = 1.4, 0.7 Hz, 3H). **^{13}C NMR** (101 MHz, CDCl_3) δ 166.0, 147.3, 145.6, 142.3, 141.0, 135.6, 125.7, 110.9, 44.9, 20.7, 20.6. **HRMS (ESI)**: m/z calculated for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{ONa} [\text{M}+\text{Na}]^+$: 213.0998, found: 213.1005. **IR (KBr)**: 3389, 3080, 1677, 1515, 1448, 1295, 1274, 1119, 894, 816, 788.

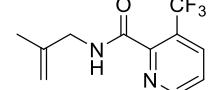
5-methyl-*N*-(2-methylallyl)picolinamide (**1a-F**)

 Colorless solid. **^1H NMR** (400 MHz, CDCl_3) δ 8.37 (dq, J = 2.2, 0.8 Hz, 1H), 8.10 (dd, J = 7.9, 0.8 Hz, 2H), 7.65 (ddd, J = 7.9, 2.2, 0.8 Hz, 1H), 4.98 – 4.82 (m, 2H), 4.03 (ddd, J = 6.3, 1.4, 0.7 Hz, 2H), 2.41 (dd, J = 0.8, 0.8 Hz, 3H), 1.80 (dd, J = 1.5, 0.8 Hz, 3H). **^{13}C NMR** (101 MHz, CDCl_3) δ 164.6, 148.7, 147.6, 142.1, 137.8, 136.5, 122.1, 111.2, 45.1, 20.6, 18.7. **HRMS (ESI)**: m/z calculated for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{ONa} [\text{M}+\text{Na}]^+$: 213.0998, found: 213.1004. **IR (KBr)**: 3390, 3080, 1674, 1606, 1525, 1294, 997, 894, 842, 784.

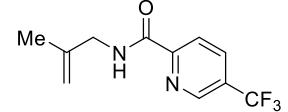
6-methyl-*N*-(2-methylallyl)picolinamide (**1a-G**)

 Colorless oil. **^1H NMR** (400 MHz, CDCl_3) δ 8.26 (s, 1H), 8.08 – 7.98 (m, 1H), 7.73 (t, J = 7.7 Hz, 1H), 7.33 – 7.24 (m, 1H), 5.00 – 4.85 (m, 2H), 4.04 (ddd, J = 6.3, 1.4, 0.7 Hz, 2H), 2.58 (s, 3H), 1.81 (dd, J = 1.5, 0.8 Hz, 3H). **^{13}C NMR** (101 MHz, CDCl_3) δ 164.6, 157.3, 149.3, 142.2, 137.6, 126.0, 119.5, 111.1, 45.0, 24.4, 20.6. **HRMS (ESI)**: m/z calculated for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{ONa} [\text{M}+\text{Na}]^+$: 213.0998, found: 213.1006. **IR (KBr)**: 3392, 3084, 1681, 1596, 1525, 1455, 897, 824, 761.

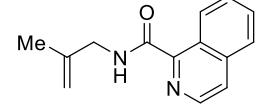
N-(2-methylallyl)-3-(trifluoromethyl)picolinamide (**1a-H**)


 Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 8.81 – 8.69 (m, 1H), 8.21 – 8.14 (m, 1H), 7.77 (br s, 1H), 7.61 – 7.53 (m, 1H), 5.01 – 4.82 (m, 2H), 4.04 (ddd, *J* = 6.3, 1.3, 0.6 Hz, 2H), 1.81 (dd, *J* = 1.3, 0.6 Hz, 3H). **13C NMR** (101 MHz, CDCl₃) δ 163.3, 150.7, 149.5 (q, *J* = 1.6 Hz), 141.7, 136.3 (q, *J* = 6.0 Hz), 126.1 (q, *J* = 34.4 Hz), 125.4, 123.0 (q, *J* = 273.5 Hz), 111.3, 45.2, 20.5. **19F NMR** (376 MHz, CDCl₃) δ -59.47. **HRMS (ESI)**: m/z calculated for C₁₁H₁₁N₂OF₃Na [M+Na]⁺: 267.0716, found: 267.0724. **IR (KBr)**: 3279, 3095, 1678, 1651, 1585, 1563, 1449, 1322, 1164, 1119, 1078, 1032, 896, 701.

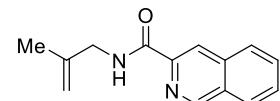
N-(2-methylallyl)-5-(trifluoromethyl)picolinamide (**1a-I**)


 Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 8.83 (dd, *J* = 2.2, 0.9 Hz, 1H), 8.37 (dt, *J* = 8.2, 0.9 Hz, 1H), 8.21 (br s, 1H), 8.13 (dd, *J* = 8.2, 2.2 Hz, 1H), 4.98 – 4.85 (m, 2H), 4.07 (ddd, *J* = 6.3, 1.2, 1.2 Hz, 2H), 1.81 (dd, *J* = 1.2, 1.2 Hz, 3H). **13C NMR** (101 MHz, CDCl₃) δ 162.9, 152.8 (q, *J* = 1.4 Hz), 145.3 (q, *J* = 3.9 Hz), 141.6, 134.9 (q, *J* = 3.5 Hz), 128.8 (q, *J* = 33.2 Hz), 123.2 (q, *J* = 272.8 Hz), 122.3, 111.3, 45.2, 20.4. **19F NMR** (376 MHz, CDCl₃) δ -62.62. **HRMS (ESI)**: m/z calculated for C₁₁H₁₁N₂OF₃Na [M+Na]⁺: 267.0716, found: 267.0721. **IR (KBr)**: 3286, 3090, 1674, 1528, 1329, 1170, 1131, 1076, 1018, 885.

N-(2-methylallyl)isoquinoline-1-carboxamide (**1a-J**)


 Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 9.62 (ddd, *J* = 8.1, 1.8, 0.8 Hz, 1H), 8.47 (d, *J* = 5.5 Hz, 1H), 8.39 (br s, 1H), 7.88 – 7.82 (m, 1H), 7.80 (dd, *J* = 5.6, 0.9 Hz, 1H), 7.75 – 7.64 (m, 2H), 5.06 – 4.85 (m, 2H), 4.09 (ddd, *J* = 6.3, 1.5, 0.8 Hz, 2H), 1.84 (dd, *J* = 1.5, 0.8 Hz, 3H). **13C NMR** (101 MHz, CDCl₃) δ 166.1, 148.3, 142.2, 140.4, 137.5, 130.6, 128.8, 128.0, 127.2, 126.9, 124.5, 111.2, 45.2, 20.7. **HRMS (ESI)**: m/z calculated for C₁₄H₁₄N₂ONa [M+Na]⁺: 249.0998, found: 249.1007. **IR (KBr)**: 3384, 3055, 1672, 1518, 1284, 1251, 1152, 895, 834.

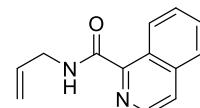
N-(2-methylallyl)isoquinoline-3-carboxamide (**1a-K**)

 Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 9.17 (d, *J* = 1.0 Hz, 1H), 8.64 (d, *J* = 1.0 Hz, 1H), 8.40 (br s, 1H), 8.08 – 8.02 (m, 1H), 8.02 – 7.95 (m, 1H), 7.77 (ddd, *J* = 8.2, 6.9, 1.4 Hz, 1H), 7.71 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 5.06 – 4.84 (m, 2H), 4.18 – 4.04 (ddd, *J* = 6.2, 1.5, 0.8 Hz, 2H), 1.84 (dd, *J* = 1.5, 0.8 Hz, 3H). **13C NMR** (101 MHz, CDCl₃) δ 164.9, 151.2, 143.7, 142.2, 136.2, 131.2, 129.8, 128.9, 128.3, 127.8, 120.6, 111.2, 45.2, 20.6. **HRMS (ESI)**: m/z calculated for C₁₄H₁₄N₂ONa [M+Na]⁺: 249.0998, found: 249.1008. **IR (KBr)**: 3356, 3060, 1669, 1524, 1288, 945, 902.

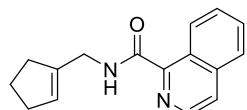
N-(2-methylallyl)quinoline-2-carboxamide (**1a-L**)

 Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 8.43 (br s, 1H), 8.33 (d, *J* = 0.7 Hz, 2H), 8.12 (ddd, *J* = 8.5, 1.4, 0.7 Hz, 1H), 7.89 (ddd, *J* = 8.2, 1.4, 0.7 Hz, 1H), 7.77 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.63 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 5.06 – 4.85 (m, 2H), 4.11 (ddd, *J* = 6.3, 1.5, 0.8 Hz, 2H), 1.84 (dd, *J* = 1.5, 0.8 Hz, 3H). **13C NMR** (101 MHz, CDCl₃) δ 164.6, 149.9, 146.6, 142.2, 137.6, 130.2, 129.9, 129.5, 128.0, 127.9, 119.1, 111.3, 45.2, 20.6. **HRMS (ESI)**: m/z calculated for C₁₄H₁₄N₂ONa [M+Na]⁺: 249.0998, found: 249.1006. **IR (KBr)**: 3391, 3075, 1679, 1527, 1501, 1427, 1166, 895, 848, 775.

N-allylisooquinoline-1-carboxamide (**1b**)

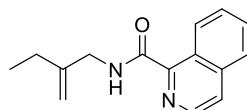
 Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 9.66 – 9.54 (m, 1H), 8.46 (d, *J* = 5.5 Hz, 1H), 8.34 (br s, 1H), 7.87 – 7.82 (m, 1H), 7.79 (dd, *J* = 5.5, 0.9 Hz, 1H), 7.74 – 7.64 (m, 2H), 6.00 (ddt, *J* = 17.2, 10.2, 5.5 Hz, 1H), 5.33 (ddt, *J* = 17.2, 1.6, 1.6 Hz, 1H), 5.20 (ddt, *J* = 10.2, 1.6, 1.6 Hz, 1H), 4.16 (dddd, *J* = 5.5, 6.0, 1.6, 1.6 Hz, 2H). **13C NMR** (101 MHz, CDCl₃) δ 166.0, 148.3, 140.3, 137.5, 134.3, 130.6, 128.7, 128.0, 127.2, 126.9, 124.5, 116.5, 42.0. **HRMS (ESI)**: m/z calculated for C₁₃H₁₂N₂ONa [M+Na]⁺: 235.0842, found: 235.0843. **IR (KBr)**: 3343, 3055, 1661, 1512, 1283, 1156, 962, 904, 835, 742.

N-(cyclopent-1-en-1-ylmethyl)isoquinoline-1-carboxamide (**1c**)



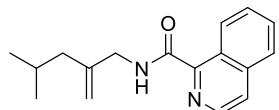
Yellow solid. **¹H NMR** (400 MHz, CDCl₃) δ 9.62 (dd, *J* = 8.5, 1.5 Hz, 1H), 8.47 (d, *J* = 5.5 Hz, 1H), 8.35 (s, 1H), 7.85 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.80 (d, *J* = 5.5 Hz, 1H), 7.70 (dd, *J* = 15.3, 8.4, 6.8, 1.5 Hz, 2H), 5.64 (tt, *J* = 2.1, 2.1 Hz, 1H), 4.19 (dd, *J* = 6.0, 2.1 Hz, 2H), 2.43 – 2.30 (m, 4H), 1.94 (tt, *J* = 7.6, 7.6 Hz, 2H). **¹³C NMR** (101 MHz, CDCl₃) δ 166.0, 148.5, 141.1, 140.4, 137.5, 130.6, 128.7, 128.1, 127.2, 126.9, 126.0, 124.4, 40.1, 33.7, 32.5, 23.5. **HRMS (ESI)**: m/z calculated for C₁₆H₁₆N₂ONa [M+Na]⁺: 275.1155, found: 275.1158. **IR (KBr)**: 3280, 3039, 1652, 1518, 1438, 1382, 1155, 1023, 977, 884, 832, 756.

N-(2-methylenebutyl)isoquinoline-1-carboxamide (**1d**)



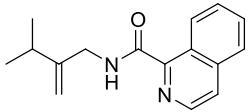
Colorless solid. **¹H NMR** (400 MHz, CDCl₃) δ 9.63 (ddd, *J* = 8.1, 1.8, 0.8 Hz, 1H), 8.47 (d, *J* = 5.5 Hz, 1H), 8.37 (br s, 1H), 7.87 – 7.82 (m, 1H), 7.80 (dd, *J* = 5.5, 0.9 Hz, 1H), 7.75 – 7.63 (m, 2H), 5.04 – 4.98 (m, 1H), 4.95 – 4.88 (m, 1H), 4.12 (ddt, *J* = 6.3, 1.6, 0.8 Hz, 2H), 2.16 (qdd, *J* = 7.5, 1.6, 0.8 Hz, 2H), 1.12 (t, *J* = 7.5 Hz, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 166.1, 148.3, 147.8, 140.3, 137.5, 130.6, 128.7, 128.0, 127.2, 126.9, 124.5, 109.2, 44.1, 27.1, 12.3. **HRMS (ESI)**: m/z calculated for C₁₅H₁₆N₂ONa [M+Na]⁺: 263.1155, found: 263.1157. **IR (KBr)**: 3386, 3065, 1672, 1516, 1283, 1184, 1151, 970, 896, 834, 743.

N-(4-methyl-2-methylenepentyl)isoquinoline-1-carboxamide (**1e**)



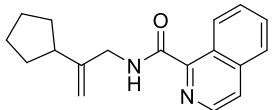
Colorless solid. **¹H NMR** (400 MHz, CDCl₃) δ 9.69 – 9.57 (m, 1H), 8.47 (dd, *J* = 5.6, 1.8 Hz, 1H), 8.37 (br s, 1H), 7.88 – 7.82 (m, 1H), 7.79 (dt, *J* = 5.6, 1.3 Hz, 1H), 7.75 – 7.64 (m, 2H), 5.08 – 5.03 (m, 1H), 4.93 – 4.87 (m, 1H), 4.08 (dd, *J* = 6.2, 1.3 Hz, 2H), 2.02 (d, *J* = 7.2 Hz, 2H), 1.96 – 1.80 (m, 1H), 0.93 (d, *J* = 6.5 Hz, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 166.0, 148.4, 145.0, 140.4, 137.5, 130.6, 128.7, 128.1, 127.2, 126.9, 124.4, 111.5, 44.2, 43.9, 26.4, 22.6. **HRMS (ESI)**: m/z calculated for C₁₇H₂₀N₂ONa [M+Na]⁺: 291.1468, found: 291.1470. **IR (KBr)**: 3304, 3050, 1651, 1522, 1290, 1157, 973, 892,

N-(3-methyl-2-methylenebutyl)isoquinoline-1-carboxamide (**1f**)



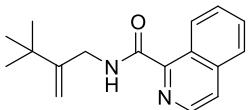
Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 9.69 – 9.59 (m, 1H), 8.46 (d, *J* = 5.5 Hz, 1H), 8.36 (br s, 1H), 7.88 – 7.82 (m, 1H), 7.80 – 7.77 (m, 1H), 7.74 – 7.63 (m, 2H), 5.01 – 4.98 (m, 1H), 4.95 – 4.92 (m, 1H), 4.15 (ddd, *J* = 6.0, 1.4, 1.4 Hz, 2H), 2.45 – 2.32 (m, 1H), 1.14 (d, *J* = 6.9 Hz, 6H). **13C NMR** (101 MHz, CDCl₃) δ 166.0, 152.1, 148.3, 140.3, 137.5, 130.6, 128.7, 128.0, 127.2, 126.8, 124.4, 108.0, 42.8, 32.3, 21.8. **HRMS (ESI)**: m/z calculated for C₁₆H₁₈N₂ONa [M+Na]⁺: 277.1311, found: 277.1316. **IR (KBr)**: 3329, 3054, 1660, 1645, 1412, 1288, 874, 742.

N-(2-cyclopentylallyl)isoquinoline-1-carboxamide (**1g**)



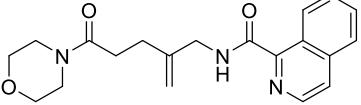
Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 9.68 – 9.59 (m, 1H), 8.46 (d, *J* = 5.5 Hz, 1H), 8.38 (t, *J* = 6.3 Hz, 1H), 7.85 – 7.81 (m, 1H), 7.78 (dd, *J* = 5.5, 0.9 Hz, 1H), 7.73 – 7.63 (m, 2H), 5.03 – 4.91 (m, 2H), 4.14 (ddd, *J* = 6.3, 1.3, 1.3 Hz, 2H), 2.50 (tt, *J* = 8.4, 8.4 Hz, 1H), 1.97 – 1.86 (m, 2H), 1.76 – 1.65 (m, 2H), 1.65 – 1.55 (m, 2H), 1.55 – 1.43 (m, 2H). **13C NMR** (101 MHz, CDCl₃) δ 166.0, 149.5, 148.3, 140.3, 137.5, 130.5, 128.7, 128.0, 127.2, 126.8, 124.4, 108.0, 44.5, 43.7, 31.6, 25.0. **HRMS (ESI)**: m/z calculated for C₁₈H₂₀N₂ONa [M+Na]⁺: 303.1468, found: 303.1470. **IR (KBr)**: 3305, 3050, 1794, 1661, 1649, 1532, 1290, 1258, 1155, 889, 831, 749.

N-(3,3-dimethyl-2-methylenebutyl)isoquinoline-1-carboxamide (**1h**)



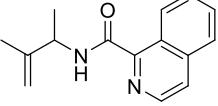
Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 9.72 – 9.57 (m, 1H), 8.47 (dd, *J* = 5.5, 0.7 Hz, 1H), 8.33 (br s, 1H), 7.87 – 7.82 (m, 1H), 7.79 (dd, *J* = 5.6, 0.9 Hz, 1H), 7.74 – 7.64 (m, 2H), 5.03 – 5.01 (m, 2H), 4.20 (dt, *J* = 6.1, 1.3 Hz, 2H), 1.18 (s, 9H). **13C NMR** (101 MHz, CDCl₃) δ 165.9, 154.2, 148.4, 140.4, 137.6, 130.6, 128.7, 128.1, 127.2, 126.9, 124.4, 107.6, 40.6, 35.6, 29.4. **HRMS (ESI)**: m/z calculated for C₁₇H₂₀N₂ONa [M+Na]⁺: 291.1468, found: 291.1468. **IR (KBr)**: 3305, 3048, 1794, 1657, 1536, 1286, 1146, 898,

N-(2-methylene-5-morpholino-5-oxopentyl)isoquinoline-1-carboxamide (**1i**)



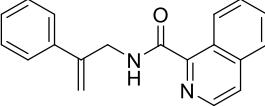
Colorless oil. **1H NMR** (400 MHz, CDCl₃) δ 9.64 – 9.54 (m, 1H), 8.50 – 8.43 (m, 2H), 7.88 – 7.83 (m, 1H), 7.81 (dd, *J* = 5.6, 0.9 Hz, 1H), 7.75 – 7.65 (m, 2H), 5.10 (td, *J* = 1.2, 1.2 Hz, 1H), 4.96 (dt, *J* = 1.2, 1.2 Hz, 1H), 4.15 (dt, *J* = 6.4, 1.2 Hz, 2H), 3.71 – 3.54 (m, 6H), 3.52 – 3.46 (m, 2H), 2.63 – 2.53 (m, 2H), 2.53 – 2.40 (m, 2H). **13C NMR** (101 MHz, CDCl₃) δ 171.0, 166.1, 148.1, 145.1, 140.4, 137.5, 130.6, 128.8, 127.8, 127.2, 126.9, 124.6, 111.6, 67.0, 66.8, 46.1, 44.0, 42.1, 31.6, 29.4. **HRMS (ESI)**: m/z calculated for C₂₀H₂₃N₃O₃Na [M+Na]⁺: 376.1632, found: 376.1629. **IR (KBr)**: 3314, 3370, 1795, 1637, 1583, 1239, 1152, 1116, 1067, 1032, 964, 900, 836, 746.

N-(3-methylbut-3-en-2-yl)isoquinoline-1-carboxamide (**1j**)



Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 9.67 – 9.67 (m, 1H), 8.46 (dd, *J* = 5.6, 1.5 Hz, 1H), 8.28 (d, *J* = 8.5 Hz, 1H), 7.88 – 7.81 (m, 1H), 7.79 (dq, *J* = 5.6, 1.1 Hz, 1H), 7.74 – 7.60 (m, 2H), 5.06 – 5.02 (m, 1H), 4.92 – 4.88 (m, 1H), 4.72 (dq, *J* = 8.5, 6.9 Hz, 1H), 1.86 (dd, *J* = 1.6, 0.8 Hz, 3H), 1.44 (d, *J* = 6.9 Hz, 3H). **13C NMR** (101 MHz, CDCl₃) δ 165.4, 148.3, 146.4, 140.3, 137.5, 130.6, 128.7, 128.1, 127.2, 126.9, 124.4, 110.5, 49.9, 19.9, 19.9. **HRMS (ESI)**: m/z calculated for C₁₅H₁₆N₂ONa [M+Na]⁺: 263.1155, found: 263.1165. **IR (KBr)**: 3365, 3082, 1664, 1648, 1512, 1158, 897, 860, 765.

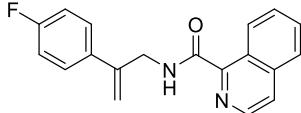
N-(2-phenylallyl)isoquinoline-1-carboxamide (**1k**)



Colorless solid. **1H NMR** (400 MHz, CDCl₃) δ 9.69 – 9.56 (m, 1H), 8.48 – 8.36 (m, 2H), 7.88 – 7.82 (m, 1H), 7.78 (dd, *J* = 5.6, 0.9 Hz, 1H), 7.75 – 7.65 (m, 2H), 7.57 – 7.50 (m, 2H), 7.40 – 7.33 (m, 2H), 7.33 – 7.27 (m, 1H), 5.54 (dt, *J* = 0.9, 0.9 Hz, 1H), 5.38 (dt, *J* = 0.9, 1.5 Hz, 1H), 4.60 (ddd, *J* = 6.0, 1.5, 0.9 Hz, 2H). **13C NMR** (101 MHz, CDCl₃) δ 166.0, 148.2, 144.4, 140.3, 138.9, 137.5, 130.6, 128.7, 128.6, 128.1, 127.9, 127.2, 126.9, 126.2, 124.5, 113.7, 43.2. **HRMS (ESI)**: m/z calculated for C₁₉H₁₆N₂ONa [M+Na]⁺:

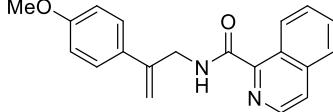
311.1155, found: 311.1160. **IR** (KBr): 3356, 3054, 1671, 1516, 1497, 1289, 1153, 895, 839, 790.

N-(2-(4-fluorophenyl)allyl)isoquinoline-1-carboxamide (**1l**)



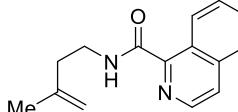
Yellow solid. **¹H NMR** (400 MHz, CDCl₃) δ 9.65 – 9.54 (m, 1H), 8.46 – 8.35 (m, 2H), 7.87 – 7.81 (m, 1H), 7.78 (dd, *J* = 5.6, 0.9 Hz, 1H), 7.75 – 7.65 (m, 2H), 7.54 – 7.46 (m, 2H), 7.08 – 6.99 (m, 2H), 5.47 (s, 1H), 5.36 (t, *J* = 1.5 Hz, 1H), 4.61 – 4.51 (m, 2H). **¹³C NMR** (101 MHz, CDCl₃) δ 166.0, 163.7 (d, *J* = 247.1 Hz), 148.1, 143.6, 140.4, 137.5, 134.9 (d, *J* = 3.3 Hz), 130.6, 128.8, 128.0, 127.9, 127.2, 126.9, 124.6, 115.5 (d, *J* = 21.4 Hz), 113.7 (d, *J* = 1.4 Hz), 43.3. **HRMS (ESI)**: m/z calculated for C₁₉H₁₅N₂OFNa [M+Na]⁺: 329.1061, found: 329.1066. **IR** (KBr): 3389, 3065, 1796, 1676, 1512, 1288, 1227, 1164, 882, 834.

N-(2-(4-methoxyphenyl)allyl)isoquinoline-1-carboxamide (**1m**)



Colorless solid. **¹H NMR** (400 MHz, CDCl₃) δ 9.69 – 9.57 (m, 1H), 8.46 – 8.29 (m, 2H), 7.86 – 7.79 (m, 1H), 7.77 (dd, *J* = 5.7, 0.9 Hz, 1H), 7.74 – 7.63 (m, 2H), 7.51 – 7.45 (m, 2H), 6.93 – 6.84 (m, 2H), 5.46 – 5.45 (m, 1H), 5.30 – 5.28 (m, 1H), 4.57 (ddd, *J* = 6.1, 1.5, 0.8 Hz, 2H), 3.79 (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 166.0, 159.6, 148.3, 143.7, 140.4, 137.5, 131.3, 130.6, 128.7, 128.0, 127.4, 127.2, 126.9, 124.5, 114.0, 112.2, 55.4, 43.3. **HRMS (ESI)**: m/z calculated for C₂₀H₁₈N₂O₂Na [M+Na]⁺: 341.1260, found: 341.1272. **IR** (KBr): 3307, 3050, 1653, 1536, 1513, 1288, 1247, 1176, 1034, 833.

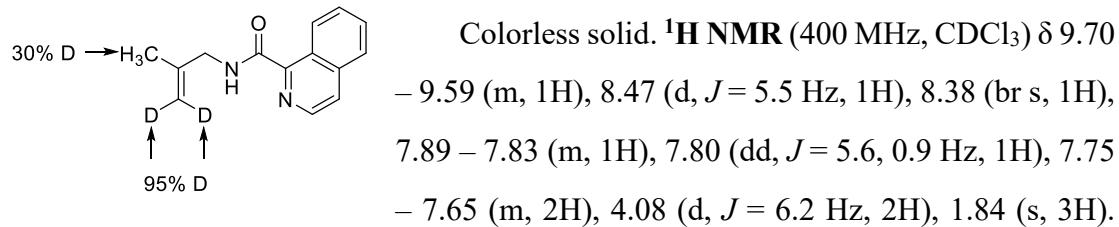
N-(3-methylbut-3-en-1-yl)isoquinoline-1-carboxamide (**1n**)



Colorless solid. **¹H NMR** (400 MHz, CDCl₃) δ 9.68 – 9.55 (m, 1H), 8.45 (dd, *J* = 5.5, 1.2 Hz, 1H), 8.23 (br s, 1H), 7.83 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.77 (dt, *J* = 5.6, 1.2 Hz, 1H), 7.69 (dtd, *J* = 8.2, 6.8, 5.4 Hz, 2H), 4.92 – 4.78 (m, 2H), 3.66 (td, *J* = 7.0, 5.9 Hz, 2H), 2.40 (t, *J* = 7.0 Hz, 2H), 1.82 (d, *J* = 1.4 Hz, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 166.1, 148.5, 142.8,

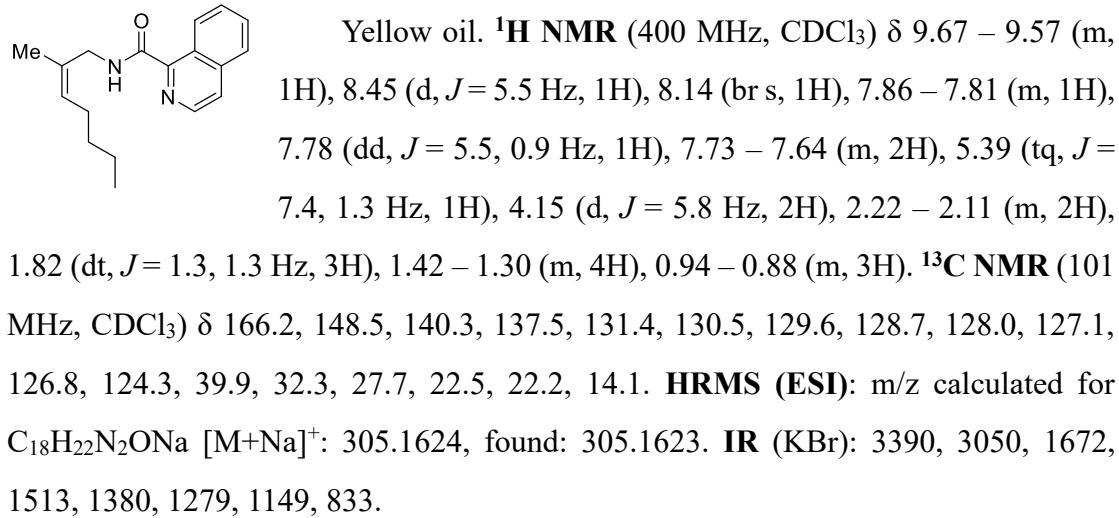
140.4, 137.5, 130.5, 128.7, 128.0, 127.1, 126.8, 124.3, 112.3, 37.6, 37.5, 22.4. **HRMS (ESI)**: m/z calculated for $C_{15}H_{16}N_2O\text{Na}$ $[M+Na]^+$: 263.1155, found: 263.1154. **IR (KBr)**: 3382, 3065, 1668, 1517, 1275, 1151, 892, 834.

N-(2-methylallyl-3,3-d2)isoquinoline-1-carboxamide (**[D₂]-1a**)

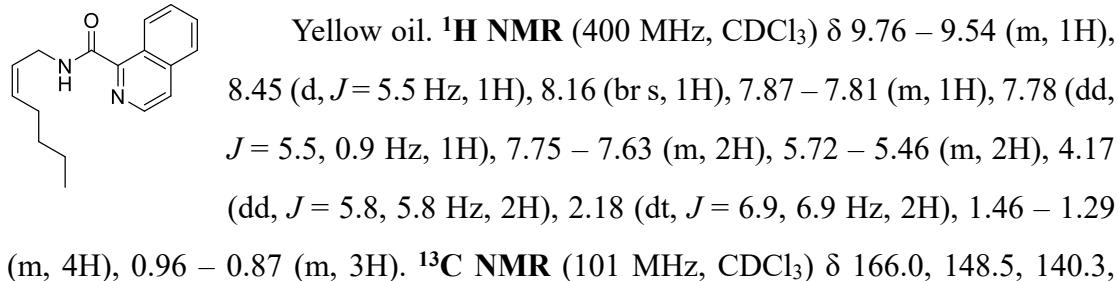


¹³C NMR (101 MHz, $CDCl_3$) δ 166.1, 148.3, 142.0, 140.4, 137.6, 130.6, 128.8, 128.1, 127.2, 126.9, 124.5, 45.1, 20.6. **HRMS (ESI)**: m/z calculated for $C_{14}H_{12}D_2N_2O\text{Na}$ $[M+Na]^+$: 251.1124, found: 251.1133. **IR (KBr)**: 3383, 3053, 1669, 1517, 1380, 1281, 1152, 833.

(*Z*)-*N*-(2-methylhept-2-en-1-yl)isoquinoline-1-carboxamide (**3a**)



(*Z*)-*N*-(hept-2-en-1-yl)isoquinoline-1-carboxamide (**3b**)



137.5, 134.1, 130.6, 128.7, 128.0, 127.1, 126.9, 125.2, 124.4, 36.8, 31.8, 27.3, 22.5, 14.1. **HRMS (ESI):** m/z calculated for $C_{17}H_{20}N_2ONa$ $[M+Na]^+$: 291.1468, found: 291.1471. **IR (KBr):** 3391, 3051, 1670, 1513, 1380, 1279, 1151, 834.

N-(2-butylcyclopent-1-en-1-yl)methyl)isoquinoline-1-carboxamide (**3c**)

Yellow oil. **1H NMR** (400 MHz, $CDCl_3$) δ 9.62 (ddd, $J = 7.7, 2.0, 0.8$ Hz, 1H), 8.44 (d, $J = 5.5$ Hz, 1H), 8.09 (t, $J = 5.7$ Hz, 1H), 7.85 – 7.80 (m, 1H), 7.77 (dd, $J = 5.6, 0.9$ Hz, 1H), 7.73 – 7.63 (m, 2H), 4.19 (dt, $J = 5.7, 1.2$ Hz, 2H), 2.51 – 2.41 (m, 2H), 2.39 – 2.31 (m, 2H), 2.19 (t, $J = 7.4$ Hz, 2H), 1.81 (tt, $J = 8.4, 6.7$ Hz, 2H), 1.44 – 1.24 (m, 4H), 0.91 (t, $J = 7.2$ Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.0, 148.6, 140.7, 140.3, 137.5, 131.2, 130.5, 128.6, 128.1, 127.1, 126.8, 124.3, 37.3, 36.2, 35.0, 30.6, 28.3, 22.8, 21.7, 14.1. **HRMS (ESI):** m/z calculated for $C_{20}H_{24}N_2ONa$ $[M+Na]^+$: 331.1781, found: 331.1788. **IR (KBr):** 3391, 3054, 1669, 1512, 1380, 1278, 1147, 833.

(*Z*)-*N*-(2-ethylhept-2-en-1-yl)isoquinoline-1-carboxamide (**3d**)

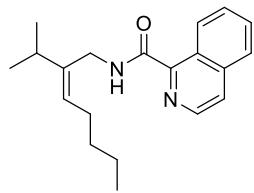
Yellow oil. **1H NMR** (400 MHz, $CDCl_3$) δ 9.63 (ddd, $J = 7.7, 2.1, 0.8$ Hz, 1H), 8.45 (d, $J = 5.5$ Hz, 1H), 8.09 (br s, 1H), 7.85 – 7.80 (m, 1H), 7.77 (dd, $J = 5.6, 0.9$ Hz, 1H), 7.74 – 7.64 (m, 2H), 5.40 (tt, $J = 7.3, 1.1$ Hz, 1H), 4.16 (d, $J = 5.7$ Hz, 2H), 2.22 – 2.09 (m, 4H), 1.45 – 1.29 (m, 4H), 1.07 (t, $J = 7.4$ Hz, 3H), 0.95 – 0.86 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.1, 148.5, 140.3, 137.5, 137.0, 130.5, 128.6, 128.3, 128.1, 127.1, 126.8, 124.3, 38.6, 32.3, 28.7, 27.6, 22.5, 14.1, 13.0. **HRMS (ESI):** m/z calculated for $C_{19}H_{24}N_2ONa$ $[M+Na]^+$: 319.1781, found: 319.1784. **IR (KBr):** 3389, 3056, 1672, 1513, 1379, 1277, 1149, 833.

(*Z*)-*N*-(2-isobutylhept-2-en-1-yl)isoquinoline-1-carboxamide (**3e**)

Brown oil. **1H NMR** (400 MHz, $CDCl_3$) δ 9.72 – 9.57 (m, 1H), 8.45 (d, $J = 5.5$ Hz, 1H), 8.08 (br s, 1H), 7.83 (dd, $J = 7.9, 1.7$ Hz, 1H), 7.77 (d, $J = 5.5$ Hz, 1H), 7.74 – 7.63 (m, 2H), 5.39 (t, $J = 7.4$ Hz, 1H), 4.12 (d, $J = 5.6$ Hz, 2H), 2.18 (dt, $J =$

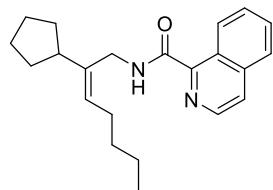
7.4, 7.1 Hz, 2H), 1.98 (d, J = 7.2 Hz, 2H), 1.85 (dtt, J = 13.5, 6.7, 6.7 Hz, 1H), 1.46 – 1.28 (m, 4H), 0.98 – 0.82 (m, 9H). **^{13}C NMR** (101 MHz, CDCl_3) δ 166.0, 148.5, 140.4, 137.5, 134.4, 131.2, 130.5, 128.6, 128.1, 127.1, 126.8, 124.3, 45.8, 38.4, 32.3, 27.7, 26.4, 22.6, 22.5, 14.1. **HRMS (ESI)**: m/z calculated for $\text{C}_{21}\text{H}_{28}\text{N}_2\text{ONa}$ $[\text{M}+\text{Na}]^+$: 347.2094, found: 347.2097. **IR (KBr)**: 3391, 3060, 1672, 1512, 1380, 1275, 1148, 832.

(Z)-*N*-(2-isopropylhept-2-en-1-yl)isoquinoline-1-carboxamide (3f**)**



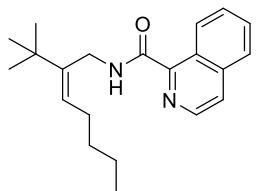
Yellow oil. **^1H NMR** (400 MHz, CDCl_3) δ 9.70 – 9.59 (m, 1H), 8.44 (d, J = 5.5 Hz, 1H), 8.02 (br s, 1H), 7.86 – 7.80 (m, 1H), 7.77 (dd, J = 5.6, 0.9 Hz, 1H), 7.74 – 7.62 (m, 2H), 5.44 (td, J = 7.3, 1.0 Hz, 1H), 4.15 (d, J = 5.4 Hz, 2H), 2.41 (qqd, J = 6.8, 6.8, 1.0 Hz, 1H), 2.17 (dt, J = 7.3, 6.8 Hz, 2H), 1.45 – 1.28 (m, 4H), 1.09 (d, J = 6.8 Hz, 6H), 0.93 – 0.86 (m, 3H). **^{13}C NMR** (101 MHz, CDCl_3) δ 165.9, 148.5, 141.4, 140.4, 137.5, 130.5, 128.6, 128.0, 127.7, 127.1, 126.8, 124.3, 37.7, 33.9, 32.3, 27.7, 22.5, 22.1, 14.2. **HRMS (ESI)**: m/z calculated for $\text{C}_{20}\text{H}_{26}\text{N}_2\text{ONa}$ $[\text{M}+\text{Na}]^+$: 333.1937, found: 333.1935. **IR (KBr)**: 3393, 3350, 1672, 1511, 1379, 1274, 1148, 833.

(Z)-*N*-(2-cyclopentylhept-2-en-1-yl)isoquinoline-1-carboxamide (3g**)**



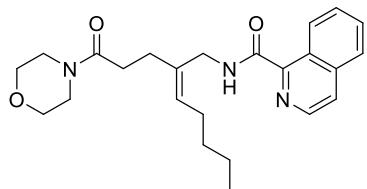
Yellow oil. **^1H NMR** (400 MHz, CDCl_3) δ 9.66 – 9.62 (m, 1H), 8.45 (d, J = 5.4 Hz, 1H), 8.04 (br s, 1H), 7.87 – 7.80 (m, 1H), 7.80 – 7.75 (m, 1H), 7.74 – 7.64 (m, 2H), 5.47 (t, J = 7.3 Hz, 1H), 4.14 (d, J = 5.4 Hz, 2H), 2.59 – 2.45 (m, 1H), 2.18 (dt, J = 7.3, 7.1 Hz, 2H), 1.94 – 1.78 (m, 2H), 1.73 – 1.63 (m, 2H), 1.63 – 1.50 (m, 2H), 1.50 – 1.28 (m, 6H), 0.89 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, CDCl_3) δ 165.9, 148.5, 140.4, 138.6, 137.5, 130.5, 128.6, 128.1, 128.1, 127.2, 126.8, 124.3, 46.3, 38.5, 32.4, 31.8, 27.7, 25.0, 22.5, 14.2. **HRMS (ESI)**: m/z calculated for $\text{C}_{22}\text{H}_{28}\text{N}_2\text{ONa}$ $[\text{M}+\text{Na}]^+$: 359.2094, found: 359.2094. **IR (KBr)**: 3393, 3052, 1671, 1511, 1379, 1274, 1148, 833.

(Z)-N-(2-(tert-butyl)hept-2-en-1-yl)isoquinoline-1-carboxamide (3h)



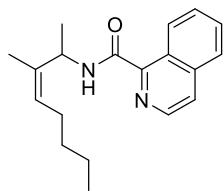
Yellow oil. **1H NMR** (400 MHz, CDCl₃) δ 9.69 – 9.57 (m, 1H), 8.44 (d, *J* = 5.5 Hz, 1H), 7.90 (br s, 1H), 7.85 – 7.80 (m, 1H), 7.76 (dd, *J* = 5.5, 0.9 Hz, 1H), 7.73 – 7.64 (m, 2H), 5.55 (t, *J* = 7.3 Hz, 1H), 4.15 (d, *J* = 4.9 Hz, 2H), 2.16 (dt, *J* = 7.3, 7.3 Hz, 2H), 1.45 – 1.27 (m, 4H), 1.13 (s, 9H), 0.87 (t, *J* = 7.2 Hz, 3H). **13C NMR** (101 MHz, CDCl₃) δ 165.6, 148.5, 143.7, 140.4, 137.5, 130.5, 128.6, 128.0, 127.9, 127.1, 126.8, 124.2, 36.7, 36.3, 32.3, 29.3, 28.1, 22.6, 14.2. **HRMS (ESI)**: m/z calculated for C₂₁H₂₈N₂ONa [M+Na]⁺: 347.2094, found: 347.2090. **IR (KBr)**: 3397, 3054, 1671, 1509, 1380, 1275, 1147, 833.

(Z)-N-(2-(3-morpholino-3-oxopropyl)hept-2-en-1-yl)isoquinoline-1-carboxamide (3i)



Yellow oil. **1H NMR** (400 MHz, CDCl₃) δ 9.61 – 9.55 (m, 1H), 8.46 (d, *J* = 5.5 Hz, 1H), 8.24 (br s, 1H), 7.88 – 7.83 (m, 1H), 7.80 (dd, *J* = 5.5, 0.8 Hz, 1H), 7.75 – 7.65 (m, 2H), 5.48 (t, *J* = 7.4 Hz, 1H), 4.19 (dd, *J* = 5.9, 0.8 Hz, 2H), 3.65 – 3.53 (m, 6H), 3.46 (dd, *J* = 5.6, 3.9 Hz, 2H), 2.58 – 2.50 (m, 2H), 2.50 – 2.40 (m, 2H), 2.18 (dt, *J* = 7.4, 7.2 Hz, 2H), 1.45 – 1.29 (m, 4H), 0.96 – 0.85 (m, 3H). **13C NMR** (101 MHz, CDCl₃) δ 171.4, 166.2, 148.3, 140.4, 137.5, 134.3, 130.7, 130.6, 128.7, 127.8, 127.1, 126.9, 124.4, 67.0, 66.8, 46.1, 42.0, 38.1, 32.4, 32.1, 31.4, 27.6, 22.4, 14.1. **HRMS (ESI)**: m/z calculated for C₂₄H₃₁N₃O₃Na [M+Na]⁺: 432.2258, found: 432.2258. **IR (KBr)**: 3333, 3059, 1637, 1529, 1386, 1270, 1114, 832.

(Z)-N-(3-methyloct-3-en-2-yl)isoquinoline-1-carboxamide (3j)

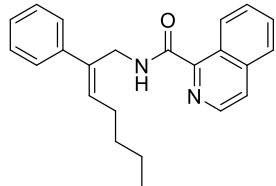


Yellow oil. **1H NMR** (400 MHz, CDCl₃) δ 9.65 (ddd, *J* = 8.2, 1.7, 0.8 Hz, 1H), 8.45 (d, *J* = 5.5 Hz, 1H), 8.33 (d, *J* = 8.2 Hz, 1H), 7.84 – 7.79 (m, 1H), 7.77 (dd, *J* = 5.5, 0.9 Hz, 1H), 7.72 – 7.62 (m, 2H), 5.28 (tq, *J* = 7.3, 1.6 Hz, 1H), 5.19 (dq, *J* = 8.2, 6.4 Hz, 1H), 2.24 (dtq, *J* = 7.3, 7.3, 1.3 Hz, 2H), 1.77 (dt, *J* = 1.6, 1.3 Hz, 3H), 1.43 – 1.31 (m, 7H), 0.95 – 0.87 (m, 3H). **13C NMR** (101 MHz, CDCl₃) δ 165.1, 148.5, 140.3, 137.5, 134.9, 130.5, 128.6, 128.2, 127.8, 127.2, 126.8, 124.3, 45.0, 32.3, 27.4, 22.6, 19.8, 18.3, 14.2.

HRMS (ESI): m/z calculated for $C_{19}H_{24}N_2O\text{Na} [M+Na]^+$: 319.1781, found: 319.1788.

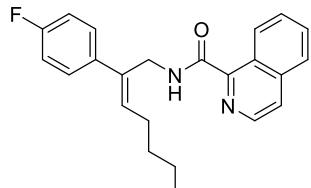
IR (KBr): 3384, 3054, 1672, 1509, 1379, 1152, 833.

(Z)-N-(2-phenylhept-2-en-1-yl)isoquinoline-1-carboxamide (3k**)**



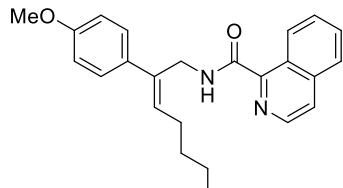
Brown-drak oil. **1H NMR** (400 MHz, $CDCl_3$) δ 9.65 – 9.52 (m, 1H), 8.35 (d, J = 5.5 Hz, 1H), 8.07 (br s, 1H), 7.85 – 7.76 (m, 1H), 7.74 – 7.63 (m, 3H), 7.52 – 7.45 (m, 2H), 7.36 – 7.28 (m, 2H), 7.25 – 7.19 (m, 1H), 6.04 (t, J = 7.5 Hz, 1H), 4.62 (d, J = 5.4 Hz, 2H), 2.39 (q, J = 7.5 Hz, 2H), 1.55 – 1.46 (m, 2H), 1.46 – 1.36 (m, 2H), 0.93 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.0, 148.4, 141.0, 140.3, 137.4, 135.5, 133.7, 130.5, 128.6, 128.6, 128.0, 127.2, 127.1, 126.8, 126.2, 124.3, 38.2, 32.1, 28.6, 22.6, 14.2. **HRMS (ESI):** m/z calculated for $C_{23}H_{24}N_2O\text{Na} [M+Na]^+$: 367.1781, found: 367.1781. **IR (KBr):** 3387, 3055, 1669, 1511, 1380, 1281, 1148, 833.

(Z)-N-(2-(4-fluorophenyl)hept-2-en-1-yl)isoquinoline-1-carboxamide (3l**)**



Brown-dark oil. **1H NMR** (400 MHz, $CDCl_3$) δ 9.62 – 9.51 (m, 1H), 8.35 (d, J = 5.5 Hz, 1H), 8.08 (br s, 1H), 7.81 – 7.75 (m, 1H), 7.75 – 7.62 (m, 3H), 7.48 – 7.39 (m, 2H), 7.04 – 6.93 (m, 2H), 5.95 (t, J = 7.5 Hz, 1H), 4.59 (d, J = 5.6 Hz, 2H), 2.37 (dt, J = 7.4, 7.4 Hz, 2H), 1.54 – 1.35 (m, 4H), 0.93 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.0, 163.2 (d, J = 245.9 Hz), 148.2, 140.3, 137.4, 137.0 (d, J = 3.3 Hz), 134.8, 133.4 (d, J = 1.4 Hz), 130.5, 128.7, 127.9, 127.8, 127.1, 126.8, 124.3, 115.3 (d, J = 21.3 Hz), 38.2, 32.1, 28.6, 22.6, 14.1. **HRMS (ESI):** m/z calculated for $C_{23}H_{23}N_2O\text{FNa} [M+Na]^+$: 385.1687, found: 385.1687. **IR (KBr):** 3387, 3054, 1669, 1510, 1380, 1281, 1161, 832.

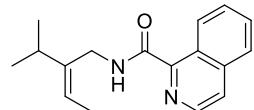
(Z)-N-(2-(4-methoxyphenyl)hept-2-en-1-yl)isoquinoline-1-carboxamide (3m**)**



Yellow oil. **1H NMR** (400 MHz, $CDCl_3$) δ 9.66 – 9.54 (m, 1H), 8.35 (d, J = 5.5 Hz, 1H), 8.05 (t, J = 5.3 Hz, 1H), 7.83 – 7.76 (m, 1H), 7.75 – 7.62 (m, 3H), 7.47 – 7.34 (m, 2H), 6.90 – 6.81 (m, 2H), 5.95 (t, J = 7.5 Hz, 1H), 4.59 (d,

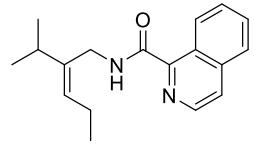
J = 5.3 Hz, 2H), 3.77 (s, 3H), 2.37 (dt, *J* = 7.3, 7.3 Hz, 2H), 1.55 – 1.30 (m, 4H), 0.93 (t, *J* = 7.2 Hz, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 166.0, 158.9, 148.4, 140.3, 137.4, 134.9, 133.4, 131.9, 130.5, 128.6, 127.9, 127.3, 127.1, 126.8, 124.2, 114.0, 55.4, 38.2, 32.2, 28.5, 22.6, 14.1. **HRMS (ESI)**: m/z calculated for C₂₄H₂₆N₂O₂Na [M+Na]⁺: 397.1886, found: 397.1894. **IR (KBr)**: 3388, 3050, 1668, 1512, 1380, 1286, 1248, 1181, 1148, 1032, 830.

(Z)-*N*-(2-isopropylbut-2-en-1-yl)isoquinoline-1-carboxamide (4b**)**



Brown oil. **¹H NMR** (400 MHz, CDCl₃) δ 9.70 – 9.58 (m, 1H), 8.44 (d, *J* = 5.5 Hz, 1H), 8.04 (br s, 1H), 7.82 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.76 (dd, *J* = 5.5, 0.9 Hz, 1H), 7.72 – 7.64 (m, 2H), 5.53 (q, *J* = 6.9 Hz, 1H), 4.17 (d, *J* = 5.4 Hz, 2H), 2.41 (hept, *J* = 6.9 Hz, 1H), 1.76 (d, *J* = 6.9 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.9, 148.5, 142.3, 140.4, 137.5, 130.5, 128.6, 128.0, 127.1, 126.8, 124.3, 121.5, 37.4, 34.0, 22.0, 13.5. **HRMS (ESI)**: m/z calculated for C₁₇H₂₀N₂ONa [M+Na]⁺: 291.1468, found: 291.1470. **IR (KBr)**: 3392, 3058, 1671, 1512, 1381, 1275, 1149, 833.

(Z)-*N*-(2-isopropylpent-2-en-1-yl)isoquinoline-1-carboxamide (4c**)**



Yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ 9.68 – 9.61 (m, 1H), 8.44 (d, *J* = 5.5 Hz, 1H), 8.02 (br s, 1H), 7.86 – 7.80 (m, 1H), 7.77 (dd, *J* = 5.5, 0.9 Hz, 1H), 7.73 – 7.64 (m, 2H), 5.43 (t, *J* = 7.3 Hz, 1H), 4.15 (d, *J* = 5.4 Hz, 2H), 2.41 (hept, *J* = 6.9 Hz, 1H), 2.18 (qd, *J* = 7.5, 7.3 Hz, 2H), 1.09 (d, *J* = 6.9 Hz, 6H), 1.02 (t, *J* = 7.5 Hz, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.9, 148.5, 140.9, 140.4, 137.5, 130.5, 129.3, 128.6, 128.1, 127.1, 126.8, 124.3, 37.6, 33.8, 22.0, 21.3, 14.7. **HRMS (ESI)**: m/z calculated for C₂₀H₂₂N₂ONa [M+Na]⁺: 305.1624, found: 305.1631. **IR (KBr)**: 3393, 3054, 1671, 1513, 1379, 1275, 1148, 834.

(Z)-N-(2-isopropylundec-2-en-1-yl)isoquinoline-1-carboxamide (4d)

Brown oil. **¹H NMR** (400 MHz, CDCl₃) δ 9.68 – 9.62 (m, 1H), 8.44 (d, *J* = 5.5 Hz, 1H), 8.02 (br s, 1H), 7.86 – 7.80 (m, 1H), 7.77 (dd, *J* = 5.6, 0.9 Hz, 1H), 7.73 – 7.64 (m, 2H), 5.44 (t, *J* = 7.3 Hz, 1H), 4.15 (d, *J* = 5.4 Hz, 2H), 2.41 (hept, *J* = 6.8 Hz, 1H), 2.16 (dt, *J* = 7.3, 7.3 Hz, 2H), 1.44 – 1.35 (m, 2H), 1.34 – 1.20 (m, 10H), 1.09 (d, *J* = 6.8 Hz, 6H), 0.89 – 0.82 (m, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.8, 148.4, 141.3, 140.3, 137.4, 130.4, 128.6, 128.0, 127.8, 127.1, 126.8, 124.2, 37.7, 33.9, 31.9, 30.1, 29.6, 29.4, 29.3, 27.9. **HRMS (ESI)**: m/z calculated for C₂₄H₃₄N₂ONa [M+Na]⁺: 389.2563, found: 389.2576. **IR (KBr)**: 3394, 3052, 1672, 1513, 1379, 1279, 1148, 833.

(Z)-N-(2-isopropyl-5-methylhex-2-en-1-yl)isoquinoline-1-carboxamide (4e)

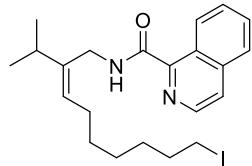
Yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ 9.68 – 9.61 (m, 1H), 8.44 (d, *J* = 5.5 Hz, 1H), 8.02 (br s, 1H), 7.85 – 7.79 (m, 1H), 7.76 (dd, *J* = 5.5, 0.8 Hz, 1H), 7.73 – 7.63 (m, 2H), 5.46 (t, *J* = 7.5 Hz, 1H), 4.15 (d, *J* = 5.4 Hz, 2H), 2.43 (hept, *J* = 6.8 Hz, 1H), 2.06 (dd, *J* = 7.5, 7.1 Hz, 2H), 1.67 (hept, *J* = 7.1, 6.6 Hz, 1H), 1.10 (d, *J* = 6.8 Hz, 6H), 0.92 (d, *J* = 6.6 Hz, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.9, 148.5, 142.1, 140.4, 137.5, 130.5, 128.6, 128.0, 127.1, 126.8, 126.5, 124.2, 37.7, 36.9, 34.0, 29.0, 22.5, 22.1. **HRMS (ESI)**: m/z calculated for C₂₀H₂₆N₂ONa [M+Na]⁺: 333.1937, found: 333.1940. **IR (KBr)**: 3393, 3060, 1672, 1512, 1381, 1274, 1148, 833.

(Z)-N-(5-fluoro-2-isopropylpent-2-en-1-yl)isoquinoline-1-carboxamide (4f)

Yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ 9.65 – 9.58 (m, 1H), 8.45 (d, *J* = 5.6 Hz, 1H), 8.11 (br s, 1H), 7.86 – 7.80 (m, 1H), 7.77 (dd, *J* = 5.6, 0.9 Hz, 1H), 7.74 – 7.63 (m, 2H), 5.49 (t, *J* = 7.3 Hz, 1H), 4.50 (dt, *J* = 47.2, 6.2 Hz, 2H), 4.17 (d, *J* = 5.6 Hz, 2H), 2.61 (ddt, *J* = 25.4, 7.3, 6.2 Hz, 2H), 2.45 (hept, *J* = 7.0 Hz, 1H), 1.11 (d, *J* = 6.9 Hz, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.9, 148.4, 145.1, 140.4, 137.5, 130.5, 128.7, 127.9, 127.1, 126.9, 124.3, 121.4 (d, *J* = 6.1 Hz), 83.5 (d, *J* = 167.4 Hz), 37.6, 34.0, 29.4 (d, *J* = 20.4 Hz), 21.9. **¹⁹F NMR** (376 MHz, CDCl₃) δ -217.17. **HRMS (ESI)**: m/z calculated for

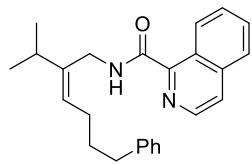
$C_{18}H_{21}N_2OFNa$ $[M+Na]^+$: 323.1530, found: 323.1536. **IR** (KBr): 3393, 3054, 1669, 1514, 1381, 1277, 1150, 1006, 878, 835.

*(Z)-N-(9-iodo-2-isopropylnon-2-en-1-yl)isoquinoline-1-carboxamide (**4g**)*



Yellow oil. **1H NMR** (400 MHz, $CDCl_3$) δ 9.68 – 9.61 (m, 1H), 8.46 (d, J = 5.5 Hz, 1H), 8.02 (br s, 1H), 7.88 – 7.81 (m, 1H), 7.79 (dd, J = 5.5, 0.9 Hz, 1H), 7.75 – 7.65 (m, 2H), 5.43 (t, J = 7.3 Hz, 1H), 4.14 (d, J = 5.4 Hz, 2H), 3.14 (t, J = 7.0 Hz, 2H), 2.40 (hept, J = 6.8 Hz, 1H), 2.17 (dt, J = 7.3, 7.2 Hz, 2H), 1.78 (tt, J = 7.2, 7.1 Hz, 2H), 1.46 – 1.28 (m, 6H), 1.09 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.9, 148.4, 141.7, 140.4, 137.5, 130.6, 128.7, 128.1, 127.5, 127.2, 126.9, 124.3, 37.7, 34.0, 33.6, 30.6, 29.9, 28.3, 27.9, 22.1, 7.3. **HRMS (ESI)**: m/z calculated for $C_{22}H_{29}N_2OINa$ $[M+Na]^+$: 487.1217, found: 487.1227. **IR** (KBr): 3390, 3052, 1670, 1511, 1379, 1274, 1274, 1148, 833.

*(Z)-N-(2-isopropyl-6-phenylhex-2-en-1-yl)isoquinoline-1-carboxamide (**4h**)*



Yellow oil. **1H NMR** (400 MHz, $CDCl_3$) δ 9.70 – 9.59 (m, 1H), 8.43 (d, J = 5.5 Hz, 1H), 8.02 (br s, 1H), 7.86 – 7.80 (m, 1H), 7.77 (dd, J = 5.5, 0.9 Hz, 1H), 7.73 – 7.65 (m, 2H), 7.26 – 7.19 (m, 2H), 7.18 – 7.10 (m, 3H), 5.46 (t, J = 7.3 Hz, 1H), 4.13 (d, J = 5.4 Hz, 2H), 2.69 – 2.57 (m, 2H), 2.42 (hept, J = 6.7 Hz, 1H), 2.22 (td, J = 7.4, 7.3 Hz, 2H), 1.80 – 1.67 (m, 2H), 1.09 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.9, 148.4, 142.5, 142.0, 140.4, 137.5, 130.5, 128.7, 128.5, 128.4, 128.1, 127.2, 126.8, 125.8, 124.3, 37.7, 35.6, 33.9, 31.8, 27.6, 22.1. **HRMS (ESI)**: m/z calculated for $C_{25}H_{28}N_2OONa$ $[M+Na]^+$: 395.2094, found: 395.2100. **IR** (KBr): 3394, 3060, 1671, 1512, 1380, 1275, 1149, 834, 743.

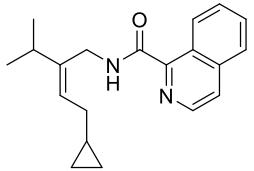
*(Z)-N-(2-isopropynona-2,8-dien-1-yl)isoquinoline-1-carboxamide (**4i**)*



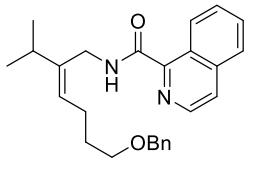
Yellow oil. **1H NMR** (400 MHz, $CDCl_3$) δ 9.68 – 9.60 (m, 1H), 8.44 (d, J = 5.5 Hz, 1H), 8.03 (br s, 1H), 7.86 – 7.80 (m, 1H), 7.79 – 7.75 (m, 1H), 7.73 – 7.64 (m, 2H), 5.78 (ddt, J = 16.9, 10.2,

6.7 Hz, 1H), 5.44 (t, J = 7.3 Hz, 1H), 4.98 (ddt, J = 16.9, 2.3, 1.6 Hz, 1H), 4.91 (ddt, J = 10.2, 2.3, 1.2 Hz, 1H), 4.15 (d, J = 5.4 Hz, 2H), 2.41 (hept, J = 6.8 Hz, 1H), 2.23 – 2.12 (m, 2H), 2.10 – 1.99 (m, 2H), 1.47 – 1.36 (m, 4H), 1.09 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (101 MHz, CDCl_3) δ 165.9, 148.4, 141.6, 140.4, 139.0, 137.5, 130.5, 128.6, 128.1, 127.5, 127.1, 126.8, 124.3, 114.4, 37.7, 34.0, 33.8, 29.6, 28.7, 27.8, 22.1. **HRMS (ESI)**: m/z calculated for $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}\text{Na}$ $[\text{M}+\text{Na}]^+$: 359.2094, found: 359.2094. **IR (KBr)**: 3393, 3065, 1672, 1512, 1380, 1274, 1149, 909, 834, 742.

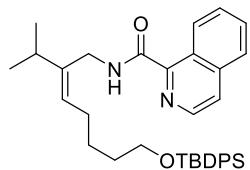
(Z)-*N*-(4-cyclopropyl-2-isopropylbut-2-en-1-yl)isoquinoline-1-carboxamide (4j**)**

 Yellow oil. **^1H NMR** (400 MHz, CDCl_3) δ 9.67 – 9.60 (m, 1H), 8.43 (d, J = 5.5 Hz, 1H), 8.03 (br s, 1H), 7.85 – 7.79 (m, 1H), 7.76 (ddd, J = 5.5, 1.0, 0.4 Hz, 1H), 7.73 – 7.64 (m, 2H), 5.54 (t, J = 7.3 Hz, 1H), 4.13 (d, J = 5.4 Hz, 2H), 2.43 (hept, J = 6.9 Hz, 1H), 2.11 (dd, J = 7.0, 6.9 Hz, 2H), 1.10 (d, J = 6.9 Hz, 6H), 0.83 – 0.72 (m, 1H), 0.50 – 0.39 (m, 2H), 0.16 – 0.08 (m, 2H). **^{13}C NMR** (101 MHz, CDCl_3) δ 165.8, 148.4, 141.6, 140.4, 137.5, 130.5, 128.6, 128.0, 127.1, 126.8, 126.6, 124.3, 37.7, 34.0, 32.5, 22.0, 11.2, 4.3. **HRMS (ESI)**: m/z calculated for $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}\text{Na}$ $[\text{M}+\text{Na}]^+$: 331.1781, found: 331.1790. **IR (KBr)**: 3390, 3075, 1671, 1511, 1380, 1275, 1149, 1016, 833, 741.

(Z)-*N*-(6-(benzyloxy)-2-isopropylhex-2-en-1-yl)isoquinoline-1-carboxamide (4k**)**

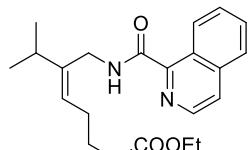
 Orange oil. **^1H NMR** (400 MHz, CDCl_3) δ 9.66 – 9.58 (m, 1H), 8.42 (d, J = 5.5 Hz, 1H), 8.04 (br s, 1H), 7.85 – 7.79 (m, 1H), 7.76 (dd, J = 5.5, 0.9 Hz, 1H), 7.73 – 7.64 (m, 2H), 7.34 – 7.21 (m, 5H), 5.43 (t, J = 7.3 Hz, 1H), 4.47 (s, 2H), 4.16 (d, J = 5.5 Hz, 2H), 3.49 (t, J = 6.5 Hz, 2H), 2.41 (hept, J = 6.8 Hz, 1H), 2.28 (td, J = 7.4, 7.3 Hz, 2H), 1.73 (tt, J = 7.4, 6.5 Hz, 2H), 1.08 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (101 MHz, CDCl_3) δ 165.9, 148.5, 142.2, 140.4, 138.6, 137.5, 130.5, 128.6, 128.4, 128.0, 127.7, 127.6, 127.1, 126.8, 126.8, 124.2, 72.9, 69.7, 37.6, 33.8, 30.0, 24.5, 22.1. **HRMS (ESI)**: m/z calculated for $\text{C}_{26}\text{H}_{30}\text{N}_2\text{O}_2\text{Na}$ $[\text{M}+\text{Na}]^+$: 425.2199, found: 425.2206. **IR (KBr)**: 3392, 3055, 1670, 1512, 1379, 1275, 1148, 1103, 834, 741.

(Z)-N-(7-((tert-butyldiphenylsilyl)oxy)-2-isopropylhept-2-en-1-yl)isoquinoline-1-carboxamide (4l)



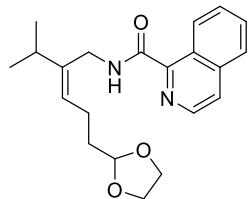
Yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ 9.68 – 9.61 (m, 1H), 8.40 (d, *J* = 5.5 Hz, 1H), 8.01 (br s, 1H), 7.84 – 7.79 (m, 1H), 7.74 (dd, *J* = 5.6, 0.9 Hz, 1H), 7.72 – 7.63 (m, 6H), 7.44 – 7.32 (m, 6H), 5.42 (t, *J* = 7.2 Hz, 1H), 4.13 (d, *J* = 5.4 Hz, 2H), 3.67 (t, *J* = 6.3 Hz, 2H), 2.41 (hept, *J* = 6.8 Hz, 1H), 2.16 (dt, *J* = 7.2, 7.2 Hz, 2H), 1.65 – 1.54 (m, 2H), 1.54 – 1.43 (m, 2H), 1.08 (d, *J* = 6.8 Hz, 6H), 1.04 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.9, 148.4, 141.7, 140.4, 137.5, 135.7, 134.2, 130.5, 129.6, 128.6, 128.1, 127.7, 127.5, 127.1, 126.8, 124.3, 64.0, 37.7, 33.9, 32.4, 27.6, 27.0, 26.3, 22.1, 19.3. **HRMS (ESI)**: m/z calculated for C₃₆H₄₄N₂O₂SiNa [M+Na]⁺: 587.3064, found: 587.3069. **IR (KBr)**: 3393, 3052, 1672, 1511, 1381, 1274, 1111, 825, 741, 703.

ethyl (Z)-6-((isoquinoline-1-carboxamido)methyl)-7-methyloct-5-enoate (4m)



Brown oil. **¹H NMR** (400 MHz, CDCl₃) δ 9.62 (ddd, *J* = 7.8, 2.1, 0.8 Hz, 1H), 8.45 (d, *J* = 5.5 Hz, 1H), 8.05 (s, 1H), 7.87 – 7.81 (m, 1H), 7.78 (dd, *J* = 5.6, 0.9 Hz, 1H), 7.74 – 7.64 (m, 2H), 5.42 (t, *J* = 7.3 Hz, 1H), 4.17 – 4.07 (m, 4H), 2.42 (hept, *J* = 6.8 Hz, 1H), 2.33 (t, *J* = 7.6 Hz, 2H), 2.23 (td, *J* = 7.4, 7.3 Hz, 2H), 1.75 (tt, *J* = 7.6, 7.4 Hz, 2H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.09 (d, *J* = 6.8 Hz, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 173.7, 165.9, 148.4, 142.7, 140.4, 137.5, 130.5, 128.7, 128.0, 127.1, 126.8, 126.3, 124.3, 60.4, 37.7, 33.9, 33.8, 27.3, 25.3, 22.0, 14.4. **HRMS (ESI)**: m/z calculated for C₂₂H₂₈N₂O₃Na [M+Na]⁺: 391.1992, found: 391.1995. **IR (KBr)**: 3391, 3056, 1732, 1671, 1513, 1377, 1346, 1276, 1249, 1151, 1033, 880, 835, 743.

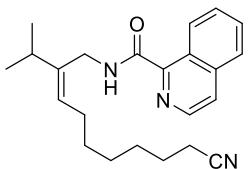
(Z)-N-(5-(1,3-dioxolan-2-yl)-2-isopropylpent-2-en-1-yl)isoquinoline-1-carboxamide (4n)



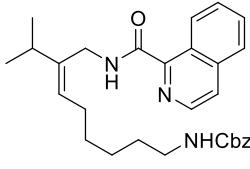
Yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ 9.63 – 9.55 (m, 1H), 8.44 (d, *J* = 5.5 Hz, 1H), 8.08 (br s, 1H), 7.87 – 7.80 (m, 1H), 7.77 (dd, *J* = 5.6, 0.9 Hz, 1H), 7.74 – 7.63 (m, 2H), 5.45 (t, *J* = 7.4 Hz, 1H), 4.88 (t, *J* = 4.9 Hz, 1H), 4.18 (d, *J* = 5.6 Hz, 2H), 3.97 –

3.87 (m, 2H), 3.85 – 3.75 (m, 2H), 2.43 (hept, $J = 6.9$ Hz, 1H), 2.33 (td, $J = 7.5, 7.4$ Hz, 2H), 1.78 (td, $J = 7.5, 4.9$ Hz, 2H), 1.09 (d, $J = 6.9$ Hz, 6H). **^{13}C NMR** (101 MHz, CDCl_3) δ 165.9, 148.8, 142.4, 140.4, 137.4, 130.5, 128.6, 128.0, 127.1, 126.8, 126.2, 124.2, 104.0, 65.0, 37.5, 34.0, 33.8, 22.7, 22.0. **HRMS (ESI)**: m/z calculated for $\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$: 377.1836, found: 377.1835. **IR (KBr)**: 3396, 3050, 1669, 1513, 1276, 1145, 1054, 835.

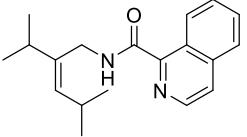
(Z)-N-(9-cyano-2-isopropylnon-2-en-1-yl)isoquinoline-1-carboxamide (4o)

 Brown oil. **^1H NMR** (400 MHz, CDCl_3) δ 9.68 – 9.61 (m, 1H), 8.45 (d, $J = 5.5$ Hz, 1H), 8.03 (br s, 1H), 7.88 – 7.82 (m, 1H), 7.79 (dd, $J = 5.5, 0.9$ Hz, 1H), 7.76 – 7.64 (m, 2H), 5.42 (t, $J = 7.3$ Hz, 1H), 4.14 (d, $J = 5.4$ Hz, 2H), 2.42 (hept, $J = 6.8$ Hz, 1H), 2.28 (t, $J = 7.2$ Hz, 2H), 2.17 (dt, $J = 7.3, 7.2$ Hz, 2H), 1.66 – 1.57 (m, 2H), 1.47 – 1.29 (m, 6H), 1.09 (d, $J = 6.8$ Hz, 6H). **^{13}C NMR** (101 MHz, CDCl_3) δ 165.8, 148.4, 141.9, 140.4, 137.5, 130.6, 128.7, 128.0, 127.3, 127.2, 126.9, 124.4, 119.9, 37.7, 34.0, 29.8, 28.7, 28.6, 27.8, 25.5, 22.1, 17.2. **HRMS (ESI)**: m/z calculated for $\text{C}_{23}\text{H}_{29}\text{N}_3\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$: 386.2203, found: 386.2210. **IR (KBr)**: 3394, 3056, 2245, 1669, 1513, 1380, 1276, 1149, 836.

benzyl **(Z)-(7-((isoquinoline-1-carboxamido)methyl)-8-methylnon-6-en-1-yl)carbamate (4p)**

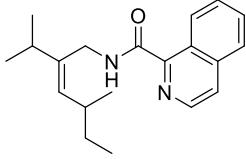
 Yellow oil. **^1H NMR** (400 MHz, CDCl_3) δ 9.69 – 9.58 (m, 1H), 8.44 (d, $J = 5.5$ Hz, 1H), 8.02 (br s, 1H), 7.85 – 7.81 (m, 1H), 7.76 (dd, $J = 5.5, 0.9$ Hz, 1H), 7.73 – 7.64 (m, 2H), 7.37 – 7.27 (m, 5H), 5.41 (t, $J = 7.3$ Hz, 1H), 5.07 (s, 2H), 4.79 (br s, 1H), 4.13 (d, $J = 5.4$ Hz, 2H), 3.16 (q, $J = 6.7$ Hz, 2H), 2.41 (hept, $J = 6.8$ Hz, 1H), 2.16 (dt, $J = 7.3, 7.3$ Hz, 2H), 1.56 – 1.28 (m, 6H), 1.08 (d, $J = 6.8$ Hz, 6H). **^{13}C NMR** (101 MHz, CDCl_3) δ 165.9, 156.5, 148.4, 141.8, 140.4, 137.5, 136.8, 130.6, 128.7, 128.6, 128.2, 128.2, 128.0, 127.3, 127.1, 126.9, 124.3, 66.7, 41.1, 37.7, 34.0, 30.0, 29.6, 27.8, 26.5, 22.1. **HRMS (ESI)**: m/z calculated for $\text{C}_{29}\text{H}_{35}\text{N}_3\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$: 496.2571, found: 496.2571. **IR (KBr)**: 3333, 3065, 1720, 1666, 1514, 1455, 1379, 1250, 1146, 1026, 834, 742.

(Z)-N-(2-isopropyl-4-methylpent-2-en-1-yl)isoquinoline-1-carboxamide (4q)



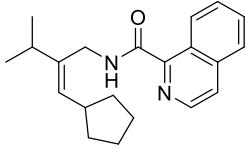
Yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ 9.68 – 9.62 (m, 1H), 8.45 (d, *J* = 5.5 Hz, 1H), 8.03 (br s, 1H), 7.87 – 7.80 (m, 1H), 7.77 (dd, *J* = 5.5, 0.9 Hz, 1H), 7.74 – 7.64 (m, 2H), 5.25 (dd, *J* = 9.6, 1.1 Hz, 1H), 4.15 (d, *J* = 5.4 Hz, 2H), 2.70 (dhept, *J* = 9.6, 6.6 Hz, 1H), 2.38 (heptd, *J* = 6.8, 1.1 Hz, 1H), 1.08 (d, *J* = 6.8 Hz, 6H), 1.00 (d, *J* = 6.6 Hz, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.8, 148.5, 140.4, 139.1, 137.5, 135.3, 130.5, 128.7, 128.1, 127.2, 126.8, 124.3, 37.8, 33.7, 27.2, 23.7, 22.1. **HRMS (ESI)**: m/z calculated for C₁₉H₂₄N₂ONa [M+Na]⁺: 319.1781, found: 319.1784. **IR (KBr)**: 3386, 3060, 1657, 1521, 1460, 1381, 1280, 1157, 974, 876, 833.

(Z)-N-(2-isopropyl-4-methylhex-2-en-1-yl)isoquinoline-1-carboxamide (4r)



Yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ 9.68 – 9.61 (m, 1H), 8.45 (d, *J* = 5.5 Hz, 1H), 8.03 (br s, 1H), 7.87 – 7.81 (m, 1H), 7.77 (dd, *J* = 5.6, 0.9 Hz, 1H), 7.74 – 7.64 (m, 2H), 5.18 (dd, *J* = 10.0, 1.0 Hz, 1H), 4.21 – 4.06 (m, 2H), 2.52 – 2.32 (m, 2H), 1.39 (dqd, *J* = 12.9, 7.4, 5.4 Hz, 1H), 1.31 – 1.19 (m, 1H), 1.09 (d, *J* = 6.9 Hz, 6H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.9, 148.5, 140.4, 140.3, 137.5, 134.0, 130.5, 128.7, 128.1, 127.2, 126.9, 124.3, 38.0, 34.1, 33.9, 30.6, 22.2, 22.1, 21.5, 12.2. **HRMS (ESI)**: m/z calculated for C₂₀H₂₆N₂ONa [M+Na]⁺: 333.1937, found: 333.1944. **IR (KBr)**: 3394, 3065, 1672, 1512, 1379, 1274, 1148, 833.

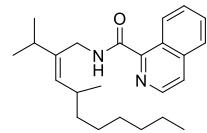
(Z)-N-(2-(cyclopentylmethylene)-3-methylbutyl)isoquinoline-1-carboxamide (4s)



Yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ 9.68 – 9.59 (m, 1H), 8.45 (d, *J* = 5.5 Hz, 1H), 8.02 (br s, 1H), 7.87 – 7.79 (m, 1H), 7.77 (dd, *J* = 5.6, 0.9 Hz, 1H), 7.74 – 7.63 (m, 2H), 5.35 (dd, *J* = 9.4, 1.0 Hz, 1H), 4.16 (d, *J* = 5.3 Hz, 2H), 2.84 – 2.70 (m, 1H), 2.39 (heptd, *J* = 6.8, 1.0 Hz, 1H), 1.91 – 1.77 (m, 2H), 1.73 – 1.48 (m, 4H), 1.34 – 1.18 (m, 2H), 1.08 (d, *J* = 6.8 Hz, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 165.8, 148.5, 140.4, 140.1, 137.5, 133.2, 130.5, 128.6, 128.0, 127.1, 126.8, 124.2, 38.8, 38.0, 34.3, 33.9, 25.6, 22.0. **HRMS (ESI)**: m/z calculated for C₂₁H₂₆N₂ONa [M+Na]⁺: 323.2118, found: 345.1942. **IR (KBr)**: 3392,

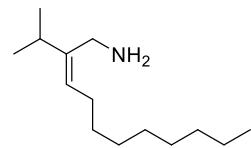
3060, 1671, 1511, 1379, 1148, 833, 742.

(Z)-N-(2-isopropyl-4-methyldec-2-en-1-yl)isoquinoline-1-carboxamide (4u)



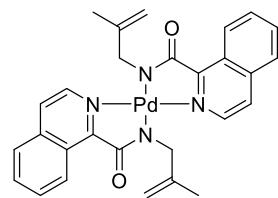
Yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ 9.74 – 9.61 (m, 1H), 8.44 (d, *J* = 5.3 Hz, 1H), 8.04 (br s, 1H), 7.87 – 7.80 (m, 1H), 7.77 (d, *J* = 5.3 Hz, 1H), 7.74 – 7.64 (m, 2H), 5.18 (d, *J* = 9.9 Hz, 1H), 4.13 (dd, *J* = 5.3, 2.0 Hz, 2H), 2.57 – 2.45 (m, 1H), 2.40 (heptd, *J* = 6.7 Hz, 1H), 1.38 – 1.16 (m, 10H), 1.09 (d, *J* = 6.8 Hz, 6H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.91 – 0.76 (m, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 164.2, 146.8, 138.9, 138.3, 136.0, 132.9, 129.0, 127.1, 126.5, 125.6, 125.4, 122.8, 36.4, 36.4, 32.4, 31.0, 30.5, 28.1, 26.3, 21.2, 20.7, 20.4, 12.7. **HRMS (ESI)**: m/z calculated for C₂₄H₃₄N₂ONa [M+Na]⁺: 389.2563, found: 389.2572. **IR (KBr)**: 3394, 3054, 1672, 1511, 1379, 1148, 833, 741.

(Z)-2-isopropylundec-2-en-1-amine (5)



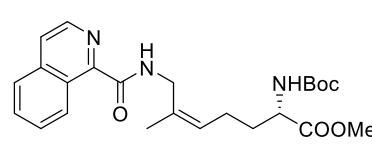
Yellow oil. **¹H NMR** (400 MHz, CDCl₃) δ 5.25 (t, *J* = 7.2 Hz, 1H), 3.29 (br s, 2H), 2.72 (s, 2H), 2.37 (hept, *J* = 6.9 Hz, 1H), 2.06 (dt, *J* = 7.2, 7.1 Hz, 2H), 1.35 – 1.24 (m, 12H), 1.03 (d, *J* = 6.9 Hz, 6H), 0.91 – 0.86 (m, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 145.0, 125.5, 39.7, 33.1, 32.0, 30.2, 29.6, 29.4, 29.4, 27.7, 22.8, 22.3, 14.2. **HRMS (ESI)**: m/z calculated for C₁₄H₃₀N [M+H]⁺: 212.2373, found: 212.2377. **IR (KBr)**: 3290, 1649, 1553, 1466, 1379, 722.

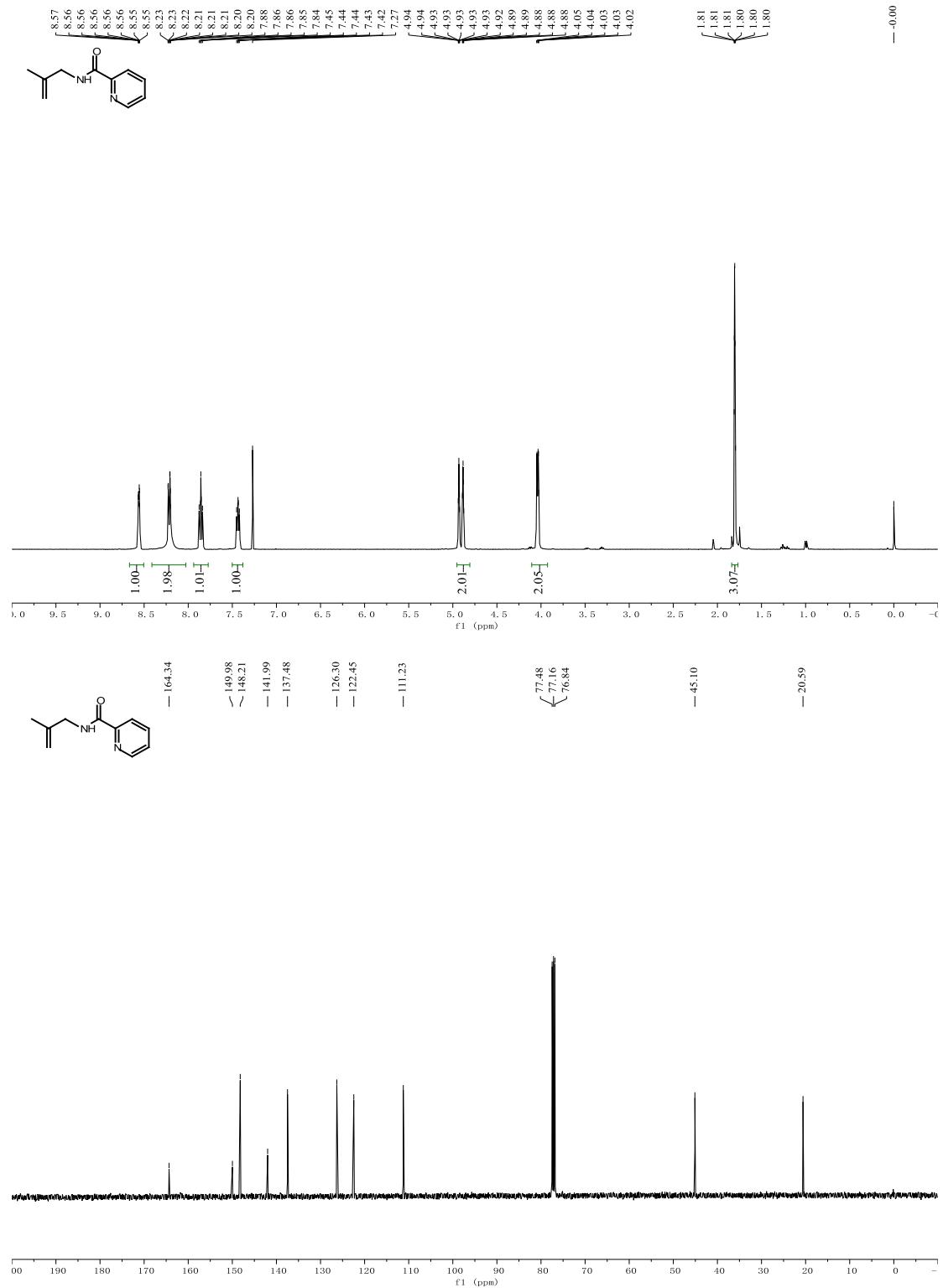
Palladium(II) complex (6)

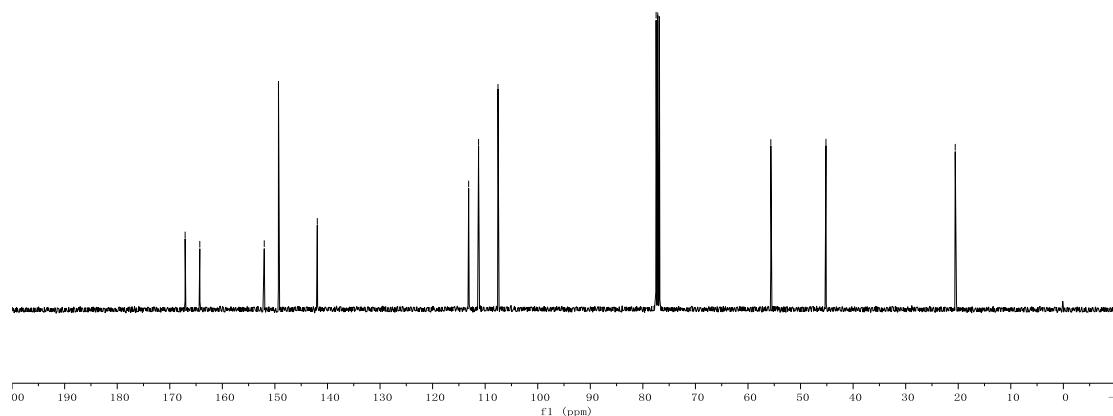
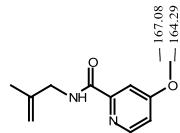
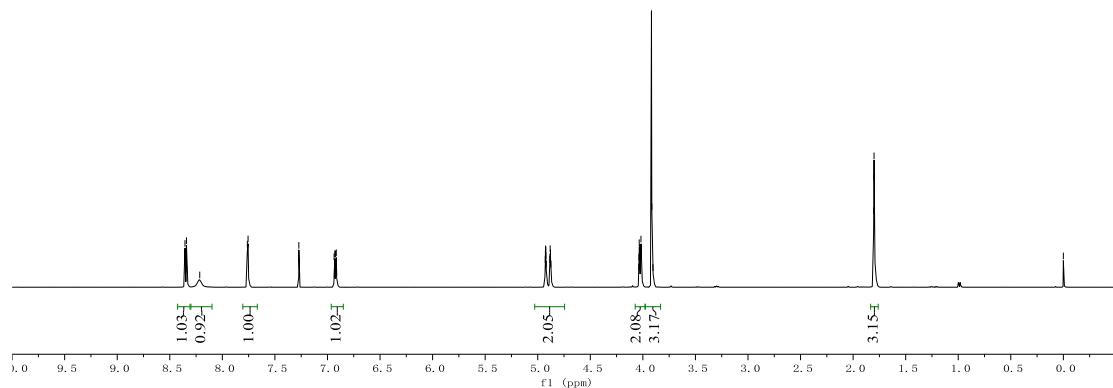
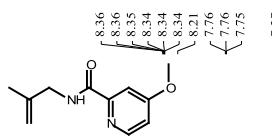


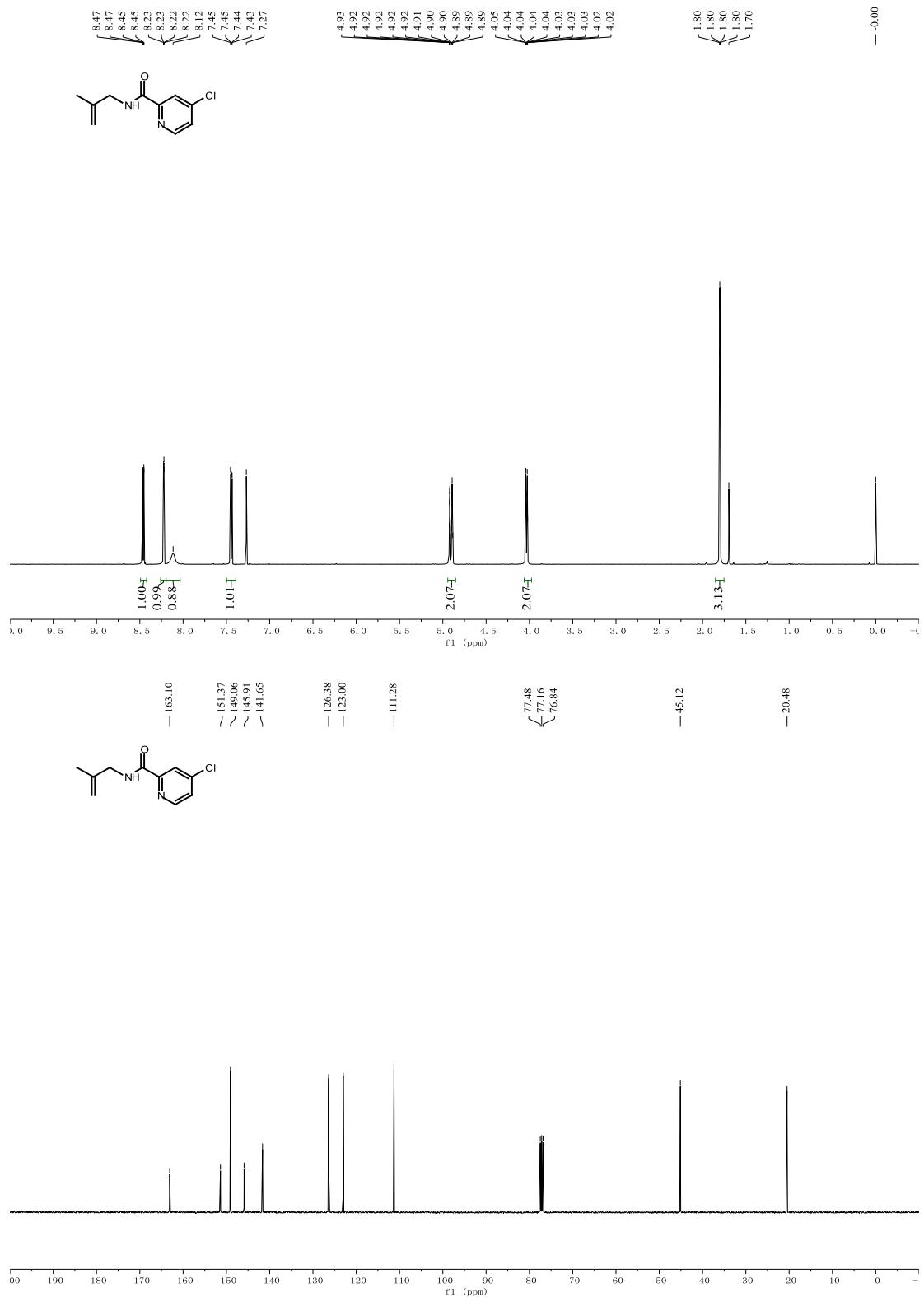
Yellow solid. **¹H NMR** (400 MHz, CDCl₃) δ 10.21 (dd, *J* = 8.7, 1.2 Hz, 2H), 8.40 (d, *J* = 6.4 Hz, 2H), 7.89 – 7.81 (m, 4H), 7.80 – 7.72 (m, 4H), 5.20 – 5.09 (m, 2H), 5.00 – 4.95 (m, 2H), 4.07 (s, 4H), 1.92 (s, 6H). **¹³C NMR** (101 MHz, CDCl₃) δ 173.7, 154.0, 144.0, 141.1, 137.7, 132.9, 129.4, 128.2, 128.1, 126.3, 124.4, 109.6, 53.3, 20.9. **HRMS (ESI)**: m/z calculated for C₂₈H₂₇N₄O₂Pd [M+H]⁺: 557.1163, found: 557.1180. **IR (KBr)**: 3437, 3082, 1601, 1363, 1337, 1268, 1160, 1021, 892, 830, 755.

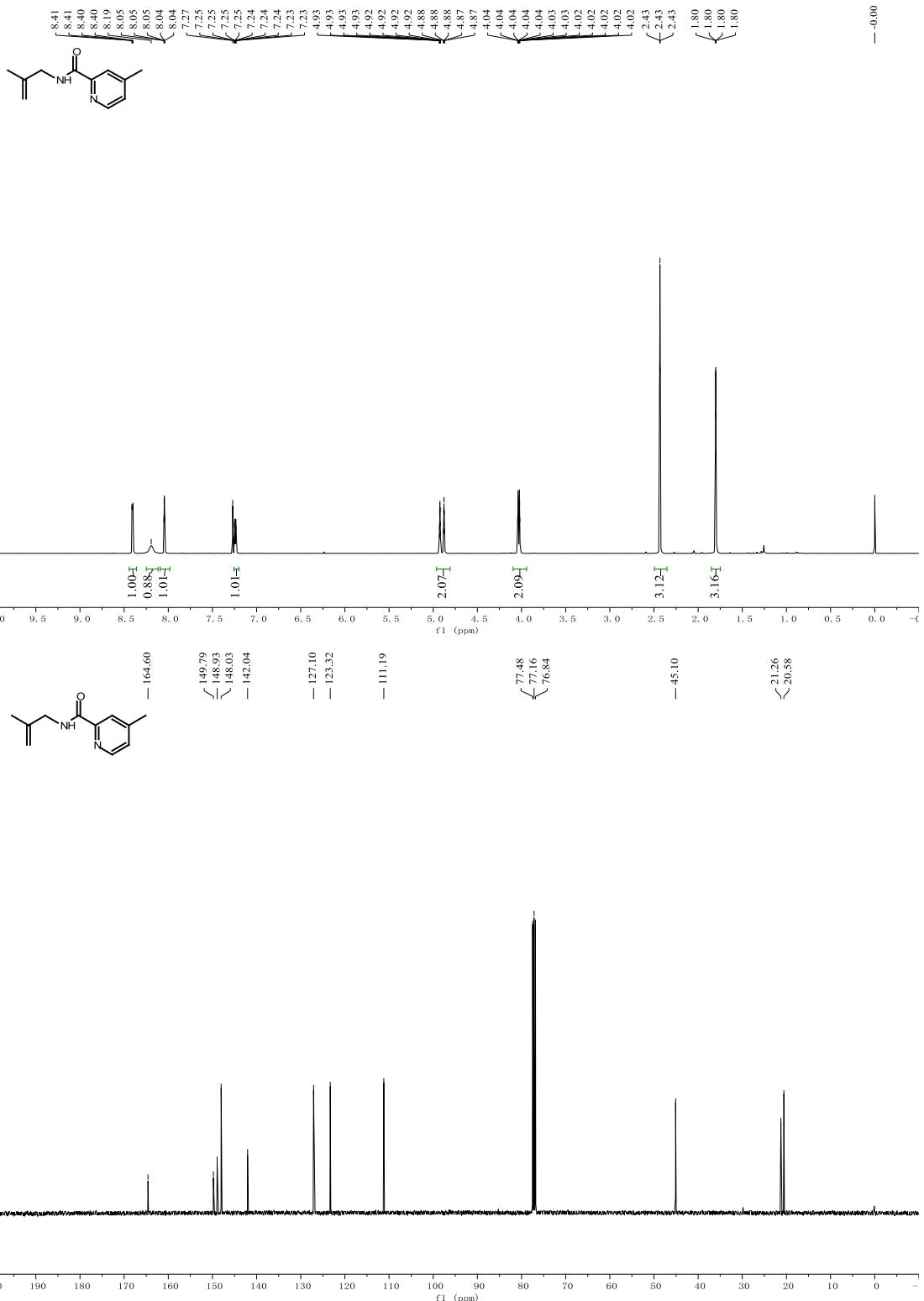
methyl (S,Z)-2-((tert-butoxycarbonyl)amino)-7-(isoquinoline-1-carboxamido)-6-methylhept-5-enoate (**3at**)

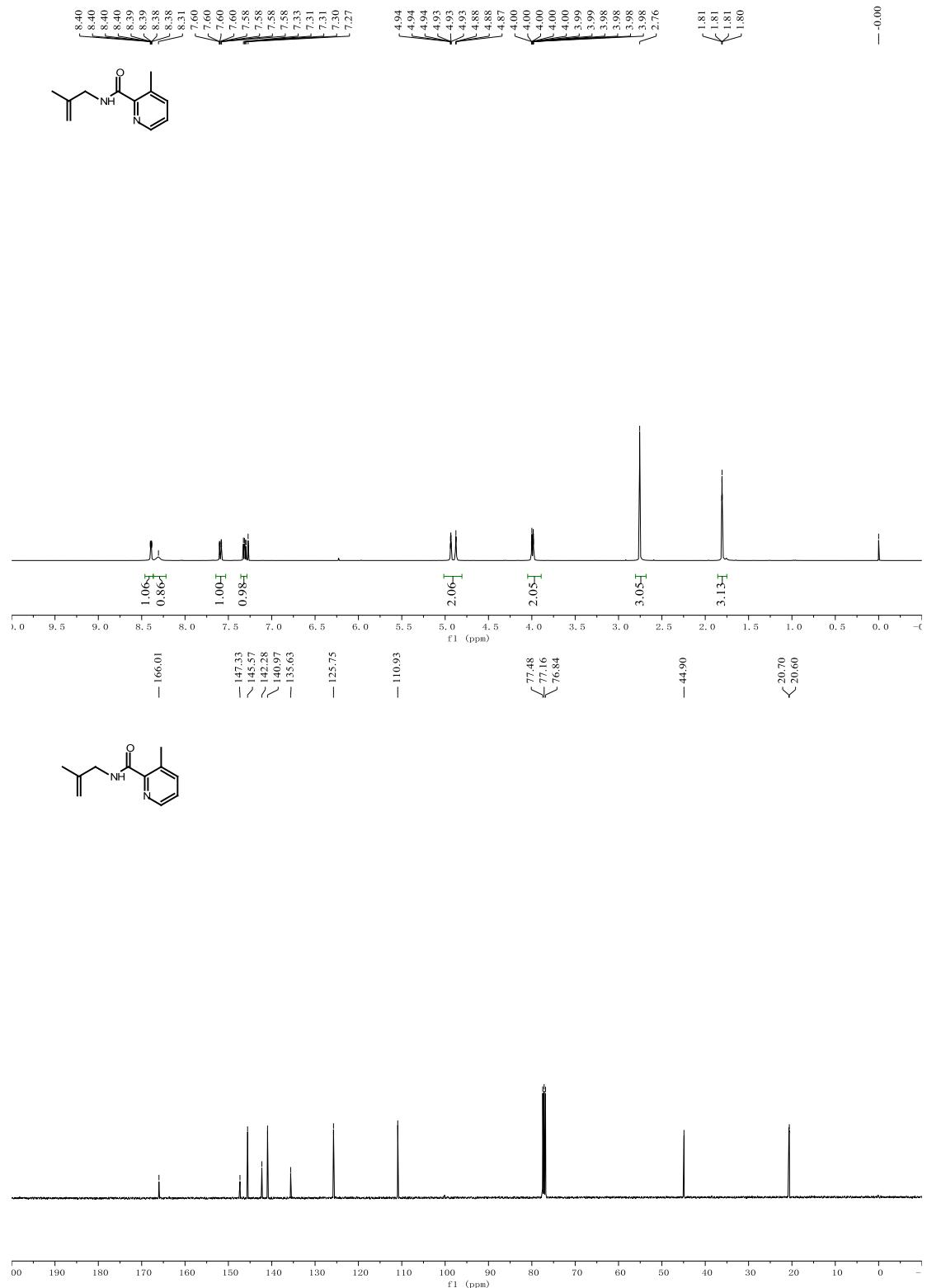
 Yellow oil. **1H NMR** (400 MHz, CDCl₃) δ 9.60 (d, *J* = 8.4 Hz, 1H), 8.47 (d, *J* = 5.5 Hz, 1H), 8.27 (br s, 1H), 7.90 – 7.77 (m, 2H), 7.77 – 7.62 (m, 2H), 5.40 – 5.27 (m, 2H), 4.34 (br s, 1H), 4.24 – 4.15 (m, 1H), 4.11 – 3.99 (m, 1H), 3.73 (s, 3H), 2.27 (dt, *J* = 7.6, 7.6 Hz, 2H), 1.99 – 1.89 (m, 1H), 1.82 (s, 3H), 1.82 – 1.69 (m, 1H), 1.42 (s, 9H). **13C NMR** (101 MHz, CDCl₃) δ 173.5, 166.3, 155.7, 148.6, 140.4, 137.5, 133.5, 130.6, 128.7, 128.0, 127.3, 127.2, 126.9, 124.4, 80.0, 53.1, 52.4, 39.8, 32.9, 28.4, 23.9, 22.3. **HRMS (ESI)**: m/z calculated for C₂₄H₃₁N₃O₅ [M+Na]⁺: 464.2156, found: 464.2170. **IR (KBr)**: 3369, 3054, 1712, 1664, 1517, 1451, 1367, 1165, 1052, 836, 745.

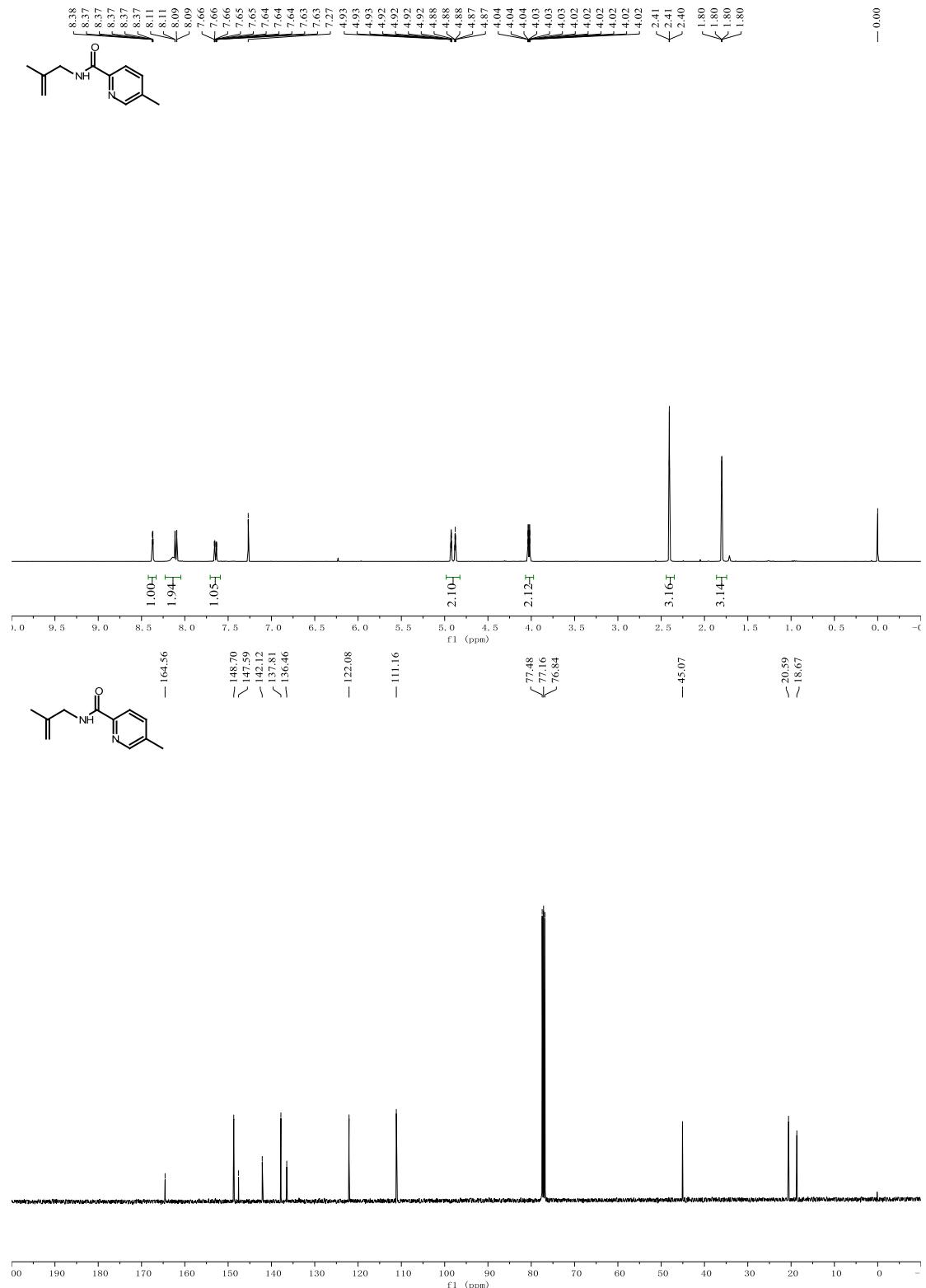


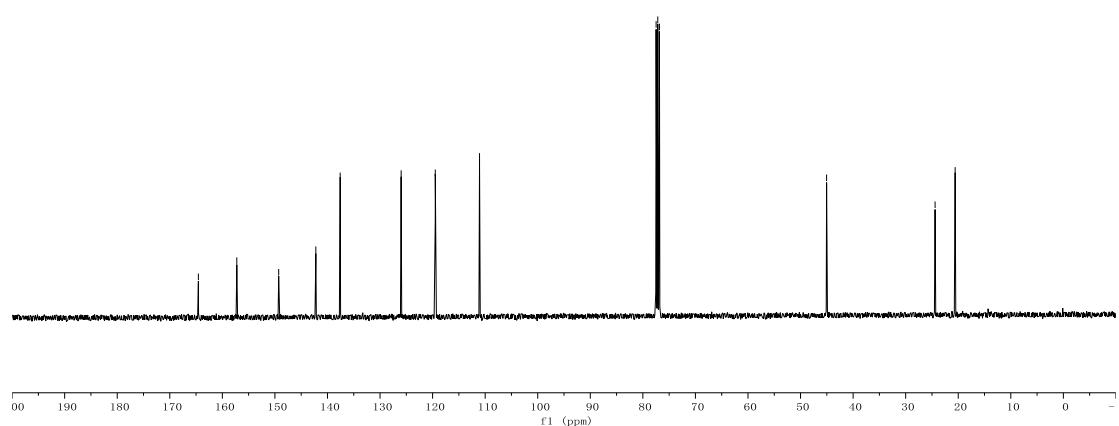
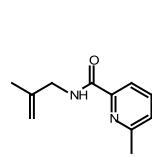
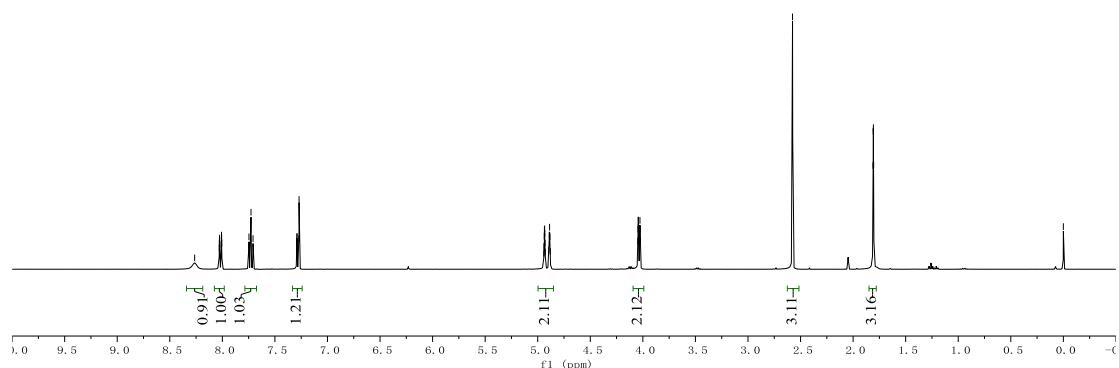
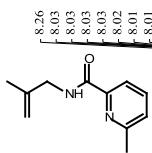


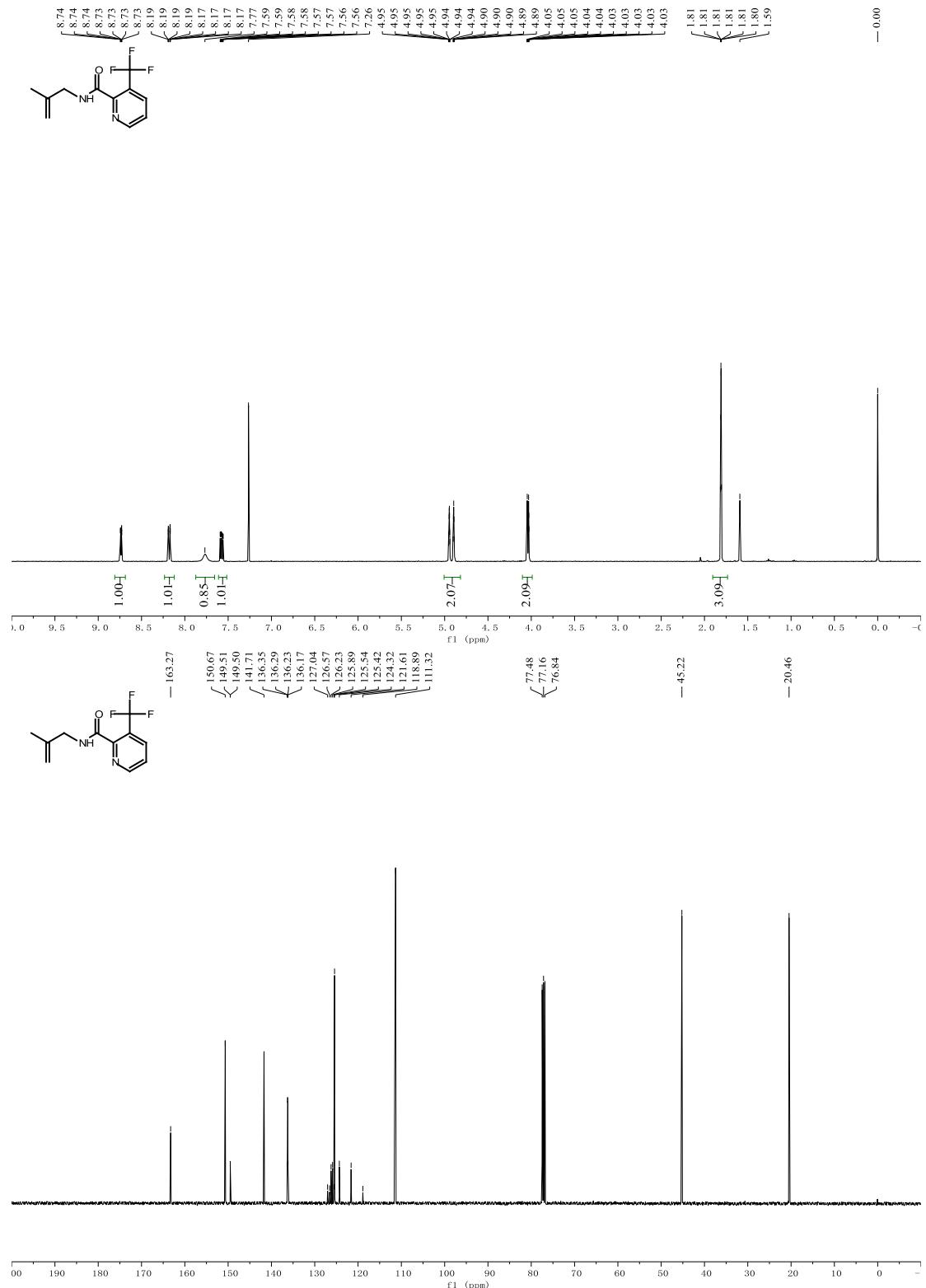


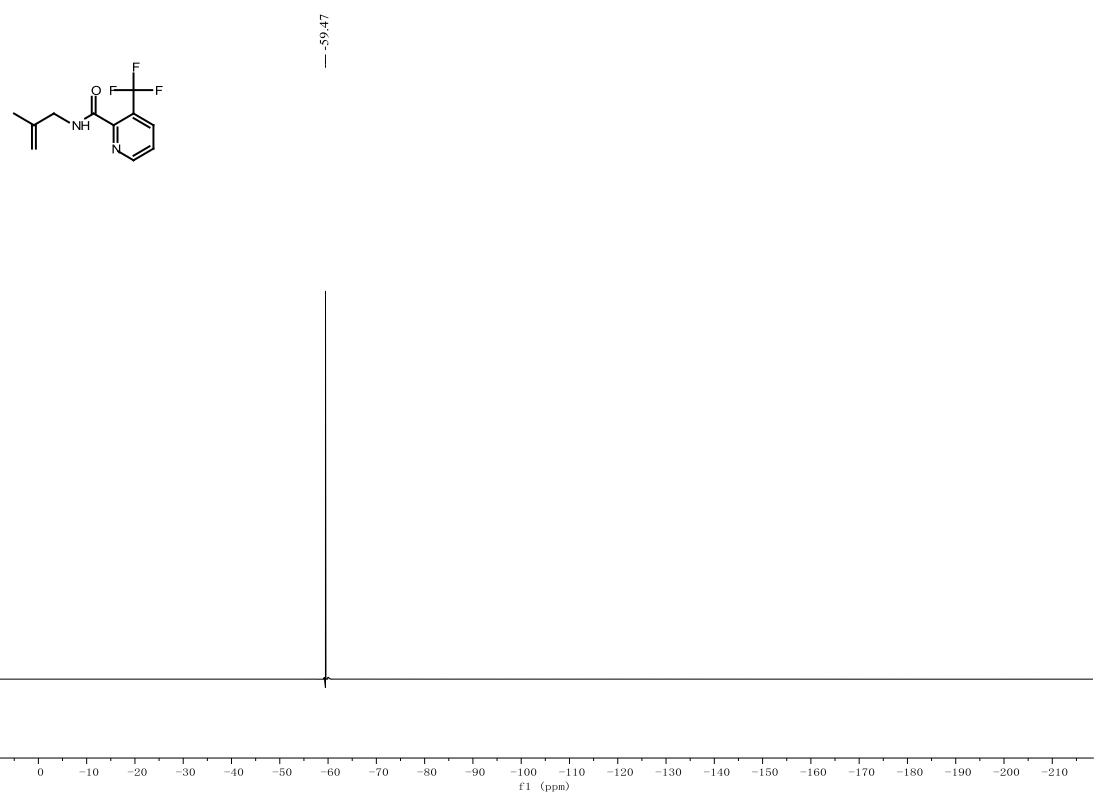


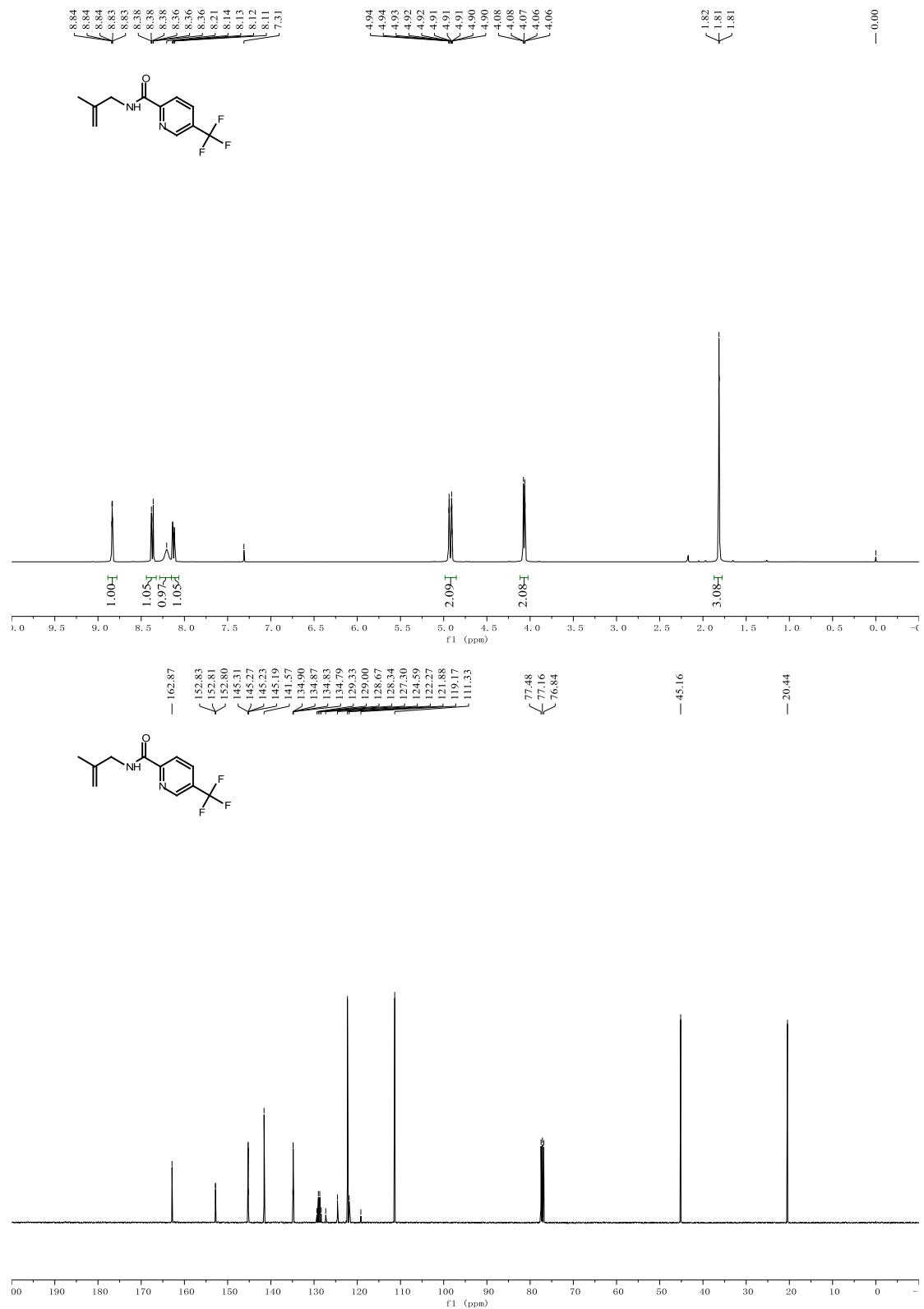


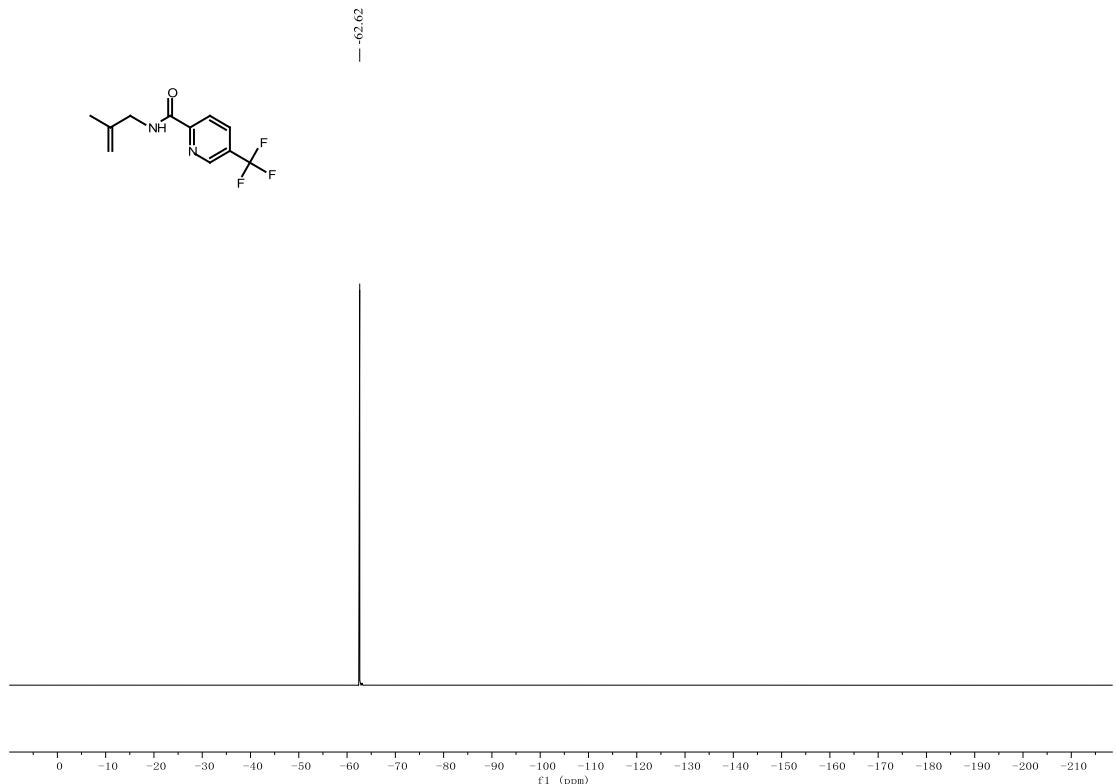


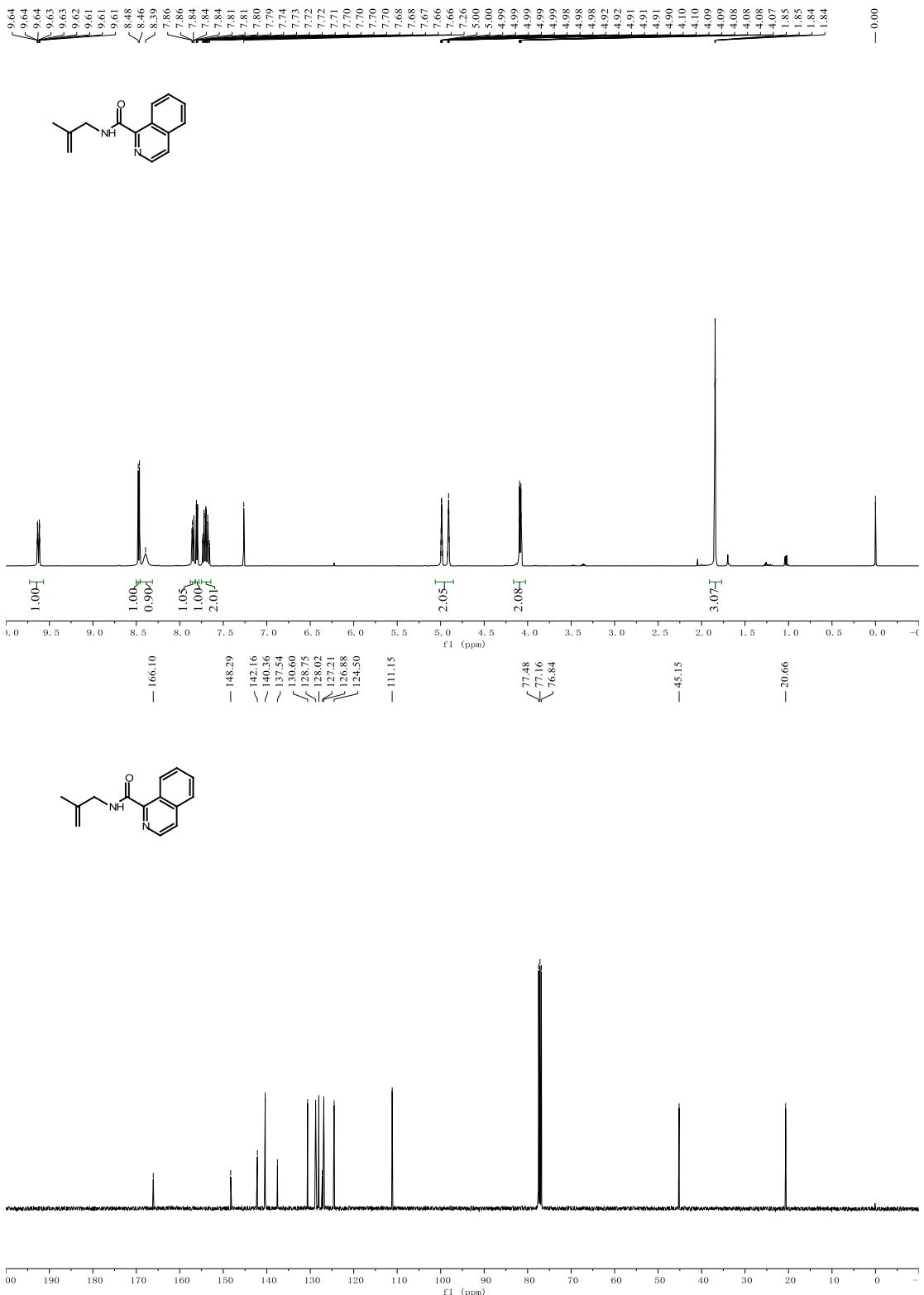


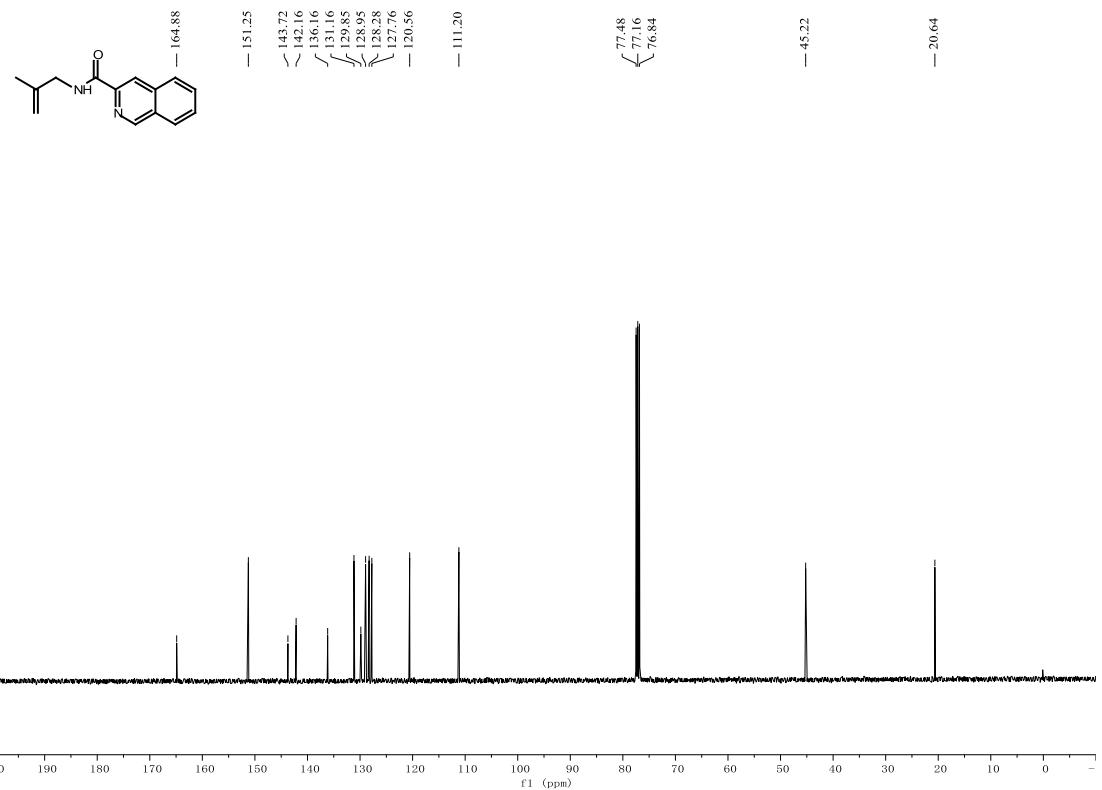
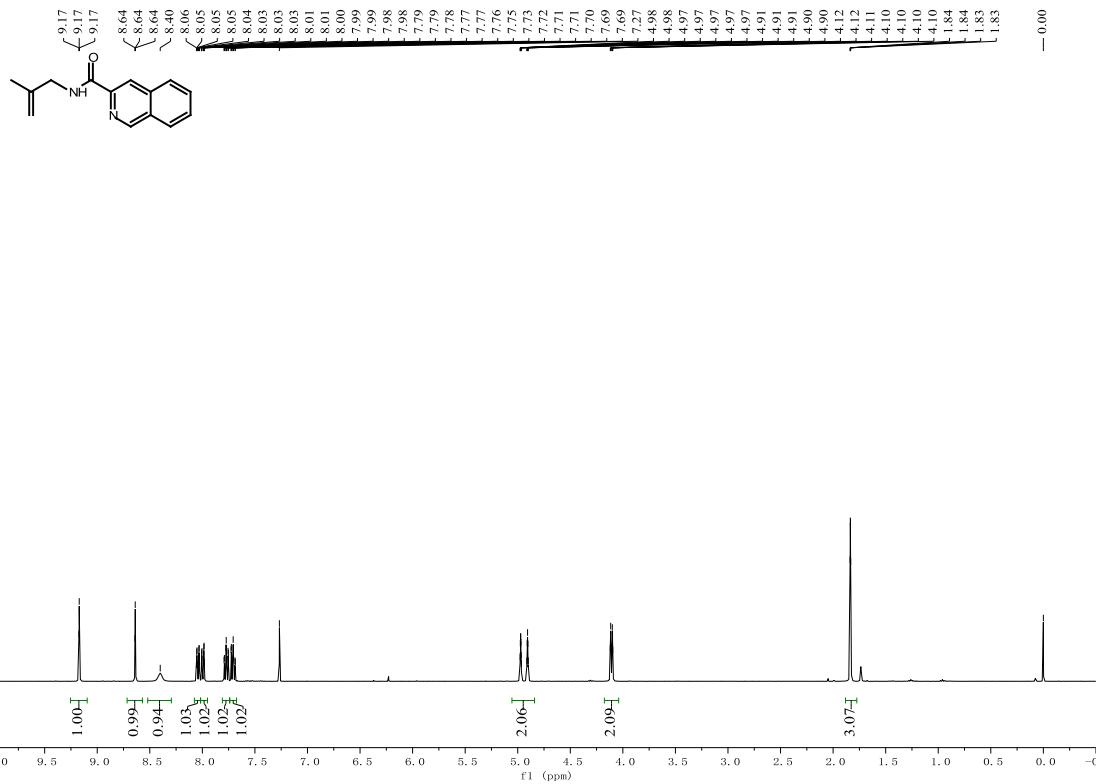


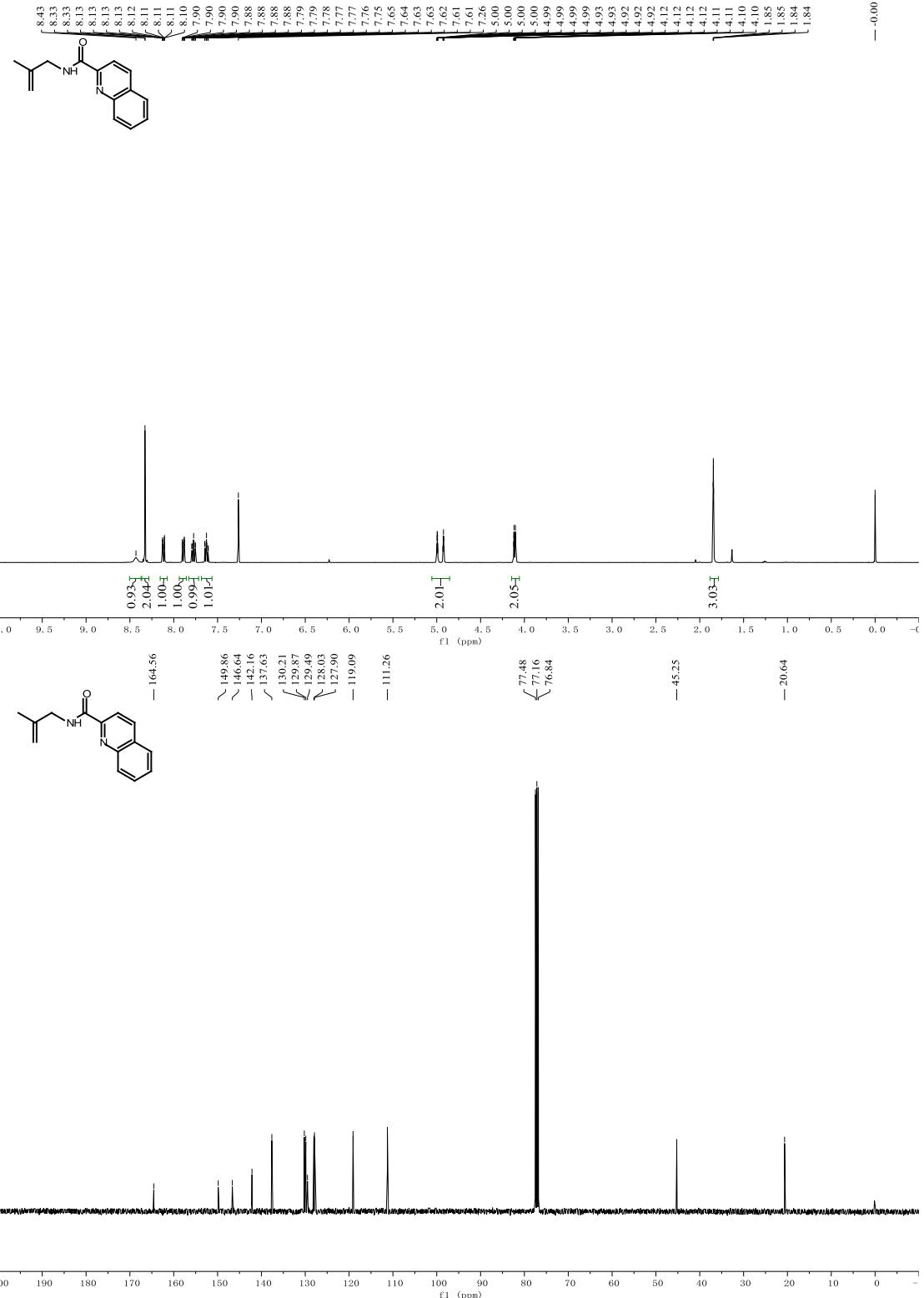


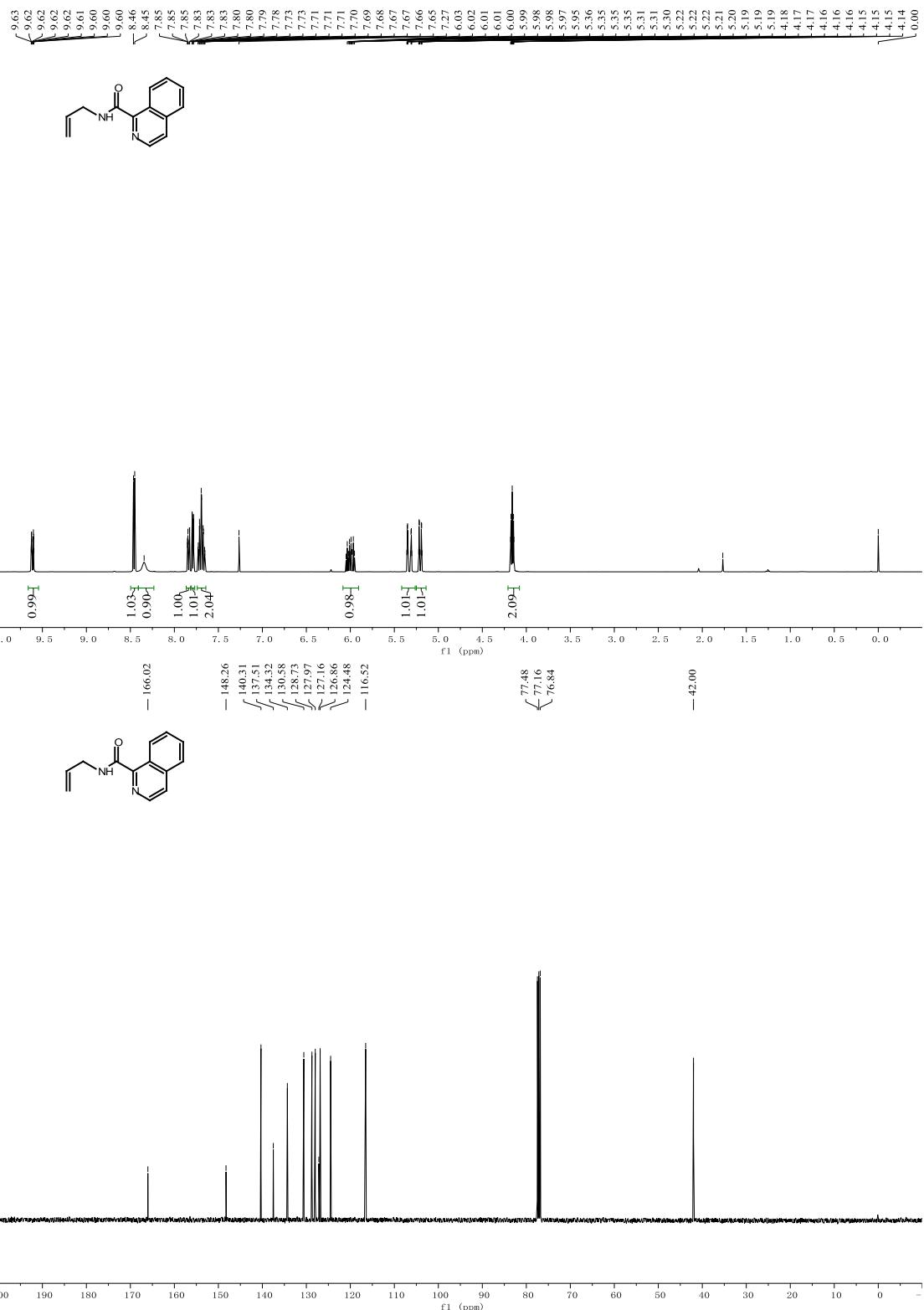


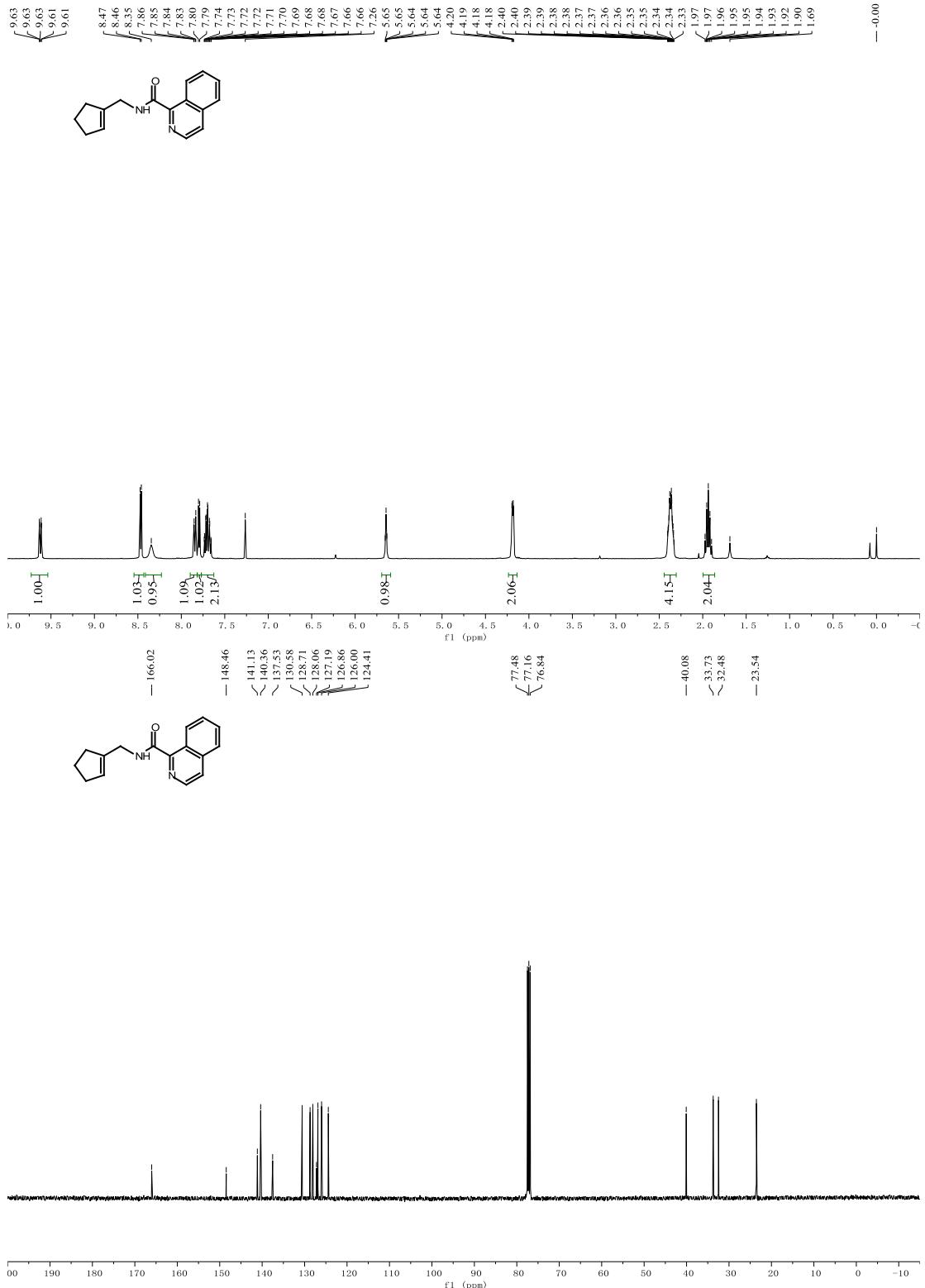


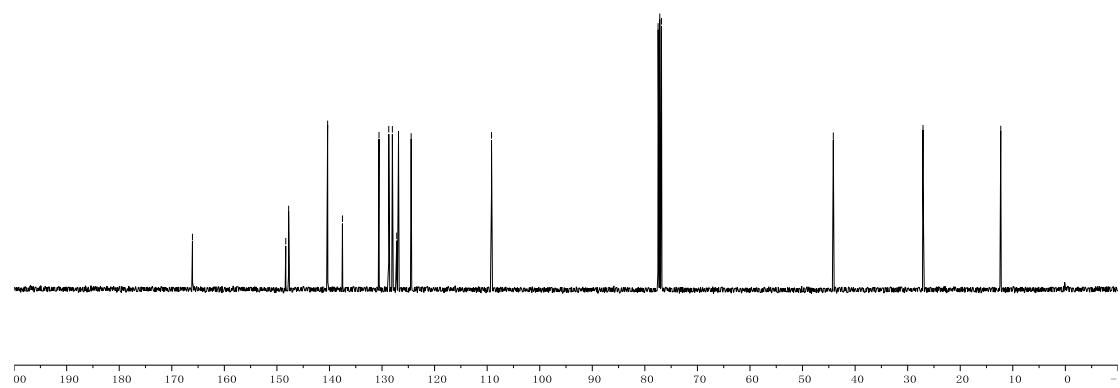
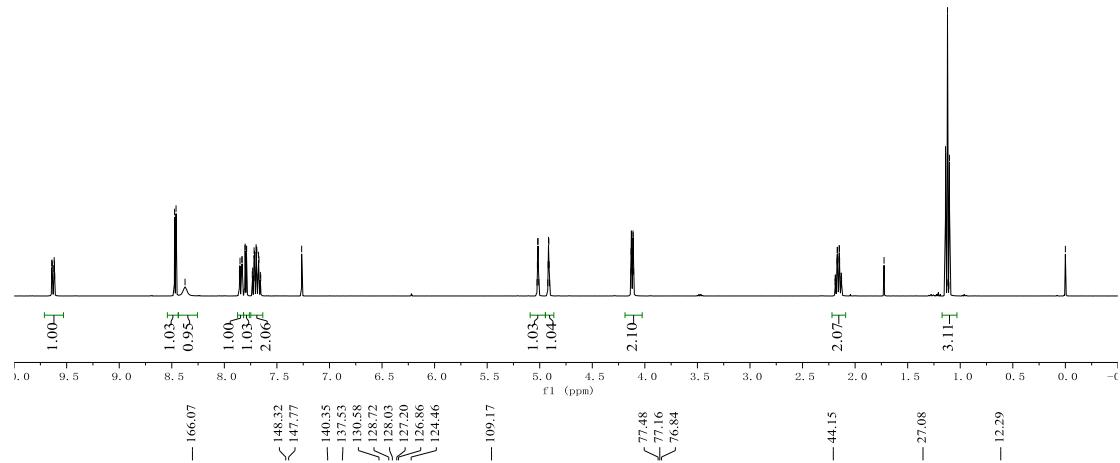
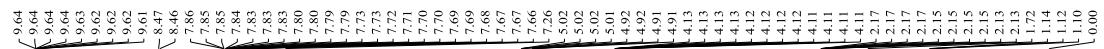


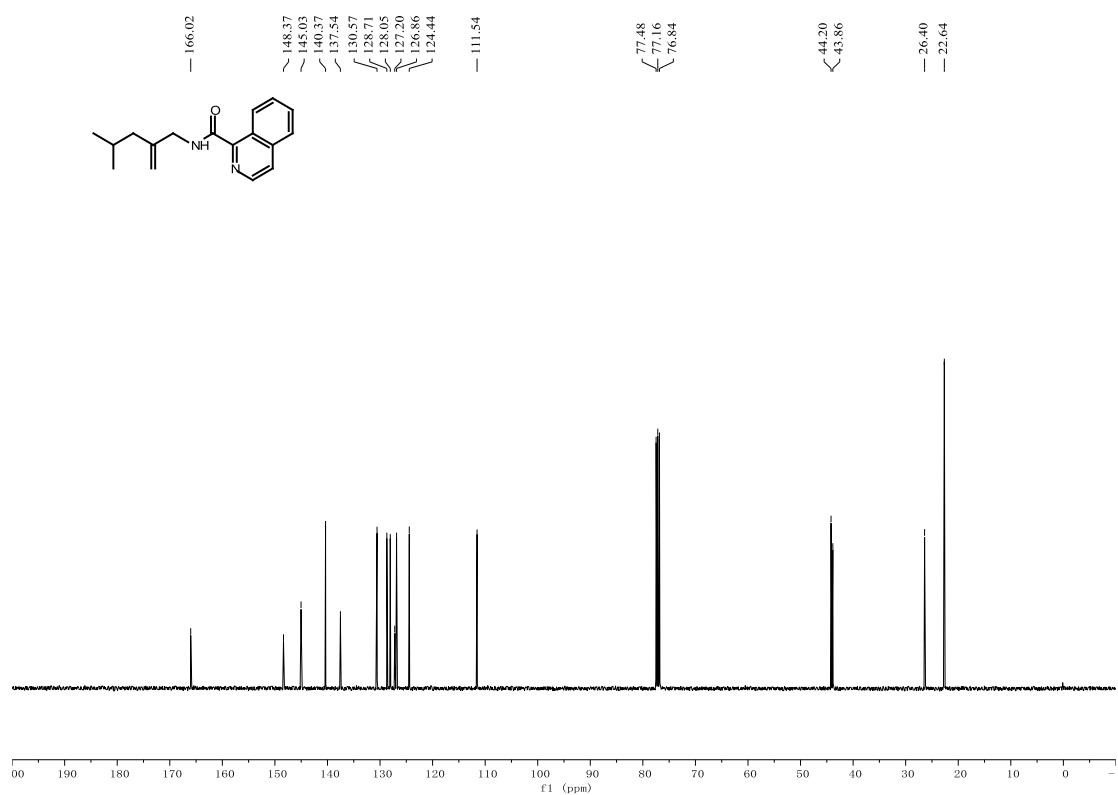
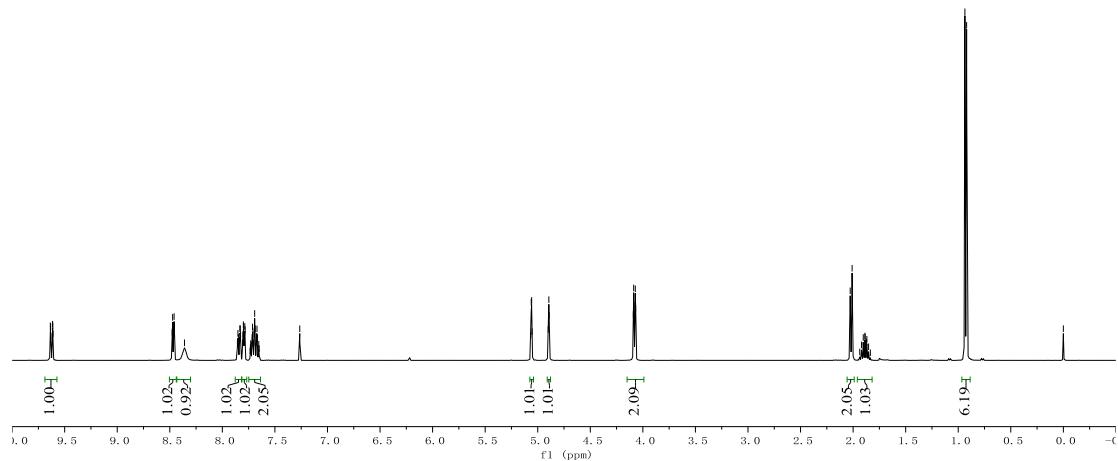
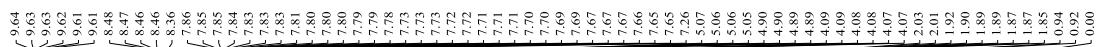


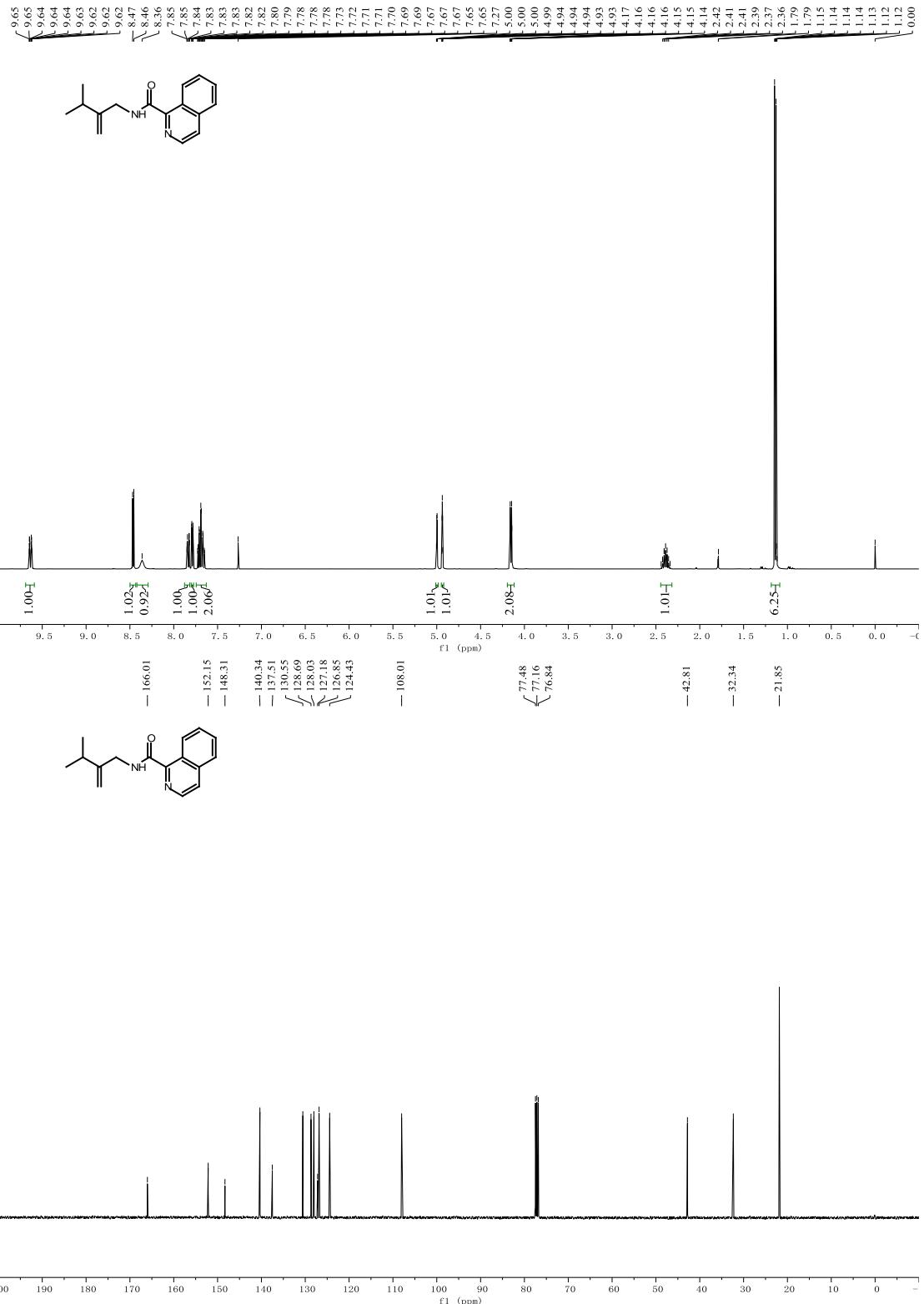


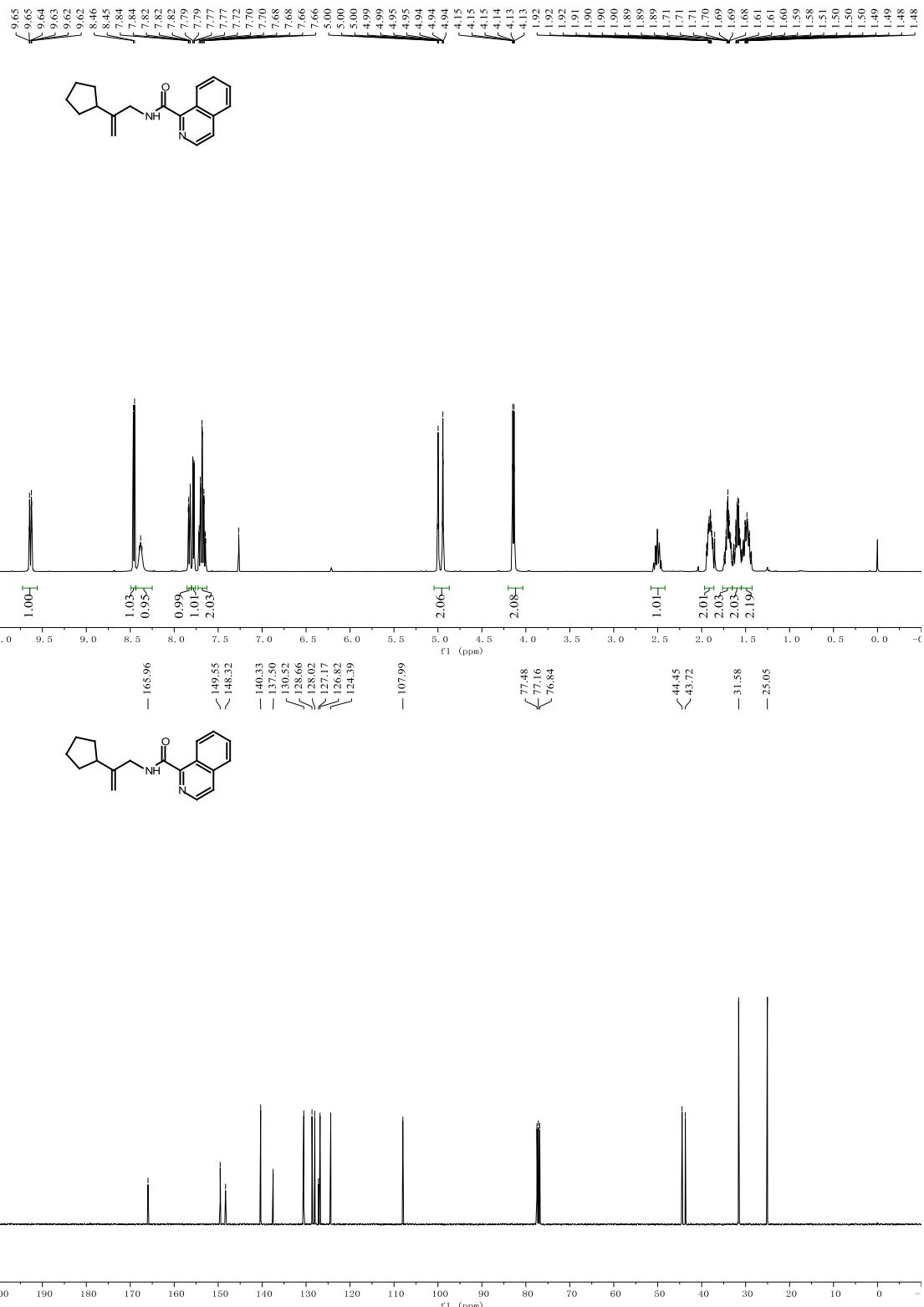


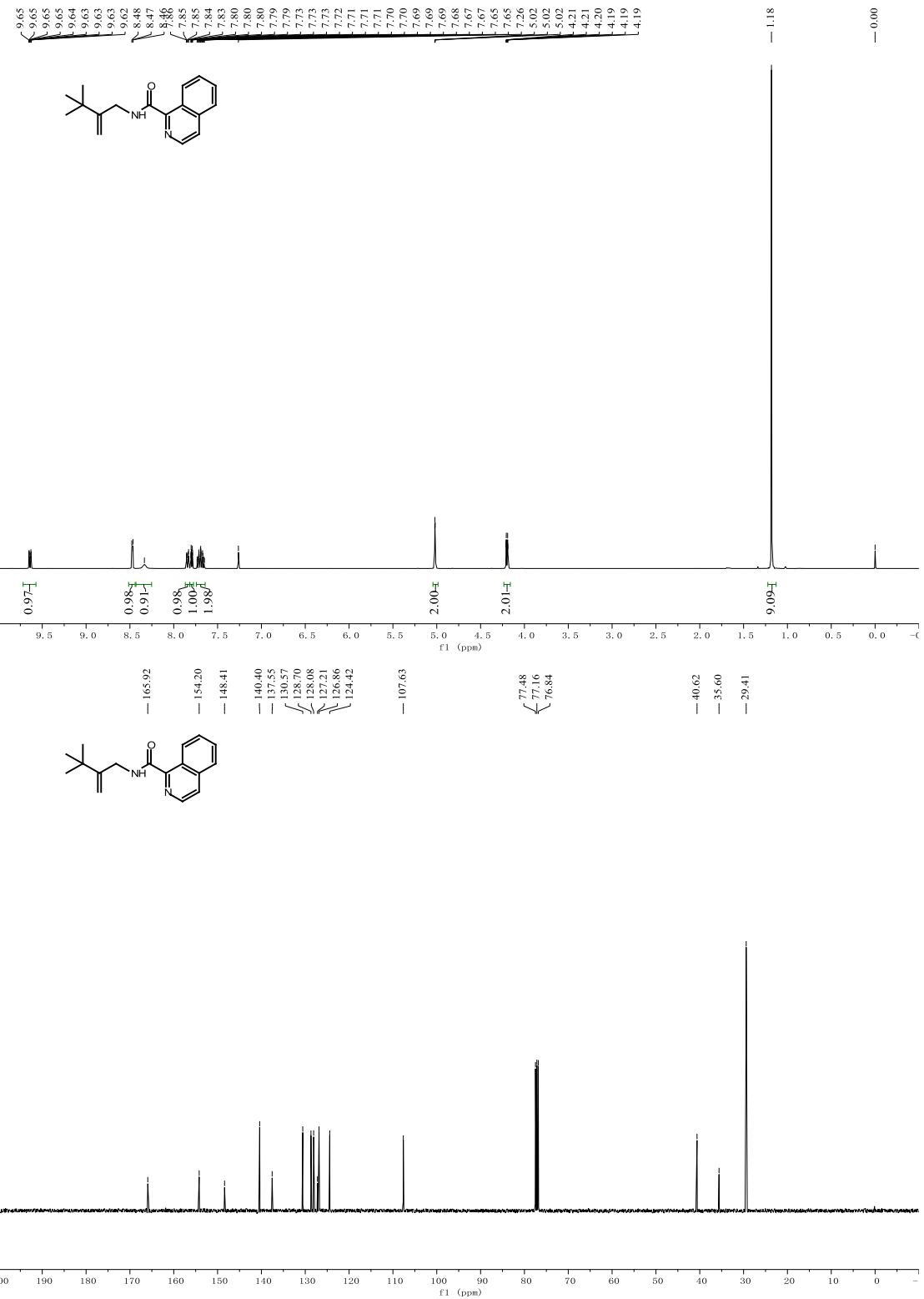


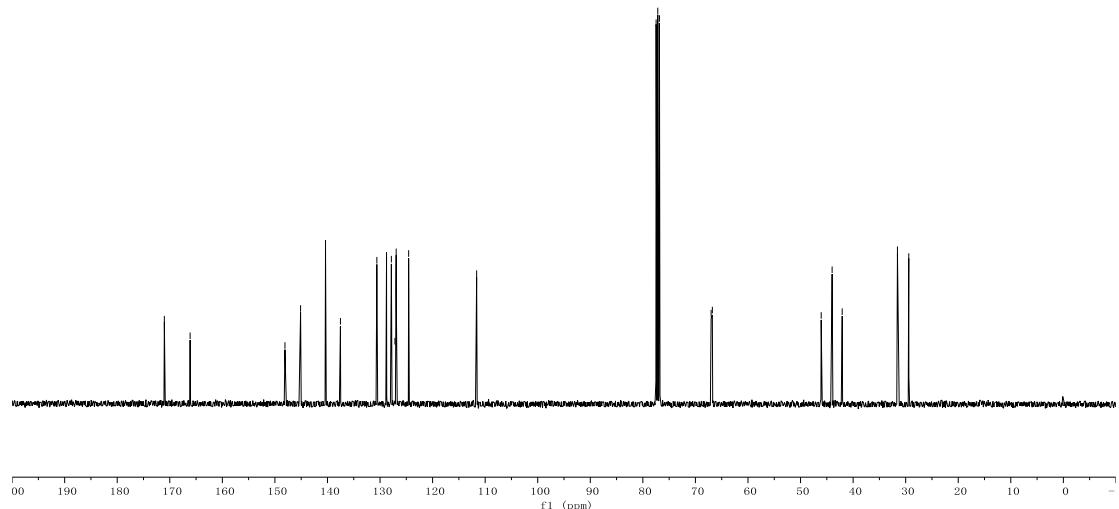
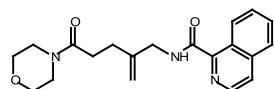
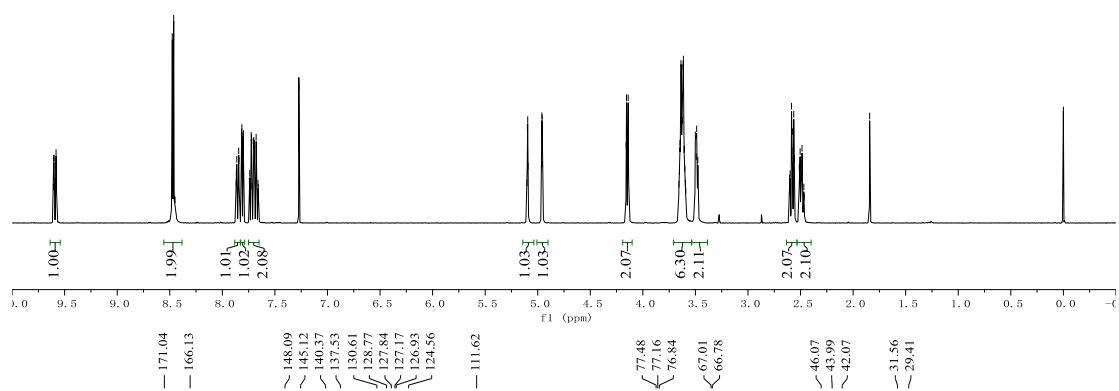
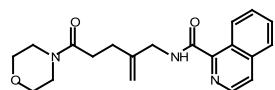
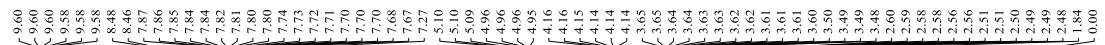


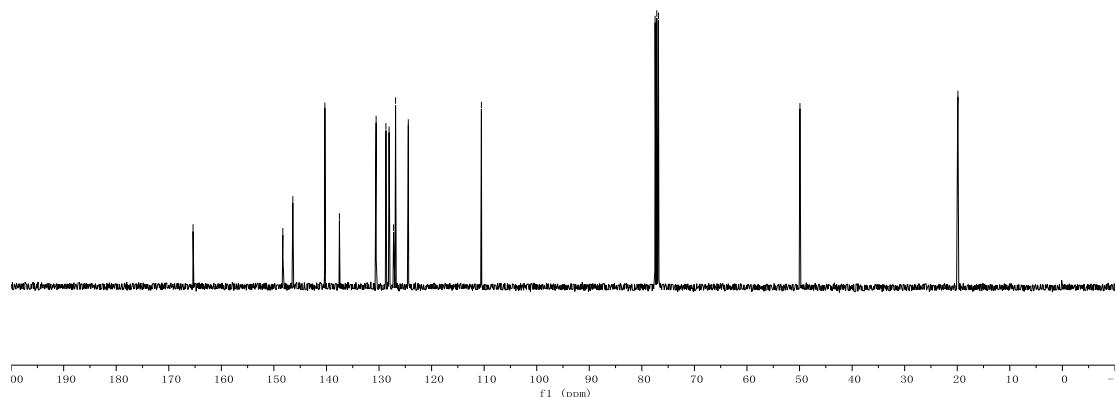
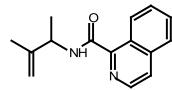
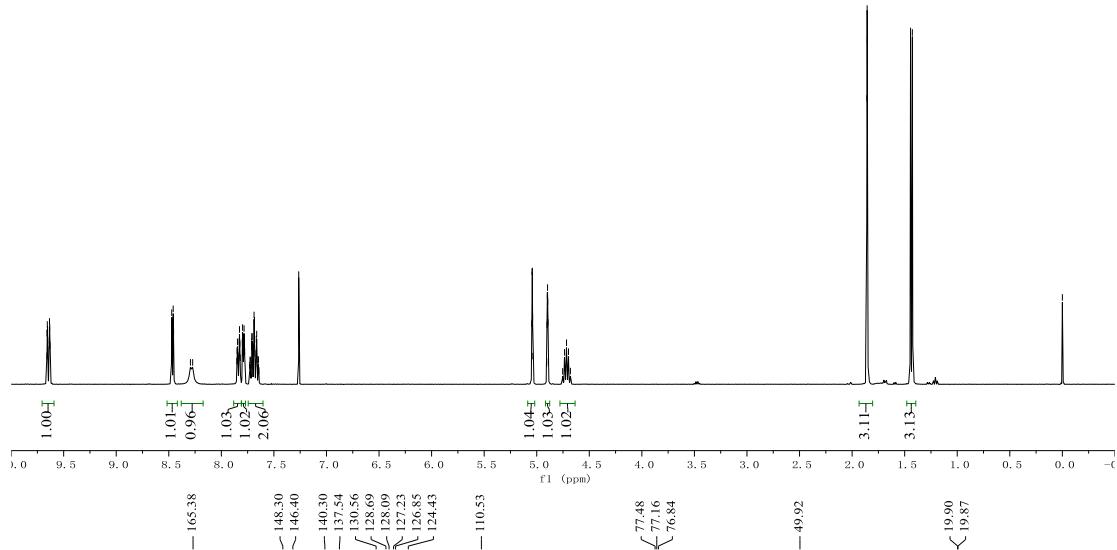
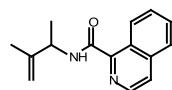


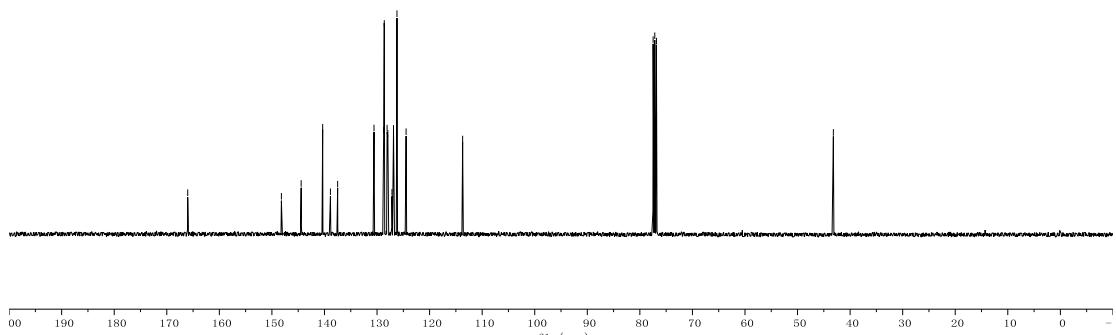
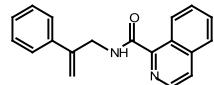
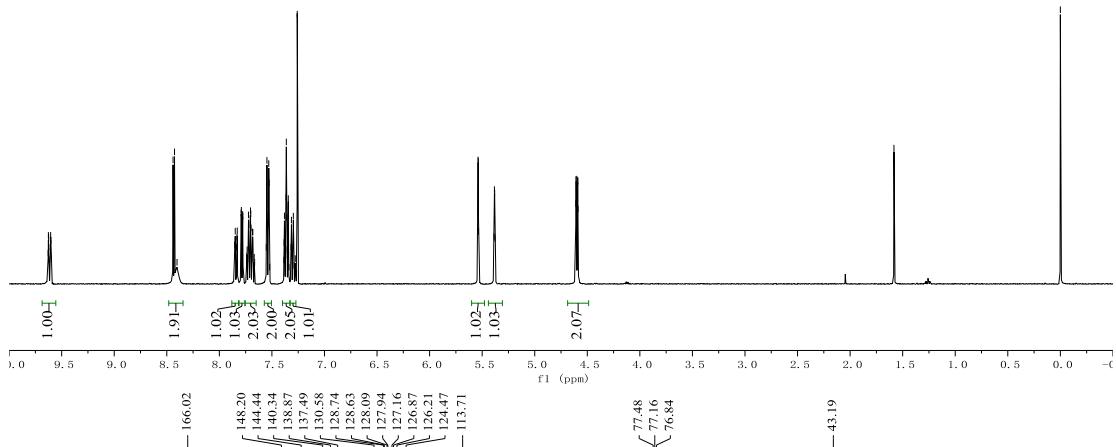
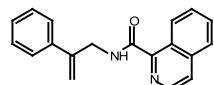
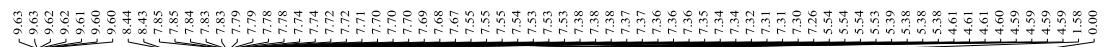


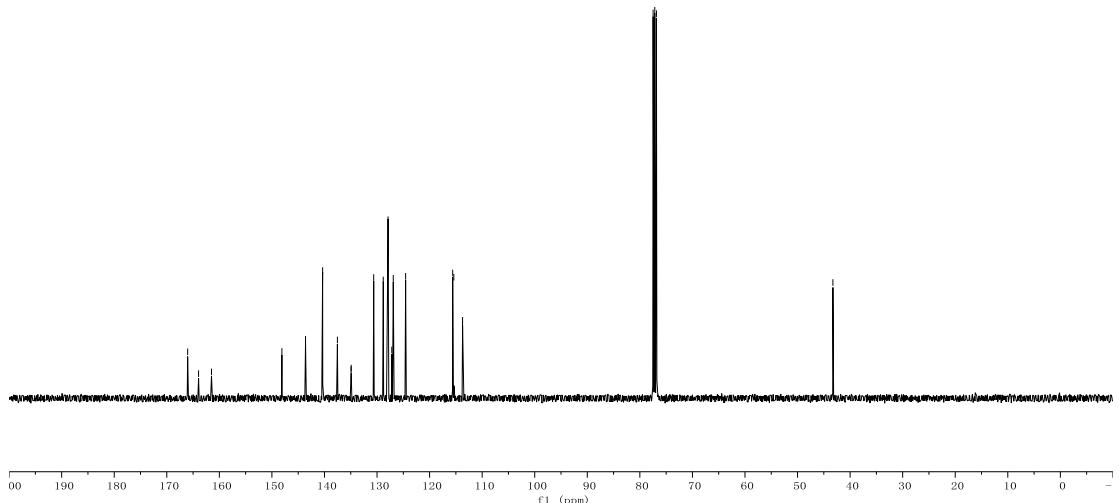
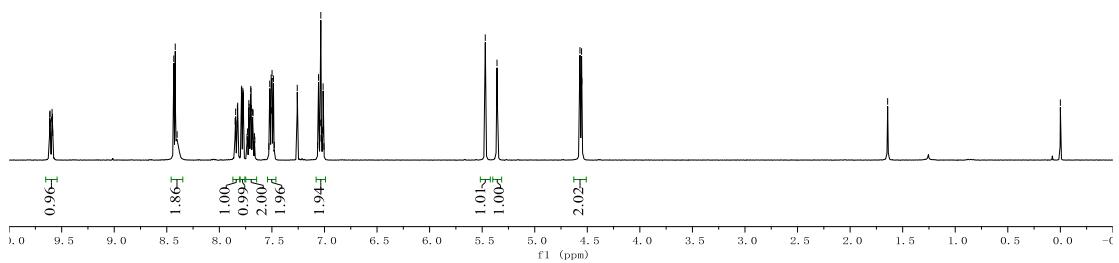
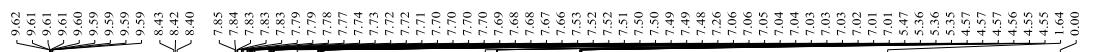


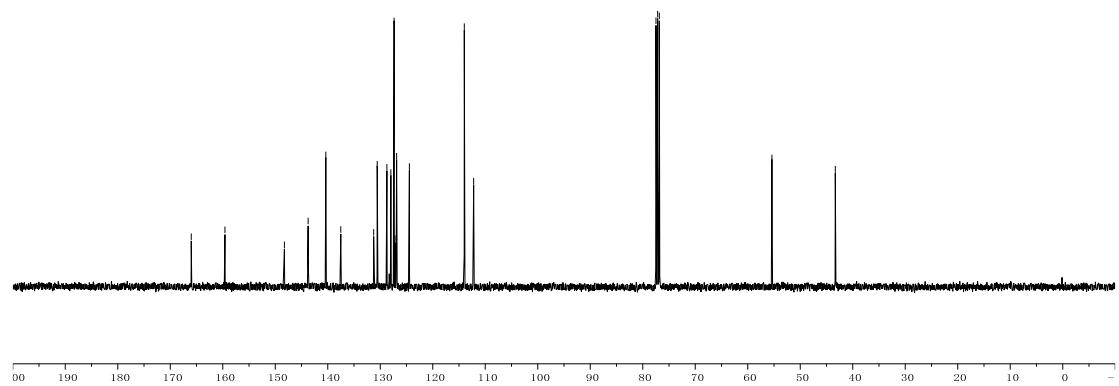
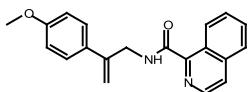
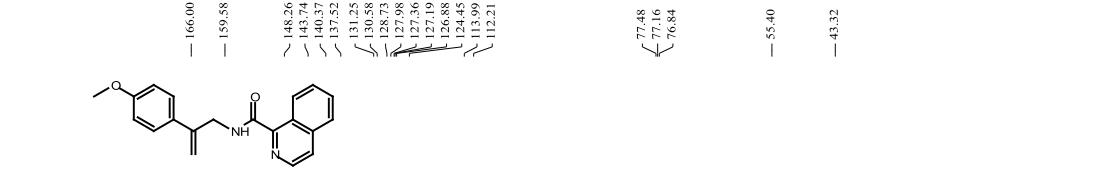
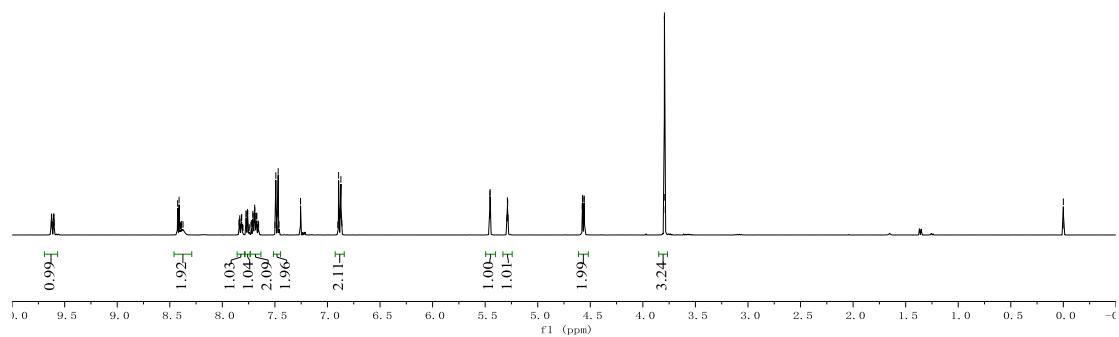
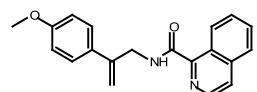
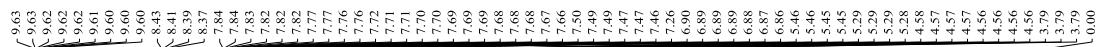


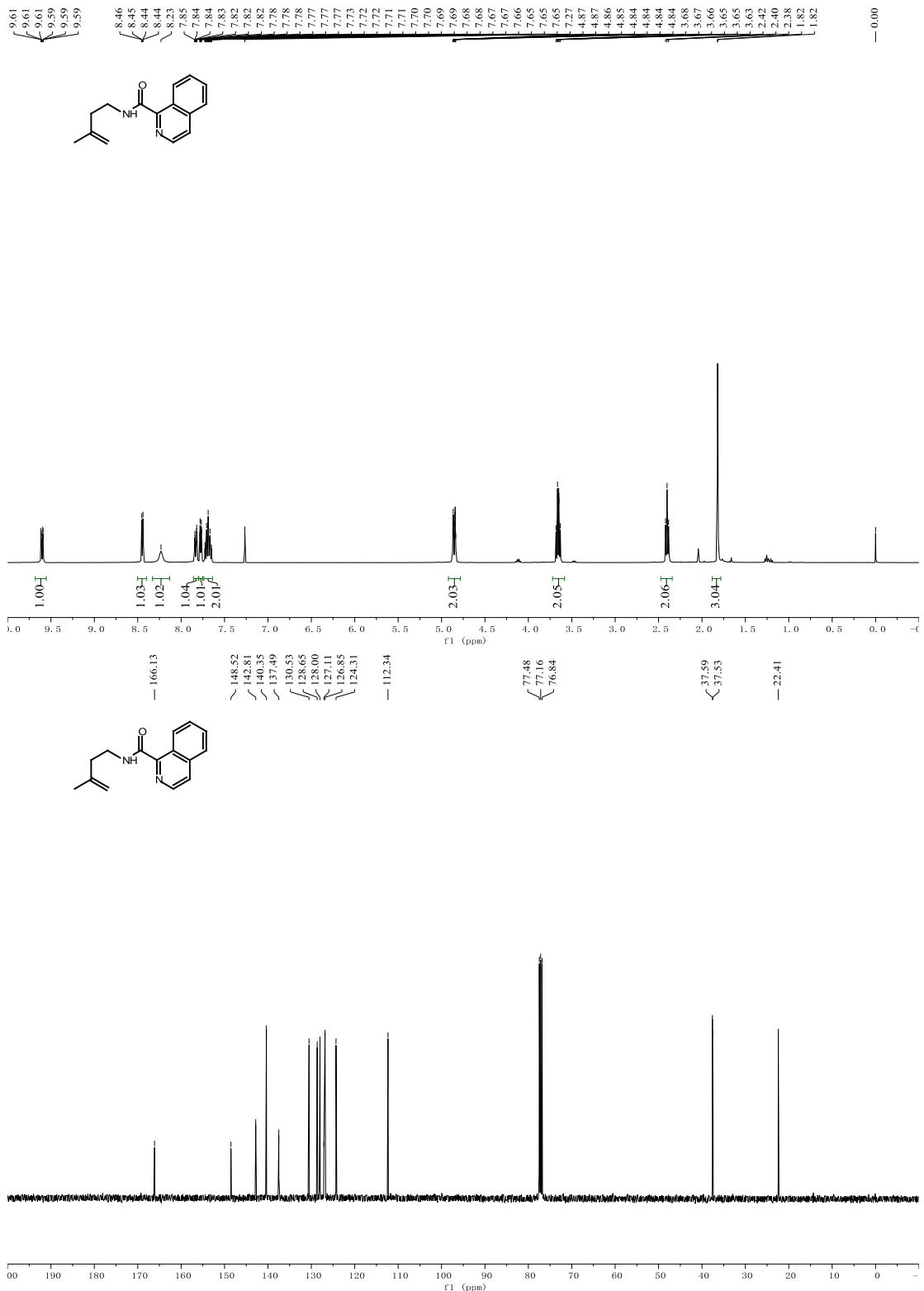


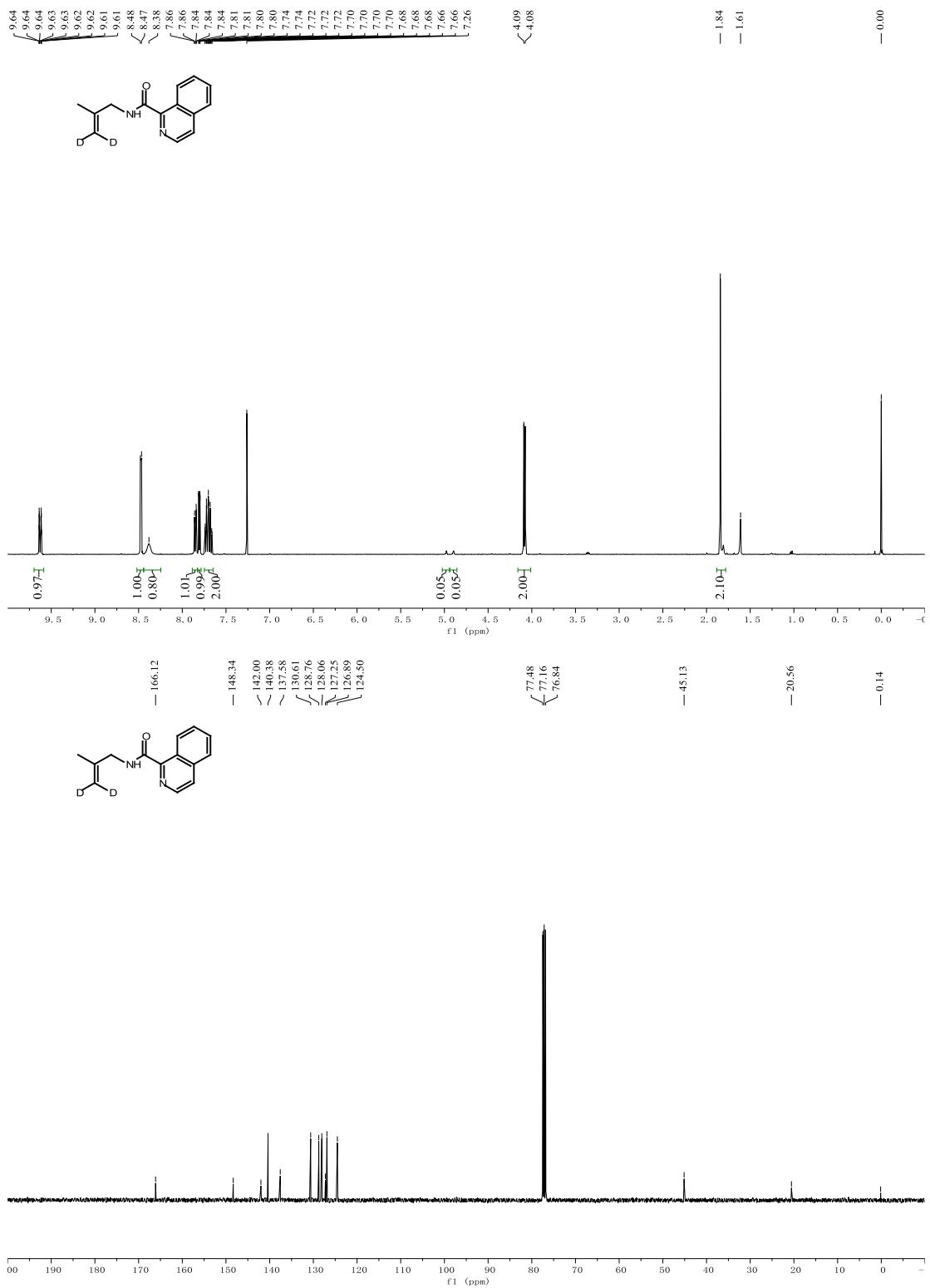


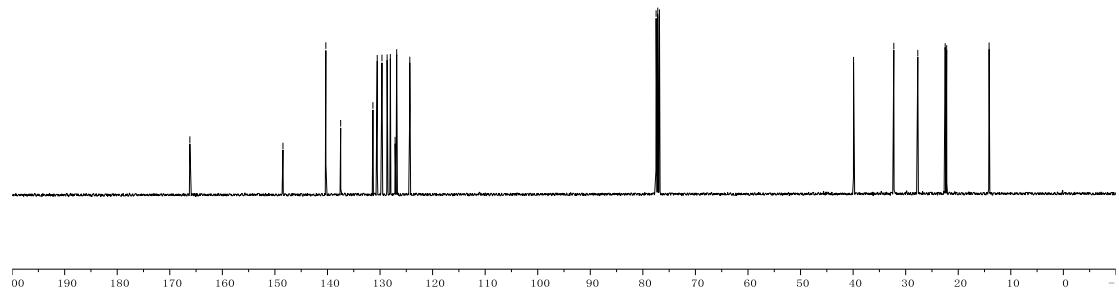
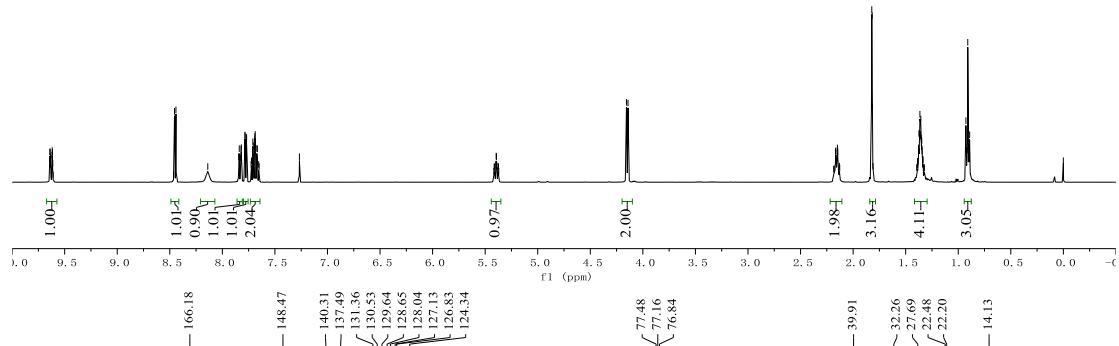
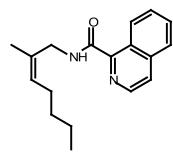
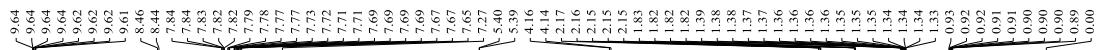


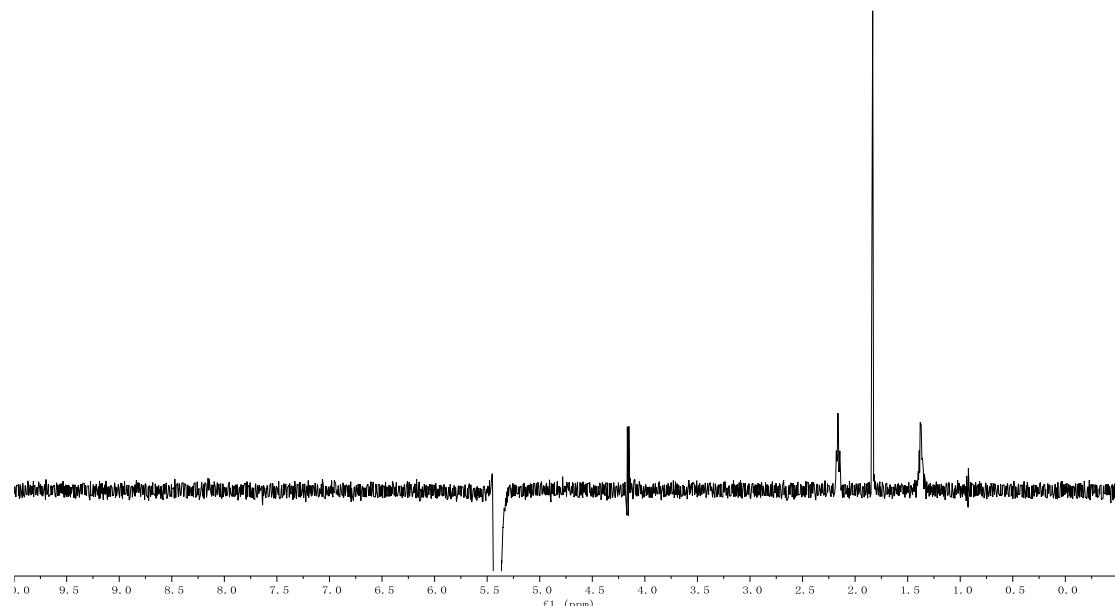
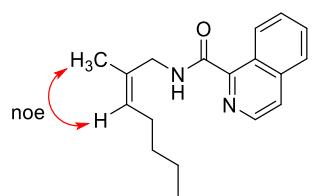


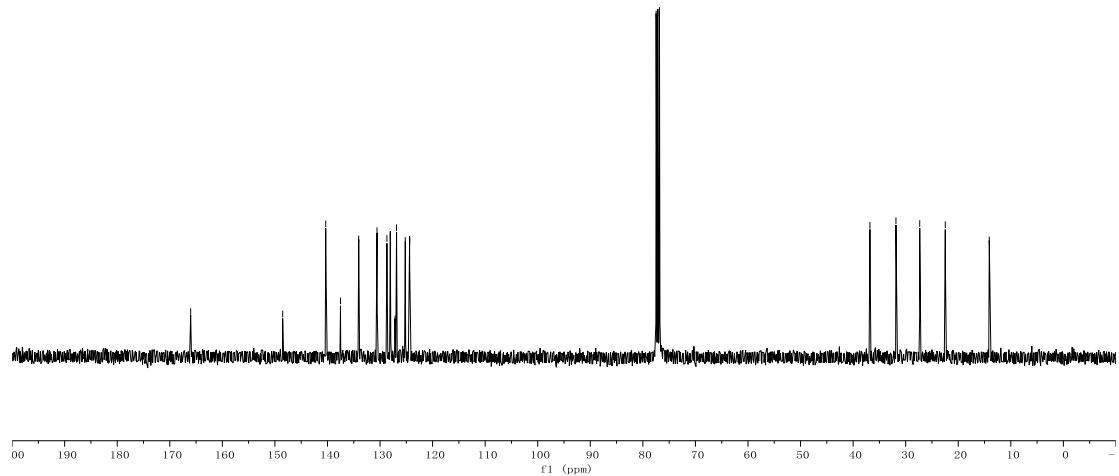
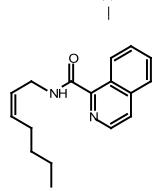
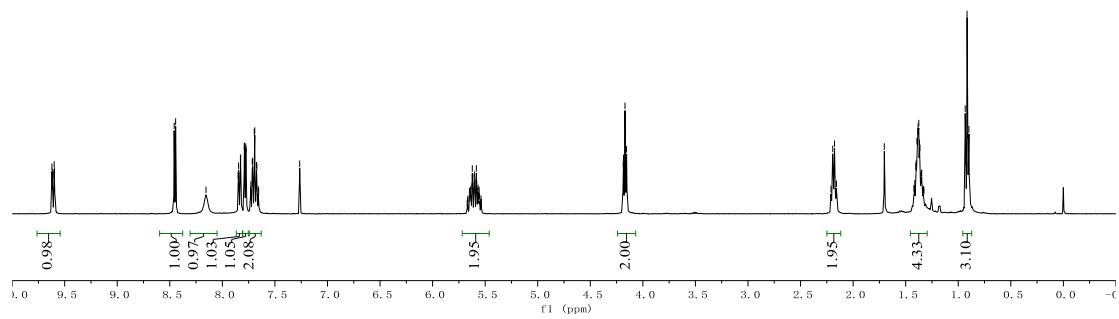
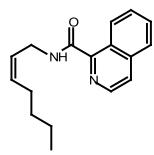
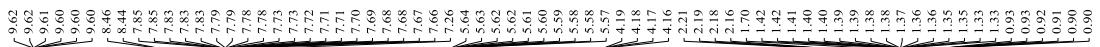


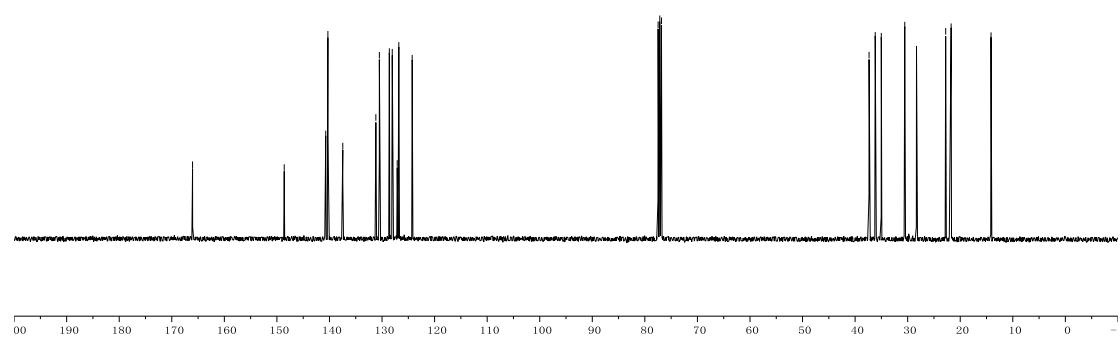
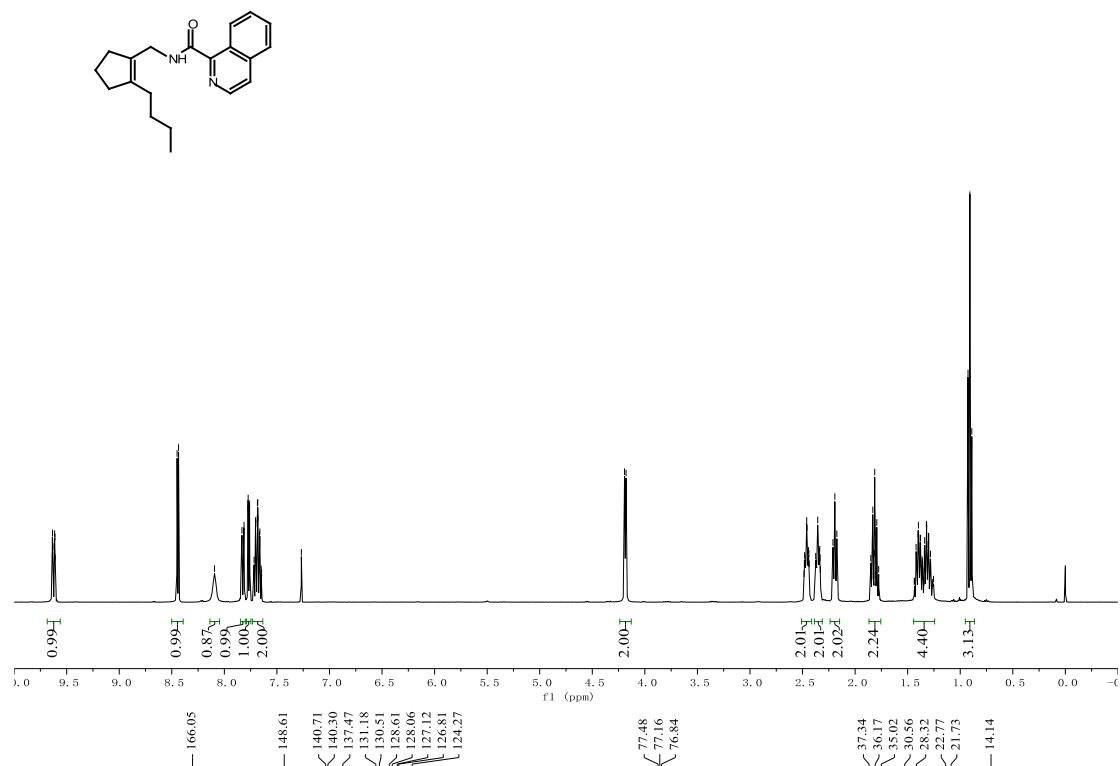
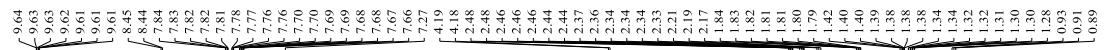


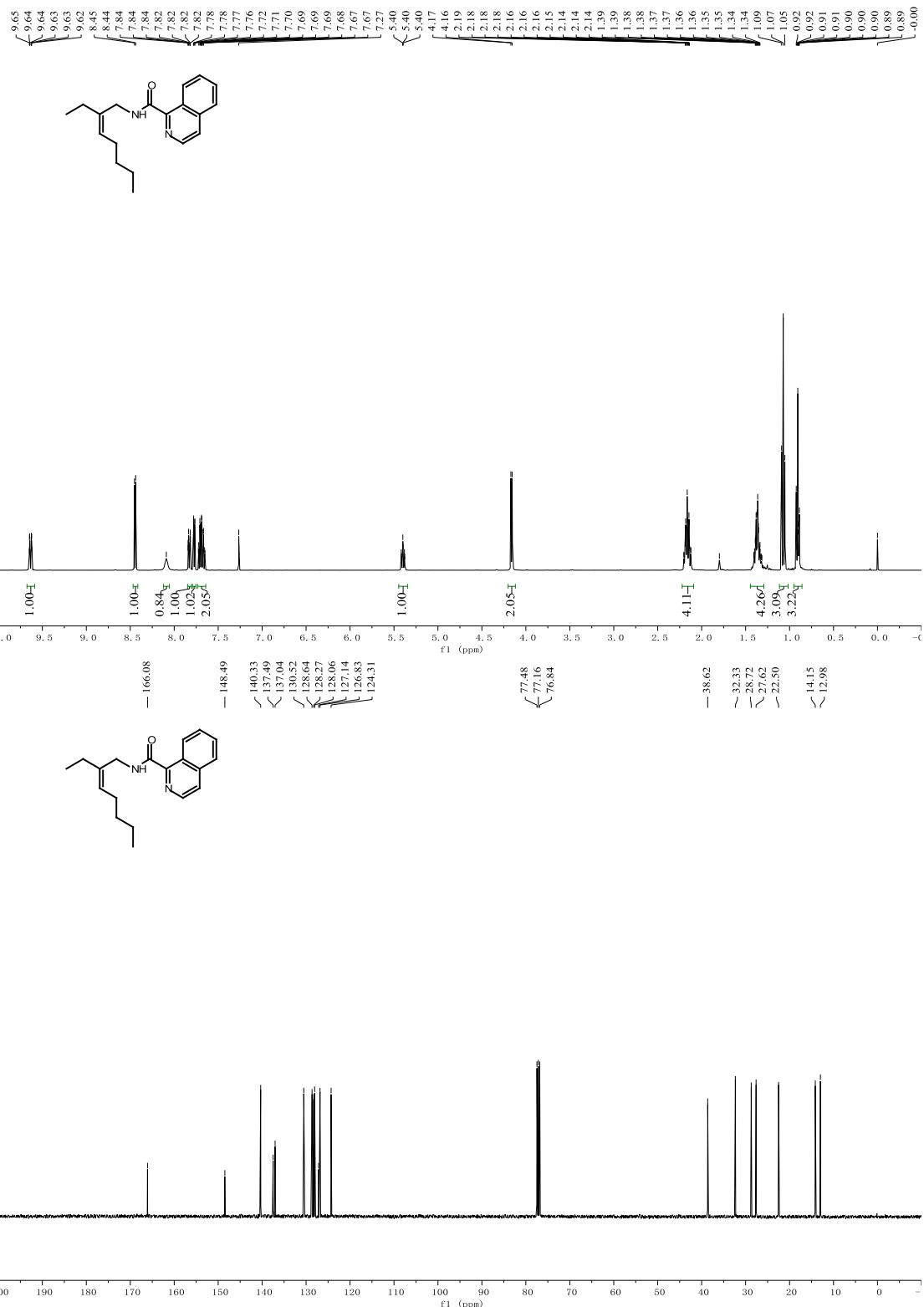


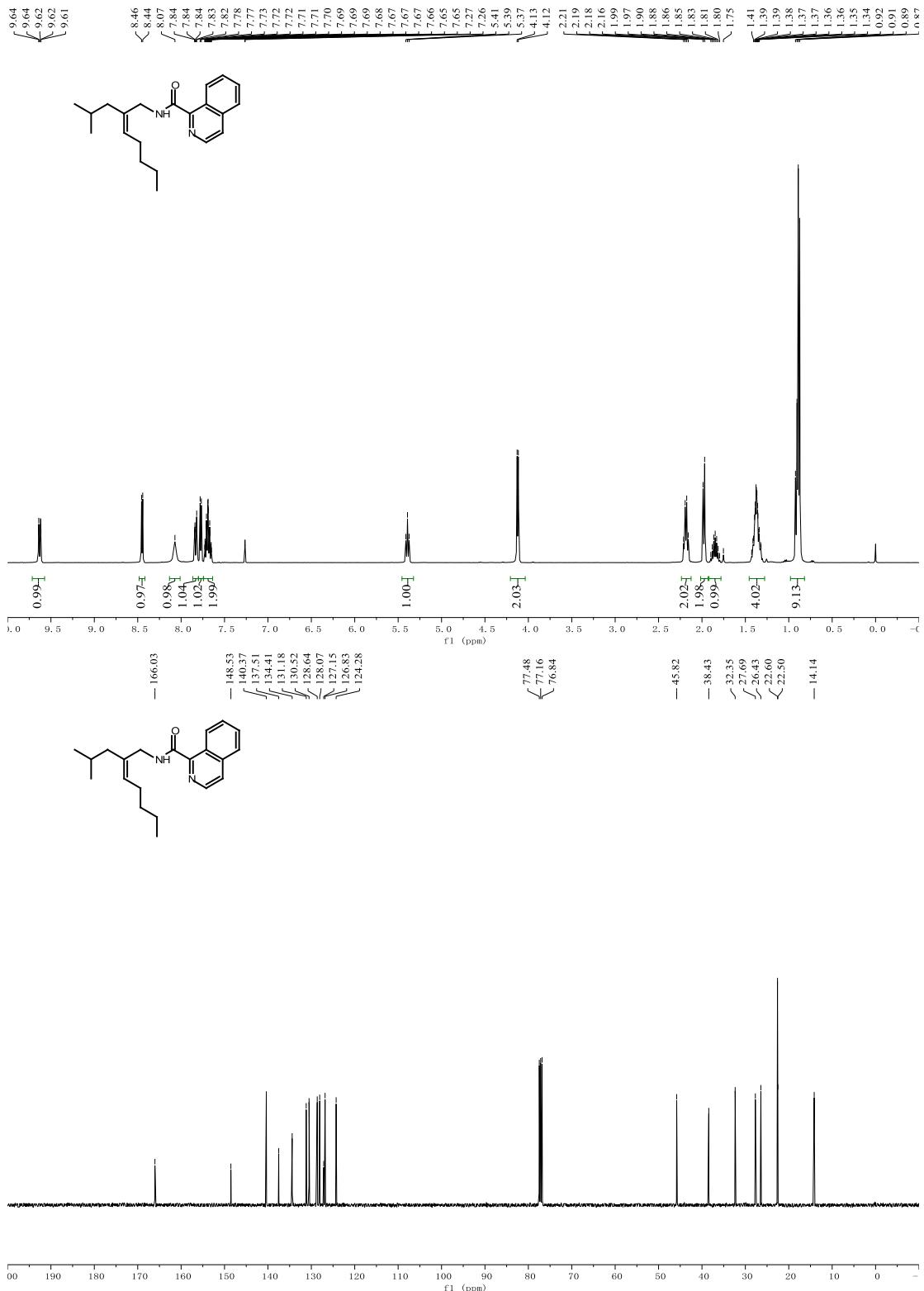


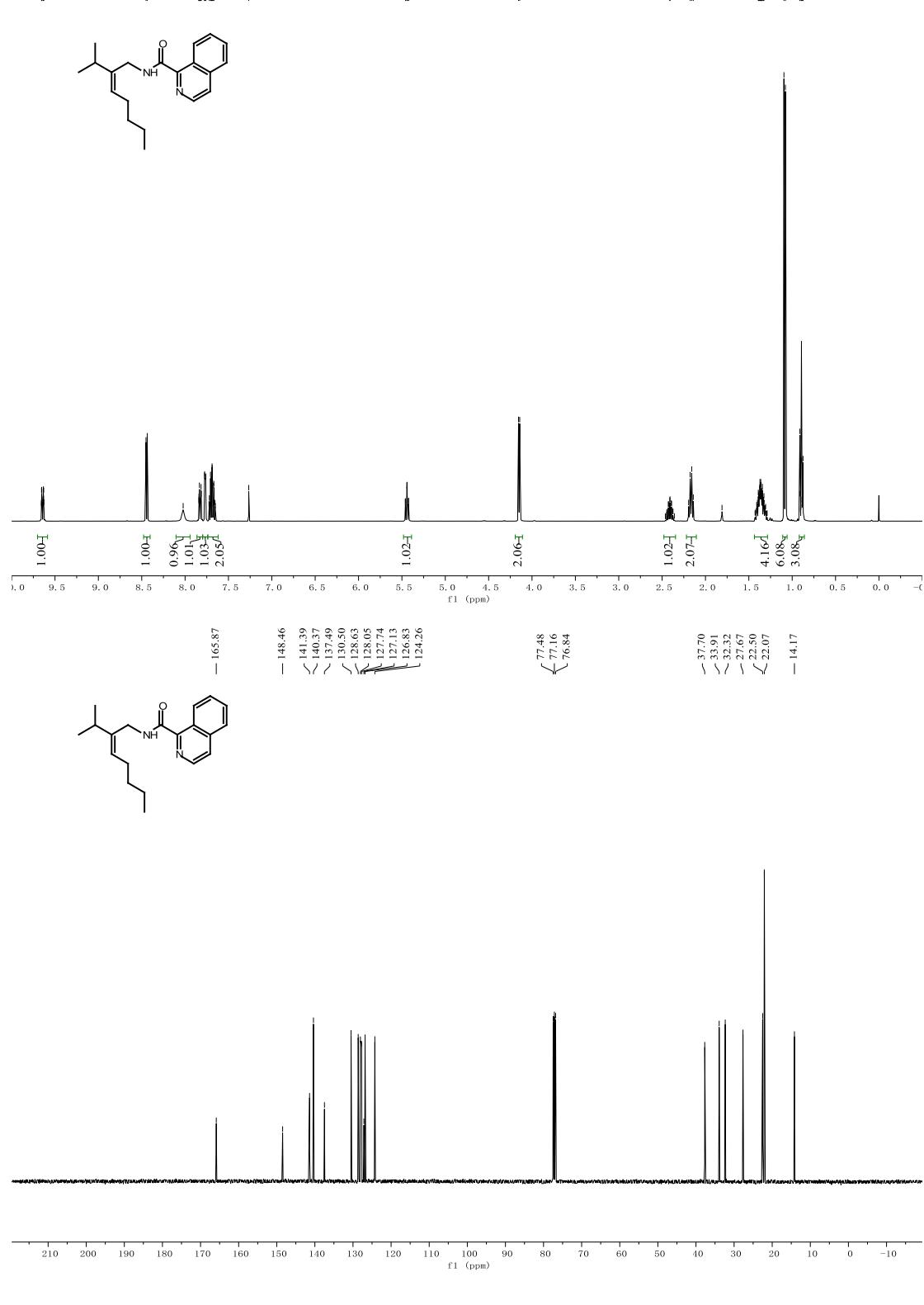
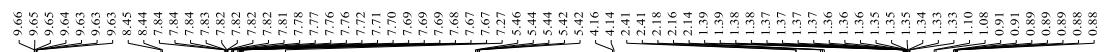


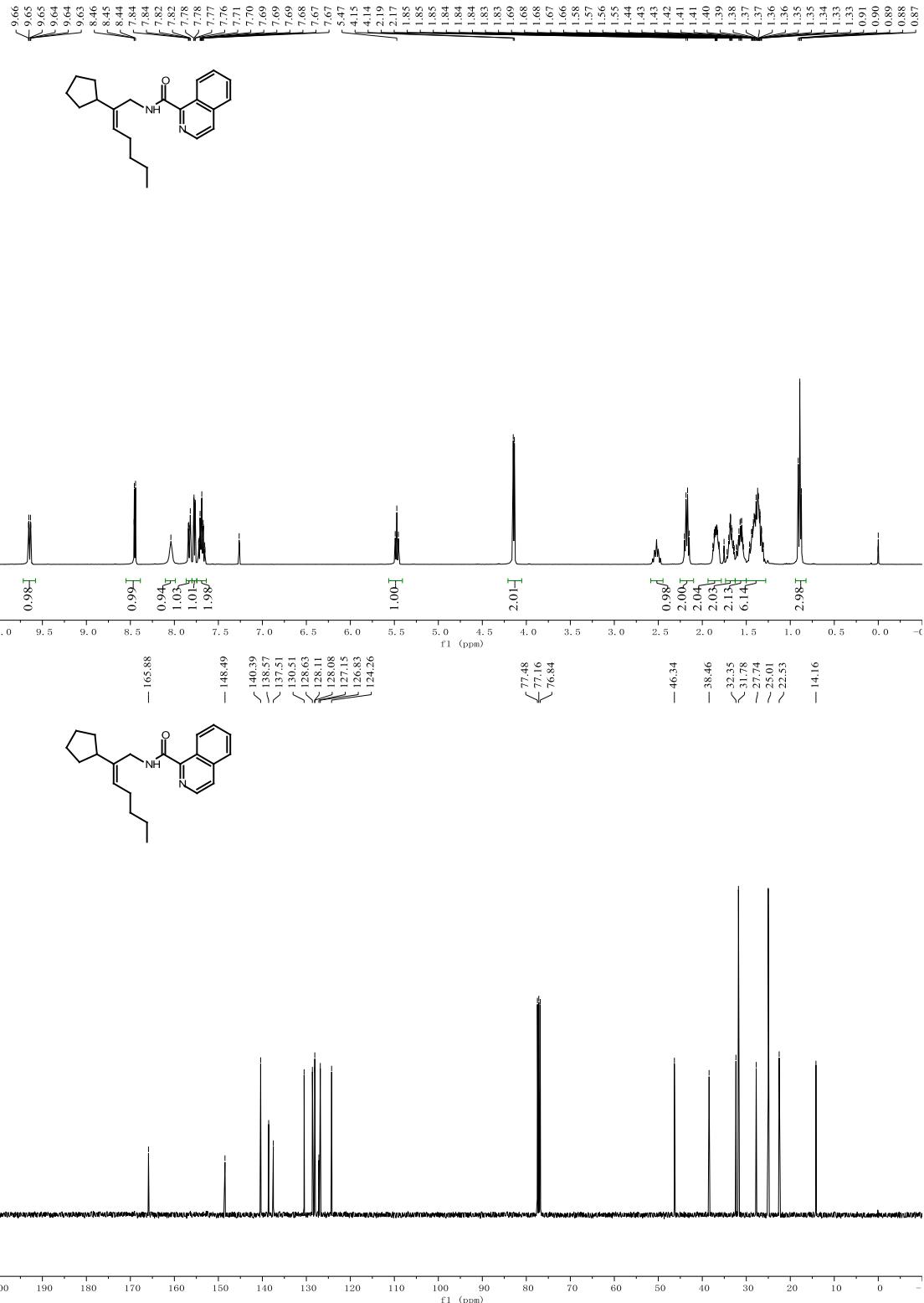


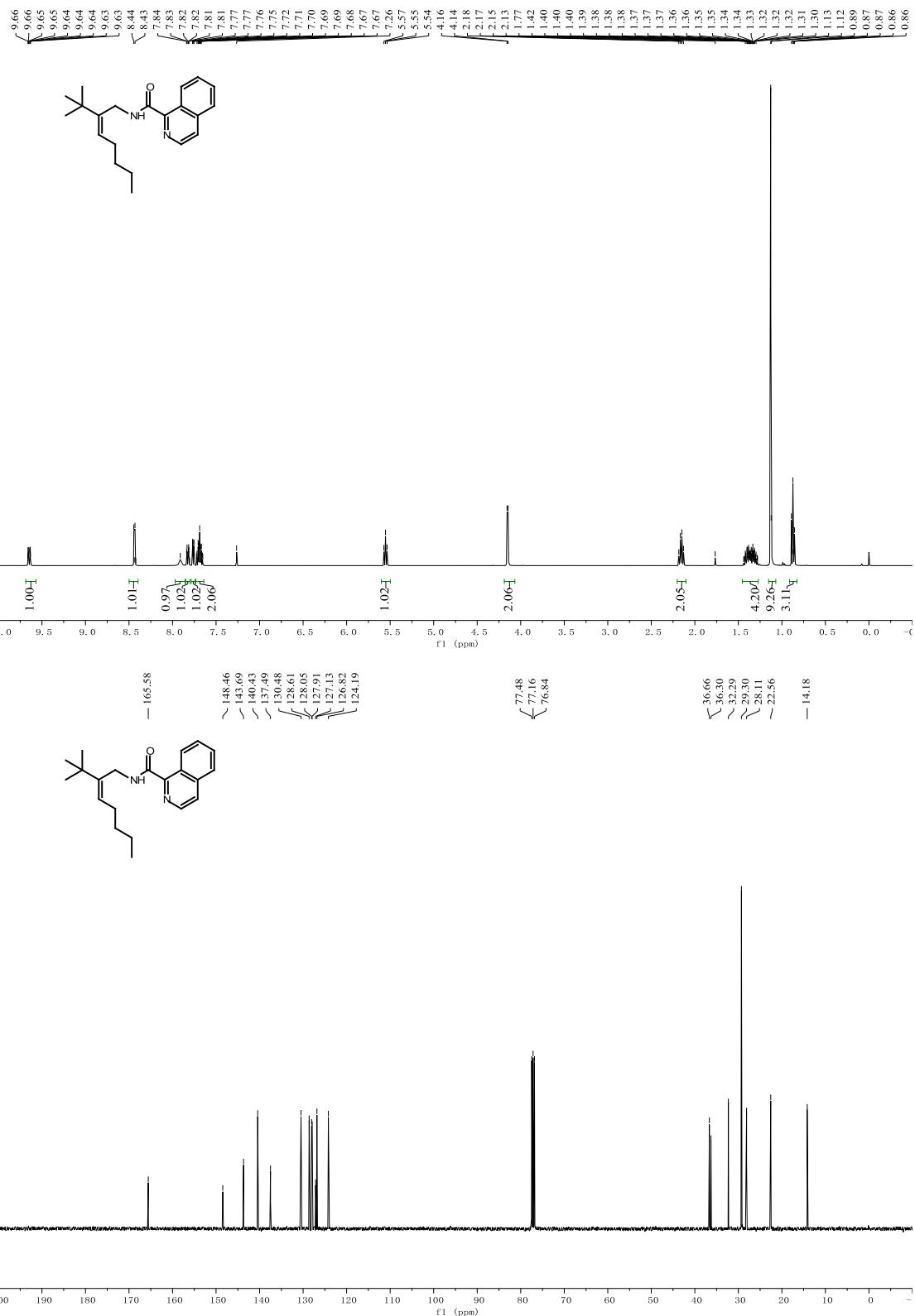


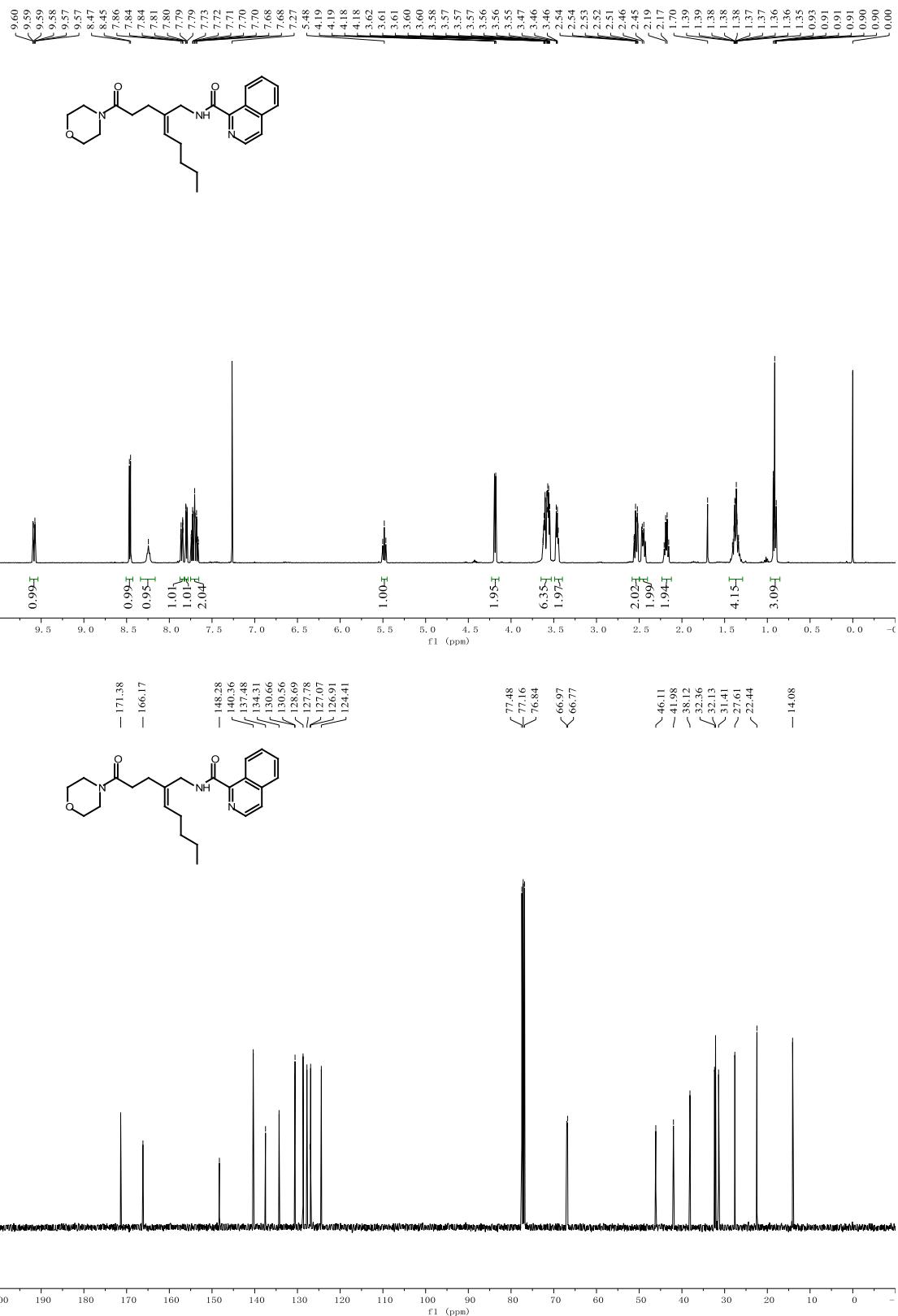


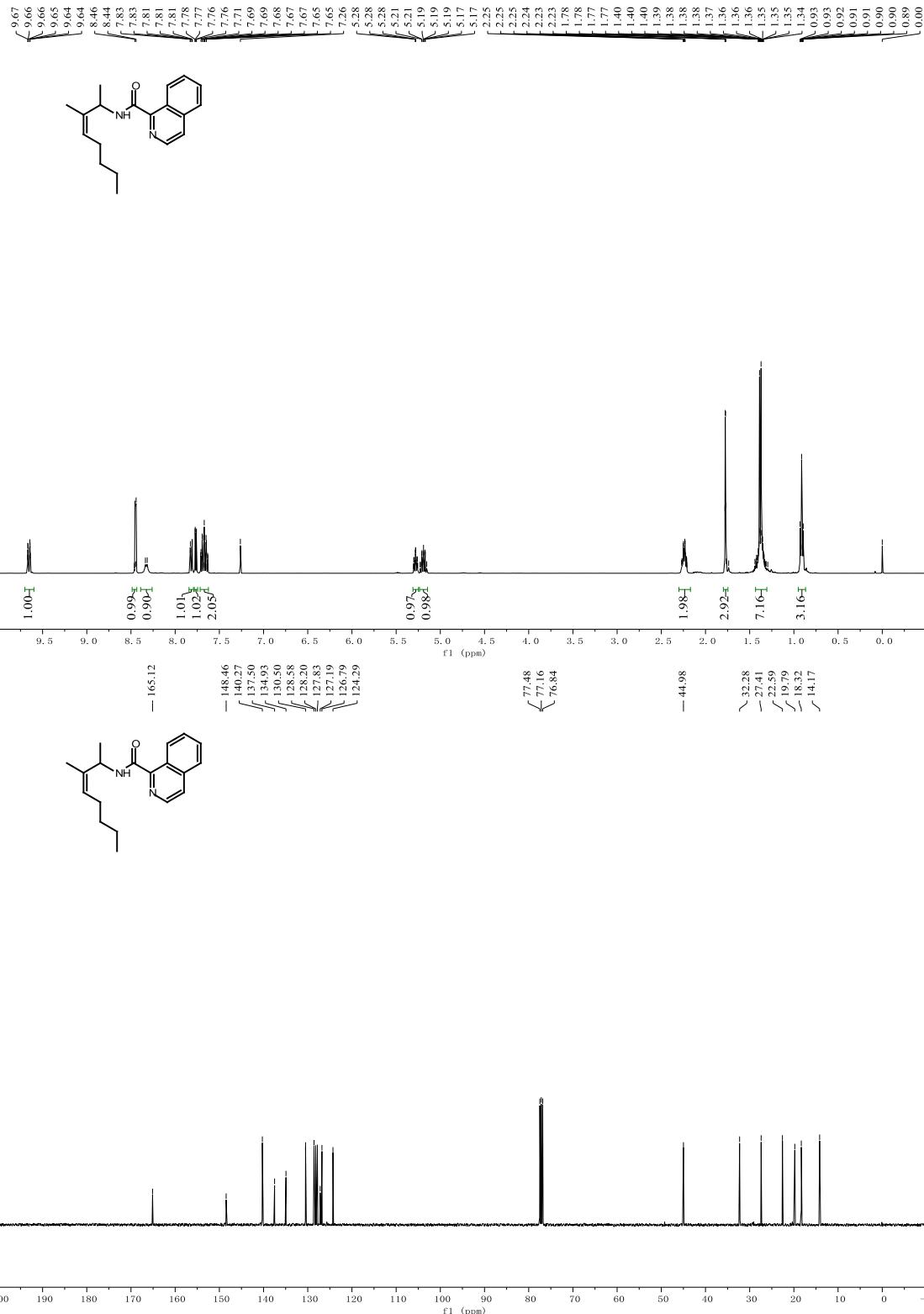


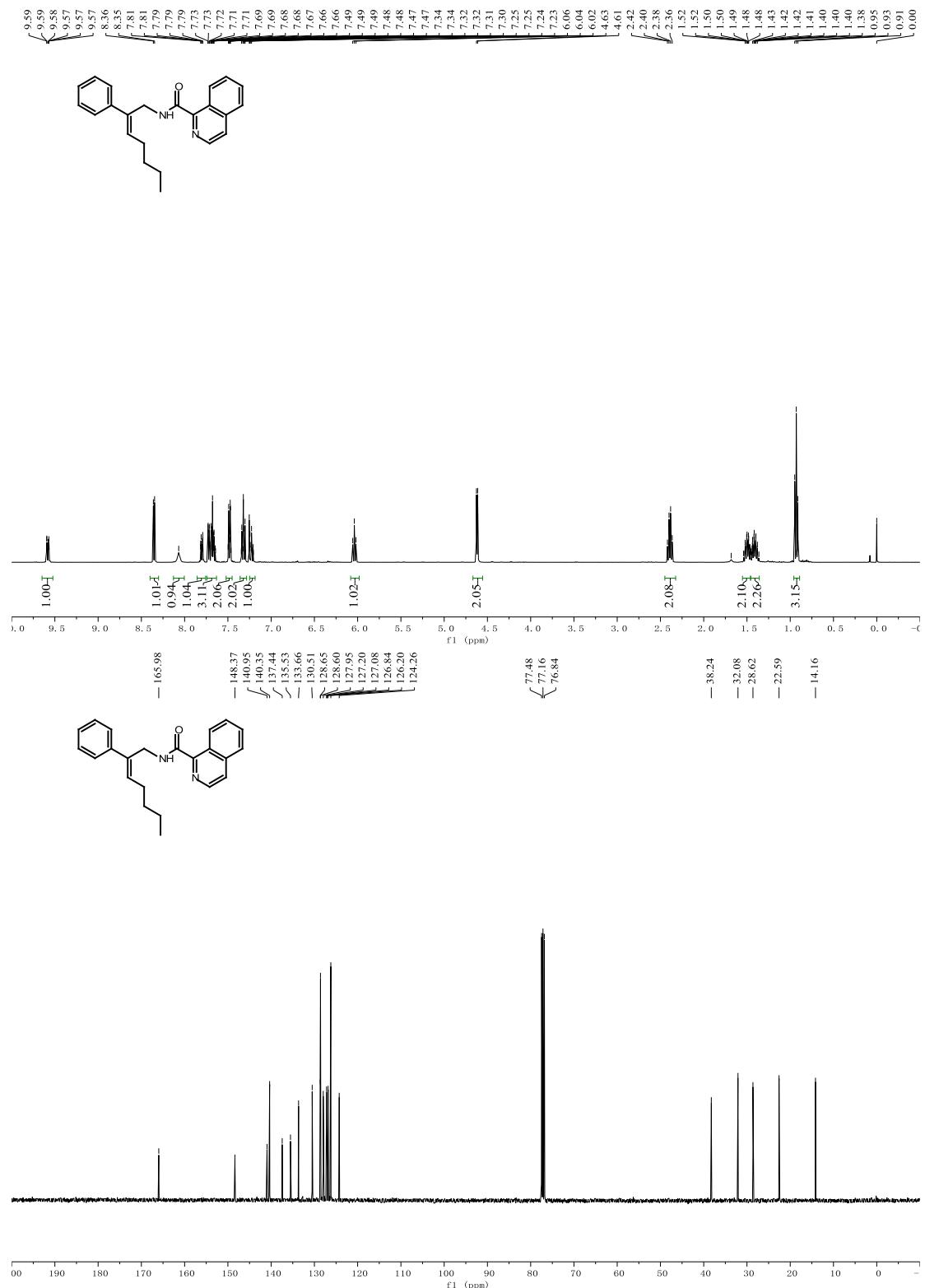


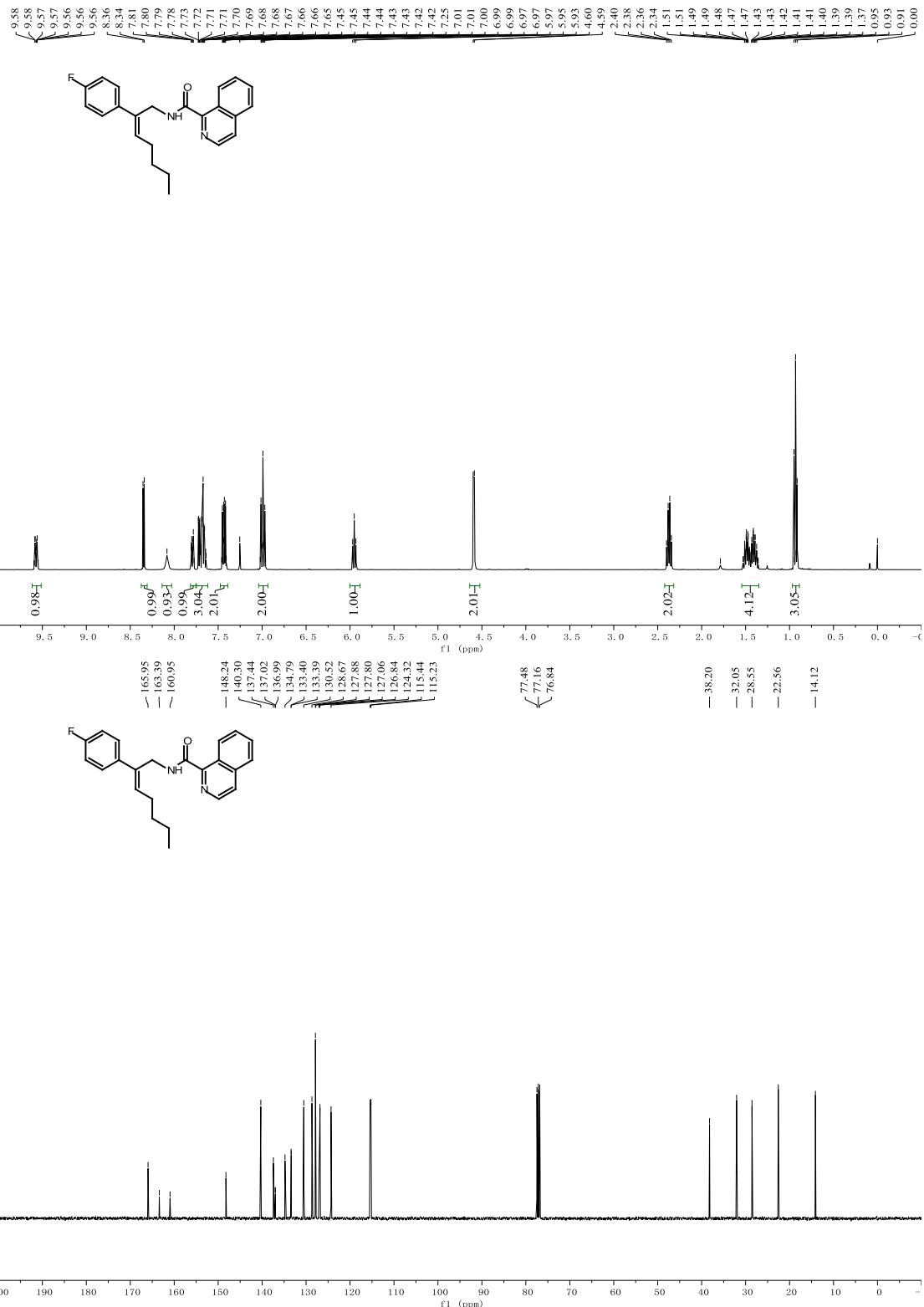


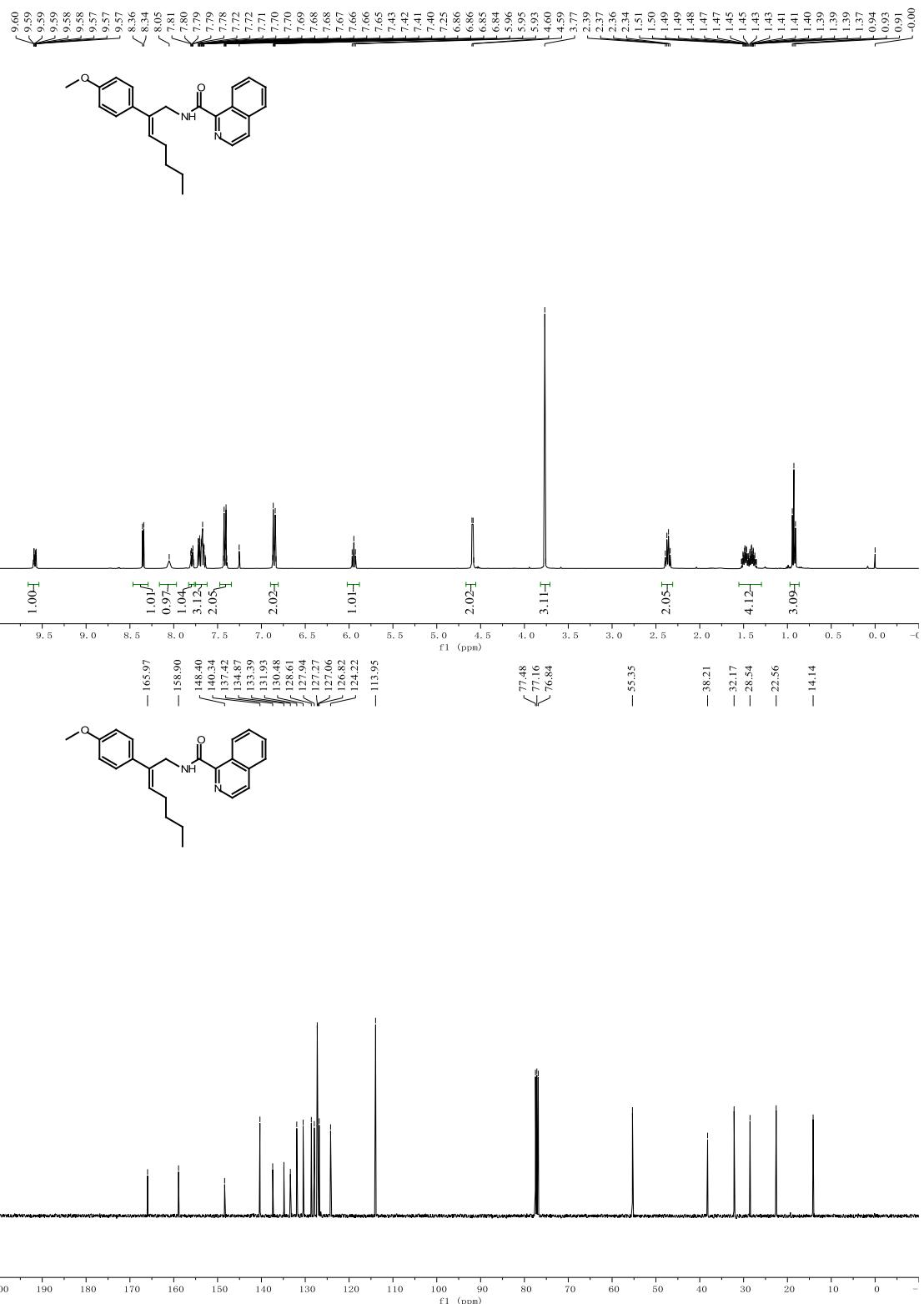


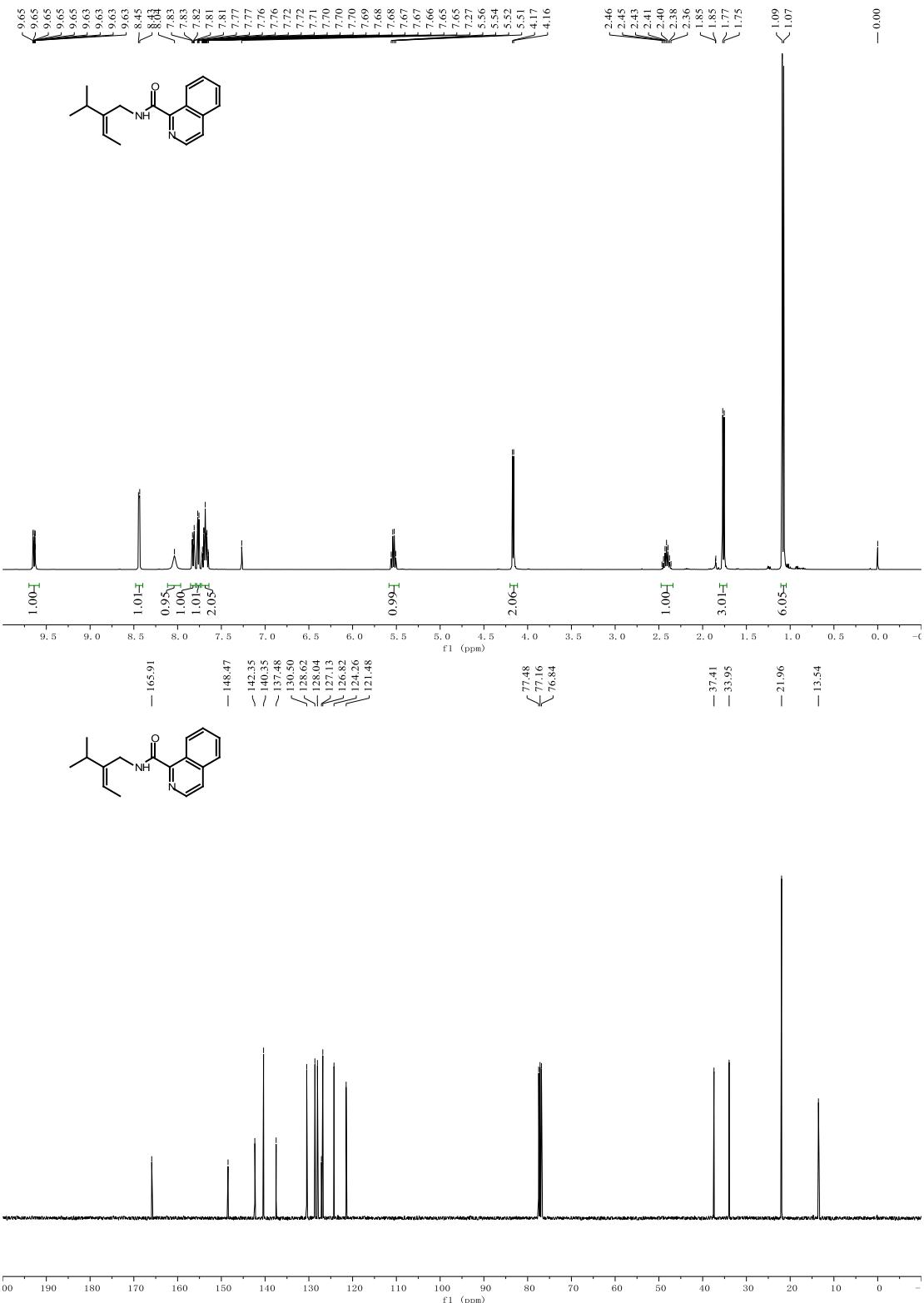


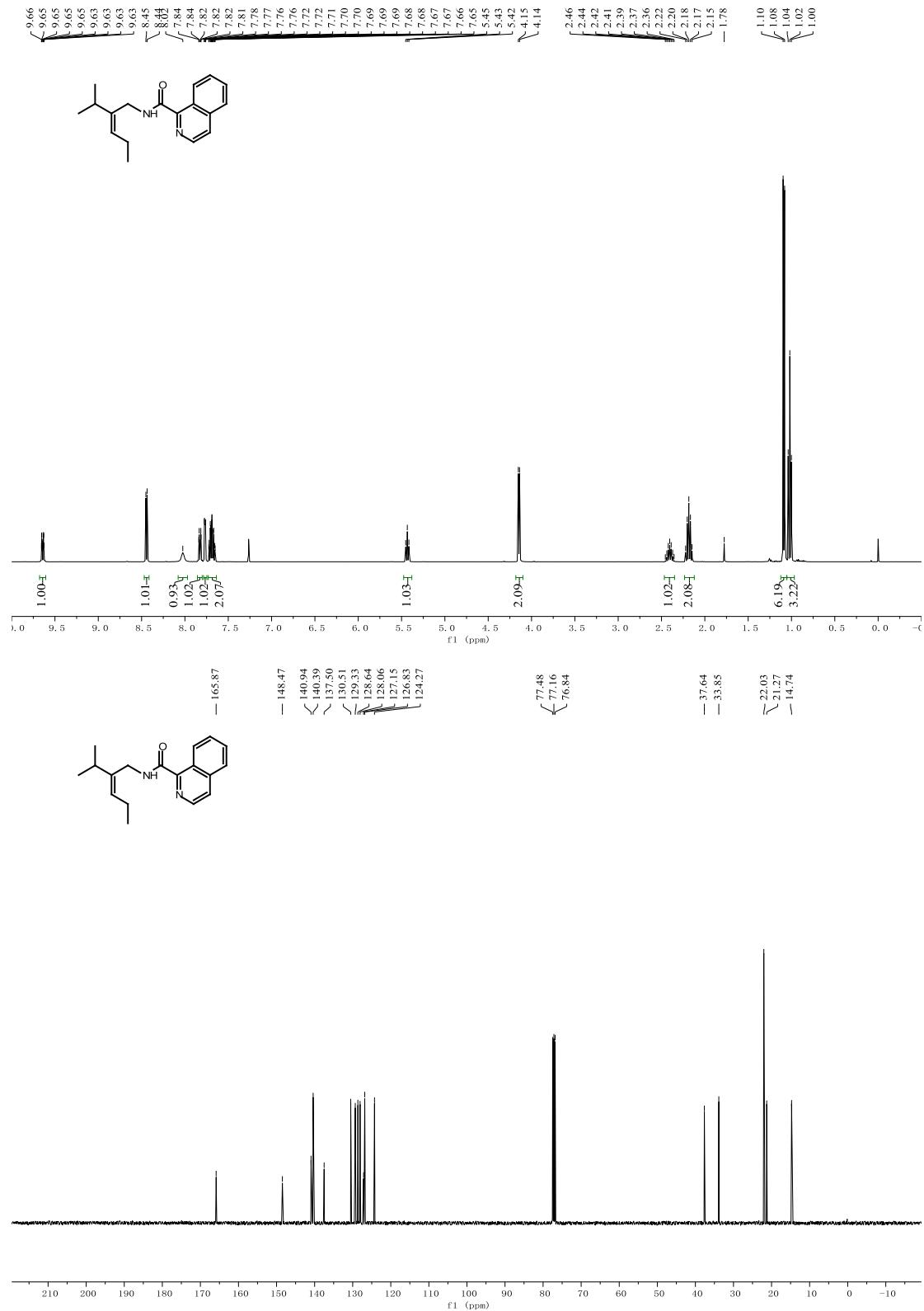


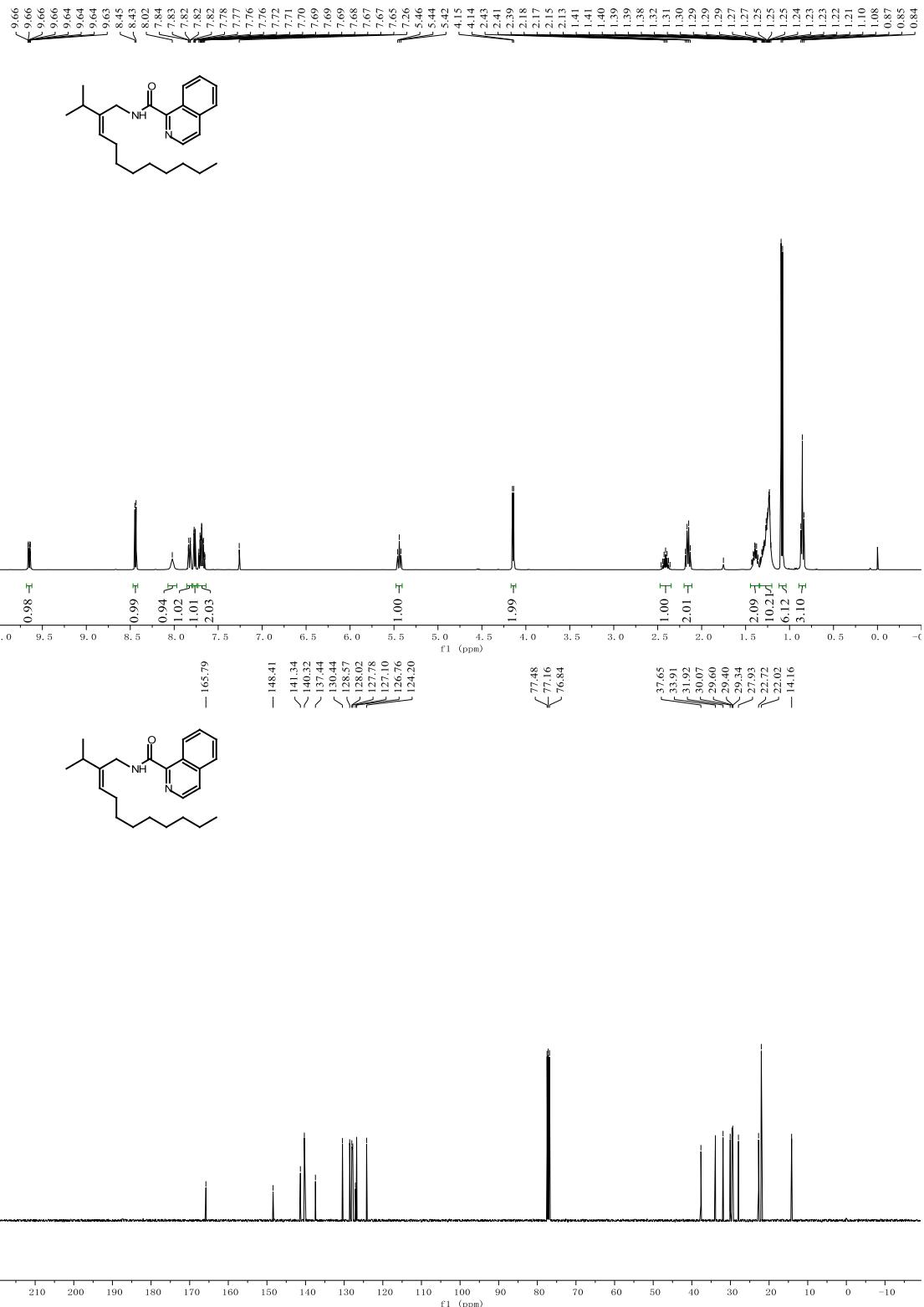


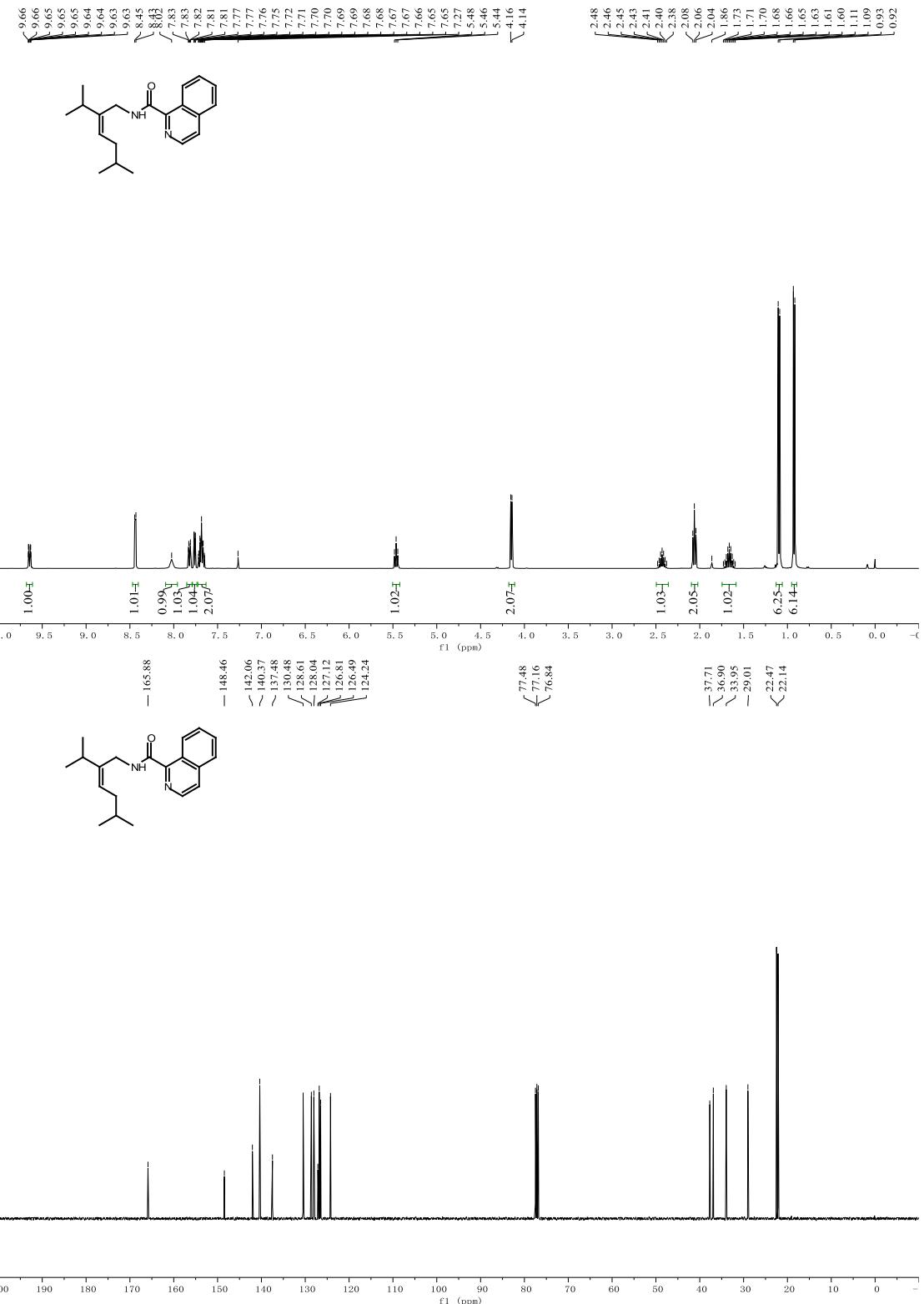


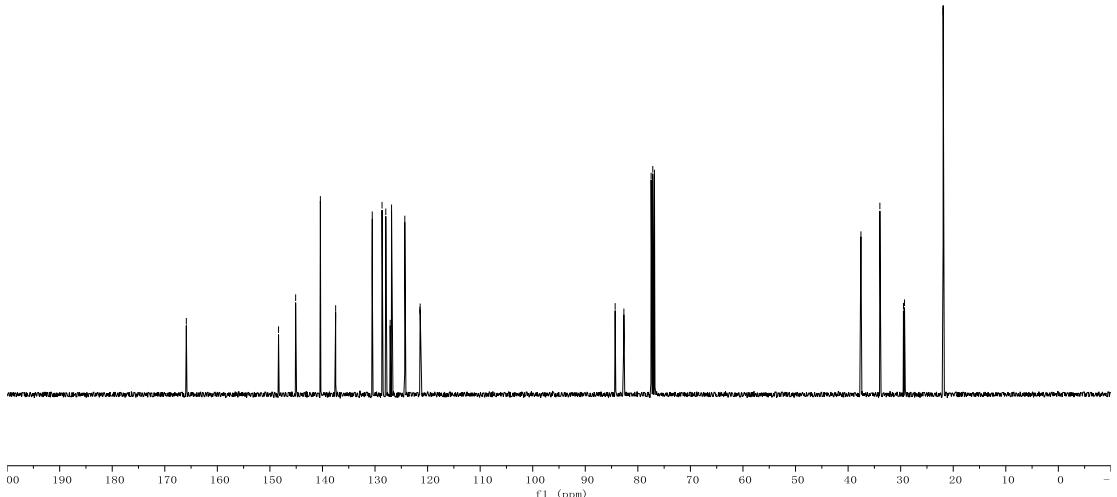
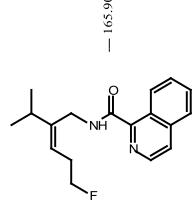
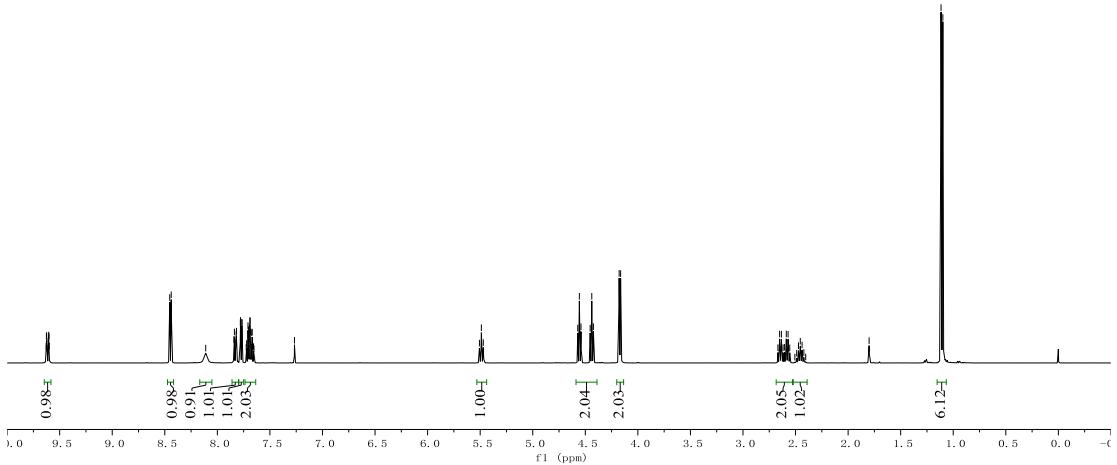


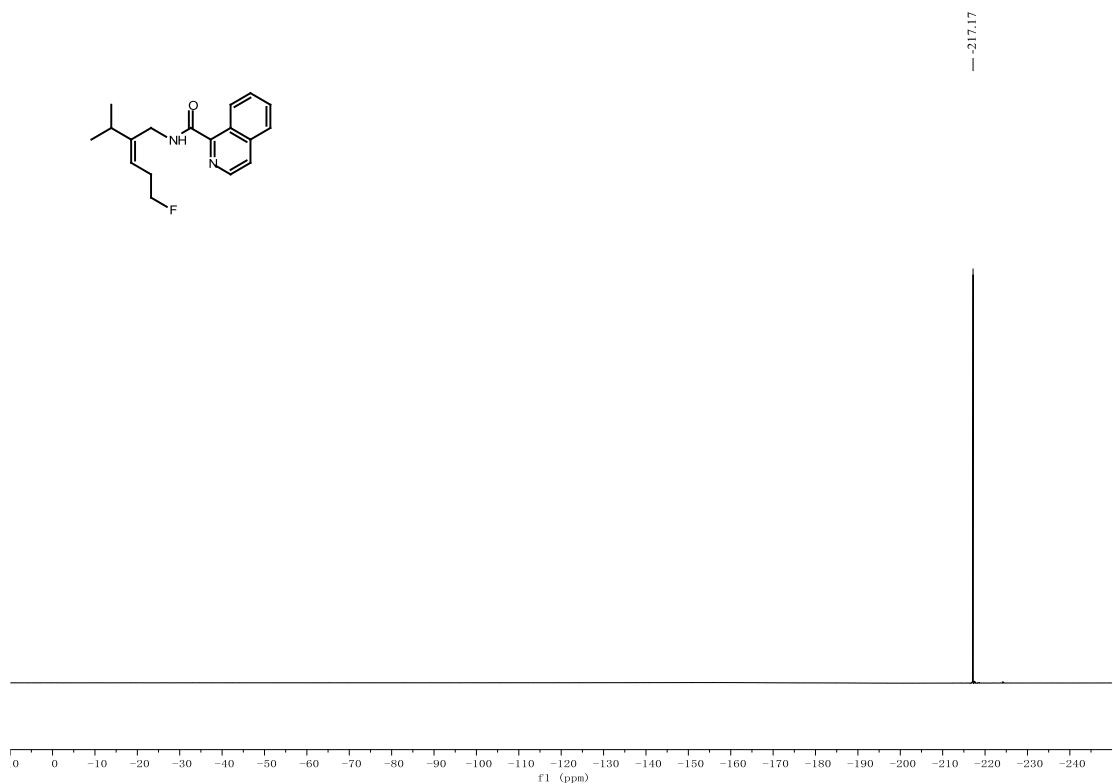


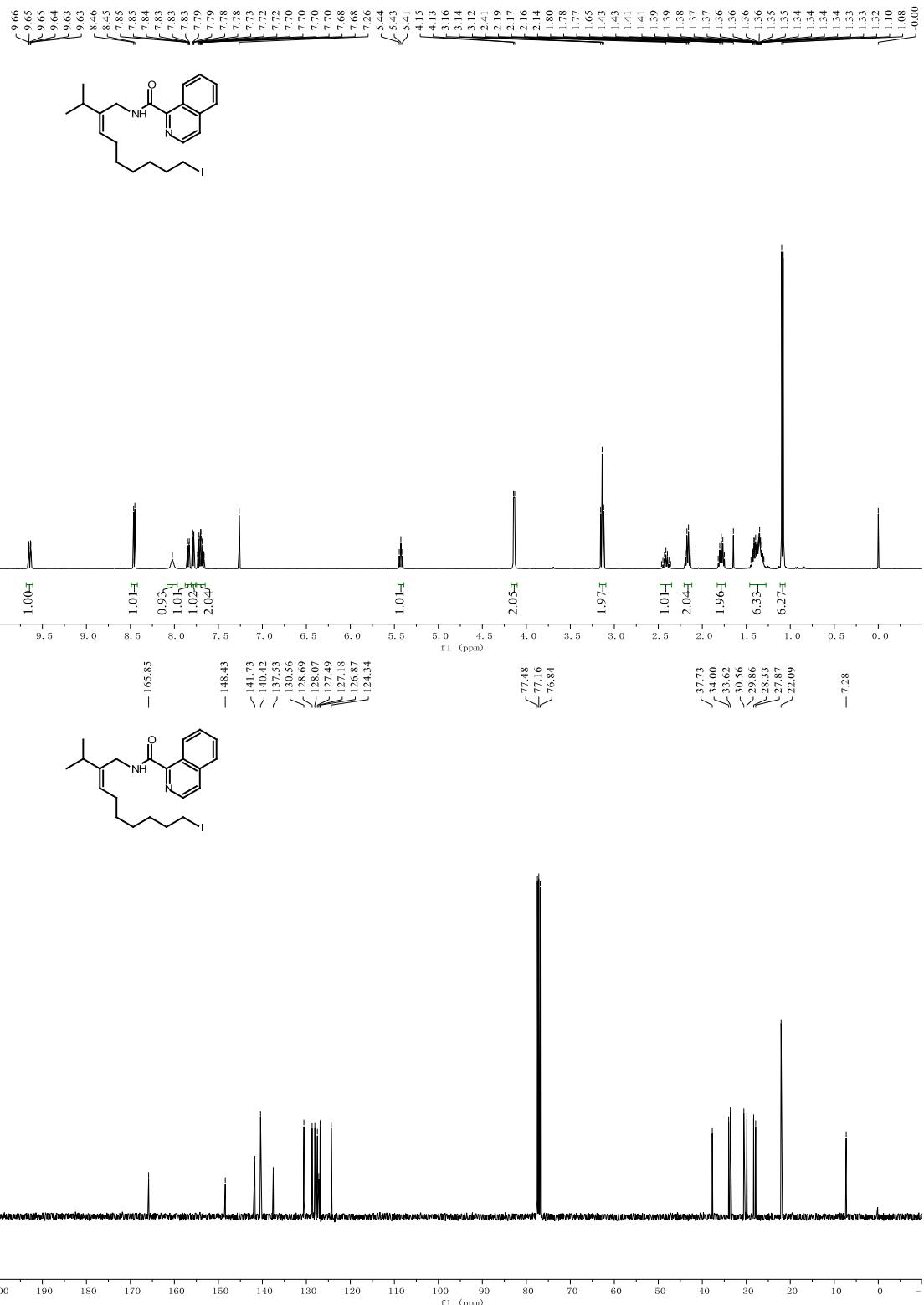


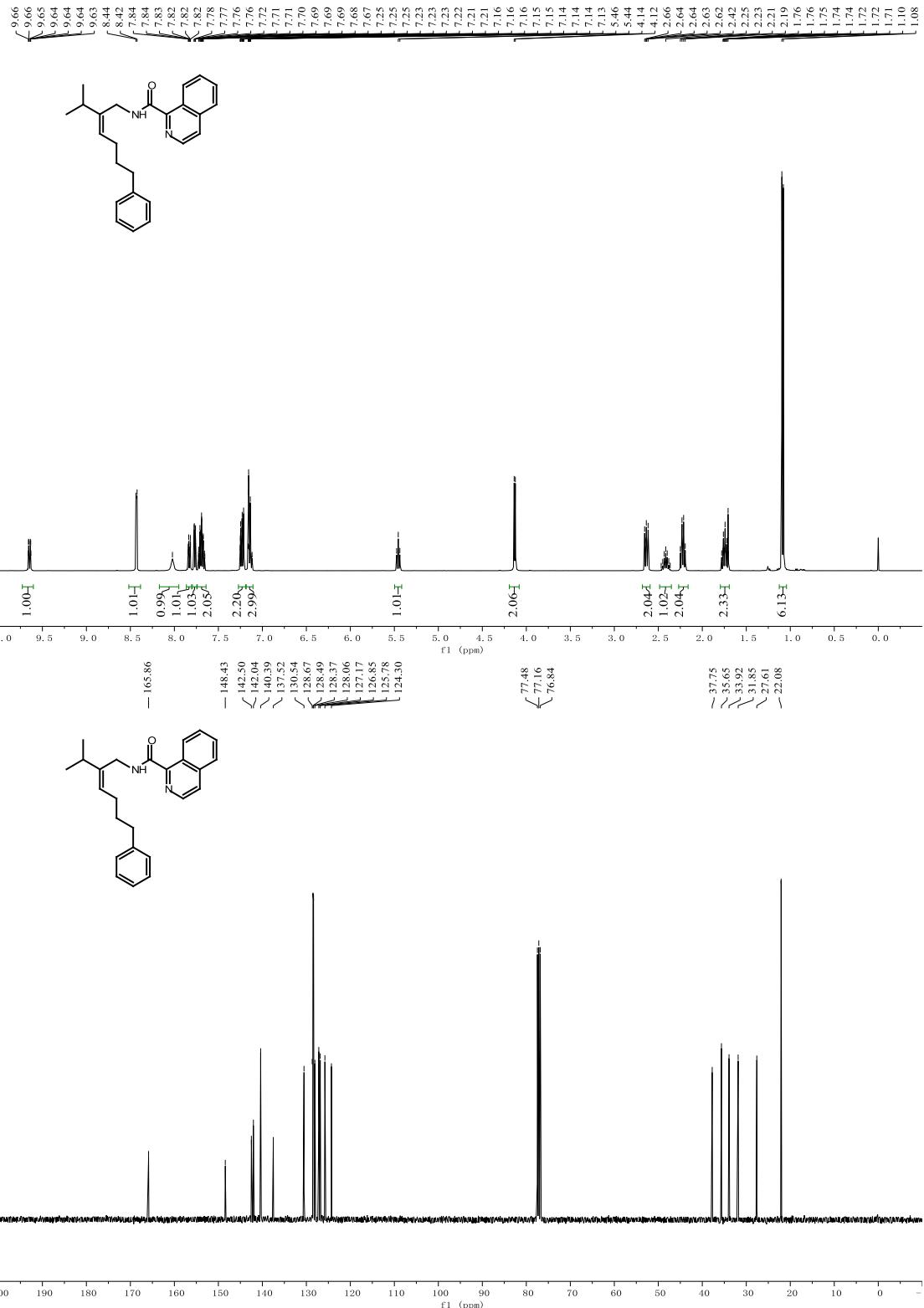


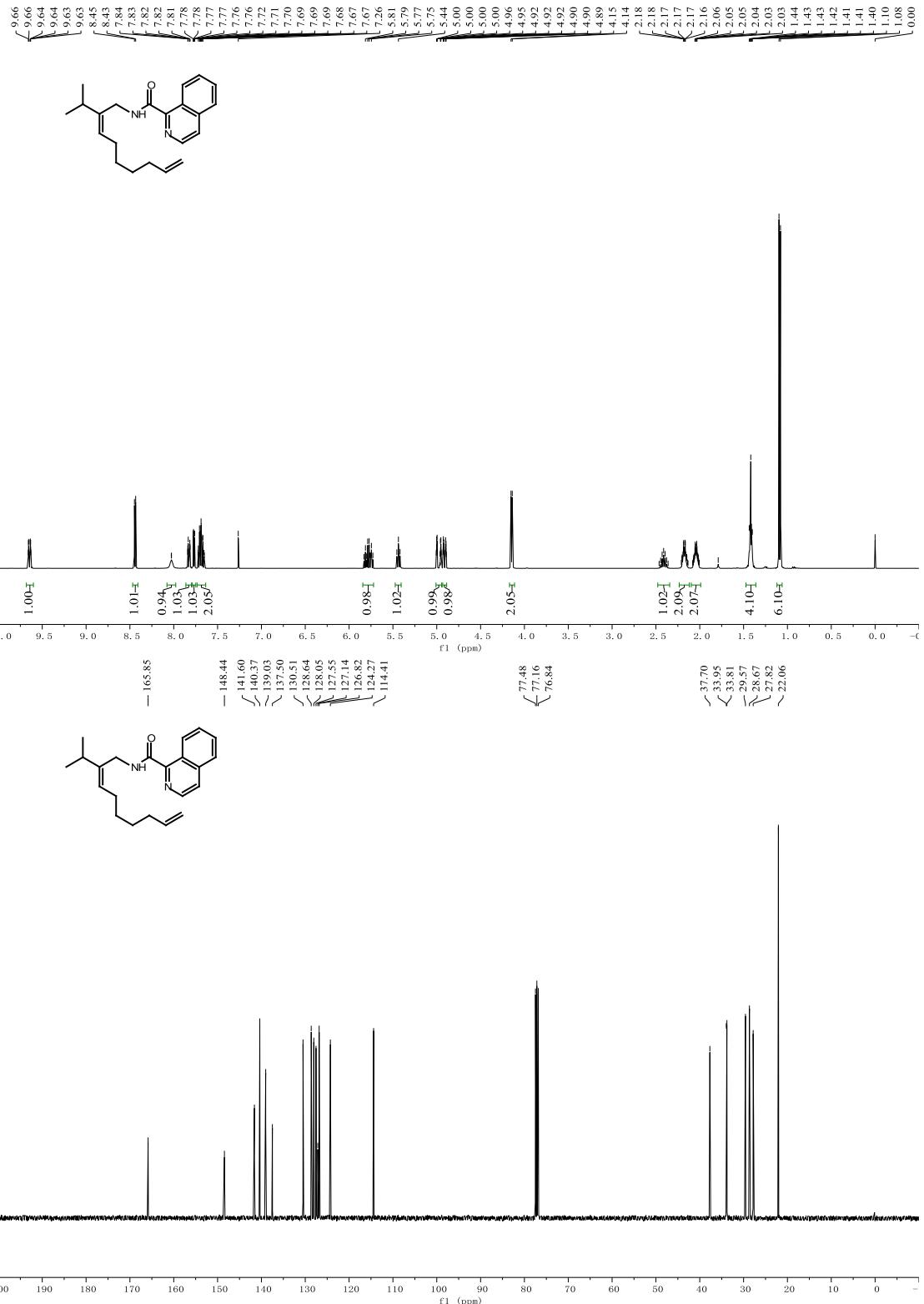


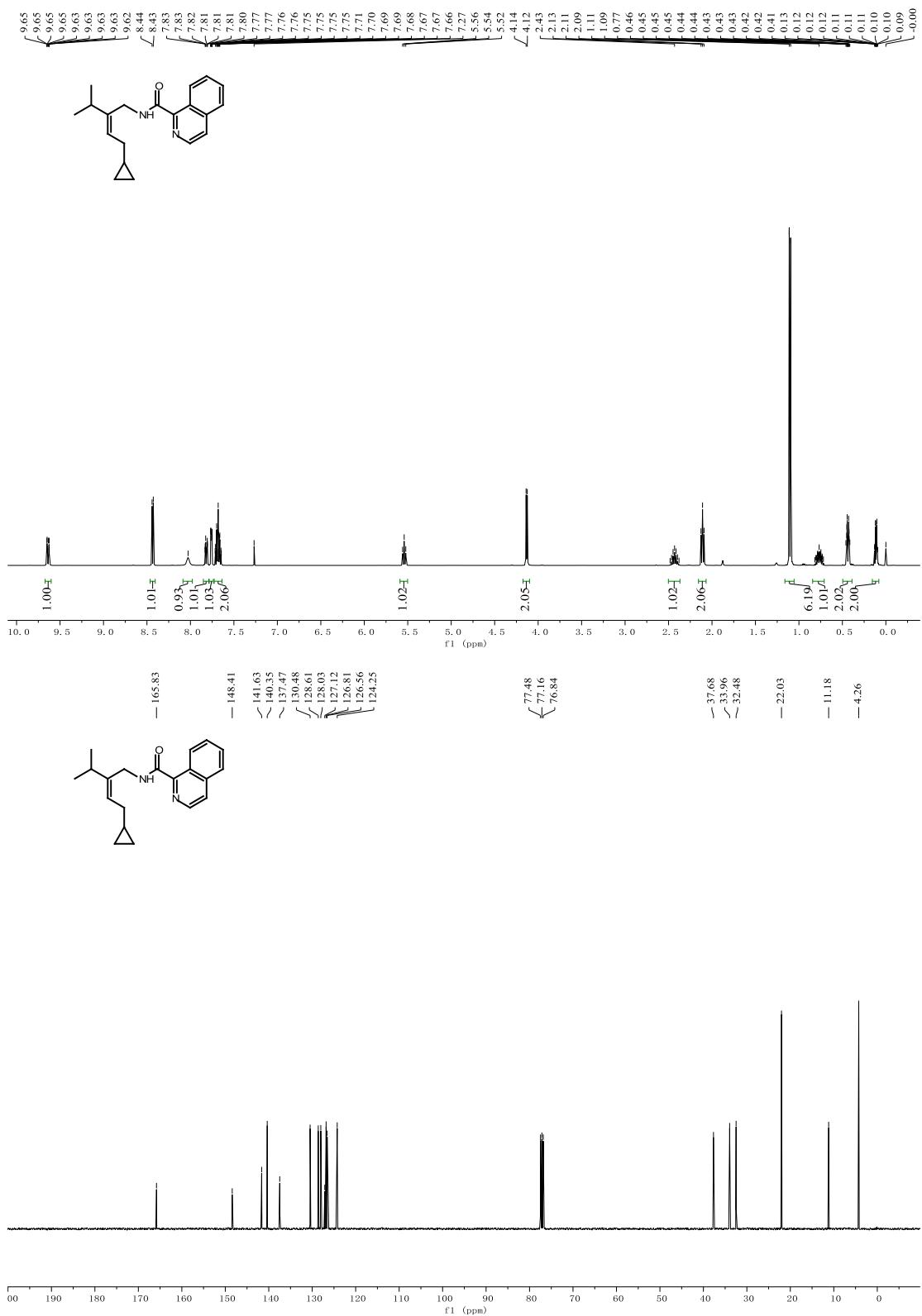


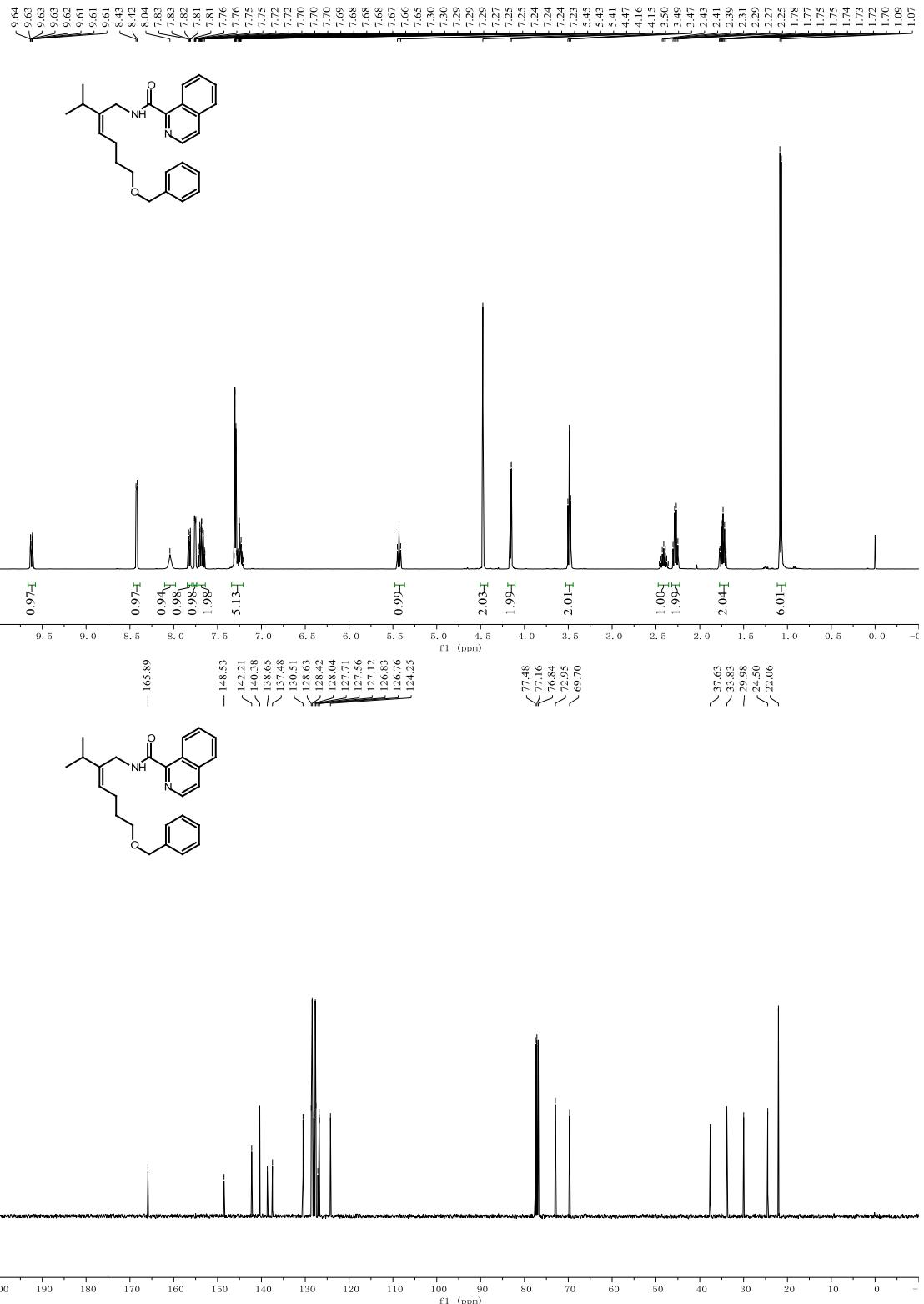


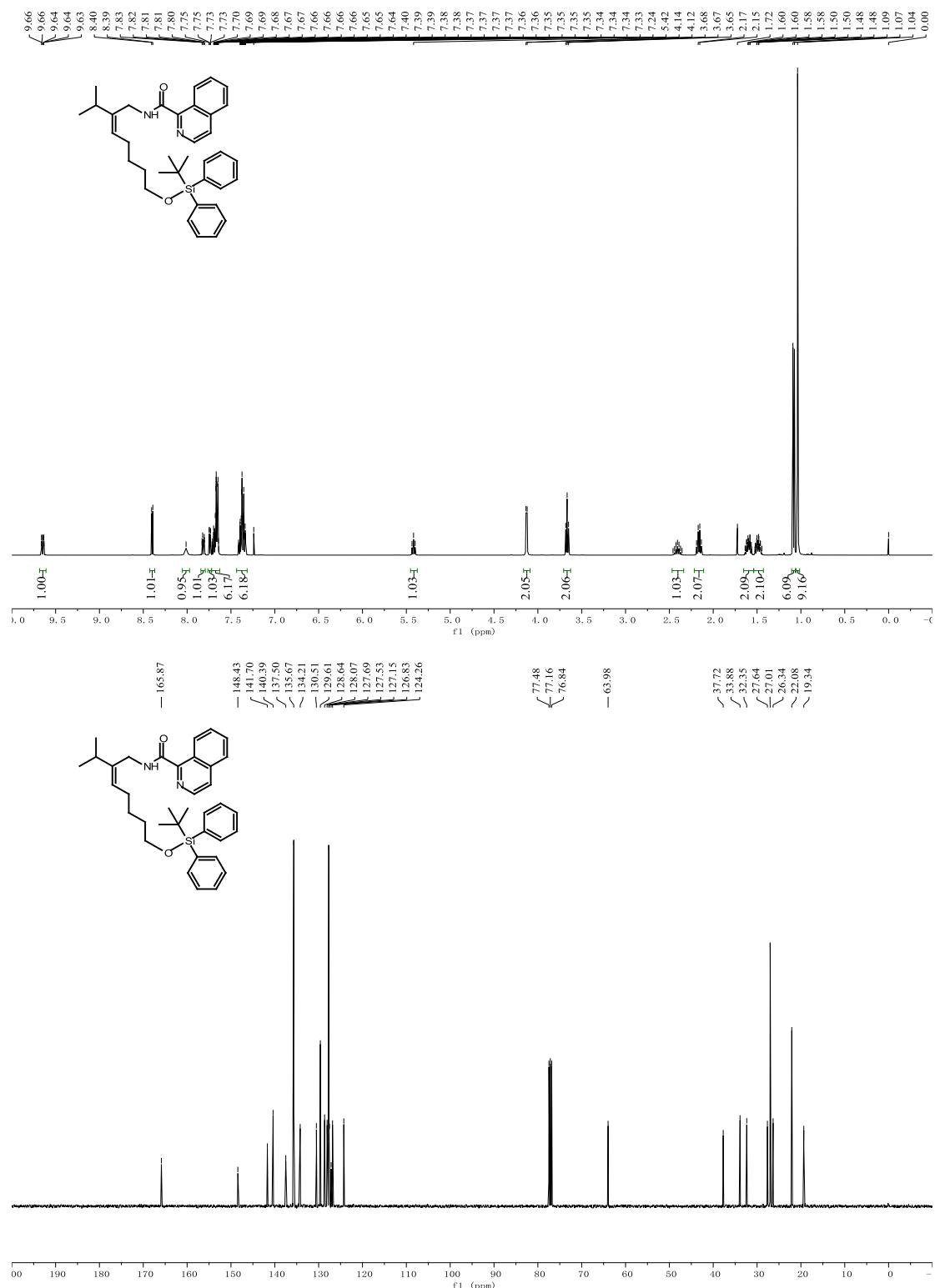


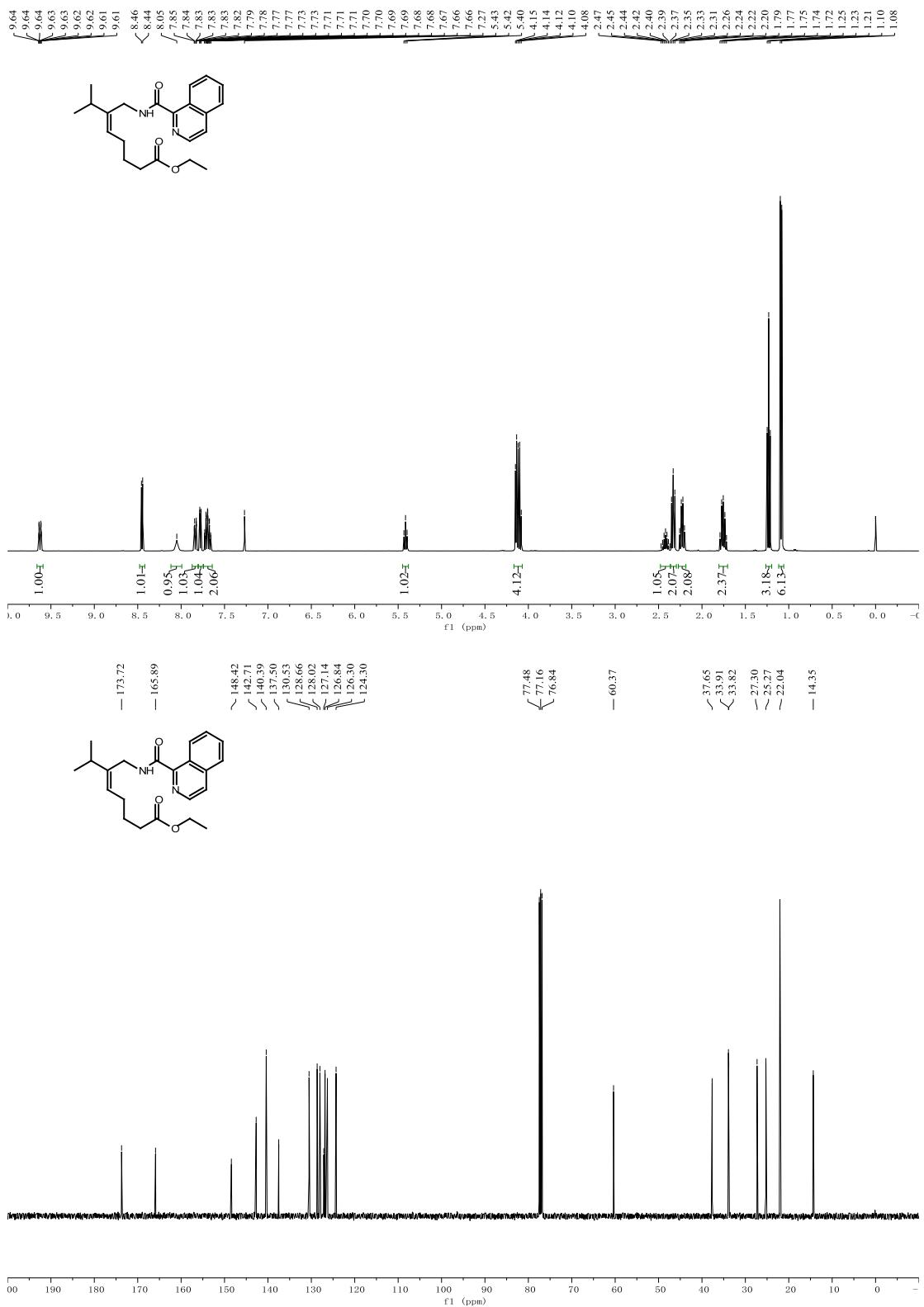


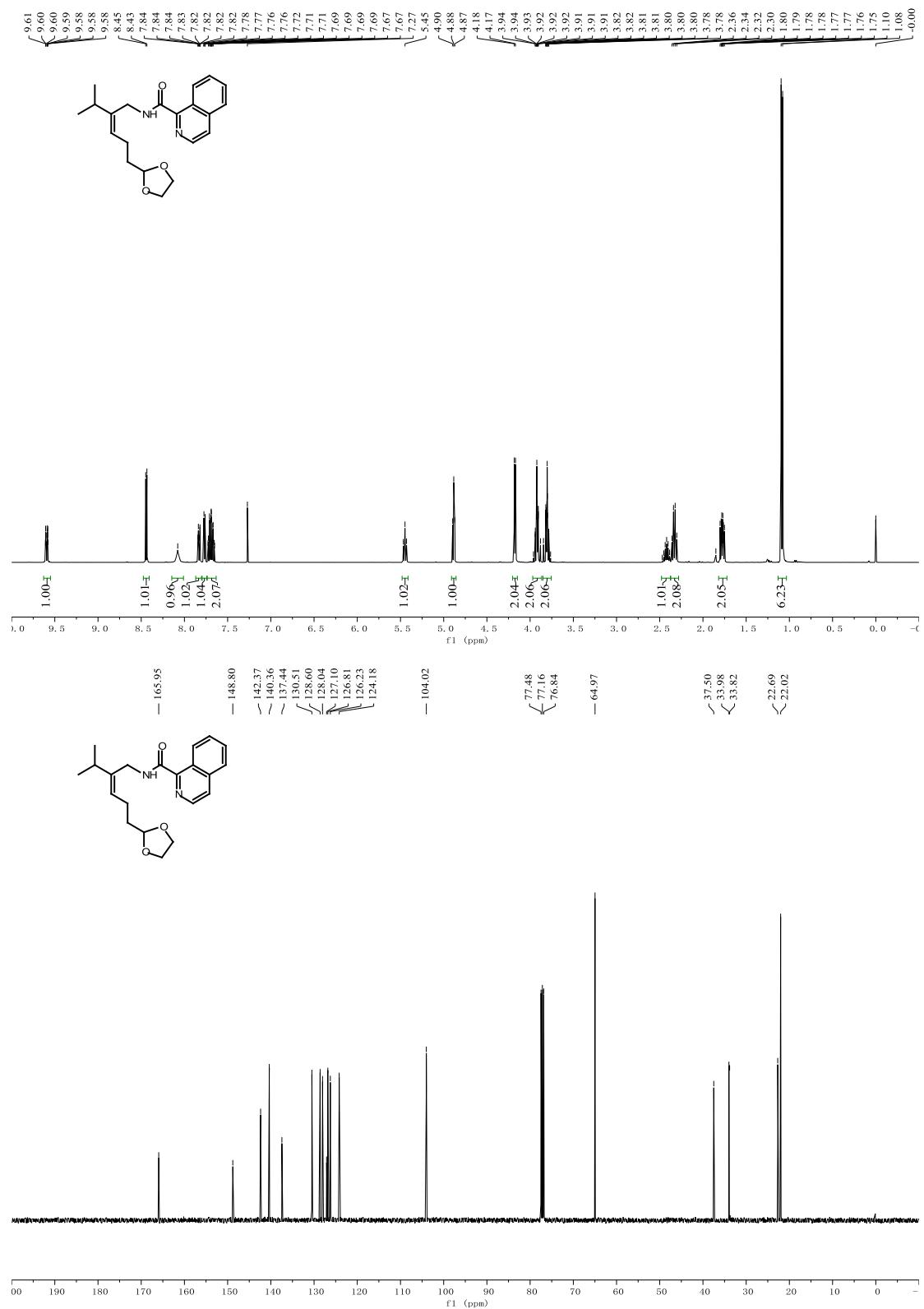


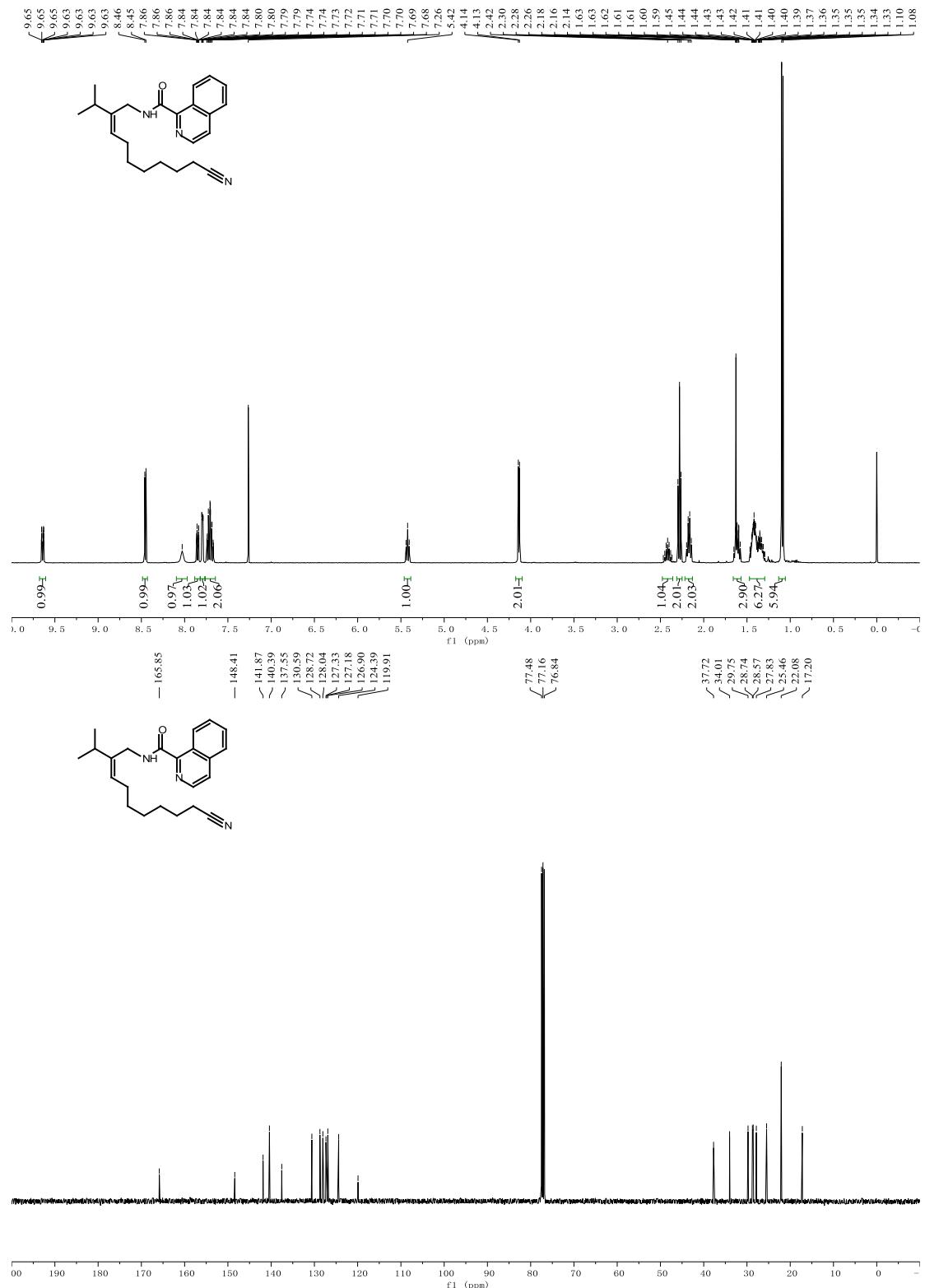


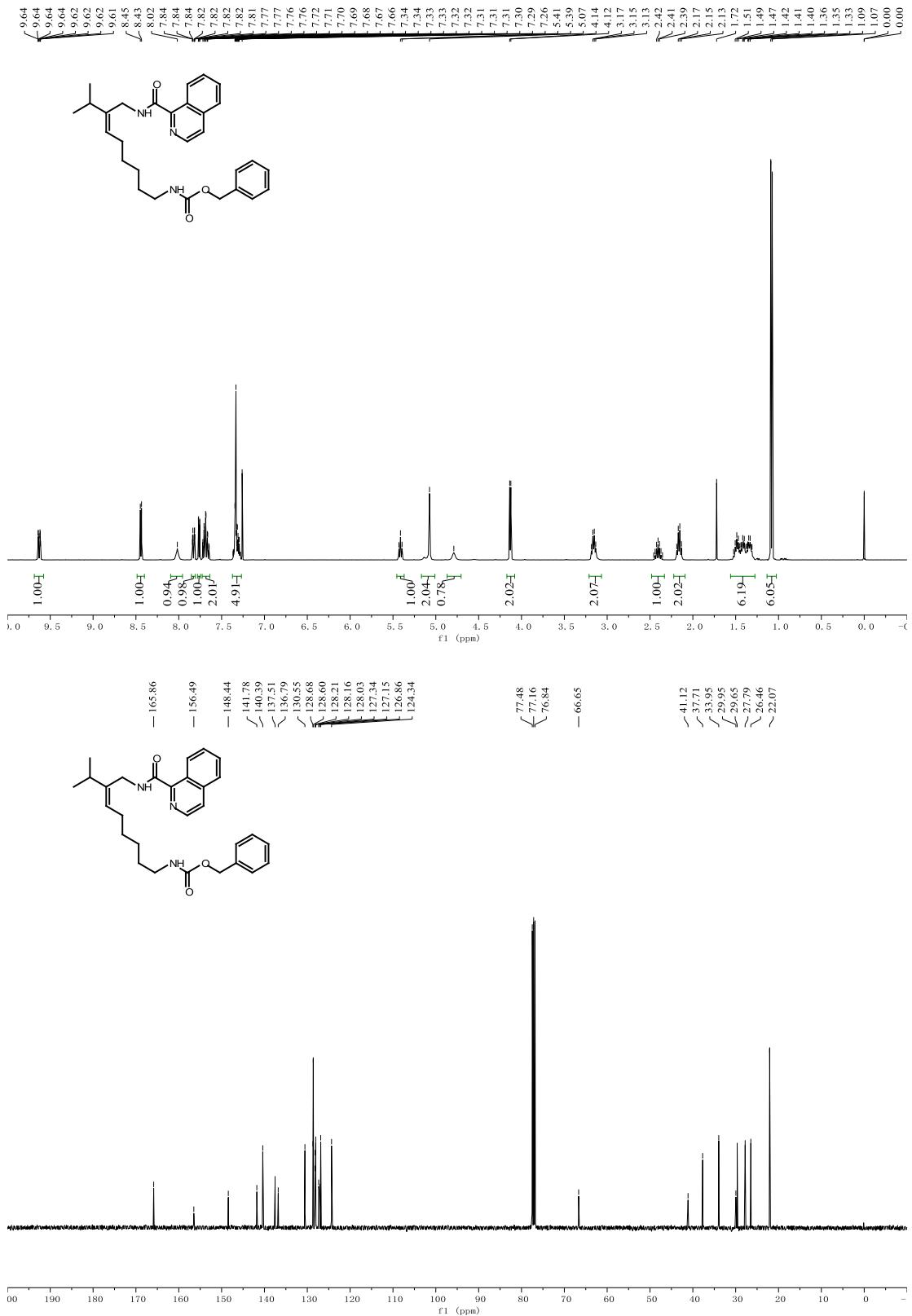


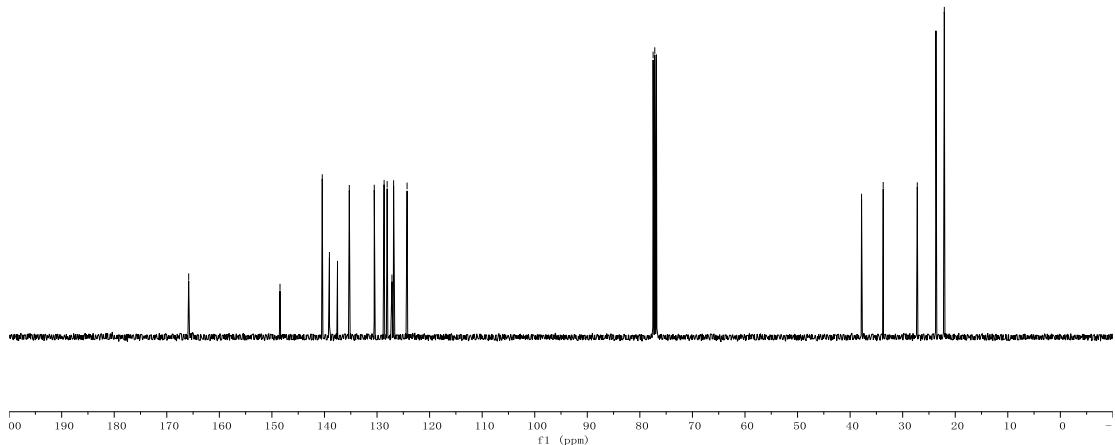
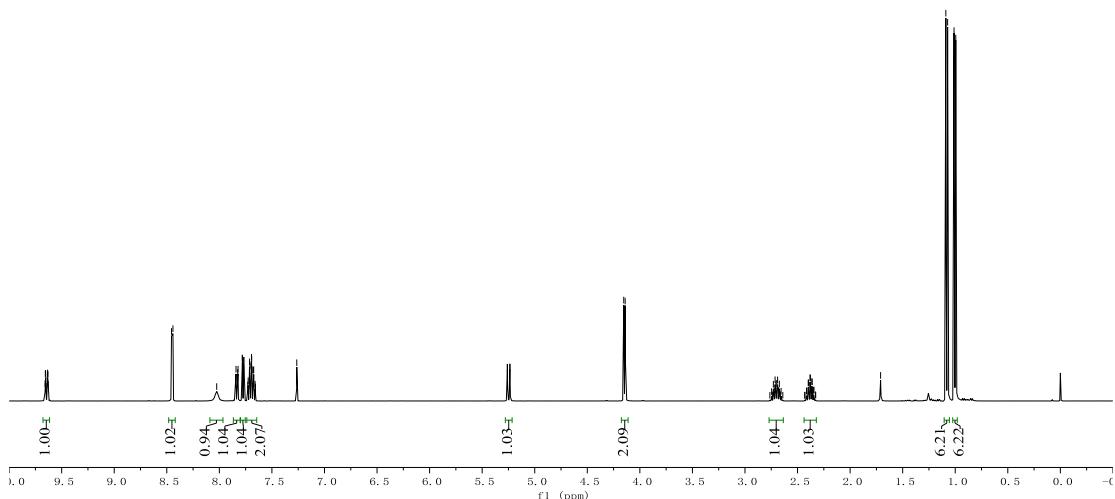
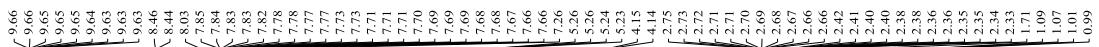


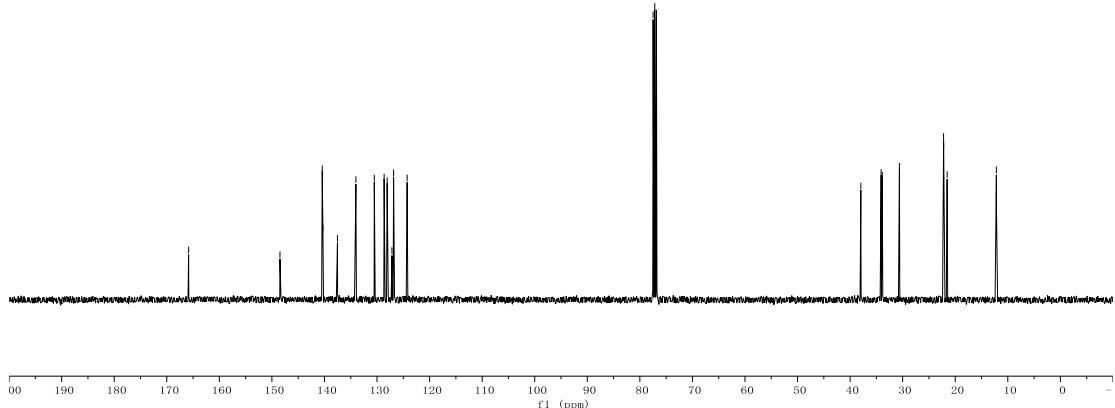
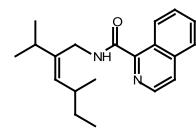
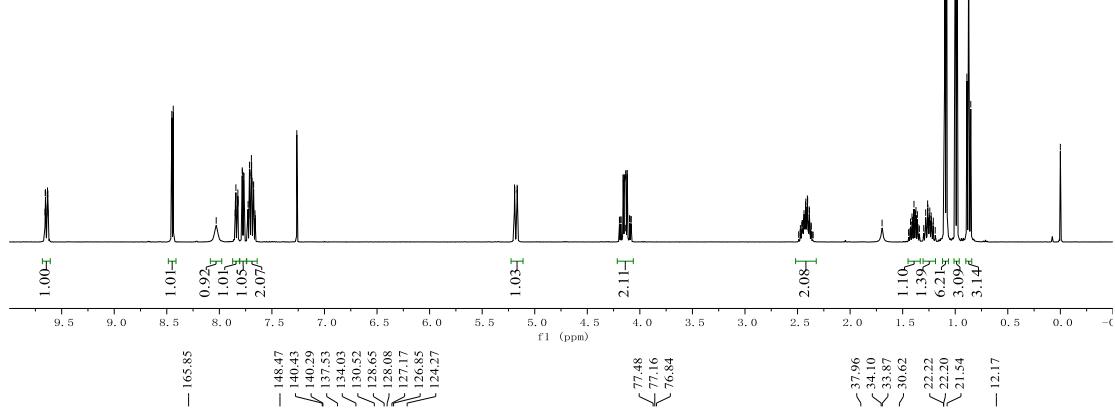
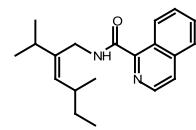
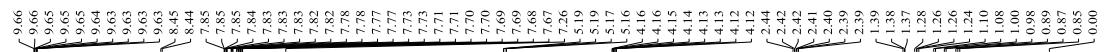


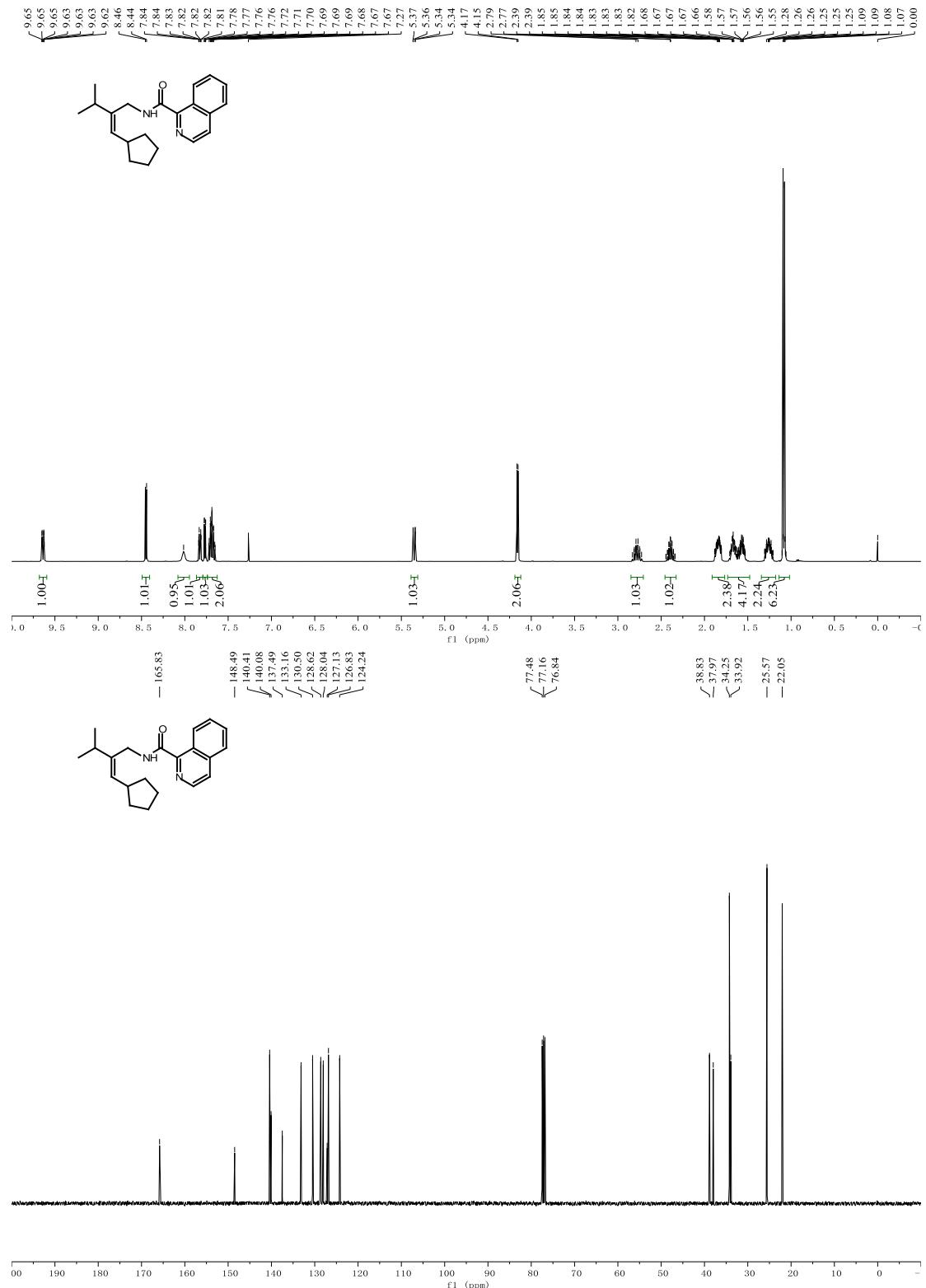


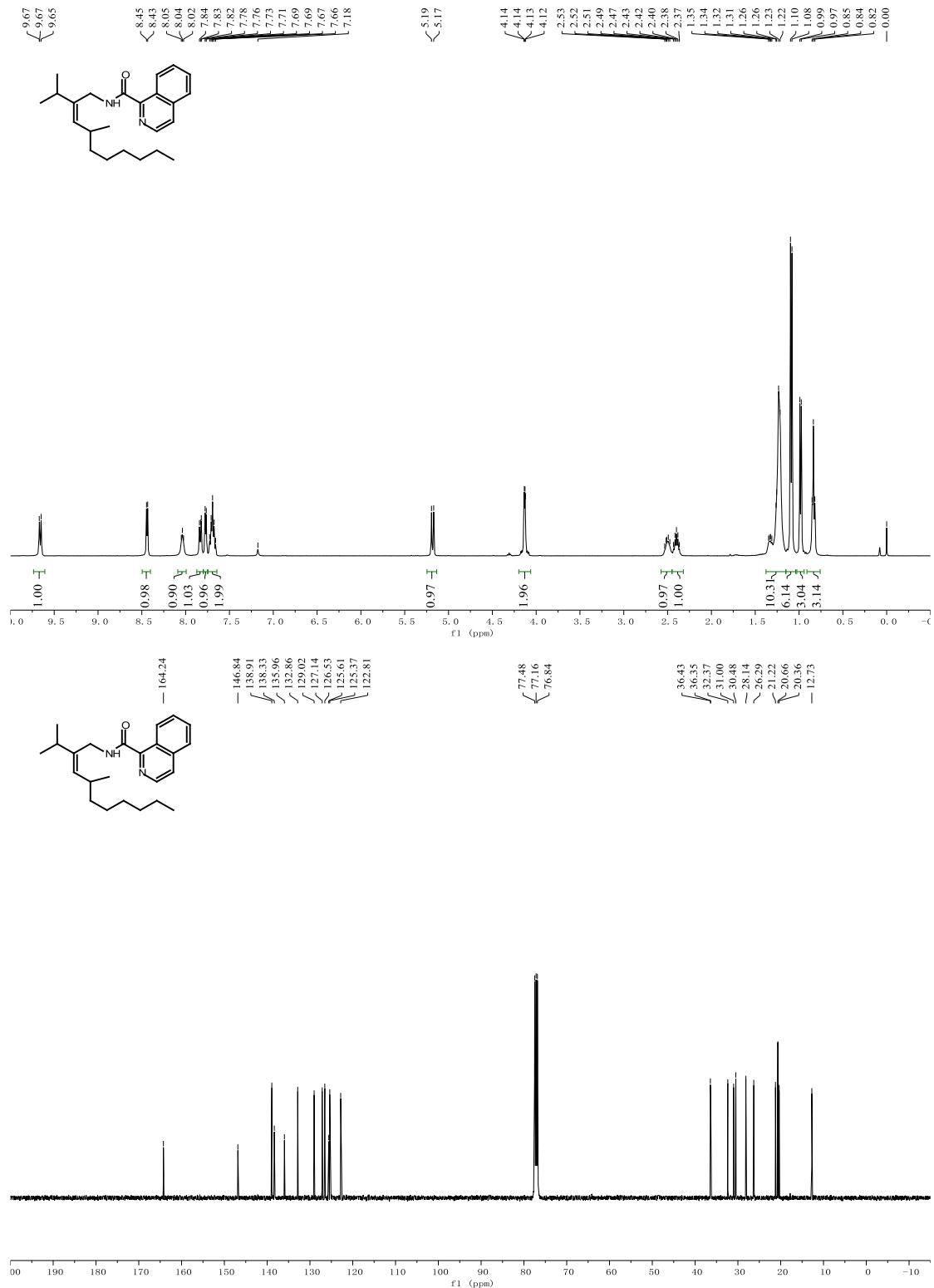


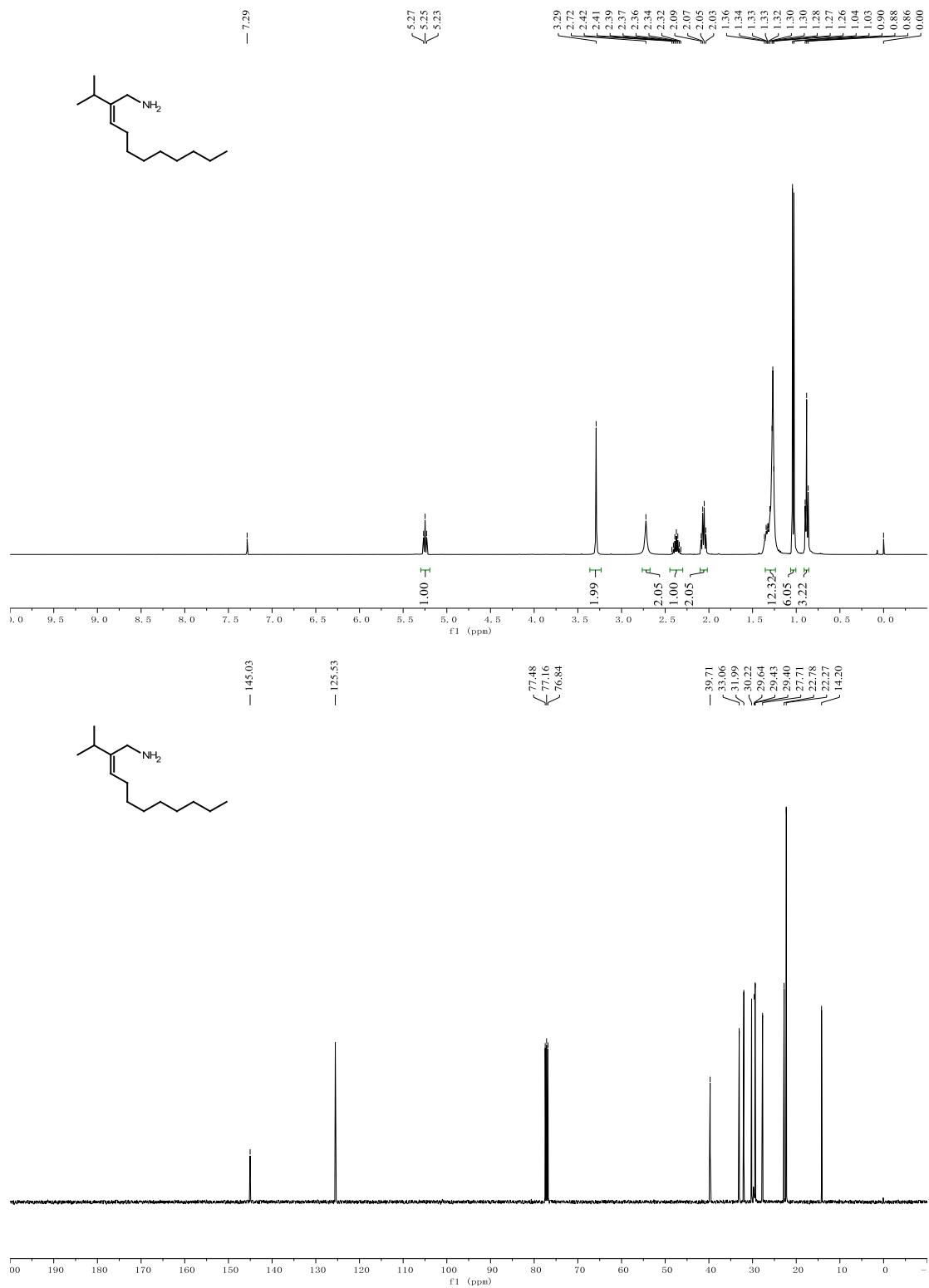


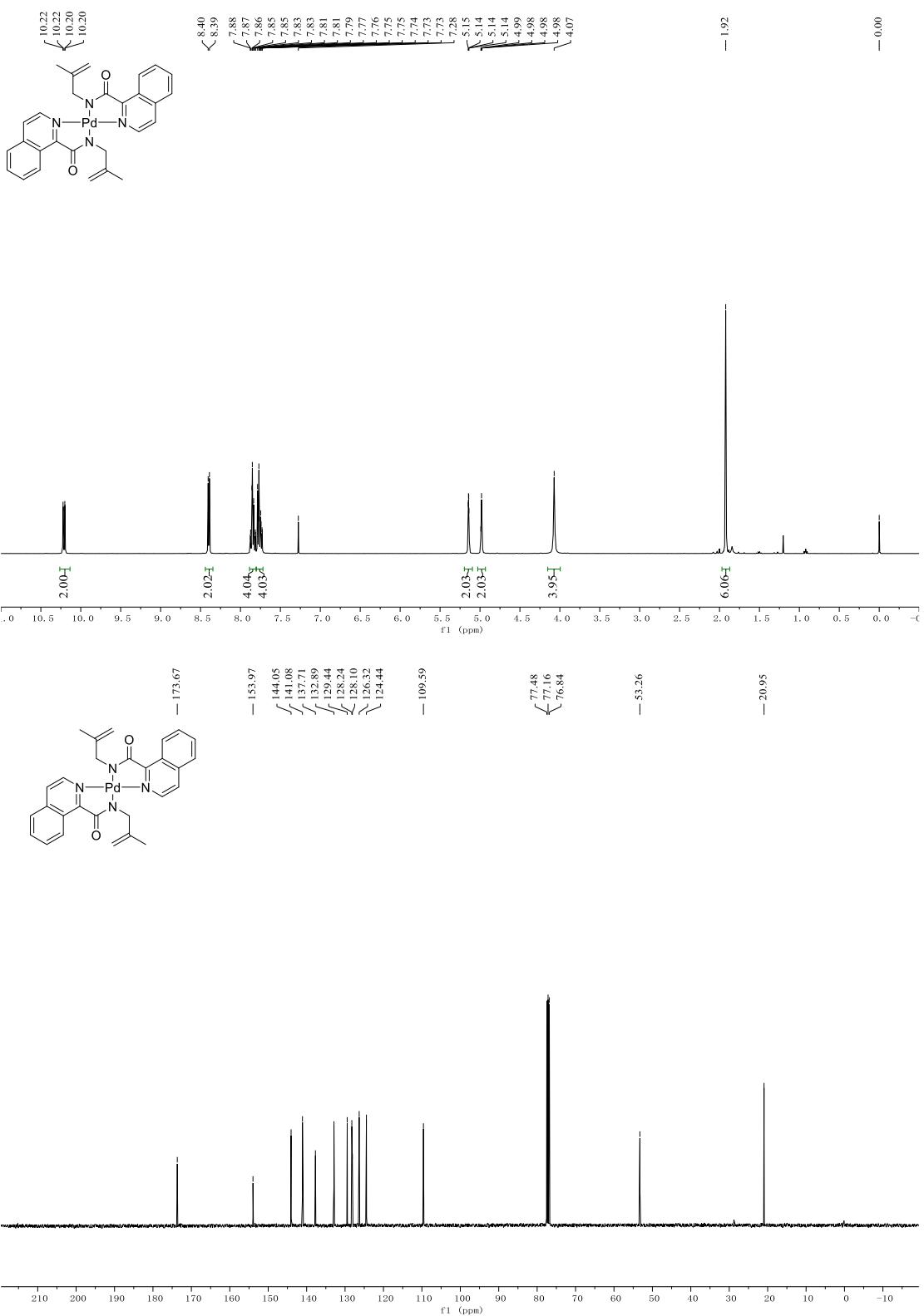


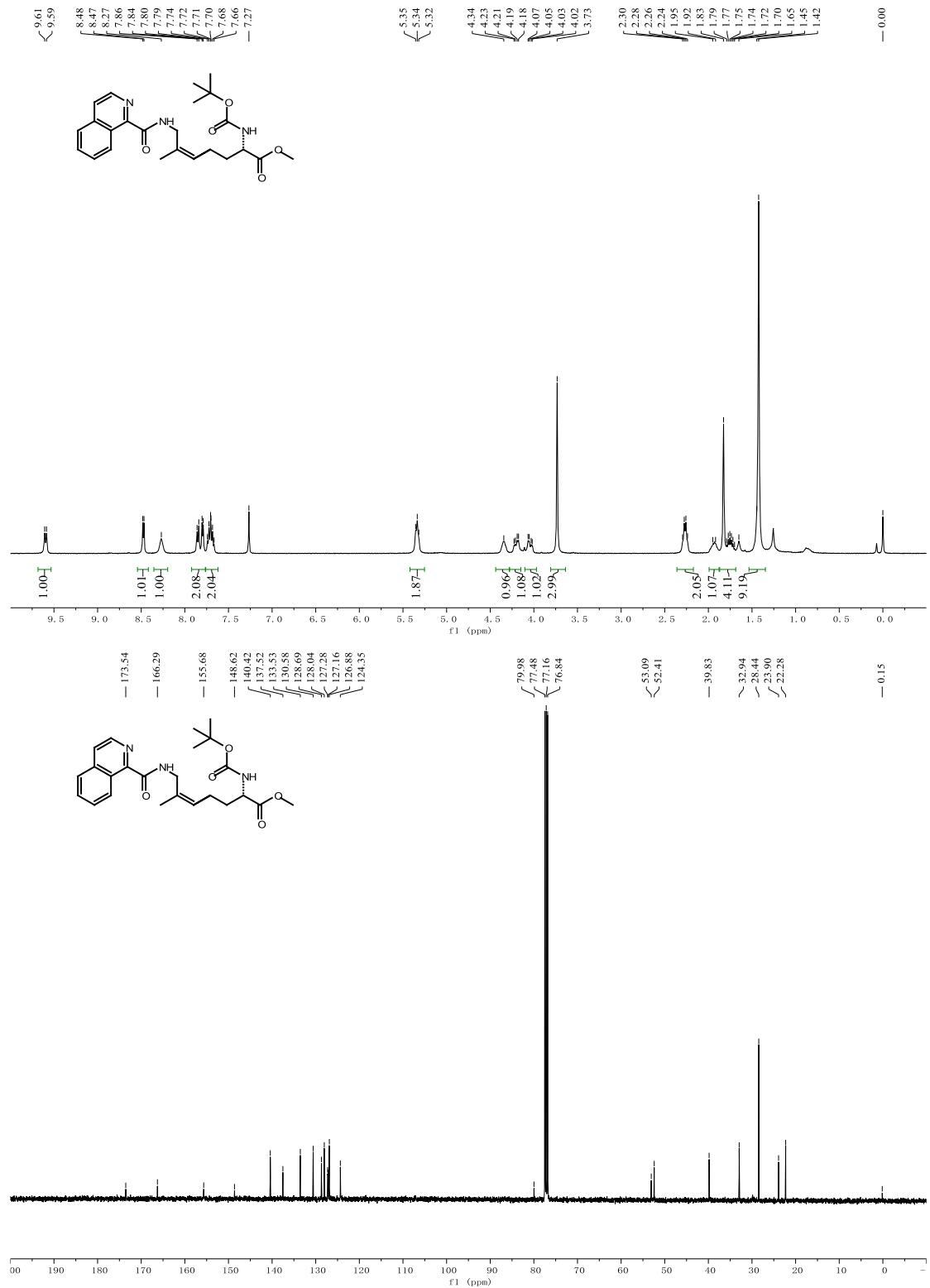












4. References

- (1) Zhang, S.-Y.; Gang He, G.; Zhao, Y.-S.; Wright, K.; Nack, W. A.; Chen, G. Efficient Alkyl Ether Synthesis via Palladium-Catalyzed, Picolinamide-Directed Alkoxylation of Unactivated C(sp³)-H and C(sp²)-H Bonds at Remote Positions. *J. Am. Chem. Soc.* **2012**, *134*, 7313–7316.
- (2) Takeda, Y.; Okumura, S.; Tone, S.; Sasaki, I.; Minakata, S. Cyclative Atmospheric CO₂ Fixation by Unsaturated Amines with *t*-BuOI Leading to Cyclic Carbamates. *Org. Lett.* **2012**, *14*, 4874–4877.
- (3) Hatano, M.; Nishimura, T.; Yorimitsu, H. Selective H/D Exchange at Vinyl and Methyldene Groups with D₂O Catalyzed by an Iridium Complex. *Org. Lett.* **2016**, *18*, 3674–3677.
- (4) Myers, M. C.; Iera, J. A.; Bang, J.-K.; Hara, T.; Saito, S.; Zambetti, G. P.; Appella D. H. A New Family of Small Molecules To Probe the Reactivation of Mutant p53. *J. Am. Chem. Soc.* **2005**, *127*, 6152–6153.
- (5) Seki, A.; Takahashi, Y.; Miyake, T. Synthesis of *cis*-3-Arylated Cycloalkylamines through Palladium-Catalyzed Methylenes sp³ Carbon–Hydrogen Bond Activation. *Tetrahedron Lett.* **2014**, *55*, 2838–2841.
- (6) Morozova, V.; Skotnitzki, J.; Moriya, K.; Karaghiosoff, K.; Knochel, P. Preparation of Optically Enriched Secondary Alkylolithium and Alkylcopper Reagents—Synthesis of (–)-Lardolure and Siphonarienal. *Angew. Chem. Int. Ed.* **2018**, *57*, 5516–5519.