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Remote Alkylation of *N*-(Quinolin-8-yl)Benzamides with Alkyl Bromides via a Ruthenium(II)-Catalyzed C-H Bond Activation

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Electronic Supplementary Information (ESI)

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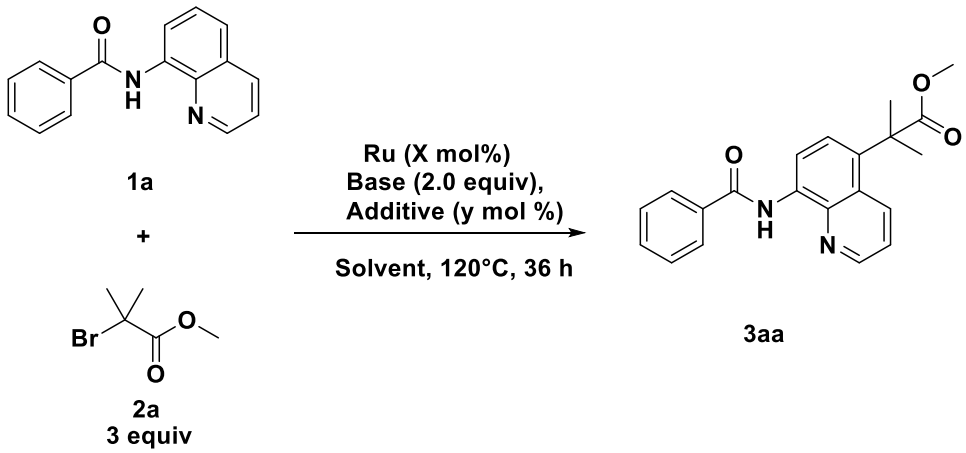
Optimization Studies

Table S1. Optimisation for Alkylation Reaction[a]



Entry	Solvent	Catalyst (mol %)	Base	Additive (mol %)	Yield (%)[b]
1	Toluene	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	MesCOOH (30)	N.R
2	Toluene	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	1-Ad-COOH(30)	N.R
3	Toluene	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	45
4	DCE	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	N.R
5	1,4 Dioxane	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	10[c]
6	DMF	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	<5[c]
7	MeCN	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	8[c]
8	DME	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	23
9	MeOH	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	28
10	THF	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	<5[c]
11	Cyclohexane	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	17
12	AcOH	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	10[c]
13	Benzene	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	41
14	*O*-Xylene	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	30

15	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	54
16	1,2 difluorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(5)	K_2CO_3	PPh_3 (40)	10[c]
17	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	K_2CO_3	PPh_3 (40)	63
18	Trifluorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	K_2CO_3	PPh_3 (40)	18
19	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	Li_2CO_3	PPh_3 (40)	13[c]
20	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	Na_2CO_3	PPh_3 (40)	30
21	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	Cs_2CO_3	PPh_3 (40)	53
22	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	$NaHCO_3$	PPh_3 (40)	16
23	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	K_3PO_4	PPh_3 (40)	23
24	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	NaOAc	PPh_3 (40)	46
25	**1,2dichlorobenzene**	**[Ru (*p*-cymene) Cl_2]$_2$(10)**	**KOAc**	**PPh_3 (40)**	**70**
26	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	KOAc	PCy_3 (40)	NR
27	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	KOAc	P(furyl)$_3$(40)	NR
28	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	KOAc	P(*O*-Tol)$_3$ (40)	NR
29	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	KOAc	P(OEt)$_3$(40)	NR
30	1,2 dichlorobenzene	[Ru (*p*-cymene) Cl_2]$_2$(10)	KOAc	-	NR
31	1,2 dichlorobenzene	-	KOAc	PPh_3 (40)	NR

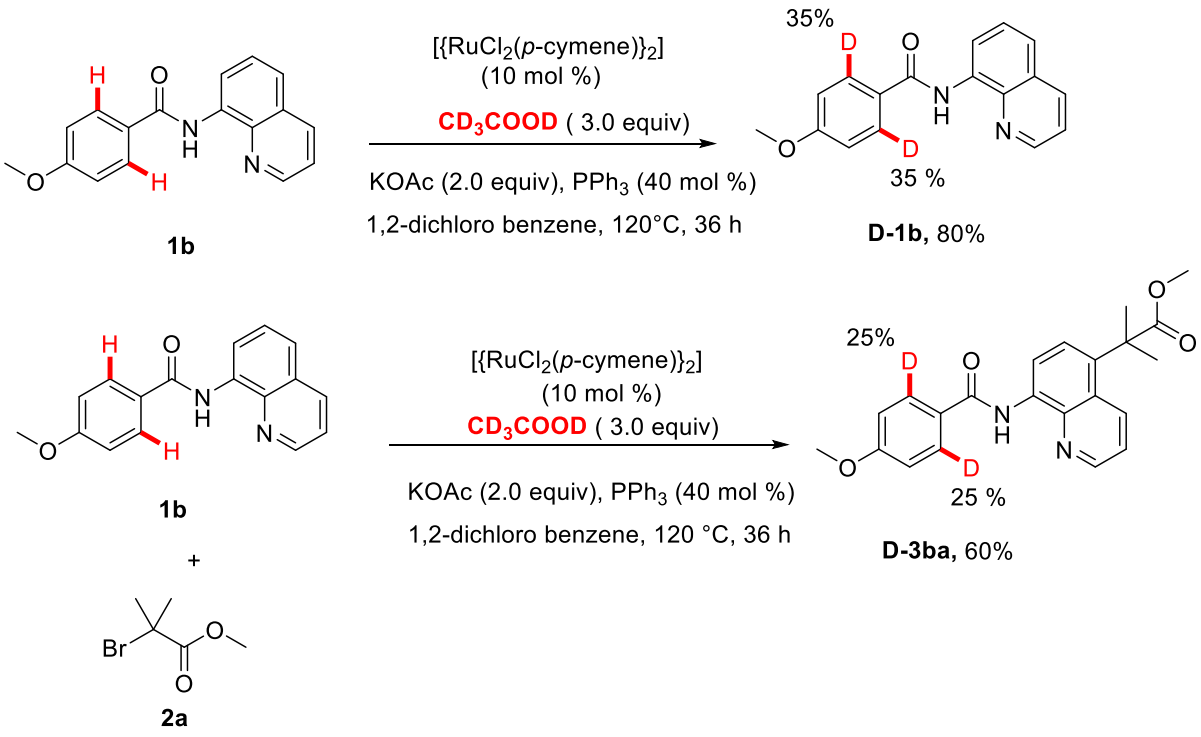
[a]All reactions were carried out using **1a** (75 mg), **2a** (3.0 equiv), Base (2.0 equiv), additive (40 mol%) in solvent (3.0 mL) under N_2 at 120 °C for 36 h. [b]Isolated yield. [c] GC yield.

Mechanistic Investigation

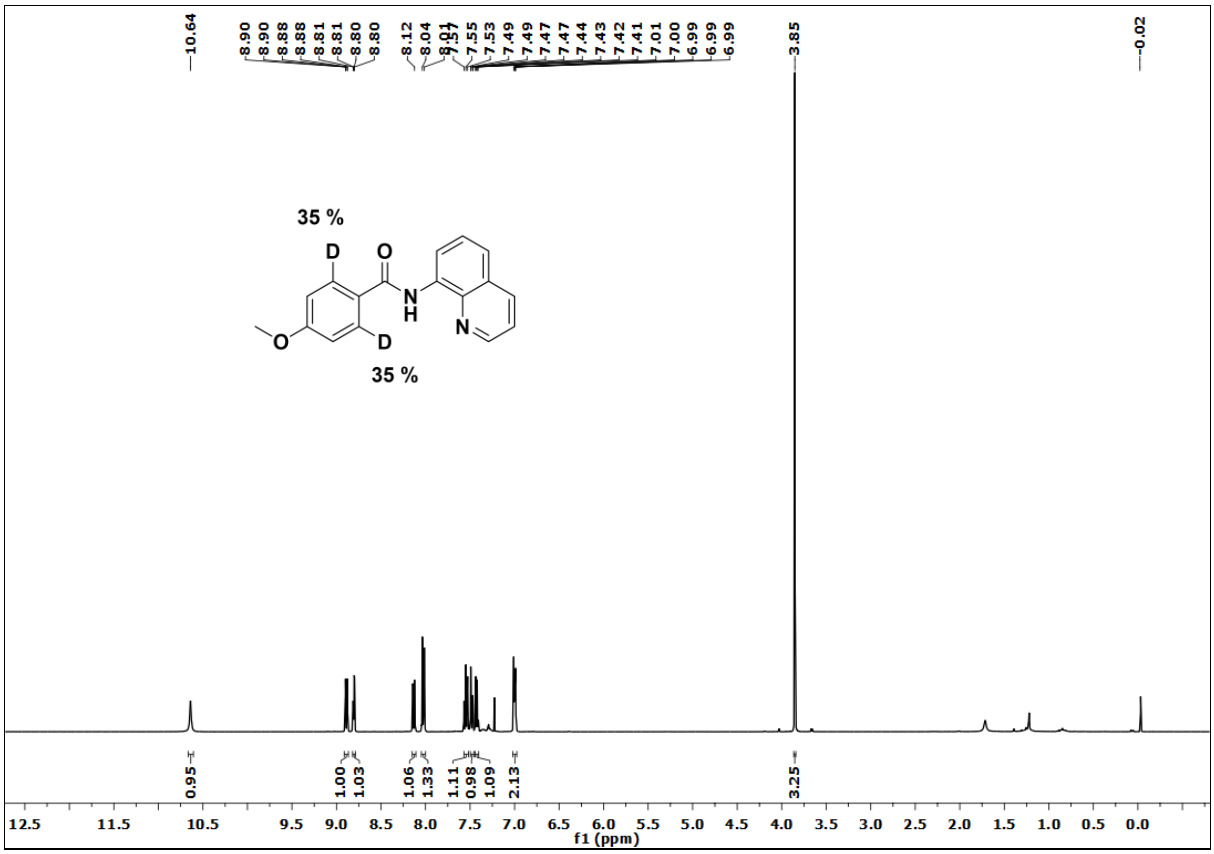
Deuterium studies

Treatment of **1b** with CD_3COOD under similar reaction conditions without **2a** gave product **D-3b** in 80% yield in which 35% of deuterium incorporation was observed at the both *ortho* C-H bonds. Meanwhile, the reaction of **1b** with **2a** in the presence of CD_3COOD provided the expected product **D-3ba** in 60% yield in which 25% of deuterium incorporation was observed at the both *ortho* C-H bonds of phenyl group. These results also clearly reveal that the C-H bond activation as a key intermediate in the reaction as well as it is the reversible process.

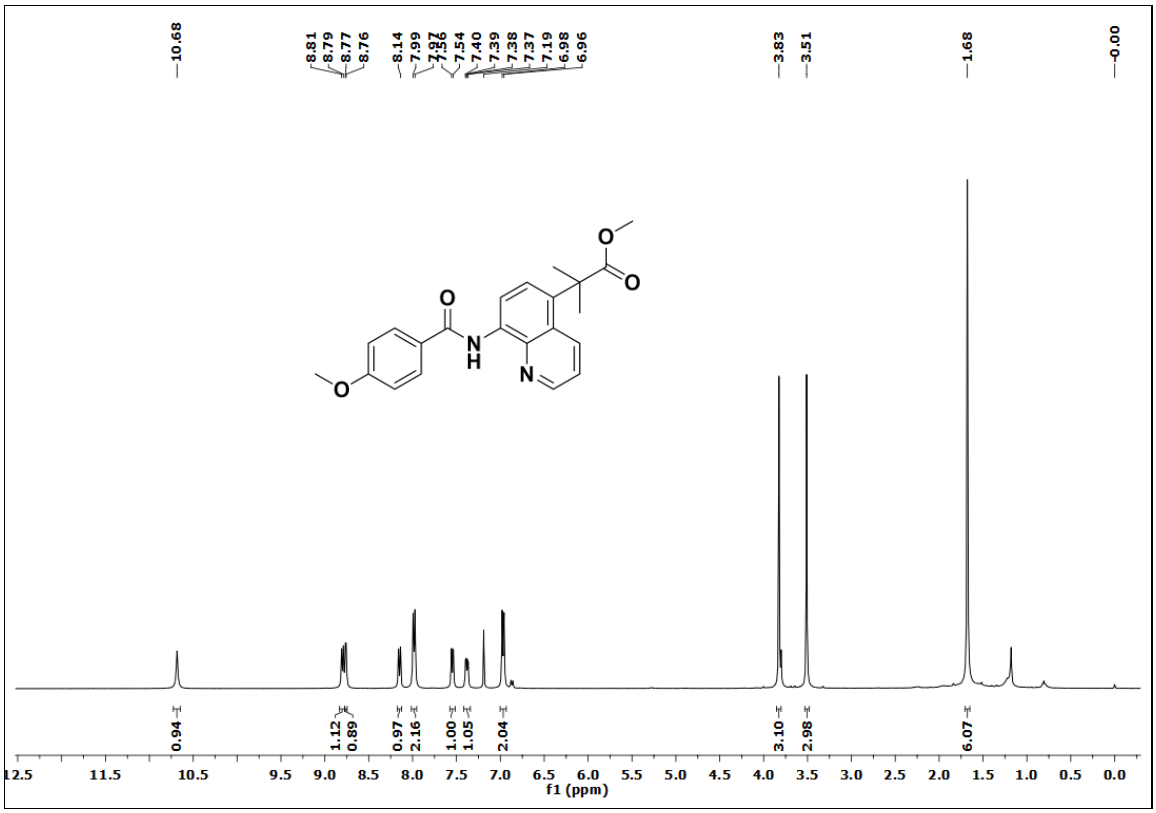
Procedure: The general reaction procedure was followed and CD_3COOD (3.0 equiv) was added via syringe before closing a screw cap in the tube.



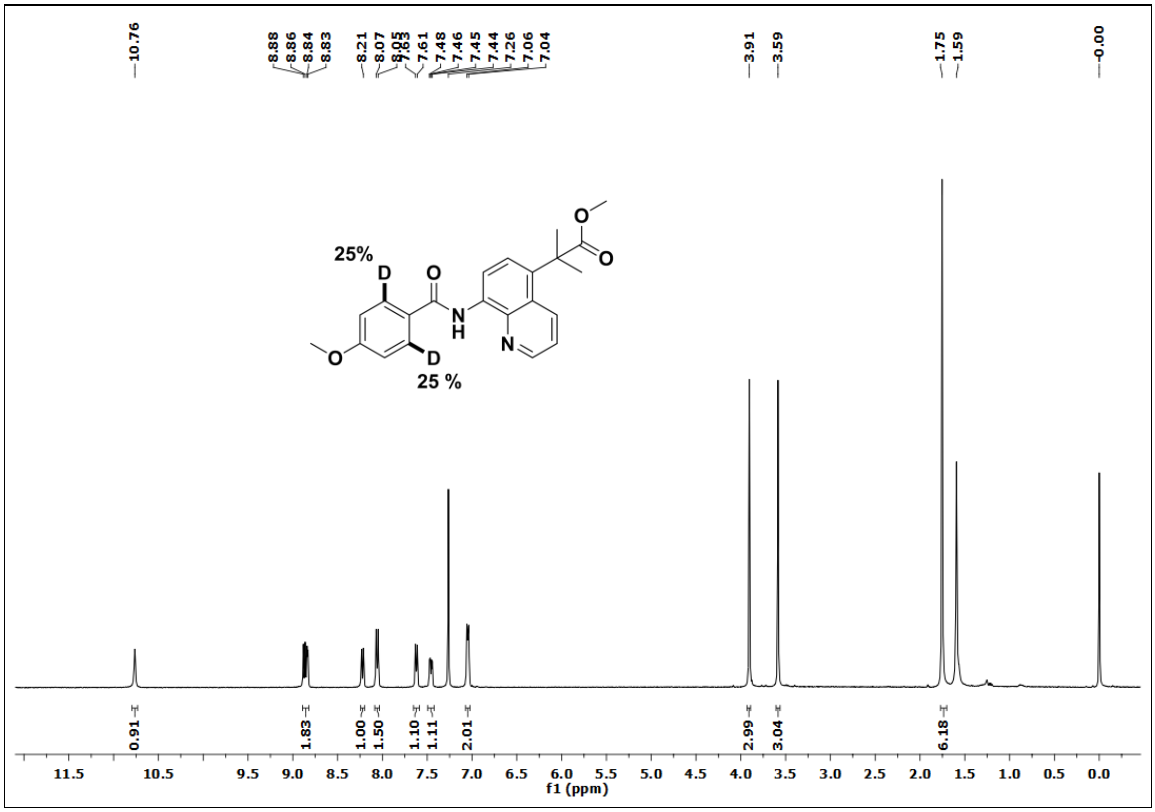
^{1}H NMR Spectra of Compound **D-1b** (DMSO-d_6 was used)**.**



^{1}H NMR Spectrum of Compound **3ba** ($CDCl_3$ was used)**.**



^{1}H NMR Spectra of Compound **D-3ba** ($CDCl_3$ was used)**.**

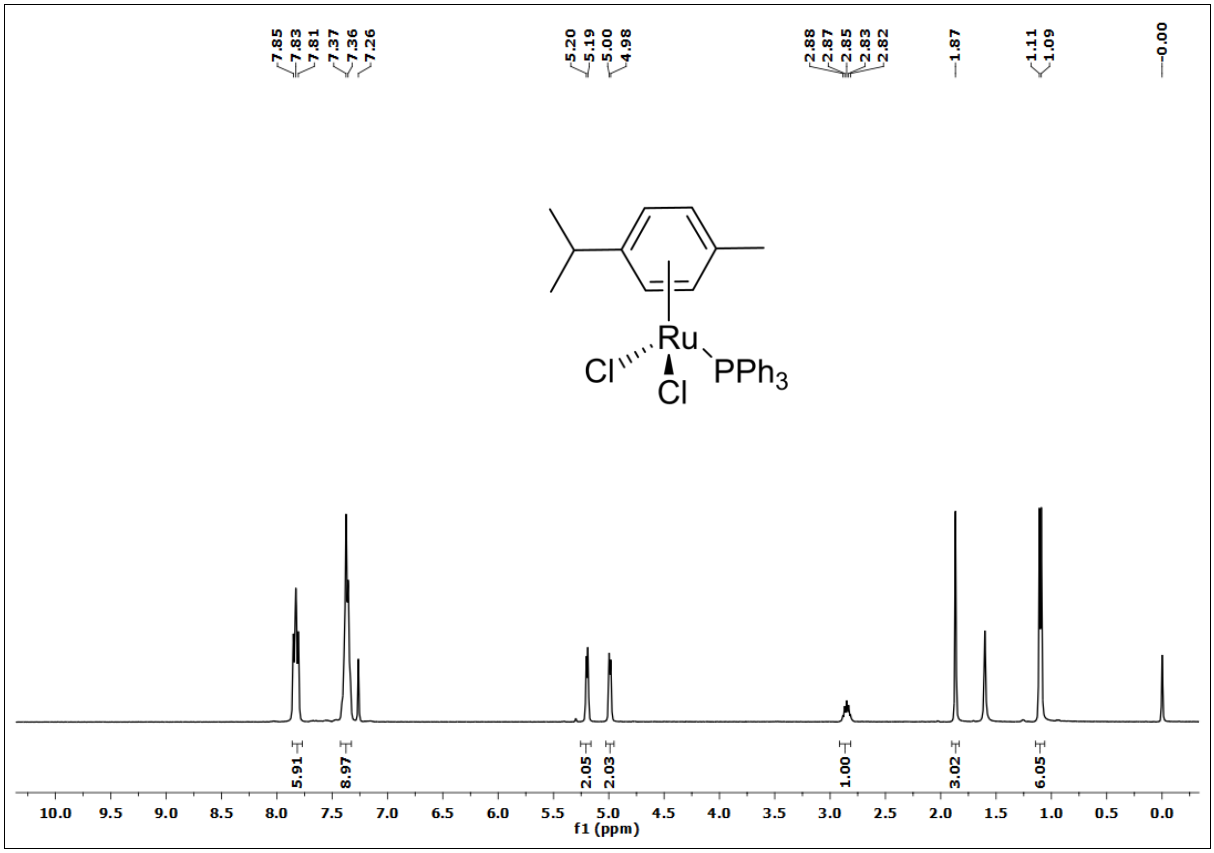


Intermediate Isolation

Procedure for the Preparation of Phosphine complex 4.

Phosphine complex **4** is prepared by the procedure mentioned in the literature.[3]

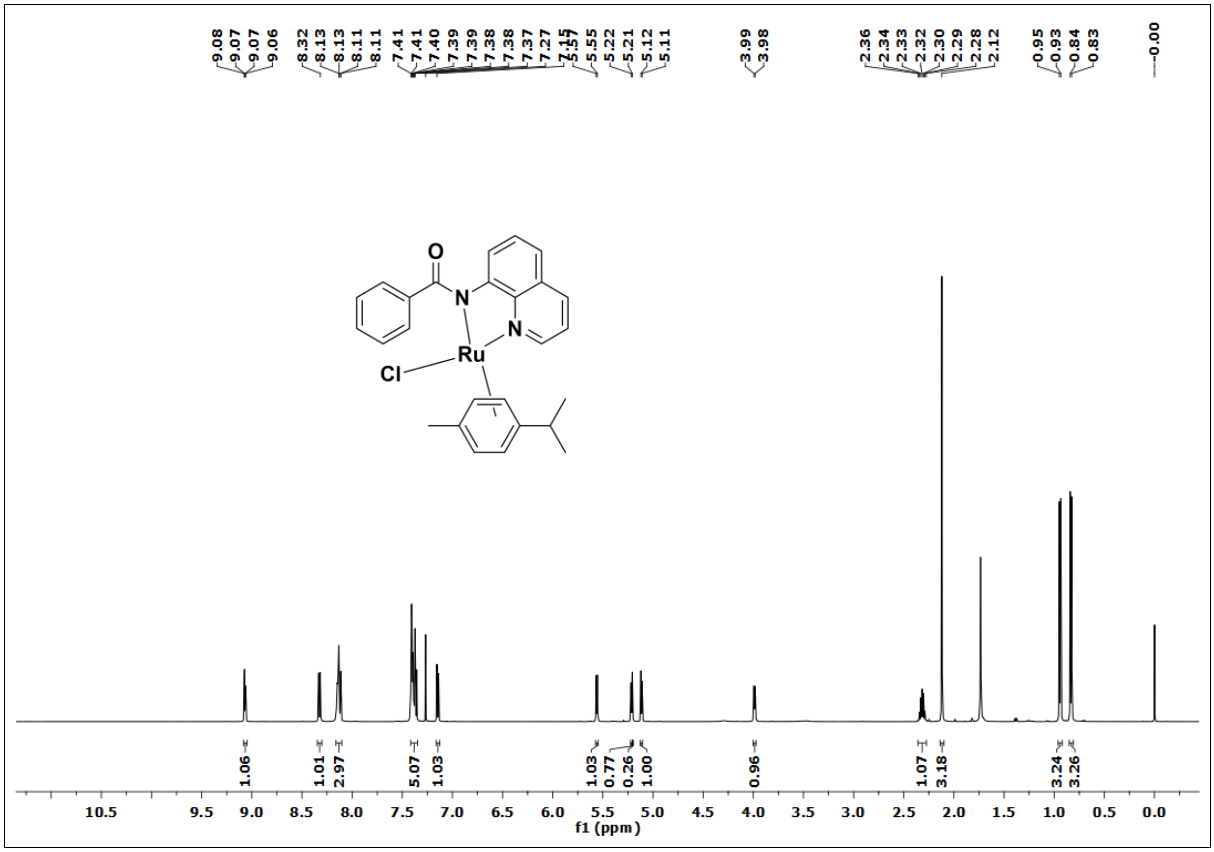
^{1}H NMR Phosphine complex **4**.



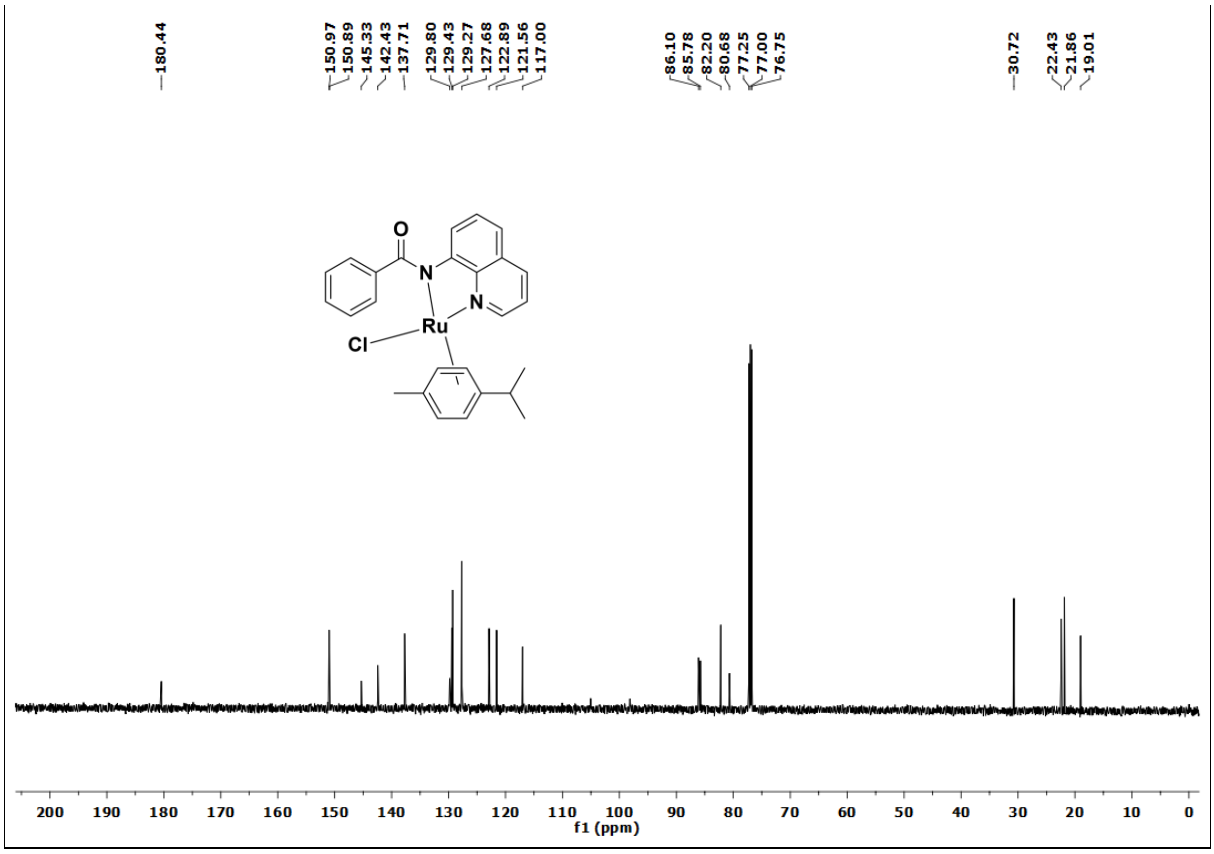
Procedure for the Preparation of Ruthenium Adduct 5.

Ruthenium adduct **5** is prepared by the procedure mentioned in the literature.[4]

^{1}H NMR Spectra of Compound **5**.



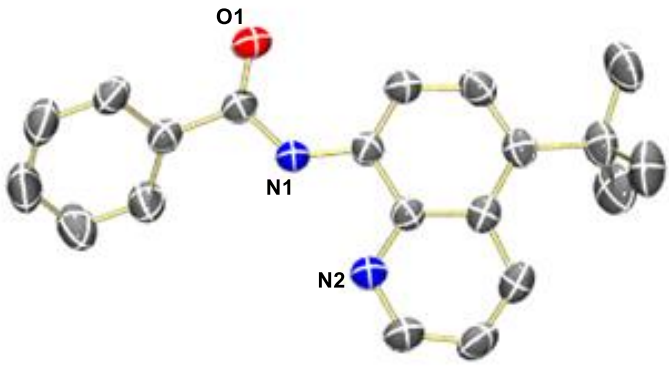
^{13}C NMR Spectra of Compound **A**.



X-Ray Analysis of Compound 3ad.

Empirical formula	$C_{20}H_{20}N_2O$
Formula weight	304.38
Temperature/K	296(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	9.5682(3)
b/Å	18.4465(7)
c/Å	9.7648(4)
α/°	90
β/°	104.8076(17)
γ/°	90
Volume/Å^3	1666.25(11)
Z	4
ρ_{calc}g/cm^3	1.213
μ/mm^{-1}	0.075
F(000)	648.0
Crystal size/mm^3	0.250 × 0.220 × 0.100
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.416 to 49.988
Index ranges	$-11 \leq h \leq 11$, $-21 \leq k \leq 21$, $-11 \leq l \leq 11$
Reflections collected	11398
Independent reflections	2938 [R_{int} = 0.0241, R_{sigma} = 0.0243]
Data/restraints/parameters	2938/0/216
Goodness-of-fit on F^2	1.042
Final R indexes [I>=2σ (I)]	R_1 = 0.0406, wR_2 = 0.0999
Final R indexes [all data]	R_1 = 0.0566, wR_2 = 0.1116
Largest diff. peak/hole / e Å^{-3}	0.16/-0.14

ORTEP Diagram of Compounds 3ad



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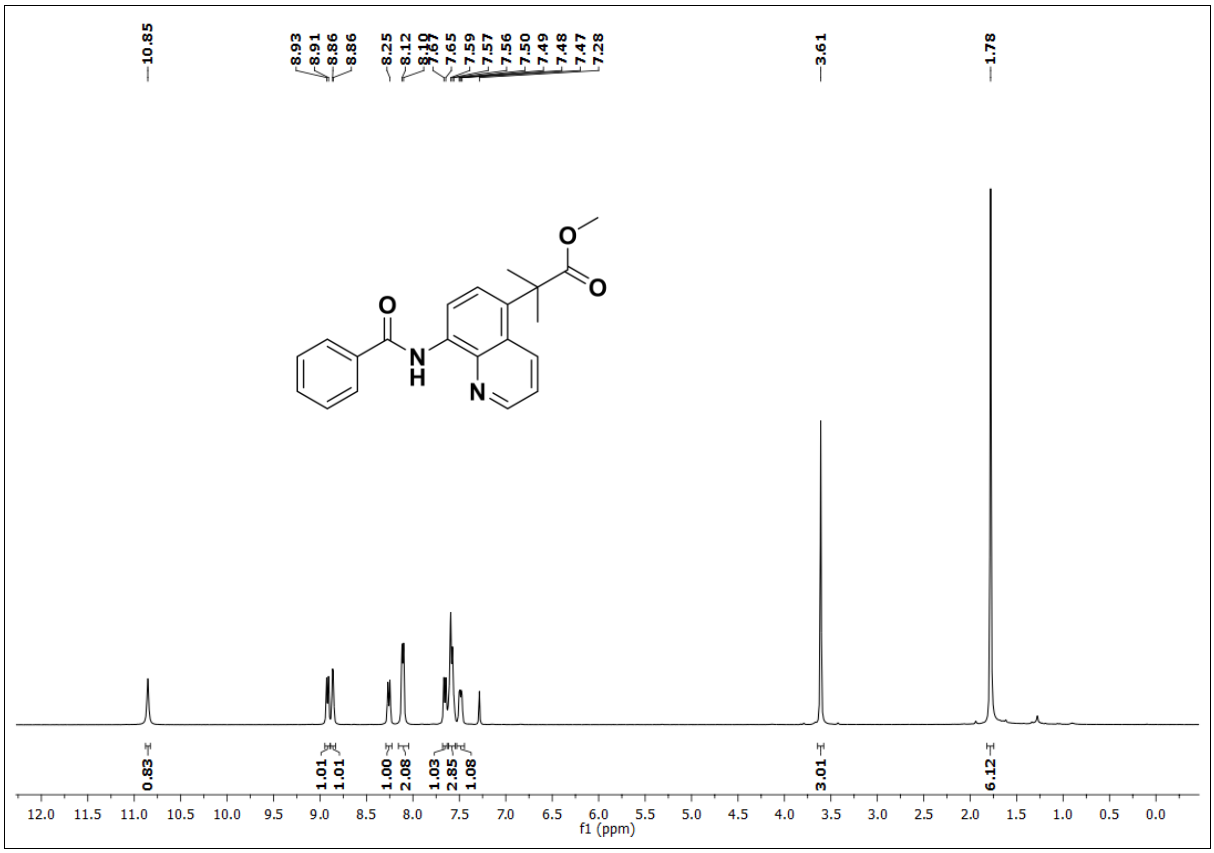
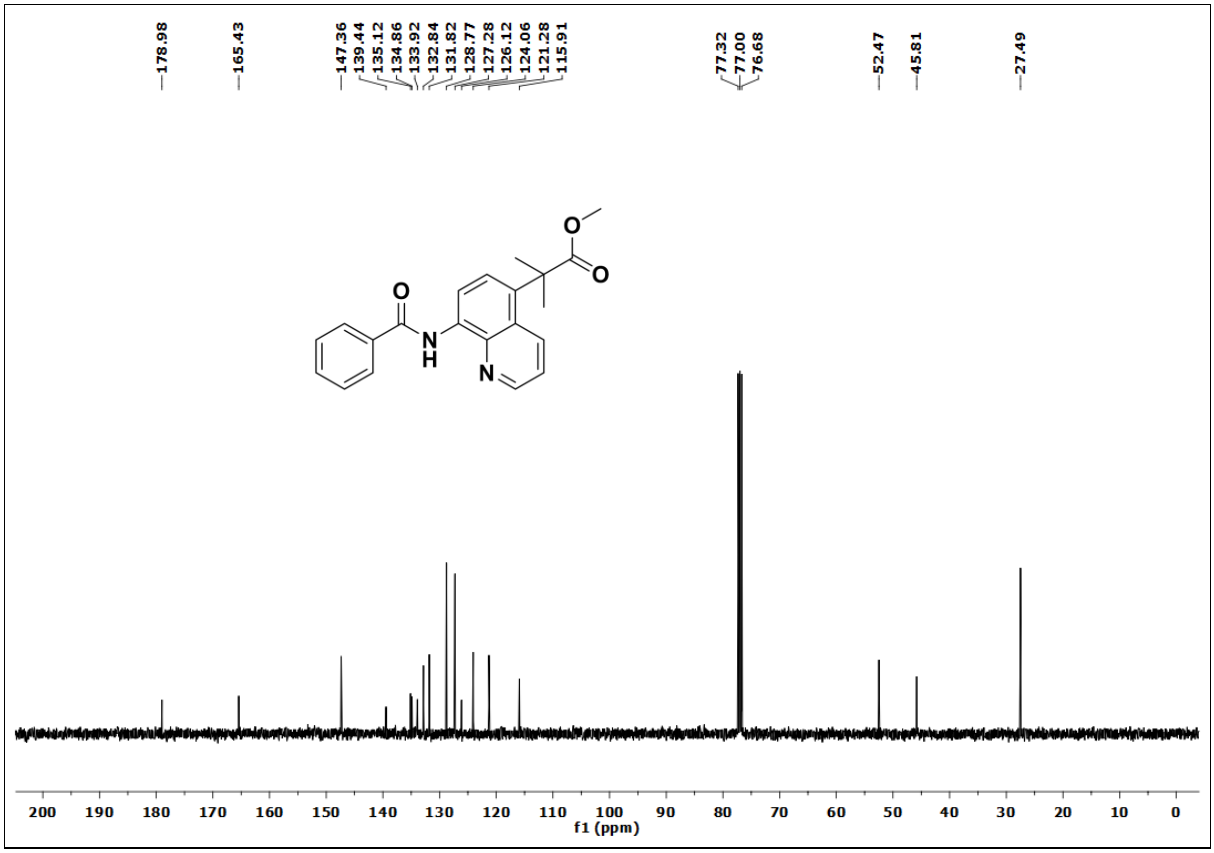
2. Bennett, M. A.; Huang, T. N.; Matheson, T. W.; Smith, A. K. *Inorganic Syntheses*. **1982**, *21*, 74.

3. Serron, S. A.; Nolan, S. P. *Organometallics.* **1995**, *14*, 4611.

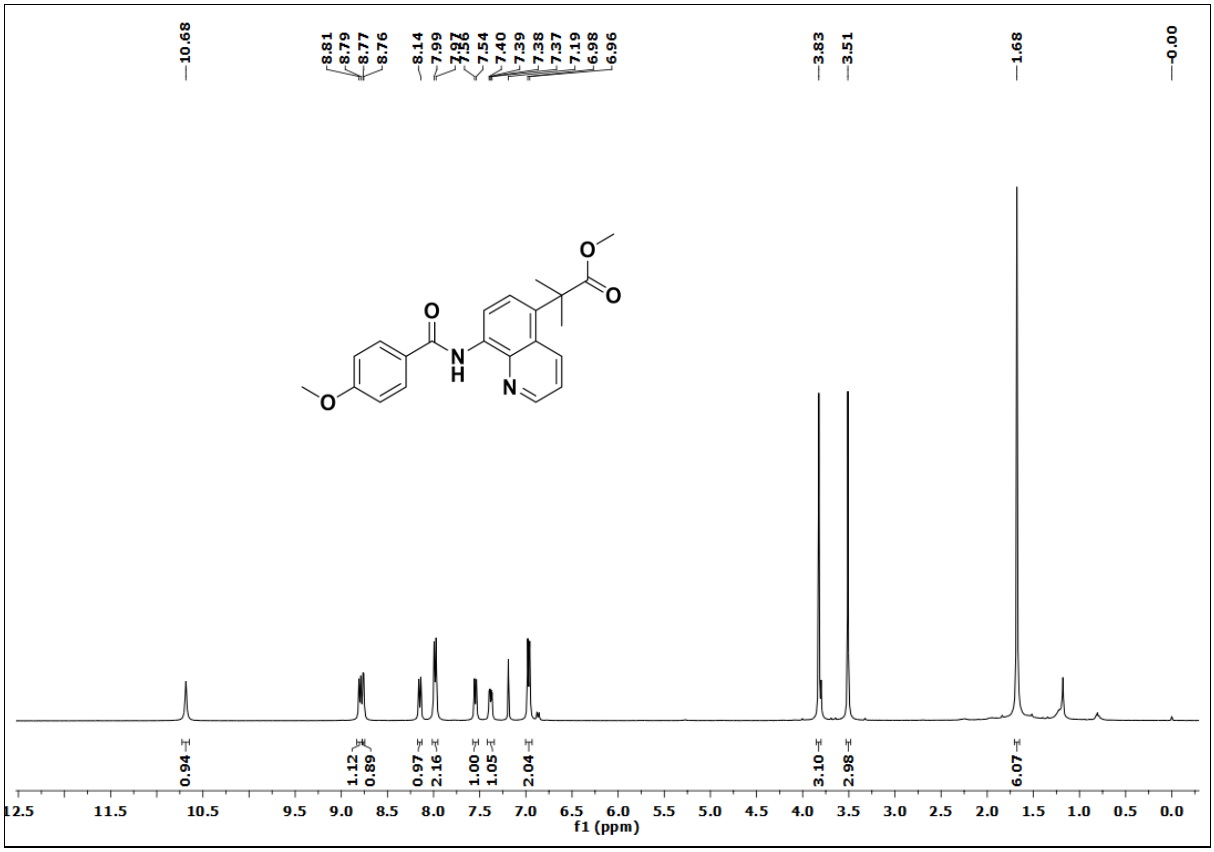
4. Allu, S.; Kumara Swamy, K. C. *J. Org. Chem.* **2014**, *79*, 3963.

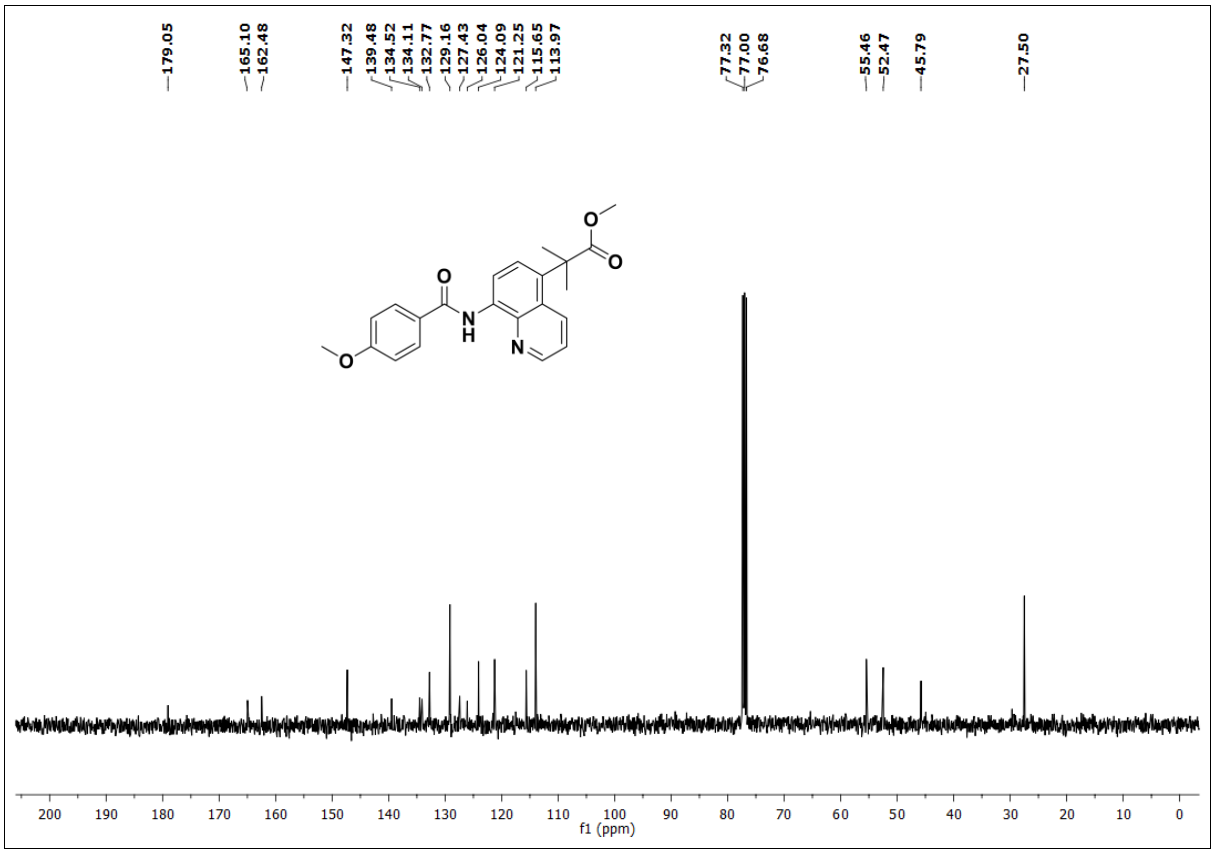
^{1}H and ^{13}C NMR Spectra of Compound **3aa.**



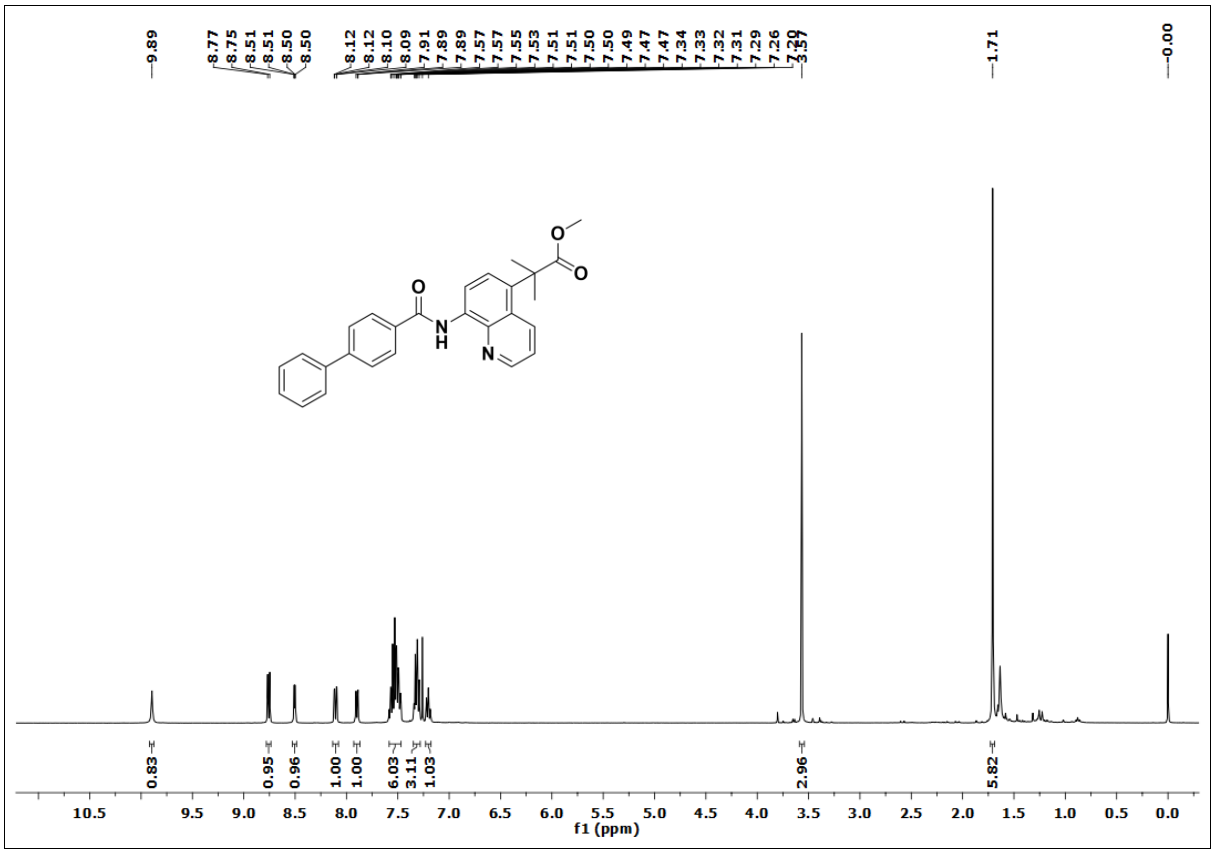


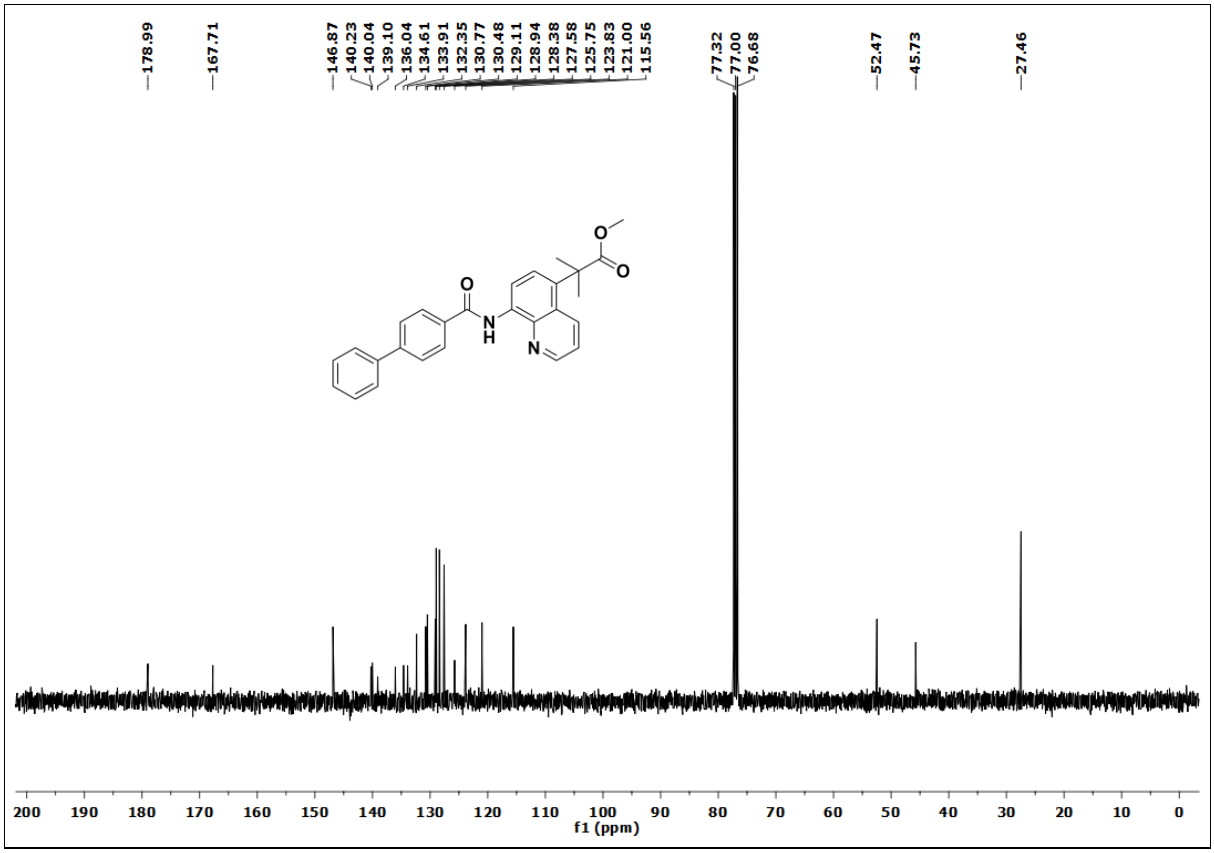
^{1}H and ^{13}C NMR Spectra of **3ba**.



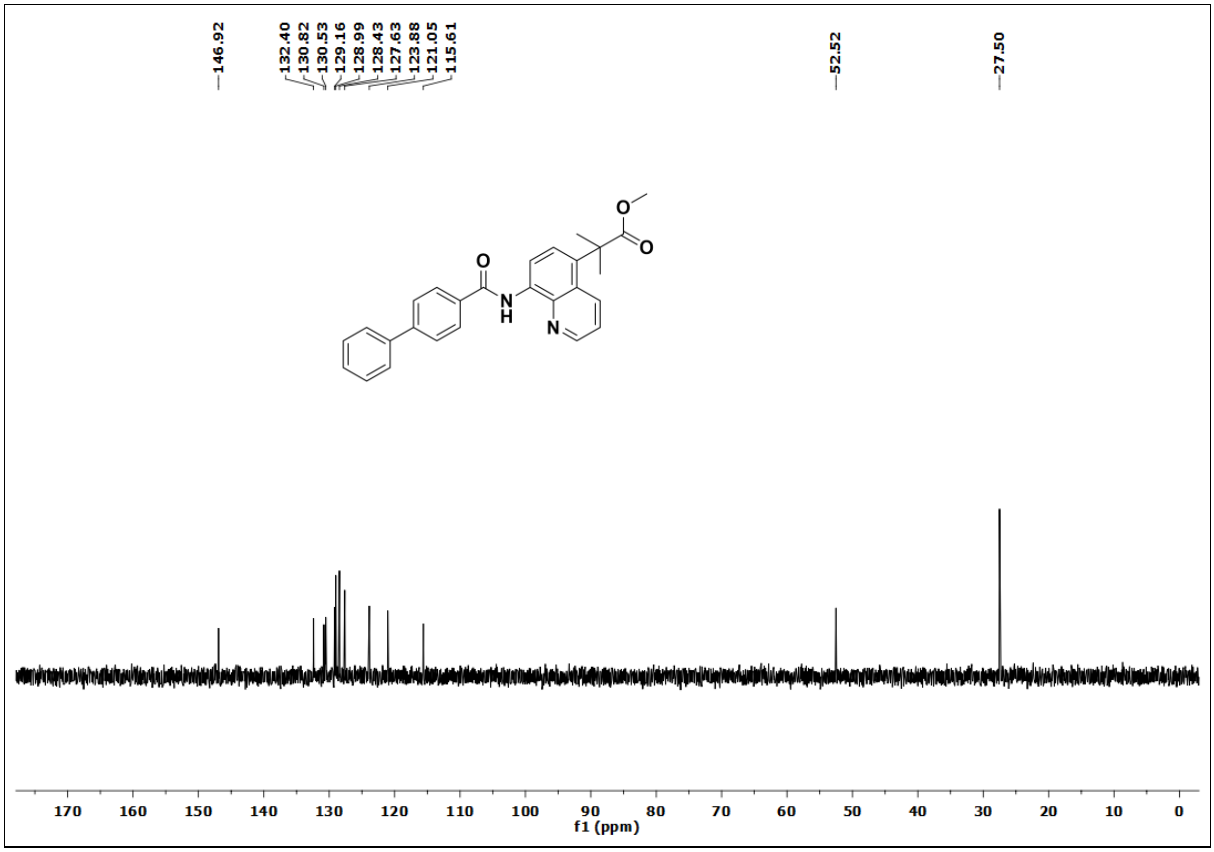


^{1}H and ^{13}C NMR Spectra of Compound **3ca.**

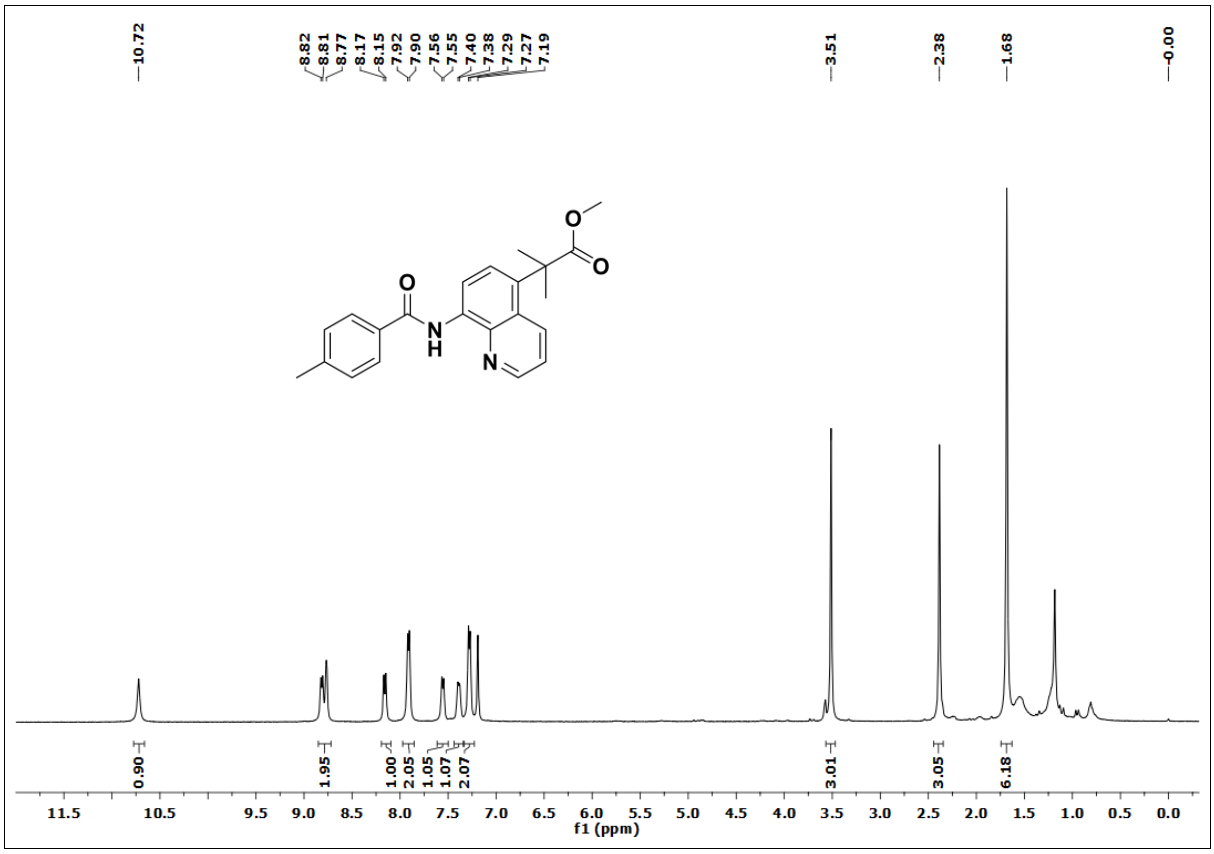


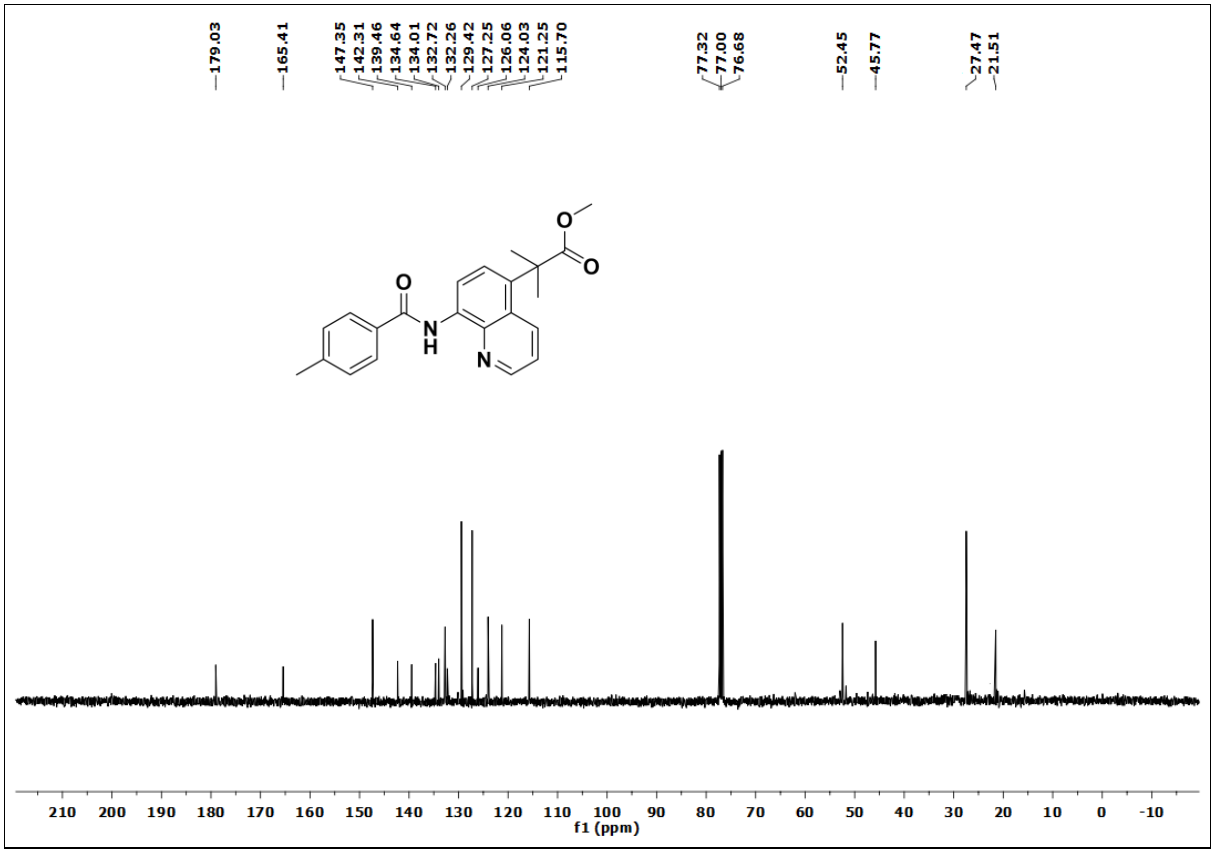


DEPT (135) NMR Spectrum of Compound **3ca.**

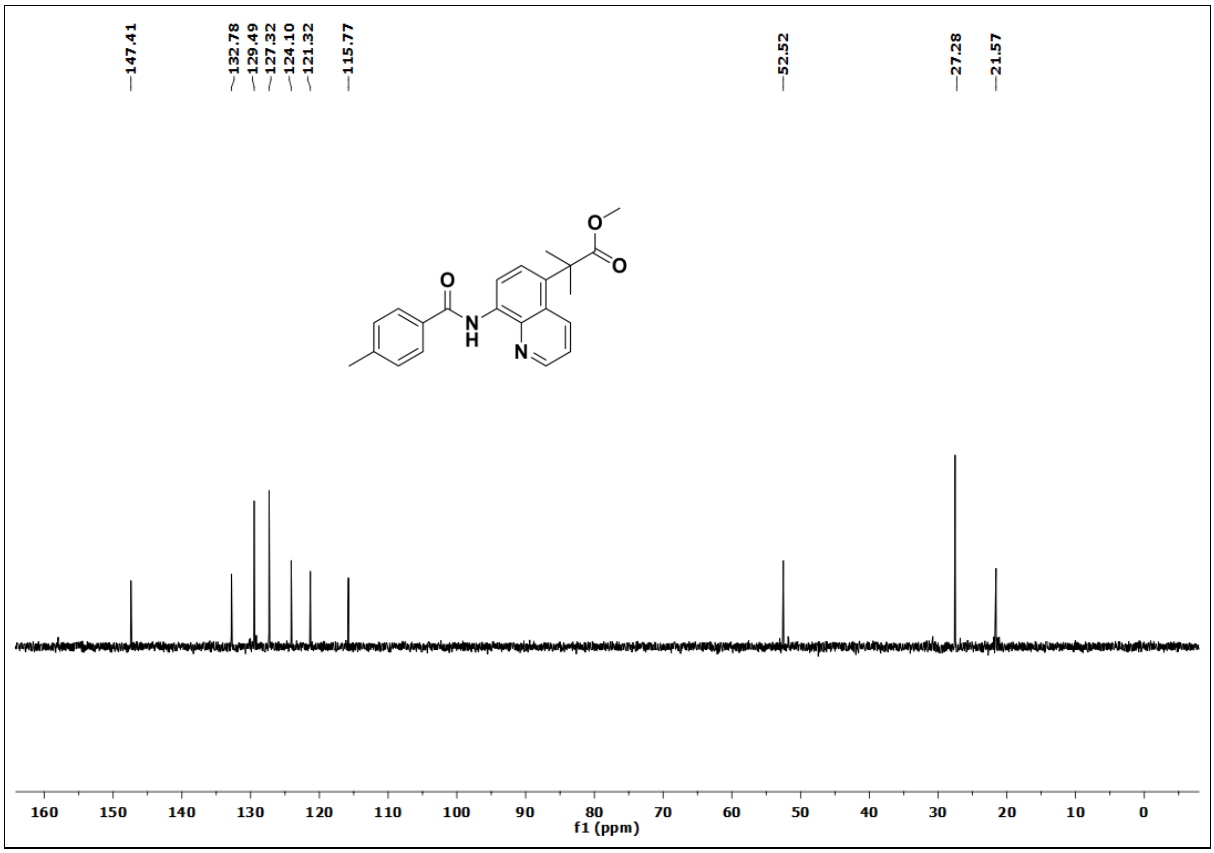


^{1}H and ^{13}C NMR Spectra of Compound **3da.**

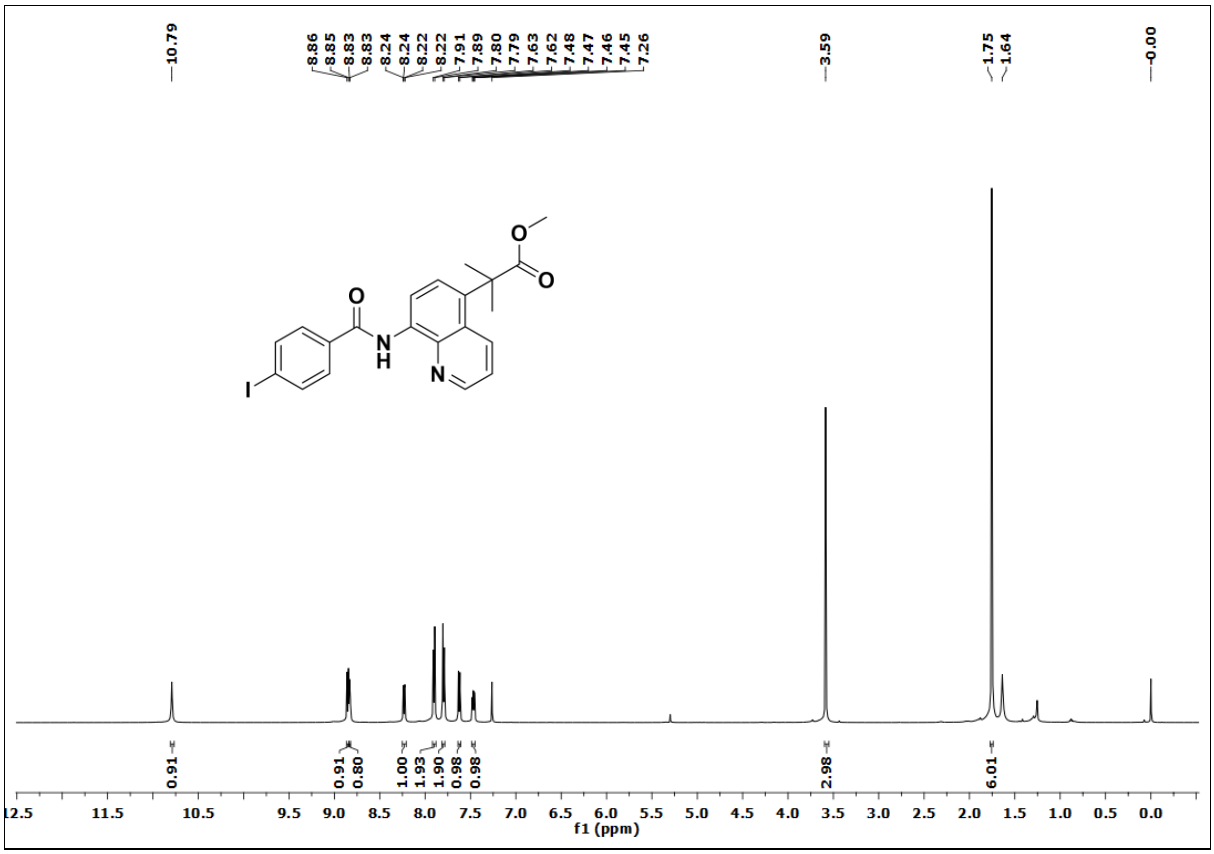


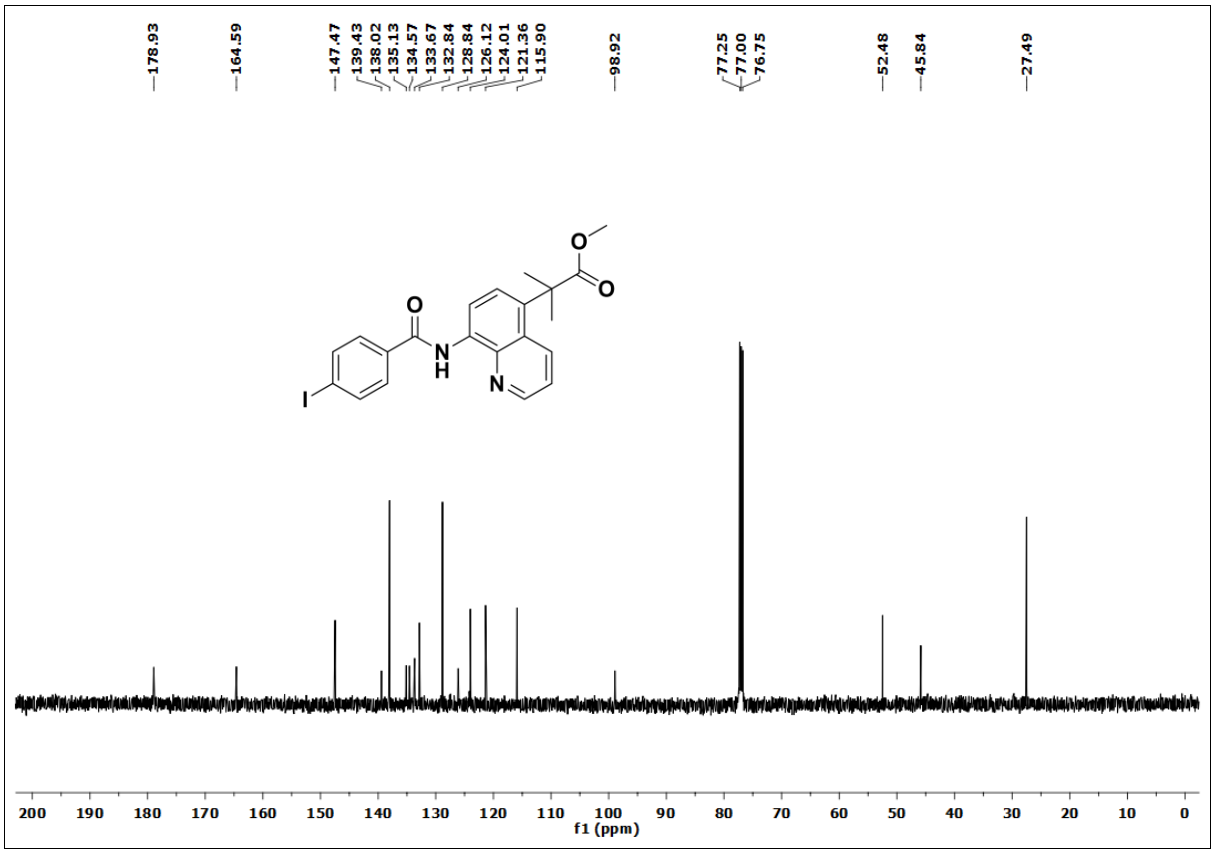


DEPT (135) NMR Spectrum of Compound **3da.**

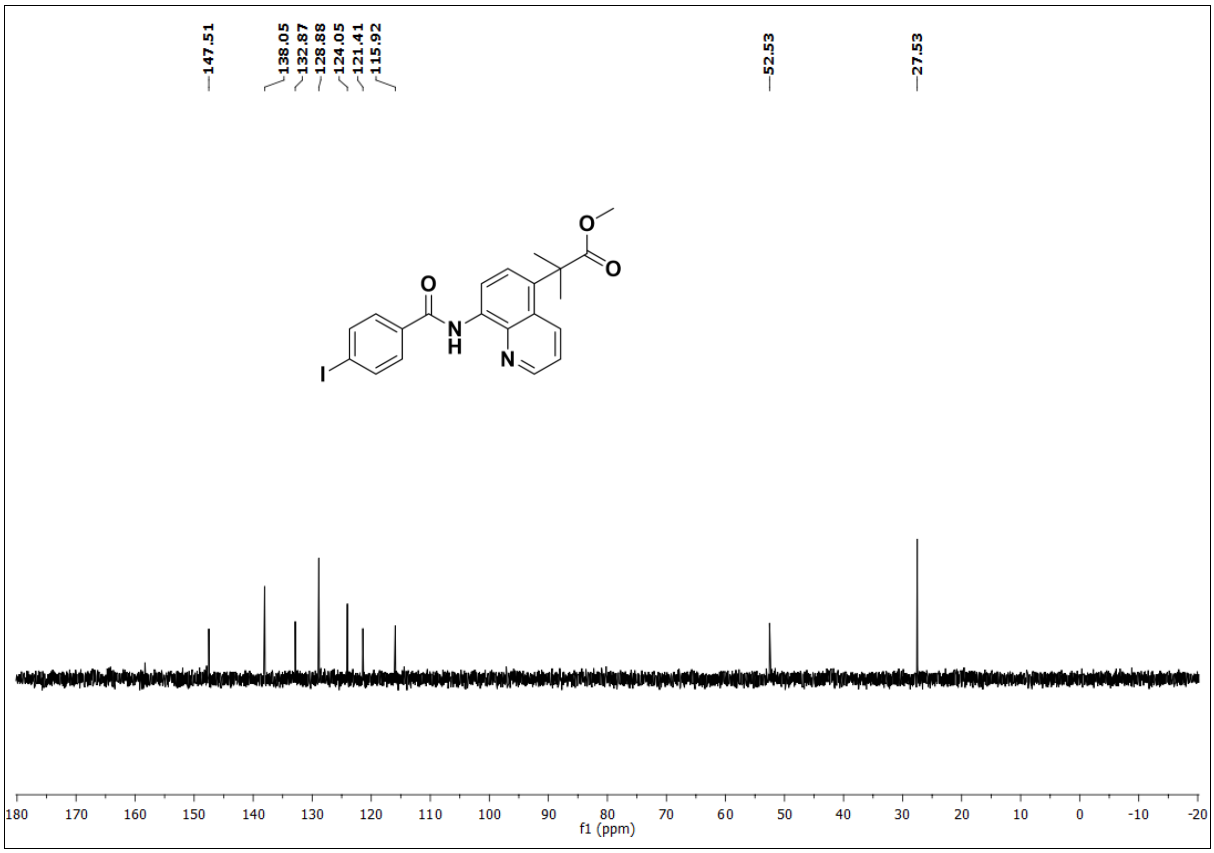


^{1}H and ^{13}C NMR Spectra of Compound **3ea.**

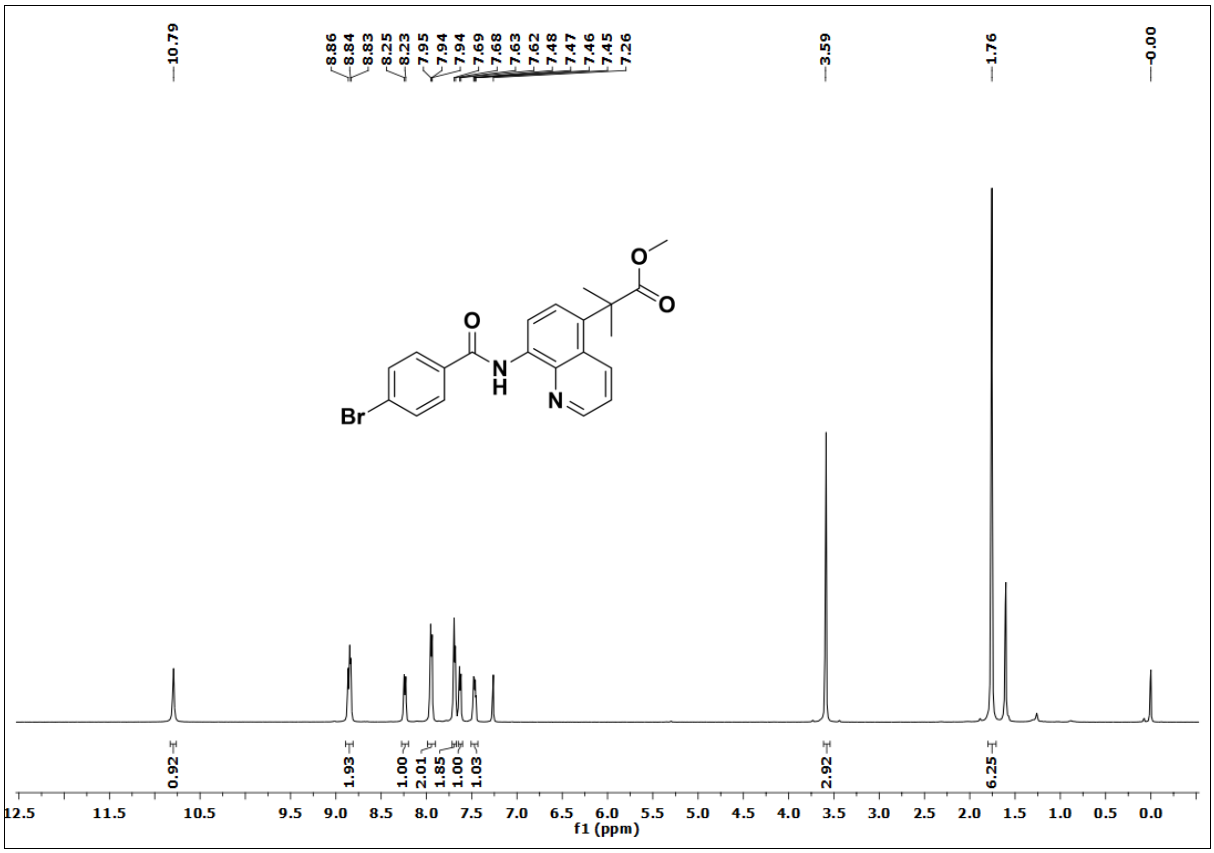


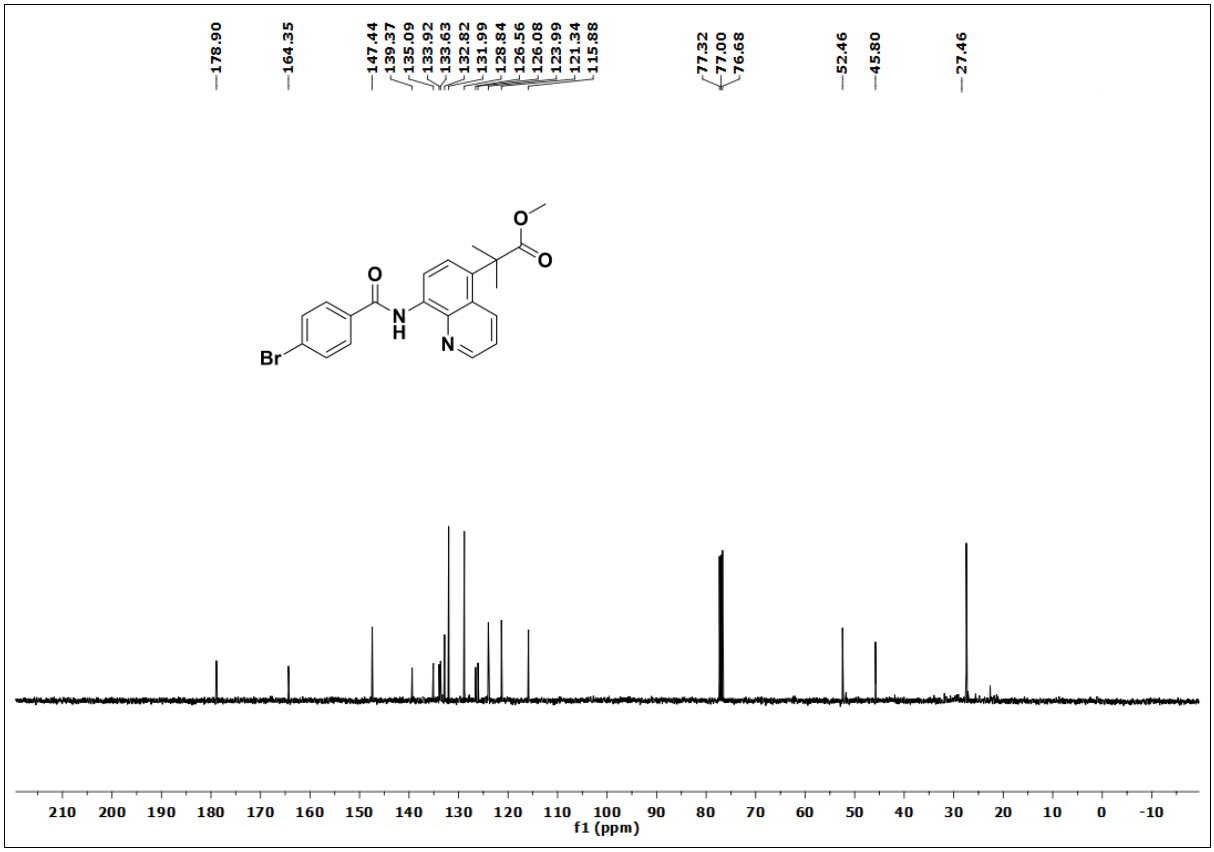


DEPT (135) NMR Spectrum of Compound **3ea.**

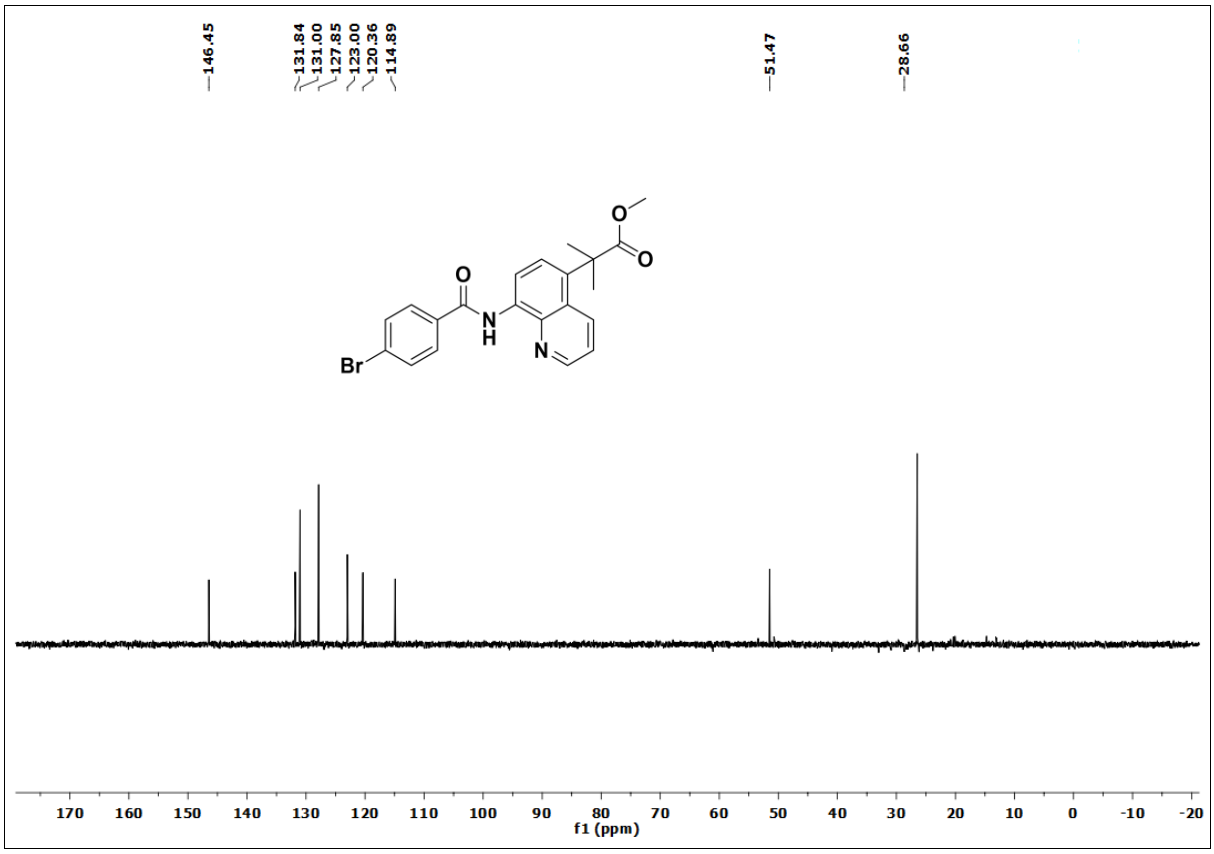


^{1}H and ^{13}C NMR Spectra of Compound **3fa.**

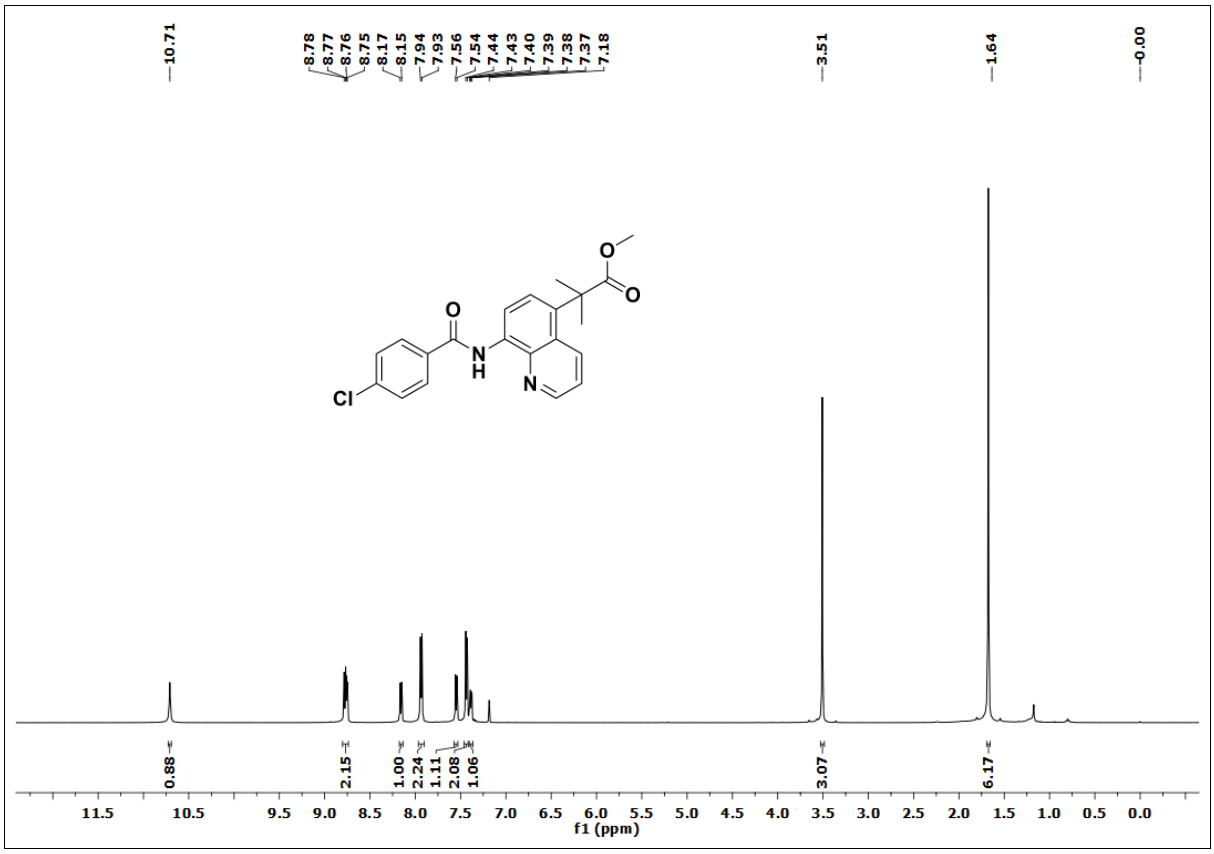


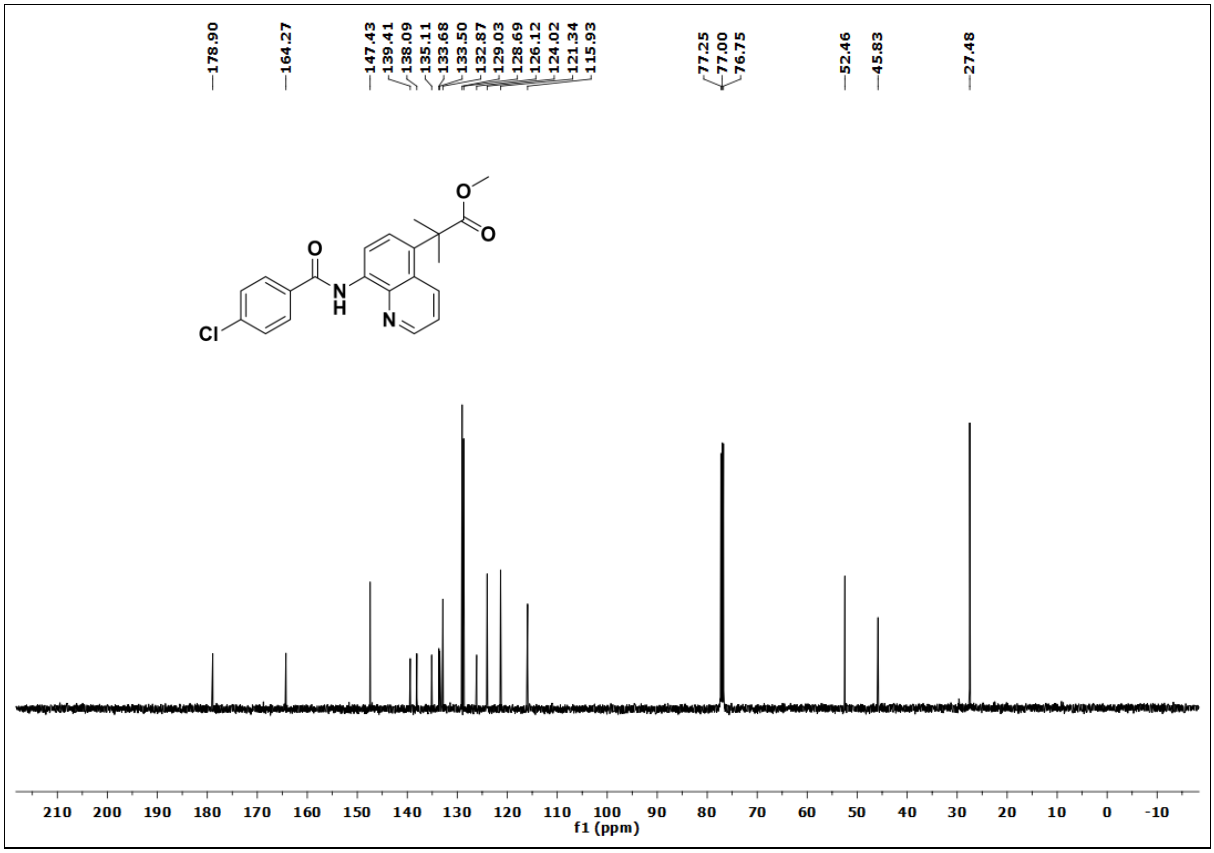


DEPT (135) NMR Spectrum of Compound **3fa.**

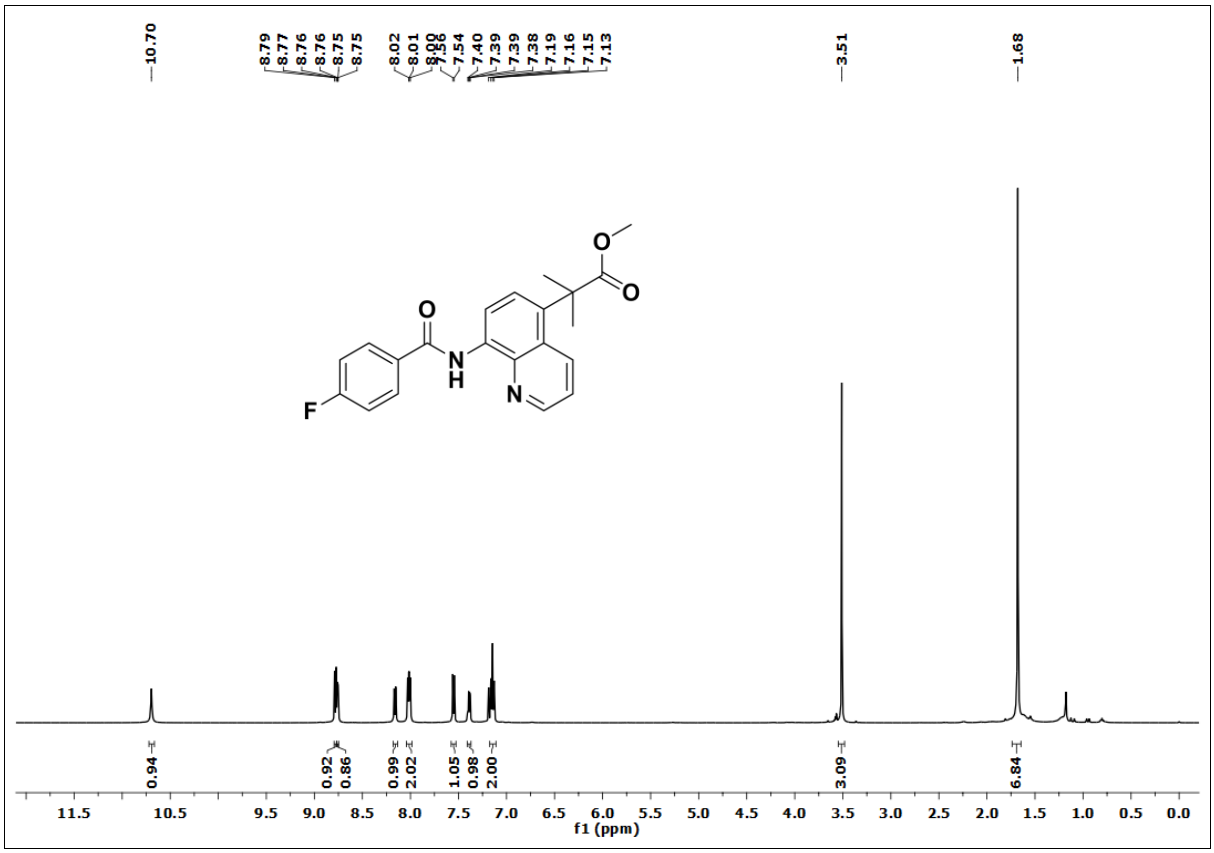


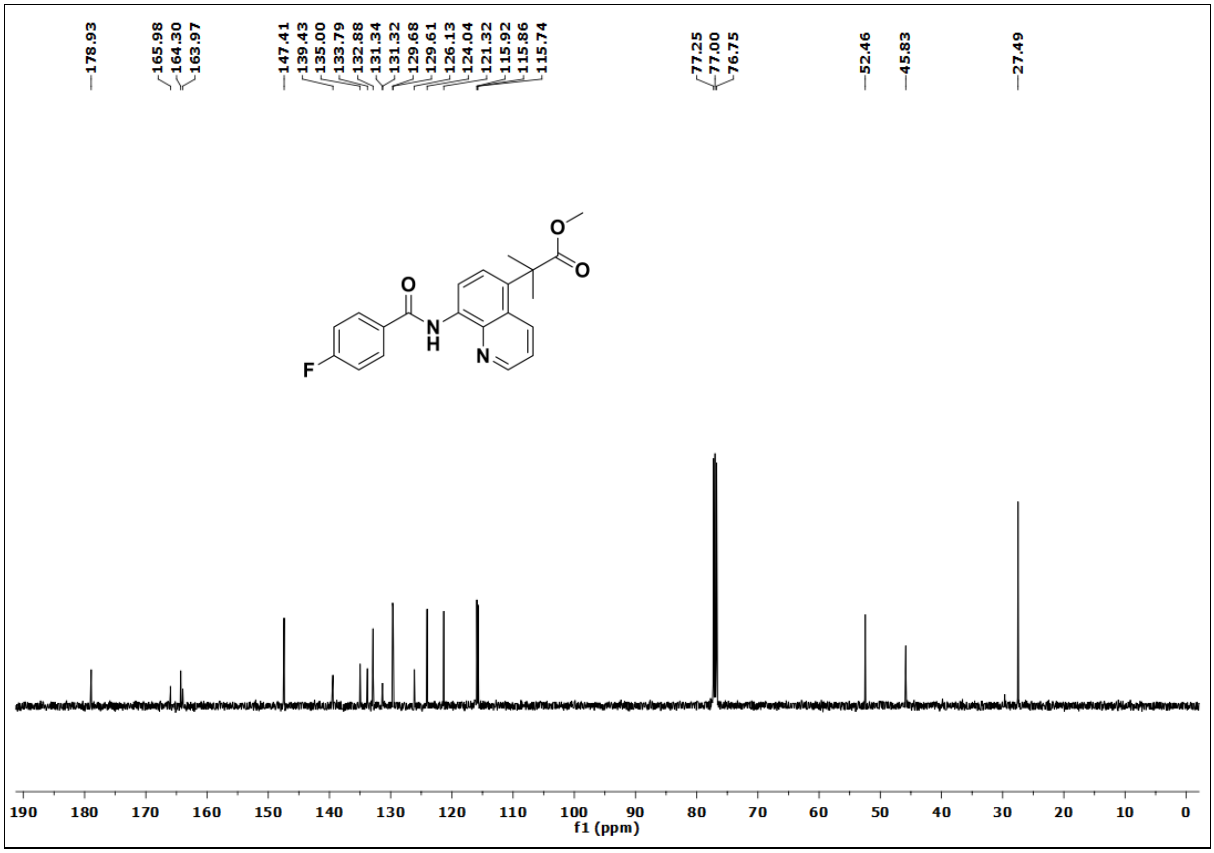
^{1}H and ^{13}C NMR Spectra of Compound **3ga.**



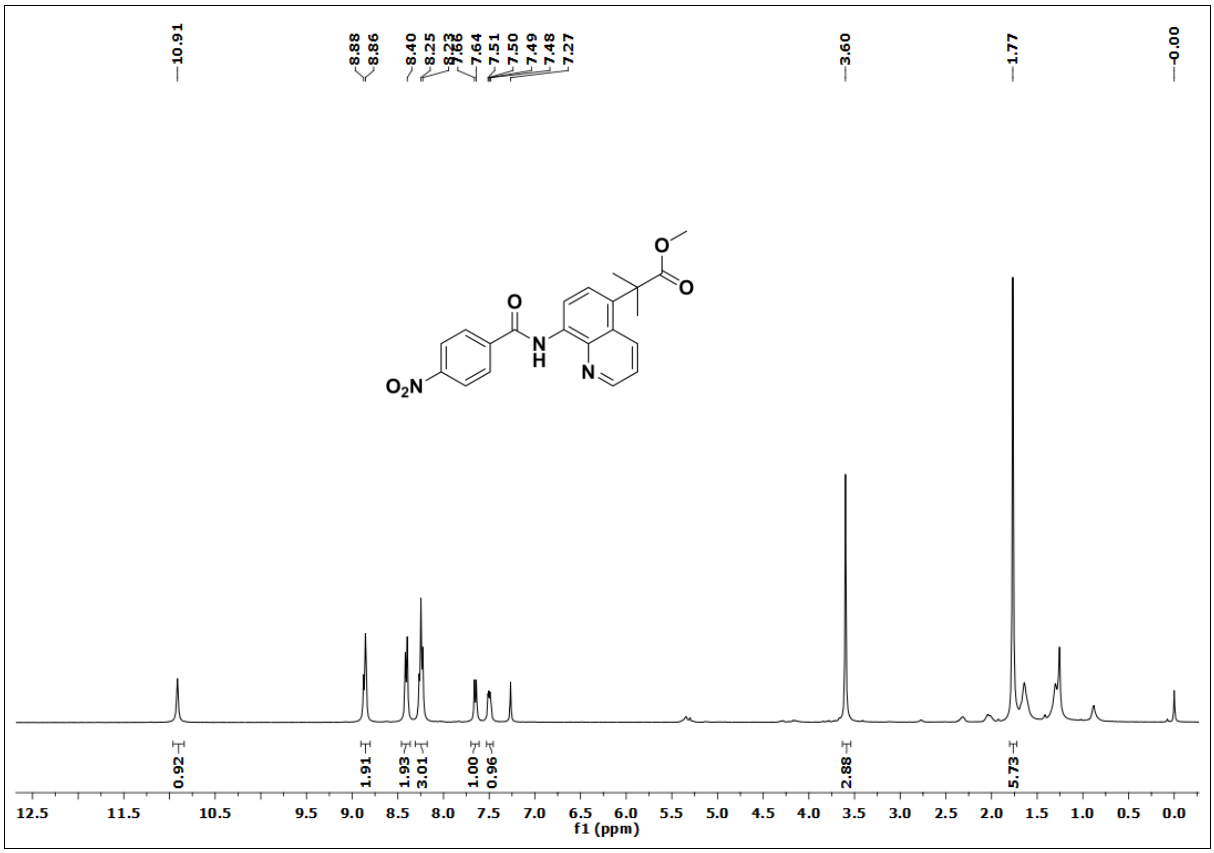


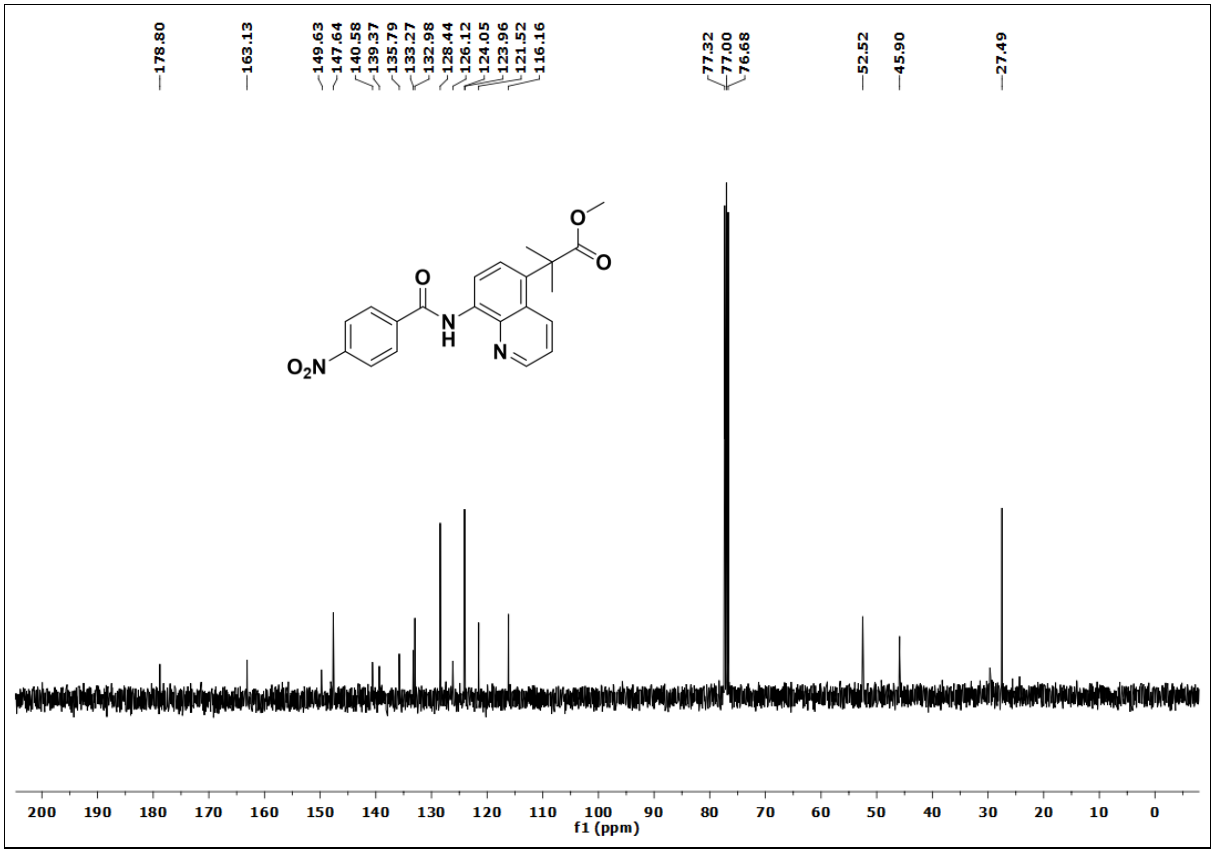
^{1}H and ^{13}C NMR Spectra of Compound **3ha.**



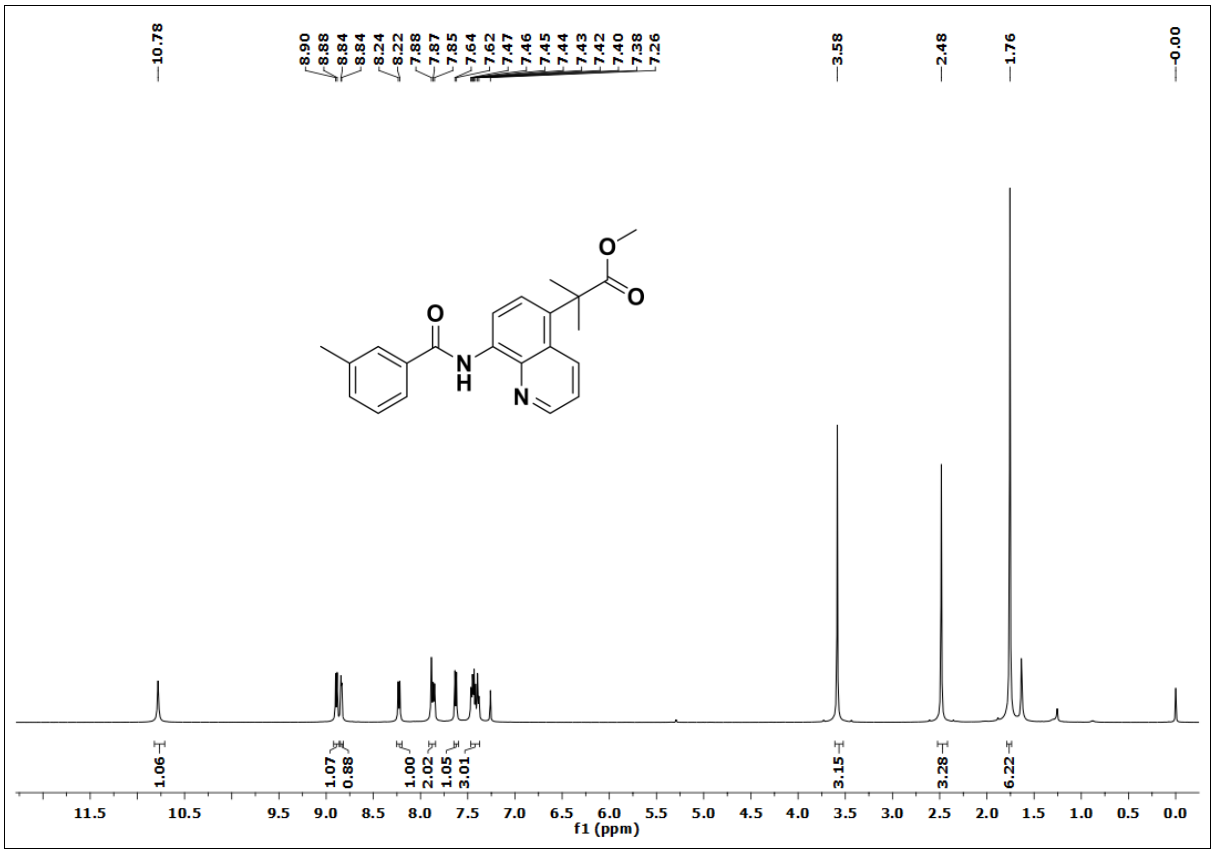


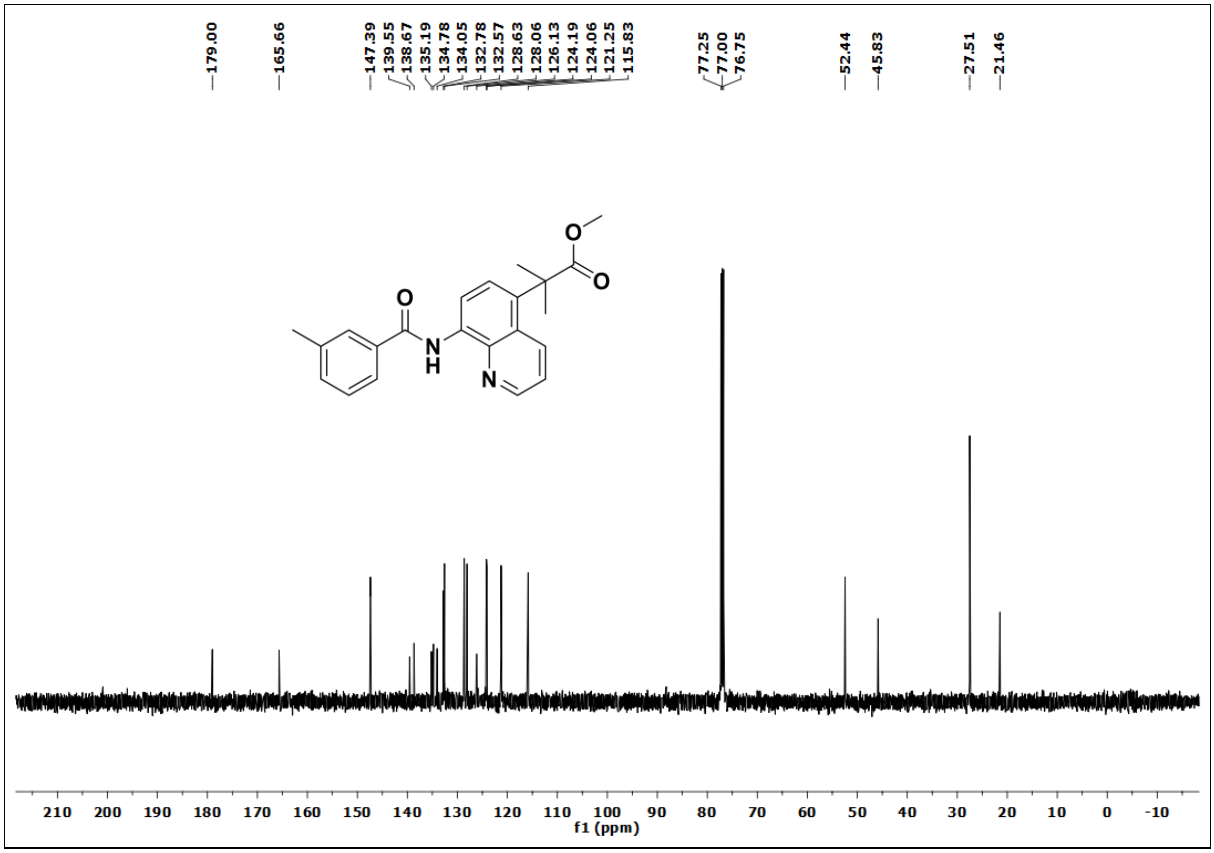
^{1}H and ^{13}C NMR Spectra of Compound **3ia.**



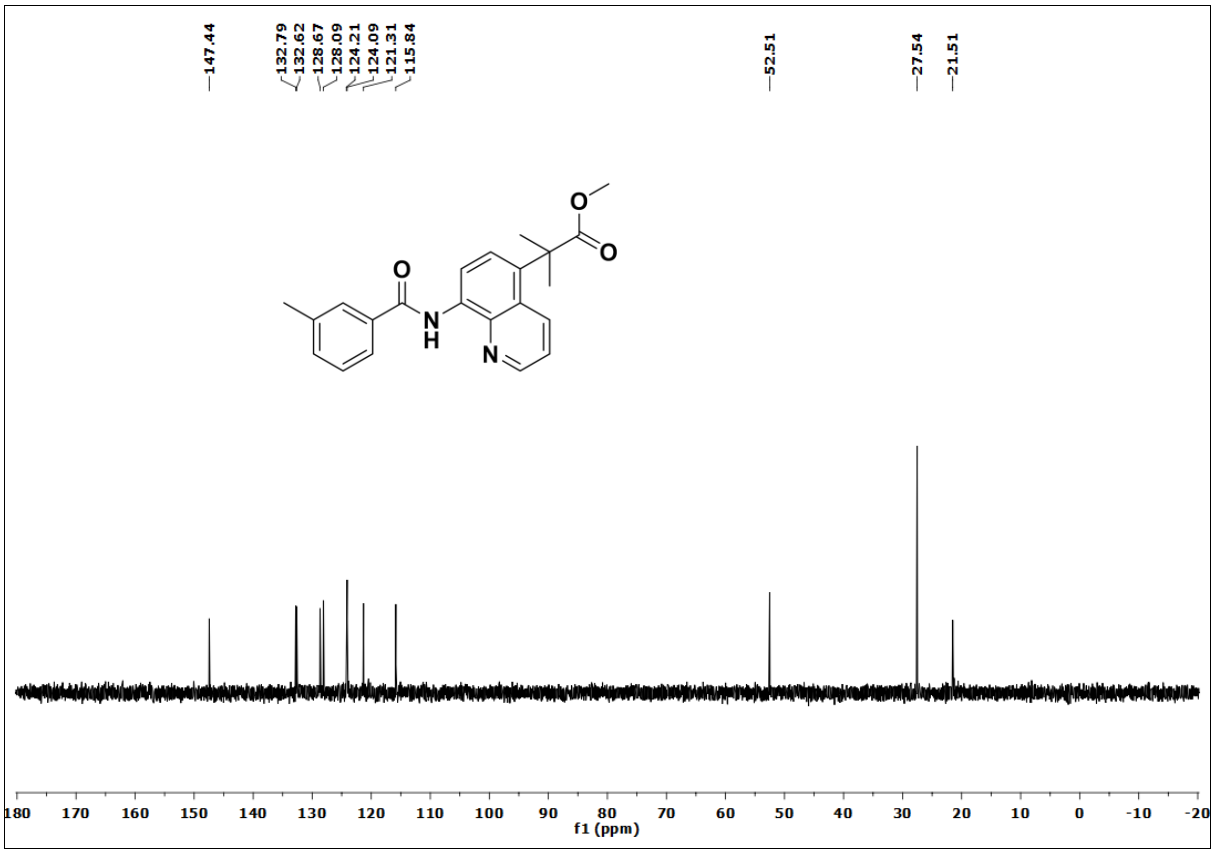


^{1}H and ^{13}C NMR Spectra of Compound **3ja.**

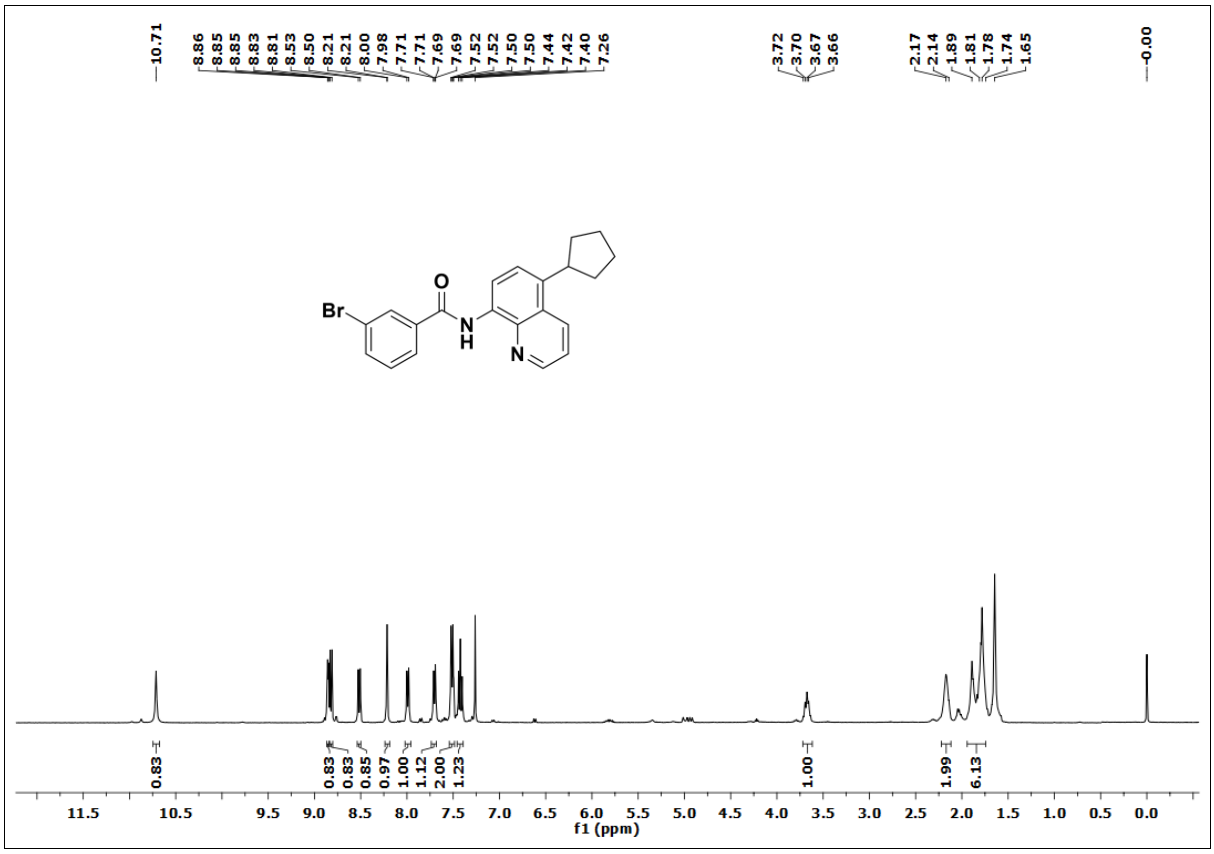


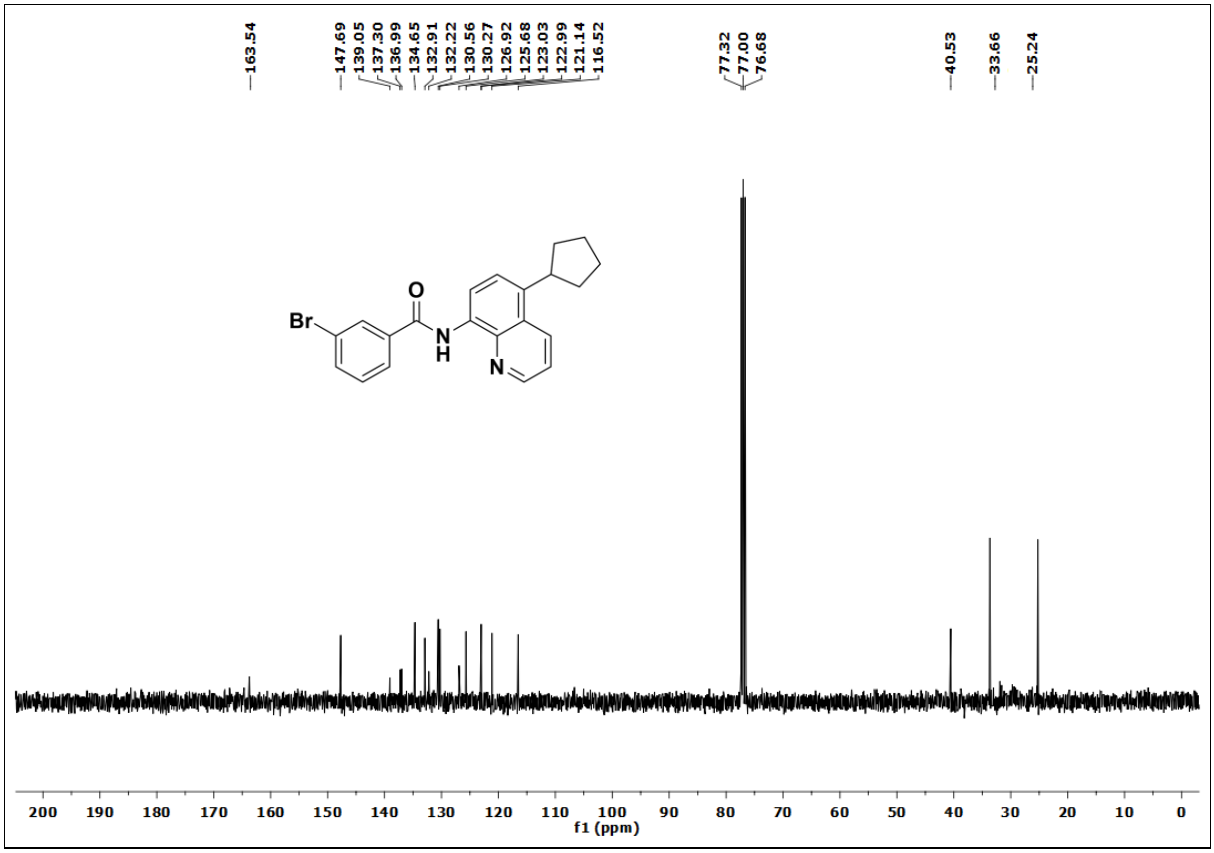


DEPT (135) NMR Spectrum of Compound **3ja.**

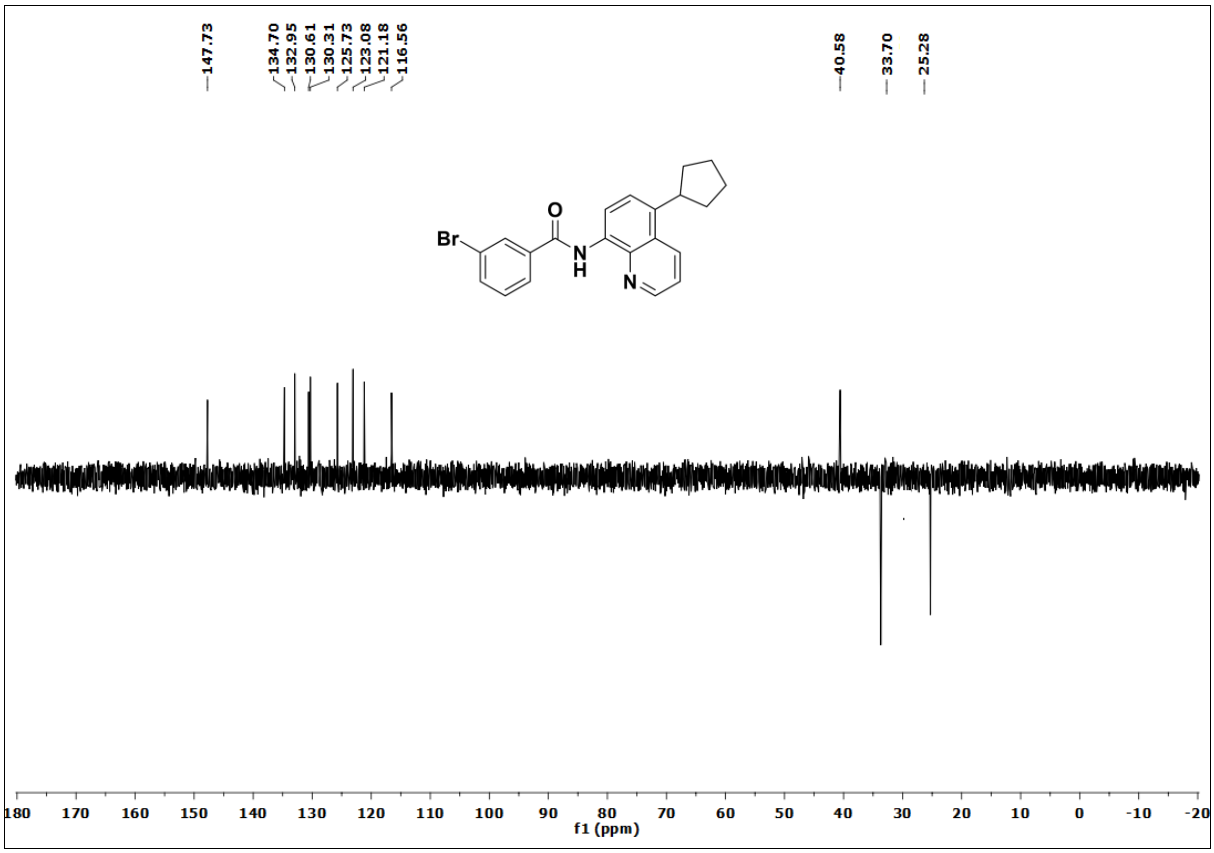


^{1}H and ^{13}C NMR Spectra of Compound **3kb.**

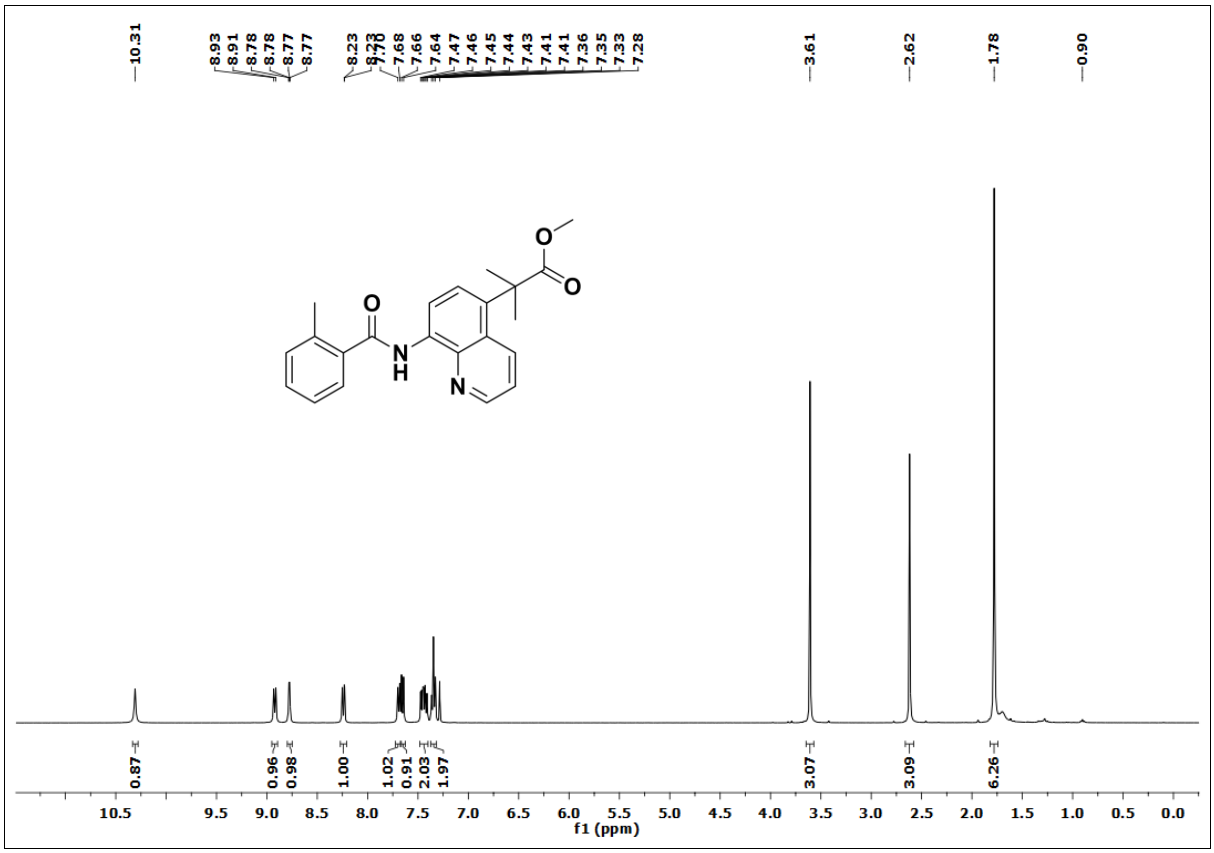


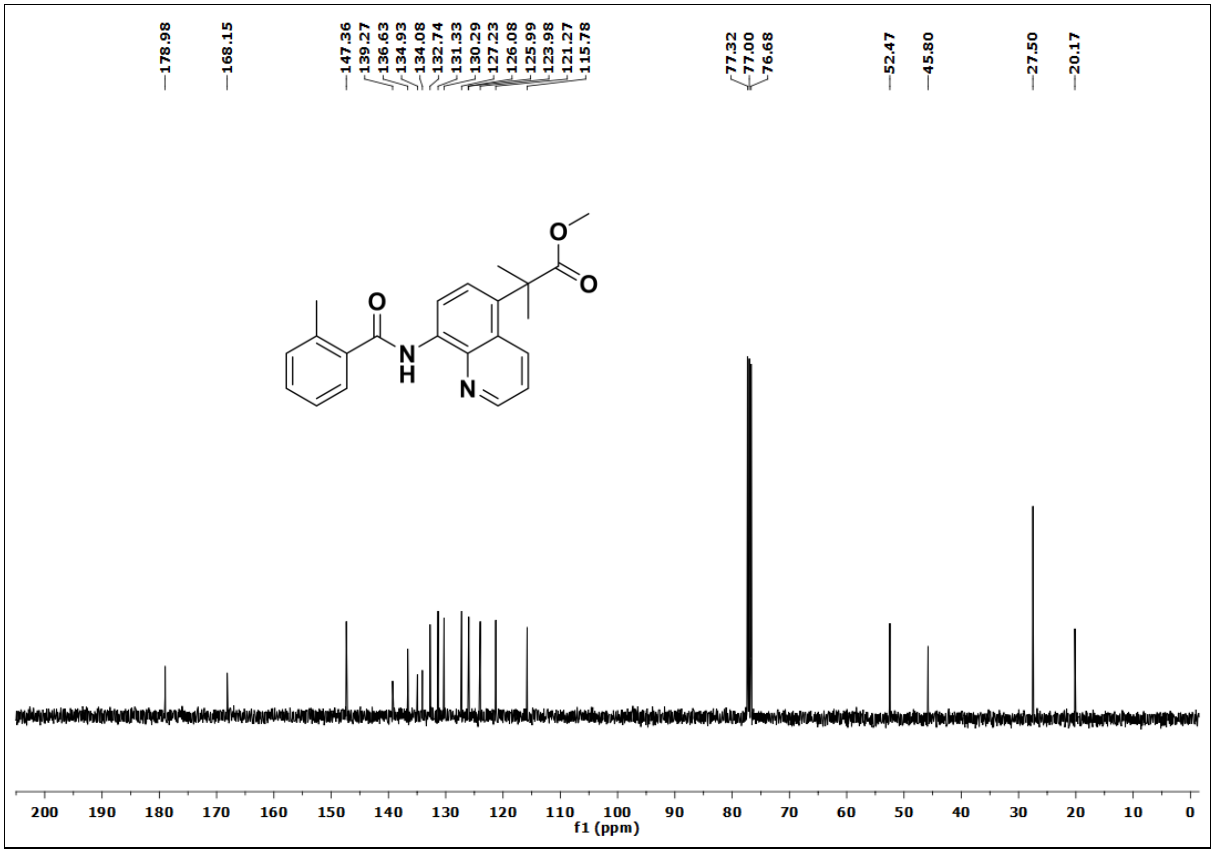


DEPT (135) NMR Spectrum of Compound **3kb.**

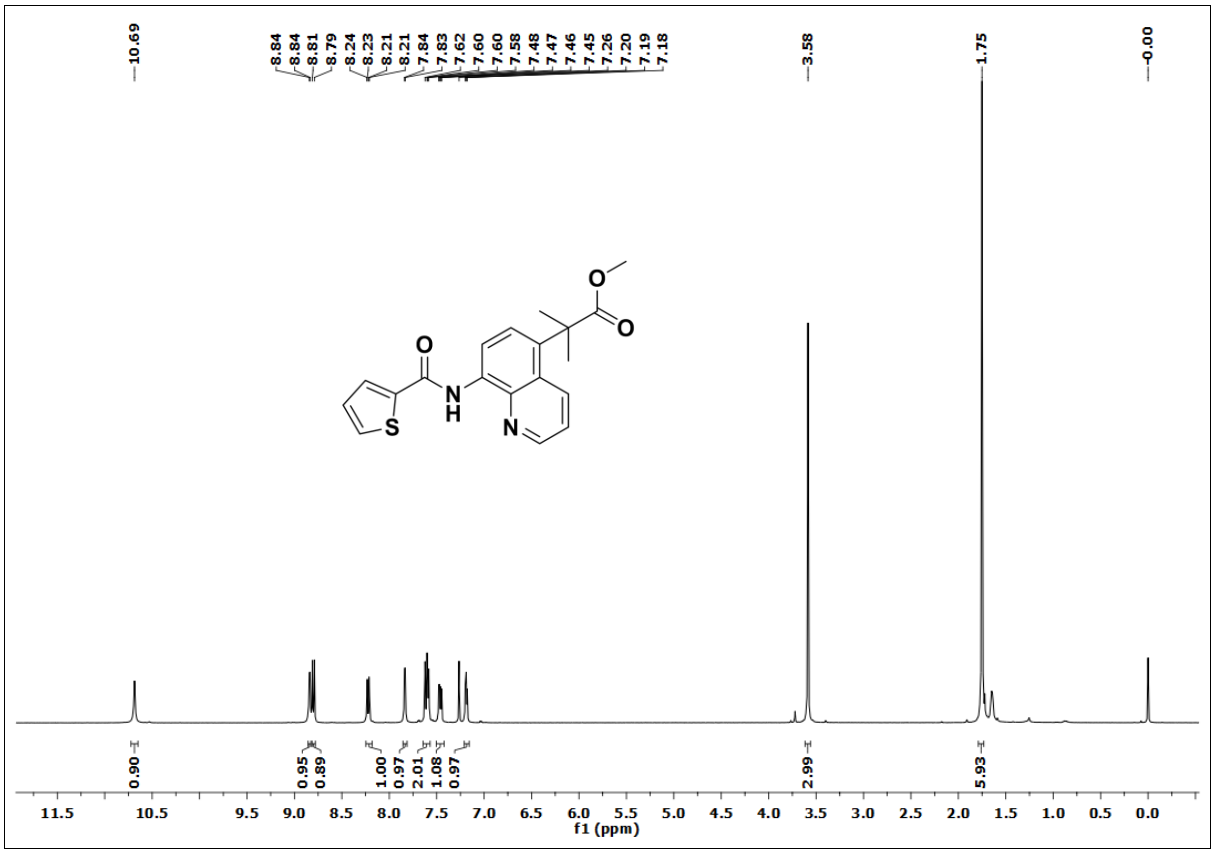


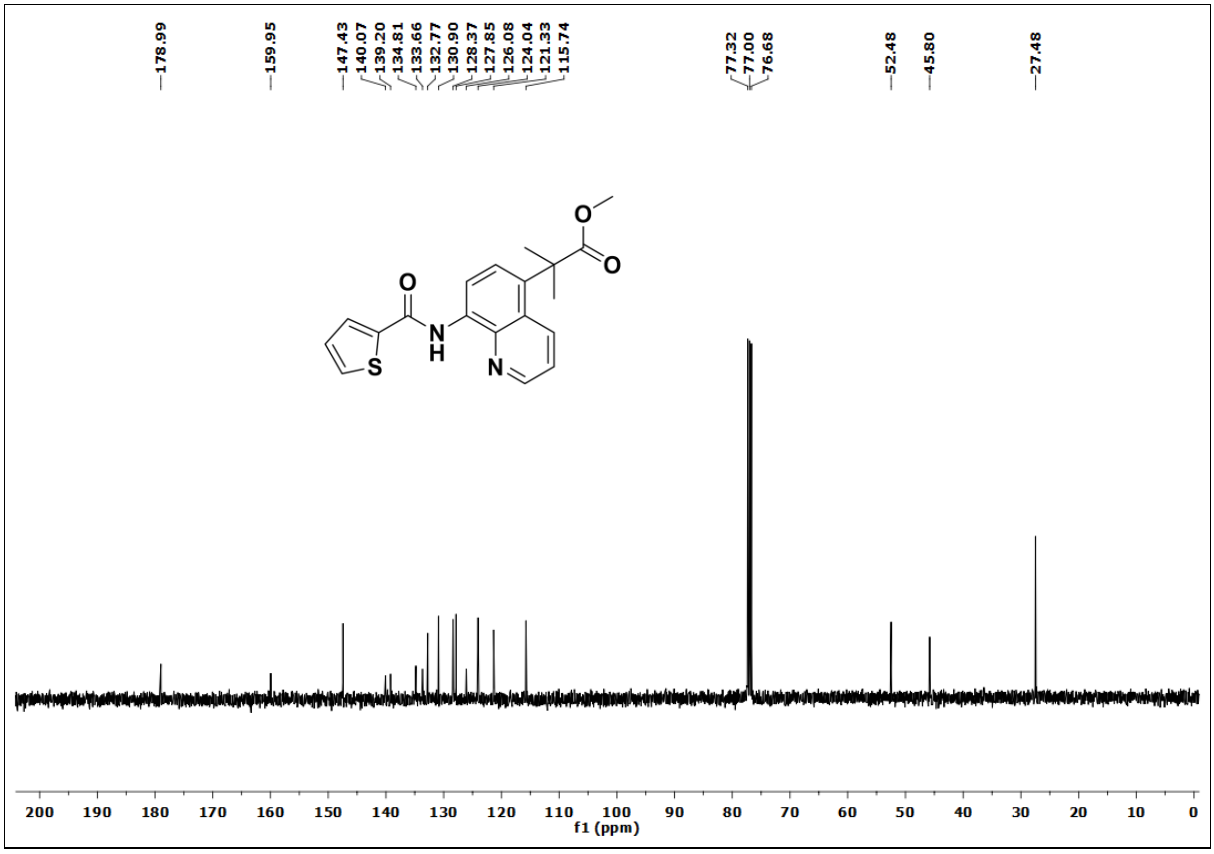
^{1}H and ^{13}C NMR Spectra of Compound **3la.**



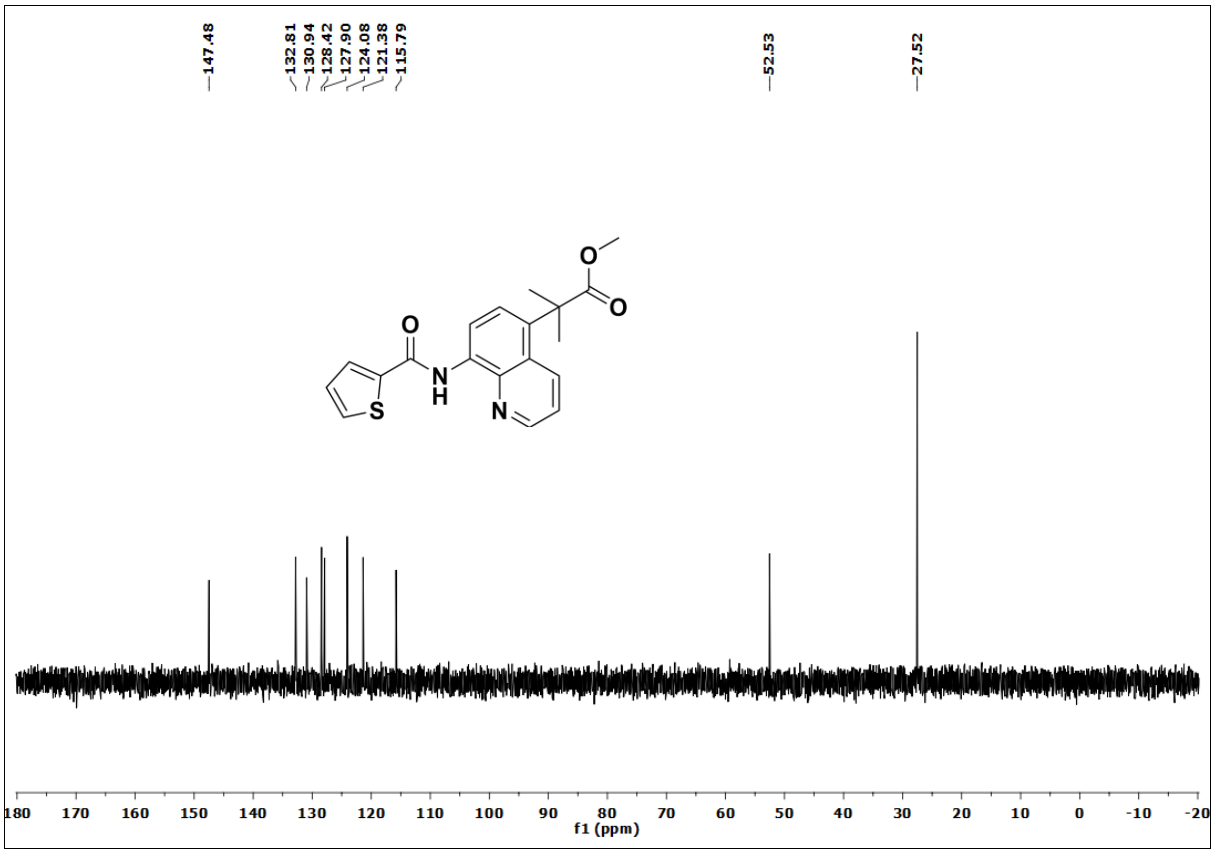


^{1}H and ^{13}C NMR Spectra of Compound **3oa.**

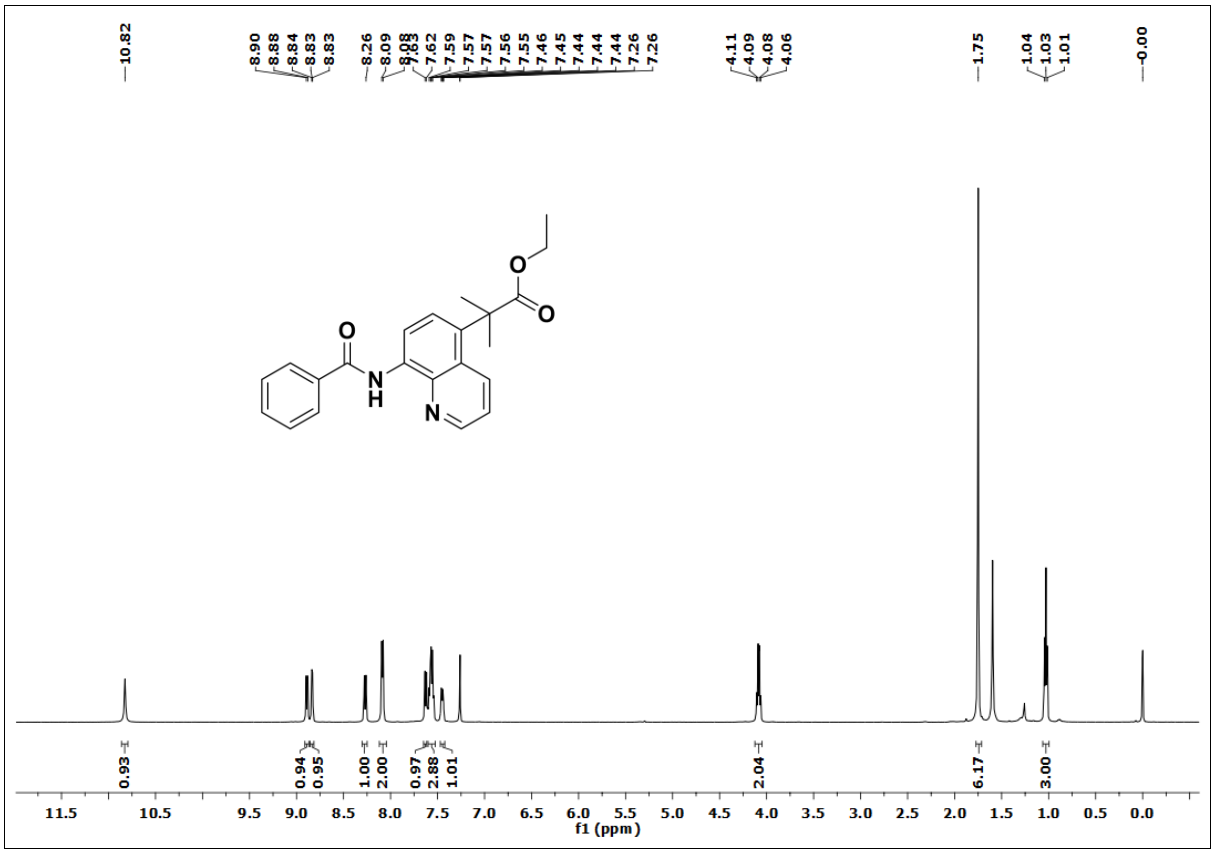


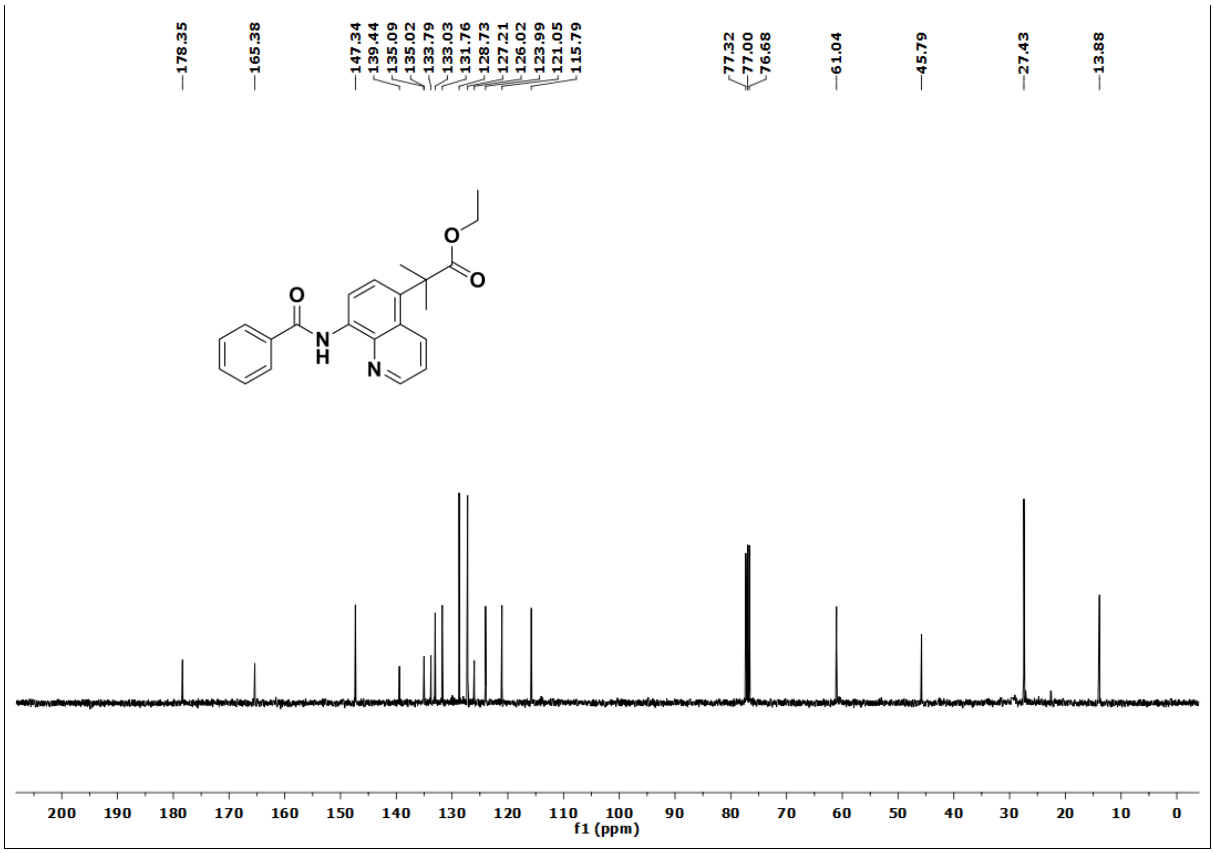


DEPT (135) NMR Spectrum of Compound **3oa.**

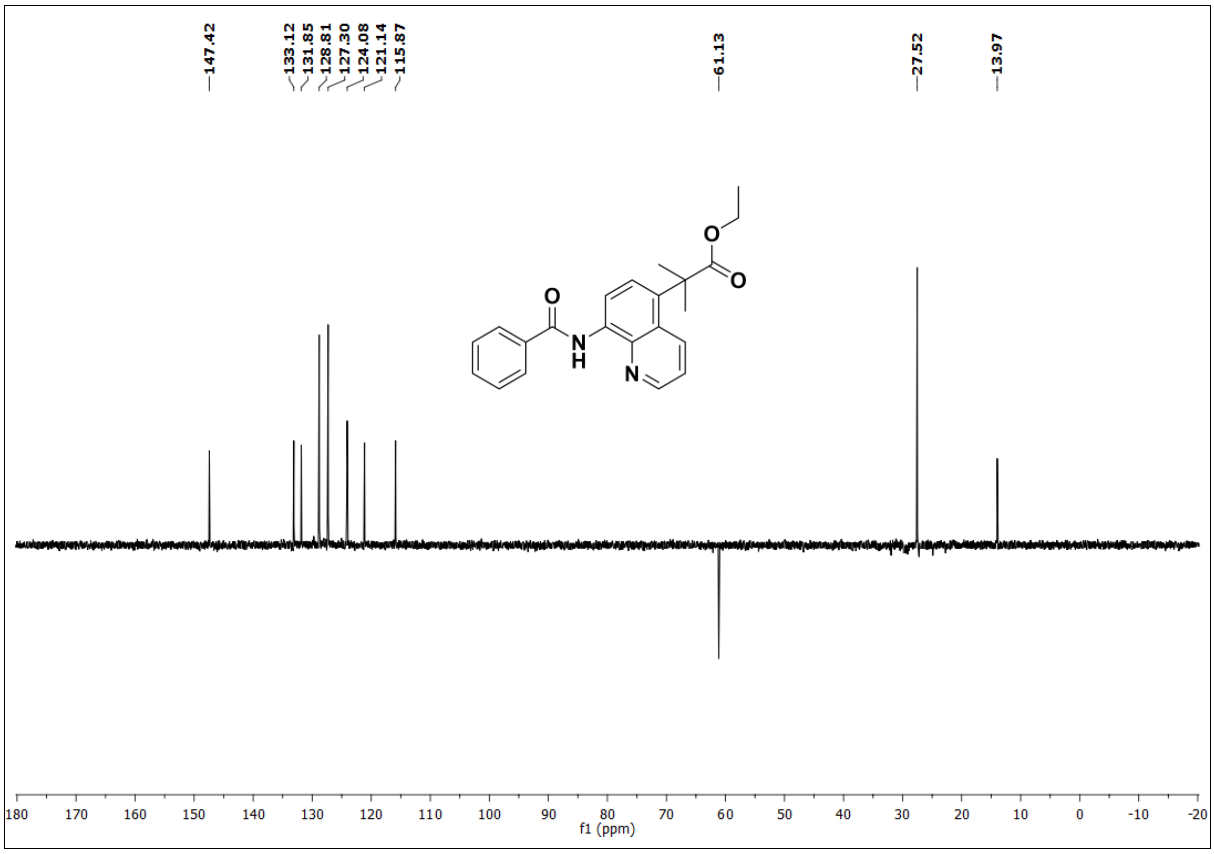


^{1}H and ^{13}C NMR Spectra of Compound **3ac.**

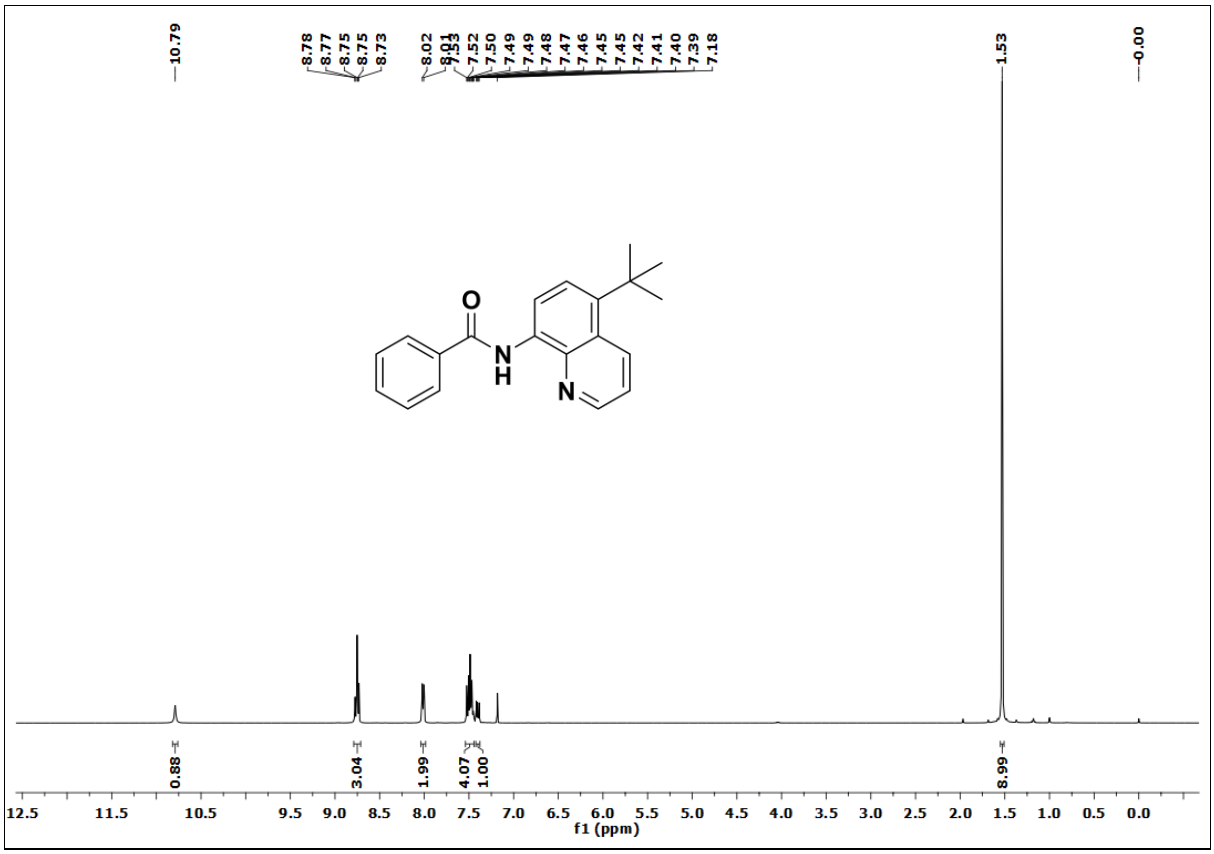


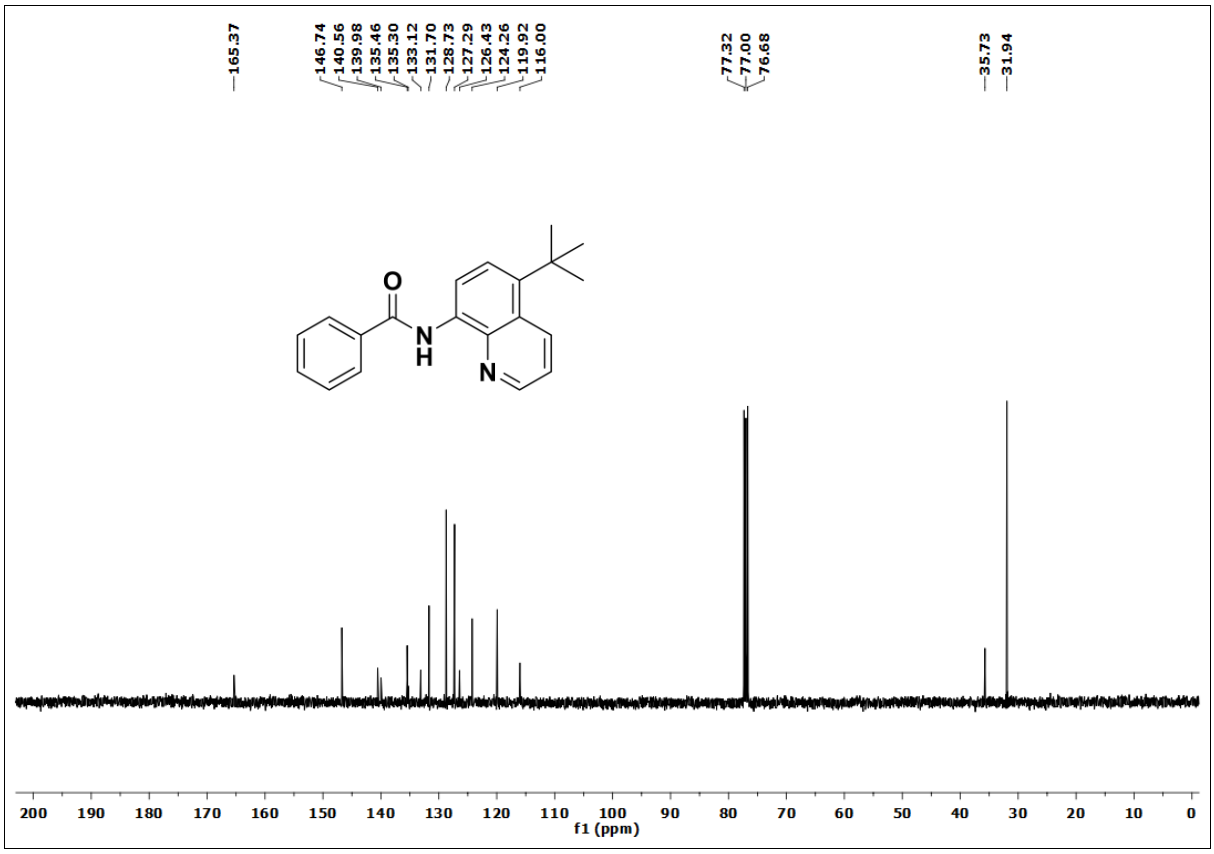


DEPT (135) NMR Spectrum of Compound **3ac.**

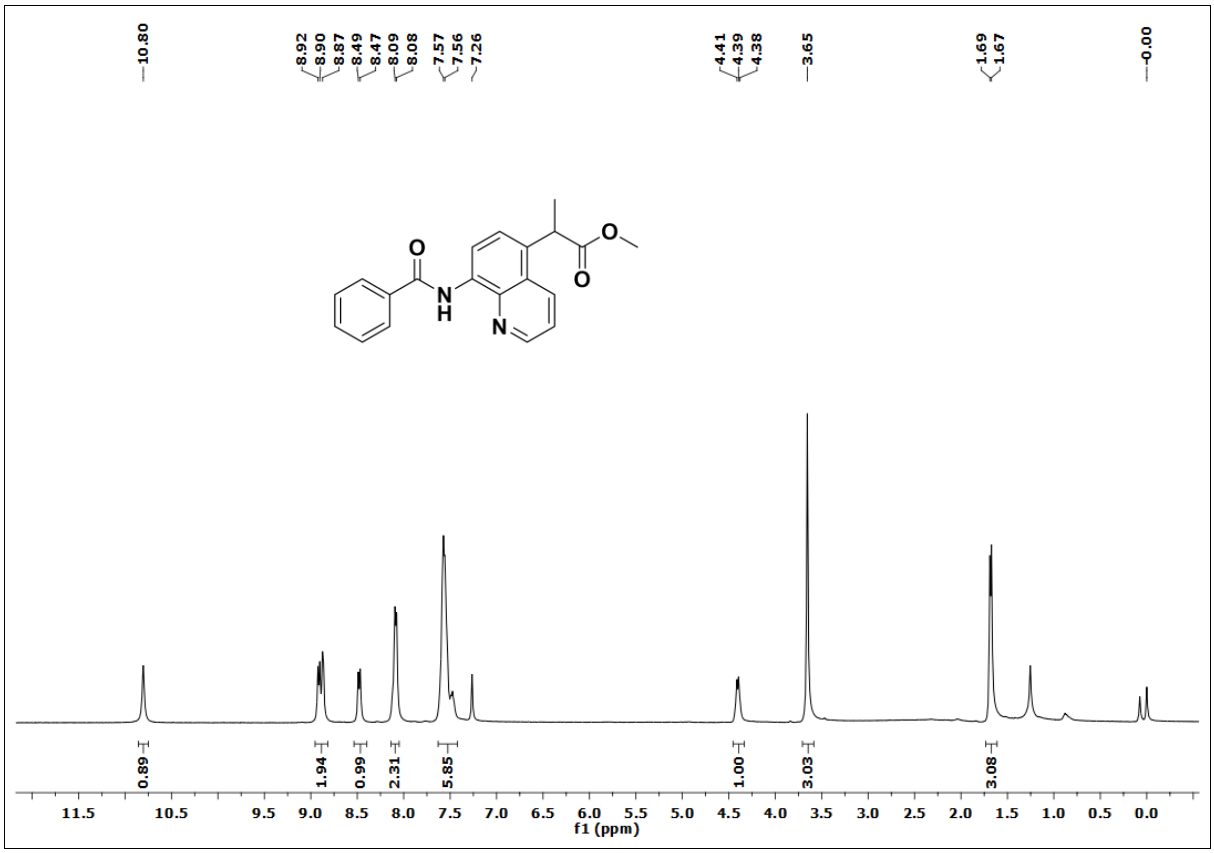


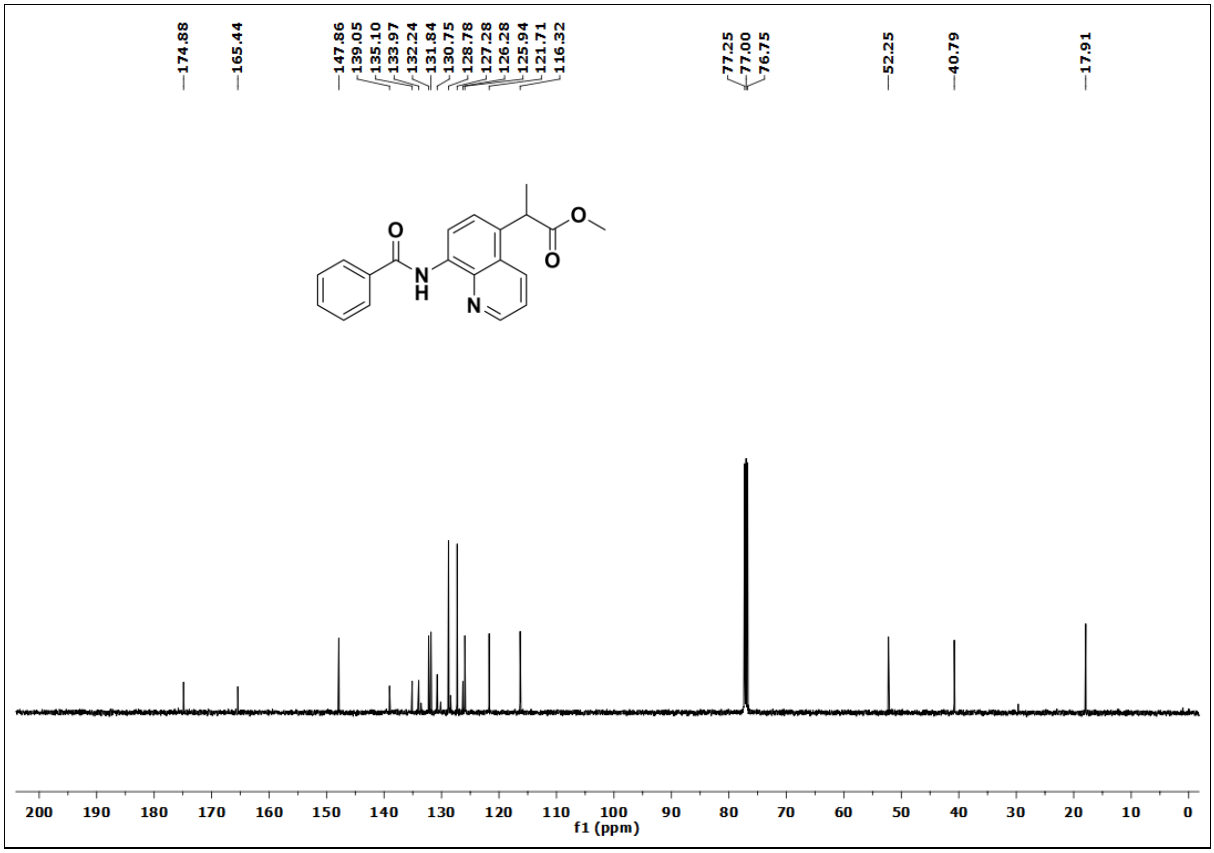
^{1}H and ^{13}C NMR Spectra of Compound **3ad.**



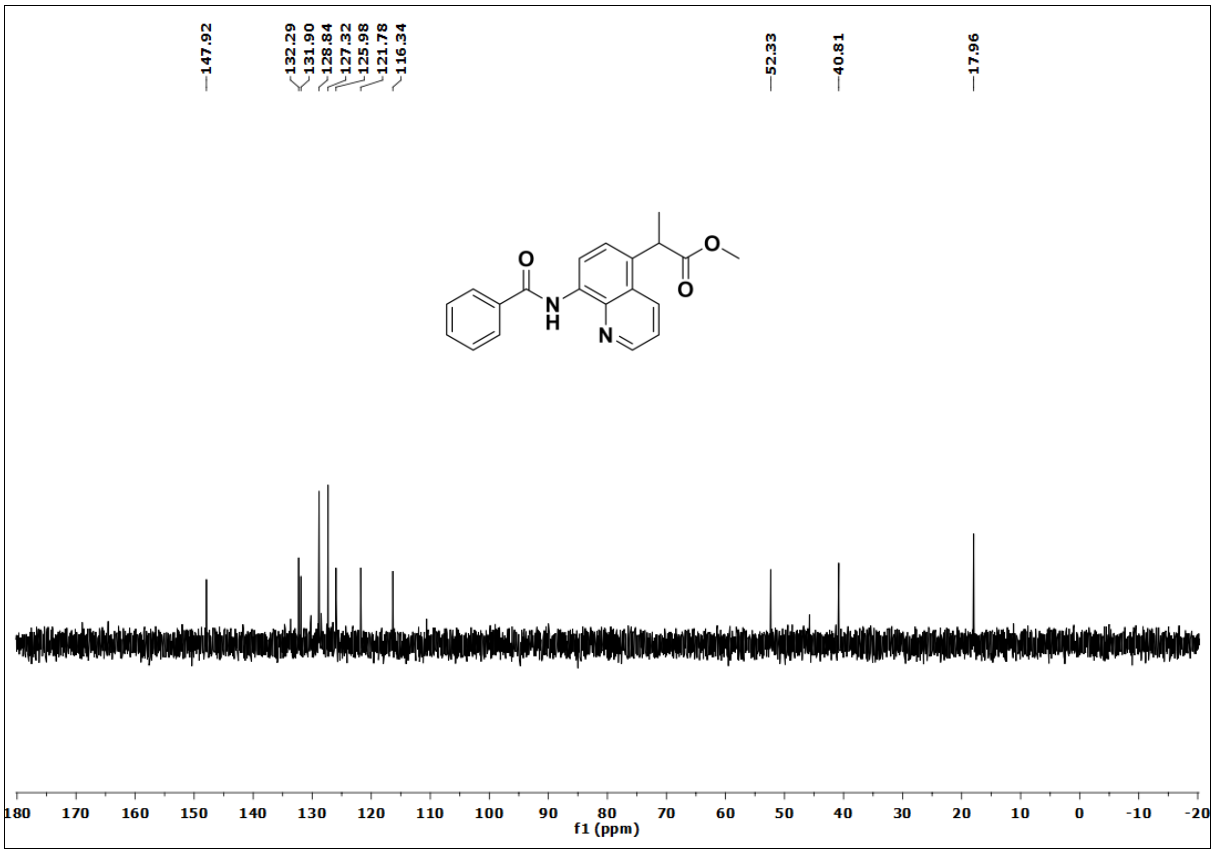


^{1}H and ^{13}C NMR Spectra of Compound **3ae.**

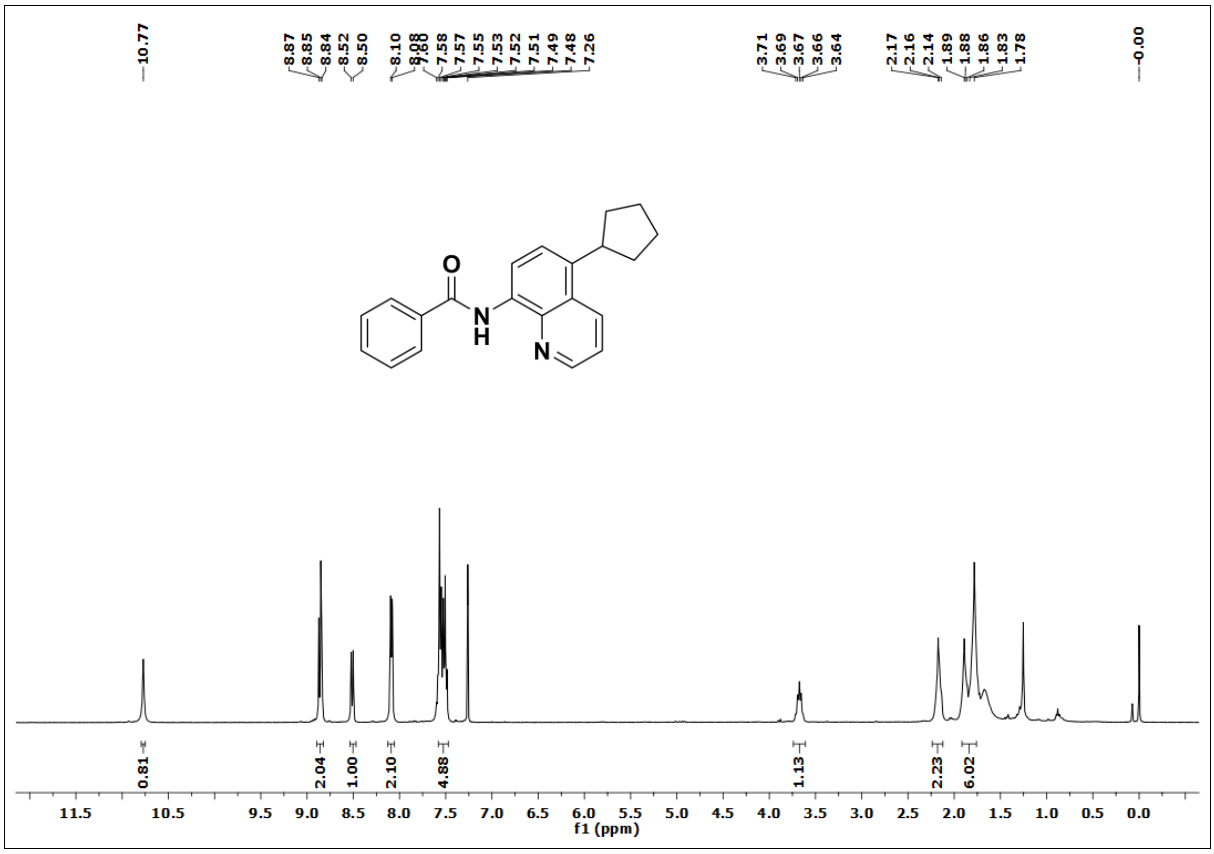


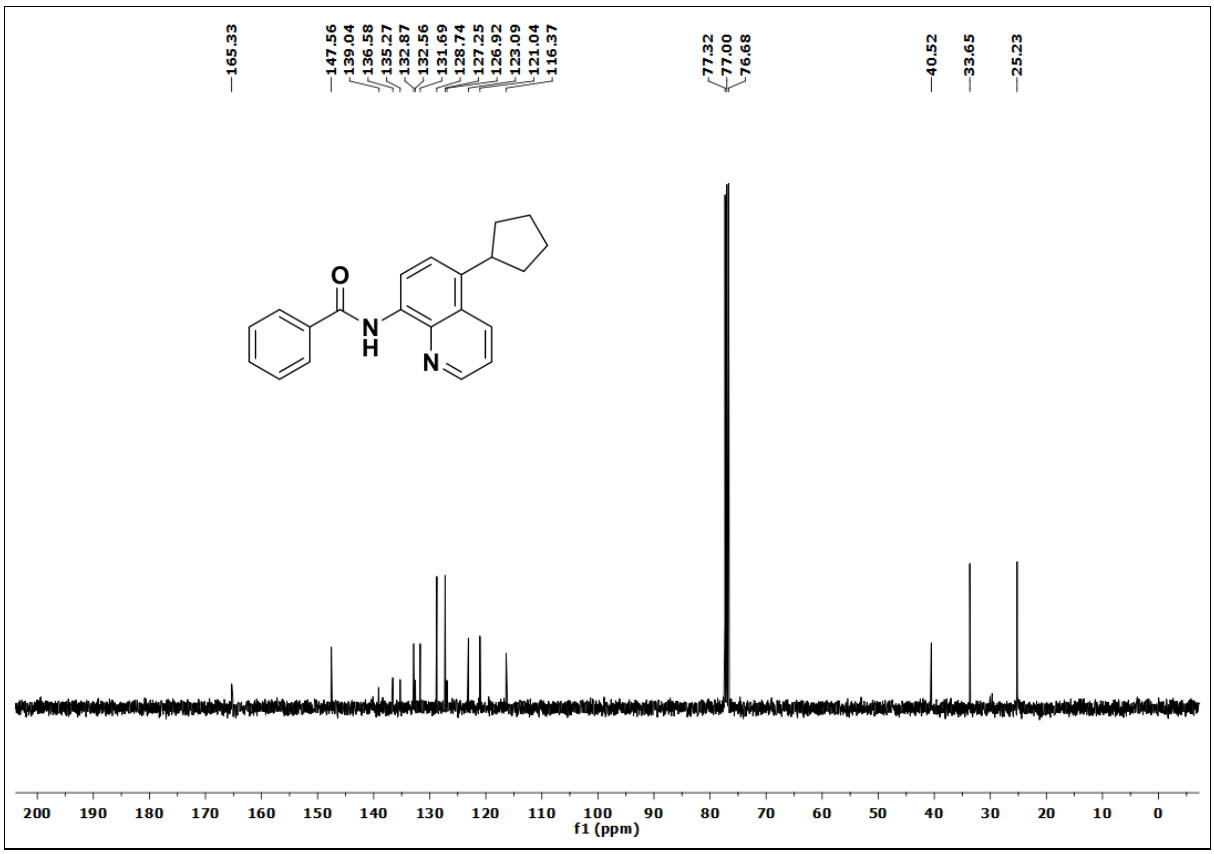


DEPT (135) NMR Spectrum of Compound **3ae.**

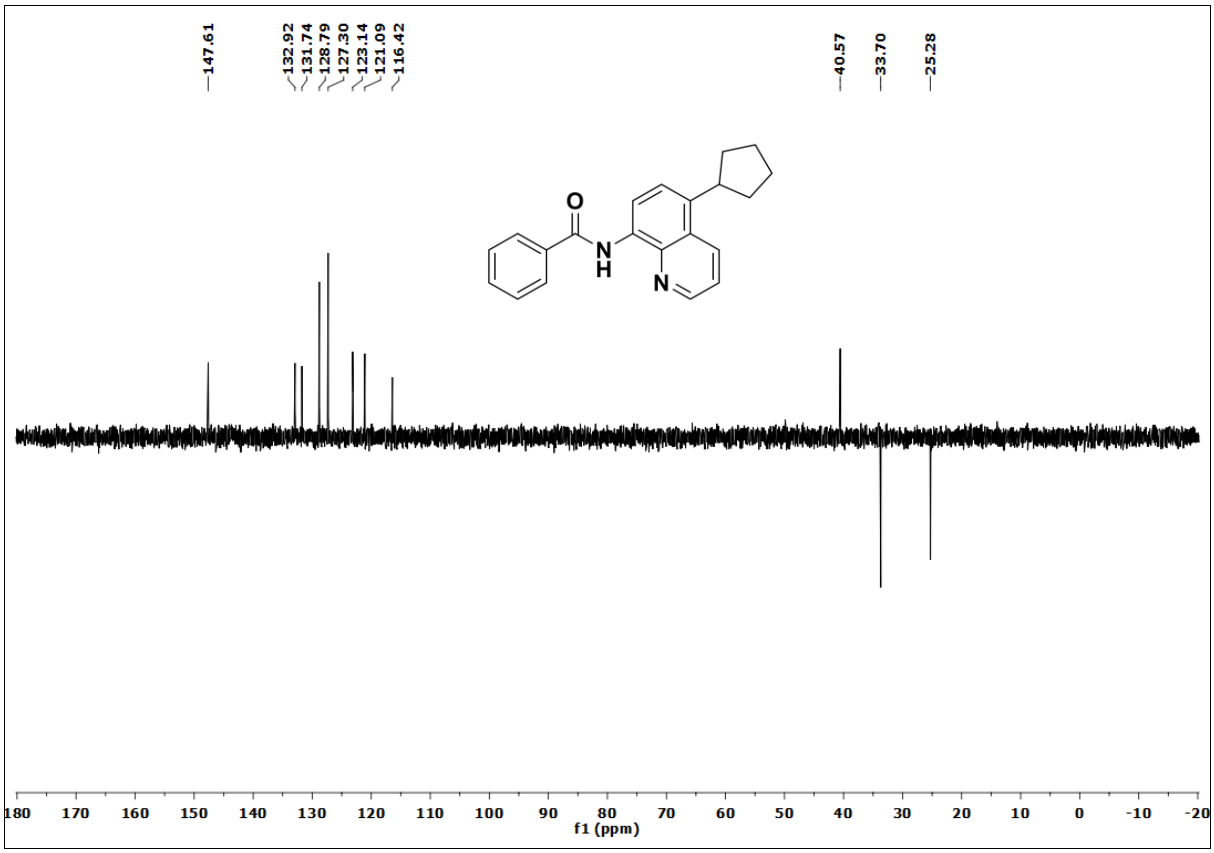


^{1}H and ^{13}C NMR Spectra of Compound **3ab.**

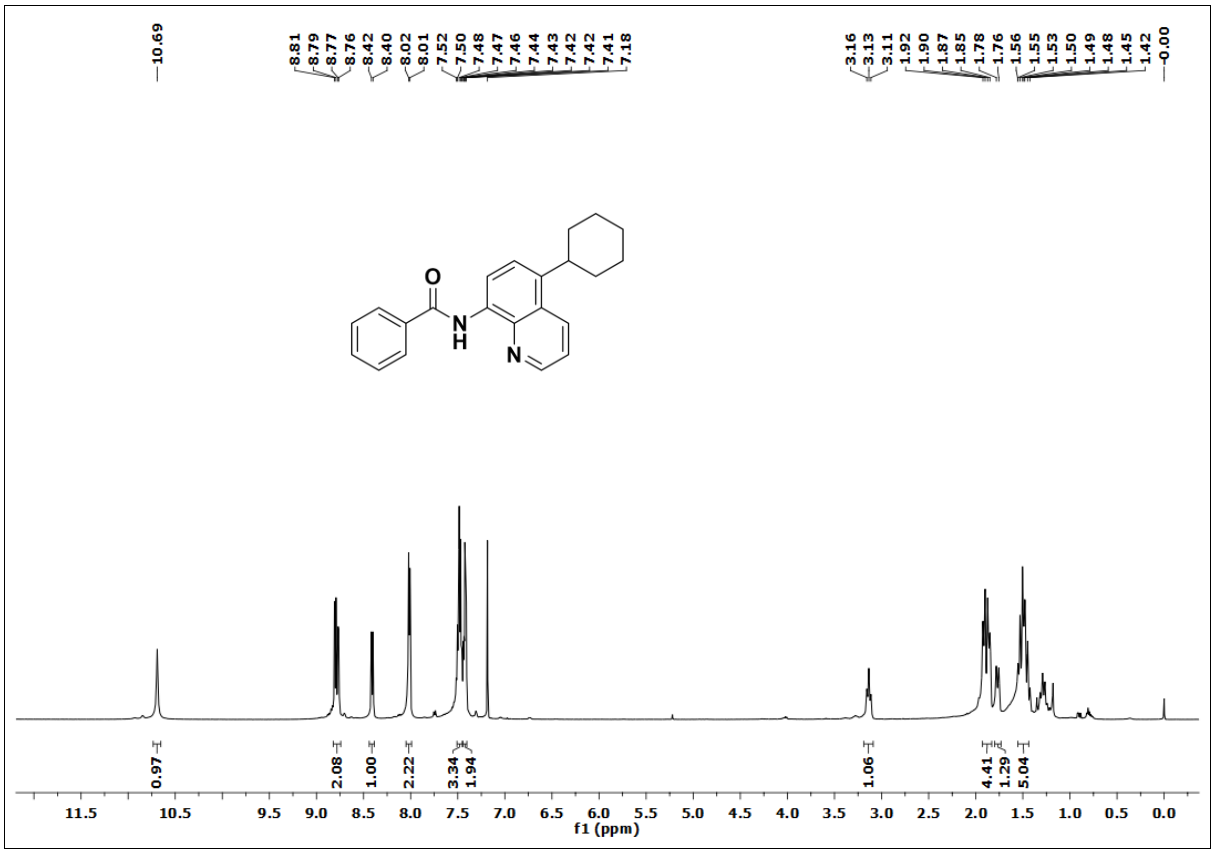


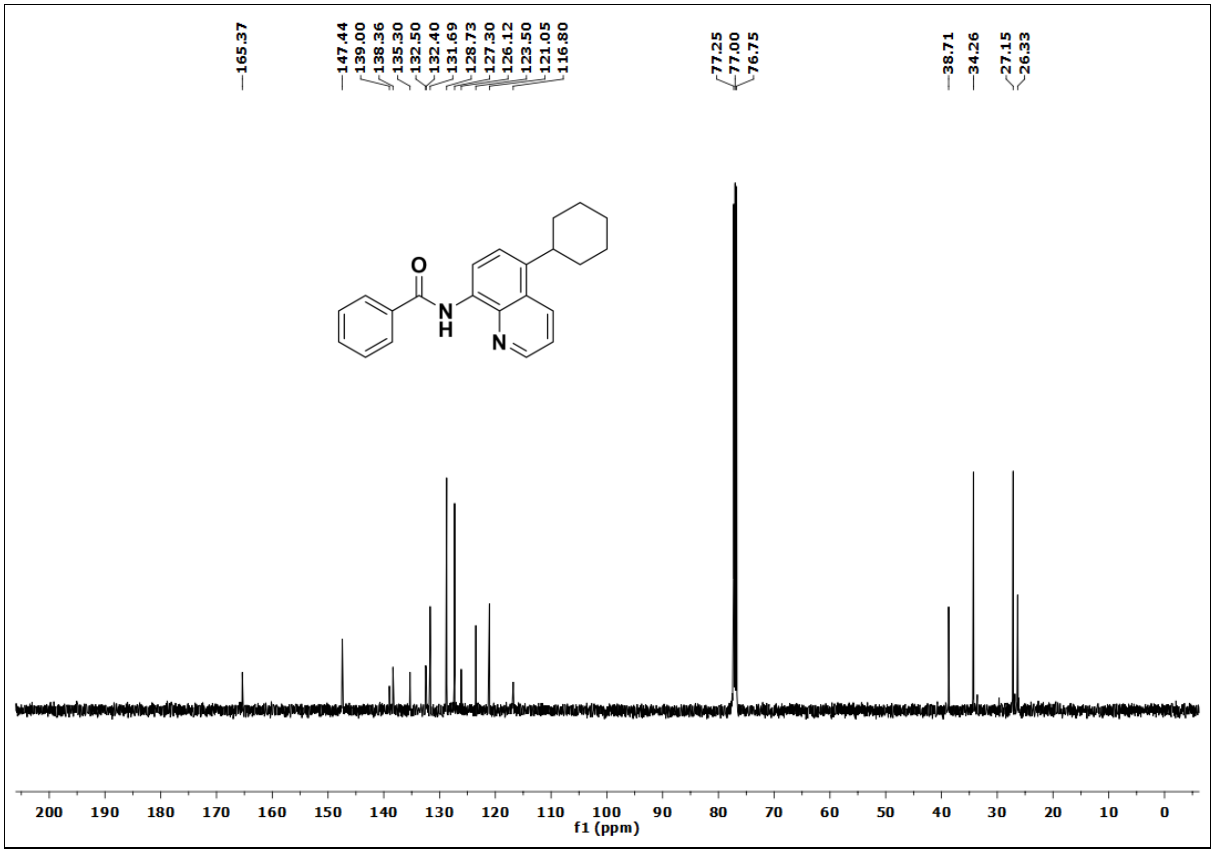


DEPT (135) NMR Spectrum of Compound **3ab.**

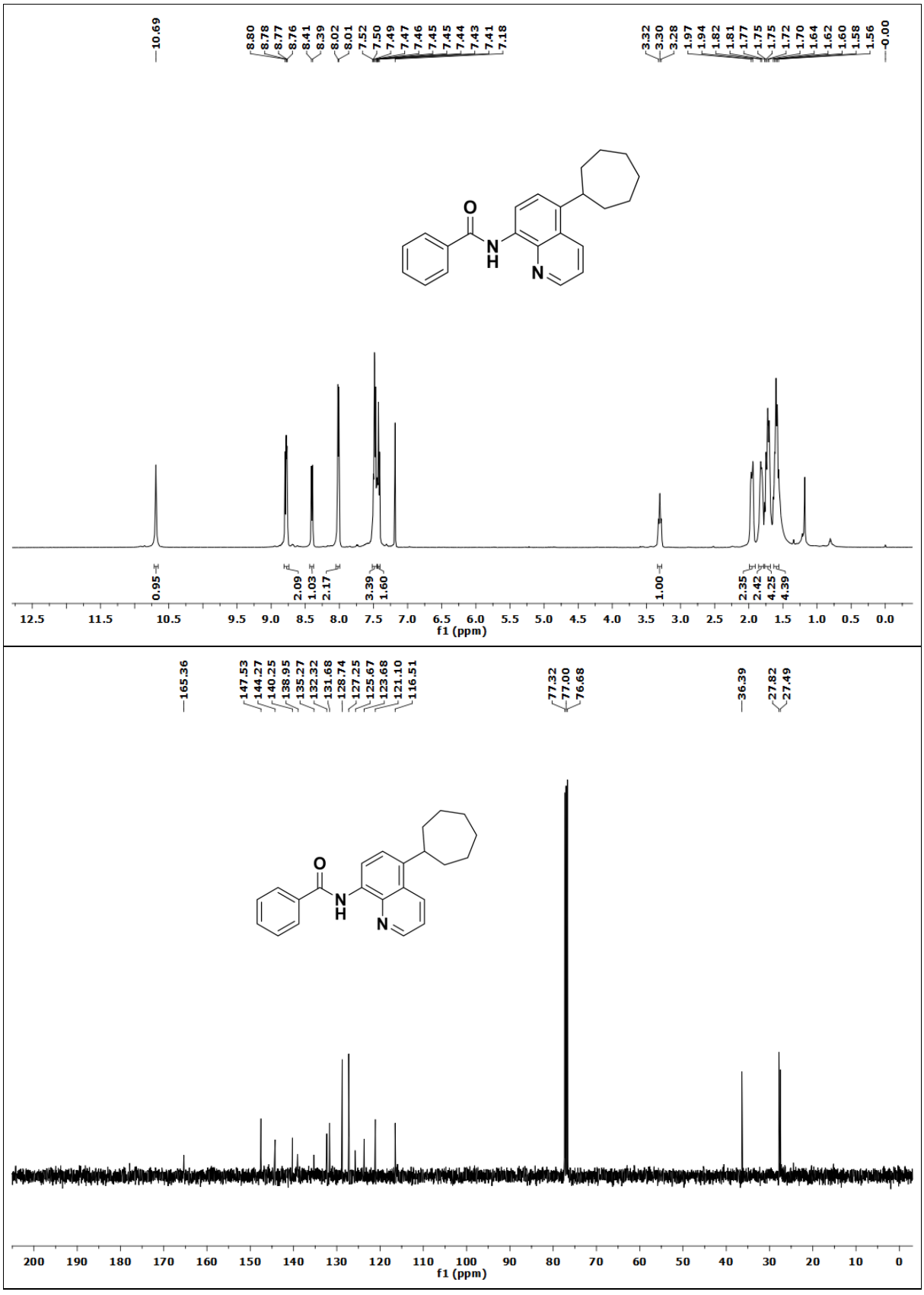


^{1}H and ^{13}C NMR Spectra of Compound **3af.**

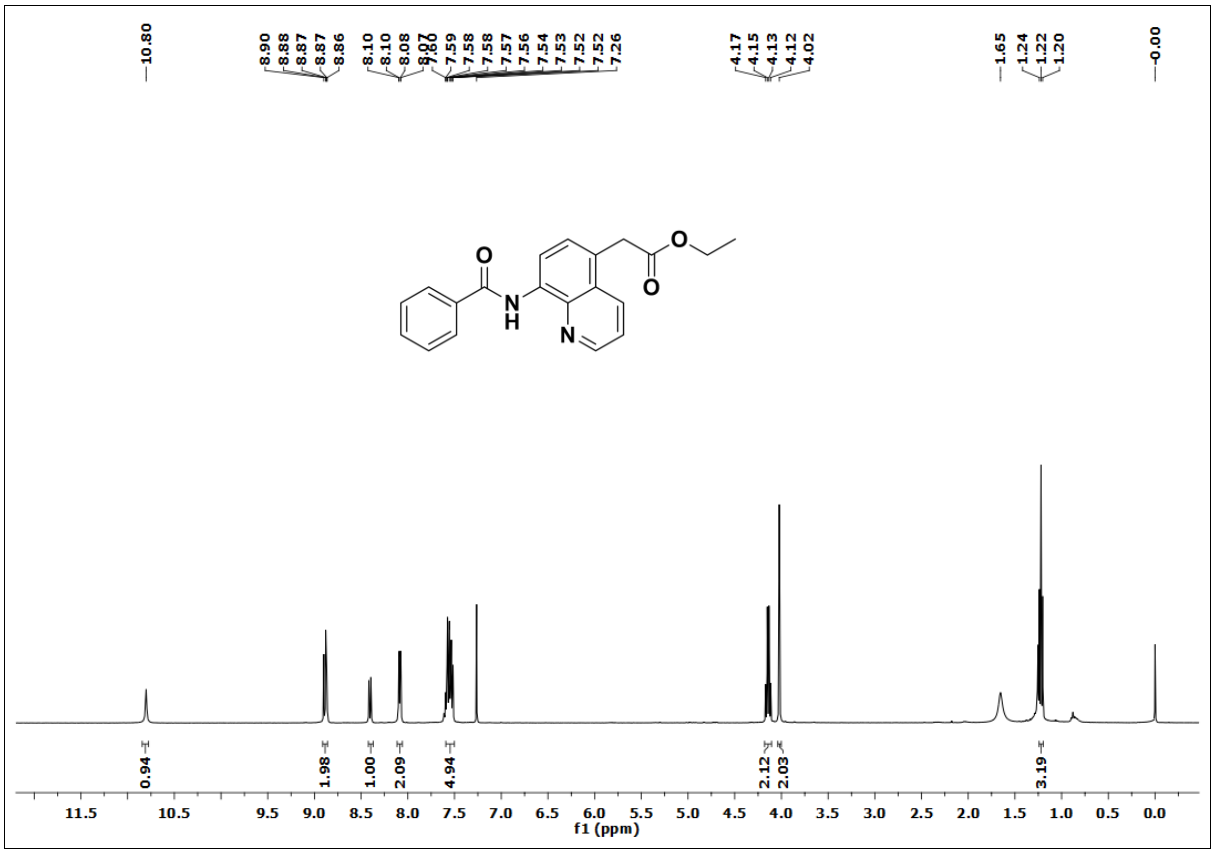


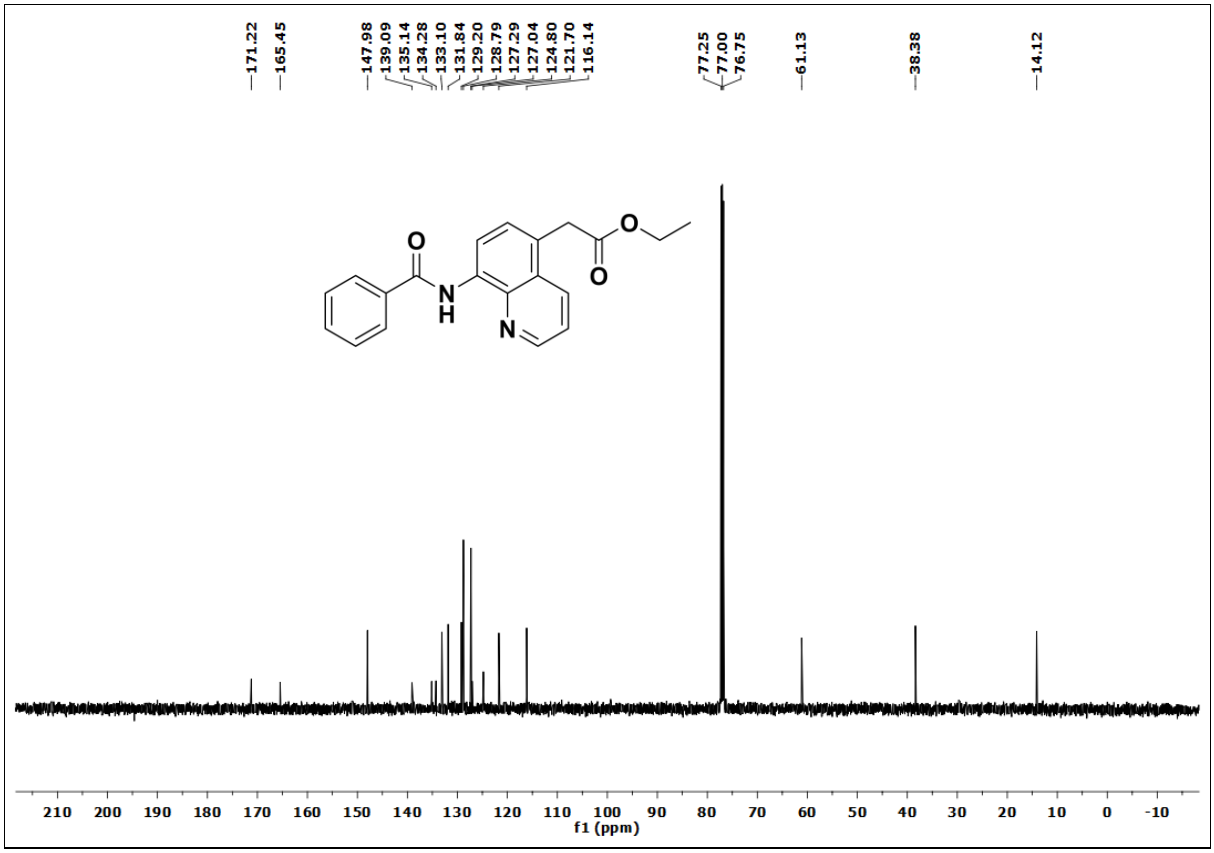


^{1}H and ^{13}C NMR Spectra of Compound **3ag.**

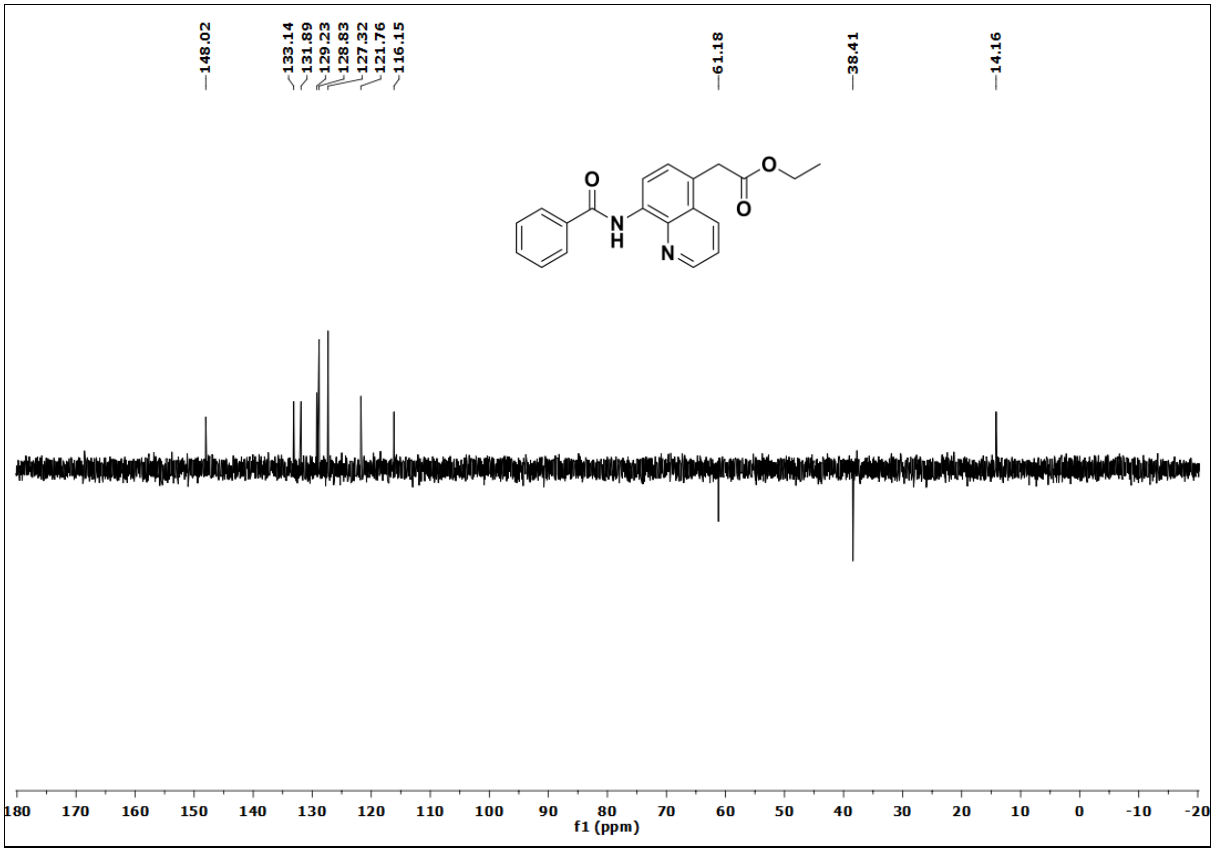


^{1}H and ^{13}C NMR Spectra of Compound **3ah.**

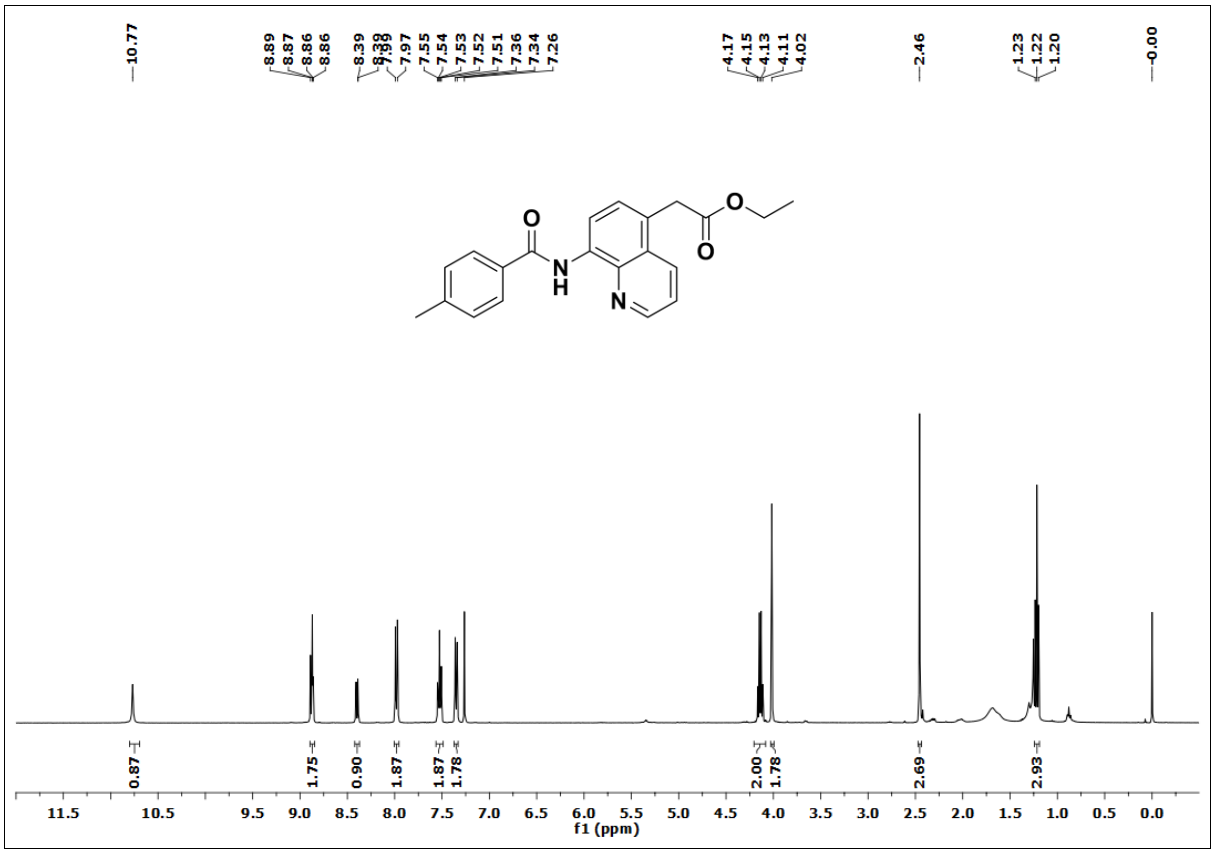


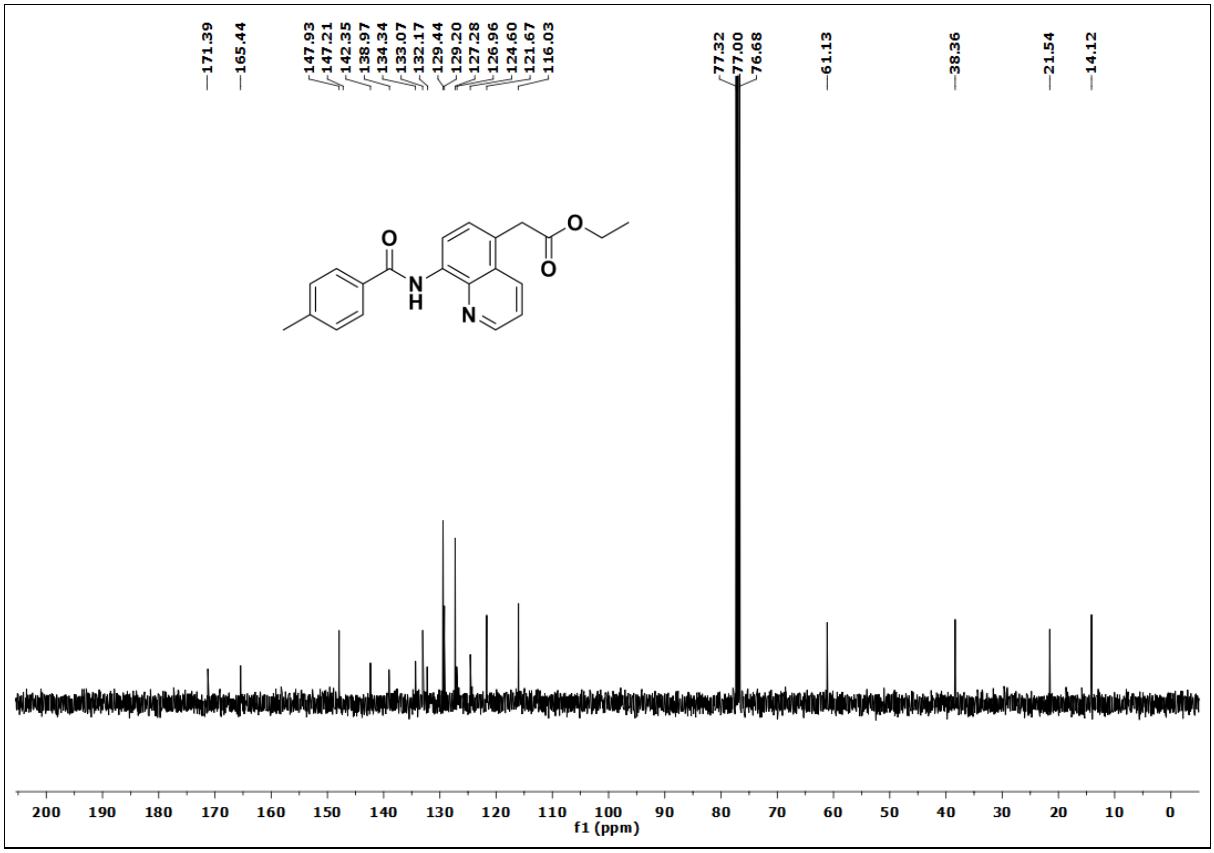


DEPT (135) NMR Spectrum of Compound **3ah.**

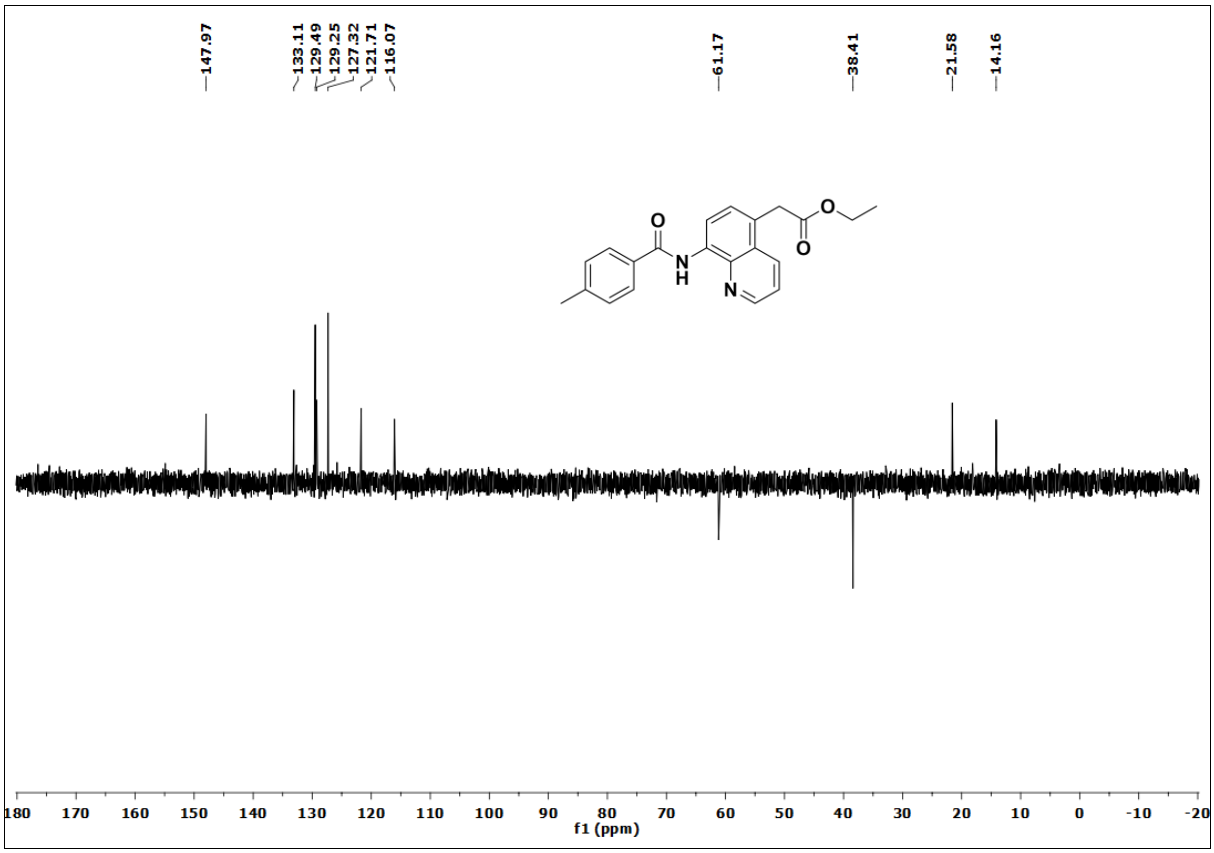


^{1}H and ^{13}C NMR Spectra of Compound **3dh.**

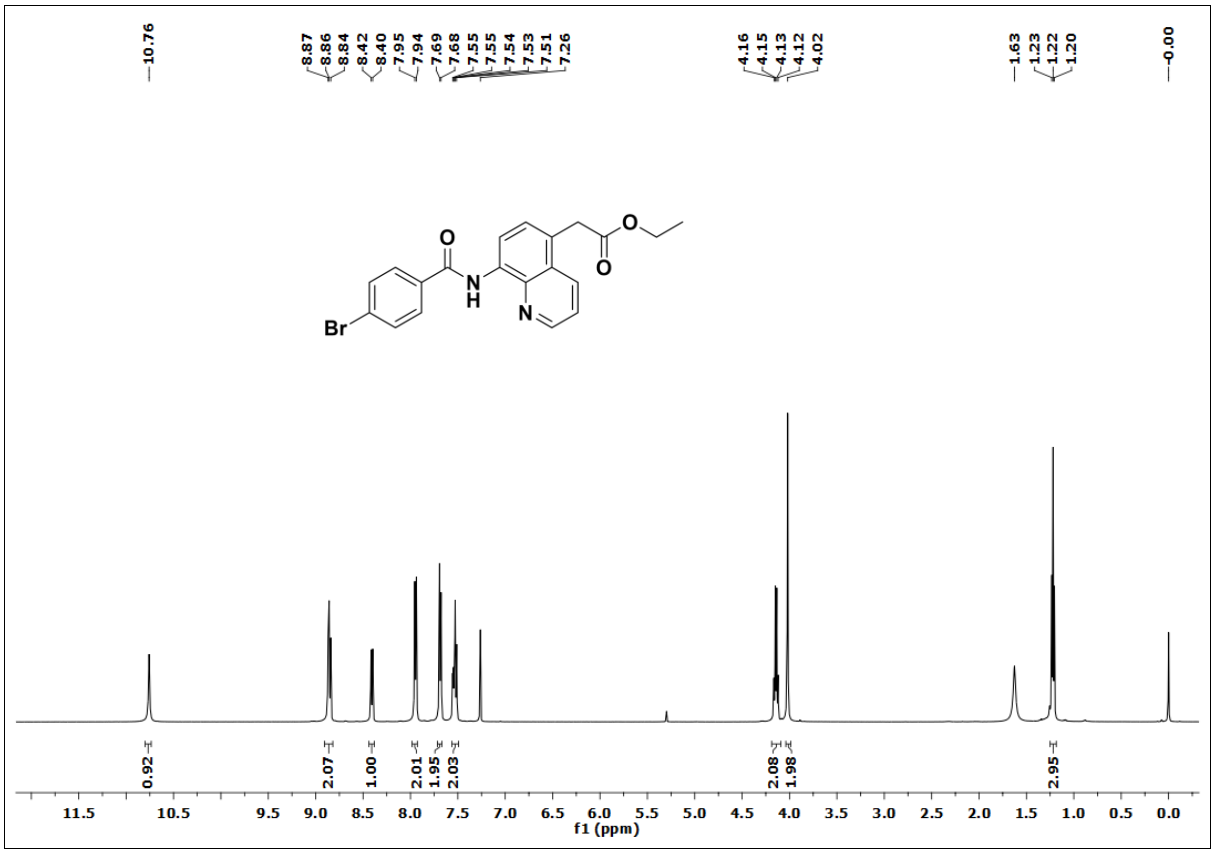


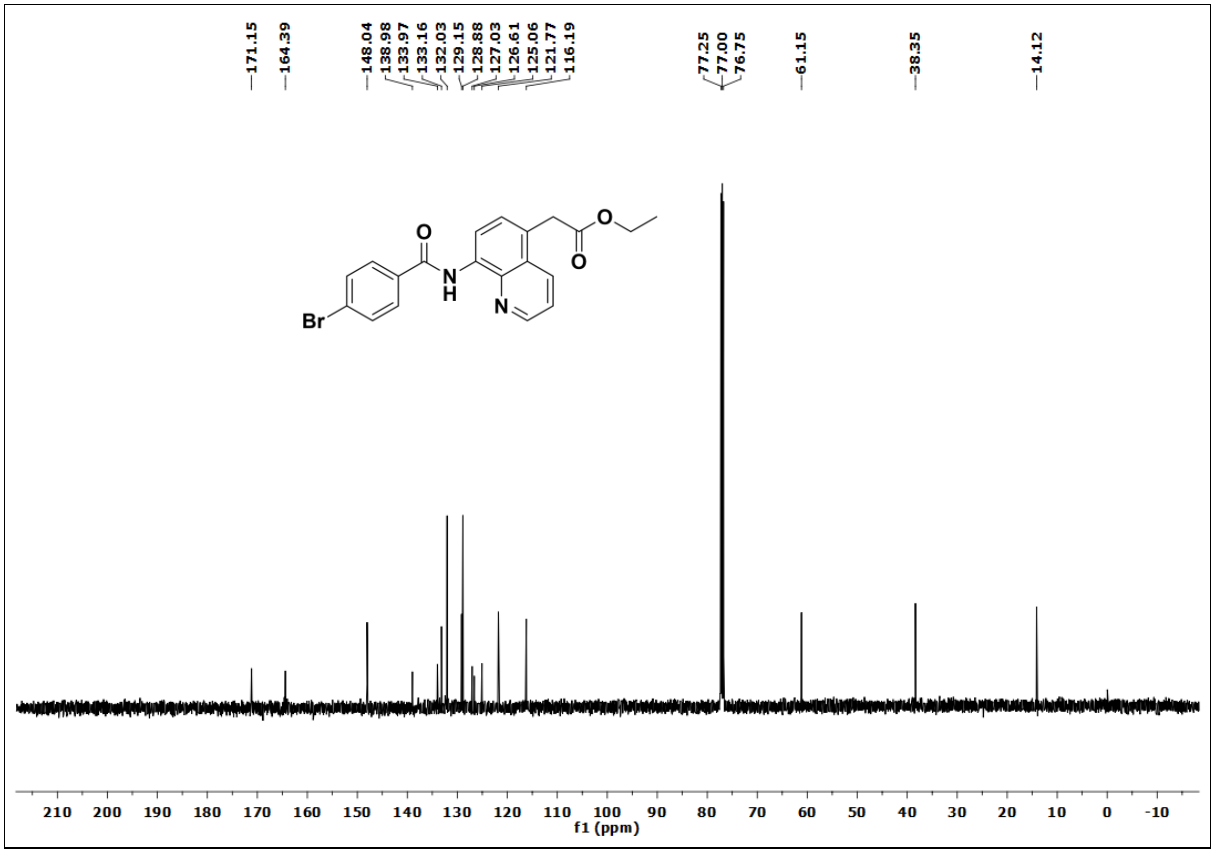


DEPT (135) NMR Spectrum of Compound **3dh.**

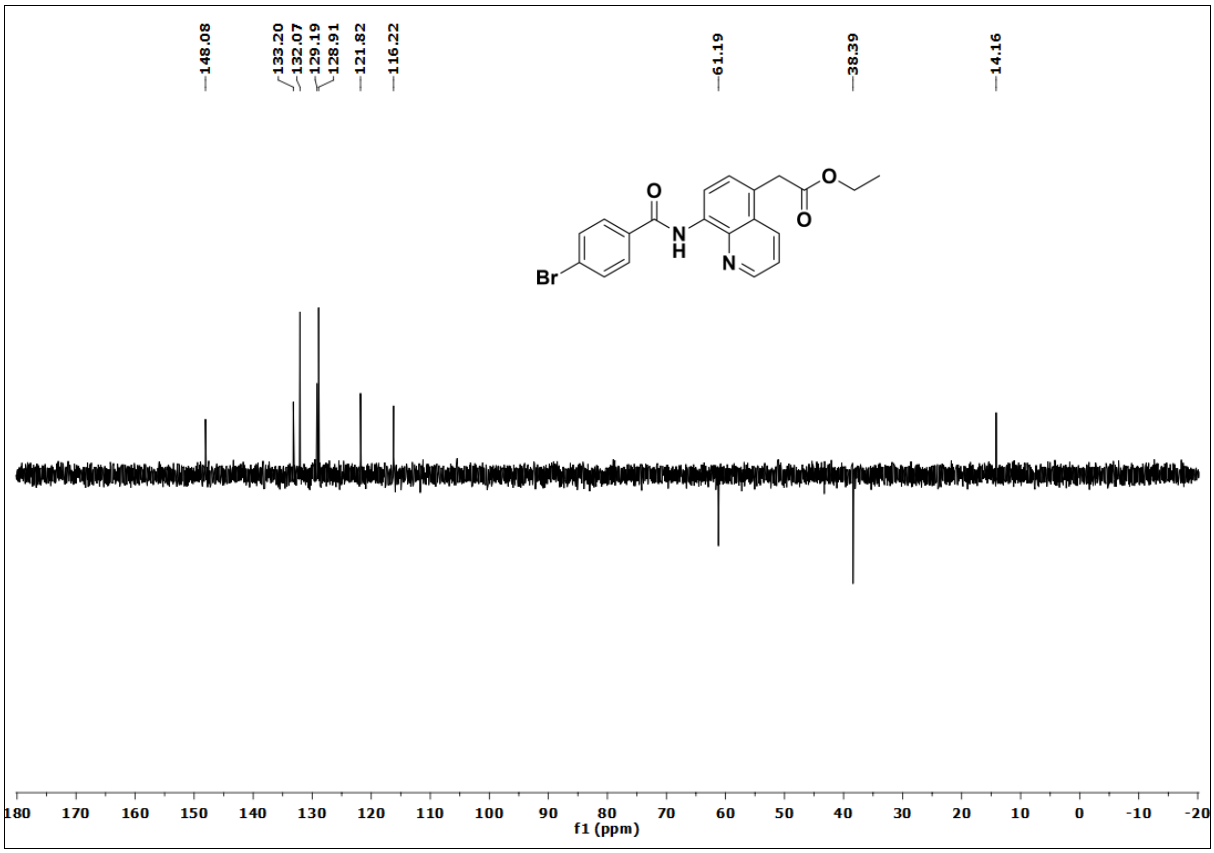


^{1}H and ^{13}C NMR Spectra of Compound **3fh.**

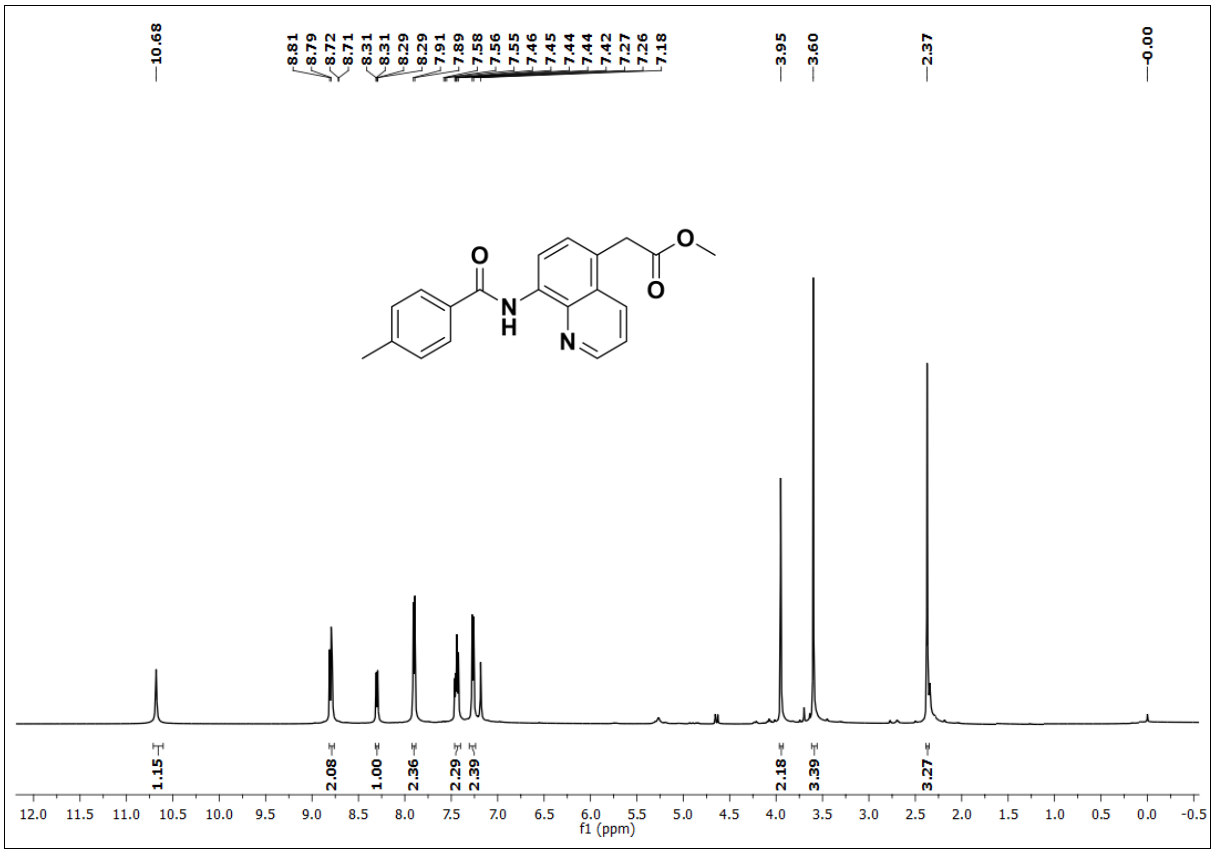


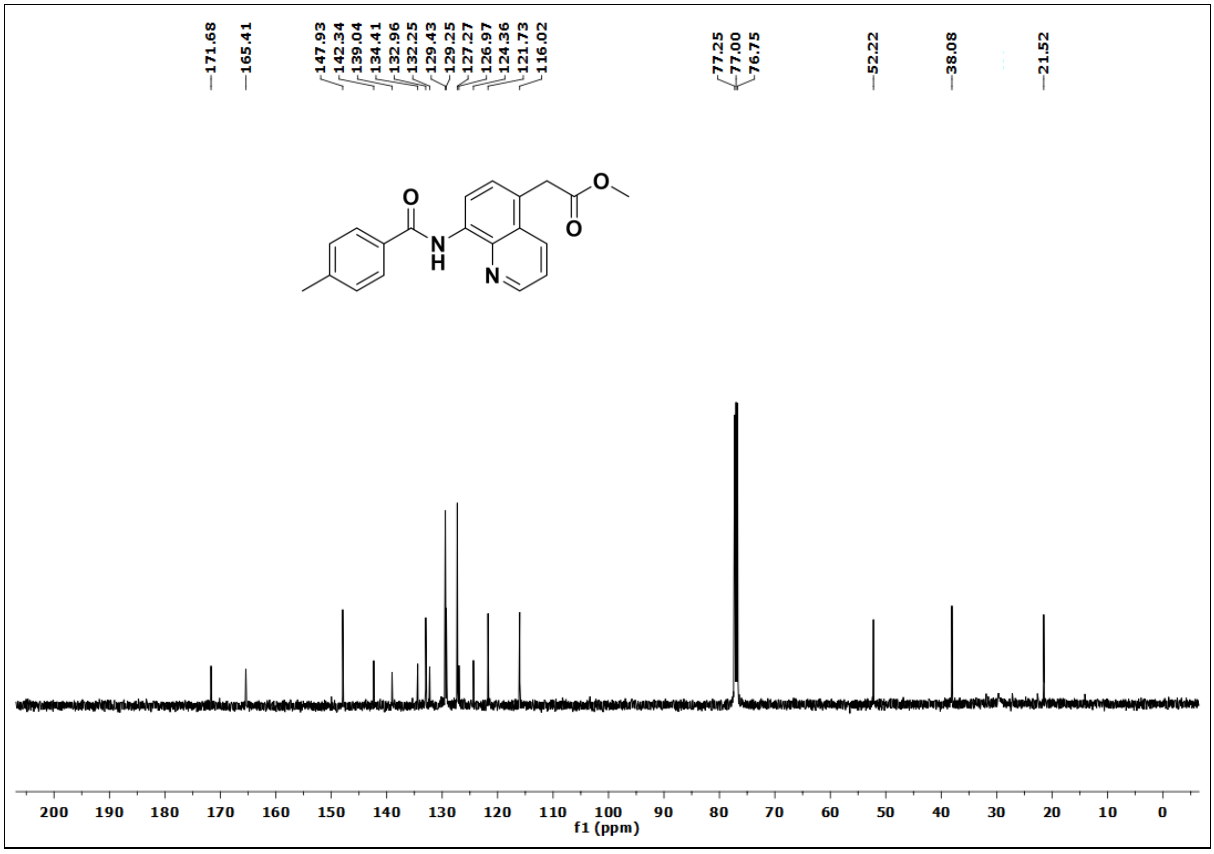


DEPT (135) NMR Spectrum of Compound **3fh.**

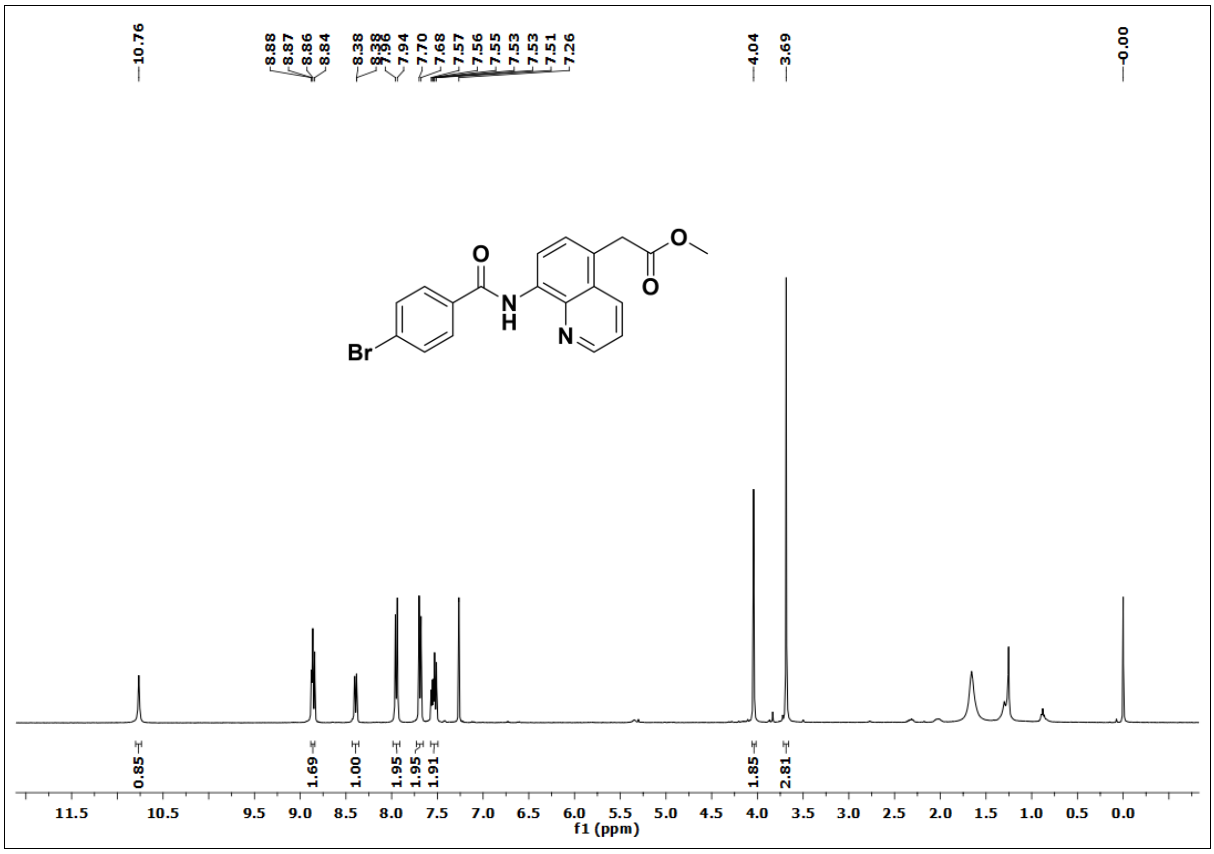


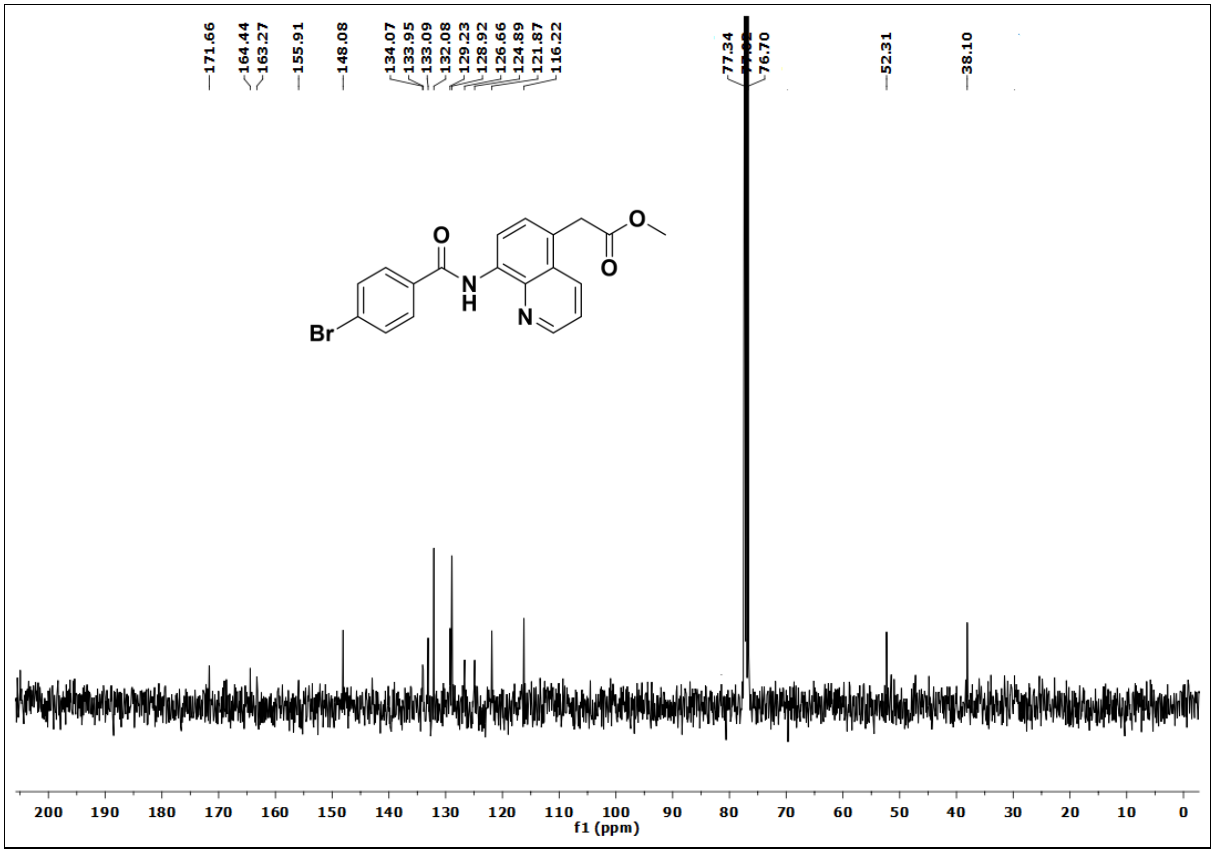
^{1}H and ^{13}C NMR Spectra of Compound **3di.**



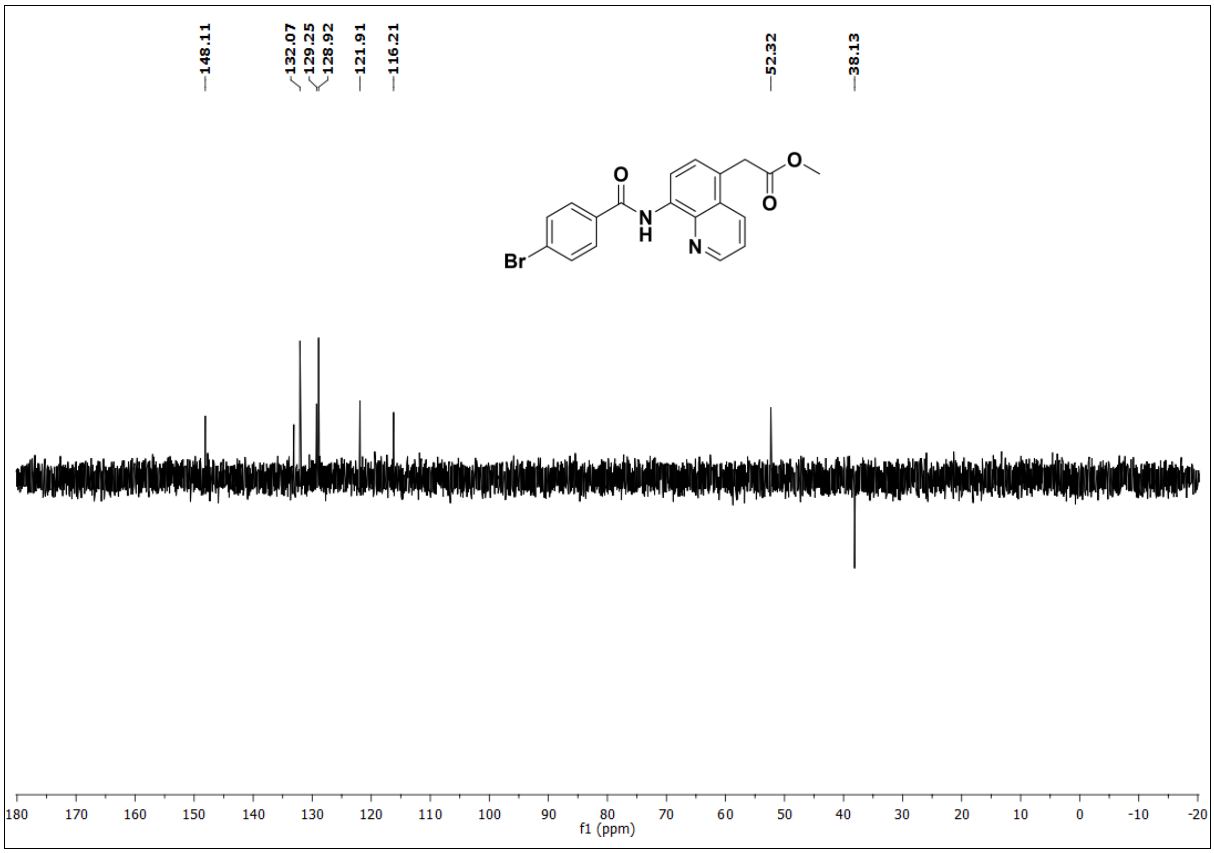


^{1}H and ^{13}C NMR Spectra of Compound **3fi.**

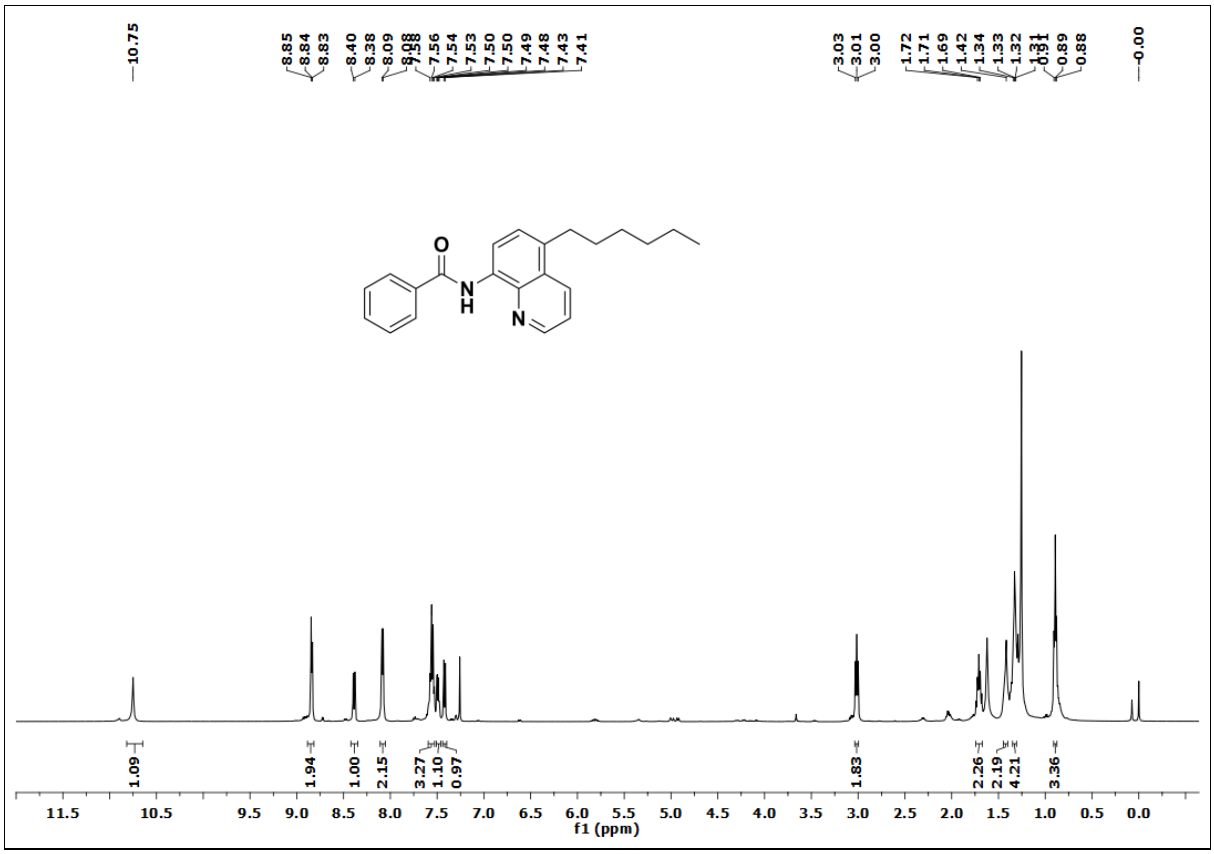


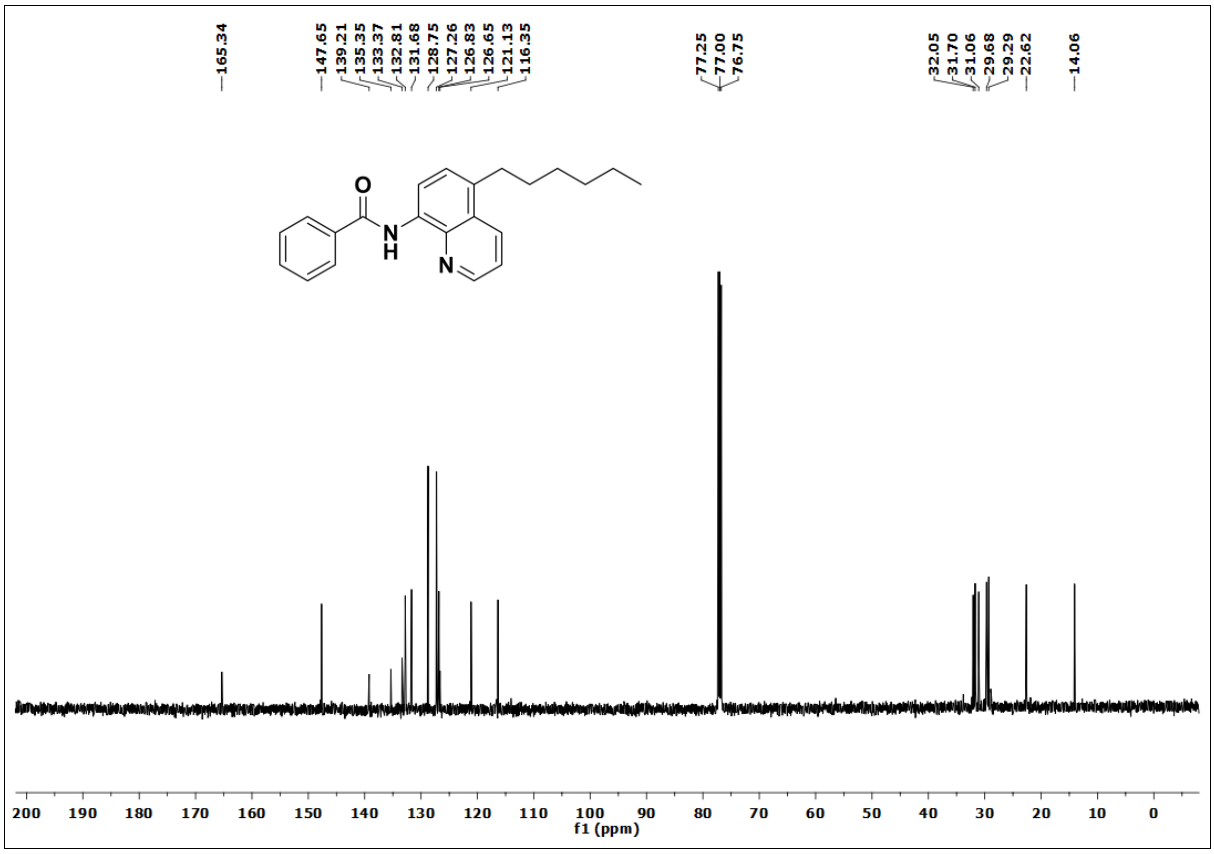


DEPT (135) NMR Spectrum of Compound **3fi.**

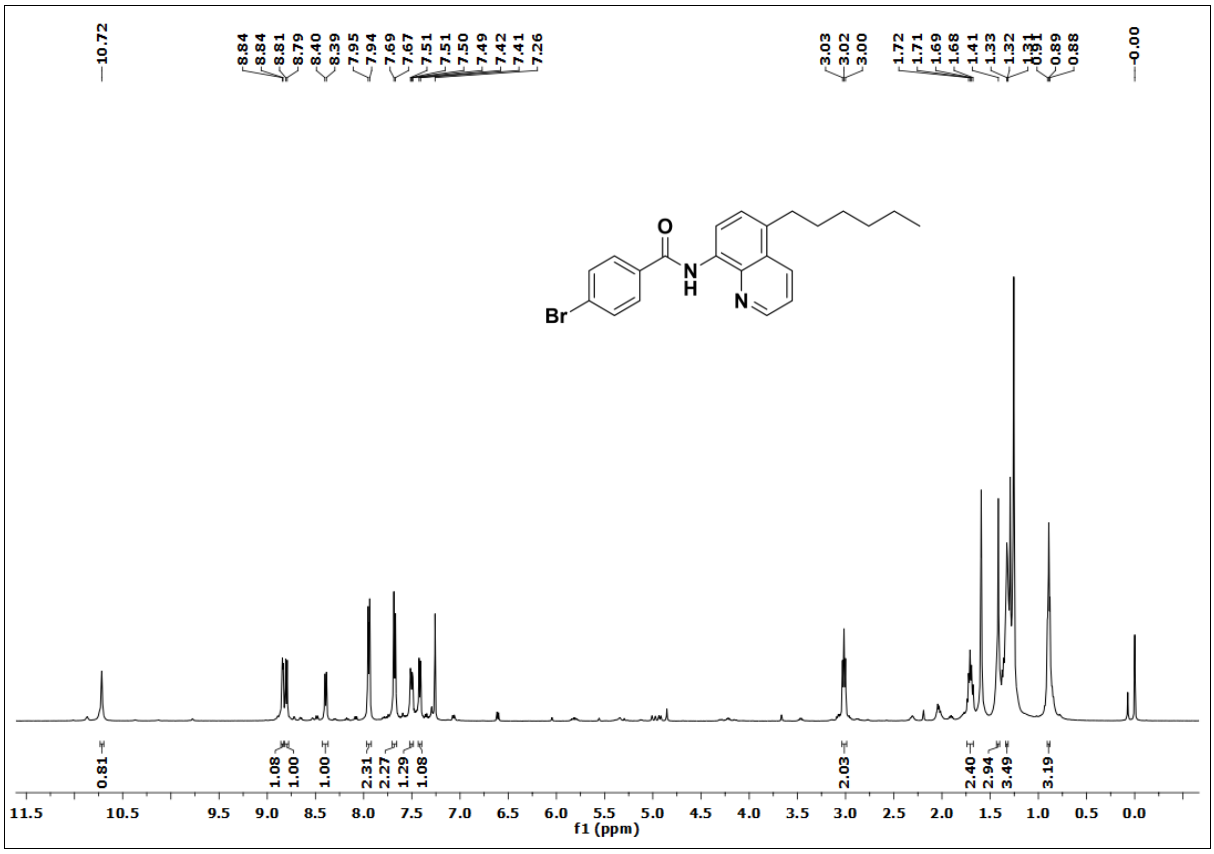


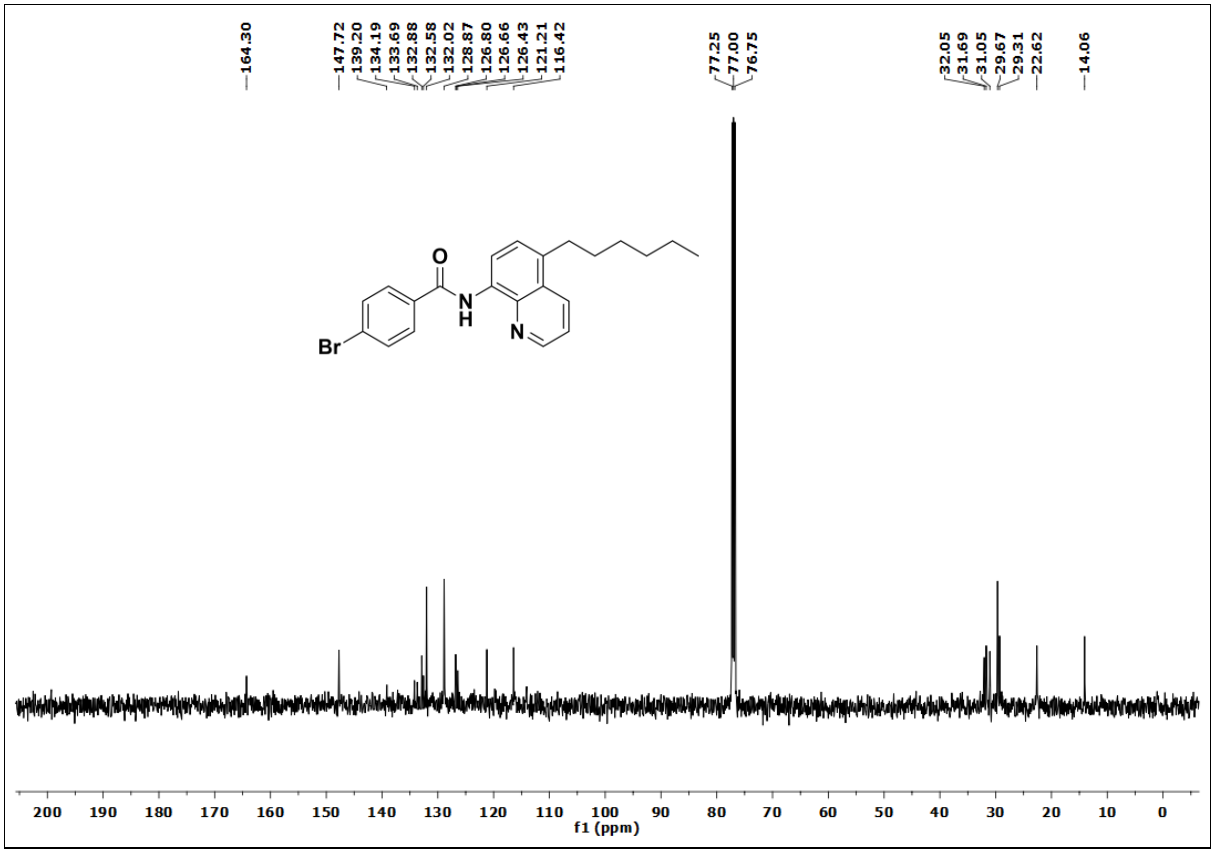
^{1}H and ^{13}C NMR Spectra of Compound **3aj.**



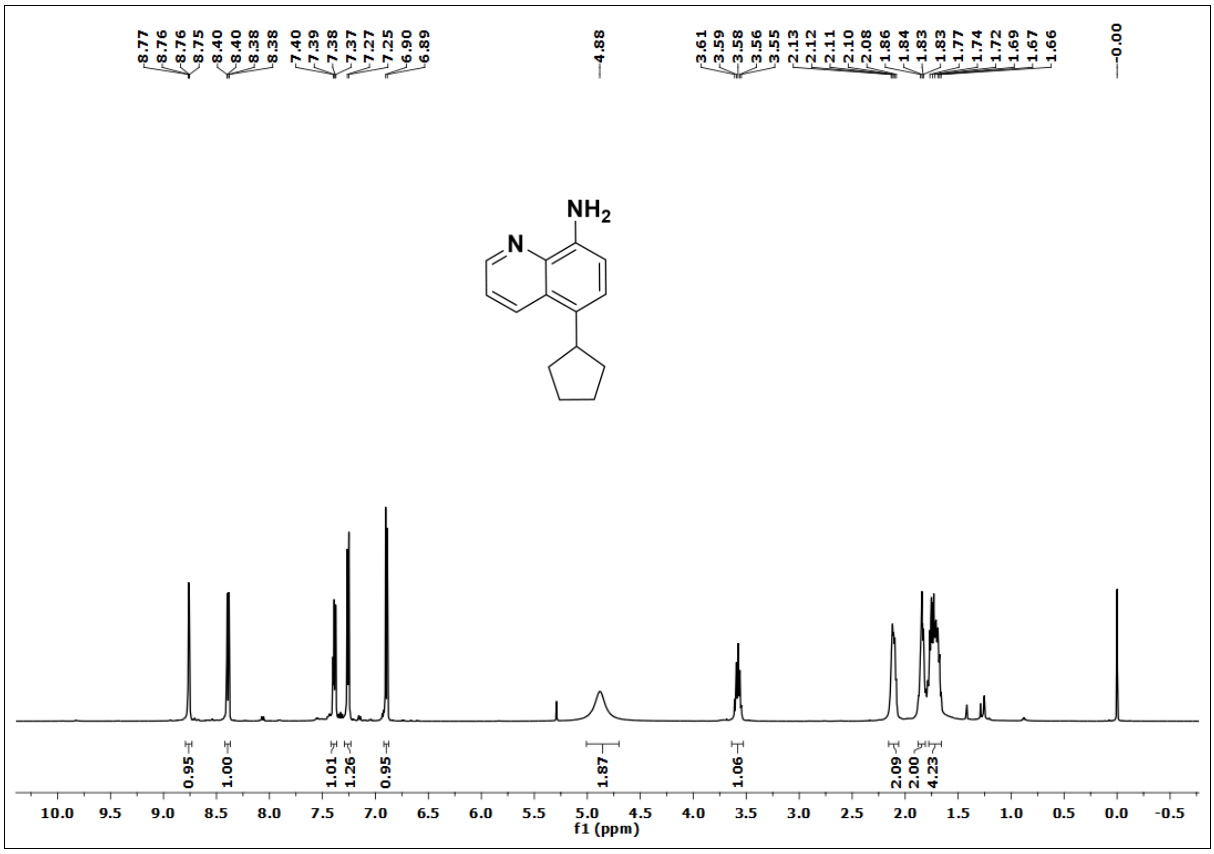


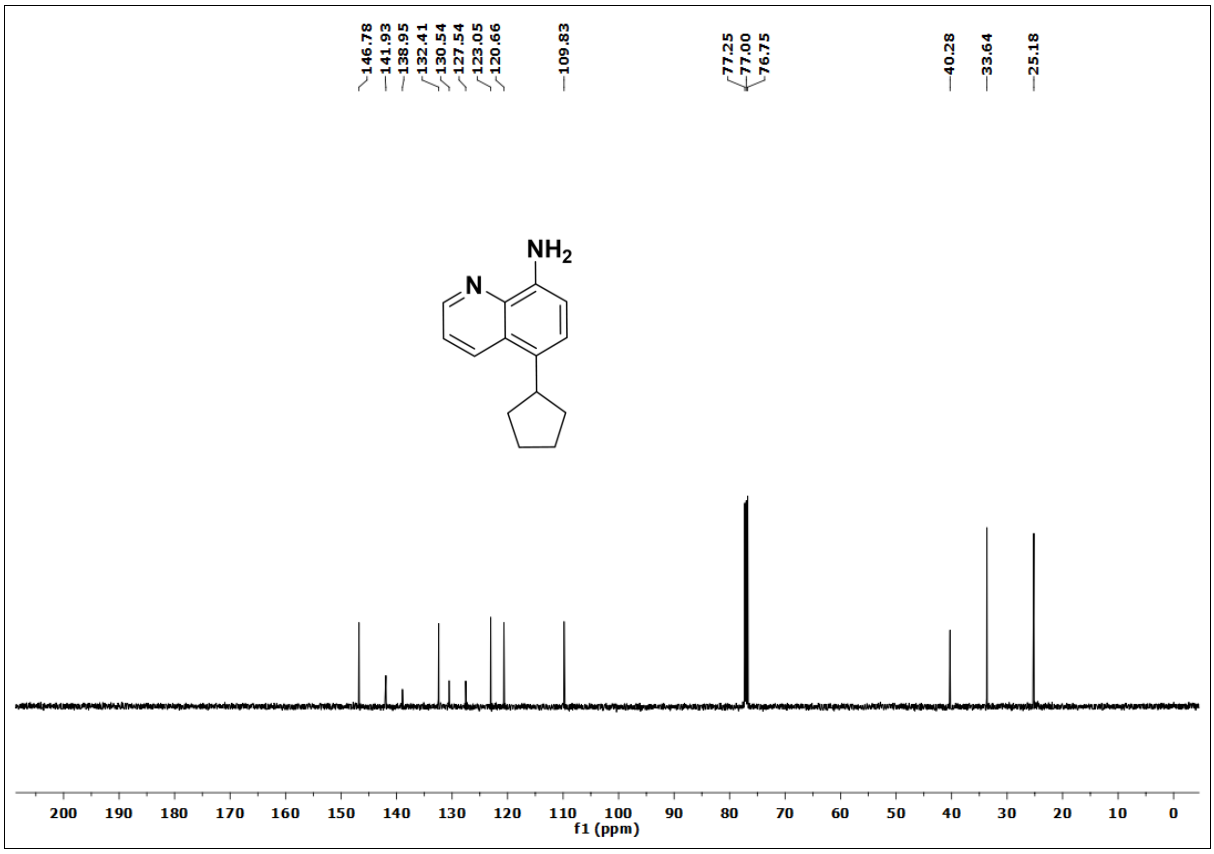
^{1}H and ^{13}C NMR Spectra of Compound **3fj.**



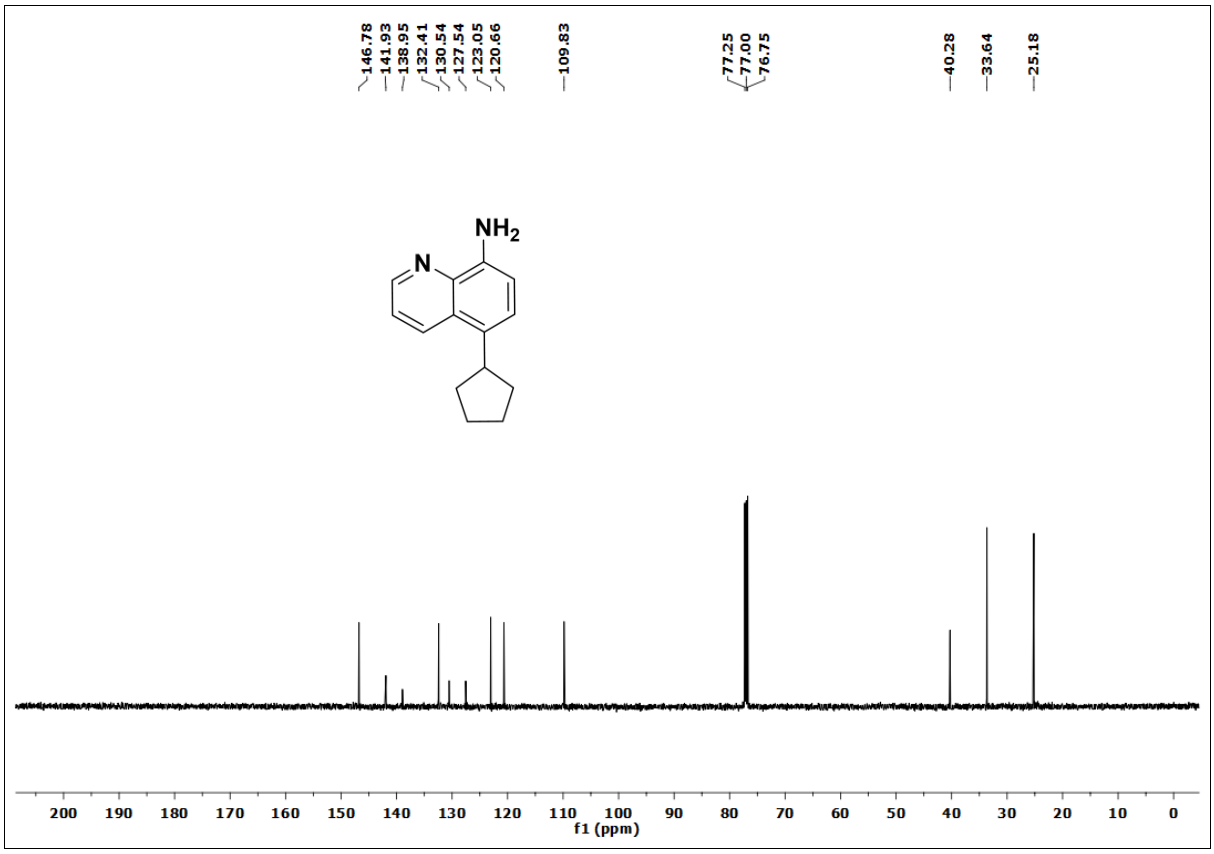


^{1}H and ^{13}C NMR Spectra of Compound **10.**





DEPT (135) NMR Spectrum of Compound **10.**



Note:

For the starting material **1m** and **1n** the final product formed is **3aa**. So we have not included the spectra again.