An Unusual 1, 2-Aryl Shift in Palladium-Catalyzed Cross-Coupling Ethoxycarbonylation of Arylboronic Acids with α-Iminoesters

Cheng Qian,[a] Jiayan Chen,[a] Meiqin Fu, [a] Shiya Zhu,[a] Wen-Hua Chen,[b] Huanfeng Jiang,[a] and Wei Zeng[a,] *

[a]*School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou, P. R. China, 510641; E-mail: zengwei@scut.edu.cn*
[b]*School of Pharmaceutical Sciences, Southern Medical University, Guangzhou 510515, P. R. China*

Supporting Information

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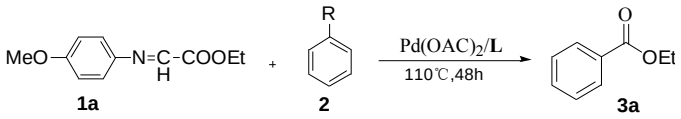
1. General experimental information

1.1 Table 1. [a]The effect of substituent groups on the aryl ring of arylboronic acid on the cross-coupling ethoxycarbonylation of arylboronic acids with α-iminoesters

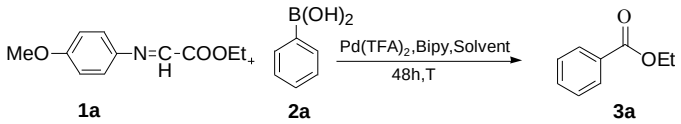


1a **2** **3a**

entry	Pd salts	R	L	Yield (%)[b]
1	$Pd(OAc)_2$	Br	Ph_3P	0
2	$Pd(OAc)_2$	I	Ph_3P	0
3	$Pd(OAc)_2$		--	0
4	$Pd(OAc)_2$	$B(OH)_2$	--	8

[a]Reaction conditions: **1a** (0.18 mmol), **2** (0.18 mmol), $Pd(TFA)_2$ (5 mol %), **L** (5 mol %), solvent: CH_3NO_2 (3.0 mL). All reactions were carried out at 110℃ for 48 h in sealed tube. [b]Isolated yield after purification; L = ligand.

1.2 Table 2. [a]The effect of solvents on the cross-coupling ethoxycarbonylation of arylboronic acids with α-iminoesters

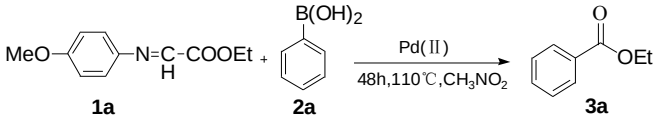


1a **2a** **3a**

entry	solvent	temp.(℃)	yield (%)[b]
1	CH_3NO_2	110	91
2	DMF	140	--
3	toluene	140	21
4	TCE	110	27
5	CH_3CN	100	23
6	CH_3OH	80	trace

[a]Reaction conditions: **1a** (0.18 mmol), **2a** (0.18 mmol), $Pd(TFA)_2$ (5 mol %), bipy (5 mol %), solvent (3.0 mL). All reactions were carried out at the given temperature for 48 h in sealed tube. [b]Isolated yield after purification. bipy = 2,2′-bipyridine.

1.3. Table 3. [a]Catalyst screening for the cross-coupling ethoxycarbonylation of arylboronic acids with α-iminoesters



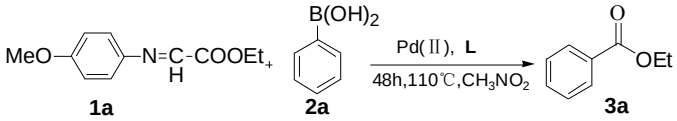
1a **2a** **3a**

entry	Pd salts	Yield (%)[b]
1	$Pd(OAc)_2$	8
2	$Pd(TFA)_2$	13
3	$PdCl_2$	27
4	$PdCl_2(CH_3CN)_2$	35
5	$PdCl_2(PhCN)_2$	37
6	$PdCl_2(PPh_3)$	--

7	$PdCl_2(CH_2CH_3)(PPh_2)_2$	<10

[a]Reaction conditions: **1a** (0.18 mmol), **2a** (0.18 mmol), Pd salts (5 mol %), solvent: CH_3NO_2 (3.0 mL). All reactions were carried out at 110℃ for 48 h in a sealed tube. [b]Isolated yield after purification.

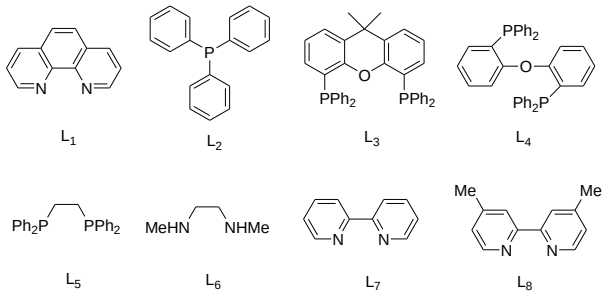
1.4 Table 4. [a]Ligand screening for the cross-coupling ethoxycarbonylation of arylboronic acids with α-iminoesters



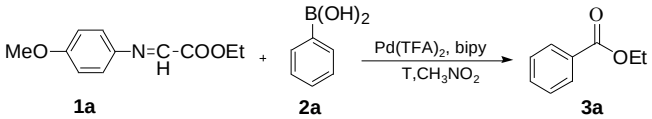
1a **2a** **3a**

entry	Pd salts	ligand	Yield (%)[b]
1	$Pd(TFA)_2$	$\mathbf{L_1}$	61
2	$Pd(TFA)_2$	$\mathbf{L_2}$	16
3	$Pd(TFA)_2$	$\mathbf{L_3}$	11
4	$Pd(TFA)_2$	$\mathbf{L_4}$	17
5	$Pd(TFA)_2$	$\mathbf{L_5}$	<10
6	$Pd(TFA)_2$	$\mathbf{L_6}$	35
7	$Pd(TFA)_2$	$\mathbf{L_7}$	91
8	$Pd(TFA)_2$	$\mathbf{L_8}$	81
9	$PdCl_2$	$\mathbf{L_7}$	27
10	$PdCl_2(CH_3CN)_2$	$\mathbf{L_7}$	53
11	$PdCl_2(PhCN)_2$	$\mathbf{L_7}$	--

[a]Reaction conditions: **1a** (0.18 mmol), **2a** (0.18 mmol), $Pd(TFA)_2$ (5 mol %), **L** (5 mol %), solvent (3.0 mL). All reactions were carried out at 110℃ for 48 h in sealed tube. [b]Isolated yield after purification; **L** = ligand.



1.5. Table 5. [a]The effect of temperature on the cross-coupling ethoxycarbonylation of arylboronic acids with α-iminoesters



1a **2a** **3a**

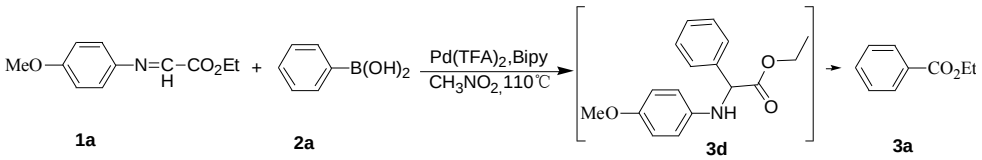
entry	solvent	Temp.(℃)	yield (%)[b]
1	CH_3NO_2	60	0
2	CH_3NO_2	90	37[c](45[c,d])
3	CH_3NO_2	100	56
4	CH_3NO_2	110	91

5	CH_3NO_2	120	77

[a]Reaction conditions: **1a** (0.174 mmol), **2a** (0.174 mmol), $Pd(TFA)_2$ (5 mol %), bipy (5 mol %), solvent: CH_3NO_2 (3.0 mL). All reactions were carried out at the given temperature for 48 h in sealed tube unless otherwise noted. [b]Isolated yield after purification. [c]The reaction temperature is 90 ℃. [d]The yield of by product *α*- (4- methoxyphenylamino)- *α*- phenyl- acetic acid ethyl ester. bipy = 2,2′- bipyridine.

1.6. The mechanism exploration of Pd(II)-catalyzed cross-coupling ethoxycarbonylation of arylboronic acids with α-iminoesters

1.6.1 The GC spectra about the the reaction progress of α-iminoesters (1a) and phenylboronic acid (2a) (see Scheme 1)



Scheme 1

To the solution of α- iminoesters **1a** (0.2 mmol, 1.0 equiv) of CH_3NO_2 (2.0 mL)，phenylboronic acid **2a** (0.2 mmol, 1.0 equiv), $Pd(TFA)_2$ (0.01 mmol, 5 mol %) and bipy (0.01 mmol, 5 mol %) was added under Ar atmosphere. Then the mixture was stirred at 110 °C for a given time, the corresponding reaction progress was monitored by GC-MS. The effect of reaction time on the GC yield of **3a** and **3d** was listed in Table 7, and the corresponding GC spectra were shown in Figure 1-6. The GC-MS spectra of **3a** and **3d** were shown in Figure 7-8.

Table 7. The effect of reaction on the GC yield of **3a** and **3d**

Entry	Reaction time (h)	Retention time (min)		GC yield (%)	
		3a	**3d**	**3a**	**3d**
1	2	2.72	6.31	15	70
2	5	2.64	6.31	30	65
3	8	2.65	6.32	46	48
4	12	2.69	6.31	54	35
5	26	2.64	6.37	87	5
6	48	2.65	6.35	>95	0

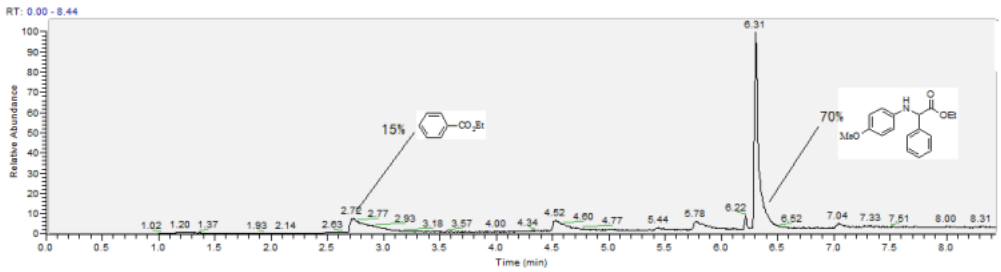


Figure 1. The GC spectra from the reaction mixture which was carried out for 2 h.

As shown in Figure 1, the GC yield of intermediate (4-methoxy-phenylamino)-phenyl-acetic acid ethyl ester **3d** was up to 70%, and the GC yield of ethyl benzoate **3a** was just 15%.

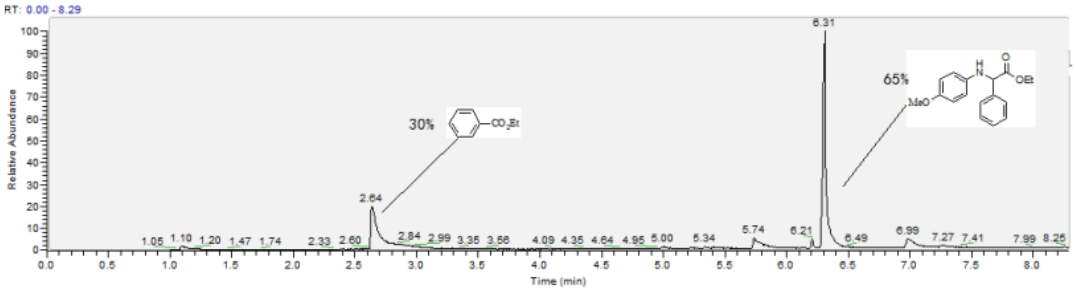


Figure 2. The GC spectra from the reaction mixture which was carried out for 5 h.

As shown in **Figure 2**, the GC yield of intermediate (4-methoxy-phenylamino)-phenyl-acetic acid ethyl ester **3d** was lowered to 65%, and the GC yield of ethyl benzoate **3a** was up to 30%.

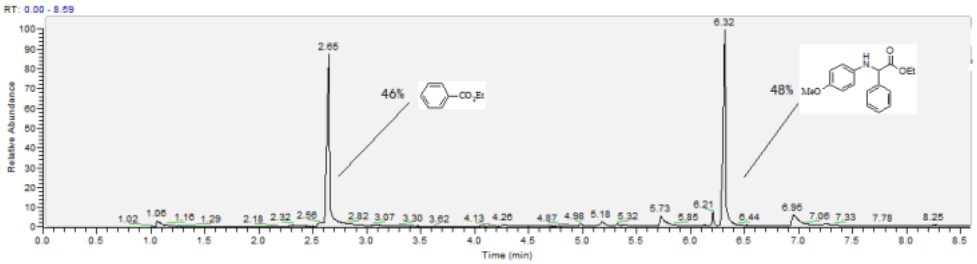


Figure 3. The GC spectra from the reaction mixture which was carried out for 8 h.

As shown in **Figure 3**, the GC yield of intermediate (4-methoxy-phenylamino)-phenyl-acetic acid ethyl ester **3d** was lowered to 48%, and the yield of ethyl benzoate **3a** was up to 46%.

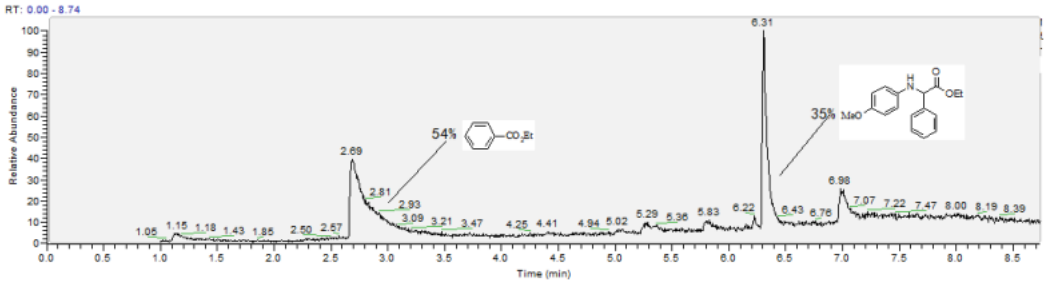


Figure 4. The GC spectra from the reaction mixture which was carried out for 12 h.

As shown in **Figure 4**, the GC yield of intermediate (4-methoxy-phenylamino)-phenyl-acetic acid ethyl ester **3d** was lowered to 35%, and the GC yield of ethyl benzoate **3a** was up to 54%.

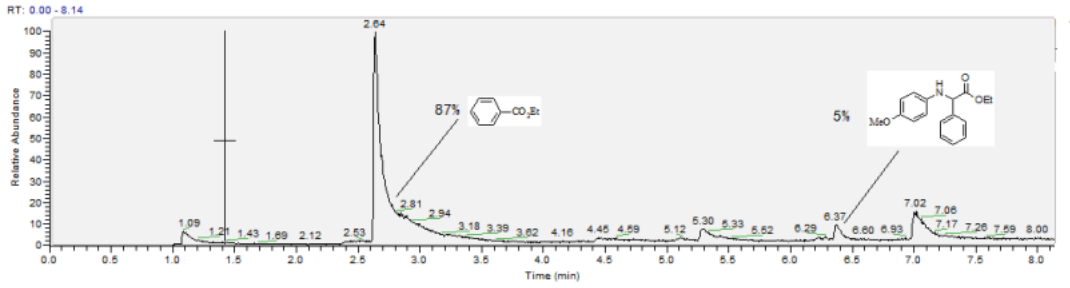


Figure 5. The GC spectra from the reaction mixture which was carried out for 26 h.

As shown in **Figure 5,** the GC yield of intermediate (4-methoxy-phenylamino)-phenyl-acetic acid ethyl ester **3d** was lowered to 5%, and the GC yield of ethyl benzoate **3a** was up to 87%.

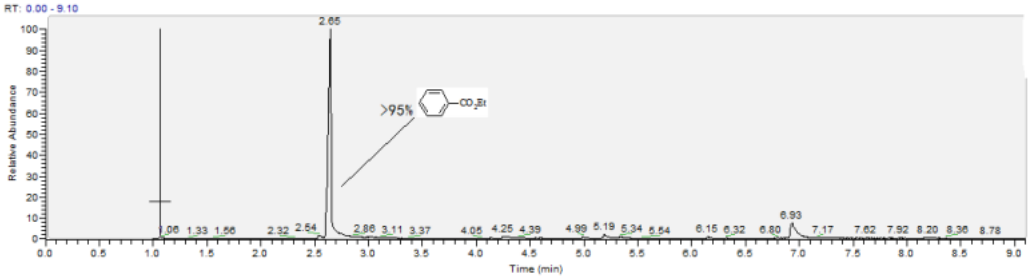


Figure 6. The GC spectra from the reaction mixture which was carried out for 48 h.

As shown in **Figure 6,** the intermediate (4-methoxy-phenylamino)-phenyl-acetic acid ethyl ester **3d** basically disappeared, and the GC yield of ethyl benzoate **3a** exceeded 95%.

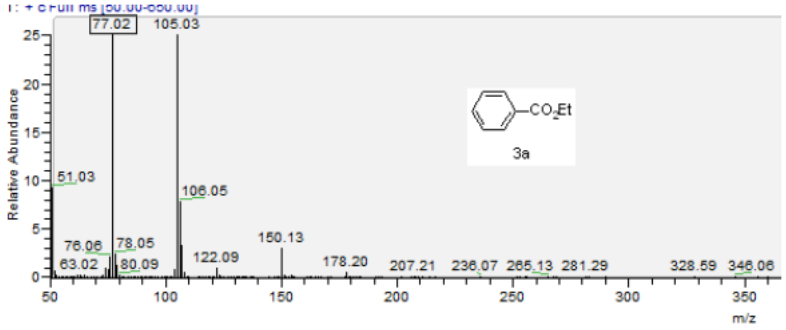


Figure 7. The **GC-MS** spectra of **3a**, FW of **3a** is 150.13.

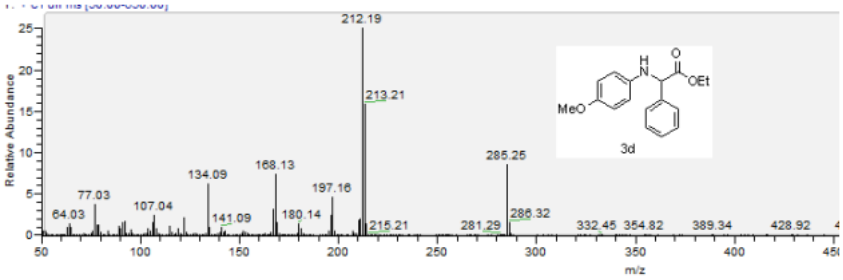


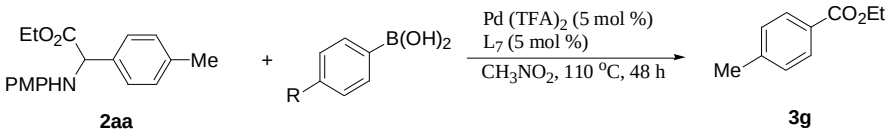
Figure 8. The **GC-MS** spectra of **3d**, The FW of **3d** is 286.32.

Conclusion: The above-mentioned GC-MS spectra indicated that ethyl 2-(4-methoxyphenylamino)-2-phenylacetate (**3d**) is a key intermediate which lead to the formation of ethyl benzoate (**3a**).

1.6.2 The electronic effect of substitutents on the aryl boronic acids of cross-coupling ethoxycarbonylation of arylboronic acids with α-iminoesters

To the solution of **2aa** (0.18 mmol, 1 equiv), substituted phenylboronic acid (0.036 mmol, 0.2 equiv), $Pd(TFA)_2$ (0.009 mmol, 5 mol %) and bipy (0.009 mmol, 5 mol %) was added in 3.0 mL of CH_3NO_2 under Ar, then the corresponding mixture was stirred at 110 ^oC for 48 h. After the reaction mixture was cooled to room temperature, then concentrated under vacuum and purified

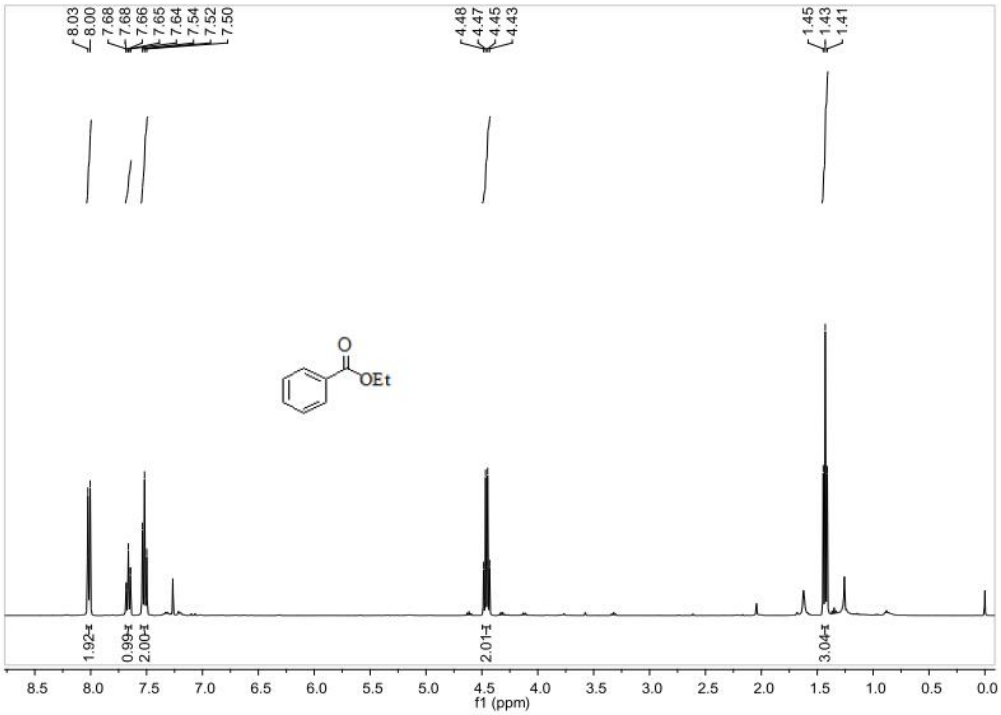
by flash chromatography (eluting with eluent consisting of Hexane/EtOAc, 20:1) to give the pure product of **3g**.

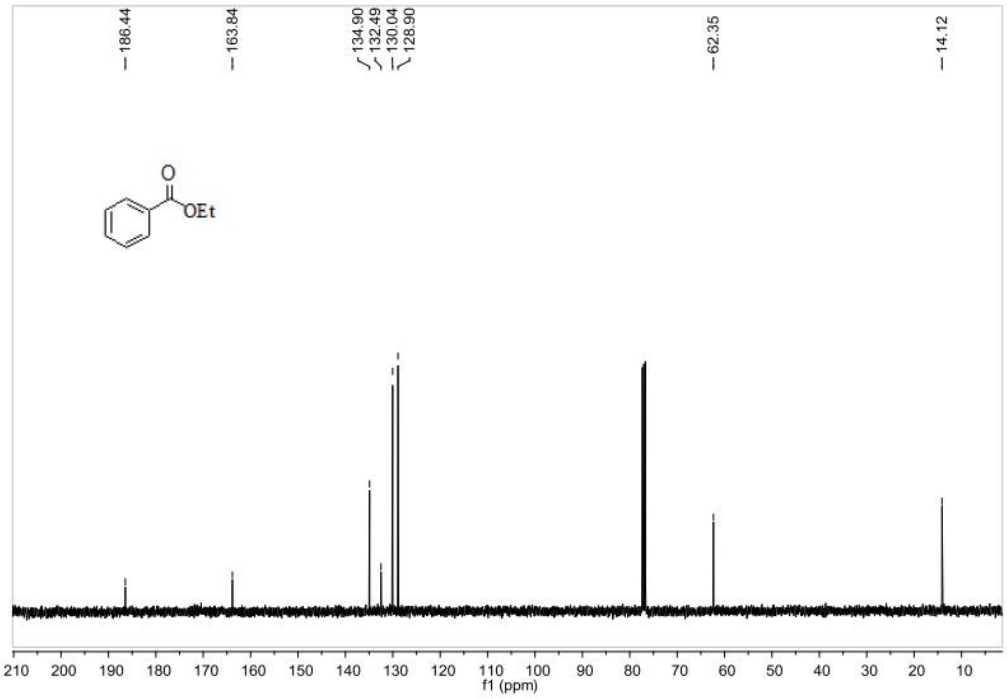


Entry	R	Yield
1	4-CH_3	82%
2	4-H	85%
3	4-Cl	84%
4	4-CF_3	64%

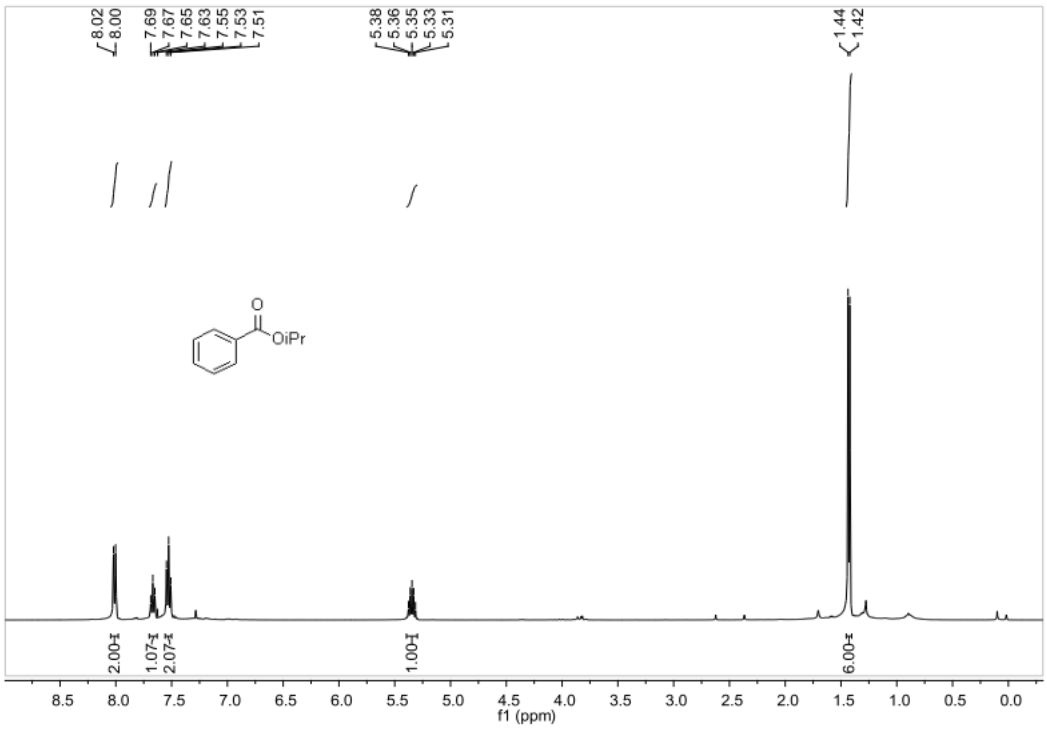
2. ^{1}H NMR and ^{13}C NMR Spectrum for products

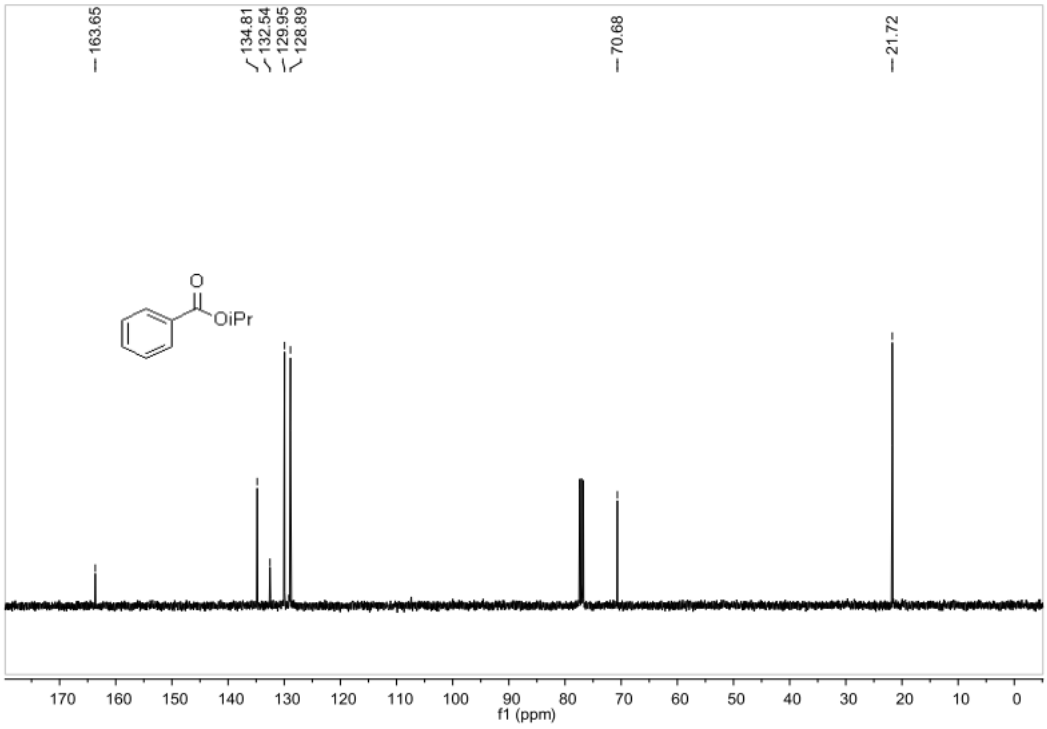
1) ^{1}H NMR and ^{13}C NMR Spectrum for ethyl benzoate **3a** (Using $CDCl_3$ as solvent)



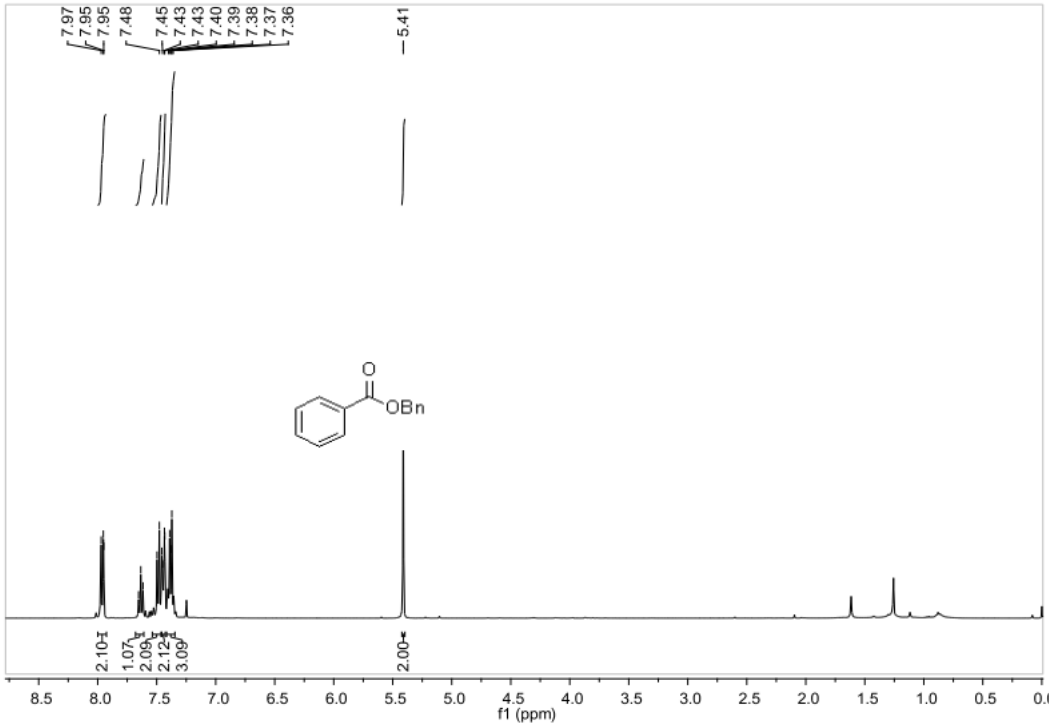


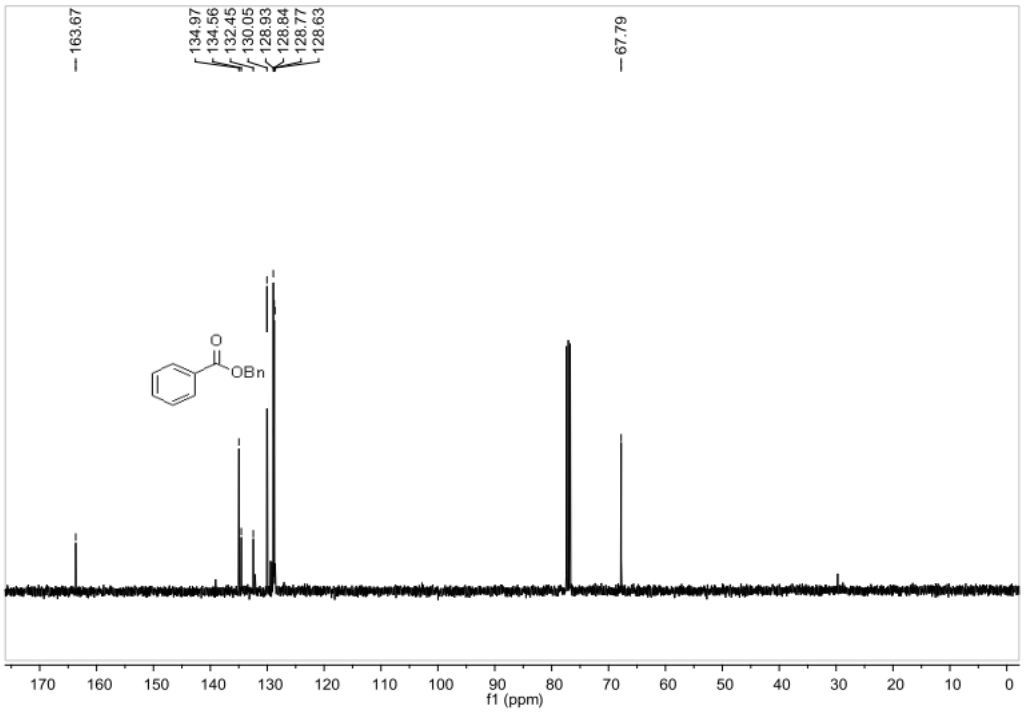
2) ^{1}H NMR and ^{13}C NMR Spectrum for isopropyl benzoate **3b** (Using $CDCl_3$ as solvent)



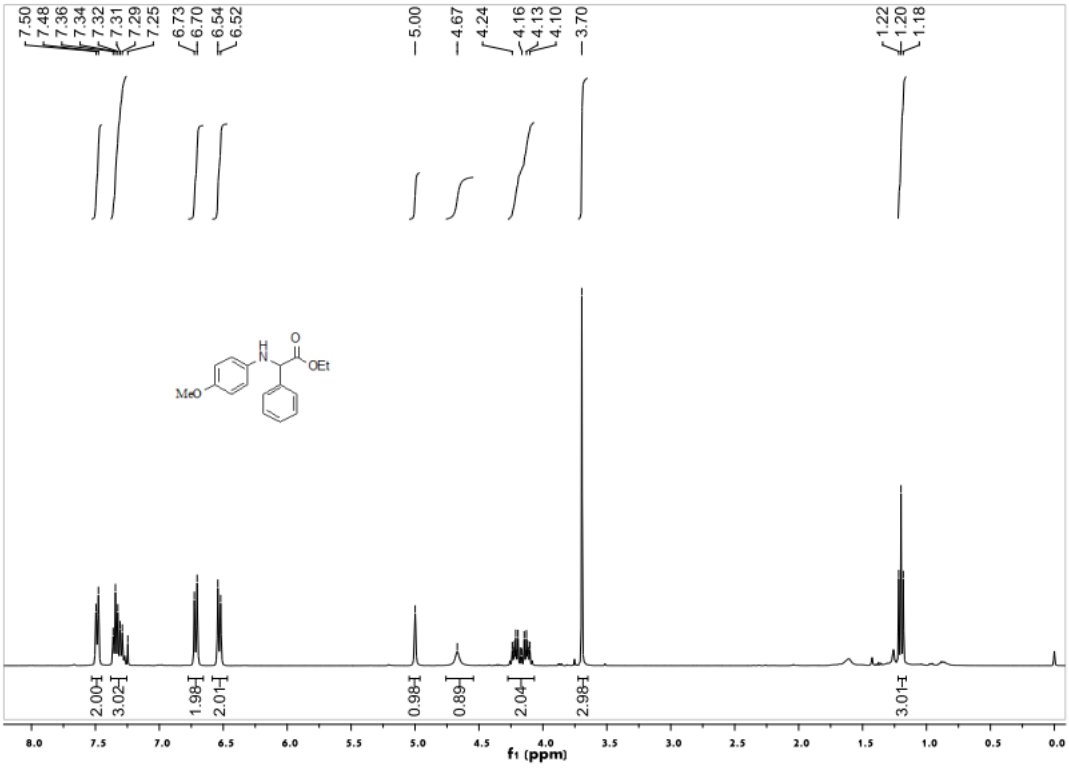


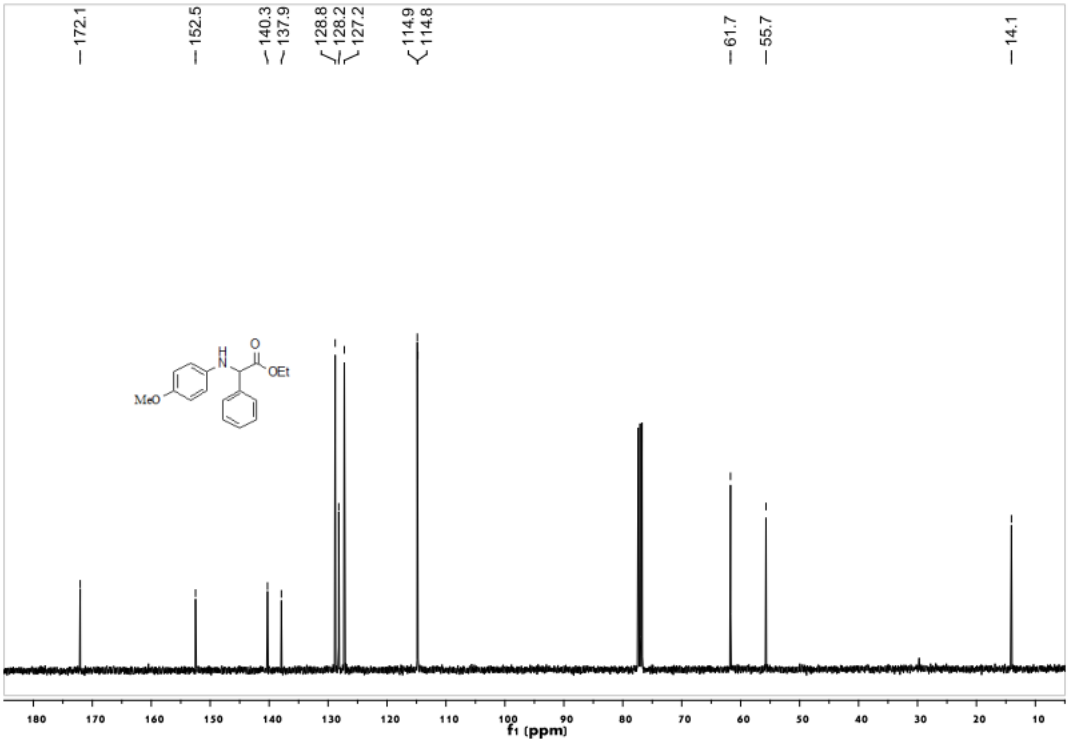
3) ^{1}H NMR and ^{13}C NMR Spectrum for benzyl benzoate **3c** (Using $CDCl_3$ as solvent)



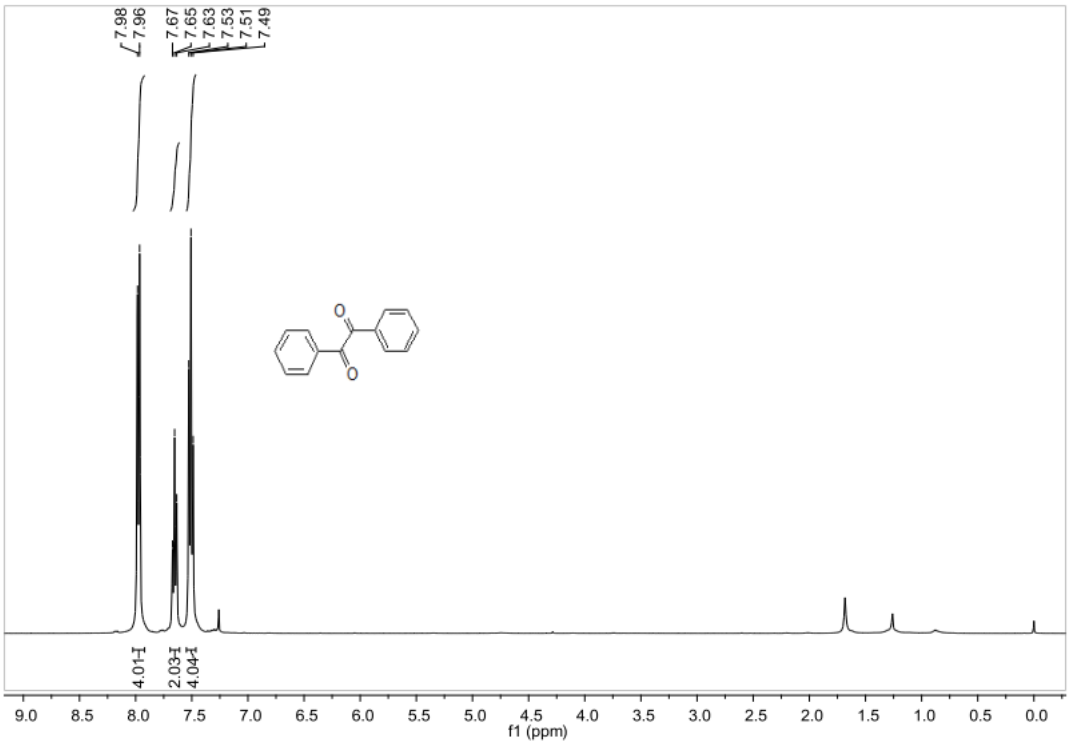


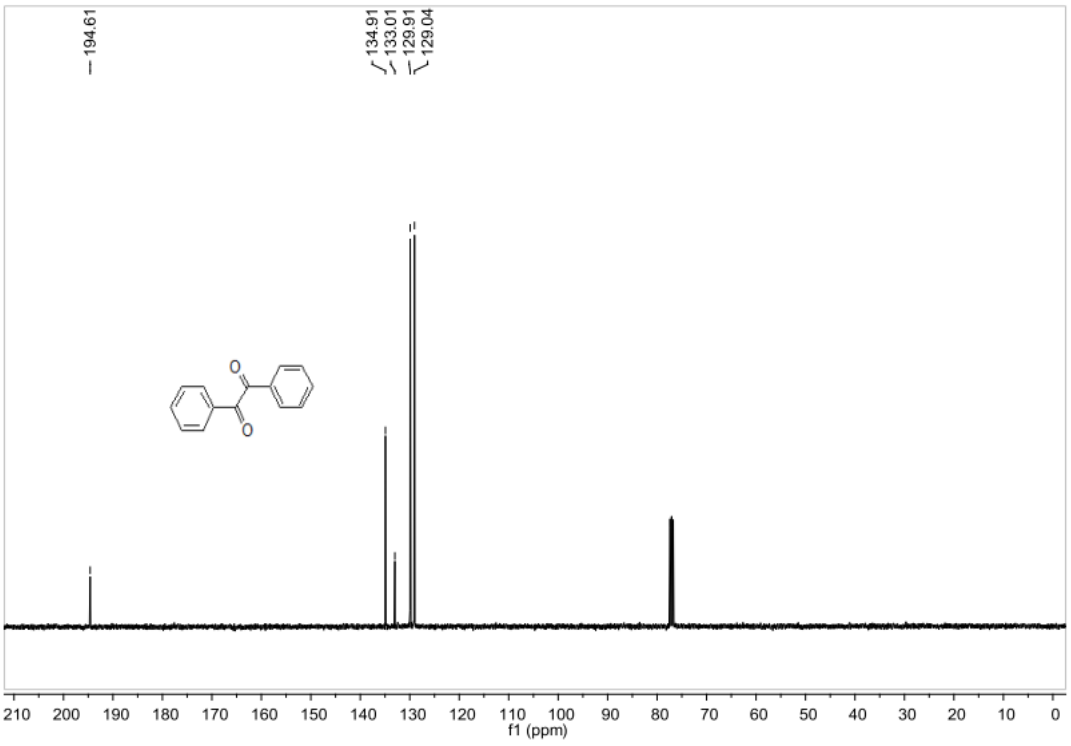
4). ^{1}H NMR and ^{13}C NMR Spectrum for ethyl 2-((4-methoxyphenyl) amino)-2-(*p*-tolyl) acetate **P2a** (Using $CDCl_3$ as solvent)



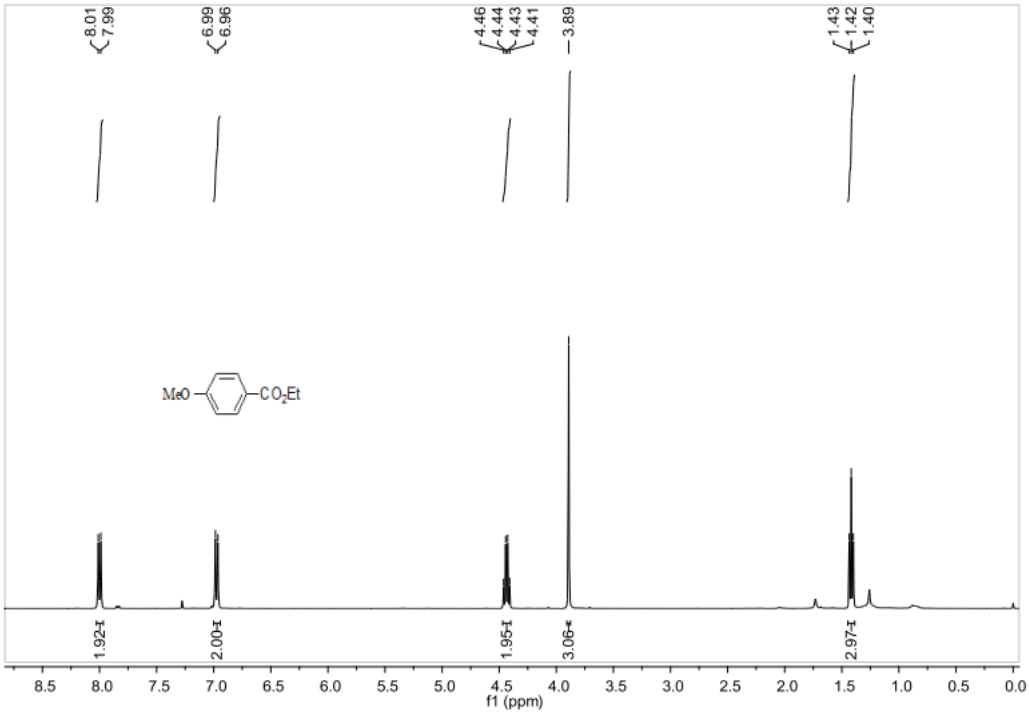


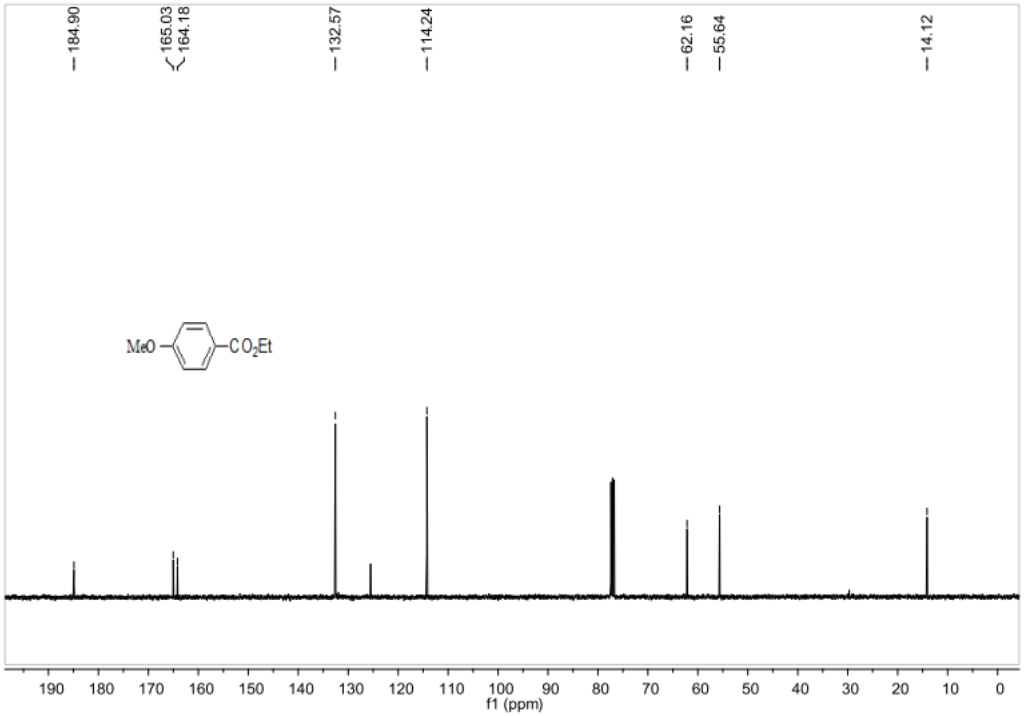
5). ^{1}H NMR and ^{13}C NMR Spectrum for benzil **3a-1** (Using $CDCl_3$ as solvent)



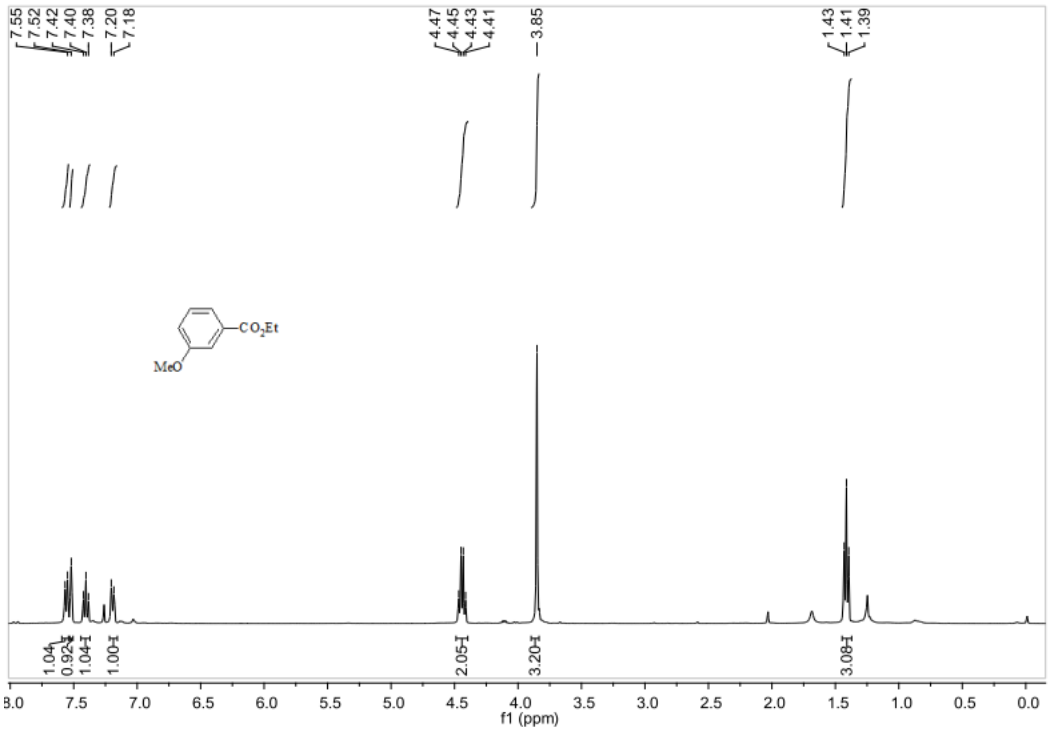


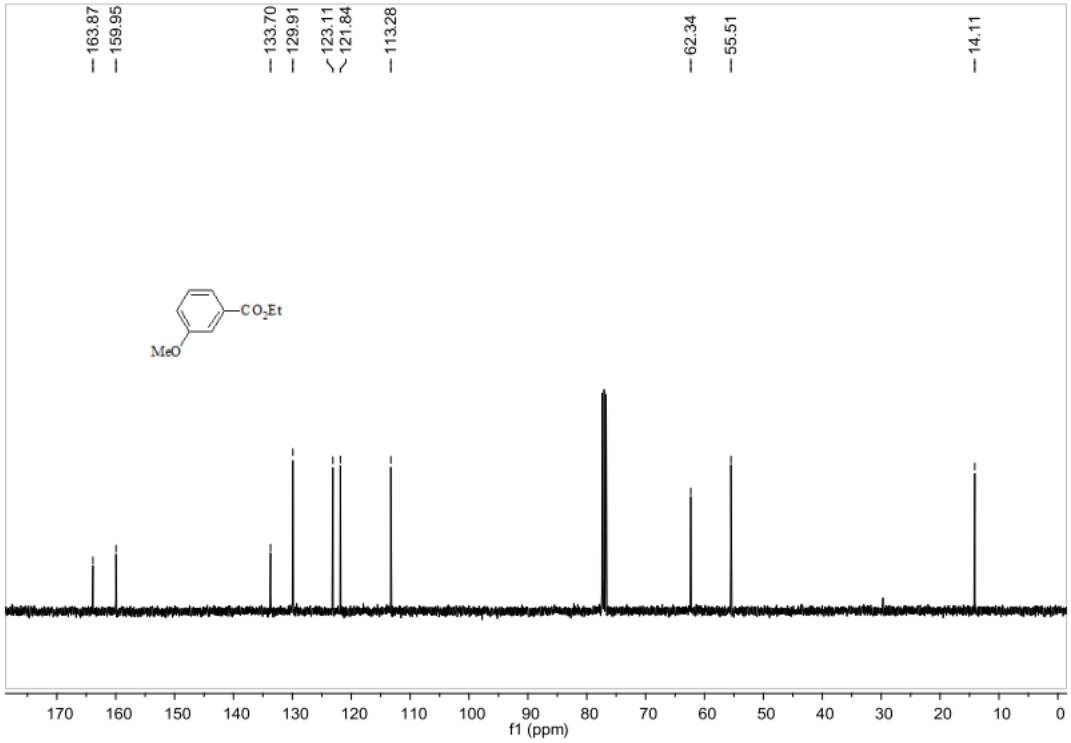
6) ^{1}H NMR and ^{13}C NMR Spectrum for 4-methoxybenzoate **3d** (Using $CDCl_3$ as solvent)



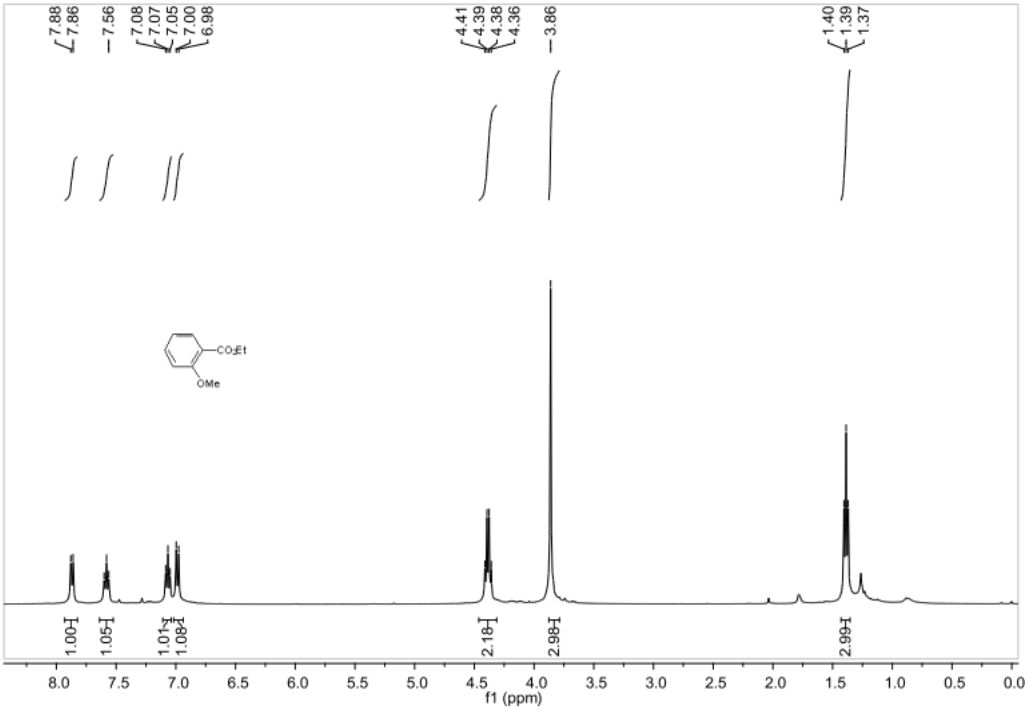


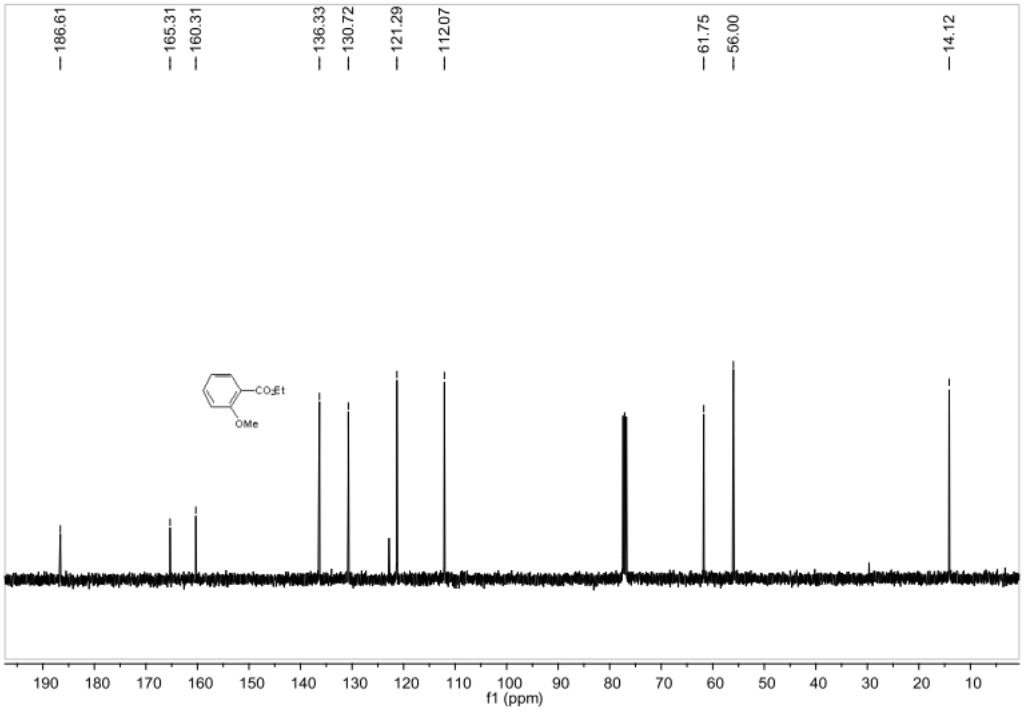
7) ^{1}H NMR and ^{13}C NMR Spectrum for ethyl 3-methoxybenzoate **3e** (Using $CDCl_3$ as solvent)



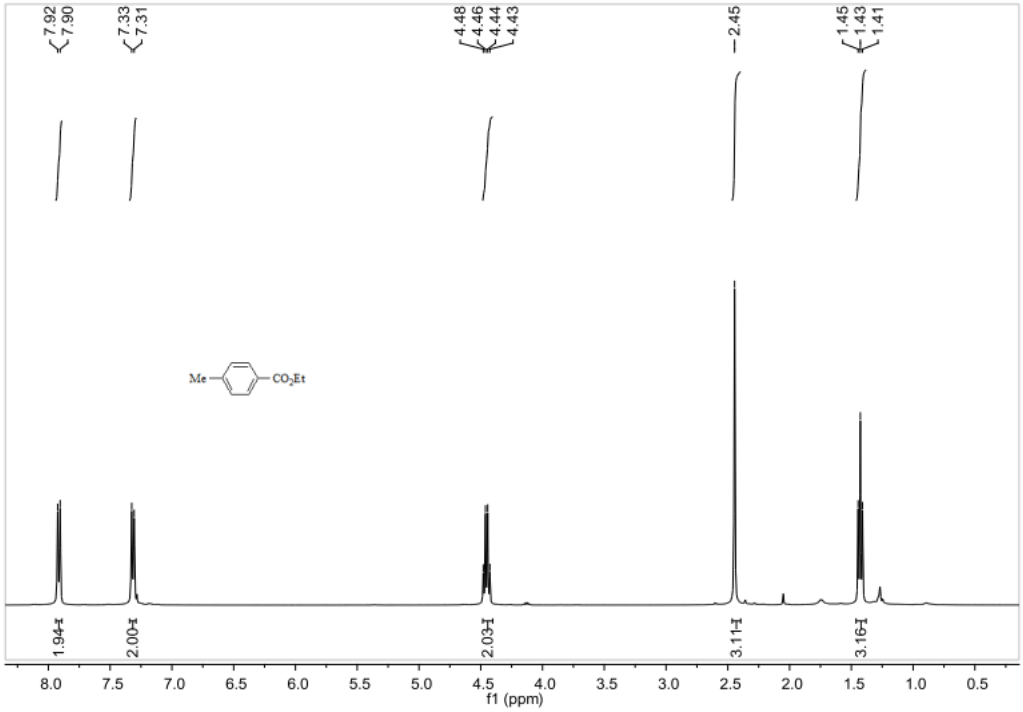


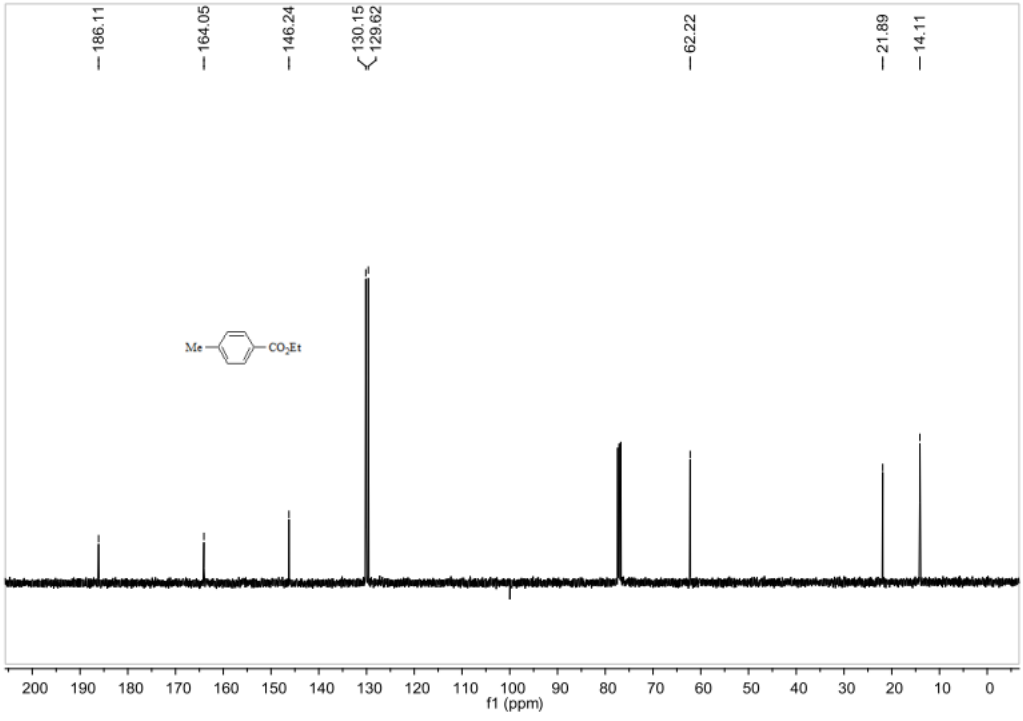
8). ^{1}H NMR and ^{13}C NMR Spectrum for ethyl 2-methoxybenzoate **3f** (Using $CDCl_3$ as solvent)



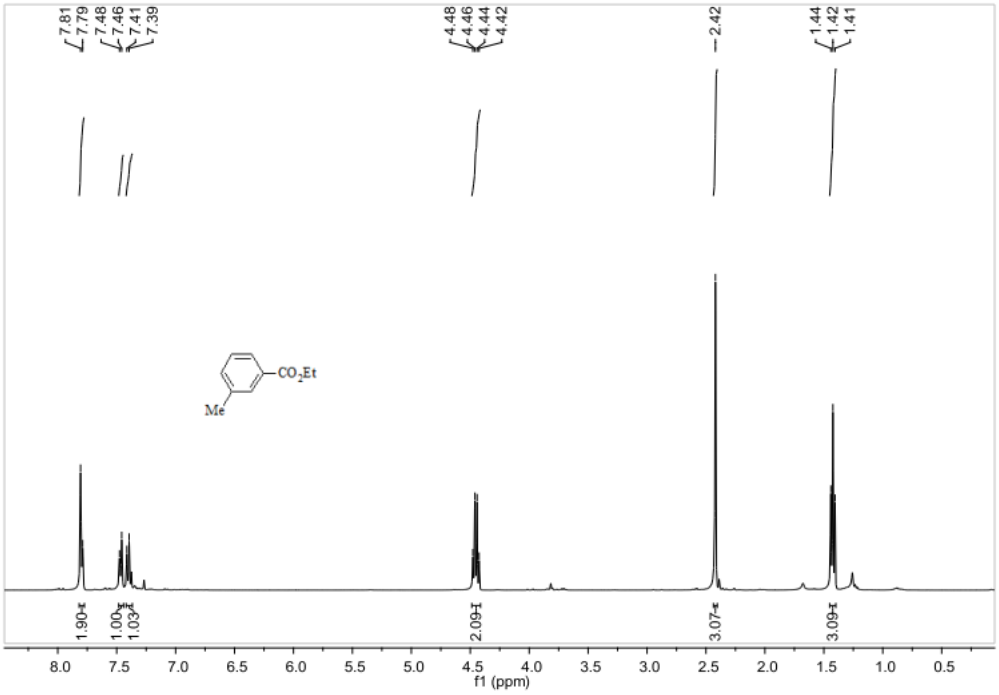


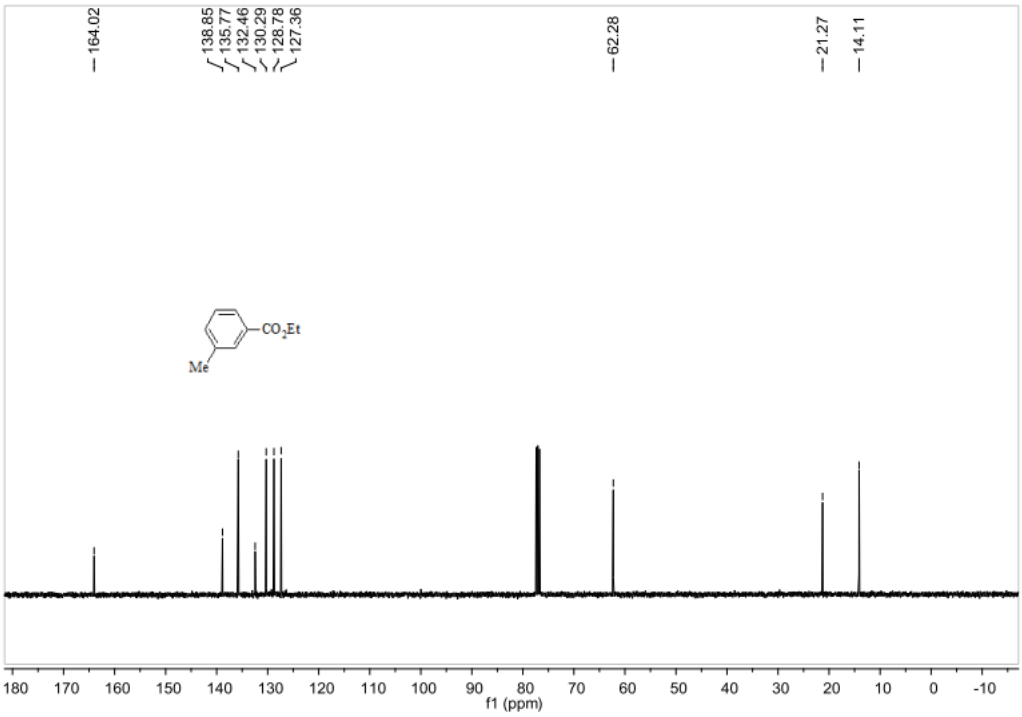
9). ^{1}H NMR and ^{13}C NMR Spectrum for ethyl 4-methylbenzoate **3g** (Using $CDCl_3$ as solvent)



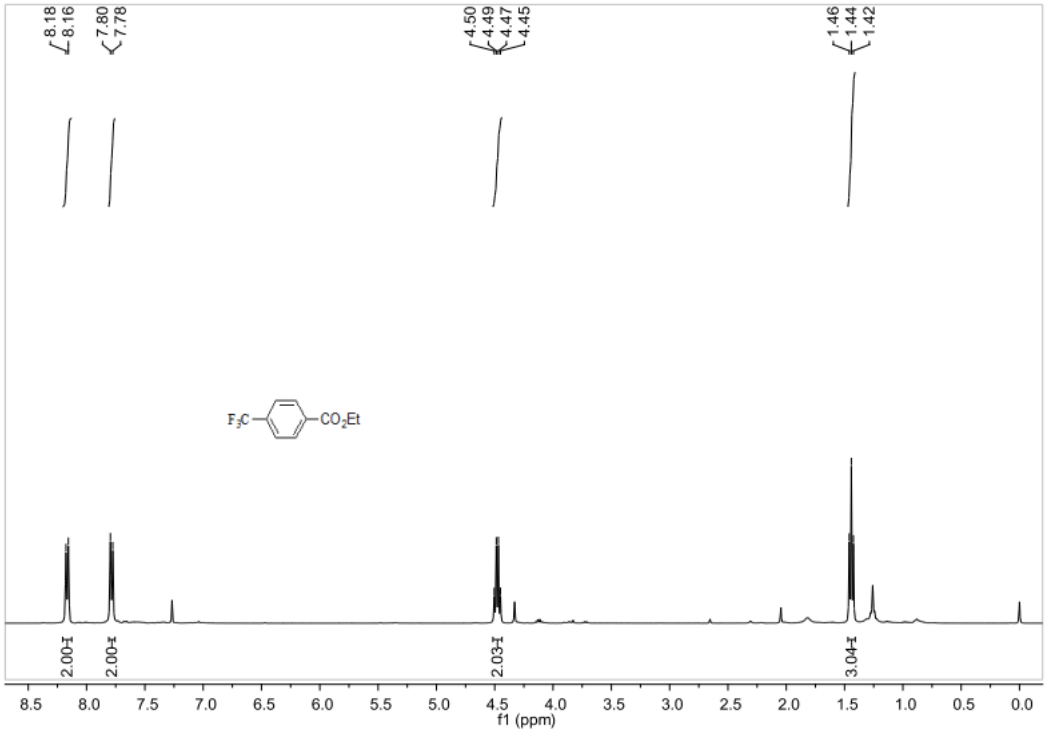


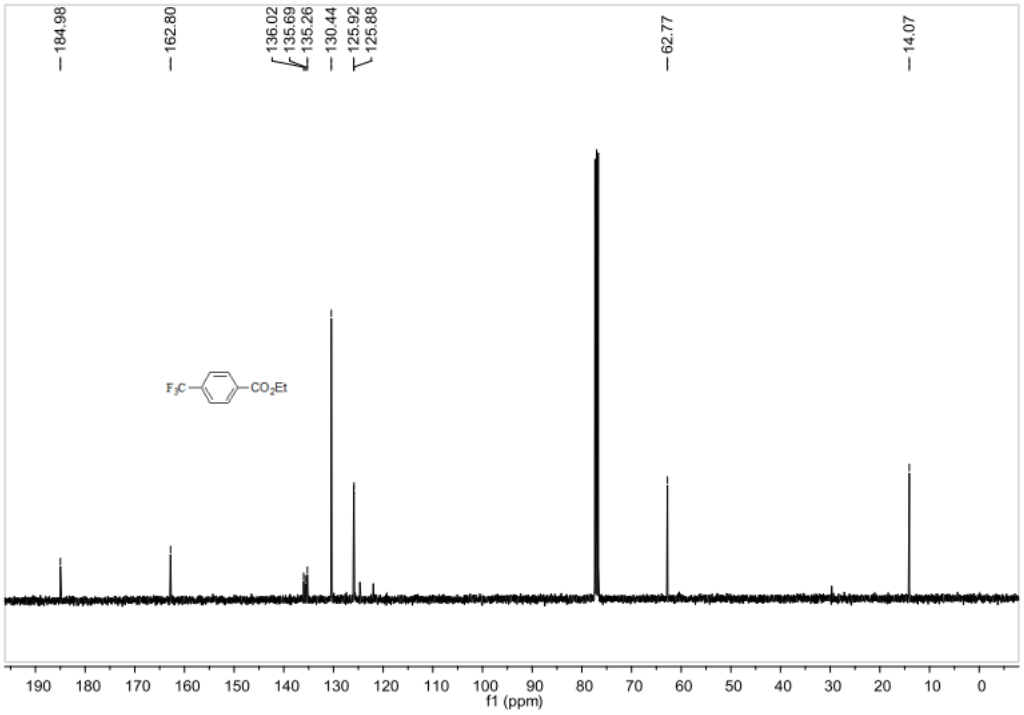
10).^{1}H NMR and ^{13}C NMR Spectrum for ethyl 3-methylbenzoate **3h** (Using $CDCl_3$ as solvent)



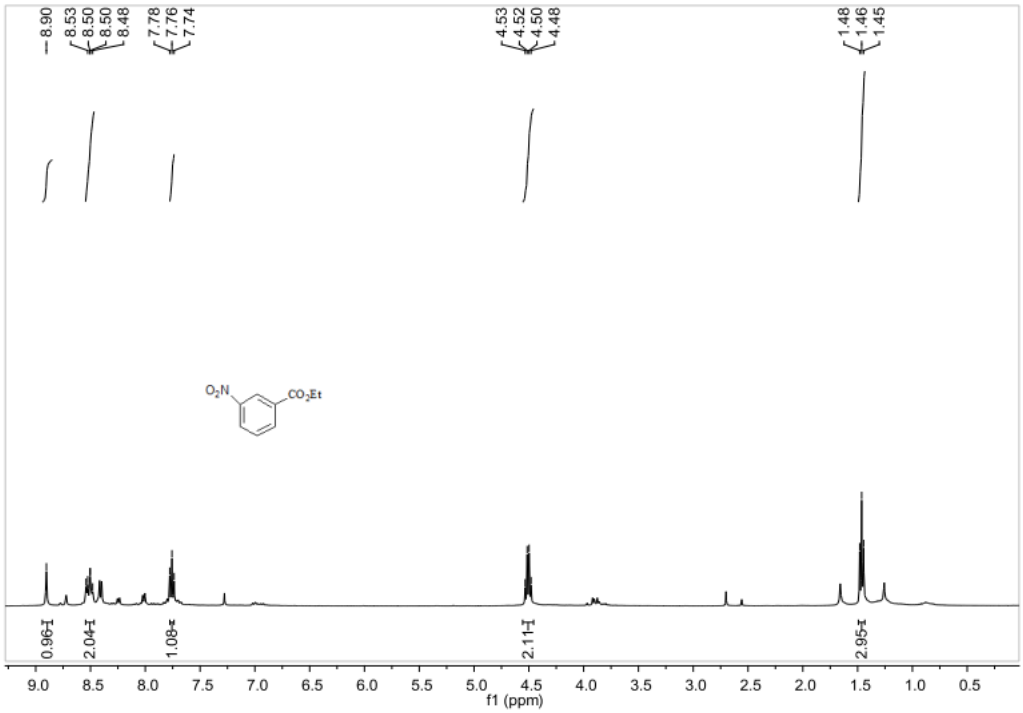


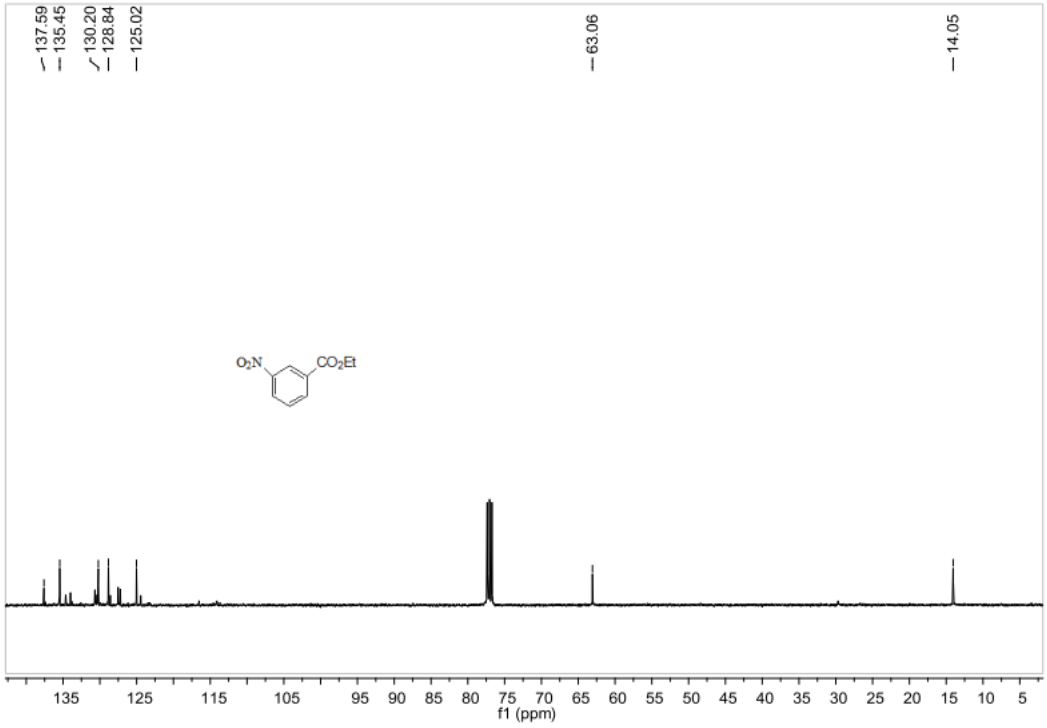
11).^{1}H NMR and ^{13}C NMR Spectrum for ethyl 4-(trifluoromethyl) benzoate **3i** (Using $CDCl_3$ as solvent)



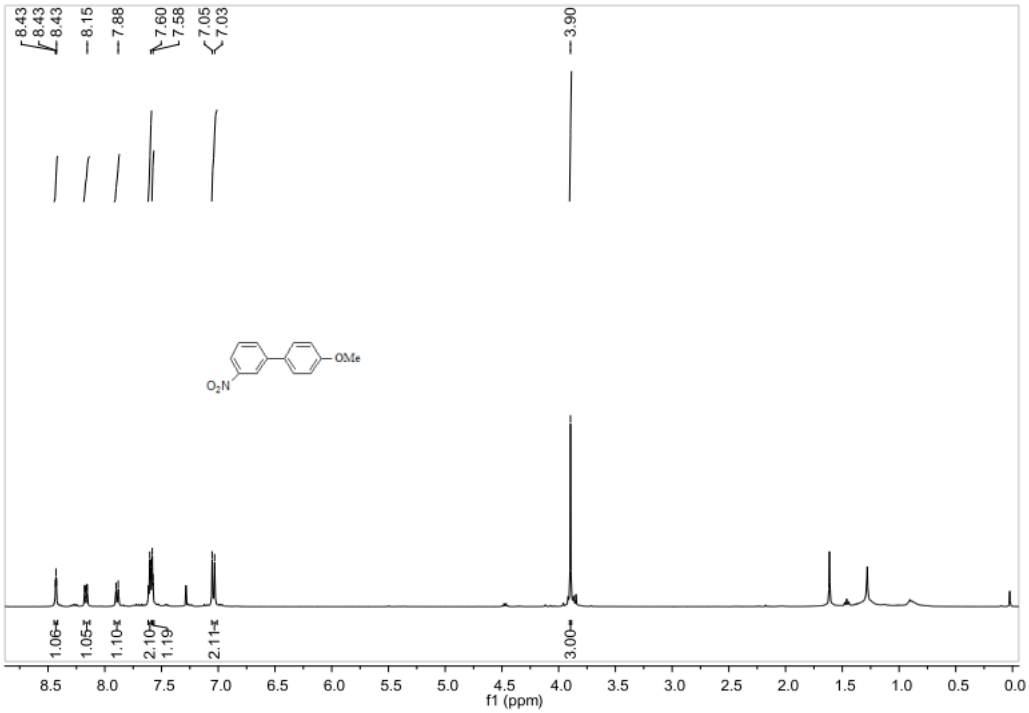


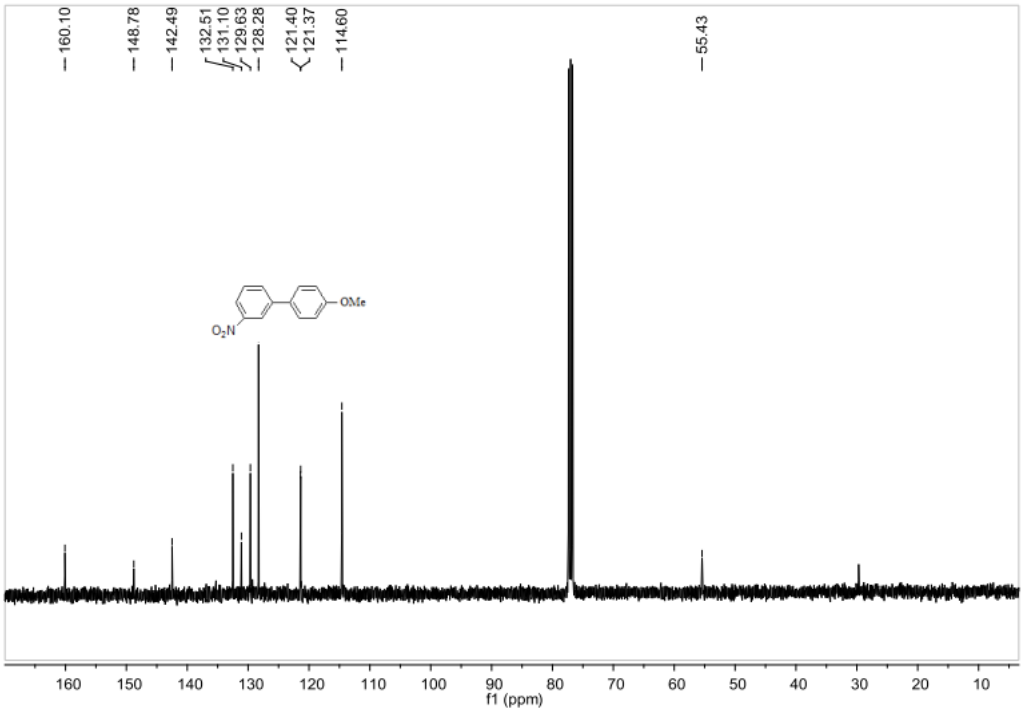
12).^{1}H NMR and ^{13}C NMR Spectrum for ethyl 3-nitrobenzoate **3j** (Using $CDCl_3$ as solvent)



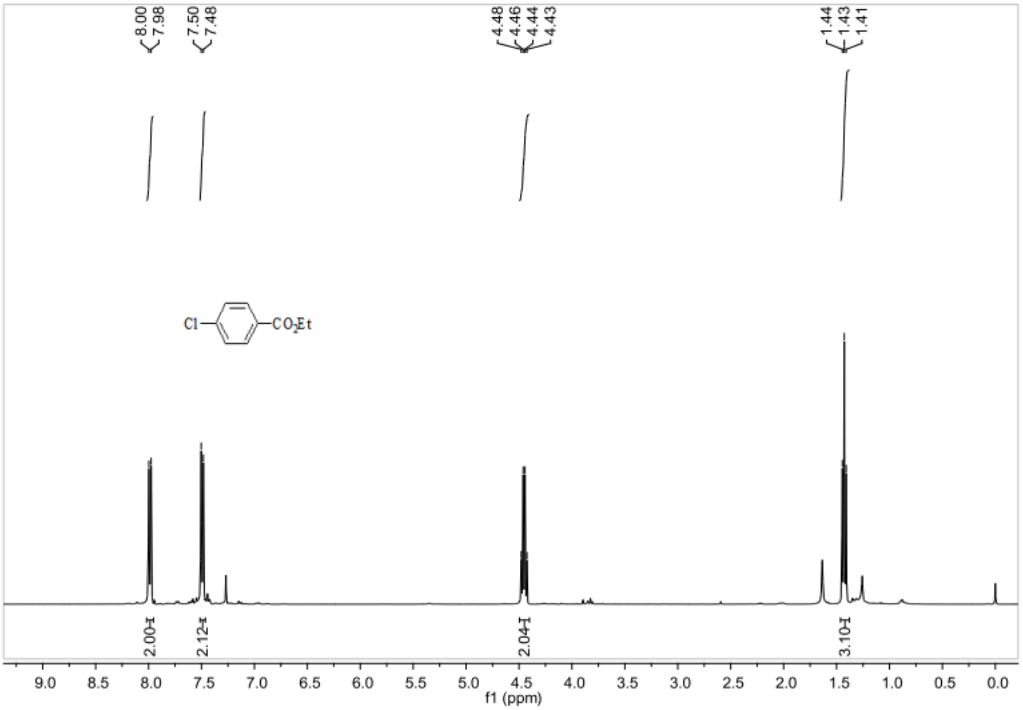


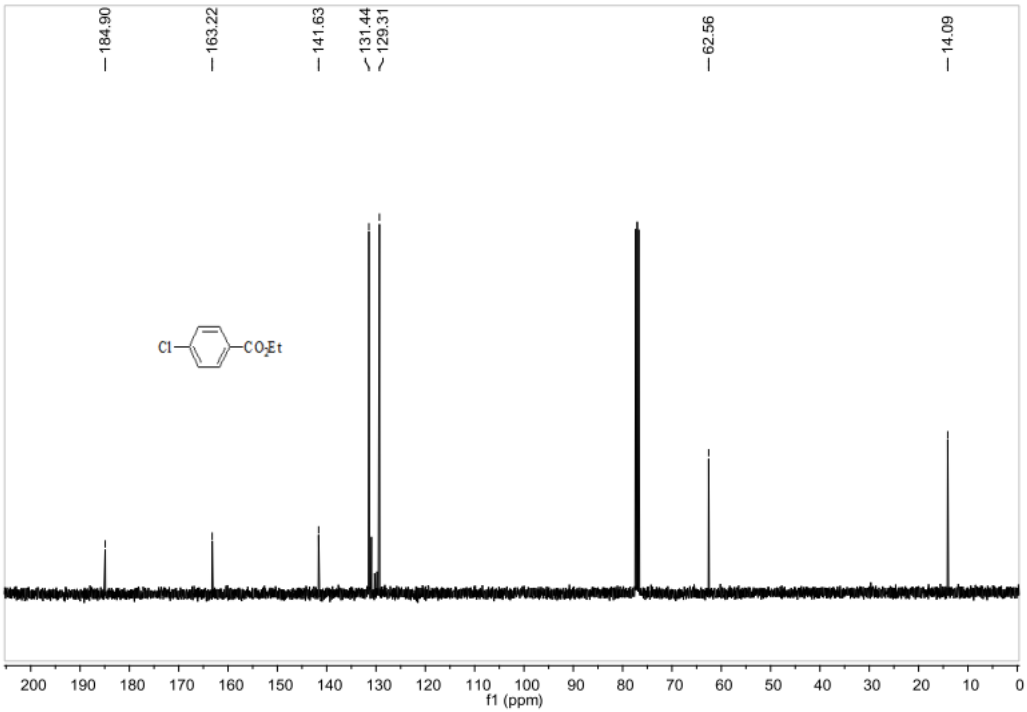
13).^{1}H NMR and ^{13}C NMR Spectrum for 4'-methoxy-3-nitro-1,1'-biphenyl **3j-1** (Using $CDCl_3$ as solvent)



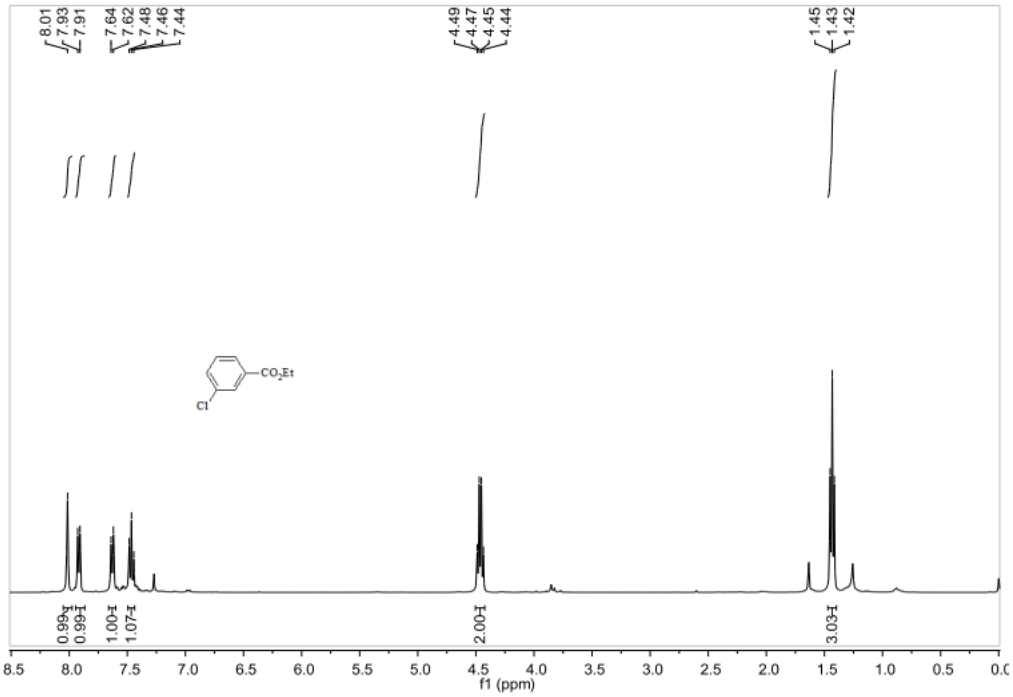


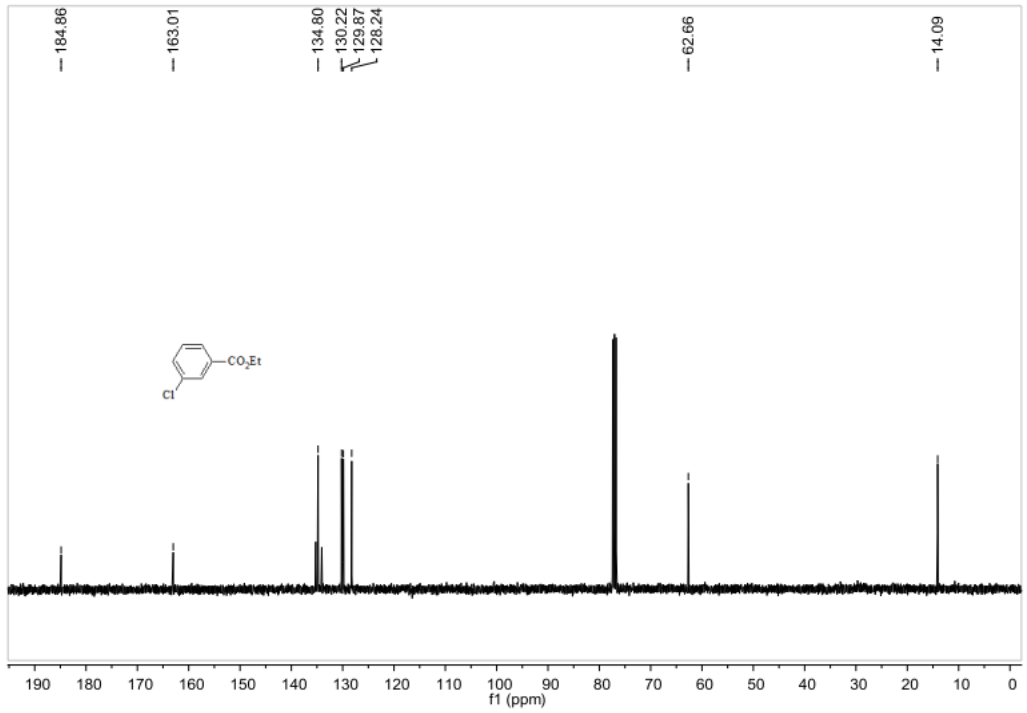
14).^{1}H NMR and ^{13}C NMR Spectrum for ethyl 4-chlorobenzoate **3k** (Using $CDCl_3$ as solvent)



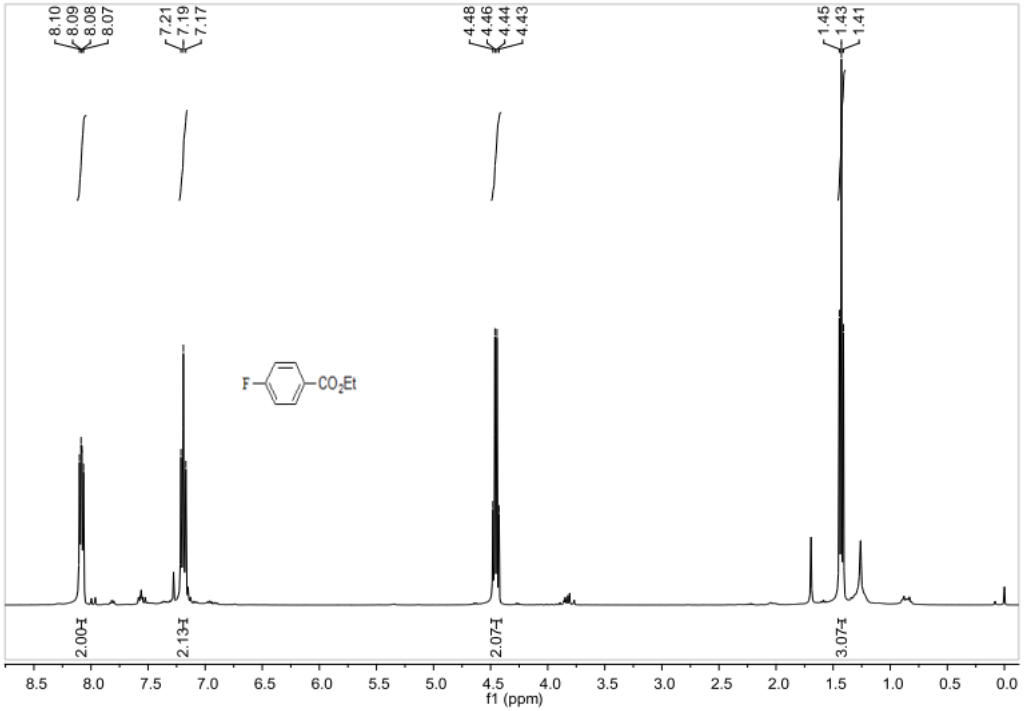


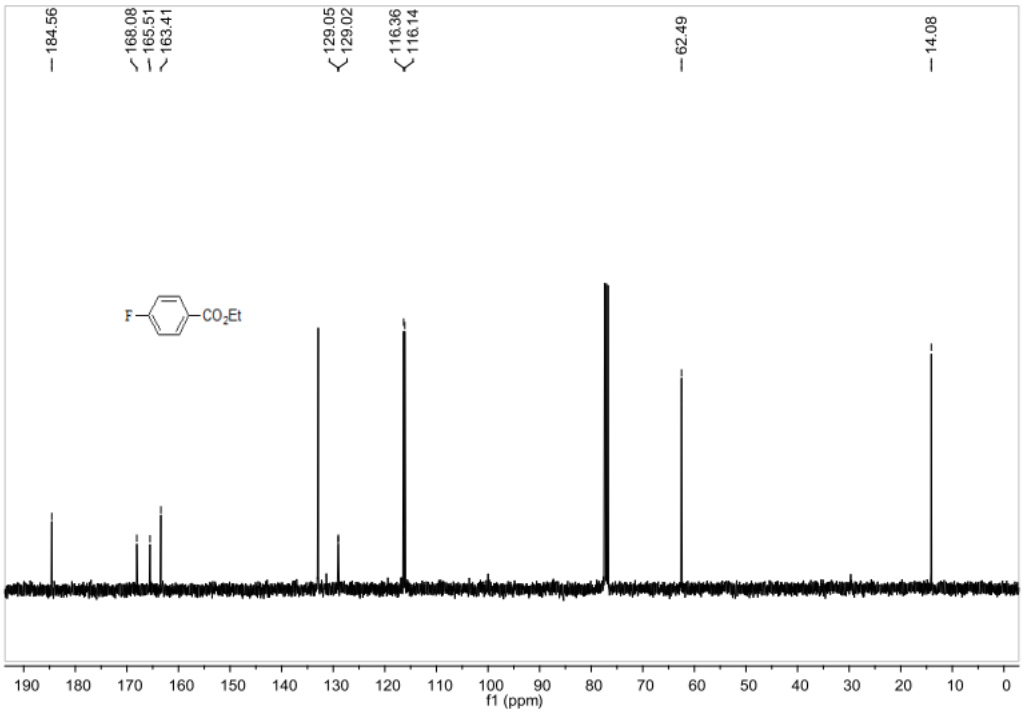
15).^{1}H NMR and ^{13}C NMR Spectrum for ethyl 3-chlorobenzoate **3l** (Using $CDCl_3$ as solvent)



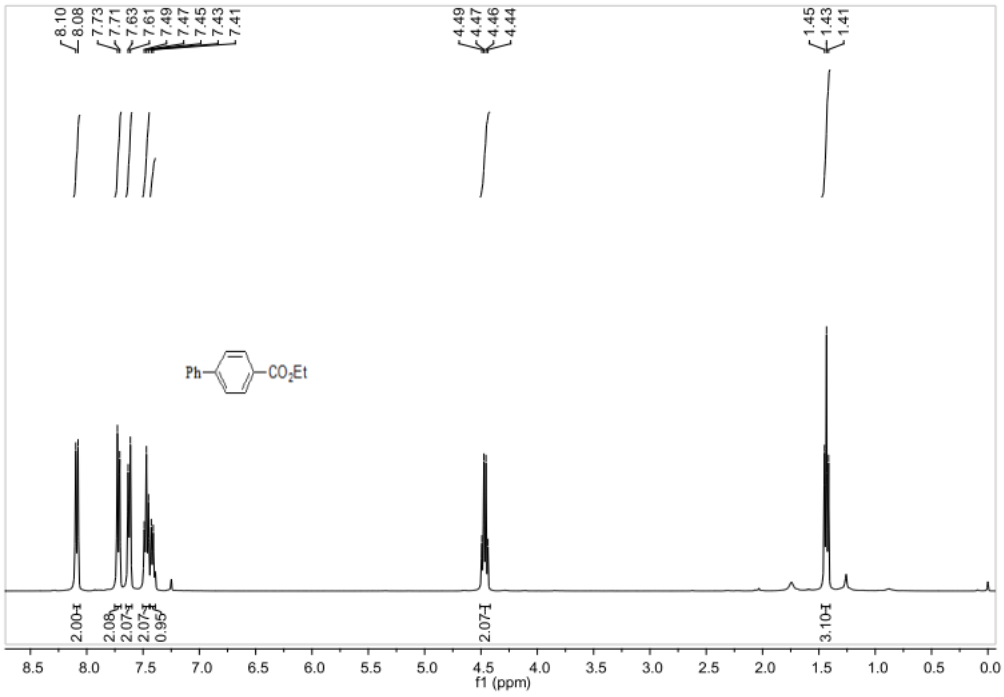


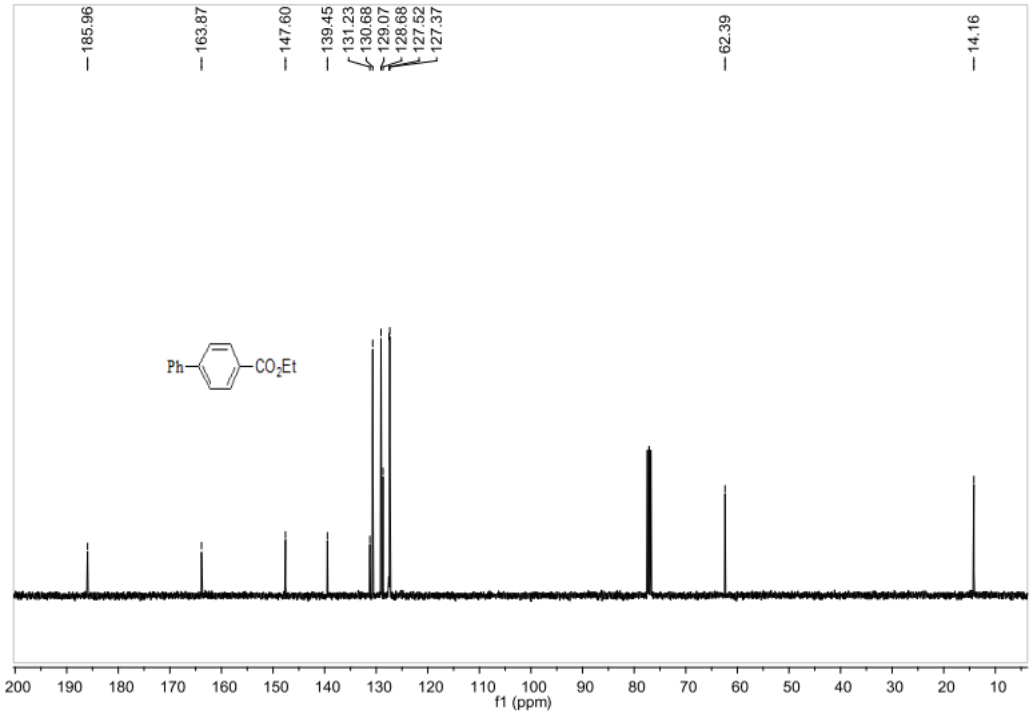
16).^{1}H NMR and ^{13}C NMR Spectrum for ethyl 4-fluorobenzoate **3m** (Using $CDCl_3$ as solvent)



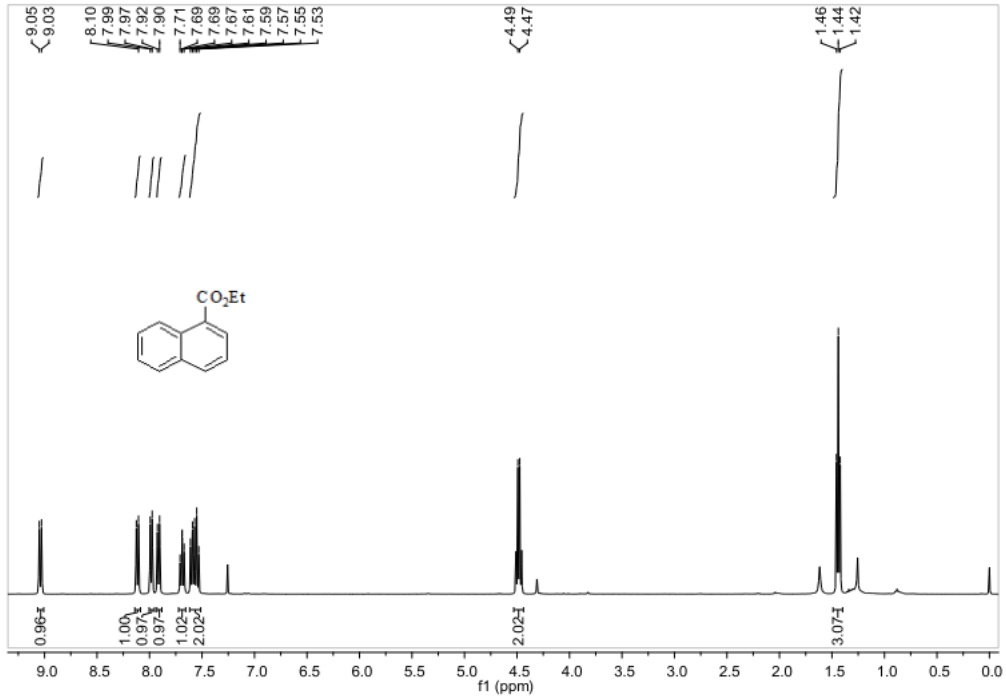


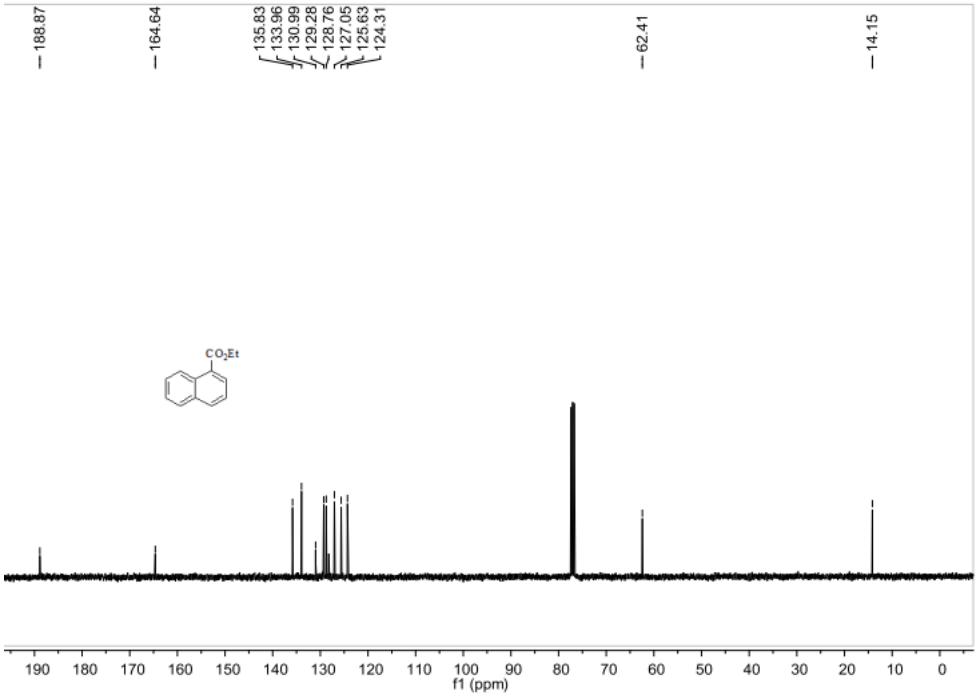
17). ^{1}H NMR and ^{13}C NMR Spectrum for ethyl [1,1'-biphenyl]-4-carboxylate **3n** (Using $CDCl_3$ as solvent)



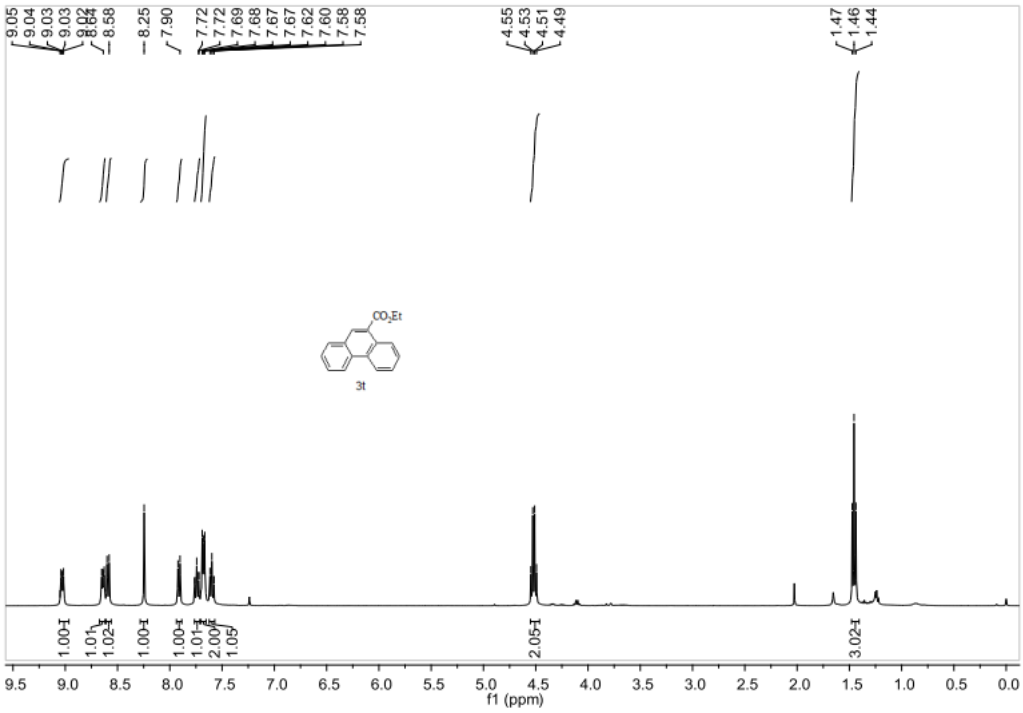


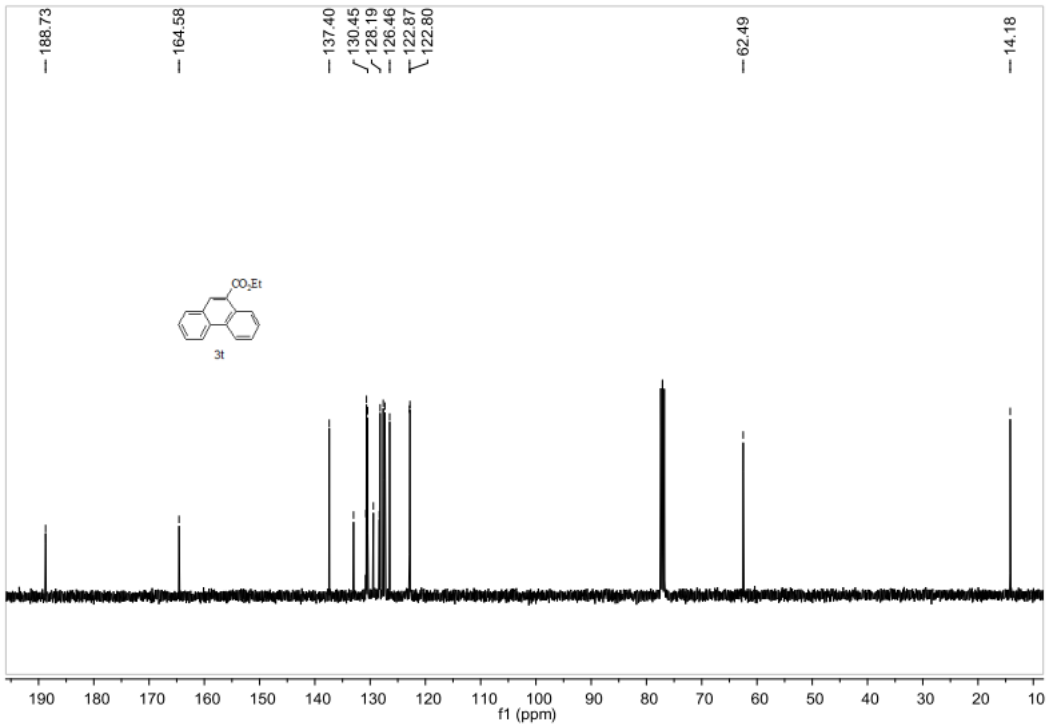
18)^{1}H NMR and ^{13}C NMR Spectrum for ethyl 1-naphthoate **3o** (Using $CDCl_3$ as solvent)



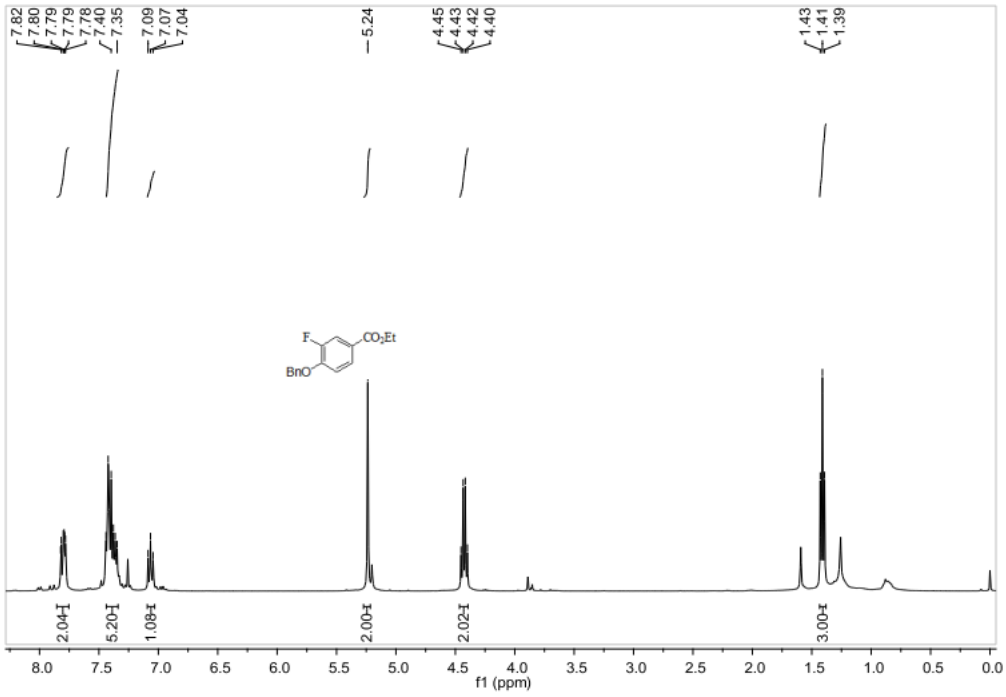


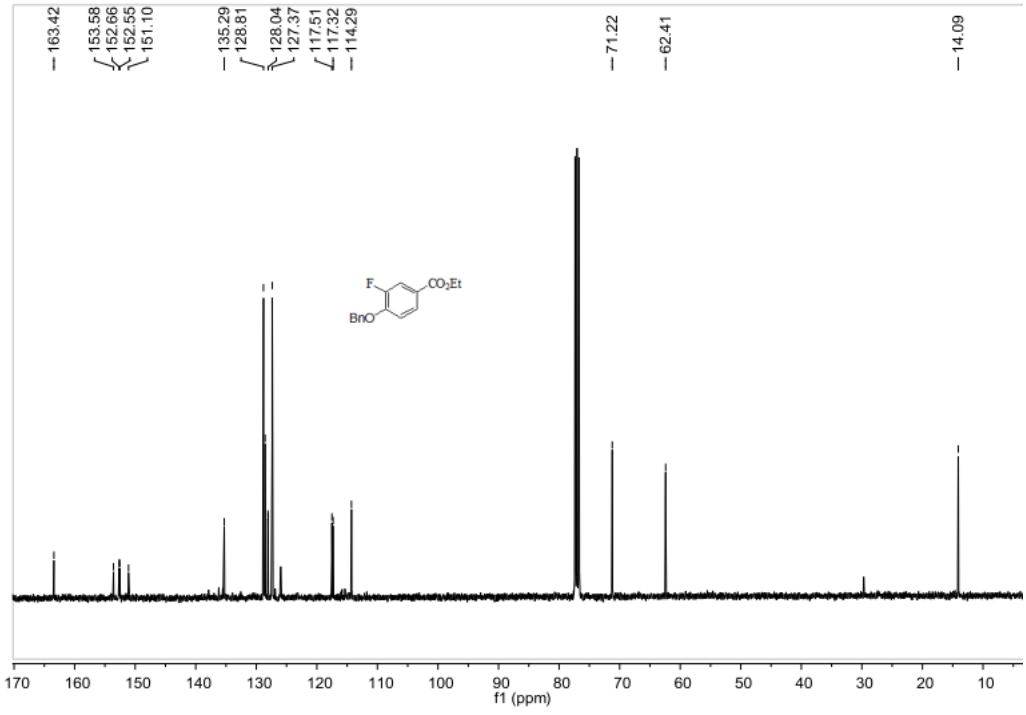
19). ^{1}H NMR and ^{13}C NMR Spectrum for ethyl phenanthrene-9-carboxylate **3p** (Using $CDCl_3$ as solvent)



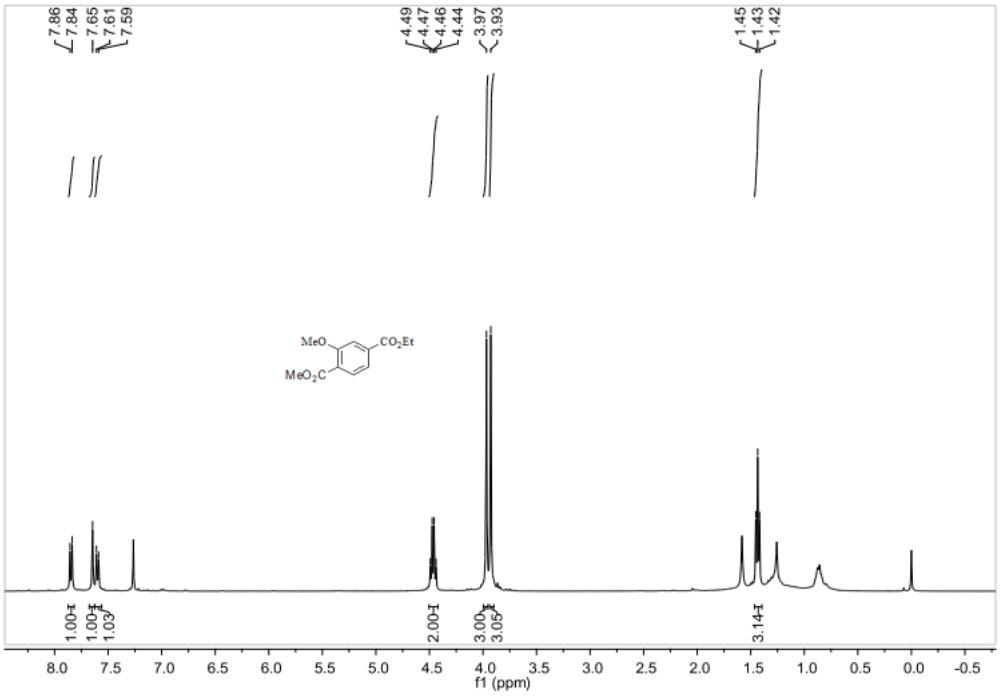


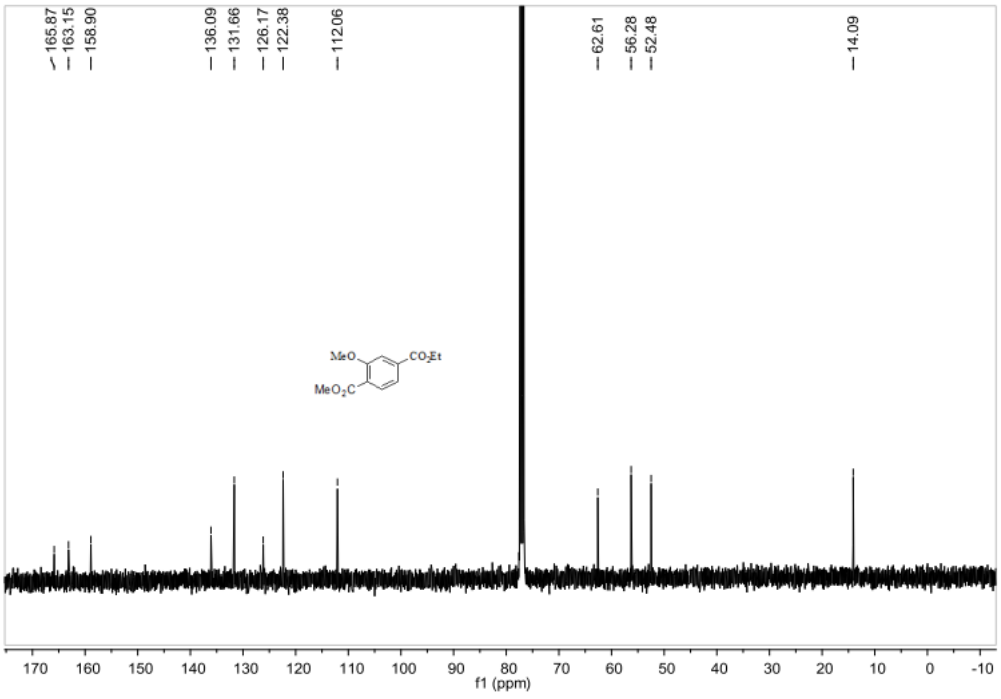
20)^{1}H NMR and ^{13}C NMR Spectrum for ethyl 4-(benzyloxy)-3-fluorobenzoate **3q** (Using $CDCl_3$ as solvent)



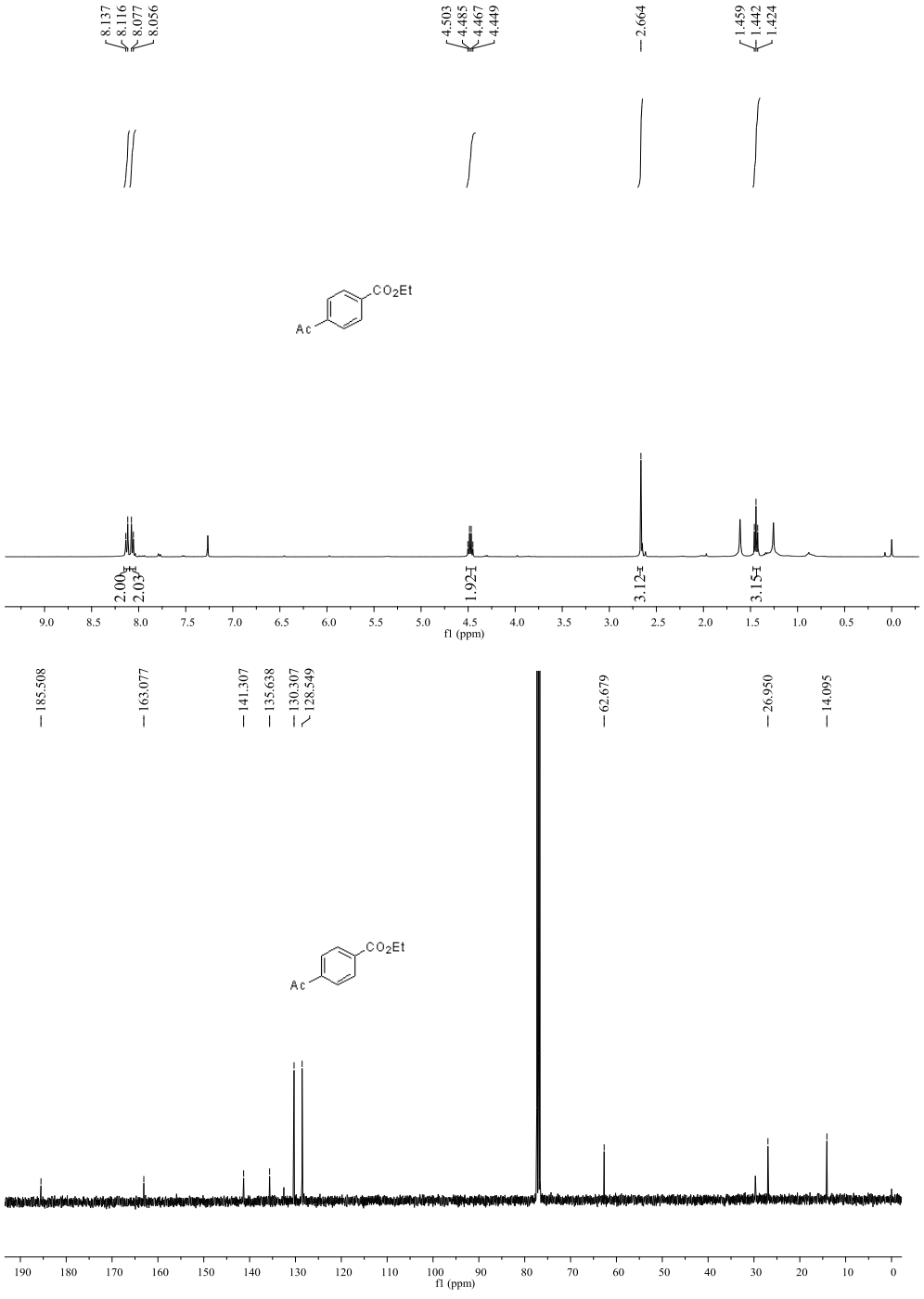


21).^{1}H NMR and ^{13}C NMR Spectrum for 4-ethyl 1-methyl 2-methoxyterephthalate **3r** (Using $CDCl_3$ as solvent)

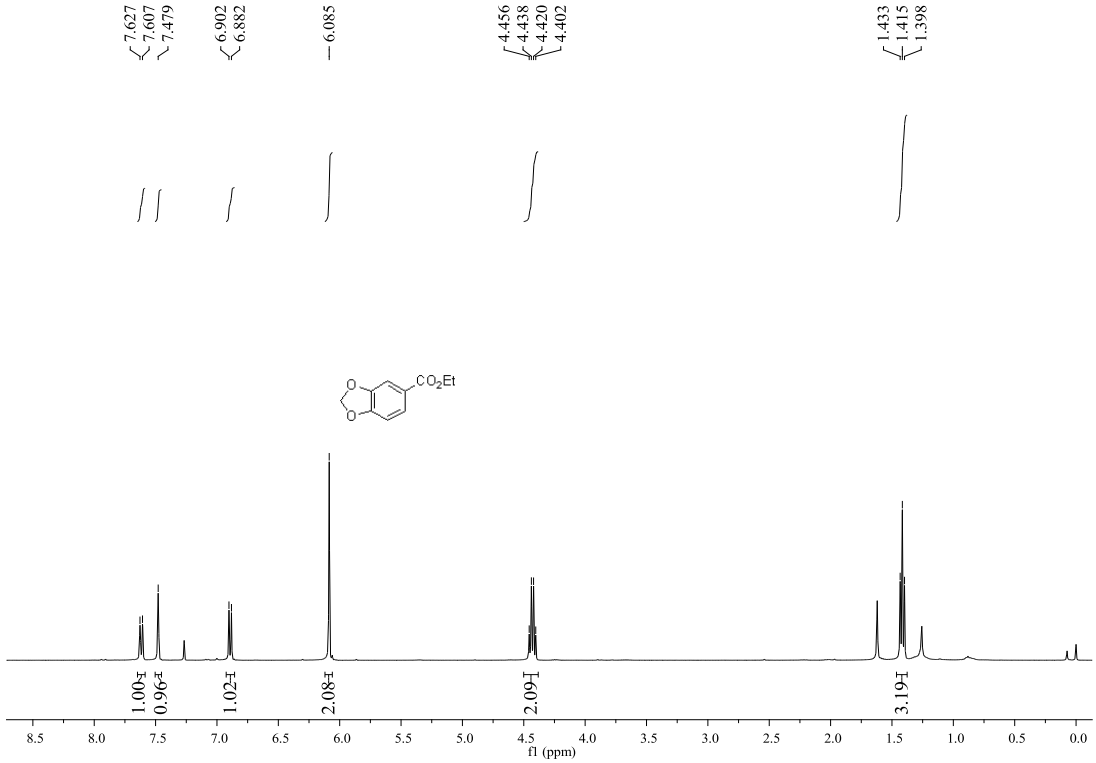


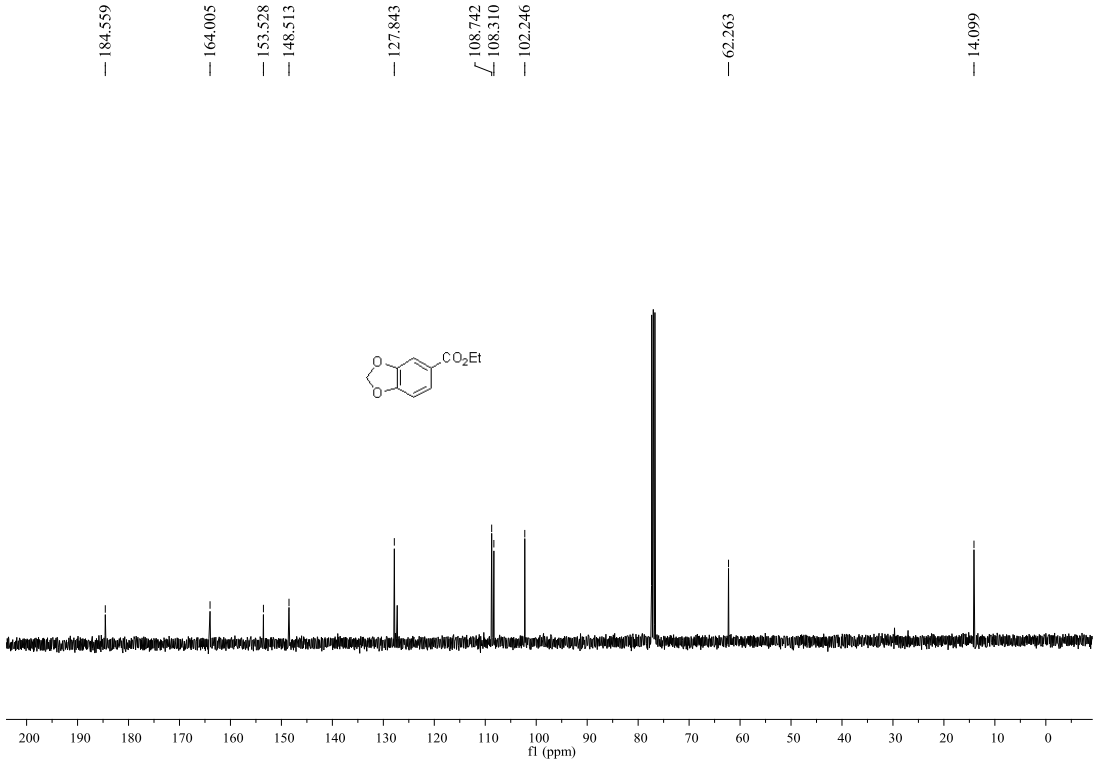


22).^{1}H NMR and ^{13}C NMR Spectrum for ethyl 4-acetylbenzoate **3s** (Using $CDCl_3$ as solvent)

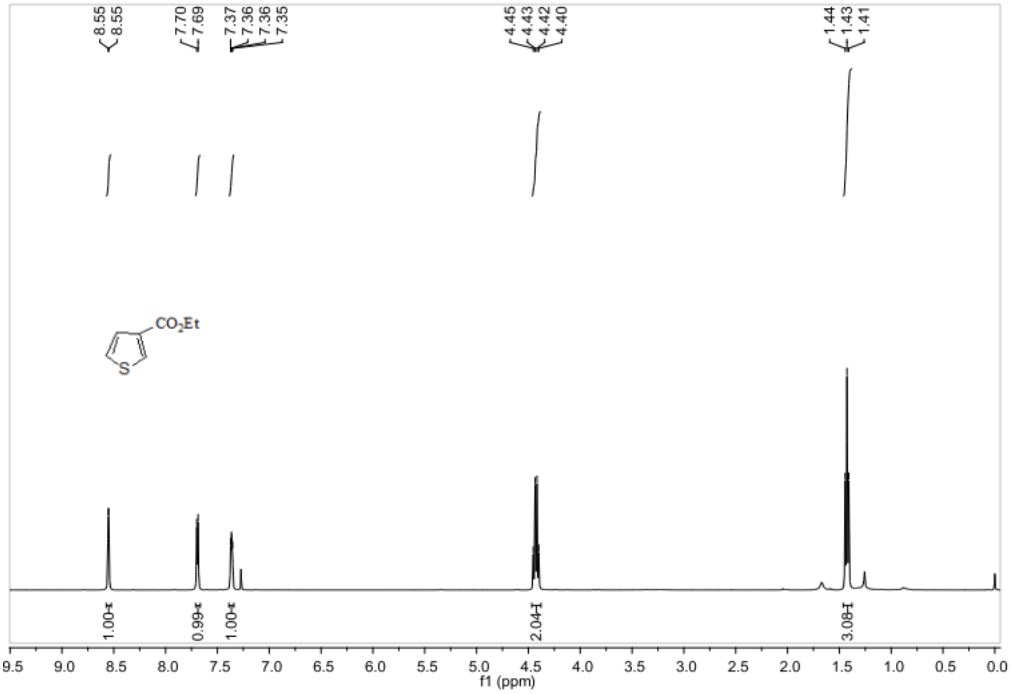


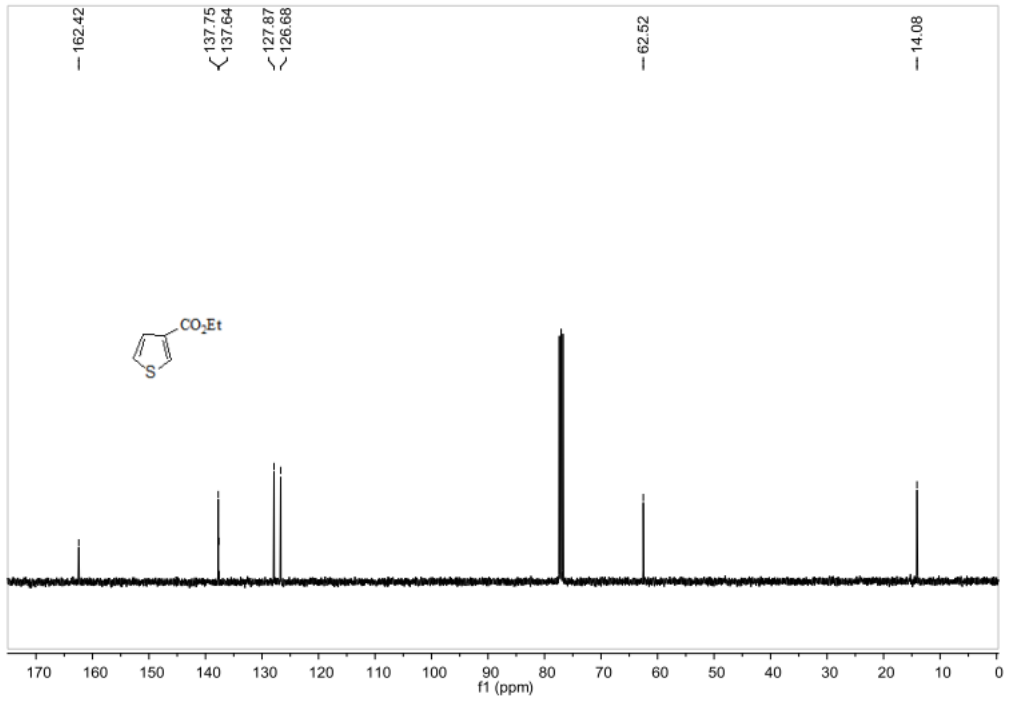
23).^{1}H NMR and ^{13}C NMR Spectrum for ethyl benzo[d][1,3]dioxole-5-carboxylate **3t** (Using $CDCl_3$ as solvent)



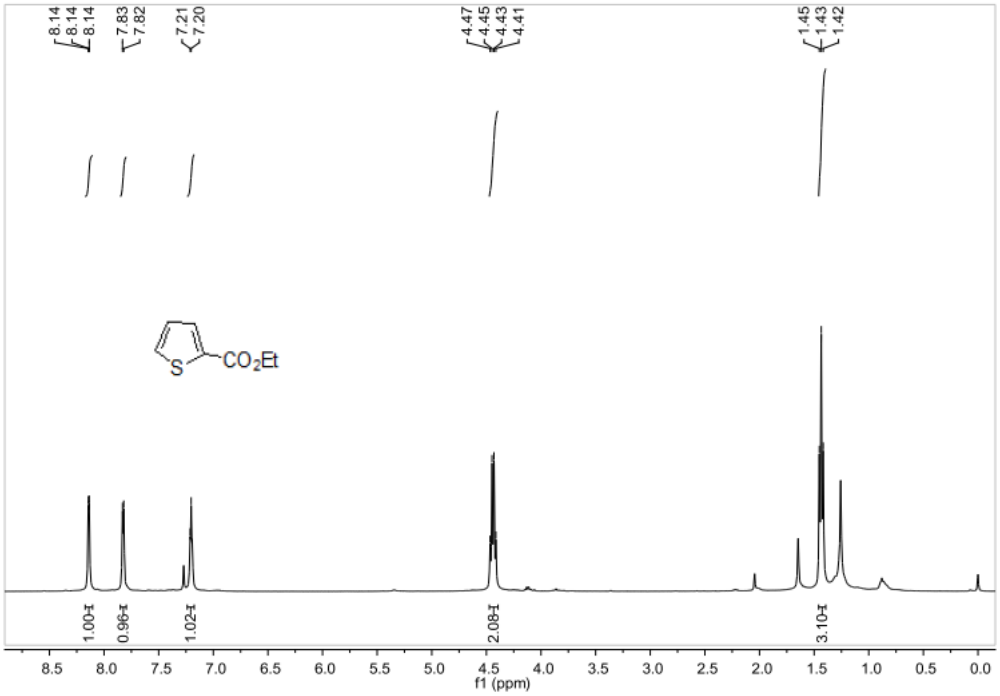


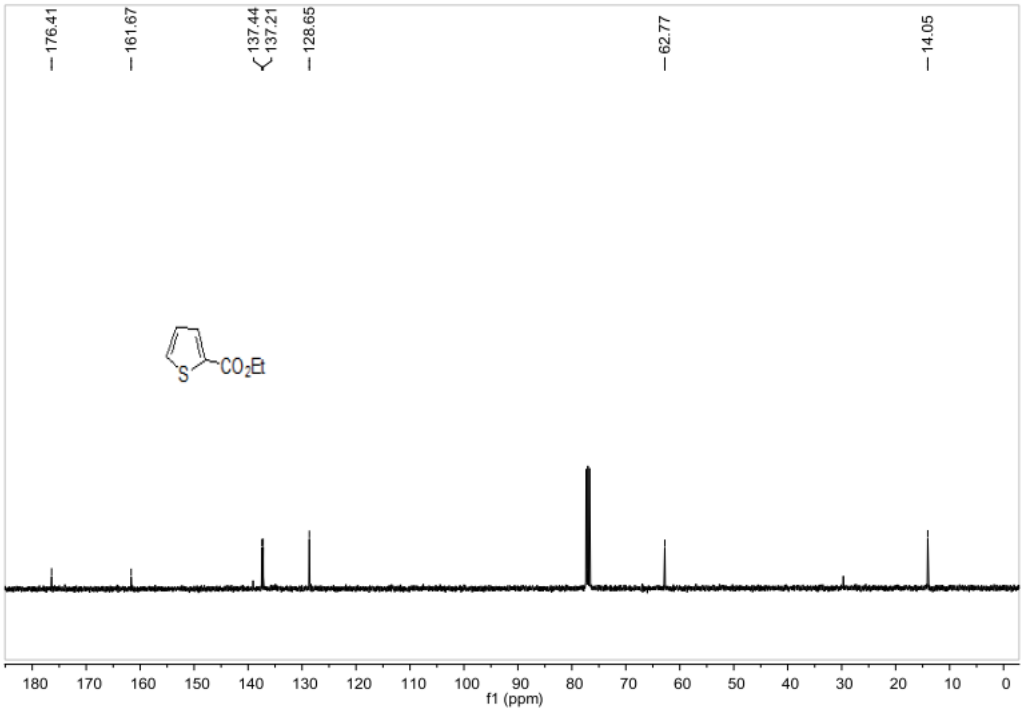
24).^{1}H NMR and ^{13}C NMR Spectrum for ethyl thiophene-3-carboxylate **3u** (Using $CDCl_3$ as solvent)



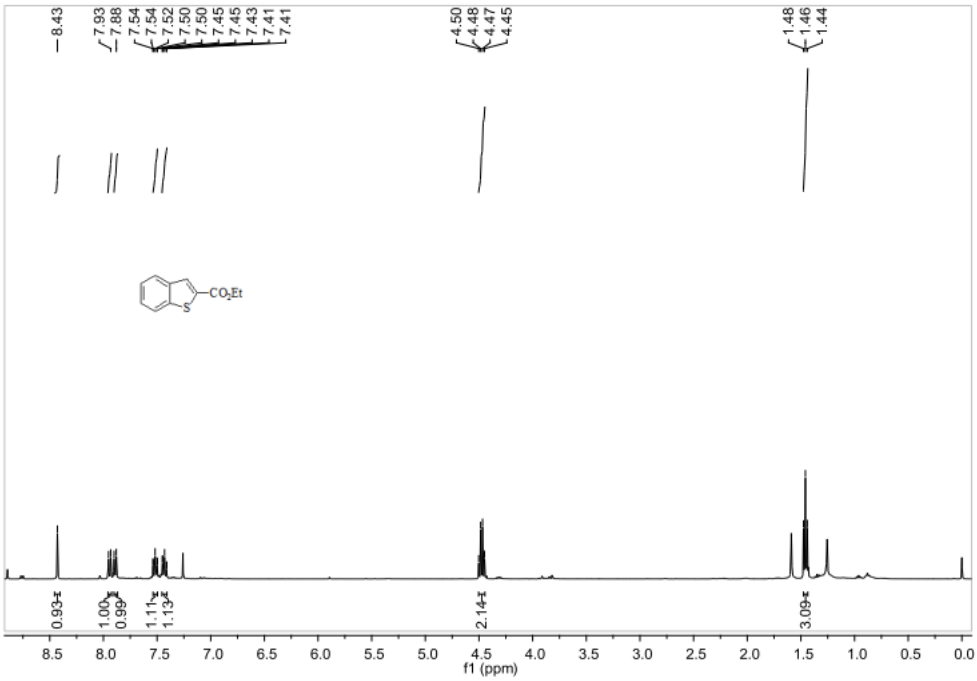


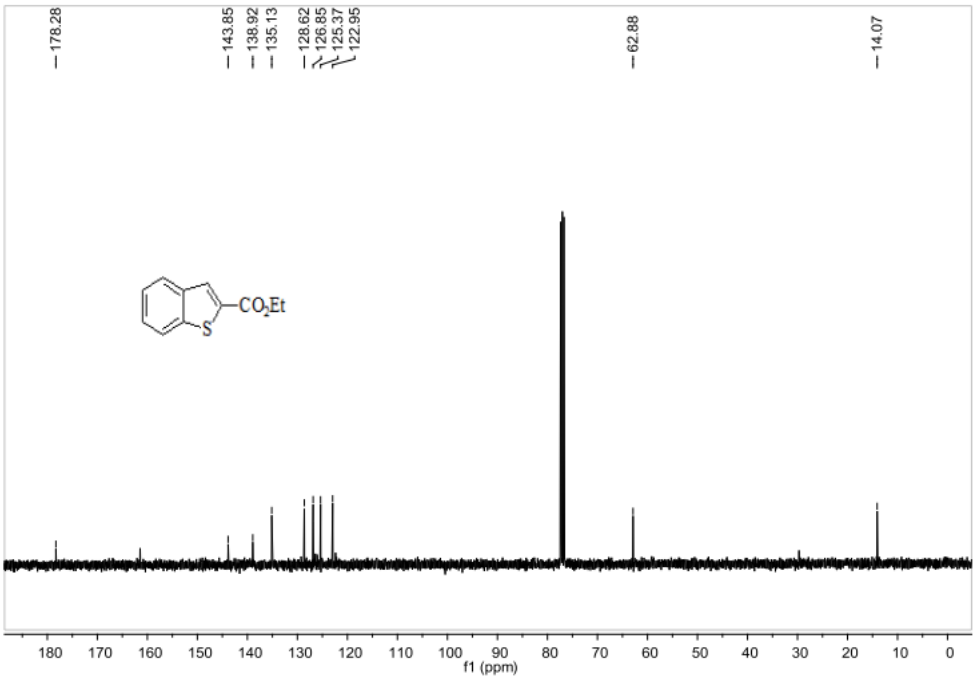
25).^{1}H NMR and ^{13}C NMR Spectrum for ethyl thiophene-2-carboxylate **3v** (Using $CDCl_3$ as solvent)



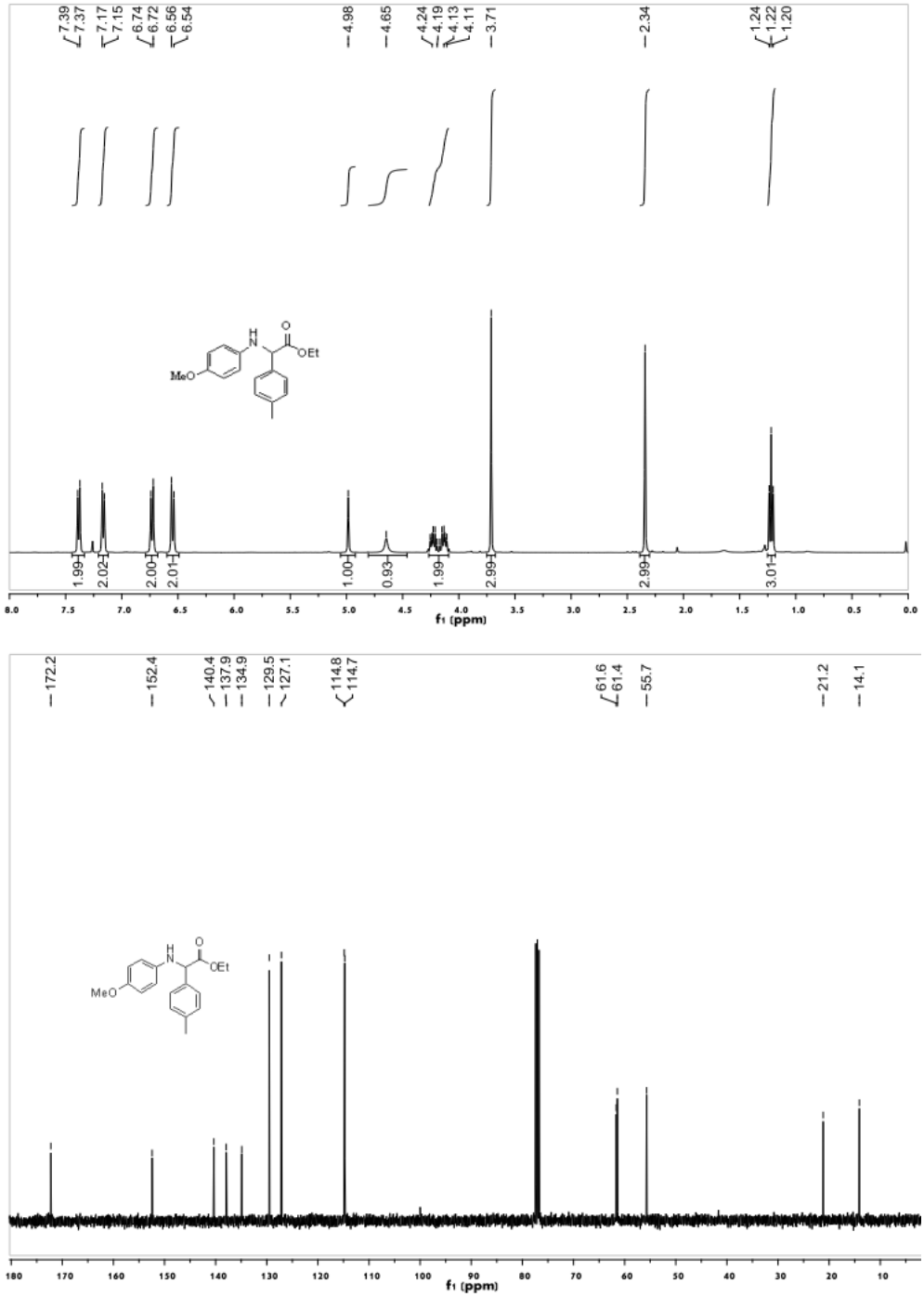


26). ^{1}H NMR and ^{13}C NMR Spectrum for ethyl benzo[b]thiophene-2-carboxylate **3w** (Using $CDCl_3$ as solvent)

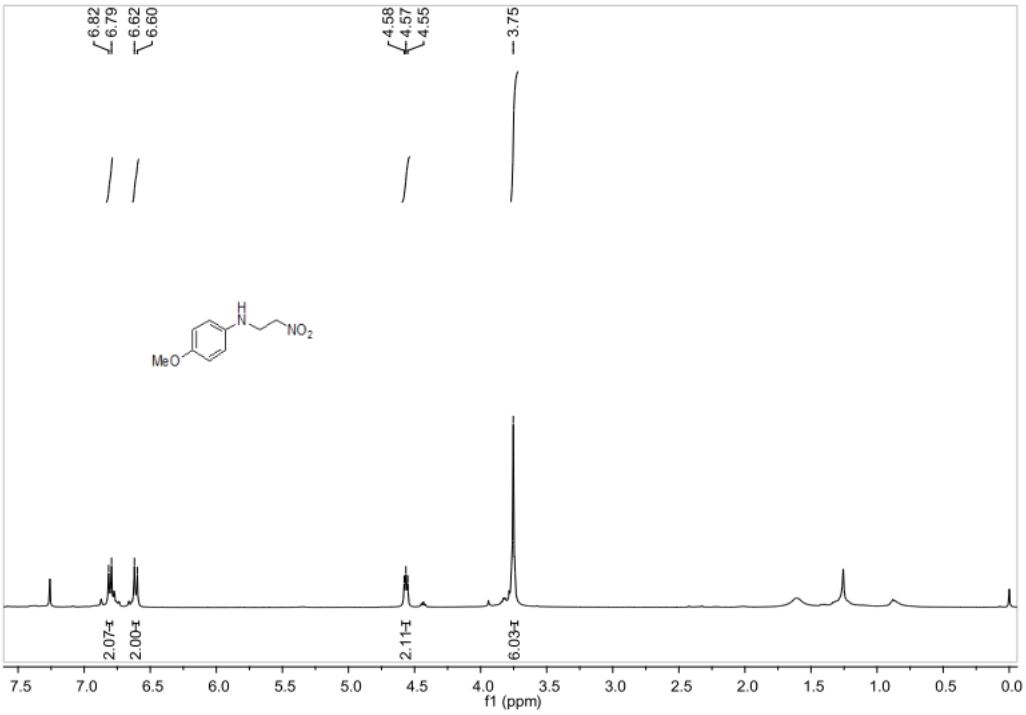


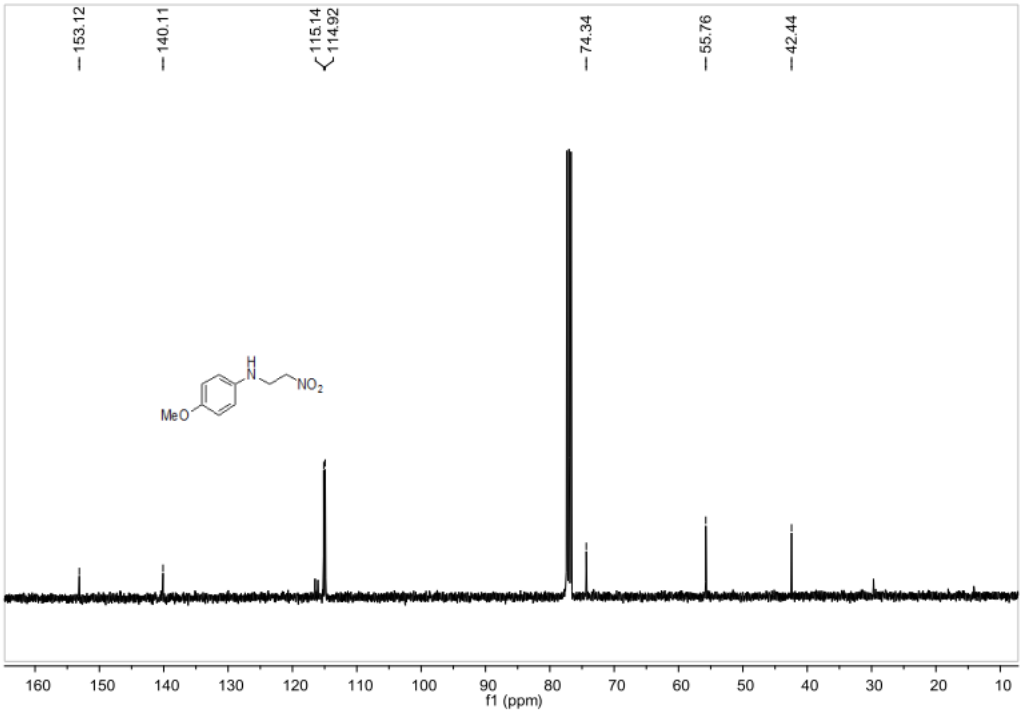


27). ^{1}H NMR and ^{13}C NMR Spectrum for ethyl 2-((4-methoxyphenyl)amino)-2-(*p*-tolyl) acetate **2aa** (Using $CDCl_3$ as solvent)

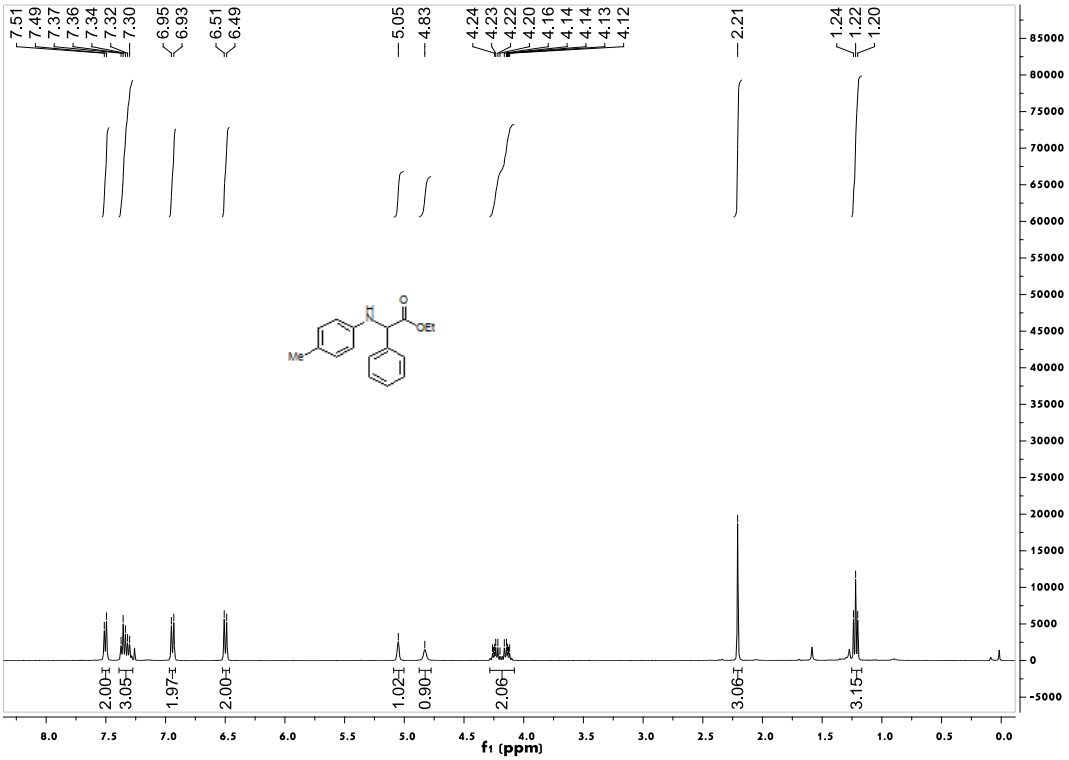


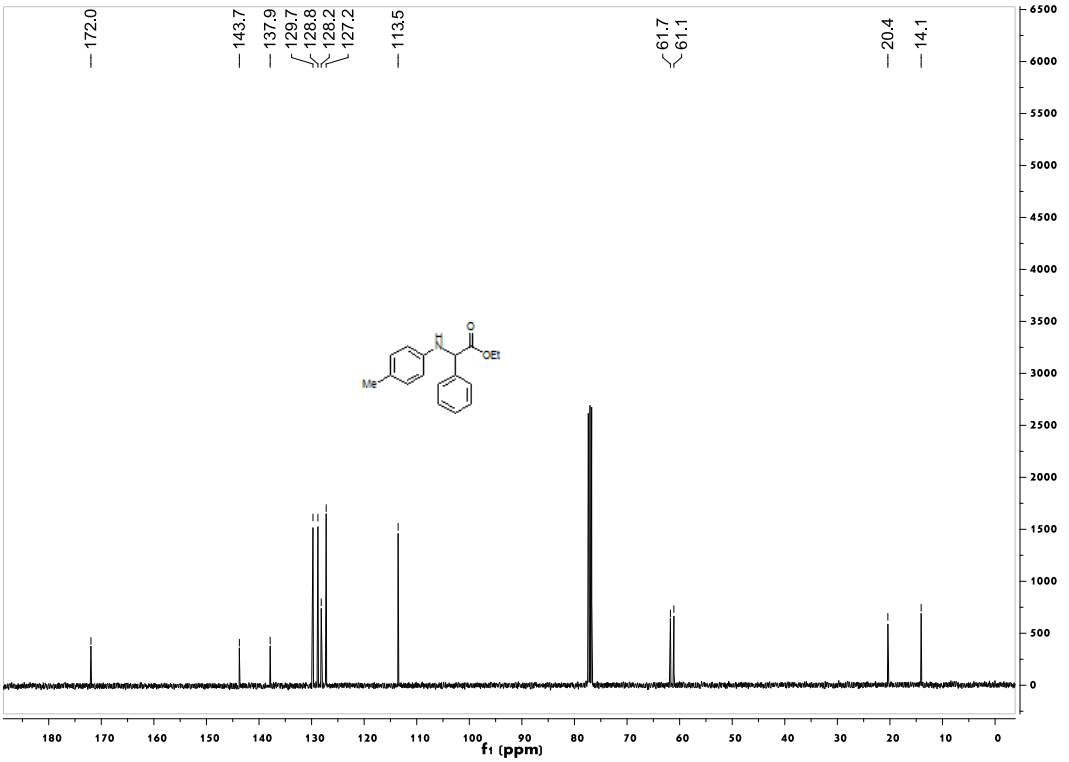
28). ^{1}H NMR and ^{13}C NMR Spectrum for 4-methoxy-*N*-(2-nitroethyl) benzenamine **4b** (Using $CDCl_3$ as solvent)



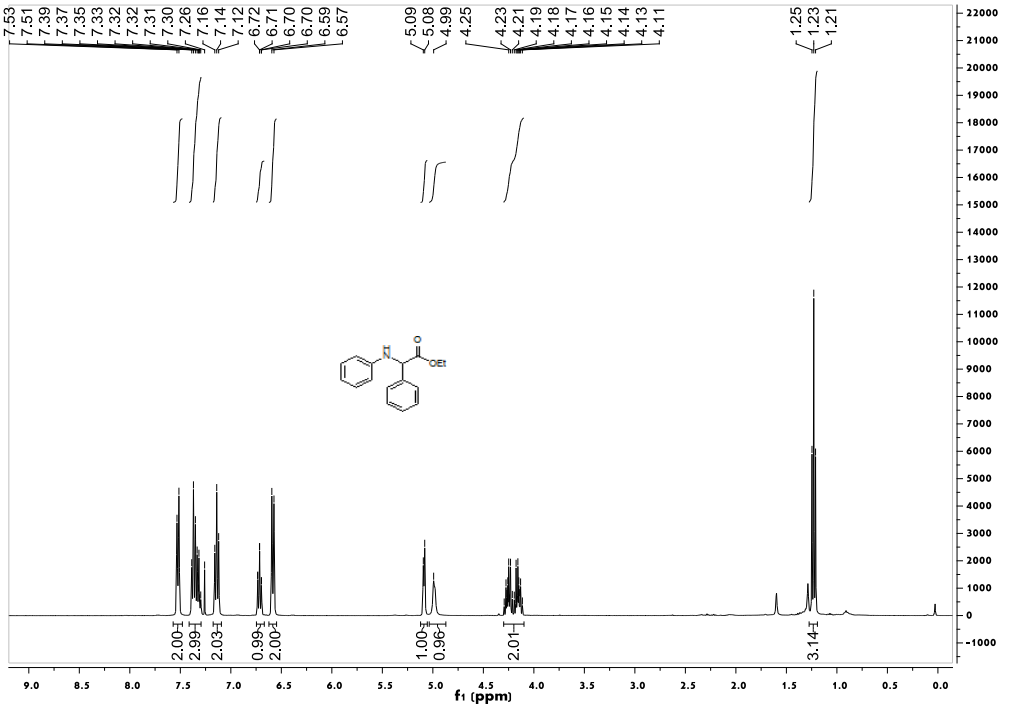


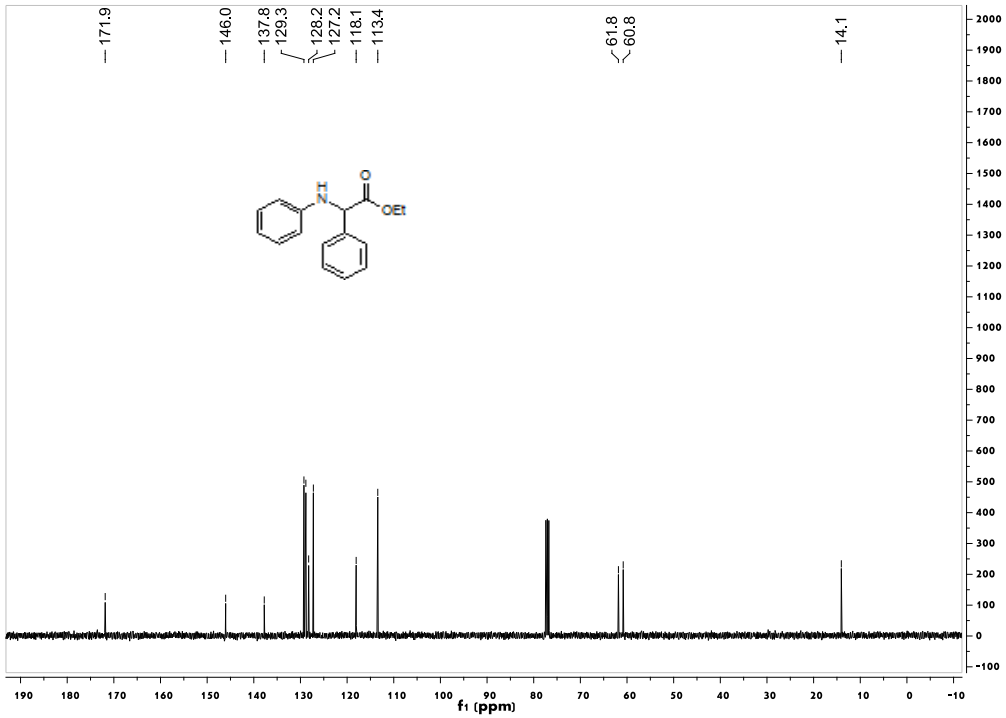
29). ^{1}H NMR and ^{13}C NMR spectrum for **P2b** (Using $CDCl_3$ as solvent)



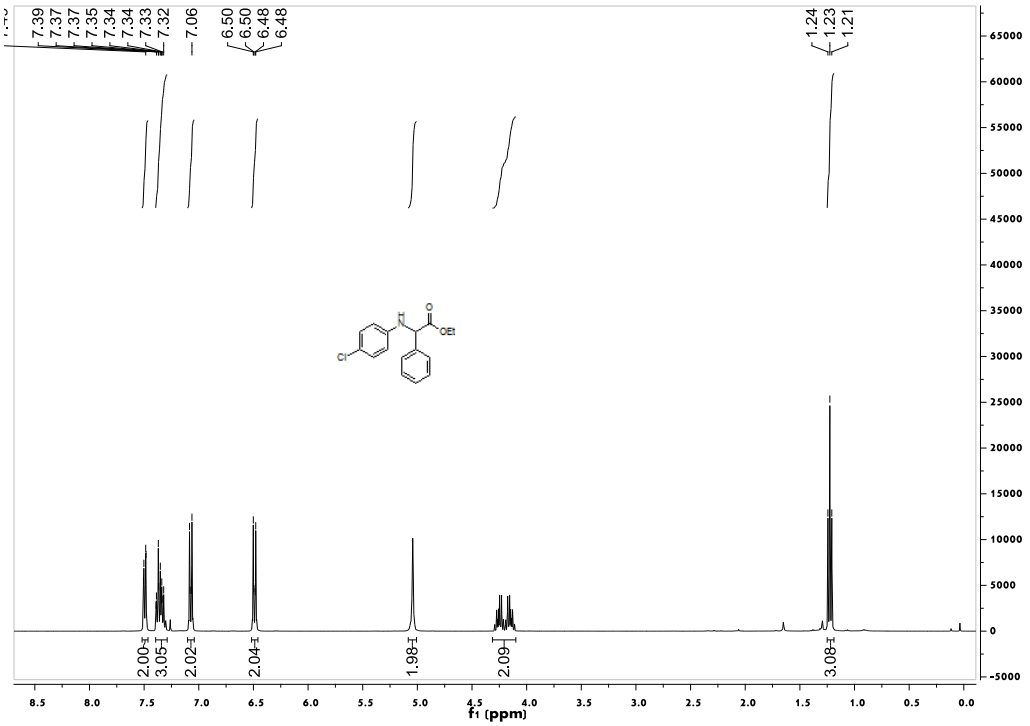


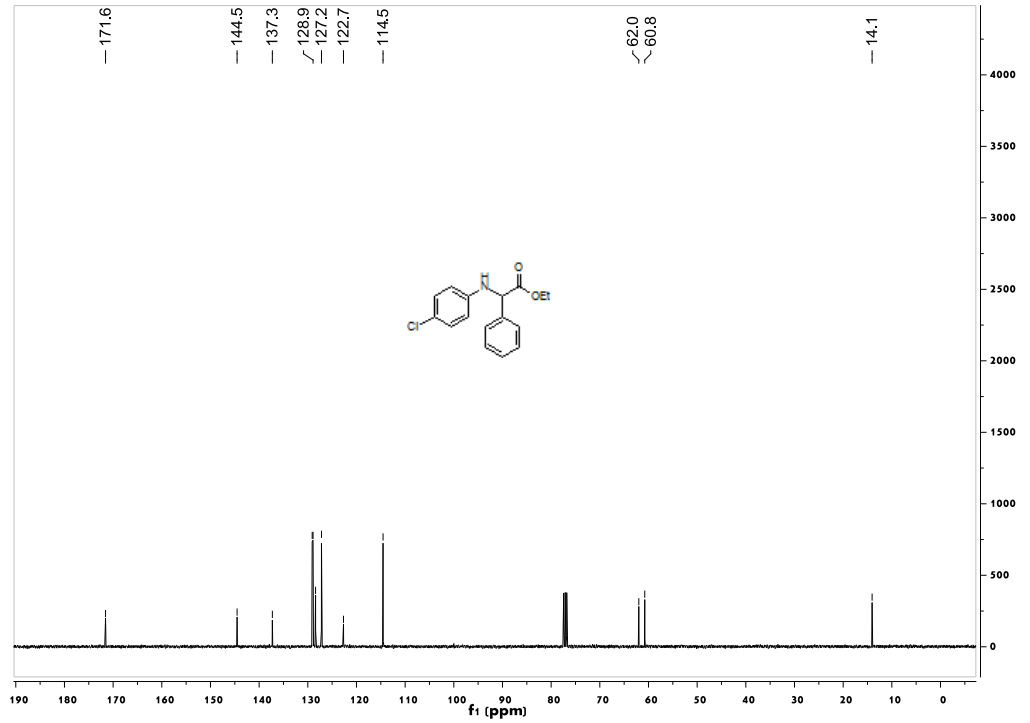
30). ^{1}H NMR and ^{13}C NMR spectrum for **P2c** (Using $CDCl_3$ as solvent)



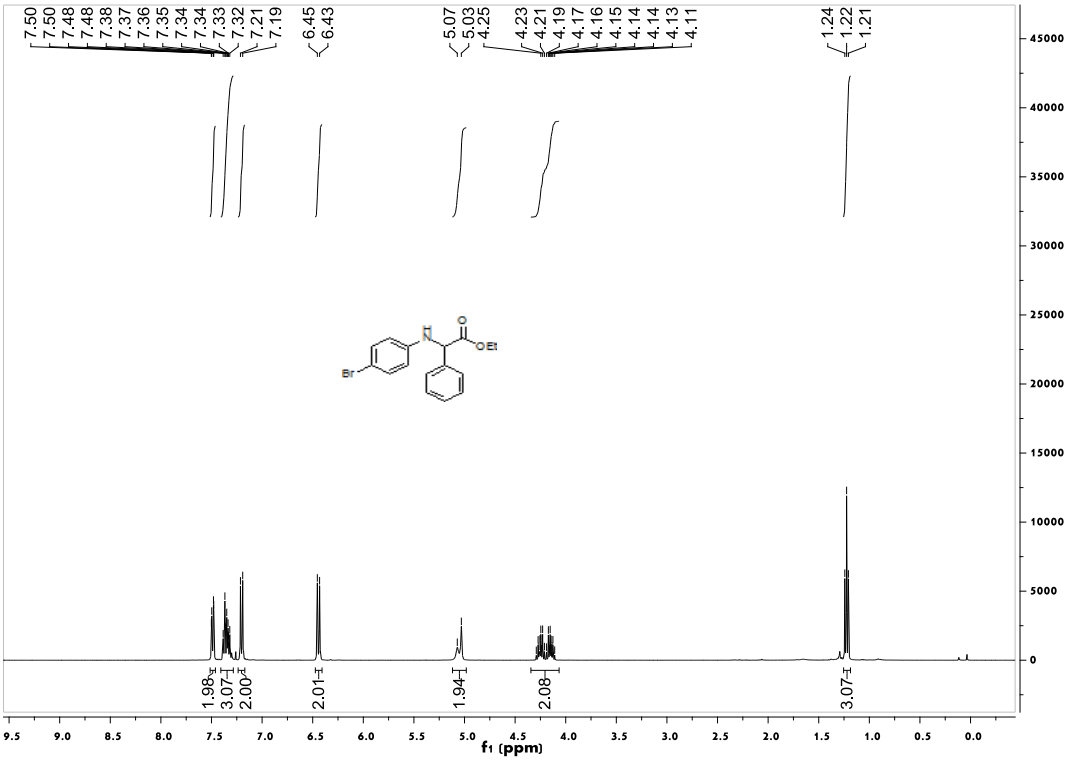


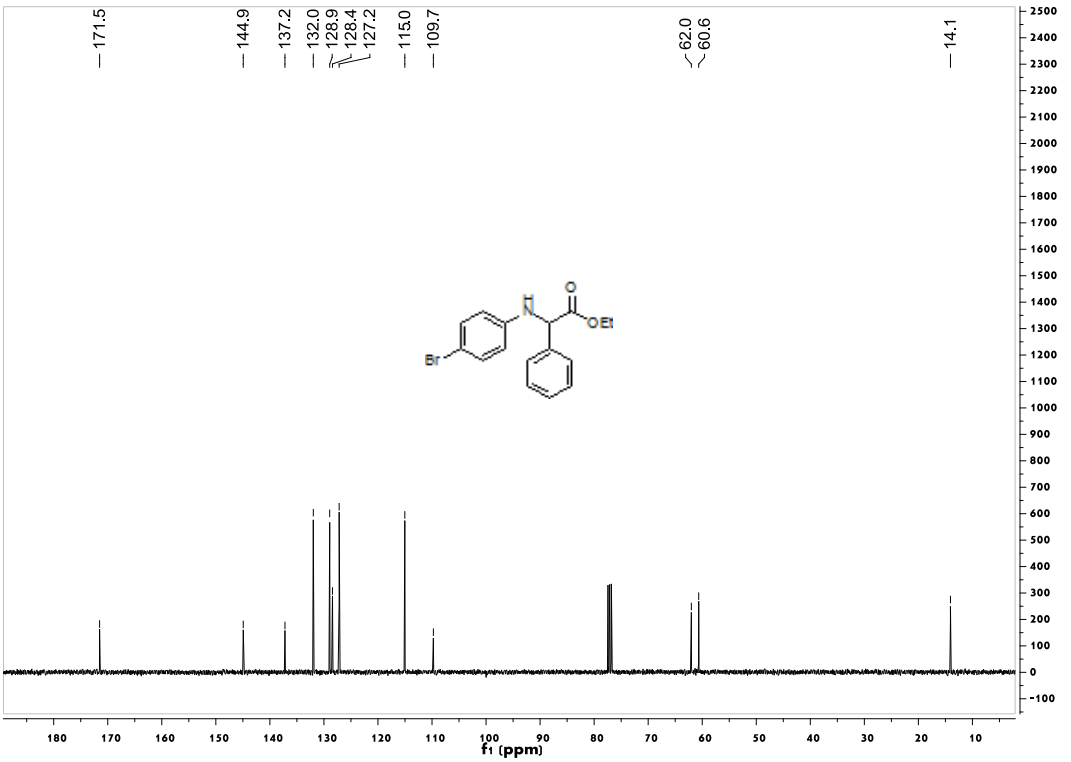
31). ^{1}H NMR and ^{13}C NMR spectrum for **P2d** (Using $CDCl_3$ as solvent)





32). ^{1}H NMR and ^{13}C NMR spectrum for **P2e** (Using $CDCl_3$ as solvent)





33). ^{1}H NMR and ^{13}C NMR spectrum for **P2f** (Using $CDCl_3$ as solvent)