Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Convenient and Flexible Syntheses of *gem*-Dimethyl Carboxylic Triggers via Mono-Selective *β*-C(sp^3)-H Arylation of Pivalic Acid with *ortho*-Substituted Aryl Iodides

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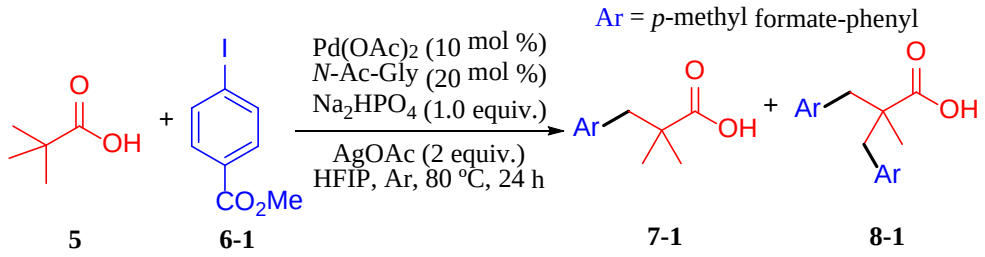
1. General Information

All reactions were performed in Schlenk tubes under an atmosphere of argon using oven-dried glassware. For reactions that require heating, oil bath was used as the heat source. Commercially available reagents were used without further purification, unless otherwise noted. Reactions were checked for completion by TLC analysis and plates were visualized with short-wave UV light (254 nm) or $KMnO_4$ aqueous. The ^{1}H, ^{13}C and ^{19}F NMR spectra were obtained in $CDCl_3$, CD_3OD or acetone-d_6 using a Bruker-BioSpin AVANCE III HD NMR spectrometer, respectively. Chemical shifts are reported in parts per million (δ value) calibrated against the residual solvent peak. Signal patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; hept, heptet; m, multiplet. Coupling constants (*J*) are given in hertz (Hz). The infrared spectra were recorded on a Bruker VERTEX 70 IR spectrometer as KBr pellets, with absorption reported in cm^{-1}. High-resolution mass spectra were recorded on a Bruker Impact II UHR TOF LC/MS Mass Spectrometry.

2. Optimization of the Reaction Conditions

Table S1: Optimization of substrate equivalent[a]

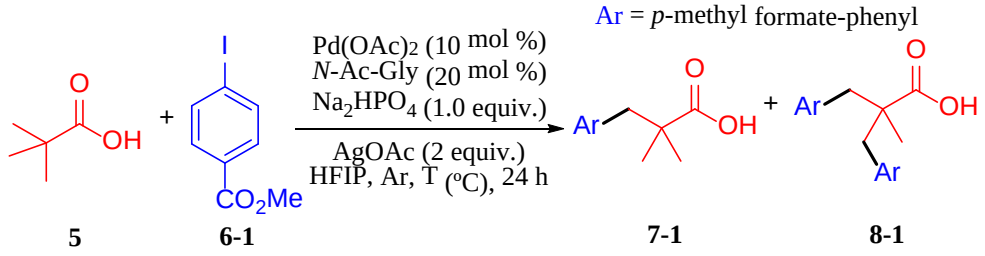


5 **6-1** **7-1** **8-1**

Entry	5:6-1	Yield (%)[b]	
		7-1	**8-1**
1	1:2	36	31
2	1:1	31	16
3	2:1	59	14
4	4:1	72	9
5	6:1	78	5
6	8:1	77	3

[a] Unless otherwise noted, reactions were carried out by using **5**, **6-1** (0.3 mmol), $Pd(OAc)_2$ (0.03mmol, 10 mol %), *N*-Ac-Gly (0.06 mmol, 20 mol %), Na_2HPO_4 (0.3 mmol, 1.0 equiv.) and AgOAc (0.6 mmol, 2 equiv.) in HFIP (1.5 mL) at 80 °C under argon atmosphere for 24 hours. [b] Yields were determined by ^{1}H-NMR spectroscopic analysis of crude mixtures using 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) as internal standard, isolated yields are given in parentheses.

Table S2: Optimization of reaction temperature[a]

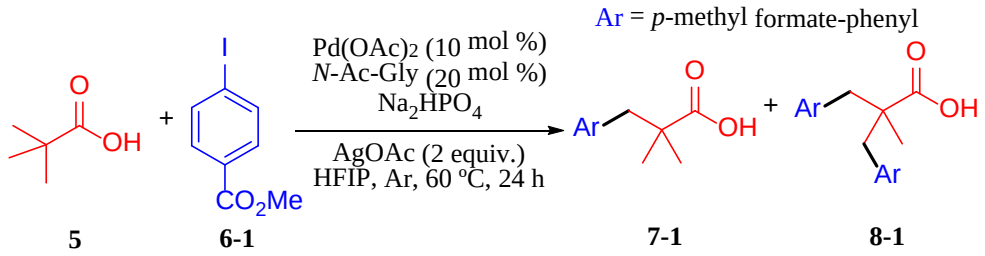


5 **6-1** **7-1** **8-1**

Entry	T (℃)	Yield (%)[b]	
		7-1	8-1
1	30	5	0
2	40	13	trace
3	50	58	2
4	60	80	4
5	70	76	5
6	80	79	6
7	90	77	5

[a] Unless otherwise noted, reactions were carried out by using **5** (1.8 mmol, 6 equiv.), **6-1** (0.3 mmol), $Pd(OAc)_2$ (0.03mmol, 10 mol %), *N*-Ac-Gly (0.06 mmol, 20 mol %), Na_2HPO_4 (0.3 mmol, 1.0 equiv.) and AgOAc (0.6 mmol, 2 equiv.) in HFIP (1.5 mL) at T °C under argon atmosphere for 24 hours. [b] Yields were determined by ^{1}H-NMR spectroscopic analysis of crude mixtures using 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) as internal standard, isolated yields are given in parentheses.

Table S3: Optimization of base amount[a]



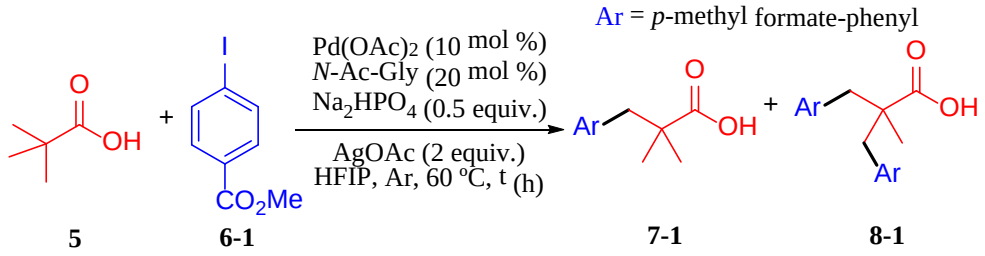
5 **6-1** **7-1** **8-1**

Entry	Base (equiv.)	Yield (%)[b]	
		7-1	8-1
1	0	52	2
2	0.5	82(84)	4

3	1	80	4
4	2	74	3

[a] Unless otherwise noted, reactions were carried out by using **5** (1.8 mmol, 6 equiv.), **6-1** (0.3 mmol), $Pd(OAc)_2$ (0.03mmol, 10 mol %), *N*-Ac-Gly (0.06 mmol, 20 mol %), Na_2HPO_4 and AgOAc (0.6 mmol, 2 equiv.) in HFIP (1.5 mL) at 60 °C under argon atmosphere for 24 hours. [b] Yields were determined by ^{1}H-NMR spectroscopic analysis of crude mixtures using 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) as internal standard, isolated yields are given in parentheses.

Table S4: Optimization of reaction time[a]

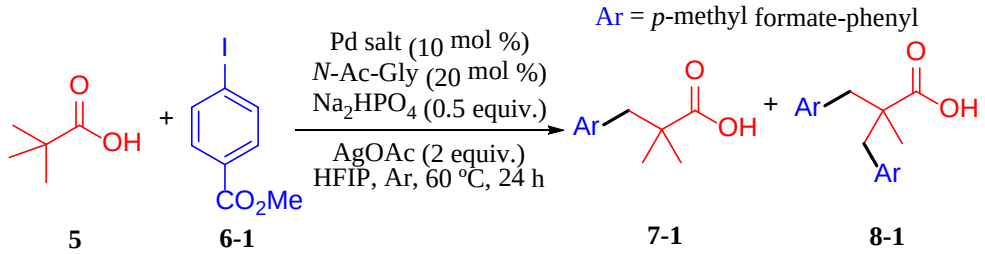


5 **6-1** **7-1** **8-1**

Entry	**t (h)**	**Yield (%)**[b]	
		7-1	**8-1**
1	6	47	1
2	12	60	3
3	24	82(84)	4
4	36	76	6

[a] Unless otherwise noted, reactions were carried out by using **5** (1.8 mmol, 6 equiv.), **6-1** (0.3 mmol), $Pd(OAc)_2$ (0.03mmol, 10 mol %), *N*-Ac-Gly (0.06 mmol, 20 mol %), Na_2HPO_4 (0.15 mmol, 0.5 equiv.) and AgOAc (0.6 mmol, 2 equiv.) in HFIP (1.5 mL) at 60 °C under argon atmosphere for t hours. [b] Yields were determined by ^{1}H-NMR spectroscopic analysis of crude mixtures using 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) as internal standard, isolated yields are given in parentheses.

Table S5: Optimization of palladium-catalyst[a]



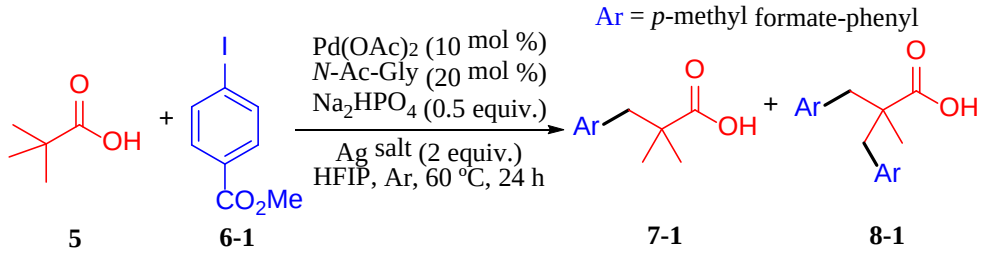
5 **6-1** **7-1** **8-1**

Entry	Palladium salt	Yield (%)[b]	
		7-1	**8-1**
1	$Pd(dba)_2$	11	0
2	$PdCl_2$	74	2
3	$Pd(PCy_3)_2Cl_2$	0	0
4	$Pd_2(dba)_3$	6	0
5	$Pd(PPh_3)_4$	12	0
6	$Pd(TFA)_2$	73	2
7	$Pd(tBuCO_2)_2$	72	1
8	$Pd(CH_3CNBF_4)_2$	75	3
9	$PdBr_2$	74	3
10	PdI_2	72	4
11	Na_2PdCl_4	73	2
12	K_2PdCl_4	75	2
13	$Pd(MeCN)_2Cl_2$	67	8
14	$Pd(OAc)_2$	82(84)	4
15	None	0	0

[a] Unless otherwise noted, reactions were carried out by using **5** (1.8 mmol, 6 equiv.), **6-1** (0.3 mmol), Pd-catalyst (0.03mmol, 10 mol %), *N*-Ac-Gly (0.06 mmol, 20 mol %),

Na_2HPO_4 (0.15 mmol, 0.5 equiv.) and AgOAc (0.6 mmol, 2 equiv.) in HFIP (1.5 mL) at 60 °C under argon atmosphere for 24 hours. [b] Yields were determined by ^{1}H-NMR spectroscopic analysis of crude mixtures using 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) as internal standard, isolated yields are given in parentheses.

Table S6: Optimization of Ag salt[a]



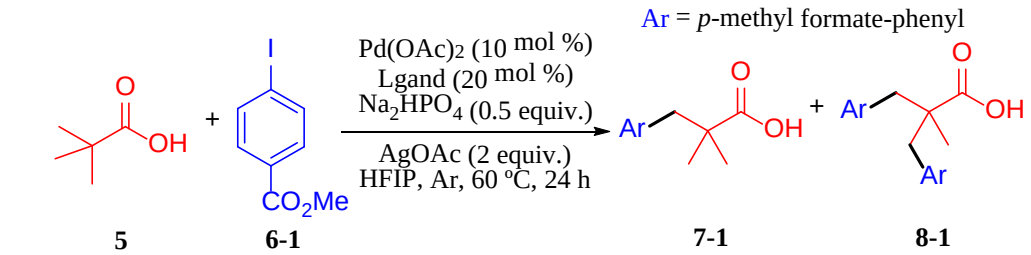
5 **6-1** **7-1** **8-1**

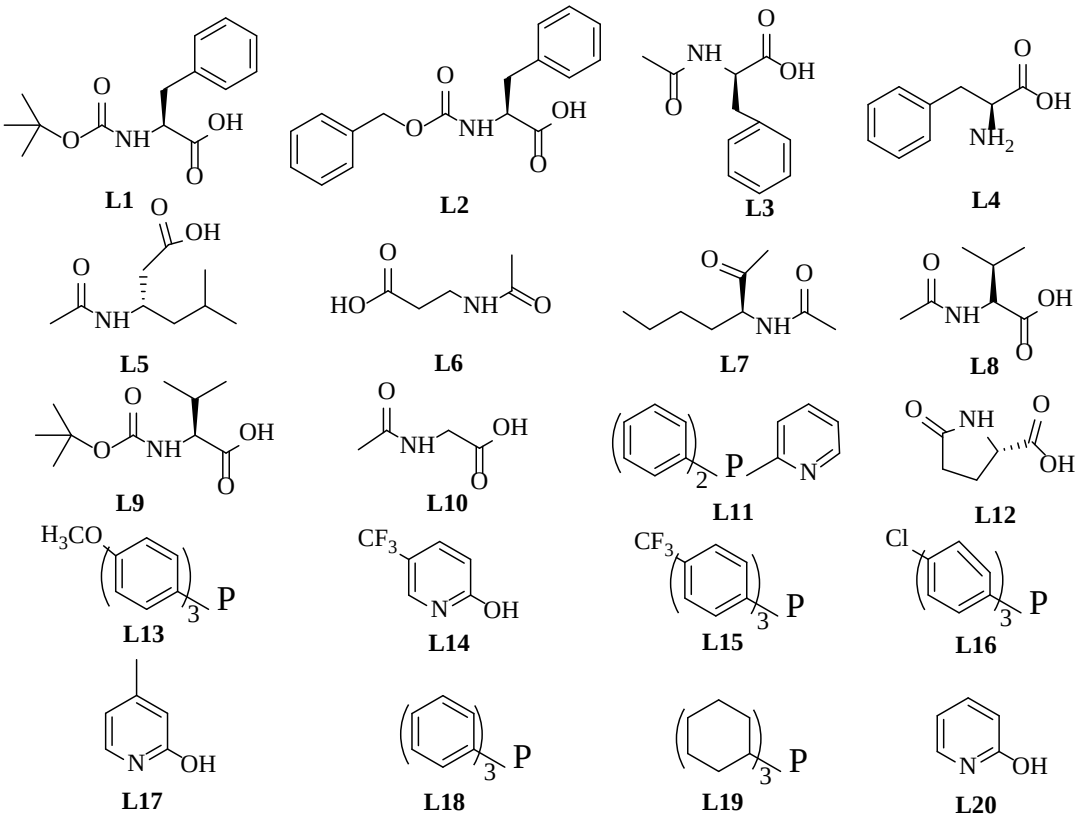
Entry	Ag salt	Yield (%)[b]	
		7-1	**8-1**
1	Ag_2CO_3	72	4
2	Ag_3PO_4	48	1
3	AgF_6Sb	19	0
4	$AgBF_4$	27	0
5	Ag_2O	64	5
6	CF_3SO_3Ag	15	0
7	AgF	22	trace
8	AgOAc	82(84)	4
9	Silver *p*-Toluenesulfonate	2	0
10	None	7	0

[a] Unless otherwise noted, reactions were carried out by using **5** (1.8 mmol, 6 equiv.), **6-1** (0.3 mmol), $Pd(OAc)_2$ (0.03mmol, 10 mol %), *N*-Ac-Gly (0.06 mmol, 20 mol %), Na_2HPO_4 (0.15 mmol, 0.5 equiv.) and Ag salt (0.6 mmol, 2 equiv.) in HFIP (1.5 mL) at

60 °C under argon atmosphere for 24 hours. [b] Yields were determined by ^{1}H-NMR spectroscopic analysis of crude mixtures using 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) as internal standard, isolated yields are given in parentheses.

Table S7: Optimization of ligand[a]



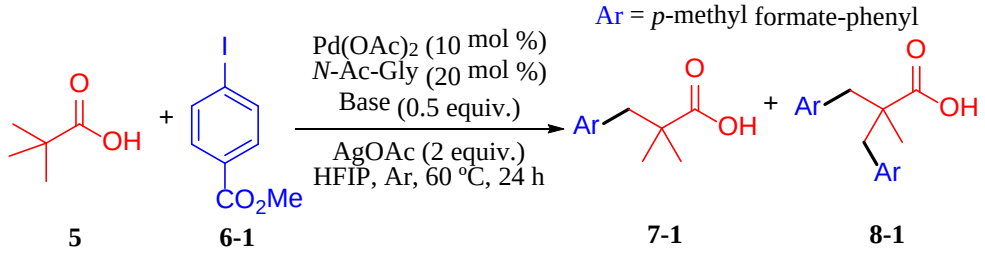


Entry	Ligand	Yield (%)[b]	
		7-1	8-1
1	L1	trace	0
2	L2	6	0
3	L3	71	2
4	L4	0	0
5	L5	69	3
6	L6	75	2
7	L7	72	3
8	L8	71	3
9	L9	7	0
10	L10	82(84)	4
11	L11	0	0
12	L12	6	0
13	L13	29	trace
14	L14	58	trace
15	L15	15	trace
16	L16	14	trace
17	L17	36	trace
18	L18	5	0
19	L19	trace	0
20	L20	39	trace
21	None	37	0

[a] Unless otherwise noted, reactions were carried out by using **5** (1.8 mmol, 6 equiv.), **6-**

1 (0.3 mmol), $Pd(OAc)_2$ (0.03mmol, 10 mol %), Ligand (0.06 mmol, 20 mol %), Na_2HPO_4 (0.15 mmol, 0.5 equiv.) and AgOAc (0.6 mmol, 2 equiv.) in HFIP (1.5 mL) at 60 °C under argon atmosphere for 24 hours. [b] Yields were determined by ^{1}H-NMR spectroscopic analysis of crude mixtures using 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) as internal standard, isolated yields are given in parentheses.

Table S8: Optimization of base[a]



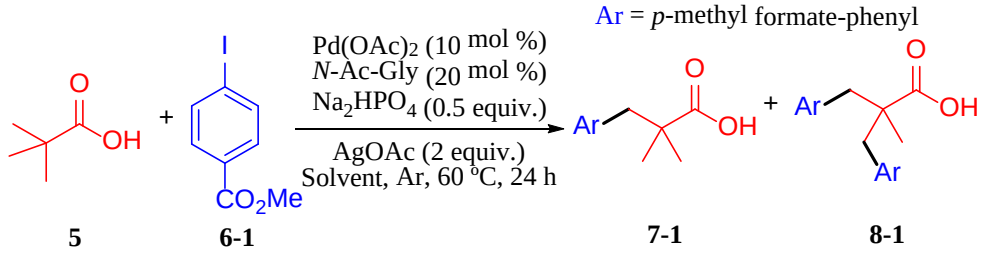
5 **6-1** **7-1** **8-1**

Entry	Base	Yield (%)[b]	
		7-1	**8-1**
1	CsF	73	4
2	$NaHCO_3$	72	3
3	$MgSO_4$	72	3
4	$KHSO_3$	77	4
5	K_2SO_4	69	4
6	K_2CO_3	68	3
7	Na_2CO_3	70	3
8	$KHSO_3$	71	4
9	$CsCO_3$	69	3
10	$LiCO_3$	56	1
11	NaOAc	71	3
12	K_2HPO_4	74	3

13	$NaHSO_3$	76	4
14	CF_3CO_2K	69	2
15	K_3PO_4	68	2
16	HCO_2K	71	2
17	Na_2HPO_4	82(84)	4
18	None	51	2

[a] Unless otherwise noted, reactions were carried out by using **5** (1.8 mmol, 6 equiv.), **6-1** (0.3 mmol), $Pd(OAc)_2$ (0.03mmol, 10 mol %), *N*-Ac-Gly (0.06 mmol, 20 mol %), Base (0.15 mmol, 0.5 equiv.) and AgOAc (0.6 mmol, 2 equiv.) in HFIP (1.5 mL) at 60 °C under argon atmosphere for 24 hours. [b] Yields were determined by ^{1}H-NMR spectroscopic analysis of crude mixtures using 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) as internal standard, isolated yields are given in parentheses.

Table S9: Optimization of solvent[a]



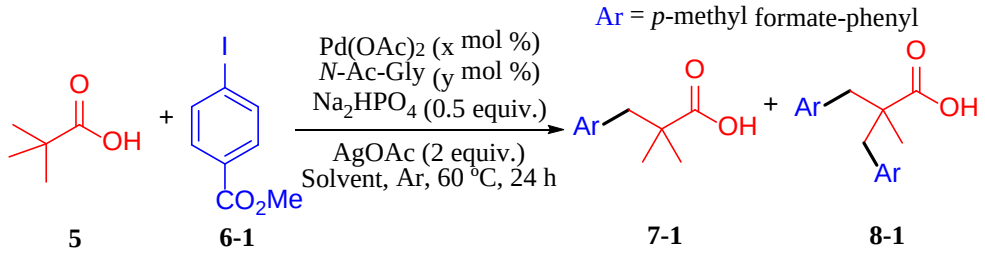
5 **6-1** **7-1** **8-1**

Entry	**Solvent**	**Yield (%)**[b]	
		7-1	**8-1**
1	1,4-dioxane	74	trace
2	toluene	4	0
3	*t*-BuOH	64	3
4	CH_3CN	trace	0
5	DCE	2	0

6	DCM	6	0
7	2-Methyl-2-butanol	53	1
8	THF	8	0
9	Hexane	1	0
10	DMF	0	0
11	DMSO	trace	0
12	EtOAc	8	0
13	HFIP	82(84)	4

[a] Unless otherwise noted, reactions were carried out by using **5** (1.8 mmol, 6 equiv.), **6-1** (0.3 mmol), $Pd(OAc)_2$ (0.03mmol, 10 mol %), *N*-Ac-Gly (0.06 mmol, 20 mol %), Na_2HPO_4 (0.15 mmol, 0.5 equiv.) and AgOAc (0.6 mmol, 2 equiv.) in Solvent (1.5 mL) at 60 °C under argon atmosphere for 24 hours. [b] Yields were determined by ^{1}H-NMR spectroscopic analysis of crude mixtures using 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) as internal standard, isolated yields are given in parentheses.

Table S10: Optimization of palladium and ligand equivalents[a]



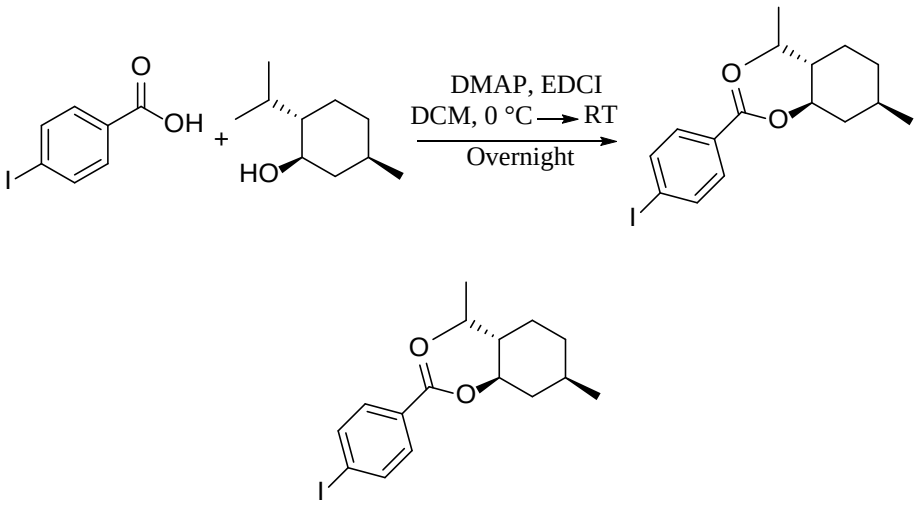
5 **6-1** **7-1** **8-1**

Entry	Palladium and ligand equivalents (x and y mol %)	Yield (%)[b]	
		7-1	**8-1**
1	2.5 and 5	33	0
2	5 and 10	78 (81)	4
3	10 and 20	82 (84)	4

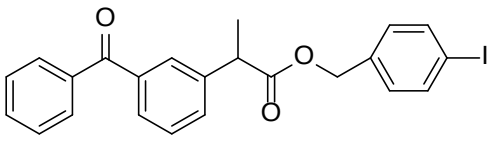
4	15 and 30	76	3

[a] Unless otherwise noted, reactions were carried out by using **5** (1.8 mmol, 6 equiv.), **6-1** (0.3 mmol), $Pd(OAc)_2$ (x mol %), *N*-Ac-Gly (y mol %), Na_2HPO_4 (0.15 mmol, 0.5 equiv.) and AgOAc (0.6 mmol, 2 equiv.) in HFIP (1.5 mL) at 60 °C under argon atmosphere for 24 hours. [b] Yields were determined by 1H-NMR spectroscopic analysis of crude mixtures using 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) as internal standard, isolated yields are given in parentheses.

3. General Synthetic Methods and Analytical Data for Substrates 6

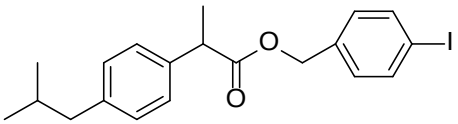


General procedure: The 4-Iodobenzoic acid (3.0 mmol, 744.0 mg), Menthol (3.0 mmol, 468.0 mg), DMAP (0.33 mmol, 42.0 mg) and EDCI (3.3 mmol, 633.0 mg) were dissolved in DCM (30 mL) and stirred at 0 °C for 1 h. Then the reaction was stirred at room temperature overnight. Upon completion, the reaction mixture was added 60 mL H_2O, then the aqueous layer was extracted with DCM (30 mL) for 3 times. The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated under vacuum. The residue was purified with column chromatography on silica gel (petroleum ether: ethyl acetate = 15:1) to yield compound **6-62** as a colorless oil (996.6 mg, 86% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.80 - 7.73 (m, 4H), 4.93 (td, *J* = 10.9, 4.4 Hz, 1H), 2.14 - 2.09 (m, 1H), 1.97 - 1.89 (m, 1H), 1.73 - 1.68 (m, 2H), 1.53 (ddt, *J* = 14.7, 10.9, 2.9 Hz, 2H), 1.17 - 1.04 (m, 2H), 0.95 - 0.85 (m, 7H), 0.79 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.4, 137.6, 131.1, 130.3, 100.5, 75.1, 47.2, 40.9, 34.3, 31.4, 26.6, 23.7, 22.1, 20.8, 16.6. **IR (KBr):** *v* (cm^{-1}) 2952, 1711, 1584, 1455, 1391, 1266, 1174, 1099, 1007, 960, 750. The spectroscopic properties of this compound are consistent with the data reported in the literature. [1]

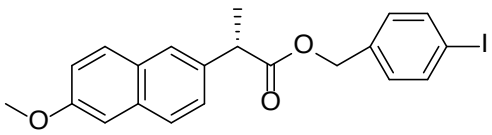


Following the general procedure and using 2-(3-benzoylphenyl)propanoic acid (3 mmol, 762.9 mg), (4-iodophenyl)methanol (3 mmol, 702.2 mg), the target compound

6-58 was obtained as a colorless oil (1.16 g, 82%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 7.1 Hz, 3H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.43 (dt, *J* = 13.2, 7.6 Hz, 3H), 6.95 (d, *J* = 8.1 Hz, 2H), 5.03 (s, 2H), 3.84 (q, *J* = 7.1 Hz, 1H), 1.54 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.3, 173.7, 140.6, 138.0, 137.6, 137.5, 135.5, 132.6, 131.6, 130.1, 129.8, 129.2, 129.1, 128.6, 128.4, 94.0, 65.9, 45.4, 18.4. **IR (KBr):** *v* (cm^{-1}) 2977, 1716, 1654, 1522, 1446, 1316, 1242, 1142, 1007, 970, 695. **HRMS** (ESI) *m*/*z*: Calculated for $C_{23}H_{19}INaO_3^+$ $[M+Na]^+$ 493.0271, found 493.0271.

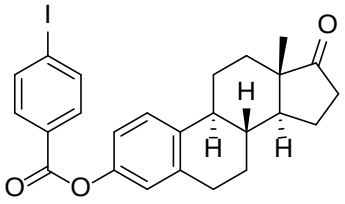


Following the general procedure and using 2-(4-isobutylphenyl)propanoic acid (3 mmol, 618.9 mg), (4-iodophenyl)methanol (3 mmol, 702.2 mg), the target compound **6-59** was obtained as a colorless oil (1.0 g, 80%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.57 - 7.51 (m, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 6.87 (d, *J* = 8.1 Hz, 2H), 4.98 (dd, *J* = 28.4 Hz, *J* = 2.8 Hz, 2H), 3.71 (q, *J* = 7.1 Hz, 1H), 2.43 (d, *J* = 7.2 Hz, 2H), 1.88 - 1.78 (m, 1H), 1.47 (d, *J* = 7.2 Hz, 3H), 0.88 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.3, 140.7, 137.6, 137.6, 135.9, 129.7, 129.5, 127.4, 93.8, 65.6, 45.2, 45.2, 30.3, 22.6, 18.5. **IR (KBr):** *v* (cm^{-1}) 2952, 1734, 1512, 1484, 1341, 1205, 1143, 1007, 970, 792. The spectroscopic properties of this compound are consistent with the data reported in the literature. [2]

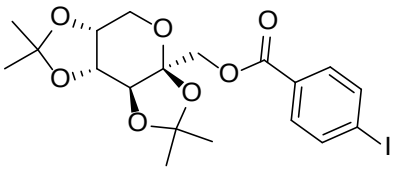


Following the general procedure and using (*S*)-2-(6-methoxynaphthalen-2-yl)propanoic acid (3 mmol, 690.8 mg), (4-iodophenyl)methanol (3 mmol, 702.2 mg), the target compound **6-60** was obtained as a colorless solid (1.07 g, 80%). **Mp:** 94-96 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.66 - 7.57 (m, 3H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.34 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.11 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.06 (d, *J* = 2.5 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 2H), 4.97 (s, 2H), 3.85 (q, *J* = 7.2 Hz, 1H), 3.82 (s, 3H), 1.55

(d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.3, 157.8, 137.6, 135.8, 135.5, 133.8, 129.9, 129.4, 129.0, 127.3, 126.3, 126.1, 119.2, 105.7, 93.9, 65.8, 55.4, 45.5, 18.6. **IR (KBr):** *v* (cm^{-1}) 2963, 1733, 1603, 1483, 1374, 1322, 1265, 1227, 1265, 1227, 1174, 1087, 1028, 1008, 964, 813. **HRMS** (ESI) *m*/*z*: Calculated for $C_{21}H_{19}INaO_3^+$ $[M+Na]^+$ 469.0271, found 469.0271.

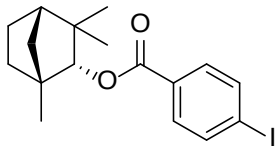


Following the general procedure and using 4-Iodobenzoic acid (3.0 mmol, 744.0 mg), Estrone (3 mmol, 811.2 mg), the target compound **6-61** was obtained as a colorless solid (1.4 g, 93%). **Mp:** 246-248 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.92 - 7.82 (m, 4H), 7.33 (d, *J* = 8.5 Hz, 1H), 6.97 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.93 (d, *J* = 2.6 Hz, 1H), 2.93 (dd, *J* = 8.0, 3.4 Hz, 2H), 2.51 (dd, *J* = 18.9, 8.6 Hz, 1H), 2.46 - 2.38 (m, 1H), 2.30 (td, *J* = 10.8, 4.0 Hz, 1H), 2.20 - 1.96 (m, 4H), 1.76 - 1.39 (m, 7H), 0.92 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 220.8, 165.0, 148.7, 138.2, 138.0, 137.7, 131.5, 129.1, 126.6, 121.6, 118.8, 101.6, 50.4, 48.0, 44.2, 38.0, 35.9, 31.6, 29.5, 26.4, 25.8, 21.6, 13.9. **IR (KBr):** *v* (cm^{-1}) 2930, 1722, 1584, 1492, 1451, 1391, 1259, 1209, 1175, 1148, 1067, 1005, 896, 749. **HRMS** (ESI) *m*/*z*: Calculated for $C_{25}H_{25}INaO_3^+$ $[M+Na]^+$ 523.0741, found 523.0741.

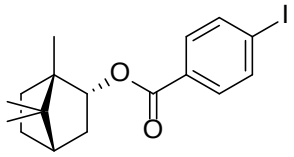


Following the general procedure and using 4-Iodobenzoic acid (3.0 mmol, 744.0 mg), Diacetonefructose (3 mmol, 780.9 mg), the target compound **6-63** was obtained as a colorless oil (1.15 g, 78%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.79 (s, 4H), 4.69 (d, *J* = 11.8 Hz, 1H), 4.64 (dd, *J* = 8.0, 2.6 Hz, 1H), 4.45 (d, *J* = 2.6 Hz, 1H), 4.32 (d, *J* = 11.8 Hz, 1H), 4.26 (d, *J* = 7.9 Hz, 1H), 3.94 (d, *J* = 12.9 Hz, 1H), 3.79 (d, *J* = 13.0 Hz, 1H), 1.54 (s, 3H), 1.46 (s, 3H), 1.36 (s, 3H), 1.34 (s, 3H). **^{13}C NMR** (101 MHz,

$CDCl_3$) δ 165.3, 137.7, 131.1, 129.4, 109.0, 108.7, 101.5, 101.0, 70.7, 70.5, 70.0, 65.5, 61.3, 26.5, 25.9, 25.5, 24.1. **IR (KBr):** *v* (cm^{-1}) 2988, 2936, 1720, 1585, 1453, 1373, 1250, 1205, 1163, 1101, 1068, 1006, 887, 750. **HRMS** (ESI) *m*/*z*: Calculated for $C_{19}H_{23}INaO_7^+$ $[M+Na]^+$ 513.0381, found 513.0381.

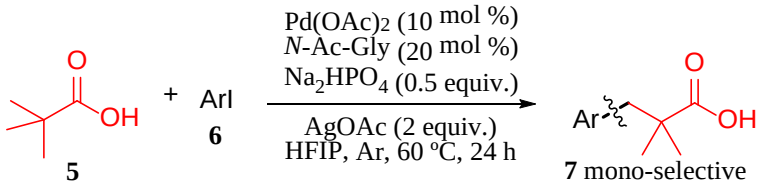


Following the general procedure and using 4-Iodobenzoic acid (3.0 mmol, 744.0 mg), (+)-Fenchol (3 mmol, 462.8 mg), the target compound **6-64** was obtained as a colorless solid (933.8 mg, 81%). **Mp:** 77-79 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.79 (q, *J* = 8.4 Hz, 4H), 4.61 (s, 1H), 1.93 - 1.86 (m, 1H), 1.81 - 1.73 (m, 2H), 1.66 (d, *J* = 10.2 Hz, 1H), 1.56 - 1.46 (m, 1H), 1.30 - 1.20 (m, 2H), 1.18 (s, 3H), 1.10 (s, 3H), 0.82 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.4, 137.8, 131.0, 130.2, 100.6, 87.0, 48.6, 48.4, 41.5, 39.9, 29.8, 26.9, 25.9, 20.3, 19.5. **IR (KBr):** *v* (cm^{-1}) 2950, 1711, 1582, 1459, 1389, 1264, 1172, 1113, 1100, 1031, 1002, 845, 749. **HRMS** (ESI) *m*/*z*: Calculated for $C_{17}H_{22}IO_2^+$ $[M+H]^+$ 385.0659, found 385.0658.



Following the general procedure and using 4-Iodobenzoic acid (3.0 mmol, 744 mg), L(-)-Borneol (3 mmol, 462.8 mg), the target compound **6-65** was obtained as a colorless solid (968.4 mg, 84%). **Mp:** 100-102 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.83 - 7.74 (m, 4H), 5.10 (ddd, *J* = 10.0, 3.5, 2.1 Hz, 1H), 2.52 - 2.42 (m, 1H), 2.08 (ddd, *J* = 13.3, 9.4, 4.4 Hz, 1H), 1.85 - 1.76 (m, 1H), 1.74 (t, *J* = 4.5 Hz, 1H), 1.45 - 1.37 (m, 1H), 1.34 - 1.27 (m, 1H), 1.10 (dd, *J* = 13.8, 3.5 Hz, 1H), 0.96 (s, 3H), 0.91 (d, *J* = 4.0 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.3, 137.7, 131.0, 130.4, 100.5, 80.9, 49.1, 47.9, 45.0, 36.9, 28.1, 27.4, 19.8, 18.9, 13.7. **IR (KBr):** *v* (cm^{-1}) 2951, 1711, 1583, 1450, 1389, 1265, 1173, 1113, 1100, 1002, 845, 741. **HRMS** (ESI) *m*/*z*: Calculated for $C_{17}H_{21}INaO_2^+$ $[M+Na]^+$ 407.0470, found 407.0478.

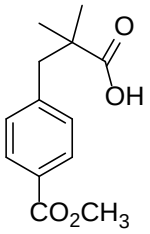
4. General Procedure for Mono-selective *β*-C(sp^3)-H Arylation of Pivalic Acid



General Procedure: In a glovebox filled with argon, a clean, oven-dried screw cap reaction tube with previously placed magnetic stir-bar was charged with pivalic acid (184.0 mg, 1.8 mmol, 6 equiv.), aryl iodide (0.3 mmol), $Pd(OAc)_2$ (6.8 mg, 0.03 mmol, 10 mol%), *N*-Ac-Gly-OH (7.1 mg, 0.06 mmol, 20 mol%), AgOAc (101.0 mg, 0.6 mmol, 2 equiv.) and Na_2HPO_4 (21.3 mg, 0.15 mmol, 0.5 equiv.), followed by addition of HFIP (1.5 mL). The vessel was sealed and moved out of the glovebox, and the reaction was stirred at room temperature for 10 minutes. Then the reaction vessel was placed in a pre-heated (60 °C) oil bath and stirring was continued at this temperature for 24 h. The reaction mixture was allowed to cool to room temperature. The resulting mixture was filtered through a celite bed using ethyl acetate as the eluent. After concentration under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum-ether / ethyl acetate / formic acid = 24:1:0.005 to 8:1:0.005) to give the desired arylated product.

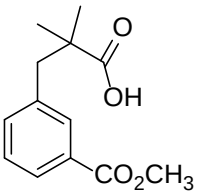
5. Characterization of Compounds

3-(4-(methoxycarbonyl)phenyl)-2,2-dimethylpropanoic acid (7-1)



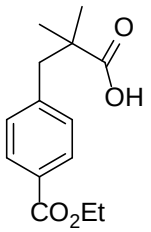
Following the general procedure and using methyl 4-iodobenzoate (78.6 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (59.5 mg, 84%). **Mp:** 95-97 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 3.91 (s, 3H), 2.95 (s, 2H), 1.22 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.8, 167.1, 143.0, 130.3, 129.4, 128.5, 52.1, 45.7, 43.5, 24.8. **IR (KBr):** *v* (cm^{-1}) 2968, 2932, 1724, 1682, 1441, 1298, 1130, 868, 712, 536. **HRMS** (ESI) *m*/*z*: Calculated for $C_{13}H_{15}O_4^-$ $[M-H]^-$ 235.0976, found 235.0976.

3-(3-(methoxycarbonyl)phenyl)-2,2-dimethylpropanoic acid (7-2)



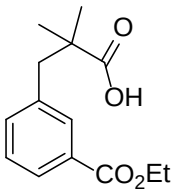
Following the general procedure and using methyl 3-iodobenzoate (78.6 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (53.9 mg, 76%). **Mp:** 91-93 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.92 (d, *J* = 7.1 Hz, 1H), 7.86 (s, 1H), 7.40 - 7.32 (m, 2H), 3.90 (s, 3H), 2.95 (s, 2H), 1.21 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.6, 167.2, 137.9, 134.8, 131.4, 129.9, 128.2, 127.9, 52.2, 45.5, 43.4, 24.6. **IR (KBr):** *v* (cm^{-1}) 2970, 2933, 1722, 1695, 1470, 1288, 1106, 954, 750, 558. **HRMS** (ESI) *m*/*z*: Calculated for $C_{13}H_{15}O_4^-$ $[M-H]^-$ 235.0976, found 235.0976.

3-(4-(ethoxycarbonyl)phenyl)-2,2-dimethylpropanoic acid (7-3)



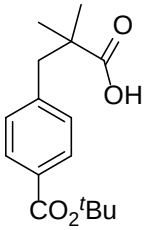
Following the general procedure and using ethyl 4-iodobenzoate (50.5 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (60.8 mg, 81%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 7.8 Hz, 2H), 7.24 (d, *J* = 7.9 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.95 (s, 2H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.21 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.5, 166.7, 142.9, 130.3, 129.3, 128.9, 60.9, 45.7, 43.4, 24.8, 14.4. The spectroscopic properties of this compound are consistent with the data reported in the literature. [3]

3-(3-(ethoxycarbonyl)phenyl)-2,2-dimethylpropanoic acid (7-4)



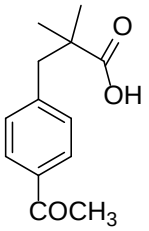
Following the general procedure and using ethyl 3-iodobenzoate (82.8 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (54.1 mg, 72%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.92 (d, *J* = 7.0 Hz, 1H), 7.86 (s, 1H), 7.39 - 7.32 (m, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.95 (s, 2H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.21 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.8, 166.7, 137.9, 134.7, 131.4, 130.3, 128.1, 127.9, 61.0, 45.4, 43.4, 24.6, 14.3. The spectroscopic properties of this compound are consistent with the data reported in the literature. [4]

3-(4-(tert-butoxycarbonyl)phenyl)-2,2-dimethylpropanoic acid (7-5)



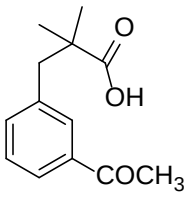
Following the general procedure and using tert-butyl 4-iodobenzoate (62.2 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (25.1 mg, 30%). **Mp:** 89-91 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 2.94 (s, 2H), 1.58 (s, 9H), 1.21 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.8, 165.8, 142.4, 130.4, 130.1, 129.2, 80.9, 45.7, 43.4, 28.2, 24.7. **IR (KBr):** *v* (cm^{-1}) 2983, 2925, 1740, 1675, 1472, 1324, 1123, 1019, 842, 752, 577. **HRMS** (ESI) *m*/*z*: Calculated for $C_{16}H_{21}O_4^-$ $[M-H]^-$ 277.1445, found 277.1445.

3-(4-acetylphenyl)-2,2-dimethylpropanoic acid (7-6)



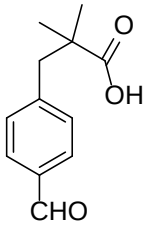
Following the general procedure and using 1-(4-iodophenyl)ethan-1-one (73.8 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (55.5 mg, 84%) **Mp:** 114-116 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.88 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 2.96 (s, 2H), 2.60 (s, 3H), 1.23 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.1, 183.6, 143.4, 135.6, 130.5, 128.2, 45.7, 43.5, 26.6, 24.8. **IR (KBr):** *v* (cm^{-1}) 2964, 2932, 1722, 1680, 1567, 1364, 1278, 1133, 916, 842, 632. **HRMS** (ESI) *m*/*z*: Calculated for $C_{13}H_{15}O_3^-$ $[M-H]^-$ 219.1027, found 219.1027.

3-(3-acetylphenyl)-2,2-dimethylpropanoic acid (7-7)



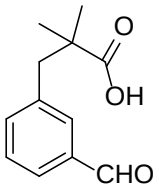
Following the general procedure and using 1-(3-iodophenyl)ethan-1-one (41.8 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (56.1 mg, 76%) **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 6.1 Hz, 1H), 7.78 (s, 1H), 7.41 - 7.34 (m, 2H), 2.96 (s, 2H), 2.58 (s, 3H), 1.22 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.5, 183.8, 138.1, 136.9, 135.0, 130.0, 128.4, 126.8, 45.6, 43.4, 26.6, 24.7. The spectroscopic properties of this compound are consistent with the data reported in the literature. [3]

3-(4-formylphenyl)-2,2-dimethylpropanoic acid (7-8)



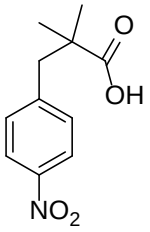
Following the general procedure and using 4-iodobenzaldehyde (69.7 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (55.1 mg, 86%) **Mp:** 82-84 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.99 (s, 1H), 7.81 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 2.98 (s, 2H), 1.24 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 183.6, 145.1, 135.0, 130.9, 129.6, 45.9, 43.5, 24.8. **IR (KBr):** *v* (cm^{-1}) 2973, 2933, 1699, 1574, 1470, 1296, 1170, 1131, 951, 835, 711. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{13}O_3^-$ $[M-H]^-$ 205.0870, found 205.0870.

3-(3-formylphenyl)-2,2-dimethylpropanoic acid (7-9)



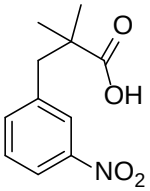
Following the general procedure and using 3-iodobenzaldehyde (69.7 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (49.5 mg, 80%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.99 (s, 1H), 7.79 - 7.74 (m, 1H), 7.69 (s, 1H), 7.48 - 7.42 (m, 2H), 2.98 (s, 2H), 1.23 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.6, 183.6, 138.7, 136.4, 136.3, 131.3, 128.8, 128.4, 45.4, 43.4, 24.7. **IR (KBr):** *v* (cm^{-1}) 2976, 2927, 1699, 1585, 1474, 1390, 1247, 1146, 807, 696. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{13}O_3^-$ $[M-H]^-$ 205.0870, found 205.0870.

2,2-dimethyl-3-(4-nitrophenyl)propanoic acid (7-10)



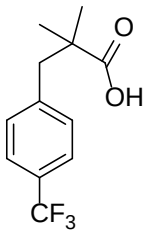
Following the general procedure and using 1-iodo-4-nitrobenzene (74.7 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (54.9 mg, 82%). **Mp:** 122-124 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 8.6 Hz, 2H), 7.35 (d, *J* = 8.6 Hz, 2H), 3.01 (s, 2H), 1.25 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.7, 146.9, 145.4, 131.1, 123.3, 45.4, 43.5, 24.8. The spectroscopic properties of this compound are consistent with the data reported in the literature. [5]

2,2-dimethyl-3-(3-nitrophenyl)propanoic acid (7-11)



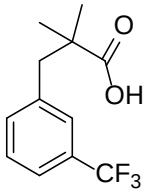
Following the general procedure and using 1-iodo-3-nitrobenzene (38.4 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (53.6 mg, 80%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 9.0 Hz, 1H), 8.05 (s, 1H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 3.01 (s, 2H), 1.25 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.0, 148.1, 139.6, 136.4, 129.0, 124.9, 121.9, 45.3, 43.5, 24.8. The spectroscopic properties of this compound are consistent with the data reported in the literature. [6]

2,2-dimethyl-3-(4-(trifluoromethyl)phenyl)propanoic acid (7-12)



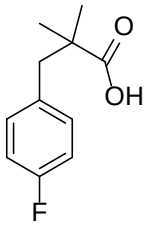
Following the general procedure and using 1-iodo-4-(trifluoromethyl)benzene (44.1 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (61.3 mg, 83%). **Mp:** 66-68 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 2.95 (s, 2H), 1.23 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.9, 141.7, 130.6, 129.0 (q, *J* = 32.4 Hz), 125.0 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 271.8 Hz), 45.5, 43.4, 24.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.43. The spectroscopic properties of this compound are consistent with the data reported in the literature. [4]

2,2-dimethyl-3-(3-(trifluoromethyl)phenyl)propanoic acid (7-13)



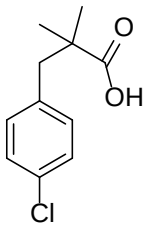
Following the general procedure and using 1-iodo-3-(trifluoromethyl)benzene (43.3 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (59.8 mg, 81%). **Mp:** 50-52 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.50 (d, *J* = 7.5 Hz, 1H), 7.43 (s, 1H), 7.41 - 7.33 (m, 2H), 2.94 (s, 2H), 1.22 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.1, 138.5, 133.6, 130.4 (q, *J* = 32.1 Hz), 128.5, 126.9 (q, *J* = 3.8 Hz), 124.2 (q, *J* = 272.1 Hz), 123.5 (q, *J* = 3.9 Hz), 45.6, 43.5, 24.6. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.63. **IR (KBr):** *v* (cm^{-1}) 2977, 2930, 1699, 1467, 1339, 1204, 1154, 1118, 1079, 814. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{12}F_3O_2^-$ $[M-H]^-$ 245.0795, found 245.0795.

3-(4-fluorophenyl)-2,2-dimethylpropanoic acid (7-14)



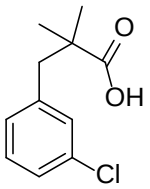
Following the general procedure and using 1-fluoro-4-iodobenzene (34.6 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (45.3 mg, 77%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.14 - 7.10 (m, 2H), 6.98 - 6.93 (m, 2H), 2.86 (s, 2H), 1.20 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.2, 161.8 (d, *J* = 244.6 Hz), 133.2 (d, *J* = 3.3 Hz), 131.6 (d, *J* = 7.9 Hz), 114.9 (d, *J* = 21.0 Hz), 45.0, 43.5, 24.6. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -116.53. The spectroscopic properties of this compound are consistent with the data reported in the literature. [6]

3-(4-chlorophenyl)-2,2-dimethylpropanoic acid (7-15)



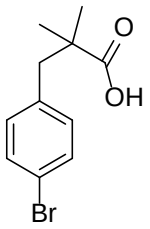
Following the general procedure and using 1-chloro-4-iodobenzene (71.6 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (47.9 mg, 75%). **Mp:** 77-79 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.24 (d, *J* = 8.5 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 2.85 (s, 2H), 1.20 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.0, 136.0, 132.6, 131.6, 128.2, 45.2, 43.4, 24.7. **IR (KBr):** *v* (cm^{-1}) 2970, 2932, 1695, 1494, 1294, 1158, 1015, 846, 508. **HRMS** (ESI) *m*/*z*: Calculated for $C_{11}H_{12}ClO_2^-$ $[M-H]^-$ 211.0531, found 211.0531.

3-(3-chlorophenyl)-2,2-dimethylpropanoic acid (7-16)



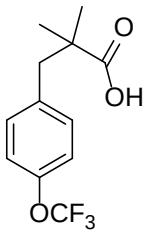
Following the general procedure and using 1-chloro-3-iodobenzene (37.2 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (46.6 mg, 73%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.20 (dd, *J* = 4.9, 2.2 Hz, 2H), 7.16 (s, 1H), 7.07 - 7.03 (m, 1H), 2.86 (s, 2H), 1.21 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.9, 139.6, 133.7, 130.3, 129.3, 128.4, 126.8, 45.4, 43.4, 24.7. **IR (KBr):** *v* (cm^{-1}) 2975, 2928, 1699, 1572, 1474, 1280, 1216, 1091, 792, 684. **HRMS** (ESI) *m*/*z*: Calculated for $C_{11}H_{12}ClO_2^-$ $[M-H]^-$ 211.0531, found 211.0532.

3-(4-bromophenyl)-2,2-dimethylpropanoic acid (7-17)



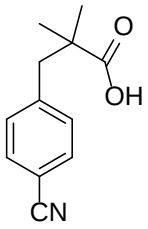
Following the general procedure and using 1-bromo-4-iodobenzene (84.9 mg, 0.3 mmol) as the arylating, agent the target compound was obtained as a colorless solid (55.5 mg, 72%). **Mp:** 117-119 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 2.84 (s, 2H), 1.20 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.0, 136.5, 132.0, 131.2, 120.7, 45.2, 43.4, 24.7. **IR (KBr):** *v* (cm^{-1}) 2970, 2947, 1692, 1489, 1290, 1058, 1011, 835, 550. The spectroscopic properties of this compound are consistent with the data reported in the literature. [6]

2,2-dimethyl-3-(4-(trifluoromethoxy)phenyl)propanoic acid (7-18)



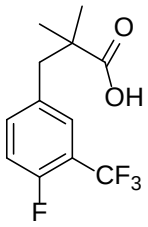
Following the general procedure and using 1-iodo-4-(trifluoromethoxy)benzene (47 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (63.7 mg, 81%). **Mp:** 41-43 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.19 (d, *J* = 8.7 Hz, 2H), 7.11 (d, *J* = 7.6 Hz, 2H), 2.89 (s, 2H), 1.21 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.2, 148.1 (q, *J* = 1.8 Hz), 136.3, 131.5, 120.5 (q, *J* = 257.8 Hz), 120.5, 45.0, 43.4, 24.7. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -57.91. **IR (KBr):** *v* (cm^{-1}) 2988, 2941, 1704, 1510, 1473, 1297, 1255, 1165, 1020, 943, 855, 547. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{12}F_3O_3^-$ $[M-H]^-$ 261.0744, found 261.0744.

3-(4-cyanophenyl)-2,2-dimethylpropanoic acid (7-19)



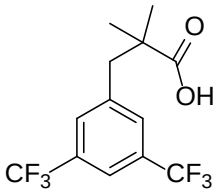
Following the general procedure and using 4-iodobenzonitrile (68.8 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (46.9 mg, 77%). **Mp:** 85-87 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 2.95 (s, 2H), 1.22 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.5, 143.2, 131.9, 131.0, 118.9, 110.6, 45.7, 43.4, 24.8. **IR (KBr):** *v* (cm^{-1}) 2982, 2924, 2222, 1694, 1472, 1306, 1217, 1132, 852, 591. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{12}NO_2^-$ $[M-H]^-$ 202.0874, found 202.0874.

3-(4-fluoro-3-(trifluoromethyl)phenyl)-2,2-dimethylpropanoic acid(7-20)



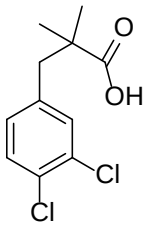
Following the general procedure and using 1-fluoro-4-iodo-2-(trifluoromethyl)benzene (44.8 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (63.4 mg, 80%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.40 (dd, *J* = 6.9, 2.3 Hz, 1H), 7.36 - 7.32 (m, 1H), 7.10 (t, *J* = 9.3 Hz, 1H), 2.90 (s, 2H), 1.22 (s, 6H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 183.6, 158.7 (dq, *J* = 256.1 Hz, *J* = 2.2 Hz), 135.5 (d, *J* = 8.3 Hz), 133.8 (d, *J* = 4.1 Hz), 128.5 (dq, *J* = 1.3 Hz, *J* = 4.7 Hz), 122.6 (q, *J* = 272.4 Hz), 117.9 (dq, *J* = 12.4 Hz, *J* = 32.7 Hz), 116.6 (d, *J* = 20.5 Hz), 44.8, 43.5, 24.6. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -61.38 (d, *J* = 12.7 Hz), -117.74 - -117.90 (m). **IR (KBr):** *v* (cm^{-1}) 2980, 2935, 1700, 1507, 1435, 1321, 1244, 1134, 1058, 835, 667. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{11}F_4O_2^-$ $[M-H]^-$ 263.0701, found 263.0701.

3-(3,5-bis(trifluoromethyl)phenyl)-2,2-dimethylpropanoic acid (7-21)



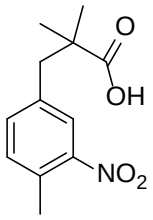
Following the general procedure and using 1-iodo-3,5-bis(trifluoromethyl)benzene (53.2 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (75.4 mg, 80%). **Mp:** 52-54 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.76 (s, 1H), 7.62 (s, 2H), 3.01 (s, 2H), 1.24 (s, 6H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 183.0, 140.0, 131.3 (q, *J* = 33.0 Hz), 130.3, 123.3 (q, *J* = 272.6 Hz), 120.9 - 120.6 (m), 45.3, 43.5, 24.6. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.96. The spectroscopic properties of this compound are consistent with the data reported in the literature. [4]

3-(3,4-dichlorophenyl)-2,2-dimethylpropanoic acid (7-22)



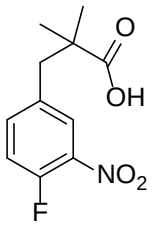
Following the general procedure and using 1,2-dichloro-4-iodobenzene (41.2 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (54.9 mg, 74%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.34 (d, *J* = 8.1 Hz, 1H), 7.01 (d, *J* = 6.2 Hz, 1H), 2.84 (s, 2H), 1.21 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.6, 137.8, 132.0, 130.8, 130.0, 129.6, 44.9, 43.3, 24.8. **IR (KBr):** *v* (cm^{-1}) 2975, 2929, 1699, 1472, 1398, 1278, 1132, 1032, 824, 667. **HRMS** (ESI) *m*/*z*: Calculated for Calculated for $C_{11}H_{11}Cl_2O_2^-$ $[M-H]^-$ 245.0142, found 245.0142.

2,2-dimethyl-3-(4-methyl-3-nitrophenyl)propanoic acid (7-23)



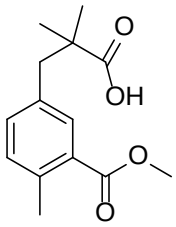
Following the general procedure and using 4-iodo-1-methyl-2-nitrobenzene (78.9 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (53.4 mg, 75%). **Mp:** 81-83 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.79 (s, 1H), 7.31 (d, *J* = 7.9 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 2.93 (s, 2H), 2.57 (s, 3H), 1.23 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.3, 148.9, 136.9, 134.9, 132.5, 131.9, 126.0, 44.9, 43.4, 24.7, 20.1. **IR (KBr):** *v* (cm^{-1}) 2979, 2930, 1693, 1527, 1343, 1200, 1131, 953, 842, 750. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{14}NO_4^-$ $[M-H]^-$ 236.0928, found 236.0928.

3-(4-fluoro-3-nitrophenyl)-2,2-dimethylpropanoic acid (7-24)



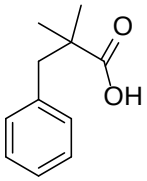
Following the general procedure and using 1-fluoro-4-iodo-2-nitrobenzene (80.1 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (55.0 mg, 76%). **Mp:** 66-68 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.88 (dd, *J* = 7.1, 2.3 Hz, 1H), 7.47-7.43 (m, 1H), 7.22 (dd, *J* = 10.7, 8.5 Hz, 1H), 2.94 (s, 2H), 1.25 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.2, 154.5 (d, *J* = 264.1 Hz), 137.3 (d, *J* = 8.4 Hz), 136.9 (d, *J* = 7.0 Hz), 134.8 (d, *J* = 4.5 Hz), 127.3 (d, *J* = 2.9 Hz), 118.1 (d, *J* = 20.7 Hz), 44.6, 43.5, 24.7. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -120.56. **IR (KBr):** *v* (cm^{-1}) 2991, 2930, 1703, 1534, 1353, 1245, 1141, 840, 547. **HRMS** (ESI) *m*/*z*: Calculated for $C_{11}H_{11}FNO_4^-$ $[M-H]^-$ 240.0678, found 240.0678.

3-(3-(methoxycarbonyl)-4-methylphenyl)-2,2-dimethylpropanoic acid (7-25)



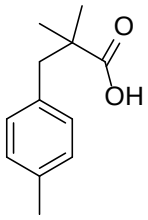
Following the general procedure and using methyl 5-iodo-2-methylbenzoate (82.8 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (55.6 mg, 74%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 11.22 (s, 1H), 7.72 (s, 1H), 7.21 (d, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 3.87 (s, 3H), 2.89 (s, 2H), 2.56 (s, 3H), 1.20 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.0, 168.2, 138.4, 135.0, 133.8, 132.4, 131.5, 129.2, 51.8, 45.1, 43.4, 24.6, 21.4. **IR (KBr):** *v* (cm^{-1}) 2970, 2926, 1722, 1694, 1435, 1296, 1250, 1197, 1082, 960, 785, 556. **HRMS**(ESI) *m*/*z*: Calculated for $C_{14}H_{17}O_4^-$ $[M-H]^-$ 249.1132, found 249.1132.

2,2-dimethyl-3-phenylpropanoic acid (7-26)



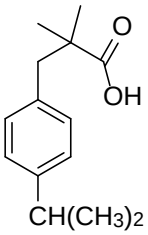
Following the general procedure and using iodobenzene (33.6 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (35.3 mg, 66%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.28 - 7.16 (m, 5H), 2.89 (s, 2H), 1.20 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.4, 137.6, 130.3, 128.1, 126.6, 45.9, 43.5, 24.7. The spectroscopic properties of this compound are consistent with the data reported in the literature. [7]

2,2-dimethyl-3-(p-tolyl)propanoic acid (7-27)



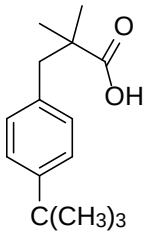
Following the general procedure and using 1-iodo-4-methylbenzene (65.4mg, 0.3 mmol) as the arylating agent the target compound was obtained as a colorless oil (36.9 mg, 64%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.09 - 7.04 (m, 4H), 2.85 (s, 2H), 2.32 (s, 3H), 1.19 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.3, 136.1, 134.5, 130.1, 128.8, 45.5, 43.5, 24.7, 21.1. The spectroscopic properties of this compound are consistent with the data reported in the literature. [6]

3-(4-isopropylphenyl)-2,2-dimethylpropanoic acid (7-28)



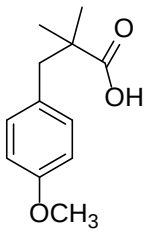
Following the general procedure and using 1-iodo-4-isopropylbenzene (48.4 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (44.9 mg, 68%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.14 - 7.08 (m, 4H), 2.93 - 2.87 (m, 1H), 2.86 (s, 2H), 1.24 (d, *J* = 6.9 Hz, 6H), 1.20 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.0, 147.0, 134.8, 130.2, 126.1, 45.4, 43.4, 33.7, 24.7, 24.0. **IR (KBr):** *v* (cm^{-1}) 2961, 2927, 1699, 1473, 1282, 1163, 1054, 944, 844, 592. **HRMS** (ESI) *m*/*z*: Calculated for $C_{14}H_{19}O_2^-$ $[M-H]^-$ 219.1391, found 219.1391.

3-(4-(tert-butyl)phenyl)-2,2-dimethylpropanoic acid (7-29)



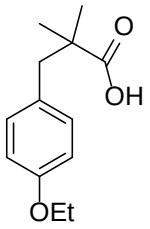
Following the general procedure and using 1-(tert-butyl)-4-iodobenzene (53.2 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (42.2 mg, 60%). **Mp:** 84-86°C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.21 (d, *J* = 8.3 Hz, 2H), 7.03 (d, *J* = 8.3 Hz, 2H), 2.79 (s, 2H), 1.23 (s, 9H), 1.13 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.2, 149.3, 134.5, 130.0, 124.9, 45.3, 43.4, 34.4, 31.4, 24.7. **IR (KBr):** *v* (cm^{-1}) 2961, 2926, 1694, 1511, 1475, 1364, 1220, 1129, 1020, 851, 592. **HRMS** (ESI) *m*/*z*: Calculated for $C_{15}H_{21}O_2^-$ $[M-H]^-$ 233.1547, found 233.1547.

3-(4-methoxyphenyl)-2,2-dimethylpropanoic acid (7-30)



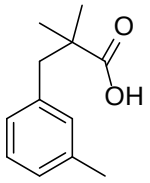
Following the general procedure and using 1-iodo-4-methoxybenzene (70.2 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (39.4 mg, 63%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.08 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 2.83 (s, 2H), 1.19 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.3, 158.3, 131.2, 129.6, 113.5, 55.2, 45.1, 43.5, 24.6. **IR (KBr):** *v* (cm^{-1}) 2972, 2934, 1699, 1513, 1473, 1249, 1179, 1037, 821, 547. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{15}O_3^-$ $[M-H]^-$ 207.1027, found 207.1027.

3-(4-ethoxyphenyl)-2,2-dimethylpropanoic acid (7-31)



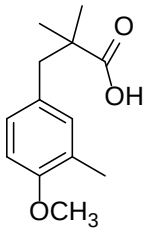
Following the general procedure and using 1-ethoxy-4-iodobenzene (45.7 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (38.7 mg, 58%). **Mp:** 53-55 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.07 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 4.00 (q, *J* = 7.0 Hz, 2H), 2.82 (s, 2H), 1.40 (t, *J* = 7.0 Hz, 3H), 1.18 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.3, 157.7, 131.2, 129.5, 114.0, 63.3, 45.1, 43.5, 24.6, 14.9. **IR (KBr):** *v* (cm^{-1}) 2970, 2928, 1704, 1517, 1474, 1261, 1217, 1131, 1047, 850, 590. **HRMS** (ESI) *m*/*z*: Calculated for $C_{13}H_{17}O_3^-$ $[M-H]^-$ 221.1183, found 221.1182.

2,2-dimethyl-3-(m-tolyl)propanoic acid (7-32)



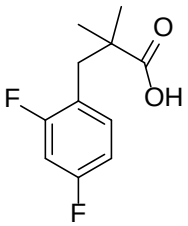
Following the general procedure and using 1-iodo-3-methylbenzene (38.6 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (34.1 mg, 59%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.15 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 7.6 Hz, 1H), 6.99 - 6.95 (m, 2H), 2.85 (s, 2H), 2.31 (s, 3H), 1.20 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.0, 137.5, 137.4, 131.1, 127.9, 127.3, 127.3, 45.8, 43.4, 24.7, 21.4. **IR (KBr):** *v* (cm^{-1}) 2973, 2925, 1699, 1473, 1286, 1217, 945, 794, 701. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{15}O_2^-$ $[M-H]^-$ 191.1078, found 191.1078.

3-(4-methoxy-3-methylphenyl)-2,2-dimethylpropanoic acid (7-33)



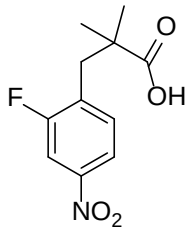
Following the general procedure and using 4-iodo-1-methoxy-2-methylbenzene (74.5 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (36.7 mg, 55%). **Mp:** 69-71 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.98 - 6.91 (m, 2H), 6.72 (d, *J* = 8.2 Hz, 1H), 3.80 (s, 3H), 2.80 (s, 2H), 2.18 (s, 3H), 1.19 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.2, 156.5, 132.6, 129.2, 128.4, 126.0, 109.5, 55.3, 45.1, 43.5, 24.6, 16.2. **IR (KBr):** *v* (cm^{-1}) 2976, 2937, 1699, 1505, 1456, 1303, 1256, 1137, 1029, 823, 754. **HRMS** (ESI) *m*/*z*: Calculated for $C_{13}H_{17}O_3^-$ $[M-H]^-$ 221.1183, found 221.1183.

3-(2,4-difluorophenyl)-2,2-dimethylpropanoic acid (7-34)



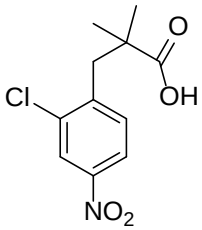
Following the general procedure and using 2,4-difluoro-1-iodobenzene (35.9 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (50.1 mg, 78%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.19 - 7.13 (m, 1H), 6.82 - 6.76 (m, 2H), 2.92 (s, 2H), 1.21 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.0, 163.0 (dd, *J* = 40.8, 11.9 Hz), 160.4 (dd, *J* = 41.4, 11.9 Hz), 132.9 (dd, *J* = 9.4, 6.1 Hz), 120.5 (dd, *J* = 16.1, 3.7 Hz), 110.9 (dd, *J* = 20.9, 3.7 Hz), 103.6 (dd, *J* = 27.1, 25.0 Hz), 43.5, 37.7, 24.4. **IR (KBr):** *v* (cm^{-1}) 2979, 2937, 1700, 1505, 1426, 1277, 1131, 967, 850, 614. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.06 (d, *J* = 7.2 Hz), -112.27 (d, *J* = 7.3 Hz). **HRMS** (ESI) *m*/*z*: Calculated for $C_{11}H_{11}F_2O_2^-$ $[M-H]^-$ 213.0733, found 213.0733.

3-(2-fluoro-4-nitrophenyl)-2,2-dimethylpropanoic acid (7-35)



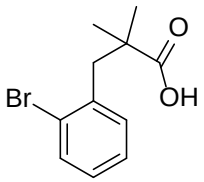
Following the general procedure and using 2-fluoro-1-iodo-4-nitrobenzene (80.1 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (55.0 mg, 76%). **Mp:** 113-115 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.98 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.92 (dd, *J* = 9.4, 2.3 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 3.06 (s, 2H), 1.26 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.4, 160.9 (d, *J* = 250.3 Hz), 147.7 (d, *J* = 9.0 Hz), 132.9 (d, *J* = 4.9 Hz), 132.8 (d, *J* = 16.2 Hz), 118.9 (d, *J* = 3.6 Hz), 111.2 (d, *J* = 28.5 Hz), 43.6, 38.1, 24.6. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -110.66. **IR (KBr):** *v* (cm^{-1}) 2988, 2948, 1699, 1527, 1355, 1291, 1230, 1159, 877, 742. **HRMS** (ESI) *m*/*z*: Calculated for $C_{11}H_{11}FNO_4^-$ $[M-H]^-$ 240.0678, found 240.0678.

3-(2-chloro-4-nitrophenyl)-2,2-dimethylpropanoic acid (7-36)



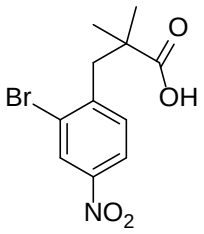
Following the general procedure and using 2-chloro-1-iodo-4-nitrobenzene (85.1 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (48.7 mg, 63%). **Mp:** 100-102 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.27 (d, *J* = 2.3 Hz, 1H), 8.06 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 1H), 3.22 (s, 2H), 1.29 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.2, 147.1, 143.4, 136.2, 132.3, 124.8, 121.4, 44.1, 41.5, 24.8. **IR (KBr):** *v* (cm^{-1}) 2982, 2929, 1699, 1512, 1349, 1219, 1130, 1047, 897, 732. **HRMS** (ESI) *m*/*z*: Calculated for $C_{11}H_{11}ClNO_4^-$ $[M-H]^-$ 256.0382, found 256.0385.

3-(2-bromophenyl)-2,2-dimethylpropanoic acid (7-37)



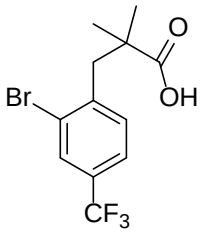
Following the general procedure and using 1-bromo-2-iodobenzene (38.6 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (52.5 mg, 68%). **Mp:** 85-87 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 7.7 Hz, 1H), 7.28 - 7.20 (m, 2H), 7.11 - 7.05 (m, 1H), 3.17 (s, 2H), 1.27 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.4, 137.5, 133.1, 131.6, 128.2, 127.2, 126.2, 44.1, 43.8, 24.7. The spectroscopic properties of this compound are consistent with the data reported in the literature. [6]

3-(2-bromo-4-nitrophenyl)-2,2-dimethylpropanoic acid (7-38)



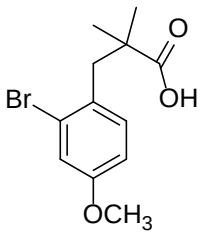
Following the general procedure and using 2-fluoro-1-iodo-4-nitrobenzene (98.4 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (54.1 mg, 60%). **Mp:** 109-111 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.45 (d, *J* = 2.4 Hz, 1H), 8.10 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.46 (d, *J* = 8.6 Hz, 1H), 3.26 (s, 2H), 1.30 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.3, 146.9, 145.2, 131.9, 128.1, 126.2, 122.0, 44.1, 43.7, 24.8. **IR (KBr):** *v* (cm^{-1}) 2983, 2930, 1698, 1517, 1345, 1219, 1121, 1038, 740. **HRMS** (ESI) *m*/*z*: Calculated for $C_{11}H_{11}BrNO_4^-$ $[M-H]^-$ 299.9877, found 299.9878.

3-(2-bromo-4-(trifluoromethyl)phenyl)-2,2-dimethylpropanoic acid (7-39)



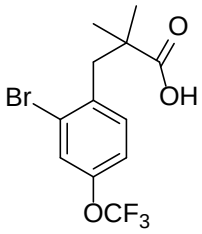
Following the general procedure and using 2-bromo-1-iodo-4-(trifluoromethyl)benzene (105.3 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (63.4 mg, 65%). **Mp:** 101-103 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.84 (s, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 3.22 (s, 2H), 1.29 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.0, 141.8, 131.8, 130.5 (q, *J* = 33.1 Hz), 130.1 (q, *J* = 3.9 Hz), δ 126.2, 123.1 (q, *J* = 273.6 Hz), 124.0 (q, *J* = 3.7 Hz), 44.1, 43.6, 24.7. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.68. **IR (KBr):** *v* (cm^{-1}) 2981, 2927, 1688, 1475, 1320, 1175, 1131, 1078, 835, 683. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{11}BrF_3O_2^-$ $[M-H]^-$ 322.9900, found 322.9900.

3-(2-bromo-4-methoxyphenyl)-2,2-dimethylpropanoic acid (7-40)



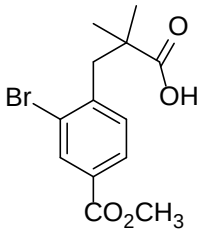
Following the general procedure and using 2-bromo-1-iodo-4-methoxybenzene (93.9 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (52.6 mg, 61%). **Mp:** 58-60 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.16 (d, *J* = 8.6 Hz, 1H), 7.11 (d, *J* = 2.6 Hz, 1H), 6.79 (dd, *J* = 8.6, 2.7 Hz, 1H), 3.78 (s, 3H), 3.09 (s, 2H), 1.25 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.9, 158.6, 131.9, 129.4, 126.2, 118.0, 113.5, 55.5, 44.1, 43.1, 24.6. **IR (KBr):** *v* (cm^{-1}) 2965, 1689, 1599, 1489, 1286, 1235, 1162, 1153, 1107, 1028, 932. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{14}BrO_3^-$ $[M-H]^-$ 285.0132, found 285.0132.

3-(2-bromo-4-(trifluoromethoxy)phenyl)-2,2-dimethylpropanoic acid (7-41)



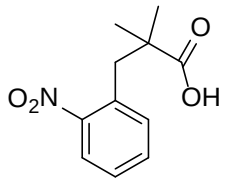
Following the general procedure and using 2-bromo-1-iodo-4-(trifluoromethoxy)benzene (110.1 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (74.7 mg, 73%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.46 (d, *J* = 2.6 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 1H), 7.11 (dd, *J* = 8.6, 2.5 Hz, 1H), 3.16 (s, 2H), 1.27 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.3, 147.8 (q, *J* = 2.0 Hz), 136.4, 132.1, 126.1, 125.5, 120.4 (q, *J* = 258.1 Hz), 119.6, 44.0, 43.1, 24.7. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -57.99. **IR (KBr):** *v* (cm^{-1}) 2981, 2936, 1700, 1487, 1259, 1218, 1169, 1040, 941, 679. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{11}BrF_3O_3^-$ [M-H]$^-$ 338.9849, found 338.9850.

3-(2-bromo-4-(methoxycarbonyl)phenyl)-2,2-dimethylpropanoic acid (7-42)



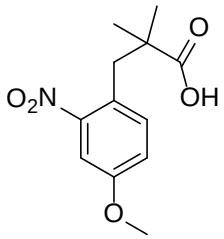
Following the general procedure and using methyl 3-bromo-4-iodobenzoate (102.3 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (60.5 mg, 64%). **Mp:** 86-88 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.24 (d, *J* = 1.7 Hz, 1H), 7.89 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 3.92 (s, 3H), 3.22 (s, 2H), 1.28 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.9, 165.7, 142.8, 134.2, 131.4, 130.1, 128.1, 126.1, 52.4, 44.1, 43.8, 24.8. **IR (KBr):** *v* (cm^{-1}) 2984, 2929, 1717, 1699, 1435, 1293, 1266, 1112, 1042, 970, 752. **HRMS** (ESI) *m*/*z*: Calculated for $C_{13}H_{14}BrO_4^-$ [M-H]$^-$ 313.0081, found 313.0081.

2,2-dimethyl-3-(2-nitrophenyl)propanoic acid (7-43)



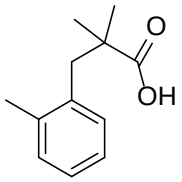
Following the general procedure and using 1-iodo-2-nitrobenzene (38.9 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (23.5 mg, 35%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 8.1 Hz, 1H), 7.51 (td, *J* = 7.6, 1.4 Hz, 1H), 7.41 - 7.36 (m, 2H), 3.37 (s, 2H), 1.19 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.3, 150.9, 133.1, 132.3, 132.1, 127.8, 124.7, 43.8, 40.3, 24.7. **IR (KBr):** *v* (cm^{-1}) 2977, 2928, 1699, 1527, 1475, 1354, 1286, 1152, 854, 731. The spectroscopic properties of this compound are consistent with the data reported in the literature. [8]

3-(4-methoxy-2-nitrophenyl)-2,2-dimethylpropanoic acid (7-44)



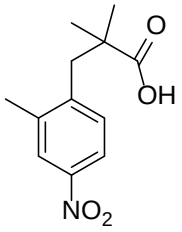
Following the general procedure and using 1-iodo-4-methoxy-2-nitrobenzene (83.7 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (40.3 mg, 53%). **Mp:** 80-82 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.34 (s, 1H), 7.26 (d, *J* = 8.3 Hz, 1H), 7.05 (d, *J* = 8.7 Hz, 1H), 3.85 (s, 3H), 3.28 (s, 2H), 1.17 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.8, 158.6, 151.2, 133.9, 123.9, 118.9, 109.4, 55.8, 43.9, 39.8, 24.6. **IR (KBr):** *v* (cm^{-1}) 2976, 2931, 1698, 1533, 1476, 1366, 1293, 1040, 915, 836, 734. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{14}NO_5^-$ $[M-H]^-$ 252.0877, found 252.0877.

2,2-dimethyl-3-(o-tolyl)propanoic acid (7-45)



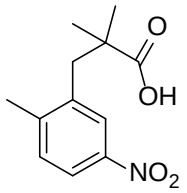
Following the general procedure and using 1-iodo-2-methylbenzene (65.5 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (57.7 mg, 47%). **Mp:** 35-37 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.17 - 7.08 (m, 4H), 2.97 (s, 2H), 2.33 (s, 3H), 1.22 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.3, 137.1, 136.0, 130.7, 130.5, 126.6, 125.6, 44.0, 41.5, 24.7, 20.3. **IR (KBr):** *v* (cm^{-1}) 2974, 2931, 1699, 1475, 1292, 1141, 943, 740. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{15}O_2^-$ $[M-H]^-$ 191.1078, found 191.1079.

2,2-dimethyl-3-(2-methyl-4-nitrophenyl)propanoic acid (7-46)



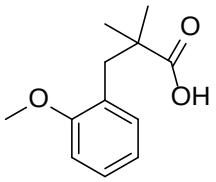
Following the general procedure and using 1-iodo-2-methyl-4-nitrobenzene (78.9 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (25.6 mg, 36%). **Mp:** 128-130 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.05 (s, 1H), 7.97 (d, *J* = 8.5 Hz, 1H), 7.31 (d, *J* = 8.5 Hz, 1H), 3.06 (s, 2H), 2.44 (s, 3H), 1.26 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.6, 146.5, 143.9, 139.0, 131.3, 125.2, 120.6, 44.0, 41.4, 24.9, 20.4. **IR (KBr):** *v* (cm^{-1}) 2970, 2920, 1696, 1507, 1475, 1347, 1141, 892, 736. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{14}NO_4^-$ $[M-H]^-$ 236.0928, found 236.0928.

2,2-dimethyl-3-(2-methyl-5-nitrophenyl)propanoic acid (7-47)



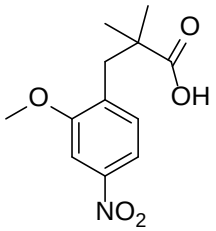
Following the general procedure and using 2-iodo-1-methyl-4-nitrobenzene (78.9 mg) as the arylating agent, the target compound was obtained as a colorless solid (24.2 mg, 34%). **Mp:** 164-166 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.04 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 8.4 Hz, 1H), 3.05 (s, 2H), 2.44 (s, 3H), 1.26 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.3, 146.1, 145.3, 137.8, 131.3, 125.3, 121.6, 44.0, 41.5, 24.7, 20.6. **IR (KBr):** *v* (cm^{-1}) 2974, 2934, 1688, 1510, 1477, 1350, 1280, 1148, 899, 741. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{14}NO_4^-$ $[M-H]^-$ 236.0928, found 236.0928.

3-(2-methoxyphenyl)-2,2-dimethylpropanoic acid (7-48)



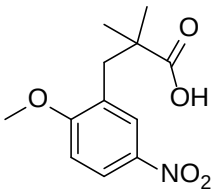
Following the general procedure and using 1-iodo-2-methoxybenzene (39.1 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (29.9 mg, 48%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.20 (t, *J* = 8.0 Hz, 1H), 7.12 (d, *J* = 7.3 Hz, 1H), 6.88 - 6.82 (m, 2H), 3.75 (s, 3H), 2.96 (s, 2H), 1.18 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.4, 158.0, 131.9, 127.9, 126.3, 120.1, 110.3, 54.9, 43.4, 39.3, 24.7. **IR (KBr):** *v* (cm^{-1}) 2971, 2935, 1699, 1495, 1289, 1247, 1140, 1031, 753, 548. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{15}O_3^-$ $[M-H]^-$ 207.1027, found 207.1027.

3-(2-methoxy-4-nitrophenyl)-2,2-dimethylpropanoic acid (7-49)



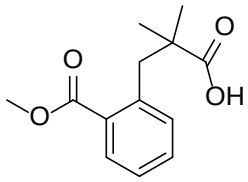
Following the general procedure and using 1-iodo-2-methoxy-4-nitrobenzene (83.8 mg, 0.3 mmol) as the arylating agent the target compound was obtained as a colorless solid (65.4 mg, 86%). **Mp:** 132-134 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 8.2 Hz, 1H), 7.70 (s, 1H), 7.28 (d, *J* = 8.3 Hz, 1H), 3.87 (s, 3H), 3.04 (s, 2H), 1.21 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.9, 158.4, 147.8, 134.3, 131.9, 115.4, 105.2, 55.6, 43.5, 39.1, 24.7. **IR (KBr):** *v* (cm^{-1}) 2960, 2931, 1694, 1520, 1461, 1348, 1249, 1032, 963, 815, 741, 591. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{14}NO_5^-$ $[M-H]^-$ 252.0877, found 252.0879.

3-(2-methoxy-5-nitrophenyl)-2,2-dimethylpropanoic acid (7-50)



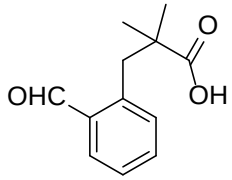
Following the general procedure and using 2-iodo-1-methoxy-4-nitrobenzene (83.8 mg, 0.3 mmol) as the arylating agent the target compound was obtained as a colorless solid (64.5 mg, 85%). **Mp:** 165-167 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 9.0 Hz, 1H), 8.06 (s, 1H), 6.91 (d, *J* = 9.1 Hz, 1H), 3.88 (s, 3H), 3.01 (s, 2H), 1.21 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.3, 163.1, 141.0, 127.6, 127.2, 124.5, 109.9, 55.7, 43.3, 39.1, 24.7. **IR (KBr):** *v* (cm^{-1}) 2975, 2930, 1698, 1506, 1477, 1351, 1264, 1150, 1023, 963, 751. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{14}NO_5^-$ $[M-H]^-$ 252.0877, found 252.0877.

3-(2-(methoxycarbonyl)phenyl)-2,2-dimethylpropanoic acid (7-51)



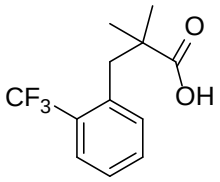
Following the general procedure and using methyl 2-iodobenzoate (44.1 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (28.4 mg, 40%). **Mp:** 42-44 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 7.8 Hz, 1H), 7.32 (td, *J* = 7.5, 1.5 Hz, 1H), 7.23 - 7.18 (m, 2H), 3.79 (s, 3H), 3.37 (s, 2H), 1.09 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.9, 168.9, 138.6, 132.2, 131.6, 131.3, 130.3, 126.6, 52.1, 43.8, 41.3, 24.6. **IR (KBr):** *v* (cm^{-1}) 2986, 2951, 1717, 1698, 1478, 1276, 1120, 1081, 968, 744, 716. **HRMS** (ESI) *m*/*z*: Calculated for $C_{13}H_{15}O_4^-$ $[M-H]^-$ 235.0976, found 235.0976.

3-(2-formylphenyl)-2,2-dimethylpropanoic acid (7-52)



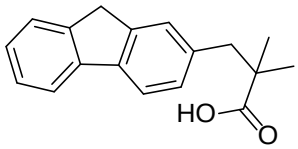
Following the general procedure and using 2-iodobenzaldehyde (69.6 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (20.4 mg, 33%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 10.29 (s, 1H), 7.87 (d, *J* = 6.2 Hz, 1H), 7.52 (td, *J* = 7.5, 1.6 Hz, 1H), 7.42 (t, *J* = 7.5, 1H), 7.31 (d, *J* = 7.7 Hz, 1H), 3.44 (s, 2H), 1.22 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.5, 183.7, 140.1, 135.1, 133.4, 132.5, 131.6, 127.3, 43.9, 39.6, 24.7. **IR (KBr):** *v* (cm^{-1}) 2980, 2929, 1705, 1474, 1410, 1271, 1130, 912, 734, 659. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{13}O_3^-$ $[M-H]^-$ 205.0870, found 205.0870.

2,2-dimethyl-3-(2-(trifluoromethyl)phenyl)propanoic acid (7-53)



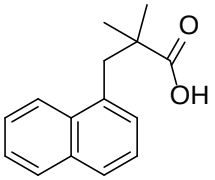
Following the general procedure and using 1-iodo-2-(trifluoromethyl)benzene (42.1 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (40.6 mg, 55%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.65 (d, *J* = 8.5 Hz, 1H), 7.45 (d, *J* = 7.0 Hz, 1H), 7.38 - 7.30 (m, 2H), 3.20 (s, 2H), 1.24 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 185.0, 137.1 (q, *J* = 1.7 Hz), 131.5, 131.1, 129.5 (q, *J* = 29.1 Hz), 126.6, 126.3 (q, *J* = 5.9 Hz), 124.5 (q, *J* = 275 Hz), 43.4, 40.5, 25.3. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -57.50. **IR (KBr):** *v* (cm^{-1}) 2984, 2938, 1700, 1477, 1131, 1121, 1039, 945, 769, 655. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{12}F_3O_2^-$ [M-H]$^-$ 245.0795, found 245.0794.

3-(9H-fluoren-2-yl)-2,2-dimethylpropanoic acid (7-54)



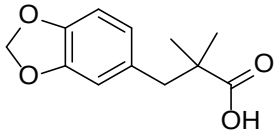
Following the general procedure and using 2-iodo-9H-fluorene (87.7 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (41.5 mg, 52%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 7.4 Hz, 1H), 7.18 (d, *J* = 7.9 Hz, 1H), 3.86 (s, 2H), 2.97 (s, 2H), 1.24 (d, *J* = 1.7 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.1, 143.2, 143.2, 141.6, 140.2, 136.2, 128.9, 126.9, 126.7, 126.5, 125.0, 119.7, 119.4, 46.1, 43.6, 36.9, 24.8. **IR (KBr):** *v* (cm^{-1}) 2923, 1695, 1455, 1322, 1291, 1221, 837, 766, 742, 602. **HRMS** (ESI) *m*/*z*: Calculated for $C_{18}H_{17}O_2^-$ [M-H]$^-$ 265.1234, found 265.1235.

2,2-dimethyl-3-(naphthalen-1-yl)propanoic acid (7-55)



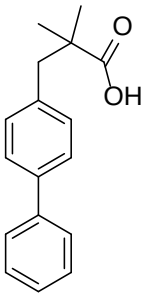
Following the general procedure and using 1-iodonaphthalene (38.9 μL, 0.3 mmol,) as the arylating agent, the target compound was obtained as a colorless oil (26.1 mg, 38%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.2 Hz, 1H), 7.85 (d, *J* = 7.9 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.51 - 7.35 (m, 4H), 3.43 (s, 2H), 1.25 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.1, 134.0, 133.9, 133.1, 128.8, 128.5, 127.4, 125.7, 125.4, 125.2, 124.5, 44.1, 40.8, 25.1. **IR (KBr):** *v* (cm^{-1}) 2971, 2931, 1693, 1508, 1462, 1287, 1154, 957, 803, 782, 528. **HRMS** (ESI) *m*/*z*: Calculated for $C_{15}H_{15}O_2^-$ $[M-H]^-$ 227.1078, found 227.1078.

3-(benzo[d][1,3]dioxol-5-yl)-2,2-dimethylpropanoic acid (7-56)



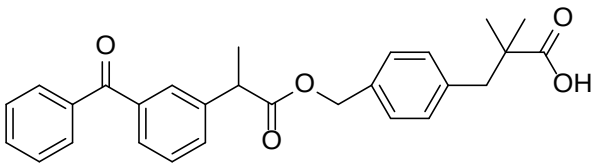
Following the general procedure and using 5-iodobenzo[d][1,3]dioxole (39.0 μL, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (32.7 mg, 49%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.72 (d, *J* = 7.9 Hz, 1H), 6.66 (d, *J* = 1.7 Hz, 1H), 6.62 (d, *J* = 7.9 Hz, 1H), 5.93 (s, 2H), 2.81 (s, 2H), 1.19 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.1, 147.3, 146.3, 131.3, 123.3, 110.6, 108.0, 100.9, 45.6, 43.6, 24.7. **IR (KBr):** *v* (cm^{-1}) 2974, 1699, 1504, 1490, 1442, 1250, 1191, 1040, 932, 813, 546. **HRMS** (ESI) *m*/*z*: Calculated for $C_{12}H_{13}O_4^-$ $[M-H]^-$ 211.0819, found 211.0819.

3-([1,1'-biphenyl]-4-yl)-2,2-dimethylpropanoic acid (7-57)



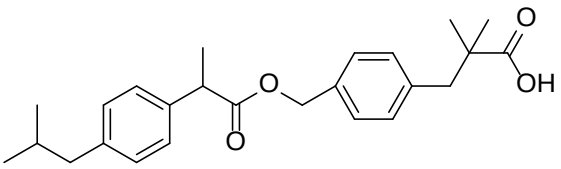
Following the general procedure and using 4-iodo-1,1'-biphenyl (84.1 mg, 0.3 mmol) as the arylating agent, Under the reaction condition of 80℃, the target compound was obtained as a colorless solid (35.1 mg, 46%). **Mp:** 133-135 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 7.5 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.24 (d, *J* = 8.2 Hz, 2H), 2.93 (s, 2H), 1.24 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.0, 140.9, 139.5, 136.7, 130.7, 128.8, 127.2, 127.0, 126.8, 45.5, 43.5, 24.8. The spectroscopic properties of this compound are consistent with the data reported in the literature. [9]

3-(4-(((2-(3-benzoylphenyl)propanoyl)oxy)methyl)phenyl)-2,2-dimethylpropanoic acid (7-58)



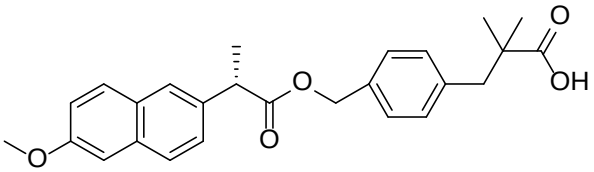
Following the general procedure and using **6-58** (141.1 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (96.0 mg, 72%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.78 (s, 1H), 7.76 (d, *J* = 5.4 Hz, 2H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.60 - 7.51 (m, 2H), 7.47 - 7.40 (m, 3H), 7.13 (q, *J* = 8.0 Hz, 4H), 5.04 (dd, *J* = 32.0 Hz, *J* = 7.2 Hz, 2H), 3.85 (q, *J* = 7.1 Hz, 1H), 2.86 (s, 2H), 1.54 (d, *J* = 7.2 Hz, 3H), 1.18 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.6, 183.9, 173.9, 140.7, 137.9, 137.7, 137.5, 134.0, 132.6, 131.6, 130.5, 130.1, 129.3, 129.1, 128.6, 128.3, 127.8, 66.5, 45.4, 45.4, 43.4, 24.7, 18.4. **IR (KBr):** *v* (cm^{-1}) 2975, 2934, 1731, 1697, 1657, 1596, 1447, 1378, 1281, 1157, 1076, 819, 719. **HRMS** (ESI) *m*/*z*: Calculated for $C_{28}H_{27}O_5^-$ $[M-H]^-$ 443.1864, found 443.1864.

3-(4-(((2-(4-isobutylphenyl)propanoyl)oxy)methyl)phenyl)-2,2 dimethylpropanoic acid (7-59)



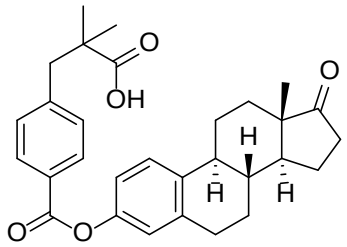
Following the general procedure and using **6-59** (126.7 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (86.9 mg, 73%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.19 (d, *J* = 7.9 Hz, 2H), 7.15 - 7.06 (m, 6H), 5.04 (dd, *J* = 32.0 Hz, *J* = 7.2 Hz, 2H), 3.74 (q, *J* = 7.1 Hz, 1H), 2.87 (s, 2H), 2.44 (d, *J* = 7.2 Hz, 2H), 1.89 - 1.79 (m, 1H), 1.50 (d, *J* = 7.2 Hz, 3H), 1.19 (s, 6H), 0.89 (d, *J* = 6.6 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.0, 174.6, 140.6, 137.7, 137.4, 134.3, 130.4, 129.3, 127.6, 127.2, 66.2, 45.4, 45.2, 45.1, 43.4, 30.2, 24.7, 22.4, 18.5. **IR (KBr):** *v* (cm^{-1}) 2953, 1733, 1697, 1513, 1463, 1366, 1285, 1198, 1155, 1072, 1021, 942, 846. **HRMS** (ESI) *m*/*z*: Calculated for $C_{25}H_{31}O_4^-$ [M-H]$^-$ 395.2228, found 395.2228.

(S)-3-(4-(((2-(6-methoxynaphthalen-2-yl)propanoyl)oxy)methyl)phenyl)-2,2-dimethylpropanoic acid (7-60)



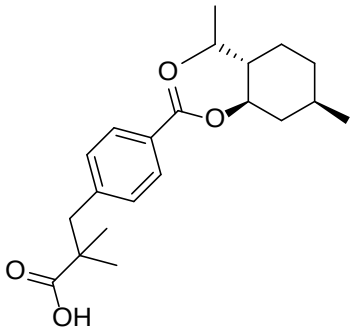
Following the general procedure and using **6-60** (133.9 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (82.0 mg, 65%). **Mp:** 205-207 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.69 - 7.63 (m, 3H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.16 - 7.06 (m, 6H), 5.04 (dd, *J* = 32.0 Hz, *J* = 7.2 Hz, 2H), 3.91 - 3.86 (m, 4H), 2.85 (s, 2H), 1.57 (d, *J* = 7.1 Hz, 3H), 1.17 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.1, 174.6, 157.7, 137.5, 135.6, 134.3, 133.7, 130.4, 129.3, 129.0, 127.9, 127.2, 126.3, 126.0, 119.0, 105.6, 66.4, 55.3, 45.5, 45.5, 43.4, 24.7, 18.6. **IR (KBr):** *v* (cm^{-1}) 2918, 1733, 1713, 1609, 1492, 1309, 1266, 1207, 1178, 1152, 1079, 1018, 855. **HRMS** (ESI) *m*/*z*: Calculated for $C_{26}H_{27}O_5^-$ [M-H]$^-$ 419.1864, found 419.1864.

2,2-dimethyl-3-(4-((((8R,9S,13S,14S)-13-methyl-17-oxo 7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)oxy)carbonyl)phenyl)propanoic acid (7-61)



Following the general procedure and using **6-61** (150.2 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (111.1 mg, 78%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.3 Hz, 2H), 7.32 (dd, *J* = 8.5, 3.7 Hz, 3H), 6.96 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.93 (d, *J* = 2.5 Hz, 1H), 2.99 (s, 2H), 2.96 - 2.90 (m, 2H), 2.52 (dd, *J* = 19.0, 8.6 Hz, 1H), 2.46 - 2.39 (m, 1H), 2.31 (td, *J* = 10.7, 4.1 Hz, 1H), 2.21 - 1.95 (m, 4H), 1.69 - 1.42 (m, 6H), 1.24 (s, 6H), 0.92 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 221.2, 183.3, 165.4, 148.9, 143.8, 138.1, 137.4, 130.5, 130.0, 128.0, 126.5, 121.7, 118.9, 50.4, 48.0, 45.8, 44.2, 43.5, 38.0, 35.9, 31.6, 29.4, 26.4, 25.8, 24.8, 21.6, 13.9. **IR (KBr):** *v* (cm^{-1}) 2973, 2934, 1730, 1696, 1605, 1453, 1391, 1323, 1263, 1216, 1150, 1030, 851. **HRMS** (ESI) *m*/*z*: Calculated for $C_{30}H_{33}O_5^-$ $[M-H]^-$ 473.2333, found 473.2333.

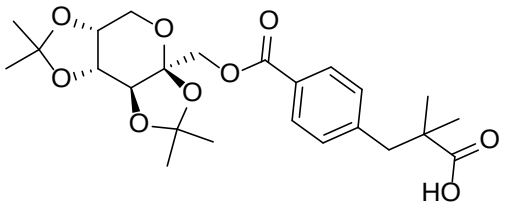
3-(4-((((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)carbonyl)phenyl)-2,2-dimethylpropanoic acid (7-62)



Following the general procedure and using **6-62** (115.9 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless oil (83.3 mg, 77%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 7.9 Hz, 2H), 7.25 (d, *J* = 7.9 Hz, 2H), 4.93 (td, *J* = 10.9, 4.3 Hz, 1H), 2.95 (s, 2H), 2.12 (d, *J* = 12.3 Hz, 1H), 2.00 - 1.93 (m,

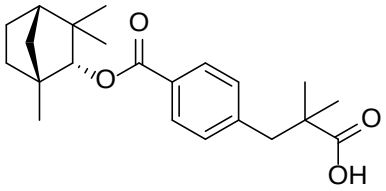
1H), 1.72 (d, *J* = 11.2 Hz, 2H), 1.61 - 1.51 (m, 2H), 1.22 (s, 6H), 1.16 - 1.04 (m, 2H), 0.92 (dd, *J* = 6.8, 4.4 Hz, 7H), 0.79 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.8, 166.1, 142.8, 130.3, 129.4, 129.2, 74.8, 47.3, 45.7, 43.4, 41.0, 34.3, 31.5, 26.5, 24.8, 24.7, 23.6, 22.1, 20.8, 16.5. **IR (KBr):** *v* (cm^{-1}) 2953, 2926, 1698, 1611, 1455, 1272, 1178, 1111, 1096, 1020, 960, 706. **HRMS** (ESI) *m*/*z*: Calculated for $C_{22}H_{31}O_4^-$ $[M-H]^-$ 359.2228, found 359.2228.

2,2-dimethyl-3-(4-((((3aS,5aR,8aR,8bS)-2,2,7,7-tetramethyltetrahydro-3aH-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-3a-yl)methoxy)carbonyl)phenyl)propanoic acid (7-63)



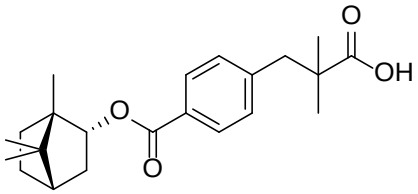
Following the general procedure and using **6-63** (147.1 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (115.7 mg, 83%). **Mp:** 56-58 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.00 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 4.70 - 4.62 (m, 2H), 4.47 (d, *J* = 2.6 Hz, 1H), 4.33 (d, *J* = 11.8 Hz, 1H), 4.26 (d, *J* = 8.0 Hz, 1H), 3.96 (dd, *J* = 13.1, 1.9 Hz, 1H), 3.81 (d, *J* = 13.0 Hz, 1H), 2.95 (s, 2H), 1.55 (s, 3H), 1.45 (s, 3H), 1.39 (s, 3H), 1.34 (s, 3H), 1.21 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.4, 166.0, 143.3, 130.3, 129.6, 128.3, 109.2, 108.8, 101.7, 70.8, 70.6, 70.1, 65.4, 61.3, 45.7, 43.4, 26.5, 25.9, 25.5, 24.7, 24.0. **IR (KBr):** *v* (cm^{-1}) 2991, 2938, 1726, 1698, 1611, 1457, 1373, 1275, 1251, 1206, 1111, 1067, 1020, 863. **HRMS** (ESI) *m*/*z*: Calculated for $C_{24}H_{31}O_9^-$ $[M-H]^-$ 463.1974, found 463.1974.

2,2-dimethyl-3-(4-((((1R,2R,4S)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-yl)oxy)carbonyl)phenyl)propanoic acid (7-64)



Following the general procedure and using **6-64** (115.3 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (86.1 mg, 80%). **Mp:** 133-135 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.99 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 4.61 (s, 1H), 2.96 (s, 2H), 1.97 - 1.90 (m, 1H), 1.82 - 1.74 (m, 2H), 1.66 (d, *J* = 10.2 Hz, 1H), 1.56 - 1.46 (m, 1H), 1.26 - 1.23 (m, 2H), 1.23 (s, 6H),1.18 (s, 3H), 1.11 (s, 3H), 0.85 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.9, 166.9, 142.9, 130.4, 129.3, 129.1, 86.6, 48.6, 48.4, 45.7, 43.4, 41.5, 39.9, 29.8, 26.9, 25.9, 24.8, 24.7, 20.4, 19.5. **IR (KBr):** *v* (cm^{-1}) 2950, 1705, 1693, 1610, 1470, 1419, 1368, 1279, 1258, 1182, 1116, 1023, 864, 735. **HRMS** (ESI) *m*/*z*: Calculated for $C_{22}H_{29}O_4^-$ $[M-H]^-$ 357.2071, found 357.2071.

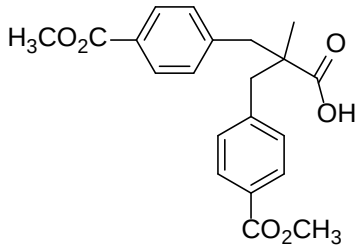
2,2-dimethyl-3-(4-((((1S,2R,4S)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)oxy)carbonyl)phenyl)propanoic acid (7-65)



Following the general procedure and using **6-65** (115.3 mg, 0.3 mmol) as the arylating agent, the target compound was obtained as a colorless solid (81.7 mg, 76%). **Mp:** 127-129 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 5.10 (dt, *J* = 9.8, 2.8 Hz, 1H), 2.96 (s, 2H), 2.51 - 2.43 (m, 1H), 2.16 - 2.10 (m, 1H), 1.83 - 1.76 (m, 1H), 1.73 (t, *J* = 4.5 Hz, 1H), 1.44 - 1.36 (m, 1H), 1.33 - 1.26 (m, 1H), 1.22 (s, 6H), 1.11 (dd, *J* = 13.8, 3.5 Hz, 1H), 0.96 (s, 3H), 0.91 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.8, 166.8, 142.9, 130.3, 129.3, 129.3, 80.5, 49.1, 47.9, 45.7, 45.0, 43.4, 36.9, 28.1, 27.4, 24.8, 24.7, 19.7, 18.9, 13.6. **IR (KBr):** *v*

(cm^{-1}) 2953, 1708, 1695, 1609, 1471, 1407, 1364, 1277, 1253, 1178, 1112, 1018, 860, 733. **HRMS** (ESI) *m*/*z*: Calculated for $C_{22}H_{29}O_4^-$ $[M-H]^-$ 357.2071, found 357.2071.

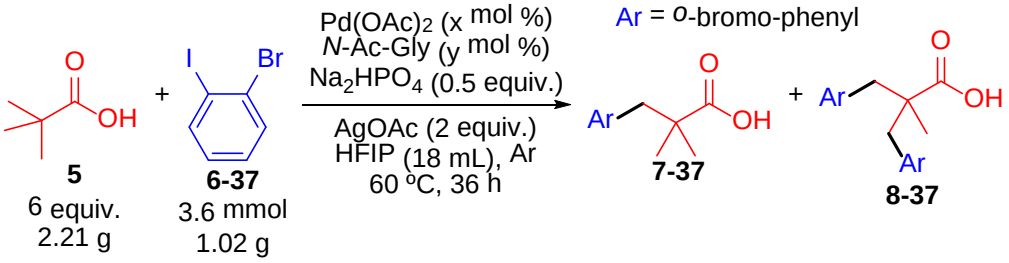
2-(4-(methoxycarbonyl)benzyl)-3-(4-(methoxycarbonyl)phenyl)-2-methylpropanoic acid (8-1)



Mp: 171-173 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 7.9 Hz, 4H), 7.25 (d, *J* = 7.3 Hz, 4H), 3.91 (s, 6H), 3.28 (d, *J* = 13.1 Hz, 2H), 2.81 (d, *J* = 13.1 Hz, 2H), 1.05 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.0, 167.0, 142.3, 130.3, 129.5, 128.8, 52.1, 48.7, 45.7, 19.9. **IR (KBr):** *v* (cm^{-1}) 2993, 2952, 1713, 1694, 1430, 1280, 1105, 859, 705. **HRMS** (ESI) *m*/*z*: Calculated for $C_{21}H_{21}O_6^-$ $[M-H]^-$ 369.1344, found 369.1345.

6. Synthetic Applications

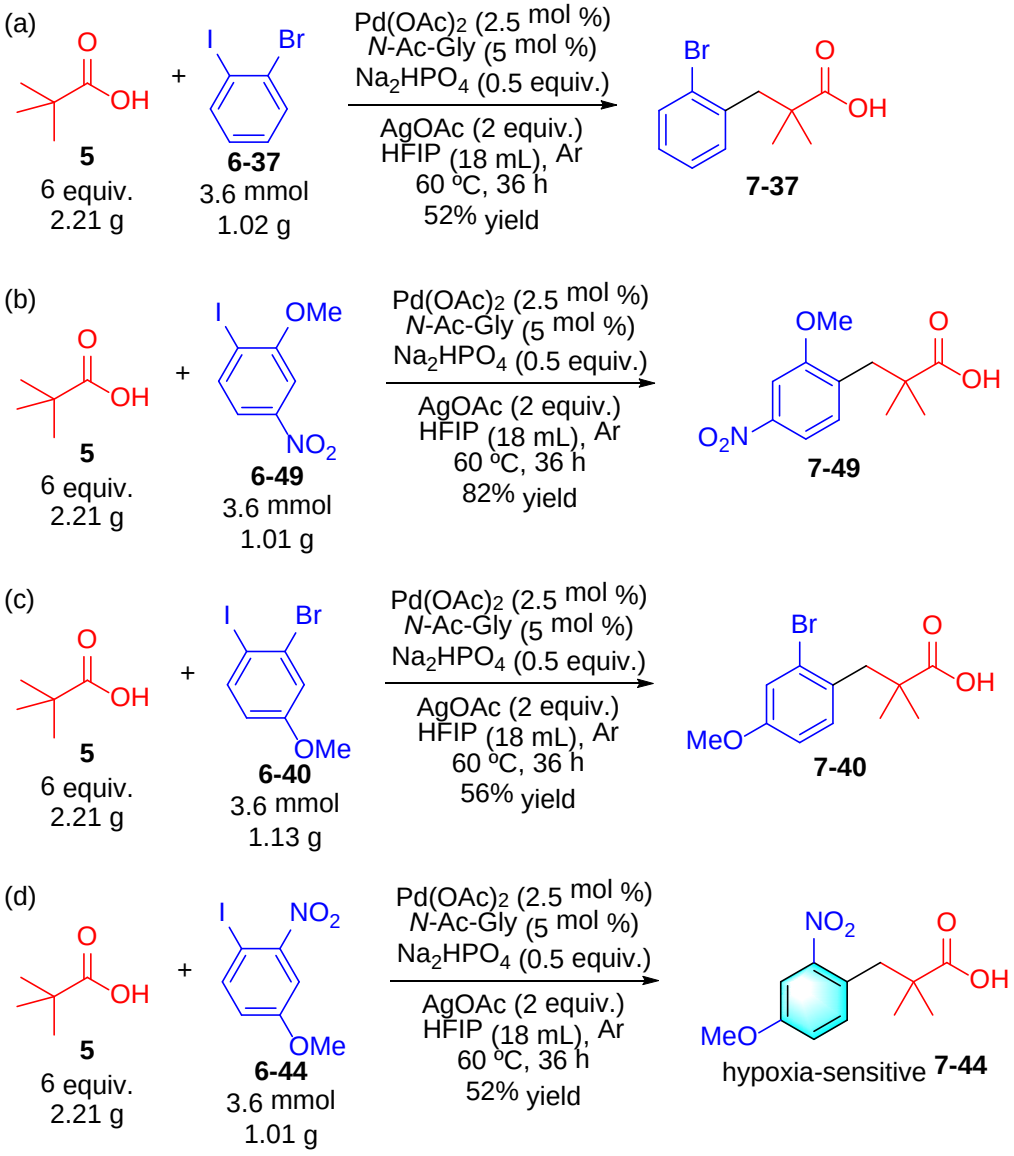
6.1. Gram-Scale Experiments



entry	x	y	Yield (%)[a]	
			7-37	**8-37**
1	10	20	50	9.8
2	5	10	58 (55)	2.5
3	2.5	5	54 (52)	trace

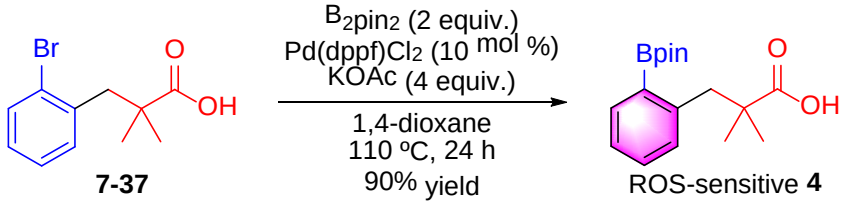
[a]All data represent the average of two independent experiments. Yields were determined by ^{1}H-NMR spectroscopic analysis of crude mixtures using 1,3,5-trimethoxybenzene (202 mg, 1.2 mmol) as internal standard, isolated yields are given in parentheses.

General Procedure for Gram-Scale Experiments: In a glovebox filled with argon, a clean, oven-dried screw cap reaction tube with previously placed magnetic stir-bar was charged with pivalic acid (2.21 g, 21.6 mmol, 6 equiv.), aryl iodide (3.6 mmol), $Pd(OAc)_2$ (20.4 mg, 0.09 mmol, 2.5 mol%), *N*-Ac-Gly-OH (21.3 mg, 0.18 mmol, 5 mol%), AgOAc (1.21 g, 7.2 mmol, 2 equiv.) and Na_2HPO_4 (255.6 mg, 1.8 mmol, 0.5 equiv.), followed by addition of HFIP (18 mL). The vessel was sealed and moved out of the glovebox, and the reaction was stirred at room temperature for 10 minutes. Then the reaction vessel was placed in a pre-heated (60 °C) oil bath and stirring was continued at this temperature for 36 h. The reaction mixture was allowed to cool to room temperature. The resulting mixture was filtered through a celite bed using ethyl acetate as the eluent. After concentration under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum-ether / ethyl acetate / formic acid = 20:1:0.005) to give the desired arylated product.

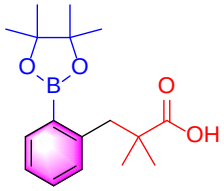


6.2. Application Potential of Developed Methodology

6.2.1 Synthesis of 2,2-dimethyl-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propanoic acid

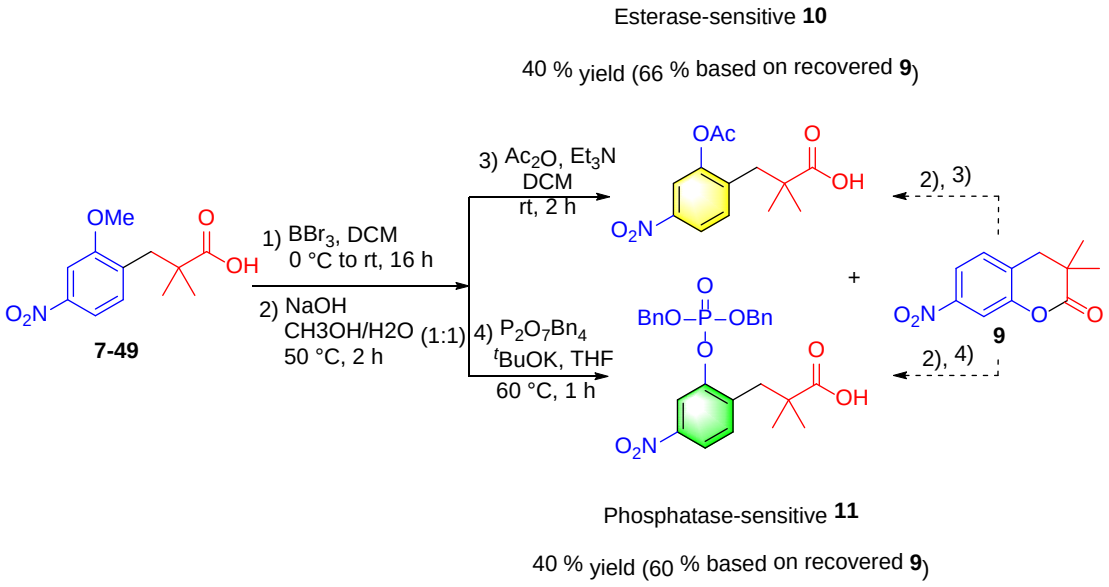


2,2-dimethyl-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propanoic acid (ROS sensitive-4)



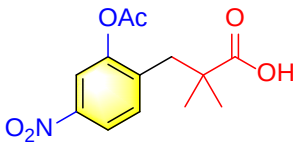
To a solution of 3-(2-bromophenyl)-2,2-dimethylpropanoic acid **7-37** (77.2 mg, 0.3 mmol) in degassed 1,4-dioxane (3 mL) was added bis(pinacolato)diboron (152.4 mg, 0.6 mmol), $Pd(dppf)Cl_2$ (22.0 mg, 0.03 mmol), and potassium acetate (117.8 mg, 1.2 mmol) and the mixture was refluxed for 24 h under an atmosphere of nitrogen. The reaction mixture was allowed to cool to room temperature and AcOH (1 mL) was added. The resulting mixture was filtered through a celite bed using ethyl acetate as the eluent. The reaction mixture was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (petroleum-ether / ethyl acetate / formic acid = 16:1:0.005) to give a pale-yellow solid (82.1 mg, 90%). **Mp:** 99-101 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 7.0 Hz, 1H), 7.33 (td, *J* = 7.5, 1.6 Hz, 1H), 7.21 (t, *J* = 7.3 Hz, 2H), 3.34 (s, 2H), 1.35 (s, 12H), 1.17 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.7, 144.1, 135.9, 130.5, 130.4, 125.7, 83.6, 43.7, 43.2, 24.9, 24.5. The spectroscopic properties of this compound are consistent with the data reported in the literature. [7]

6.2.2 Synthesis of 3-(2-acetoxy-4-nitrophenyl)-2,2-dimethylpropanoic acid (esterase sensitive-10) and 3-(2-((bis(benzyloxy)phosphoryl)oxy)-4-nitrophenyl)-2,2-dimethylpropanoic acid (phosphatase sensitive-11)



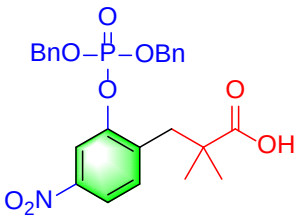
In an argon flushed 100 mL round bottom flask, 3-(2-methoxy-4-nitrophenyl)-2,2-dimethylpropanoic acid **7-49** (759 mg, 3.0 mmol) was dissolved in CH_2Cl_2 (40 mL) and the solution was cooled to 0 °C. A solution of BBr_3 in CH_2Cl_2 (2 M, 3.0 mL, 6.0 mmol, 2.0 eq) was added dropwise at this temperature. The mixture was allowed to warm to room temperature and stirring was continued for 16 hours. The reaction was quenched trough the addition of ice. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were concentrated under reduced pressure to give the crude product, which was added to a cooled solution of NaOH (480 mg, 12 mmol, 4 eq) in CH_3OH/H_2O (1:1v/v, 20 mL). The reaction was heated to 50 °C for 2 h. After cooling to room temperature, the pH was adjusted to 2-3 with 1N HCl. The mixture was extracted with EtOAc (3 × 40 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was directly used for next step synthesis without further purification.

3-(2-acetoxy-4-nitrophenyl)-2,2-dimethylpropanoic acid (esterase sensitive-10)



The crude product obtained in the previous step was added to 7 mL of dry CH_2Cl_2 followed by addition of Ac_2O (855 µL, 9.0 mmol, 3.0 eq) and Et_3N (1.26 mL, 9.0 mmol, 3.0 eq). After stirring at room temperature for 2h, the reaction was quenched trough the addition of H_2O (10 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification was achieved using column chromatography on silica gel (petroleum-ether / ethyl acetate / formic acid = 20:1:0.005) to give **10** as a colorless solid (338 mg, 40 %) and compound **9** (258 mg, 39 %). **Mp:** 92-94 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.04 (dd, *J* = 8.5, 2.4 Hz, 1H), 8.01 (d, *J* = 2.3 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 2.96 (s, 2H), 2.36 (s, 3H), 1.24 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.4, 168.7, 149.6, 147.2, 137.4, 132.7, 120.4, 118.3, 43.5, 39.5, 24.8, 20.9. **IR (KBr):** *v* (cm^{-1}) 2981, 2935, 1769, 1695, 1523, 1347, 1201, 1166, 1076, 947, 742. **HRMS** (ESI) *m/z*: Calculated for $C_{13}H_{14}NO_6^-$ $[M-H]^-$ 280.0827, found 280.0827.

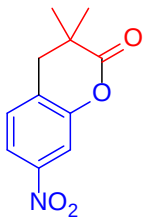
3-(2-((bis(benzyloxy)phosphoryl)oxy)-4-nitrophenyl)-2,2-dimethylpropanoic acid (phosphatase sensitive-11) [10]



The crude product obtained in the previous step was added to 20 mL of dry THF followed by addition of solid potassium tert-butoxide (744.0 mg, 6.6 mmol, 2.2 eq). The mixture was heated to 60 °C in an oil bath for approximately 5 min. To this warm reaction mixture was added the solid tetrabenzyl pyrophosphate (1.78 g, 3.3 mmol, 1.1 eq). Approximately 10 min after the addition of the tetrabenzyl pyrophosphate, an insoluble white precipitate formed. The reaction mixture was kept under continuous

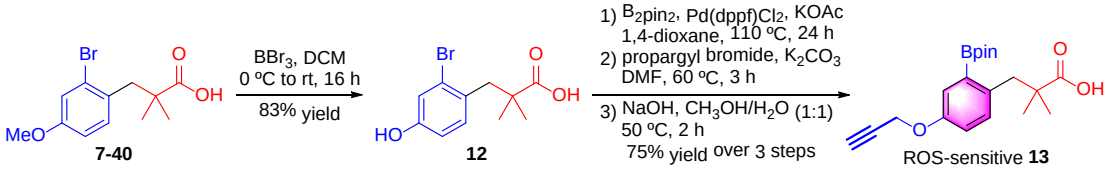
stirring at 60 °C for 1h and then allowed to cool to room temperature. To the reaction milieu was added hexane (60 mL), and the insoluble white precipitate was removed by filtration. After removal of all solvents by rotary evaporation, a viscous residue was obtained. Purification was achieved using column chromatography on silica gel (petroleum-ether / ethyl acetate / formic acid = 20:1:0.005) to give **11** as a colorless solid (599 mg, 40 %) and compound **9** (219 mg, 33%). **Mp:** 136-138 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.09 (s, 1H), 7.88 (d, *J* = 8.5 Hz, 1H), 7.32 (s, 11H), 5.21 - 5.11 (m, 4H), 2.96 (s, 2H), 1.15 (s, 6H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 181.9, 149.4 (d, *J* = 7.0 Hz), 147.1, 136.9 (d, *J* = 7.3 Hz), 134.9 (d, *J* = 6.2 Hz), 132.6, 129.0, 128.7, 128.3, 119.5, 115.1 (d, *J* = 2.2 Hz), 70.7 (d, *J* = 5.9 Hz), 43.5, 39.0, 24.8. **^{31}P NMR** (162 MHz, $CDCl_3$) δ -6.63. **IR (KBr):** *v* (cm^{-1}) 2974, 1712, 1522, 1342, 1243, 1176, 1143, 1009, 970, 696. **HRMS** (ESI) *m/z*: Calculated for $C_{25}H_{25}NO_8P^-$ $[M-H]^-$ 498.1323, found 498.1319.

3,3-dimethyl-7-nitrochroman-2-one (9)

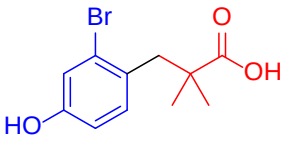


Compound **9** was obtained as a colorless solid. Purification was achieved by column chromatography on silica gel (petroleum ether / ethyl acetate = 16:1). **Mp:** 126-128 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.87 (d, *J* = 2.2 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 3.00 (s, 2H), 1.33 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.8, 151.7, 147.8, 129.6, 129.3, 119.2, 111.8, 38.3, 36.8, 24.6. **IR (KBr):** *v* (cm^{-1}) 2977, 2939, 1777, 1513, 1421, 1336, 1264, 1231, 1121, 1091, 1019, 905, 753. **HRMS** (ESI) *m/z*: Calculated for $C_{11}H_{12}NO_4^+$ $[M+H]^+$ 222.0761, found 222.0761.

6.2.3 Synthesis of 2,2-dimethyl-3-(4-(prop-2-yn-1-yloxy)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propanoic acid (ROS sensitive-13)

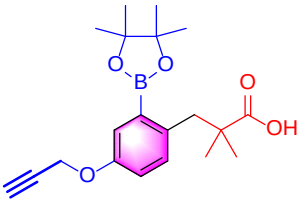


3-(2-bromo-4-hydroxyphenyl)-2,2-dimethylpropanoic acid (12)



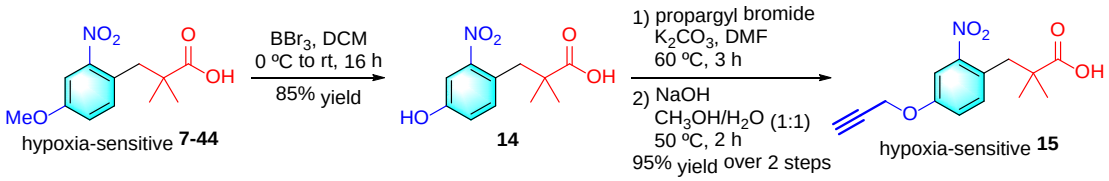
In an argon flushed 100 mL round bottom flask, 3-(2-bromo-4-methoxyphenyl)-2,2-dimethylpropanoic acid **7-40** (1.5 g, 5.2 mmol) was dissolved in CH_2Cl_2 (50 mL) and the solution was cooled to 0 °C. A solution of BBr_3 in CH_2Cl_2 (2 M, 5.2 mL, 10.4 mmol, 2 eq) was added dropwise at this temperature. The mixture was allowed to warm to room temperature and stirring was continued for 16 hours. The reaction was quenched trough the addition of ice. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 60 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification was achieved using column chromatography on silica gel (petroleum-ether / ethyl acetate / formic acid = 15:1:0.005) to give a colorless solid (1.18 g, 83 %). **Mp:** 125-127 °C. **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.09 (d, J = 8.5 Hz, 1H), 7.04 (d, J = 2.5 Hz, 1H), 6.71 (dd, J = 8.5, 2.6 Hz, 1H), 3.03 (s, 2H), 1.19 (s, 6H). **^{13}C NMR** (101 MHz, Methanol-d_4) δ 180.6, 156.3, 131.7, 128.3, 125.6, 119.2, 114.3, 43.8, 42.9, 24.1. **IR (KBr):** ν (cm^{-1}) 3300, 2972, 1682, 1604, 1491, 1344, 1242, 1038, 994, 821.**HRMS** (ESI) m/z: Calculated for $C_{11}H_{12}BrO_3^-$ $[M-H]^-$ 270.9975, found 270.9981.

2,2-dimethyl-3-(4-(prop-2-yn-1-yloxy)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propanoic acid (ROS sensitive-13)

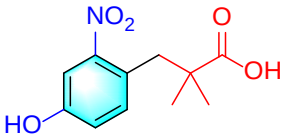


To a solution of 3-(2-bromo-4-hydroxyphenyl)-2,2-dimethylpropanoic acid **12** (700 mg, 2.56 mmol) in degassed 1,4-dioxane (25 mL) was added bis(pinacolato)diboron (1.3 mg, 5.12 mmol), Pd(dppf)Cl_2 (187.3 mg, 0.256 mmol, 0.1 eq), and potassium acetate (1.26 g, 12.8 mmol, 5 eq). The mixture was refluxed for 24 h under an atmosphere of nitrogen. The reaction mixture was allowed to cool to room temperature and AcOH (1.5 mL) was added. The resulting mixture was filtered through a celite bed using ethyl acetate as the eluent and concentrated under reduced pressure. The crude product was dissolved in DMF (15 ml) and crushed anhydrous K_2CO_3 (1.06 g, 7.68 mmol, 3 eq) was added to form a suspension. Propargyl bromide (670 µL, 7.68 mmol, 3 eq) was added and the flask was heated to 60 °C for 3 hours. After cooling to room temperature, the reaction mixture was filtered through celite. The organic solvents were removed in vacuum. The obtained oily residue was redissolved with a cooled solution of NaOH (307 mg, 7.68 mmol, 3 eq.) in CH_3OH:H_2O (1:1v/v, 8 mL), heated at 50 °C for 2 h. The reaction mixture was allowed to cool to room temperature. Then the pH was adjusted to 2-3 with 1N HCl. The phases were separated and the aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Further purification was achieved using column chromatography on silica gel (petroleum-ether / ethyl acetate / formic acid = 15:1:0.005) to give a colorless solid (1.16 g, 75 %). **Mp:** 86-88 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.37 (d, *J* = 2.9 Hz, 1H), 7.14 (d, *J* = 8.5 Hz, 1H), 6.96 (dd, *J* = 8.5, 3.0 Hz, 1H), 4.68 (d, *J* = 2.4 Hz, 2H), 3.27 (s, 2H), 2.50 (t, *J* = 2.4 Hz, 1H), 1.34 (s, 12H), 1.15 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.4, 155.5, 137.2, 131.5, 121.6, 117.2, 83.7, 78.8, 75.3, 55.9, 43.7, 42.4, 24.9, 24.5. **IR (KBr):** *v* (cm^{-1}) 3260, 2976, 1694, 1568, 1417, 1330, 1281, 1199, 1139, 1057, 1029, 853. **HRMS** (ESI) *m*/*z*: Calculated for $C_{20}H_{26}BO_5^-$ $[M-H]^-$ 357.1879, found 357.1881.

6.2.4 Synthesis of 2,2-dimethyl-3-(2-nitro-4-(prop-2-yn-1-yloxy)phenyl)propanoic acid (hypoxia sensitive-15)

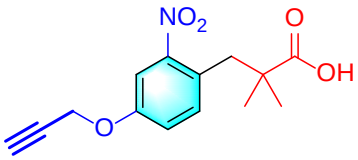


3-(4-hydroxy-2-nitrophenyl)-2,2-dimethylpropanoic acid (14)



In an argon flushed 100 mL round bottom flask, 3-(4-methoxy-2-nitrophenyl)-2,2-dimethylpropanoic acid **7-44** (1.02 g, 4 mmol) was dissolved in CH_2Cl_2 (25 mL) and the solution was cooled to 0 °C. A solution of BBr_3 in CH_2Cl_2 (2 M, 4 mL, 8.0 mmol, 2 eq) was added dropwise at this temperature. The mixture was allowed to warm to room temperature and stirring was continued for 16 hours. The reaction was quenched trough the addition of ice. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification was achieved using column chromatography on silica gel (petroleum-ether / ethyl acetate / formic acid = 20:1:0.005) to give a red solid (813.4 mg, 85 %). **Mp:** 128-130 °C. **^{1}H NMR** (400 MHz, Acetone-d_6) δ 7.33 - 7.28 (m, 2H), 7.08 (dd, J = 8.5, 2.7 Hz, 1H), 3.22 (s, 2H), 1.12 (s, 6H). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 178.0, 156.5, 151.6, 134.2, 122.4, 119.5, 110.8, 43.3, 39.3, 24.2. **IR (KBr):** ν (cm^{-1}) 3416, 2977, 1696, 1621, 1517, 1370, 1193, 1156, 1013, 816. **HRMS** (ESI) m/z: Calculated for $C_{11}H_{12}NO_5^-$ $[M-H]^-$ 238.0721, found 238.0720.

2,2-dimethyl-3-(2-nitro-4-(prop-2-yn-1-yloxy)phenyl)propanoic acid (hypoxia sensitive-15)



3-(4-hydroxy-2-nitrophenyl)-2,2-dimethylpropanoic acid **14** (1.0 g, 3.95 mmol) was dissolved in DMF (20 ml) and crushed anhydrous K_2CO_3 (1.64 g, 11.9 mmol, 3 eq) was added to form a suspension. Propargyl bromide (1.03 mL, 11.9 mmol, 3 eq) was added and the flask was heated to 60°C for 3 hours. After cooling to room temperature, the reaction mixture was filtered through celite. The organic solvents were removed in vacuum. The obtained oily residue was redissolved with a cooled solution of NaOH (475 mg, 11.9 mmol, 3 eq.) in CH_3OH:H_2O (1:1v/v, 8 mL), heated at 50 °C for 2 h. The reaction mixture was allowed to cool to room temperature. Then the pH was adjusted to 2-3 with 1N HCl. The phases were separated and the aqueous phase was extracted with EtOAc (3 × 20 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Further purification was achieved using column chromatography on silica gel (petroleum-ether / ethyl acetate / formic acid = 15:1:0.005) to give a yellow solid (1.04 g, 95 %). **Mp:** 100-102 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.45 (d, *J* = 2.7 Hz, 1H), 7.29 (d, *J* = 8.6 Hz, 1H), 7.14 (dd, *J* = 8.6, 2.8 Hz, 1H), 4.74 (d, *J* = 2.4 Hz, 2H), 3.29 (s, 2H), 2.58 (t, *J* = 2.4 Hz, 1H), 1.18 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.8, 156.4, 151.0, 134.0, 124.8, 119.5, 110.8, 77.4, 76.7, 56.3, 43.9, 39.8, 24.7. **IR (KBr):** *v* (cm^{-1}) 3293, 2978, 1681, 1526, 1495, 1330, 1268, 1211, 1152, 1028, 863. **HRMS** (ESI) *m*/*z*: Calculated for $C_{14}H_{14}NO_5^-$ $[M-H]^-$ 276.0877, found 276.0879.

7. Some Incompatible Substrates

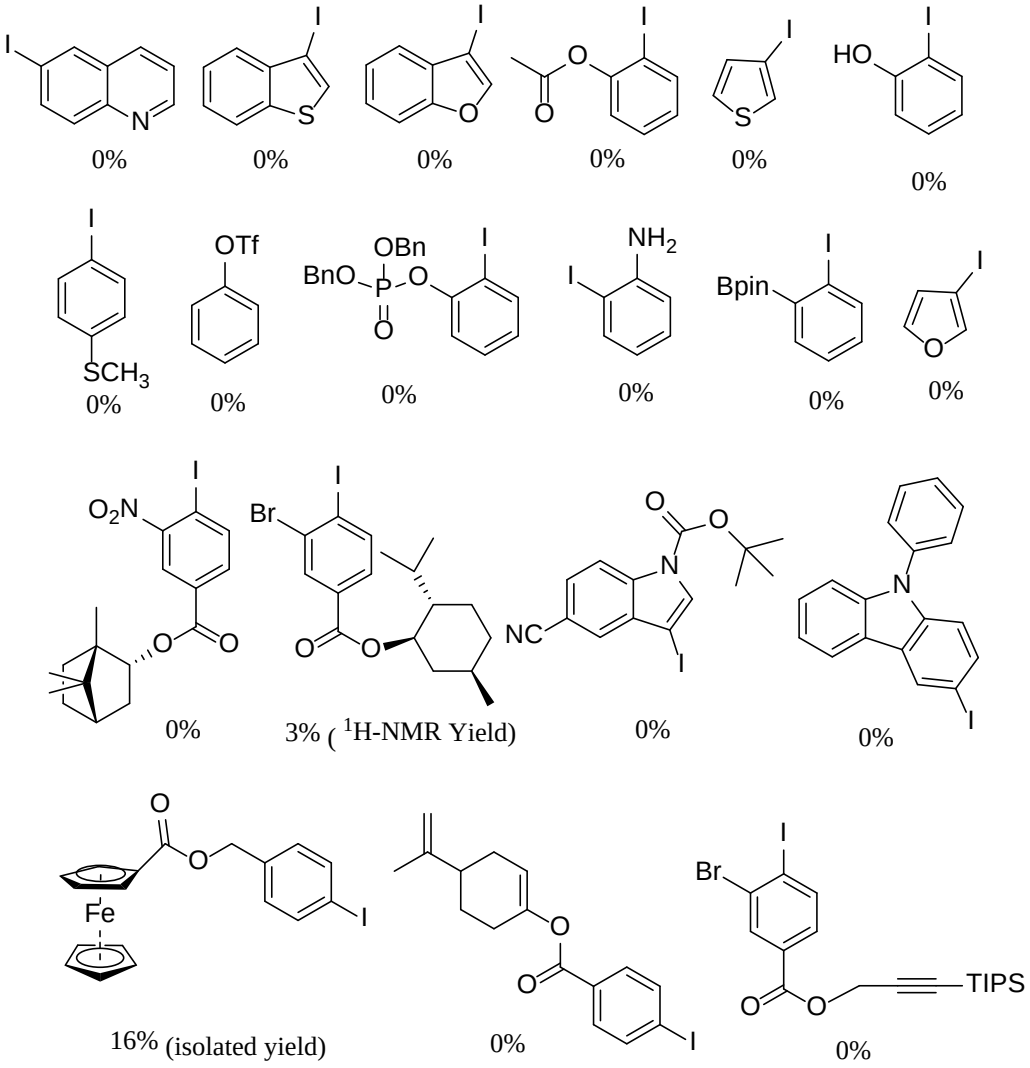


Figure S1. Some incompatible substrates.

8. References

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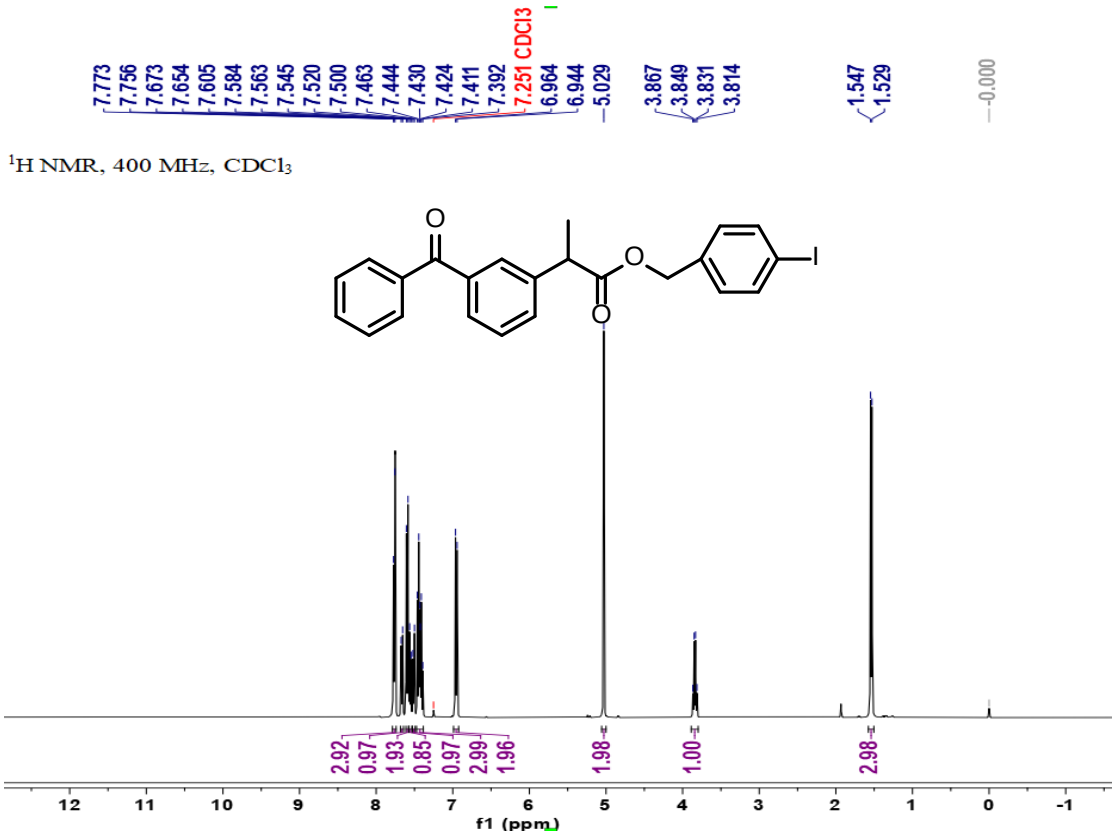
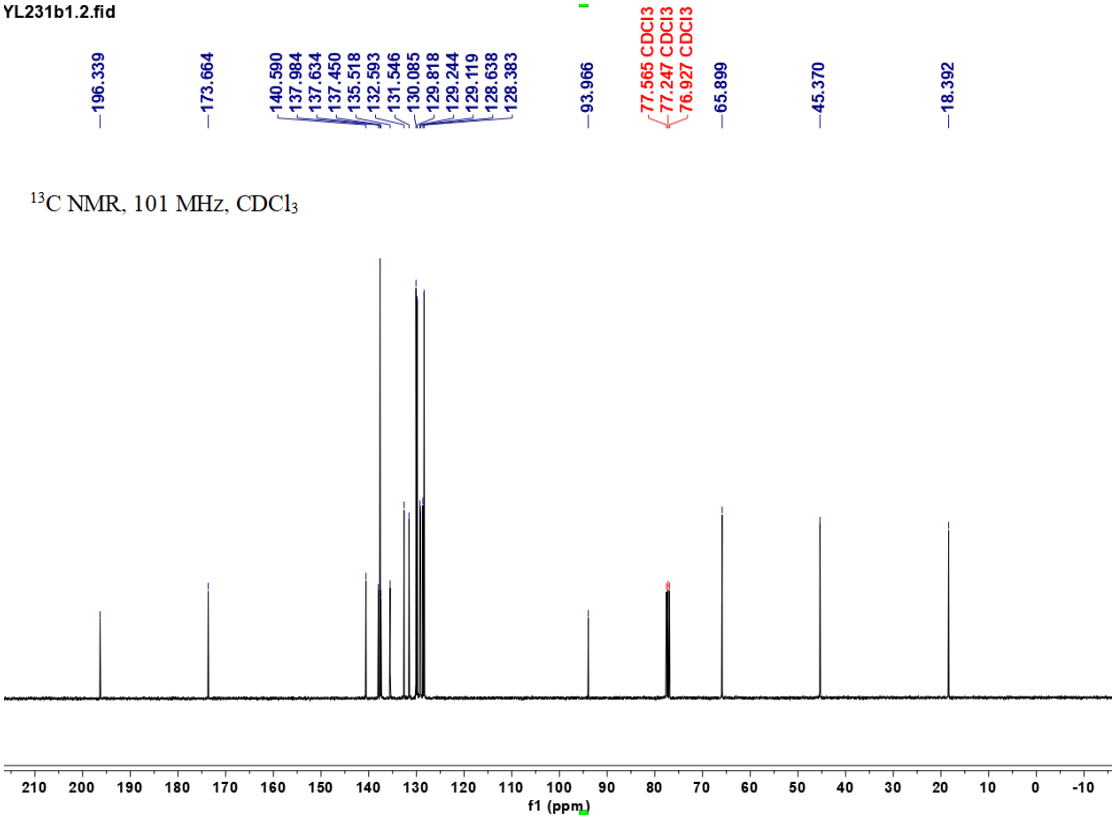
9. NMR Spectra

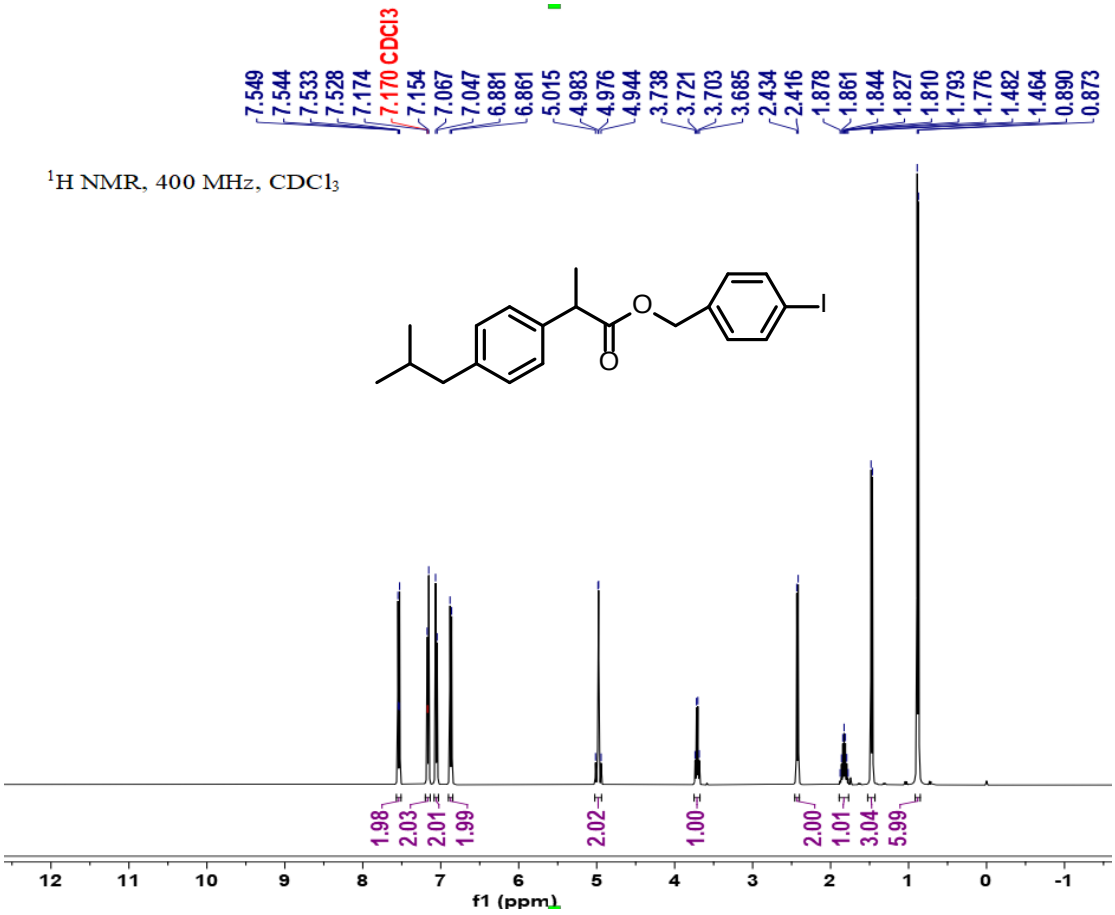


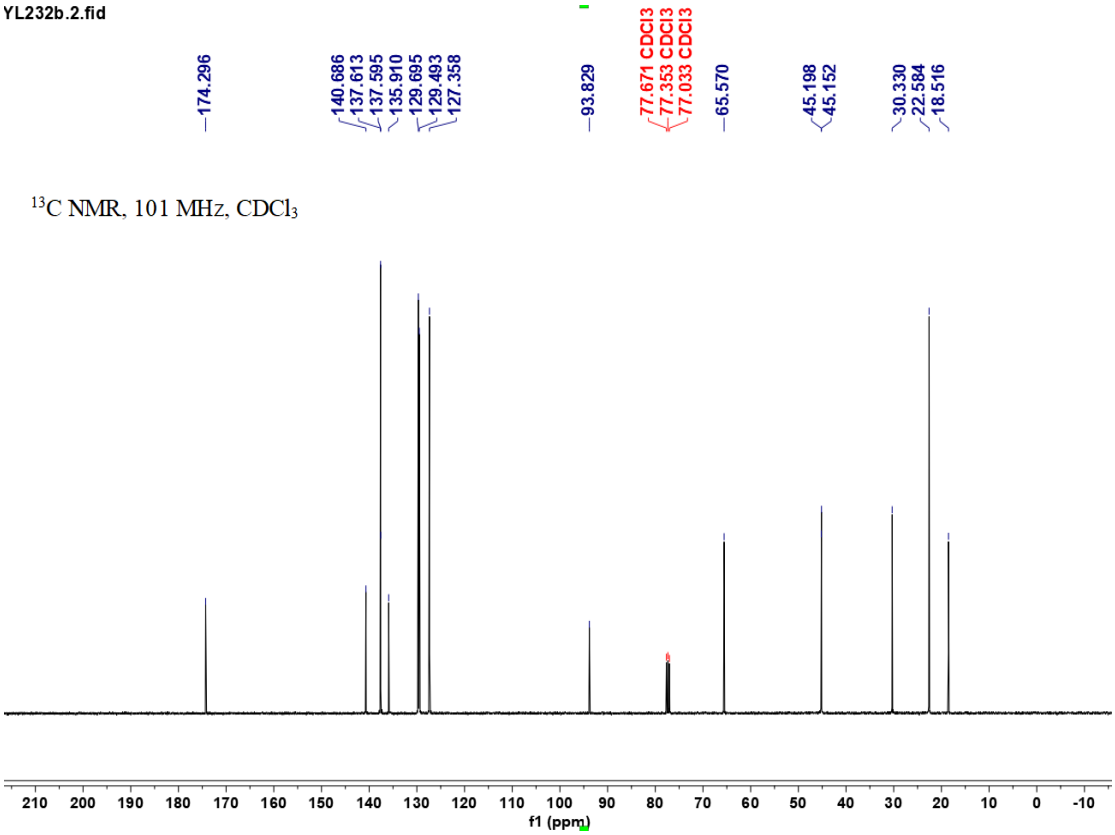
^{1}H NMR, 400 MHz, $CDCl_3$



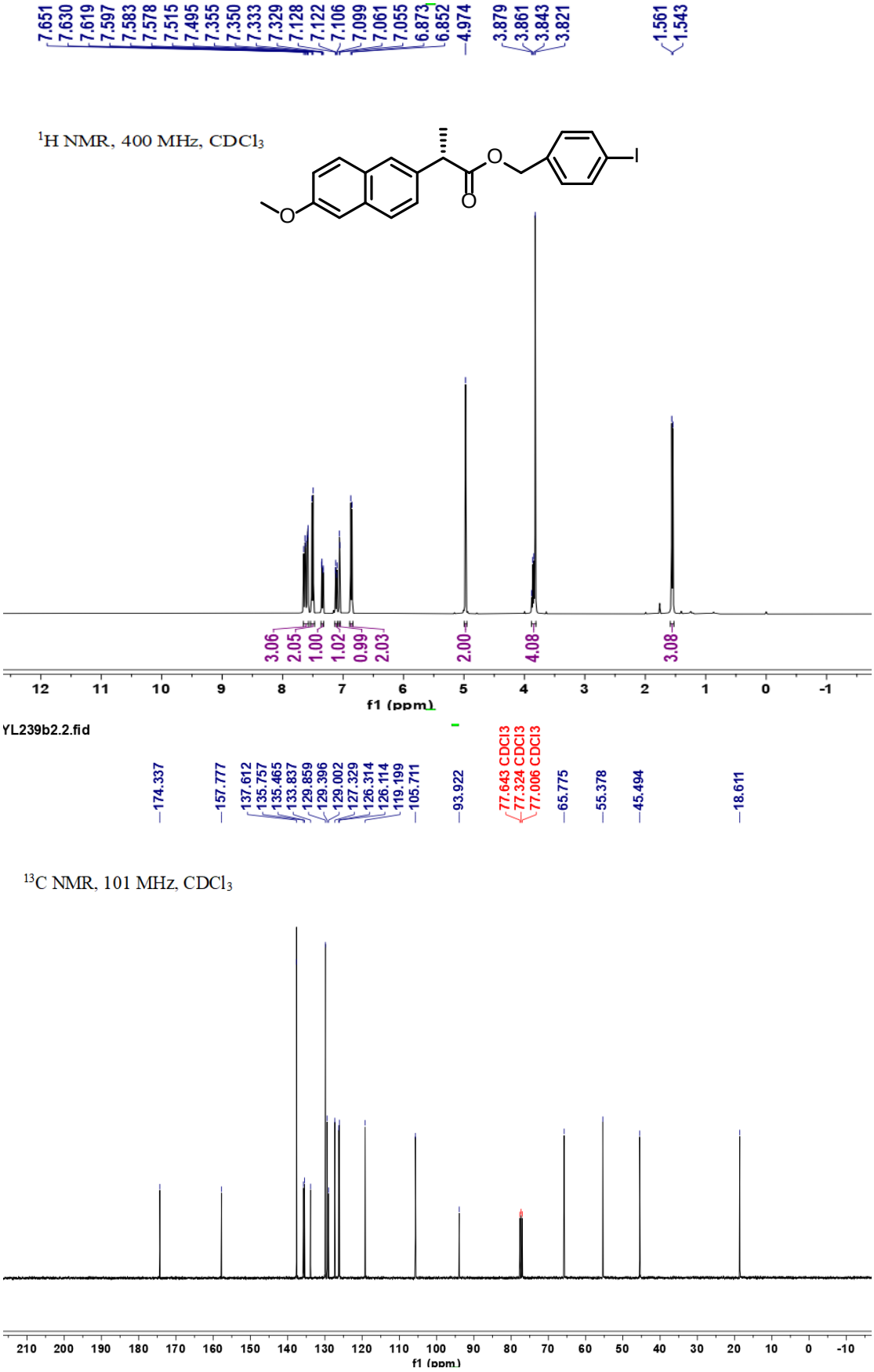
^{13}C NMR, 101 MHz, $CDCl_3$

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **6-58**

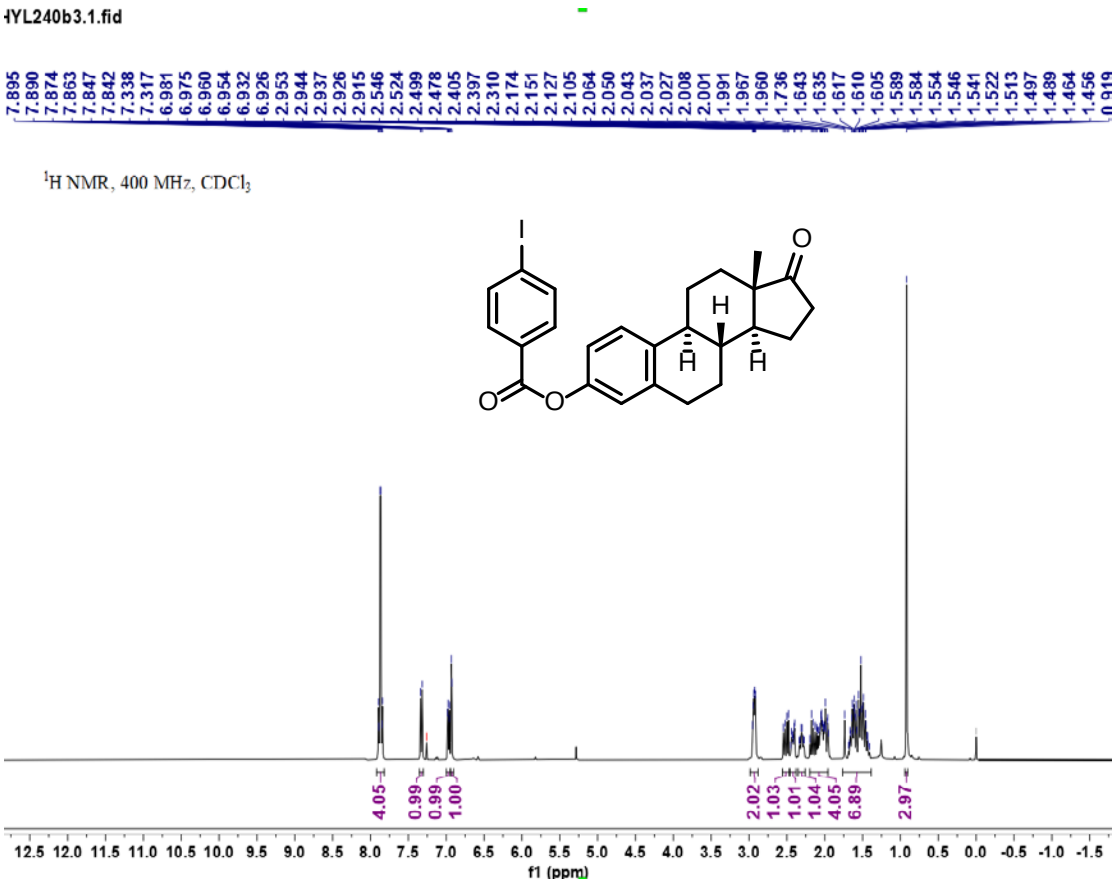




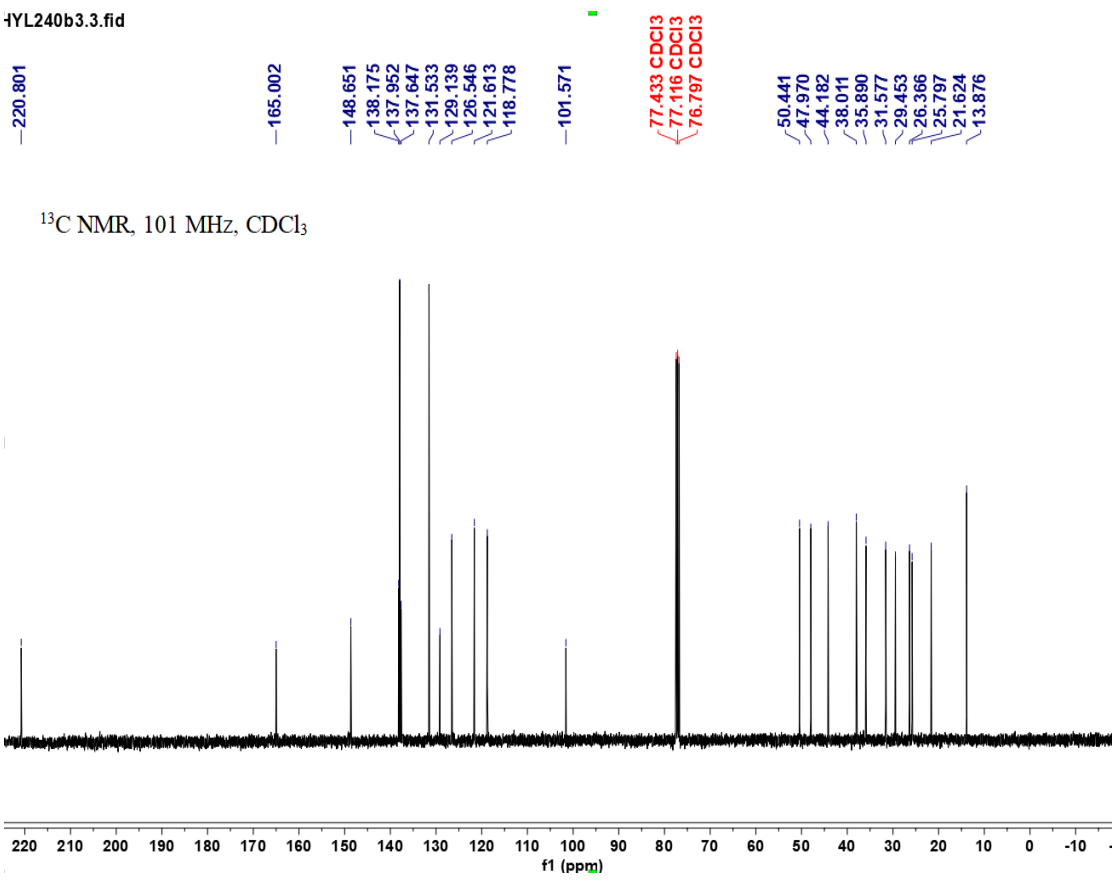
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **6-59**



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **6-60**

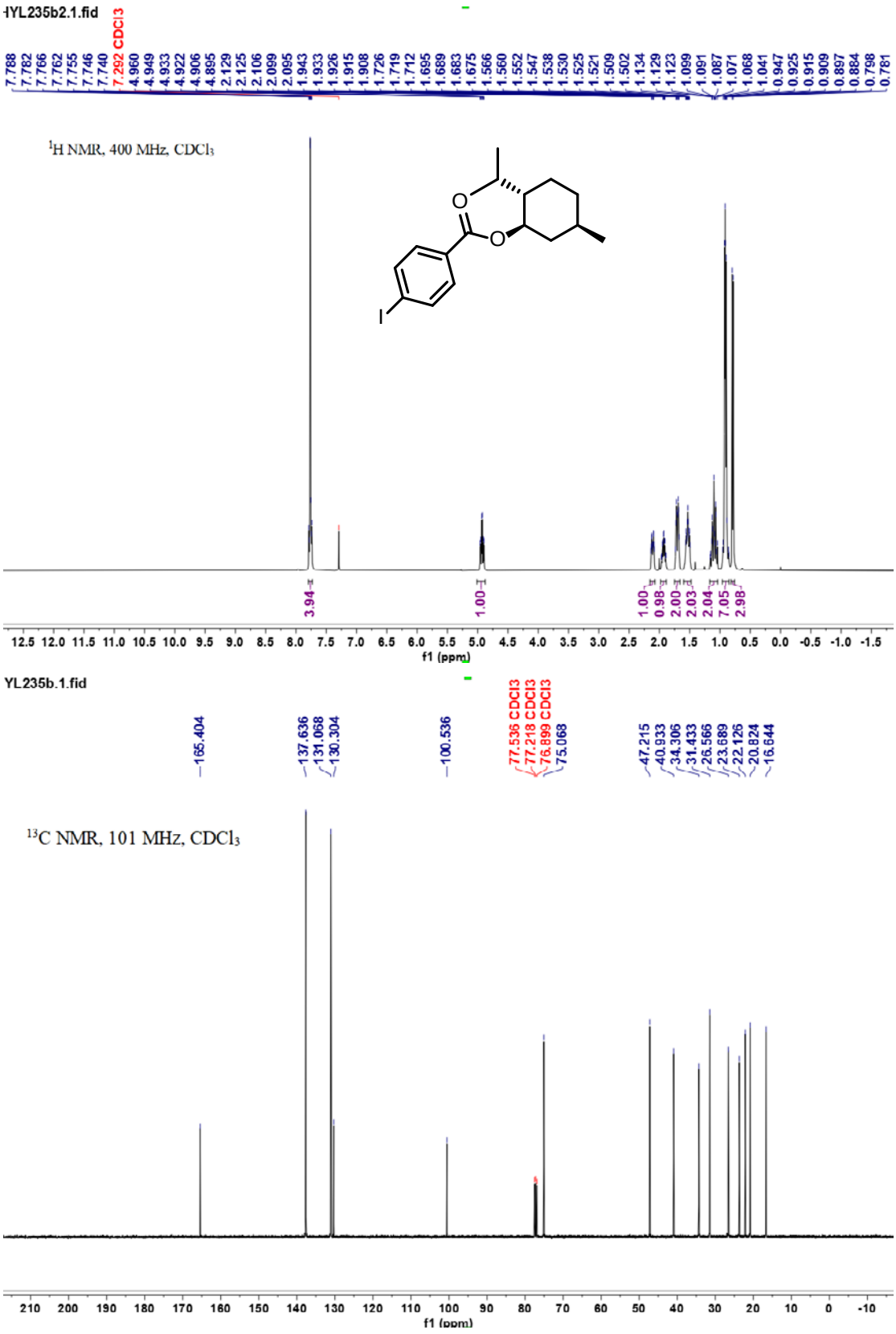


^{1}H NMR, 400 MHz, $CDCl_3$

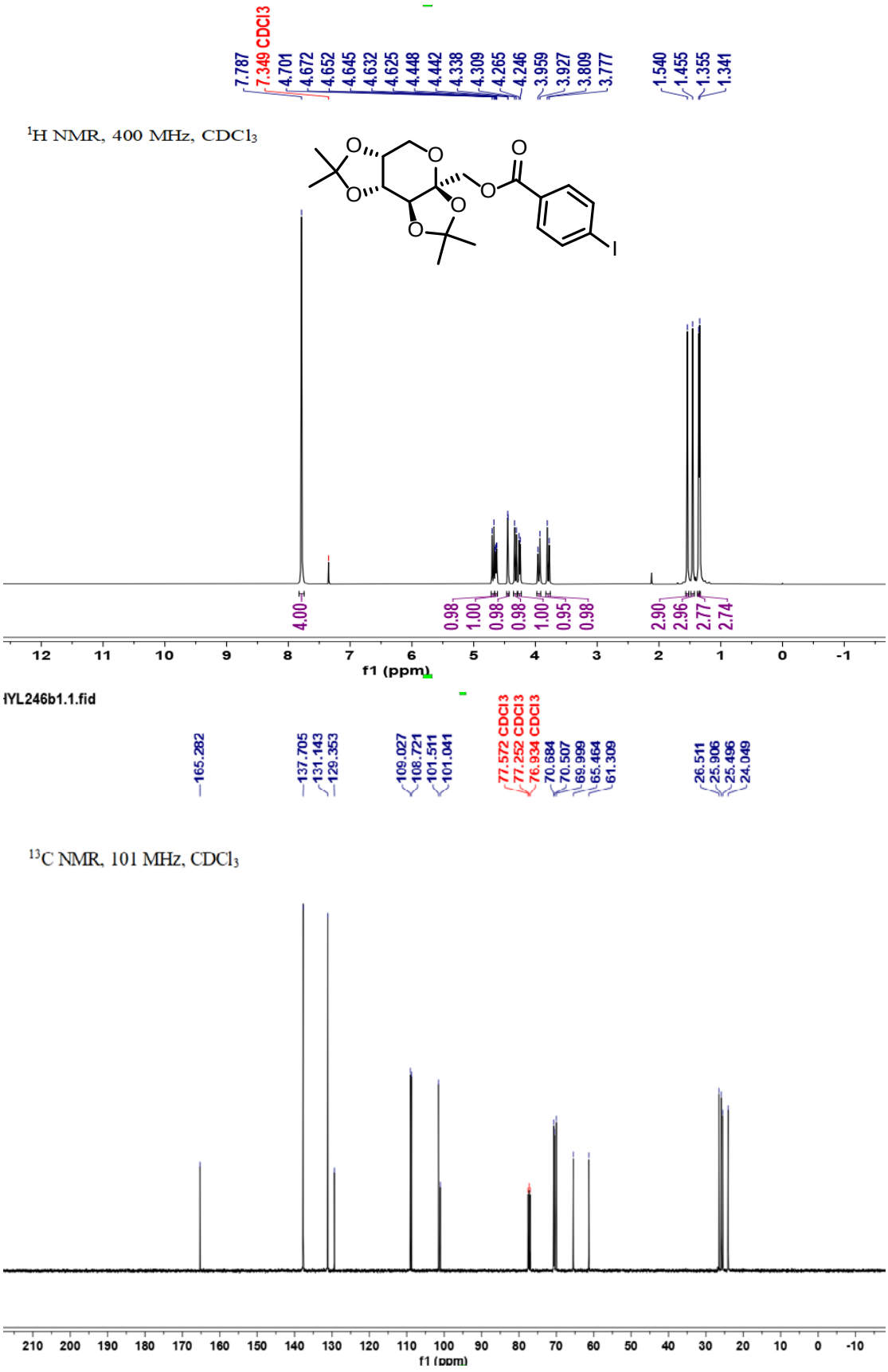


^{13}C NMR, 101 MHz, $CDCl_3$

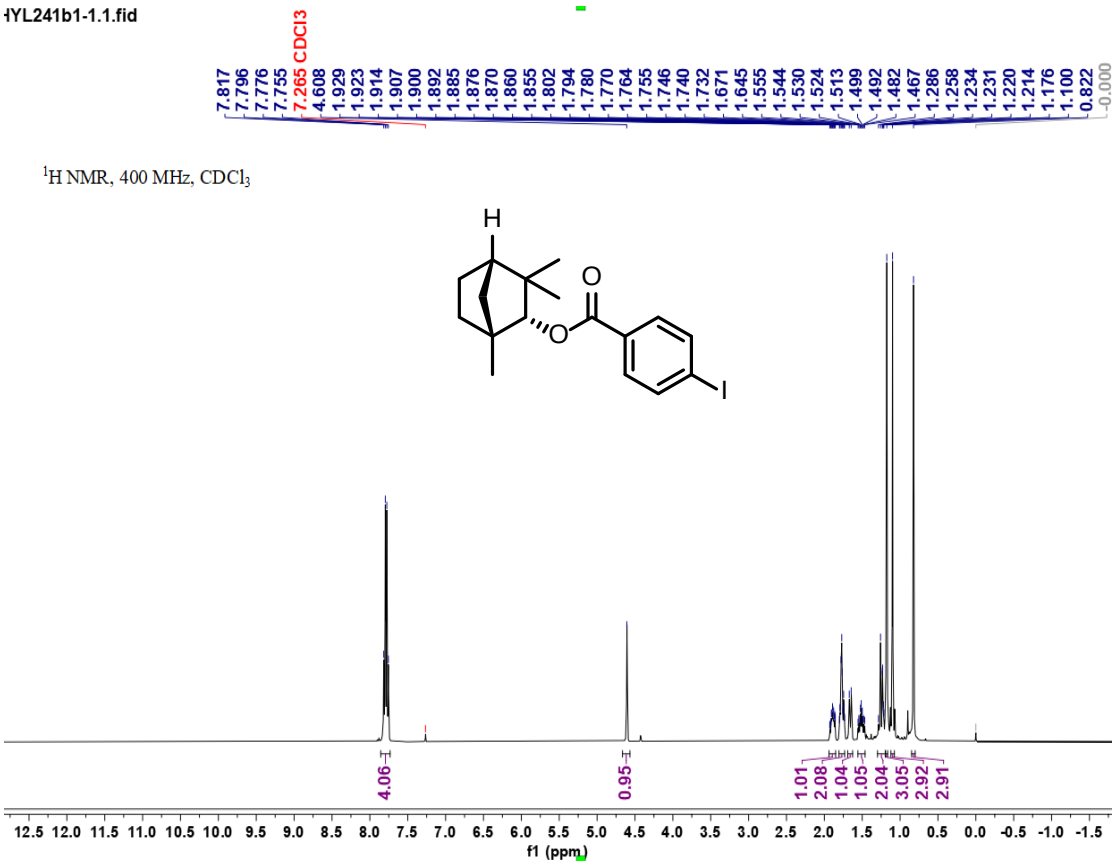
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **6-61**



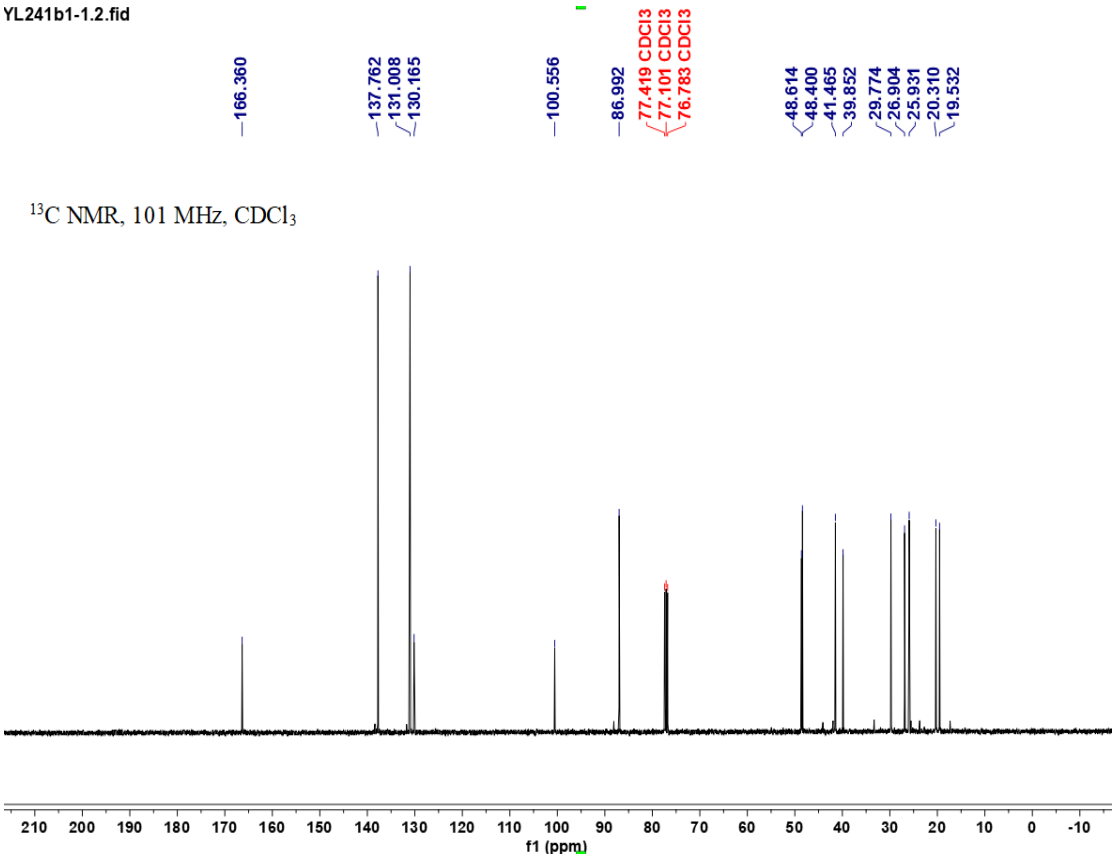
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **6-62**



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **6-63**

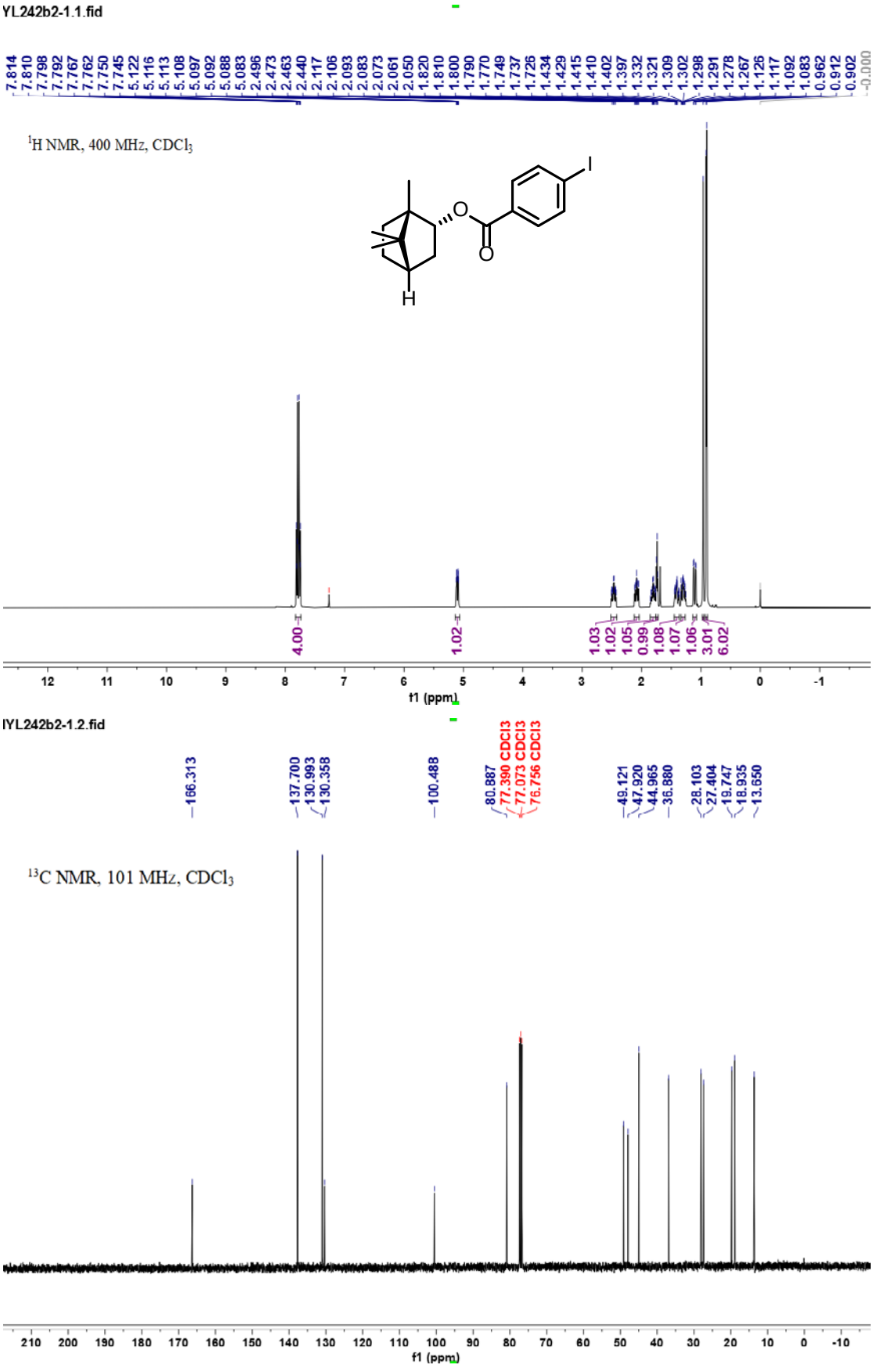


^{1}H NMR, 400 MHz, $CDCl_3$

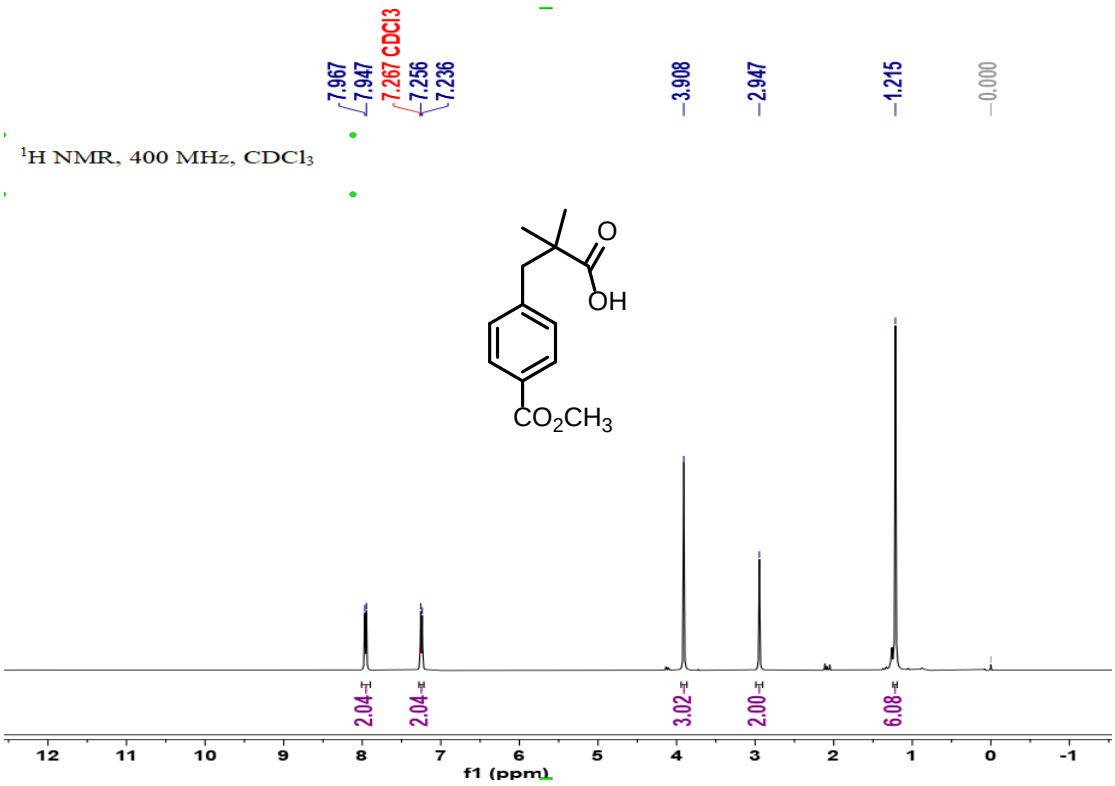


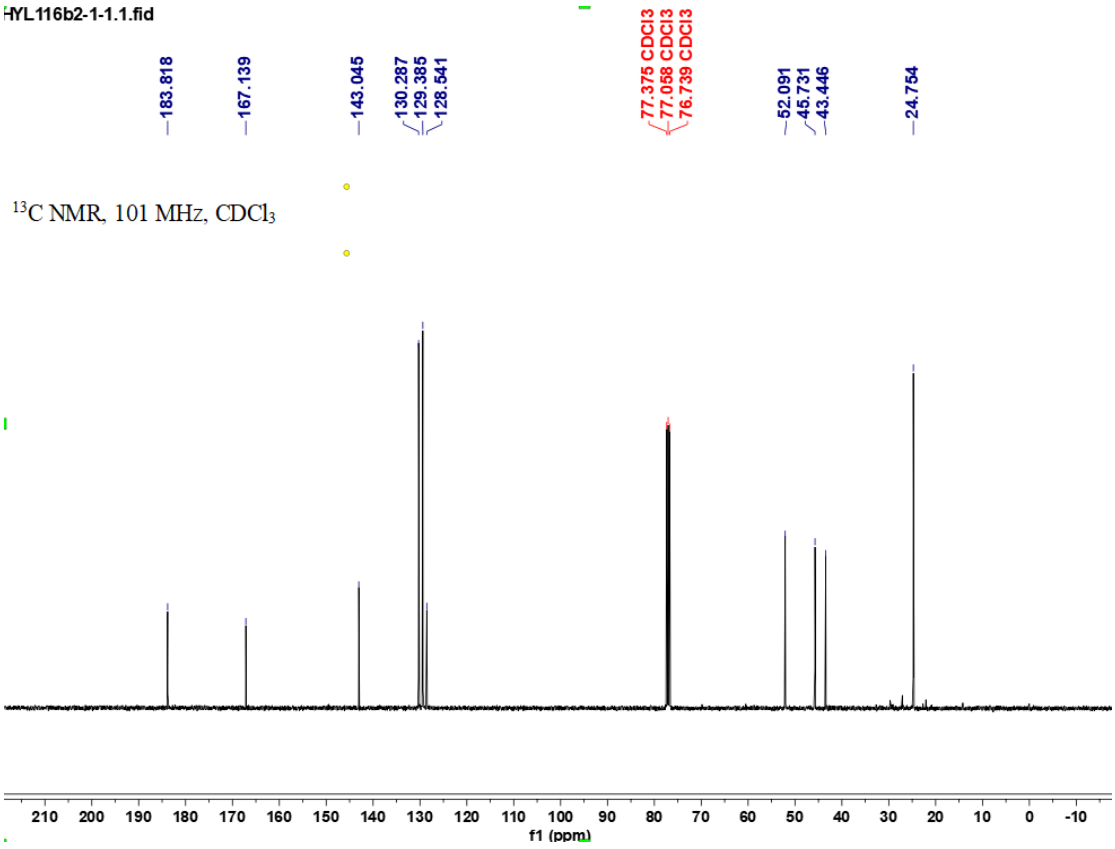
^{13}C NMR, 101 MHz, $CDCl_3$

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **6-64**

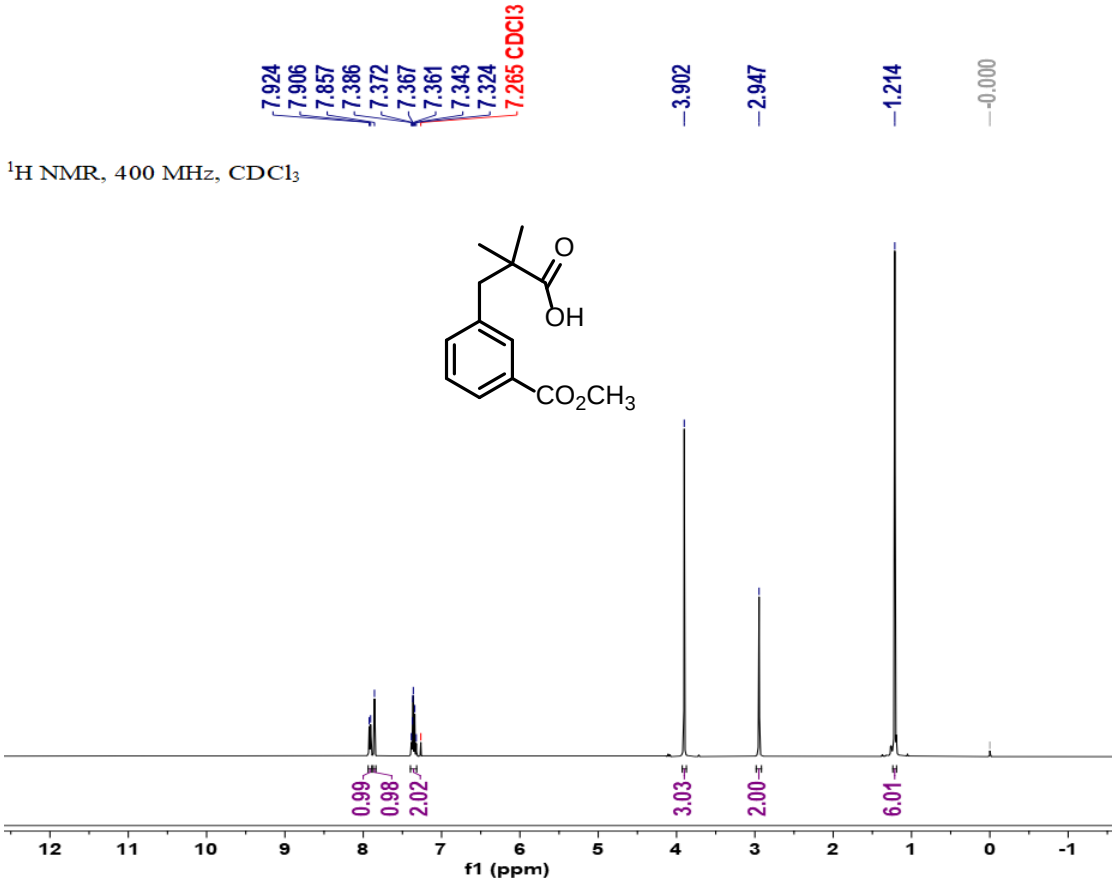


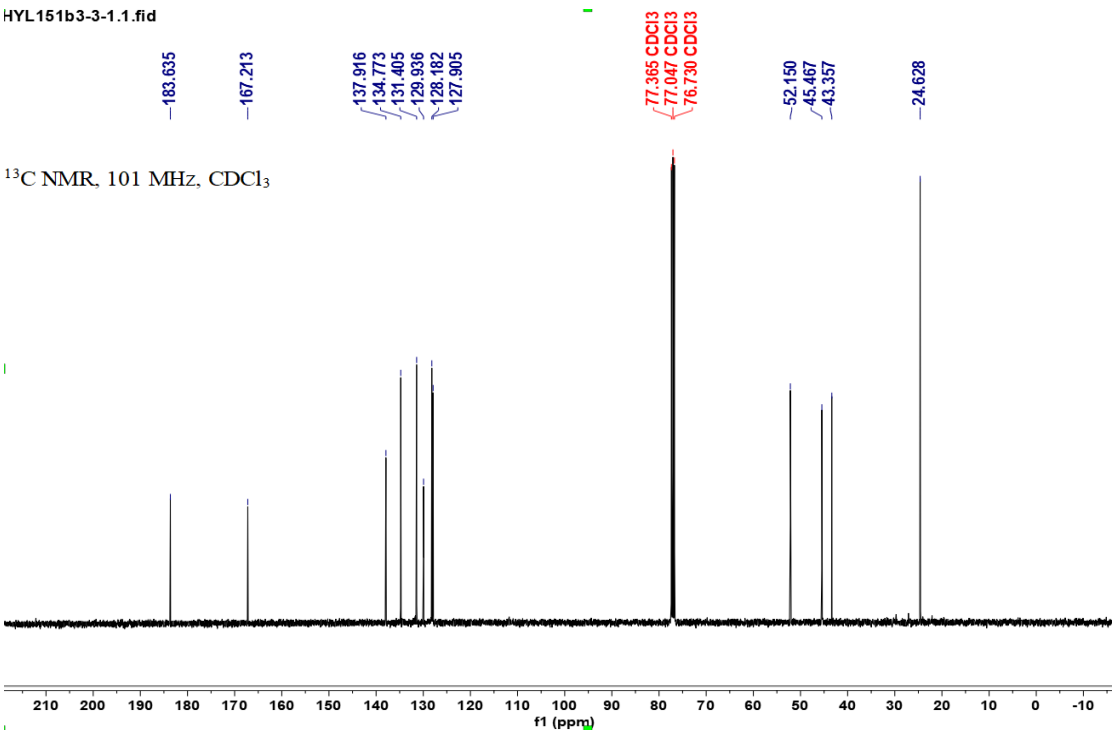
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **6-65**



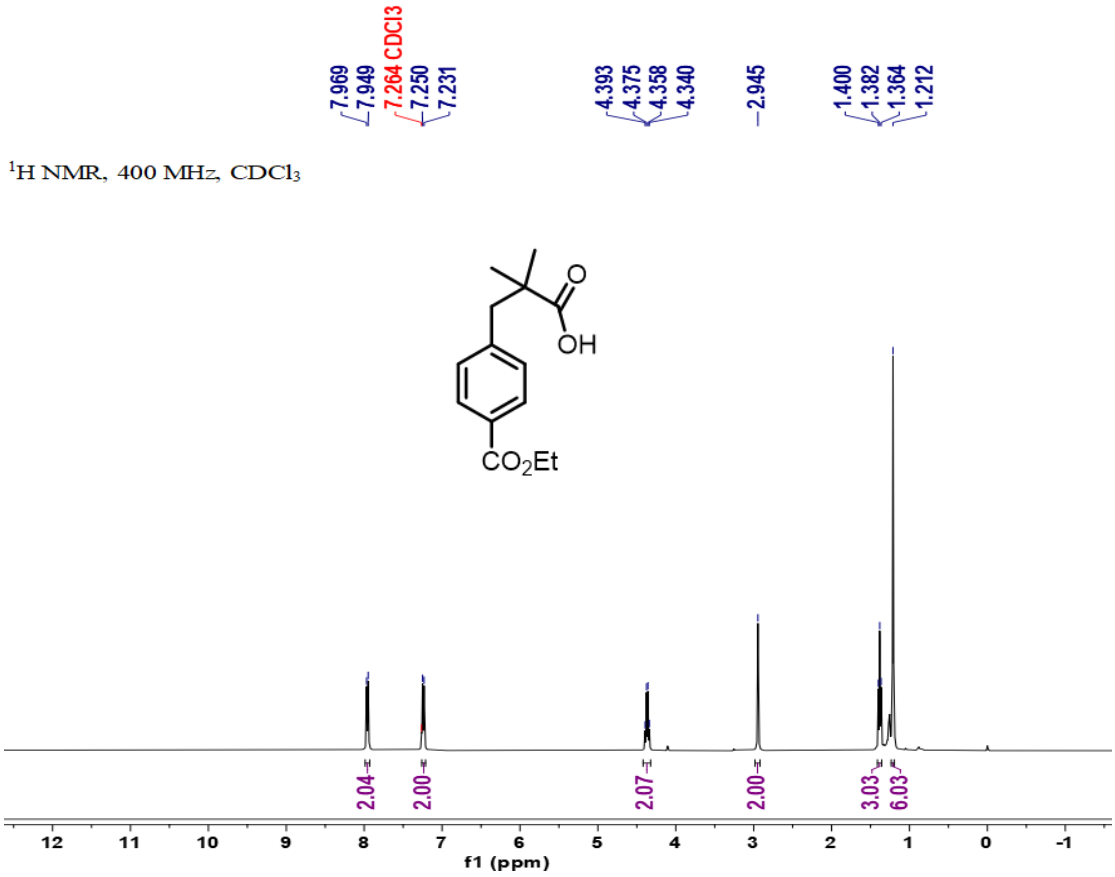


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-1**

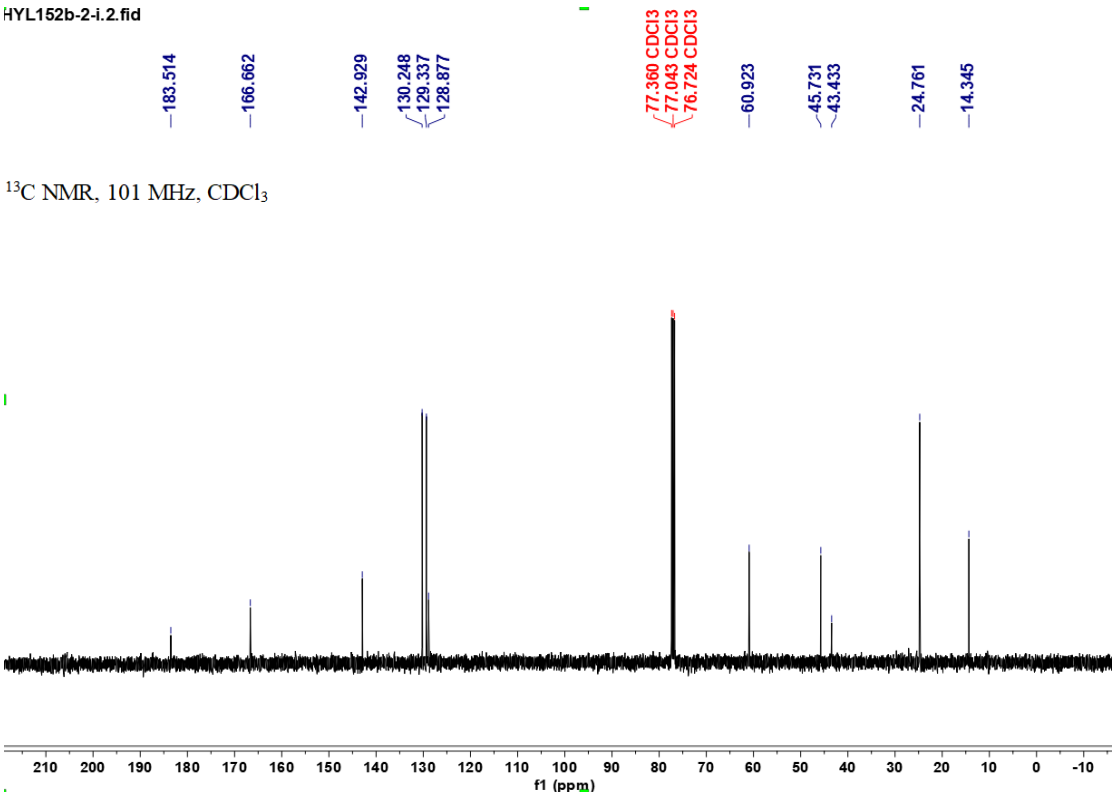




^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-2**

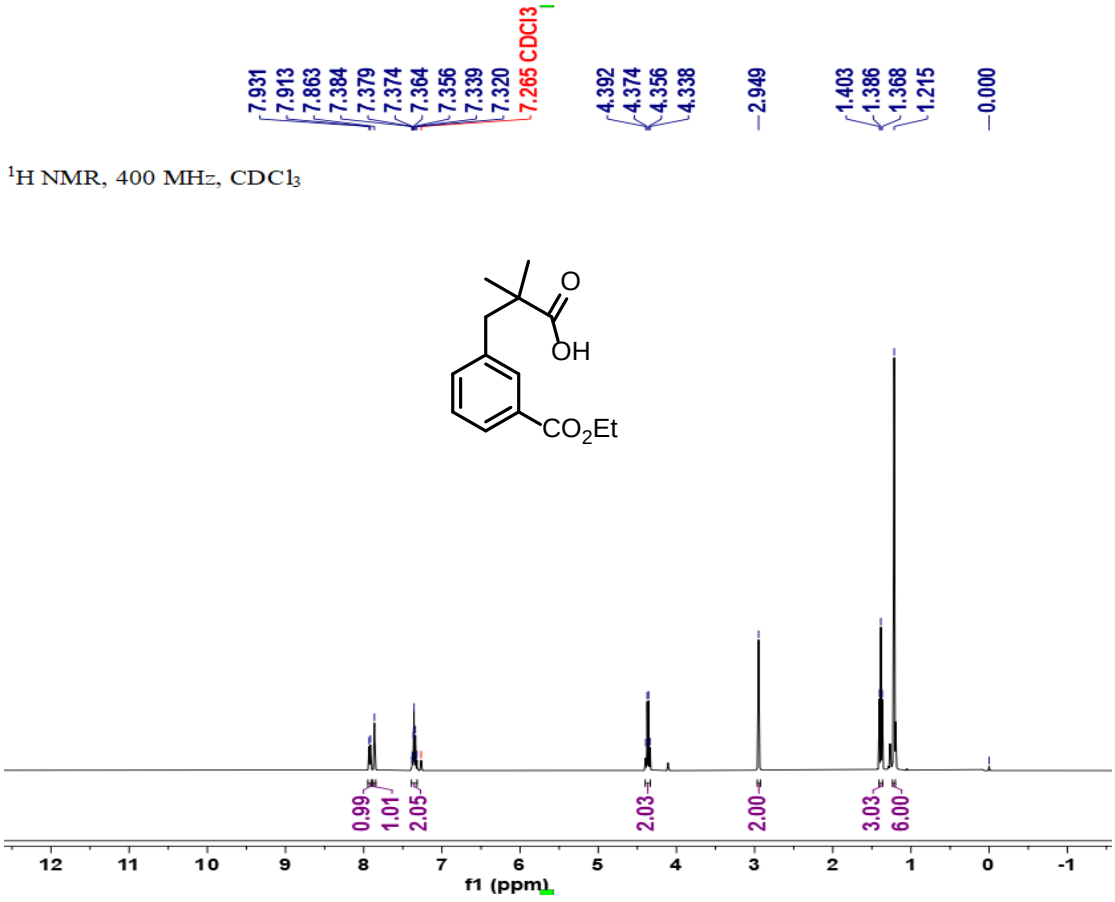


^{1}H NMR, 400 MHz, $CDCl_3$

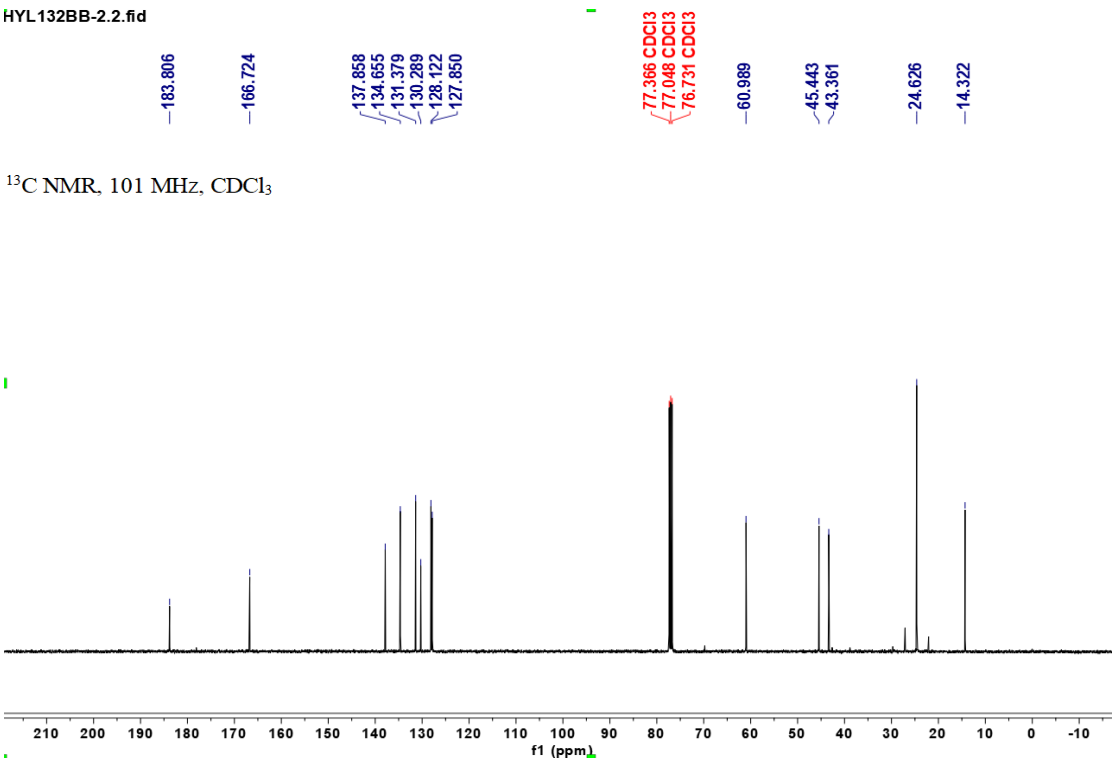


^{13}C NMR, 101 MHz, $CDCl_3$

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-3**

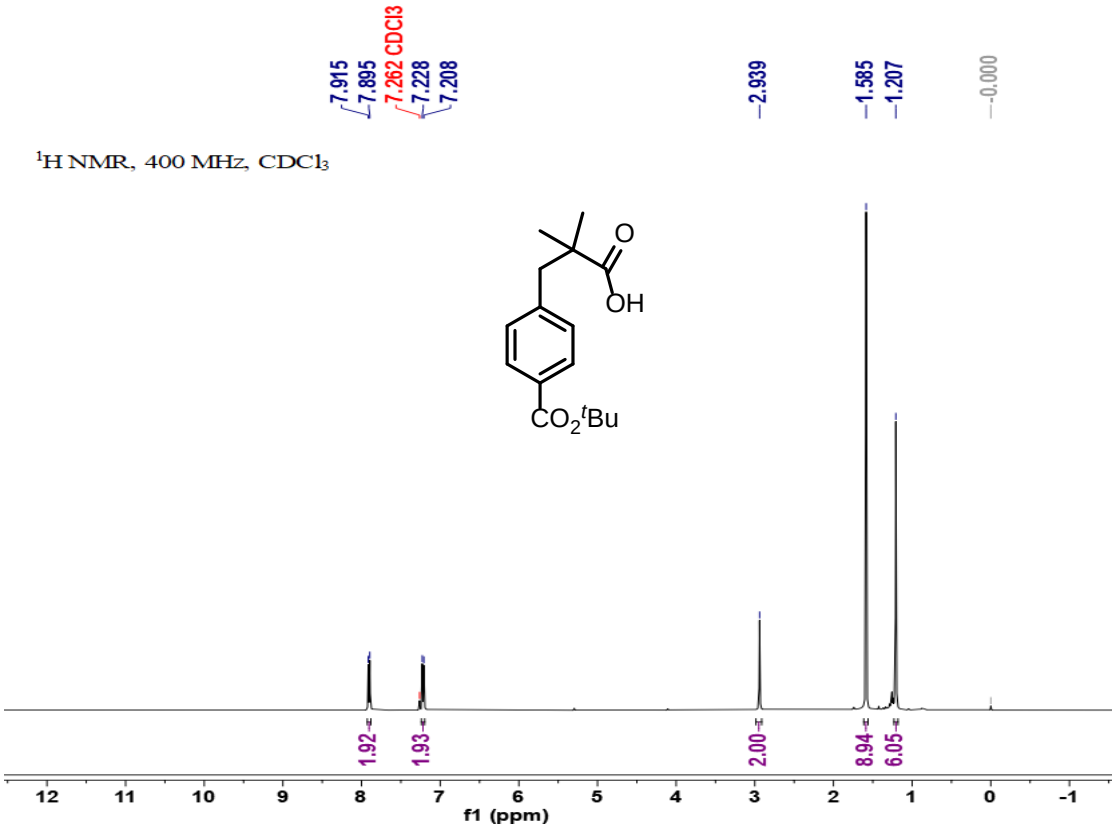


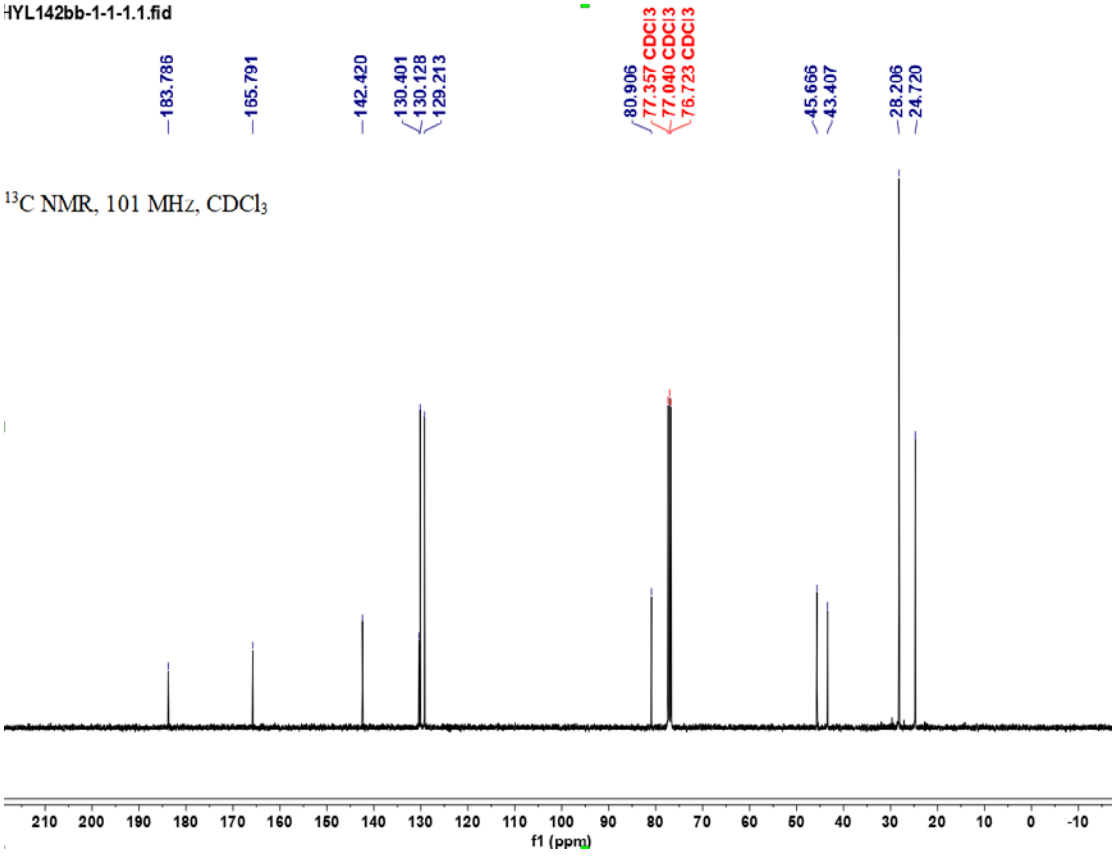
^{1}H NMR, 400 MHz, $CDCl_3$



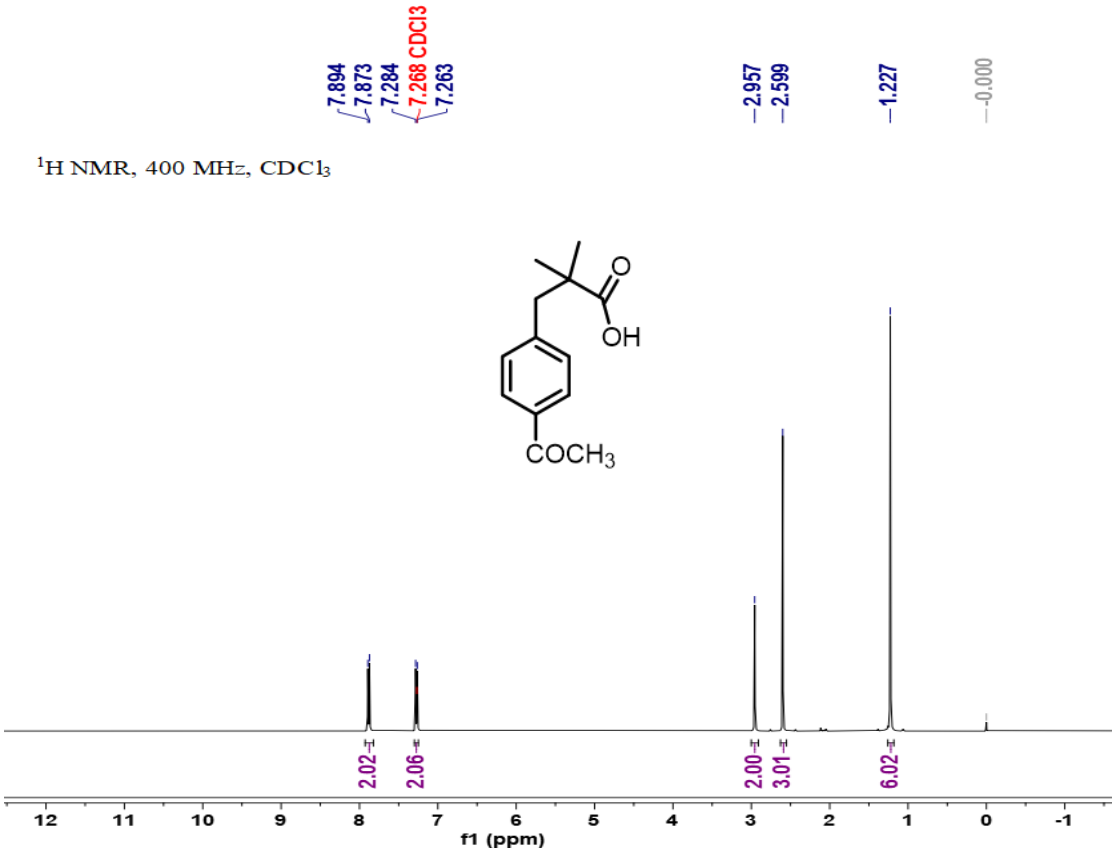
^{13}C NMR, 101 MHz, $CDCl_3$

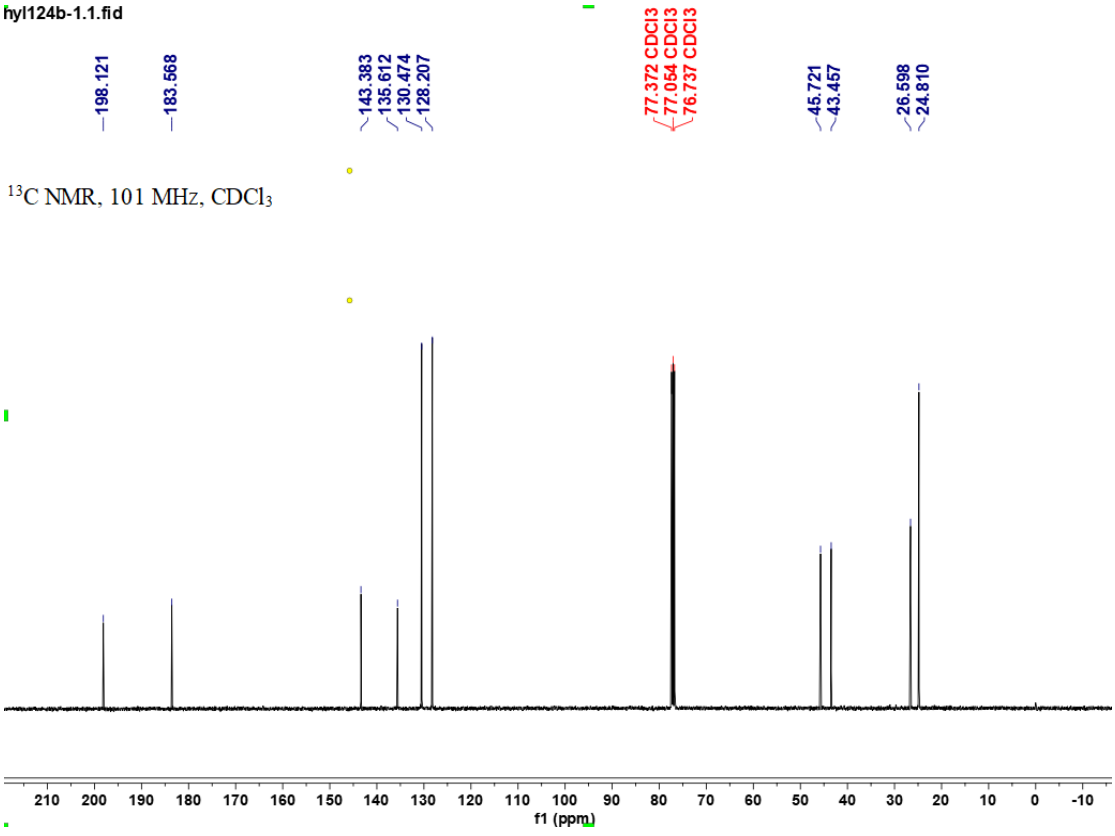
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-4**



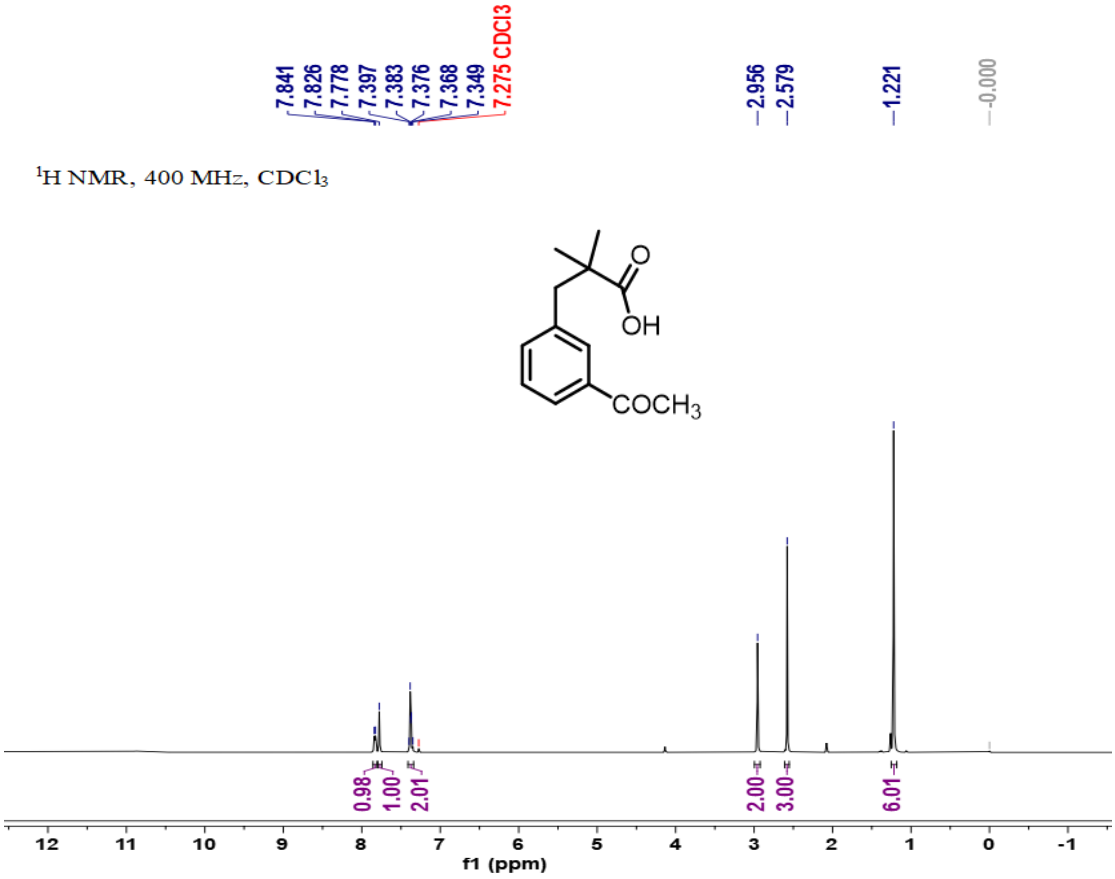


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-5**

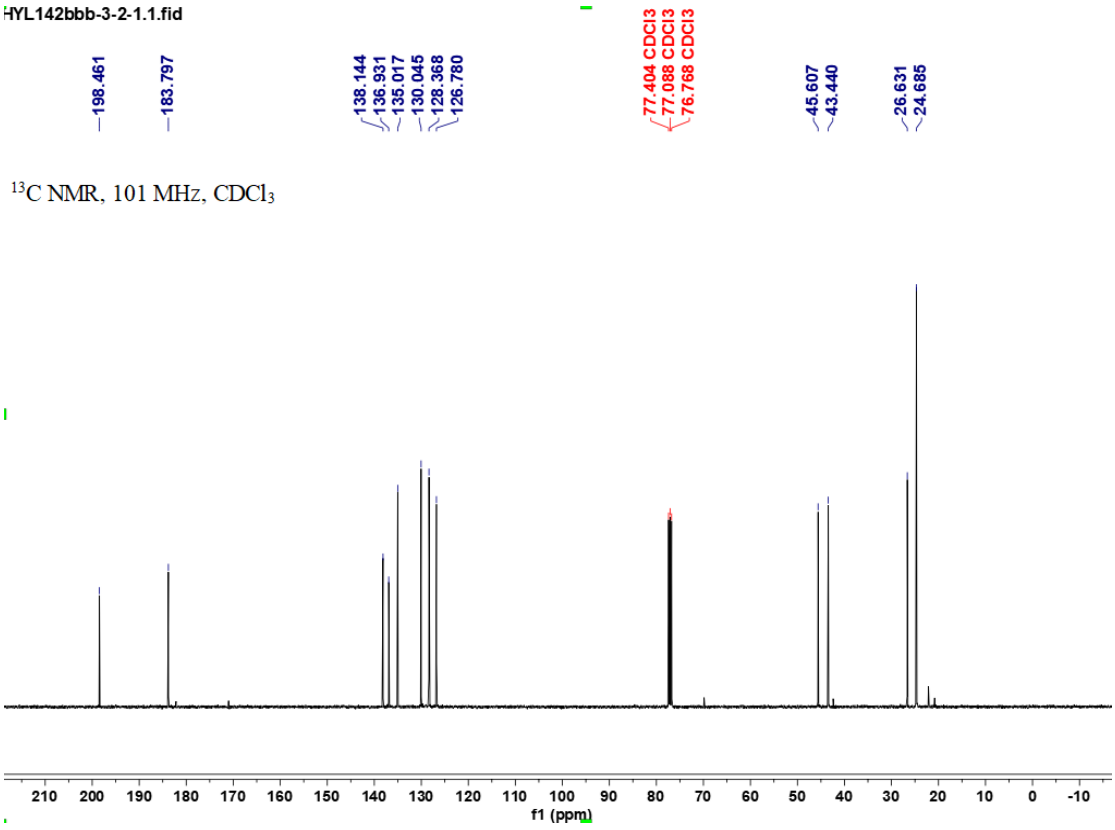




^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 7-6

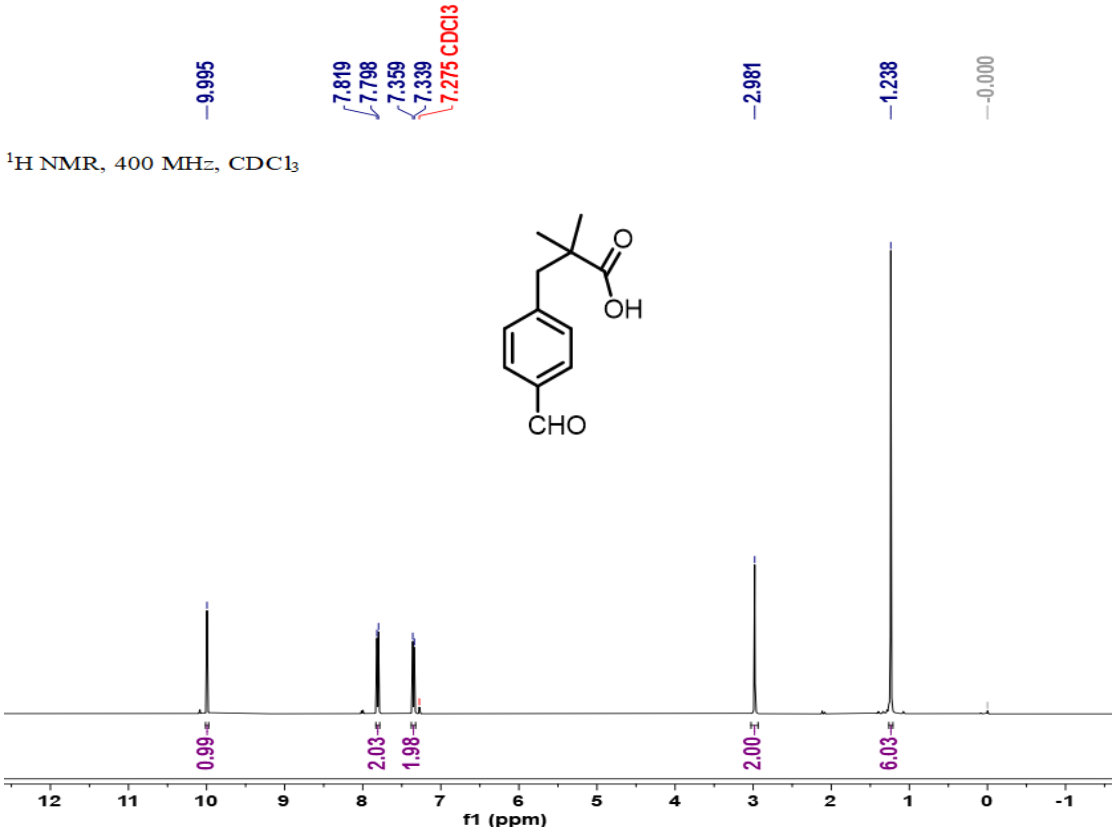


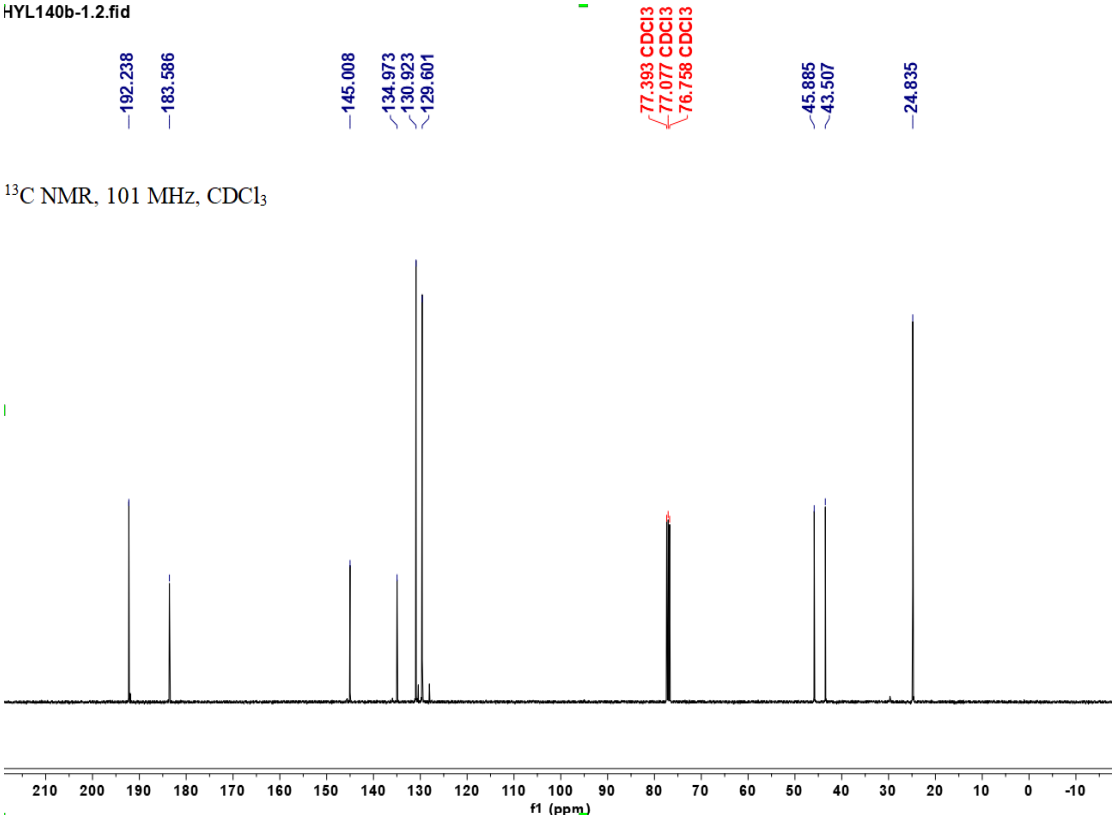
^{1}H NMR, 400 MHz, $CDCl_3$



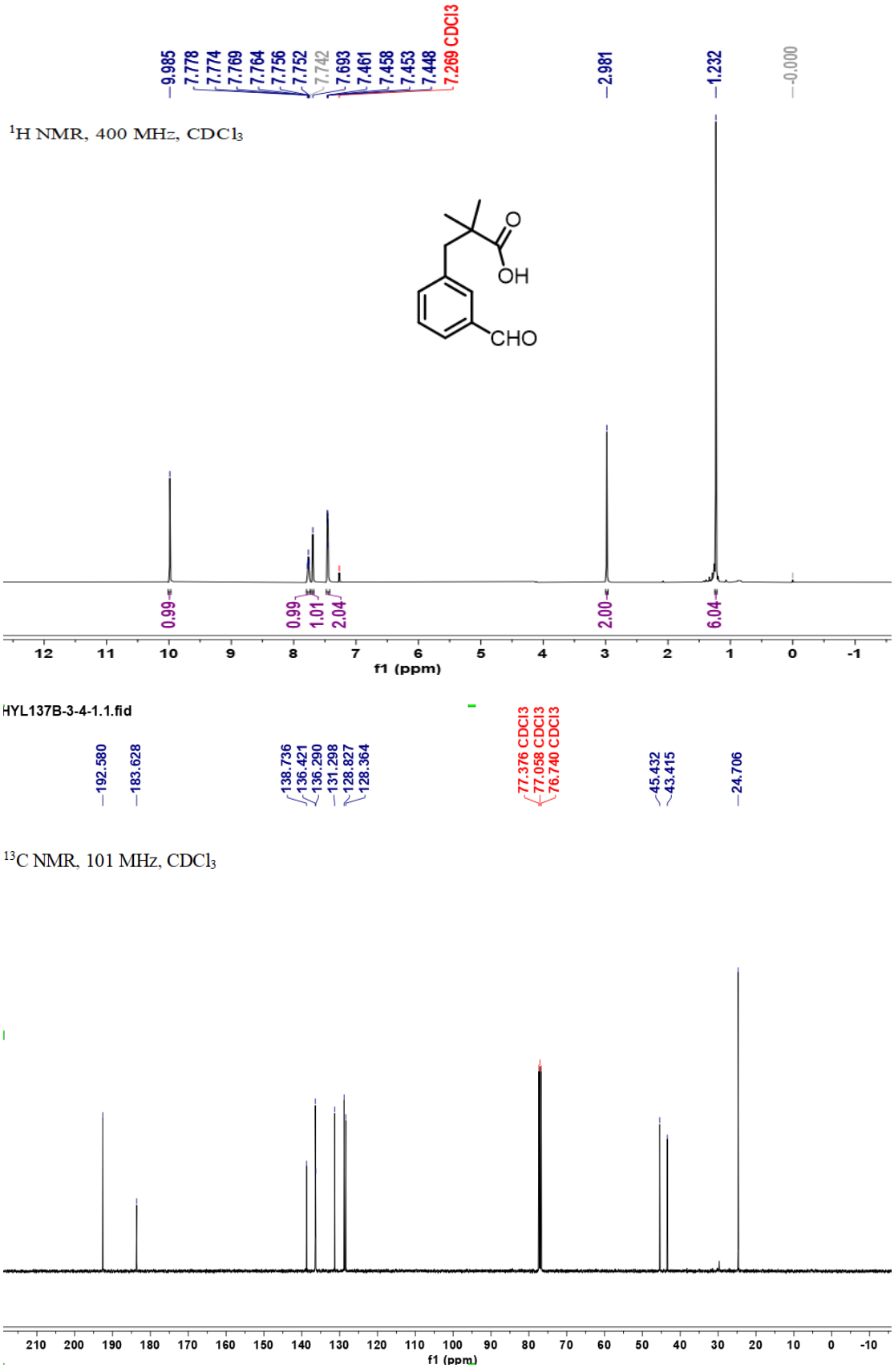
^{13}C NMR, 101 MHz, $CDCl_3$

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-7**

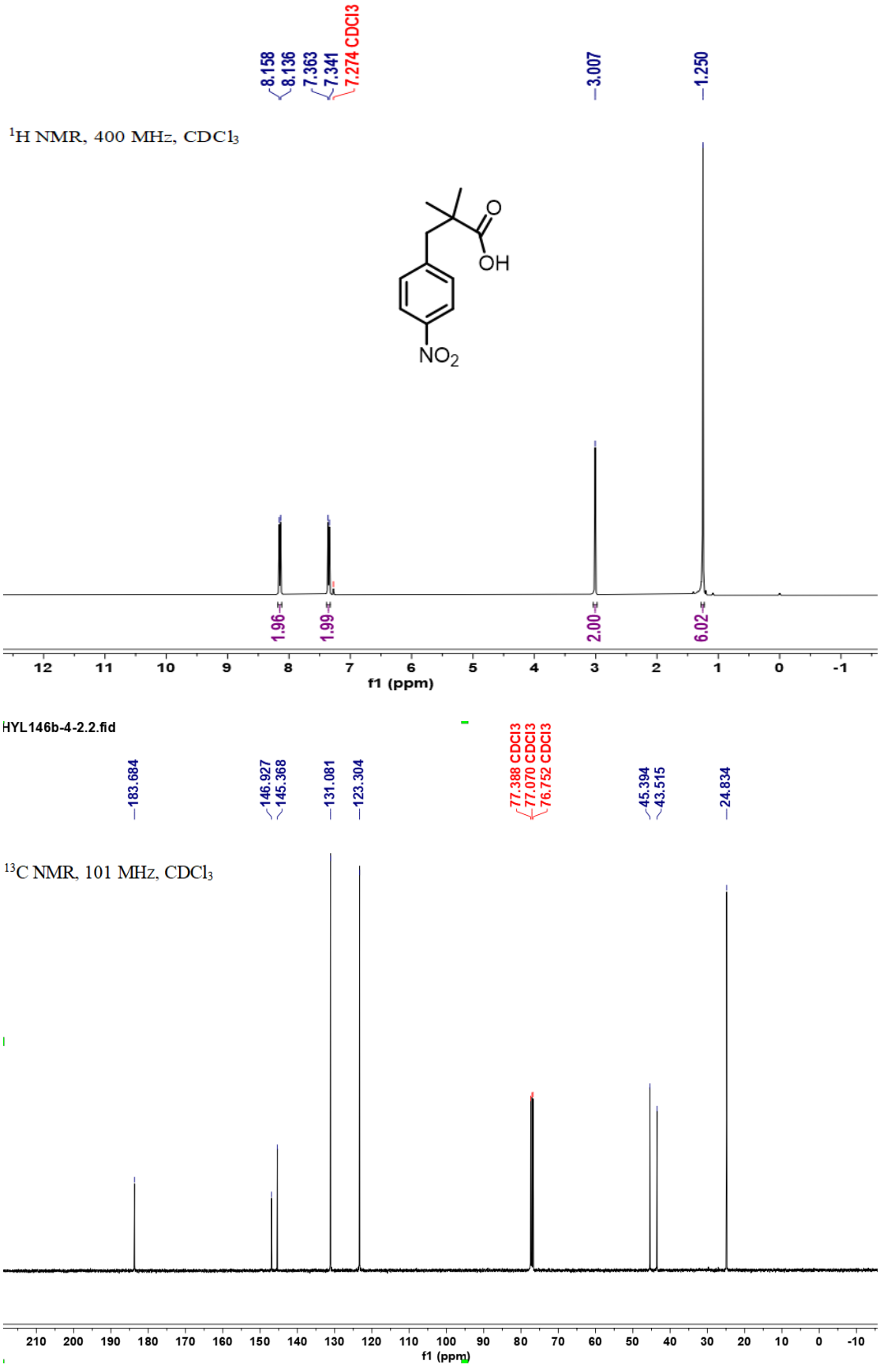




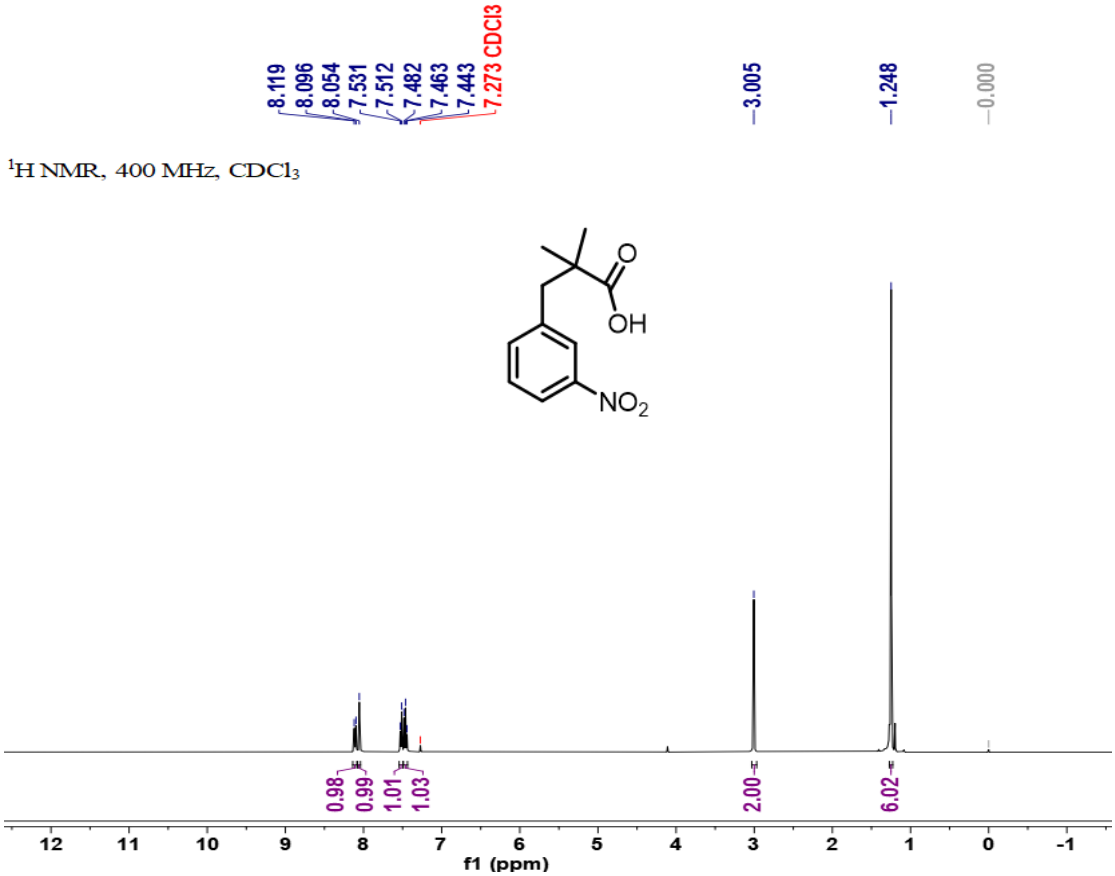
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-8**

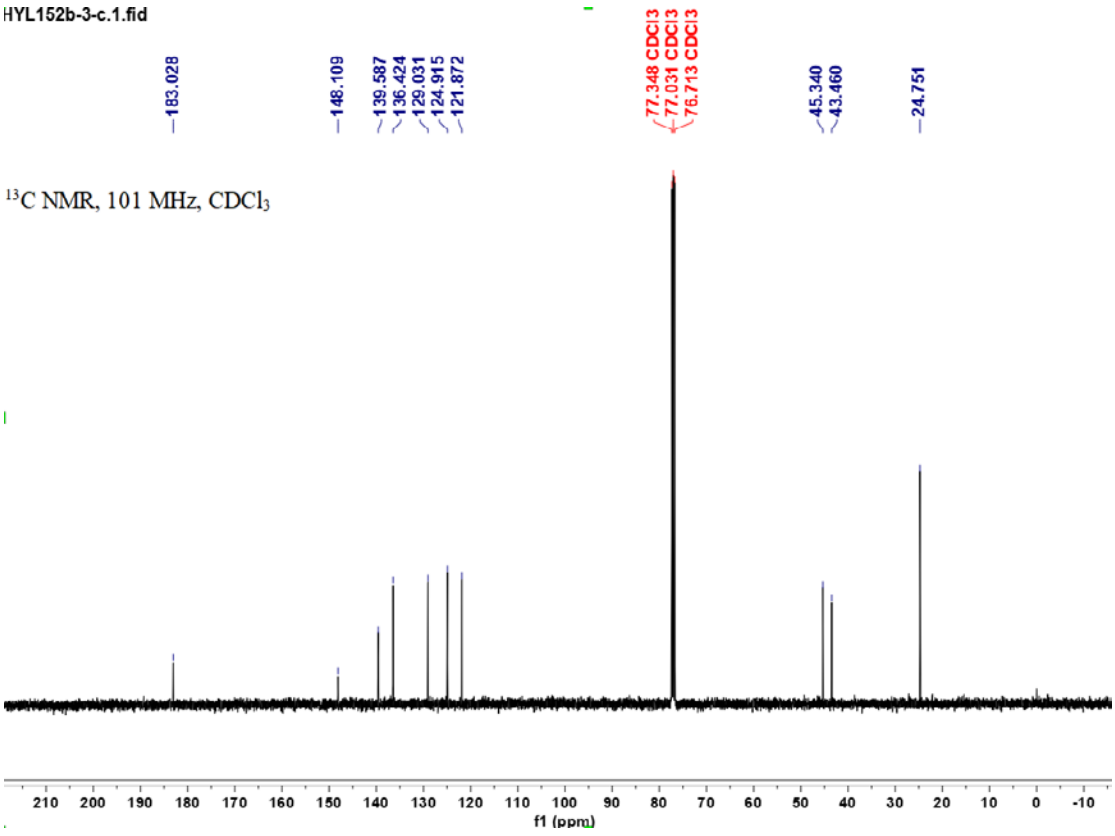


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-9**

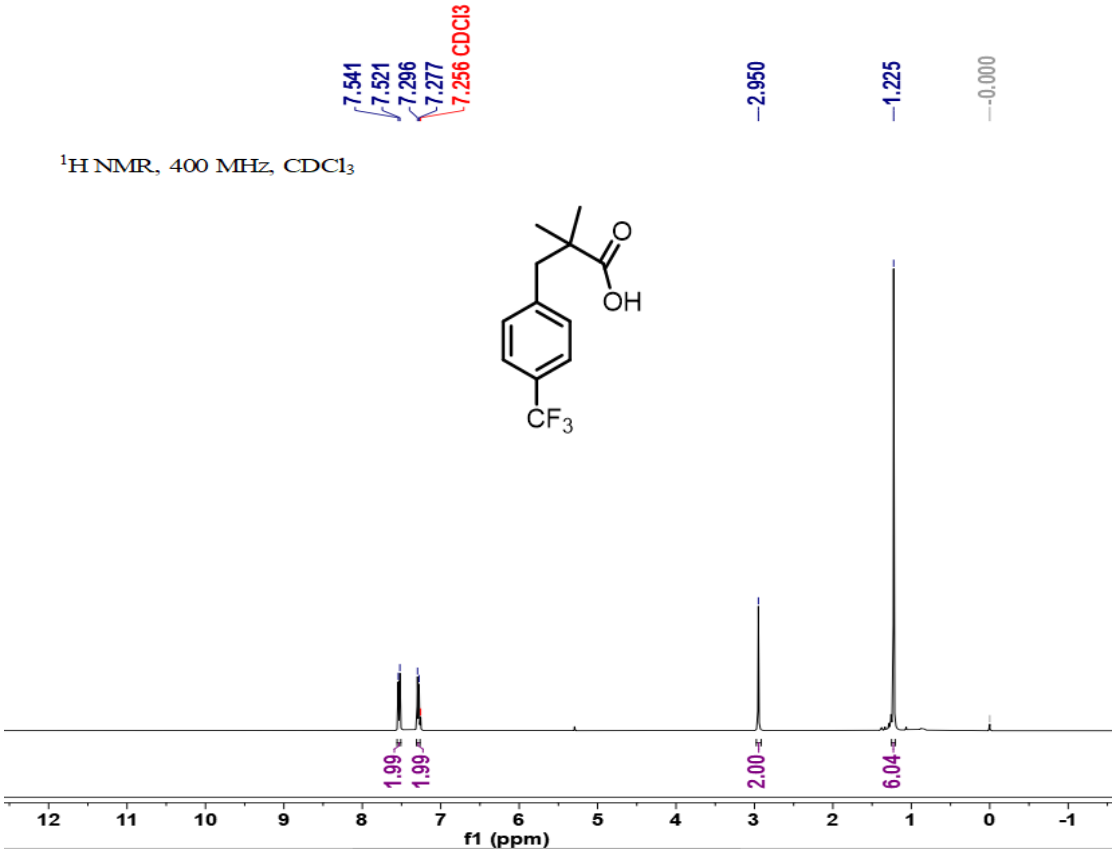


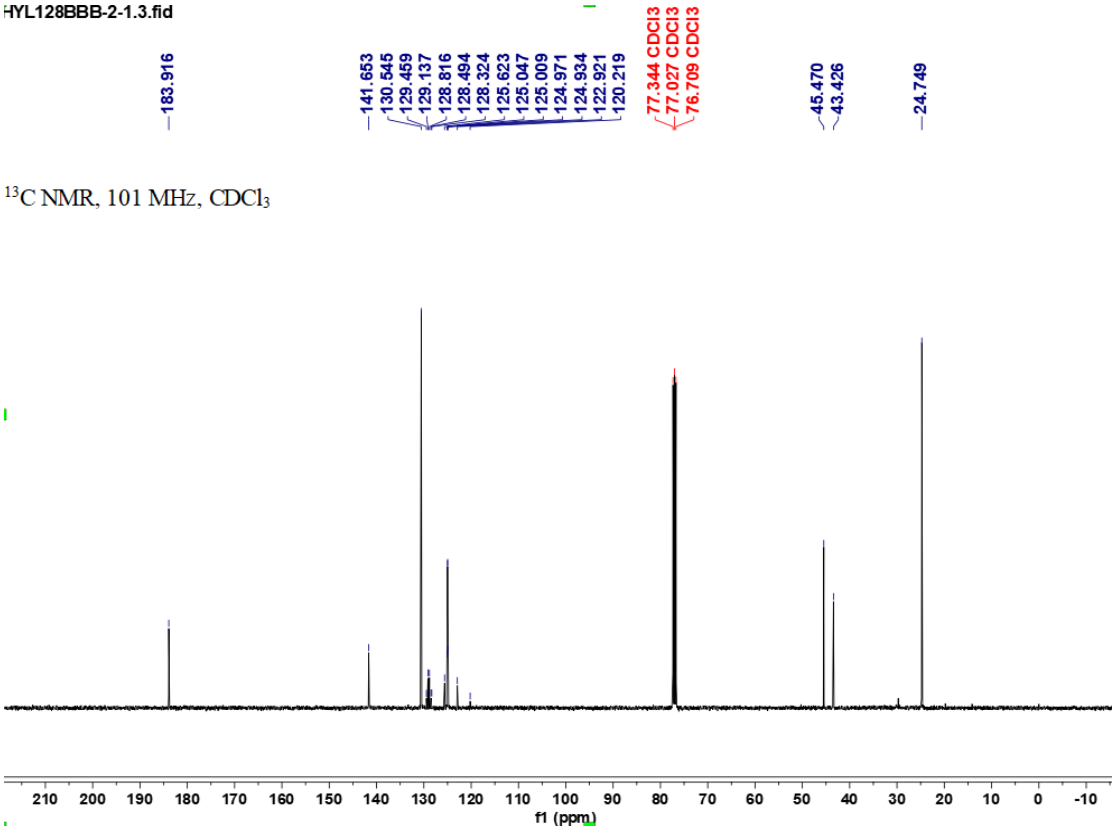
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7**-**10**

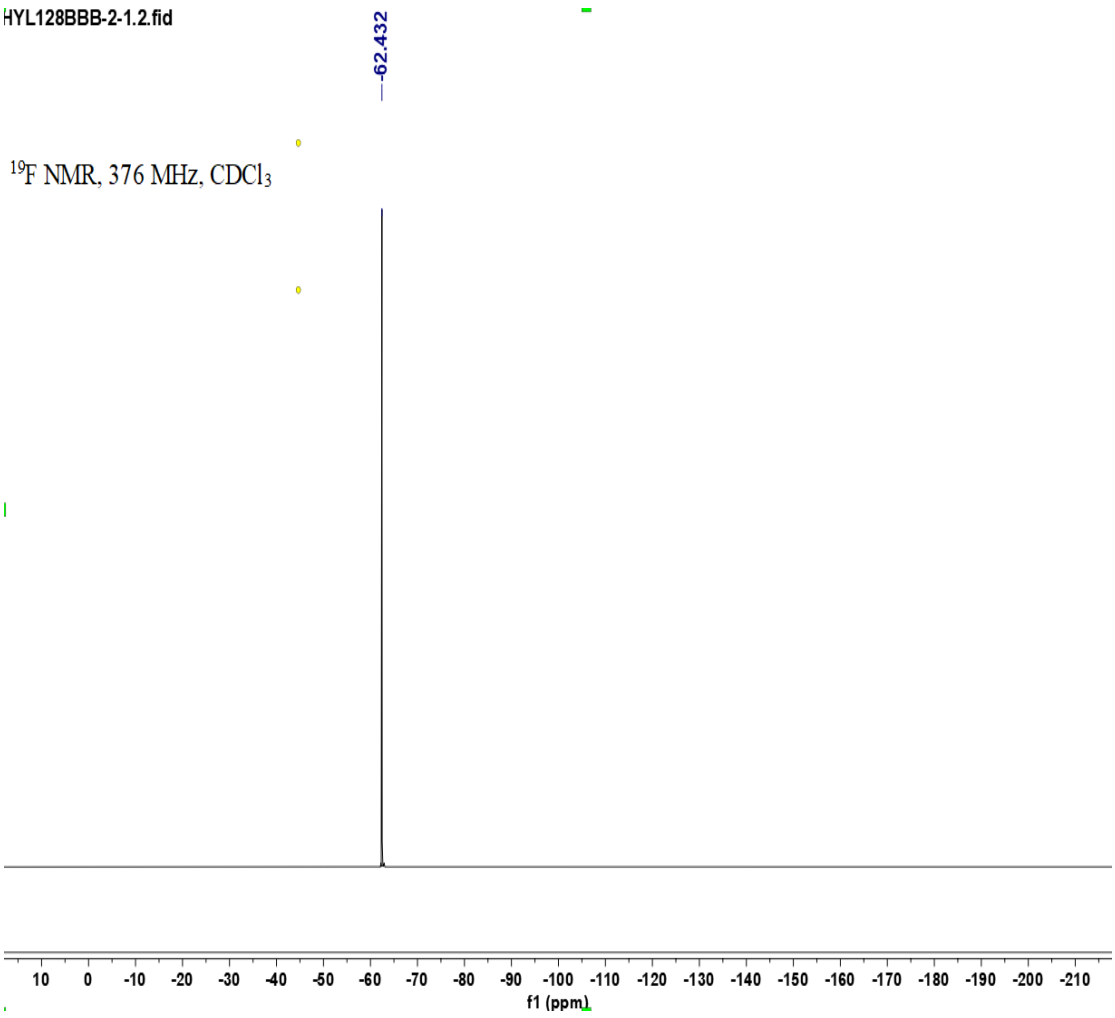




^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-11**

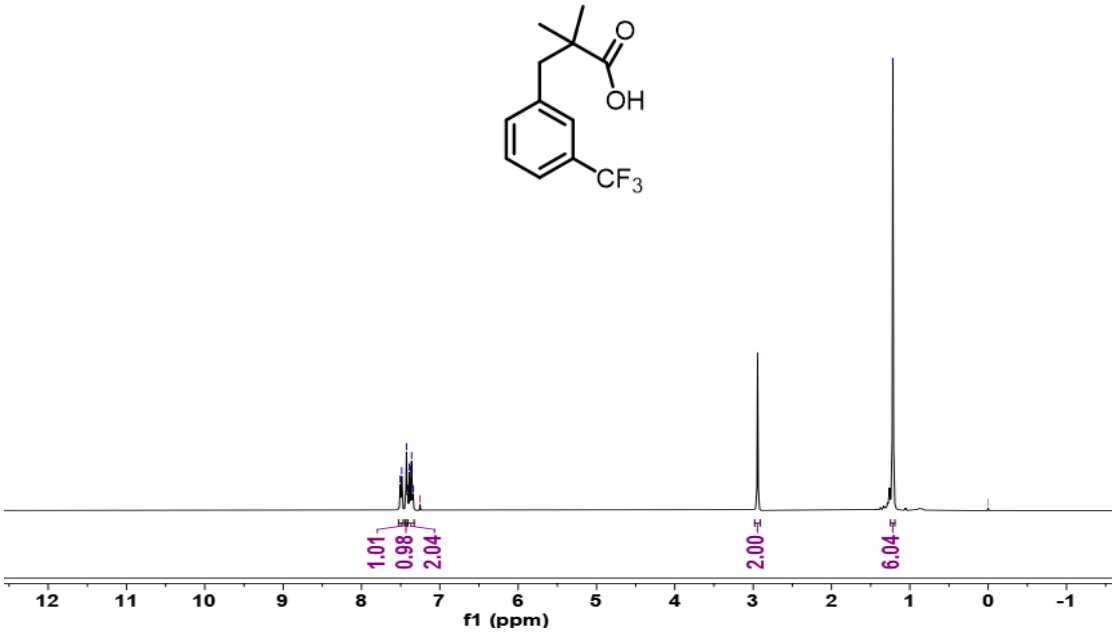

7.541
7.521
7.296
7.277
7.256 CDCl3
2.950
1.225
0.000
1H NMR, 400 MHz, CDCl3
O
OH
CF3
1.99
1.99
2.00
6.04
12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)


HYL128BBB-2-1.3.fid
183.916
141.653
130.545
129.459
129.137
128.816
128.494
128.324
125.623
125.047
125.009
124.971
124.934
122.921
120.219
77.344 CDCl3
77.027 CDCl3
76.709 CDCl3
45.470
43.426
24.749
13C NMR, 101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

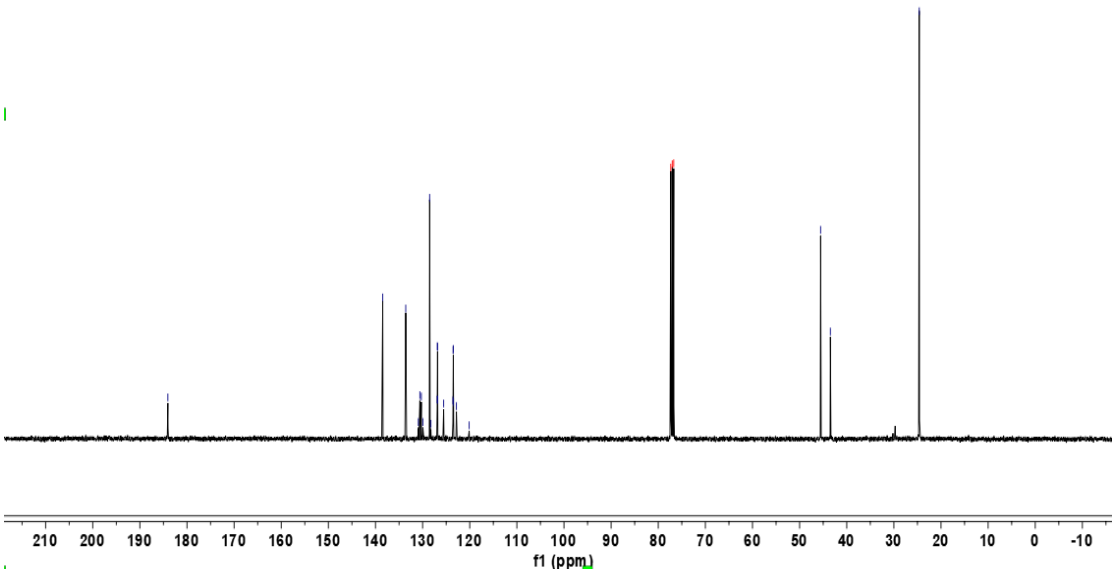


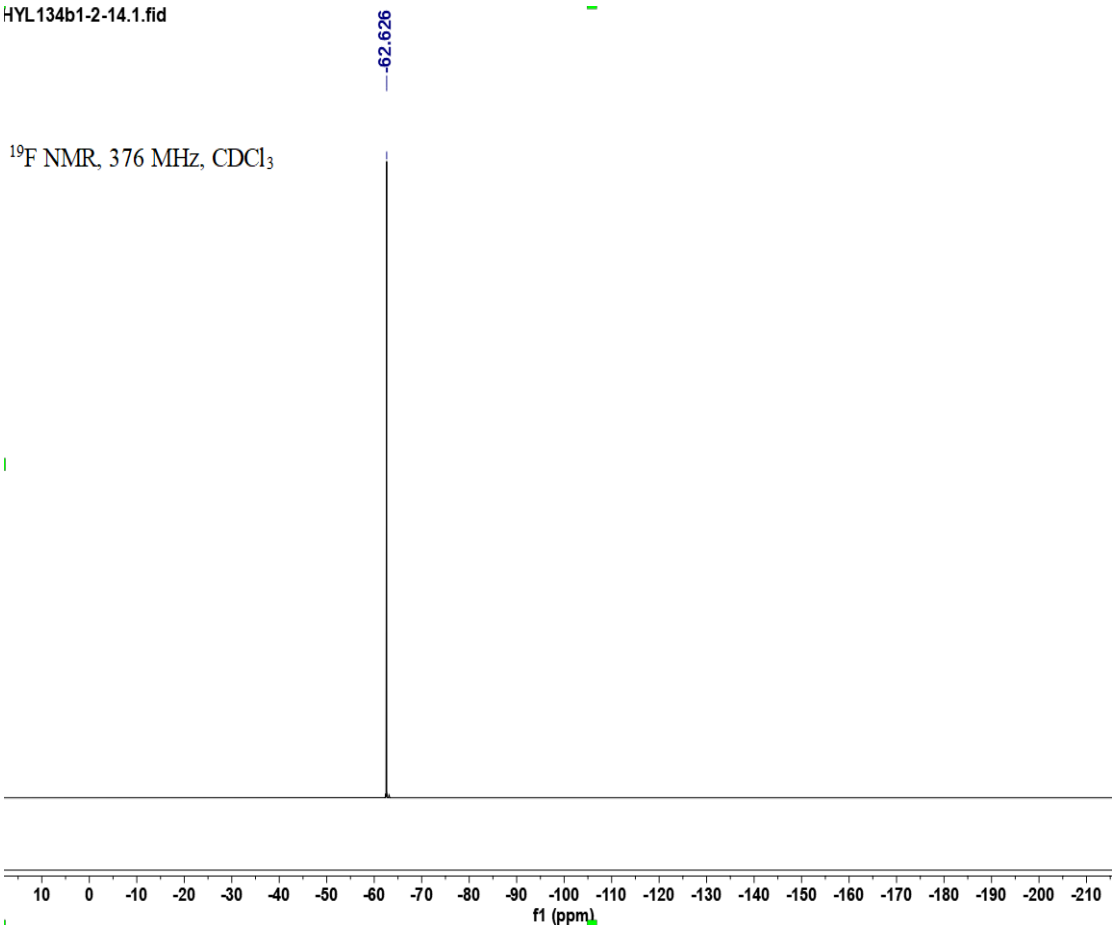
^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra of **7-12**

^{1}H NMR, 400 MHz, $CDCl_3$

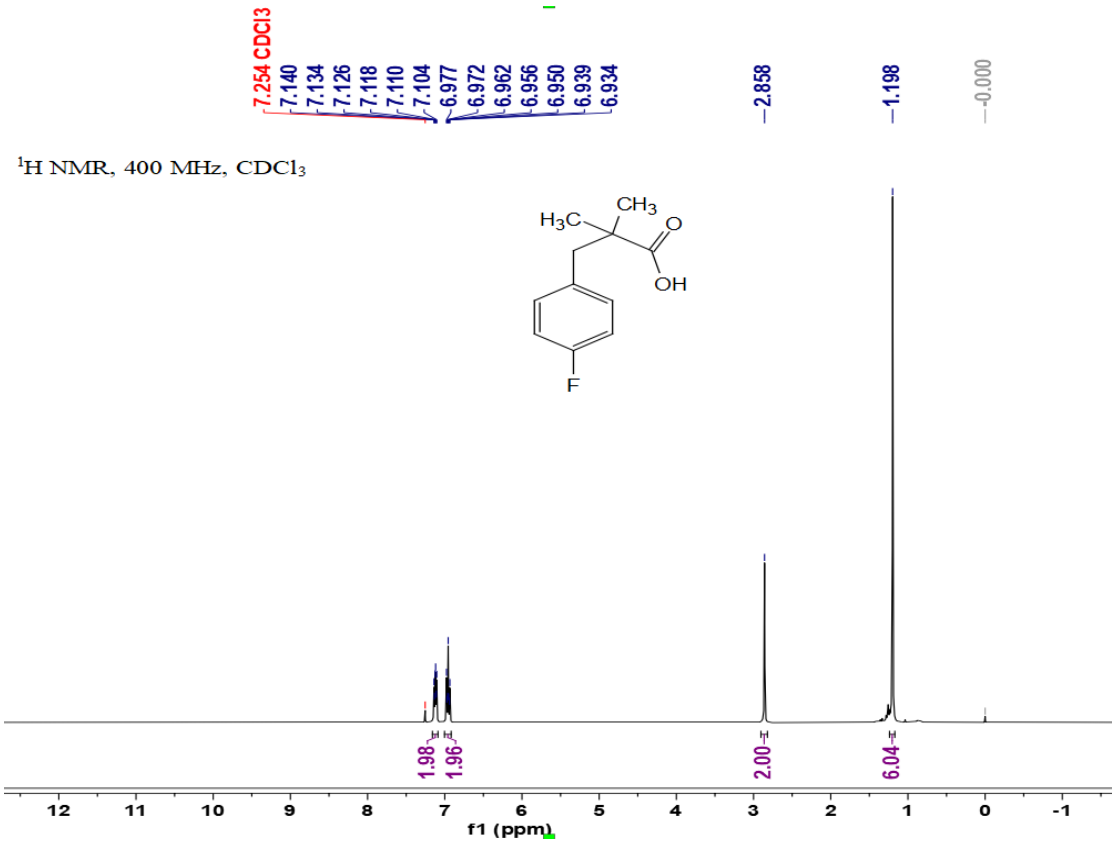


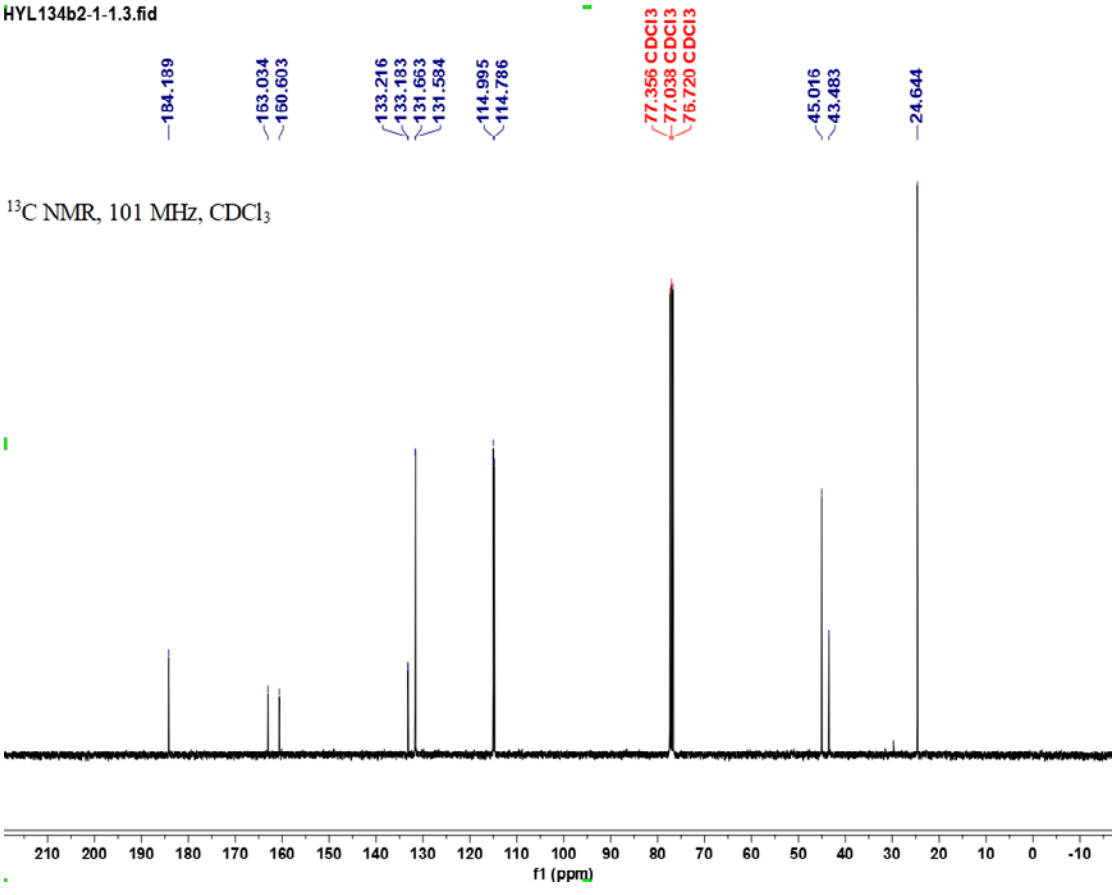
^{13}C NMR, 101 MHz, $CDCl_3$

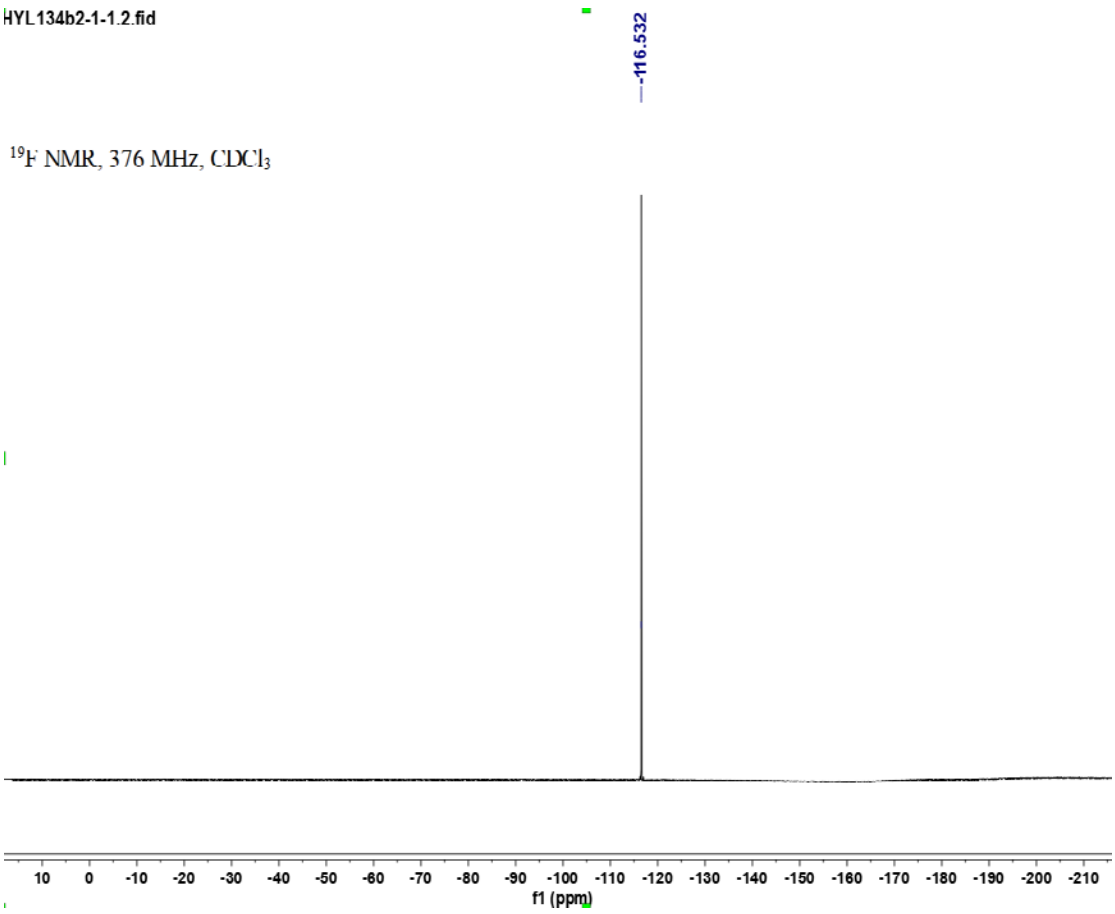




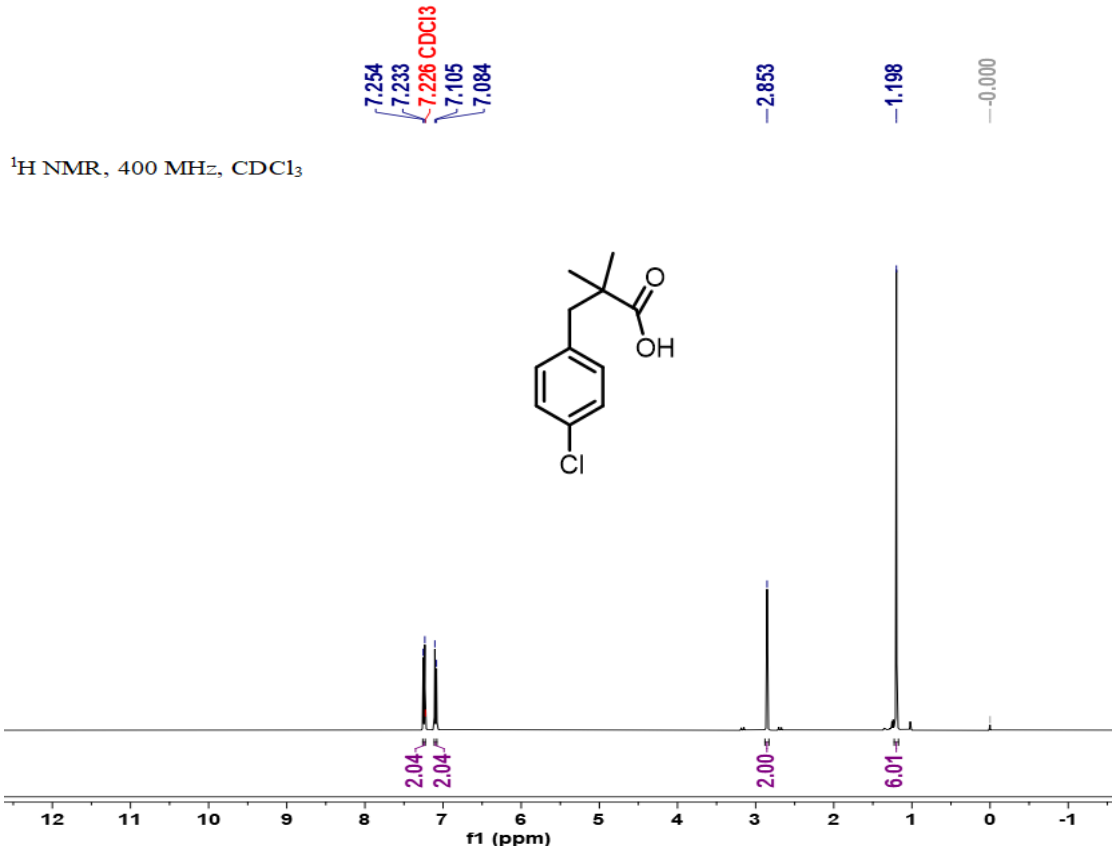
^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra of **7-13**


7.254 CDCl3
7.140
7.134
7.126
7.118
7.110
7.104
6.977
6.972
6.962
6.956
6.950
6.939
6.934
2.858
1.198
0.000
^{1}H NMR, 400 MHz, CDCl$_3$
H$_3$C
CH$_3$
O
OH
F
1.98
1.96
2.00
6.04
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

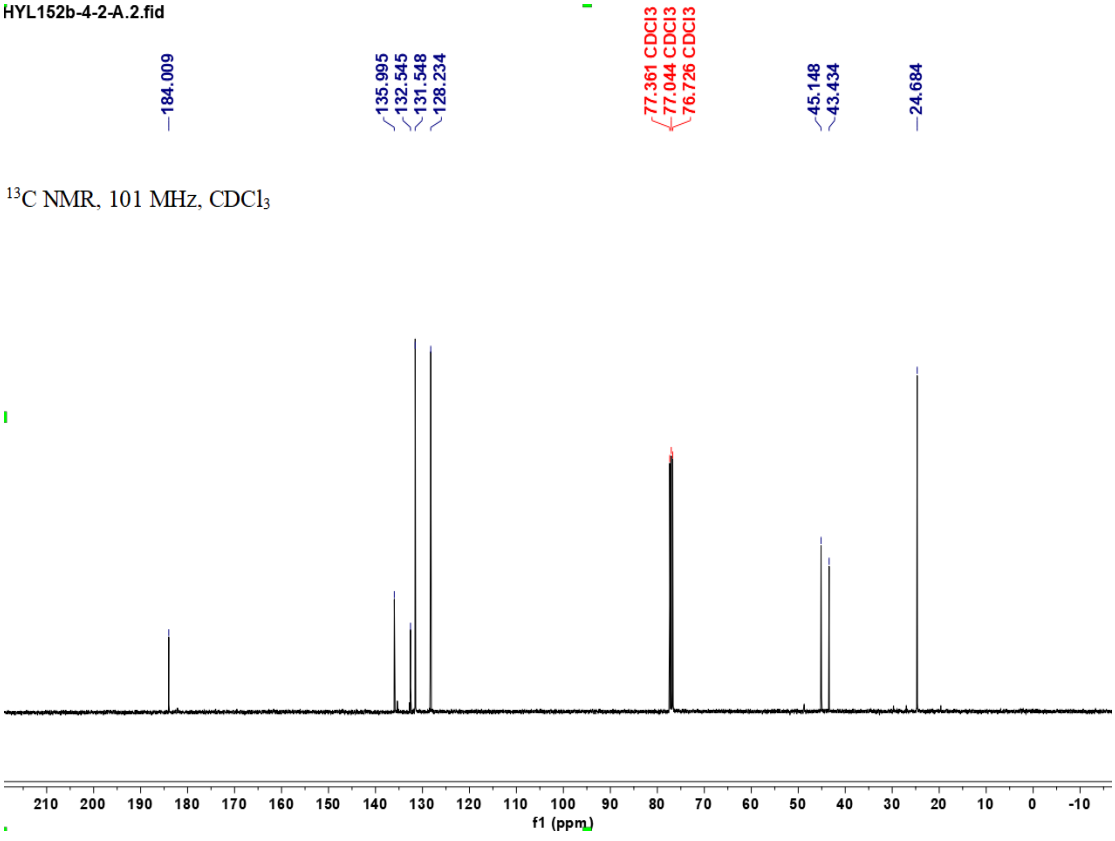

HYL134b2-1-1.3.fid
184.189
163.034
160.603
133.216
133.183
131.663
131.584
114.995
114.786
77.356 CDCl3
77.038 CDCl3
76.720 CDCl3
45.016
43.483
24.644
^{13}C NMR, 101 MHz, CDCl$_3$
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra of **7-14**

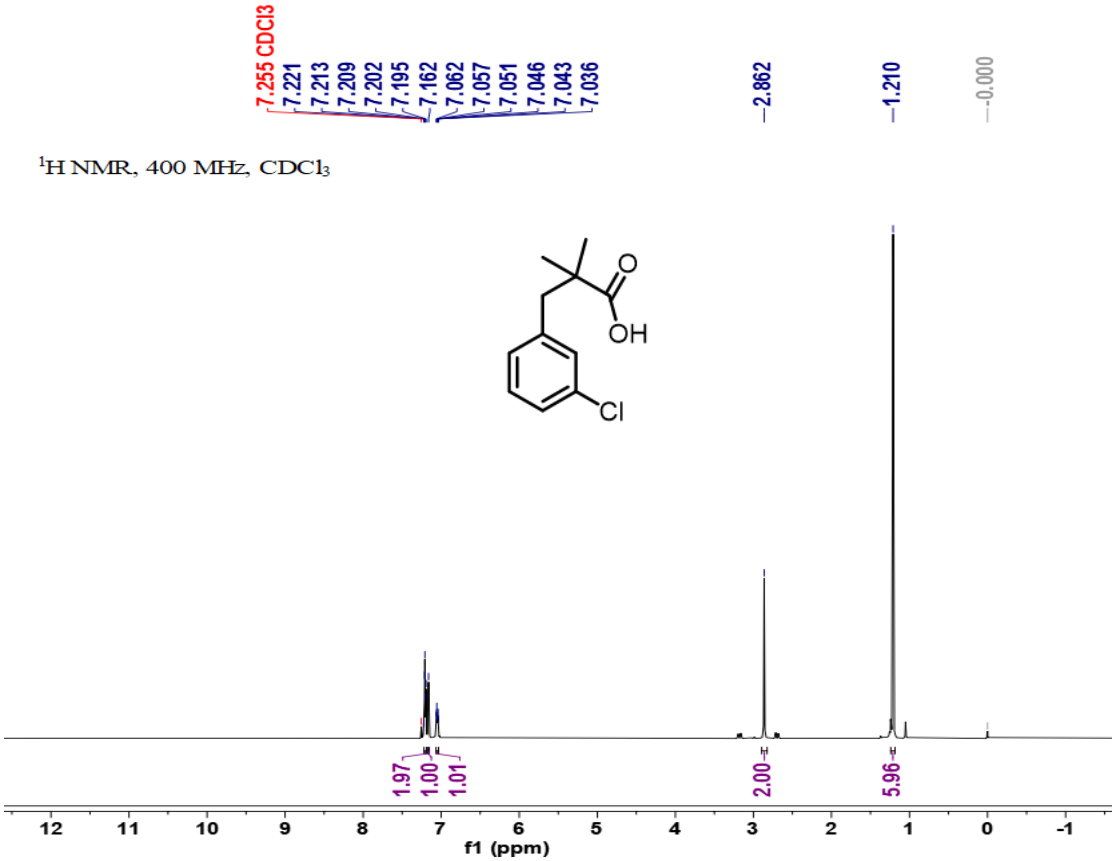


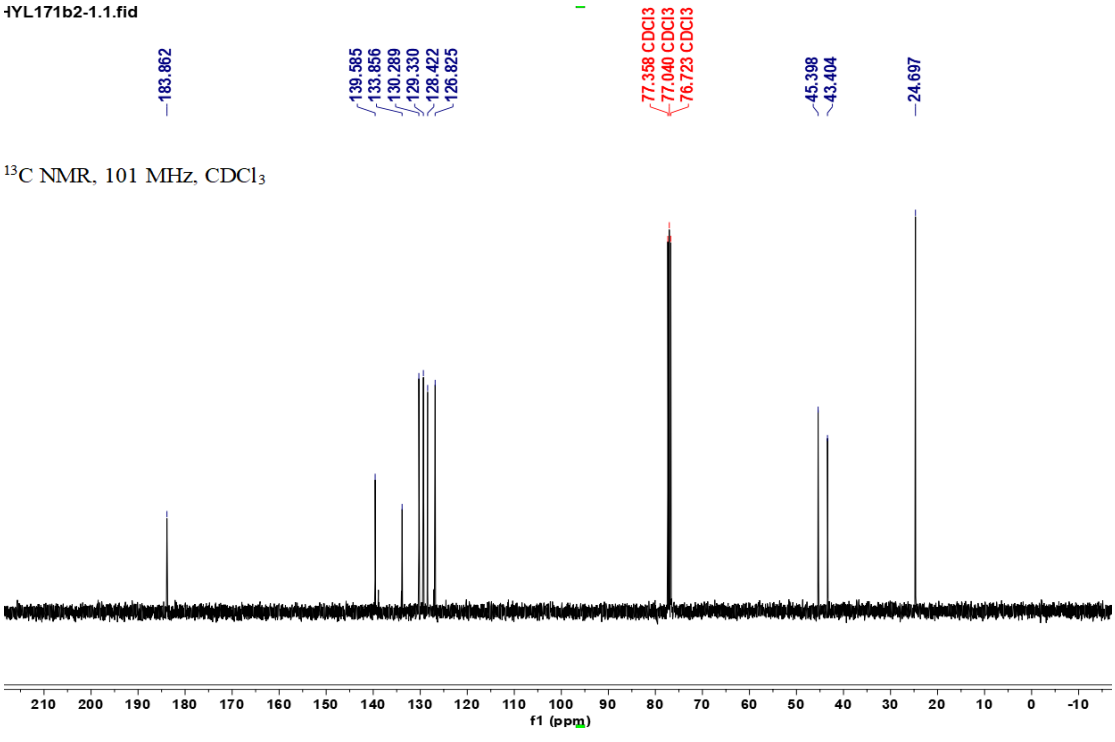
^{1}H NMR, 400 MHz, $CDCl_3$



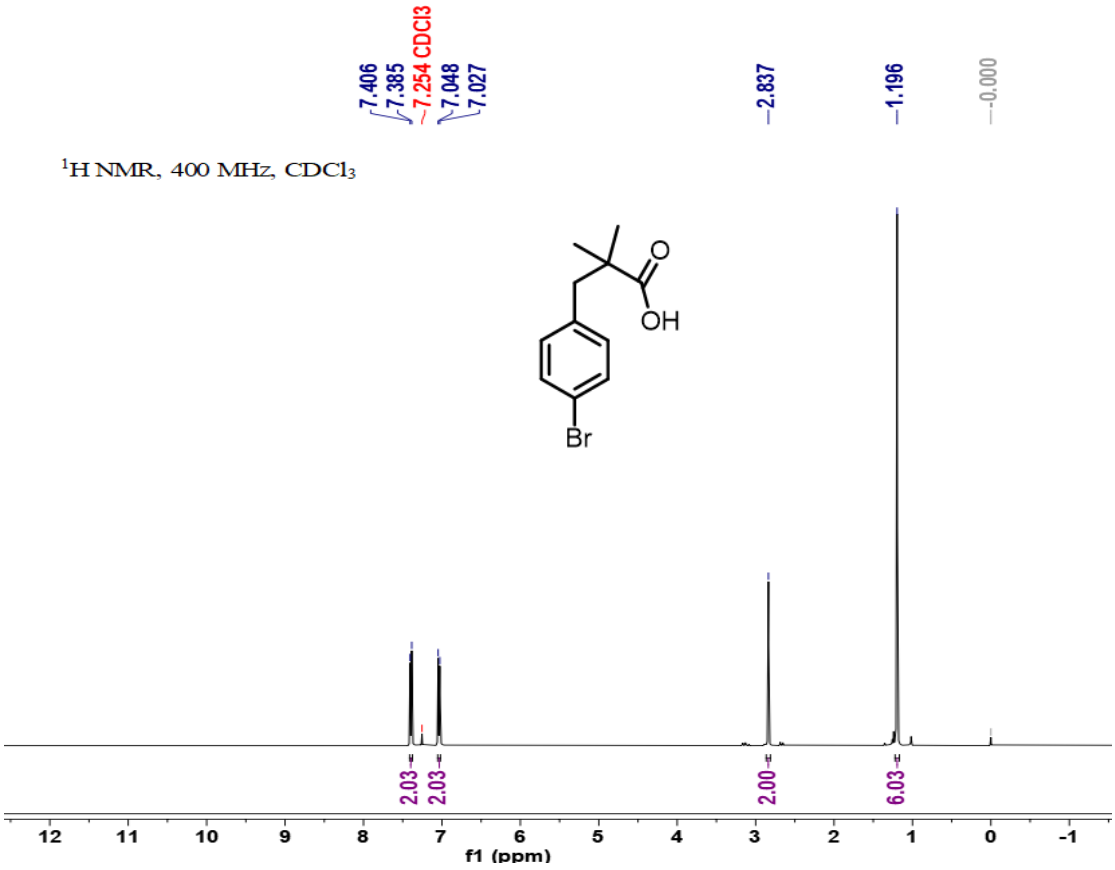
^{13}C NMR, 101 MHz, $CDCl_3$

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-15**

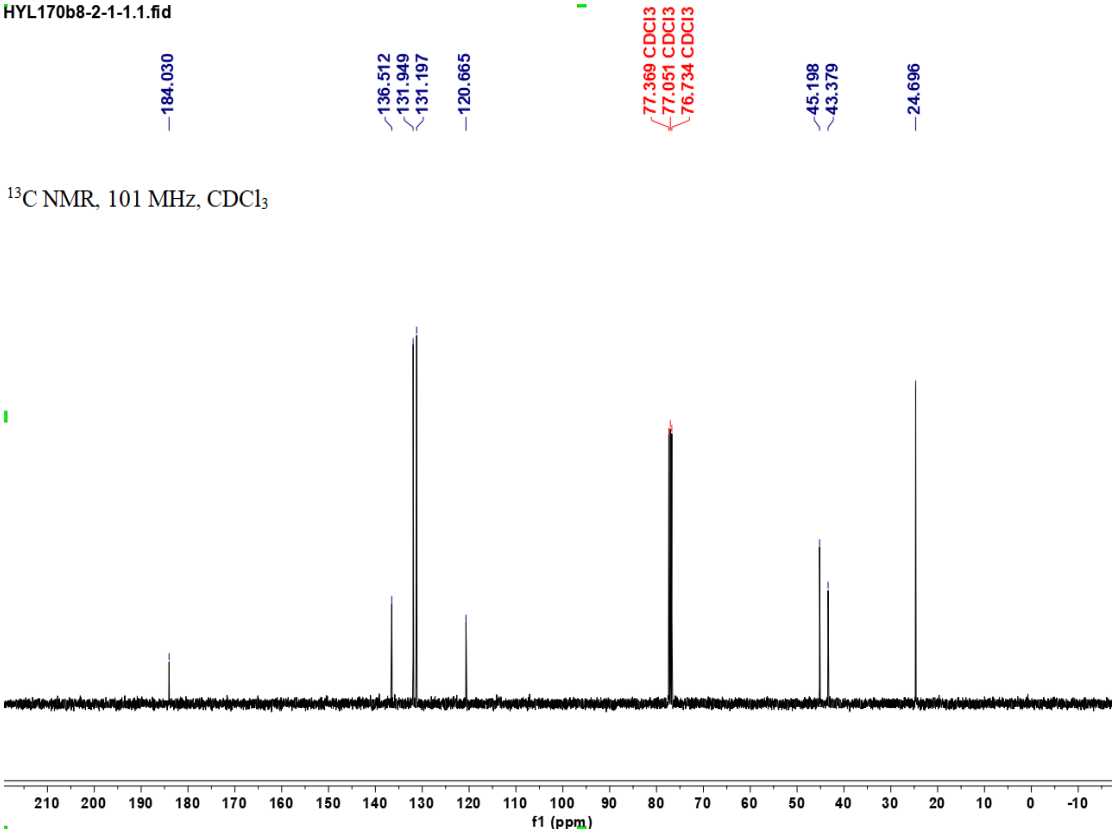




^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-16**



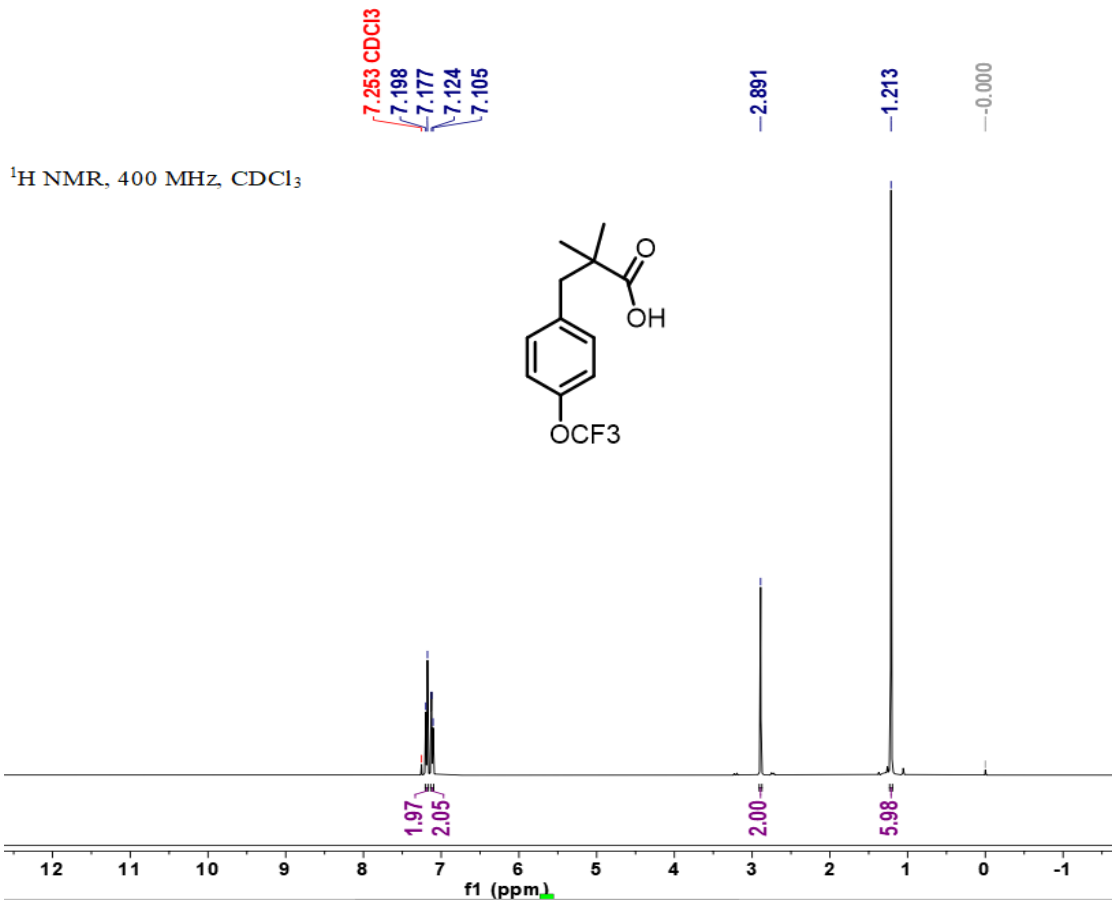
^{1}H NMR, 400 MHz, $CDCl_3$



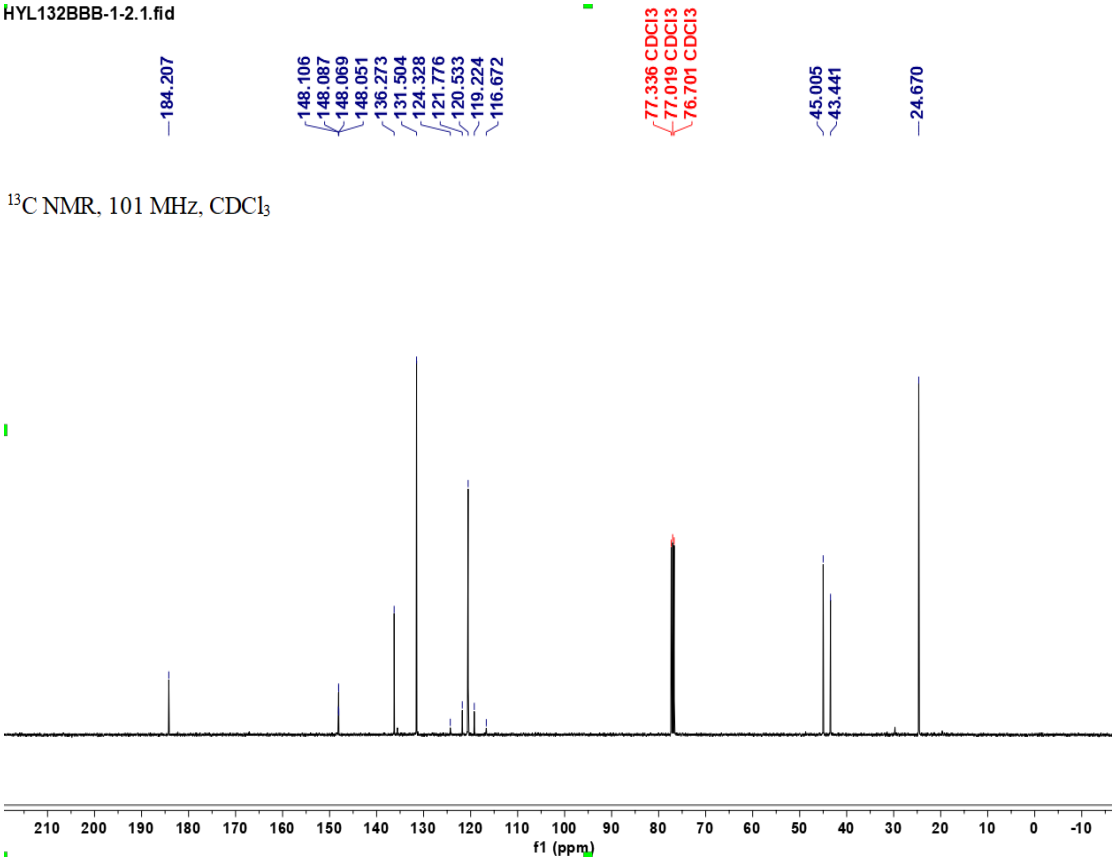
^{13}C NMR, 101 MHz, $CDCl_3$

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-17**

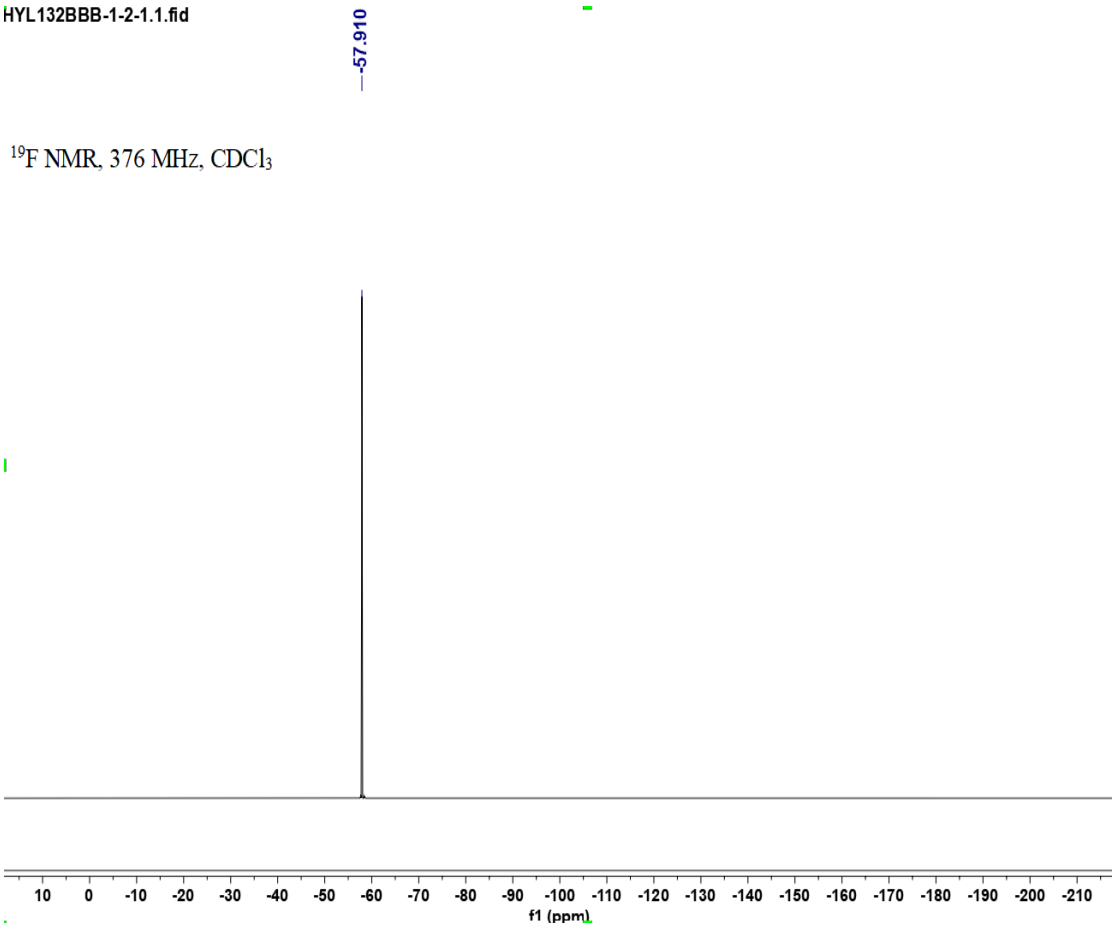
^{1}H NMR, 400 MHz, $CDCl_3$



HYL132BBB-1-2.1.fid

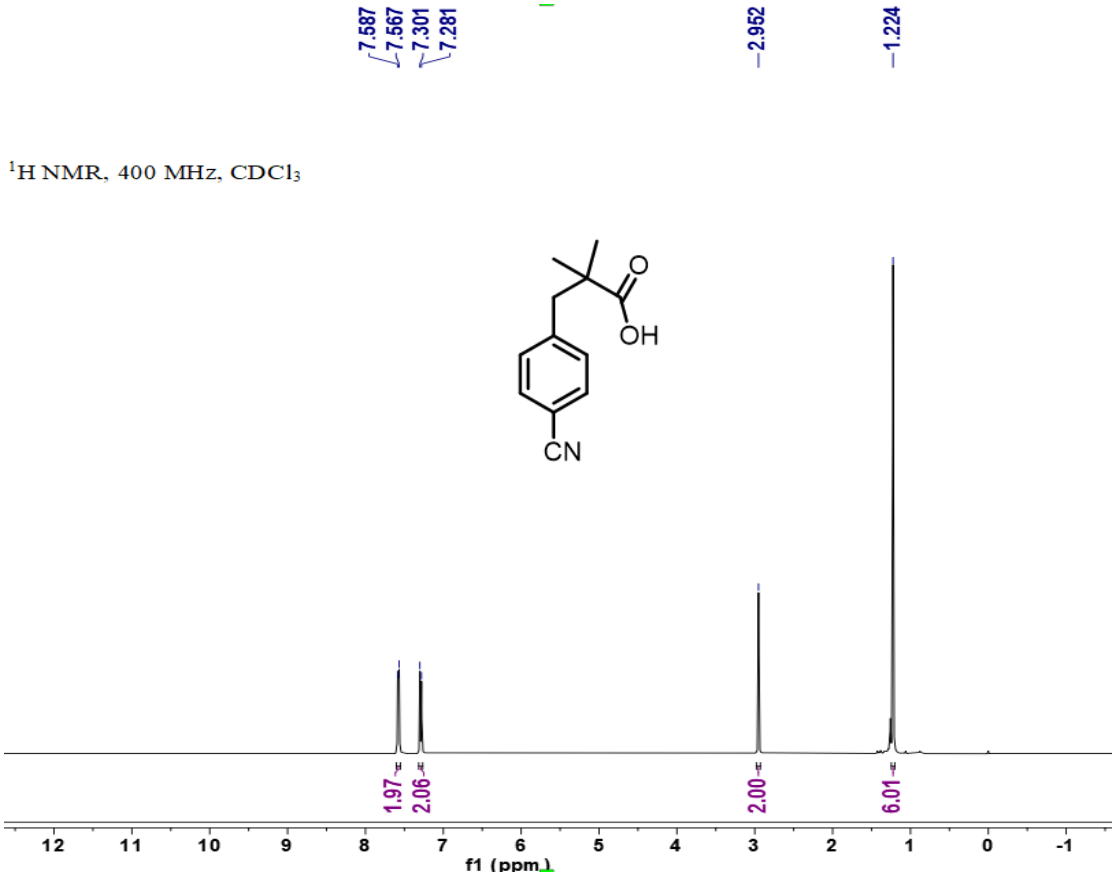


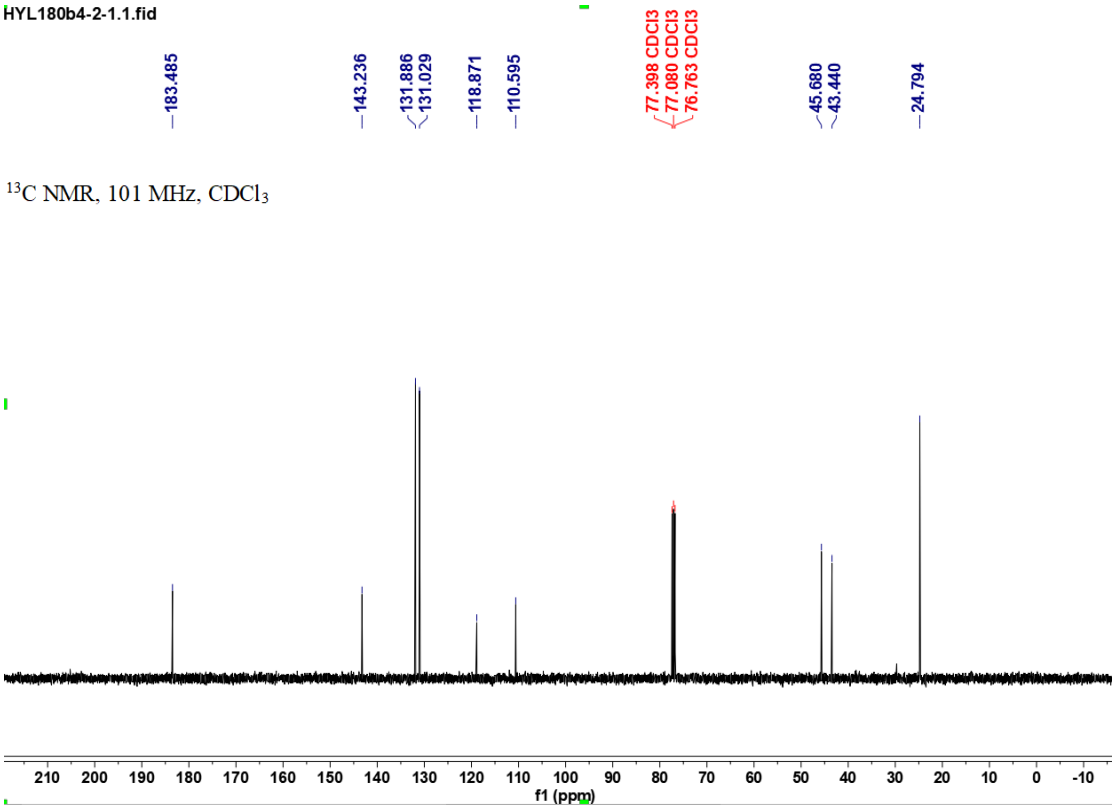
^{13}C NMR, 101 MHz, $CDCl_3$



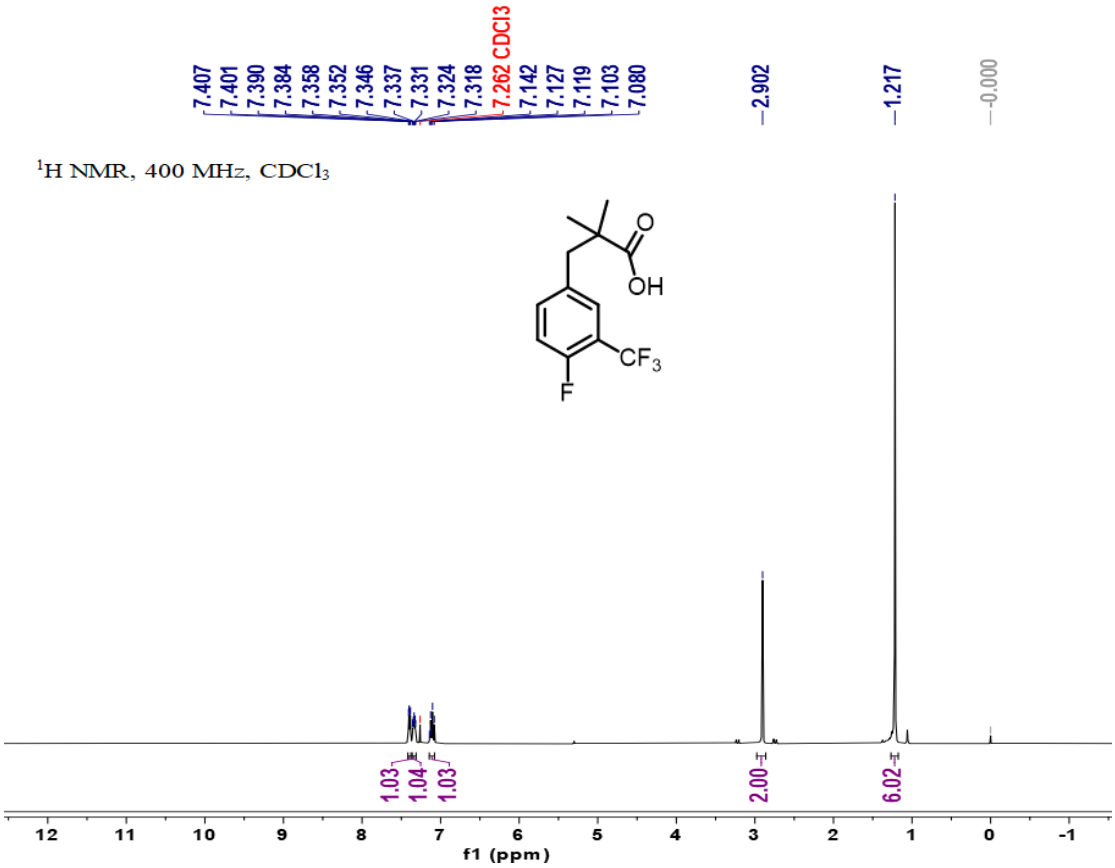
^{19}F NMR, 376 MHz, $CDCl_3$

^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra of **7-18**

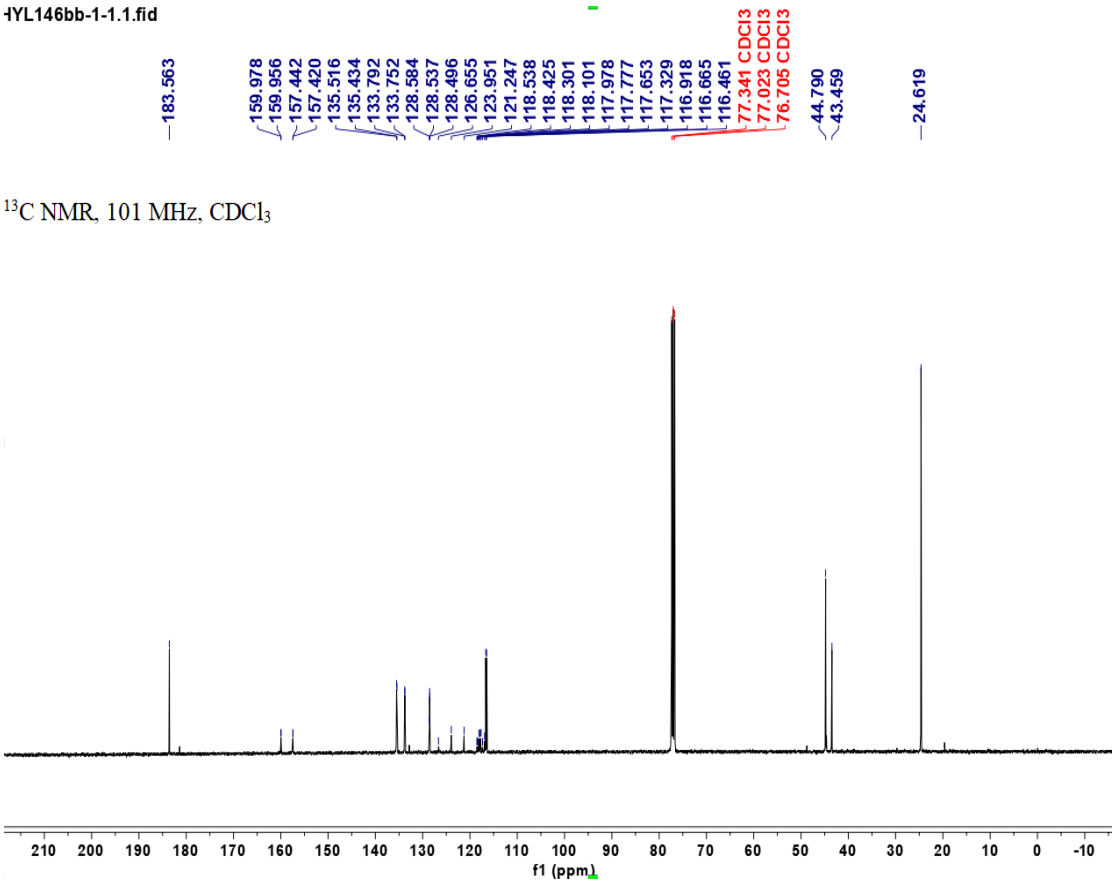




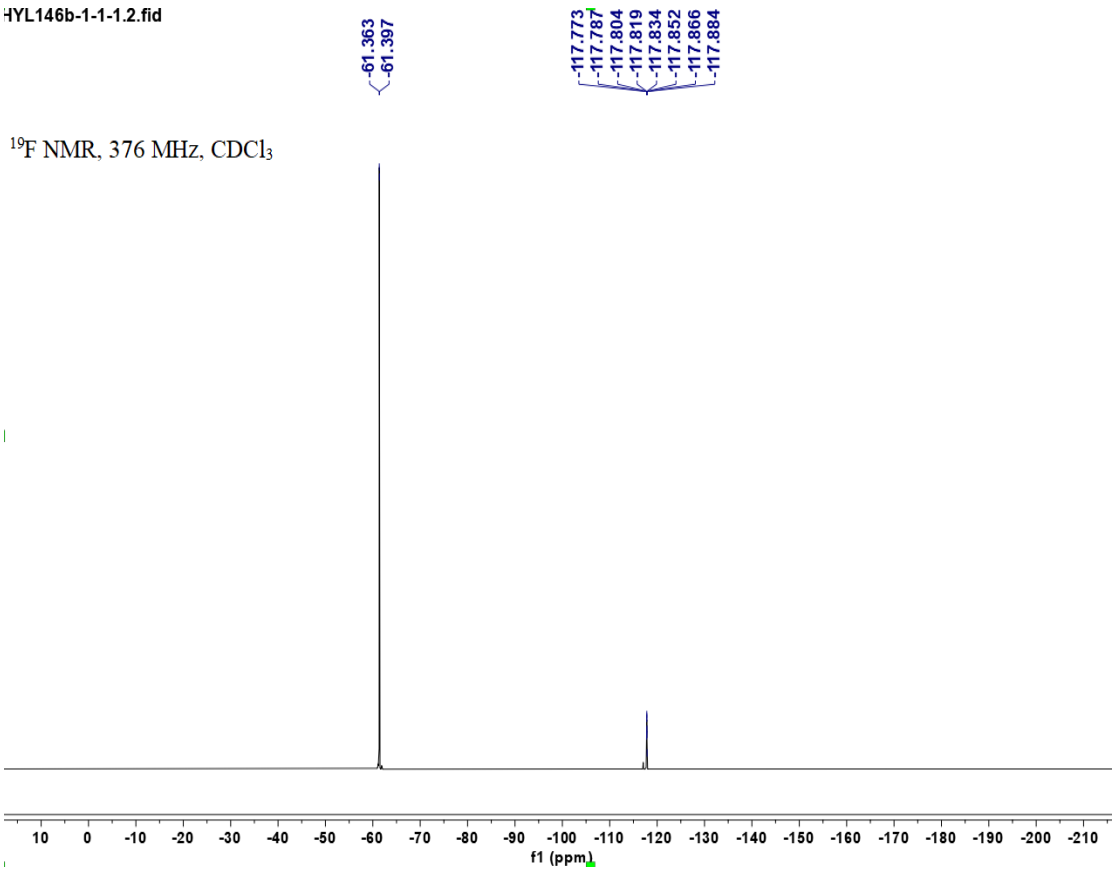
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-19**



^{1}H NMR, 400 MHz, $CDCl_3$

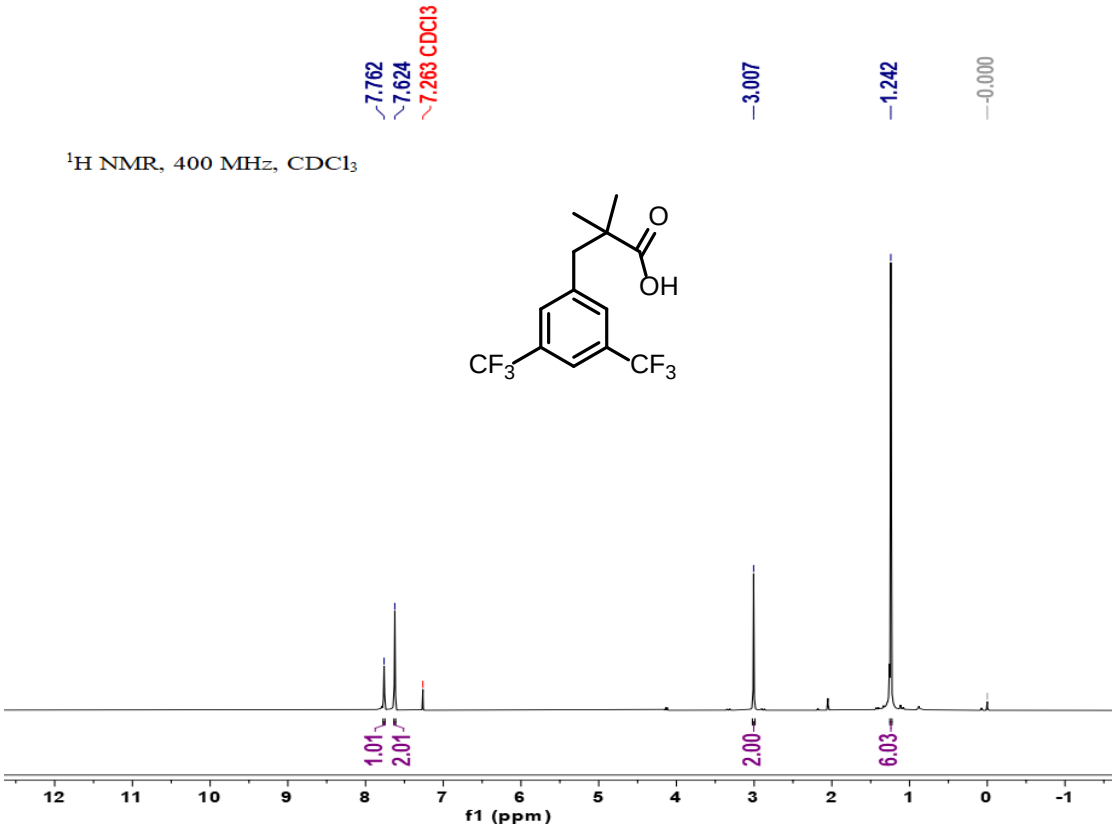


^{13}C NMR, 101 MHz, $CDCl_3$

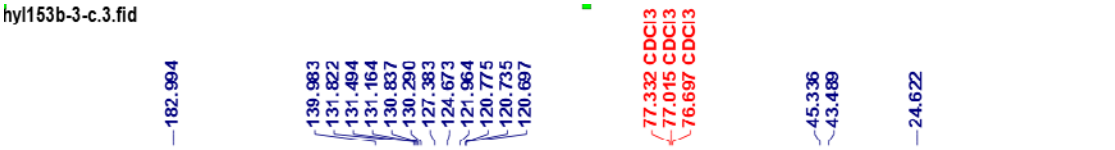


^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra of **7**-**20**

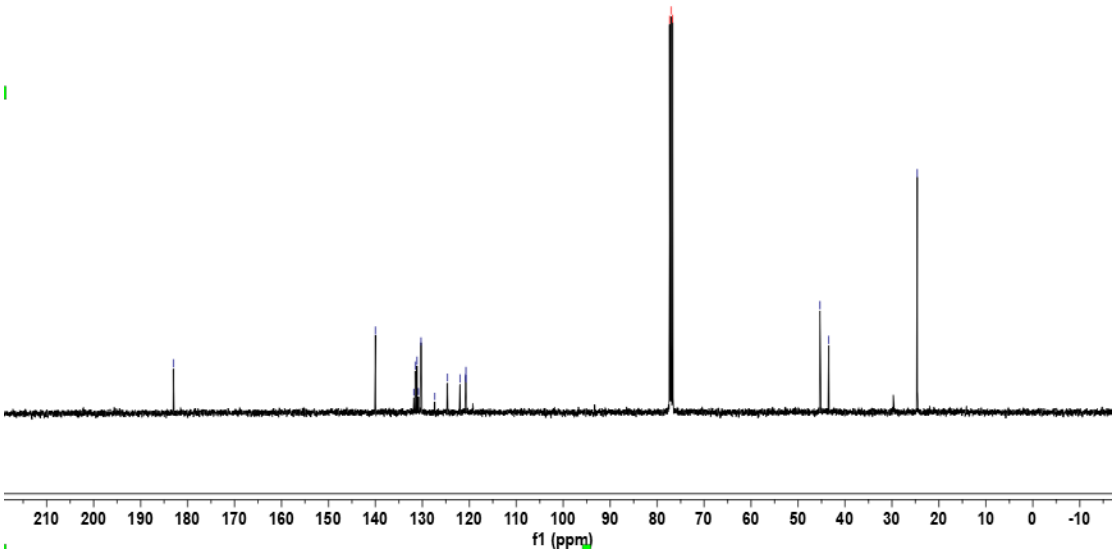
^{1}H NMR, 400 MHz, $CDCl_3$

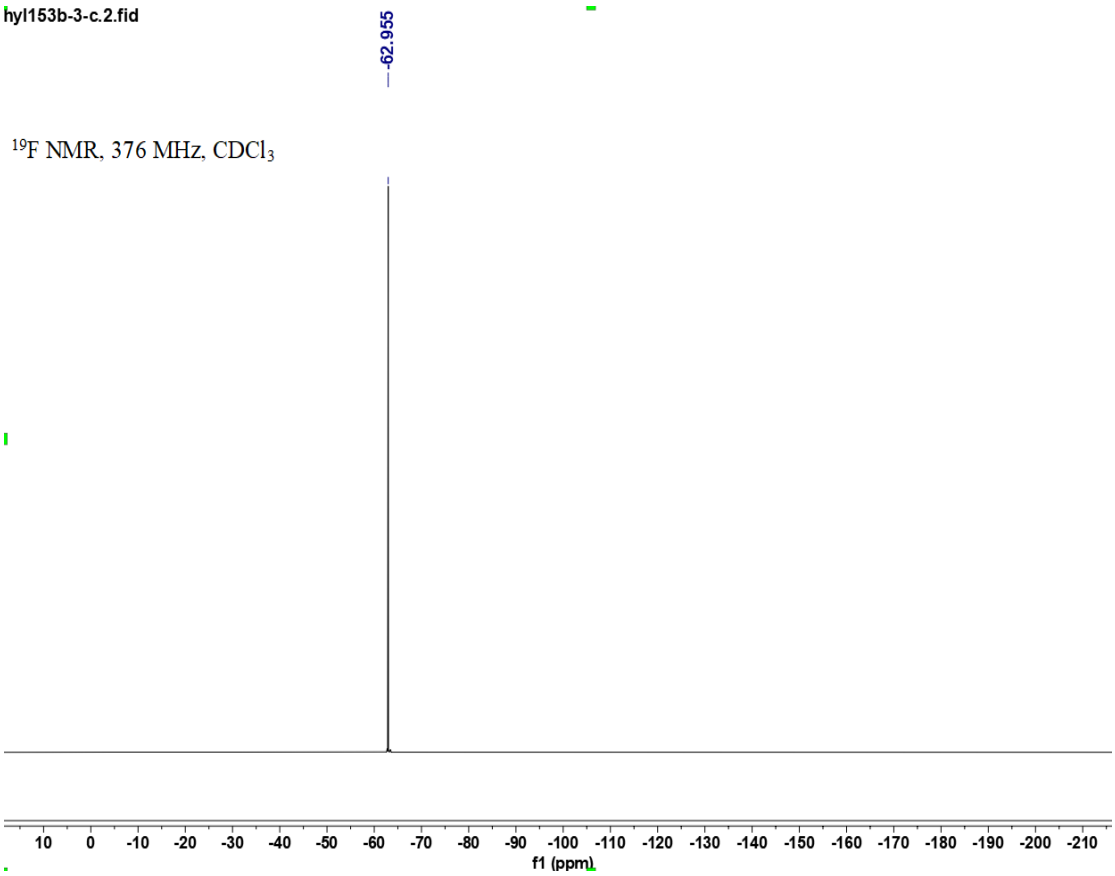


hyl153b-3-c.3.fid

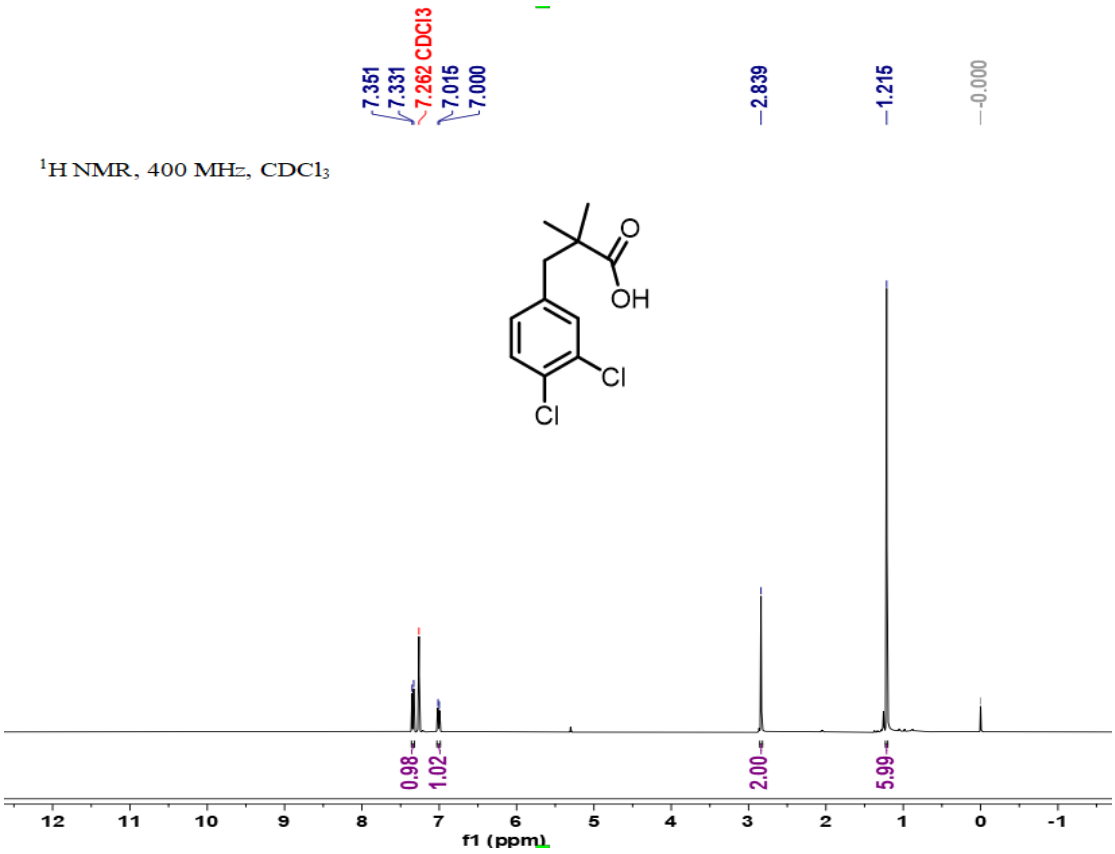


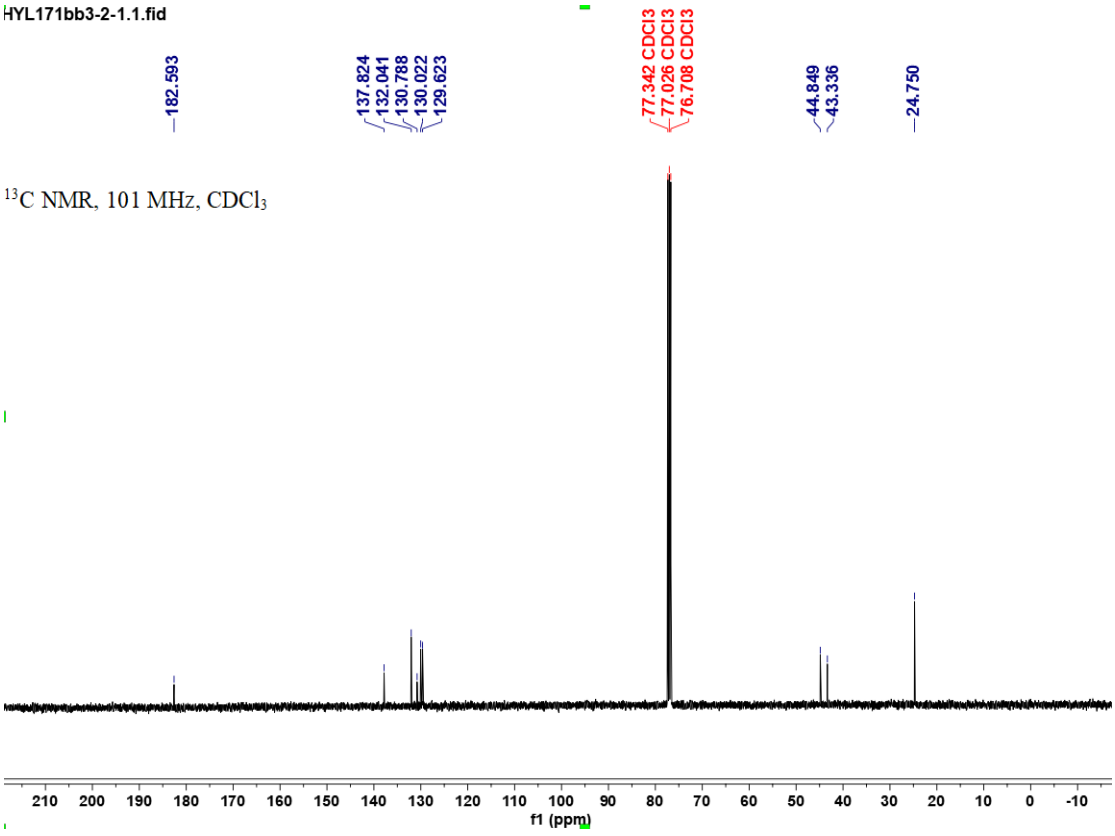
^{13}C NMR, 101 MHz, $CDCl_3$



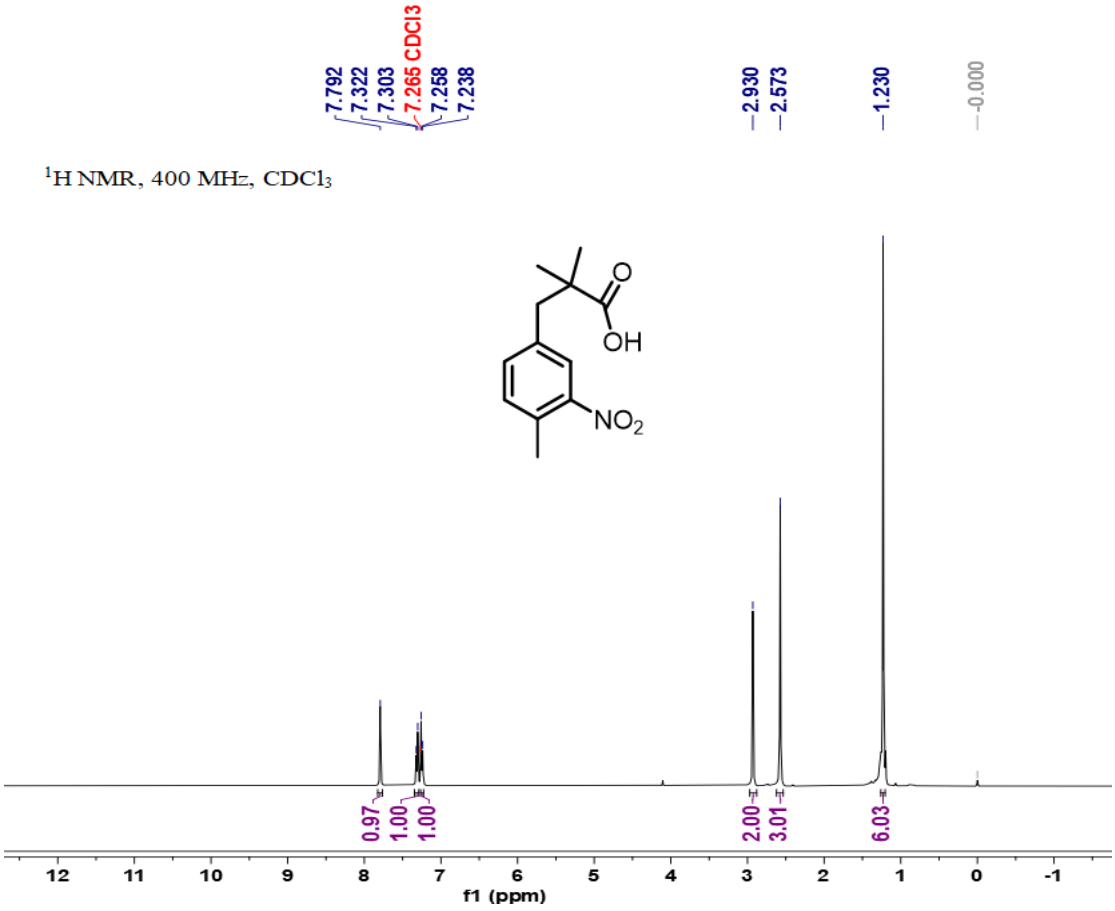


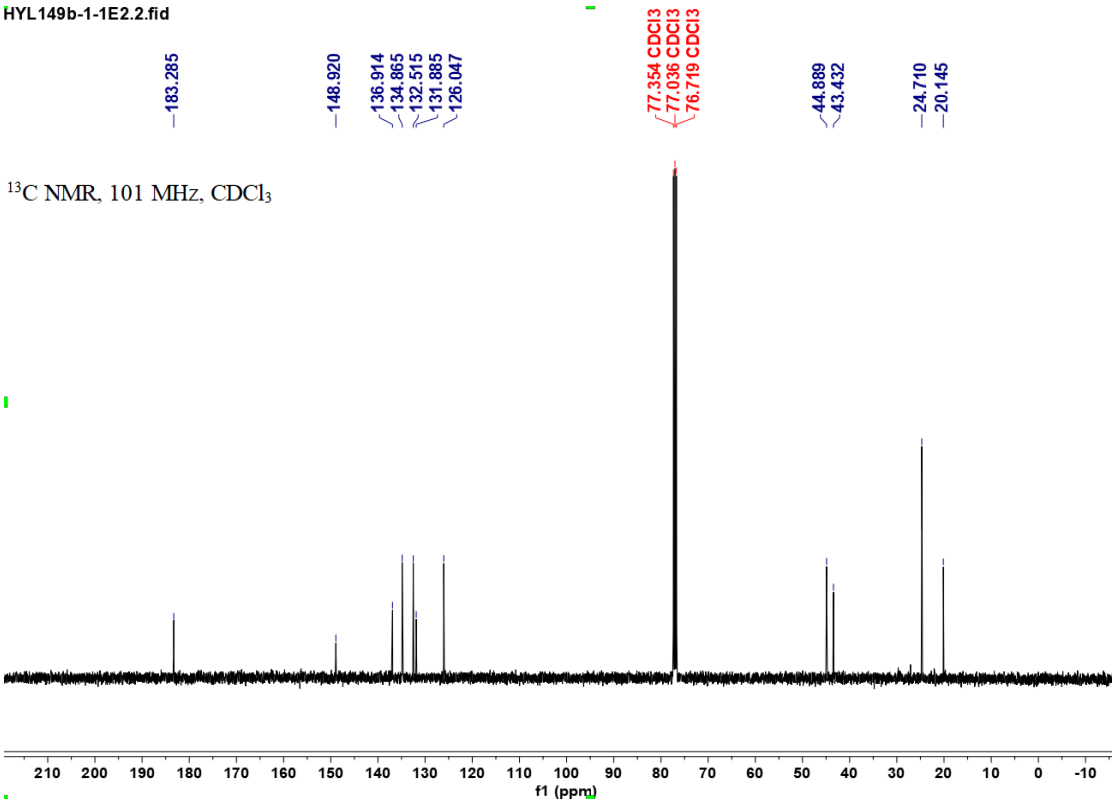
^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra of **7-21**





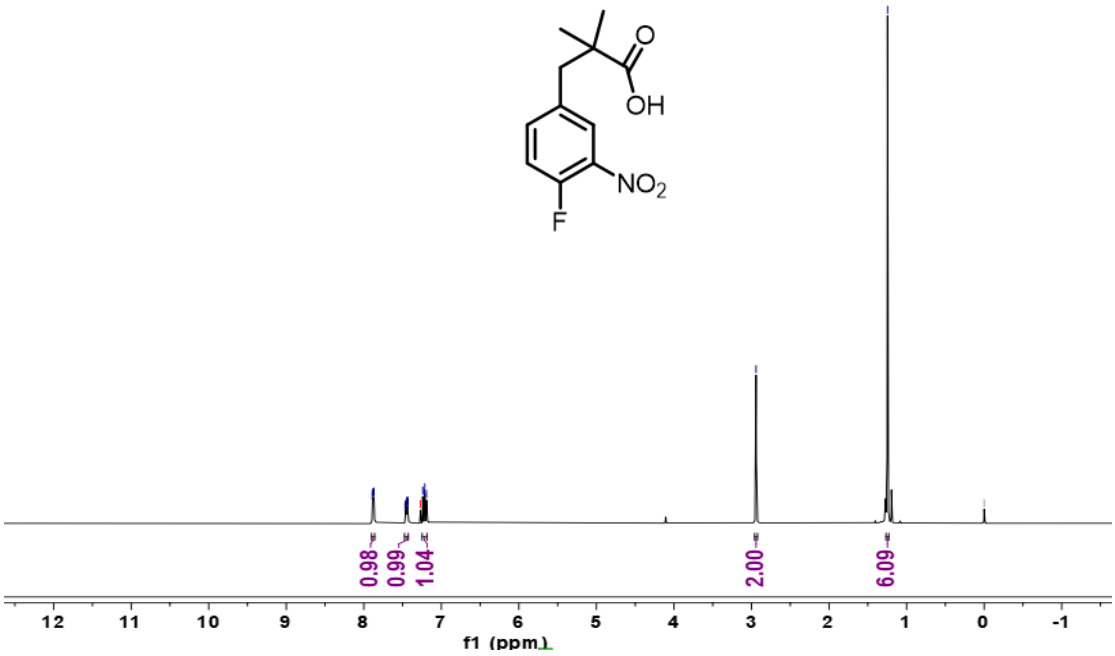
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-22**





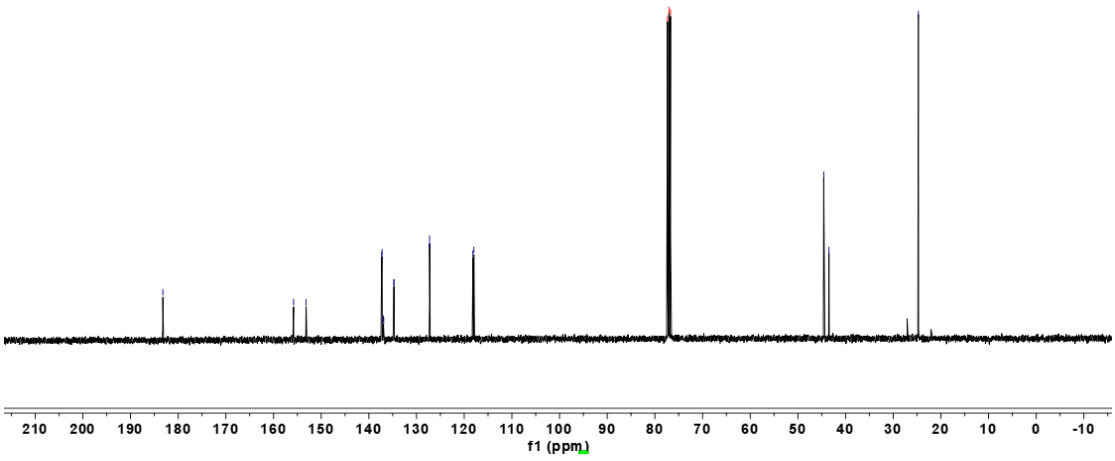
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 7-23

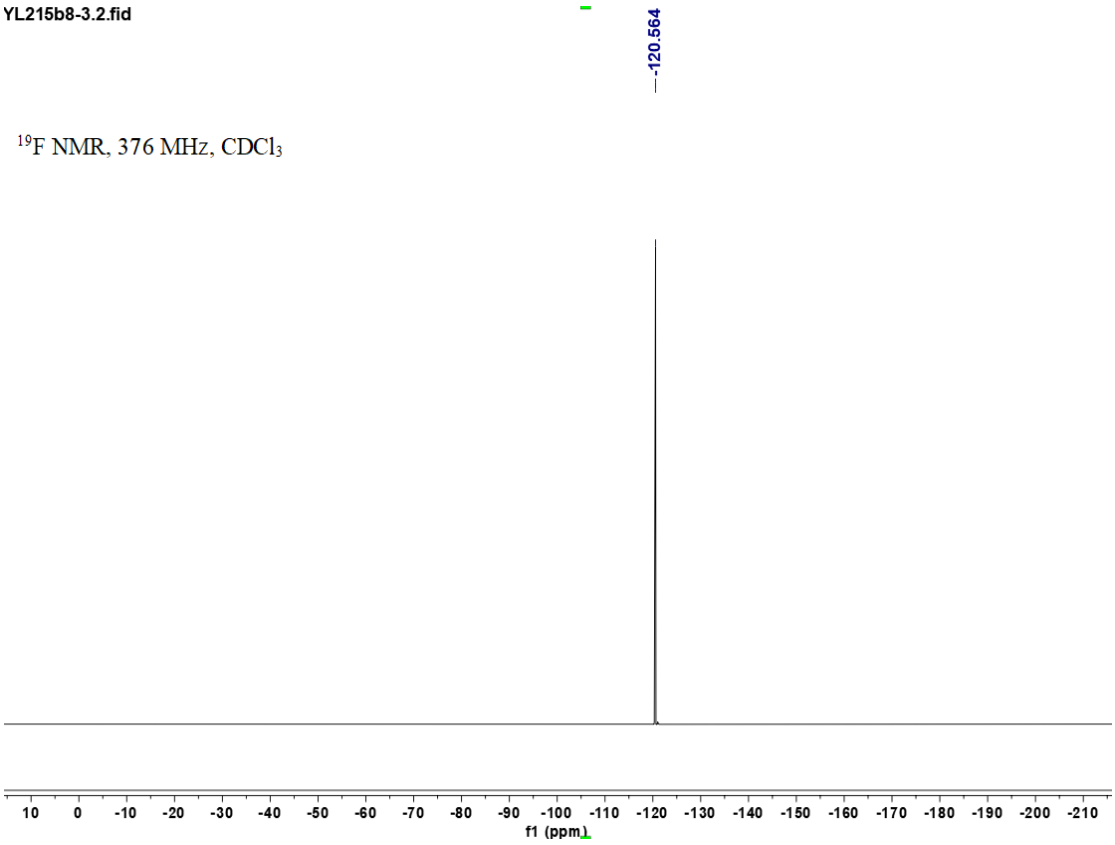
^{1}H NMR, 400 MHz, $CDCl_3$



YL215b8-3-1.1.fid

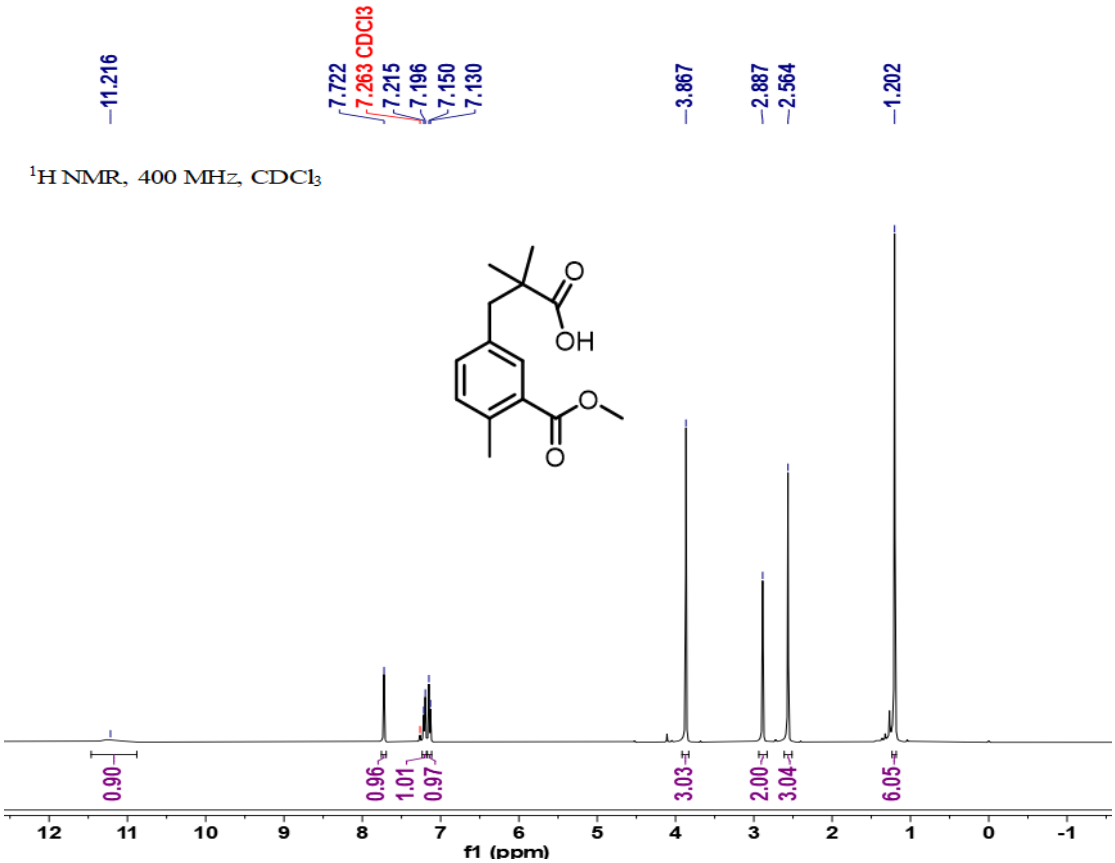
^{13}C NMR, 101 MHz, $CDCl_3$

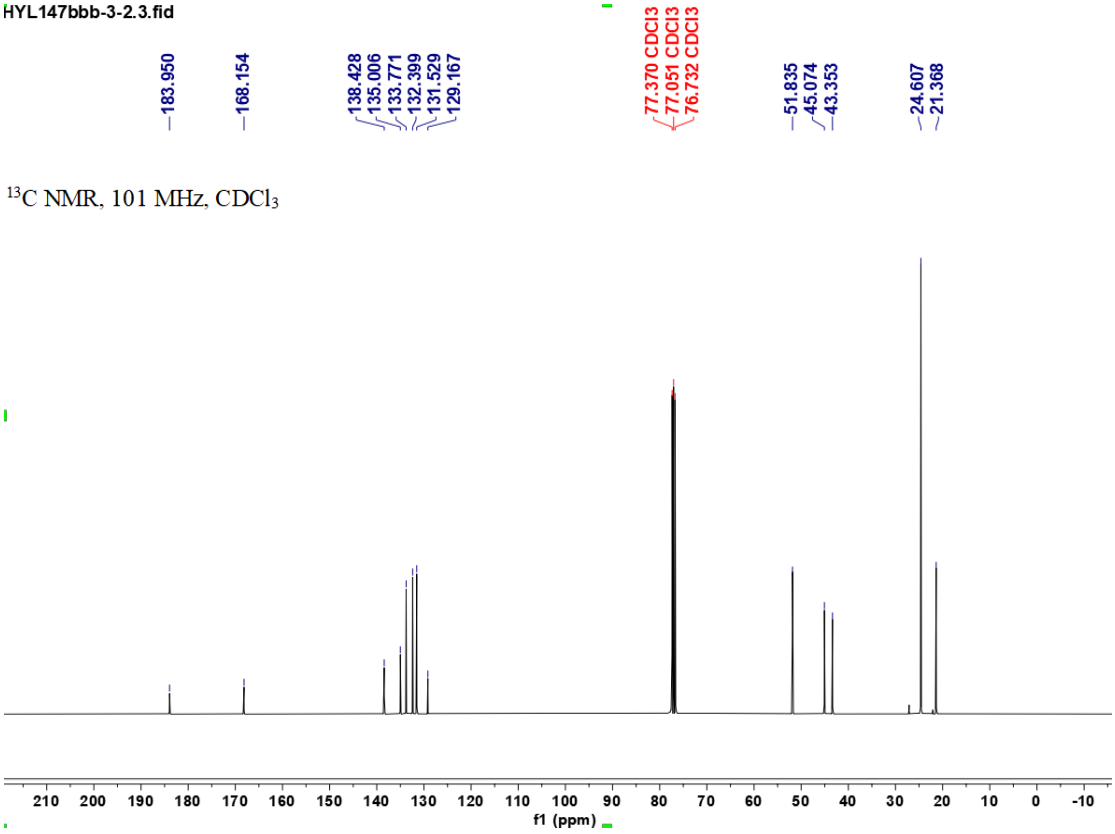




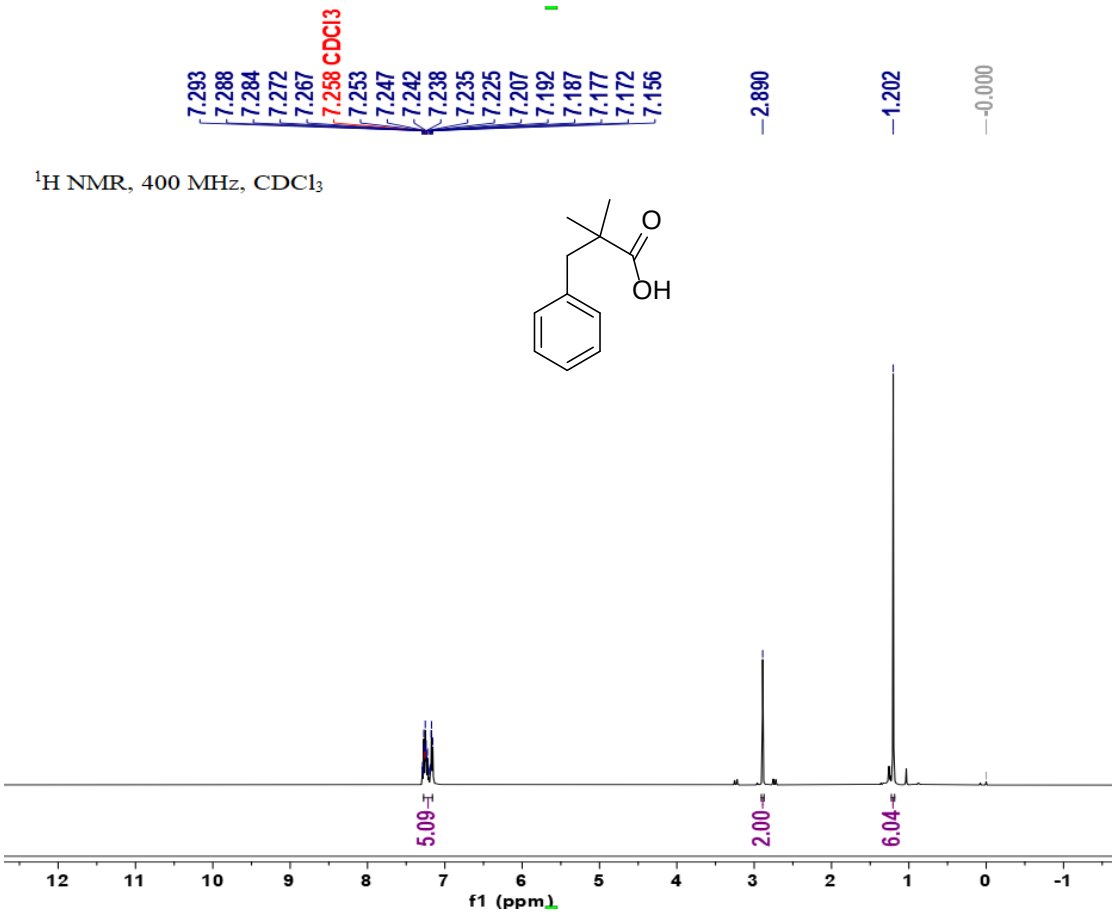
^{19}F NMR, 376 MHz, $CDCl_3$

^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra of **7**-**24**

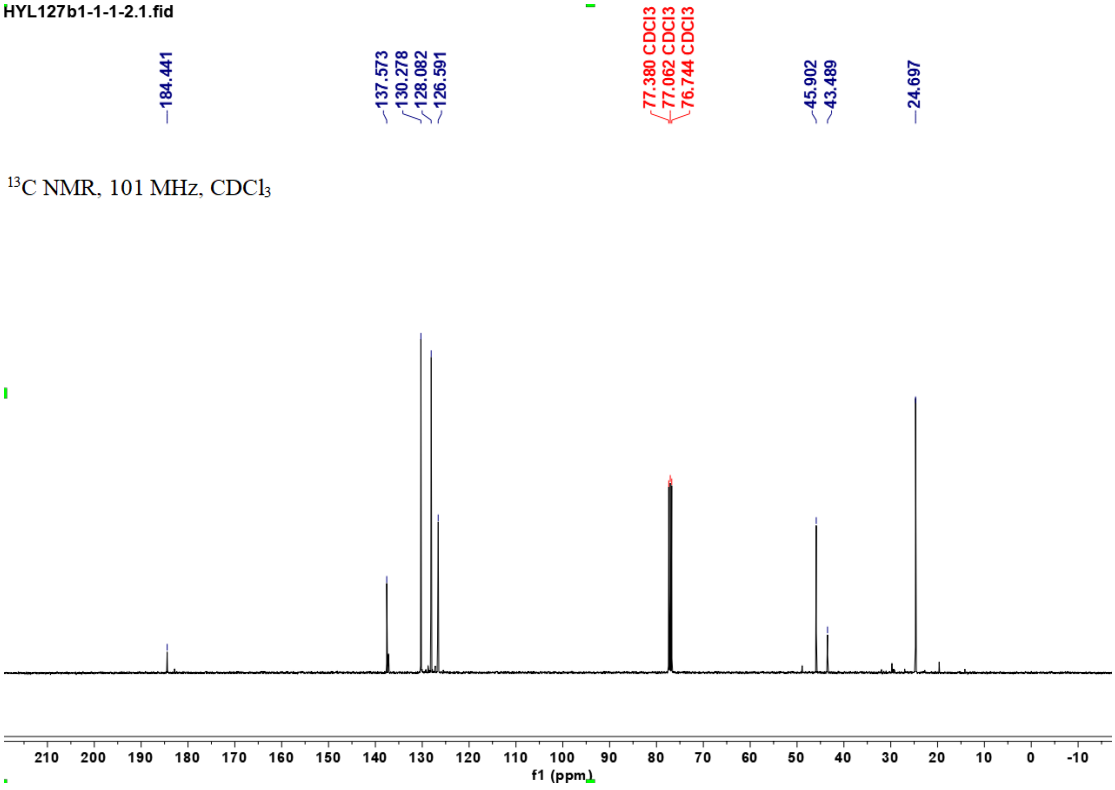




^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 7-25

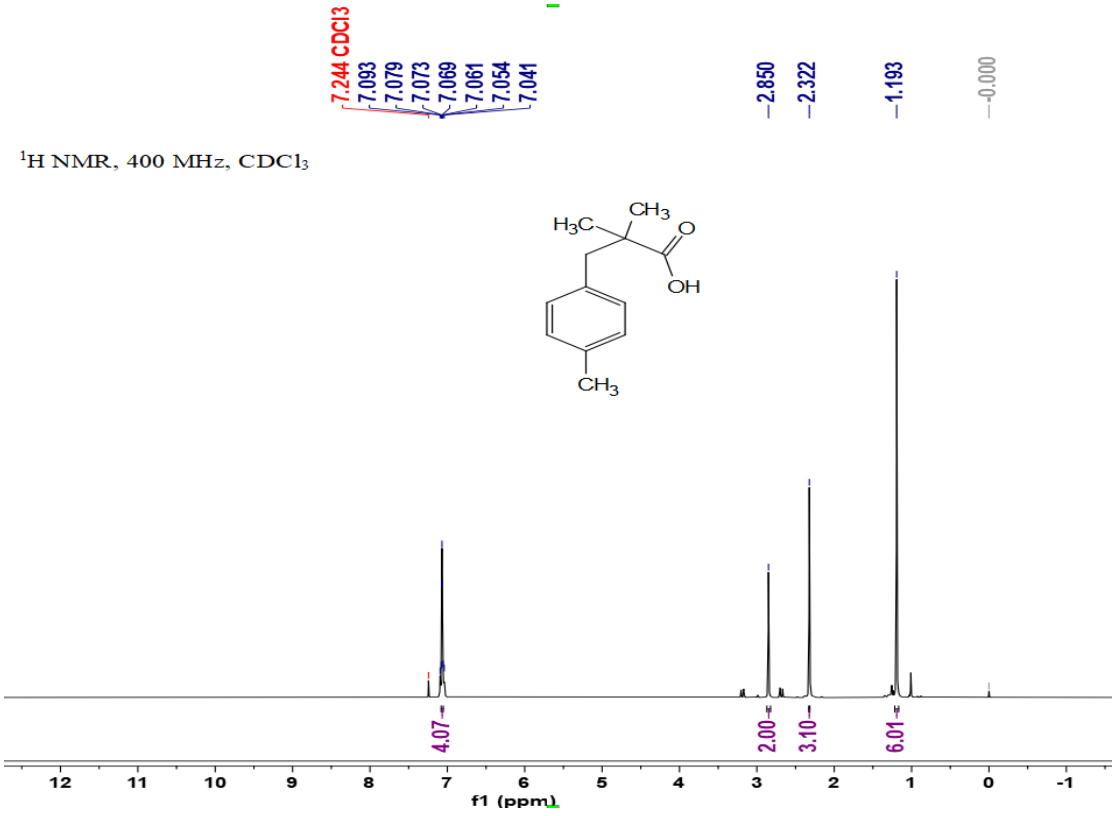


^{1}H NMR, 400 MHz, $CDCl_3$

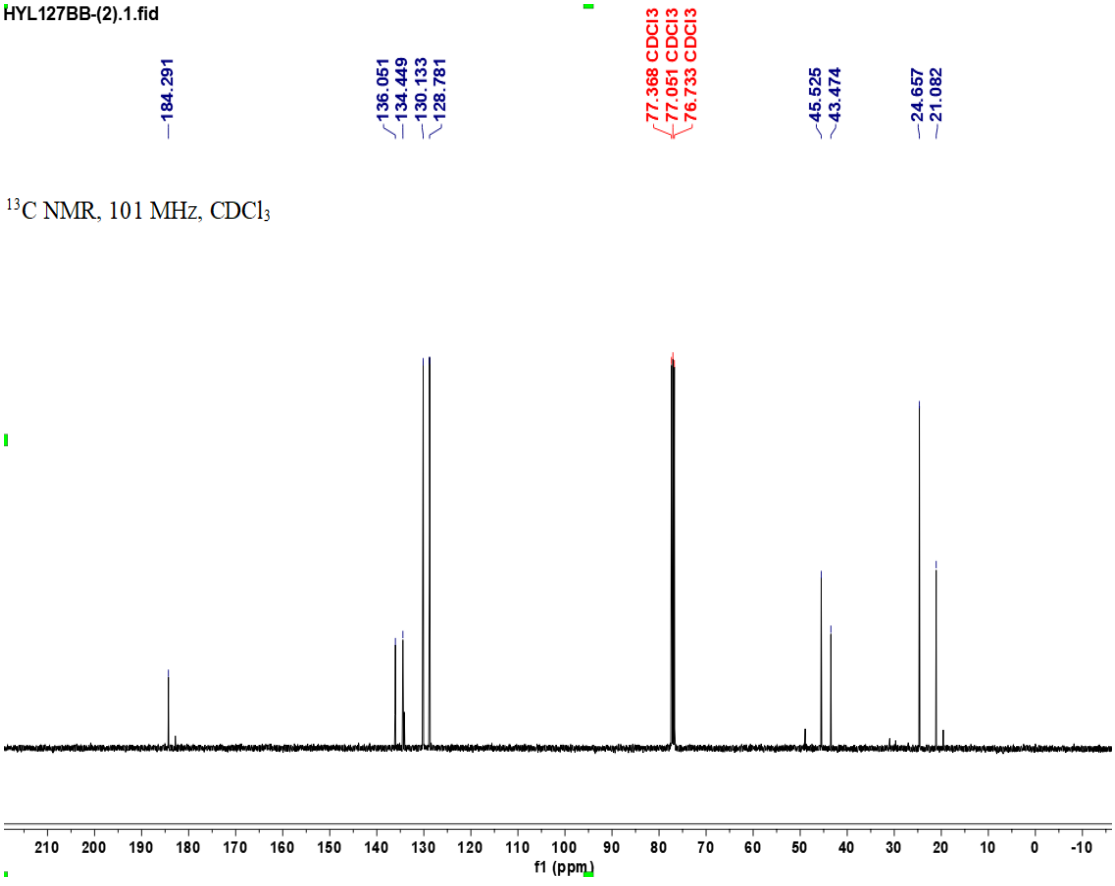


^{13}C NMR, 101 MHz, $CDCl_3$

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-26**

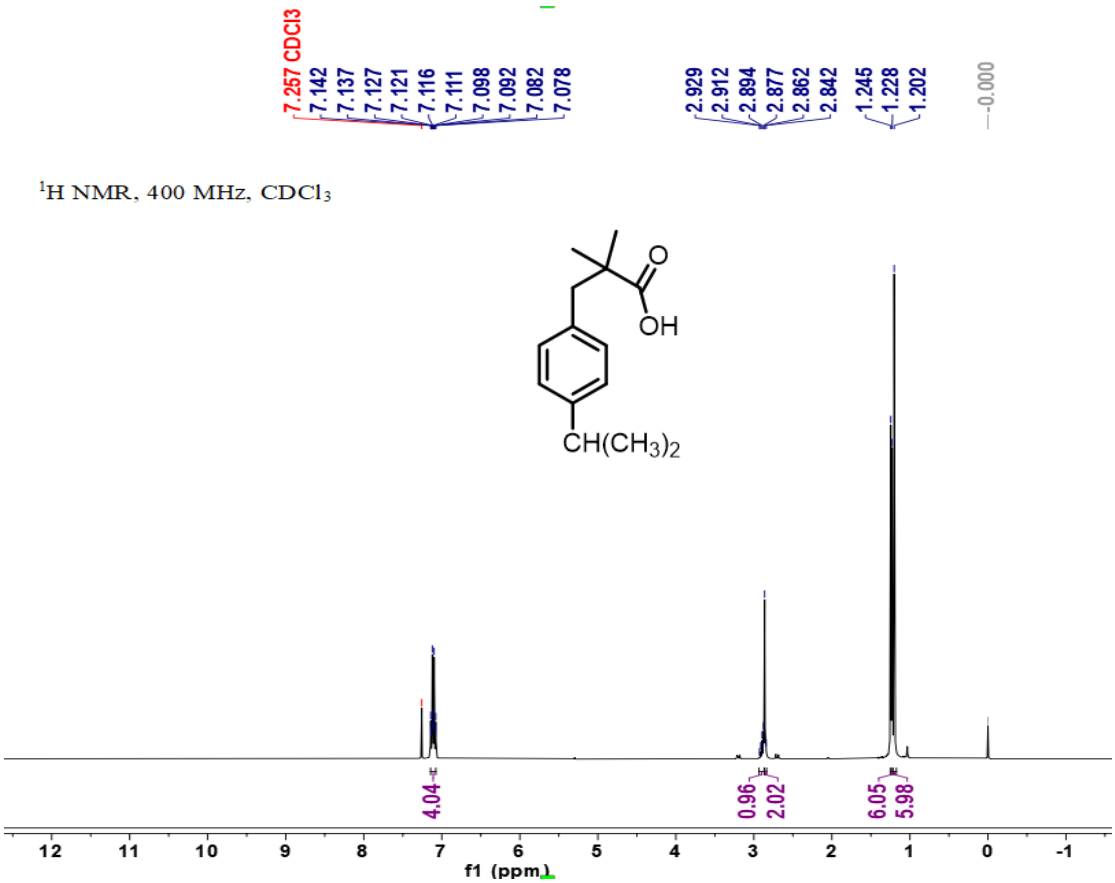


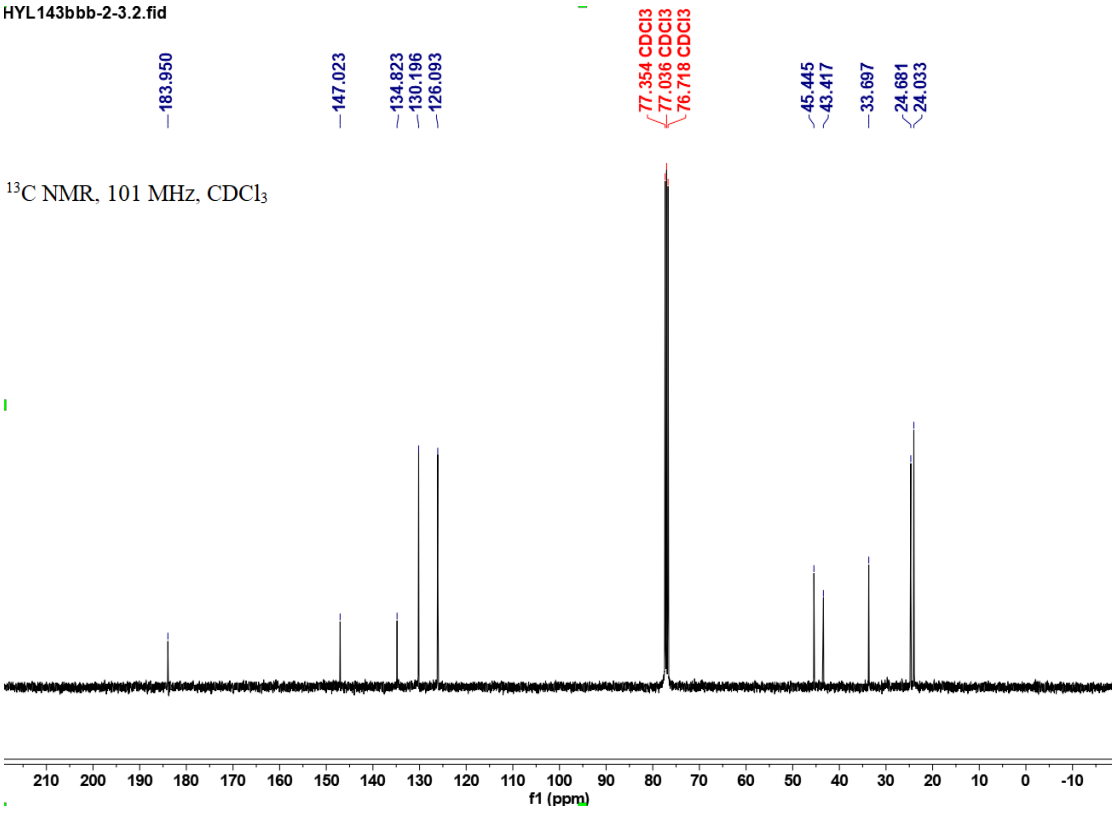
^{1}H NMR, 400 MHz, $CDCl_3$



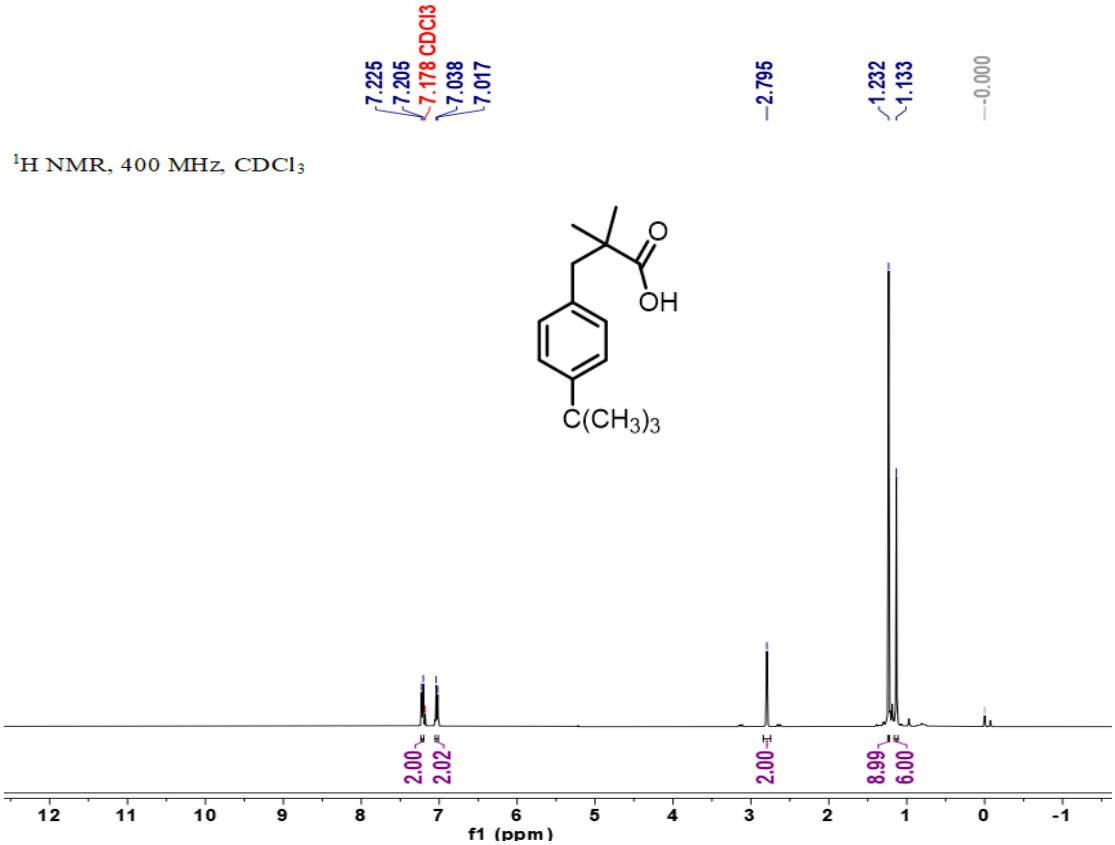
^{13}C NMR, 101 MHz, $CDCl_3$

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-27**

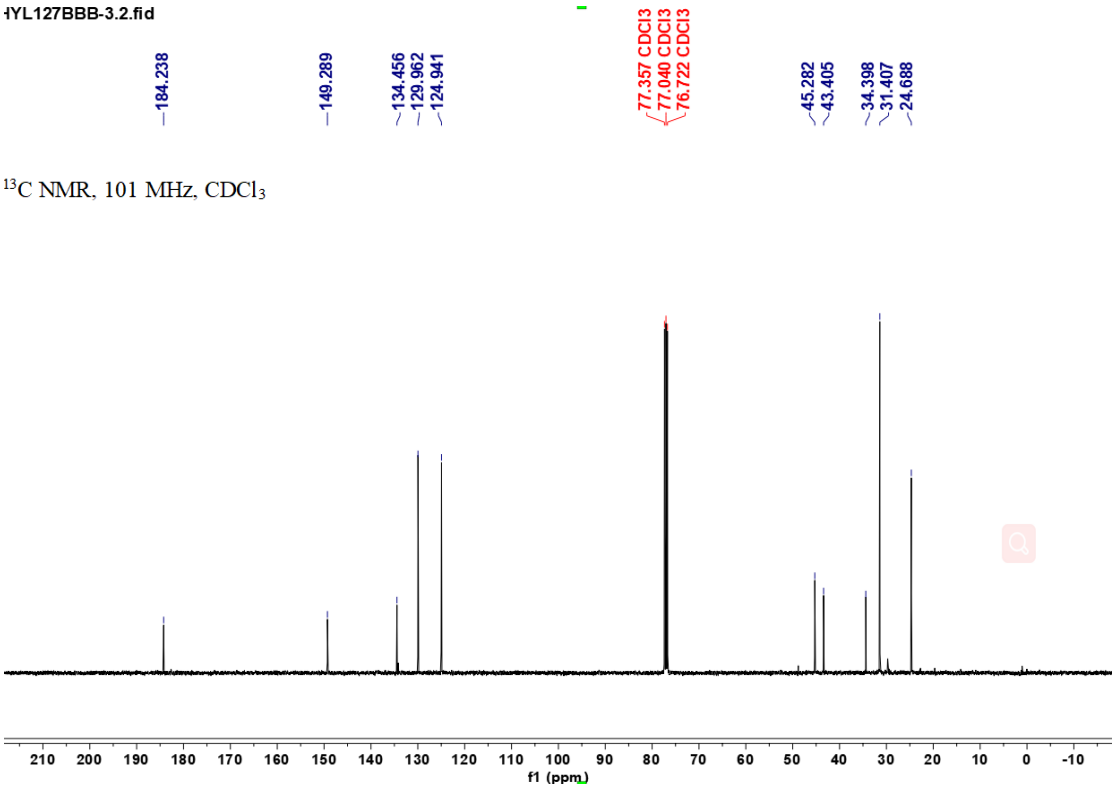




^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-28**

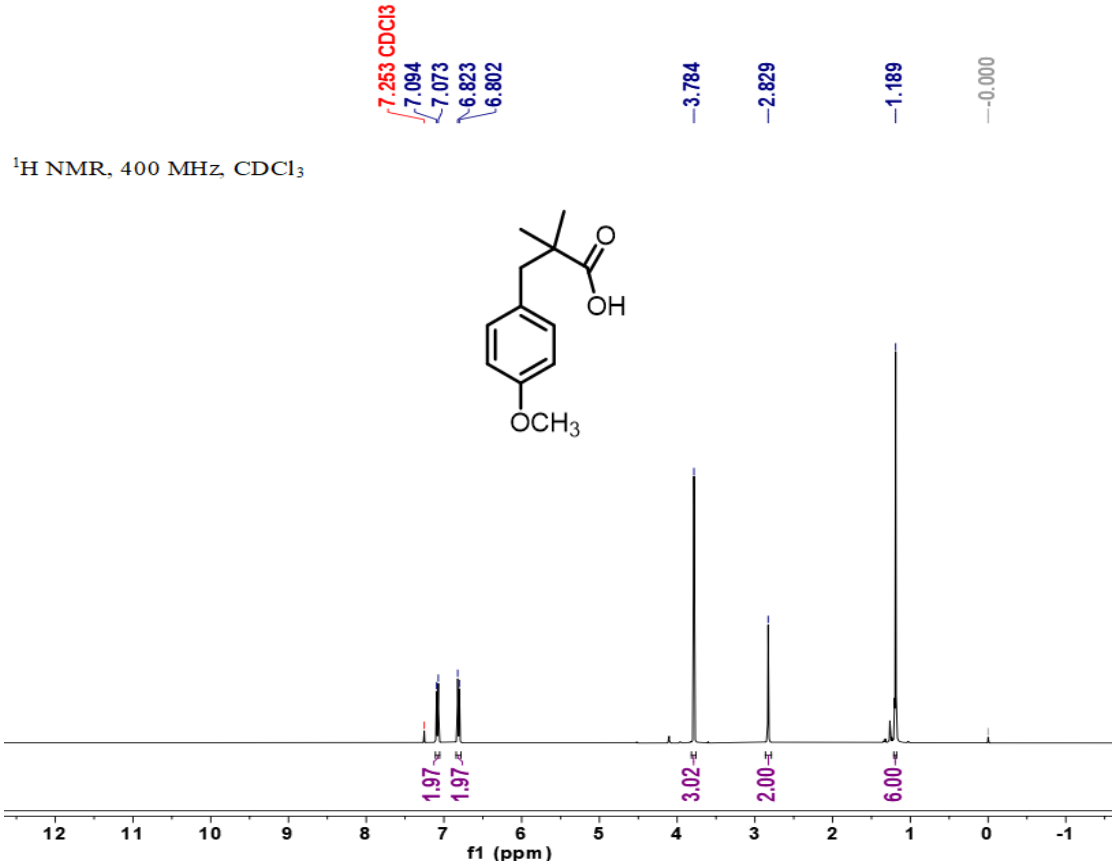


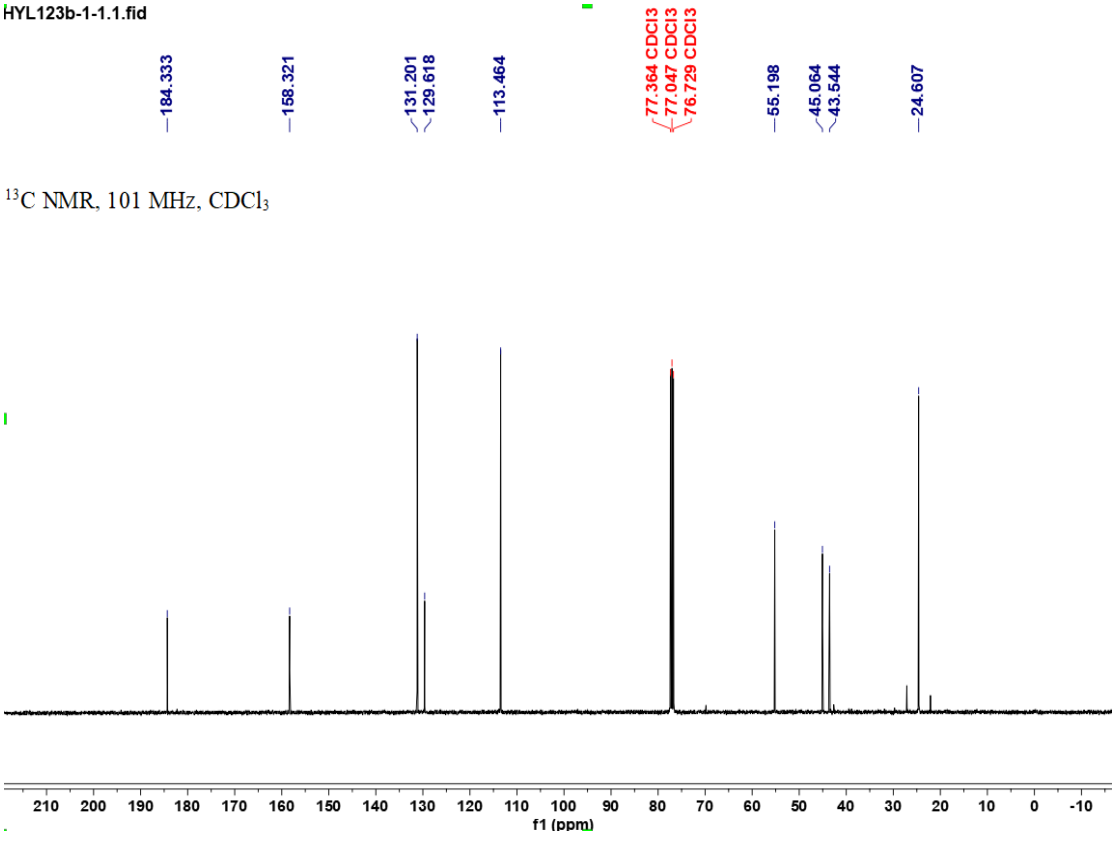
^{1}H NMR, 400 MHz, $CDCl_3$



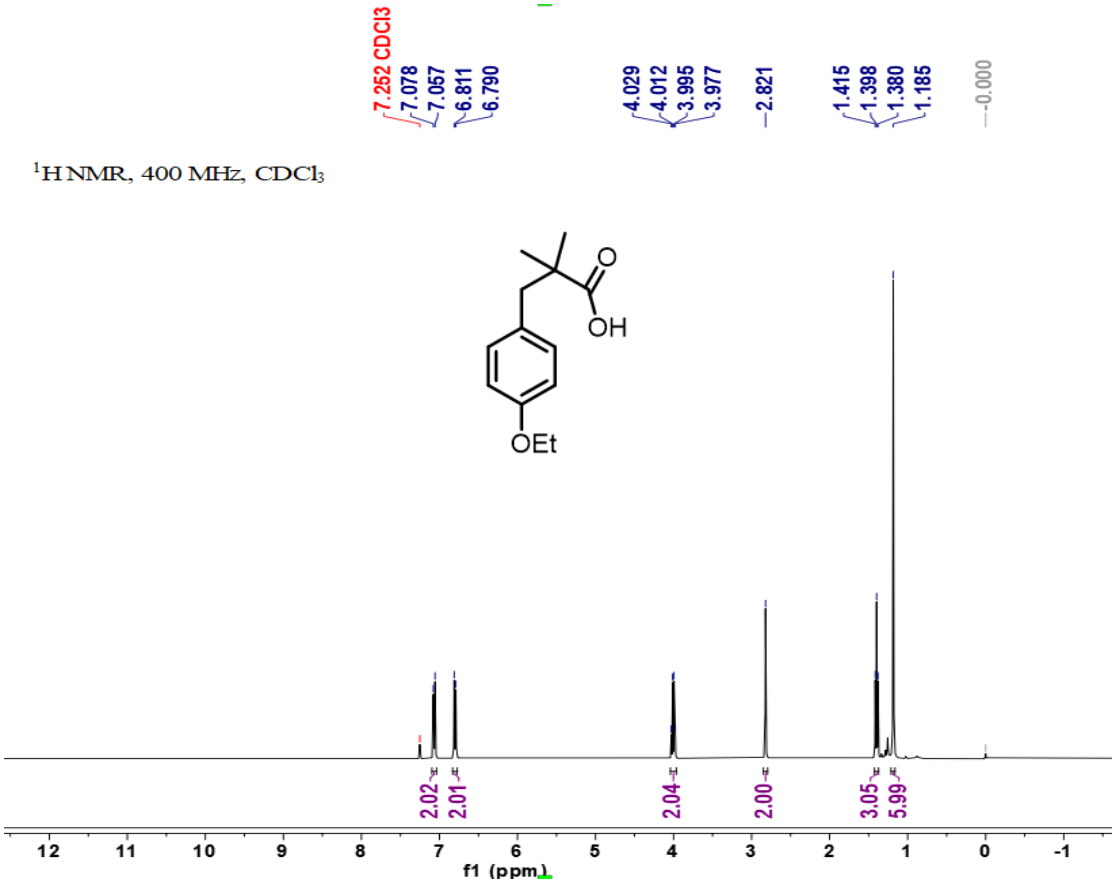
^{13}C NMR, 101 MHz, $CDCl_3$

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-29**

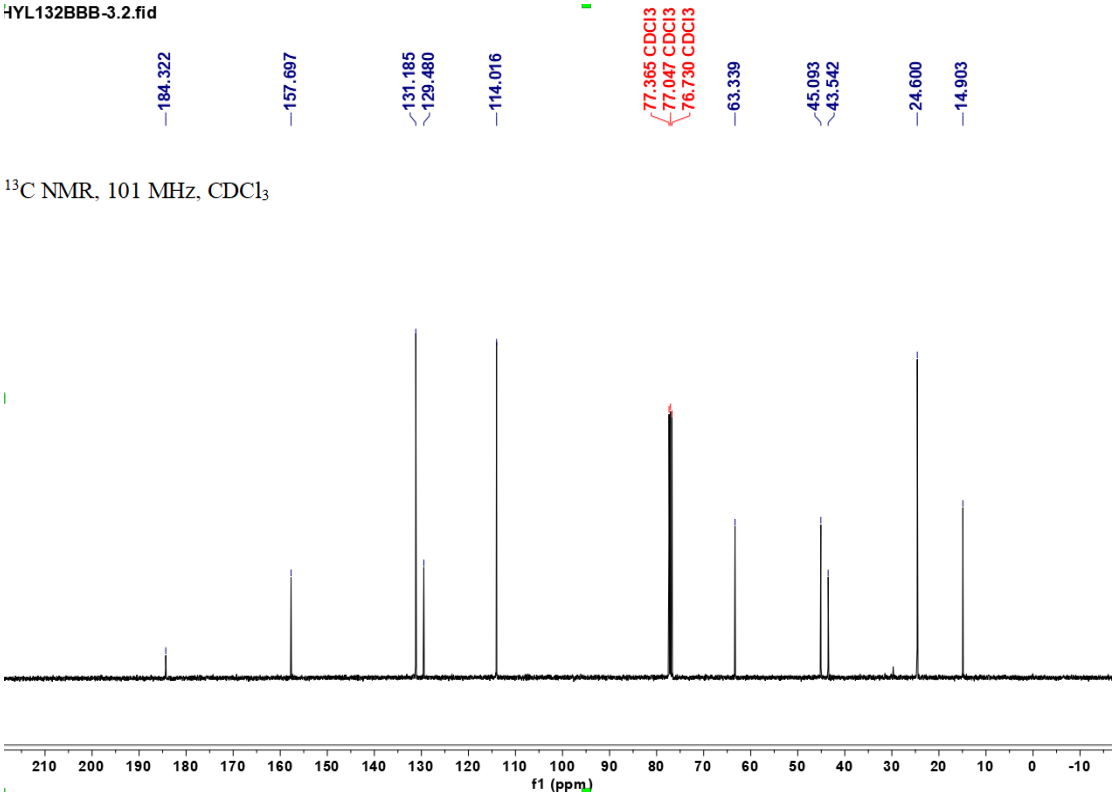




^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-30**

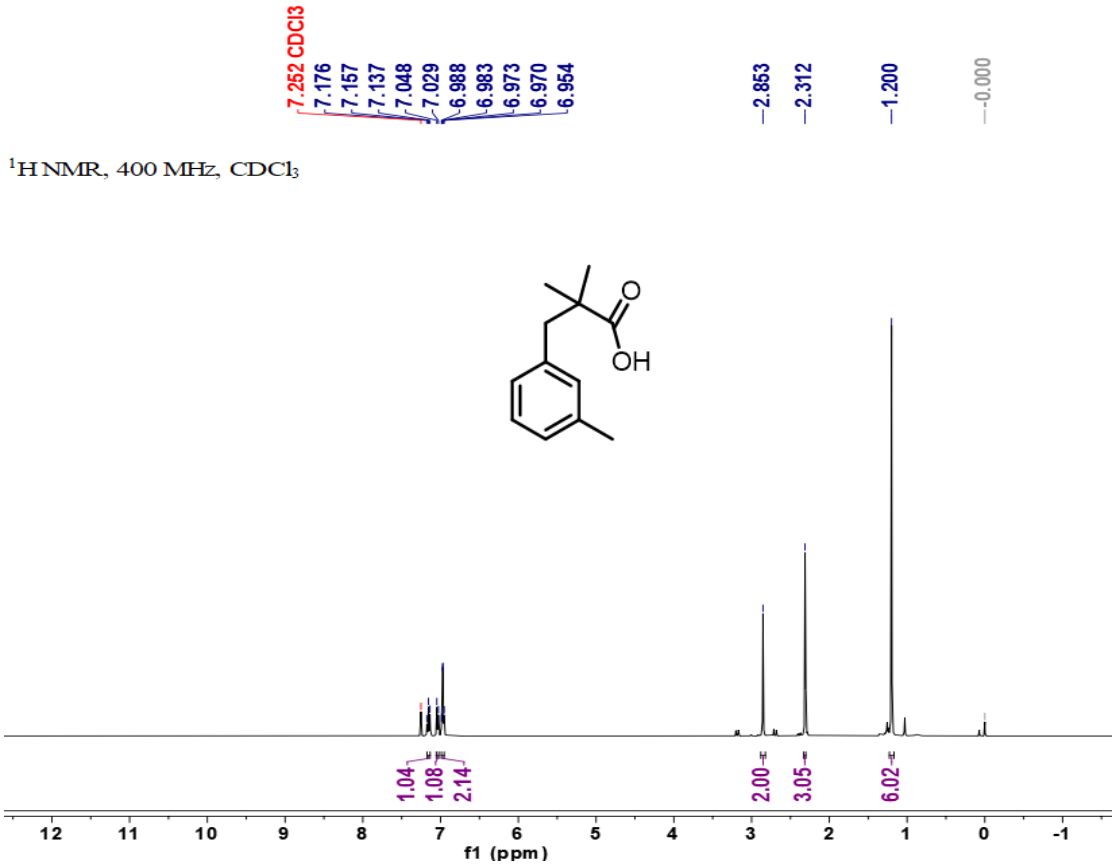


^{1}H NMR, 400 MHz, $CDCl_3$

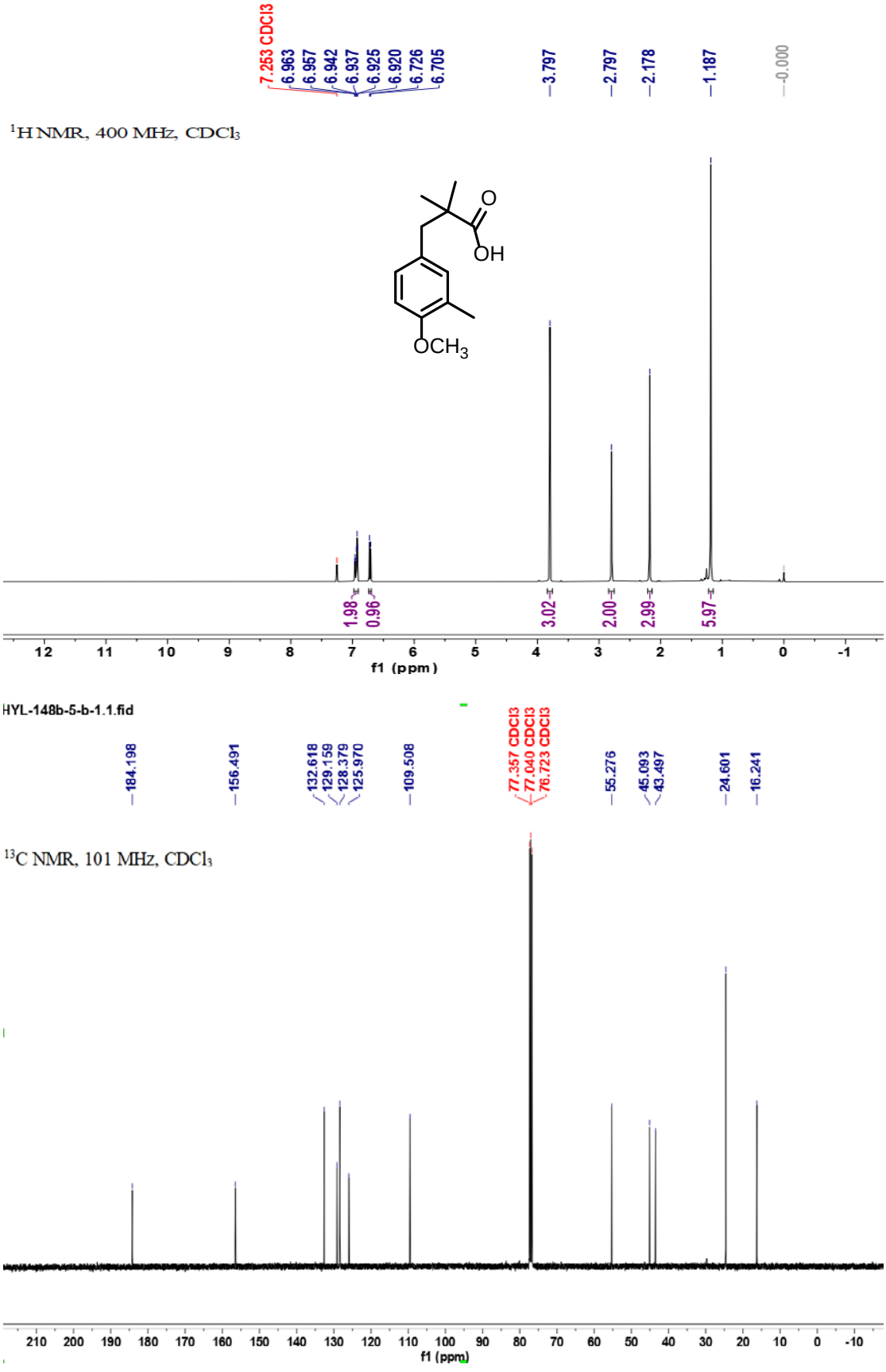


^{13}C NMR, 101 MHz, $CDCl_3$

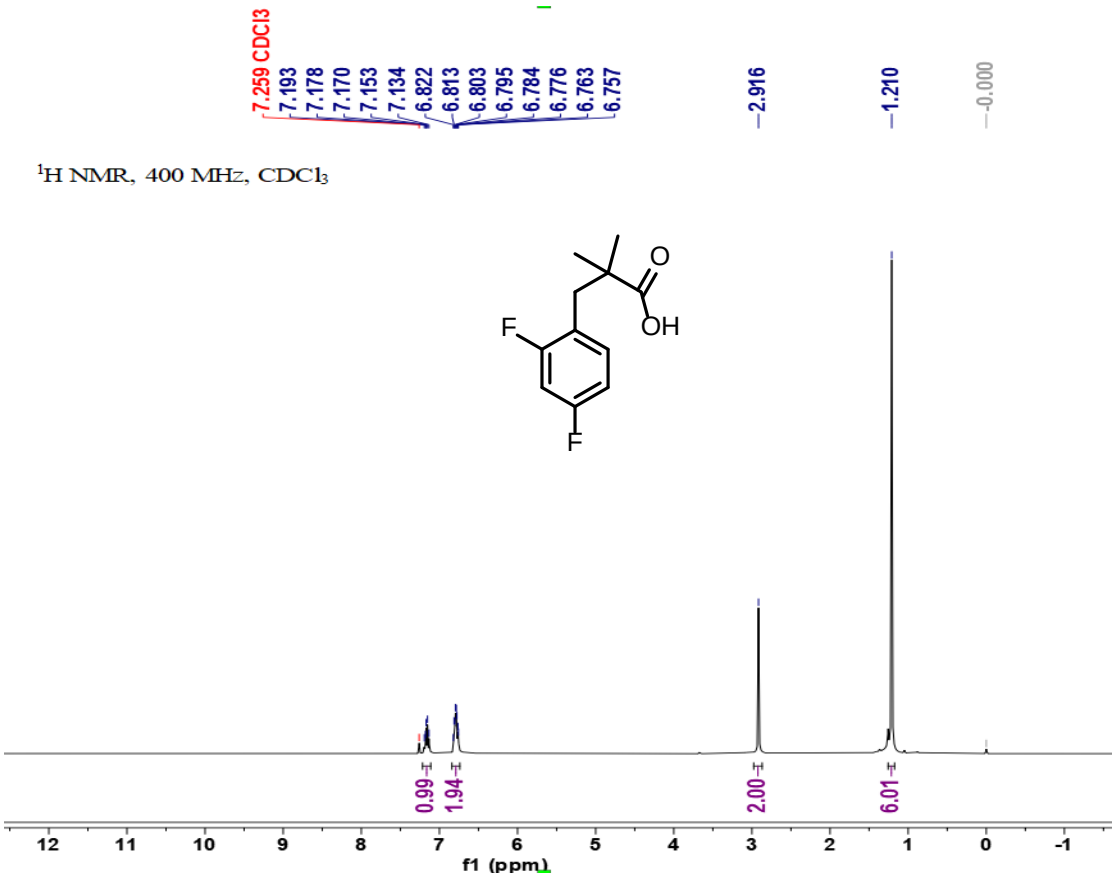
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-31**



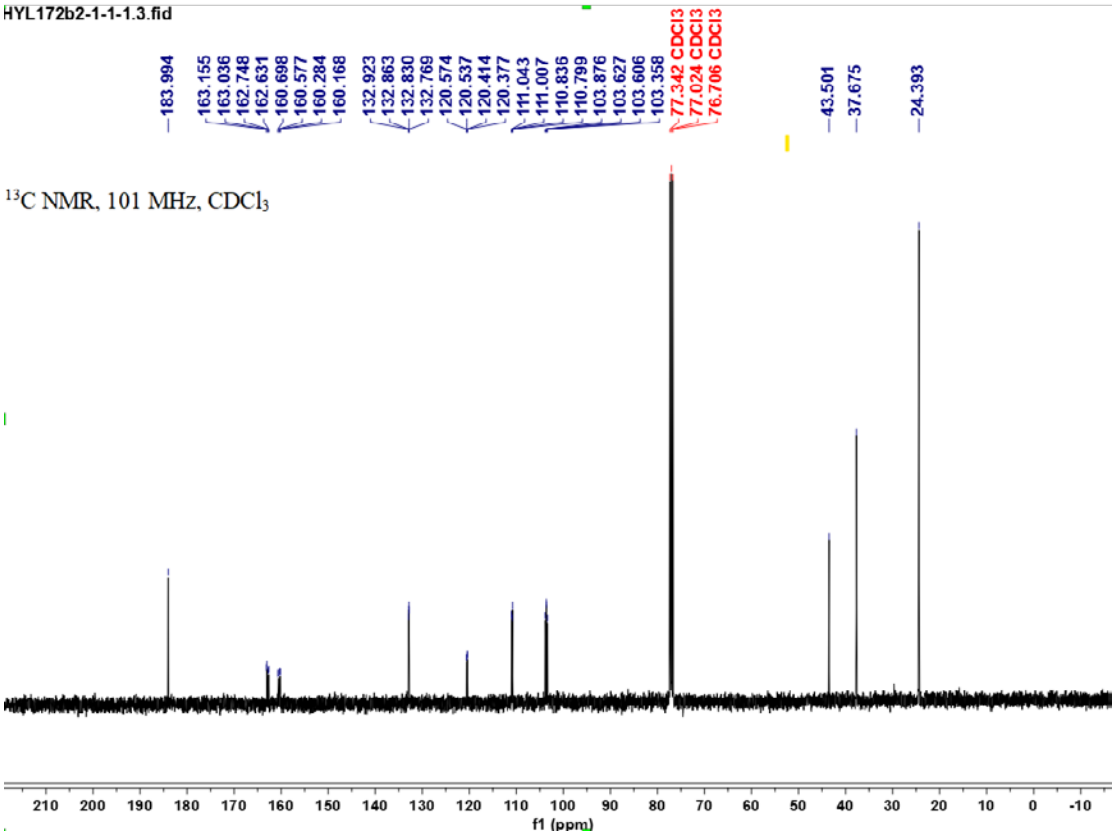
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-32**



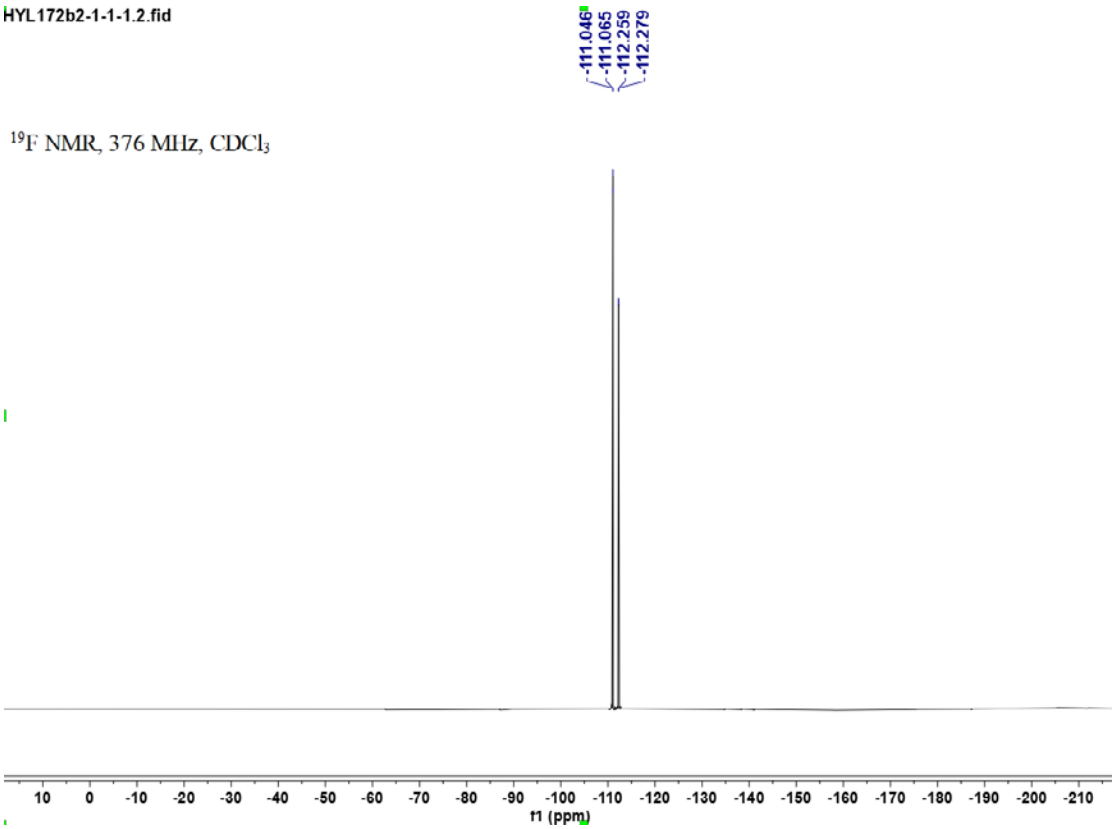
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-33**



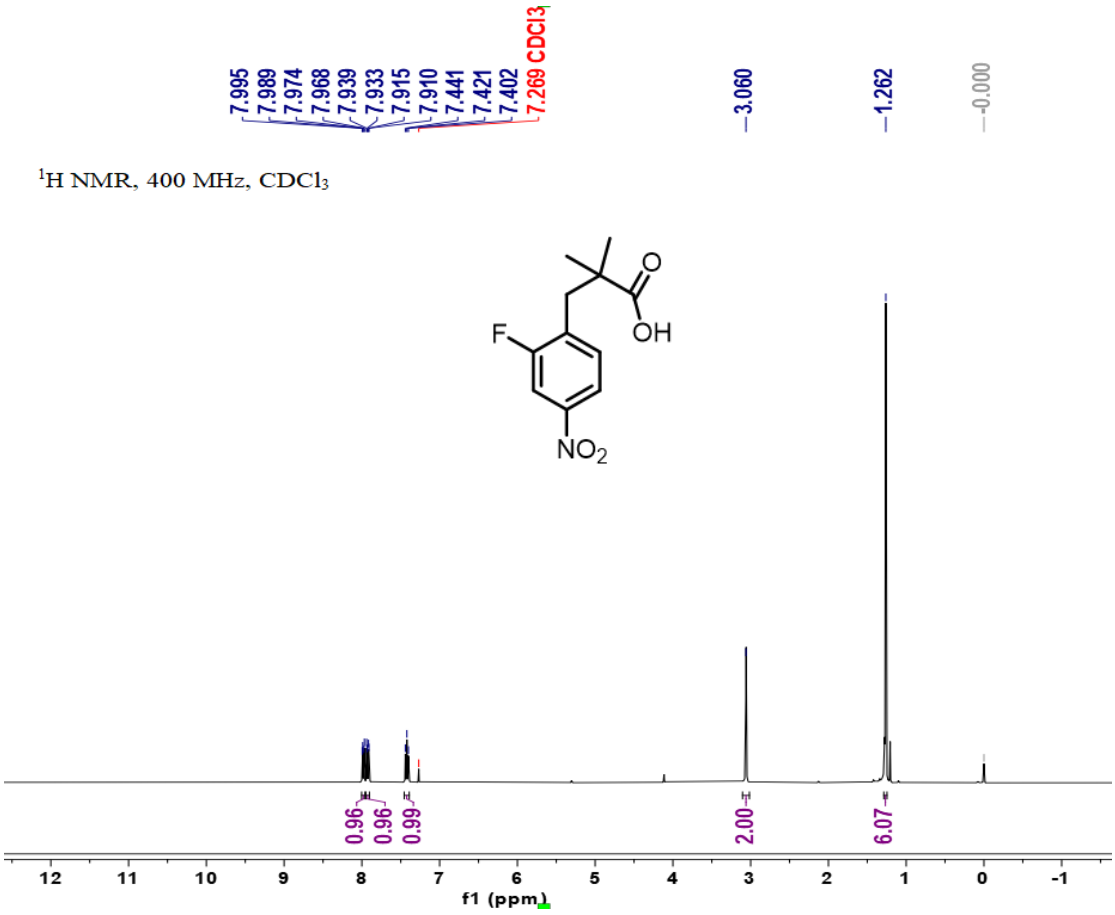
^{1}H NMR, 400 MHz, $CDCl_3$



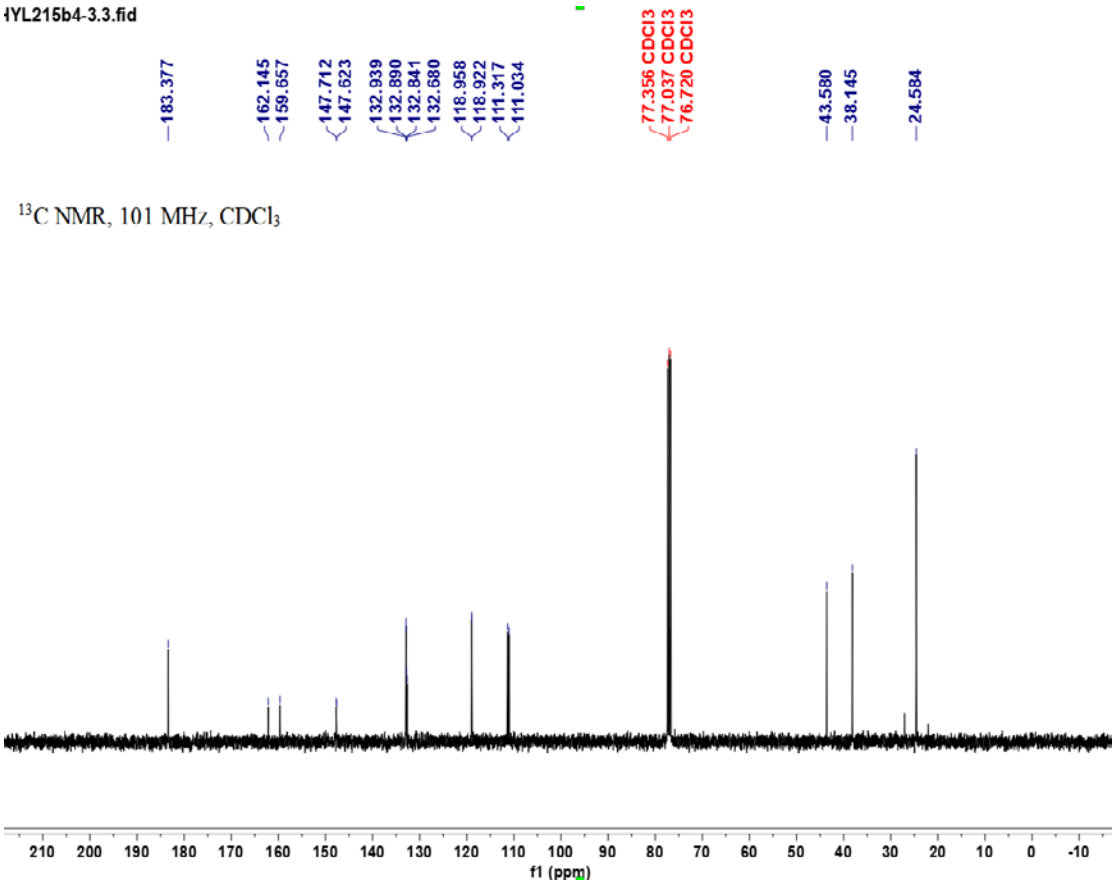
^{13}C NMR, 101 MHz, $CDCl_3$



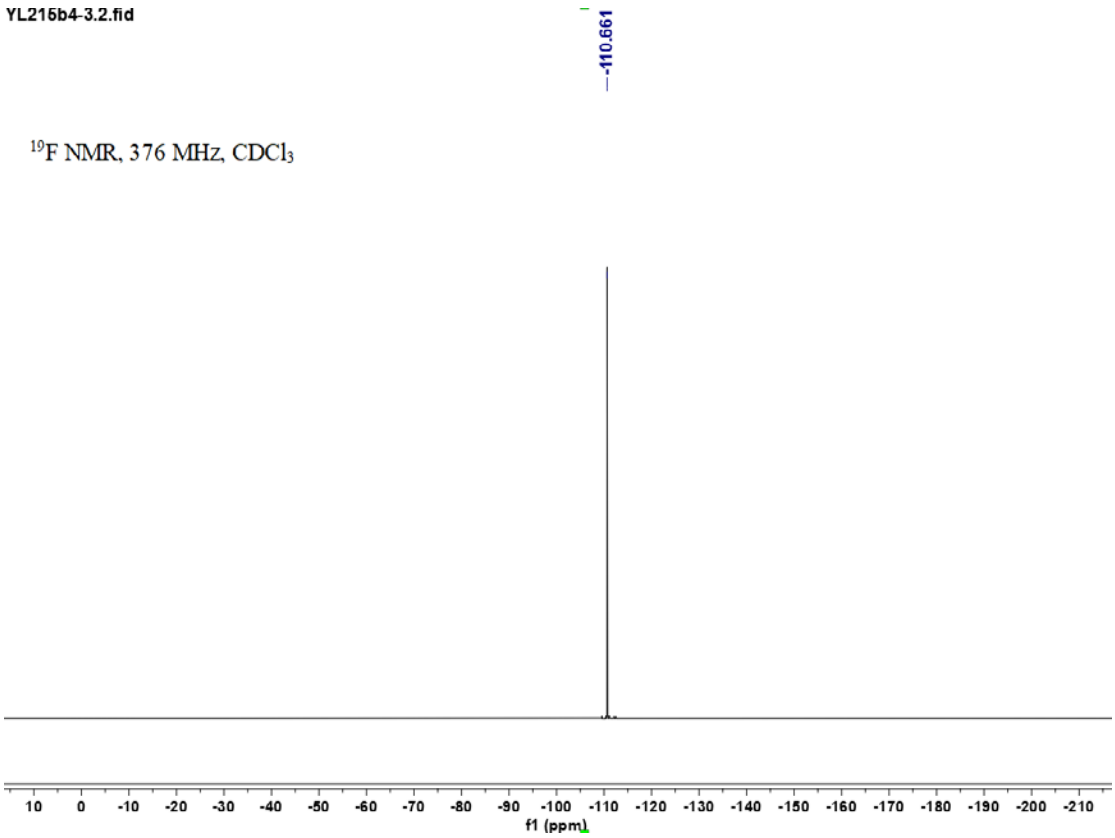
^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra of **7-34**



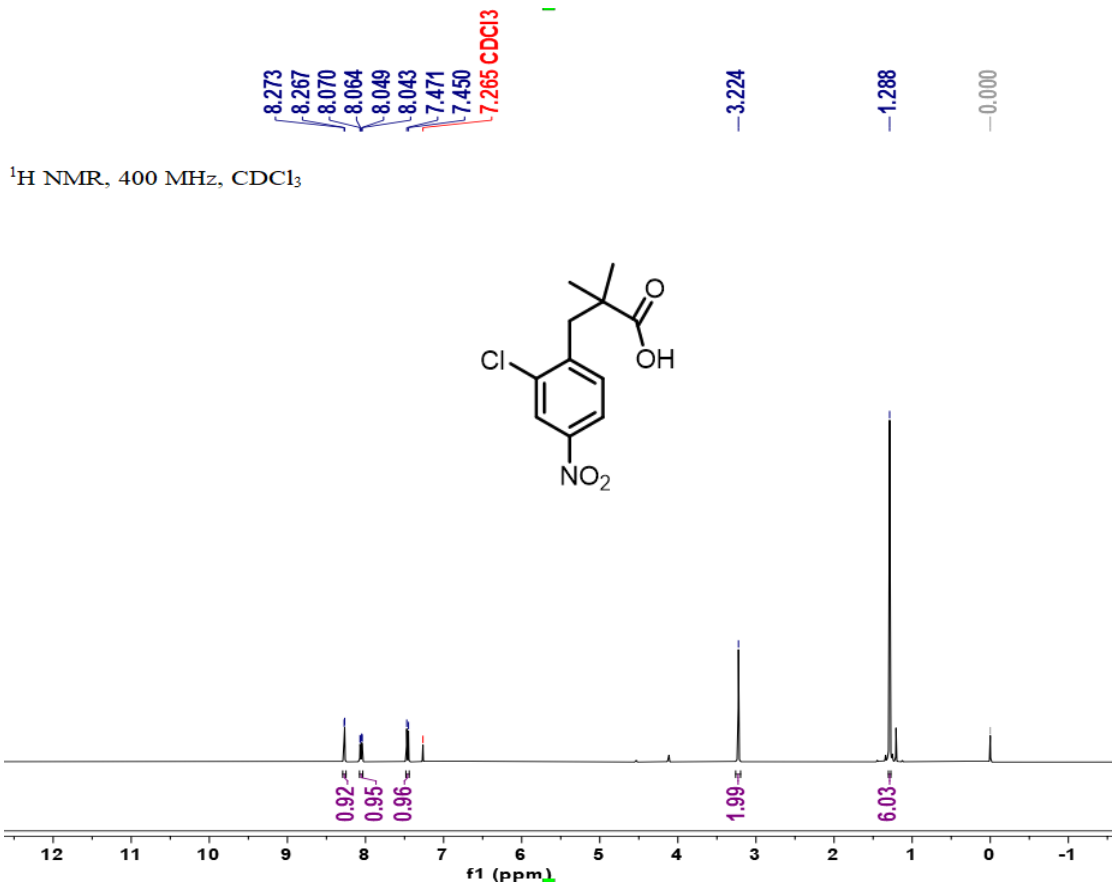
^{1}H NMR, 400 MHz, $CDCl_3$



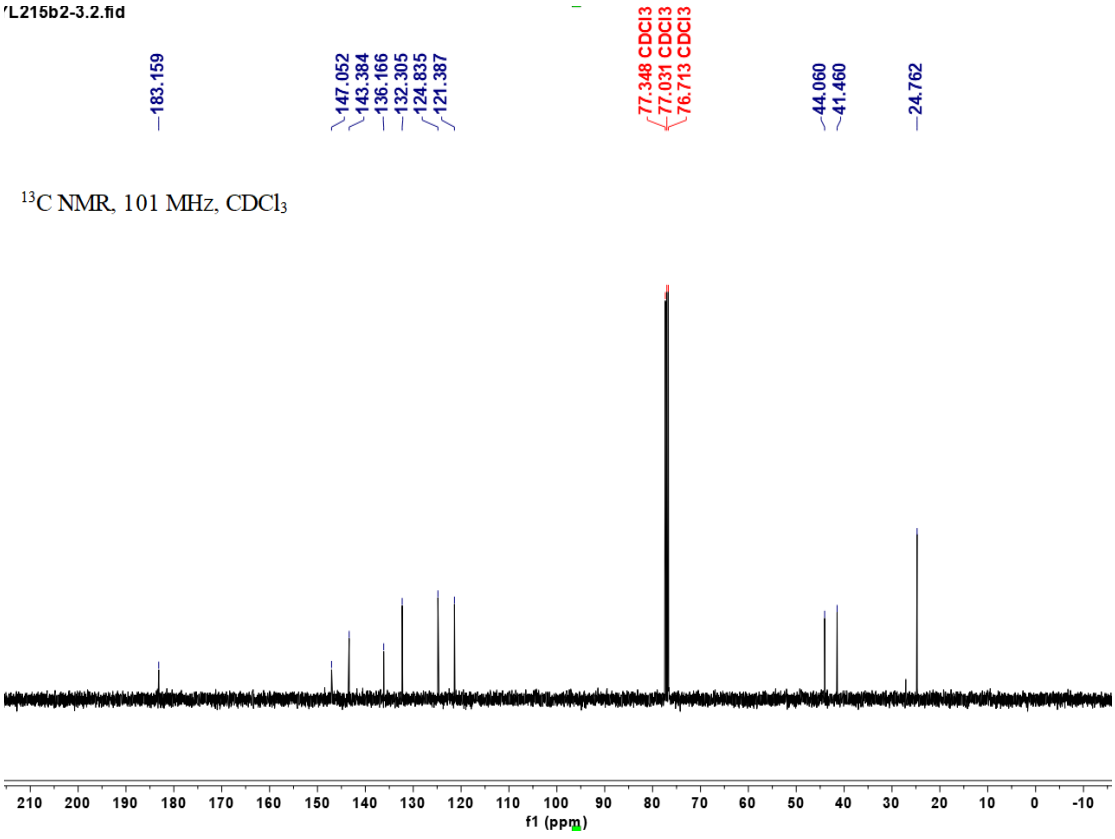
^{13}C NMR, 101 MHz, $CDCl_3$



^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra of **7-35**

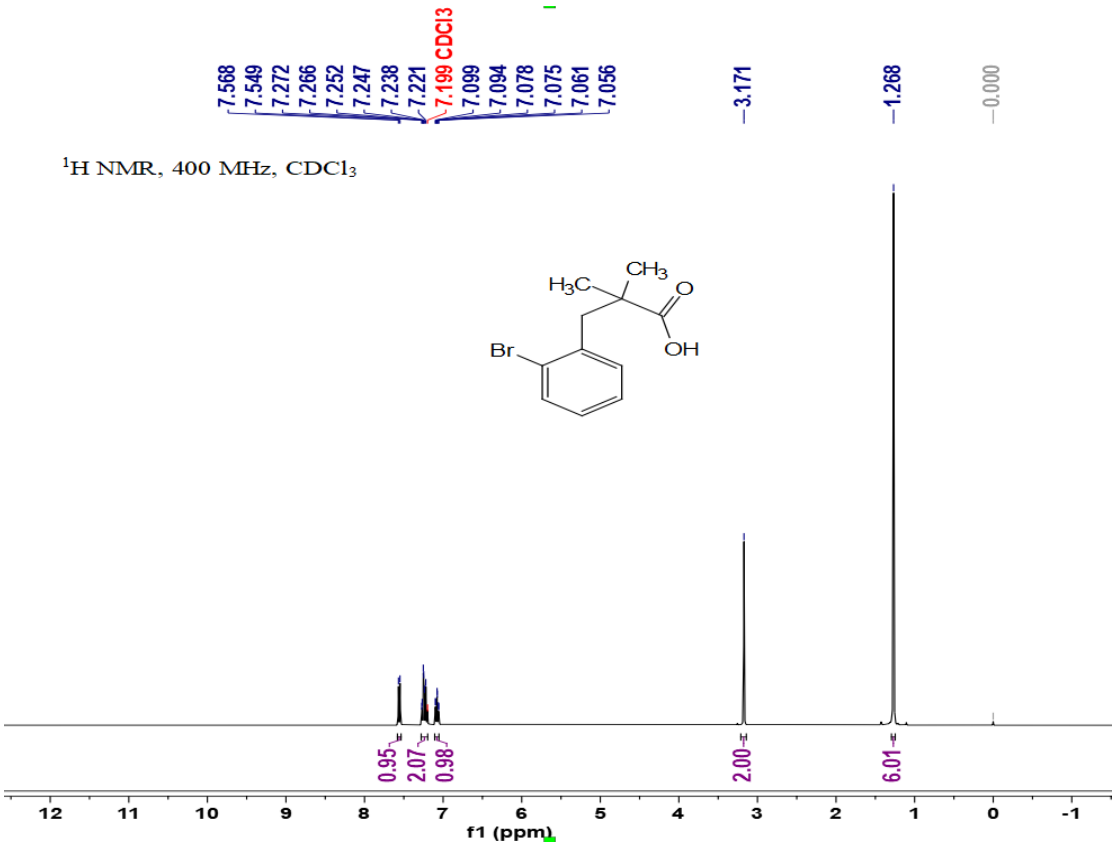


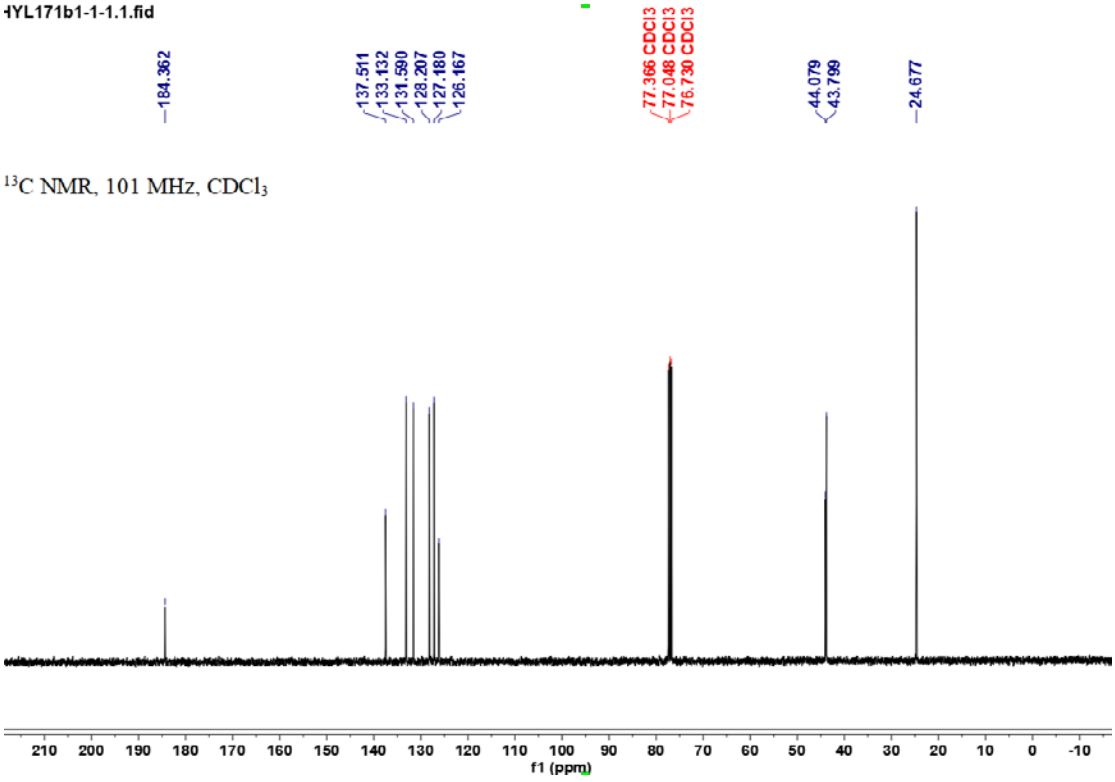
^{1}H NMR, 400 MHz, $CDCl_3$



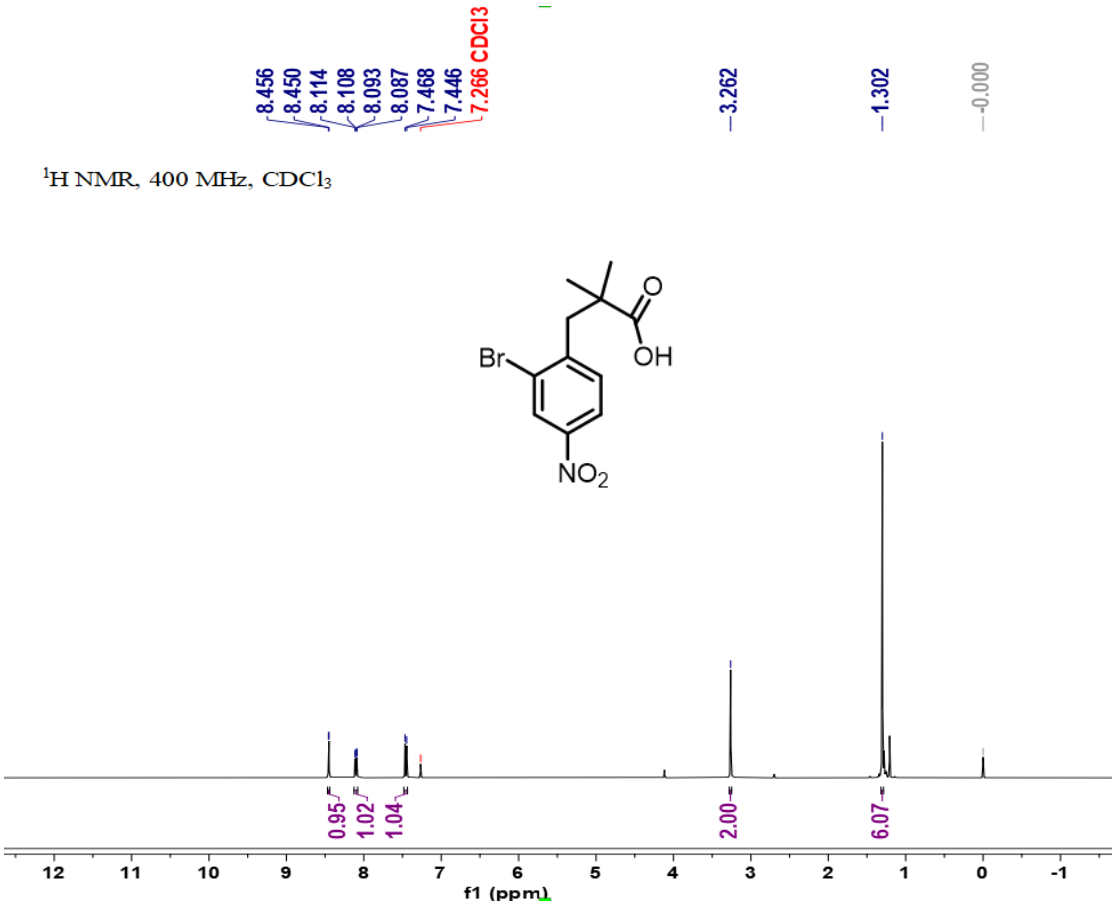
^{13}C NMR, 101 MHz, $CDCl_3$

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-36**

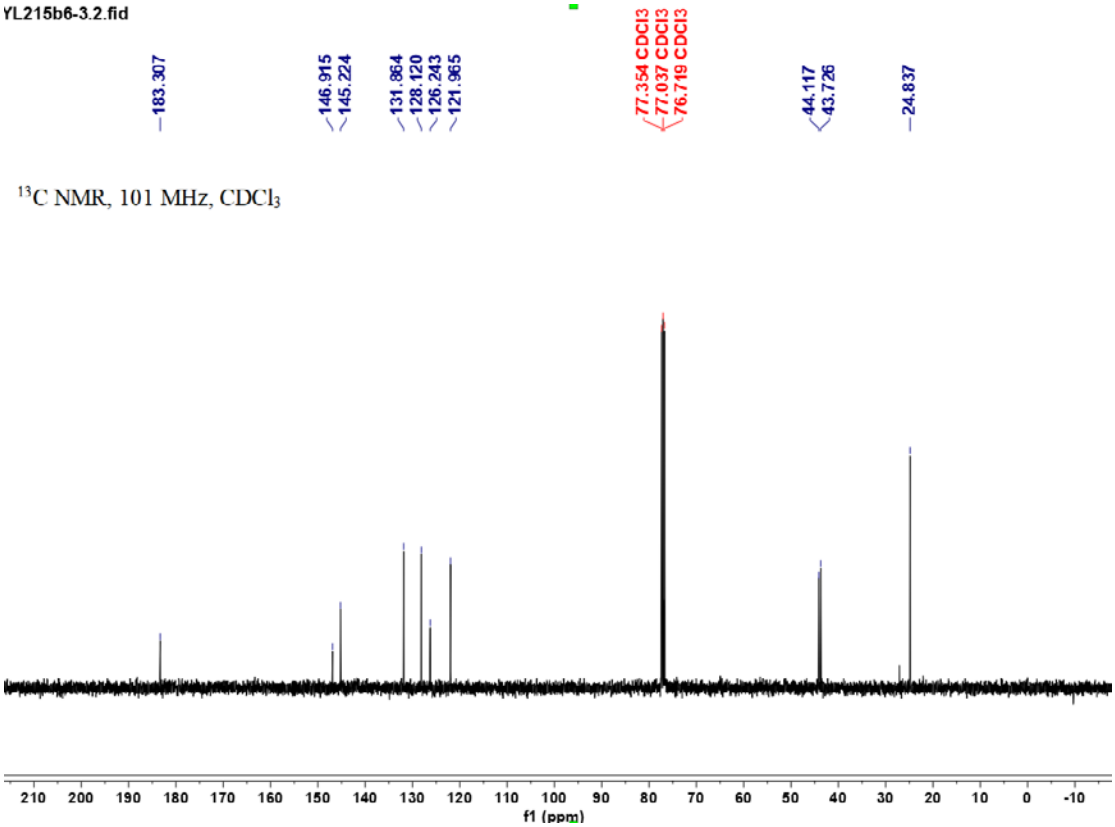




^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-37**

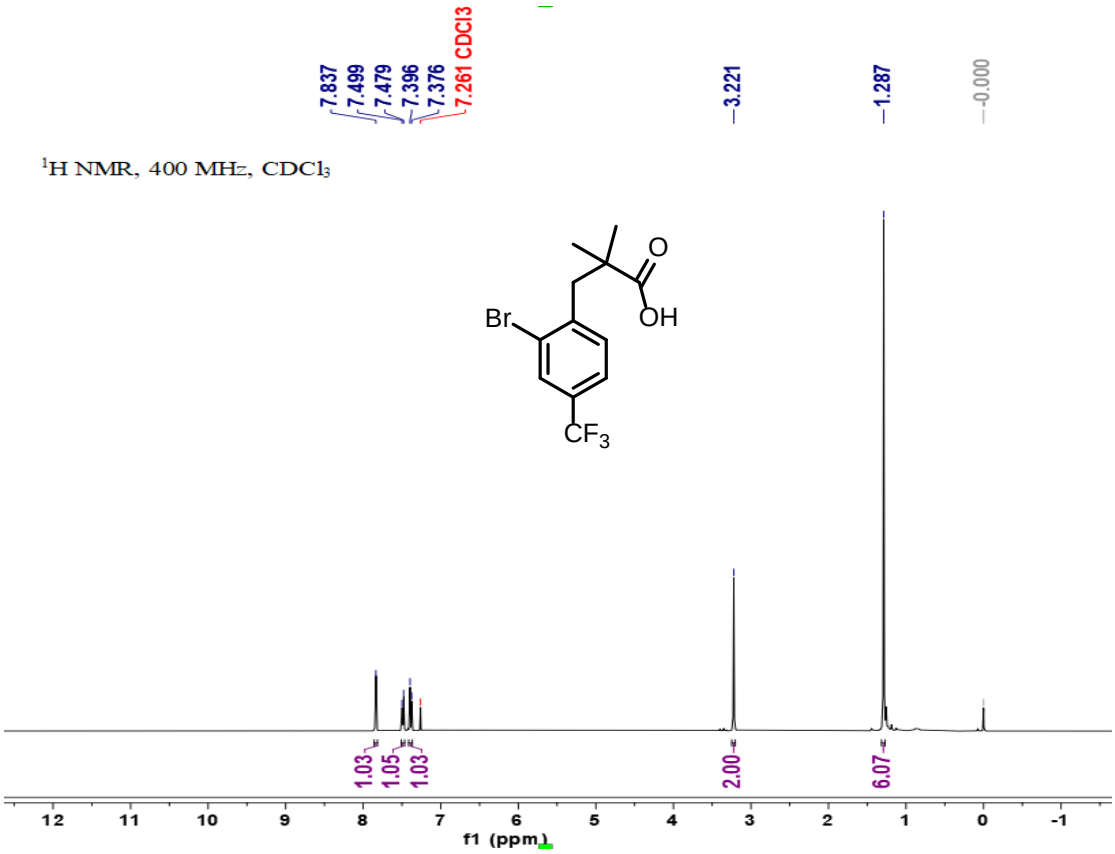


^{1}H NMR, 400 MHz, $CDCl_3$

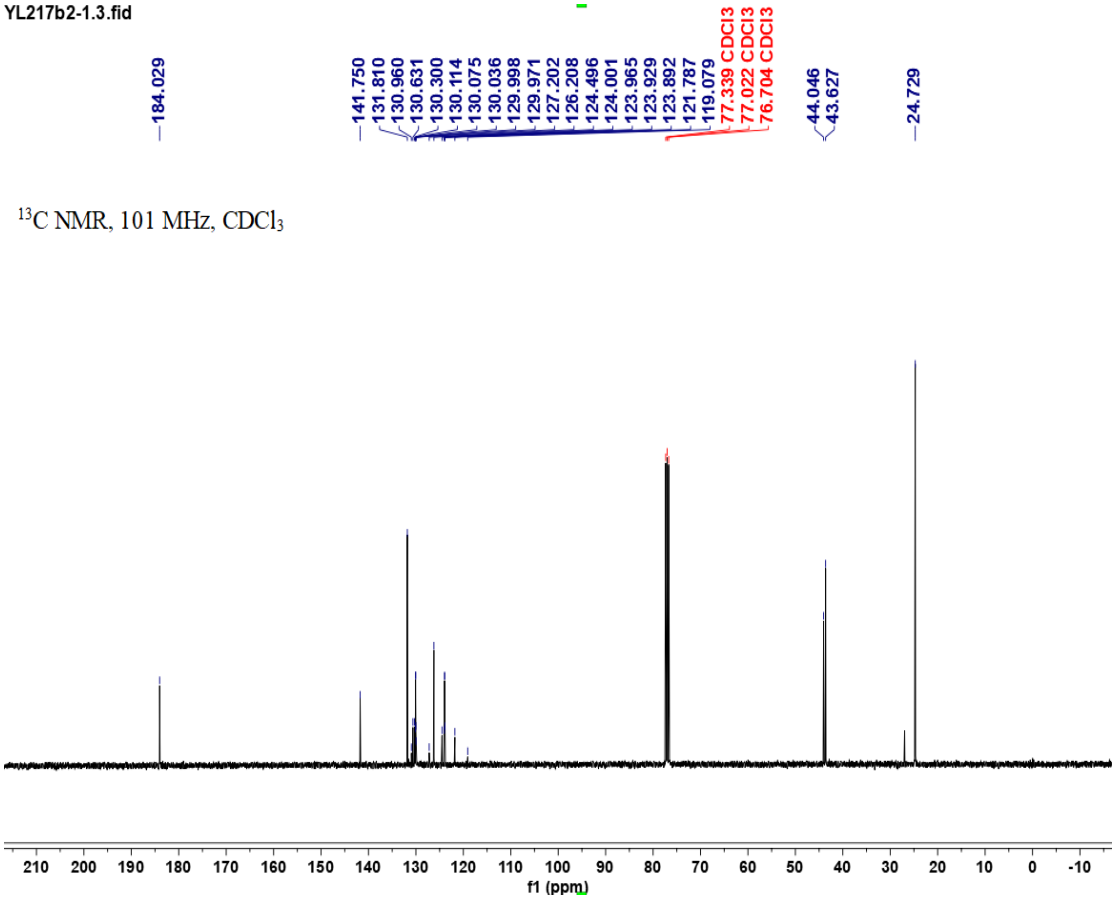


^{13}C NMR, 101 MHz, $CDCl_3$

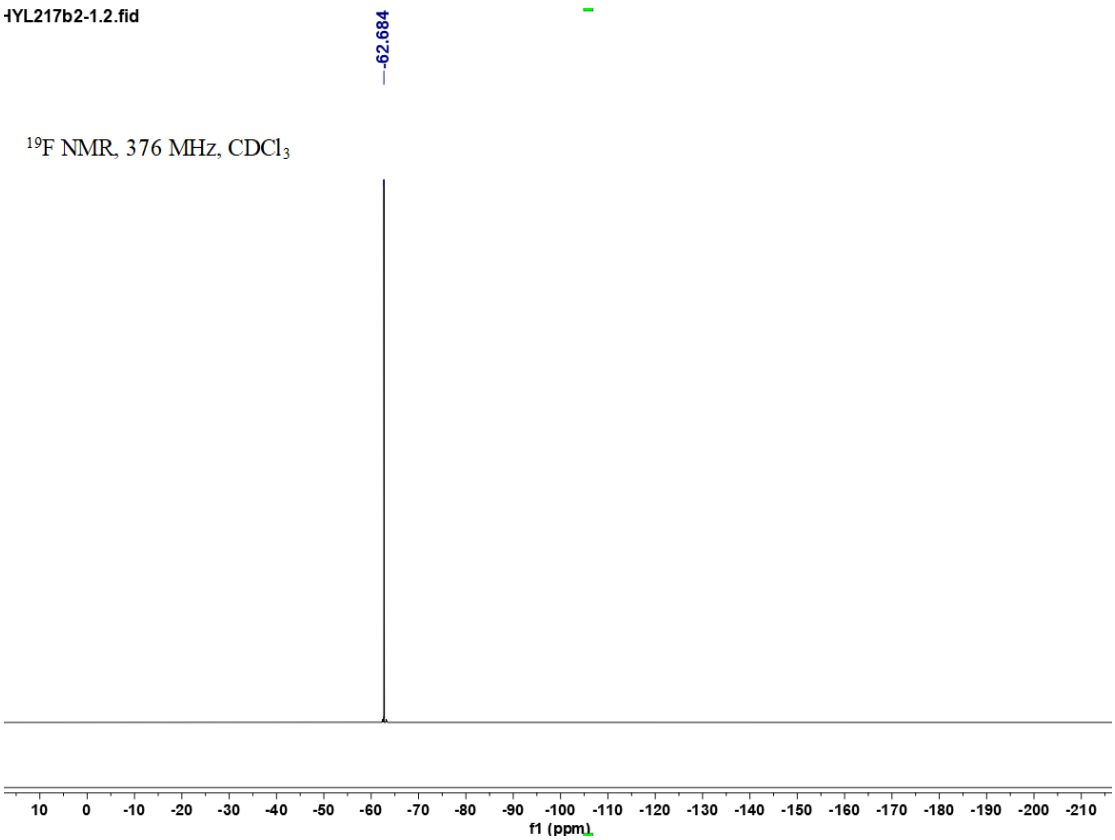
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-38**



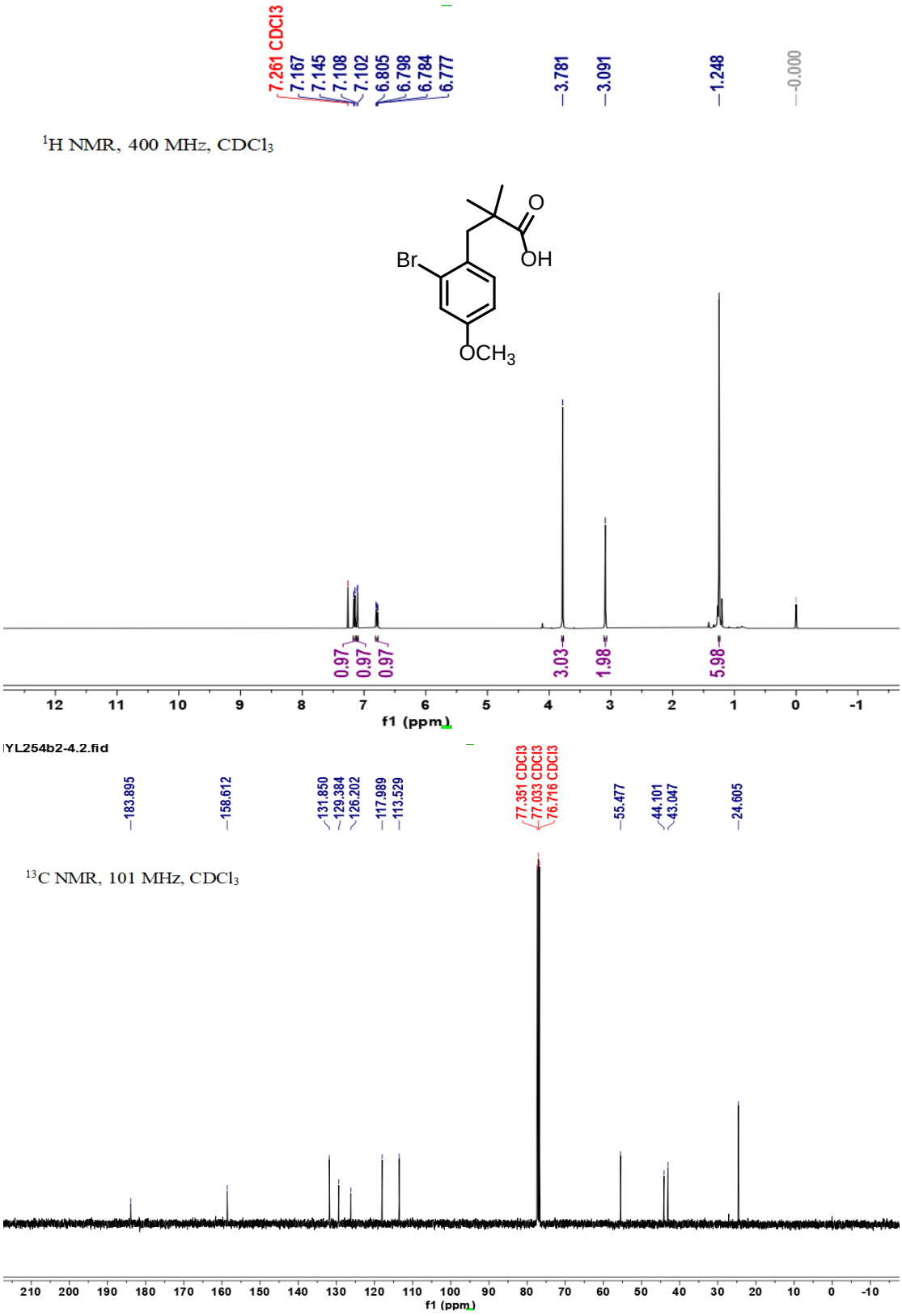
^{1}H NMR, 400 MHz, $CDCl_3$



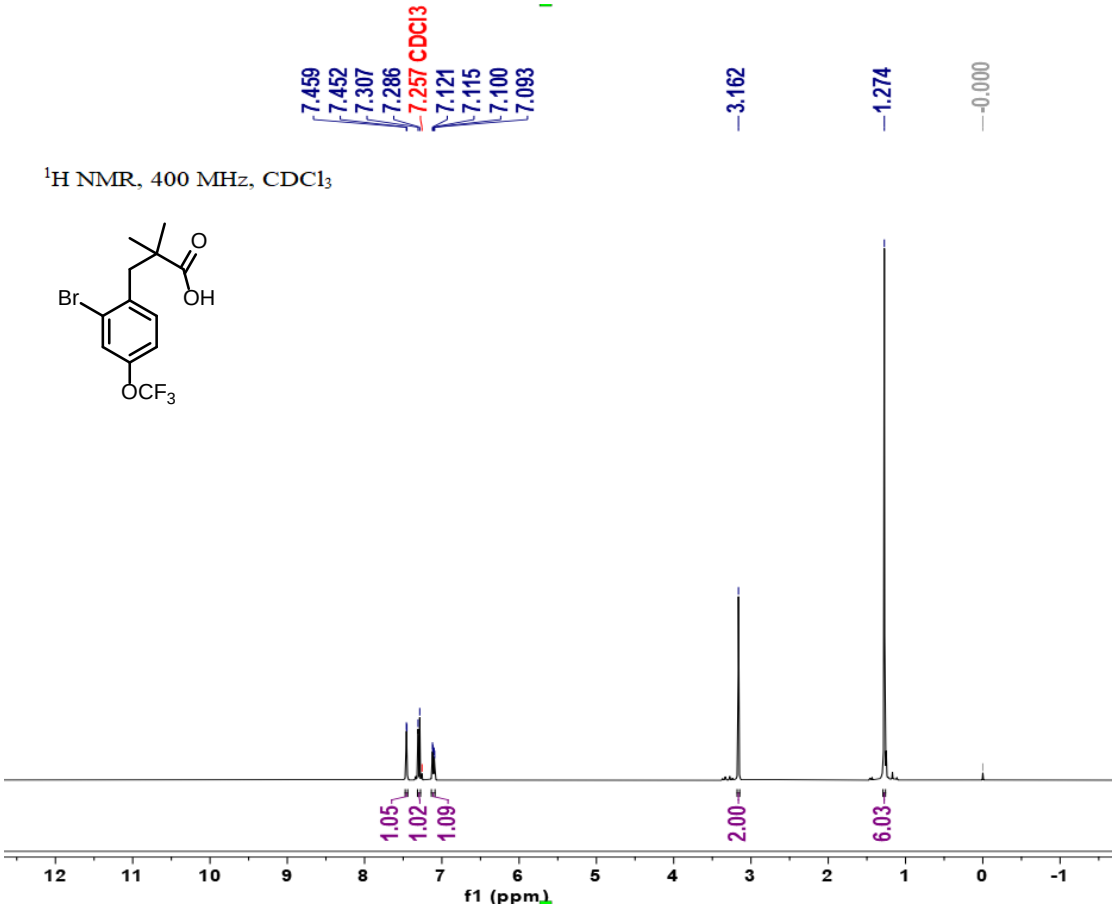
^{13}C NMR, 101 MHz, $CDCl_3$



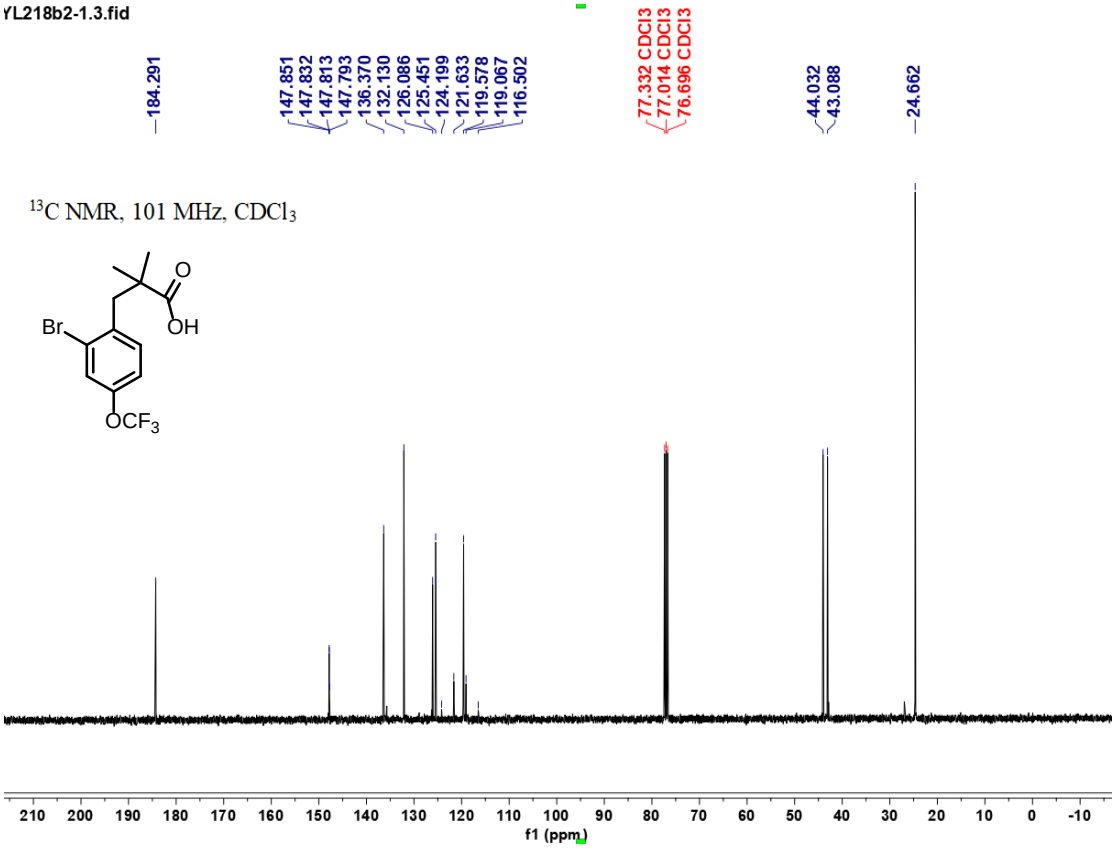
^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra of **7-39**



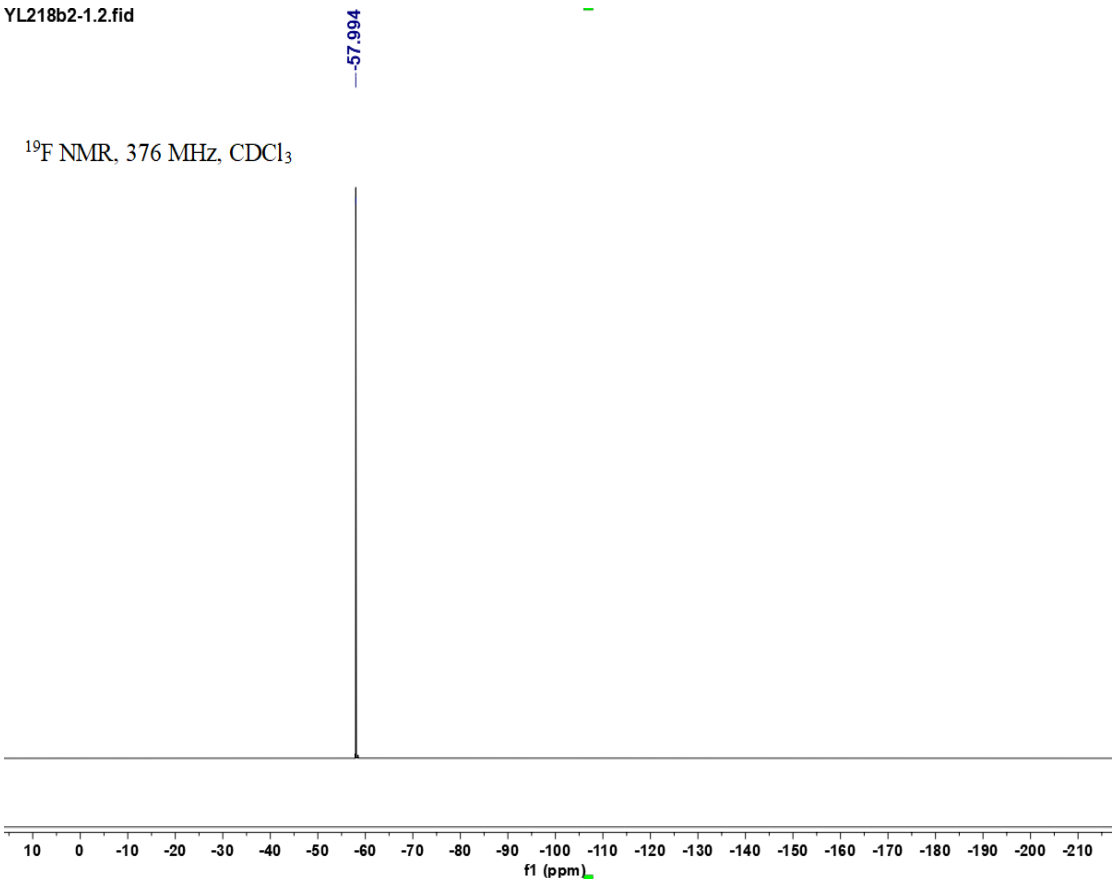
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-40**



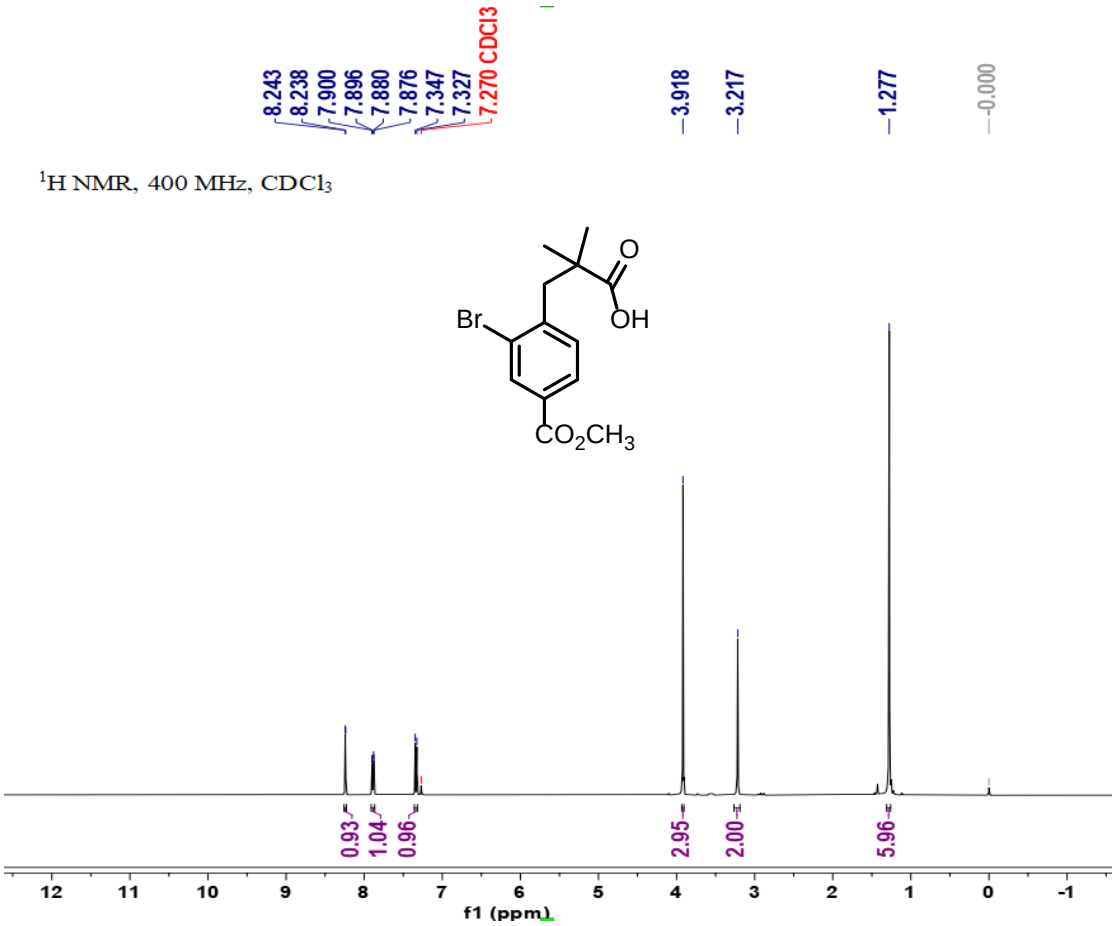
^{1}H NMR, 400 MHz, $CDCl_3$



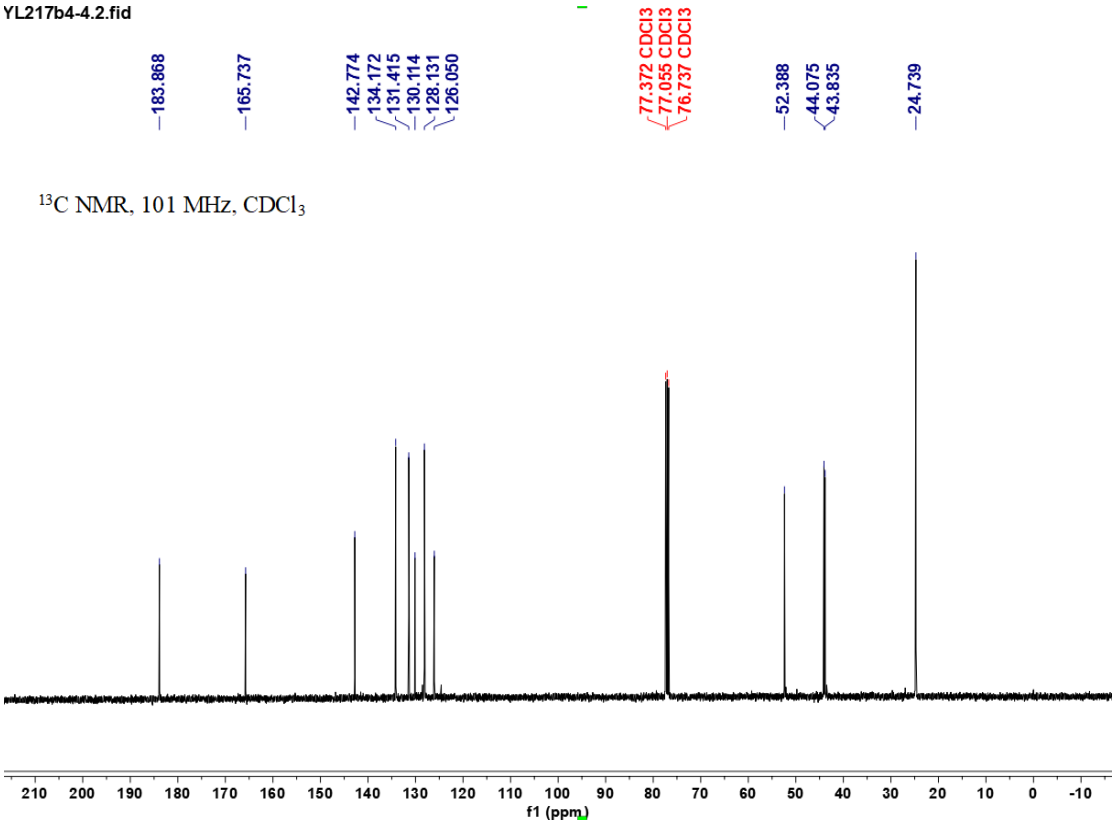
^{13}C NMR, 101 MHz, $CDCl_3$



^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra of **7-41**

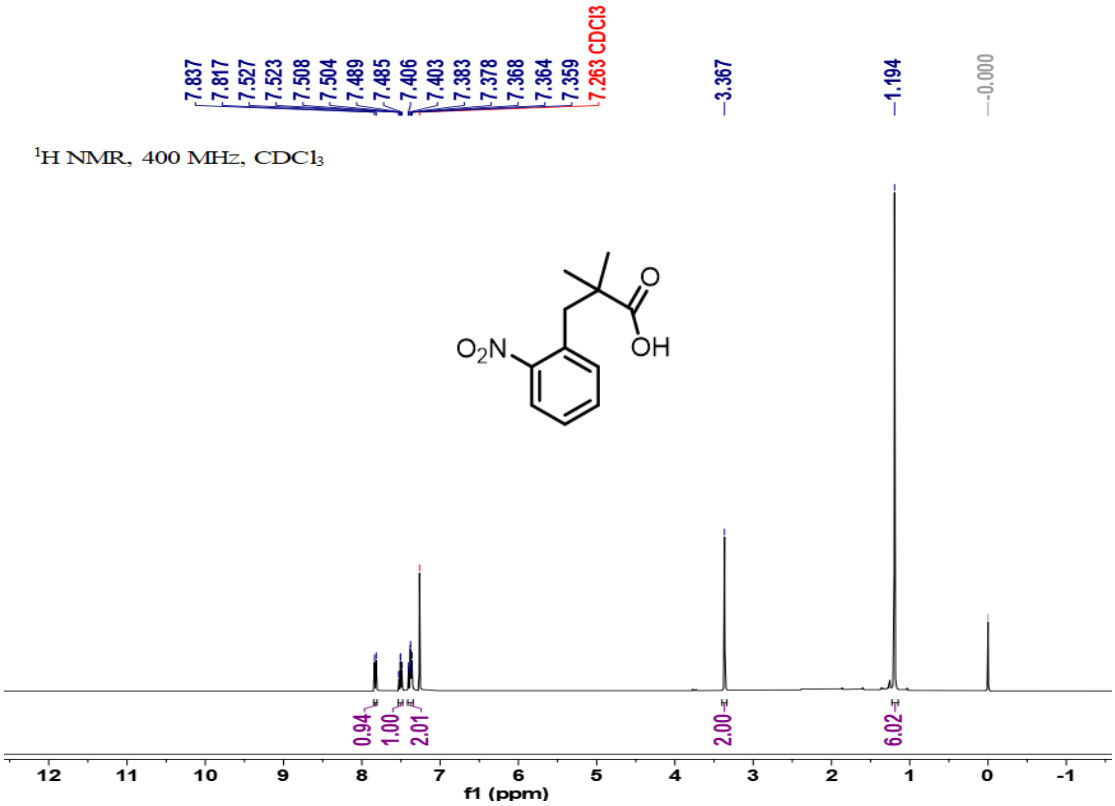


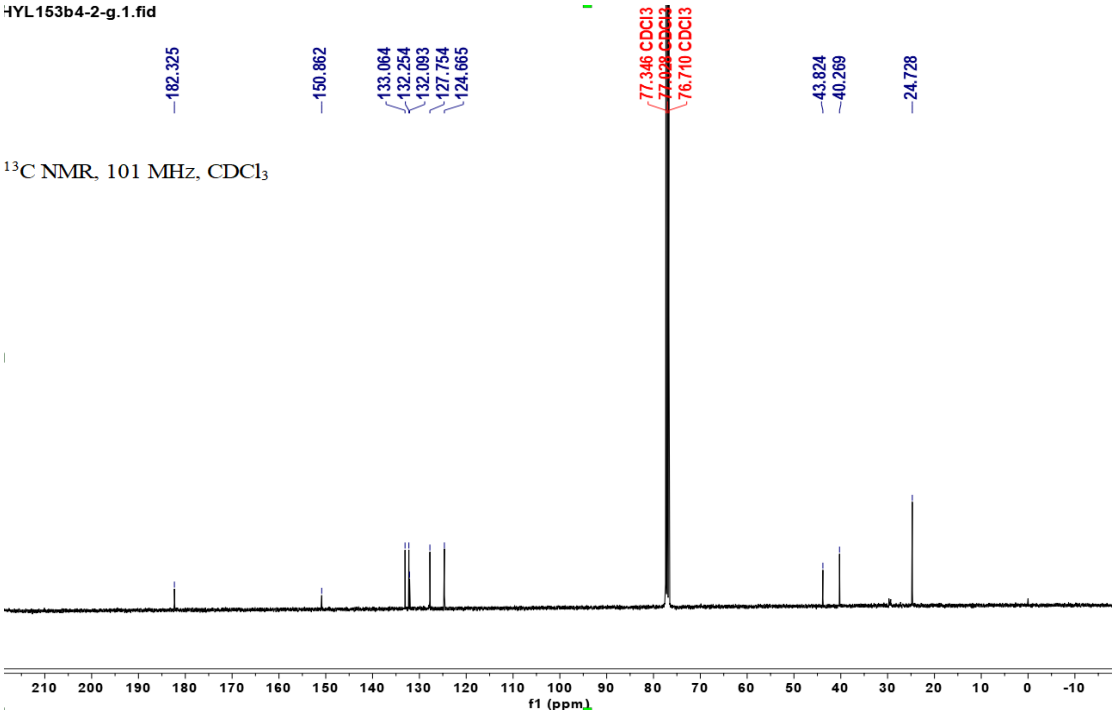
^{1}H NMR, 400 MHz, $CDCl_3$



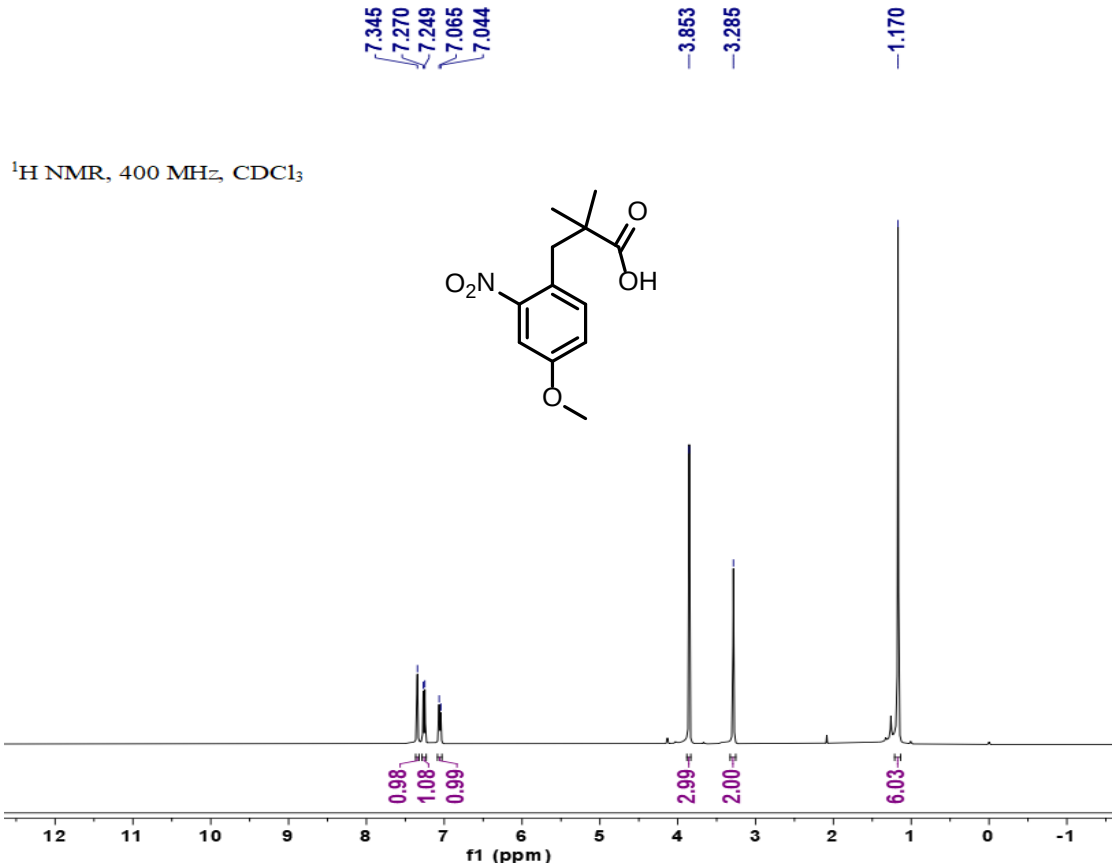
^{13}C NMR, 101 MHz, $CDCl_3$

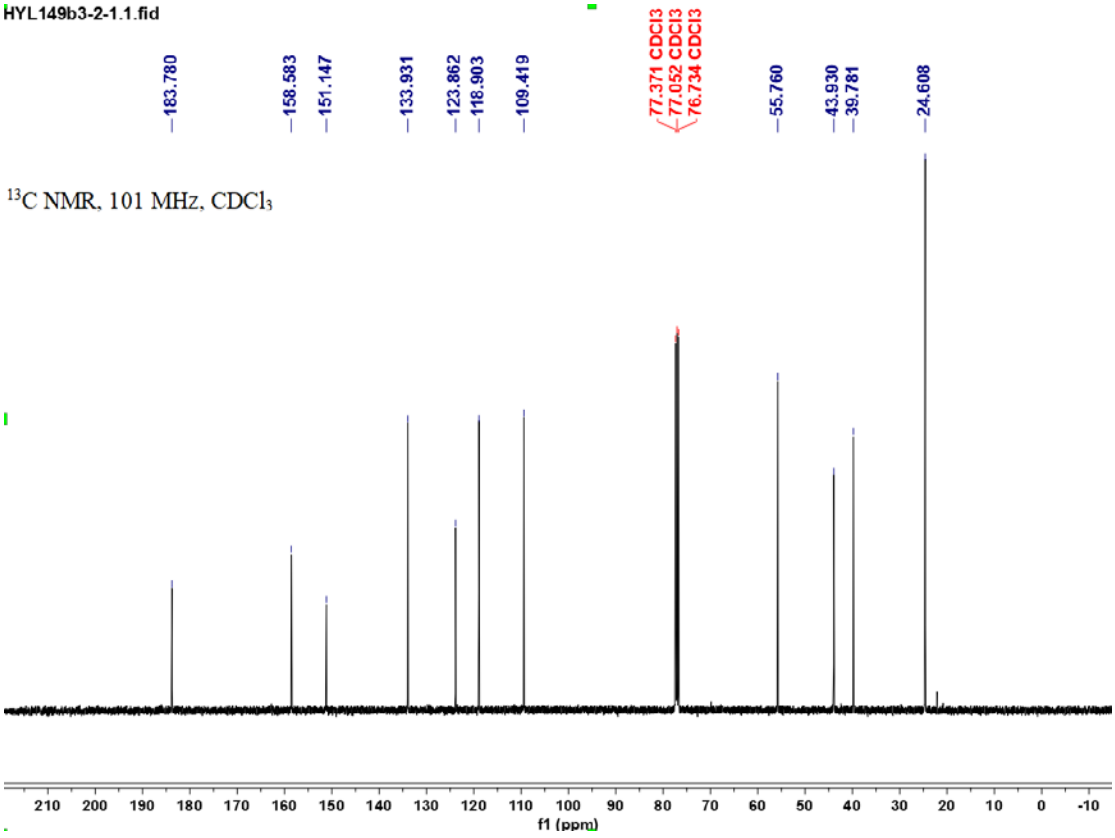
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-42**



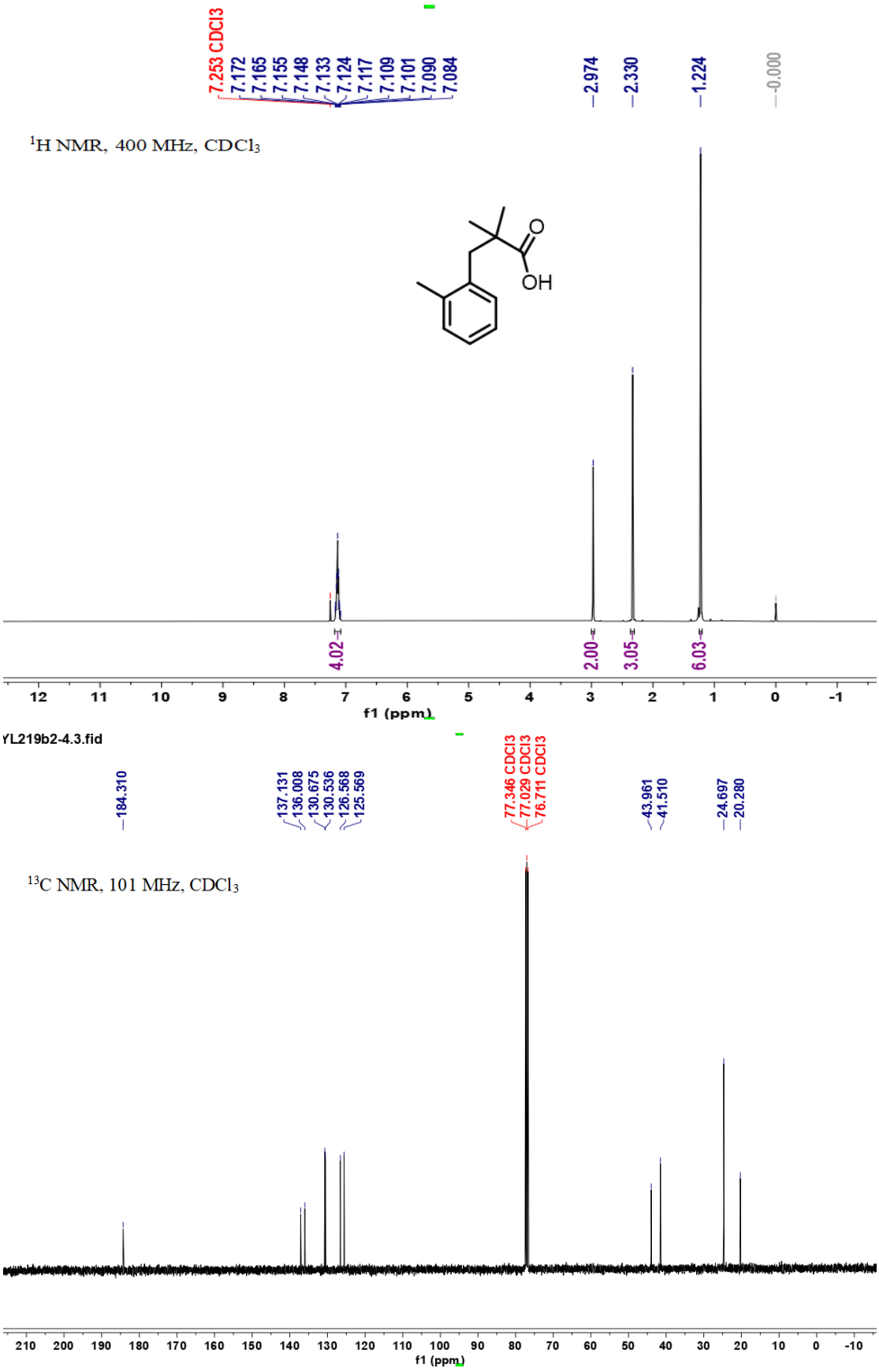


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-43**

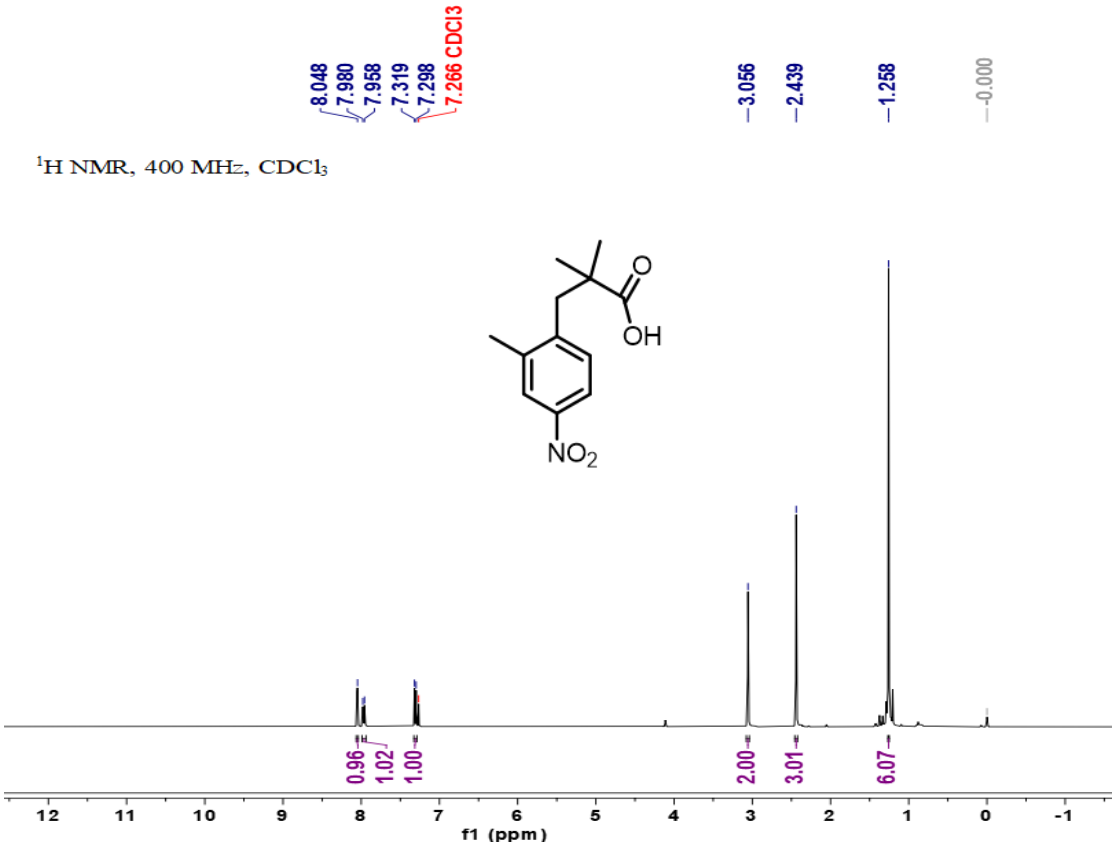




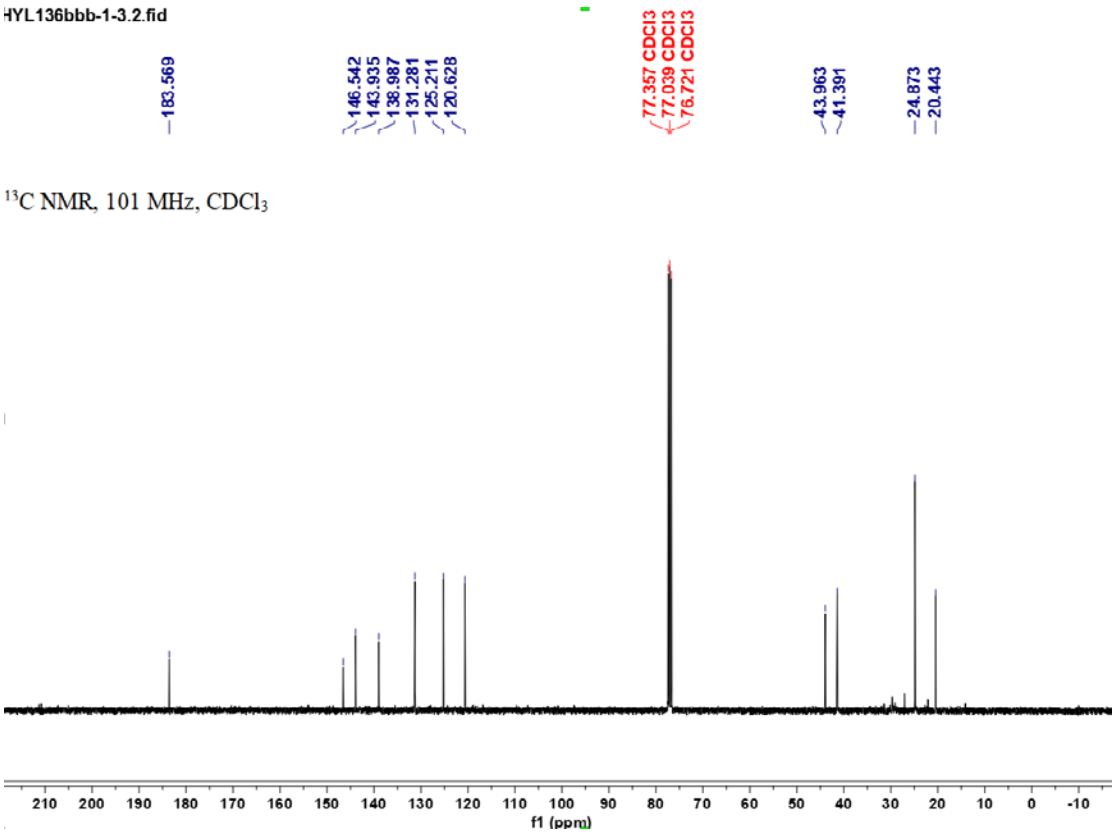
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-44**



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-45**

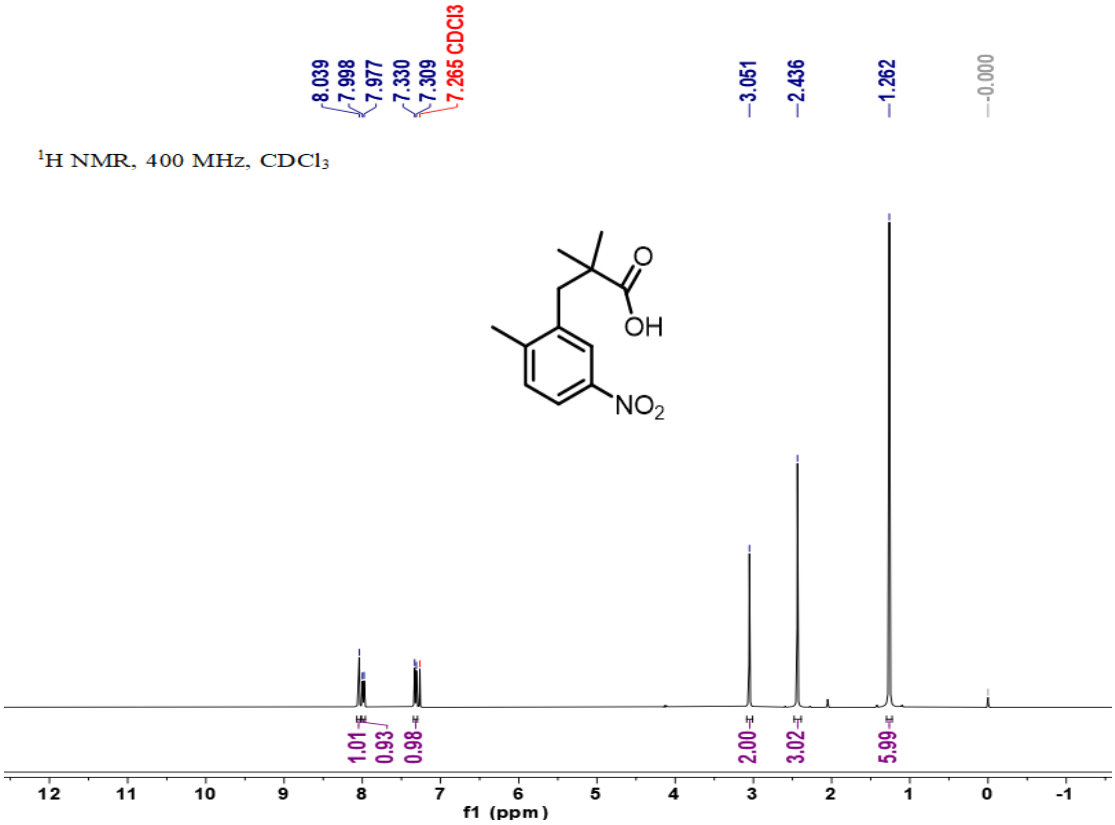


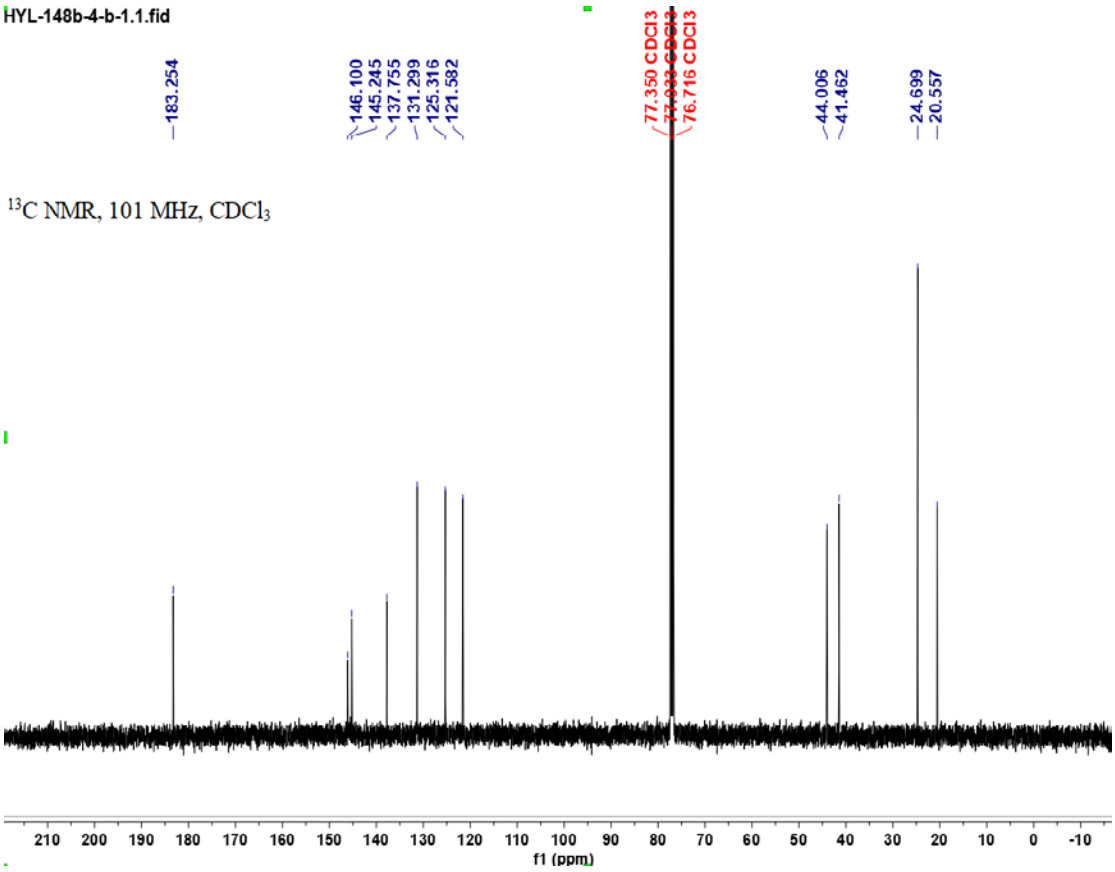
^{1}H NMR, 400 MHz, $CDCl_3$



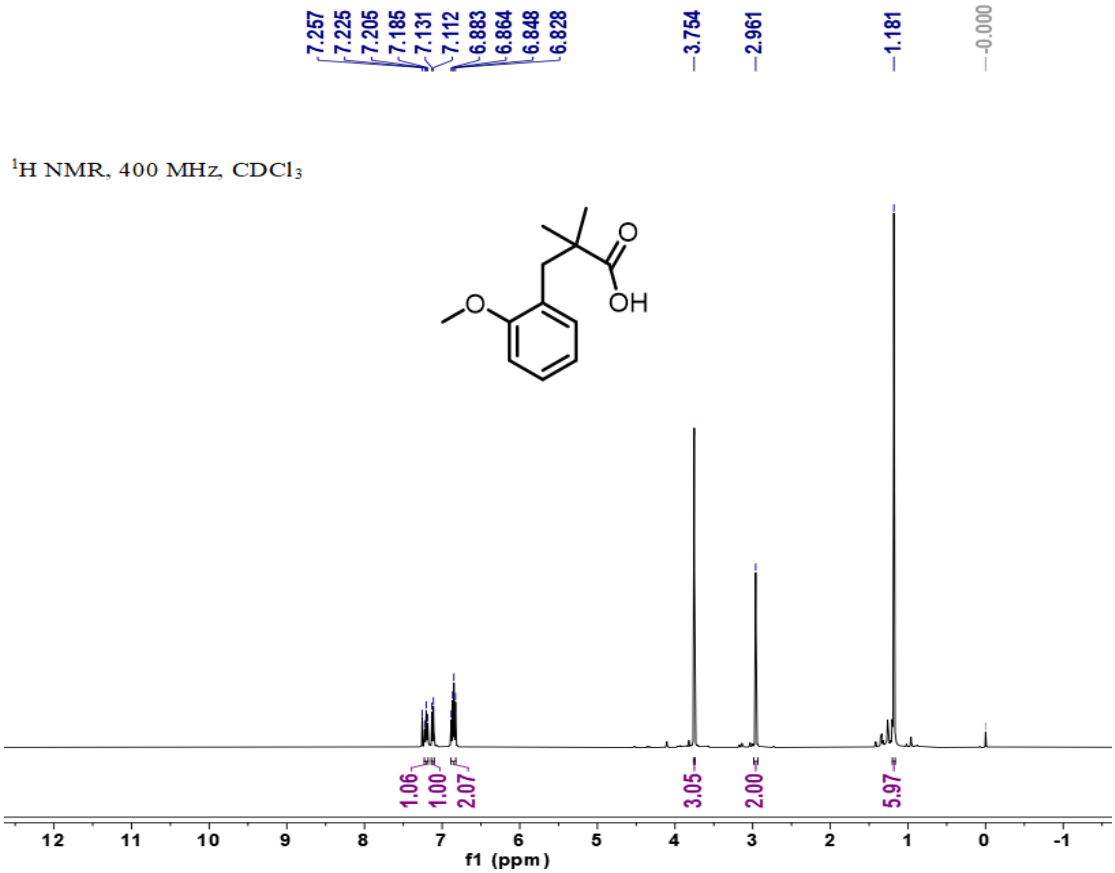
^{13}C NMR, 101 MHz, $CDCl_3$

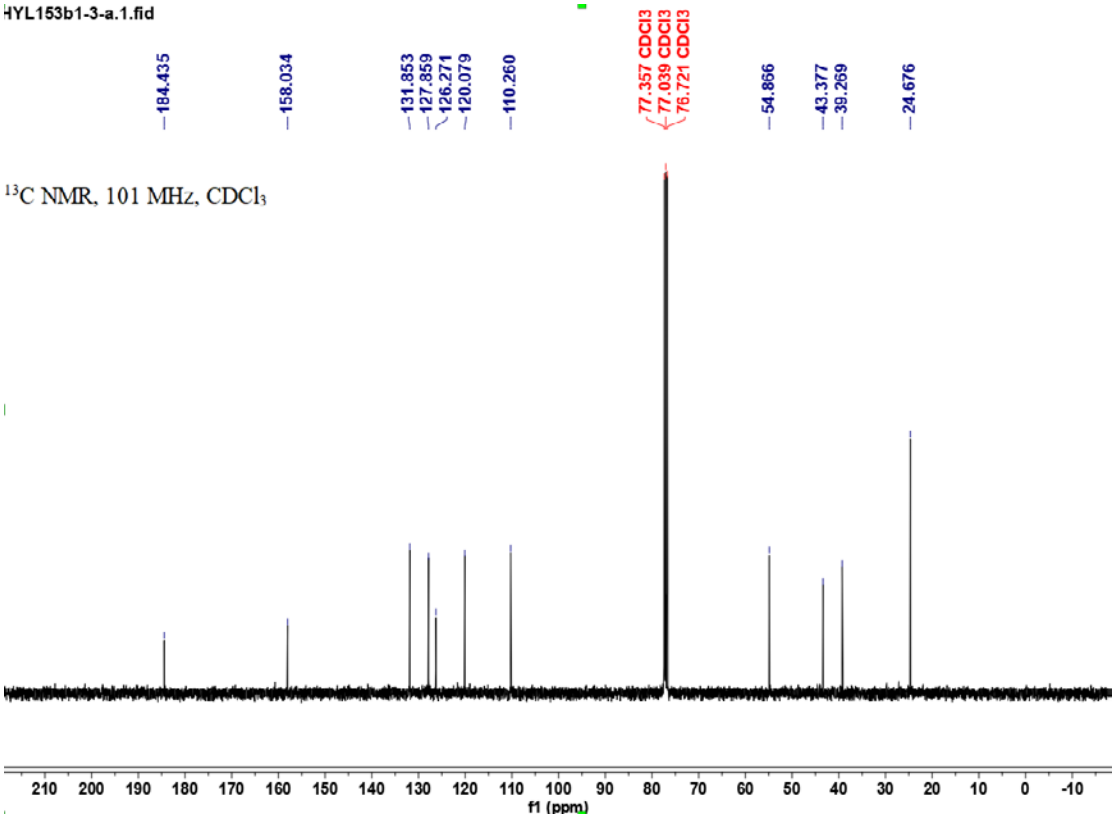
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-46**



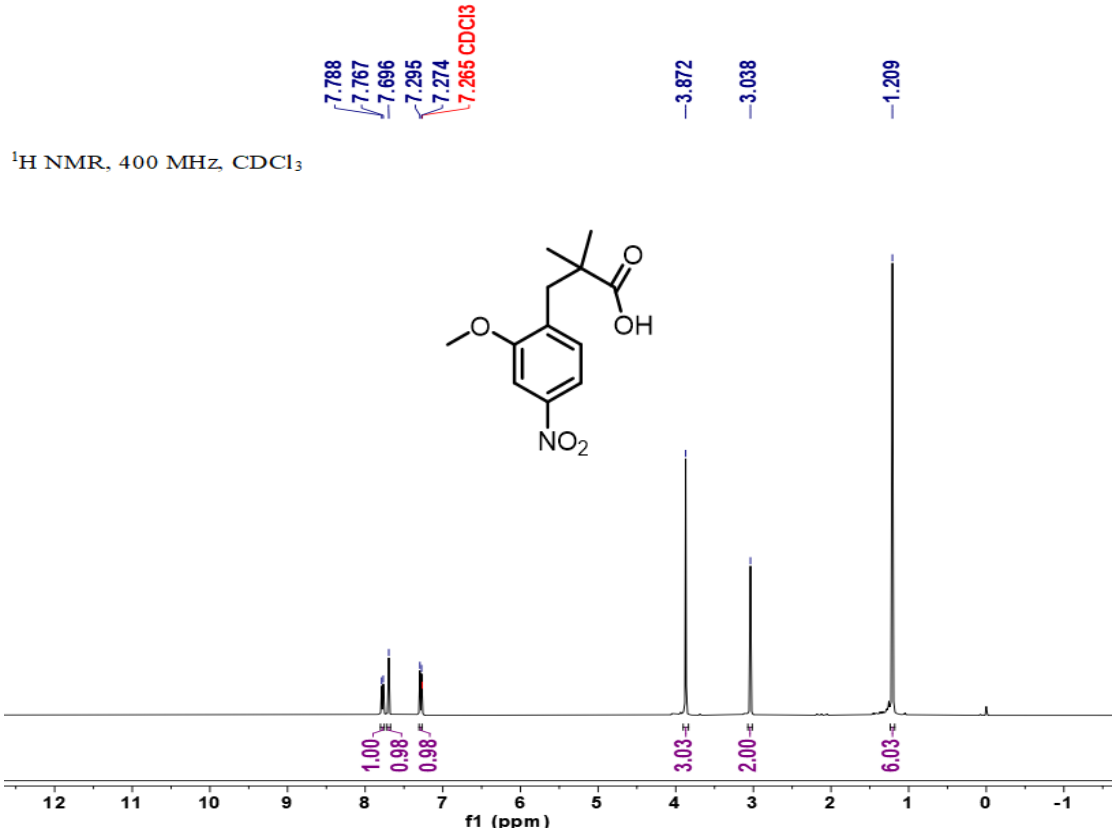


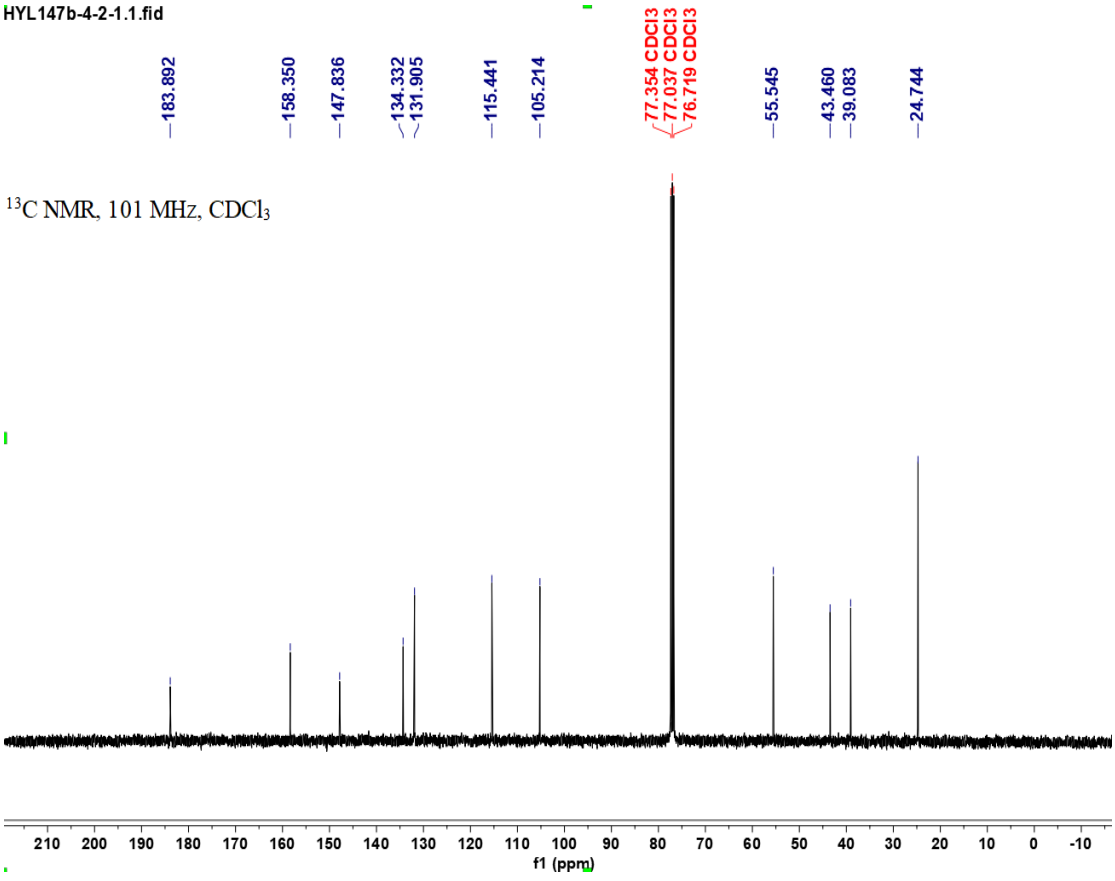
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-47**



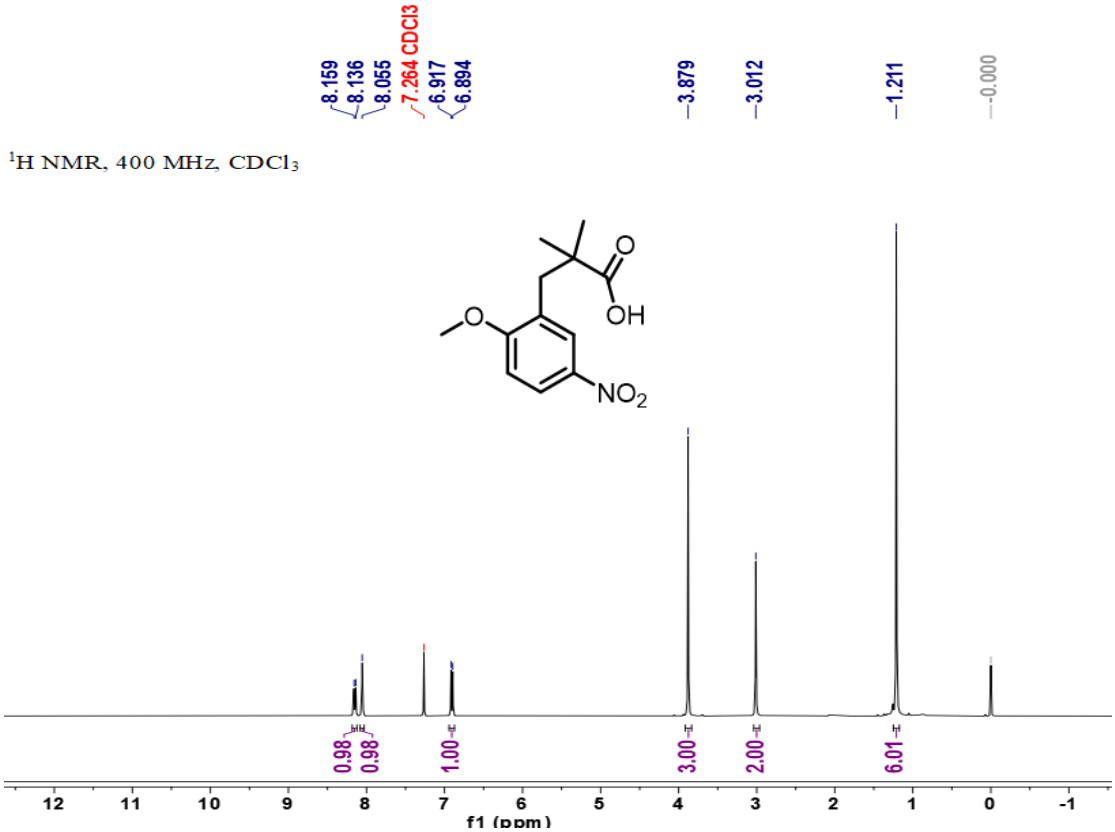


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-48**

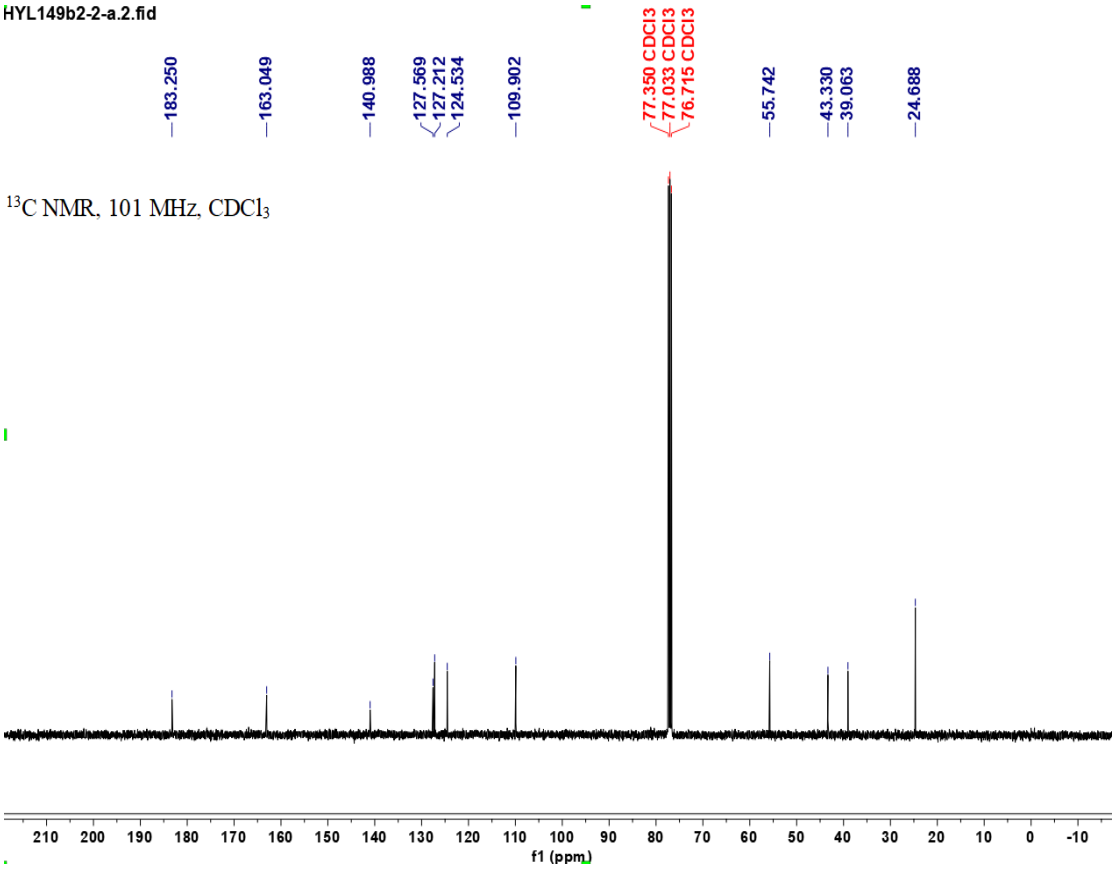




^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-49**

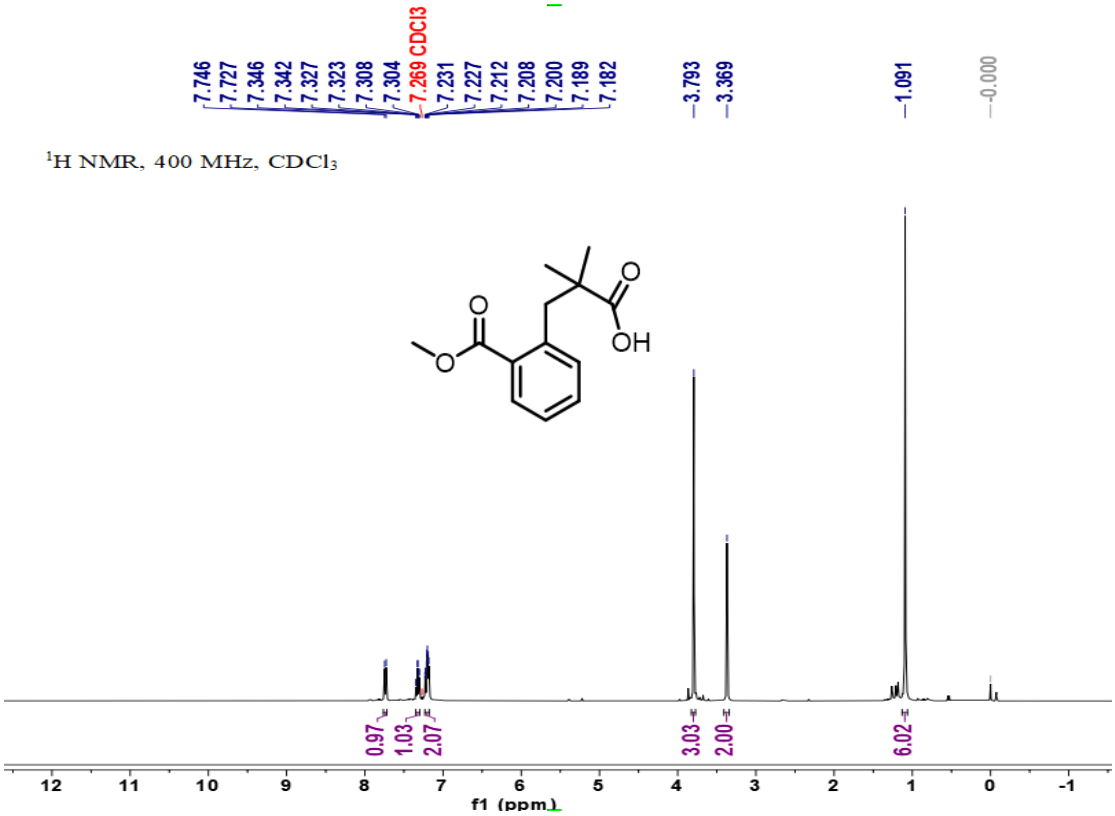


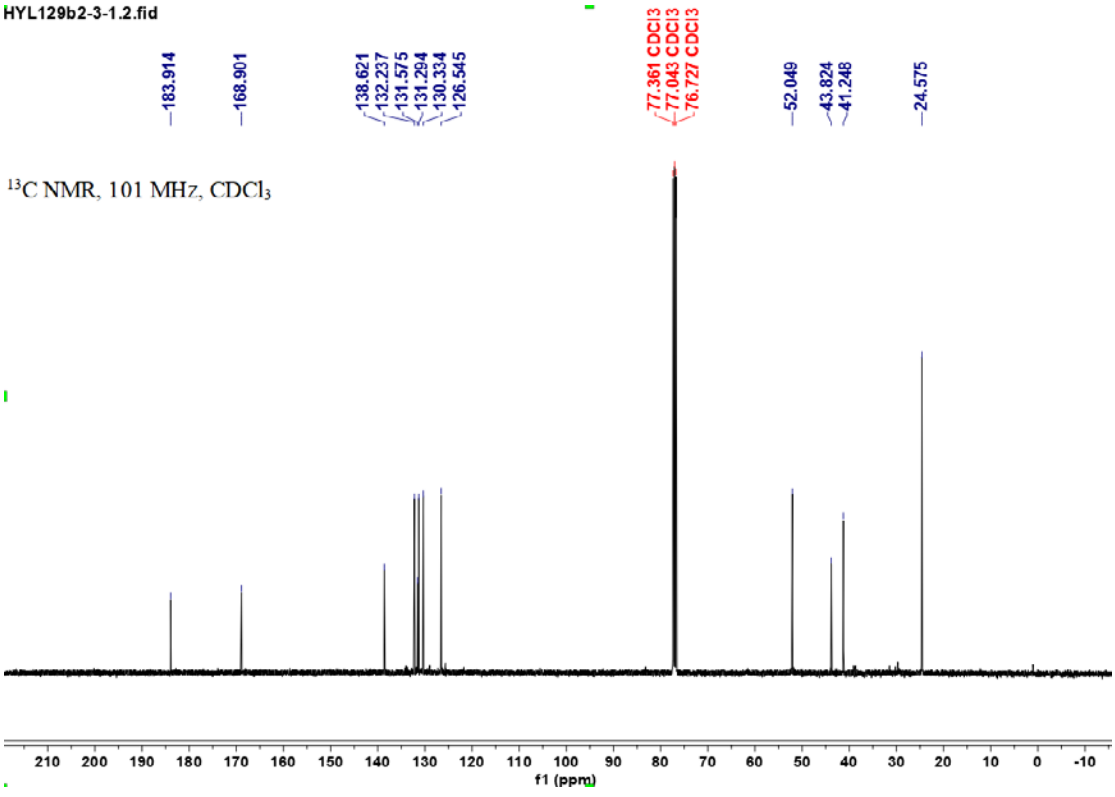
^{1}H NMR, 400 MHz, $CDCl_3$



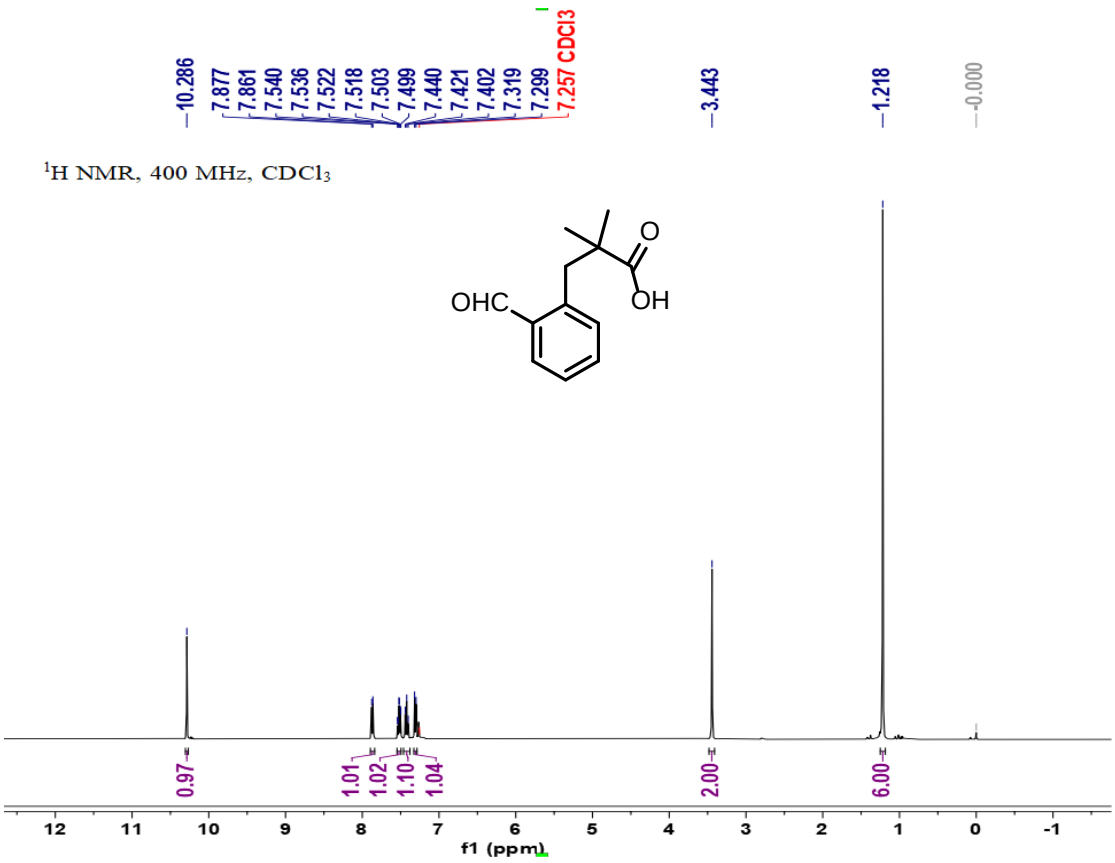
^{13}C NMR, 101 MHz, $CDCl_3$

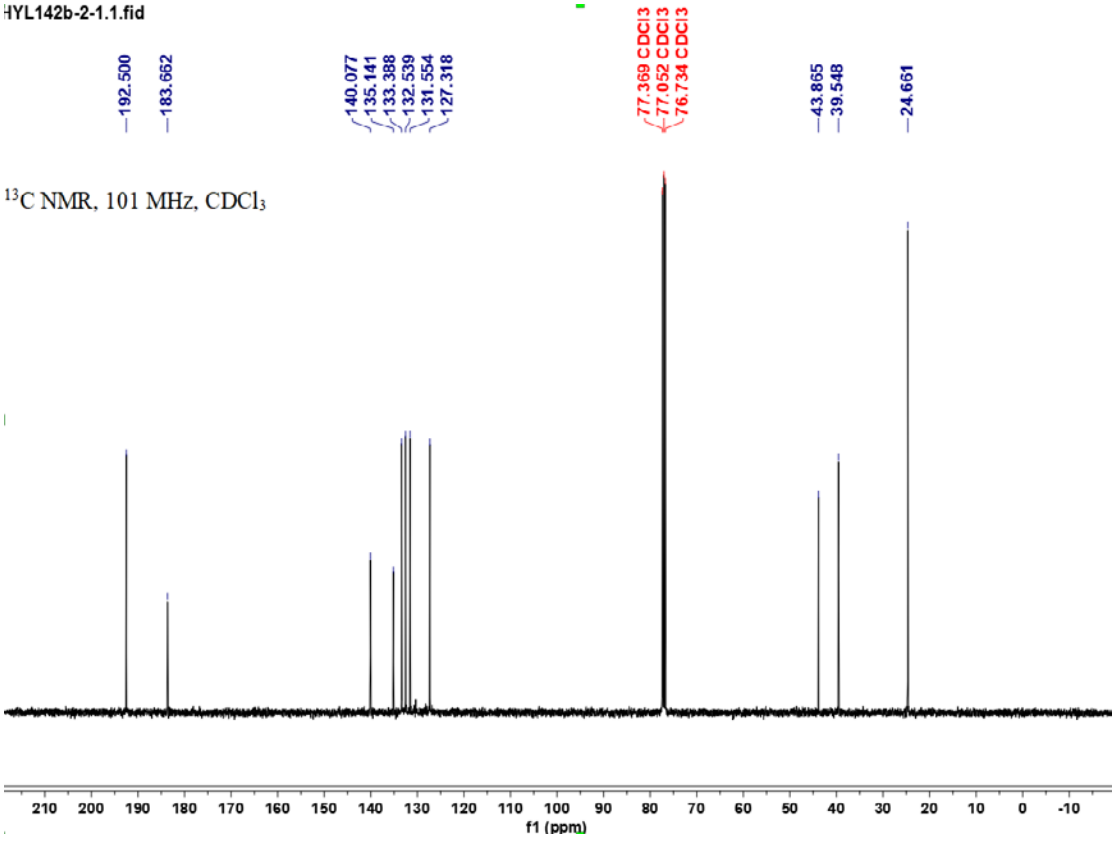
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-50**



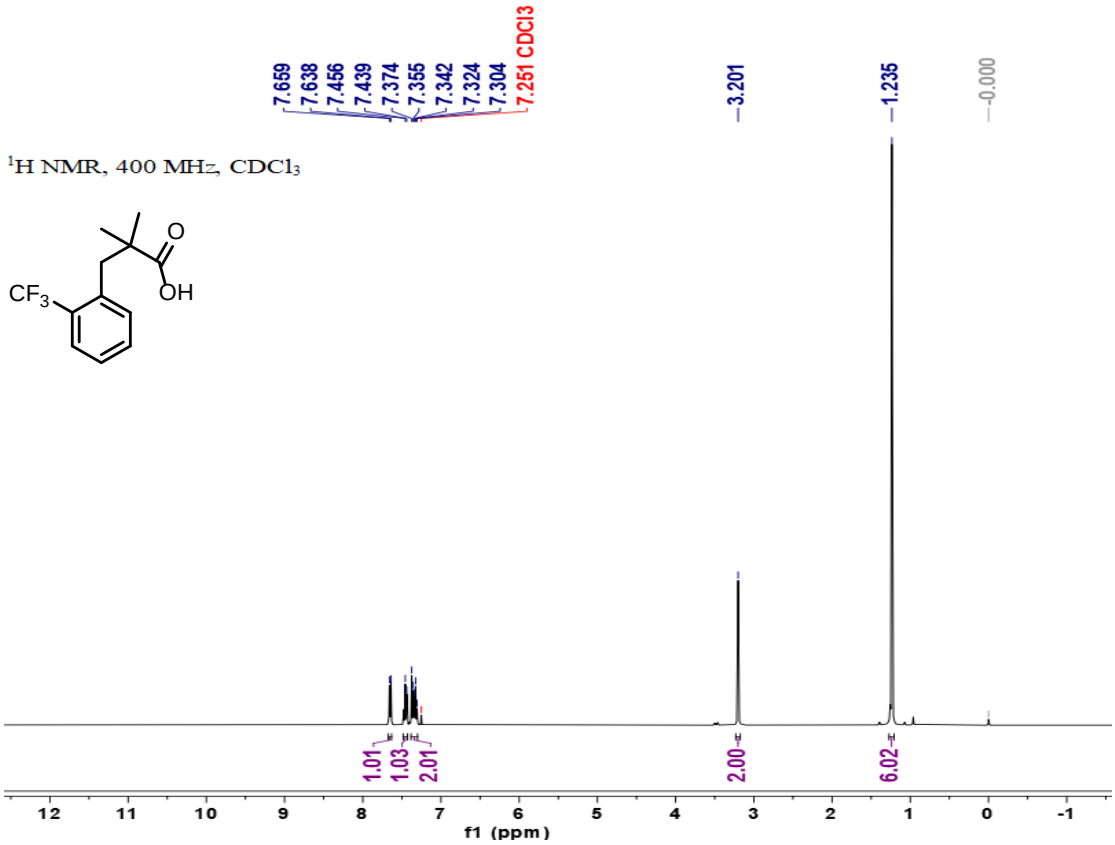


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-51**

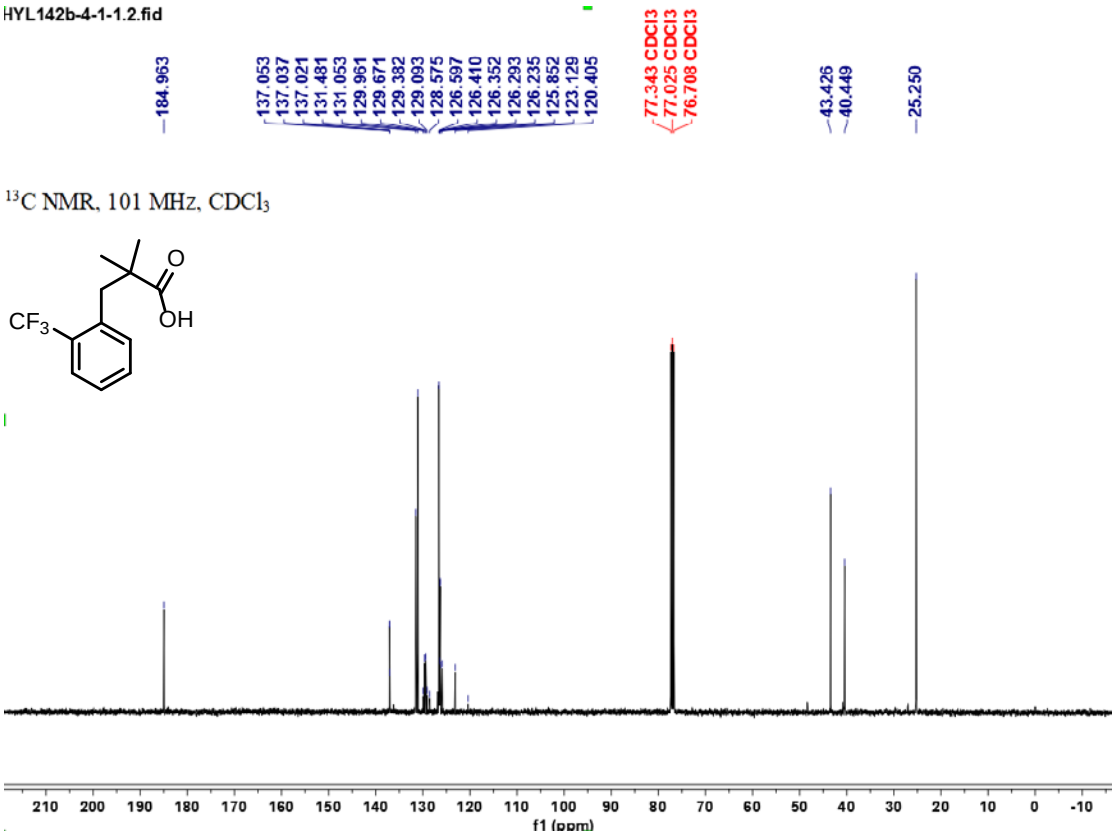




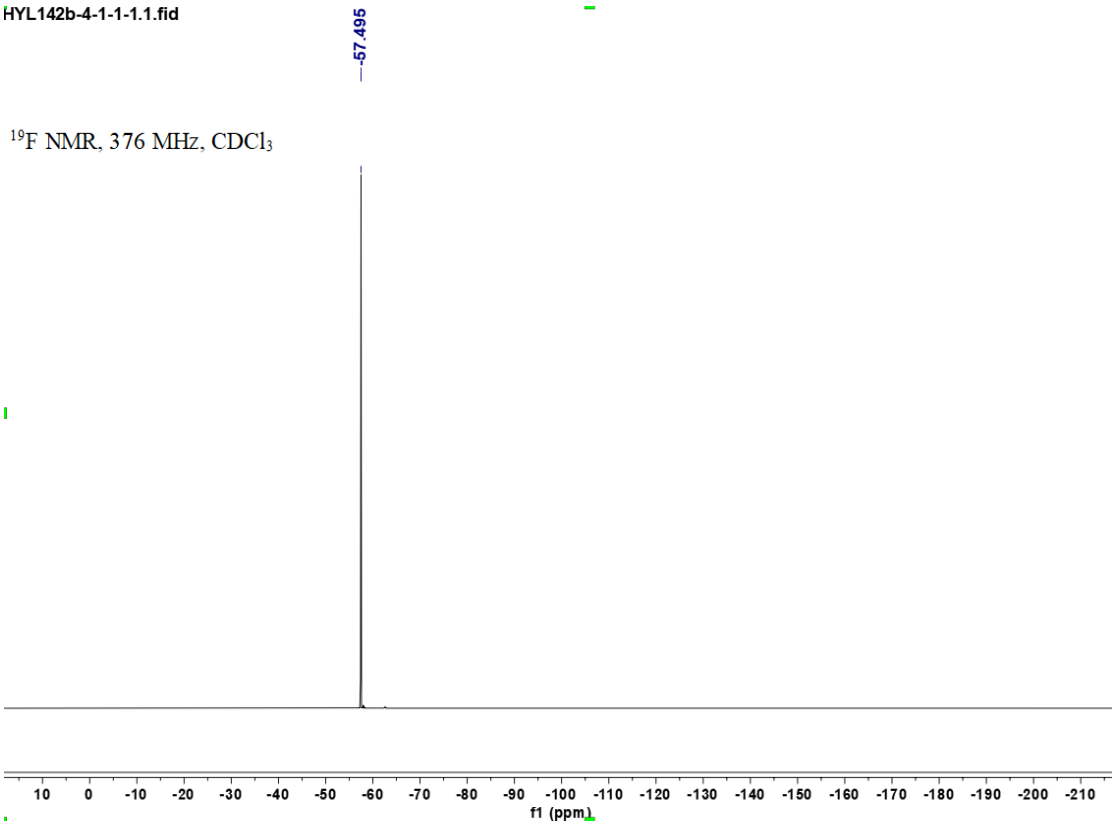
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-52**



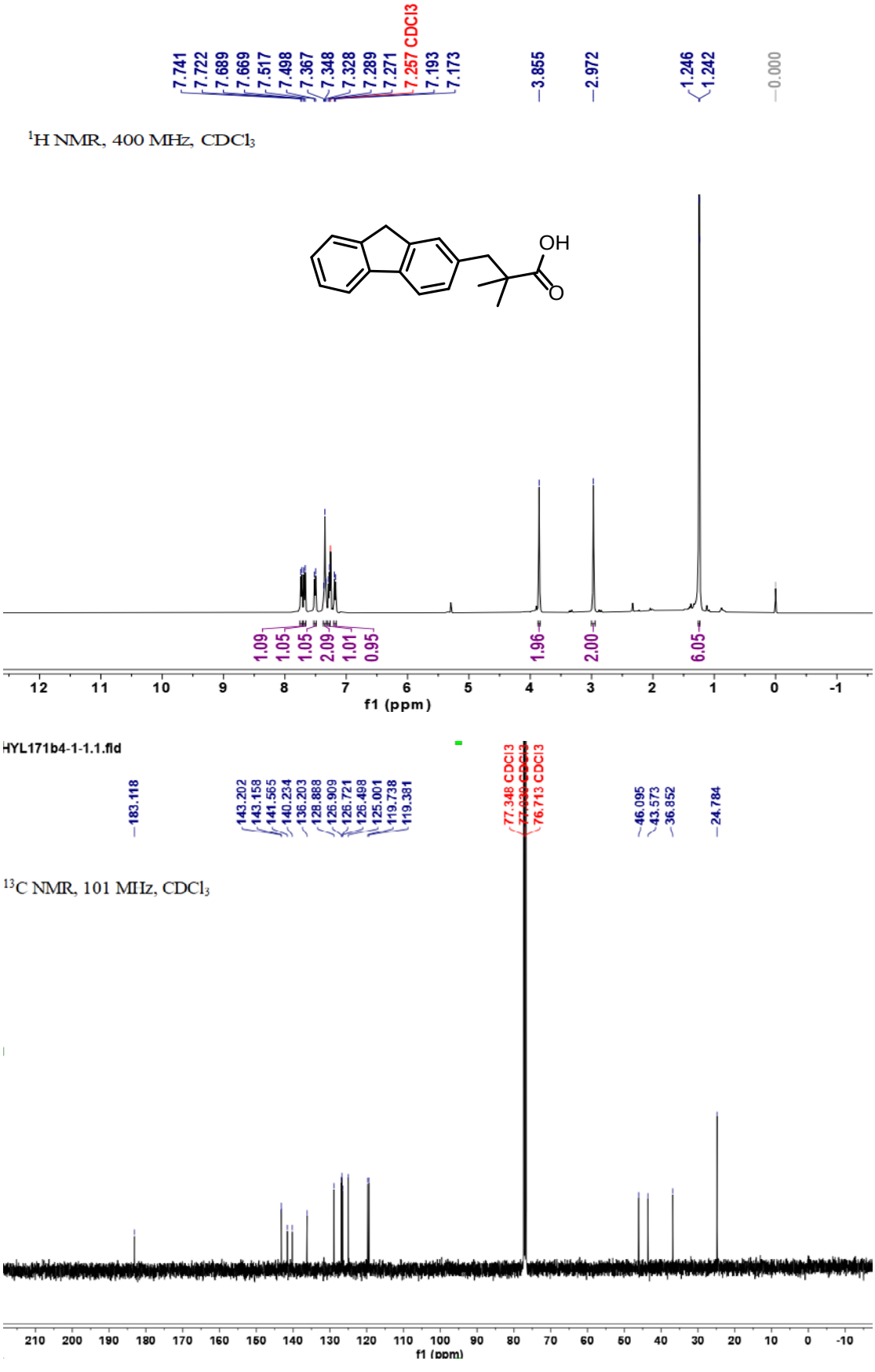
^{1}H NMR, 400 MHz, $CDCl_3$



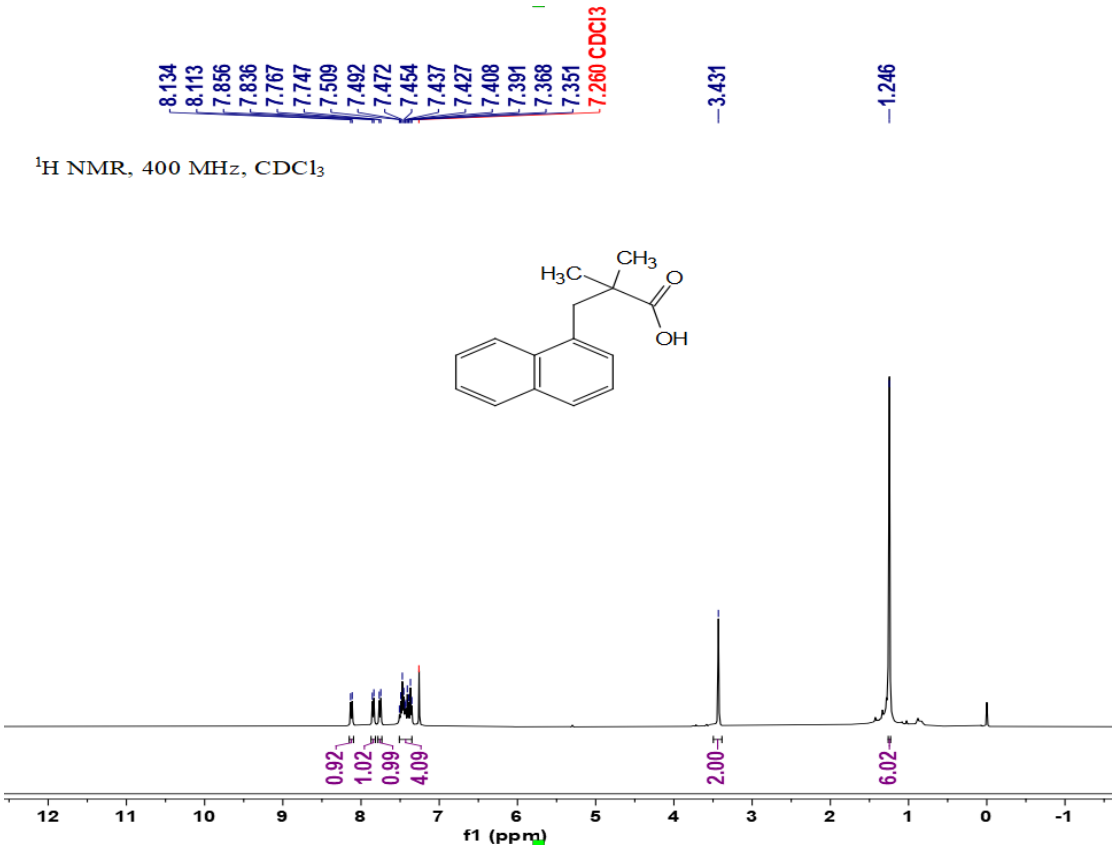
^{13}C NMR, 101 MHz, $CDCl_3$



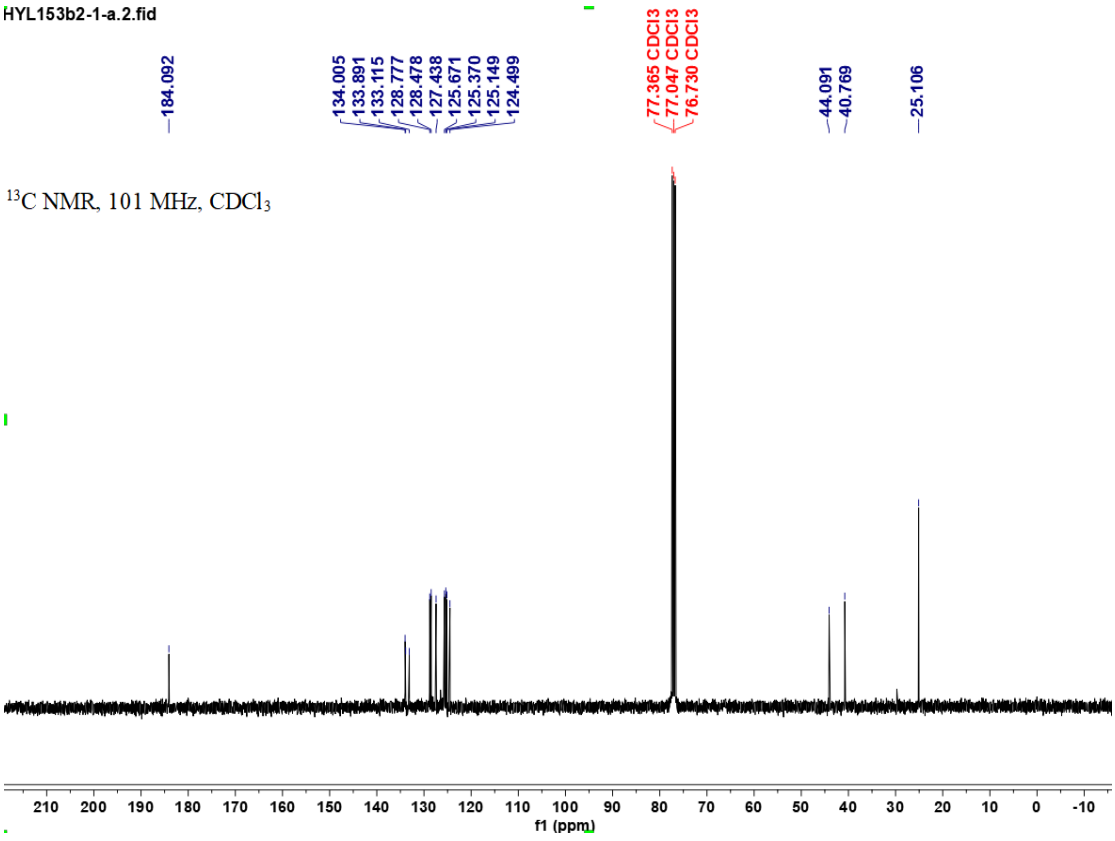
^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) spectra of **7-53**



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-54**

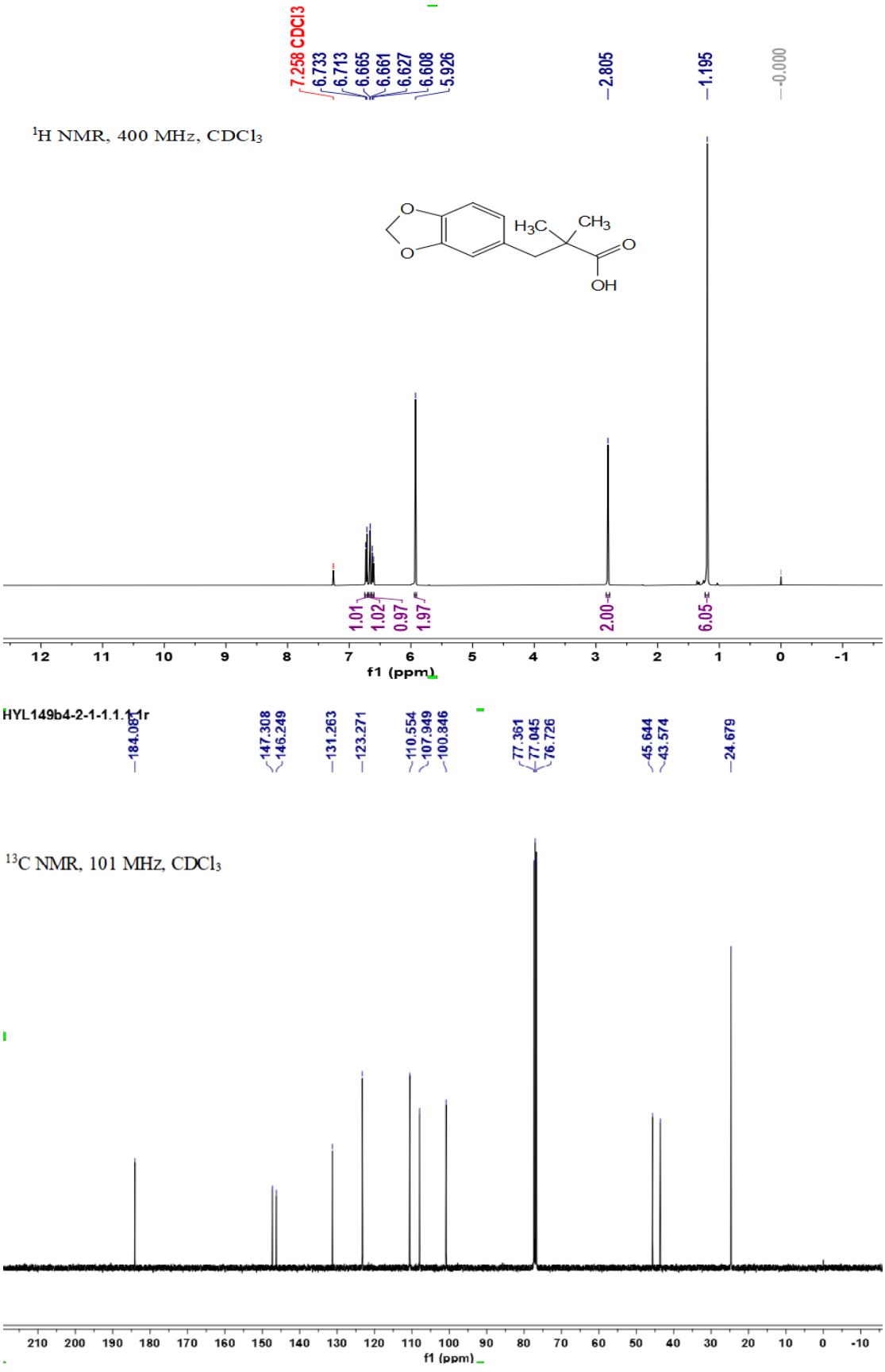


^{1}H NMR, 400 MHz, $CDCl_3$

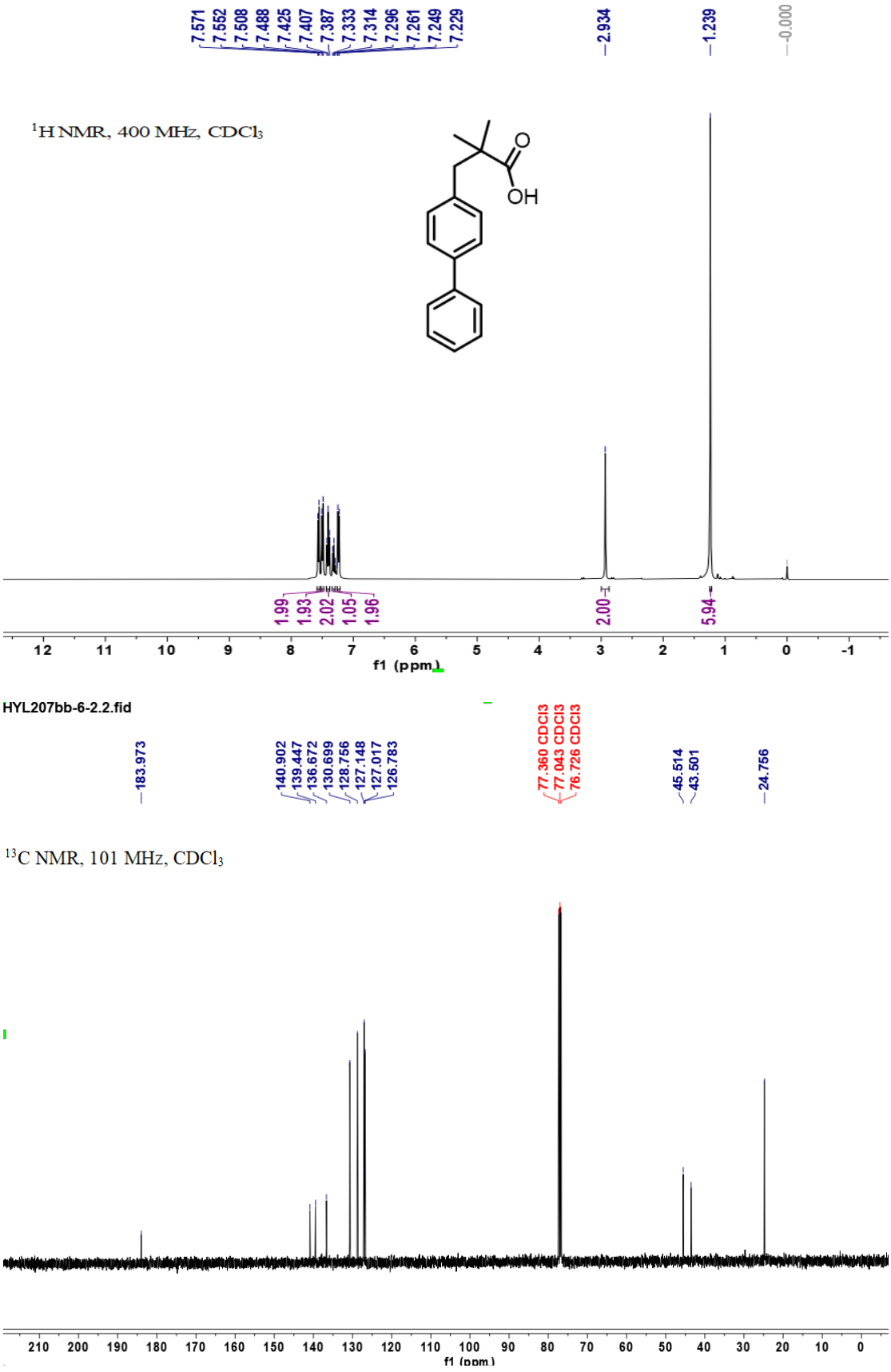


^{13}C NMR, 101 MHz, $CDCl_3$

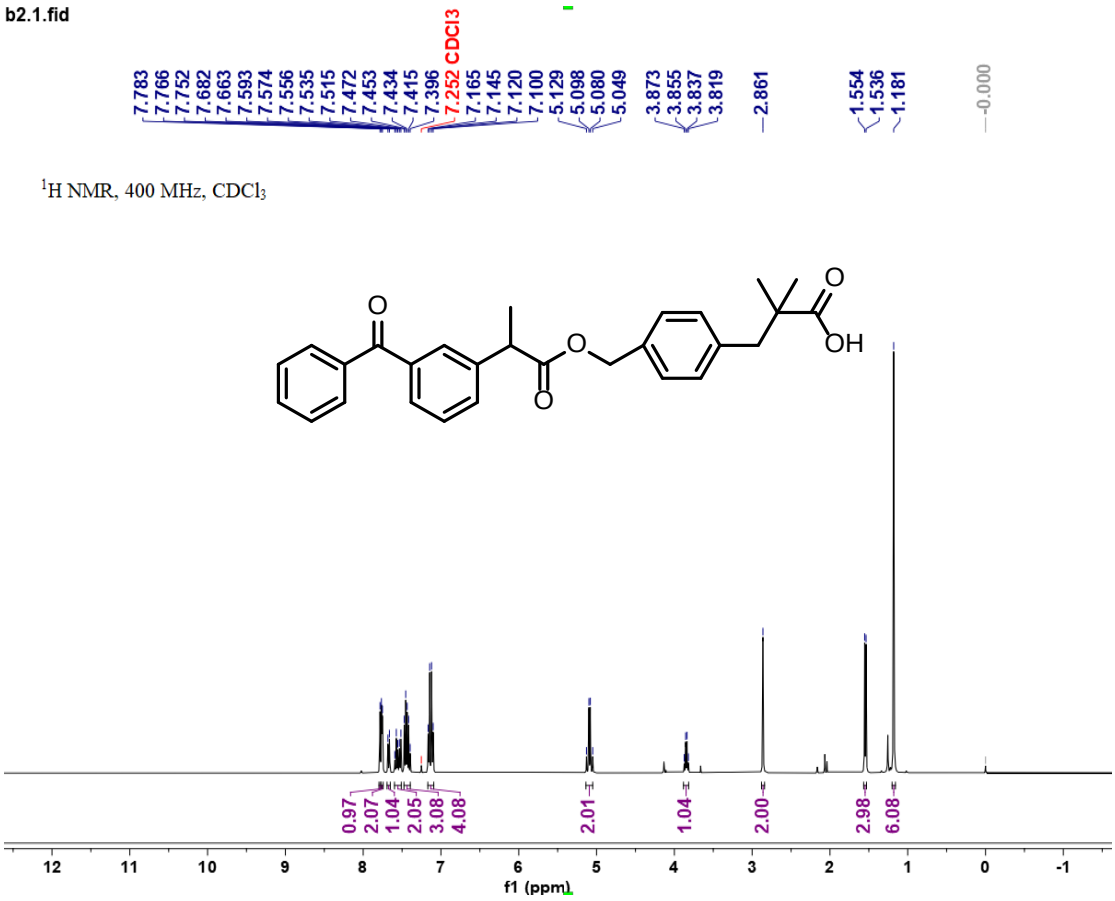
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-55**



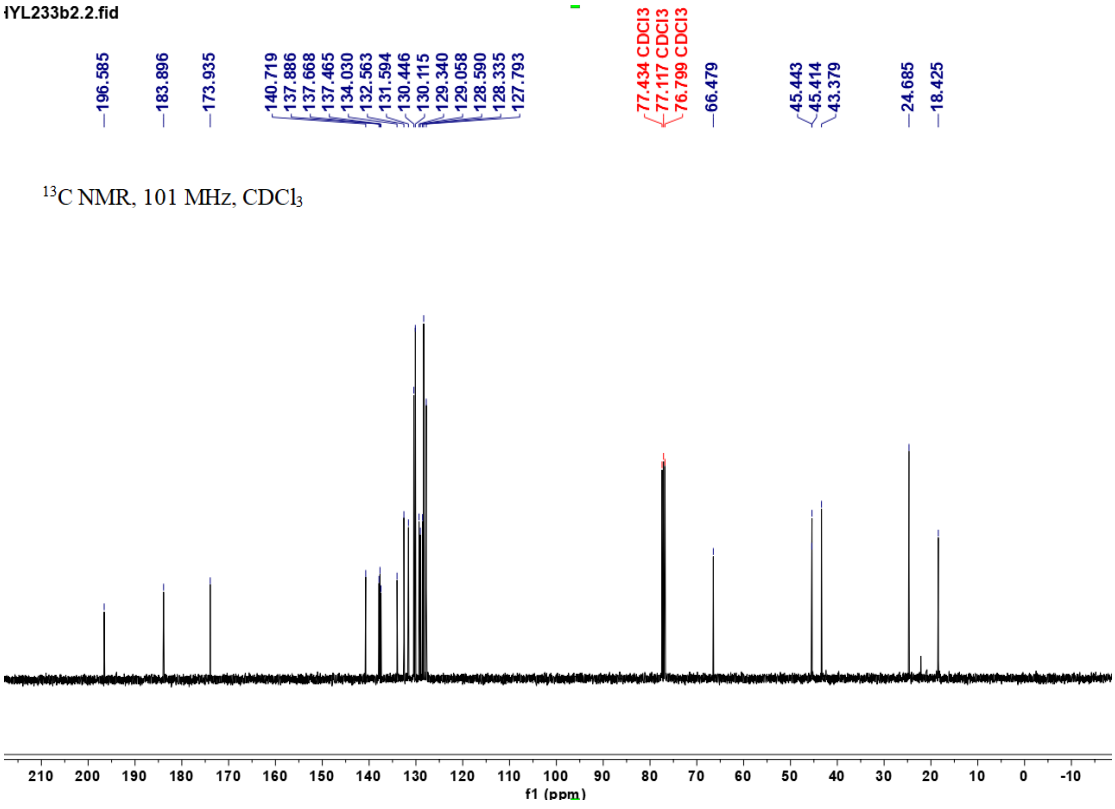
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-56**



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-57**

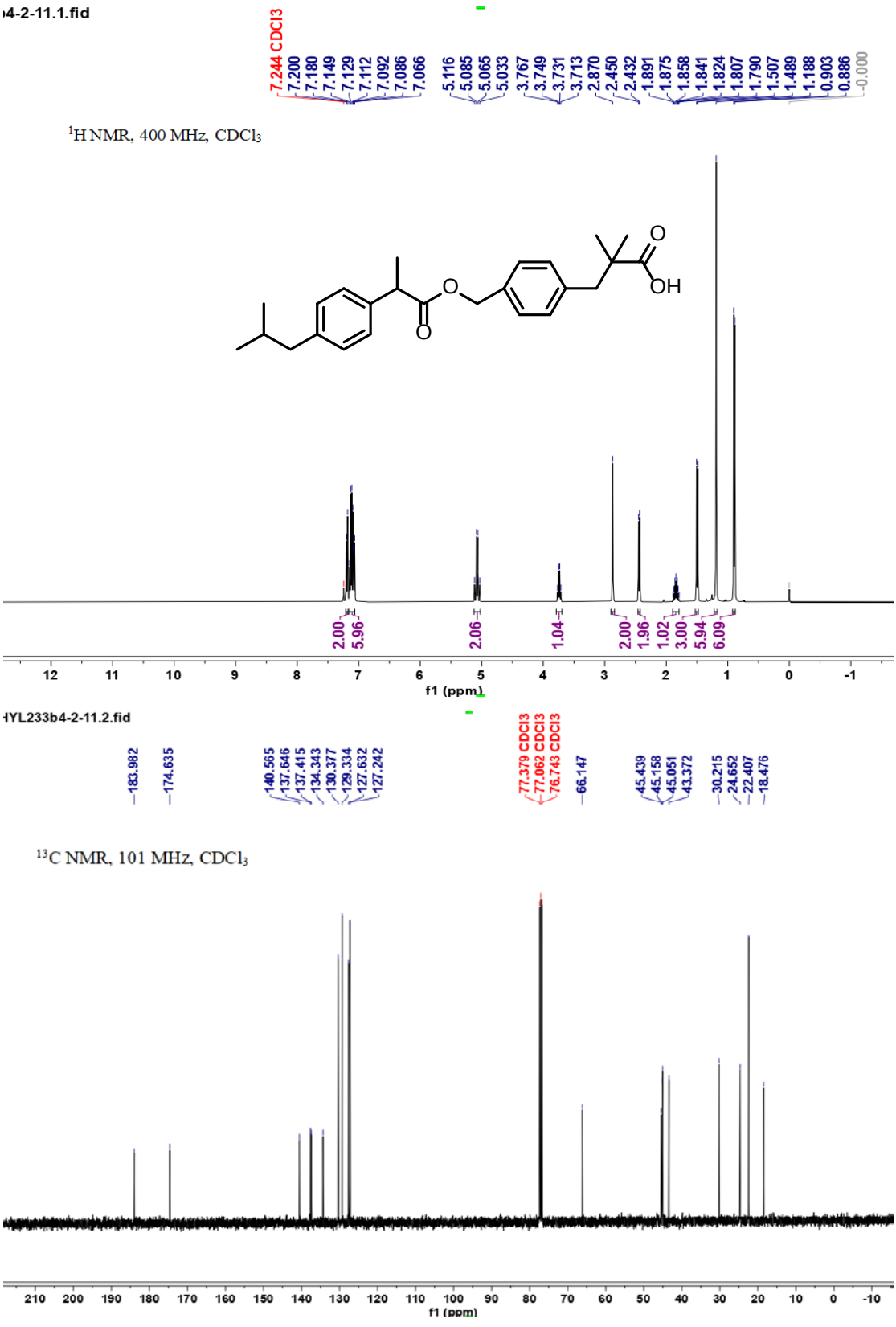


^{1}H NMR, 400 MHz, $CDCl_3$

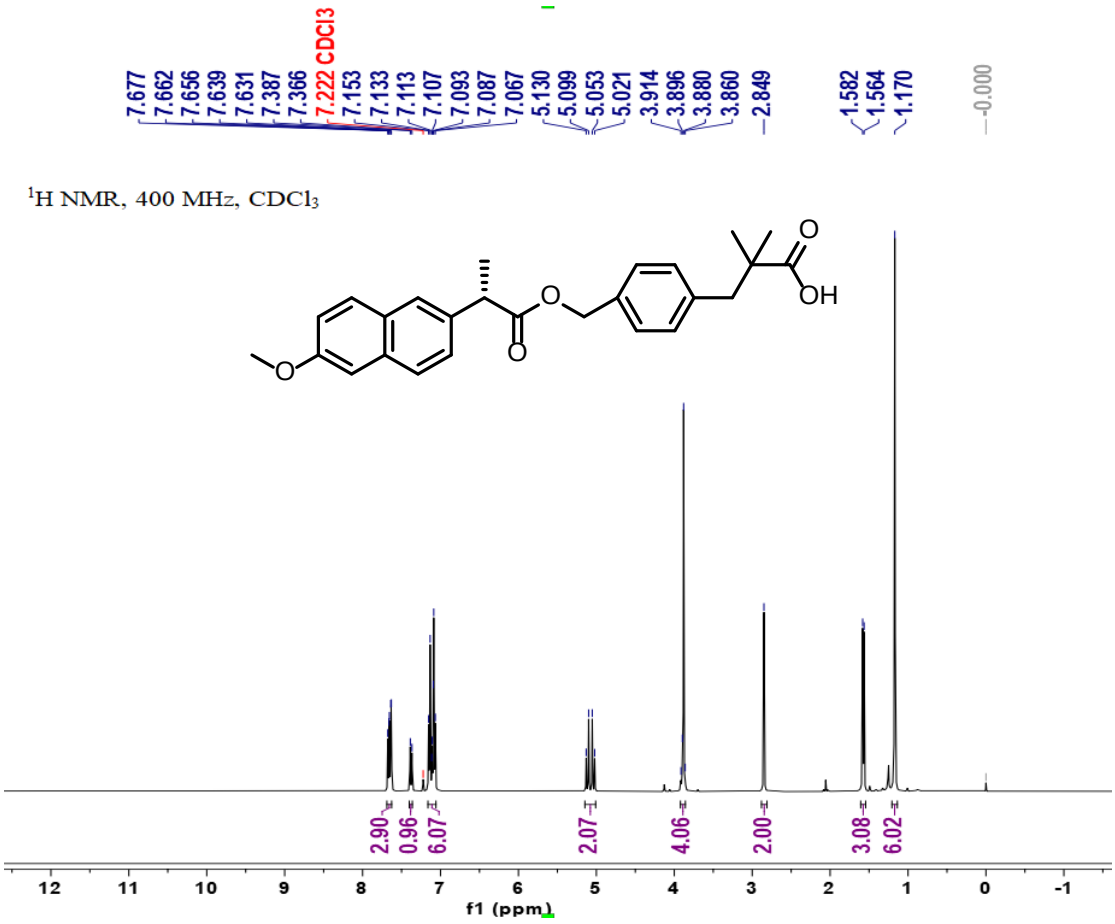


^{13}C NMR, 101 MHz, $CDCl_3$

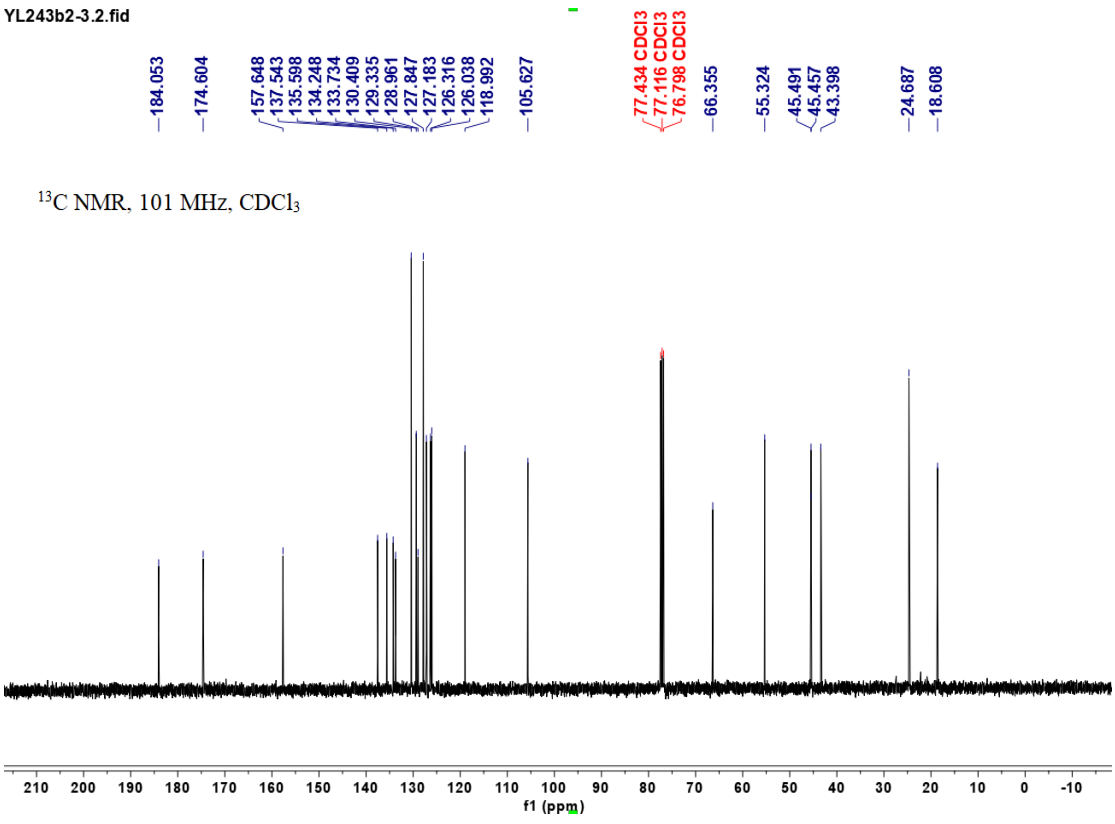
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-58**



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-59**

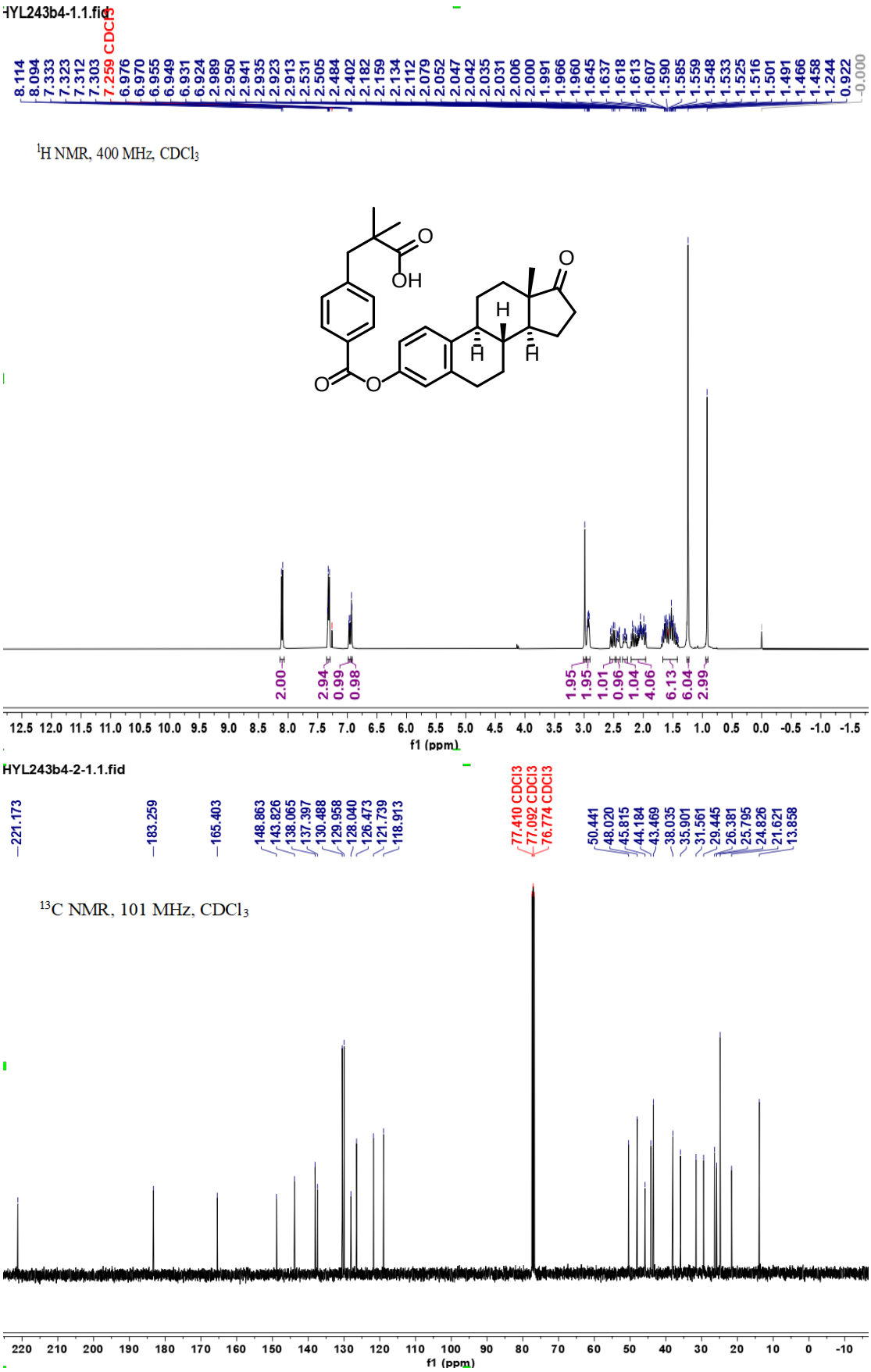


^{1}H NMR, 400 MHz, $CDCl_3$

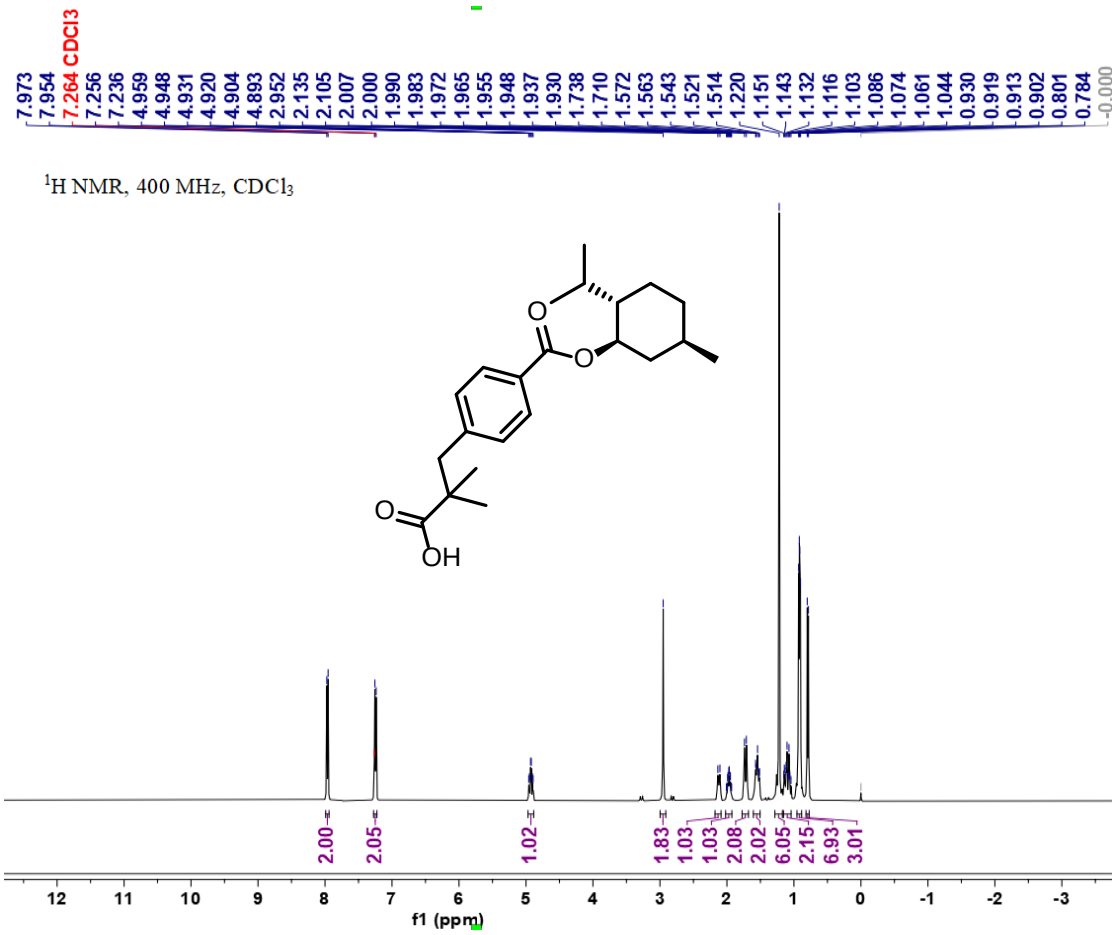


^{13}C NMR, 101 MHz, $CDCl_3$

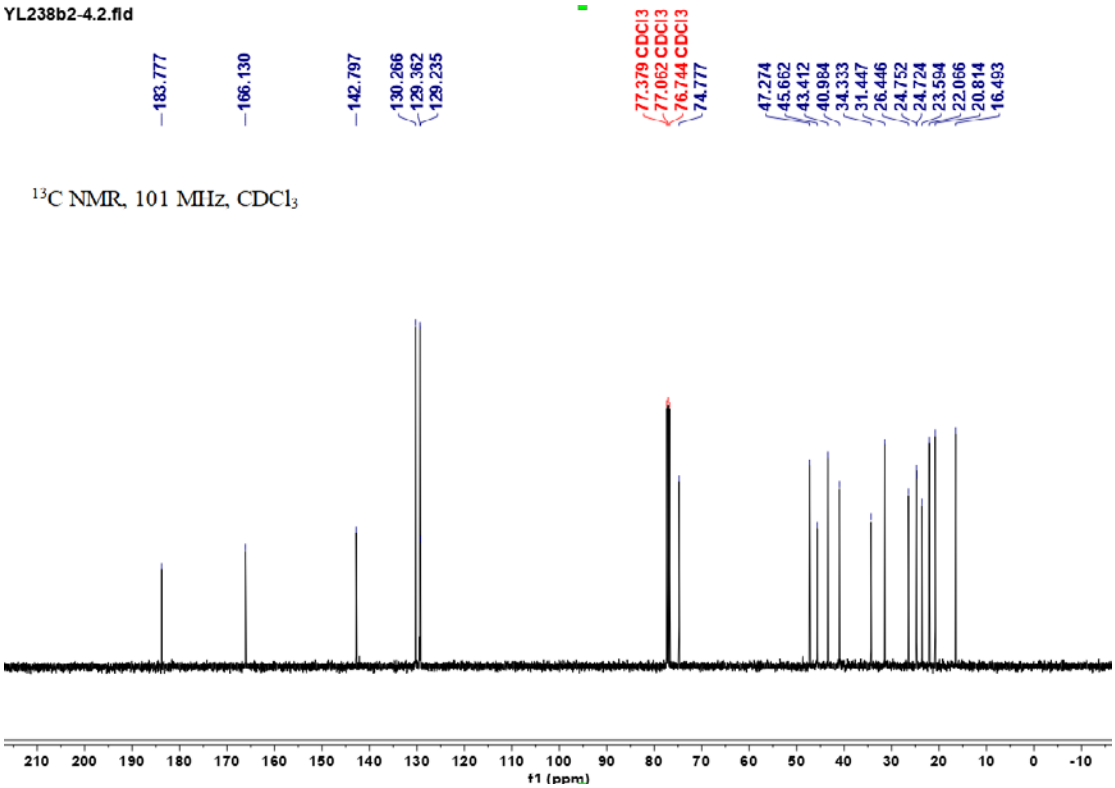
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-60**



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-61**

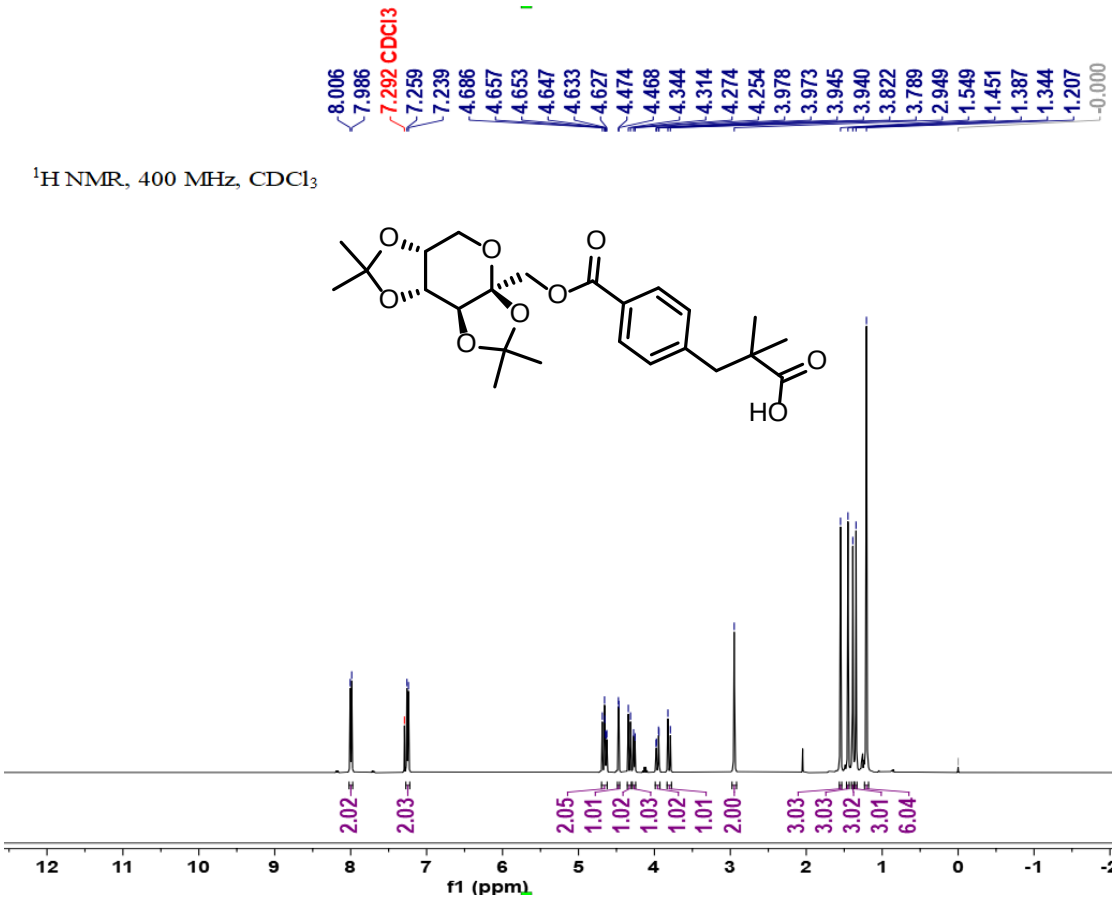


^{1}H NMR, 400 MHz, $CDCl_3$

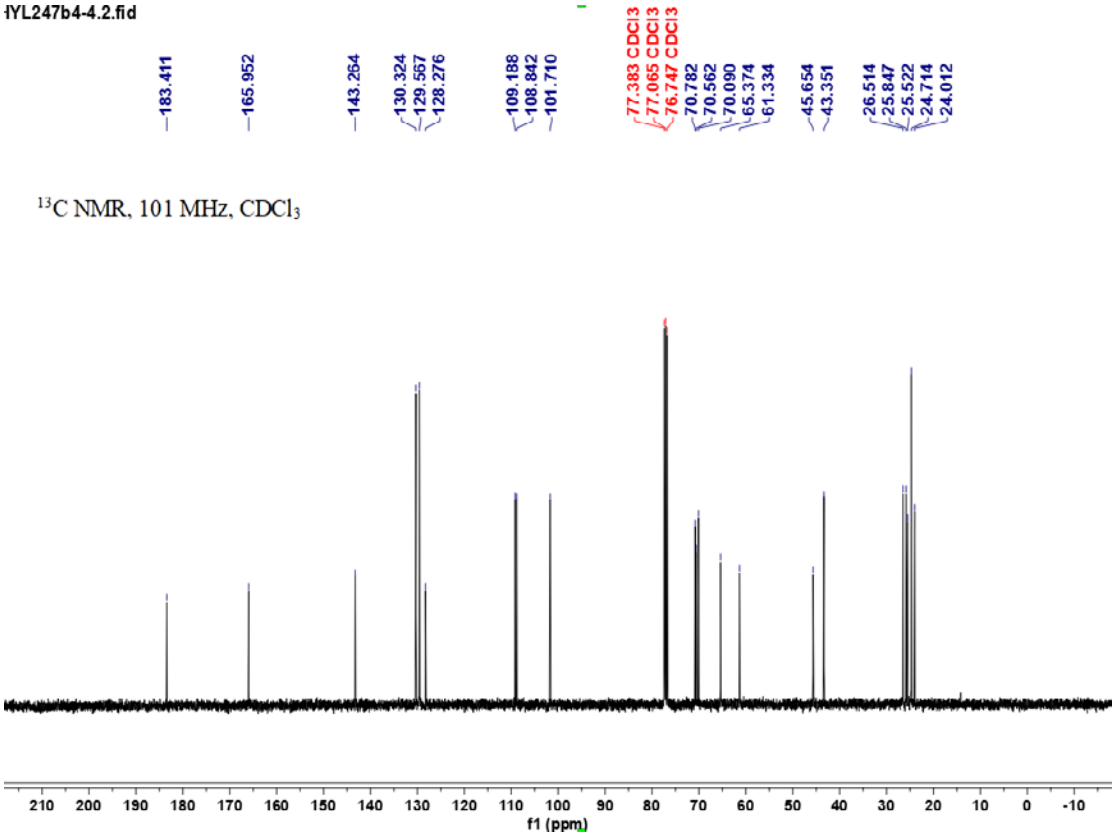


^{13}C NMR, 101 MHz, $CDCl_3$

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-62**

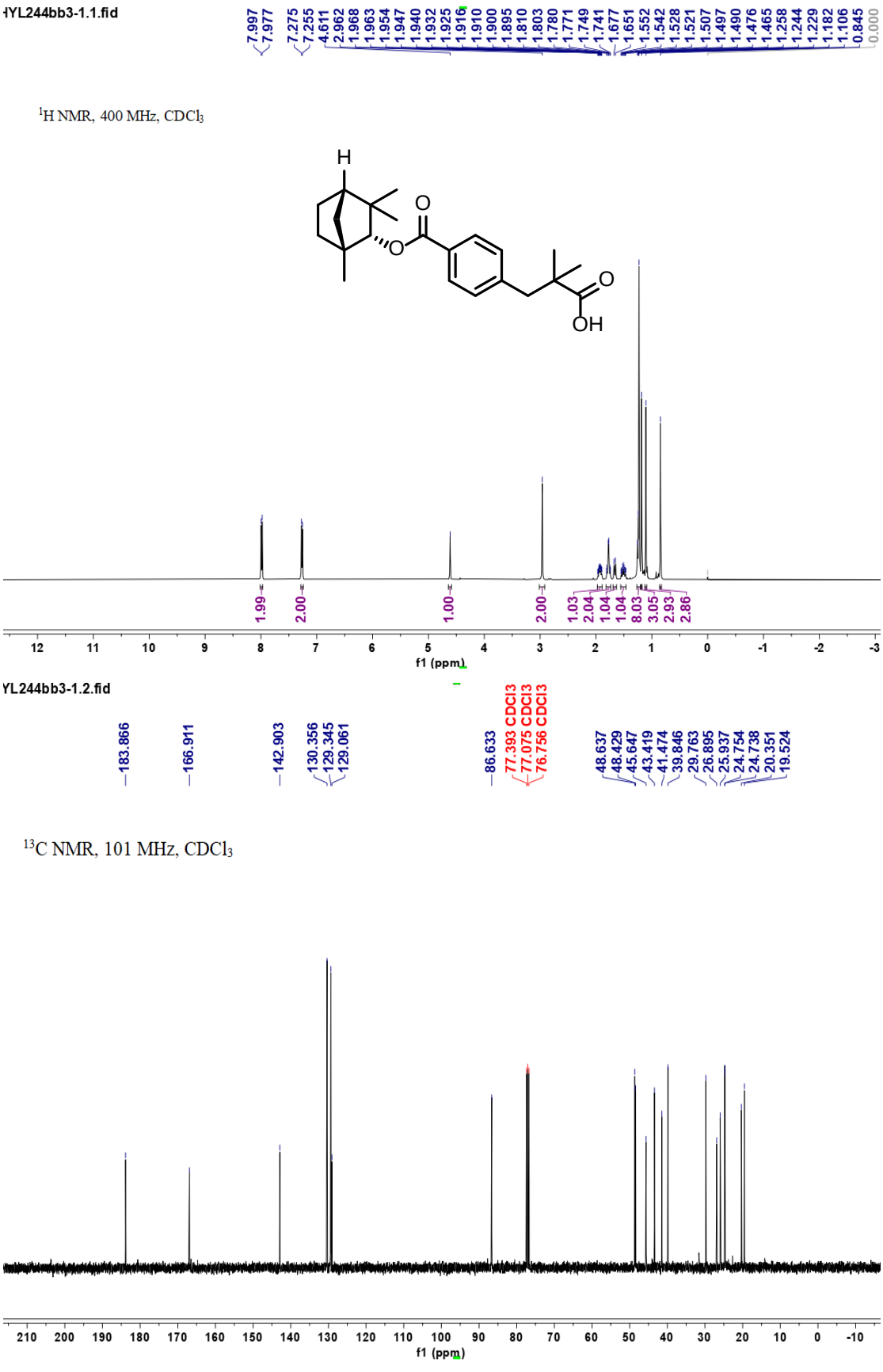


^{1}H NMR, 400 MHz, $CDCl_3$

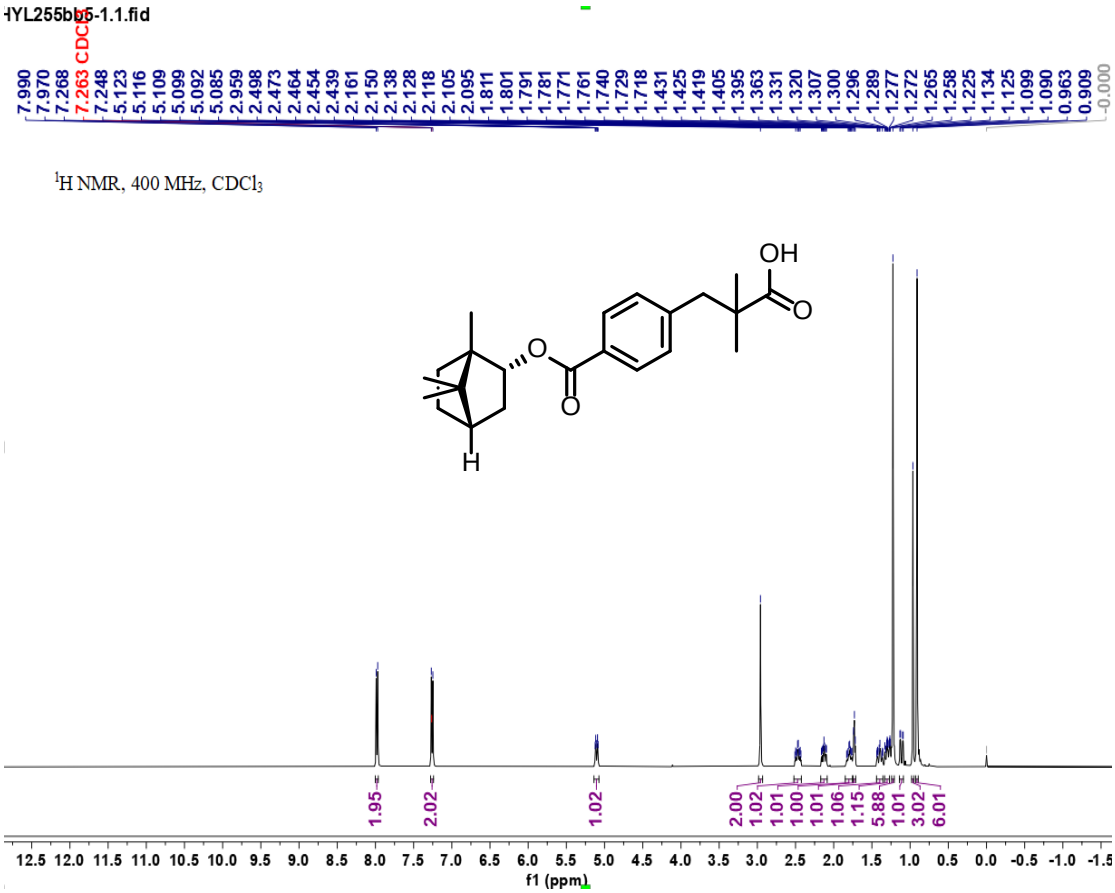


^{13}C NMR, 101 MHz, $CDCl_3$

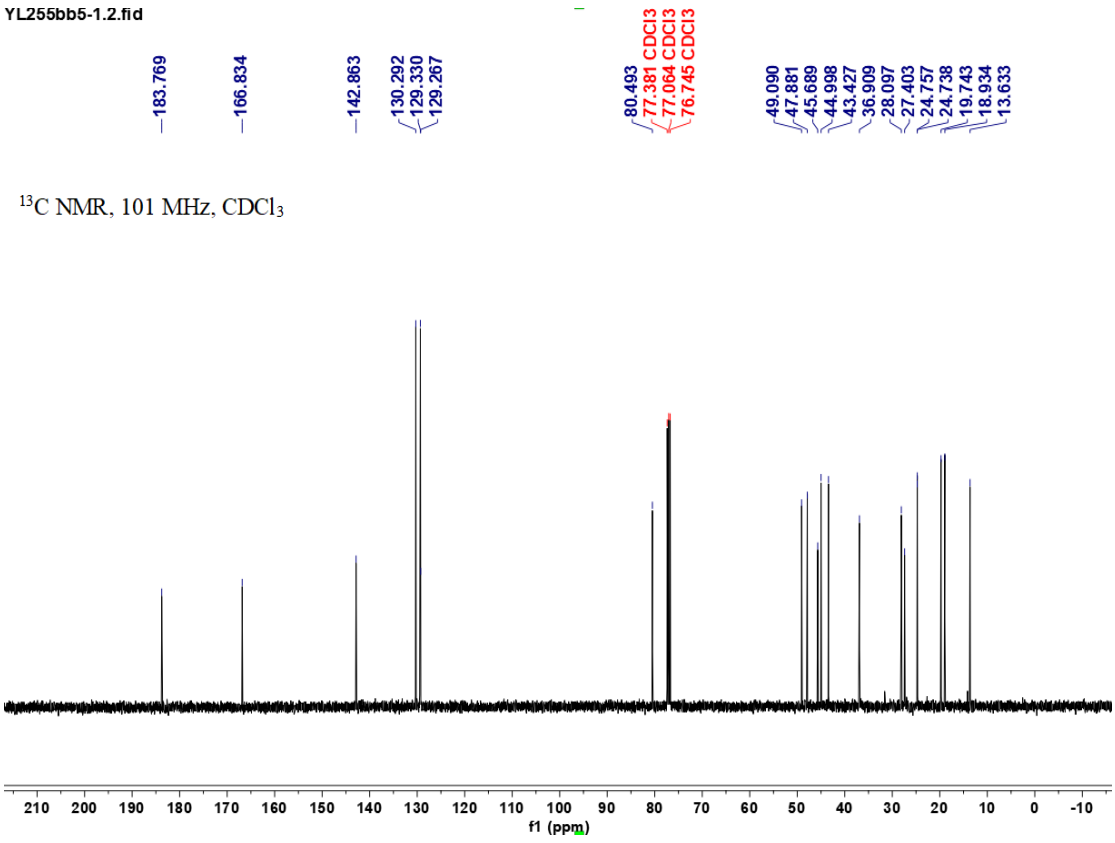
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-63**



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-64**

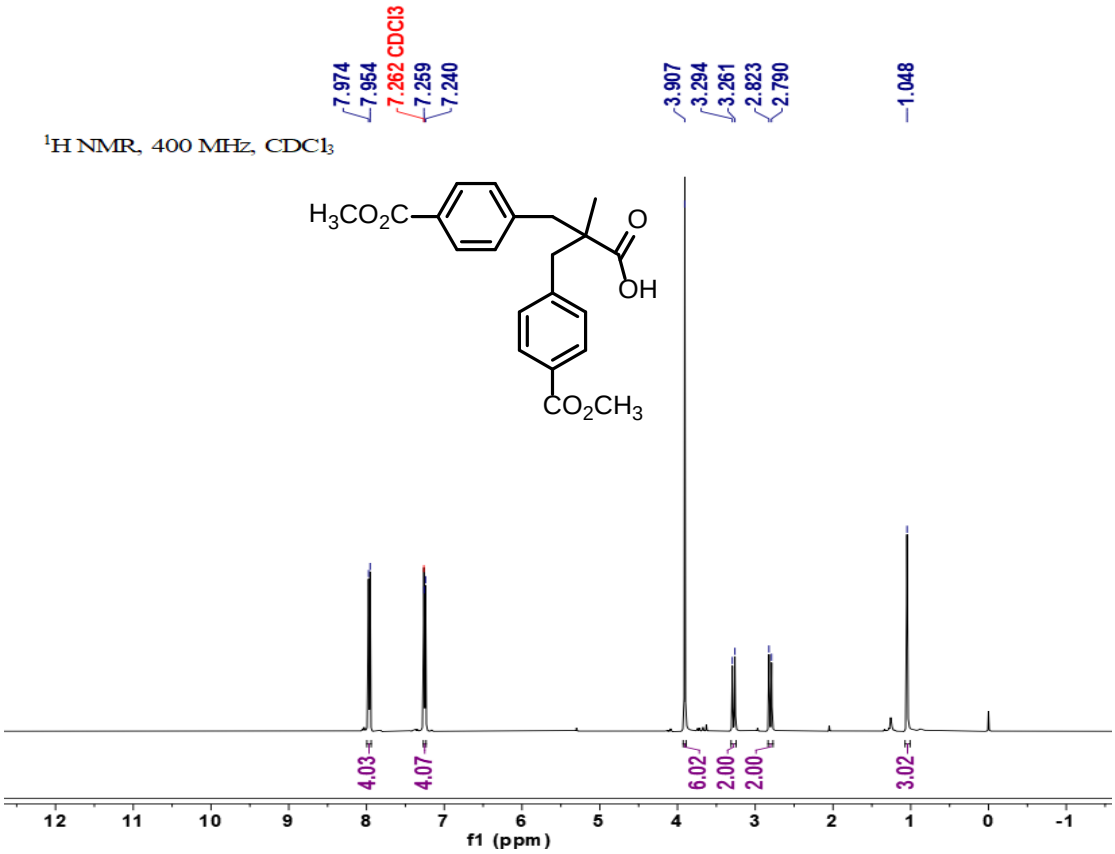


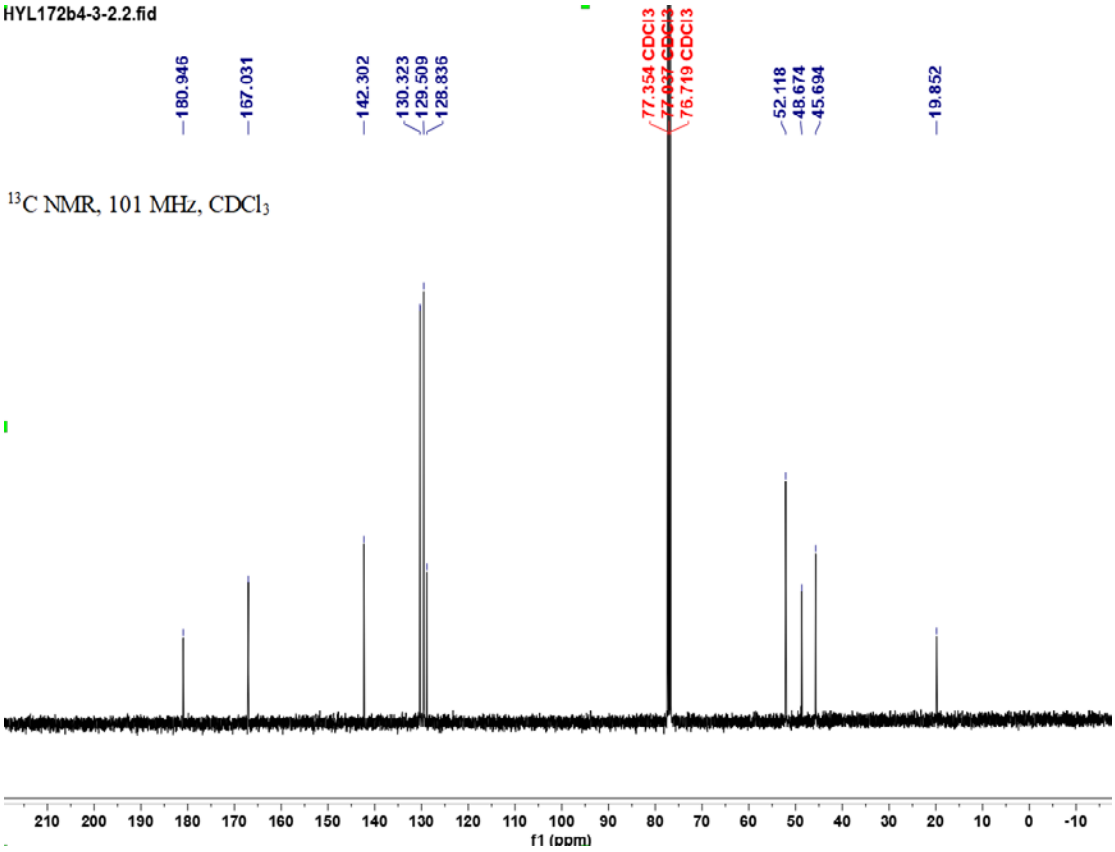
^{1}H NMR, 400 MHz, $CDCl_3$



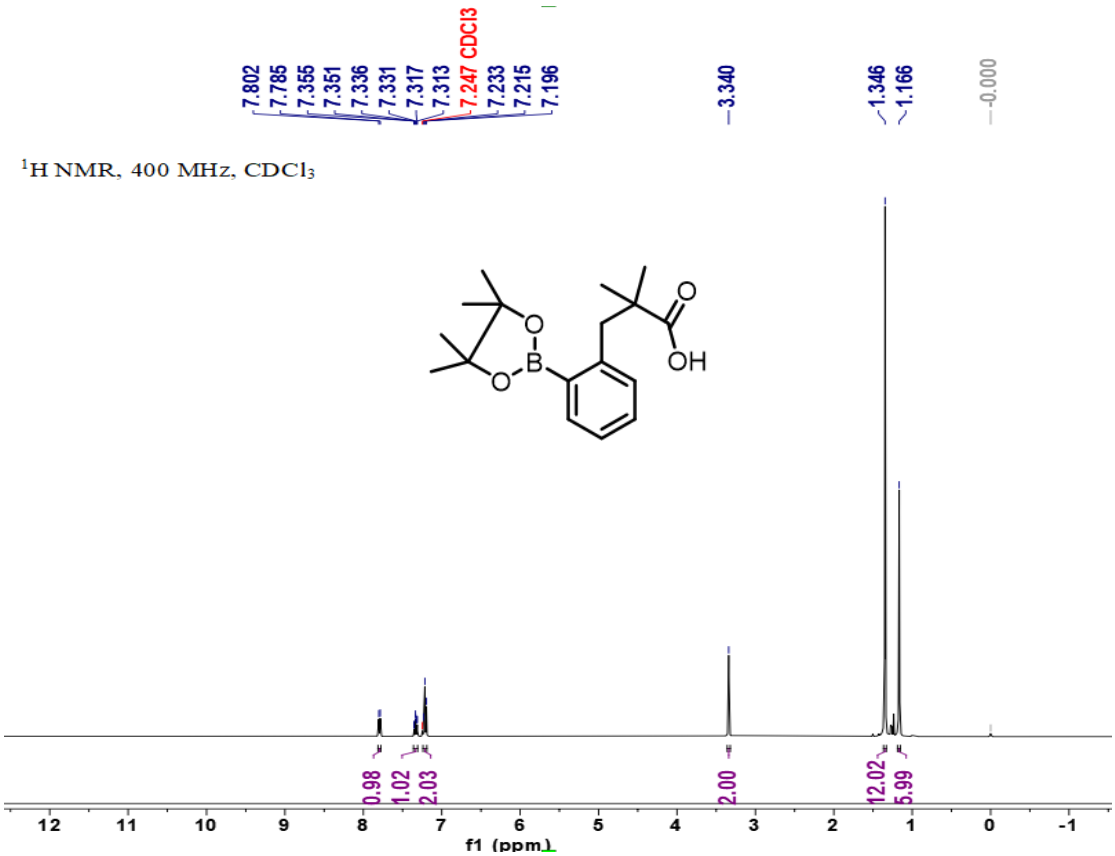
^{13}C NMR, 101 MHz, $CDCl_3$

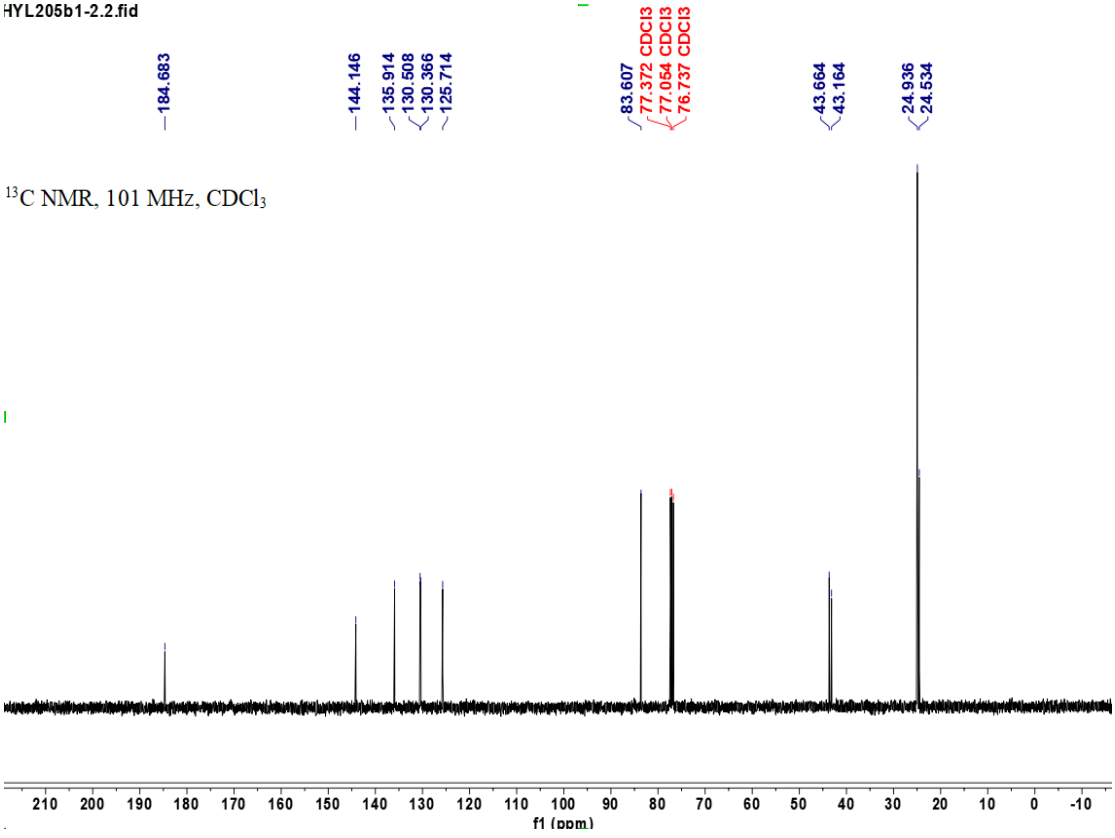
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **7-65**



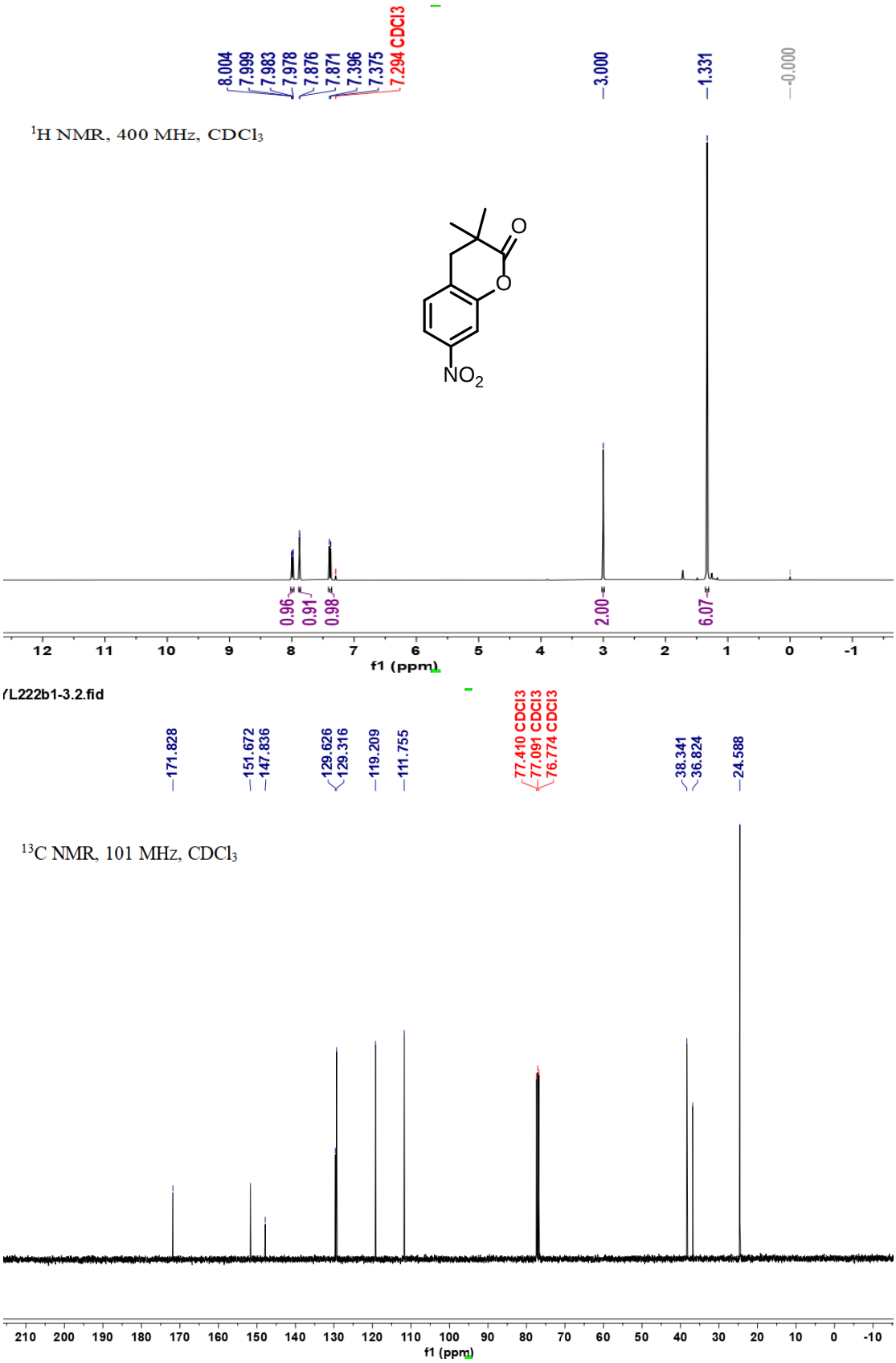


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **8-1**

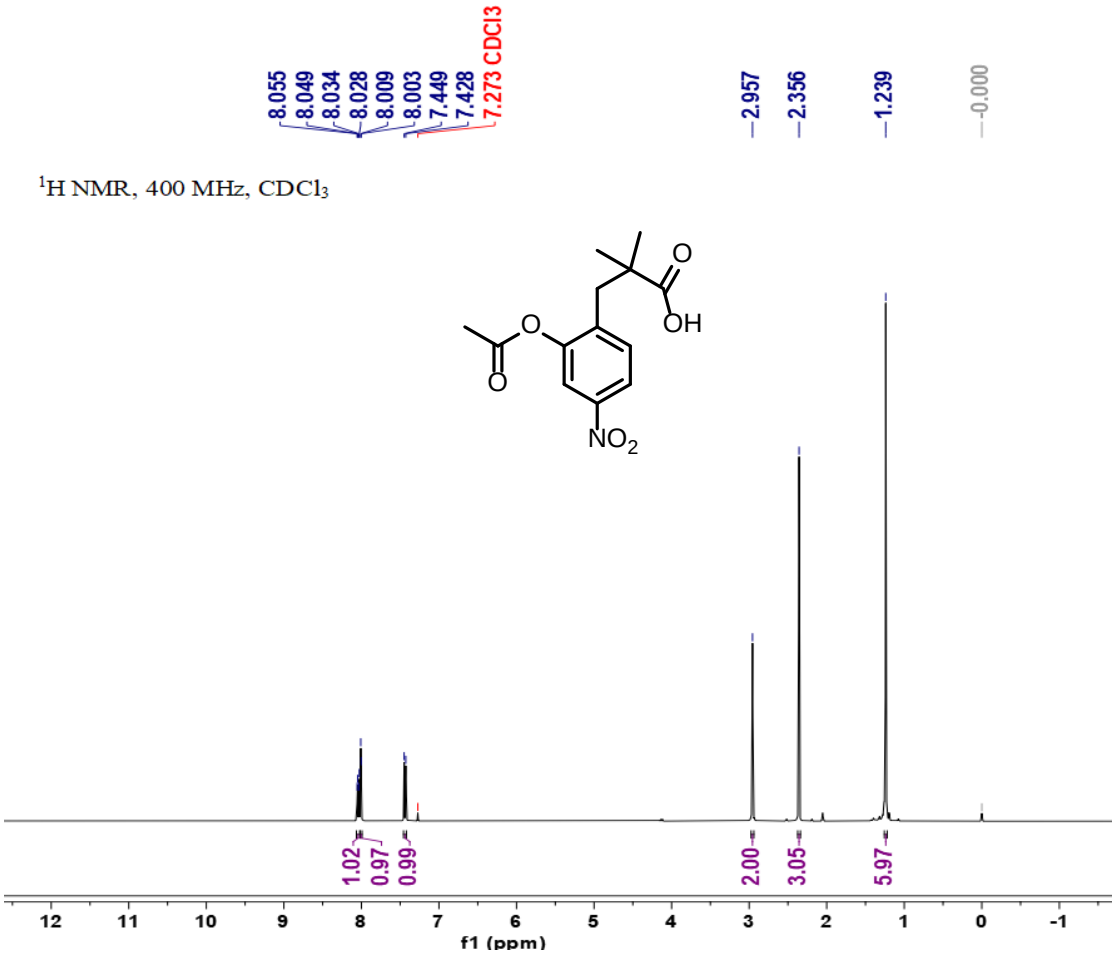


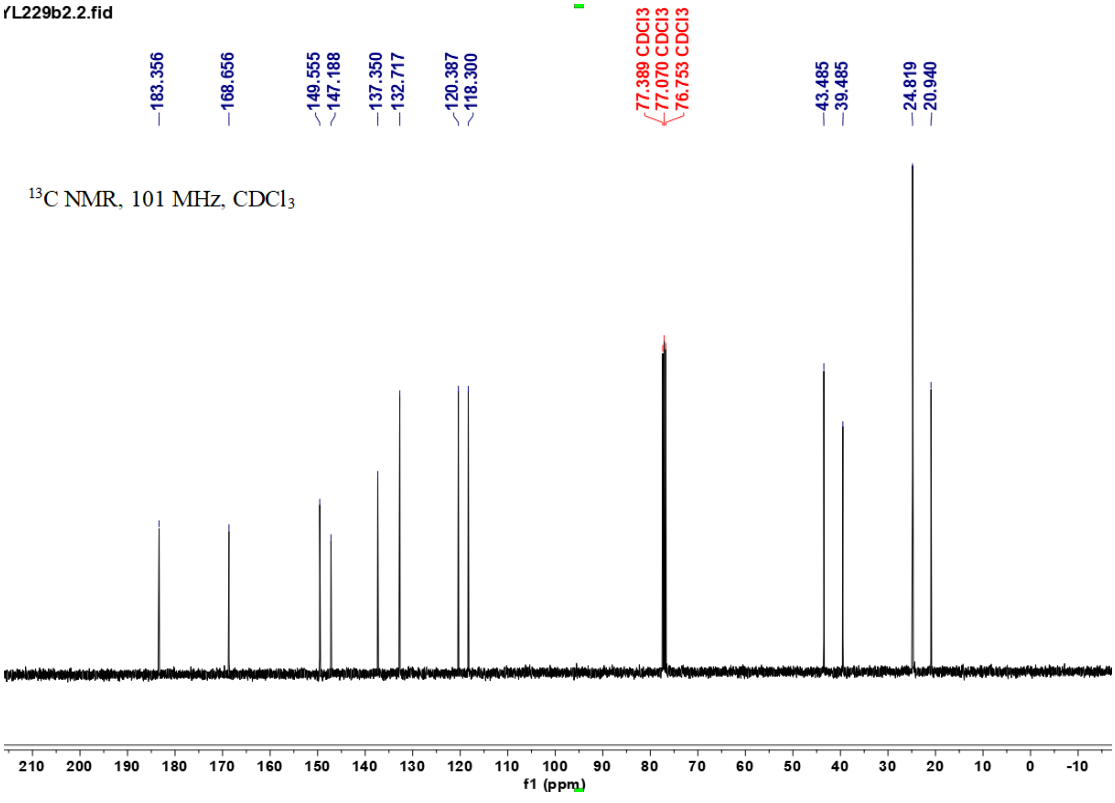


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **ROS sensitive-4**

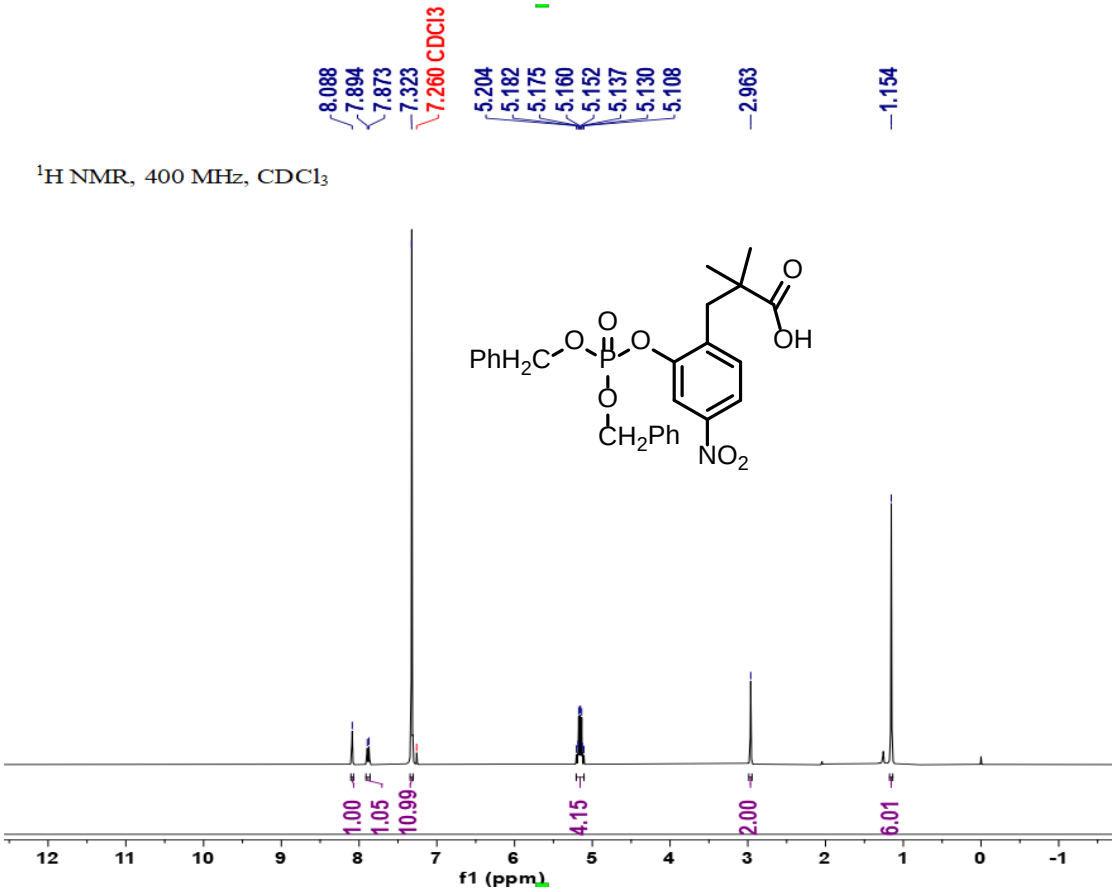


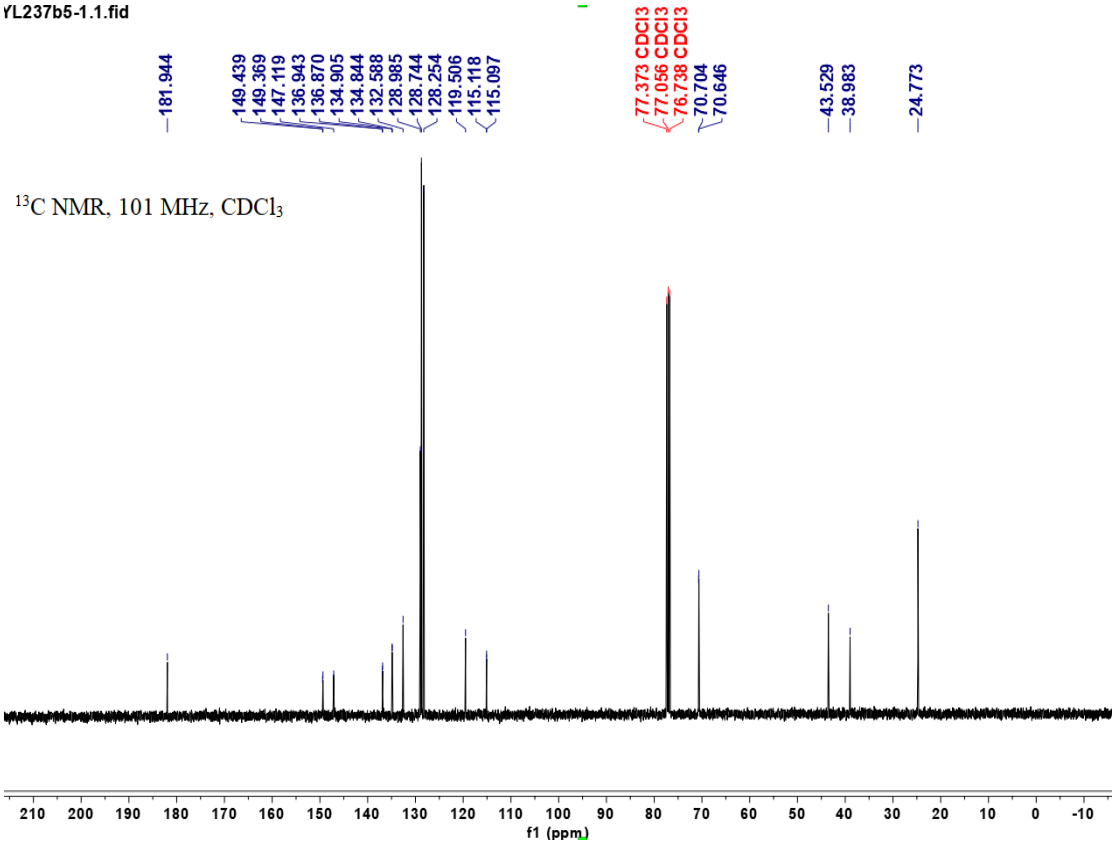
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **9**

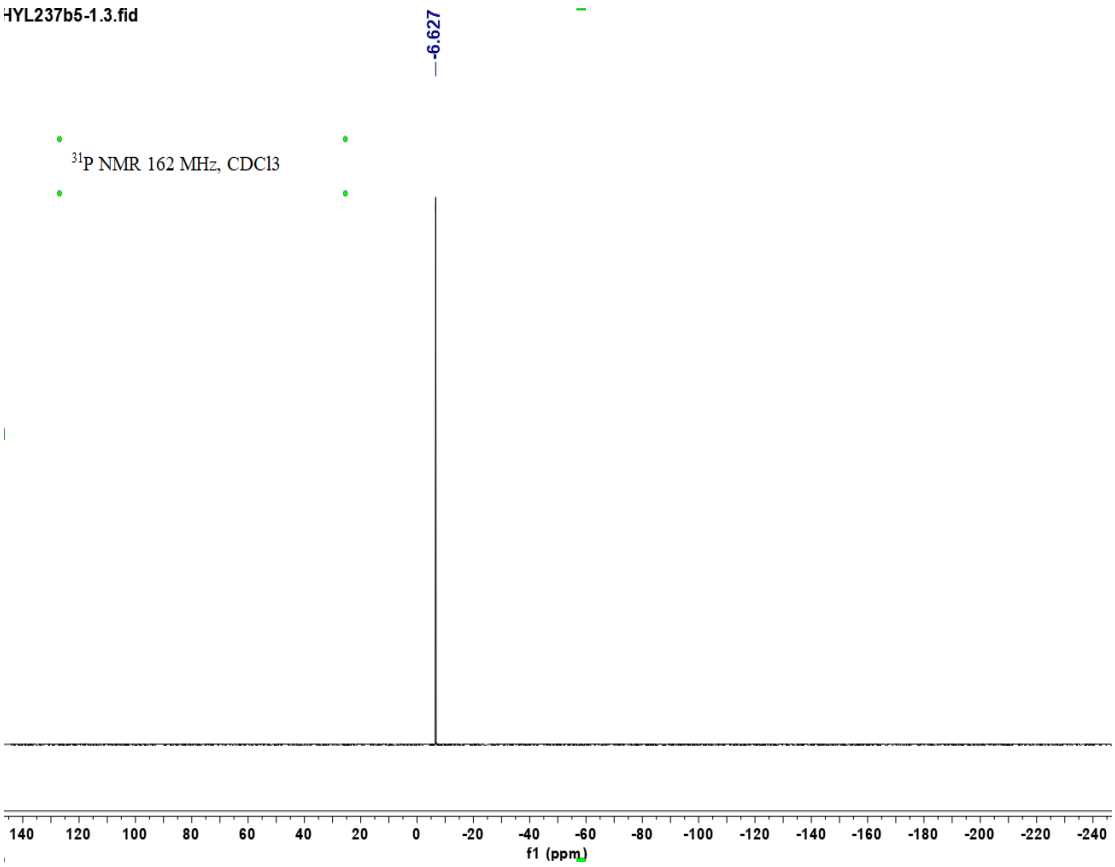




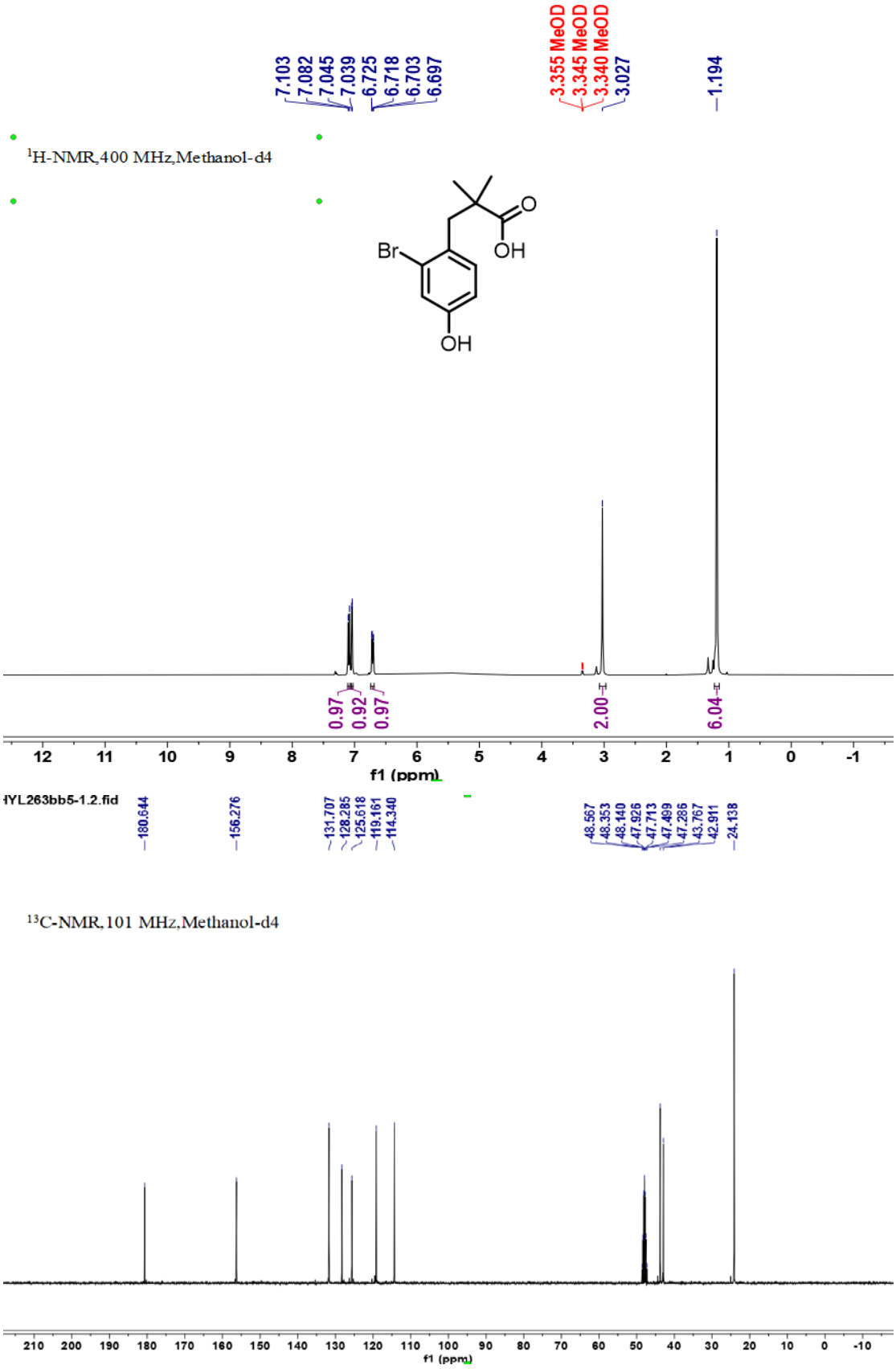
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **esterase sensitive-10**


8.088
7.894
7.873
7.323
7.260 CDCl3
5.204
5.182
5.175
5.160
5.152
5.137
5.130
5.108
2.963
1.154
1H NMR, 400 MHz, CDCl3
PhH2C
O
O
P
O
O
O
CH2Ph
O
OH
NO2
1.00
1.05
10.99
4.15
2.00
6.01
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

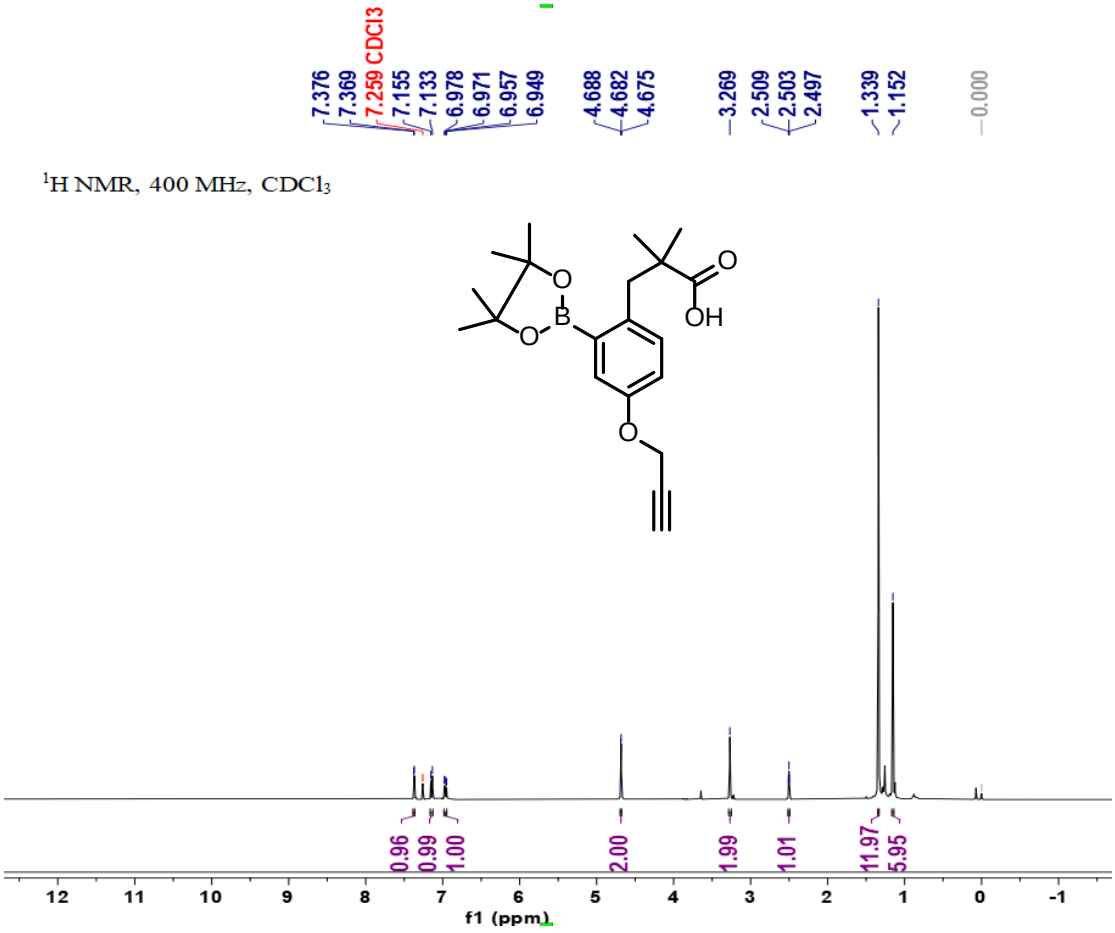

YL237b5-1.1.fid
181.944
149.439
149.369
147.119
136.943
136.870
134.905
134.844
132.588
128.985
128.744
128.254
119.506
115.118
115.097
77.373 CDCl3
77.056 CDCl3
76.738 CDCl3
70.704
70.646
43.529
38.983
24.773
13C NMR, 101 MHz, CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



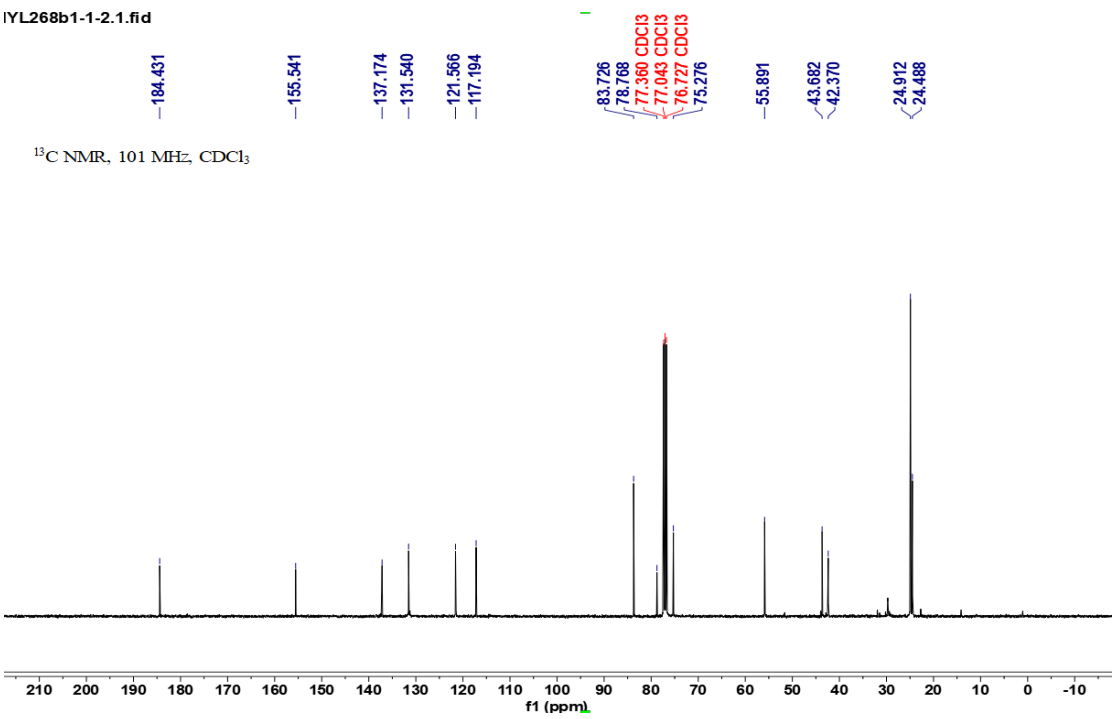
^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{31}P NMR (162 MHz, $CDCl_3$) spectra of **phosphatase sensitive-11**



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **12**

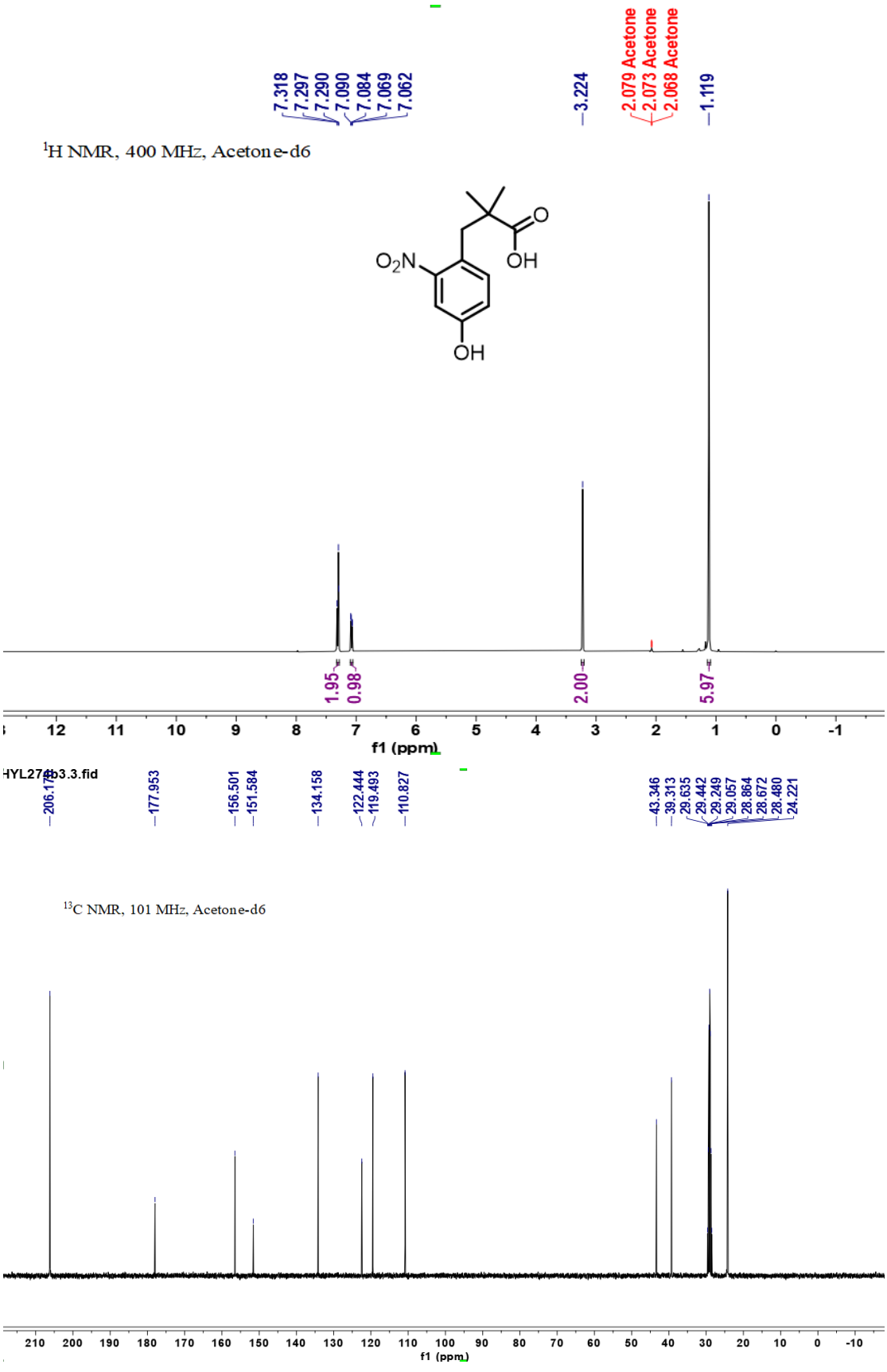


^{1}H NMR, 400 MHz, $CDCl_3$

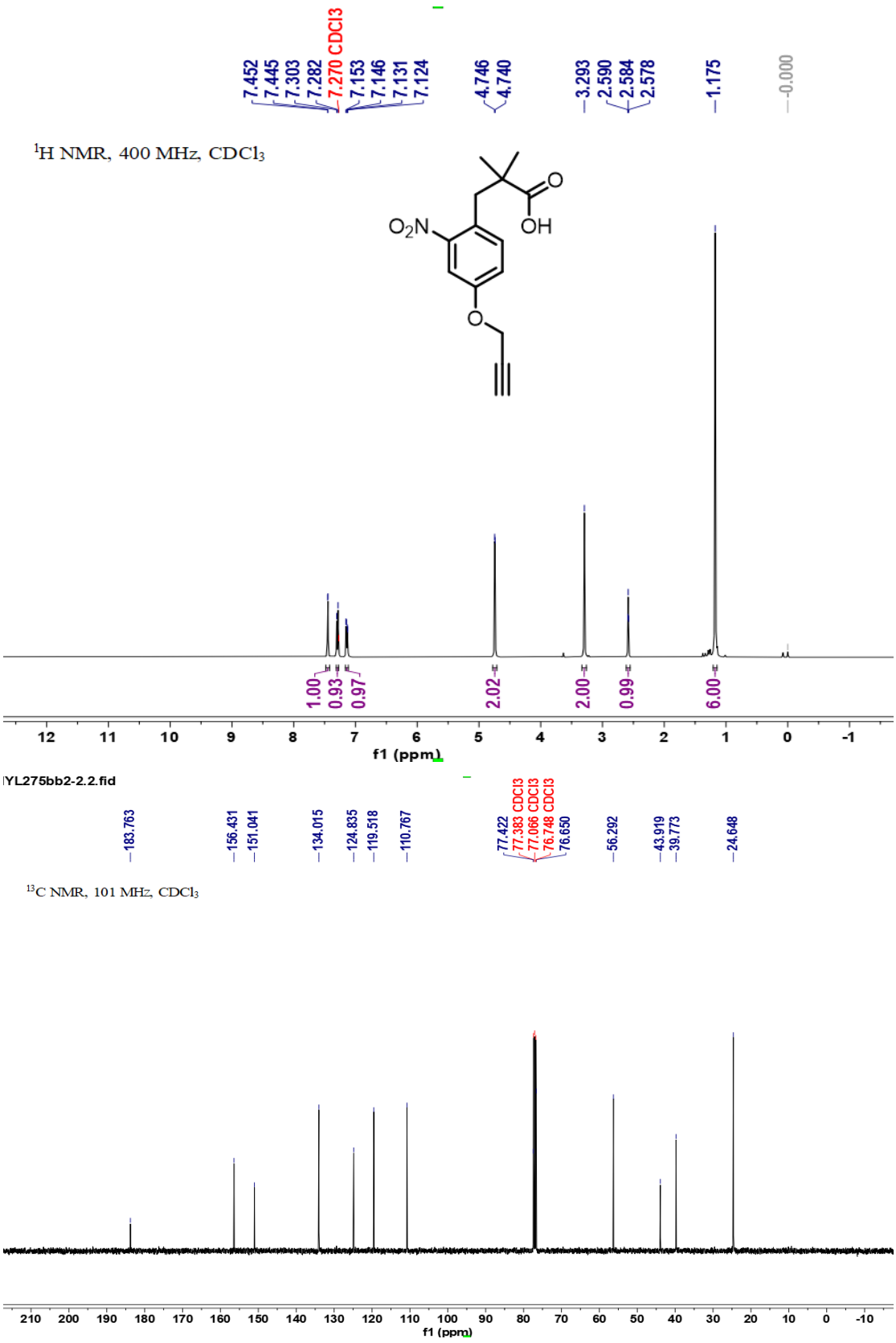


^{13}C NMR, 101 MHz, $CDCl_3$

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **ROS sensitive-13**



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **14**



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of **hypoxia sensitive-15**