Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Electronic Supporting Information for

Oxidative Activation of Stable Dihydropyridine Amides to Reactive Acyl Donors

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Table of Contents

Stability of DHP amide 1 towards amide bond formation ($CDCl_3$)

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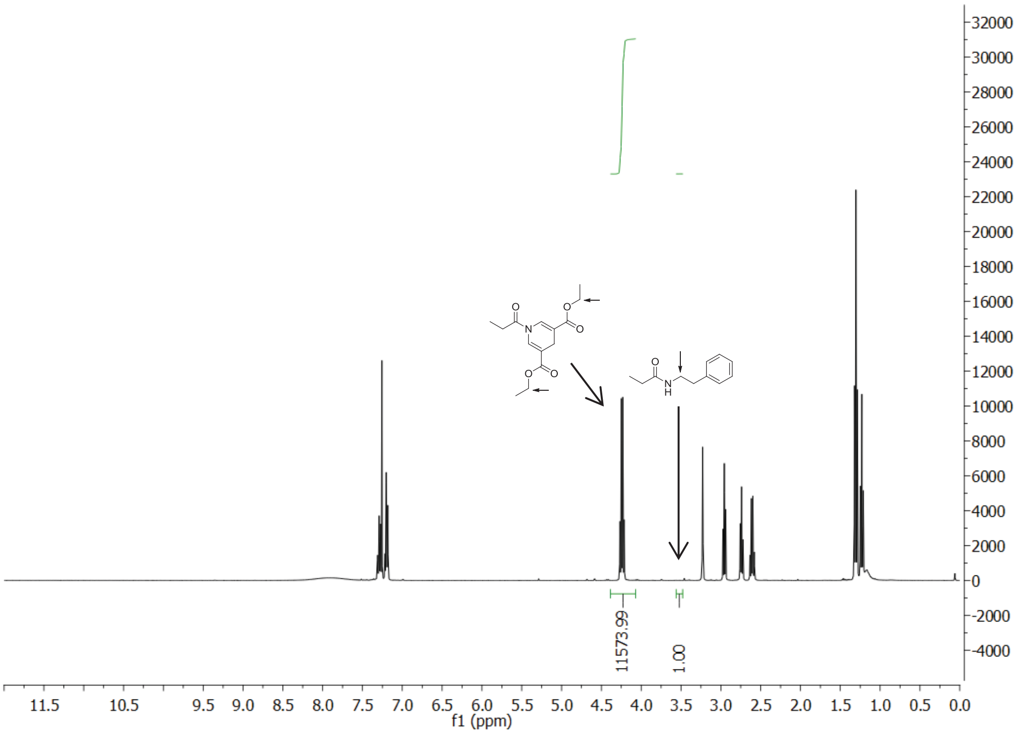
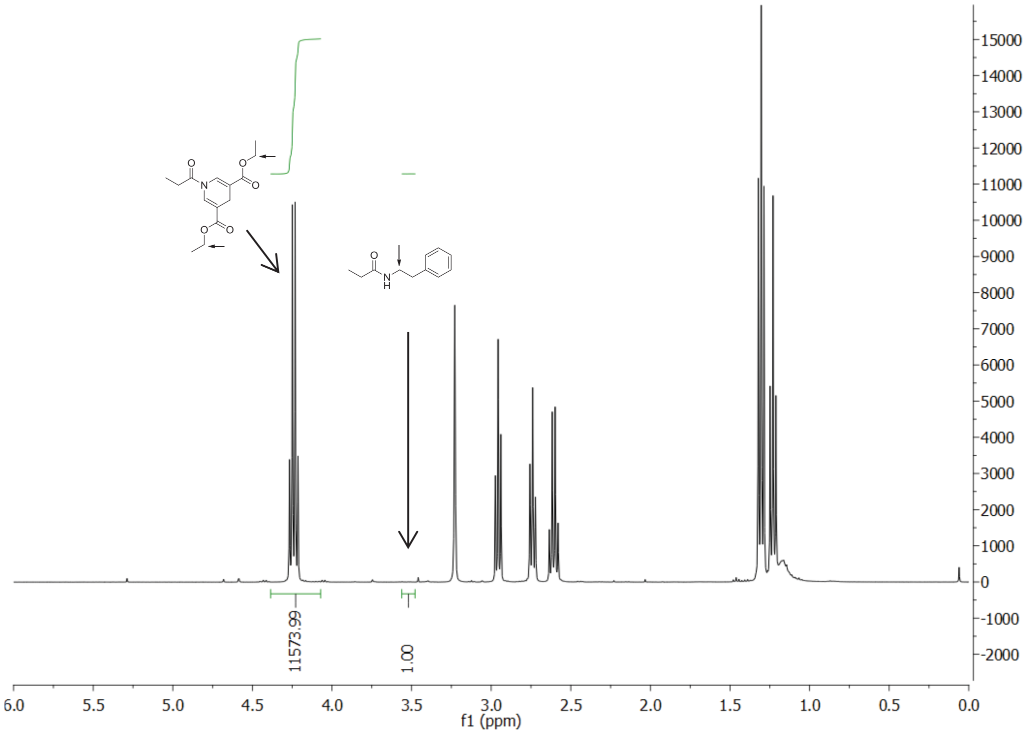
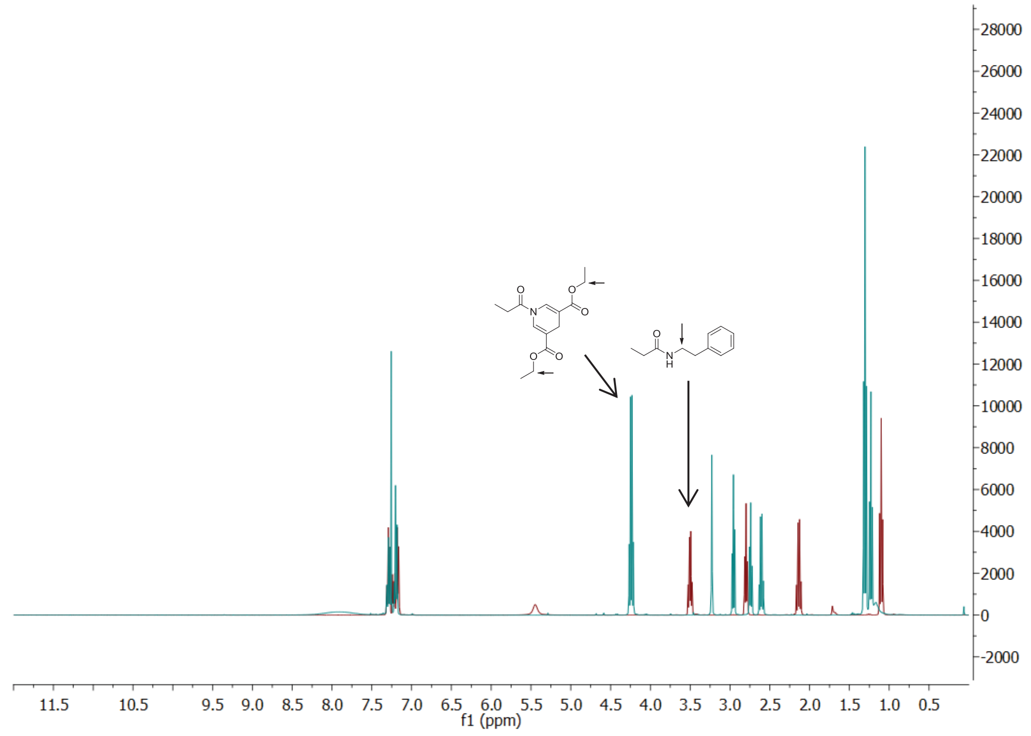


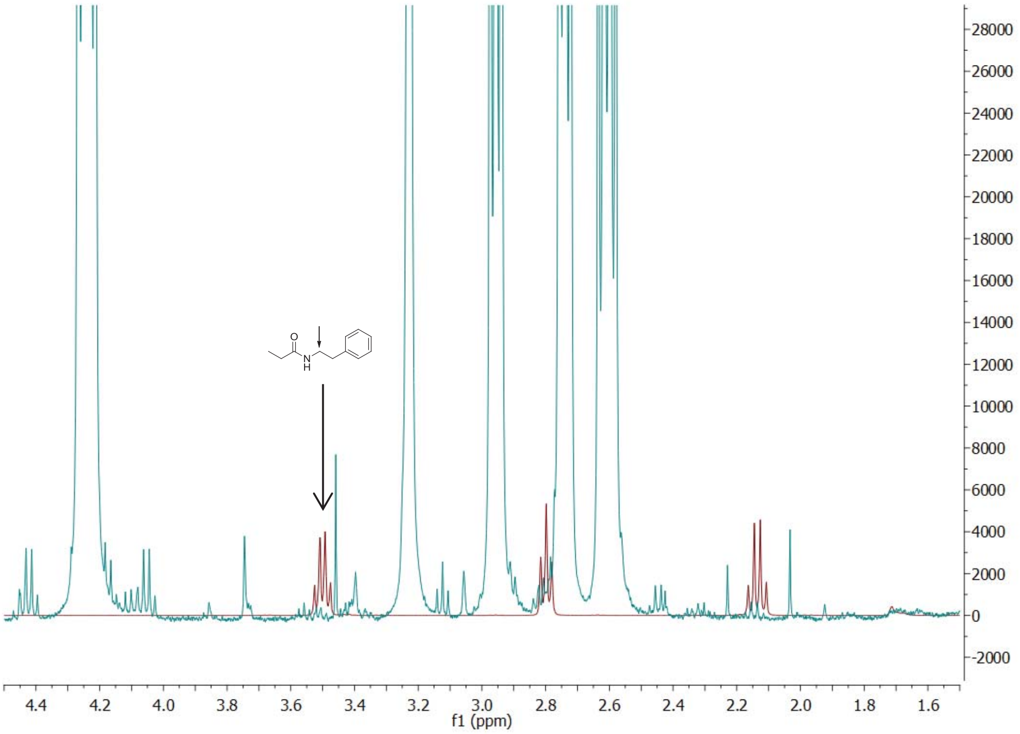
Zoom 0-6 ppm



Overlay spectra. The crude mixture (shown in blue) with overlay of the reference product (shown in red)



Zoomed overlay spectra with increased intensity of peaks in the crude mixture



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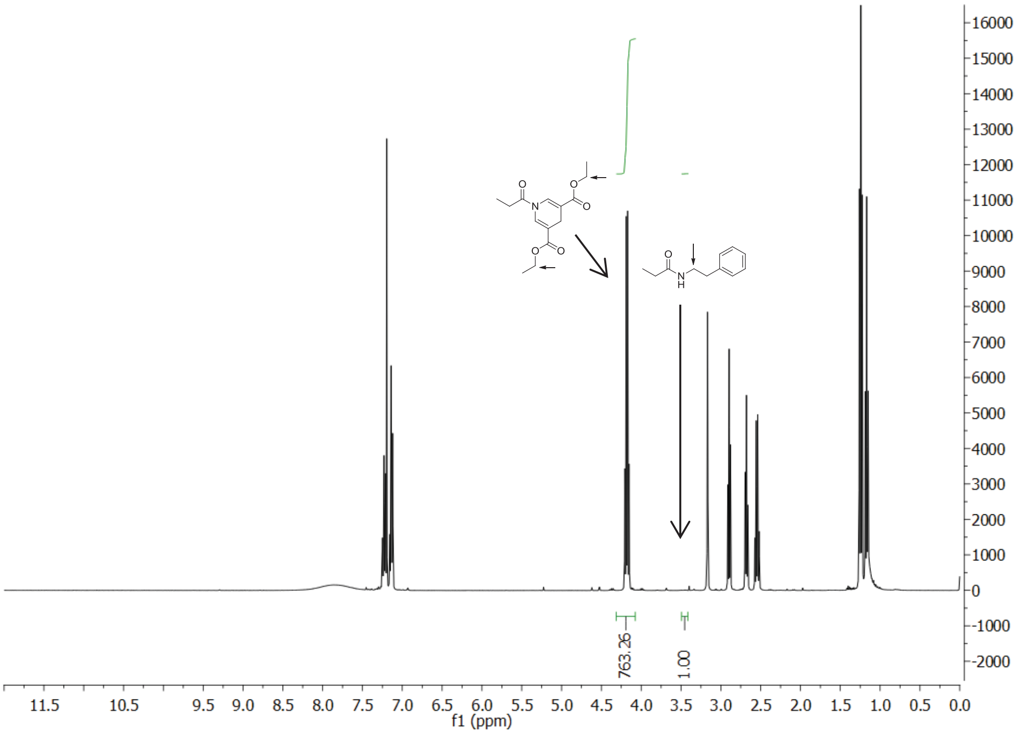
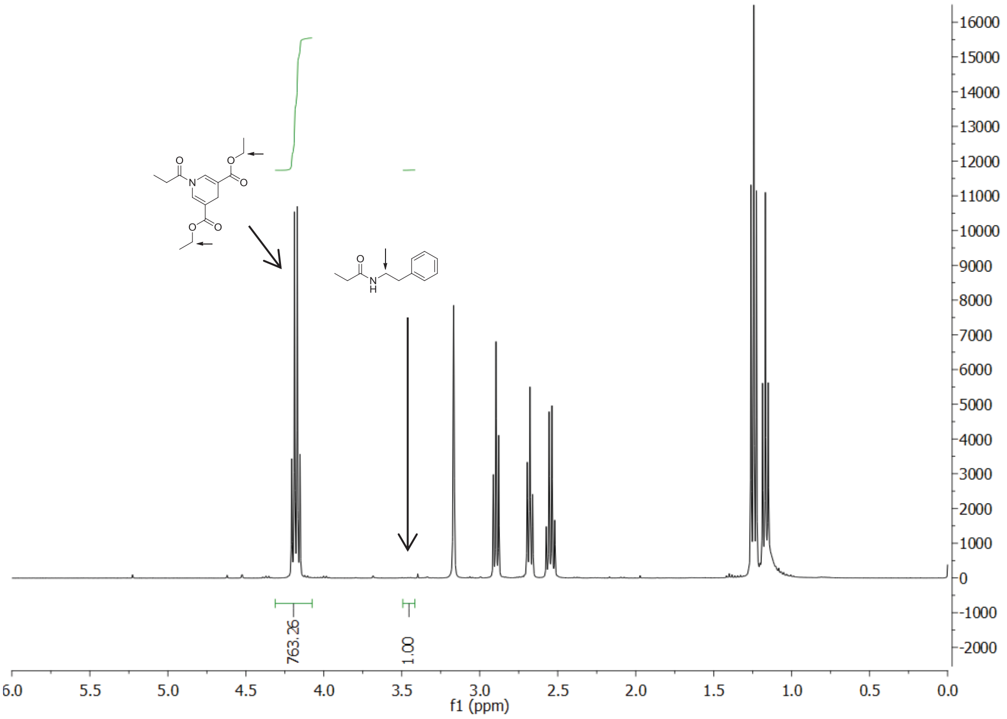
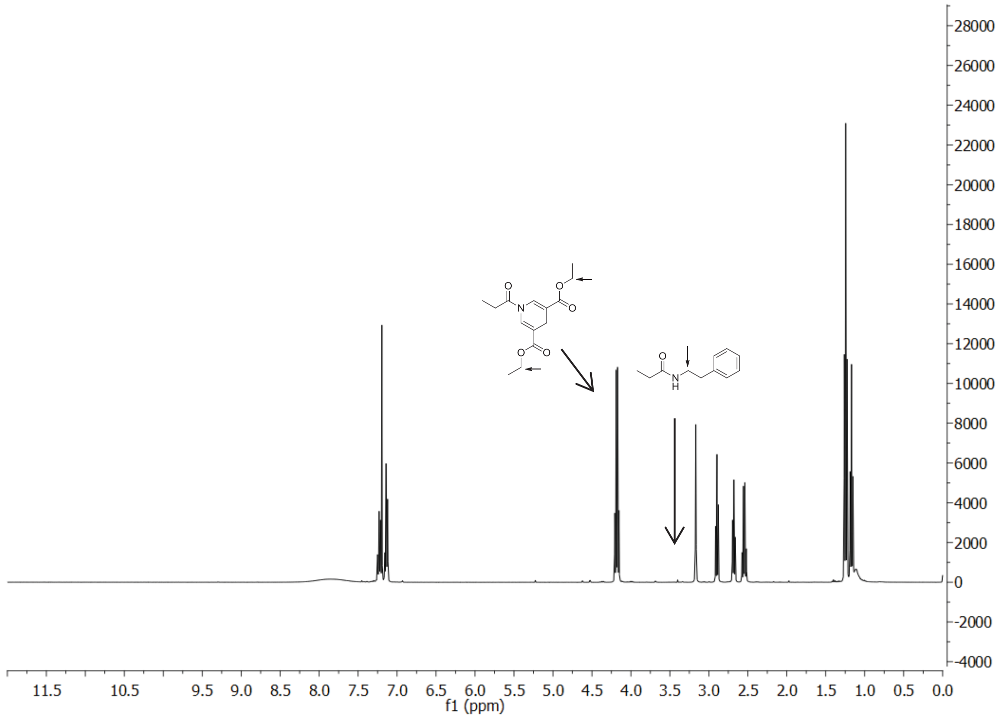


After 48 h at rt. < 1% product formation. (Propionyl DHP (1 eq.) and phenylethyl amine (1 eq.) in $CDCl_3$). Zoom 6-0 ppm



After 24 h at 40 ˚C < 1% product formation. (Propionyl DHP (1 eq.) and phenylethyl amine (1 eq.) in $CDCl_3$)



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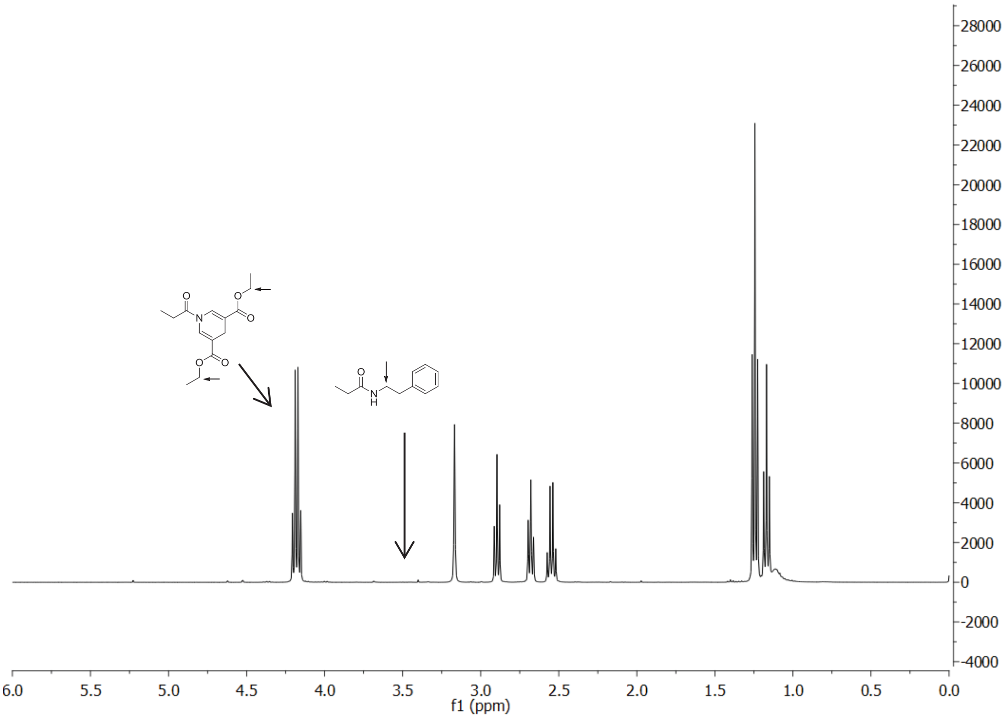

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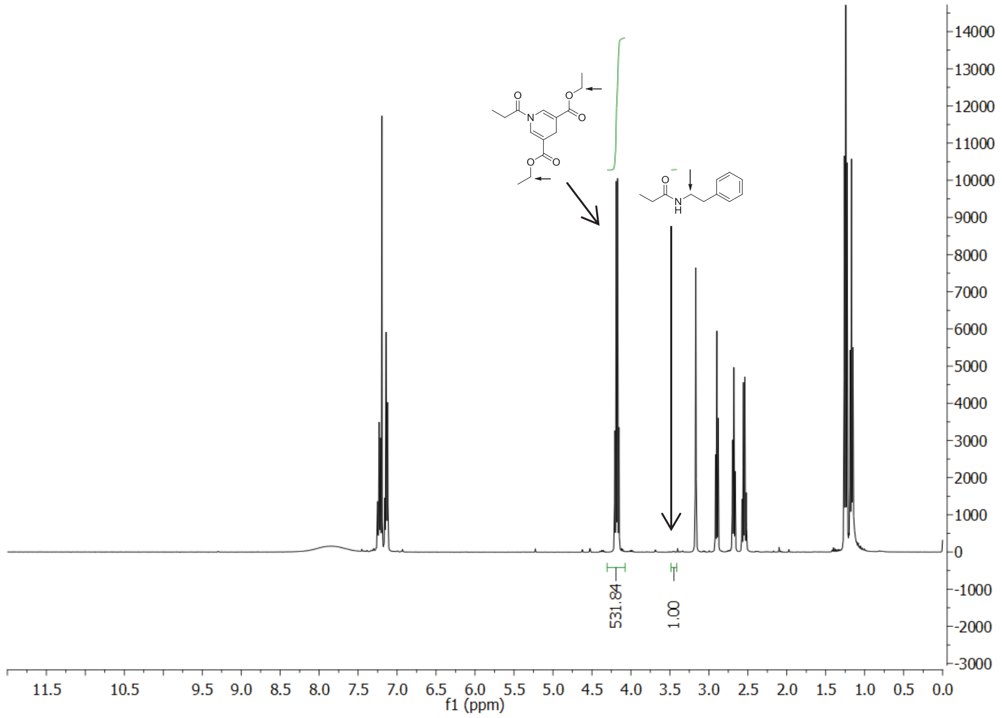

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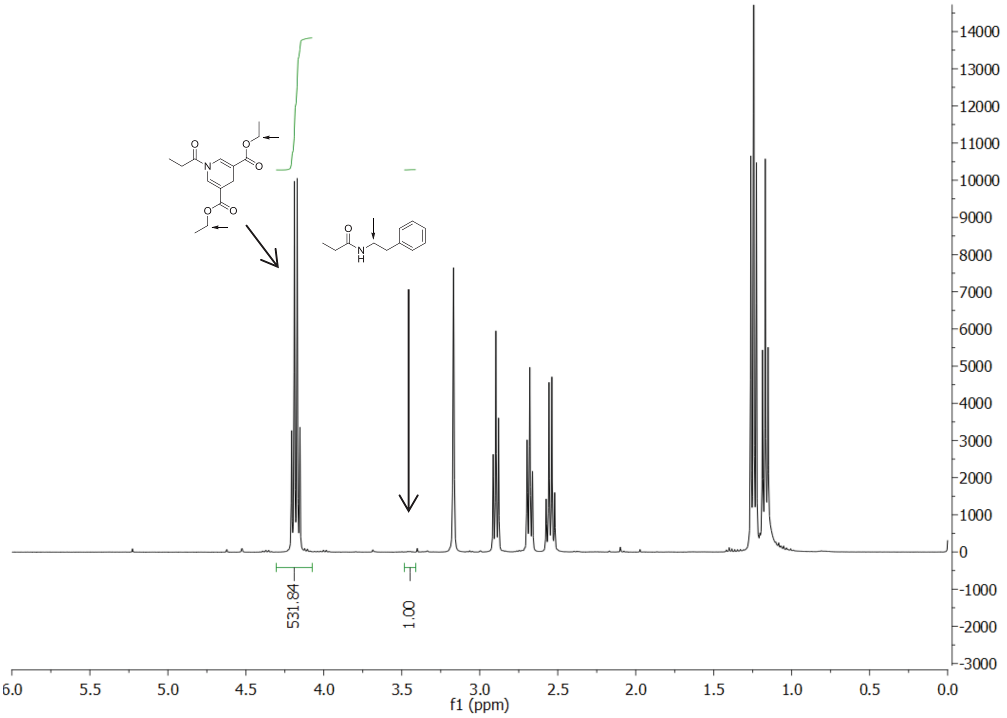
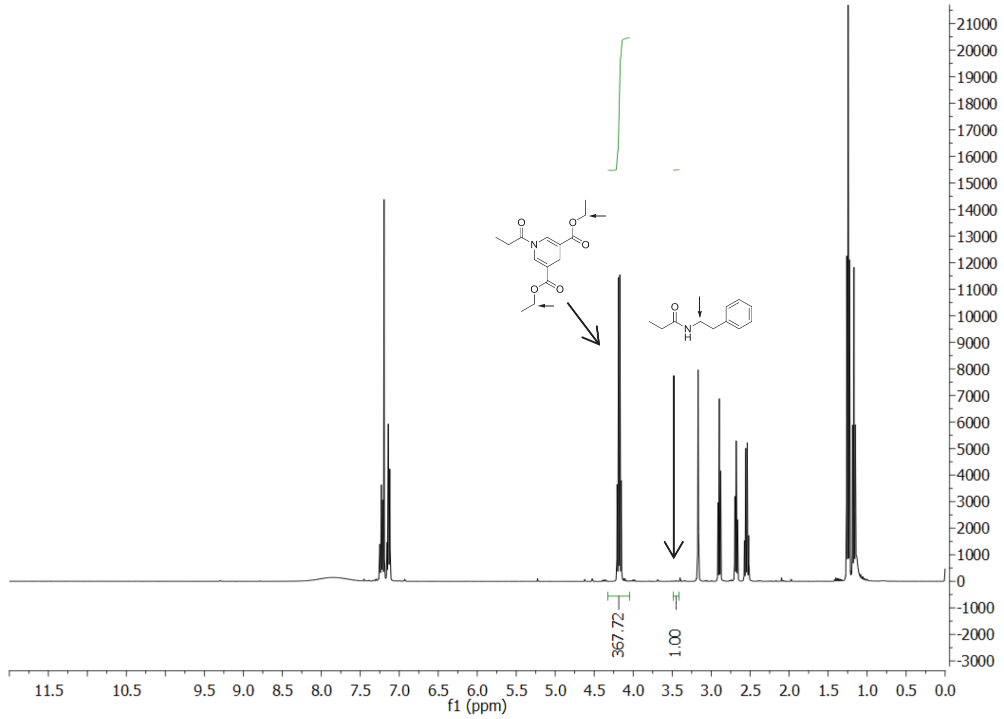
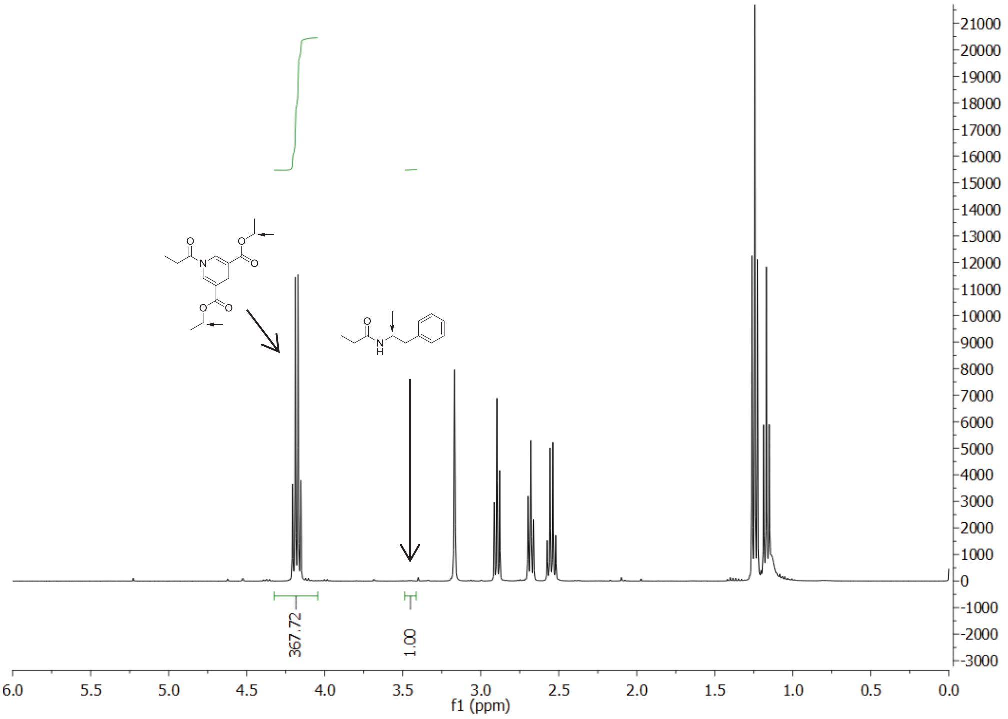


After 24 h at 60 ˚C < 1% product formation. (Propionyl DHP (1 eq.) and phenylethyl amine (1 eq.) in $CDCl_3$).



After 24 h at 60 ˚C < 1% product formation. (Propionyl DHP (1 eq.) and phenylethyl amine (1 eq.) in CDCl$_3$). Zoom 6-0 ppm



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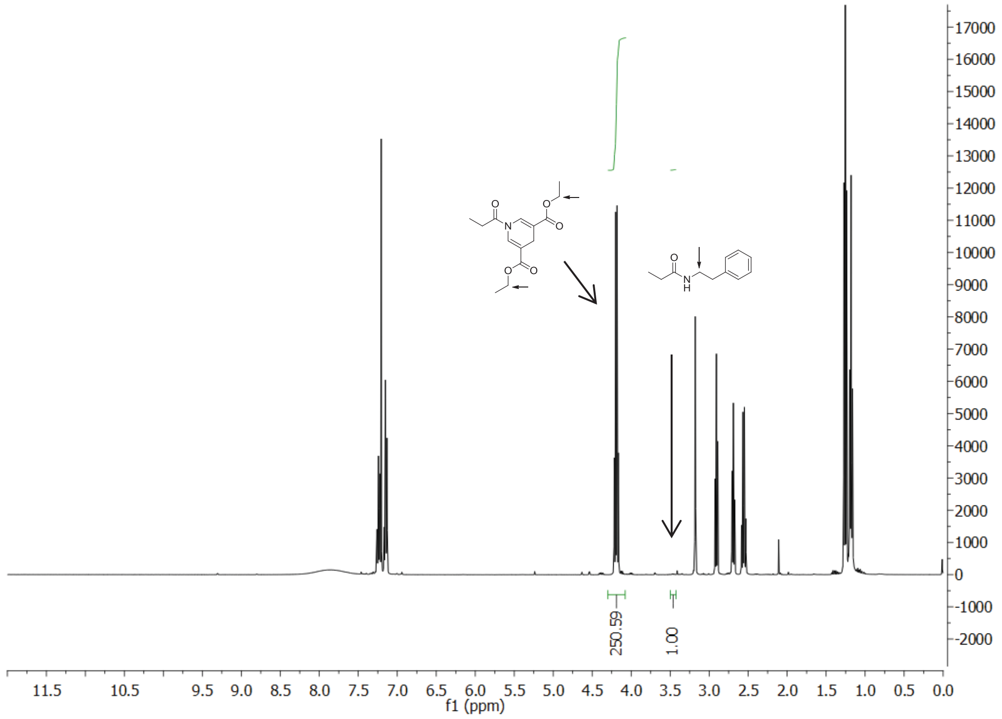

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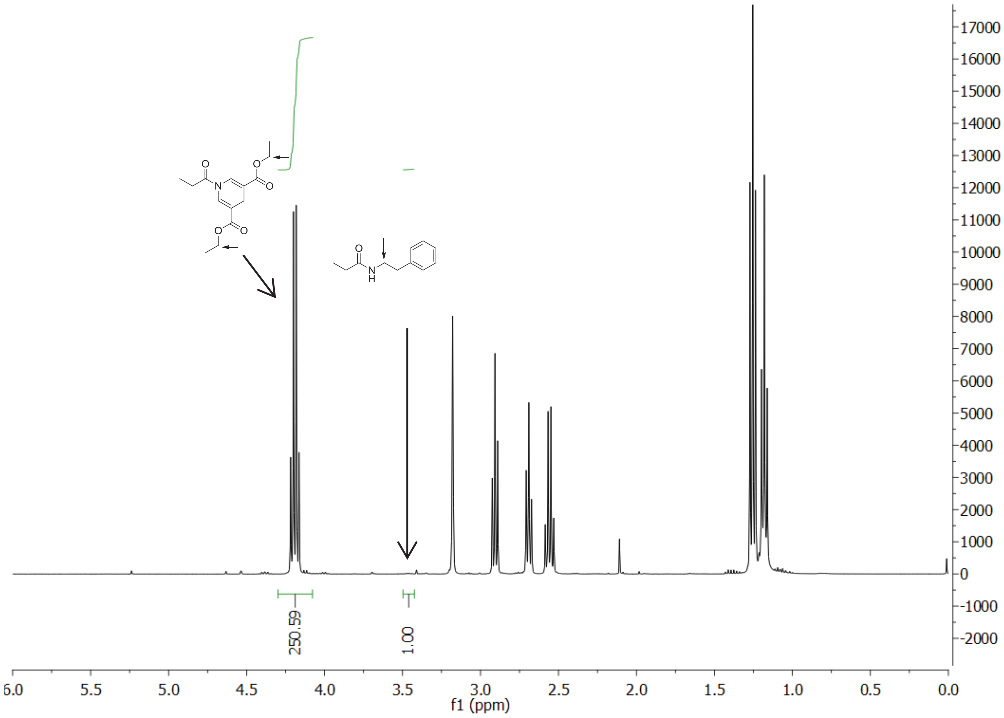

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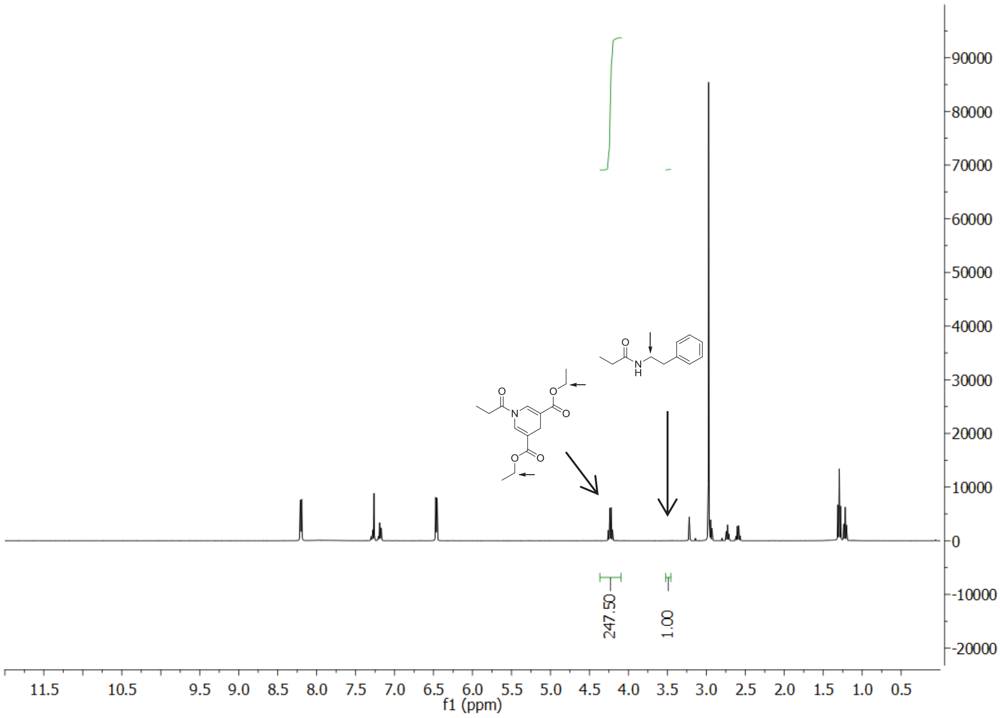
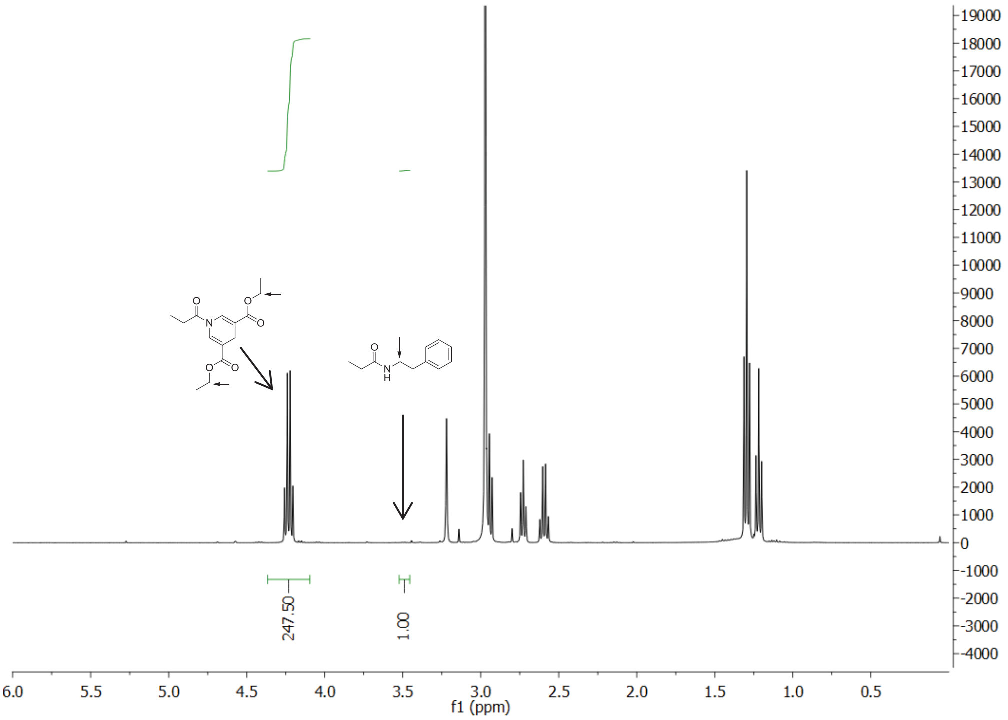
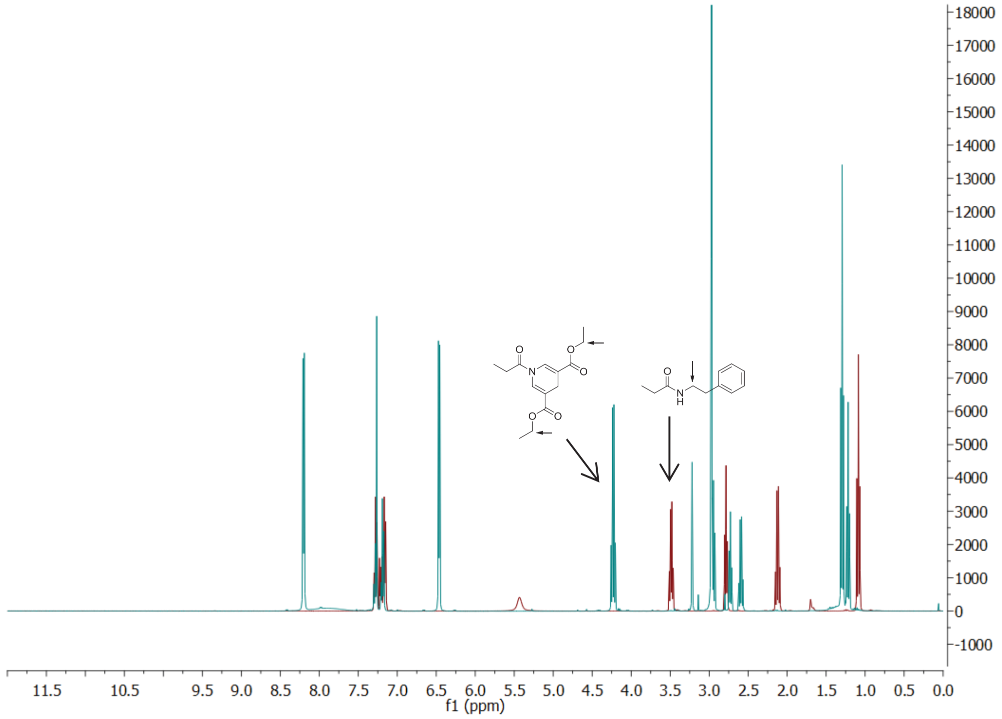


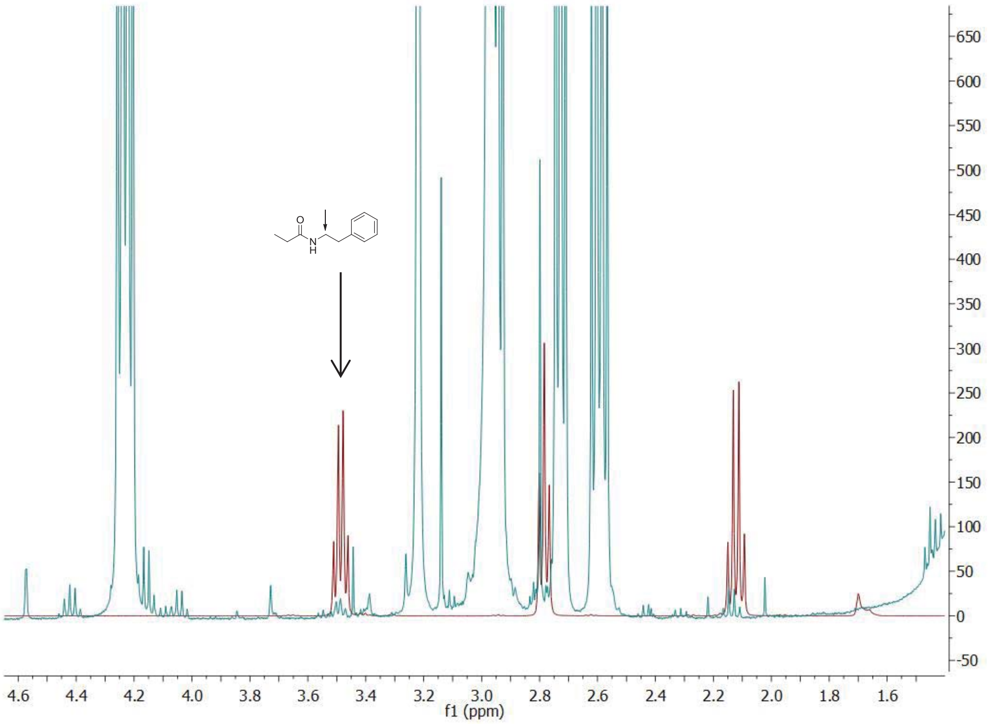
Zoom 0-6 ppm



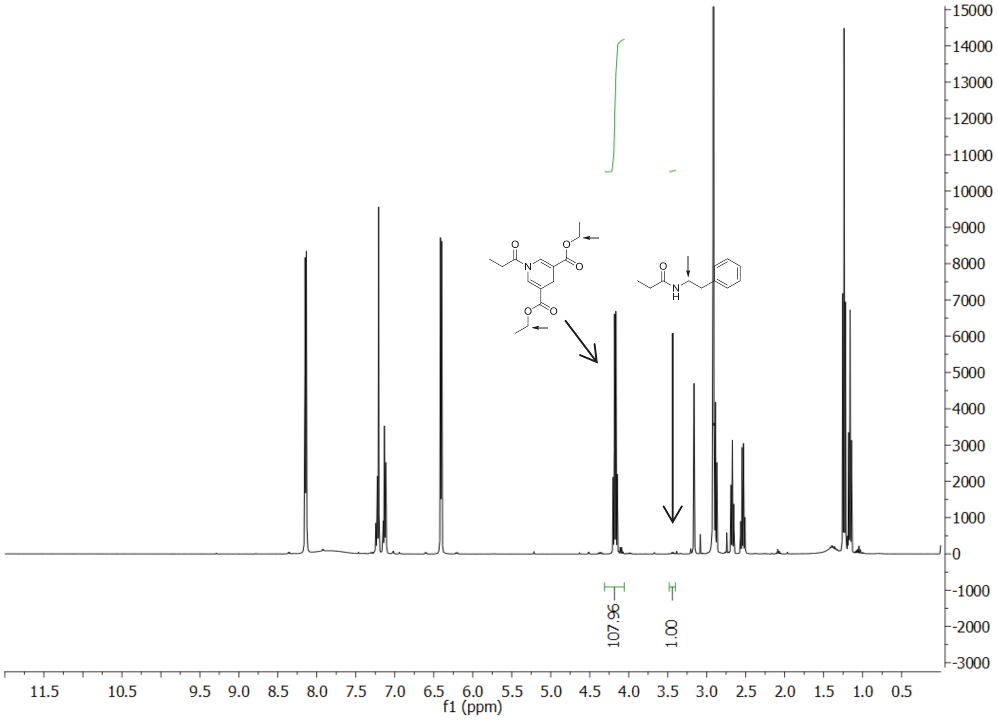
Overlay spectra. The crude mixture (shown in blue) with overlay of the reference product (shown in red)



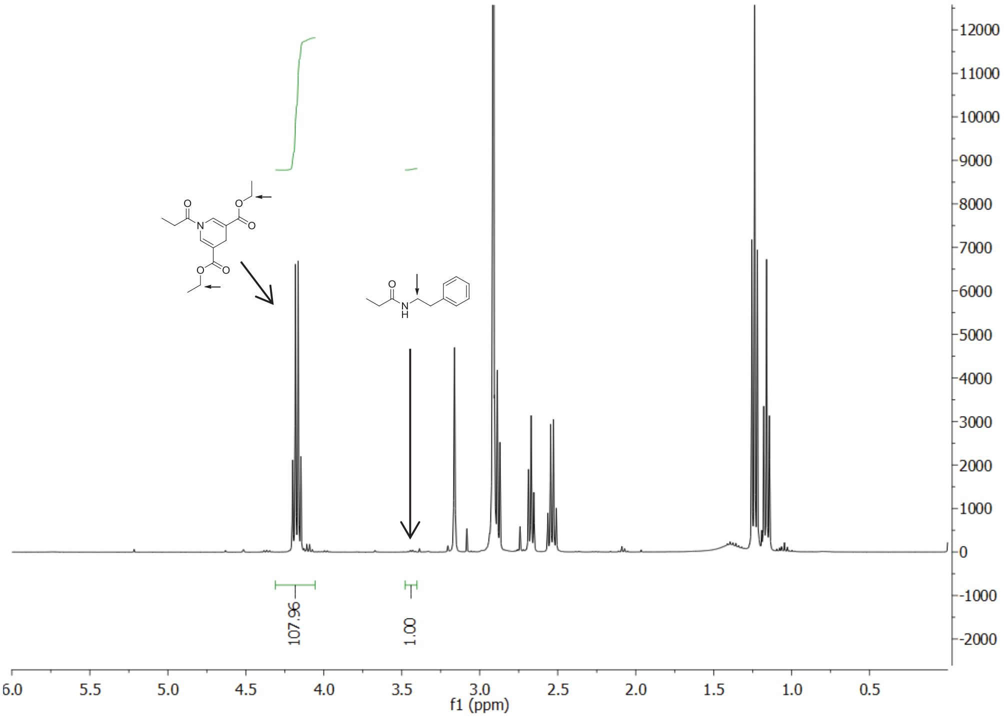
Zoomed overlay spectra with increased intensity of peaks in the crude mixture



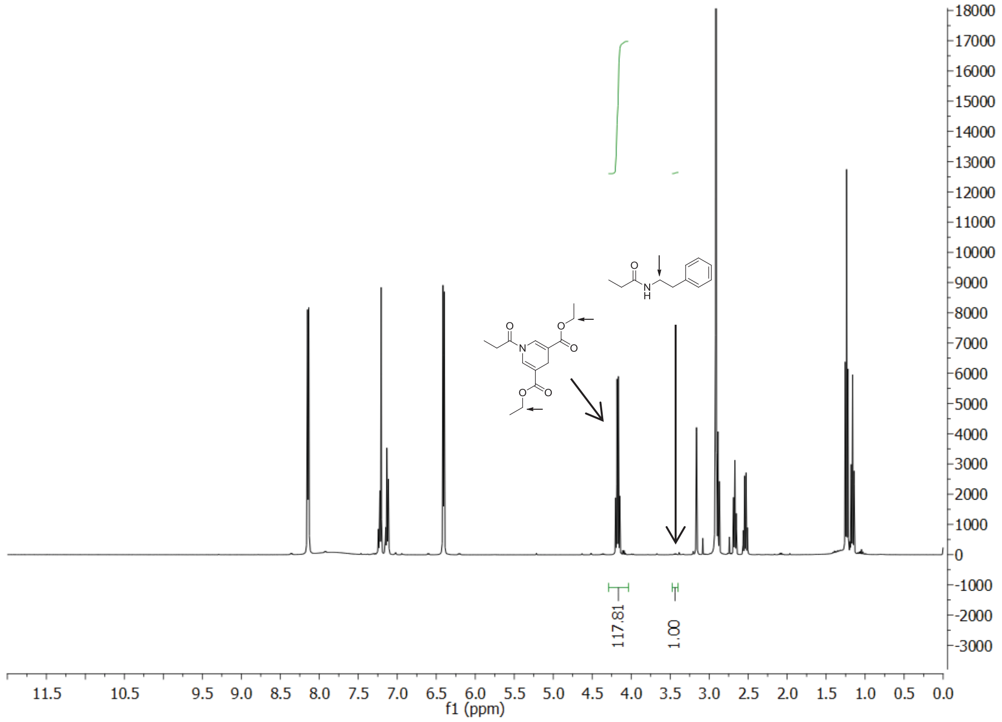
After 48 h at rt. < 2% product formation. (Propionyl DHP (1 eq.), phenylethyl amine (1 eq.), and DMAP (3 eq.) in $CDCl_3$).



After 48 h at rt. < 2% product formation. (Propionyl DHP (1 eq.), phenylethyl amine (1 eq.), and DMAP (3 eq.) in $CDCl_3$). Zoom 6-0 ppm



After 24 h at 40 ˚C < 2% product formation. (Propionyl DHP (1 eq.), phenylethyl amine (1 eq.), and DMAP (3 eq.) in $CDCl_3$).



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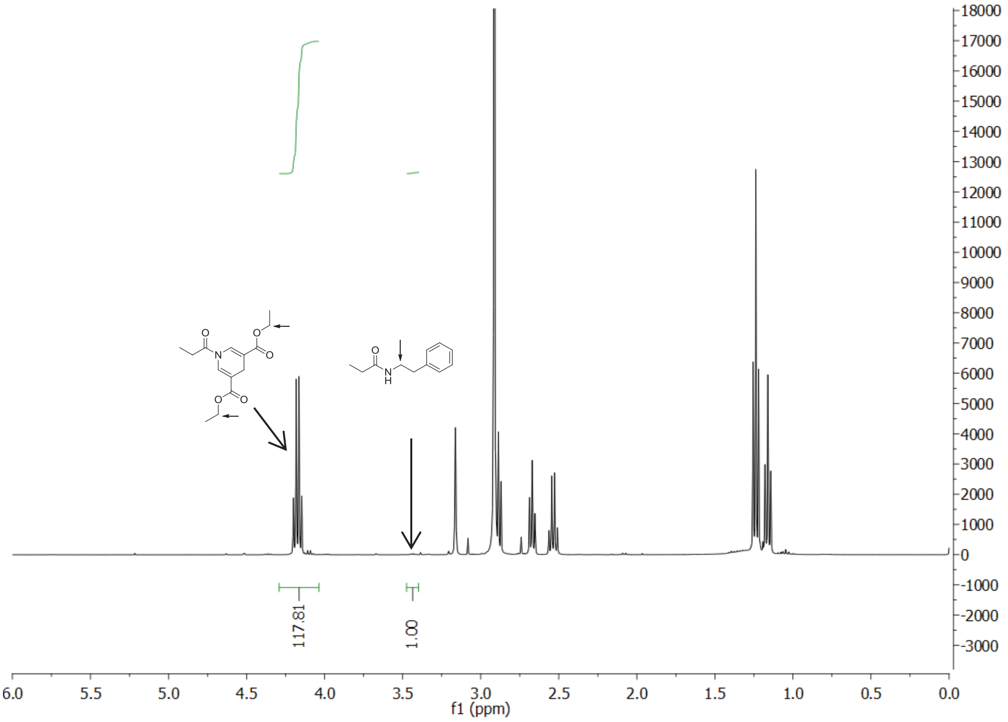
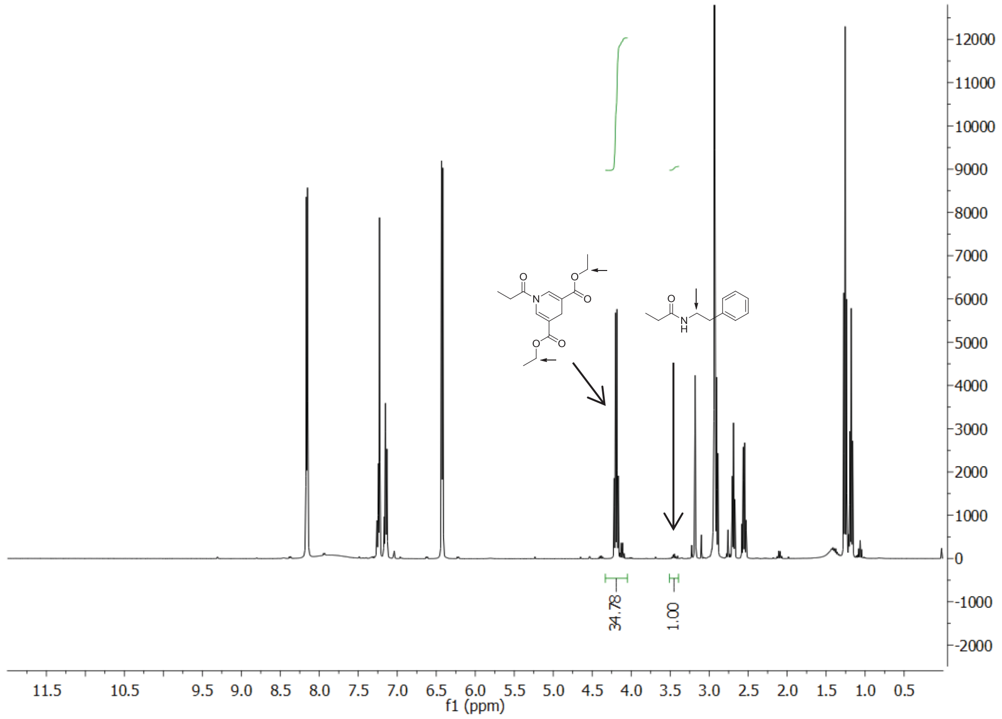


After 48 h at 40 ˚C < 6% product formation. (Propionyl DHP (1 eq.), phenylethyl amine (1 eq.), and DMAP (3 eq.) in $CDCl_3$).



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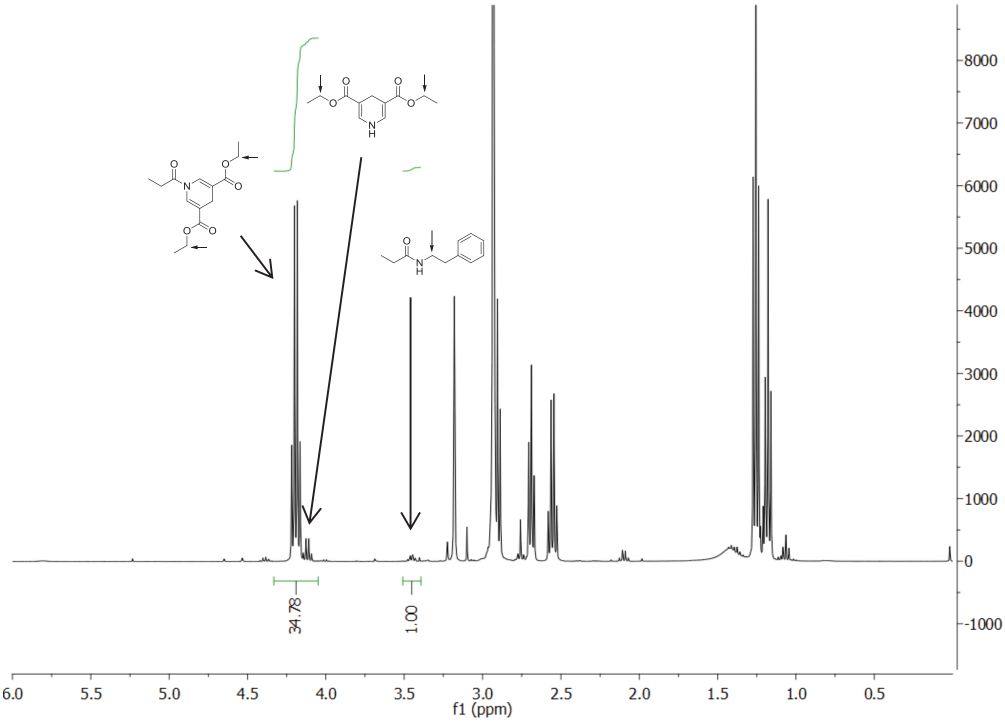

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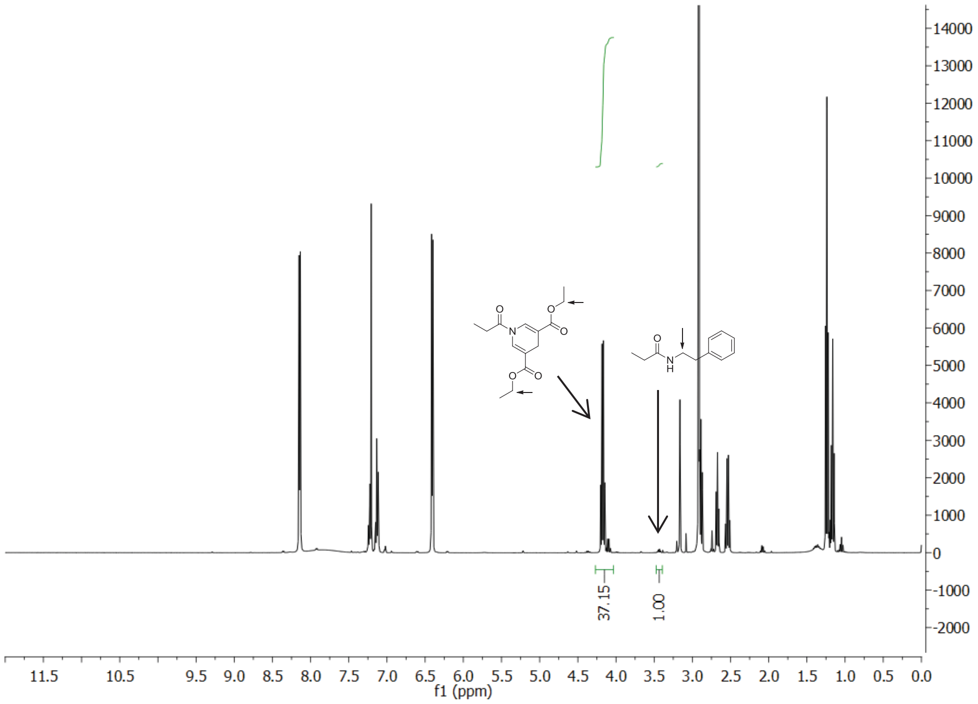

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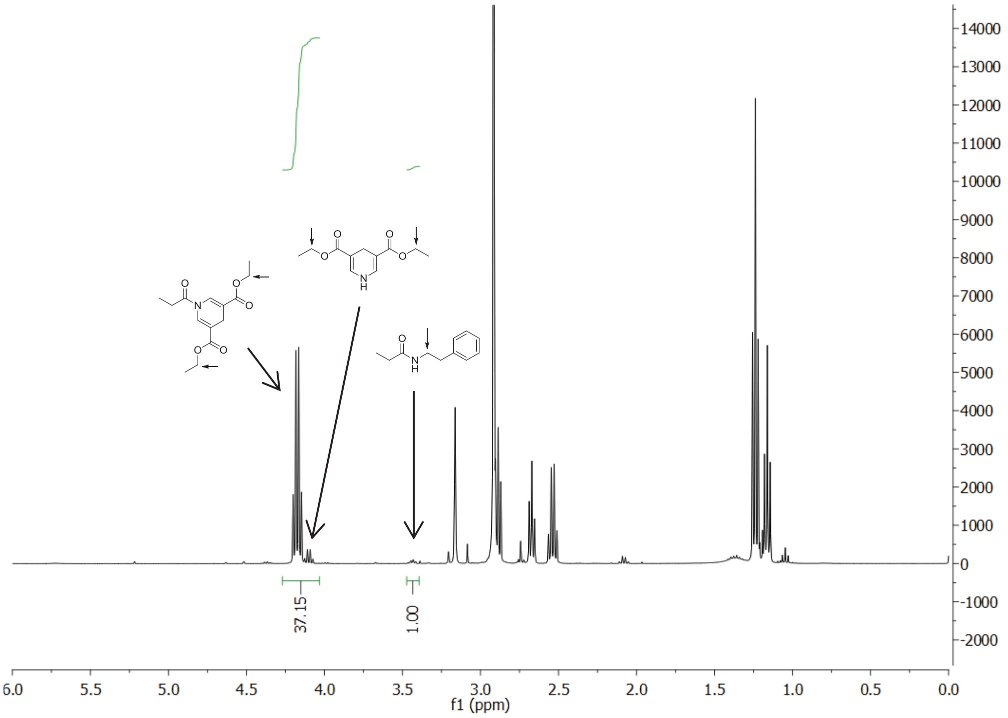
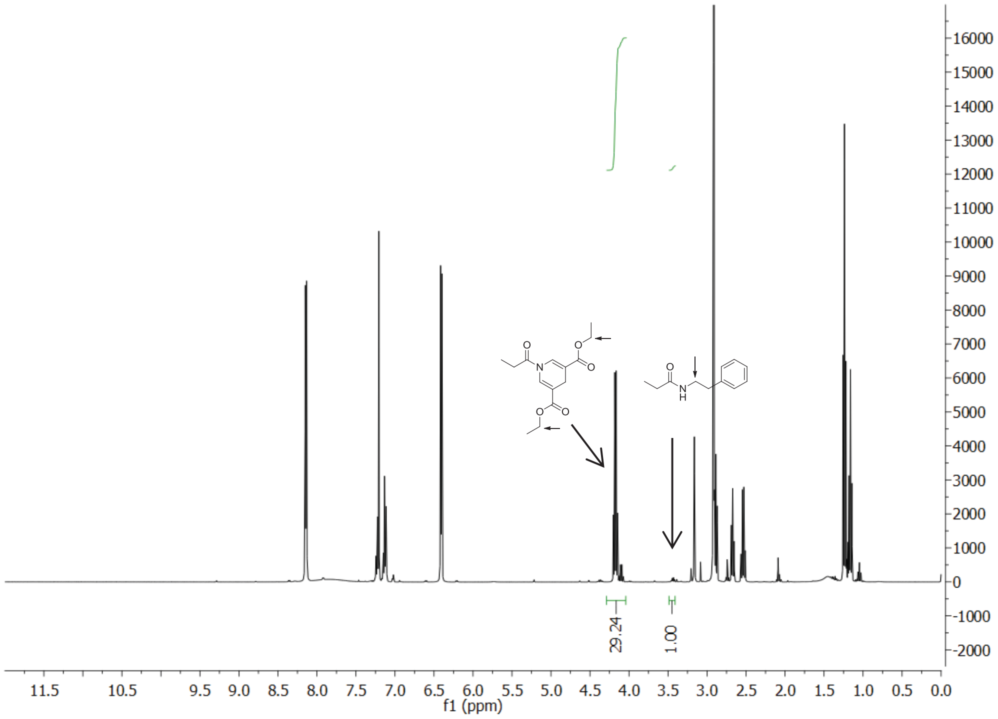


After 48 h at 60 ˚C < 7% product formation. (Propionyl DHP (1 eq.), phenylethyl amine (1 eq.), and DMAP (3 eq.) in CDCl$_3$).



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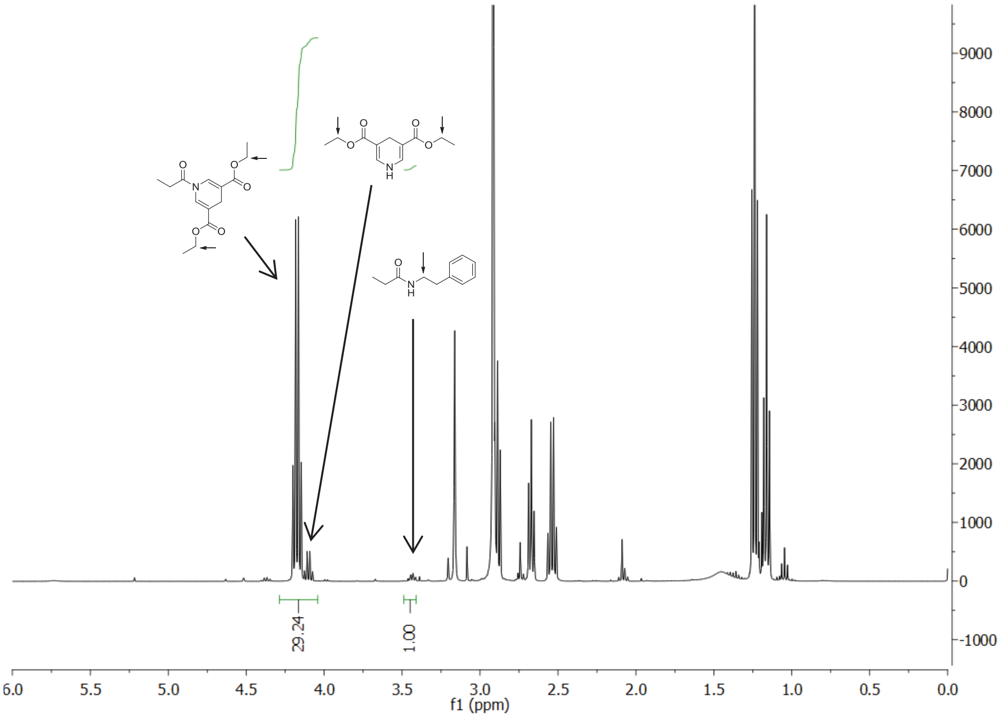

Stability of DHP amide 1 towards amide bond formation (DCM)

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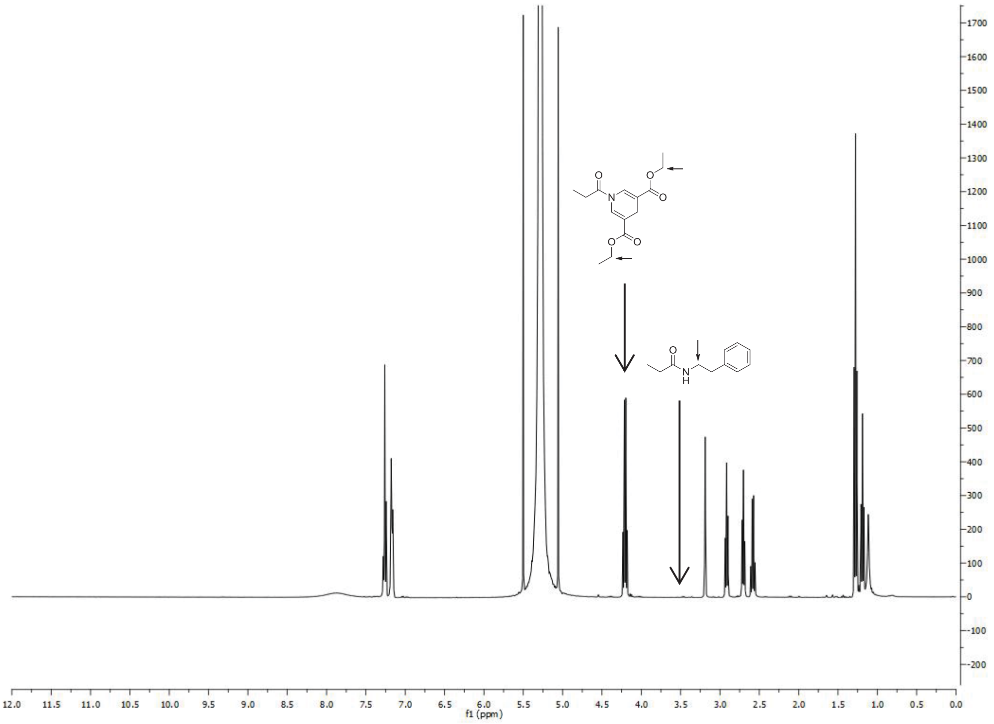
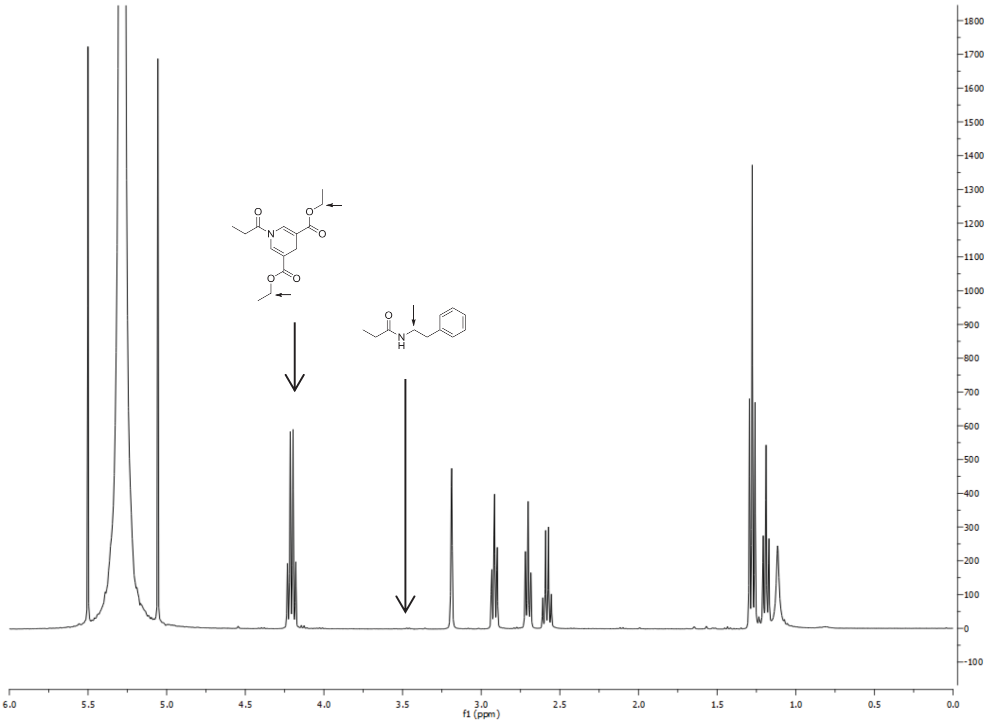


Zoom 0-6 ppm



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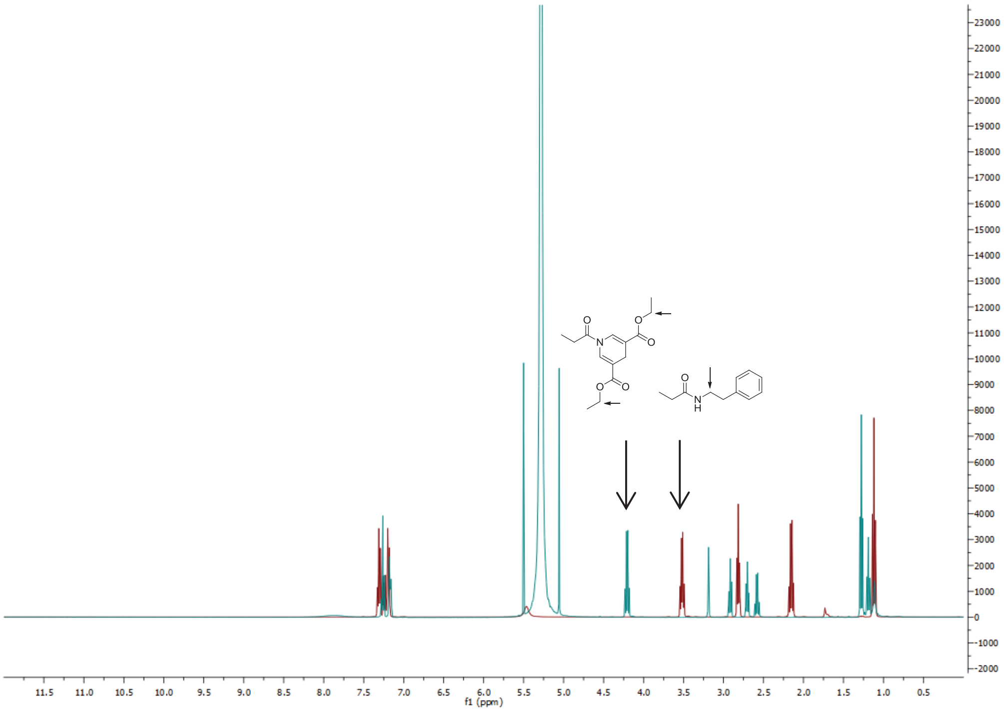
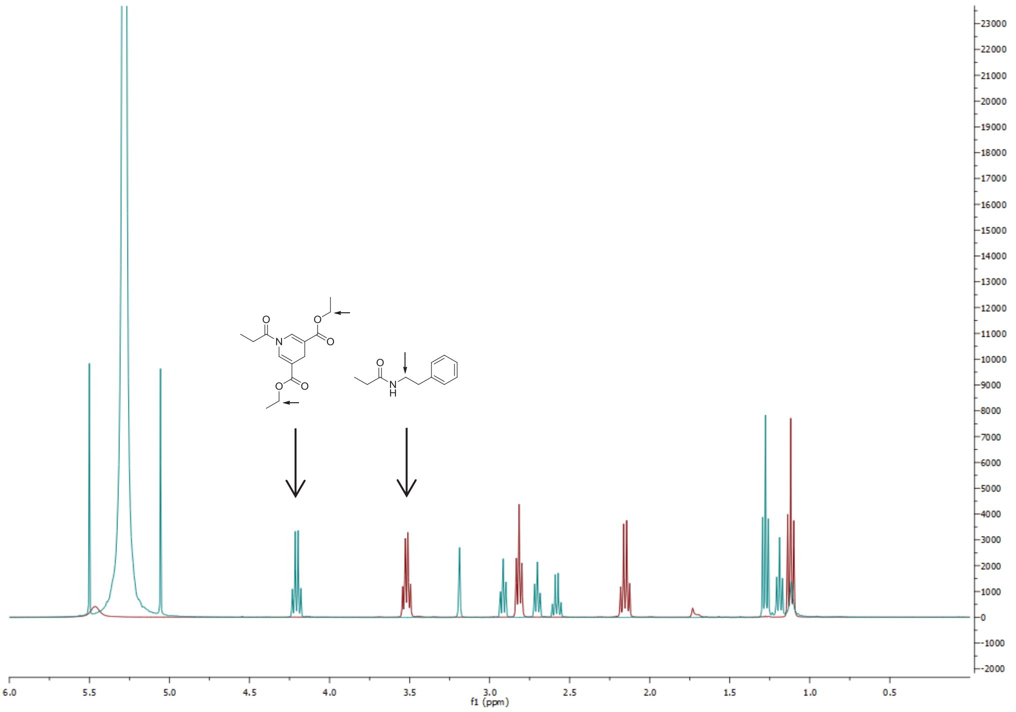


Zoomed overlay spectra with increased intensity of peaks in the crude mixture



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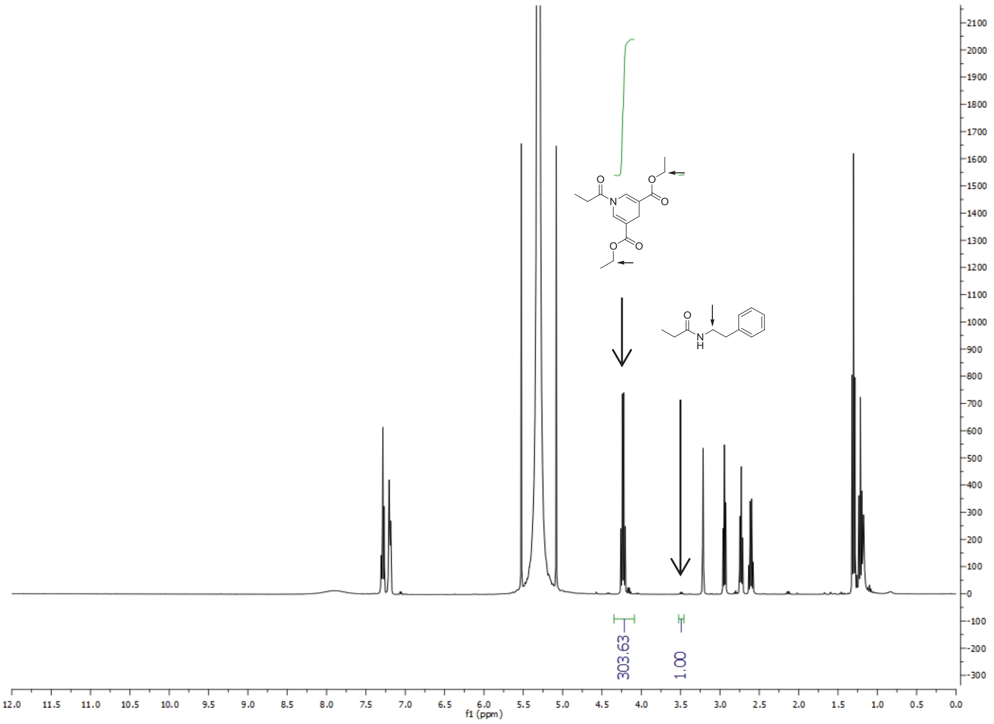

After 48 h < 1% product formation. (Propionyl DHP (1 eq.) and phenylethyl amine (1 eq.) in DCM).
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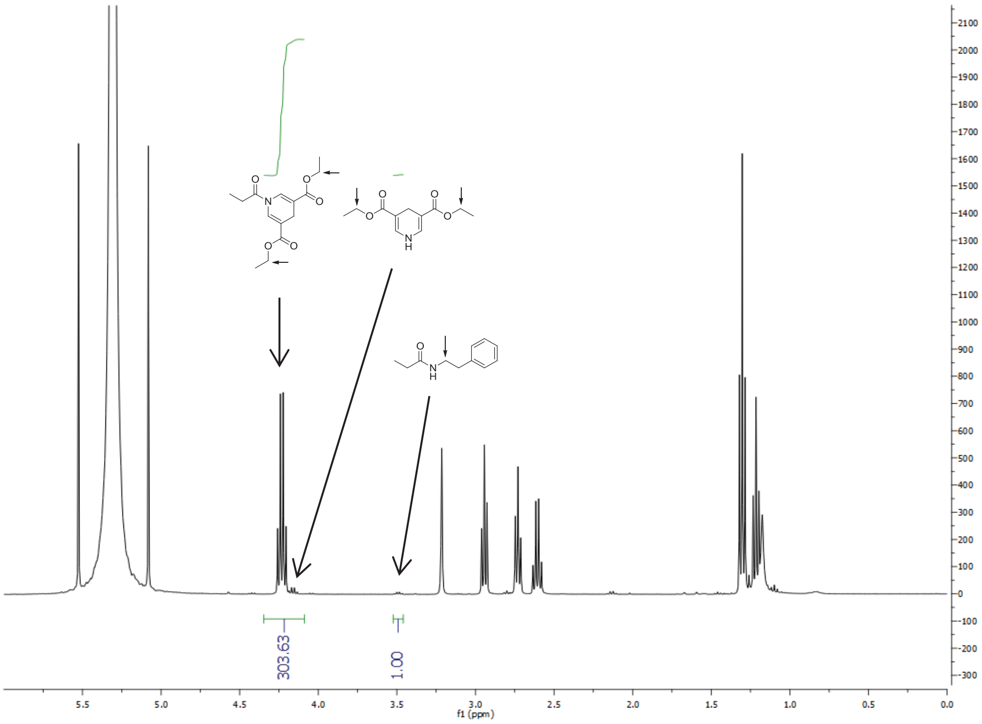

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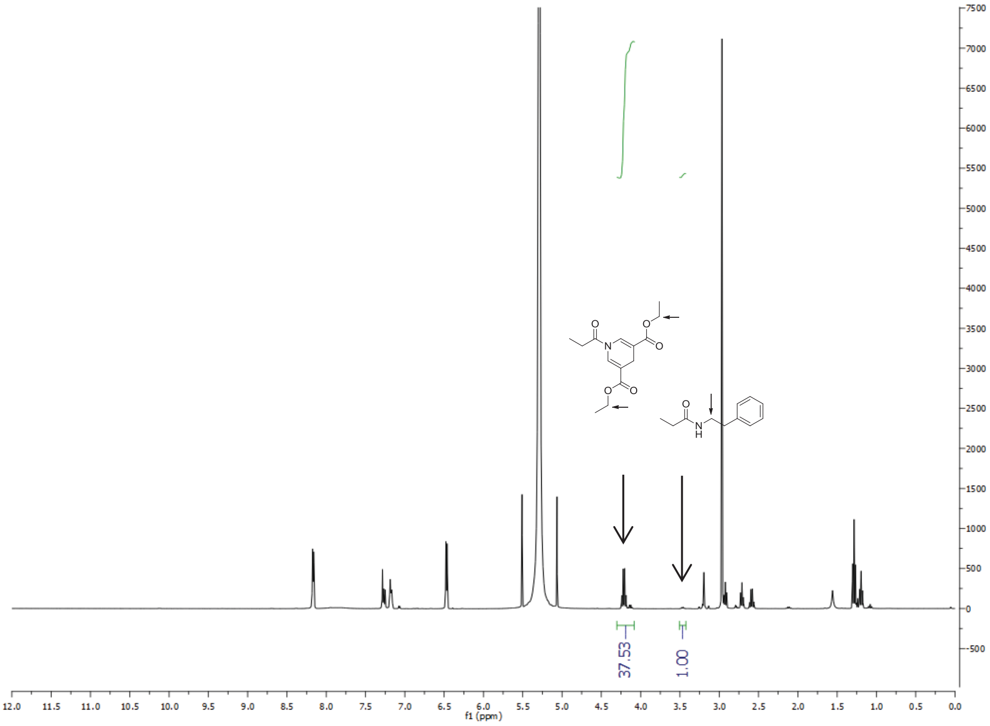
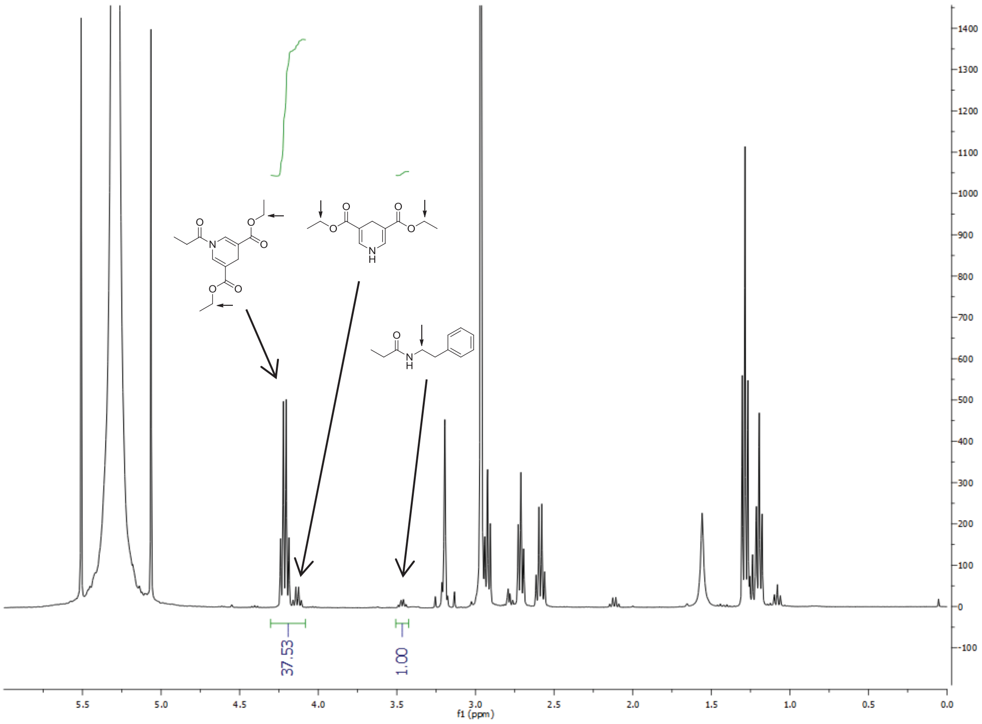
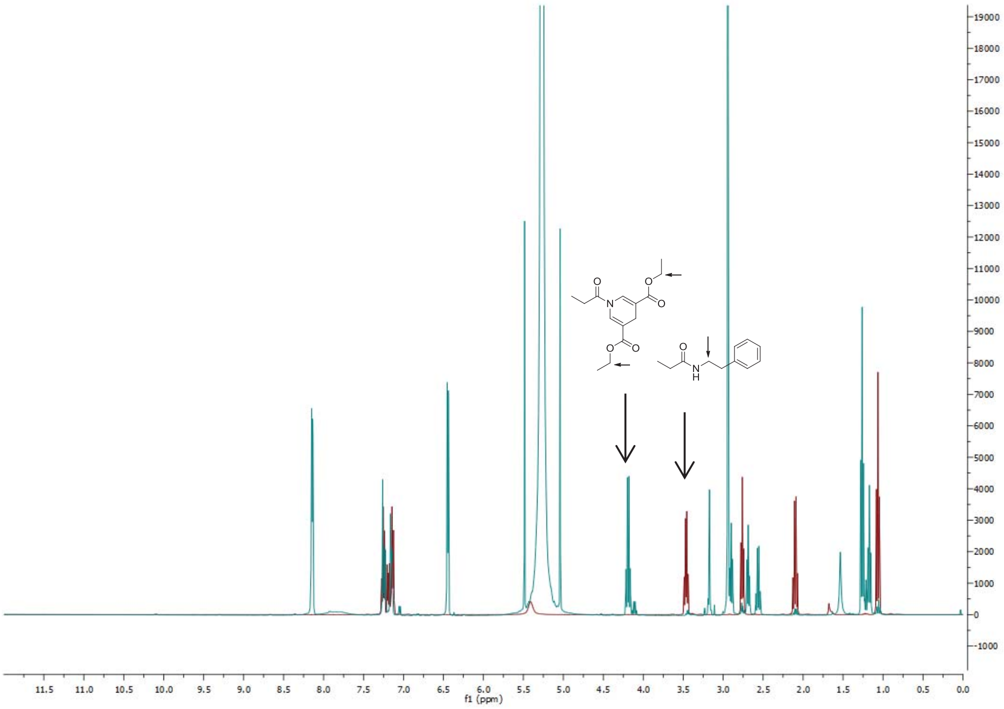


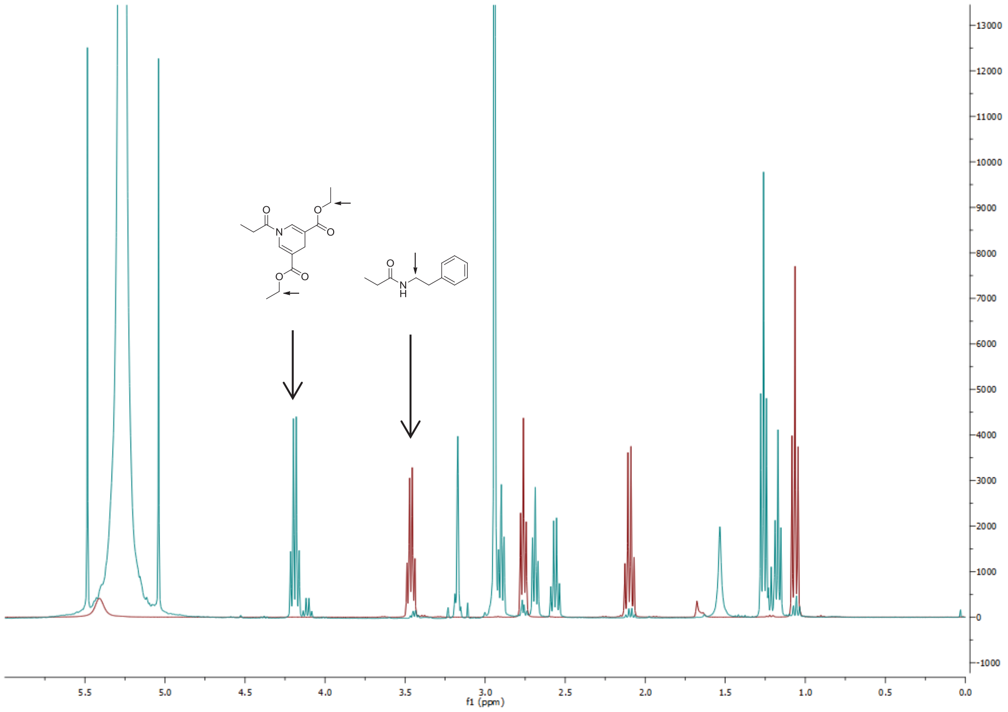
Zoom 0-6 ppm



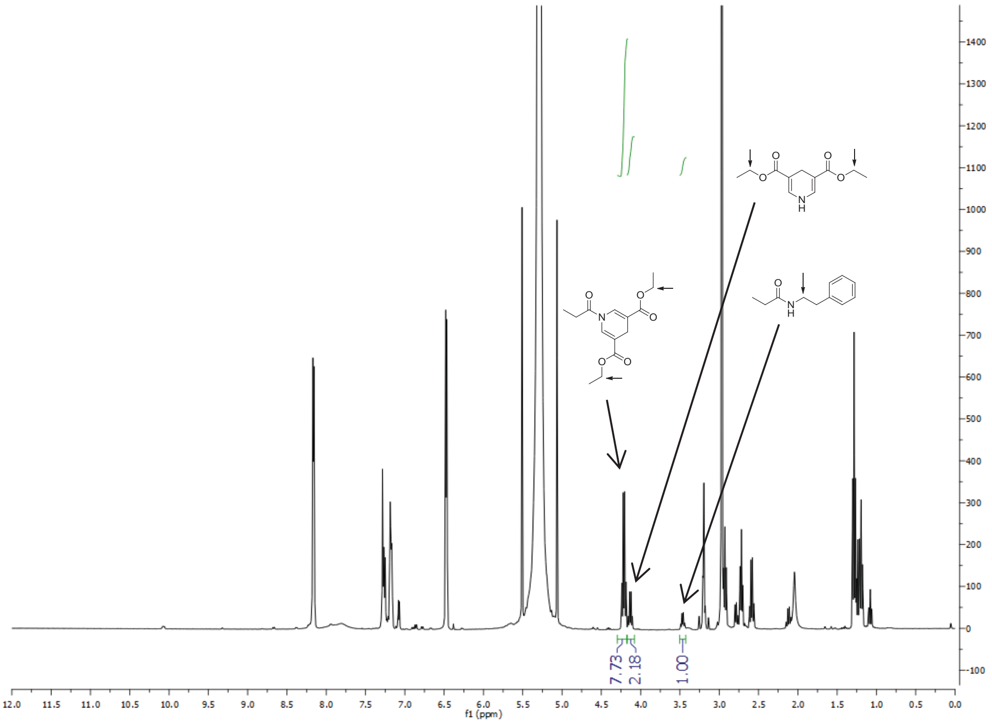
Overlay spectra. The crude mixture (shown in blue) with overlay of the reference product (shown in red)



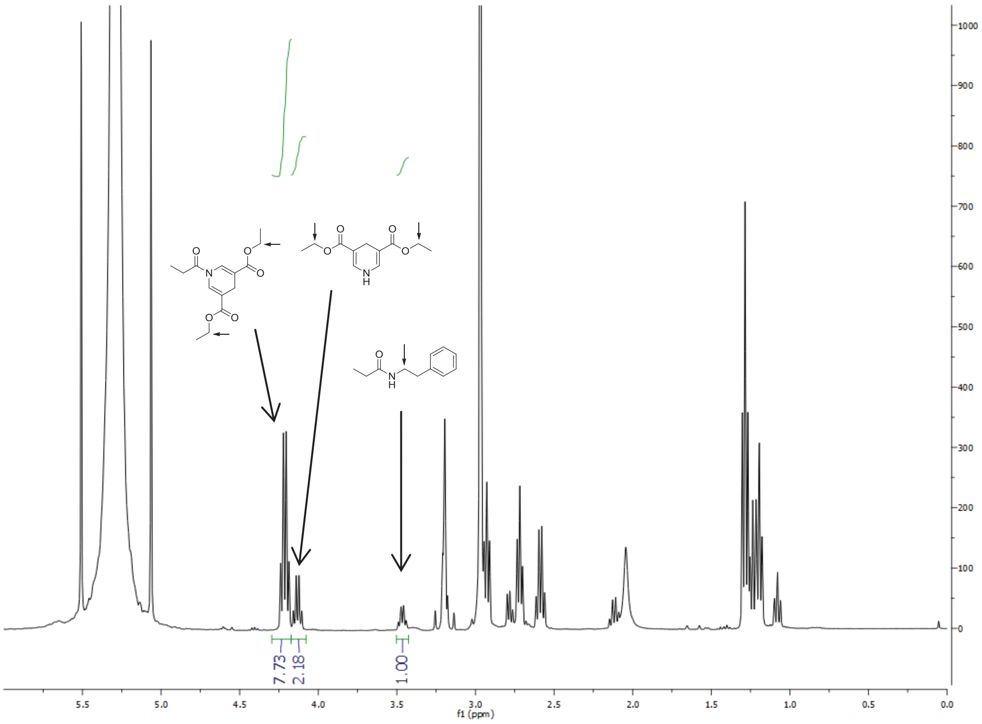
Zoomed overlay spectra with increased intensity of peaks in the crude mixture



After 48 h < 18% product formation. (Propionyl DHP (1 eq.), phenylethyl amine (1 eq.), and DMAP (3 eq.) in DCM)

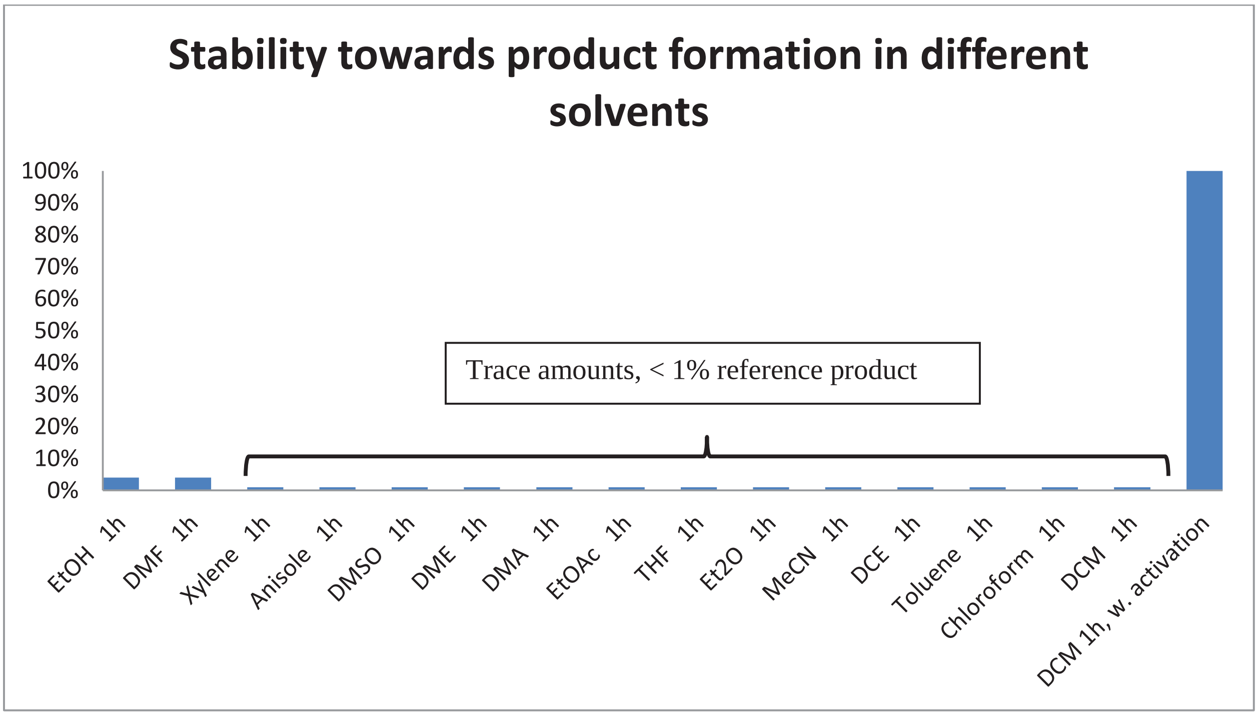


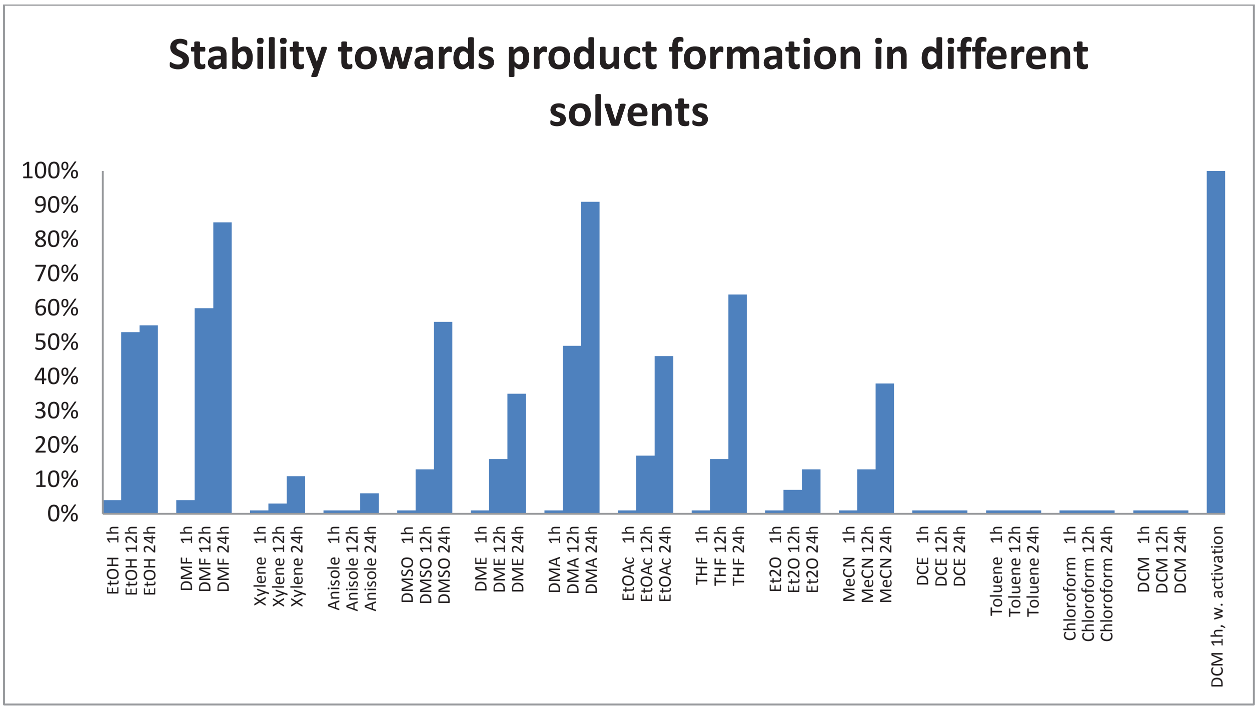
After 48 h < 18% product formation. (Propionyl DHP (1 eq.), phenylethyl amine (1 eq.), and DMAP (3 eq.) in DCM. Zoom 0-6 ppm



Stability of DHP amide 1 towards amide bond formation in various solvents

To a solution of propionyl DHP (10 mg) in the solvent specified (0.6 mL) was phenylethyl amine (71 µL, 1 eq.) from 0.5 M solution in the solvent specified, added. The solution was stirred in a 4 mL vial at rt. and the product formation was monitored by crude ^{1}H-NMR spectroscopy of the crude reaction mixture.



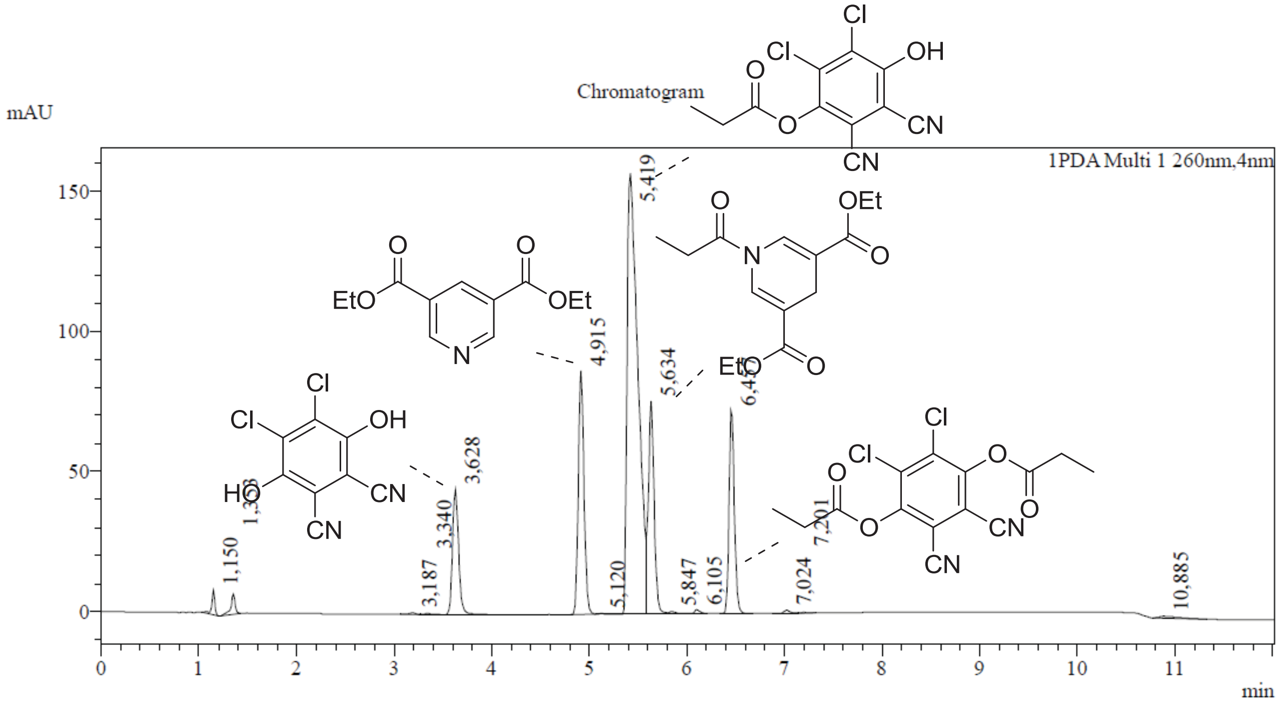

Stability towards product formation in different solvents

Investigation of reaction intermediates by LC-MS

Reaction conditions:

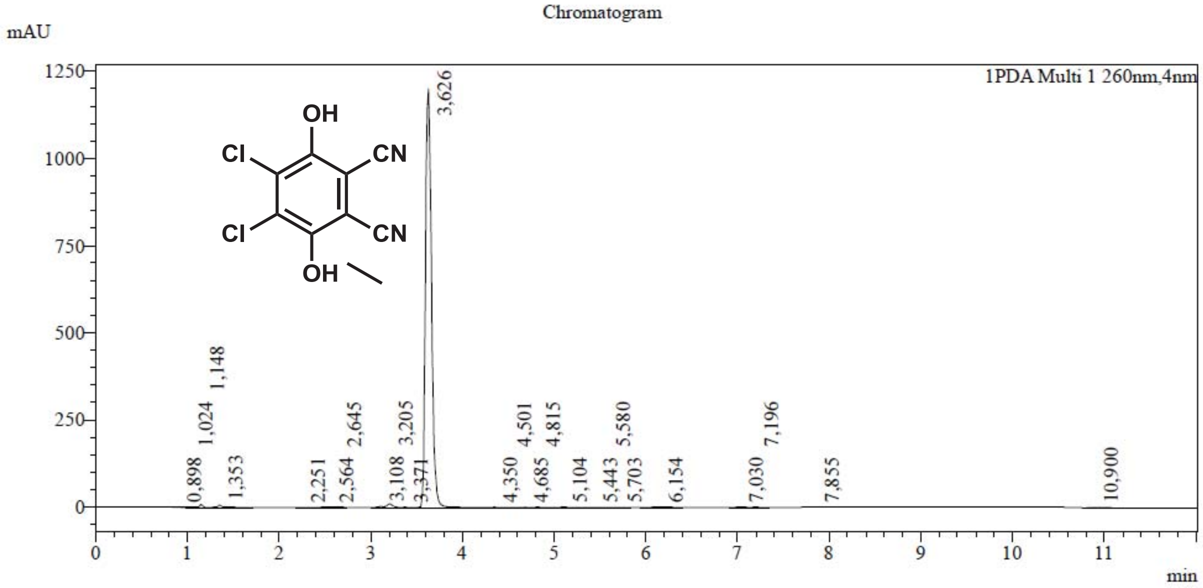
To a solution of DHP amide **1** (14 mg, 0.048 mmol, 1.1 eq.) in DCM (0.8 mL) was DDQ (10 mg, 0.044 mmol, 1 eq.) added. After 30 minutes the reaction was monitored by LC-MS. The peaks in the resulting LC chromatogram were then identified by doing separate LC chromatograms for the individual compounds. A small drift in retention time is in some cases observed.

The LC chromatogram obtained after 30 minutes of oxidation w. DDQ is the following:

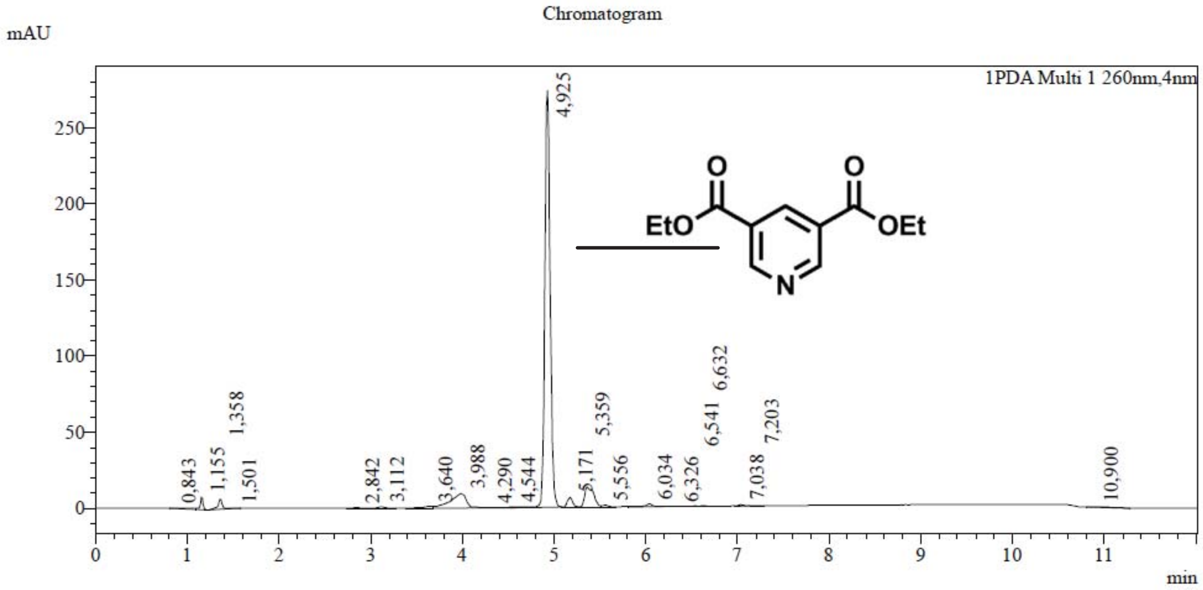


Individual LC chromatograms for the individual compounds proposed as reaction intermediates:

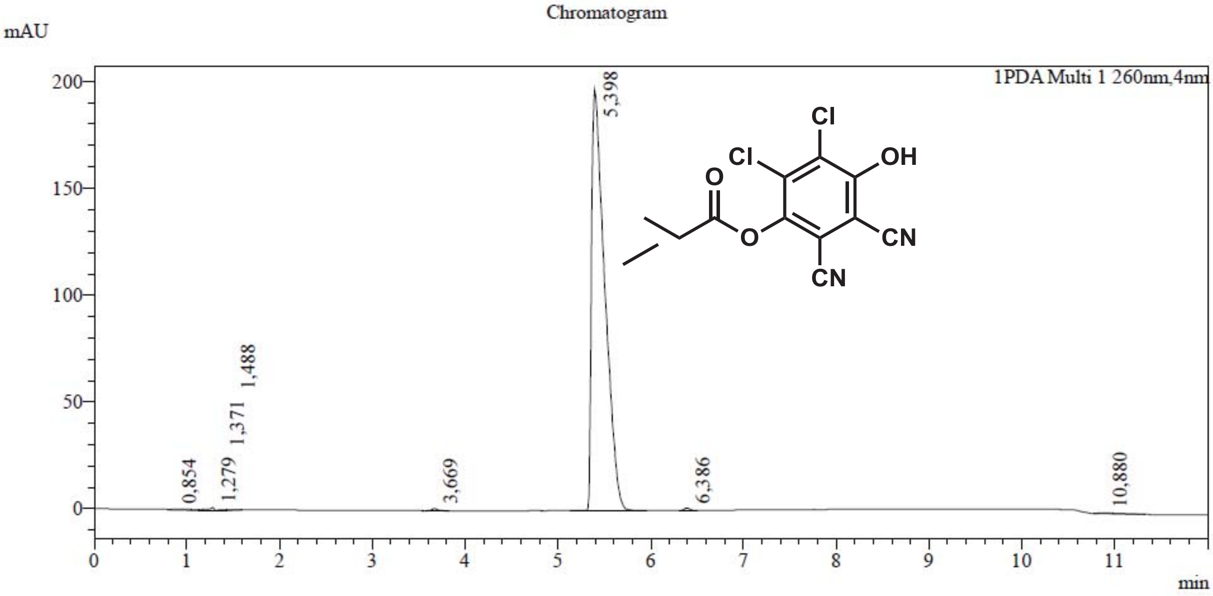
Reduced DDQ



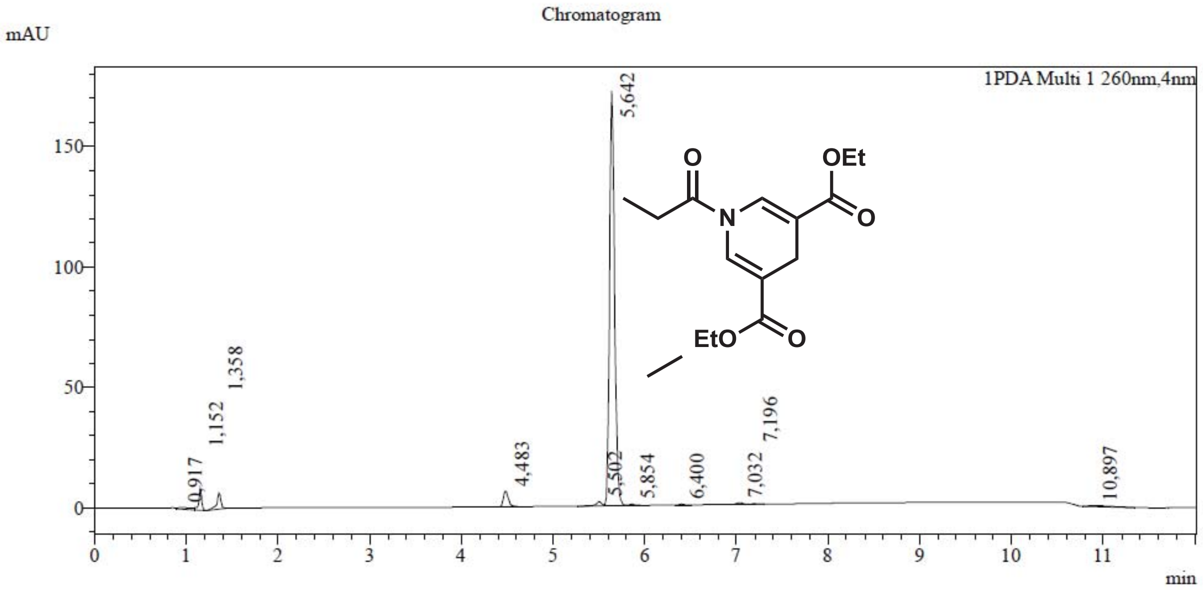
Di-ethyl pyridine ester 4



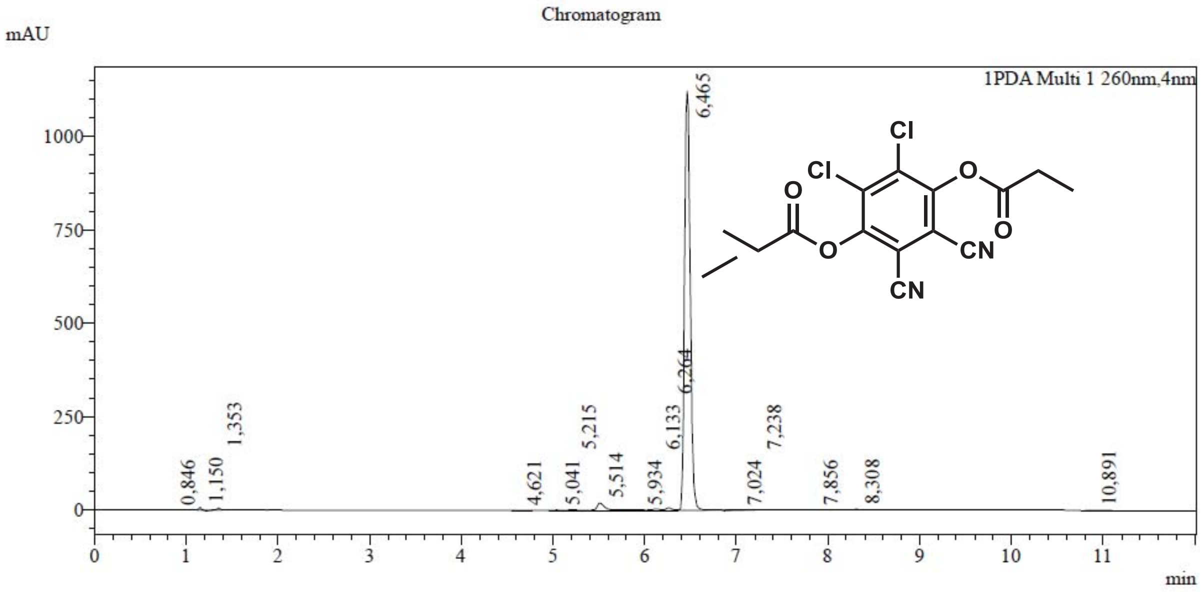
Mono ester of reduced DDQ



DHP amide 1

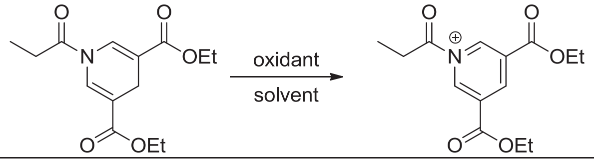

Chromatogram
mAU
1PDA Multi 1 260nm,4nm
150
100
50
0
0,917
1,152
1,358
4,483
5,502
5,642
5,854
6,400
7,032
7,196
10,897
0
1
2
3
4
5
6
7
8
9
10
11
min
O
OEt
N
O
EtO
O

Di ester of reduced DDQ



Optimization of DDP (1) oxidation

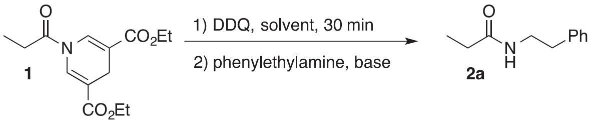
Optimization of reaction conditions for the oxidation of DDP amide **1**.[a]



Entry[a]	Oxidant	Solvent	Temp (°C)	Time (h)	Conversion (%)
1	$Cu(NO_3)_2$	$CDCl_3$	rt	5	-
2	$CuCl_2$	$CDCl_3$	rt	5	-
3	$Cu(OAc)_2$	$CDCl_3$	rt	5	-
4	CuI	$CDCl_3$	rt	2	-
5	TBAI	$CDCl_3$	rt	2	-
6	NIS	$CDCl_3$	rt	2	51
7	ICl	$CDCl_3$	rt	1.5	51
8	ZnI_2	$CDCl_3$	rt	11	64
9	ZnI_2	MeCN	rt	2	11
10	ZnI_2[b]	$CDCl_3$	rt	2	78
11	ZnI_2 NaIO4[c]	$CDCl_3$	rt	2	88
12	$ZnBr_2$	$CDCl_3$	rt	2	-
13	$ZnCl_2$	$CDCl_3$	rt	2	-
14	$ZnSO_4$	$CDCl_3$	rt	2	-
15	Silica[d]	$CDCl_3$	rt	11	5
16	DDQ	$CDCl_3$	rt	0.33	99
17	TPAP, NMO	$CDCl_3$	rt	5	-
18	MnO_2	$CDCl_3$	rt	5	-
19	CAN	$CDCl_3$	rt	5	7
20	CAN	MeCN	rt	2	42
21	TetrafluoroQ	$CDCl_3$	rt	2	2
22	Chloranil	$CDCl_3$	rt	11	-
23	O_2 (balloon)	$CDCl_3$	rt	24	<5
24	NAD^+	$CDCl_3$	rt	48	10

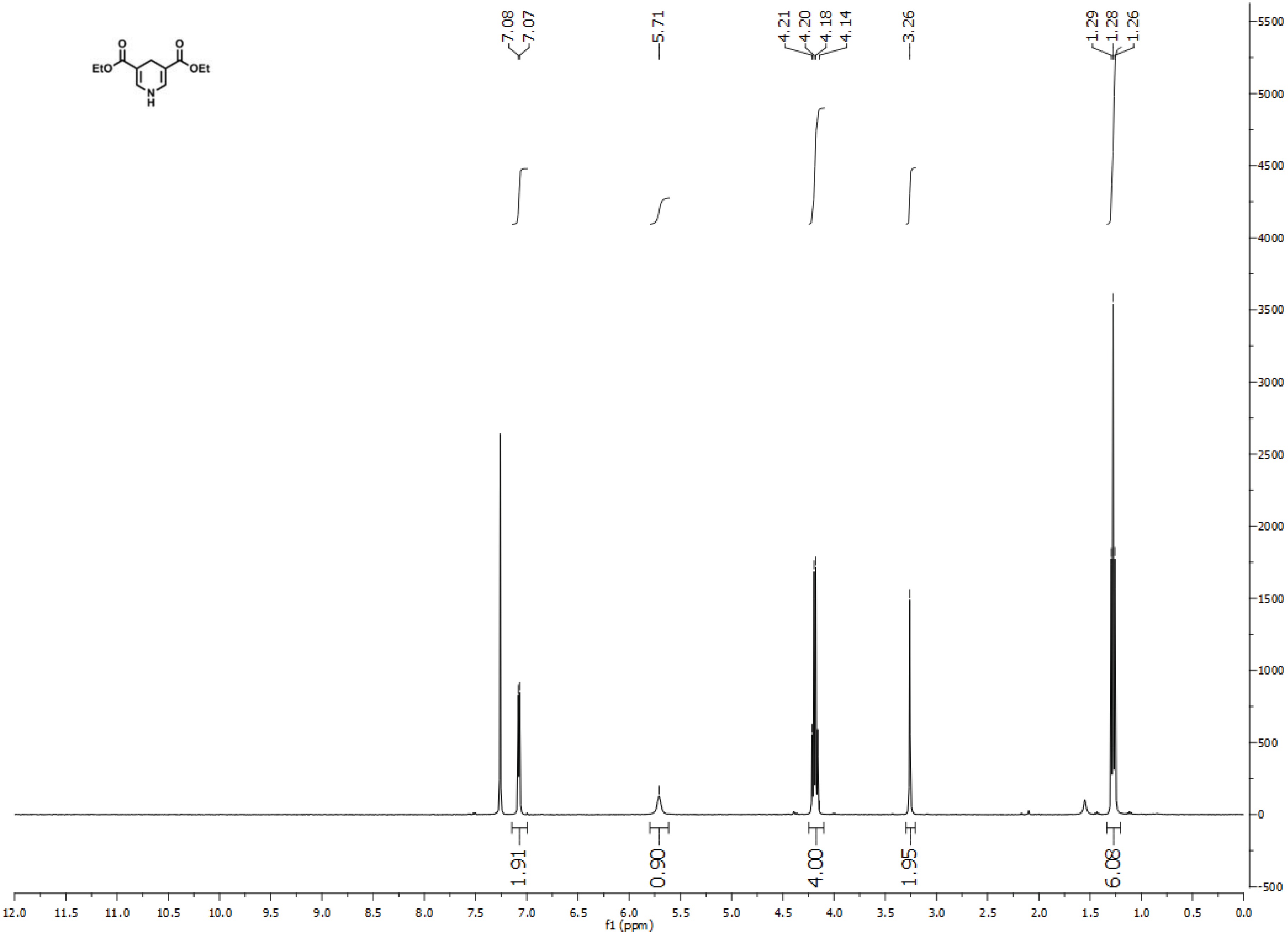
[a] Reaction conditions: **1** (0.040 mmol), oxidant (0.040 mmol) were stirred in 0.6 mL of solvent in a sealed vial. [b] Reaction was performed with 3 eq. oxidant. [c] Reaction was performed with 1 and 2 eq. oxidant. [d] Reaction was performed with 20 mg silica [e] Conversions were determined by ^1H NMR spectroscopy based on **1**.

Optimization of reaction conditions for the oxidation of 1 and subsequent reaction with phenylethylamine[a]



Entry	Base	Amine (eq.)	Solvent	Time (h)	Conversion (%)
1	-	3	$CDCl_3$	17	72
2	DIPEA	3	$CDCl_3$	2	47
3	2,6-Lutidine	3	$CDCl_3$	2	65
4	Pyridine	3	$CDCl_3$	2	75
5	K_2CO_3	3	$CDCl_3$	2	77
6	Cs_2CO_3	3	$CDCl_3$	2	100 (50)
7	DMAP	3	$CDCl_3$	1	100 (86)
8	DMAP	3	DCM	1	100 (87)
9	DMAP	3	EtOAc	26	(44)
10	DMAP	3	Dioxane	26	(65)
11	DMAP (0.2 eq.)	3	DCM	4	(84)
12	DMAP (1 eq.)	3	DCM	1.5	(94)
13	DMAP (1 eq.)	1	DCM	6	(83)
14	DMAP (3 eq.)	1.1	DCM	1	(90)

[a] Reaction conditions for entry 1-10: **1** (0.036 mmol) and DDQ (0.036 mmol) were stirred in 0.6 mL of solvent in a sealed vial (all reactions with isolated yields were performed on 0.18 mmol scale using 3.0 mL of solvent). After 30 minutes phenylethylamine (0.11 mmol) and base (0.11 mmol) were added. Reaction conditions for entry 11-14: **1** (0.18 mmol) and DDQ (0.18 mmol) were stirred in 3 mL DCM in a sealed vial (entry 14 was perfomed with DDQ (1 eq.) and **1** (1.1 eq.). After 30 minutes phenylethylamine and base were added according to the table. [b] Conversions were determined by ^1H NMR spectroscopy based on **1**. Isolated yields are reported in paranthesis.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OEt
O
O
N
H
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7.07
5.71
4.21
4.20
4.18
4.14
3.26
1.29
1.28
1.26
1.91
0.90
4.00
1.95
6.08
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.5
3.0
2.5
2.0
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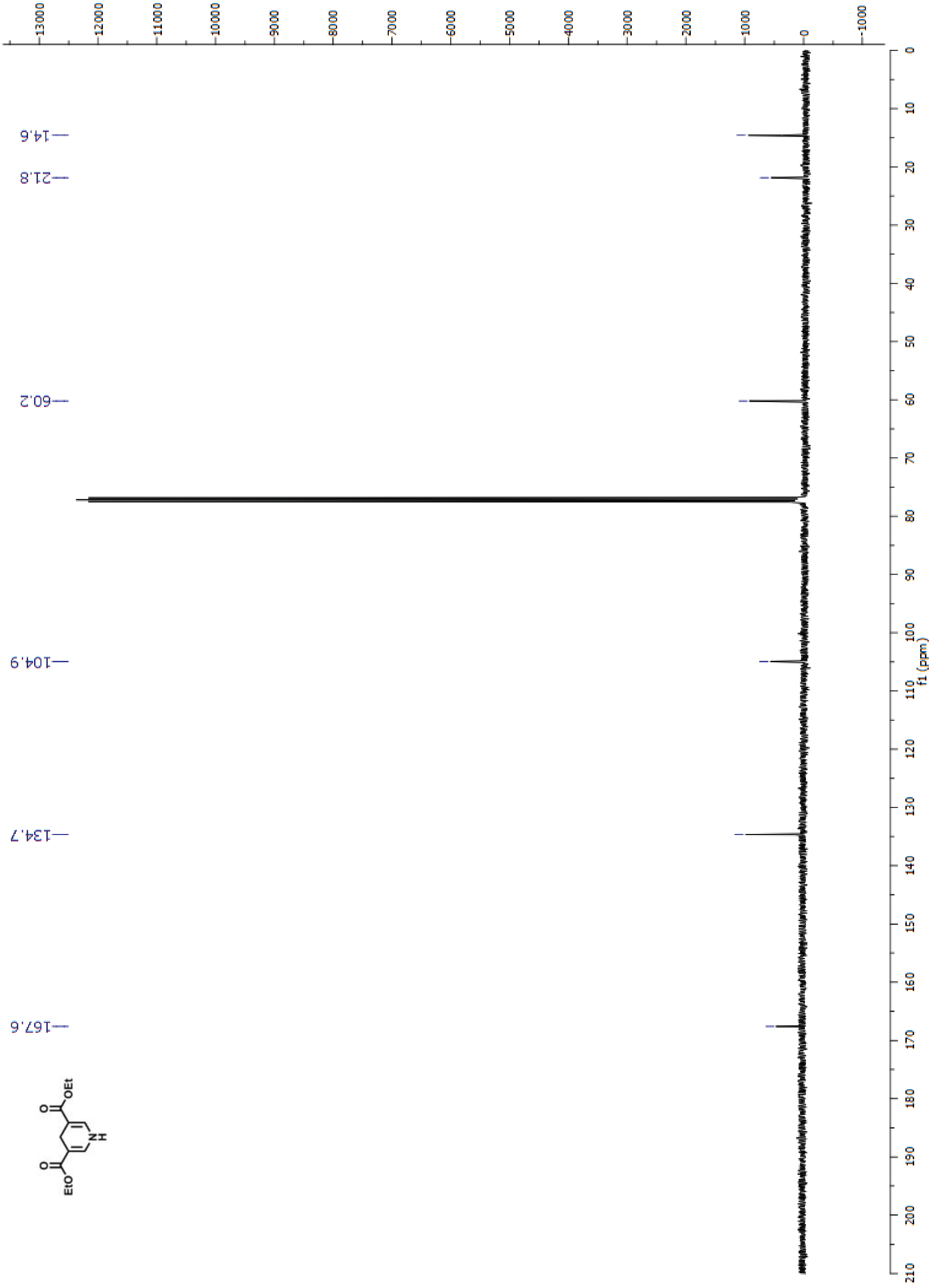
f1 (ppm)



14.6
21.8
60.2
104.9
134.7
167.6
EtO
OEt
O
O
N
H
f1 (ppm)
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10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
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0
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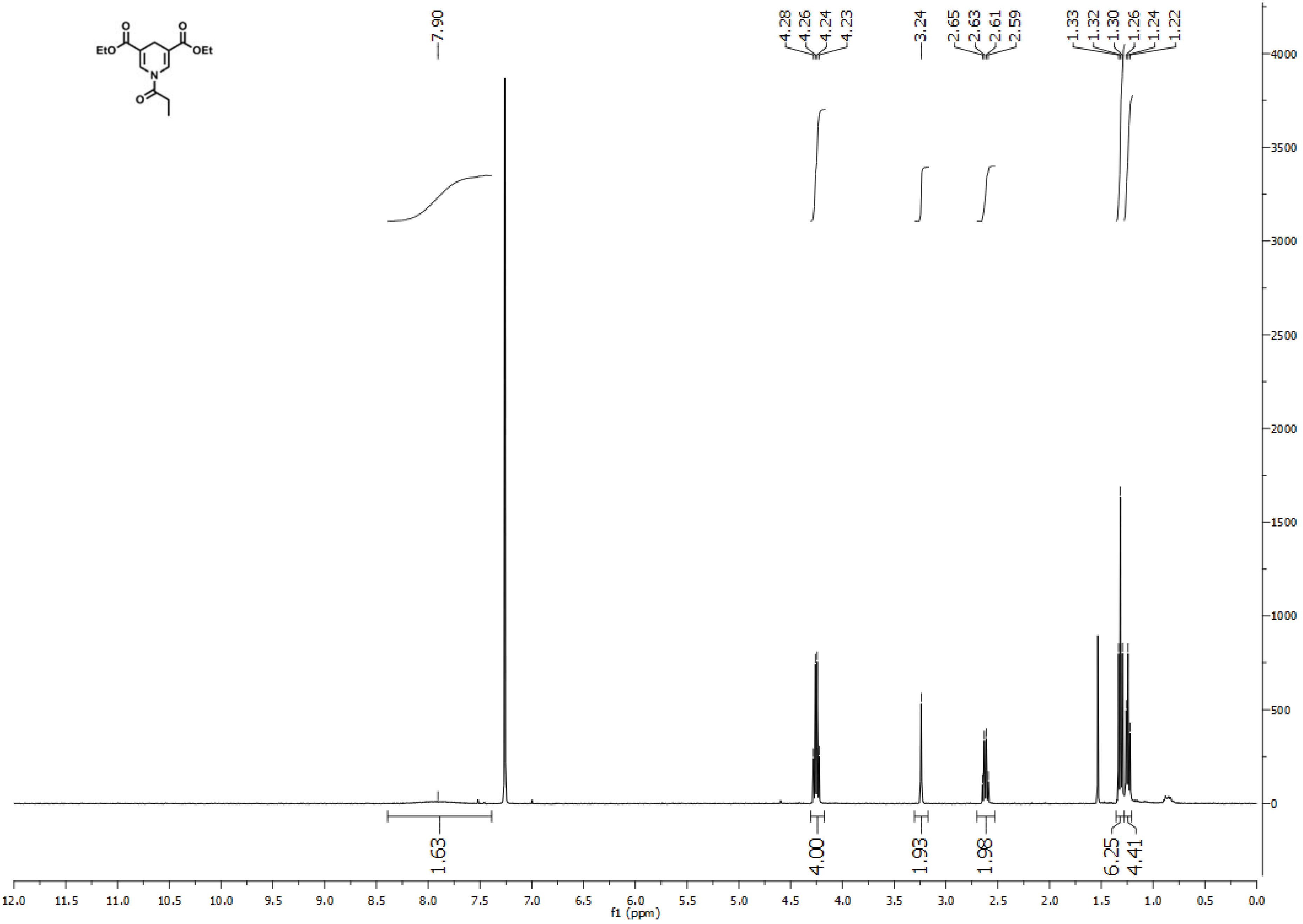
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OEt
O
O
N
O
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4.26
4.24
4.23
—3.24
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2.61
2.59
1.33
1.32
1.30
1.26
1.24
1.22
1.63
4.00
1.93
1.98
6.25
4.41
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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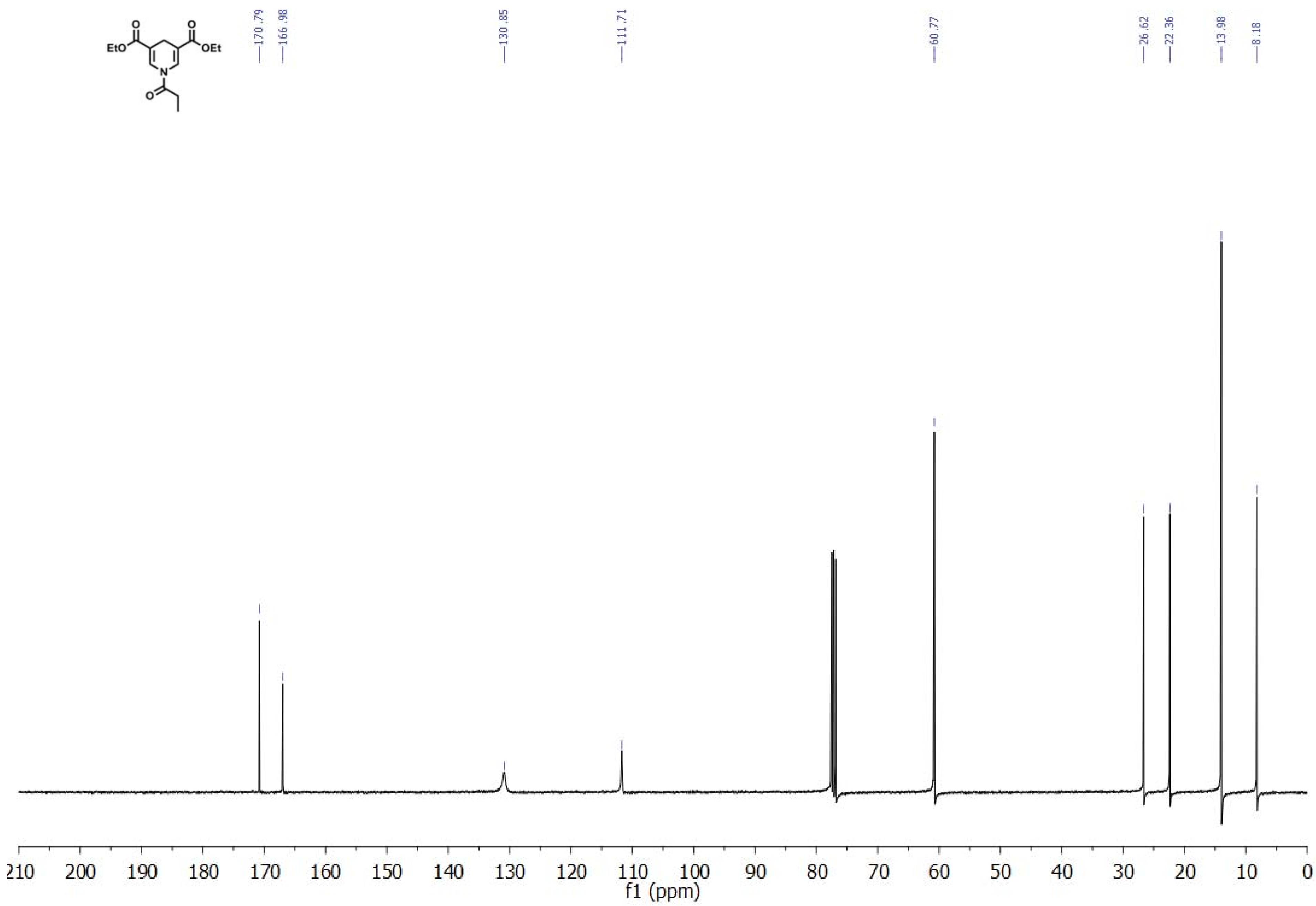
3000
2500
2000
1500
1000
500
0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O
OEt
N
O
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111.71
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26.62
22.36
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210
200
190
180
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50
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10
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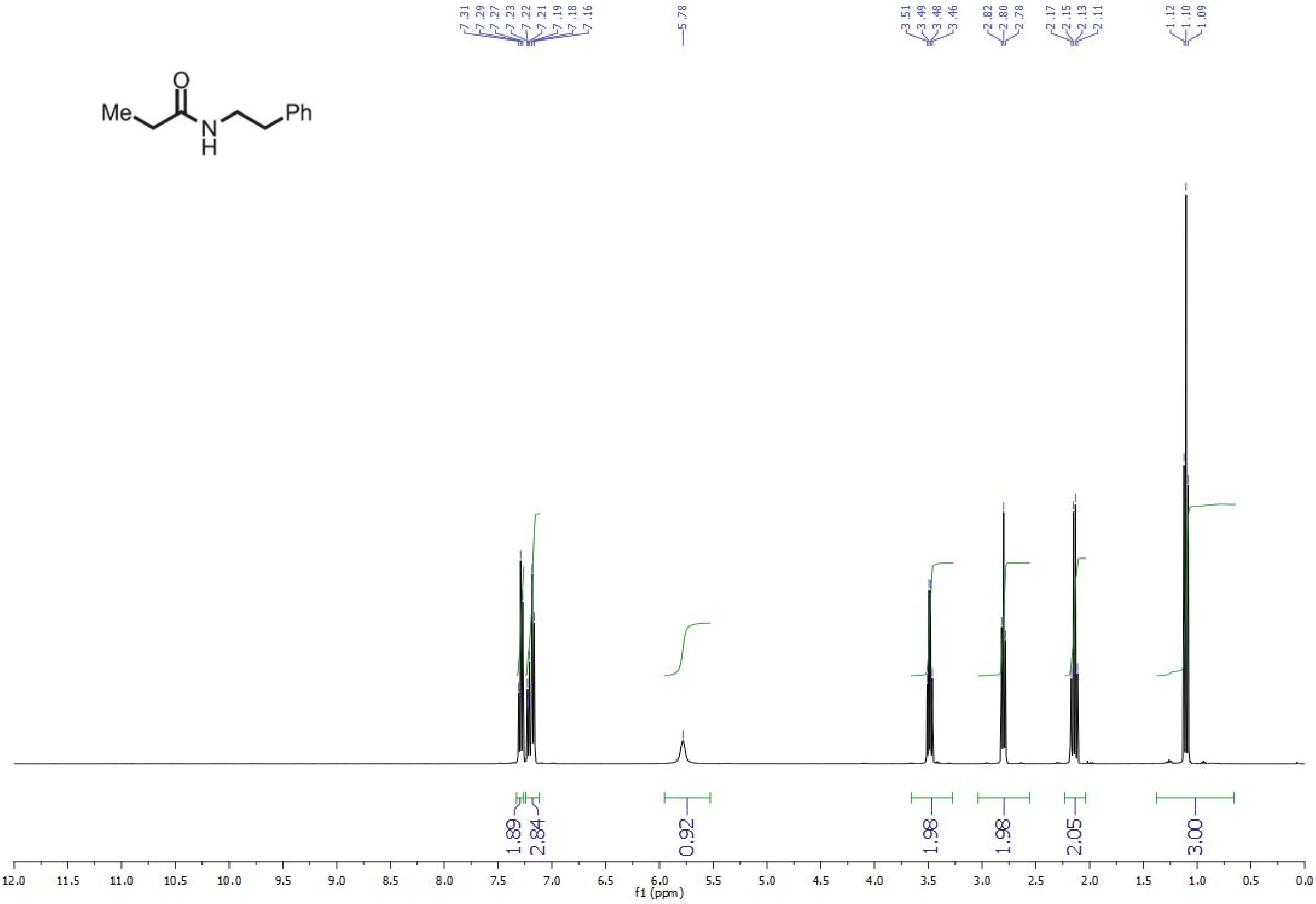
f1 (ppm)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7.19
7.18
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3.49
3.48
3.46
2.82
2.80
2.78
2.17
2.15
2.13
2.11
1.12
1.10
1.09
Me
O
N
H
Ph
1.89
2.84
0.92
1.98
1.98
2.05
3.00
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.0
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2.0
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1.0
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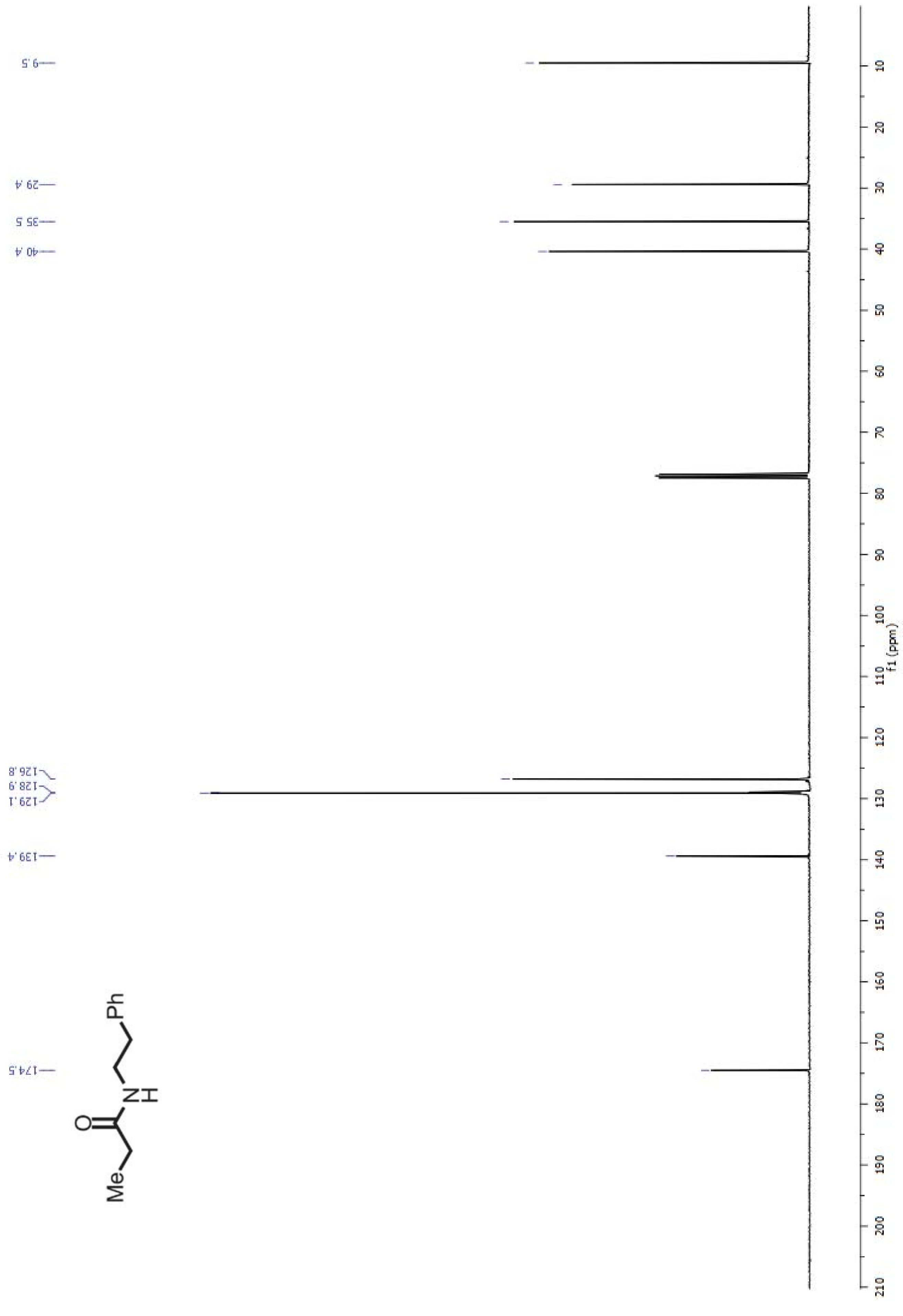
f1 (ppm)


9.5
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35.5
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128.9
129.1
139.4
174.5
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O
N
H
Ph
10
20
30
40
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60
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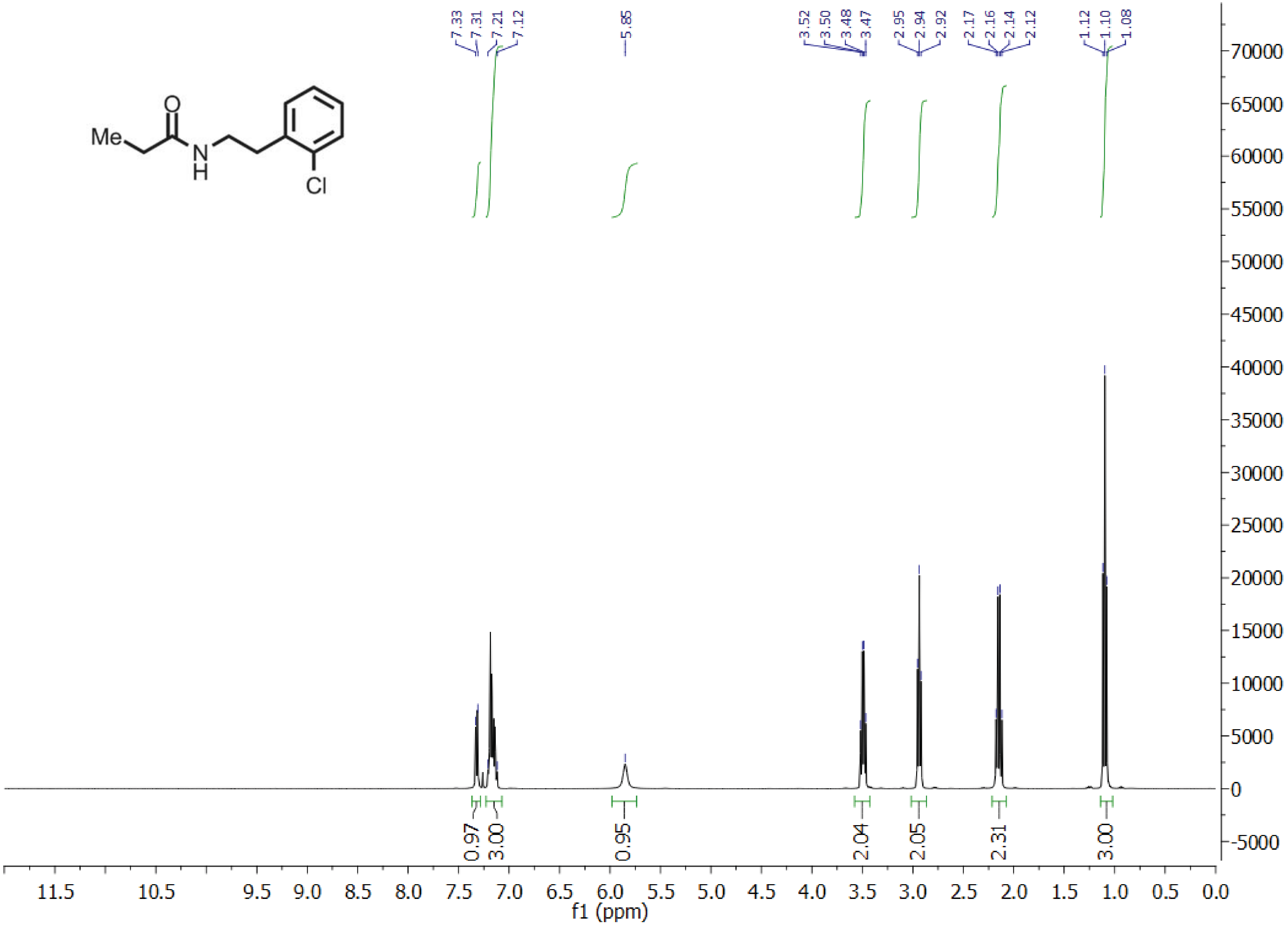
80
90
100
110
120
130
140
150
160
170
180
190
200
210
f1 (ppm)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N
H
Cl
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3.50
3.48
3.47
2.95
2.94
2.92
2.17
2.16
2.14
2.12
1.12
1.10
1.08
0.97
3.00
0.95
2.04
2.05
2.31
3.00
70000
65000
60000
55000
50000
45000
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30000
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20000
15000
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5000
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9.0
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7.0
6.5
6.0
5.5
5.0
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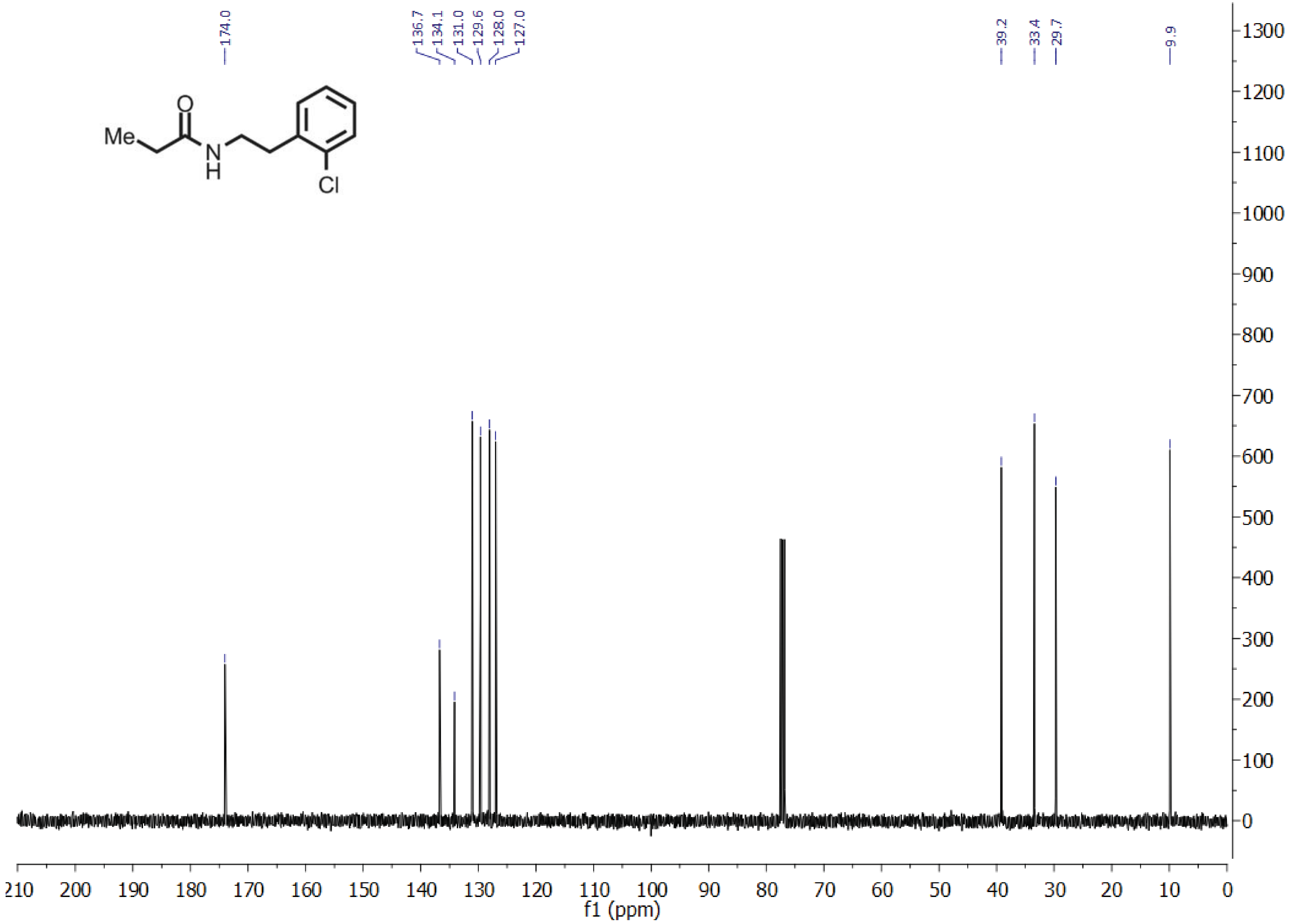
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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134.1
131.0
129.6
128.0
127.0
39.2
33.4
29.7
9.9
Me
O
N
H
Cl
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
210
200
190
180
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150
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130
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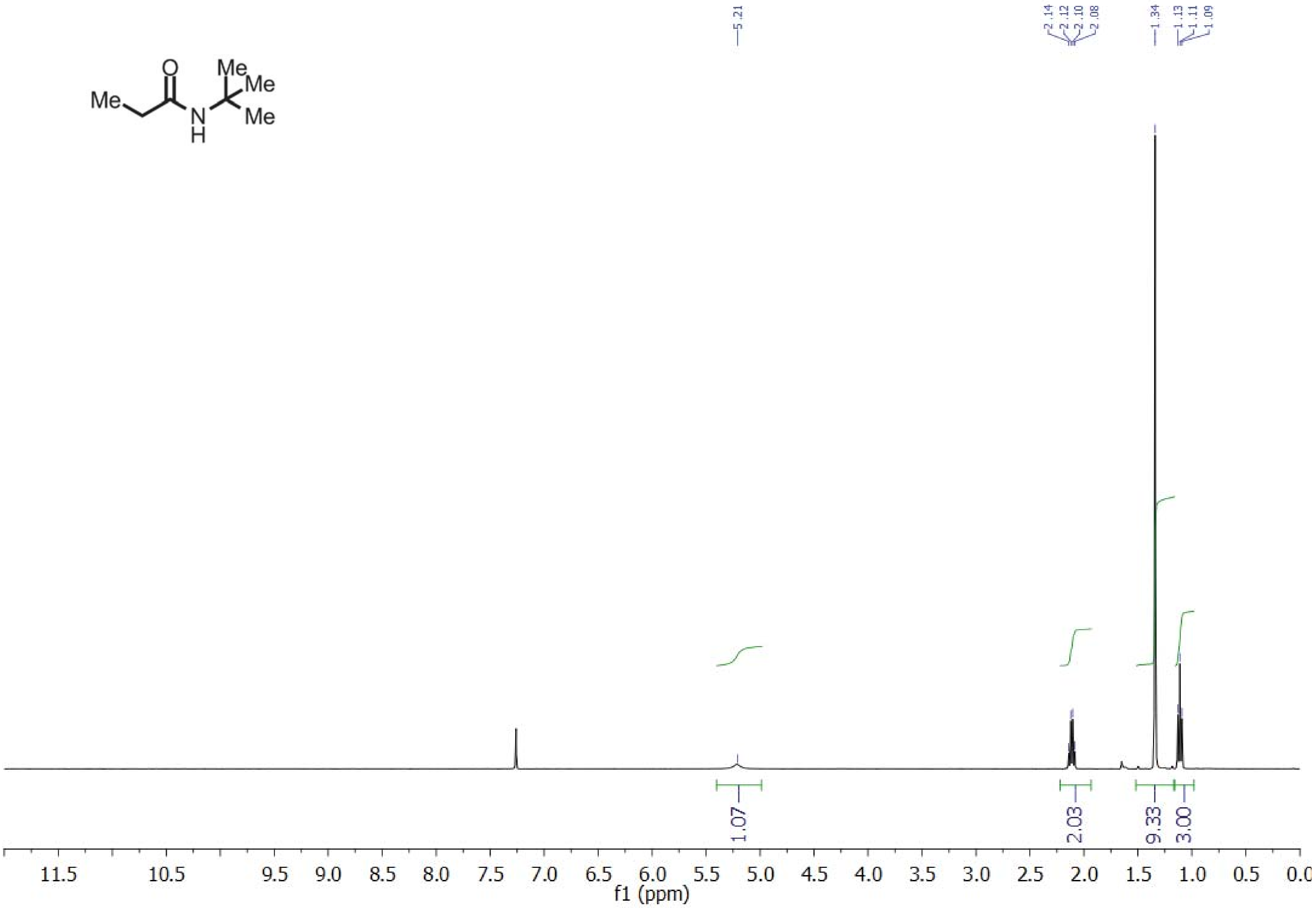
50
40
30
20
10
0
f1 (ppm)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H
Me
Me
Me
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1.34
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1.11
1.09
1.07
2.03
9.33
3.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.5
3.0
2.5
2.0
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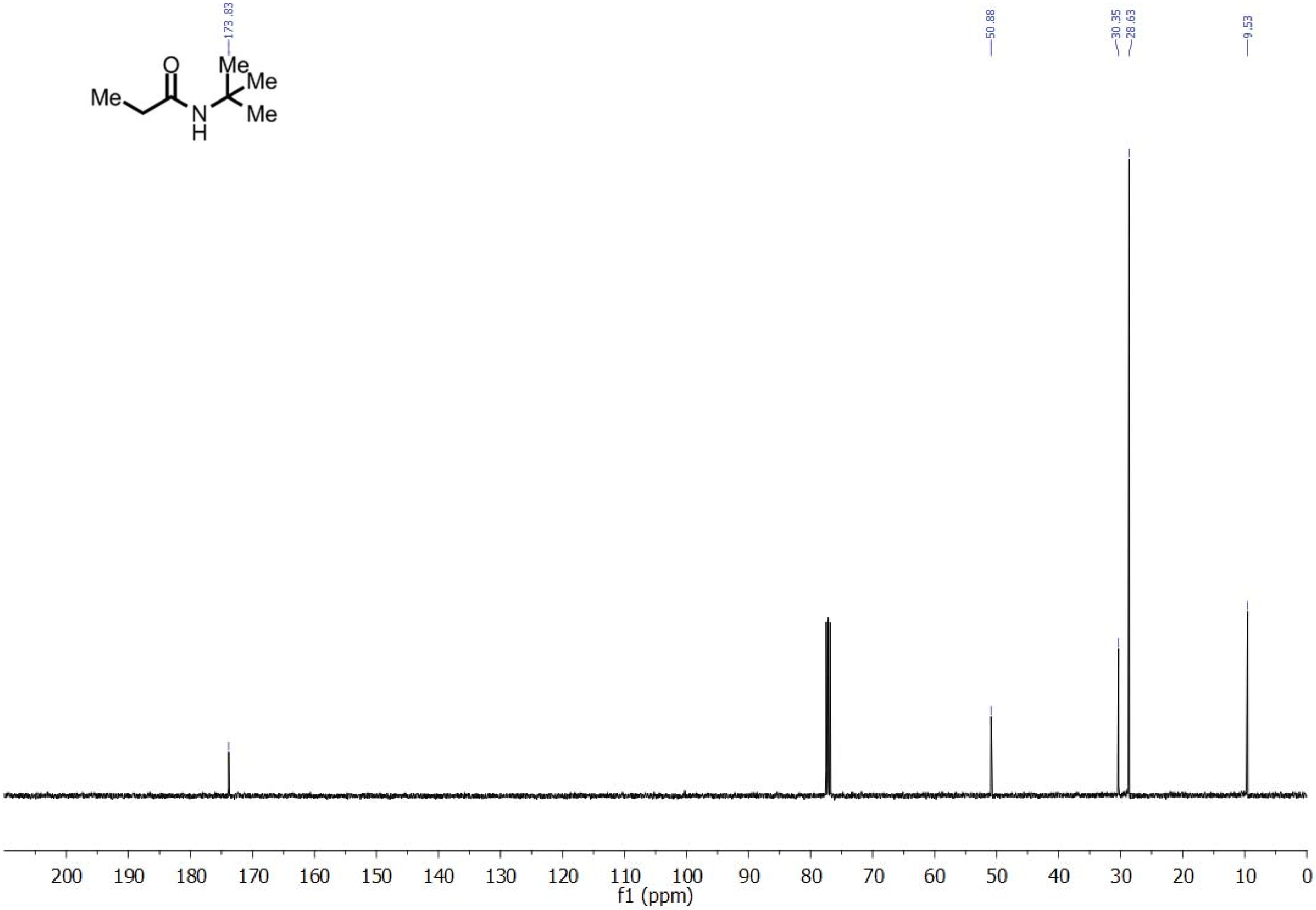
0.0
f1 (ppm)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Me
Me
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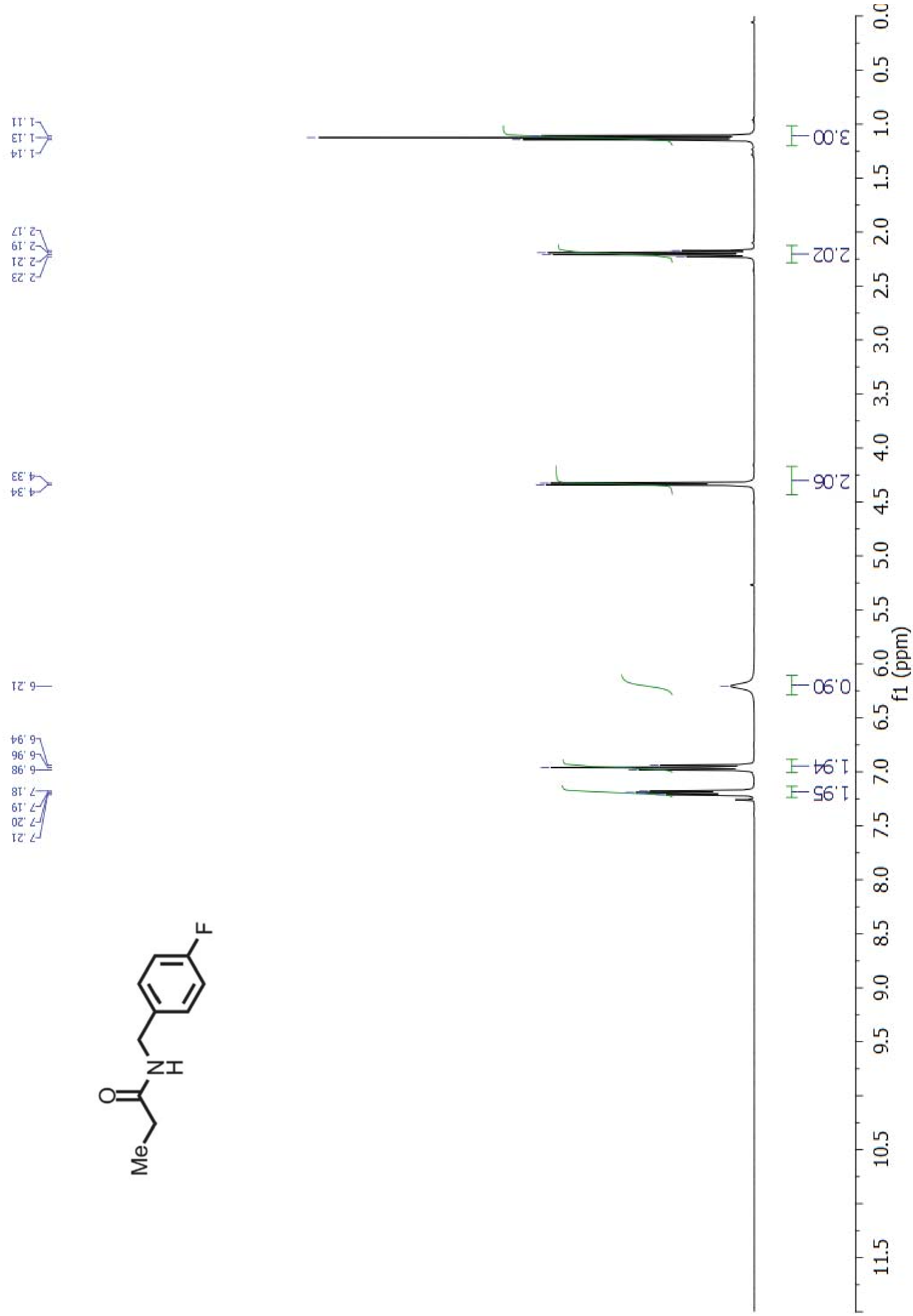
50
40
30
20
10
0
f1 (ppm)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2.21
2.23
4.33
4.34
6.21
6.94
6.96
6.98
7.18
7.19
7.20
7.21
3.00
2.02
2.06
0.90
1.94
1.95
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
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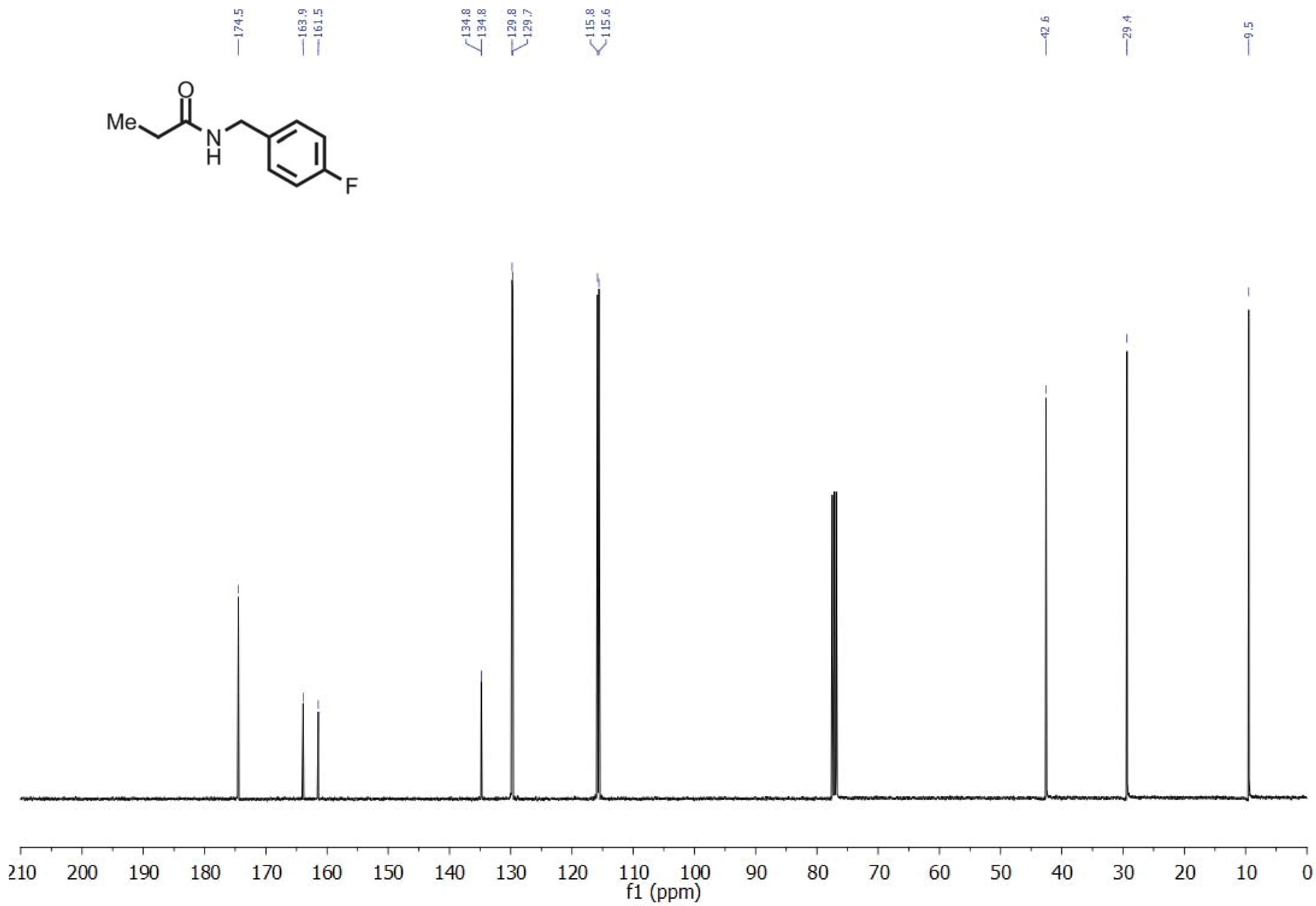
8.5
9.0
9.5
10.5
11.5
f1 (ppm)
Me
O
N
H
F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129.8
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42.6
29.4
9.5
Me
O
N
H
F
210
200
190
180
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130
120
110
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90
80
70
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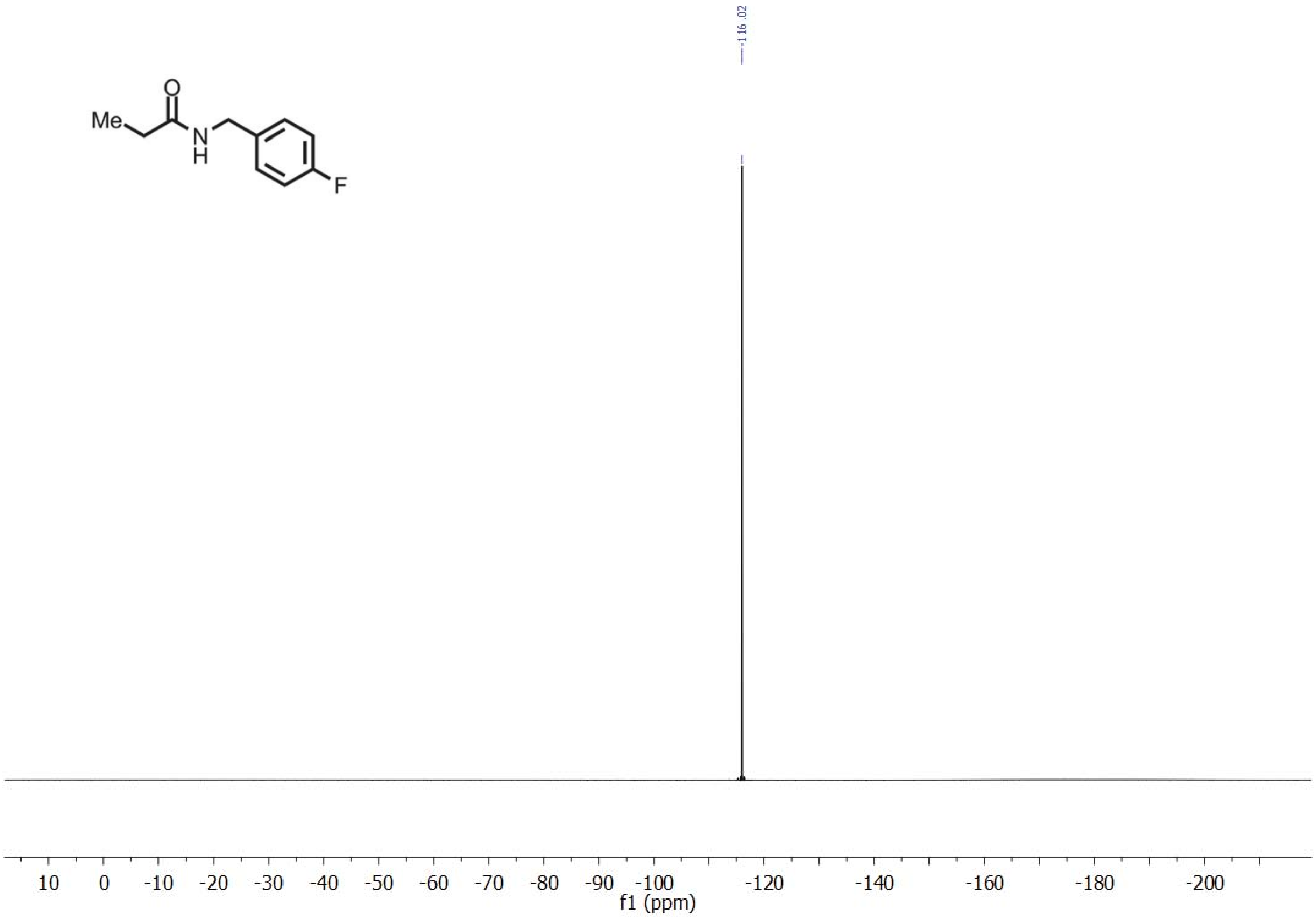
50
40
30
20
10
0
f1 (ppm)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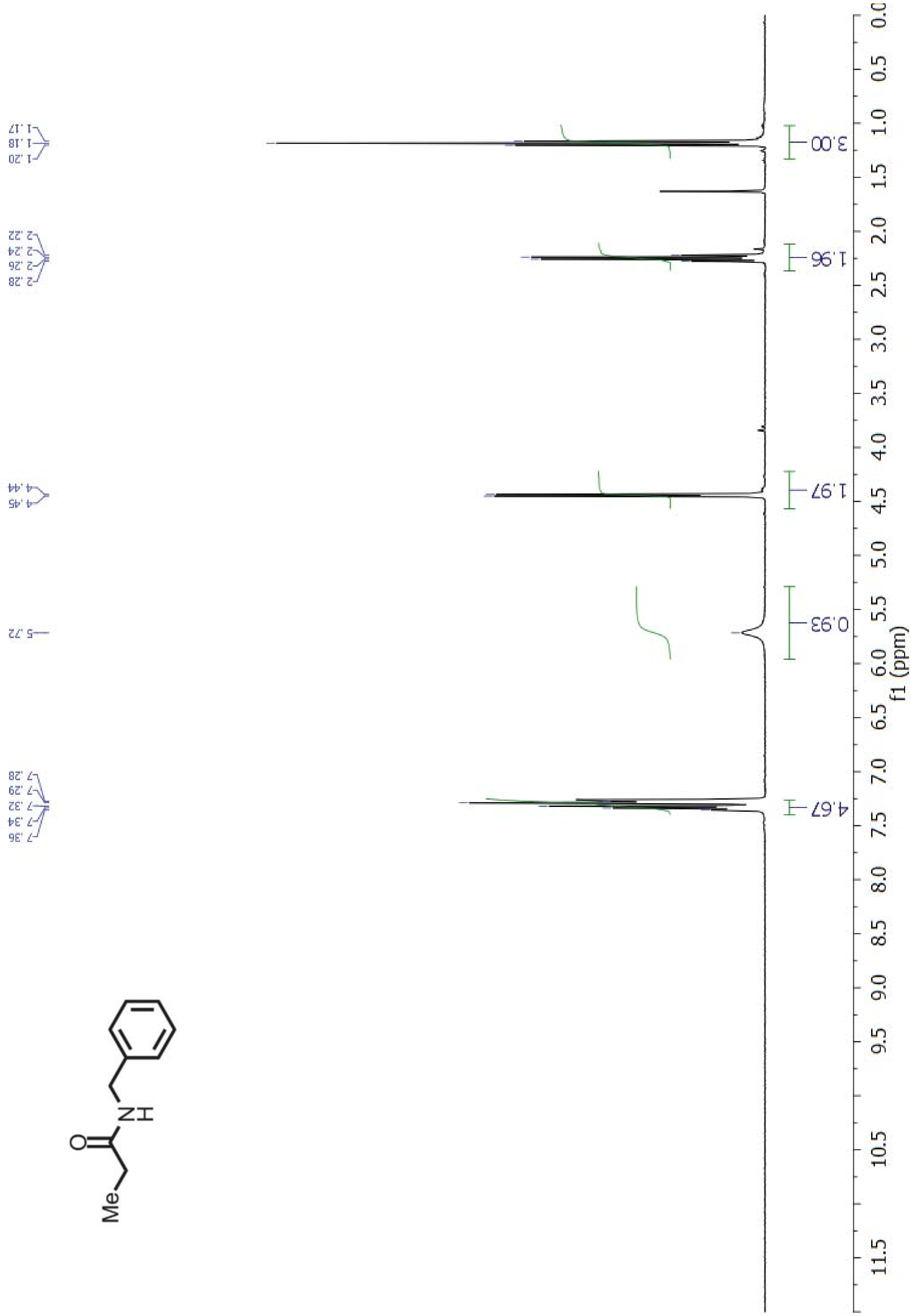
-160
-180
-200
f1 (ppm)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7.29
7.32
7.34
7.36
3.00
1.96
1.97
0.93
4.67
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
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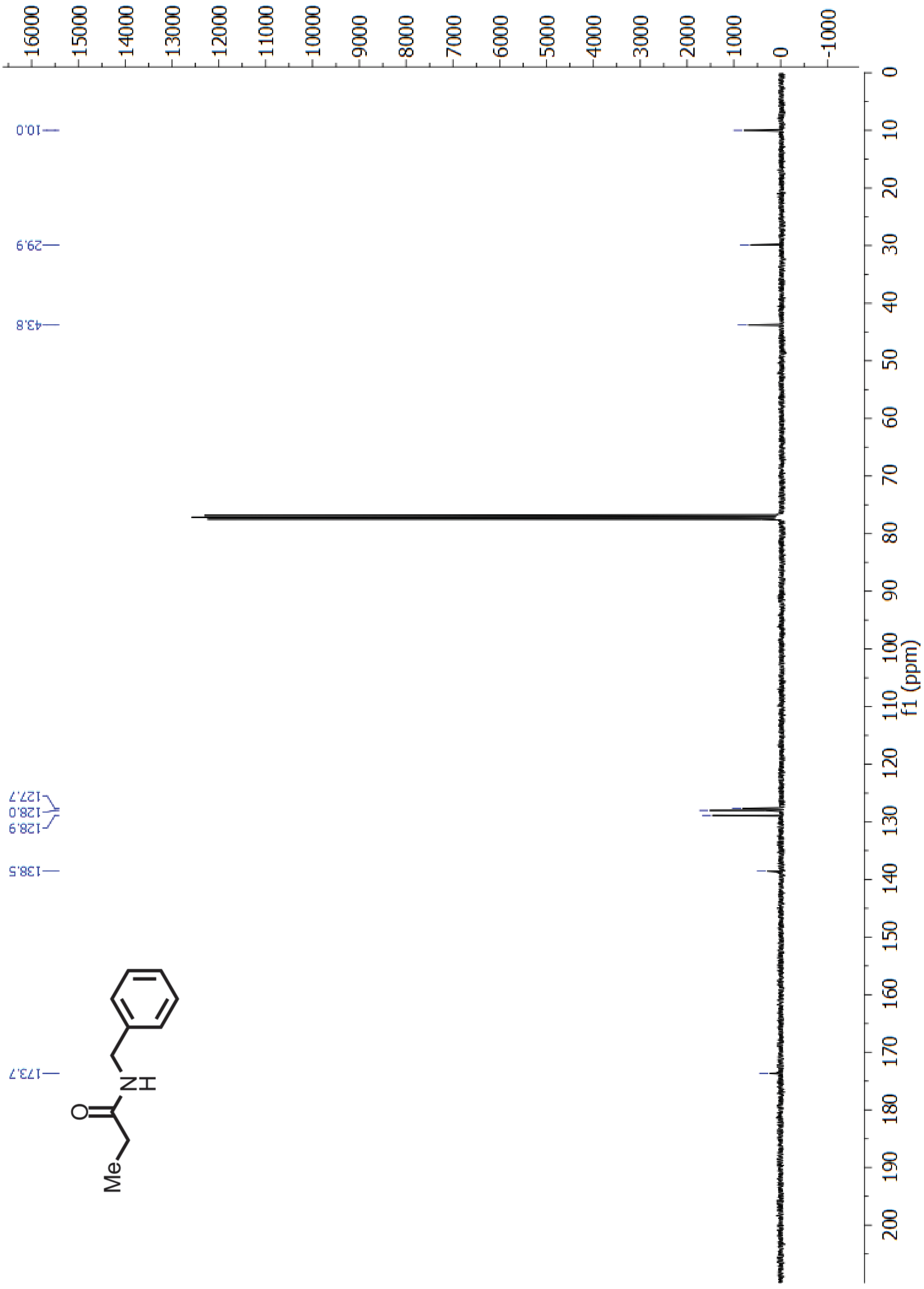
8.0
8.5
9.0
9.5
10.5
11.5
f1 (ppm)
Me
O
N
H



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128.9
138.5
173.7
Me
O
NH
f1 (ppm)
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10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
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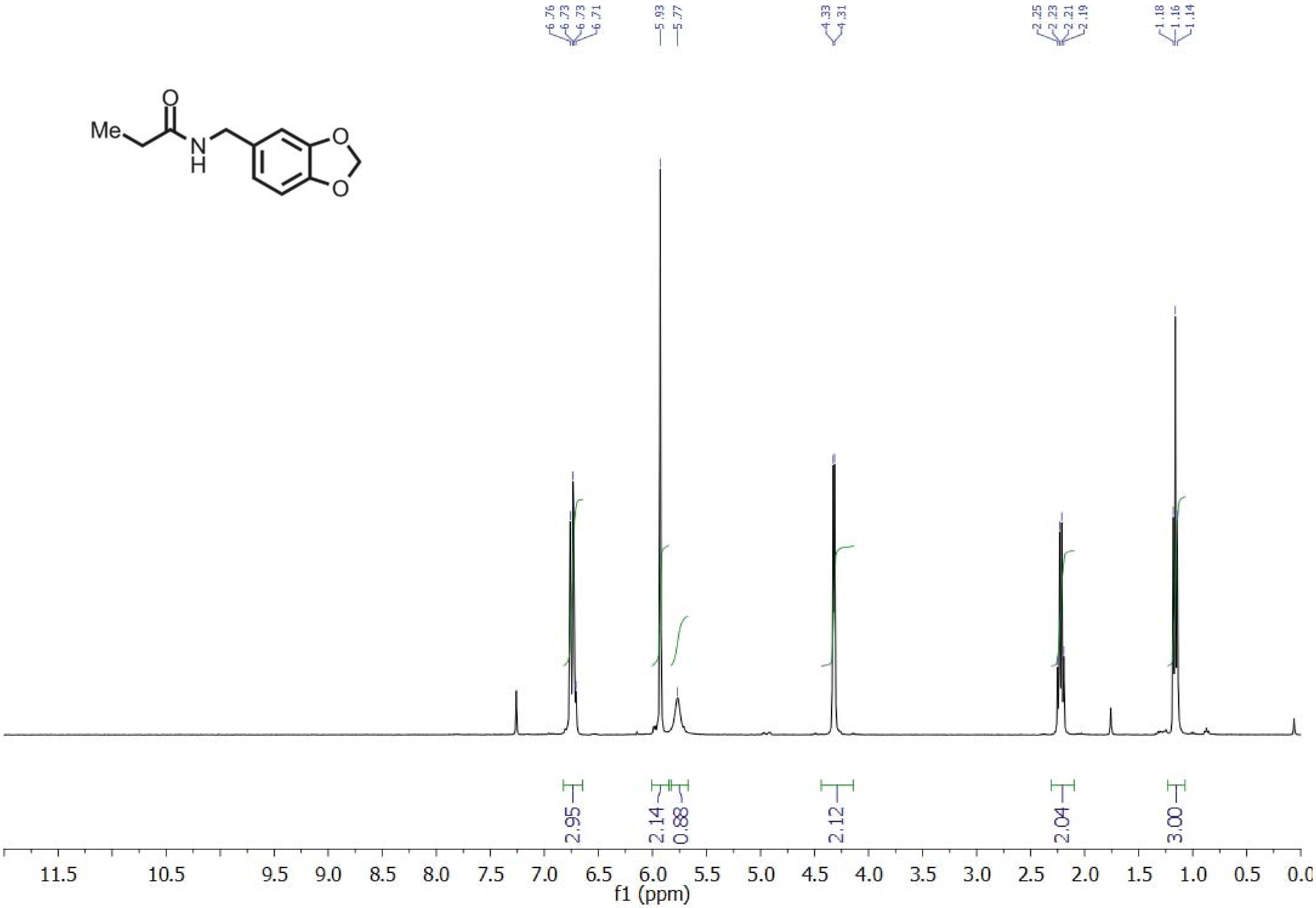
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1.14
Me
O
N
H
O
O
2.95
2.14
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2.12
2.04
3.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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1.0
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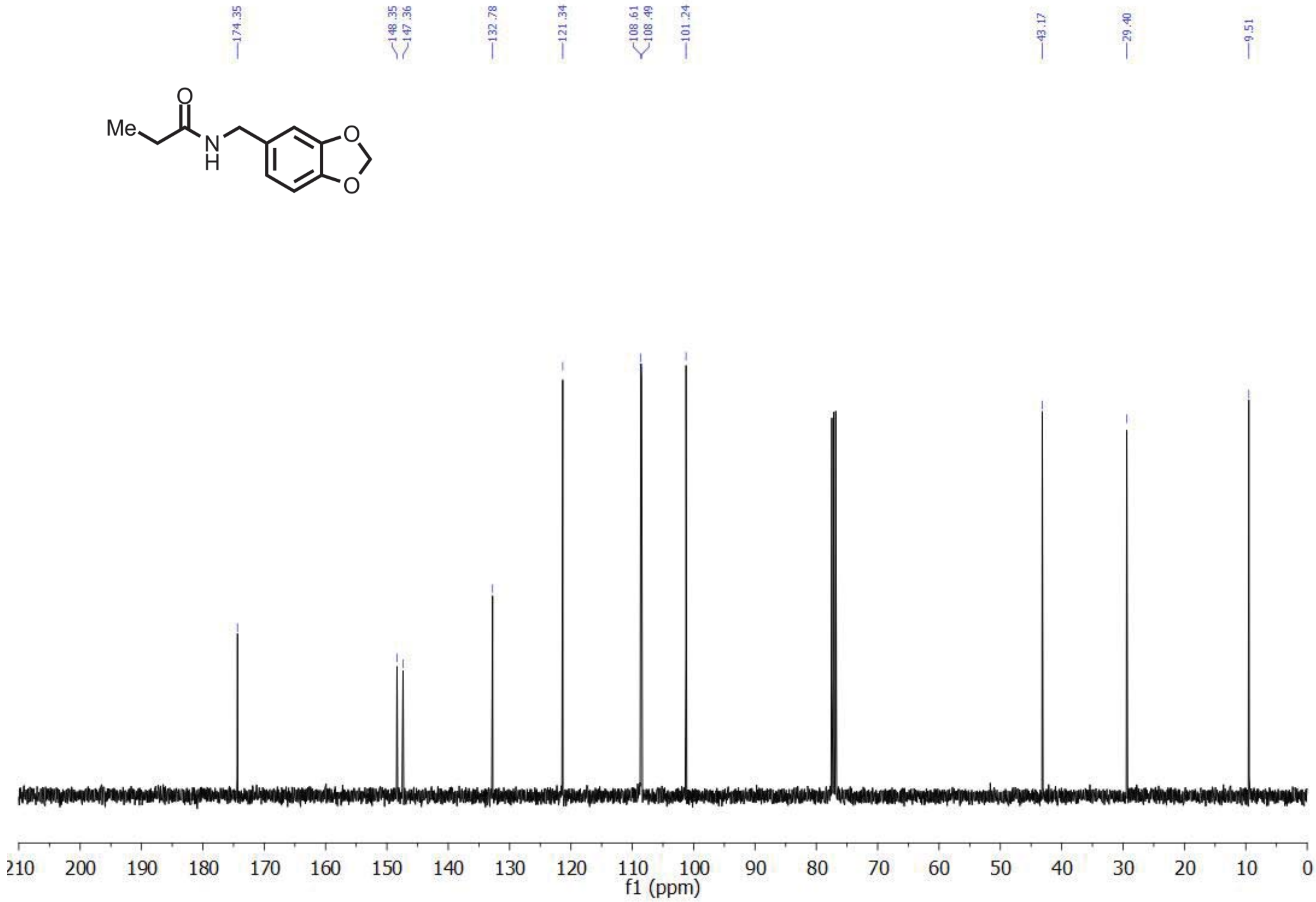
f1 (ppm)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O
N
H
O
O
210
200
190
180
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130
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90
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50
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30
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10
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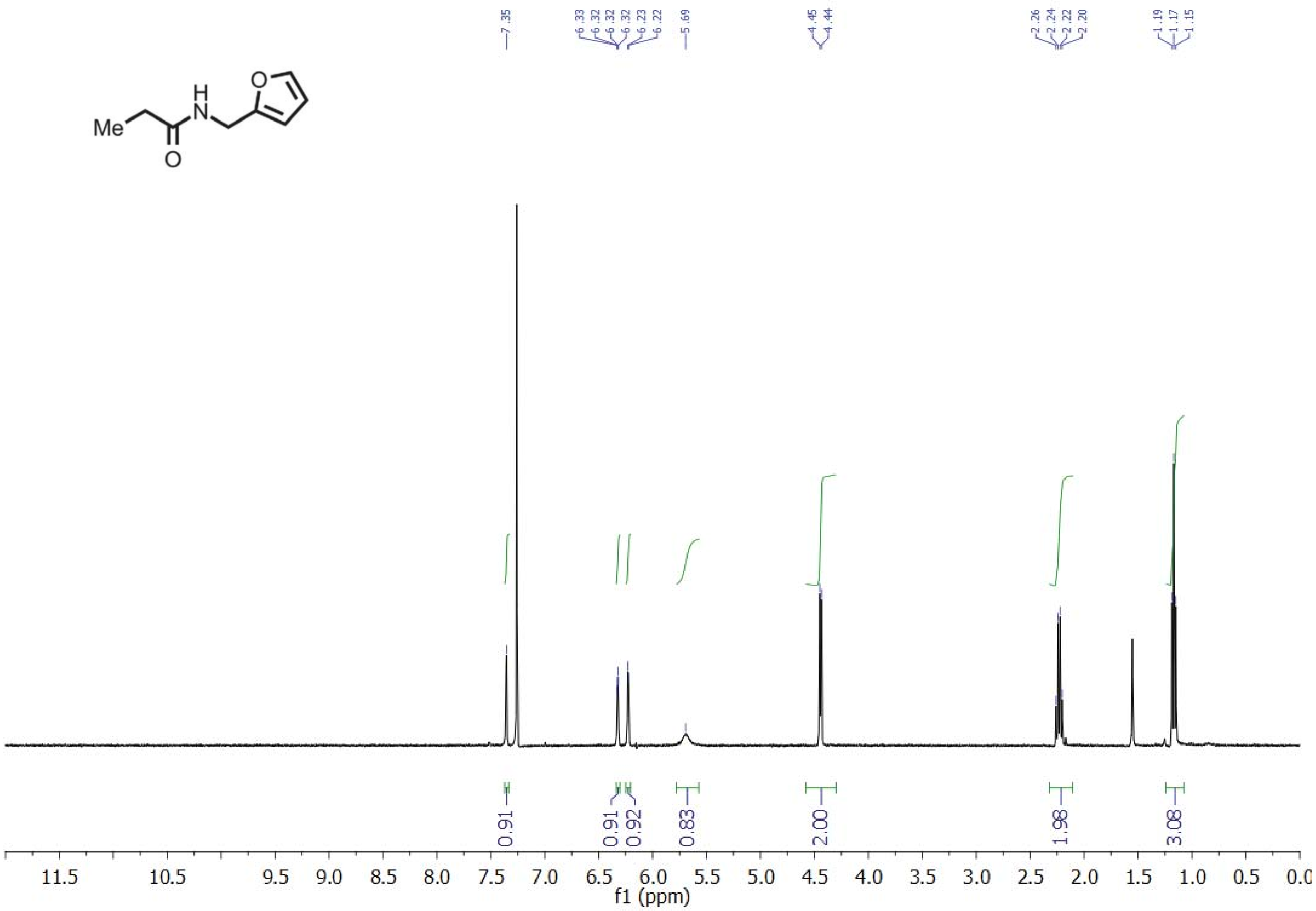
f1 (ppm)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2.22
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1.15
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0.91
0.92
0.83
2.00
1.98
3.08
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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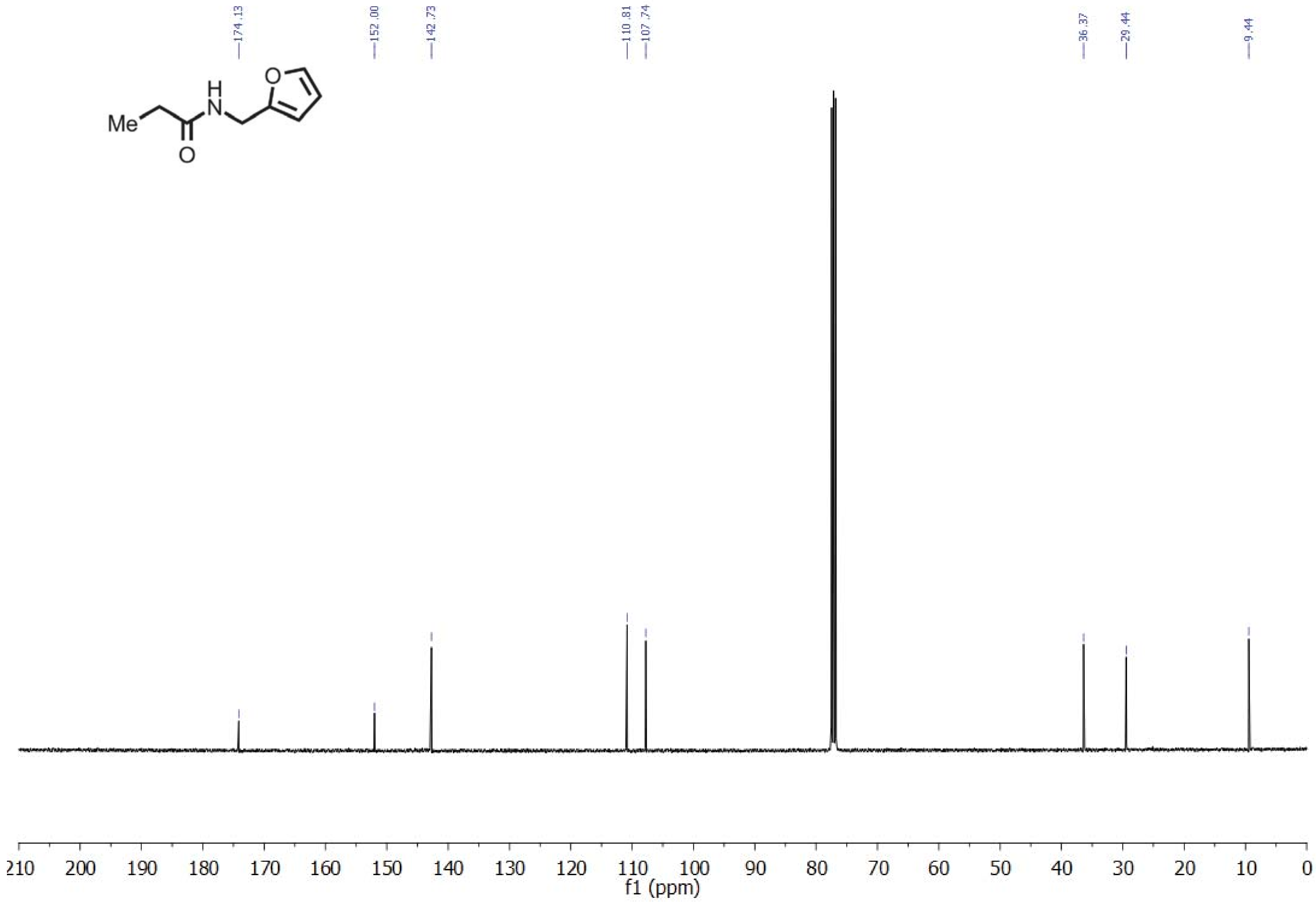
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180
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110
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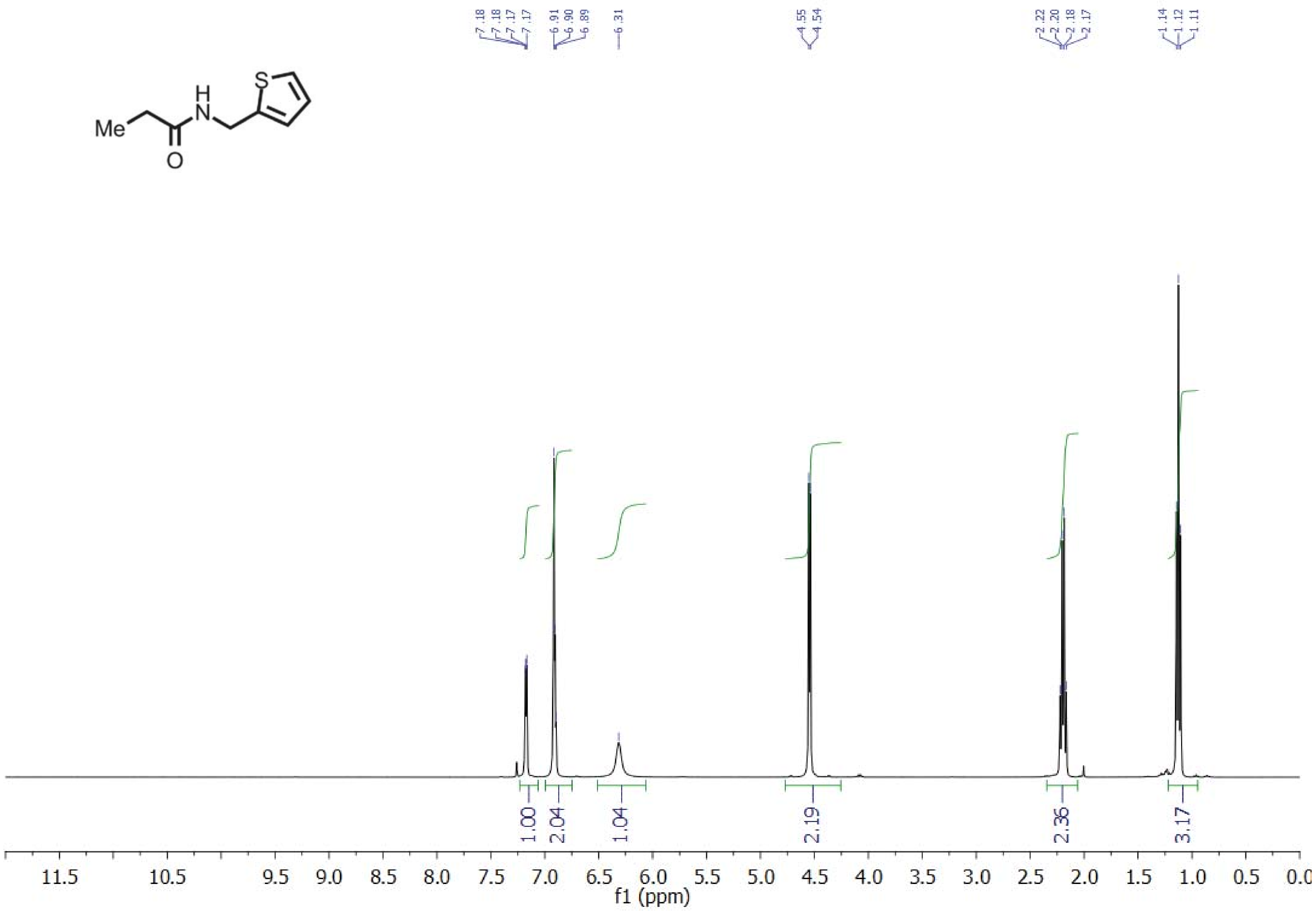
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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S
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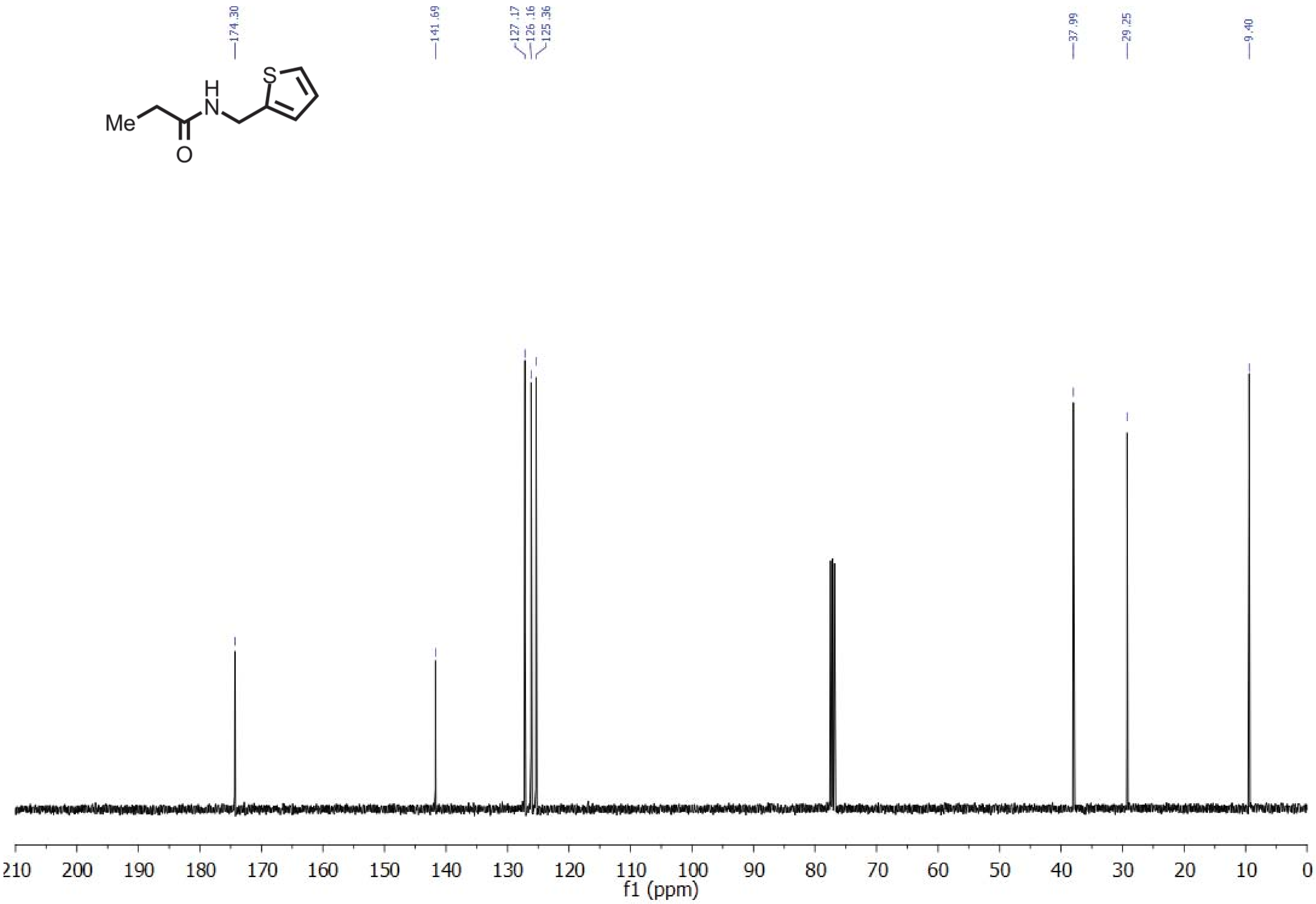
4.54
2.22
2.20
2.18
2.17
1.14
1.12
1.11
1.00
2.04
1.04
2.19
2.36
3.17
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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29.25
9.40
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N
O
S
210
200
190
180
170
160
150
140
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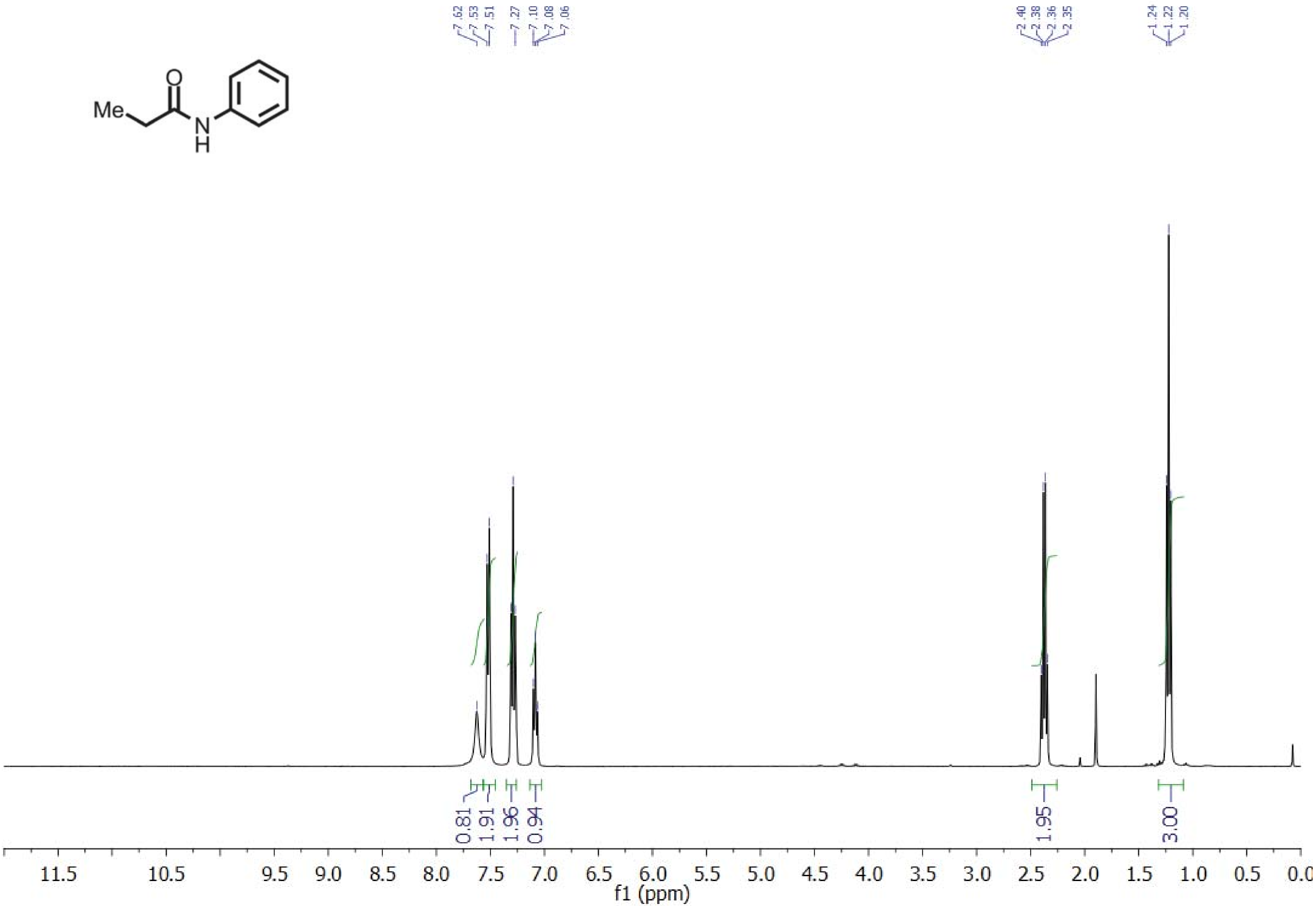
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Me
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7.08
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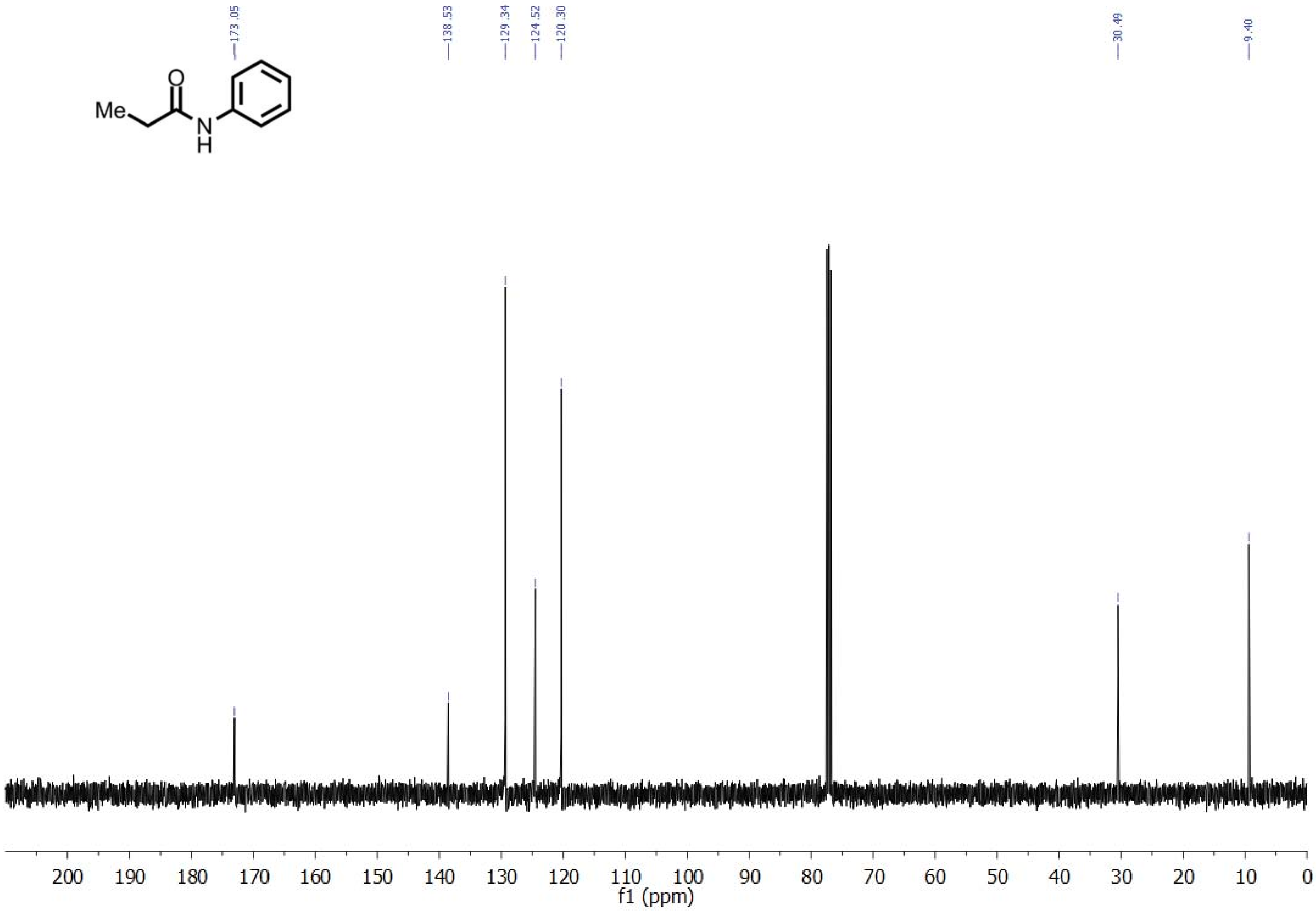
2.36
2.35
1.24
1.22
1.20
0.81
1.91
1.96
0.94
1.95
3.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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110
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90
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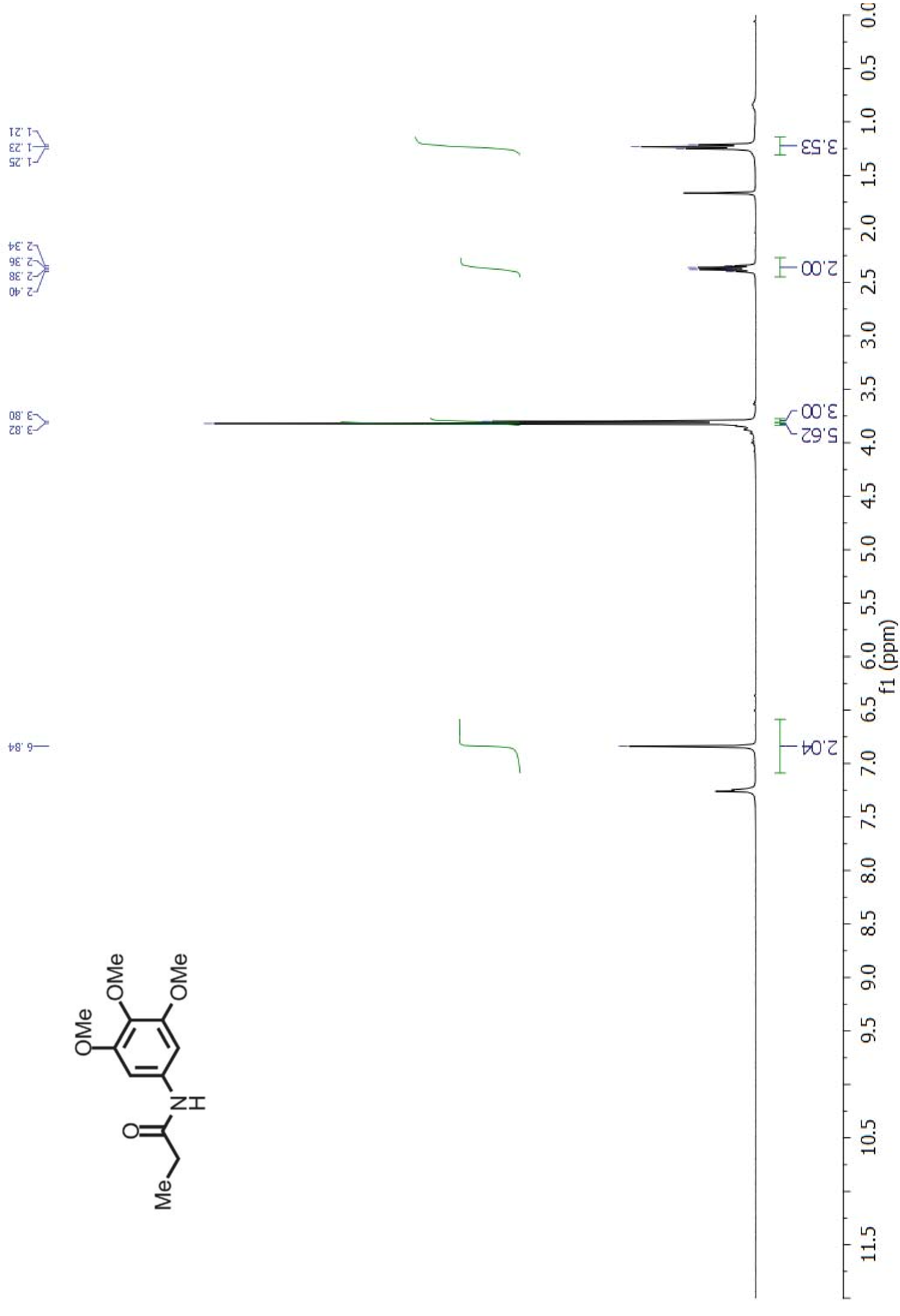
50
40
30
20
10
0
f1 (ppm)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2.5
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3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
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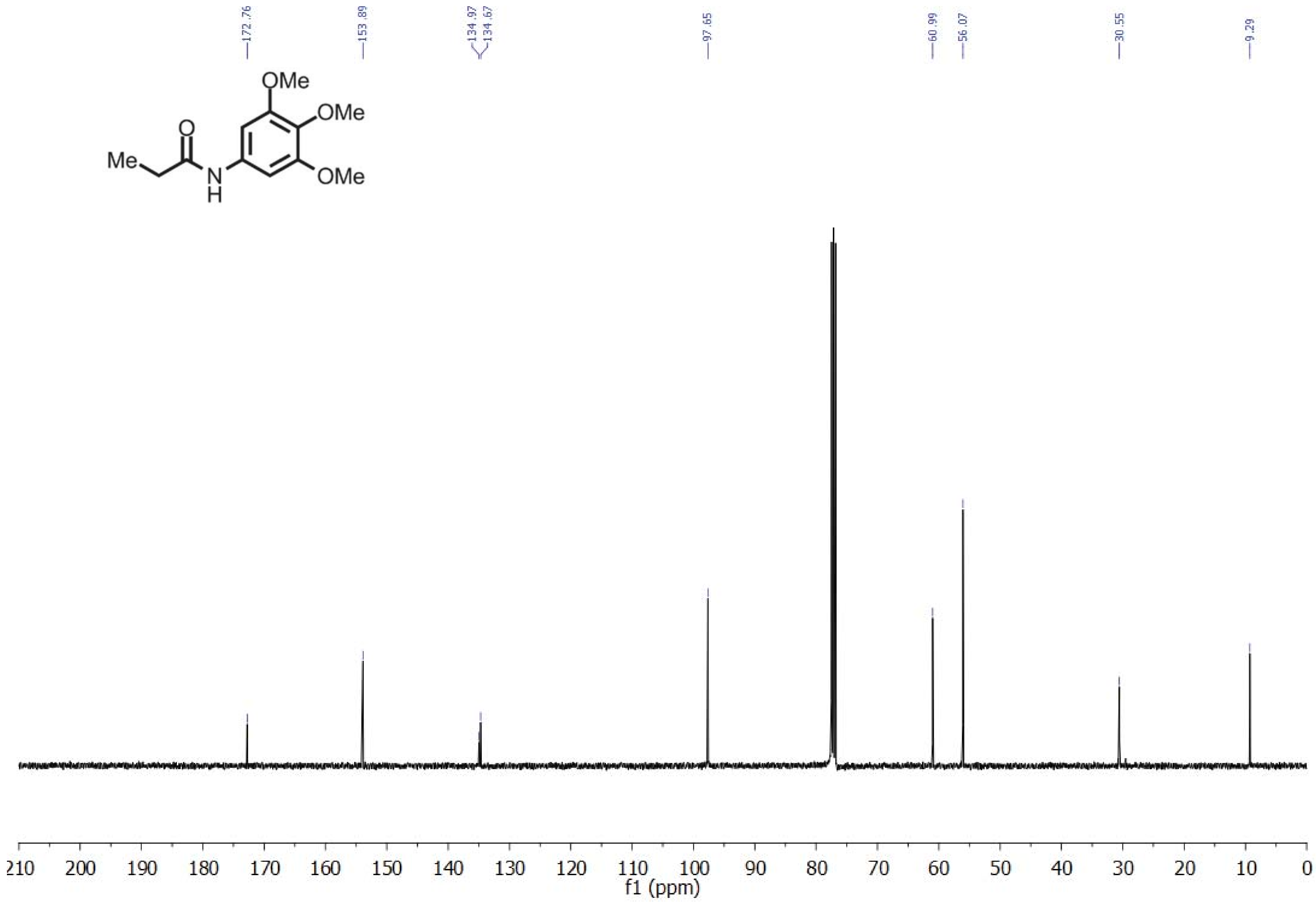
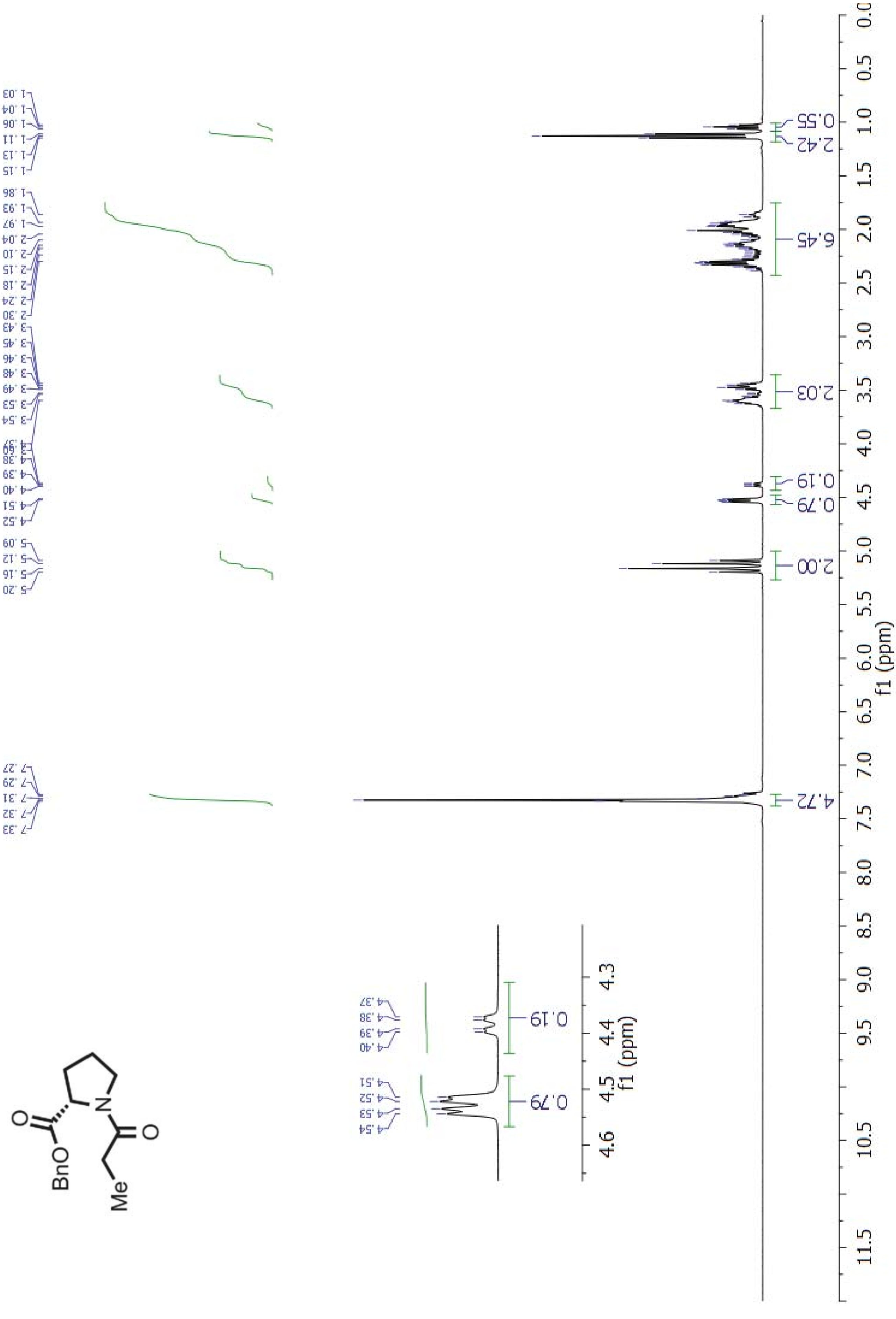
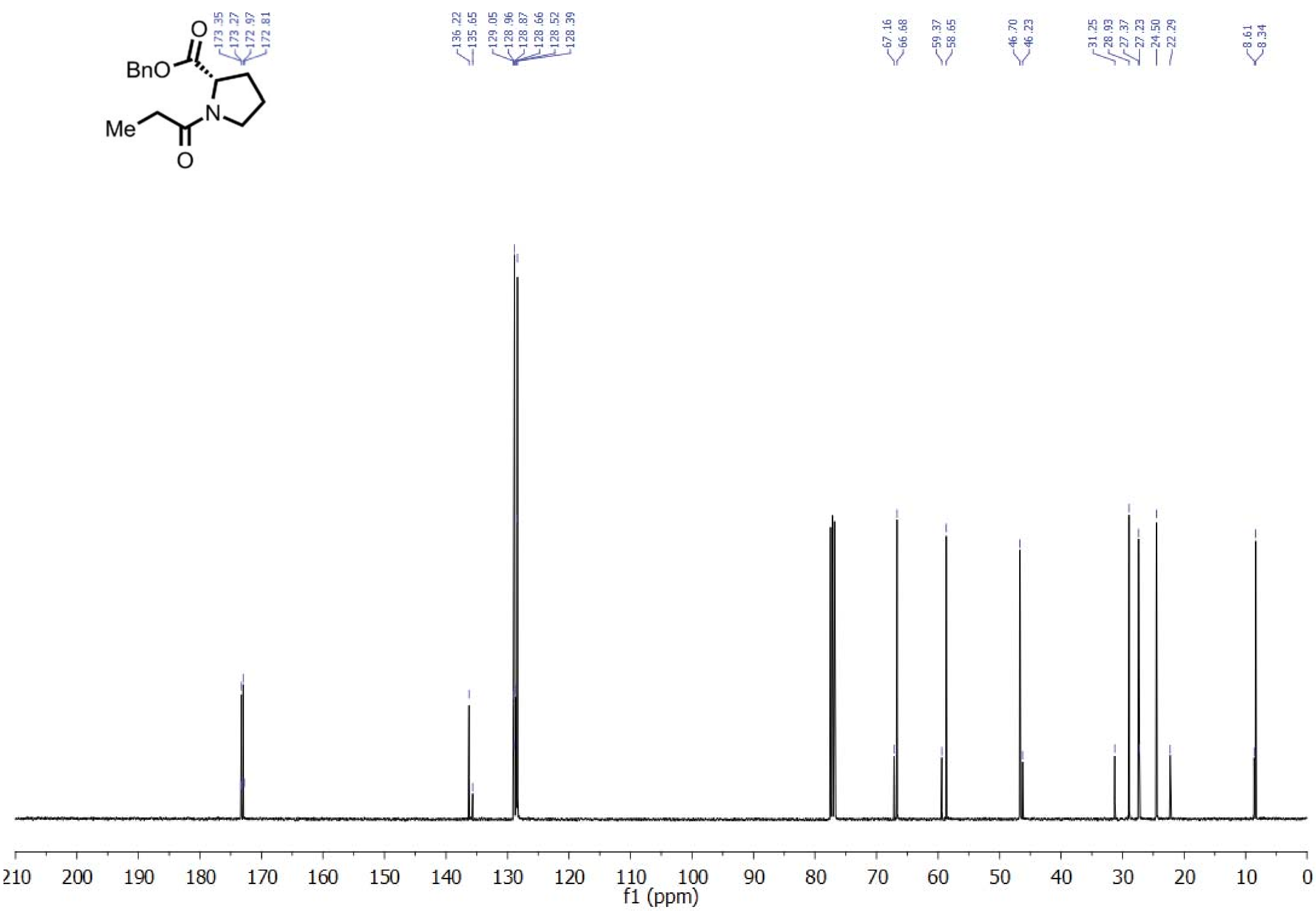
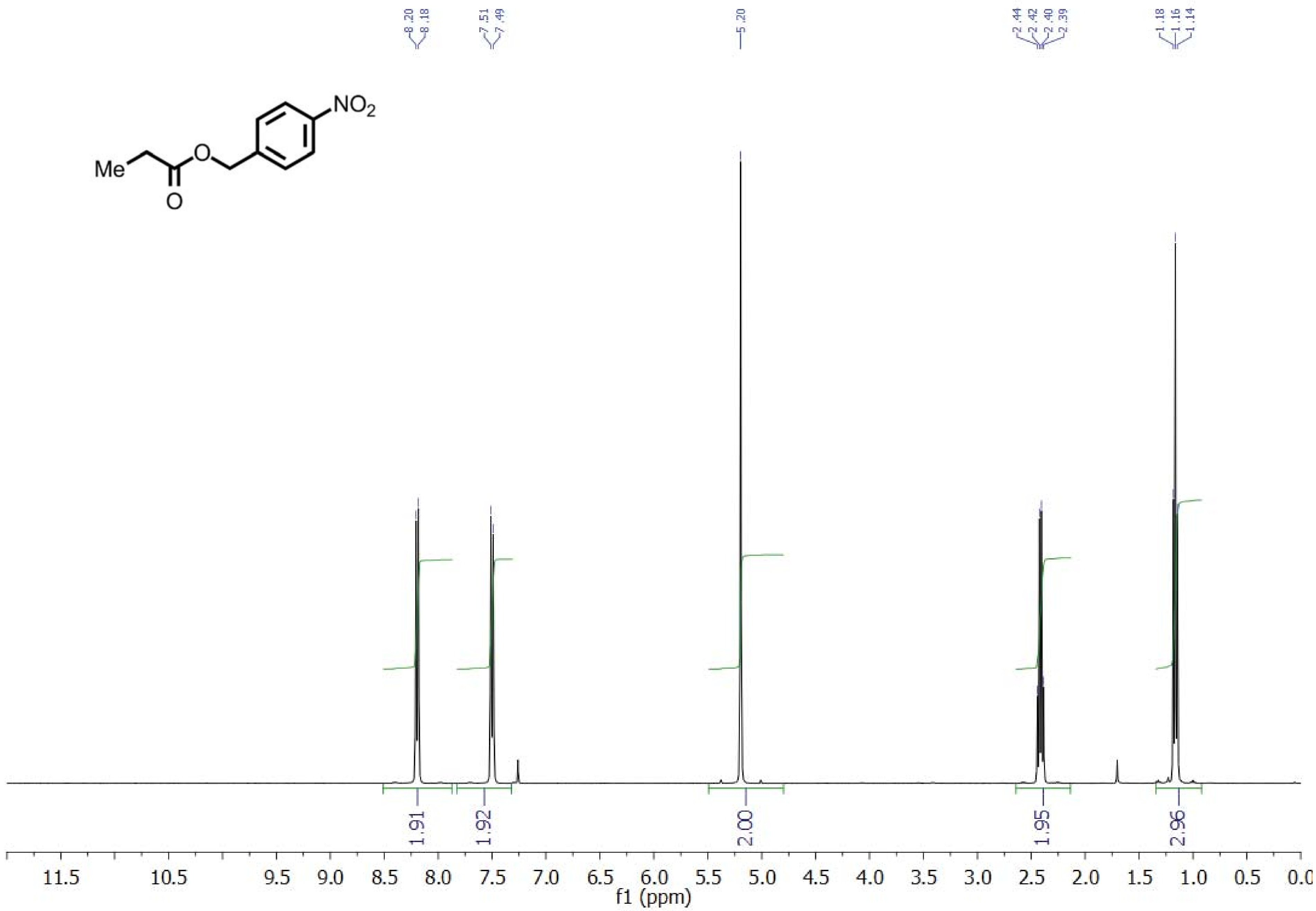
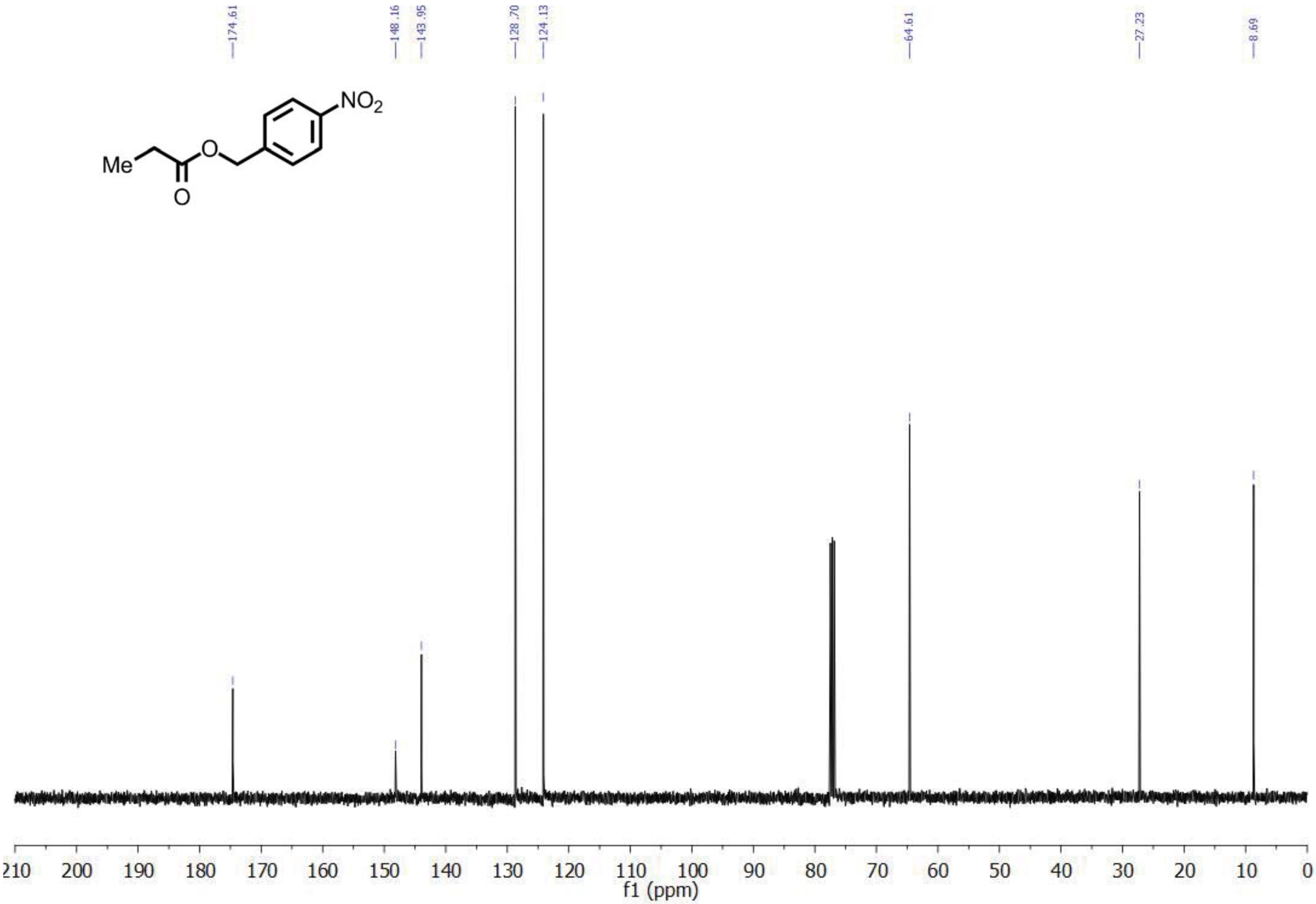
8.0
8.5
9.0
9.5
10.5
11.5
f1 (ppm)
OMe
OMe
OMe
Me
O
N
H

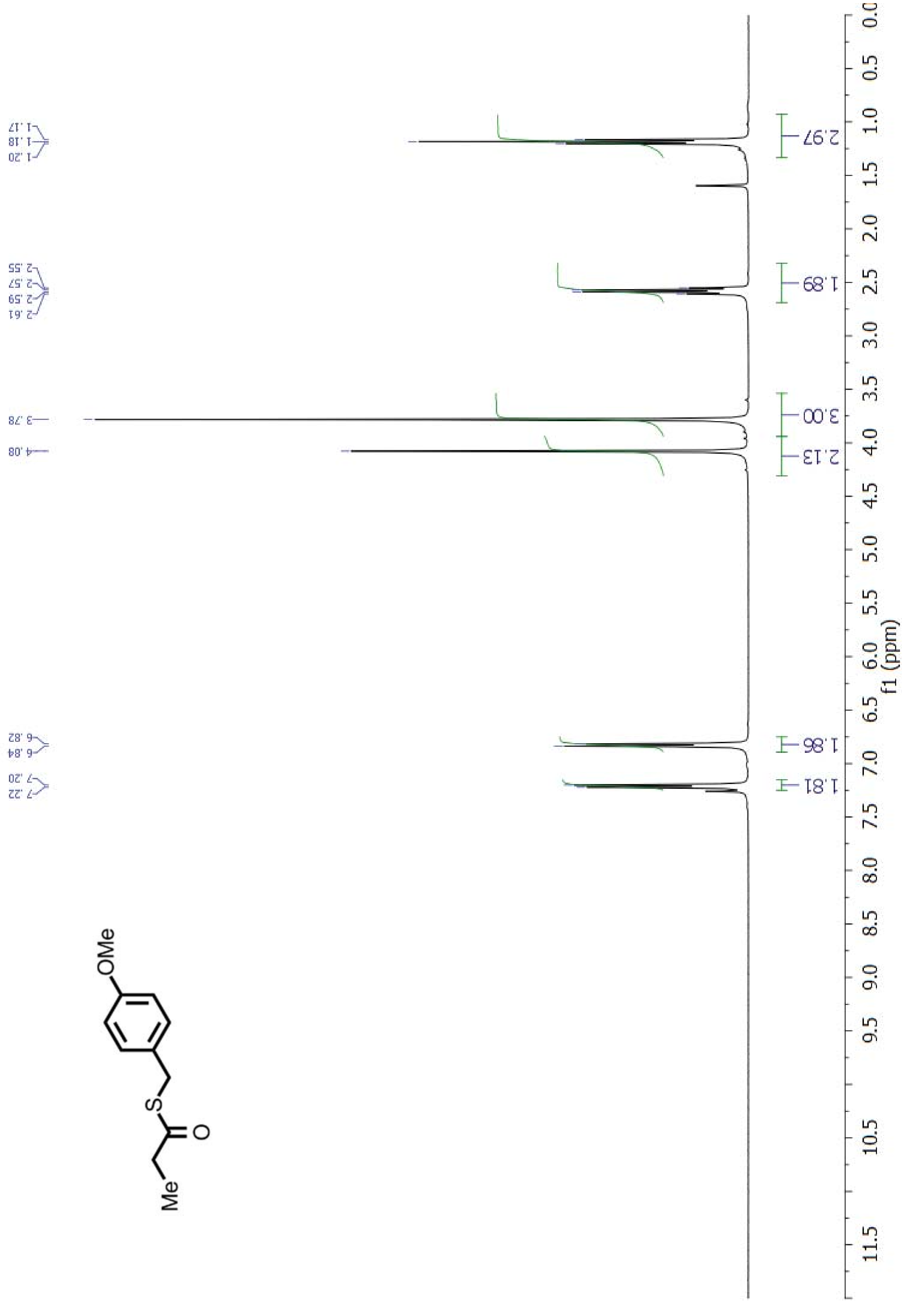

172.76
153.89
134.97
134.67
97.65
60.99
56.07
30.55
9.29
OMe
OMe
OMe
O
Me
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


1.03
1.04
1.06
1.11
1.13
1.15
1.86
1.93
1.97
2.04
2.10
2.15
2.18
2.24
2.30
3.43
3.45
3.46
3.48
3.49
3.53
3.54
4.37
3.60
4.38
4.39
4.40
4.51
4.52
5.09
5.12
5.16
5.20
7.27
7.29
7.31
7.32
7.33
0.55
2.42
6.45
2.03
0.19
0.79
2.00
4.72
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.5
11.5
f1 (ppm)
4.37
4.38
4.39
4.40
4.51
4.52
4.53
4.54
0.19
0.79
4.3
4.4
4.5
4.6
f1 (ppm)
BnO
O
N
O
Me

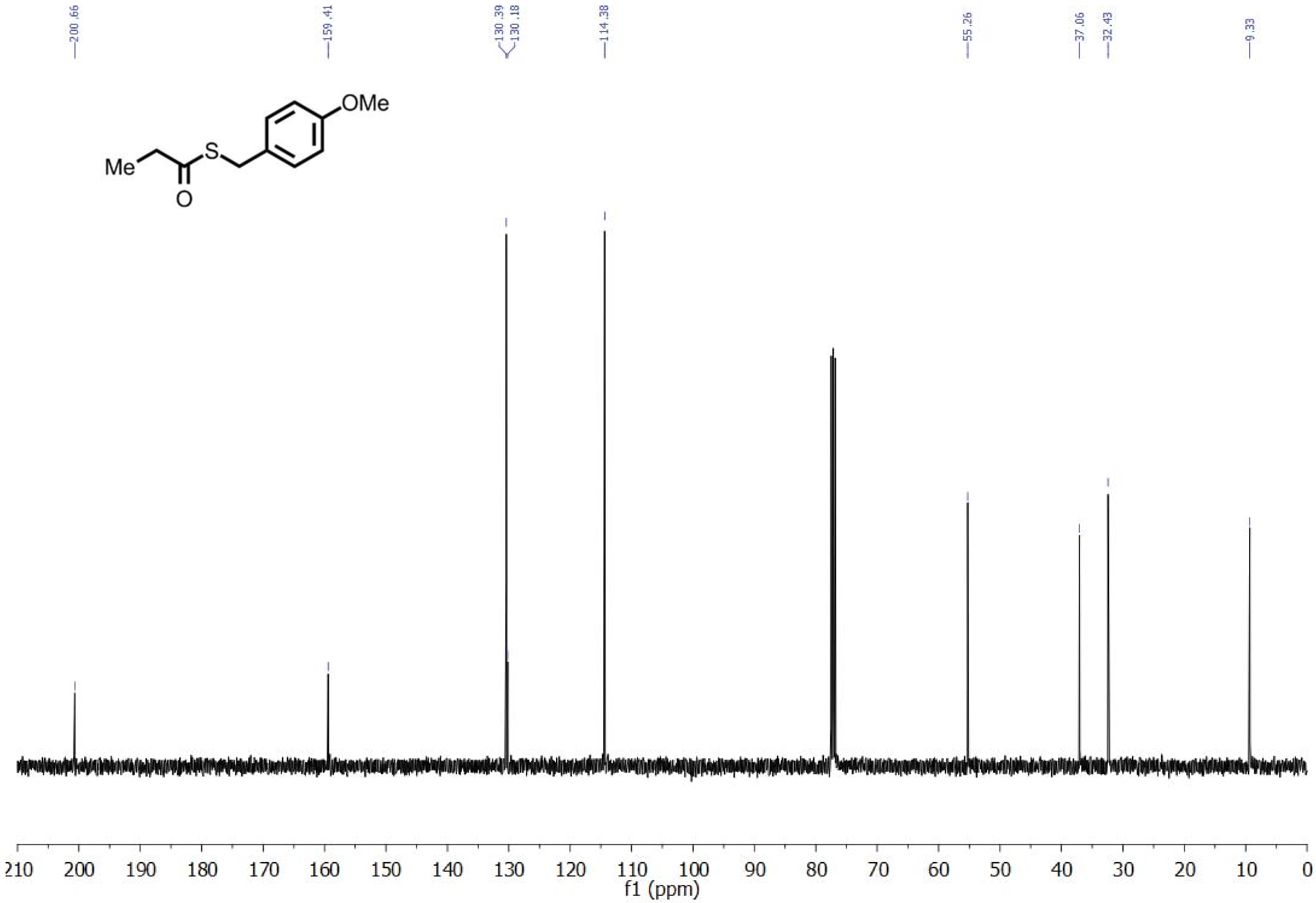

173.35
173.27
172.97
172.81
136.22
135.65
129.05
128.96
128.87
128.66
128.52
128.39
67.16
66.68
59.37
58.65
46.70
46.23
31.25
28.93
27.37
27.23
24.50
22.29
8.61
8.34
BnO
O
N
Me
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

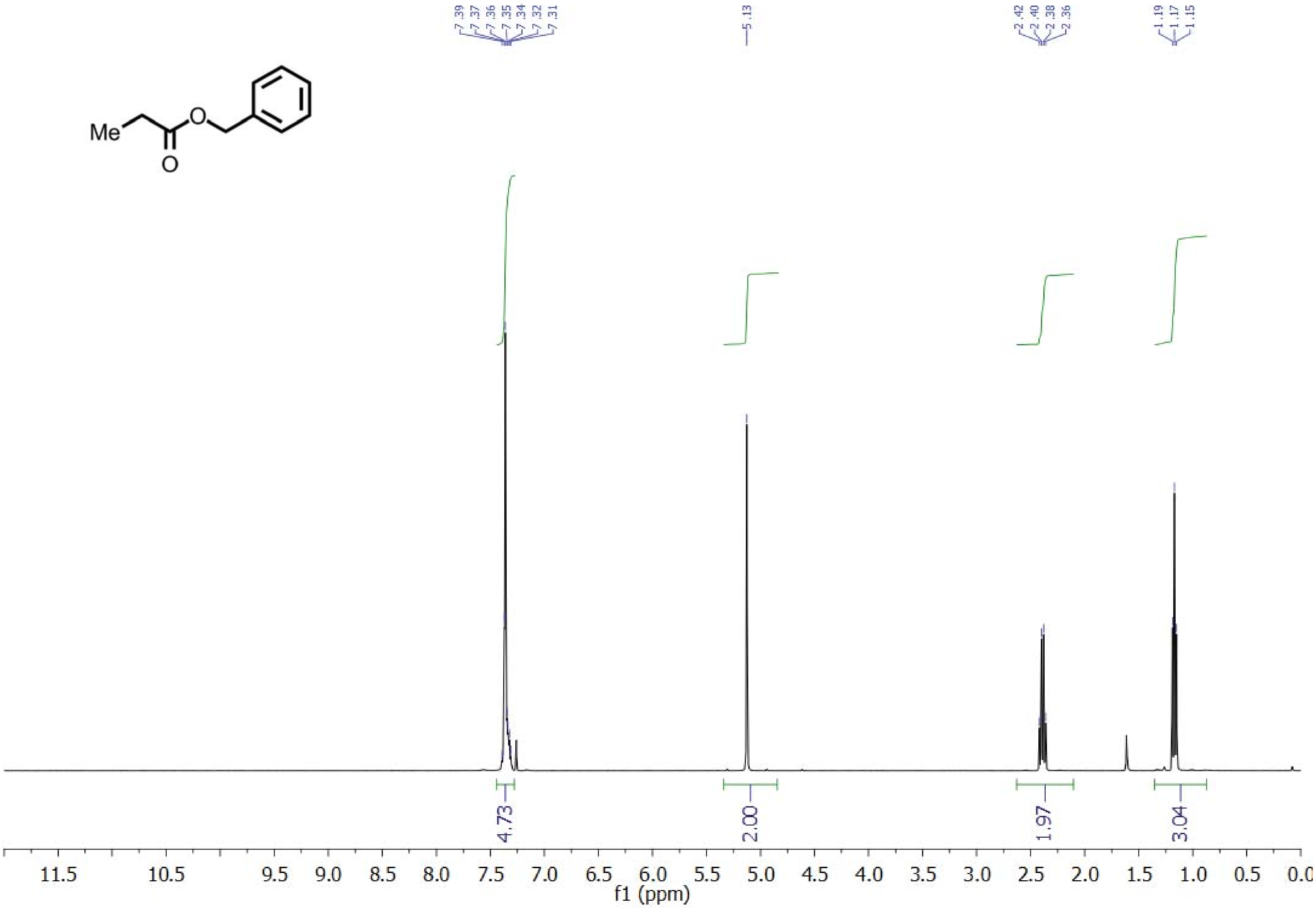

8.20
8.18
7.51
7.49
5.20
2.44
2.42
2.40
2.39
1.18
1.16
1.14
Me
O
O
NO$_2$
1.91
1.92
2.00
1.95
2.96
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

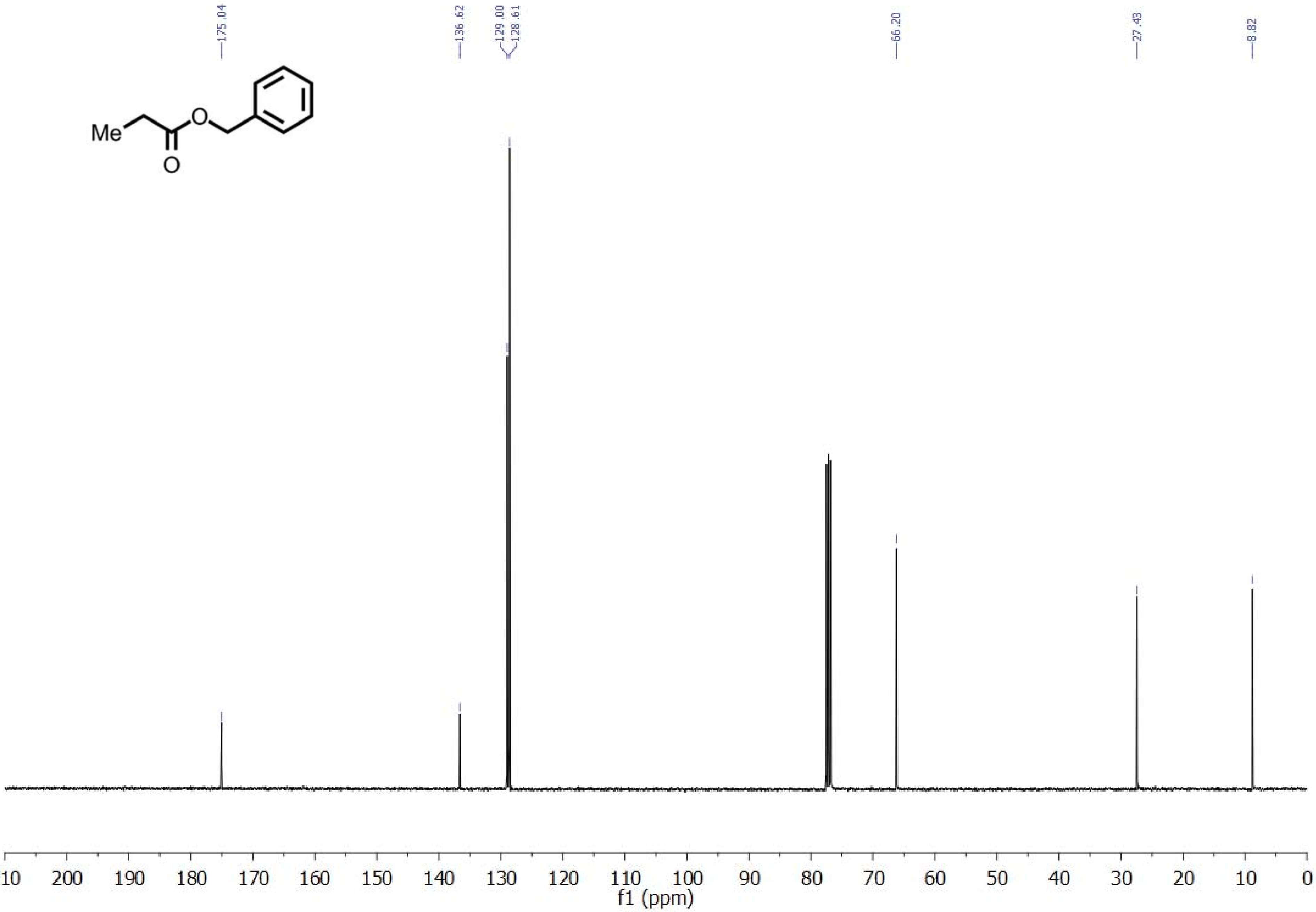

174.61
148.16
143.95
128.70
124.13
64.61
27.23
8.69
Me
O
O
NO2
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

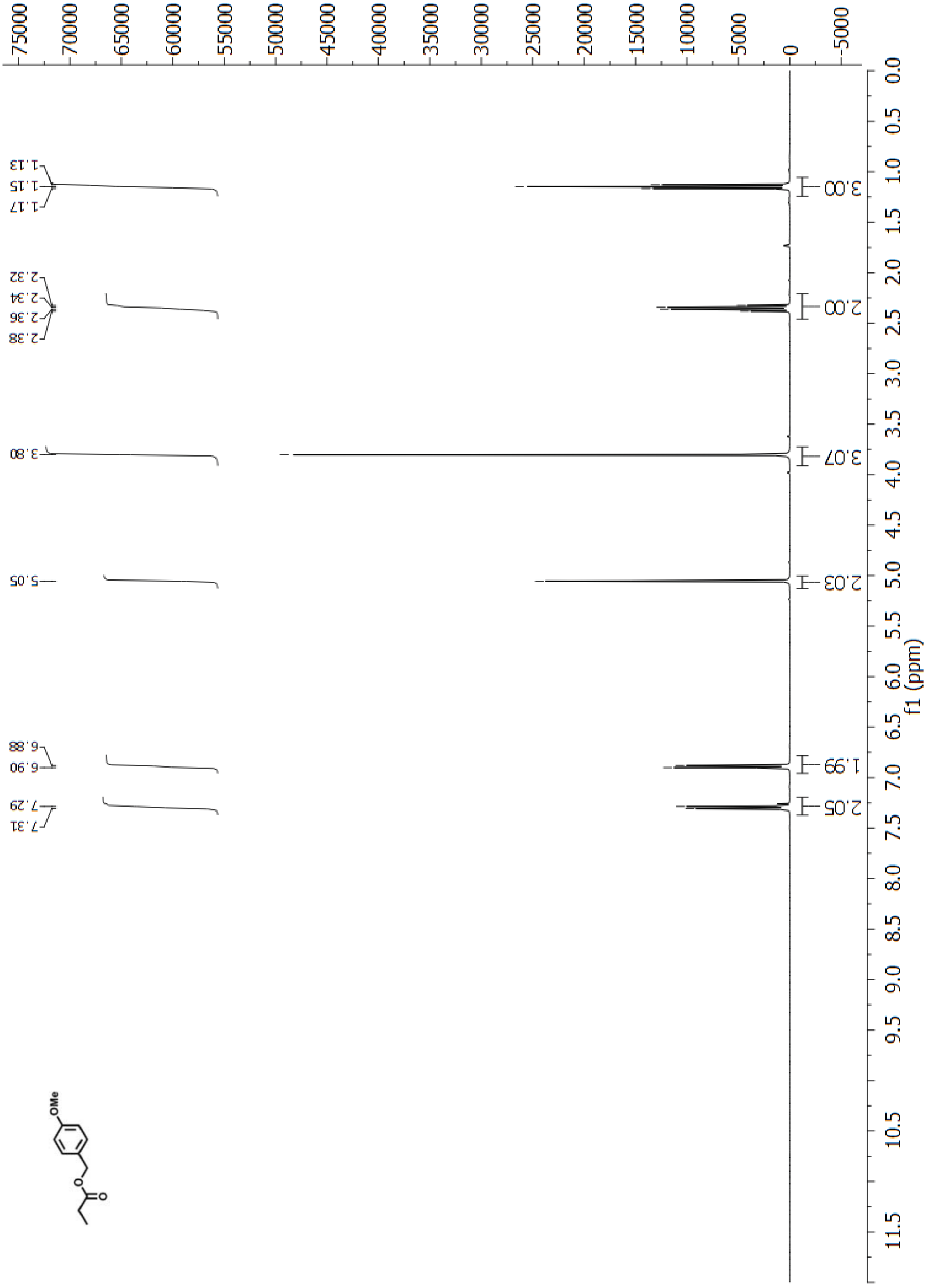


1.17
1.18
1.20
2.55
2.57
2.59
2.61
3.78
4.08
6.82
6.84
7.20
7.22
2.97
1.89
3.00
2.13
1.86
1.81
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.5
11.5
f1 (ppm)
OMe
S
O
Me

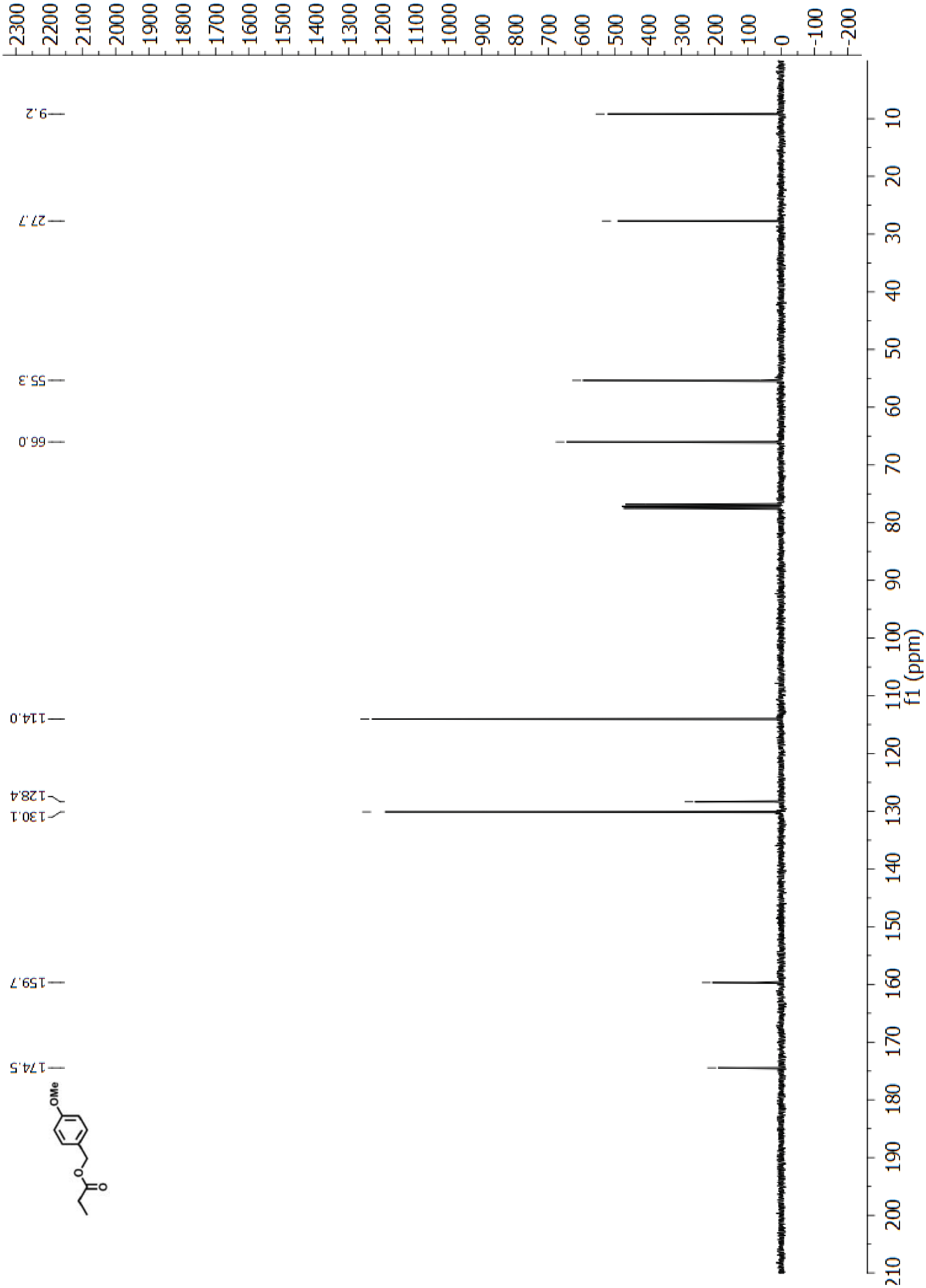

200.66
159.41
130.39
130.18
114.38
55.26
37.06
32.43
9.33
OMe
S
Me
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

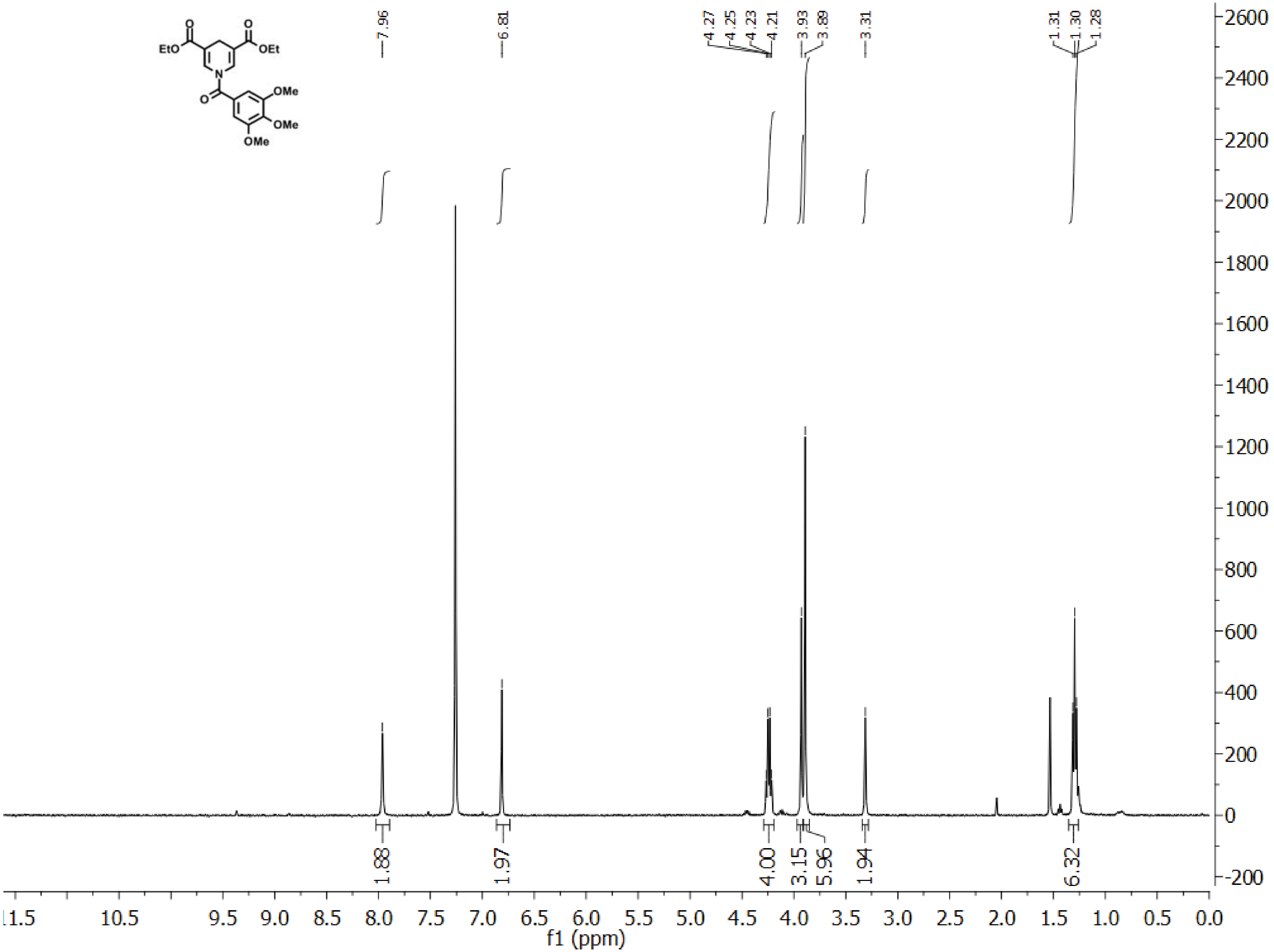

7.39
7.37
7.36
7.35
7.34
7.32
7.31
5.13
2.42
2.40
2.38
2.36
1.19
1.17
1.15
Me
O
O
4.73
2.00
1.97
3.04
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

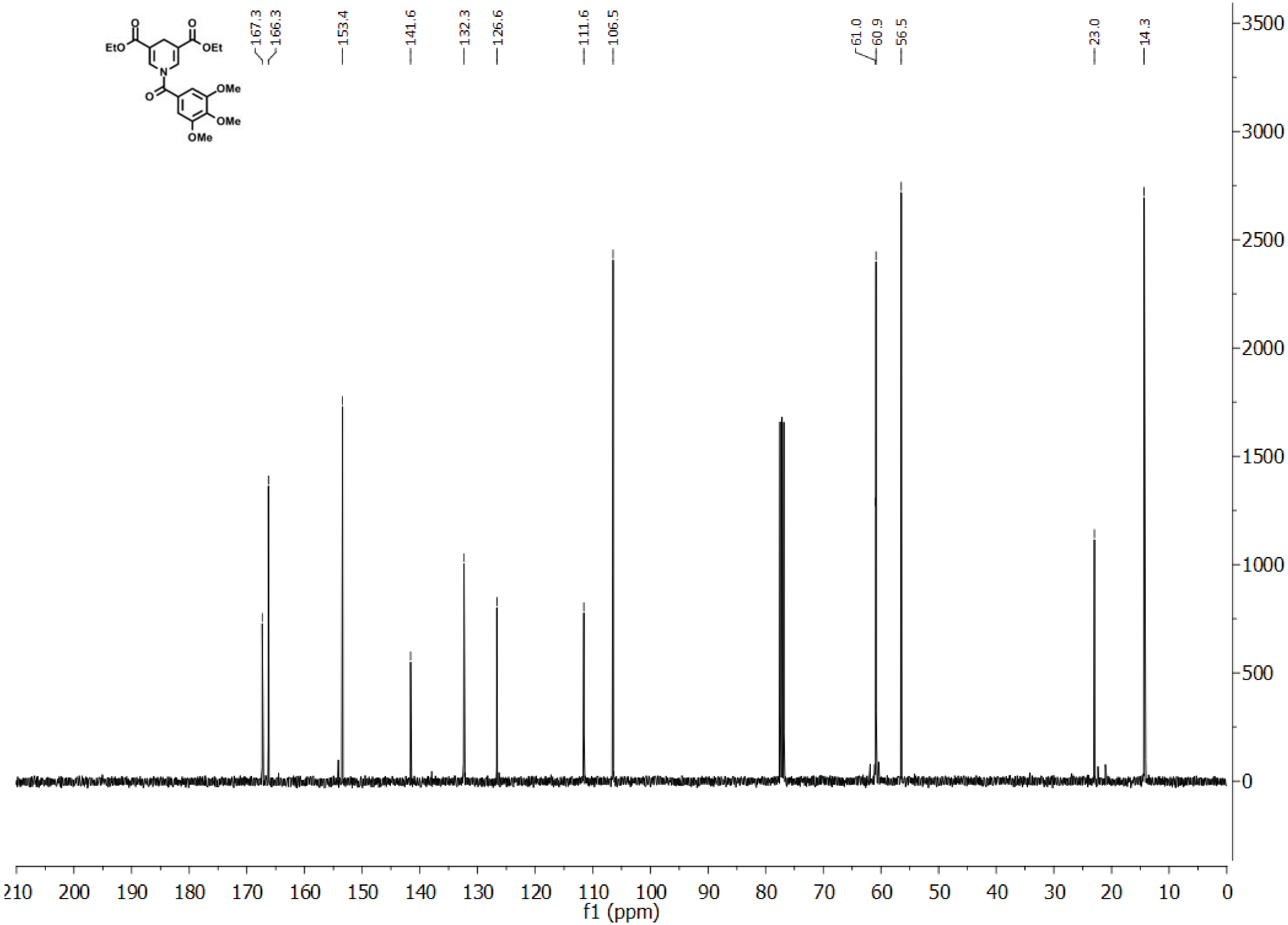

175.04
136.62
129.00
128.61
66.20
27.43
8.82
Me
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

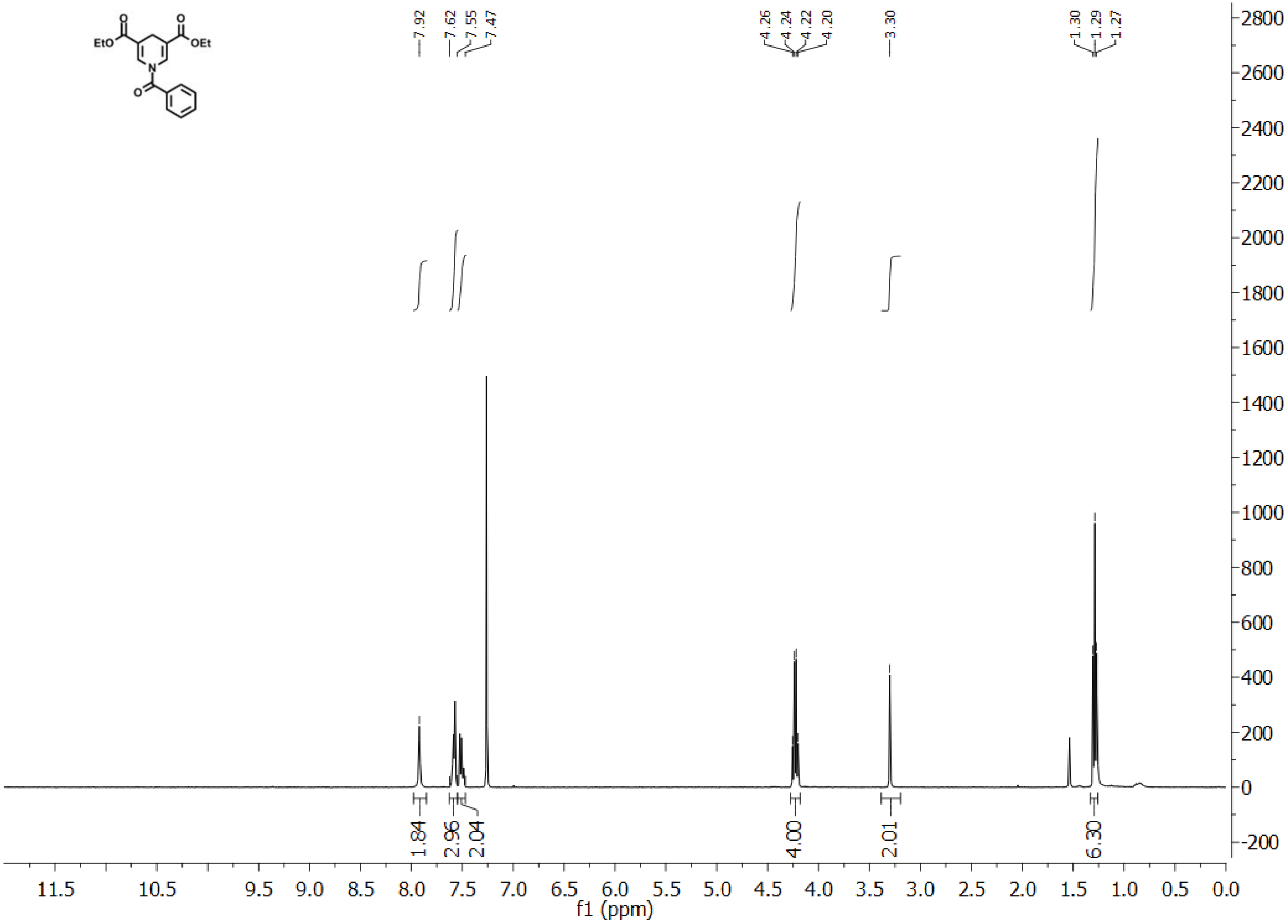


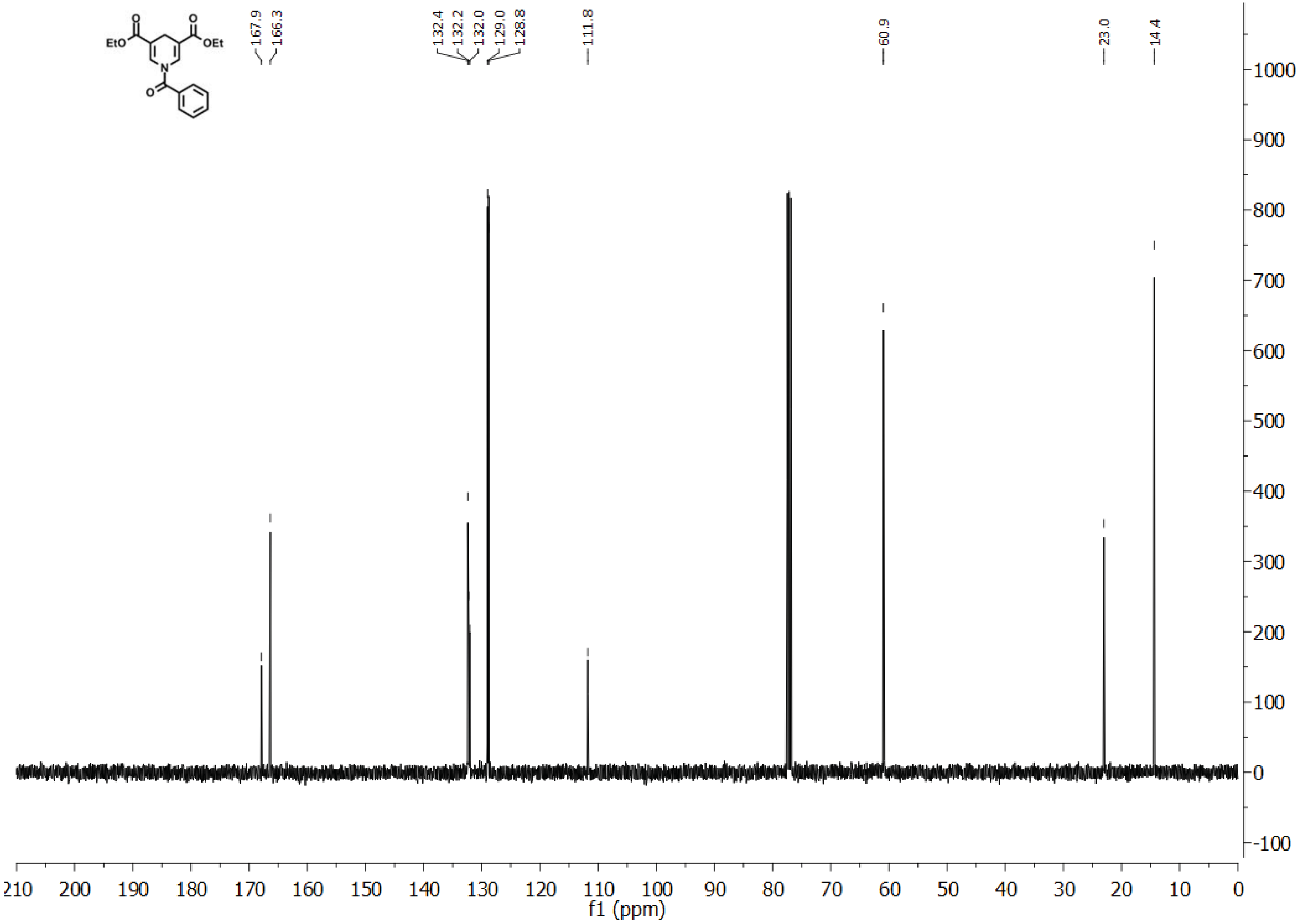
OMe
1.13
1.15
1.17
2.32
2.34
2.36
2.38
3.80
5.05
6.88
6.90
7.29
7.31
3.00
2.00
3.07
2.03
1.99
2.05
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.5
11.5
f1 (ppm)

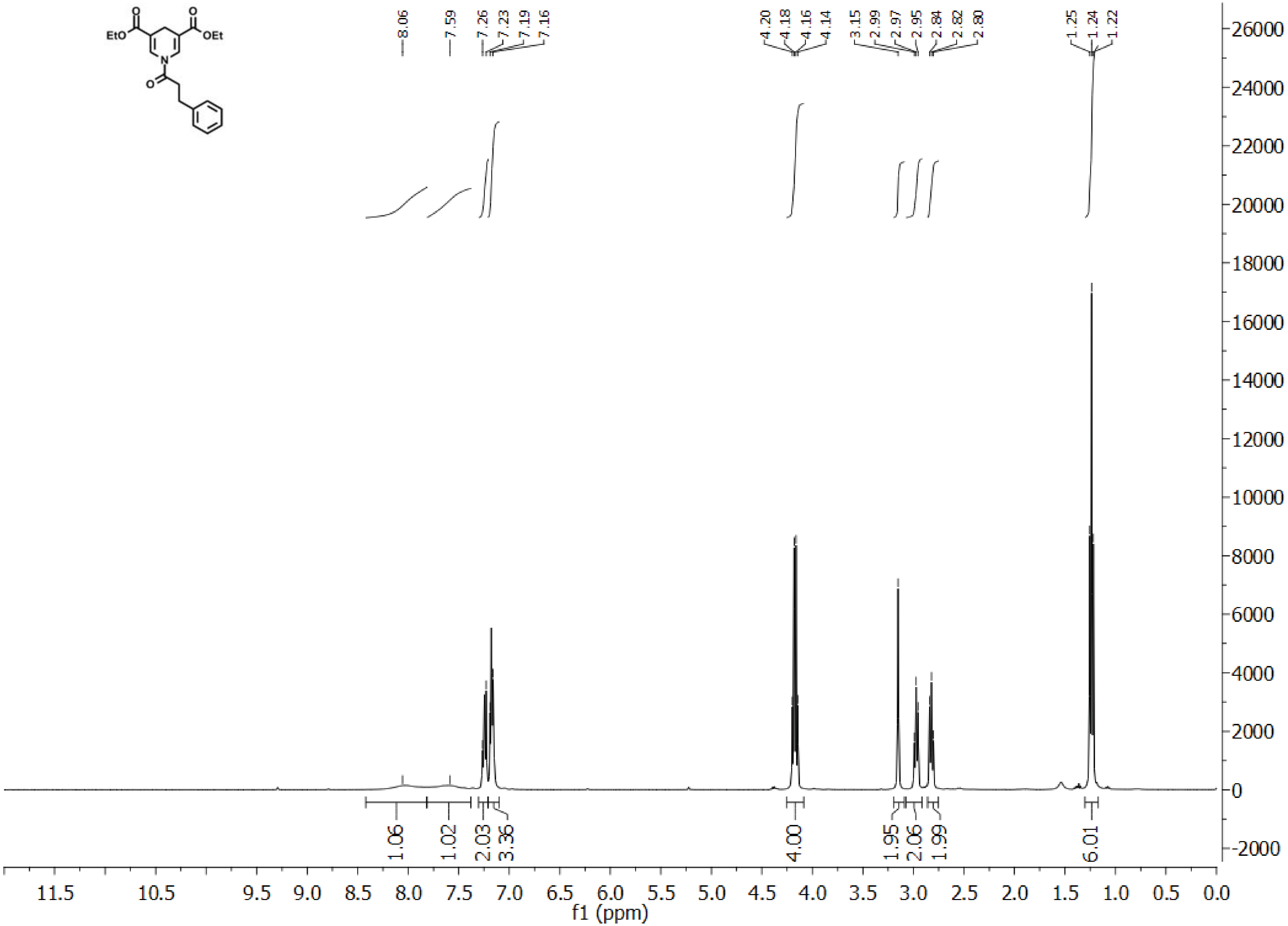

OMe
174.5
159.7
130.1
128.4
114.0
66.0
55.3
27.7
9.2
f1 (ppm)
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
2300
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200

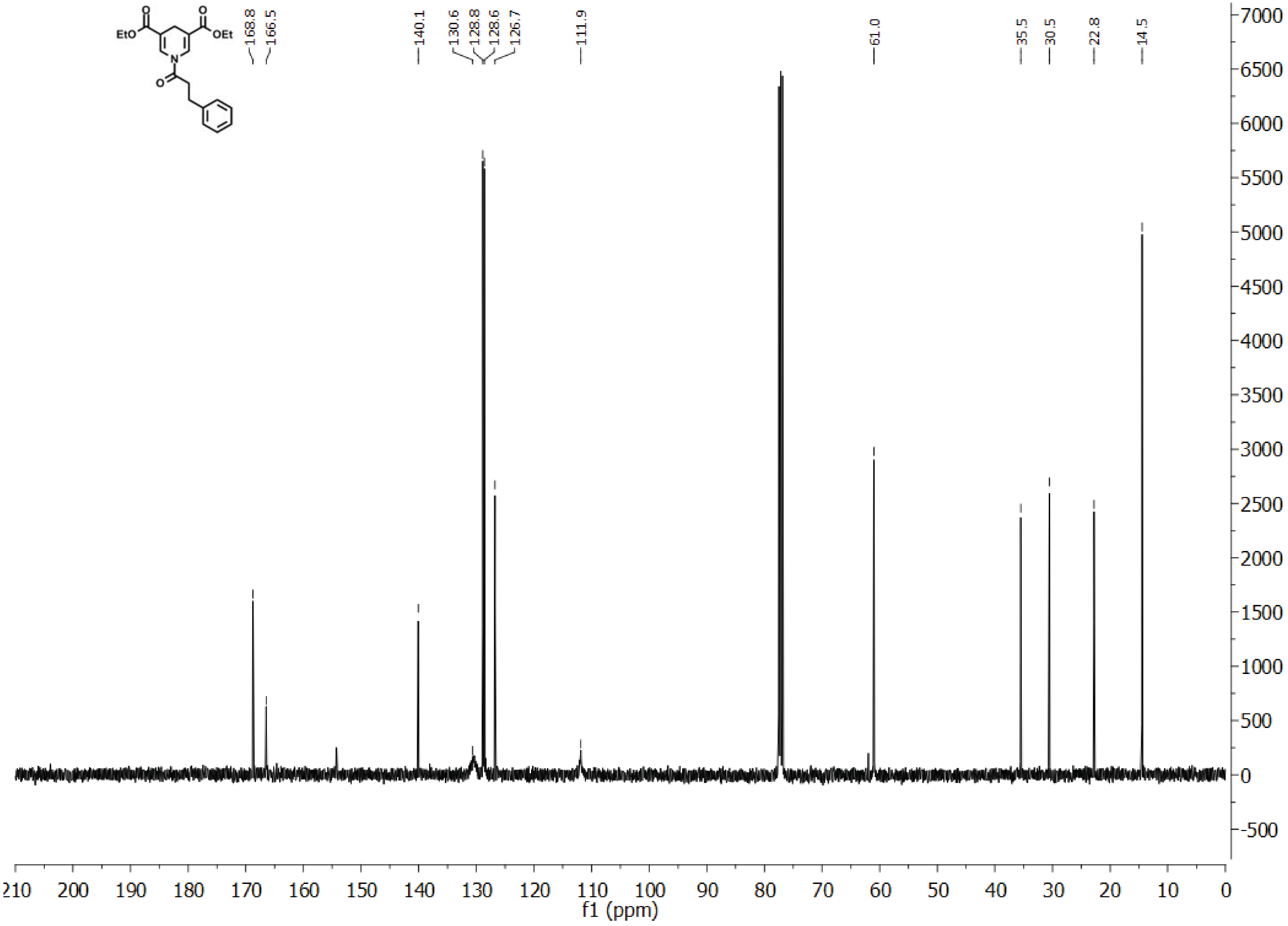

7.96
6.81
4.27
4.25
4.23
4.21
3.93
3.89
3.31
1.31
1.30
1.28
1.88
1.97
4.00
3.15
5.96
1.94
6.32
EtO
OEt
N
OMe
OMe
OMe
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200

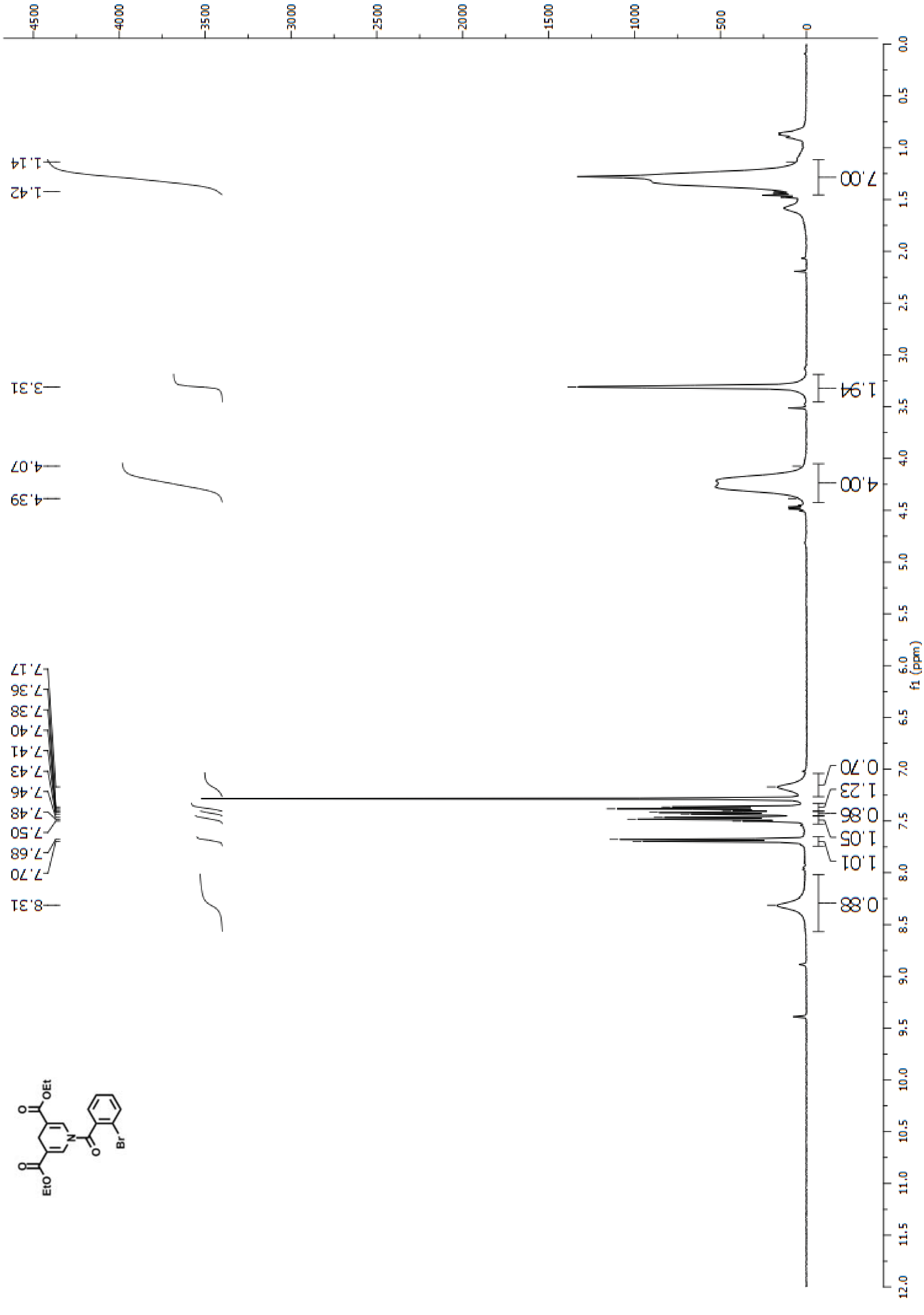

EtO
OEt
O
O
N
O
OMe
OMe
OMe
167.3
166.3
153.4
141.6
132.3
126.6
111.6
106.5
61.0
60.9
56.5
23.0
14.3
3500
3000
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

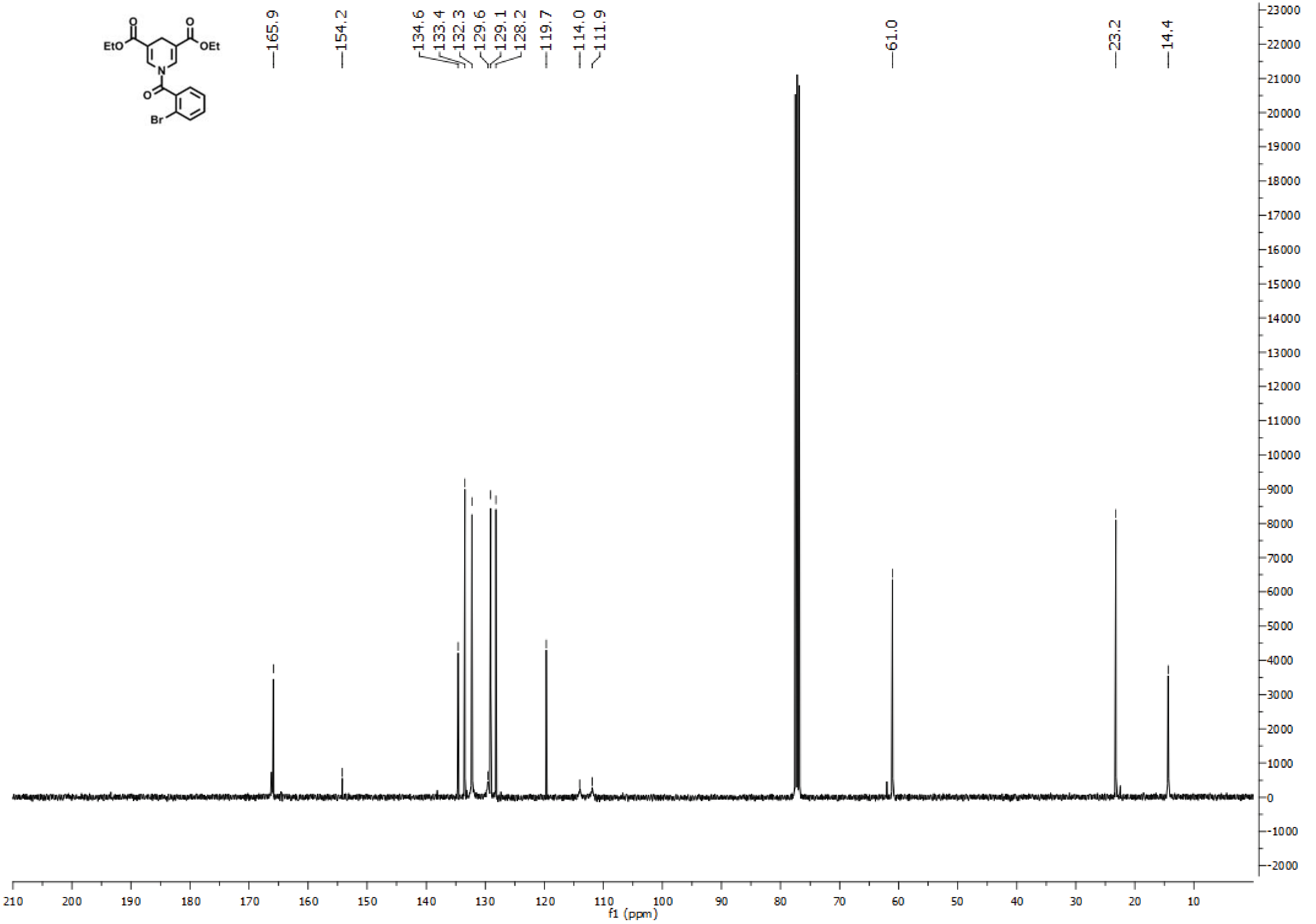

EtO
OEt
O
O
N
O
7.92
7.62
7.55
7.47
4.26
4.24
4.22
4.20
3.30
1.30
1.29
1.27
1.84
2.96
2.04
4.00
2.01
6.30
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

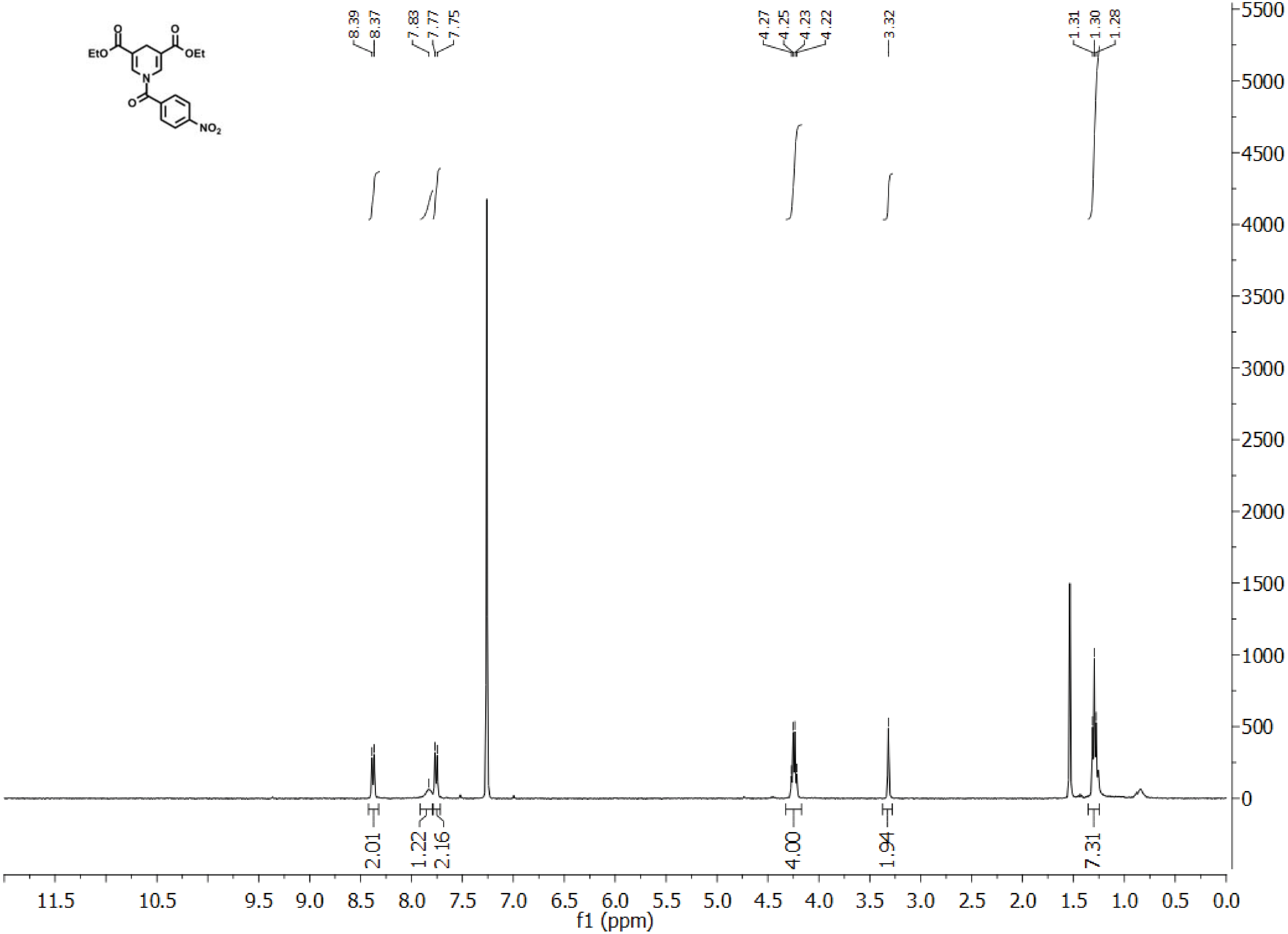

EtO
OEt
O
N
167.9
166.3
132.4
132.2
132.0
129.0
128.8
111.8
60.9
23.0
14.4
1000
900
800
700
600
500
400
300
200
100
0
-100
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

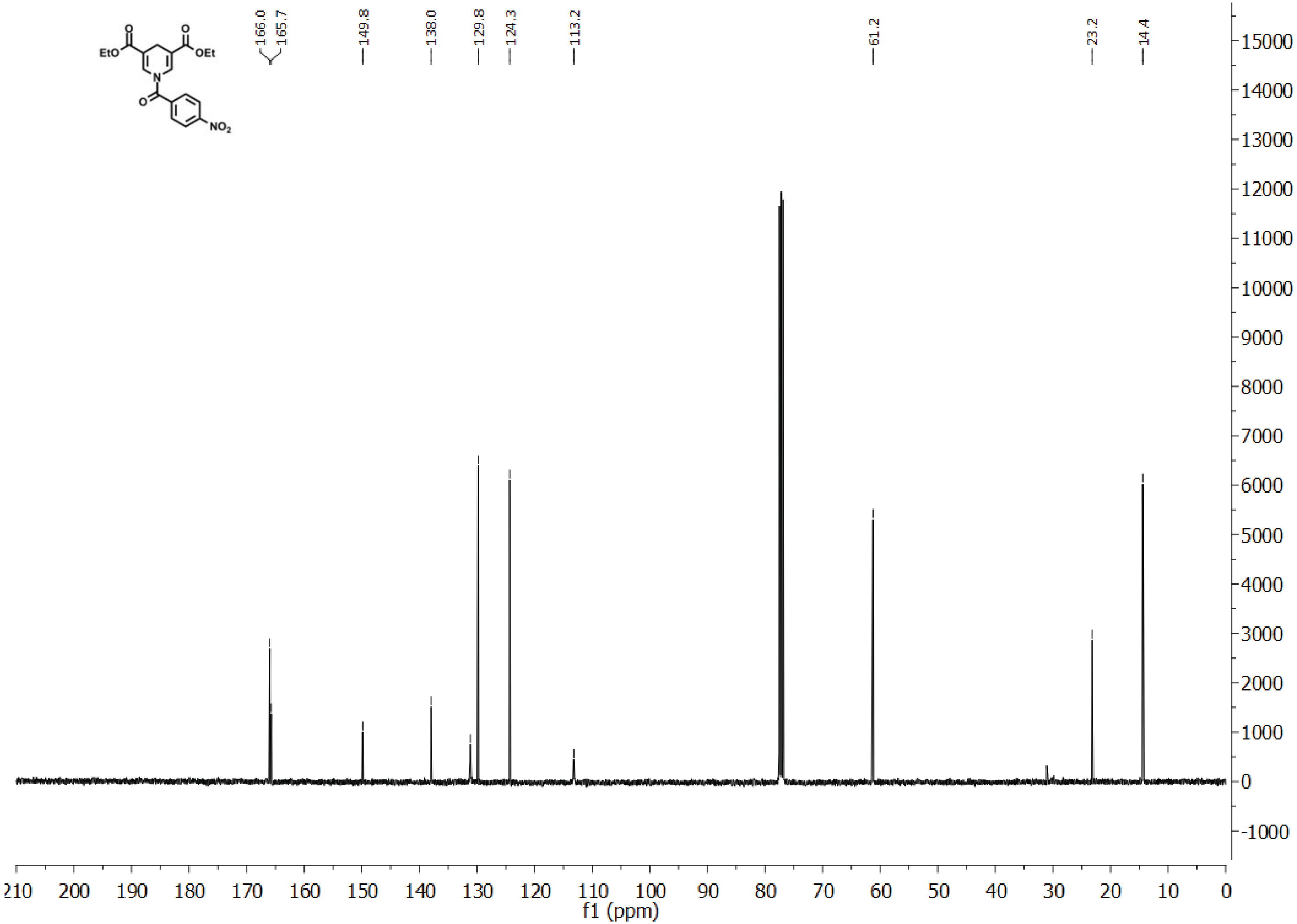

EtO
OEt
O
O
N
O
8.06
7.59
7.26
7.23
7.19
7.16
4.20
4.18
4.16
4.14
3.15
2.99
2.97
2.95
2.84
2.82
2.80
1.25
1.24
1.22
1.06
1.02
2.03
3.36
4.00
1.95
2.06
1.99
6.01
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


EtO
OEt
O
O
N
O
168.8
166.5
140.1
130.6
128.8
128.6
126.7
111.9
61.0
35.5
30.5
22.8
14.5
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

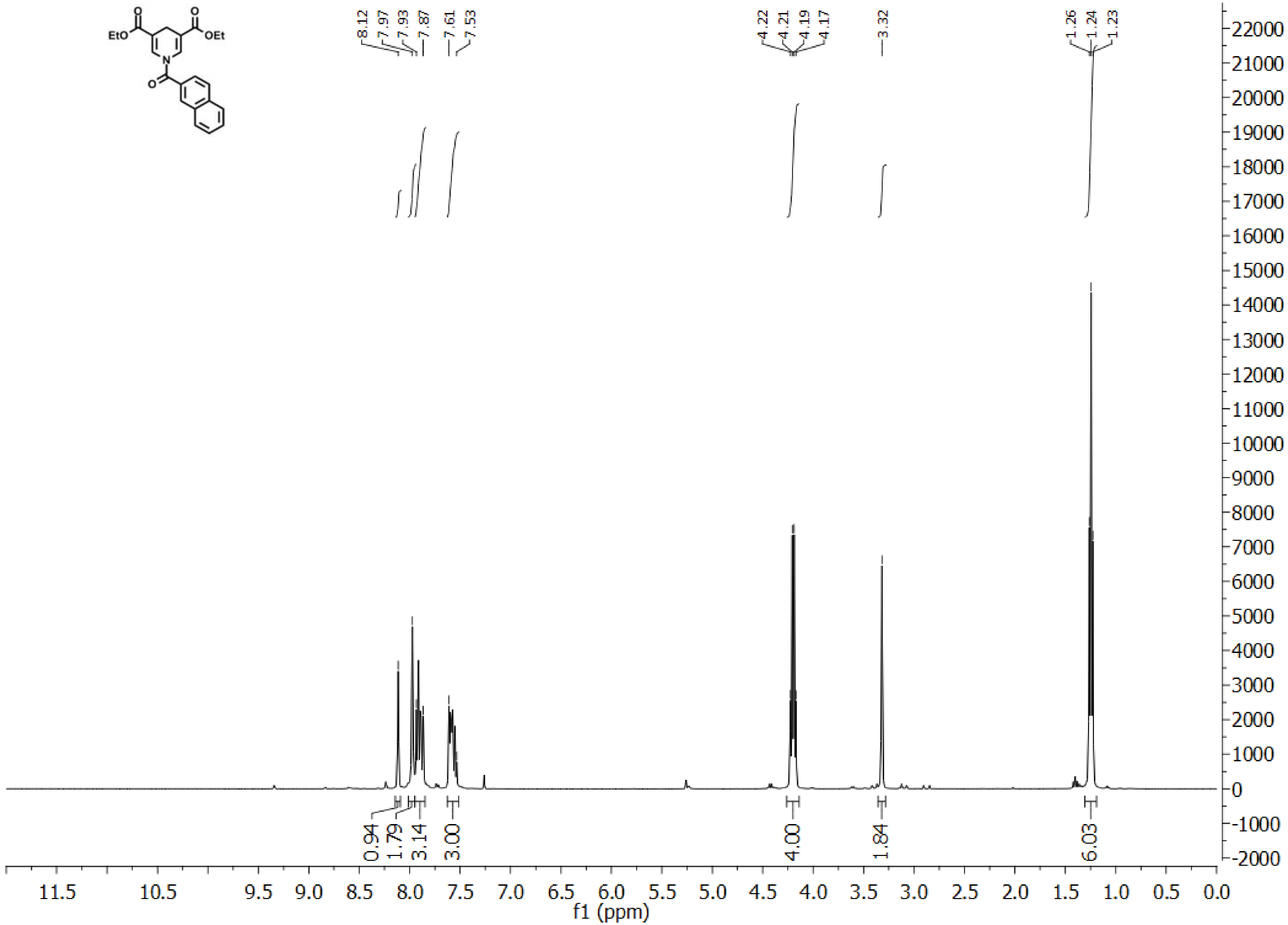

1.14
1.42
3.31
4.07
4.39
7.17
7.36
7.38
7.40
7.41
7.43
7.46
7.48
7.50
7.68
7.70
8.31
7.00
1.94
4.00
0.70
1.23
0.86
1.05
1.01
0.88
f1 (ppm)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.0
10.5
11.0
11.5
12.0
0
500
1000
1500
2000
2500
3000
3500
4000
4500
EtO
OEt
O
O
N
O
Br

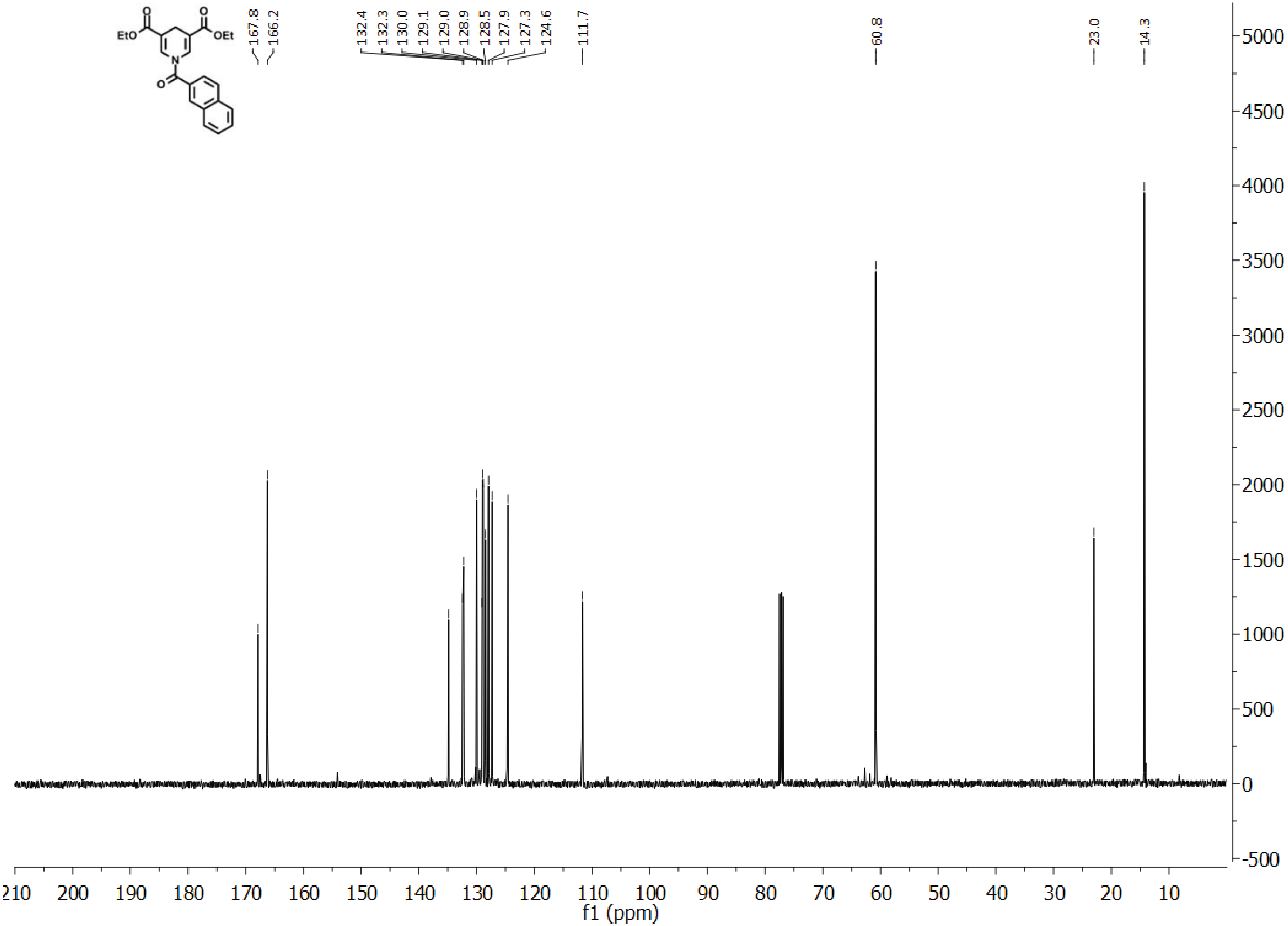

EtO
O
O
OEt
N
O
Br
165.9
154.2
134.6
133.4
132.3
129.6
129.1
128.2
119.7
114.0
111.9
61.0
23.2
14.4
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

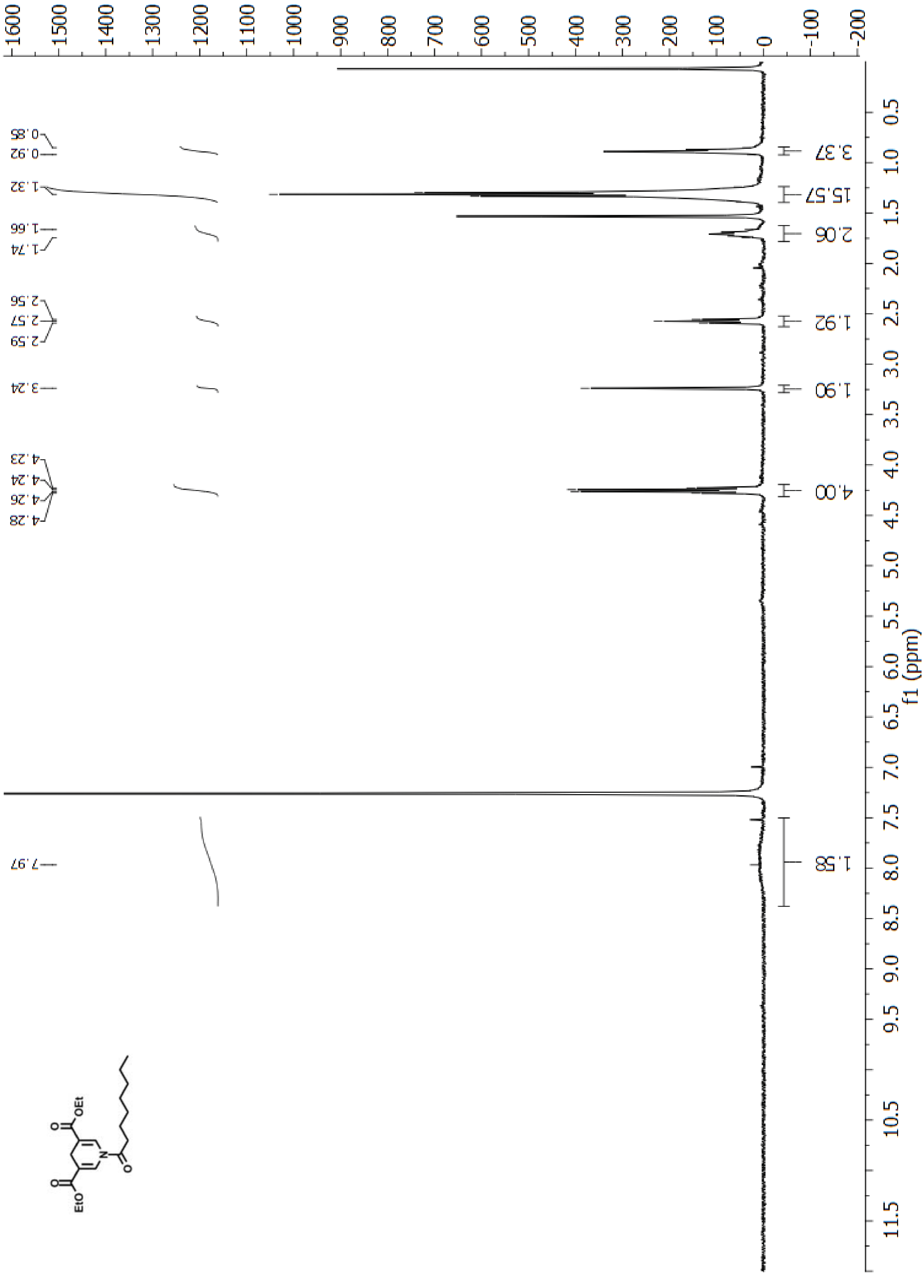

EtO
OEt
N
O
NO2
8.39
8.37
7.83
7.77
7.75
4.27
4.25
4.23
4.22
3.32
1.31
1.30
1.28
2.01
1.22
2.16
4.00
1.94
7.31
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

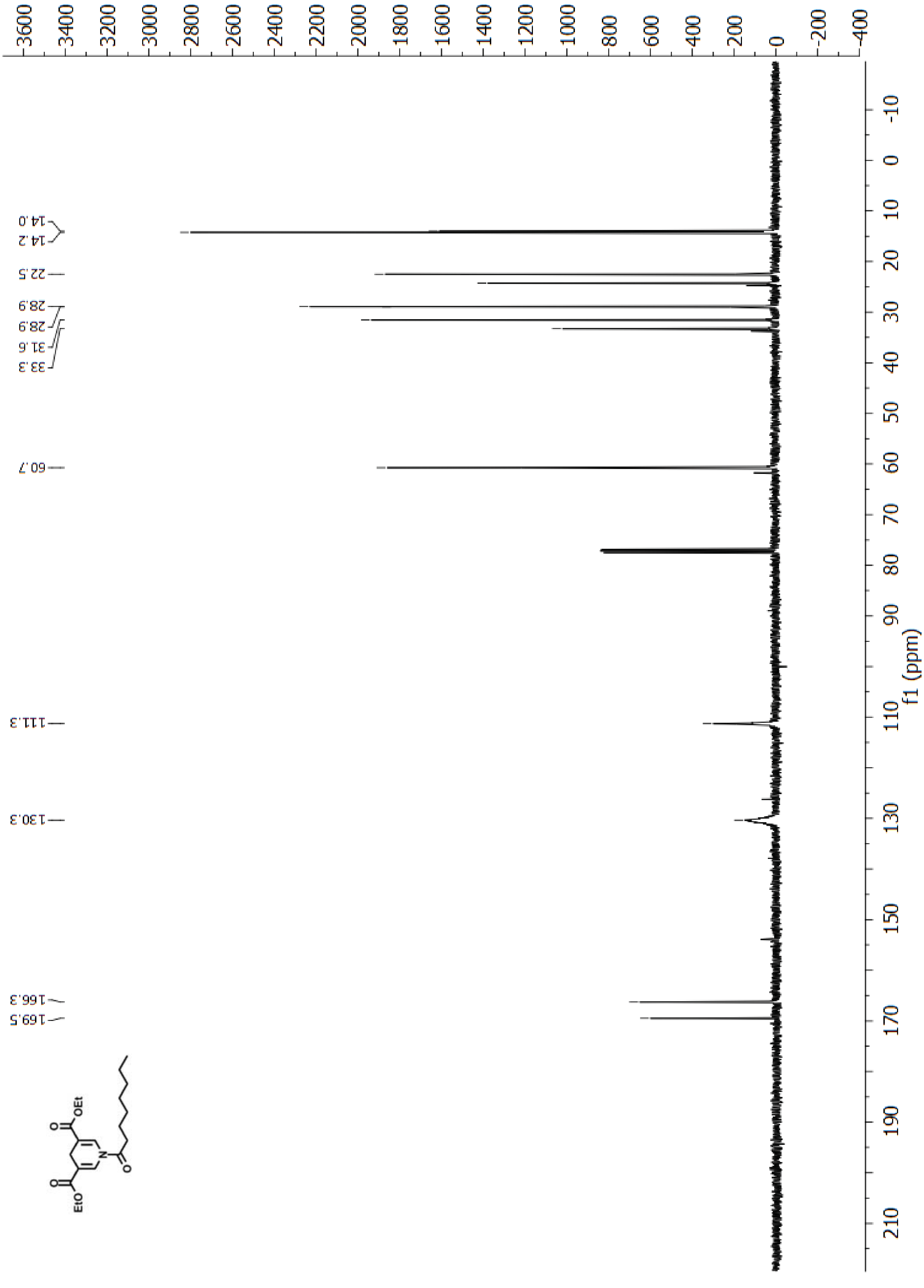


EtO
OEt
O
O
N
O
NO$_2$
166.0
165.7
149.8
138.0
129.8
124.3
113.2
61.2
23.2
14.4
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

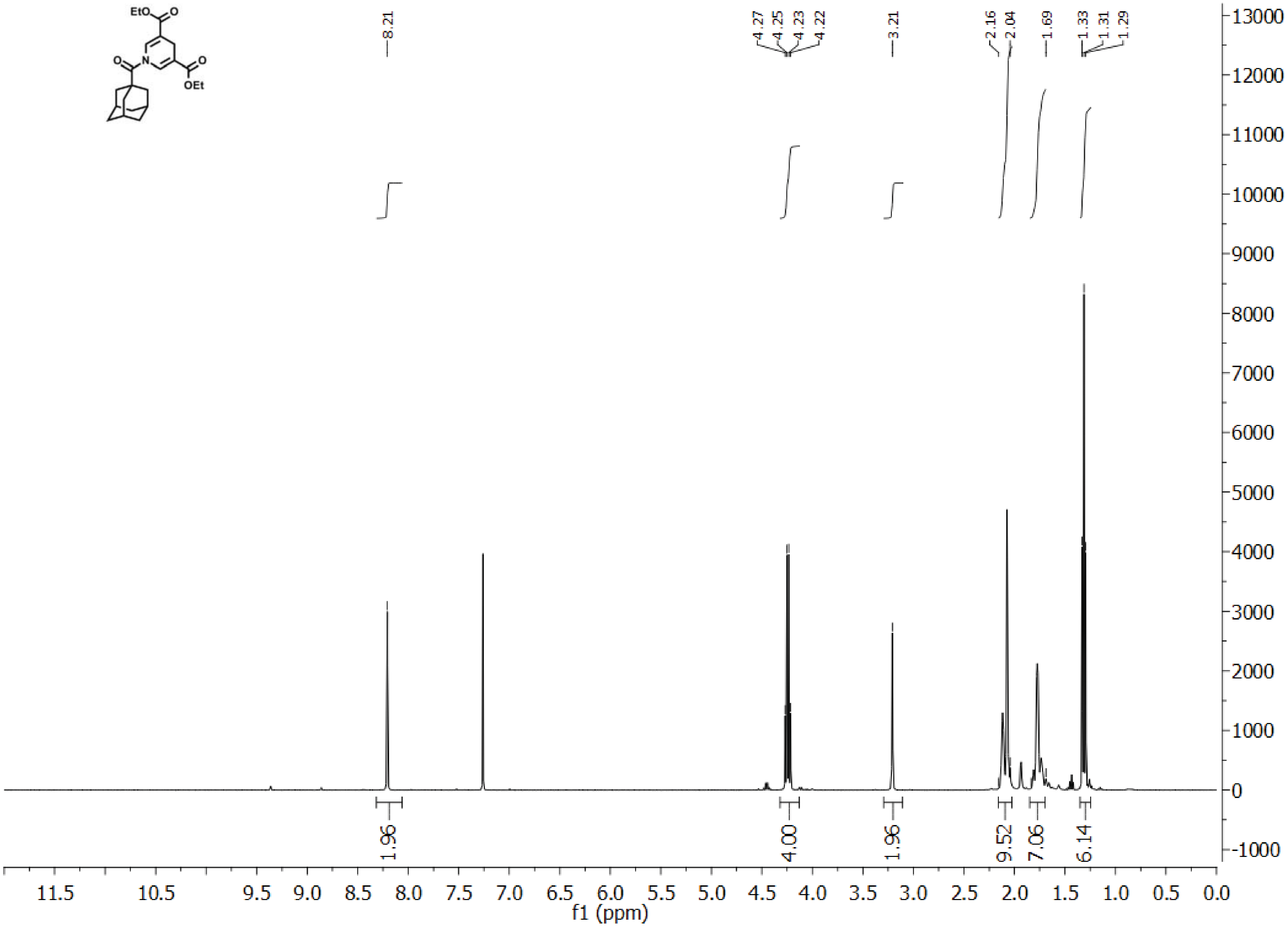

EtO
OEt
N
O
O
O
8.12
7.97
7.93
7.87
7.61
7.53
4.22
4.21
4.19
4.17
3.32
1.26
1.24
1.23
0.94
1.79
3.14
3.00
4.00
1.84
6.03
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

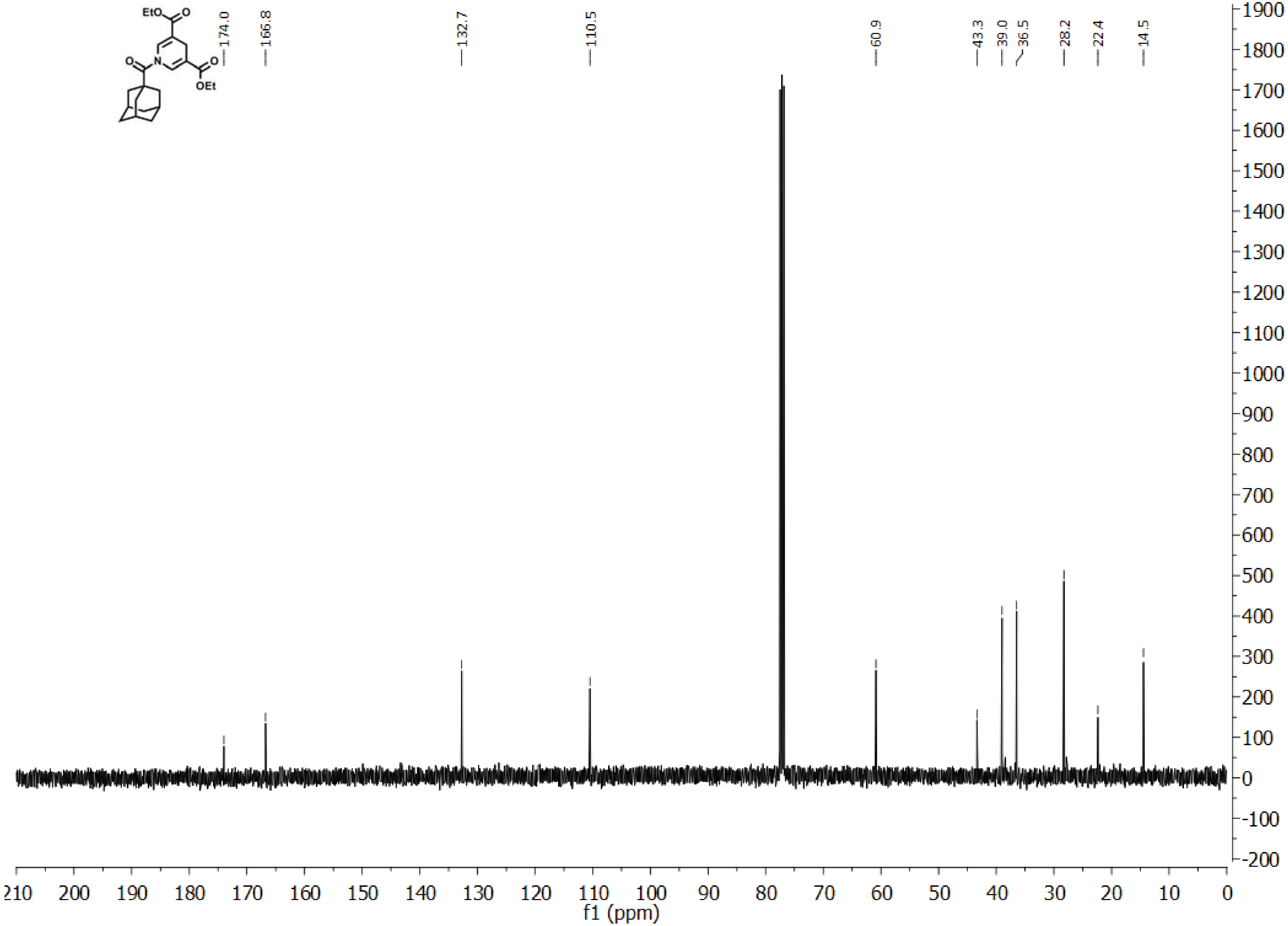

EtO
OEt
N
O
167.8
166.2
132.4
132.3
130.0
129.1
129.0
128.9
128.5
127.9
127.3
124.6
111.7
60.8
23.0
14.3
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

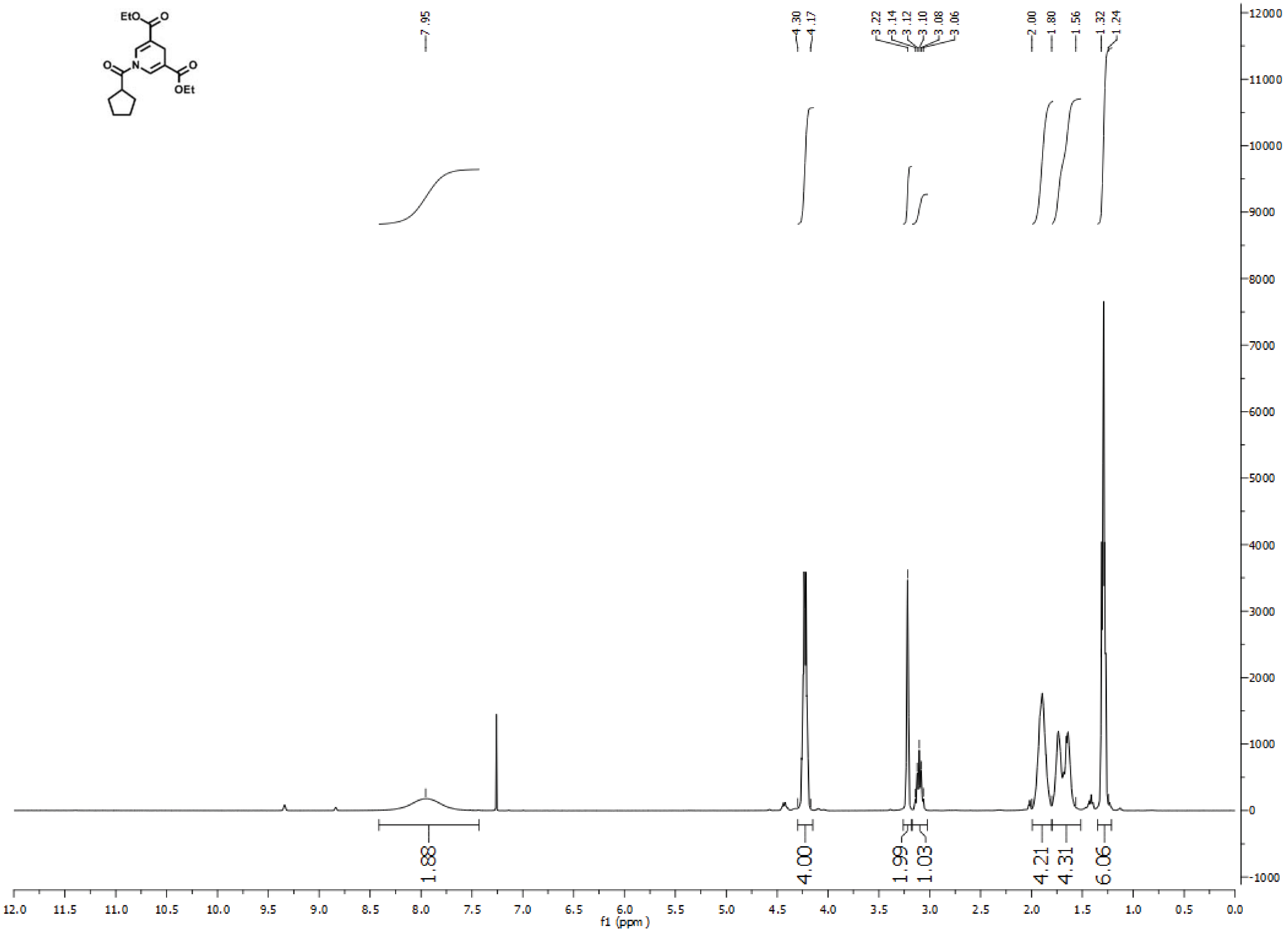
7.97
4.28
4.26
4.24
4.23
3.24
2.59
2.57
2.56
1.74
1.66
1.32
0.92
0.85
1.58
4.00
1.90
1.92
2.06
15.57
3.37
EtO
O
O
OEt
N
O
f1 (ppm)
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200

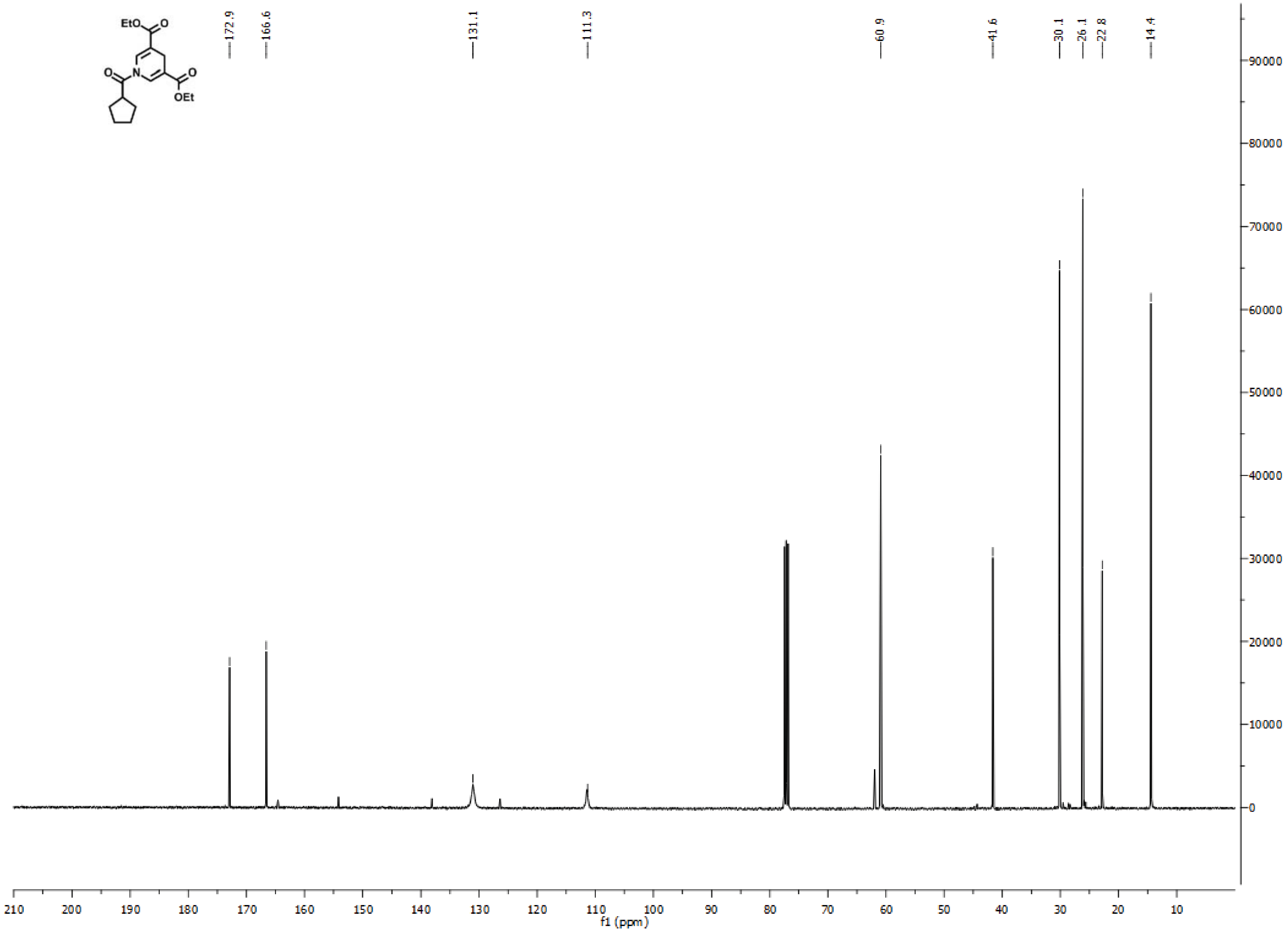


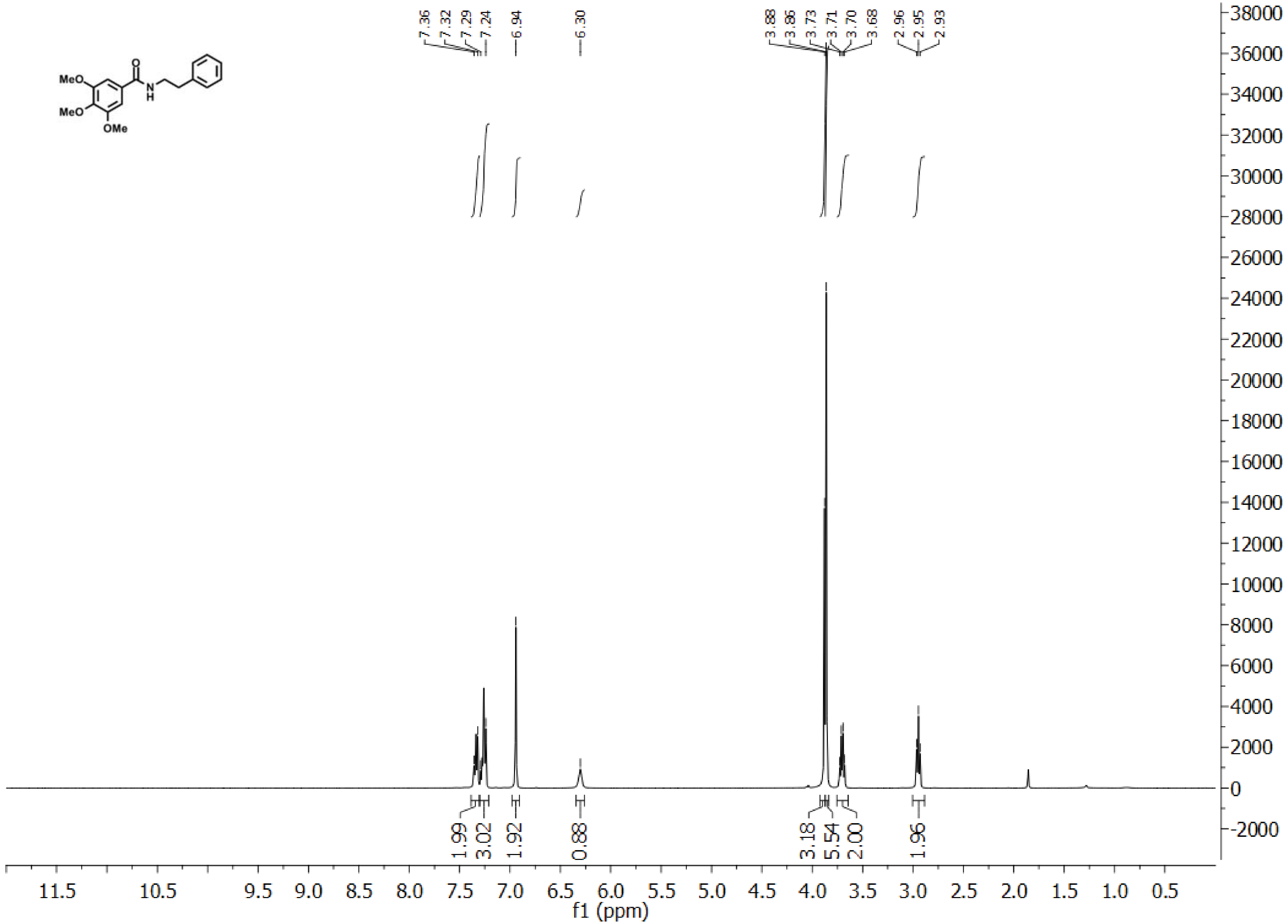
14.0
14.2
22.5
28.9
28.9
31.6
33.3
60.7
111.3
130.3
166.3
169.5
EtO
OEt
O
O
N
O
f1 (ppm)
-10
0
10
20
30
40
50
60
70
80
90
110
130
150
170
190
210
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
-400

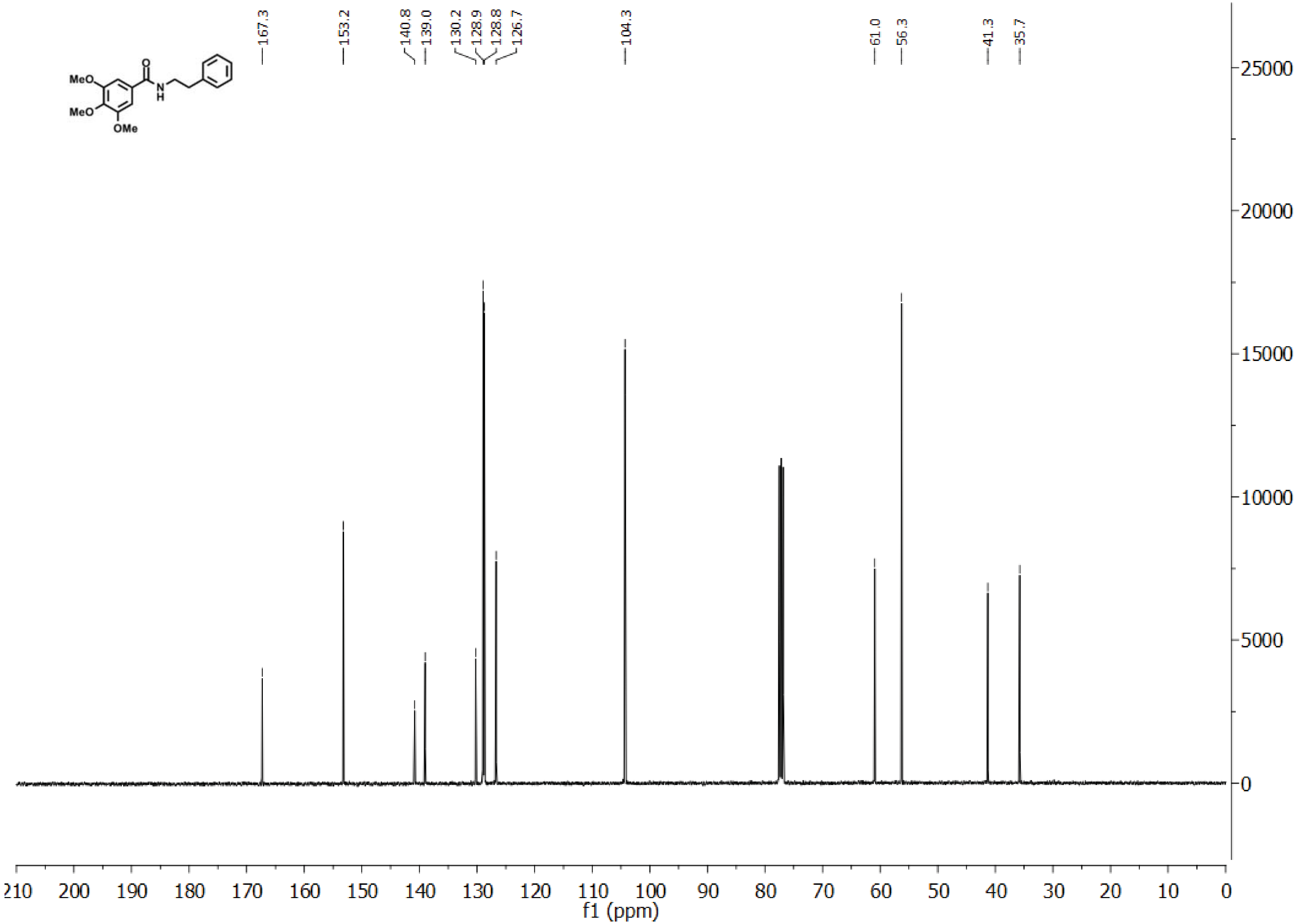

EtO
O
N
O
O
OEt
8.21
4.27
4.25
4.23
4.22
3.21
2.16
2.04
1.69
1.33
1.31
1.29
1.96
4.00
1.96
9.52
7.06
6.14
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


EtO
O
N
O
O
OEt
174.0
166.8
132.7
110.5
60.9
43.3
39.0
36.5
28.2
22.4
14.5
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

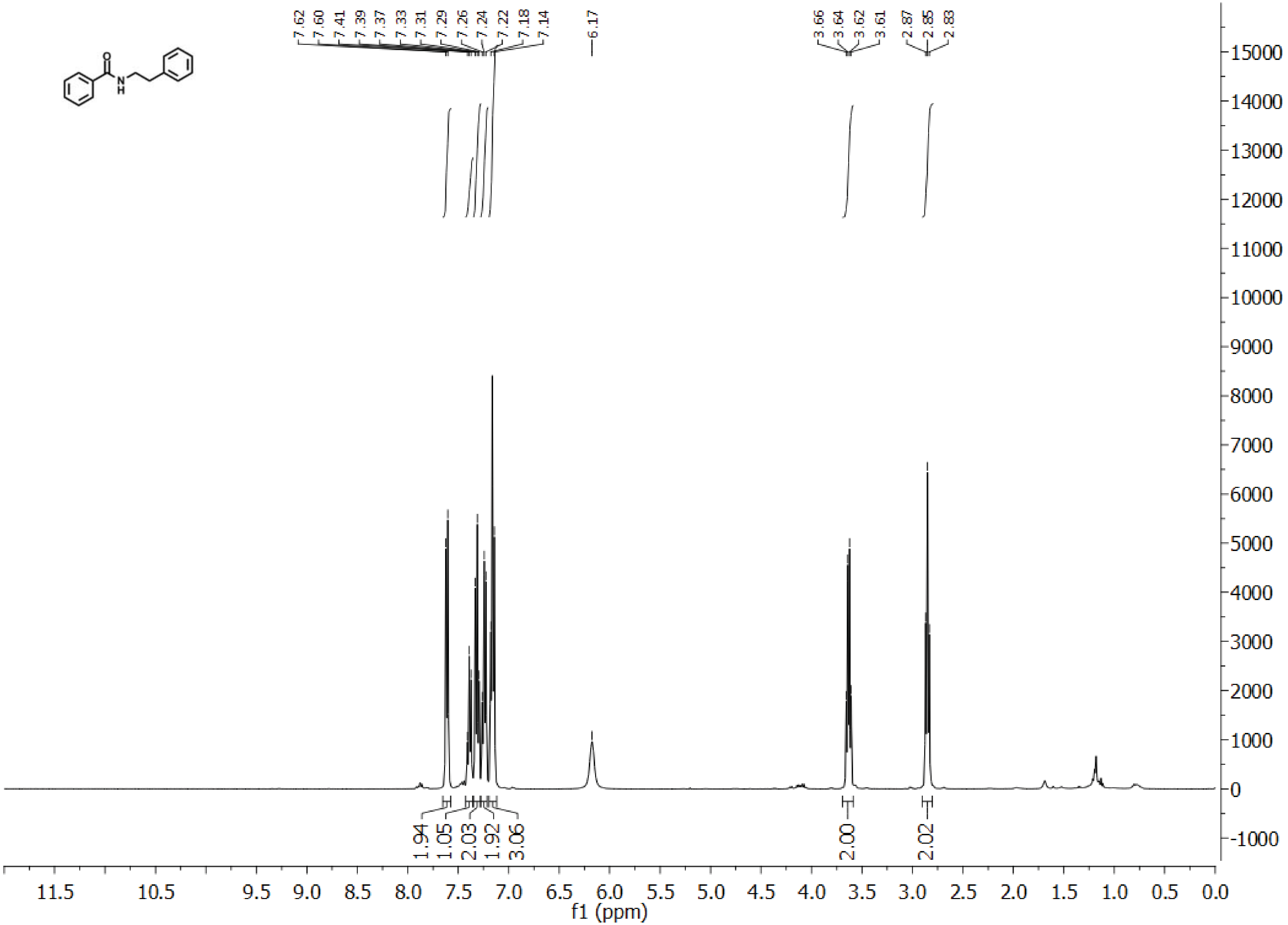

EtO
O
N
O
OEt
7.95
4.30
4.17
3.22
3.14
3.12
3.10
3.08
3.06
2.00
1.80
1.56
1.32
1.24
1.88
4.00
1.99
1.03
4.21
4.31
6.06
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000


EtO
O
N
O
O
OEt
172.9
166.6
131.1
111.3
60.9
41.6
30.1
26.1
22.8
14.4
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

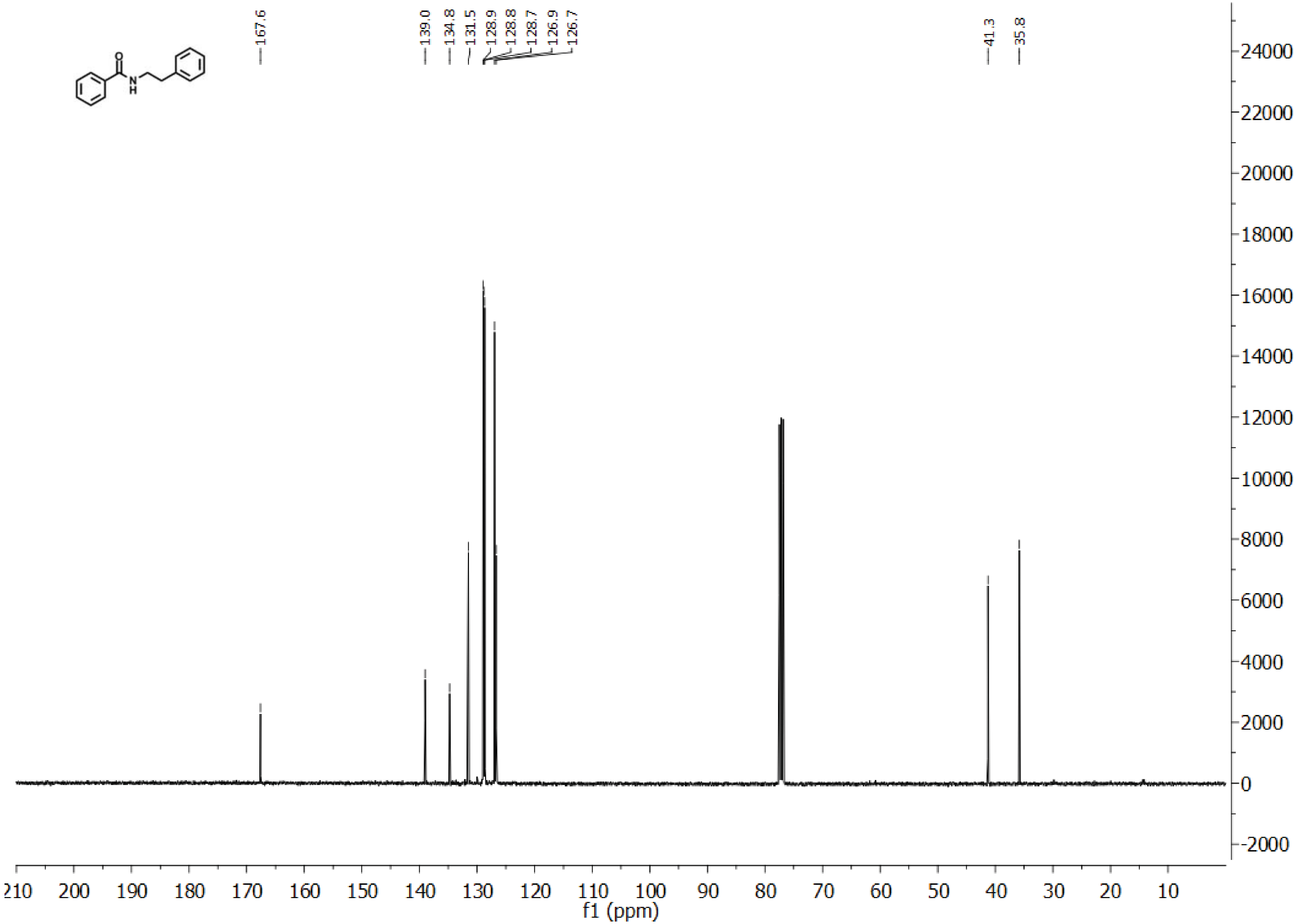

MeO
MeO
OMe
O
N
H
7.36
7.32
7.29
7.24
6.94
6.30
3.88
3.86
3.73
3.71
3.70
3.68
2.96
2.95
2.93
1.99
3.02
1.92
0.88
3.18
5.54
2.00
1.96
38000
36000
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

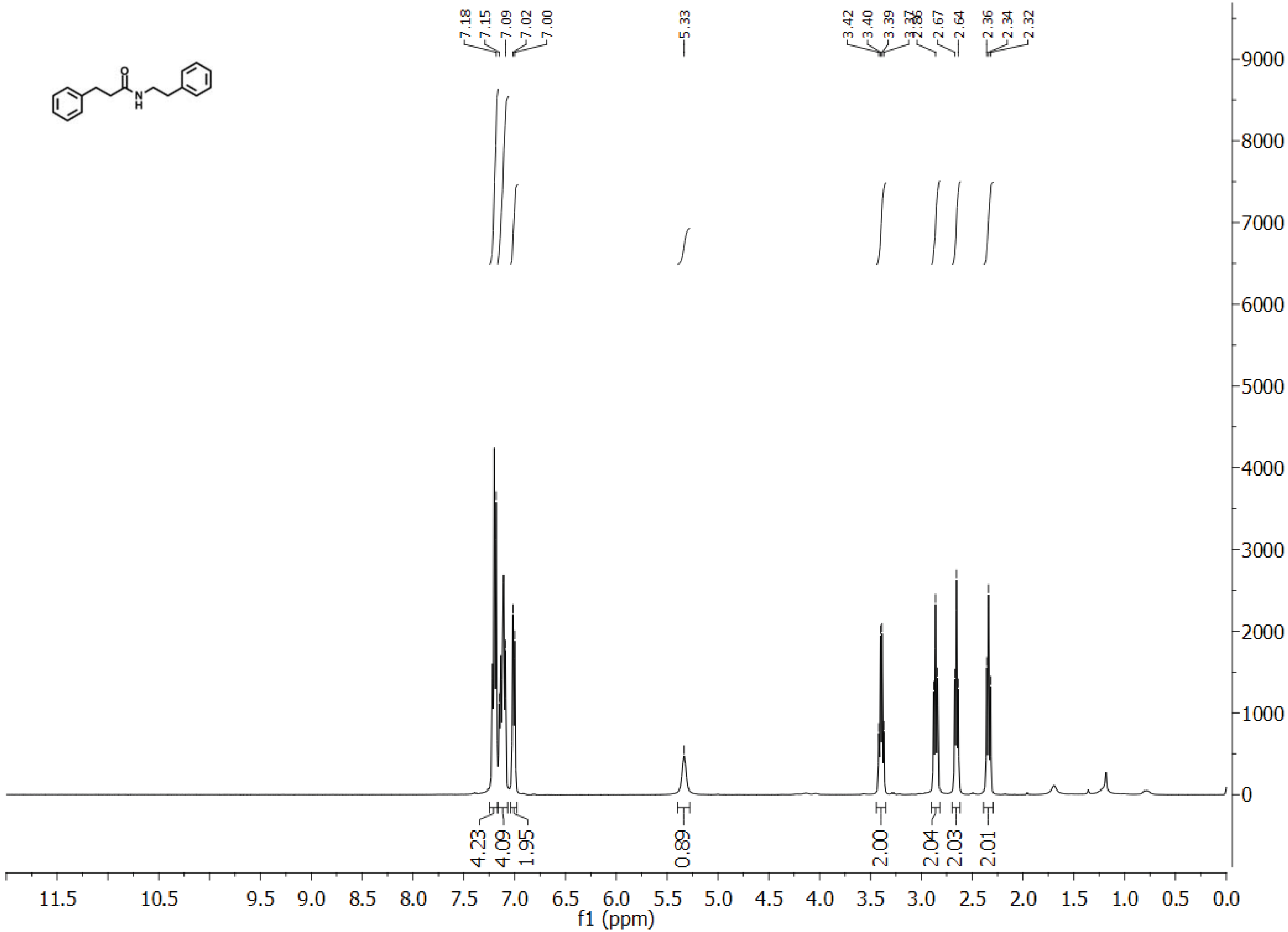


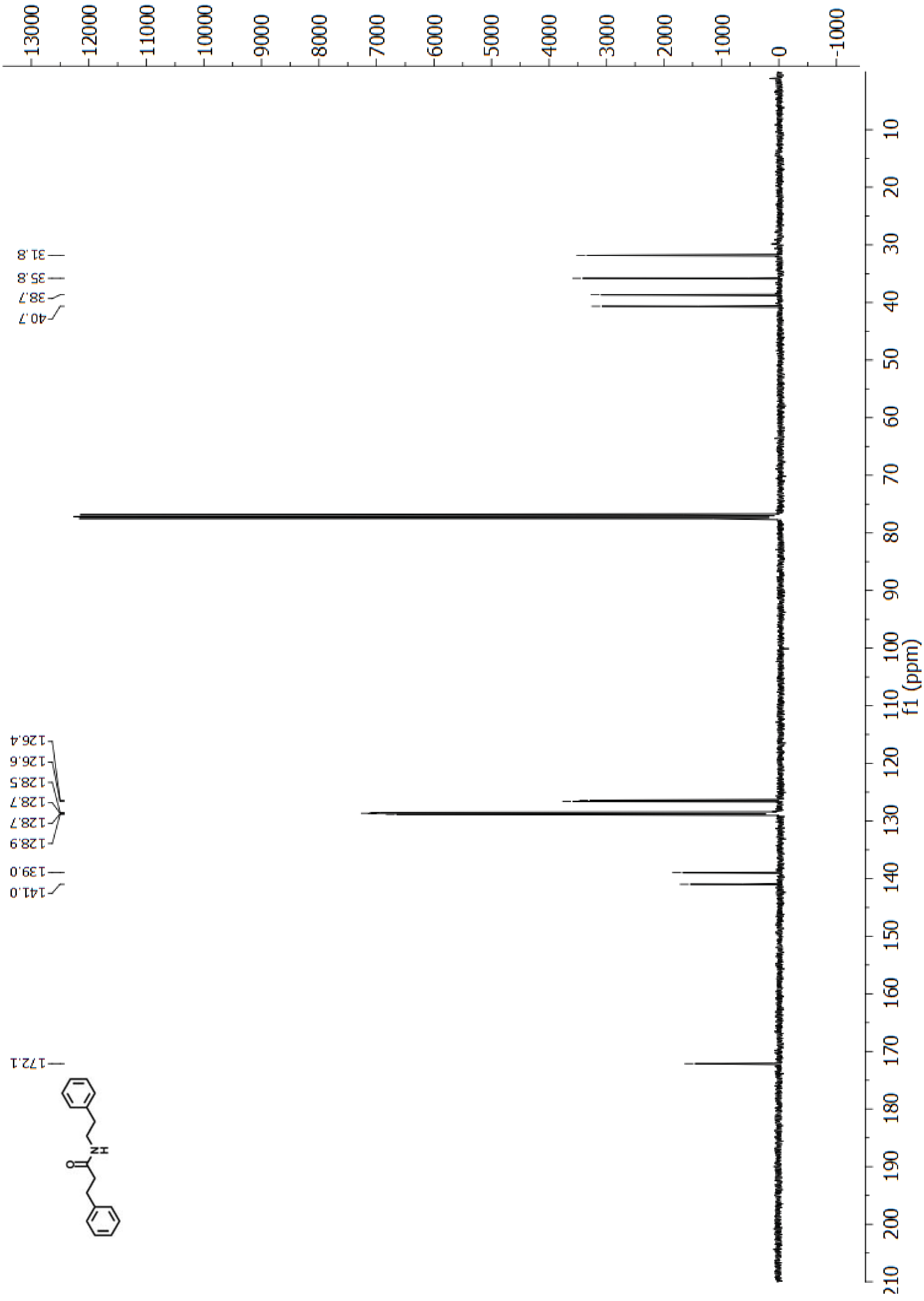
167.3
153.2
140.8
139.0
130.2
128.9
128.8
126.7
104.3
61.0
56.3
41.3
35.7
MeO
MeO
OMe
O
N
H
25000
20000
15000
10000
5000
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



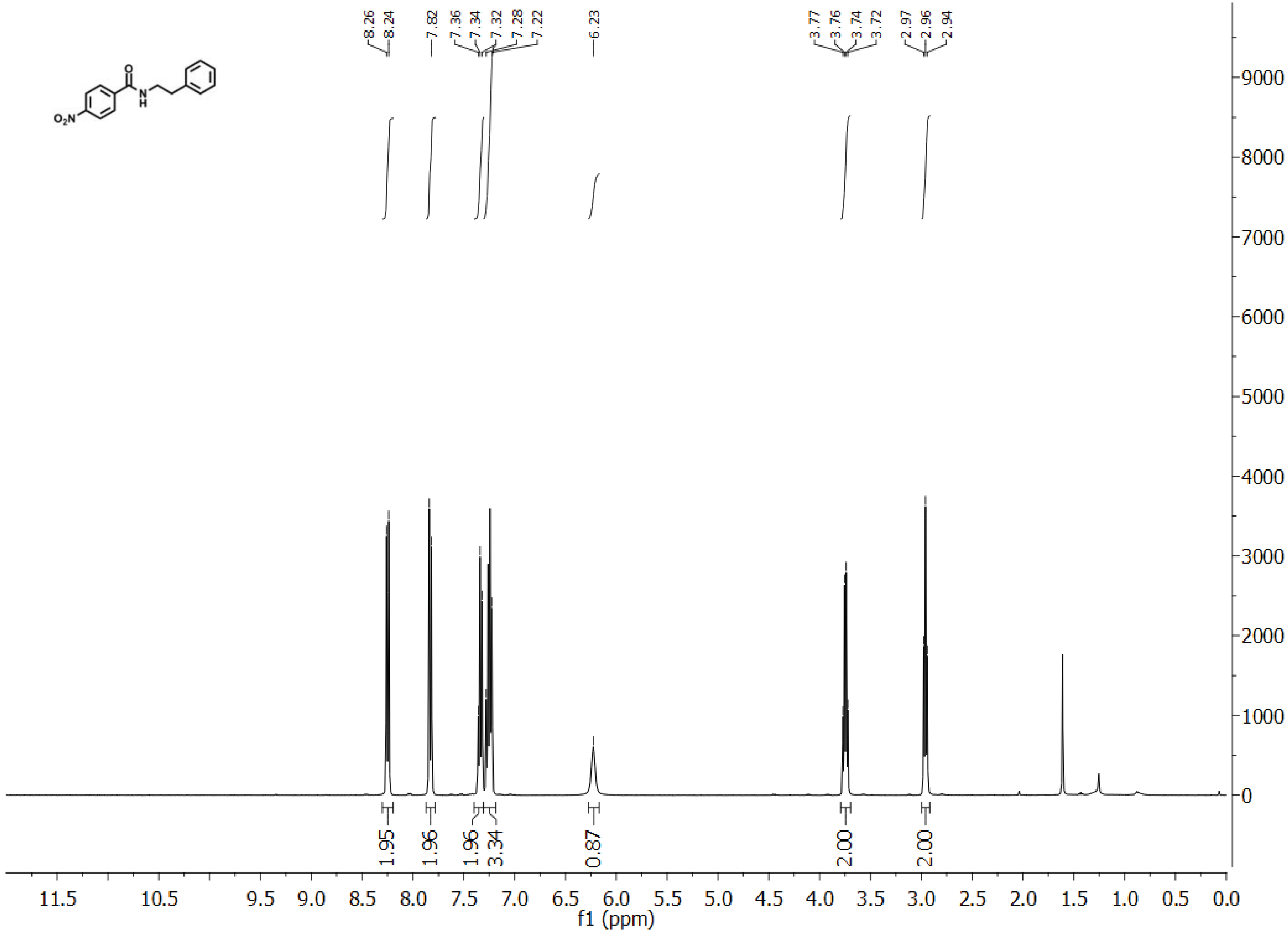
7.62
7.60
7.41
7.39
7.37
7.33
7.31
7.29
7.26
7.24
7.22
7.18
7.14
6.17
3.66
3.64
3.62
3.61
2.87
2.85
2.83
O
N
H
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
1.94
1.05
2.03
1.92
3.06
2.00
2.02
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

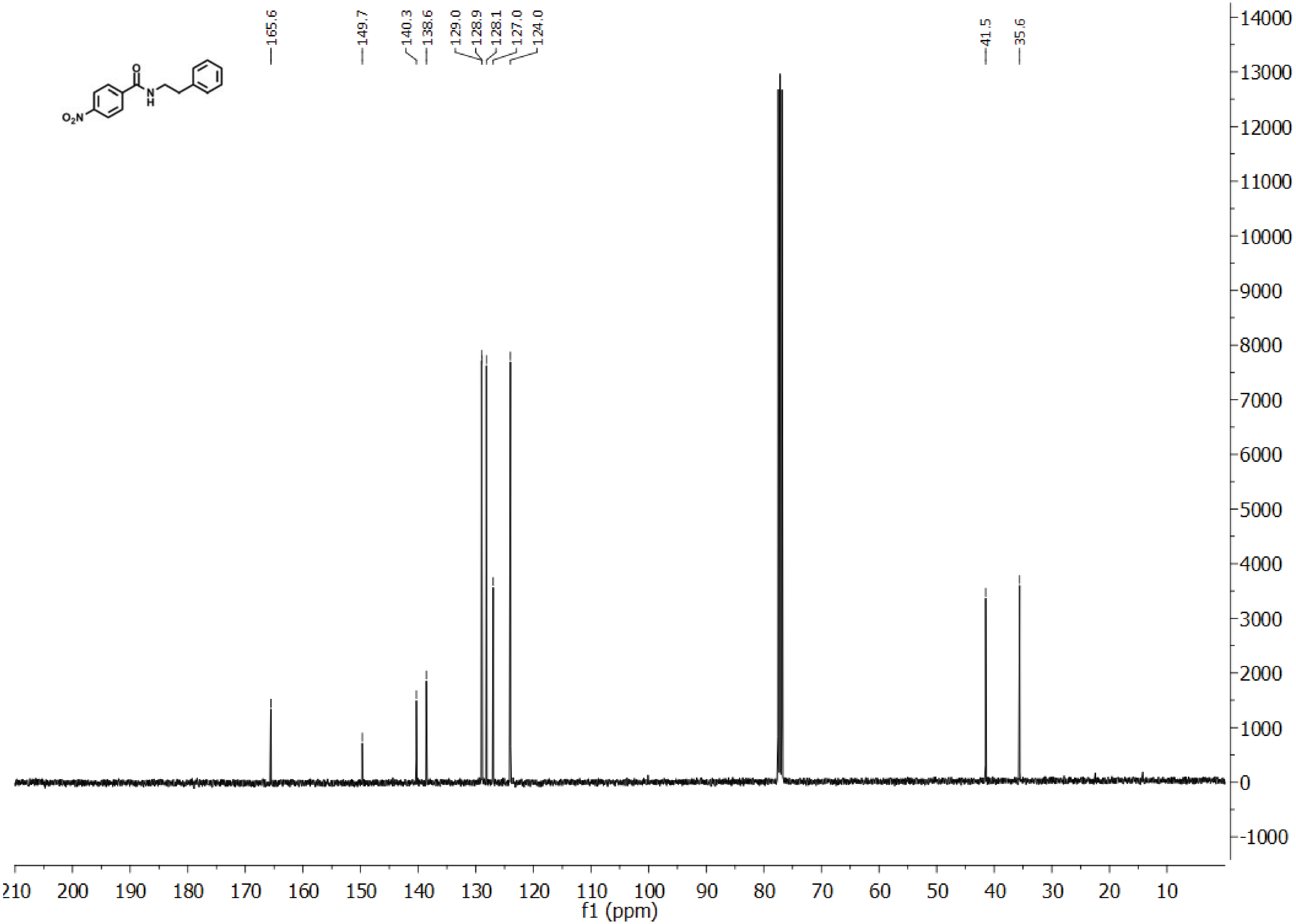

167.6
139.0
134.8
131.5
128.9
128.8
128.7
126.9
126.7
41.3
35.8
N
H
O
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

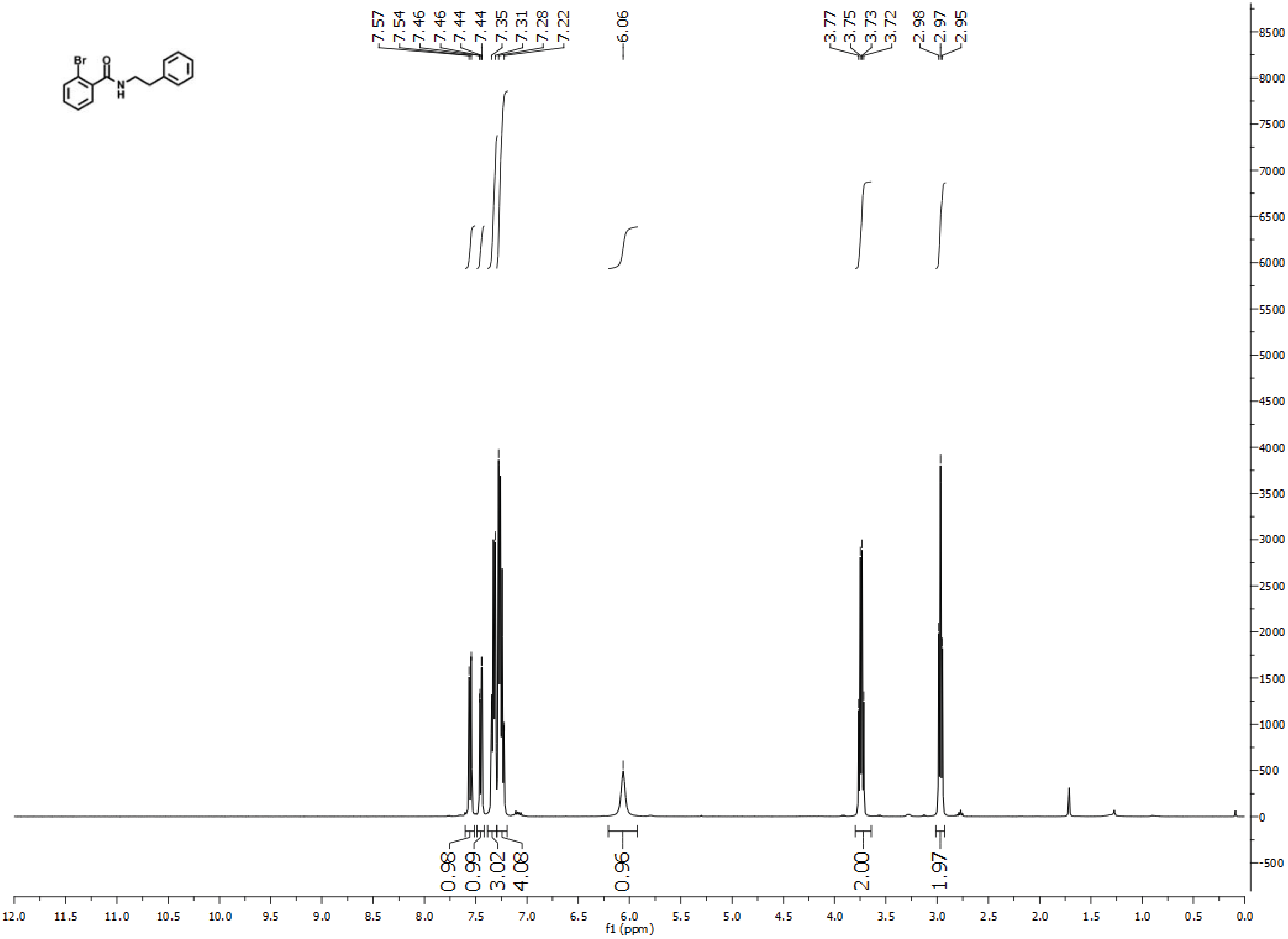

7.18
7.15
7.09
7.02
7.00
5.33
3.42
3.40
3.39
3.37
2.86
2.67
2.64
2.36
2.34
2.32
O
N
H
4.23
4.09
1.95
0.89
2.00
2.04
2.03
2.01
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

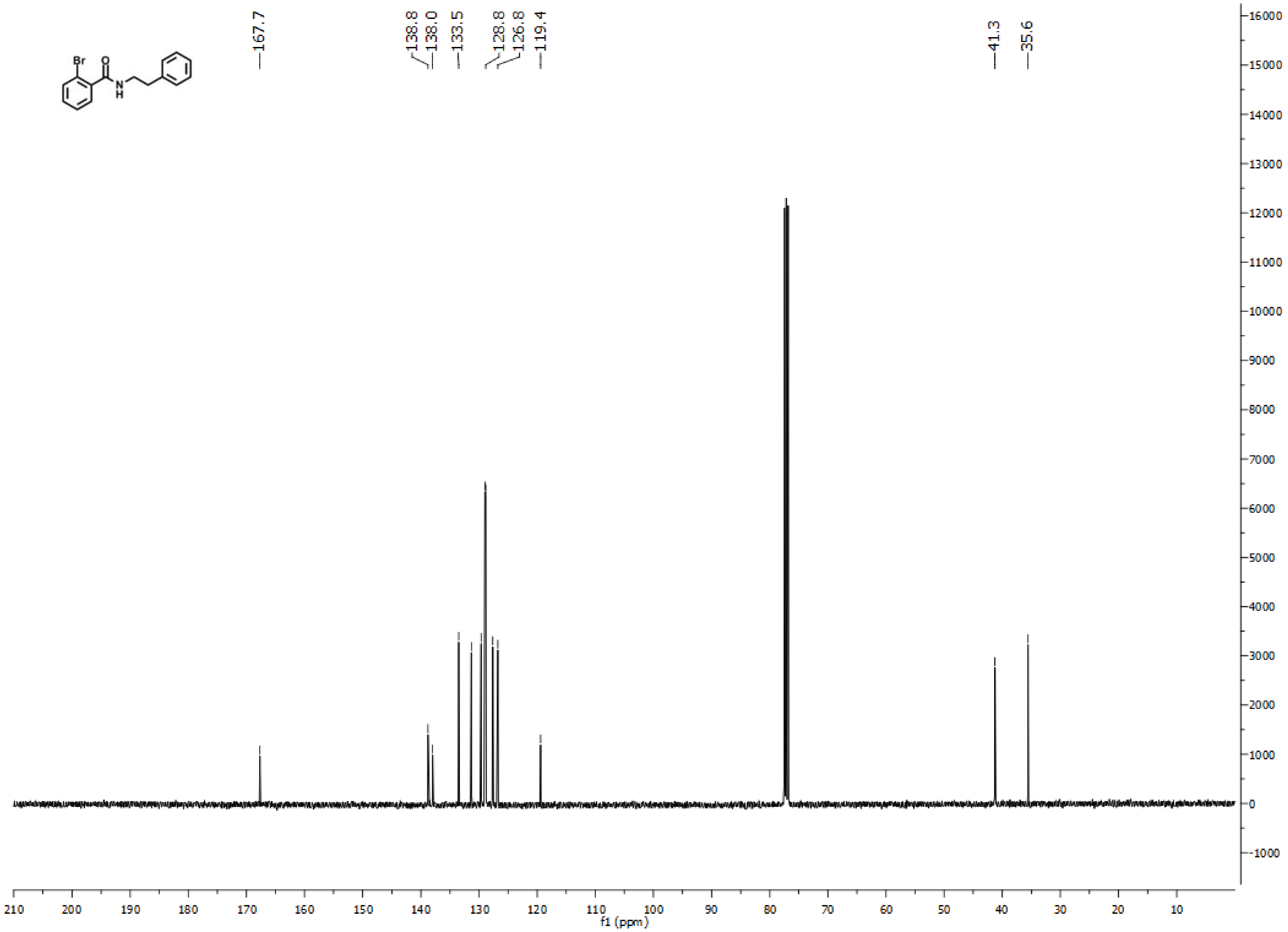


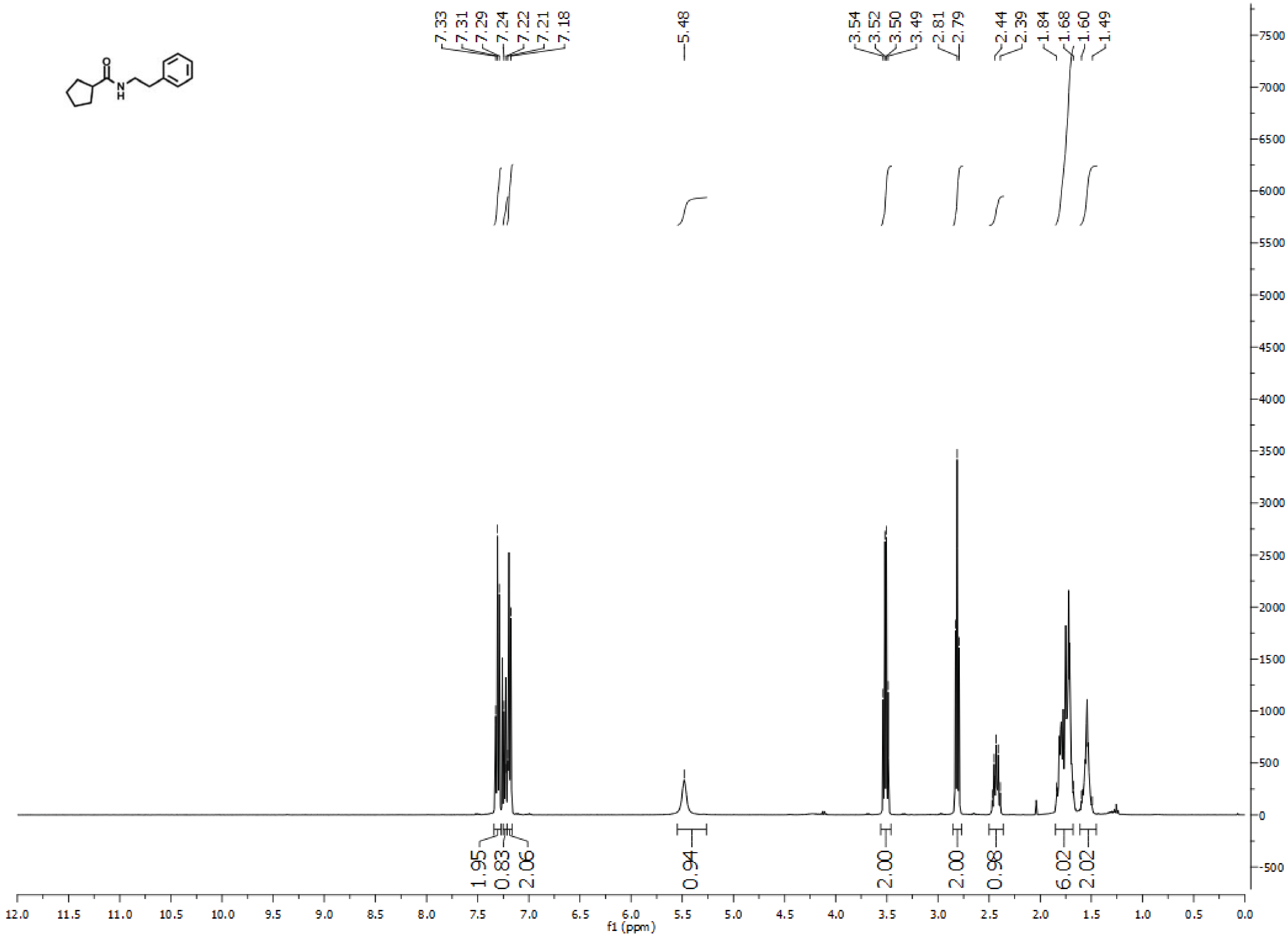
172.1
141.0
139.0
128.9
128.7
128.7
128.5
126.6
126.4
40.7
38.7
35.8
31.8
O
N
H
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000


8.26
8.24
7.82
7.36
7.34
7.32
7.28
7.22
6.23
3.77
3.76
3.74
3.72
2.97
2.96
2.94
O$_2$N
O
N
H
1.95
1.96
1.96
3.34
0.87
2.00
2.00
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


O2N
O
N
H
165.6
149.7
140.3
138.6
129.0
128.9
128.1
127.0
124.0
41.5
35.6
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


Br
O
N
H
7.57
7.54
7.46
7.46
7.44
7.44
7.35
7.31
7.28
7.22
6.06
3.77
3.75
3.73
3.72
2.98
2.97
2.95
0.98
0.99
3.02
4.08
0.96
2.00
1.97
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Br
O
N
H
167.7
138.8
138.0
133.5
128.8
126.8
119.4
41.3
35.6
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.33
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7.24
7.22
7.21
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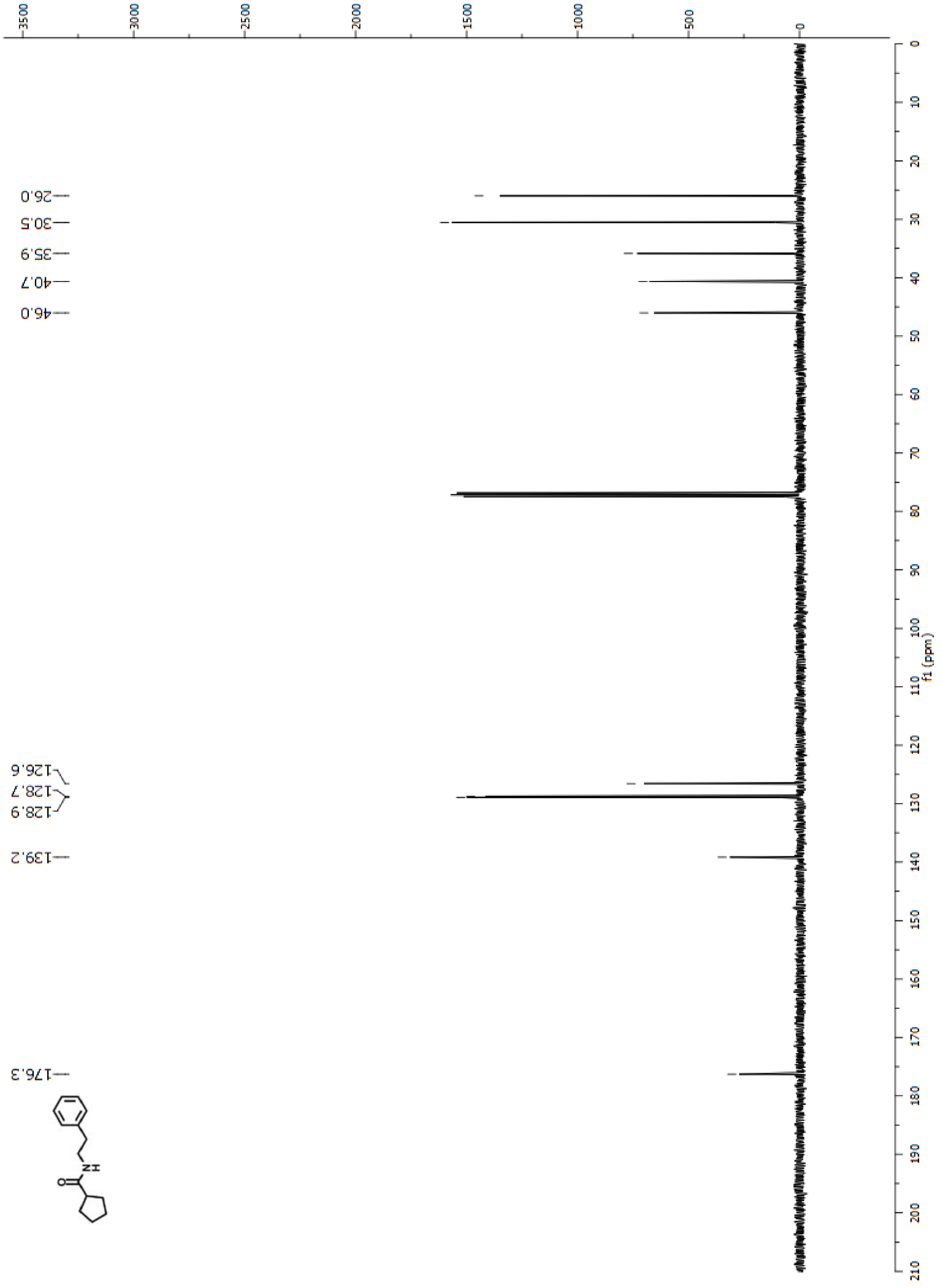
5.48
3.54
3.52
3.50
3.49
2.81
2.79
2.44
2.39
1.84
1.68
1.60
1.49
1.95
0.83
2.06
0.94
2.00
2.00
0.98
6.02
2.02
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
O
N
H



176.3
139.2
128.9
128.7
126.6
46.0
40.7
35.9
30.5
26.0
HN
O
f1 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
3500
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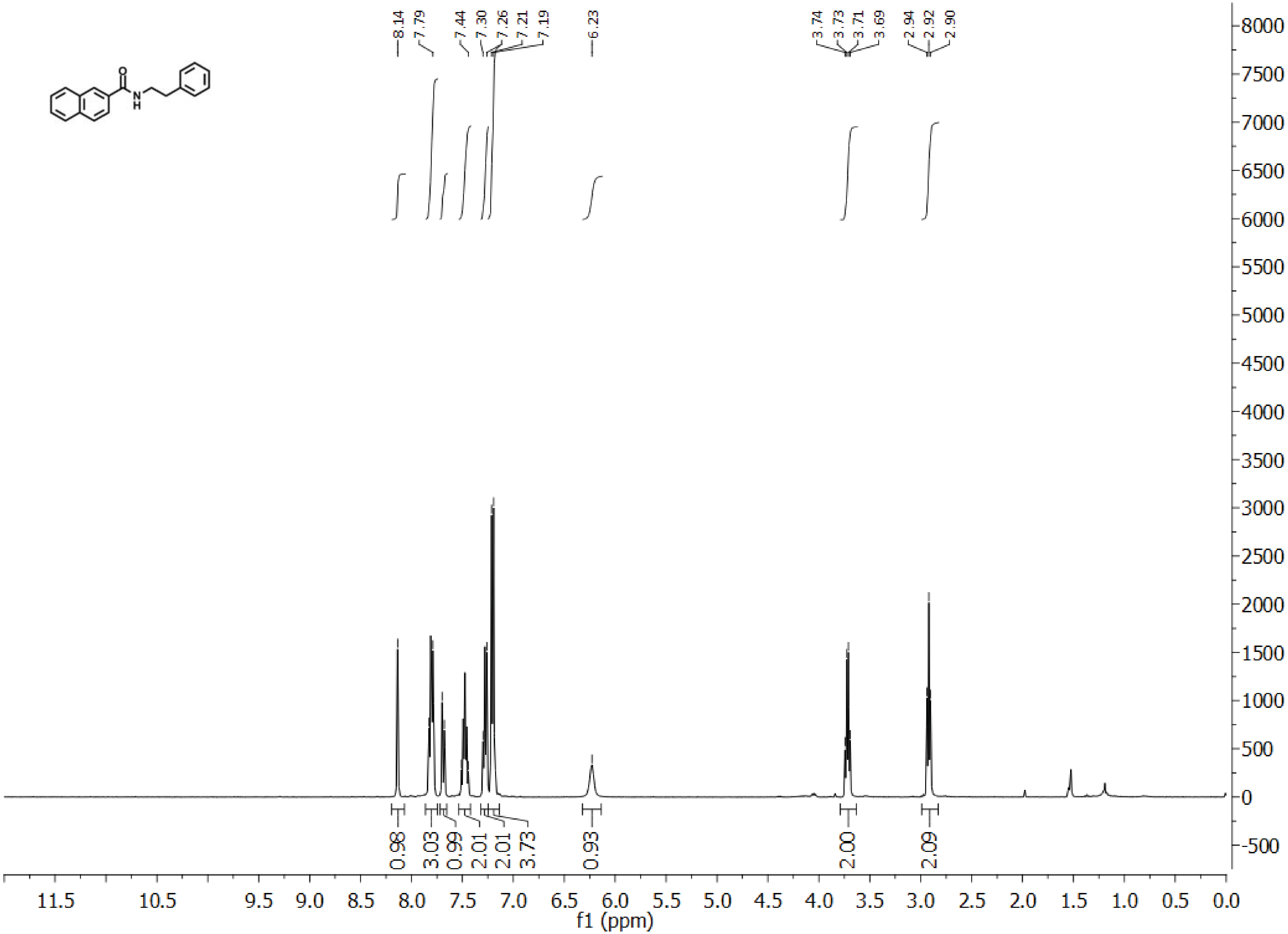
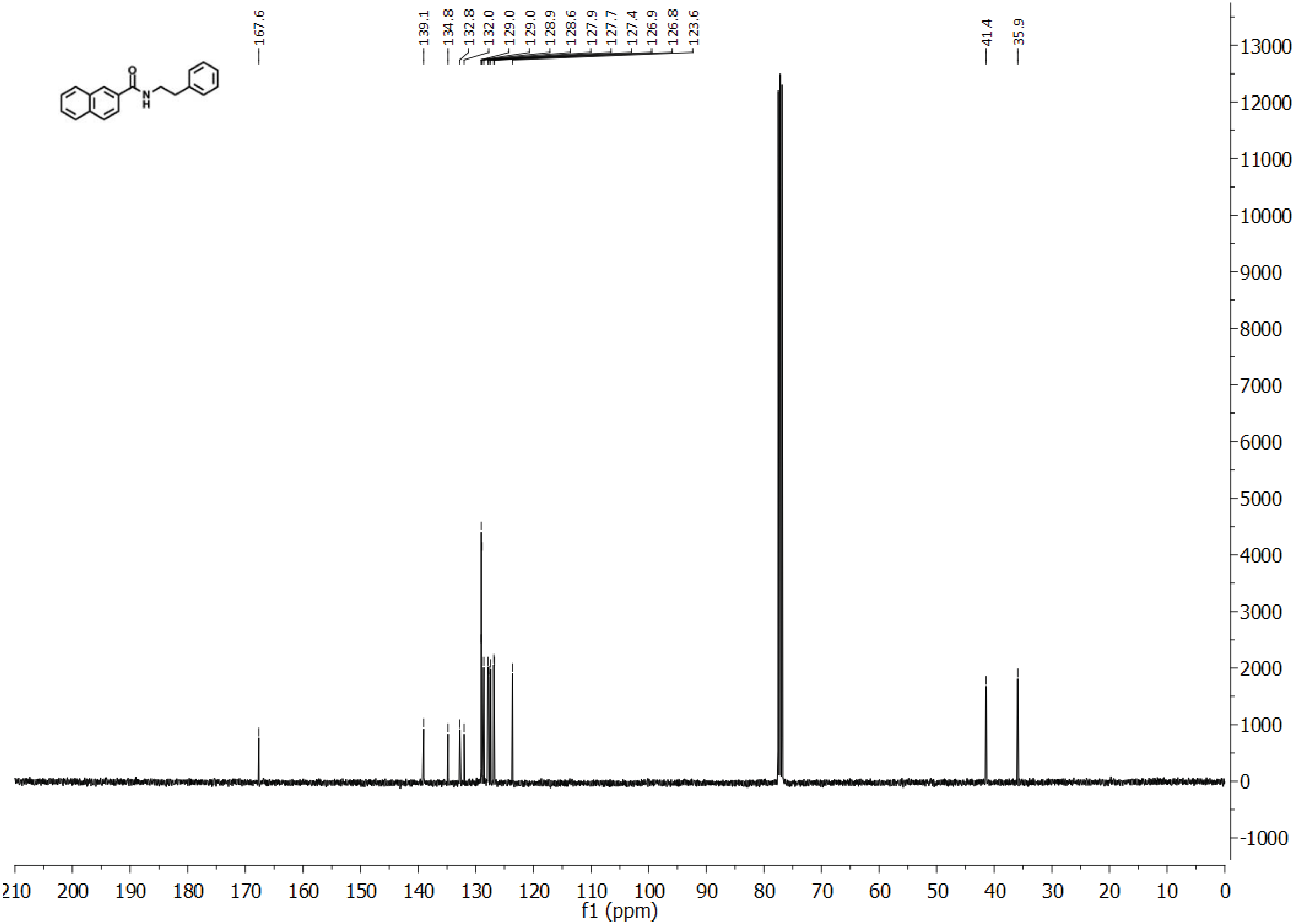
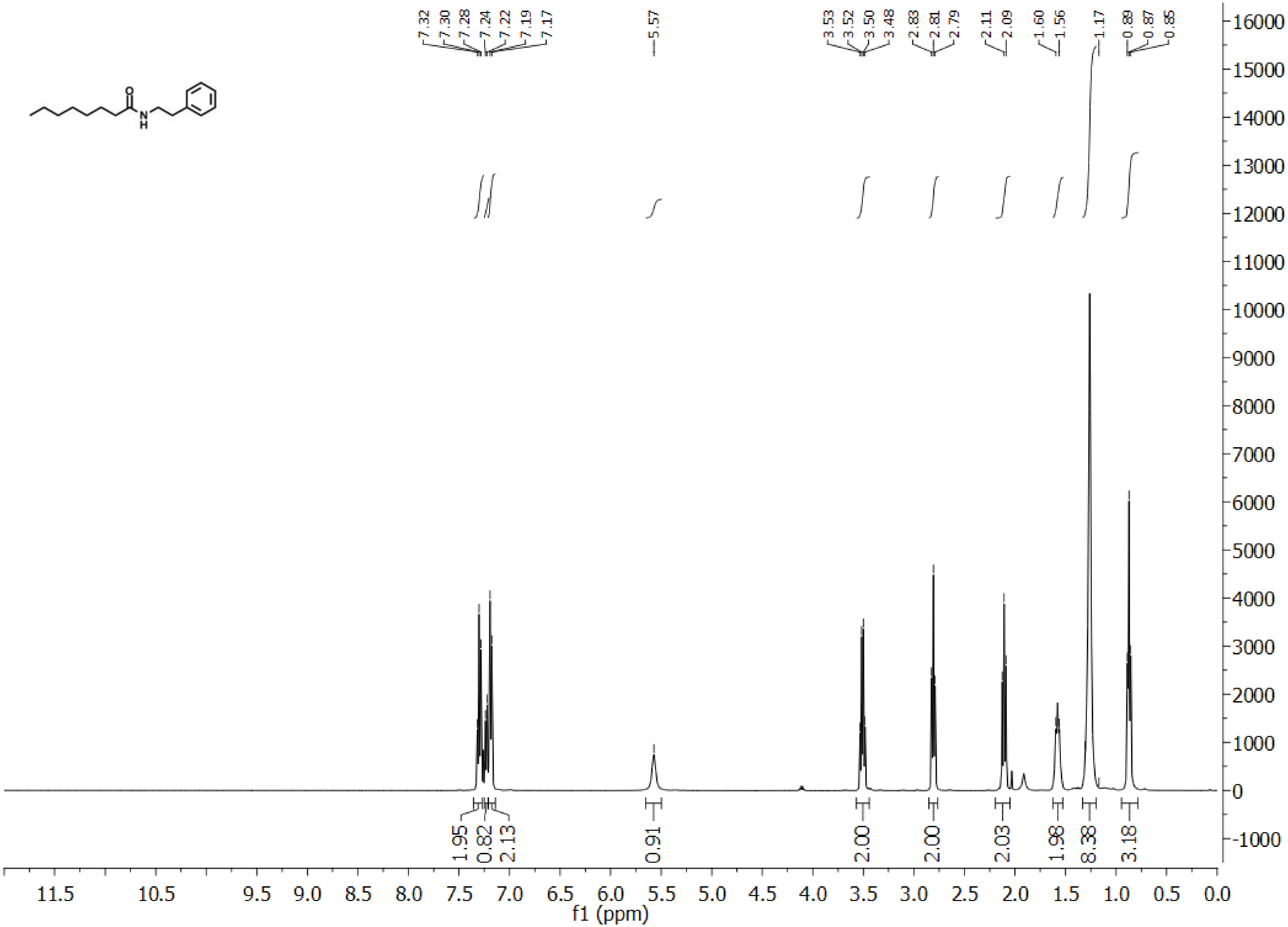
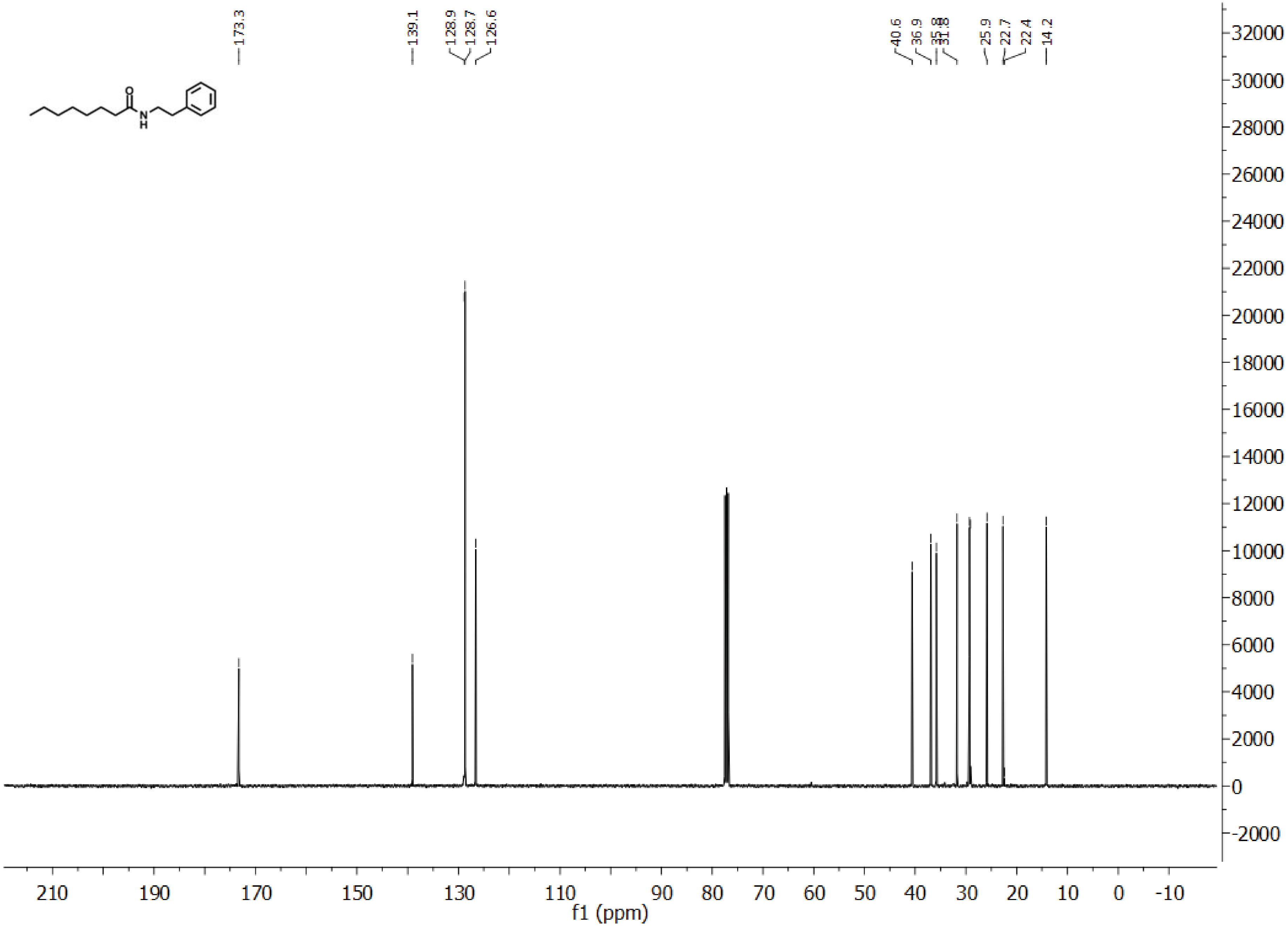
2500
2000
1500
1000
500
0

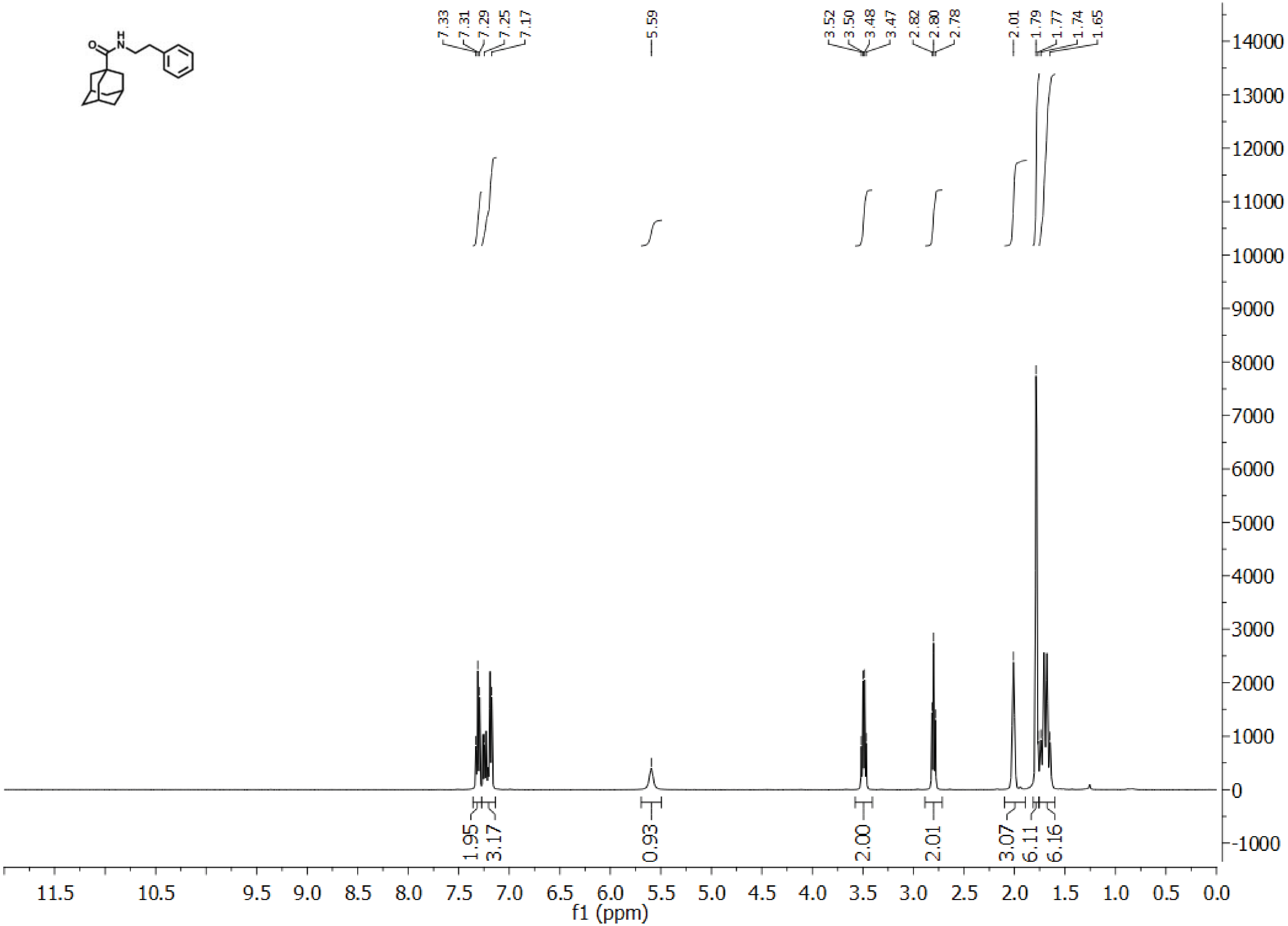


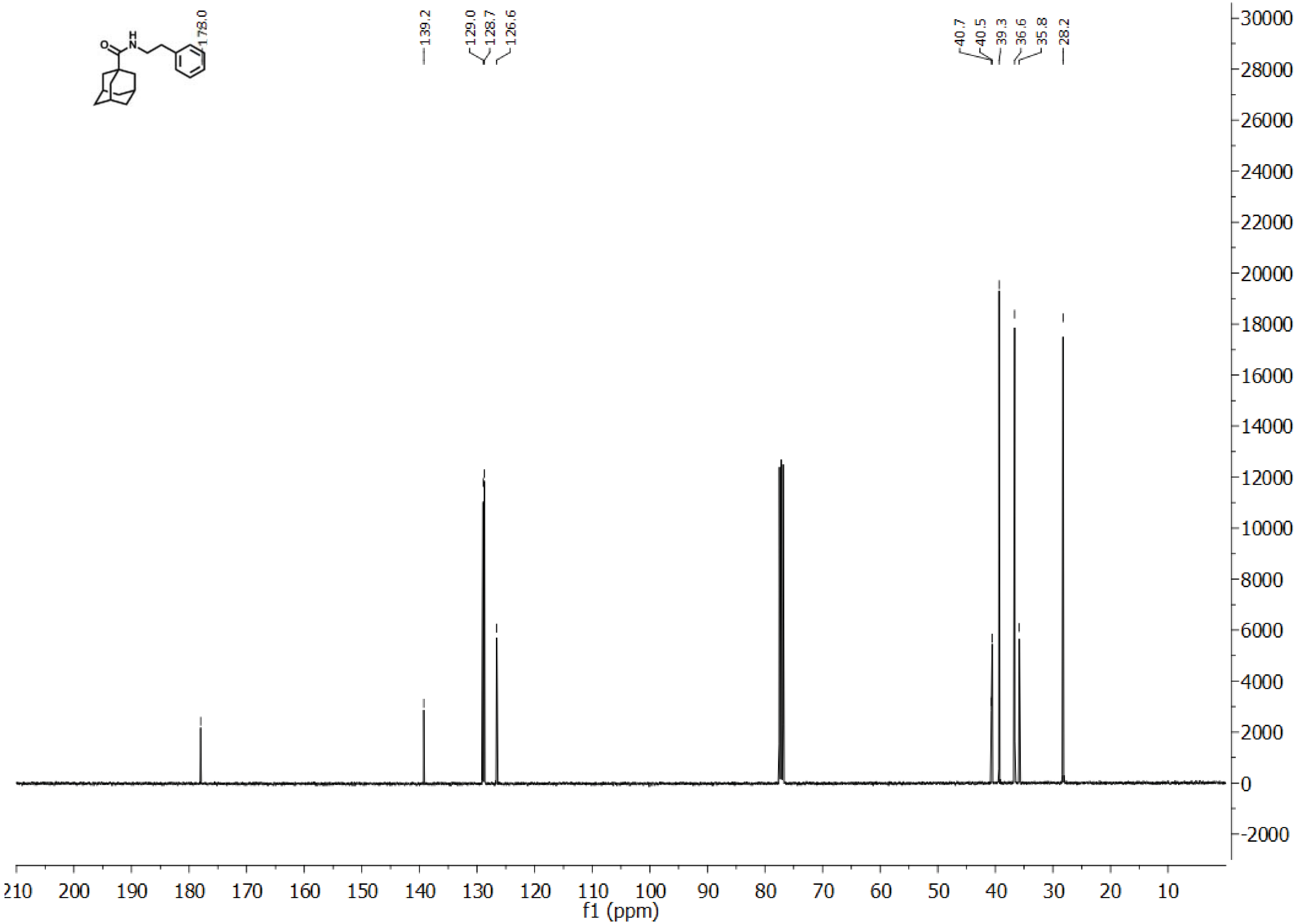
8.14
7.79
7.44
7.30
7.26
7.21
7.19
6.23
3.74
3.73
3.71
3.69
2.94
2.92
2.90
0.98
3.03
0.99
2.01
2.01
3.73
0.93
2.00
2.09
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
O
N
H

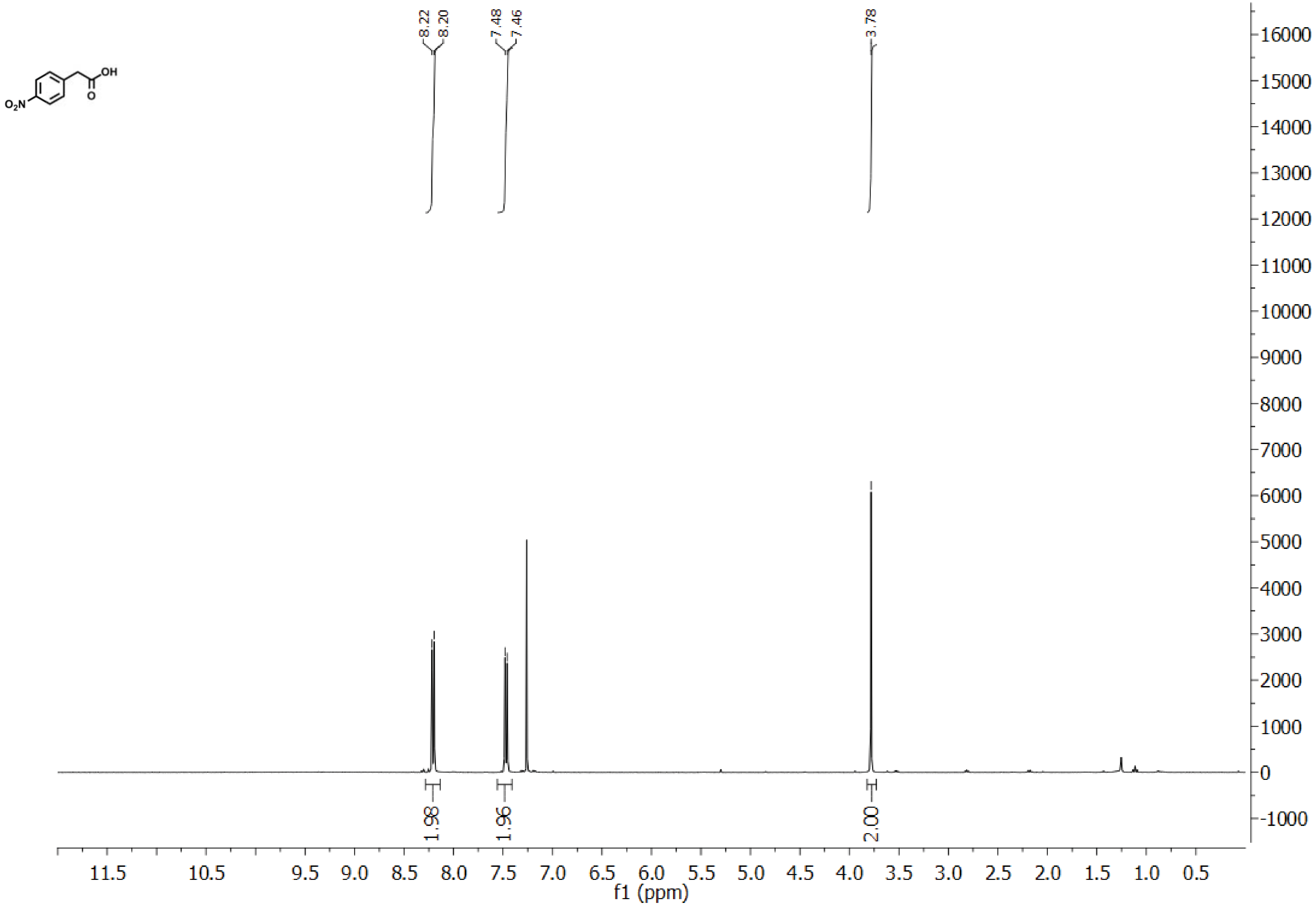

O
N
H
167.6
139.1
134.8
132.8
132.0
129.0
129.0
128.9
128.6
127.9
127.7
127.4
126.9
126.8
123.6
41.4
35.9
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

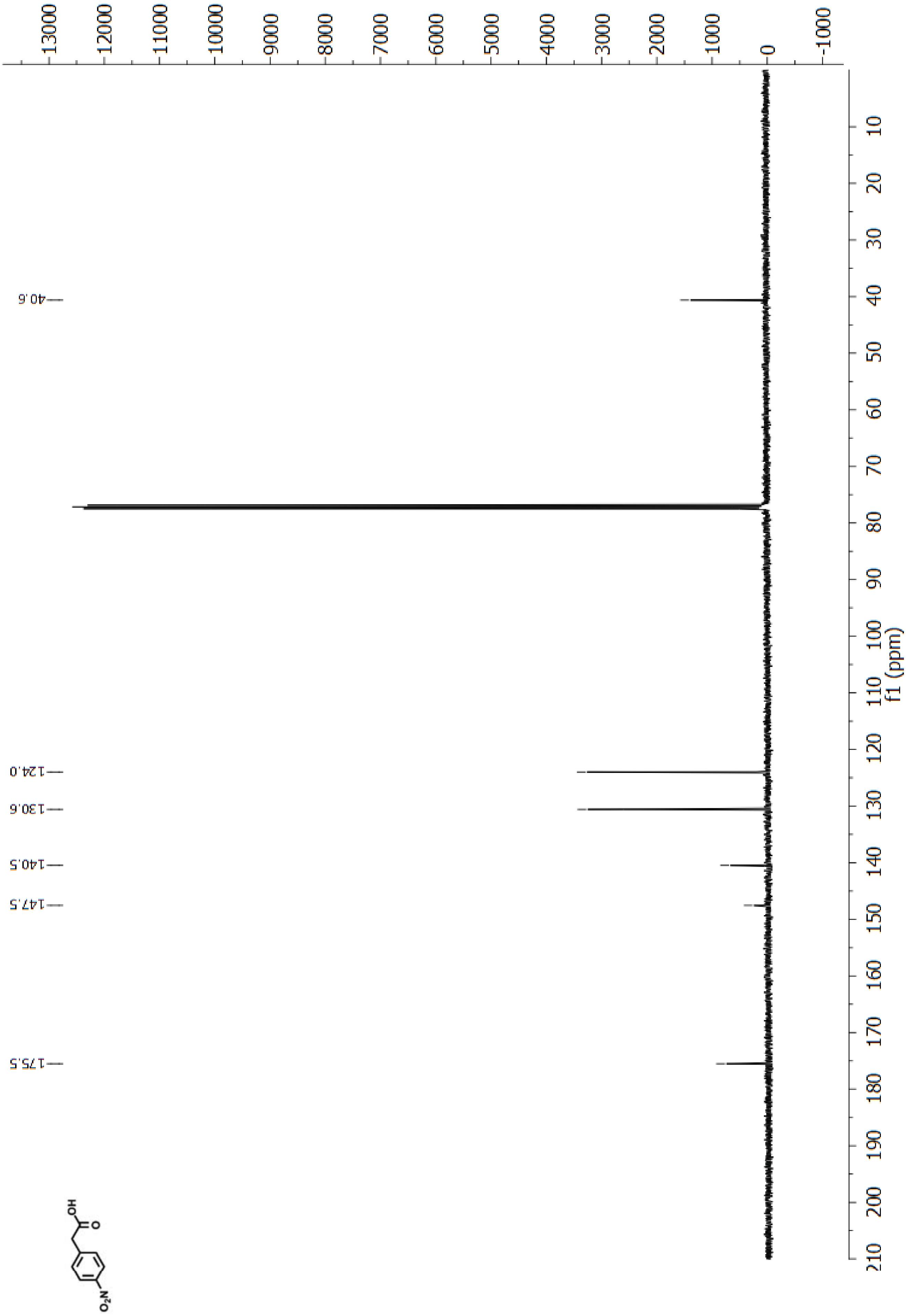

7.32
7.30
7.28
7.24
7.22
7.19
7.17
5.57
3.53
3.52
3.50
3.48
2.83
2.81
2.79
2.11
2.09
1.60
1.56
1.17
0.89
0.87
0.85
1.95
0.82
2.13
0.91
2.00
2.00
2.03
1.98
8.38
3.18
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
O
N
H

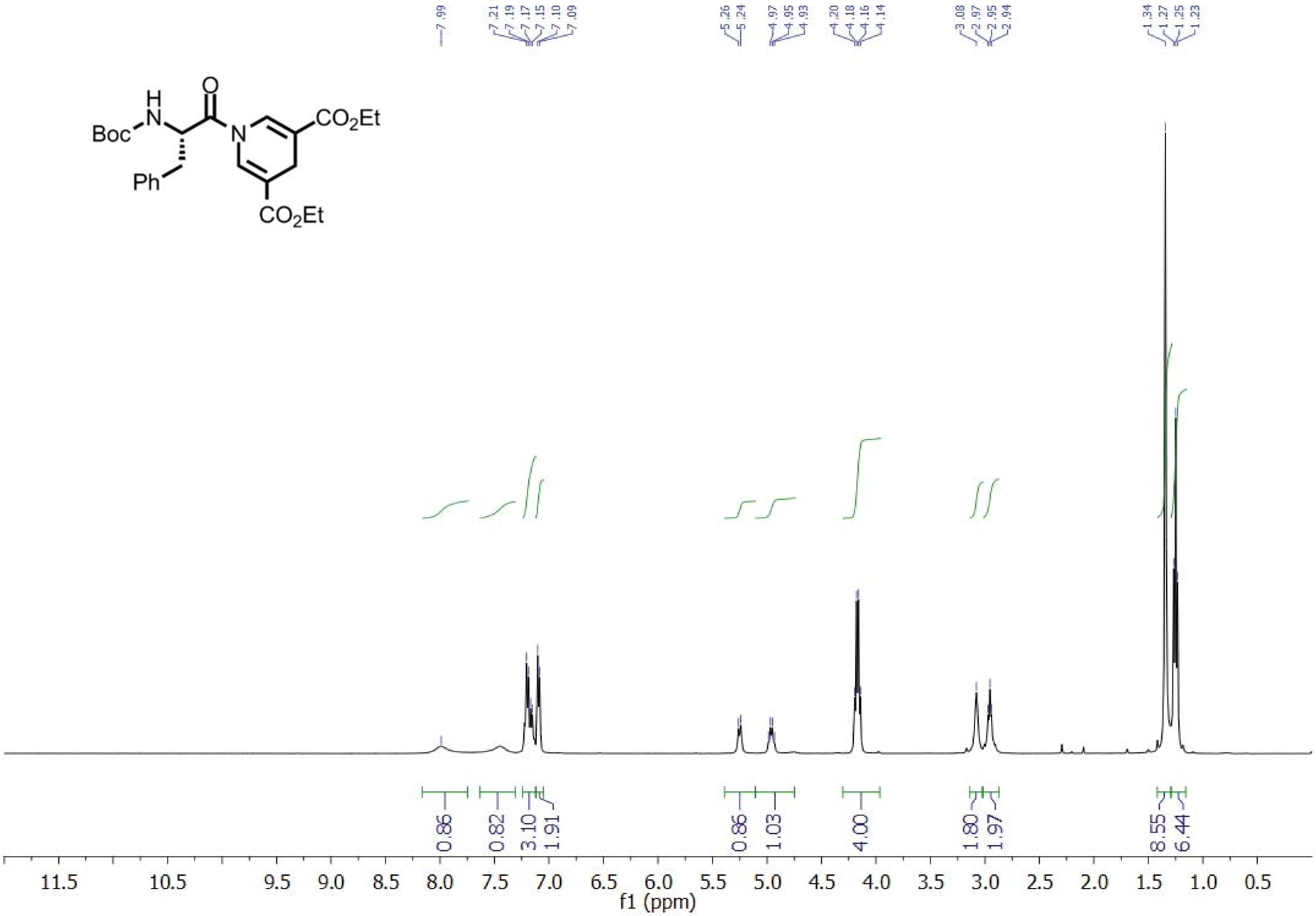

173.3
139.1
128.9
128.7
126.6
40.6
36.9
35.8
31.8
25.9
22.7
22.4
14.2
O
N
H
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

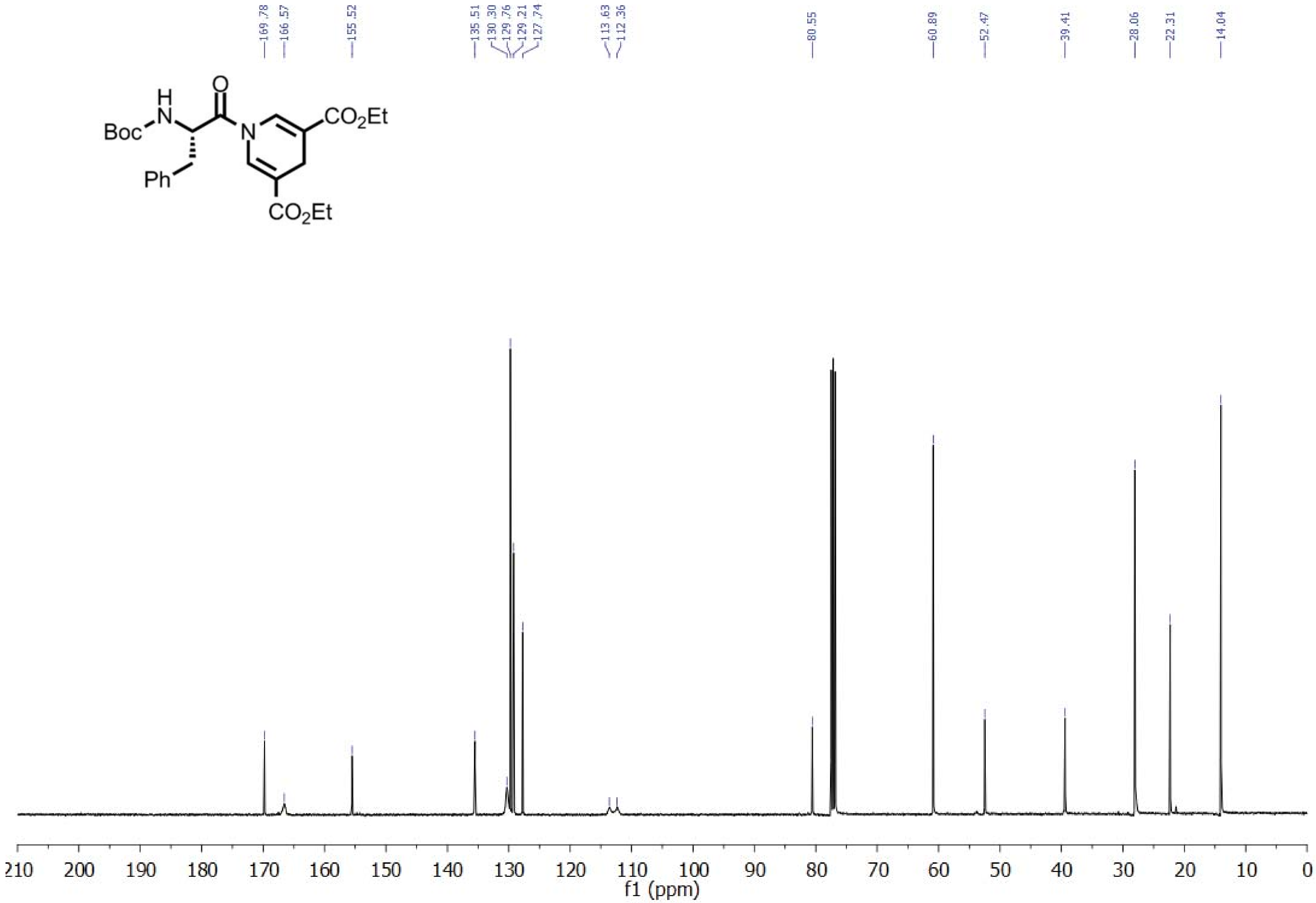

7.33
7.31
7.29
7.25
7.17
5.59
3.52
3.50
3.48
3.47
2.82
2.80
2.78
2.01
1.79
1.77
1.74
1.65
1.95
3.17
0.93
2.00
2.01
3.07
6.11
6.16
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
O
N
H

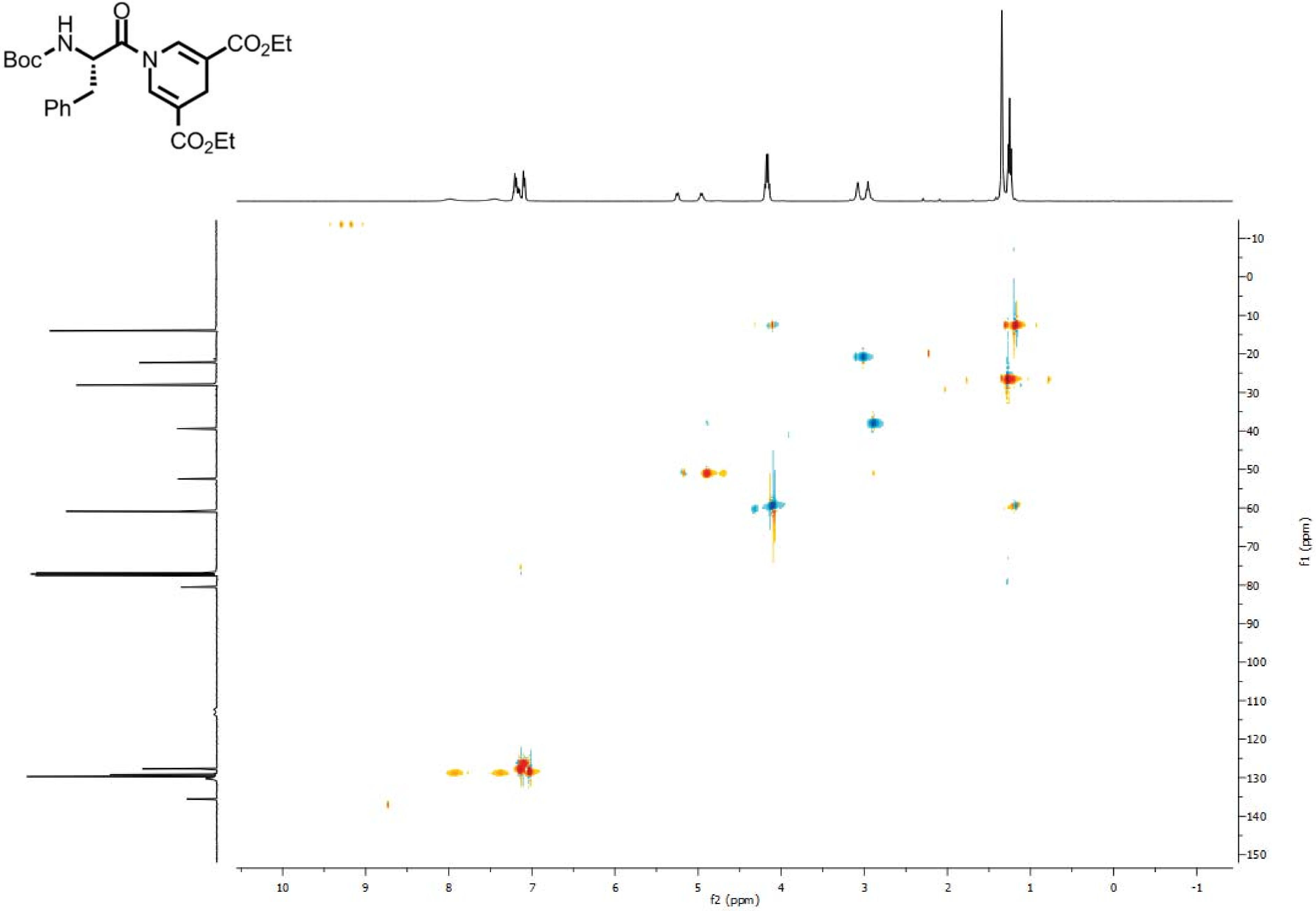

178.0
139.2
129.0
128.7
126.6
40.7
40.5
39.3
36.6
35.8
28.2
O
H
N
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

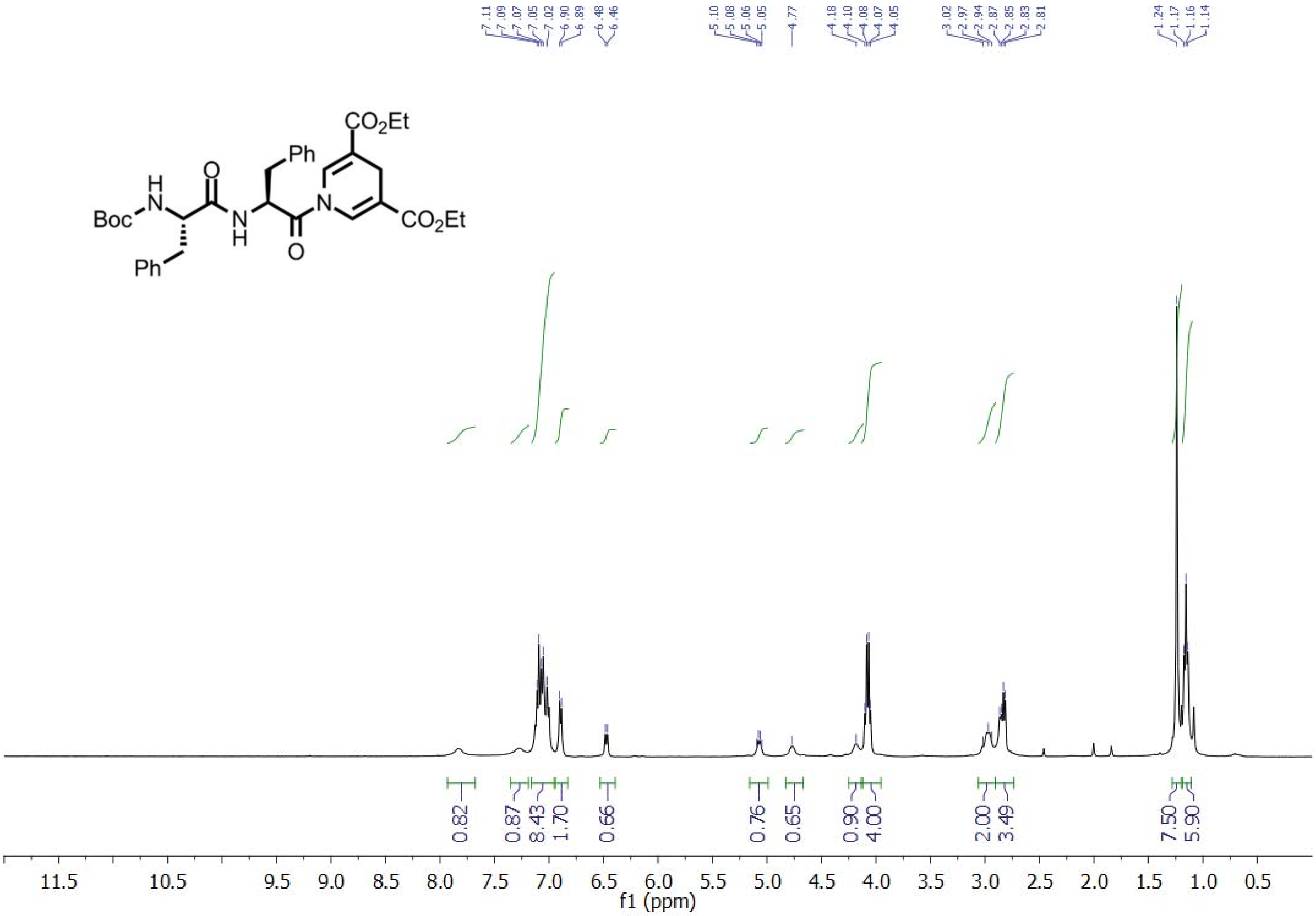

O2N
OH
O
8.22
8.20
7.48
7.46
3.78
1.98
1.96
2.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000

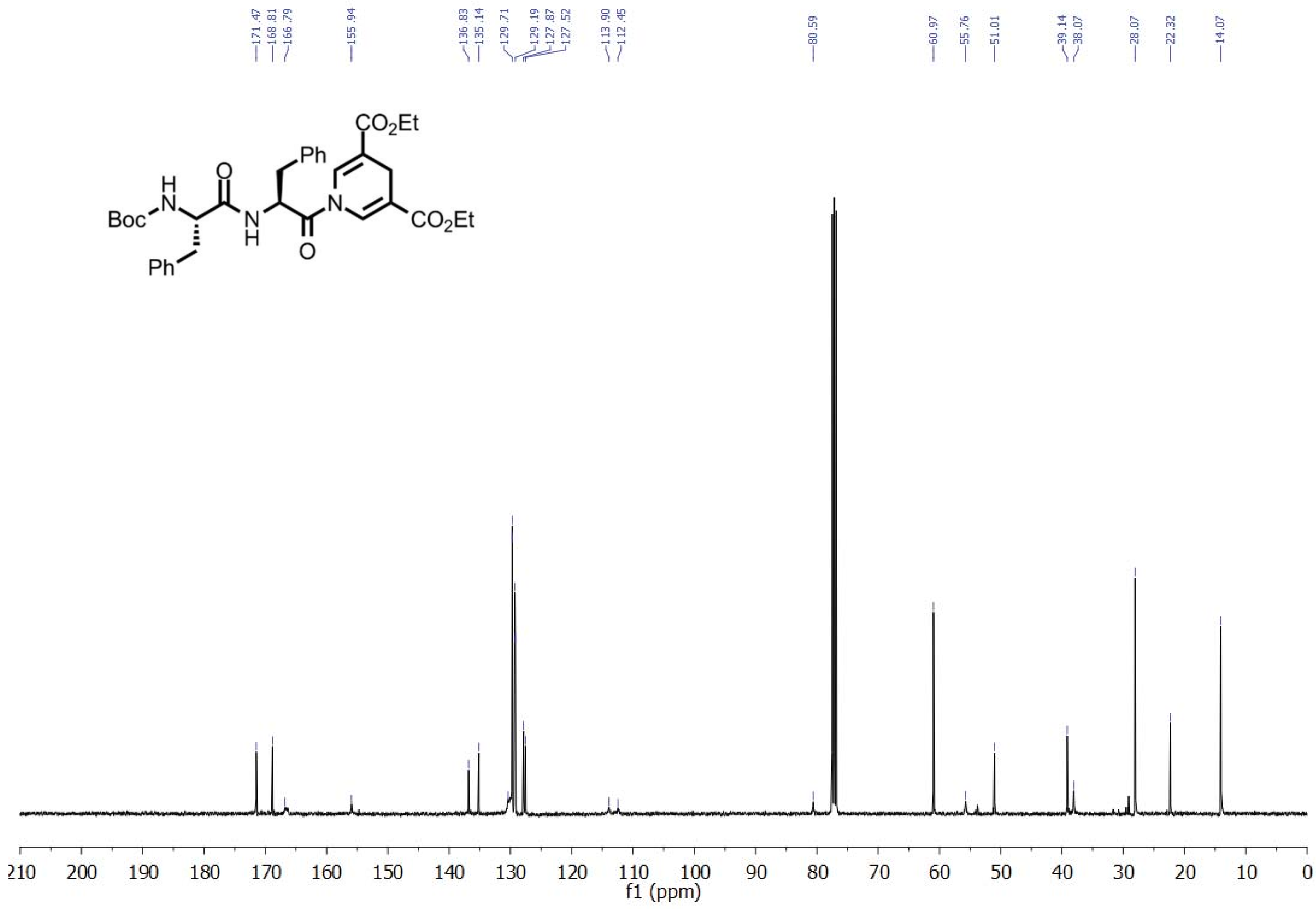

40.6
124.0
130.6
140.5
147.5
175.5
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
f1 (ppm)
OH
O
O2N

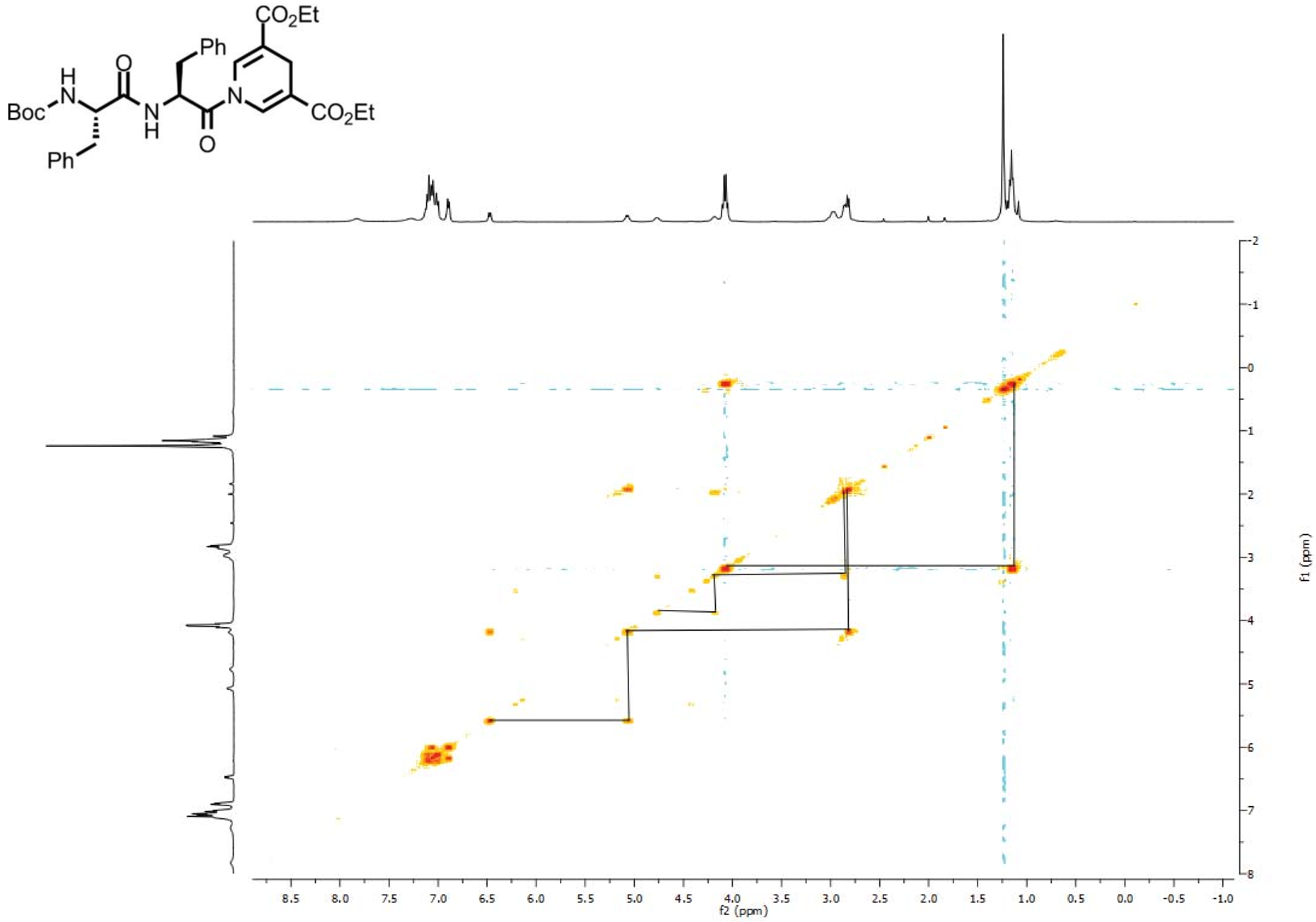

7.99
7.21
7.19
7.17
7.15
7.10
7.09
5.26
5.24
4.97
4.95
4.93
4.20
4.18
4.16
4.14
3.08
2.97
2.95
2.94
1.34
1.27
1.25
1.23
Boc
H
N
O
N
CO2Et
Ph
CO2Et
0.86
0.82
3.10
1.91
0.86
1.03
4.00
1.80
1.97
8.55
6.44
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

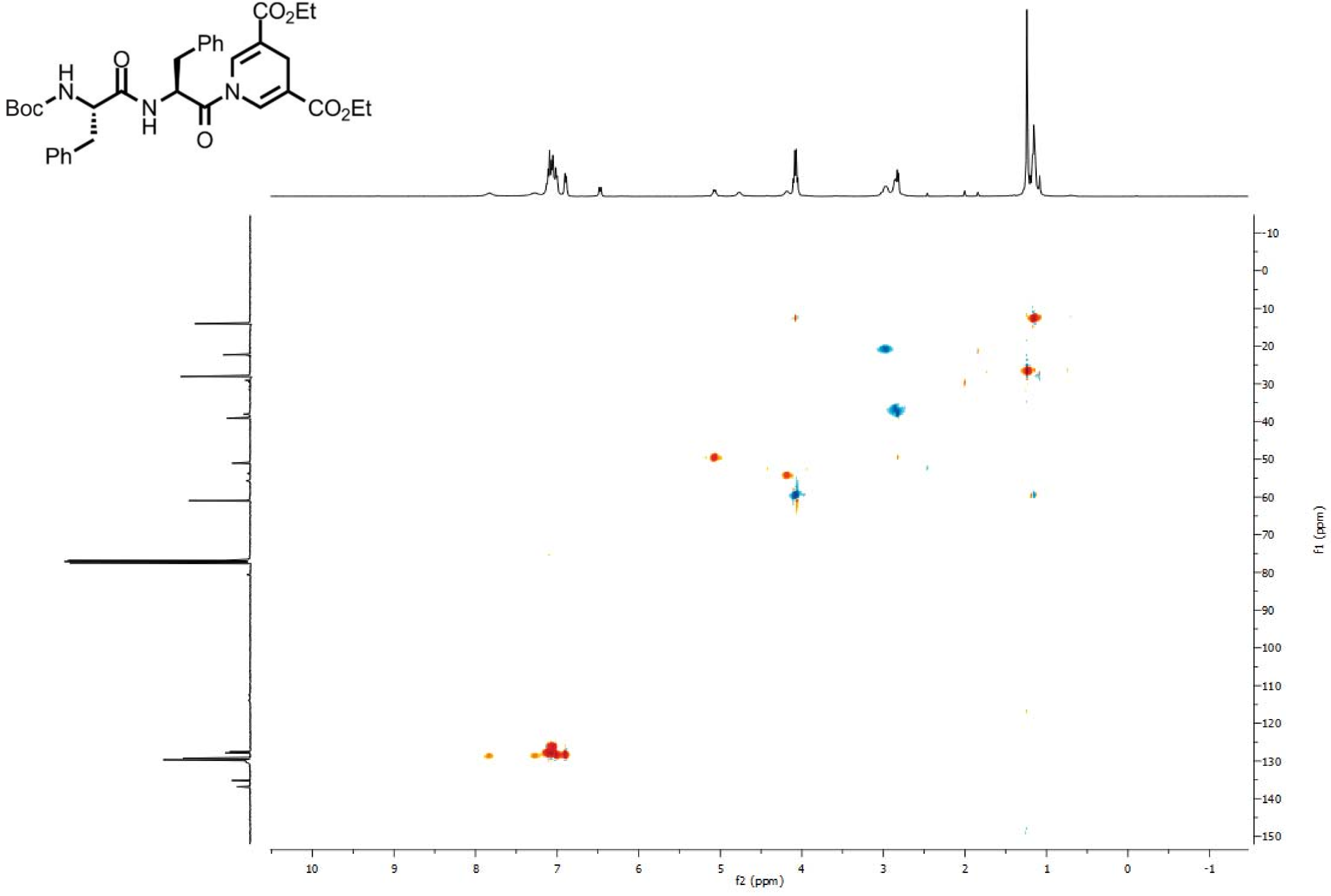

169.78
166.57
155.52
135.51
130.30
129.76
129.21
127.74
113.63
112.36
80.55
60.89
52.47
39.41
28.06
22.31
14.04
Boc
H
N
O
N
CO2Et
Ph
CO2Et
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

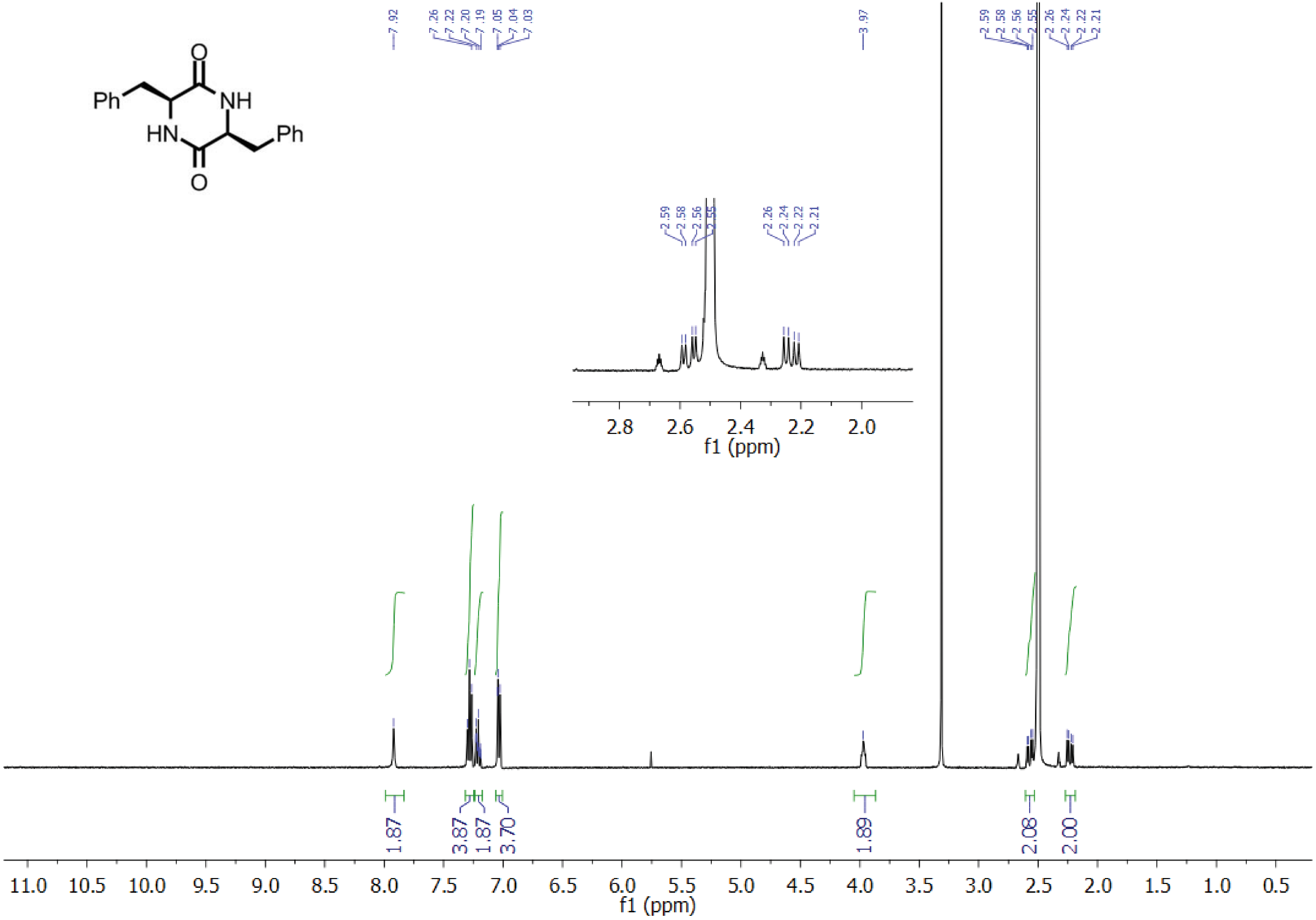

Boc
H
N
O
N
CO2Et
CO2Et
Ph
10
9
8
7
6
5
4
3
2
1
0
-1
f2 (ppm)
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
f1 (ppm)

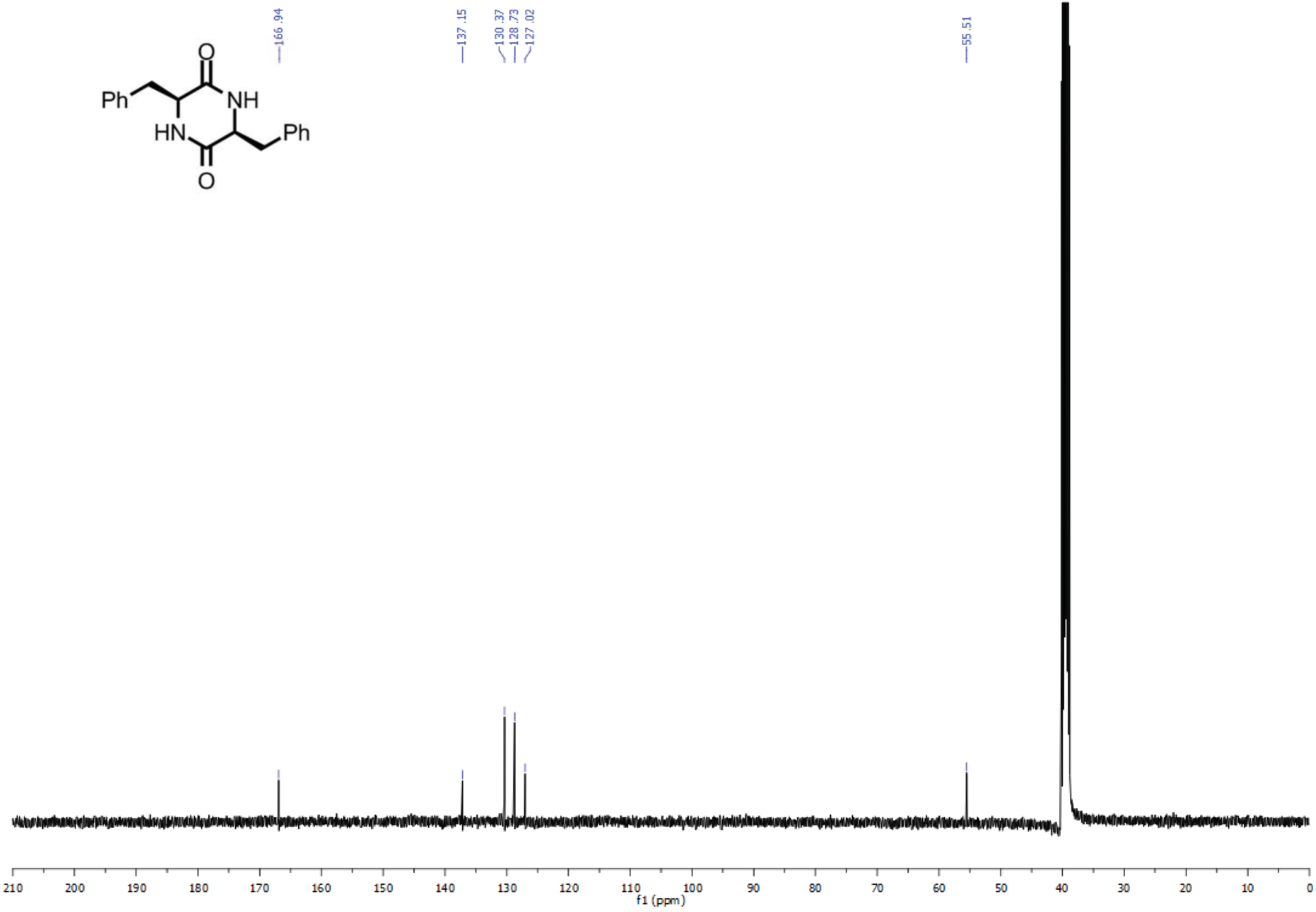

7.11
7.09
7.07
7.05
7.02
6.90
6.89
6.48
6.46
5.10
5.08
5.06
5.05
4.77
4.18
4.10
4.08
4.07
4.05
3.02
2.97
2.94
2.87
2.85
2.83
2.81
1.24
1.17
1.16
1.14
CO2Et
Ph
H
N
Boc
O
N
H
O
N
CO2Et
Ph
0.82
0.87
8.43
1.70
0.66
0.76
0.65
0.90
4.00
2.00
3.49
7.50
5.90
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

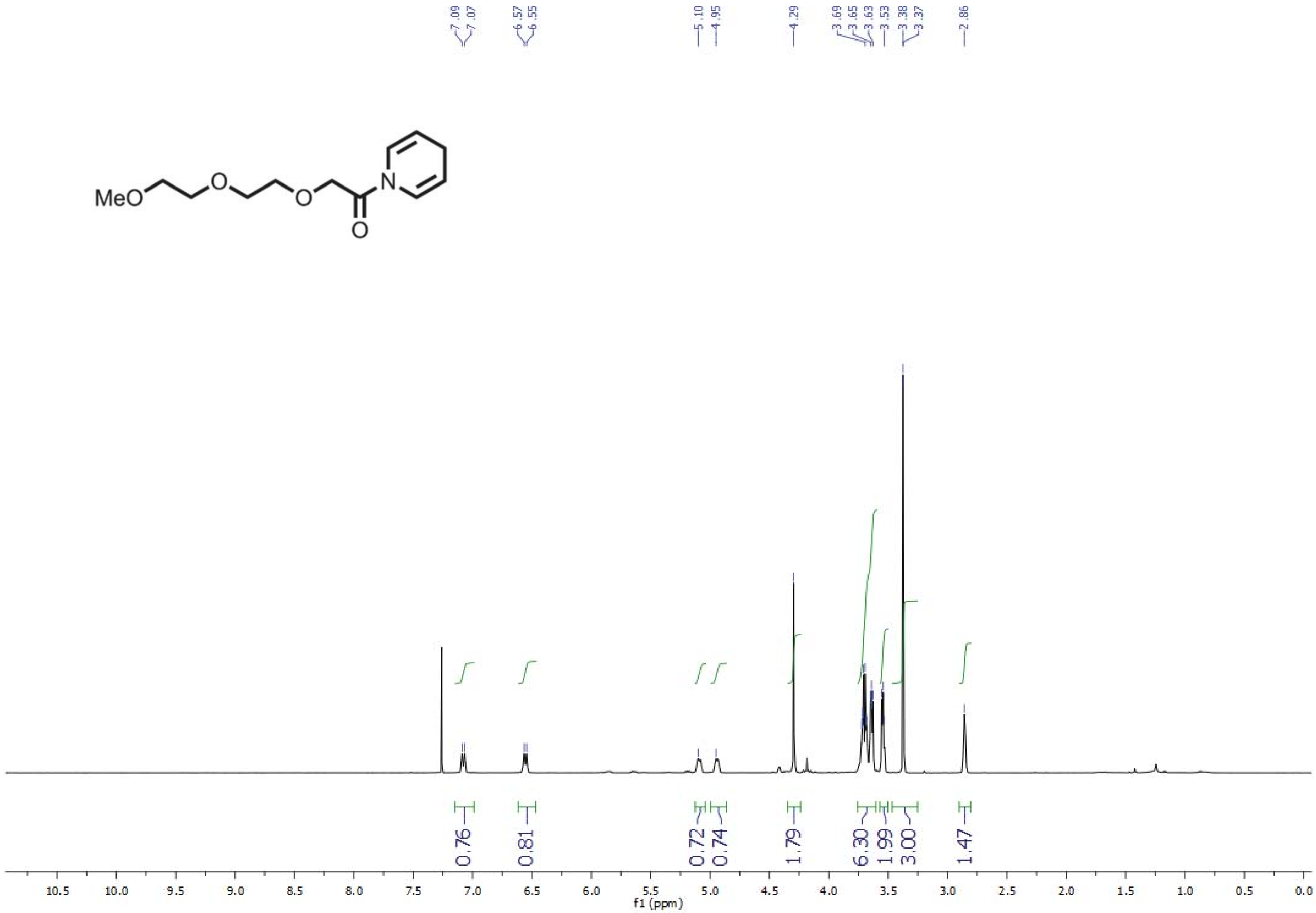

171.47
168.81
166.79
155.94
136.83
135.14
129.71
129.19
127.87
127.52
113.90
112.45
80.59
60.97
55.76
51.01
39.14
38.07
28.07
22.32
14.07
Boc
H
N
O
N
H
Ph
Ph
O
N
CO2Et
CO2Et
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

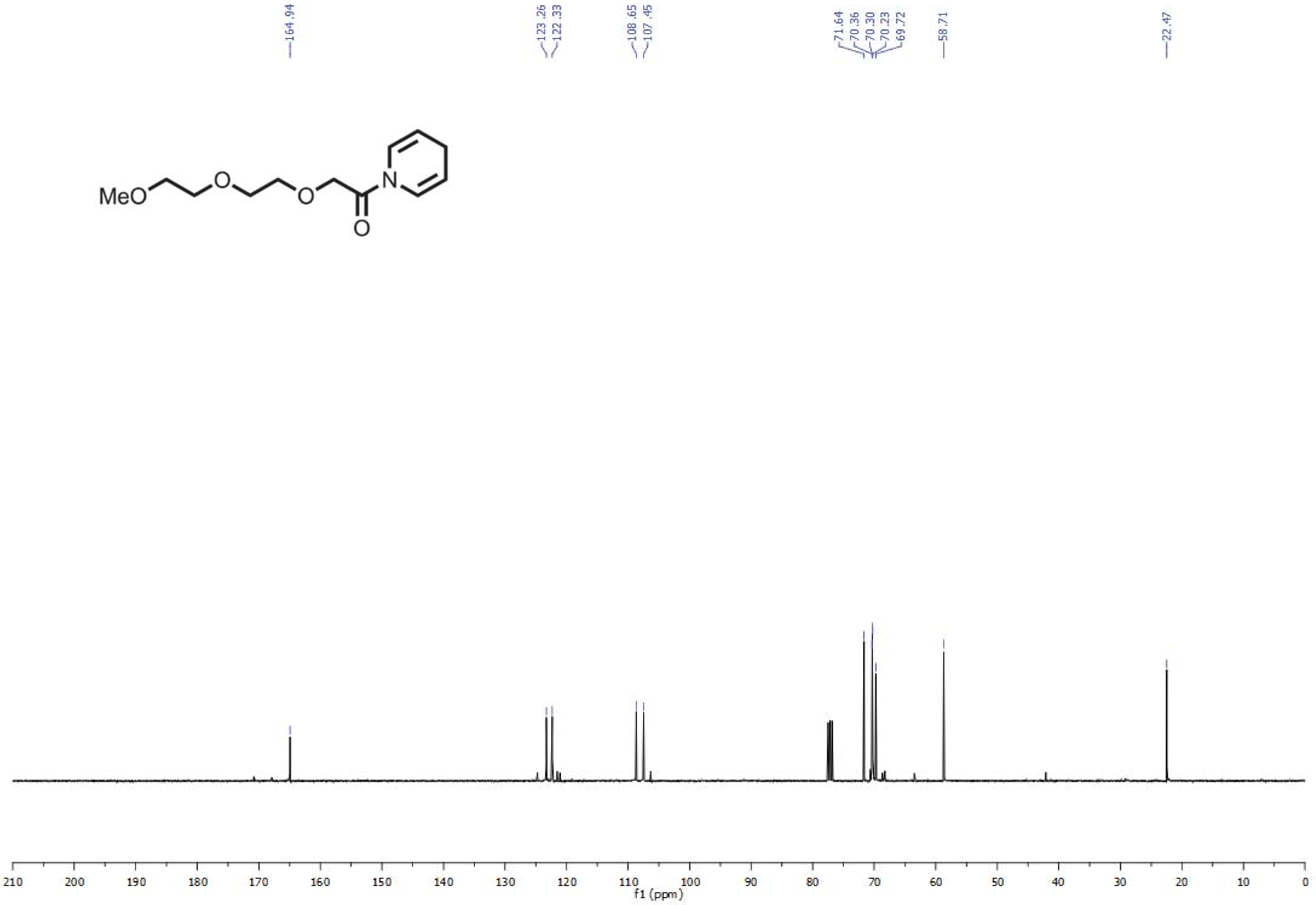

Boc
H
N
O
N
H
Ph
Ph
N
O
CO2Et
CO2Et
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f2 (ppm)
-2
-1
0
1
2
3
4
5
6
7
8
f1 (ppm)

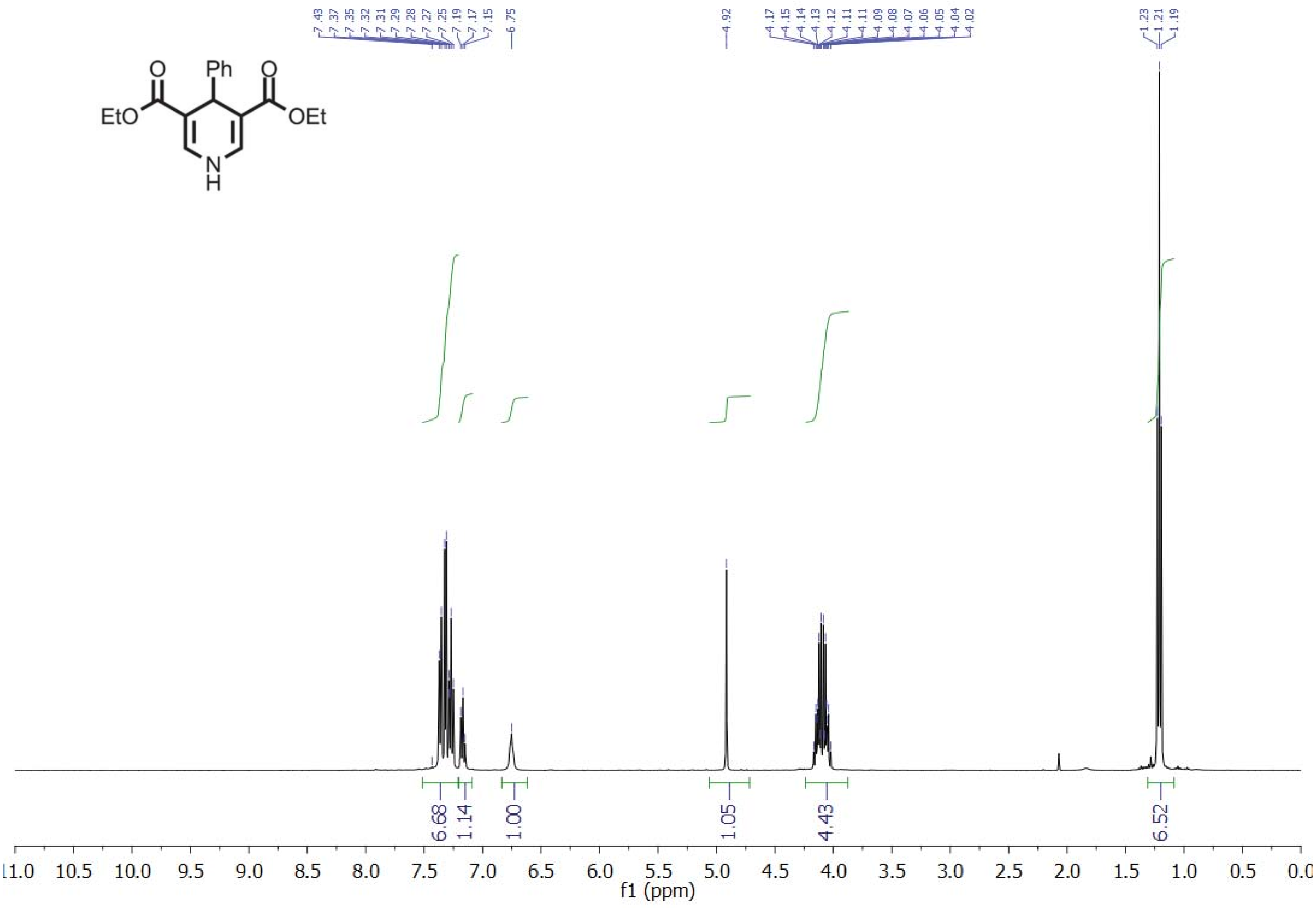

Boc
H
N
O
N
H
O
N
Ph
Ph
CO2Et
CO2Et
f2 (ppm)
f1 (ppm)
10
9
8
7
6
5
4
3
2
1
0
-1
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150

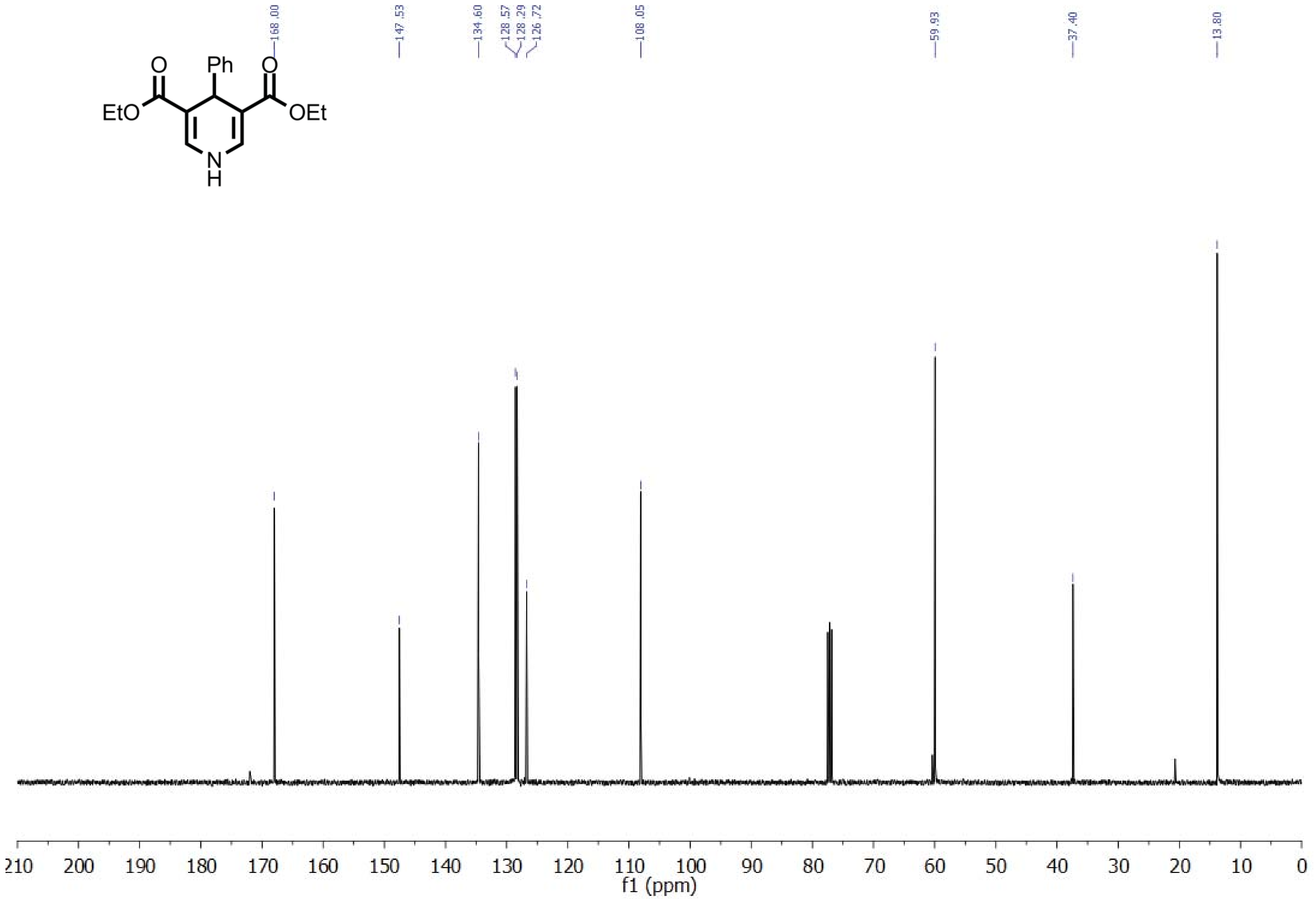

Ph
NH
HN
Ph
O
O
7.92
7.26
7.22
7.20
7.19
7.05
7.04
7.03
3.97
2.59
2.58
2.56
2.55
2.26
2.24
2.22
2.21
2.8
2.6
2.4
2.2
2.0
f1 (ppm)
1.87
3.87
1.87
3.70
1.89
2.08
2.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

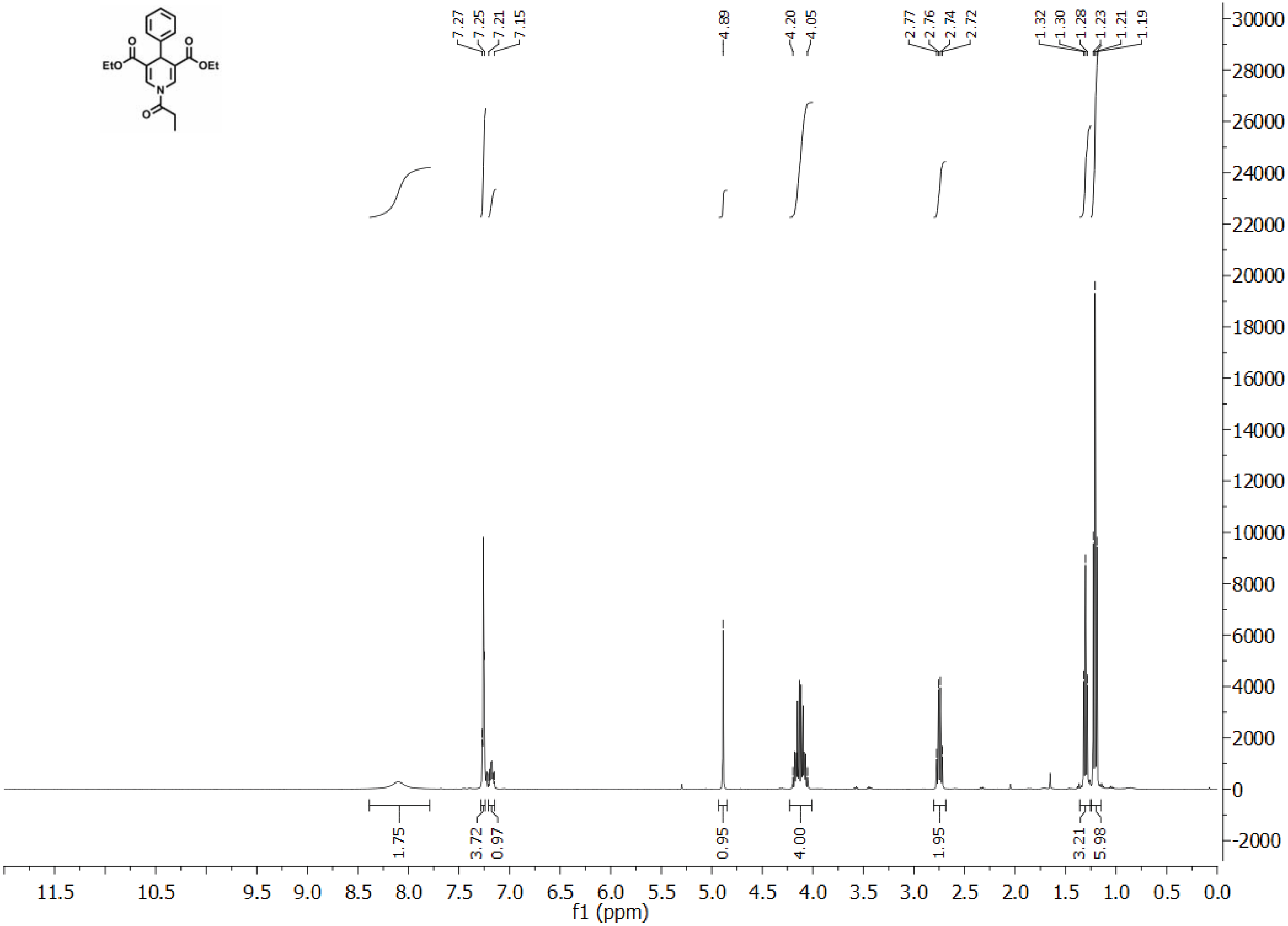

166.94
137.15
130.37
128.73
127.02
55.51
Ph
NH
HN
Ph
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

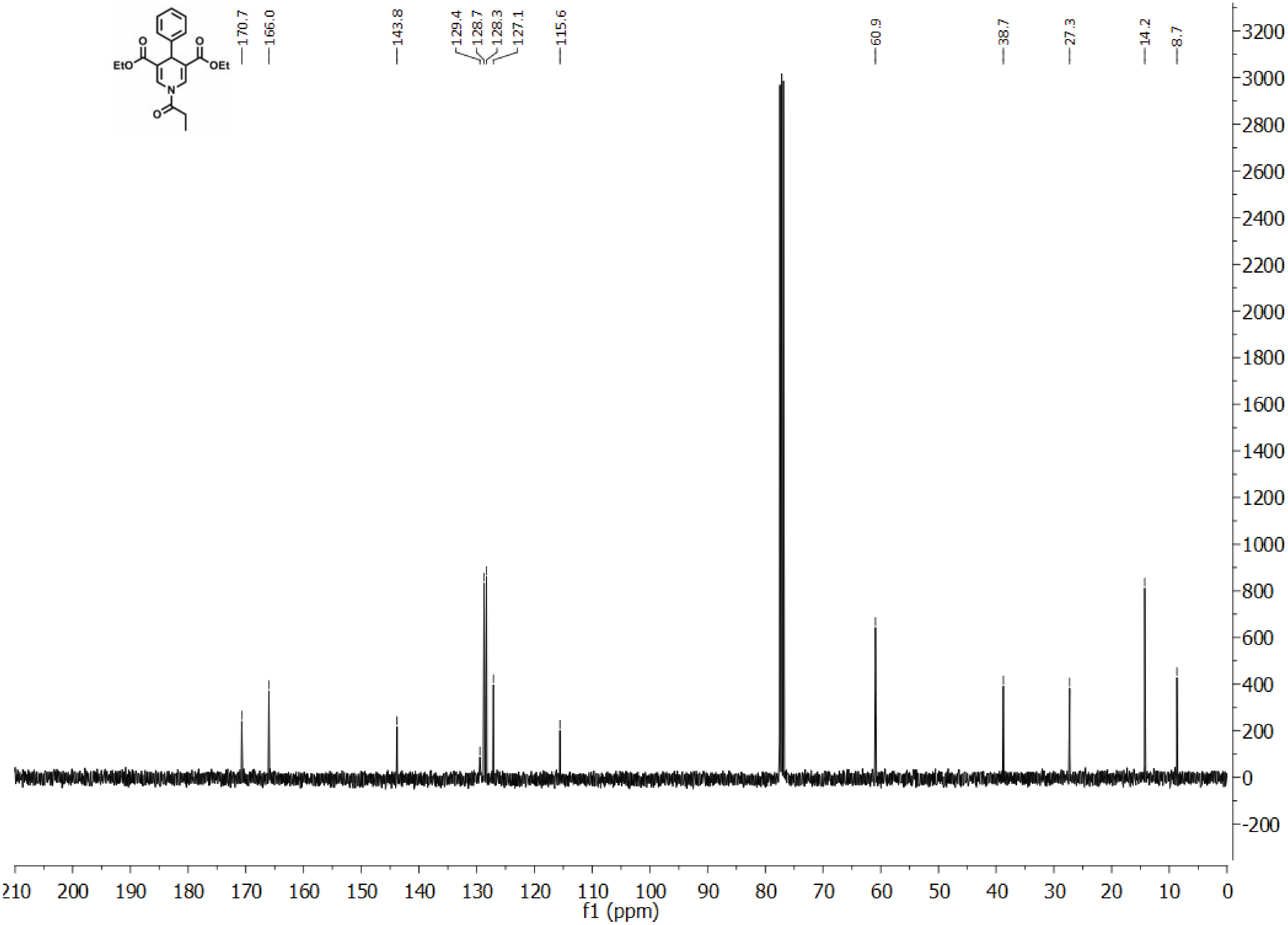

7.09
7.07
6.57
6.55
5.10
4.95
4.29
3.69
3.65
3.63
3.53
3.38
3.37
2.86
MeO
O
O
O
N
0.76
0.81
0.72
0.74
1.79
6.30
1.99
3.00
1.47
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


164.94
123.26
122.33
108.65
107.45
71.64
70.36
70.30
70.23
69.72
58.71
22.47
MeO
O
O
N
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.43
7.37
7.35
7.32
7.31
7.29
7.28
7.27
7.25
7.19
7.17
7.15
6.75
4.92
4.17
4.15
4.14
4.13
4.12
4.11
4.11
4.09
4.08
4.07
4.06
4.05
4.04
4.02
1.23
1.21
1.19
O
Ph
O
EtO
OEt
N
H
6.68
1.14
1.00
1.05
4.43
6.52
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


168.00
147.53
134.60
128.57
128.29
126.72
108.05
59.93
37.40
13.80
EtO
O
Ph
O
OEt
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


EtO
OEt
N
O
7.27
7.25
7.21
7.15
4.89
4.20
4.05
2.77
2.76
2.74
2.72
1.32
1.30
1.28
1.23
1.21
1.19
1.75
3.72
0.97
0.95
4.00
1.95
3.21
5.98
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000


EtO
OEt
O
O
N
O
170.7
166.0
143.8
129.4
128.7
128.3
127.1
115.6
60.9
38.7
27.3
14.2
8.7
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)