Polycyclic Ring Formation Using *Bis*-Diazolactams for Cascade Stitching

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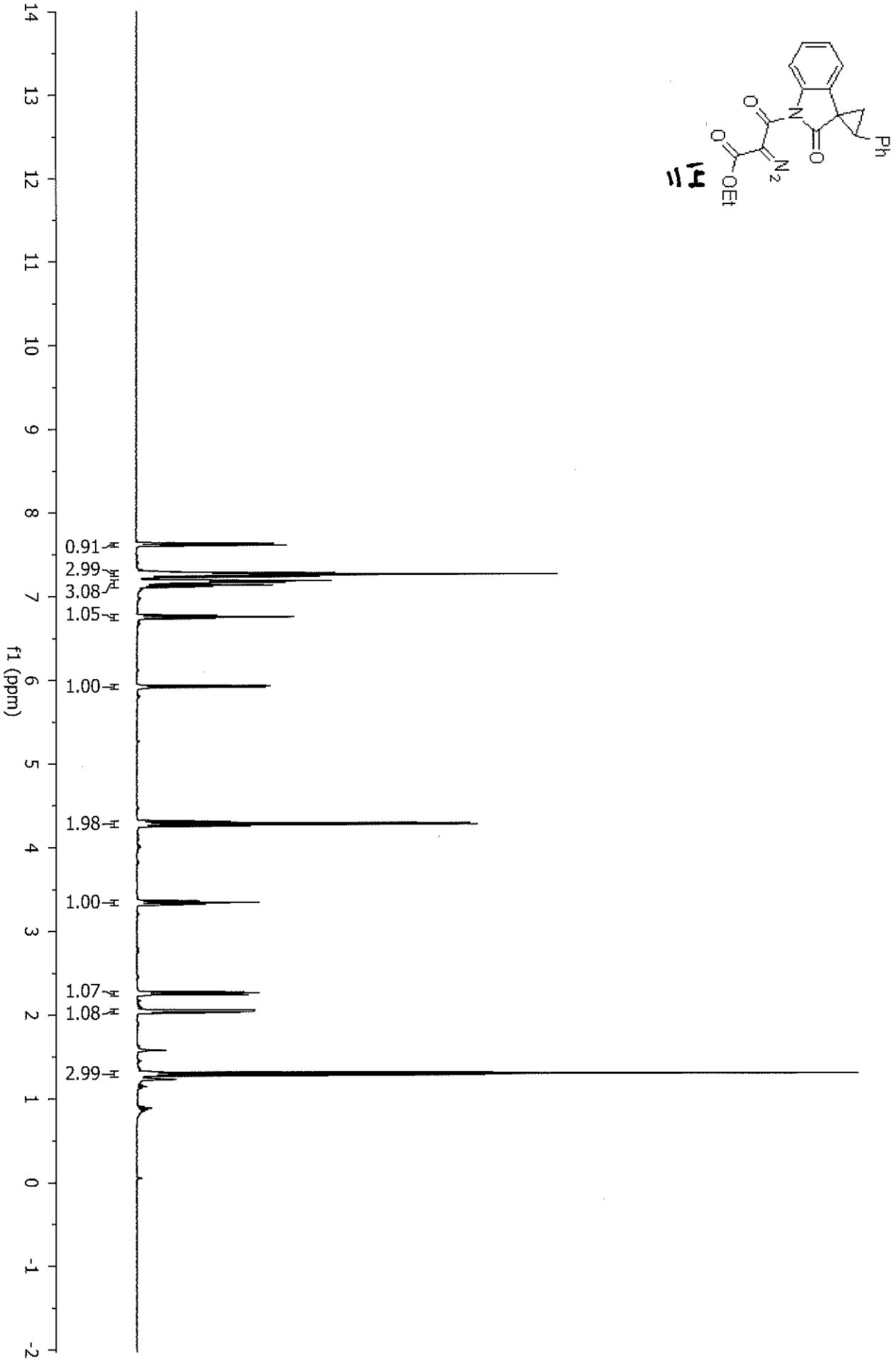
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2.99
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1.08
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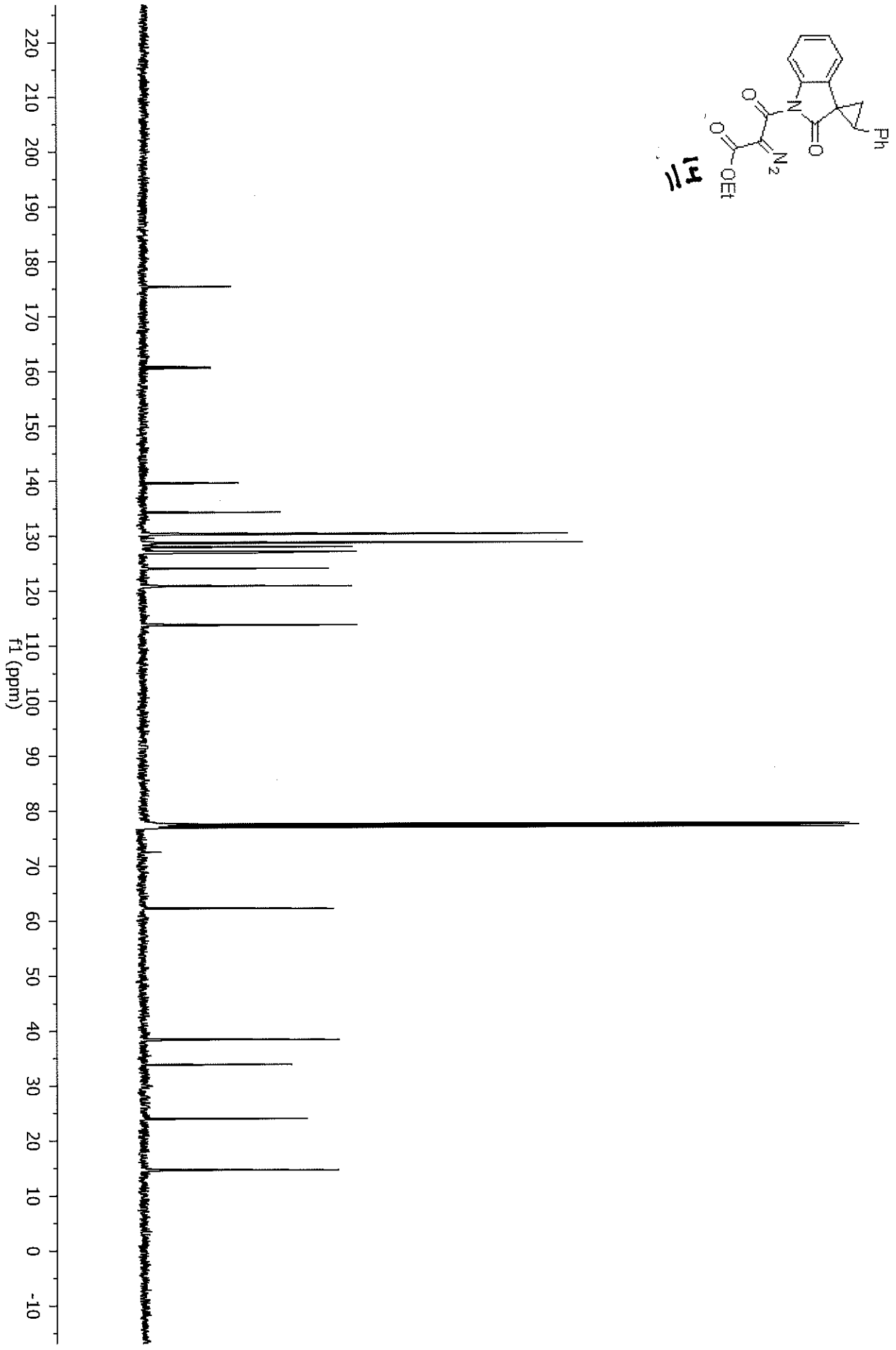
O
O
N2
OEt
Ph

11i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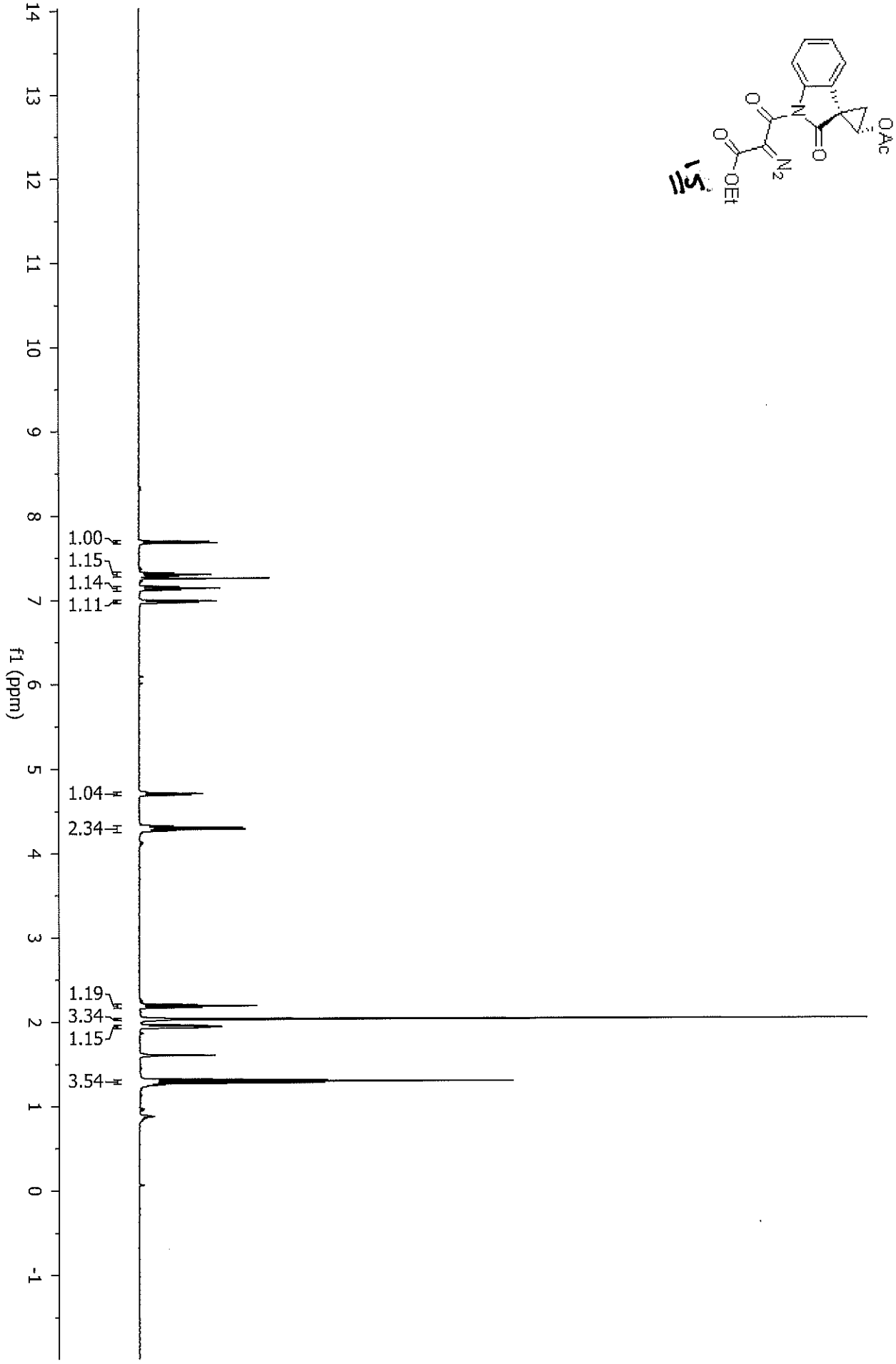
f1 (ppm)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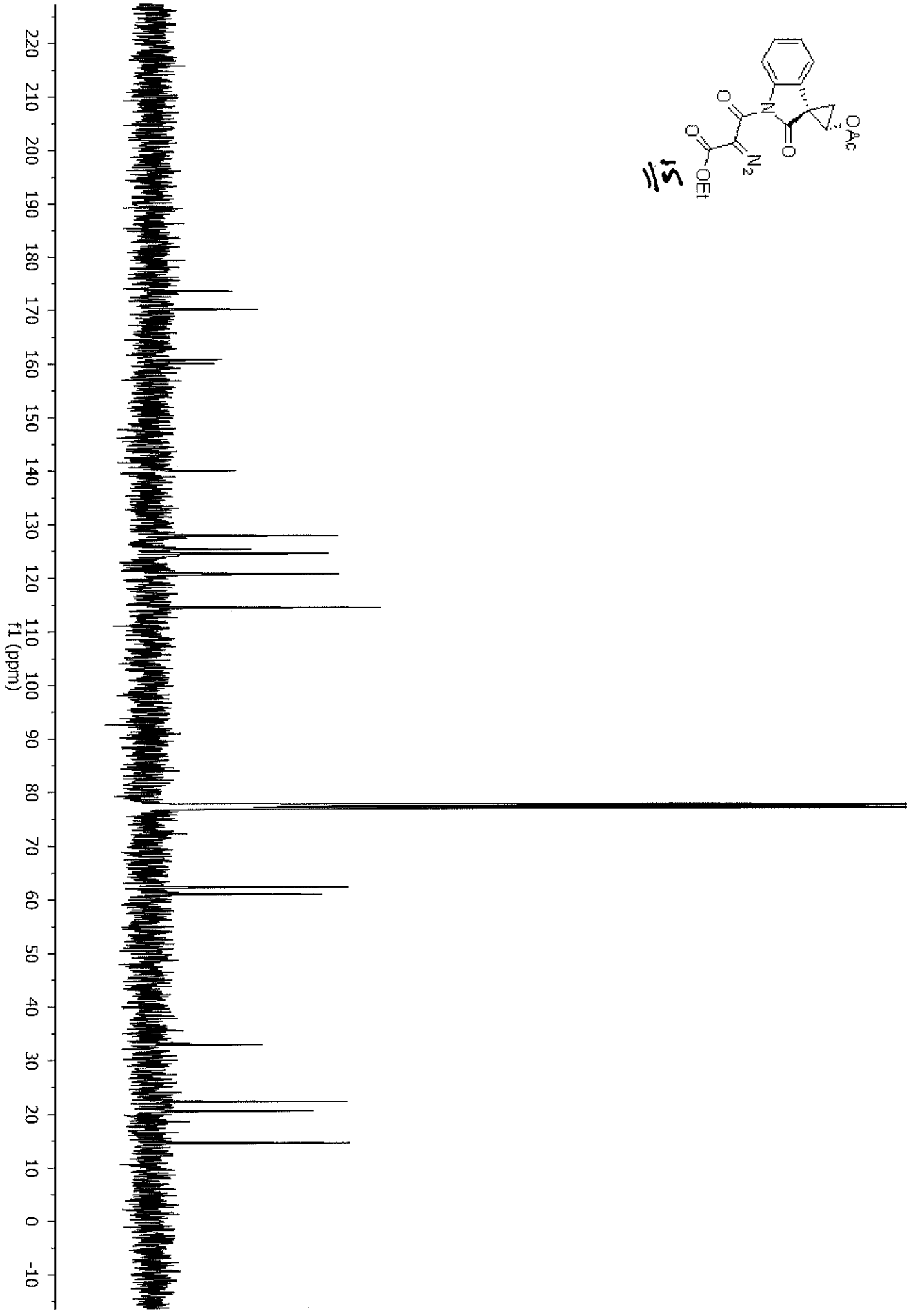
N2
OEt
1h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O
O
N2
OEt
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50
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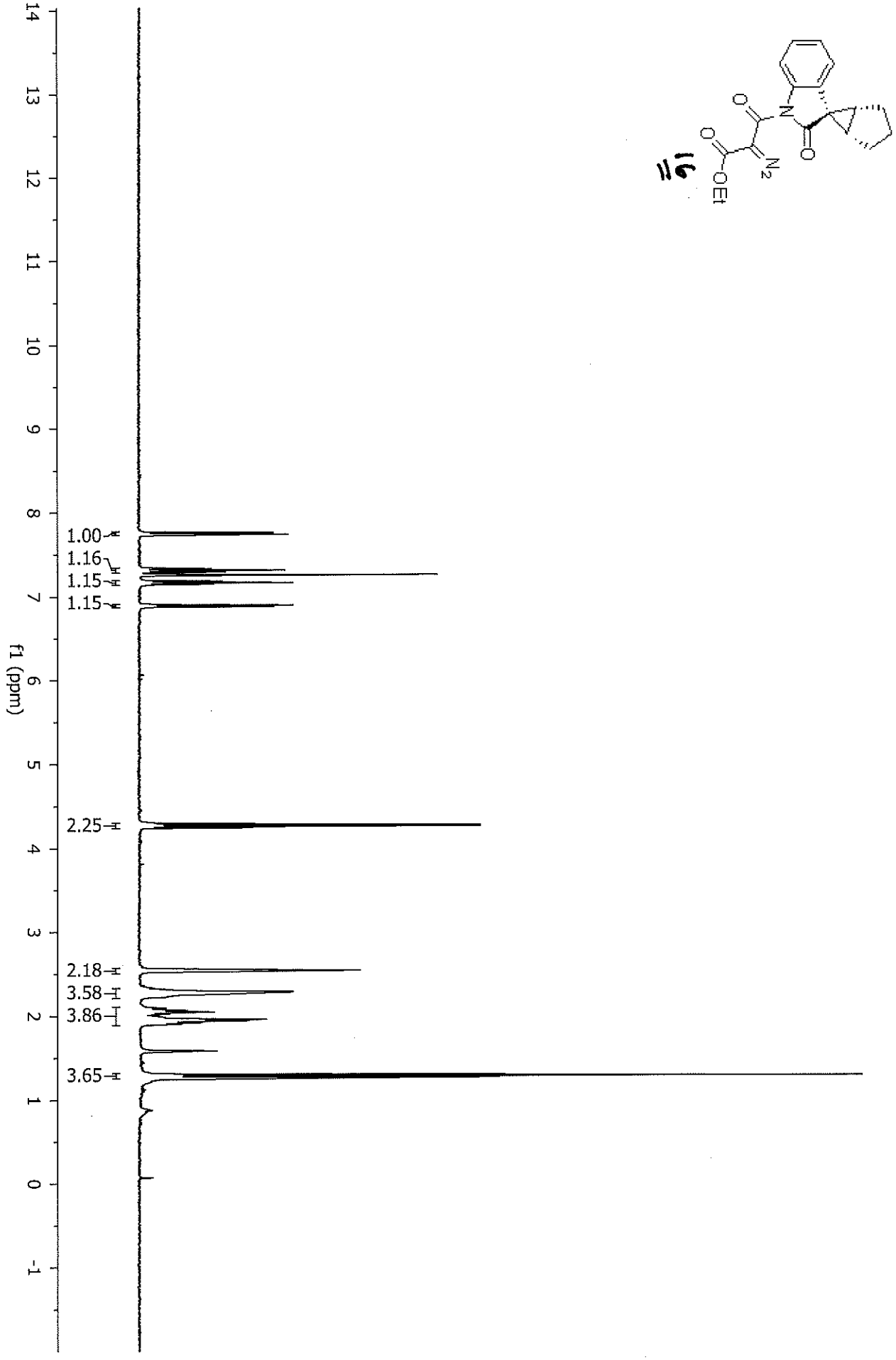
-10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O
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N2
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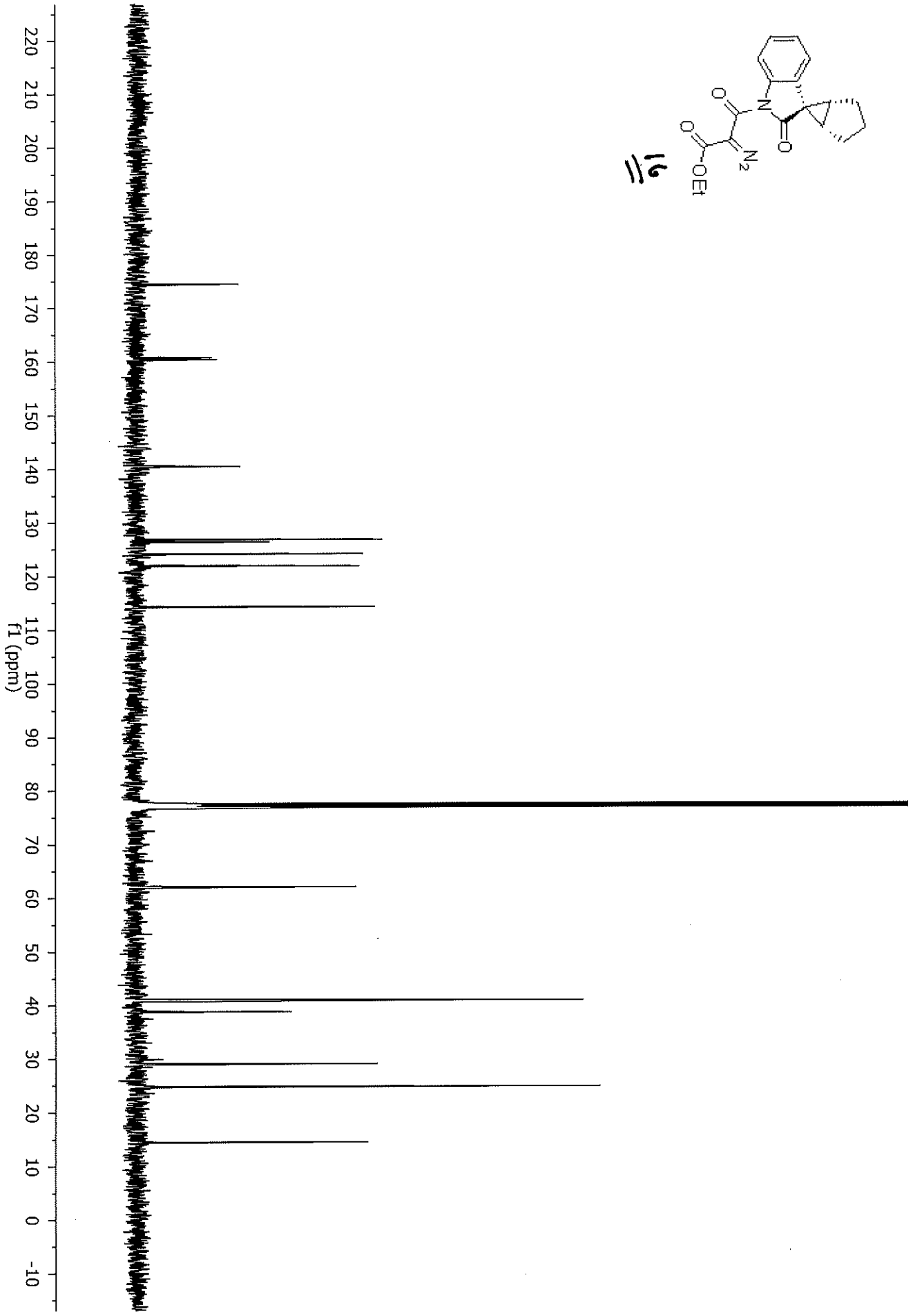
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f1 (ppm)
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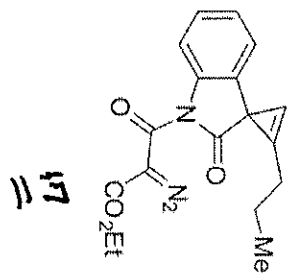
O
O
N2
O
OEt


O
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O
N2
CO2Et
Me

1i

f1 (ppm)
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13
12
11
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9
8
7
6
5
4
3
2
1
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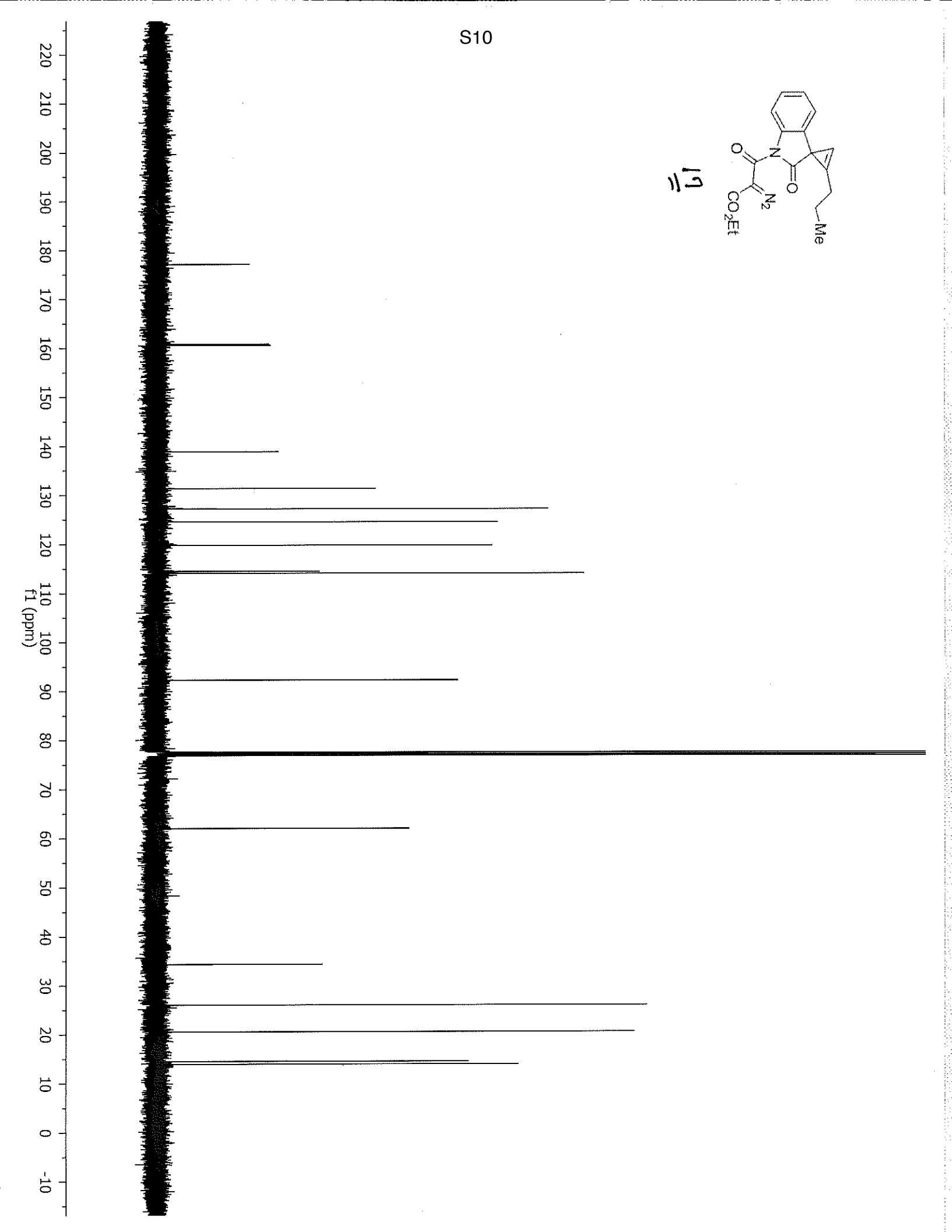
3.03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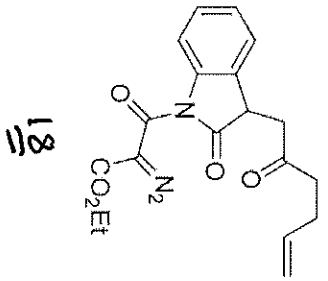
0
-10
f1 (ppm)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N2
CO2Et

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0.95
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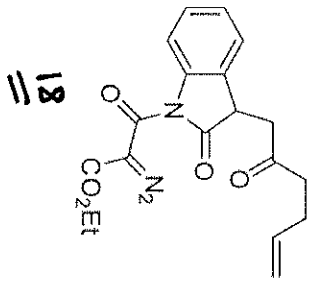
1.09
2.02
2.00
3.10
f1 (ppm)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O
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O
N2
CO2Et

1l

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210
200
190
180
170
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80
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40
30
20
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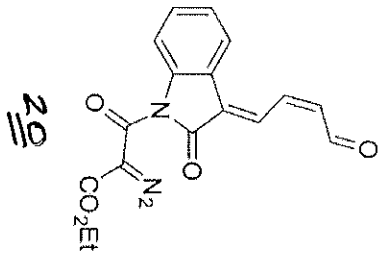
0
-10
f1 (ppm)



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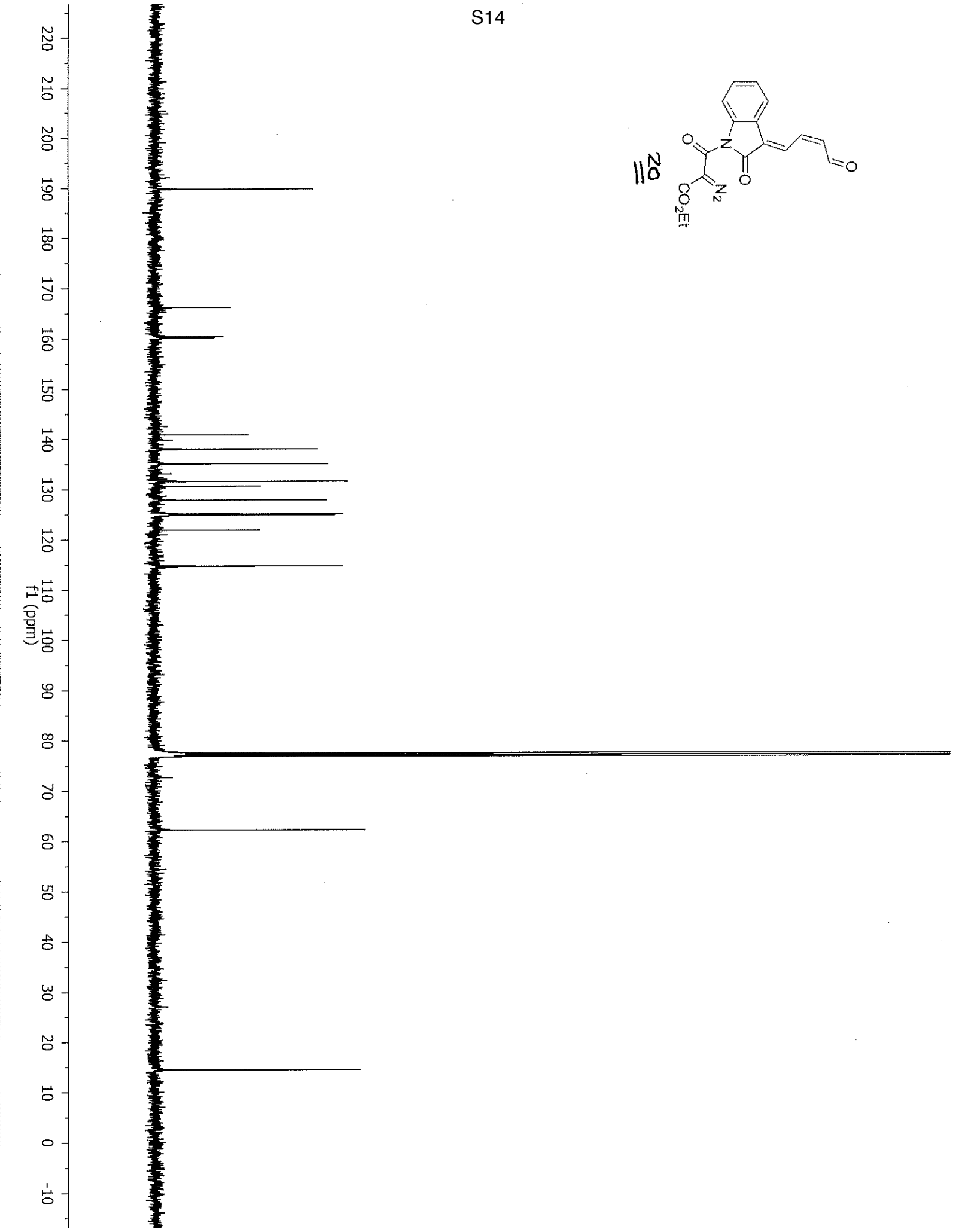
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100
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80
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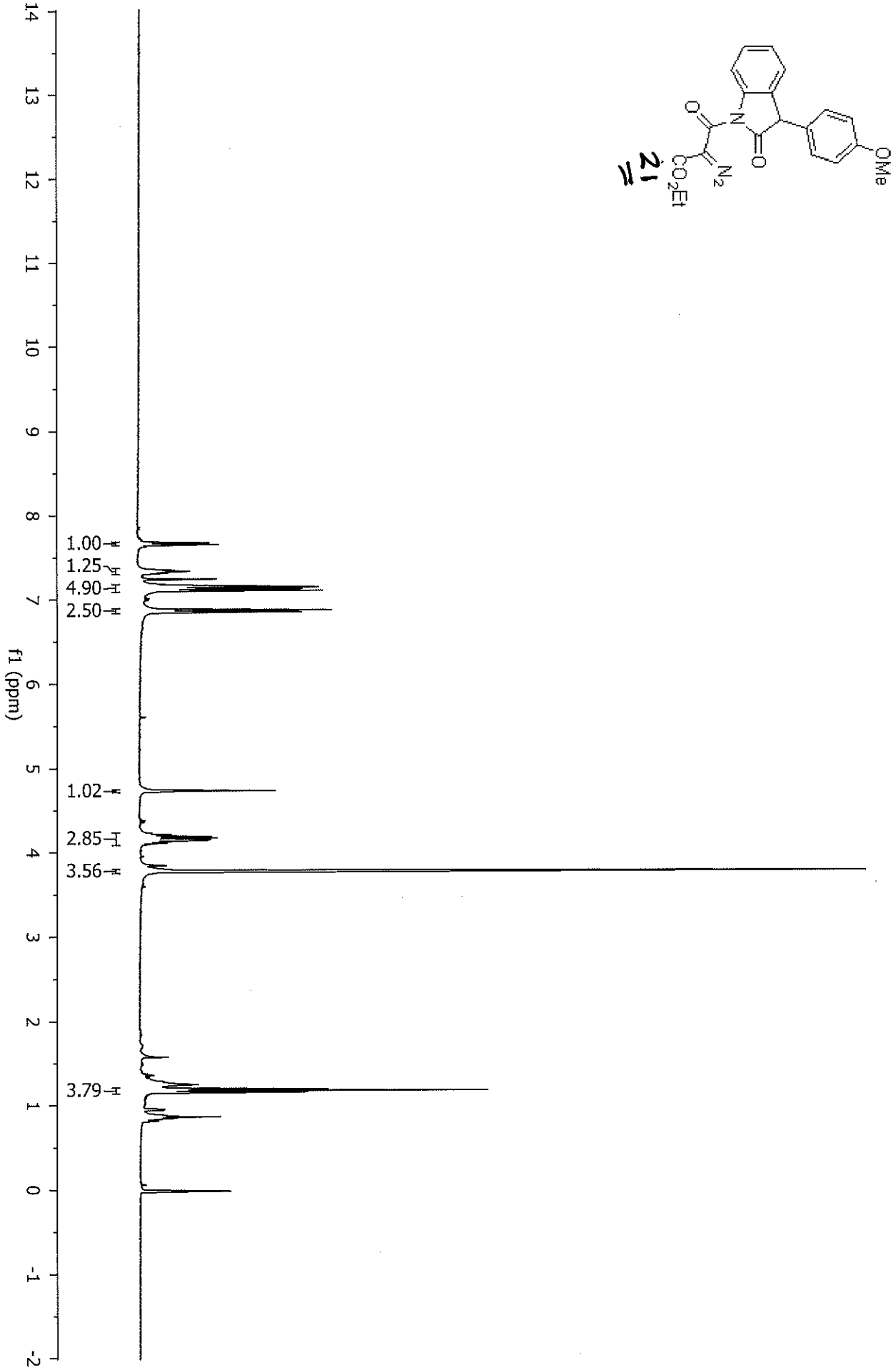
20
10
0
-10
f1 (ppm)
20
N
O
O
O
N2
CO2Et
O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4
3
2
1
0
-1
-2
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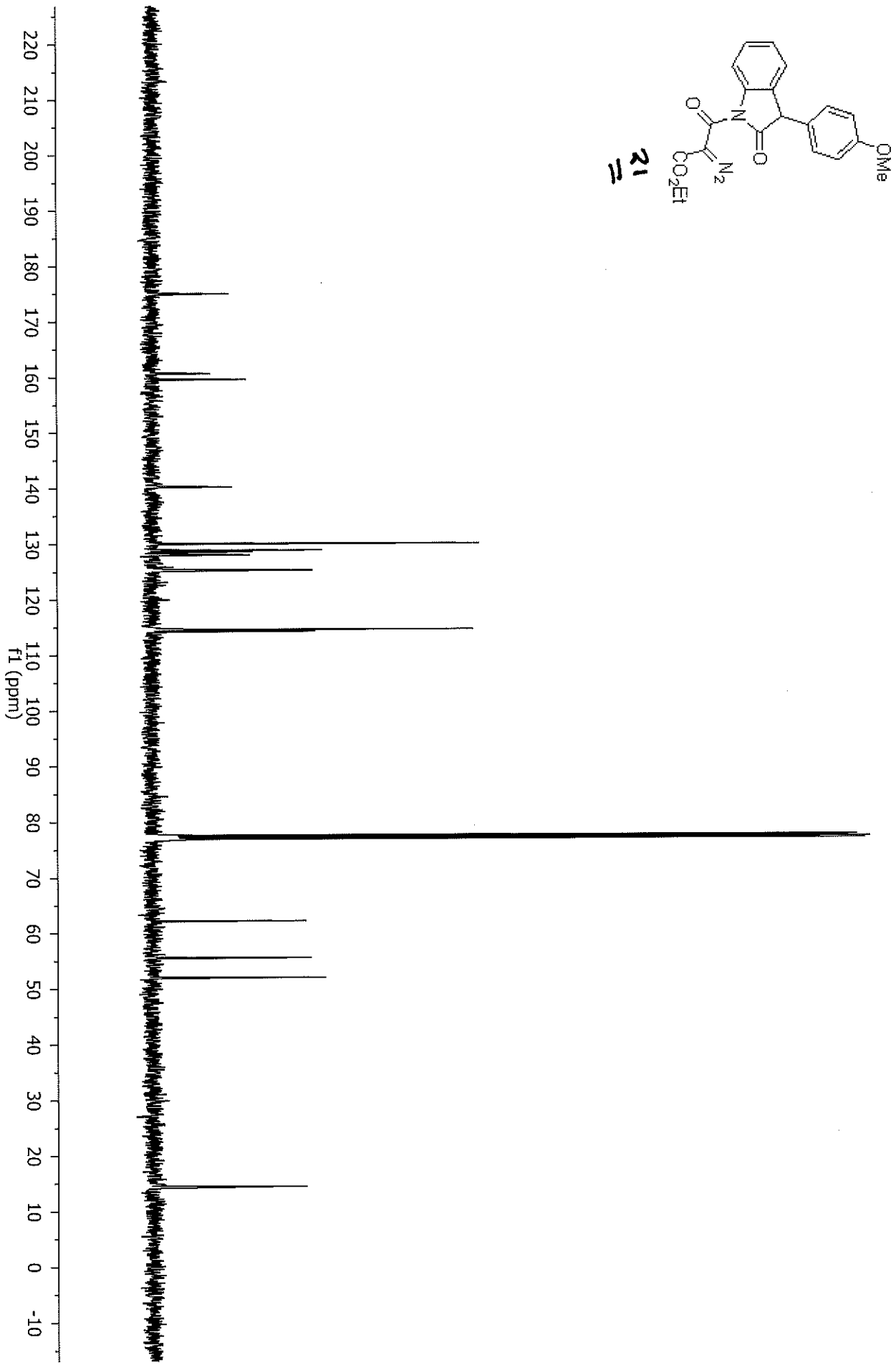
2.85
3.56
3.79
OMe
N2
CO2Et
21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O
O
N2
CO2Et
2l
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210
200
190
180
170
160
150
140
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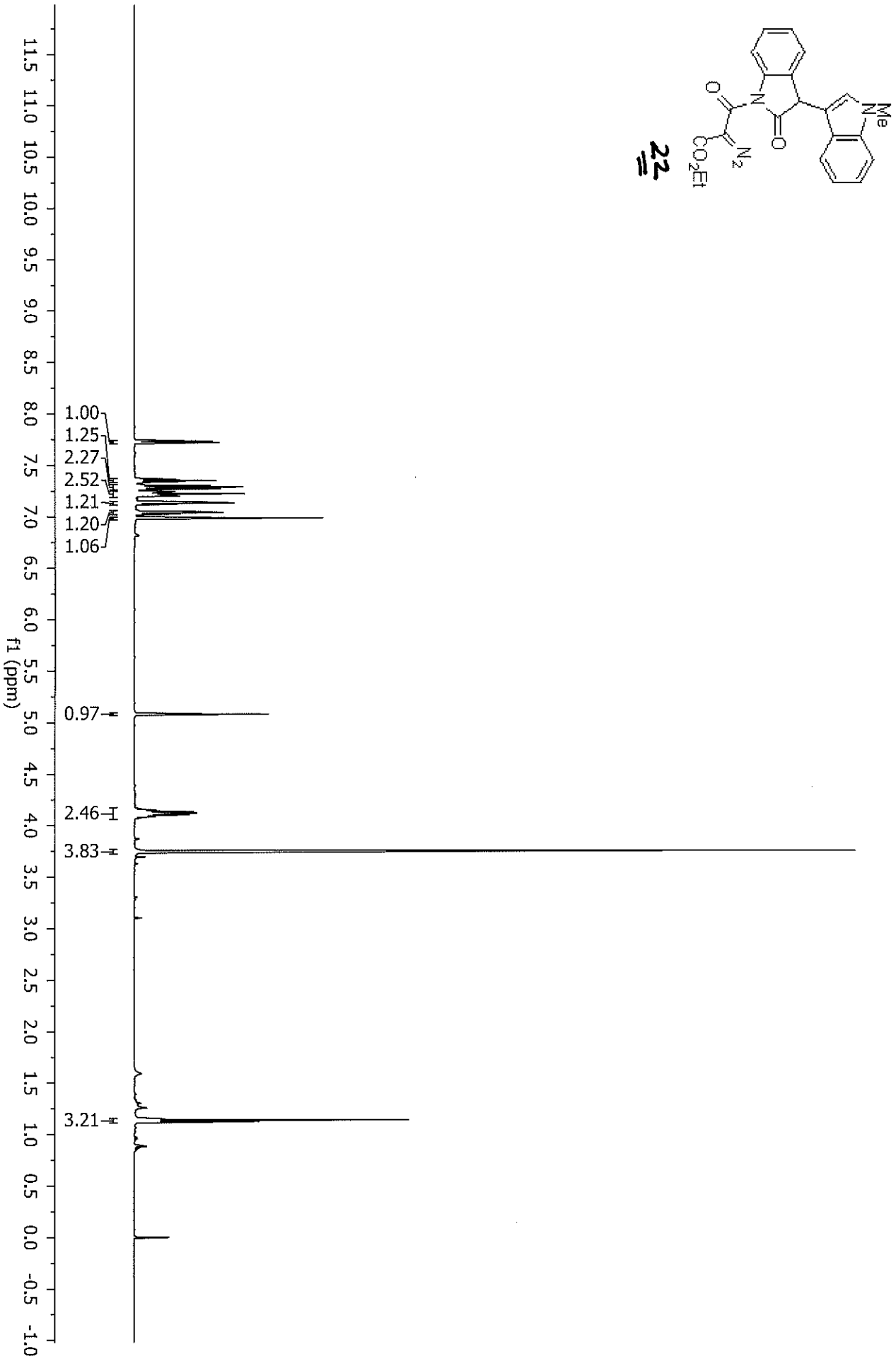
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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N
N2
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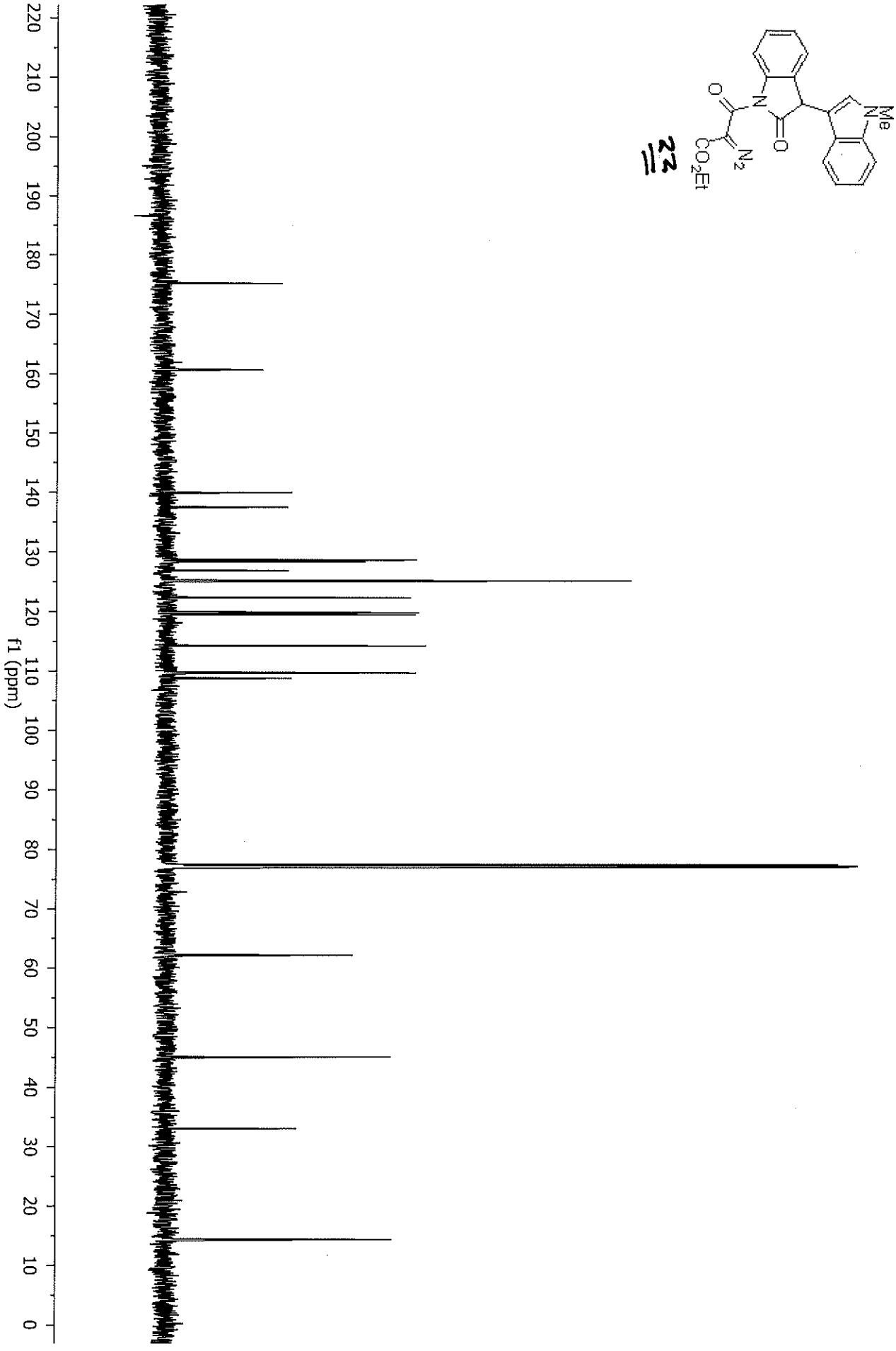
f1 (ppm)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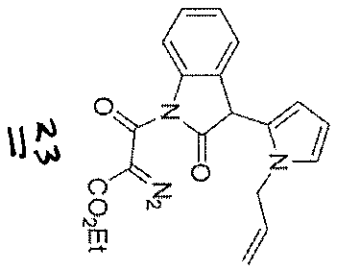
10
0
f1 (ppm)
Me
N
N
O
O
N2
CO2Et

22


O
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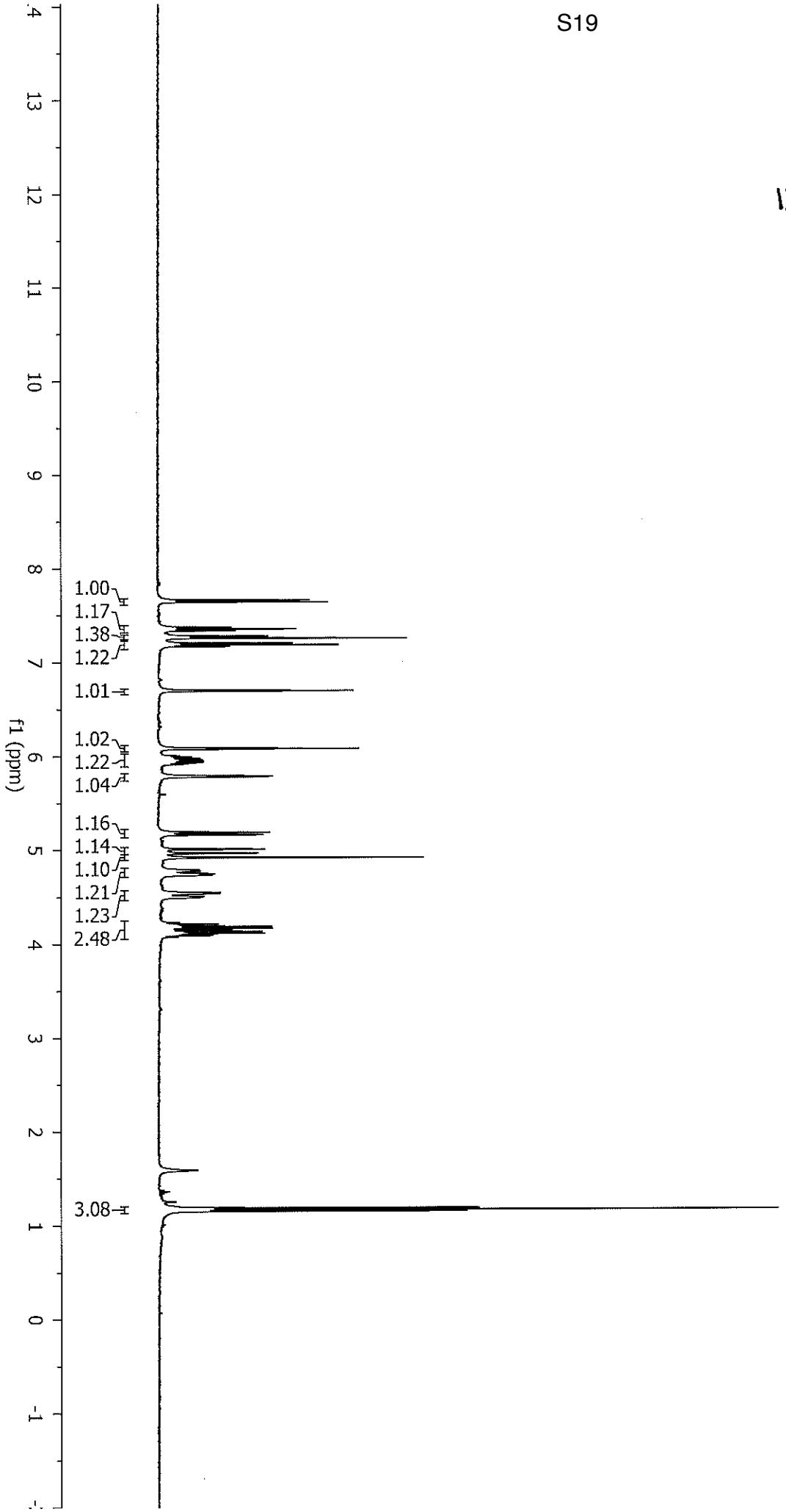
O
N
N2
CO2Et

23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1.21
1.23
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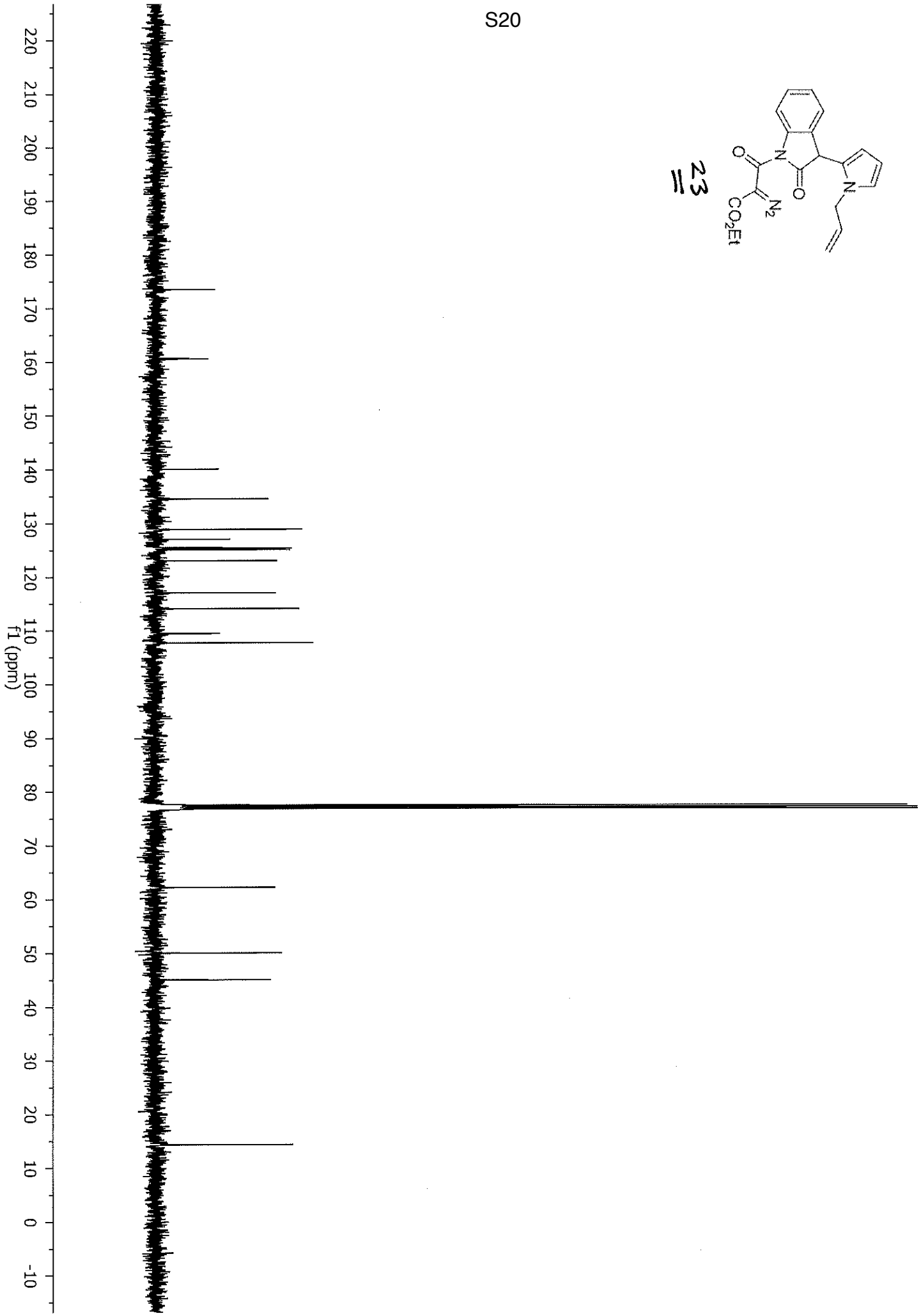
3.08
f1 (ppm)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100
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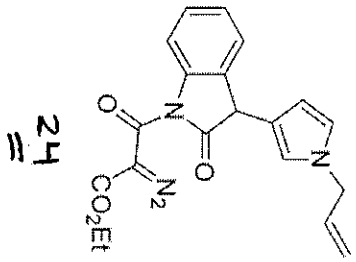
60
50
40
30
20
10
0
-10
f1 (ppm)

23


24
O
N
O
N2
CO2Et
N

0.95
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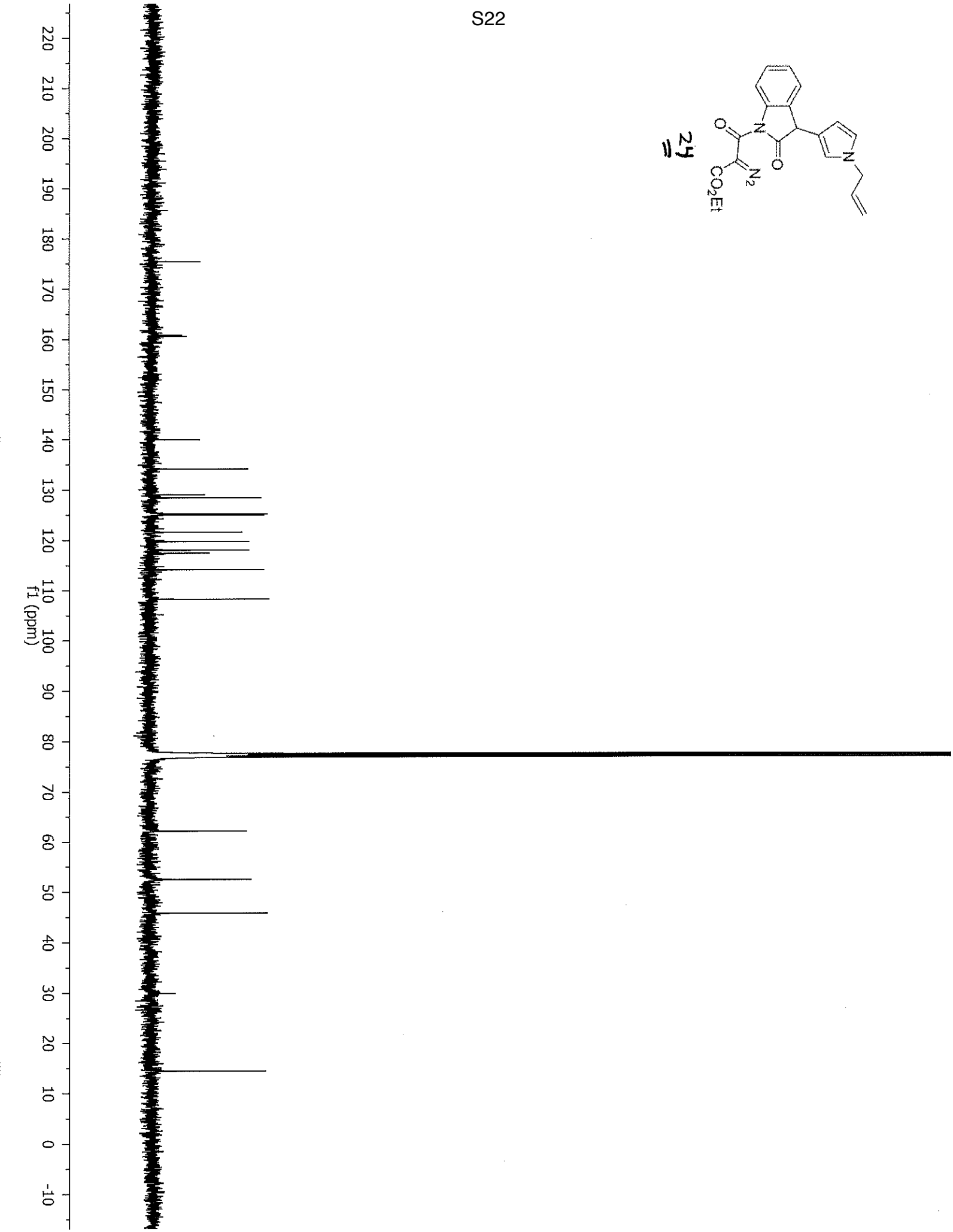
1.07
0.94
0.81
0.85
0.98
1.01
1.01
0.84
2.04
2.35
3.00
f1 (ppm)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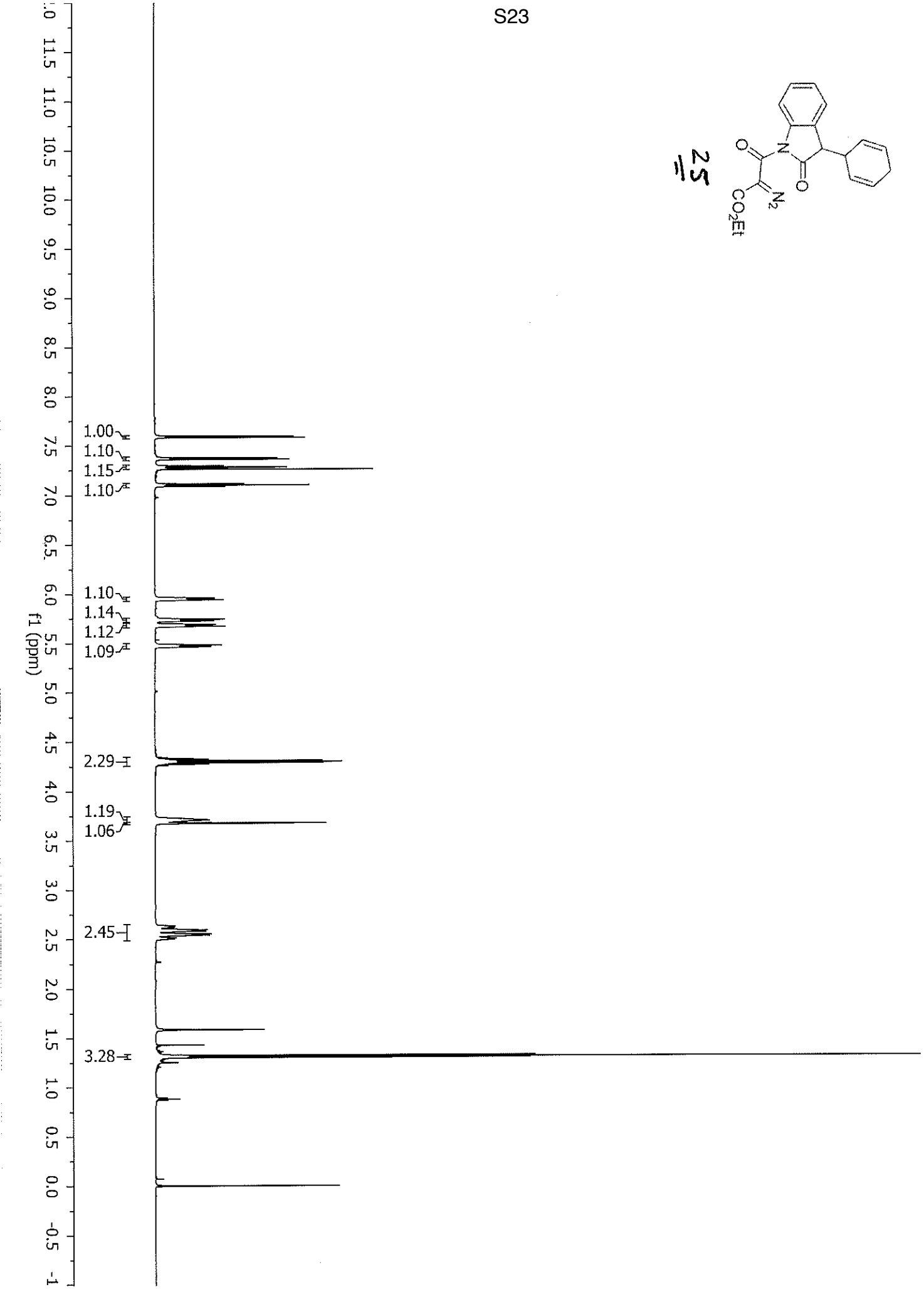
f1 (ppm)


2s
N
O
O
N2
CO2Et
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1.10
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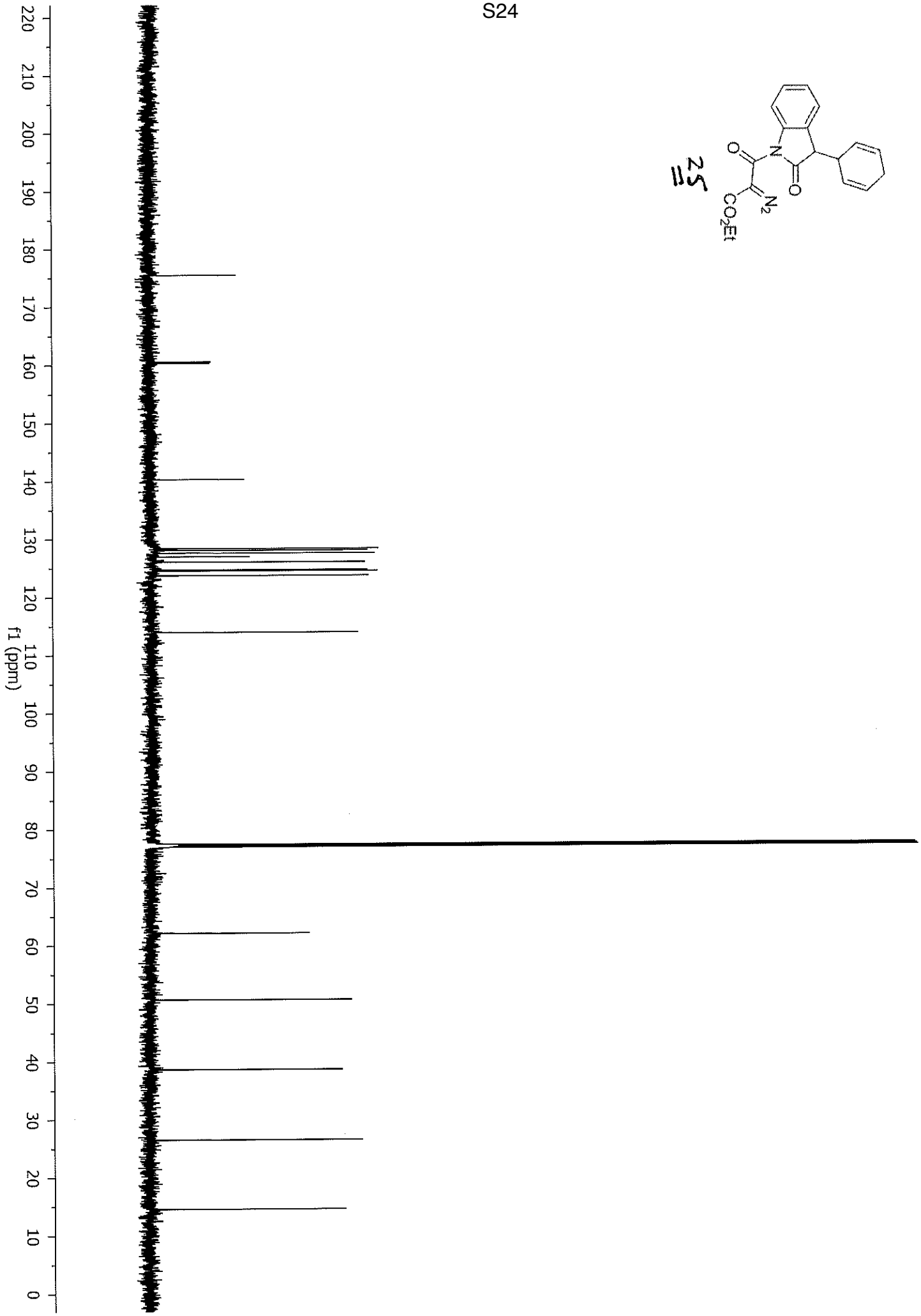
1.10
1.10
1.14
1.12
1.09
2.29
1.19
1.06
2.45
3.28
f1 (ppm)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200
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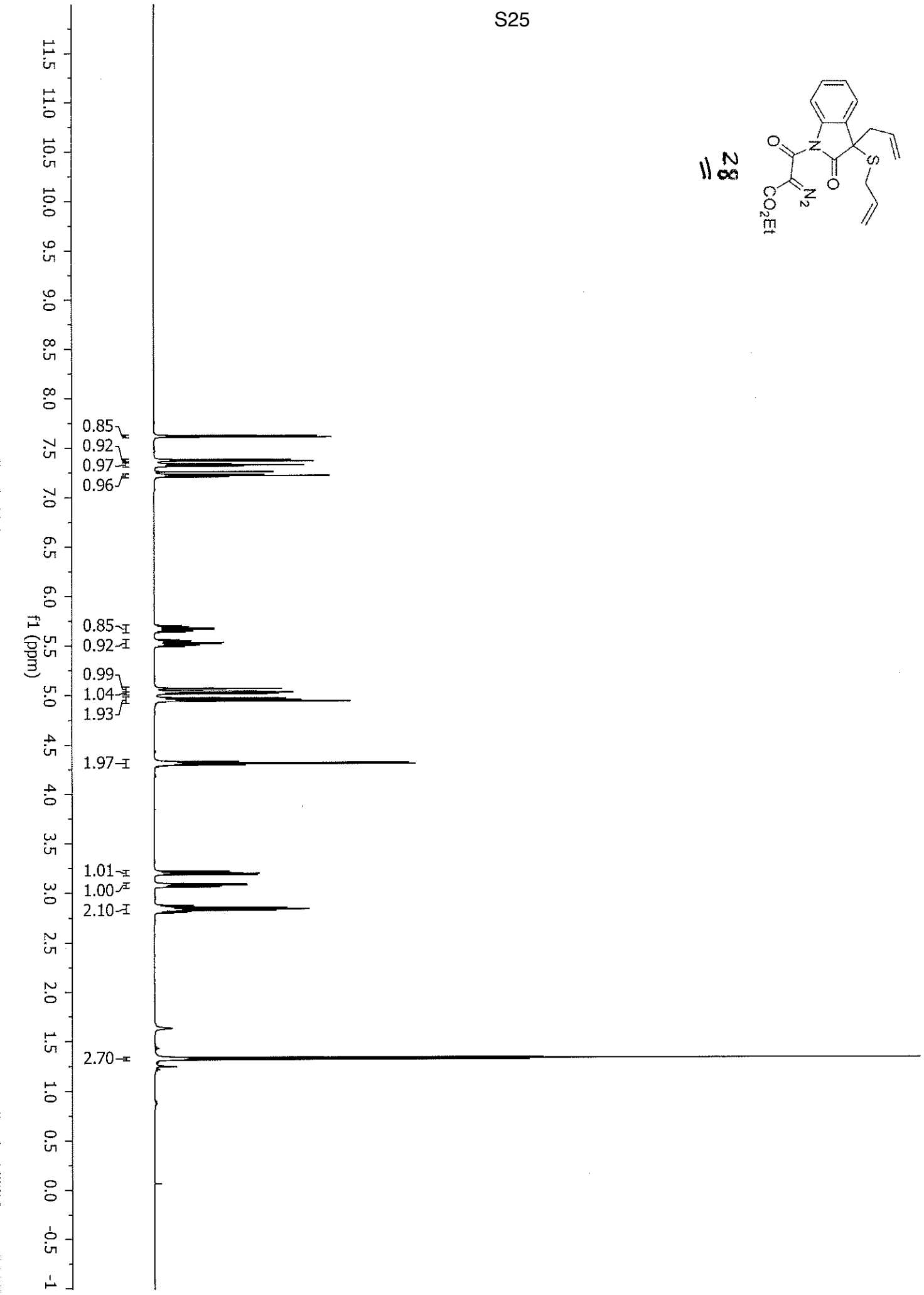
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

O
N
O
N2
CO2Et

25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f1 (ppm)
0.85
0.92
0.97
0.96
0.85
0.92
0.99
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1.01
1.00
2.10
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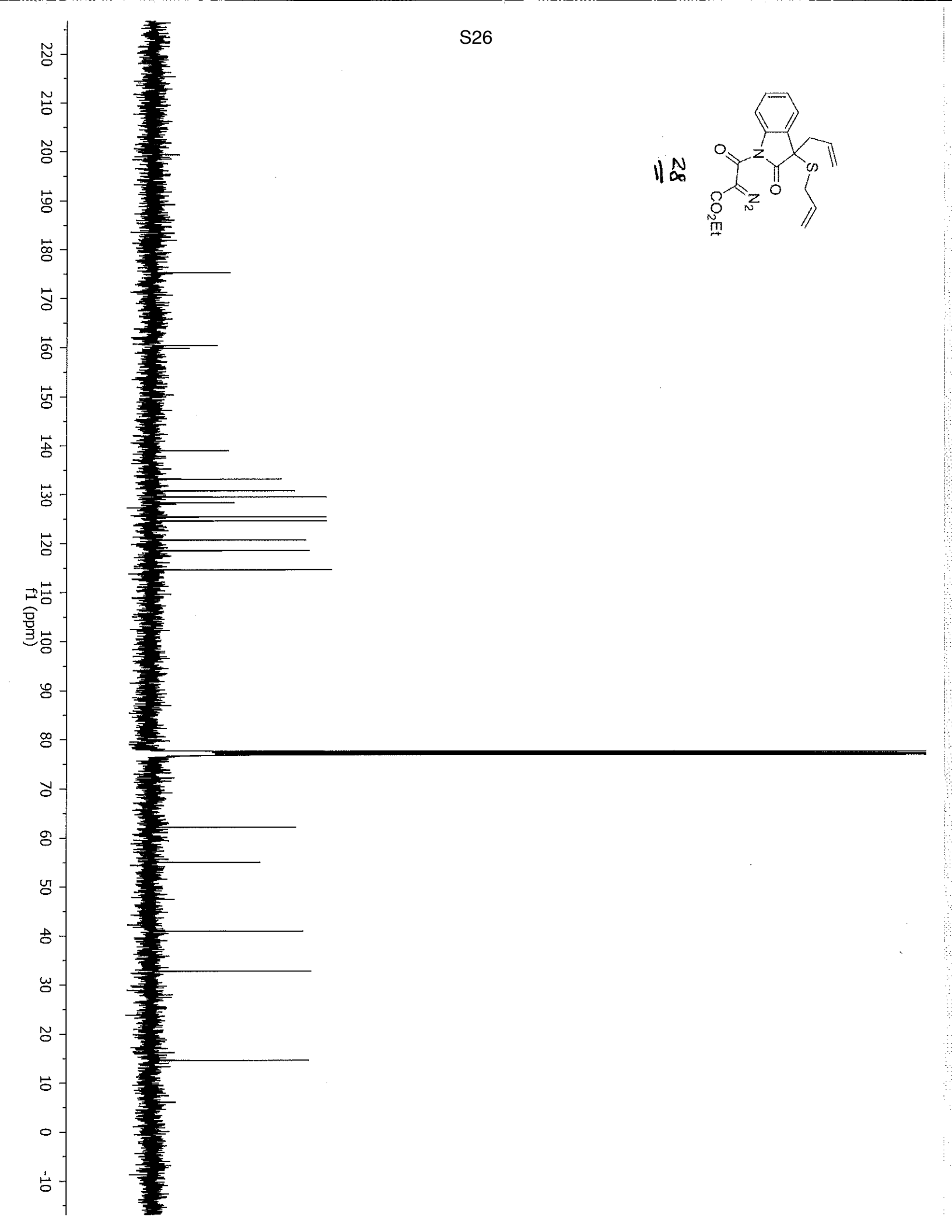
N
O
O
O
S
N2
CO2Et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200
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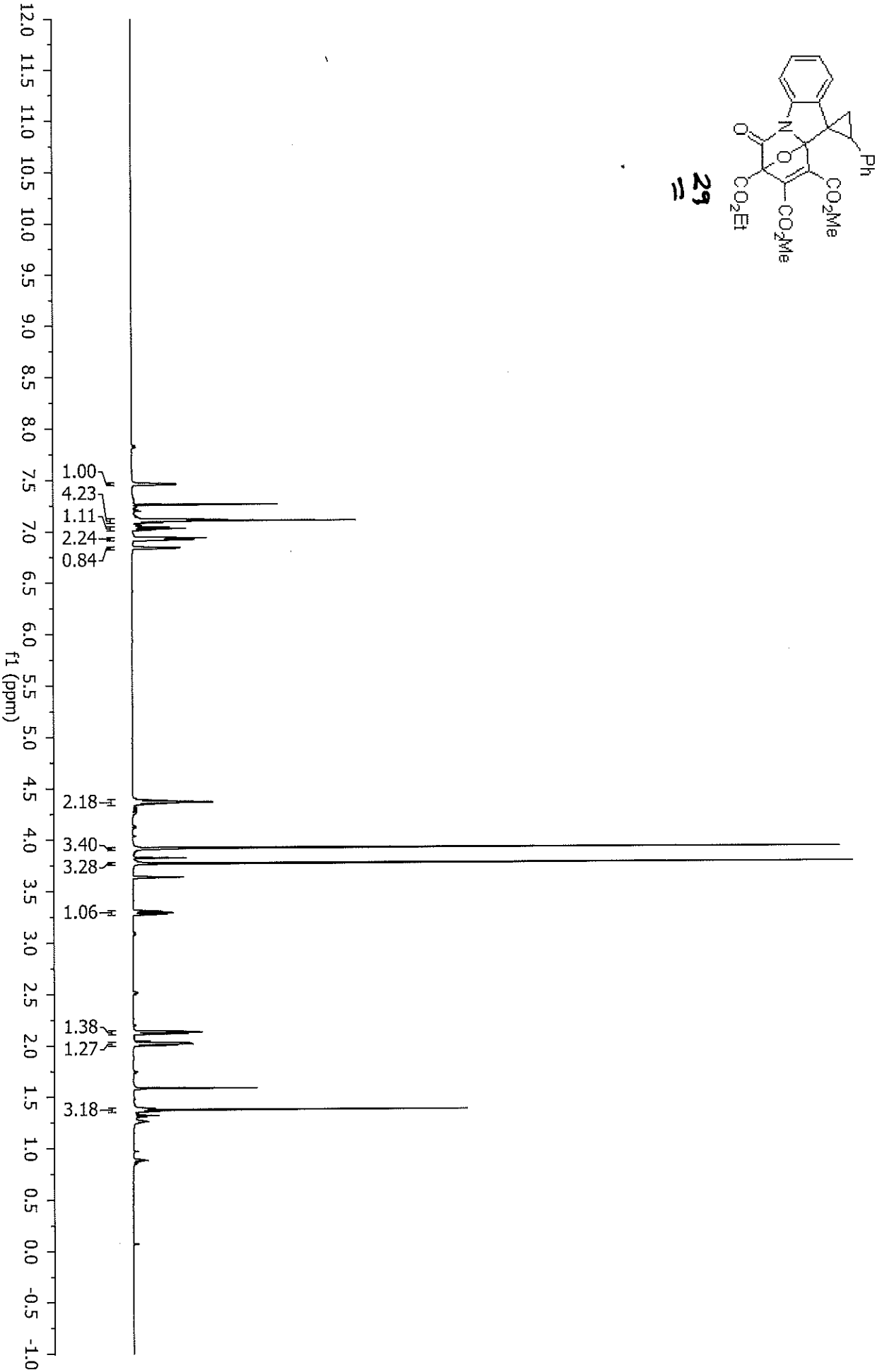
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

28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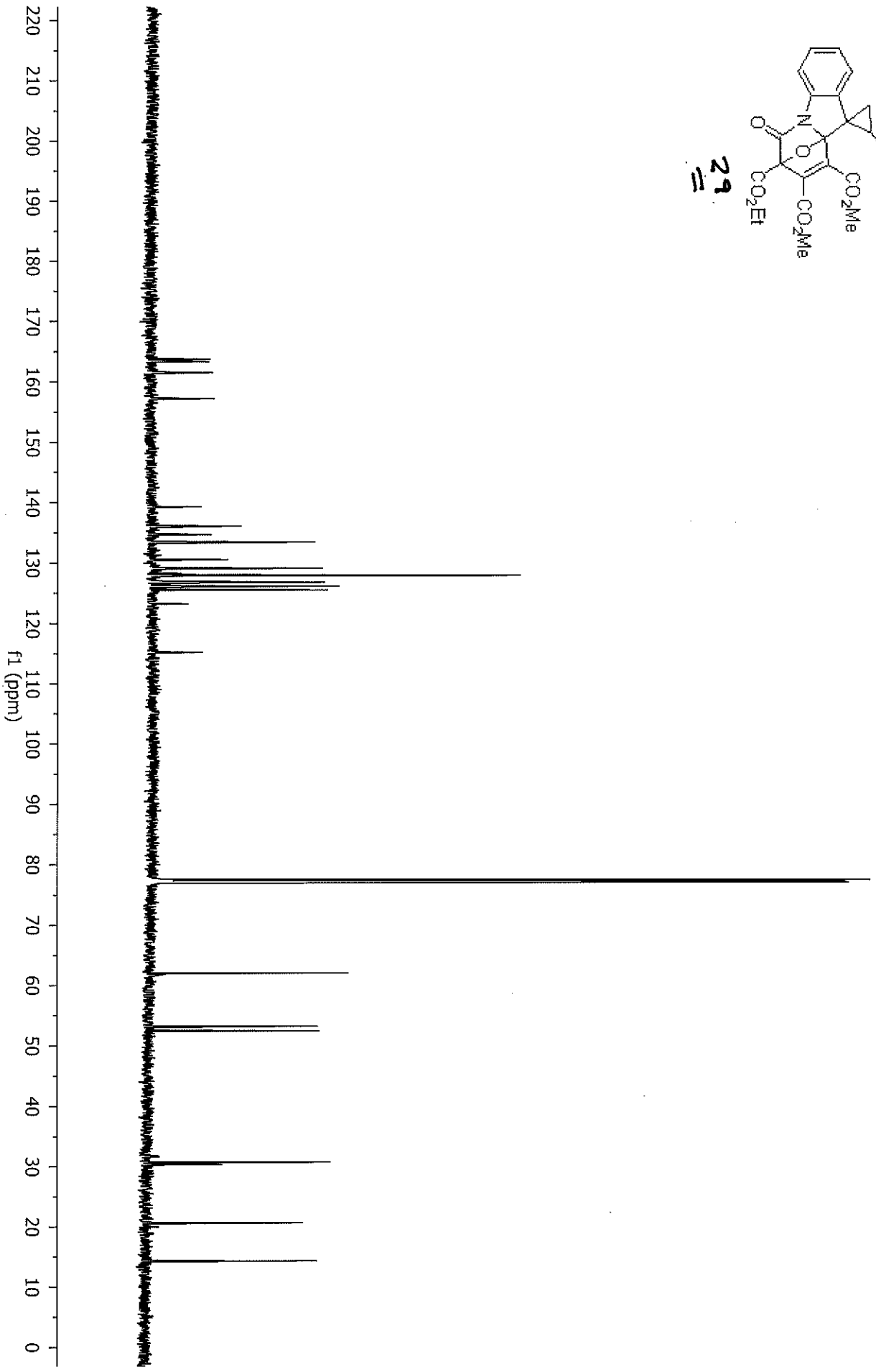
f1 (ppm)
1.00
4.23
1.11
2.24
0.84
2.18
3.40
3.28
1.06
1.38
1.27
3.18
N
O
O
Ph
CO2Me
CO2Me
CO2Et

29


Ph
CO2Me
CO2Me
CO2Et
O
N
O
29
f1 (ppm)
220
210
200
190
180
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150
140
130
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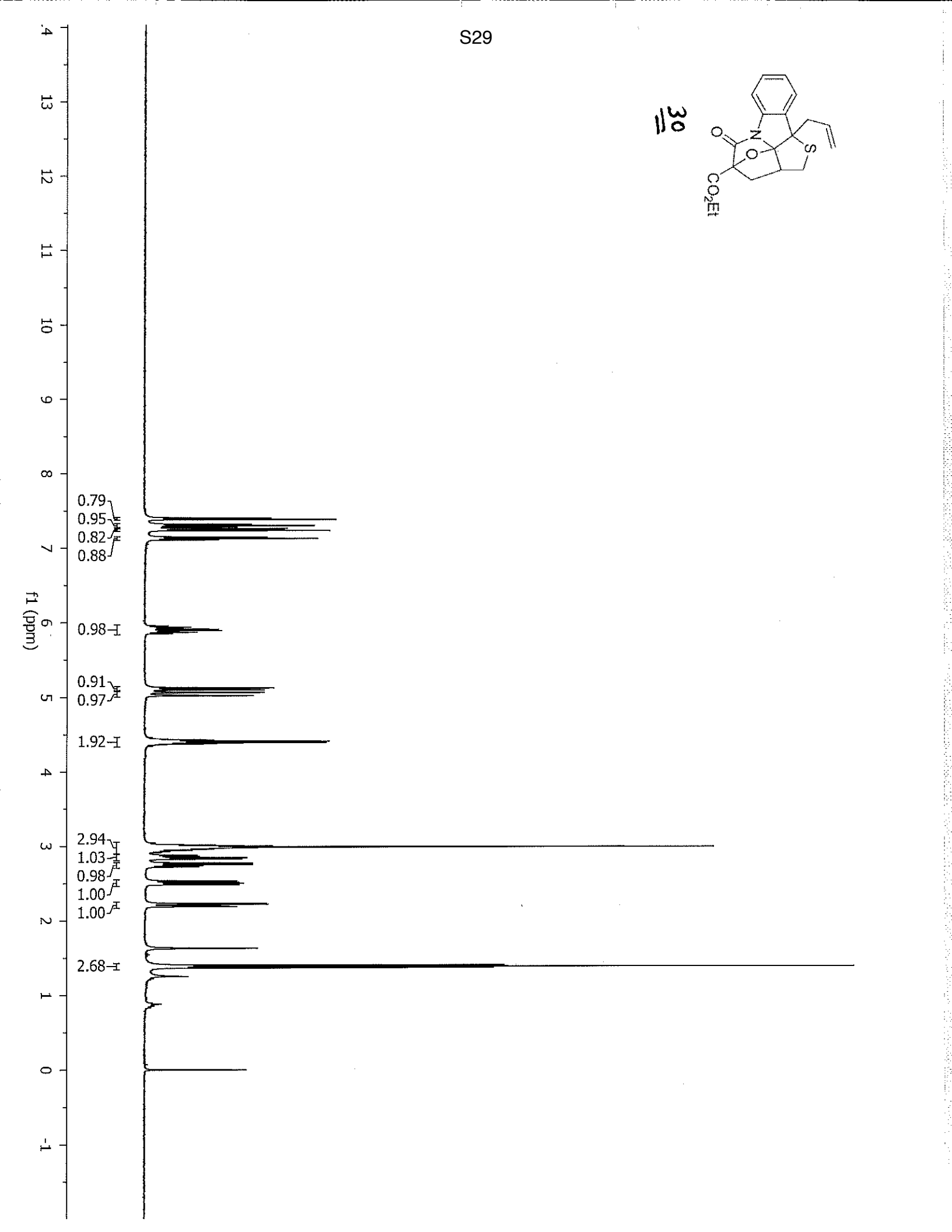
100
90
80
70
60
50
40
30
20
10
0


30
CO2Et
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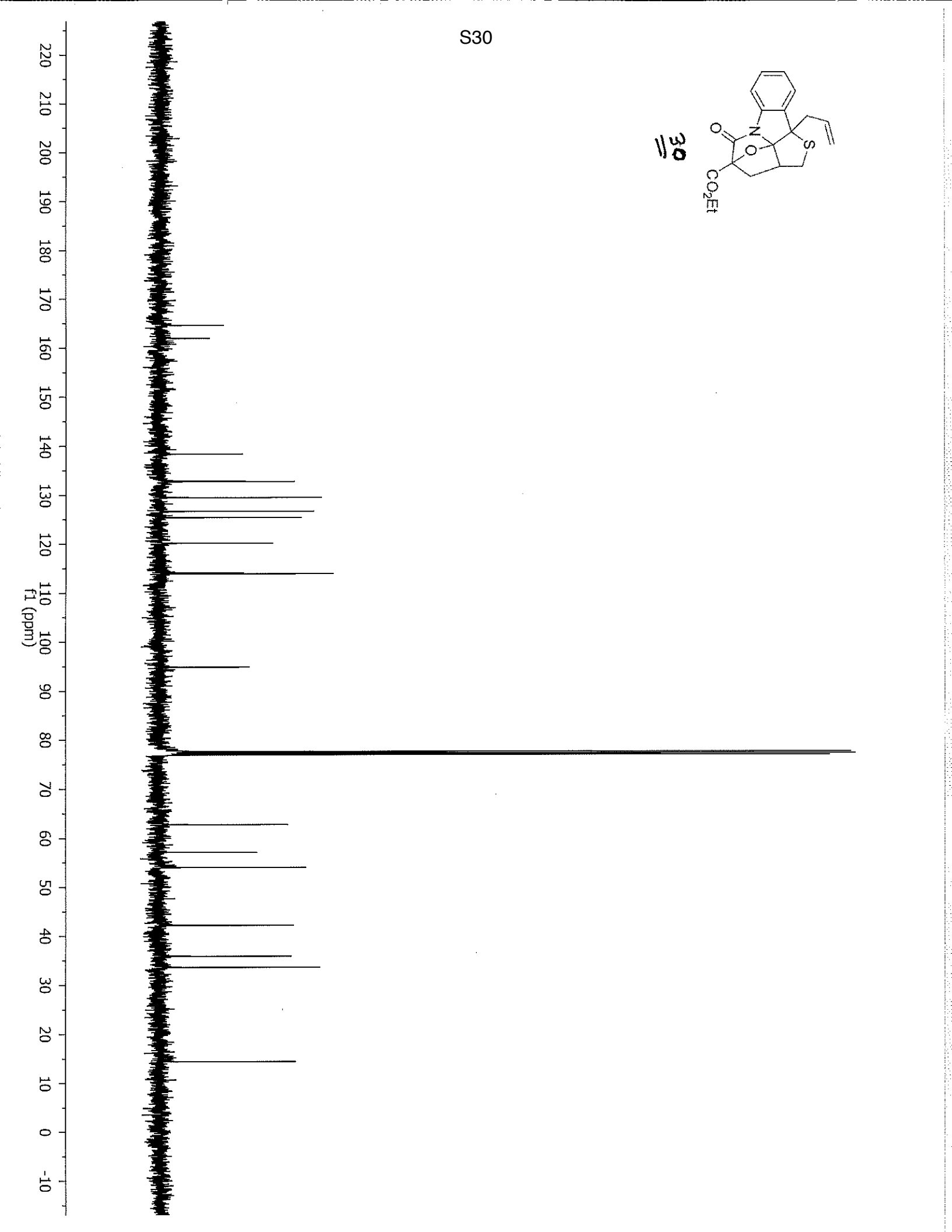
0.95
0.82
0.88
0.98
0.91
0.97
1.92
2.94
1.03
0.98
1.00
1.00
2.68
f1 (ppm)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N
O
S
O
CO2Et
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180
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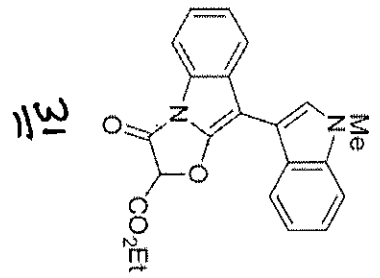
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



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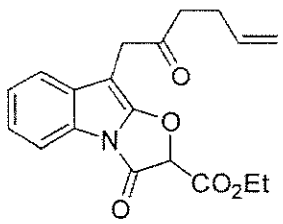
O
N
O
O
CO_2Et

31

220
210
200
190
180
170
160
150
140
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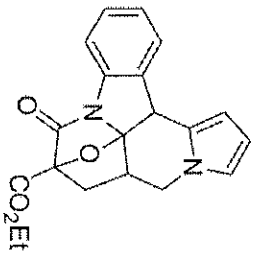
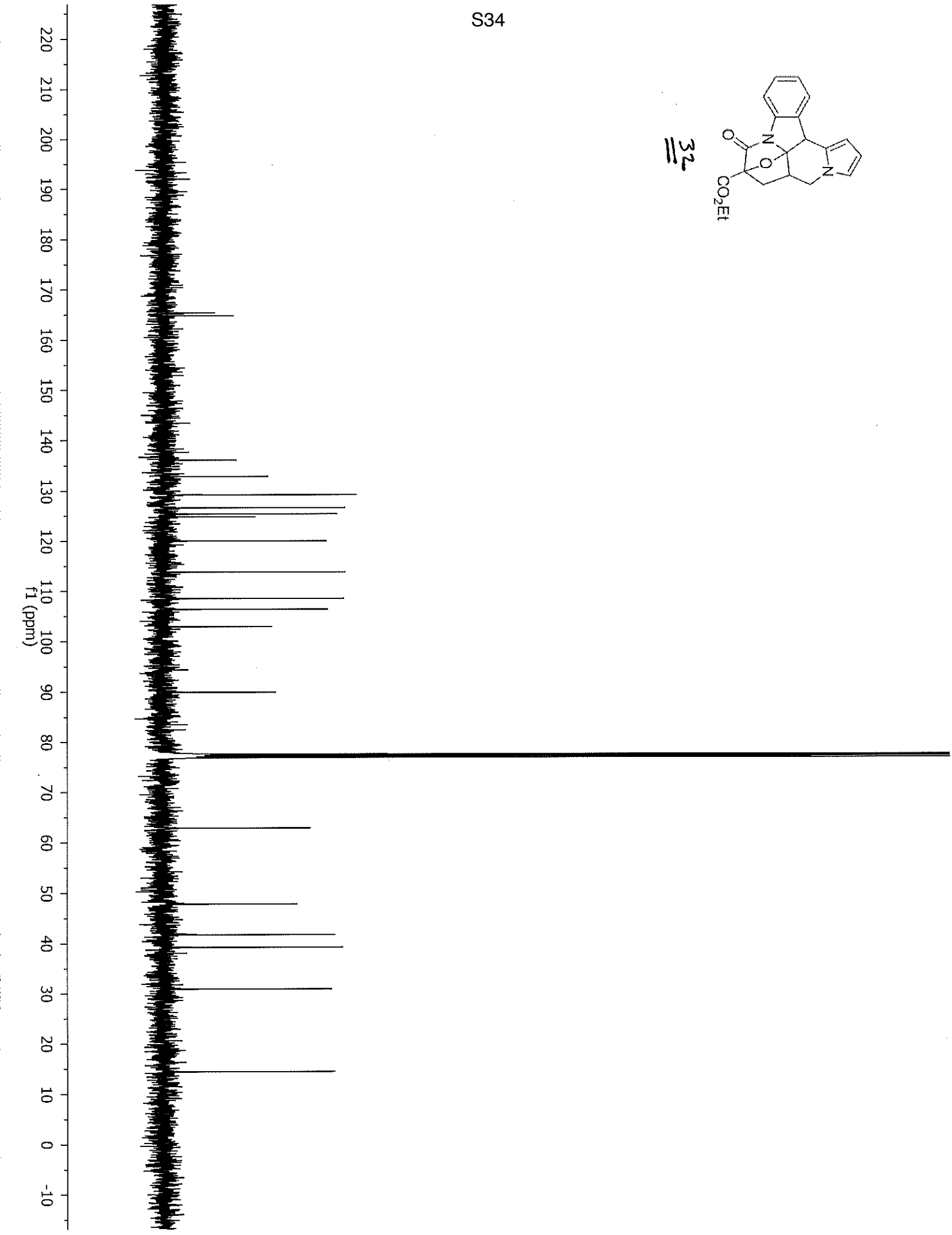
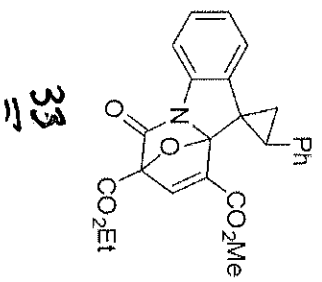
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
N
O
N
CO2Et

32

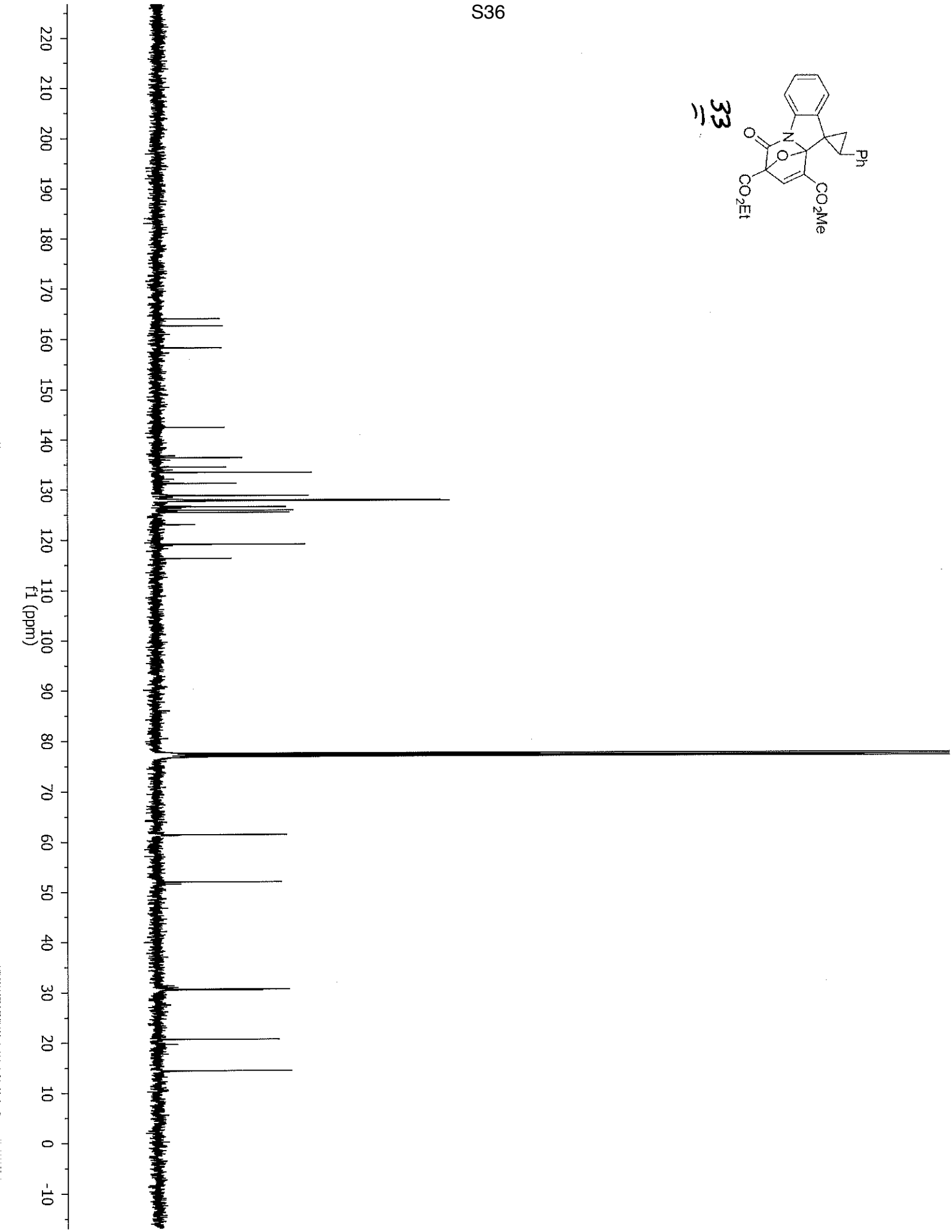
1.00
0.93
1.06
1.05
0.94
0.95
0.92
0.88
2.26
1.14
1.17
1.08
1.14
1.11
3.03
f1 (ppm)


32
O
N
O
N
CO2Et
220
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)


O
N
O
Ph
CO2Et
CO2Me

33

f1 (ppm)
1.00
0.89
3.64
1.96
1.97
0.96
2.27
2.93
0.52
1.08
0.29
0.26
1.13
1.09
0.50
2.93
0.79


33
Ph
CO2Et
CO2Me
f1 (ppm)
220
210
200
190
180
170
160
150
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120
110
100
90
80
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60
50
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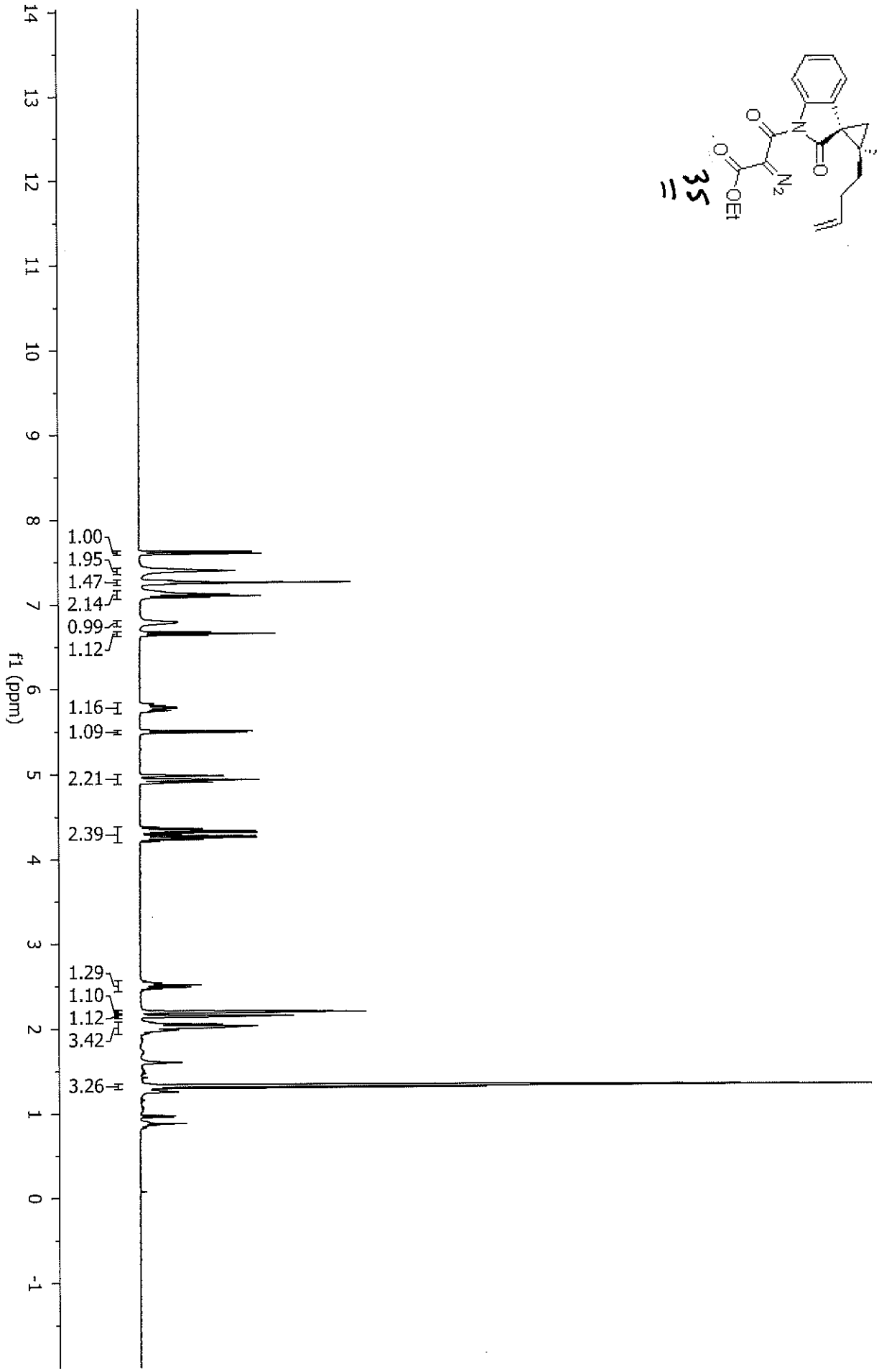
0
-10


35
Ph
N
O
O
OEt
N2
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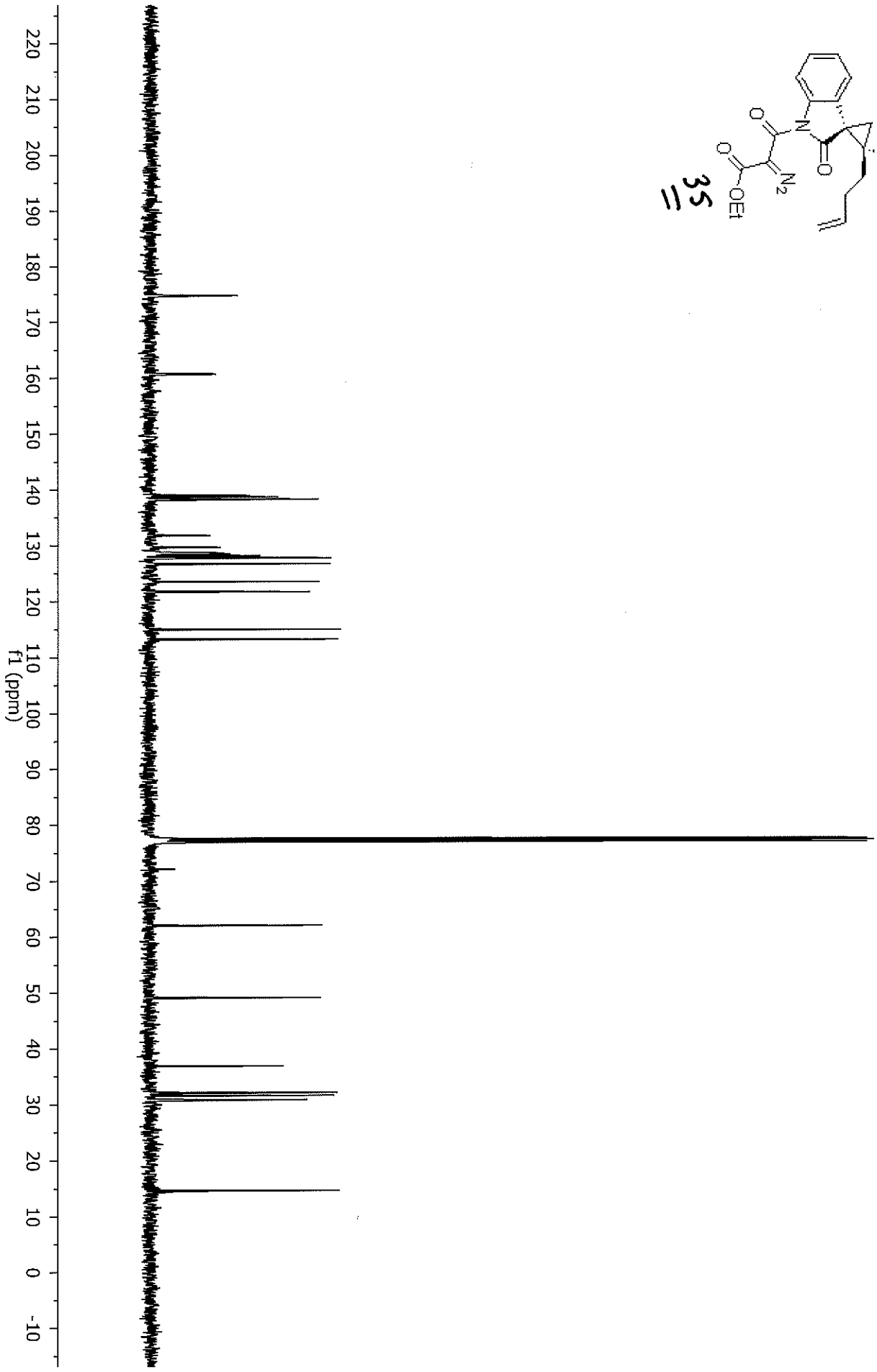
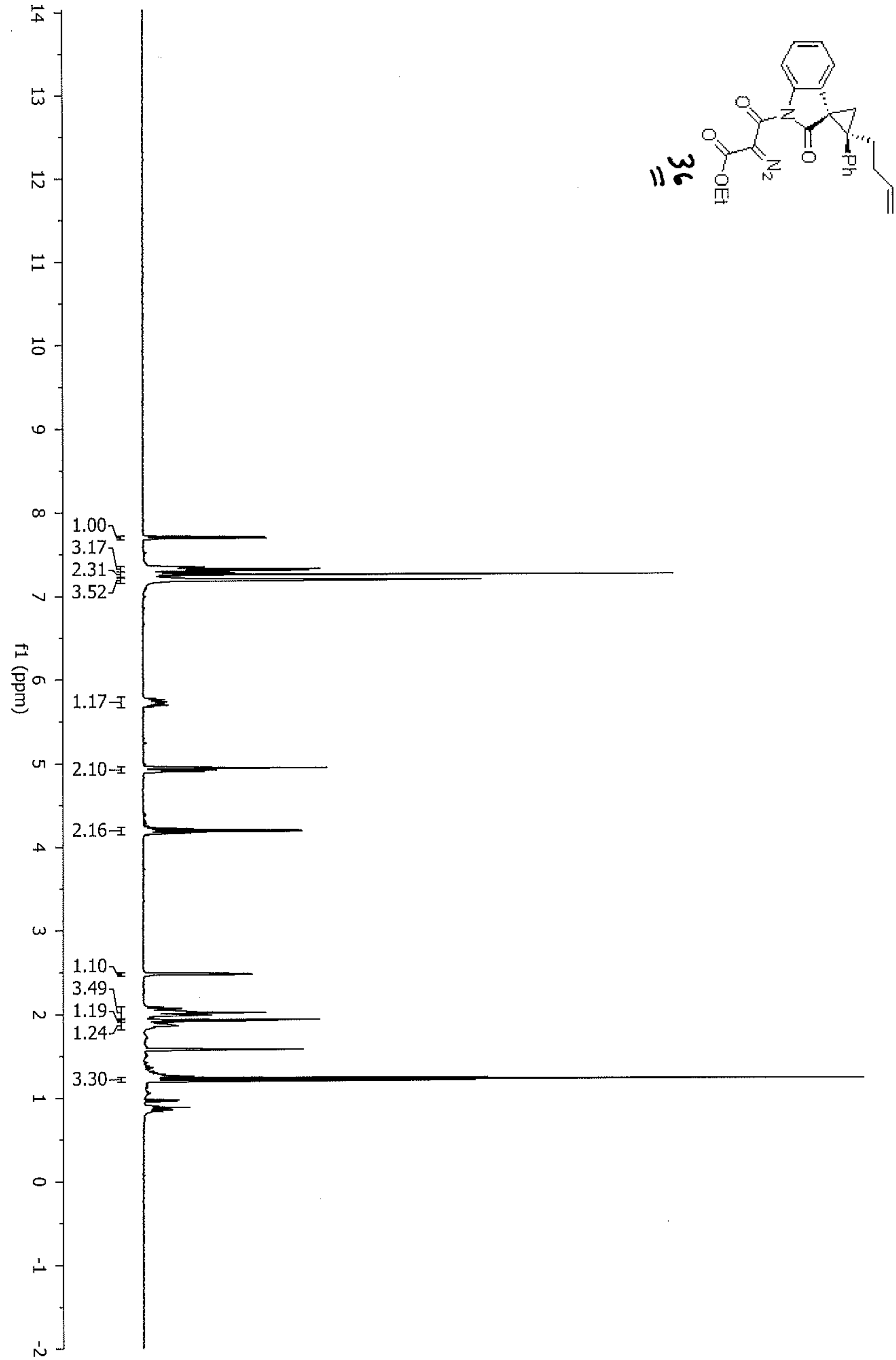
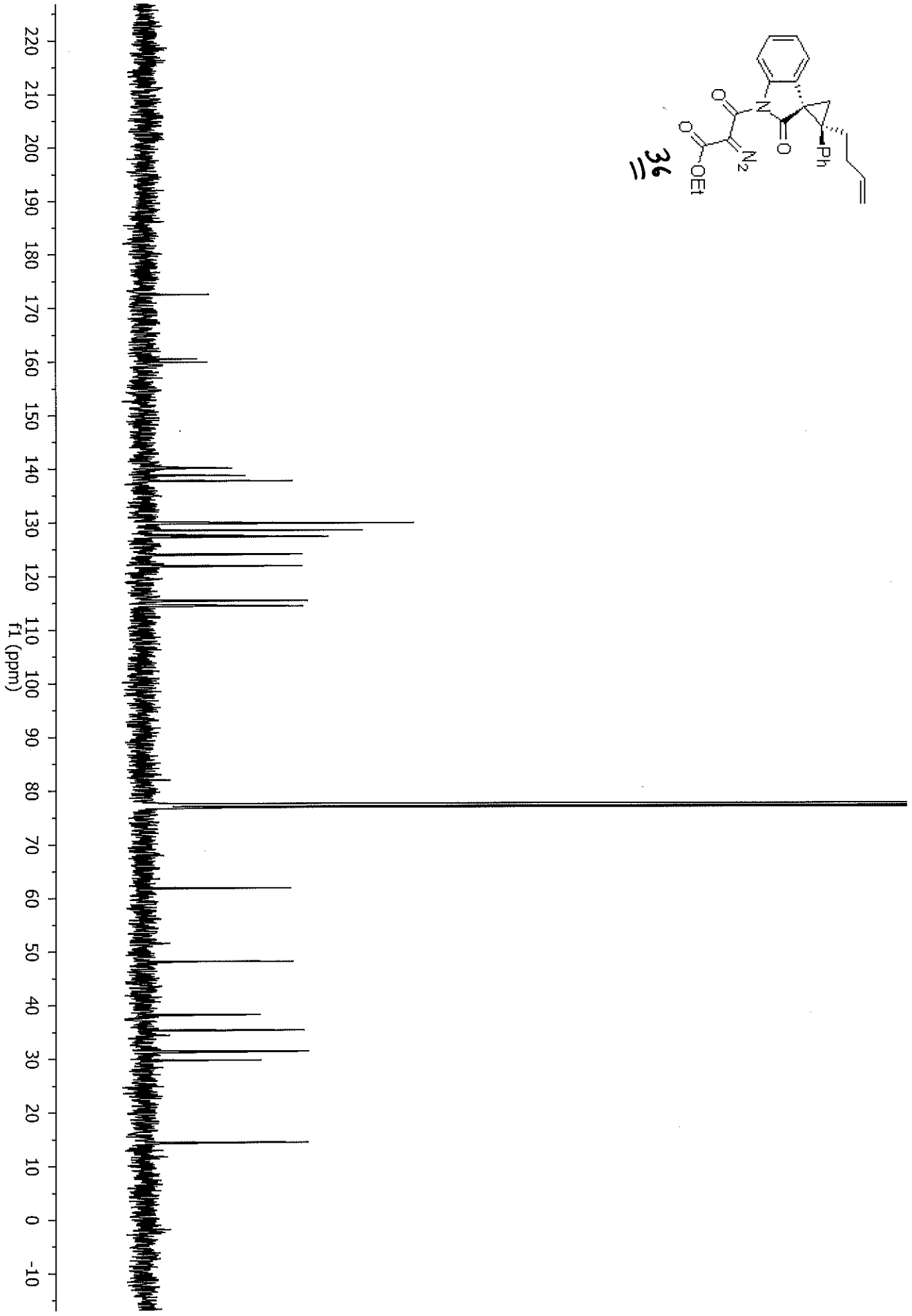
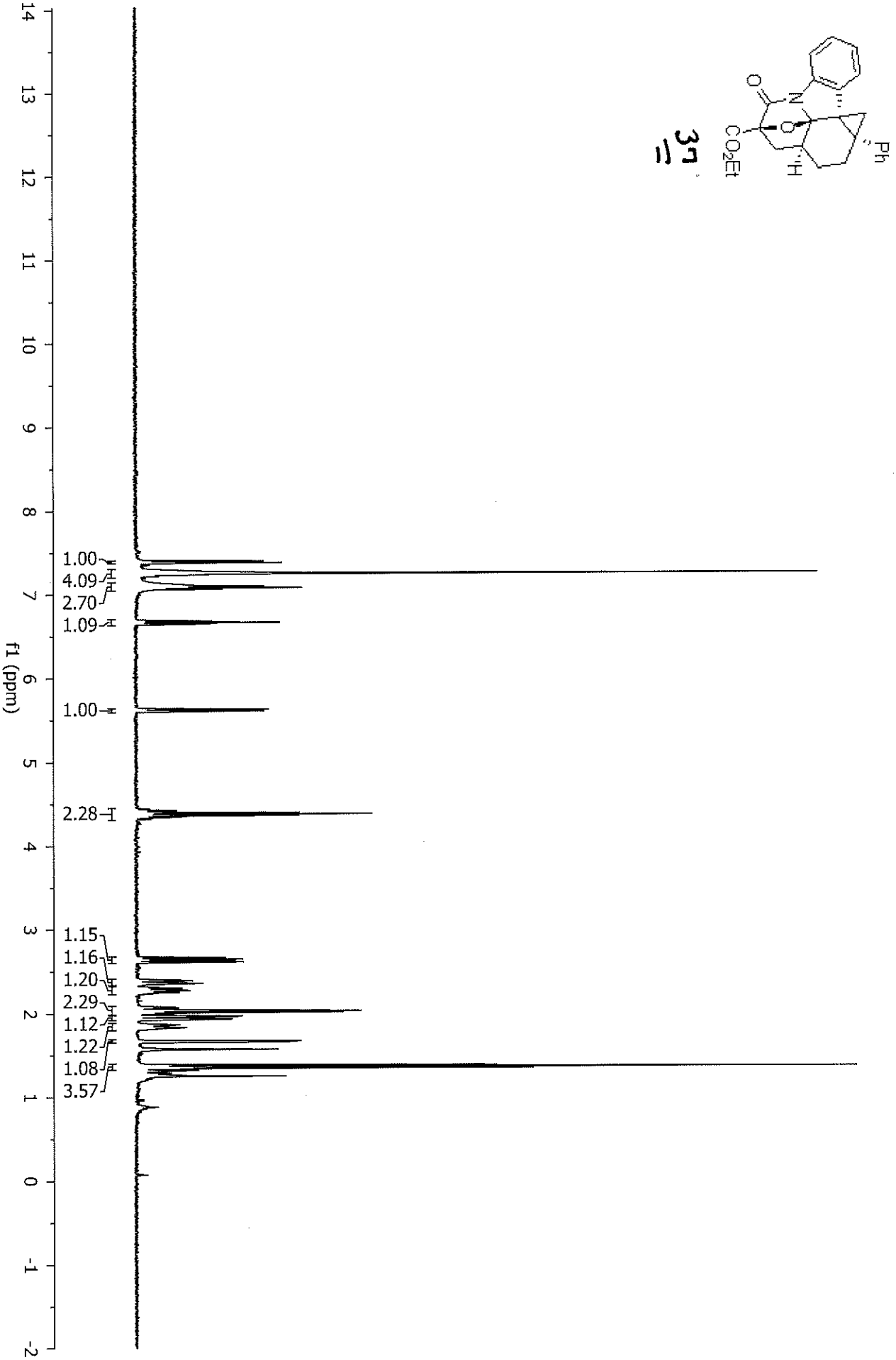
1.95
1.47
2.14
0.99
1.12
1.16
1.09
2.21
2.39
1.29
1.10
1.12
3.42
3.26
f1 (ppm)

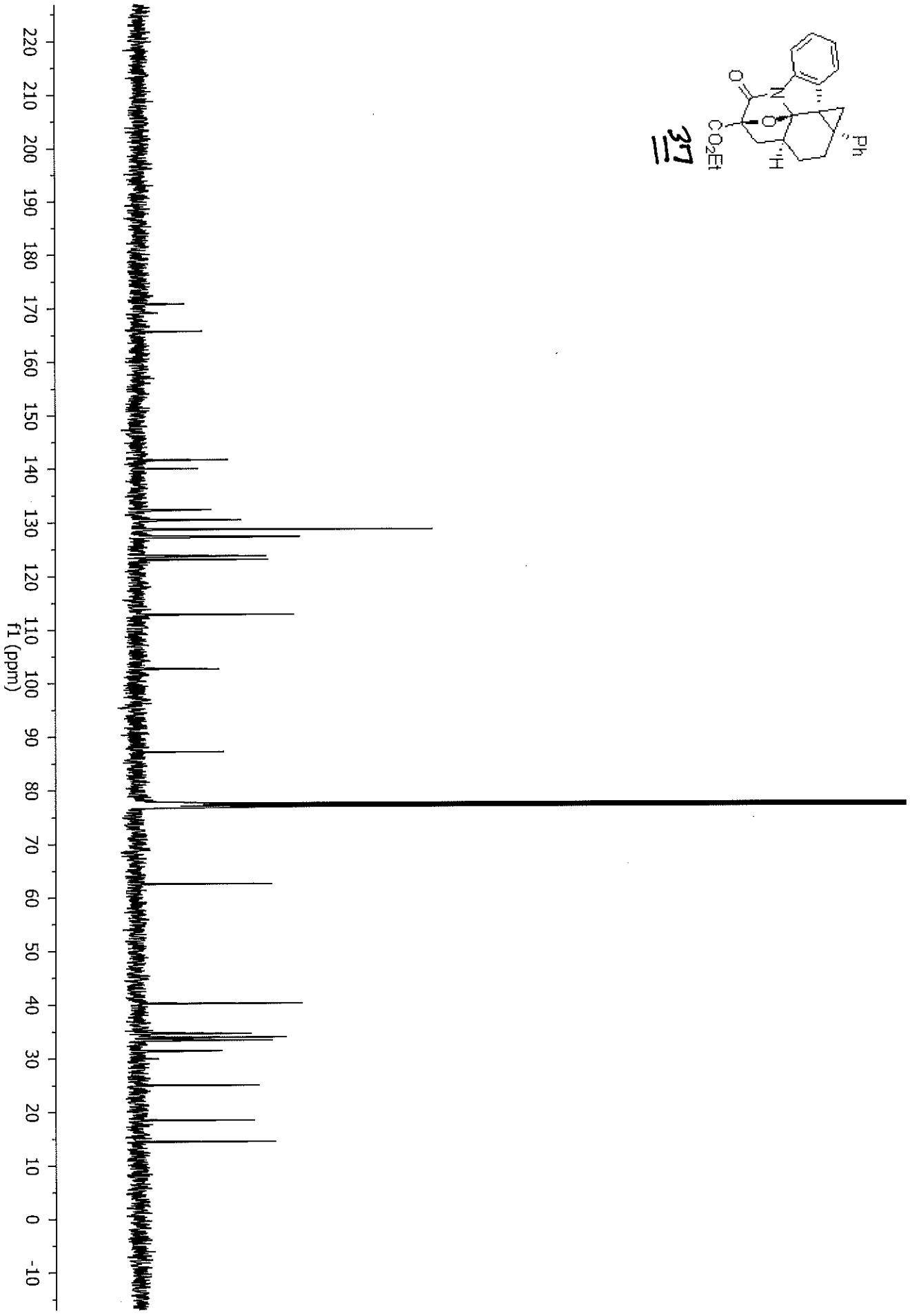

35
Ph
N
O
O
O
N2
OEt
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

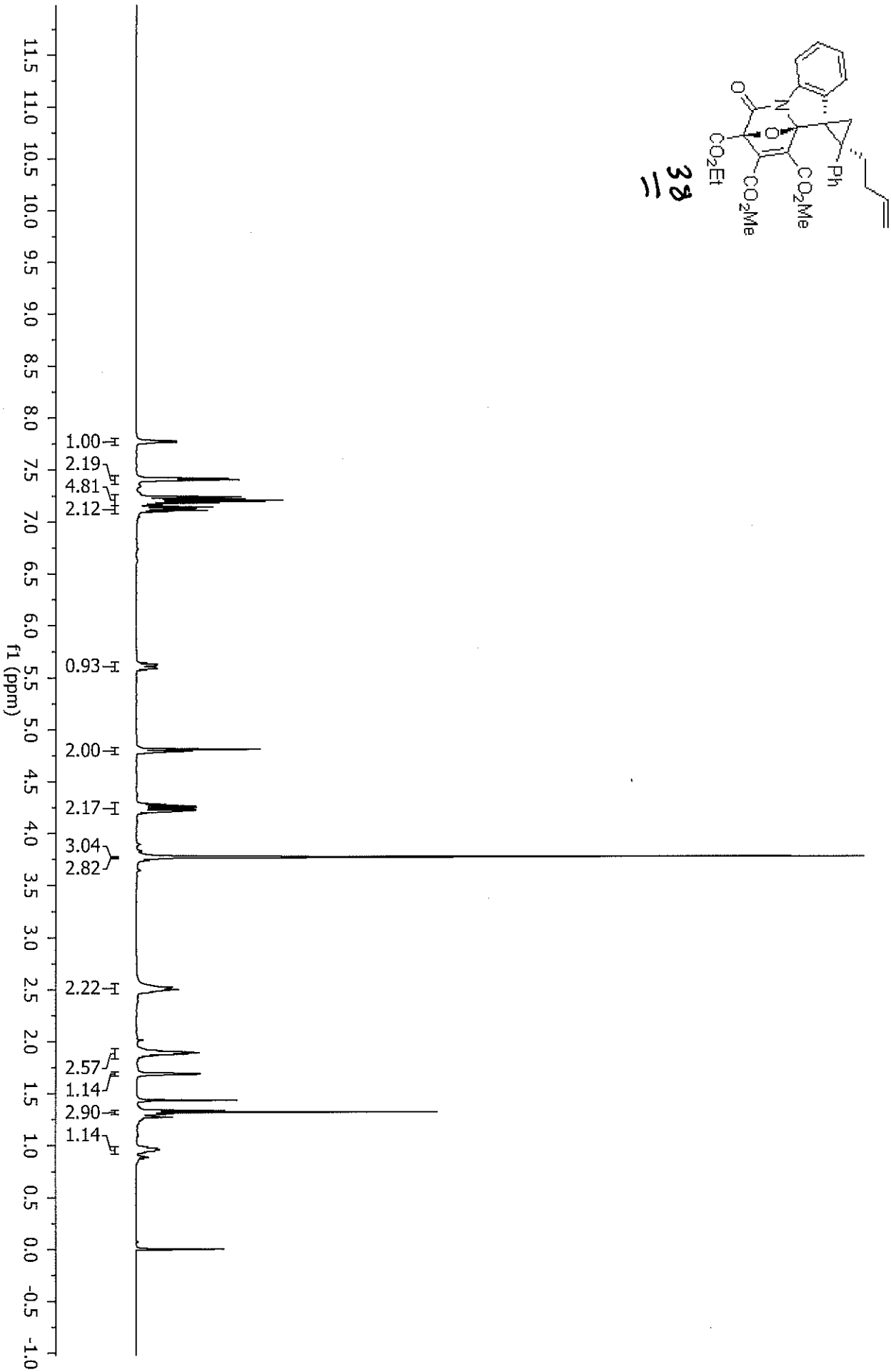


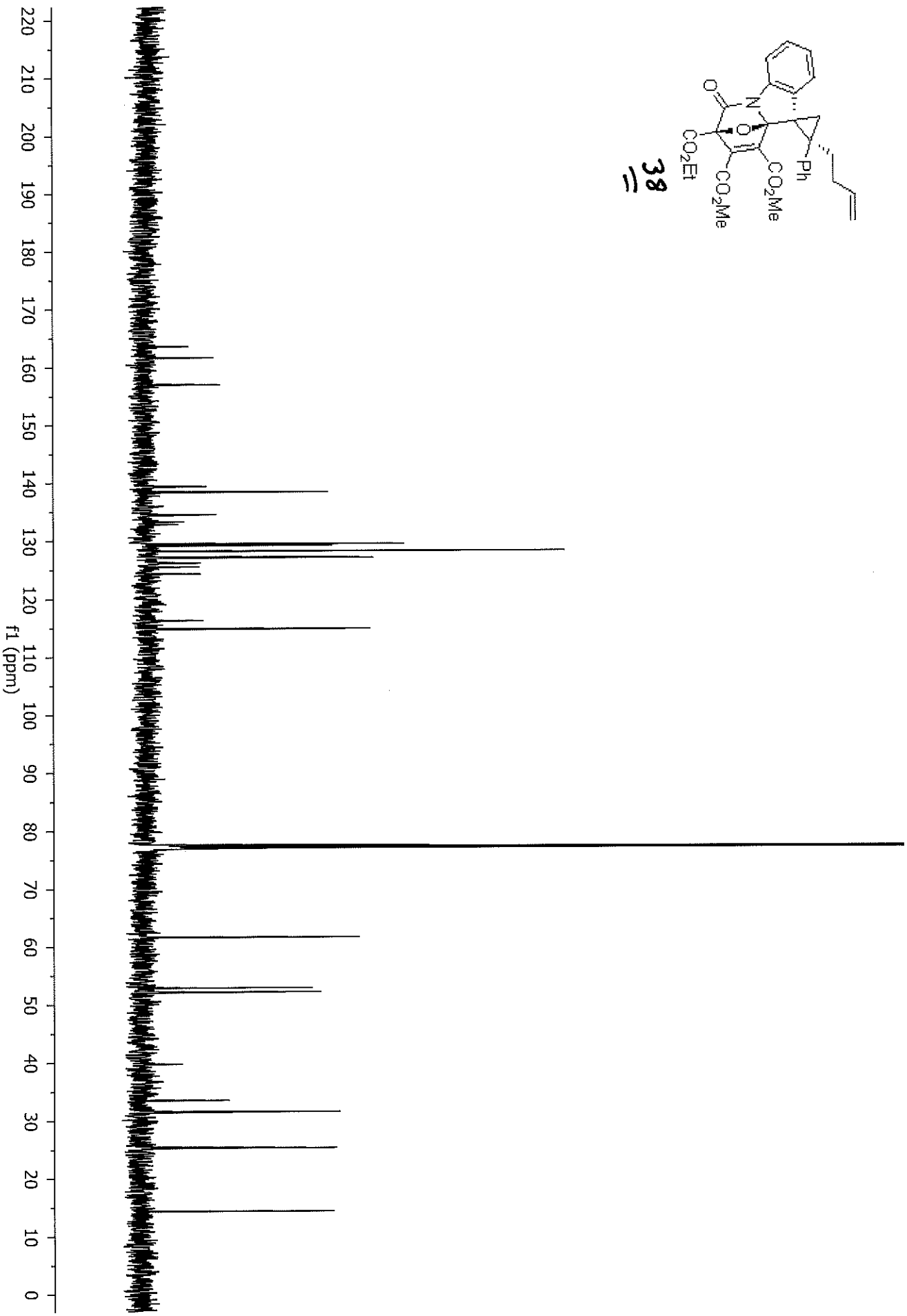
O
N
O
N2
O
OEt
Ph
36
1.00
3.17
2.31
3.52
1.17
2.10
2.16
1.10
3.49
1.19
1.24
3.30
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

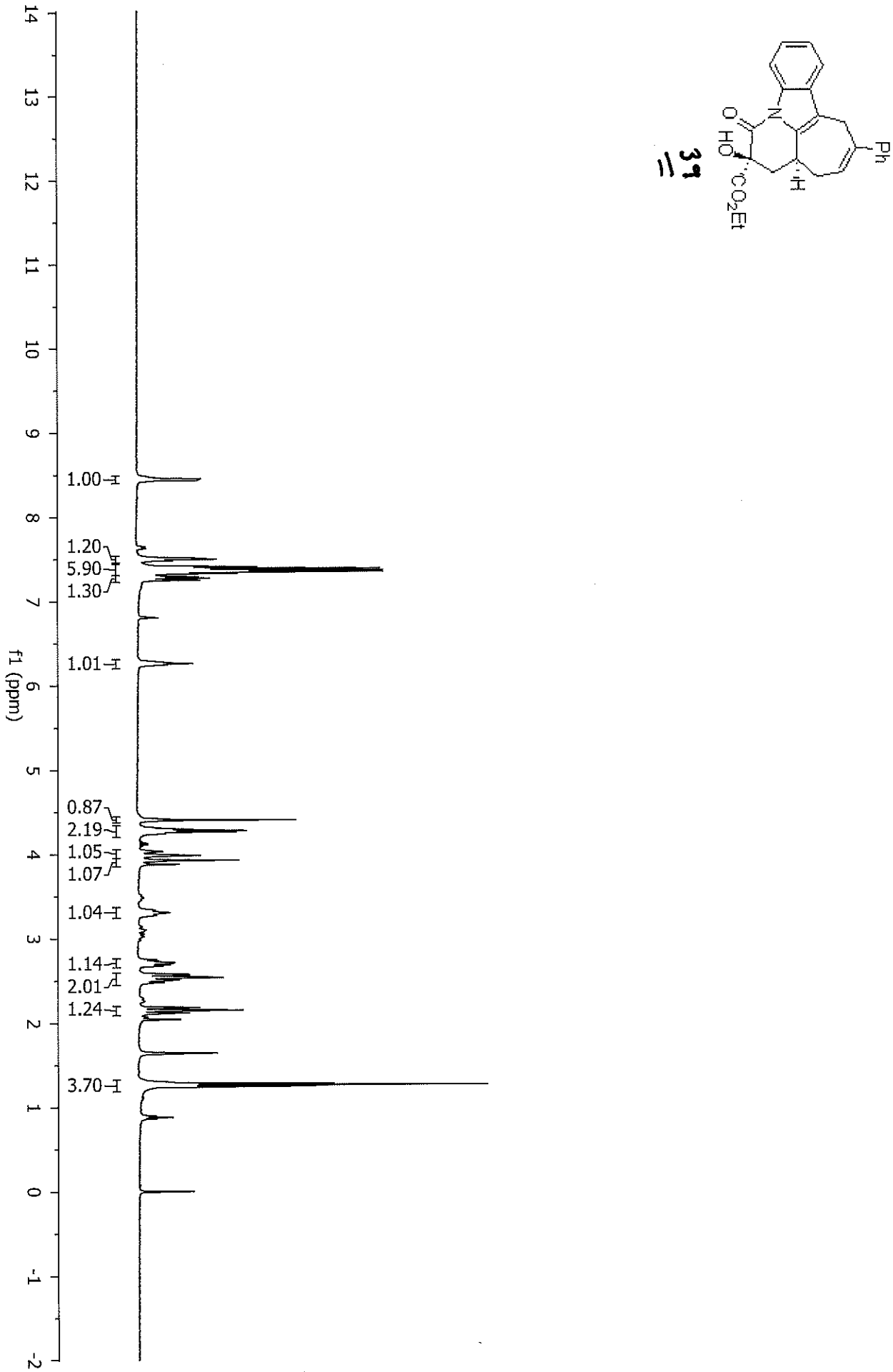

36
N
O
O
O
N2
OEt
Ph
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

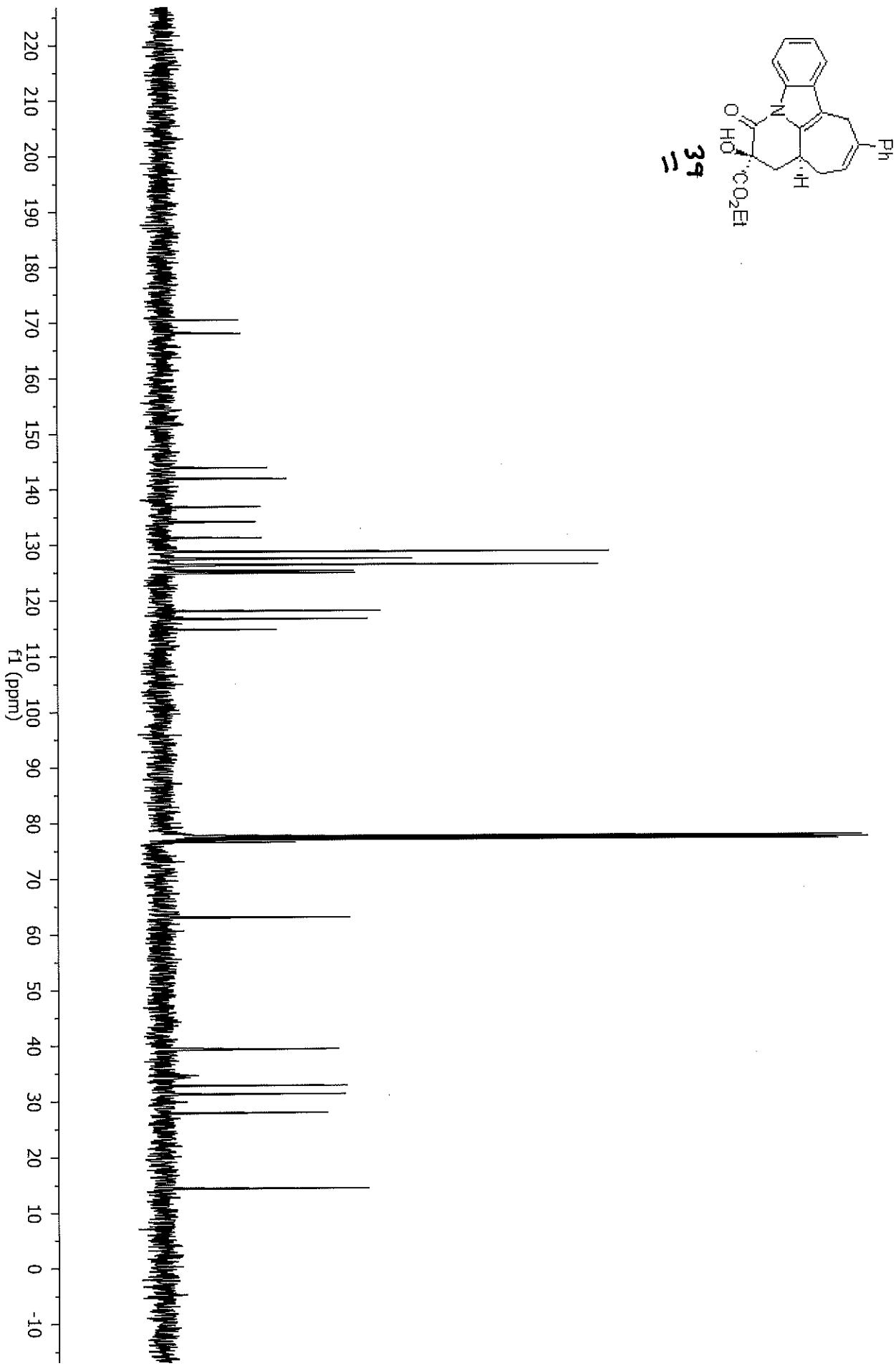

3n
Ph
H
CO2Et
O
N
O
1.00
4.09
2.70
1.09
1.00
2.28
1.15
1.16
1.20
2.29
1.12
1.22
1.08
3.57
f1 (ppm)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2

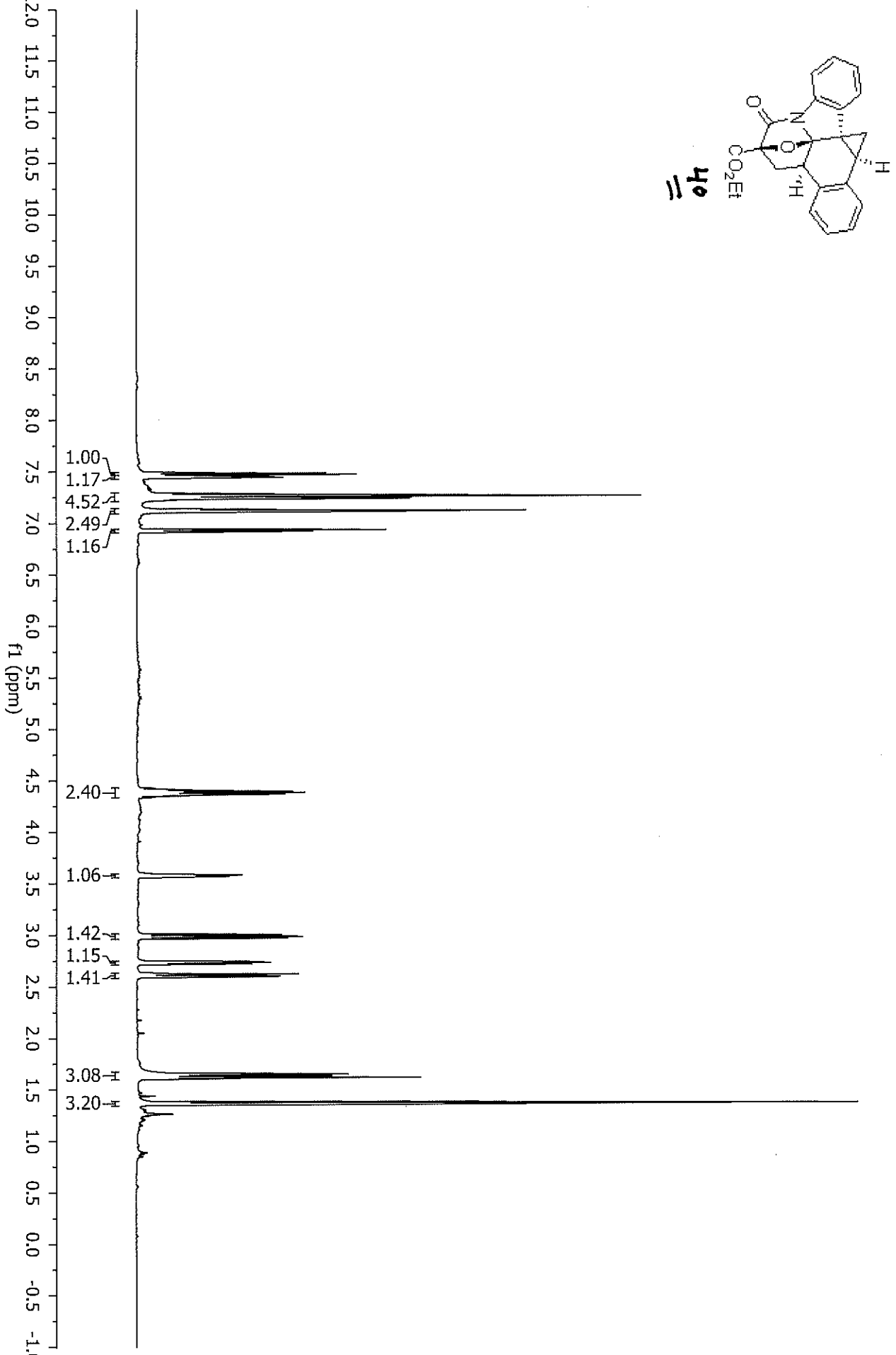

O
N
O
CO2Et
H
Ph
37
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

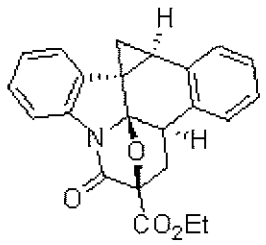

3a
Ph
CO2Me
CO2Me
CO2Et
O
N
O
1.00
2.19
4.81
2.12
0.93
2.00
2.17
3.04
2.82
2.22
2.57
1.14
2.90
1.14
f1 (ppm)
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0


Ph
CO2Me
CO2Me
CO2Et
N
O
O
3g
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

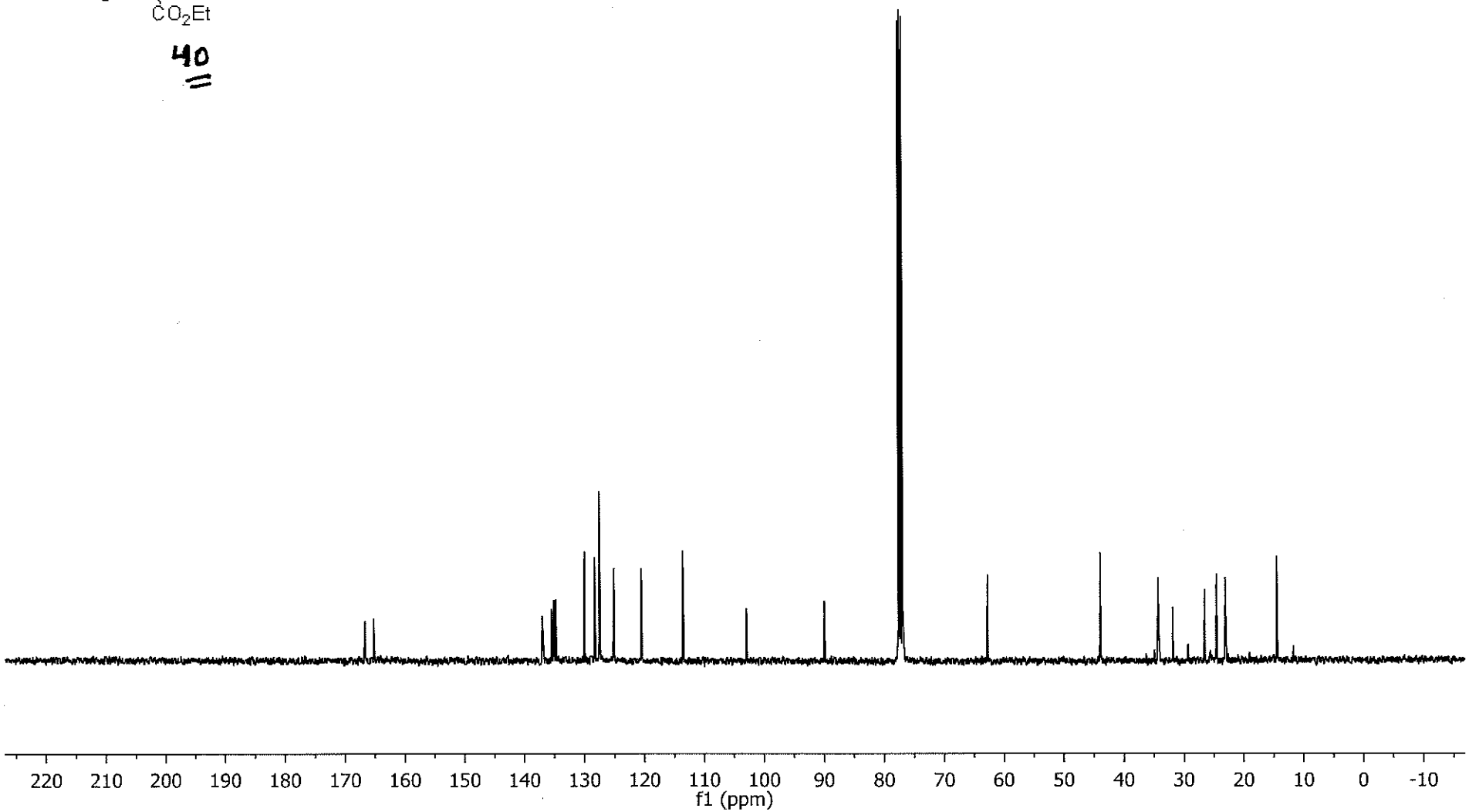

3g
Ph
H
CO_2Et
HO
O
N
1.00
1.20
5.90
1.30
1.01
0.87
2.19
1.05
1.07
1.04
1.14
2.01
1.24
3.70
f1 (ppm)

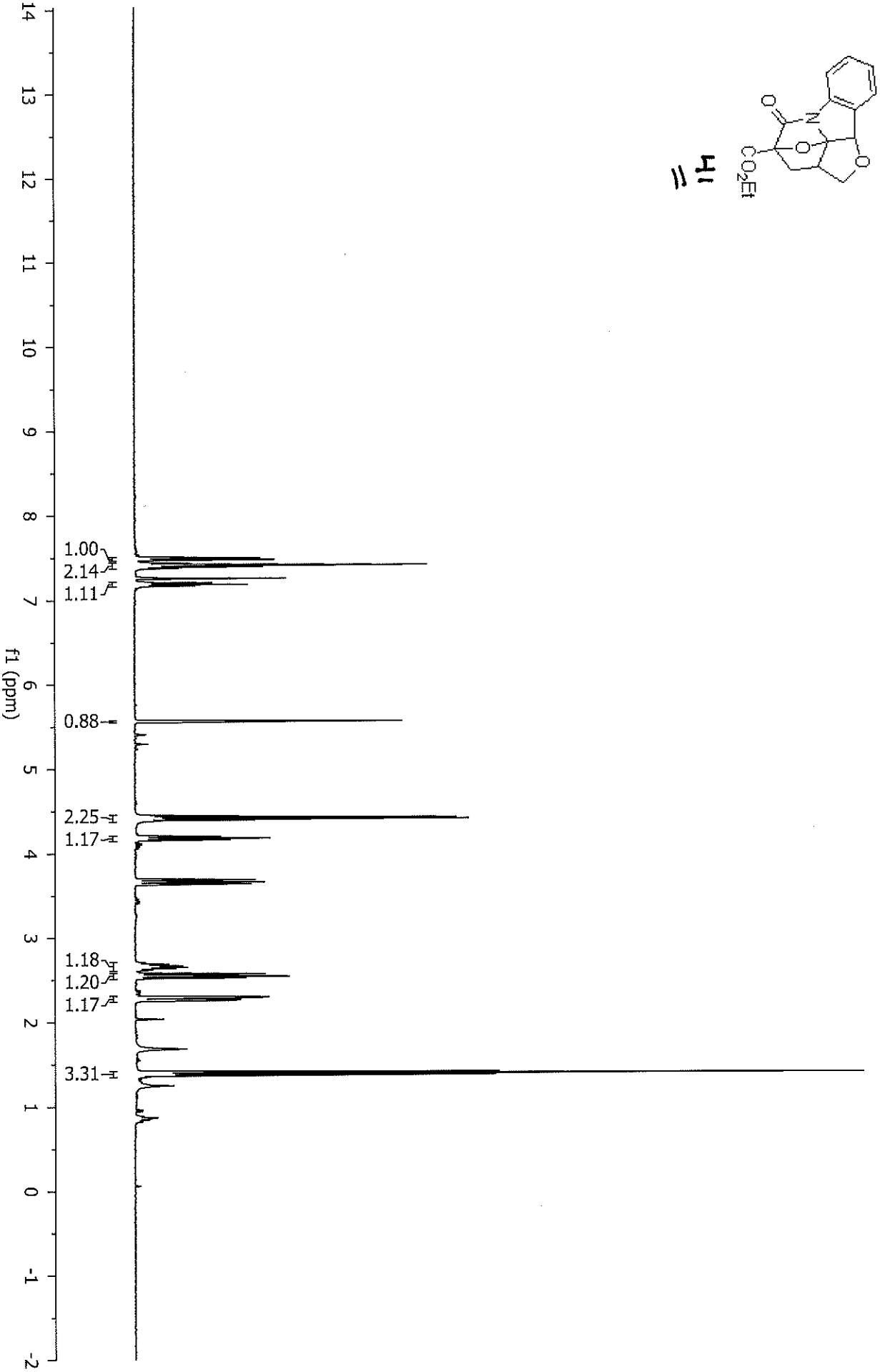

Ph
N
O
HO
H
CO2Et
39
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

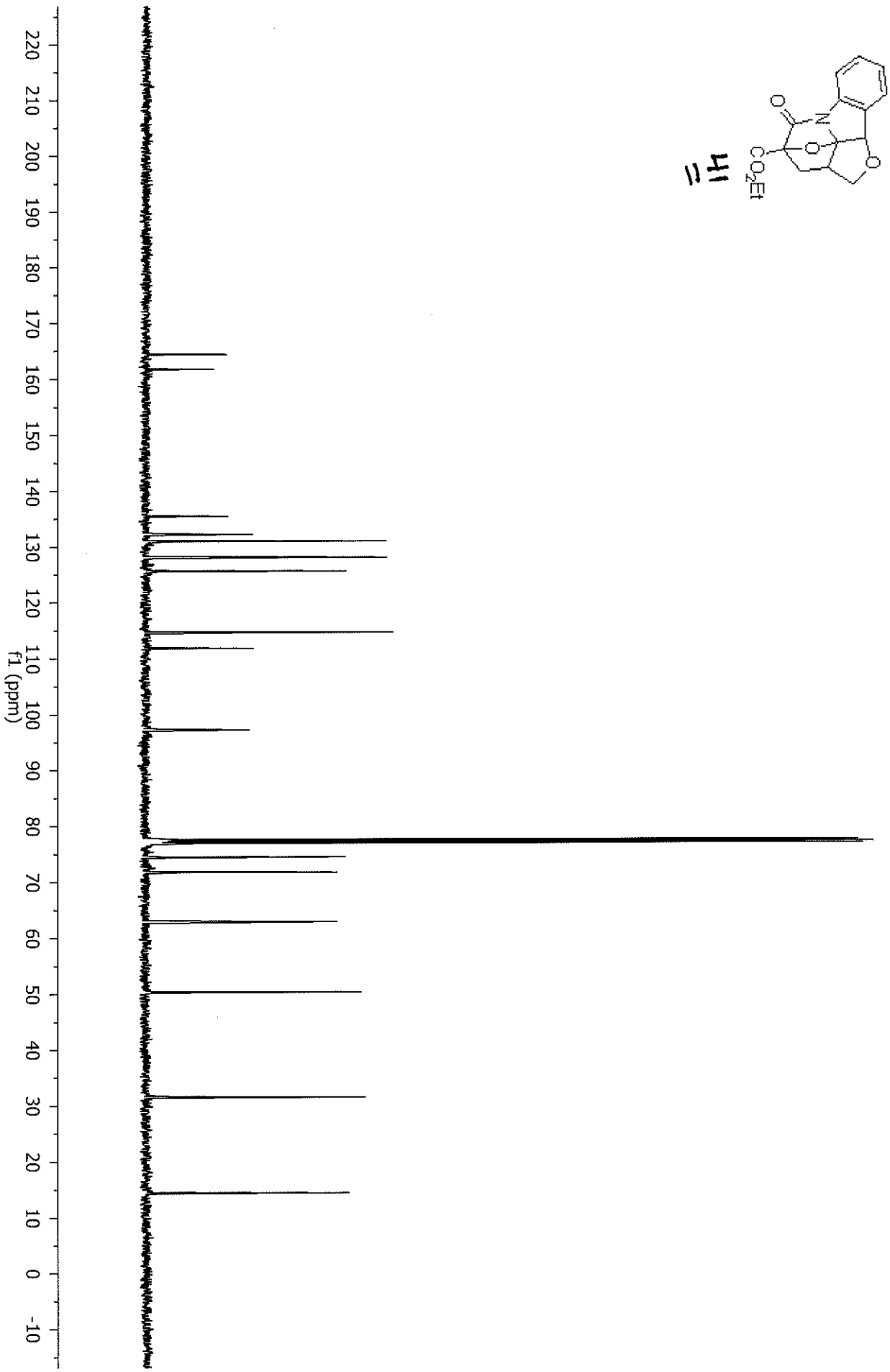

12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)
1.00
1.17
4.52
2.49
1.16
2.40
1.06
1.42
1.15
1.41
3.08
3.20
4h
CO2Et
H
H
O
N
O

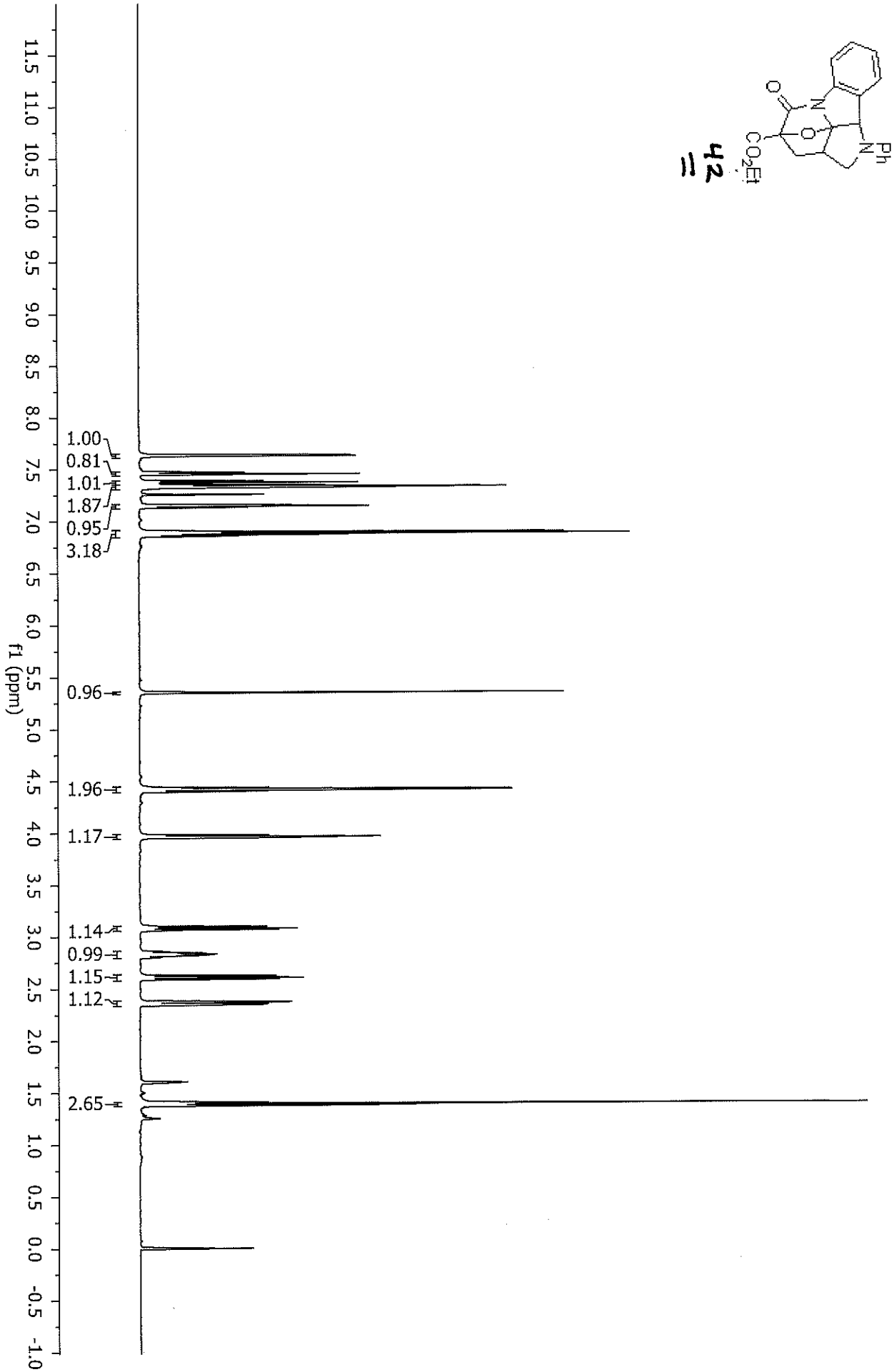

H
N
O
H
O
CO2Et

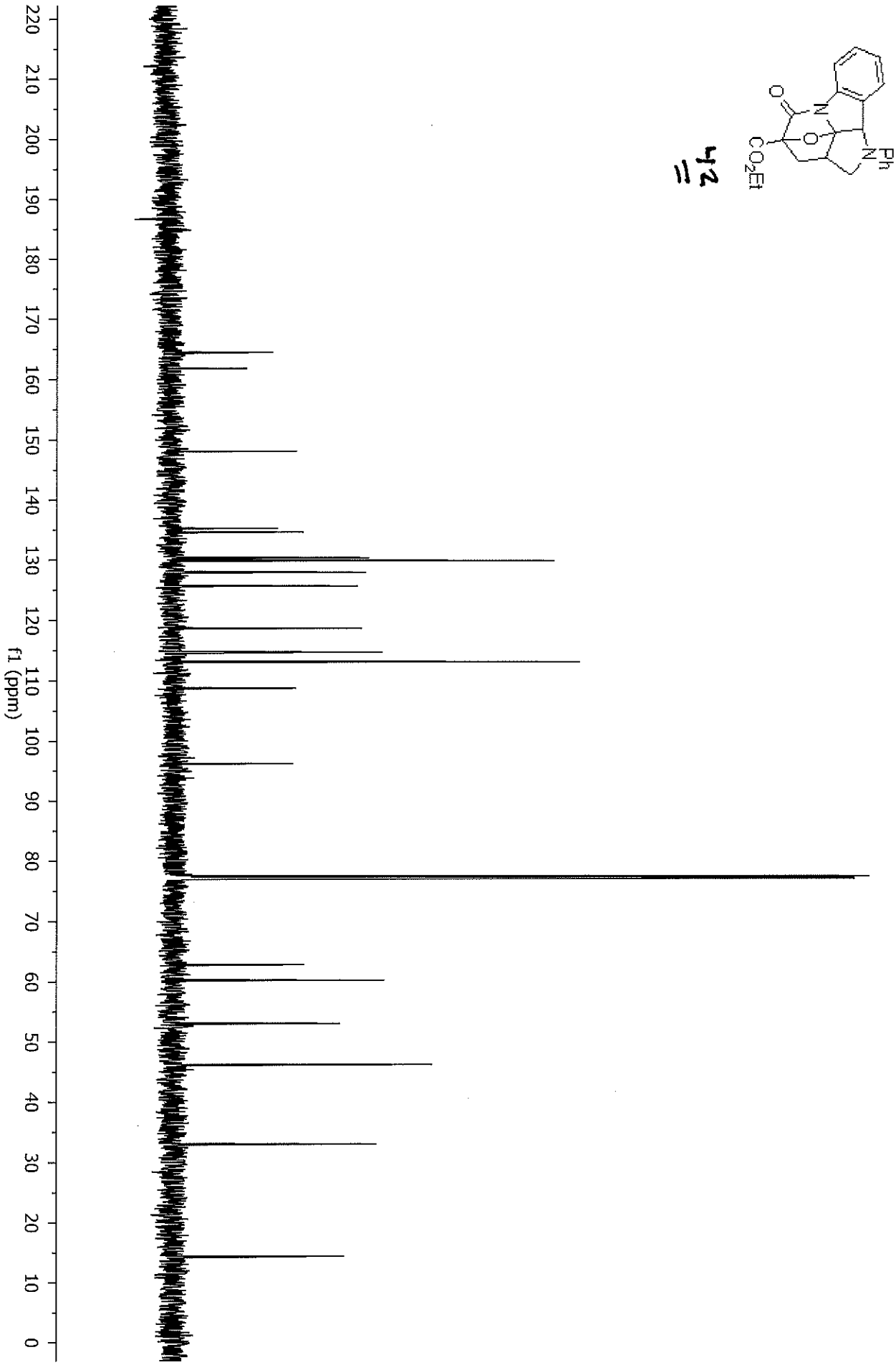
40

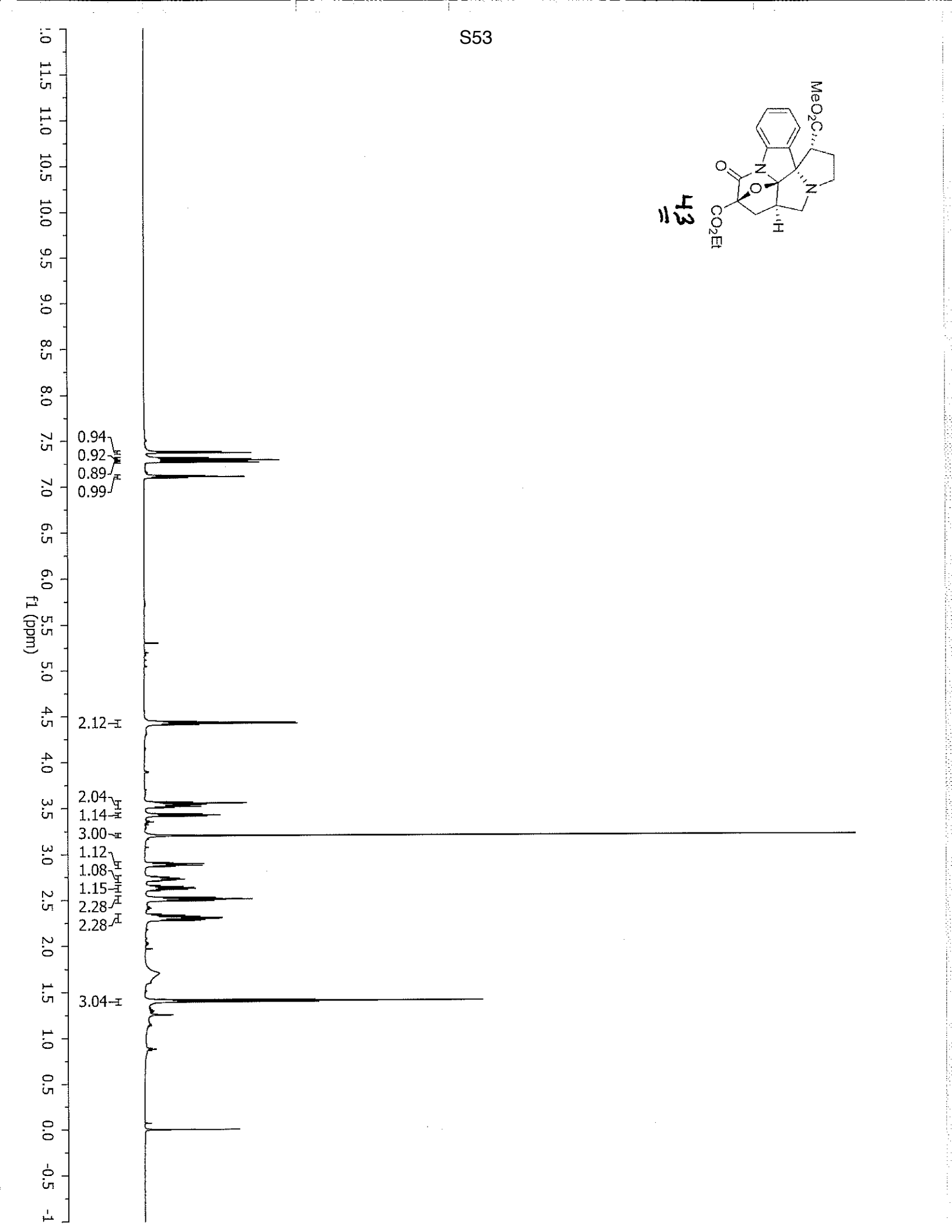

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

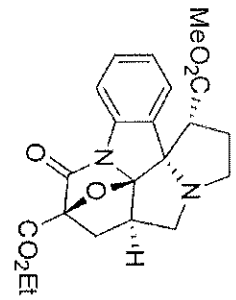

1H
CO2Et
O
N
O
O
f1 (ppm)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
1.00
2.14
1.11
0.88
2.25
1.17
1.18
1.20
1.17
3.31


O
N
O
O
CO2Et
H
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


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 -0.5 -1.0
f1 (ppm)
1.00
0.81
1.01
1.87
0.95
3.18
0.96
1.96
1.17
1.14
0.99
1.15
1.12
2.65
4z
CO2Et
Ph
N
O
O
N


42
Ph
N
O
N
O
CO2Et
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

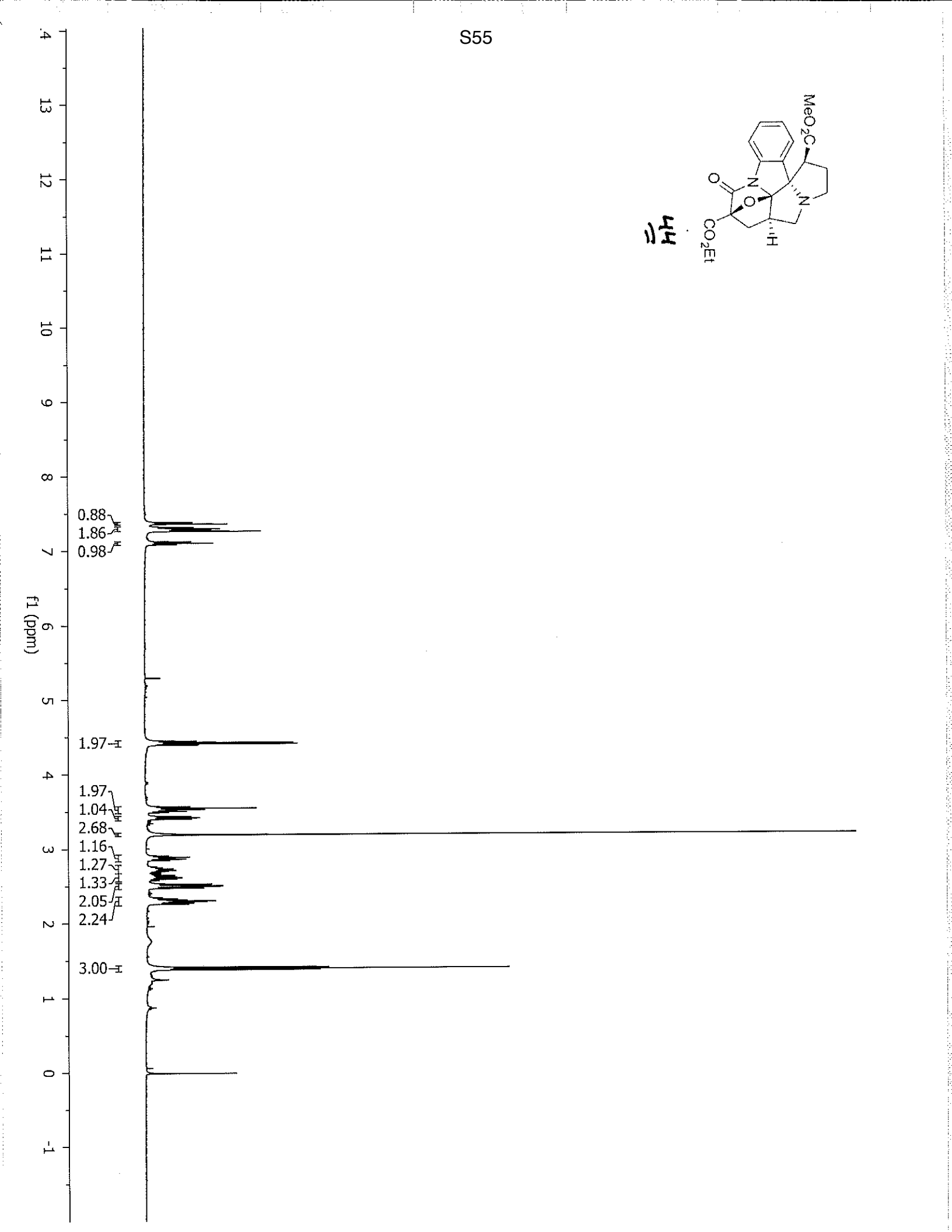

MeO2C
N
O
N
O
CO2Et
H
43
0.94
0.92
0.89
0.99
2.12
2.04
1.14
3.00
1.12
1.08
1.15
2.28
2.28
3.04
f1 (ppm)

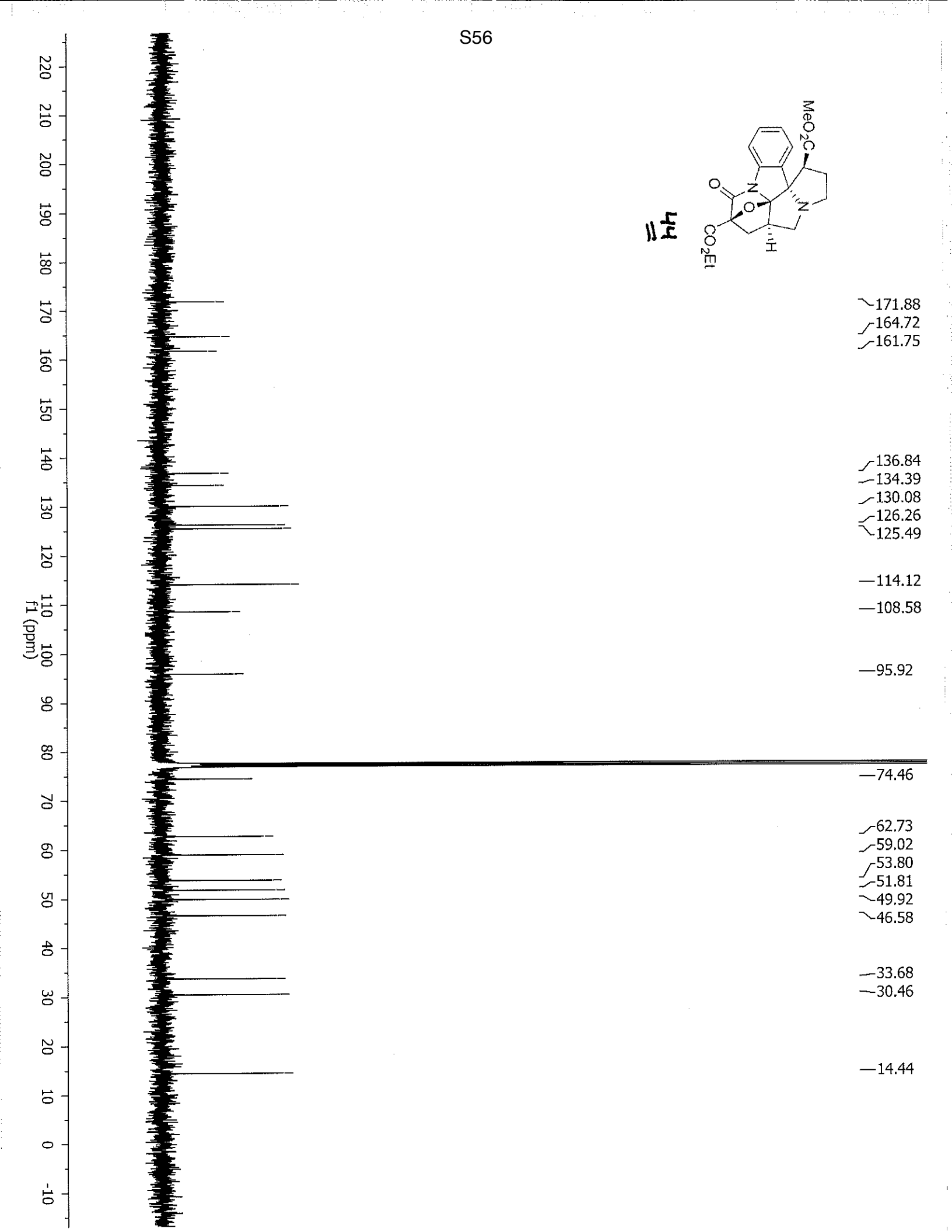


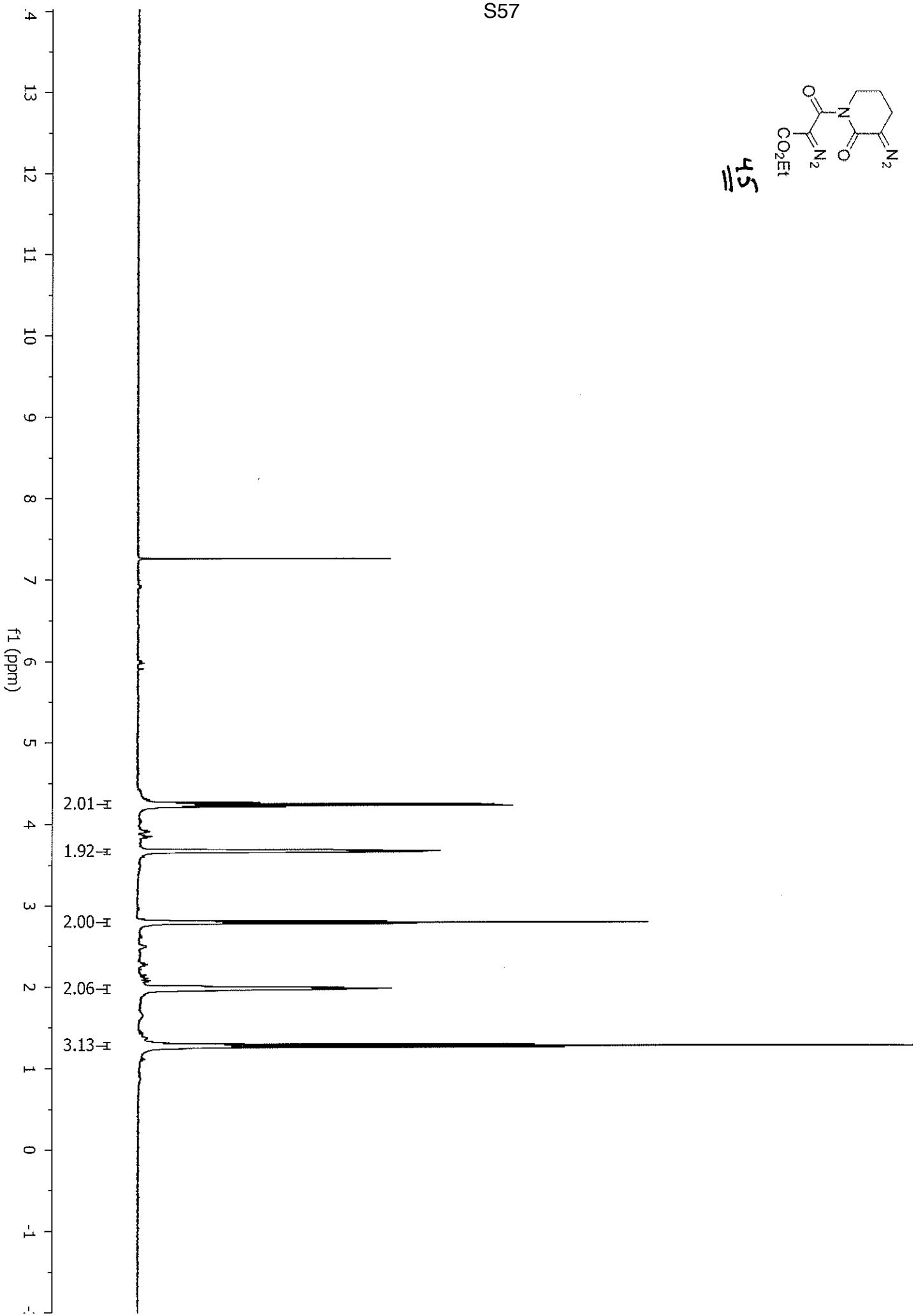
43

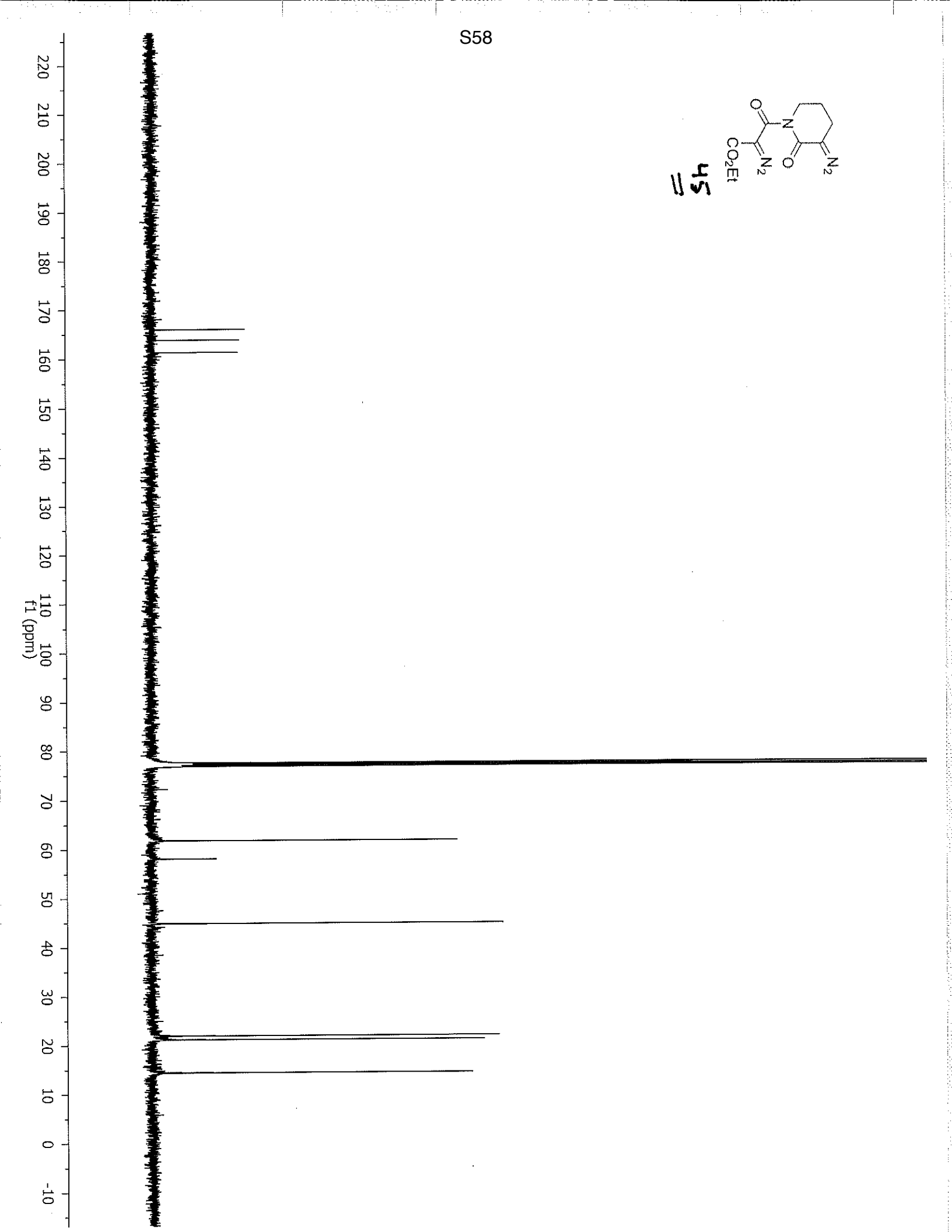
171.88
164.73
161.76
136.84
134.40
130.09
126.27
125.49
114.12
108.58
95.93
74.47
62.74
59.02
53.80
51.81
49.92
46.59
33.68
30.46
14.44

f1 (ppm)


MeO2C
N
O
O
N
H
CO2Et
14h
0.88
1.86
0.98
1.97
1.97
1.04
2.68
1.16
1.27
1.33
2.05
2.24
3.00
f1 (ppm)

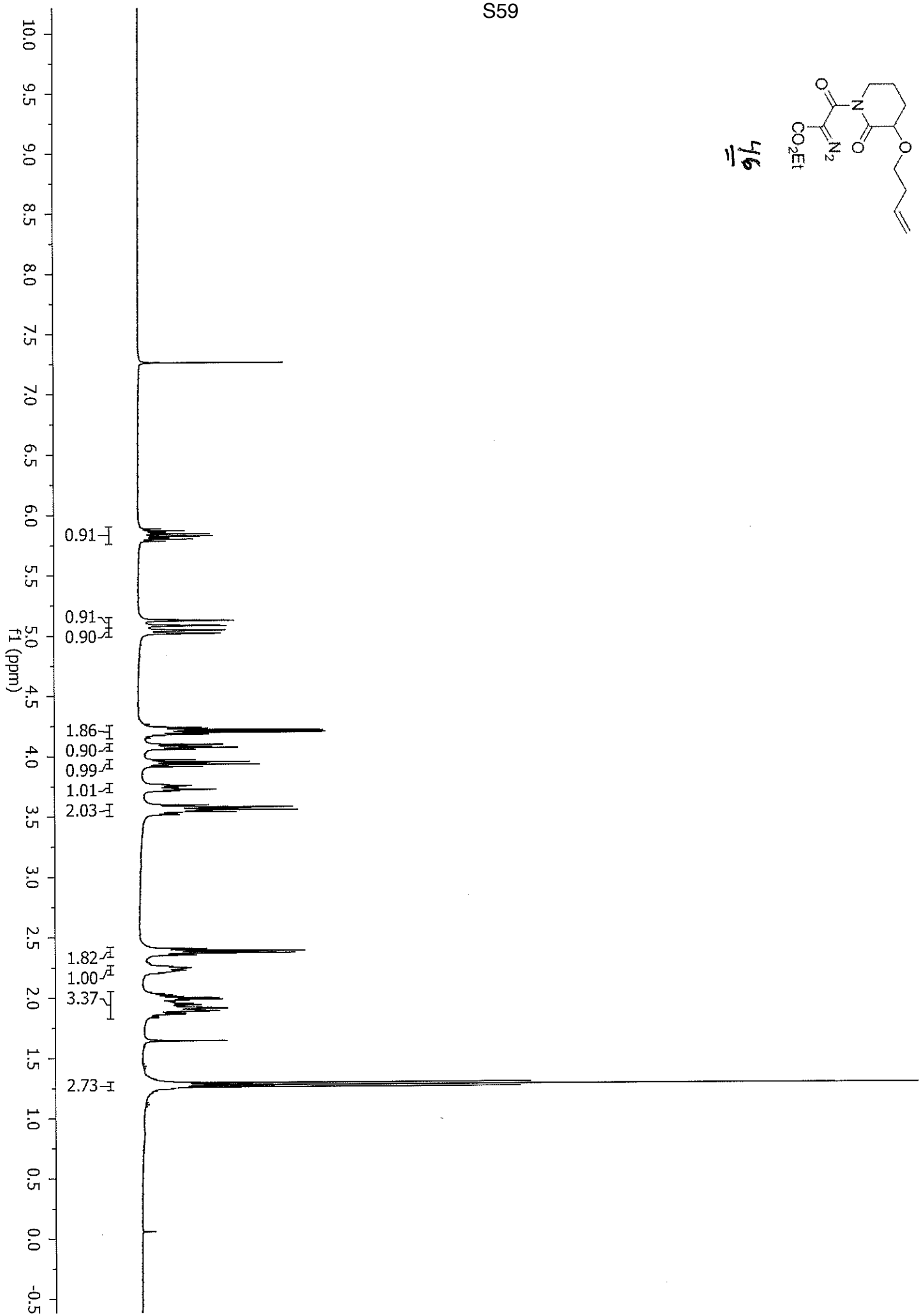

MeO2C
CO2Et
H
171.88
164.72
161.75
136.84
134.39
130.08
126.26
125.49
114.12
108.58
95.92
74.46
62.73
59.02
53.80
51.81
49.92
46.58
33.68
30.46
14.44
f1 (ppm)


4h
2.01
1.92
2.00
2.06
3.13
f1 (ppm)

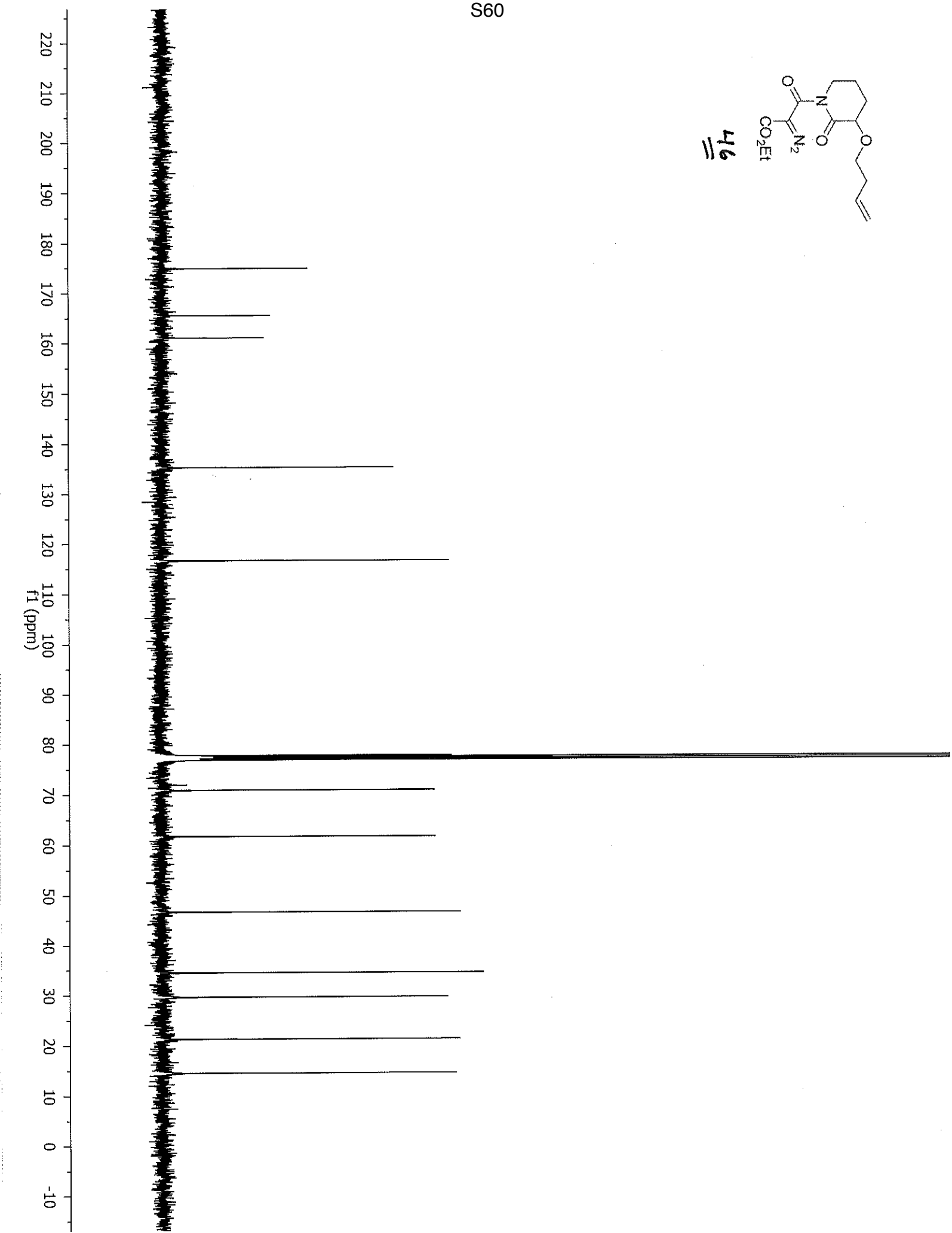

220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

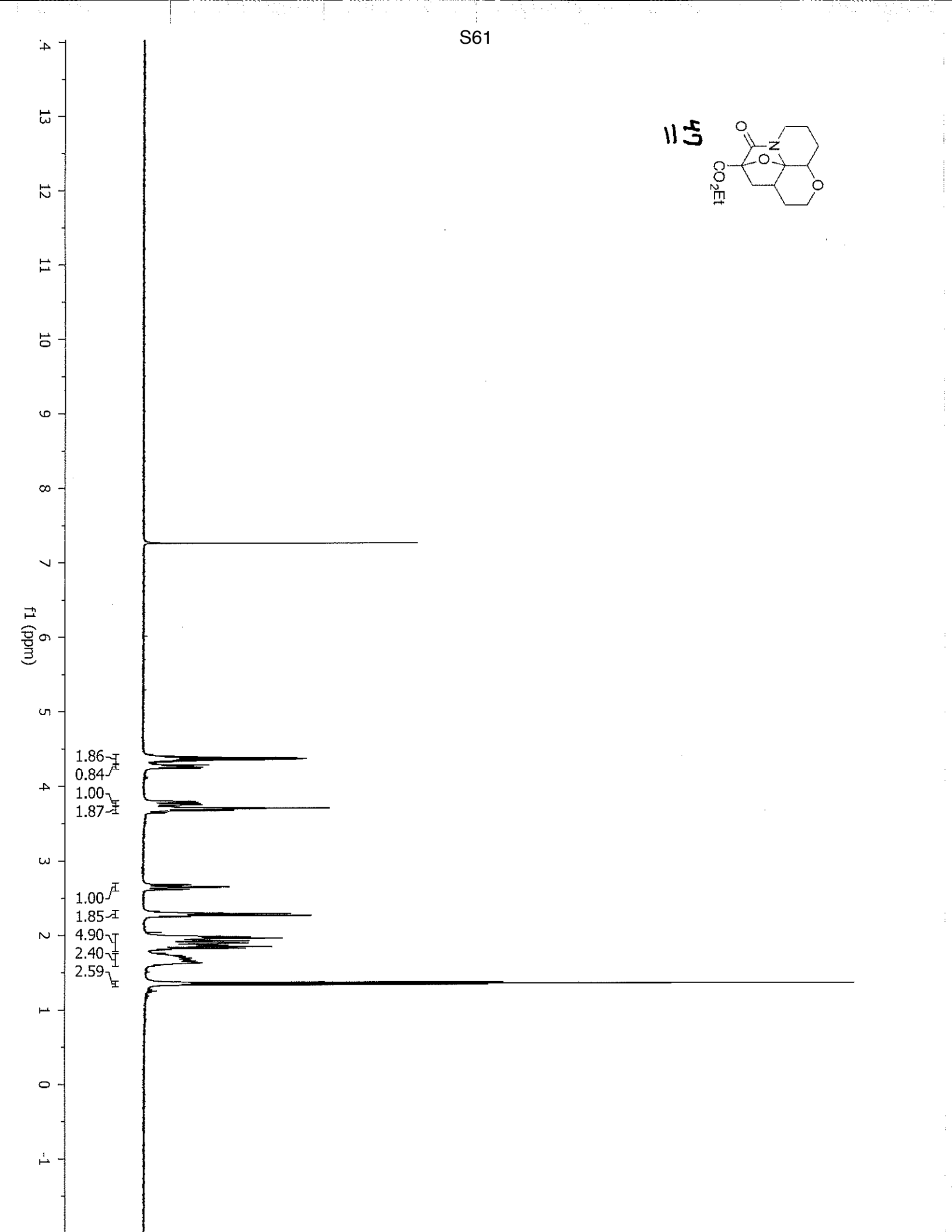
O
N
O
N2
CO2Et
N2

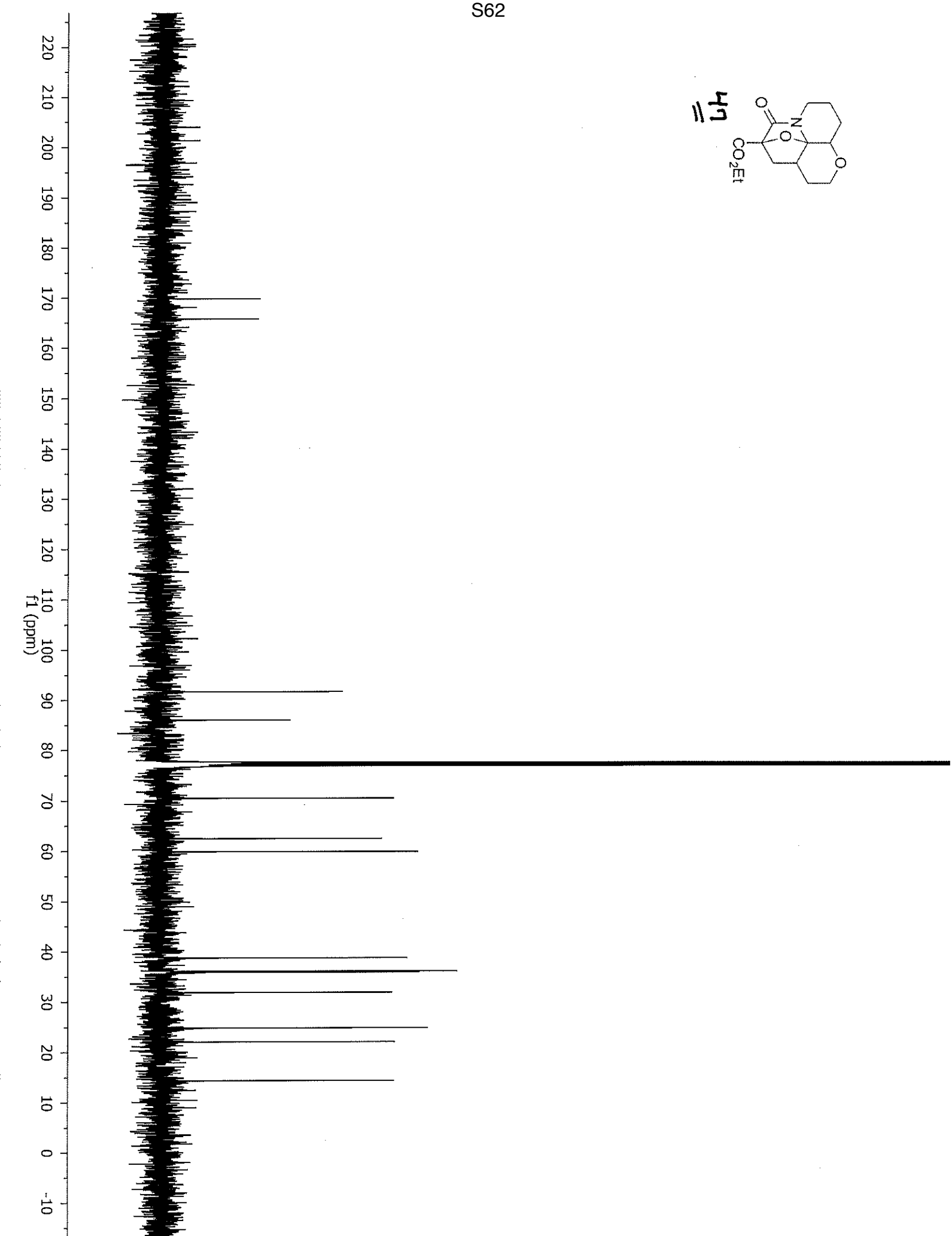
5h


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
-0.5
f1 (ppm)
0.91
0.91
0.90
1.86
0.90
0.99
1.01
2.03
1.82
1.00
3.37
2.73
O
N
O
CO2Et
N2
O
O

46

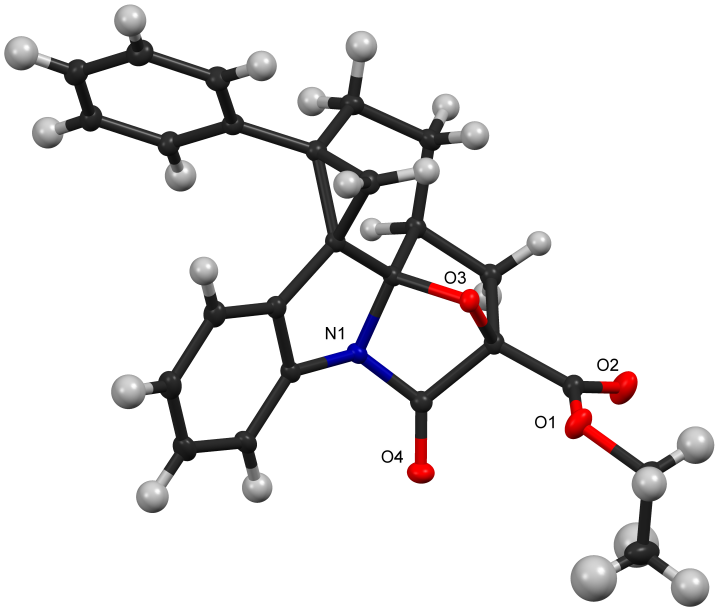

4b
CO2Et
N2
O
N
O
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


11g
O
N
O
O
CO2Et
f1 (ppm)
1.86
0.84
1.00
1.87
1.00
1.85
4.90
2.40
2.59


14
N
O
O
O
CO2Et
220
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)

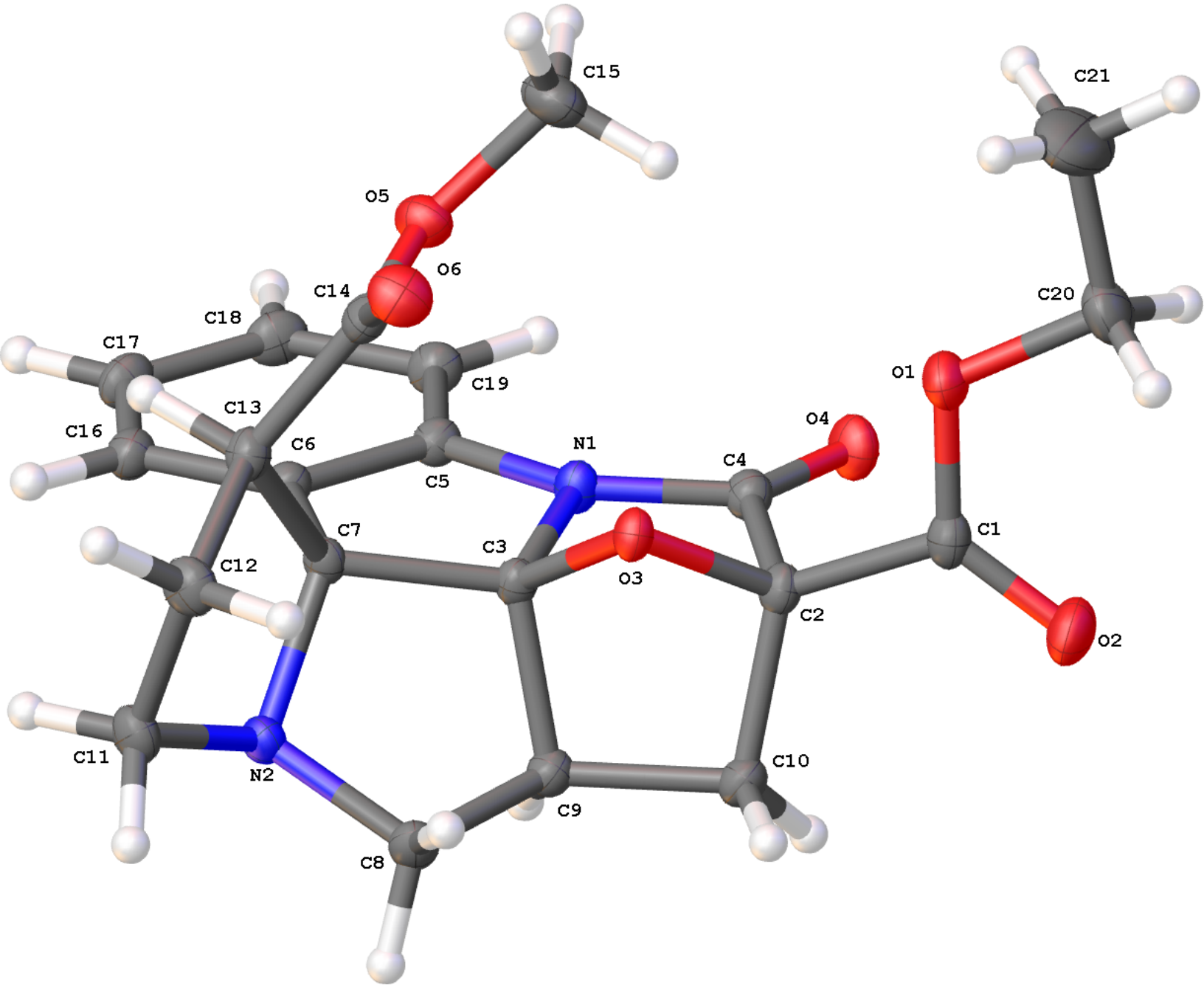
Thermal ellipsoid plot for compound **37**

The ellipsoid contour percent probability level = 50%



Thermal ellipsoid plot for compound **44**

The ellipsoid contour percent probability level = 50%



Crystal Data and Experimental for Compounds **37** and **44**

Single clear colorless prism-shaped crystals of both compounds **37** and **44** were crystallised from ether/hexane. A suitable crystal (0.73×0.68×0.42 mm^3) was selected and mounted on a loop with paratone oil on a Bruker APEX-II CCD diffractometer. The crystal was cooled to T = 100(2) K during data collection. The structures were solved with the **ShelXT-2014/4** (Sheldrick, 2015) structure solution program using the Charge Flipping solution method and by using **Olex2** (Dolomanov et al., 2009) as the graphical interface. The model was refined with version 2014/7 of **ShelXL-2014/7** (Sheldrick, 2014) using Least Squares minimisation.

A clear colourless prism-shaped crystal with dimensions 0.73×0.68×0.42 mm^3 was mounted on a loop with paratone oil. Data were collected using a Bruker APEX-II CCD diffractometer equipped with a Oxford Cryosystems low-temperature device, operating at T = 100(2) K.

Data were measured using *f* and *w* scans using MoK_a radiation (fine-focus sealed tube, 45 kV, 35 mA). The total number of runs and images was based on the strategy calculation from the program **APEX2** (Bruker). The maximum resolution that was achieved was Q = 37.858°.

The diffraction patterns were indexed using **SAINT** (Bruker, V8.27A, 2012) and the unit cells were refined using **SAINT** (Bruker, V8.27A, 2012) on 9990 reflections, 24 % of the observed reflections. Data reduction, scaling and absorption corrections were performed using **SAINT** (Bruker, V8.27A, 2012) and **SADABS-2012/1** (Bruker, 2012). The values of wR_2(int) were 0.0824 before and 0.0598 after correction. The ratio of minimum to maximum transmission is 0.8393.The *l*/2 correction factor is 0.0015. The final completeness is 99.9% out to 37.858° in Q. The absorption coefficient m of this material is 0.091 mm^{-1} at this wavelength (l = 0.71073 Å) and the minimum and maximum transmissions are 0.8393 and 1.0000.

The structures were solved and the space group P-1 (# 2) determined by the **ShelXT-2014/4** (Sheldrick, 2015) structure solution program using Charge Flipping and refined by Least Squares using version 2014/7 of ShelXL-2014/7 (Sheldrick, 2014). All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model.

Table 1. Crystal data and structure refinement for compound **37**

Empirical formula	C25H23NO4
Formula weight	401.44
Temperature/K	172.3
Crystal system	triclinic
Space group	P-1
a/Å	9.0316(2)
b/Å	10.4052(2)
c/Å	10.9083(3)
α/°	99.9550(10)
β/°	97.1890(10)
γ/°	97.4110(10)
Volume/Å^3	989.77(4)
Z	2
ϱ_{calc}mg/mm^3	1.347
m/mm^{-1}	0.091
F(000)	424.0
Crystal size/mm^3	0.735 × 0.675 × 0.418
2Θ range for data collection	3.834 to 75.716°
Index ranges	-15 ≤ h ≤ 15, -17 ≤ k ≤ 17, -18 ≤ l ≤ 18
Reflections collected	40859
Independent reflections	10498[R(int) = 0.0476]
Data/restraints/parameters	10498/0/363
Goodness-of-fit on F^2	1.028
Final R indexes [I>=2σ (I)]	R_1 = 0.0466, wR_2 = 0.1265
Final R indexes [all data]	R_1 = 0.0535, wR_2 = 0.1355
Largest diff. peak/hole / e Å^{-3}	0.74/-0.37

Table 2. Crystal data and structure refinement for compound **44**

Empirical formula	C21 H22 N2 O6	
Formula weight	398.40	
Temperature	110(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 12.7648(13) Å	α= 90°.
	b = 9.0440(9) Å	β= 92.9810(10)°.
	c = 16.8162(18) Å	γ = 90°.
Volume	1938.7(3) $Å^3$	
Z	4	
Density (calculated)	1.365 Mg/m^3	
Absorption coefficient	0.101 mm^{-1}	
F(000)	840	
Crystal size	0.672 x 0.458 x 0.158 mm^3	
Theta range for data collection	2.426 to 30.995°.	
Index ranges	-18<=h<=18, -12<=k<=13, -24<=l<=24	
Reflections collected	22767	
Independent reflections	6142 [R(int) = 0.0318]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7463 and 0.5813	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6142 / 27 / 337	
Goodness-of-fit on F^2	1.126	
Final R indices [I>2sigma(I)]	R1 = 0.0503, wR2 = 0.1192	
R indices (all data)	R1 = 0.0683, wR2 = 0.1451	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.607 and -0.309 $e.Å^{-3}$	