Supplementary Material

A modular approach for the installation of functionalized phosphonates to heterocycles

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Email: justin.lopchuk@moffitt.org

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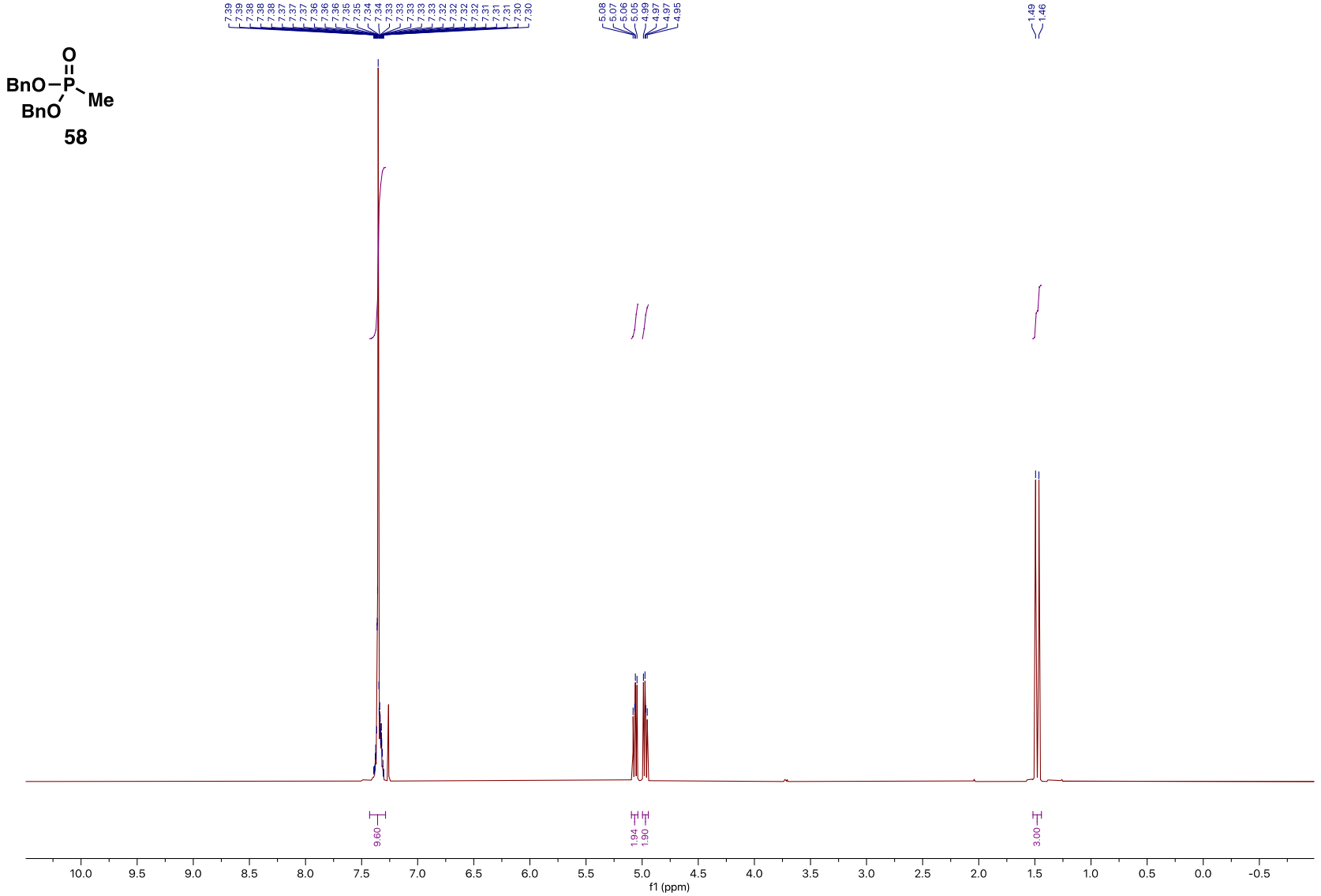
Phosphonate nucleophiles and heterocyclic electrophiles:



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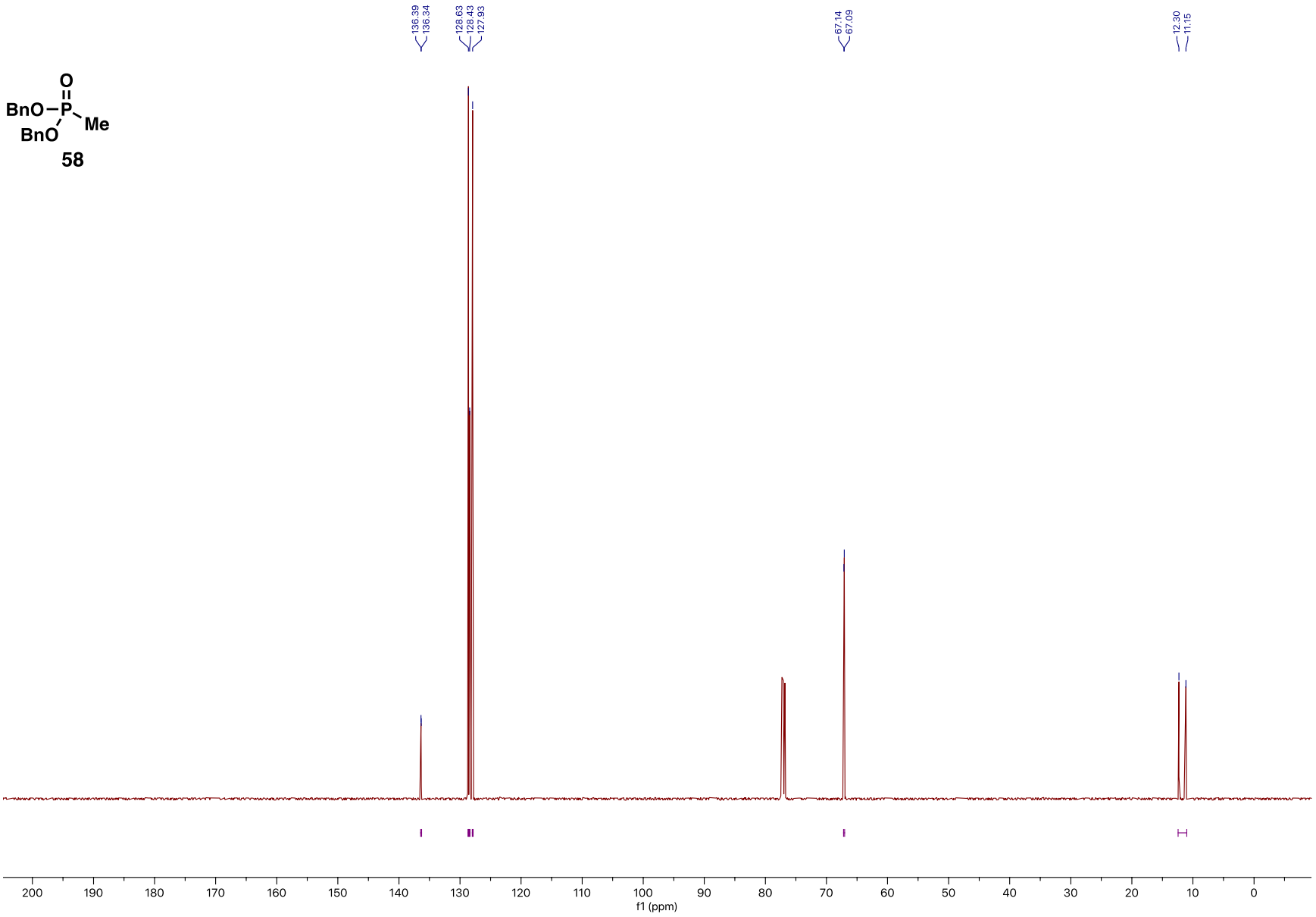
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BnO
BnO
Me
58
200
190
180
170
160
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20
10
0
f1 (ppm)

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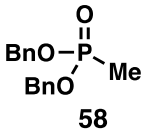
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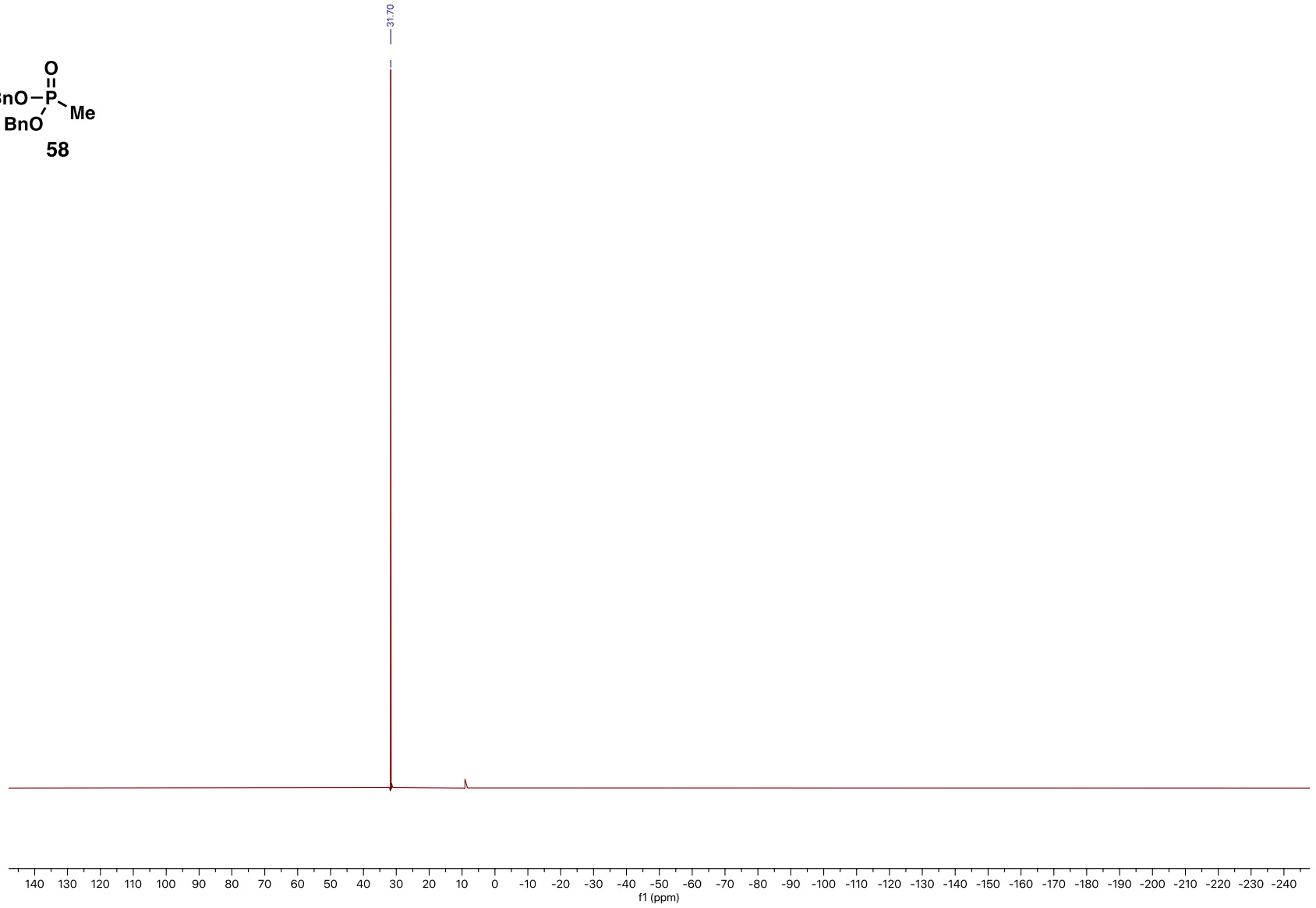
P
Me
BnO

58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f1 (ppm)

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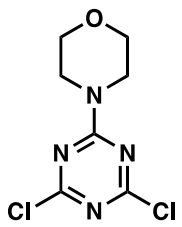

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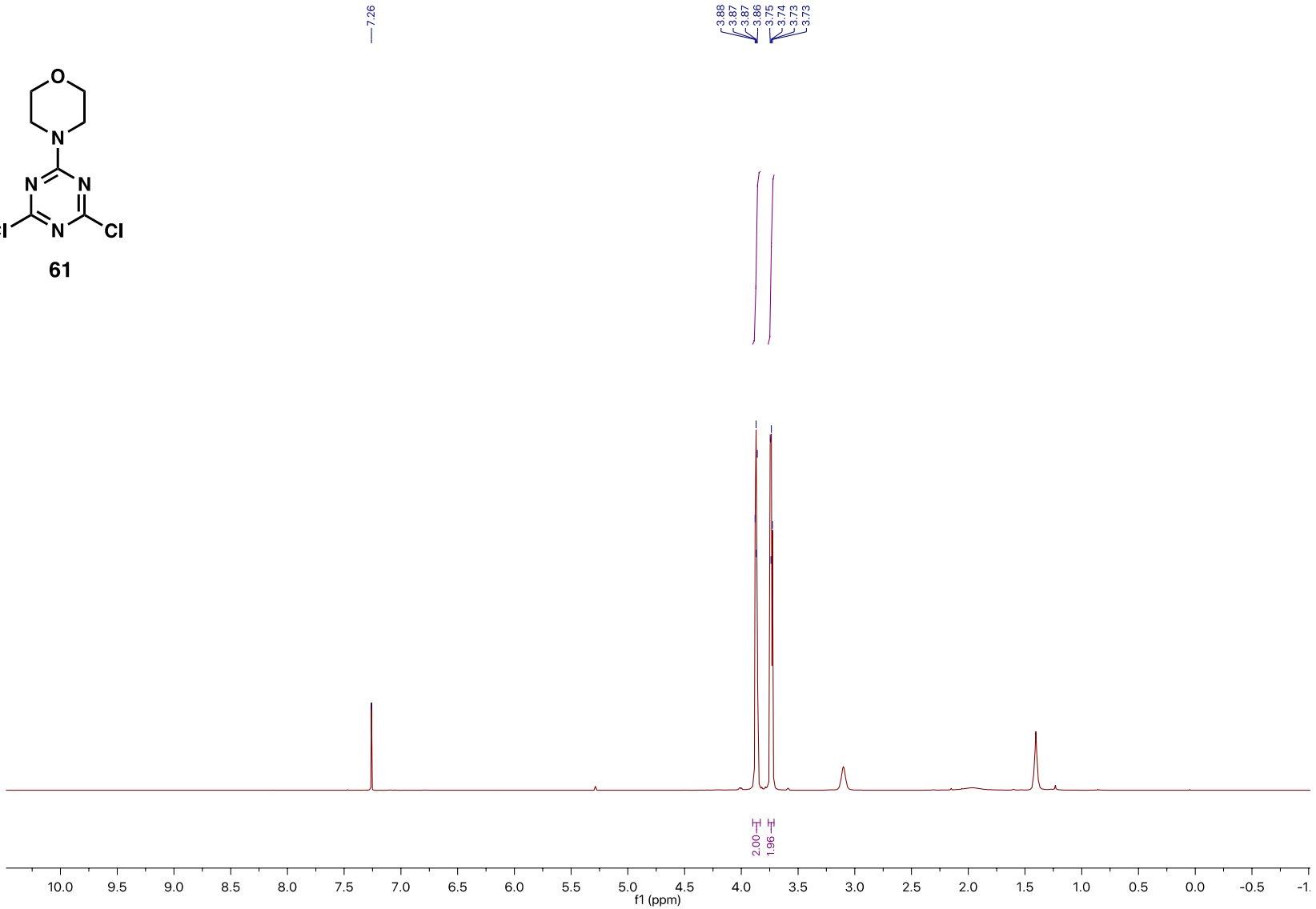
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3.87
3.87
3.86
3.75
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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f1 (ppm)

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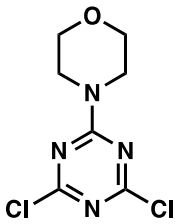

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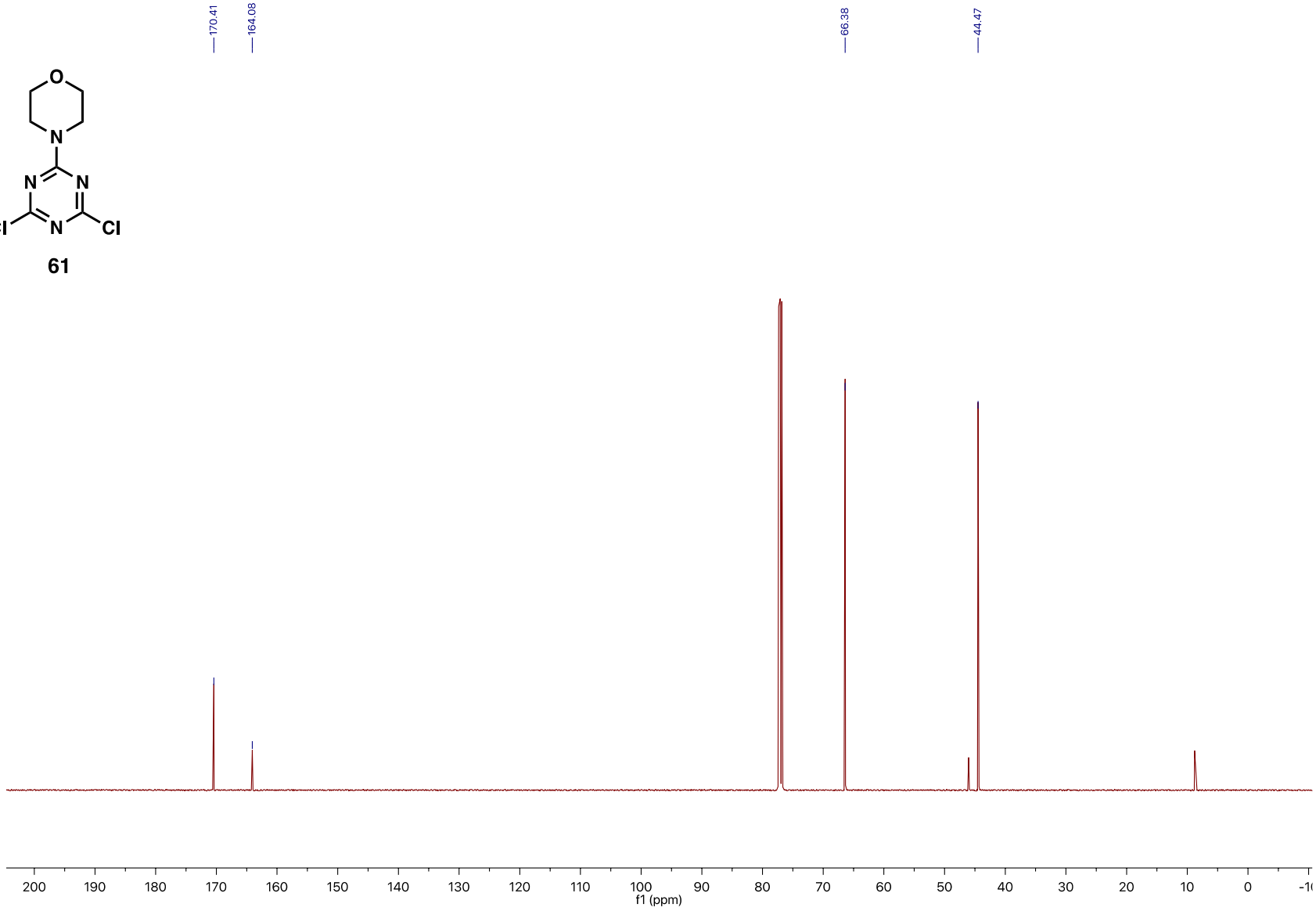
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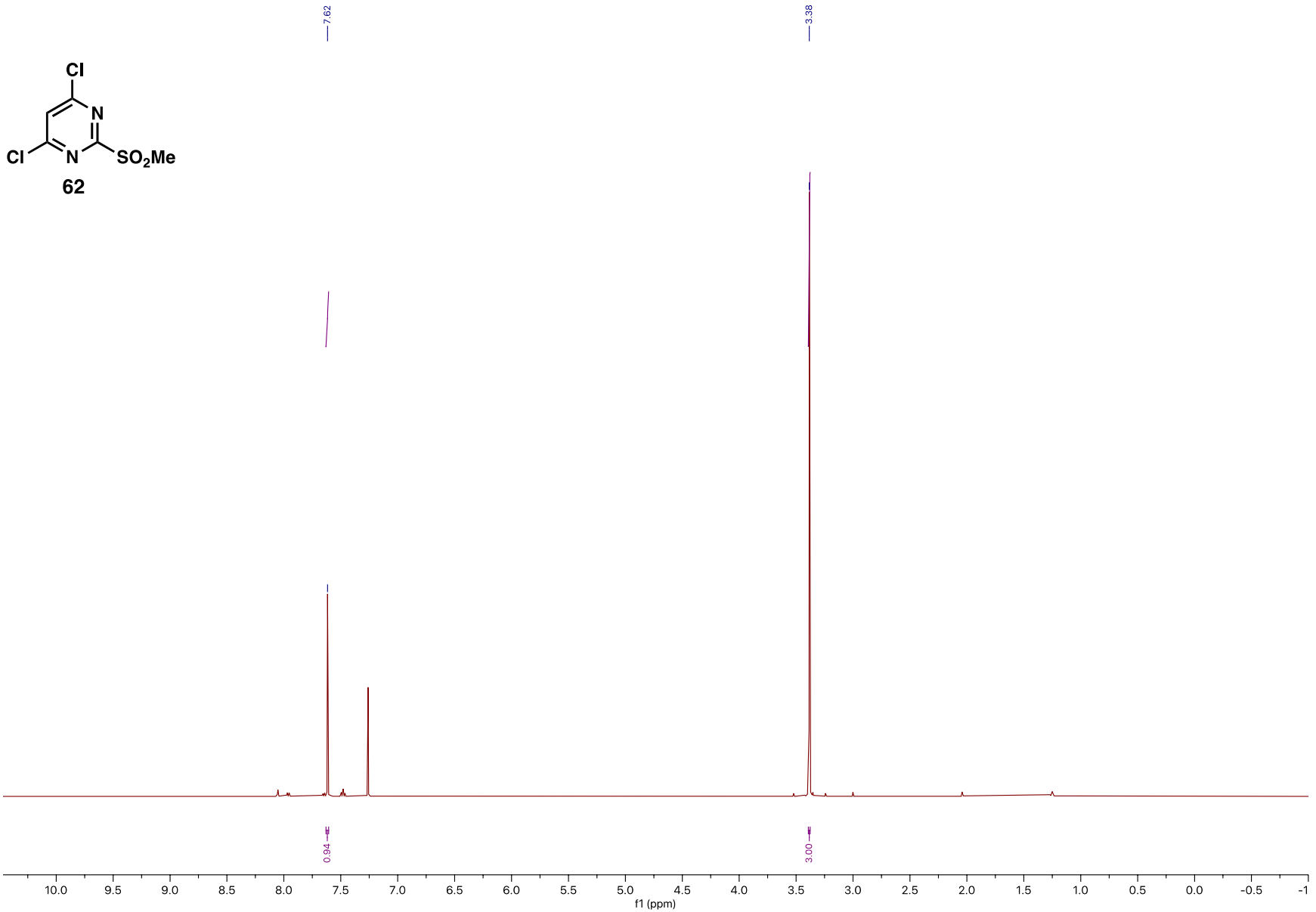
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

©AUTHOR(S)

Cl
N
Cl
N
SO2Me

62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5.5
5.0
4.5
4.0
3.5
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1.5
1.0
0.5
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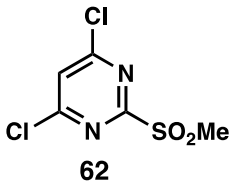
-0.5
-1
f1 (ppm)

©AUTHOR(S)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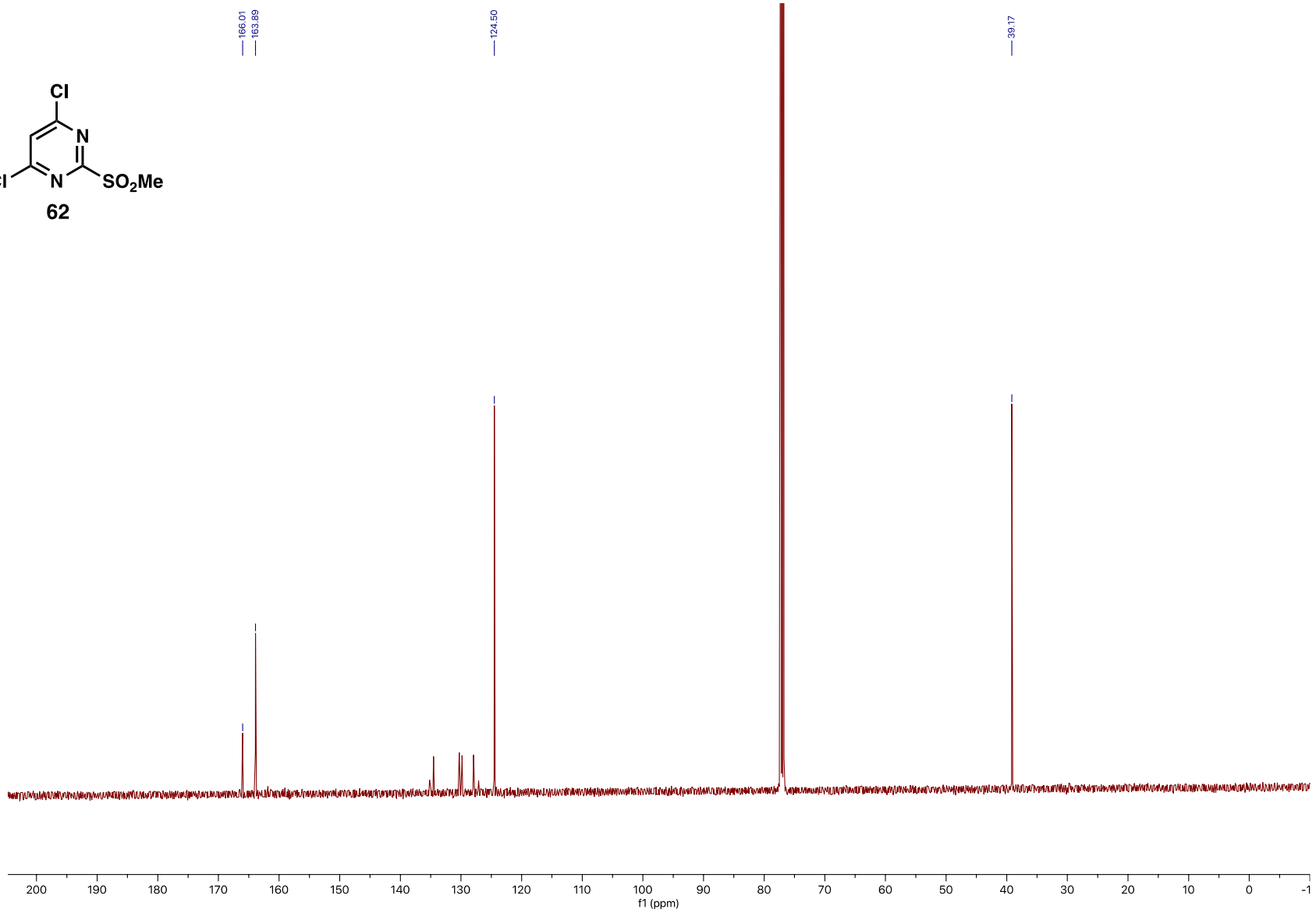
N
Cl
N
SO2Me

62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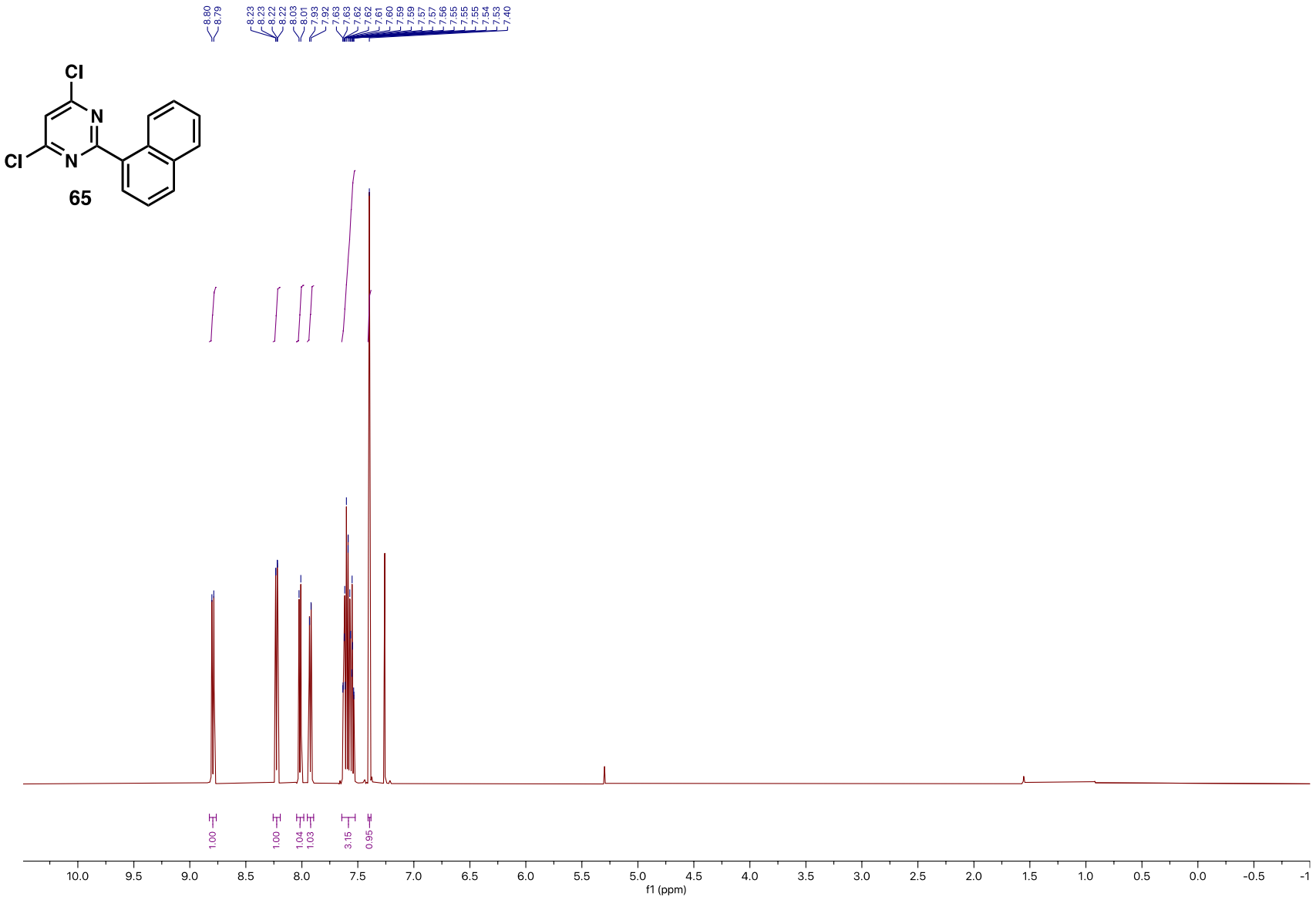
39.17
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

©AUTHOR(S)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7.61
7.60
7.59
7.59
7.57
7.57
7.56
7.55
7.55
7.55
7.54
7.53
7.40
Cl
N
Cl
N
65
1.00
1.00
1.04
1.03
3.15
0.95
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.0
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f1 (ppm)

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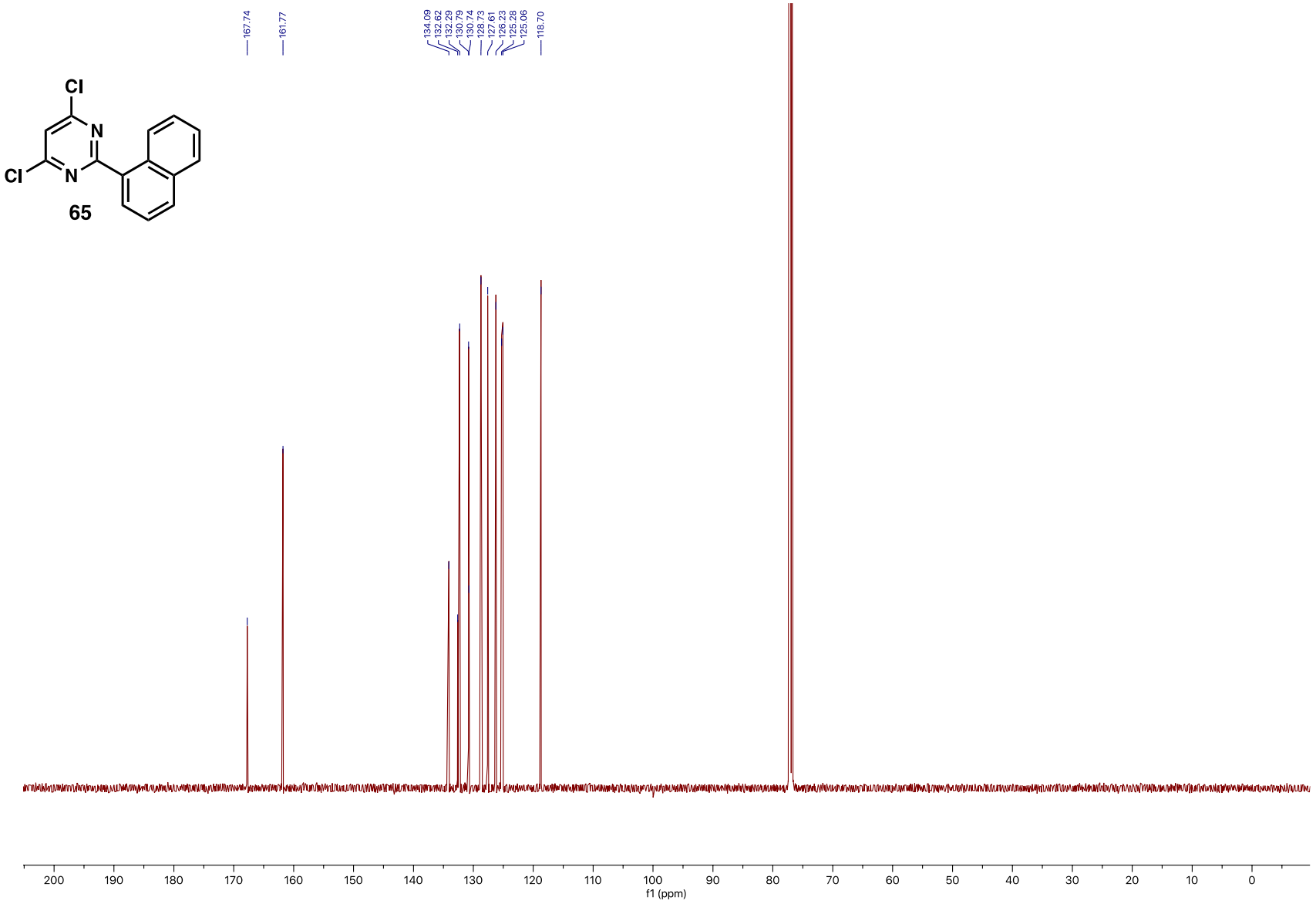
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Cl
N
65
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130.74
128.73
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126.23
125.28
125.06
118.70
200
190
180
170
160
150
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90
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70
60
50
40
30
20
10
0
f1 (ppm)

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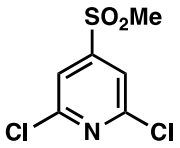
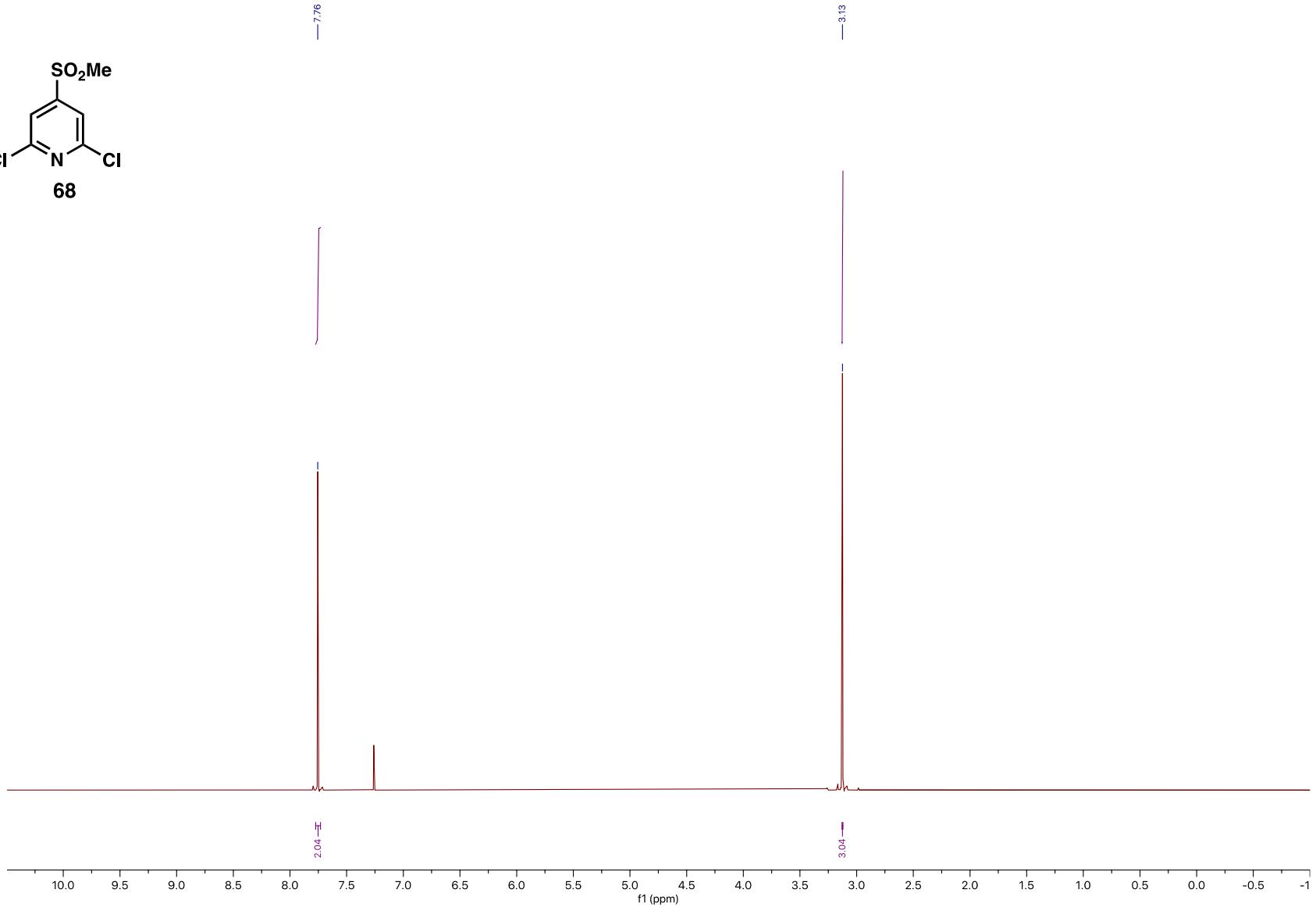

SO2Me
Cl
N
Cl

68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4.5
4.0
3.5
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1.5
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-0.5
-1
f1 (ppm)

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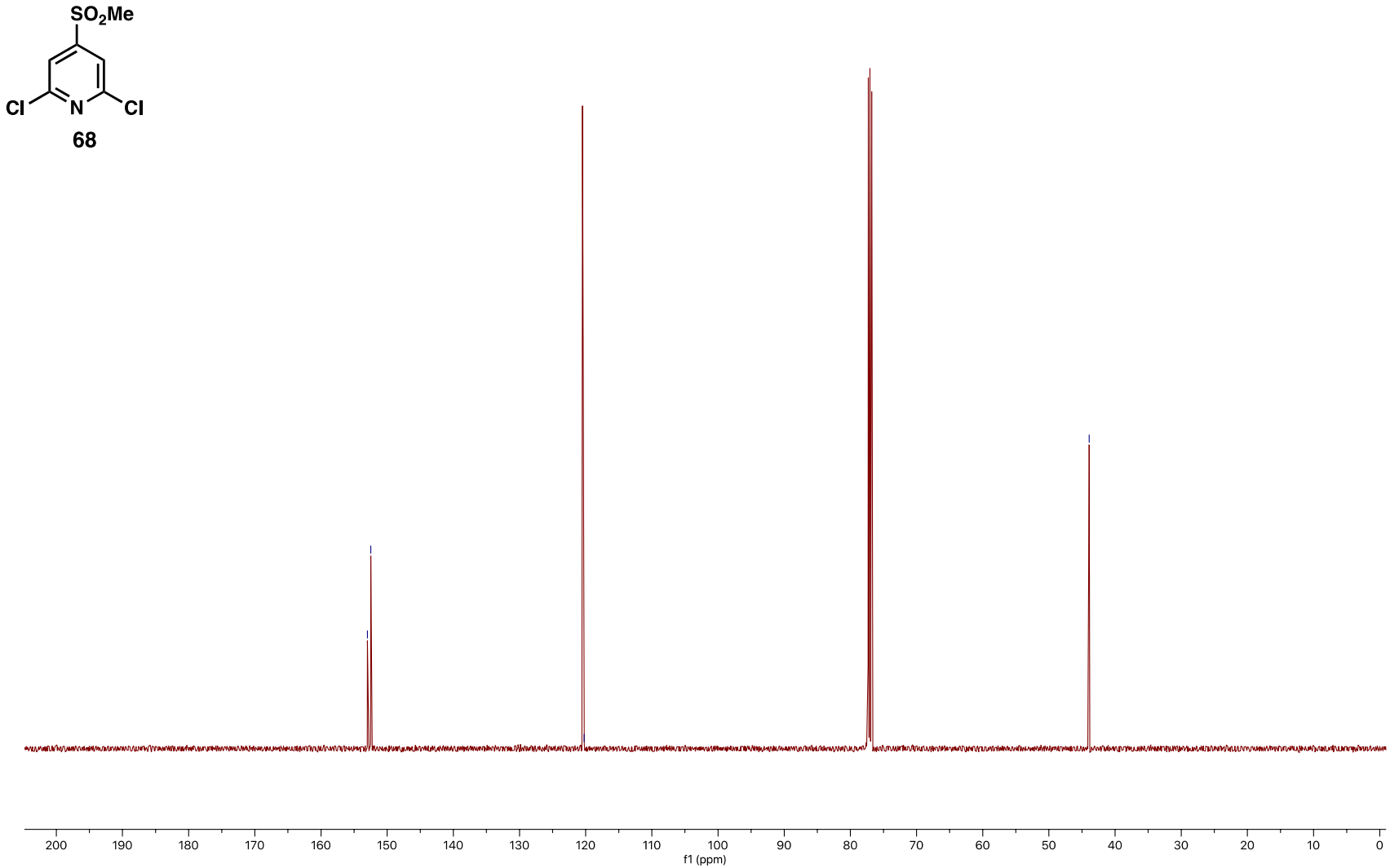
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SO2Me
Cl
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Cl
68
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f1 (ppm)

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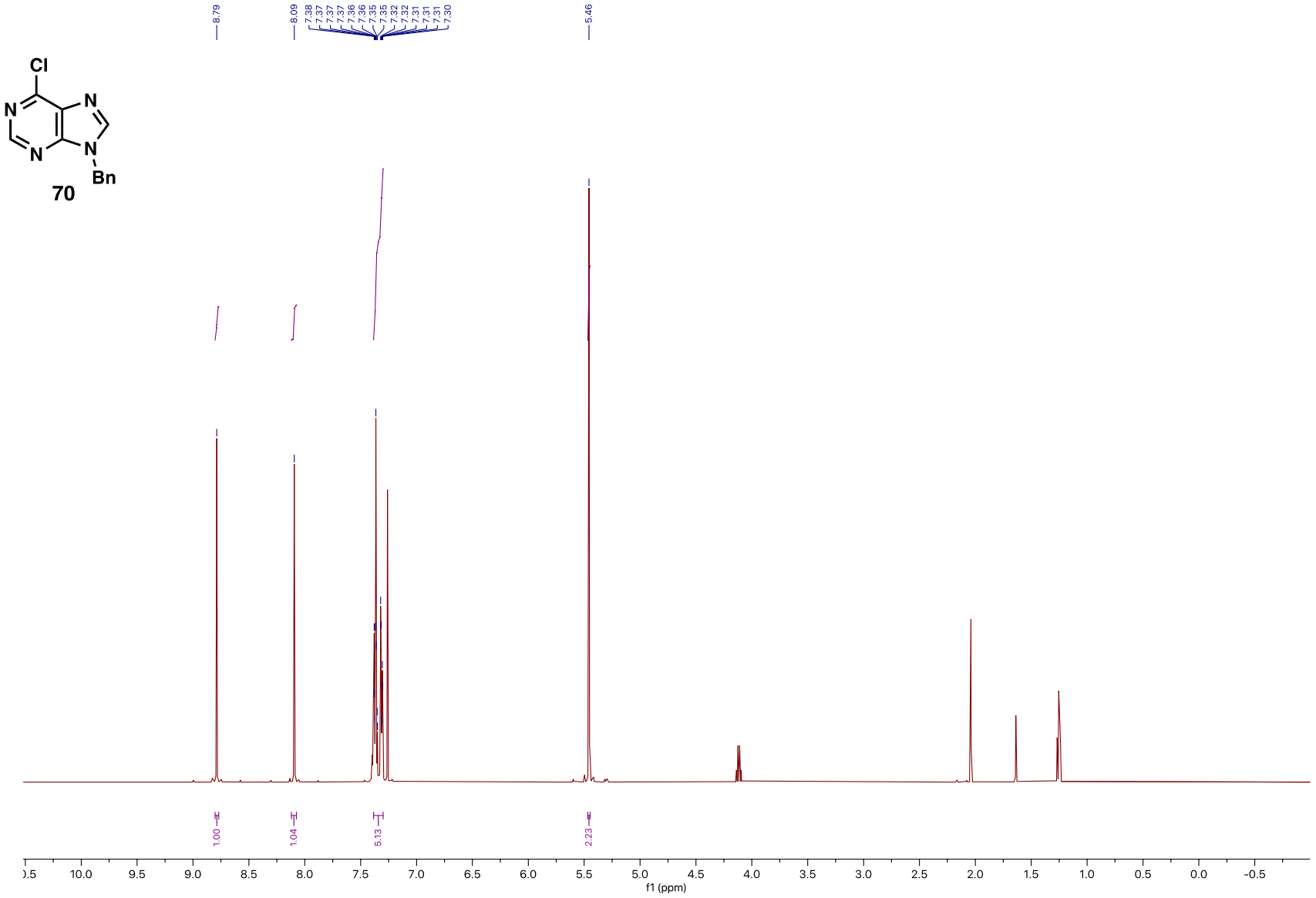

Phosphonate nucleophile scope:

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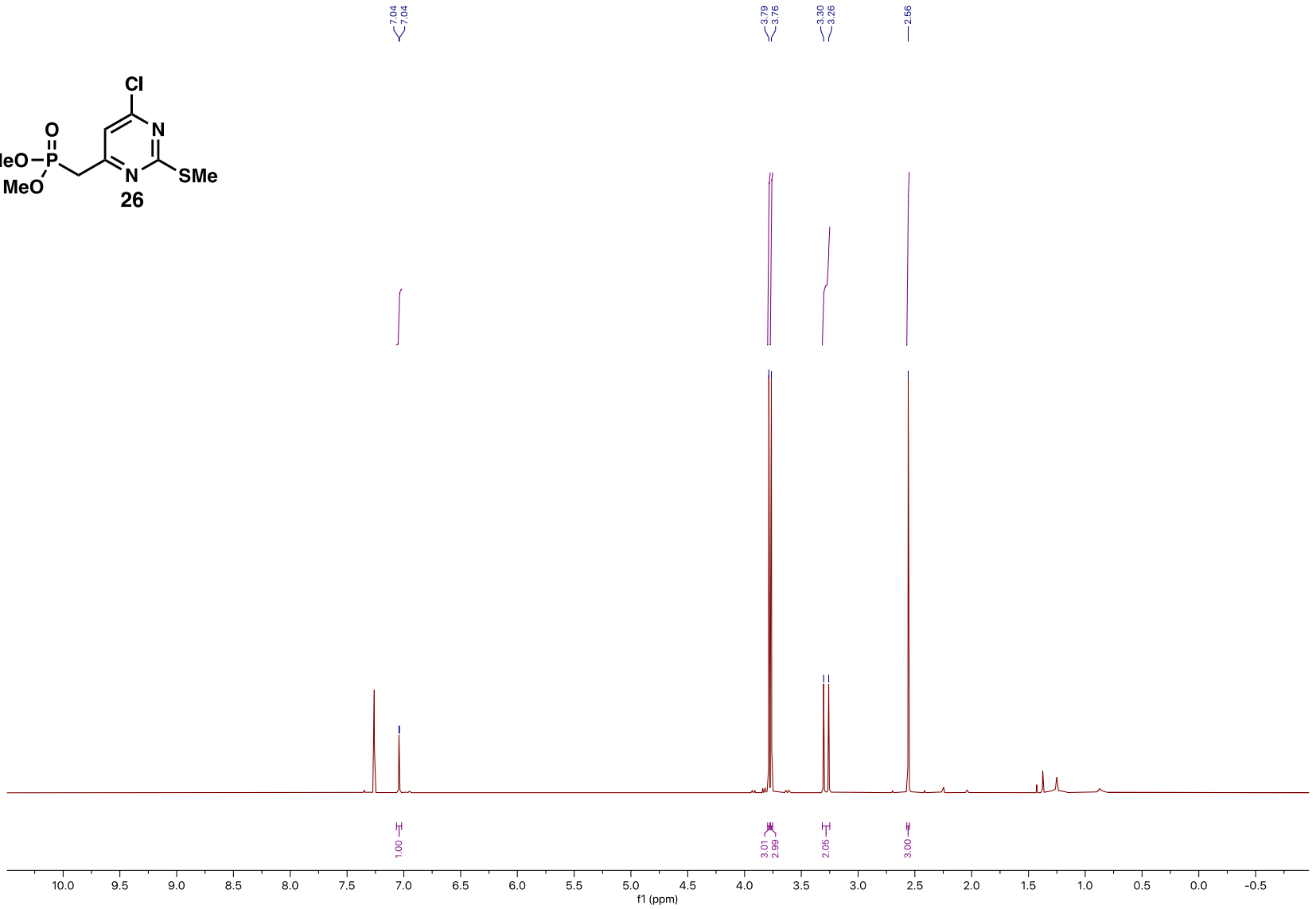
Cl
O
N
MeO
P
N
SMe
MeO

26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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
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2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

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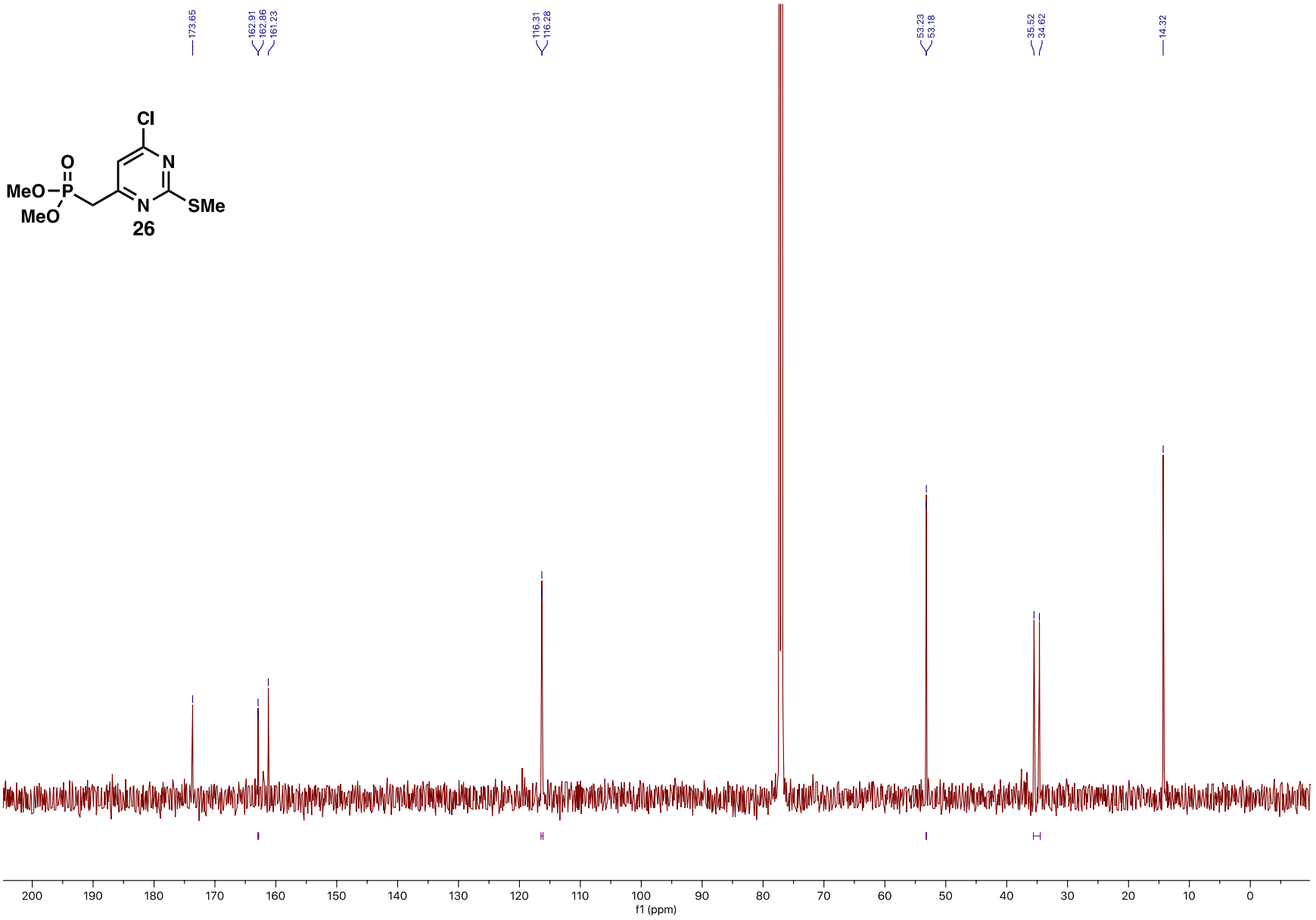
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162.91
162.86
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116.31
116.28
53.23
53.18
35.52
34.62
14.32
Cl
O
MeO
P
MeO
N
N
SMe
26
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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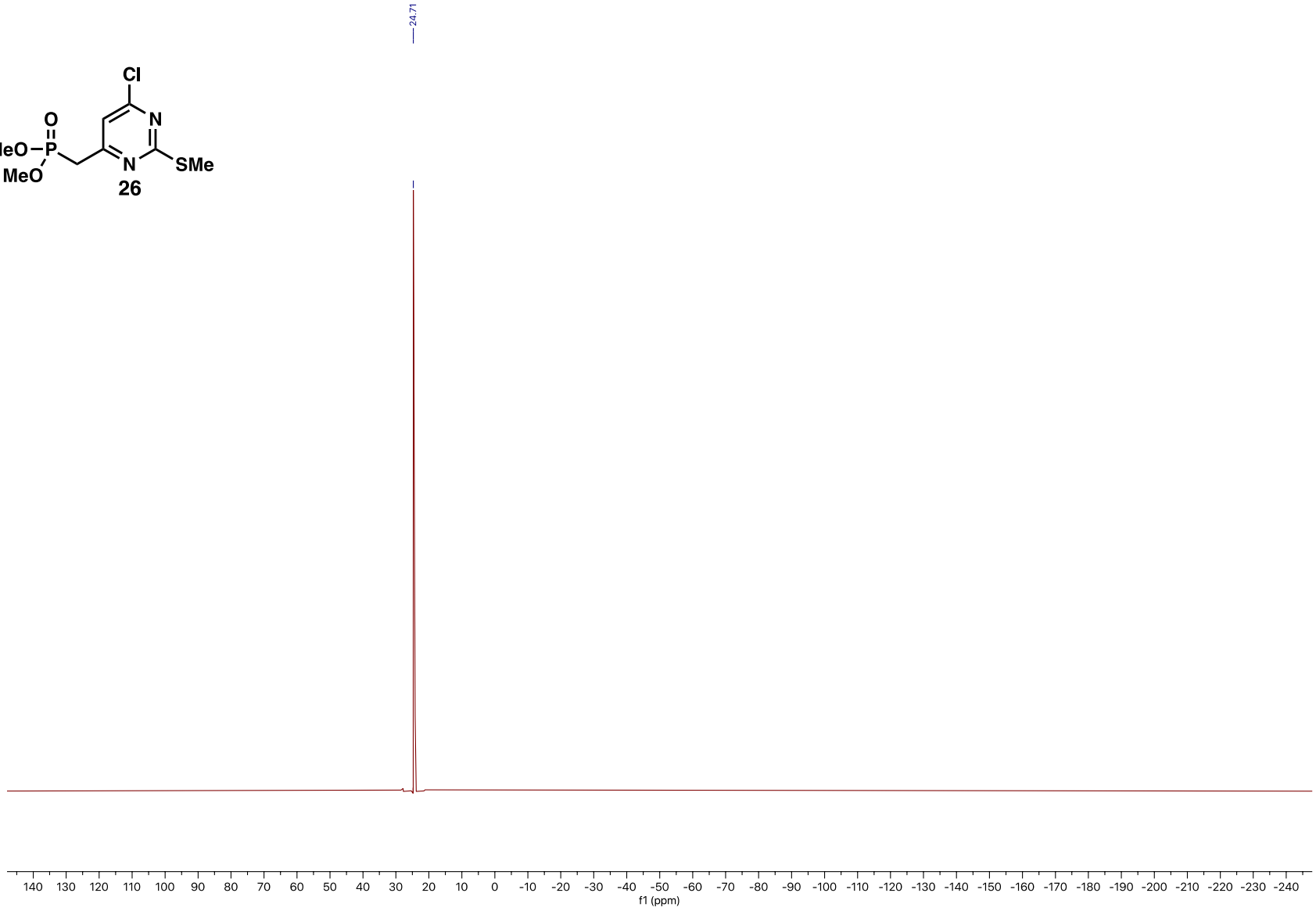
Cl
O
N
MeO
P
MeO
N
SMe

26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f1 (ppm)

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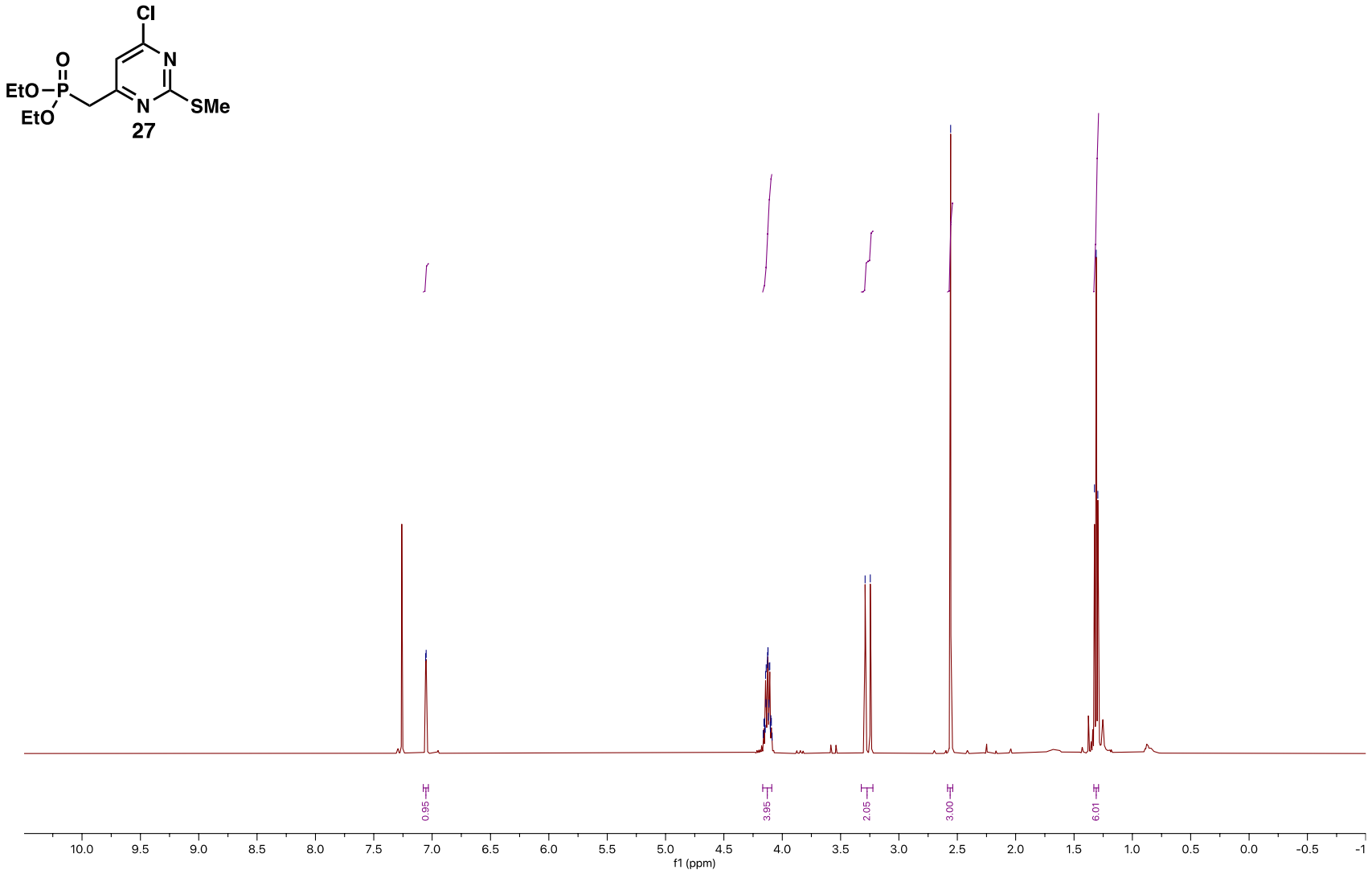
Cl
O
N
EtO
P
N
SMe
EtO
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4.15
4.14
4.14
4.14
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4.12
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f1 (ppm)

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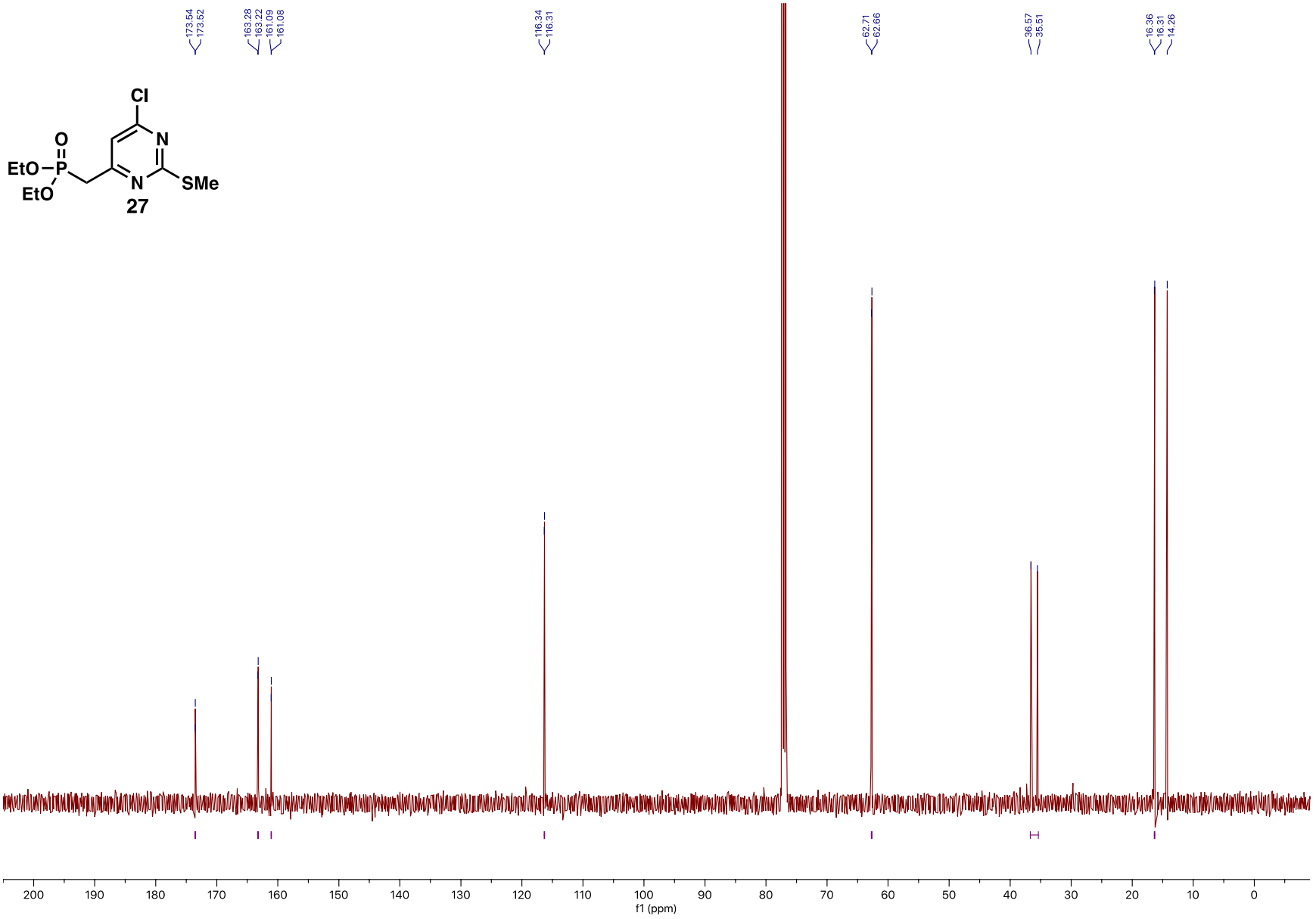
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16.31
14.26
Cl
O
N
EtO
P
N
SMe
EtO
27
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
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0
f1 (ppm)

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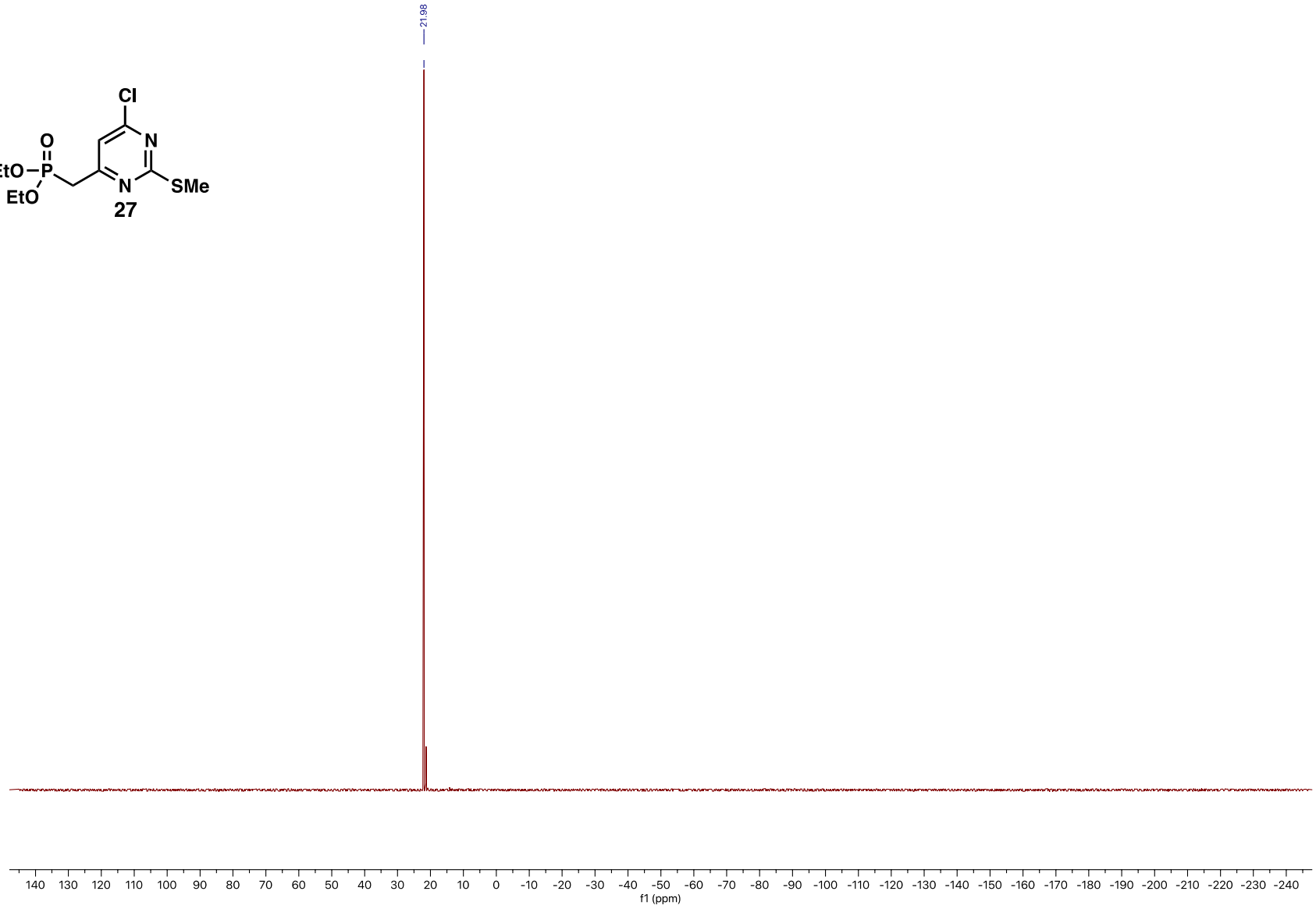
Cl
O
N
EtO
P
N
SMe
EtO

27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f1 (ppm)

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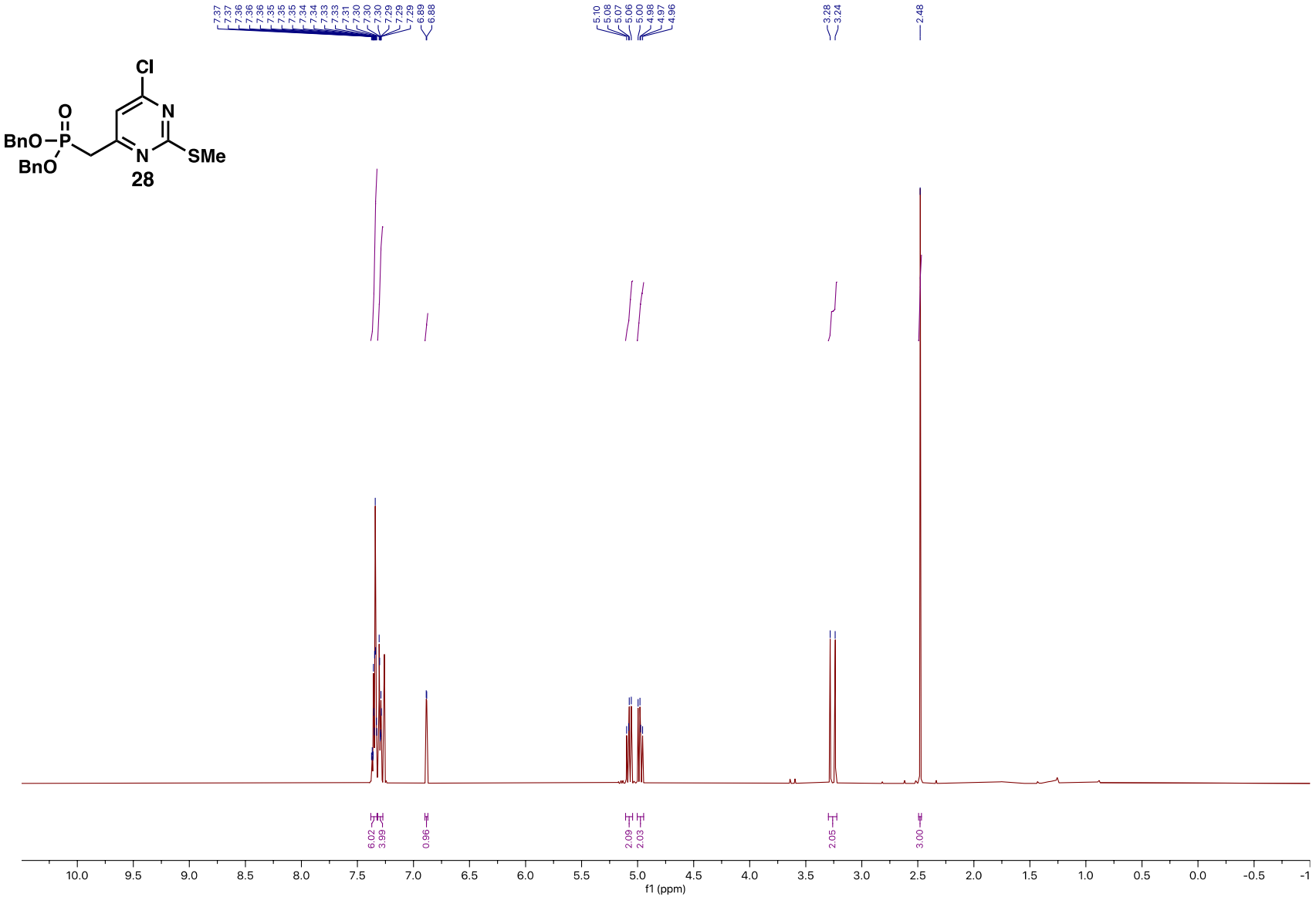
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7.30
7.30
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7.29
7.29
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6.88
5.10
5.08
5.07
5.06
5.00
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4.96
3.28
3.24
2.48
Cl
O
N
BnO–P
BnO
N
SMe
28
6.02
3.99
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2.09
2.03
2.05
3.00
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6.0
5.5
5.0
4.5
4.0
3.5
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-0.5
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f1 (ppm)

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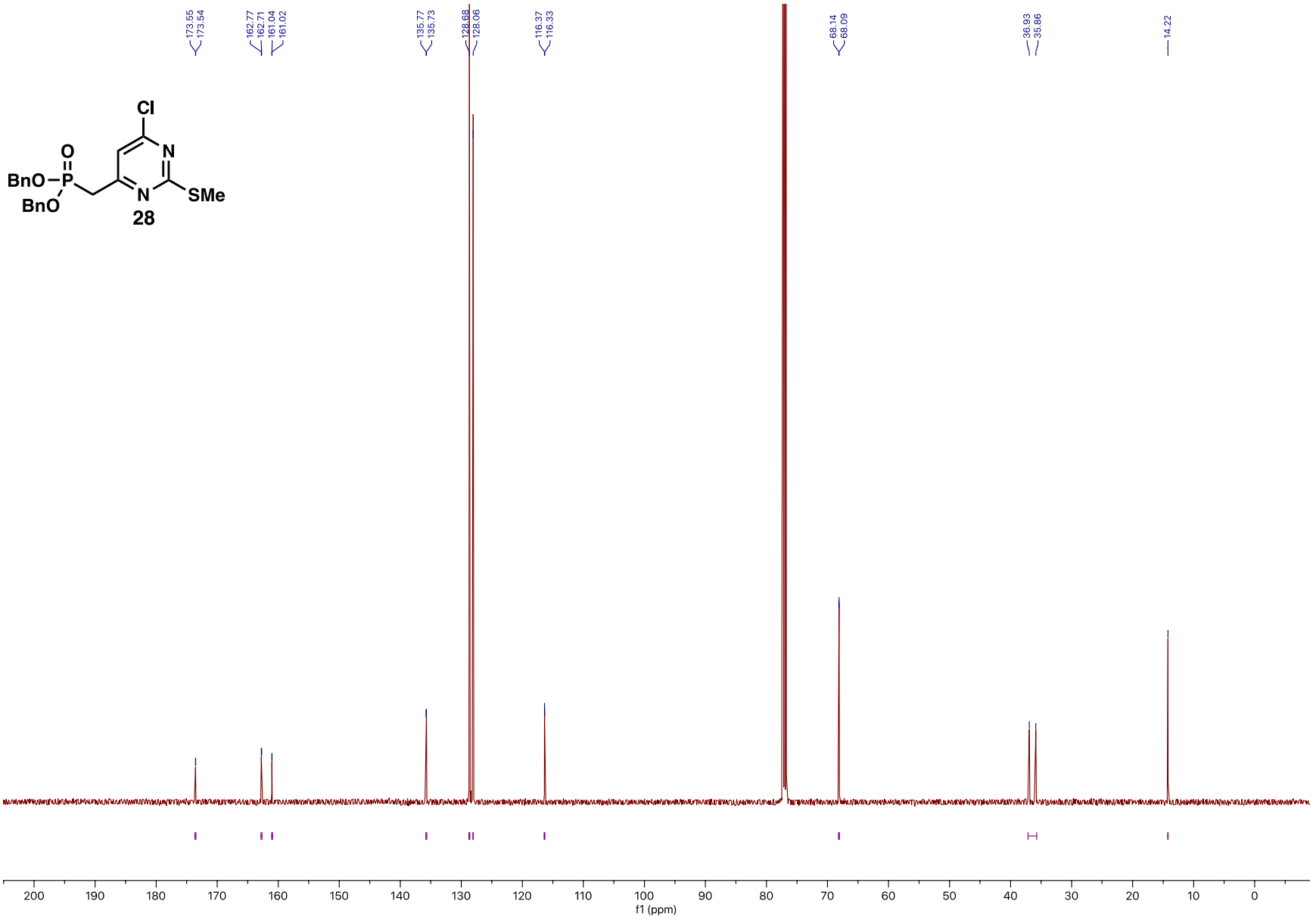
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161.04
161.02
135.77
135.73
128.68
128.06
116.37
116.33
68.14
68.09
36.93
35.86
14.22
Cl
O
N
BnO
P
BnO
N
SMe
28
200
190
180
170
160
150
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30
20
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f1 (ppm)

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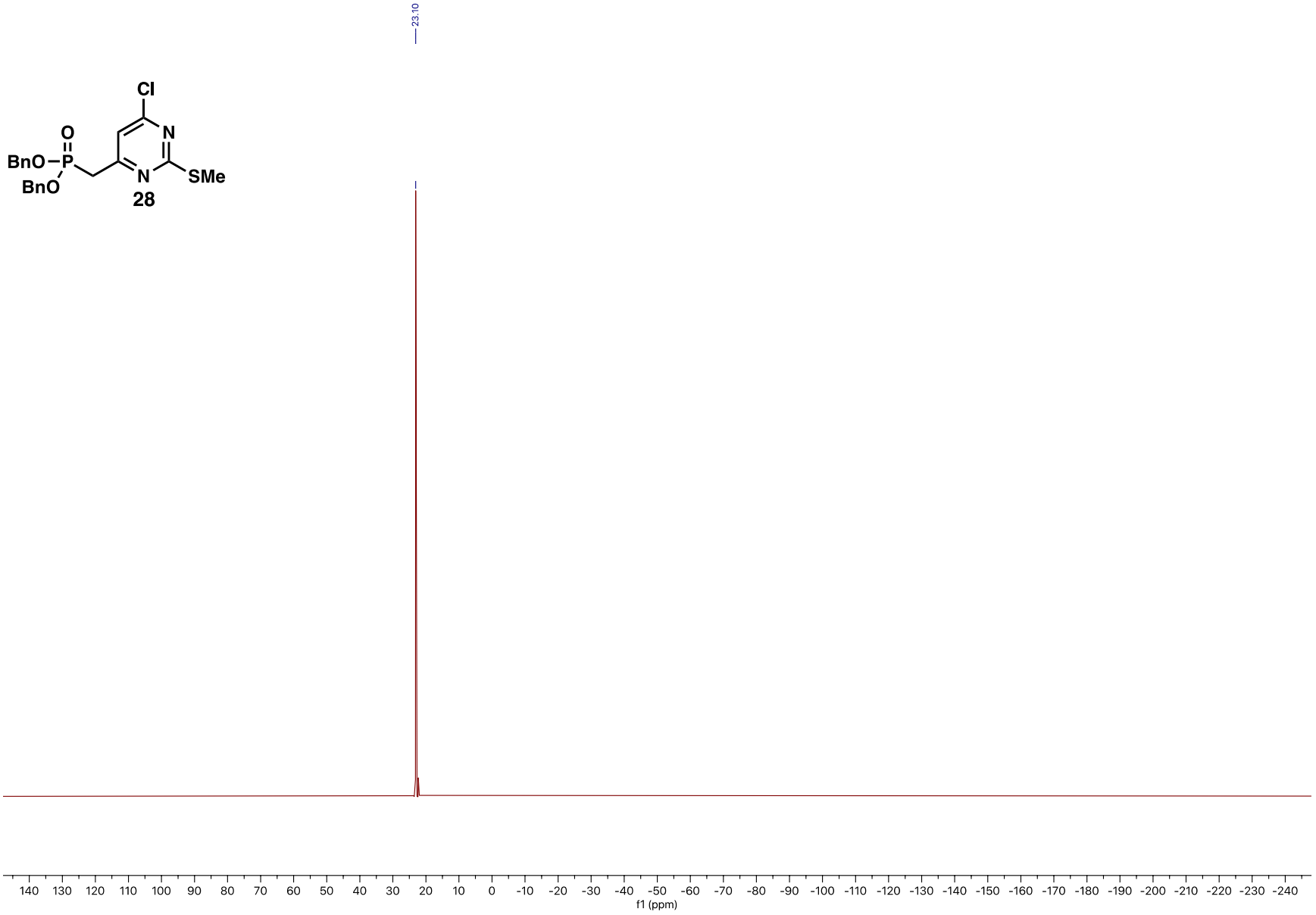
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BnO
P
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28
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f1 (ppm)

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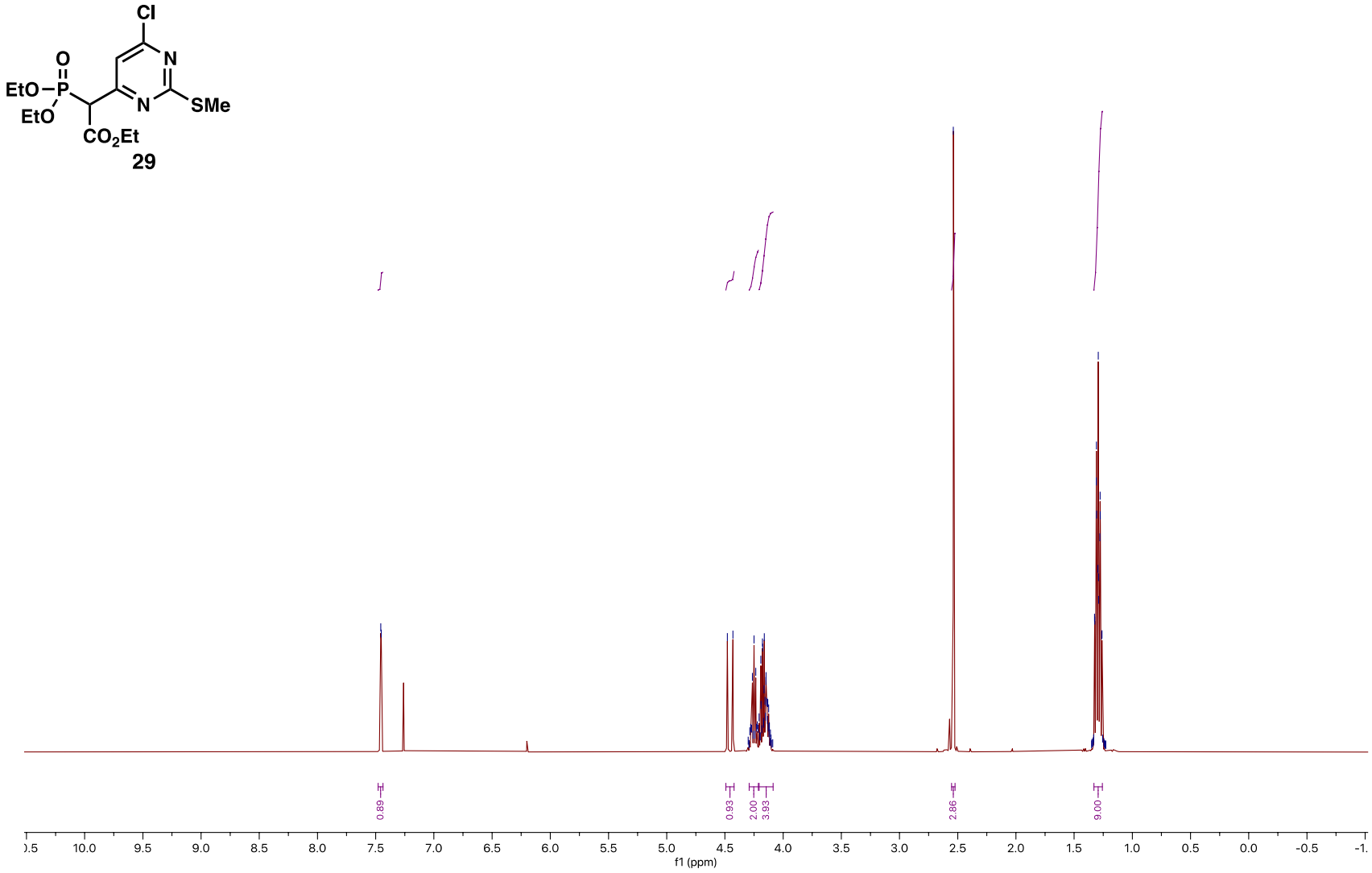

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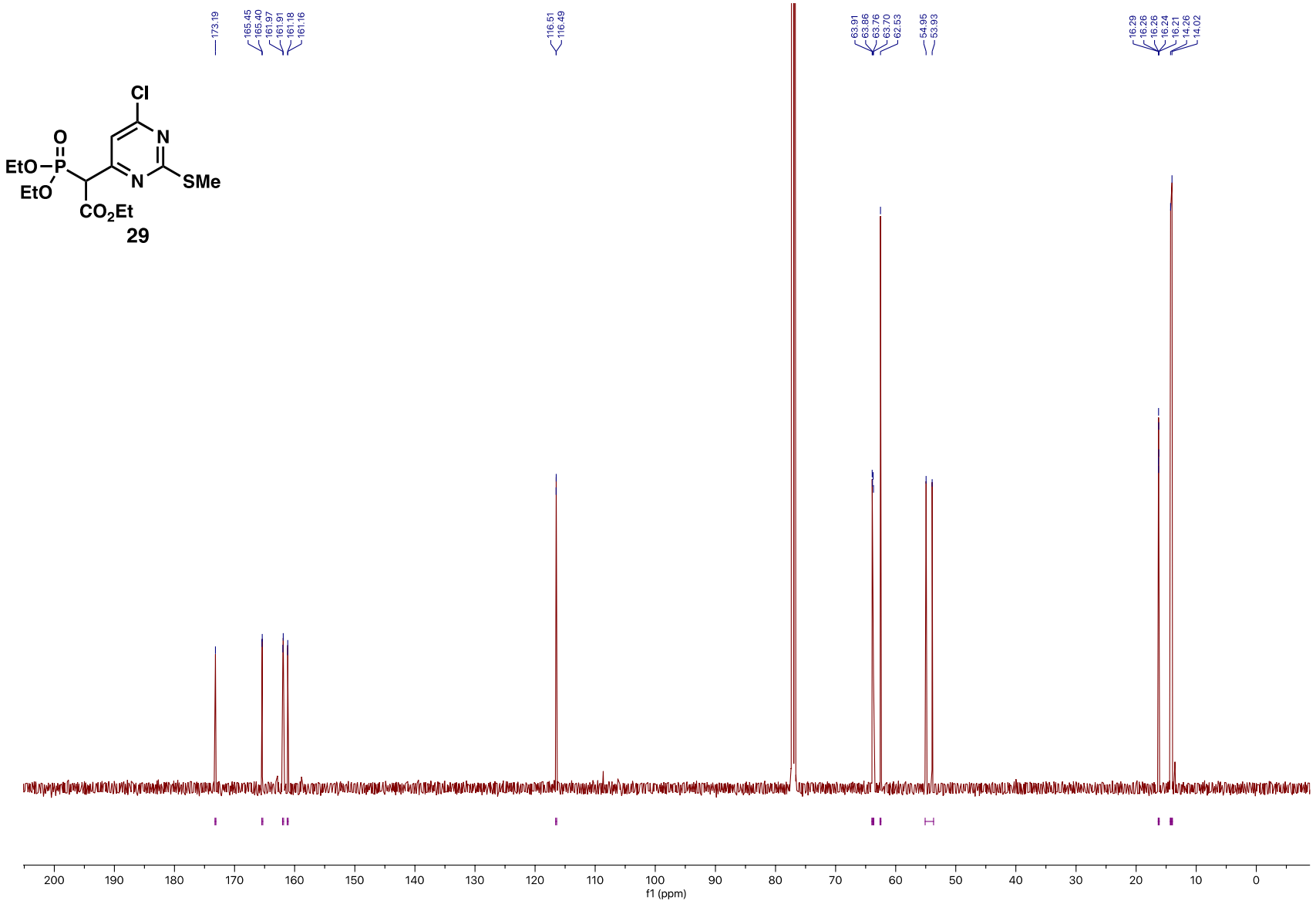
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161.91
161.18
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116.51
116.49
63.91
63.86
63.76
63.70
62.53
54.95
53.93
16.29
16.26
16.26
16.24
16.21
14.26
14.02
Cl
N
O
EtO
P
EtO
N
SMe
CO2Et
29
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
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0
f1 (ppm)

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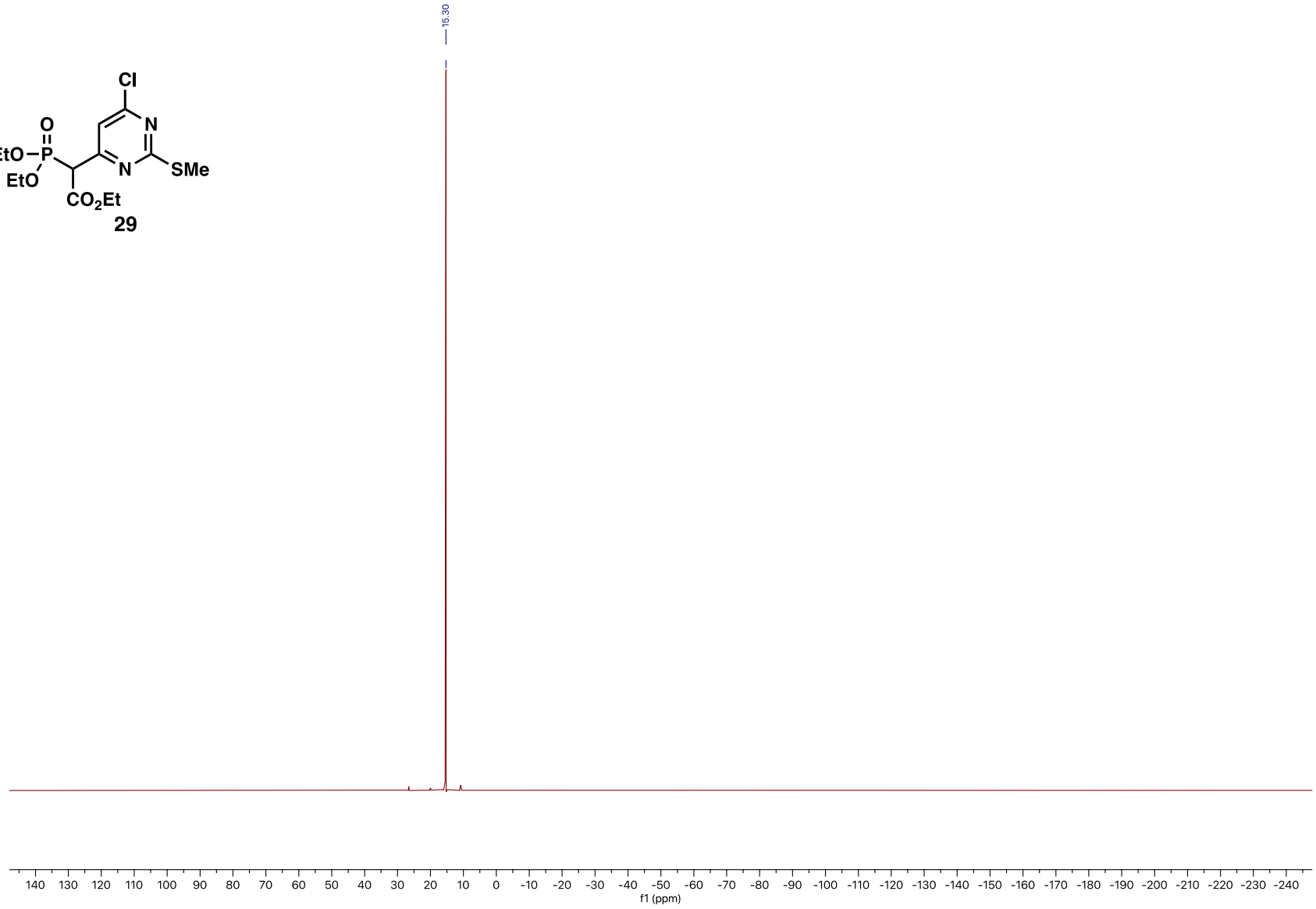
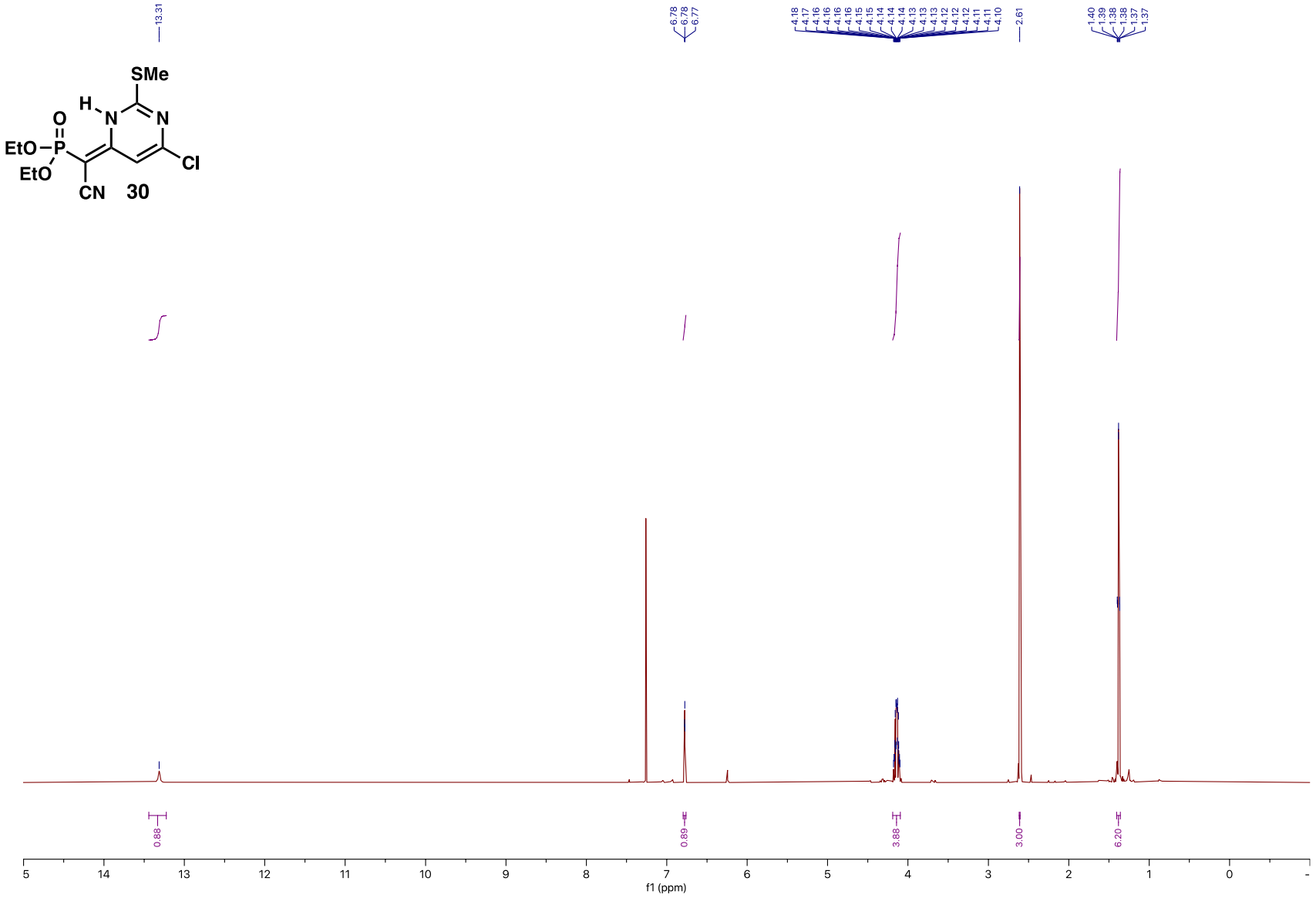
Cl
O
N
EtO
P
N
SMe
EtO
CO2Et

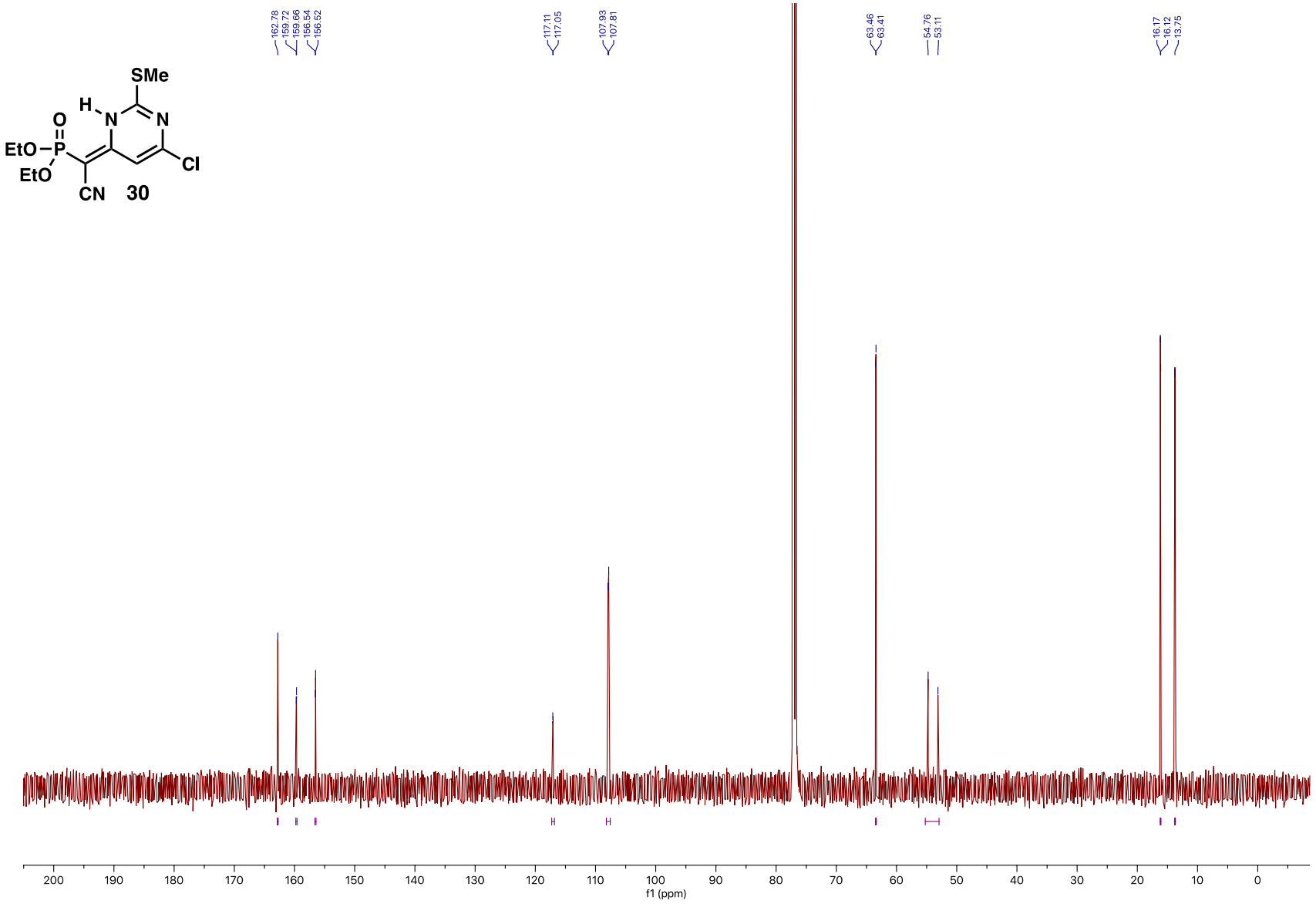
29


15.30
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

©AUTHOR(S)

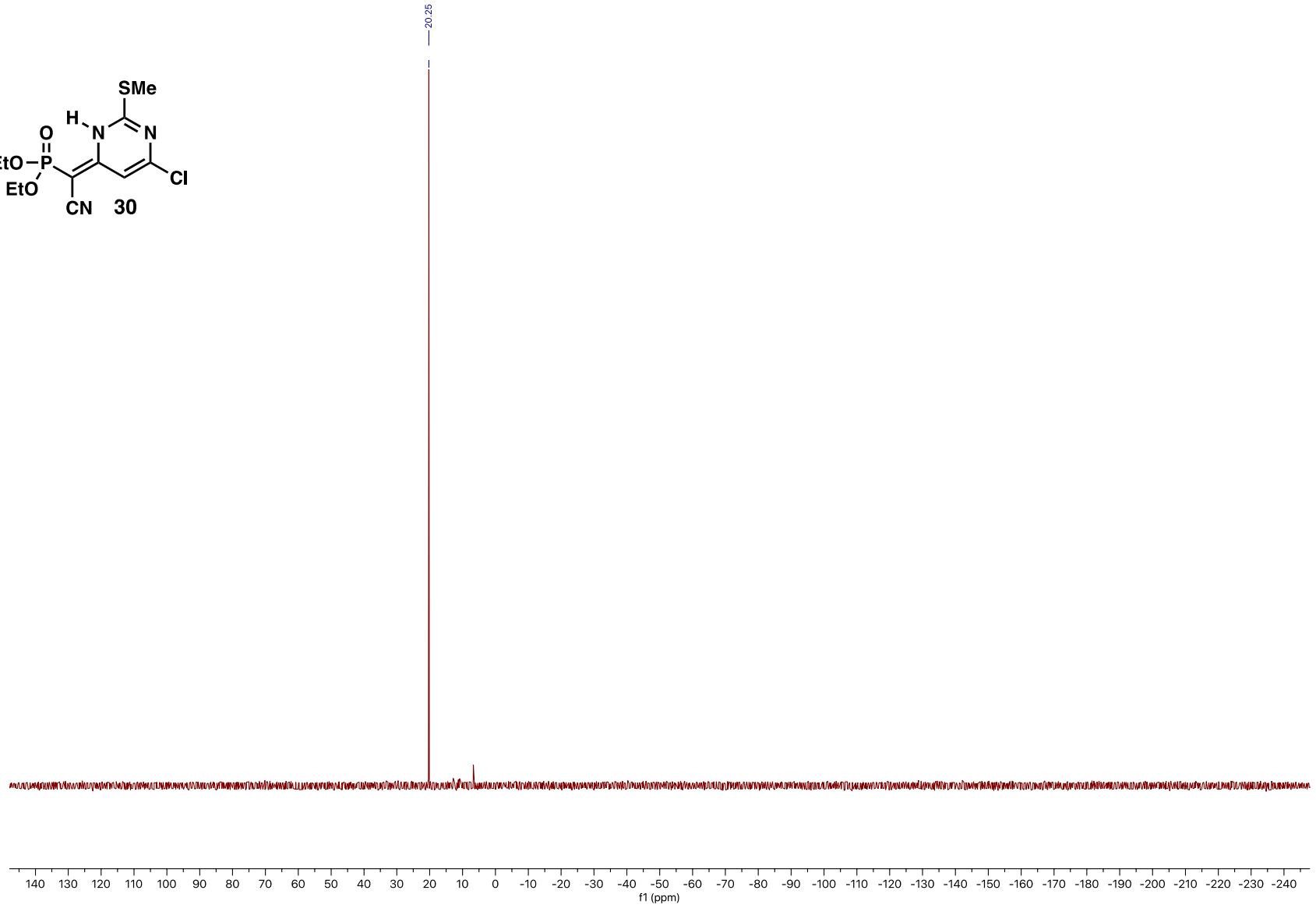

13.31
6.78
6.78
6.77
4.18
4.17
4.16
4.16
4.16
4.16
4.15
4.15
4.14
4.14
4.14
4.13
4.13
4.13
4.12
4.12
4.12
4.12
4.11
4.11
4.10
2.61
1.40
1.39
1.38
1.38
1.37
1.37
SMe
H
N
N
O
EtO
P
EtO
Cl
CN
30
0.88
0.89
3.88
3.00
6.20
5
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)

©AUTHOR(S)

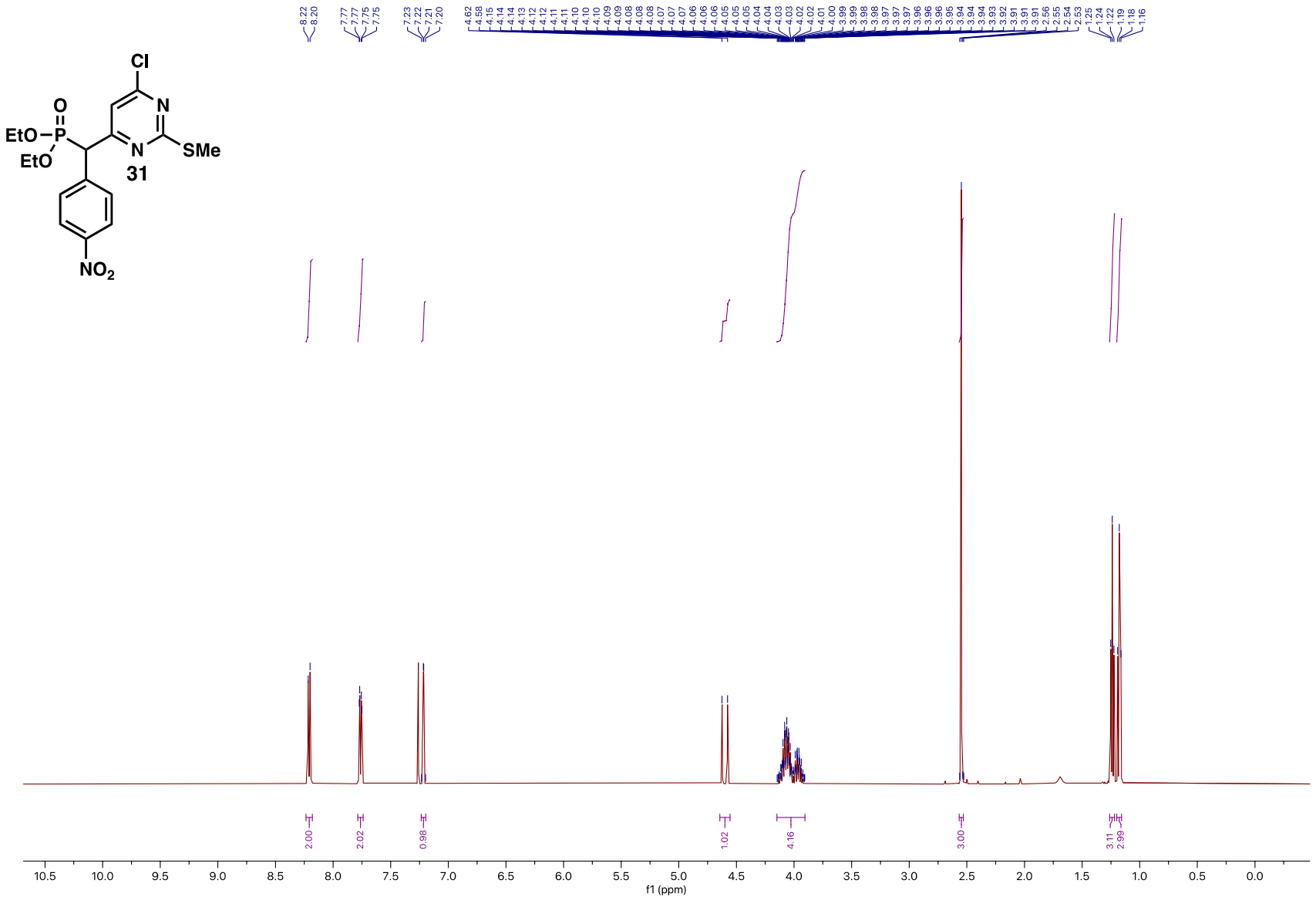

162.78
159.72
159.66
156.54
156.52
117.11
117.05
107.93
107.81
63.46
63.41
54.76
53.11
16.17
16.12
13.75
SMe
H
N
N
O
EtO
P
EtO
Cl
CN
30
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

©AUTHOR(S)

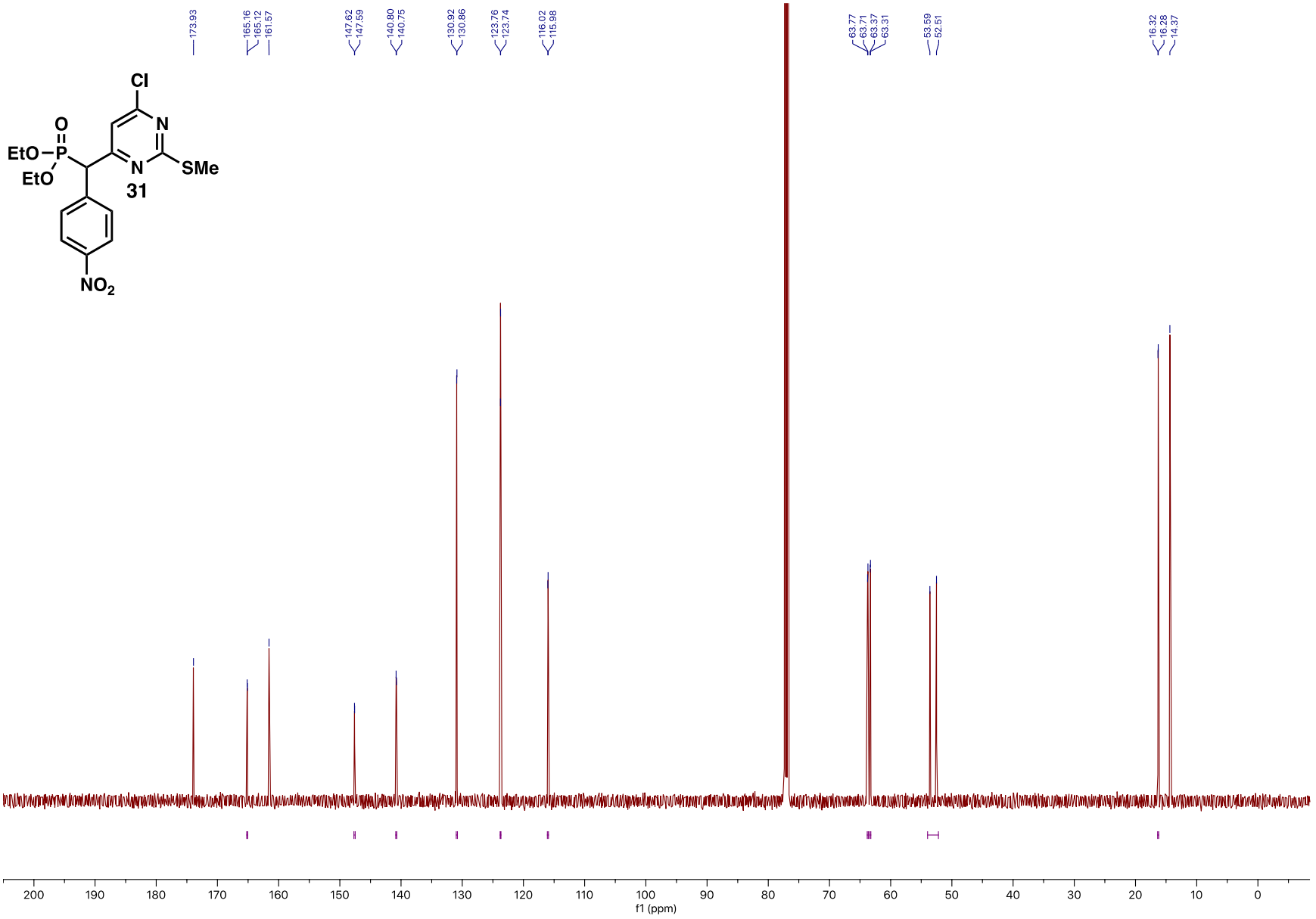
SMe
H
N
N
O
EtO
P
EtO
Cl
CN
30


20.25
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

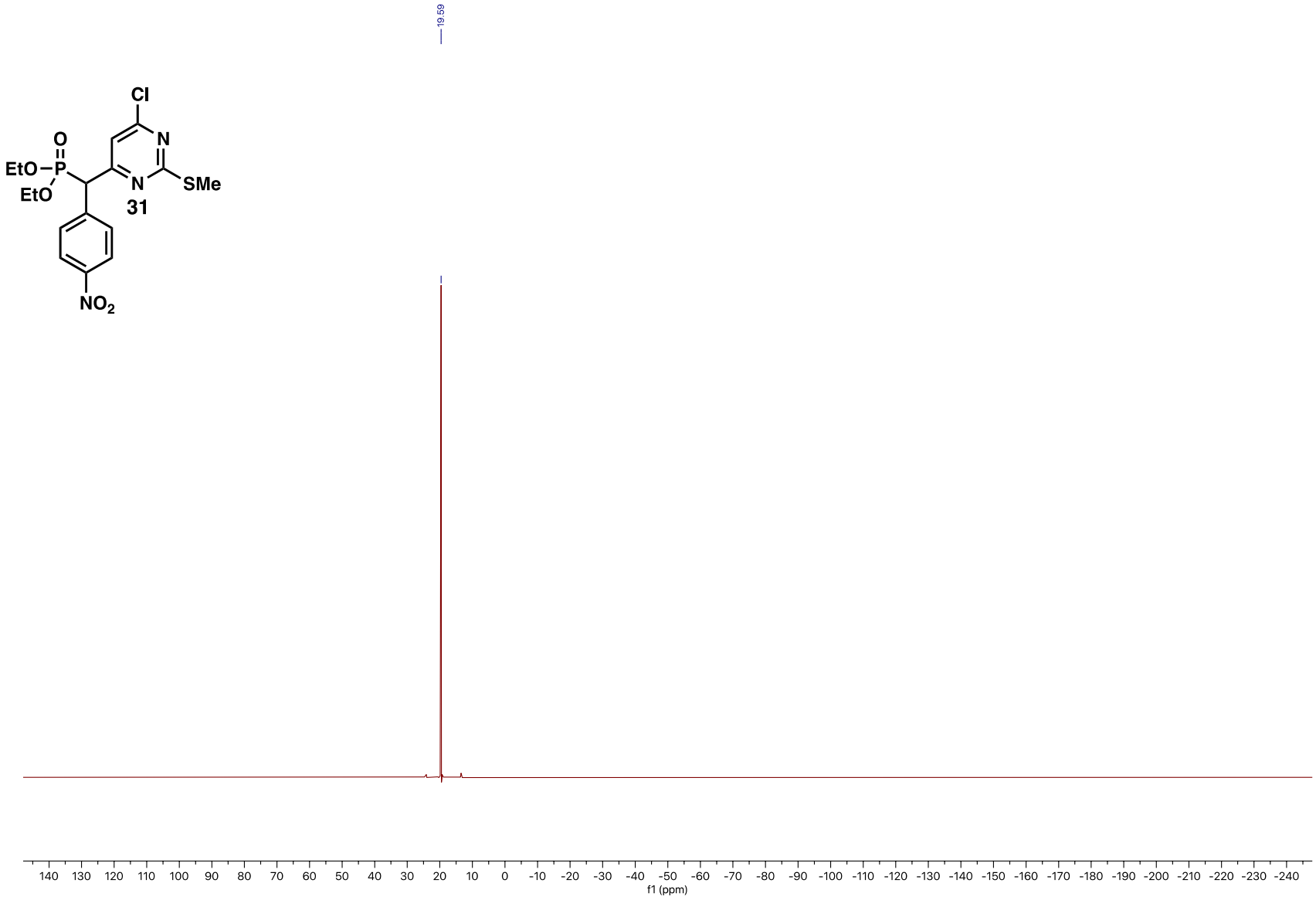
©AUTHOR(S)


Cl
O
N
EtO
P
EtO
N
SMe
31
NO2
8.22
8.20
7.77
7.75
7.23
7.22
7.21
7.20
4.62
4.58
4.15
4.14
4.13
4.12
4.11
4.10
4.09
4.08
4.07
4.06
4.05
4.04
4.03
4.02
4.01
4.00
3.99
3.98
3.97
3.96
3.95
3.94
3.93
3.92
3.91
2.56
2.55
2.54
2.53
1.25
1.24
1.22
1.19
1.18
1.16
2.00
2.02
0.98
1.02
4.16
3.00
3.11
2.99
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)

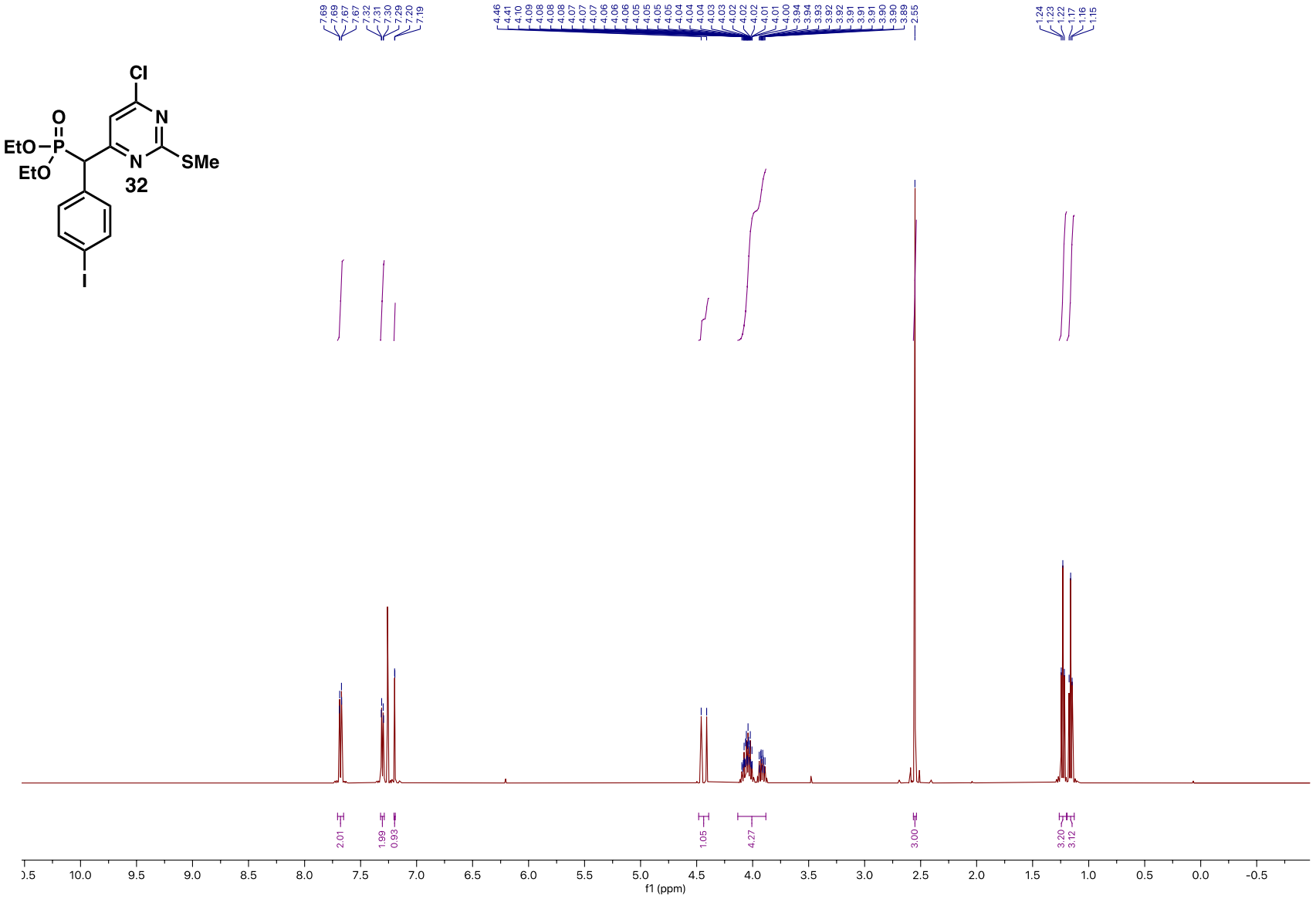
©AUTHOR(S)


173.93
165.16
165.12
161.57
147.62
147.59
140.80
140.75
130.92
130.86
123.76
123.74
116.02
115.98
63.77
63.71
63.37
63.31
53.59
52.51
16.32
16.28
14.37
Cl
O
EtO
P
EtO
N
N
SMe
31
NO2
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

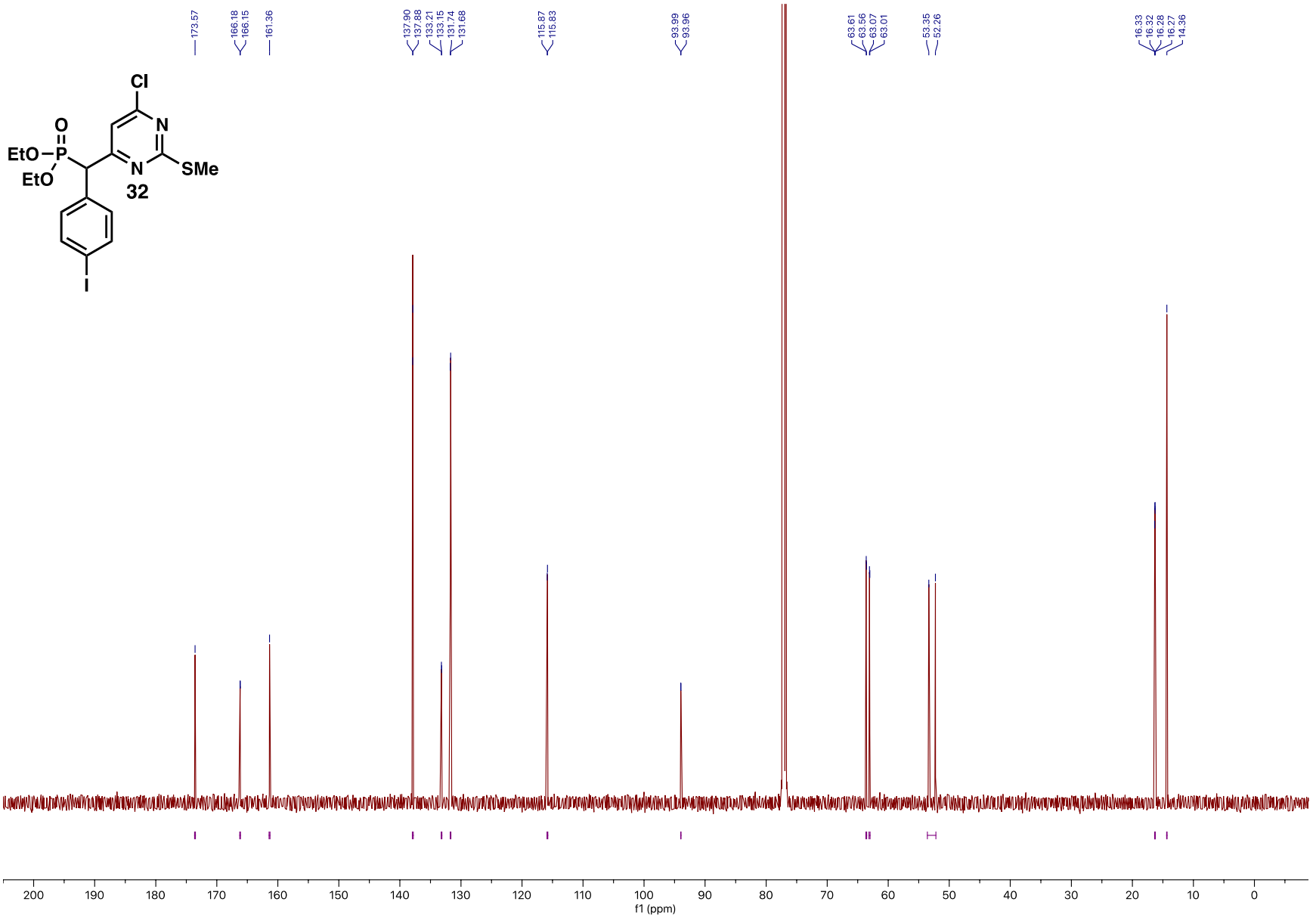
©AUTHOR(S)


19.59
Cl
O
N
EtO
P
N
SMe
EtO
31
NO2
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

©AUTHOR(S)

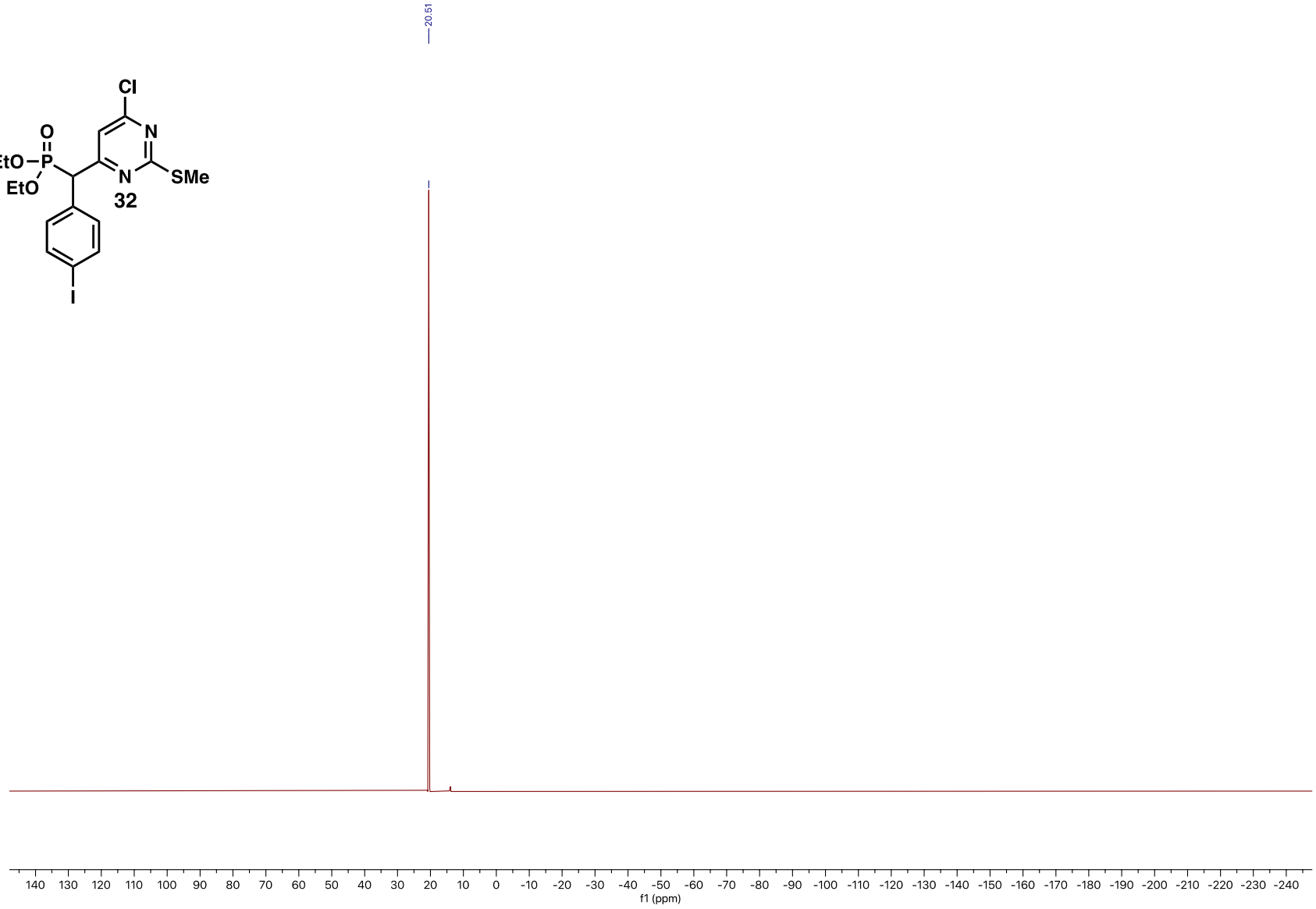


©AUTHOR(S)


173.57
166.18
166.15
161.36
137.90
137.88
133.21
133.15
131.74
131.68
115.87
115.83
93.99
93.96
63.61
63.56
63.07
63.01
53.35
52.26
16.33
16.32
16.28
16.27
14.36
Cl
O
N
EtO
P
N
SMe
EtO
32
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

©AUTHOR(S)

Cl
O
EtO
P
EtO
N
N
SMe
32
I


20.51
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

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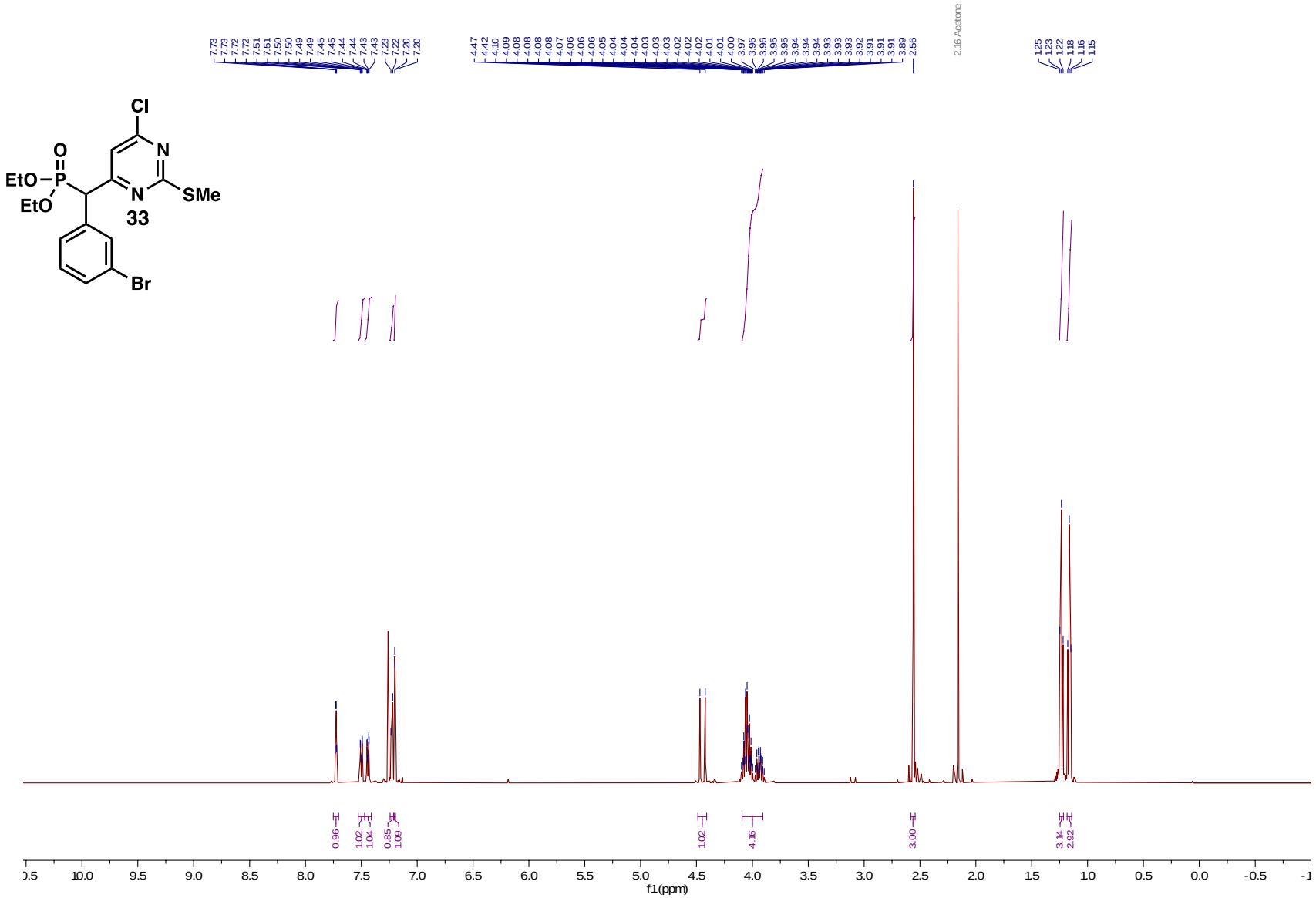
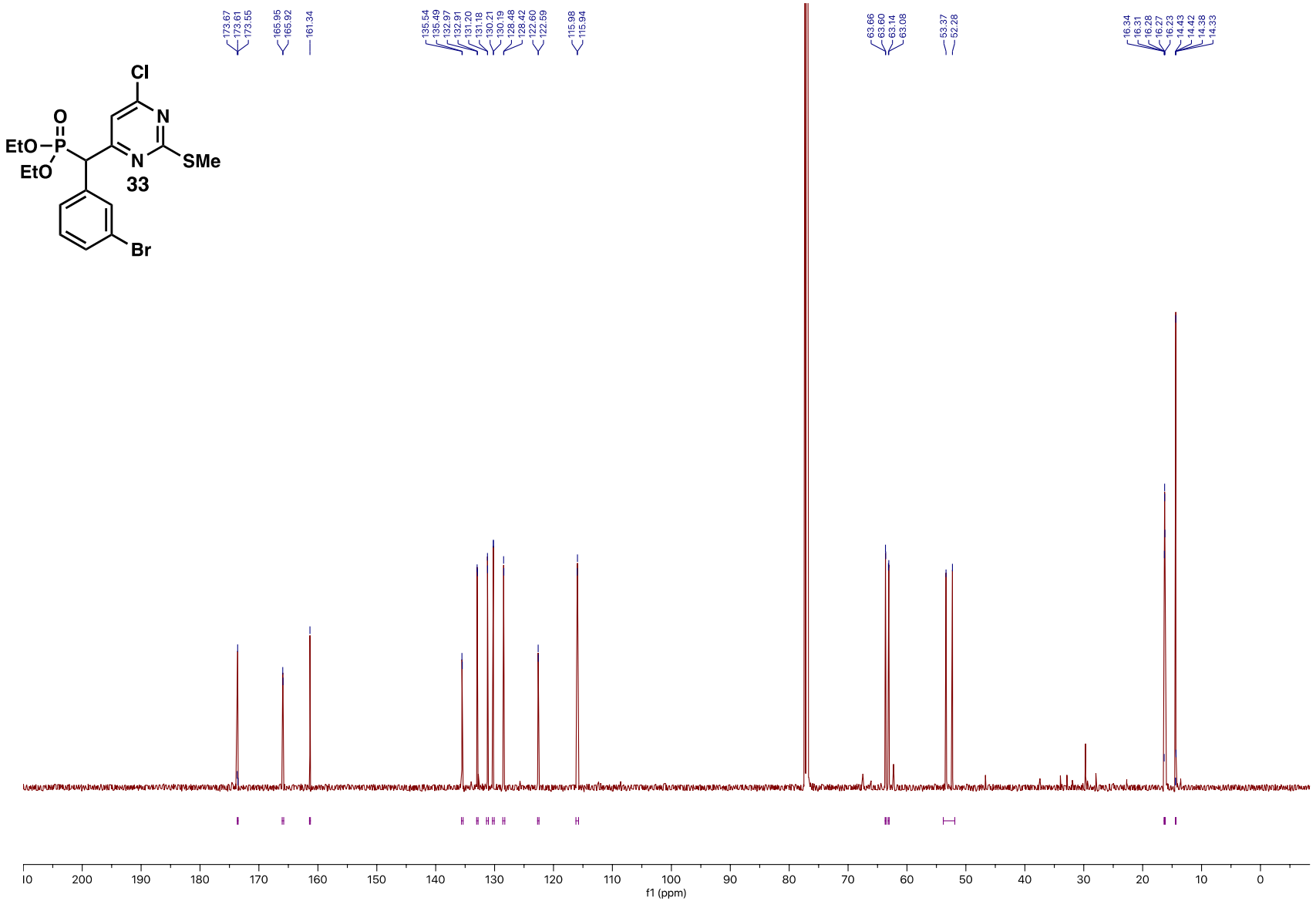
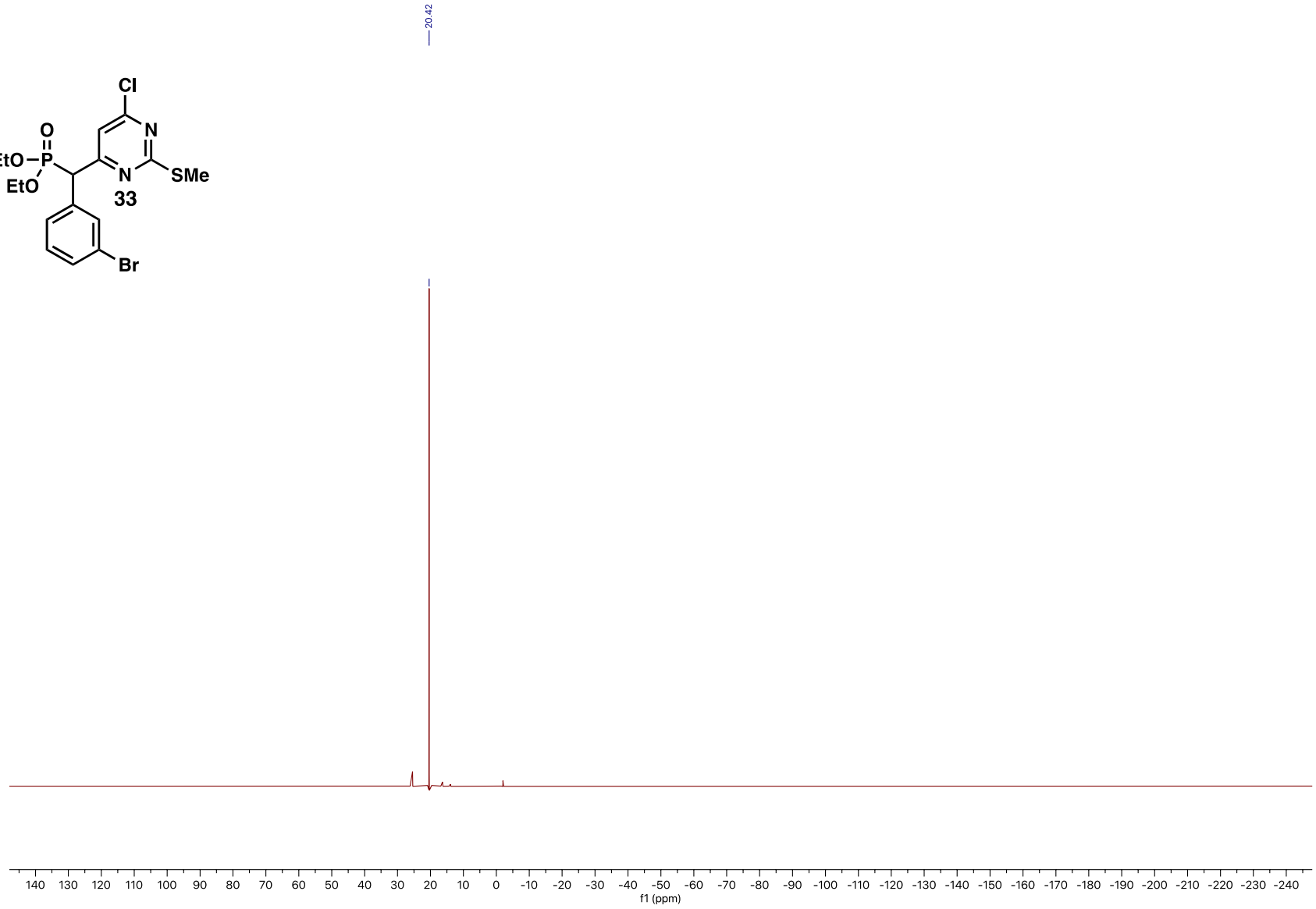


©AUTHOR(S)


173.67
173.61
173.55
165.95
165.92
161.34
135.54
135.49
132.97
132.91
131.20
131.18
130.21
130.19
128.48
128.42
122.60
122.59
115.98
115.94
63.66
63.60
63.14
63.08
53.37
52.28
16.34
16.31
16.28
16.27
16.23
14.43
14.42
14.38
14.33
Cl
N
O
EtO
P
EtO
N
SMe
33
Br
f1 (ppm)

©AUTHOR(S)

Cl
O
N
EtO
P
N
SMe
EtO
33
Br


20.42
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

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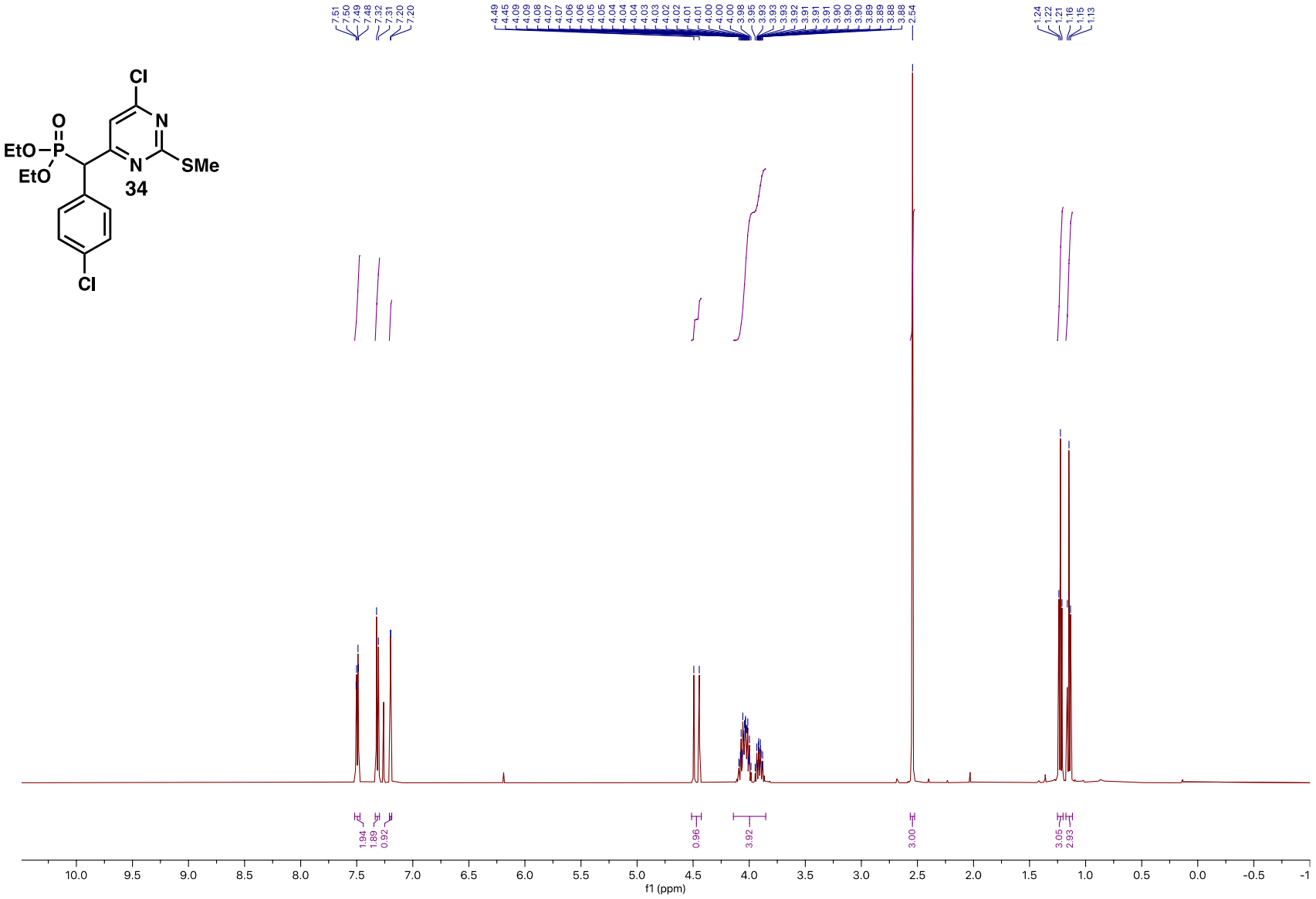
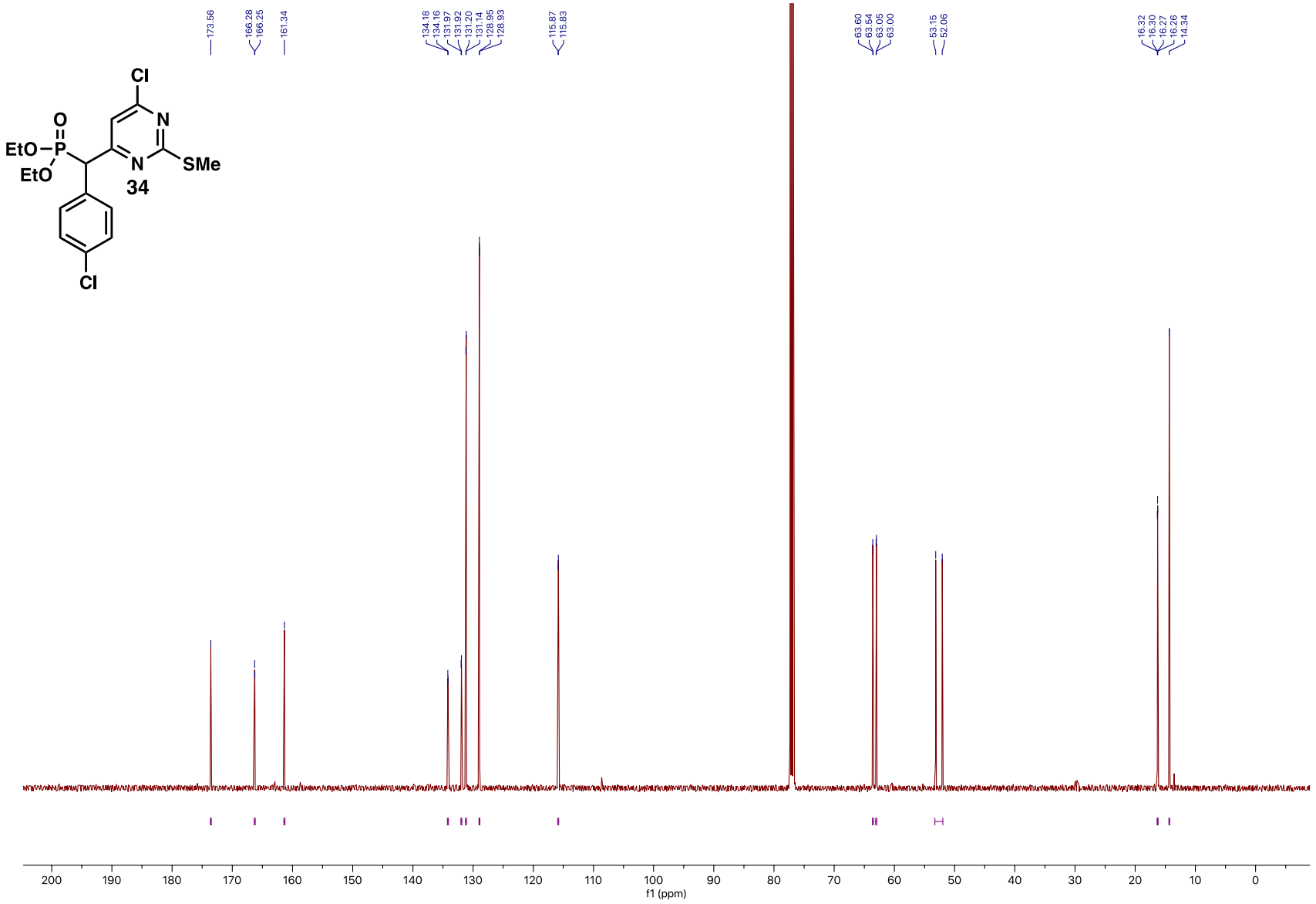

Cl
O
N
EtO–P
N
SMe
EtO
34
Cl
7.51
7.50
7.49
7.48
7.32
7.31
7.20
7.20
4.49
4.45
4.09
4.09
4.08
4.07
4.07
4.06
4.06
4.05
4.05
4.04
4.04
4.04
4.03
4.03
4.02
4.02
4.01
4.01
4.00
4.00
4.00
3.98
3.95
3.93
3.93
3.92
3.91
3.91
3.90
3.90
3.89
3.89
3.88
3.88
2.54
1.24
1.22
1.21
1.16
1.15
1.13
1.94
1.89
0.92
0.96
3.92
3.00
3.05
2.93
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
f1 (ppm)

©AUTHOR(S)


173.56
166.28
166.25
161.34
134.18
134.16
131.97
131.92
131.20
131.14
128.95
128.93
115.87
115.83
63.60
63.54
63.05
63.00
53.15
52.06
16.32
16.30
16.27
16.26
14.34
Cl
O
N
EtO
P
EtO
N
SMe
34
Cl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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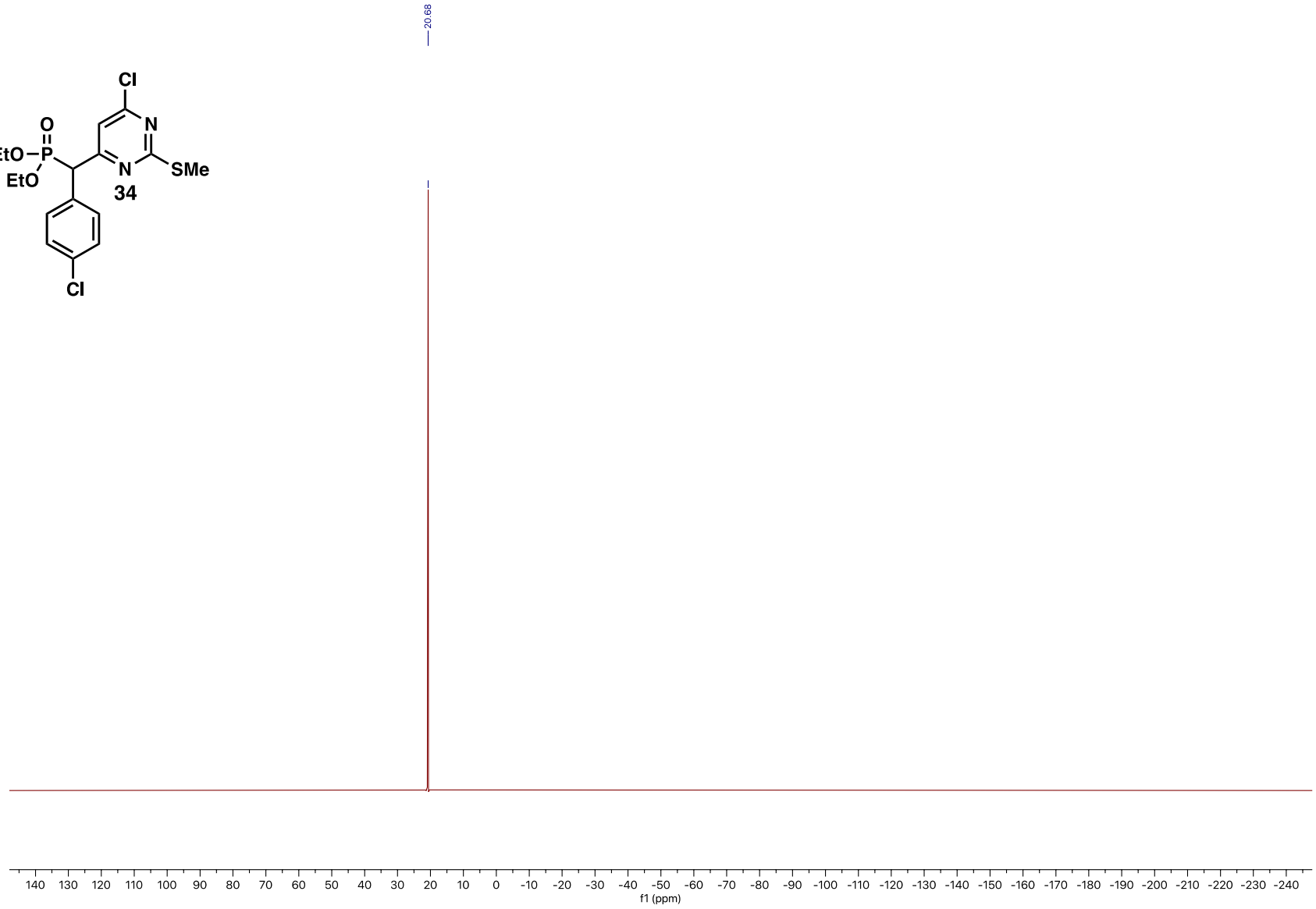
Cl
O
N
EtO
P
N
SMe
EtO
34
Cl


20.68
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

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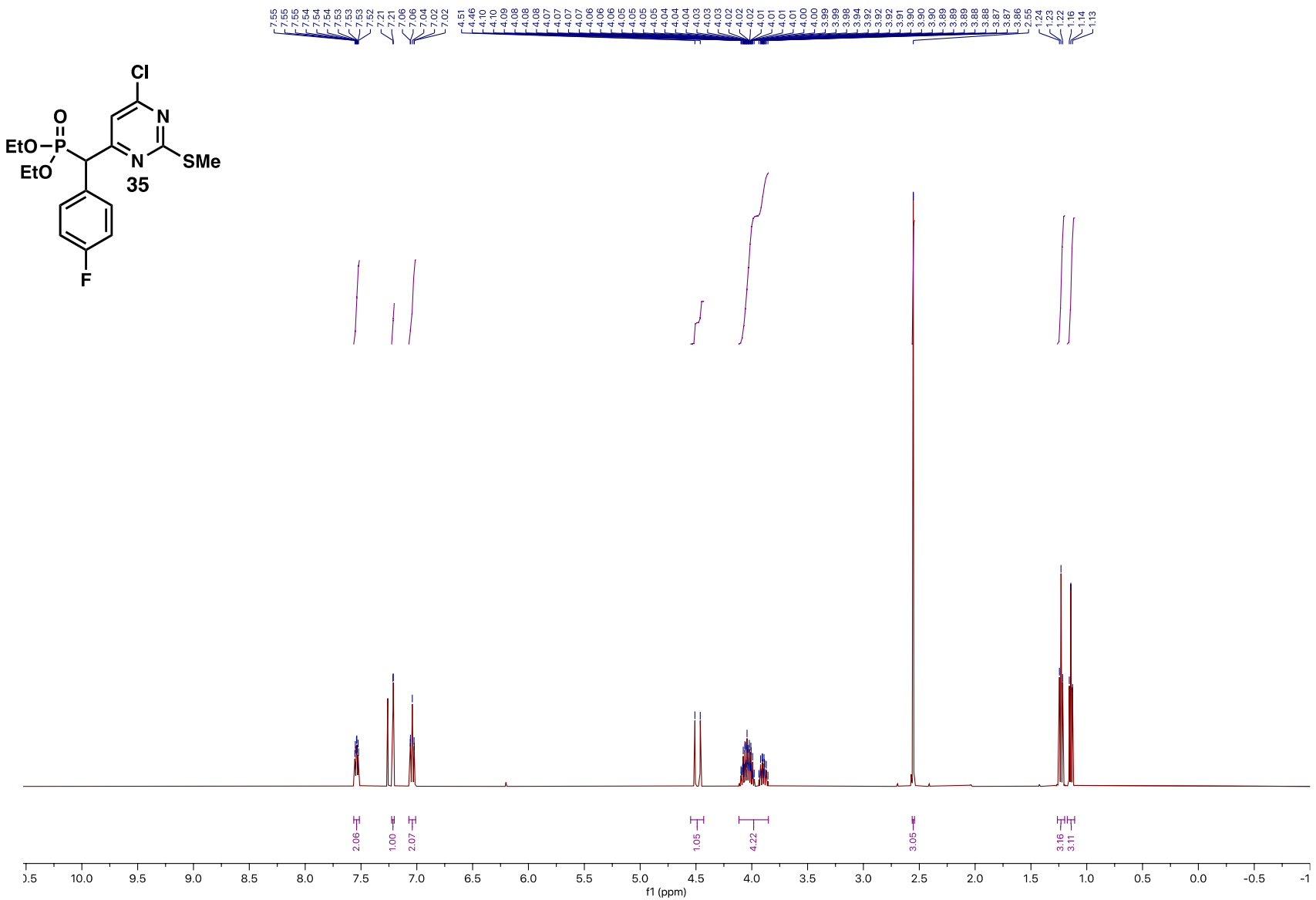

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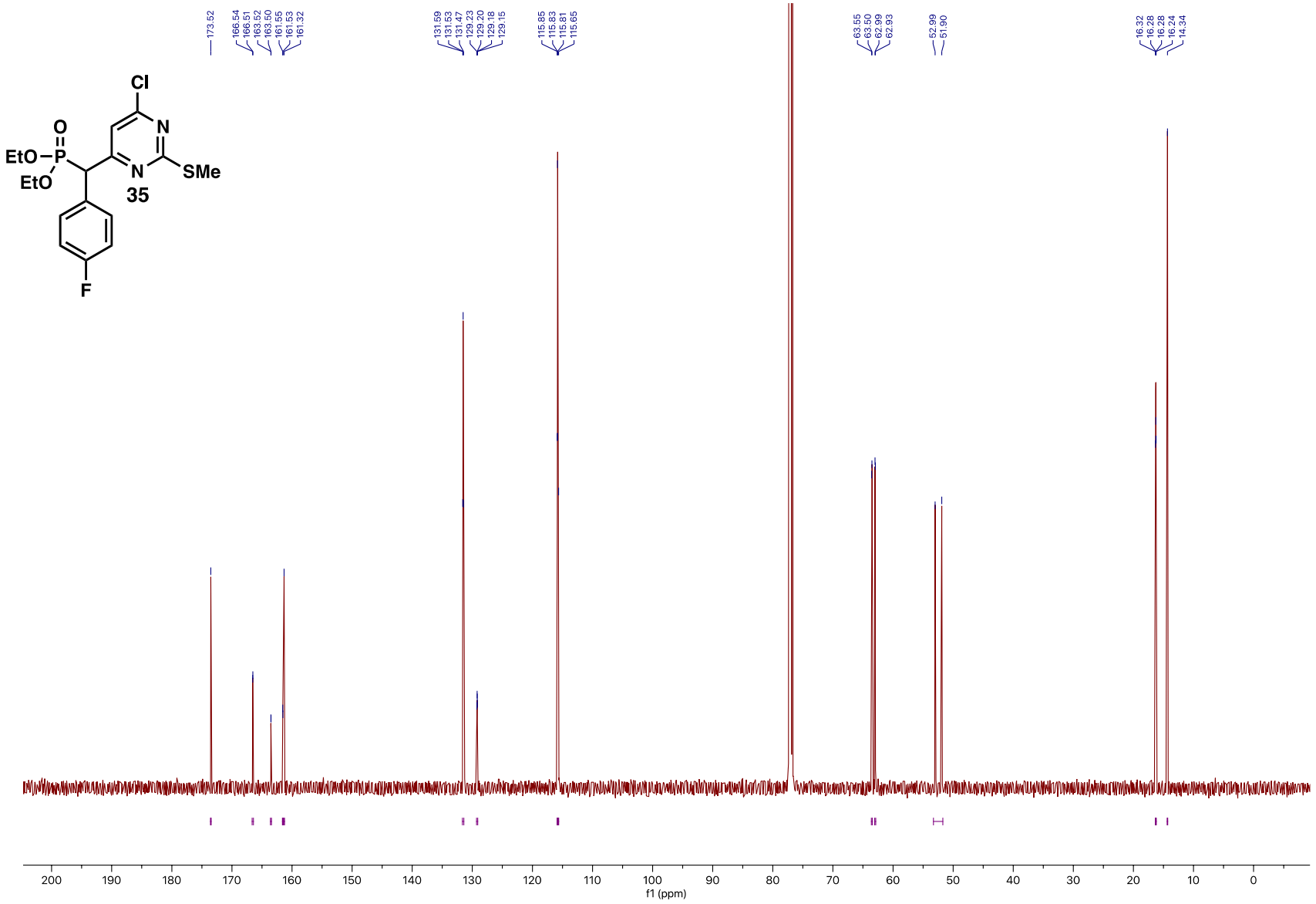
173.52
166.54
166.51
163.52
163.50
161.55
161.53
161.32
131.59
131.53
131.47
129.23
129.20
129.18
129.15
115.85
115.83
115.81
115.65
63.55
63.50
62.99
62.93
52.99
51.90
16.32
16.28
16.28
16.24
14.34
Cl
O
N
EtO
P
EtO
N
SMe
35
F
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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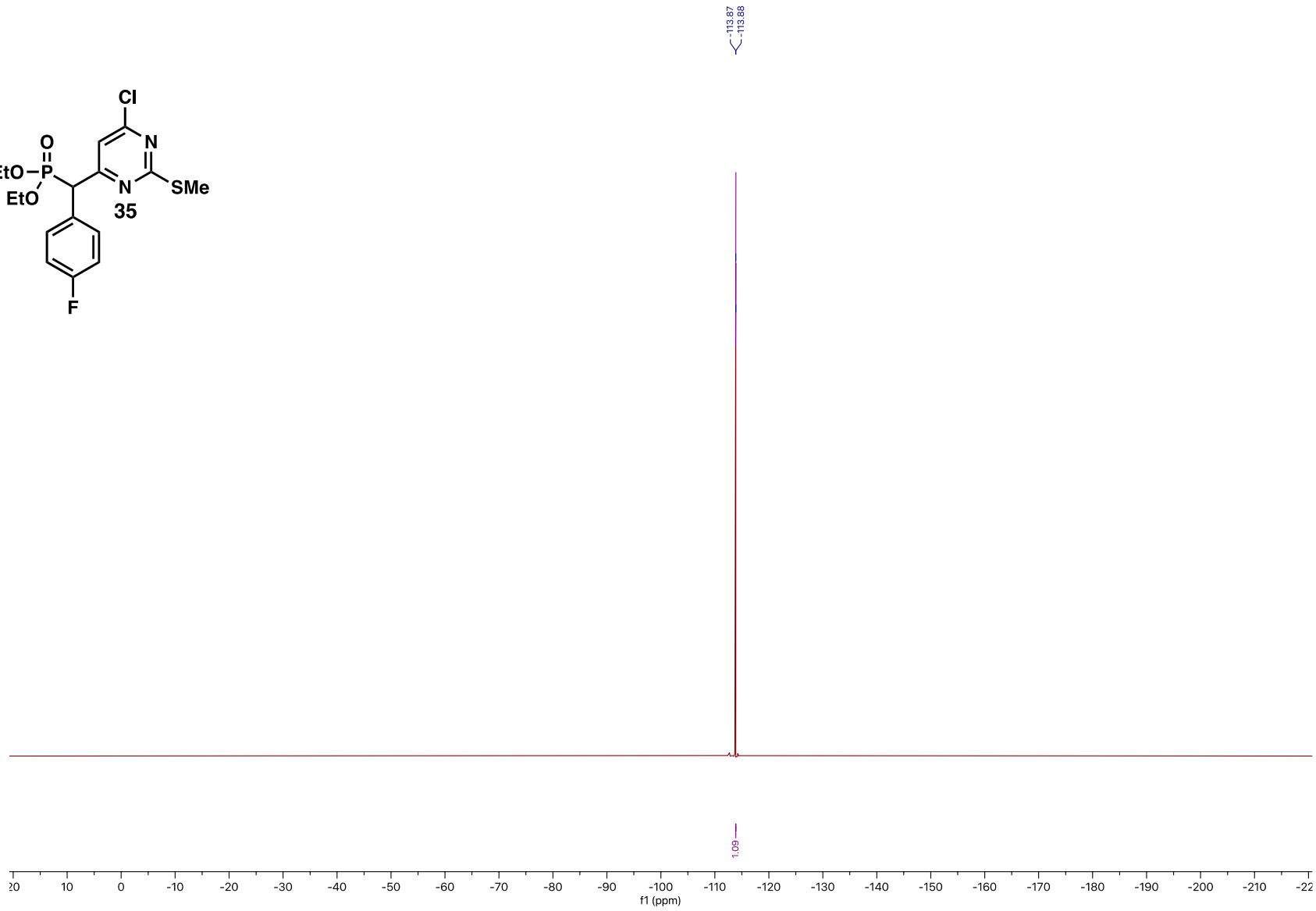
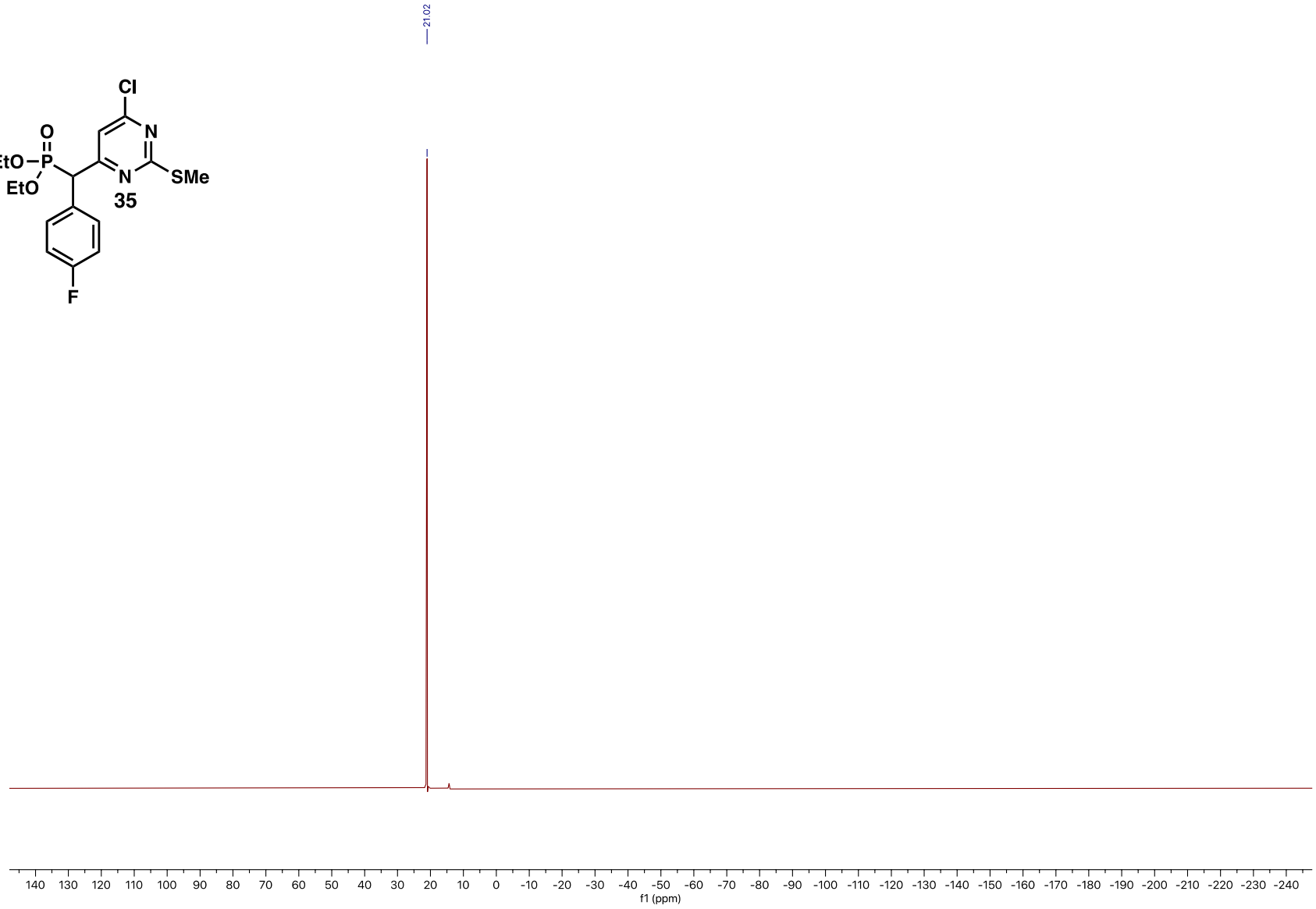
Cl
O
N
EtO
P
N
SMe
EtO
35
F


-113.87
-113.88
1.09
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-22
f1 (ppm)

©AUTHOR(S)



Heterocycle electrophile scope:

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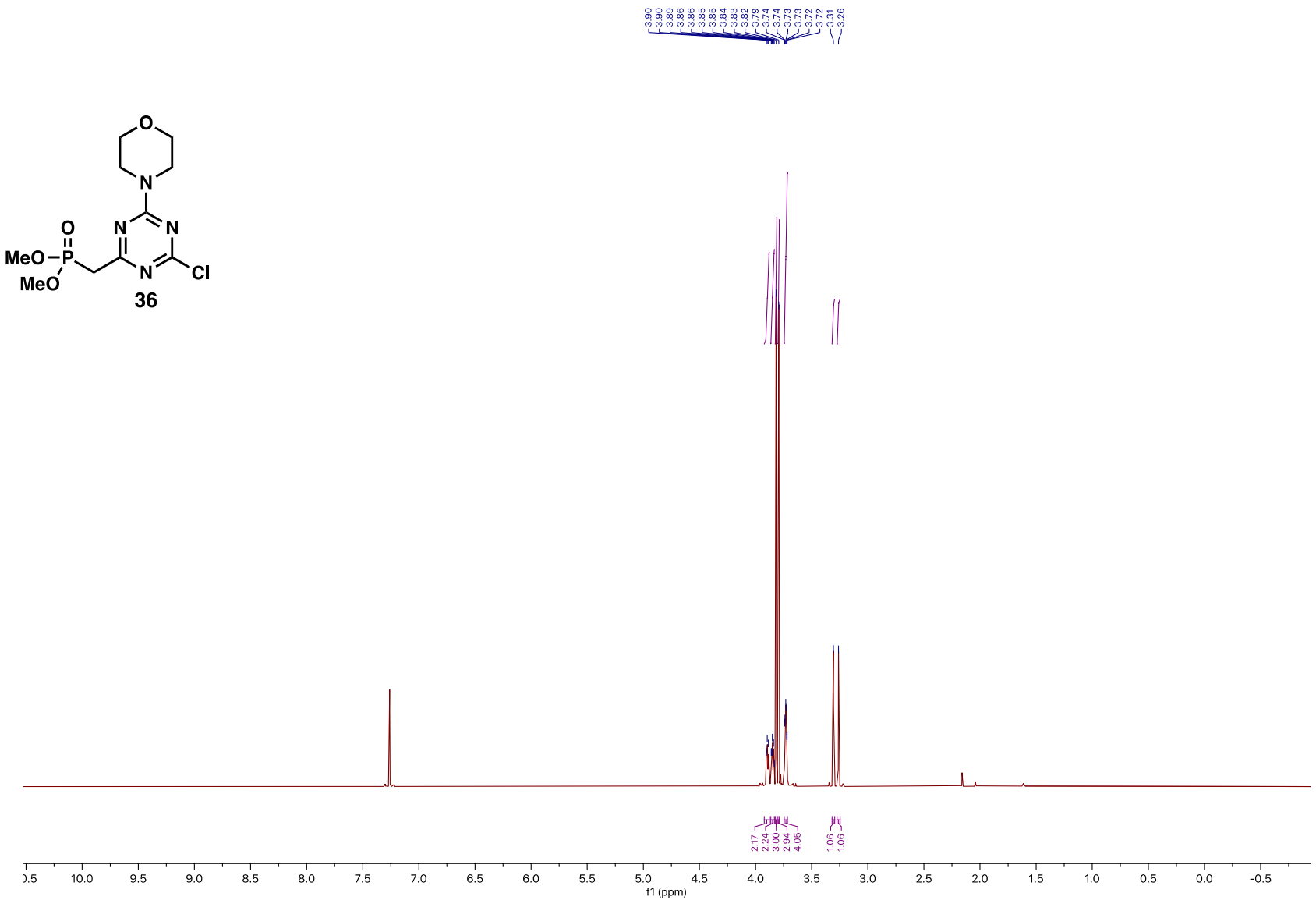
3.90
3.90
3.89
3.86
3.86
3.85
3.85
3.84
3.83
3.82
3.79
3.74
3.74
3.73
3.73
3.72
3.72
3.31
3.26
O
N
O
N
N
MeO
P
N
Cl
MeO
36
2.17
2.24
3.00
2.94
4.05
1.06
1.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

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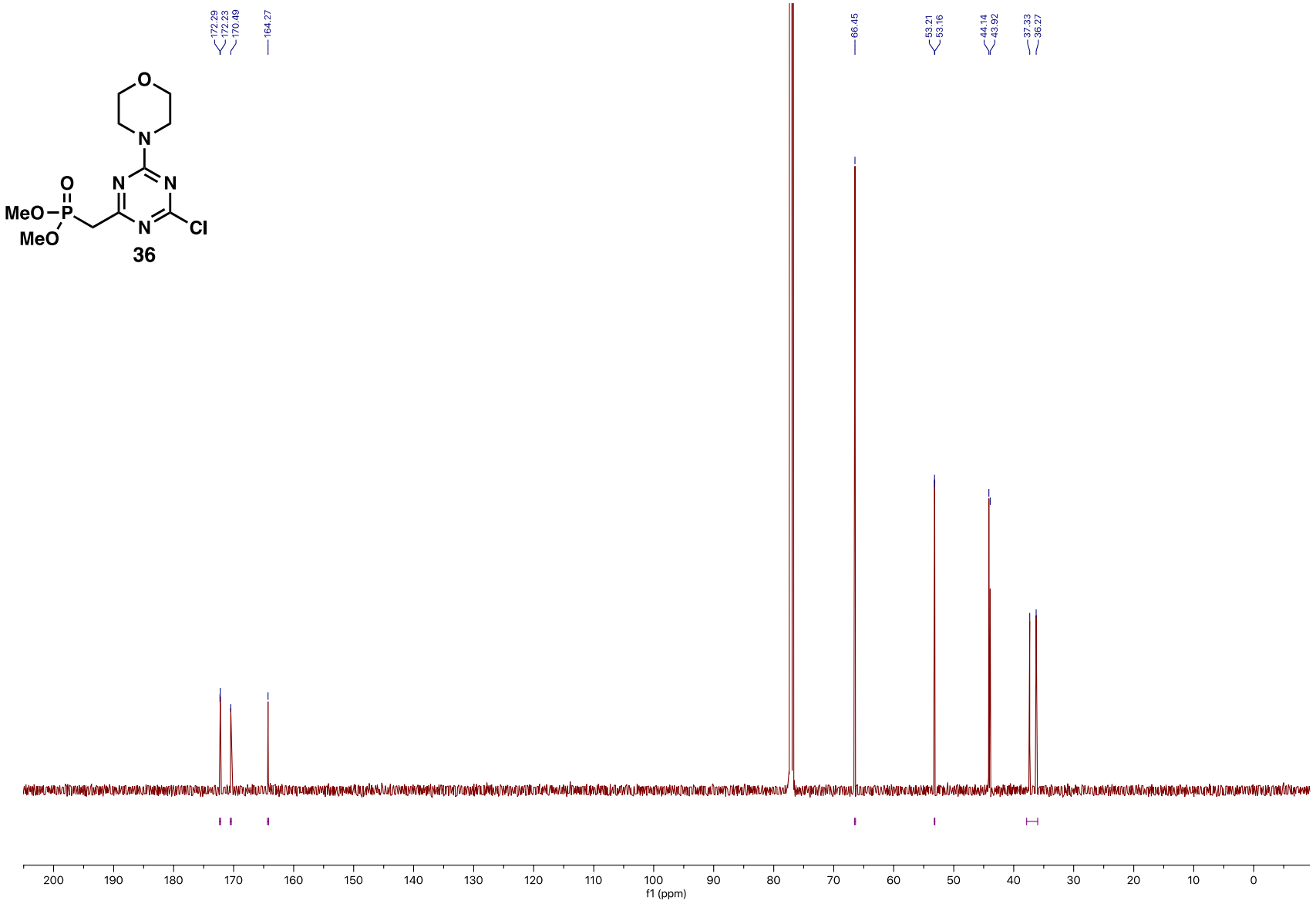
172.29
172.23
170.49
164.27
66.45
53.21
53.16
44.14
43.92
37.33
36.27
O
N
N
N
N
O
MeO
P
MeO
Cl
36
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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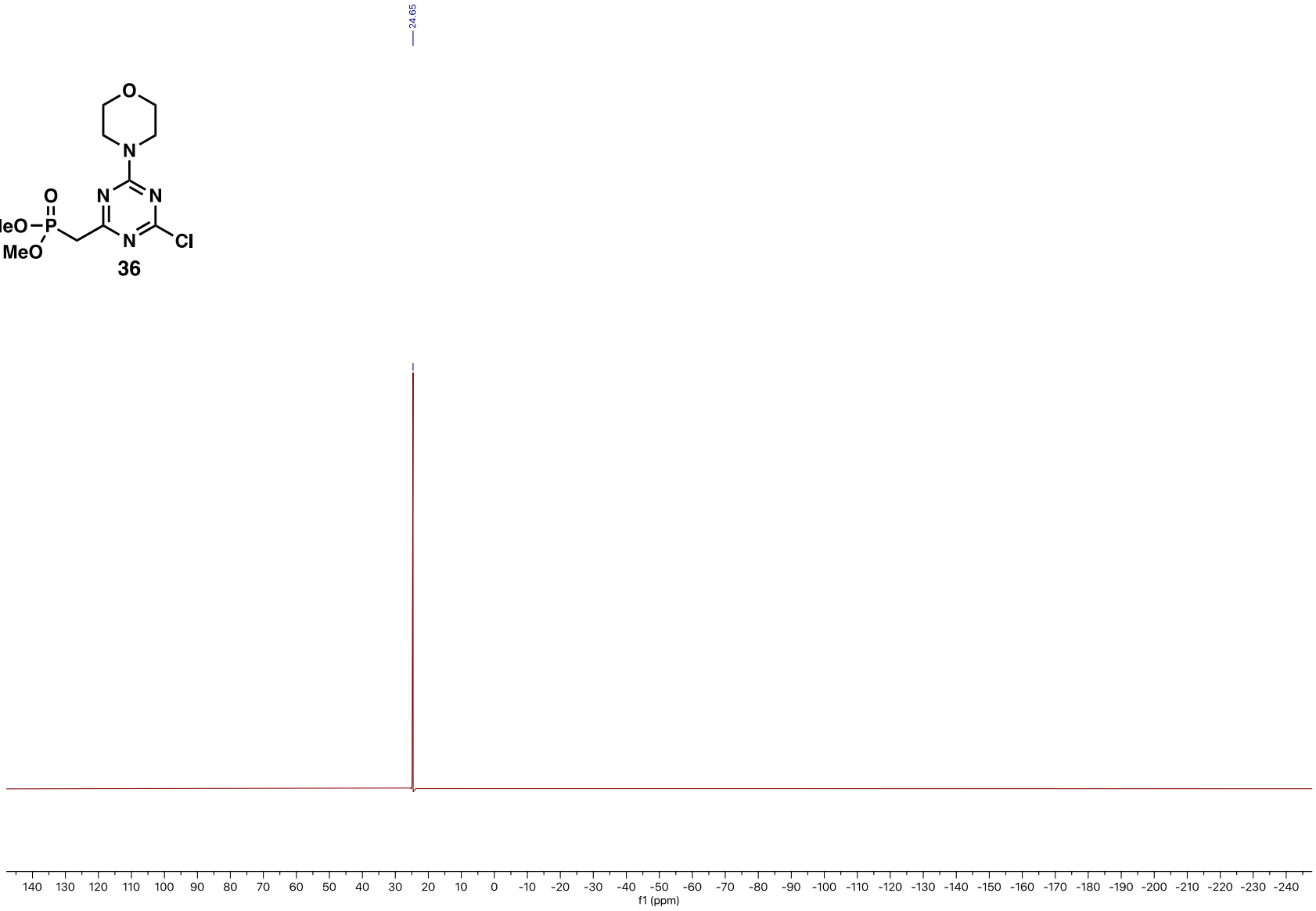
O
N
O
N
N
MeO–P
MeO
N
Cl

36


24.65
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

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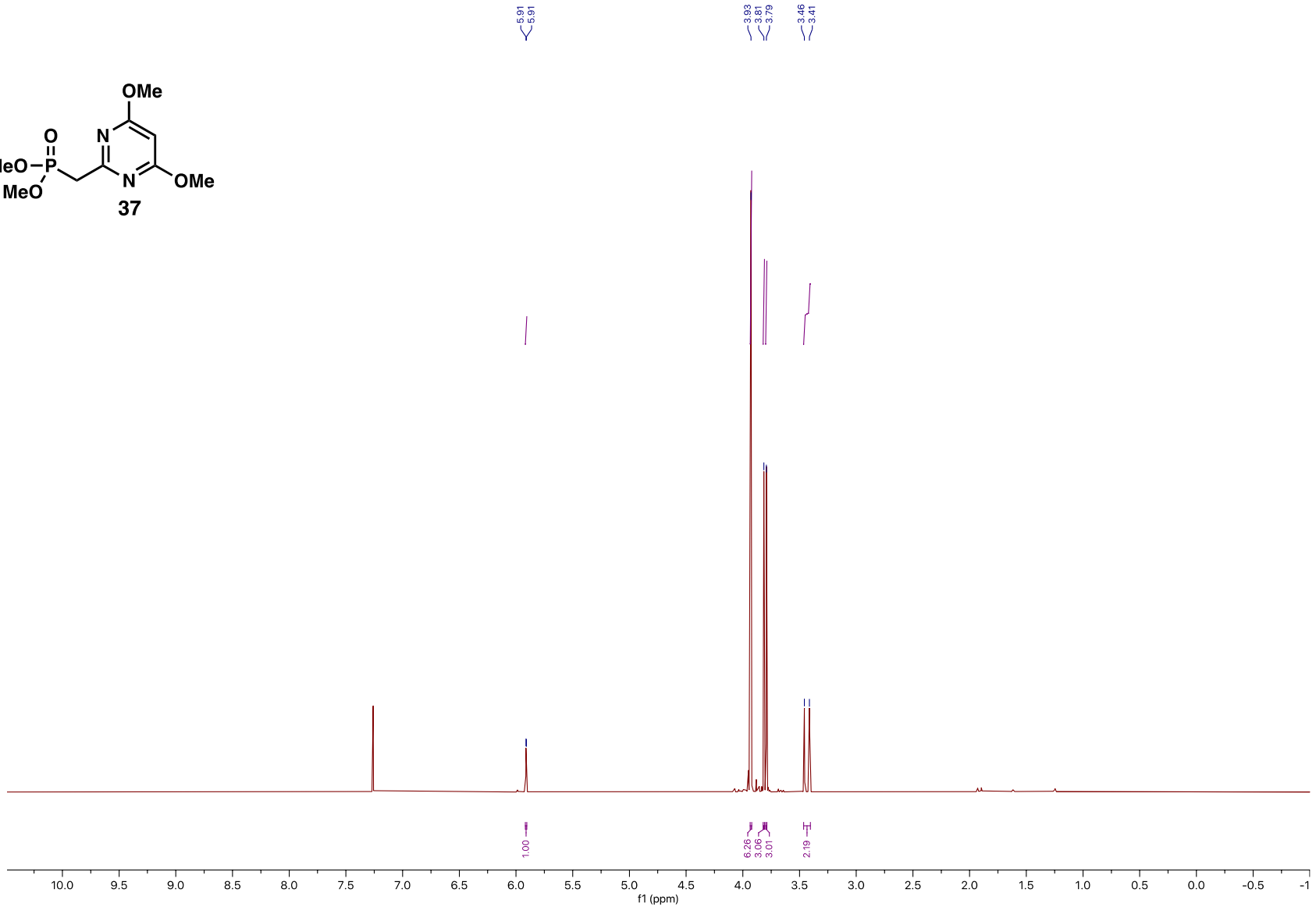
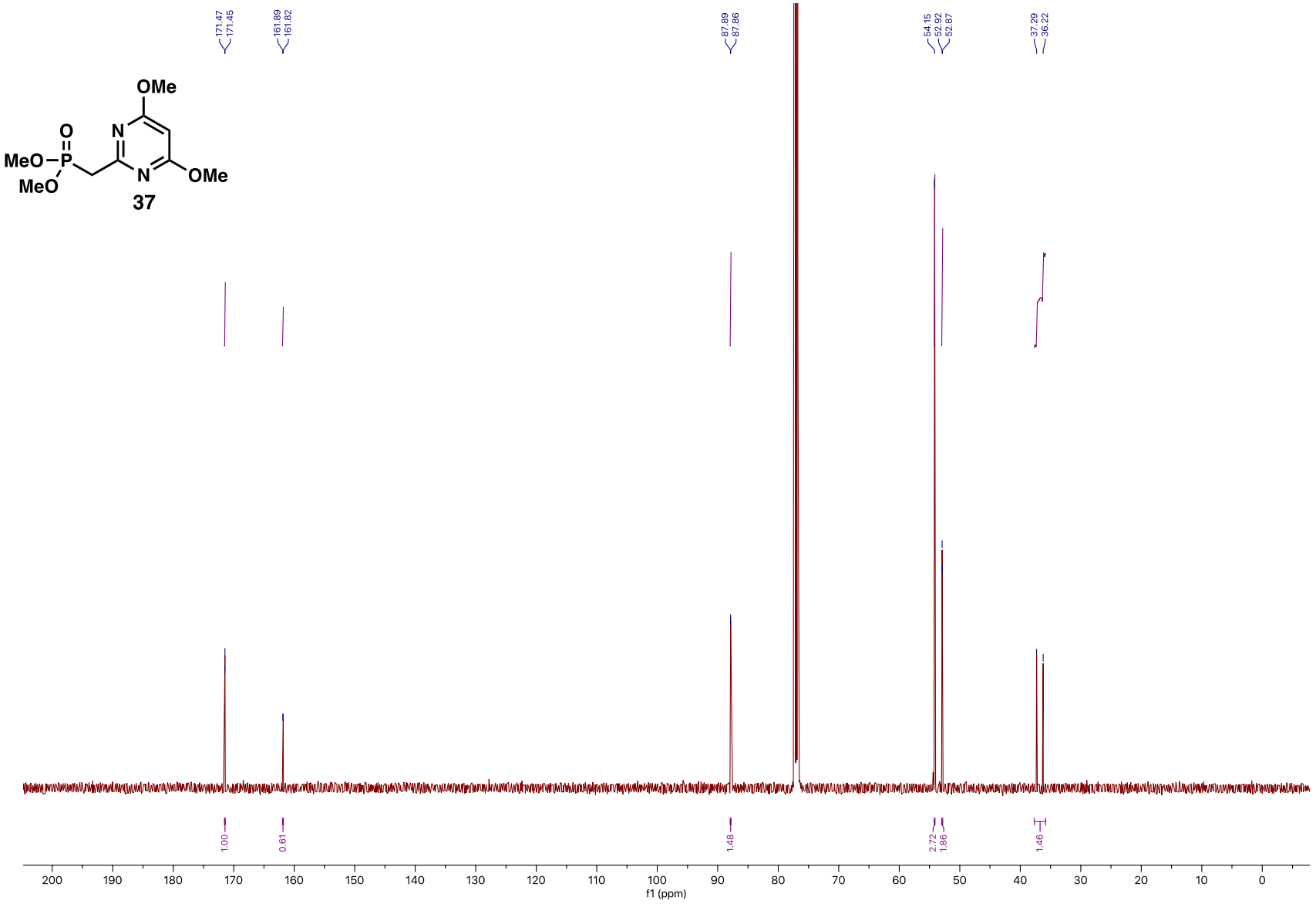
OMe
O
N
MeO
P
N
OMe
MeO

37


5.91
5.91
3.93
3.81
3.79
3.46
3.41
1.00
6.26
3.06
3.01
2.19
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
f1 (ppm)

©AUTHOR(S)


171.47
171.45
161.89
161.82
87.89
87.86
54.15
52.92
52.87
37.29
36.22
OMe
O
N
MeO
P
MeO
N
OMe
37
1.00
0.61
1.48
2.72
1.86
1.46
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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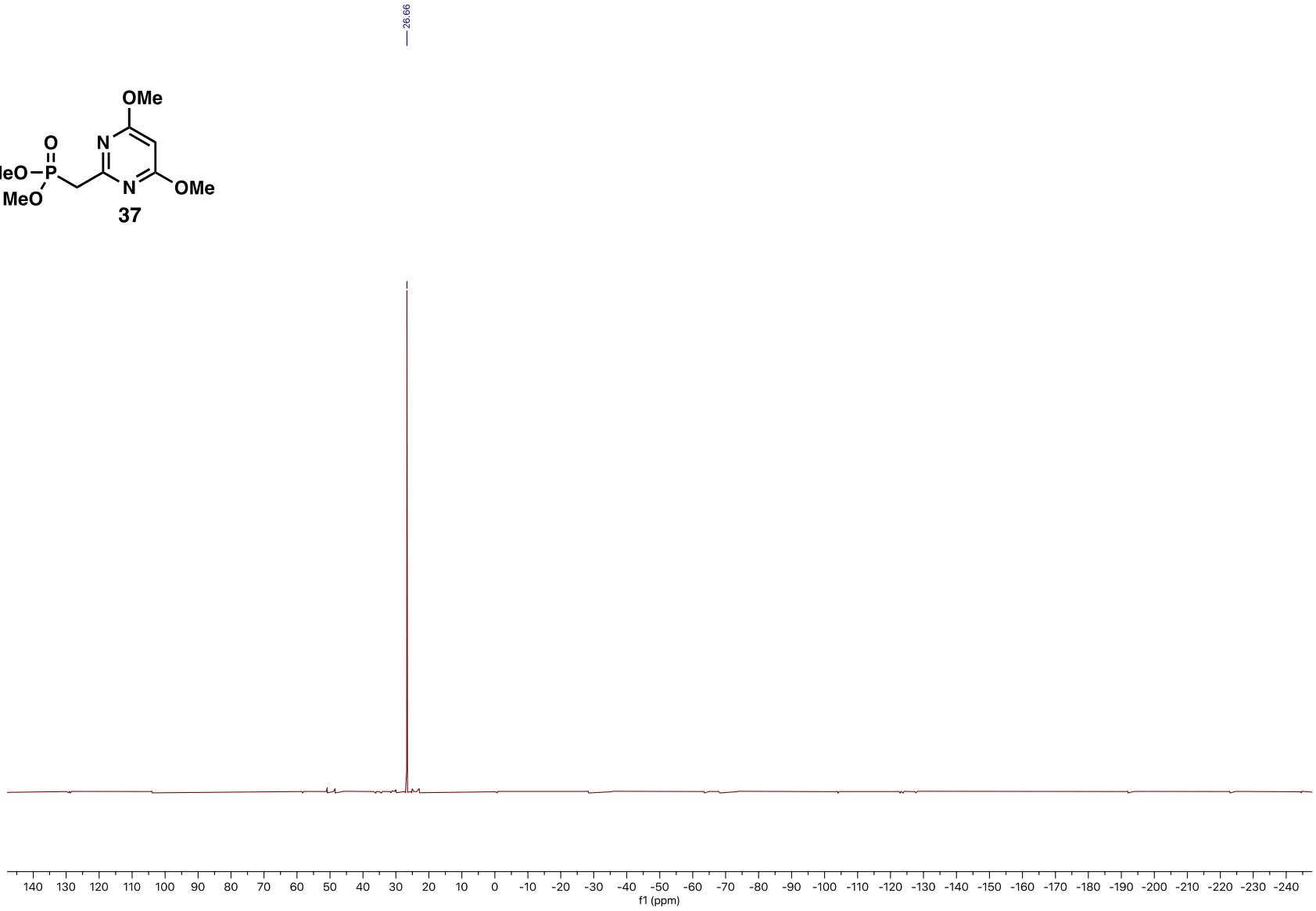
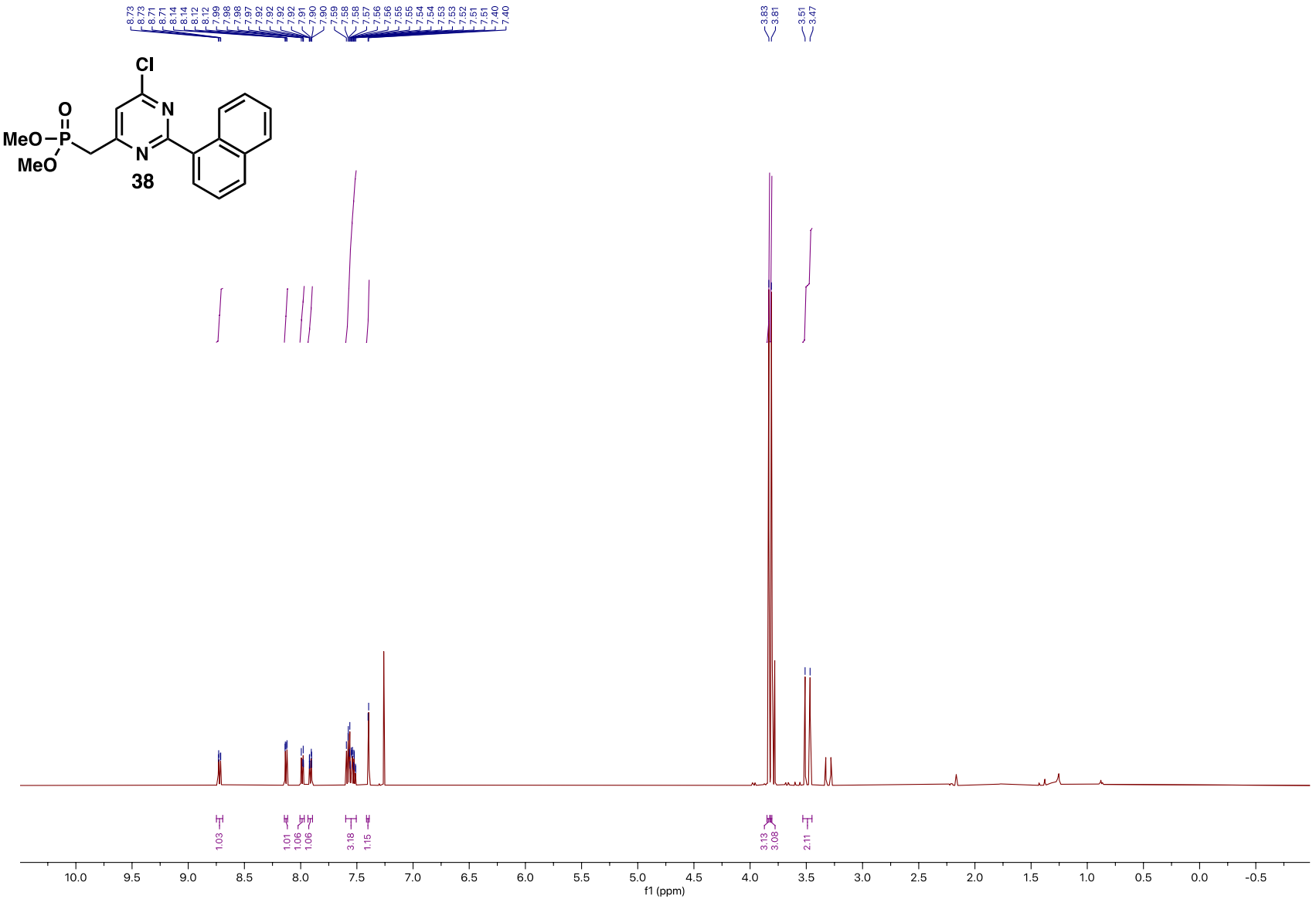
OMe
O
N
MeO–P
N
OMe
MeO

37


26.66
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

©AUTHOR(S)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8.73
8.71
8.71
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8.14
8.12
8.12
7.99
7.98
7.98
7.97
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7.92
7.92
7.92
7.91
7.90
7.90
7.59
7.58
7.58
7.57
7.56
7.56
7.55
7.55
7.54
7.54
7.53
7.53
7.52
7.51
7.51
7.40
7.40
3.83
3.81
3.51
3.47
Cl
N
N
O
MeO
P
MeO
38
1.03
1.01
1.06
1.06
3.18
1.15
3.13
3.08
2.11
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
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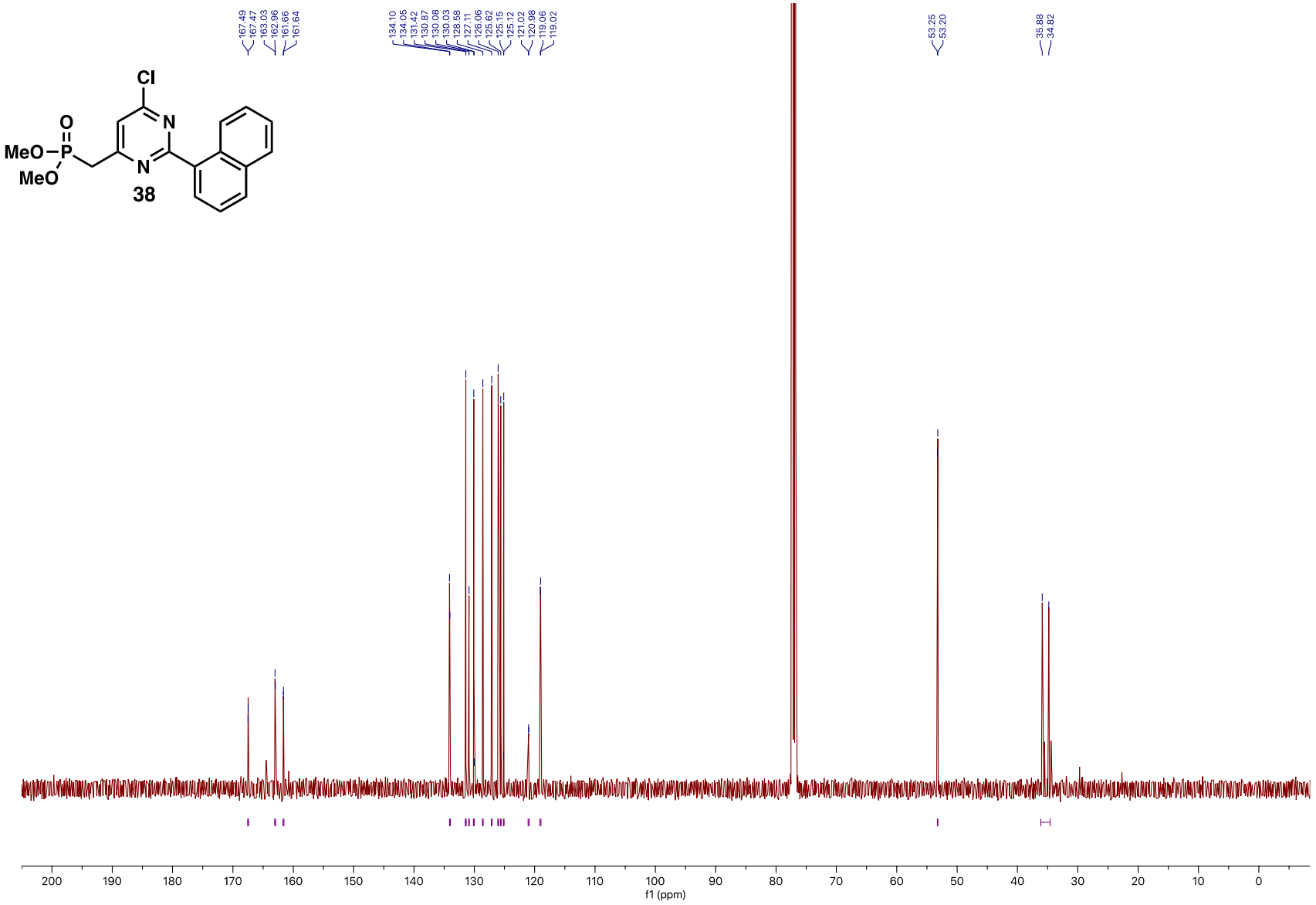
0.0
-0.5
f1 (ppm)

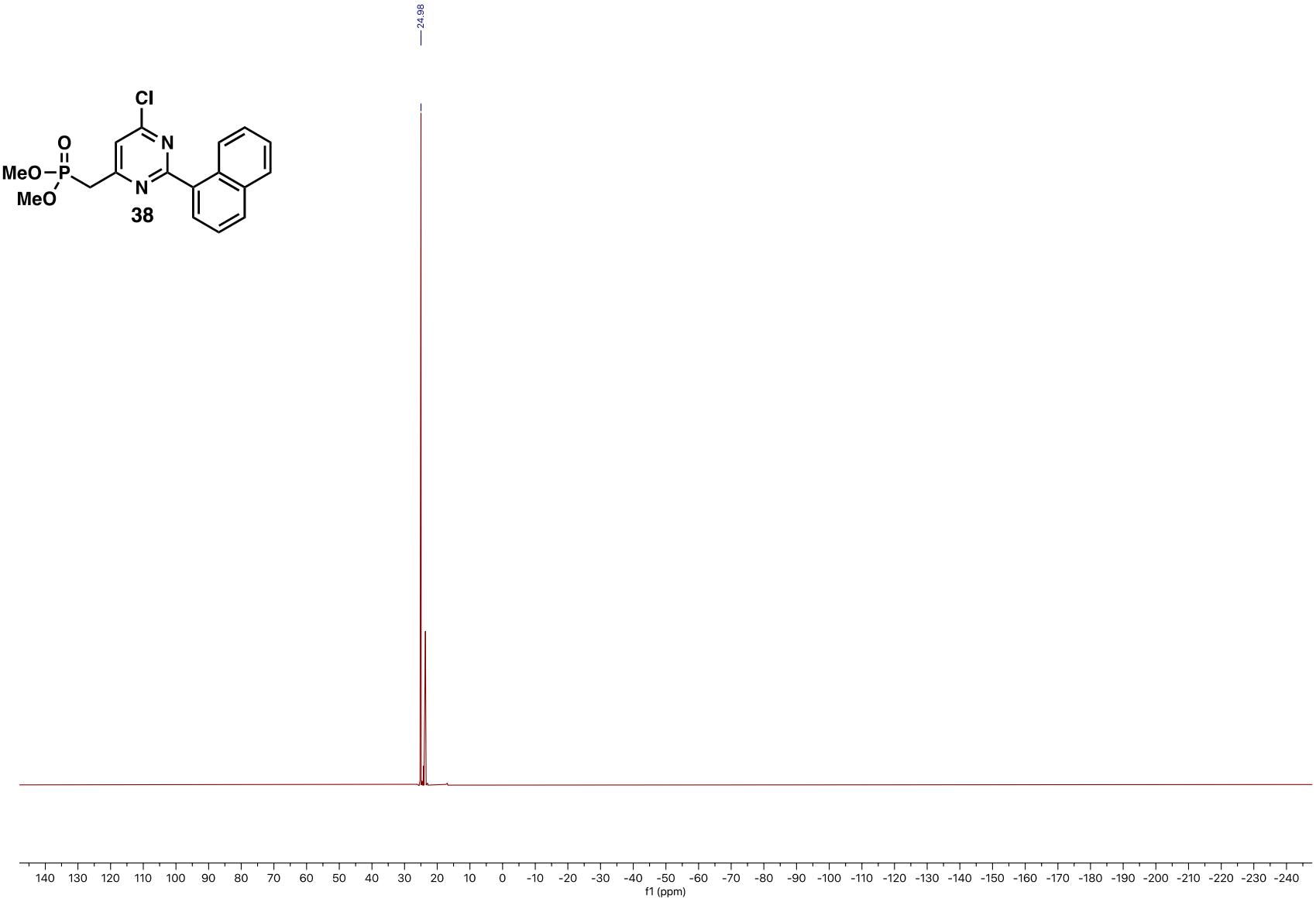
©AUTHOR(S)


167.49
167.47
163.03
162.96
161.66
161.64
134.10
134.05
131.42
130.87
130.08
130.03
128.58
127.11
126.06
125.62
125.15
125.12
121.02
120.98
119.06
119.02
53.25
53.20
35.88
34.82
Cl
O
N
MeO
P
MeO
N
38
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

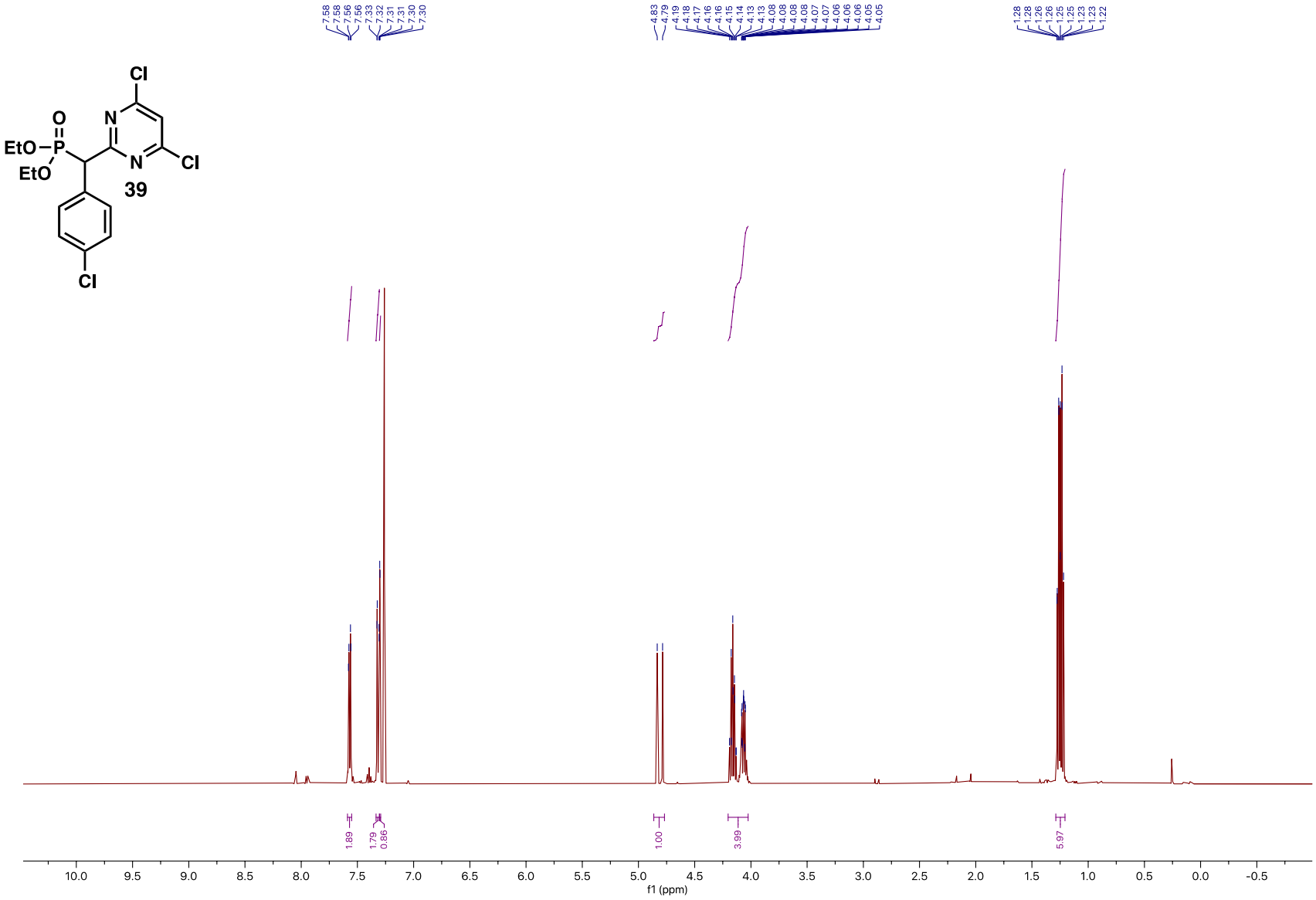
©AUTHOR(S)

Cl
O
N
MeO–P
MeO
N

38


24.98
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

©AUTHOR(S)


Cl
O
N
EtO–P
N
Cl
EtO
39
Cl
7.58
7.58
7.56
7.56
7.33
7.32
7.31
7.31
7.30
7.30
4.83
4.79
4.19
4.18
4.17
4.16
4.16
4.15
4.14
4.13
4.13
4.08
4.08
4.08
4.08
4.07
4.07
4.06
4.06
4.06
4.05
4.05
1.28
1.28
1.26
1.26
1.25
1.25
1.23
1.23
1.22
1.89
1.79
0.86
1.00
3.99
5.97
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
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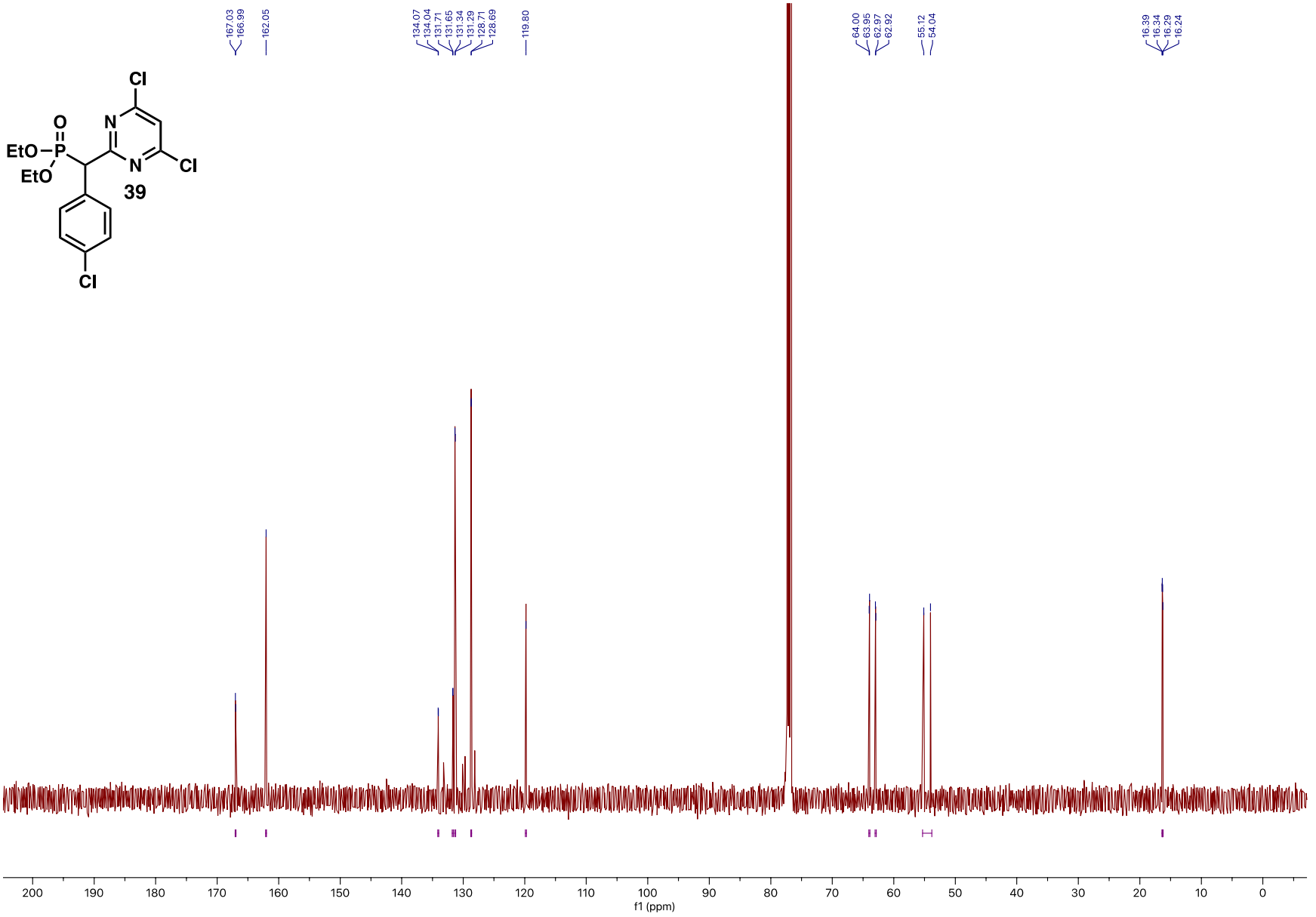
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

©AUTHOR(S)


167.03
166.99
162.05
134.07
134.04
131.71
131.65
131.34
131.29
128.71
128.69
119.80
64.00
63.95
62.97
62.92
55.12
54.04
16.39
16.34
16.29
16.24
Cl
O
N
EtO–P
EtO
N
Cl
39
Cl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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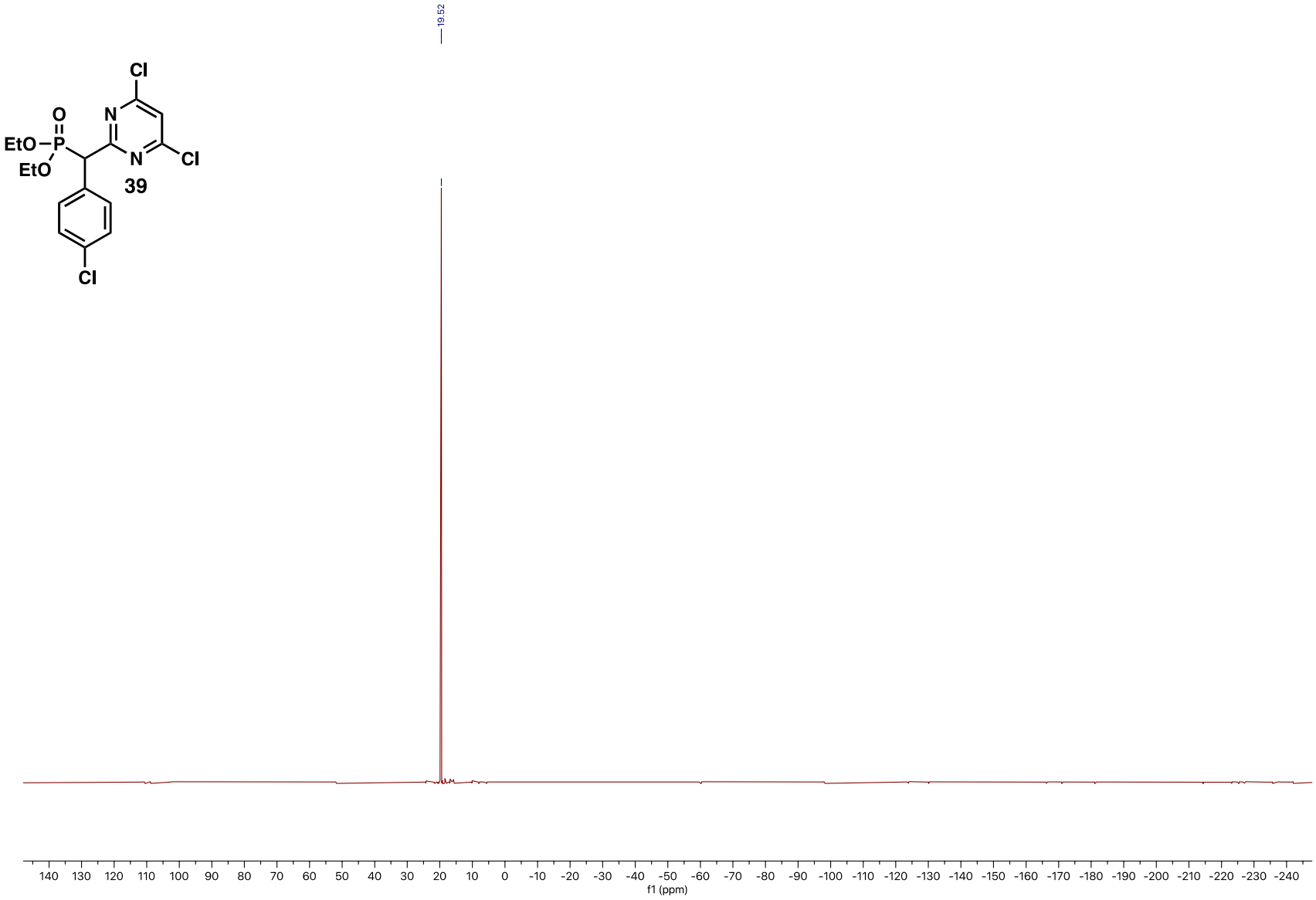
19.52
Cl
O
N
EtO
P
N
Cl
EtO
39
Cl
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

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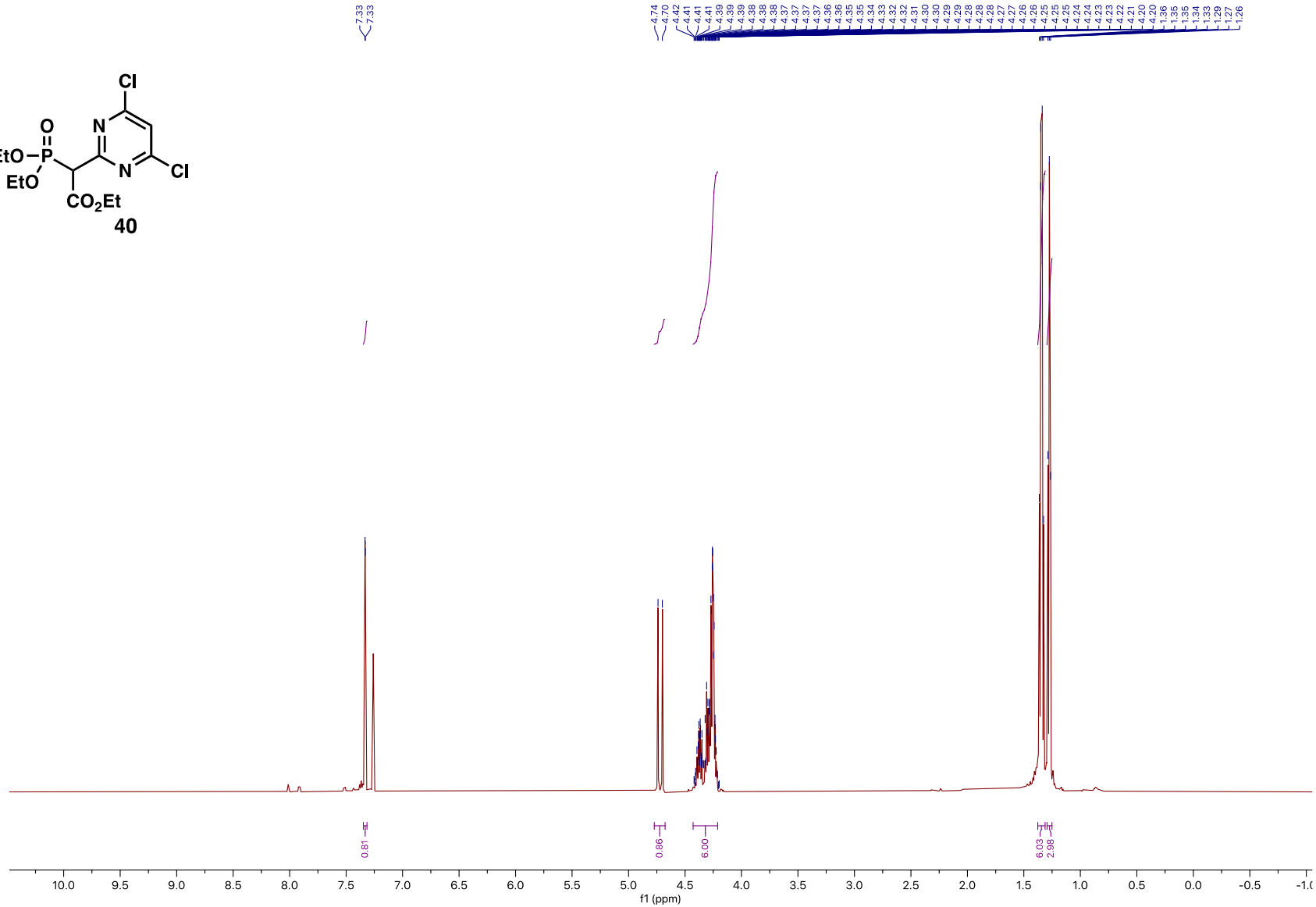
Cl
O
N
EtO
P
N
Cl
EtO
CO2Et

40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4.42
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4.41
4.39
4.39
4.39
4.38
4.38
4.38
4.37
4.37
4.37
4.36
4.36
4.35
4.35
4.34
4.33
4.32
4.32
4.31
4.30
4.30
4.29
4.29
4.28
4.28
4.28
4.27
4.27
4.26
4.26
4.25
4.25
4.25
4.24
4.24
4.23
4.23
4.22
4.21
4.20
4.20
1.36
1.35
1.35
1.34
1.33
1.29
1.27
1.26
0.81
0.86
6.00
6.03
2.98
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)

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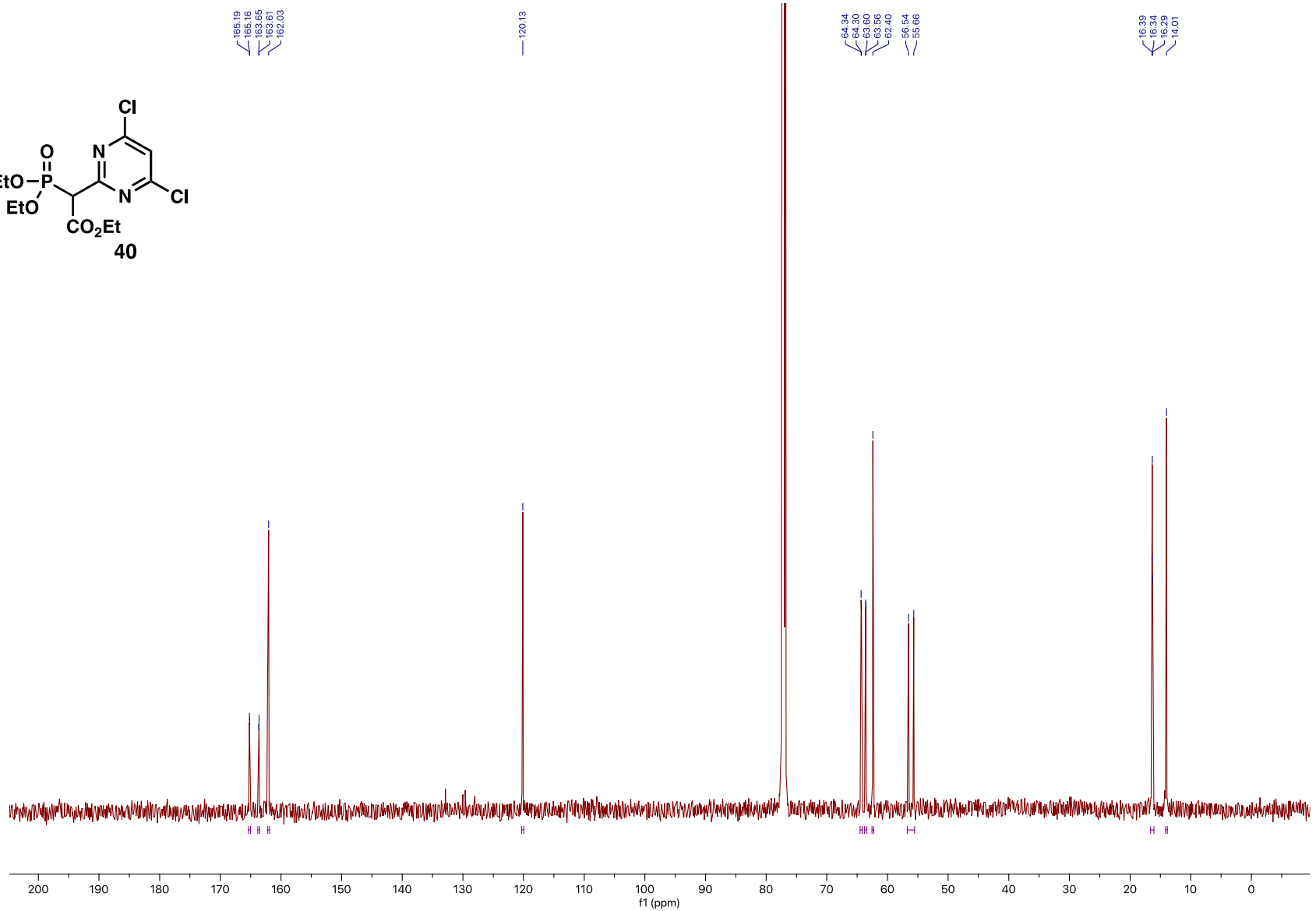
Cl
O
N
EtO
P
N
Cl
EtO
CO2Et

40


165.19
165.16
163.65
163.61
162.03
120.13
64.34
64.30
63.60
63.56
62.40
56.54
55.66
16.39
16.34
16.29
14.01
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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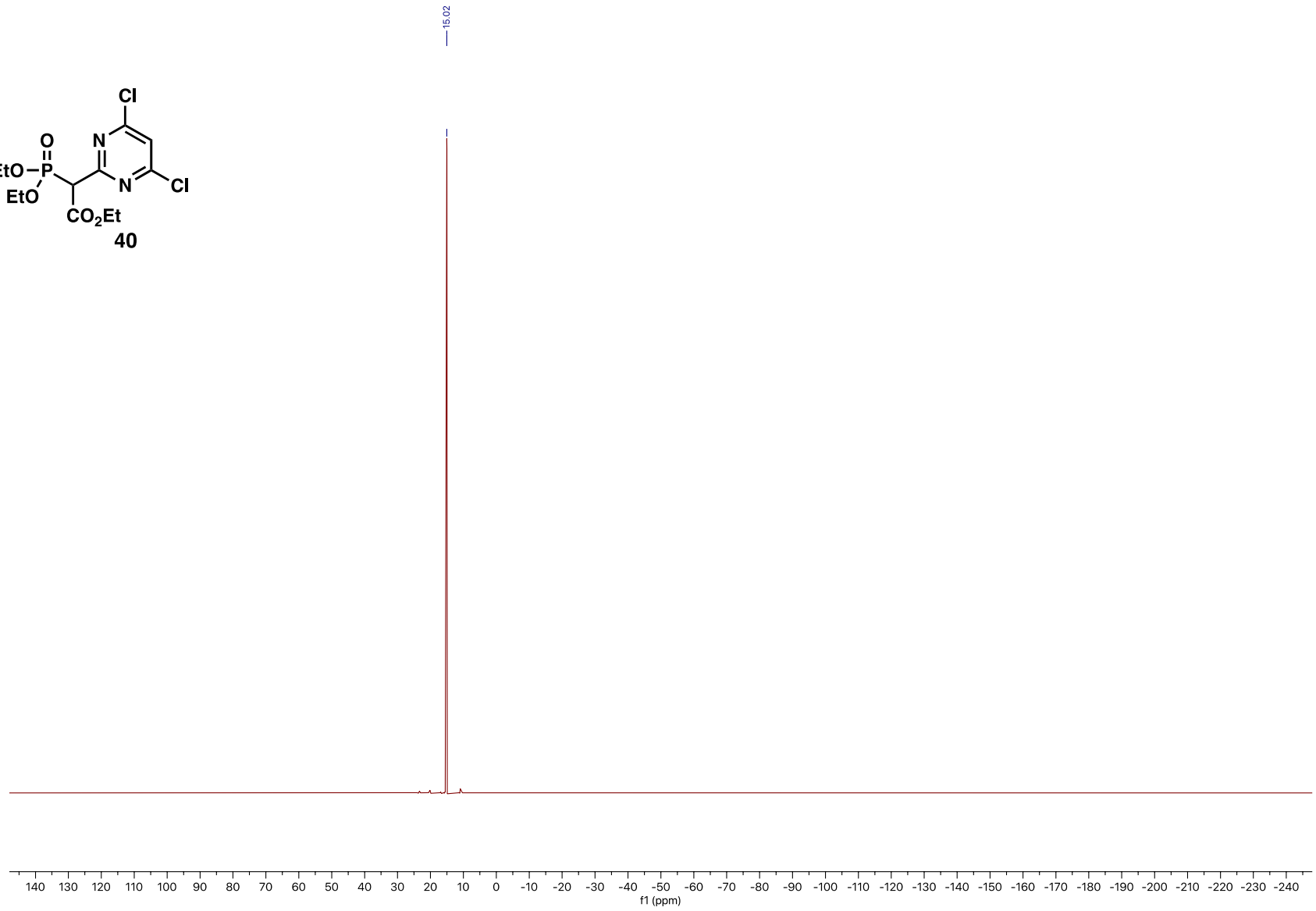
Cl
O
N
EtO
P
N
Cl
EtO
CO2Et

40


15.02
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

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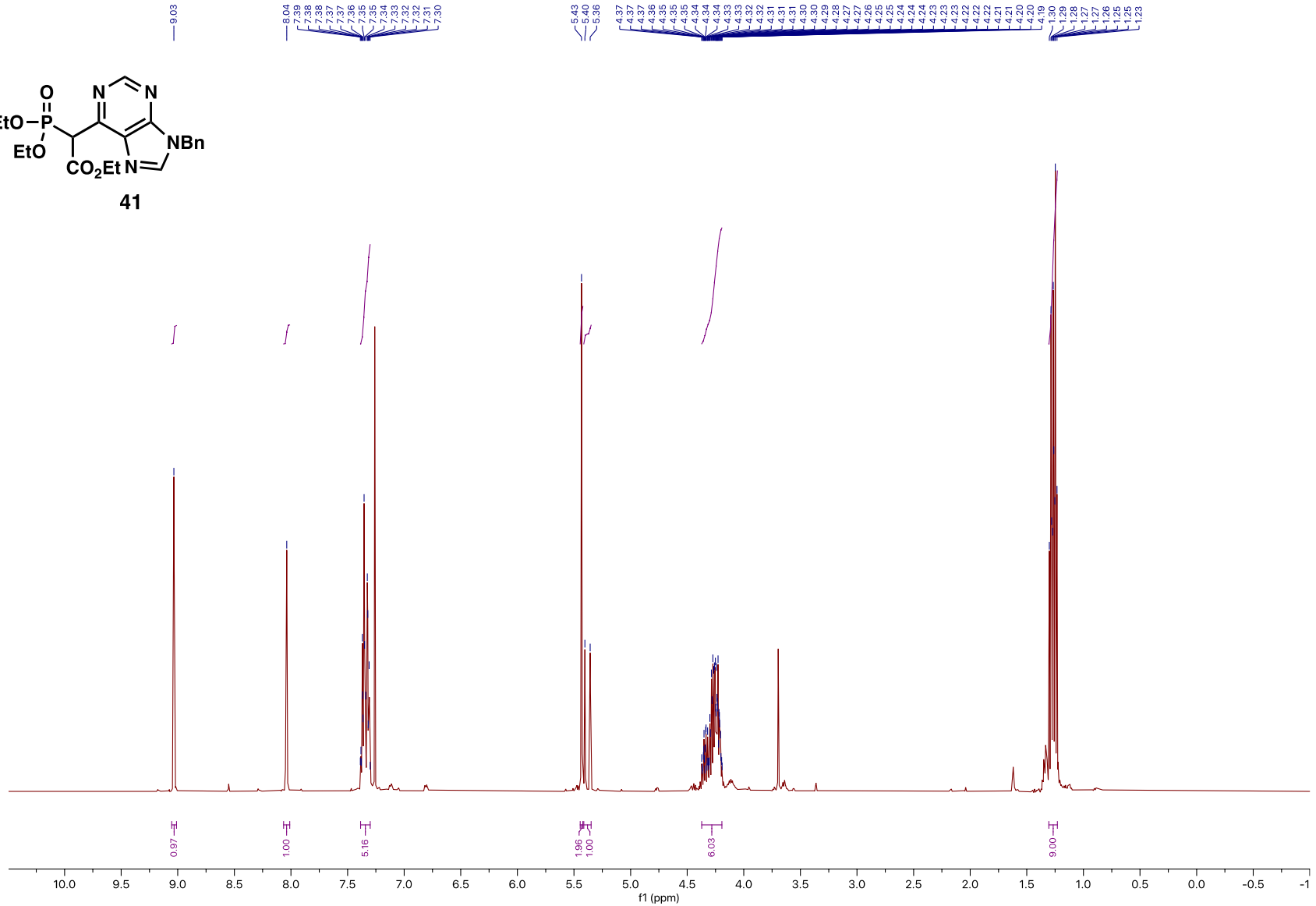
O
N
N
EtO
P
EtO
NBn
CO2Et
N

41


9.03
8.04
7.39
7.38
7.38
7.37
7.37
7.36
7.35
7.35
7.34
7.33
7.32
7.32
7.31
7.30
5.43
5.40
5.36
4.37
4.37
4.37
4.36
4.35
4.35
4.35
4.34
4.34
4.34
4.33
4.32
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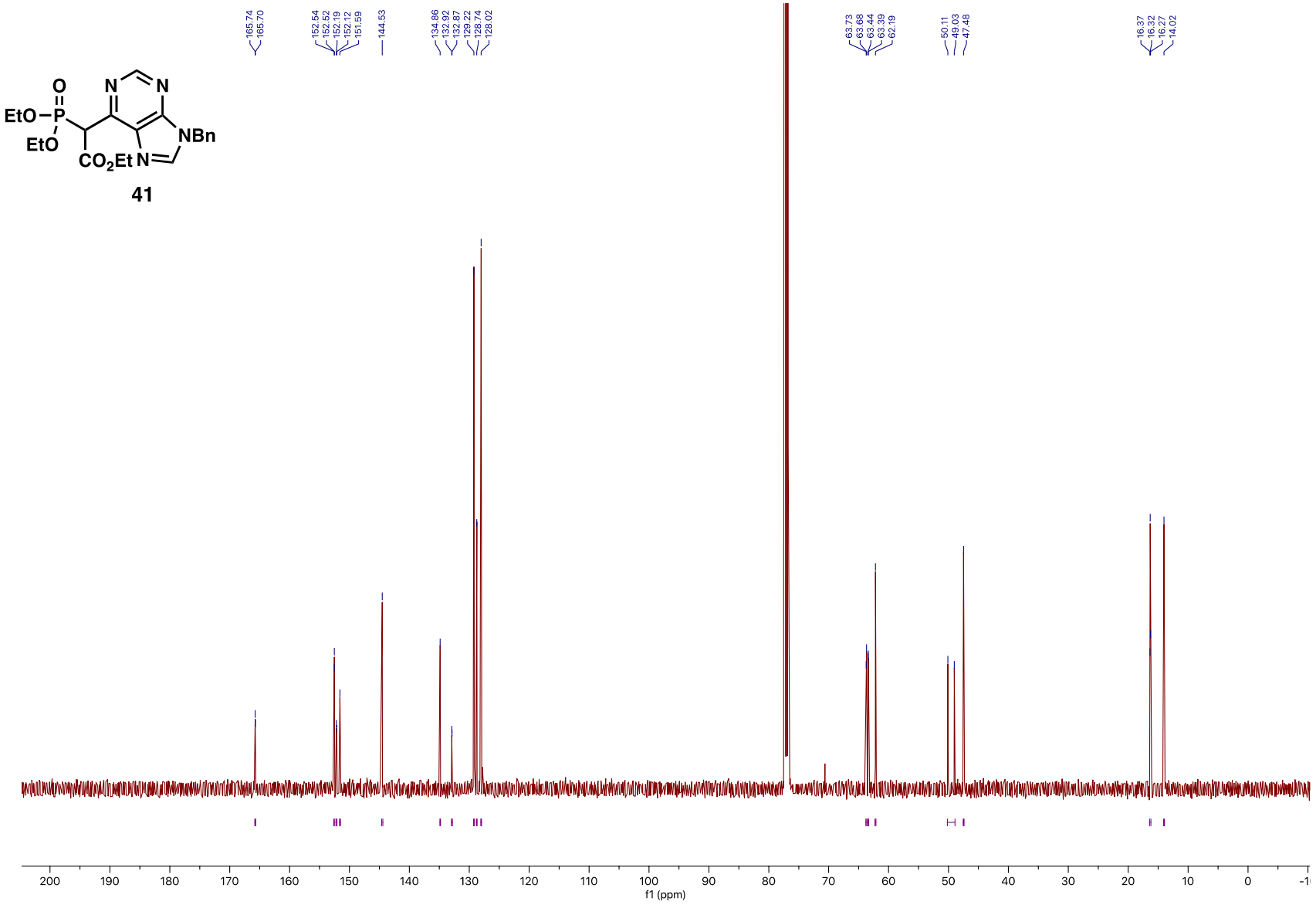
4.31
4.31
4.31
4.30
4.30
4.29
4.28
4.27
4.27
4.26
4.25
4.25
4.24
4.24
4.24
4.23
4.23
4.23
4.22
4.22
4.22
4.21
4.21
4.20
4.20
4.19
1.30
1.29
1.28
1.27
1.27
1.26
1.25
1.25
1.23
0.97
1.00
5.16
1.96
1.00
6.03
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

©AUTHOR(S)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165.70
152.54
152.52
152.19
152.12
151.99
144.53
134.86
132.92
132.87
129.22
128.74
128.02
63.73
63.68
63.44
63.39
62.19
50.11
49.03
47.48
16.37
16.32
16.27
14.02
O
N
N
EtO
P
EtO
NBn
CO2Et
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

41

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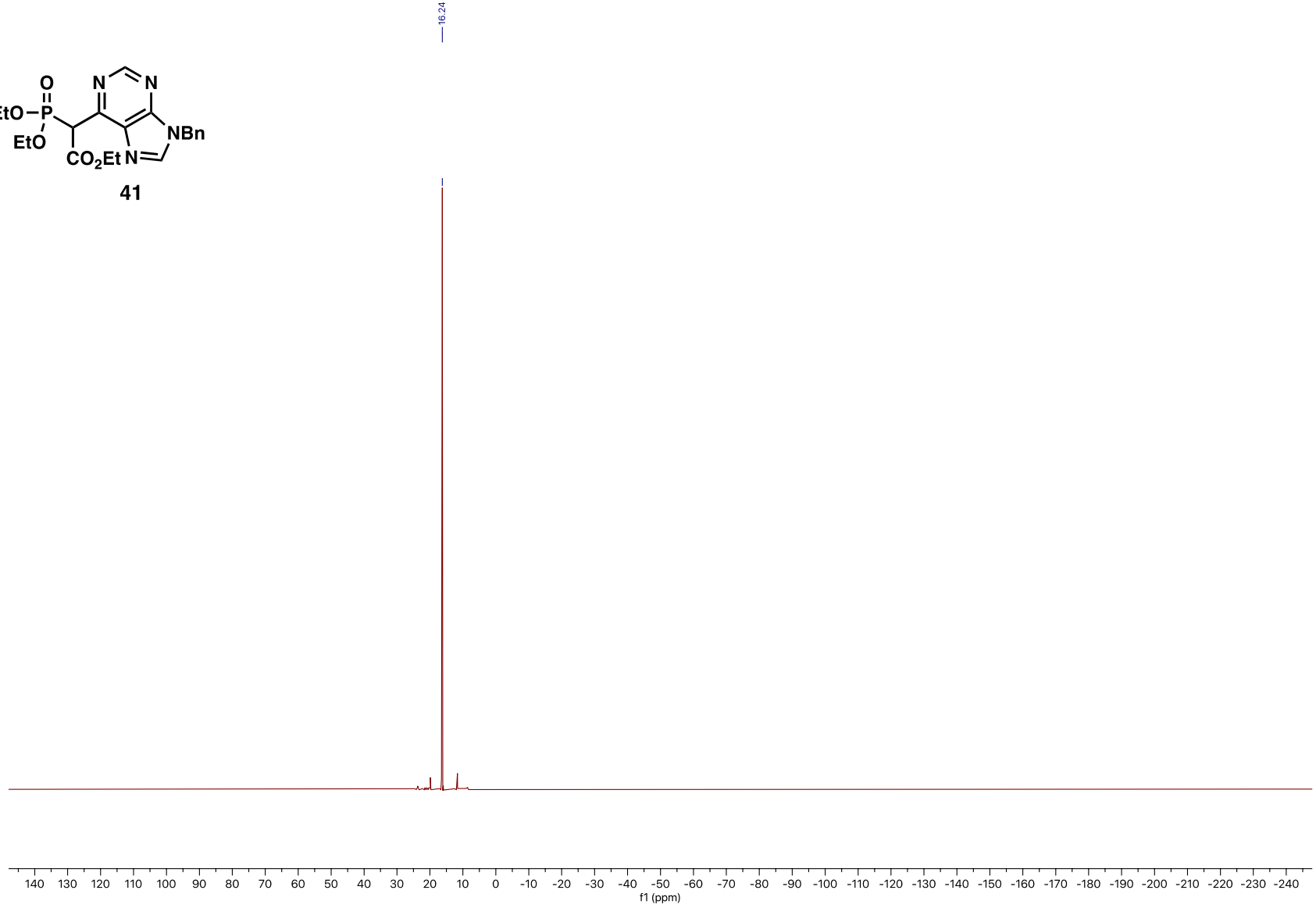
O
N
N
EtO
P
EtO
NBn
CO2Et
N

41


16.24
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

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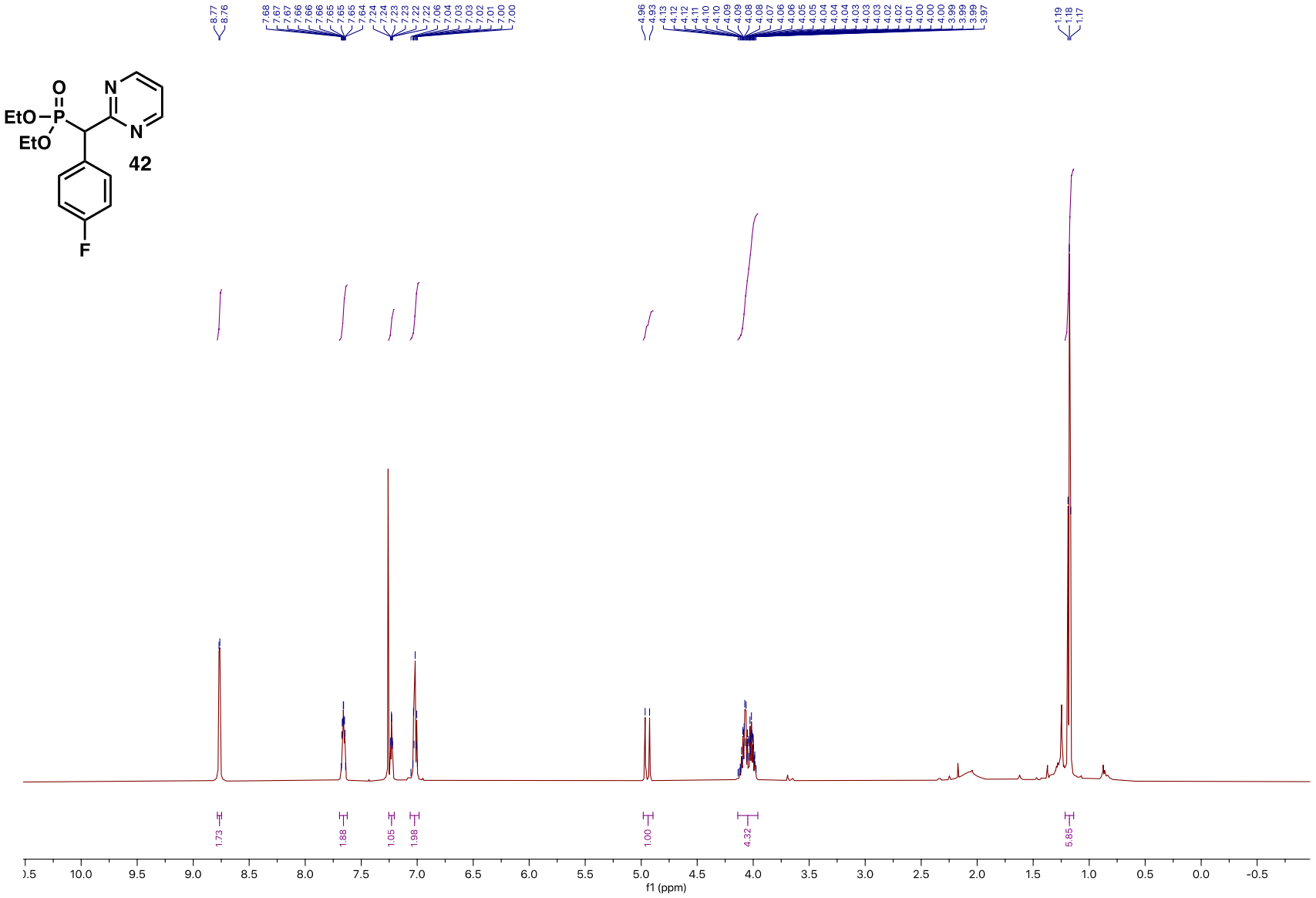
8.77
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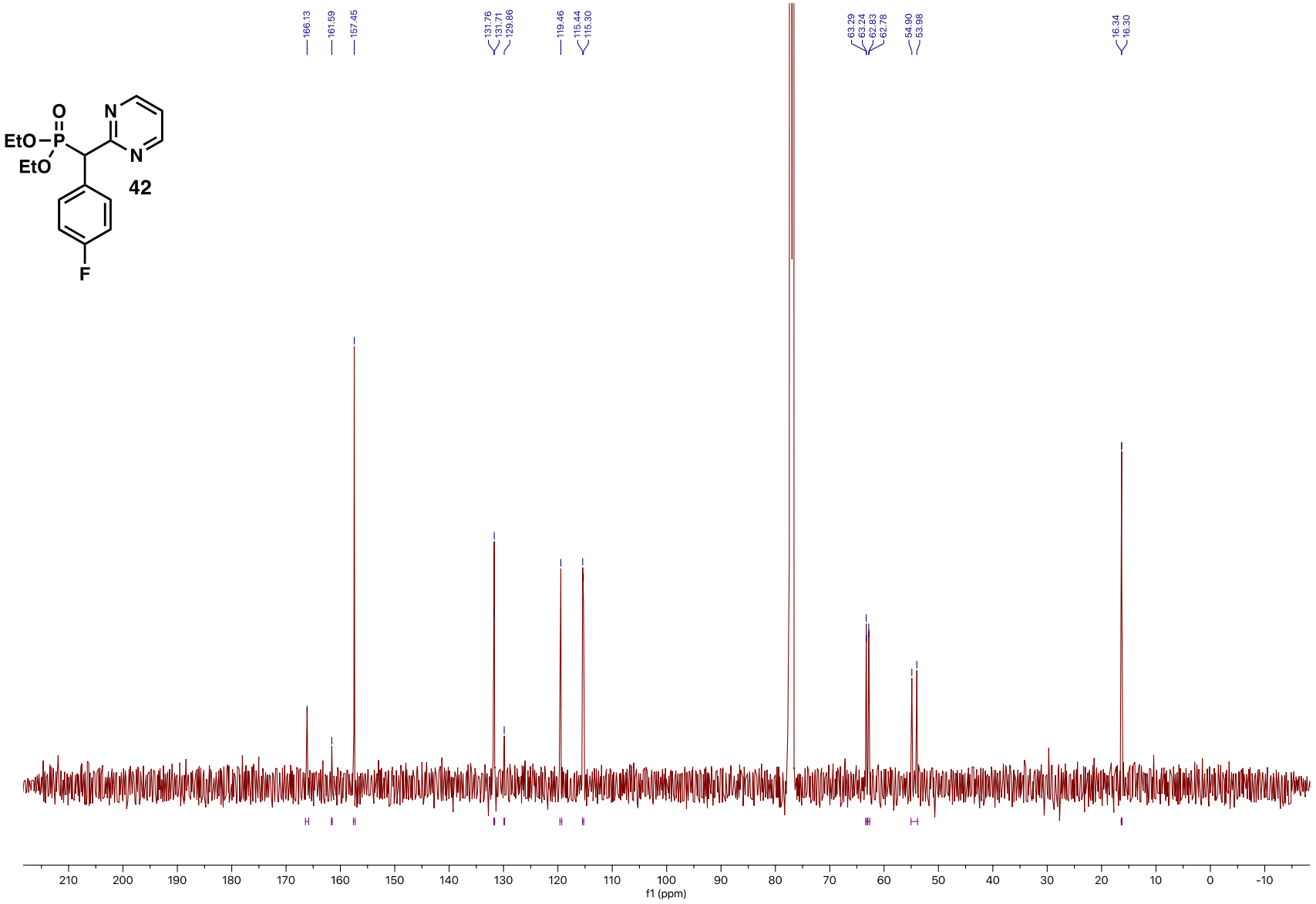
7.65
7.65
7.65
7.64
7.24
7.23
7.23
7.22
7.22
7.06
7.04
7.03
7.03
7.02
7.01
7.00
7.00
4.96
4.93
4.13
4.12
4.12
4.11
4.10
4.10
4.09
4.09
4.08
4.08
4.07
4.06
4.06
4.05
4.04
4.04
4.04
4.03
4.03
4.02
4.02
4.01
4.00
4.00
4.00
3.99
3.99
3.99
3.97
1.19
1.18
1.17
O
N
EtO
P
EtO
N
42
F
1.73
1.88
1.05
1.98
1.00
4.32
5.85
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)

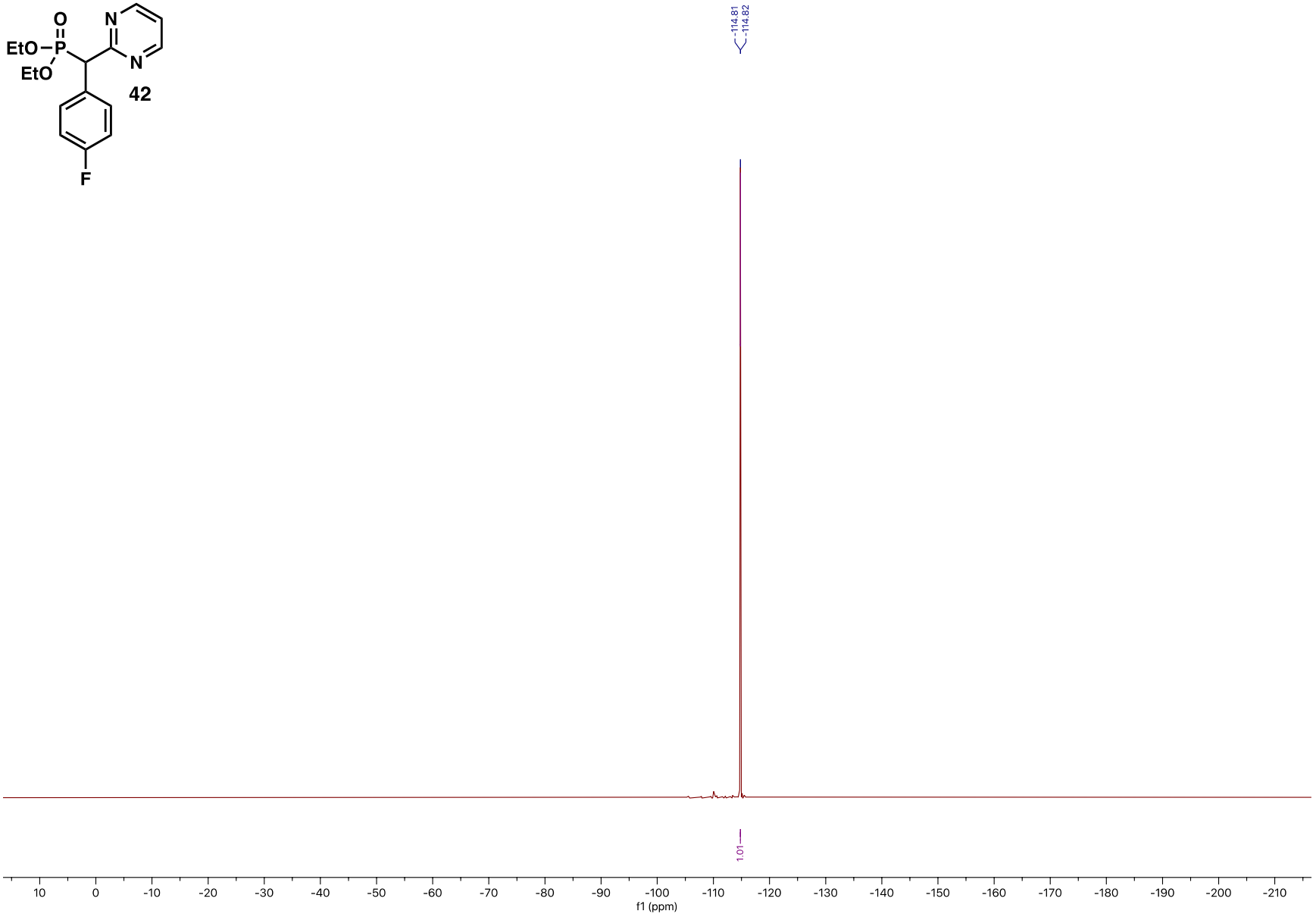
©AUTHOR(S)


166.13
161.59
157.45
131.76
131.71
129.86
119.46
115.44
115.30
63.29
63.24
62.83
62.78
54.90
53.98
16.34
16.30
O
N
EtO
P
EtO
N
F
42
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)

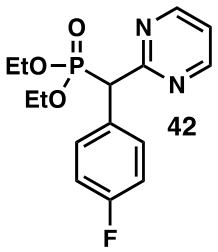
©AUTHOR(S)

O
N
EtO
P
N
EtO
F

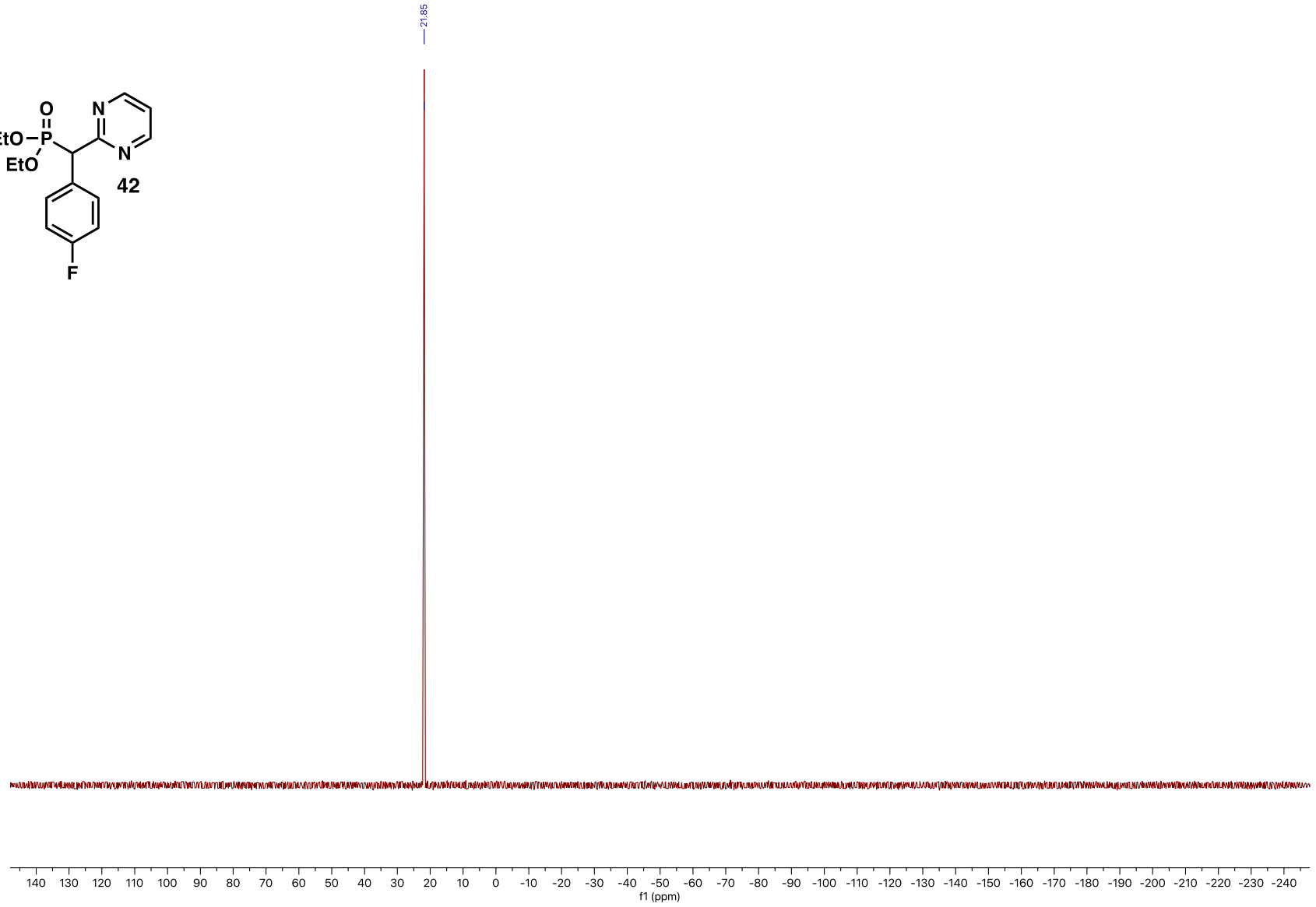
42


-114.81
-114.82
1.01
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

©AUTHOR(S)


O
N
EtO
P
N
EtO
F

42


21.85
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

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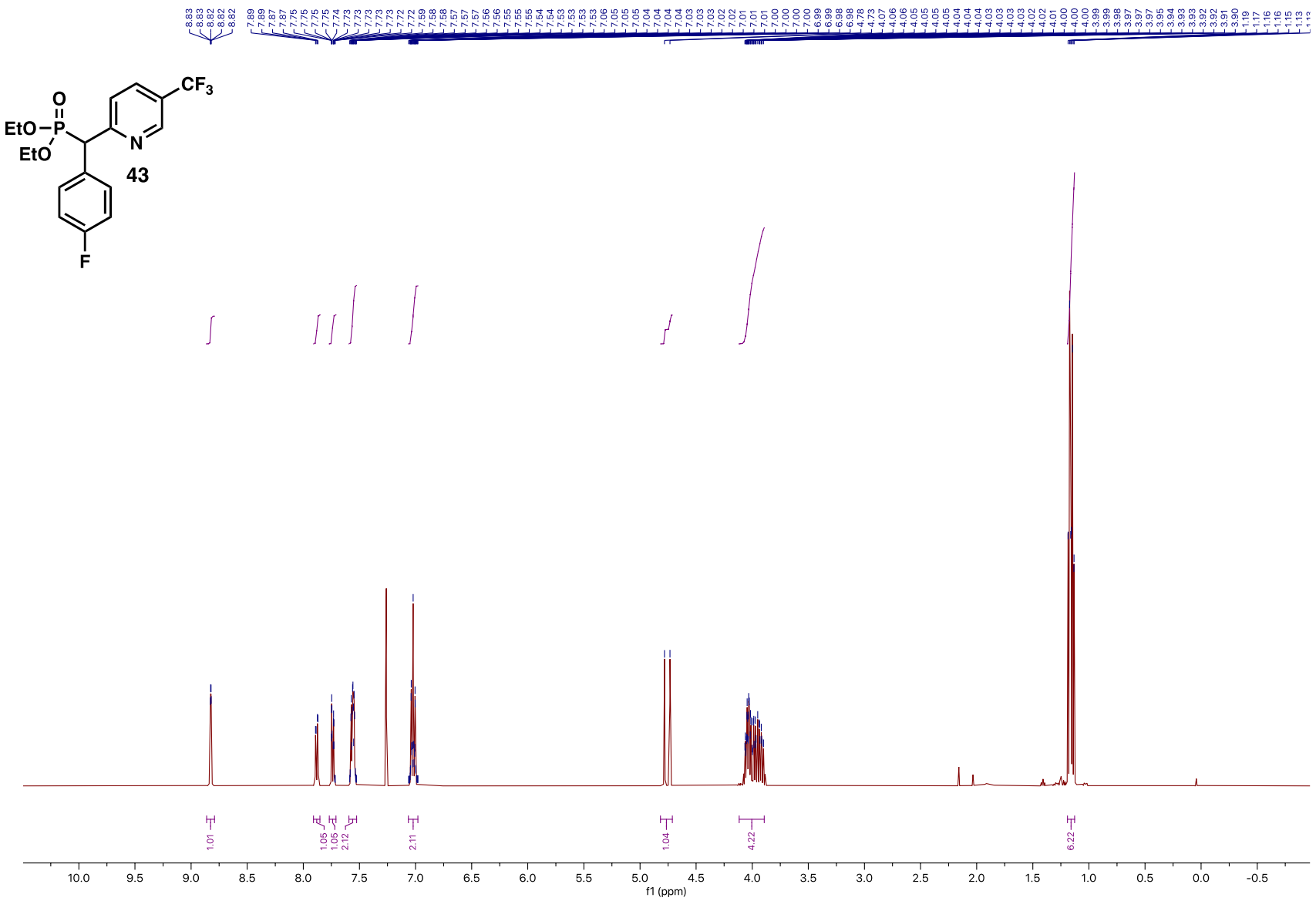
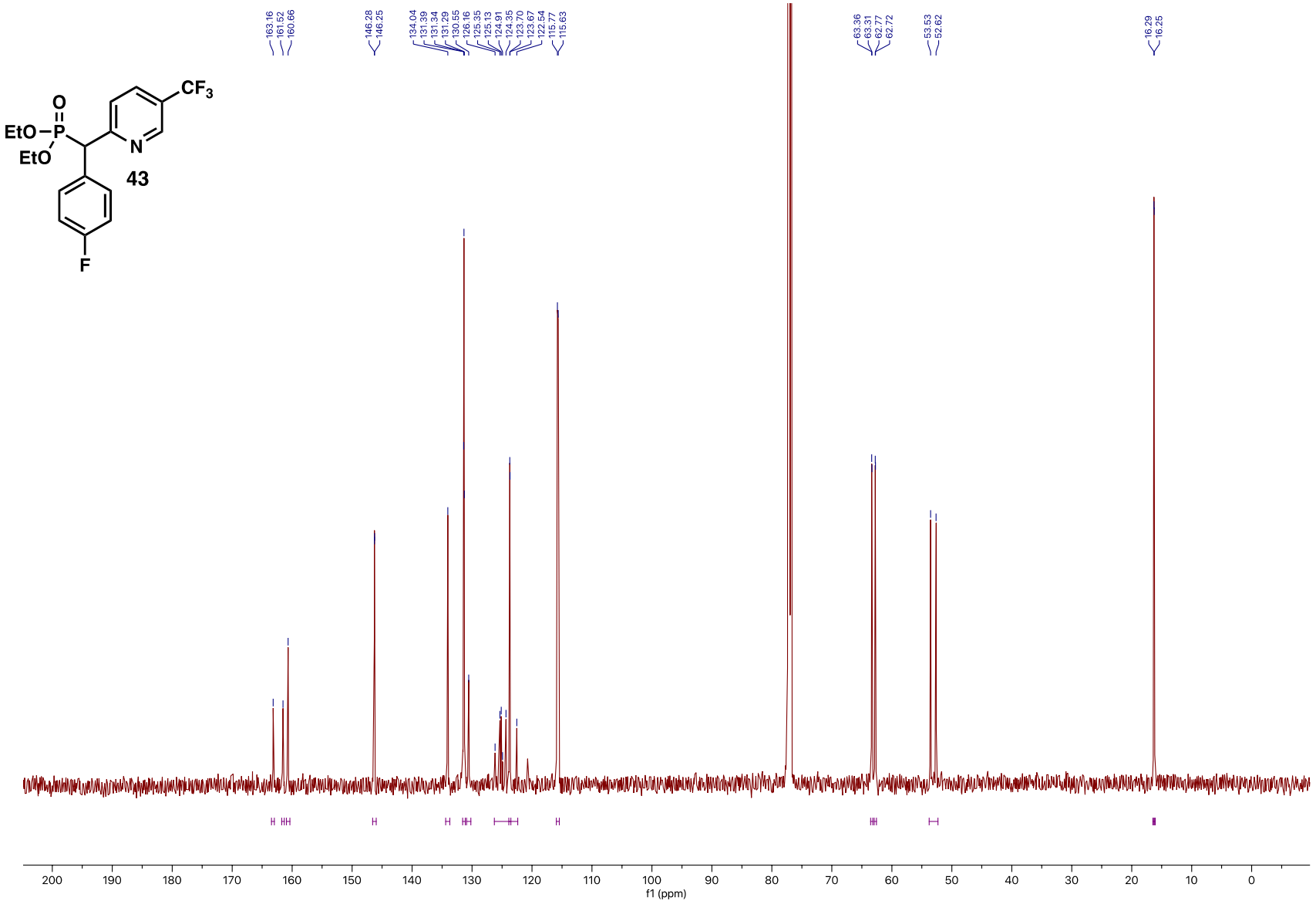
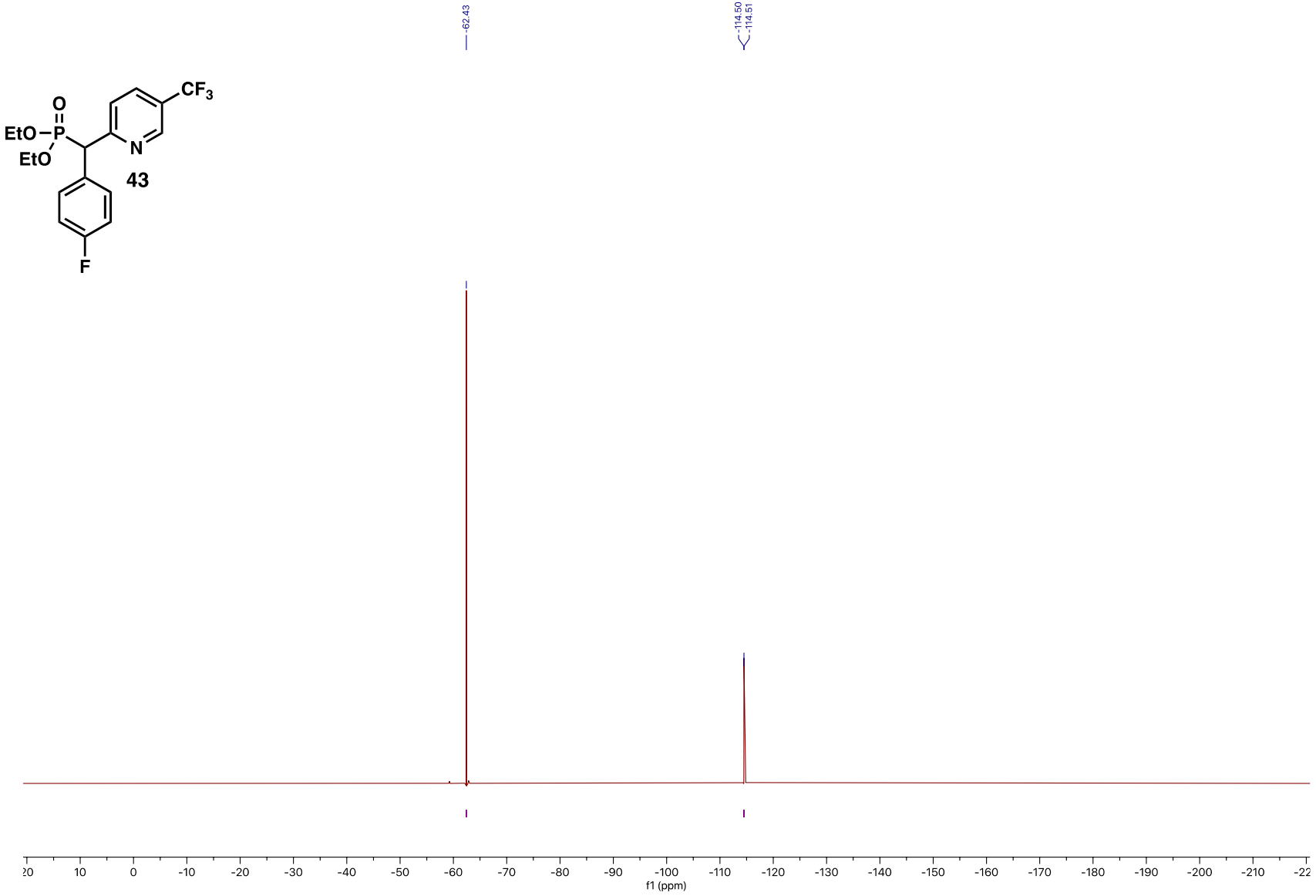


©AUTHOR(S)


163.16
161.52
160.66
146.28
146.25
134.04
131.39
131.34
131.29
130.65
126.96
125.35
125.13
124.91
124.35
123.70
123.67
122.54
115.77
115.63
63.36
63.31
62.77
62.72
53.53
52.62
16.29
16.25
O
EtO–P
EtO
N
CF3
43
F
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

©AUTHOR(S)



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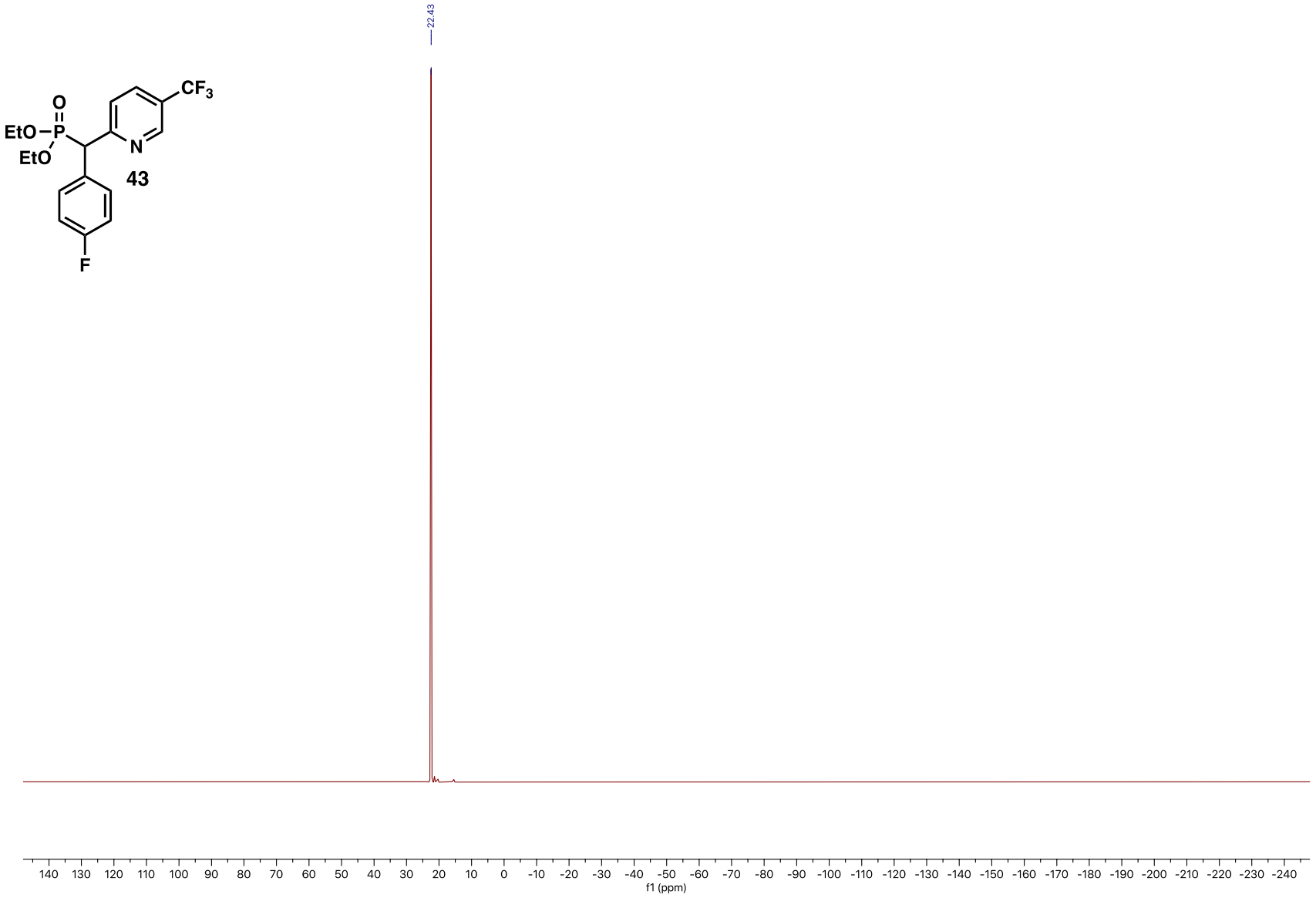
22.43
O
EtO
P
EtO
N
CF3
F
43
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

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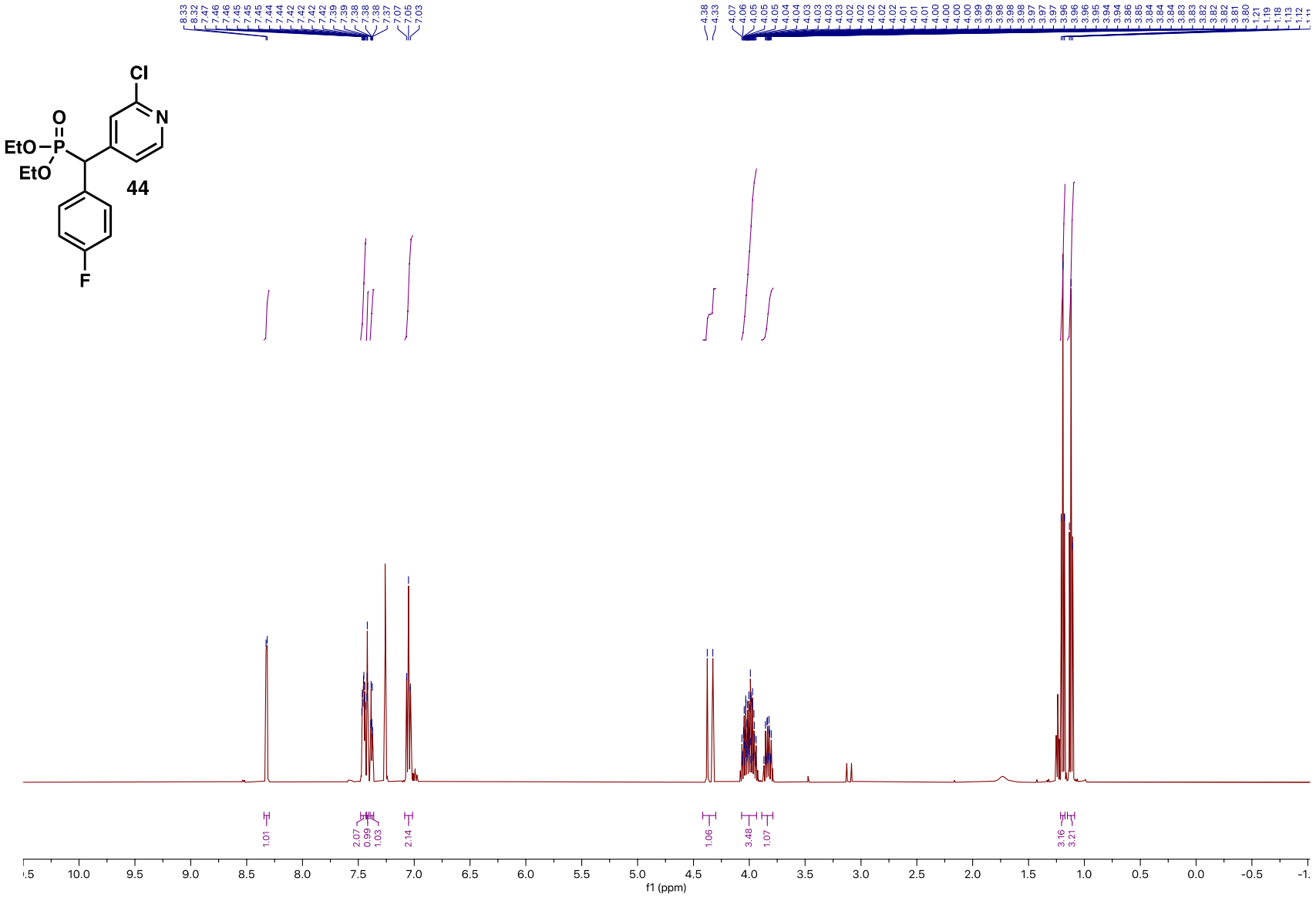
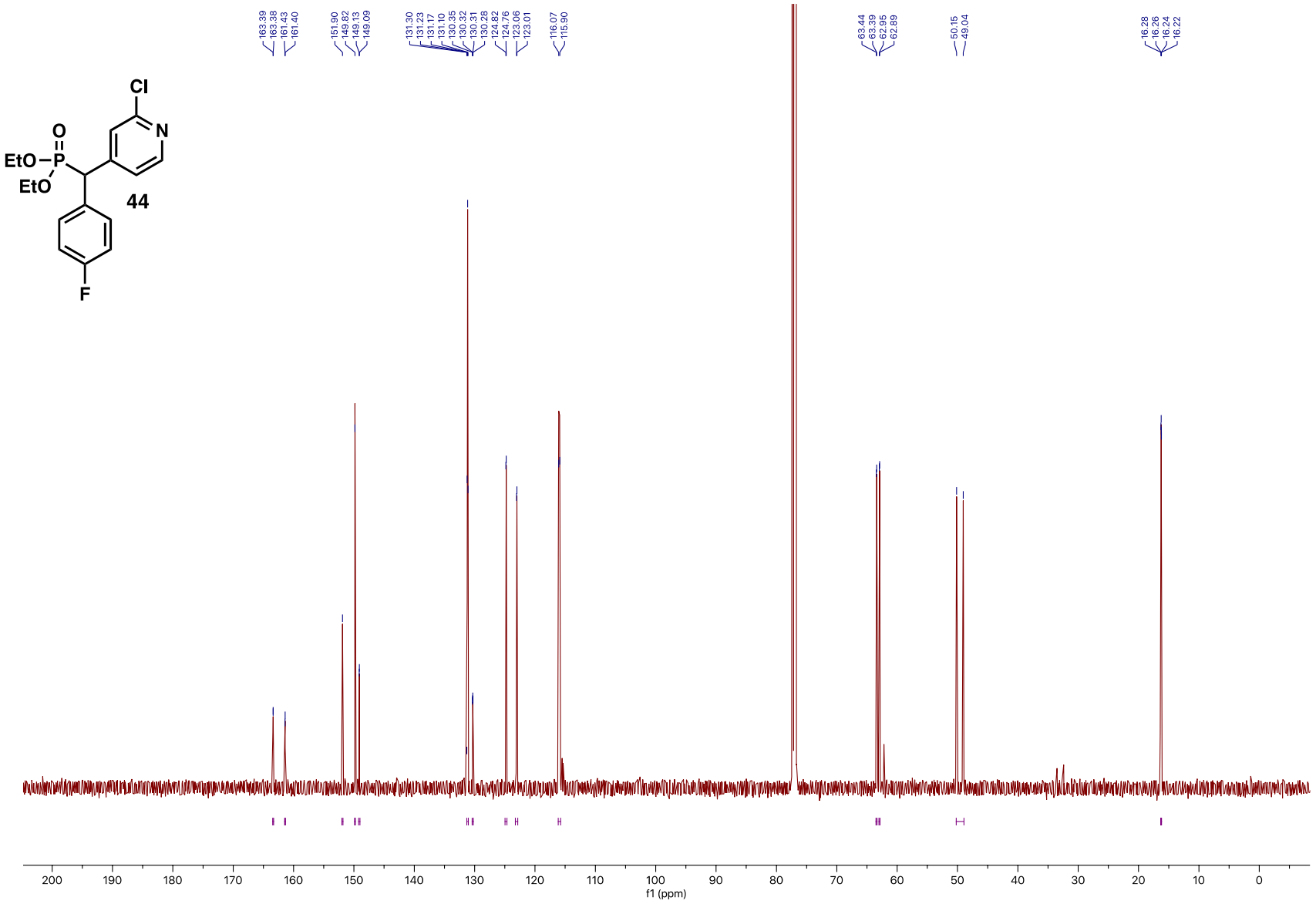


©AUTHOR(S)


163.39
163.38
161.43
161.40
151.90
149.82
149.13
149.09
131.30
131.23
131.17
131.10
130.35
130.32
130.31
130.28
124.82
124.76
123.06
123.01
116.07
115.90
63.44
63.39
62.95
62.89
50.15
49.04
16.28
16.26
16.24
16.22
Cl
N
O
EtO
P
EtO
44
F
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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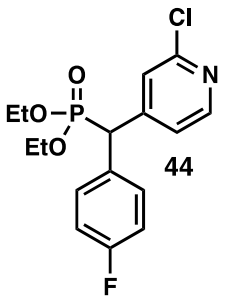
Cl
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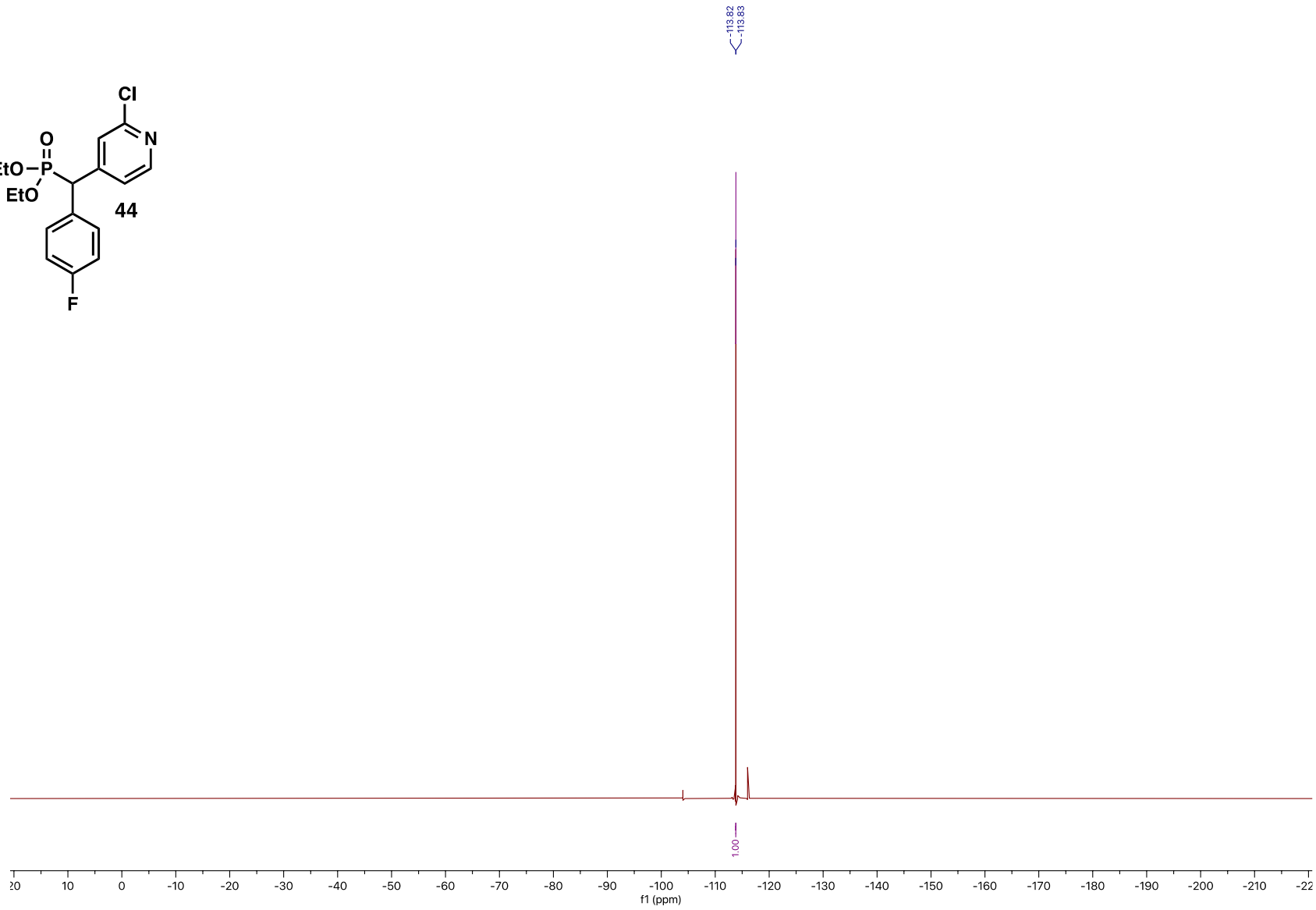
O
EtO
P
EtO
F

44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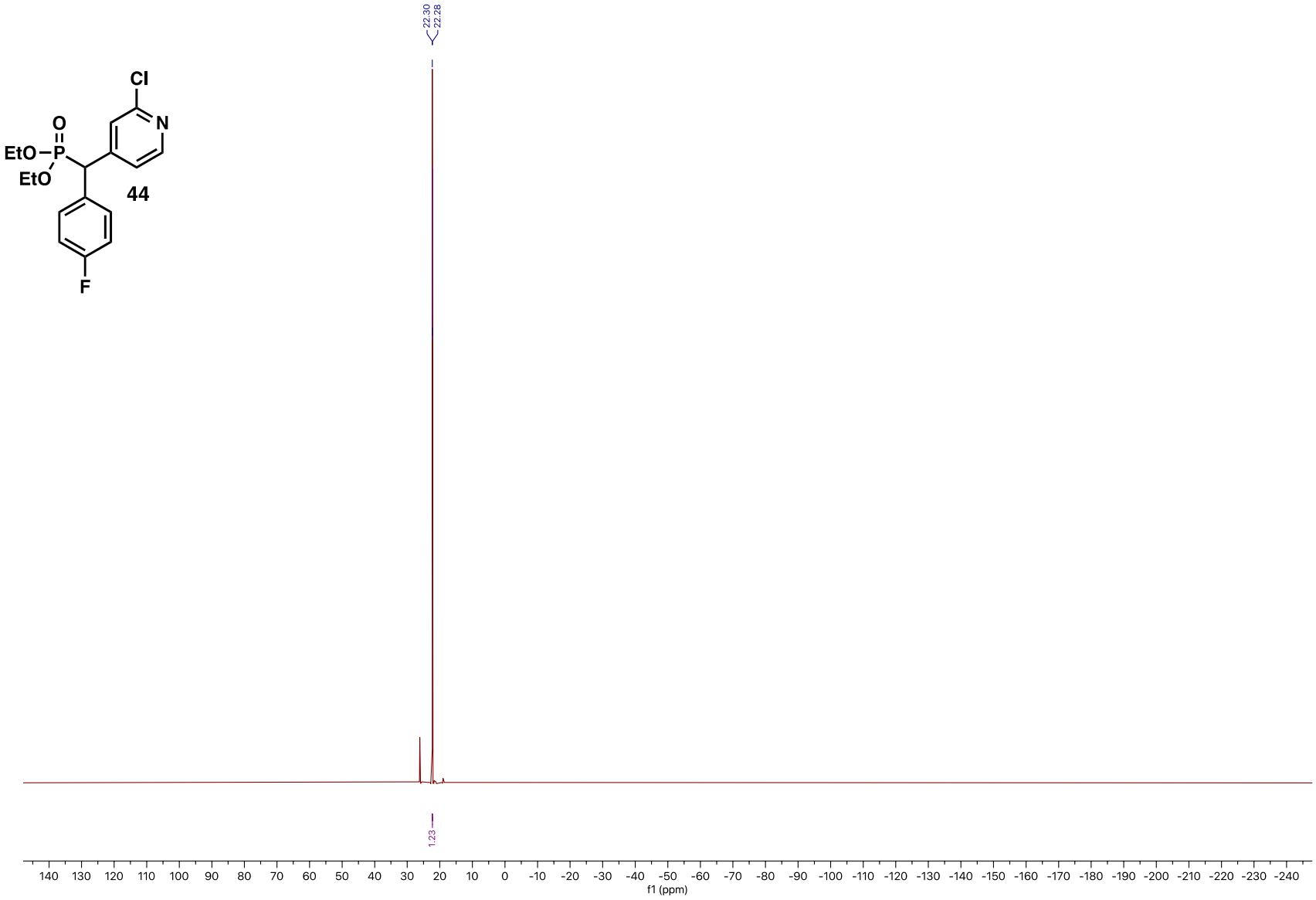
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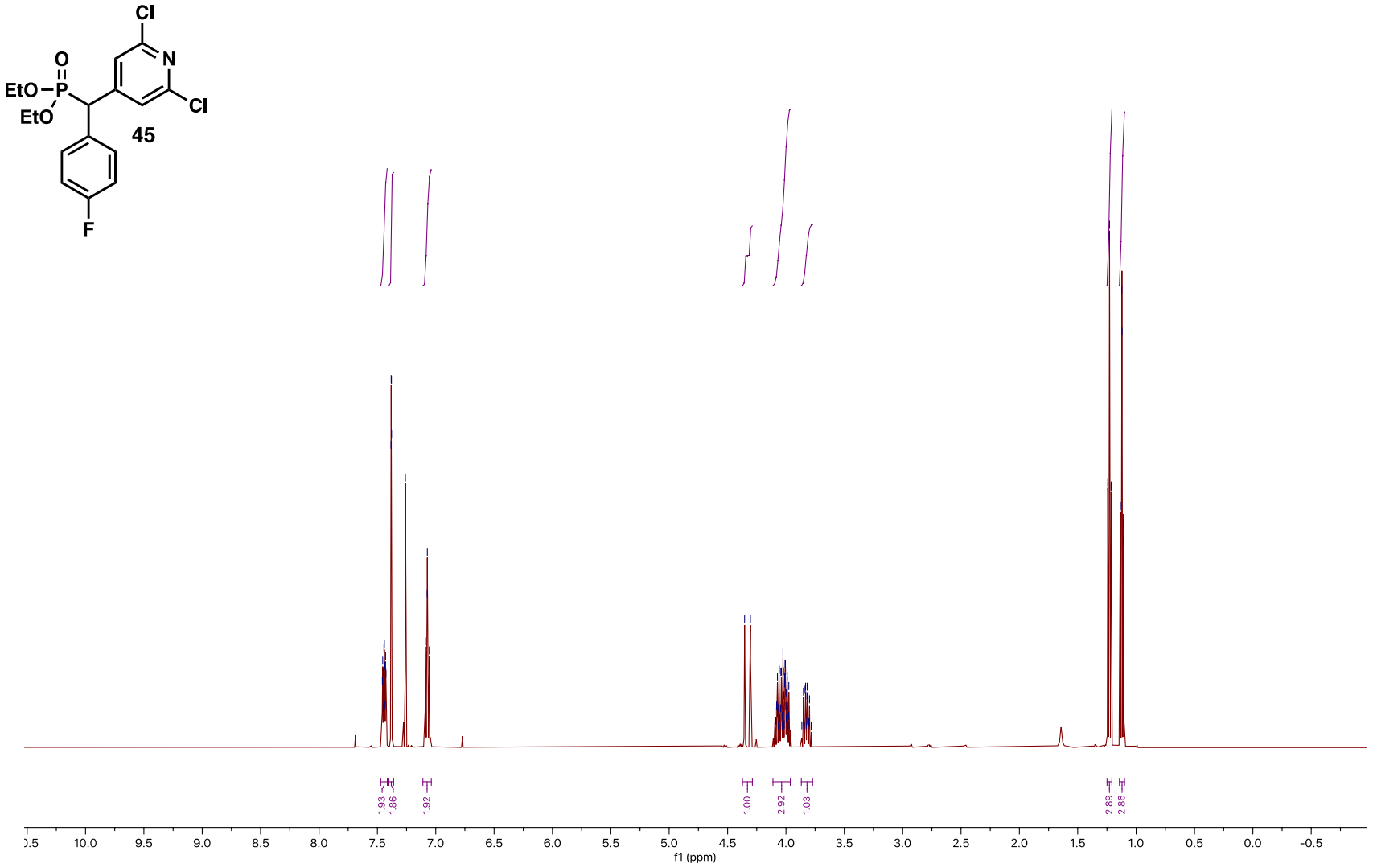
f1 (ppm)

©AUTHOR(S)



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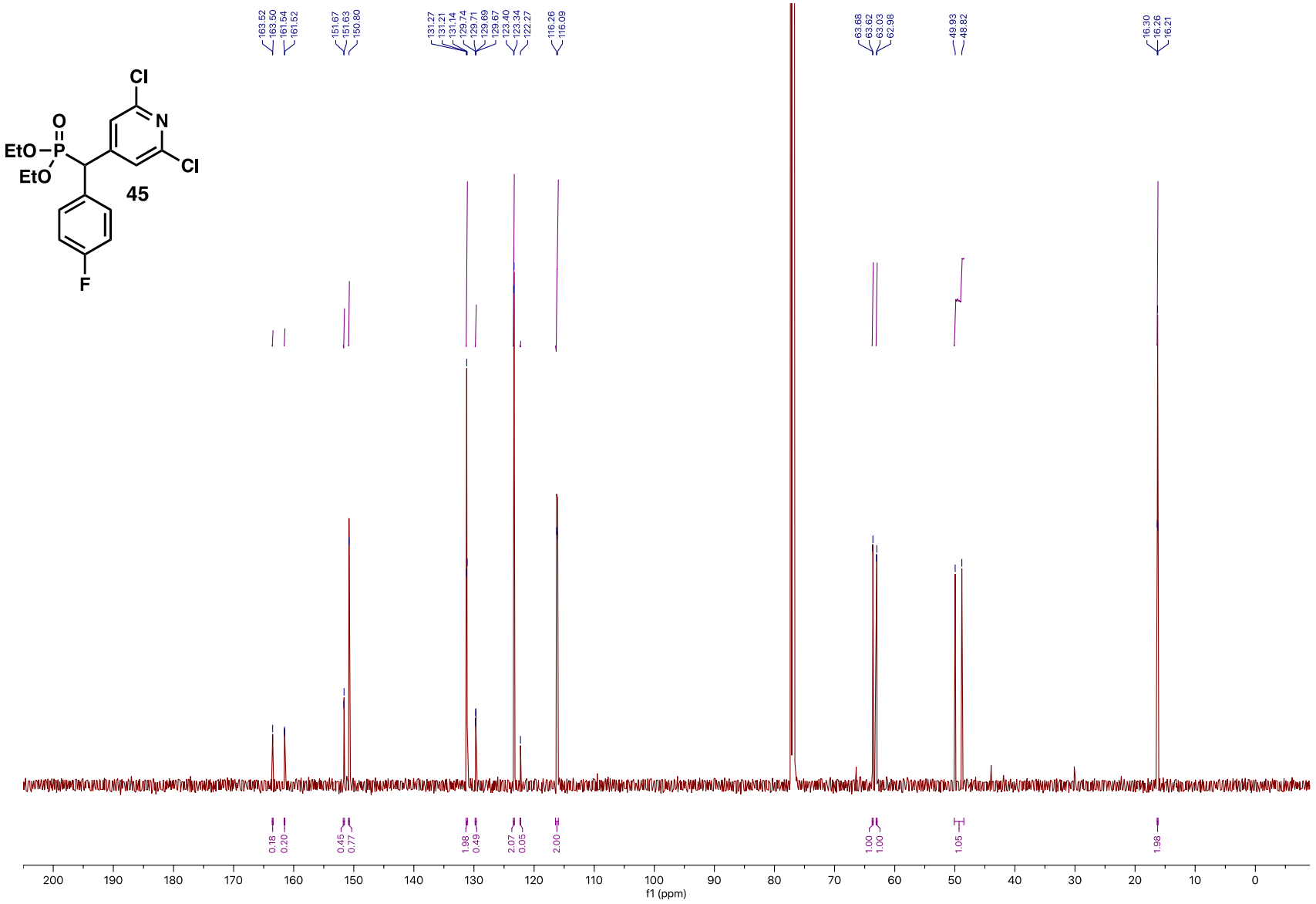
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63.62
63.03
62.98
49.93
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16.30
16.26
16.21
Cl
O
N
EtO
P
EtO
Cl
45
F
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0.20
0.45
0.77
1.98
0.49
2.07
0.05
2.00
1.00
1.00
1.05
1.98
200
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100
90
80
70
60
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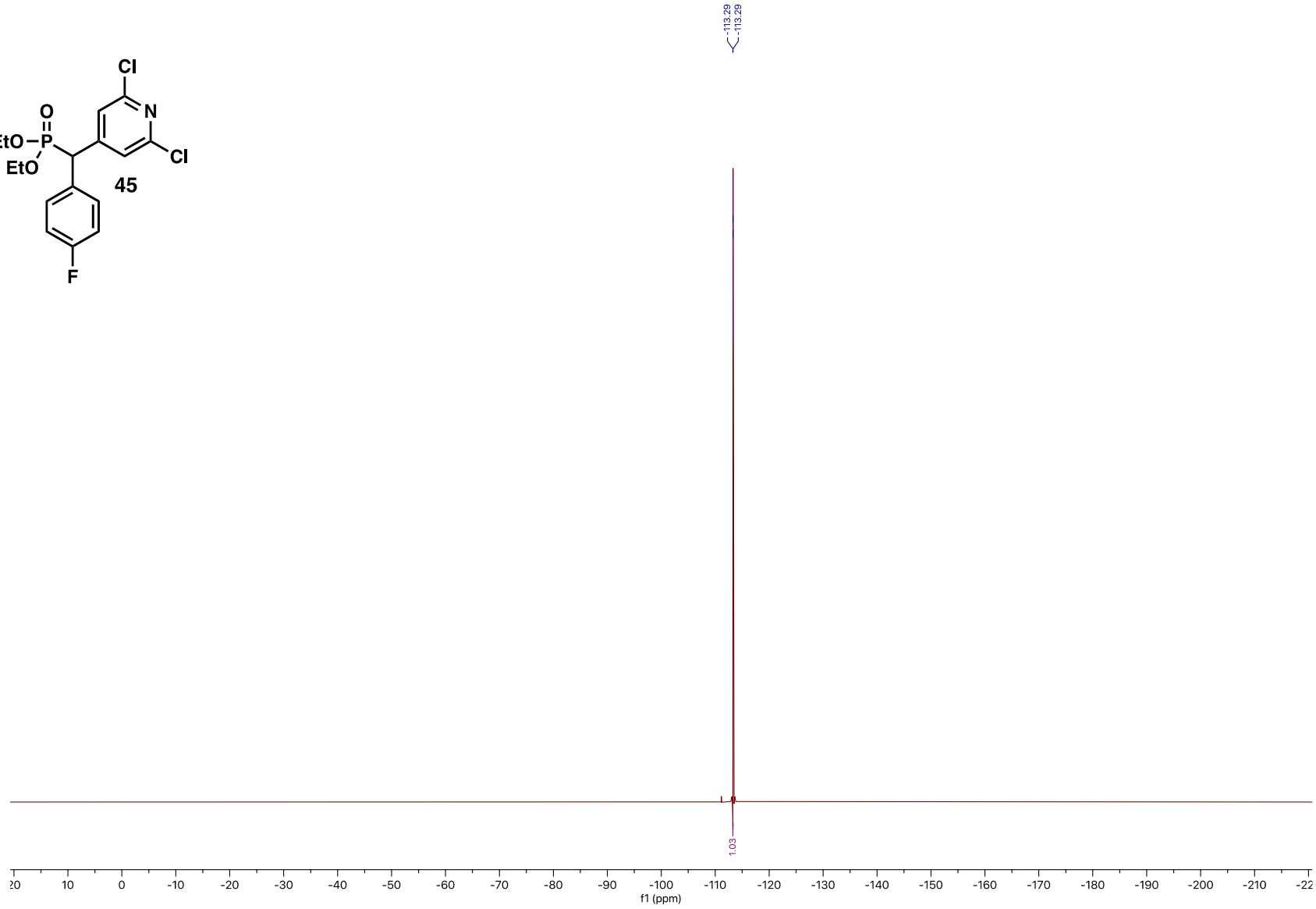
f1 (ppm)

©AUTHOR(S)

Cl
O
N
EtO–P
EtO
Cl
F

45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-113.29
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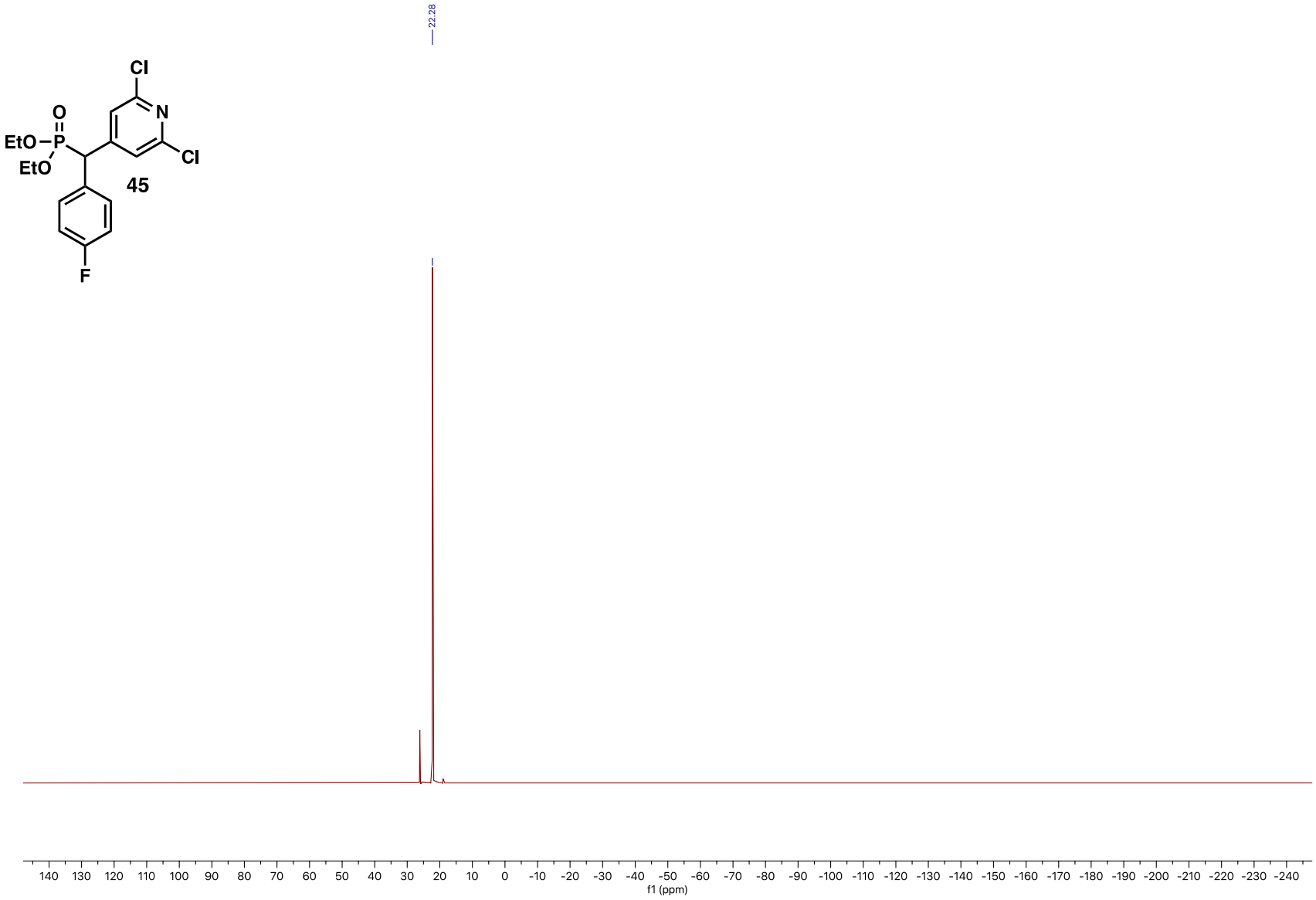
f1 (ppm)

©AUTHOR(S)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EtO
Cl
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F
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f1 (ppm)

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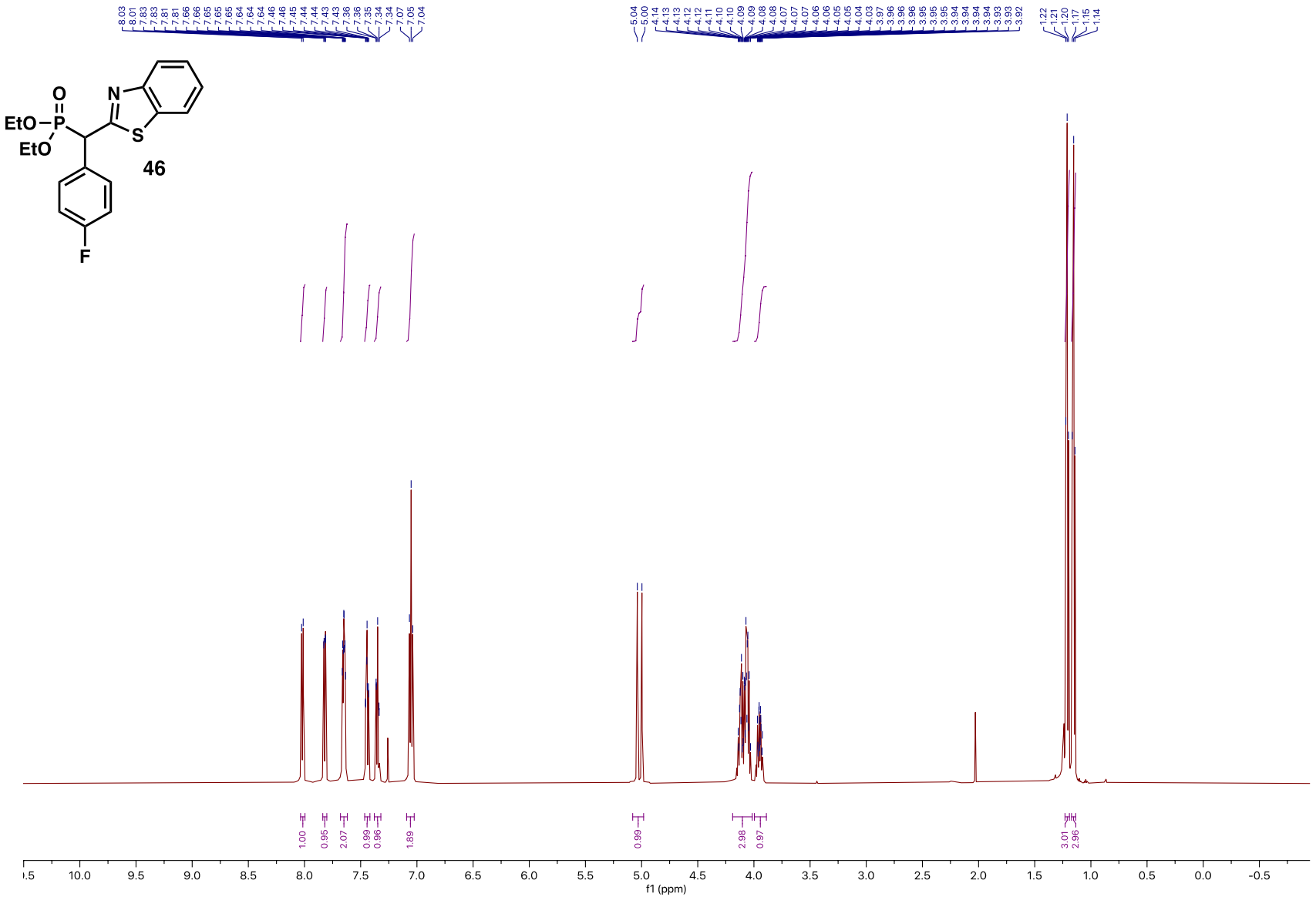
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1.20
1.17
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1.14
O
N
EtO
P
S
EtO
46
F
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2.07
0.99
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2.96
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f1 (ppm)

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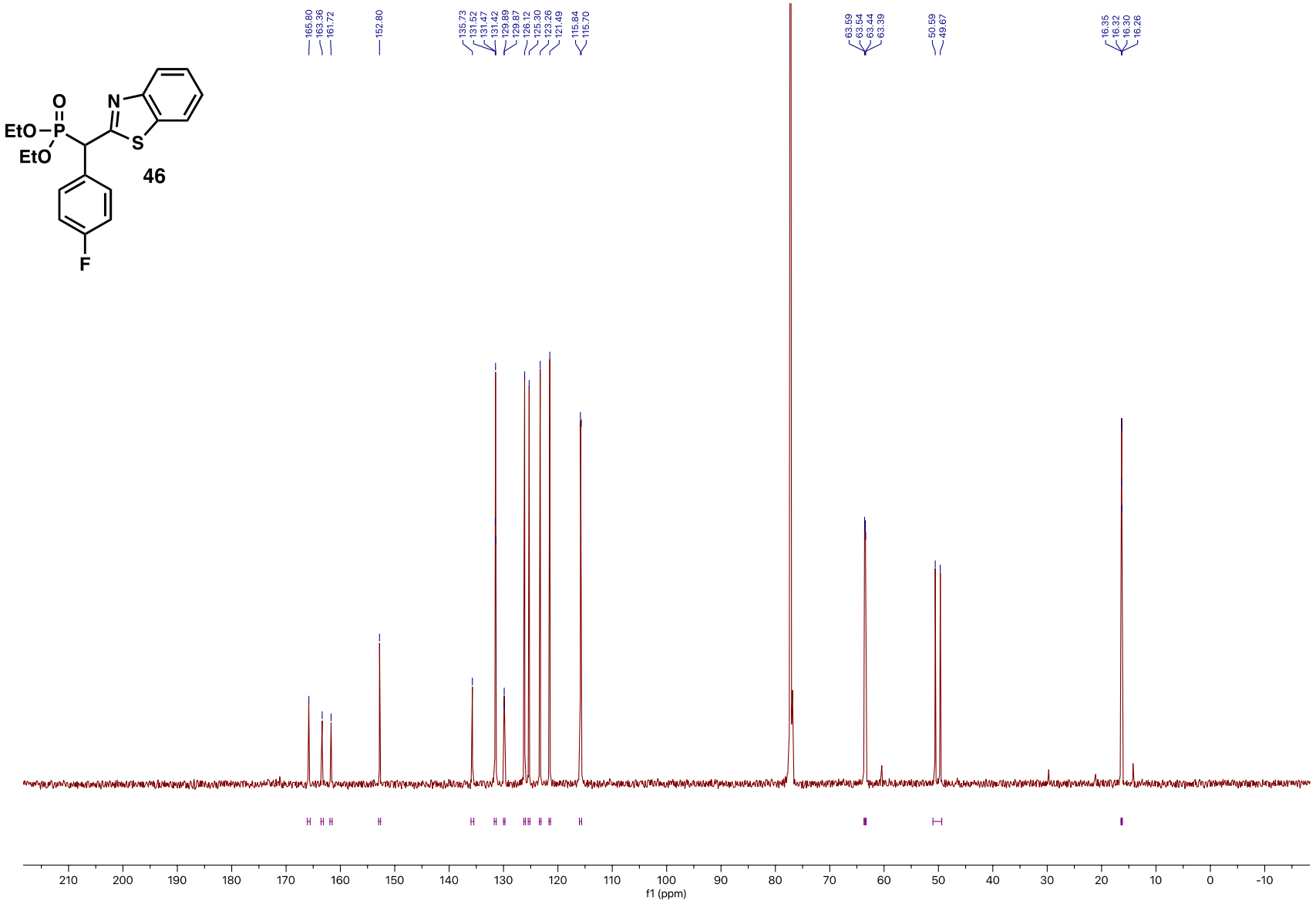
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63.54
63.44
63.39
50.59
49.67
16.35
16.32
16.30
16.26
O
N
EtO
P
EtO
S
F
46
210
200
190
180
170
160
150
140
130
120
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100
90
80
70
60
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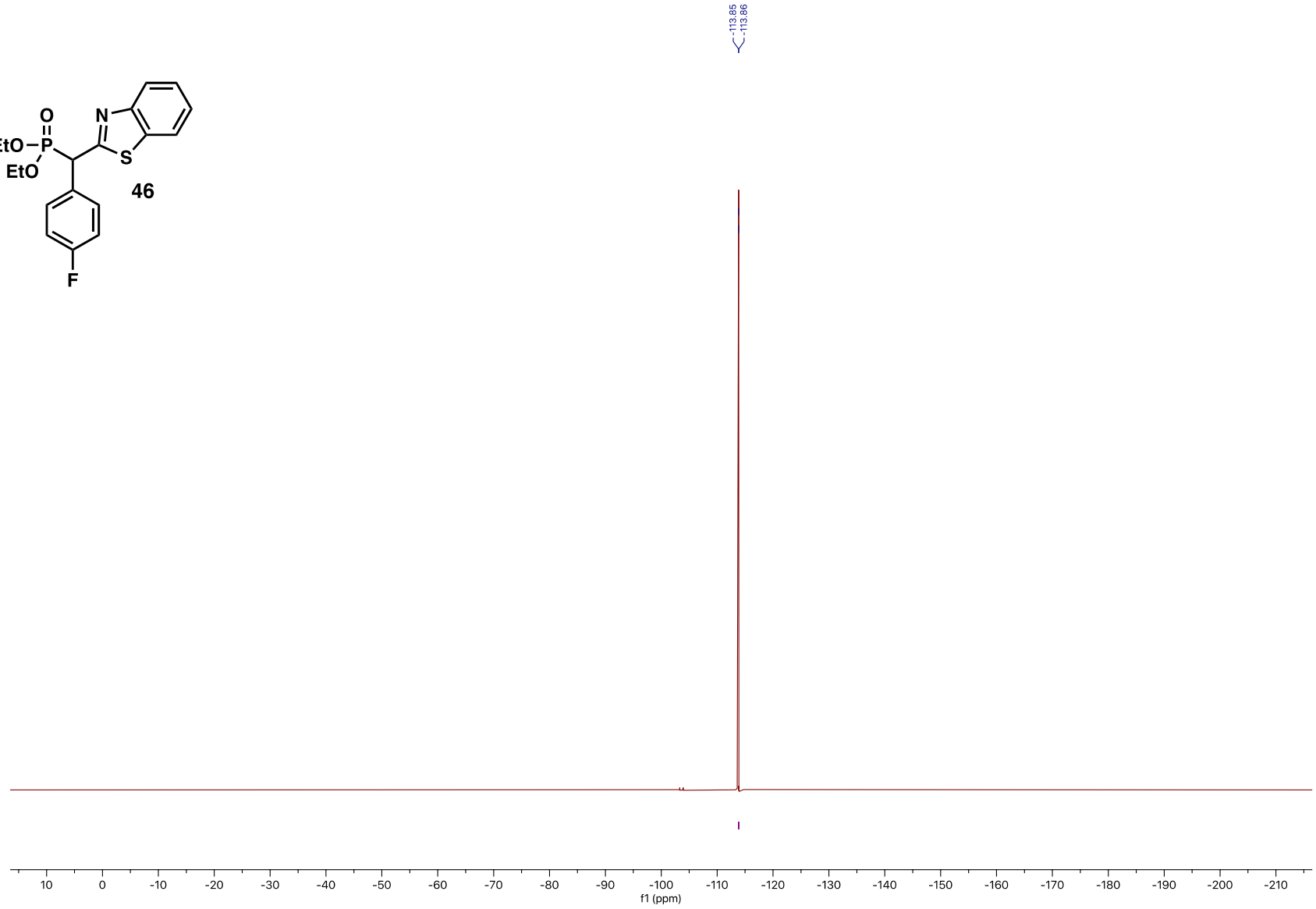
f1 (ppm)

©AUTHOR(S)

O
N
EtO
P
S
EtO
F

46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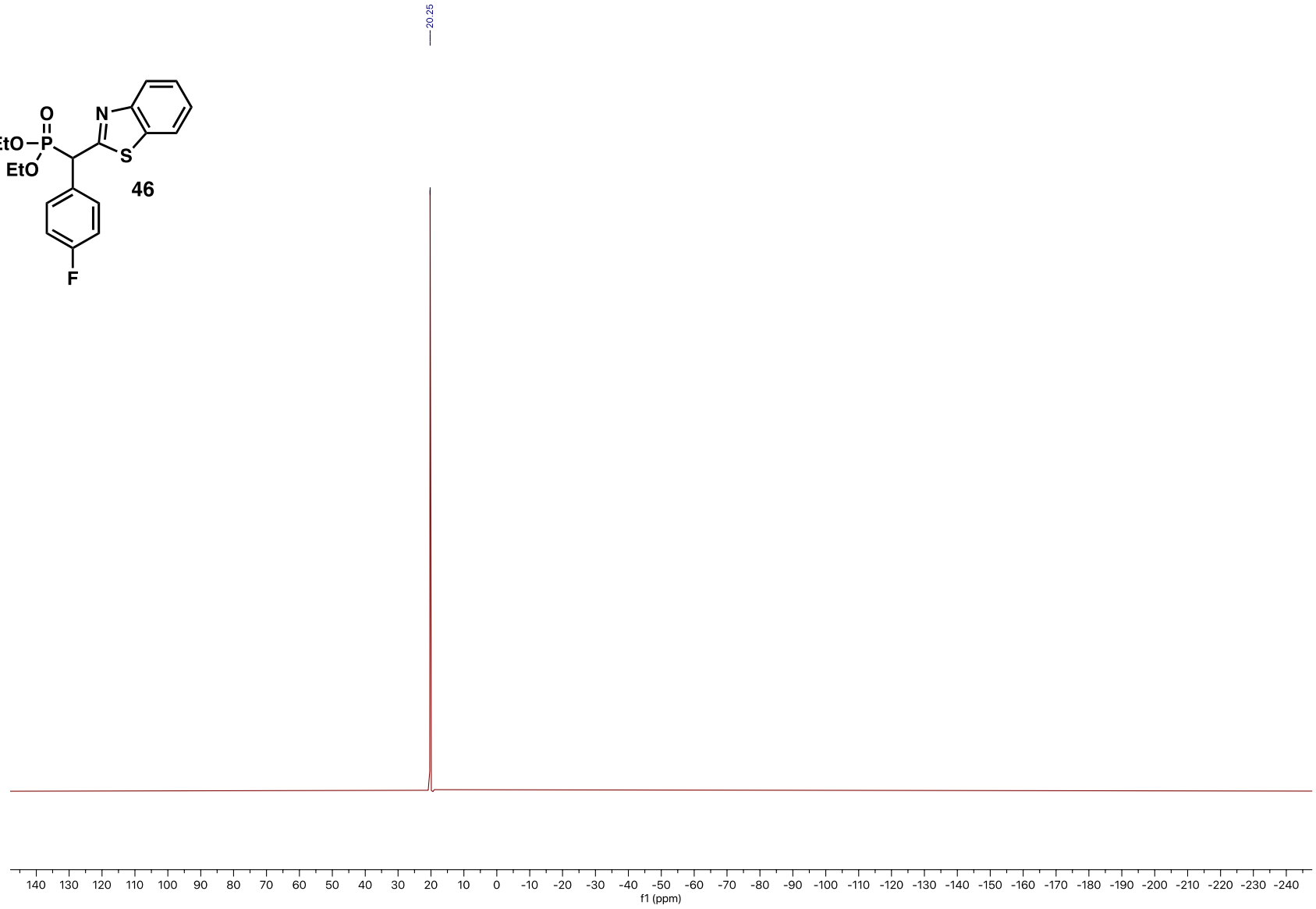
f1 (ppm)

©AUTHOR(S)

O
N
EtO
P
S
EtO
F

46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f1 (ppm)

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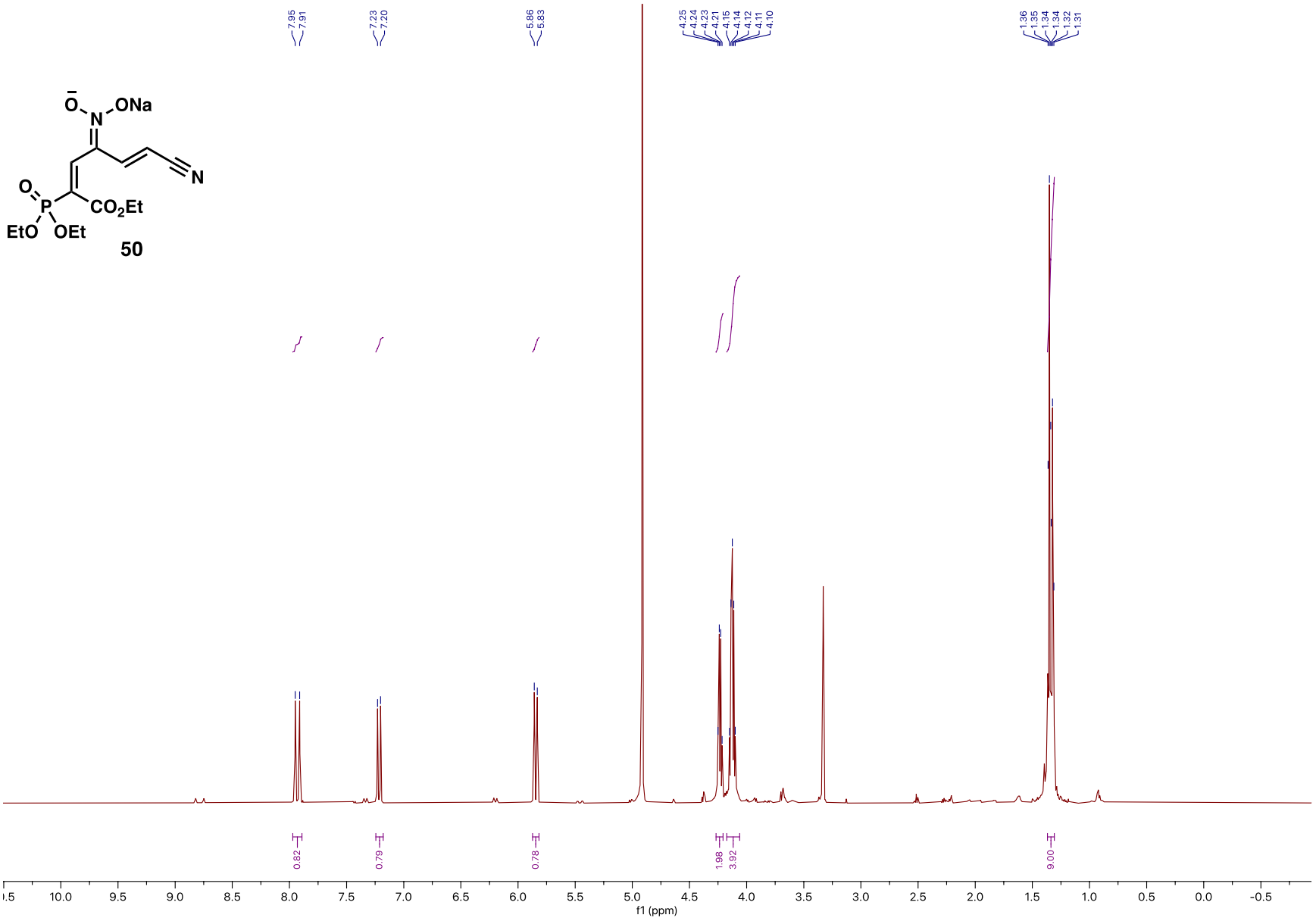
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4.15
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4.12
4.11
4.10
1.36
1.35
1.34
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0.82
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9.00
f1 (ppm)

50

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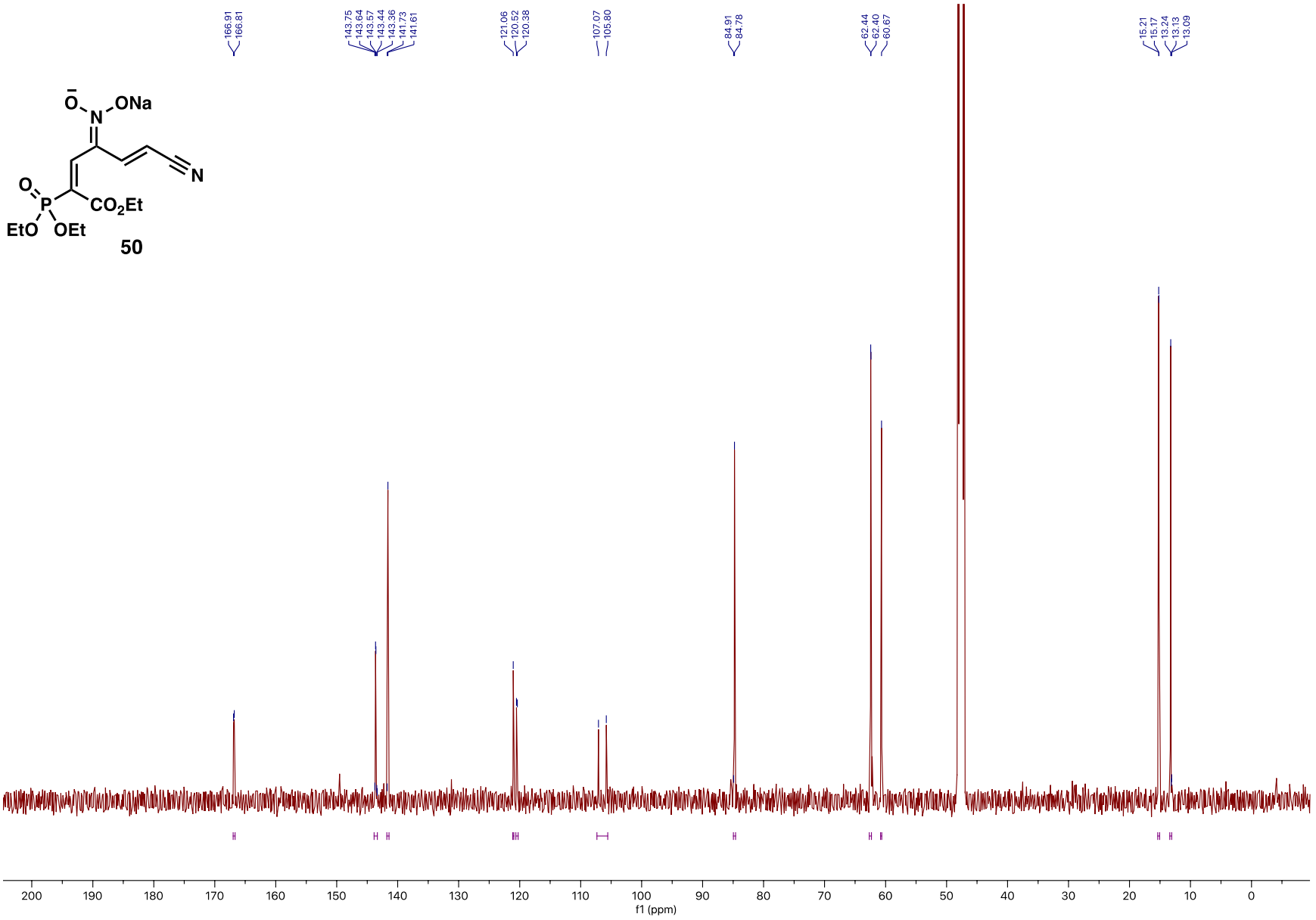
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60.67
15.21
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13.13
13.09
O
N
ONa
N
O
P
CO2Et
EtO
OEt
50
200
190
180
170
160
150
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f1 (ppm)

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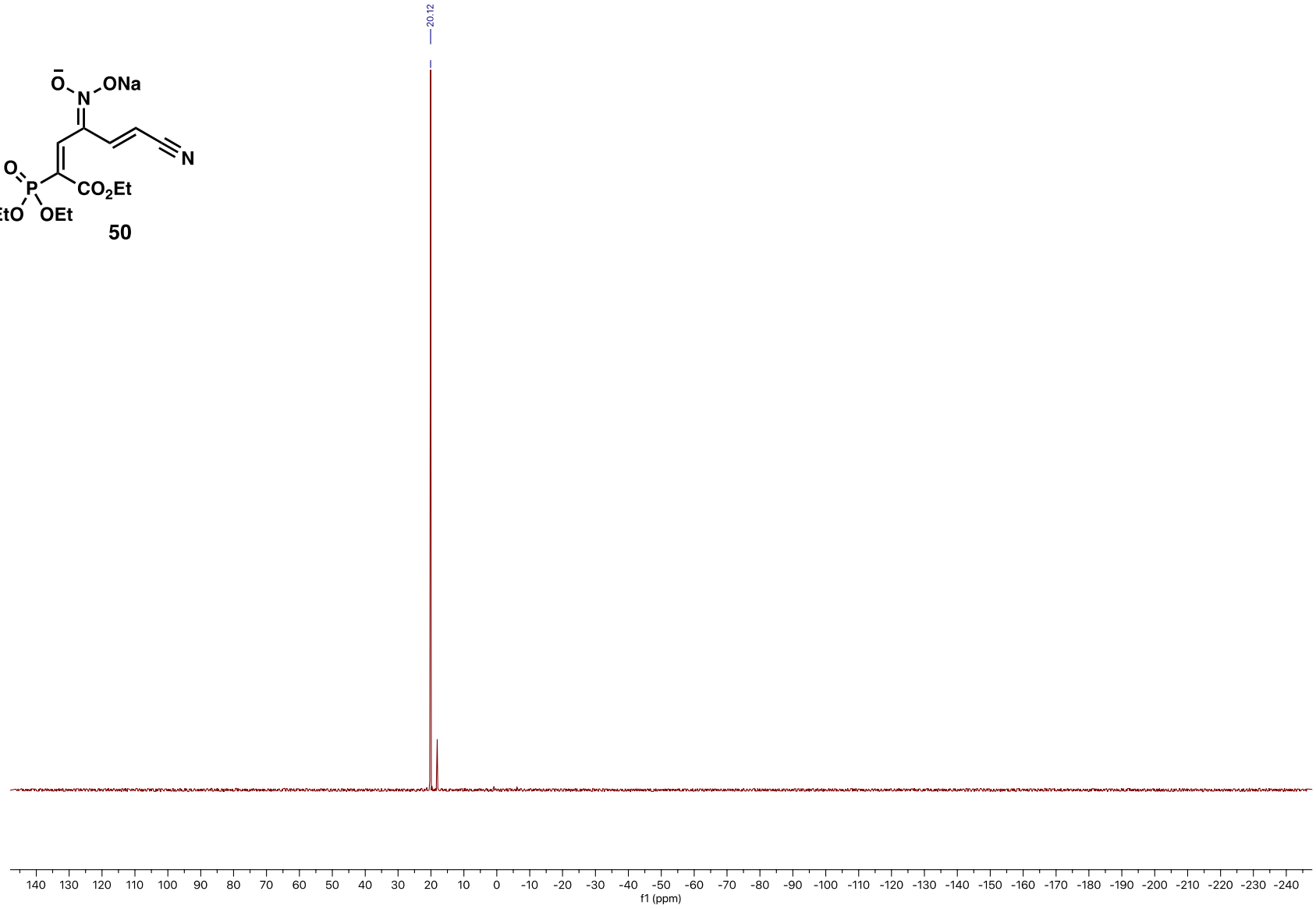
50



HSQC of 50:

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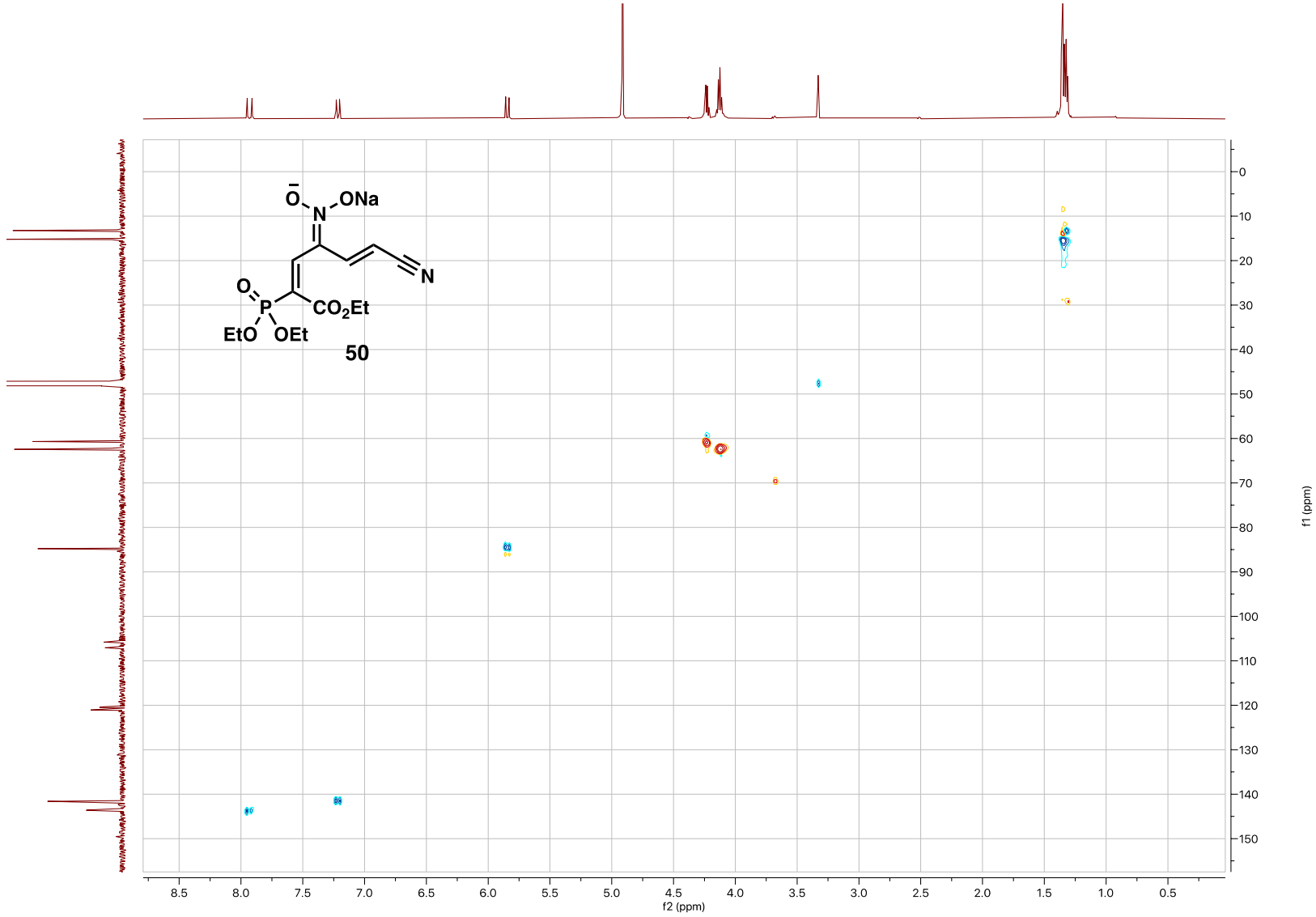

Single-Crystal X-Ray Crystallography of Compound 30

X-ray diffraction data were measured on Bruker D8 Venture PHOTON II CPAD diffractometer equipped with a Cu K_α INCOATEC ImuS micro-focus source (λ = 1.54178 Å). Indexing was performed using *APEX3* [1] (Difference Vectors method). Data integration and reduction were performed using SaintPlus [2]. Absorption correction was performed by multi-scan method implemented in SADABS [3]. Space groups were determined using XPREP

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implemented in APEX3 [1]. Structure was solved using SHELXT [4] and refined using SHELXL-2018 [5] (full-matrix least-squares on F^2) through OLEX2 interface program [6]. Disordered -OEt group was refined with restraints / constraint. Crystal data and refinement conditions are shown in Table 1.

[1] Bruker (2019). *APEX3* Bruker AXS Inc., Madison, Wisconsin, USA.
[2] Bruker (2019) SAINT V8.35A. Data Reduction Software.
[3] Sheldrick, G. M. (1996). *SADABS. Program for Empirical Absorption Correction.* University of Gottingen, Germany.
[4] XT, G.M. Sheldrick, Acta Cryst. (2015). A71, 3-8
[5] XL, Sheldrick, G. M. (2008). Acta Cryst. A64, 112-122.
[6] Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J.A.K.; Puschmann, H., OLEX2: A complete structure solution, refinement and analysis program (2009). J. Appl. Cryst., 42, 339-341

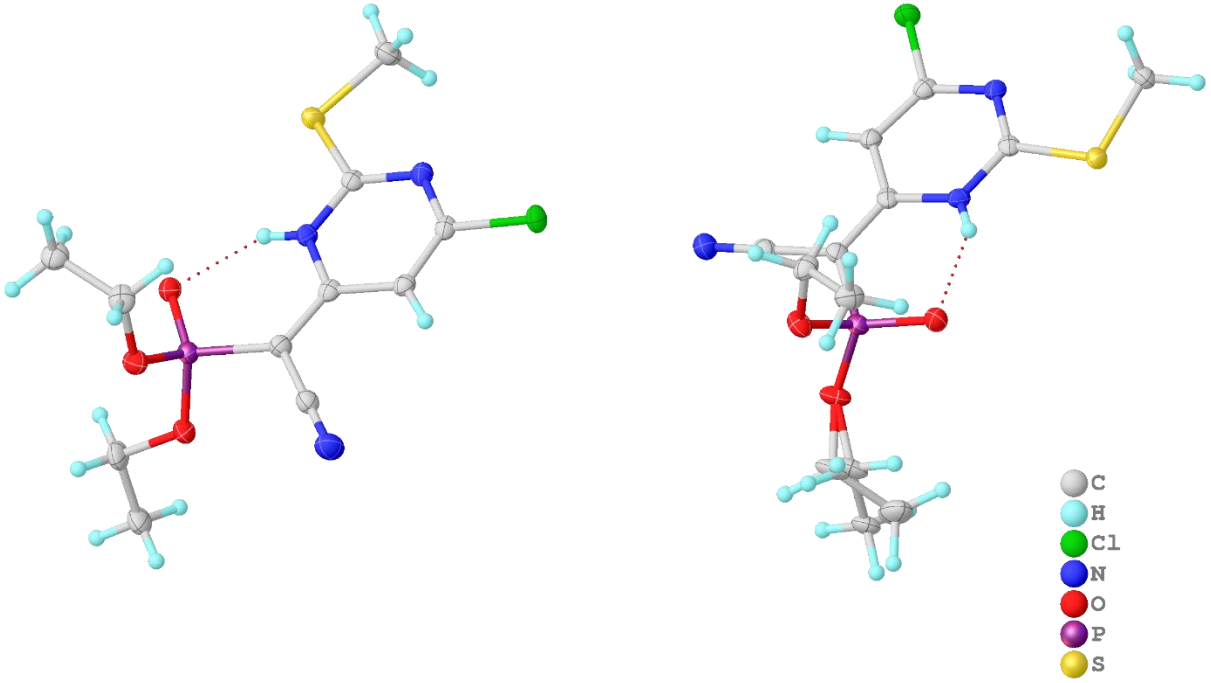

Figure S1. Asymmetric unit of ZS_820 **(30)**. Anisotropic displacement parameters were drawn at 50% probability level.

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Table S1. Crystal data and structure refinement for ZS_820 **(30).**	
Identification code	ZS_820
Empirical formula	$C_{11}H_{15}ClN_3O_3PS$
Formula weight	335.74
Temperature/K	100.0
Crystal system	triclinic
Space group	P-1
a/Å	10.5147(4)
b/Å	12.3363(4)
c/Å	12.9255(5)
α/°	63.702(2)
β/°	83.475(2)
γ/°	83.211(2)
Volume/Å^3	1489.00(10)
Z	4
ρ_{calc}g/cm^3	1.498
μ/mm^{-1}	4.706
F(000)	696.0
Crystal size/mm^3	0.67 × 0.08 × 0.01
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	7.648 to 158.31
Index ranges	-13 ≤ h ≤ 13, -15 ≤ k ≤ 15, -16 ≤ l ≤ 16
Reflections collected	27051
Independent reflections	6068 [R_{int} = 0.0640, R_{sigma} = 0.0516]
Data/restraints/parameters	6068/33/389
Goodness-of-fit on F^2	1.038
Final R indexes [I>=2σ (I)]	R_1 = 0.0404, wR_2 = 0.1016
Final R indexes [all data]	R_1 = 0.0492, wR_2 = 0.1086
Largest diff. peak/hole / e Å^{-3}	0.51/-0.39

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Single-Crystal X-Ray Crystallography for Compound 50

X-ray diffraction data were measured on Bruker D8 Venture PHOTON II CPAD diffractometer equipped with a Cu Kα INCOATEC ImuS micro-focus source (λ = 1.54178 Å). Indexing was performed using APEX3 [1] (Difference Vectors method). Data integration and reduction were performed using SaintPlus [2]. Absorption correction was performed by multi-scan method implemented in TWINABS [3]. Space group was determined using XPREP implemented in APEX3 [1]. Structure weas solved using SHELXT [4] and refined using SHELXL-2018/3 [5] (full-matrix least-squares on F2) through OLEX2 interface program [6]. Ellipsoid plot was drawn with Platon [7]. Crystal was a twin. Data were integrated with Bruker-Saint using two orientation matrices determined in APEX3/RLATT based on two manually selected reciprocal lattices. Twin law from Saint: -1.00005 0.00008 0.02110 / -0.00011 -1.00040 0.08615 / 0.00404 -0.01146 1.00045. Reflections were scaled and merged with TWINABS. Detwinned data were used for refinement. Data and refinement conditions are shown in Table 1.

[1] Bruker (2019). APEX3. Bruker AXS LLC, Madison, Wisconsin, USA.
[2] Bruker (2019) SAINT. Bruker AXS LLC, Madison, Wisconsin, USA.
[3] Krause, L., Herbst-Irmer, R., Sheldrick, G. M., Stalke, D. (2015). "Comparison of silver and molybdenum microfocus X-ray sources for single-crystal structure determination" J. Appl. Cryst. 48, 3-10.
[4] Sheldrick, G. M. (2015). "SHELXT - Integrated space-group and crystal-structure determination", Acta Cryst. A71, 3-8.
[5] Sheldrick, G. M. (2015) "Crystal structure refinement with SHELXL", Acta Cryst., C71, 3-8
[6] Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J.A.K.; Puschmann, H., OLEX2: A complete structure solution, refinement and analysis program (2009). J. Appl. Cryst., 42, 339-341
[7] Spek, A. L. (2009). "Structure validation in chemical crystallography", Acta Cryst. D65, 148-155.

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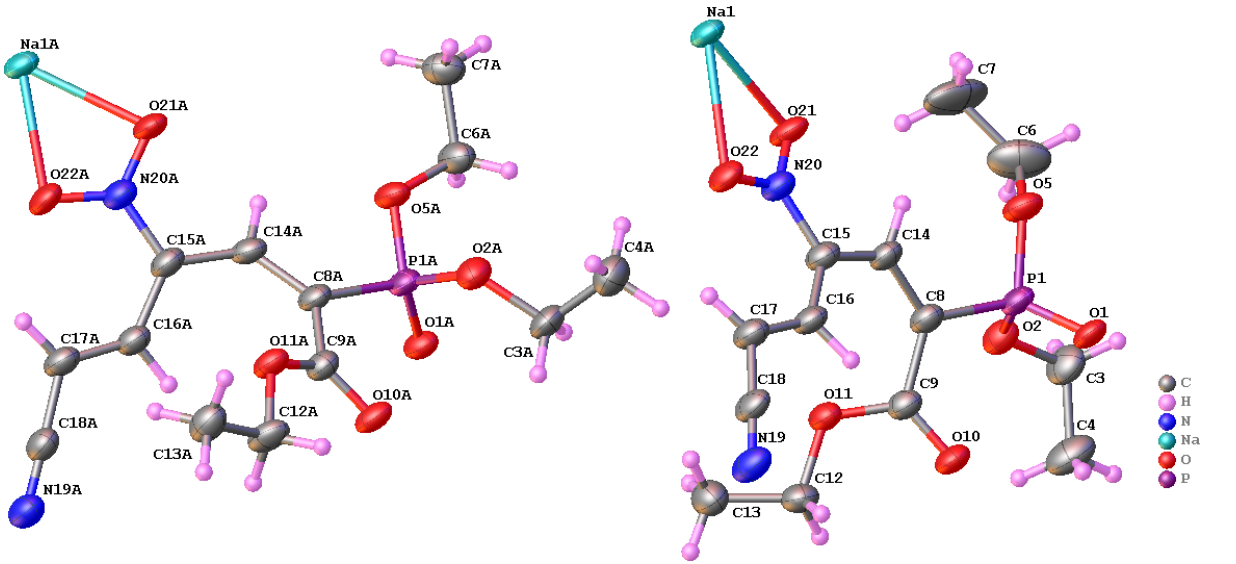

Figure S2. Asymmetric unit of JL_ZS1_837_2_tw_4. Anisotropic displacement parameters were drawn at 50% probability level.

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Table S2. Crystal data and structure refinement for JL_ZS1_837_2_tw_4 (**50**).	
Identification code	JL_ZS1_837_2_tw_4
Empirical formula	$C_{13}H_{18}N_2NaO_7P$
Formula weight	368.25
Temperature/K	100.0
Crystal system	triclinic
Space group	P-1
a/Å	9.3192(3)
b/Å	11.1085(4)
c/Å	18.3315(6)
α/°	85.750(2)
β/°	88.791(2)
γ/°	66.538(2)
Volume/Å^3	1735.96(10)
Z	4
ρ_{calc}g/cm^3	1.409
μ/mm^{-1}	1.999
F(000)	768.0
Crystal size/mm^3	0.33 × 0.13 × 0.03
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	4.834 to 133.788
Index ranges	-11 ≤ h ≤ 11, -13 ≤ k ≤ 13, 0 ≤ l ≤ 21
Reflections collected	6147
Independent reflections	6147 [R_{int} = 0.0946, R_{sigma} = 0.0622]
Data/restraints/parameters	6147/3/439
Goodness-of-fit on F^2	1.044
Final R indexes [I>=2σ (I)]	R_1 = 0.0752, wR_2 = 0.2218
Final R indexes [all data]	R_1 = 0.0887, wR_2 = 0.2288

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