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2021

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Verónica Juste Navarro

Síntesis de pirrolidinas quirales. Aplicación al diseño de inhibidores de glicosiltranferasas Anexos

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Merino Filella, Pedro

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Tesis Doctoral

SÍNTESIS DE PIRROLIDINAS QUIRALES. APLICACIÓN AL DISEÑO DE INHIBIDORES DE GLICOSILTRANFERASAS
ANEXOS

Autor

Verónica Juste Navarro

Director/es

Tejero López, Tomás
Merino Filella, Pedro

UNIVERSIDAD DE ZARAGOZA
Escuela de Doctorado

2019

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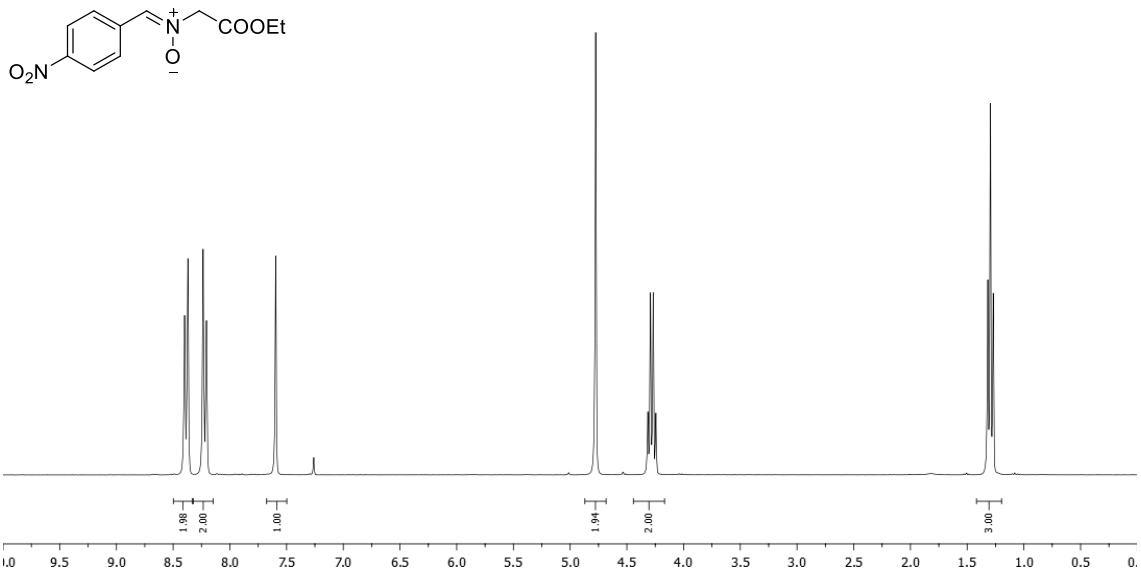

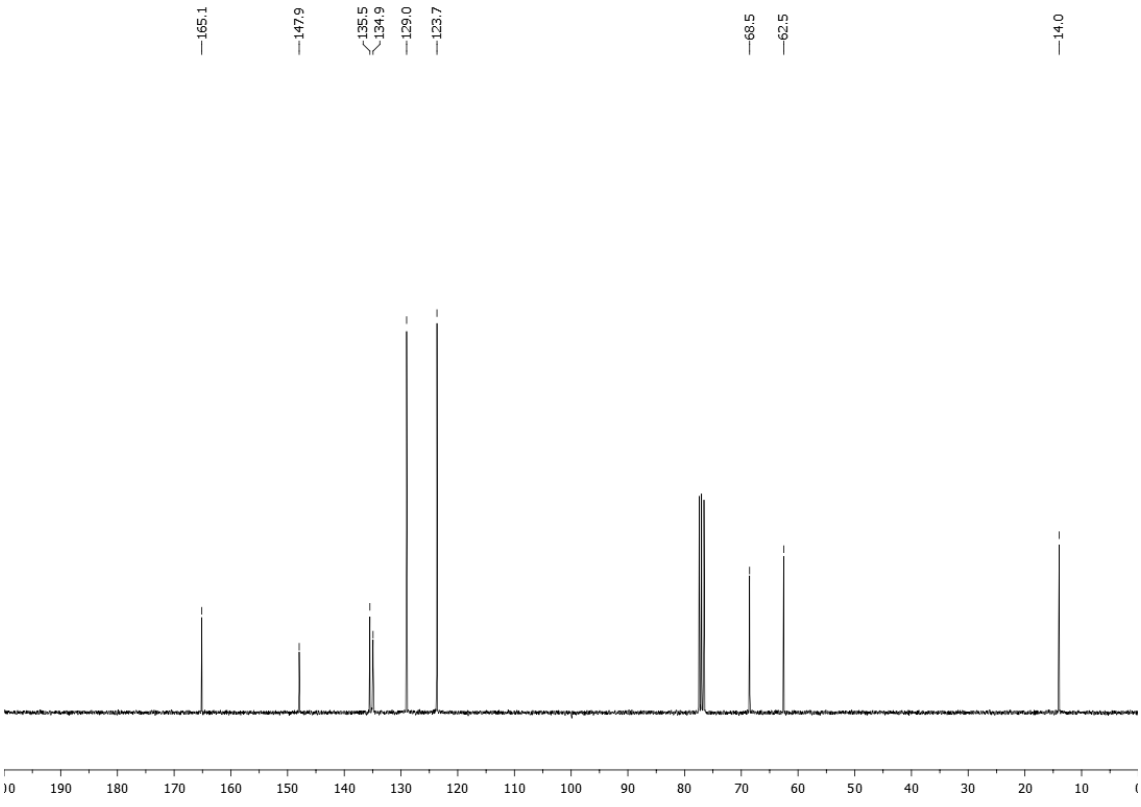

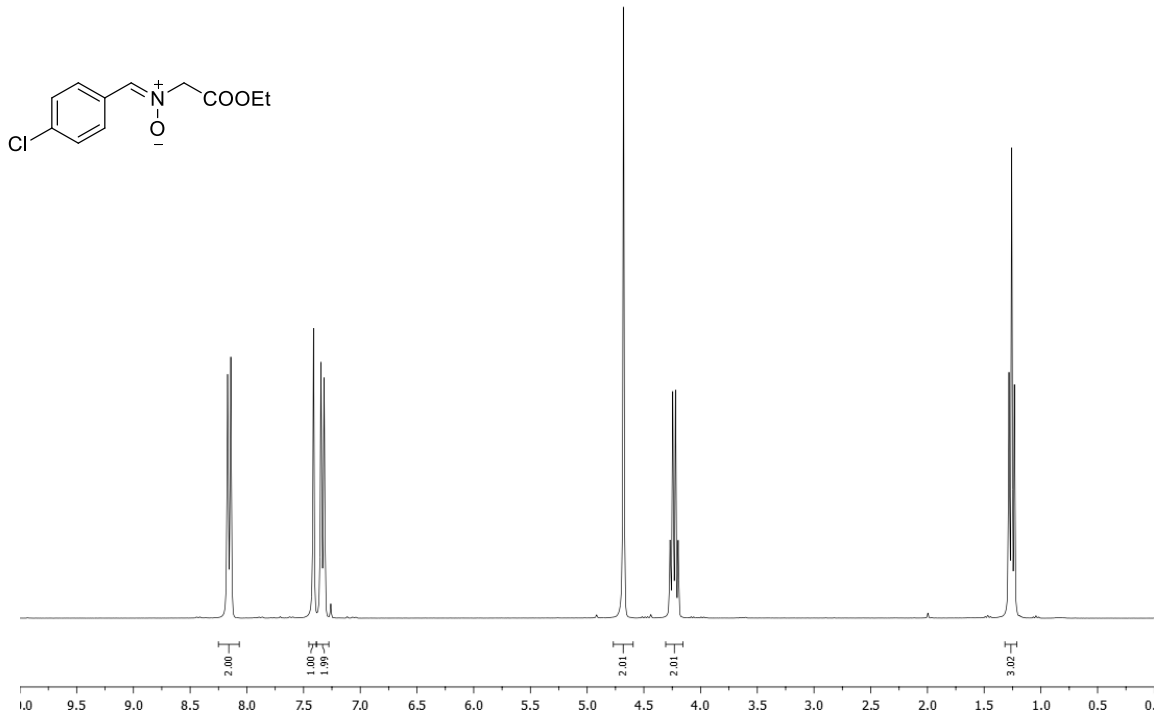
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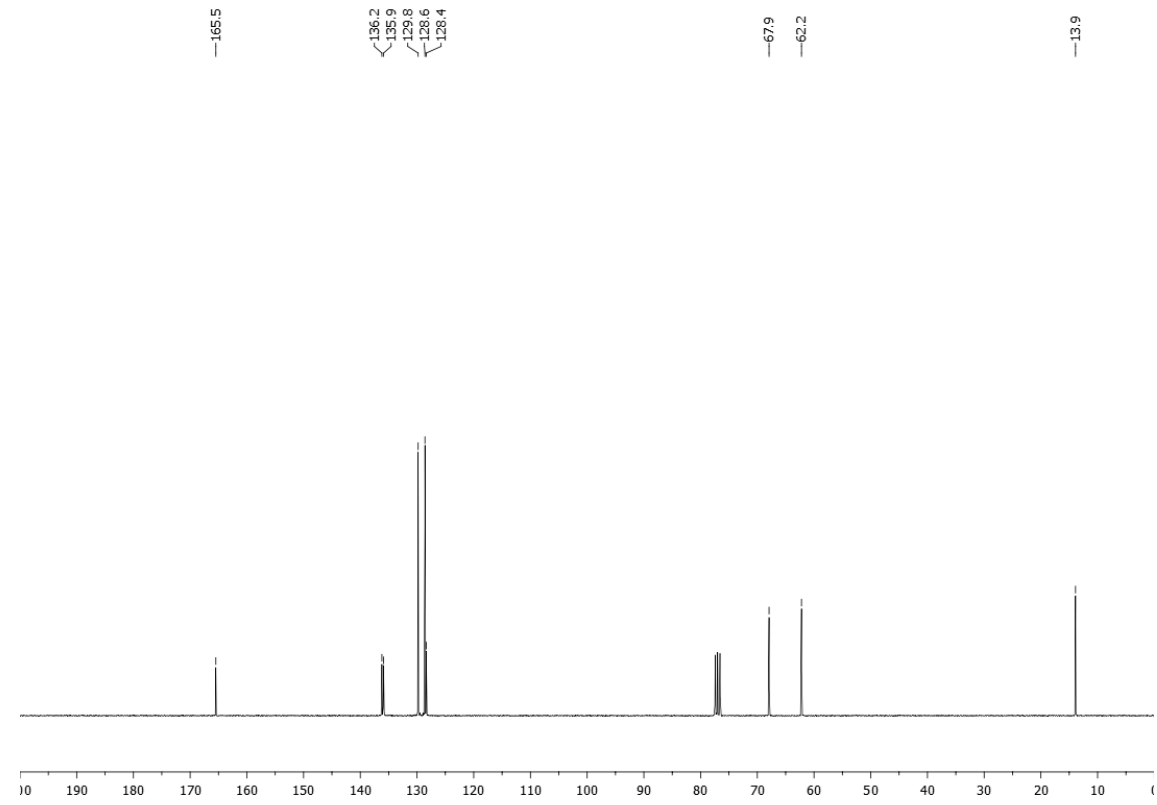
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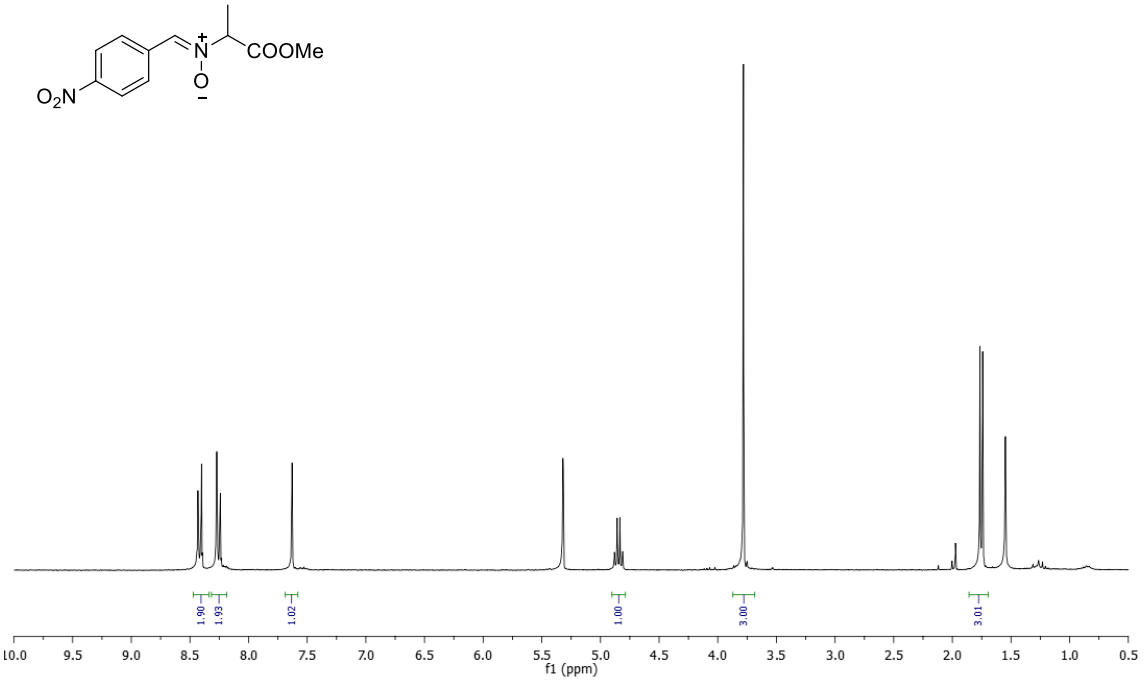
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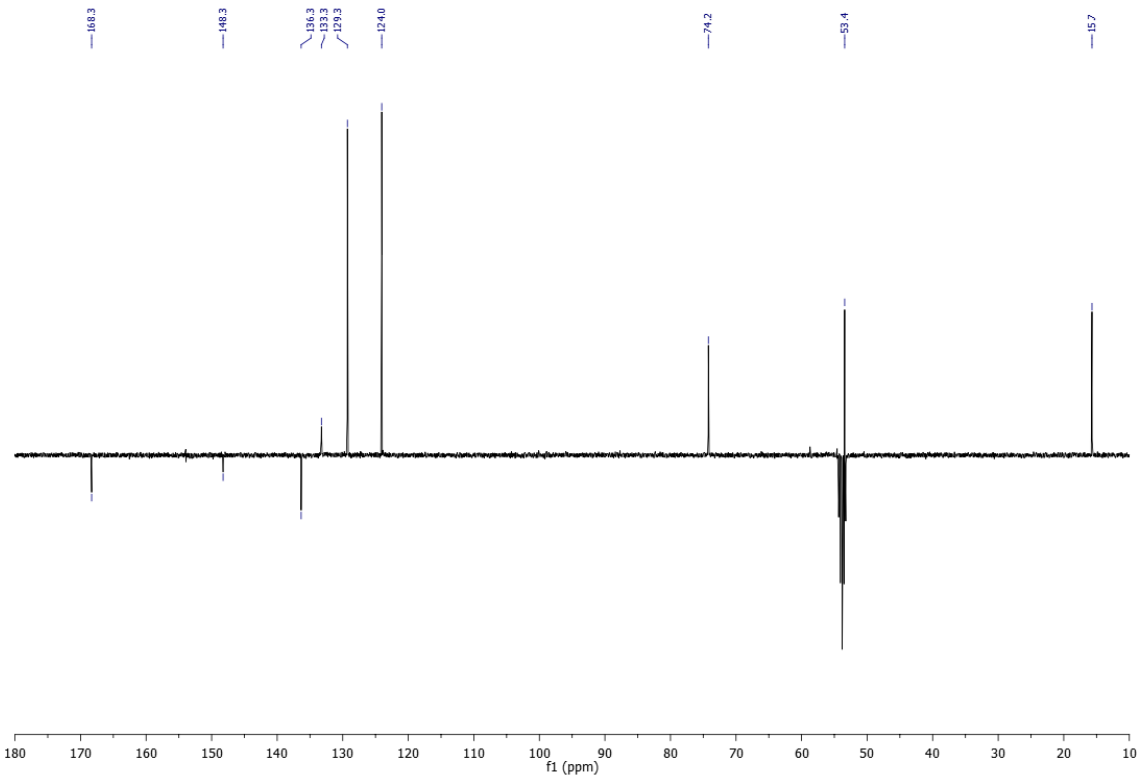
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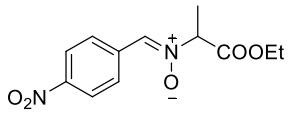
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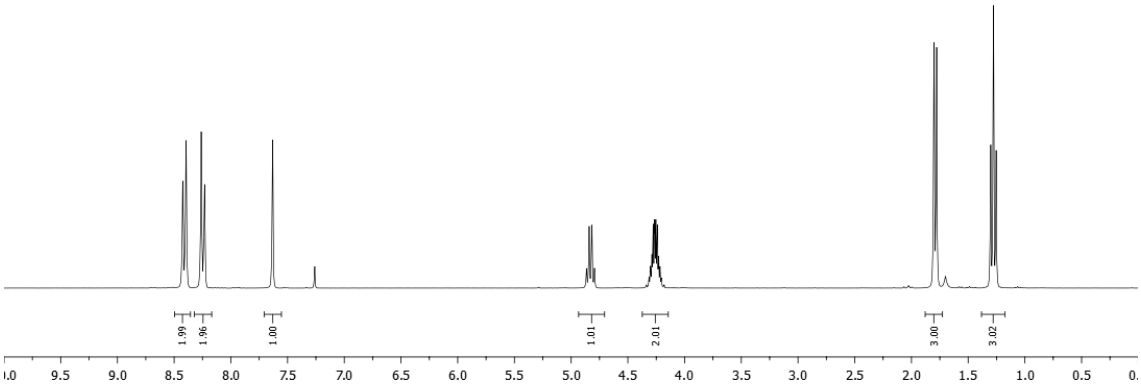
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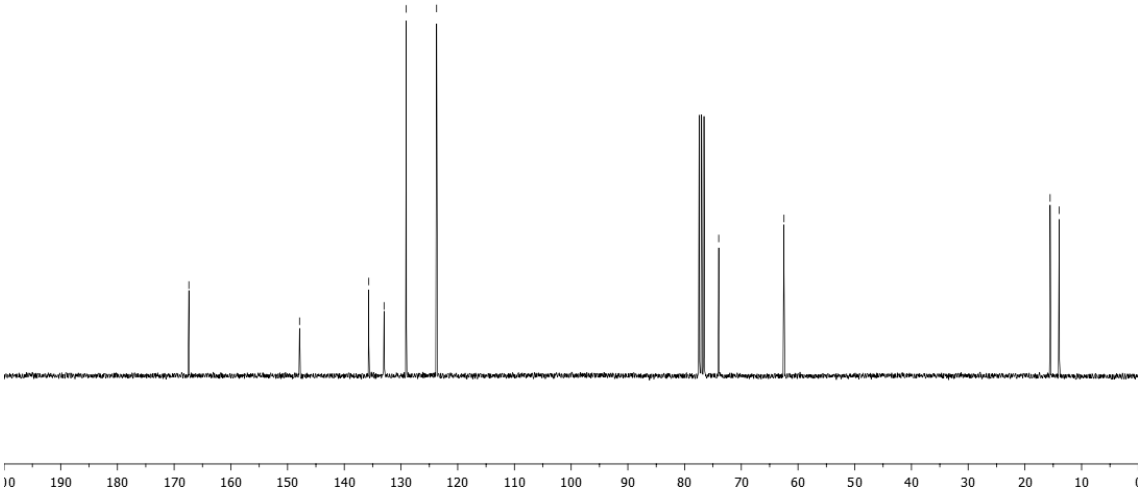
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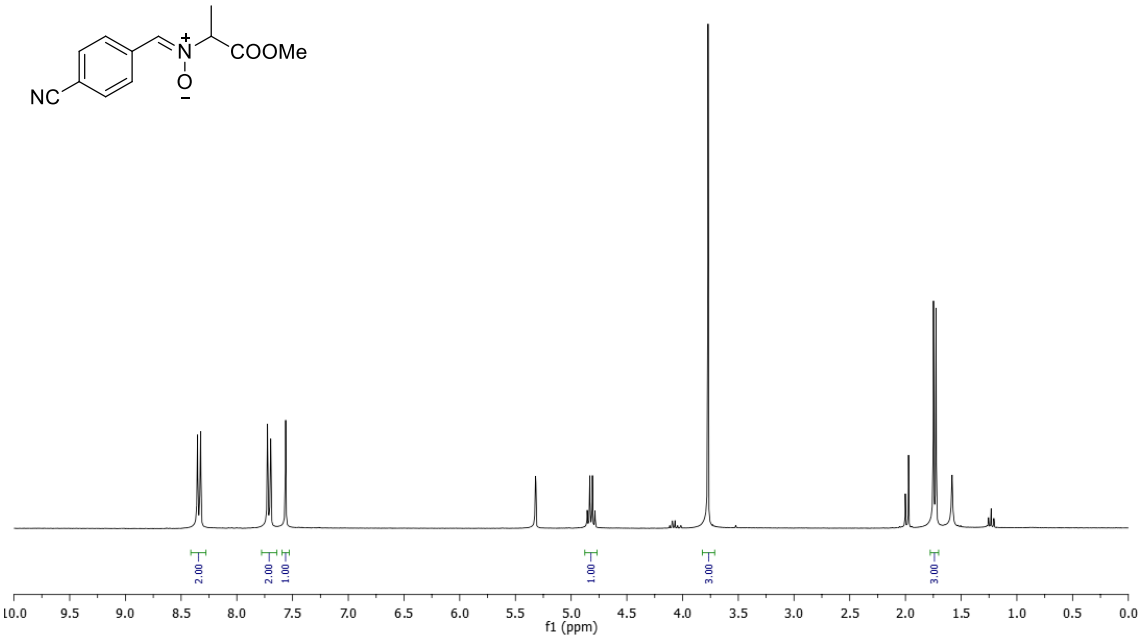
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O
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3.00
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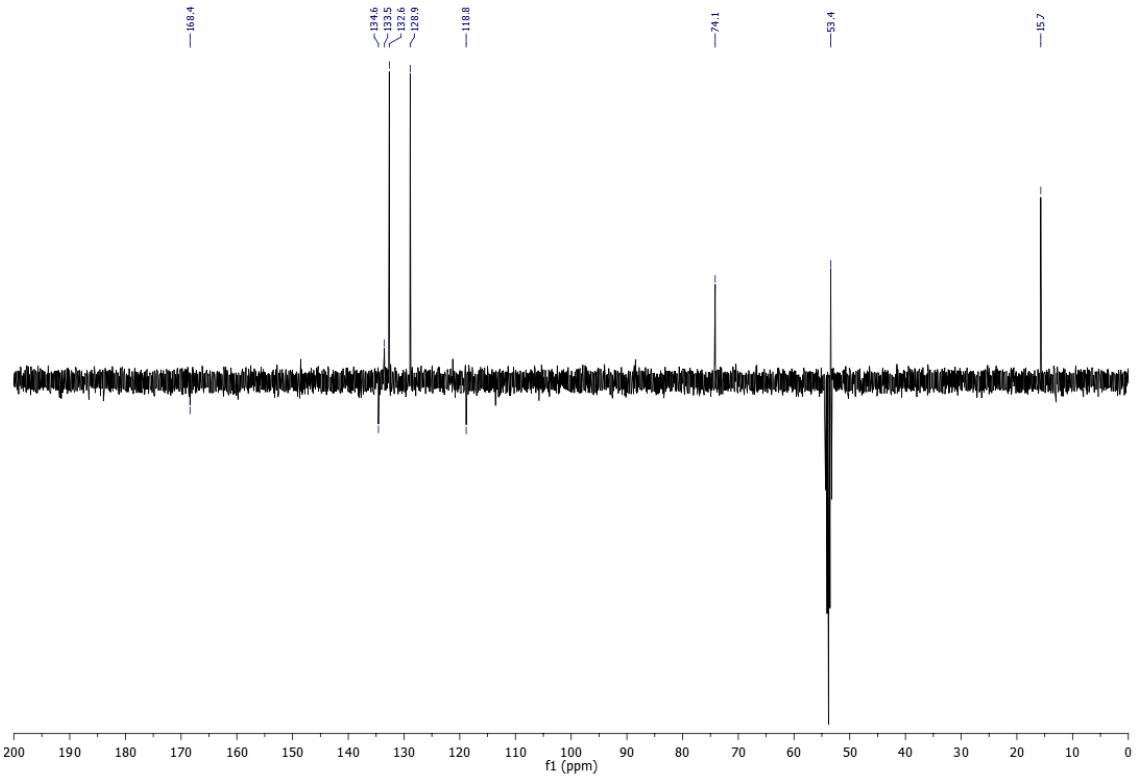
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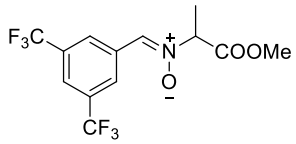
f1 (ppm)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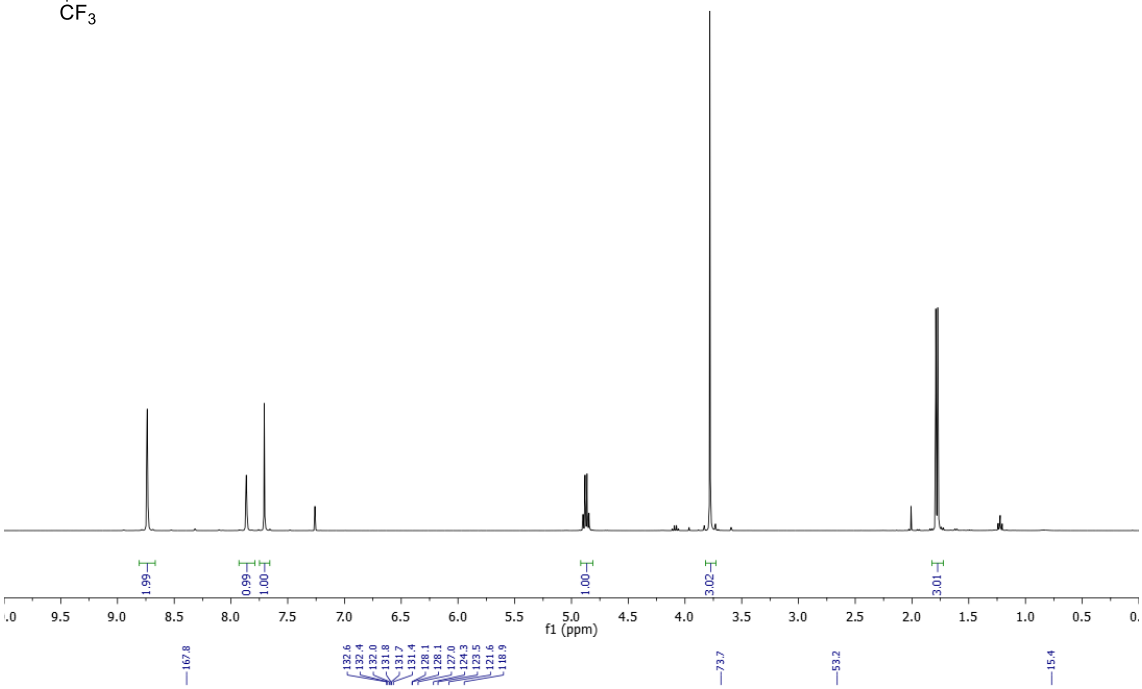
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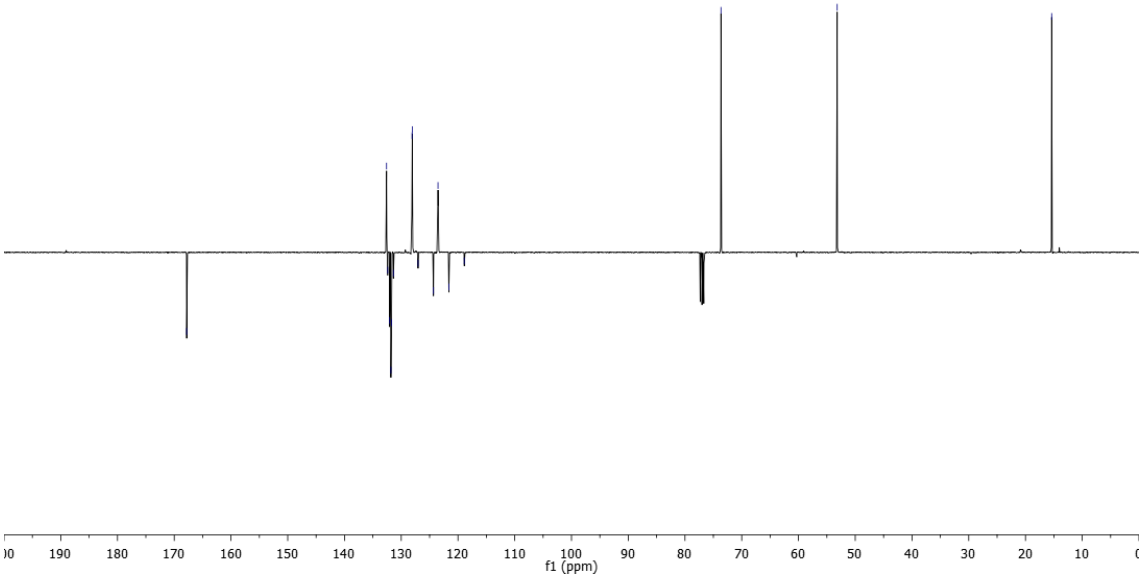
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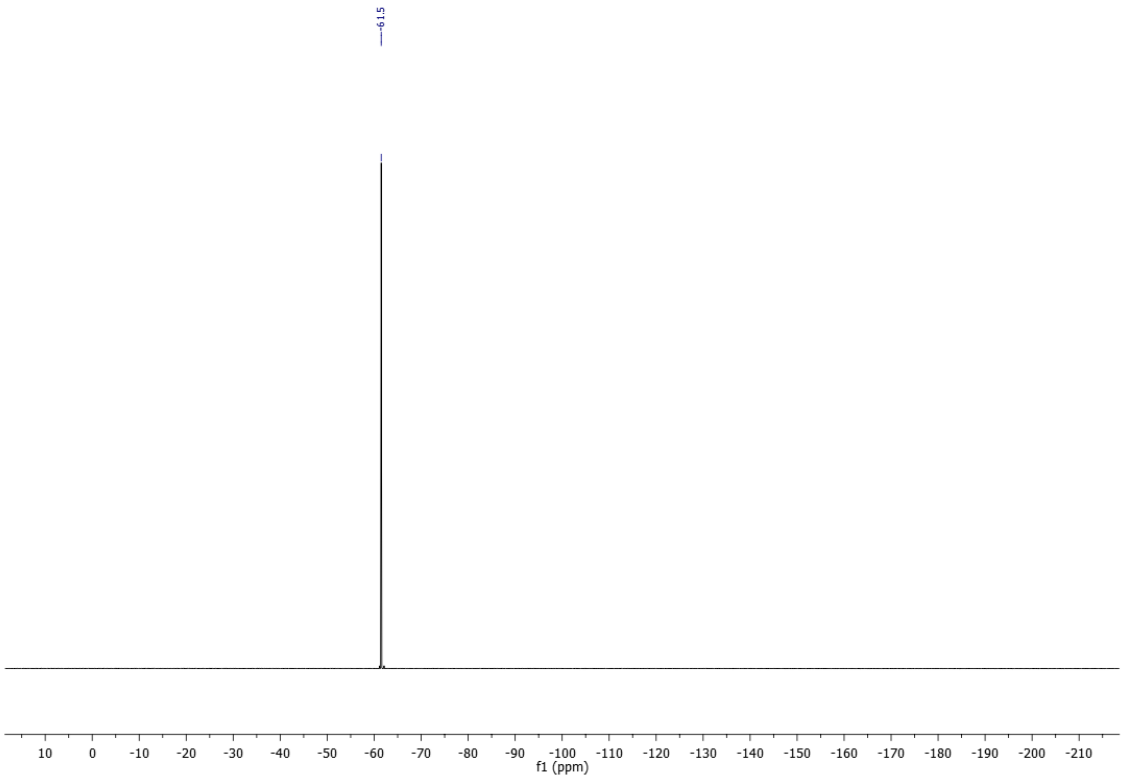
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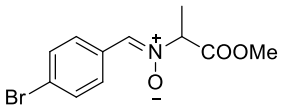
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N
O
COOMe

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3.00
3.01
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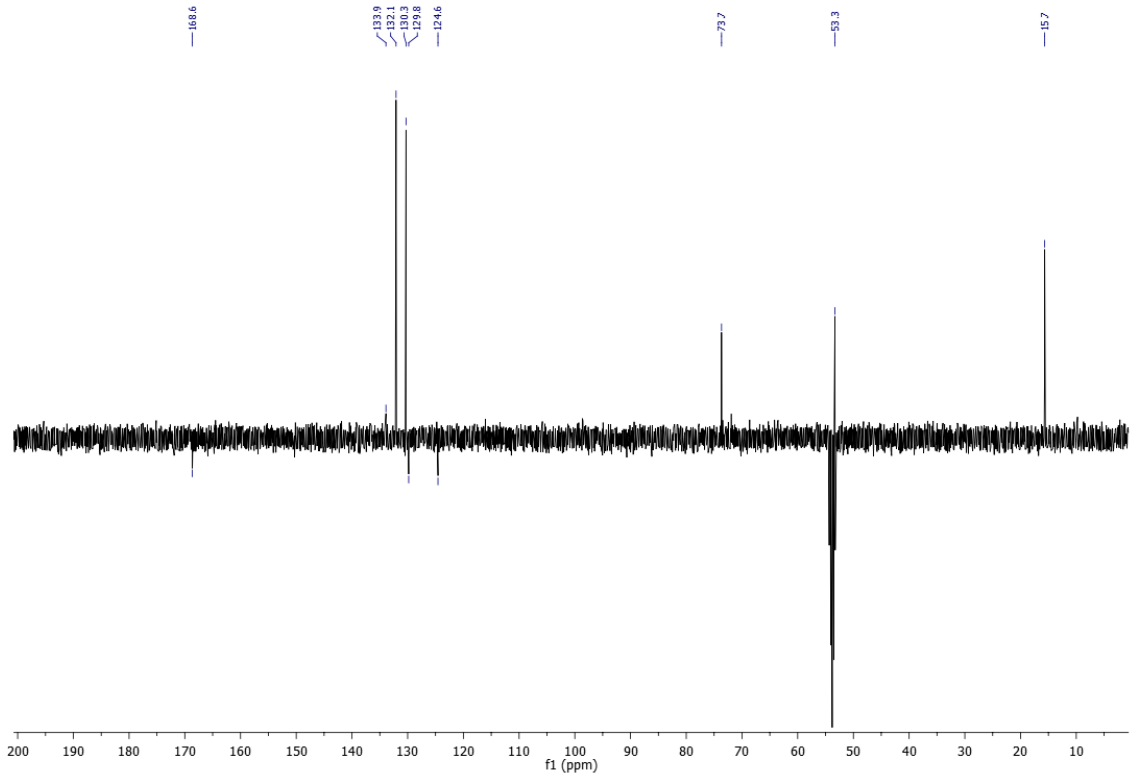
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15.7
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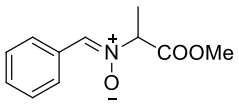
f1 (ppm)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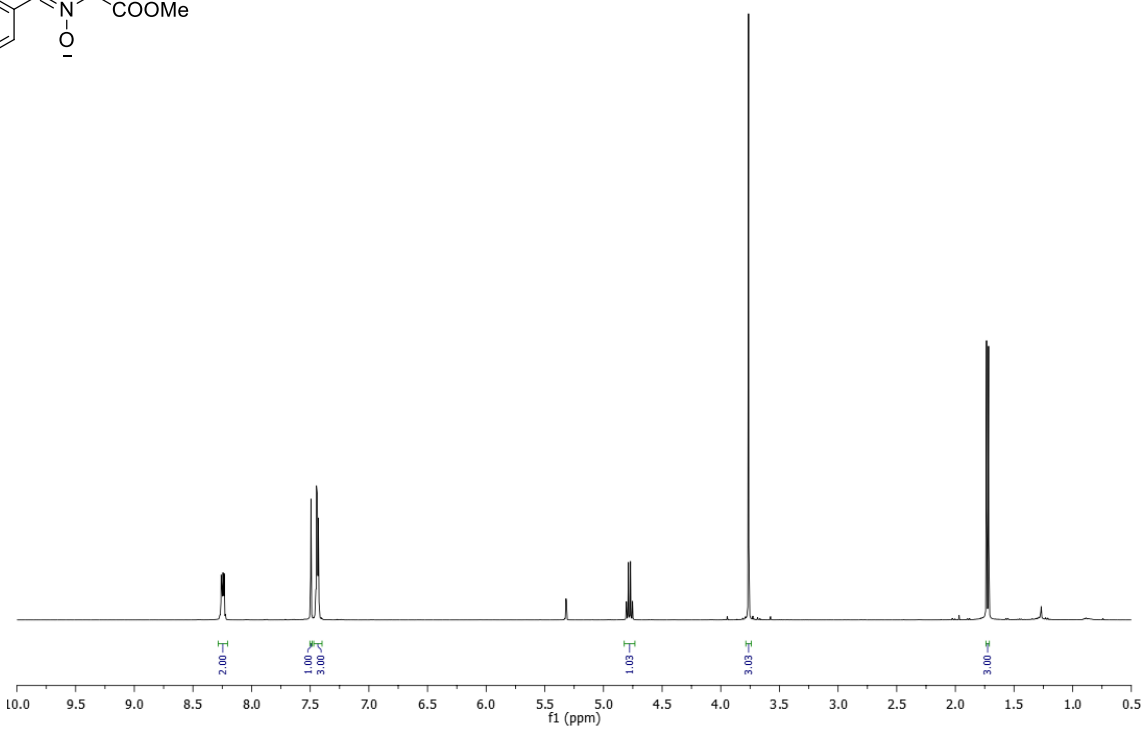
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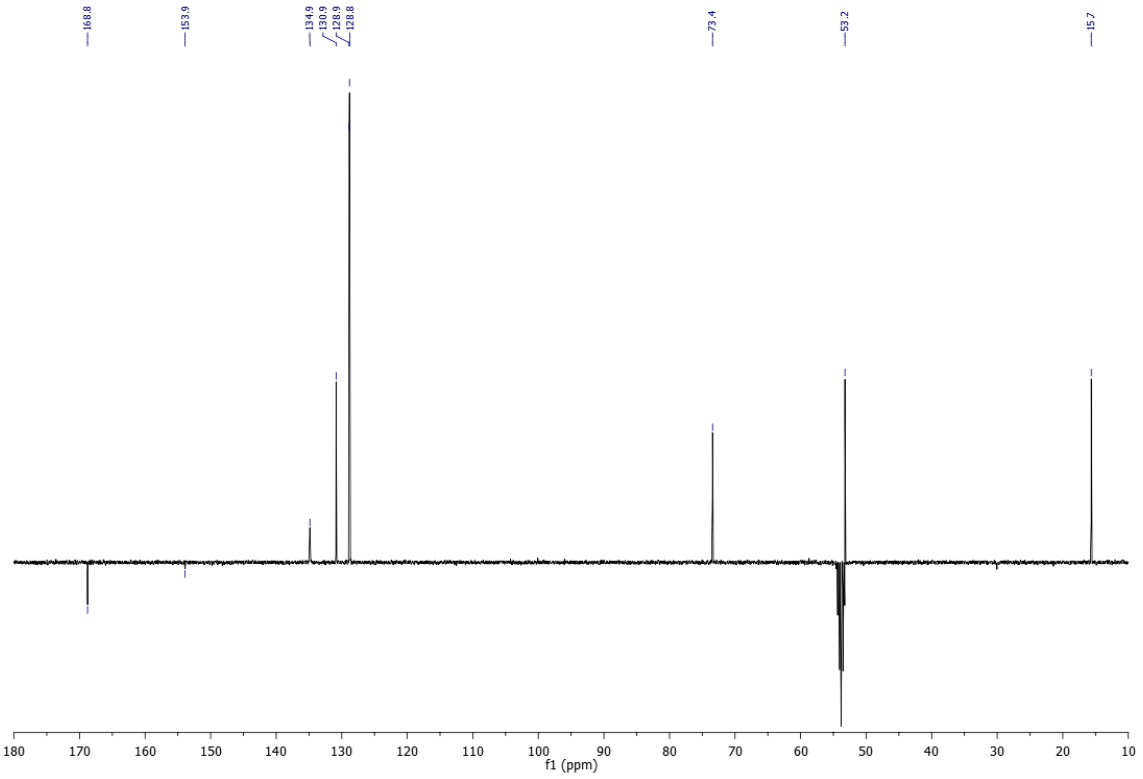
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128.9
128.8
73.4
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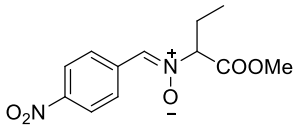
15.7
f1 (ppm)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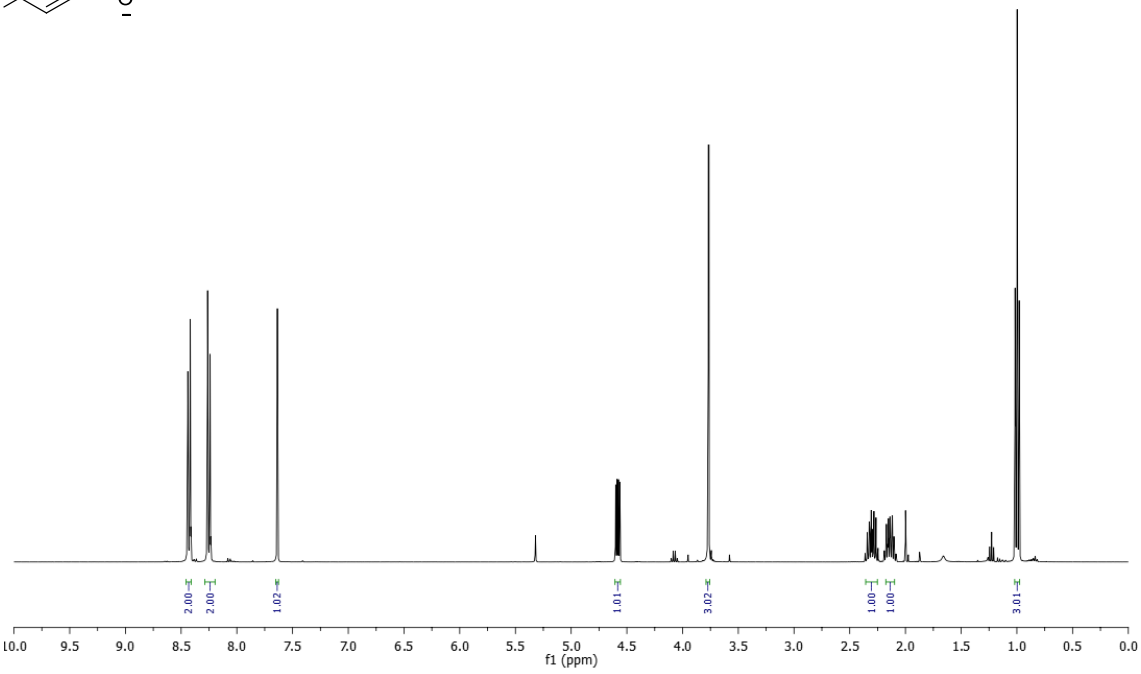
N
O
COOMe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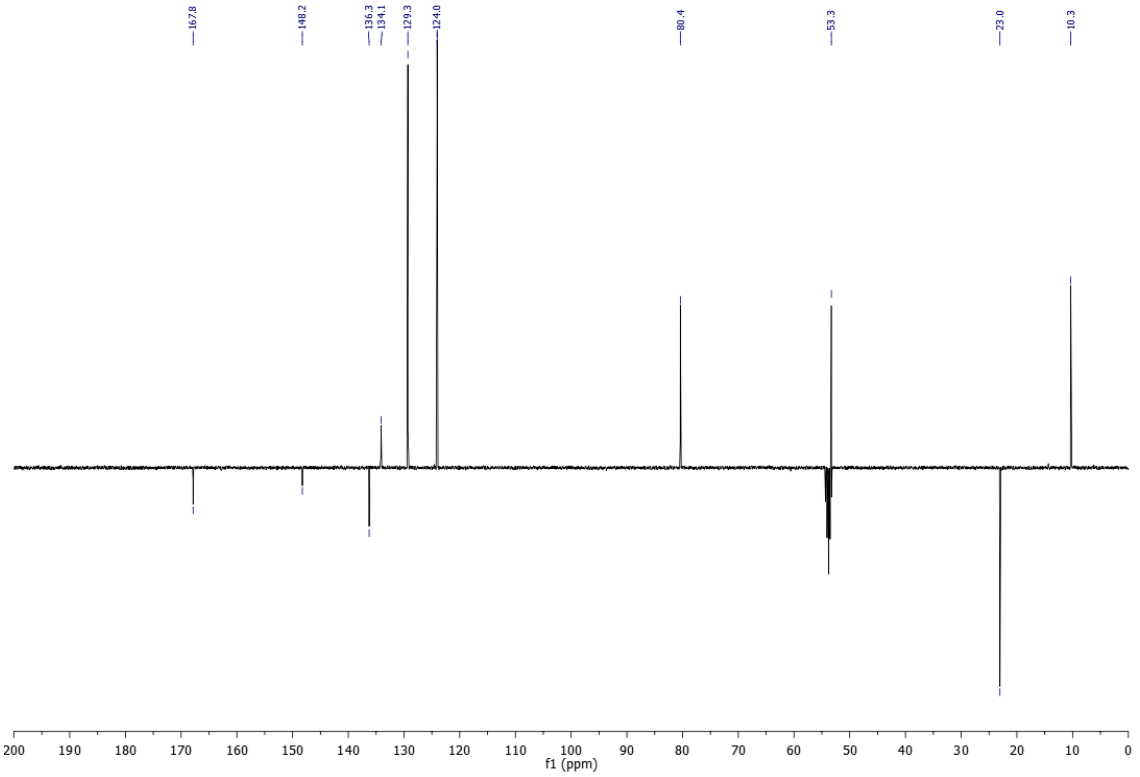
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134.1
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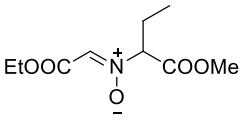
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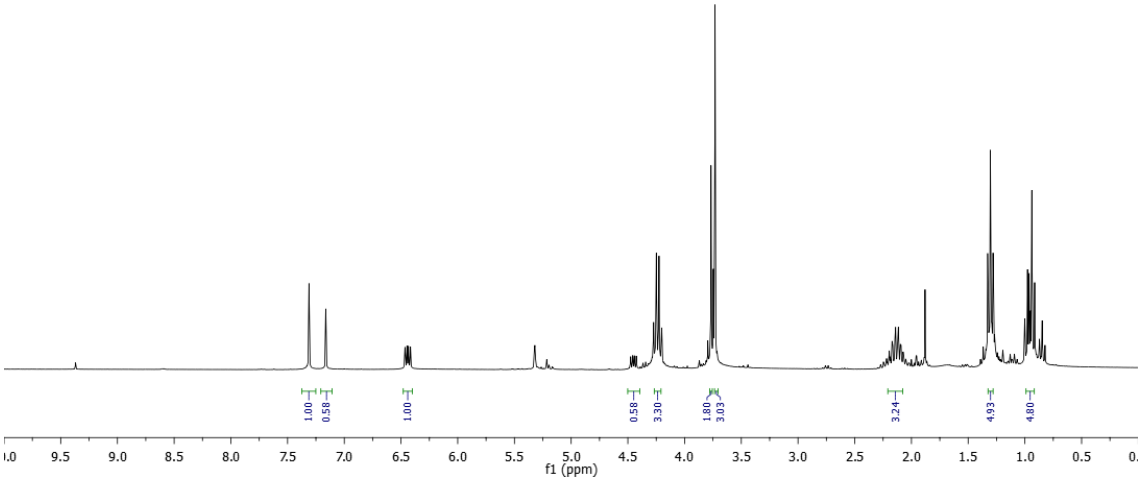
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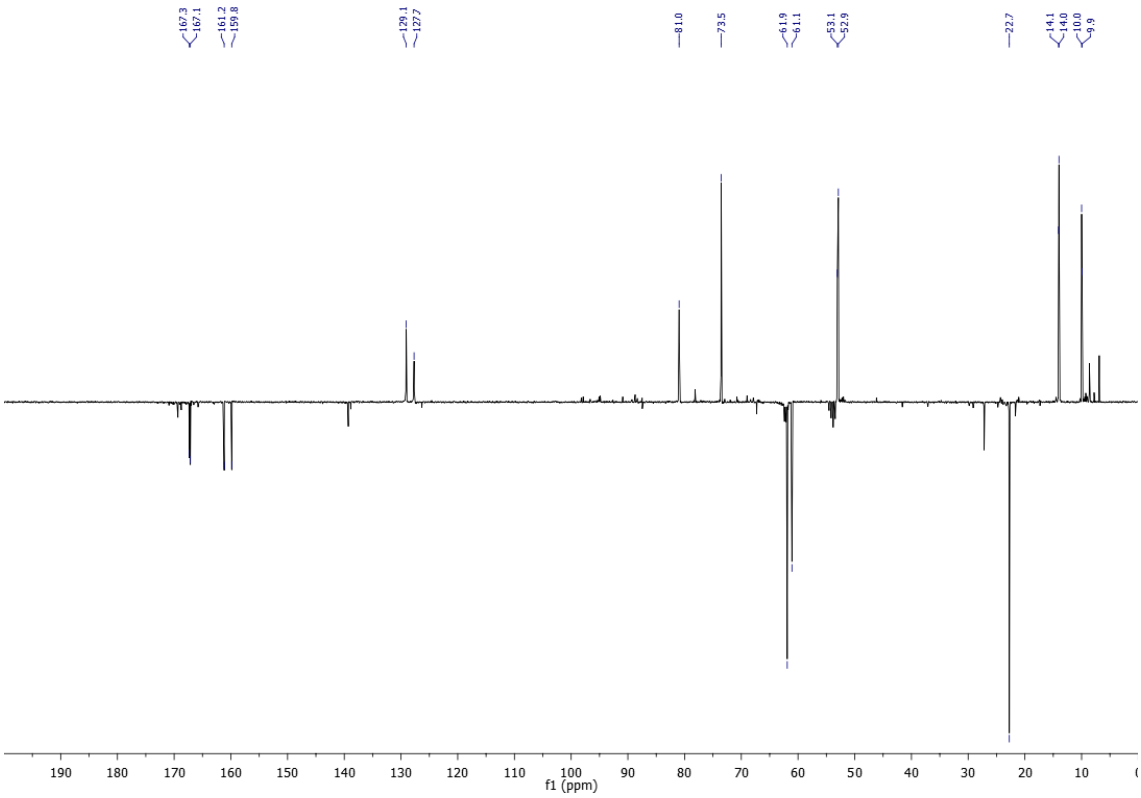
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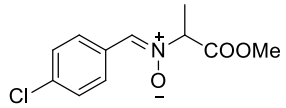
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COOMe

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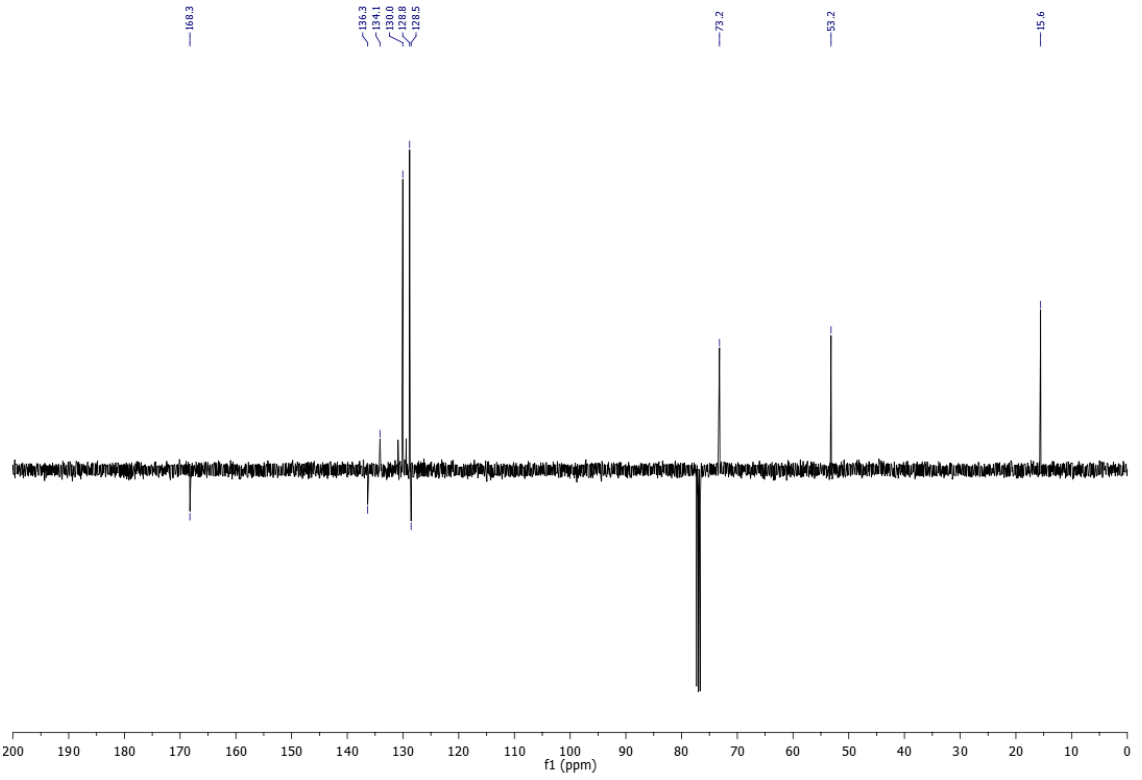
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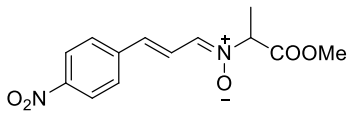
f1 (ppm)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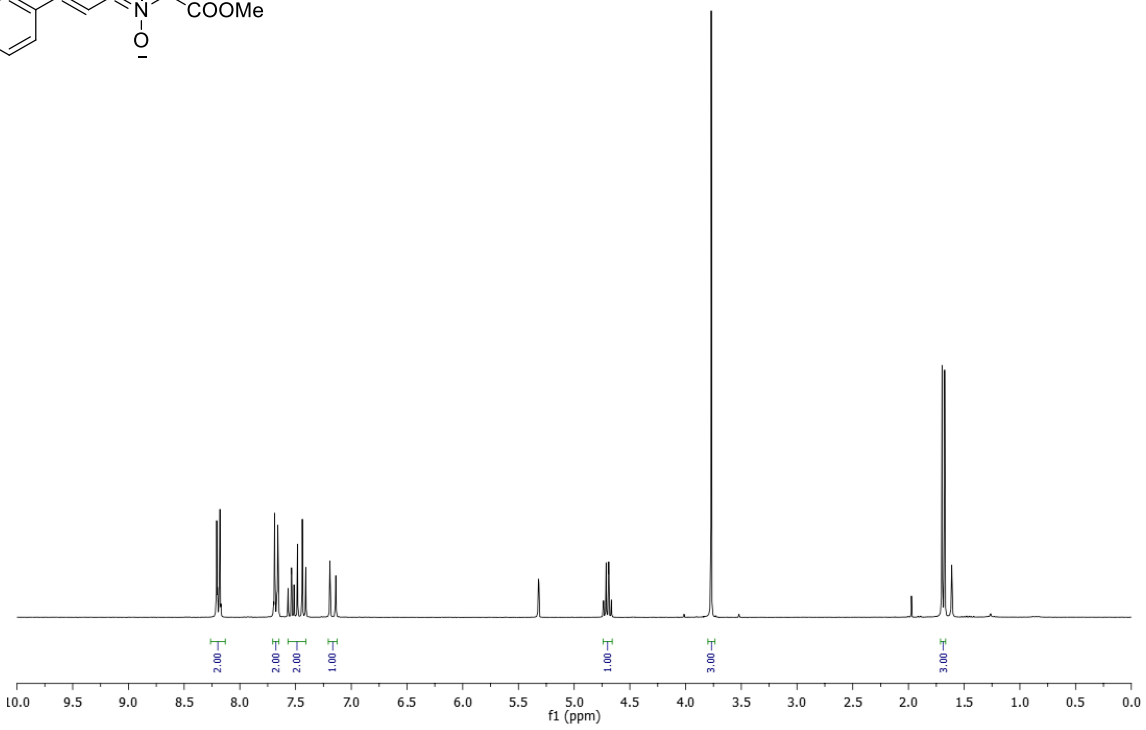
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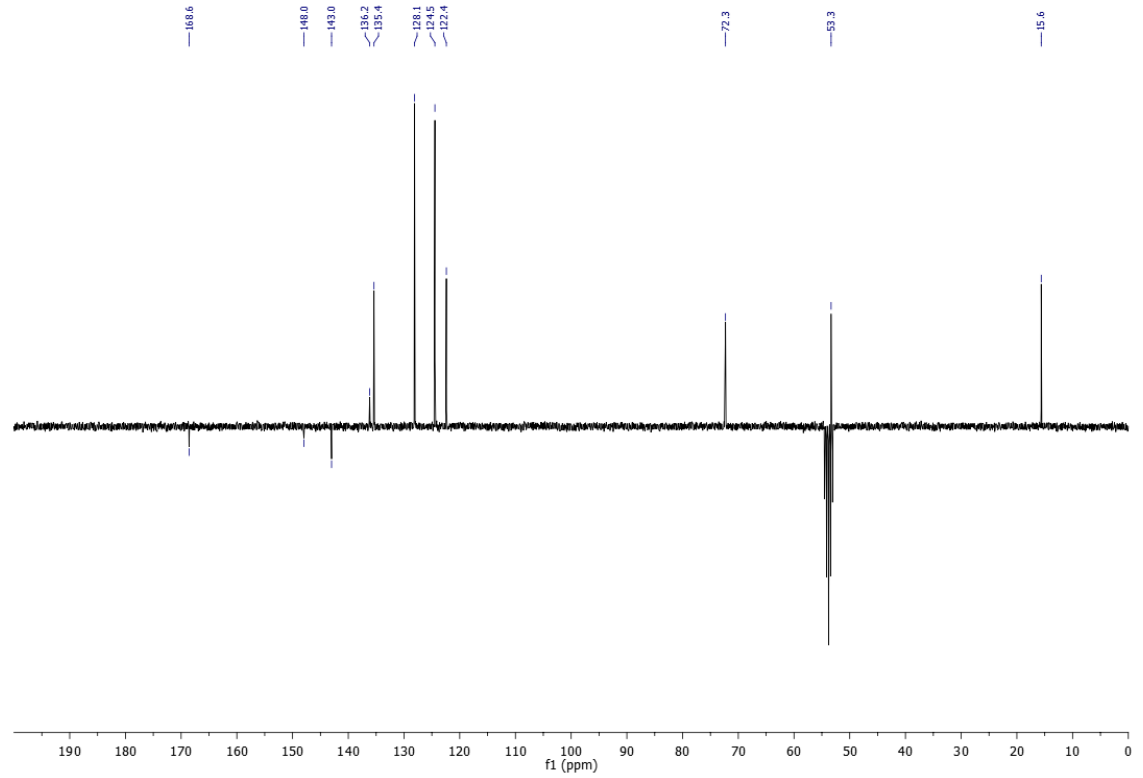
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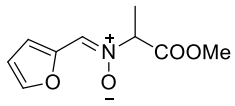
COOMe
O
N
O

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1.00
1.00
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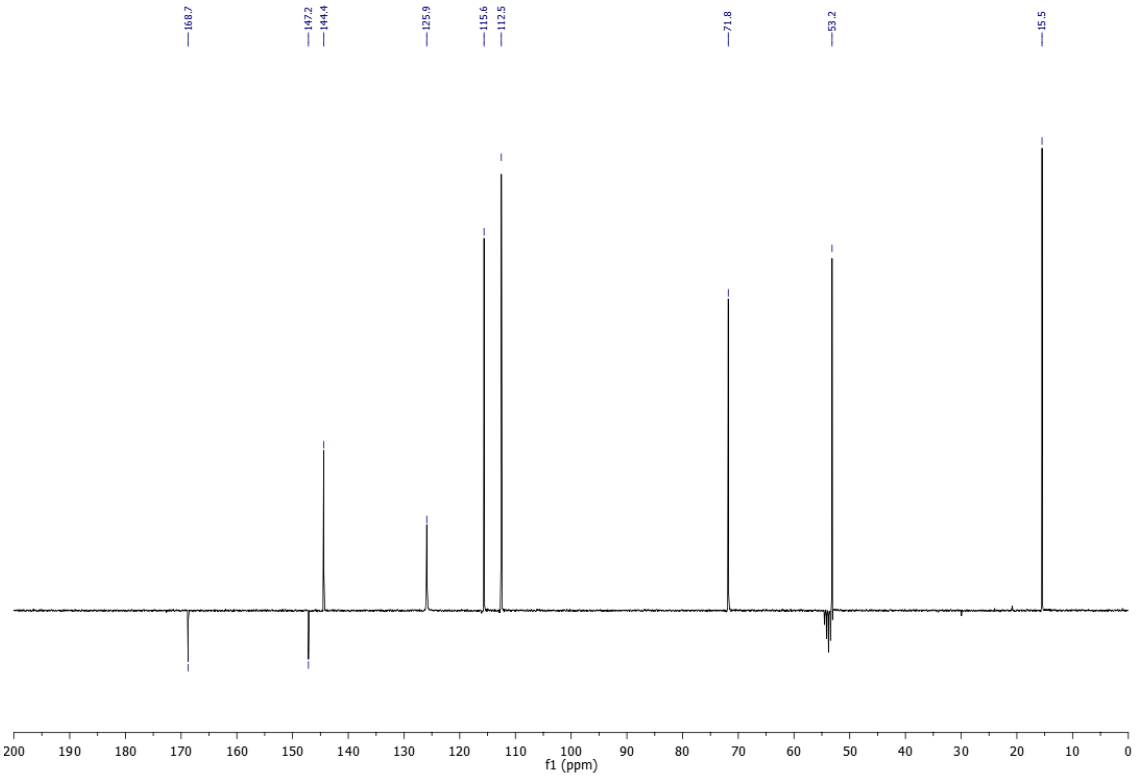
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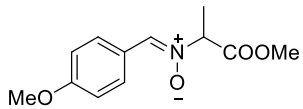
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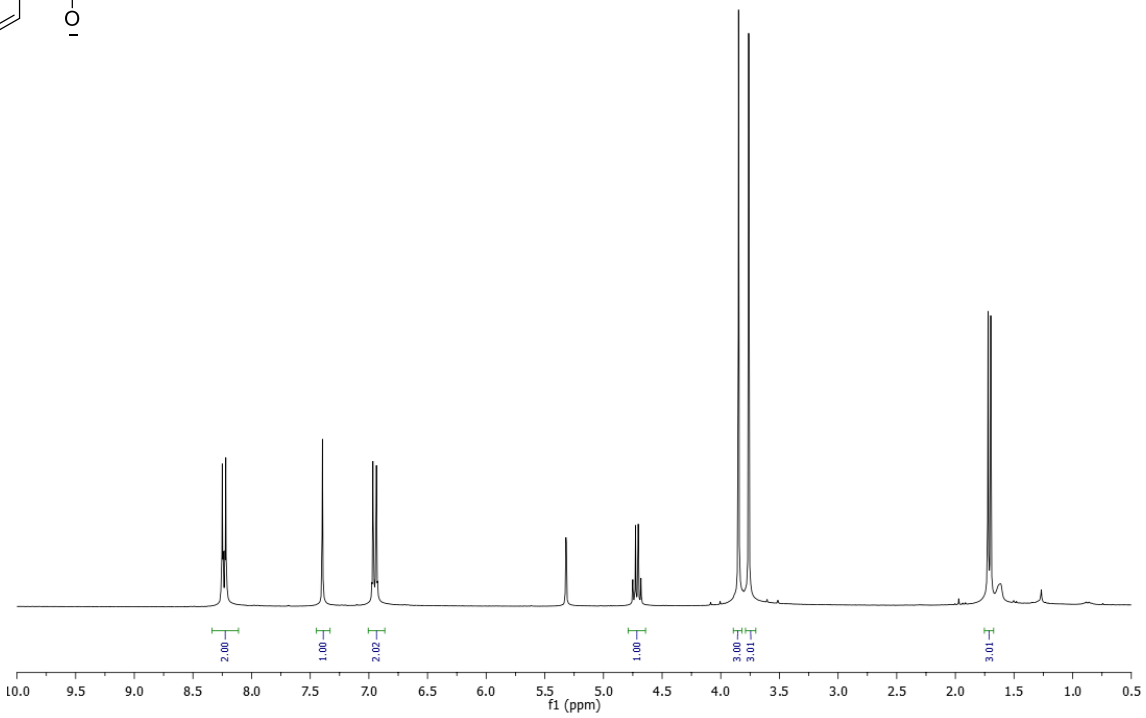
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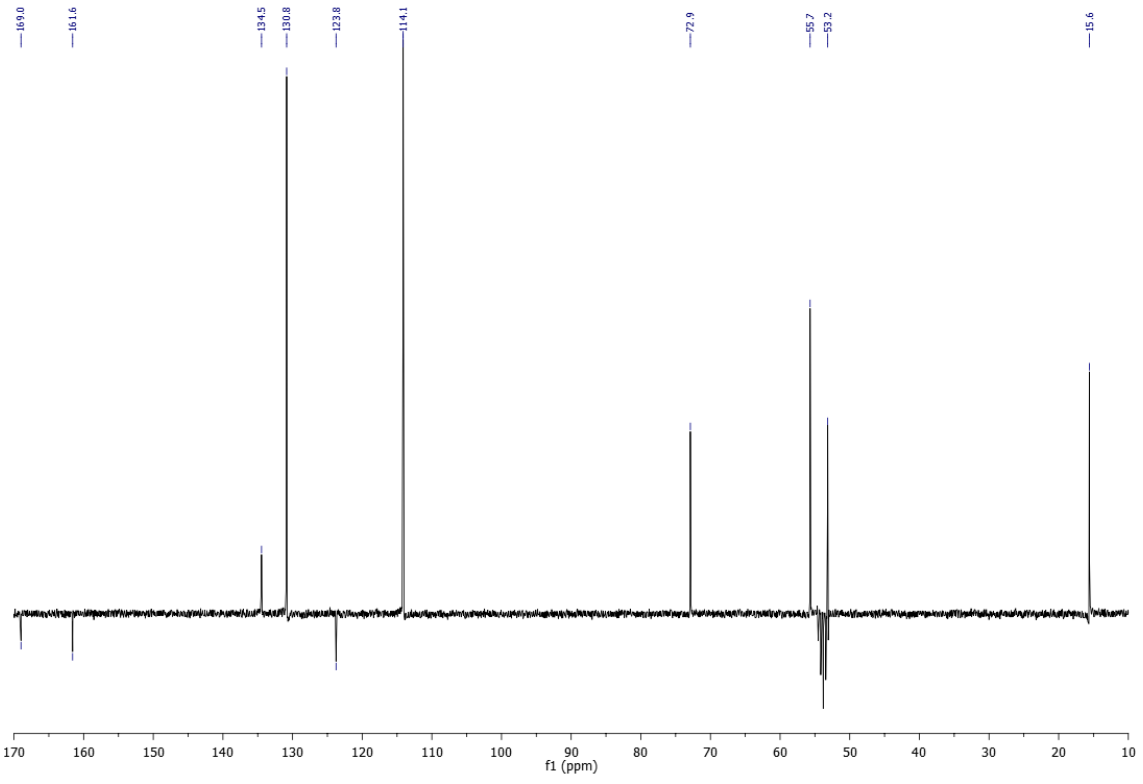
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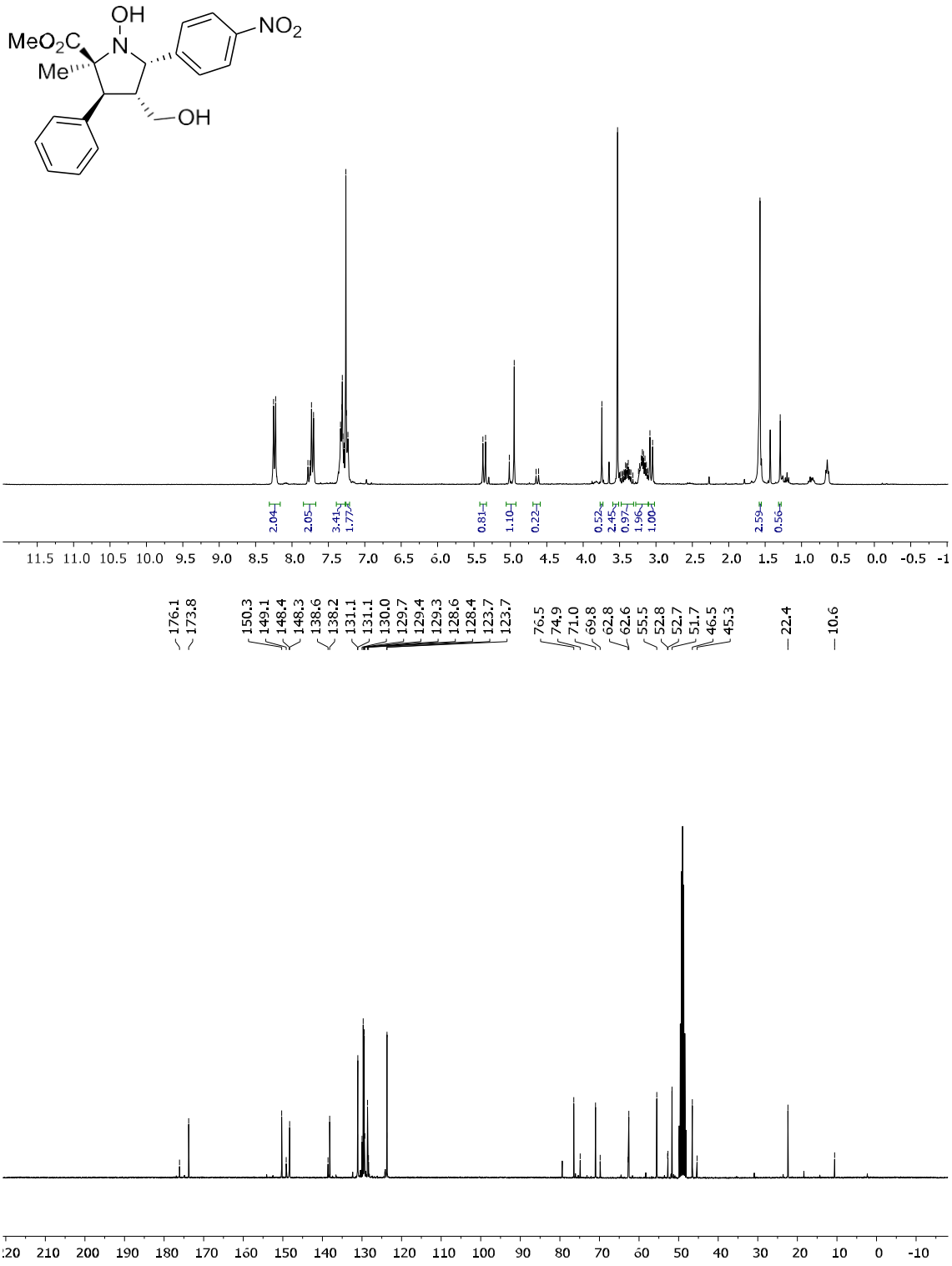
15.6
f1 (ppm)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MeO2C
N
NO2
Me
OH
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2.05
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1.77
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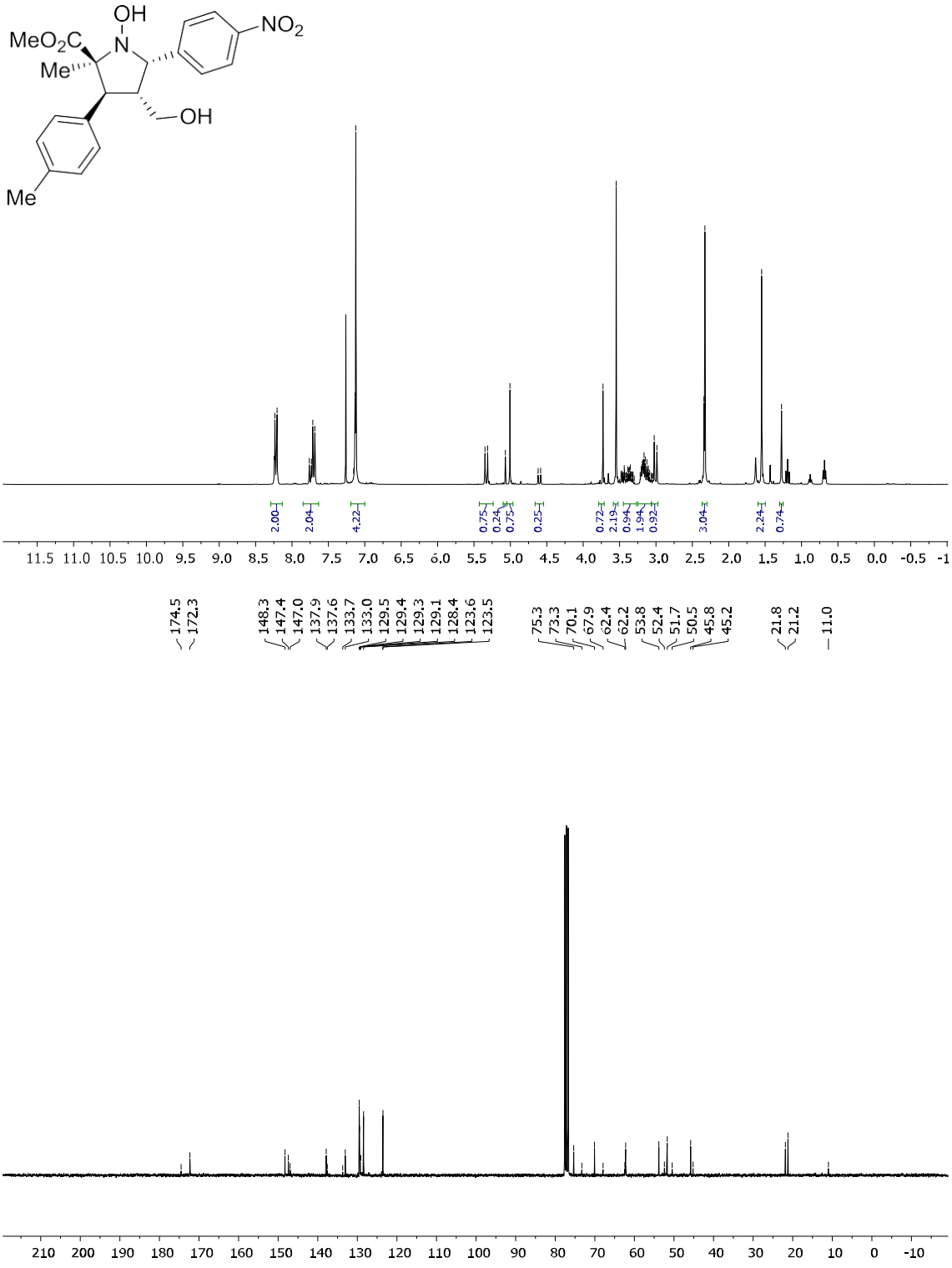
1.10
0.22
0.52
2.45
0.97
1.96
1.00
2.59
0.56
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
176.1
173.8
150.3
149.1
148.4
148.3
138.6
138.2
131.1
131.1
130.0
129.7
129.4
129.3
128.6
128.4
123.7
123.7
76.5
74.9
71.0
69.8
62.8
62.6
55.5
52.8
52.7
51.7
46.5
45.3
22.4
10.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10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MeO2C
N
NO2
Me
OH
Me
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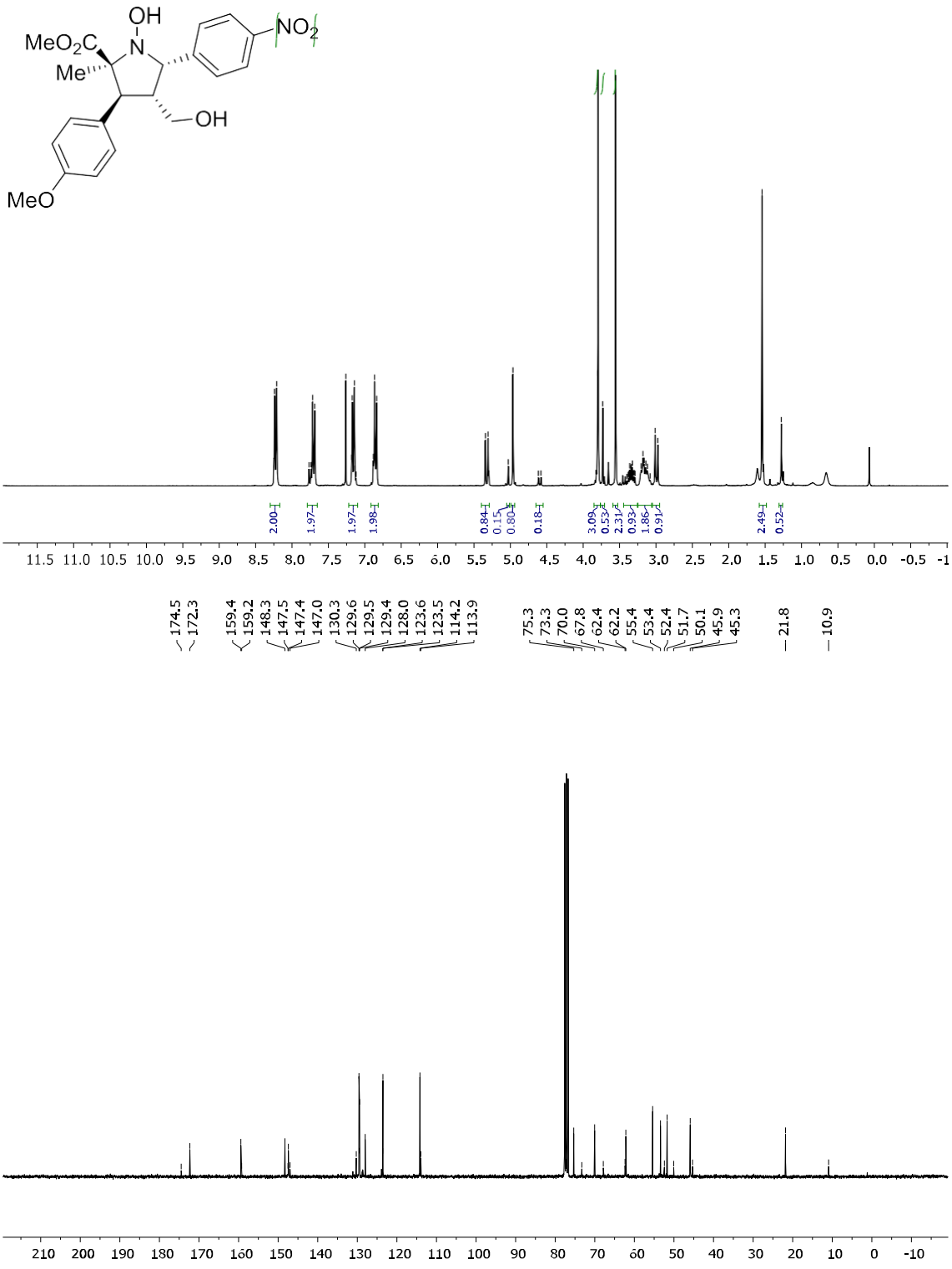
2.04
4.22
0.75
0.24
0.75
0.25
0.72
2.19
0.94
1.94
0.92
3.04
2.24
0.74
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
174.5
172.3
148.3
147.4
147.0
137.9
137.6
133.7
133.0
129.5
129.4
129.3
129.1
128.4
123.6
123.5
75.3
73.3
70.1
67.9
62.4
62.2
53.8
52.4
51.7
50.5
45.8
45.2
21.8
21.2
11.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10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MeO2C
N
NO2
Me
OH
MeO
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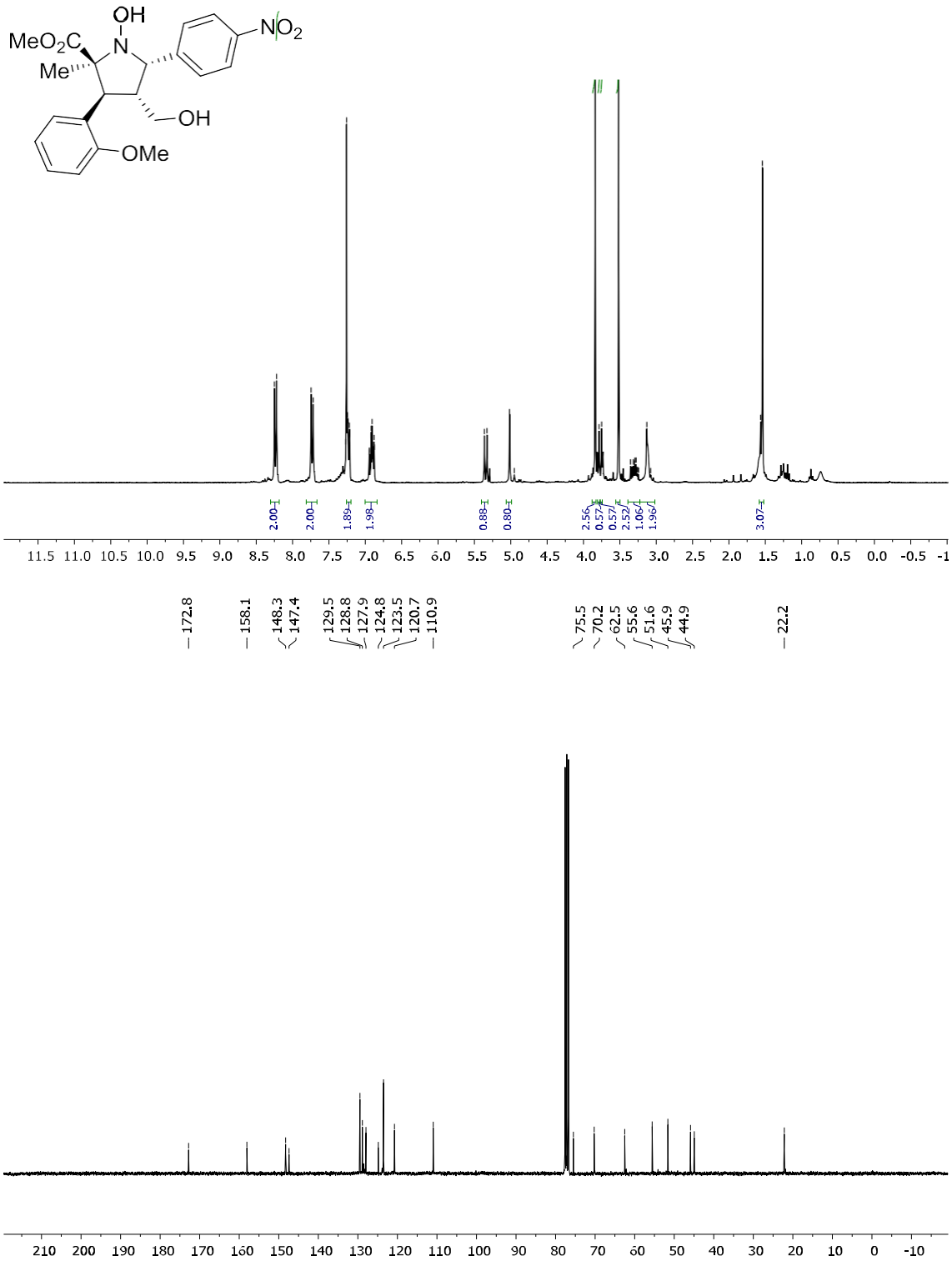
1.97
1.98
0.84
0.15
0.80
0.18
3.09
0.53
2.31
0.93
1.86
0.91
2.49
0.52
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
174.5
172.3
159.4
159.2
148.3
147.5
147.4
147.0
130.3
129.6
129.5
129.4
128.0
123.6
123.5
114.2
113.9
75.3
73.3
70.0
67.8
62.4
62.2
55.4
53.4
52.4
51.7
50.1
45.9
45.3
21.8
10.9
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10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N
MeO2C
Me
NO2
OH
OMe
2.00
2.00
1.89
1.98
0.88
0.80
2.56
0.57
0.57
2.52
1.06
1.96
3.07
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
172.8
158.1
148.3
147.4
129.5
128.8
127.9
124.8
123.5
120.7
110.9
75.5
70.2
62.5
55.6
51.6
45.9
44.9
22.2
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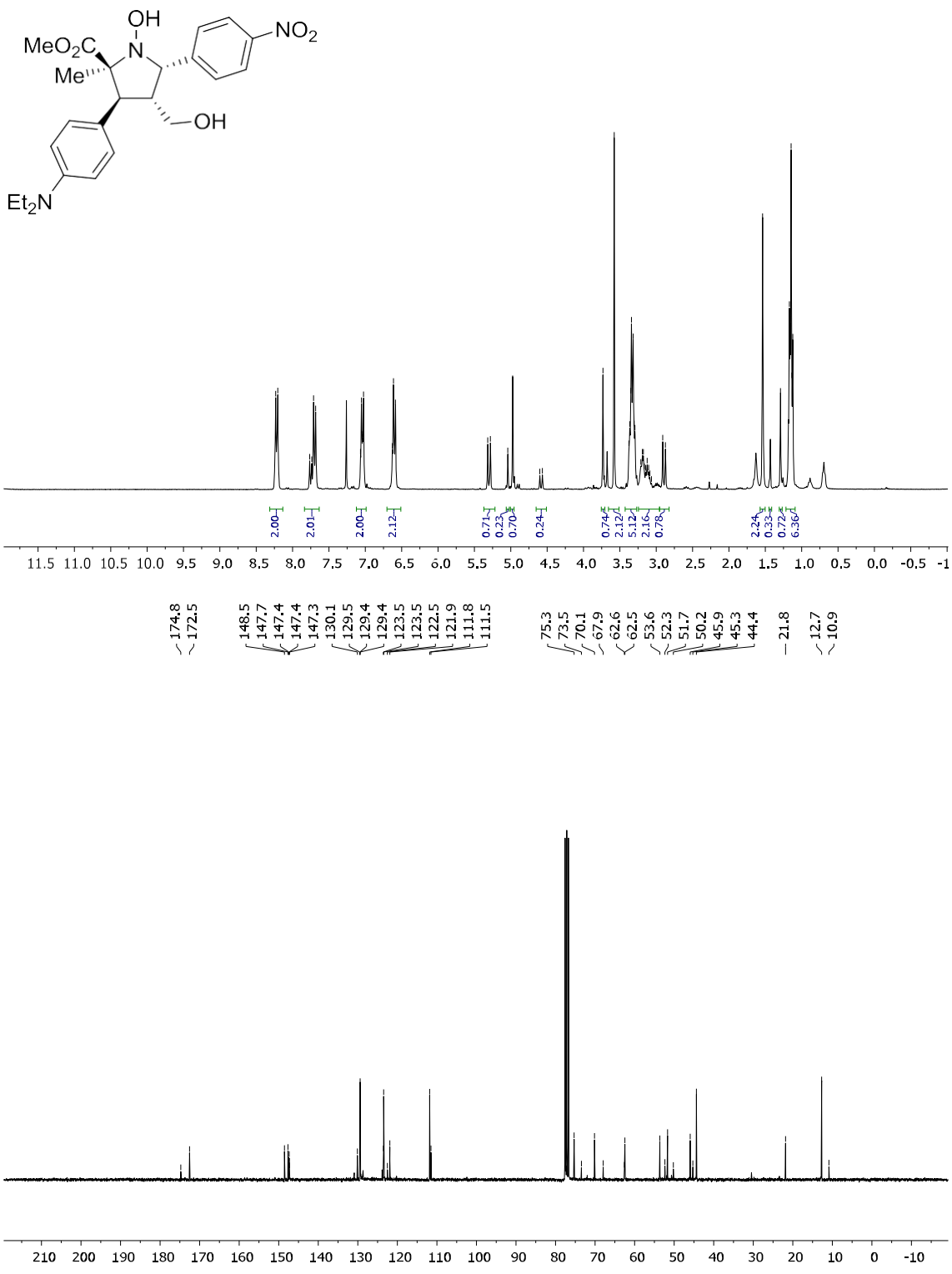
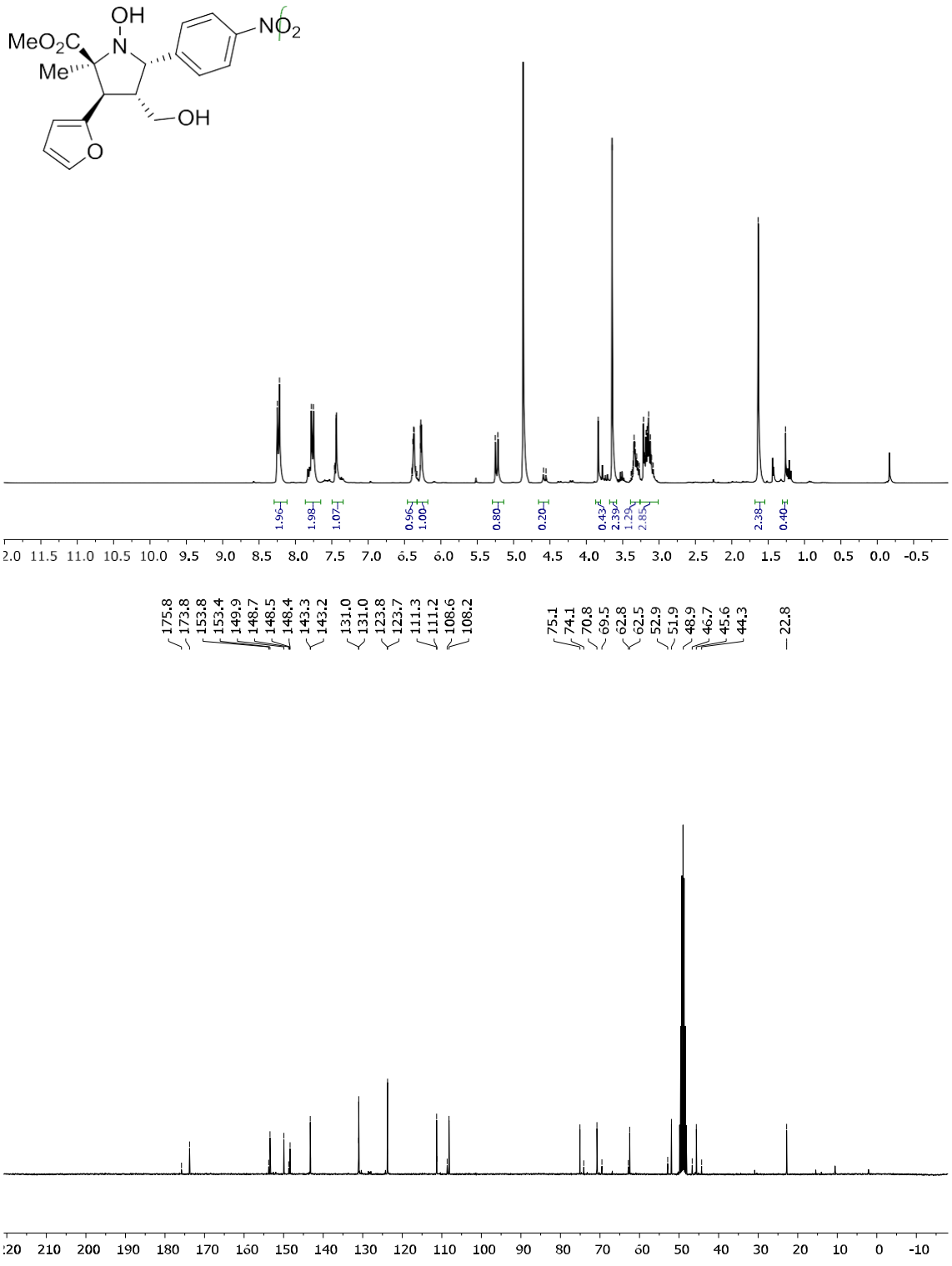
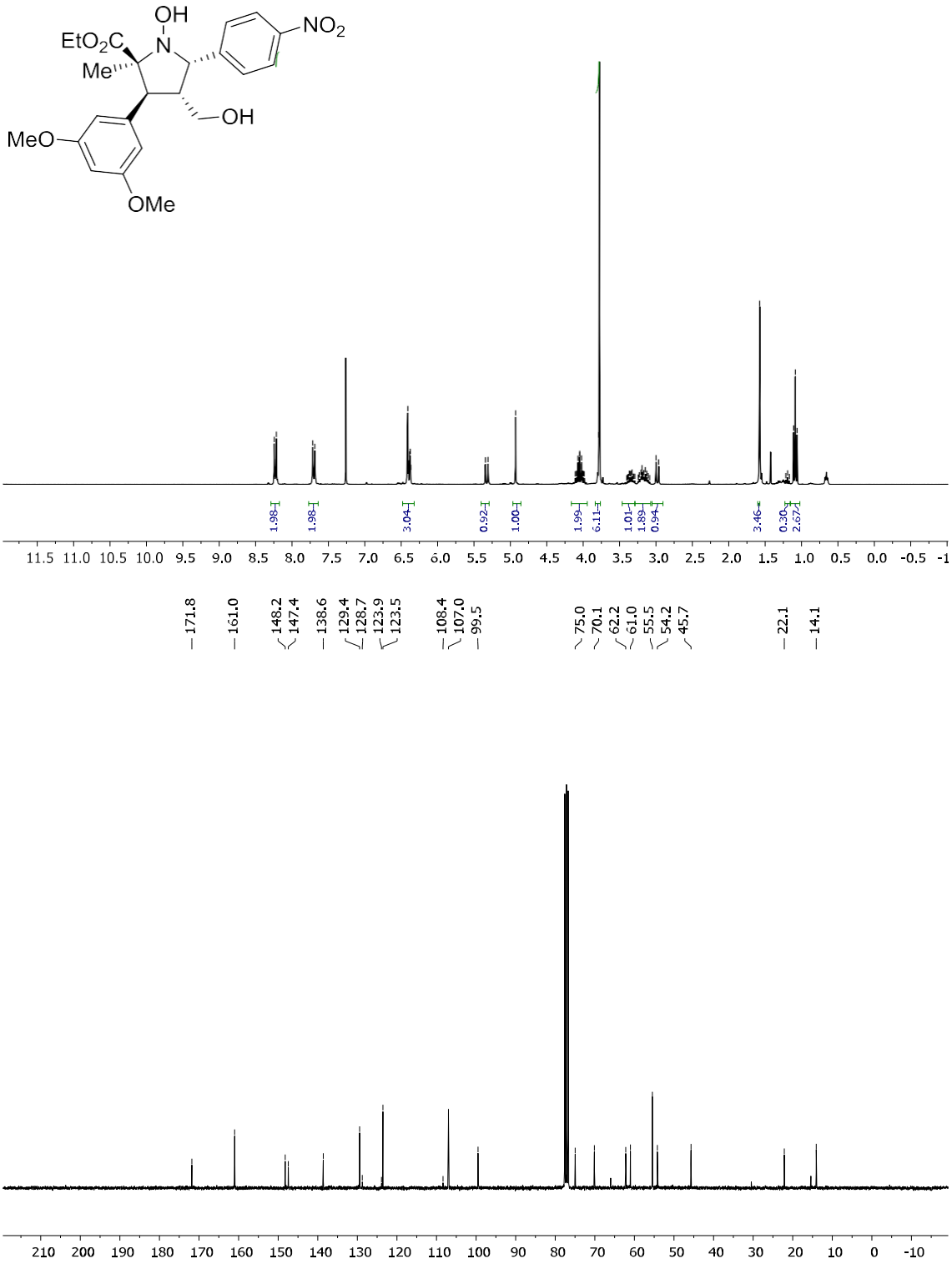
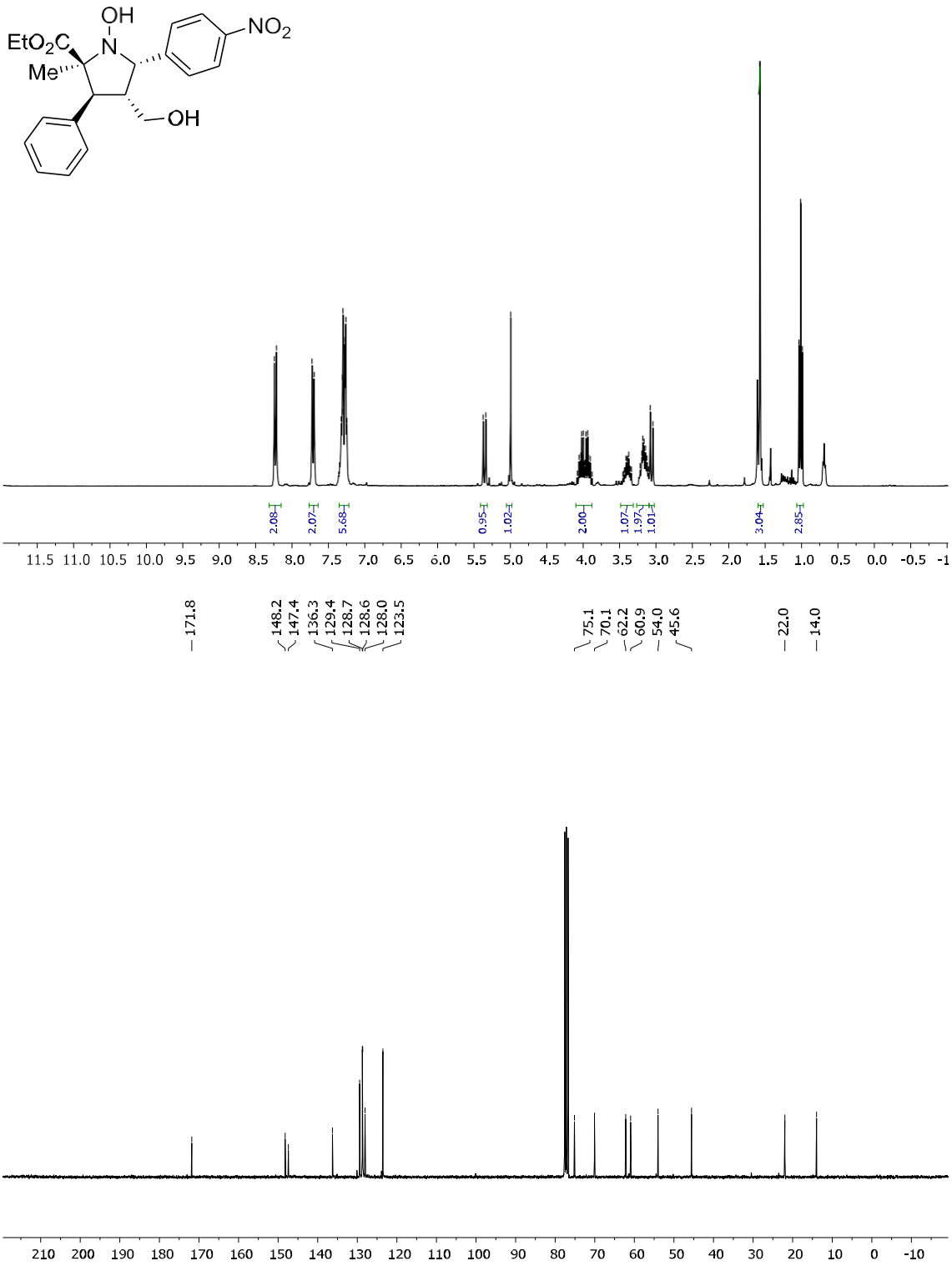
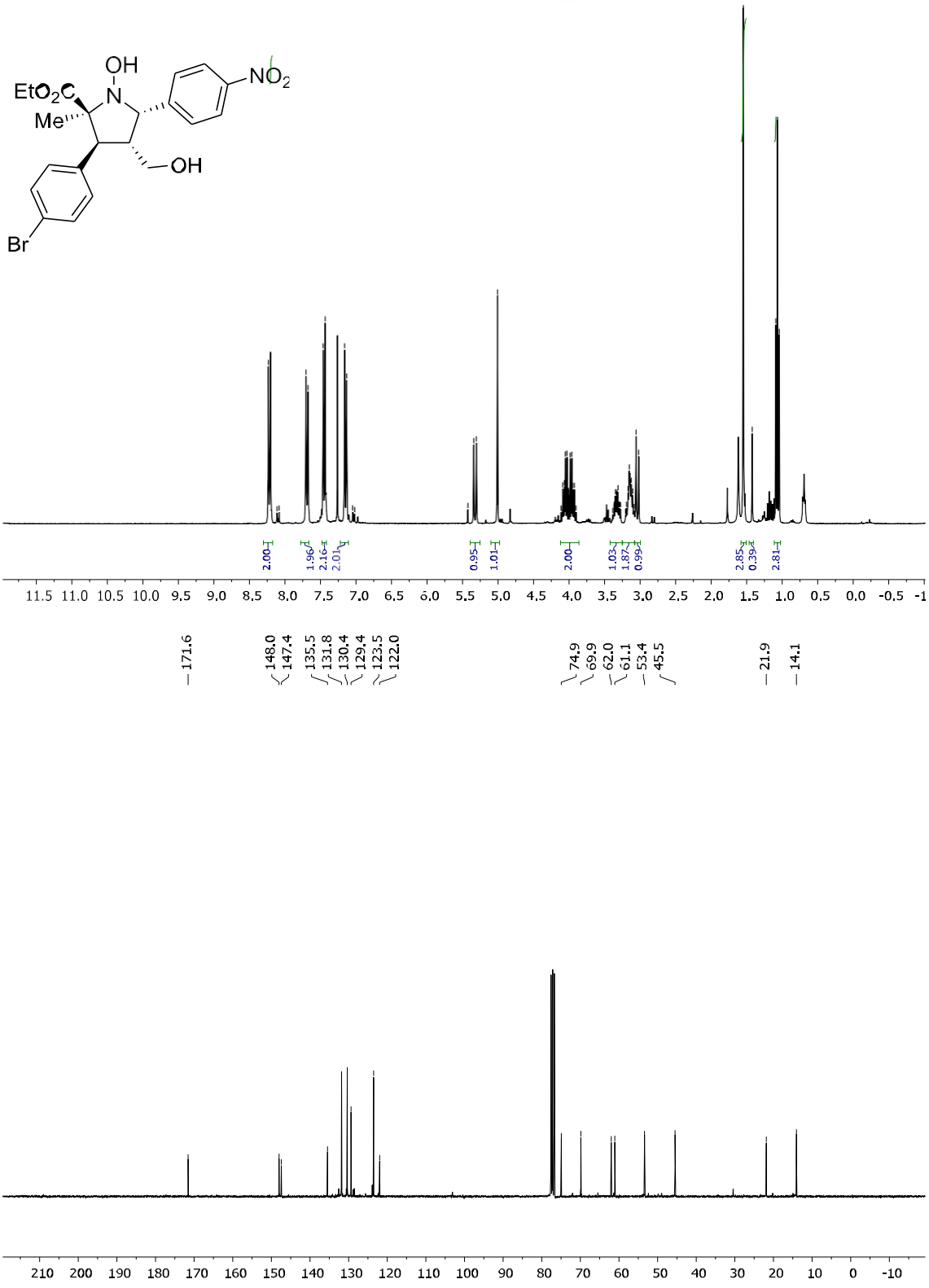
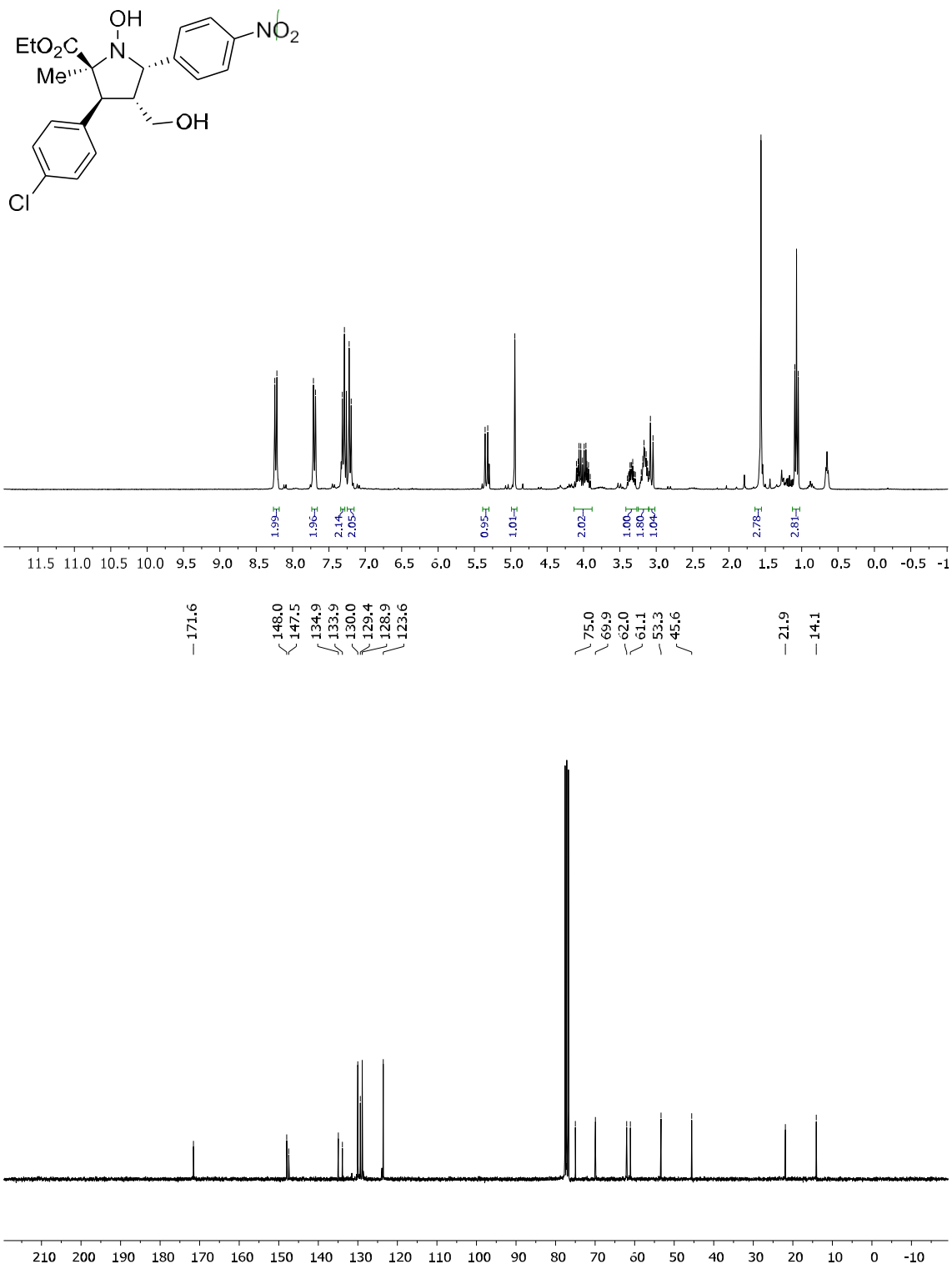

OH
MeO2C
N
NO2
Me
OH
Et2N
2.00
2.01
2.00
2.12
0.71
0.23
0.70
0.24
0.74
2.12
5.12
2.16
0.78
2.24
0.33
0.72
6.36
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
174.8
172.5
148.5
147.7
147.4
147.4
147.3
130.1
129.5
129.4
129.4
123.5
123.5
122.5
121.9
111.8
111.5
75.3
73.5
70.1
67.9
62.6
62.5
53.6
52.3
51.7
50.2
45.9
45.3
44.4
21.8
12.7
10.9
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


OH
MeO2C
N
NO2
Me
OH
O
1.96
1.98
1.07
0.96
1.00
0.80
0.20
0.43
2.39
1.29
2.85
2.38
0.40
175.8
173.8
153.8
153.4
149.9
148.7
148.5
148.4
143.3
143.2
131.0
131.0
123.8
123.7
111.3
111.2
108.6
108.2
75.1
74.1
70.8
69.5
62.8
62.5
52.9
51.9
48.9
46.7
45.6
44.3
22.8


OH
EtO2C
N
NO2
Me
OH
MeO
OMe
1.98
1.98
3.04
0.92
1.00
1.99
6.11
1.01
1.89
0.94
3.46
0.30
2.67
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
171.8
161.0
148.2
147.4
138.6
129.4
128.7
123.9
123.5
108.4
107.0
99.5
75.0
70.1
62.2
61.0
55.5
54.2
45.7
22.1
14.1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


OH
EtO2C
N
NO2
Me
OH
2.08
2.07
5.68
0.95
1.02
2.00
1.07
1.97
1.01
3.04
2.85
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
171.8
148.2
147.4
136.3
129.4
128.7
128.6
128.0
123.5
75.1
70.1
62.2
60.9
54.0
45.6
22.0
14.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


OH
EtO2C
N
NO2
Me
OH
Br
2.00
1.96
2.16
2.01
0.95
1.01
2.00
1.03
1.87
0.99
2.85
0.39
2.81
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
171.6
148.0
147.4
135.5
131.8
130.4
129.4
123.5
122.0
74.9
69.9
62.0
61.1
53.4
45.5
21.9
14.1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


OH
EtO2C
N
NO2
Me
OH
Cl
1.99
1.96
2.14
2.05
0.95
1.01
2.02
1.00
1.80
1.04
2.78
2.81
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
171.6
148.0
147.5
134.9
133.9
130.0
129.4
128.9
123.6
75.0
69.9
62.0
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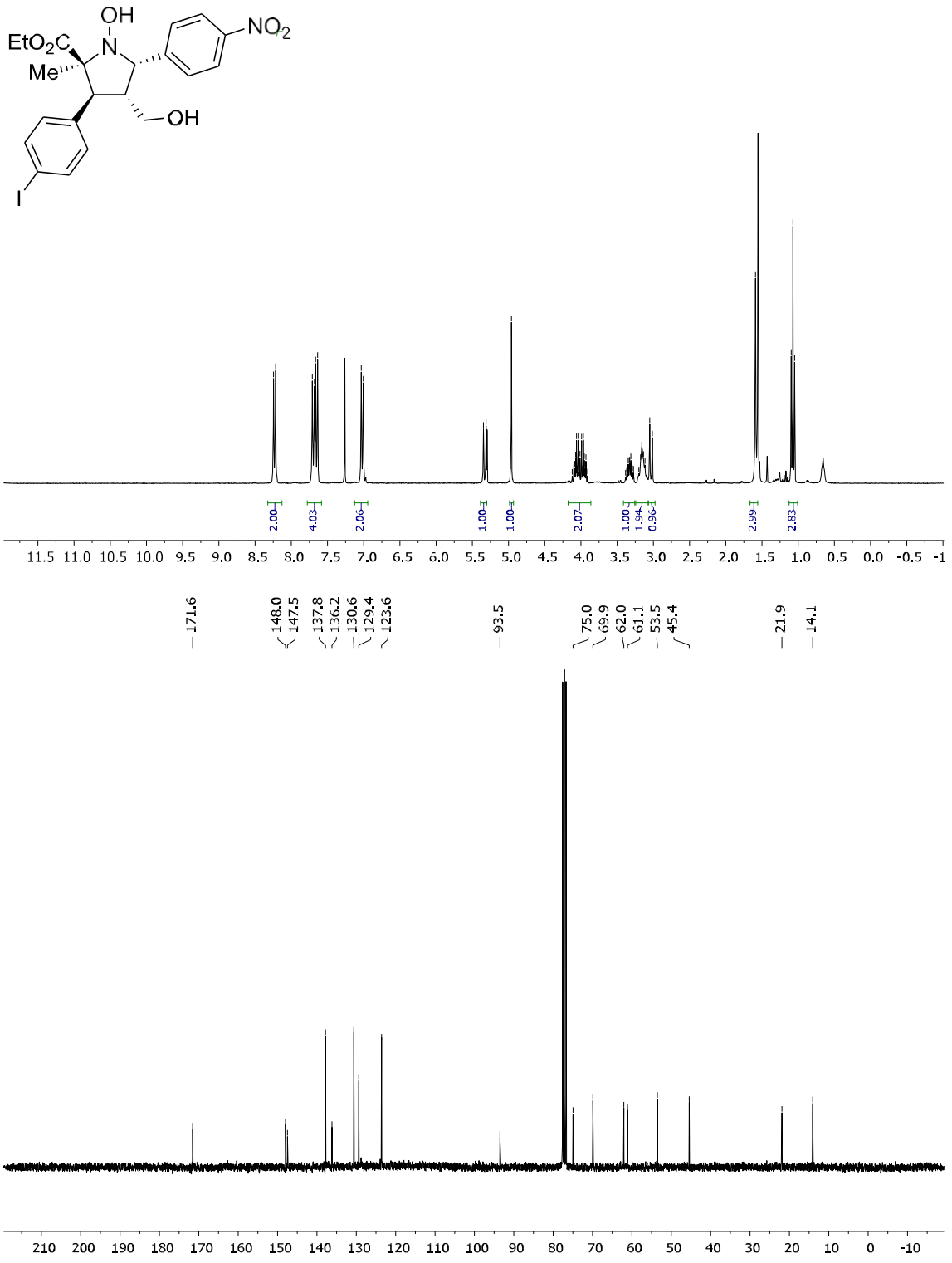
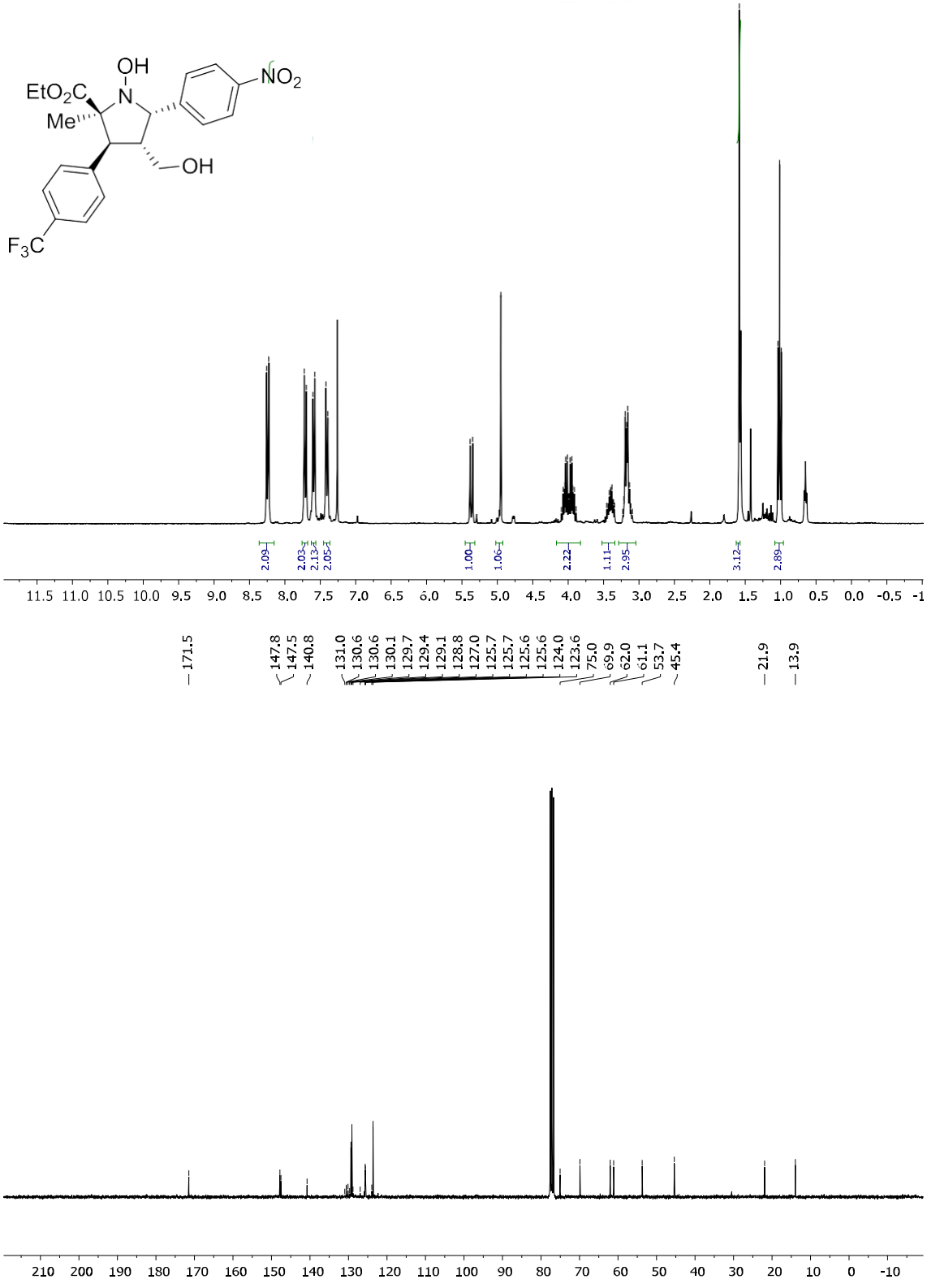
53.3
45.6
21.9
14.1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


OH
EtO2C
N
NO2
Me
OH
I
2.00
4.03
2.06
1.00
1.00
2.07
1.00
1.94
0.96
2.99
2.83
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
171.6
148.0
147.5
137.8
136.2
130.6
129.4
123.6
93.5
75.0
69.9
62.0
61.1
53.5
45.4
21.9
14.1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


OH
EtO2C
N
NO2
Me
OH
F3C
2.09
2.03
2.13
2.05
1.00
1.06
2.22
1.11
2.95
3.12
2.89
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
171.5
147.8
147.5
140.8
131.0
130.6
130.6
130.1
129.7
129.4
129.1
128.8
127.0
125.7
125.7
125.6
125.6
124.0
123.6
75.0
69.9
62.0
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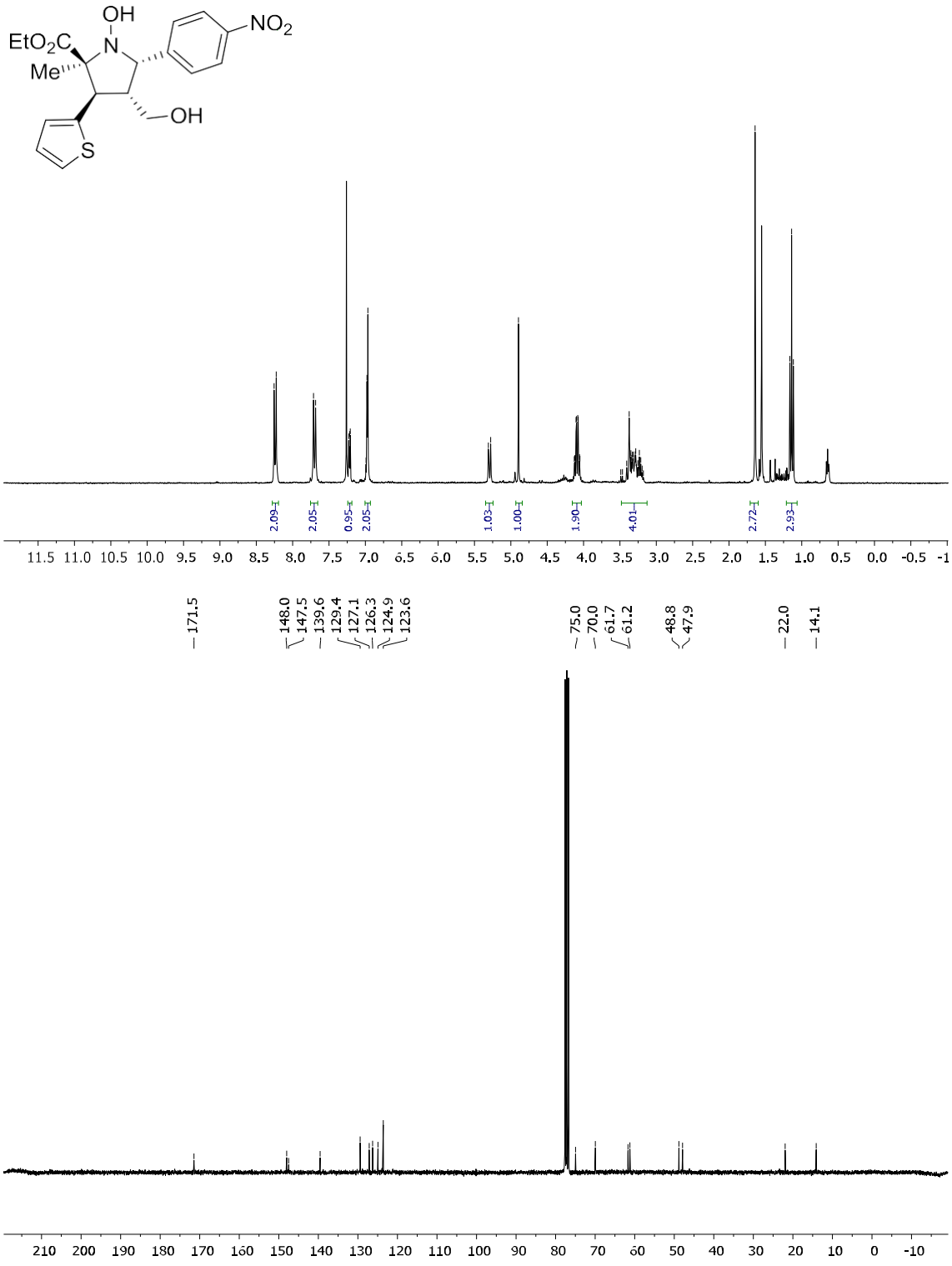
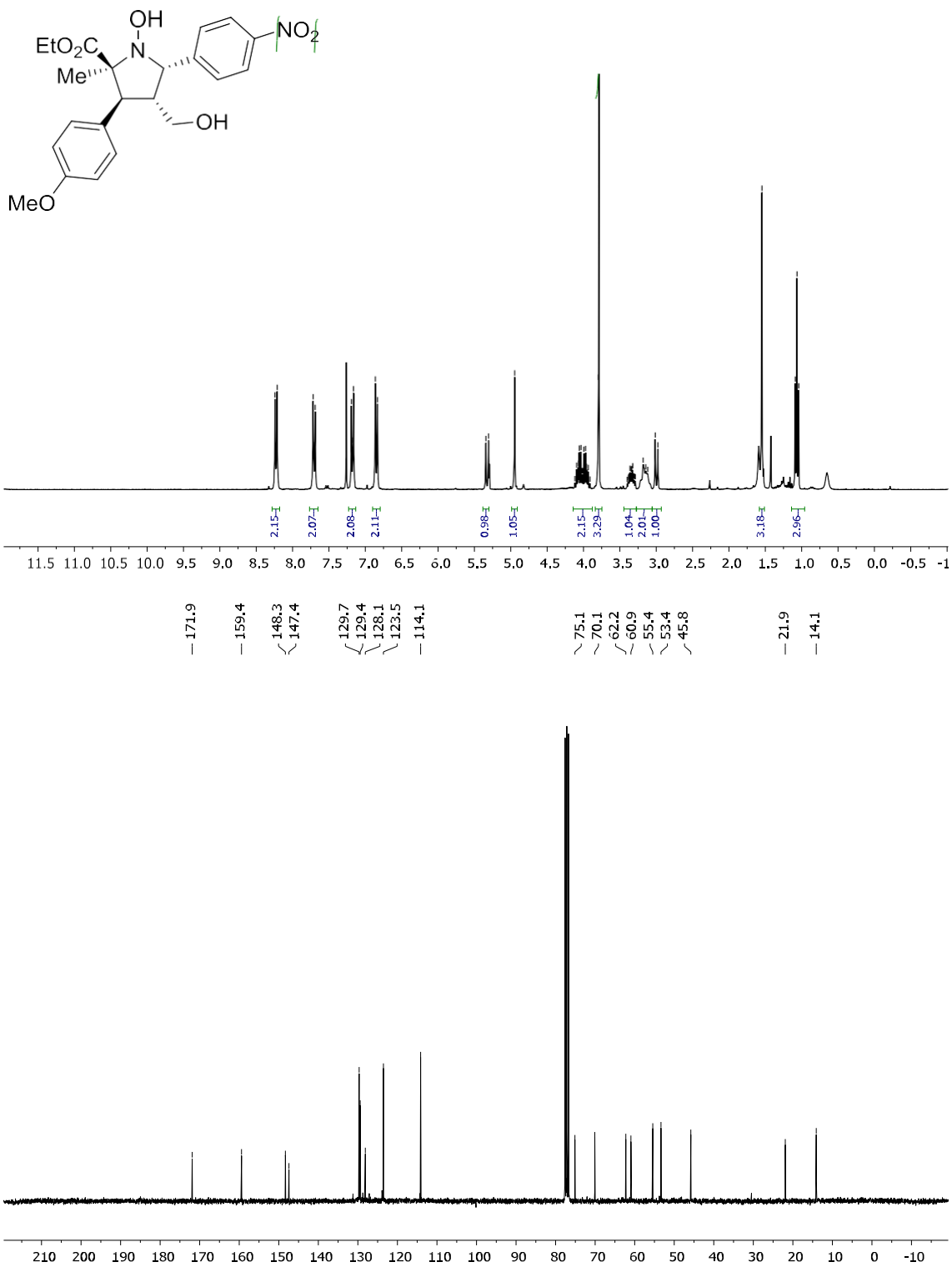
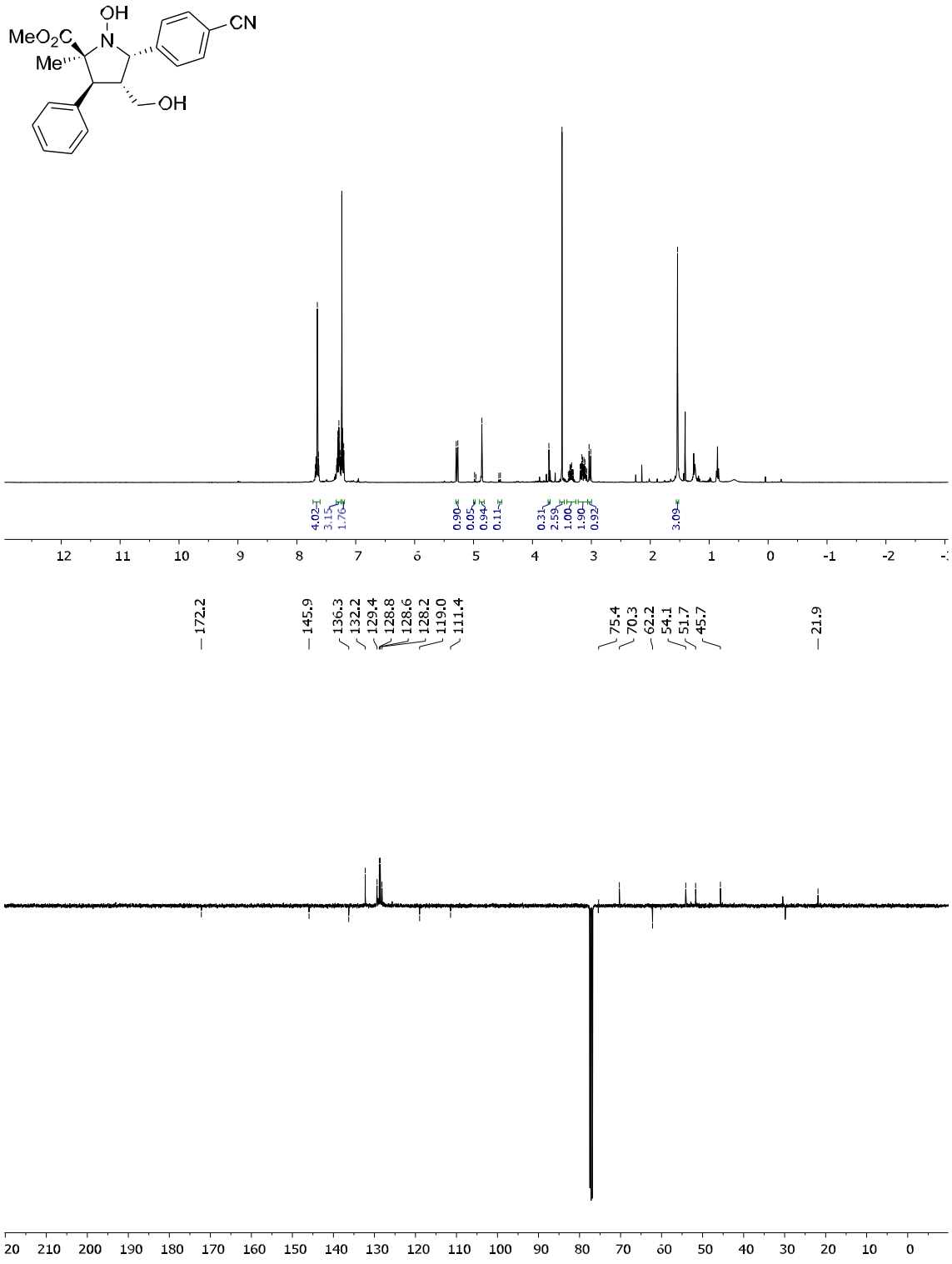
53.7
45.4
21.9
13.9
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


OH
EtO2C
N
NO2
Me
OH
S
2.09
2.05
0.95
2.05
1.03
1.00
1.90
4.01
2.72
2.93
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
171.5
148.0
147.5
139.6
129.4
127.1
126.3
124.9
123.6
75.0
70.0
61.7
61.2
48.8
47.9
22.0
14.1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


OH
EtO2C
N
NO2
Me
OH
MeO
2.15
2.07
2.08
2.11
0.98
1.05
2.15
3.29
1.04
2.01
1.00
3.18
2.96
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
171.9
159.4
148.3
147.4
129.7
129.4
128.1
123.5
114.1
75.1
70.1
62.2
60.9
55.4
53.4
45.8
21.9
14.1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


OH
MeO2C
N
CN
Me
OH
4.02
3.15
1.76
0.90
0.05
0.94
0.11
0.31
2.59
1.00
1.90
0.92
3.09
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
172.2
145.9
136.3
132.2
129.4
128.8
128.6
128.2
119.0
111.4
75.4
70.3
62.2
54.1
51.7
45.7
21.9
220
210
200
190
180
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150
140
130
120
110
100
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70
60
50
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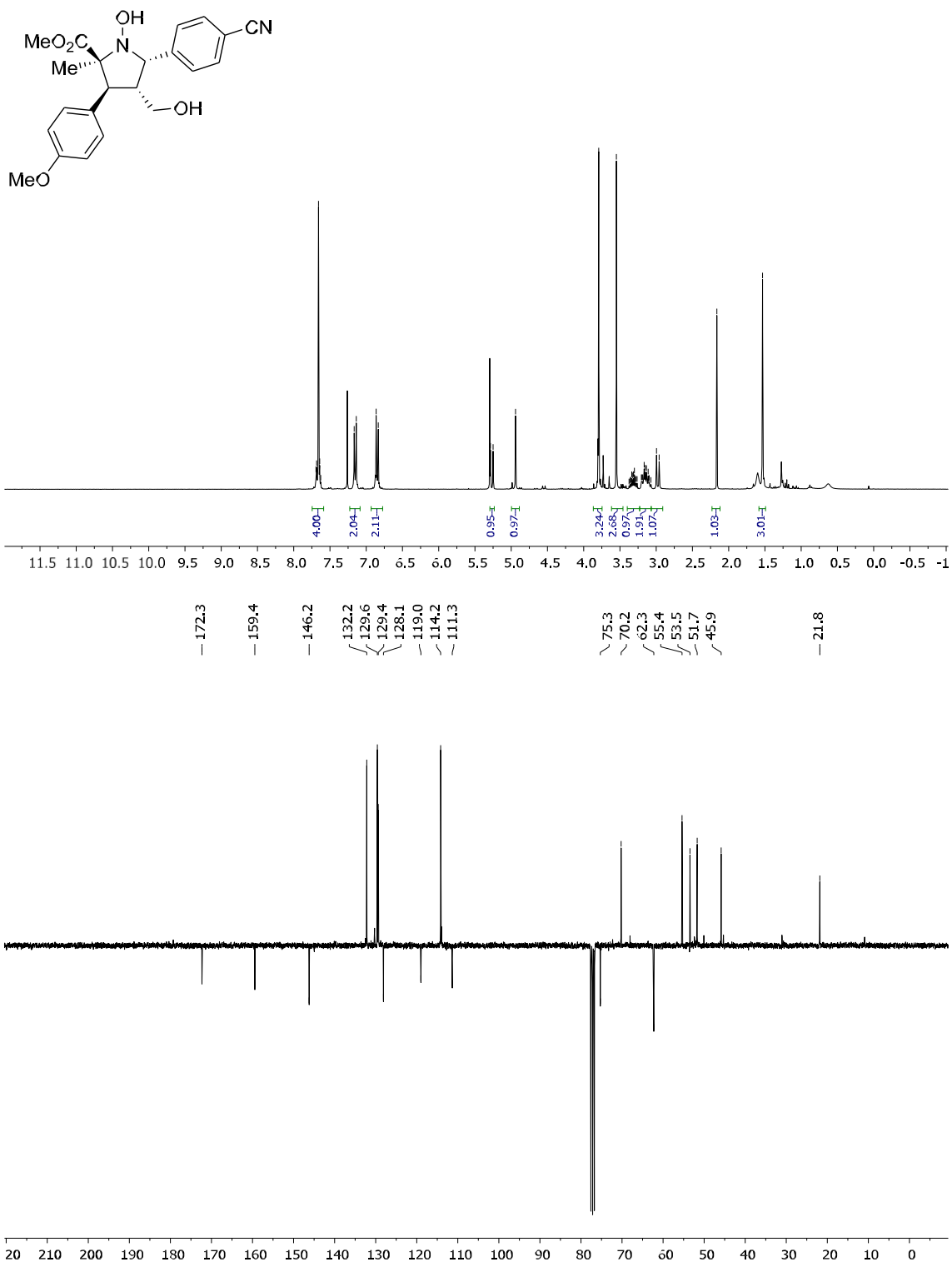
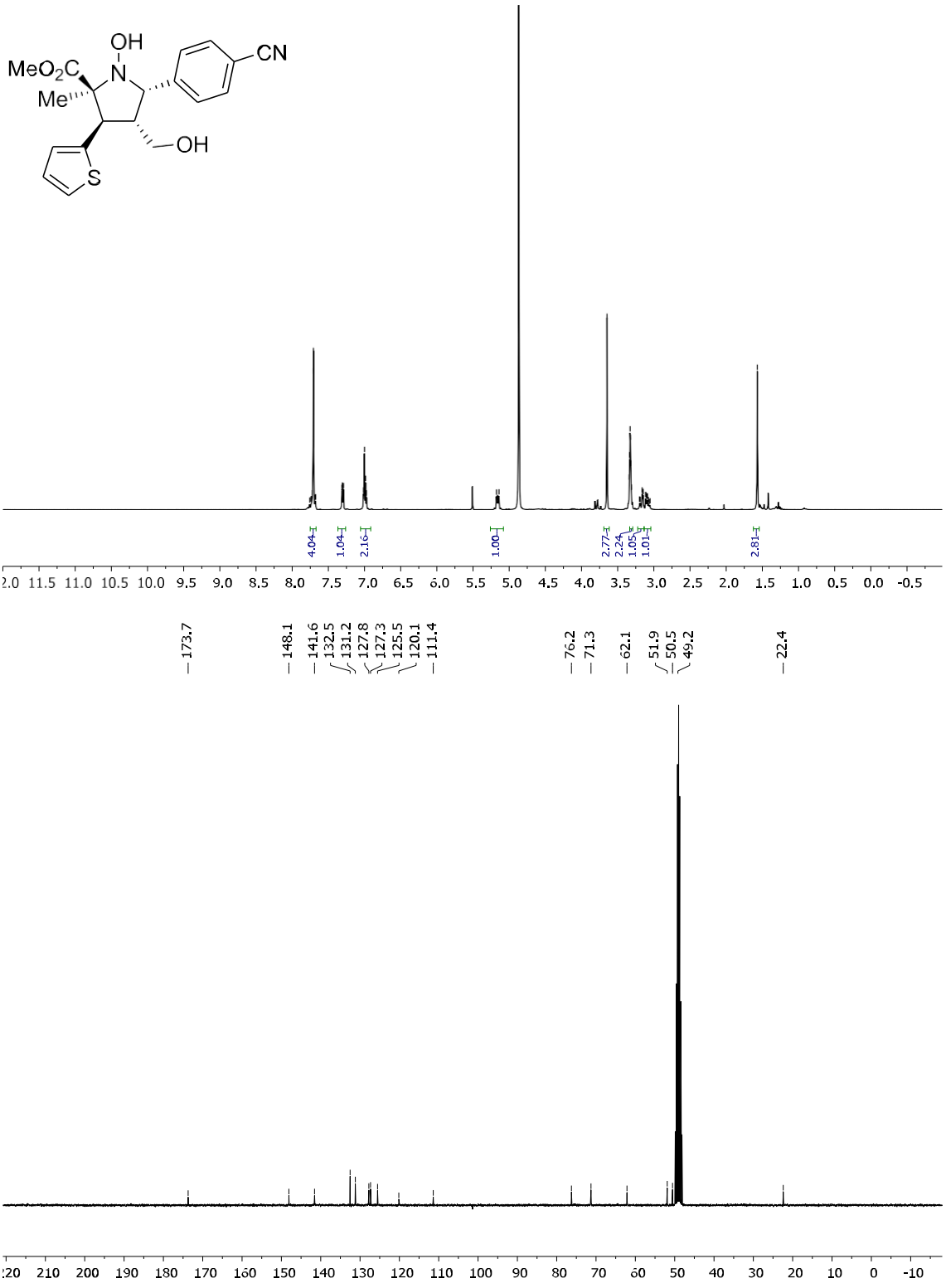
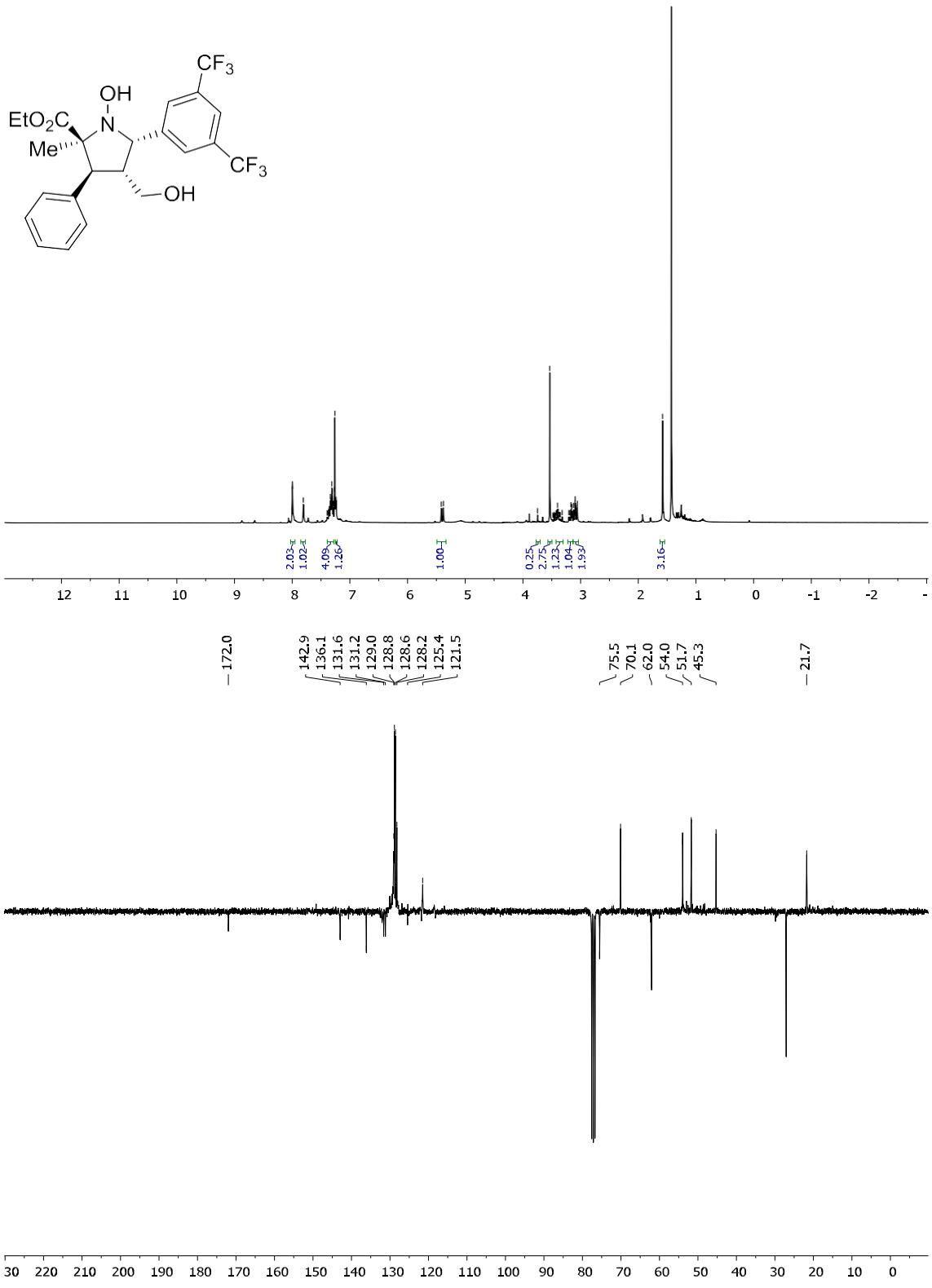
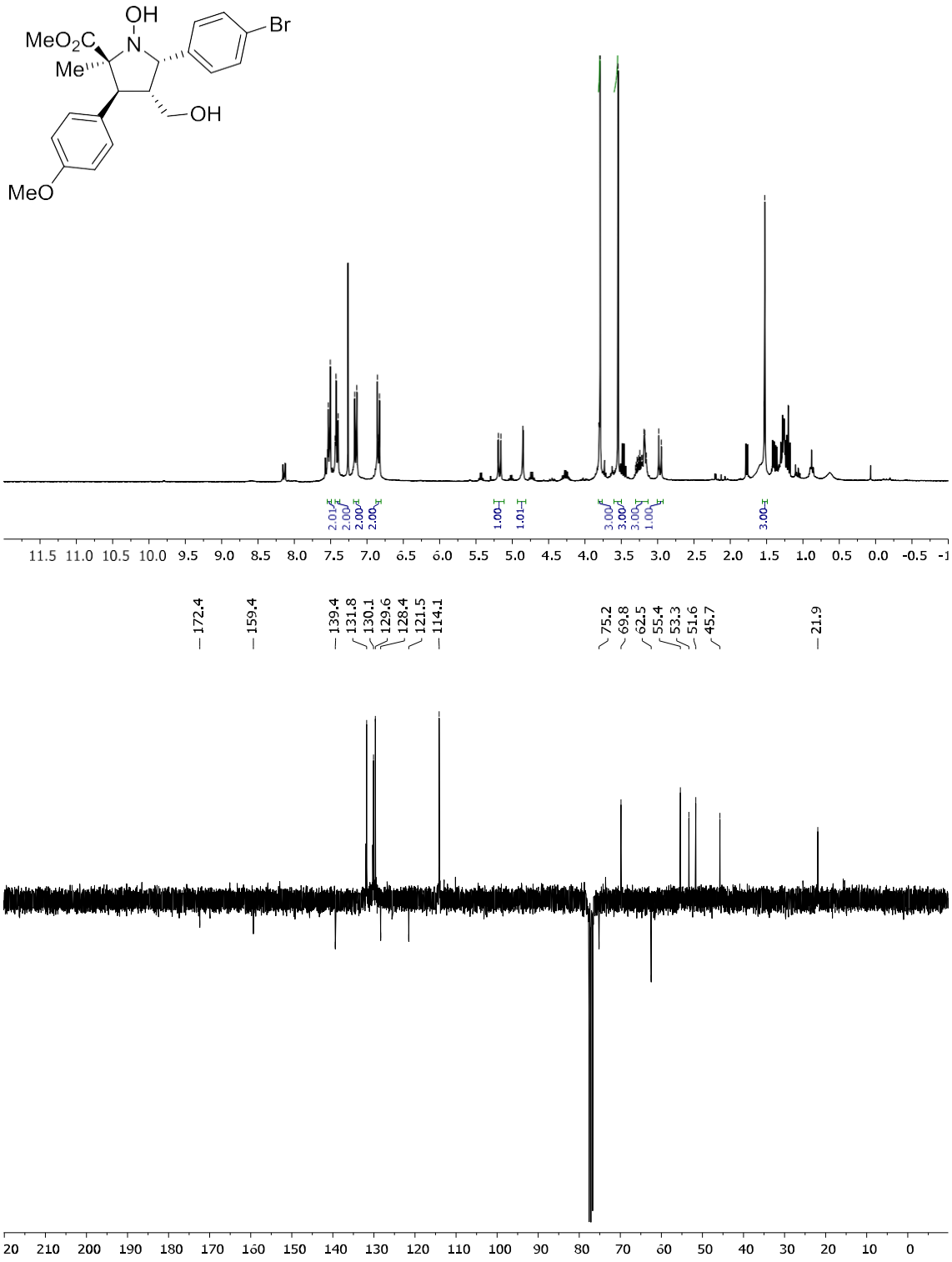
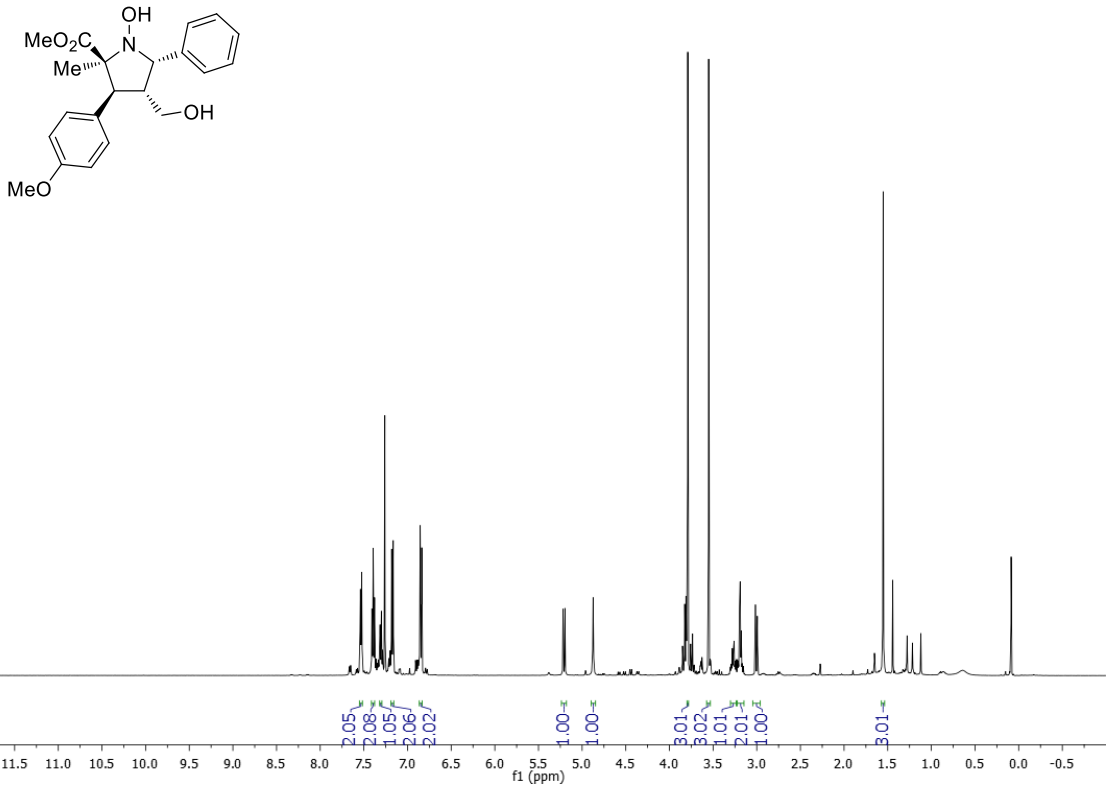
30
20
10
0

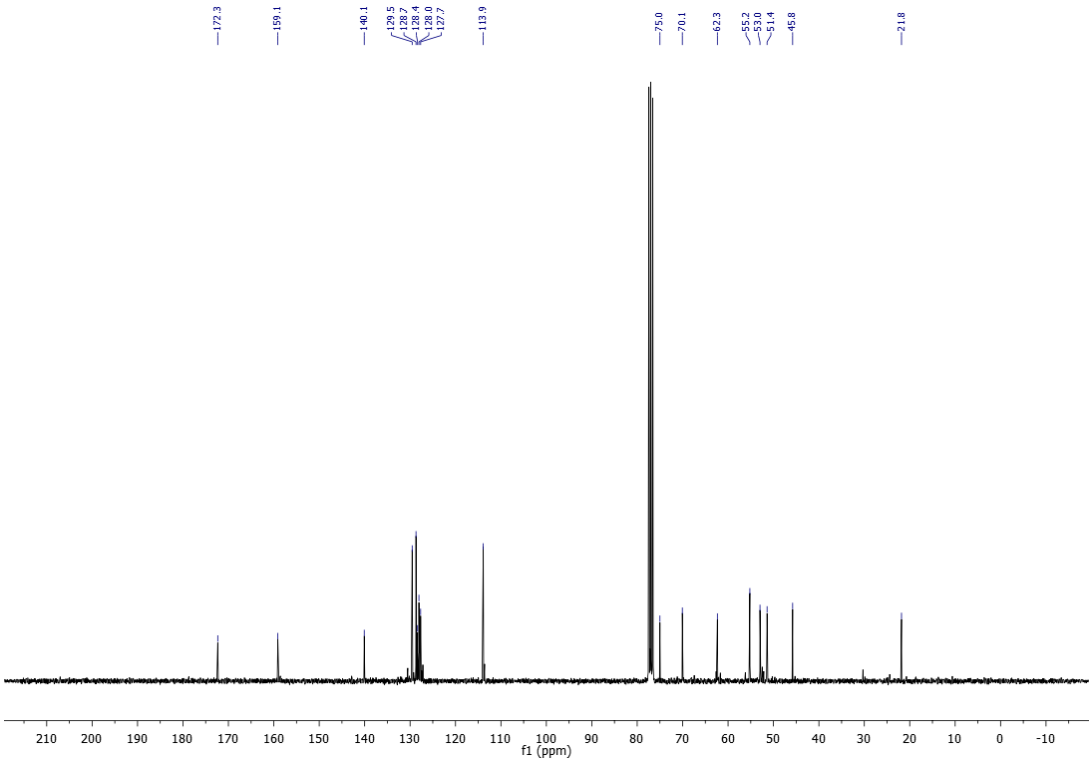

OH
MeO2C
N
Me
CN
OH
MeO
4.00
2.04
2.11
0.95
0.97
3.24
2.68
0.97
1.91
1.07
1.03
3.01
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
172.3
159.4
146.2
132.2
129.6
129.4
128.1
119.0
114.2
111.3
75.3
70.2
62.3
55.4
53.5
51.7
45.9
21.8
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

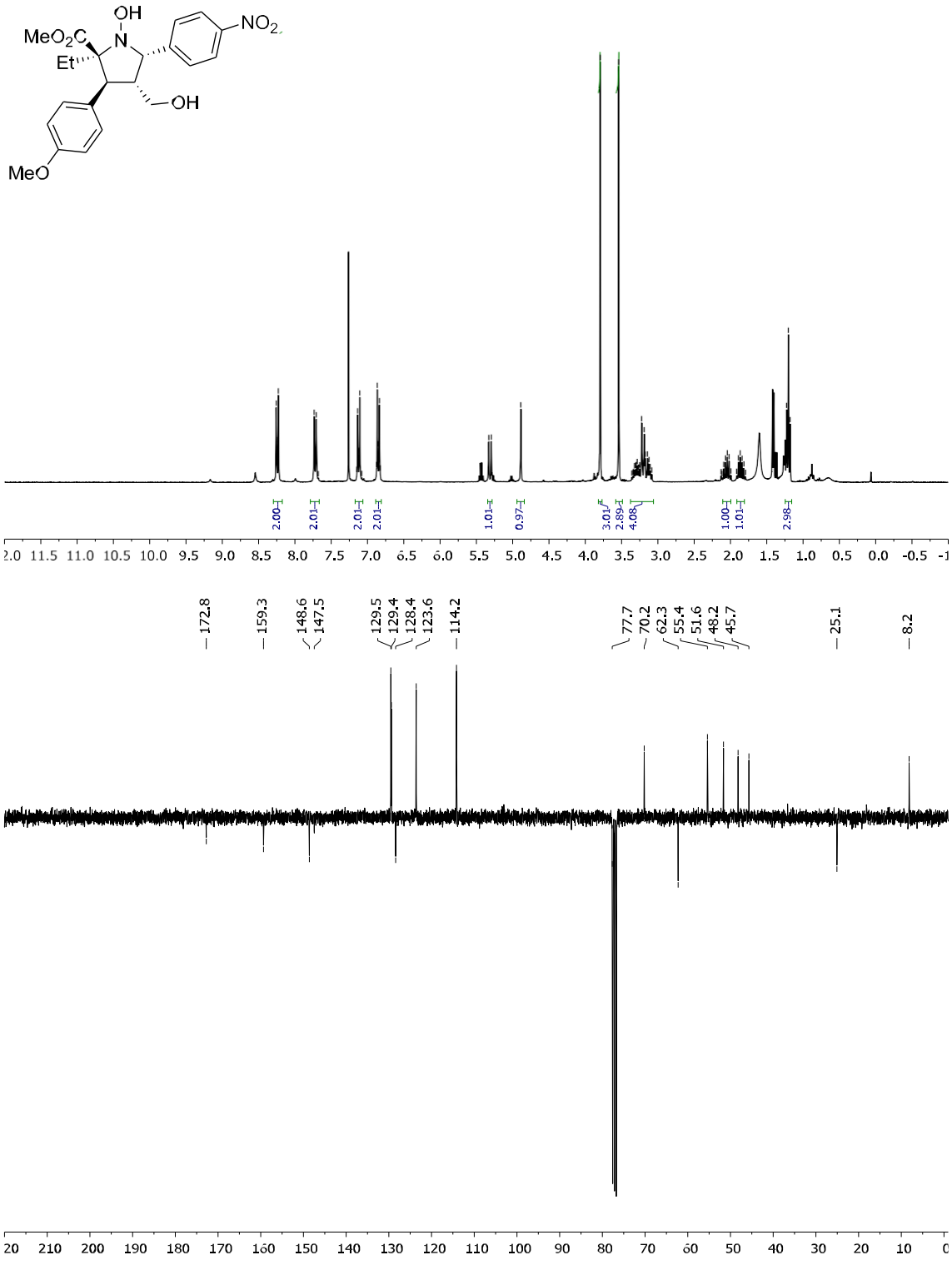

OH
MeO2C
N
CN
Me
OH
S
4.04
1.04
2.16
1.00
2.77
2.24
1.05
1.01
2.81
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
173.7
148.1
141.6
132.5
131.2
127.8
127.3
125.5
120.1
111.4
76.2
71.3
62.1
51.9
50.5
49.2
22.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

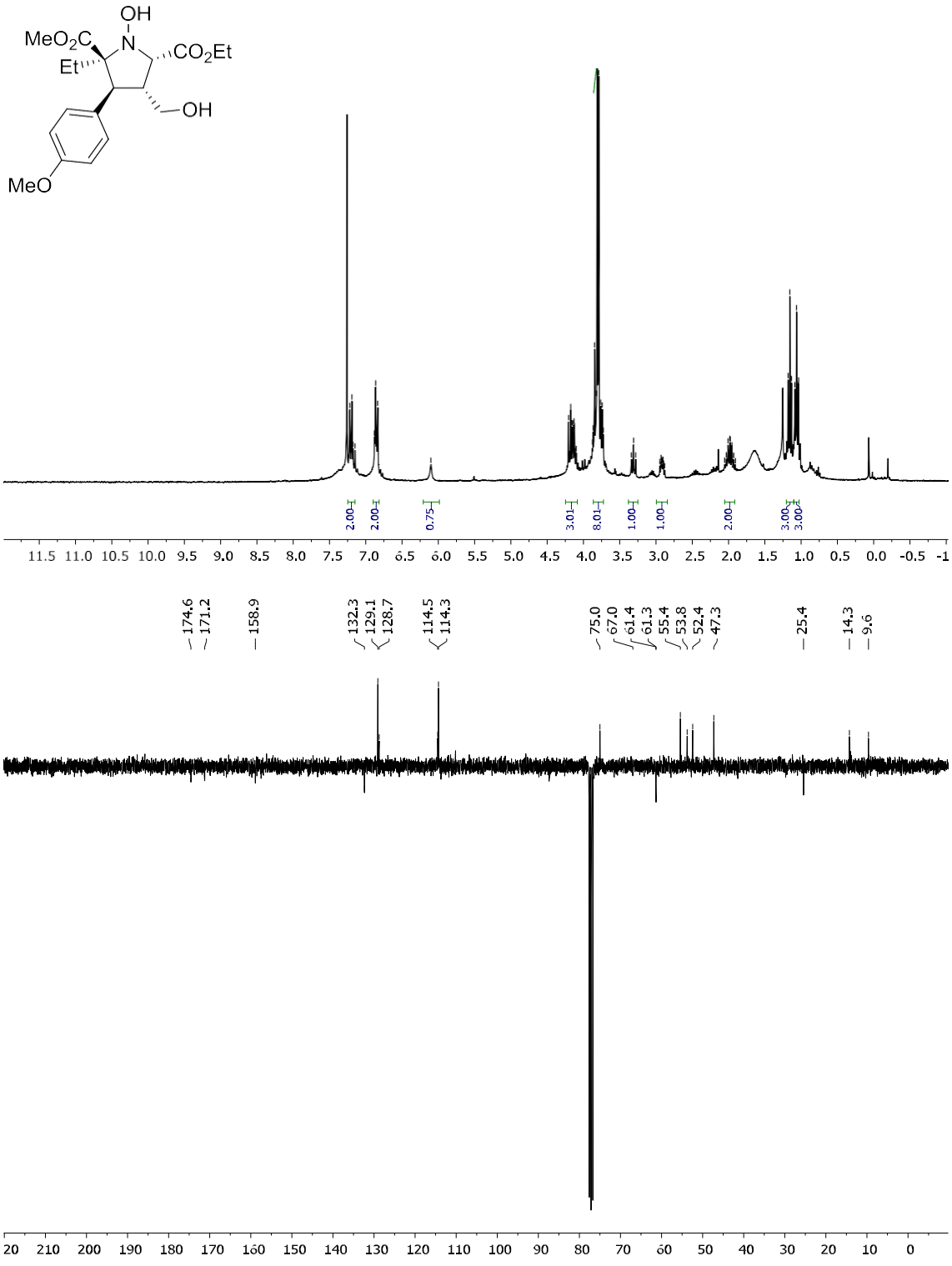

CF3
OH
EtO2C
N
Me
CF3
OH
2.03
1.02
4.09
1.26
1.00
0.25
2.75
1.23
1.04
1.93
3.16
12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
172.0
142.9
136.1
131.6
131.2
129.0
128.8
128.6
128.2
125.4
121.5
75.5
70.1
62.0
54.0
51.7
45.3
21.7
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

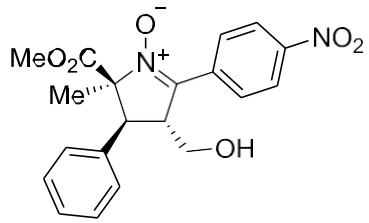

OH
MeO2C
N
Br
Me
OH
MeO
2.01
2.00
2.00
2.00
1.00
1.01
3.00
3.00
3.00
1.00
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
172.4
159.4
139.4
131.8
130.1
129.6
128.4
121.5
114.1
75.2
69.8
62.5
55.4
53.3
51.6
45.7
21.9
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

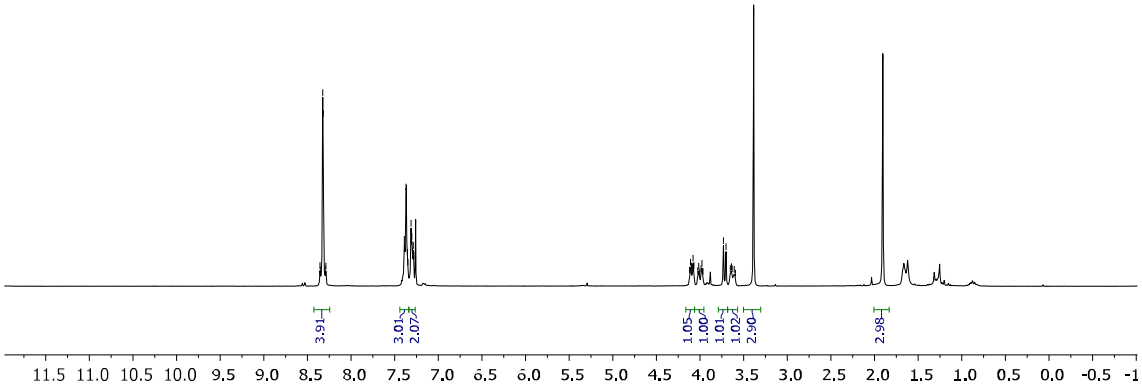

OH
MeO2C
N
Me
OH
MeO
2.05
2.08
1.05
2.06
2.02
1.00
1.00
3.01
3.02
1.01
2.01
1.00
3.01
f1 (ppm)

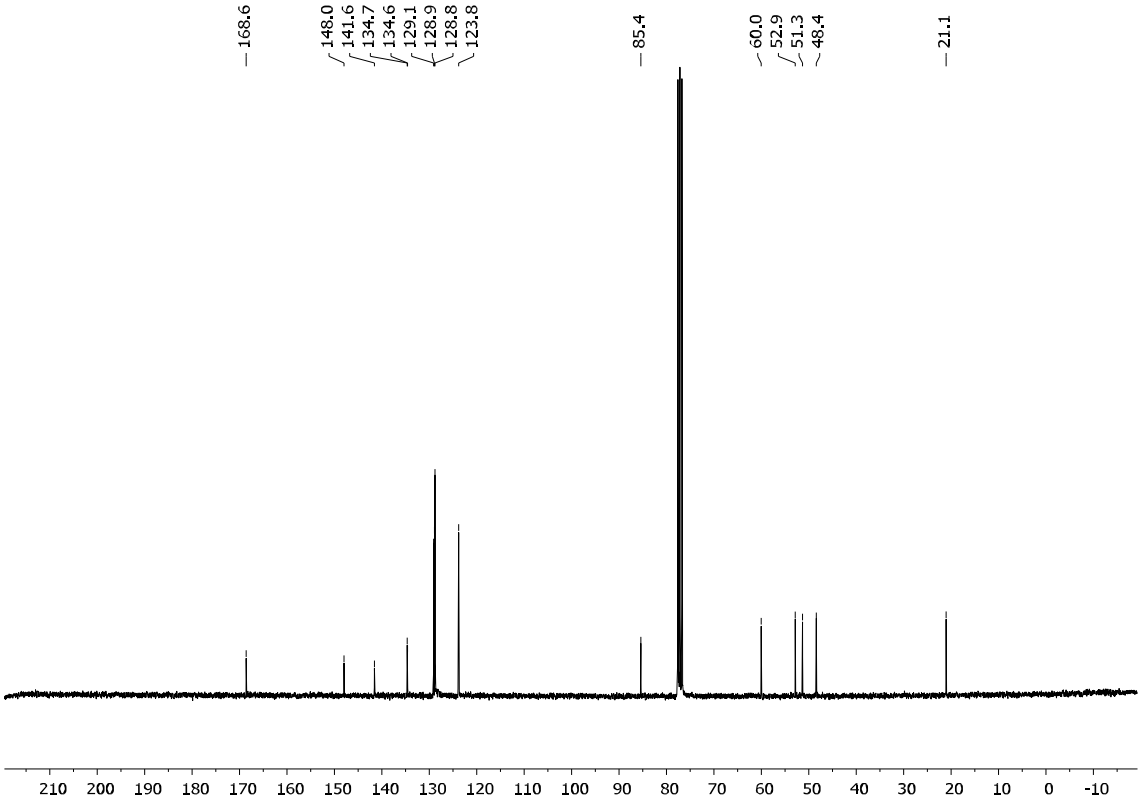

172.3
159.1
140.1
129.5
128.7
128.4
128.0
127.7
113.9
75.0
70.1
62.3
55.2
53.0
51.4
45.8
21.8
f1 (ppm)

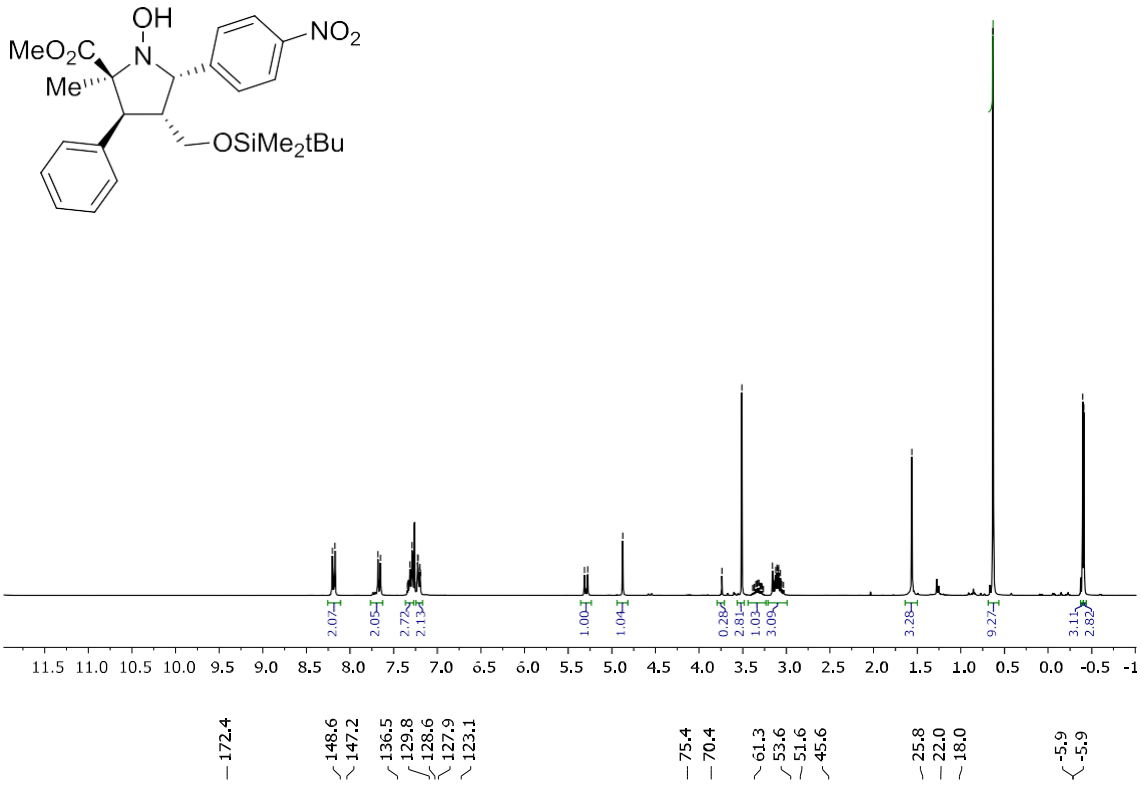

OH
MeO2C
N
Et
NO2
OH
MeO
2.00
2.01
2.01
2.01
1.01
0.97
3.01
2.89
4.08
1.00
1.01
2.98
172.8
159.3
148.6
147.5
129.5
129.4
128.4
123.6
114.2
77.7
70.2
62.3
55.4
51.6
48.2
45.7
25.1
8.2

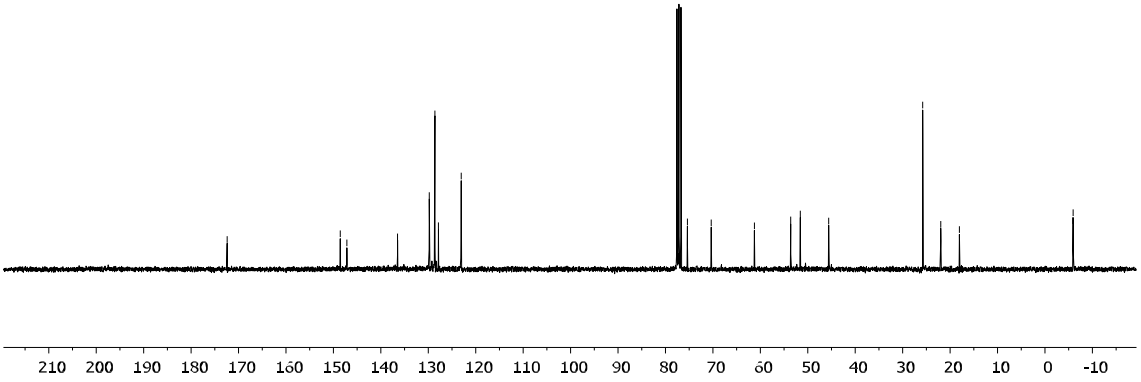

OH
MeO2C
N
CO2Et
Et
OH
MeO
2.00
2.00
0.75
3.01
8.01
1.00
1.00
2.00
3.00
3.00
174.6
171.2
158.9
132.3
129.1
128.7
114.5
114.3
75.0
67.0
61.4
61.3
55.4
53.8
52.4
47.3
25.4
14.3
9.6

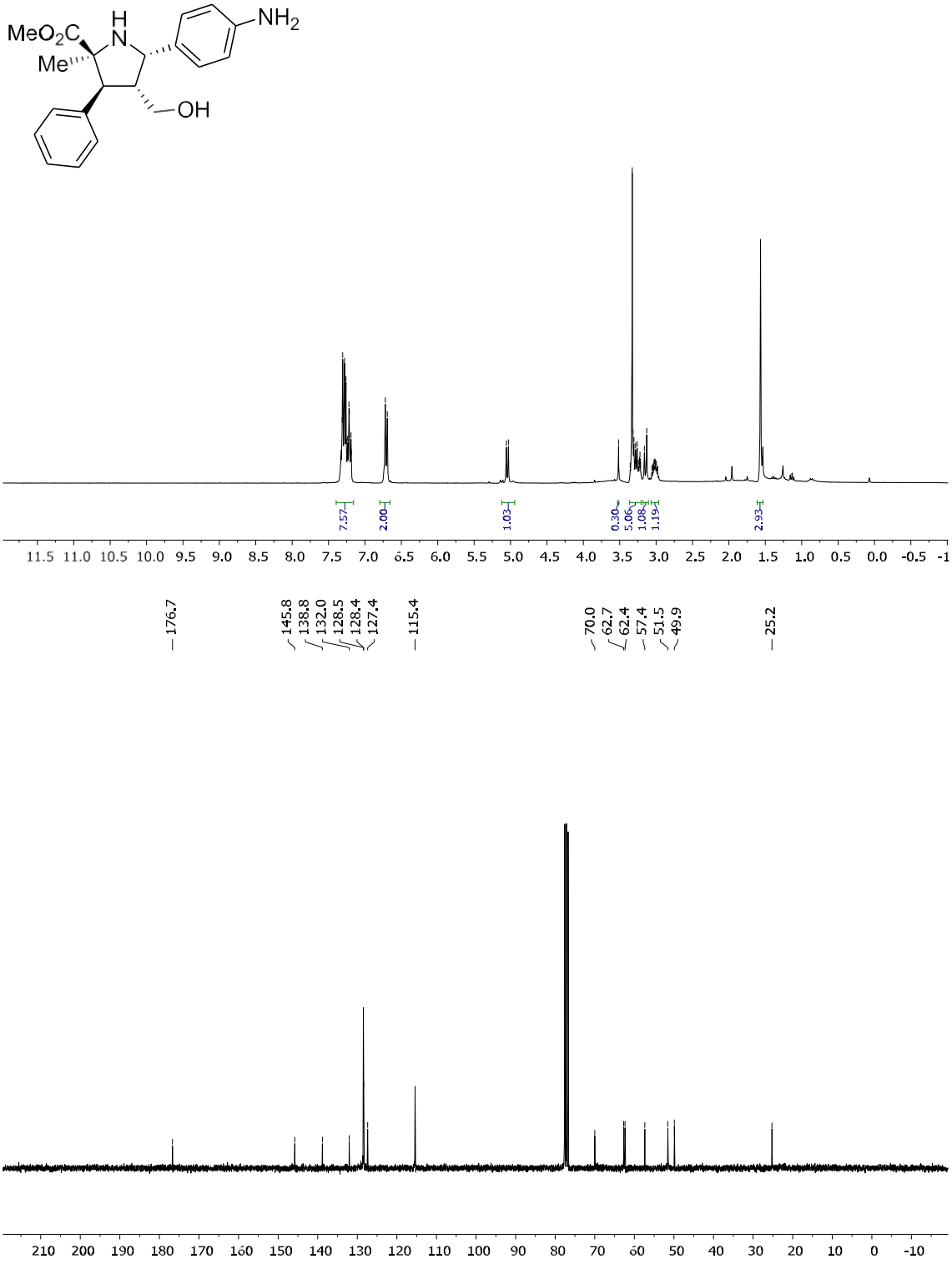

MeO2C
Me
O
N+
NO2
OH

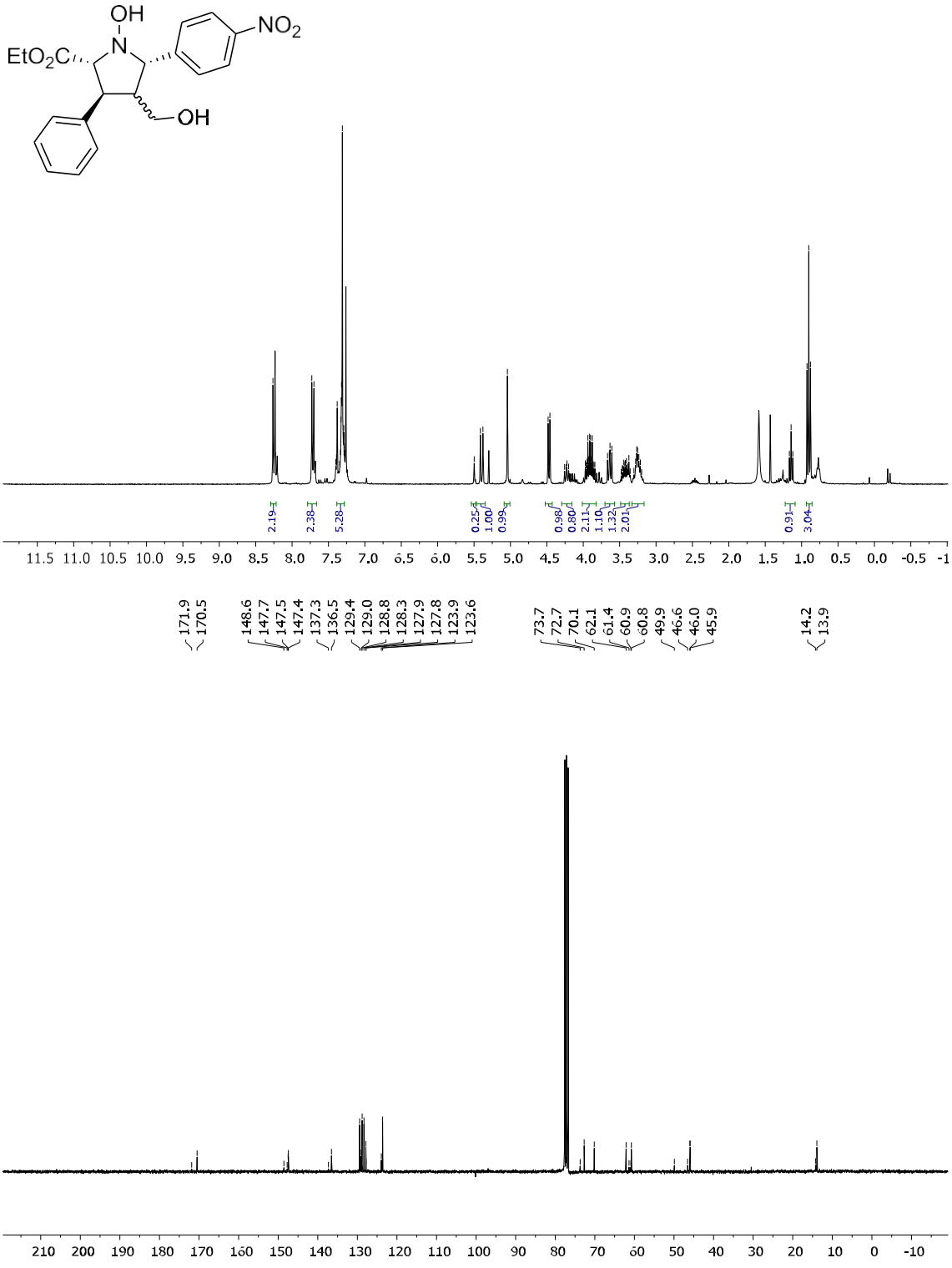

3.91
3.01
2.07
1.05
1.00
1.01
1.02
2.90
2.98
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1

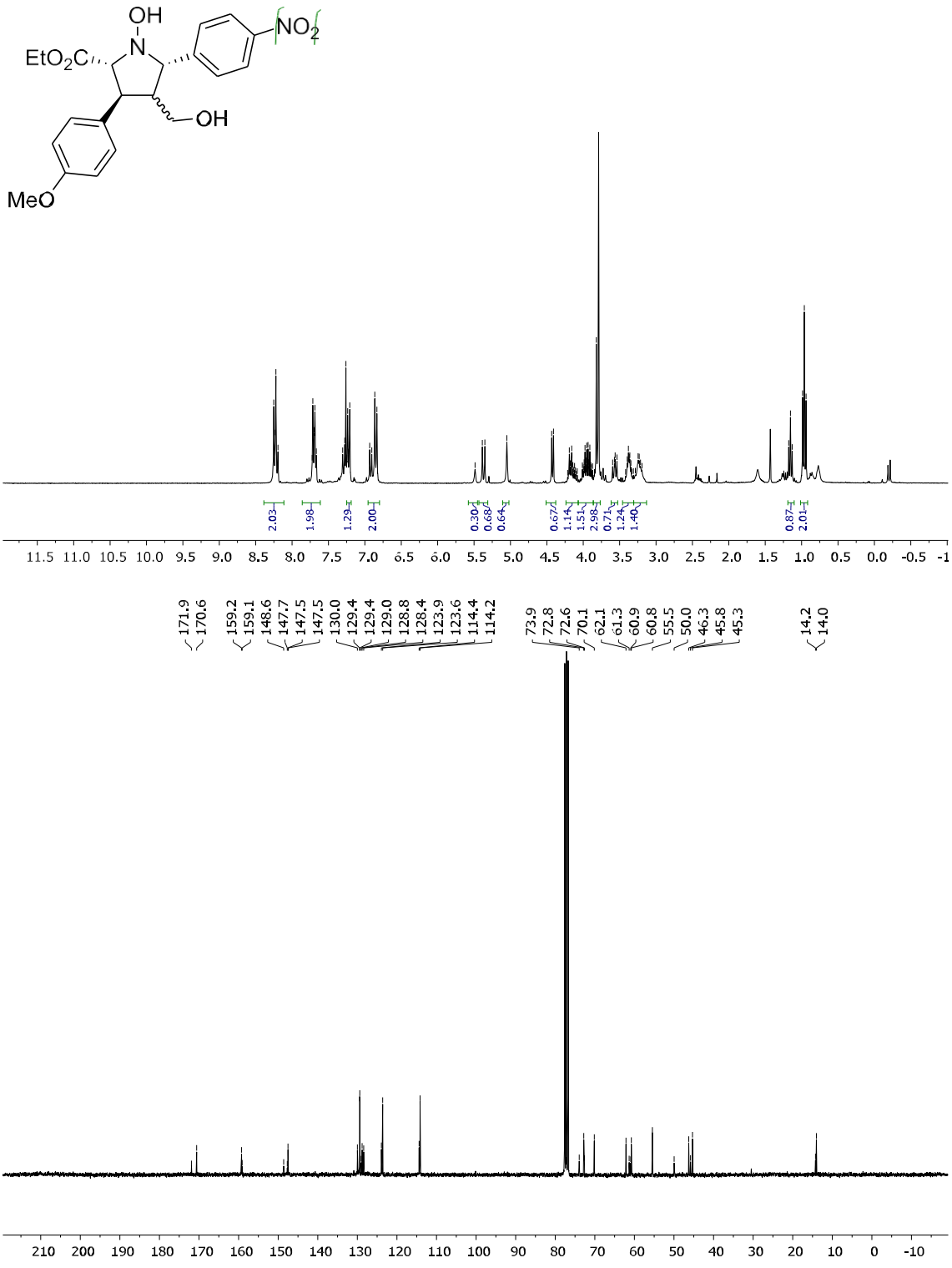

168.6
148.0
141.6
134.7
134.6
129.1
128.9
128.8
123.8
85.4
60.0
52.9
51.3
48.4
21.1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

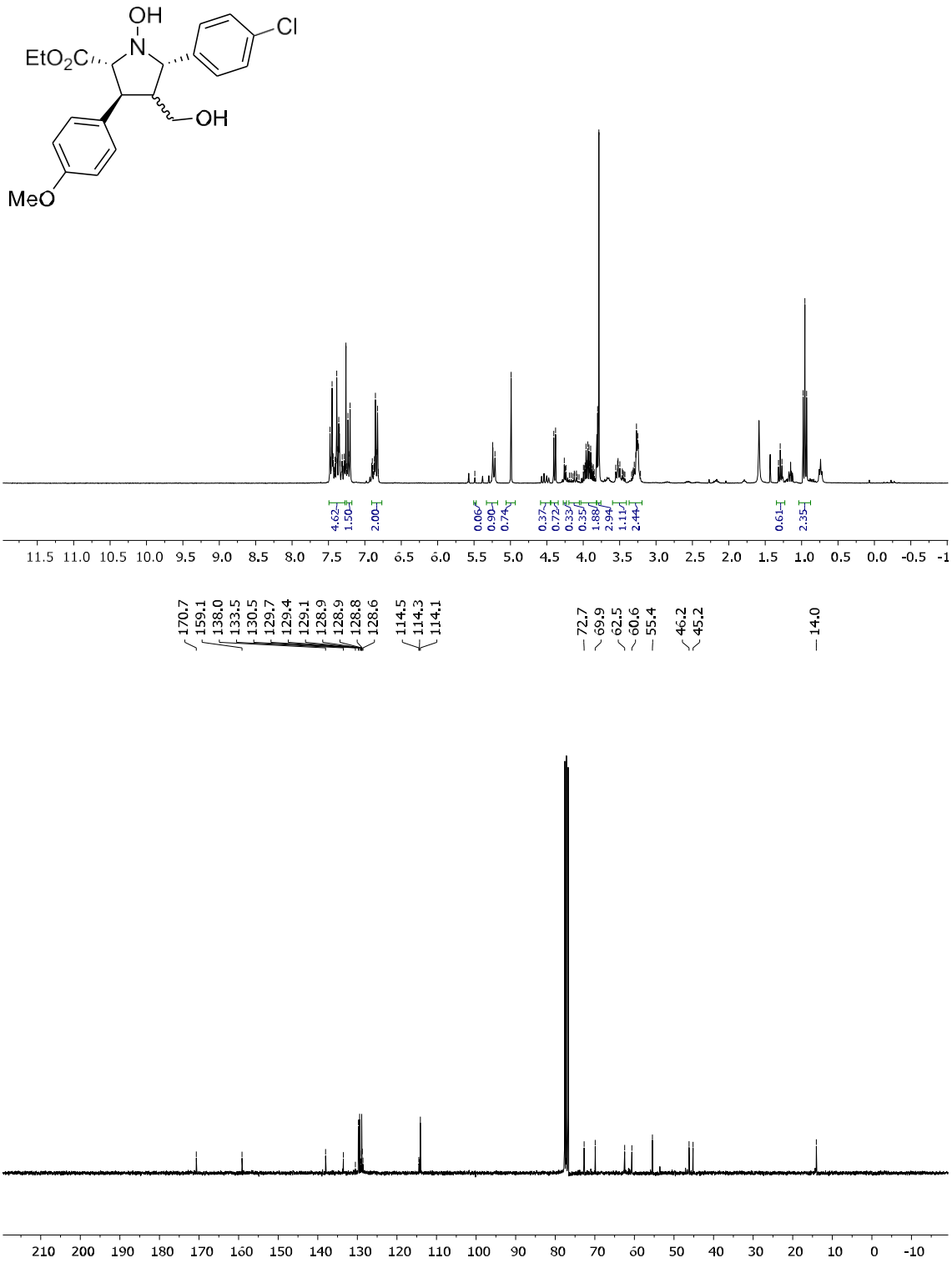

OH
N
MeO2C
Me
NO2
OSiMe2tBu
2.07
2.05
2.72
2.13
1.00
1.04
0.28
2.81
1.03
3.09
3.28
9.27
3.11
2.82
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
172.4
148.6
147.2
136.5
129.8
128.6
127.9
123.1
75.4
70.4
61.3
53.6
51.6
45.6
25.8
22.0
18.0
-5.9
-5.9

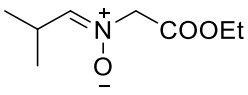

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

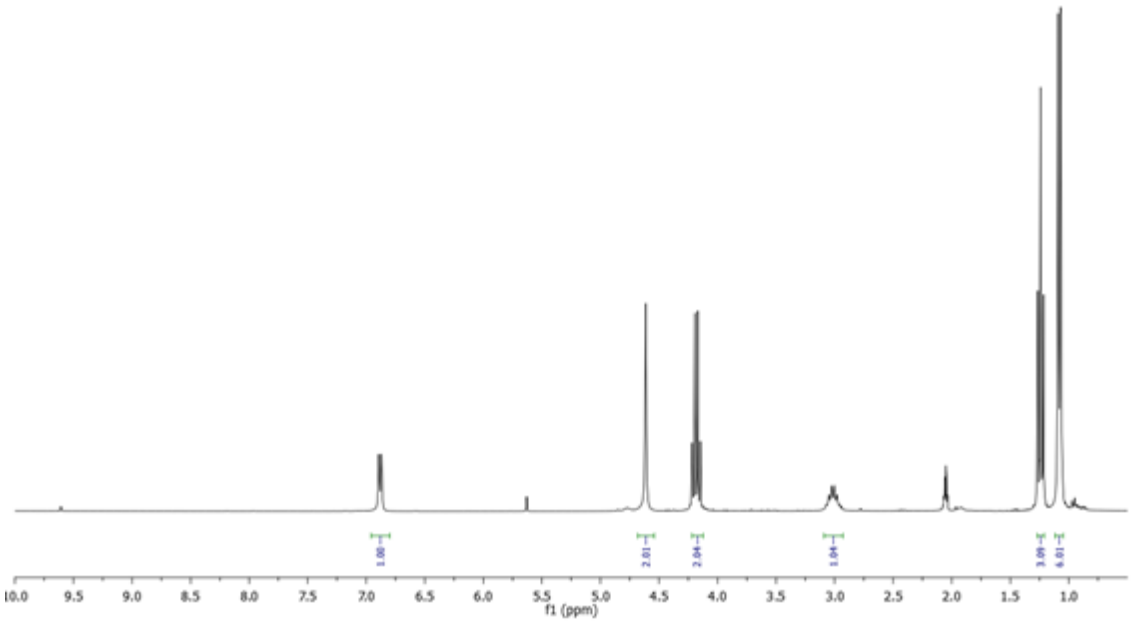

MeO2C
Me
H
N
NH2
OH
7.57
2.00
1.03
0.30
5.06
1.08
1.19
2.93
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
176.7
145.8
138.8
132.0
128.5
128.4
127.4
115.4
70.0
62.7
62.4
57.4
51.5
49.9
25.2
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

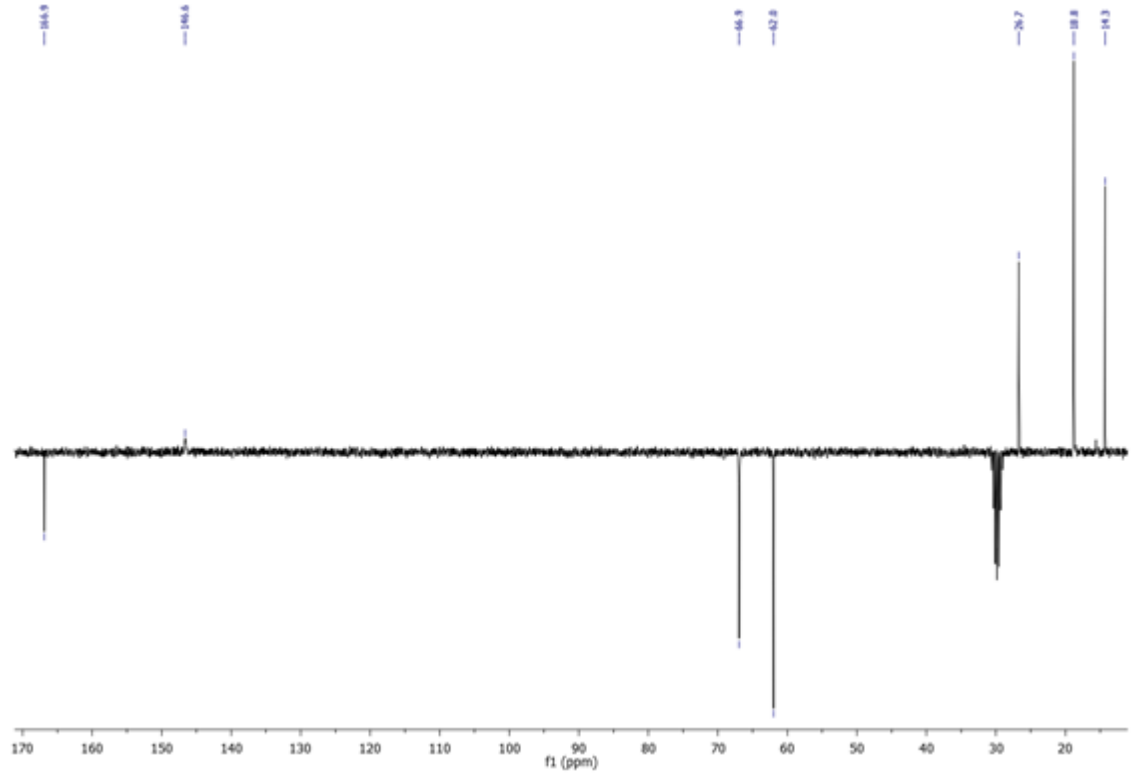

OH
N
NO2
EtO2C
OH
2.19
2.38
5.28
0.25
1.00
0.99
0.98
0.80
2.11
1.10
1.32
2.01
0.91
3.04
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
171.9
170.5
148.6
147.7
147.5
147.4
137.3
136.5
129.4
129.0
128.8
128.3
127.9
127.8
123.9
123.6
73.7
72.7
70.1
62.1
61.4
60.9
60.8
49.9
46.6
46.0
45.9
14.2
13.9
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

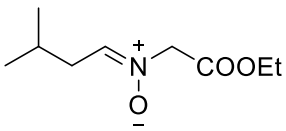

OH
N
EtO2C
NO2
OH
MeO
2.03
1.98
1.29
2.00
0.30
0.68
0.64
0.67
1.14
1.51
2.98
0.71
1.24
1.40
0.87
2.01
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
171.9
170.6
159.2
159.1
148.6
147.7
147.5
147.5
130.0
129.4
129.4
129.0
128.8
128.4
123.9
123.6
114.4
114.2
73.9
72.8
72.6
70.1
62.1
61.3
60.9
60.8
55.5
50.0
46.3
45.8
45.3
14.2
14.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


OH
N
EtO2C
Cl
OH
MeO
4.62
1.50
2.00
0.06
0.90
0.74
0.37
0.72
0.33
0.35
1.88
2.94
1.11
2.44
0.61
2.35
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
170.7
159.1
138.0
133.5
130.5
129.7
129.4
129.1
128.9
128.9
128.8
128.6
114.5
114.3
114.1
72.7
69.9
62.5
60.6
55.4
46.2
45.2
14.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

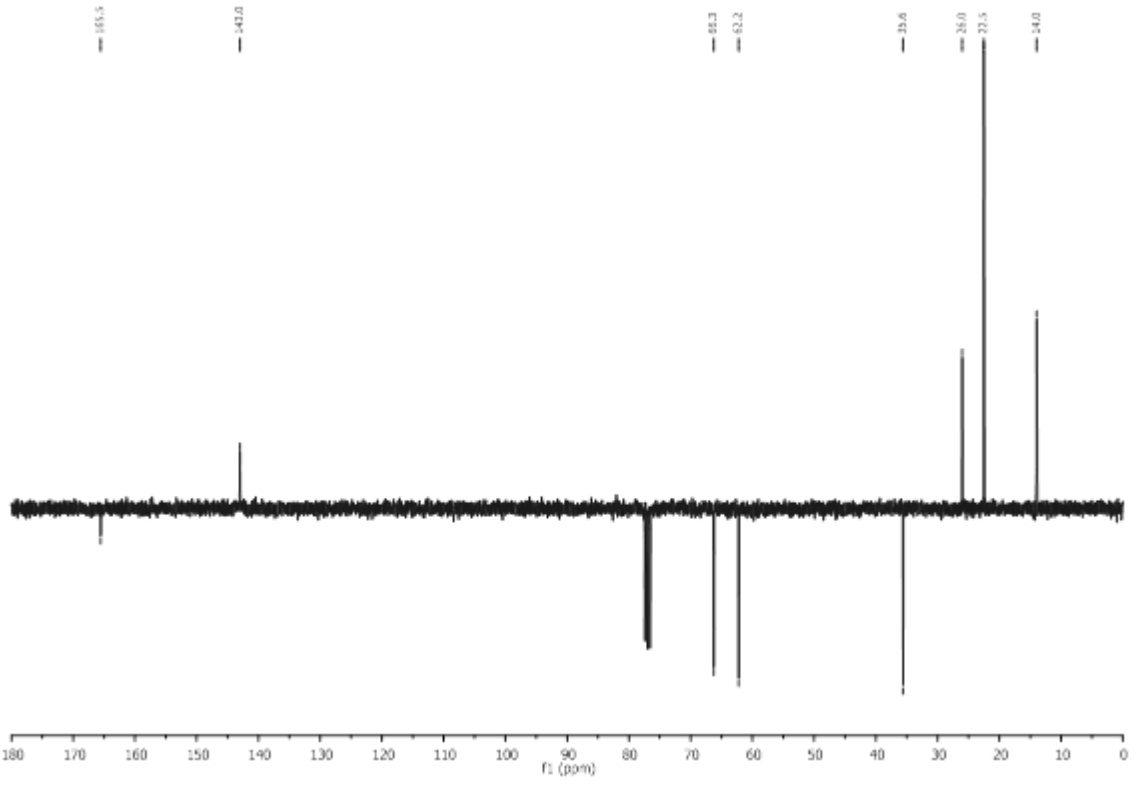

COOEt

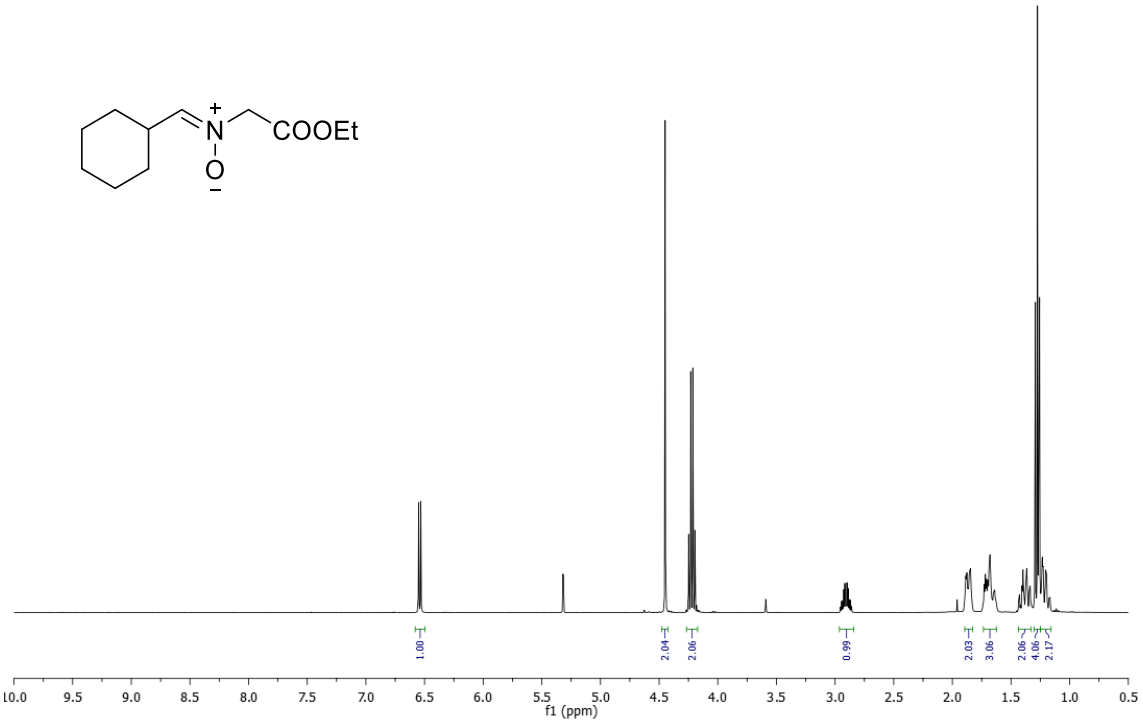

1.00
2.01
2.04
1.04
3.09
6.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)

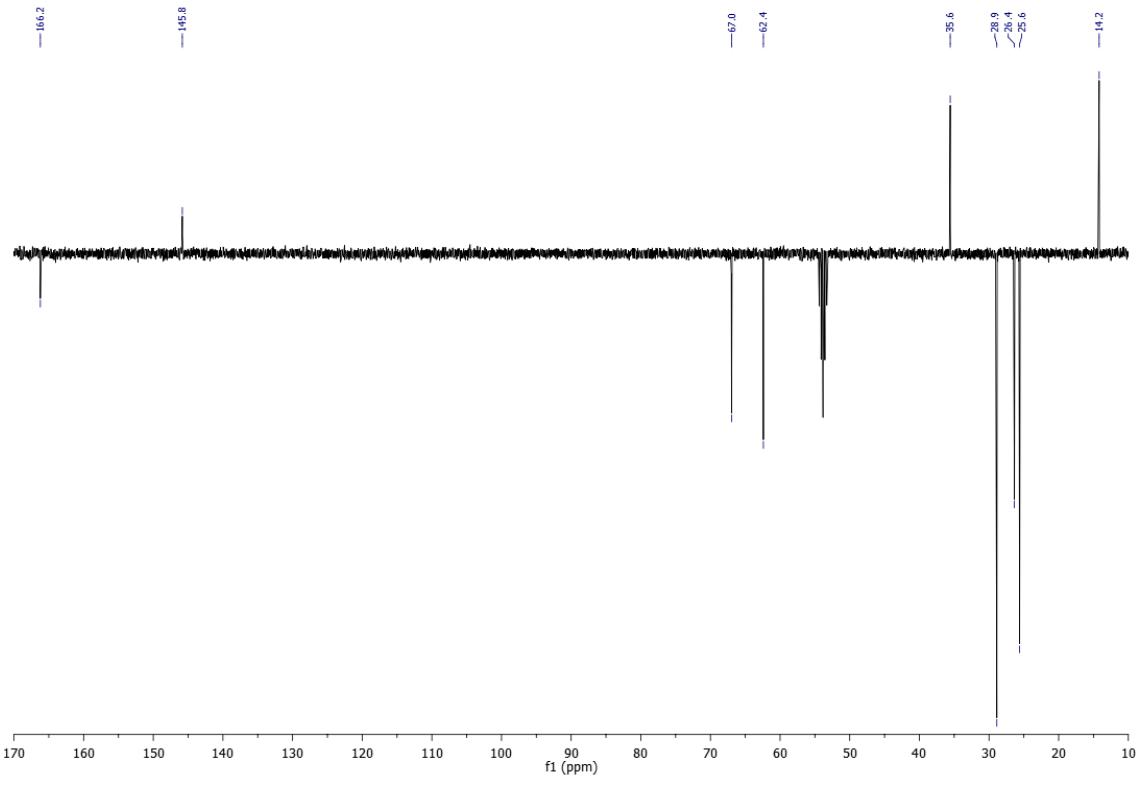

164.9
146.6
66.9
62.0
26.7
18.8
14.3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

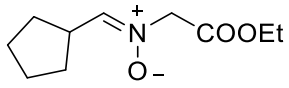

COOEt

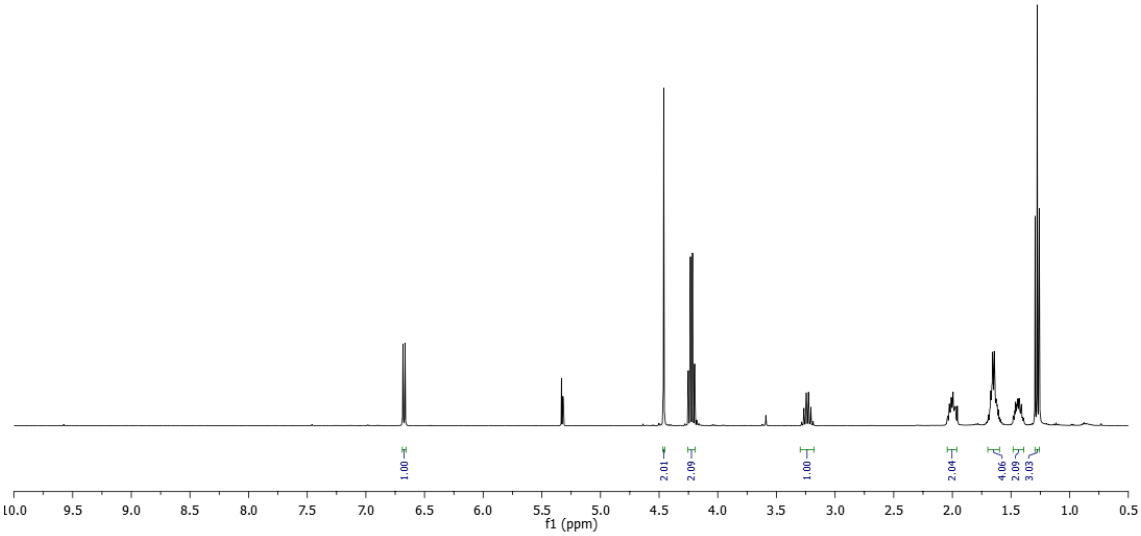
f1 (ppm)

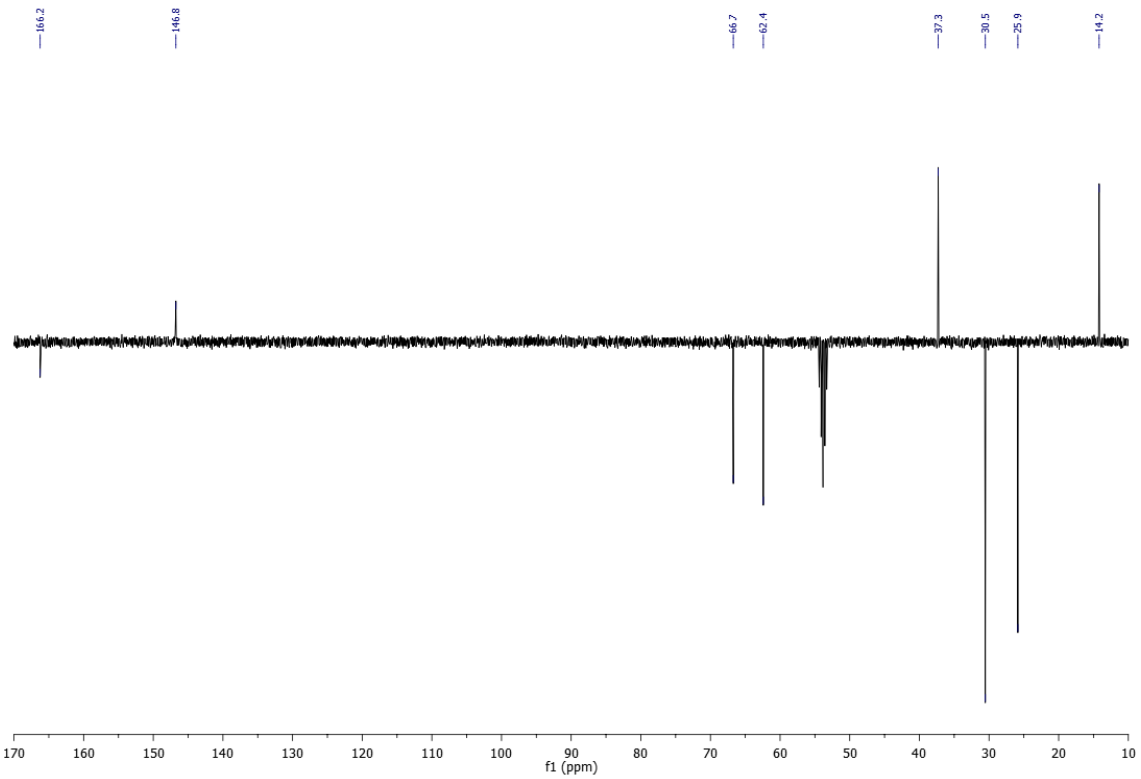

f1 (ppm)

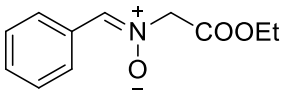

COOEt
1.00
2.04
2.06
0.99
2.03
3.06
2.06
4.06
2.17
f1 (ppm)

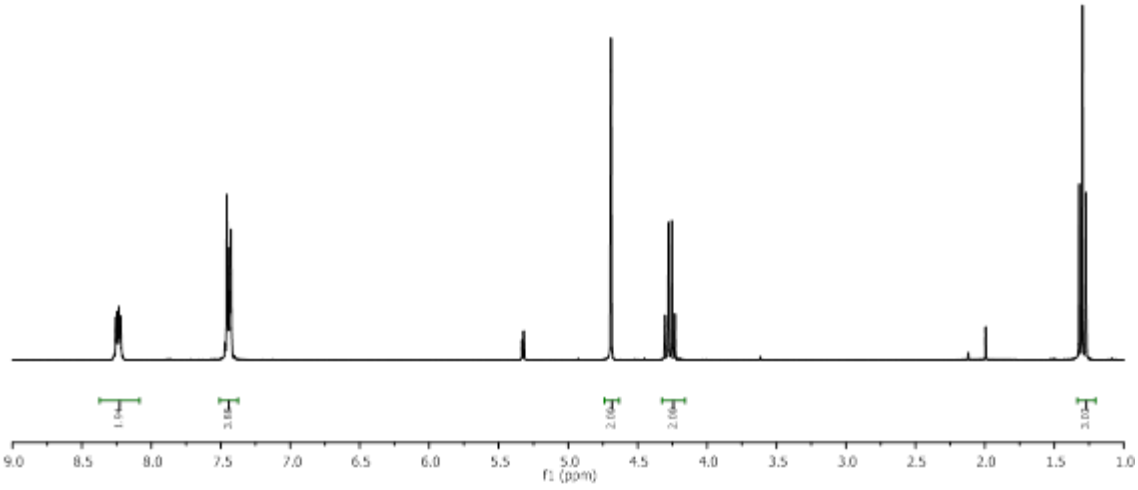

166.2
145.8
67.0
62.4
35.6
28.9
26.4
25.6
14.2
f1 (ppm)

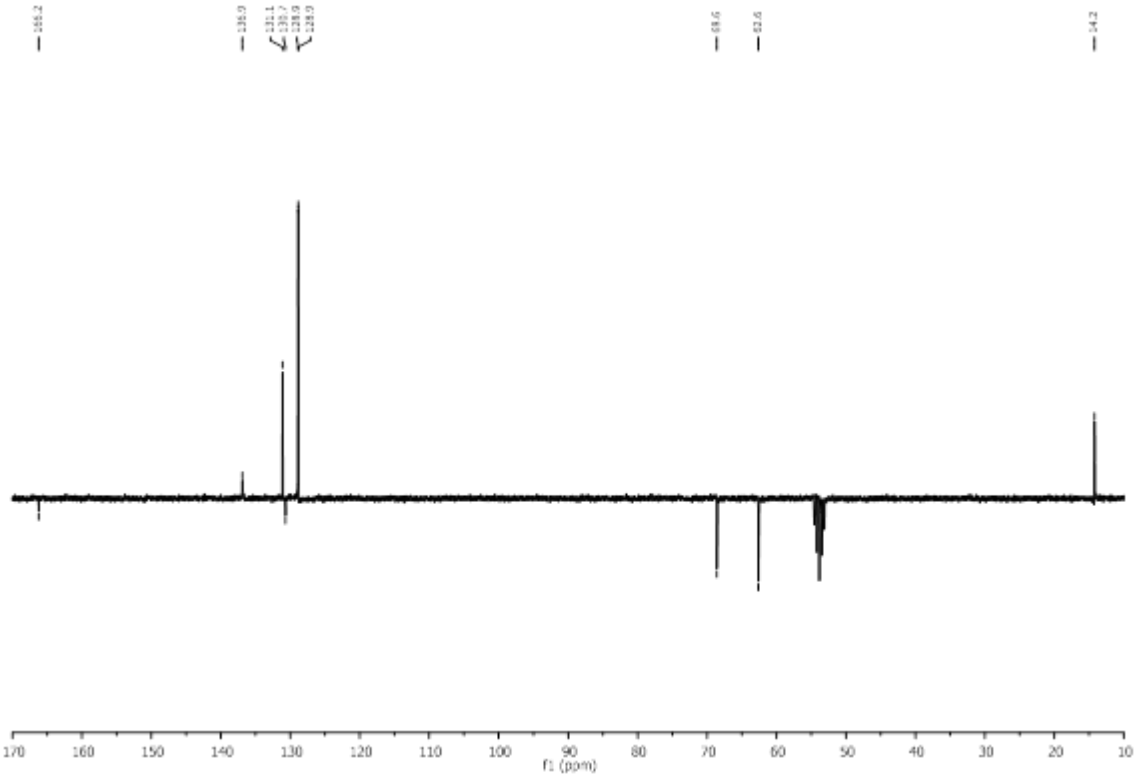

COOEt
N
O

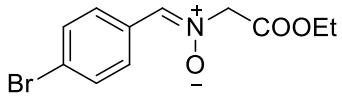

1.00
2.01
2.09
1.00
2.04
4.06
2.09
3.03
f1 (ppm)


166.2
146.8
66.7
62.4
37.3
30.5
25.9
14.2
f1 (ppm)

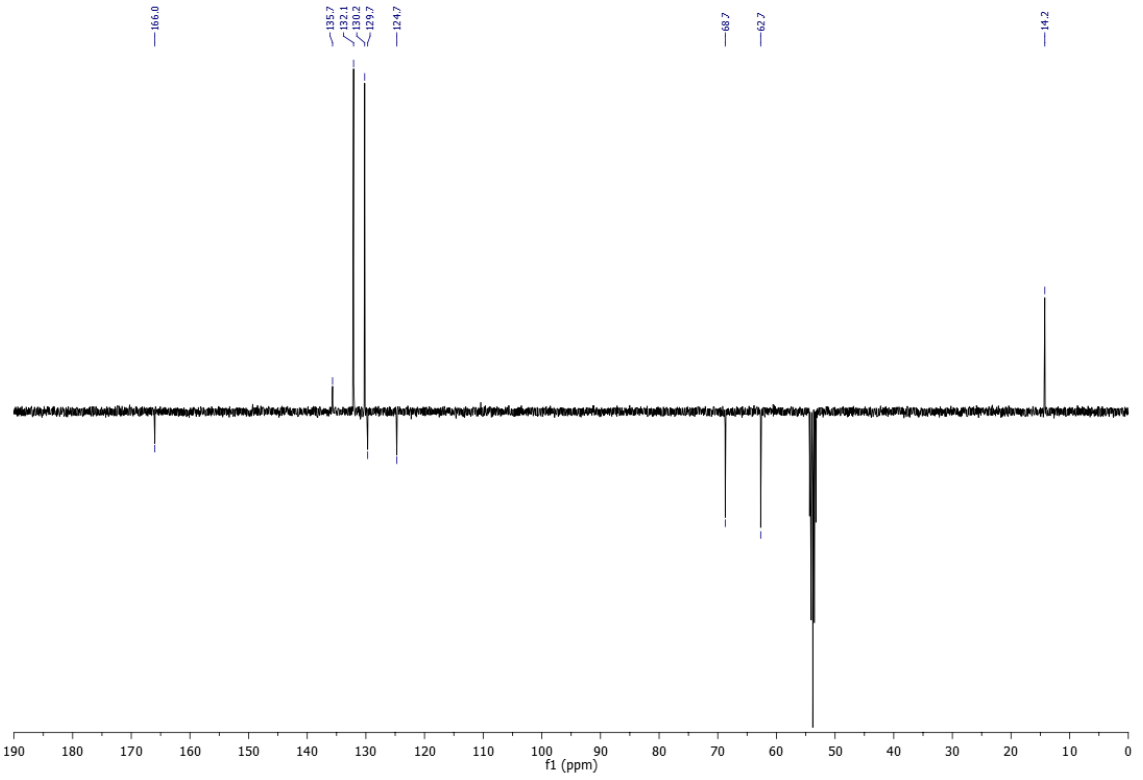

COOEt

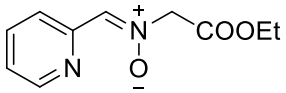

f1 (ppm)

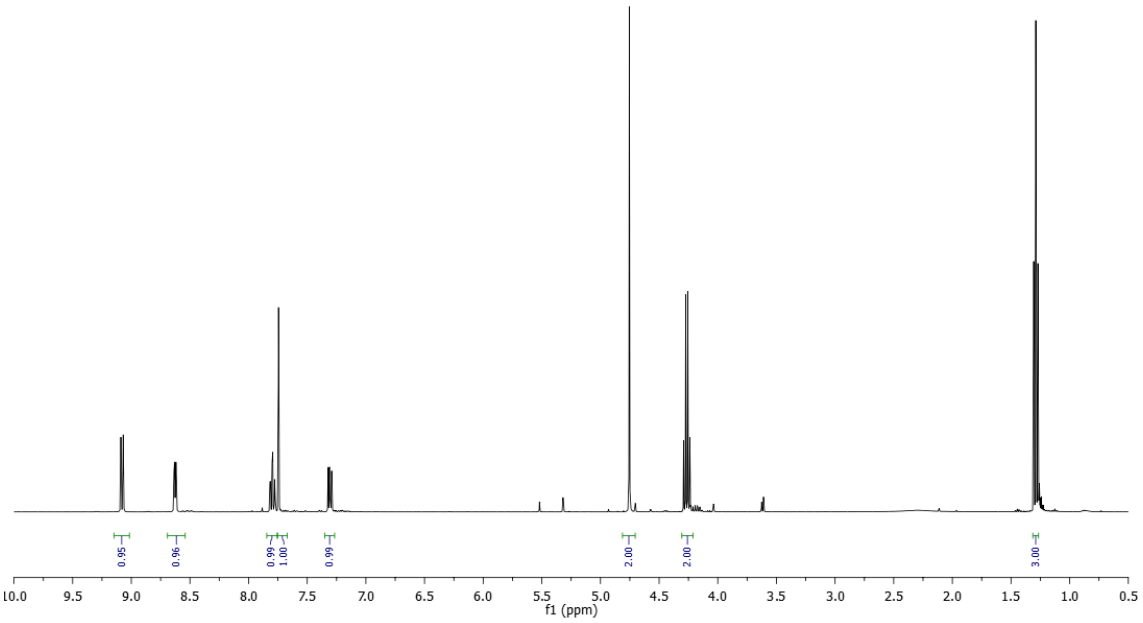

f1 (ppm)

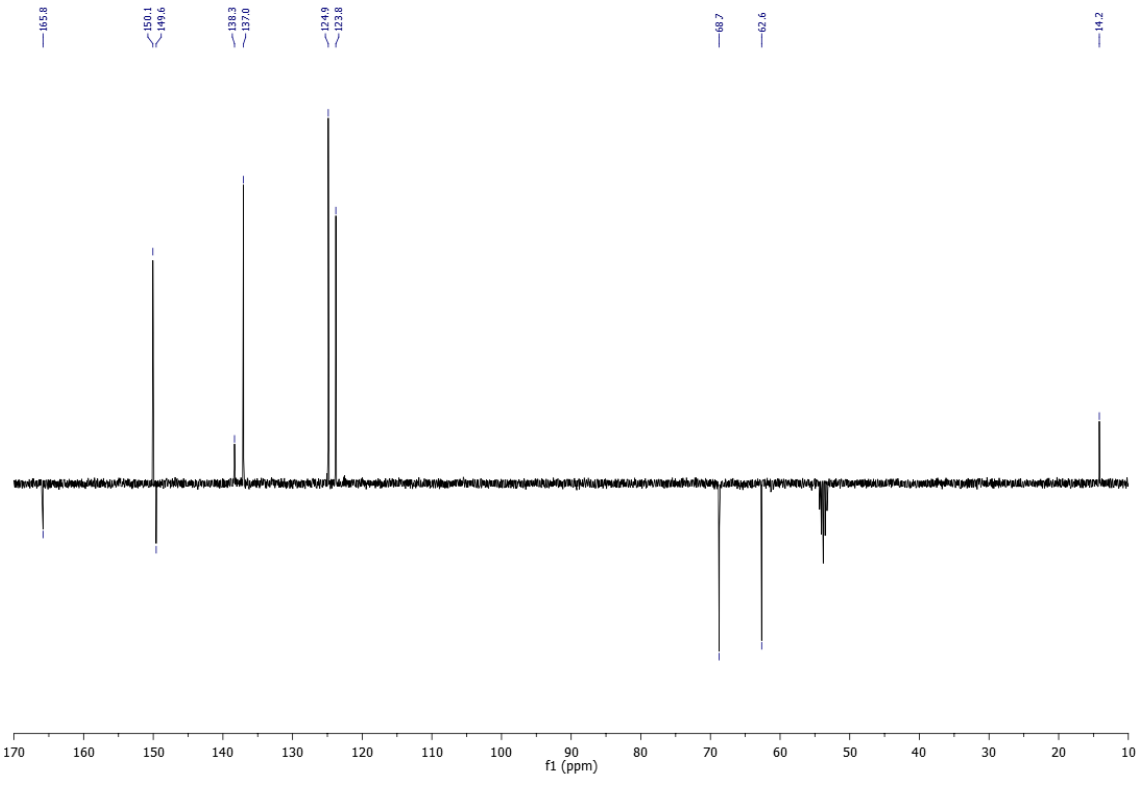

Br
N
O
COOEt

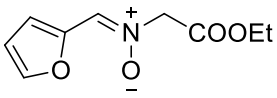
1.99
1.95
1.00
2.00
2.00
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

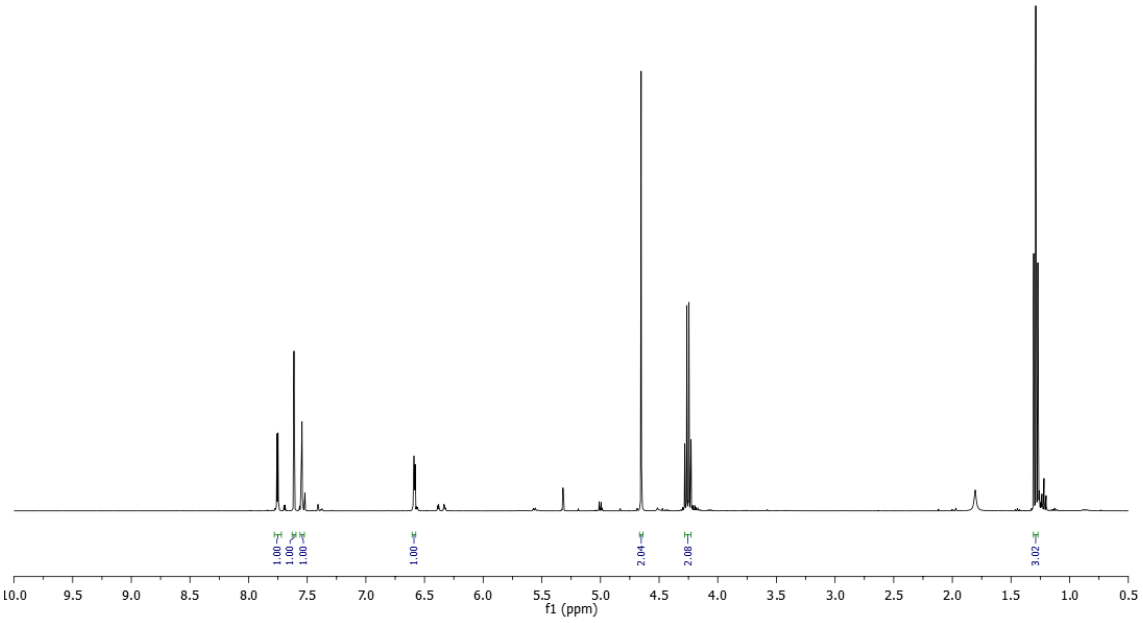

166.0
135.7
132.1
130.2
129.7
124.7
68.7
62.7
14.2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


COOEt
N
O


0.95
0.96
0.99
1.00
0.99
2.00
2.00
3.00
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
f1 (ppm)


165.8
150.1
149.6
138.3
137.0
124.9
123.8
68.7
62.6
14.2
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


COOEt
O
N
O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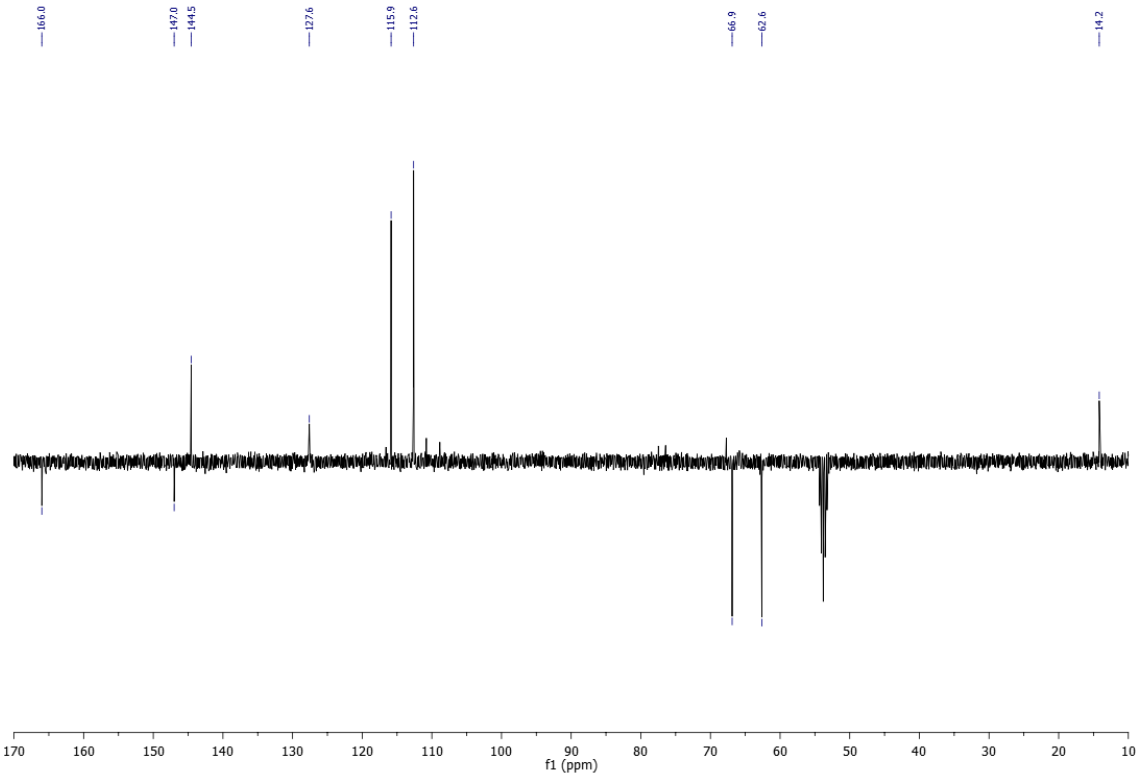
1.00
1.00
1.00
2.04
2.08
3.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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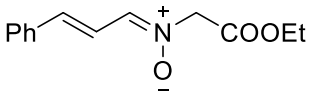
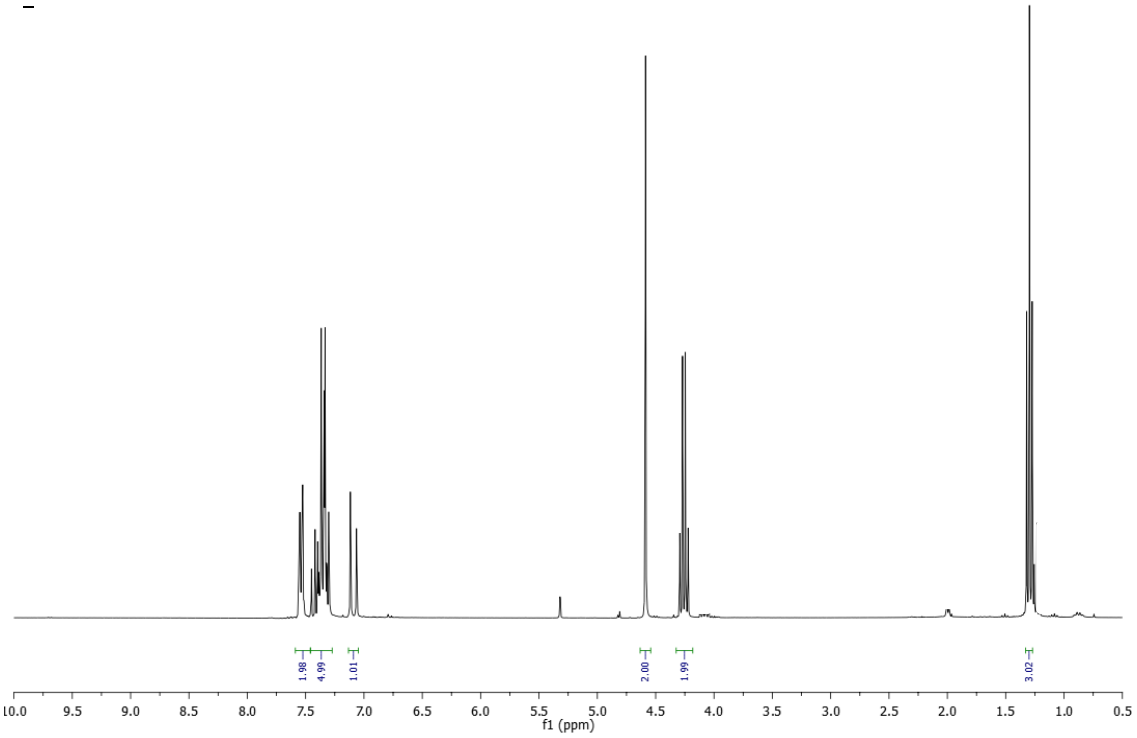
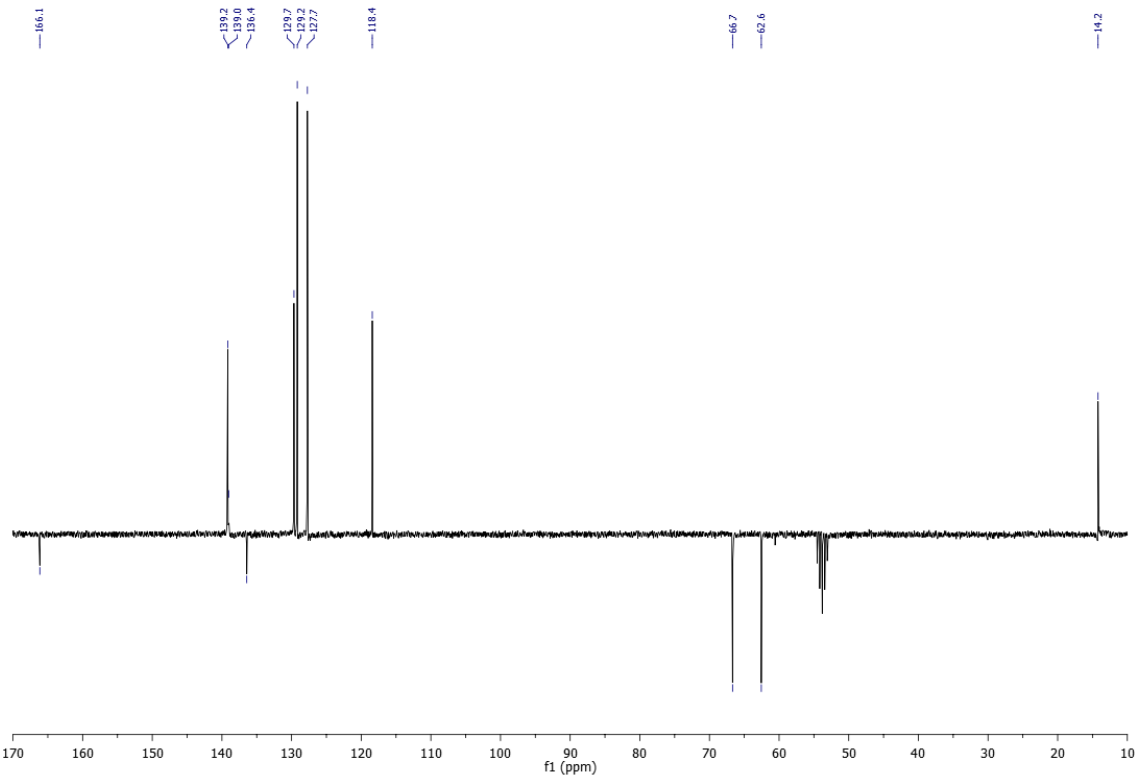
147.0
144.5
127.6
115.9
112.6
66.9
62.6
14.2
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


Ph
N
COOEt
O


1.98
4.99
1.01
2.00
1.99
3.02
f1 (ppm)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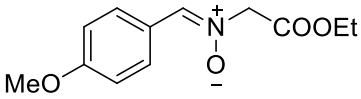
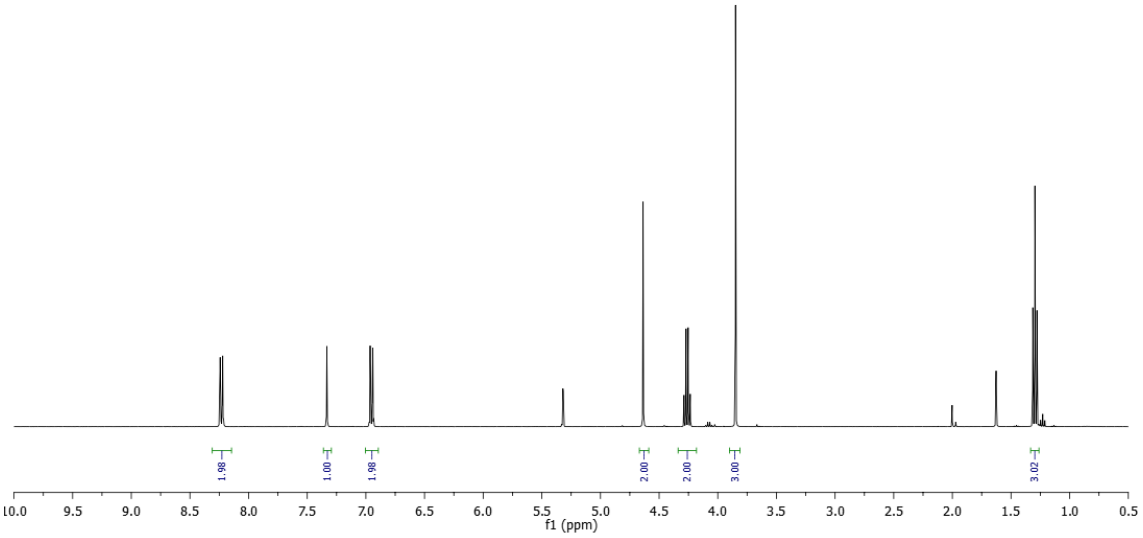
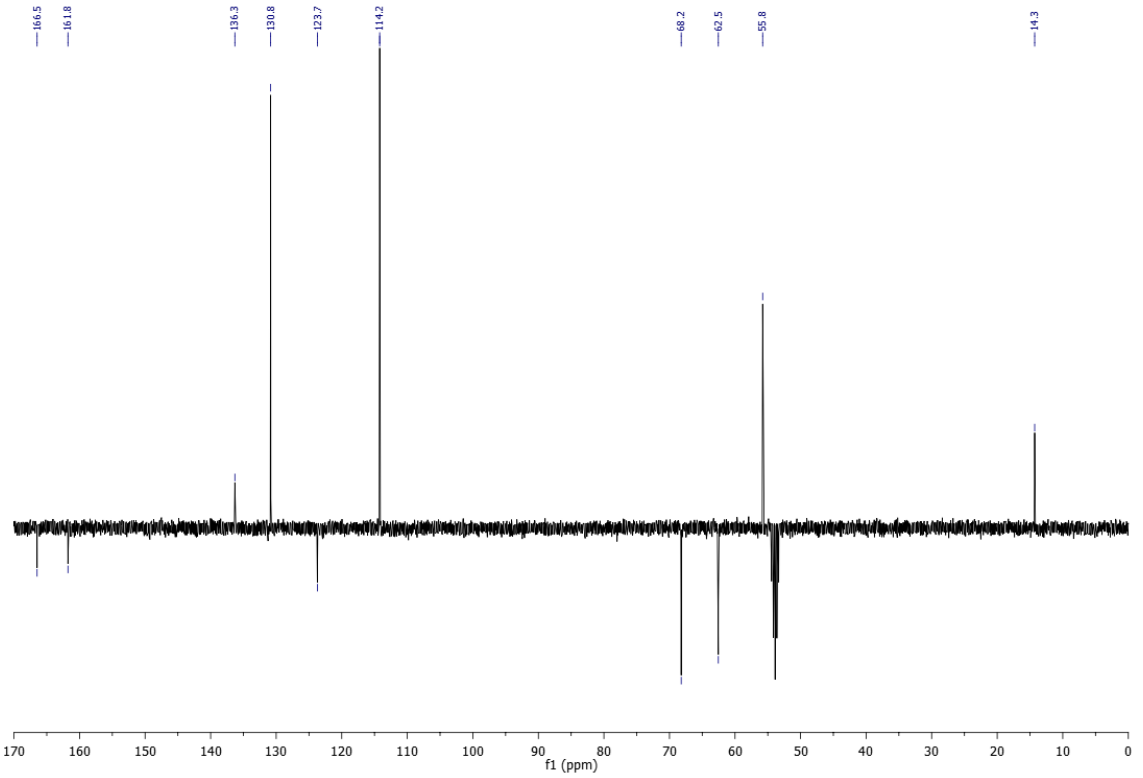
139.2
139.0
136.4
129.7
129.2
127.7
118.4
66.7
62.6
14.2
f1 (ppm)


MeO
N
O
COOEt


1.98
1.00
1.98
2.00
2.00
3.00
3.02
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)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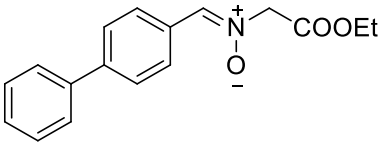
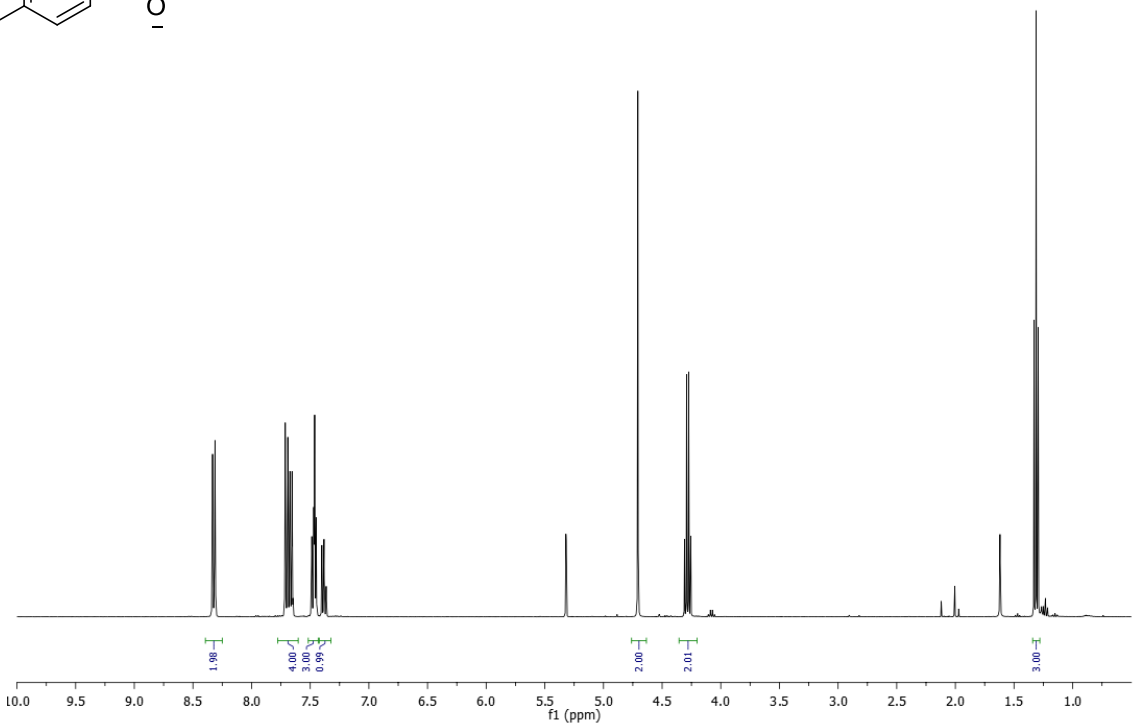
161.8
136.3
130.8
123.7
114.2
68.2
62.5
55.8
14.3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


COOEt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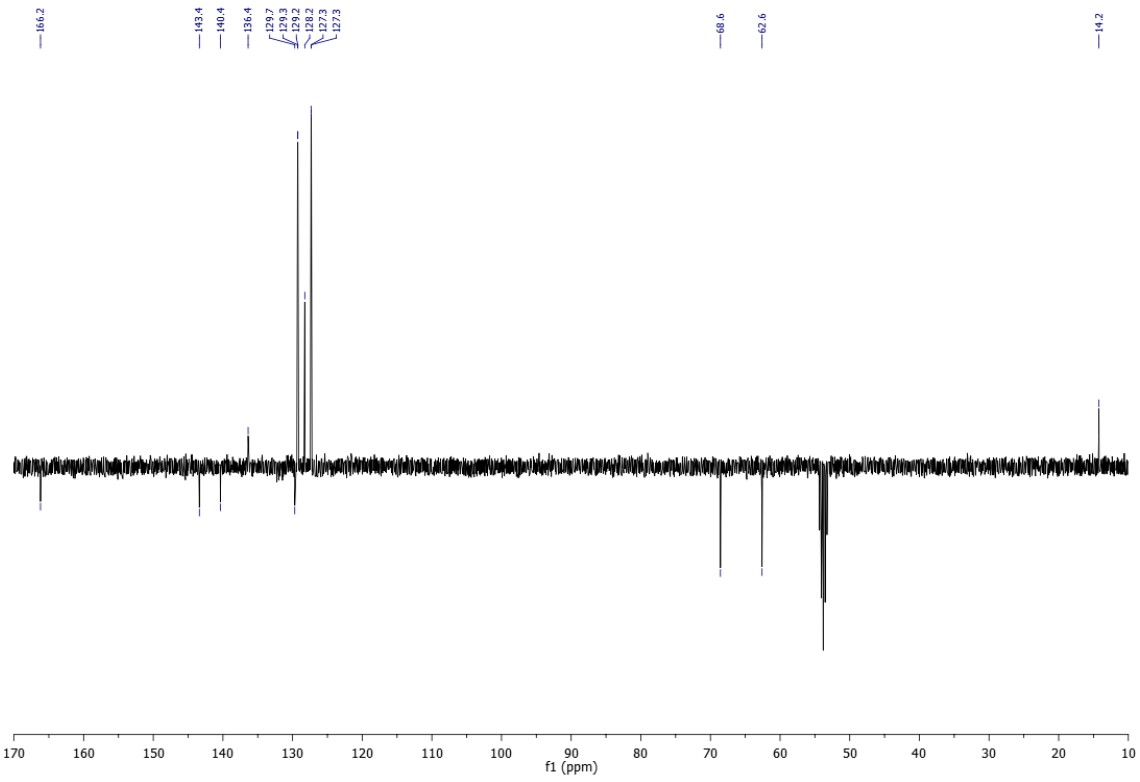
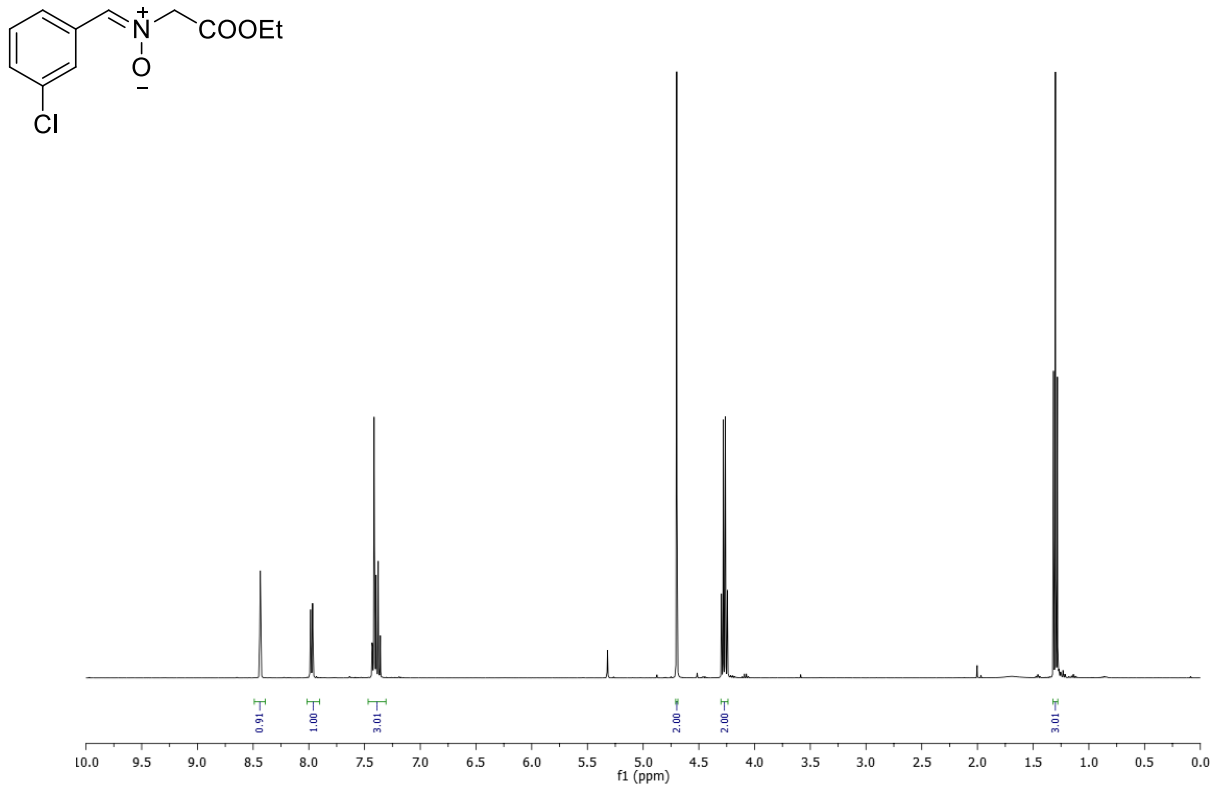
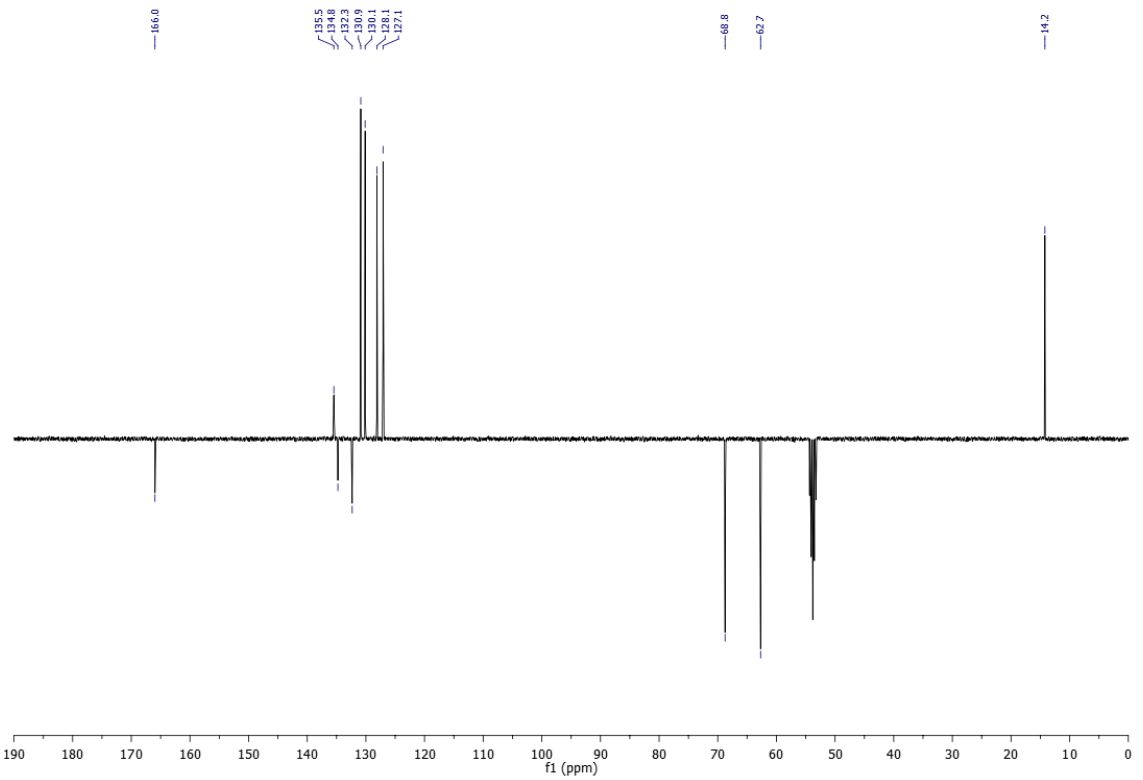
4.00
3.00
0.99
2.00
2.01
3.00
f1 (ppm)


166.2
143.4
140.4
136.4
129.7
129.3
129.2
128.2
127.3
127.3
68.6
62.6
14.2
f1 (ppm)


COOEt
Cl
0.91
1.00
3.01
2.00
2.00
3.01
f1 (ppm)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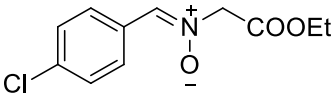
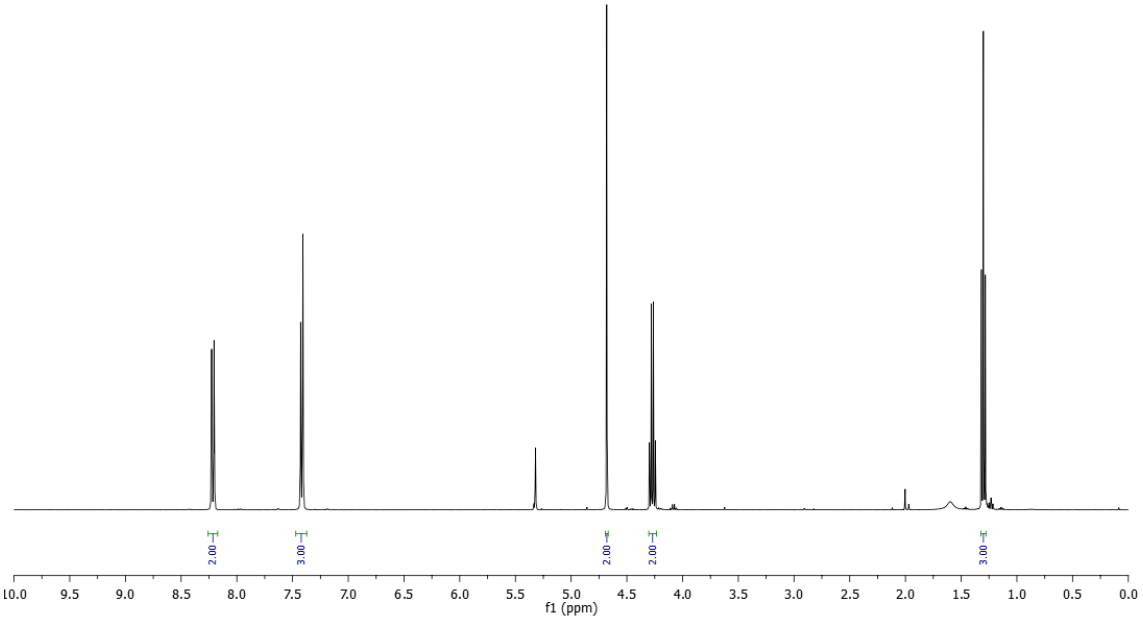
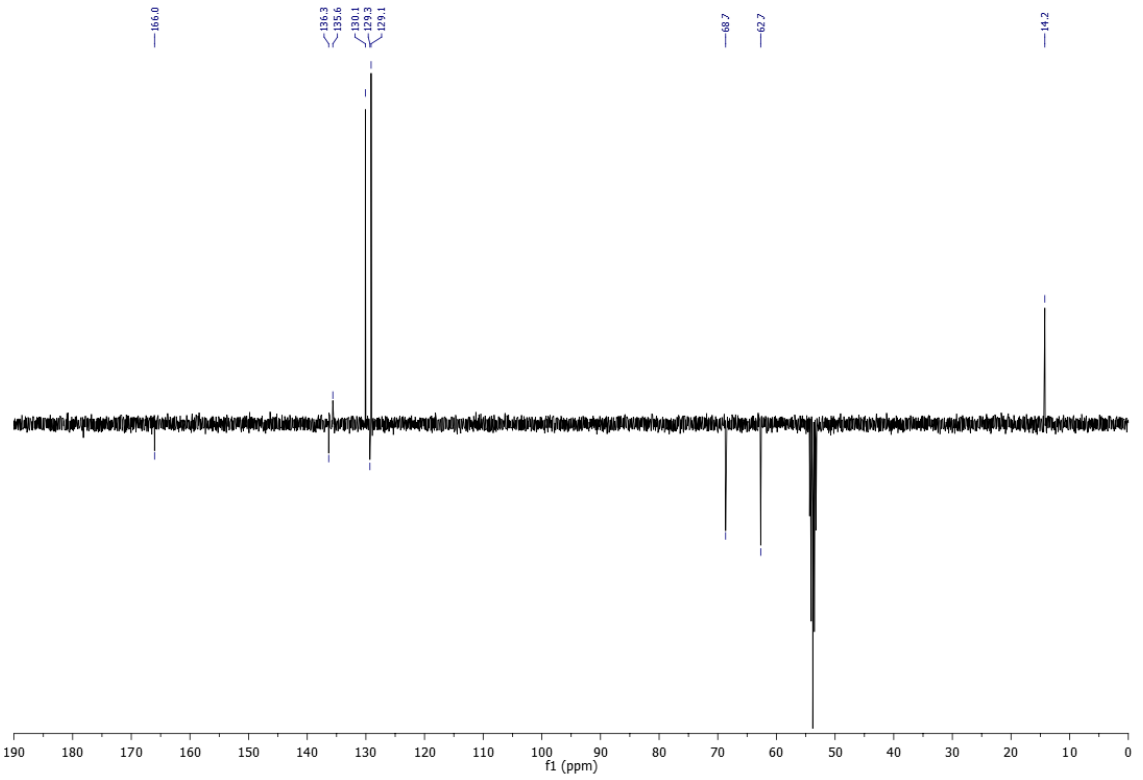
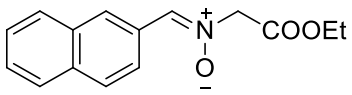
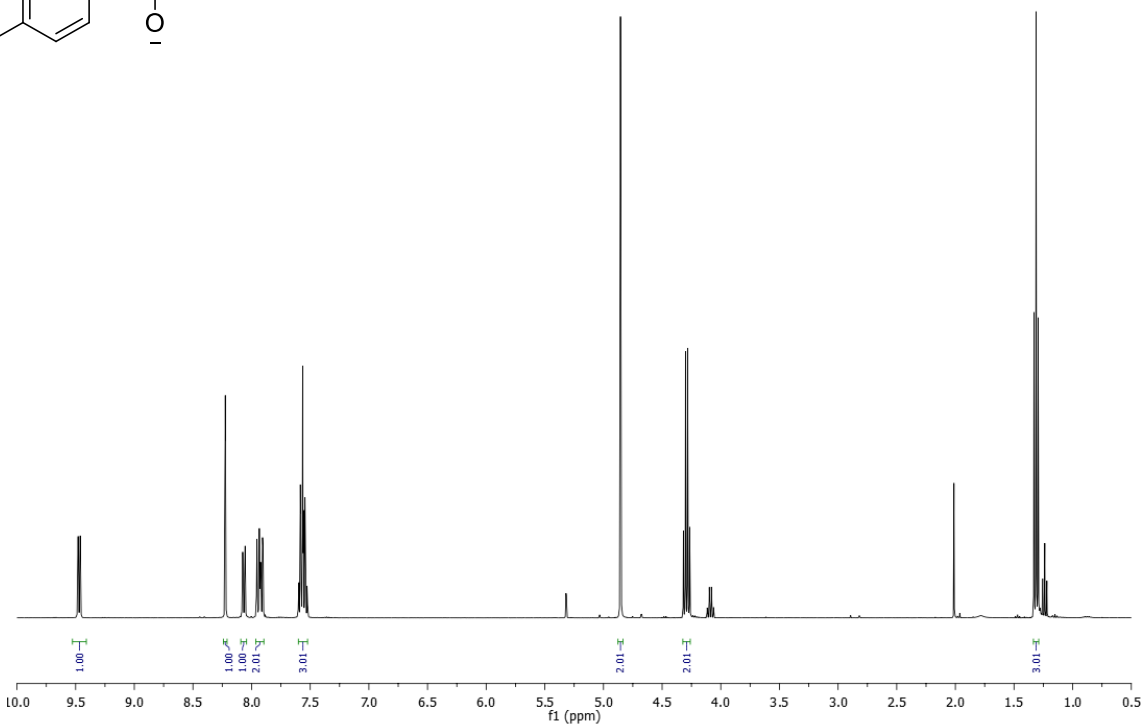
135.5
134.8
132.3
130.9
130.1
128.1
127.1
68.8
62.7
14.2
f1 (ppm)

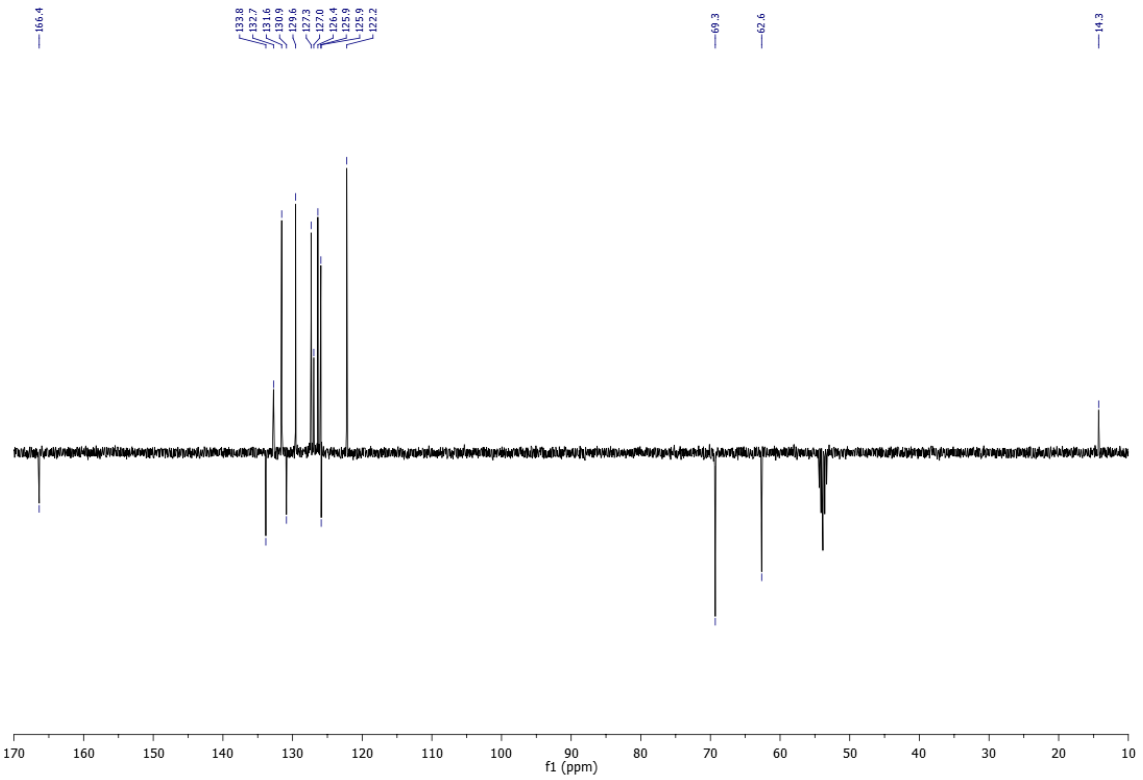

Cl
N
O
COOEt


2.00
3.00
2.00
2.00
3.00
f1 (ppm)


166.0
136.3
135.6
130.1
129.3
129.1
68.7
62.7
14.2
f1 (ppm)


COOEt


1.00
1.00
1.00
2.01
3.01
2.01
2.01
3.01
f1 (ppm)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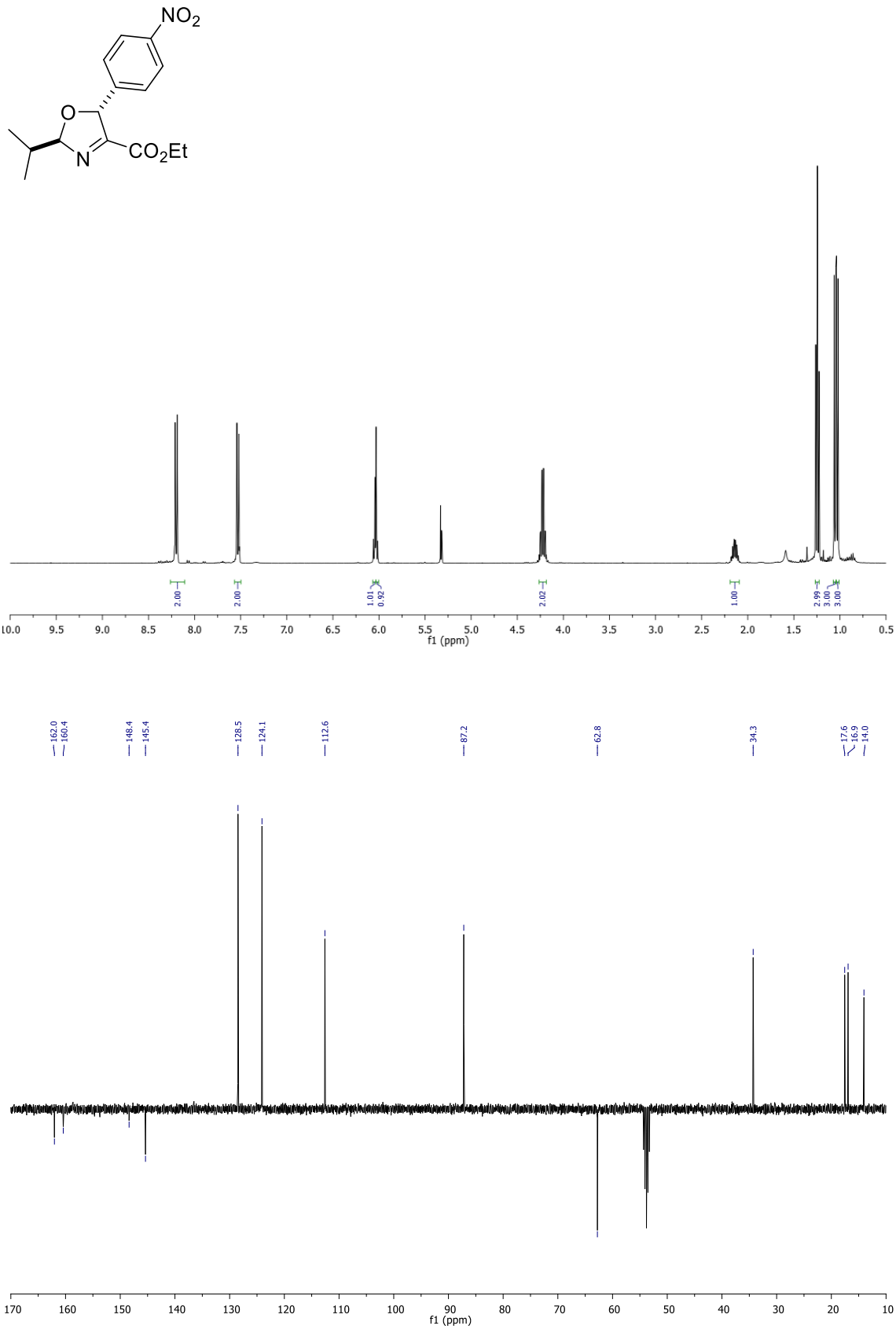
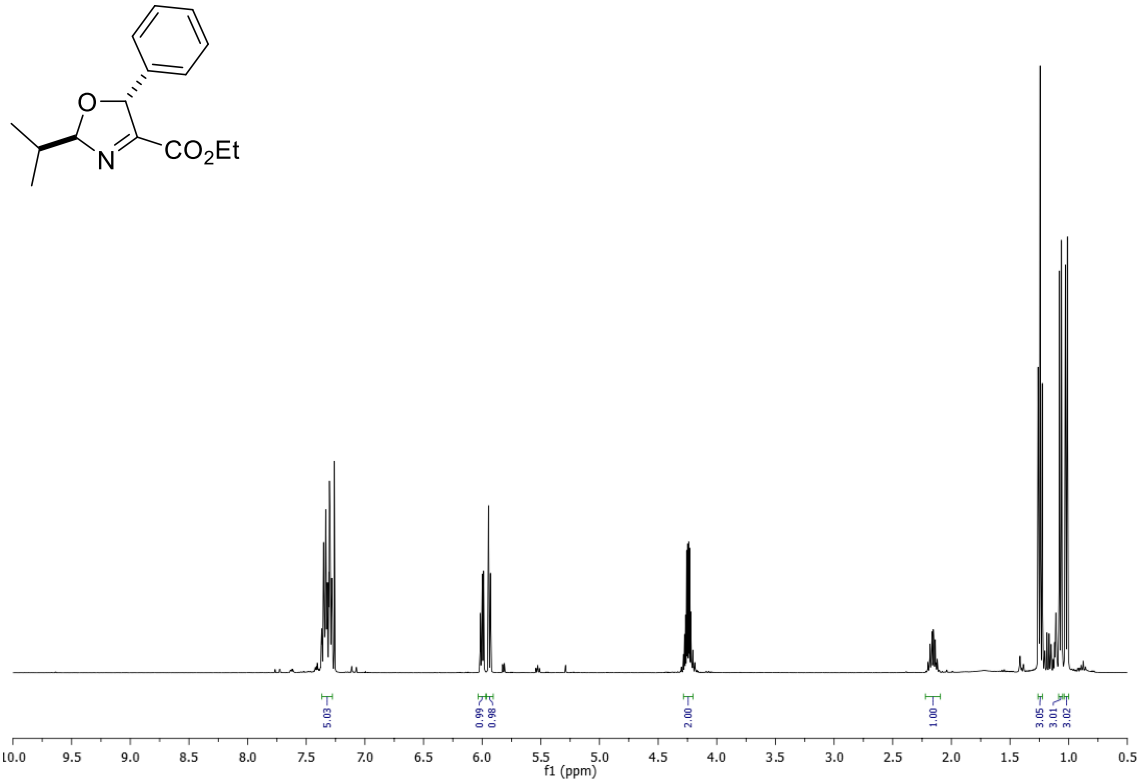
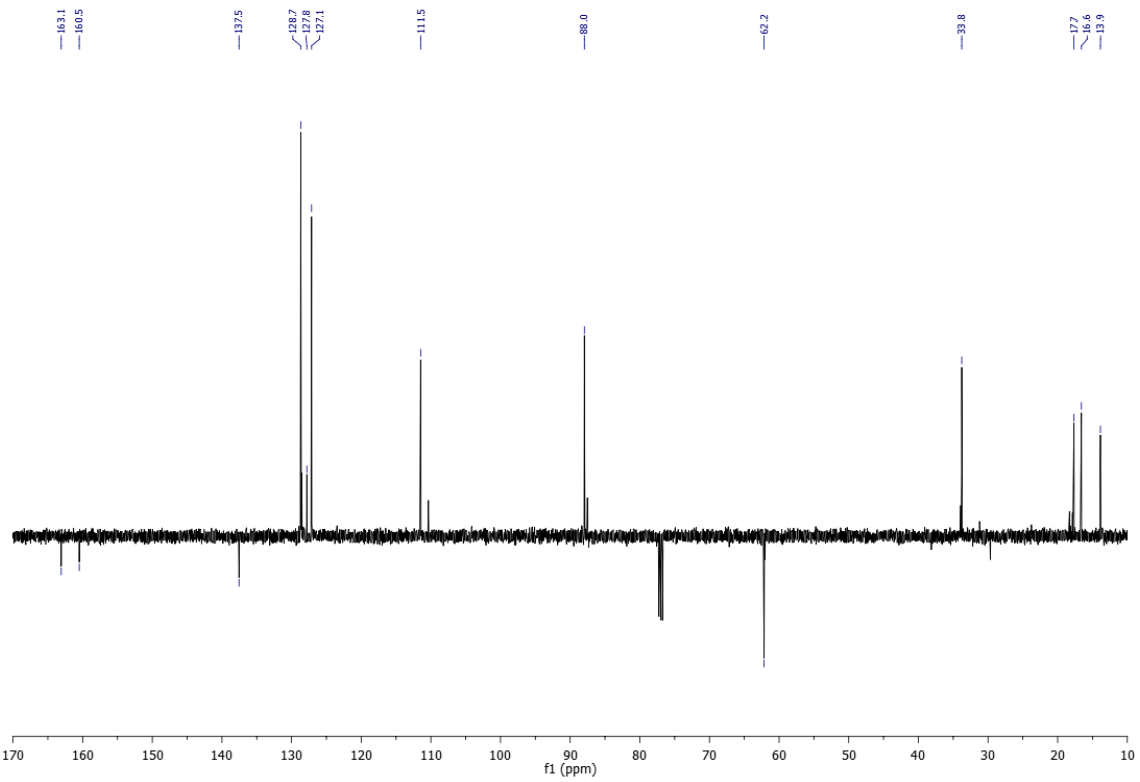
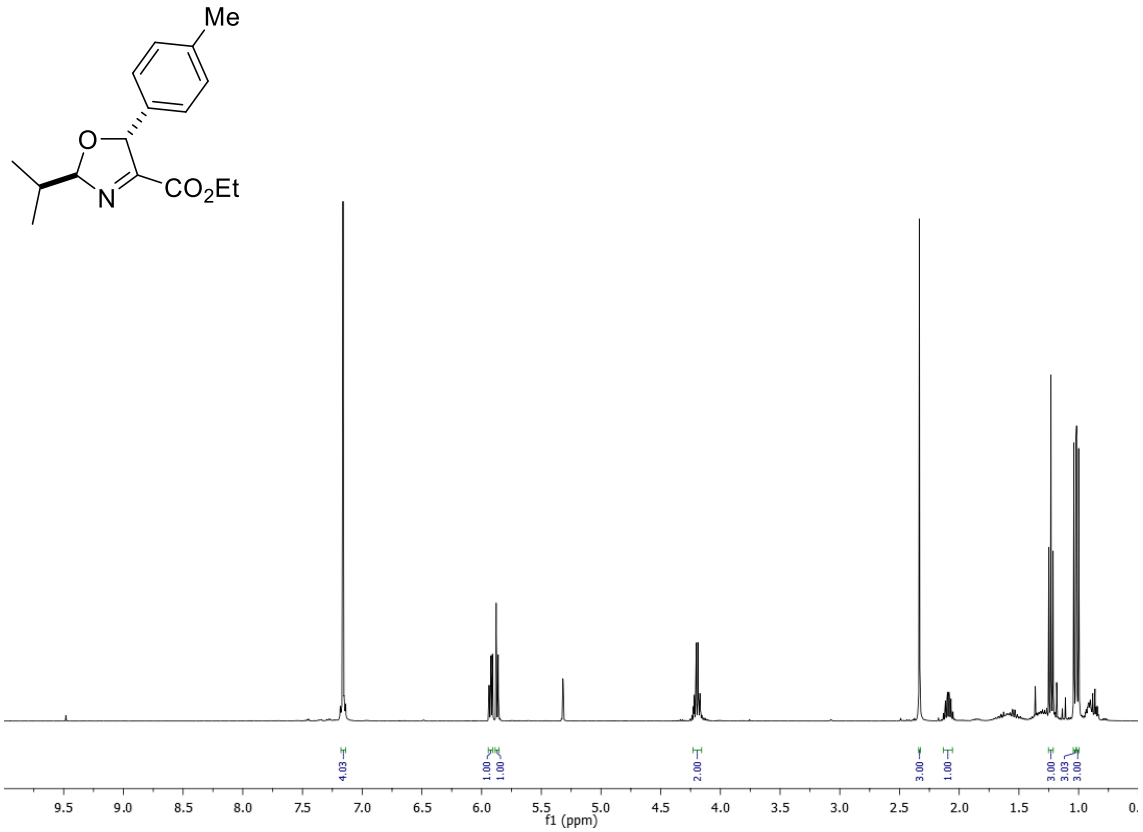
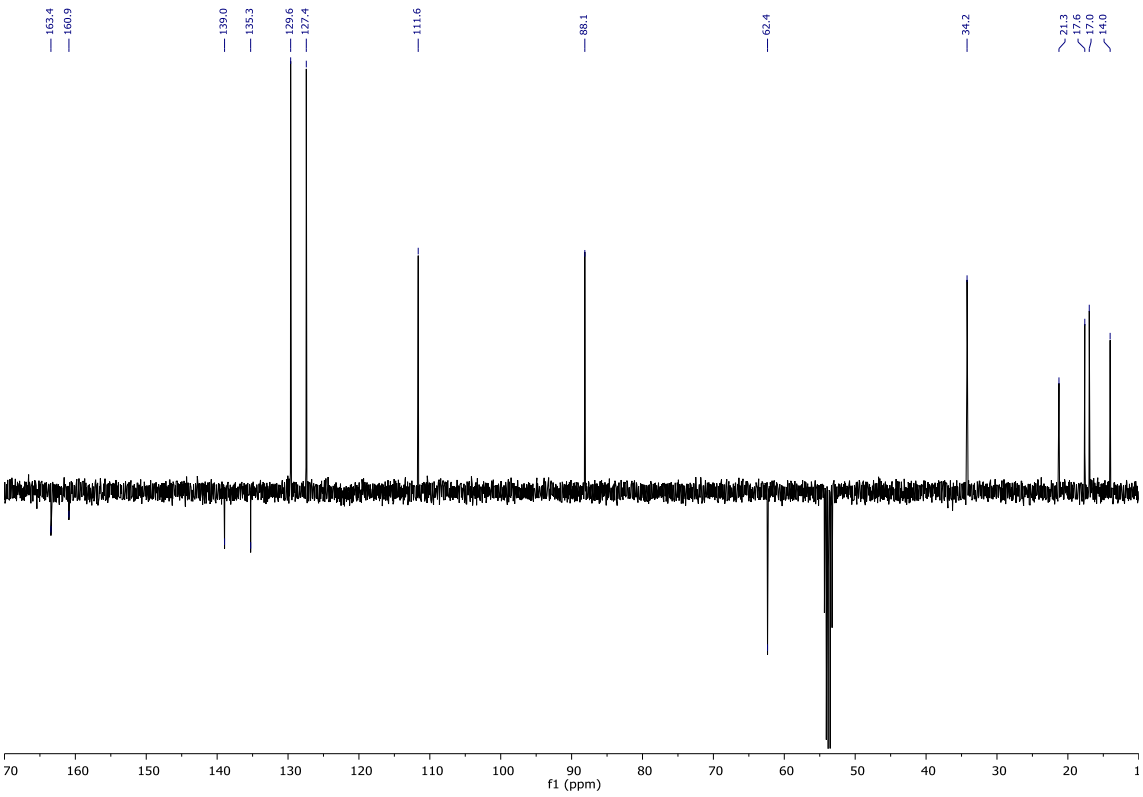
133.8
132.7
131.6
130.9
129.6
127.3
127.0
126.4
125.9
125.9
122.2
69.3
62.6
14.3
f1 (ppm)

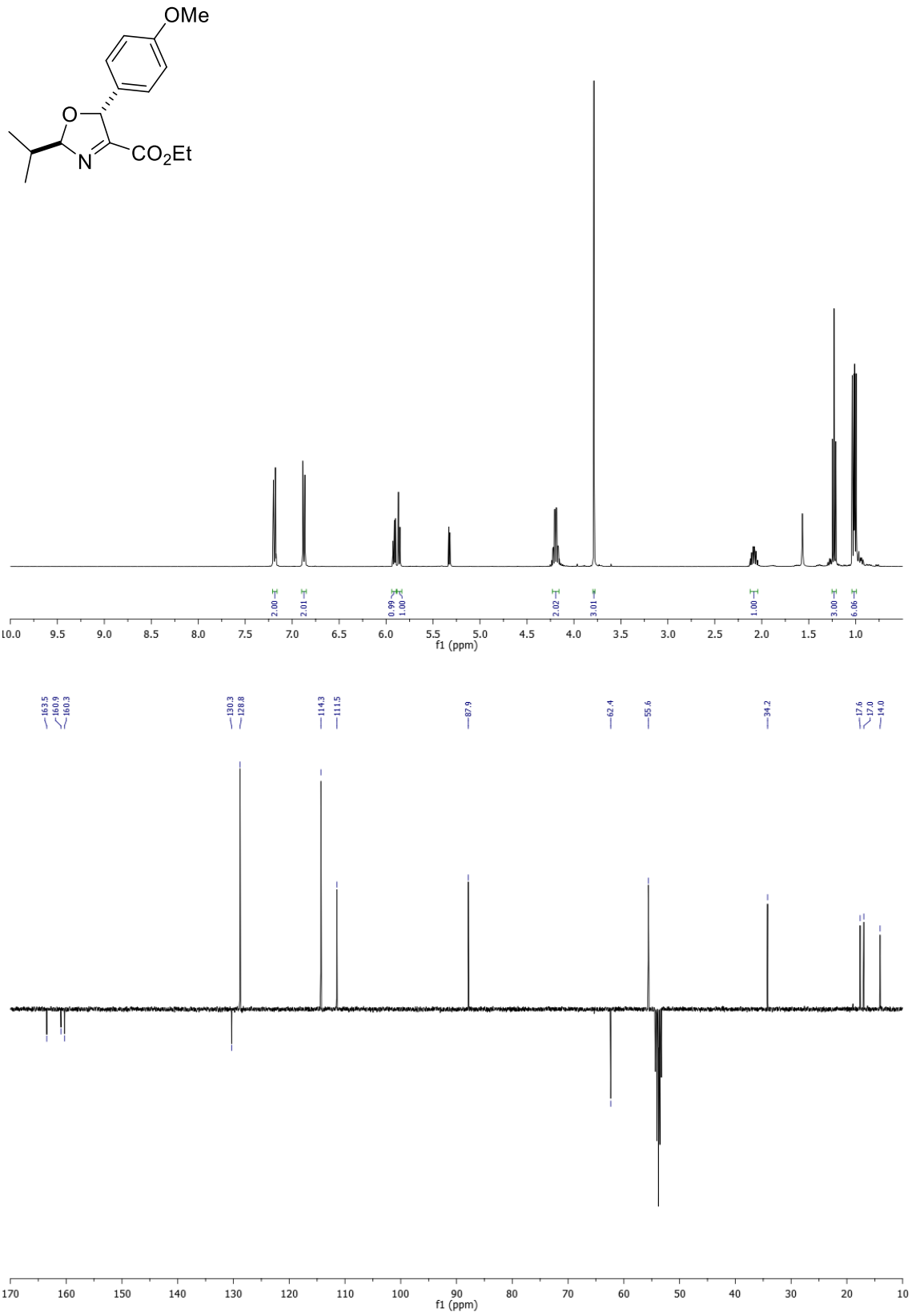

NO2
O
N
CO2Et
2.00
2.00
1.01
0.92
2.02
1.00
2.99
3.00
3.00
f1 (ppm)
162.0
160.4
148.4
145.4
128.5
124.1
112.6
87.2
62.8
34.3
17.6
16.9
14.0
f1 (ppm)

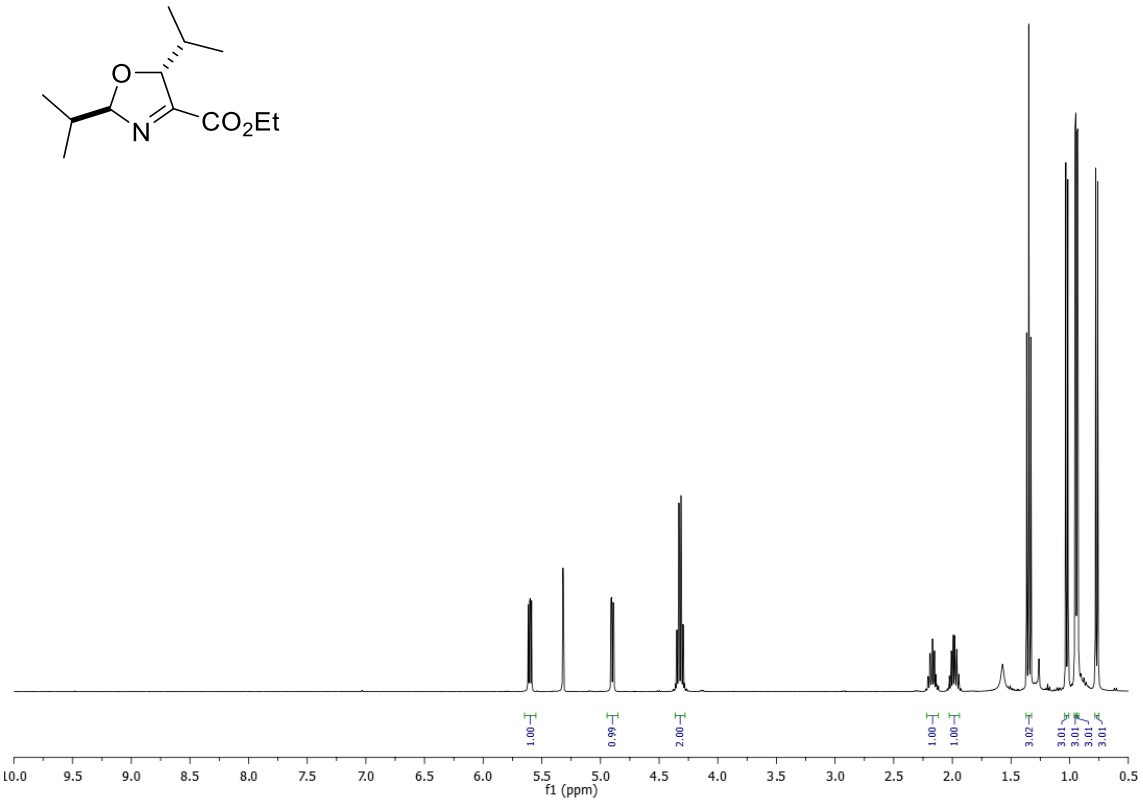

O
N
CO2Et
5.03
0.99
0.98
2.00
1.00
3.05
3.01
3.02
f1 (ppm)

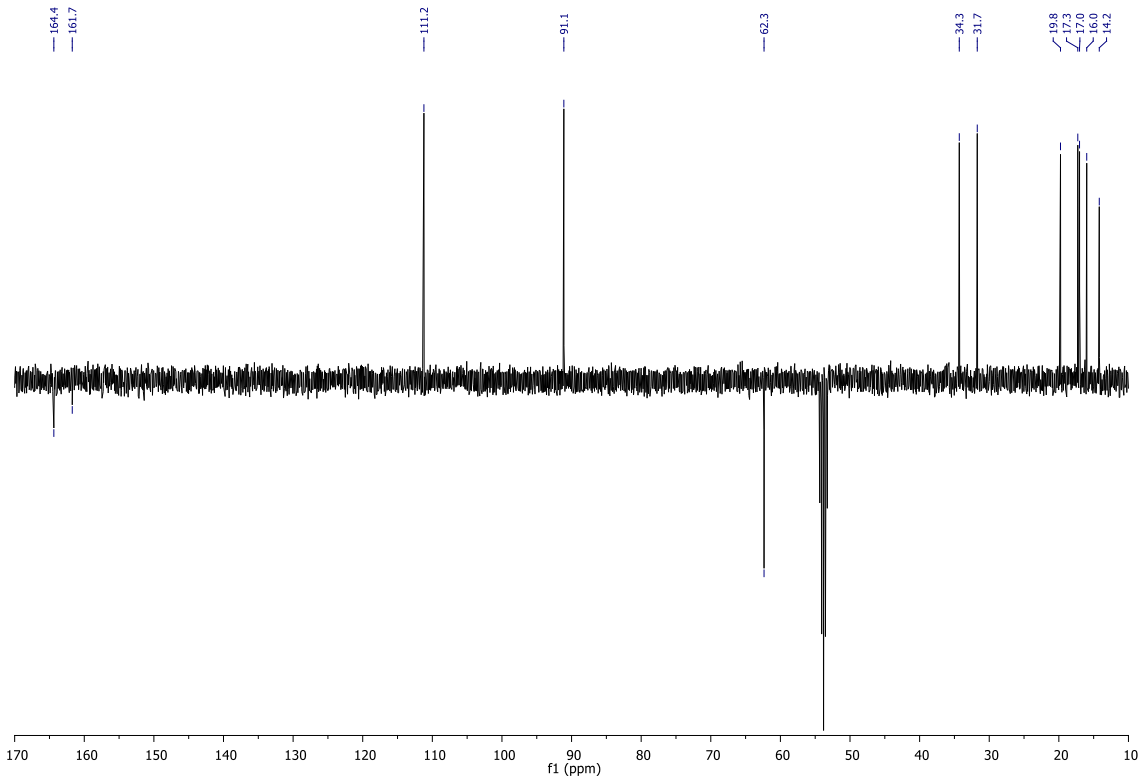

163.1
160.5
137.5
128.7
127.8
127.1
111.5
88.0
62.2
33.8
17.7
16.6
13.9
f1 (ppm)

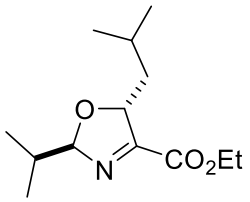

Me
O
N
CO2Et
4.03
1.00
1.00
2.00
3.00
1.00
3.00
3.03
3.00
f1 (ppm)


163.4
160.9
139.0
135.3
129.6
127.4
111.6
88.1
62.4
34.2
21.3
17.6
17.0
14.0
f1 (ppm)

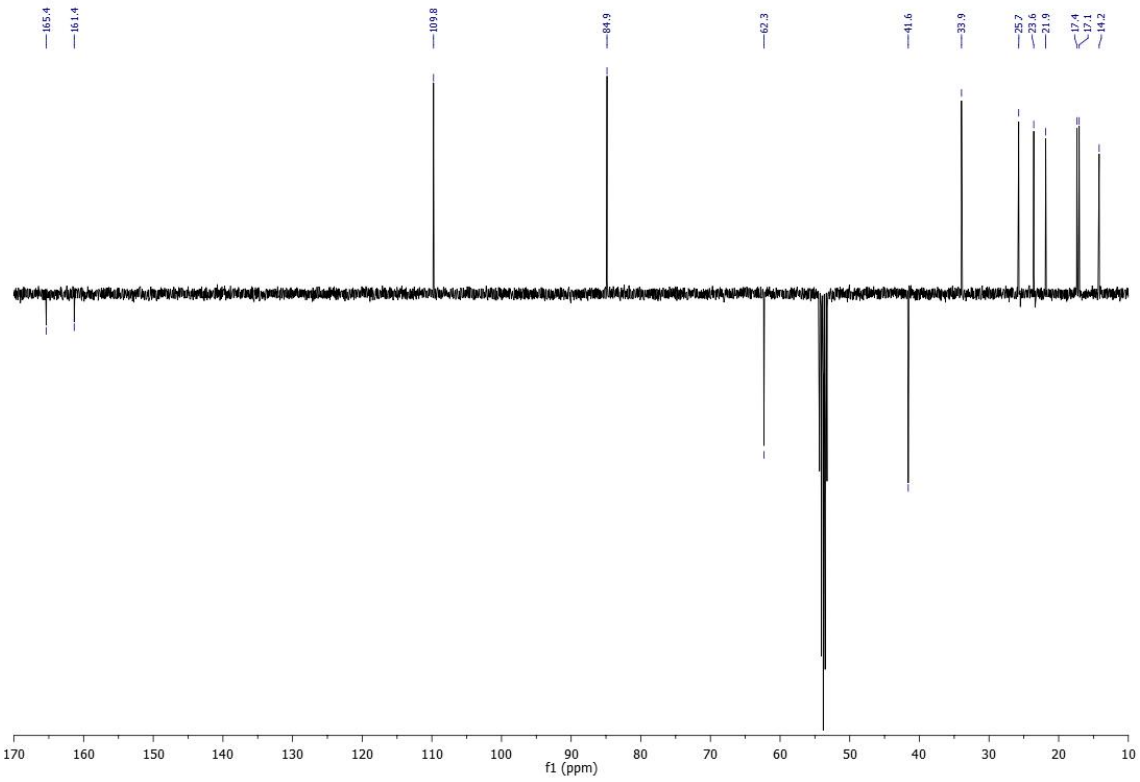

OMe
O
N
CO2Et
2.00
2.01
0.99
1.00
2.02
3.01
1.00
3.00
6.06
f1 (ppm)
163.5
160.9
160.3
130.3
128.8
114.3
111.5
87.9
62.4
55.6
34.2
17.6
17.0
14.0
f1 (ppm)

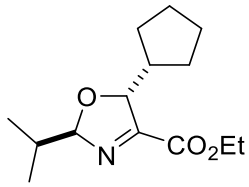

O
N
CO2Et
1.00
0.99
2.00
1.00
1.00
3.02
3.01
3.01
3.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

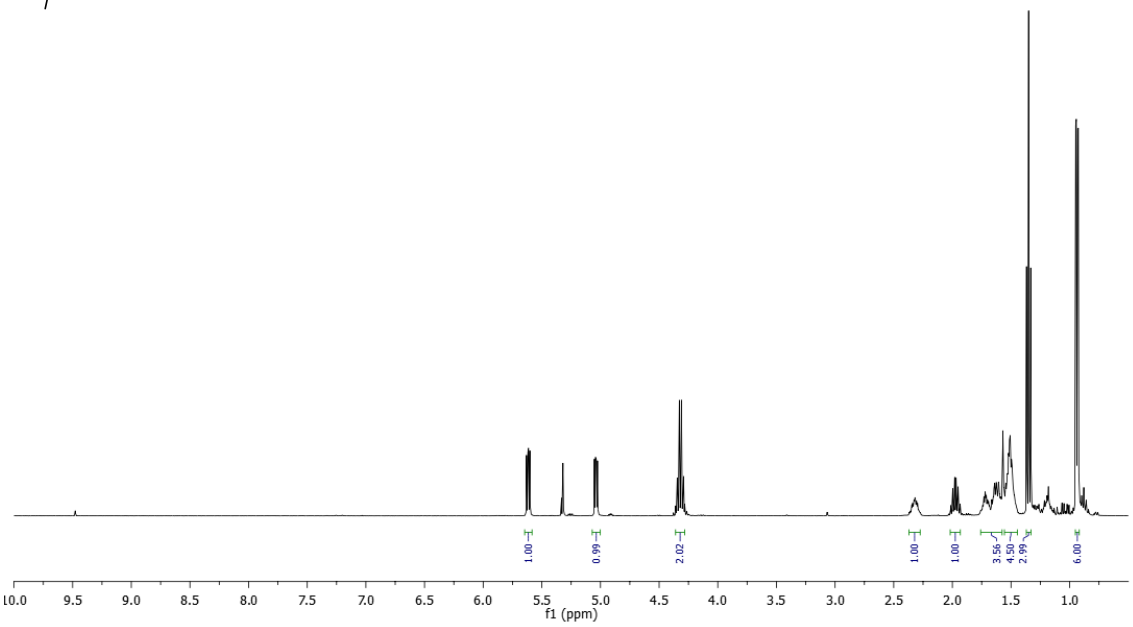

164.4
161.7
111.2
91.1
62.3
34.3
31.7
19.8
17.3
17.0
16.0
14.2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

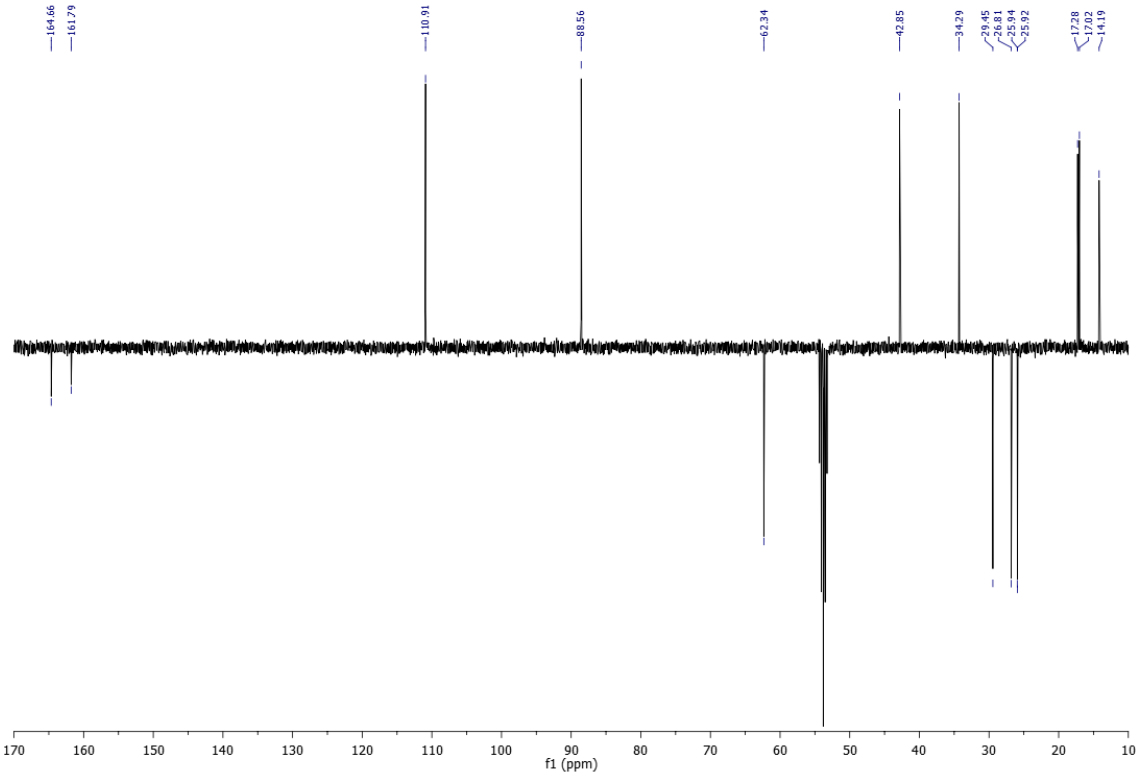

O
N
CO2Et

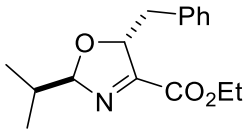
1.00
1.00
2.01
1.04
1.01
1.00
1.04
3.02
12.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

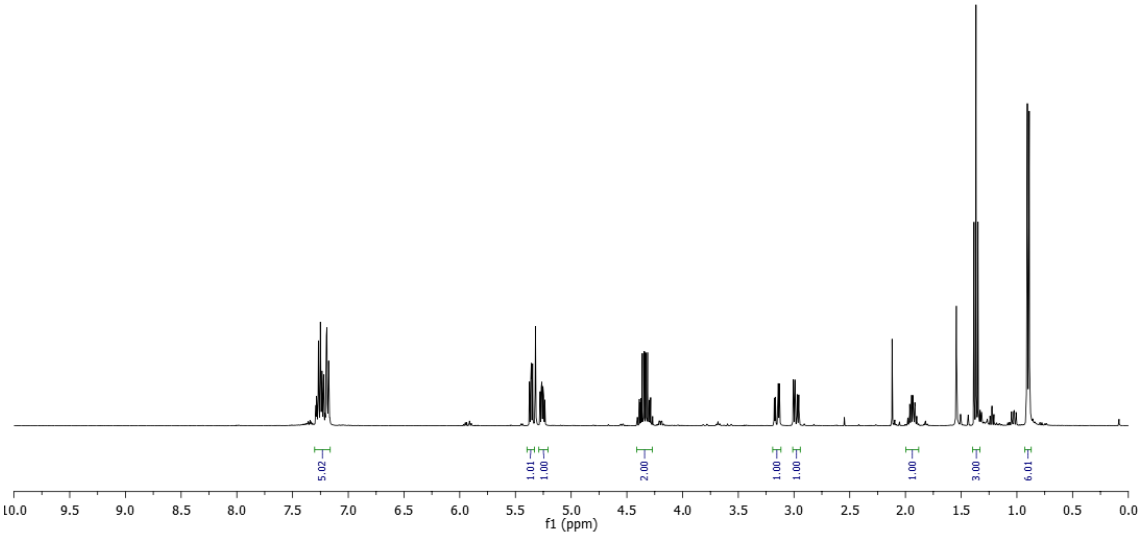

165.4
161.4
109.8
84.9
62.3
41.6
33.9
25.7
23.6
21.9
17.4
17.1
14.2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

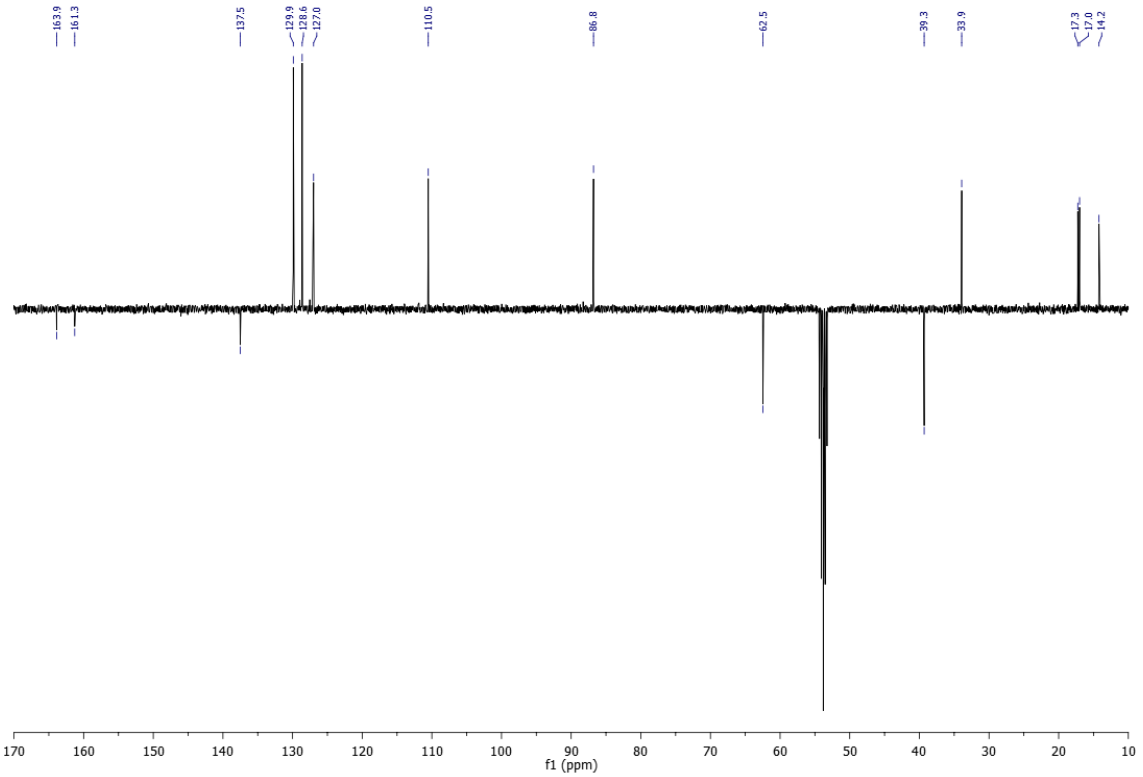

O
N
CO2Et


1.00
0.99
2.02
1.00
1.00
3.56
4.50
2.99
6.00
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
f1 (ppm)


164.66
161.79
110.91
88.56
62.34
42.85
34.29
29.45
26.81
25.94
25.92
17.28
17.02
14.19
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


Ph
O
N
CO2Et


5.02
1.01
1.00
2.00
1.00
1.00
1.00
3.00
6.01
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)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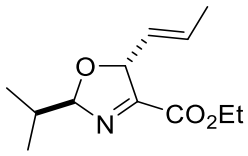
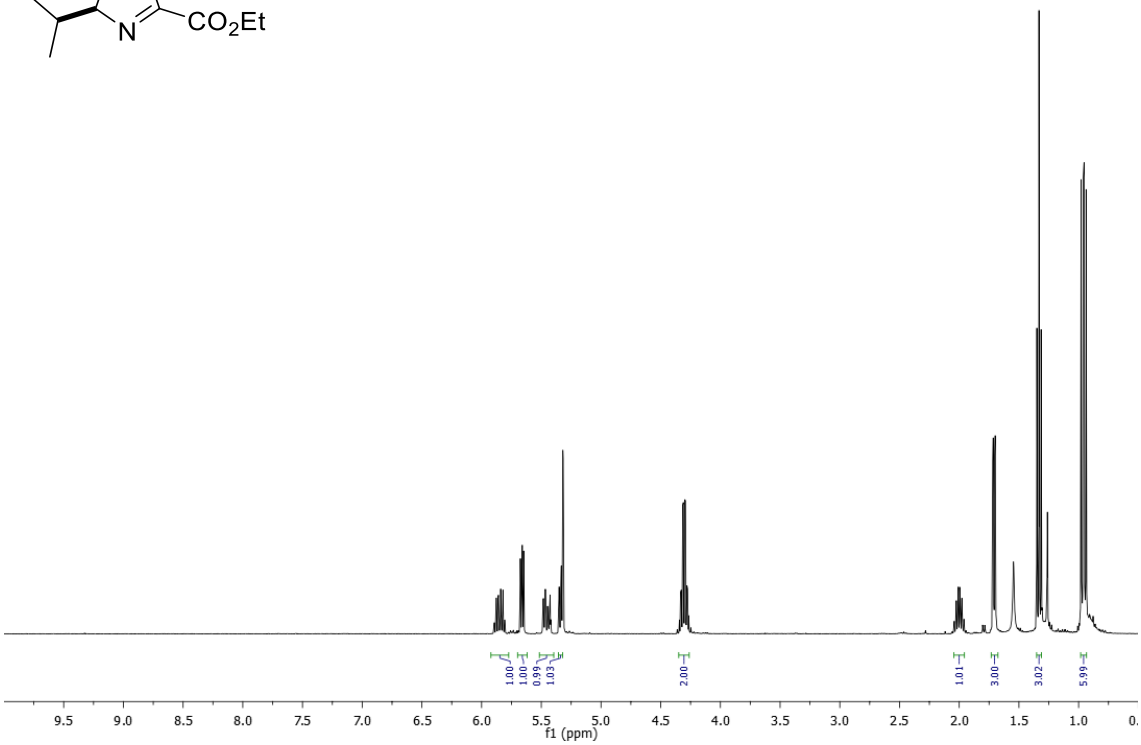
161.3
137.5
129.9
128.6
127.0
110.5
86.8
62.5
39.3
33.9
17.3
17.0
14.2
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


O
N
CO2Et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1.00
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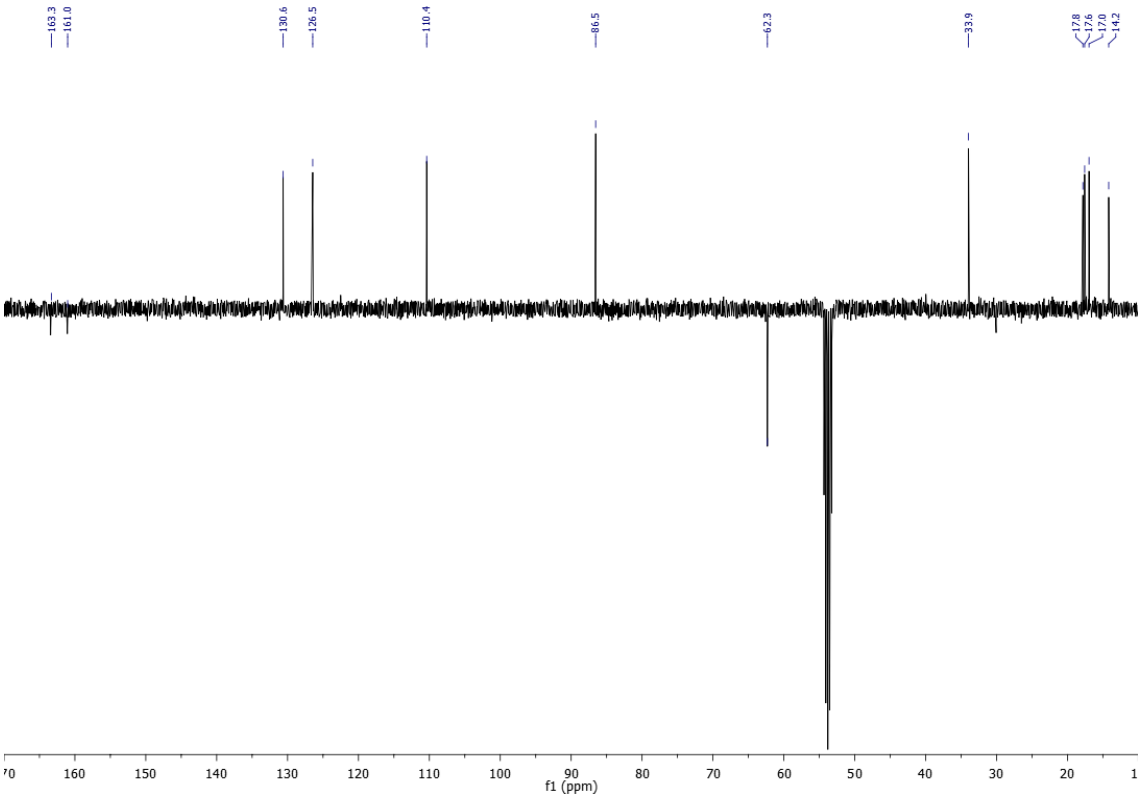
2.00
1.01
3.00
3.02
5.99
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)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130.6
126.5
110.4
86.5
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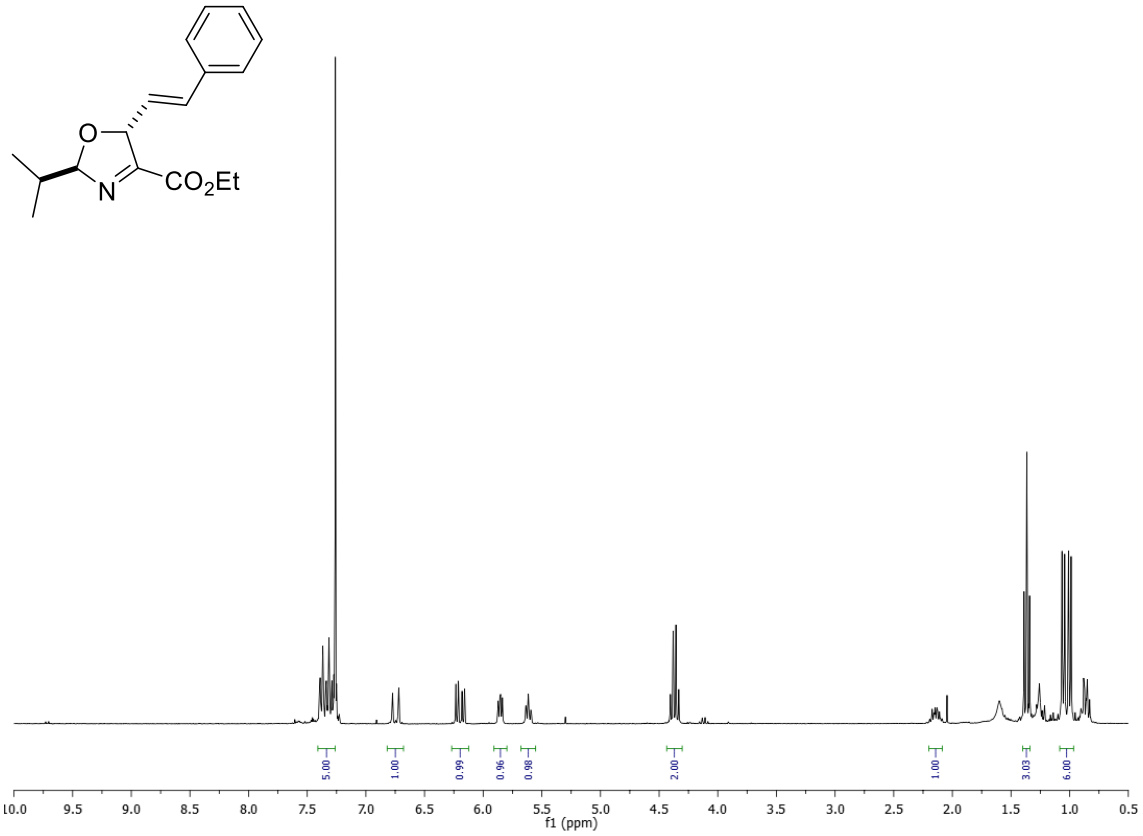
33.9
17.8
17.6
17.0
14.2
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)


O
N
CO2Et
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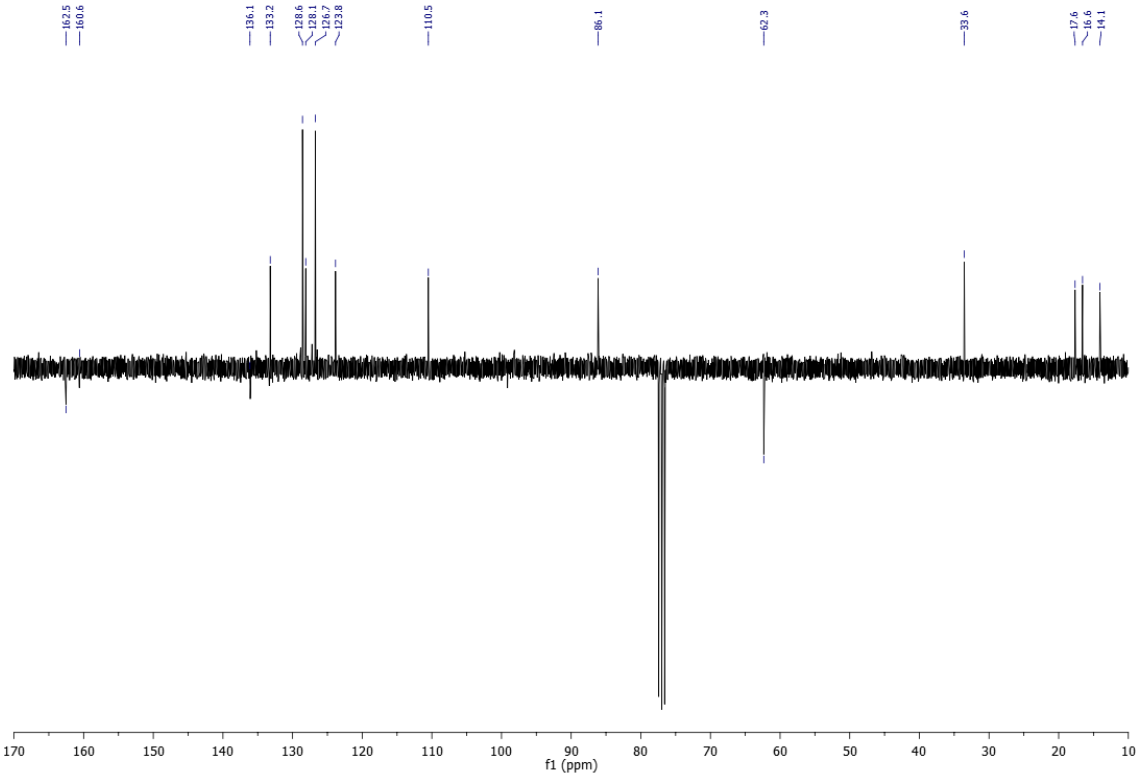
0.96
0.98
2.00
1.00
3.03
6.00
f1 (ppm)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160.6
136.1
133.2
128.6
128.1
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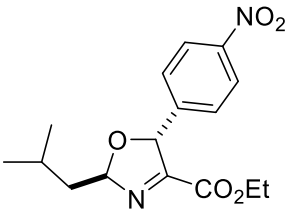
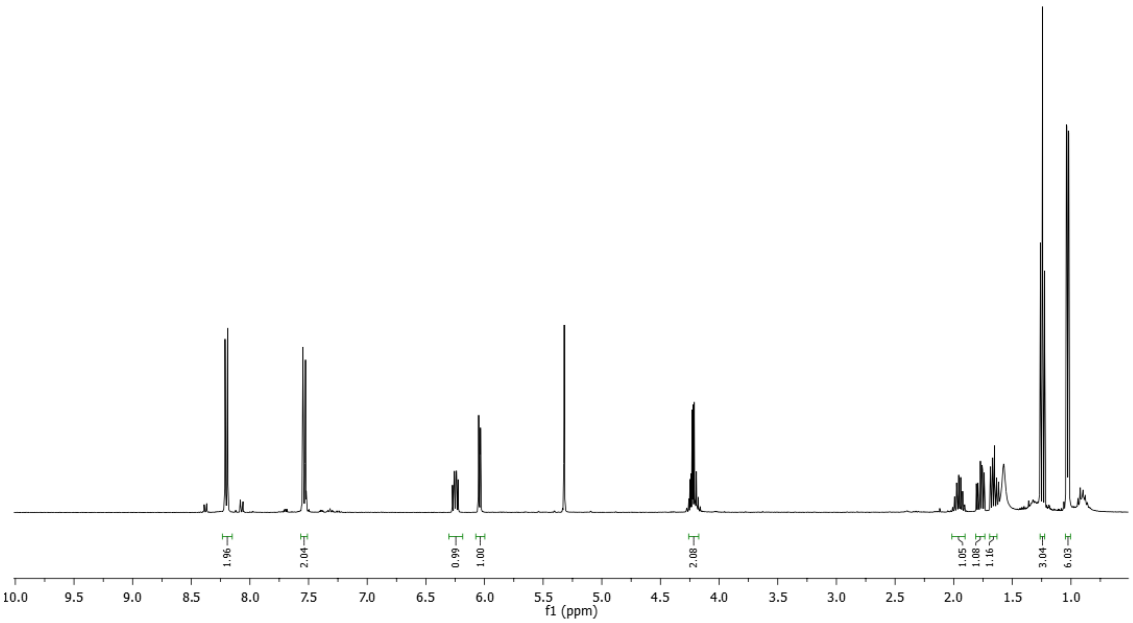
123.8
110.5
86.1
62.3
33.6
17.6
16.6
14.1
f1 (ppm)


NO2
O
N
CO2Et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1.00
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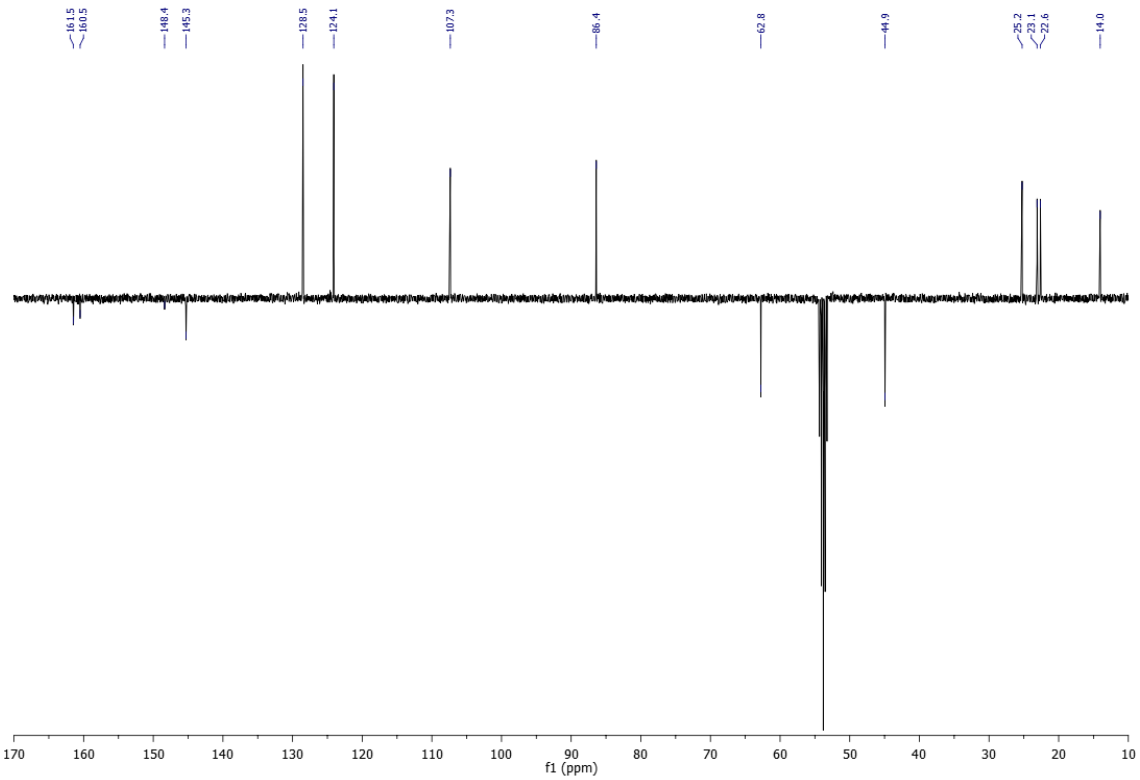
1.05
1.08
1.16
3.04
6.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)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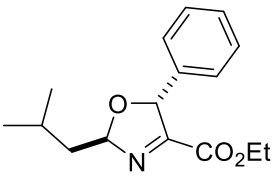
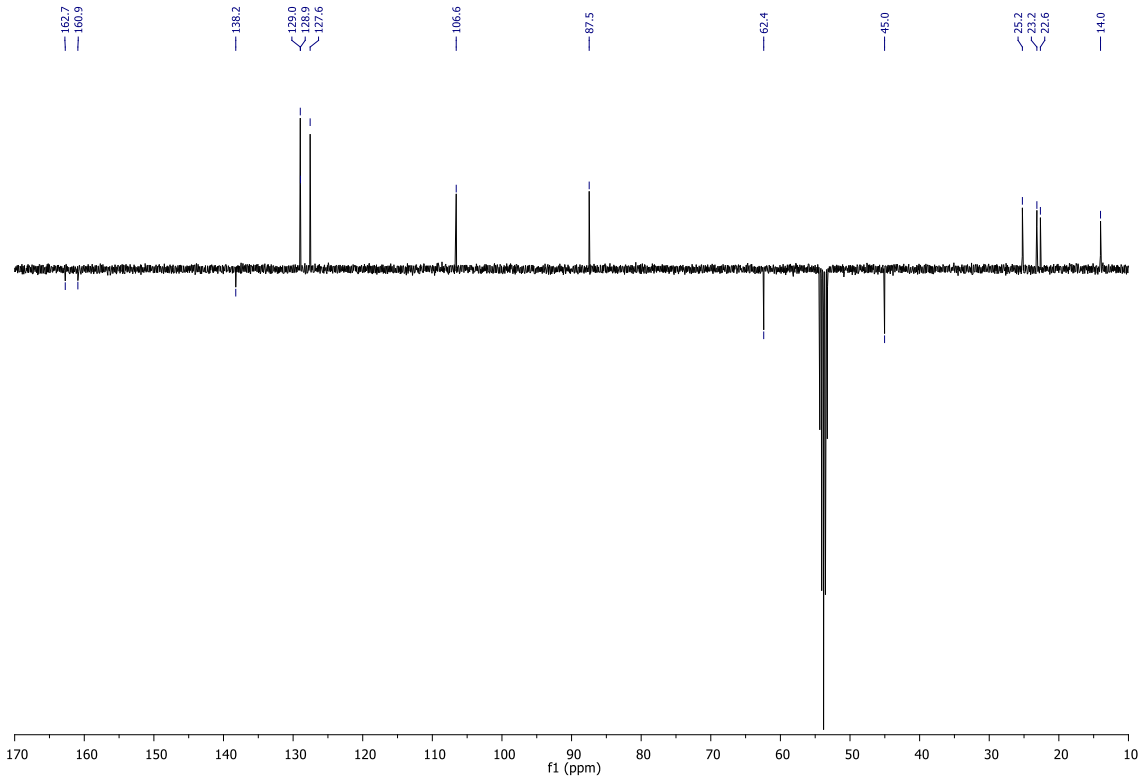
160.5
148.4
145.3
128.5
124.1
107.3
86.4
62.8
44.9
25.2
23.1
22.6
14.0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O
N
CO2Et

4.98
1.00
1.00
2.01
1.03
1.08
1.11
3.03
6.00
f1 (ppm)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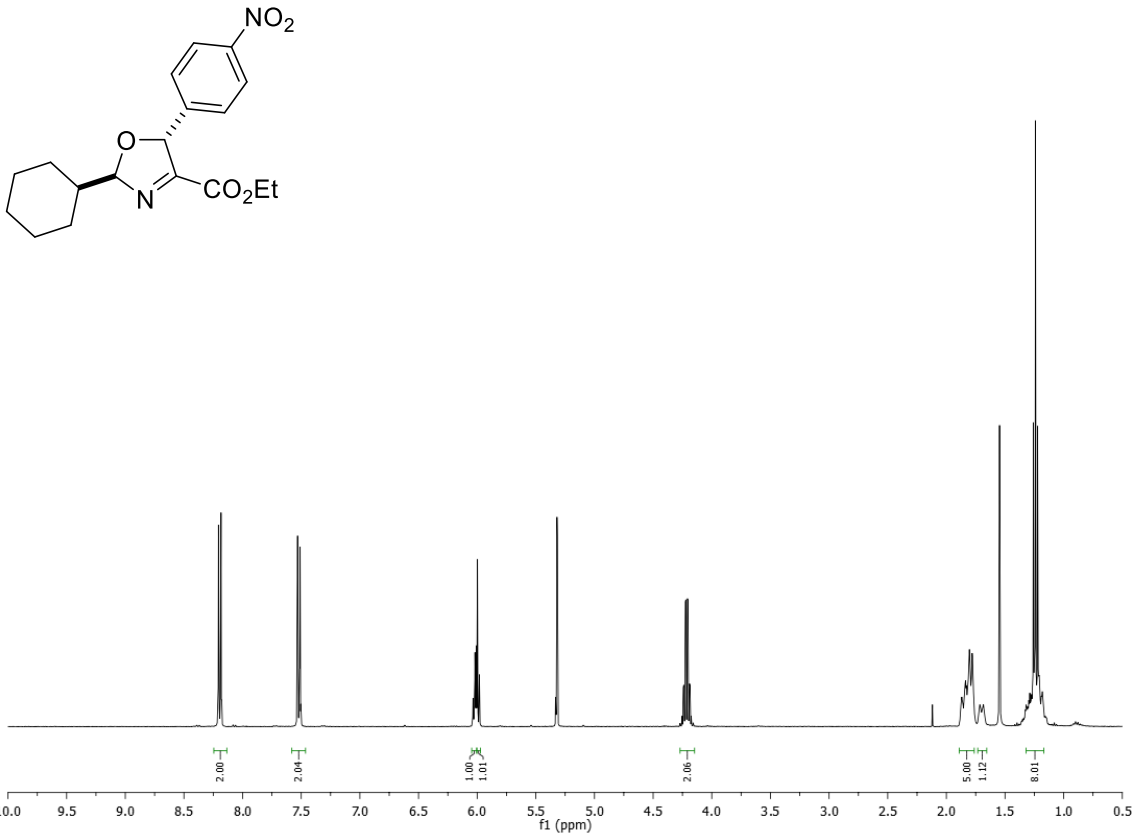
160.9
138.2
129.0
128.9
127.6
106.6
87.5
62.4
45.0
25.2
23.2
22.6
14.0
f1 (ppm)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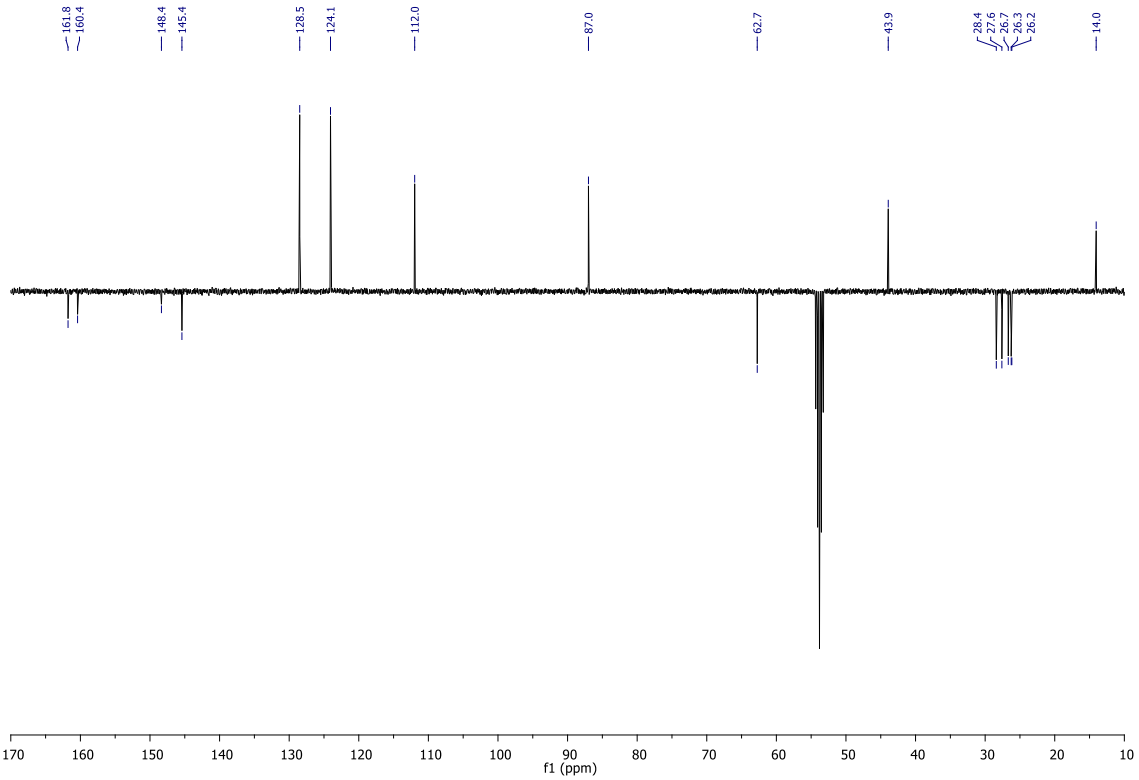
O
N
CO2Et
2.00
2.04
1.00
1.01
2.06
5.00
1.12
8.01
f1 (ppm)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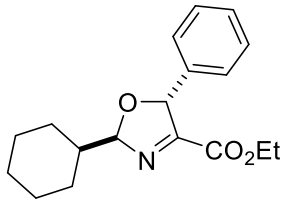
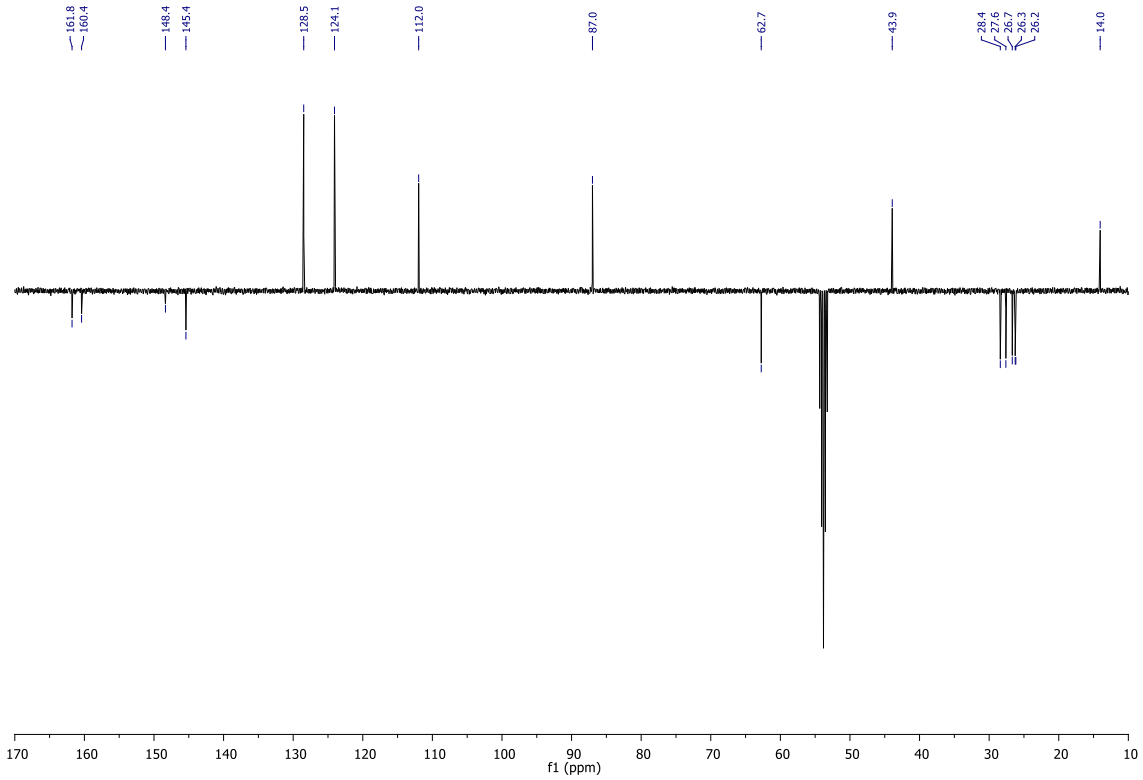
160.4
148.4
145.4
128.5
124.1
112.0
87.0
62.7
43.9
28.4
27.6
26.7
26.3
26.2
14.0
f1 (ppm)


O
N
CO2Et

2.00
2.04
1.00
1.01
2.06
5.00
1.12
8.01
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)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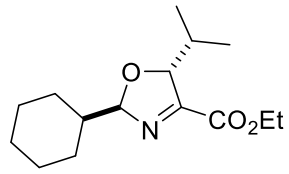
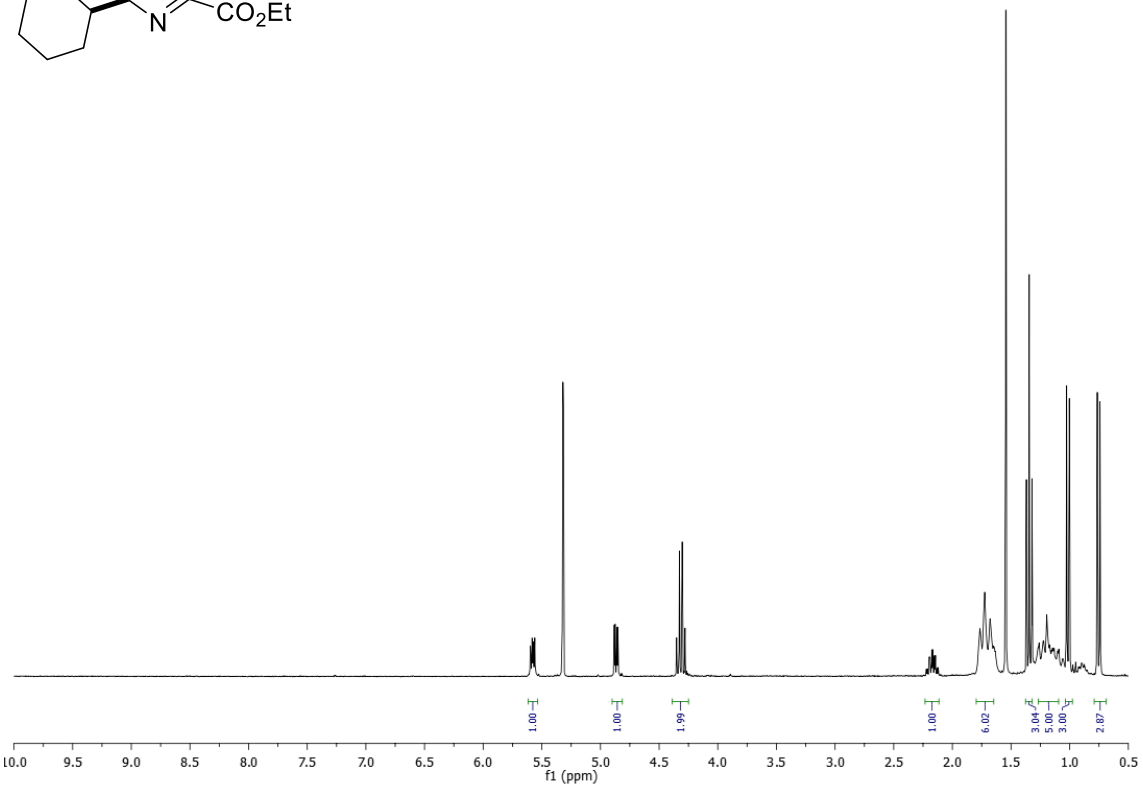
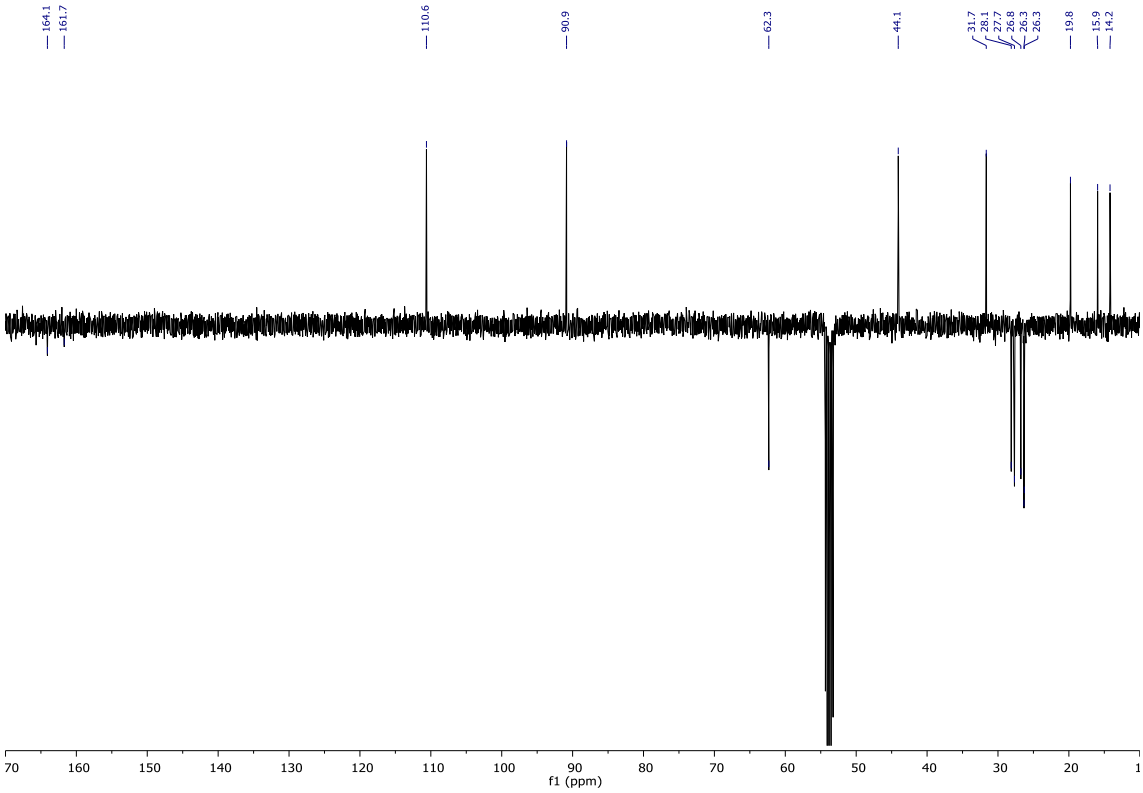
160.4
148.4
145.4
128.5
124.1
112.0
87.0
62.7
43.9
28.4
27.6
26.7
26.3
26.2
14.0
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


O
N
CO2Et


1.00
1.00
1.99
1.00
6.02
3.04
5.00
3.00
2.87
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)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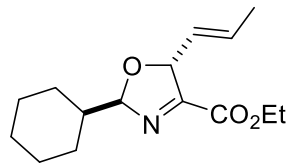
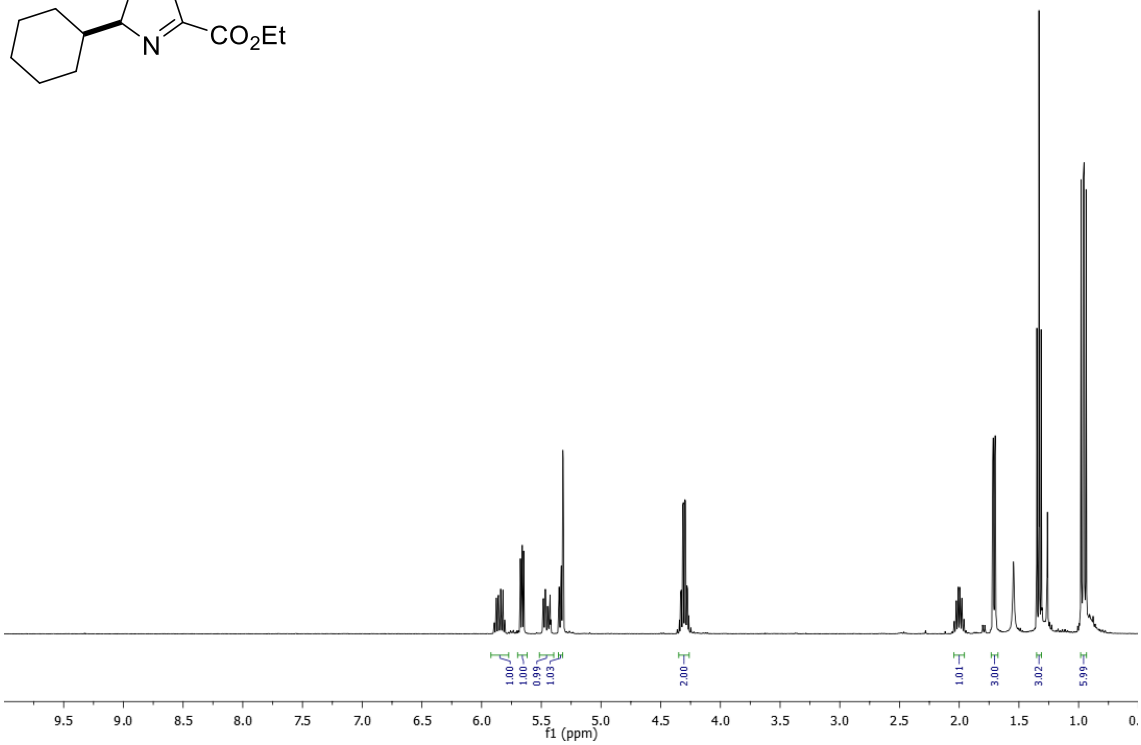
161.7
110.6
90.9
62.3
44.1
31.7
28.1
27.7
26.8
26.3
26.3
19.8
15.9
14.2
70 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 1
f1 (ppm)


O
N
CO2Et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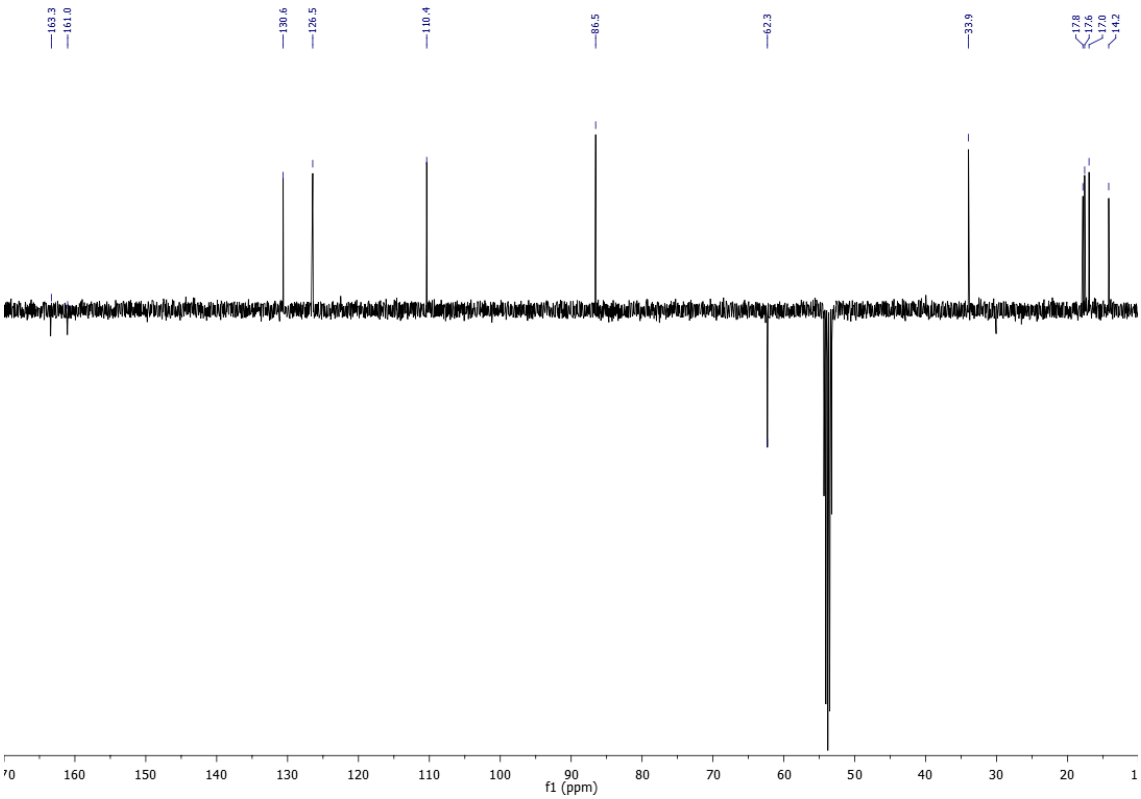
1.00
0.99
1.03
2.00
1.01
3.00
3.02
5.99
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)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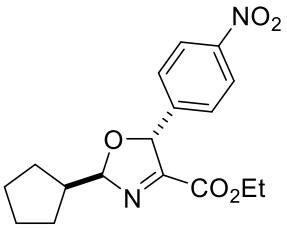
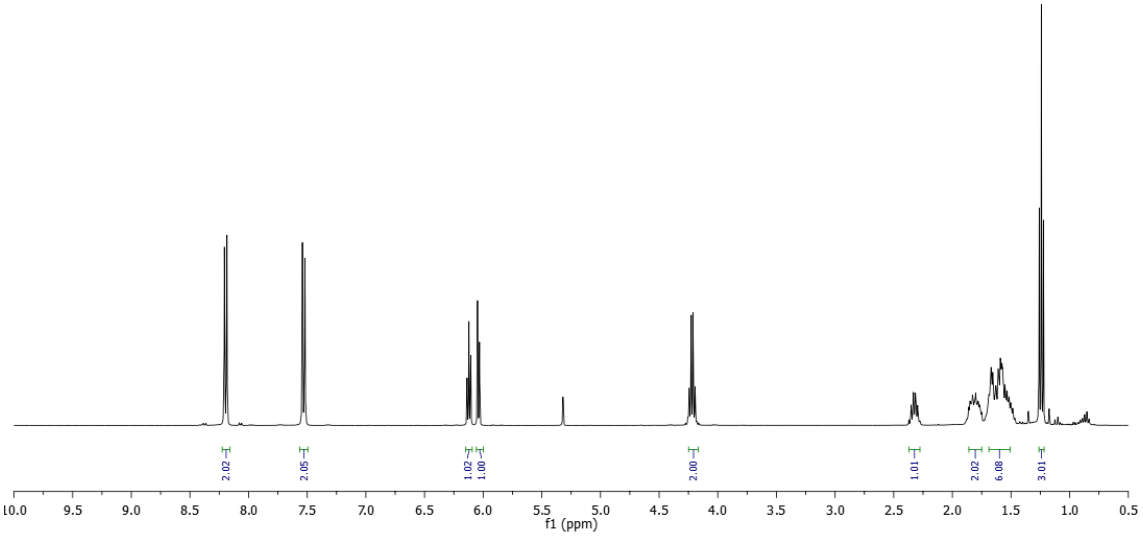
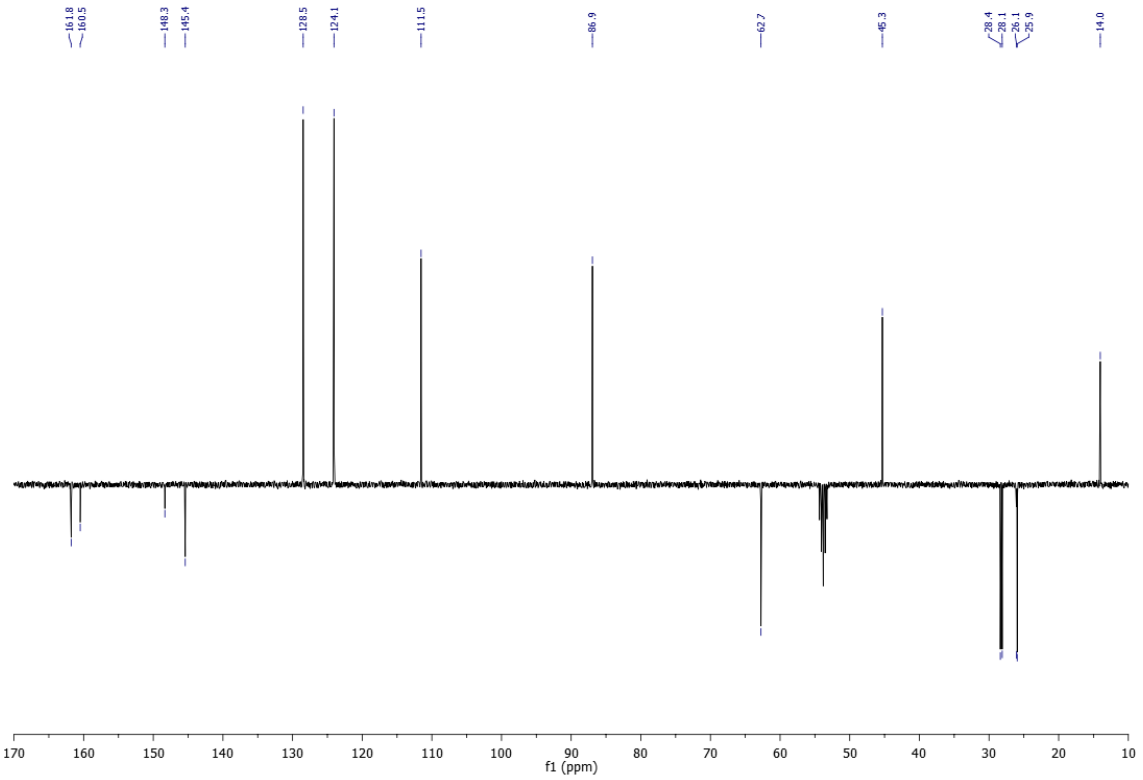
161.0
130.6
126.5
110.4
86.5
62.3
33.9
17.8
17.6
17.0
14.2
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)


NO2
O
N
CO2Et


2.02
2.05
1.02
1.00
2.00
1.01
2.02
6.08
3.01
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)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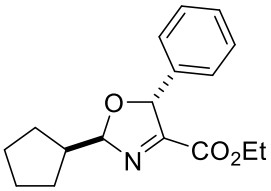
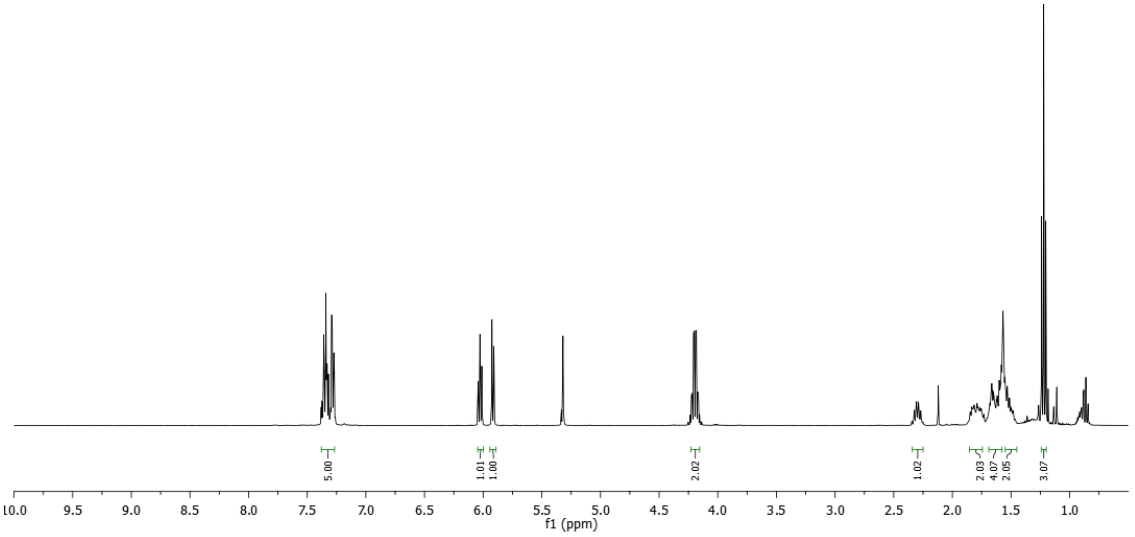
160.5
148.3
145.4
128.5
124.1
111.5
86.9
62.7
45.3
28.4
28.1
26.1
25.9
14.0
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


O
N
CO2Et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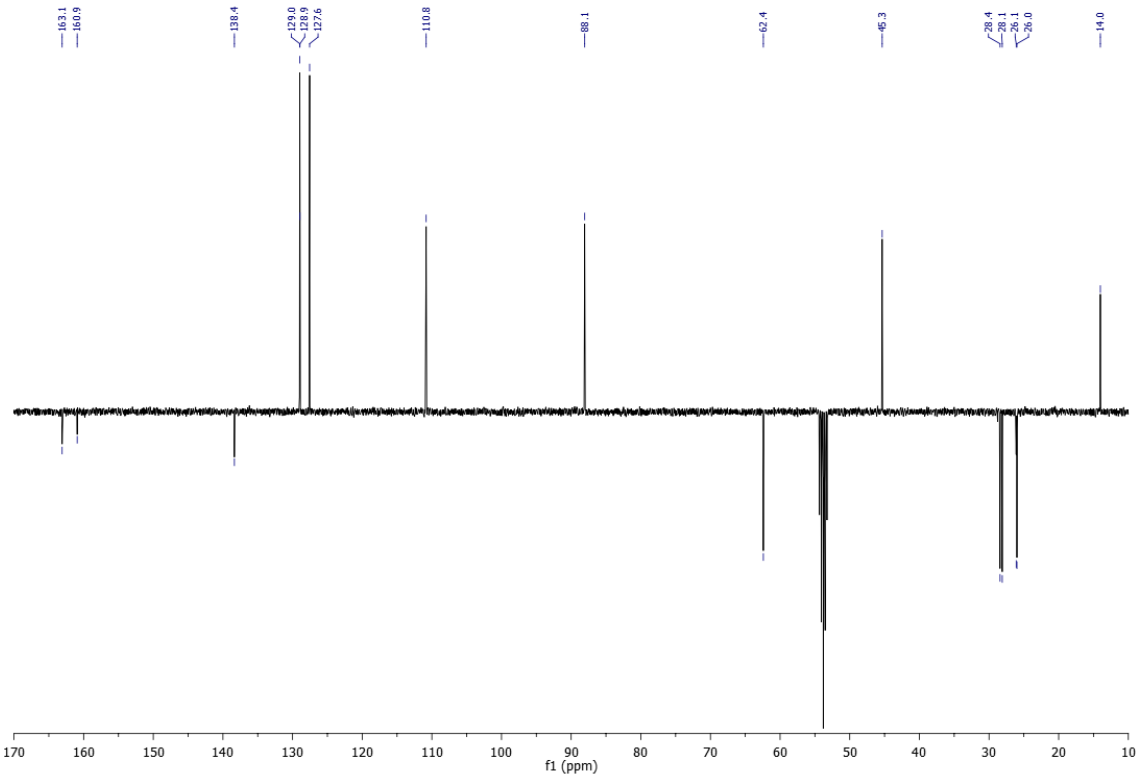
1.01
1.00
2.02
1.02
2.03
4.07
2.05
3.07
f1 (ppm)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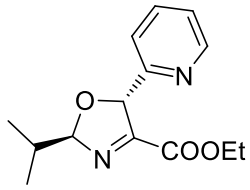
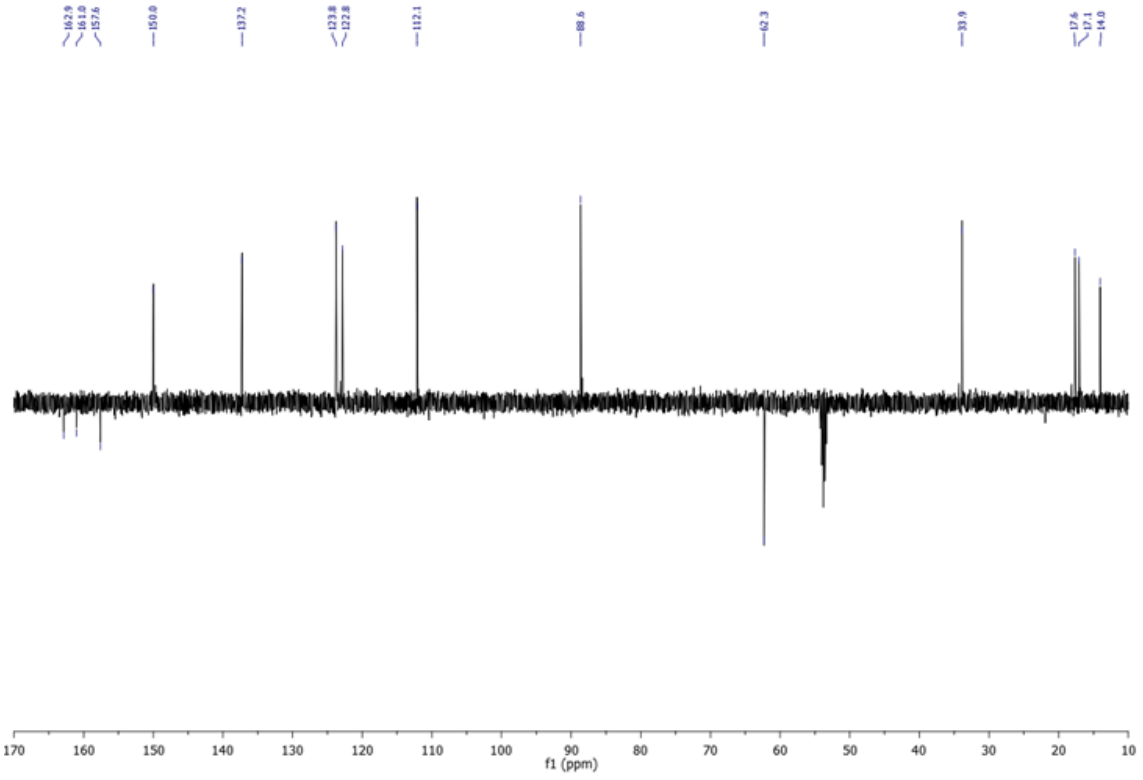
138.4
129.0
128.9
127.6
110.8
88.1
62.4
45.3
28.4
28.1
26.1
26.0
14.0
f1 (ppm)


O
N
N
COOEt

1.00
1.00
1.00
1.00
0.98
1.00
2.01
0.99
3.00
6.01
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)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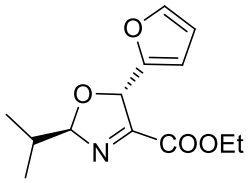
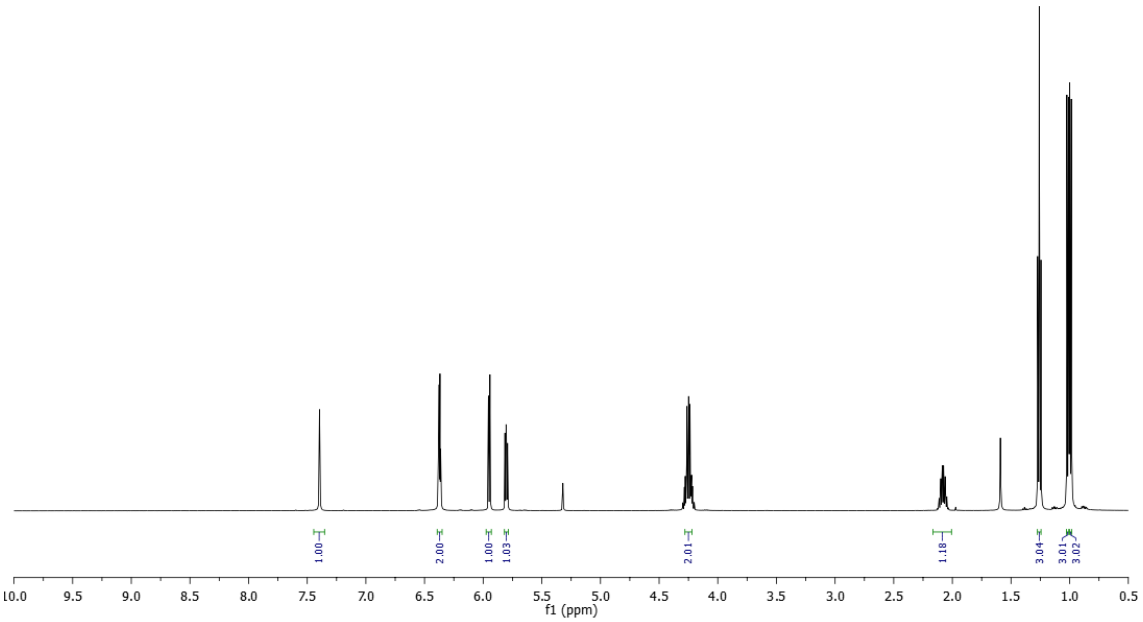
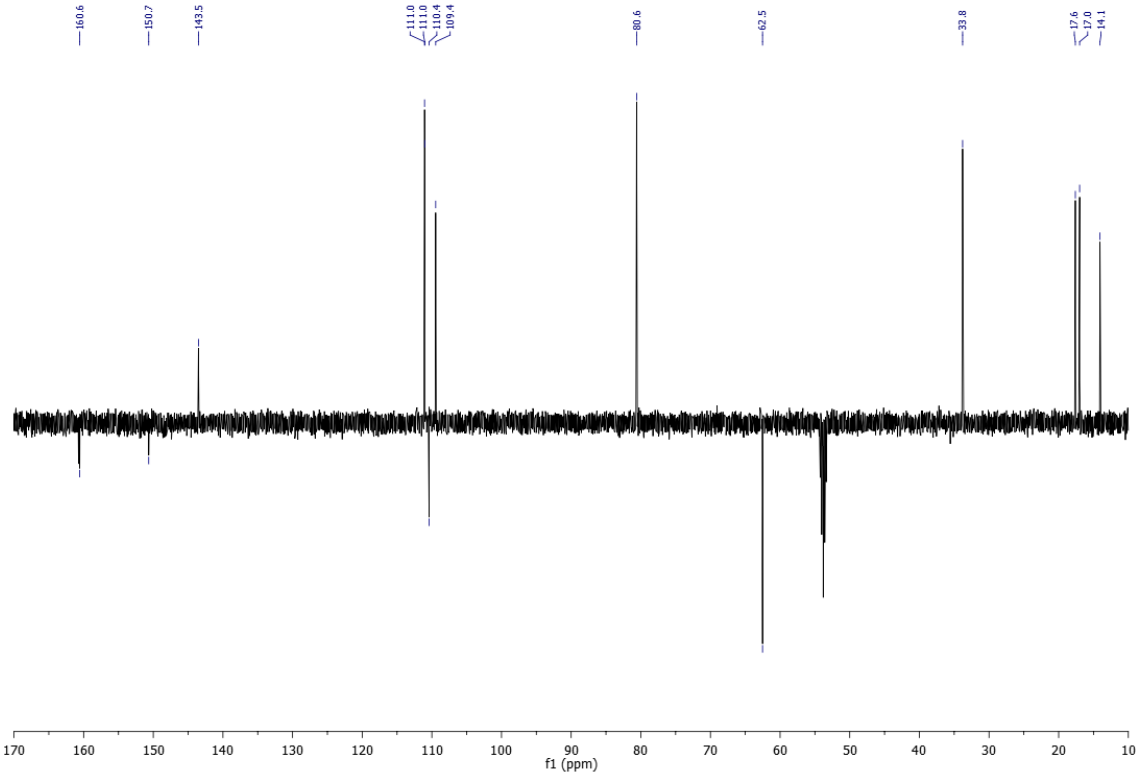
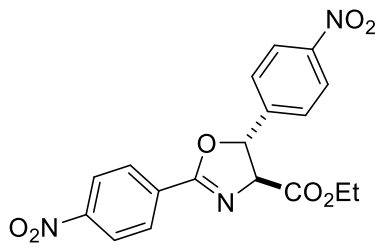
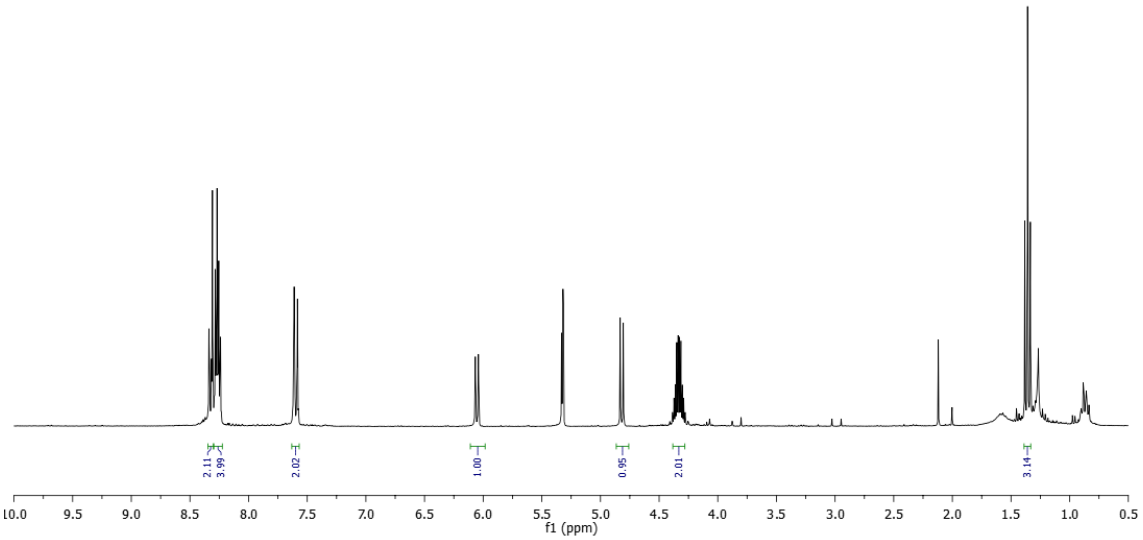
161.0
157.6
150.0
137.2
123.8
122.8
112.1
88.6
62.3
33.9
17.6
17.1
14.0
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

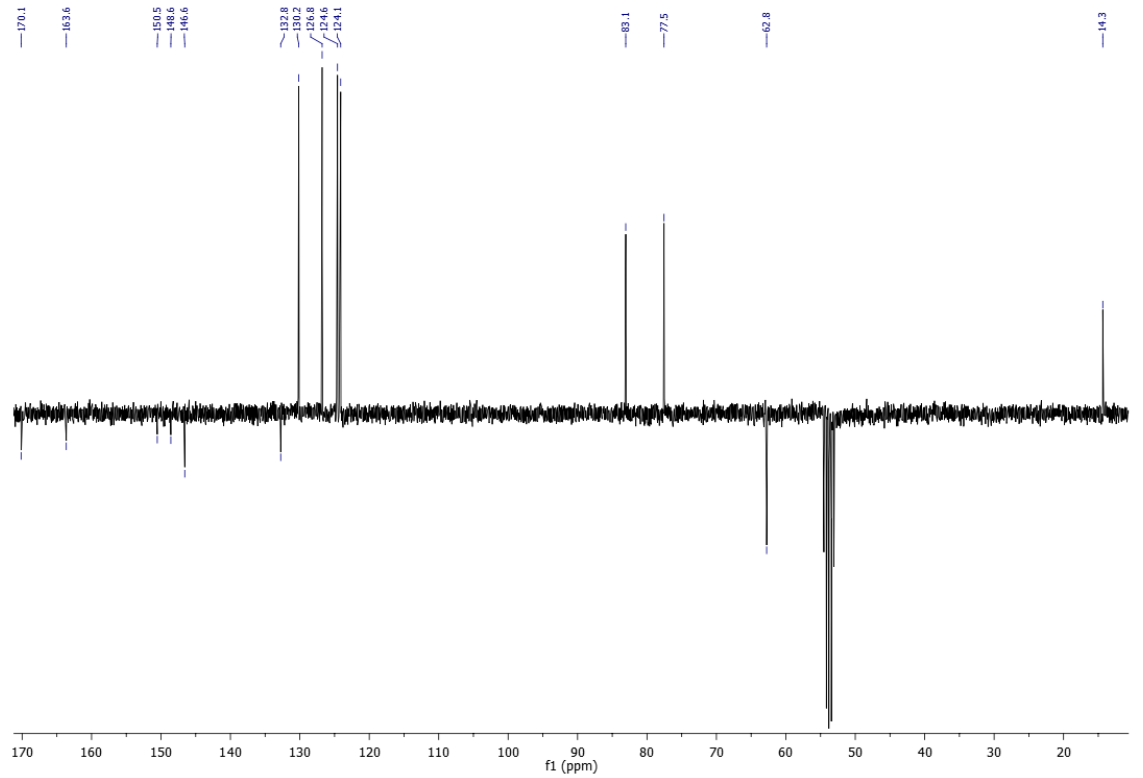

O
O
N
COOEt

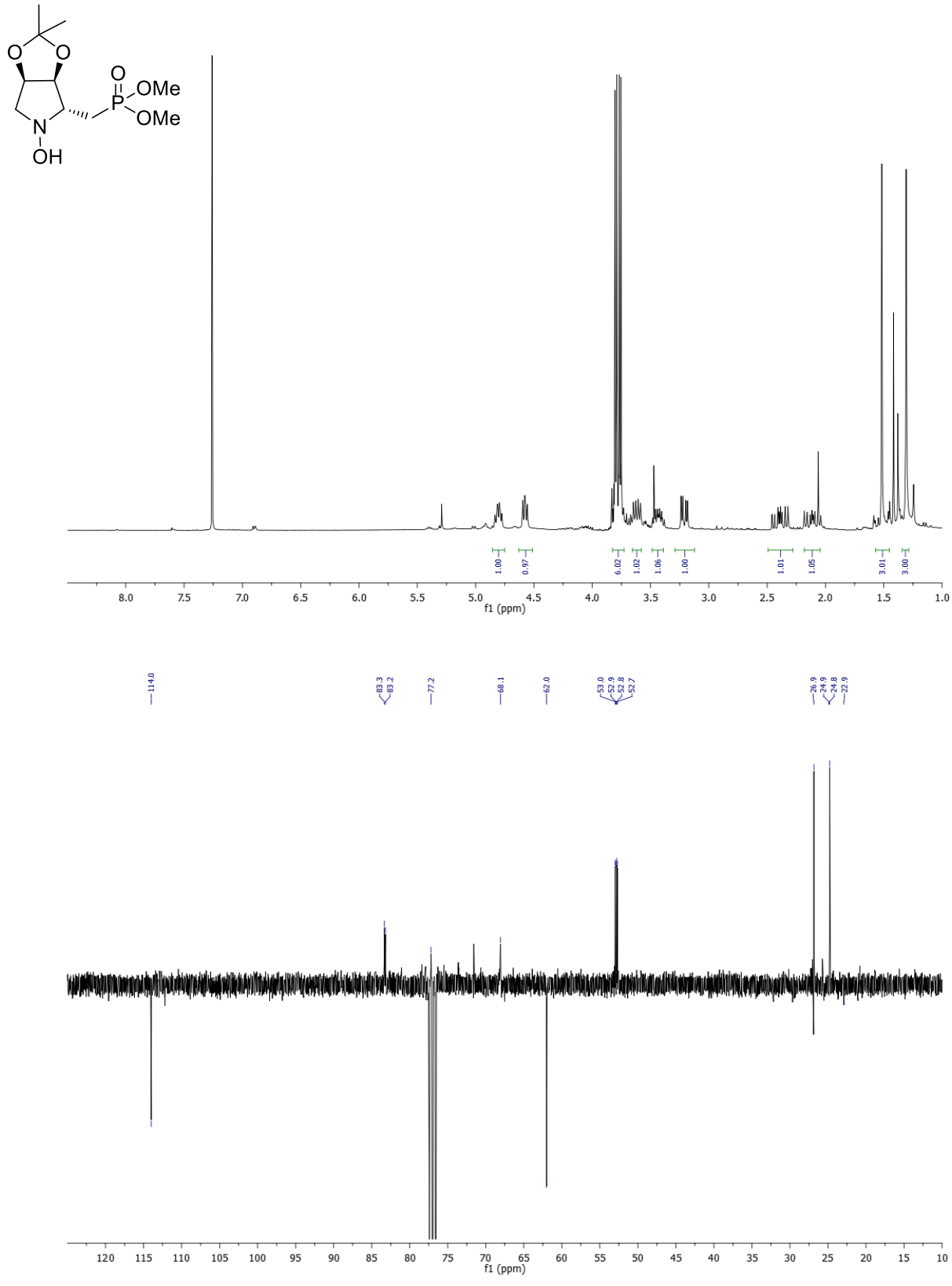

1.00
2.00
1.00
1.03
2.01
1.18
3.04
3.01
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

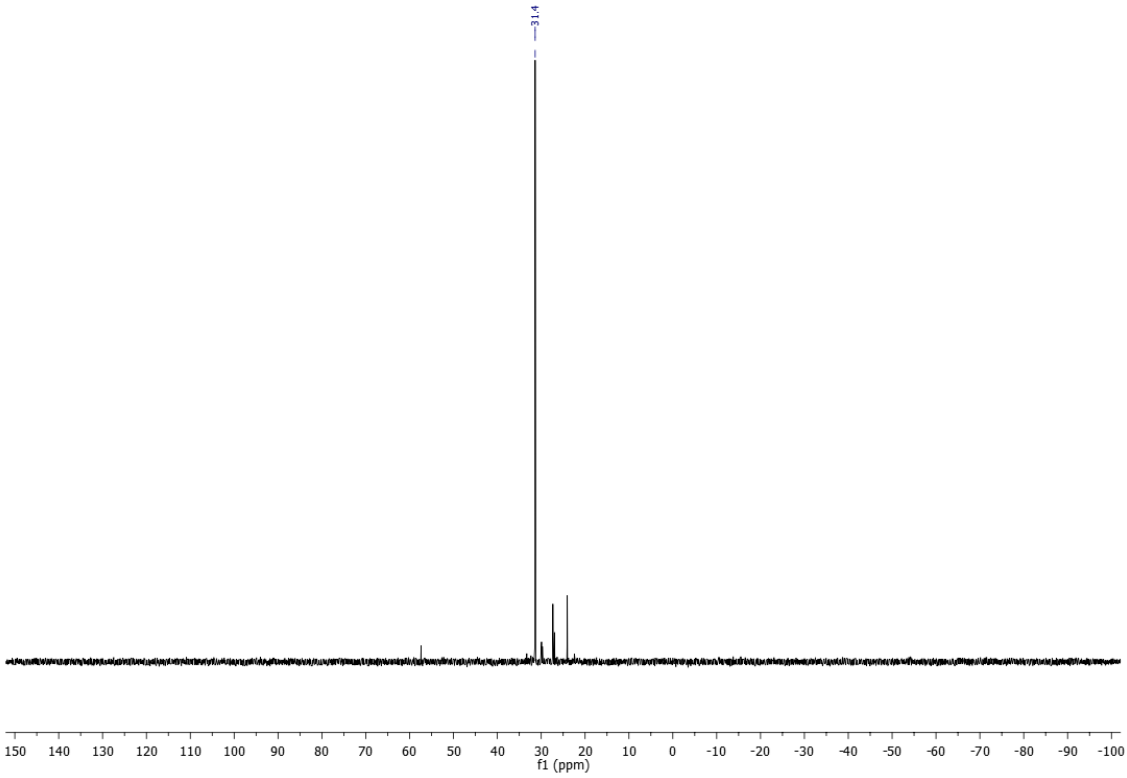

160.6
150.7
143.5
111.0
111.0
110.4
109.4
80.6
62.5
33.8
17.6
17.0
14.1
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

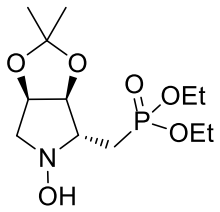

NO2
O
N
CO2Et
O2N


2.11
3.99
2.02
1.00
0.95
2.01
3.14
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)

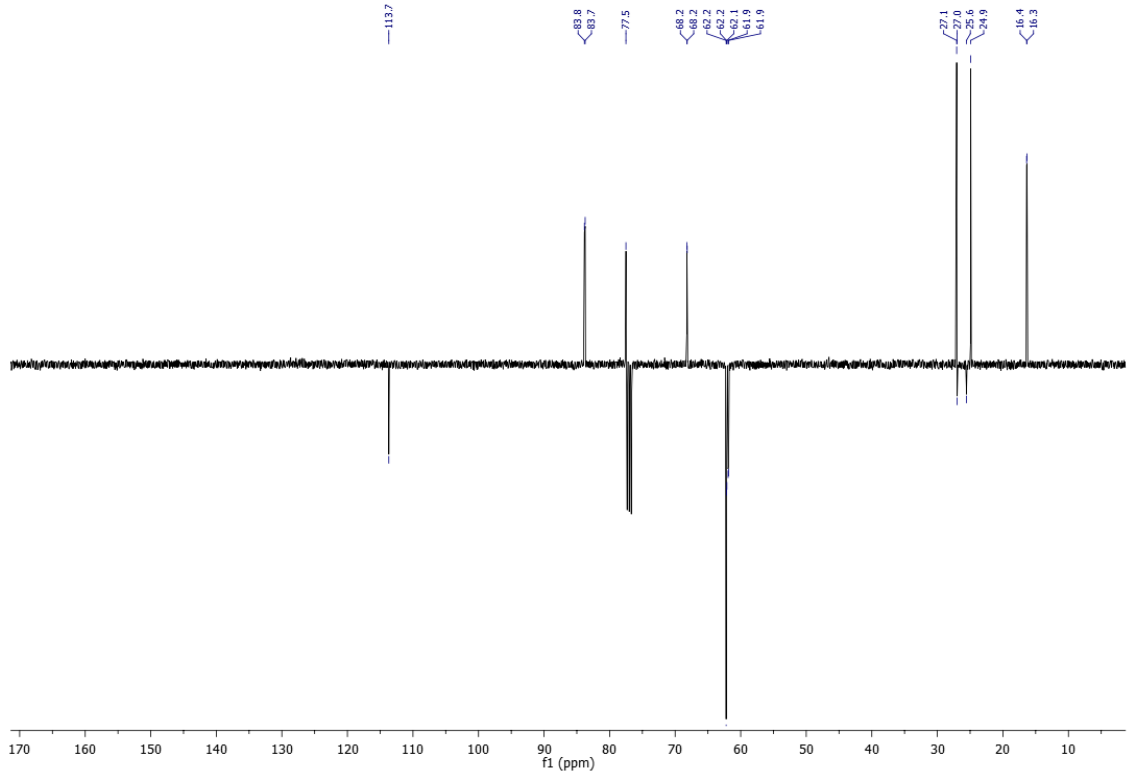

170.1
163.6
150.5
148.6
146.6
132.8
130.2
126.8
124.6
124.1
83.1
77.5
62.8
14.3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

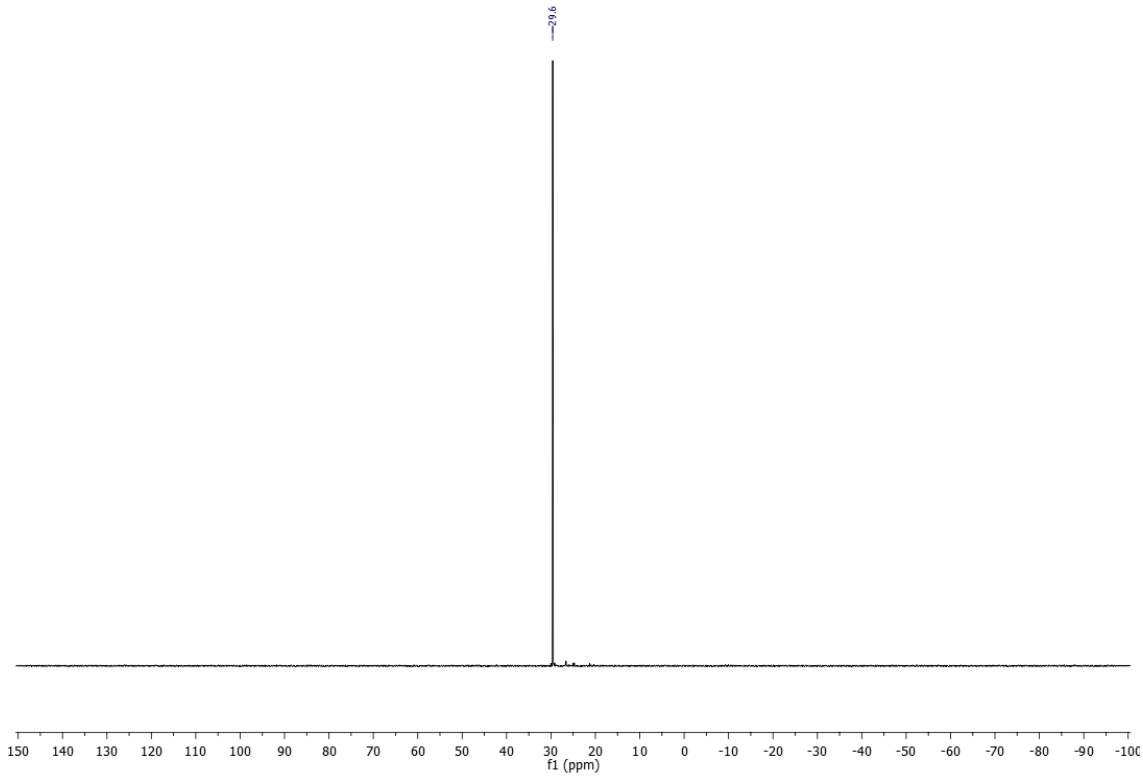

O
O
O
OMe
P
OMe
N
OH
1.00
0.97
6.02
1.02
1.06
1.00
1.01
1.05
3.01
3.00
f1 (ppm)
114.0
83.3
83.2
77.2
68.1
62.0
53.0
52.9
52.8
52.7
26.9
24.9
24.8
22.9
f1 (ppm)

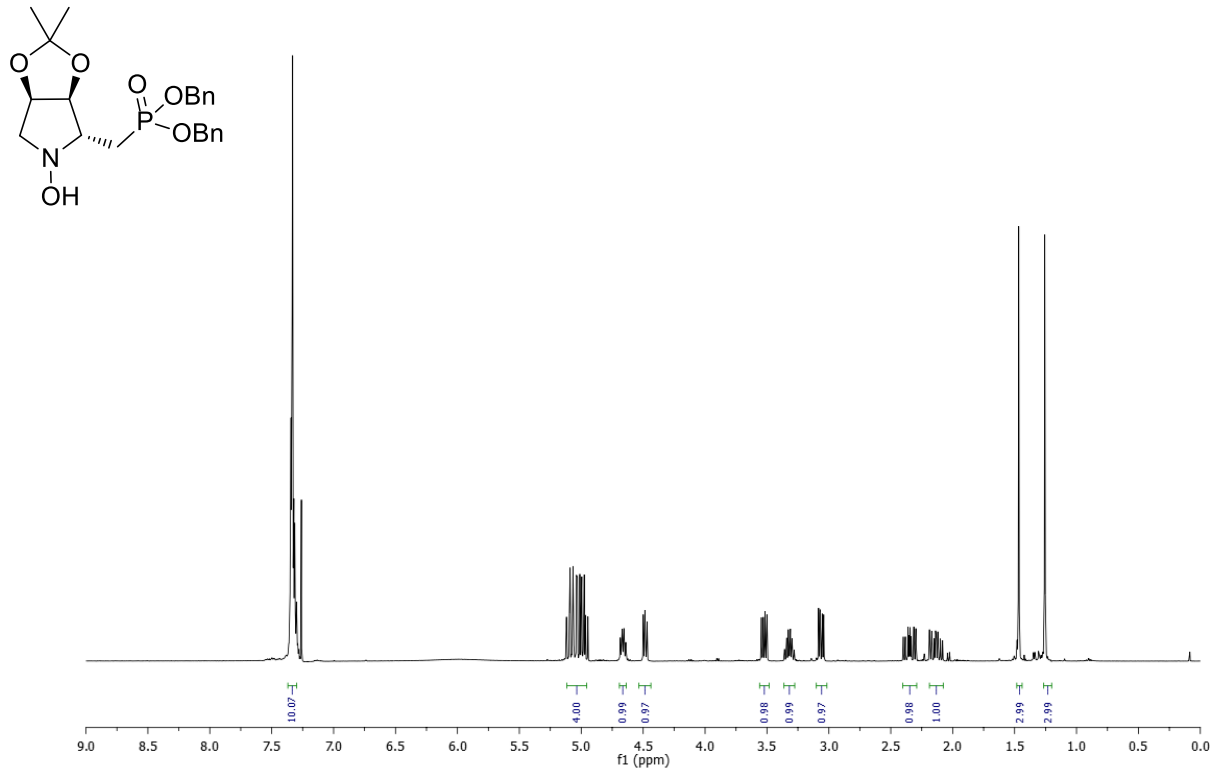

31.4
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

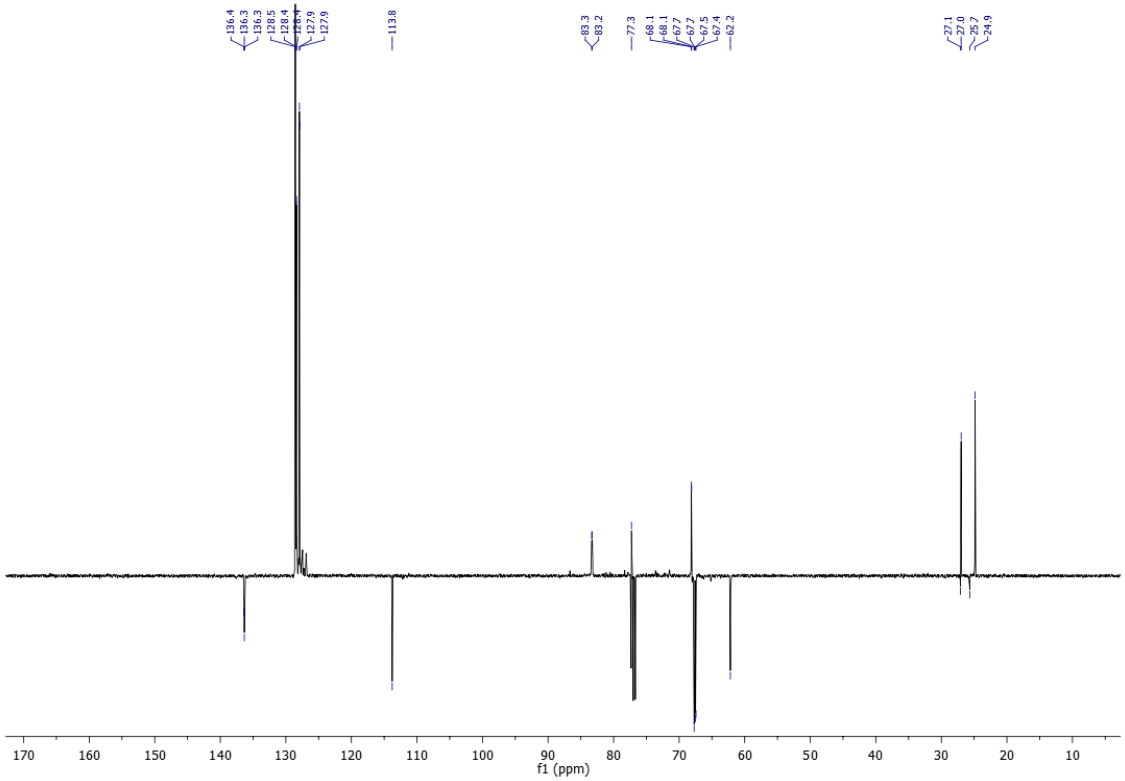

O
O
O
OEt
P
OEt
N
OH

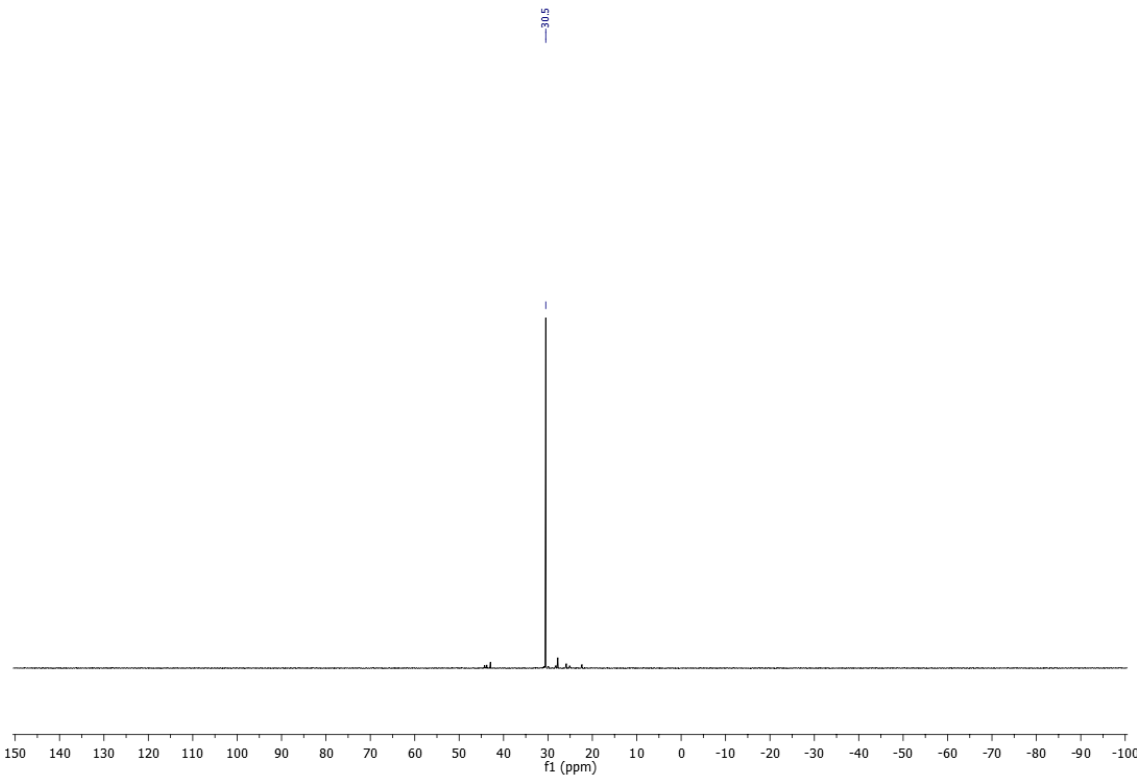
1.00
1.00
3.75
1.00
1.00
1.00
1.00
1.08
3.01
5.99
2.98
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

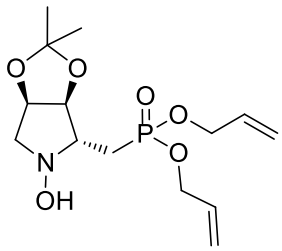

113.7
83.8
83.7
77.5
68.2
68.2
62.2
62.2
62.1
61.9
61.9
27.1
27.0
25.6
24.9
16.4
16.3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


29.6
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

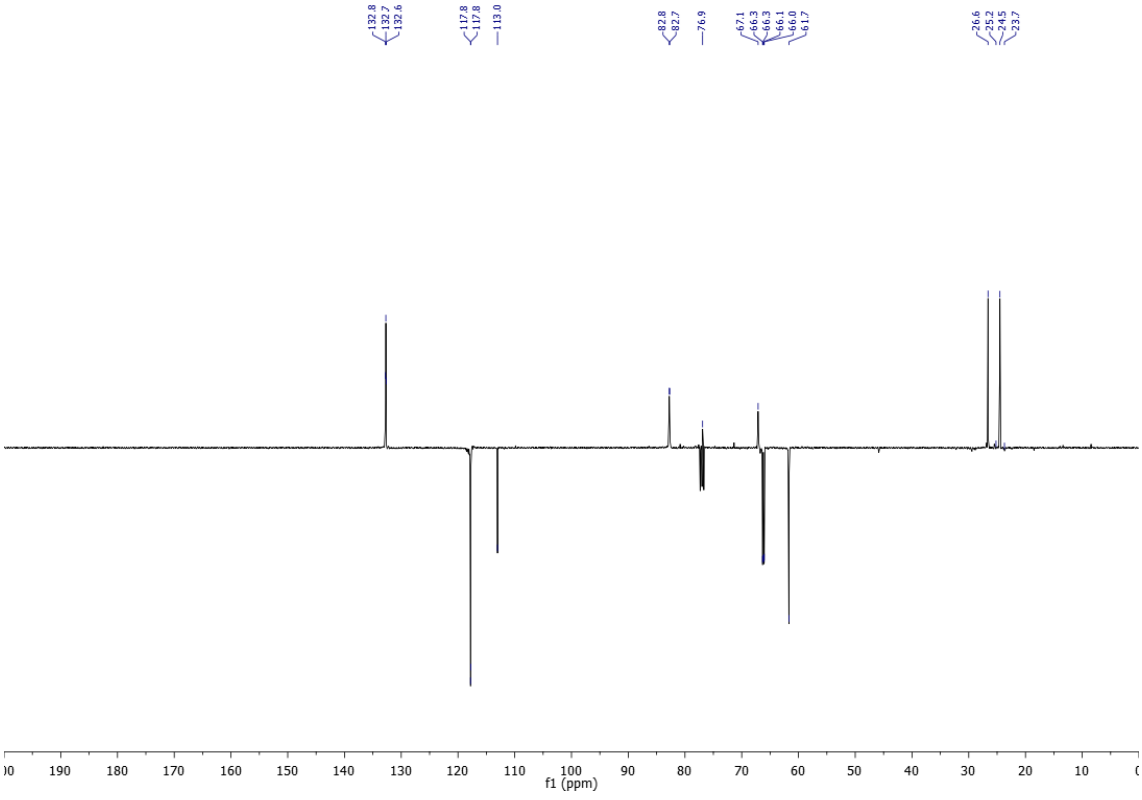

O
O
O
OBn
P
OBn
N
OH
10.07
4.00
0.99
0.97
0.98
0.99
0.97
0.98
1.00
2.99
2.99
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

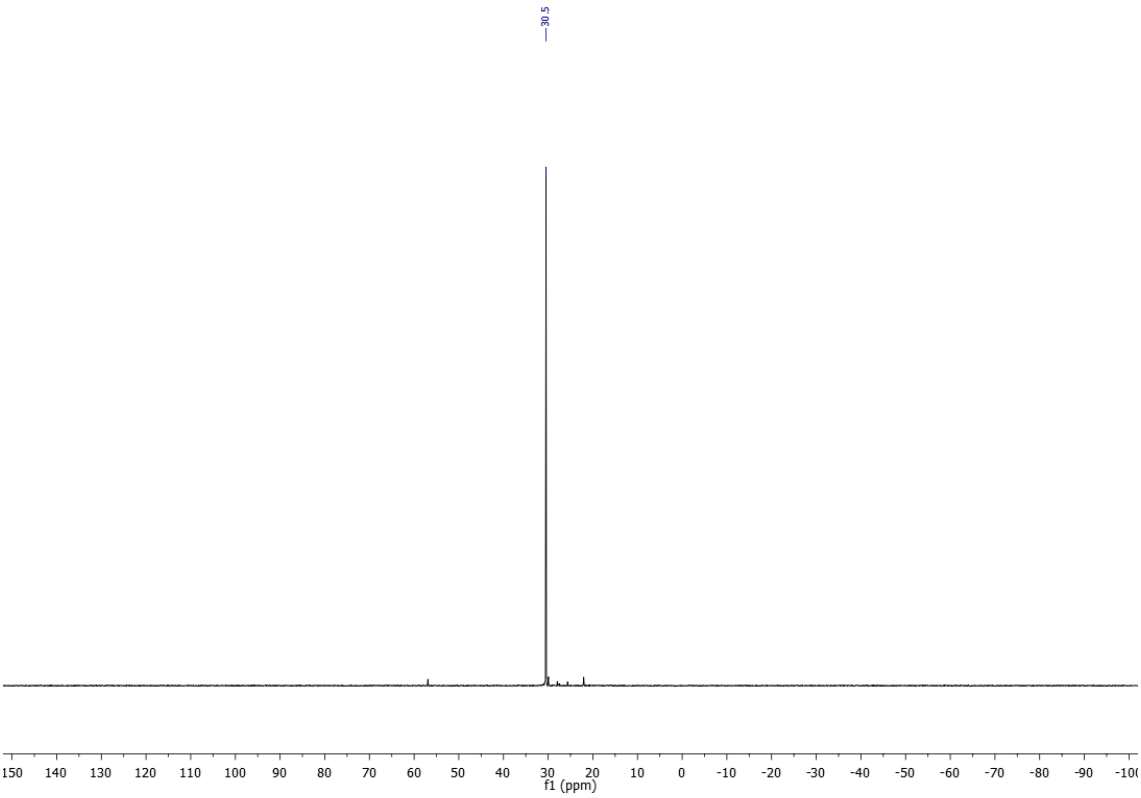

136.4
136.3
136.3
128.5
128.4
128.4
127.9
127.9
113.8
83.3
83.2
77.3
68.1
68.1
67.7
67.7
67.5
67.4
62.2
27.1
27.0
25.7
24.9
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

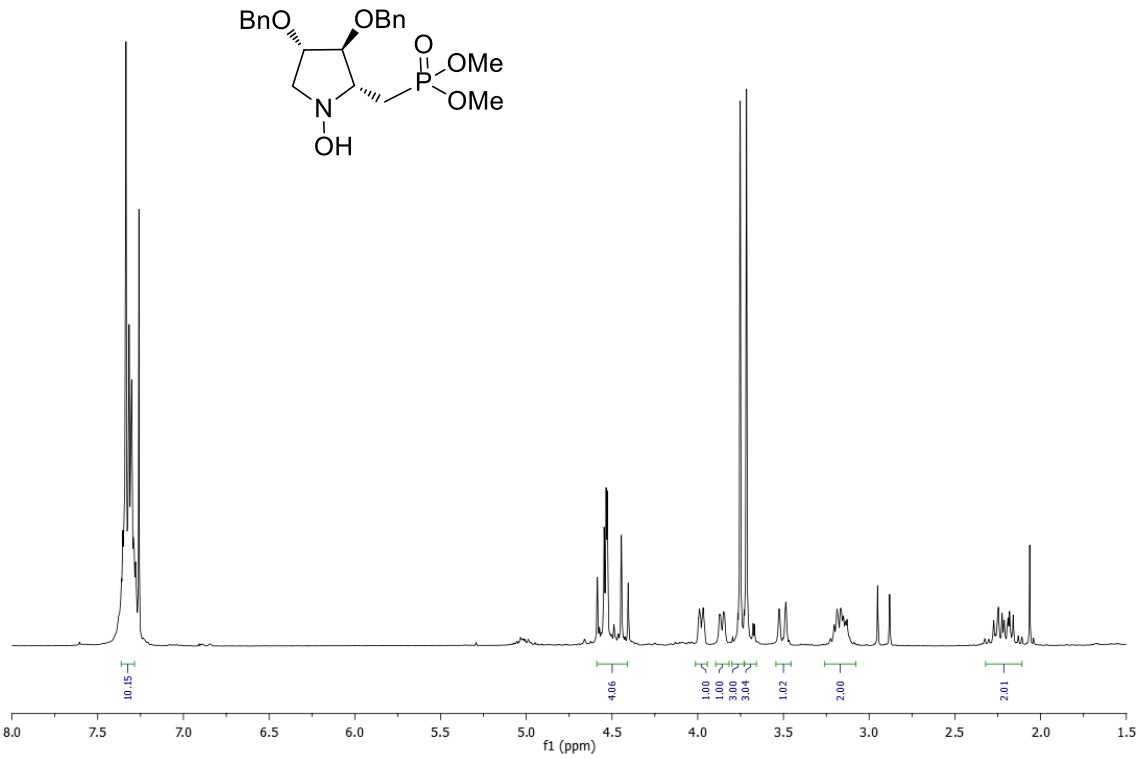

30.5
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

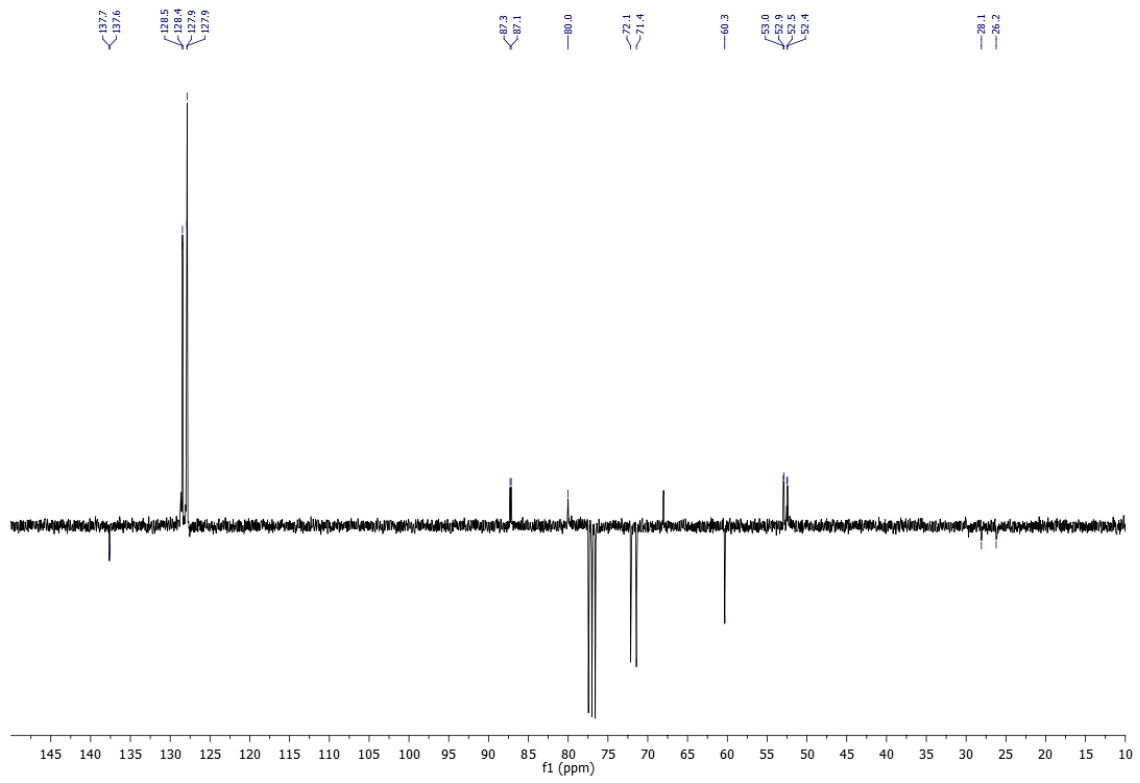

O
O
O
P
O
O
N
OH

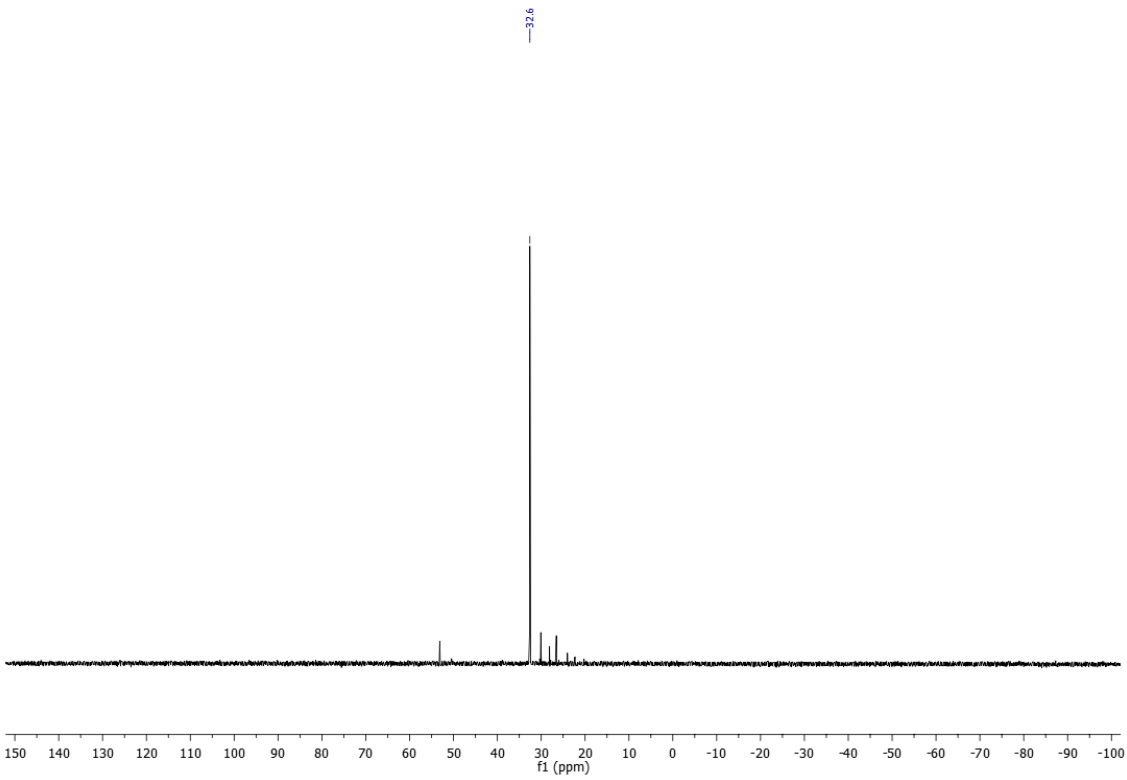
2.00
2.00
2.00
1.00
5.00
0.97
0.98
0.98
0.91
1.00
3.00
3.00
f1 (ppm)

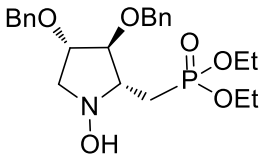

132.8
132.7
132.6
117.8
117.8
113.0
82.8
82.7
76.9
67.1
66.3
66.3
66.1
66.0
61.7
26.6
25.2
24.5
23.7
f1 (ppm)

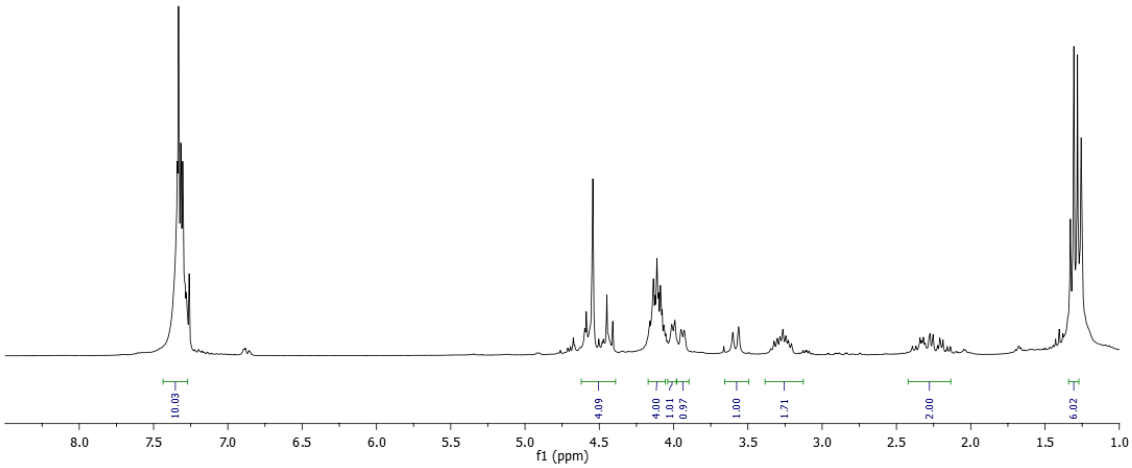

30.5
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)

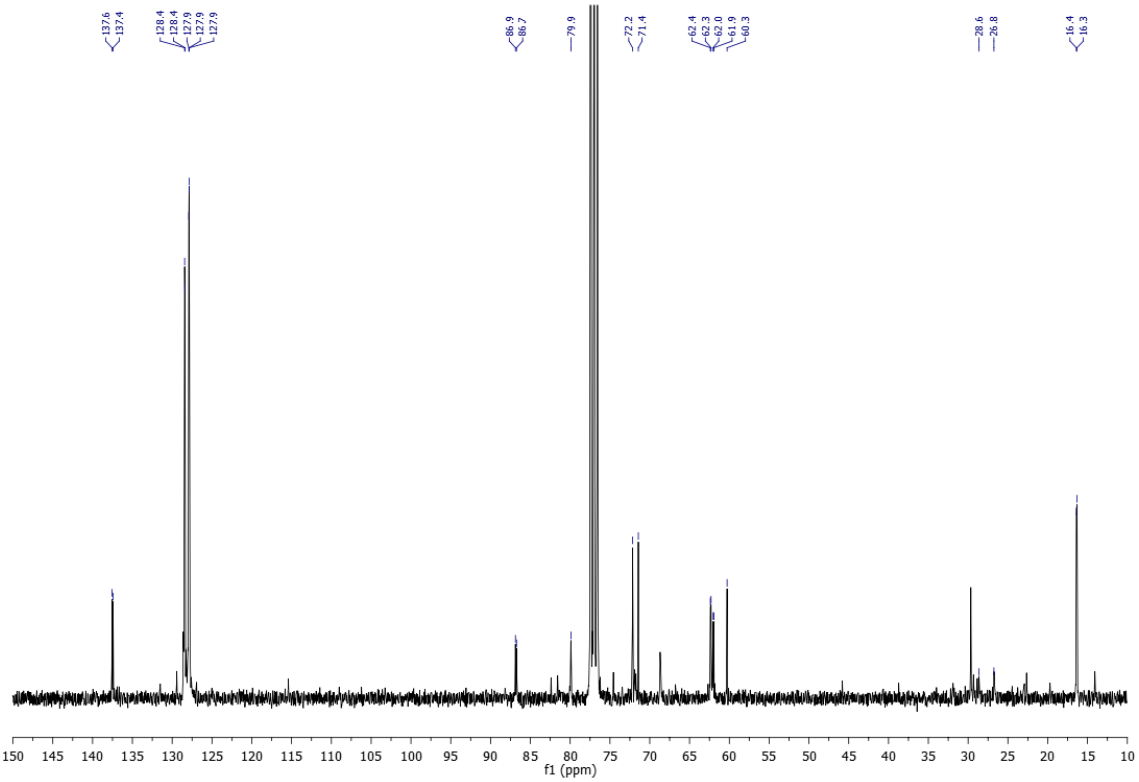

BnO
OBn
O
OMe
P
OMe
N
OH
10.15
4.06
1.00
1.00
3.00
3.04
1.02
2.00
2.01
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

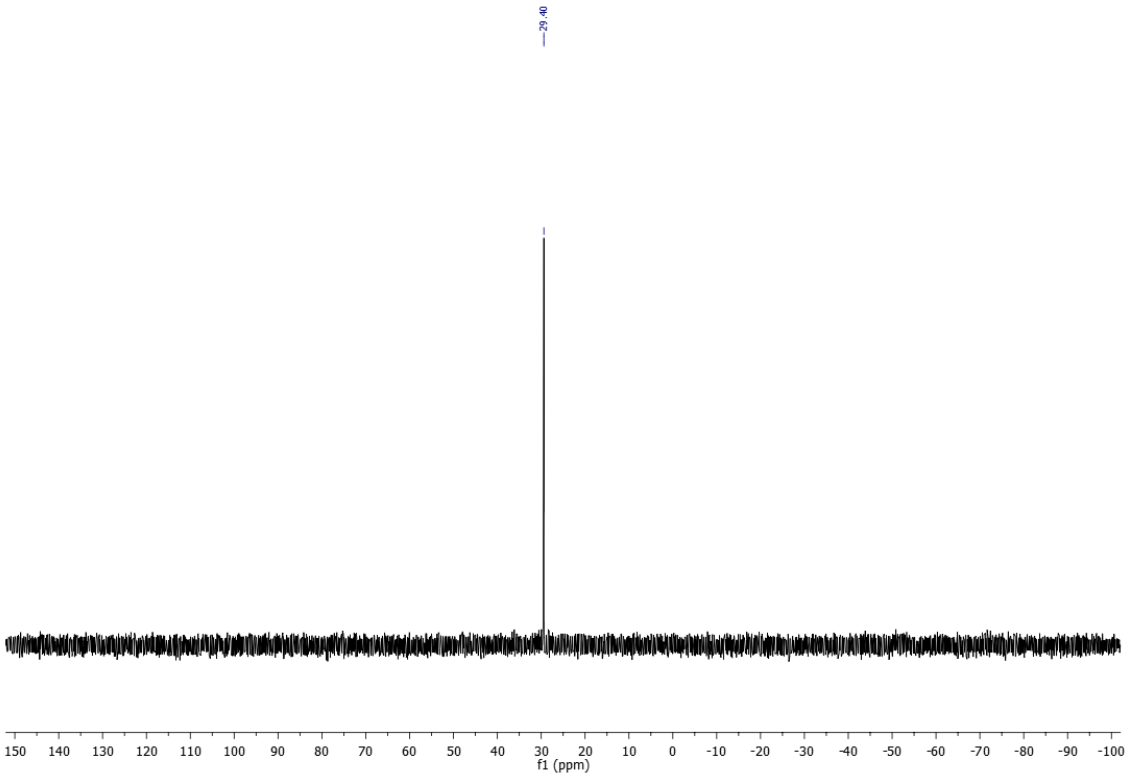

137.7
137.6
128.5
128.4
127.9
127.9
87.3
87.1
80.0
72.1
71.4
60.3
53.0
52.9
52.5
52.4
28.1
26.2
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
f1 (ppm)

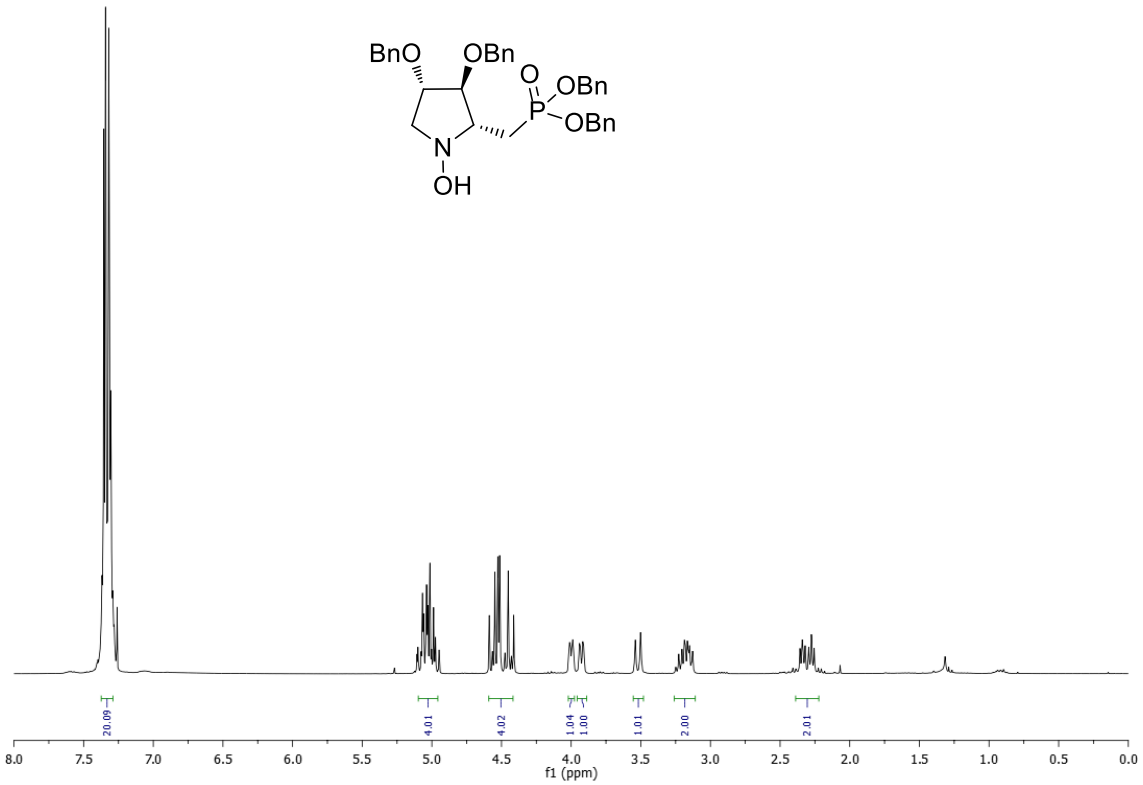

32.6
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

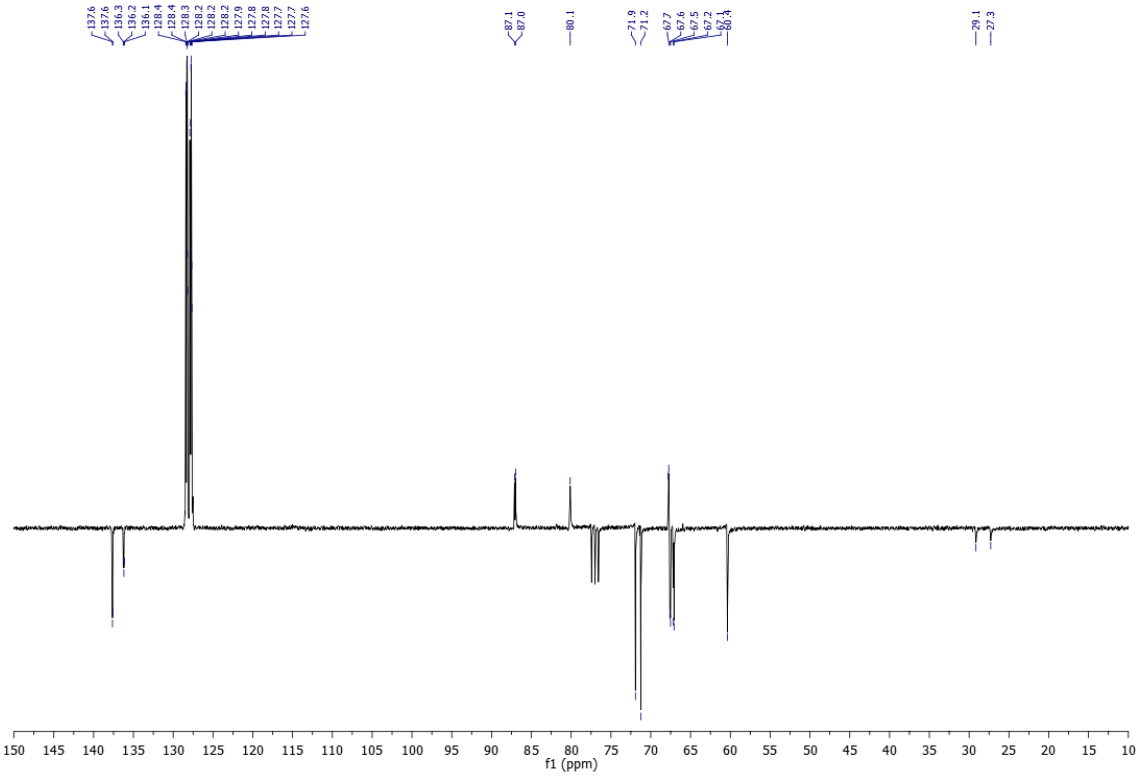

BnO
OBn
O
OEt
P
OEt
N
OH

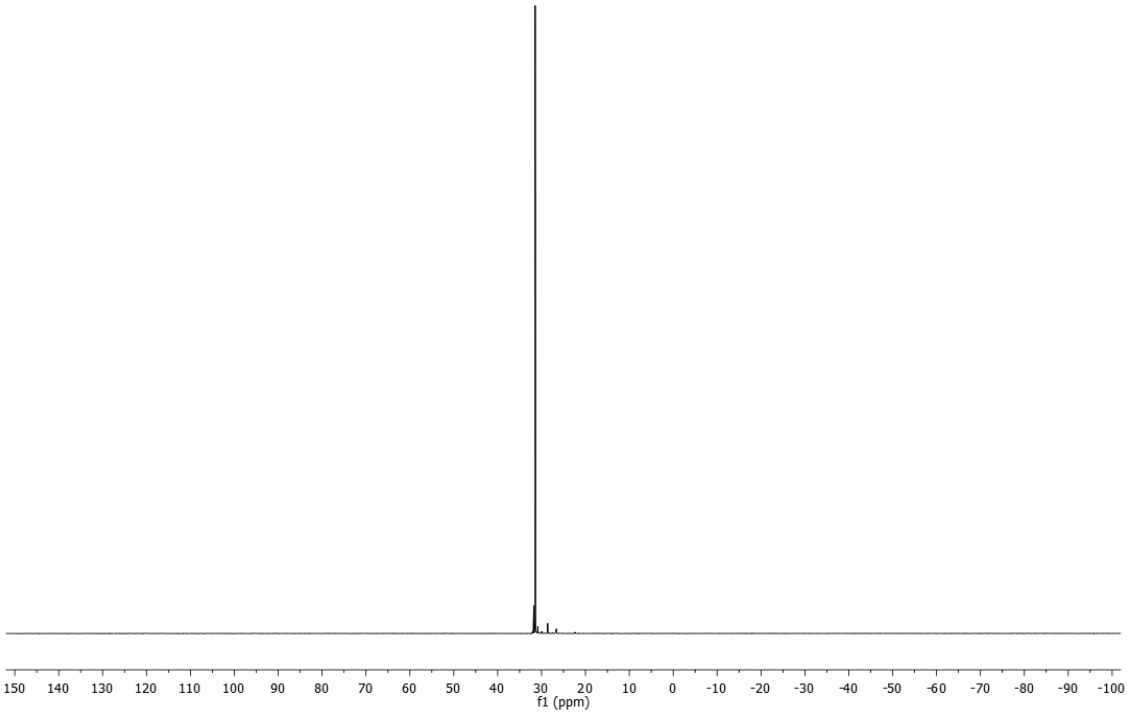

10.03
4.09
4.00
1.01
0.97
1.00
1.71
2.00
6.02
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

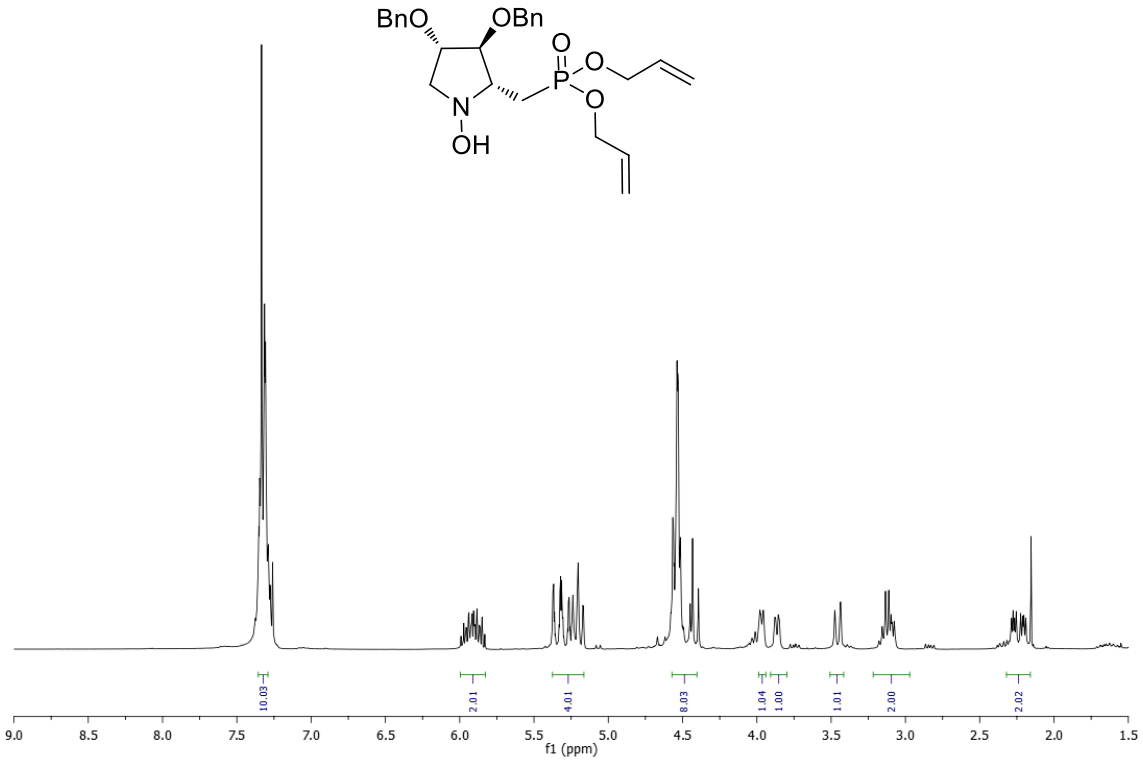

137.6
137.4
128.4
128.4
127.9
127.9
127.9
86.9
86.7
79.9
72.2
71.4
62.4
62.3
62.0
61.9
60.3
28.6
26.8
16.4
16.3
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
f1 (ppm)

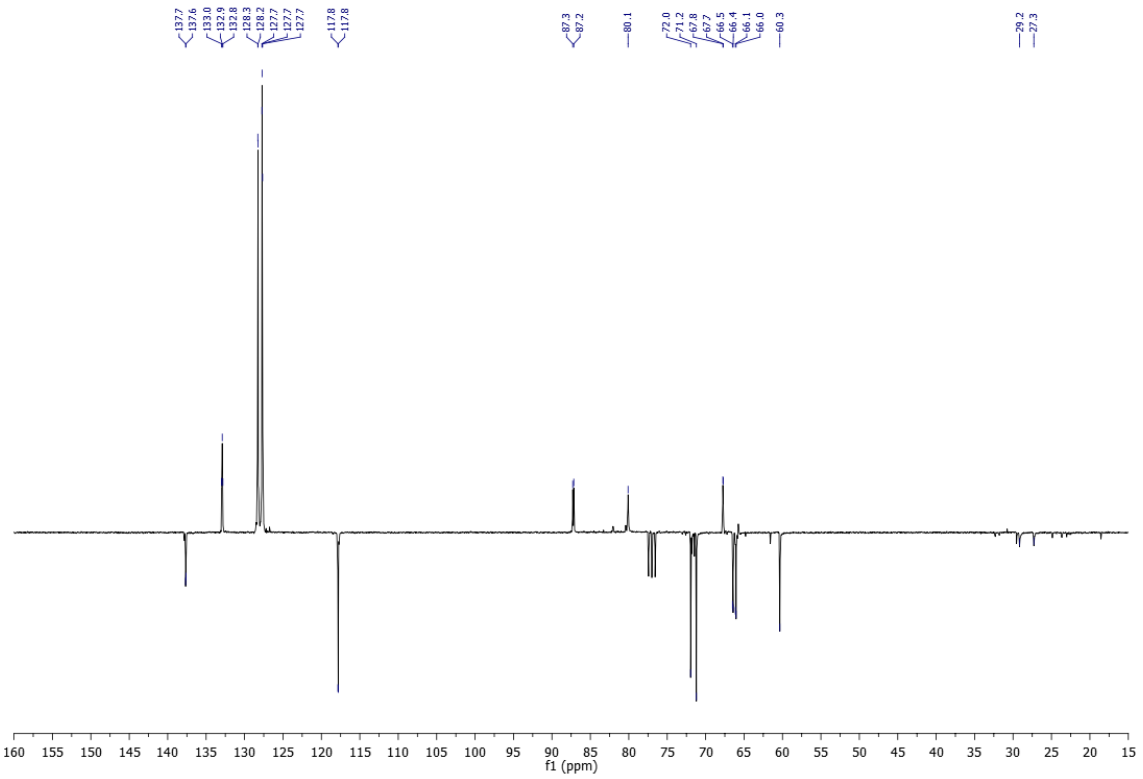

29.40
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

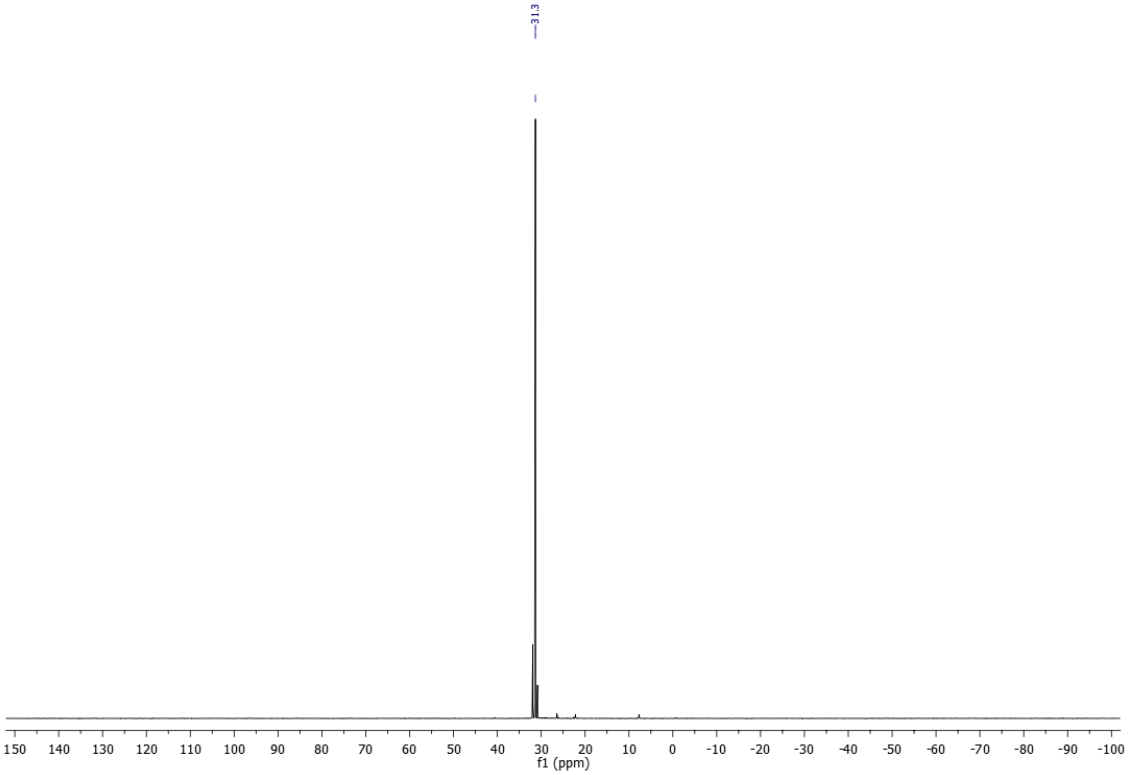

BnO
OBn
O
OBn
P
OBn
N
OH
20.09
4.01
4.02
1.04
1.00
1.01
2.00
2.01
f1 (ppm)

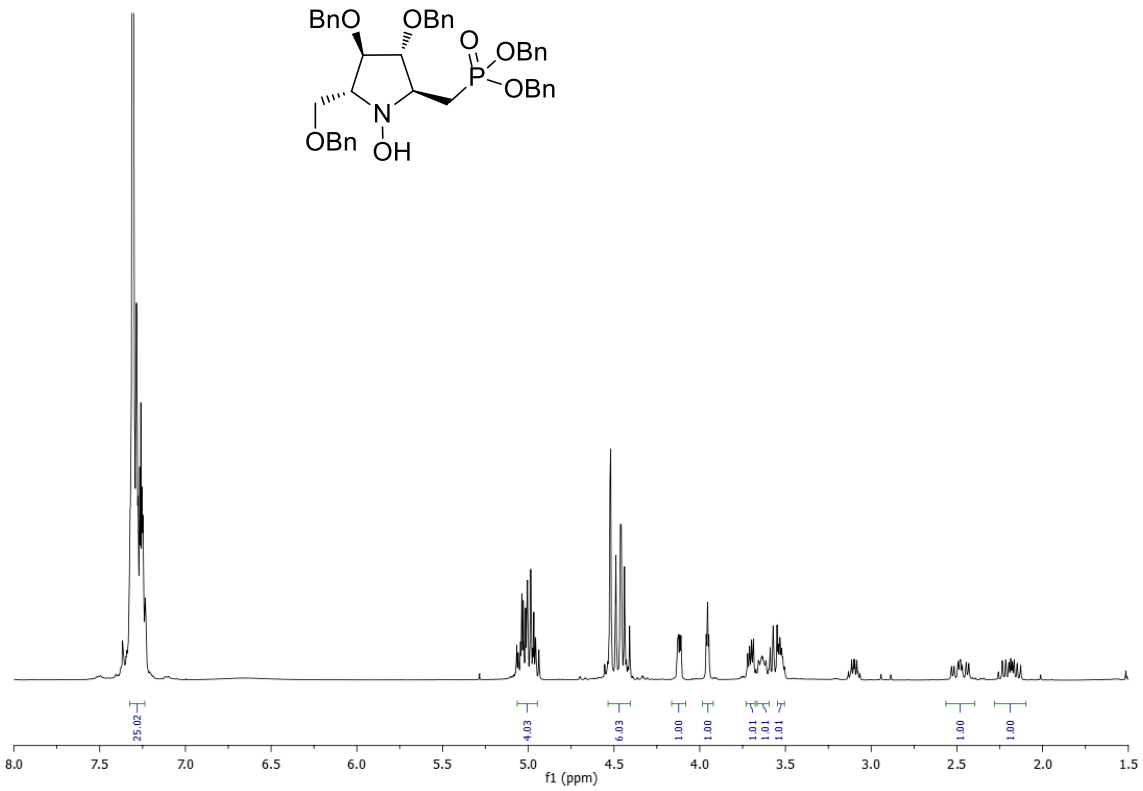

137.6
137.6
136.3
136.2
136.1
128.4
128.4
128.3
128.2
128.2
128.2
127.9
127.8
127.8
127.7
127.7
127.6
87.1
87.0
80.1
71.9
71.2
67.7
67.6
67.5
67.2
67.1
60.4
29.1
27.3
f1 (ppm)

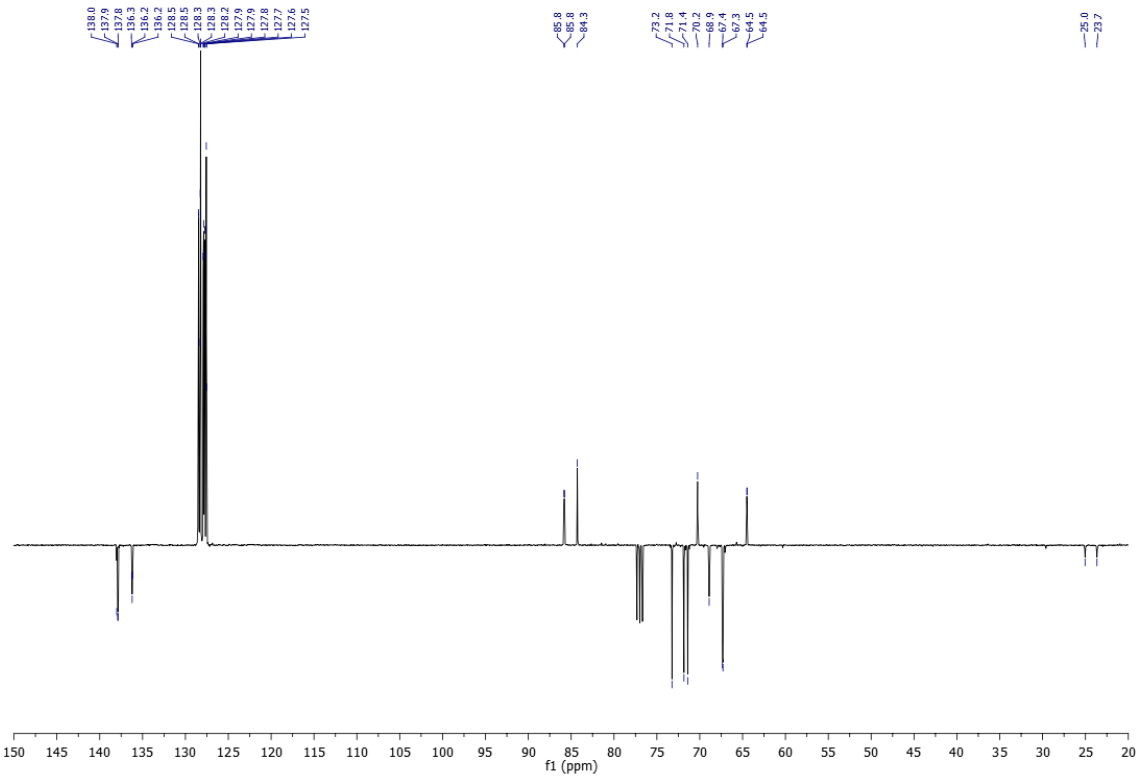

150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

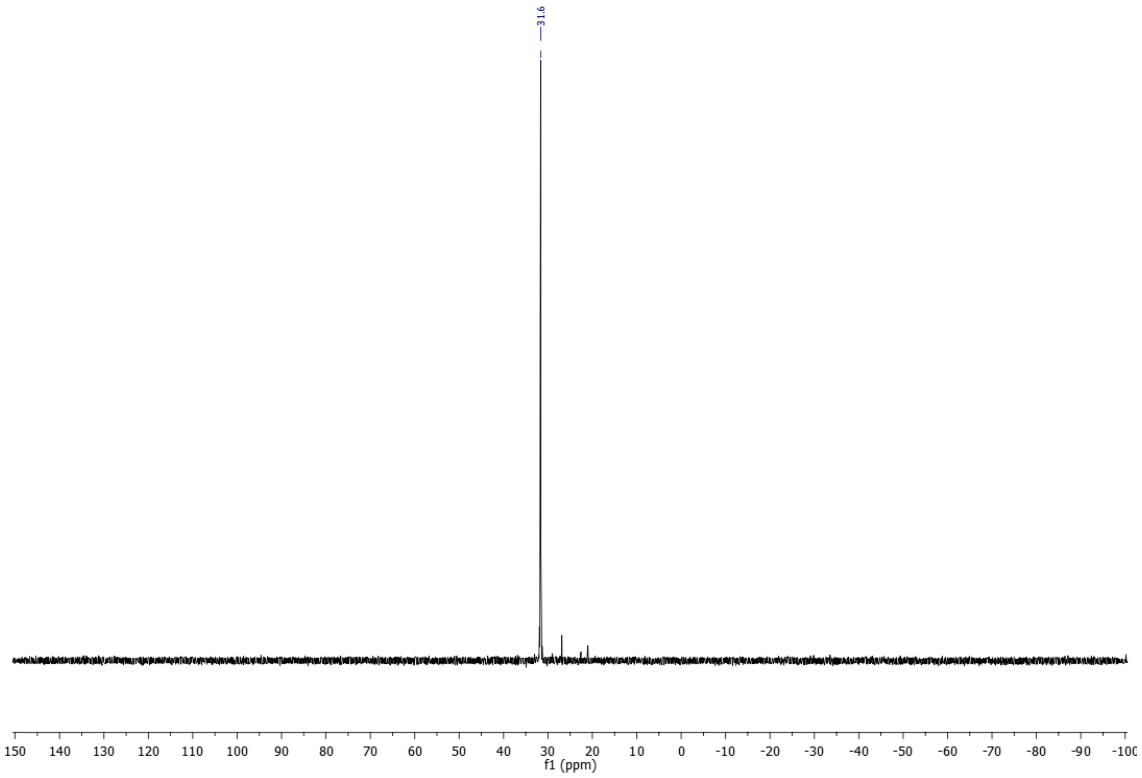

BnO
OBn
O
O
P
O
N
OH
10.03
2.01
4.01
8.03
1.04
1.00
1.01
2.00
2.02
f1 (ppm)

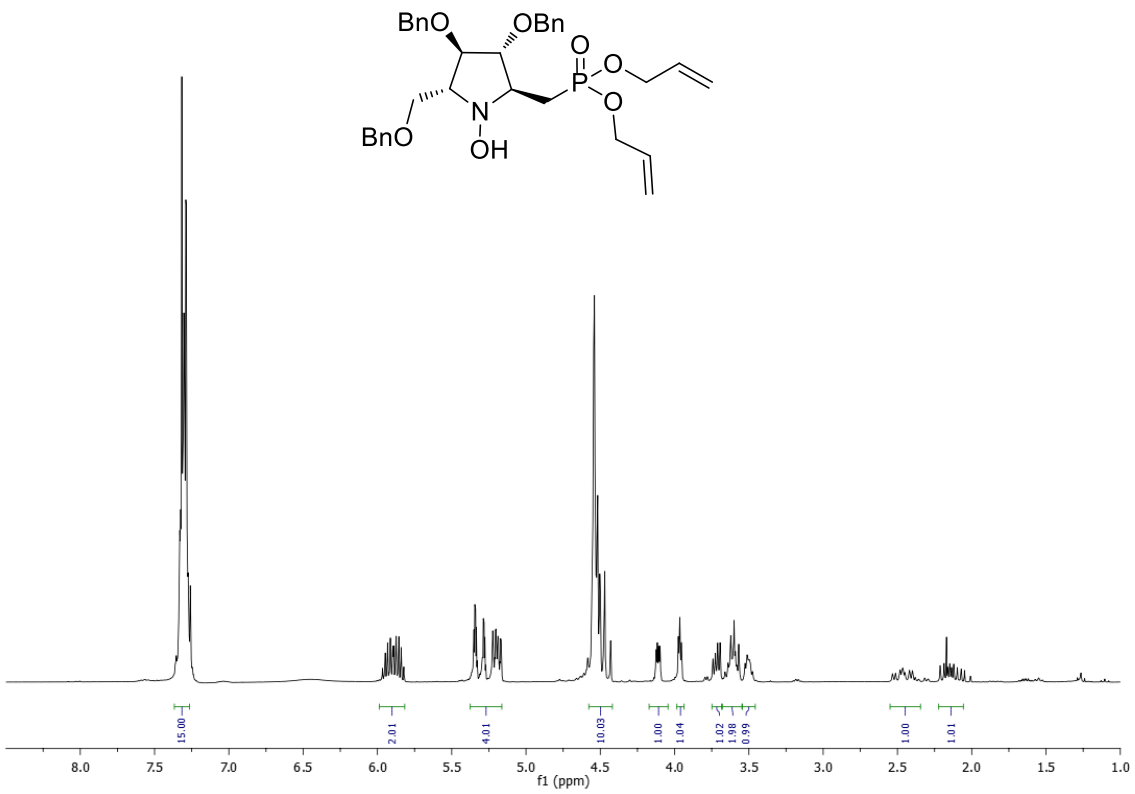

137.7
137.6
133.0
132.9
132.8
128.3
128.2
127.7
127.7
127.7
117.8
117.8
87.3
87.2
80.1
72.0
71.2
67.8
67.7
66.5
66.4
66.1
66.0
60.3
29.2
27.3
f1 (ppm)

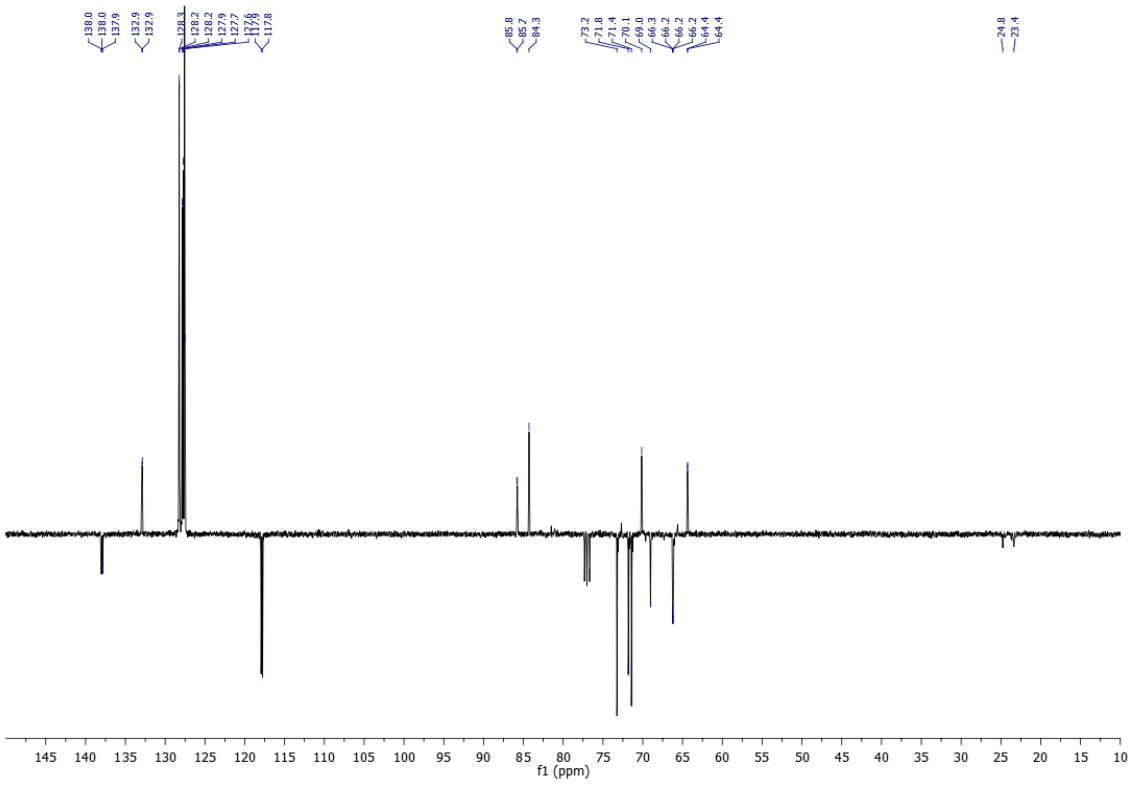

31.3
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

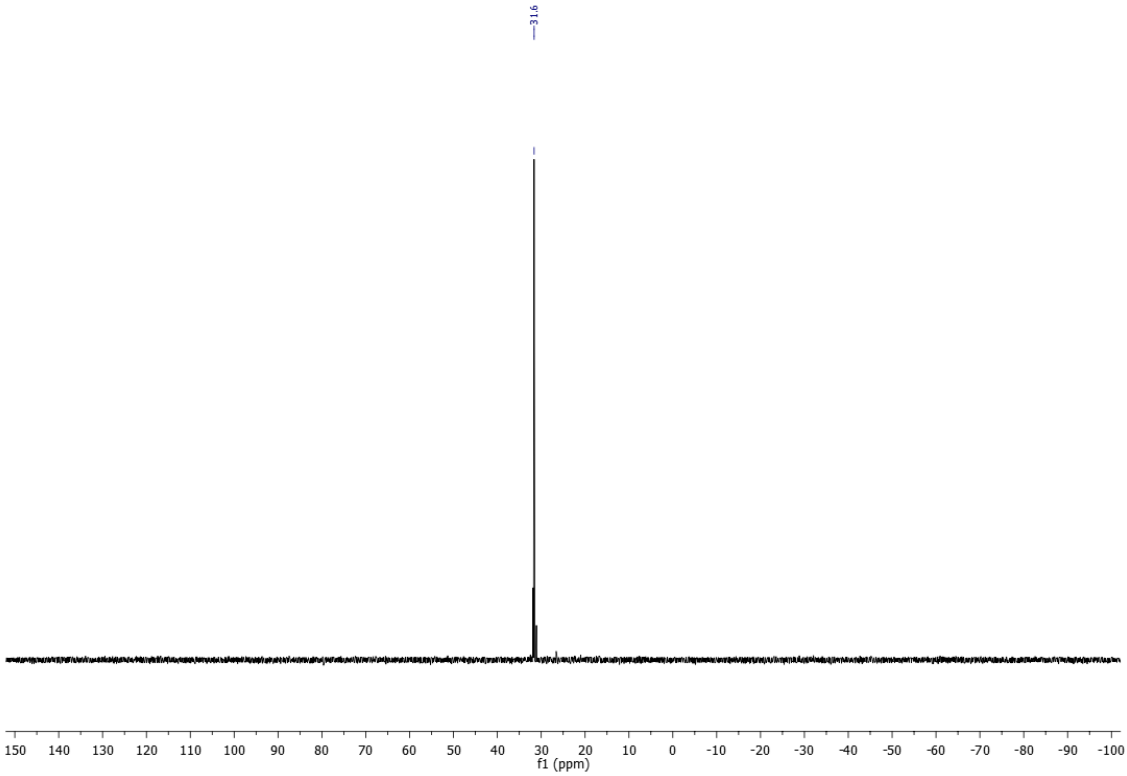

BnO
OBn
O
OBn
P
OBn
N
OBn
OH
25.02
4.03
6.03
1.00
1.00
1.01
1.01
1.01
1.00
1.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

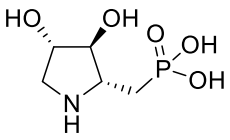

138.0
137.9
137.8
136.3
136.2
136.2
128.5
128.5
128.3
128.3
128.2
127.9
127.9
127.8
127.7
127.6
127.5
85.8
85.8
84.3
73.2
71.8
71.4
70.2
68.9
67.4
67.3
64.5
64.5
25.0
23.7
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
f1 (ppm)


31.6
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

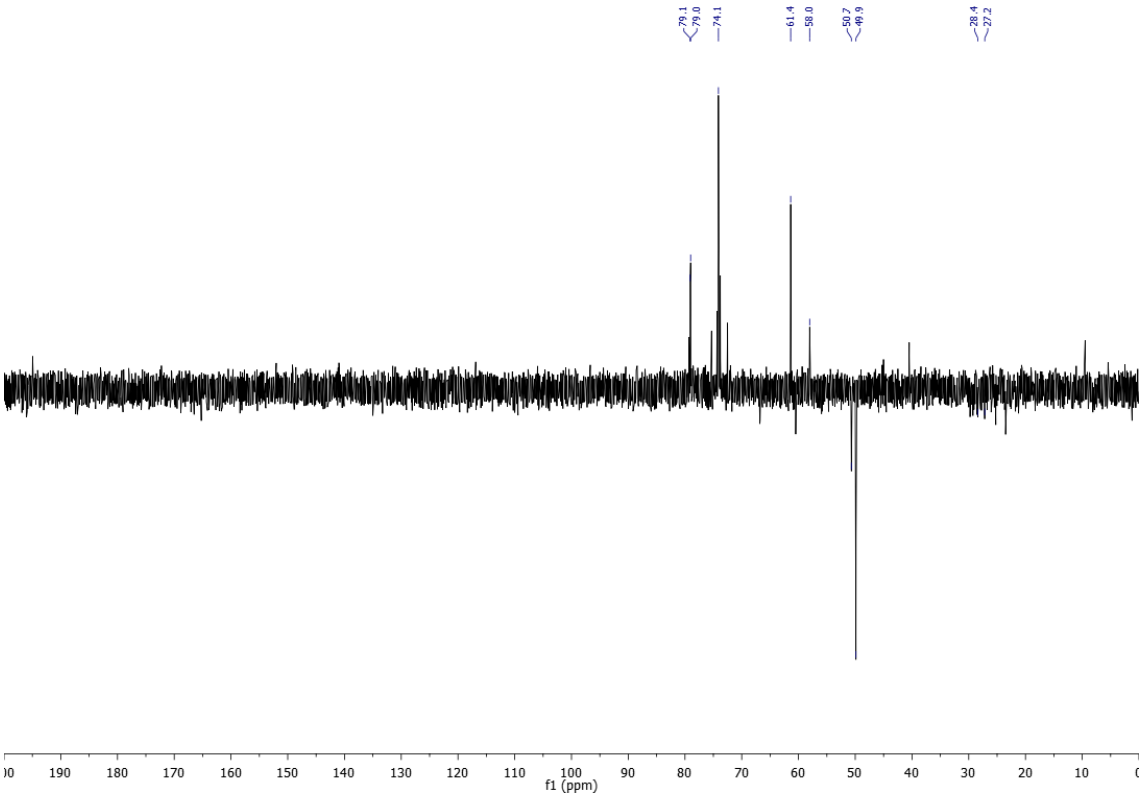

BnO
OBn
O
O
P
O
N
OH
BnO
15.00
2.01
4.01
10.03
1.00
1.04
1.02
1.98
0.99
1.00
1.01
f1 (ppm)

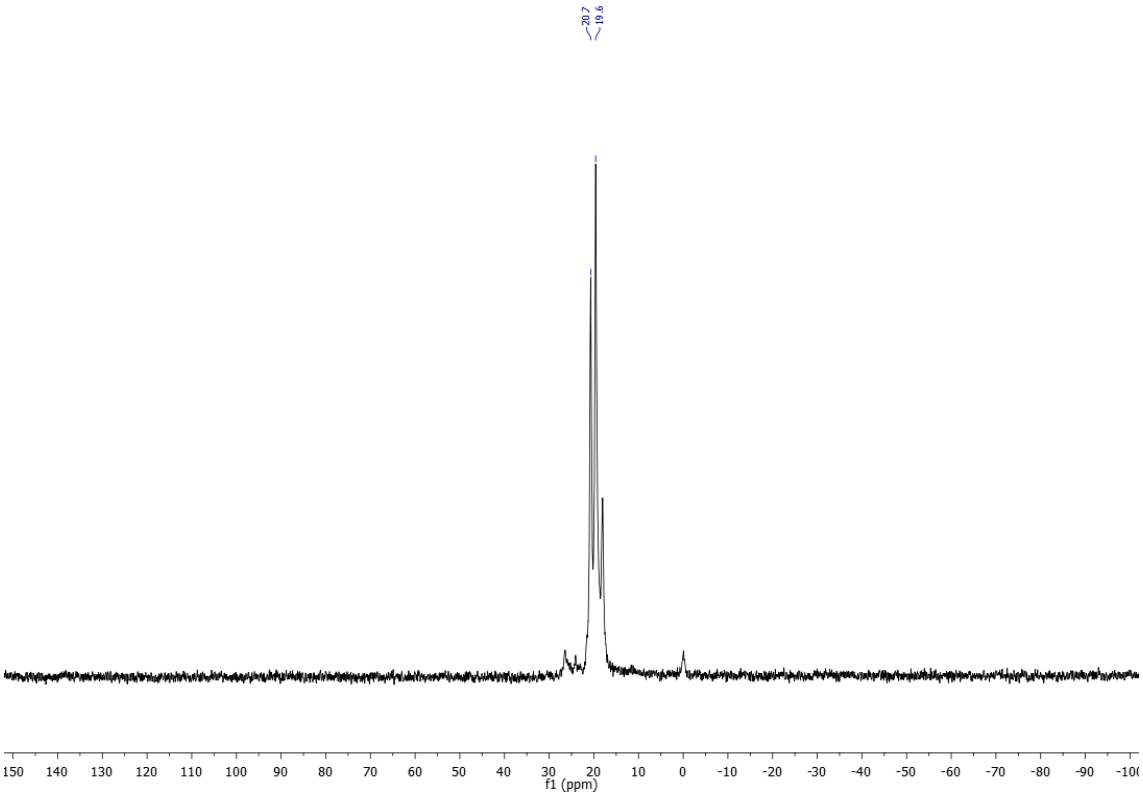

138.0
138.0
137.9
132.9
132.9
128.3
128.2
128.2
127.9
127.7
85.8
85.7
84.3
73.2
71.8
71.4
70.1
69.0
66.3
66.2
66.2
66.2
64.4
64.4
24.8
23.4
f1 (ppm)

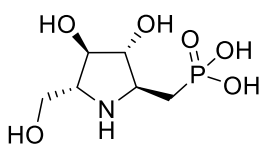

31.6
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)


HO
OH
O
OH
P
OH
N
H

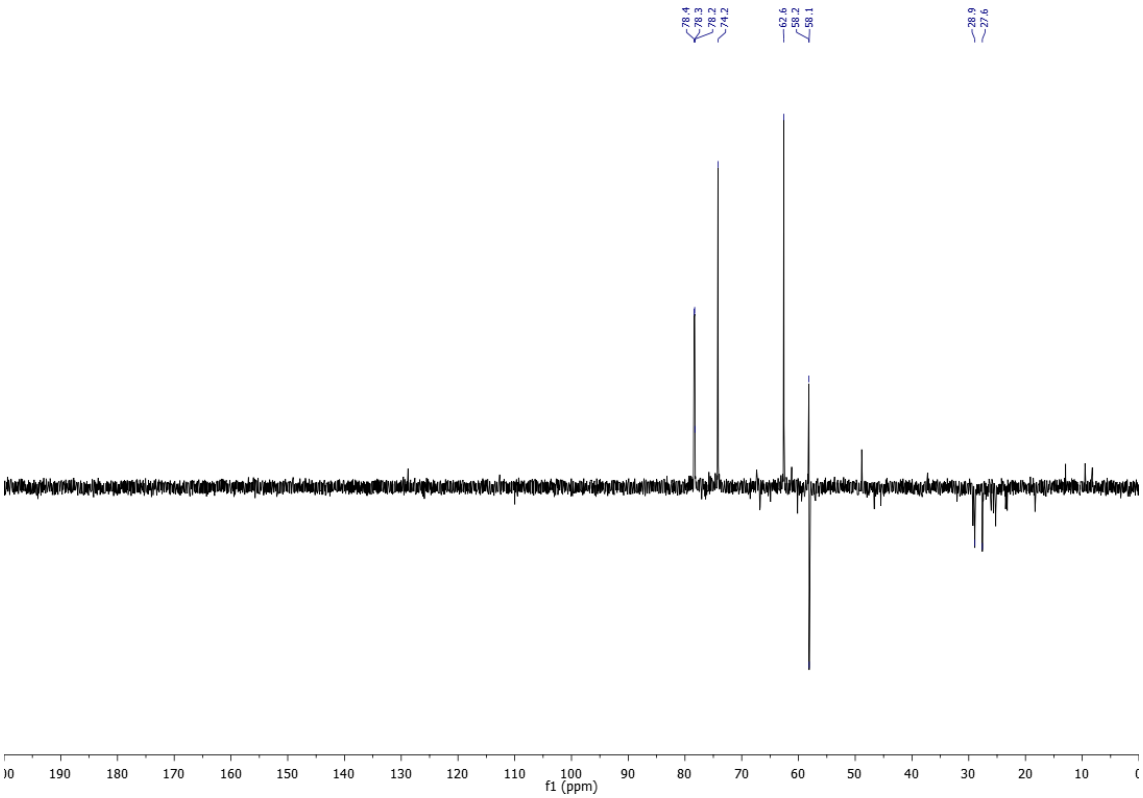
0.20
0.86
0.23
0.68
0.27
0.69
0.36
0.67
0.33
0.67
2.00
f1 (ppm)

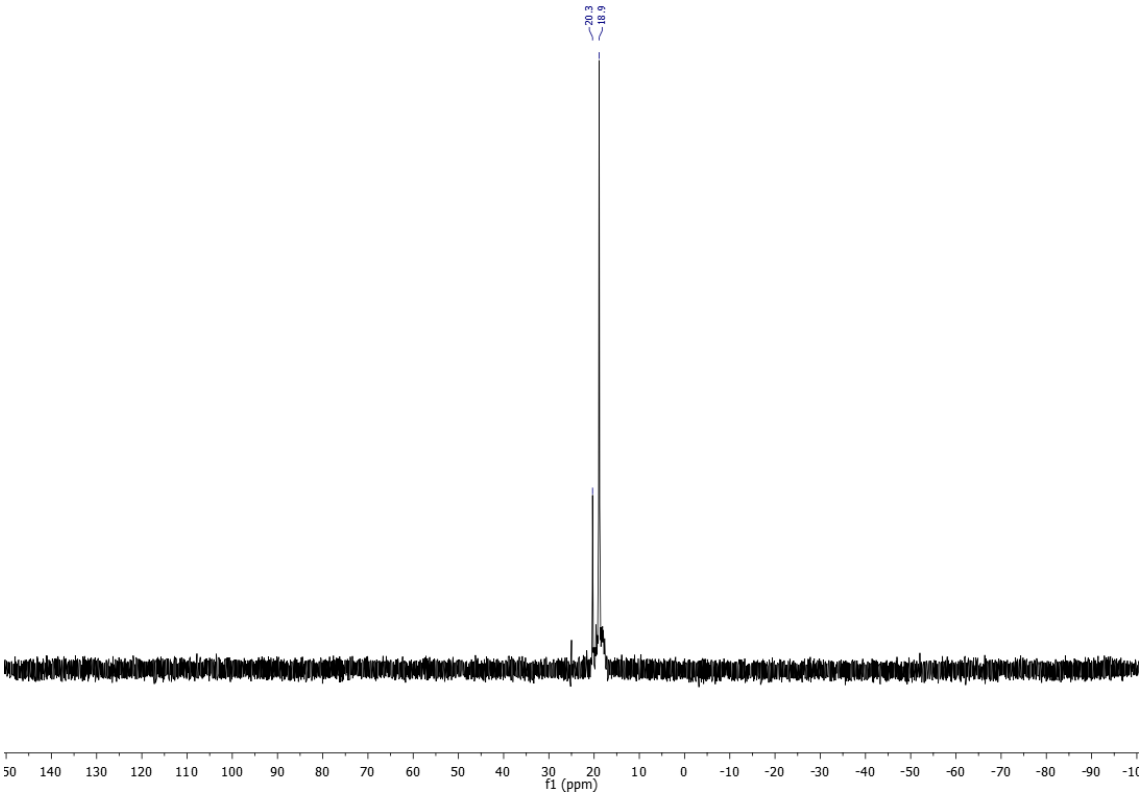

79.1
79.0
74.1
61.4
58.0
50.7
49.9
28.4
27.2
f1 (ppm)

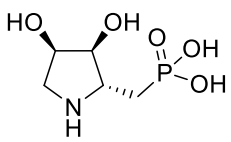

20.7
19.6
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)


HO
OH
O
OH
P
OH
N
H
HO

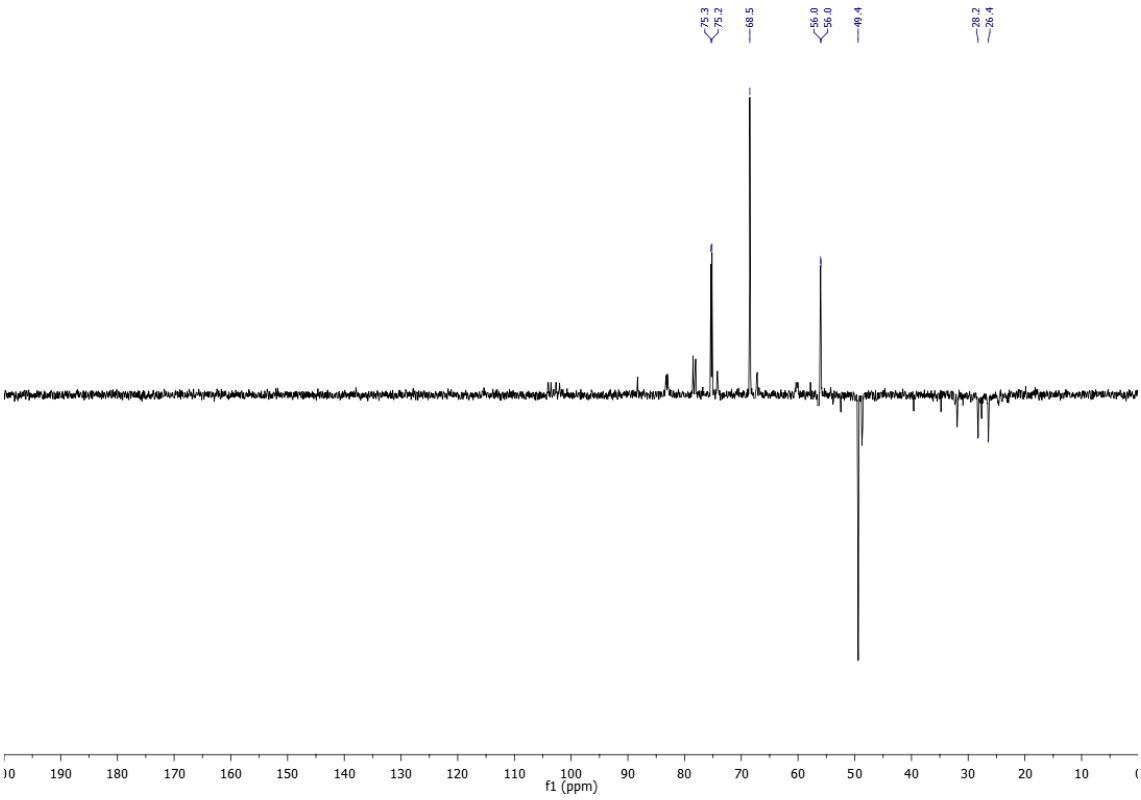
2.00
1.00
1.01
2.00
2.00
f1 (ppm)

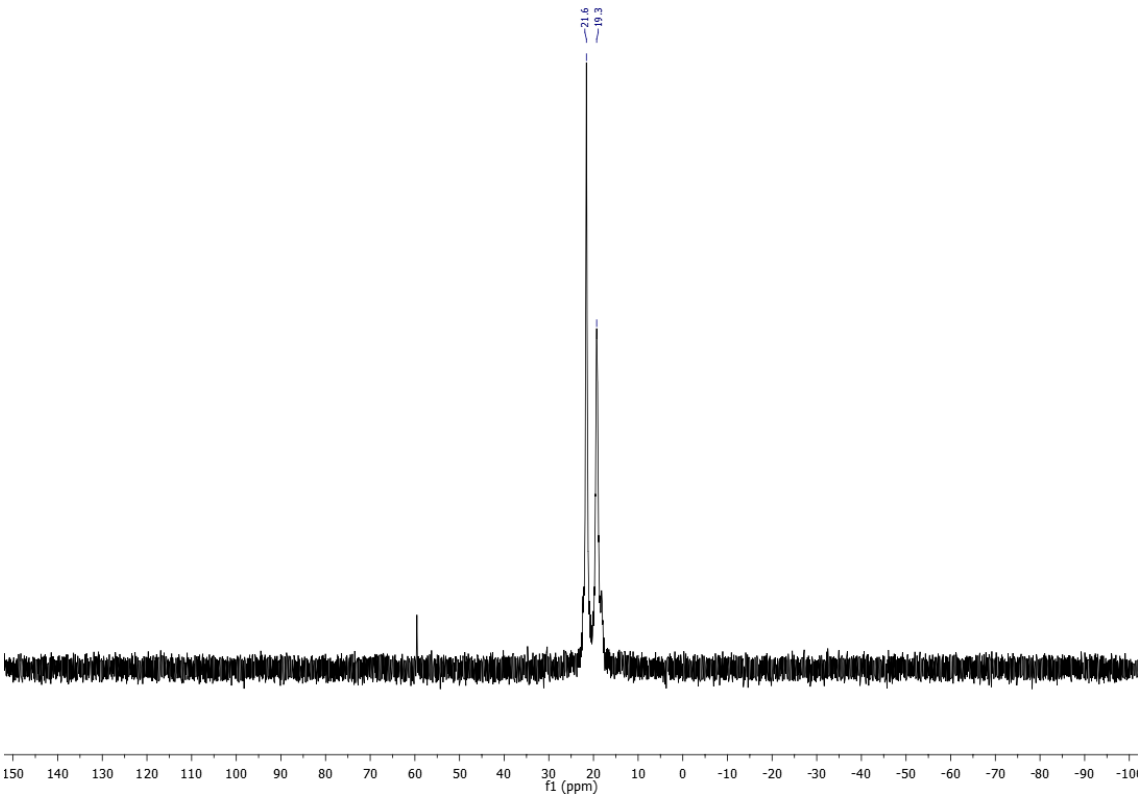

78.4
78.3
78.2
74.2
62.6
58.2
58.1
28.9
27.6
f1 (ppm)

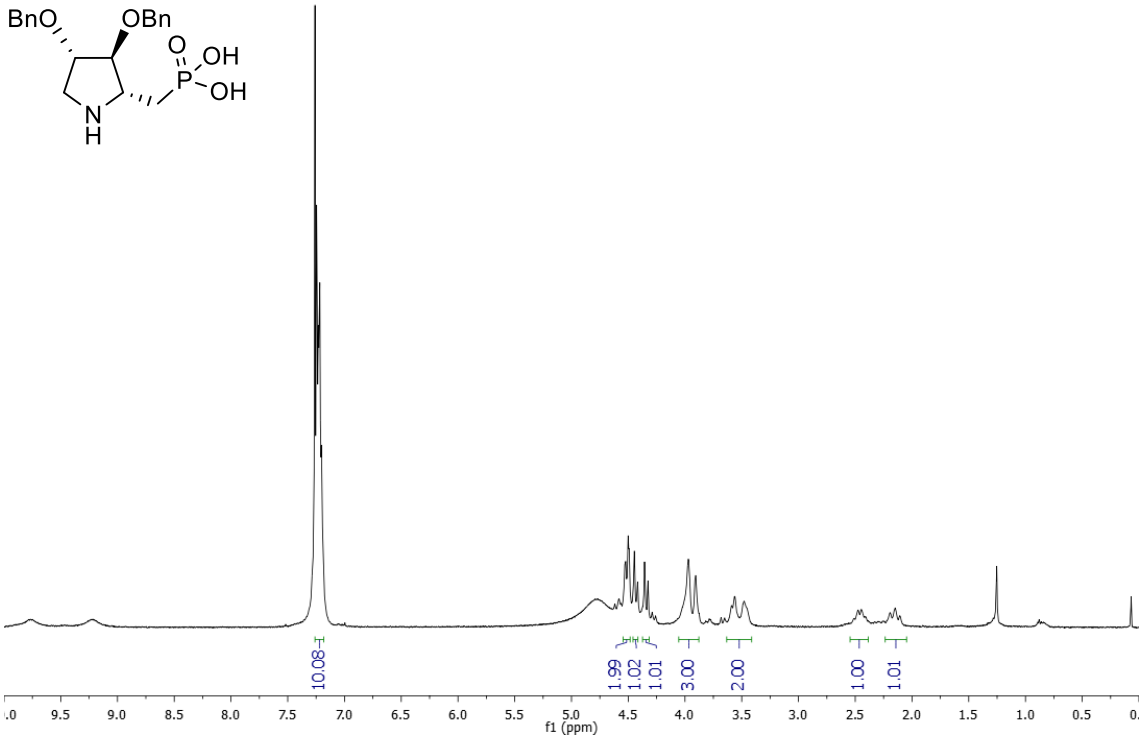

20.3
18.9
50 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -10
f1 (ppm)

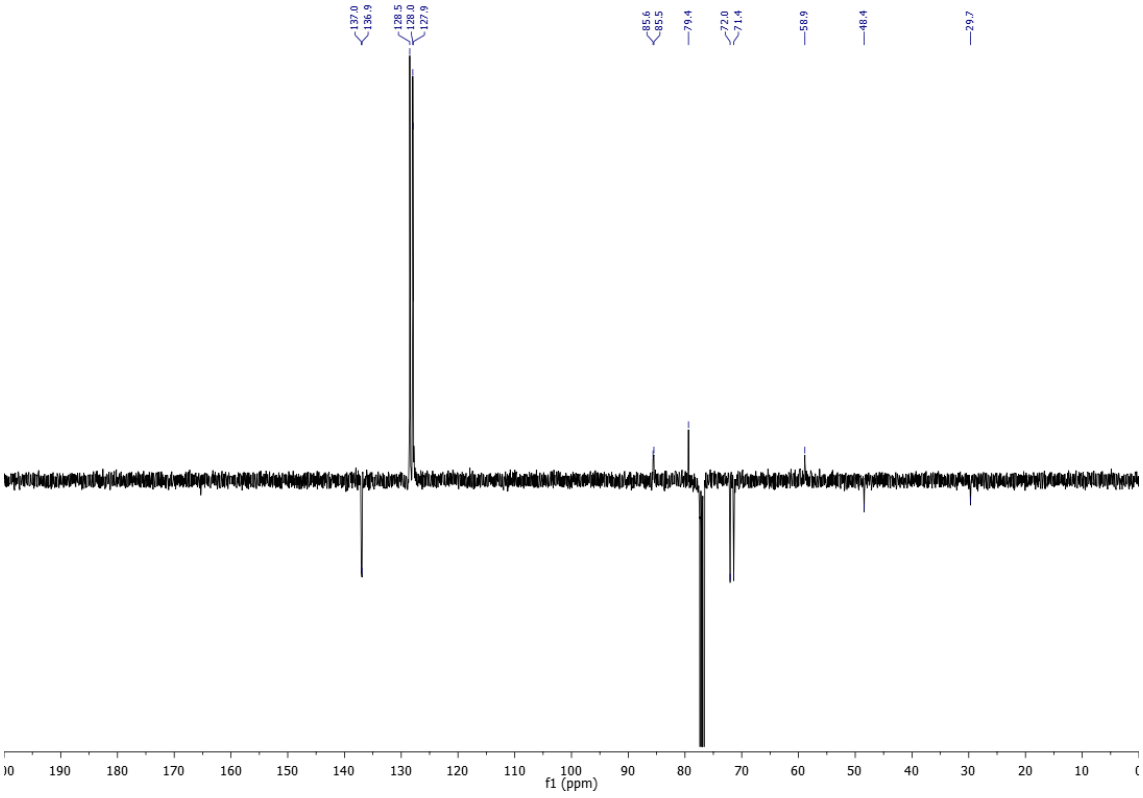

HO
OH
O
OH
P
OH
N
H

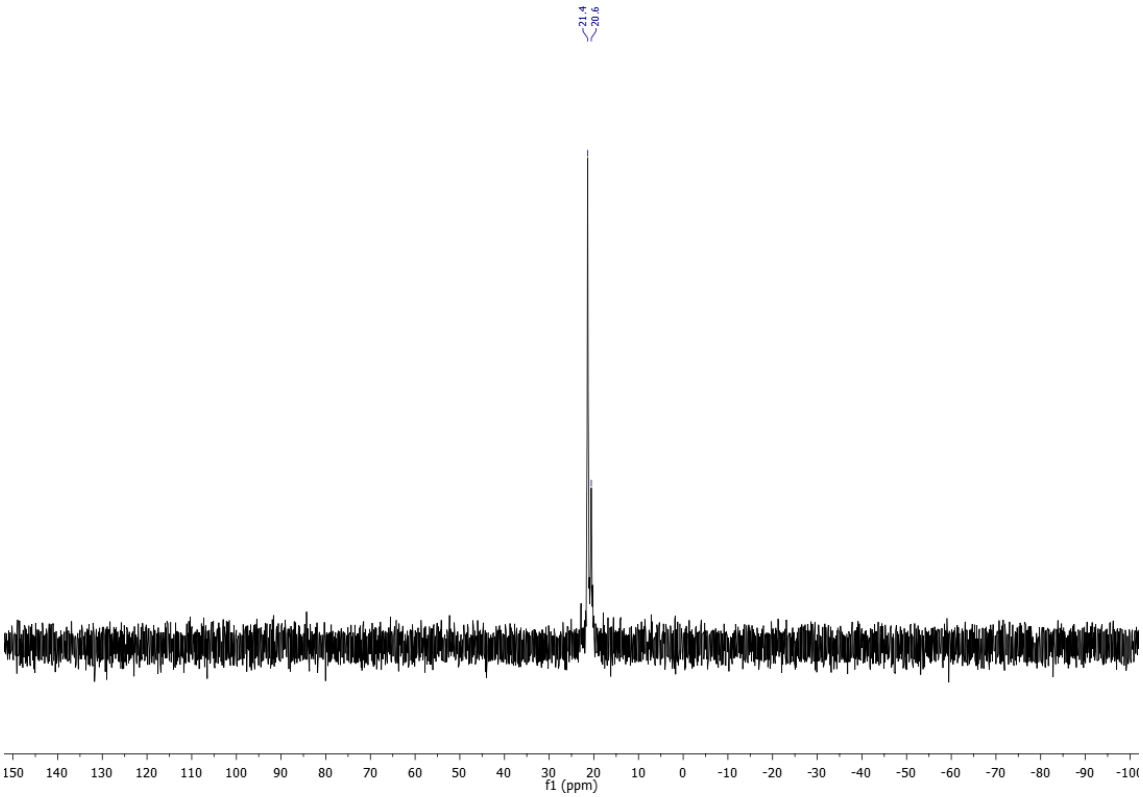
1.00
1.00
1.04
1.09
1.09
2.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

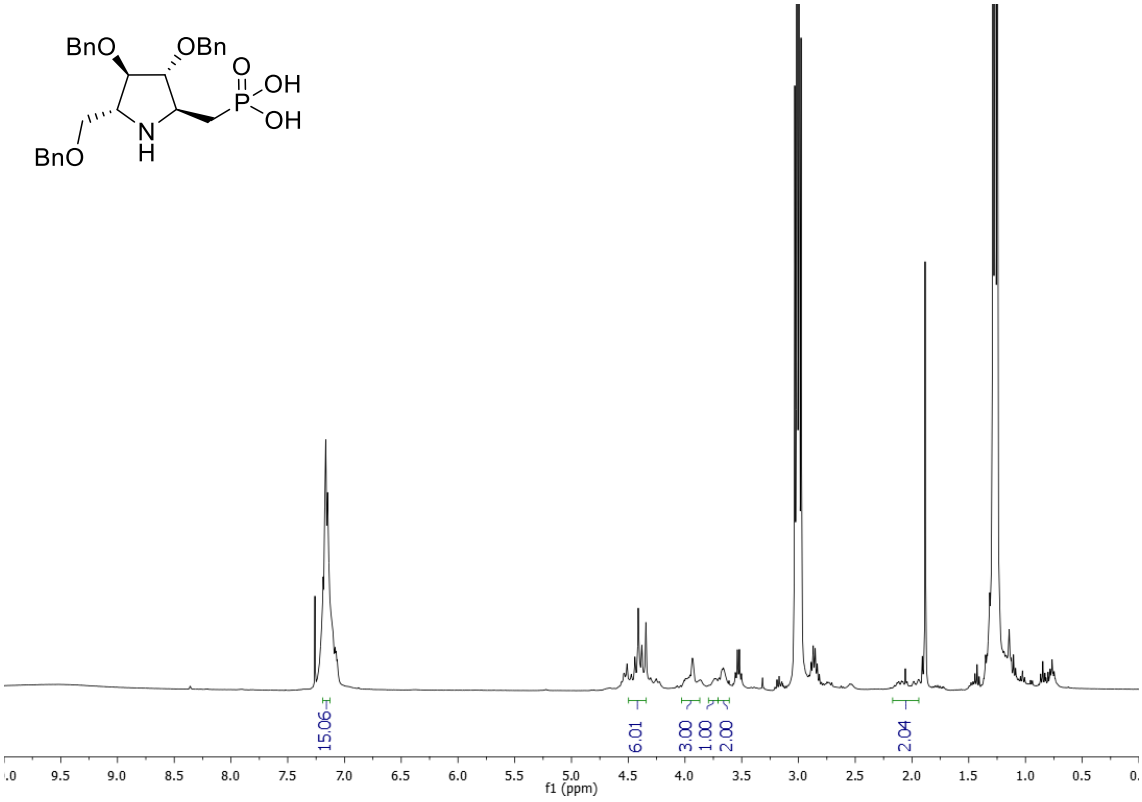

75.3
75.2
68.5
56.0
56.0
49.4
28.2
26.4
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

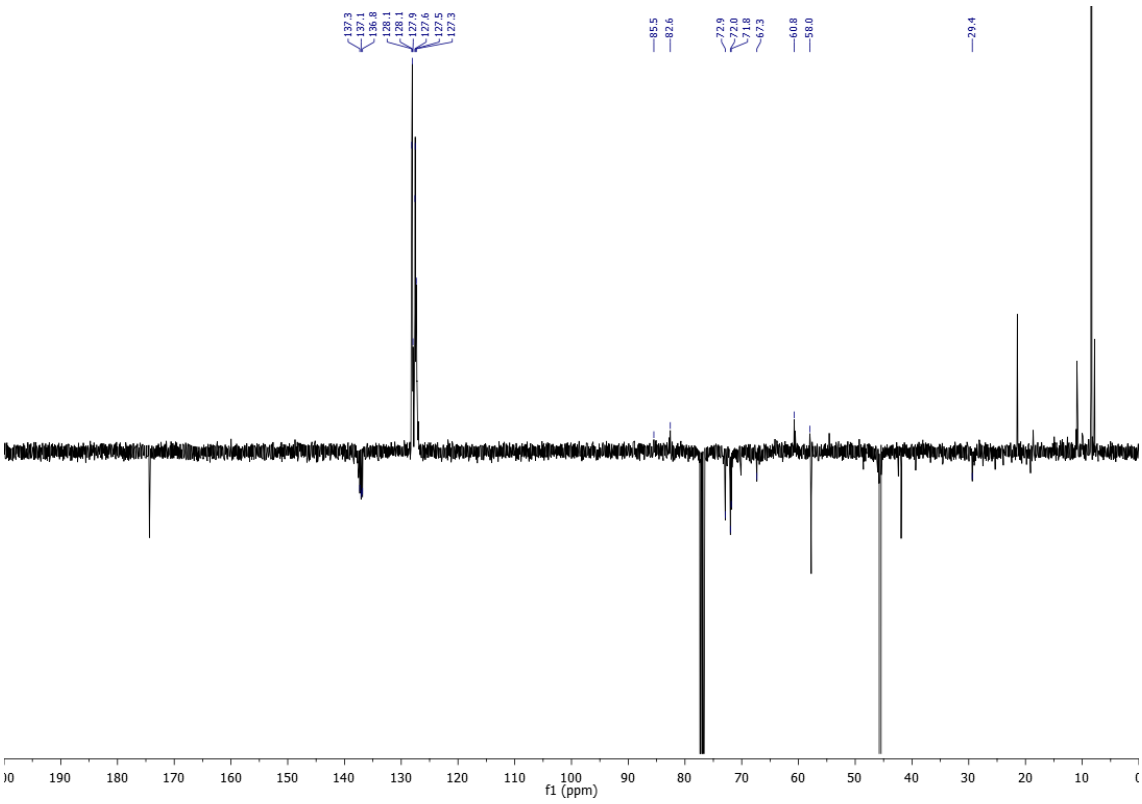

21.6
19.3
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)

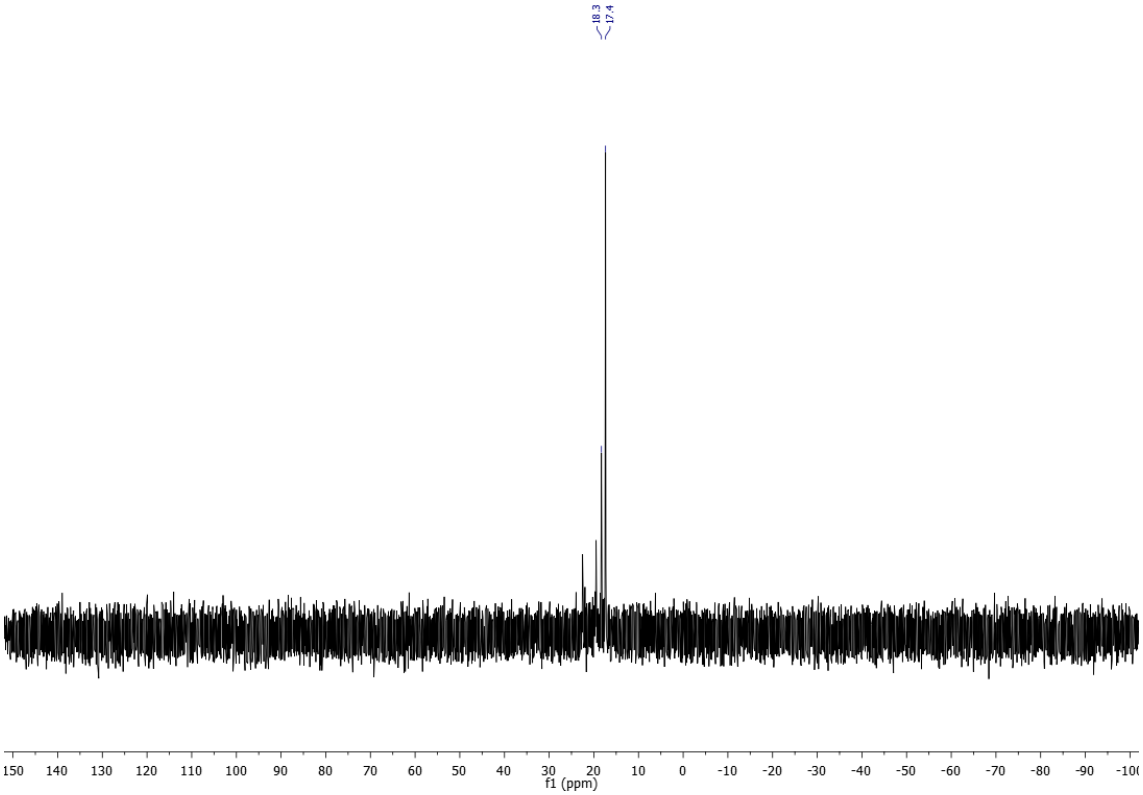

BnO
OBn
O
OH
P
OH
N
H
10.08
1.99
1.02
1.01
3.00
2.00
1.00
1.01
f1 (ppm)

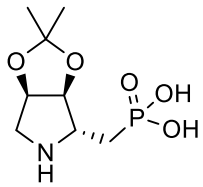

137.0
136.9
128.5
128.0
127.9
85.6
85.5
79.4
72.0
71.4
58.9
48.4
29.7
f1 (ppm)

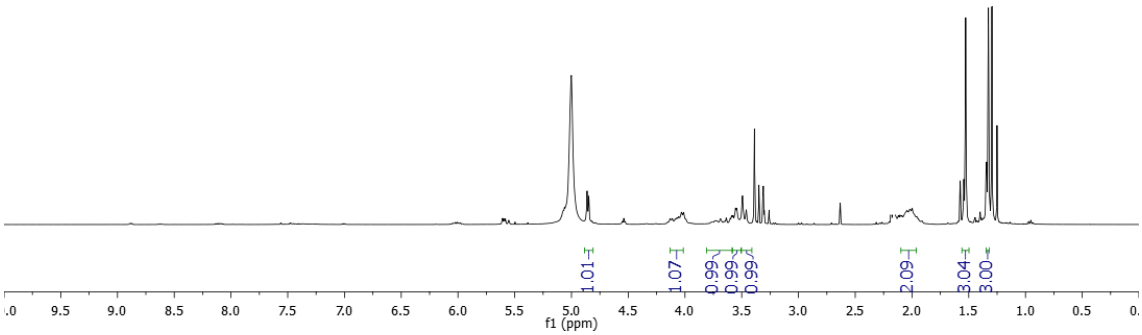

21.4
20.6
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -10
f1 (ppm)

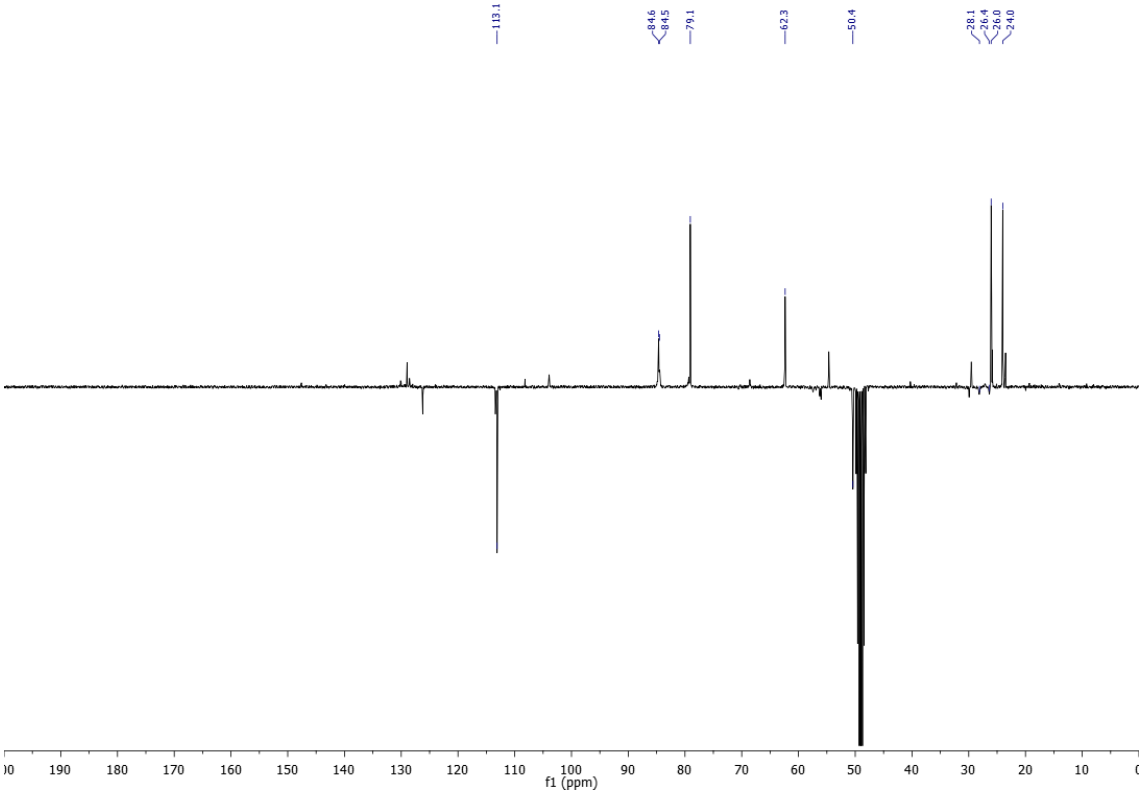

BnO
OBn
O
OH
P
OH
N
H
BnO
15.06
6.01
3.00
1.00
2.00
2.04
f1 (ppm)

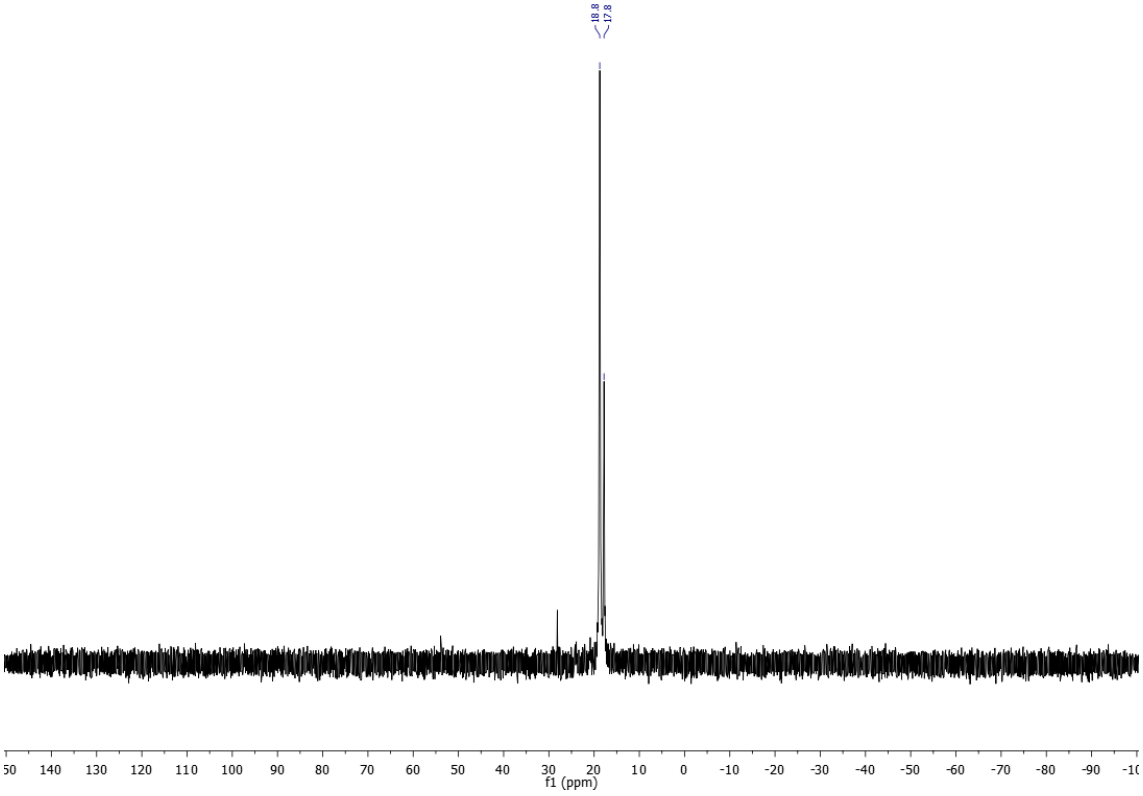

137.3
137.1
136.8
128.1
127.9
127.6
127.5
127.3
85.5
82.6
72.9
72.0
71.8
67.3
60.8
58.0
29.4
f1 (ppm)

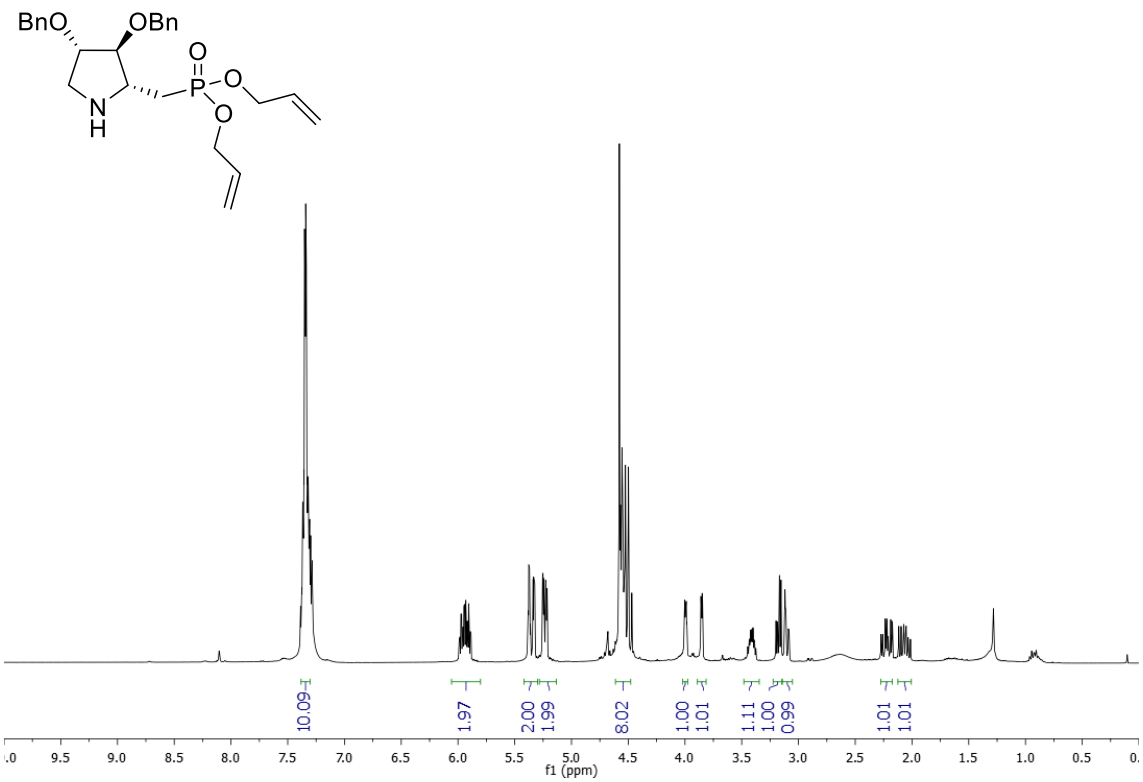

18.3
17.4
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)

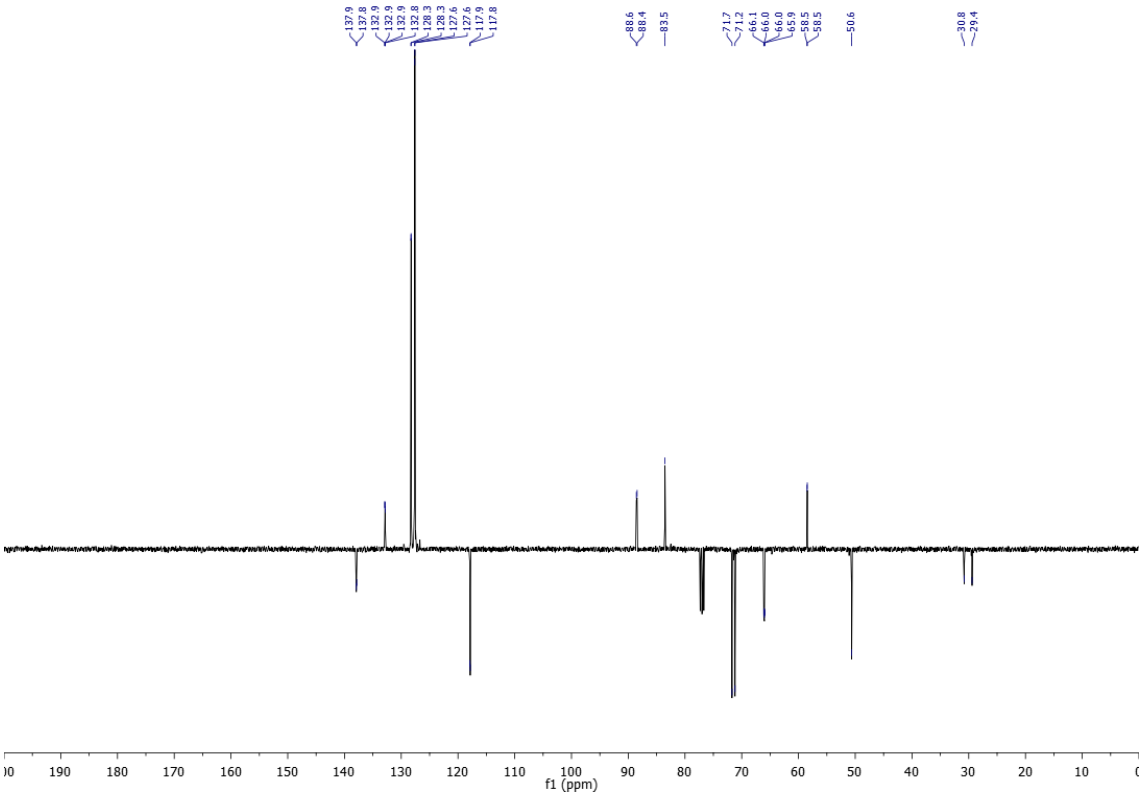

O
O
O
OH
P
OH
N
H

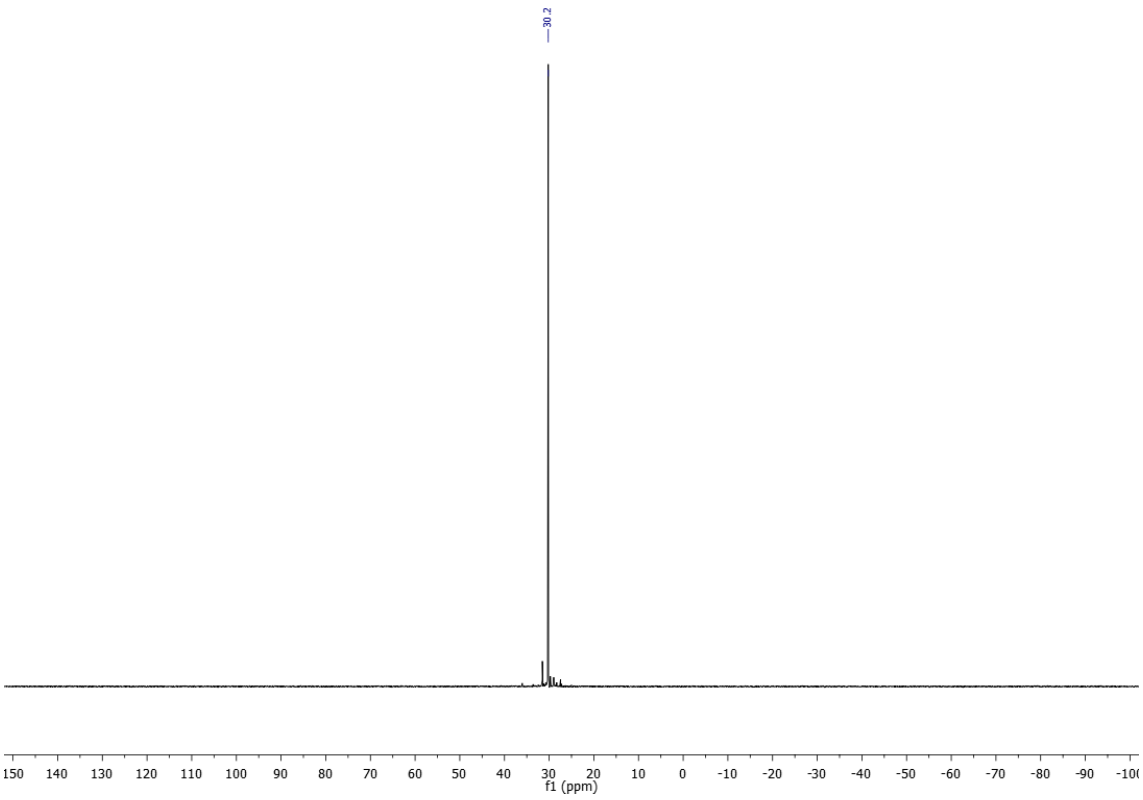

1.01
1.07
0.99
0.99
0.99
2.09
3.04
3.00
f1 (ppm)

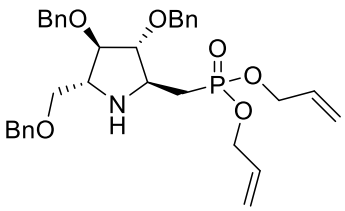

113.1
84.6
84.5
79.1
62.3
50.4
28.1
26.4
26.0
24.0
f1 (ppm)

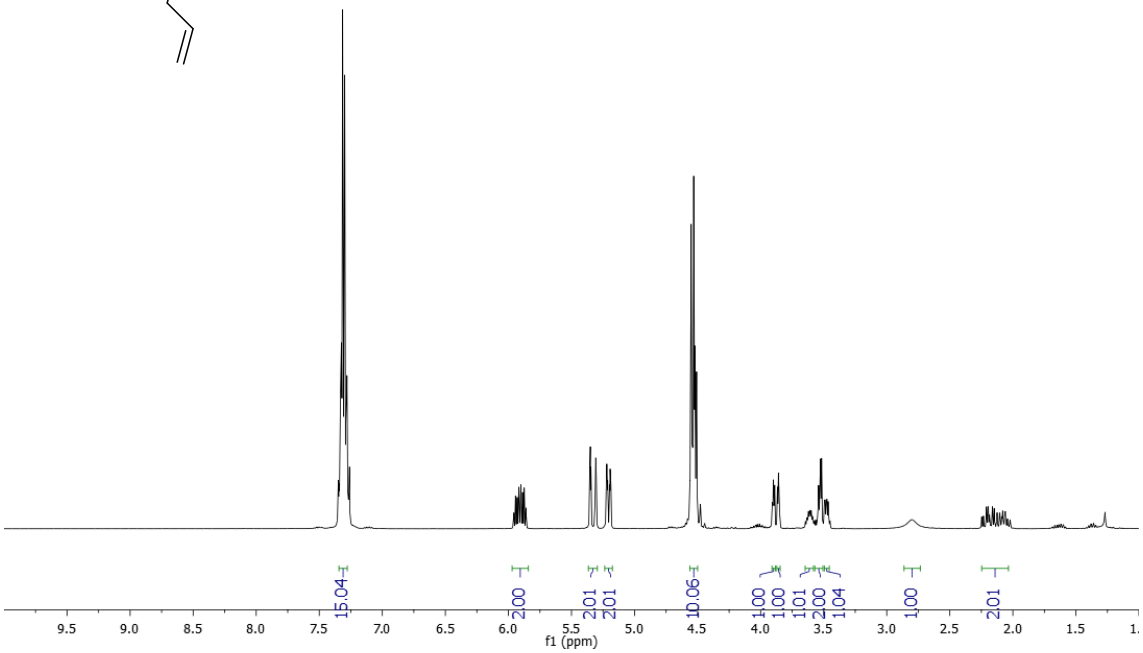

18.8
17.8
50 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -10
f1 (ppm)

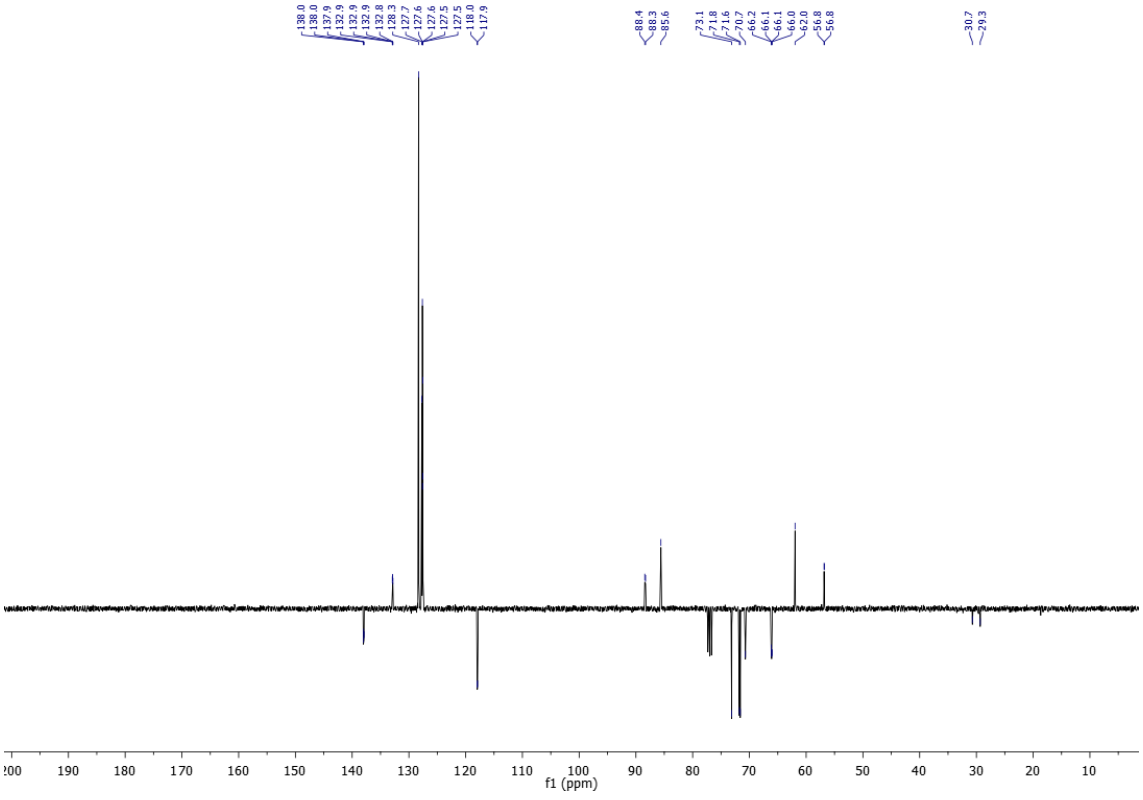

BnO
OBn
O
P
O
O
N
H
10.09
1.97
2.00
1.99
8.02
1.00
1.01
1.11
1.00
0.99
1.01
1.01
f1 (ppm)

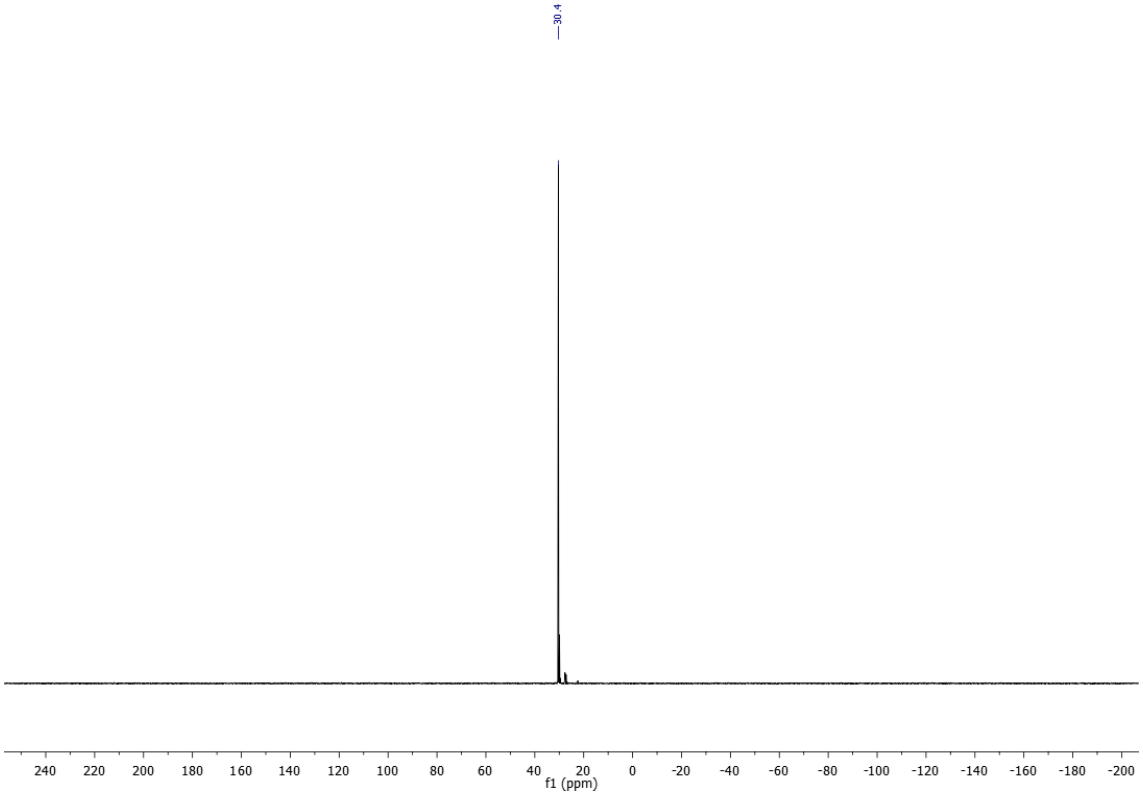

137.9
137.8
132.9
132.9
132.9
132.8
128.3
128.3
127.6
127.6
117.9
117.8
88.6
88.4
83.5
71.7
71.2
66.1
66.0
66.0
65.9
58.5
58.5
50.6
30.8
29.4
f1 (ppm)

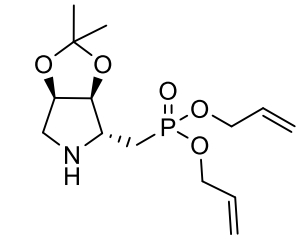

30.2
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)

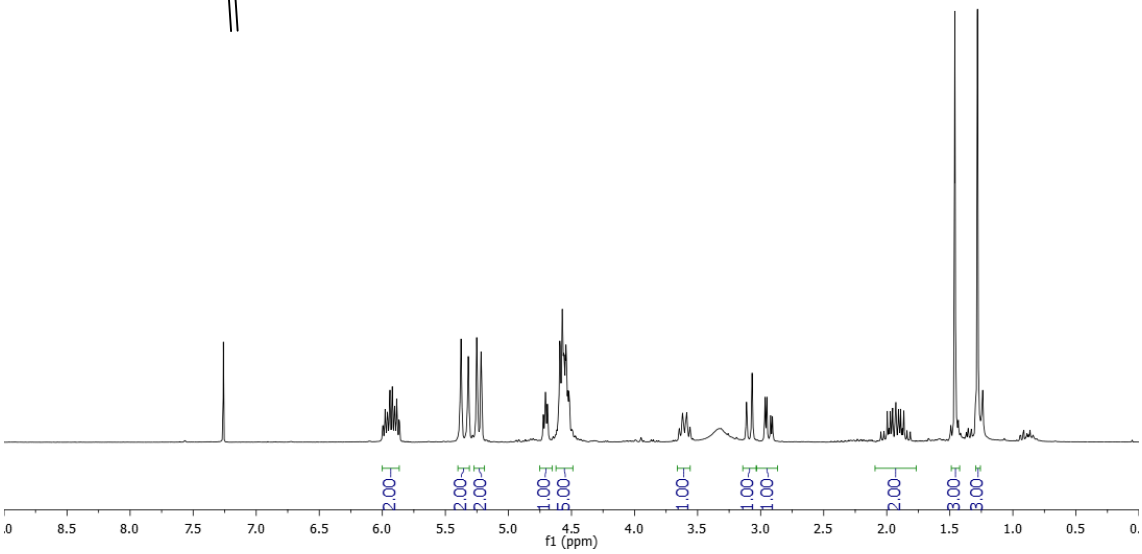

BnO
OBn
O
P
O
O
N
H
BnO

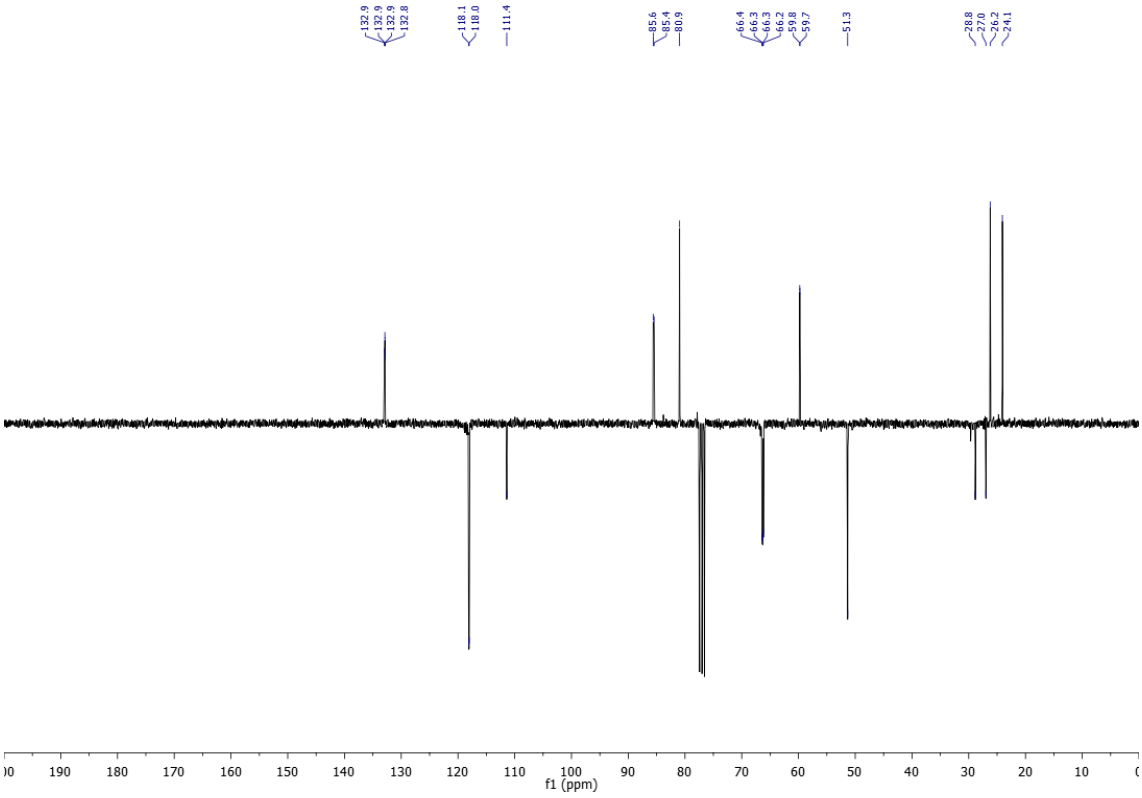

15.04
2.00
2.01
2.01
10.06
1.00
1.00
1.01
2.00
1.04
1.00
2.01
f1 (ppm)

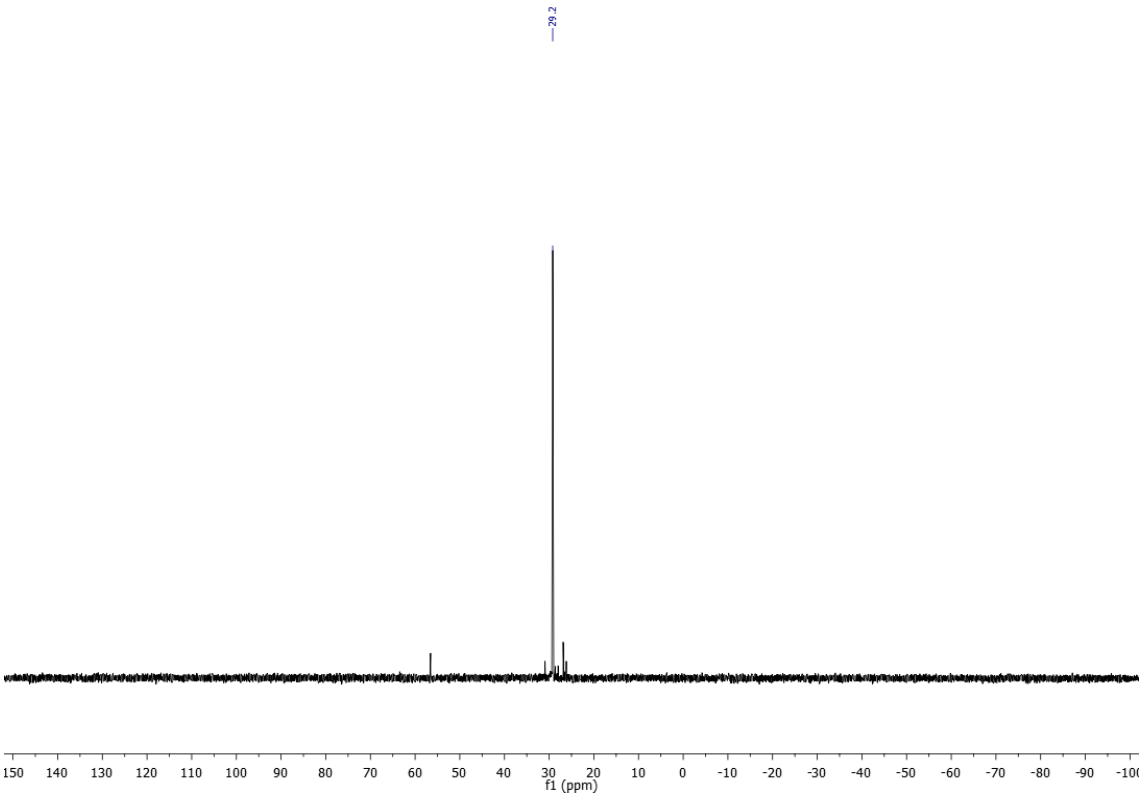

138.0
138.0
137.9
132.9
132.9
132.8
128.3
127.7
127.6
127.6
127.5
118.0
117.9
88.4
88.3
85.6
73.1
71.8
71.6
70.7
66.2
66.1
66.1
66.0
62.0
56.8
56.8
30.7
29.3
f1 (ppm)

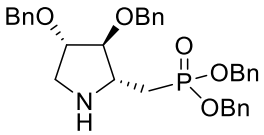

30.4
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)



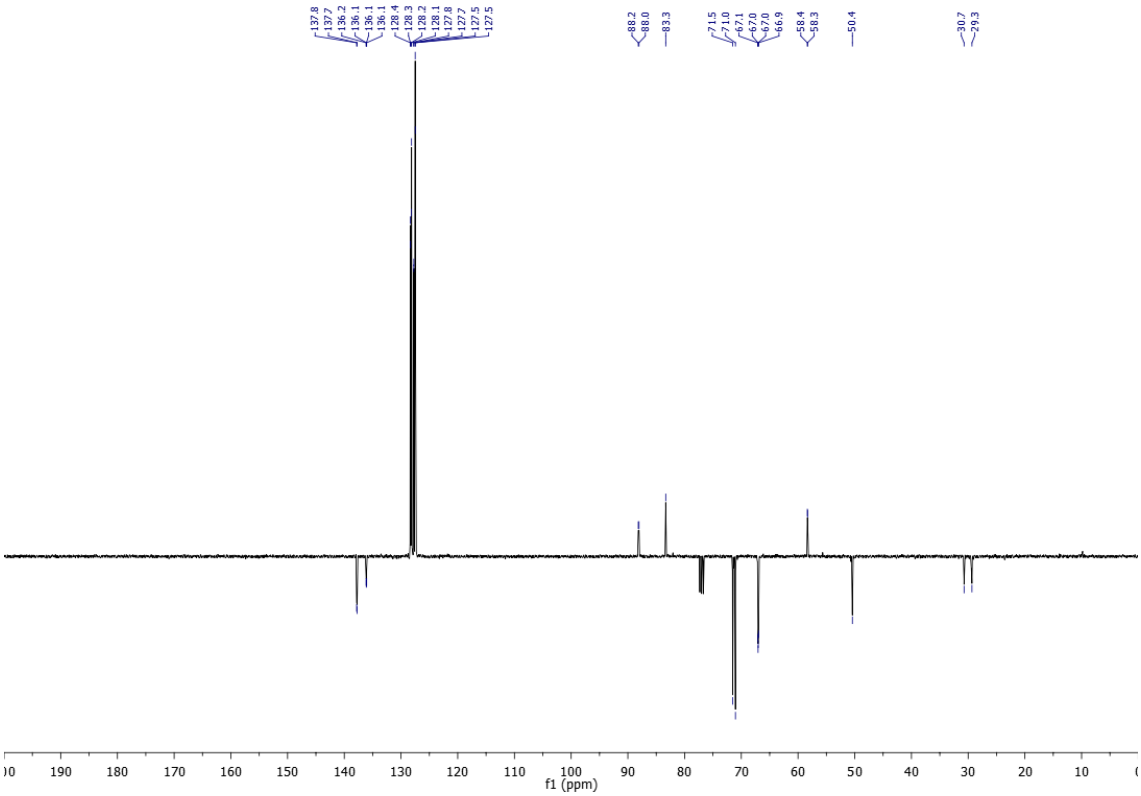

2.00
2.00
2.00
1.00
5.00
1.00
1.00
1.00
2.00
3.00
3.00
f1 (ppm)

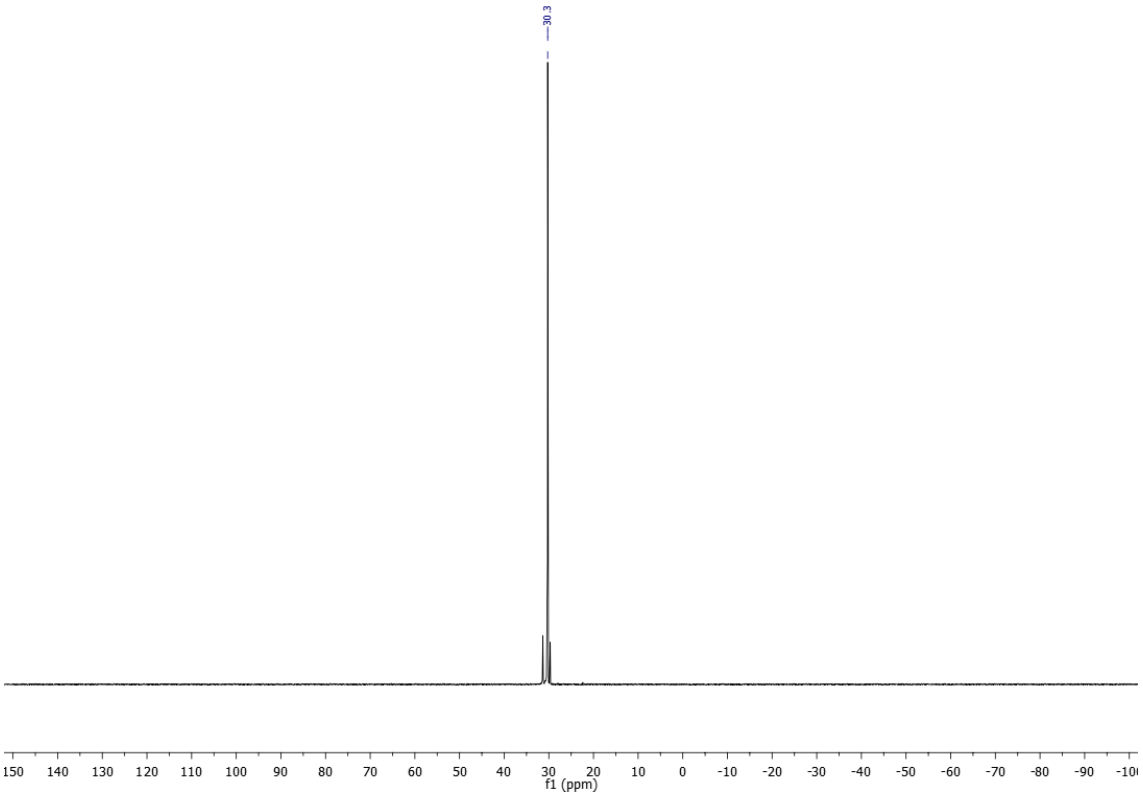

132.9
132.9
132.9
132.8
118.1
118.0
111.4
85.6
85.4
80.9
66.4
66.3
66.3
66.2
59.8
59.7
51.3
28.8
27.0
26.2
24.1
f1 (ppm)

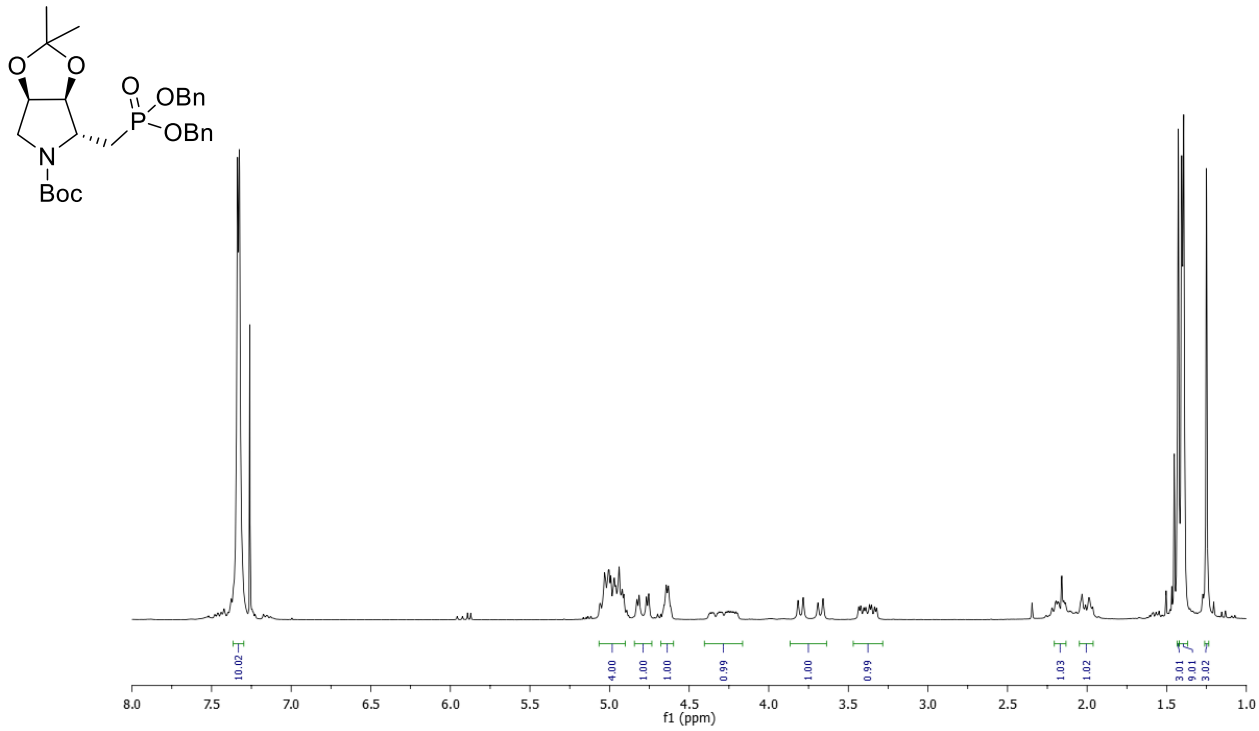

29.2
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)

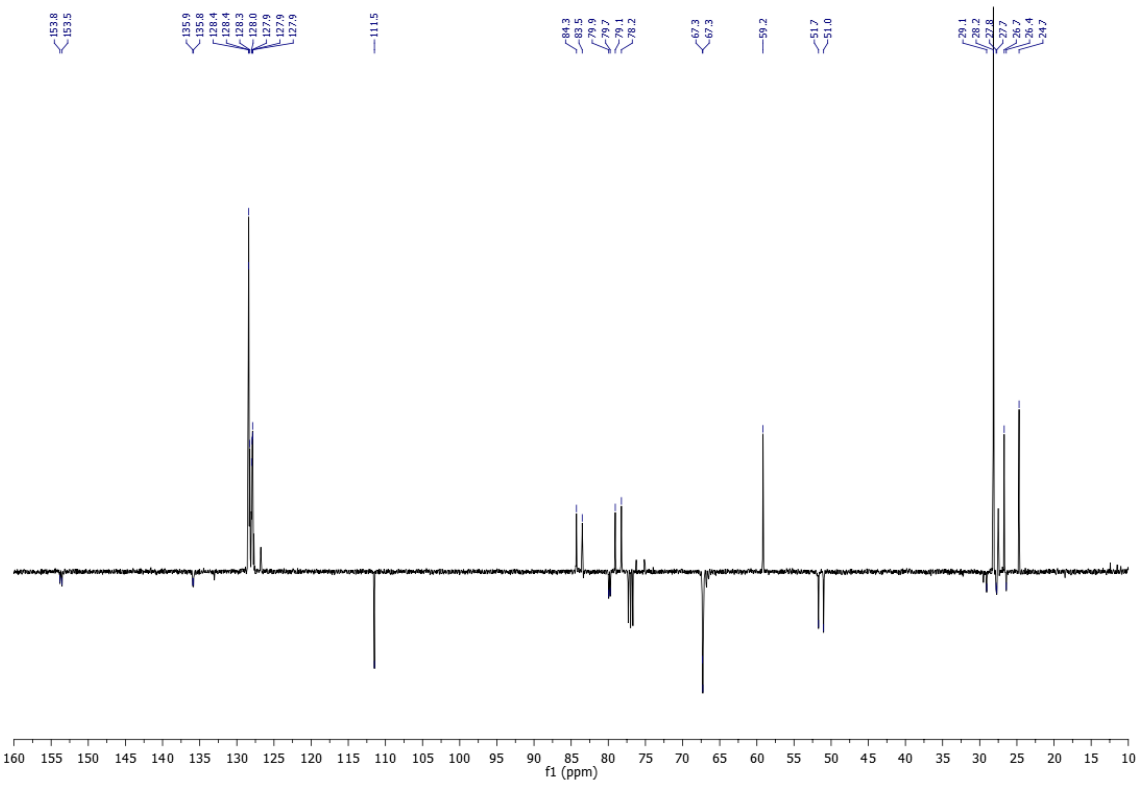

BnO
OBn
O
P
OBn
OBn
N
H

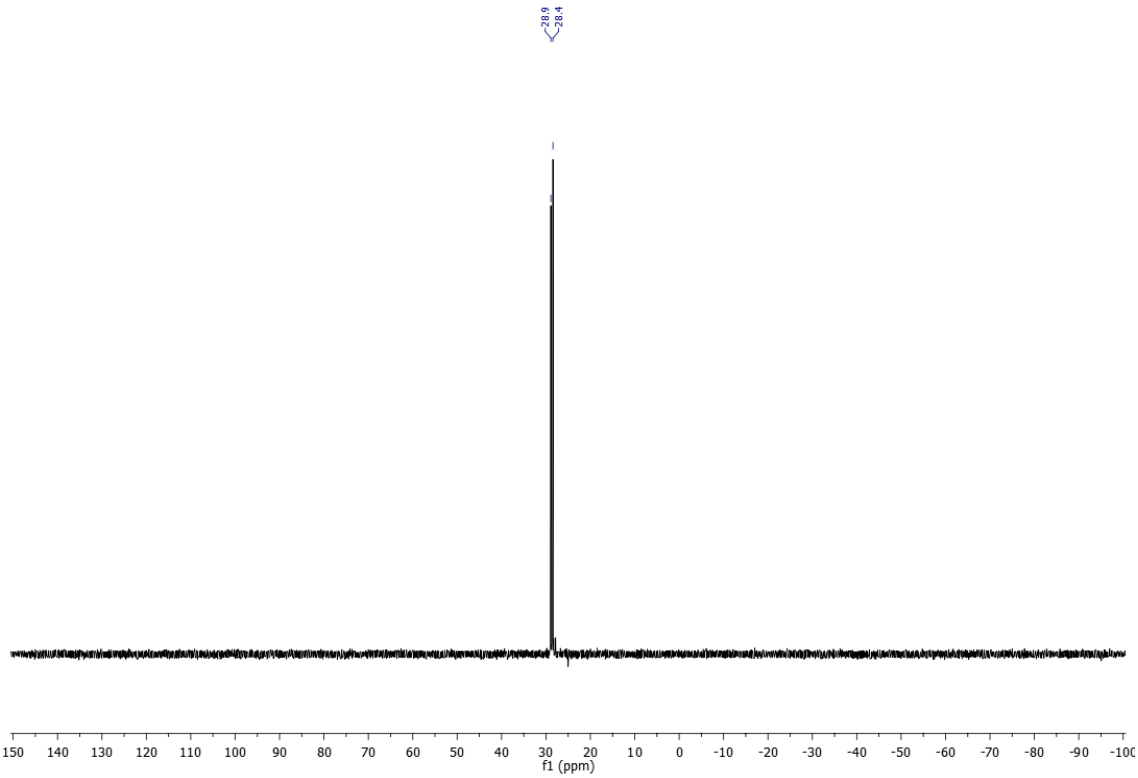
20.00
4.01
4.01
1.01
1.00
1.00
3.01
2.03
f1 (ppm)

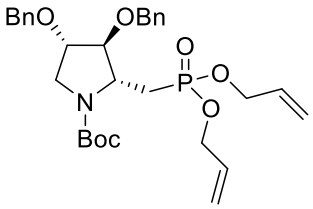

137.8
137.7
136.2
136.1
136.1
128.4
128.3
128.2
128.1
127.8
127.7
127.5
127.5
88.2
88.0
83.3
71.5
71.0
67.1
67.0
67.0
66.9
58.4
58.3
50.4
30.7
29.3
f1 (ppm)


30.3
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)

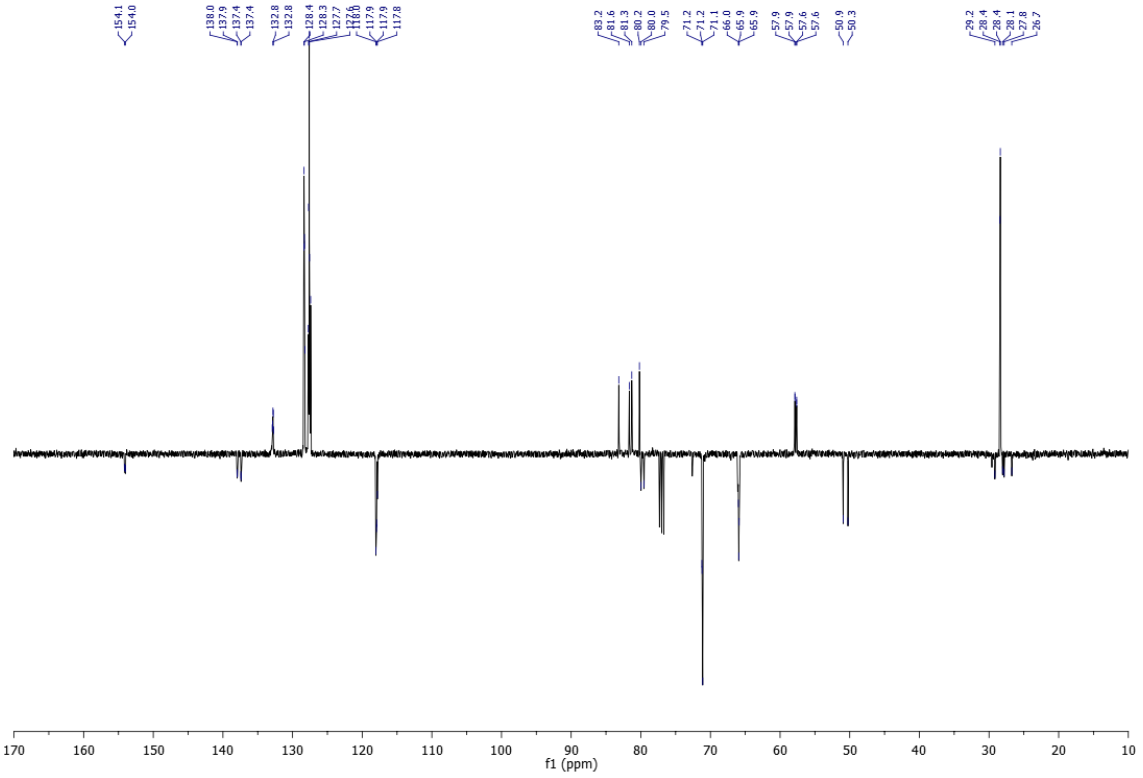

O
O
O
OBn
P
OBn
N
Boc
10.02
4.00
1.00
1.00
0.99
1.00
0.99
1.03
1.02
3.01
9.01
3.02
f1 (ppm)

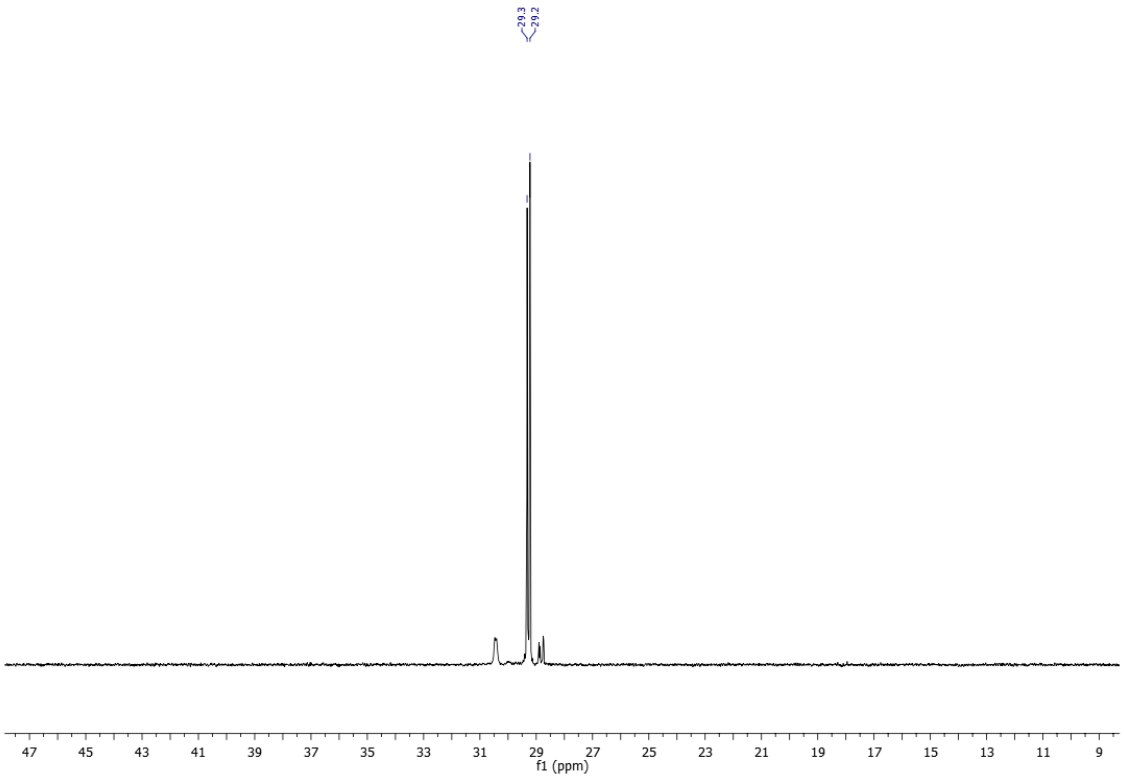

153.8
153.5
135.9
135.8
138.4
138.4
138.3
128.0
127.9
127.9
127.9
111.5
84.3
83.5
79.9
79.2
79.1
78.2
67.3
67.3
59.2
51.7
51.0
29.1
28.2
27.8
27.7
26.2
26.4
24.7
f1 (ppm)

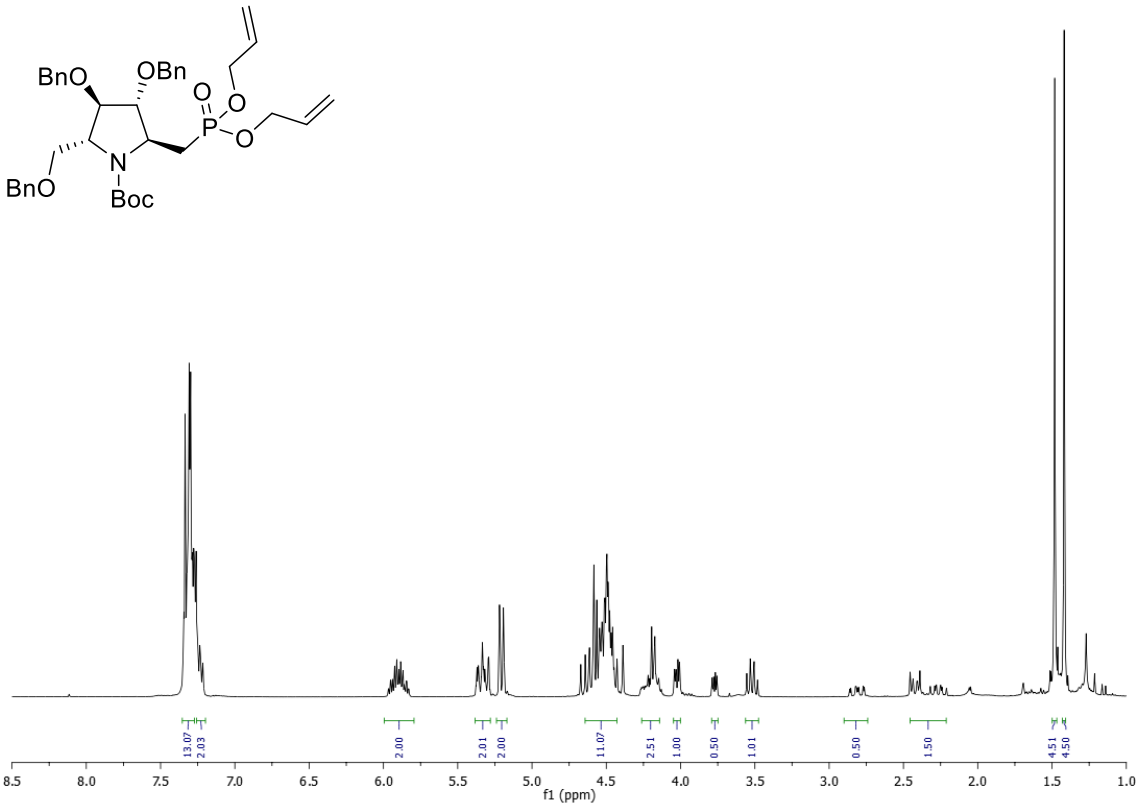

28.9
28.4
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

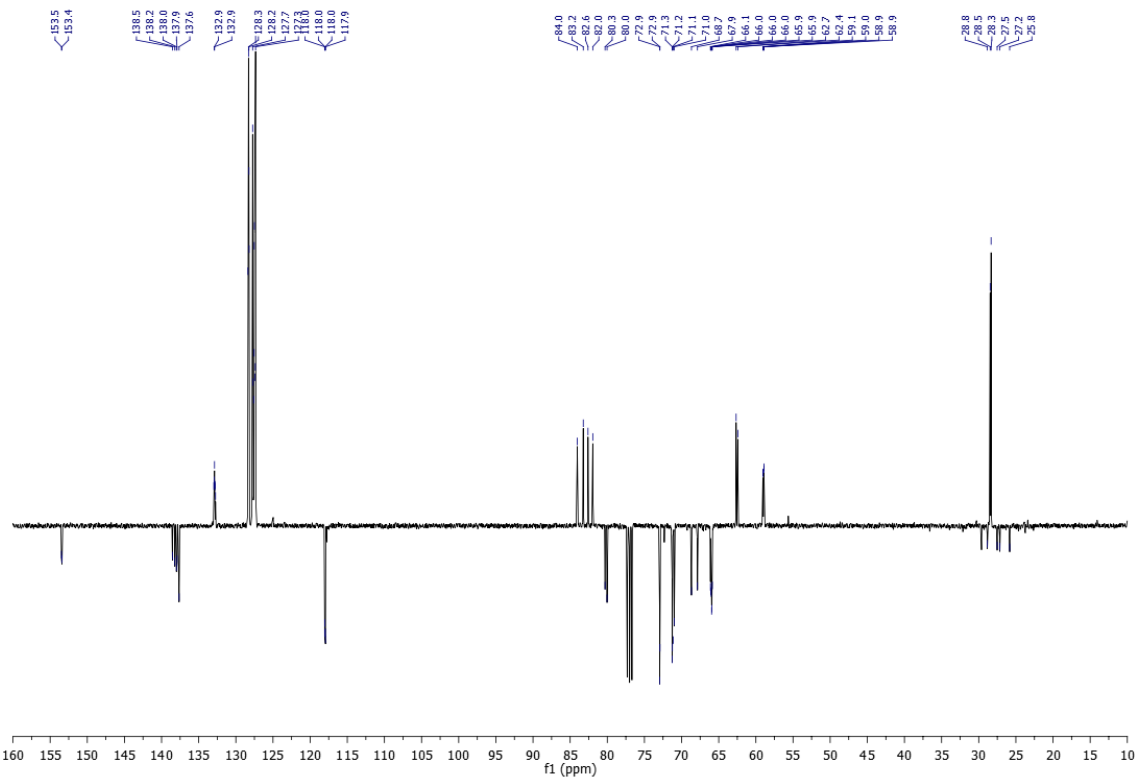

BnO
OBn
O
P
O
O
N
Boc

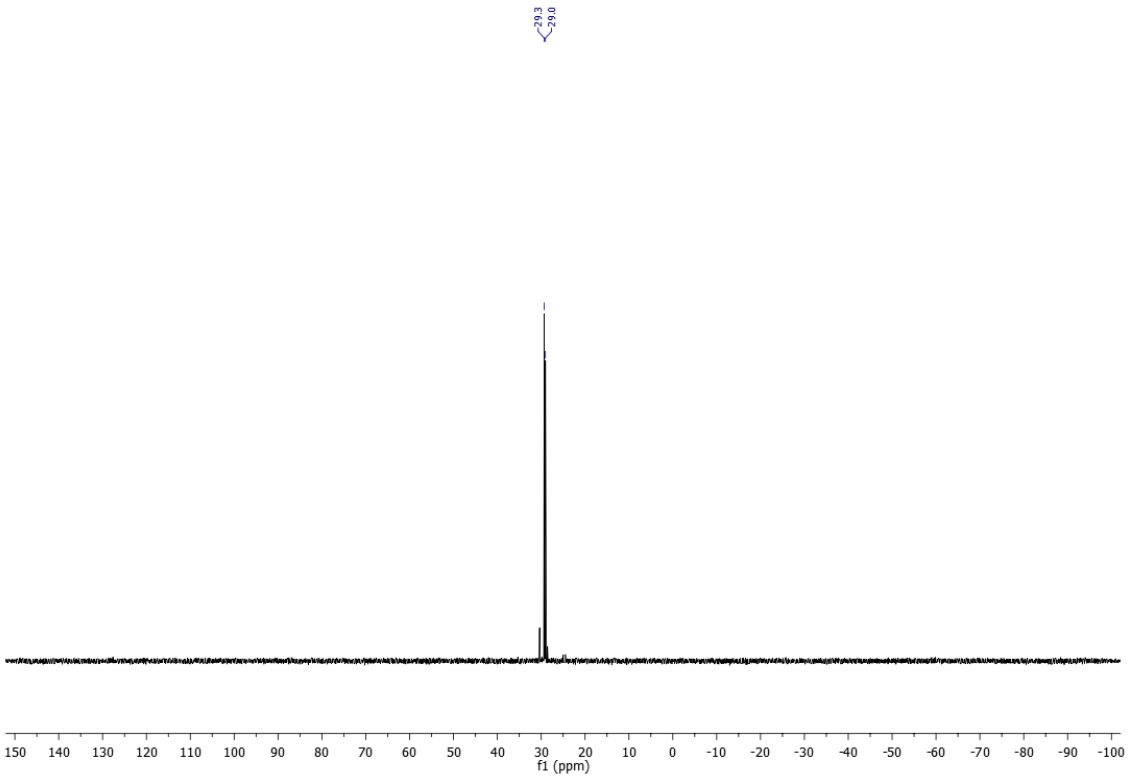
10.01
2.00
2.00
2.00
8.53
1.44
1.01
2.00
0.46
1.51
4.50
4.49
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

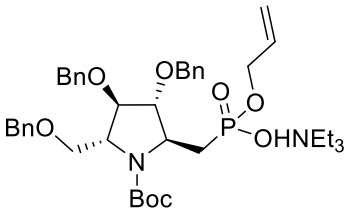

154.1
154.0
138.0
137.9
137.4
137.4
132.8
132.8
128.4
128.3
127.7
127.6
118.0
117.9
117.9
117.8
83.2
81.6
81.3
80.2
80.0
79.5
71.2
71.2
71.1
66.0
65.9
65.9
57.9
57.9
57.6
57.6
50.9
50.3
29.2
28.4
28.4
28.1
27.8
26.7
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

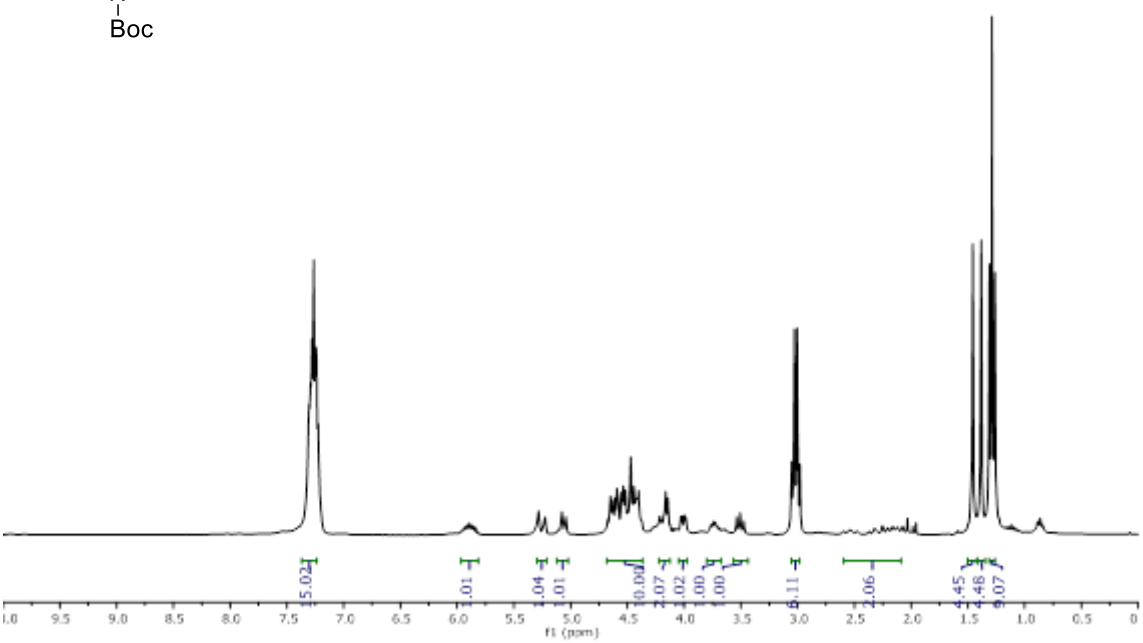

29.3
29.2
47
45
43
41
39
37
35
33
31
29
27
25
23
21
19
17
15
13
11
9
f1 (ppm)

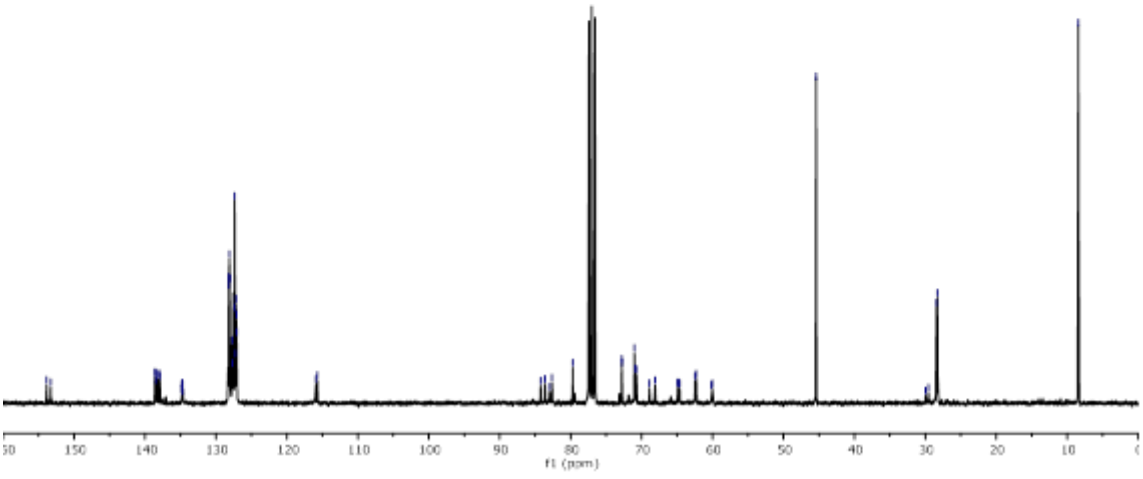

BnO
OBn
O
O
P
O
N
Boc
BnO
13.07
2.03
2.00
2.01
2.00
11.07
2.51
1.00
0.50
1.01
0.50
1.50
4.51
4.50
f1 (ppm)

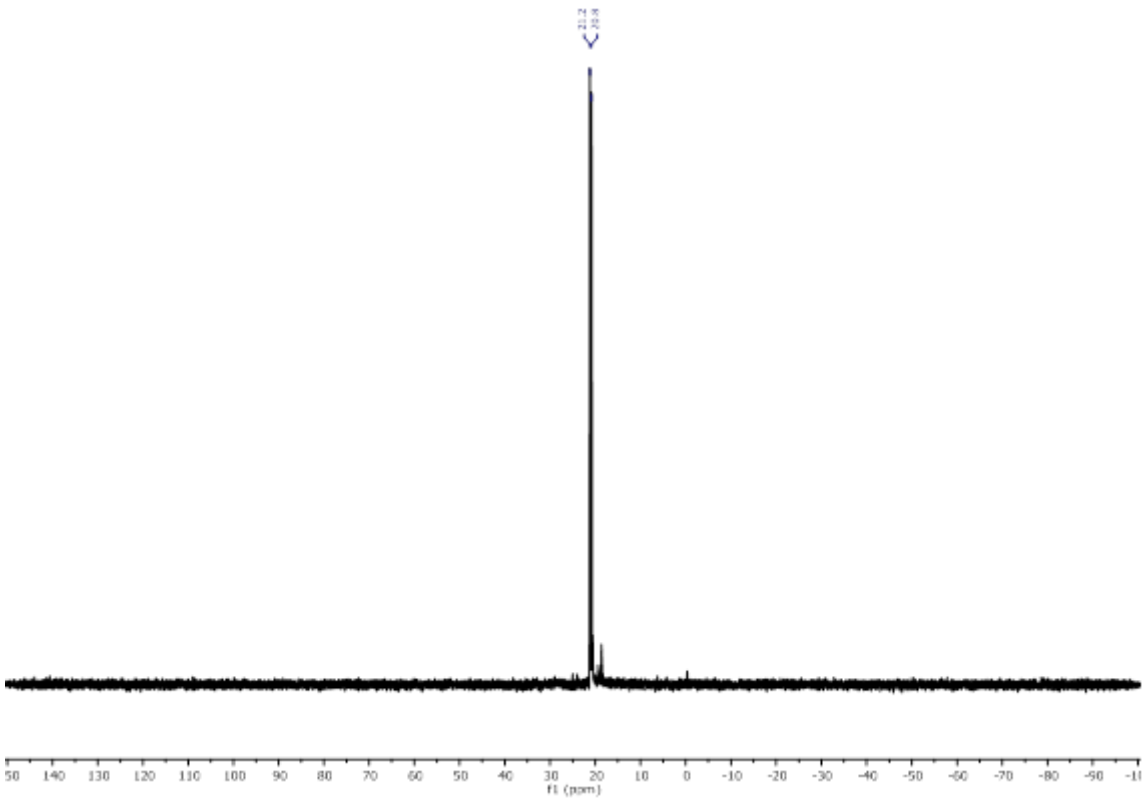

153.5
153.4
138.5
138.2
138.0
137.9
137.6
132.9
132.9
128.3
128.2
127.7
118.0
118.0
117.9
84.0
83.2
82.6
82.0
80.3
80.0
72.9
72.9
71.3
71.2
71.1
71.0
68.7
67.9
66.1
66.0
66.0
66.0
65.9
65.9
62.7
62.4
59.1
59.0
58.9
58.9
28.8
28.5
28.3
27.5
27.2
25.8
f1 (ppm)

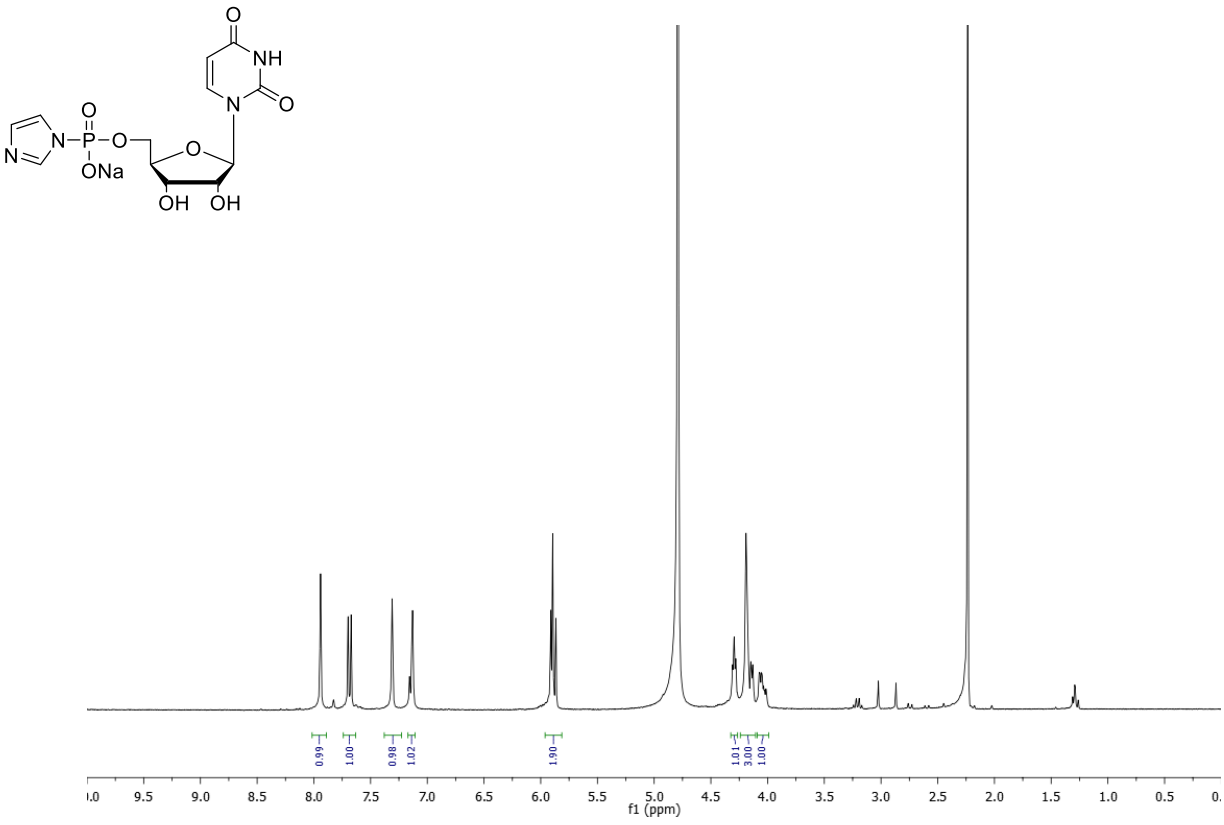

29.3
29.0
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

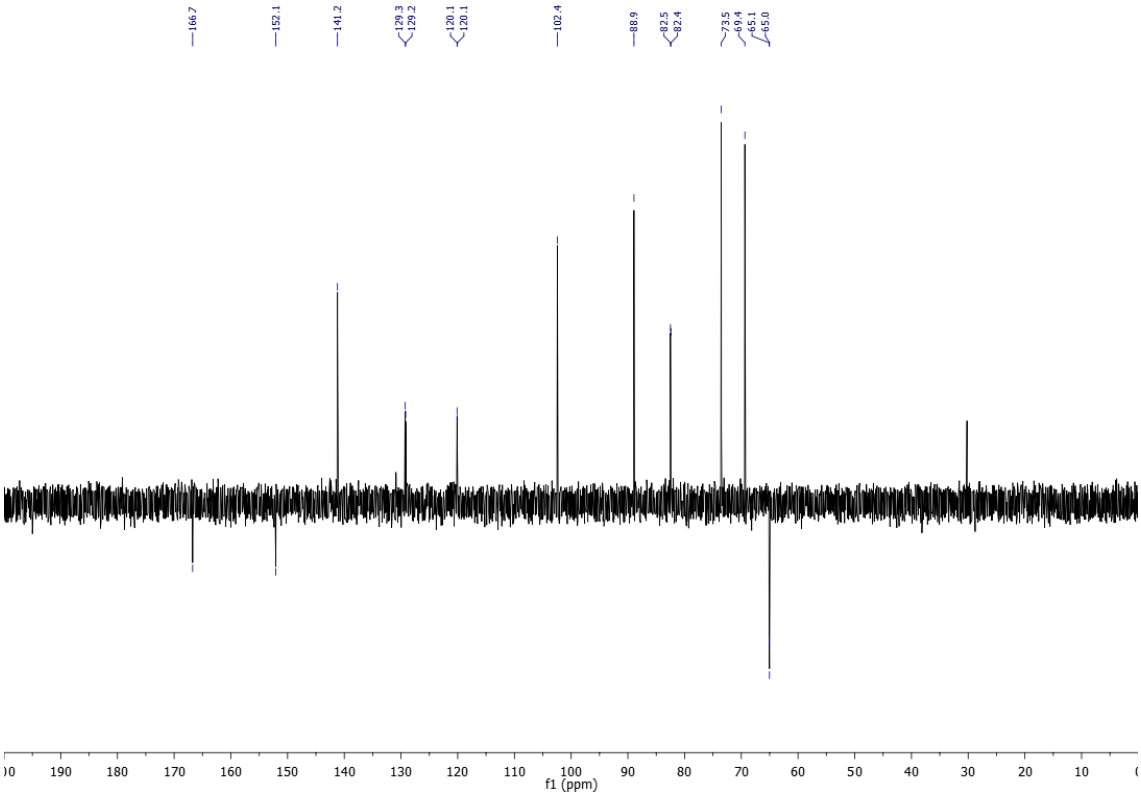

BnO
OBn
O
O
BnO
P
OHNEt3
N
Boc

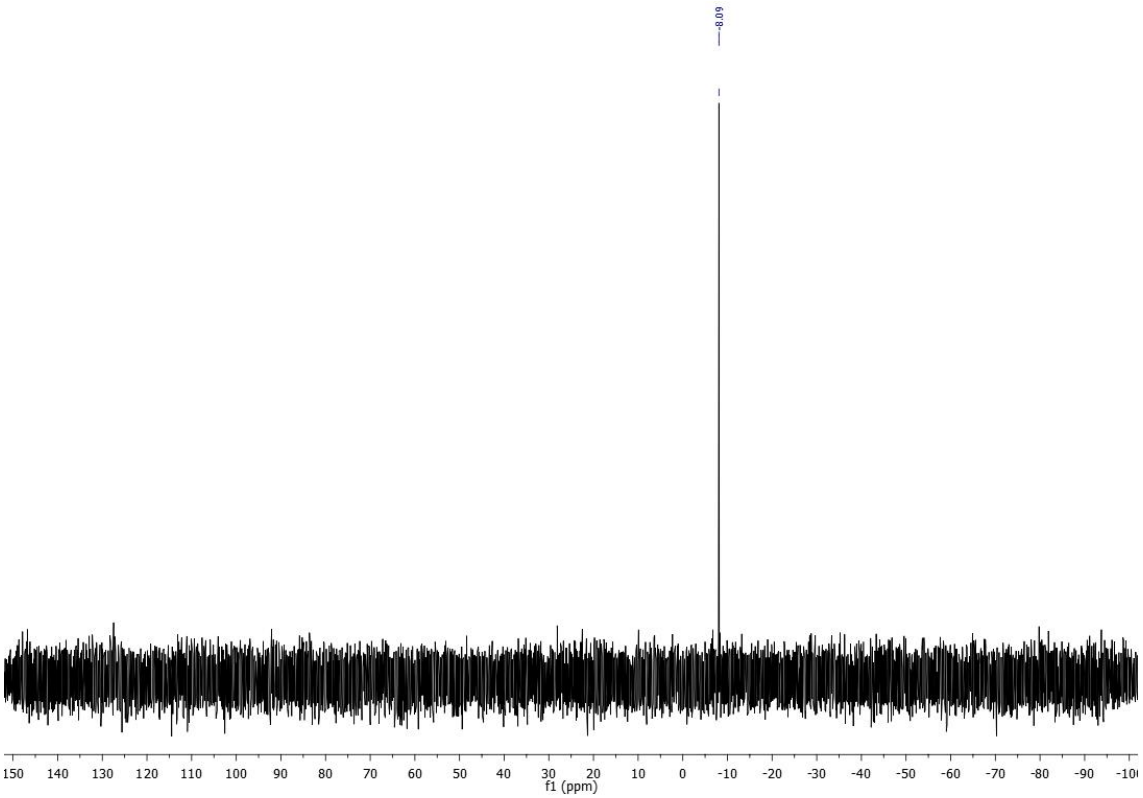

5.02
1.01
1.04
1.01
10.00
2.07
1.02
1.00
1.00
6.11
2.06
4.45
4.46
9.07
f1 (ppm)

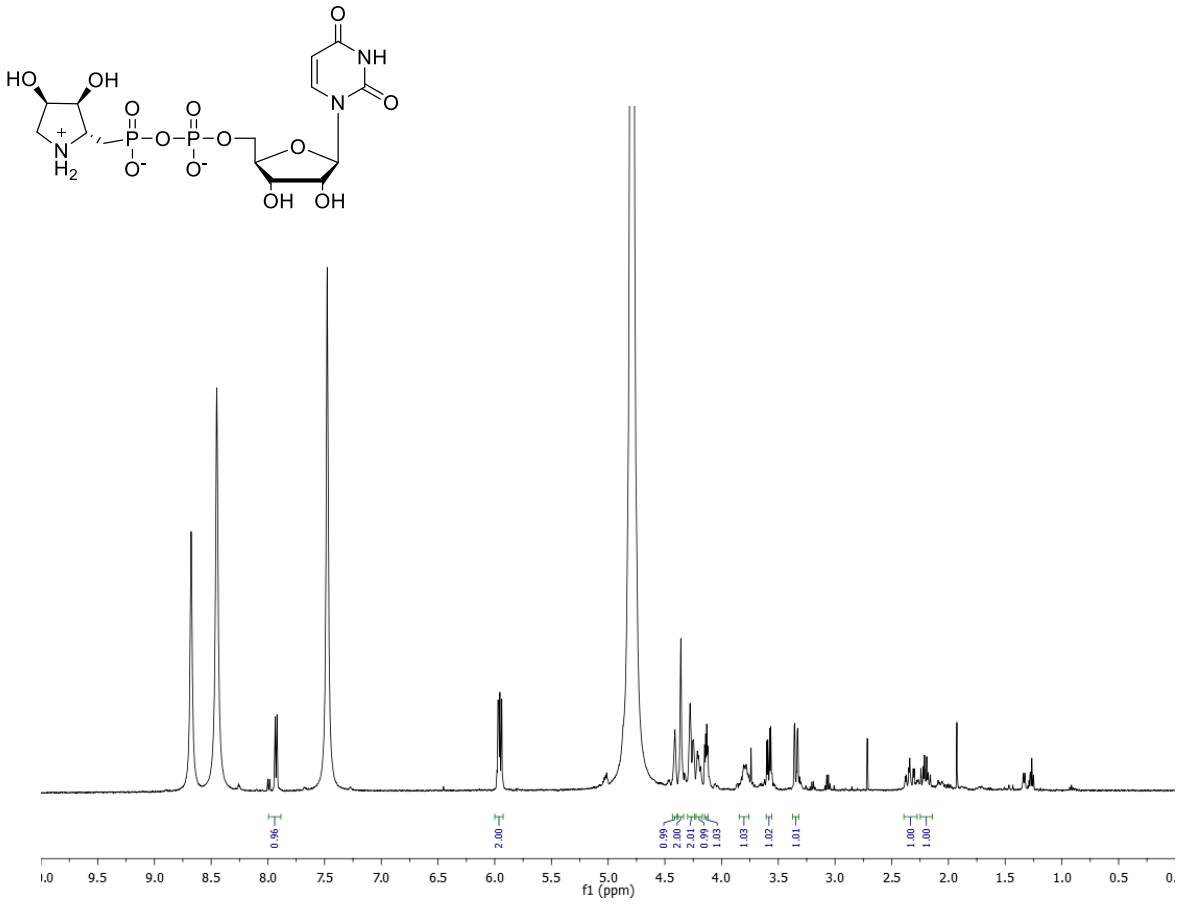

f1 (ppm)

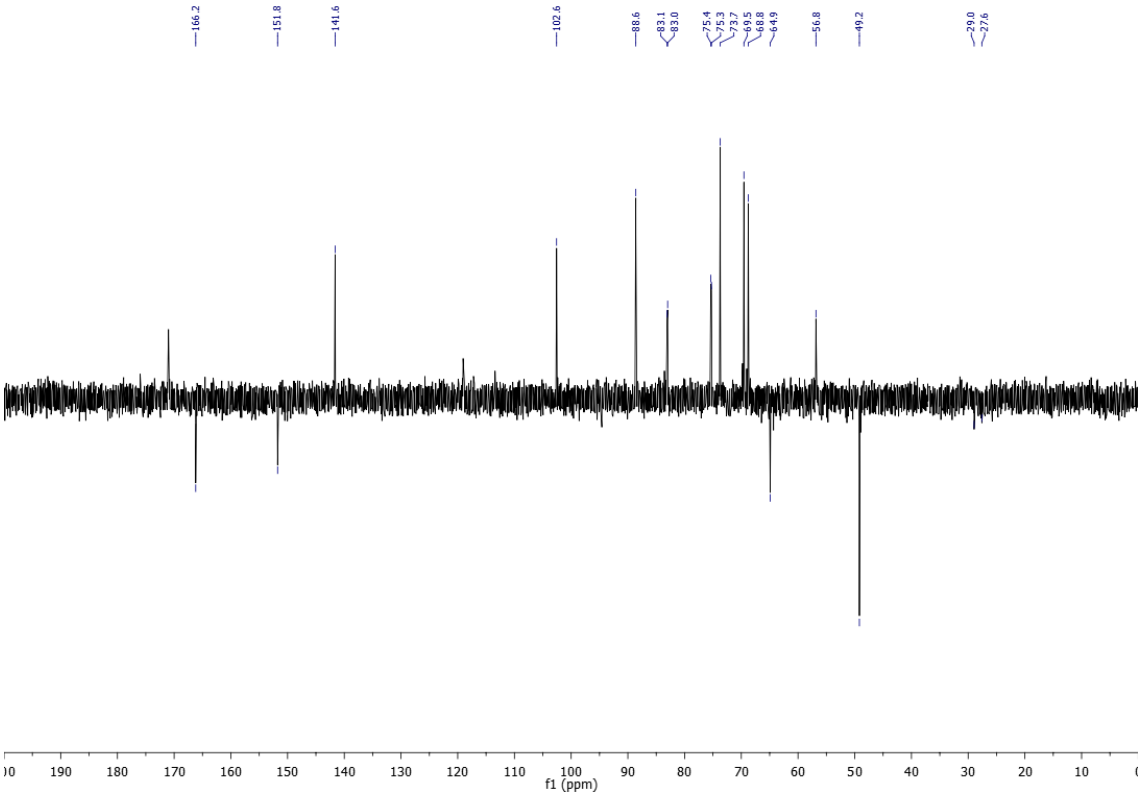

f1 (ppm)

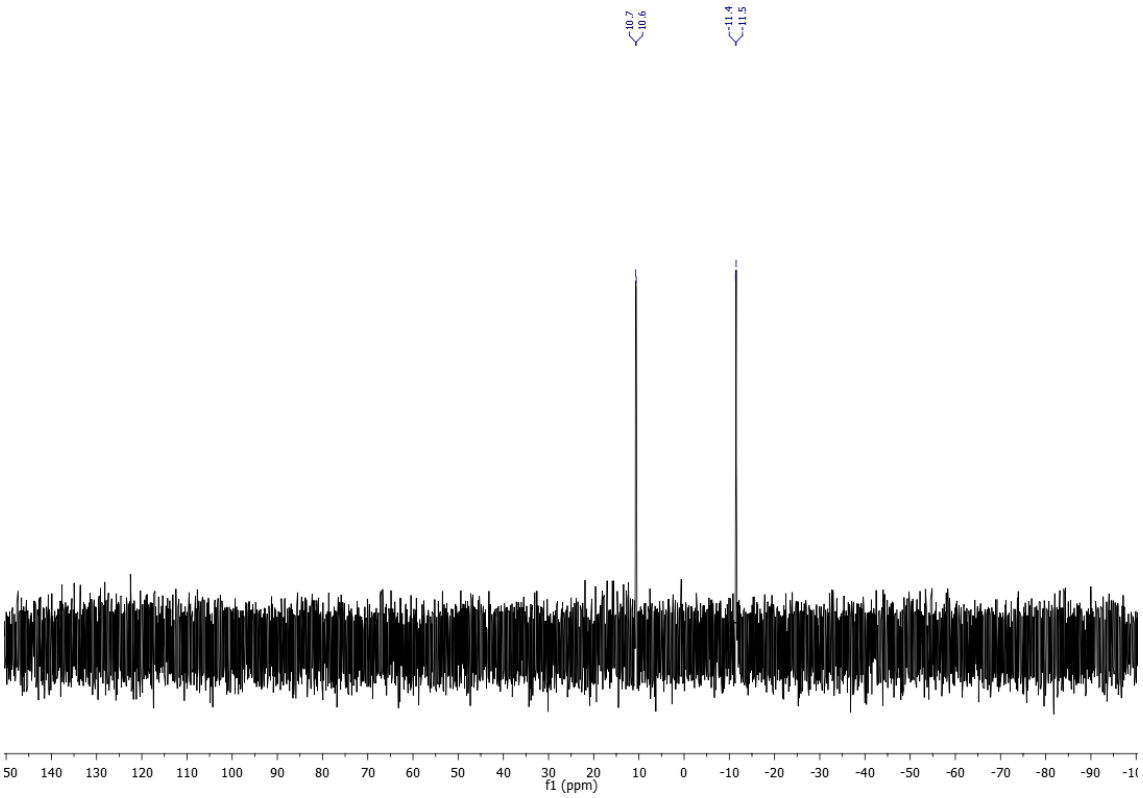

O
NH
N
O
O
N
P
O
ONa
O
OH
OH
0.99
1.00
0.98
1.02
1.90
1.01
3.00
1.00
f1 (ppm)

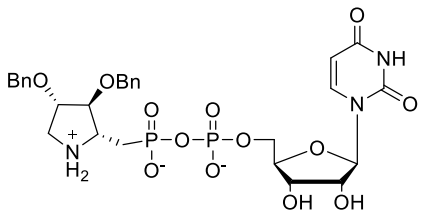

166.7
152.1
141.2
129.3
129.2
120.1
120.1
102.4
88.9
82.5
82.4
73.5
69.4
65.1
65.0
f1 (ppm)


8.09
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)

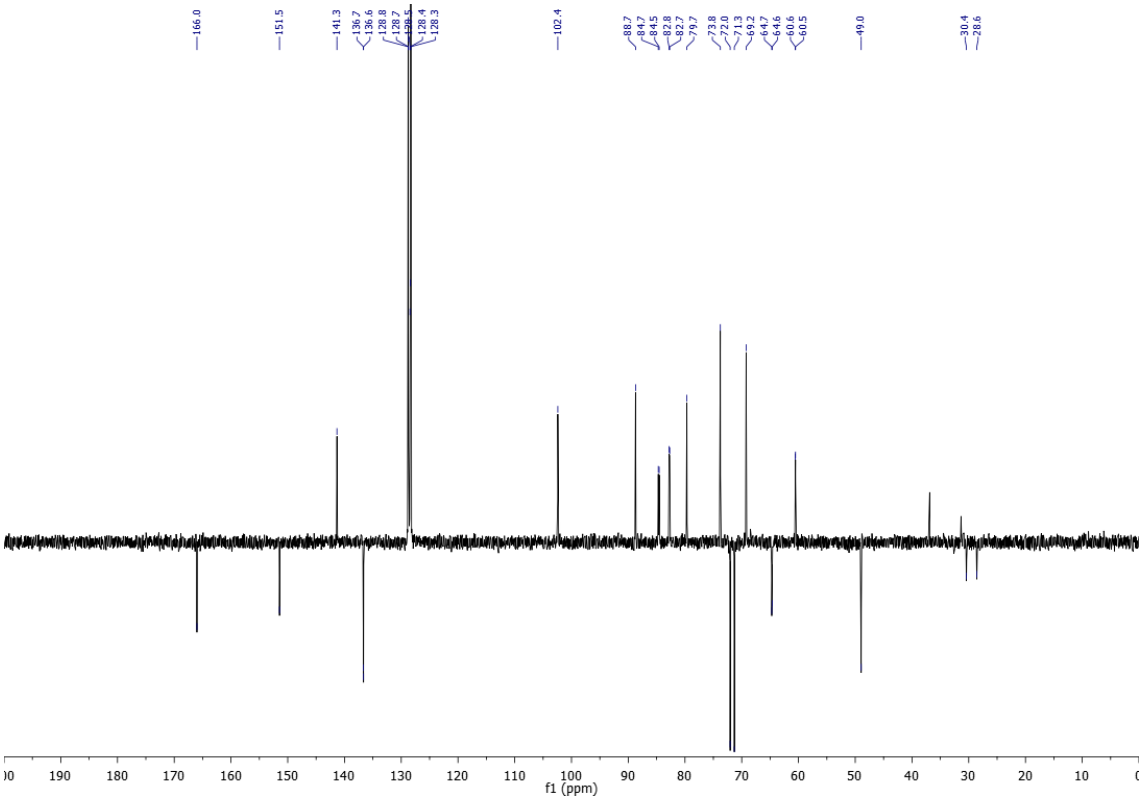

HO
OH
NH
O
N
O
O
P
O
O
P
O
O
O
O
O
N
H2
OH
OH
0.96
2.00
0.99
2.00
2.01
0.99
1.03
1.03
1.02
1.01
1.00
1.00
f1 (ppm)

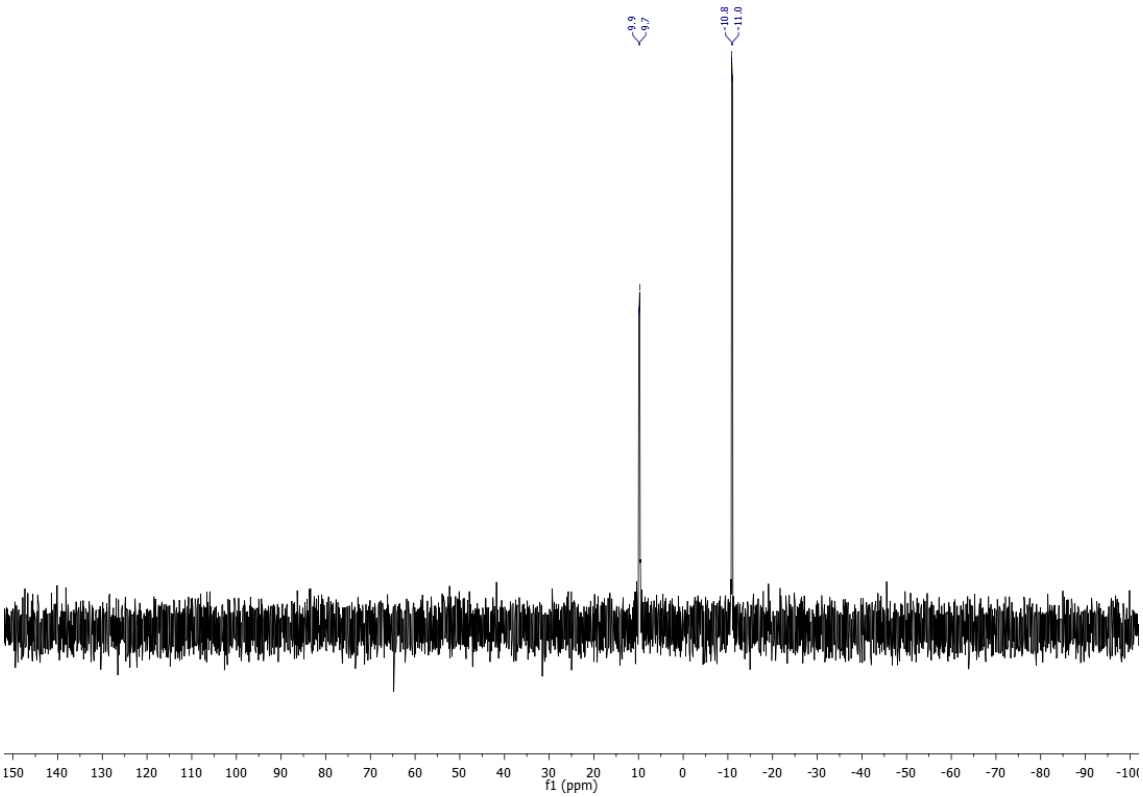

166.2
151.8
141.6
102.6
88.6
83.1
83.0
75.4
75.3
73.7
69.5
68.8
64.9
56.8
49.2
29.0
27.6
f1 (ppm)

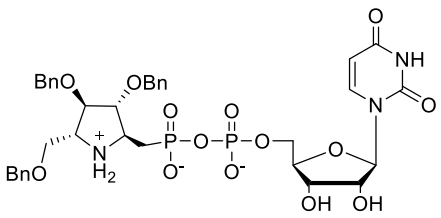

10.7
10.6
11.4
11.5
50 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -10
f1 (ppm)

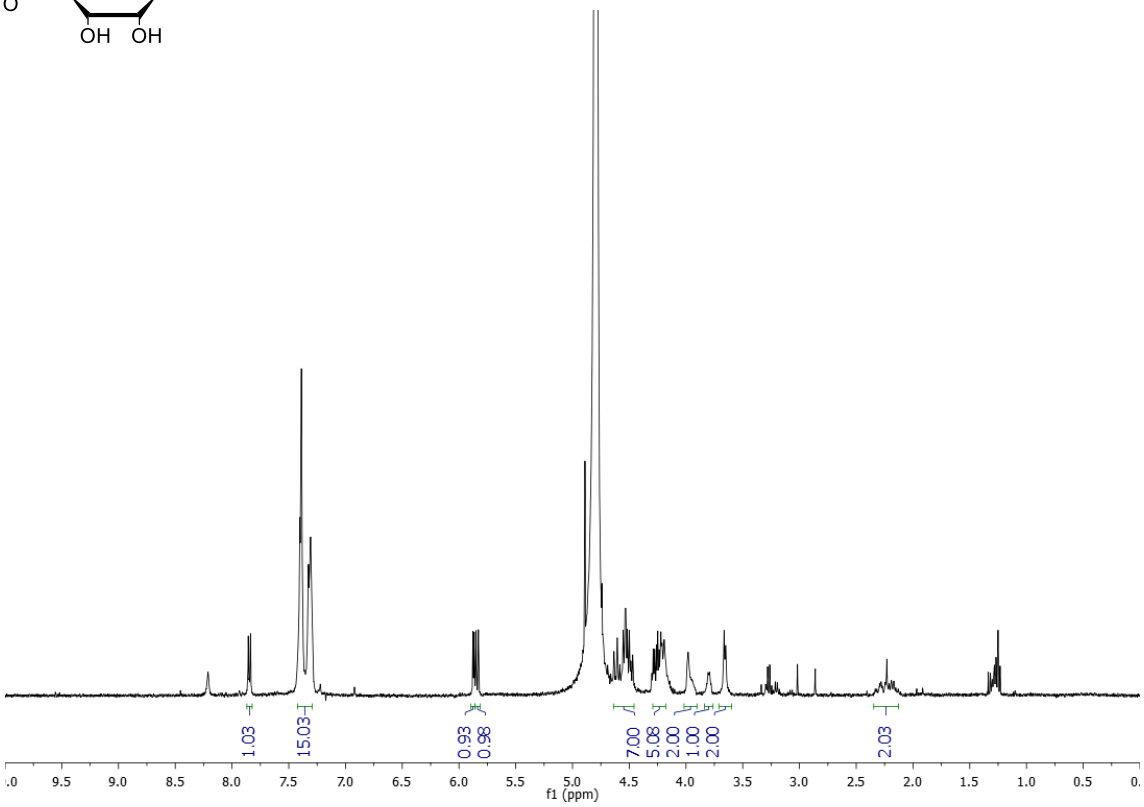

BnO
OBn
O
NH
N
O
O
P
O
P
O
O
O
N
H2
O-
O-
OH
OH

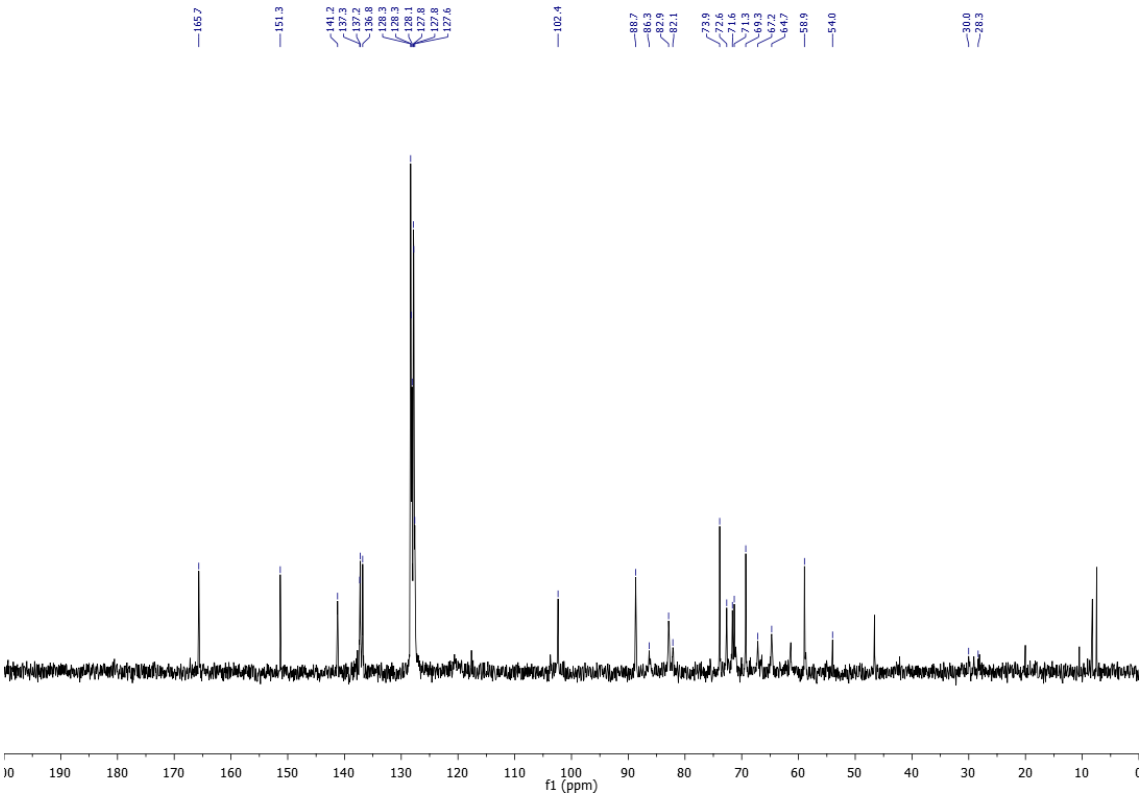
1.03
10.00
1.00
1.00
4.00
6.99
1.00
2.00
2.00
f1 (ppm)

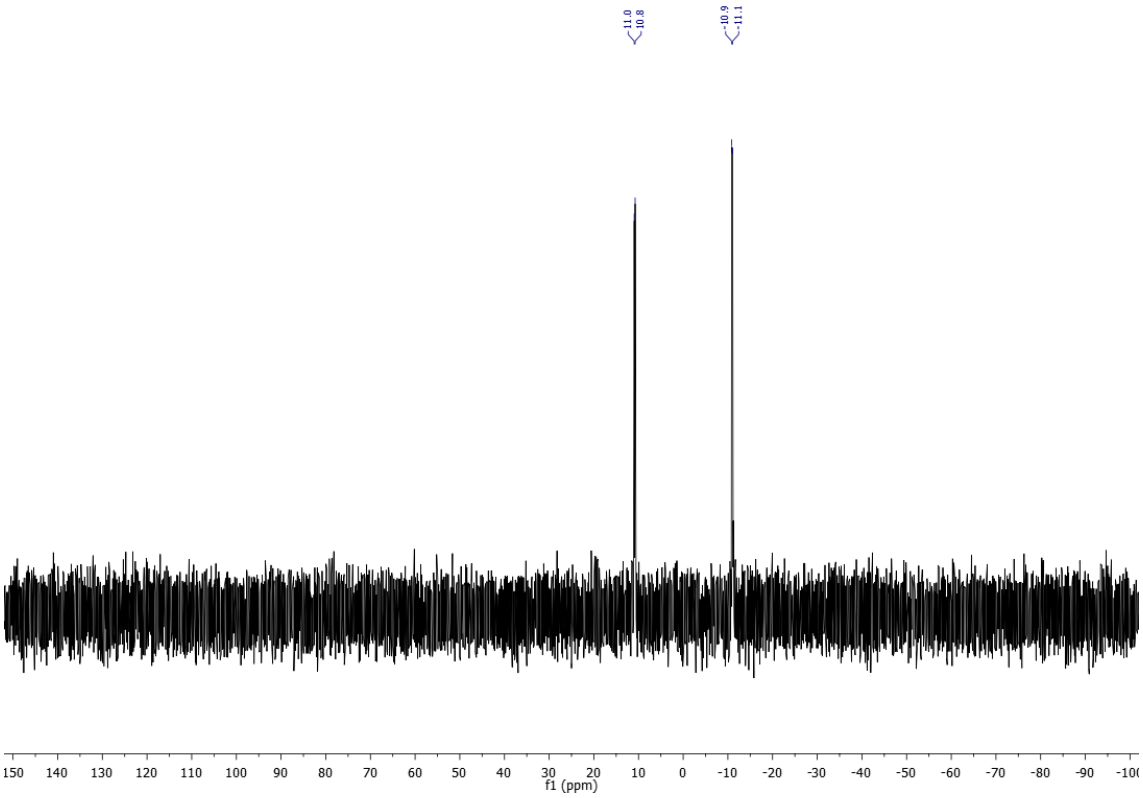

166.0
151.5
141.3
136.7
136.6
128.8
128.7
128.5
128.4
128.3
102.4
88.7
84.7
84.5
82.8
82.7
79.7
73.8
72.0
71.3
69.2
64.7
64.6
60.6
60.5
49.0
30.4
28.6
f1 (ppm)

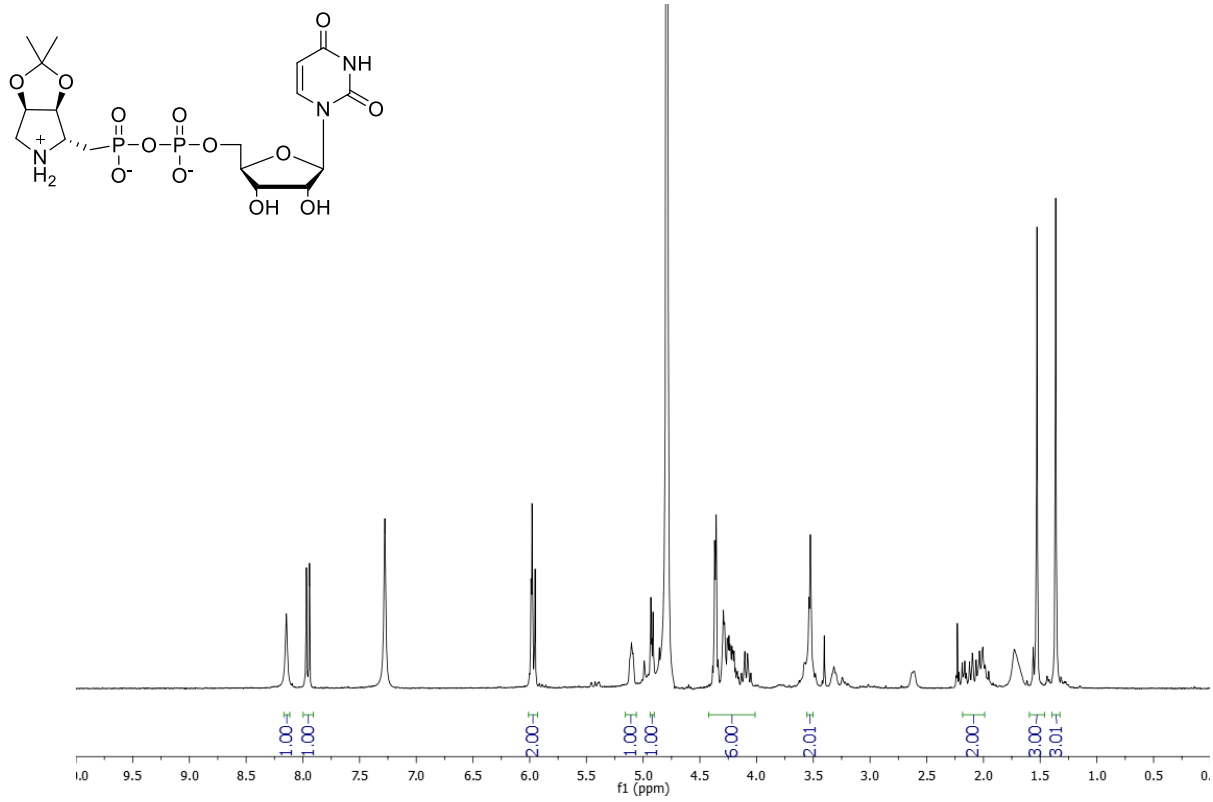

9.9
9.7
10.8
11.0
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

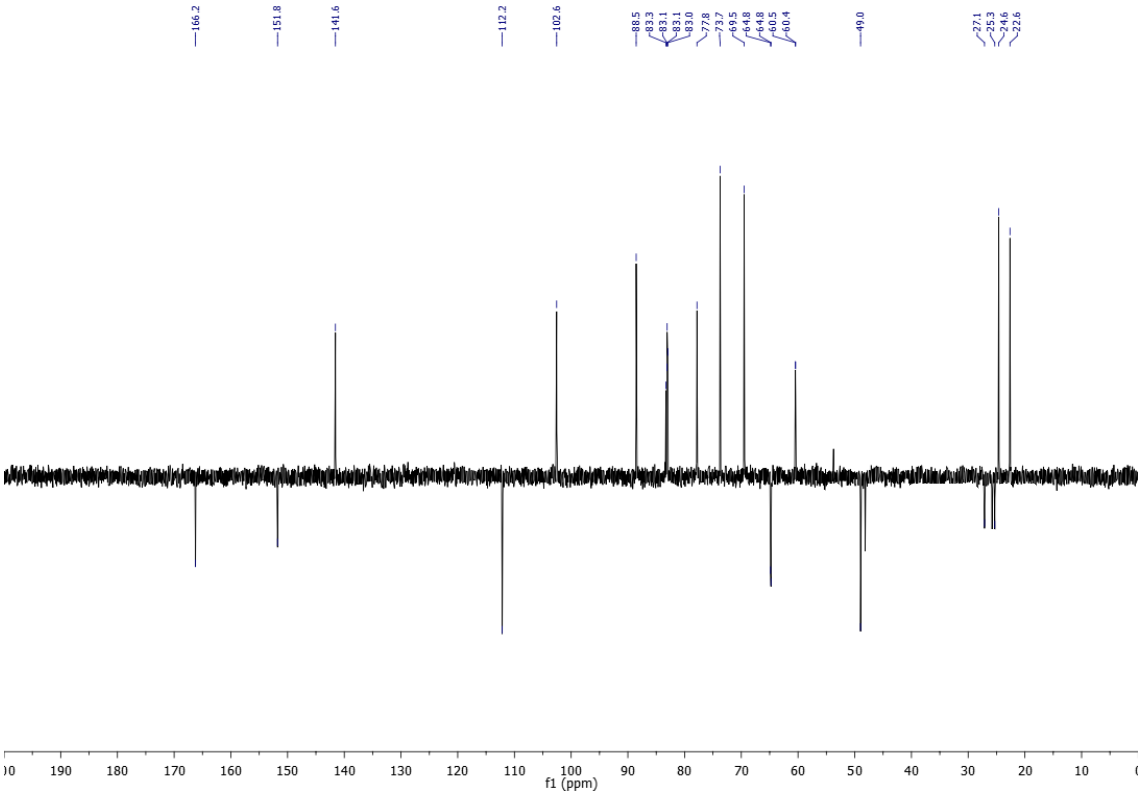

BnO
OBn
BnO
N
H2
O
P
O-
O
P
O-
O
O
N
NH
O
OH
OH

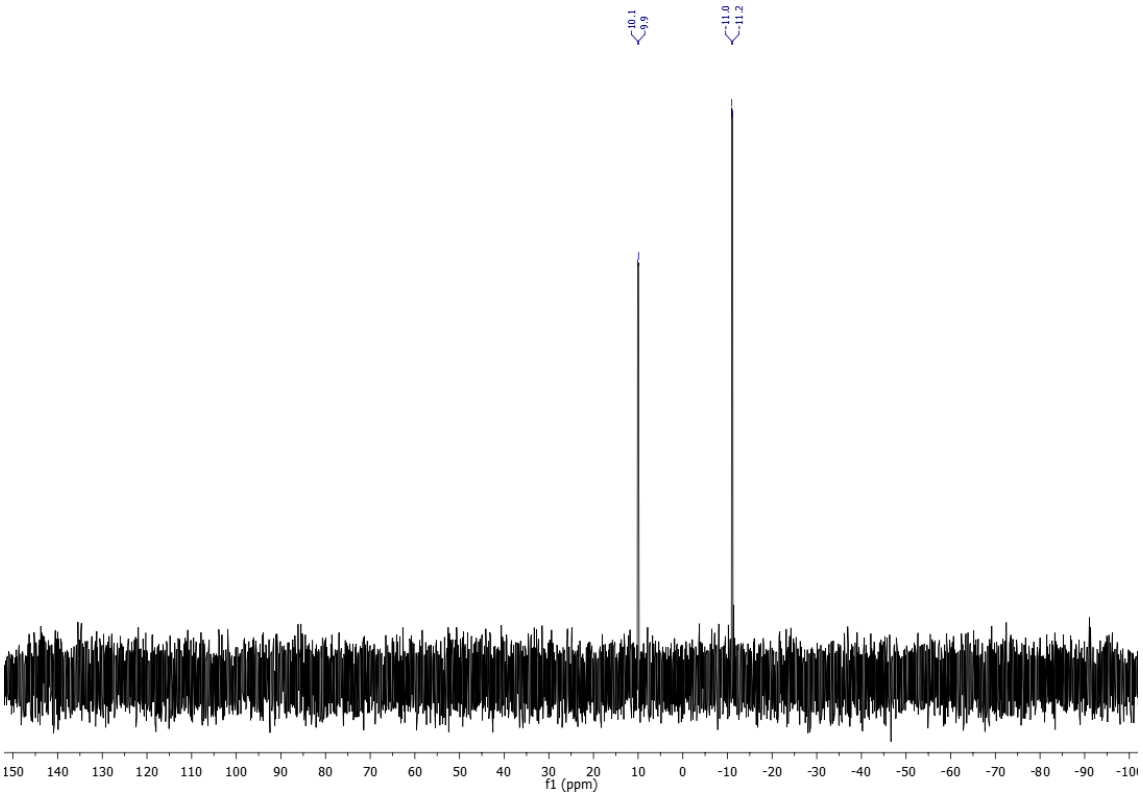

1.03
15.03
0.93
0.98
7.00
5.08
2.00
1.00
2.00
2.03
f1 (ppm)


165.7
151.3
141.2
137.3
137.2
136.8
128.3
128.3
128.1
127.8
127.6
102.4
88.7
86.3
82.9
82.1
73.9
72.6
71.6
71.3
69.3
67.2
64.7
58.9
54.0
30.0
28.3
f1 (ppm)

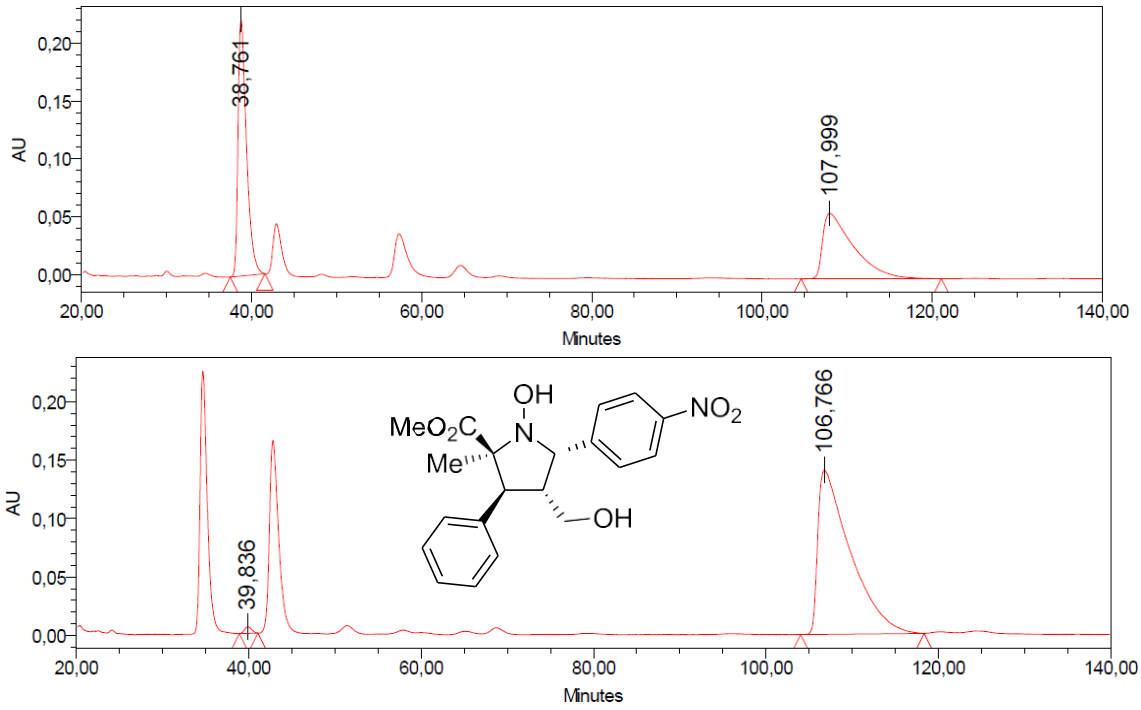

11.0
10.8
10.9
11.1
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)


NH
O
N
O
O
O
O
P
O
O
P
O
O
O
O
N
H2
OH
OH
1.00
1.00
2.00
1.00
1.00
5.00
2.01
2.00
3.00
3.01
f1 (ppm)


166.2
151.8
141.6
112.2
102.6
88.5
83.3
83.1
83.1
83.0
77.8
73.7
69.5
64.8
64.8
60.5
60.4
49.0
27.1
25.3
24.6
22.6
f1 (ppm)

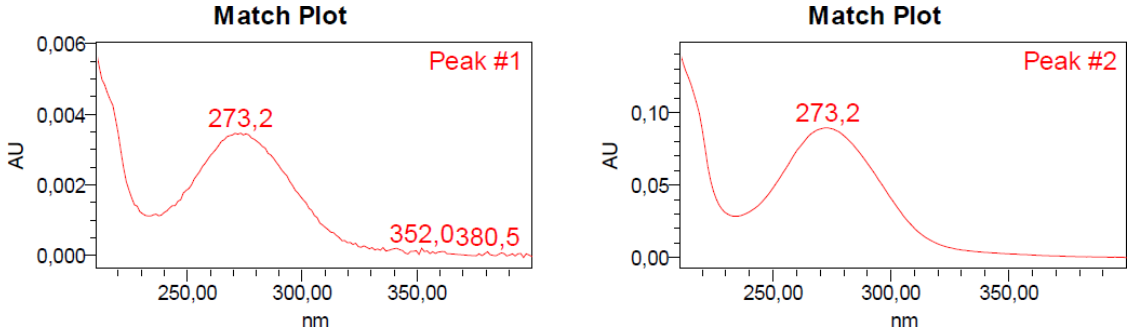

10.1
9.9
11.0
11.2
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -10
f1 (ppm)

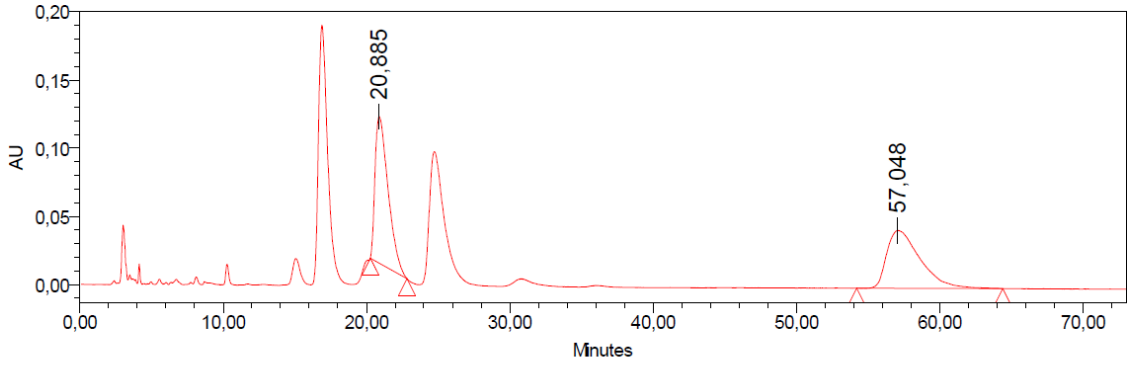
2. HPLC Cromatograms

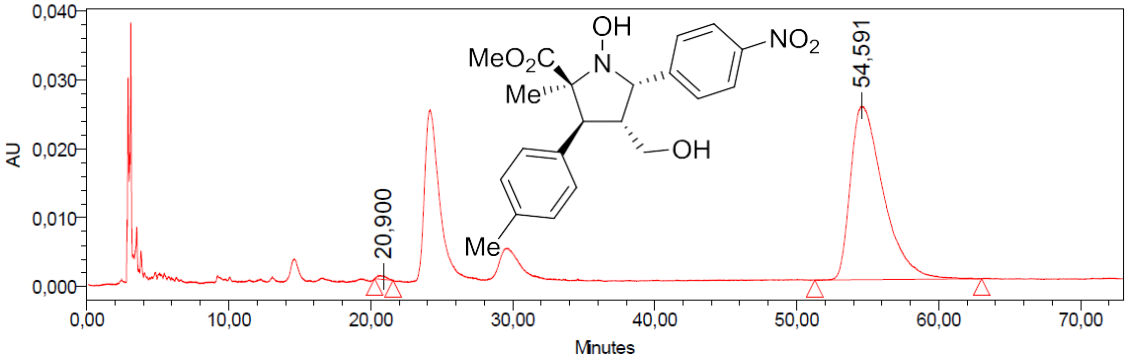


Peak Results

	Name	RT	Area	Height	% Area
1		39,836	325315	5663	0,88
2		106,766	36724437	140775	99,12



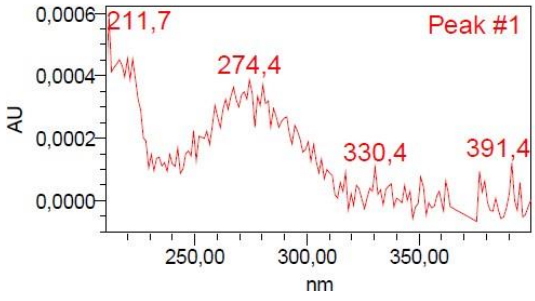




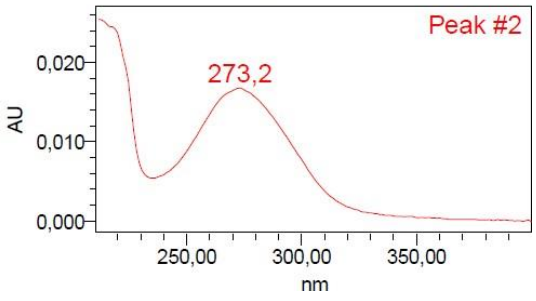
Peak Results

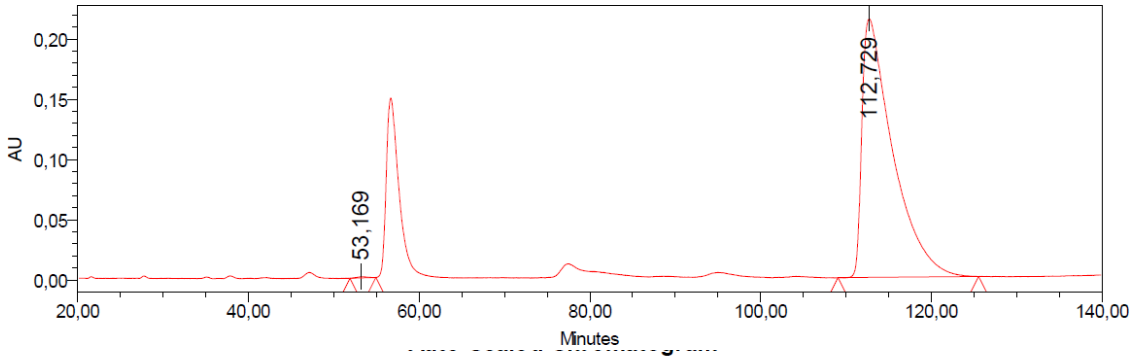
	Name	RT	Area	Height	% Area
1		20,900	23245	566	0,57
2		54,591	4042091	25320	99,43

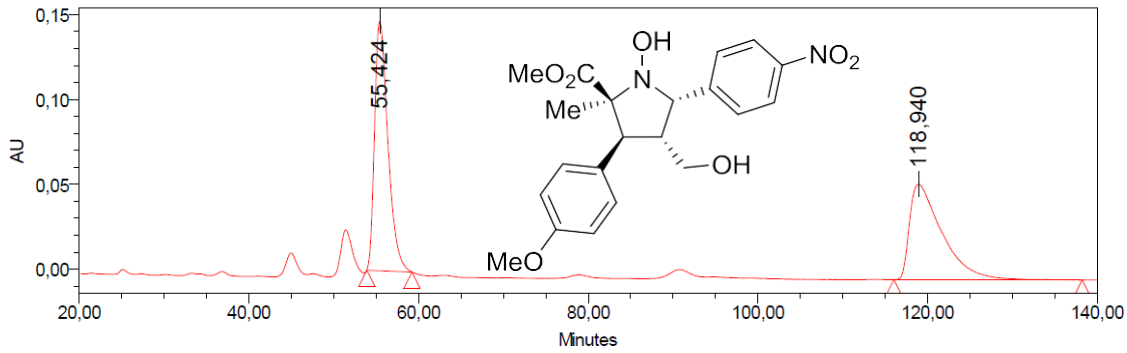
Match Plot



Match Plot

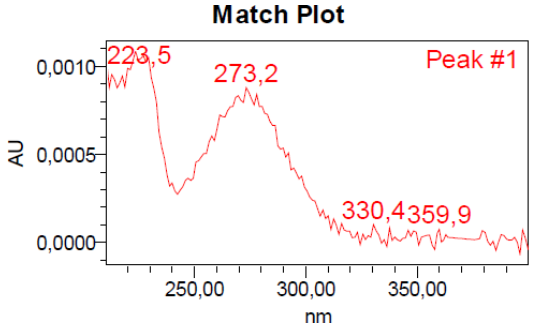


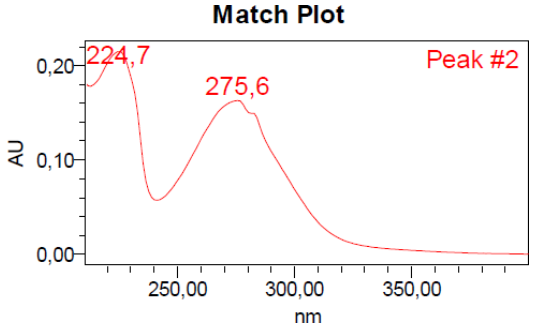


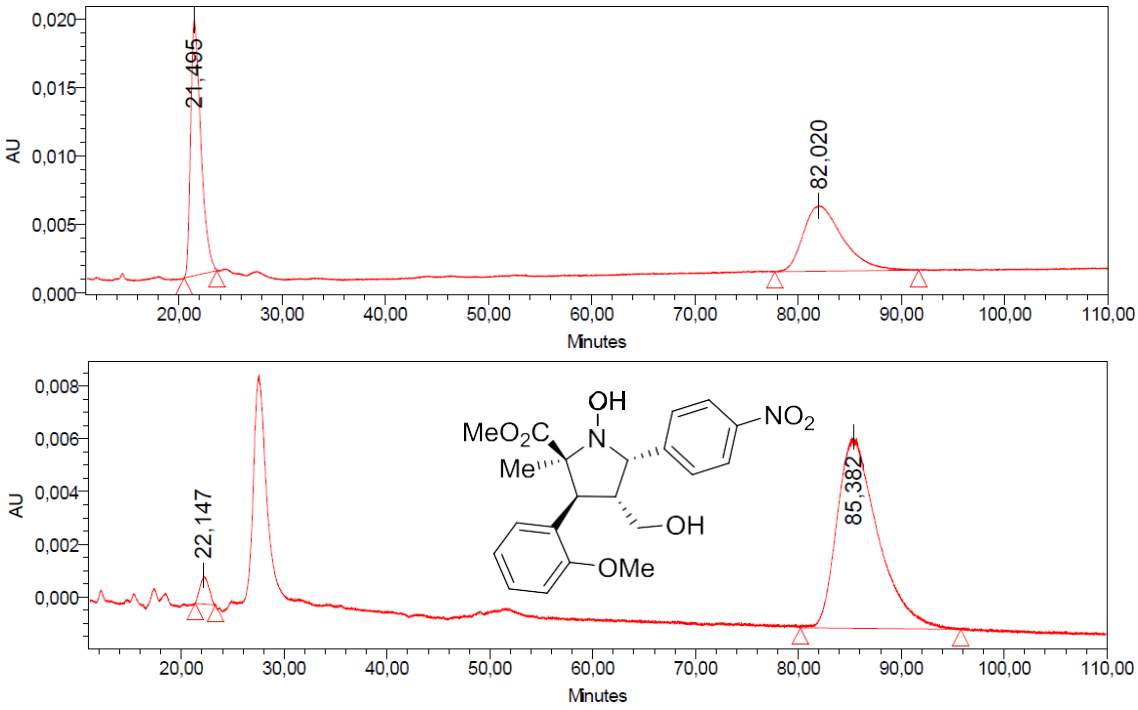


Peak Results

	Name	RT	Area	Height	% Area
1		53,169	78152	1031	0,15
2		112,729	53553262	214269	99,85

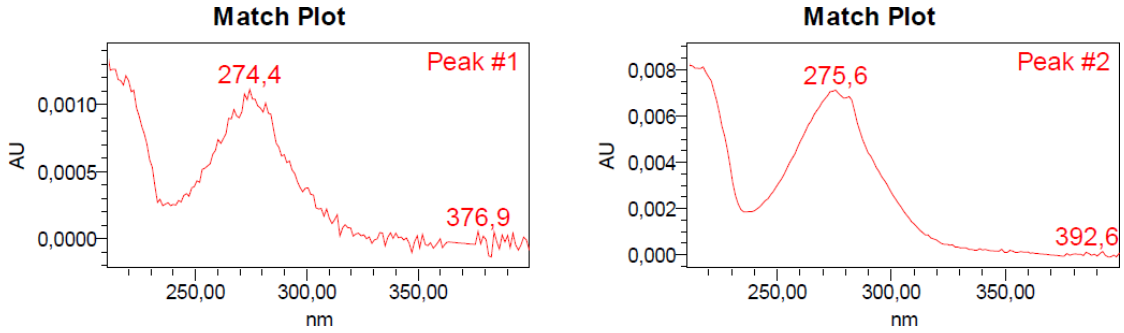


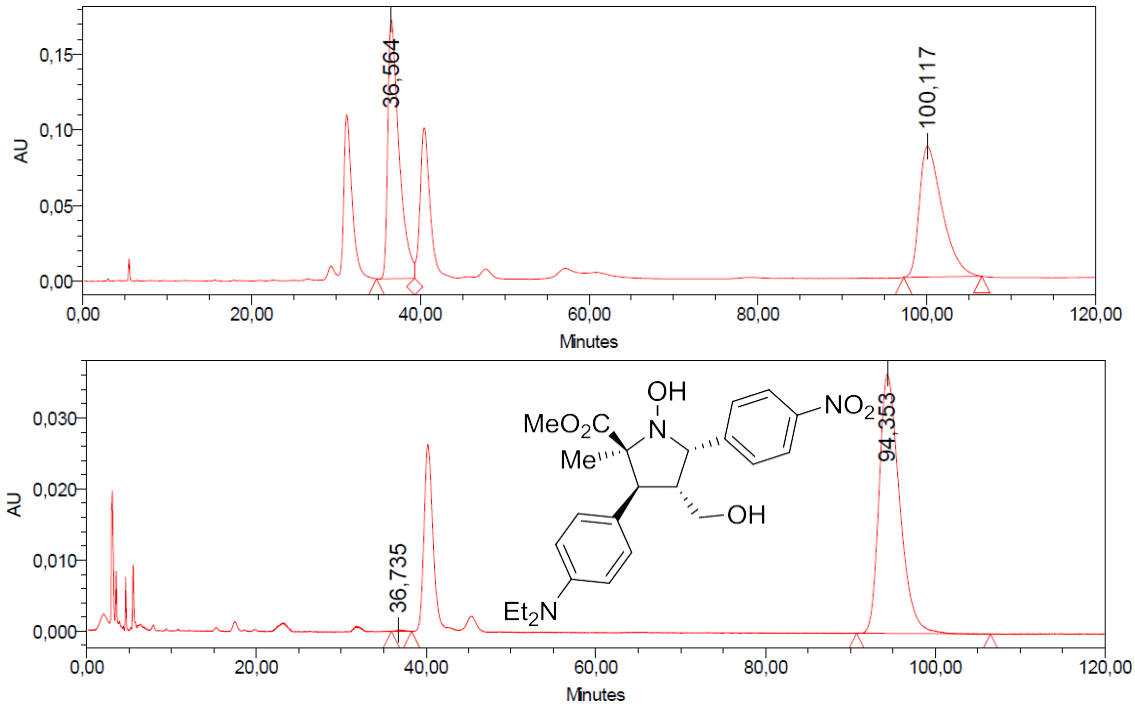




Peak Results

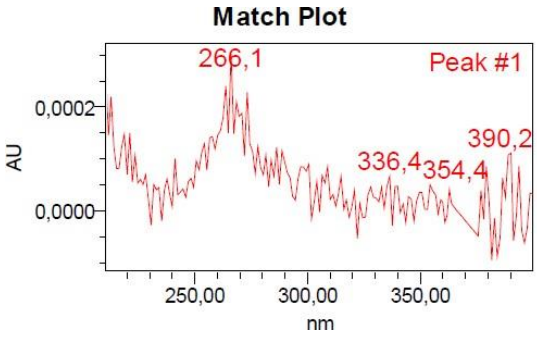
	Name	RT	Area	Height	% Area
1		22,147	62879	1085	3,07
2		85,382	1984825	7266	96,93

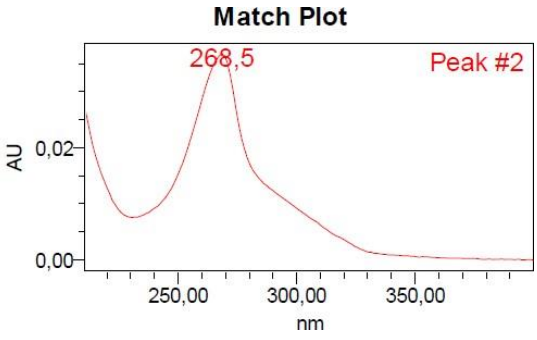


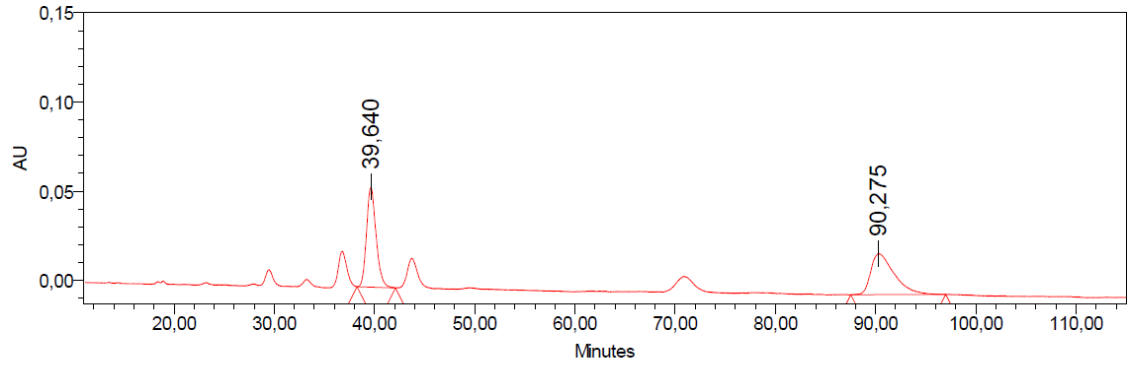


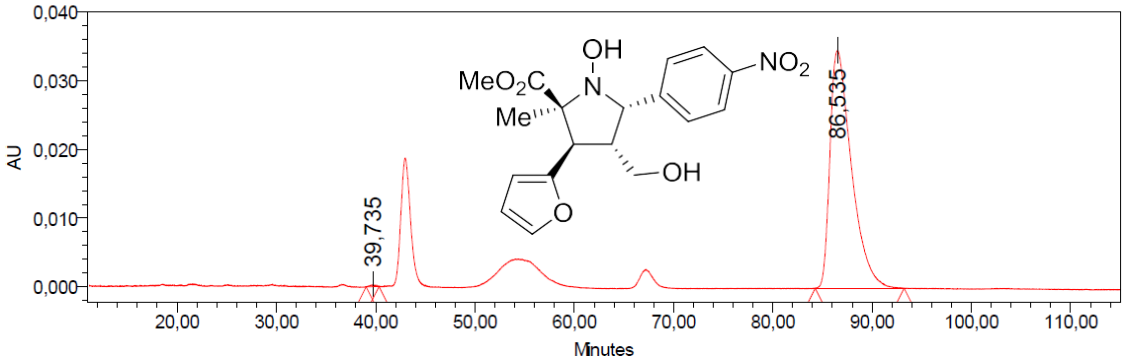
Peak Results

	Name	RT	Area	Height	% Area
1		36,735	14040	221	0,23
2		94,353	6091675	36504	99,77



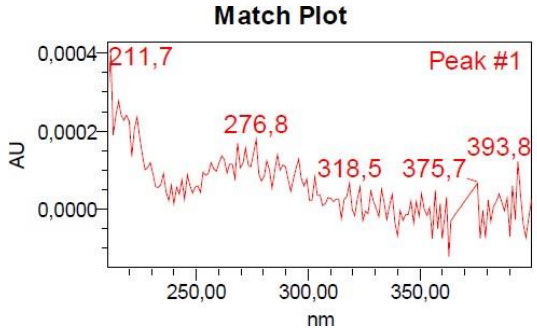


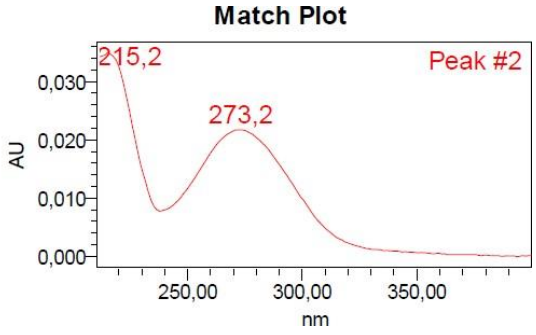


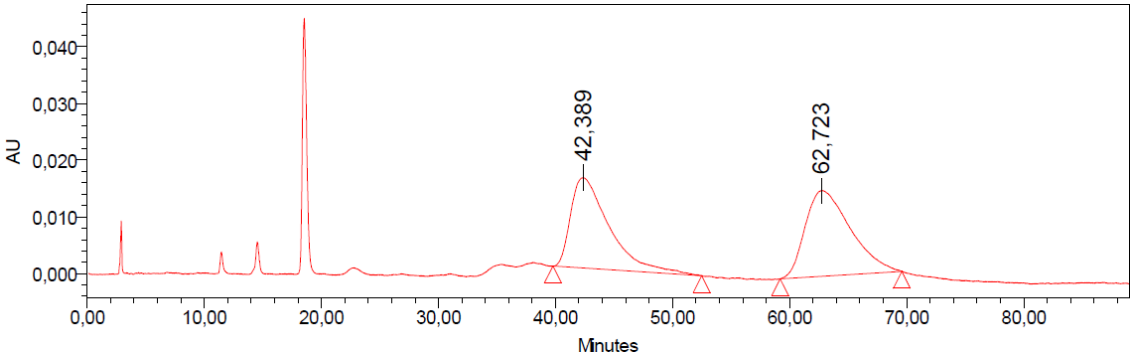


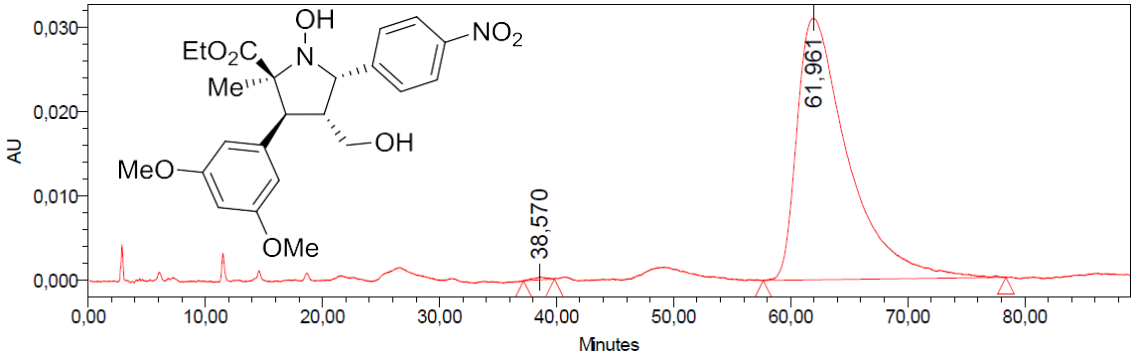
Peak Results

	Name	RT	Area	Height	% Area
1		39,735	9751	354	0,19
2		86,535	5209909	34663	99,81



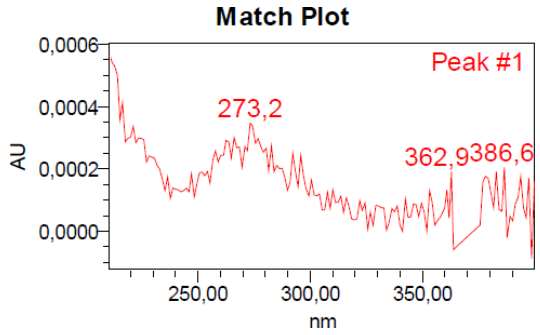


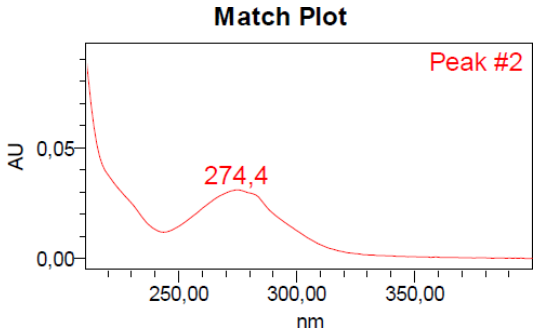


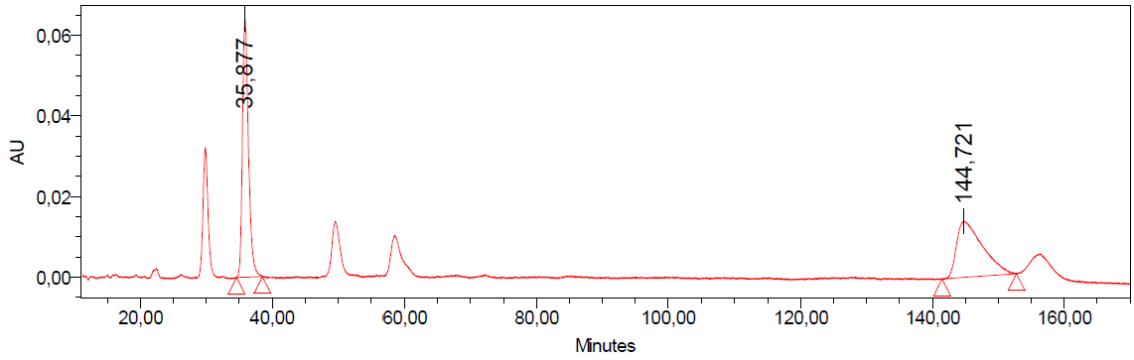


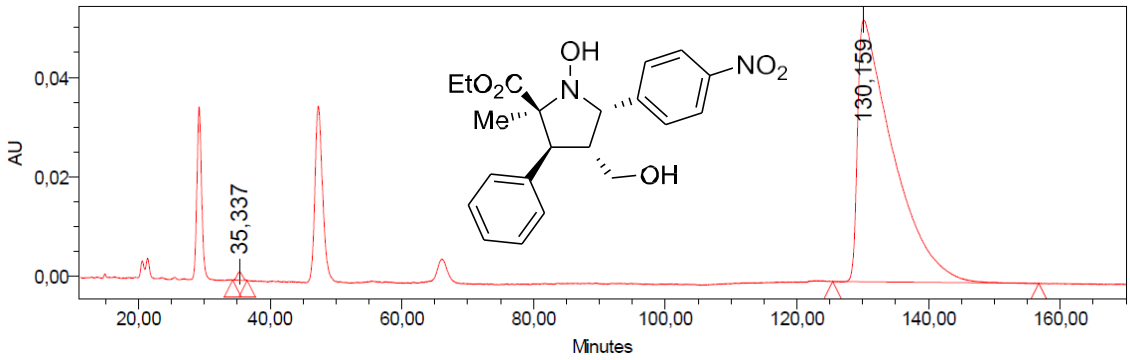
Peak Results

	Name	RT	Area	Height	% Area
1		38,570	25180	339	0,27
2		61,961	9375649	31021	99,73





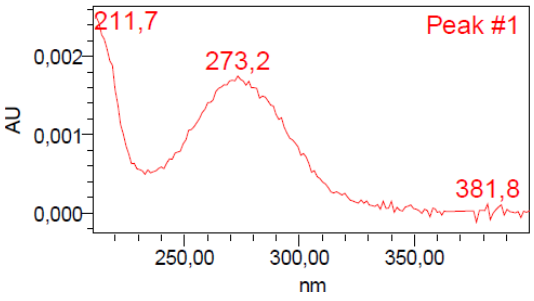




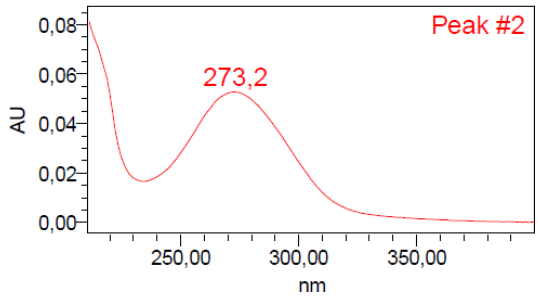
Peak Results

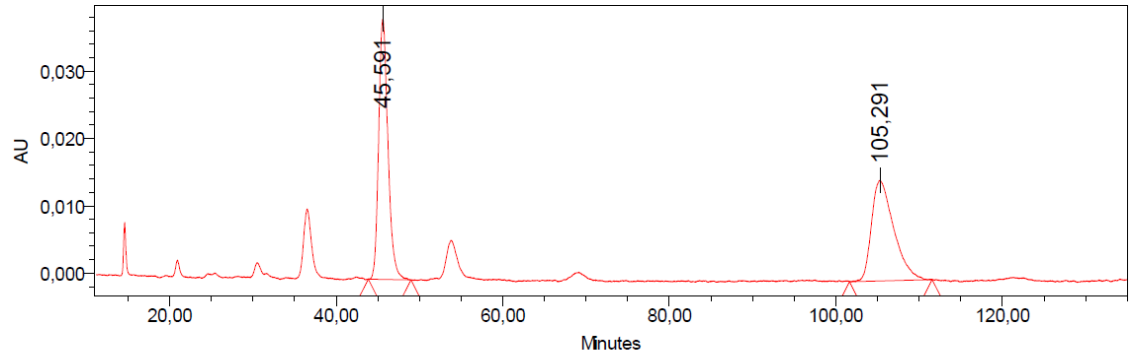
	Name	RT	Area	Height	% Area
1		35,337	93858	1735	0,47
2		130,159	19739873	52720	99,53

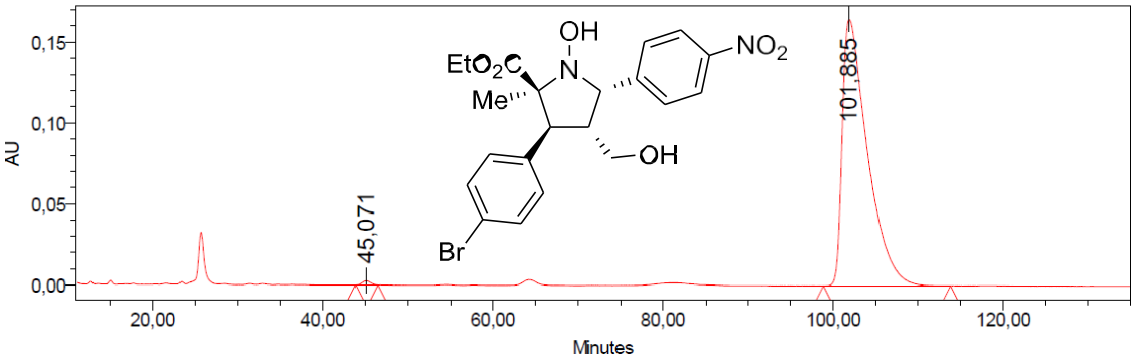
Match Plot



Match Plot

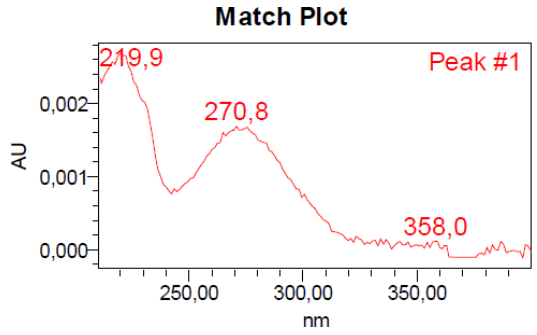


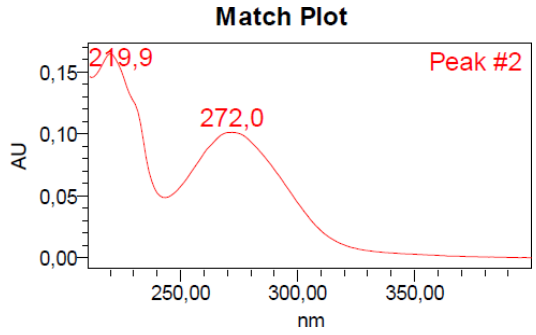


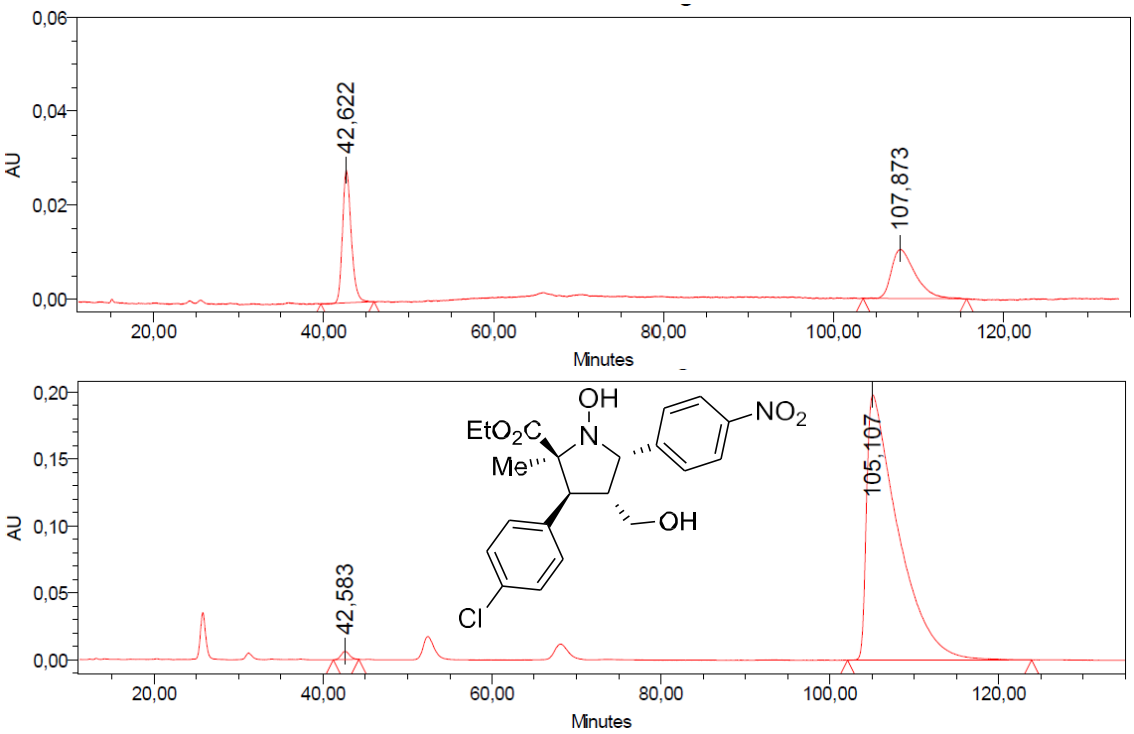


Peak Results

	Name	RT	Area	Height	% Area
1		45,071	185488	2684	0,54
2		101,885	33974963	164621	99,46

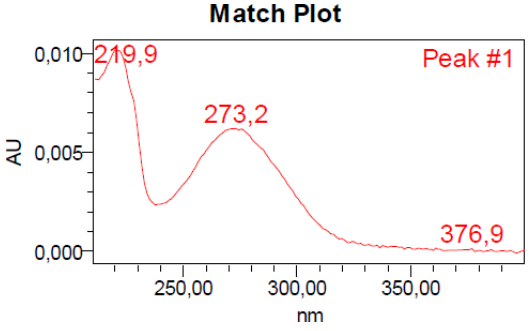


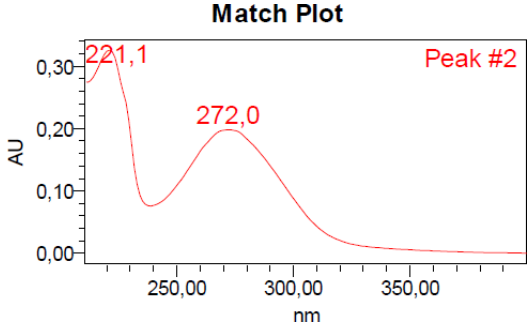


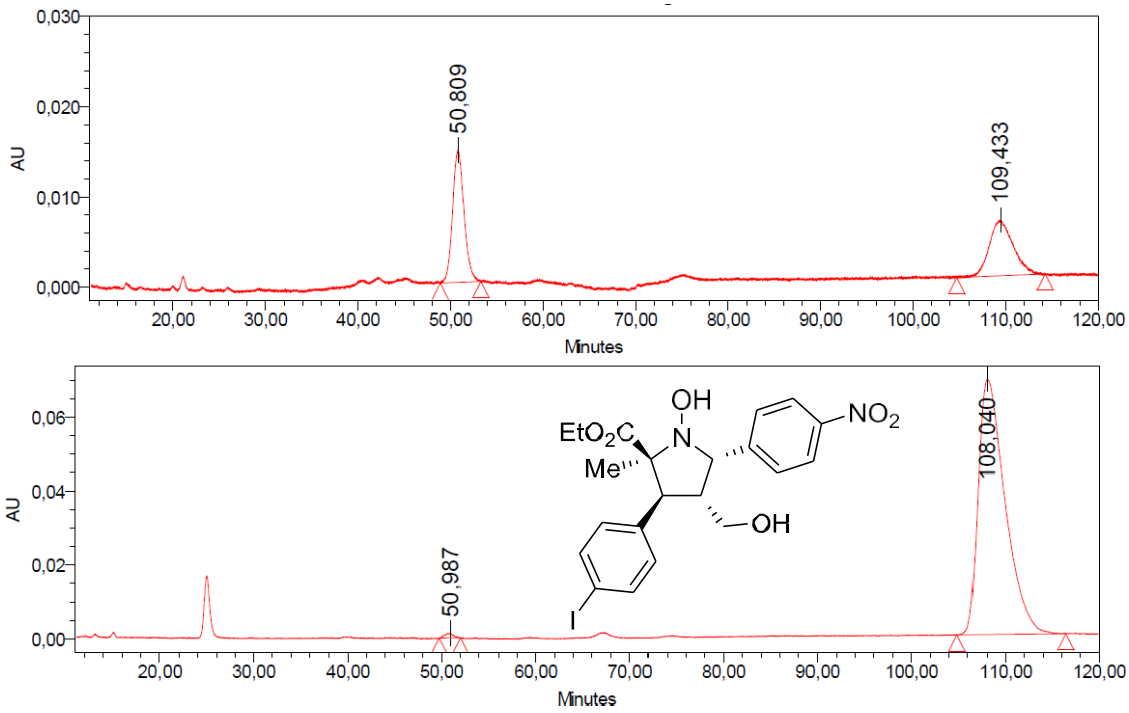


Peak Results

	Name	RT	Area	Height	% Area
1		42,583	424256	6203	0,82
2		105,107	51178236	197980	99,18

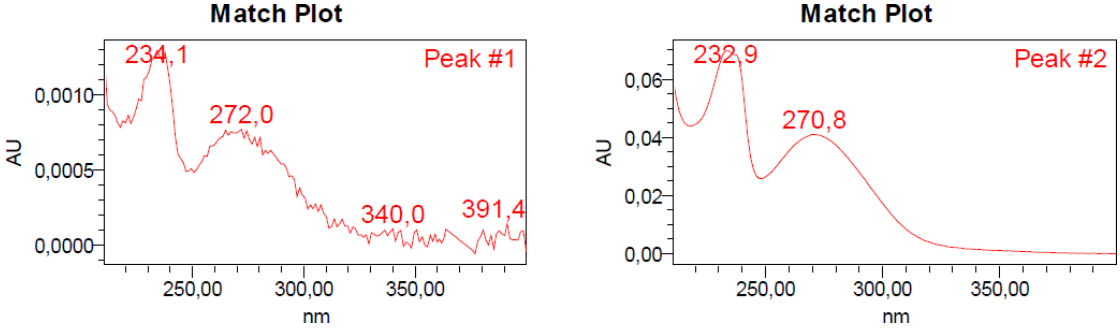


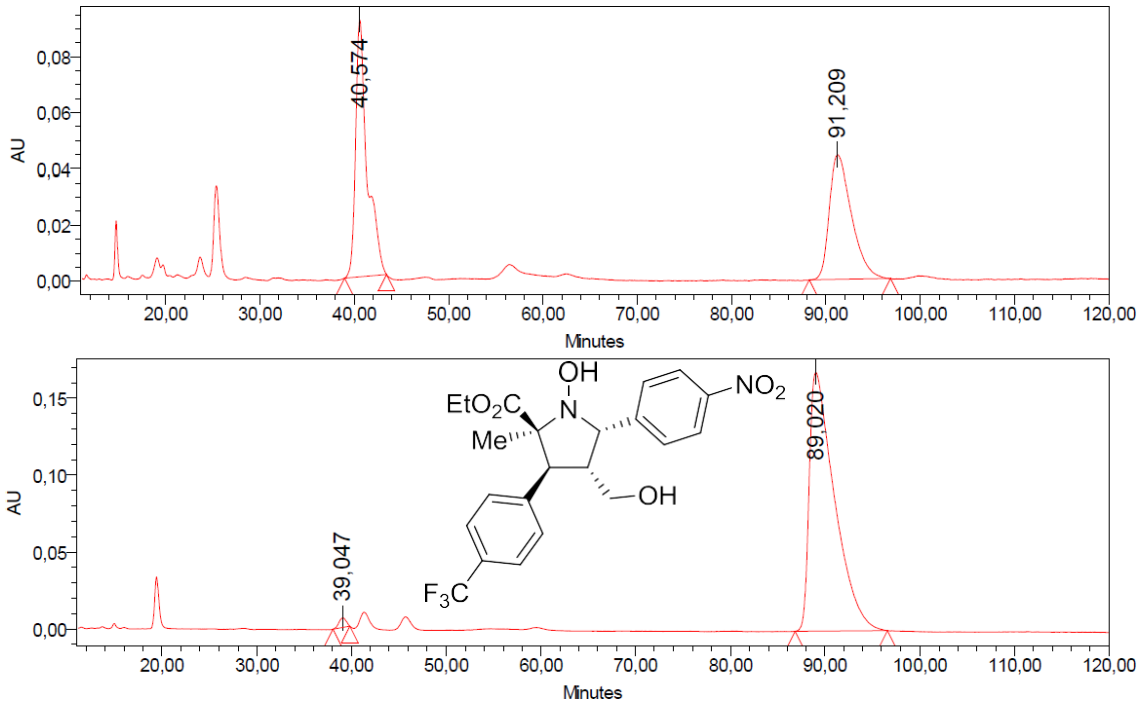




Peak Results

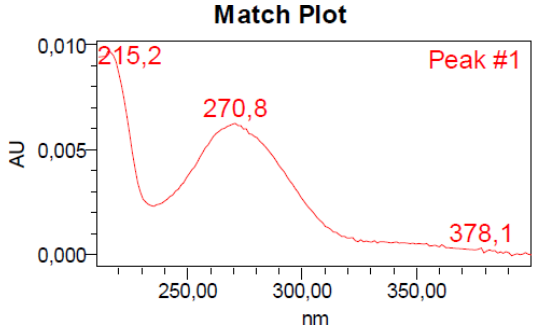
	Name	RT	Area	Height	% Area
1		50,987	75669	1229	0,55
2		108,040	13642378	69026	99,45

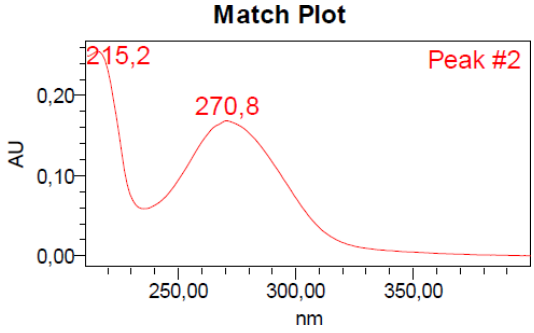


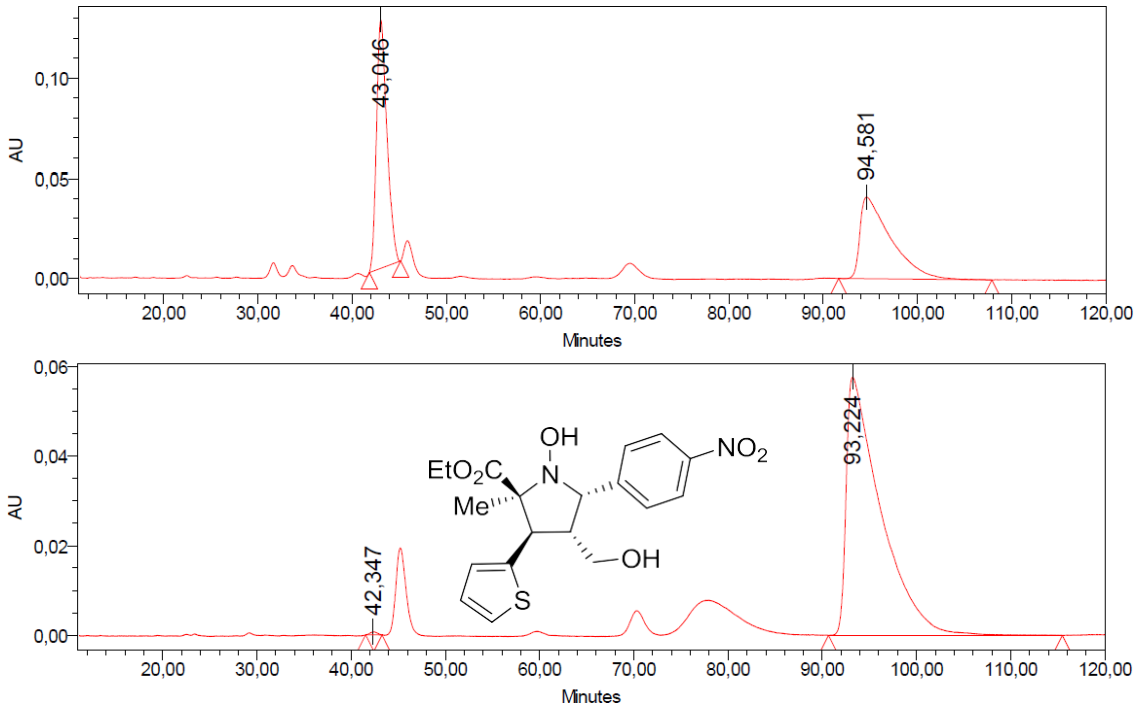


Peak Results

	Name	RT	Area	Height	% Area
1		39,047	329975	6244	1,04
2		89,020	31267751	168239	98,96

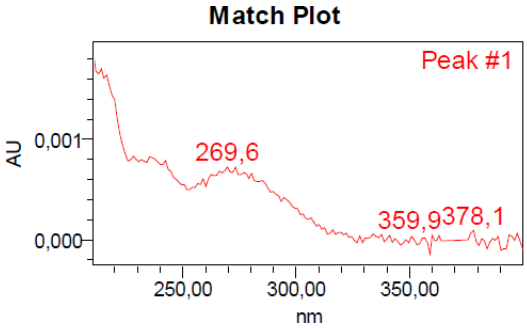


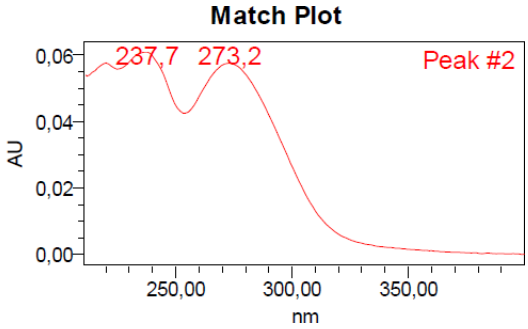


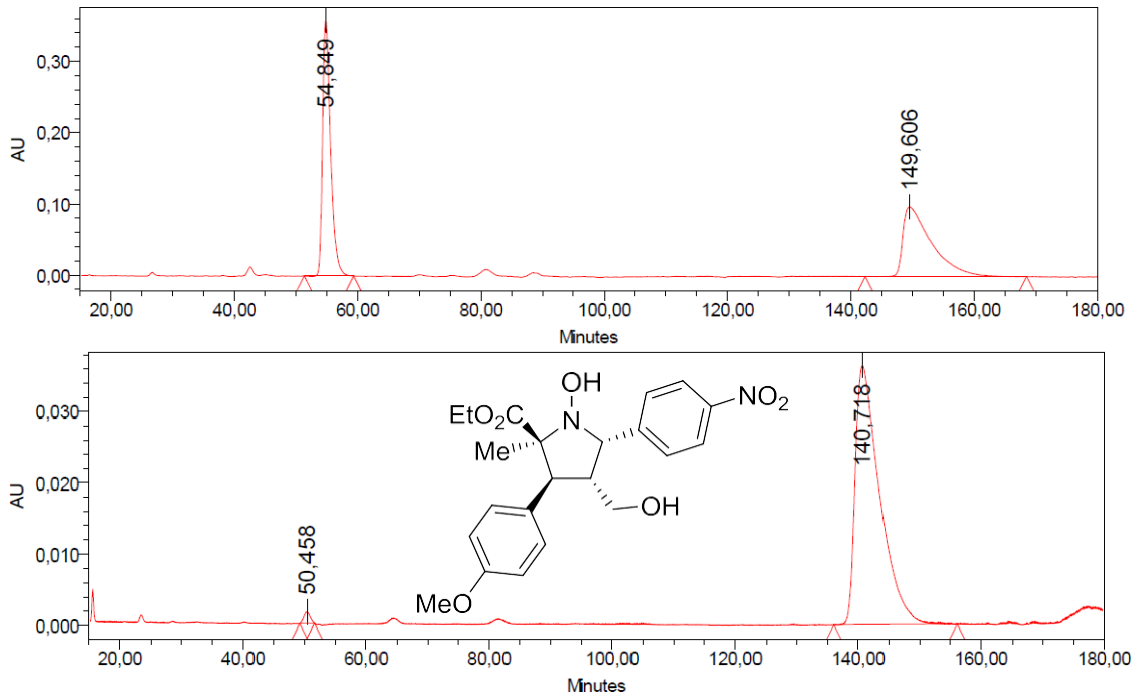


Peak Results

	Name	RT	Area	Height	% Area
1		42,347	36814	716	0,25
2		93,224	14633060	57616	99,75

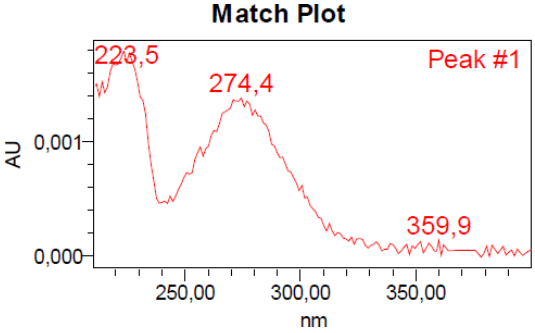


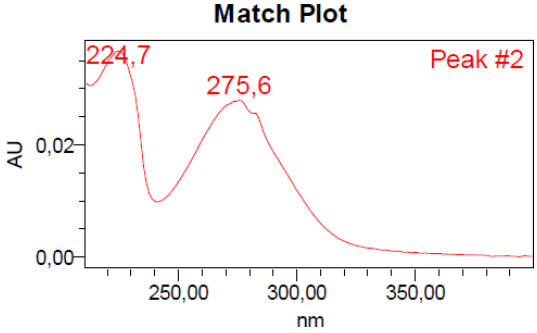


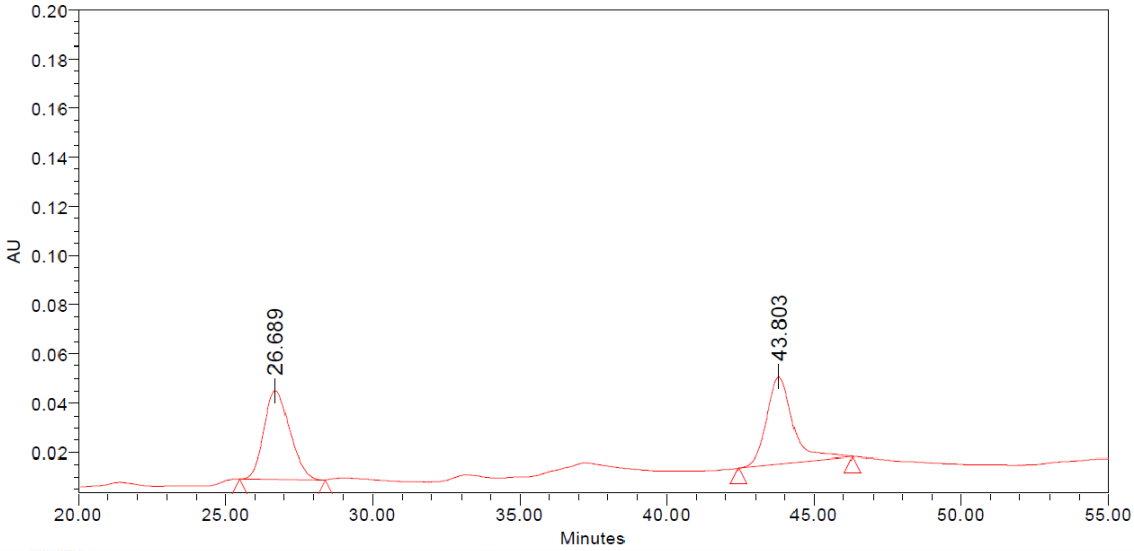


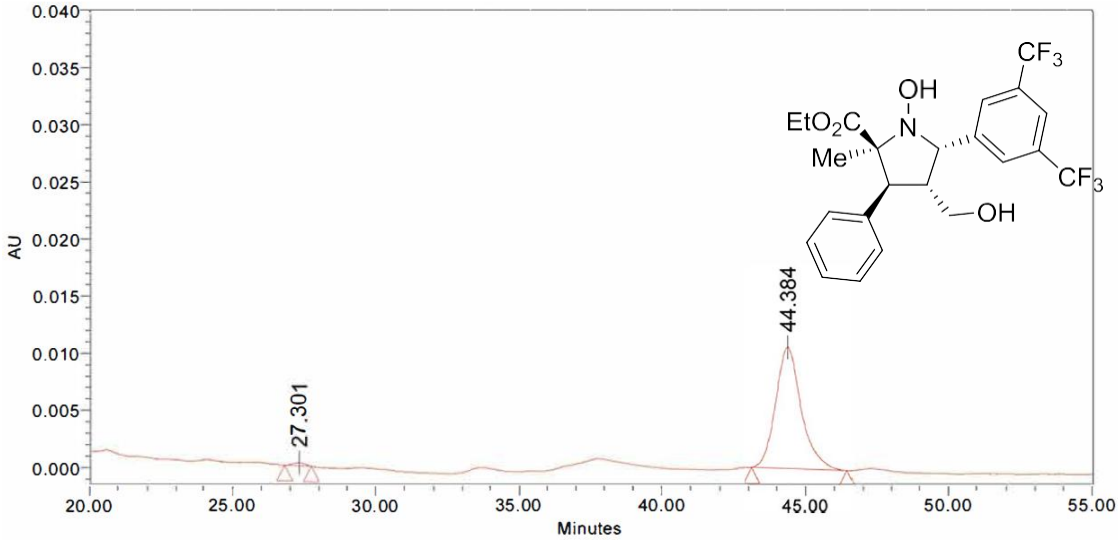
Peak Results

	Name	RT	Area	Height	% Area
1		50,458	112788	1624	1,11
2		140,718	10043455	36408	98,89



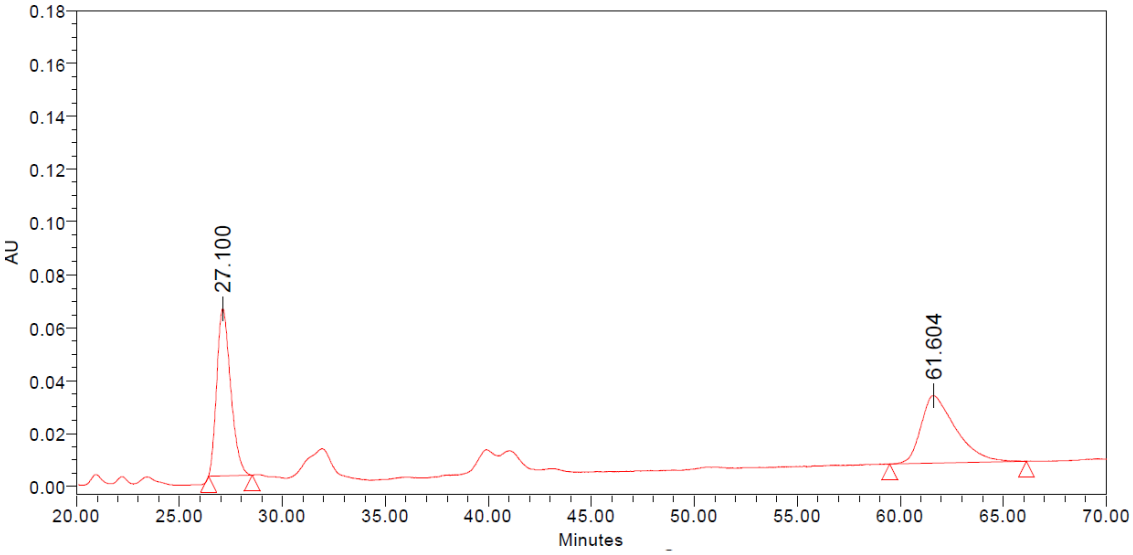


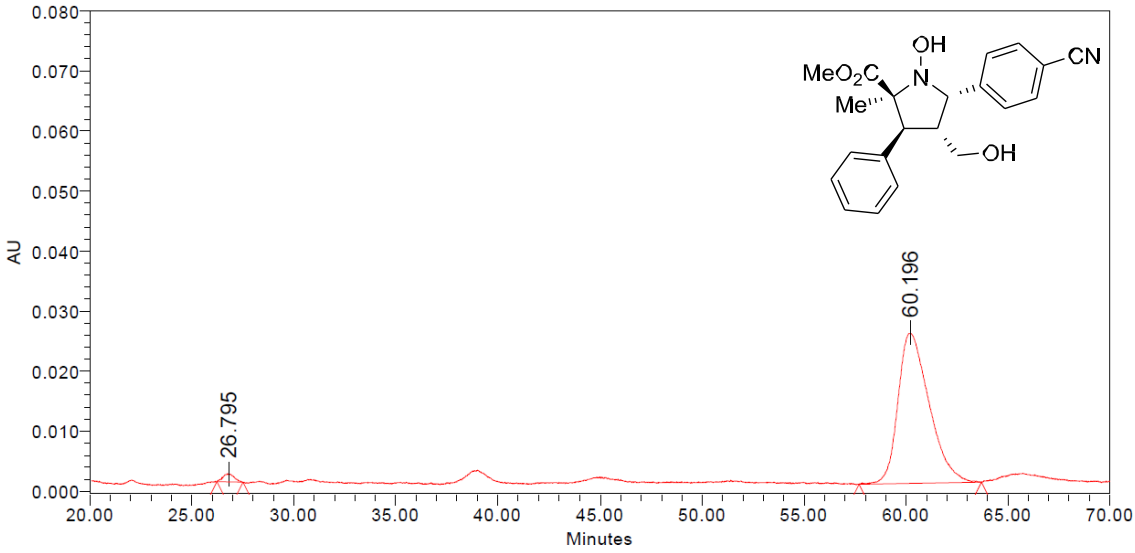




Peak Results

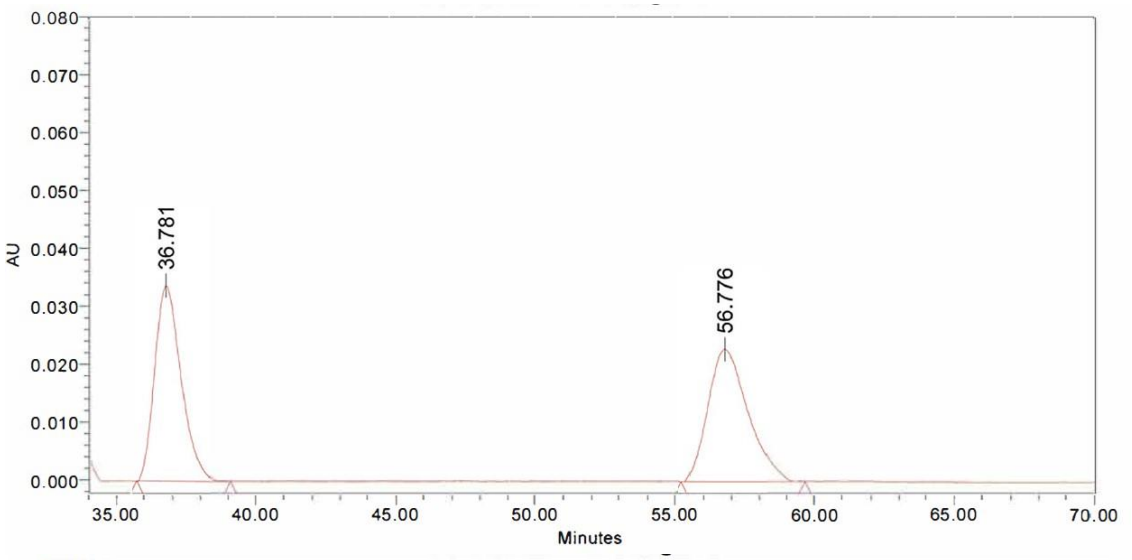
	RT	% Area
1	27.301	1.05
2	44.384	98.95

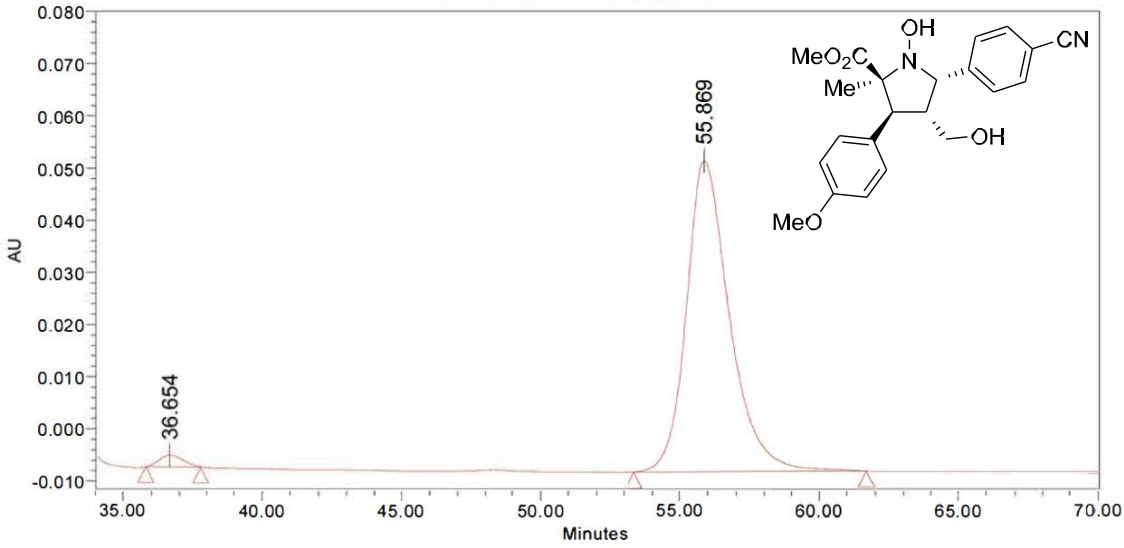




Peak Results

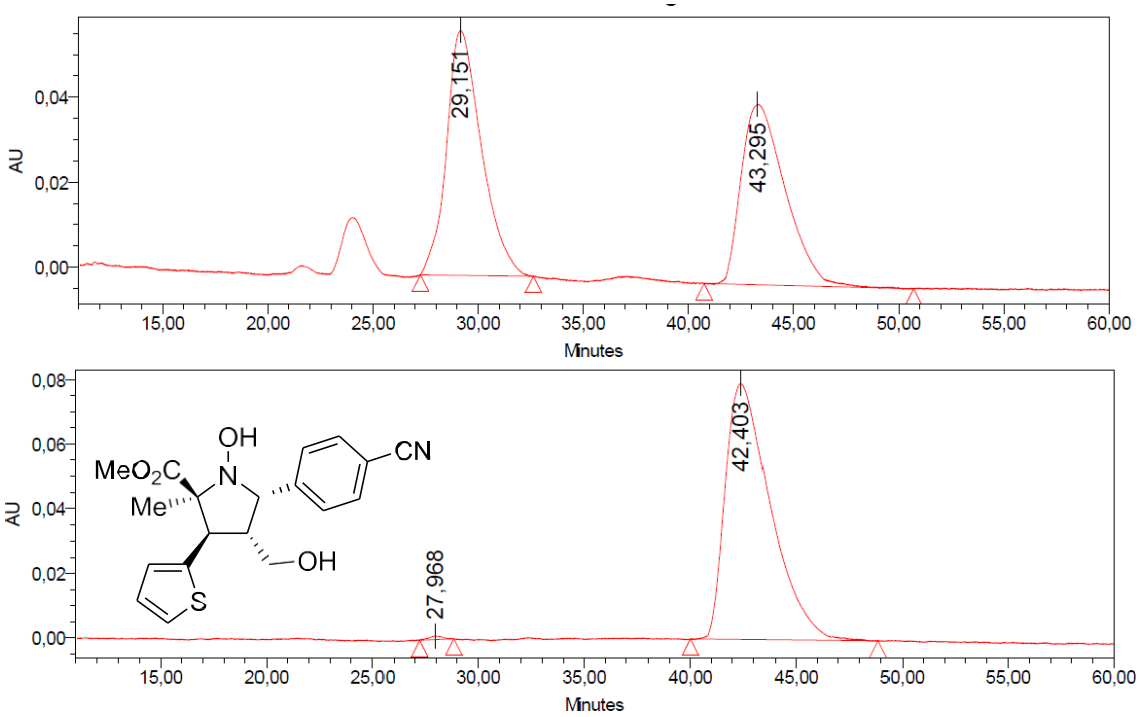
	RT	% Area
1	26.795	1.95
2	60.196	98.05





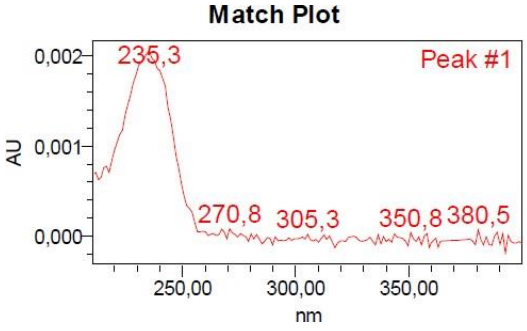
Peak Results

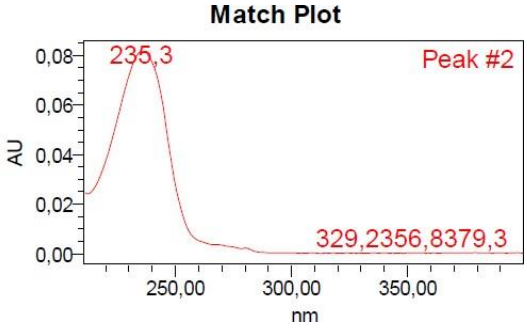
	RT	% Area
1	36.654	2.00
2	55.869	98.00

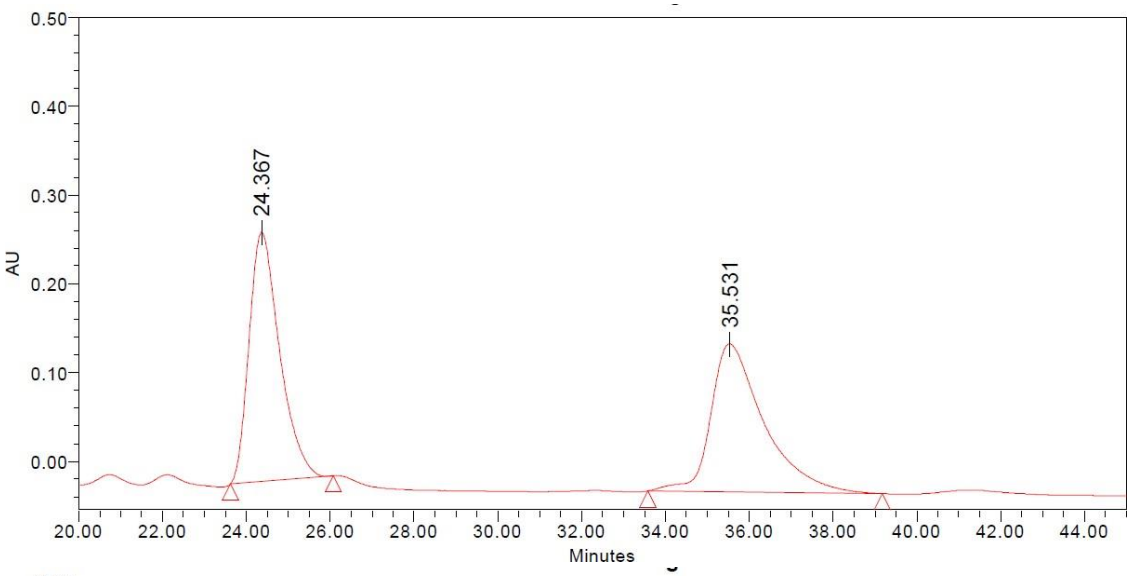


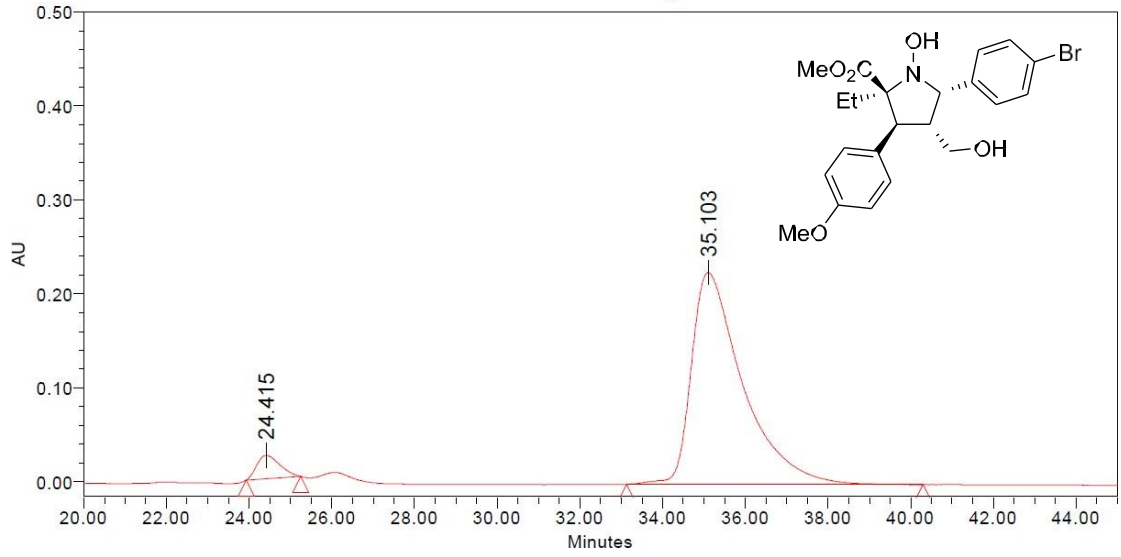
Peak Results

	Name	RT	Area	Height	% Area
1		27,968	49873	1096	0,43
2		42,403	11679666	79319	99,57



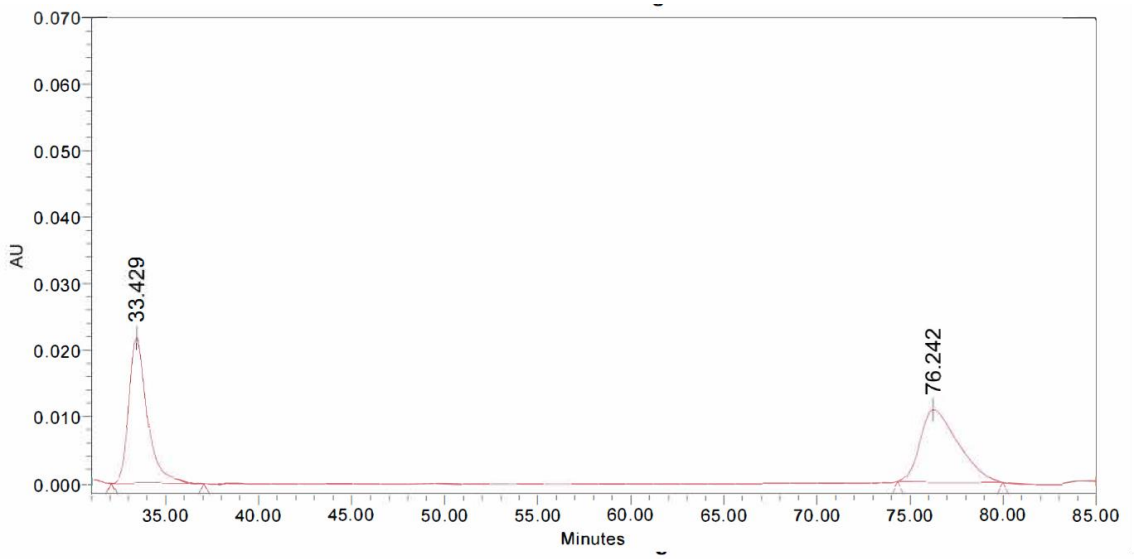


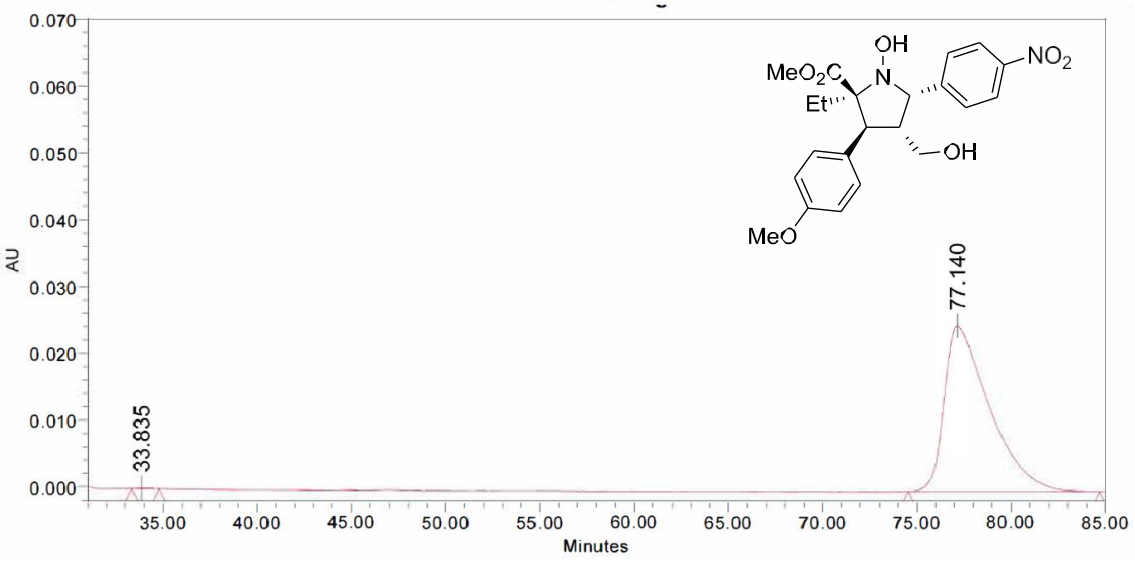




Peak Results

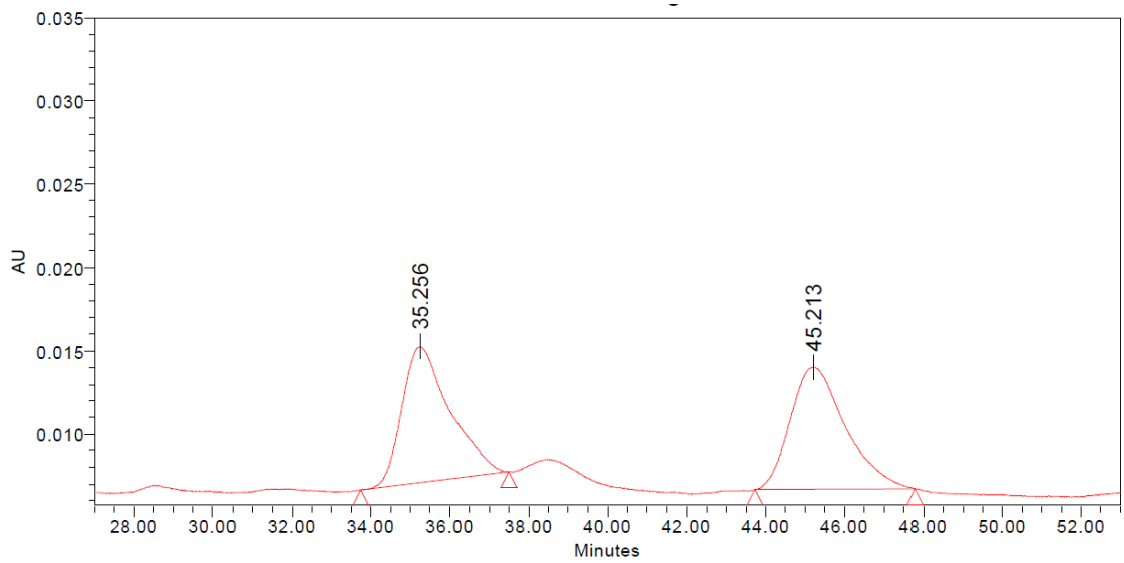
	RT	% Area
1	24.415	4.76
2	35.103	95.24

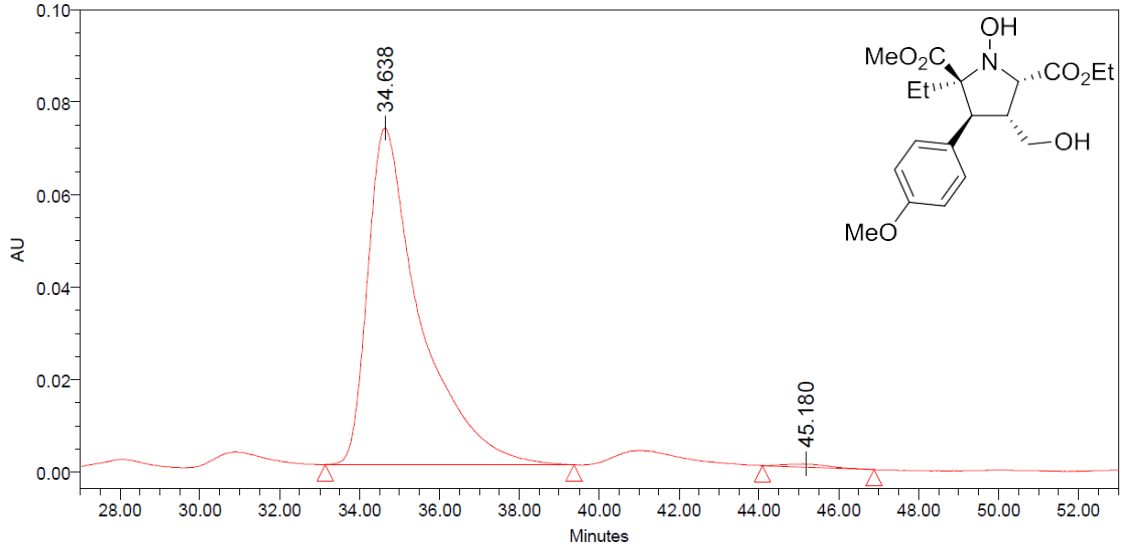




Peak Results

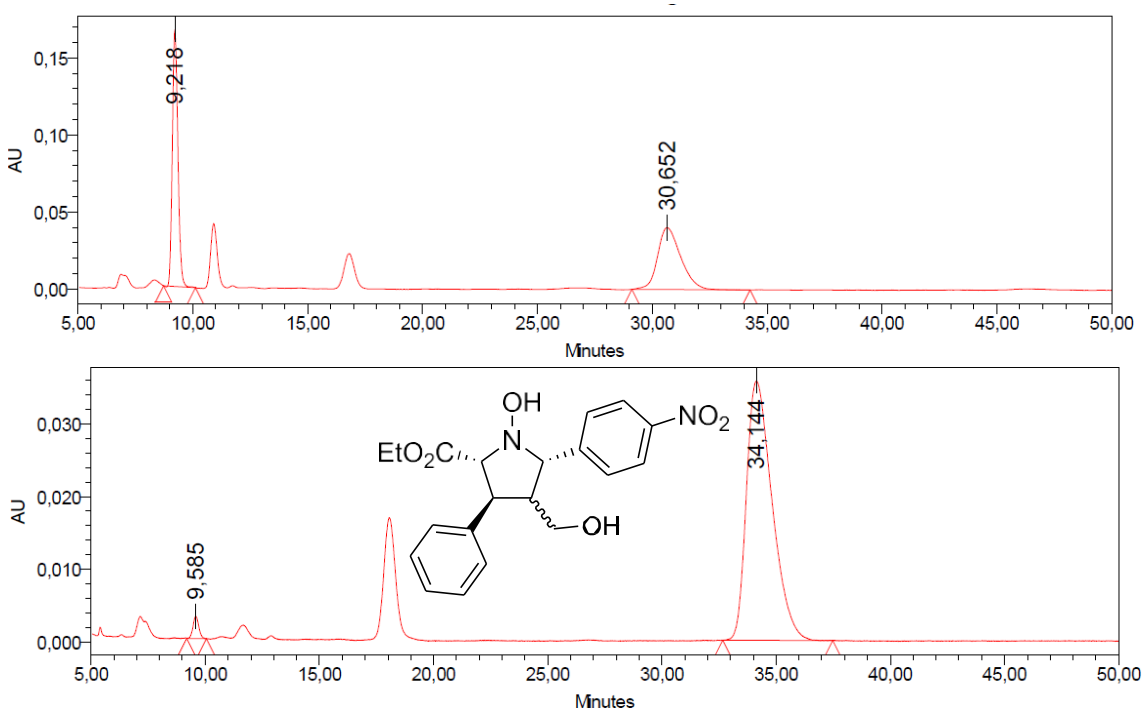
	RT	% Area
1	33.835	0.12
2	77.140	99.88





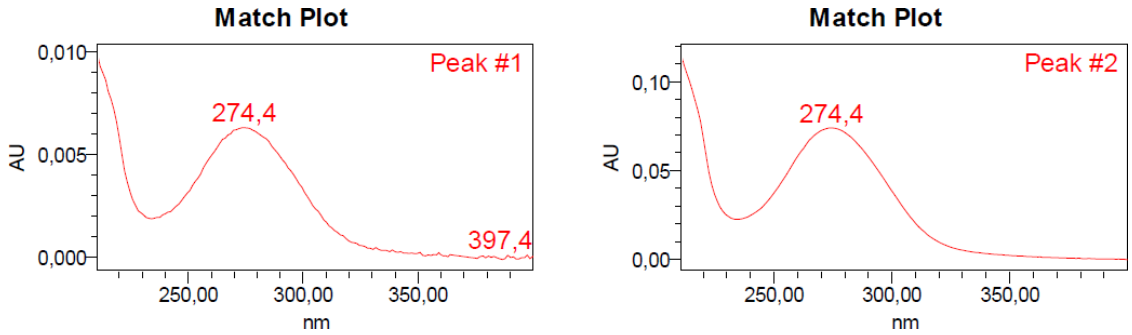
Peak Results

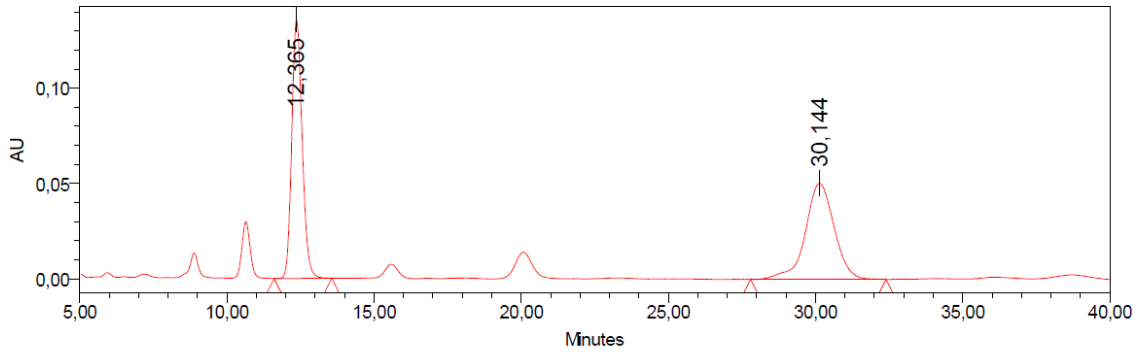
	RT	% Area
1	34.638	99.23
2	45.180	0.77

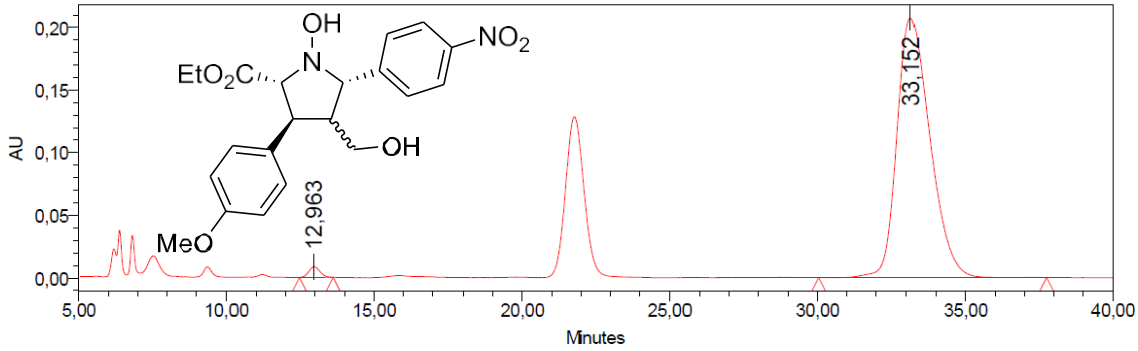


Peak Results

	Name	RT	Area	Height	% Area
1		9,585	54459	3068	1,92
2		34,144	2788697	35708	98,08

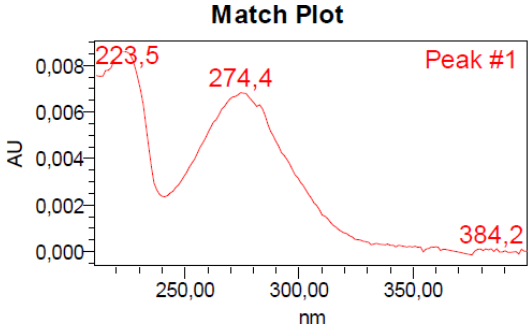


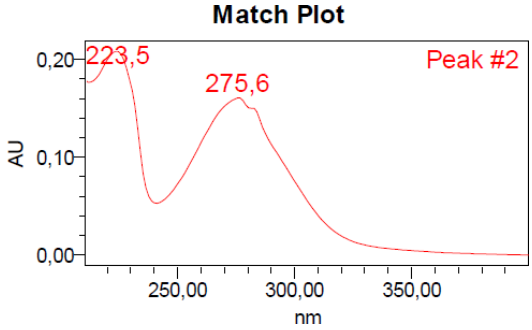


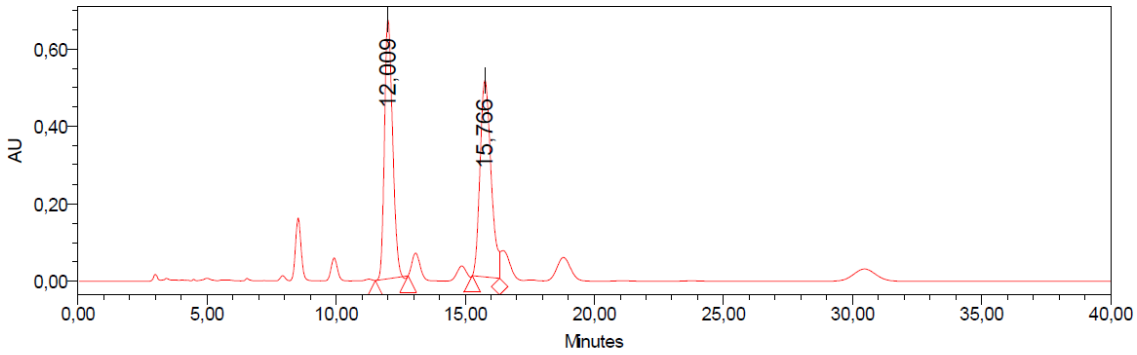


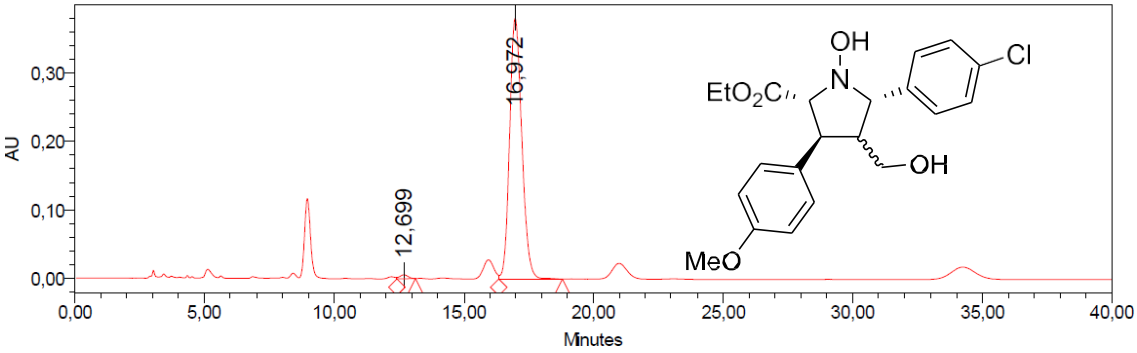
Peak Results

	Name	RT	Area	Height	% Area
1		12,963	222179	8549	1,39
2		33,152	15782734	207125	98,61





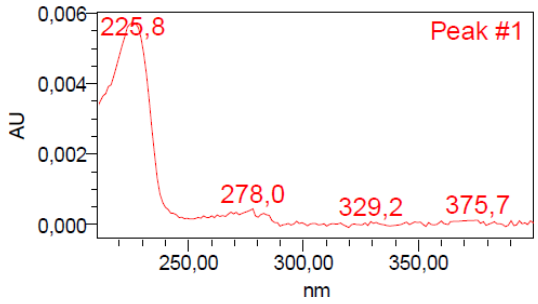




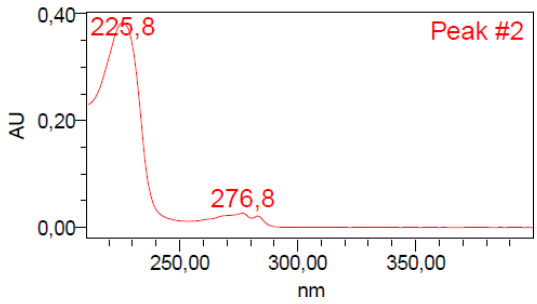
Peak Results

	Name	RT	Area	Height	% Area
1		12,699	125976	5700	1,00
2		16,972	12515573	381339	99,00

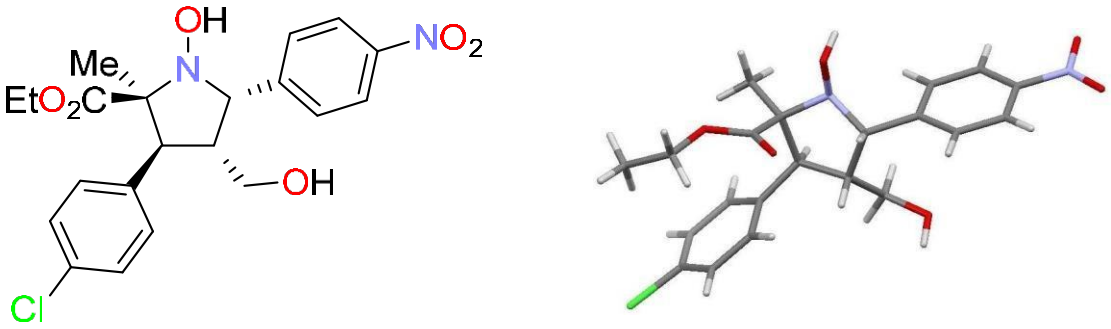
Match Plot



Match Plot

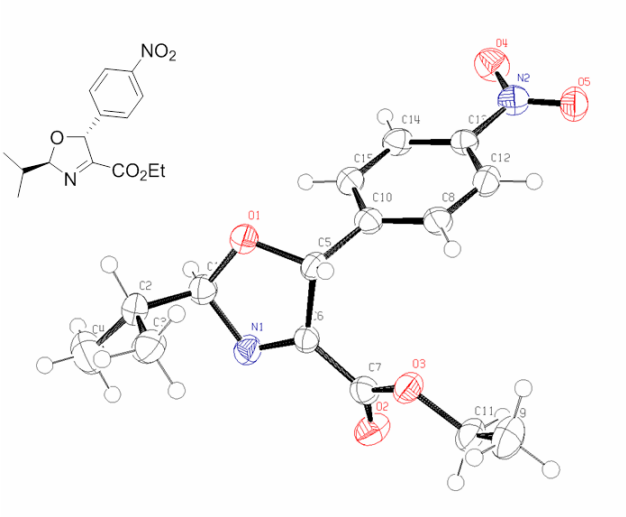


3. X-Ray Structures



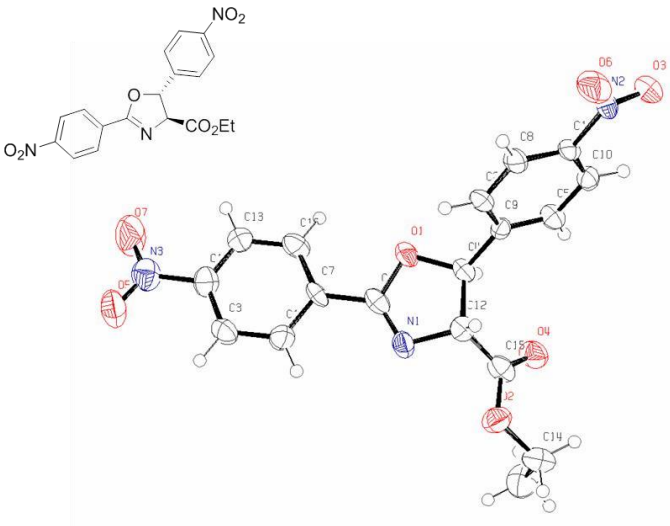
ORTEP representation of compound **7j**.

Represented as sticks. CCDC: 1511107



ORTEP representation of compound **20b**.

Ellipsoids are represented at 50% probability level. CCDC: 1444429



ORTEP representation of compound **21**.

Ellipsoids are represented at 50% probability level. CCDC: 1444430

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_audit_block_doi 10.5517/ccdc.csd.cc1mqfd5

_database_code_depnum_ccdc_archive 'CCDC 1511107'

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_citation_year

1 10.1002/chem.201605350 2017

_audit_update_record

2016-10-21 deposited with the CCDC. 2019-02-14 downloaded from the CCDC.

_audit_creation_date 2016-10-21T14:01:32-00:00

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CHEMICAL INFORMATION

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_chemical_name_systematic

'Ethyl (2S,3S,4R,5S)-3-(4-chlorophenyl)-1-hydroxy-4-(hydroxymethyl)-2-methyl-5-(4-nitrophenyl)pyrrolidine-2-carboxylate'

_chemical_formula_moiety 'C21 H23 Cl1 N2 O6'

_chemical_formula_sum 'C21 H23 Cl N2 O6'

_chemical_formula_weight 434.86

_chemical_compound_source 'synthesis as described'

_chemical_absolute_configuration ad

#---#

UNIT CELL INFORMATION

#---#

_space_group_crystal_system monoclinic

_space_group_name_H-M_alt 'P 1 21 1'

_space_group_name_Hall 'P 2yb'

_space_group_IT_number 4

_symmetry_cell_setting monoclinic

_symmetry_space_group_name_H-M 'P 1 21 1'

_symmetry_space_group_name_Hall 'P 2yb'

_symmetry_Int_Tables_number 4

loop_

_space_group_symop_operation_xyz

'x, y, z'

'-x, y+1/2, -z'

_cell_length_a 7.82808(13)

_cell_length_b 11.08346(17)

_cell_length_c 23.9907(4)

_cell_angle_alpha 90

_cell_angle_beta 91.6094(14)

_cell_angle_gamma 90

_cell_volume 2080.66(6)

_cell_formula_units_Z 4

_cell_measurement_temperature 120.00(10)

_cell_measurement_reflns_used 19466

_cell_measurement_theta_min 3.661

_cell_measurement_theta_max 73.973

_cell_measurement_wavelength 1.54184

#---#

CRYSTAL INFORMATION

#---#

_exptl_crystal_description plate

_exptl_crystal_colour colourless

_exptl_crystal_size_max 0.7093

_exptl_crystal_size_mid 0.1006

_exptl_crystal_size_min 0.0263

_exptl_crystal_density_diffrn 1.389

_exptl_crystal_density_method 'not measured'

_exptl_crystal_F_000 912

loop_

_exptl_crystal_face_index_h

_exptl_crystal_face_index_k

_exptl_crystal_face_index_l

_exptl_crystal_face_perp_dist

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0 -7 1 0.0524

5 0 -2 0.328

0 0 1 0.0148

-5 2 2 0.3464

0 0 -1 0.0115

#---#

ABSORPTION CORRECTION

#---#

_exptl_absorpt_coefficient_mu 1.985

_exptl_absorpt_correction_type analytical

_exptl_absorpt_process_details

CrysAlisPro, Agilent Technologies,

Version 1.171.36.24 (release 03-12-2012 CrysAlis171 .NET)

(compiled Dec 3 2012,18:21:49)

Analytical numeric absorption correction using a multifaceted crystal

model based on expressions derived by R.C. Clark & J.S.

(Clark, R. C. & Reid, J. S. (1995). Acta Cryst. A51, 887-897)

_exptl_absorpt_correction_T_min 0.369

_exptl_absorpt_correction_T_max 0.949

#---#

DATA COLLECTION

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_diffrn_ambient_temperature 120.00(10)

_diffrn_radiation_wavelength 1.54184

_diffrn_radiation_type CuK\a

_diffrn_radiation_source 'Nova (Cu) X-ray micro-source'

_diffrn_radiation_monochromator 'Multilayer optics'

_diffrn_source_voltage 50

_diffrn_source_current 0.8

_diffrn_source_power 0.04

_diffrn_radiation_probe x-ray

_diffrn_detector_area_resol_mean 10.4023

_diffrn_orient_matrix_ub_11 -0.0806729

_diffrn_orient_matrix_ub_12 0.0016795

_diffrn_orient_matrix_ub_13 -0.0593217

_diffrn_orient_matrix_ub_21 0.1720034

_diffrn_orient_matrix_ub_22 -0.0393658

_diffrn_orient_matrix_ub_23 -0.0238559

_diffrn_orient_matrix_ub_31 -0.051624

_diffrn_orient_matrix_ub_32 -0.1332833

_diffrn_orient_matrix_ub_33 0.0062867

_diffrn_measurement_device_type 'Agilent SuperNova'

_diffrn_detector 'CCD plate'

_diffrn_detector_type Atlas

_diffrn_measurement_device '\k-geometry diffractometer'

_diffrn_measurement_method '\w scans'

_diffrn_reflns_av_R_equivalents 0.0717

_diffrn_reflns_av_unetI/netI 0.0638

_diffrn_reflns_number 38789

_diffrn_reflns_limit_h_min -9

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_diffrn_reflns_limit_k_max 13

_diffrn_reflns_limit_l_min -29

_diffrn_reflns_limit_l_max 29

_diffrn_reflns_theta_min 3.687

_diffrn_reflns_theta_max 69.996

_diffrn_reflns_theta_full 67.684

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_diffrn_reflns_Laue_measured_fraction_full 1

_diffrn_reflns_Laue_measured_fraction_max 1

_diffrn_reflns_point_group_measured_fraction_max 0.999

_reflns_number_total 11647

_reflns_number_gt 11194

_reflns_threshold_expression 'I > 2\s(I)'

_diffrn_measurement_details

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omega____ theta____ kappa____ phi_____ frames

- 41.3256 38.0000 60.0000 27

#__ type_ start__ end____ width___ exp.time_

2 omega -20.00 83.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

- 41.3256 -99.0000 -150.0000 103

#__ type_ start__ end____ width___ exp.time_

3 omega 20.00 47.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

- 41.3256 57.0000 90.0000 27

#__ type_ start__ end____ width___ exp.time_

4 omega 9.00 119.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

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    -       41.3256   77.0000  120.0000 110
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  5 omega   58.00  112.00   1.0000    1.5000
omega____ theta____ kappa____ phi_____ frames
    -       41.3256  150.0000 -135.0000 54
#__ type_ start__ end____ width___ exp.time_
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omega____ theta____ kappa____ phi_____ frames
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#__ type_ start__ end____ width___ exp.time_
  7 omega -131.00 -104.00   1.0000   10.0000
omega____ theta____ kappa____ phi_____ frames
    -      -83.0000  -74.0000  129.9045 27
#__ type_ start__ end____ width___ exp.time_
  8 omega  -77.00  -51.00   1.0000   10.0000
omega____ theta____ kappa____ phi_____ frames
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omega____ theta____ kappa____ phi_____ frames
    -      -83.0000  -72.0000   38.6606 31
#__ type_ start__ end____ width___ exp.time_
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omega____ theta____ kappa____ phi_____ frames
    -      -83.0000  -69.0000   59.6494 68
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 11 omega -126.00  -52.00   1.0000   10.0000
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- -83.0000 -72.0000 89.6453 74

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12 omega -74.00 -49.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- -83.0000 -77.0000 120.0000 25

#__ type_ start__ end____ width___ exp.time_

13 omega -85.00 -52.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- -83.0000 -71.0000 27.1134 33

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14 omega -76.00 -51.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- -83.0000 -72.0000 101.4431 25

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15 omega -77.00 -50.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- -83.0000 -77.0000 150.0000 27

#__ type_ start__ end____ width___ exp.time_

16 omega -76.00 -50.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- -83.0000 -74.0000 129.9045 26

#__ type_ start__ end____ width___ exp.time_

17 omega -76.00 -51.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- -83.0000 -77.0000 30.0000 25

#__ type_ start__ end____ width___ exp.time_

18 omega -75.00 -49.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- -83.0000 -77.0000 0.0000 26

#__ type_ start__ end____ width___ exp.time_

19 omega -75.00 -50.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- -83.0000 -77.0000 90.0000 25

#__ type_ start__ end____ width___ exp.time_

20 omega -78.00 -51.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- -83.0000 -69.0000 114.4649 27

#__ type_ start__ end____ width___ exp.time_

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omega____ theta____ kappa____ phi_____ frames

- 108.3609 61.0000 150.0000 27

#__ type_ start__ end____ width___ exp.time_

22 omega 79.00 104.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 61.0000 90.0000 25

#__ type_ start__ end____ width___ exp.time_

23 omega 40.00 66.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -45.0000 60.0000 26

#__ type_ start__ end____ width___ exp.time_

24 omega 60.00 121.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -125.0000 -180.0000 61

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25 omega 75.00 107.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 77.0000 30.0000 32

#__ type_ start__ end____ width___ exp.time_

26 omega 78.00 140.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 77.0000 60.0000 62

#__ type_ start__ end____ width___ exp.time_

27 omega 31.00 68.00 1.0000 10.0000

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- 108.3609 -30.0000 -120.0000 37

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28 omega 30.00 67.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -30.0000 90.0000 37

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29 omega 75.00 134.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 77.0000 90.0000 59

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30 omega 47.00 73.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -45.0000 30.0000 26

#__ type_ start__ end____ width___ exp.time_

31 omega 34.00 62.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -30.0000 60.0000 28

#__ type_ start__ end____ width___ exp.time_

32 omega 77.00 132.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 77.0000 150.0000 55

#__ type_ start__ end____ width___ exp.time_

33 omega 74.00 153.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 125.0000 150.0000 79

#__ type_ start__ end____ width___ exp.time_

34 omega 34.00 72.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -45.0000 -150.0000 38

#__ type_ start__ end____ width___ exp.time_

35 omega 84.00 111.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 45.0000 60.0000 27

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36 omega 38.00 64.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -30.0000 -60.0000 26

#__ type_ start__ end____ width___ exp.time_

37 omega 83.00 121.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 61.0000 60.0000 38

#__ type_ start__ end____ width___ exp.time_

38 omega 73.00 148.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 125.0000 -180.0000 75

#__ type_ start__ end____ width___ exp.time_

39 omega 75.00 150.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 77.0000 120.0000 75

#__ type_ start__ end____ width___ exp.time_

40 omega 26.00 67.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

- 41.3256 -122.0000 -18.0000 41

#__ type_ start__ end____ width___ exp.time_

41 omega 69.00 96.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

- 41.3256 -122.0000 -18.0000 27

#__ type_ start__ end____ width___ exp.time_

42 omega 58.00 97.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -94.0000 -90.0000 39

#__ type_ start__ end____ width___ exp.time_

43 omega 61.00 109.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -94.0000 30.0000 48

#__ type_ start__ end____ width___ exp.time_

44 omega 40.00 72.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -45.0000 -60.0000 32

#__ type_ start__ end____ width___ exp.time_

45 omega 41.00 67.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -30.0000 120.0000 26

#__ type_ start__ end____ width___ exp.time_

46 omega 75.00 101.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -94.0000 -150.0000 26

#__ type_ start__ end____ width___ exp.time_

47 omega 65.00 124.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -61.0000 120.0000 59

#__ type_ start__ end____ width___ exp.time_

48 omega 38.00 103.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- 108.3609 -94.0000 -30.0000 65

#__ type_ start__ end____ width___ exp.time_

49 omega -124.00 -79.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

- -41.3256 -99.0000 90.0000 45

#__ type_ start__ end____ width___ exp.time_

50 omega -99.00 -2.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

- -41.3256 125.0000 -30.0000 97

#__ type_ start__ end____ width___ exp.time_

51 omega -124.00 -79.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

- -41.3256 -99.0000 -120.0000 45

#__ type_ start__ end____ width___ exp.time_

52 omega -120.00 -8.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

- -41.3256 -77.0000 0.0000 112

#__ type_ start__ end____ width___ exp.time_

53 omega -115.00 -12.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

- -41.3256 -57.0000 -60.0000 103

#__ type_ start__ end____ width___ exp.time_

54 omega 8.00 120.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

- 41.3256 77.0000 -30.0000 112

#__ type_ start__ end____ width___ exp.time_

55 omega 8.00 120.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

- 41.3256 77.0000 -150.0000 112

#__ type_ start__ end____ width___ exp.time_

56 omega 12.00 115.00 1.0000 1.5000

omega____ theta____ kappa____ phi_____ frames

- 41.3256 57.0000 -90.0000 103

#__ type_ start__ end____ width___ exp.time_

57 omega -162.00 -78.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

- -83.0000 -77.0000 -60.0000 84

#__ type_ start__ end____ width___ exp.time_

58 omega -162.00 -49.00 1.0000 10.0000

omega____ theta____ kappa____ phi_____ frames

```
   -      -83.0000  -77.0000 -120.0000 113
#__ type_ start__ end____ width___ exp.time_
 59 omega   34.00   77.00   1.0000   10.0000
omega____ theta____ kappa____ phi______ frames
   -      108.3609  -45.0000 -180.0000 43
#__ type_ start__ end____ width___ exp.time_
 60 omega   81.00  158.00   1.0000   10.0000
omega____ theta____ kappa____ phi______ frames
   -      108.3609   45.0000    0.0000 77
#__ type_ start__ end____ width___ exp.time_
 61 omega   78.00  158.00   1.0000   10.0000
omega____ theta____ kappa____ phi______ frames
   -      108.3609   30.0000  -60.0000 80
#------------------------------------------------------------------------------#
#                  COMPUTER PROGRAMS USED                                      #
#------------------------------------------------------------------------------#
_computing_data_collection       'CrysAlis Pro (Oxford Diffraction Ltd., 2011)'
_computing_cell_refinement       'CrysAlis Pro (Oxford Diffraction Ltd., 2011)'
_computing_data_reduction        'CrysAlis Pro (Oxford Diffraction Ltd., 2011)'
_computing_structure_solution    'OLEX2 (Dolomanov et al, 2009)'
_computing_structure_refinement  'SHELXL-97 (Sheldrick, 2008)'
_computing_molecular_graphics    'Diamond v.3.2f (Crystal Impact GbR, 2008)'
_computing_publication_material  'WinGX publication routines (Farrugia, 1999)'
#------------------------------------------------------------------------------#
#                  STRUCTURE SOLUTION
#------------------------------------------------------------------------------#
_atom_sites_solution_primary     direct
```

_atom_sites_solution_hydrogens geom

#---#

REFINEMENT INFORMATION

#---#

_refine_special_details

Refinement of F^2^ against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2^, conventional R-factors R are based on F, with F set to zero for negative F^2^. The threshold expression of F^2^ > 2\s(F^2^) is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2^ are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

Refined as a 2-component twin.

loop_

_diffrn_oxdiff_twin_id

_diffrn_oxdiff_twin_ratio

_diffrn_oxdiff_twin_reflns_isolated

_diffrn_oxdiff_twin_reflns_overlapped

1 0.5812 10988 27401

2 0.4188 10925 27401

loop_

_cell_oxdiff_twin_id

_cell_oxdiff_twin_matrix_11

_cell_oxdiff_twin_matrix_12

_cell_oxdiff_twin_matrix_13

_cell_oxdiff_twin_matrix_21

_cell_oxdiff_twin_matrix_22

_cell_oxdiff_twin_matrix_23

_cell_oxdiff_twin_matrix_31

_cell_oxdiff_twin_matrix_32

_cell_oxdiff_twin_matrix_33

1 1.0000 0.0000 0.0000 0.0000 1.0000 0.0000 0.0000 0.0000 1.0000

2 1.0003 -0.0001 0.0002 -0.0016 -0.9996 -0.0005 -0.1710 0.0021 -0.9997

_refine_ls_structure_factor_coef Fsqd

_refine_ls_matrix_type full

_refine_ls_weighting_scheme calc

_refine_ls_weighting_details

'w=1/[\s^2^(Fo^2^)+(0.0946P)^2^+1.8635P] where P=(Fo^2^+2Fc^2^)/3'

_refine_ls_hydrogen_treatment constr

_refine_ls_extinction_method none

_refine_ls_number_reflns 11647

_refine_ls_number_parameters 550

_refine_ls_number_restraints 7

_refine_ls_R_factor_all 0.0555

_refine_ls_R_factor_gt 0.0529

_refine_ls_wR_factor_ref 0.1547

_refine_ls_wR_factor_gt 0.1522

_refine_ls_goodness_of_fit_ref 1.07

_refine_ls_restrained_S_all 1.071

_refine_ls_shift/su_max 0

_refine_ls_shift/su_mean 0

_refine_ls_abs_structure_details

The Friedel pair coverage of the experiment is almost complete (98%).

Analysis of the absolute structure using likelihood methods

(Hooft, Straver & Spek, 2008) was performed using OLEX2 (Dolomanov, 2009). The results indicated that the absolute structure had been correctly assigned. The method calculated that the probability that the structure is inverted is smaller than 10-99. The absolute structure parameter y (Hooft, Straver & Spek, 2008) was calculated using OLEX2 (Dolomanov, 2009). The resulting value was y=0.019(2), which together with Flack parameter value, indicate that the absolute structure has sureley been determined correctly.

Flack, H. D. (1983), Acta Cryst. A39, 876-881

Flack & G. Bernardinelli, Acta Cryst. 1999, A55, 908-915;

H. D. Flack & G. Bernardinelli, J. Appl. Cryst. 2000, 33, 1143-1148.

Dolomanov, O.V., J. Appl. Cryst., 2009, 42, 339-341.

R. W. W. Hooft, L. H. Straver & A. L. Spek, J. Appl. Cryst. 2008, 41, 96-103

A. L. Spek (2010) PLATON, Utrecht, The Netherlands;

A. L. Spek, J. Appl. Cryst. 2003, 36, 7-13

A. L. Thompson & D. J. Watkin, Tetrahedron: Asymmetry 2009, 20, 712--717

_refine_ls_abs_structure_Flack 0.036(17)

_refine_diff_density_max 0.494

_refine_diff_density_min -0.39

_refine_diff_density_rms 0.065

#---#

ATOMIC TYPES, COORDINATES AND THERMAL PARAMETERS

#---#

loop_

_atom_type_symbol

_atom_type_description

_atom_type_scat_dispersion_real

_atom_type_scat_dispersion_imag

_atom_type_scat_source

C C 0.0181 0.0091 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

H H 0 0 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

Cl Cl 0.3639 0.7018 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

N N 0.0311 0.018 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

O O 0.0492 0.0322 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

loop_

_atom_site_label

_atom_site_type_symbol

_atom_site_fract_x

_atom_site_fract_y

_atom_site_fract_z

_atom_site_U_iso_or_equiv

_atom_site_adp_type

_atom_site_occupancy

_atom_site_calc_flag

_atom_site_disorder_assembly

_atom_site_disorder_group

Cl1A Cl 0.9830(2) 0.38959(16) 0.22666(7) 0.0328(4) Uani 1 d . .

O1A O 0.1629(6) 0.8361(4) 0.06324(18) 0.0241(9) Uani 1 d . .

H1A H 0.0604 0.8551 0.0566 0.036 Uiso 1 calc . .

O2A O 0.5386(6) 0.7662(4) 0.06654(17) 0.0252(9) Uani 1 d . .

O3A O 0.5063(6) 0.8190(5) 0.15558(19) 0.0293(10) Uani 1 d . .

O4A O 0.1790(5) 0.3885(4) -0.02760(17) 0.0251(9) Uani 1 d . .

H4A H 0.2649 0.3501 -0.038 0.038 Uiso 1 calc . .

O5A O -0.2260(8) 0.6087(8) -0.2029(2) 0.063(2) Uani 1 d . .

O6A O -0.4249(7) 0.6290(6) -0.1432(2) 0.0438(14) Uani 1 d . .

N1A N 0.1754(7) 0.7066(5) 0.0708(2) 0.0208(10) Uani 1 d . .

N2A N -0.2722(9) 0.6204(6) -0.1553(3) 0.0372(15) Uani 1 d . .

C1A C 0.3006(8) 0.6825(5) 0.1163(2) 0.0190(12) Uani 1 d . .

C2A C 0.3354(8) 0.5459(5) 0.1046(2) 0.0195(12) Uani 1 d . .

H2A H 0.2387 0.5008 0.1212 0.023 Uiso 1 calc . .

C3A C 0.3142(7) 0.5291(6) 0.0405(2) 0.0192(12) Uani 1 d . .

H3A H 0.4287 0.5154 0.0242 0.023 Uiso 1 calc . .

C4A C 0.2403(8) 0.6529(6) 0.0193(2) 0.0221(12) Uani 1 d . .

H4AA H 0.3362 0.7037 0.0057 0.026 Uiso 1 calc . .

C5A C 0.4633(8) 0.7594(6) 0.1095(2) 0.0217(12) Uani 1 d . .

C6A C 0.6535(8) 0.9009(7) 0.1527(3) 0.0306(14) Uani 1 d . .

H6AA H 0.6464 0.9621 0.1826 0.037 Uiso 1 calc . .

H6AB H 0.6489 0.9437 0.1164 0.037 Uiso 1 calc . .

C7A C 0.8212(9) 0.8353(7) 0.1588(3) 0.0333(15) Uani 1 d . .

H7AA H 0.8311 0.777 0.1283 0.05 Uiso 1 calc . .

H7AB H 0.8263 0.7926 0.1946 0.05 Uiso 1 calc . .

H7AC H 0.9153 0.8934 0.1574 0.05 Uiso 1 calc . .

C8A C 0.2221(8) 0.7014(6) 0.1728(3) 0.0247(13) Uani 1 d . .

H8AA H 0.1964 0.7872 0.1779 0.037 Uiso 1 calc . .

H8AB H 0.3029 0.6748 0.2023 0.037 Uiso 1 calc . .

H8AC H 0.1164 0.6544 0.1748 0.037 Uiso 1 calc . .

C9A C 0.4970(8) 0.4955(6) 0.1321(3) 0.0238(13) Uani 1 d . .

C10A C 0.6575(8) 0.5161(6) 0.1095(3) 0.0242(13) Uani 1 d . .

H10A H 0.6649 0.5552 0.0744 0.029 Uiso 1 calc . .

C11A C 0.8061(8) 0.4801(6) 0.1380(3) 0.0252(13) Uani 1 d . .

H11A H 0.9148 0.4928 0.1224 0.03 Uiso 1 calc . .

C12A C 0.7924(10) 0.4257(6) 0.1892(3) 0.0281(15) Uani 1 d . .

C13A C 0.6398(8) 0.3983(7) 0.2115(3) 0.0266(14) Uani 1 d . .

H13A H 0.6337 0.355 0.2456 0.032 Uiso 1 calc . .

C14A C 0.4929(9) 0.4360(6) 0.1827(3) 0.0262(14) Uani 1 d . .

H14A H 0.3851 0.4201 0.1983 0.031 Uiso 1 calc . .

C15A C 0.2008(8) 0.4190(6) 0.0294(3) 0.0247(13) Uani 1 d . .

H15A H 0.2512 0.3489 0.0495 0.03 Uiso 1 calc . .

H15B H 0.0871 0.4344 0.0449 0.03 Uiso 1 calc . .

C16A C 0.1019(8) 0.6457(5) -0.0259(3) 0.0215(12) Uani 1 d . .

C17A C 0.1436(8) 0.6634(6) -0.0810(3) 0.0248(13) Uani 1 d . .

H17A H 0.2582 0.6826 -0.0895 0.03 Uiso 1 calc . .

C18A C 0.0236(9) 0.6539(6) -0.1237(3) 0.0270(13) Uani 1 d . .

H18A H 0.0544 0.665 -0.1614 0.032 Uiso 1 calc . .

C19A C -0.1441(9) 0.6277(6) -0.1102(3) 0.0264(14) Uani 1 d . .

C20A C -0.1928(8) 0.6122(6) -0.0556(3) 0.0243(13) Uani 1 d . .

H20A H -0.3082 0.5951 -0.0473 0.029 Uiso 1 calc . .

C21A C -0.0690(9) 0.6222(6) -0.0136(3) 0.0249(13) Uani 1 d . .

H21A H -0.1002 0.6131 0.0242 0.03 Uiso 1 calc . .

Cl1B Cl 0.8802(2) 1.08214(18) 0.27585(7) 0.0390(4) Uani 1 d . .

O1B O 0.1217(7) 0.6038(4) 0.4369(2) 0.0354(11) Uani 1 d . .

H1B H 0.0193 0.5809 0.4354 0.053 Uiso 1 calc . .

O2B O 0.4895(6) 0.6726(5) 0.43339(19) 0.0333(11) Uani 1 d . .

O3B O 0.4689(7) 0.6713(5) 0.3404(2) 0.0398(13) Uani 1 d . .

O4B O 0.2088(6) 1.0433(4) 0.54133(18) 0.0291(10) Uani 1 d . .

H4B H 0.3036 1.0753 0.5493 0.044 Uiso 1 calc . .

O5B O -0.4885(8) 0.8470(7) 0.6252(2) 0.0558(18) Uani 1 d . .

O6B O -0.3026(7) 0.8364(7) 0.6926(2) 0.0478(15) Uani 1 d . .

N1B N 0.1283(7) 0.7330(5) 0.4319(2) 0.0265(12) Uani 1 d . .

N2B N -0.3404(8) 0.8366(6) 0.6431(2) 0.0349(14) Uani 1 d . .

C1B C 0.2413(9) 0.7637(7) 0.3868(3) 0.0276(14) Uani 1 d . .

C2B C 0.2757(8) 0.8995(6) 0.4011(3) 0.0259(13) Uani 1 d . .

H2B H 0.1724 0.9453 0.3877 0.031 Uiso 1 calc . .

C3B C 0.2778(8) 0.9047(7) 0.4655(2) 0.0268(13) Uani 1 d . .

H3B H 0.3996 0.9049 0.4793 0.032 Uiso 1 calc . .

C4B C 0.1931(9) 0.7850(6) 0.4847(3) 0.0269(14) Uani 1 d . .

H4BA H 0.2837 0.7307 0.5009 0.032 Uiso 1 calc . .

C5B C 0.4118(10) 0.6943(6) 0.3902(3) 0.0311(15) Uani 1 d . .

C6B C 0.6482(11) 0.6307(8) 0.3357(3) 0.045(2) Uani 1 d . .

H6BA H 0.7204 0.6651 0.3663 0.054 Uiso 1 calc . .

H6BB H 0.6551 0.5416 0.3377 0.054 Uiso 1 calc . .

C7B C 0.7059(10) 0.6741(8) 0.2811(3) 0.0386(17) Uani 1 d . .

H7BA H 0.6298 0.6425 0.2514 0.058 Uiso 1 calc . .

H7BB H 0.8228 0.6461 0.2752 0.058 Uiso 1 calc . .

H7BC H 0.7033 0.7625 0.2804 0.058 Uiso 1 calc . .

C8B C 0.1480(9) 0.7468(7) 0.3314(3) 0.0343(16) Uani 1 d . .

H8BA H 0.1269 0.6607 0.325 0.051 Uiso 1 calc . .

H8BB H 0.2178 0.7788 0.3015 0.051 Uiso 1 calc . .

H8BC H 0.0388 0.79 0.3317 0.051 Uiso 1 calc . .

C9B C 0.4266(9) 0.9549(6) 0.3729(3) 0.0244(14) Uani 1 d . .

C10B C 0.5940(9) 0.9410(7) 0.3942(3) 0.0301(15) Uani 1 d . .

H10B H 0.6127 0.9019 0.4291 0.036 Uiso 1 calc . .

C11B C 0.7330(9) 0.9834(7) 0.3653(3) 0.0300(14) Uani 1 d . .

H11B H 0.846 0.9749 0.3802 0.036 Uiso 1 calc . .

C12B C 0.7031(10) 1.0382(6) 0.3142(3) 0.0303(14) Uani 1 d . .

C13B C 0.5435(10) 1.0565(6) 0.2930(3) 0.0303(14) Uani 1 d . .

H13B H 0.5258 1.0975 0.2585 0.036 Uiso 1 calc . .

C14B C 0.4059(9) 1.0141(6) 0.3225(3) 0.0270(14) Uani 1 d . .

H14B H 0.2935 1.0263 0.3076 0.032 Uiso 1 calc . .

C15B C 0.1952(9) 1.0231(6) 0.4834(3) 0.0288(14) Uani 1 d . .

H15C H 0.2502 1.0908 0.4638 0.035 Uiso 1 calc . .

H15D H 0.0728 1.0221 0.4717 0.035 Uiso 1 calc . .

C16B C 0.0515(9) 0.7971(6) 0.5259(3) 0.0276(14) Uani 1 d . .

C17B C -0.1158(9) 0.8209(7) 0.5085(3) 0.0295(15) Uani 1 d . .

H17B H -0.1423 0.8292 0.4698 0.035 Uiso 1 calc . .

C18B C -0.2444(9) 0.8329(7) 0.5463(3) 0.0298(14) Uani 1 d . .

H18B H -0.3586 0.8479 0.5337 0.036 Uiso 1 calc . .

C19B C -0.2062(9) 0.8231(6) 0.6024(3) 0.0295(15) Uani 1 d . .

C20B C -0.0400(9) 0.7982(7) 0.6215(3) 0.0300(15) Uani 1 d . .

H20B H -0.0148 0.7901 0.6603 0.036 Uiso 1 calc . .

C21B C 0.0872(8) 0.7856(6) 0.5834(3) 0.0260(13) Uani 1 d . .

H21B H 0.2008 0.7689 0.5961 0.031 Uiso 1 calc . .

loop_

_atom_site_aniso_label

_atom_site_aniso_U_11

_atom_site_aniso_U_22

_atom_site_aniso_U_33

_atom_site_aniso_U_23

_atom_site_aniso_U_13

_atom_site_aniso_U_12

Cl1A 0.0212(8) 0.0372(9) 0.0395(8) 0.0056(7) -0.0090(6) 0.0045(7)

O1A 0.022(2) 0.015(2) 0.036(2) 0.0000(17) -0.0015(19) 0.0036(18)

O2A 0.021(2) 0.028(2) 0.027(2) 0.0008(17) 0.0002(17) -0.0056(19)

O3A 0.022(3) 0.035(3) 0.032(2) -0.007(2) 0.0009(17) -0.006(2)

O4A 0.020(2) 0.026(2) 0.029(2) -0.0040(18) -0.0007(17) 0.005(2)

O5A 0.047(4) 0.107(6) 0.034(3) -0.011(3) -0.010(3) -0.015(4)

O6A 0.025(3) 0.055(4) 0.051(3) 0.000(3) -0.012(2) -0.001(3)

N1A 0.014(3) 0.017(2) 0.031(3) 0.0005(19) -0.001(2) 0.000(2)

N2A 0.038(4) 0.040(4) 0.033(3) -0.003(3) -0.013(3) -0.005(3)

C1A 0.014(3) 0.019(3) 0.024(3) 0.002(2) 0.000(2) -0.001(2)

C2A 0.010(3) 0.018(3) 0.030(3) 0.003(2) 0.003(2) -0.001(2)

C3A 0.006(3) 0.020(3) 0.031(3) 0.002(2) 0.000(2) 0.004(2)

C4A 0.016(3) 0.021(3) 0.029(3) -0.001(2) 0.000(2) 0.000(2)

C5A 0.021(3) 0.018(3) 0.026(3) 0.000(2) -0.003(2) 0.007(2)

C6A 0.015(3) 0.030(3) 0.047(4) -0.011(3) -0.003(3) -0.007(3)

C7A 0.024(4) 0.034(4) 0.041(4) 0.000(3) -0.002(3) -0.001(3)

C8A 0.016(3) 0.027(3) 0.031(3) -0.002(3) 0.000(2) 0.002(3)

C9A 0.026(4) 0.024(3) 0.022(3) 0.000(2) 0.000(2) -0.002(3)

C10A 0.015(3) 0.029(3) 0.029(3) 0.004(2) 0.000(2) -0.001(2)

C11A 0.010(3) 0.033(3) 0.032(3) 0.001(3) -0.001(2) -0.002(2)

C12A 0.037(4) 0.019(3) 0.028(3) 0.001(2) -0.007(3) 0.009(3)

C13A 0.018(3) 0.035(4) 0.027(3) 0.011(3) -0.003(2) -0.002(3)

C14A 0.022(4) 0.023(3) 0.033(3) 0.001(2) 0.000(3) 0.000(3)

C15A 0.020(3) 0.026(3) 0.028(3) 0.000(2) 0.000(2) 0.001(2)

C16A 0.020(3) 0.018(3) 0.026(3) 0.001(2) -0.003(2) 0.001(2)

C17A 0.018(3) 0.027(3) 0.029(3) 0.000(2) 0.000(2) 0.003(3)

C18A 0.031(4) 0.027(3) 0.023(3) -0.002(2) 0.001(3) -0.002(3)

C19A 0.025(4) 0.022(3) 0.031(3) -0.003(2) -0.007(3) -0.001(3)

C20A 0.016(3) 0.022(3) 0.035(3) 0.000(2) -0.001(2) -0.001(2)

C21A 0.025(3) 0.025(3) 0.025(3) 0.000(2) 0.000(2) 0.005(3)

Cl1B 0.0352(10) 0.0506(11) 0.0315(8) 0.0038(7) 0.0046(7) -0.0162(8)

O1B 0.033(3) 0.023(2) 0.050(3) 0.000(2) 0.011(2) -0.001(2)

O2B 0.025(2) 0.038(3) 0.037(2) 0.002(2) 0.005(2) 0.013(2)

O3B 0.039(3) 0.047(3) 0.034(2) -0.001(2) 0.008(2) 0.018(3)

O4B 0.027(3) 0.028(2) 0.032(2) -0.0069(19) 0.0034(19) -0.004(2)

O5B 0.026(3) 0.098(5) 0.043(3) -0.008(3) 0.007(2) 0.001(3)

O6B 0.031(3) 0.082(4) 0.030(3) -0.009(3) 0.009(2) -0.008(3)

N1B 0.023(3) 0.025(3) 0.032(3) 0.000(2) 0.007(2) 0.001(2)

N2B 0.024(3) 0.047(4) 0.034(3) -0.006(3) 0.006(2) -0.003(3)

C1B 0.023(3) 0.032(4) 0.027(3) 0.000(3) 0.002(3) -0.001(3)

C2B 0.021(3) 0.024(3) 0.032(3) 0.004(3) 0.000(2) 0.006(3)

C3B 0.022(3) 0.033(4) 0.026(3) 0.000(3) 0.000(2) 0.003(3)

C4B 0.022(3) 0.030(3) 0.028(3) 0.001(3) 0.000(3) 0.005(3)

C5B 0.041(4) 0.027(4) 0.026(3) 0.002(3) 0.005(3) -0.005(3)

C6B 0.045(5) 0.046(5) 0.044(4) 0.004(3) 0.003(4) 0.018(4)

C7B 0.026(4) 0.044(4) 0.046(4) -0.003(3) 0.007(3) -0.002(3)

C8B 0.029(4) 0.039(4) 0.034(3) -0.007(3) -0.001(3) 0.000(3)

C9B 0.023(4) 0.027(3) 0.023(3) -0.003(2) 0.002(2) 0.002(3)

C10B 0.030(4) 0.036(4) 0.024(3) 0.009(3) 0.000(3) 0.003(3)

C11B 0.021(4) 0.033(4) 0.036(3) 0.004(3) -0.002(3) 0.002(3)

C12B 0.040(3) 0.028(3) 0.023(3) 0.002(2) 0.000(2) -0.004(3)

C13B 0.038(3) 0.031(4) 0.022(3) 0.004(2) -0.001(2) 0.002(3)

C14B 0.025(3) 0.029(3) 0.027(3) 0.002(2) -0.005(3) 0.005(3)

C15B 0.028(4) 0.023(3) 0.035(3) -0.001(3) 0.003(3) 0.000(3)

C16B 0.029(4) 0.025(3) 0.029(3) -0.002(2) 0.004(3) -0.003(3)

C17B 0.027(4) 0.037(4) 0.025(3) 0.003(3) -0.002(2) 0.003(3)

C18B 0.016(3) 0.041(4) 0.032(3) 0.001(3) -0.002(3) -0.002(3)

C19B 0.031(4) 0.028(4) 0.029(3) -0.001(3) 0.003(3) -0.006(3)

C20B 0.026(4) 0.040(4) 0.024(3) 0.000(3) -0.001(2) -0.004(3)

C21B 0.015(3) 0.032(3) 0.031(3) 0.001(3) -0.001(2) 0.001(3)

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MOLECULAR GEOMETRY

#---#

_geom_special_details

All esds (except the esd in the dihedral angle between two l.s. planes)
are estimated using the full covariance matrix. The cell esds are taken
into account individually in the estimation of esds in distances, angles
and torsion angles; correlations between esds in cell parameters are only
used when they are defined by crystal symmetry. An approximate (isotropic)
treatment of cell esds is used for estimating esds involving l.s. planes.

loop_

_geom_bond_atom_site_label_1

_geom_bond_atom_site_label_2

_geom_bond_distance

_geom_bond_site_symmetry_2

_geom_bond_publ_flag

Cl1A C12A 1.766(7) . ?

O1A H1A 0.84 . ?

O1A N1A 1.449(6) . ?

O2A C5A 1.204(8) . ?

O3A C5A 1.324(7) . ?

O3A C6A 1.470(8) . ?

O4A H4A 0.84 . ?

O4A C15A 1.413(7) . ?

O5A N2A 1.215(9) . ?

O6A N2A 1.241(8) . ?

N1A C1A 1.470(7) . ?

N1A C4A 1.475(8) . ?

N2A C19A 1.455(8) . ?

C1A C2A 1.565(8) . ?

C1A C5A 1.544(9) . ?

C1A C8A 1.519(8) . ?

C2A H2A 1 . ?

C2A C3A 1.553(8) . ?

C2A C9A 1.517(9) . ?

C3A H3A 1 . ?

C3A C4A 1.568(8) . ?

C3A C15A 1.528(8) . ?

C4A H4AA 1 . ?

C4A C16A 1.514(8) . ?

C6A H6AA 0.99 . ?

C6A H6AB 0.99 . ?

C6A C7A 1.504(10) . ?

C7A H7AA 0.98 . ?

C7A H7AB 0.98 . ?

C7A H7AC 0.98 . ?

C8A H8AA 0.98 . ?

C8A H8AB 0.98 . ?

C8A H8AC 0.98 . ?

C9A C10A 1.400(9) . ?

C9A C14A 1.382(9) . ?

C10A H10A 0.95 . ?

C10A C11A 1.390(9) . ?

C11A H11A 0.95 . ?

C11A C12A 1.375(9) . ?

C12A C13A 1.357(10) . ?

C13A H13A 0.95 . ?

C13A C14A 1.390(9) . ?

C14A H14A 0.95 . ?

C15A H15A 0.99 . ?

C15A H15B 0.99 . ?

C16A C17A 1.383(9) . ?

C16A C21A 1.402(9) . ?

C17A H17A 0.95 . ?

C17A C18A 1.374(9) . ?

C18A H18A 0.95 . ?

C18A C19A 1.392(10) . ?

C19A C20A 1.386(9) . ?

C20A H20A 0.95 . ?

C20A C21A 1.383(9) . ?

C21A H21A 0.95 . ?

Cl1B C12B 1.754(8) . ?

O1B H1B 0.84 . ?

O1B N1B 1.438(7) . ?

O2B C5B 1.212(8) . ?

O3B C5B 1.312(8) . ?

O3B C6B 1.481(9) . ?

O4B H4B 0.84 . ?

O4B C15B 1.410(8) . ?

O5B N2B 1.231(8) . ?

O6B N2B 1.215(8) . ?

N1B C1B 1.458(8) . ?

N1B C4B 1.468(8) . ?

N2B C19B 1.462(9) . ?

C1B C2B 1.565(10) . ?

C1B C5B 1.540(10) . ?

C1B C8B 1.511(9) . ?

C2B H2B 1 . ?

C2B C3B 1.547(8) . ?

C2B C9B 1.508(9) . ?

C3B H3B 1 . ?

C3B C4B 1.559(10) . ?

C3B C15B 1.529(10) . ?

C4B H4BA 1 . ?

C4B C16B 1.512(9) . ?

C6B H6BA 0.99 . ?

C6B H6BB 0.99 . ?

C6B C7B 1.480(11) . ?

C7B H7BA 0.98 . ?

C7B H7BB 0.98 . ?

C7B H7BC 0.98 . ?

C8B H8BA 0.98 . ?

C8B H8BB 0.98 . ?

C8B H8BC 0.98 . ?

C9B C10B 1.401(9) . ?

C9B C14B 1.380(9) . ?

C10B H10B 0.95 . ?

C10B C11B 1.389(10) . ?

C11B H11B 0.95 . ?

C11B C12B 1.381(9) . ?

C12B C13B 1.351(10) . ?

C13B H13B 0.95 . ?

C13B C14B 1.388(10) . ?

C14B H14B 0.95 . ?

C15B H15C 0.99 . ?

C15B H15D 0.99 . ?

C16B C17B 1.389(9) . ?

C16B C21B 1.404(9) . ?

C17B H17B 0.95 . ?

C17B C18B 1.381(10) . ?

C18B H18B 0.95 . ?

C18B C19B 1.373(9) . ?

C19B C20B 1.395(10) . ?

C20B H20B 0.95 . ?

C20B C21B 1.379(9) . ?

C21B H21B 0.95 . ?

loop_

_geom_angle_atom_site_label_1

_geom_angle_atom_site_label_2

_geom_angle_atom_site_label_3

_geom_angle

_geom_angle_site_symmetry_1

_geom_angle_site_symmetry_3

_geom_angle_publ_flag

N1A O1A H1A 109.5 . . ?

C5A O3A C6A 116.8(5) . . ?

C15A O4A H4A 109.5 . . ?

O1A N1A C1A 108.3(4) . . ?

O1A N1A C4A 108.5(4) . . ?

C1A N1A C4A 108.1(5) . . ?

O5A N2A O6A 122.7(6) . . ?

O5A N2A C19A 119.1(7) . . ?

O6A N2A C19A 118.1(6) . . ?

N1A C1A C2A 99.1(5) . . ?

N1A C1A C5A 110.8(5) . . ?

N1A C1A C8A 111.1(5) . . ?

C5A C1A C2A 111.5(5) . . ?

C8A C1A C2A 111.8(5) . . ?

C8A C1A C5A 111.9(5) . . ?

C1A C2A H2A 105.9 . . ?

C3A C2A C1A 106.2(5) . . ?

C3A C2A H2A 105.9 . . ?

C9A C2A C1A 115.2(5) . . ?

C9A C2A H2A 105.9 . . ?

C9A C2A C3A 116.9(5) . . ?

C2A C3A H3A 109.4 . . ?

C2A C3A C4A 104.1(5) . . ?

C4A C3A H3A 109.4 . . ?

C15A C3A C2A 108.3(5) . . ?

C15A C3A H3A 109.4 . . ?

C15A C3A C4A 115.8(5) . . ?

N1A C4A C3A 102.3(5) . . ?

N1A C4A H4AA 109 . . ?

N1A C4A C16A 111.4(5) . . ?

C3A C4A H4AA 109 . . ?

C16A C4A C3A 115.9(5) . . ?

C16A C4A H4AA 109 . . ?

O2A C5A O3A 124.3(6) . . ?

O2A C5A C1A 123.4(5) . . ?

O3A C5A C1A 112.3(5) . . ?

O3A C6A H6AA 109.1 . . ?

O3A C6A H6AB 109.1 . . ?

O3A C6A C7A 112.3(6) . . ?

H6AA C6A H6AB 107.9 . . ?

C7A C6A H6AA 109.1 . . ?

C7A C6A H6AB 109.1 . . ?

C6A C7A H7AA 109.5 . . ?

C6A C7A H7AB 109.5 . . ?

C6A C7A H7AC 109.5 . . ?

H7AA C7A H7AB 109.5 . . ?

H7AA C7A H7AC 109.5 . . ?

H7AB C7A H7AC 109.5 . . ?

C1A C8A H8AA 109.5 . . ?

C1A C8A H8AB 109.5 . . ?

C1A C8A H8AC 109.5 . . ?

H8AA C8A H8AB 109.5 . . ?

H8AA C8A H8AC 109.5 . . ?

H8AB C8A H8AC 109.5 . . ?

C10A C9A C2A 121.2(6) . . ?

C14A C9A C2A 121.2(6) . . ?

C14A C9A C10A 117.4(6) . . ?

C9A C10A H10A 119.6 . . ?

C11A C10A C9A 120.7(6) . . ?

C11A C10A H10A 119.6 . . ?

C10A C11A H11A 120.7 . . ?

C12A C11A C10A 118.6(6) . . ?

C12A C11A H11A 120.7 . . ?

C11A C12A Cl1A 117.9(6) . . ?

C13A C12A Cl1A 119.2(5) . . ?

C13A C12A C11A 122.8(6) . . ?

C12A C13A H13A 121.3 . . ?

C12A C13A C14A 117.5(6) . . ?

C14A C13A H13A 121.3 . . ?

C9A C14A C13A 122.7(7) . . ?

C9A C14A H14A 118.6 . . ?

C13A C14A H14A 118.6 . . ?

O4A C15A C3A 114.4(5) . . ?

O4A C15A H15A 108.7 . . ?

O4A C15A H15B 108.7 . . ?

C3A C15A H15A 108.7 . . ?

C3A C15A H15B 108.7 . . ?

H15A C15A H15B 107.6 . . ?

C17A C16A C4A 119.6(6) . . ?

C17A C16A C21A 118.7(6) . . ?

C21A C16A C4A 121.8(6) . . ?

C16A C17A H17A 119.1 . . ?

C18A C17A C16A 121.8(6) . . ?

C18A C17A H17A 119.1 . . ?

C17A C18A H18A 120.9 . . ?

C17A C18A C19A 118.2(6) . . ?

C19A C18A H18A 120.9 . . ?

C18A C19A N2A 118.3(6) . . ?

C20A C19A N2A 119.5(6) . . ?

C20A C19A C18A 122.1(6) . . ?

C19A C20A H20A 120.8 . . ?

C21A C20A C19A 118.3(6) . . ?

C21A C20A H20A 120.8 . . ?

C16A C21A H21A 119.5 . . ?

C20A C21A C16A 120.9(6) . . ?

C20A C21A H21A 119.5 . . ?

N1B O1B H1B 109.5 . . ?

C5B O3B C6B 118.4(6) . . ?

C15B O4B H4B 109.5 . . ?

O1B N1B C1B 108.5(5) . . ?

O1B N1B C4B 109.4(5) . . ?

C1B N1B C4B 110.3(5) . . ?

O5B N2B C19B 117.6(6) . . ?

O6B N2B O5B 122.8(6) . . ?

O6B N2B C19B 119.6(6) . . ?

N1B C1B C2B 99.6(5) . . ?

N1B C1B C5B 112.8(5) . . ?

N1B C1B C8B 109.6(6) . . ?

C5B C1B C2B 109.0(6) . . ?

C8B C1B C2B 112.8(6) . . ?

C8B C1B C5B 112.4(6) . . ?

C1B C2B H2B 106.6 . . ?

C3B C2B C1B 104.5(5) . . ?

C3B C2B H2B 106.6 . . ?

C9B C2B C1B 115.2(5) . . ?

C9B C2B H2B 106.6 . . ?

C9B C2B C3B 116.5(5) . . ?

C2B C3B H3B 108.3 . . ?

C2B C3B C4B 105.7(5) . . ?

C4B C3B H3B 108.3 . . ?

C15B C3B C2B 108.6(5) . . ?

C15B C3B H3B 108.3 . . ?

C15B C3B C4B 117.4(5) . . ?

N1B C4B C3B 102.6(5) . . ?

N1B C4B H4BA 108.9 . . ?

N1B C4B C16B 110.9(5) . . ?

C3B C4B H4BA 108.9 . . ?

C16B C4B C3B 116.3(6) . . ?

C16B C4B H4BA 108.9 . . ?

O2B C5B O3B 124.4(7) . . ?

O2B C5B C1B 123.8(6) . . ?

O3B C5B C1B 111.5(6) . . ?

O3B C6B H6BA 110.5 . . ?

O3B C6B H6BB 110.5 . . ?

H6BA C6B H6BB 108.7 . . ?

C7B C6B O3B 106.3(6) . . ?

C7B C6B H6BA 110.5 . . ?

C7B C6B H6BB 110.5 . . ?

C6B C7B H7BA 109.5 . . ?

C6B C7B H7BB 109.5 . . ?

C6B C7B H7BC 109.5 . . ?

H7BA C7B H7BB 109.5 . . ?

H7BA C7B H7BC 109.5 . . ?

H7BB C7B H7BC 109.5 . . ?

C1B C8B H8BA 109.5 . . ?

C1B C8B H8BB 109.5 . . ?

C1B C8B H8BC 109.5 . . ?

H8BA C8B H8BB 109.5 . . ?

H8BA C8B H8BC 109.5 . . ?

H8BB C8B H8BC 109.5 . . ?

C10B C9B C2B 121.9(6) . . ?

C14B C9B C2B 120.8(6) . . ?

C14B C9B C10B 117.2(6) . . ?

C9B C10B H10B 119.4 . . ?

C11B C10B C9B 121.2(6) . . ?

C11B C10B H10B 119.4 . . ?

C10B C11B H11B 120.8 . . ?

C12B C11B C10B 118.4(7) . . ?

C12B C11B H11B 120.8 . . ?

C11B C12B Cl1B 118.1(6) . . ?

C13B C12B Cl1B 119.8(5) . . ?

C13B C12B C11B 122.1(7) . . ?

C12B C13B H13B 120.7 . . ?

C12B C13B C14B 118.6(6) . . ?

C14B C13B H13B 120.7 . . ?

C9B C14B C13B 122.3(6) . . ?

C9B C14B H14B 118.9 . . ?

C13B C14B H14B 118.9 . . ?

O4B C15B C3B 113.1(6) . . ?

O4B C15B H15C 109 . . ?

O4B C15B H15D 109 . . ?

C3B C15B H15C 109 . . ?

C3B C15B H15D 109 . . ?

H15C C15B H15D 107.8 . . ?

C17B C16B C4B 121.5(6) . . ?

C17B C16B C21B 118.3(6) . . ?

C21B C16B C4B 120.3(6) . . ?

C16B C17B H17B 119.4 . . ?

C18B C17B C16B 121.2(6) . . ?

C18B C17B H17B 119.4 . . ?

C17B C18B H18B 120.2 . . ?

C19B C18B C17B 119.6(6) . . ?

C19B C18B H18B 120.2 . . ?

C18B C19B N2B 120.4(6) . . ?

C18B C19B C20B 120.9(7) . . ?

C20B C19B N2B 118.7(6) . . ?

C19B C20B H20B 120.5 . . ?

C21B C20B C19B 119.0(6) . . ?

C21B C20B H20B 120.5 . . ?

C16B C21B H21B 119.5 . . ?

C20B C21B C16B 121.0(6) . . ?

C20B C21B H21B 119.5 . . ?

loop_

_geom_torsion_atom_site_label_1

_geom_torsion_atom_site_label_2

_geom_torsion_atom_site_label_3

_geom_torsion_atom_site_label_4

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_geom_torsion_site_symmetry_2

_geom_torsion_site_symmetry_3

_geom_torsion_site_symmetry_4

_geom_torsion_publ_flag

Cl1A C12A C13A C14A 175.5(6) . . . . ?

O1A N1A C1A C2A -163.1(4) . . . . ?

O1A N1A C1A C5A -45.8(6) . . . . ?

O1A N1A C1A C8A 79.3(6) . . . . ?

O1A N1A C4A C3A 158.6(4) . . . . ?

O1A N1A C4A C16A -77.0(6) . . . . ?

O5A N2A C19A C18A 17.2(10) . . . . ?

O5A N2A C19A C20A -164.7(7) . . . . ?

O6A N2A C19A C18A -161.3(6) . . . . ?

O6A N2A C19A C20A 16.7(10) . . . . ?

N1A C1A C2A C3A 31.6(5) . . . . ?

N1A C1A C2A C9A 162.6(5) . . . . ?

N1A C1A C5A O2A -49.2(8) . . . . ?

N1A C1A C5A O3A 128.9(5) . . . . ?

N1A C4A C16A C17A 144.5(6) . . . . ?

N1A C4A C16A C21A -35.2(8) . . . . ?

N2A C19A C20A C21A -178.6(6) . . . . ?

C1A N1A C4A C3A 41.3(6) . . . . ?

C1A N1A C4A C16A 165.7(5) . . . . ?

C1A C2A C3A C4A -8.5(6) . . . . ?

C1A C2A C3A C15A -132.3(5) . . . . ?

C1A C2A C9A C10A -79.1(7) . . . . ?

C1A C2A C9A C14A 95.6(7) . . . . ?

C2A C1A C5A O2A 60.2(8) . . . . ?

C2A C1A C5A O3A -121.7(5) . . . . ?

C2A C3A C4A N1A -18.1(6) . . . . ?

C2A C3A C4A C16A -139.5(5) . . . . ?

C2A C3A C15A O4A -176.3(5) . . . . ?

C2A C9A C10A C11A 173.5(6) . . . . ?

C2A C9A C14A C13A -174.0(6) . . . . ?

C3A C2A C9A C10A 46.6(8) . . . . ?

C3A C2A C9A C14A -138.7(6) . . . . ?

C3A C4A C16A C17A -99.1(7) . . . . ?

C3A C4A C16A C21A 81.3(7) . . . . ?

C4A N1A C1A C2A -45.7(5) . . . . ?

C4A N1A C1A C5A 71.6(6) . . . . ?

C4A N1A C1A C8A -163.3(5) . . . . ?

C4A C3A C15A O4A 67.2(7) . . . . ?

C4A C16A C17A C18A 177.8(6) . . . . ?

C4A C16A C21A C20A -177.9(6) . . . . ?

C5A O3A C6A C7A -80.9(7) . . . . ?

C5A C1A C2A C3A -85.2(5) . . . . ?

C5A C1A C2A C9A 45.9(7) . . . . ?

C6A O3A C5A O2A 1.7(9) . . . . ?

C6A O3A C5A C1A -176.4(5) . . . . ?

C8A C1A C2A C3A 148.7(5) . . . . ?

C8A C1A C2A C9A -80.3(6) . . . . ?

C8A C1A C5A O2A -173.8(6) . . . . ?

C8A C1A C5A O3A 4.3(7) . . . . ?

C9A C2A C3A C4A -138.5(5) . . . . ?

C9A C2A C3A C15A 97.6(6) . . . . ?

C9A C10A C11A C12A -1.1(10) . . . . ?

C10A C9A C14A C13A 0.9(10) . . . . ?

C10A C11A C12A Cl1A -175.9(5) . . . . ?

C10A C11A C12A C13A 4.6(10) . . . . ?

C11A C12A C13A C14A -5.1(10) . . . . ?

C12A C13A C14A C9A 2.2(11) . . . . ?

C14A C9A C10A C11A -1.4(9) . . . . ?

C15A C3A C4A N1A 100.7(6) . . . . ?

C15A C3A C4A C16A -20.7(8) . . . . ?

C16A C17A C18A C19A 1.0(10) . . . . ?

C17A C16A C21A C20A 2.5(9) . . . . ?

C17A C18A C19A N2A 178.6(6) . . . . ?

C17A C18A C19A C20A 0.6(10) . . . . ?

C18A C19A C20A C21A -0.6(10) . . . . ?

C19A C20A C21A C16A -0.9(10) . . . . ?

C21A C16A C17A C18A -2.5(10) . . . . ?

Cl1B C12B C13B C14B 176.0(6) . . . . ?

O1B N1B C1B C2B -162.8(5) . . . . ?

O1B N1B C1B C5B -47.4(7) . . . . ?

O1B N1B C1B C8B 78.7(7) . . . . ?

O1B N1B C4B C3B 152.4(5) . . . . ?

O1B N1B C4B C16B -82.7(6) . . . . ?

O5B N2B C19B C18B 5.7(11) . . . . ?

O5B N2B C19B C20B -173.2(7) . . . . ?

O6B N2B C19B C18B -174.7(7) . . . . ?

O6B N2B C19B C20B 6.4(11) . . . . ?

N1B C1B C2B C3B 34.6(6) . . . . ?

N1B C1B C2B C9B 163.8(5) . . . . ?

N1B C1B C5B O2B -38.6(10) . . . . ?

N1B C1B C5B O3B 146.8(6) . . . . ?

N1B C4B C16B C17B -32.5(9) . . . . ?

N1B C4B C16B C21B 148.2(6) . . . . ?

N2B C19B C20B C21B -179.9(6) . . . . ?

C1B N1B C4B C3B 33.2(7) . . . . ?

C1B N1B C4B C16B 158.1(5) . . . . ?

C1B C2B C3B C4B -16.3(6) . . . . ?

C1B C2B C3B C15B -143.2(6) . . . . ?

C1B C2B C9B C10B -82.7(8) . . . . ?

C1B C2B C9B C14B 92.4(7) . . . . ?

C2B C1B C5B O2B 71.0(9) . . . . ?

C2B C1B C5B O3B -103.5(7) . . . . ?

C2B C3B C4B N1B -8.3(6) . . . . ?

C2B C3B C4B C16B -129.5(6) . . . . ?

C2B C3B C15B O4B -173.0(5) . . . . ?

C2B C9B C10B C11B 174.2(7) . . . . ?

C2B C9B C14B C13B -174.0(6) . . . . ?

C3B C2B C9B C10B 40.3(9) . . . . ?

C3B C2B C9B C14B -144.5(6) . . . . ?

C3B C4B C16B C17B 84.2(8) . . . . ?

C3B C4B C16B C21B -95.1(8) . . . . ?

C4B N1B C1B C2B -43.0(6) . . . . ?

C4B N1B C1B C5B 72.4(7) . . . . ?

C4B N1B C1B C8B -161.5(6) . . . . ?

C4B C3B C15B O4B 67.2(7) . . . . ?

C4B C16B C17B C18B -179.5(7) . . . . ?

C4B C16B C21B C20B 179.0(6) . . . . ?

C5B O3B C6B C7B -149.8(7) . . . . ?

C5B C1B C2B C3B -83.7(6) . . . . ?

C5B C1B C2B C9B 45.4(7) . . . . ?

C6B O3B C5B O2B -8.3(11) . . . . ?

C6B O3B C5B C1B 166.2(6) . . . . ?

C8B C1B C2B C3B 150.7(5) . . . . ?

C8B C1B C2B C9B -80.1(7) . . . . ?

C8B C1B C5B O2B -163.2(7) . . . . ?

C8B C1B C5B O3B 22.2(9) . . . . ?

C9B C2B C3B C4B -144.7(6) . . . . ?

C9B C2B C3B C15B 88.4(7) . . . . ?

C9B C10B C11B C12B -1.1(11) . . . . ?

C10B C9B C14B C13B 1.4(10) . . . . ?

C10B C11B C12B Cl1B -175.8(6) . . . . ?

C10B C11B C12B C13B 3.1(11) . . . . ?

C11B C12B C13B C14B -2.8(11) . . . . ?

C12B C13B C14B C9B 0.5(10) . . . . ?

C14B C9B C10B C11B -1.1(10) . . . . ?

C15B C3B C4B N1B 113.0(6) . . . . ?

C15B C3B C4B C16B -8.2(8) . . . . ?

C16B C17B C18B C19B 1.1(11) . . . . ?

C17B C16B C21B C20B -0.3(10) . . . . ?

C17B C18B C19B N2B 179.5(7) . . . . ?

C17B C18B C19B C20B -1.6(11) . . . . ?

C18B C19B C20B C21B 1.1(11) . . . . ?

C19B C20B C21B C16B -0.2(11) . . . . ?

C21B C16B C17B C18B -0.1(11) . . . . ?

_iucr_refine_instructions_details

a20160354_lp1252.res created by SHELXL-2014/7

TITL a20160354_lp1252_a.res in P2(1)

CELL 1.54184 7.8273 11.0828 23.9892 90 91.607 90

ZERR 4 0.0001 0.0002 0.0004 0 0.001 0

LATT -1

SYMM -X,0.5+Y,-Z

SFAC C H Cl N O

UNIT 84 92 4 8 24

RIGU 0.001 0.001 C12B C13B

```
RIGU 0.001 0.001 C11A C10A
L.S. 10
PLAN  20
TEMP -153
MORE -1
BOND $H
CONF
LIST 4
fmap 2
acta
MERG 0
OMIT -2 140
OMIT -1 -7 0
OMIT 3 -7 -2
REM <olex2.extras>
REM <HklSrc "%.\\a20160354_LP1252_twin1_hklf5.hkl">
REM </olex2.extras>
WGHT    0.094600    1.863500
BASF   0.38526
FVAR       4.01870
CL1A  3    0.982960    0.389589    0.226660    11.00000    0.02115    0.03721 =
       0.03949    0.00557   -0.00903    0.00452
O1A   5    0.162863    0.836066    0.063241    11.00000    0.02177    0.01456 =
       0.03572    0.00004   -0.00146    0.00365
AFIX 147
H1A   2    0.060442    0.855076    0.056554    11.00000   -1.50000
AFIX   0
```

O2A 5 0.538639 0.766224 0.066542 11.00000 0.02071 0.02763 =
0.02709 0.00083 0.00016 -0.00557
O3A 5 0.506333 0.819019 0.155580 11.00000 0.02167 0.03459 =
0.03157 -0.00671 0.00092 -0.00589
O4A 5 0.179049 0.388547 -0.027604 11.00000 0.02022 0.02626 =
0.02888 -0.00400 -0.00069 0.00497
AFIX 147
H4A 2 0.264907 0.350063 -0.038036 11.00000 -1.50000
AFIX 0
O5A 5 -0.225999 0.608672 -0.202883 11.00000 0.04698 0.10691 =
0.03366 -0.01113 -0.01038 -0.01511
O6A 5 -0.424871 0.628952 -0.143232 11.00000 0.02475 0.05500 =
0.05075 -0.00010 -0.01247 -0.00145
N1A 4 0.175421 0.706601 0.070841 11.00000 0.01431 0.01656 =
0.03148 0.00049 -0.00104 0.00008
N2A 4 -0.272202 0.620377 -0.155254 11.00000 0.03779 0.03976 =
0.03318 -0.00266 -0.01289 -0.00531
C1A 1 0.300643 0.682487 0.116306 11.00000 0.01365 0.01931 =
0.02393 0.00235 0.00038 -0.00058
C2A 1 0.335443 0.545918 0.104571 11.00000 0.01029 0.01796 =
0.03026 0.00336 0.00273 -0.00060
AFIX 13
H2A 2 0.238661 0.500829 0.121217 11.00000 -1.20000
AFIX 0
C3A 1 0.314153 0.529098 0.040482 11.00000 0.00623 0.01990 =
0.03131 0.00174 -0.00039 0.00354
AFIX 13

```
H3A   2    0.428730    0.515375    0.024182    11.00000   -1.20000
AFIX   0
C4A   1    0.240293    0.652890    0.019287    11.00000    0.01621    0.02094 =
      0.02896   -0.00119   -0.00050    0.00033
AFIX  13
H4AA  2    0.336180    0.703687    0.005712    11.00000   -1.20000
AFIX   0
C5A   1    0.463278    0.759364    0.109502    11.00000    0.02115    0.01802 =
      0.02556    0.00000   -0.00321    0.00658
C6A   1    0.653546    0.900911    0.152661    11.00000    0.01476    0.02954 =
      0.04729   -0.01125   -0.00274   -0.00668
AFIX  23
H6AA  2    0.646354    0.962112    0.182564    11.00000   -1.20000
H6AB  2    0.648892    0.943687    0.116421    11.00000   -1.20000
AFIX   0
C7A   1    0.821153    0.835271    0.158780    11.00000    0.02432    0.03443 =
      0.04099    0.00046   -0.00216   -0.00095
AFIX 137
H7AA  2    0.831105    0.777009    0.128313    11.00000   -1.50000
H7AB  2    0.826312    0.792610    0.194570    11.00000   -1.50000
H7AC  2    0.915279    0.893416    0.157445    11.00000   -1.50000
AFIX   0
C8A   1    0.222137    0.701391    0.172832    11.00000    0.01600    0.02719 =
      0.03077   -0.00152   -0.00017    0.00182
AFIX 137
H8AA  2    0.196443    0.787182    0.177863    11.00000   -1.50000
H8AB  2    0.302878    0.674805    0.202285    11.00000   -1.50000
```

H8AC 2 0.116438 0.654383 0.174819 11.00000 -1.50000

AFIX 0

C9A 1 0.497048 0.495498 0.132095 11.00000 0.02556 0.02410 =

0.02173 0.00032 -0.00041 -0.00248

C10A 1 0.657488 0.516133 0.109544 11.00000 0.01511 0.02850 =

0.02904 0.00405 -0.00031 -0.00078

AFIX 43

H10A 2 0.664903 0.555162 0.074437 11.00000 -1.20000

AFIX 0

C11A 1 0.806059 0.480116 0.137979 11.00000 0.01037 0.03292 =

0.03216 0.00120 -0.00061 -0.00220

AFIX 43

H11A 2 0.914799 0.492812 0.122361 11.00000 -1.20000

AFIX 0

C12A 1 0.792370 0.425742 0.189172 11.00000 0.03655 0.01904 =

0.02829 0.00127 -0.00689 0.00936

C13A 1 0.639813 0.398319 0.211510 11.00000 0.01797 0.03503 =

0.02656 0.01074 -0.00290 -0.00239

AFIX 43

H13A 2 0.633682 0.355028 0.245576 11.00000 -1.20000

AFIX 0

C14A 1 0.492879 0.435978 0.182654 11.00000 0.02244 0.02349 =

0.03251 0.00057 0.00026 0.00016

AFIX 43

H14A 2 0.385062 0.420138 0.198344 11.00000 -1.20000

AFIX 0

C15A 1 0.200842 0.418969 0.029363 11.00000 0.01994 0.02563 =

0.02846 0.00029 0.00025 0.00104

AFIX 23

H15A 2 0.251211 0.348935 0.049480 11.00000 -1.20000

H15B 2 0.087061 0.434431 0.044902 11.00000 -1.20000

AFIX 0

C16A 1 0.101851 0.645739 -0.025924 11.00000 0.02029 0.01769 =

0.02638 0.00059 -0.00314 0.00113

C17A 1 0.143563 0.663401 -0.080981 11.00000 0.01809 0.02694 =

0.02926 0.00006 -0.00045 0.00259

AFIX 43

H17A 2 0.258208 0.682608 -0.089488 11.00000 -1.20000

AFIX 0

C18A 1 0.023629 0.653912 -0.123706 11.00000 0.03091 0.02684 =

0.02329 -0.00160 0.00062 -0.00196

AFIX 43

H18A 2 0.054400 0.664959 -0.161391 11.00000 -1.20000

AFIX 0

C19A 1 -0.144130 0.627677 -0.110249 11.00000 0.02542 0.02214 =

0.03119 -0.00276 -0.00745 -0.00077

C20A 1 -0.192766 0.612191 -0.055621 11.00000 0.01642 0.02168 =

0.03463 -0.00046 -0.00073 -0.00102

AFIX 43

H20A 2 -0.308186 0.595112 -0.047251 11.00000 -1.20000

AFIX 0

C21A 1 -0.069003 0.622229 -0.013588 11.00000 0.02466 0.02471 =

0.02519 -0.00005 -0.00047 0.00470

AFIX 43

H21A 2 -0.100180 0.613069 0.024165 11.00000 -1.20000

AFIX 0

CL1B 3 0.880202 1.082141 0.275854 11.00000 0.03524 0.05057 =

0.03151 0.00376 0.00464 -0.01621

O1B 5 0.121691 0.603782 0.436866 11.00000 0.03309 0.02344 =

0.05014 0.00031 0.01091 -0.00064

AFIX 147

H1B 2 0.019347 0.580914 0.435417 11.00000 -1.50000

AFIX 0

O2B 5 0.489478 0.672583 0.433392 11.00000 0.02525 0.03803 =

0.03695 0.00249 0.00486 0.01347

O3B 5 0.468904 0.671255 0.340385 11.00000 0.03857 0.04749 =

0.03365 -0.00066 0.00764 0.01848

O4B 5 0.208755 1.043291 0.541335 11.00000 0.02703 0.02798 =

0.03236 -0.00688 0.00336 -0.00401

AFIX 147

H4B 2 0.303600 1.075304 0.549305 11.00000 -1.50000

AFIX 0

O5B 5 -0.488528 0.847019 0.625187 11.00000 0.02636 0.09848 =

0.04290 -0.00787 0.00678 0.00149

O6B 5 -0.302648 0.836427 0.692573 11.00000 0.03121 0.08250 =

0.03031 -0.00907 0.00933 -0.00806

N1B 4 0.128260 0.733012 0.431949 11.00000 0.02337 0.02490 =

0.03152 0.00025 0.00655 0.00080

N2B 4 -0.340368 0.836582 0.643097 11.00000 0.02392 0.04671 =

0.03435 -0.00607 0.00564 -0.00327

C1B 1 0.241341 0.763704 0.386822 11.00000 0.02314 0.03246 =
0.02725 -0.00014 0.00245 -0.00060
C2B 1 0.275747 0.899497 0.401051 11.00000 0.02130 0.02418 =
0.03212 0.00417 0.00014 0.00640
AFIX 13
H2B 2 0.172424 0.945348 0.387724 11.00000 -1.20000
AFIX 0
C3B 1 0.277832 0.904731 0.465518 11.00000 0.02152 0.03259 =
0.02618 -0.00037 -0.00027 0.00269
AFIX 13
H3B 2 0.399619 0.904865 0.479276 11.00000 -1.20000
AFIX 0
C4B 1 0.193087 0.784952 0.484725 11.00000 0.02201 0.03035 =
0.02818 0.00135 -0.00016 0.00453
AFIX 13
H4BA 2 0.283661 0.730707 0.500947 11.00000 -1.20000
AFIX 0
C5B 1 0.411823 0.694334 0.390156 11.00000 0.04079 0.02695 =
0.02573 0.00216 0.00470 -0.00454
C6B 1 0.648215 0.630679 0.335742 11.00000 0.04499 0.04570 =
0.04386 0.00418 0.00299 0.01793
AFIX 23
H6BA 2 0.720407 0.665125 0.366326 11.00000 -1.20000
H6BB 2 0.655089 0.541581 0.337728 11.00000 -1.20000
AFIX 0
C7B 1 0.705897 0.674111 0.281053 11.00000 0.02640 0.04387 =
0.04590 -0.00339 0.00673 -0.00214

AFIX 137

H7BA 2 0.629792 0.642511 0.251381 11.00000 -1.50000

H7BB 2 0.822772 0.646078 0.275191 11.00000 -1.50000

H7BC 2 0.703327 0.762506 0.280371 11.00000 -1.50000

AFIX 0

C8B 1 0.147986 0.746830 0.331379 11.00000 0.02930 0.03947 =

0.03392 -0.00692 -0.00085 0.00046

AFIX 137

H8BA 2 0.126853 0.660708 0.324999 11.00000 -1.50000

H8BB 2 0.217803 0.778828 0.301493 11.00000 -1.50000

H8BC 2 0.038758 0.790012 0.331689 11.00000 -1.50000

AFIX 0

C9B 1 0.426647 0.954925 0.372874 11.00000 0.02343 0.02705 =

0.02290 -0.00282 0.00193 0.00182

C10B 1 0.594014 0.941032 0.394177 11.00000 0.02956 0.03617 =

0.02447 0.00857 0.00035 0.00333

AFIX 43

H10B 2 0.612720 0.901923 0.429055 11.00000 -1.20000

AFIX 0

C11B 1 0.733020 0.983371 0.365250 11.00000 0.02083 0.03334 =

0.03567 0.00428 -0.00232 0.00208

AFIX 43

H11B 2 0.846024 0.974864 0.380226 11.00000 -1.20000

AFIX 0

C12B 1 0.703123 1.038152 0.314185 11.00000 0.04033 0.02760 =

0.02285 0.00196 -0.00012 -0.00369

C13B 1 0.543479 1.056484 0.292958 11.00000 0.03779 0.03051 =

0.02238 0.00367 -0.00107 0.00186

AFIX 43

H13B 2 0.525797 1.097520 0.258509 11.00000 -1.20000

AFIX 0

C14B 1 0.405898 1.014118 0.322526 11.00000 0.02460 0.02914 =

0.02691 0.00227 -0.00538 0.00489

AFIX 43

H14B 2 0.293532 1.026290 0.307588 11.00000 -1.20000

AFIX 0

C15B 1 0.195194 1.023067 0.483365 11.00000 0.02836 0.02296 =

0.03509 -0.00081 0.00270 -0.00001

AFIX 23

H15C 2 0.250167 1.090812 0.463817 11.00000 -1.20000

H15D 2 0.072835 1.022054 0.471747 11.00000 -1.20000

AFIX 0

C16B 1 0.051451 0.797086 0.525923 11.00000 0.02885 0.02519 =

0.02890 -0.00210 0.00413 -0.00321

C17B 1 -0.115827 0.820940 0.508464 11.00000 0.02655 0.03693 =

0.02472 0.00272 -0.00242 0.00293

AFIX 43

H17B 2 -0.142285 0.829162 0.469760 11.00000 -1.20000

AFIX 0

C18B 1 -0.244402 0.832925 0.546334 11.00000 0.01633 0.04092 =

0.03205 0.00108 -0.00234 -0.00156

AFIX 43

H18B 2 -0.358561 0.847867 0.533702 11.00000 -1.20000

AFIX 0

C19B 1 -0.206185 0.823109 0.602359 11.00000 0.03122 0.02802 =

0.02934 -0.00099 0.00309 -0.00557

C20B 1 -0.039956 0.798219 0.621538 11.00000 0.02647 0.03952 =

0.02390 0.00042 -0.00097 -0.00379

AFIX 43

H20B 2 -0.014797 0.790098 0.660328 11.00000 -1.20000

AFIX 0

C21B 1 0.087212 0.785590 0.583359 11.00000 0.01534 0.03181 =

0.03083 0.00079 -0.00150 0.00063

AFIX 43

H21B 2 0.200758 0.768855 0.596102 11.00000 -1.20000

AFIX 0

HKLF 5

REM a20160354_lp1252_a.res in P2(1)

REM R1 = 0.0529 for 11194 Fo > 4sig(Fo) and 0.0555 for all 11647 data

REM 550 parameters refined using 7 restraints

END

WGHT 0.0946 1.8635

REM Highest difference peak 0.494, deepest hole -0.390, 1-sigma level 0.065

Q1 1 0.8715 1.0896 0.3163 11.00000 0.05 0.49

Q2 1 0.9731 0.3873 0.2693 11.00000 0.05 0.48

Q3 1 0.8758 0.3760 0.2210 11.00000 0.05 0.44

Q4 1 0.9903 0.3855 0.1863 11.00000 0.05 0.42

Q5 1 0.8845 1.0841 0.2330 11.00000 0.05 0.41

Q6 1 0.7426 0.4002 0.2225 11.00000 0.05 0.36

Q7 1 0.7691 1.0999 0.2701 11.00000 0.05 0.35

Q8 1 1.0887 0.3947 0.2334 11.00000 0.05 0.34

Q9	1	0.5685	0.5621	0.3337	11.00000	0.05	0.33
Q10	1	0.2515	0.7422	0.3462	11.00000	0.05	0.32
Q11	1	0.2254	0.6943	0.1301	11.00000	0.05	0.31
Q12	1	0.5668	0.4960	0.1127	11.00000	0.05	0.30
Q13	1	0.9811	1.0848	0.2805	11.00000	0.05	0.29
Q14	1	1.0999	1.1285	0.2759	11.00000	0.05	0.27
Q15	1	0.7383	0.8701	0.1569	11.00000	0.05	0.26
Q16	1	0.2237	0.7531	0.4294	11.00000	0.05	0.25
Q17	1	0.1349	0.7013	0.1688	11.00000	0.05	0.25
Q18	1	-0.4054	0.8370	0.6900	11.00000	0.05	0.25
Q19	1	0.7393	0.6590	0.3214	11.00000	0.05	0.25
Q20	1	0.1387	0.7438	0.3760	11.00000	0.05	0.25

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_audit_block_doi 10.5517/ccdc.csd.cc1kh1hl

_database_code_depnum_ccdc_archive 'CCDC 1444429'

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_citation_id

_citation_doi

_citation_year

1 10.1002/chem.201602159 2016

_audit_update_record

2015-12-26 deposited with the CCDC. 2019-02-14 downloaded from the CCDC.

_audit_creation_method SHELXL-97

_chemical_name_systematic

'(2R,5R)-ethyl 2-isopropyl-5-(4-nitrophenyl)-2,5-dihydrooxazole-4-carboxylate'

_chemical_melting_point '357 K'

_chemical_formula_sum 'C15 H18 N2 O5'

_chemical_formula_weight 306.31

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_atom_type_description

_atom_type_scat_dispersion_real

_atom_type_scat_dispersion_imag

_atom_type_scat_source

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H H 0.0000 0.0000 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

N N 0.0061 0.0033 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

O O 0.0106 0.0060 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

_symmetry_cell_setting triclinic

_symmetry_space_group_name_H-M P-1

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_symmetry_equiv_pos_as_xyz

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'-x, -y, -z'

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_cell_length_c 10.582

_cell_angle_alpha 89.14

_cell_angle_beta 85.49

_cell_angle_gamma 74.58

_cell_volume 774.2

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_cell_measurement_reflns_used 992

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_exptl_crystal_density_method 'not measured'

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_exptl_absorpt_correction_T_max 1.00000

_exptl_absorpt_correction_type multi-scan

_exptl_absorpt_process_details

CrysAlisPro, Agilent Technologies,

Version 1.171.37.35 (release 13-08-2014 CrysAlis171 .NET)

(compiled Aug 13 2014,18:06:01)

Empirical absorption correction using spherical harmonics,

implemented in SCALE3 ABSPACK scaling algorithm.

_diffrn_ambient_temperature 293(2)

_diffrn_radiation_wavelength 0.71073

_diffrn_radiation_type MoK\a

_diffrn_radiation_source 'fine-focus sealed tube'

_diffrn_radiation_monochromator graphite

_diffrn_measurement_device_type 'Xcalibur, Sapphire3'

_diffrn_measurement_method '\w scans'

_diffrn_detector 'CCD plate'

_diffrn_detector_type Sapphire3

_diffrn_detector_area_resol_mean 16.3990

_diffrn_standards_number 3

_diffrn_standards_interval_count 97

_diffrn_standards_decay_% 0.90

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_diffrn_reflns_av_sigmaI/netI 0.1445

_diffrn_reflns_limit_h_min -9

_diffrn_reflns_limit_h_max 9

_diffrn_reflns_limit_k_min -11

_diffrn_reflns_limit_k_max 12

_diffrn_reflns_limit_l_min -13

_diffrn_reflns_limit_l_max 12

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_diffrn_reflns_theta_max 26.55

_reflns_number_total 2769

_reflns_number_gt 1251

_reflns_threshold_expression >2\s(I)

_computing_data_collection

CrysAlisPro, Agilent Technologies,

Version 1.171.37.35 (release 13-08-2014 CrysAlis171 .NET)

(compiled Aug 13 2014,18:06:01)

_computing_cell_refinement

CrysAlisPro, Agilent Technologies,

Version 1.171.37.35 (release 13-08-2014 CrysAlis171 .NET)

(compiled Aug 13 2014,18:06:01)

_computing_data_reduction

CrysAlisPro, Agilent Technologies,

Version 1.171.37.35 (release 13-08-2014 CrysAlis171 .NET)

(compiled Aug 13 2014,18:06:01)

_computing_structure_solution 'SHELXS-97 (Sheldrick, 1990)'

_computing_structure_refinement 'SHELXL-97 (Sheldrick, 1997)'

_computing_molecular_graphics 'Siemens SHELXTL'

_computing_publication_material 'Siemens SHELXTL'

_refine_special_details

Refinement of F^2^ against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2^, conventional R-factors R are based on F, with F set to zero for negative F^2^. The threshold expression of F^2^ > 2\s(F^2^) is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2^ are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

_refine_ls_structure_factor_coef Fsqd

_refine_ls_matrix_type full

_refine_ls_weighting_scheme calc

_refine_ls_weighting_details

'calc w=1/[\s^2^(Fo^2^)+(0.0671P)^2^+0.0000P] where P=(Fo^2^+2Fc^2^)/3'

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_atom_sites_solution_secondary difmap

_atom_sites_solution_hydrogens geom

_refine_ls_hydrogen_treatment mixed

_refine_ls_extinction_method none

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_refine_ls_number_parameters 199

_refine_ls_number_restraints 0

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_refine_ls_R_factor_gt 0.0610

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_refine_ls_restrained_S_all 0.935

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_refine_ls_shift/su_mean 0.003

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_atom_site_type_symbol

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_atom_site_fract_y

_atom_site_fract_z

_atom_site_U_iso_or_equiv

_atom_site_adp_type

_atom_site_occupancy

_atom_site_symmetry_multiplicity

_atom_site_calc_flag

_atom_site_refinement_flags

_atom_site_disorder_assembly

_atom_site_disorder_group

O1 O 0.1405(4) 0.6036(3) 0.2417(2) 0.0346(7) Uani 1 1 d . . .

O2 O 0.2686(4) 0.1792(3) 0.4730(3) 0.0417(8) Uani 1 1 d . . .

O3 O 0.4166(3) 0.1736(3) 0.2816(2) 0.0333(7) Uani 1 1 d . . .

O4 O -0.4528(4) 0.3042(3) -0.0178(3) 0.0447(8) Uani 1 1 d . . .

O5 O -0.2438(4) 0.1192(3) -0.0853(3) 0.0412(8) Uani 1 1 d . . .

N1 N 0.1926(4) 0.4885(3) 0.4364(3) 0.0314(9) Uani 1 1 d . . .

N2 N -0.2972(5) 0.2334(4) -0.0265(3) 0.0357(9) Uani 1 1 d . . .

C1 C 0.1299(5) 0.6290(4) 0.3774(3) 0.0315(10) Uani 1 1 d . . .

H1 H 0.0070 0.6718 0.4077 0.038 Uiso 1 1 calc R . .

C2 C 0.2392(5) 0.7315(4) 0.4059(4) 0.0346(11) Uani 1 1 d . . .

H2 H 0.1972 0.8187 0.3559 0.041 Uiso 1 1 calc R . .

C3 C 0.4331(5) 0.6690(4) 0.3644(4) 0.0429(12) Uani 1 1 d . . .

H3A H 0.4977 0.7364 0.3837 0.064 Uiso 1 1 calc R . .

H3B H 0.4464 0.6507 0.2747 0.064 Uiso 1 1 calc R . .

H3C H 0.4774 0.5805 0.4085 0.064 Uiso 1 1 calc R . .

C4 C 0.2110(7) 0.7763(5) 0.5437(4) 0.0597(15) Uani 1 1 d . . .

H4A H 0.2819 0.8403 0.5591 0.090 Uiso 1 1 calc R . .

H4B H 0.2439 0.6925 0.5958 0.090 Uiso 1 1 calc R . .

H4C H 0.0892 0.8246 0.5636 0.090 Uiso 1 1 calc R . .

C5 C 0.2014(5) 0.4533(4) 0.2169(3) 0.0282(10) Uani 1 1 d . . .

H5 H 0.3124 0.4323 0.1637 0.034 Uiso 1 1 calc R . .

C6 C 0.2343(5) 0.3941(4) 0.3500(4) 0.0258(9) Uani 1 1 d . . .

C7 C 0.3057(5) 0.2389(4) 0.3774(4) 0.0314(10) Uani 1 1 d . . .

C8 C 0.1233(5) 0.2735(4) 0.0799(4) 0.0321(10) Uani 1 1 d . . .

H8 H 0.2426 0.2272 0.0682 0.039 Uiso 1 1 calc R . .

C9 C 0.6379(6) -0.0285(4) 0.1943(4) 0.0506(13) Uani 1 1 d . . .

H9A H 0.6878 -0.1306 0.2008 0.076 Uiso 1 1 calc R . .

H9B H 0.7265 0.0207 0.2057 0.076 Uiso 1 1 calc R . .

H9C H 0.5944 -0.0066 0.1121 0.076 Uiso 1 1 calc R . .

C10 C 0.0679(5) 0.3958(4) 0.1542(3) 0.0266(10) Uani 1 1 d . . .

C11 C 0.4896(5) 0.0197(4) 0.2943(4) 0.0366(11) Uani 1 1 d . . .

H11A H 0.3999 -0.0302 0.2840 0.044 Uiso 1 1 calc R . .

H11B H 0.5323 -0.0021 0.3777 0.044 Uiso 1 1 calc R . .

C12 C 0.0030(5) 0.2187(4) 0.0225(4) 0.0327(10) Uani 1 1 d . . .

H12 H 0.0406 0.1353 -0.0267 0.039 Uiso 1 1 calc R . .

C13 C -0.1719(5) 0.2891(4) 0.0393(3) 0.0254(9) Uani 1 1 d . . .

C14 C -0.2310(5) 0.4113(4) 0.1132(4) 0.0324(10) Uani 1 1 d . . .

H14 H -0.3503 0.4581 0.1236 0.039 Uiso 1 1 calc R . .

C15 C -0.1100(5) 0.4633(4) 0.1717(4) 0.0332(11) Uani 1 1 d . . .

H15 H -0.1486 0.5446 0.2234 0.040 Uiso 1 1 calc R . .

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_atom_site_aniso_U_22

_atom_site_aniso_U_33

_atom_site_aniso_U_23

_atom_site_aniso_U_13

_atom_site_aniso_U_12

O1 0.0486(19) 0.0262(16) 0.0285(16) 0.0003(13) -0.0075(14) -0.0080(14)

O2 0.0433(19) 0.0371(18) 0.0393(17) 0.0081(15) 0.0020(16) -0.0032(15)

O3 0.0394(18) 0.0232(16) 0.0331(16) 0.0020(13) -0.0026(15) -0.0013(14)

O4 0.0312(19) 0.055(2) 0.0478(19) -0.0017(16) -0.0060(16) -0.0096(16)

O5 0.044(2) 0.0331(18) 0.0469(19) -0.0074(15) -0.0064(16) -0.0094(16)

N1 0.039(2) 0.026(2) 0.0314(19) 0.0013(16) -0.0040(17) -0.0108(17)

N2 0.031(2) 0.040(2) 0.037(2) 0.0033(19) -0.0044(19) -0.010(2)

C1 0.038(3) 0.028(2) 0.028(2) -0.0018(19) -0.004(2) -0.007(2)

C2 0.042(3) 0.027(2) 0.036(2) -0.001(2) -0.006(2) -0.010(2)

C3 0.046(3) 0.036(3) 0.051(3) 0.008(2) -0.012(2) -0.014(2)

C4 0.077(4) 0.060(3) 0.048(3) -0.009(3) -0.005(3) -0.029(3)

C5 0.029(2) 0.022(2) 0.032(2) -0.0001(18) -0.003(2) -0.0032(19)

C6 0.023(2) 0.025(2) 0.029(2) -0.0014(19) -0.0030(19) -0.0055(19)

C7 0.028(3) 0.034(3) 0.031(2) -0.004(2) -0.005(2) -0.004(2)

C8 0.025(2) 0.034(3) 0.033(2) -0.004(2) -0.006(2) -0.001(2)

C9 0.055(3) 0.034(3) 0.054(3) -0.005(2) 0.009(3) -0.001(2)

C10 0.030(2) 0.027(2) 0.024(2) 0.0032(18) -0.003(2) -0.009(2)

C11 0.044(3) 0.023(2) 0.040(3) 0.005(2) -0.003(2) -0.005(2)

C12 0.035(3) 0.027(2) 0.035(2) -0.0046(19) -0.001(2) -0.005(2)

C13 0.022(2) 0.027(2) 0.027(2) 0.0021(19) -0.0039(19) -0.0076(19)

C14 0.023(2) 0.036(3) 0.034(2) -0.003(2) -0.002(2) 0.002(2)

C15 0.034(3) 0.028(2) 0.034(2) -0.0050(19) -0.007(2) -0.002(2)

_geom_special_details

All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes)
are estimated using the full covariance matrix. The cell s.u.'s are taken
into account individually in the estimation of s.u.'s in distances, angles
and torsion angles; correlations between s.u.'s in cell parameters are only
used when they are defined by crystal symmetry. An approximate (isotropic)
treatment of cell s.u.'s is used for estimating s.u.'s involving l.s. planes.

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_geom_bond_atom_site_label_2

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_geom_bond_site_symmetry_2

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O1 C1 1.452(4) . ?

O2 C7 1.210(4) . ?

O3 C7 1.333(4) . ?

O3 C11 1.449(4) . ?

O4 N2 1.235(4) . ?

O5 N2 1.227(4) . ?

N1 C6 1.261(4) . ?

N1 C1 1.460(4) . ?

N2 C13 1.469(5) . ?

C1 C2 1.521(5) . ?

C2 C4 1.509(5) . ?

C2 C3 1.523(5) . ?

C5 C10 1.515(5) . ?

C5 C6 1.526(5) . ?

C6 C7 1.483(5) . ?

C8 C10 1.376(5) . ?

C8 C12 1.386(5) . ?

C9 C11 1.497(5) . ?

C10 C15 1.383(5) . ?

C12 C13 1.368(5) . ?

C13 C14 1.375(5) . ?

C14 C15 1.380(5) . ?

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_geom_angle_atom_site_label_3

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_geom_angle_site_symmetry_3

_geom_angle_publ_flag

C5 O1 C1 109.4(3) . . ?

C7 O3 C11 115.9(3) . . ?

C6 N1 C1 108.1(3) . . ?

O5 N2 O4 123.4(3) . . ?

O5 N2 C13 119.0(3) . . ?

O4 N2 C13 117.5(4) . . ?

O1 C1 N1 106.8(3) . . ?

O1 C1 C2 110.0(3) . . ?

N1 C1 C2 112.2(3) . . ?

C4 C2 C1 111.2(4) . . ?

C4 C2 C3 112.0(4) . . ?

C1 C2 C3 111.8(3) . . ?

O1 C5 C10 112.3(3) . . ?

O1 C5 C6 101.4(3) . . ?

C10 C5 C6 113.1(3) . . ?

N1 C6 C7 122.2(3) . . ?

N1 C6 C5 114.2(3) . . ?

C7 C6 C5 123.6(3) . . ?

O2 C7 O3 124.5(4) . . ?

O2 C7 C6 125.0(4) . . ?

O3 C7 C6 110.5(4) . . ?

C10 C8 C12 120.7(4) . . ?

C8 C10 C15 119.2(4) . . ?

C8 C10 C5 119.9(3) . . ?

C15 C10 C5 120.9(3) . . ?

O3 C11 C9 108.2(3) . . ?

C13 C12 C8 118.9(4) . . ?

C12 C13 C14 121.6(4) . . ?

C12 C13 N2 118.4(4) . . ?

C14 C13 N2 120.0(4) . . ?

C13 C14 C15 118.8(4) . . ?

C14 C15 C10 120.7(4) . . ?

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_diffrn_measured_fraction_theta_full 0.9986

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_refine_diff_density_rms 0.063

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_audit_block_doi 10.5517/ccdc.csd.cc1kh1jm

_database_code_depnum_ccdc_archive 'CCDC 1444430'

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_citation_id

_citation_doi

_citation_year

1 10.1002/chem.201602159 2016

_audit_update_record

2015-12-26 deposited with the CCDC. 2019-02-14 downloaded from the CCDC.

_audit_creation_method SHELXL-97

_chemical_name_systematic

'ethyl (4R,5S)-2,5-bis(4-nitrophenyl)-4,5-dihydrooxazole-4-carboxylate'

_chemical_name_common ?

_chemical_melting_point '363 K'

_chemical_formula_sum 'C18 H15 N3 O7'

_chemical_formula_weight 385.33

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_atom_type_description

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_atom_type_scat_source

C C 0.0033 0.0016 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

H H 0.0000 0.0000 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

N N 0.0061 0.0033 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

O O 0.0106 0.0060 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

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_symmetry_space_group_name_H-M P21/c

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'-x, -y, -z'

'x, -y-1/2, z-1/2'

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_exptl_absorpt_correction_T_min 0.73538

_exptl_absorpt_correction_T_max 1.00000

_exptl_absorpt_process_details

CrysAlisPro, Agilent Technologies,

Version 1.171.37.35 (release 13-08-2014 CrysAlis171 .NET)

(compiled Aug 13 2014,18:06:01)

Empirical absorption correction using spherical harmonics,

implemented in SCALE3 ABSPACK scaling algorithm.

_diffrn_ambient_temperature 293(2)

_diffrn_radiation_wavelength 0.71073

_diffrn_radiation_type MoK\a

_diffrn_radiation_source 'fine-focus sealed tube'

_diffrn_radiation_monochromator graphite

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_diffrn_measurement_method '\w scans'

_diffrn_detector 'CCD plate'

_diffrn_detector_type Sapphire3

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_diffrn_standards_interval_count 97

_diffrn_standards_decay_% 0.90

_diffrn_reflns_number 13318

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_diffrn_reflns_av_sigmaI/netI 0.3906

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_diffrn_reflns_limit_h_max 23

_diffrn_reflns_limit_k_min -9

_diffrn_reflns_limit_k_max 8

_diffrn_reflns_limit_l_min -18

_diffrn_reflns_limit_l_max 18

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_diffrn_reflns_theta_max 27.90

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_reflns_number_gt 996

_reflns_threshold_expression >2\s(I)

_computing_data_collection

CrysAlisPro, Agilent Technologies,

Version 1.171.37.35 (release 13-08-2014 CrysAlis171 .NET)

(compiled Aug 13 2014,18:06:01)

_computing_cell_refinement

CrysAlisPro, Agilent Technologies,

Version 1.171.37.35 (release 13-08-2014 CrysAlis171 .NET)

(compiled Aug 13 2014,18:06:01)

_computing_data_reduction

CrysAlisPro, Agilent Technologies,

Version 1.171.37.35 (release 13-08-2014 CrysAlis171 .NET)

(compiled Aug 13 2014,18:06:01)

_computing_structure_solution 'SHELXS-97 (Sheldrick, 1990)'

_computing_structure_refinement 'SHELXL-97 (Sheldrick, 1997)'

_computing_molecular_graphics 'Siemens SHELXTL'

_computing_publication_material 'Siemens SHELXTL'

_refine_special_details

Refinement of F^2^ against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2^, conventional R-factors R are based on F, with F set to zero for negative F^2^. The threshold expression of F^2^ > 2\s(F^2^) is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2^ are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

_refine_ls_structure_factor_coef Fsqd

_refine_ls_matrix_type full

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N2 N 0.4349(4) 0.3167(8) 0.3363(5) 0.0387(17) Uani 1 1 d . . .

O3 O 0.3662(3) 0.3015(6) 0.2772(4) 0.0547(16) Uani 1 1 d . . .

O4 O 0.6592(3) 0.5163(7) 0.0298(3) 0.0509(15) Uani 1 1 d . . .

O5 O 1.1611(3) -0.1825(8) 0.4835(4) 0.0677(19) Uani 1 1 d . . .

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C5 C 0.5478(4) 0.2973(9) 0.1629(5) 0.0341(19) Uani 1 1 d . . .

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O7 O 1.0859(3) -0.4296(8) 0.4443(5) 0.102(3) Uani 1 1 d . . .

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C7 C 0.8957(4) 0.0898(10) 0.3054(5) 0.0312(18) Uani 1 1 d . . .

C8 C 0.5790(4) 0.2819(9) 0.3638(5) 0.038(2) Uani 1 1 d . . .

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C9 C 0.6254(4) 0.2754(8) 0.2267(5) 0.0280(17) Uani 1 1 d . . .

C10 C 0.4849(4) 0.3147(9) 0.1982(5) 0.0370(19) Uani 1 1 d . . .

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C12 C 0.7421(4) 0.4441(9) 0.1955(5) 0.0363(19) Uani 1 1 d . . .

H12 H 0.7318 0.5249 0.2449 0.044 Uiso 1 1 calc R . .

C13 C 0.9512(4) -0.2156(10) 0.3657(5) 0.047(2) Uani 1 1 d . . .

H13 H 0.9451 -0.3447 0.3761 0.056 Uiso 1 1 calc R . .

C14 C 0.7358(4) 0.8470(10) 0.0271(6) 0.055(2) Uani 1 1 d . . .

H14A H 0.6778 0.8567 0.0037 0.066 Uiso 1 1 calc R . .

H14B H 0.7579 0.9719 0.0500 0.066 Uiso 1 1 calc R . .

C15 C 0.7168(5) 0.5556(10) 0.1001(6) 0.042(2) Uani 1 1 d . . .

C16 C 0.8855(4) -0.1027(10) 0.3200(5) 0.043(2) Uani 1 1 d . . .

H16 H 0.8343 -0.1553 0.2988 0.051 Uiso 1 1 calc R . .

C17 C 0.7620(4) 0.7853(10) -0.0542(5) 0.065(3) Uani 1 1 d . . .

H17A H 0.7435 0.8752 -0.1072 0.098 Uiso 1 1 calc R . .

H17B H 0.7400 0.6617 -0.0768 0.098 Uiso 1 1 calc R . .

H17C H 0.8195 0.7789 -0.0313 0.098 Uiso 1 1 calc R . .

C18 C 0.9724(4) 0.1685(10) 0.3350(5) 0.043(2) Uani 1 1 d . . .

H18 H 0.9790 0.2973 0.3245 0.051 Uiso 1 1 calc R . .

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N2 0.031(4) 0.039(4) 0.053(5) 0.005(4) 0.023(4) 0.011(3)

O3 0.033(4) 0.059(4) 0.073(4) 0.010(3) 0.019(3) -0.005(3)

O4 0.039(4) 0.065(4) 0.041(3) 0.002(3) 0.004(3) -0.011(3)

O5 0.043(4) 0.074(4) 0.072(4) -0.001(3) 0.003(3) 0.011(3)

N1 0.026(4) 0.052(4) 0.039(4) 0.006(4) 0.006(3) 0.004(4)

O6 0.059(4) 0.088(5) 0.061(4) 0.006(4) 0.039(3) 0.006(3)

C2 0.024(5) 0.044(5) 0.045(5) 0.007(4) 0.006(4) -0.009(4)

C3 0.032(5) 0.046(5) 0.047(5) -0.004(4) 0.008(4) -0.009(4)

C5 0.032(5) 0.042(5) 0.030(5) -0.006(4) 0.014(4) -0.001(4)

C4 0.023(4) 0.041(5) 0.039(5) -0.001(4) 0.012(4) -0.002(4)

N3 0.053(5) 0.059(5) 0.058(5) -0.003(4) 0.024(4) 0.010(5)

O7 0.064(5) 0.050(4) 0.175(7) 0.009(4) 0.020(4) 0.019(4)

C6 0.029(5) 0.054(6) 0.049(5) -0.002(5) 0.022(4) 0.000(5)

C7 0.019(4) 0.045(5) 0.033(4) -0.009(4) 0.014(3) -0.001(4)

C8 0.025(5) 0.048(5) 0.034(5) 0.007(4) 0.002(4) -0.006(4)

C9 0.029(5) 0.026(4) 0.030(5) 0.004(4) 0.012(4) 0.004(3)

C10 0.029(5) 0.027(4) 0.053(6) 0.001(4) 0.012(4) 0.001(3)

C11 0.031(5) 0.024(4) 0.050(5) 0.000(4) 0.027(4) 0.005(3)

C12 0.038(5) 0.036(5) 0.036(5) -0.004(4) 0.014(4) 0.001(4)

C13 0.042(6) 0.037(5) 0.061(6) 0.009(4) 0.017(5) 0.000(4)

C14 0.055(6) 0.052(5) 0.065(6) -0.003(5) 0.029(5) -0.015(4)

C15 0.037(5) 0.038(5) 0.053(6) -0.017(5) 0.019(4) -0.008(4)

C16 0.034(5) 0.042(5) 0.051(5) -0.009(4) 0.013(4) -0.012(4)

C17 0.071(7) 0.071(6) 0.058(6) 0.004(5) 0.026(5) 0.008(5)

C18 0.040(5) 0.037(5) 0.044(5) 0.004(4) 0.007(4) -0.005(4)

C19 0.043(6) 0.041(5) 0.048(5) -0.006(4) 0.019(4) 0.012(5)

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All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes)
are estimated using the full covariance matrix. The cell s.u.'s are taken
into account individually in the estimation of s.u.'s in distances, angles
and torsion angles; correlations between s.u.'s in cell parameters are only
used when they are defined by crystal symmetry. An approximate (isotropic)
treatment of cell s.u.'s is used for estimating s.u.'s involving l.s. planes.

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N2 O3 1.228(6) . ?

N2 C11 1.479(8) . ?

O4 C15 1.199(7) . ?

O5 N3 1.225(7) . ?

N1 C6 1.254(8) . ?

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C2 C9 1.391(8) . ?

C3 C19 1.367(8) . ?

C3 C18 1.394(8) . ?

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C5 C10 1.390(8) . ?

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C4 C12 1.532(8) . ?

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N3 C19 1.472(9) . ?

C6 C7 1.465(9) . ?

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C7 C18 1.392(8) . ?

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O6 N2 C11 117.5(6) . . ?

O3 N2 C11 117.5(7) . . ?

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C8 C2 C9 120.8(7) . . ?

C19 C3 C18 117.6(7) . . ?

C9 C5 C10 120.6(7) . . ?

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O1 C4 C12 102.7(5) . . ?

C9 C4 C12 114.2(6) . . ?

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O7 N3 C19 119.2(7) . . ?

O5 N3 C19 118.8(7) . . ?

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C16 C7 C18 120.3(6) . . ?

C16 C7 C6 121.2(6) . . ?

C18 C7 C6 118.5(7) . . ?

C2 C8 C11 118.3(7) . . ?

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C2 C9 C4 120.0(6) . . ?

C11 C10 C5 118.6(6) . . ?

C10 C11 C8 122.0(7) . . ?

C10 C11 N2 119.3(7) . . ?

C8 C11 N2 118.7(7) . . ?

N1 C12 C15 115.9(6) . . ?

N1 C12 C4 105.3(5) . . ?

C15 C12 C4 112.9(6) . . ?

C19 C13 C16 118.5(7) . . ?

C17 C14 O2 110.3(6) . . ?

O4 C15 O2 125.8(7) . . ?

O4 C15 C12 123.6(7) . . ?

O2 C15 C12 110.4(6) . . ?

C13 C16 C7 120.0(6) . . ?

C7 C18 C3 119.8(7) . . ?

C3 C19 C13 123.8(7) . . ?

C3 C19 N3 118.4(7) . . ?

C13 C19 N3 117.8(7) . . ?

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4. Publications and supporting information

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Asymmetric Synthesis

Regioselectivity Change in the Organocatalytic Enantioselective (3+2) Cycloaddition with Nitrones through Cooperative Hydrogen-Bonding Catalysis/Iminium Activation

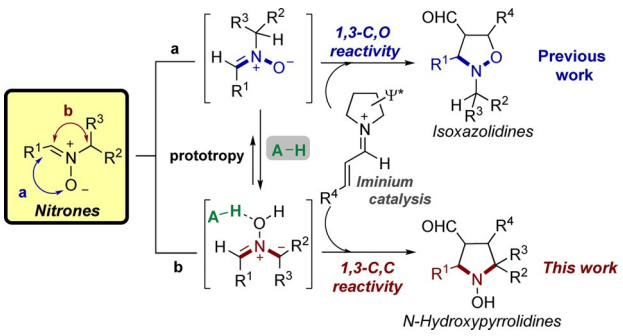
Liher Prieto,[a] Veronica Juste-Navarro,[b] Uxue Uria,[a] Ignacio Delso,[b] Efraim Reyes,[a] Tomas Tejero,[b] Luisa Carrillo,[a] Pedro Merino,*[b] and Jose L. Vicario*[a]

Dedicated to Professor Dieter Enders on the on the occasion of his 70th birthday

Abstract: The reaction of nitrones with enals through iminium activation can be modulated by using cooperative hydrogen-bonding catalysis to induce the participation of a nitrone ylide (C-N-C) instead of the classical C-N-O dipole. As a consequence, *N*-hydroxypyrrolidines are obtained, rather than the expected isoxazolidines. The reaction proceeds smoothly and high enantioselectivities are observed in all cases. By using the appropriate substrate, polysubstituted pyrrolidines incorporating quaternary stereocenters can be efficiently prepared.

Cycloadditions are powerful reactions that enable the construction of complex molecular architectures through the simultaneous generation of two new bonds.[1] Moreover, the stereochemical requirements associated with cycloaddition processes make this type of reaction a very appropriate candidate for the development of stereospecific variants. In this sense, catalytic and enantioselective (3+2) cycloadditions emerge as very convenient tools for the preparation of stereospecific 5-membered heterocyclic ring scaffolds, and in the past few years research has been intense in trying to develop catalytic and enantioselective versions with a variety of 1,3-dipoles.[2] In particular, the ability of chiral primary or secondary amines to activate α,β-unsaturated aldehydes or ketones as dipolarophiles in (3+2) cycloadditions under the so-called iminium activation manifold[3] has been explored by several authors[4] after the initial discovery of the concept by MacMillan.[5] Specifically, this approach has been successfully applied to reactions using 1,3-dipoles such as nitrones,[6] azomethine ylides[7] and azomethine imines[8]. Despite these intensive efforts, the range of dipoles for which this approach has been employed is still very limited. In particular, nitrones have been one of the most widely used 1,3-dipoles in (3+2) cycloaddition reactions, mainly because these are stable compounds that can be easily synthesized and handled in comparison with other 1,3-dipoles.[9] In fact, the 1,3-dipolar cycloaddition between nitrones and enals was the first example of an organocatalytic enantioselective (3+2) cycloaddition under iminium activation.[6a] This reaction enables the direct synthesis of isoxazolidines as single stereoisomers, in which the nitrone simultaneously reacts through the C and O termini. As an alternative, we envisaged that this standard 1,3-C,O reactivity of nitrones could be modified into a less conventional 1,3-C,C-type reactivity in (3+2) cycloaddition chemistry using some specific nitrone compounds able to give nitrone ylides, in combination with a hydrogen-bond co-catalyst,[10] leading to the formation of *N*-hydroxypyrrolidines in a single step (see Scheme 1). Moreover, the iminium activation approach could also render the overall process enantioselective by the incorporation of a chiral secondary amine as a catalyst.

We started our work by surveying the viability of the cycloaddition reaction using nitrone **1a** and cinnamaldehyde (**2a**) as a model system (Table 1). Introducing an electron-withdrawing group on the α-substituent to the nitrogen atom on the nitrone was predicted to increase the acidity of the adjacent proton and therefore assist the formation of the required ni-



Scheme 1. Bidentate reactivity of nitrones towards (3+2) cycloaddition with enals under cooperative H-bonding catalysis/iminium activation (Ψ* denotes a substituent incorporating chiral information).

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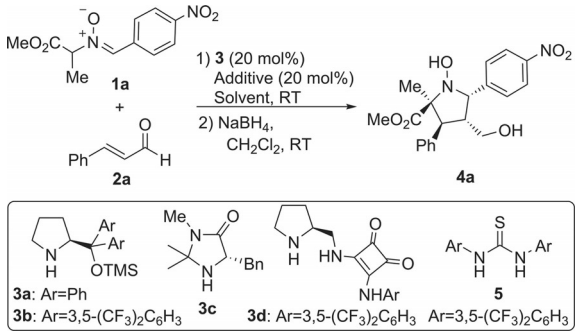
Supporting information and the ORCID number(s) for the author(s) of this article can be found under http://dx.doi.org/10.1002/chem.201605350.

Table 1. Screening for the best experimental conditions.



Entry	Catalyst	Additive	Solvent	Yield [%][a]	d.r.[b]	*ee* [%][c]
1	**3a**	none	$CHCl_3$	<5	n.d.[d]	n.d.[d]
2	**3a**	$PhCO_2$-	$CHCl_3$	<5	n.d.[d]	n.d.[d]
3	**3a**	5	$CHCl_3$	47	5:1	97
4	**3b**	5	$CHCl_3$	<5	n.d.[d]	n.d.[d]
5	**3c**	HCl	$MeNO_2$	<5	n.d.[d]	n.d.[d]
6	**3d**	none	$CHCl_3$	40	4:1	20
7[e]	**3a**	5	$CHCl_3$	92	5:1	98
8[f]	**3a**	5	$CHCl_3$	27	5:1	98
9[e]	**3a**	–	$CHCl_3$	9	2:1	98
10[g]	**3a**	5	$CHCl_3$	62	6:1	97
11[e]	**3a**	5	CH_2Cl_2	82	3:1	98
12[e]	**3a**	5	toluene	53	4:1	98
13[e]	**3a**	5	THF	28	4:1	98
14[e]	**3a**	5	EtOAc	22	4:1	97

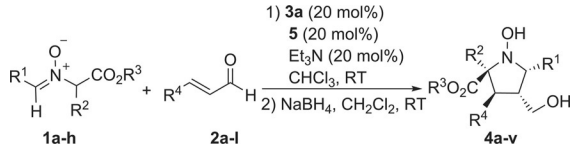
[a] Yield of pure product after flash column chromatography. [b] Diastereomeric ratio (d.r.) determined by NMR spectroscopic analysis of the crude reaction mixture. [c] Enantiomeric excess (*ee*) determined by HPLC analysis on a chiral stationary phase of the corresponding alcohol after reduction (see Supporting Information). [d] n.d.: not determined. [e] Et_3N (20 mol%) was incorporated as additive. [f] Et_3N (40 mol%) was incorporated as additive. [g] Reaction carried out using 1 equivalent of **5** and 1 equivalent of Et_3N.

trone ylide tautomer. When the reaction was carried out in the presence of the archetypal *O*-TMS diphenylprolinol **3a**, which is recognized as a reliable catalyst for the activation of enals through iminium salt intermediates,[11] no reaction was observed (entry 1). Incorporating benzoic acid as a protic additive with the aim of stabilizing the nitrone ylide intermediate also led to no reactivity (entry 2). Remarkably, using achiral thiourea **5** as co-catalyst, which had been previously used in other reactions under aminocatalytic activation for the stabilization of ionic intermediates through hydrogen-bonding interactions,[12] led to the formation of an *N*-hydroxypyrrolidine adduct, albeit in moderate yield. Importantly, the presence of isoxazolidine cycloadducts was not detected in the crude reaction mixture, meaning that the nitrone did not participate as 1,3-C,O dipole. The adduct was isolated as a complex mixture of four diastereoisomers, including the two epimers at C3 (the stereocentre containing the formyl substituent) that appeared during chromatographic purification. In order to avoid this epimerization process, the crude reaction mixture was subjected to in situ reduction, resulting in the clean formation of adduct **4a** in 47% yield and as a 5:1 mixture of diastereoisomers, in which the major diastereomer showed a very high *ee* (entry 3).

The use of the bulkier diarylprolinol-based catalyst **3b** under these conditions did not give any cycloaddition product (entry 4). The same was observed when the (3+2) reaction with nitrone **1a** was tested under the conditions reported by MacMillan[6a] for the generation of isoxazolidines (entry 5).[13] We also surveyed the possibility of using bifunctional pyrrolidine/squaramide catalyst **3d**, but this was unable to provide good enantiocontrol (entry 6). An important improvement was observed when a basic additive such as Et_3N was incorporated (20 mol%) into the reaction, resulting in adduct **4a** in high yield, diastereo- and enantiocontrol after 48 h (entry 7).[14] Using a larger amount of base led to poorer yield of **4a** (entry 8); yield was also poor when the reaction was carried out in the presence of Et_3N but without thiourea **5** (entry 9); this last experiment demonstrates the key role played by thiourea in the stabilization of the nitrone ylide intermediate. Using stoichiometric amounts of both additives, the reaction was observed to proceed much faster, producing complete conversion after 12 h but with a lower isolated yield of **4a** because of some decomposition (entry 10). Finally, other solvents were also screened (entries 11–14) without any significant improvement, it was therefore concluded that the conditions summarized in entry 7 of Table 1 were the most appropriate for this transformation. It should be highlighted that these conditions enable the generation of nitrone ylides from substrates in which the proton undergoing prototropy is activated by a single electron-withdrawing group, in contrast to what was previously found for the generation of azomethine ylides, for which the presence of two activating groups is necessary to form the ylide.[7a,k] This is a relevant issue since it also opens the door to the synthesis of pyrrolidines with one single electron-withdrawing substituent at the stereocentre.

Having established a robust experimental protocol for the reaction, we next proceeded to explore the scope of the nitrone and enal reagents. As seen in Table 2, the reaction proceeded efficiently with a family of structurally different β-aryl-substituted enals **2a–l**. This produced the hydroxypyrrolidine adducts **4a–n** in high yields, and excellent diastereoselectivity (entries 1–14), regardless of the electronic nature of the aryl substituent (compare entries 1–7 with entries 9–12) or the aryl ring position (compare entries 3, 4 and 7).[16] Also, β-heteroaryl-substituted enals performed well (entries 6, 13 and 18). The formation of isoxazolidine byproducts were not observed in the crude reaction mixture in any of these cases. The reaction also showed a similar level of performance when the structure of the ester moiety on the nitrone was changed (see entries 1–6 vs. 7–14). It also proceeded efficiently when nitrones with different substitution patterns on the aryl substituent were employed (entries 15–19), although results indicated that the yield was significantly higher when strongly electron-withdrawing groups were placed at this position (entries 15–18 vs. entries 19 and 20). Remarkably, a larger ethyl group at the α-position to the ester moiety of the nitrone also led to excellent results, which points to a wide tolerance towards the incorporation of substituents at this position, leading to the formation

Table 2. Scope of the reaction.



1a-h 2a-l 4a-v

Entry	Product	R^1	R^2	R^3	R^4	Yield [%][a]	d.r.[b]	*ee* [%][c]
1	**4a**	4-$NO_2C_6H_4$	Me	Me	Ph	92	5:1	98
2	**4b**	4-$NO_2C_6H_4$	Me	Me	4-MeC_6H_4	84	6:1	99
3	**4c**	4-$NO_2C_6H_4$	Me	Me	4-$MeOC_6H_4$	85	6:1	>99
4	**4d**	4-$NO_2C_6H_4$	Me	Me	2-$MeOC_6H_4$	72	4:1	94
5	**4e**	4-$NO_2C_6H_4$	Me	Me	4-$Et_2NC_6H_4$	74	2:1	>99
6	**4f**	4-$NO_2C_6H_4$	Me	Me	2-furyl	93	9:1	>99
7	**4g**	4-$NO_2C_6H_4$	Me	Et	3,5-$(MeO)_2C_6H_3$	83	4:1	>99
8	**4h**	4-$NO_2C_6H_4$	Me	Et	Ph	84	4:1	99
9	**4i**	4-$NO_2C_6H_4$	Me	Et	4-BrC_6H_4	81	4:1	99
10	**4j**	4-$NO_2C_6H_4$	Me	Et	4-ClC_6H_4	94	4:1	98
11	**4k**	4-$NO_2C_6H_4$	Me	Et	4-IC_6H_4	86	5:1	99
12	**4l**	4-$NO_2C_6H_4$	Me	Et	4-$CF_3C_6H_4$	85	4:1	99
13	**4m**	4-$NO_2C_6H_4$	Me	Et	2-thienyl	78	7:1	>99
14	**4n**	4-$NO_2C_6H_4$	Me	Et	4-$MeOC_6H_4$	82	5:1	98
15	**4o**	3,5-$(CF_3)_2C_6H_3$	Me	Me	Ph	80	9:1	98
16	**4p**	4-CNC_6H_4	Me	Me	Ph	82	9:1	96
17	**4q**	4-CNC_6H_4	Me	Me	4-$MeOC_6H_4$	84	9:1	96
18	**4r**	4-CNC_6H_4	Me	Me	2-thienyl	82	10:1	99
19[d]	**4s**	4-BrC_6H_4	Me	Me	4-$MeOC_6H_4$	46	1:1	90
20[d]	**4t**	Ph	Me	Me	4-$MeOC_6H_4$	45	1:1	92
21	**4u**	4-$NO_2C_6H_4$	Et	Me	4-$MeOC_6H_4$	96	>20:1	>99
22[d]	**4v**	CO_2Et	Et	Me	4-$MeOC_6H_4$	25	>20:1	98

[a] Combined yield of the diastereomeric mixture after purification. [b] Determined by NMR spectroscopic analysis of the crude reaction mixture before the reduction step. [c] Determined by HPLC analysis on a chiral stationary phase (see Supporting Information). [d] 1 Equivalent of additive **5** and Et_3N was used.

of a quaternary stereocentre (entry 21). Finally, a glyoxylate-derived nitrone was employed,[17] also illustrating the possible participation of nonaromatic nitrones as substrates (entry 22).[18] A possible limitation to this methodology arose when electron-rich aryl substituents were placed on the nitrone reagent (R^1); in this case reactions were found to be significantly slower.[19] In the same regard, the reaction using β-alkyl-substituted enals was also tested, but without observing any product after several days.

Crystals suitable for X-ray analysis could be grown for adduct **4j**, which allowed its absolute configuration as (2*S*,3*S*,4*R*,5*S*) to be ascertained.[20] The absolute configuration of the other adducts **4a**–**u** was established by assuming an analogous mechanistic pathway for all reactions. This configuration is also in agreement with the stereochemical outcome of other reactions proceeding through iminium intermediates, and involving facial stereoselection through the steric bulk exerted by catalyst **3a**.[11] In this sense we propose the formation of a nitrone ylide thiourea complex, stabilized through hydrogen-bonding interactions, which approaches the activated iminium ion through its less hindered face as shown in a simplified manner in Figure 1. The observed stereostructure can only be

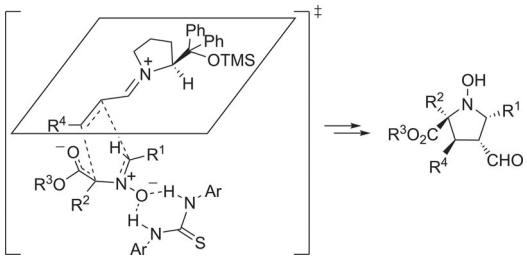
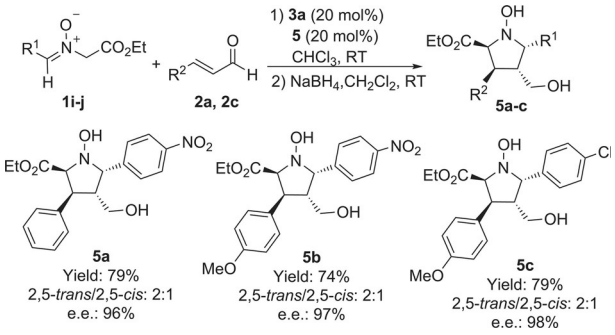


Figure 1. Proposed model to explain the stereochemical outcome of the reaction.

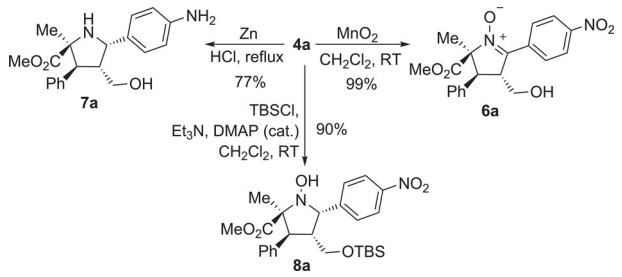
reached by assuming the participation of an ylide with an *S*-type geometry, in which the thiourea can only interact with one of the two negatively charged oxygen atoms of the ylide. It is therefore assumed that interaction with the nitrone oxygen is more likely to occur, since it helps to generate an azomethine functionality, which is more likely to react with the incipient nucleophilic α-carbon of the iminium ion that is produced as the reaction moves forward. Detailed mechanistic features such as the concerted or stepwise nature of the cycloaddition process or the nature of the hydrogen-bonding interactions between the ylide and the thiourea are currently under investigation.

The reaction using glycinate-based nitrones was also screened with a variety of substrates (Scheme 2). The reaction proceeded satisfactorily,[21] giving cycloadducts **5a**–**c** in excellent yield, as 2:1 mixtures of 2,5-*trans* and 2,5-*cis* diastereoisomers, but with excellent enantiocontrol, and without the production of isoxazolidine byproducts.



Scheme 2. Some reactions using glycinate-based nitrones.

Finally, we also evaluated some possible manipulations of the obtained *N*-hydroxypyrrolidines **4** in order to demonstrate their potential as chiral building-blocks in synthesis (Scheme 3). Taking **4a** as representative example, this compound could be easily oxidized to give highly-substituted cyclic nitrone **6a** with great synthetic value.[9a] Moreover, the reduction to the corresponding pyrrolidine **7a** could also be easily accomplished using Zn/HCl. Finally, we also demonstrated the feasibility of the selective protection of the primary alcohol moiety in the presence of the hydroxylamino functionality (**8a**).



Scheme 3. Some useful transformations on adduct **4a**.

In conclusion, this novel organocatalyzed asymmetric (3+2) cycloaddition of nitrones with α,β-unsaturated aldehydes provides a new entry to the enantioselective synthesis of a variety of highly substituted *N*-hydroxypyrrolidines bearing a quaternary center adjacent to the nitrogen atom.[22] The combined use of organocatalyst **3a** together with thiourea **5** enabled the first successful use of *N*-(alkoxycarbonylmethyl)nitrones in highly enantioselective (3+2) cycloadditions participating as 1,3-C–C dipoles, as an alternative to their well-known 1,3-C,O reactivity.

Acknowledgements

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Keywords: asymmetric catalysis · cycloaddition · nitrones · organocatalysis · pyrrolidines

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[13] *p*-Nitrobenzaldehyde and the corresponding cinnamaldehyde-derived nitrone were cleanly isolated after 36 h of reaction in both cases.

[14] Other Brønsted bases such as DMAP, DBU, DABCO, Na_2CO_3 or LiOAc were tested, but did not produce better results than Et_3N.

[15] The obtained aldehydes proved to be configurationally unstable and epimerization was observed upon manipulation.

[16] In all cases, the minor diastereoisomers obtained were identified to be those with opposite configuration at both C2 and C5 positions.

[17] The starting nitrone was employed as a mixture of *Z*/*E* diastereoisomers, from which only one was found to be reactive, which explained the low yield. This behavior is under investigation.
[18] Nitrones derived from aliphatic aldehydes (R^1 = alkyl) reacted through the undesired 1,2-addition pathway. See also reference [10].
[19] The reaction with tolualdehyde-derived nitrone (R^1 = 4-MeC_6H_4, R^2 = Me, R^3 = Me) with cinnamaldehyde produced a 20% conversion after 72 h.
[20] CCDC 1511107 (**4j**) contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.
[21] The reaction produced slightly better yield in the absence of Et_3N.
[22] During the revision of this manuscript, a related example of a (3+2) cycloaddition between isatin-based nitrone ylides and enals proceeding under iminium activation was reported: Y.-R. Chen, G. Zhan, W. Du, Y.-C. Chen, *Adv. Synth. Catal.* **2016**, *358*, 3759.

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Regioselectivity Change in the Organocatalytic Enantioselective (3+2) Cycloaddition with Nitrones Through Cooperative H-Bonding Catalysis/Iminium Activation

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Contents

General Methods.[1]

NMR: Monodimensional nuclear magnetic resonance proton and carbon spectra (^{1}H-NMR and ^{13}C-NMR) were acquired at 25ºC on a Bruker AC-300 spectrometer (300 MHz for ^{1}H, 75.5 MHz for ^{13}C and 282 MHz for ^{19}F). Chemical shifts (δ) are reported in ppm relative to residual solvent signals[2] ($CHCl_3$, 7.26 ppm for ^{1}H NMR, $CDCl_3$, 77.0 ppm for ^{13}C NMR; MeOH, 3.31 ppm for ^{1}H NMR, MeOD, 49.0 ppm for ^{13}C NMR) and coupling constants (*J*) in hertz (Hz). The following abbreviations are used to indicate the multiplicity in ^{1}H NMR spectra: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad signal. ^{13}C NMR spectra were acquired on a broad band decoupled mode using DEPT experiments (Distortionless Enhancement by Polarization Transfer) for nucleus assignement.

IR: Infrared spectra (IR) were measured in a Jasco FT/IR 4100, a Perkin-Elmer 1600 and a Perkin-Elmer Spectrum BX apparatus, in the interval between 4000 and 400 cm^{-1} with a 4 cm^{-1} resolution. Only characteristic bands are given in each case.

HRMS: High-resolution mass spectra (HRMS) on an Acquity UPLC coupled to a QTOF mass spectrometer (SYNAPT G2 HDMS) using electrospray ionization (ESI).

HPLC: High performance liquid chromatography on a chiral stationary phase was performed in a Waters 2695 chromatograph coupled to a Waters 2998 photodiode array detector. Daicel Chiralpak *AD-H, IA, IC, OD-H* columns (0.46 cm x 25 cm) were used; specific conditions are indicated for each case.

X-ray data collections were performed in an Agilent Supernova diffractometer equipped with an Atlas CCD area detector, and a CuKα micro-focus source with multilayer optics (λ = 1.54184Å, 250μm FWHM beam size). The sample was kept at 120 K with a Oxford Cryosystems Cryostream 700 cooler. The quality of the crystals was checked under a polarizing miscroscope, and a suitable crystal or fragment was mounted on a Mitegen Micromount™ using Paratone N inert oil and transferred to the diffractometer.

Miscellaneous: Analytical grade solvents and commercially available reagents were used without further purification. Anhydrous solvents were purified and dried with activated molecular sieves prior to use. For reactions carried out under inert conditions, the argon was previously dried through a column of P_2O_5 and a column of KOH and $CaCl_2$. All the glassware was dried for 12 hours prior to use in an oven at 140ºC, and allowed to cool under a dehumidified atmosphere.[3] Reactions were monitored using analytical thin layer chromatography (TLC), in pre-coated silica-backed plates (Merck Kieselgel 60 F254). These were visualized by ultraviolet irradiation, permanganate potasium or *p*-anisaldehyde dips.[4] For flash chromatography Silicycle 40-63, 230-400 mesh silica gel was used.[5] For the removal of solvents under reduced pressure Büchi R-210 rotary evaporators were used.

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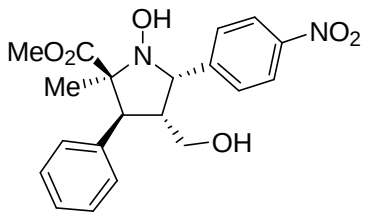
Experimental Procedures and Characterizations.

General Procedure A for the Preparation of 1-Hydroxypyrrolidine Adducts 4a-r, 4u. The corresponding nitrone **1a-d**, **1g**, (0.20 mmol), 1,3-bis(3,5-bis(trifluoromethyl)phenyl)thiourea **5** (0.04 mmol) and triethylamine (0.04 mmol) were added to a solution of (2*S*)-2-[diphenyl[(trimethylsilyl)oxy]methyl]pyrrolidine **3a** (0.04 mmol) and the corresponding α,β-unsaturated aldehyde **2a-l** (0.24 mmol) in dry chloroform (0.4 mL) in an screw capped vial equipped with a magnetic stirring bar. The reaction mixture was stirred at room temperature, until achievement of full conversion. The crude reaction mixture was concentrated and redissolved in dry dichloromethane (2 ml) and $NaBH_4$ (0.80 mmol) was added. The reaction was stirred at room temperature for 4 hours, then 4 mL of water were added. The organic layer was separated and the aqueous layer was extracted with dichloromethane (3 x 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-Pentane/Et_2O 1:1 to 3:7) to afford pure alcohols **4a-r, 4u**.

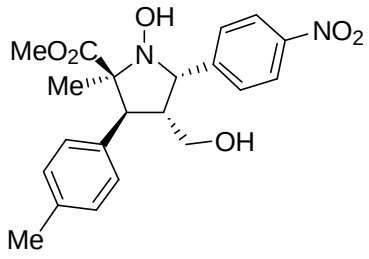
General Procedure B for the Preparation of 1-Hydroxypyrroldine Adducts 4s, 4t, 4t', 4v. The corresponding nitrone **1e-f**, **1h** (0.40 mmol), 1,3-bis(3,5-bis(trifluoromethyl)phenyl)thiourea **5** (0.20 mmol) and triethylamine (0.20 mmol) were added to a solution of (2*S*)-2-[diphenyl[(trimethylsilyl)oxy]methyl]pyrrolidine **3a** (0.04 mmol) and the corresponding α,β-unsaturated aldehyde **2a**, **2c** (0.20 mmol) in dry chloroform (0.4 mL) in an screw capped vial equipped with a magnetic stirring bar. The reaction mixture was stirred at room temperature, until achievement of full conversion. The crude reaction mixture was concentrated and redissolved in dry dichloromethane (2 ml) and $NaBH_4$ (0.80 mmol) was added. The reaction was stirred at room temperature for 4 hours, then 4 mL of water were added. The organic layer was separated and the aqueous layer was extracted with dichloromethane (3 x 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography (n-Pentane/Et_2O 1:1 to 3:7) to afford pure alcohols **4s, 4t, 4t', 4v.**

General Procedure C for the Preparation of 1-Hydroxypyrroldine Adducts 5a-c. The corresponding nitrone **1i-j** (0.20 mmol) and 1,3-bis(3,5-bis(trifluoromethyl)phenyl)thiourea **5** (0.04 mmol) were added to a solution of (2*S*)-2-[diphenyl[(trimethylsilyl)oxy]methyl]pyrrolidine **3a** (0.04 mmol) and the corresponding α,β-unsaturated aldehyde **2a, 2c** (0.20 mmol) in dry CH_2Cl_2 (0.4 mL) in an screw capped vial equipped with a magnetic stirring bar. The reaction mixture was stirred at room temperature for 16h. To the crude reaction mixture $NaBH_4$ (0.80 mmol) was added. The reaction was stirred at room temperature for 4 hours, then 4 mL of water were added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-Pentane/Et_2O 1:1 to 3:7) to afford pure alcohols **5a-c**.

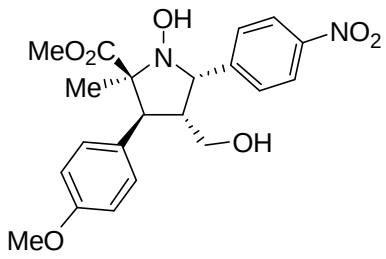
The racemic standards in order to find conditions for HPLC separation were prepared using a mixture of enantiomers of catalyst **3a** (*R* and *S*).



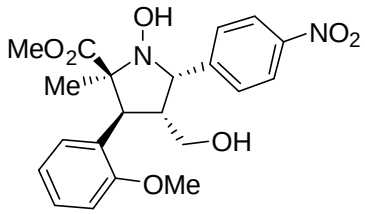
Methyl (2S,3S,4R,5S)-1-hydroxy-4-(hydroxymethyl)-2-methyl-5-(4-nitrophenyl)-3-phenylpyrrolidine-2-carboxylate (4a). Following the general procedure **A**, **4a** (71 mg, 0.18 mmol) was isolated as a pale yellow oil, starting from aldehyde **2a** (32 mg, 0.24 mmol) and nitrone **1a** (50 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 92%. d.r. 5:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 1.29* (s, 3H, CH_3C), 1.57 (s, 3H, CH_3C), 3.06 (d, *J* = 10.9 Hz, 1H, C_3-H), 3.10-3.26 (m, 2H, CH_2), 3.40 (tdd, *J* = 11.0, 6.8, 4.5 Hz, 1H, C_4-H), 3.53 (s, 3H, CH_3O), 3.74* (s, 3H, CH_3O), 4.63* (d, *J* = 10.5 Hz, 1H, C_5-H), 4.95 (s, 1H, NOH), 5.01* (s, 1H, NOH), 5.36 (d, *J* = 10.9 Hz, 1H, C_5-H), 7.19-7.37 (m, 5H, C_{arom}-H), 7.72 (d, *J* = 8.5 Hz, 2H, C_{arom}-H), 7.77* (d, *J* = 8.7 Hz, 2H, C_{arom}-H), 8.24 (d, *J* = 8.8 Hz, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, MeOD) (* denotes minor diastereomer resonances) δ 10.6* (CH_3C), 22.4 (CH_3C), 45.3* (C_4), 46.5 (C_4), 51.7 (C_3), 52.7* (C_3), 52.8 (CH_3O), 55.5 (CH_3O), 62.6 (CH_2OH), 62.8* (CH_2OH), 68.8* (C_5), 71.0 (C_5), 74.9*(C_2), 76.5 (C_2), 123.7 (C_{arom}-H), 128.4* (C_{arom}-H), 128.6 (C_{arom}-H), 129.3* (C_{arom}-H), 129.4 (C_{arom}-H), 129.7 (C_{arom}-H), 130.0* (C_{arom}-H), 131.1* (C_{arom}-H), 131.1 (C_{arom}-H), 138.2 (**C**$_{arom}$-C_3), 138.6* (**C**$_{arom}$-C_3), 148.3 (C_{arom}-NO_2), 148.4* (C_{arom}-NO_2), 149.1* (**C**$_{arom}$-C_5), 150.3 (**C**$_{arom}$-C_5), 173.8 (CO), 176.1* (CO). IR ($CHCl_3$): 3476, 2951, 1725, 1597, 1518, 1345 cm^{-1}. HRMS: Calculated for $[C_{20}H_{22}N_2NaO_6]^+$: 409.1370 (M^++Na); found: 409.1369. The ee (98%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=39.84 min, τ_{major}=106.77 min.



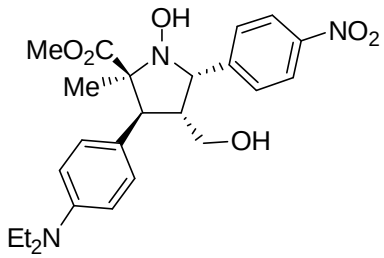
Methyl (2S,3S,4R,5S)-1-hydroxy-4-(hydroxymethyl)-2-methyl-5-(4-nitrophenyl)-3-(p-tolyl)pyrrolidine-2-carboxylate (4b). Following the general procedure **A**, **4b** (67 mg, 0.17 mmol) was isolated as a pale yellow oil, starting from aldehyde **2b** (39 mg, 0.24 mmol) and nitrone **1a** (50 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 84%. d.r. 6:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 1.28* (s, 3H, CH_3C). 1.55 (s, 3H, CH_3C), 2.33 (s, 3H, C_{arom}-CH_3), 2.34* (s, *J* = 1.8 Hz, 3H, C_{arom}-CH_3), 3.01 (d, *J* = 11.0 Hz, 1H, C_3-H), 3.04-3.24 (m, 2H, CH_2), 3.29-3.44 (m, 1H, C_4-H), 3.55 (s, 3H, CH_3O), 3.73* (s, 3H, CH_3O), 4.60* (d, *J* = 10.4 Hz, 1H, C_5-H), 5.01 (s, 1H, NOH), 5.07* (s, 1H, NOH), 5.33 (d, *J* = 11.0 Hz, 1H, C_5-H), 7.10-7.16 (m, 4H, C_{arom}-H), 7.70 (d, *J* = 8.7 Hz, 2H, C_{arom}-H), 7.75* (d, *J* = 8.7 Hz, 2H, C_{arom}-H), 8.22 (d, *J* = 8.8 Hz, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) (* denotes minor diastereomer resonances) δ 11.0* (CH_3C), 21.2 (CH_3C), 21.8 (C_{arom}-CH_3), 45.2* (C_4), 45.8 (C_4), 50.5* (C_3), 51.7 (C_3), 52.4* (CH_3O), 53.8 (CH_3O), 62.2 (CH_2), 62.4* (CH_2), 67.9* (C_5), 70.1 (C_5), 73.3* (C_2), 75.3 (C_2), 123.5 (C_{arom}-H), 123.5* (C_{arom}-H), 128.4 (C_{arom}-H), 129.1* (C_{arom}-H), 129.3* (C_{arom}-H), 129.4 (C_{arom}-H), 129.5 (C_{arom}-H), 133.0 (**C**$_{arom}$-CH_3), 133.7* (**C**$_{arom}$-CH_3), 137.6* (**C**$_{arom}$-C_3), 137.9 (**C**$_{arom}$-C_3), 147.0* (C_{arom}-NO_2), 147.4 (C_{arom}-NO_2), 148.3 (**C**$_{arom}$-C_5), 172.3 (CO), 174.5* (CO). IR ($CHCl_3$): 3468, 2951, 1724, 1597, 1517, 1454, 1345 cm^{-1}. HRMS: Calculated for $[C_{21}H_{24}N_2NaO_6]^+$: 423.1527 (M^++Na); found: 423.1533. The ee (99%) was determined by HPLC using a *Chiralpak OD-3* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=20.90 min, τ_{major}=54.59 min.



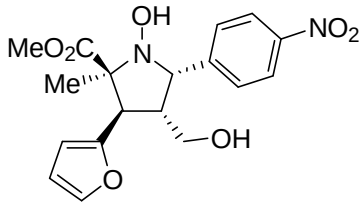
Methyl (2S,3S,4R,5S)-1-hydroxy-4-(hydroxymethyl)-3-(4-methoxyphenyl)-2-methyl-5-(4-nitrophenyl)pyrrolidine-2-carboxylate (4c). Following the general procedure **A**, **4c** (71 mg, 0.17 mmol) was isolated as a yellow oil, starting from aldehyde **2c** (40 mg, 0.24 mmol) and nitrone **1a** (50 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 85%. d.r. 6:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 1.28* (s, 3H, CH_3C), 1.54 (s, 3H, CH_3C), 2.99 (d, *J* = 11.0 Hz, 1H, C_3-H), 3.06-3.25 (m, 2H, CH_2), 3.34 (tdd, *J* = 11.1, 6.9, 4.5 Hz, 1H, C_4-H), 3.55 (s, 3H, CH_3O_2C), 3.73* (s, 3H, CH_3O_2C), 3.79 (s, 3H, C_{arom}-OCH_3), 3.80* (s, 3H, C_{arom}-OCH_3), 4.60* (d, *J* = 10.5 Hz, 1H, C_5-H), 4.97 (s, 1H, NOH), 5.03* (s, 1H, NOH), 5.33 (d, *J* = 10.9 Hz, 1H, C_5-H), 6.85 (d, *J* = 8.7 Hz, 2H, C_{arom}-H), 7.16 (d, *J* = 8.7 Hz, 2H, C_{arom}-H), 7.70 (d, *J* = 8.6 Hz, 2H, C_{arom}-H), 7.75* (d, *J* = 8.7 Hz, 2H, C_{arom}-H), 8.22 (d, *J* = 8.8 Hz, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) (* denotes minor diastereomer resonances) δ 10.9* (CH_3C), 21.8 (CH_3C), 45.3* (C_4), 45.9 (C_4), 50.1* (C_3), 51.7 (C_3), 52.4* (**C**H_3O_2C), 53.4 (**C**H_3O_2C), 55.4 (C_{arom}-O**C**H_3), 62.2 (CH_2), 62.4* (CH_2), 67.8* (C_5), 70.0 (C_5), 73.2* (C_2), 75.3 (C_2), 113.9* (C_{arom}-H), 114.7 (C_{arom}-H), 123.5 (C_{arom}-H), 123.6* (C_{arom}-H), 128.0 (**C**$_{arom}$-C_3), 129.4 (C_{arom}-H), 129.5* (C_{arom}-H), 129.6* (C_{arom}-H), 130.3 (C_{arom}-H), 131.1* (C_{arom}-H), 131.1 (C_{arom}-H), 138.2 (C_{arom}), 138.6* (C_{arom}), 147.0* (**C**$_{arom}$-NO_2), 147.4 (**C**$_{arom}$-NO_2), 147.5* (**C**$_{arom}$-C_5), 148.3 (**C**$_{arom}$-C_5), 159.2* (**C**$_{arom}$-OCH_3), 159.4 (**C**$_{arom}$-OCH_3), 172.3 (CO), 174.5* (CO). IR ($CHCl_3$): 3462, 2951, 1724, 1612, 1514, 1345 cm^{-1}. HRMS: Calculated for $[C_{21}H_{24}N_2NaO_7]^+$: 439.1476 (M^++Na); found: 439.1476. The ee (>99%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=53.17 min, τ_{major}=112.73 min.



Methyl (2S,3S,4R,5S)-1-hydroxy-4-(hydroxymethyl)-3-(2-methoxyphenyl)-2-methyl-5-(4-nitrophenyl)pyrrolidine-2-carboxylate (4d). Following the general procedure **A**, **4d** (60 mg, 0.14 mmol) was isolated as a yellow oil, starting from aldehyde **2d** (40 mg, 0.24 mmol) and nitrone **1a** (50 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 72%. d.r. 4:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 1.55 (s, 3H, CH_3C), 1.57* (s, 3H, CH_3C), 3.09-3.18 (m, 2H, CH_2), 3.24-3.37 (m, 1H, C_4-H), 3.52 (s, 3H, CH_3O_2C), 3.76* (s, 3H, CH_3O_2C), 3.79* (s, 3H, C_{arom}-OCH_3), 3.84 (s, 3H, C_{arom}-OCH_3), 4.96* (s, 1H, NOH), 5.02 (s, 1H, NOH), 5.35 (d, *J* = 10.7 Hz, 1H, C_5-H), 6.86-6.98 (m, 2H, C_{arom}-H), 7.19-7.31 (m, 2H, C_{arom}-H), 7.73 (d, *J* = 8.7 Hz, 2H, C_{arom}-H), 8.24 (d, *J* = 8.8 Hz, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 22.2 (CH_3C), 44.9 (C_4), 45.9 (C_3), 51.6 (**C**H_3O_2C), 55.6 (C_{arom}-O**C**H_3), 62.5 (CH_2), 70.2 (C_5), 75.5 (C_2), 110.9, 120.7, 123.5 (C_{arom}-H), 124.8 (**C**$_{arom}$-C_3), 127.9 (C_{arom}-H), 128.8 (C_{arom}-H), 129.5 (C_{arom}-H), 147.4 (C_{arom}-NO_2), 148.3 (**C**$_{arom}$-C_5), 158.1 (**C**$_{arom}$-OCH_3), 172.8 (CO). IR ($CHCl_3$): 3476, 2948, 1725, 1598, 1518, 1492, 1345, 1246 cm^{-1}. HRMS: Calculated for $[C_{21}H_{24}N_2NaO_7]^+$: 439.1476 (M^++Na); found: 439.1467. The ee (94%) was determined by HPLC using a *Chiralpak OD-3* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=22.14 min, τ_{major}=85.38 min. $[\alpha]_D^{20}$: +22.9 (*c* = 1.0, $CHCl_3$).

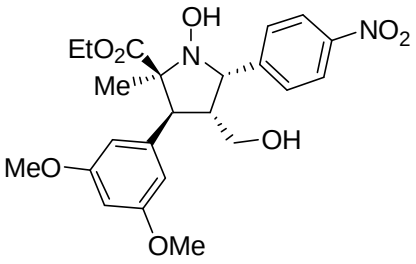


Methyl (2S,3S,4R,5S)-3-(4-(diethylamino)phenyl)-1-hydroxy-4-(hydroxymethyl)-2-methyl-5-(4-nitrophenyl)pyrrolidine-2-carboxylate (4e). Following the general procedure **A**, **4e** (68 mg, 0.15 mmol) was isolated as a yellow oil, starting from aldehyde **2e** (49 mg, 0.24 mmol) and nitrone **1a** (50 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 74%. d.r. 2:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 1.07-1.22 (m, 6H, C**H**$_3$CH$_2$), 1.29* (s, 3H, CH_3C), 1.54 (s, 3H, CH_3C), 2.89 (d, *J* = 11.0 Hz, 1H, C_3-H), 2.93-3.26 (m, 2H, C**H**$_2$OH), 3.26-3.40 (m, 5H, C_4-H, CH_3C**H**$_2$), 3.58 (s, 3H, CH_3O), 3.73* (s, 3H, CH_3O), 4.58* (d, *J* = 10.5 Hz, 1H, C_5-H), 4.97 (s, 1H, NOH), 5.04* (s, 1H, NOH), 5.30 (d, *J* = 11.0 Hz, 1H, C_5-H), 6.55-6.64 (m, 2H, C_{arom}-H), 6.99-7.09 (m, 2H, C_{arom}-H), 7.70 (d, *J* = 8.5 Hz, 2H, C_{arom}-H), 7.75* (d, *J* = 8.6 Hz, 2H, C_{arom}-H), 8.22 (d, *J* = 8.7 Hz, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) (* denotes minor diastereomer resonances) δ 10.9* (CH_3C), 12.7 (**C**H$_3$CH$_2$), 21.8 (CH_3C), 44.4 (CH_3**C**H$_2$), 45.3* (C_4), 45.9 (C_4), 50.2* (CH_3O), 51.7 (C_3), 52.3* (C_3), 53.6 (CH_3O), 62.5 (CH_2OH), 62.6* (CH_2OH), 67.9* (C_5), 70.1 (C_5), 73.5*(C_2), 75.3 (C_2), 111.5* (C_{arom}-H), 111.8 (C_{arom}-H), 121.9 (**C**$_{arom}$-C_3), 122.5* (**C**$_{arom}$-C_3), 123.4 (C_{arom}-H), 123.5* (C_{arom}-H), 129.4 (C_{arom}-H), 129.4 (C_{arom}-H), 129.5* (C_{arom}-H), 130.1* (C_{arom}-H), 147.3* (C_{arom}-NO_2), 147.4 (C_{arom}-NO_2), 147.4* (**C**$_{arom}$-C_5), 147.7 (**C**$_{arom}$-C_5), 148.5 (C_{arom}-NCH_2), 172.5 (CO), 174.8* (CO). IR ($CHCl_3$): 3541, 3314, 2978, 1715, 1613, 1518, 1342 cm^{-1}. HRMS: Calculated for $[C_{24}H_{32}N_3O_6]^+$: 458.2286 (M^++H); found: 458.2296. The ee (>99%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=36.73 min, τ_{major}=94.35 min.

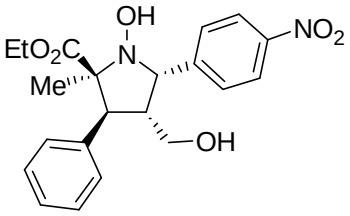


Methyl (2S,3R,4R,5S)-3-(furan-2-yl)-1-hydroxy-4-(hydroxymethyl)-2-methyl-5-(4-nitrophenyl)pyrrolidine-2-carboxylate (4f). Following the general procedure **A**, **4f** (70 mg, 0.19 mmol) was isolated as a colorless oil, starting from aldehyde **2f** (29 mg, 0.24 mmol) and nitrone **1a** (50 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 93%. d.r. 9:1. ^{1}H NMR (300 MHz, MeOD) (* indicates minor diastereomer resonances) δ 1.26* (s, 3H, CH_3C), 1.64 (s, 3H, CH_3C), 3.07-3.23 (m, 3H, C_3-H, C**H**$_2$OH), 3.27-3.39 (m, 1H, C_4-H), 3.65 (s, 3H, CH_3O), 3.84* (s, 3H, CH_3O), 4.57* (d, *J* = 10.2 Hz, 1H, C_5-H), 5.23 (d, *J* = 10.6 Hz, 1H, C_5-H), 6.18-6.31 (m, 1H, $C_{Heteroarom}$-H), 6.38 (dd, *J* = 3.3, 1.9 Hz, 1H, $C_{Heteroarom}$-H), 7.44 (dd, *J* = 1.9, 0.9 Hz, 1H, $C_{Heteroarom}$-H), 7.77 (d, *J* = 8.6 Hz, 2H, C_{arom}-H), 8.23 (d, *J* = 8.8 Hz, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, MeOD) (* denotes minor diastereomer resonances) δ 22.8 (CH_3C), 44.3* (CH_3**C**H$_2$), 45.6 (C_4), 46.7* (C_3), 48.9 (C_3), 51.9 (CH_3O), 52.9* (CH_3O), 62.5 (CH_2OH), 62.8* (CH_2OH), 69.5* (C_5), 70.8 (C_5), 74.1* (C_2), 75.1 (C_2), 108.2 ($C_{Heteroarom}$-H), 108.6* ($C_{Heteroarom}$-H), 111.2* ($C_{Heteroarom}$-H), 111.3 ($C_{Heteroarom}$-H), 123.7 (C_{arom}-H), 123.8* (C_{arom}-H), 131.0 (C_{arom}-H), 143.2* ($C_{Heteroarom}$-H), 143.3 ($C_{Heteroarom}$-H), 148.4 (C_{arom}-NO_2), 148.5* (C_{arom}-NO_2), 148.7 (**C**$_{arom}$-C_5), 149.9 (**C**$_{arom}$-C_5), 153.4 (**C**$_{arom}$-C_3), 153.8* (**C**$_{arom}$-C_3), 173.8 (CO), 175.8* (CO). IR ($CHCl_3$): 3347, 2951, 1725, 1598, 1517, 1345 cm^{-1}. HRMS: Calculated for $[C_{18}H_{20}N_2NaO7]^+$: 399.1163 (M^++Na); found: 399.1164. The ee (>99%) was determined by

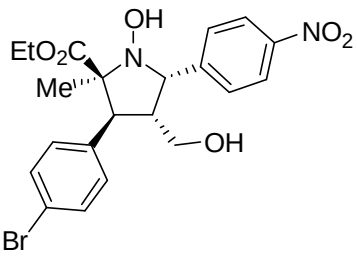
HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=39.73 min, τ_{major}=86.53 min. $[\alpha]_D^{20}$: +10.1 (*c* = 1.0, MeOH).



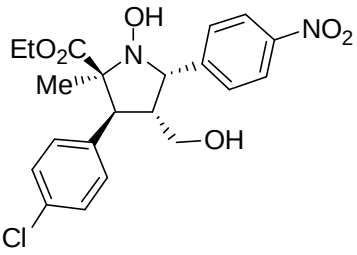
Ethyl (2S,3S,4R,5S)-3-(3,5-dimethoxyphenyl)-1-hydroxy-4-(hydroxymethyl)-2-methyl-5-(4-nitrophenyl)pyrrolidine-2-carboxylate (4g). Following the general procedure **A**, **4g** (77 mg, 0.17 mmol) was isolated as a yellow oil, starting from aldehyde **2g** (46 mg, 0.24 mmol) and nitrone **1b** (50 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 83%. d.r. 4:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 1.09 (t, *J* = 7.1 Hz, 3H, C**H**$_3$CH$_2$), 1.20* (t, *J* = 7.1 Hz, 3H, C**H**$_3$CH$_2$), 1.58 (s, 3H, CH$_3$C), 2.98 (d, *J* = 10.9 Hz, 1H, C$_3$-H), 3.07-3.26 (m, 2H, C**H**$_2$OH), 3.35 (tdd, *J* = 11.0, 6.8, 4.5 Hz, 1H, C$_4$-H), 3.78 (s, 6H, CH$_3$O), 3.95-4.14 (m, 2H, CH$_3$C**H**$_2$), 4.93 (s, 1H, NOH), 5.33 (d, *J* = 10.9 Hz, 1H, C$_5$-H), 6.34-6.54 (m, 3H, C$_{arom}$-H), 7.70 (d, *J* = 8.6 Hz, 2H, C$_{arom}$-H), 8.23 (d, *J* = 8.8 Hz, 2H, C$_{arom}$-H). ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 14.1 (**C**H$_3$CH$_2$), 22.1 (**C**H$_3$C), 45.7 (C$_4$), 54.2 (C$_3$), 55.5 (CH$_3$O), 61.0 (CH$_3$**C**H$_2$), 62.2 (CH$_2$OH), 70.1 (C$_5$), 75.0 (C$_2$), 99.5 (C$_{arom}$-H), 107.0 (C$_{arom}$-H), 108.4* (C$_{arom}$-H), 123.5 (C$_{arom}$-H), 123.9* (C$_{arom}$-H), 128.7* (C$_{arom}$-H), 129.4 (C$_{arom}$-H), 138.6 (**C**$_{arom}$-C$_3$), 147.4 (C$_{arom}$-NO$_2$), 148.2 (**C**$_{arom}$-C$_5$), 171.8 (CO). IR ($CHCl_3$): 3458, 2984, 1720, 1597, 1518, 1462, 1346 cm^{-1}. HRMS: Calculated for $[C_{23}H_{28}N_2NaO_8]^+$: 483.1738 (M^++Na); found: 483.1719. The ee (>99%) was determined by HPLC using a *Chiralpak OD-3* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=38.57 min, τ_{major}=61.96 min. $[\alpha]_D^{20}$: +13.4 (*c* = 1.0, $CHCl_3$).



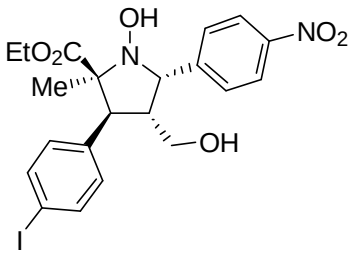
Ethyl (2S,3S,4R,5S)-1-hydroxy-4-(hydroxymethyl)-2-methyl-5-(4-nitrophenyl)-3-phenylpyrrolidine-2-carboxylate (4h). Following the general procedure **A**, **4h** (67 mg, 0.17 mmol) was isolated as a pale yellow oil, starting from aldehyde **2a** (32 mg, 0.24 mmol) and nitrone **1b** (53 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 84%. d.r. 4:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.01 (t, *J* = 7.2 Hz, 3H, C**H**$_3$CH$_2$), 1.57 (s, 3H, CH$_3$C), 3.06 (d, *J* = 10.8 Hz, 1H, C$_3$-H), 3.10-3.25 (m, 2H, C**H**$_2$OH), 3.39 (tdd *J* = 10.9, 6.8, 4.5 Hz, 1H, C$_4$-H), 3.87-4.09 (m, 2H, CH$_3$C**H**$_2$), 5.00 (s, 1H, NOH), 5.36 (d, *J* = 10.9 Hz, 1H, C$_5$-H), 7.19-7.39 (m, 5H, C$_{arom}$-H), 7.71 (d, *J* = 8.7 Hz, 2H, C$_{arom}$-H), 8.23 (d, *J* = 8.8 Hz, 2H, C$_{arom}$-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.0 (**C**H$_3$CH$_2$), 22.0 (CH$_3$C), 45.6 (C$_4$), 54.0 (C$_3$), 60.9 (CH$_3$**C**H$_2$), 62.2 (CH$_2$OH), 70.1 (C$_5$), 75.1 (C$_2$), 123.5 (C$_{arom}$-H), 128.0 (C$_{arom}$-H), 128.6 (C$_{arom}$-H), 128.7 (C$_{arom}$-H), 129.4 (C$_{arom}$-H), 136.2 (**C**$_{arom}$-C$_3$), 147.4 (C$_{arom}$-NO$_2$), 148.2 (**C**$_{arom}$-C$_5$), 171.8 (CO). IR ($CHCl_3$): 3468, 2980, 1716, 1602, 1518, 1345 cm^{-1}. HRMS: Calculated for $[C_{21}H_{24}N_2NaO_6]^+$: 423.1527 (M^++Na); found: 423.1530.The ee (99%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major}=130.16 min, τ_{minor}=35.34 min. $[\alpha]_D^{20}$: +17.9 (*c* = 1.0, $CHCl_3$).



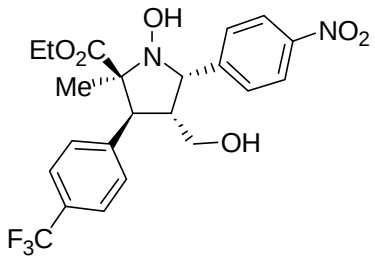
Ethyl (2S,3S,4R,5S)-3-(4-bromophenyl)-1-hydroxy-4-(hydroxymethyl)-2-methyl-5-(4-nitrophenyl)pyrrolidine-2-carboxylate (4i). Following the general procedure **A**, **4i** (78 mg, 0.16 mmol) was isolated as a colorless oil, starting from aldehyde **2h** (52 mg, 0.24 mmol) and nitrone **1b** (53 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 µL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 81%. d.r. 4:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 1.07 (t, *J* = 7.1 Hz, 3H, C**H**$_3$CH$_2$), 1.43* (s, 3H, CH$_3$C), 1.55 (s, 3H, CH$_3$C), 3.04 (d, *J* = 10.8 Hz, 1H, C$_3$-H), 3.06-3.23 (m, 2H, C**H**$_2$OH), 3.33 (tdd, *J* = 11.0, 6.6, 4.5 Hz, 1H, C$_4$-H), 3.87-4.15 (m, 2H, CH$_3$C**H**$_2$), 5.01 (s, 1H, NOH), 5.33 (d, *J* = 10.9 Hz, 1H, C$_5$-H), 5.43* (s, 1H, NOH), 7.04* (d, *J* = 8.4 Hz, 2H, C$_{arom}$-H), 7.15 (d, *J* = 8.5 Hz, 2H, C$_{arom}$-H), 7.45 (d, *J* = 8.4 Hz, 2H, C$_{arom}$-H), 7.69 (d, *J* = 8.6 Hz, 2H, C$_{arom}$-H), 8.10* (d, *J* = 8.7 Hz, 2H, C$_{arom}$-H), 8.22 (d, *J* = 9.0 Hz, 2H, C$_{arom}$-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.1 (**C**H$_3$CH$_2$), 21.9 (CH$_3$C), 45.5 (C$_4$), 53.4 (C$_3$), 61.1 (CH$_3$**C**H$_2$), 62.0 (CH$_2$OH), 69.9 (C$_5$), 74.9 (C$_2$), 122.0 (C$_{arom}$-Br), 123.5, 129.4, 130.4, 131.8 (C$_{arom}$-H), 135.5 (**C**$_{arom}$-C$_3$), 147.4 (C$_{arom}$-NO$_2$), 148.0 (**C**$_{arom}$-C$_5$), 171.6 (CO). IR ($CHCl_3$): 3465, 2984, 1717, 1598, 1518, 1490, 1345 cm^{-1}. HRMS: Calculated for $[C_{21}H_{23}BrN_2NaO_6]^+$: 501.0534 (M$^+$+Na); found: 501.0632. The ee (99%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=45.07 min, τ_{major}=101.88 min. $[\alpha]_D^{20}$: +24.7 (*c* = 1.0, $CHCl_3$).



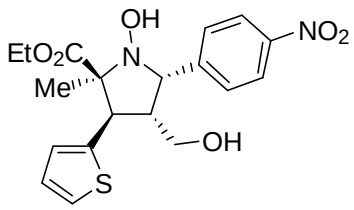
Ethyl (2S,3S,4R,5S)-3-(4-chlorophenyl)-1-hydroxy-4-(hydroxymethyl)-2-methyl-5-(4-nitrophenyl)pyrrolidine-2-carboxylate (4j). Following the general procedure **A**, **4j** (82 mg, 0.19 mmol) was isolated as a colorless oil, starting from aldehyde **2i** (42 mg, 0.24 mmol) and nitrone **1b** (53 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 µL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 94%. d.r. 4:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 1.07 (t, *J* = 7.1 Hz, 3H, C**H**$_3$CH$_2$), 1.56 (s, 3H, CH$_3$C), 3.06 (d, *J* = 10.8 Hz, 1H, C$_3$-H), 3.09-3.24 (m, 2H, C**H**$_2$OH), 3.34 (tdd, *J* = 10.8, 6.7, 4.6 Hz, 1H, C$_4$-H), 3.88-4.13 (m, 2H, CH$_3$C**H**$_2$), 4.94 (s, 1H, NOH), 5.33 (d, *J* = 10.9 Hz, 1H, C$_5$-H), 7.21 (d, *J* = 8.5 Hz, 2H, C$_{arom}$-H), 7.30 (d, *J* = 8.5 Hz, 2H, C$_{arom}$-H), 7.70 (d, *J* = 8.6 Hz, 2H, C$_{arom}$-H), 8.23 (d, *J* = 8.7 Hz, 2H, C$_{arom}$-H).^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.1 (**C**H$_3$CH$_2$), 21.9 (CH$_3$C), 45.6 (C$_4$), 53.3 (C$_3$), 61.1 (CH$_3$**C**H$_2$), 62.0 (CH$_2$OH), 69.9 (C$_5$), 75.0 (C$_2$), 123.6 (C$_{arom}$-H), 128.9 (C$_{arom}$-H), 129.4 (C$_{arom}$-H), 130.0 (C$_{arom}$-H), 133.9 (C$_{arom}$-Cl), 134.9 (**C**$_{arom}$-C$_3$), 147.5 (C$_{arom}$-NO$_2$), 148.0 (**C**$_{arom}$-C$_5$), 171.6 (CO). IR ($CHCl_3$): 3447, 2980, 1715, 1598, 1518, 1493, 1346 cm^{-1}. HRMS: Calculated for $[C_{21}H_{23}ClN_2NaO_6]^+$: 457.1142 (M$^+$+Na); found: 457.1111. The ee (98%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=42.58 min, τ_{major}=105.11 min. $[\alpha]_D^{20}$: +28.1 (*c* = 1.0, $CHCl_3$).



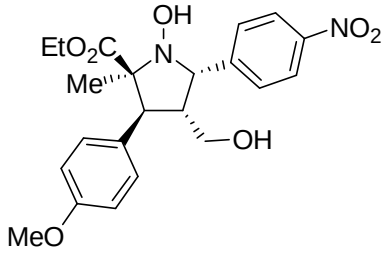
Ethyl (2S,3S,4R,5S)-1-hydroxy-4-(hydroxymethyl)-3-(4-iodophenyl)-2-methyl-5-(4-nitrophenyl)pyrrolidine-2-carboxylate (4k). Following the general procedure **A**, **4k** (91 mg, 0.17 mmol) was isolated as a pale yellow oil, starting from aldehyde **2j** (62 mg, 0.24 mmol) and nitrone **1b** (53 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 86%. d.r. 5:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.07 (t, *J* = 7.1 Hz, 3H, C**H**$_3$CH$_2$), 1.59 (s, 3H, CH$_3$C), 3.03 (d, *J* = 10.7 Hz, 1H, C$_3$-H), 3.07-3.24 (m, 2H, C**H**$_2$OH), 3.33 (tdd, *J* = 10.9, 6.6, 4.6 Hz, 1H, C$_4$-H), 3.89-4.14 (m, 2H, CH$_3$C**H**$_2$), 4.96 (s, 1H, NOH), 5.33 (d, *J* = 10.9 Hz, 1H, C$_5$-H), 7.02 (d, *J* = 8.4 Hz, 2H, C$_{arom}$-H), 7.65 (d, *J* = 8.4 Hz, 2H, C$_{arom}$-H), 7.70 (d, *J* = 8.7 Hz, 2H, C$_{arom}$-H), 8.23 (d, *J* = 8.8 Hz, 2H, C$_{arom}$-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.1 (**C**H$_3$CH$_2$), 21.9 (**C**H$_3$C), 45.4 (C$_4$), 53.5 (C$_3$), 60.9 (CH$_3$**C**H$_2$), 62.2 (CH$_2$OH), 69.9 (C$_5$), 75.0 (C$_2$), 93.5 (C$_{arom}$-I), 123.6 (C$_{arom}$-H), 129.4 (C$_{arom}$-H), 130.6 (C$_{arom}$-H), 136.2 (**C$_{arom}$**-C$_3$), 137.9 (C$_{arom}$-H), 147.5 (C$_{arom}$-NO$_2$), 148.0 (**C$_{arom}$**-C$_5$), 171.6 (CO). IR ($CHCl_3$): 3465, 2984, 1716, 1598, 1517, 1487, 1345 cm^{-1}. HRMS: Calculated for $[C_{21}H_{23}IN_2NaO_6]^+$: 549.0493 ($M^+$+Na); found: 549.0503. The ee (99%) was determined by HPLC using a *Chiralpak ID-3* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=50.99 min, τ_{major}=108.04 min. $[\alpha]_D^{20}$: +52.6 (*c* = 1.0, $CHCl_3$).



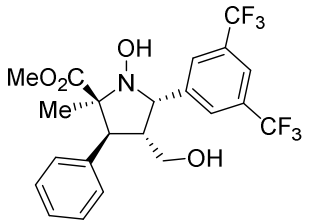
Ethyl (2S,3S,4R,5S)-1-hydroxy-4-(hydroxymethyl)-2-methyl-5-(4-nitrophenyl)-3-(4-(trifluoromethyl)phenyl)pyrrolidine-2-carboxylate (4l). Following the general procedure **A**, **4l** (80 mg, 0.17 mmol) was isolated as a pale yellow oil, starting from aldehyde **2k** (80 mg, 0.40 mmol) and nitrone **1b** (53 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 85%. d.r. 4:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 (t, *J* = 7.1 Hz, 3H, C**H**$_3$CH$_2$), 1.59 (s, 3H, CH$_3$C), 3.09-3.26 (m, 3H, C$_3$-H, CH$_2$OH), 3.34-3.47 (m, 1H, C$_4$-H), 3.88-4.12 (m, 2H, CH$_3$C**H**$_2$), 4.95 (s, 1H, NOH), 5.37 (d, *J* = 10.8 Hz, 1H, C$_5$-H), 7.41 (d, *J* = 8.2 Hz, 2H, C$_{arom}$-H), 7.59 (d, *J* = 8.2 Hz, 2H, C$_{arom}$-H), 7.71 (d, *J* = 8.6 Hz, 2H, C$_{arom}$-H), 8.25 (d, *J* = 8.9 Hz, 2H, C$_{arom}$-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 13.9 (**C**H$_3$CH$_2$), 21.9 (**C**H$_3$C), 45.4 (C$_4$), 53.7 (C$_3$), 61.1 (CH$_3$**C**H$_2$), 62.0 (CH$_2$OH), 69.9 (C$_5$), 75.0 (C$_2$), 123.6 (C$_{arom}$-H), 124.0* (C$_{arom}$-H), 125.6 (q, $^3J_{C\text{-}F}$ = 3.6 Hz, **C$_{arom}$**H-F), 128.8 (q, $^1J_{C\text{-}F}$ = 272.4 Hz, C-F), 128.8* (C$_{arom}$-H), 129.1 (C$_{arom}$-H), 129.4 (C$_{arom}$-H), 130.3 (q, $^2J_{C\text{-}F}$ = 32.8 Hz, F-**C$_{arom}$**), 140.8 (**C$_{arom}$**-C$_3$), 147.5 (C$_{arom}$-NO$_2$), 147.8 (**C$_{arom}$**-C$_5$), 171.5 (CO). ^{19}F NMR (282 MHz, $CDCl_3$) δ -62.5. IR ($CHCl_3$): 3476, 2987, 1716, 1601, 1518, 1346, 1326 cm^{-1}. HRMS: Calculated for $[C_{22}H_{23}F_3N_2NaO_6]^+$: 491.1400 ($M^+$+Na); found: 491.1387. The ee (99%) was determined by HPLC using a *Chiralpak IC* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=39.05 min, τ_{major}=89.02 min. $[\alpha]_D^{20}$: +23.6 (*c* = 1.0, $CHCl_3$).



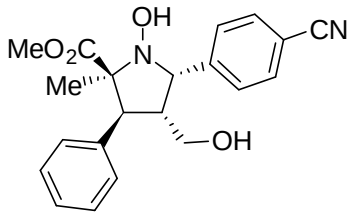
Ethyl (2S,3R,4R,5S)-1-hydroxy-4-(hydroxymethyl)-2-methyl-5-(4-nitrophenyl)-3-(thiophen-2-yl)pyrrolidine-2-carboxylate (4m). Following the general procedure **A**, **4m** (63 mg, 0.16 mmol) was isolated as a pale yellow oil, starting from aldehyde **2l** (33 mg, 0.24 mmol) and nitrone **1b** (53 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 78%. d.r. 7:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (t, *J* = 7.1 Hz, 3H, C**H**$_3$CH$_2$), 1.64 (s, 3H, CH$_3$C), 3.13-3.44 (m, 4H, C$_3$-H, C$_4$-H, C**H**$_2$OH), 4.02-4.16 (m, 2H, CH$_3$C**H**$_2$), 4.89 (s, 1H, NOH), 5.29 (d, *J* = 7.2 Hz, 1H, C$_5$-H), 6.94-7.02 (m, 2H, C$_{Hetarom}$-H), 7.18-7.24 (m, 1H, C$_{Hetarom}$-H), 7.70 (d, *J* = 8.6 Hz, 2H, C$_{arom}$-H), 8.24 (d, *J* = 8.7 Hz, 2H, C$_{arom}$-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.1 (**C**H$_3$CH$_2$), 22.0 (**C**H$_3$C), 47.9 (C$_4$), 48.8 (C$_3$), 61.2 (CH$_3$**C**H$_2$), 61.7 (CH$_2$OH), 70.0 (C$_5$), 75.0 (C$_2$), 123.6 (C$_{arom}$-H), 124.9 (C$_{Heteroarom}$-H), 126.3 (C$_{Heteroarom}$-H), 127.1 (C$_{Heteroarom}$-H), 129.4 (C$_{arom}$-H), 129.4 (C$_{arom}$-H), 139.6 (C$_{Heteroarom}$-C$_3$), 147.5 (C$_{arom}$-NO$_2$), 148.0 (**C**$_{arom}$-C$_5$), 171.5 (CO). IR ($CHCl_3$): 3458, 2984, 1718, 1598, 1518, 1345 cm^{-1}. HRMS: Calculated for $[C_{19}H_{22}N_2NaO_6S]^+$: 429.1019 ($M^+$+Na); found: 429.1091. The ee (>99%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=42.35 min, τ_{major}=93.22 min. $[\alpha]_D^{20}$: +61.8 (*c* = 0.7, $CHCl_3$).



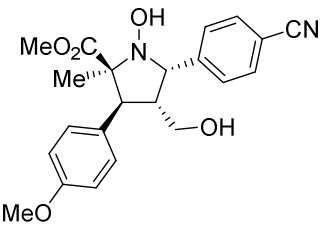
Ethyl (2S,3S,4R,5S)-1-hydroxy-4-(hydroxymethyl)-3-(4-methoxyphenyl)-2-methyl-5-(4-nitrophenyl)pyrrolidine-2-carboxylate (4n). Following the general procedure **A**, **4n** (71 mg, 0.16 mmol) was isolated as a pale yellow oil, starting from aldehyde **2c** (40 mg, 0.24 mmol) and nitrone **1b** (53 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 48h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 82%. d.r. 5:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 1.07 (t, *J* = 7.1 Hz, 3H, C**H**$_3$CH$_2$), 1.17* (t, *J* = 7.1 Hz, 3H, C**H**$_3$CH$_2$), 1.53* (s, 3H, CH$_3$C), 1.55 (s, 3H, CH$_3$C), 3.00 (d, *J* = 10.9 Hz, 1H, C$_3$-H), 3.06-3.24 (m, 2H, C**H**$_2$OH), 3.34 (tdd, *J* = 11.0, 6.8, 4.5 Hz, 1H, C$_4$-H), 3.48* (d, *J* = 10.8 Hz, 1H, C$_3$-H), 3.79 (s, 3H, CH$_3$O), 3.91-4.14 (m, 2H, CH$_3$C**H**$_2$), 4.95 (s, 1H, NOH), 5.33 (d, *J* = 10.9 Hz, 1H, C$_5$-H), 6.85 (d, *J* = 8.7 Hz, 2H, C$_{arom}$-H), 7.18 (d, *J* = 8.7 Hz, 2H, C$_{arom}$-H), 7.53* (d, *J* = 8.6 Hz, 2H, C$_{arom}$-H), 7.71 (d, *J* = 8.6 Hz, 2H, C$_{arom}$-H), 8.23 (d, *J* = 8.7 Hz, 2H, C$_{arom}$-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 14.1 (**C**H$_3$CH$_2$), 21.9 (**C**H$_3$C), 45.8 (C$_4$), 53.4 (C$_3$), 55.4 (CH$_3$O), 60.9 (CH$_3$**C**H$_2$), 62.2 (CH$_2$OH), 70.1 (C$_5$), 75.1 (C$_2$), 114.1 (C$_{arom}$-H), 123.5 (C$_{arom}$-H), 128.1 (**C**$_{arom}$-C$_3$), 129.4 (C$_{arom}$-H), 129.7 (C$_{arom}$-H), 147.4 (C$_{arom}$-NO$_2$), 148.3 (**C**$_{arom}$-C$_5$), 159.4 (C$_{arom}$-O), 171.9 (CO). IR ($CHCl_3$): 3458, 2987, 1718, 1598, 1514, 1345, 1251 cm^{-1}. HRMS: Calculated for $[C_{22}H_{26}N_2NaO_7]^+$: 453.1632 (M^++Na); found: 453.1613. The ee (98%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=50.46 min, τ_{major}=140.72 min. $[\alpha]_D^{20}$: +19.25 (*c* = 1.0, $CHCl_3$).



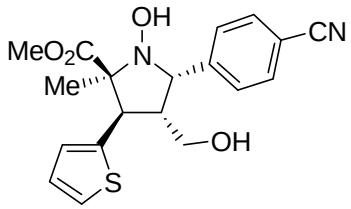
Methyl (2S,3S,4R,5S)-5-(3,5-bis(trifluoromethyl)phenyl)-1-hydroxy-4-(hydroxymethyl)-2-methyl-3-phenylpyrrolidine-2-carboxylate (4o). Following the general procedure **A**, **4o** (76 mg, 0.16 mmol) was isolated as a pale yellow oil, starting from aldehyde **2a** (32 mg, 0.24 mmol) and nitrone **1c** (69 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 120h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 80%. d.r. 9:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 1.58 (s, 3H, CH_3C), 3.04-3.14 (m, 2H, C_3-H, C**H**$_a$H$_b$), 3.18 (dd, 1H, *J* = 11.1, 4.6 Hz, CH$_a$**H**$_b$), 3.30-3.43 (m, 1H, C_4-H), 3.54 (s, 3H, CH_3O), 3.75* (s, 3H, CH_3O), 4.94 (s, 1H, NOH), 5.40 (d, 1H, *J* = 10.9 Hz, C_5-H), 7.27-7.38 (m, 5H, C_{arom}-H), 7.81 (s, 1H, C_{arom}-H), 7.95-8.03 (m, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.7 (CH_3C), 45.3 (C_4), 51.7 (CH_3O), 54.0 (C_3), 62.0 (CH_2OH), 70.1 (C_5), 75.5 (C_2), 121.5 (C_{arom}-H), 125.4 (C-F), 128.2 (C_{arom}-H), 128.6 (C_{arom}-H), 128.8 (C_{arom}-H), 129.0 (C_{arom}-H), 131.2 (C_{arom}-CF_3), 131.6 (C_{arom}-CF_3), 136.3 (**C**$_{arom}$-C_3), 142.9 (**C**$_{arom}$-C_5), 172.0 (CO). ^{19}F NMR (282 MHz, $CDCl_3$) δ -62.6. HRMS: Calculated for $[C_{22}H_{21}F_6NNaO_4]^+$: 500.1267 ($M^+$+Na); found: 500.1263. The ee (98%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (99:1)]; flow rate 0.9 mL/min; τ_{minor}=27.30 min, τ_{major}=44.38 min. $[\alpha]_D^{20}$: +15.6 (*c* = 0.69, $CHCl_3$).



Methyl (2S,3S,4R,5S)-5-(4-cyanophenyl)-1-hydroxy-4-(hydroxymethyl)-2-methyl-3-phenylpyrrolidine-2-carboxylate (4p). Following the general procedure **A**, **4p** (60 mg, 0.16 mmol) was isolated as a pale yellow oil, starting from aldehyde **2a** (32 mg, 0.24 mmol) and nitrone **1d** (46 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 96h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 82%. d.r. 9:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 1.54 (s, 3H, CH_3C), 3.03 (d, 1H, *J* = 10.9 Hz, C_3-H), 3.12 (dd, 1H, *J* = 11.4, 6.8 Hz, C**H**$_a$H$_b$), 3.17 (dd, 1H, *J* = 11.5, 4.7 Hz, CH$_a$**H**$_b$), 3.35 (tdd, *J* = 11.0, 6.8, 4.5 Hz, 1H, C_4-H), 3.50 (s, 3H, CH_3O), 3.72* (s, 3H, CH_3O), 4.56*(d, 1H, *J* = 10.5 Hz, C_5-H), 4.86 (s, 1H, NOH), 4.98* (s, 1H, NOH), 5.28 (d, 1H, *J* = 11.0 Hz, C_5-H), 7.19-7.33 (m, 5H, C_6H_5), 7.62-7.71 (m, 4H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.9 (CH_3C), 45.7 (C_4), 51.7 (CH_3O), 54.1 (C_3), 62.2 (CH_2OH), 70.3 (C_5), 75.4 (C_2), 111.4 (**C**$_{arom}$-CN), 119.0 (CN), 128.2 (C_{arom}-H), 128.6 (C_{arom}-H), 128.8 (C_{arom}-H), 129.4 (C_{arom}-H), 132.2 (C_{arom}-H), 136.3 (**C**$_{arom}$-C_3), 145.9 (**C**$_{arom}$-C_5), 172.2 (CO). HRMS: Calculated for $[C_{21}H_{22}N_2NaO_4]^+$: 389.1472 (M^++Na); found: 389.1464. The ee (96%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=26.79 min, τ_{major}=60.19 min. $[\alpha]_D^{20}$: +25.6 (*c* = 0.17, $CHCl_3$).

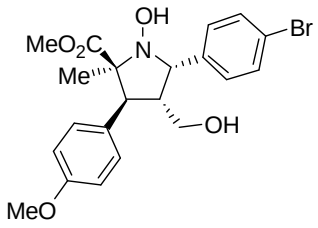


Methyl (2S,3S,4R,5S)-5-(4-cyanophenyl)-1-hydroxy-4-(hydroxymethyl)-3-(4-methoxyphenyl)-2-methylpyrrolidine-2-carboxylate (4q). Following the general procedure **A**, **4q** (67 mg, 0.17 mmol) was isolated as a pale yellow oil, starting from aldehyde **2c** (40 mg, 0.24 mmol) and nitrone **1d** (46 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 96h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 84%. d.r. 9:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53 (s, 3H, CH_3C), 2.16 (s, 1H, CH_2O**H**), 2.98 (d, 1H, *J* = 11.0 Hz, C_3-H), 3.06-3.21 (m, 2H, CH_2), 3.32 (tdd, *J* = 11.1, 6.8, 4.5 Hz, 1H, C_4-H), 3.55 (s, 3H, CH_3O_2C), 3.79 (s, 3H, C_{arom}-OCH_3), 4.94 (s, 1H, NOH), 5.27 (d, 1H, *J* = 10.9 Hz, C_5-H), 6.75-6.92 (m, 2H, C_{arom}-H), 7.05-7.21 (m, 2H, C_{arom}-H), 7.61-7.75 (m, 4H, C_{arom}-H). ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 21.8 (CH_3C), 45.9 (C_4), 51.7 (**C**H_3O_2C), 53.5 (C_3), 55.4 (C_{arom}-O**C**H_3), 62.3 (CH_2OH), 70.2 (C_5), 75.3 (C_2), 111.3 (**C**$_{arom}$-CN), 114.2 (C_{arom}-H), 119.0 (CN), 128.1 (**C**$_{arom}$-C_3), 129.4 (C_{arom}-H), 129.6 (C_{arom}-H), 132.2 (C_{arom}-H), 146.2 (**C**$_{arom}$-C_5), 159.4 (**C**$_{arom}$-OCH_3), 172.3 (CO). HRMS: Calculated for $[C_{22}H_{22}N_2NaO_5]^+$: 4191567 (M^++Na); found: 419.1571. The ee (96%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=36.65 min, τ_{major}=55.87 min. $[\alpha]_D^{20}$: +33.3 (*c* = 0.18, $CHCl_3$).



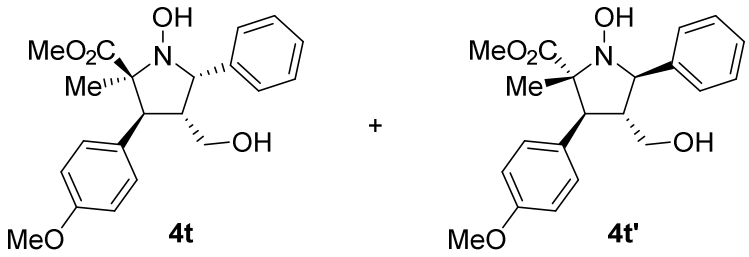
Methyl (2S,3R,4R,5S)-5-(4-cyanophenyl)-1-hydroxy-4-(hydroxymethyl)-2-methyl-3-(thiophen-2-yl)pyrrolidine-2-carboxylate (4r). Following the general procedure **A**, **4r** (61 mg, 0.16 mmol) was isolated as a pale yellow oil, starting from aldehyde **2l** (33 mg, 0.24 mmol) and nitrone **1d** (46 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 96h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 82%. d.r. 10:1. ^{1}H NMR (300 MHz, MeOD) δ 1.57 (s, 3H, CH_3C), 3.05-3.13 (m, 1H, C**H**$_a$H$_b$OH), 3.14-3.21 (m, 1H, CH$_a$**H**$_b$OH), 3.29-3.36 (m, 2H, C_3-H, C_4-H), 3.65 (s, 3H, CH_3O), 5.11-5.23 (m, 1H, C_5-H), 6.94-7.06 (m, 2H, $C_{Hetarom}$-H), 7.30 (dd, *J* = 4.8, 1.6 Hz, 1H, $C_{Hetarom}$-H), 7.66-7.77 (m, 4H, C_{arom}-H). ^{13}C NMR (75.5 MHz, MeOD) δ 22.4 (CH_3), 49.2 (C_4), 50.5 (C_3), 51.9 (CH_3O), 62.1 (CH_2OH), 71.3 (C_5), 76.2 (C_2), 111.4 (**C**$_{arom}$-CN), 120.1 (C≡N), 125.5 ($C_{Heteroarom}$-H), 127.3 ($C_{Heteroarom}$-H), 127.8 ($C_{Heteroarom}$-H), 131.2 (C_{arom}-H), 132.5 (C_{arom}-H), 141.6 ($C_{Heteroarom}$), 148.1(C_{arom}),, 173.7 (CO). IR ($CHCl_3$): 3389, 3218, 3009, 2237, 1716, 1609 cm^{-1}. HRMS: Calculated for $[C_{19}H_{20}N_2NaO_4S]^+$: 395.1036 ($M^+$+Na); found: 395.1037. The ee (99%) was determined by HPLC using a *Chiralpak OD-3* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=27.97 min, τ_{major}=42.40 min. $[\alpha]_D^{20}$: +14.2 (*c* = 1.0, MeOH).

Methyl (2S,3S,4R,5S)-5-(4-bromophenyl)-1-hydroxy-4-(hydroxymethyl)-3-(4-methoxyphenyl)-2-methylpyrrolidine-2-carboxylate (4s). Following the general procedure **B**,



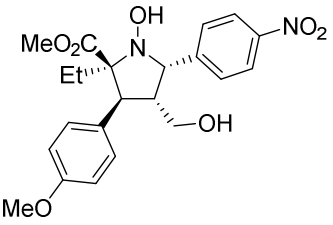
4s (46 mg, 0.10 mmol) was isolated as a pale yellow oil, starting from aldehyde **2c** (34 mg, 0.20 mmol) and nitrone **1e** (114 mg, 0.40 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (100 mg, 0.20 mmol, 100 mol%) and Et_3N (28 μL, 0.20 mmol, 100 mol%) using $CHCl_3$ (0.4 mL) as solvent for 120h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 51%. d.r. 1:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53 (t, *J* = 7.4 Hz, 3H, C**H**$_3$CH$_2$), 2.97 (d, *J* = 10.7 Hz, 1H, C_3-H, 3.10-3.36 (m, 3H, C_4-H, C**H**$_2$OH), 3.55 (s, 3H, CH_3O_2C), 3.79 (s, 3H, C_{arom}-OCH$_3$), 4.85 (s, 1H, NOH), 5.18 (d, 1H, *J* = 10.6 Hz, C_5-H), 6.81-6.88 (m, 2H, C_{arom}-H), 7.13-7.20 (m, 2H, C_{arom}-H), 7.39-7.44 (m, 2H, C_{arom}-H), 7.50-7.54 (m, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.9 (**C**H$_3$CH$_2$), 45.7 (C_4), 51.6 (**C**H$_3$O$_2$C), 53.3 (C_3), 55.4 (C_{arom}-O**C**H$_3$), 62.5 (CH_2OH), 69.8 (C_5), 75.2 (C_2), 114.1 (C_{arom}-H), 121.5 (C_{arom}-Br), 128.4 (**C**$_{arom}$-C_3), 129.6 (C_{arom}-H), 130.1 (**C**$_{arom}$-H), 131.8 (**C**$_{arom}$-H), 139.4 (**C**$_{arom}$-C_5), 159.4 (**C**$_{arom}$-OCH$_3$), 172.4 (CO). HRMS: Calculated for $[C_{21}H_{24}BrNNaO_5]^+$: 472.0736 (M^++Na); found: 472.0700. The ee (90%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=24.41 min, τ_{major}=35.10 min. $[\alpha]_D^{20}$: +27.0 (*c* = 0.18, $CHCl_3$).

Methyl (2S,3S,4R,5S)-1-hydroxy-4-(hydroxymethyl)-3-(4-methoxyphenyl)-2-methyl-5-phenylpyrrolidine-2-carboxylate (4t) and Methyl (2R,3S,4R,5S)-1-hydroxy-4-(hydroxymethyl)-3-(4-methoxyphenyl)-2-methyl-5-phenylpyrrolidine-2-carboxylate (4t').

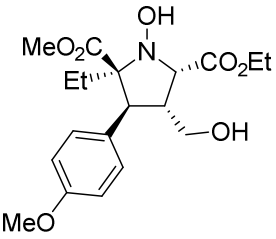


Following the general procedure **B**, **4t** and **4t'** (34 mg, 0.09 mmol) were isolated as yellow oil, starting from aldehyde **2c** (33 mg, 0.20 mmol) and nitrone **1f** (83 mg, 0.40 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (100 mg, 0.20 mmol, 100 mol%) and Et_3N (28 μL, 0.20 mmol, 100 mol%) using $CHCl_3$ (0.4 mL) as solvent for 96h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 46%. d.r. 1:1. Data for **4t**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.54 (s, 3H, CH_3C), 2.99 (d, *J* = 10.7 Hz, 1H, C_3-H), 3.13-3.32 (m, 3H, CH_2, C_4-H), 3.55 (s, 3H, CH_3O_2C), 3.79 (s, 3H, C_{arom}-OCH$_3$), 4.89 (s, 1H, NOH), 5.22 (d, *J* = 10.5 Hz, 1H, C_5-H), 6.82-6.86 (m, 2H, C_{arom}-H), 7.14-7.21 (m, 2H, C_{arom}-H), 7.27-7.35 (m, 1H, C_{arom}-H), 7.37-7.43 (m, 2H, C_{arom}-H), 7.50-7.58 (m, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, CDCl3) δ 22.0 (CH_3C), 45.9 (C_4), 51.6 (C_3), 53.1 (**C**H$_3$O$_2$C), 55.4 (C_{arom}-O**C**H$_3$), 62.5 (CH_2), 70.2 (C_5), 75.2 (C_2), 114.0 (C_{arom}-H), 127.8 (C_{arom}-H), 128.2 (C_{arom}-H), 128.5 (**C**$_{arom}$-C_3), 128.9 (C_{arom}-H), 129.7 (C_{arom}-H), 140.2 (C_{arom}-C_5), 159.3 (**C**$_{arom}$-OCH$_3$), 172.5 (CO). IR ($CHCl_3$): 3440, 2951, 1726, 1612, 1514, 1251 cm^{-1}. HRMS: Calculated for $[C_{21}H_{26}NO_5]^+$: 372.1811 (M^++H); found: 372.1816. The ee (94%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (85:15)]; flow rate 1.0 mL/min; τ_{major}=14.63 min, τ_{minor}=19.83 min. $[\alpha]_D^{20}$: +12.3 (*c* = 1.0, $CHCl_3$). Data for **4t'**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (s, 3H, CH_3C), 2.34 (ddd, *J* = 9.5, 7.3, 4.5 Hz, 1H, C_3-H), 3.57-3.68 (m, 3H, CH_2, C_4-H), 3.80 (s, 3H, CH_3O_2C), 3.83 (s, 3H, C_{arom}-OCH$_3$), 4.45 (d, *J* = 9.6 Hz, 1H, C_5-H), 5.46 (s, 1H, NOH), 6.84-6.90 (m, 2H, C_{arom}-H), 7.21 (d, *J* = 2.0 Hz, 2H, C_{arom}-H), 7.31-7.35 (m, 1H, C_{arom}-H), 7.37-7.44 (m, 2H, C_{arom}-H), 7.52-7.58 (m, 2H, C_{arom}-H). ^{13}C

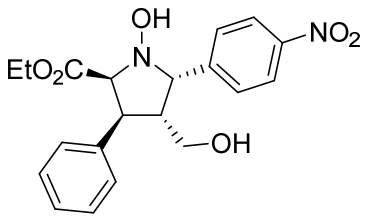
NMR (75.5 MHz, CDCl3) δ 20.9 (CH_3C), 50.4 (C_4), 52.3 (C_3), 53.1 (**C**H_3O_2C), 55.4 (C_{arom}-O**C**H_3), 61.9 (CH_2), 70.0 (C_5), 72.6 (C_2), 113.9 (C_{arom}-H), 127.7 (C_{arom}-H), 127.9 (C_{arom}-H), 128.9 (C_{arom}-H), 130.8 (C_{arom}-H), 132.8 (**C**$_{arom}$-C_3), 141.2 (C_{arom}-C_5), 158.8 (**C**$_{arom}$-OCH_3), 176.3 (CO). IR ($CHCl_3$): 3440, 2951, 1726, 1612, 1514, 1251 cm^{-1}. HRMS: $[C_{21}H_{26}NO_5]^+$: 372.1811 (M^++H); found: 372.1816. The ee (92%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (85:15)]; flow rate 1.0 mL/min; τ_{major}=17.18 min, τ_{minor}=23.98 min. $[\alpha]_D^{20}$: +34.5 (*c* = 1.0, $CHCl_3$).



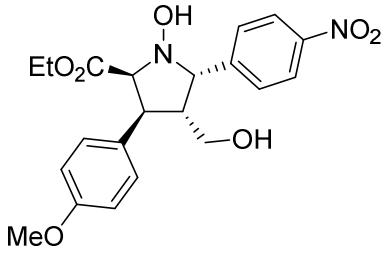
Methyl (2S,3S,4R,5S)-2-ethyl-1-hydroxy-4-(hydroxymethyl)-3-(4-methoxyphenyl)-5-(4-nitrophenyl)pyrrolidine-2-carboxylate (4u). Following the general procedure **A**, **4u** (83 mg, 0.19 mmol) was isolated as a pale yellow oil, starting from aldehyde **2c** (40 mg, 0.24 mmol) and nitrone **1g** (43 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (20 mg, 0.04 mmol, 20 mol%) and Et_3N (5.5 μL, 0.04 mmol, 20 mol%) using $CHCl_3$ (0.4 mL) as solvent for 72h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 96%. d.r. >20:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20 (t, *J* = 7.4 Hz, 3H, C**H**$_3$$CH_2$), 1.85 (dq, *J* = 14.6, 7.3 Hz, 1H, CH_3C**H**$_a$$H_b$), 2.06 (dq, *J* = 14.6, 7.3 Hz, 1H, CH_3CH_a**H**$_b$), 2.06-3.37 (m, 4H, C_3-H, C_4-H, C**H**$_2$OH), 3.54 (s, 3H, CH_3O_2C), 3.80 (s, 3H, C_{arom}-OCH_3), 4.89 (s, 1H, NOH), 5.31 (d, *J* = 10.5 Hz, 1H, C_5-H), 6.81-6.90 (m, 2H, C_{arom}-H), 7.06-7.19 (m, 2H, C_{arom}-H), 7.68-7.73 (m, 2H, C_{arom}-H), 8.20-8.30 (m, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 8.2 (**C**H_3CH_2), 25.1 (**C**H_2), 45.7 (C_4), 48.2 (C_3), 51.6 (**C**H_3O_2C), 55.4 (C_{arom}-O**C**H_3), 62.3 (CH_2OH), 70.2 (C_5), 77.7 (C_2), 114.2, 123.6 (C_{arom}-H), 128.4 (**C**$_{arom}$-C_3), 129.4, 129.5 (**C**$_{arom}$-H), 147.5 (**C**$_{arom}$-NO_2), 148.5 (**C**$_{arom}$-C_5), 159.3 (**C**$_{arom}$-OCH_3), 172.8 (CO). HRMS: Calculated for $[C_{22}H_{26}N_2NaO_7]^+$: 453.1632 (M^++Na); found: 453.1625. The ee (>99%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor}=33.83 min, τ_{major}=77.14 min. $[\alpha]_D^{20}$: +48.7 (*c* = 0.56, $CHCl_3$).



5-Ethyl 2-methyl (2S,3S,4R,5S)-2-ethyl-1-hydroxy-4-(hydroxymethyl)-3-(4-methoxyphenyl)pyrrolidine-2,5-dicarboxylate (4v). Following the general procedure **B**, **4v** (19 mg, 0.05 mmol) was isolated as a pale yellow oil, starting from aldehyde **2c** (34 mg, 0.20 mmol) and nitrone **1h** (87 mg, 0.40 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%), thiourea **5** (100 mg, 0.20 mmol, 100 mol%) and Et_3N (28 μL, 0.20 mmol, 100 mol%) using $CHCl_3$ (0.4 mL) as solvent for 144h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 25%. d.r. >20:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (t, *J* = 7.4 Hz, 3H, C**H**$_3$$CH_2C_2$), 1.16 (t, *J* = 7.1 Hz, 3H, C**H**$_3$$CH_2OOC$), 1.85-2.07 (m, 2H, CH_2C_2), 2.91 (ddd, *J* = 8.6, 6.5, 4.6 Hz, 1H, C_4-H), 3.31 (t, *J* = 8.8 Hz, C**H**$_a$$H_b$OH), 3.69-3.93 (m, 8H, CH_3OC_{arom}, CH_3OOC, C_2-H, CH_a**H**$_b$OH), 4.08-4.27 (m, 3H, C_5-H CH_2CO), 6.10 (s, 1H, NOH), 6.77-6.89 (m, 2H, C_{arom}-H), 7.12-7.24 (m, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 9.6 (**C**$H_3CH_2C_2$), 14.3 (**C**H_3CH_2CO), 25.4 (CH_3**C**H_2C_2), 47.3 (C_4), 53.4 (C_3), 53.8 (**C**H_3OOC), 55.4 (**C**H_3OC_{arom}), 61.3 (CH_2OH), 61.4 (CH_3**C**H_2CO), 67.0 (C_2), 75.0 (C_2), 114.3 (C_{arom}-H), 129.1 (C_{arom}-H), 132.3 (**C**$_{aroom}$-C_3), 158.9 (C_{aroom}-O), 171.2 (**C**$OOCH_2$), 174.6 (**C**$OOCH_3$). HRMS: Calculated for $[C_{19}H_{27}NNaO_8]^+$: 404.1685 (M^++Na); found: 404.1675. The ee (98%) was determined by HPLC using a *Chiralpak IA* column [*hexane*/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major}=34.64 min, τ_{minorr}=45.18 min. $[\alpha]_D^{20}$: +5.3 (*c* = 0.47, $CHCl_3$).

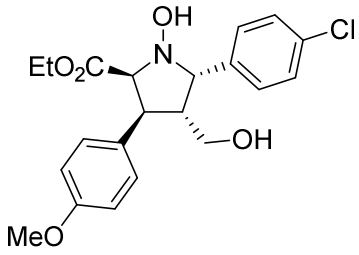


Ethyl (2R,3S,5S)-1-hydroxy-4-(hydroxymethyl)-5-(4-nitrophenyl)-3-phenylpyrrolidine-2-carboxylate (5a). Following the general procedure **C**, **5a** (61 mg, 0.16 mmol) was isolated as a pale yellow oil, starting from aldehyde **2a** (32 mg, 0.24 mmol) and nitrone **1i** (50 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%) and thiourea **5** (20 mg, 0.04 mmol, 20 mol%) using CH_2Cl_2 (0.4 mL) as solvent for 16h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 79%. d.r. (2,5-*trans*/2,5-*cis*): 2:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, *J* = 7.1 Hz, 3H, C**H$_3$**CH$_2$), 1.14* (t, *J* = 7.1 Hz, 3H, C**H$_3$**CH$_2$), 3.19-3.33 (m, 2H, C**H$_2$**OH), 3.35-3.50 (m, 1H, C_4-H), 3.64 (dd, *J* = 10.1, 7.4 Hz, 1H, C_3-H), 3.81-4.01 (m, 2H, CH$_3$C**H$_2$**), 4.12-4.27* (m, 2H, CH$_3$C**H$_2$**), 4.47 (d, *J* = 7.4 Hz, 1H, C_2-H), 5.04 (s, 1H, NOH), 5.40 (d, *J* = 10.6 Hz, 1H, C_5-H), 5.50* (s, 1H, NOH), 7.28-7.41 (m, 5H, C_6H_5), 7.71 (d, *J* = 8.7 Hz, 2H, C_{arom}-H), 8.25 (d, *J* = 8.7 Hz, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 13.9 (**C**H$_3$CH$_2$), 14.2* (**C**H$_3$CH$_2$), 45.9 (C_4), 46.0 (C_3), 46.6* (C_4), 49.9* (C_3), 60.8 (CH$_2$OH), 60.9* (CH$_2$OH), 61.4* (COO**C**H$_2$), 62.1 (COO**C**H$_2$), 70.1 (C_5), 72.7 (C_2), 73.7* (C_2), 123.6 (C_{arom}-H), 123.9* (C_{arom}-H), 127.8* (C_{arom}-H), 127.9 (C_{arom}-H), 128.3 (C_{arom}-H), 128.8 (C_{arom}-H), 129.0* (C_{arom}-H), 129.0* (C_{arom}-H), 129.4 (C_{arom}-H), 136.5 (**C**$_{arom}$-C_3), 147.4 (C_{arom}-NO_2), 147.5 (**C**$_{arom}$-C_5), 147.4* (**C**$_{arom}$-C_5), 148.6* (C_{arom}-NO_2), 170.5 (CO), 171.9* (CO). IR ($CHCl_3$): 3432, 2952, 1730, 1598, 1519, 1246, 1192 cm^{-1}. HRMS: Calculated for $[C_{20}H_{23}N_2O_6]^+$: 387.1556 (M^++H); found: 387.1561. The ee (96%) was determined by HPLC using a *Chiralpak ADH* column [*hexane*/*i*-PrOH (70:30)]; flow rate 1.0 mL/min; τ_{minor}=9.58 min, τ_{major}=34.14 min.

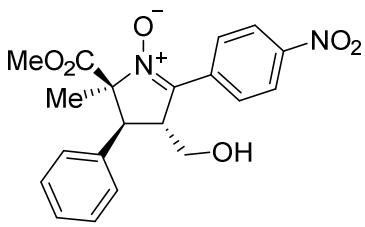


Ethyl (2R,3S,5S)-1-hydroxy-4-(hydroxymethyl)-3-(4-methoxyphenyl)-5-(4-nitrophenyl)pyrrolidine-2-carboxylate (5b). Following the general procedure **C**, **5b** (61 mg, 0.15 mmol) was isolated as a pale yellow oil, starting from aldehyde **2c** (40 mg, 0.24 mmol) and nitrone **1i** (50 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%) and thiourea **5** (20 mg, 0.04 mmol, 20 mol%) using CH_2Cl_2 (0.4 mL) as solvent for 16h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 74%. d.r. (2,5-*trans*/2,5-*cis*): 2:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 0.96 (t, *J* = 7.1 Hz, 3H, C**H$_3$**CH$_2$), 1.15* (t, *J* = 7.1 Hz, 3H, C**H$_3$**CH$_2$), 3.12-3.31 (m, 2H, C**H$_2$**OH), 3.31-3.46* (m, 1H, C_4-H), 3.57 (dd, *J* = 10.2, 7.3 Hz, C_3-H), 3.82 (s, 1H, CH$_3$O), 3.87-4.03 (m, 2H, CH$_3$C**H$_2$**), 4.06-4.25* (m, 2H, CH$_3$C**H$_2$**), 4.17* (d, *J* = 9.7 Hz, 2H, C_2-H), 4.42 (d, *J* = 7.4 Hz, 1H, C_2-H), 5.05 (s, 1H, NOH), 5.37 (d, *J* = 10.5 Hz, 1H, C_5-H), 5.49* (s, 1H, NOH), 6.85 (d, *J* = 8.7 Hz, 2H, C_{arom}-H), 6.92* (d, *J* = 8.7 Hz, 2H, C_{arom}-H), 7.22(d, *J* = 8.7 Hz, 2H, C_{arom}-H), 7.29* (d, *J* = 8.7 Hz, 2H, C_{arom}-H), 7.65-7.73 (m, 2H, C_{arom}-H),8.18-8.27 (m, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) (* indicates minor diastereomer resonances, d.r. 1:1) δ 14.0 (**C**H$_3$CH$_2$), 14.2* (**C**H$_3$CH$_2$), 45.3 (C_4), 45.6* (C_4), 46.3 (C_3), 50.0* (C_3), 55.5 (CH$_3$O), 60.8 (CH$_2$OH), 60.9* (CH$_2$OH), 61.3* (COO**C**H$_2$), 62.1 (COO**C**H$_2$), 70.1 (C_5), 72.6* (C_5), 72.8 (C_2), 73.9* (C_2), 114.2 (C_{arom}-H), 114.4* (C_{arom}-H), 123.6 (C_{arom}-H), 123.9* (C_{arom}-H), 128.4* (C_{arom}-H), 128.8* (C_{arom}-H), 129.0* (**C**$_{arom}$-C_3), 129.4 (C_{arom}-H), 129.4 (C_{arom}-H), 130.0 (**C**$_{arom}$-C_3), 147.5 (C_{arom}-NO_2), 147.7* (**C**$_{arom}$-C_5), 148.6* (C_{arom}-NO_2), 159.1* (C_{arom}-O), 159.2 (C_{arom}-O), 170.6 (CO), 171.9* (CO). IR ($CHCl_3$): 3426, 2941, 1729, 1605, 1515, 1346 cm^{-1}. HRMS: Calculated for $[C_{21}H_{25}N_2O_7]^+$: 417.1262 (M^++H); found: 417.1669. The ee (97%) was determined by HPLC using a *Chiralpak ADH* column

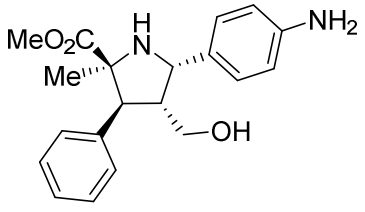
[*hexane*/*i*-PrOH (70:30)]; flow rate 1.0 mL/min; τ_{minor}=12.96 min, τ_{major}=33.15 min. $[\alpha]_D^{20}$: +5.8 (*c* = 0.15, $CHCl_3$).



Ethyl (2R,3S,5S)-5-(4-chlorophenyl)-1-hydroxy-4-(hydroxymethyl)-3-(4-methoxyphenyl)pyrrolidine-2-carboxylate (5c). Following the general procedure **C**, **5c** (64 mg, 0.16 mmol) was isolated as a pale yellow oil, starting from aldehyde **2c** (40 mg, 0.24 mmol) and nitrone **1j** (48 mg, 0.20 mmol) in the presence of catalyst **3a** (13 mg, 0.04 mmol, 20 mol%) and thiourea **5** (20 mg, 0.04 mmol, 20 mol%) using CH_2Cl_2 (0.4 mL) as solvent for 16h and after reduction with $NaBH_4$ (30 mg, 0.80 mmol). Yield: 79%. d.r. (2,5-*trans*/2,5-*cis*): 2:1. ^{1}H NMR (300 MHz, $CDCl_3$) (* indicates minor diastereomer resonances) δ 0.96 (t, *J* = 7.1 Hz, 3H, C**H**$_3$CH$_2$), 1.29* (t, *J* = 7.1 Hz, 3H, C**H**$_3$CH$_2$), 3.20-3.34 (m, 2H, C**H**$_2$OH), 3.45 (d, *J* = 7.3, 3.5 Hz, 1H, C_4-H), 3.46-3.59 (m, 1H, C_3-H), 3.79 (s, 1H, CH_3O), 3.80* (s, 1H, CH_3O), 3.85-4.03 (m, 2H, CH$_3$C**H**$_2$), 4.05-4.19* (m, 2H, CH$_3$C**H**$_2$), 4.25* (d, *J* = 6.9 Hz, 1H, C_2-H), 4.39 (d, *J* = 7.4 Hz, 1H, C_2-H), 4.99 (s, 1H, NOH), 5.23 (d, *J* = 9.3 Hz, 1H, C_5-H), 5.49* (s, 1H, NOH), 6.80-6.92 (m, 2H, C_{arom}-H), 7.17-7.49 (m, 6H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) (* indicates minor diastereomer resonances, d.r. 1:1) δ 14.0 (**C**H$_3$CH$_2$), 45.2 (C_4), 46.2 (C_3), 55.4 (CH_3O), 60.6 (CH_2OH), 62.5 (COO**C**H$_2$), 69.9 (C_5), 72.7 (C_2), 114.1 (C_{arom}-H), 114.3* (C_{arom}-H), 128.9 (C_{arom}-H), 129.4 (C_{arom}-H), 129.7 (C_{arom}-H), 130.5 (C_{arom}-Cl), 133.5 (**C**$_{arom}$-C_3), 138.0 (**C**$_{arom}$-C_5), 159.1 (C_{arom}-O), 170.7 (CO). IR ($CHCl_3$): 3414, 2930, 1730, 1612, 1514, 1250 cm^{-1}. HRMS: Calculated for $[C_{21}H_{25}ClNO_5]^+$: 406.1421 (M^++H); found: 406.1428. The ee (98%) was determined by HPLC using a *Chiralpak ADH* column [*hexane*/*i*-PrOH (75:25)]; flow rate 1.0 mL/min; τ_{minor}=12.70 min, τ_{major}=16.97 min. $[\alpha]_D^{20}$: +8.6 (*c* = 1.0, $CHCl_3$). The stereostructure of **5c** was established assuming the same configuration at C-3, C-4 and C-5 than that proposed for the other adducts. The relative configuration at C-2 was then established by X-ray analysis (CCDC Number: 1522262).

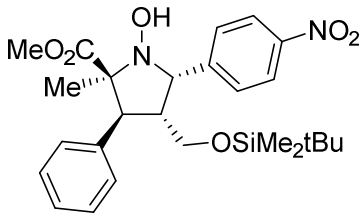


(2S,3S,4R)-4-(hydroxymethyl)-2-(methoxycarbonyl)-2-methyl-5-(4-nitrophenyl)-3-phenyl-3,4-dihydro-2H-pyrrole 1-oxide (6a). To a solution of **4a (**38 mg, 0.10 mmol) in CH_2Cl_2 (0.2 mL), MnO_2 activated (100 mg, 1.0 mmol) was added. The mixture was stirred for 12h at room temperature. Then the crude mixture was filtered through a short pad of silica gel yielding the pure product **6a** (38 mg, 0.10 mmol) as a yellow solid. Yield: 99%. d.r. > 20:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.91 (s, 3H), 3.39 (s, 3H), 3.57-3.68 (m, 1H), 3.72 (d, *J* = 8.8 Hz, 1H), 4.00 (dt, *J* = 11.3, 3.3 Hz, 1H), 4.09 (dt, *J* = 8.6, 3.1 Hz, 1H), 7.26-7.34 (m, 2H), 7.34-7.43 (m, 3H), 8.25-8.38 (m, 4H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.0, 48.4 (C_3), 51.3 (C_4), 52.9, 60.0, 85.4, 123.8, 128.8, 128.9, 129.1, 134.6, 141.6, 148.0, 168.6. IR ($CHCl_3$): 3322, 2955, 1731, 1605, 1518, 1344 cm^{-1}. HRMS: Calculated for $[C_{20}H_{21}N_2O_6]^+$: 385.1400 (M^++H); found: 385.1405. $[\alpha]_D^{20}$: +144.9 (*c* = 1.0, $CHCl_3$).



Methyl (2S,3S,4R,5S)-5-(4-aminophenyl)-4-(hydroxymethyl)-2-methyl-3-phenylpyrrolidine-2-carboxylate (7a). To a suspension of **4a** (38 mg, 0.10 mmol) in H_2O (2 mL), HCl conc. (1mL) and Zn dust (260 mg, 4.0 mmol) were added. The mixture was heated to reflux for 3h until the solution turned from yellow to colorless. The mixture

was cooled and basified to pH > 12 with aqueous NaOH 2.5 M, extracted with Et_2O (5 x 5mL), dried over anhydrous Na_2SO_4, filtrated, evaporated and purified by flash column chromatography on triethylamine deactivated SiO_2 (PE/EtOAc 3:7 to 0:100) to afford pure **7a** (26 mg, 0.08 mmol) as a pale yellow oil. Yield: 77%. d.r. > 20:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.76 (s, 3H, CH_3C), 3.02 (dtd, *J* = 11.6, 6.0, 3.1 Hz, 1H, C_3-H), 3.14 (d, *J* = 9.7 Hz, 1H, C_2), 3.21-3.36 (m, 5H, CH_2O, CH_3O), 3.52* (s, 3H, CH_3O), 5.04 (d, *J* = 8.5 Hz, 1H, C_5-H), 6.59-6.75 (m, 2H, C_{arom}-H), 7.13-7.36 (m, 7H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 25.2 (C_2**C**H_3), 49.9 (C_4), 51.5 (C_3), 57.4 (CH_3O), 62.4 (CH_2O), 62.7 (C_5), 70.0 (C_2), 115.4 (C_{arom}-H), 127.4 (C_{arom}-H), 128.5 (C_{arom}-H), 132.0 (C_{arom}-H), 138.8 (C_{arom}-C_5), 145.8 (C_{arom}-C_3), 148.6 (C_{arom}-NH_2), 176.7 (CO). IR ($CHCl_3$): 3551, 3350, 2945, 1720, 1623, 1516, 1281 cm^{-1}. HRMS: Calculated for $[C_{20}H_{25}N_2O_3]^+$: 341.1865 (M^++H); found: 341.1874. $[\alpha]_D^{20}$: +62.1 (*c* = 1.0, $CHCl_3$).



Methyl (2S,3S,4R,5S)-4-(((tert-butyldimethylsilyl)oxy)methyl)-1-hydroxy-2-methyl-5-(4-nitrophenyl)-3-phenylpyrrolidine-2-carboxylate (8a).

To a solution of **4a** (38 mg, 0.10 mmol) and 4-(dimethylamino)pyridine (1 mg, 0.01 mmol) in CH_2Cl_2 at room temperature, tert-buthyldimethylsilyl chloride (30 mg, 0.20 mmol) and triethylamine (28 µL ,0.20 mmol) were added. The mixture was stirred at room temperature for 12h. Then, the solvent was evaporated and the crude mixture was purified by flash column chromatography (PE/EtOAc 9:1 to 7:3) to afford pure **8a** (45 mg, 0.09 mmol) as a colorless oil. Yield: 90%. d.r. > 20:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ -0.41 (s, 3H, SiC**H**$_3$$CH_3$), -0.40 (s, 3H, $SiCH_3$C**H**$_3$), 0.63 (s, 9H, $C(CH_3)_3$), 1.56 (s, 3H, CH_3C), 3.00-3.19 (m, 3H, C_3-H, CH_2), 3.33 (tdd, *J* = 10.8, 6.1, 4.0 Hz, 1H, C_4-H), 3.51 (s, 3H, CH_3O), 3.74* (s, 3H, CH_3O), 4.88 (s, 1H, NOH), 5.24-5.35 (m 1H, C_5-H), 7.15-7.36 (m, 5H, C_{arom}-H), 7.62-7.77 (m, 2H, C_{arom}-H), 8.13-8.25 (m, 2H, C_{arom}-H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ -5.9 ($SiCH_3$), 18.0 (C_2**C**H_3), 22.0 (**C**$(CH_3)_3$), 25.8 (C(**C**$H_3)_3$), 45.6 (C_4), 51.6 (C_3), 53.6 (CH_3O), 61.3 (CH_2O), 70.4 (C_5), 75.4 (C_2), 123.1 (C_{arom}-H), 127.9 (C_{arom}-H), 128.6 (C_{arom}-H), 129.8 (C_{arom}-H), 136.5 (C_{arom}-C_3), 147.2 (C_{arom}-NO_2), 148.6 (C_{arom}-C_5), 172.4 (CO). IR ($CHCl_3$): 3479, 2952, 1729, 1602, 1520, 1345, 1252, 1109, 836 cm^{-1}. HRMS: Calculated for $[C_{26}H_{36}N_2O_6Si]^+$: 501.2421 (M^++H); found: 501.2420. $[\alpha]_D^{20}$: +18.2 (*c* = 1.0, $CHCl_3$).

X-Ray analysis of compound 4j

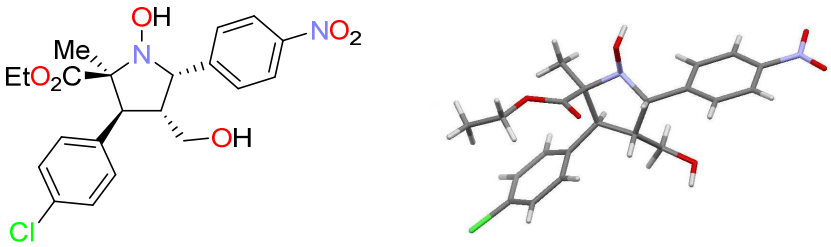


Figure SI-1. ORTEP diagram for compound **(2*S*,3*S*,4*R*,5*S*)-4j**

Crystal data for $C_{21}H_{23}ClN_2O_6$ (M = 434.86 g/mol) (CCDC 1511107): monoclinic, space group $P2_1$, a = 7.82808(13) Å, b = 11.08346(17) Å, c = 23.9907(4) Å, $\alpha = \gamma = 90^o$ β = 91.6094(14), V = 2080.66(6) Å^3, Z = 4, T = 120(2) K, μ(CuKα) = 1.985 mm^{-1}, ρ_{calc} = 1.389 g/cm^3, 38789 reflections measured (7.374° ≤ 2Θ ≤ 139.992°), 11647 unique (R_{int} = 0.0717, R_{sigma} = 0. 0638) which were used in all calculations. The final R_1 was 0.0555 (I > 2σ(I)) (all data) and wR_2 was 0.1547 (all data).

Table SI-1. Crystal data and structure refinement for **4j**.

Empirical formula	$C_{21}H_{23}ClN_2O_6$
Formula weight	434.86
Temperature/K	120.00(10)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	7.82808(13)
b/Å	11.08346(17)
c/Å	23.9907(4)
α/°	90
β/°	91.6094(14)
γ/°	90
Volume/Å^3	2080.66(6)
Z	4
ρ_{calc}g/cm^3	1.389
μ/mm^{-1}	1.985
F(000)	912.0
Crystal size/mm^3	0.7093 × 0.1006 × 0.0263
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.374 to 139.992
Index ranges	-9 ≤ h ≤ 9, -13 ≤ k ≤ 13, -29 ≤ l ≤ 29
Reflections collected	38789
Independent reflections	11647 [R_{int} = 0.0717, R_{sigma} = 0.0638]
Data/restraints/parameters	11647/7/550
Goodness-of-fit on F^2	1.070
Final R indexes [I>=2σ (I)]	R_1 = 0.0529, wR_2 = 0.1522
Final R indexes [all data]	R_1 = 0.0555, wR_2 = 0.1547
Largest diff. peak/hole / e Å^{-3}	0.49/-0.39
Flack parameter	0.036(17)

Table SI-2. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **4j**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
Cl1A	9830(2)	3895.9(16)	2266.6(7)	32.8(4)
O1A	1629(6)	8361(4)	632.4(18)	24.1(9)
O2A	5386(6)	7662(4)	665.4(17)	25.2(9)
O3A	5063(6)	8190(5)	1555.8(19)	29.3(10)
O4A	1790(5)	3885(4)	-276.0(17)	25.1(9)
O5A	-2260(8)	6087(8)	-2029(2)	63(2)
O6A	-4249(7)	6290(6)	-1432(2)	43.8(14)
N1A	1754(7)	7066(5)	708(2)	20.8(10)
N2A	-2722(9)	6204(6)	-1553(3)	37.2(15)
C1A	3006(8)	6825(5)	1163(2)	19.0(12)
C2A	3354(8)	5459(5)	1046(2)	19.5(12)
C3A	3142(7)	5291(6)	405(2)	19.2(12)
C4A	2403(8)	6529(6)	193(2)	22.1(12)
C5A	4633(8)	7594(6)	1095(2)	21.7(12)
C6A	6535(8)	9009(7)	1527(3)	30.6(14)
C7A	8212(9)	8353(7)	1588(3)	33.3(15)
C8A	2221(8)	7014(6)	1728(3)	24.7(13)
C9A	4970(8)	4955(6)	1321(3)	23.8(13)
C10A	6575(8)	5161(6)	1095(3)	24.2(13)
C11A	8061(8)	4801(6)	1380(3)	25.2(13)
C12A	7924(10)	4257(6)	1892(3)	28.1(15)
C13A	6398(8)	3983(7)	2115(3)	26.6(14)
C14A	4929(9)	4360(6)	1827(3)	26.2(14)
C15A	2008(8)	4190(6)	294(3)	24.7(13)
C16A	1019(8)	6457(5)	-259(3)	21.5(12)
C17A	1436(8)	6634(6)	-810(3)	24.8(13)
C18A	236(9)	6539(6)	-1237(3)	27.0(13)
C19A	-1441(9)	6277(6)	-1102(3)	26.4(14)
C20A	-1928(8)	6122(6)	-556(3)	24.3(13)
C21A	-690(9)	6222(6)	-136(3)	24.9(13)
Cl1B	8802(2)	10821.4(18)	2758.5(7)	39.0(4)
O1B	1217(7)	6038(4)	4369(2)	35.4(11)
O2B	4895(6)	6726(5)	4333.9(19)	33.3(11)
O3B	4689(7)	6713(5)	3404(2)	39.8(13)
O4B	2088(6)	10433(4)	5413.3(18)	29.1(10)
O5B	-4885(8)	8470(7)	6252(2)	55.8(18)
O6B	-3026(7)	8364(7)	6926(2)	47.8(15)
N1B	1283(7)	7330(5)	4319(2)	26.5(12)
N2B	-3404(8)	8366(6)	6431(2)	34.9(14)
C1B	2413(9)	7637(7)	3868(3)	27.6(14)
C2B	2757(8)	8995(6)	4011(3)	25.9(13)
C3B	2778(8)	9047(7)	4655(2)	26.8(13)
C4B	1931(9)	7850(6)	4847(3)	26.9(14)
C5B	4118(10)	6943(6)	3902(3)	31.1(15)
C6B	6482(11)	6307(8)	3357(3)	45(2)
C7B	7059(10)	6741(8)	2811(3)	38.6(17)
C8B	1480(9)	7468(7)	3314(3)	34.3(16)
C9B	4266(9)	9549(6)	3729(3)	24.4(14)
C10B	5940(9)	9410(7)	3942(3)	30.1(15)
C11B	7330(9)	9834(7)	3653(3)	30.0(14)
C12B	7031(10)	10382(6)	3142(3)	30.3(14)
C13B	5435(10)	10565(6)	2930(3)	30.3(14)
C14B	4059(9)	10141(6)	3225(3)	27.0(14)
C15B	1952(9)	10231(6)	4834(3)	28.8(14)
C16B	515(9)	7971(6)	5259(3)	27.6(14)
C17B	-1158(9)	8209(7)	5085(3)	29.5(15)
C18B	-2444(9)	8329(7)	5463(3)	29.8(14)
C19B	-2062(9)	8231(6)	6024(3)	29.5(15)
C20B	-400(9)	7982(7)	6215(3)	30.0(15)
C21B	872(8)	7856(6)	5834(3)	26.0(13)

5. NMR Spectra

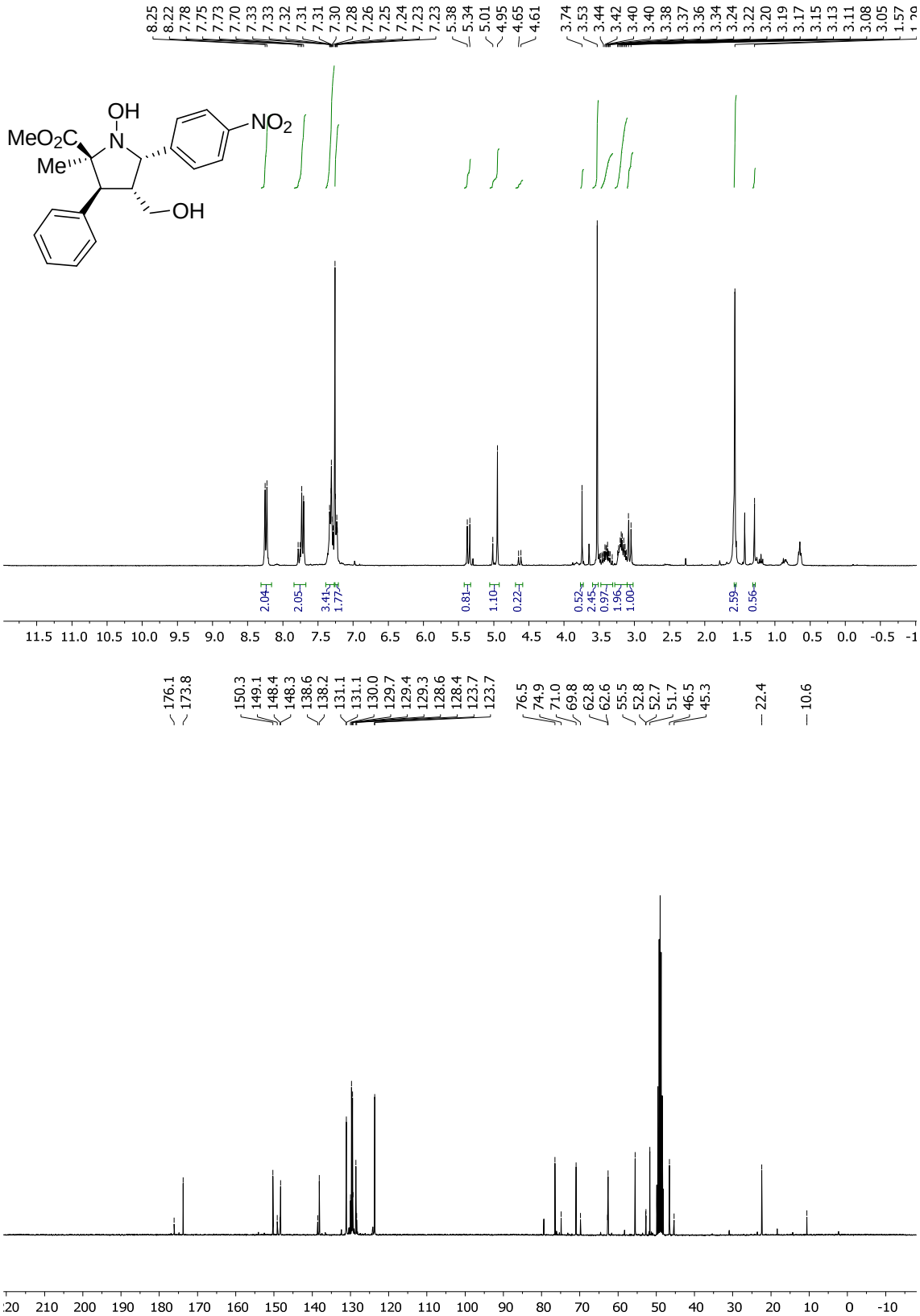


Figure SI-2. NMR spectra of compound **4a**.

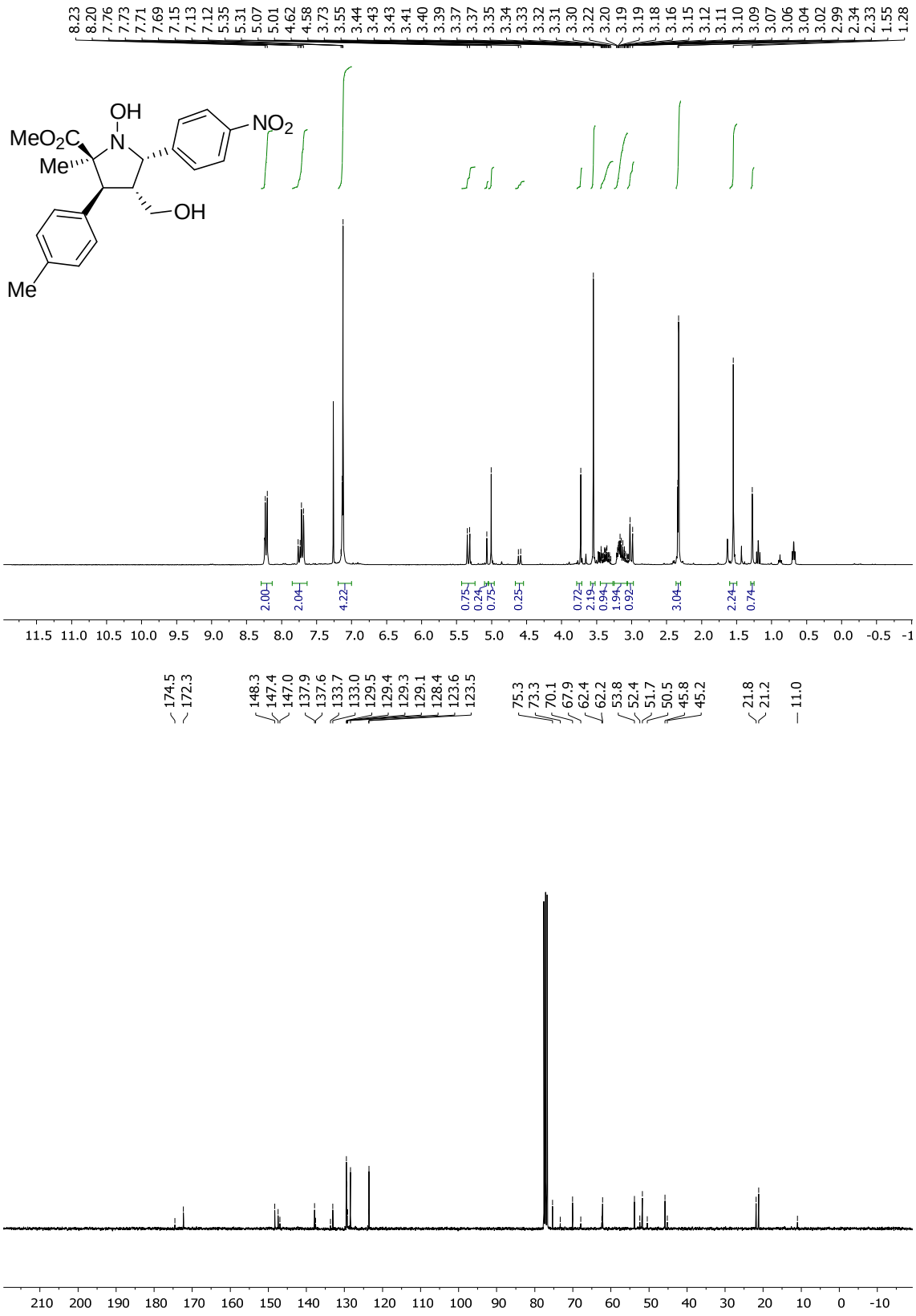


Figure SI-3. NMR spectra of compound **4b**.

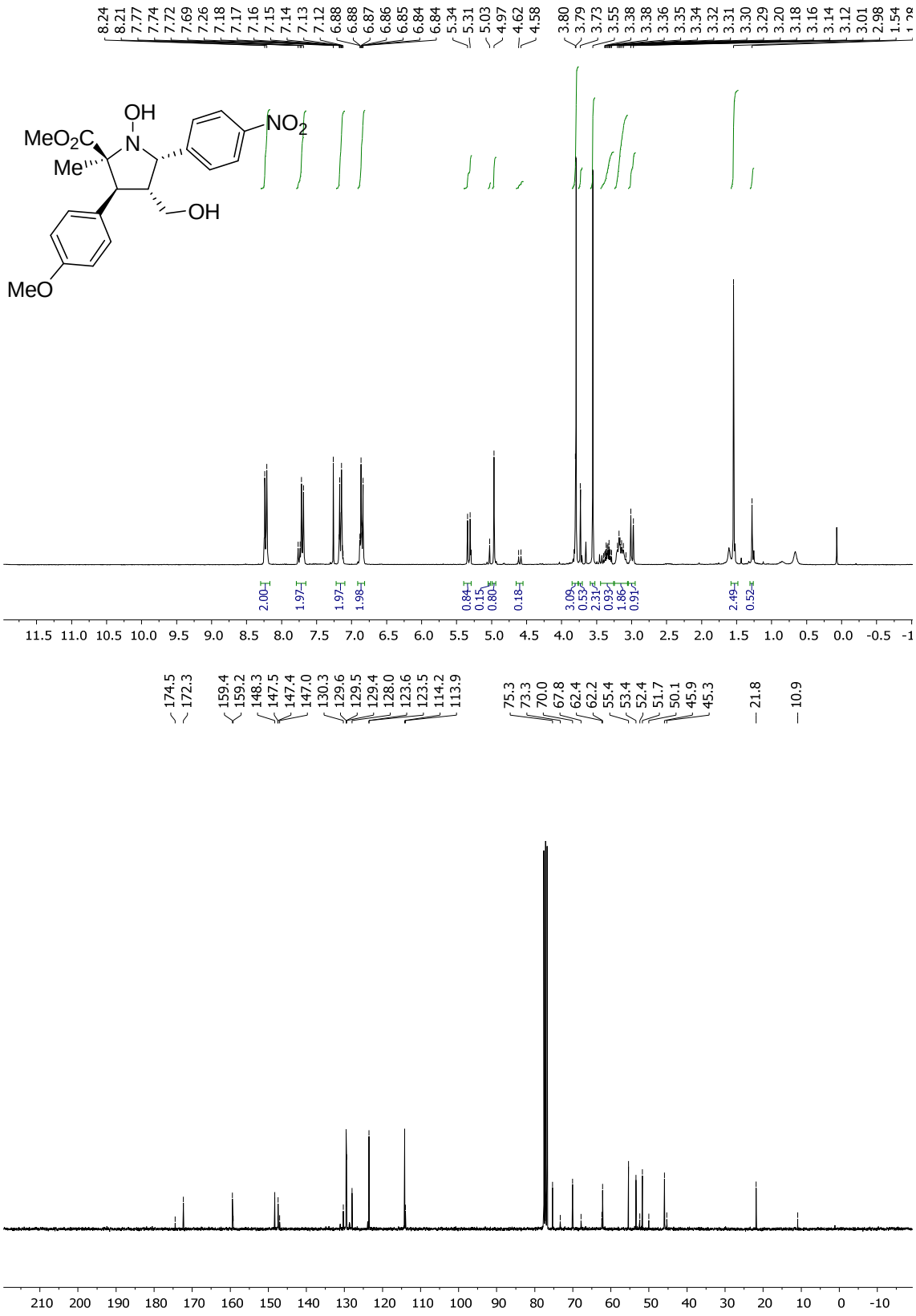


Figure SI-4. NMR spectra of compound **4c**.

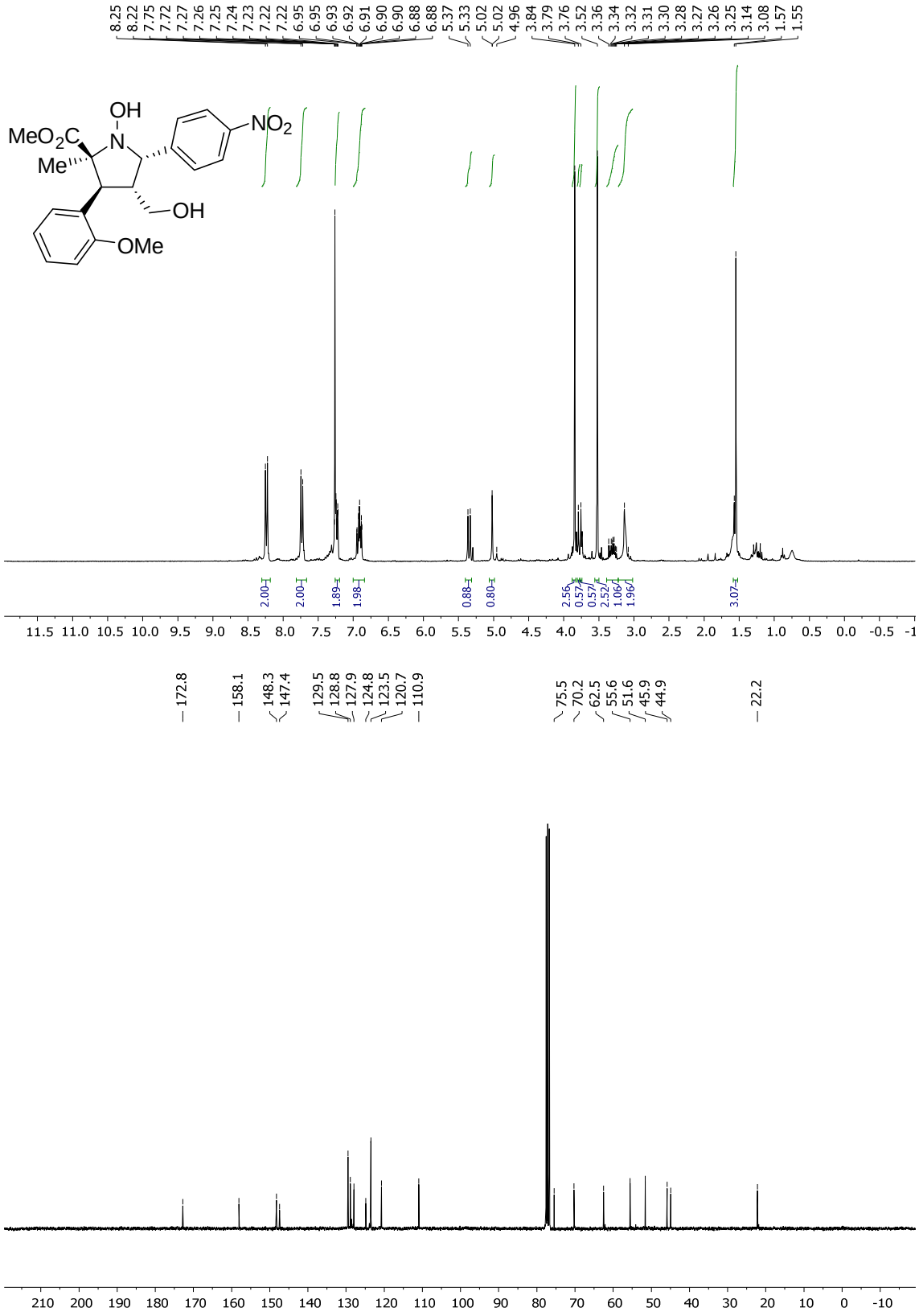


Figure SI-5. NMR spectra of compound **4d**.

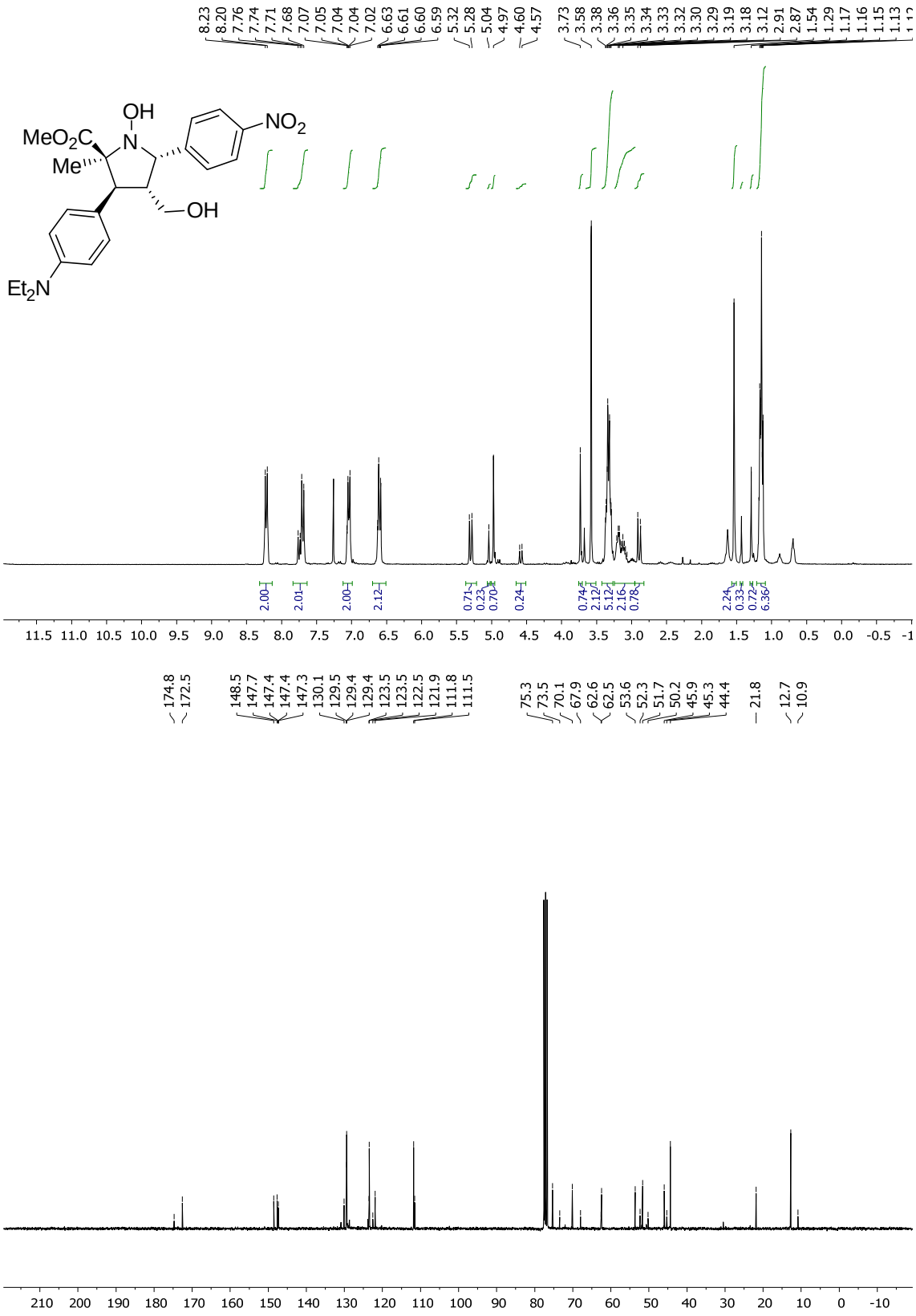


Figure SI-6. NMR spectra of compound **4e**.

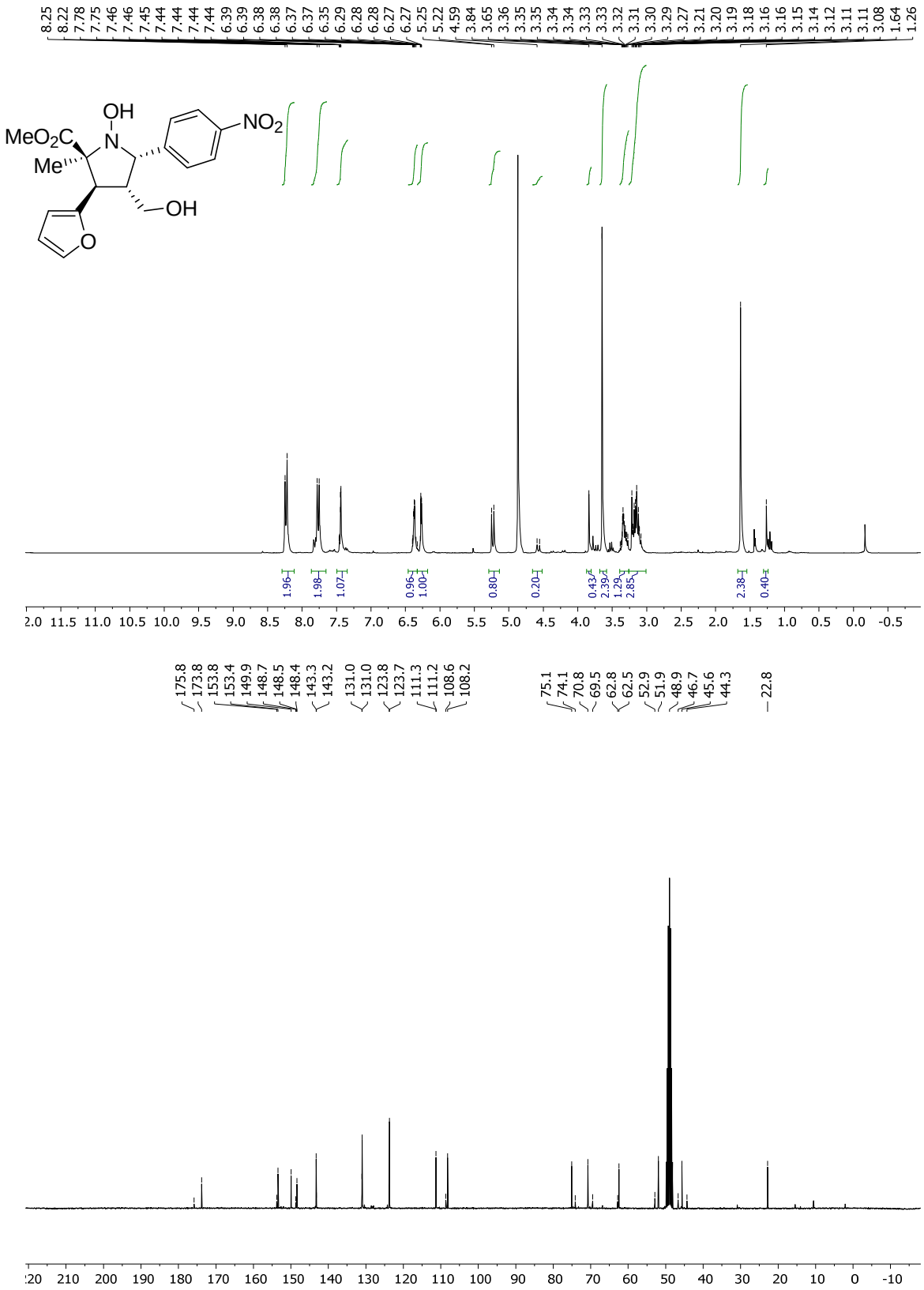


Figure SI-7. NMR spectra of compound **4f**.

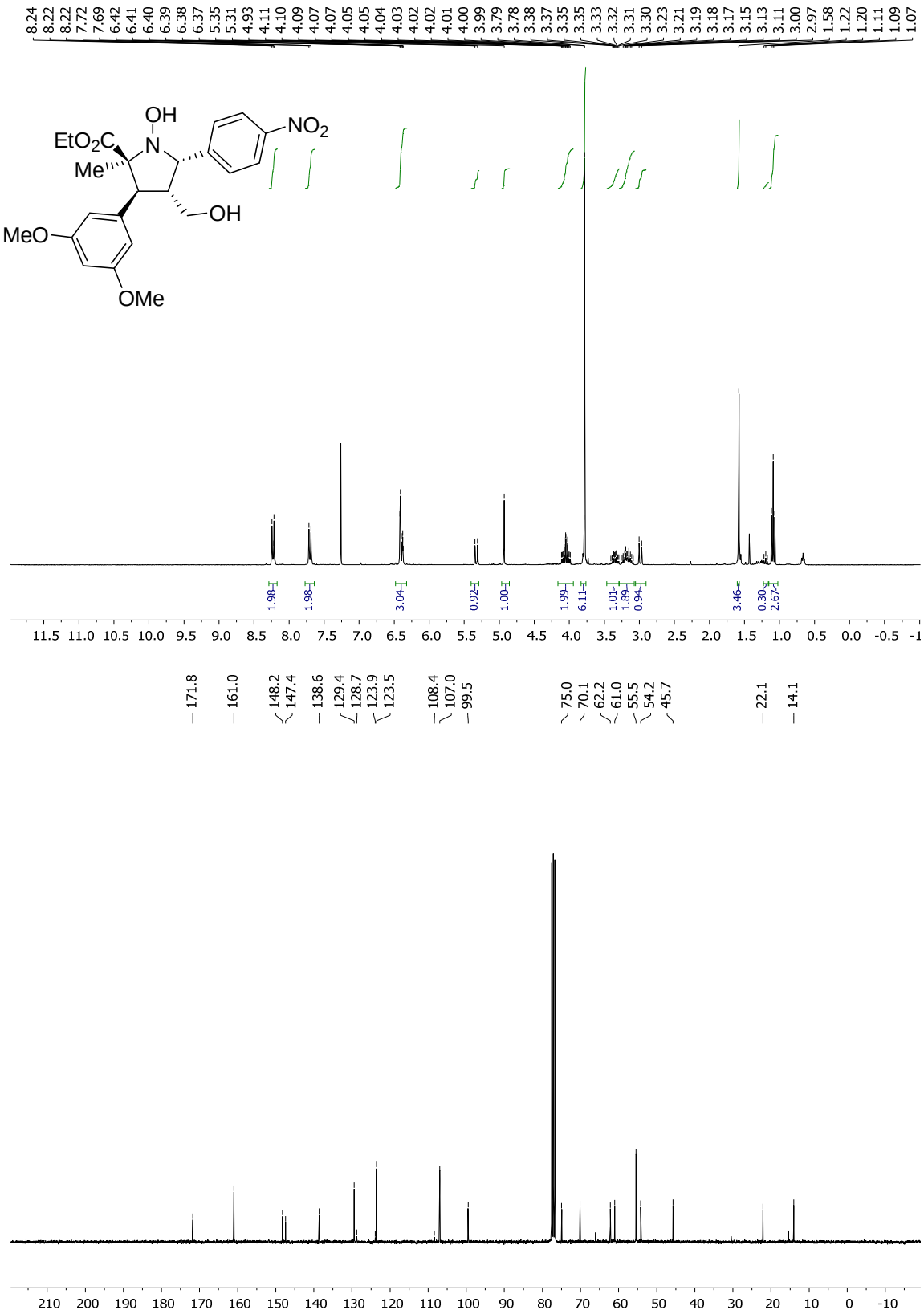


Figure SI-8. NMR spectra of compound **4g**.

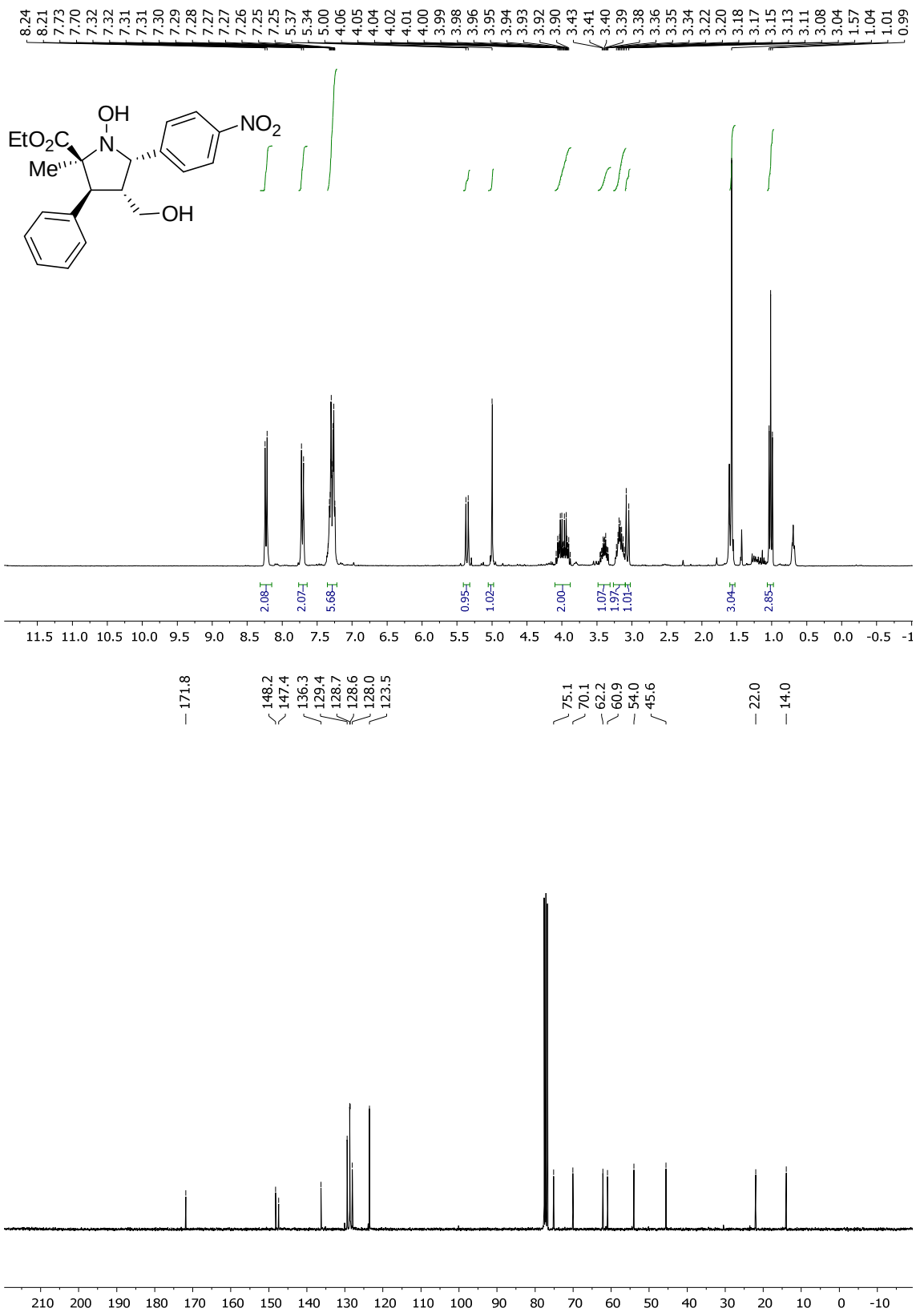


Figure SI-9. NMR spectra of compound **4h**.

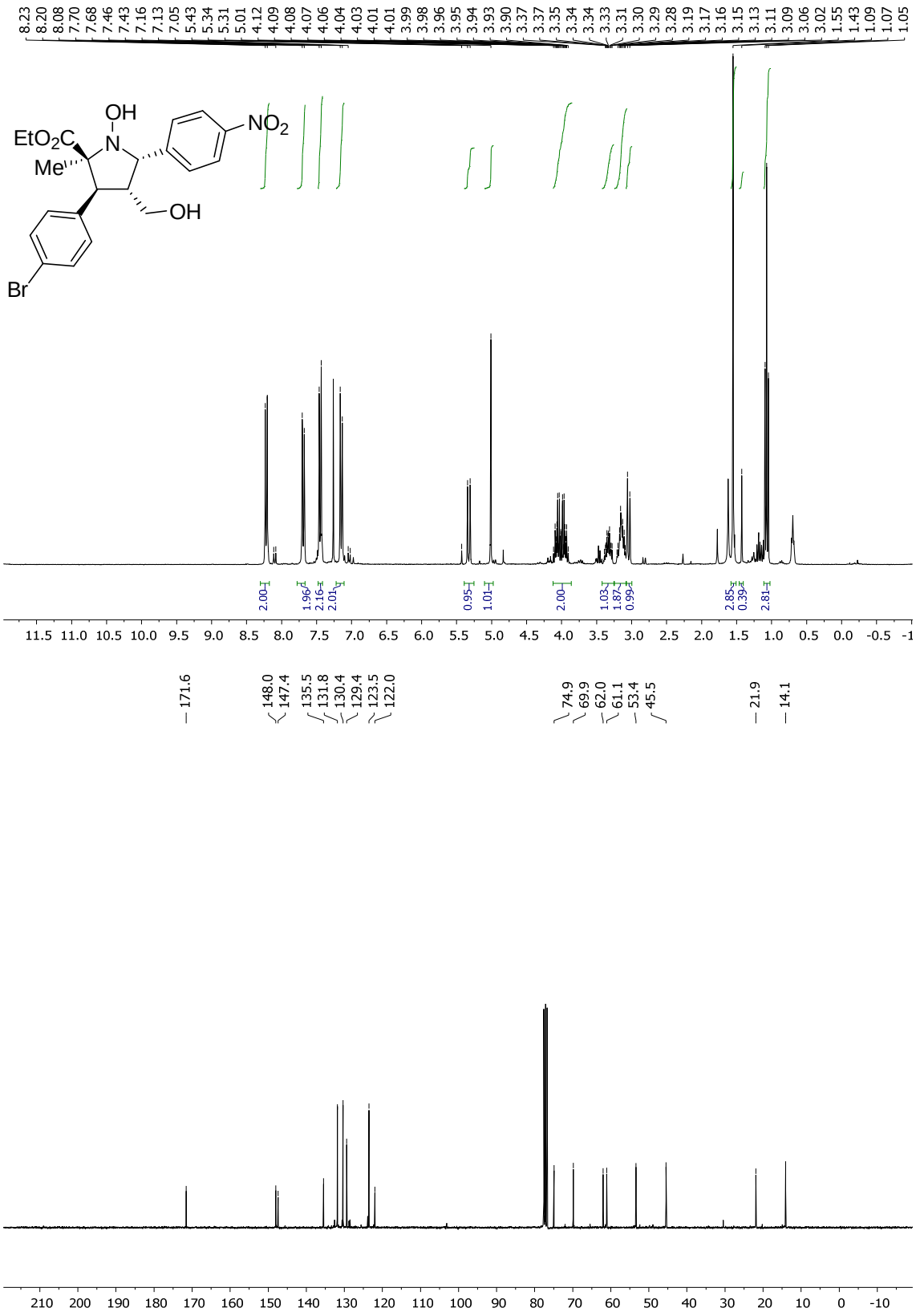


Figure SI-10. NMR spectra of compound **4i**.

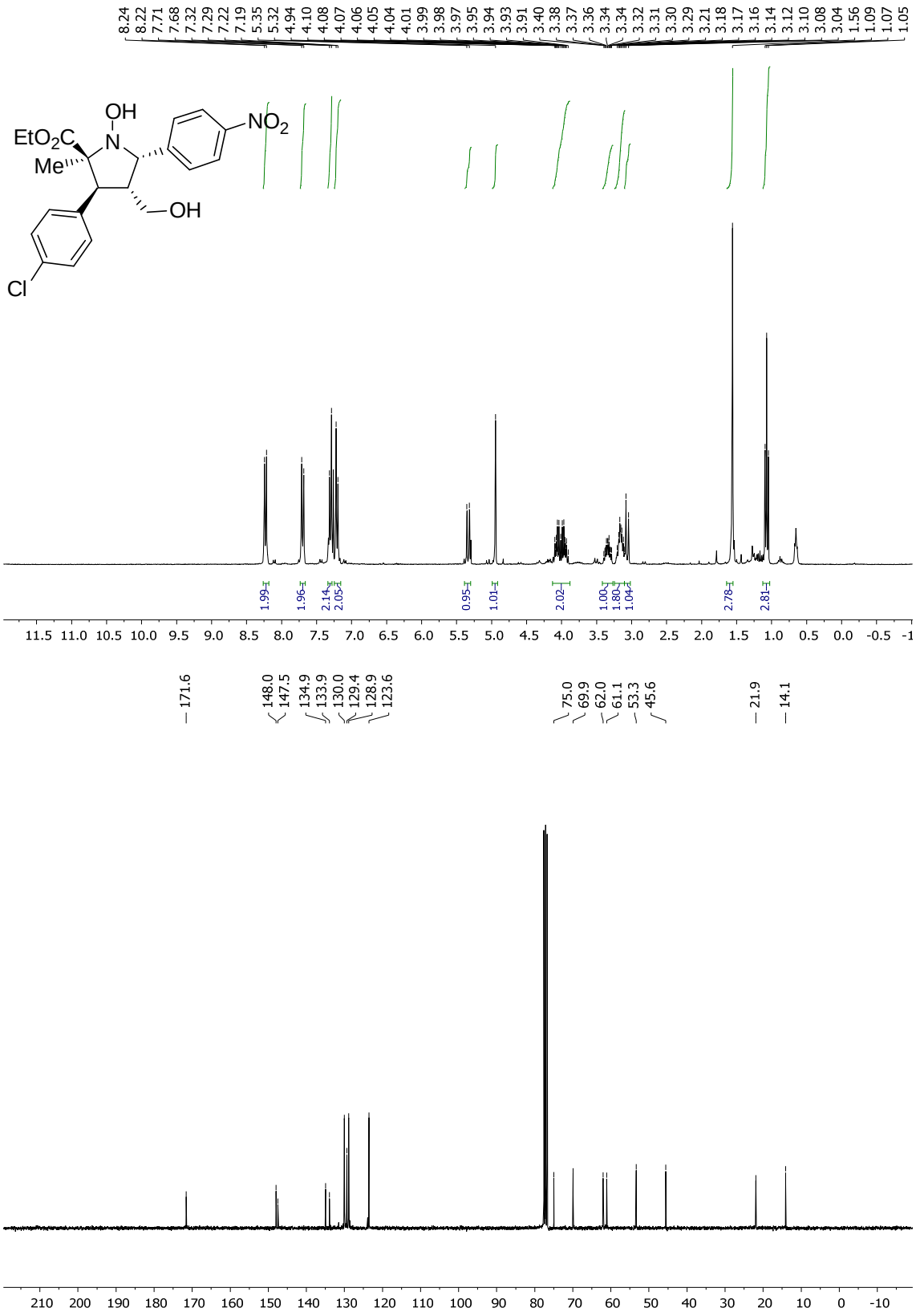


Figure SI-11. NMR spectra of compound **4j**.

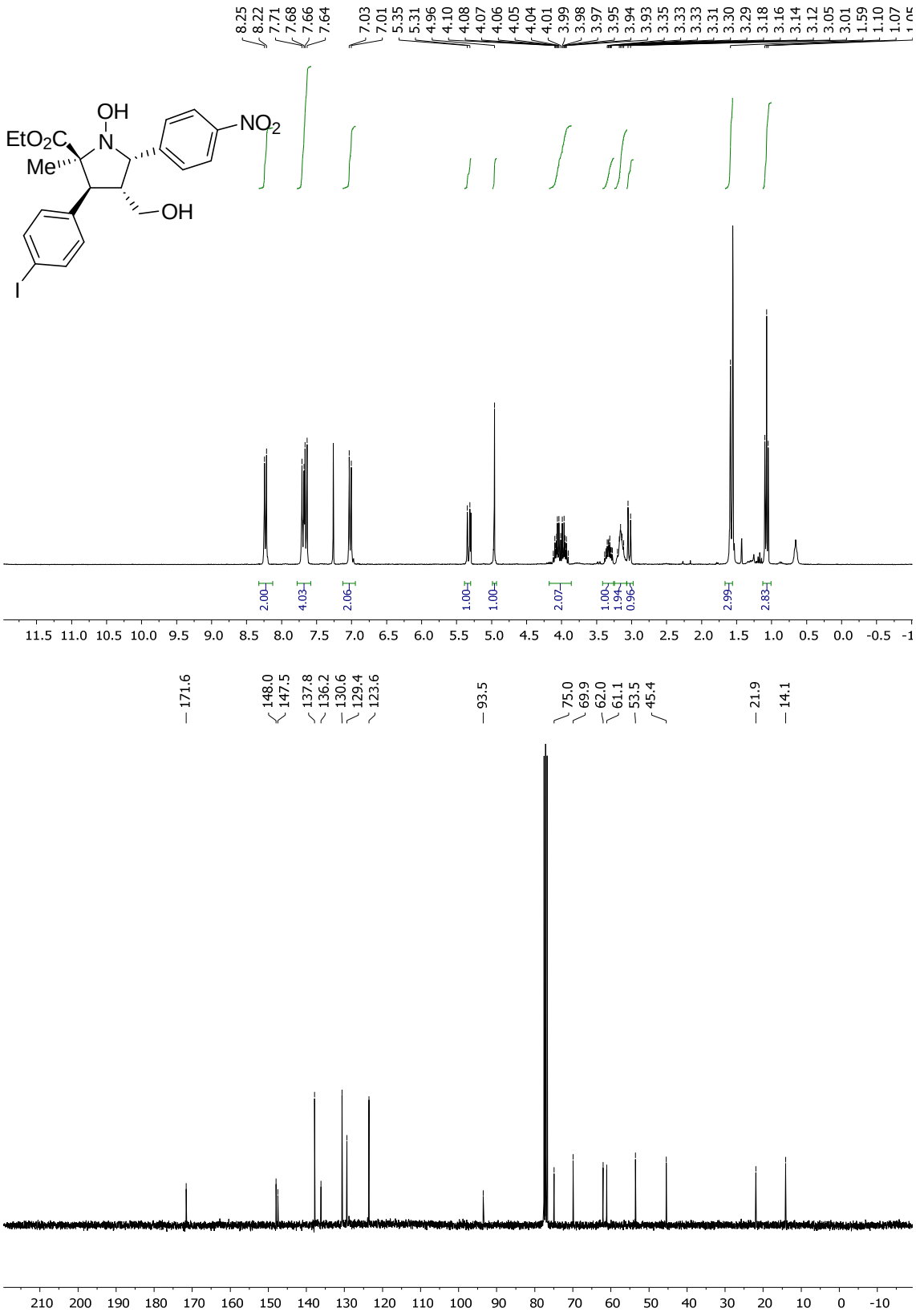


Figure SI-12. NMR spectra of compound **4k**.

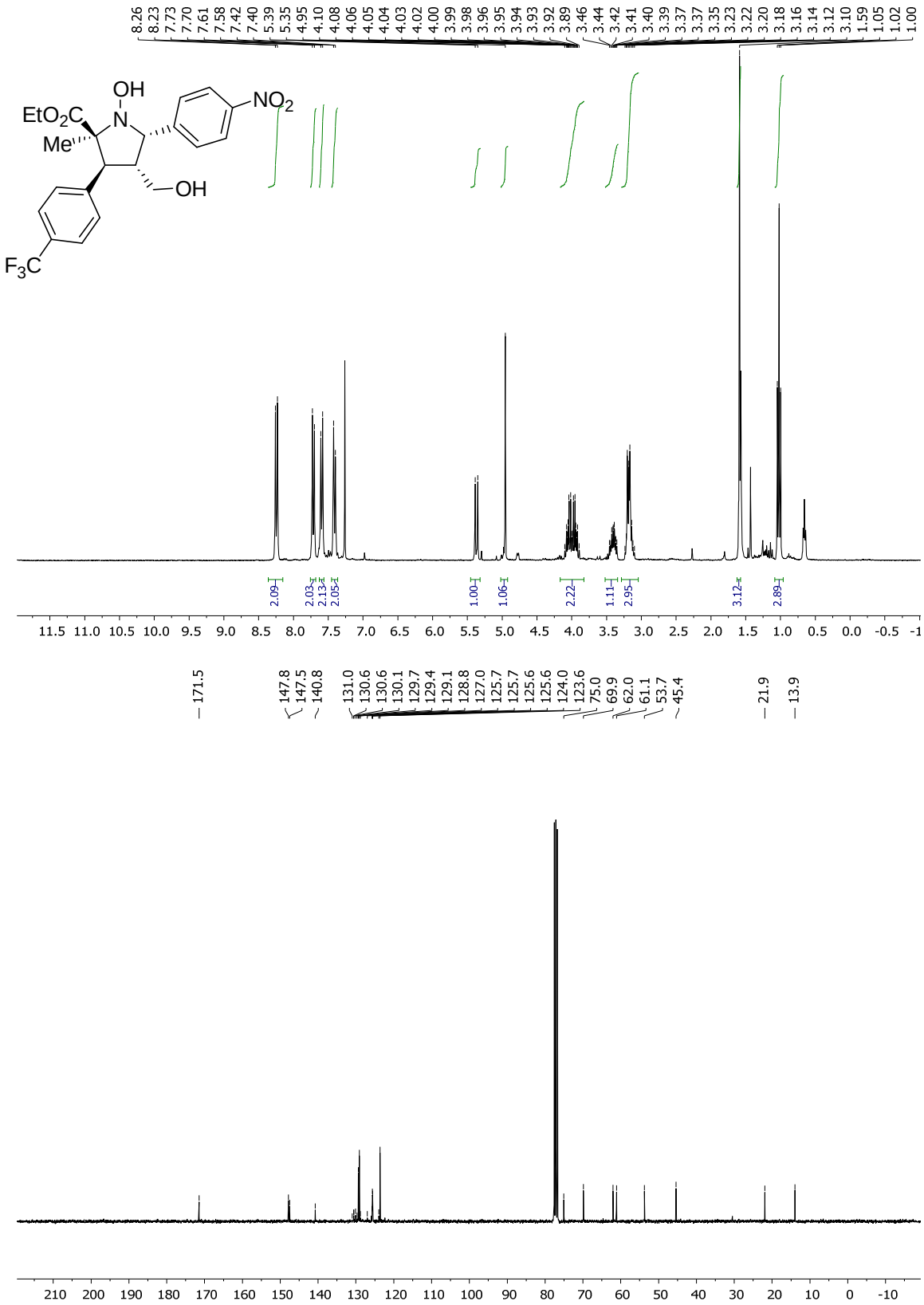


Figure SI-13. NMR spectra of compound **4l**.

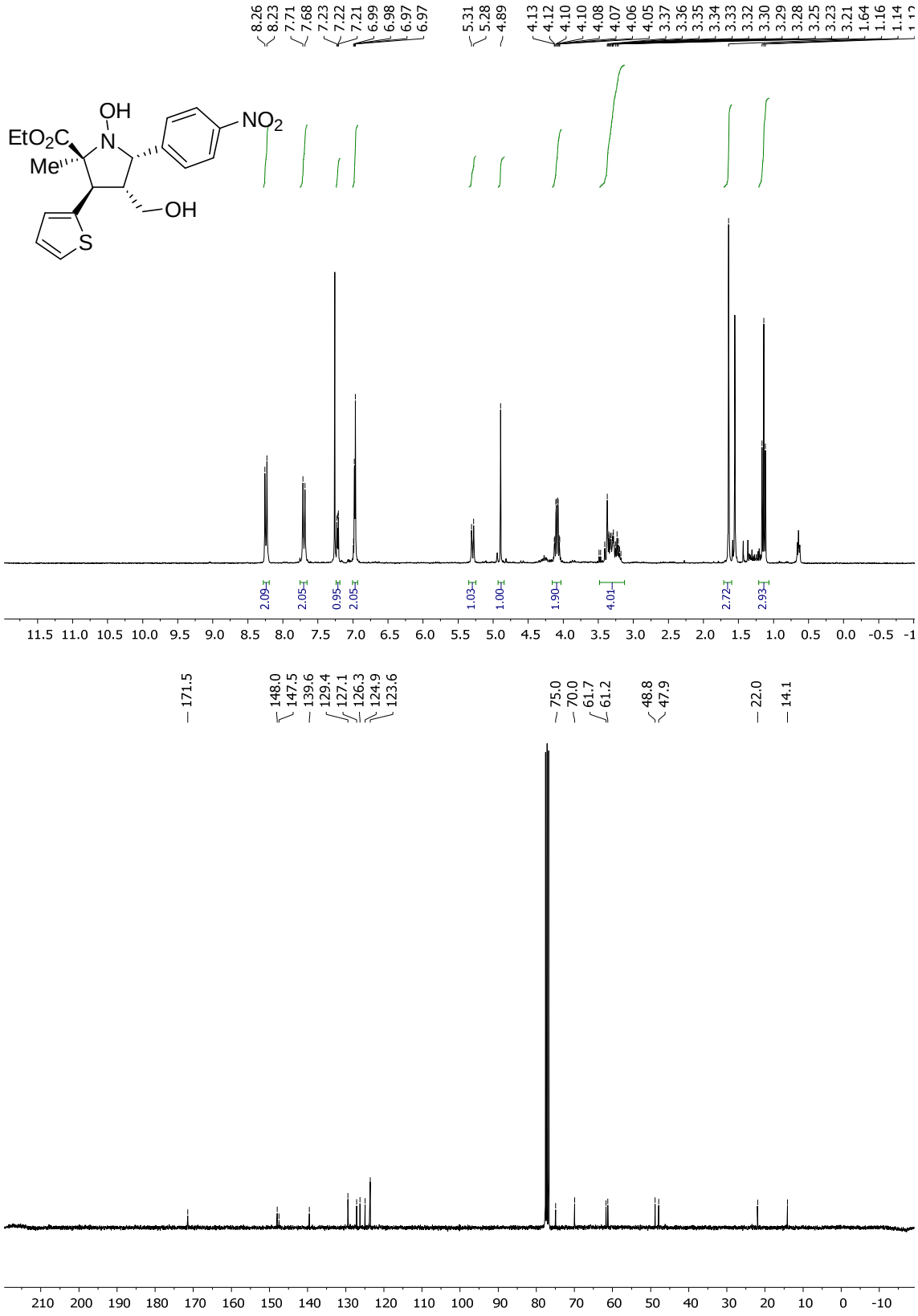


Figure SI-14. NMR spectra of compound **4m**.

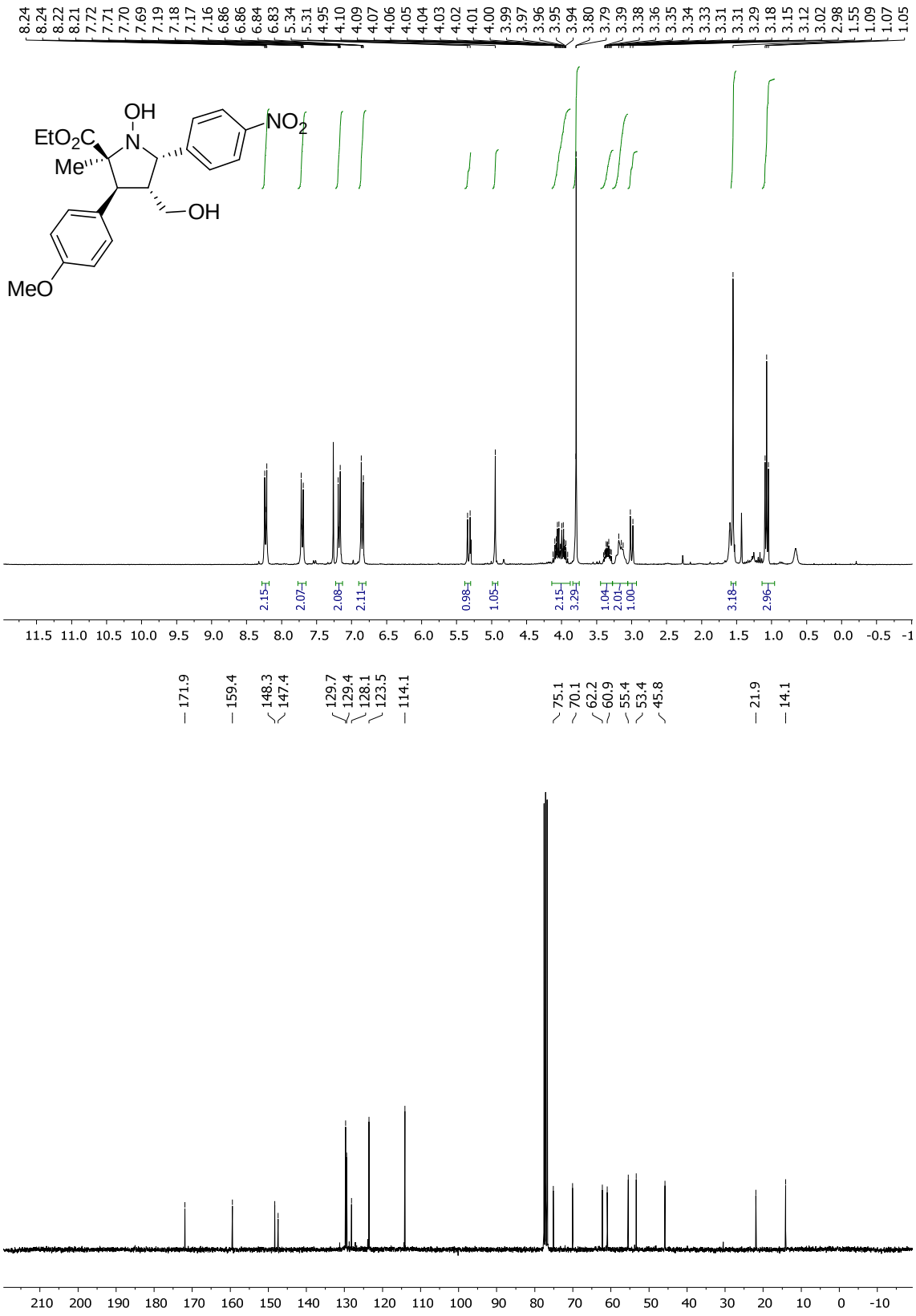


Figure SI-15. NMR spectra of compound **4n**.

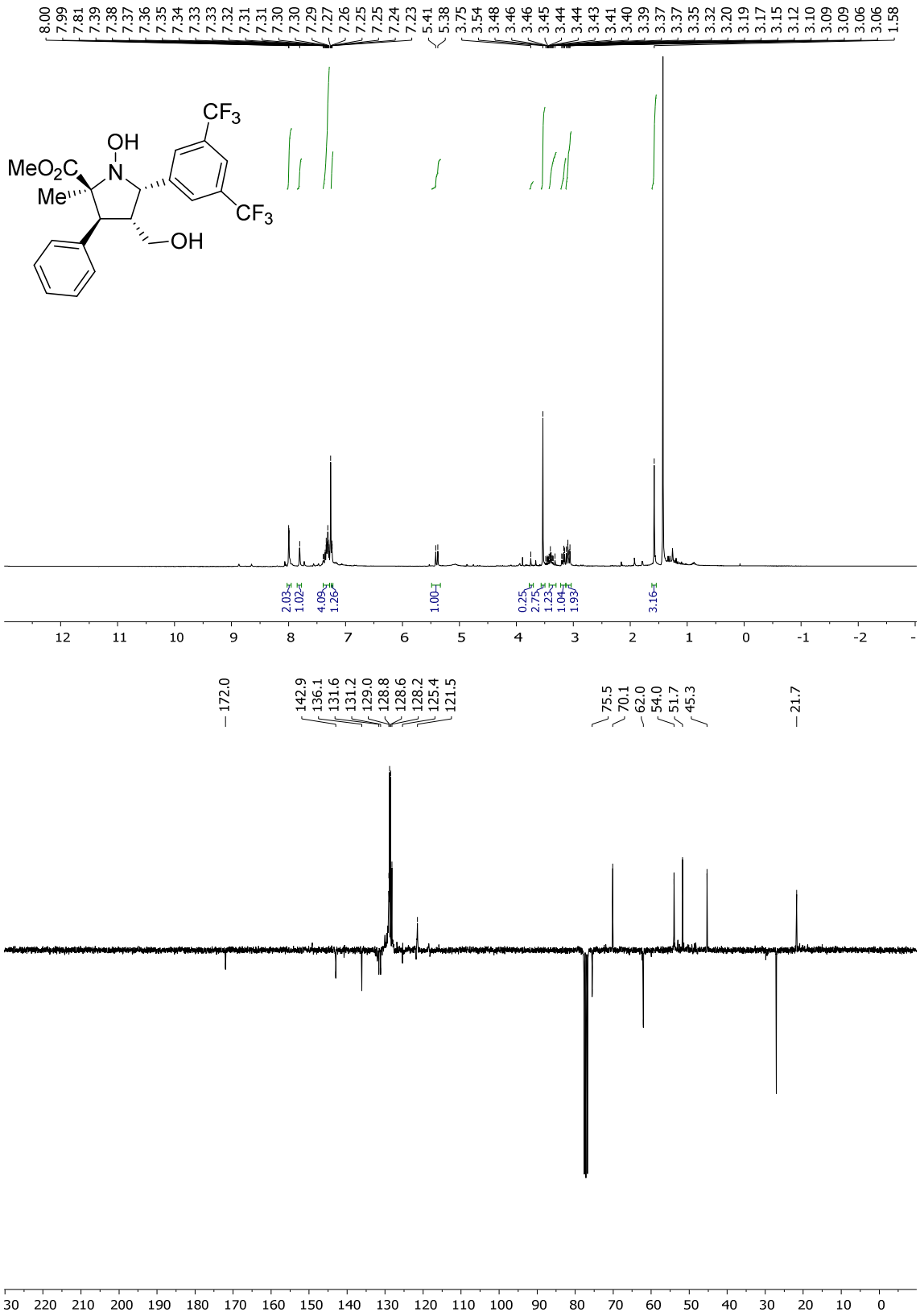


Figure SI-16. NMR spectra of compound **4o**.

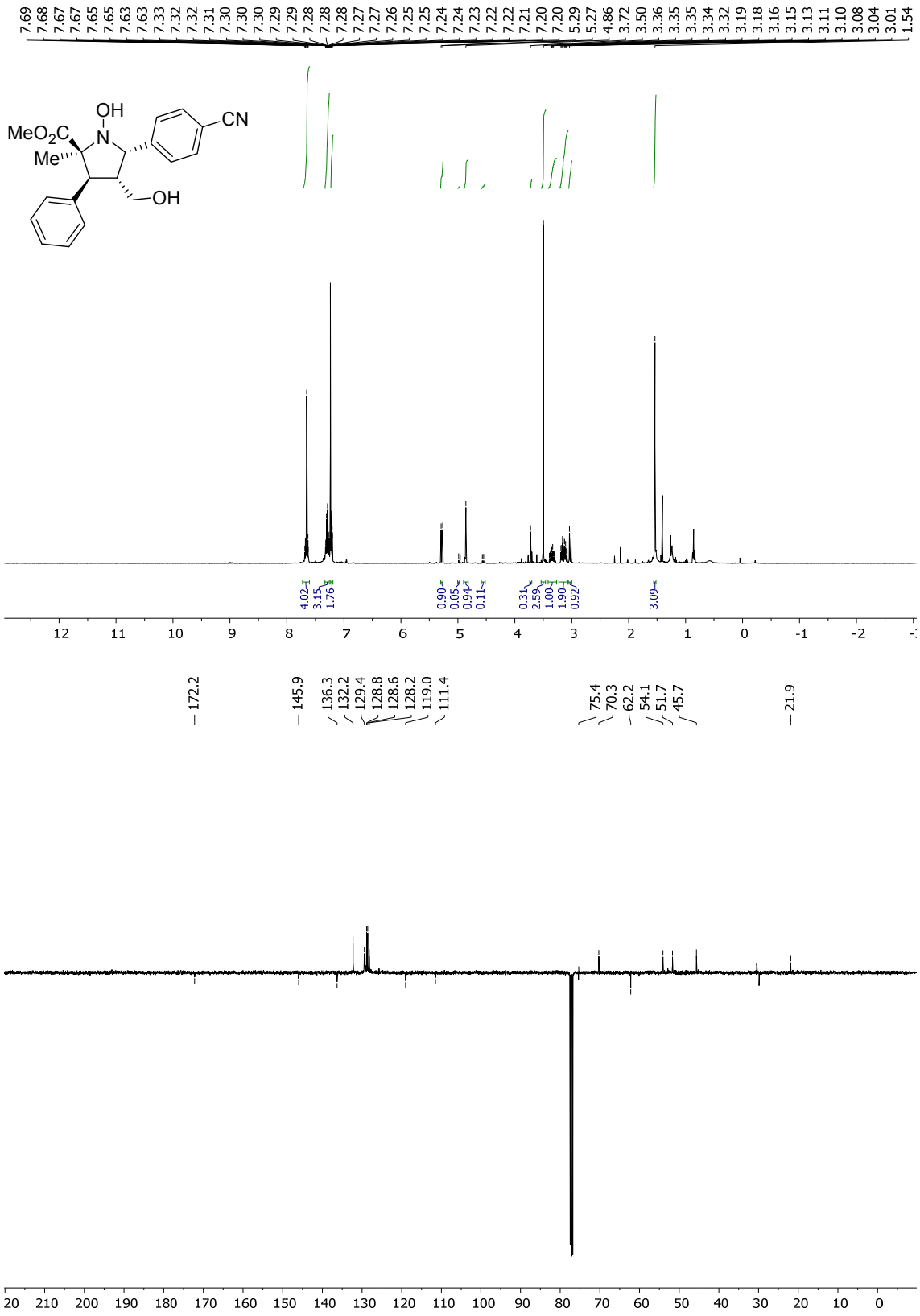


Figure SI-17. NMR spectra of compound **4p**.

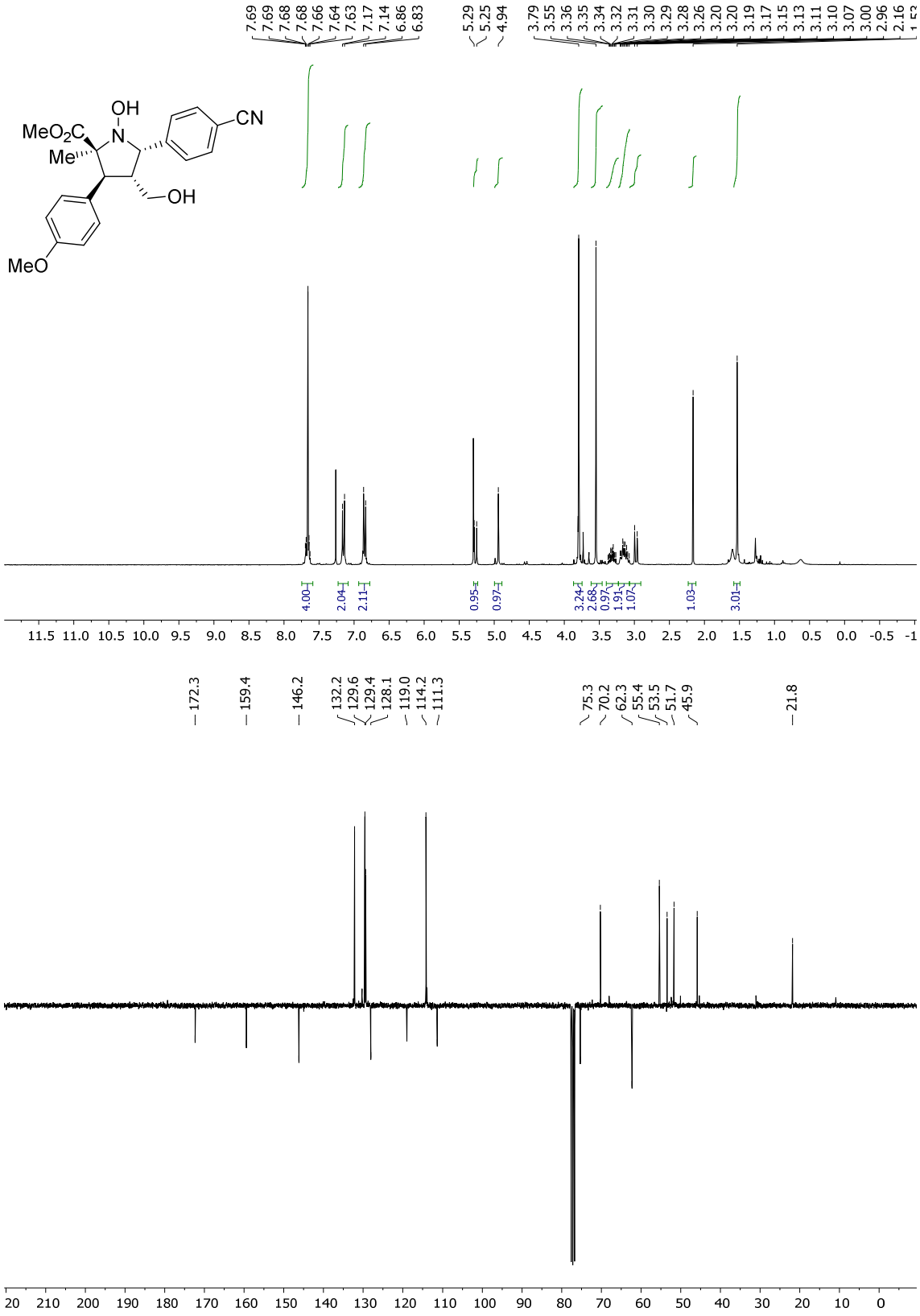


Figure SI-18. NMR spectra of compound **4q**.

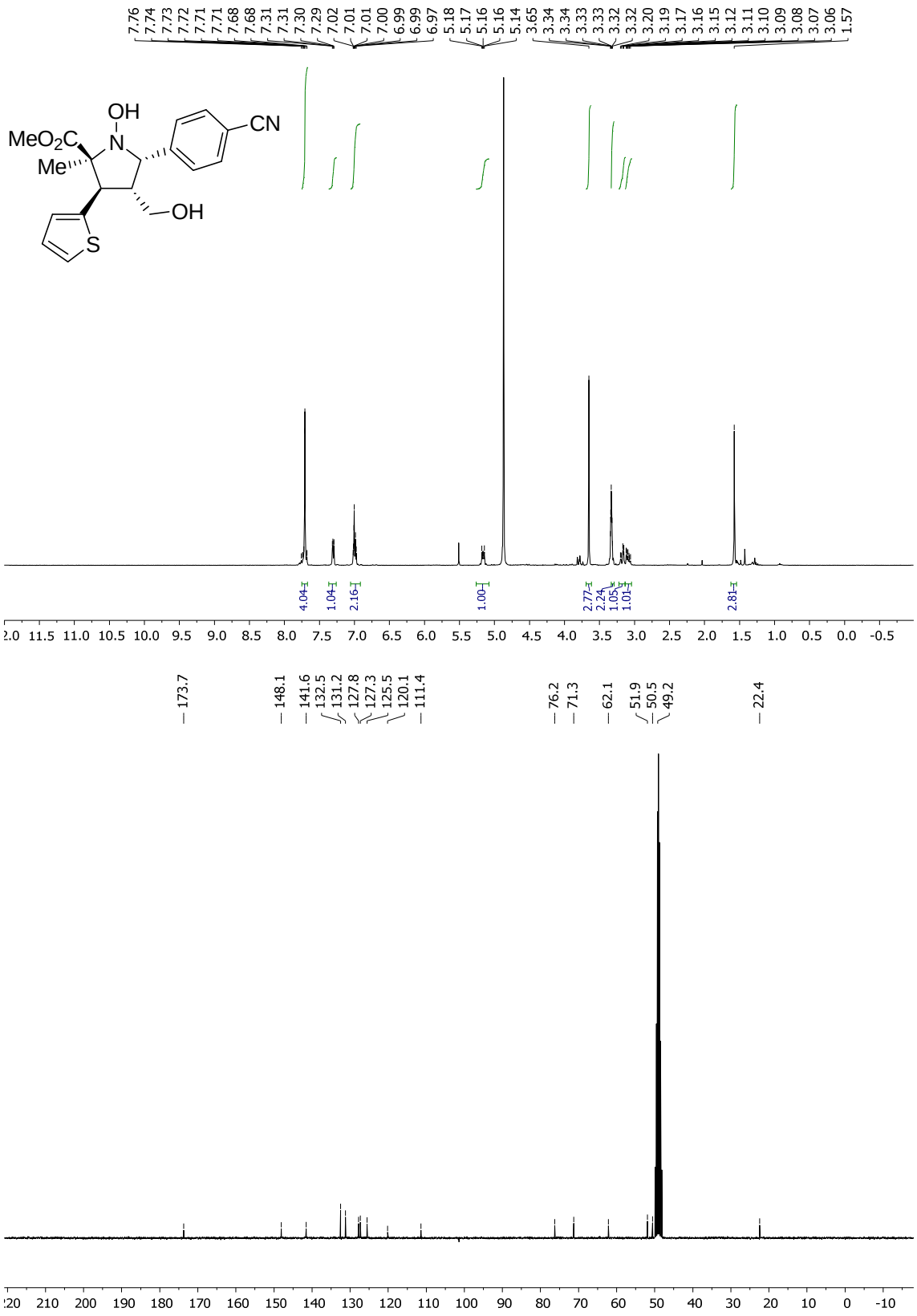


Figure SI-19. NMR spectra of compound **4r**.

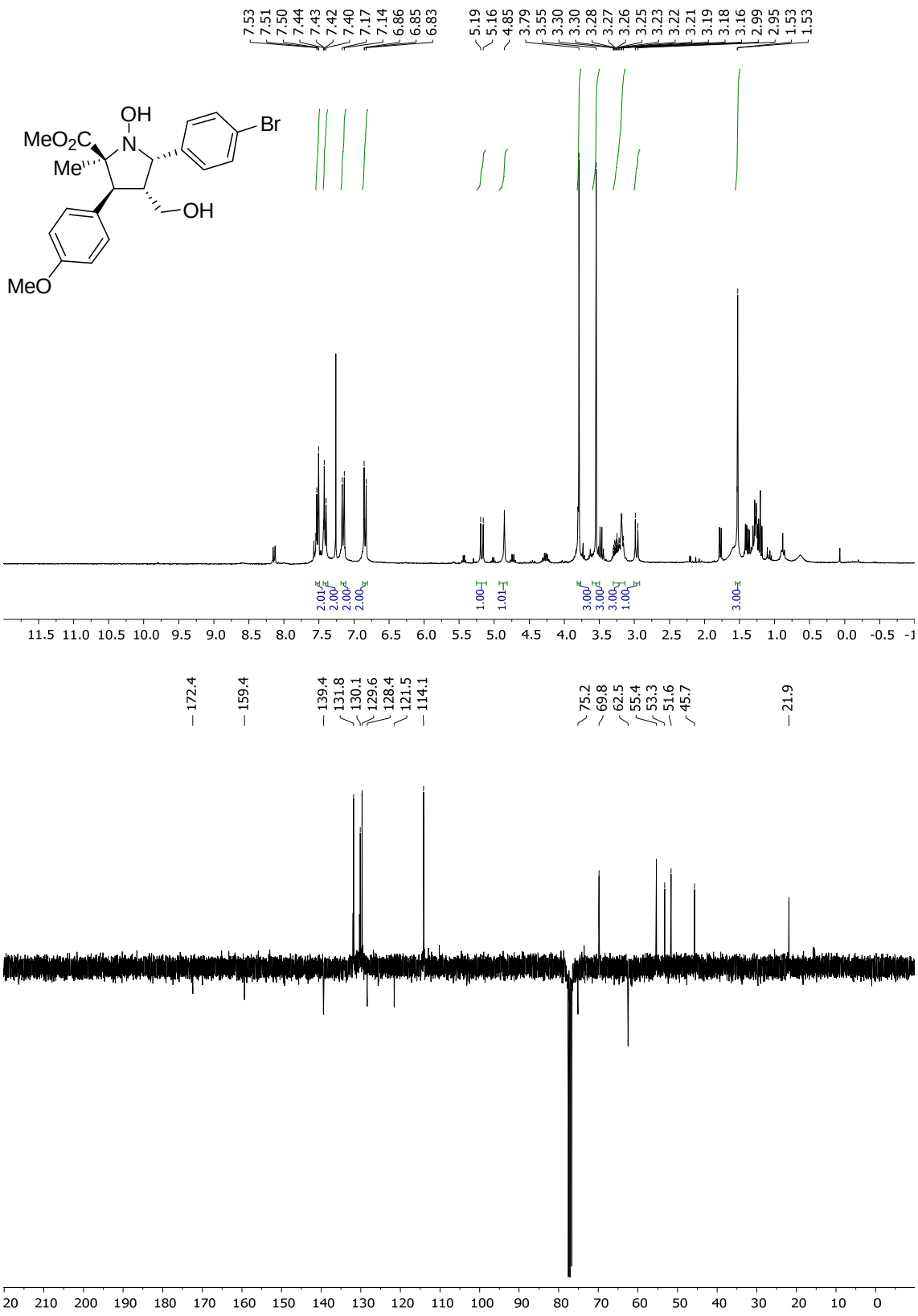


Figure SI-20. NMR spectra of compound **4s**.

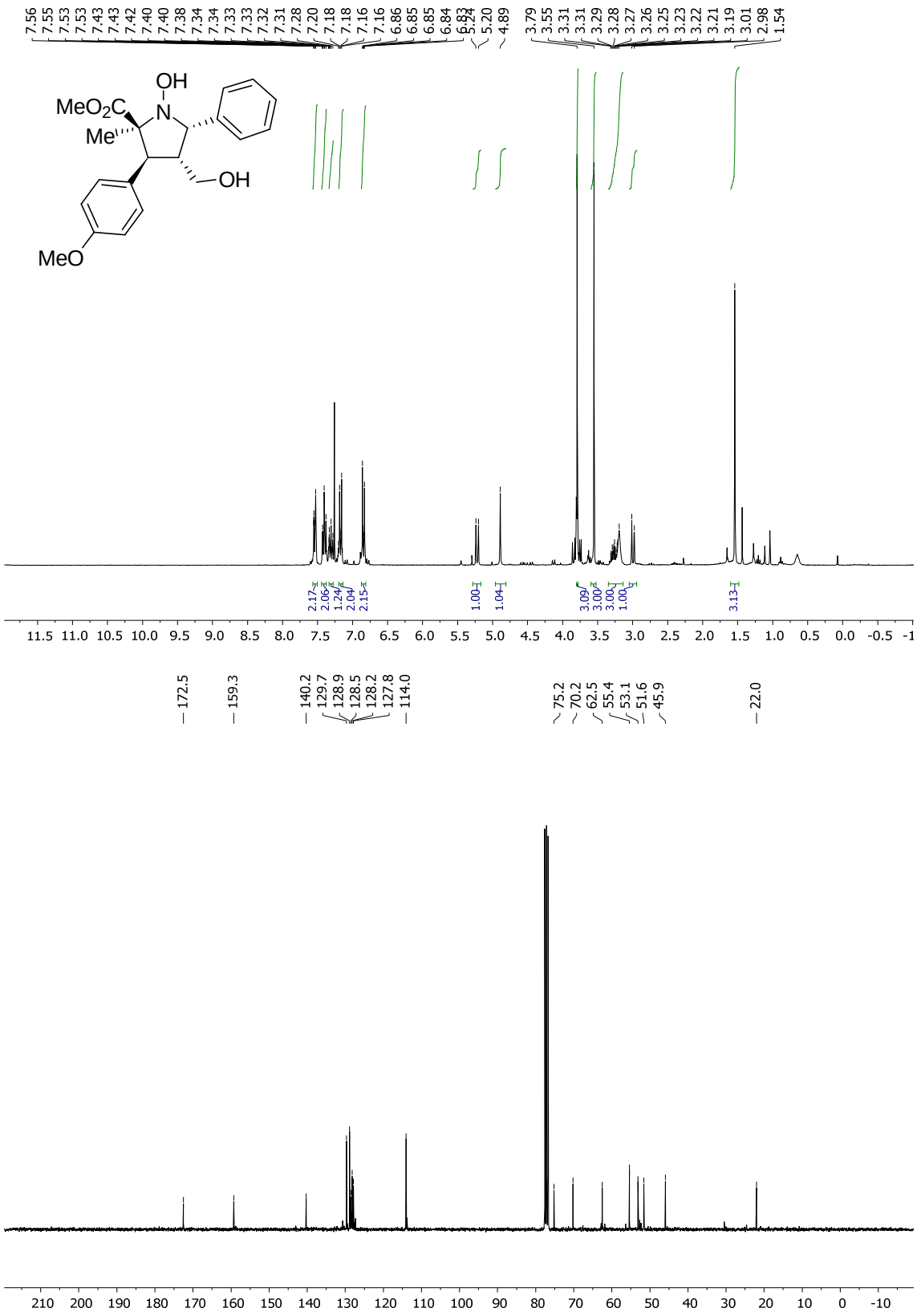


Figure SI-21. NMR spectra of compound **4t**.

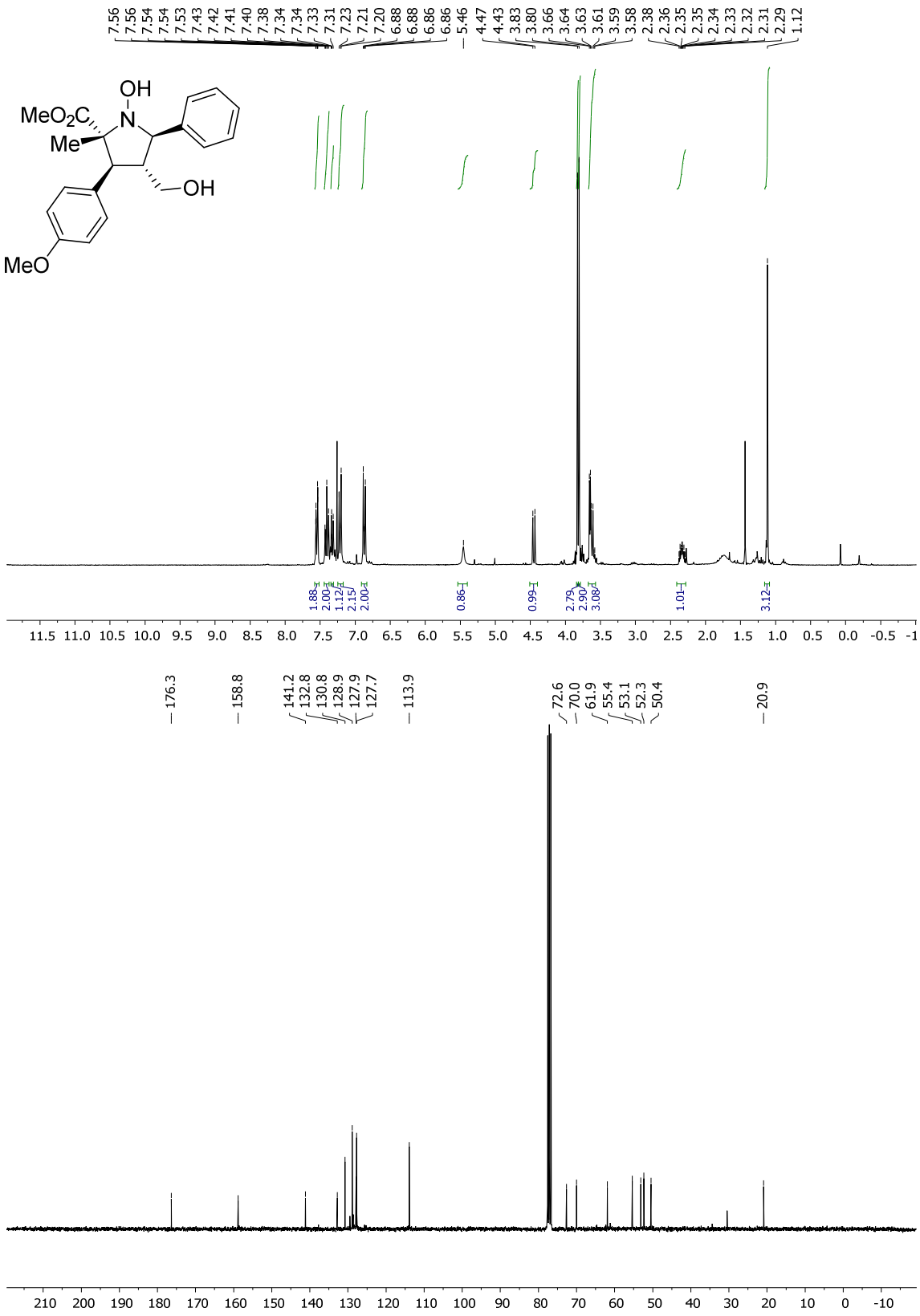


Figure SI-22. NMR spectra of compound **4t'**.

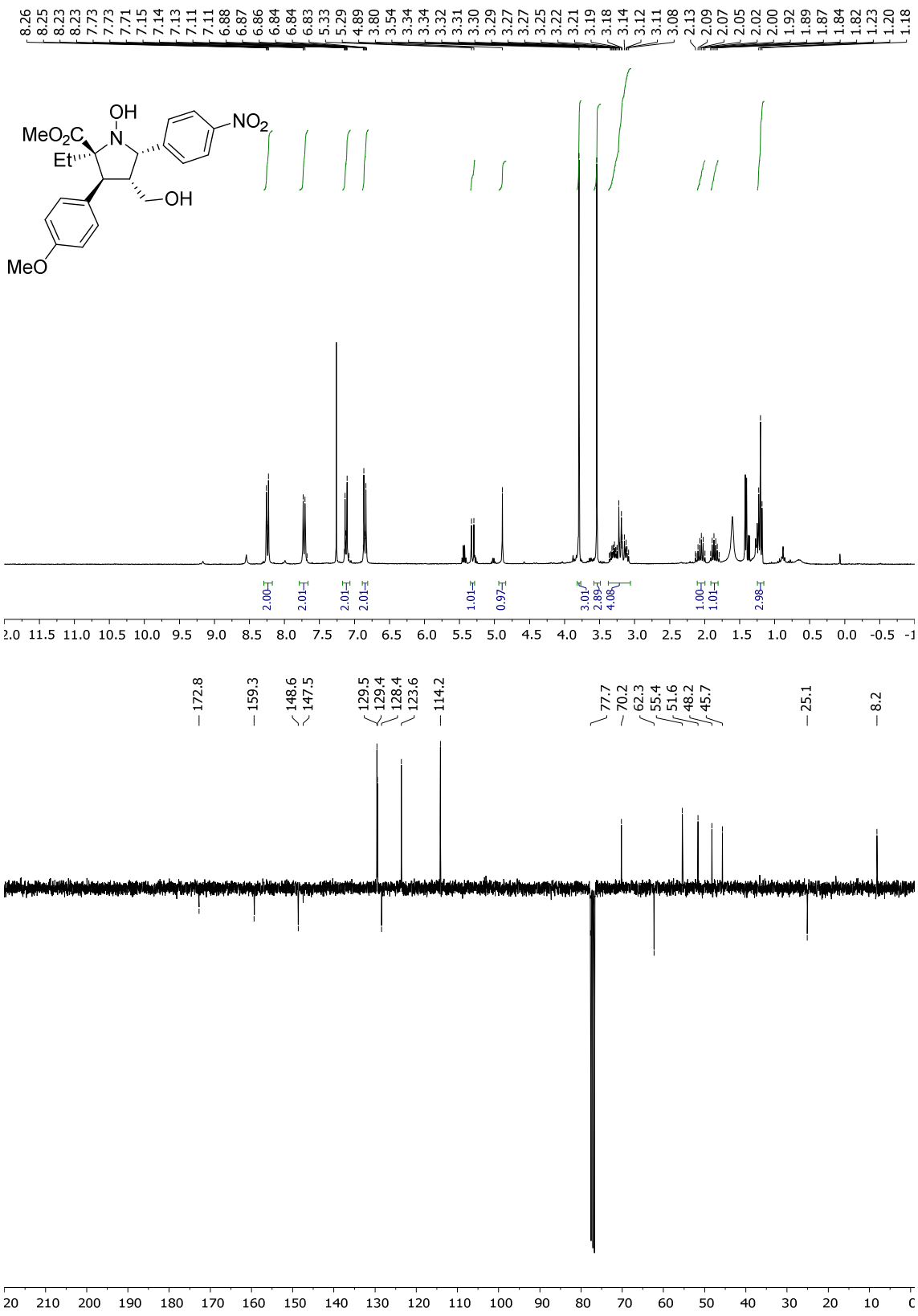


Figure SI-23. NMR spectra of compound **4u**.

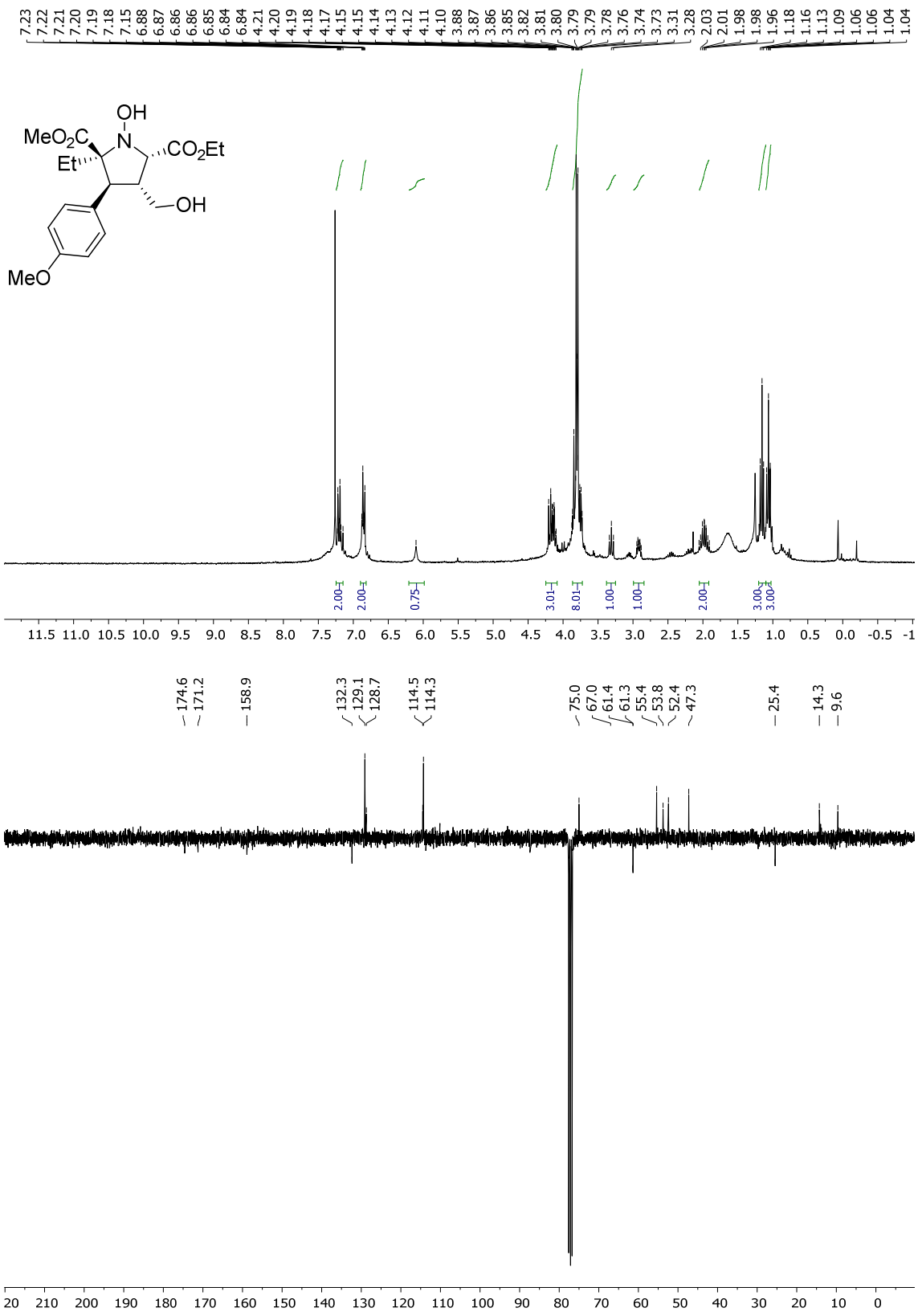


Figure SI-24. NMR spectra of compound **4v**.

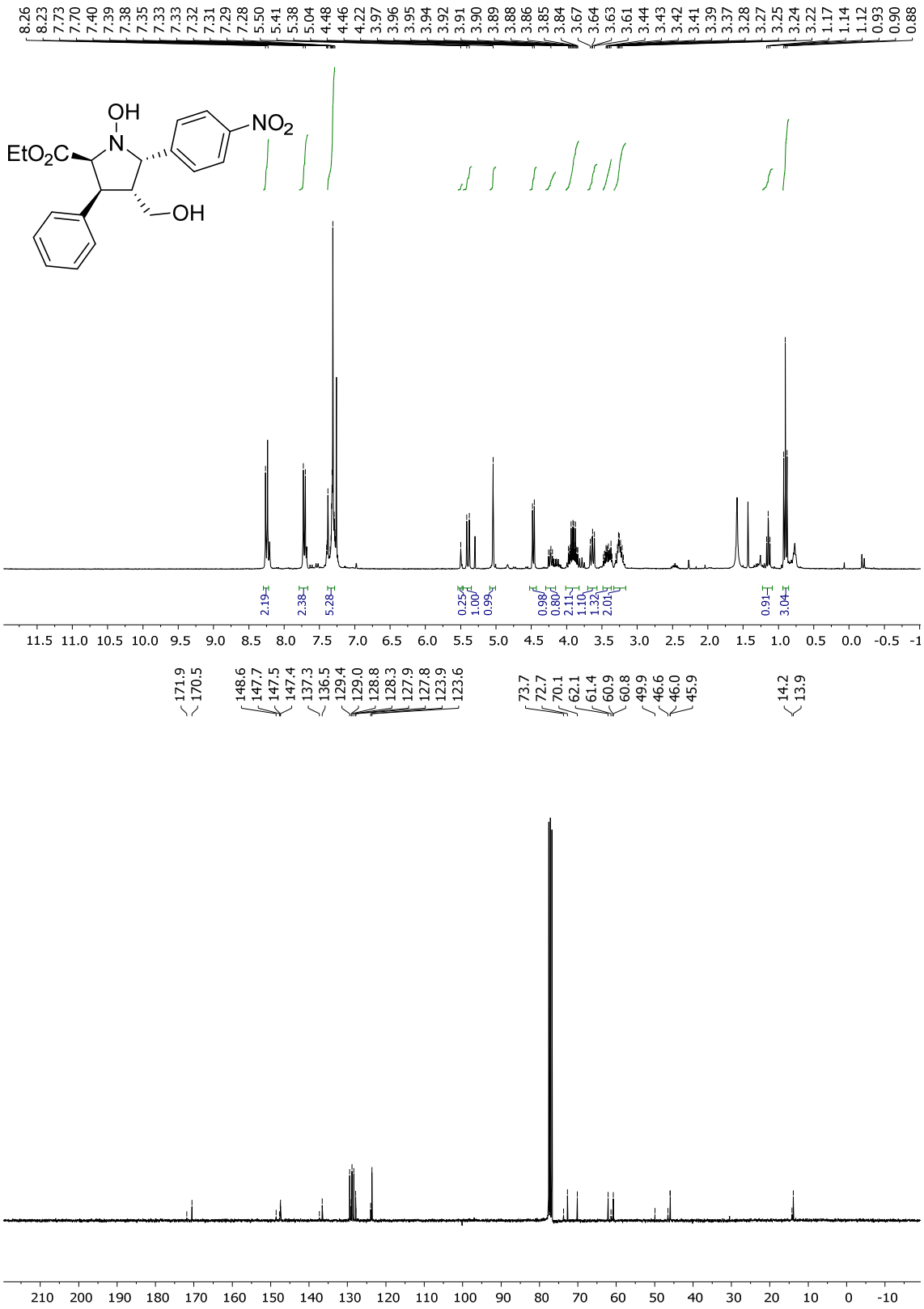


Figure SI-25. NMR spectra of compound **5a**.

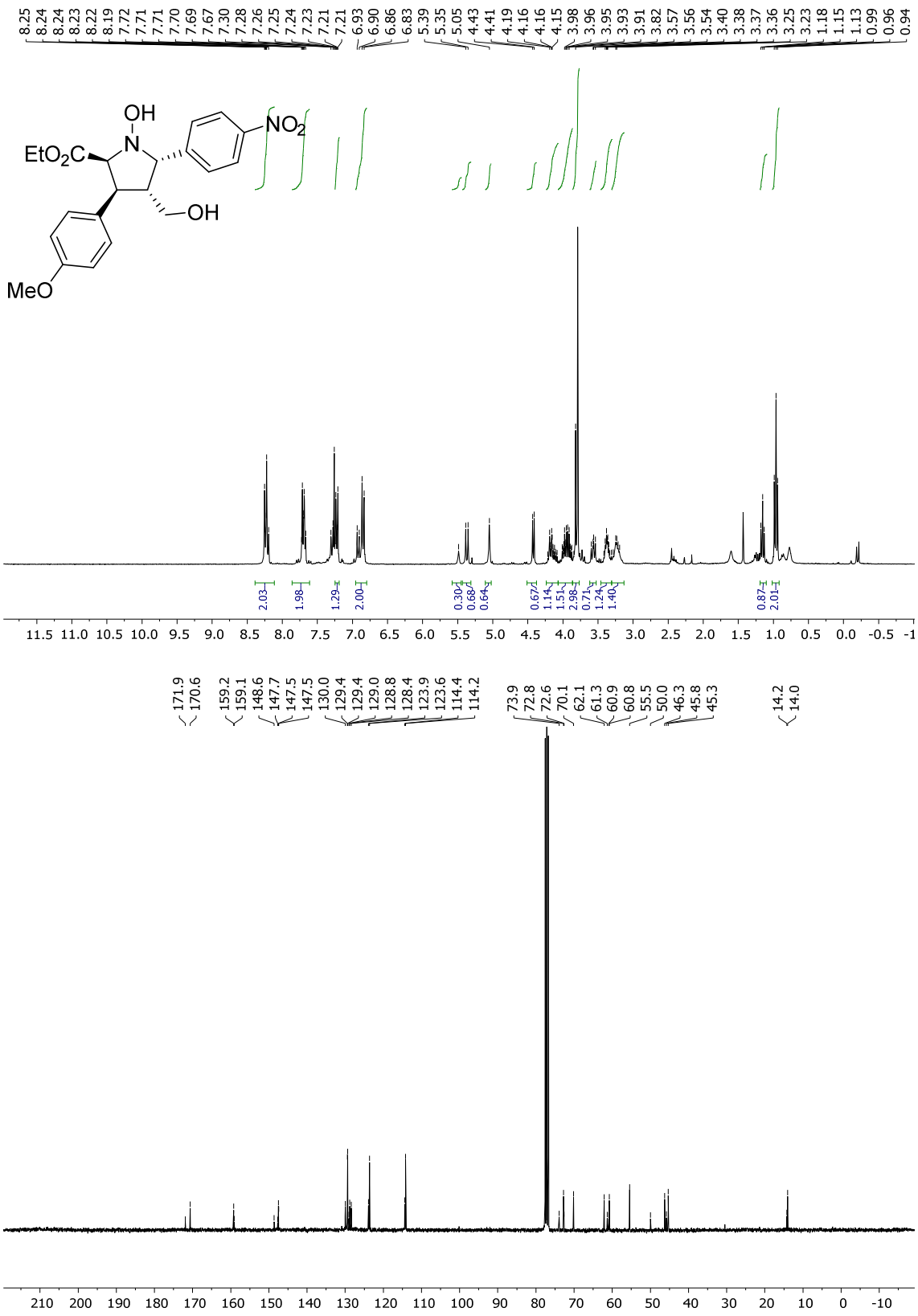


Figure SI-26. NMR spectra of compound **5b**.

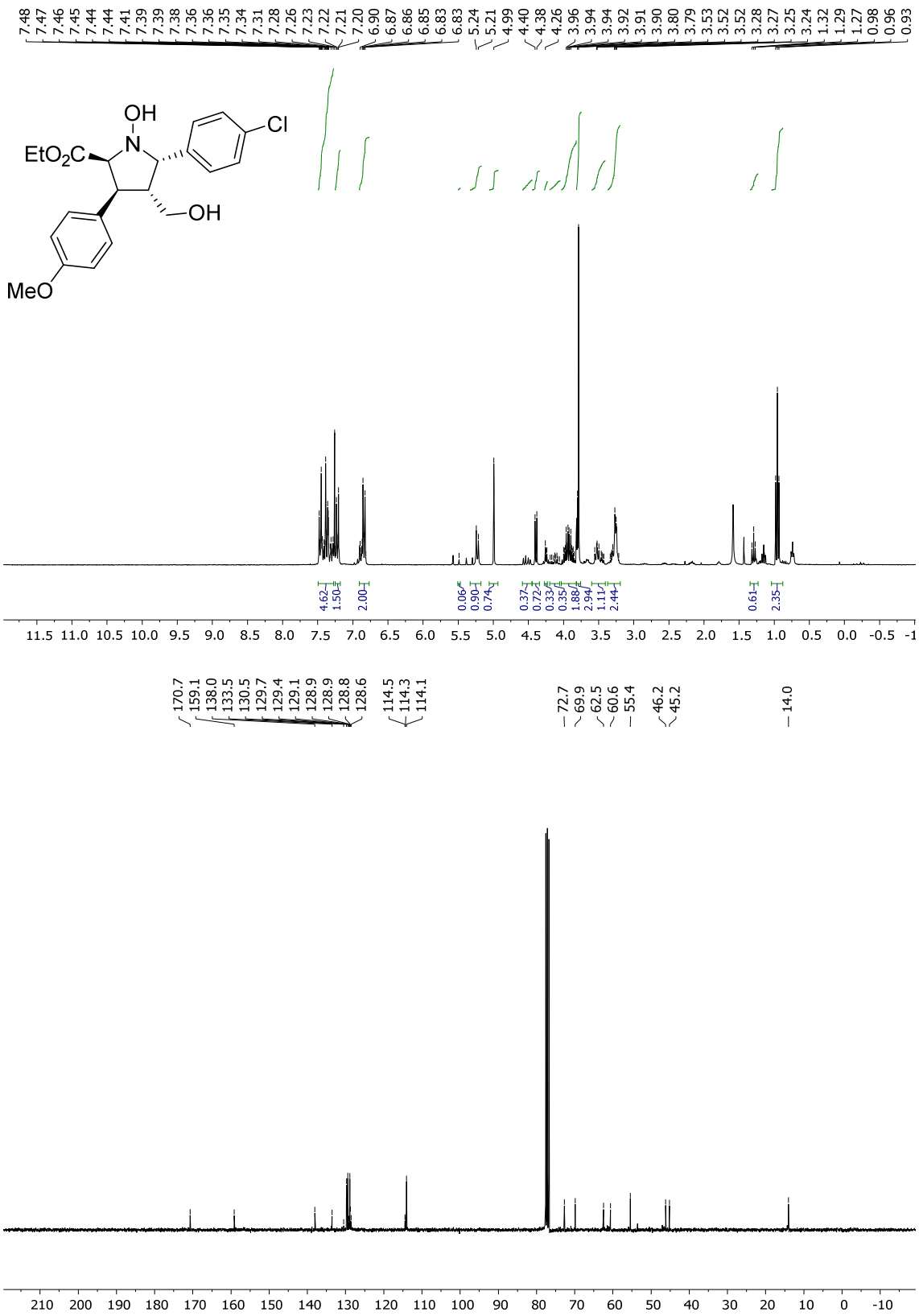


Figure SI-27. NMR spectra of compound **5c**.

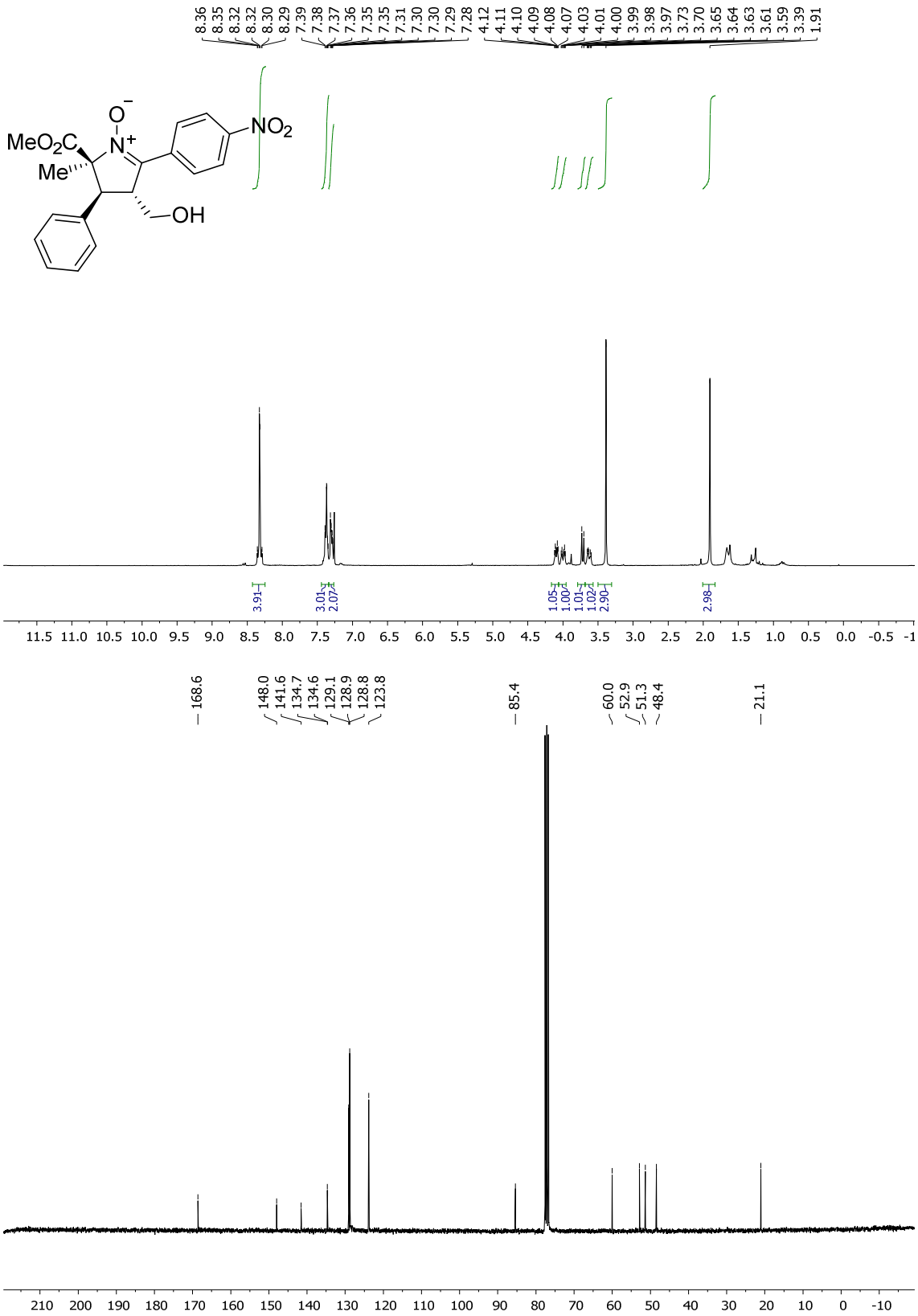


Figure SI-28. NMR spectra of compound **6a**.

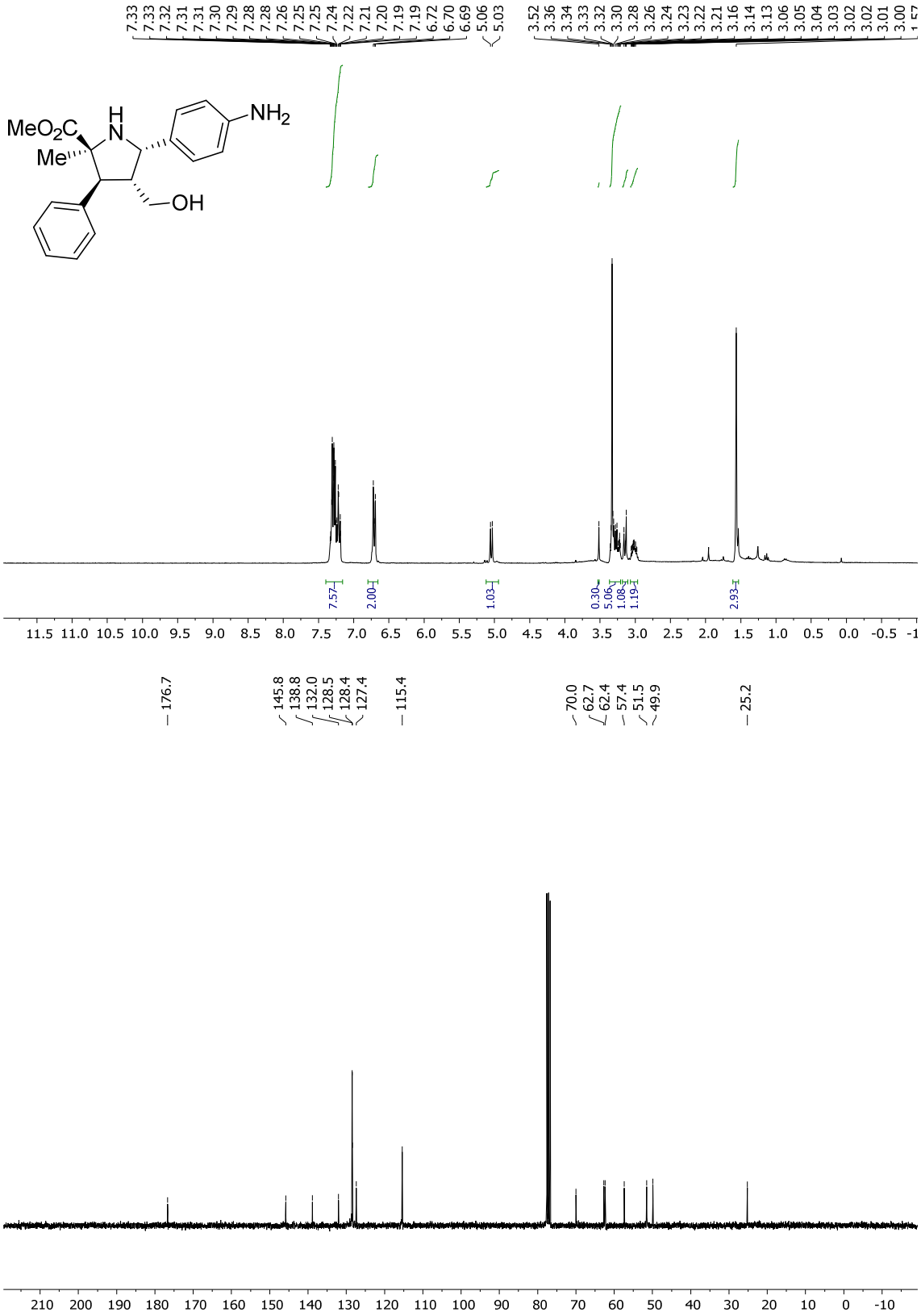


Figure SI-29. NMR spectra of compound **7a**.

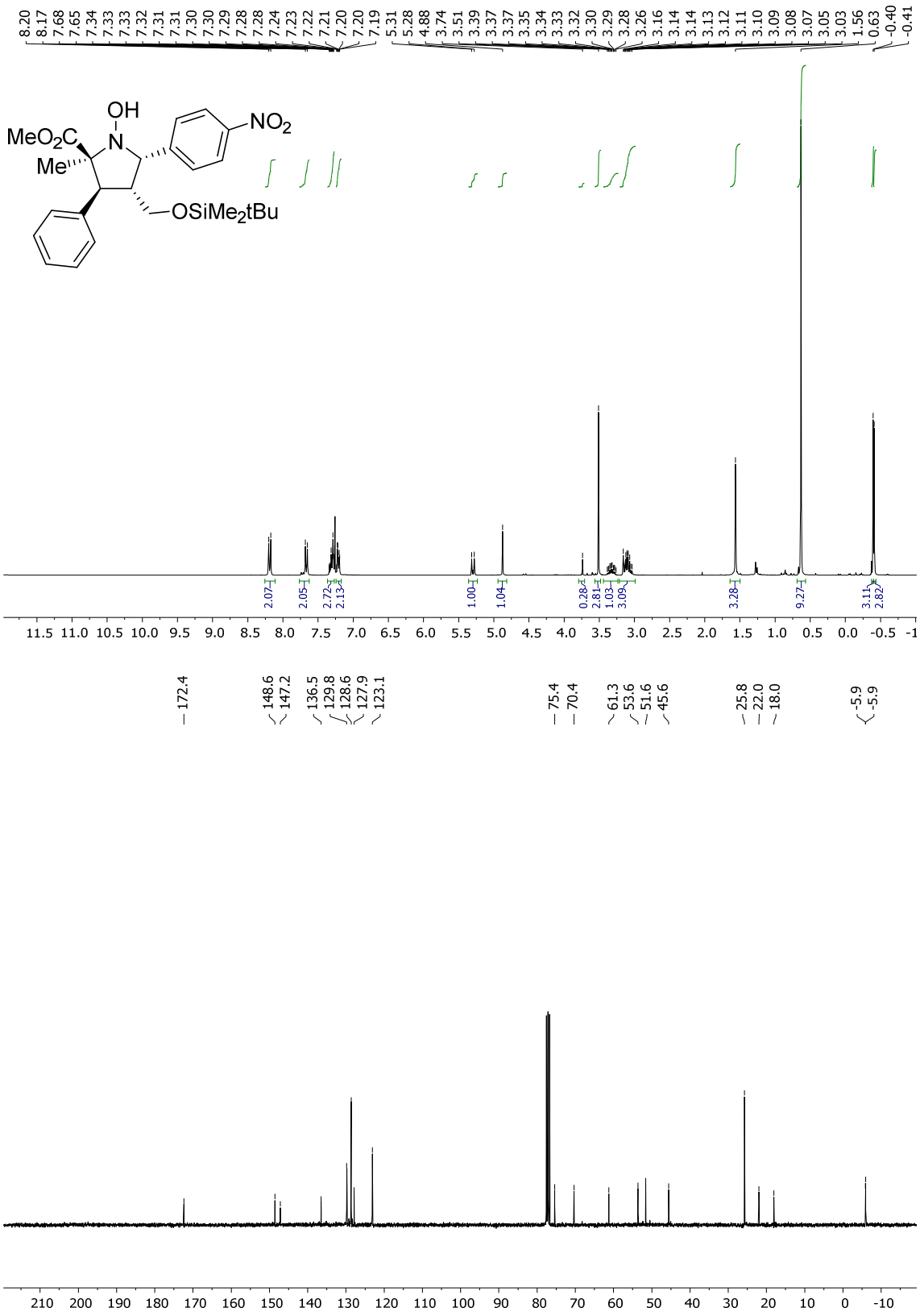
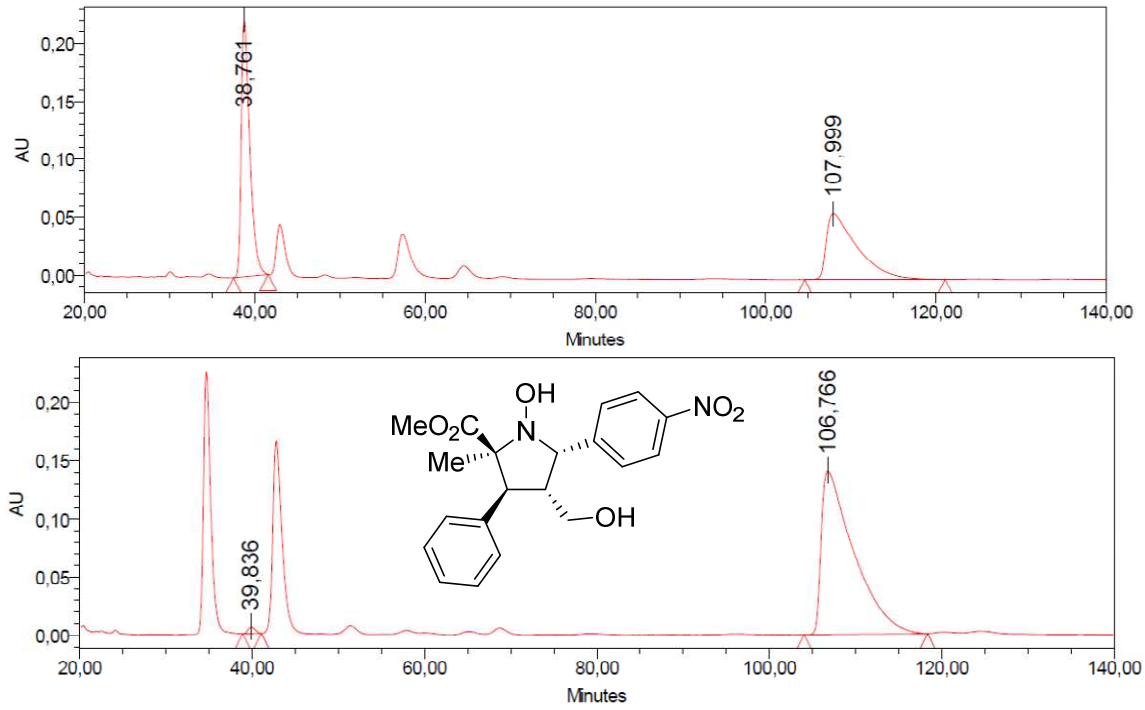


Figure SI-30. NMR spectra of compound **8a**.

HPLC traces



Peak Results

	Name	RT	Area	Height	% Area
1		39,836	325315	5663	0,88
2		106,766	36724437	140775	99,12

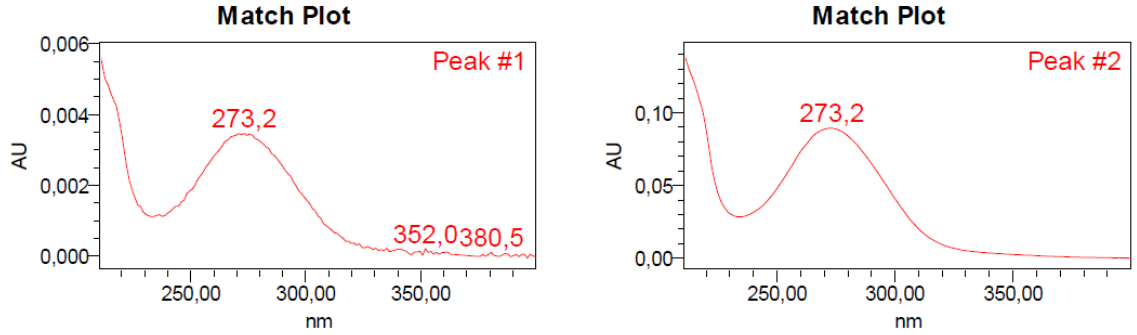
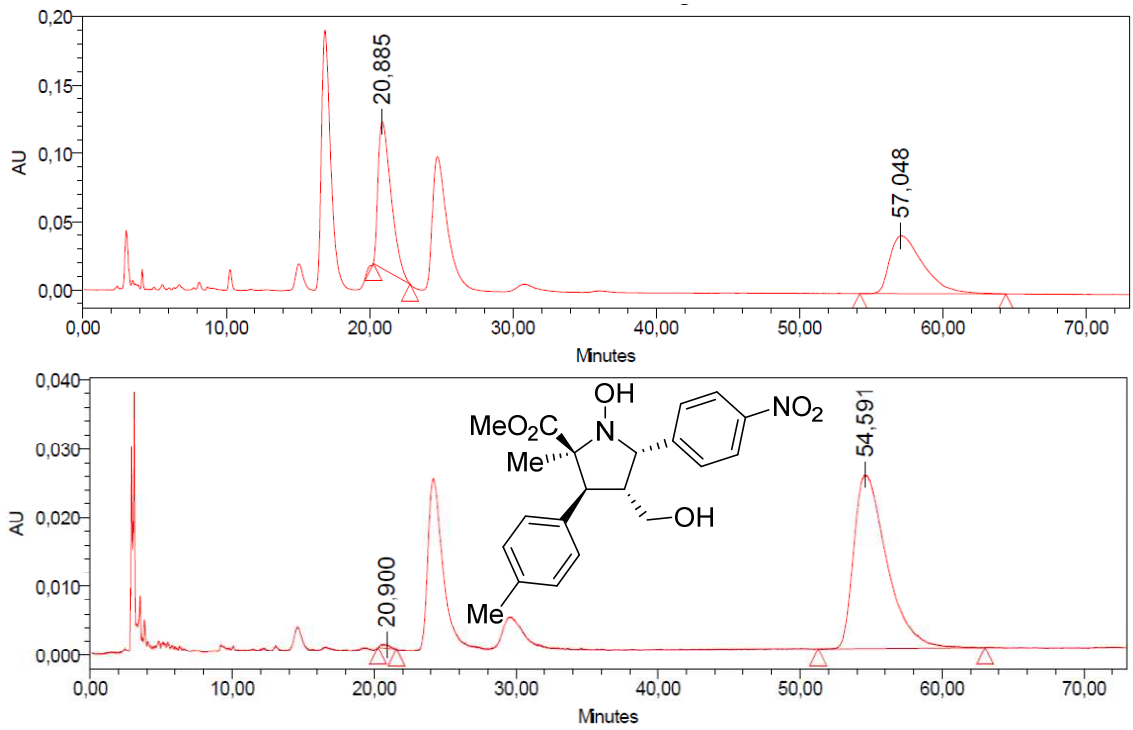


Figure SI-31. HPLC traces of compound **4a**.



Peak Results

	Name	RT	Area	Height	% Area
1		20,900	23245	566	0,57
2		54,591	4042091	25320	99,43

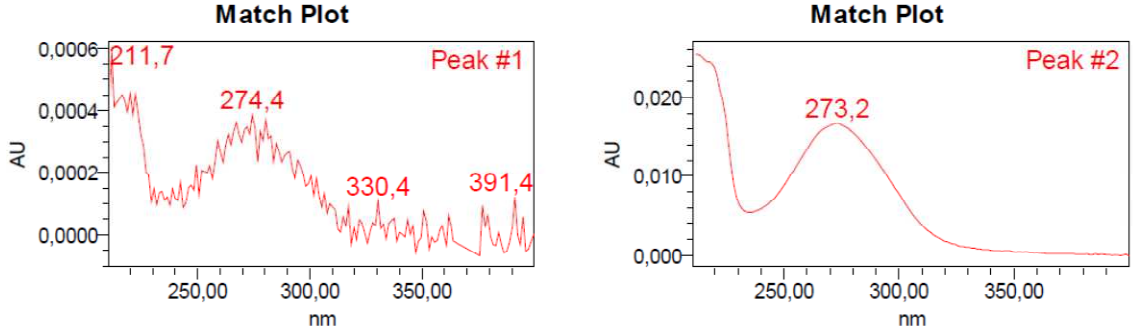
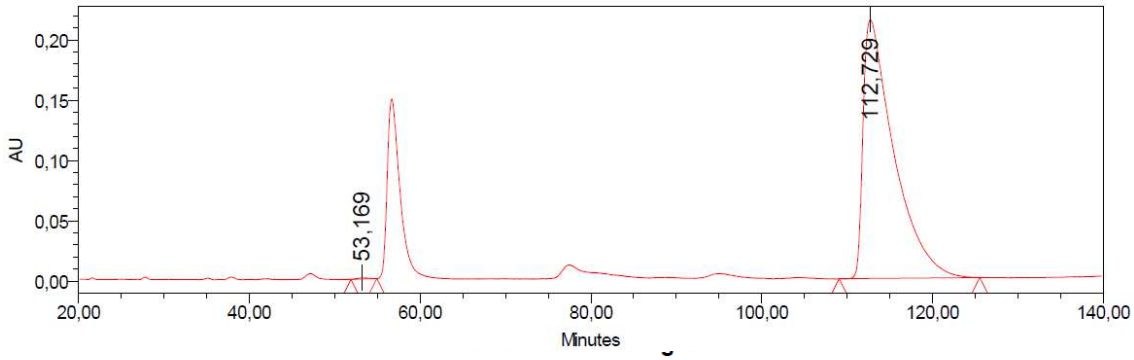
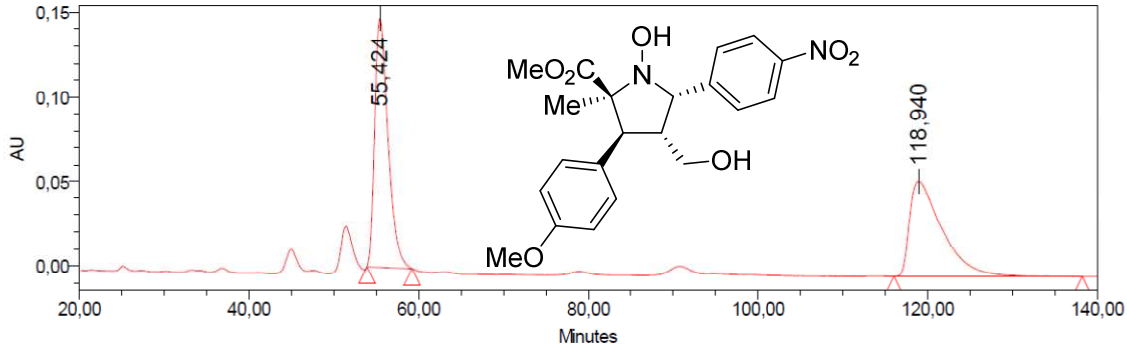


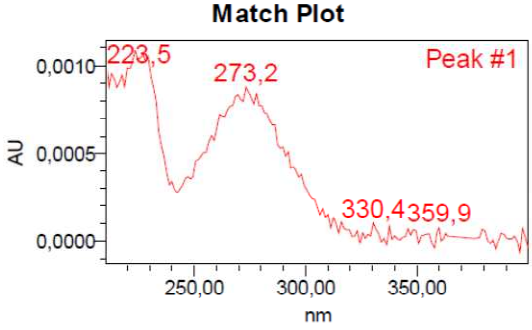
Figure SI-32. HPLC traces of compound **4b**.





Peak Results

	Name	RT	Area	Height	% Area
1		53,169	78152	1031	0,15
2		112,729	53553262	214269	99,85



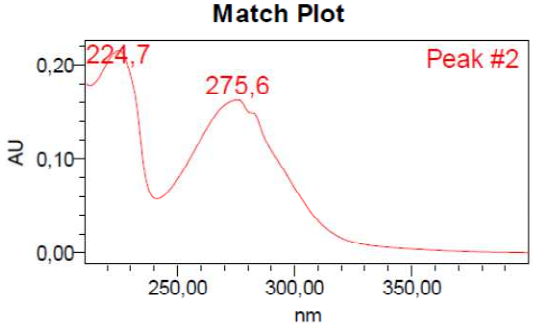
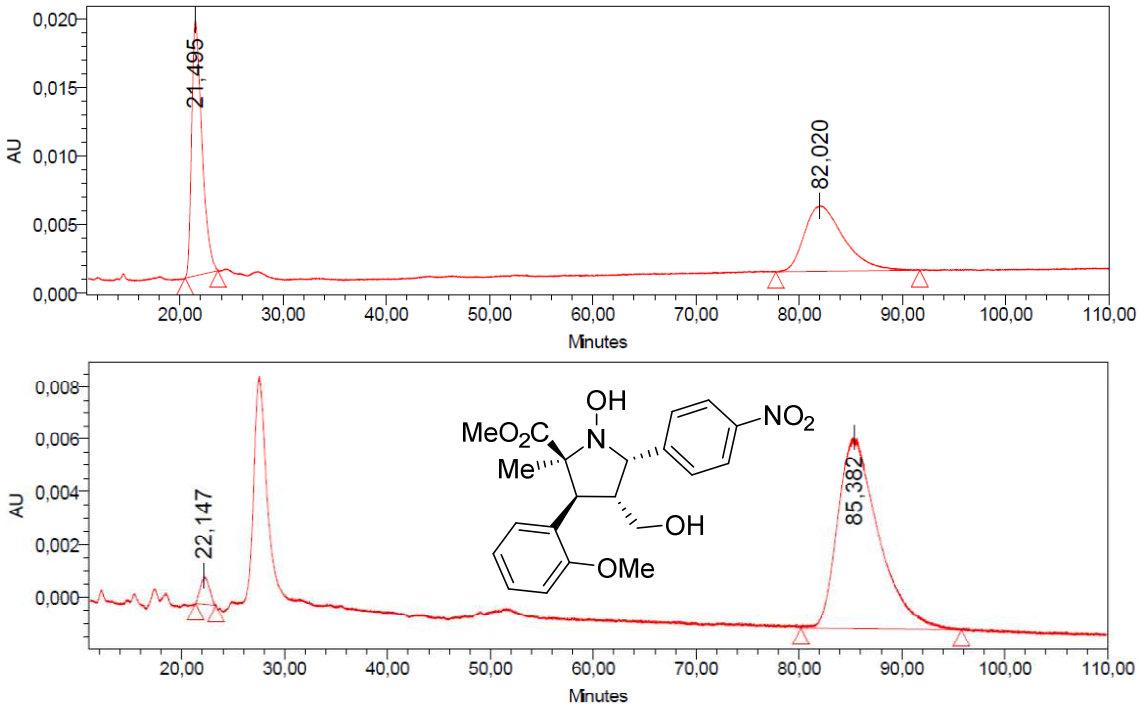


Figure SI-33. HPLC traces of compound **4c**.



Peak Results

	Name	RT	Area	Height	% Area
1		22,147	62879	1085	3,07
2		85,382	1984825	7266	96,93

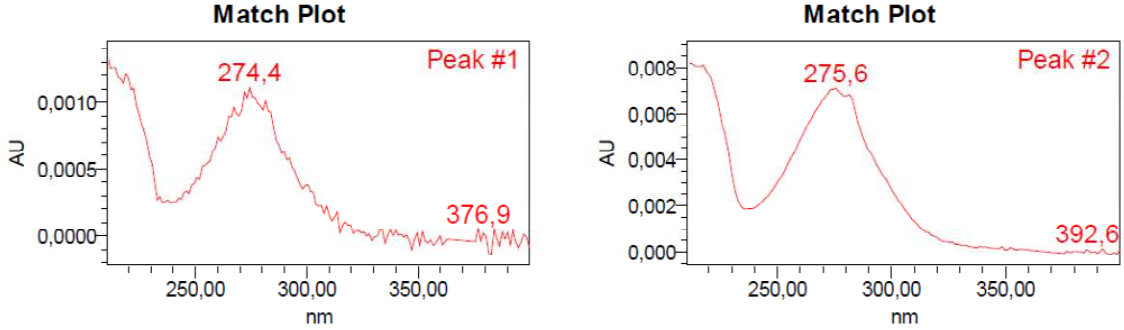
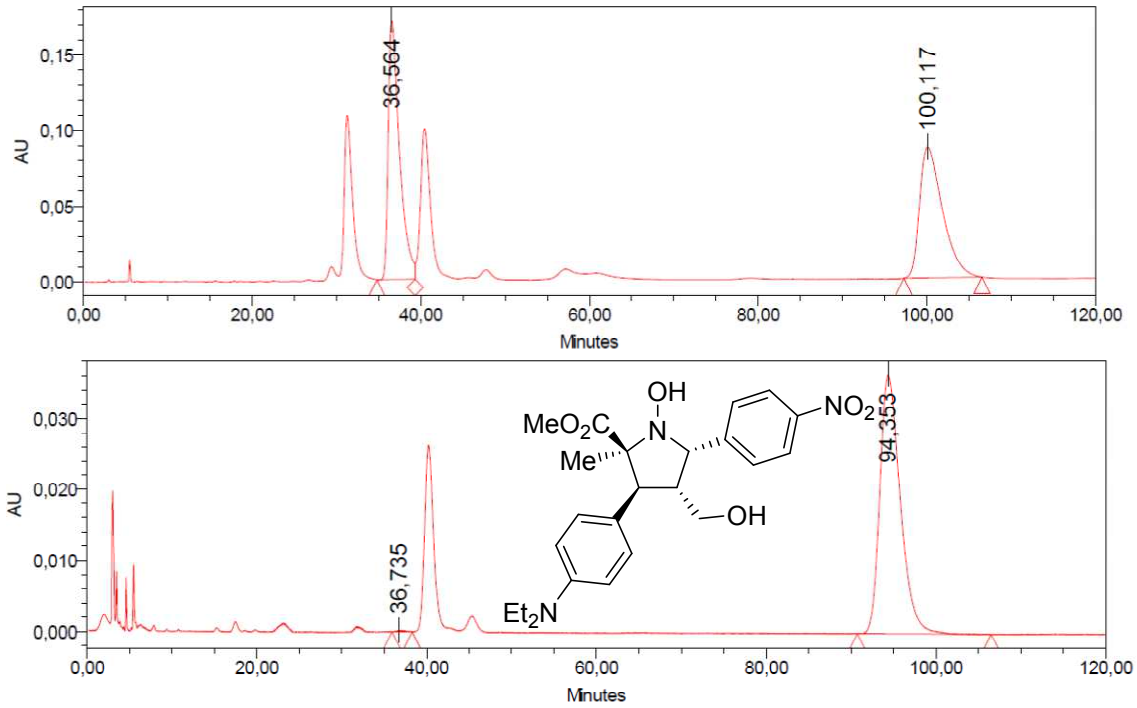


Figure SI-34. HPLC traces of compound **4d**.



Peak Results

	Name	RT	Area	Height	% Area
1		36,735	14040	221	0,23
2		94,353	6091675	36504	99,77

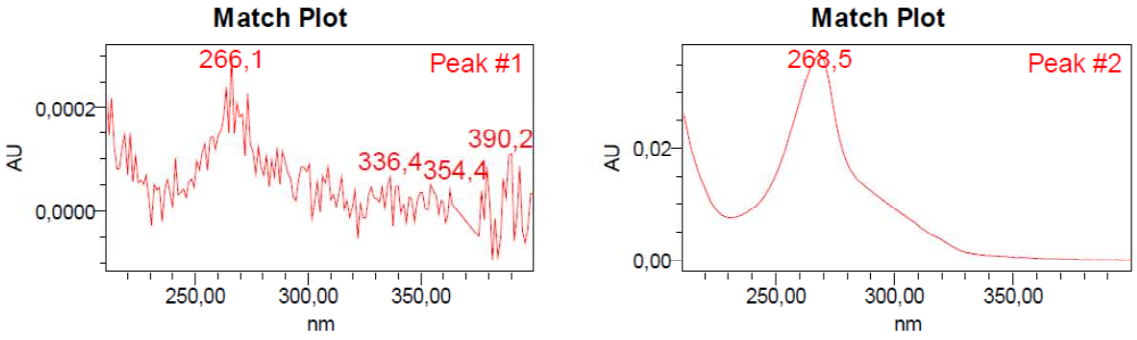
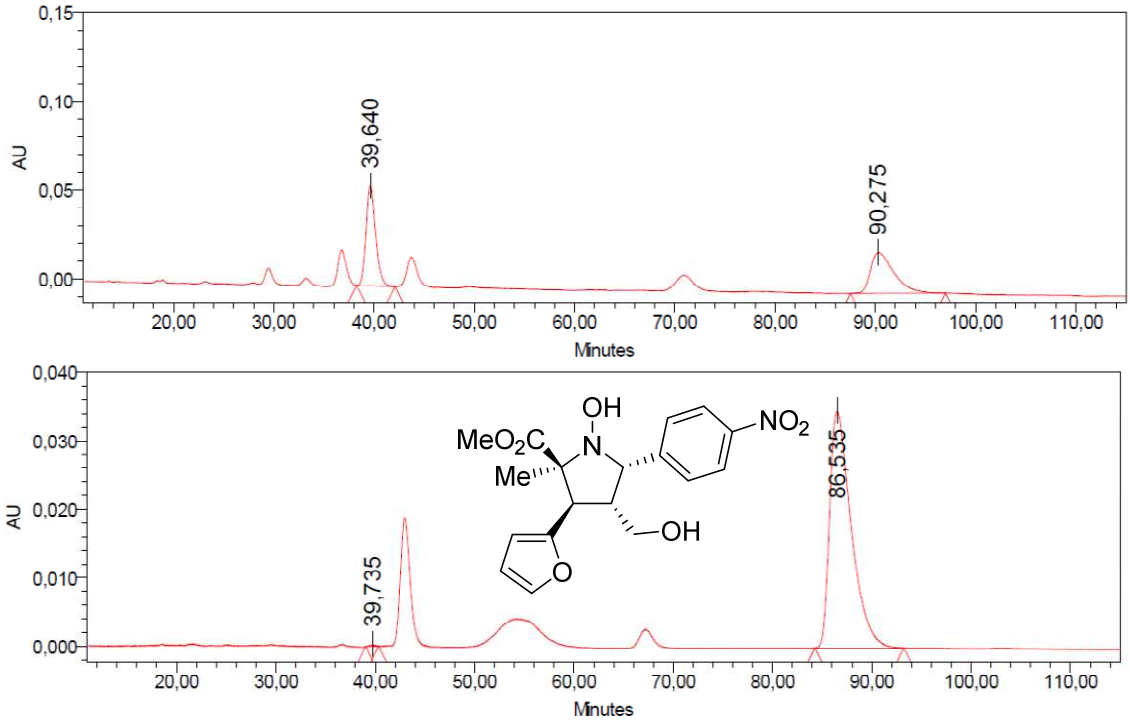


Figure SI-35. HPLC traces of compound **4e**.



Peak Results

	Name	RT	Area	Height	% Area
1		39,735	9751	354	0,19
2		86,535	5209909	34663	99,81

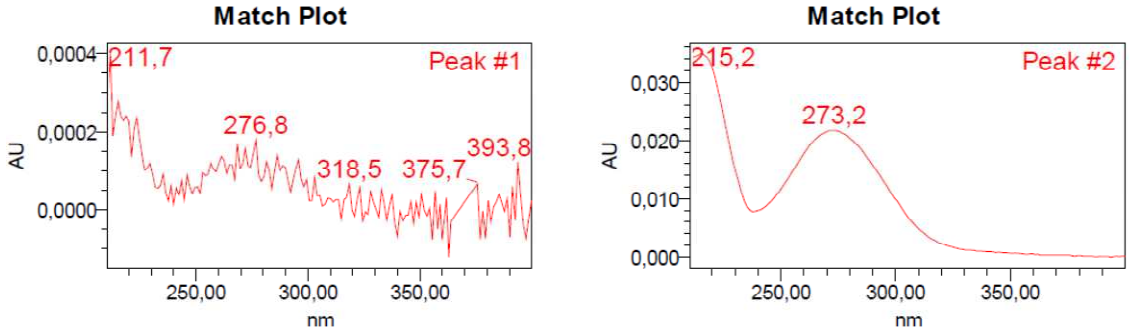
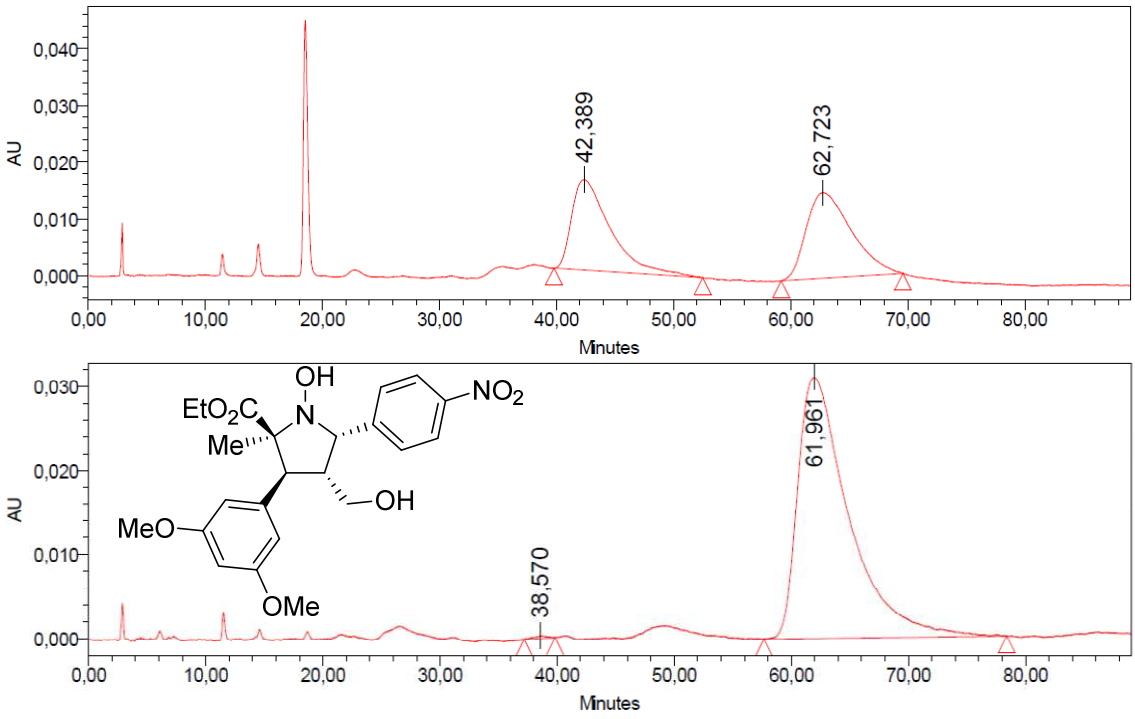


Figure SI-36. HPLC traces of compound **4f**.



Peak Results

	Name	RT	Area	Height	% Area
1		38,570	25180	339	0,27
2		61,961	9375649	31021	99,73

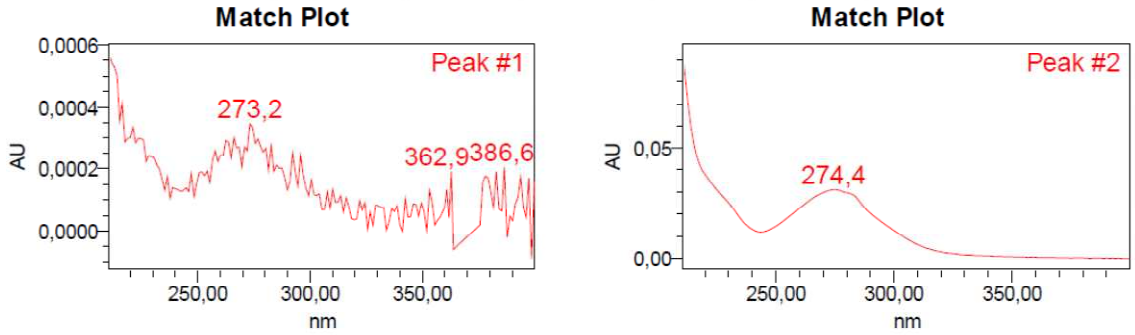
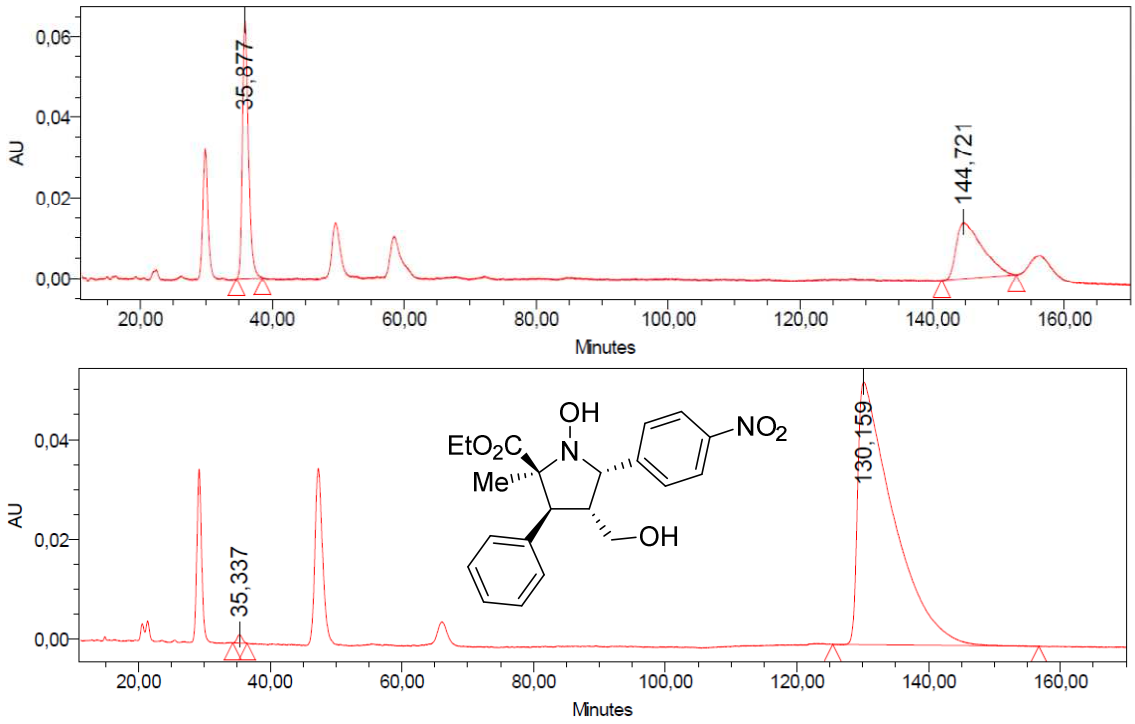


Figure SI-37. HPLC traces of compound **4g**.



Peak Results

	Name	RT	Area	Height	% Area
1		35,337	93858	1735	0,47
2		130,159	19739873	52720	99,53

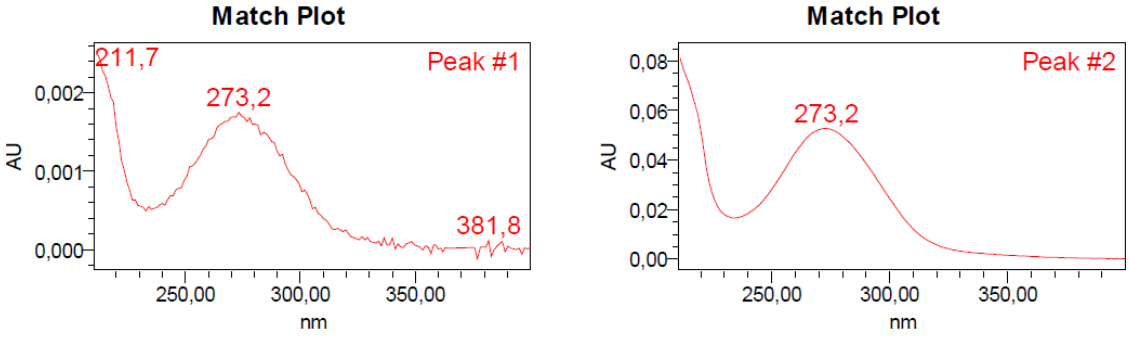
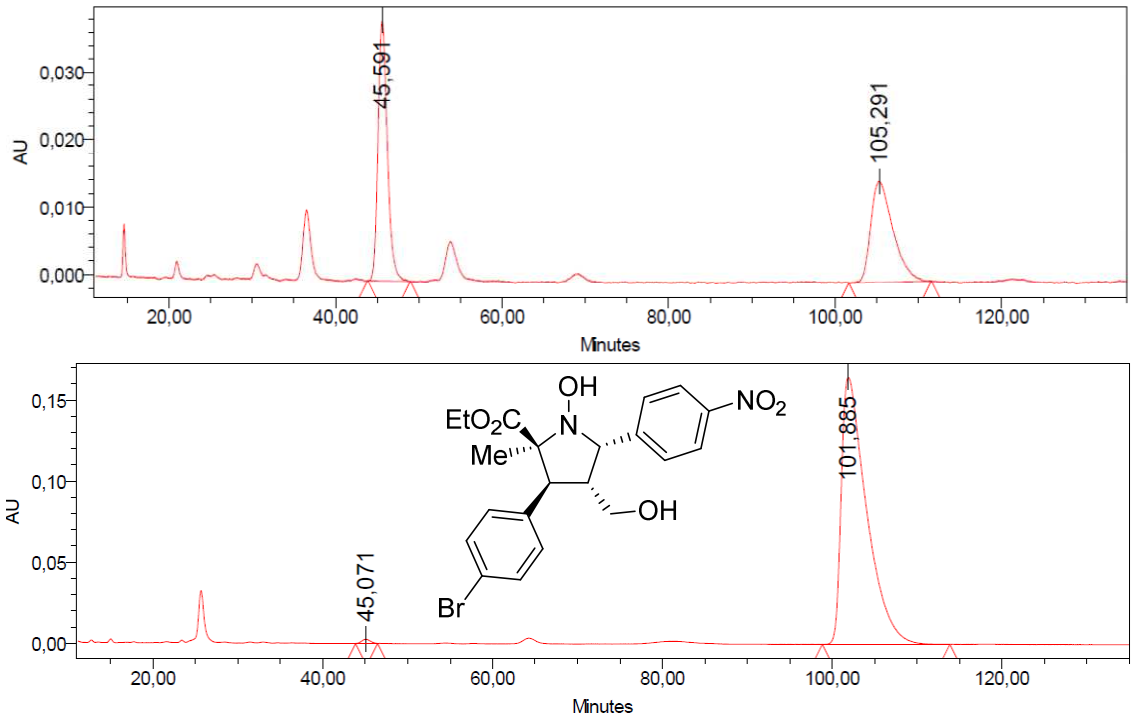


Figure SI-38. HPLC traces of compound **4h**.



Peak Results

	Name	RT	Area	Height	% Area
1		45,071	185488	2684	0,54
2		101,885	33974963	164621	99,46

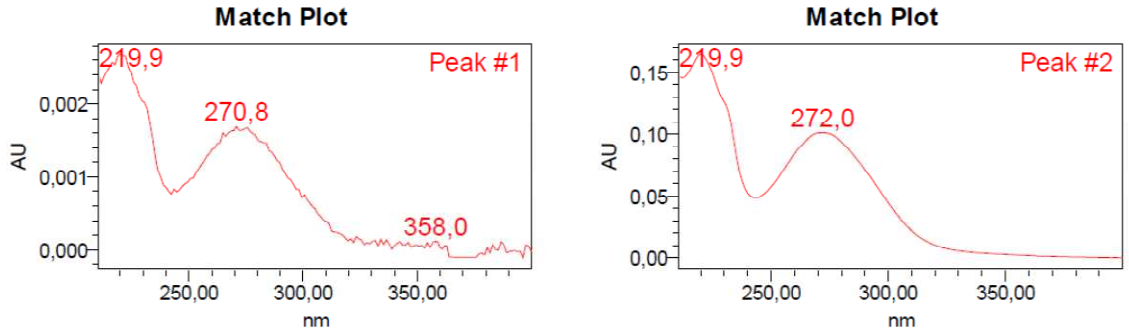
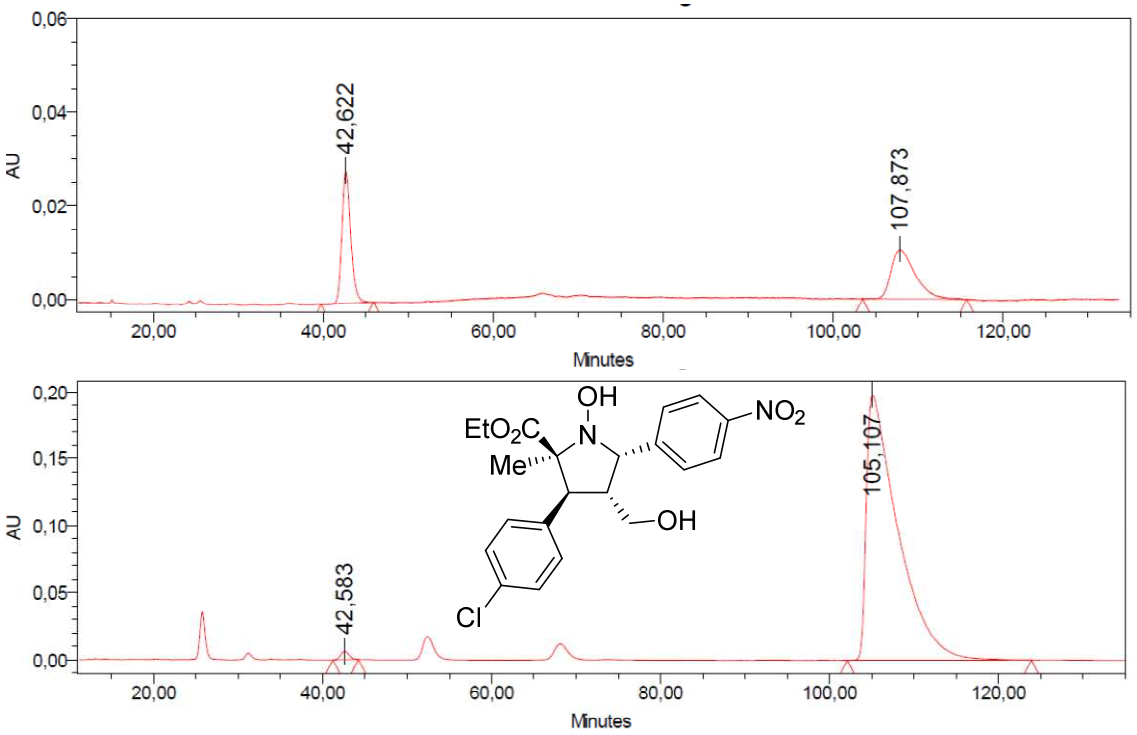


Figure SI-39. HPLC traces of compound **4i**.



Peak Results

	Name	RT	Area	Height	% Area
1		42,583	424256	6203	0,82
2		105,107	51178236	197980	99,18

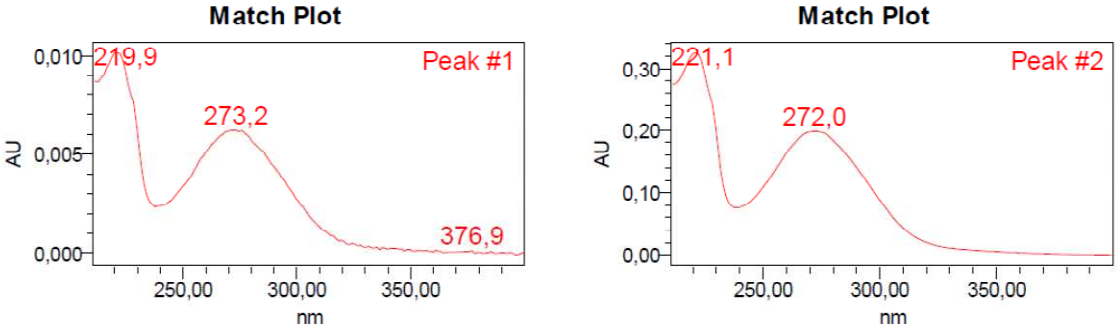
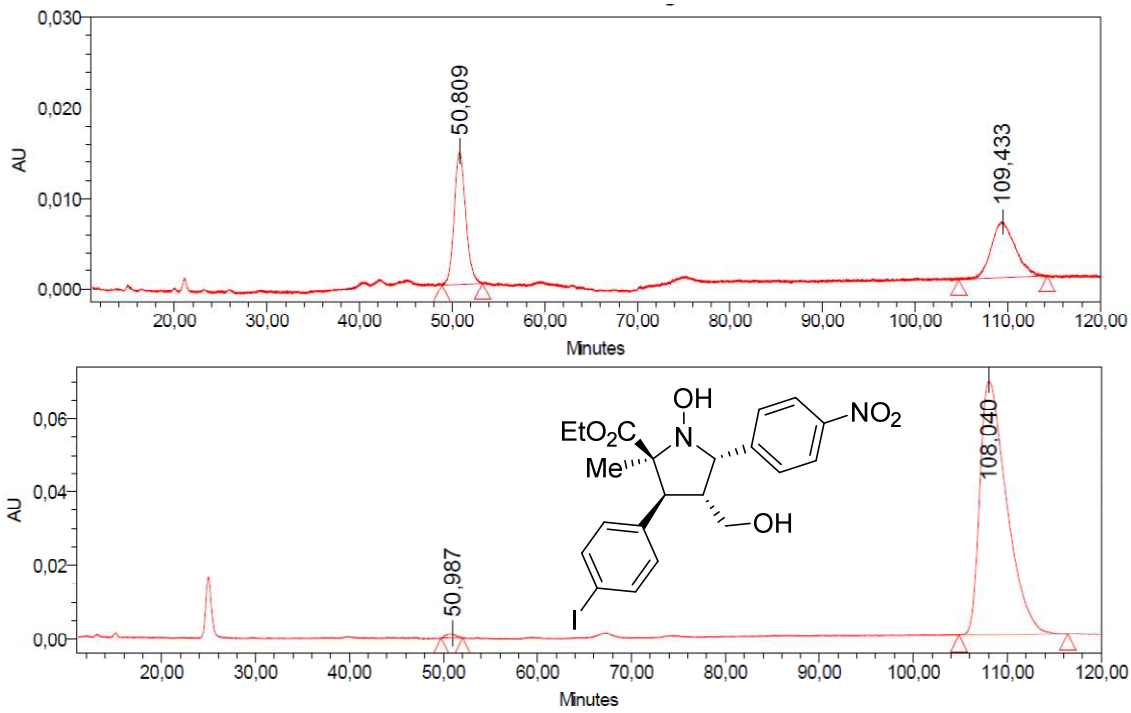


Figure SI-40. HPLC traces of compound **4j**.



Peak Results

	Name	RT	Area	Height	% Area
1		50,987	75669	1229	0,55
2		108,040	13642378	69026	99,45

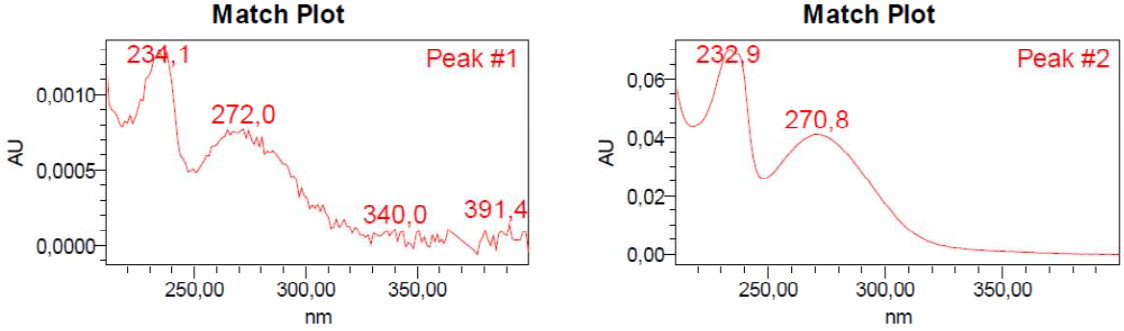
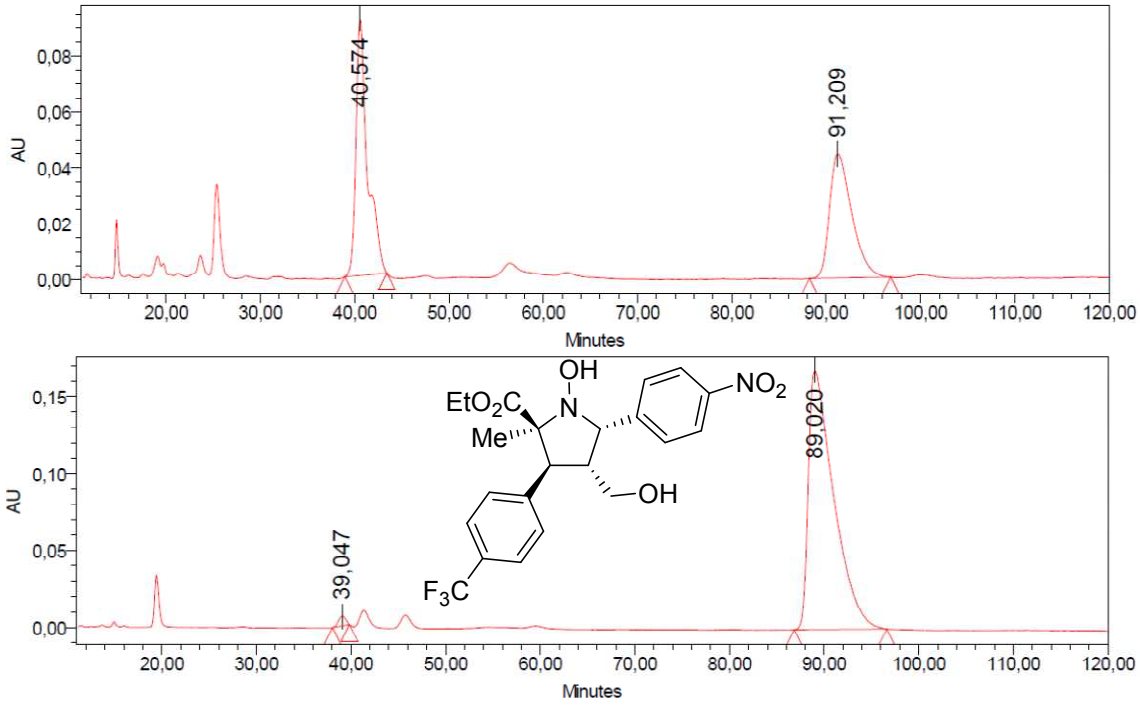


Figure SI-41. HPLC traces of compound **4k**.



Peak Results

	Name	RT	Area	Height	% Area
1		39,047	329975	6244	1,04
2		89,020	31267751	168239	98,96

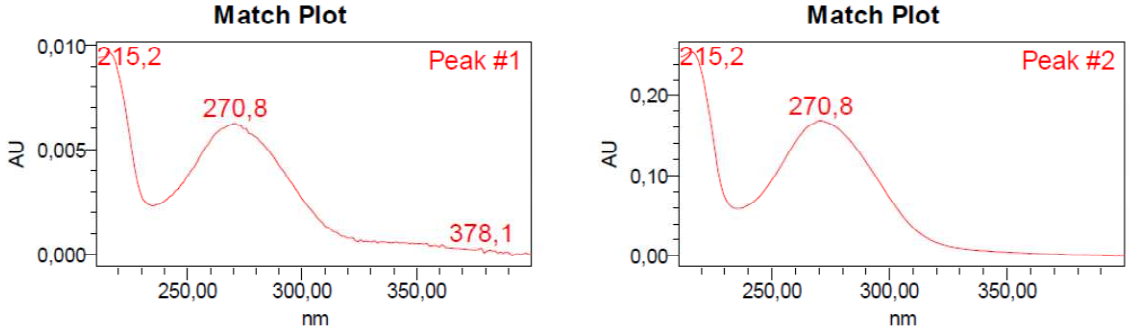
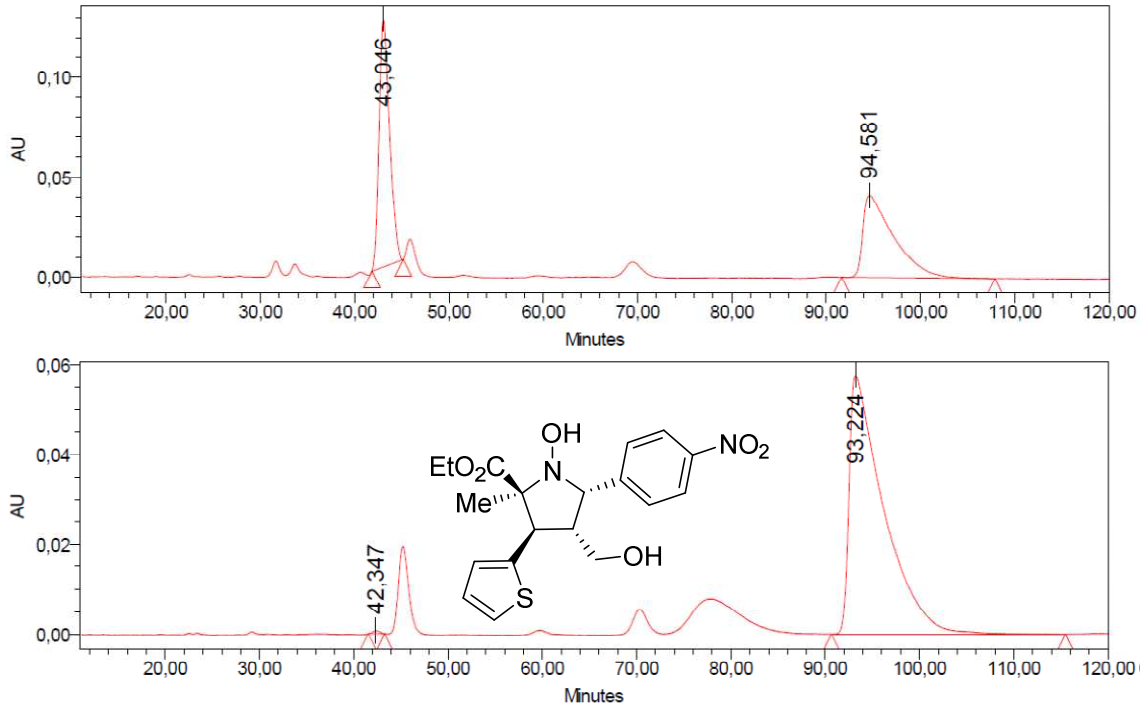


Figure SI-42. HPLC traces of compound **4l**.



Peak Results

	Name	RT	Area	Height	% Area
1		42,347	36814	716	0,25
2		93,224	14633060	57616	99,75

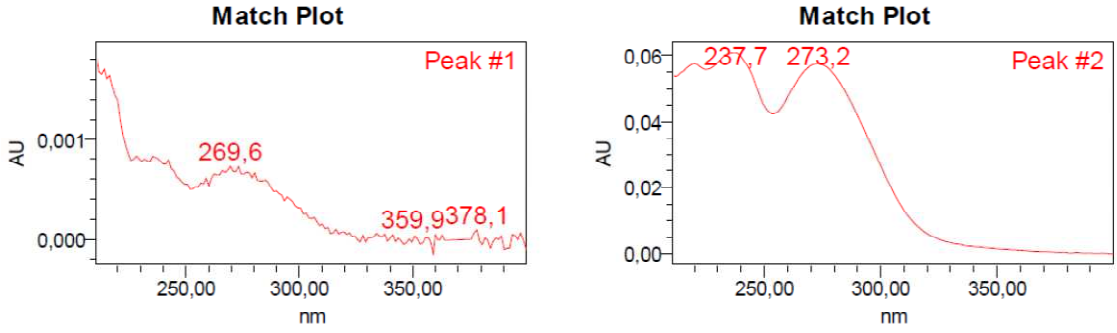
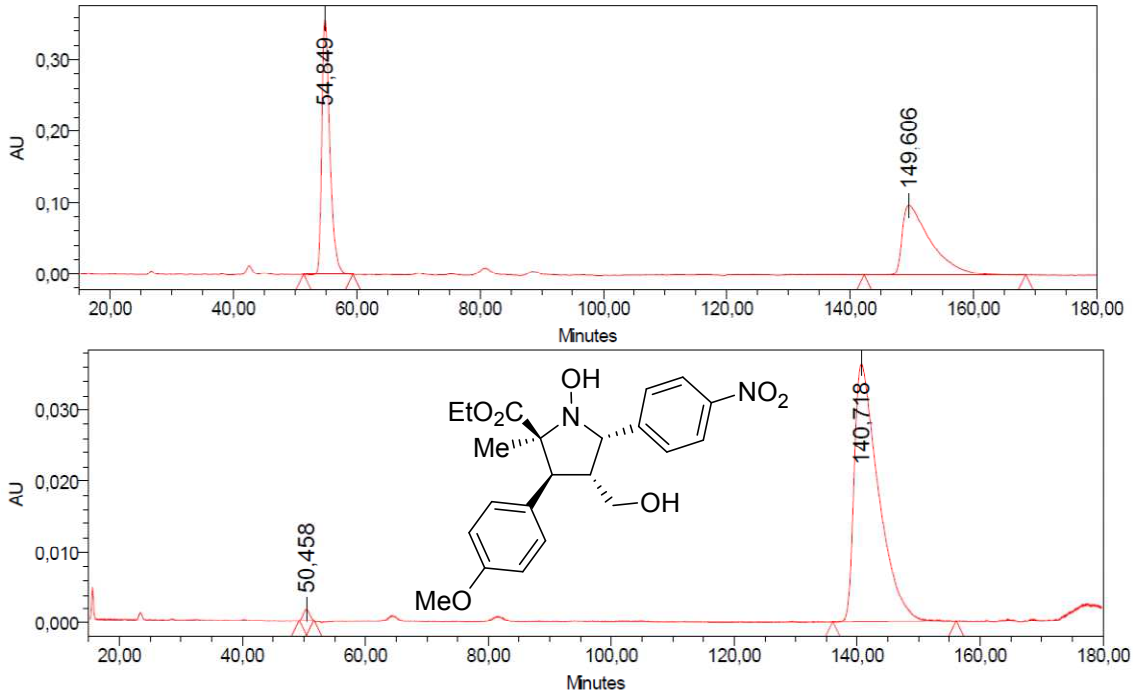


Figure SI-43. HPLC traces of compound **4m**.



Peak Results

	Name	RT	Area	Height	% Area
1		50,458	112788	1624	1,11
2		140,718	10043455	36408	98,89

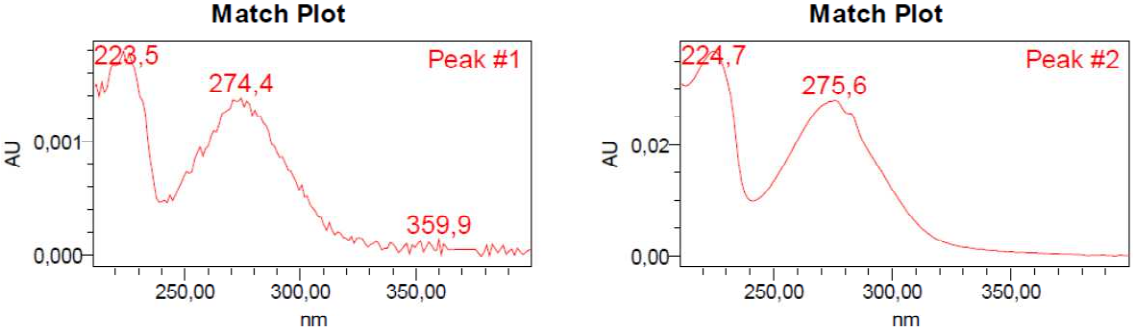
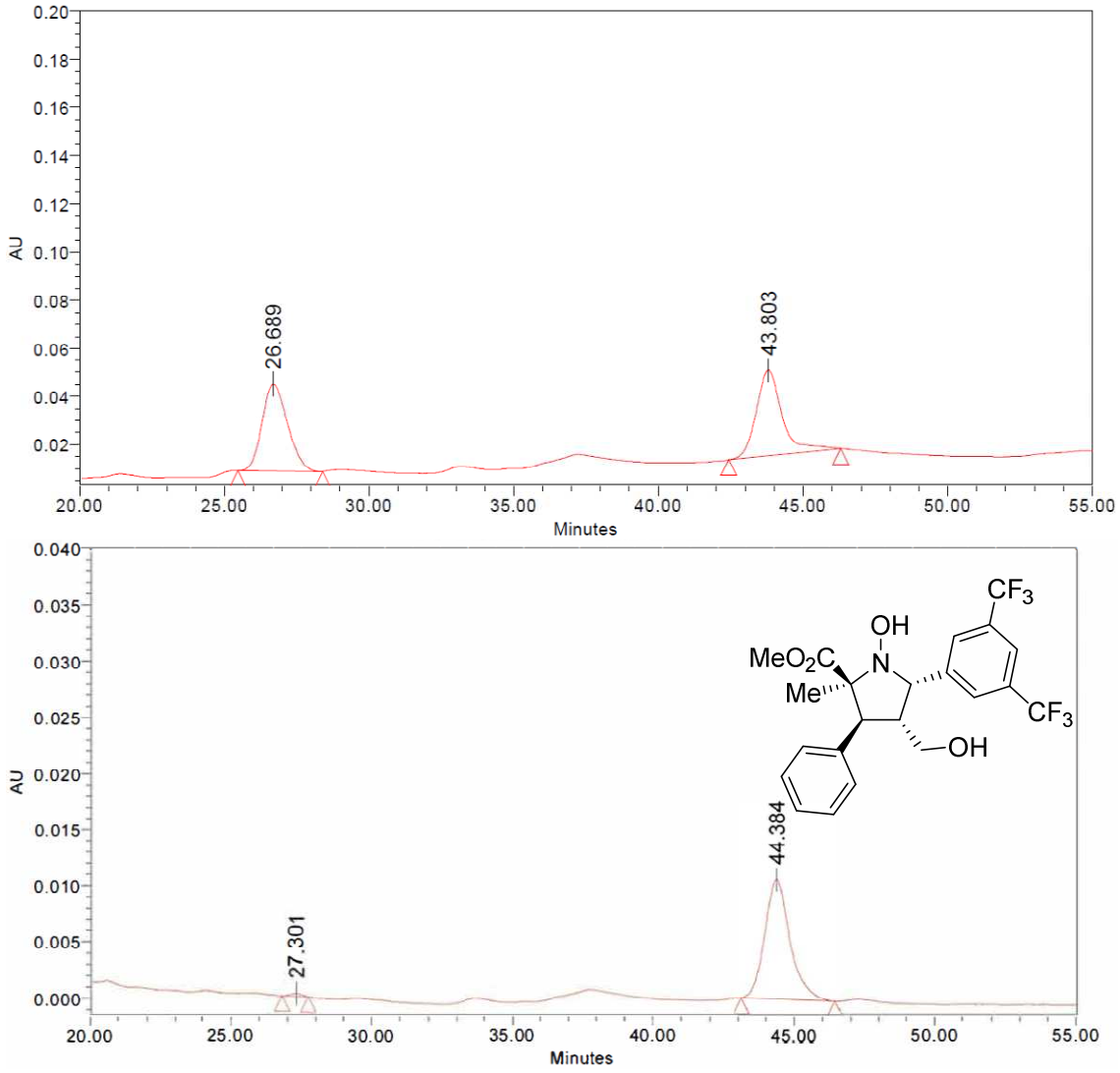


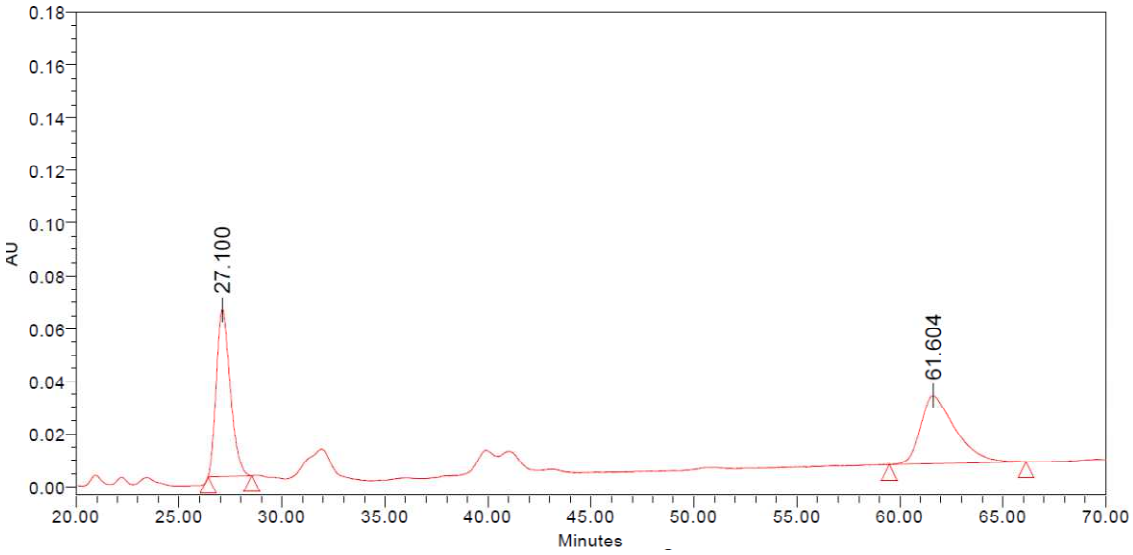
Figure SI-44. HPLC traces of compound **4n**.

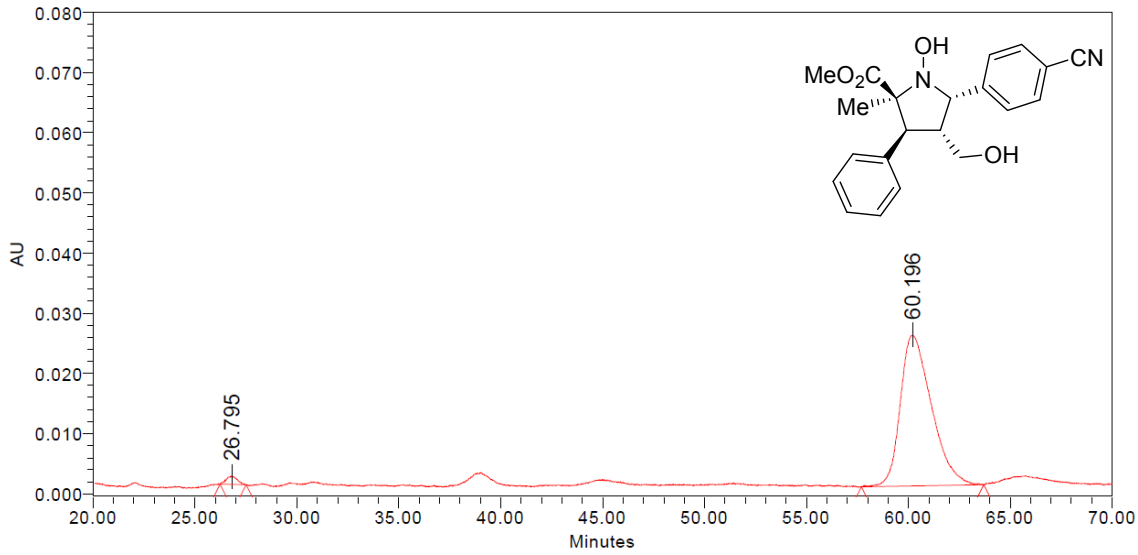


Peak Results

	RT	% Area
1	27.301	1.05
2	44.384	98.95

Figure SI-45. HPLC traces of compound **4o**.

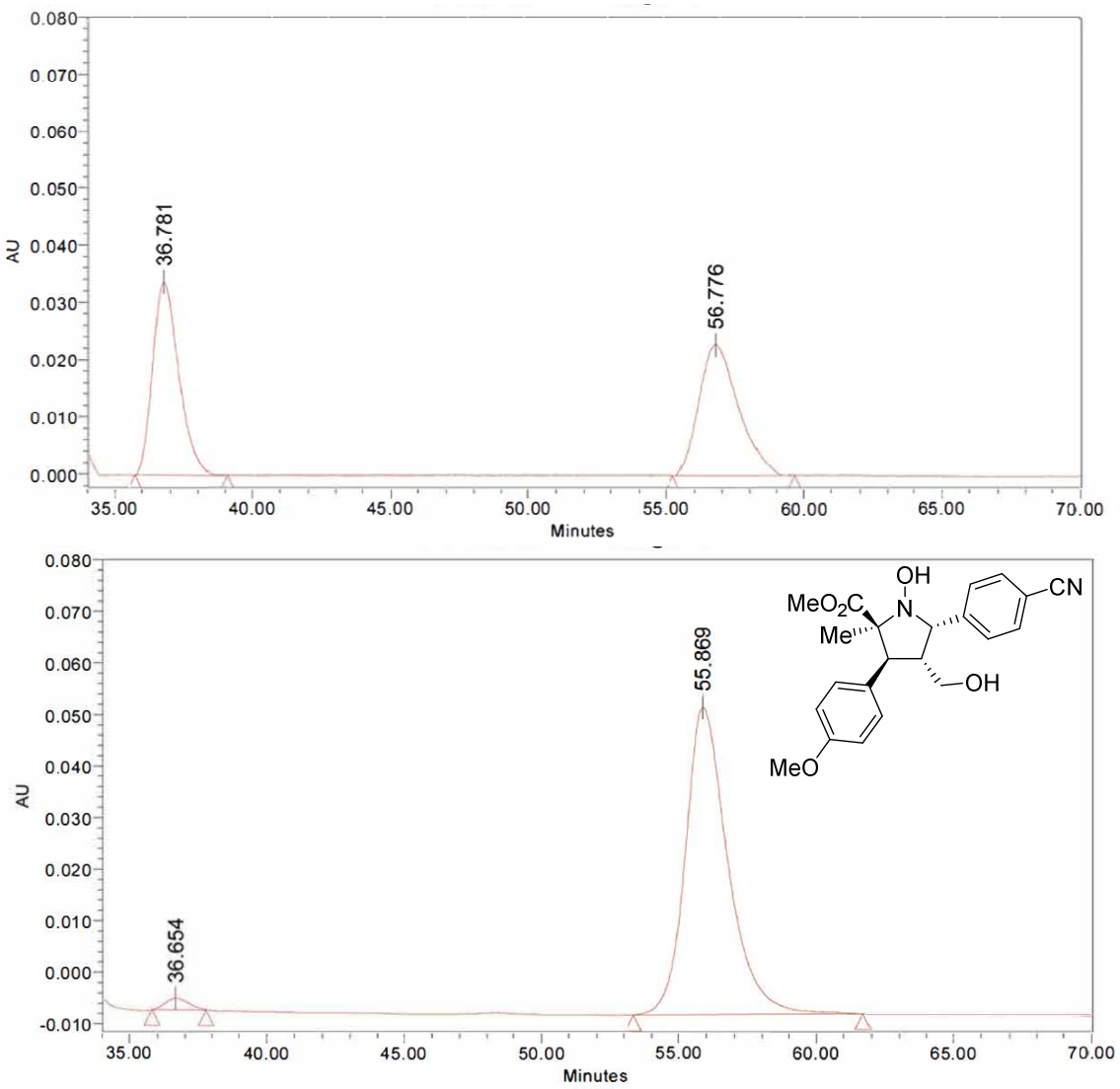




Peak Results

	RT	% Area
1	26.795	1.95
2	60.196	98.05

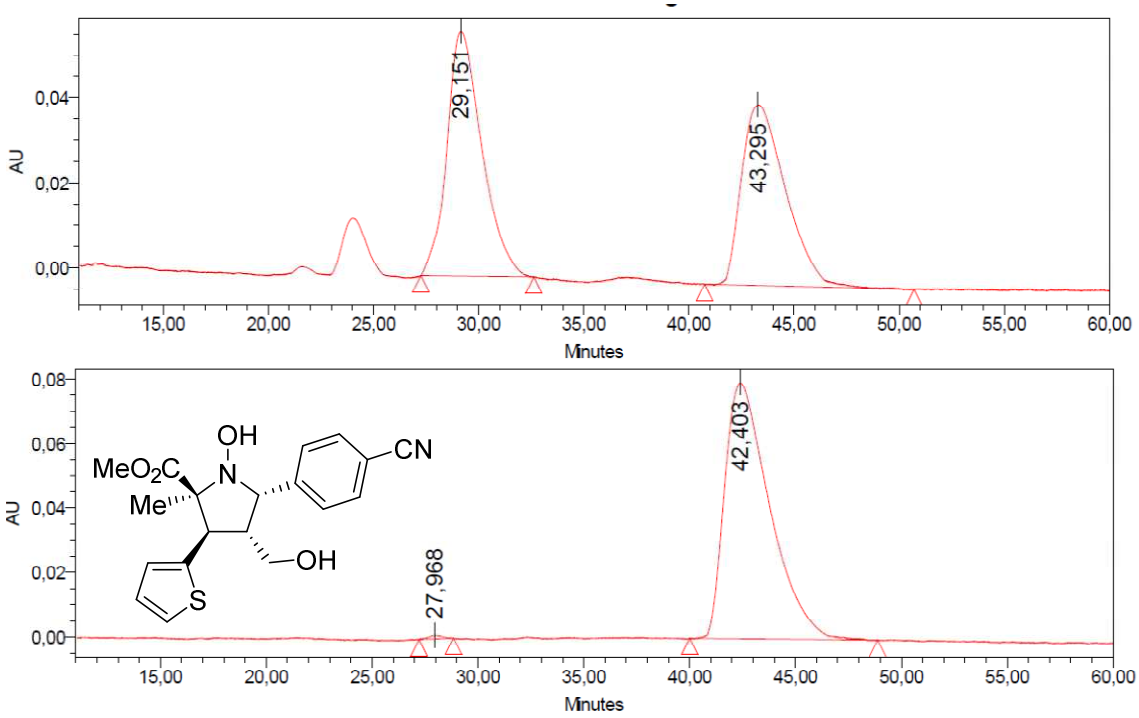
Figure SI-46. HPLC traces of compound **4p**.



Peak Results

	RT	% Area
1	36.654	2.00
2	55.869	98.00

Figure SI-47. HPLC traces of compound **4q**.



Peak Results

	Name	RT	Area	Height	% Area
1		27,968	49873	1096	0,43
2		42,403	11679666	79319	99,57

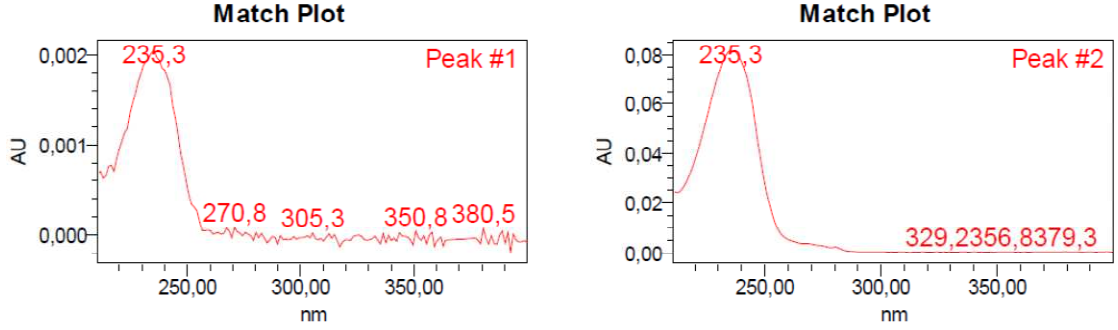
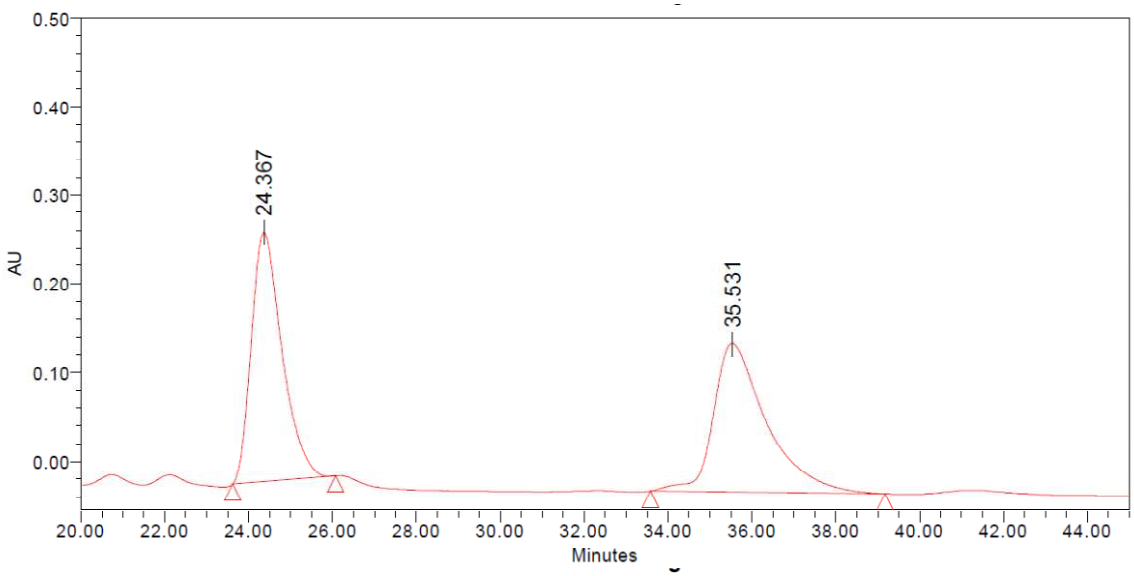
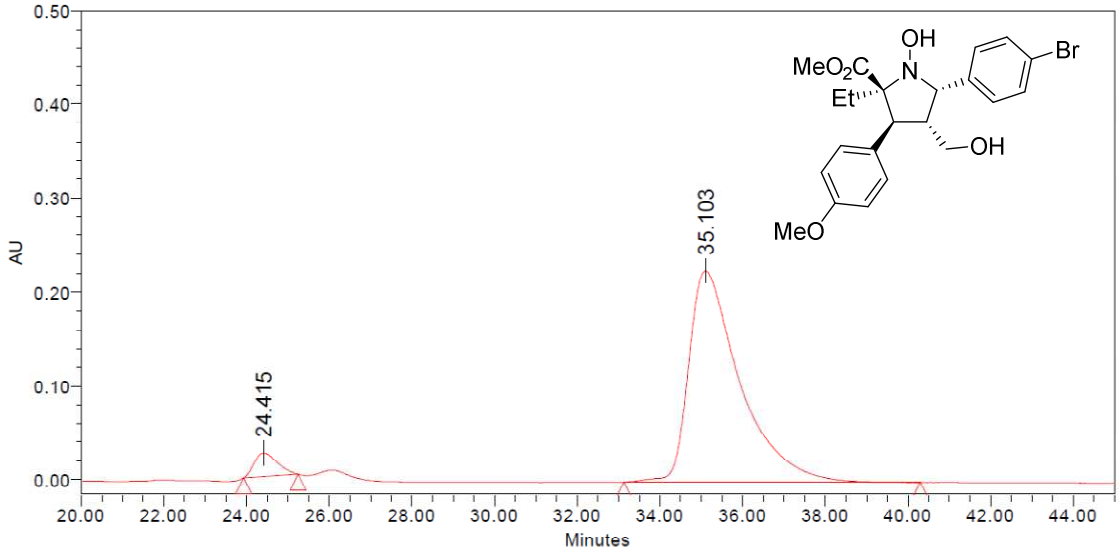


Figure SI-48. HPLC traces of compound **4r**.

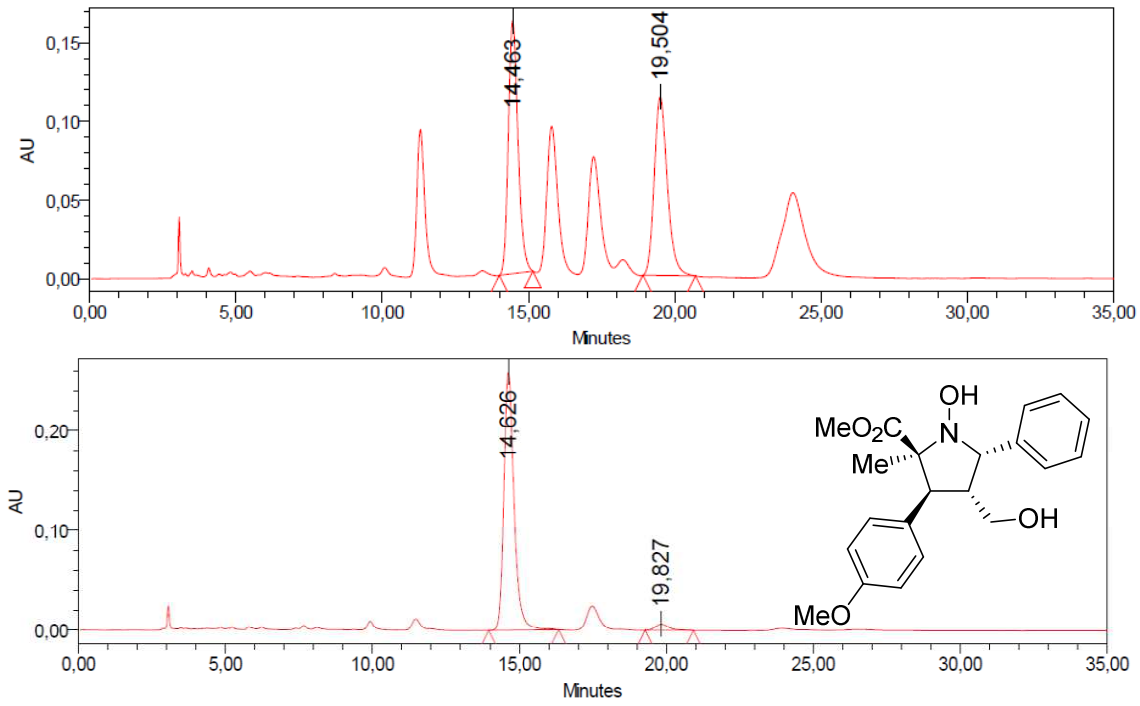




Peak Results

	RT	% Area
1	24.415	4.76
2	35.103	95.24

Figure SI-49. HPLC traces of compound **4s**.



Peak Results

	Name	RT	Area	Height	% Area
1		14,626	6230903	259136	96,95
2		19,827	196012	6077	3,05

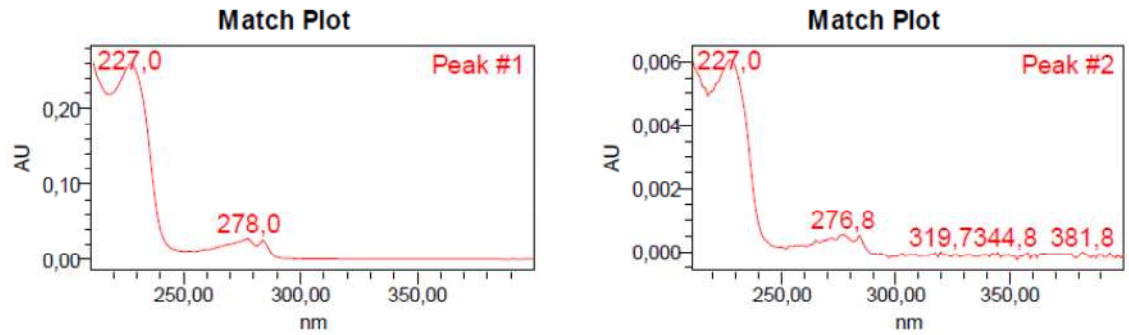
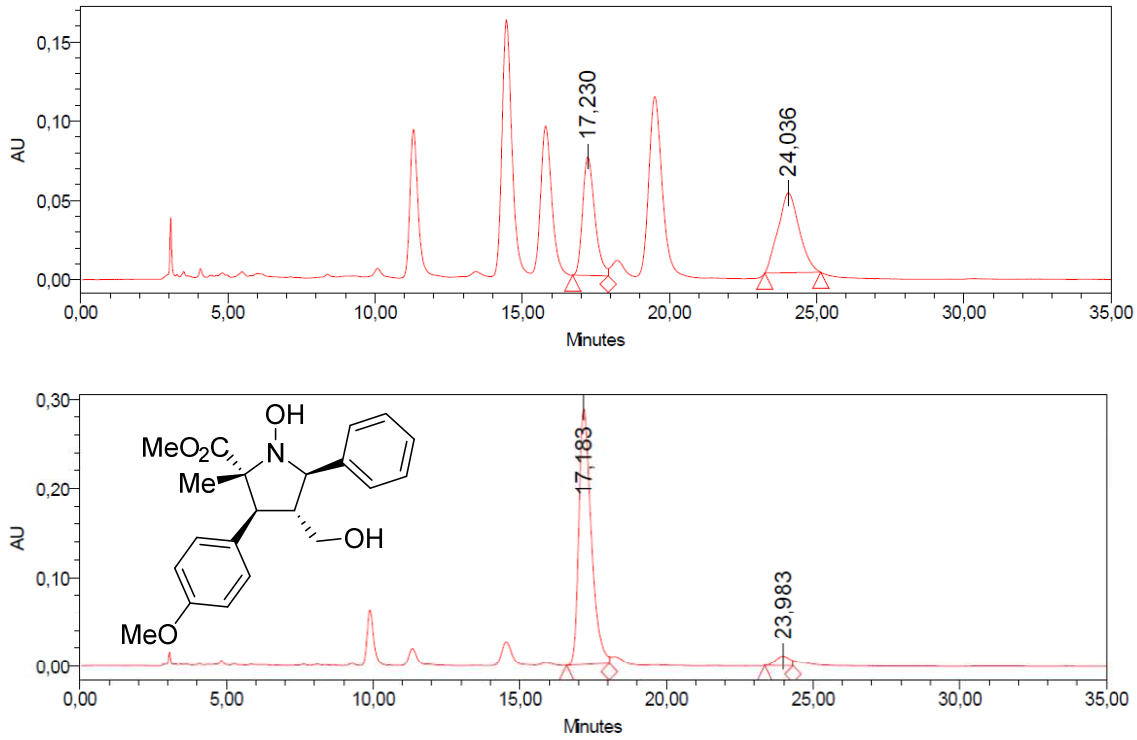


Figure SI-50. HPLC traces of compound **4t**.



Peak Results

	Name	RT	Area	Height	% Area
1		17,183	8452203	288611	96,03
2		23,983	349712	10440	3,97

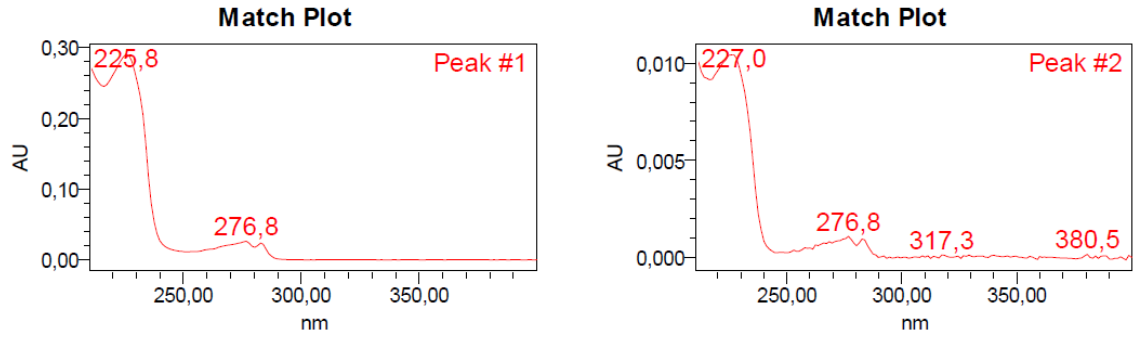
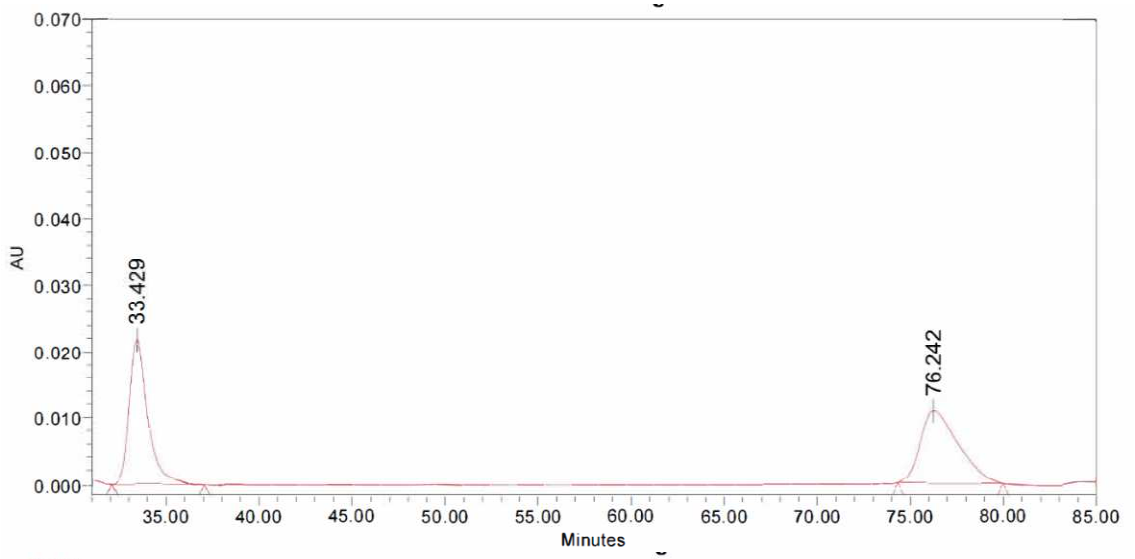
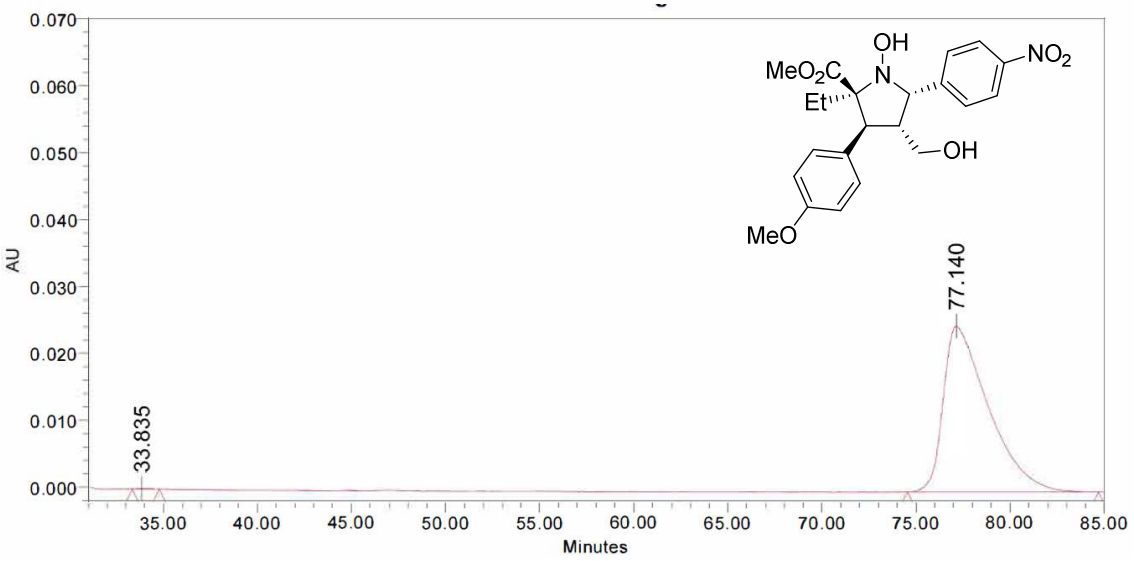


Figure SI-51. HPLC traces of compound **4t'**.

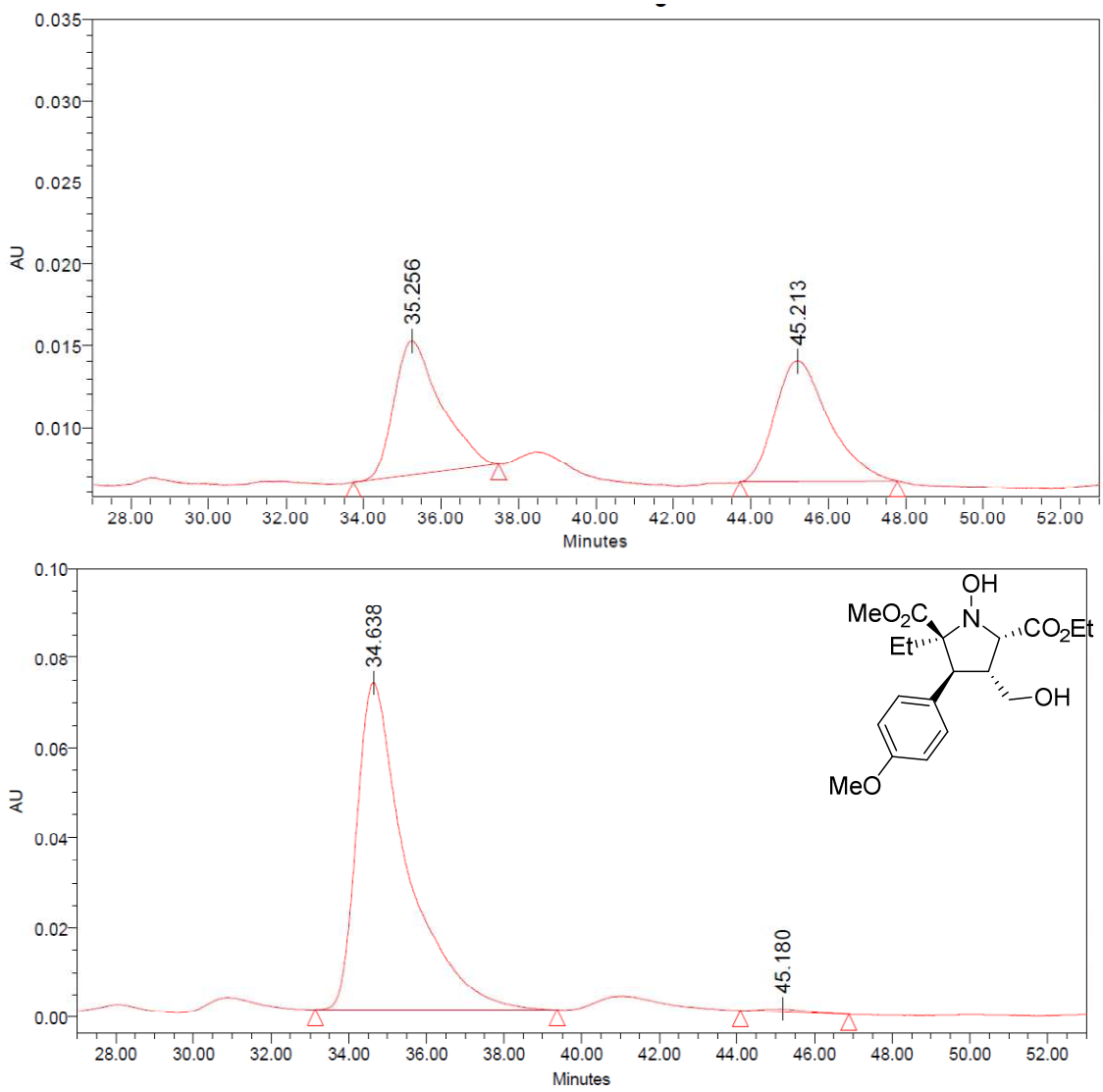




Peak Results

	RT	% Area
1	33.835	0.12
2	77.140	99.88

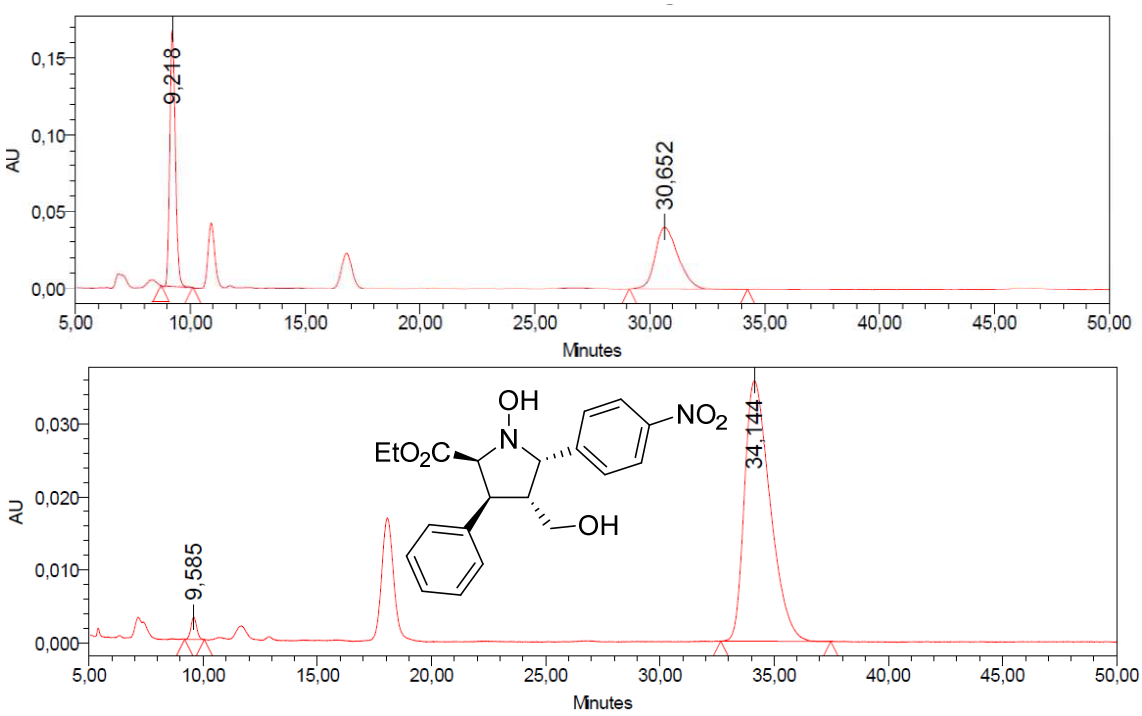
Figure SI-52. HPLC traces of compound **4u**.



Peak Results

	RT	% Area
1	34.638	99.23
2	45.180	0.77

Figure SI-53. HPLC traces of compound **4v**.



Peak Results

	Name	RT	Area	Height	% Area
1		9,585	54459	3068	1,92
2		34,144	2788697	35708	98,08

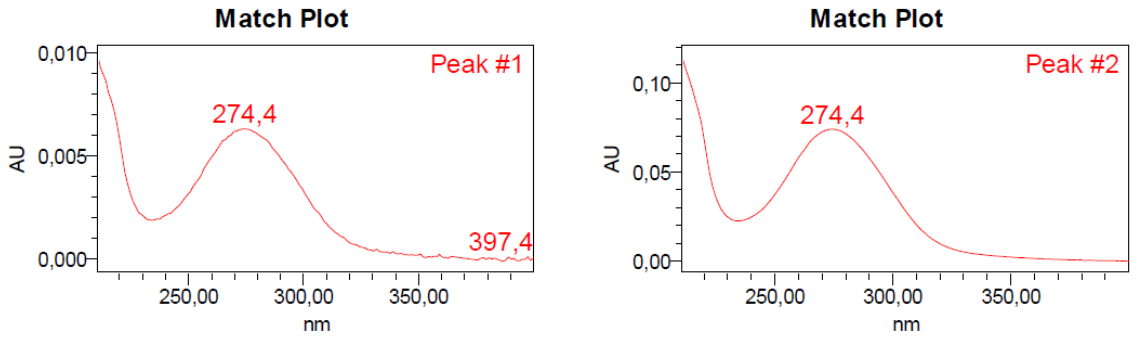
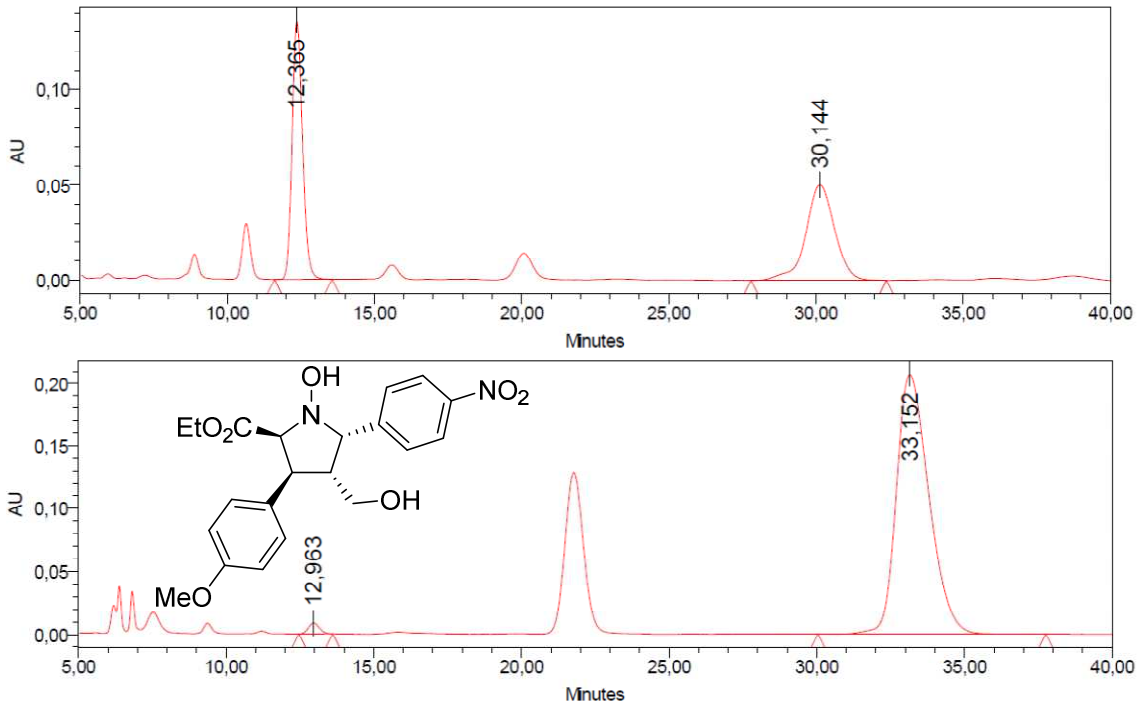


Figure SI-54. HPLC traces of compound **5a**.



Peak Results

	Name	RT	Area	Height	% Area
1		12,963	222179	8549	1,39
2		33,152	15782734	207125	98,61

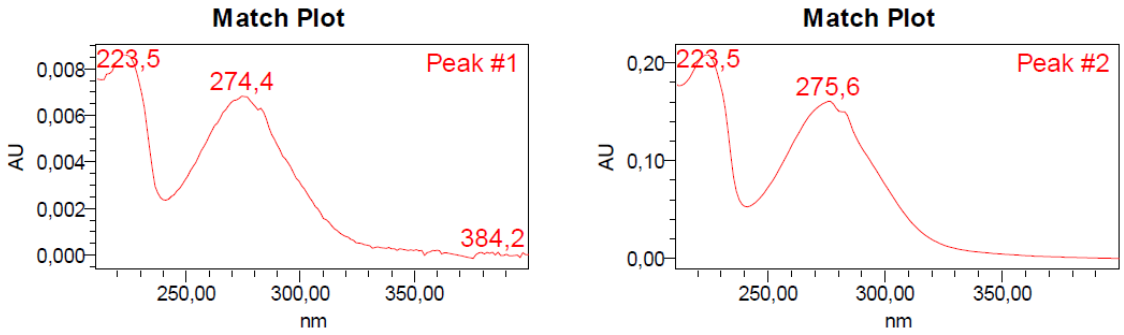
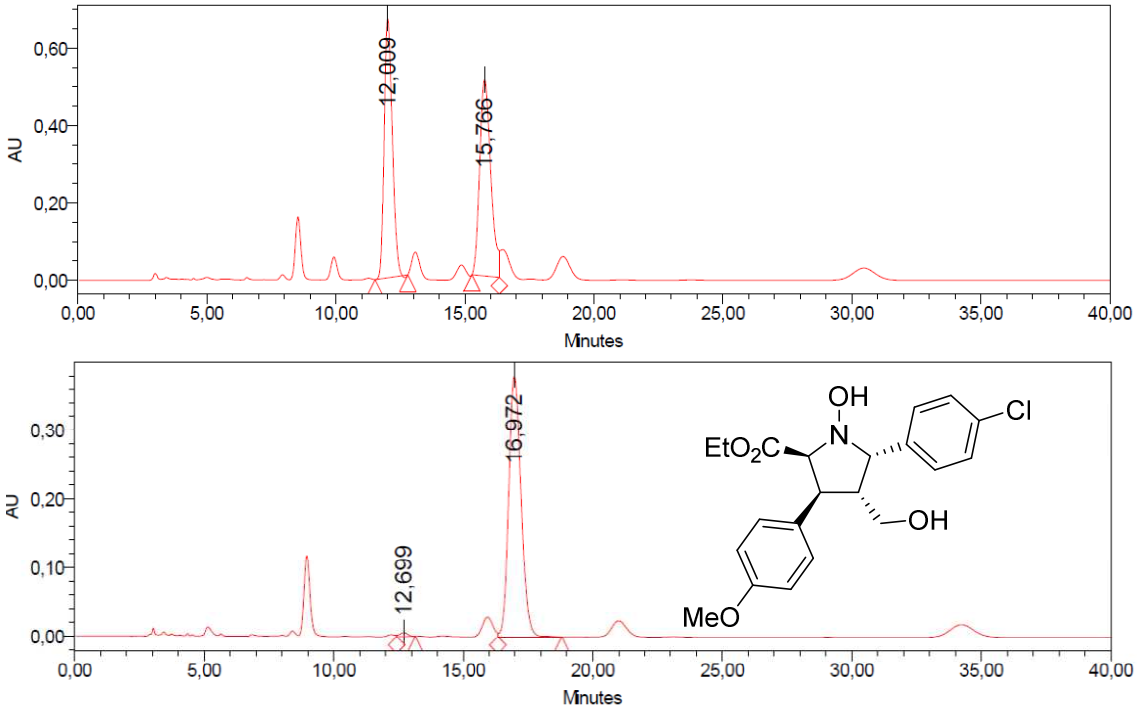


Figure SI-55. HPLC traces of compound **5b**.



Peak Results

	Name	RT	Area	Height	% Area
1		12,699	125976	5700	1,00
2		16,972	12515573	381339	99,00

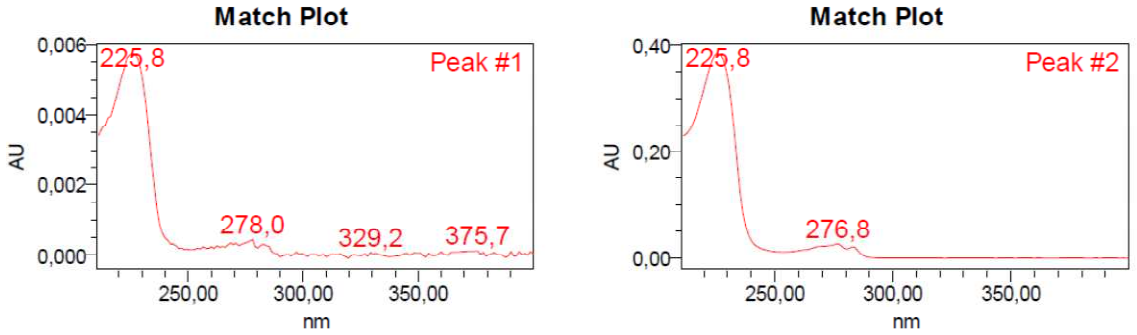


Figure SI-56. HPLC traces of compound **5c**.

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Advanced Synthesis & Catalysis

A Case Study of Thiourea-Assisted Iminium Formation by Hydroxyl Anion Binding: Kinetic, Spectroscopic and Computational Evidences

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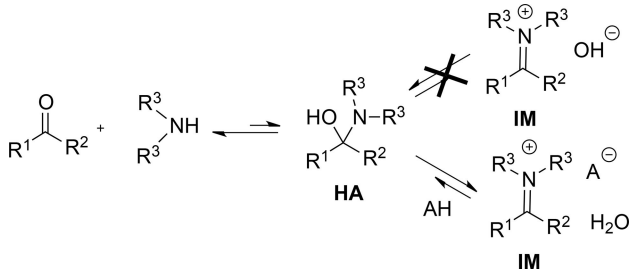
Abstract: The experimental and computational study of the mechanism of the iminium-organocatalyzed formation of *N*-hydroxypyrrolidines from nitrones, revealed up to three activation levels of the Schreiner's thiourea used as co-catalyst, i.e: (i) formation of the iminium ion through hydroxyl anion recognition forming a stable ion pair; (ii) enolization of the nitrone through a H-bond network and (iii) activation of the nitrone moiety towards the final ring closure. The computational model supports the mechanism and the catalytic cycle. This mechanistic rationale is supported by the lack of reactivity of preformed iminium ion with the nitrone in the absence of thiourea-hydroxyl complex and the observed reactivity when a complex thiourea-tetrabutylammonium hydroxide is added.

Keywords: Thioureas; Iminium catalysis; Nitrones; Hydroxide binding; Squaramides

Iminium catalysis has emerged over the past twenty years as one of the most powerful methods in organocatalysis.[1] When a carbonyl compound is placed in the presence of a secondary amine, an equilibrium with the hemiaminal **HA** is established. **HA** can lead to the corresponding iminium ion **IM** but this process is not spontaneous (Scheme 1).[2]

In particular cases, a reagent can assist – by means of H-bond interactions- the elimination of the hydroxyl group and subsequent iminium formation, as in the case of an oxa-Michael reaction recently reported from our laboratories.[3] Depending on substrates and reaction, the formation of the iminium ion might not be strictly required,[4] although it is a rare circumstance. In any case, the commonest situation is that a Brønsted acid (AH) helps to form **IM** by protonation of the hydroxyl group of the hemiaminal. In fact, iminium catalysis generally involves a secondary amine and an acid co-catalyst, the iminium ion forming an ion pair with the counteranion of the acid. By using strong acids such as trifluoroacetic acid or perchloric acid, iminium ions have been isolated and characterized.[5] In this respect, the non-nucleophilic character of the counterion is crucial.[6]

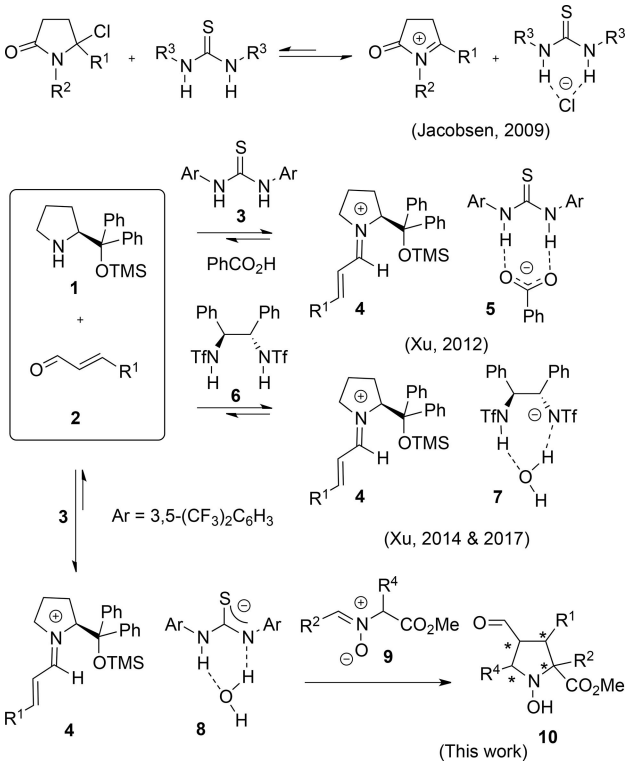


Scheme 1. Formation of iminium ions assisted by a Brønsted acid.

The reversibility of the process illustrated in Scheme 1 is often a drawback for many organo-

catalytic reactions requiring long reaction times due to the limited availability of the iminium ion.

Thioureas are known as reagents for anion recognition[7] and, in particular, Schreiner's thiourea[8] has been used in oxyanion recognition to promote tetrahydropyranylation of hydroxyl functionalities.[9] Organocatalytic activity of thioureas,[10] including their role in bifunctional catalysts,[11] is closely related with their role in molecular recognition processes.[7] Jacobsen and co-workers reported that recognition of chloride by an amidothiourea was crucial for generating the required iminium ion in an asymmetric Pictet-Spengler-type reaction (Scheme 2).[12] In general, thioureas act as co-catalysts either facilitating the action of the chiral catalyst or activating one of the reagents,[13] typically electrophiles such as carbonyl compounds, imines and nitroalkenes, among others, against nucleophiles.[14] The use of Schreiner's thiourea **3**, capable of sequestering the counteranion (typically a benzoate), has been reported by Xu and co-workers in 2012 (Scheme 2).[15] Two years later,[16] the same authors reported that bis(trifluoromethane) sulfonamide **6** led to the formation of a stable ion pair **4·7** in the course of the vinylogous Michael addition. In the same work, the use of thiourea **3**, presumably leading to **4·8** was discarded because it provided low regioselectivity. More recently,[17] ion pair **4·7** was used in a similar reaction and **3** was again discarded because it led to low yields and ee's. Both **3** and **6** were discarded as co-catalysts in a recently published vinylogous Michael/Stetter relay sequence.[18]



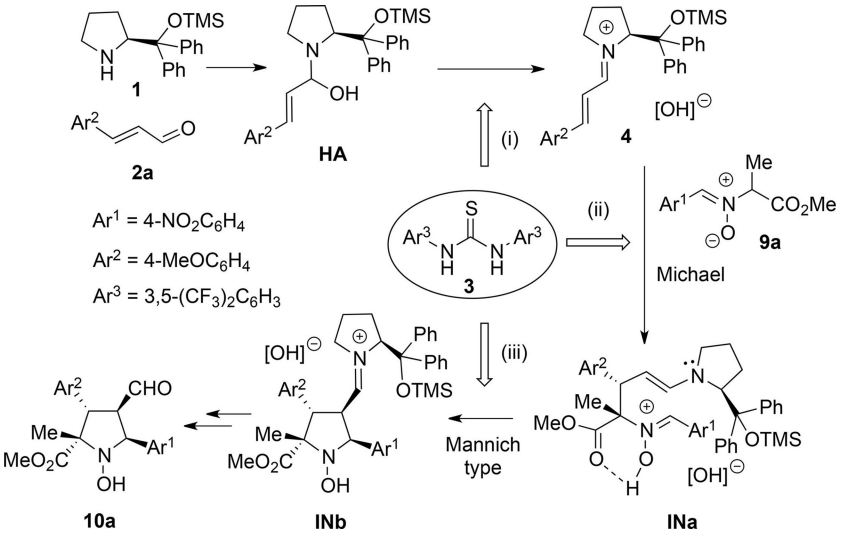
Scheme 2. Recognition of anions by H-bond donors.

In this work, we report experimental and computational evidences confirming hydroxyl anion recognition by thiourea **3** that promotes the formation of iminium salt **4** from amine **1** and aldehyde **2** through ion pair **4·8**. We chose as a case study our recently reported reaction of **2** with nitrones **9**, catalyzed by **1** leading to *N*-hydroxypyrrolidines **10** (Scheme 2).[22] Schreiner's thiourea **3** was used for the study; further studies were also made with other thioureas and squaramides. Actually, the basicity of hydroxide (pK_a of water ca. 15) is so high so that deprotonation of Schreiner's thiourea (pK_a ca. 8.5)[19] will occur quantitatively. The formation of counterion **8** agrees with previous investigations reporting anion-induced deprotonation of (thio)ureas,[20] and with the only reported measured recognition of hydroxyl anion by a thiourea.[21] Once formed the iminium ion, the thiourea·OH complex **8** led to a reactive anion-binding-stabilized ion pair with concomitant loss of water that reacts with **9** to form **10** in good yields and enantioselectivities.

The crucial role of the **4·8** ion pair in the reaction and the full mechanism, including the catalytic cycle, have also been studied experimental- and computationally. The effect of hydrogen bonds, and the factors that influenced the stereochemistry were explored to get useful information on organocatalytic reactions of nitrone ylides and the potential role of thiourea in iminium catalysis.

Both in our preliminary communication[22] and a previous similar study with isatin-derived nitrones,[23] triethylamine was used to deprotonate the nitrone **9** and generate the nitrone ylide assuming a mechanism involving the anion derived from **9**. Under this hypothesis the role of thiourea **3** was limited to activate the carbonyl group in the first step and/or the nitrone moiety in the second one.[24] However, a more in-depth analysis of the reaction conditions showed that the reaction with nitrones **9** does not require the presence of any base. On the other hand, the presence of thiourea **3** in catalytic amounts was essential for the progress of the reaction, which does not work in the absence of **3**. The results in the absence of triethylamine were similar in yield and identical in dr and ee to those obtained in the presence of triethylamine (see SI).[22]

To investigate in detail the mechanism of the reaction we carried out some kinetic analysis of the reaction (see SI). We used as representative substrates nitrone **9a** and aldehyde **2a** (Scheme 3) and determined that the reaction is first-order in both **9a** and **2a**. The kinetic measurements also confirmed the reaction to be first-order in **1** and **3**. The observed linear effects between ee and catalyst loading confirmed that the active catalyst is a monomeric species.



Scheme 3. Reaction between **2a** and **9a** in the presence of **1** and possible steps in which thiourea **3** might be involved. (i) formation of the iminium ion; (ii) enolization of nitrone and (iii) activation of nitrone in Mannich step. *Reaction conditions*: **2a** (1.0 eq, 015 M), **9a** (1.0 eq, 0.15 M), **1** (20 mol%), **3** (20 mol%), $CHCl_3$, rt, 4 days.

The first-order dependence on both aldehyde and nitrone observed experimentally indicates that both reactants are not associated in the resting state, suggesting a typical mechanism via formation of an iminium ion. Once the iminium ion is formed, the reaction can take place in a concerted way or in two steps through a tandem Michael-Mannich reaction as we previously reported for electron-poor alkenes.[25] In principle, thiourea activation can occur at different non-exclusive levels, i.e.: (i) by promoting the formation of the iminium ion; (ii) by facilitating enolization of the nitrone required for both mechanisms, considering that the reaction does not need the presence of a base, and (iii) by activating the nitrone towards the electrophilic addition. The stepwise mechanism, involving an initial nucleophilic attack to the iminium ion followed by a second nucleophilic attack of the intermediate enamine to the nitrone moiety, should be much more sensitive to electronic effects at the substituents. To evaluate such effects, we measured the rates of the reaction for several substituted nitrones and aldehydes. Hammett plots revealed a clear dependence of the electronic effects of the substituents indicating that the most favorable situation corresponds to nitrones with electron-withdrawing groups and aldehydes with electron-donating groups (ee SI). These data provide compelling evidence in favor of a stepwise mechanism based on nucleophilic attacks to iminium intermediate and nitrone (Scheme 3).[26]

The whole process, in which the precise involvement(s) of thiourea should still be investigated, can be divided in three parts, i.e: 1) formation of the iminium ion from the precursor hemiaminal **HA**, 2) reaction between iminium ion and nitrone and 3) formation of the final product.

Firstly, we studied the formation of the iminium ion by ^{1}H NMR. Our results (see SI) fully confirmed the previous observations reported by Xu and co-workers.[16] Moreover, when the reaction mixture was submitted to ESI-MS strong signals at m/z 470.2584 and m/z 499.0214 were observed corresponding to the iminium cation (m/z calcd 470.2510) and the thiourea anion (m/z calcd 499.0144) resulting from **8** after loss of water. The binding properties of thiourea **3** towards hydroxide anion have been evaluated and a value of log $K = 5.5 \pm 0.20$ was obtained (see SI) in agreement with a previous report for other thioureas.[21]

The binding of thiourea **3** to hydroxide ion was corroborated by monitoring the changes in the ^{1}H NMR spectrum of **3** upon addition of lyophilized Bu_4NOH. Complete disappearance of both NH signals was observed after the addition of 1.0 eq of Bu_4NOH (see SI). As expected, addition of nitrone **9a** to the reaction mixture in which the ion pair **4·8** had been identified resulted in the rapid formation of the *N*-hydroxypyrrolidine **10a**. From these results, it became evident that *thiourea **3** is capable of promoting the formation of the iminium ion without the help of any acid co-catalyst.*

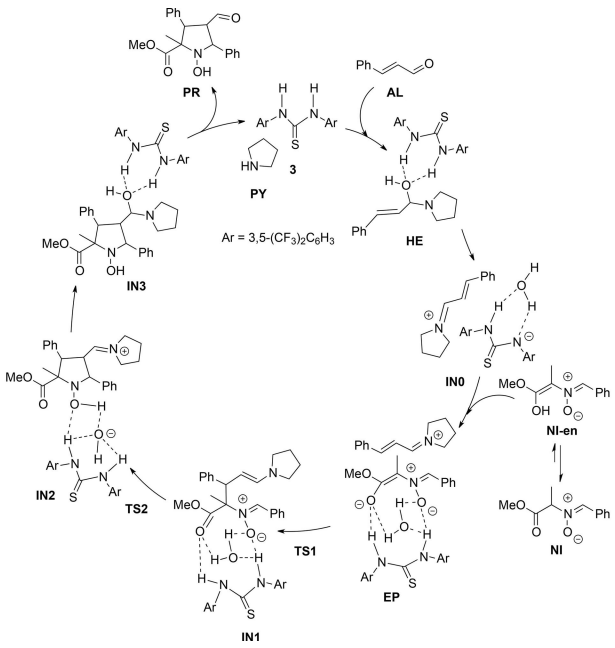
Then we studied the second part of the catalytic cycle, i.e. the reaction of iminium ion with the nitrone. Remarkably, when nitrone **9a** was added to a freshly prepared[5] solution of iminium perchlorate **4·ClO$_4$** no reaction was observed after 2 days.[27] The situation was the same when up to 1.0 equiv. of thiourea was added. In fact, no reaction was observed between **2a** and **9a** in the only presence of **1** and an acidic co-

catalyst (benzoic, 2- and 4-nitrobenzoic, acetic, oxalic, trifluoroacetic, methanesulfonic and hydrochloric acids were checked) or by moving to high polar solvents like nitromethane. This result suggests that not only a high iminium concentration is required but additional activation of the nitrone should be exerted (see below).

The addition of a base (Et_3N) resulted in a very slow reaction (20% of conversion after 4 days). On the contrary, when a solution of a 1:1 mixture of thiourea **3** and lyophilized Bu_4NOH was added, the reaction proceeded as in the conditions reported in SI. Similarly, when Bu_4NOH was added to the non-reacting mixture **4·ClO$_4$/9a/3** a complete reaction was observed suggesting that the combination thiourea-OH-nitrone is necessary for the progress of the reaction. These results suggest a second point of activation of the reaction, indicating that *the formation of ion pair **4·8** is required for promoting enolization of nitrone by the action of counteranion **8***.

Finally, we studied the formation of the final product. The process is more efficient with the ion pair **4·8** than using a base for generating the enolate of **9a**,[28] but an enolate should be more nucleophilic and should favor the second step of the reaction (Mannich-type). However, Mannich-type reactions with nitrones require activation of the nitrone;[29] the higher efficiency of ion pair **4·8** suggests a third point of activation of the reaction, i.e. *the presence of a H-bonding network responsible for activating the nitrone towards the intramolecular Mannich-type reaction.* We also monitored the reaction with ESI-MS and after 1 day of reaction signals at m/z 470.2672 and m/z 722.3203 were observed corresponding to iminium cations **4** (m/z calcd 470.2510) and that integrating **INb** (m/z calcd 722.3256), definitively confirming the process illustrated in Scheme 3.

With the aim of giving support to our hypotheses and to propose precise structures of the species involved in the catalytic cycle considering thiourea participation, we carried out a computational study of the whole catalytic process at B3LYP-D3(BJ)/def2SVP level of theory considering chloroform as a solvent (CPCM model, see SI for details). We used for our model pyrrolidine as the catalyst, and phenyl rings at both nitrone and aldehyde.[30]. The proposed catalytic cycle according to calculations is given in Scheme 4. The cycle begins with the formation of complex **HE** from the catalyst **PY,** aldehyde **AL** and thiourea **3**. The formation of iminium ion pair **IN0** is favored by 10.8 kcal/mol in agreement with the experimental observations. The higher stability of **IN0** is also due to the presence of favorable dispersion interactions between the phenyl ring of the iminium ion and one of the aromatic rings of thiourea **3** (see SI).



Scheme 4. Catalytic cycle for the reaction between **AL** and **NI** in the presence of **PY** and **3**.

Incorporation of nitrone **NI** results in the formation of encounter pair **EP** in which the counteranion of the iminium salt stabilizes the enol tautomer of the nitrone. After the first transition state, **TS1**, located at 3.1 kcal/mol and identified as the rate-limiting step, the enamine intermediate **IN1** is formed. This intermediate is ready for the next step through a second transition state, **TS2**, located at 1.8 kcal/mol. In this transition structure thiourea facilitates a H-bond network responsible of activating the nitrone moiety towards the intramolecular nucleophilic attack. This step yields **IN2** formed by a new iminium ion (detected by ESI-MS) having complex **8** as counteranion which interacts with the hydroxyamino functionality through H-bonds. Intermediate **IN2** evolves to hemiaminal **IN3**, a transformation thermodynamically favored by 4.4 kcal/mol (for the preferred diastereomer). Releasing of product **PR** regenerates catalyst **PY** and co-catalyst **3**. The driving force of the catalytic cycle is determined by the regeneration of **HE** from **IN3** with concomitant release of the final product. This final catalyst-turnover step involves a favored energy of $\Delta G = -22.8$ kcal/mol (for a complete energy profile see SI). Two approaches of the iminium ion to the activated enolized nitrone are possible in **EP**, leading to two diastereomers. The corresponding transition structures **TS1a** and **TS1b** differ in 2.4 kcal/mol in favor of that leading to (2*S**,3*S**,4*R**,5*S**)-isomer, in excellent agreement with the experiments. The almost complete enantioselectivity is due to the essentially exclusive attack by the less hindered face

of the iminium formed from catalyst **1** as reported elsewhere.[30]

The calculated catalytic cycle is in good agreement with the experimental observations, including ESI-MS monitoring that allowed identifying iminium ions from **IN0** and **IN2**. Calculations also support the three keypoints of the reaction in which thiourea acts on the reaction, i.e. promoting formation of iminium ion, nitrone enol and activating nitrone functionality in the second step.

In addition to **3** we also studied the formation of iminium **4** mediated by thioureas **11** and **12**, and squaramides **13** and **14**. The observed rates for **3** and **12–14** (a very slow reaction was observed with **11** ($pK_a = 13.4$)[19] are illustrated in Figure 1.

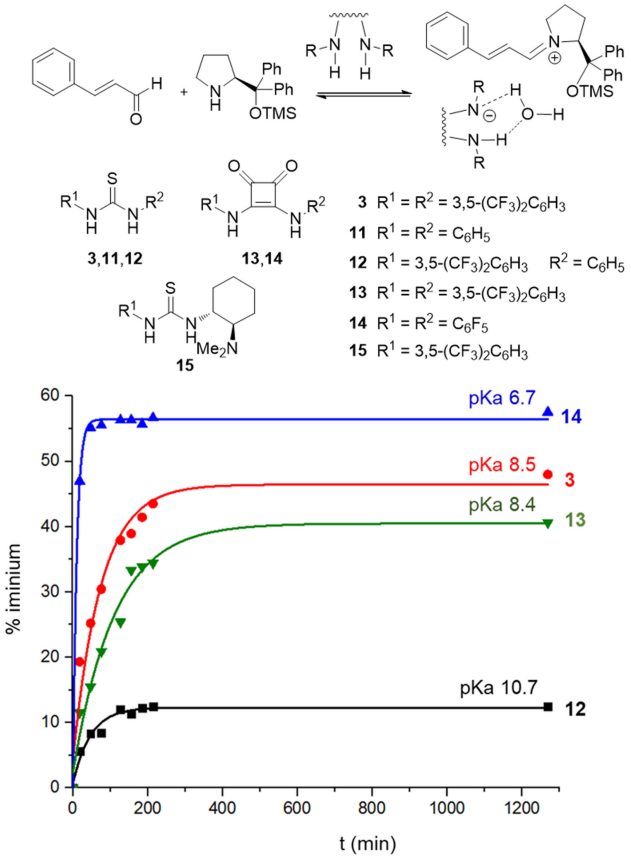


Figure 1. Reaction rates for the formation of iminium ion **4** from catalyst **1** and cinnamaldehyde **2a** in the presence of thioureas **3**, **11** and **12,** and squaramides **13** and **14**. Reaction rate with **15** is not shown because it was too slow.

Once the equilibrium is reached, the most acidic squaramide **14** showed the best result with ca. 56% of iminium formed, corresponding to $k_{eq} = 19.3 \pm 0.18\ dm^3 \cdot mol^{-1}$.[31] The equilibrium constants for thiourea **3** and squaramide **13** were $k_{eq} = 10.3 \pm 0.15\ dm^3 \cdot mol^{-1}$ (46% of iminium) and $k_{eq} = 7.7 \pm 0.21\ dm^3 \cdot mol^{-1}$ (41% of iminium formed), respectively. For thiourea **12** with an only electron-withdrawing group the value drops to $k_{eq} = 1.1 \pm 0.19\ dm^3 \cdot mol^{-1}$. Indeed, the iminium formation showed to be dependent on the pK_a (we determined $pK_a = 6.7$ for **14**, see SI), the higher acidity, the higher rate of iminium formation. The amount of iminium at the equilibrium was found to be linearly dependent on the relative stability between the iminium and the precursor hemiaminal.[32]

The reaction between **2a** and **7a** catalyzed by **1** in the presence of squaramides **13** and **14** led to essentially identical results in yield and enantioselectivity without observable effects in the rate of the reaction. This result agrees with calculations, which showed **TS1** (and not the formation of the iminium ion) as the rate-limiting step. Accordingly, the observed rates of iminium ion formation for thiourea **3** and squaramides **13** and **14** are enough for feeding the catalytic cycle. When both enantiomers of Takemoto's thiourea[33] **15** were employed the reaction was considerably slower (24% of conversion after 6 days) than with thiourea **3** in agreement with the lower acidity of **15** ($pK_a = 13.8$).[34] The reaction between cinnamaldehyde and nitrone **9b** ($R^4 = H$ according to Scheme 2) using **1** as catalyst in the presence of (*R*,*R*)-**15** provided the corresponding cycloadduct with a diastereoselectivity of ca 1:1 and a 97% e.e., while the same reaction in the presence of (*S*,*S*)-**15** provided the same 1:1 mixture of diastereoisomers but with a slightly improved e.e. (>99%). This almost non-existed match/mismatch effect indicated that the aminocatalyst is the main element with respect to face selection in this cycloaddition reaction.

In summary, we have confirmed that thioureas promote the formation of iminium ions without the presence of a Brønsted acid. We have also expanded the utility of such recognition and demonstrated that squaramides can exert the same effect. The case study has confirmed that hydroxide anion recognition is the main driving force helped by dispersion interactions between aromatic rings of co-catalyst and iminium, which thermodynamically favors the formation of the ionic pair **IN0** (formed by iminium ion **4** and complex [**3**·OH]$^-$) from the precursor hemiaminal (**HE**) in equilibrium with the reagents. Because of the absence of those favourable dispersion interactions in the final iminium ion (**IN2**), the formation of hemiaminal (**IN3**) is thermodynamically favoured closing the catalytic cycle. The formed anion [**3**·OH]$^-$ has an additional effect facilitating enolization of the nitrone and promoting the attack to the iminium ion **4**; this step is the rate-limiting step (**TS1**).

Rates and enantioselectivities of the reaction between **2a** and **9a** using thiourea **3** as the only co-catalyst compare with other reactions in which no H-bond donors are present and only acidic co-catalysts

are used. In our case however, thiourea is additionally required for activating the nitrone and no reaction is observed in their absence, independently of the acidic co-catalyst employed. Consequently, it is possible to predict that the use of thioureas or squaramides might promote cascade reactions starting and ending with iminium ions, which should be formed and hydrolyzed, respectively. The formation of anion $[\mathbf{3}\cdot OH]^-$, which can be considered a weak base with capability of promoting H-bond networks, could also exert additional effects on the substrates. In this respect, it should of great interest to consider reagents requiring enolization or any kind of H-bond activation.

It is expected that these findings, in particular generation of iminium ions in a neutral or weakly basic medium, will allow evaluating the significance of iminium formation in other organocatalytic reactions. Moreover, the observation of the same behaviour with squaramides expands considerably the number of organocatalytic processes susceptible to be modulated.

Acknowledgements

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[26] The concerted pathway involve a typical normal demand dipolar cycloaddition in which the dipole acts as a nucleophile. Accordingly, electron-donating groups at the nitrone-carbon should favor the reaction, which is just the opposite to that observed in Hammett plots. However, the second step of the stepwise mechanism involves a nucleophilic attack to the nitrone, which is clearly favored by the presence of electron-withdrawing groups at the nitrone carbon.

[27] The same lack of reactivity was observed with the trifluoroacetate evidencing that it is not a matter of counteranion.

[28] Treatment of **7a** with Et_3N and with a solution of a 1:1 mixture of thiourea **3** and Bu_4NOH in the presence of deuterium oxide showed the same proton-deuterium

A Case Study of Thiourea-Assisted Iminium Formation by Hydroxyl Anion Binding: Kinetic, Spectroscopic and Computational Evidences

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Supporting Information

Synthesis of *N*-Hydroxypyrrolidines in the absence of a base

Table S1. Synthesis of *N*-hydroxypyrrolidines

entry	nitrone	Ar^1	aldehyde	Ar^2	product	Yield (%)[a]	d.r. [b]	ee (%)[c]
1	**7a**	4-$NO_2C_6H_4$	**2a**	4-$MeOC_6H_4$	**8a**	90	6:1	99
2[d]	**7a**	4-$NO_2C_6H_4$	**2a**	4-$MeOC_6H_4$	**8a**	10	-	-
3[e]	**7a**	4-$NO_2C_6H_4$	**2a**	4-$MeOC_6H_4$	**8a**	< 5	-	-
4	**7b**	3,5-di$CF_3C_6H_4$	**2a**	4-$MeOC_6H_4$	**8b**	87	9:1	98
5	**7c**	4-CNC_6H_4	**2a**	4-$MeOC_6H_4$	**8c**	84	9:1	96
6	**7d**	4-BrC_6H_4	**2a**	4-$MeOC_6H_4$	**8d**	55	1:1	90
7	**7e**	C_6H_5	**2a**	4-$MeOC_6H_4$	**8e**	46	1:1	92
8	**7a**	4-$NO_2C_6H_4$	**2b**	4-ClC_6H_4	**8f**	95	4:1	98
9	**7a**	4-$NO_2C_6H_4$	**2c**	4-$CF_3C_6H_4$	**8g**	88	4:1	99
10	**7a**	4-$NO_2C_6H_4$	**2d**	C_6H_5	**8h**	93	5:1	98

[a] Combined yield of the diastereomeric mixture after purification. [b] Determined by NMR spectroscopic analysis of the crude reaction mixture before the reduction step. [c] Determined by HPLC analysis on a chiral stationary phase. [d] In the absence of thiourea and in the presence of 1.0 eq of Et_3N. [e] In the absence of thiourea.

Kinetic Studies

The reaction was carried out in $CDCl_3$ at 25ºC using the pseudo-first-order kinetics method. When the reaction was carried out with a large excess of **2a**, plotting in ln([**7a**]/[**7a**]$_0$) versus time gave a straight line (Figure S1, A), which indicates the reaction is first-order in **7a**. By the same procedure, it was determined that the reaction was first-order in **2a** (Figure S1, B).

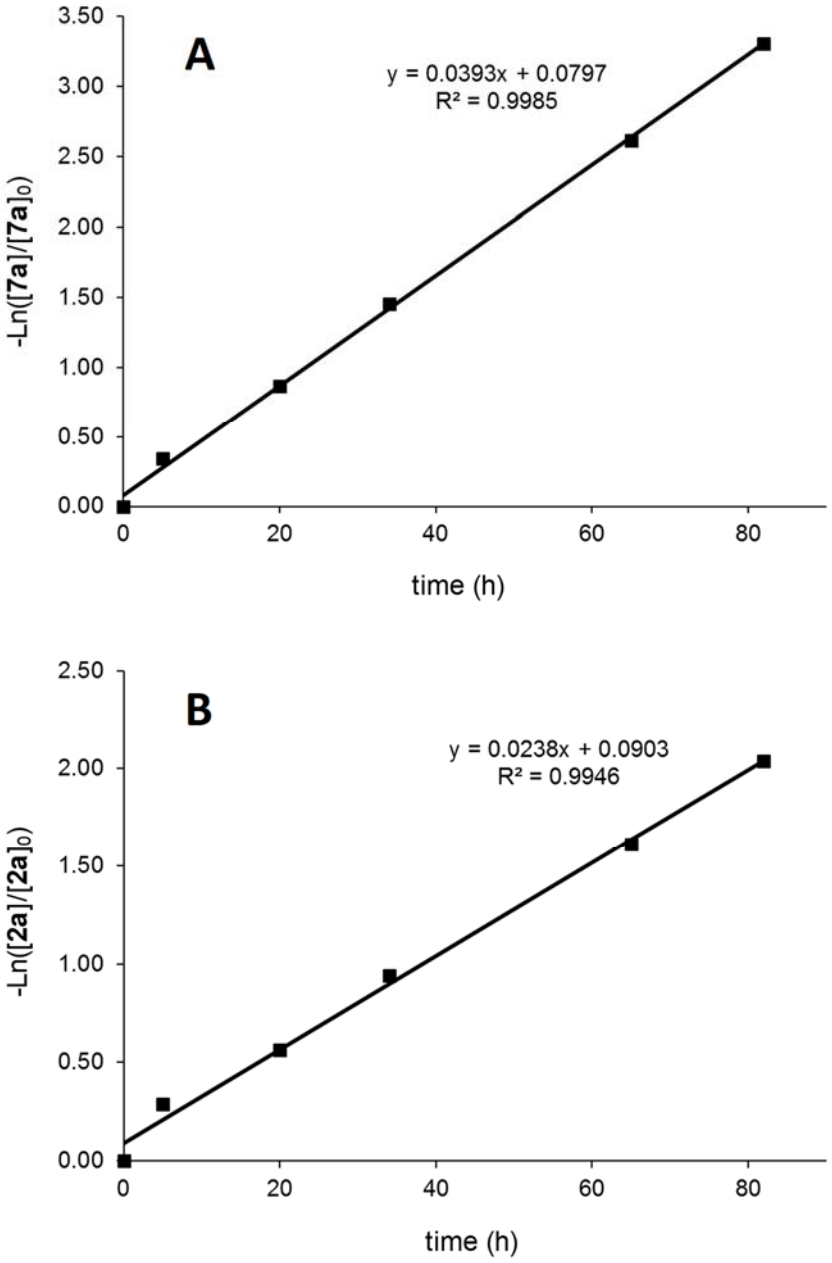

Figure S1. Kinetic studies on the reaction between **2a** and **7a** in the presence of **1** and **4**.

The order in catalyst **1** and thiourea **3** was also examined by plotting the kinetic rate constant (k_{obs}) against the loading of both **1** (Figure S2, A) and **3** (Figure S2, B), in separated experiments, which indicates that the reaction is also first-order in **1** and **3.**

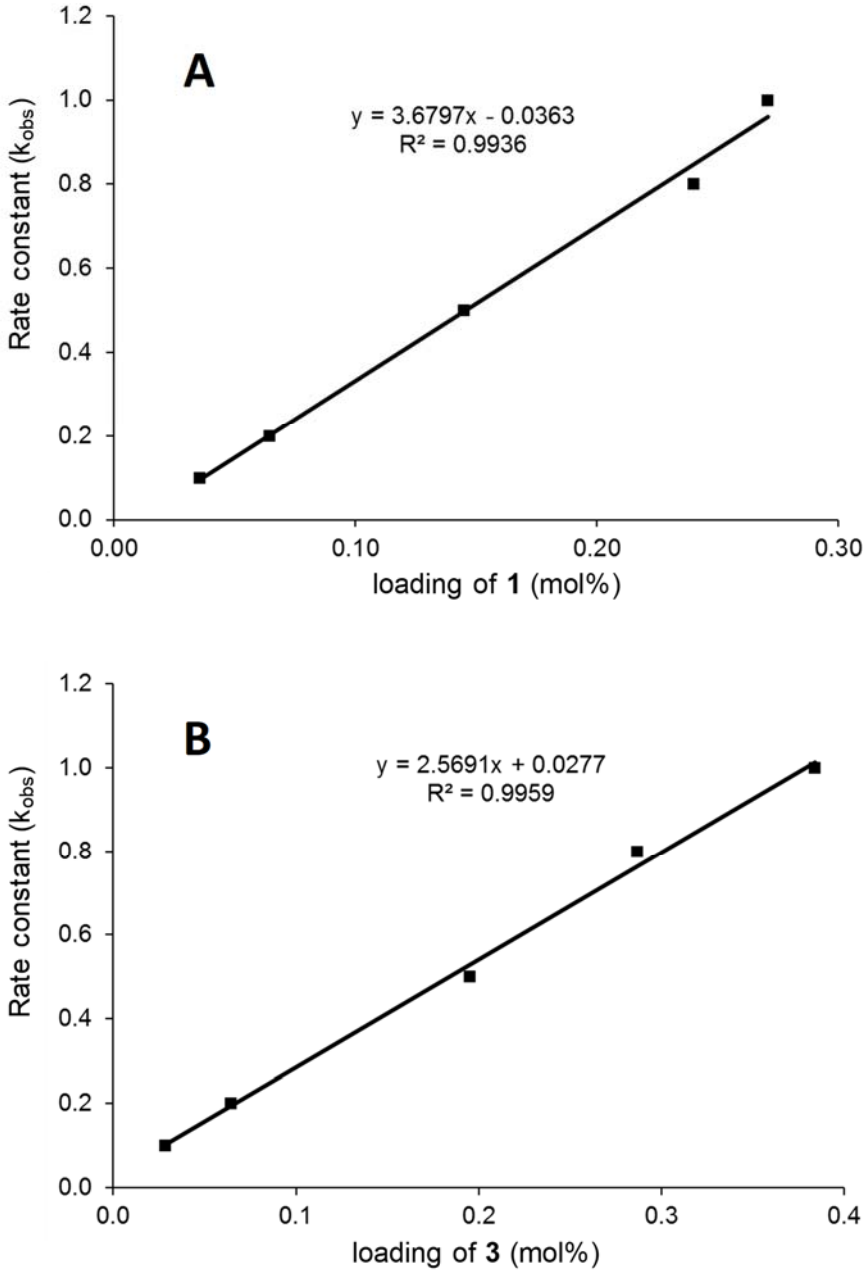

Figure S2. Linearity studies for catalyst **1** and co-catalyst **3** .

The relationship between the ee value of catalyst **1** and the ee value of the product **8a** is represented in Figure S3. The observed absence of non-linear effects suggested that the active catalyst is a monomeric species.[1]

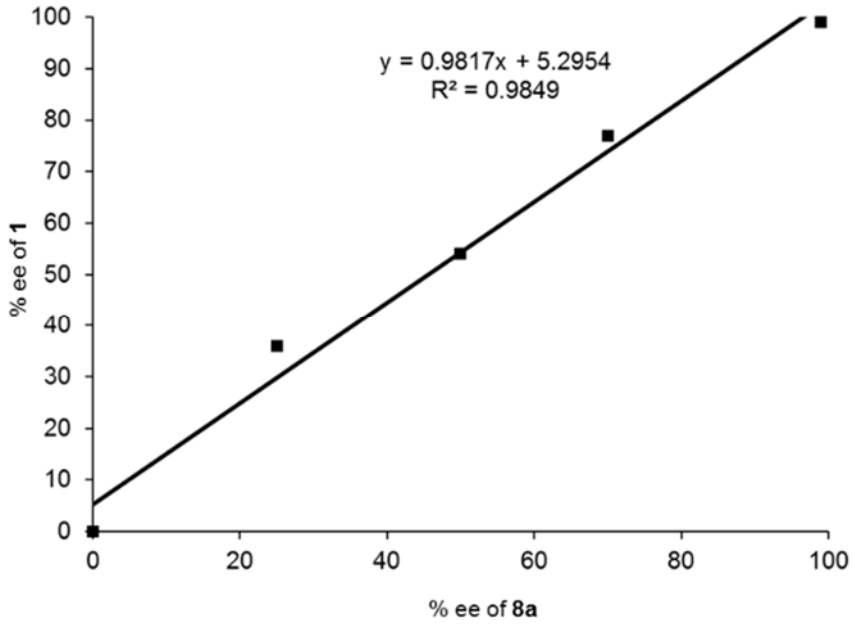

Figure S3. Kinetic studies on the reaction between **2a** and **7a** in the presence of **1** and **4**.

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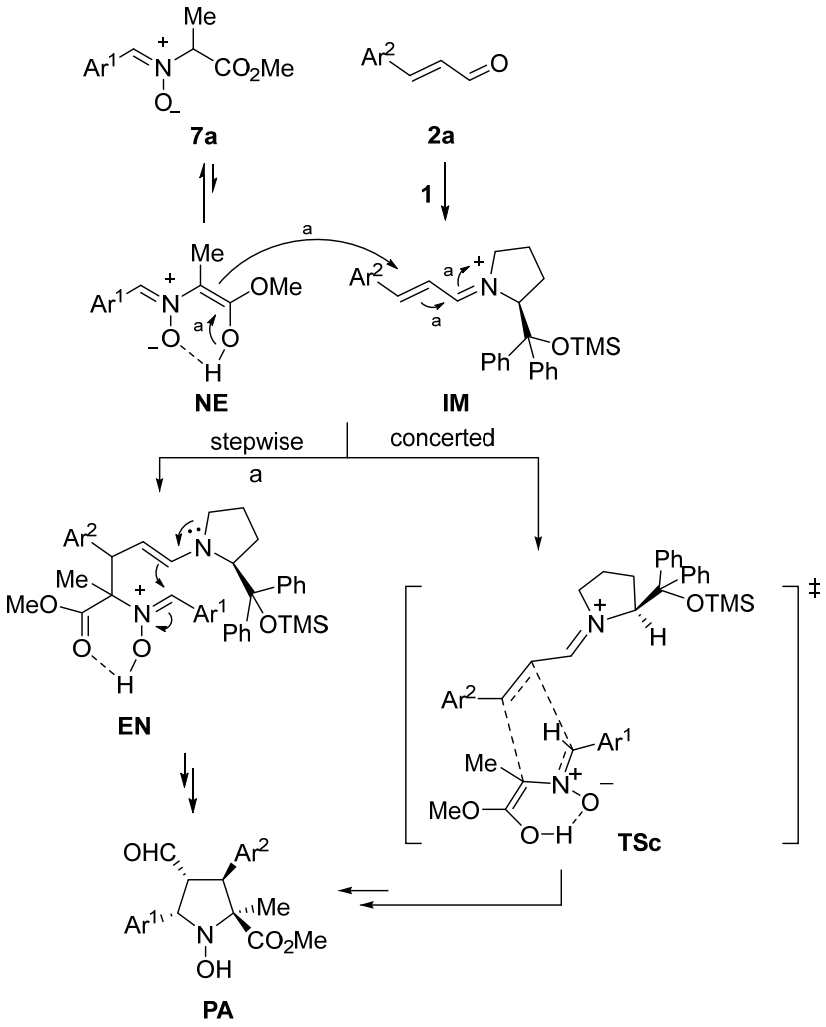
Concerted vs. Stepwise mechanisms for the reaction

Once the iminium ion is formed, the reaction can take place in a concerted way or in two steps through a tandem Michael-Mannich reaction (Scheme S1).



Scheme S1. Concerted and stepwise plausible mechanisms for the reaction between **2a** and **7a** in the presence of **1** and **3** (not showed). Ar^1 = 4-$NO_2C_6H_5$, Ar^2 = 4-$MeOC_6H_5$.

Hammett Plots

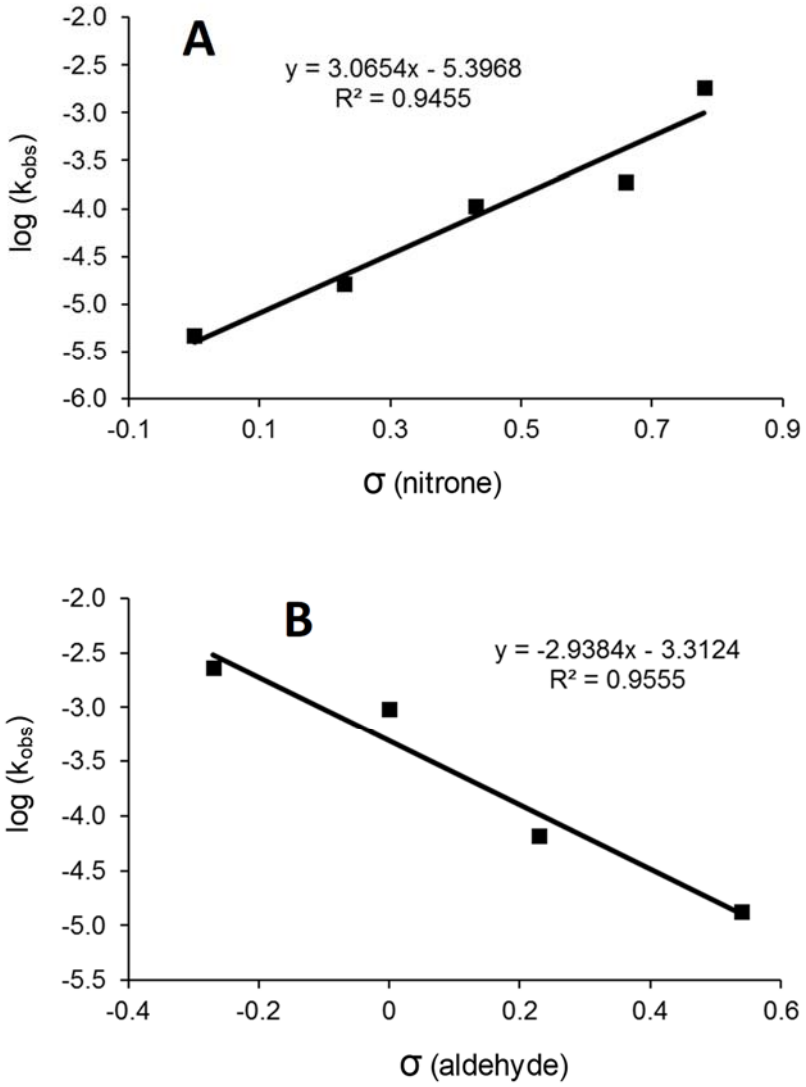
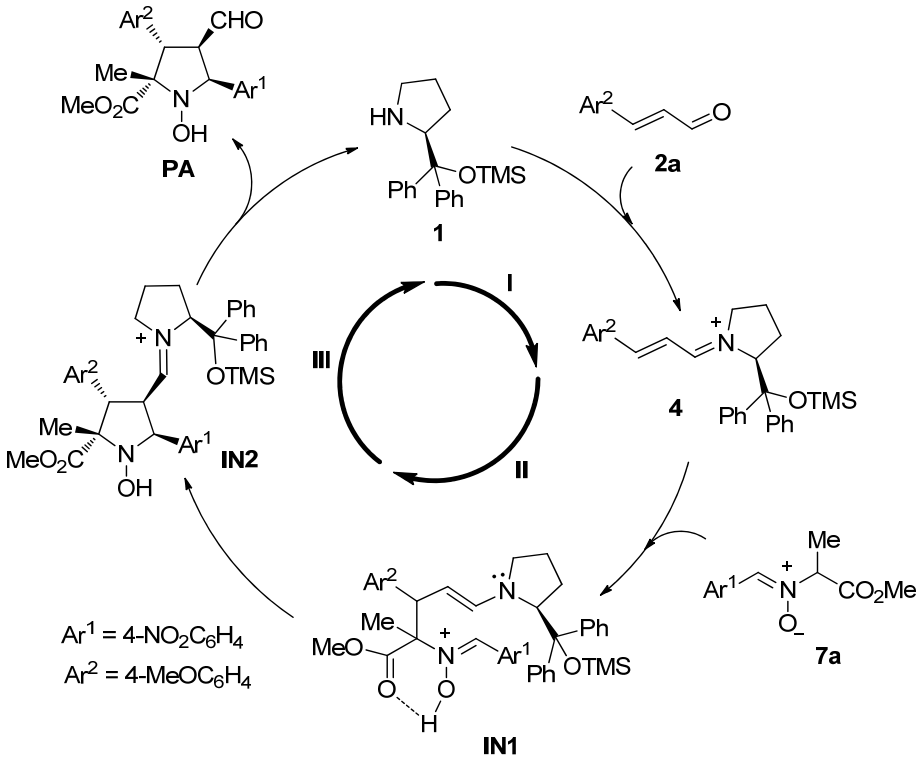


Figure S4. Rate dependence of the reaction between aldehydes and nitrones on substrate electronic properties. A: Reaction of nitrone **7a** with aldehydes **2a-d**. B: Reaction of nitrones **7a-d** with aldehyde **2a**.

Hammett plots show the most favorable situations those corresponding to nitrones with electron-withdrawing groups and aldehydes with electron-donating groups. These data point to a stepwise mechanism based on nucleophilic attacks to iminium intermediate and nitrone. The concerted pathway would involve a typical normal demand dipolar cycloaddition in which the dipole acts as a nucleophile. Accordingly, electron-donating groups at the nitrone-carbon should favor the reaction, which is just the opposite to that observed in Hammett plots.

Proposed Catalytic Cycle

According to a stepwise mechanism a catalytic cycle in which the role of thiourea should still be investigated can be advanced:



Scheme S2. Advanced catalytic cycle according to a stepwise mechanism (the role of thiourea is still pending of being investigated).

Mass Spectra

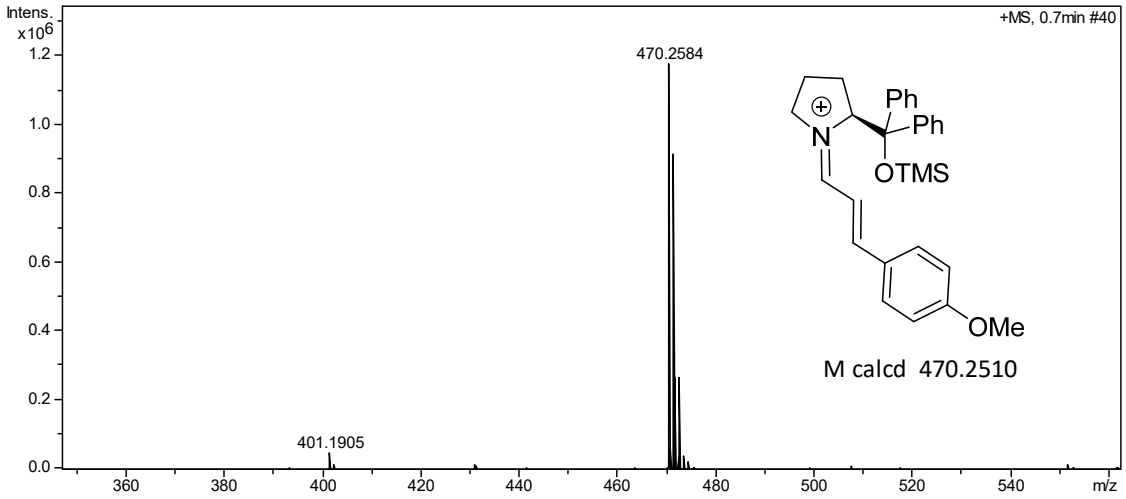


Figure S5. (+)-ESI-MS scan of the reaction of **2a** with **1** in the presence of **3** as co-catalyst (1.0 eq of all reagents were used)

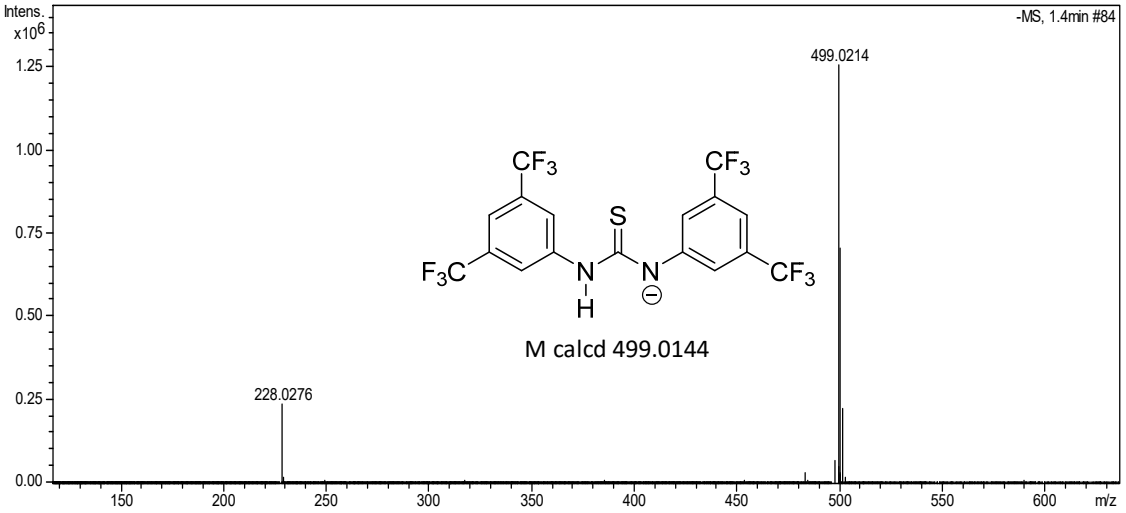


Figure S6. (-)-ESI-MS scan of the reaction of **2a** with **1** in the presence of **3** as co-catalyst (1.0 eq of all reagents were used).

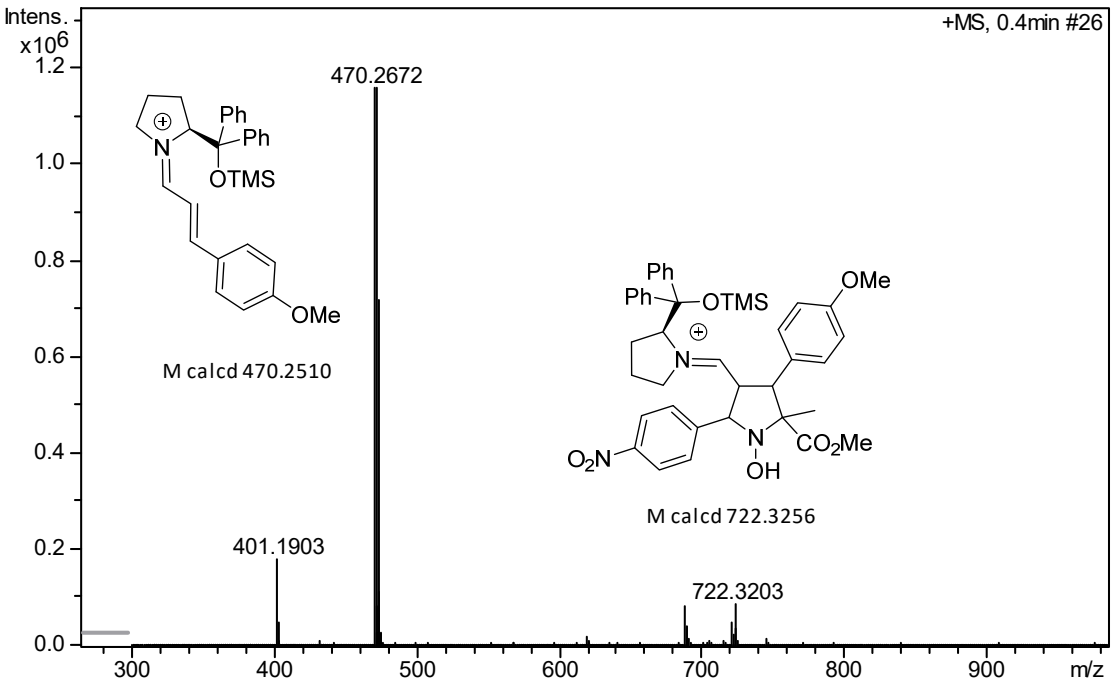


Figure S7. (+)-ESI-MS scan of the reaction of **2a** with **7a** catalyzed by **1** in the presence of **3** as co-catalyst. (1.0 eq of all reagents were used)

^{1}H NMR Spectra

Formation of iminium ion

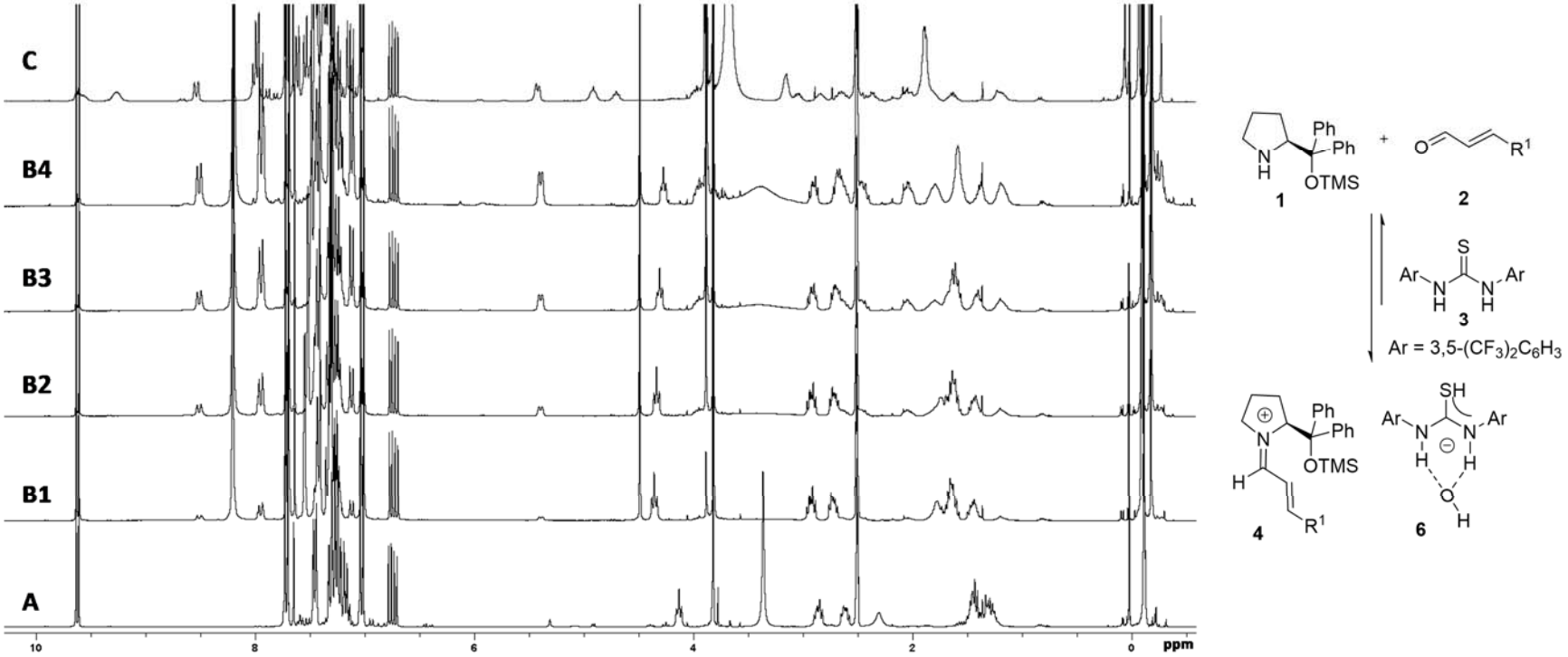


Figure S8. Full spectra corresponding to those showed in Fig1. of main text. A: Equimolar mixture of **1** and **2a**. B1-B4: A after adding 1.0 equiv of thiourea **3**; B1: after 1 h; B2: after 2 h; B3: after 6 h; B4: after 10 h. C: Iminium ion prepared from **1**, **2a** and trifluoroacetic acid as reported.[2]

[2] H. Gotoh, T. Uchimaru, Y. Hayashi, *Chem. Eur. J.* **2015**, *21*, 12337-12346.

*Binding of thiourea **3** to hydroxide ion*

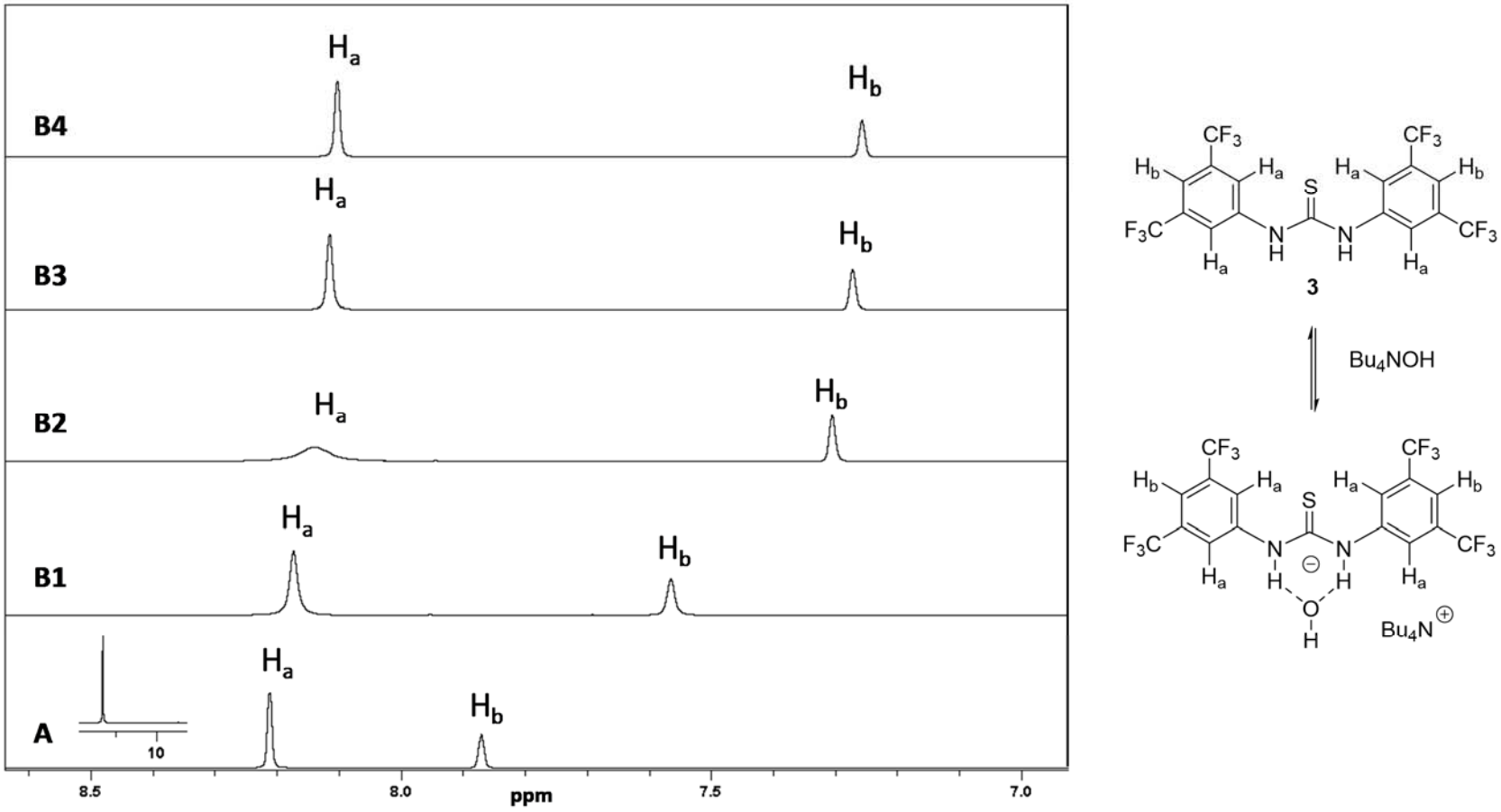


Figure S9. A: Thiourea **3**. B1-B4: A after adding commercial 1.0 M aqueous solution of Bu_4NOH**;** B1: after adding 0.5 equiv of Bu_4NOH; B2: after adding 1.0 equiv of Bu_4NOH; B3: after adding 1.5 equiv of Bu_4NOH; B4: after adding 2 equiv of Bu_4NOH

In order to check the effect of **6** (generated during the reaction from the formation of iminium ion **4**) over the nitrone, we treated nitrone **7a** with $Bu_4N\cdot$**6**, which was obtained as a yellow solid by mixing equimolar amounts of thiourea **3** and an aqueous 1M solution of Bu_4NOH, stirring for 1 hour and lyophilizing. When nitrone **7a** is treated with 0.1 equiv of $Bu_4N\cdot$**6**, partial disappearance of the signal corresponding to H_a was observed, H_a : H_b integration going from 2:1 in the nitrone to 2:0.5 after the addition of $Bu_4N\cdot$**6**.This fact indicates the formation of an equilibrium, presumably that illustrated in Figure S10. After addition of 0.3 equiv. of $Bu_4N\cdot$**6**, all signals disappeared indicating a rapid equilibrium.

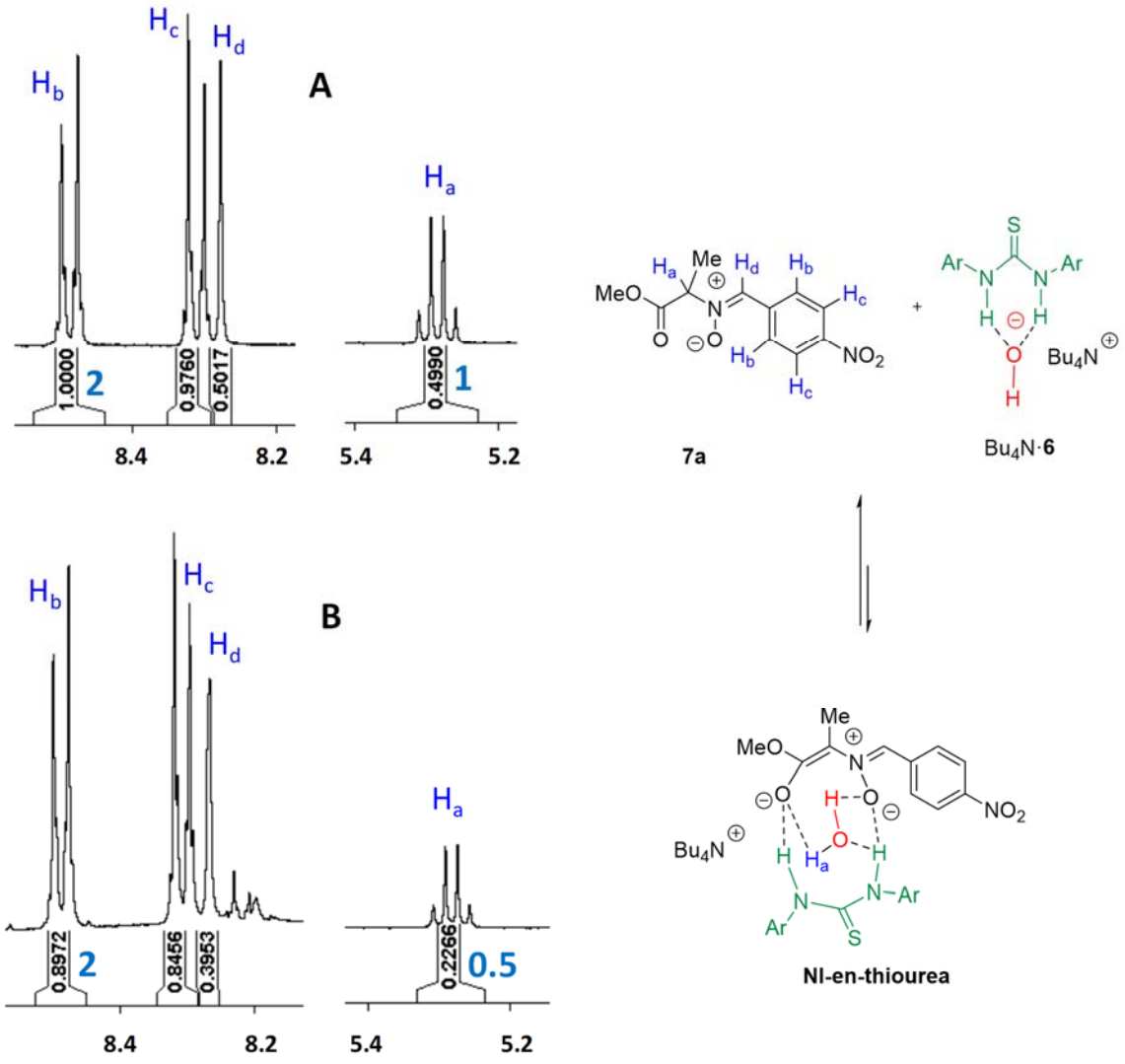


Figure S10. Enolization of nitrone **7a** upon addition of **6** (generated from thiourea **3** and Bu_4NOH). A: Nitrone **7a**. B: After addition of 0.1 equiv of $Bu_4N\cdot$**6**.

UV Spectra

Study of binding properties of thiourea 3 *to hydroxide ion*

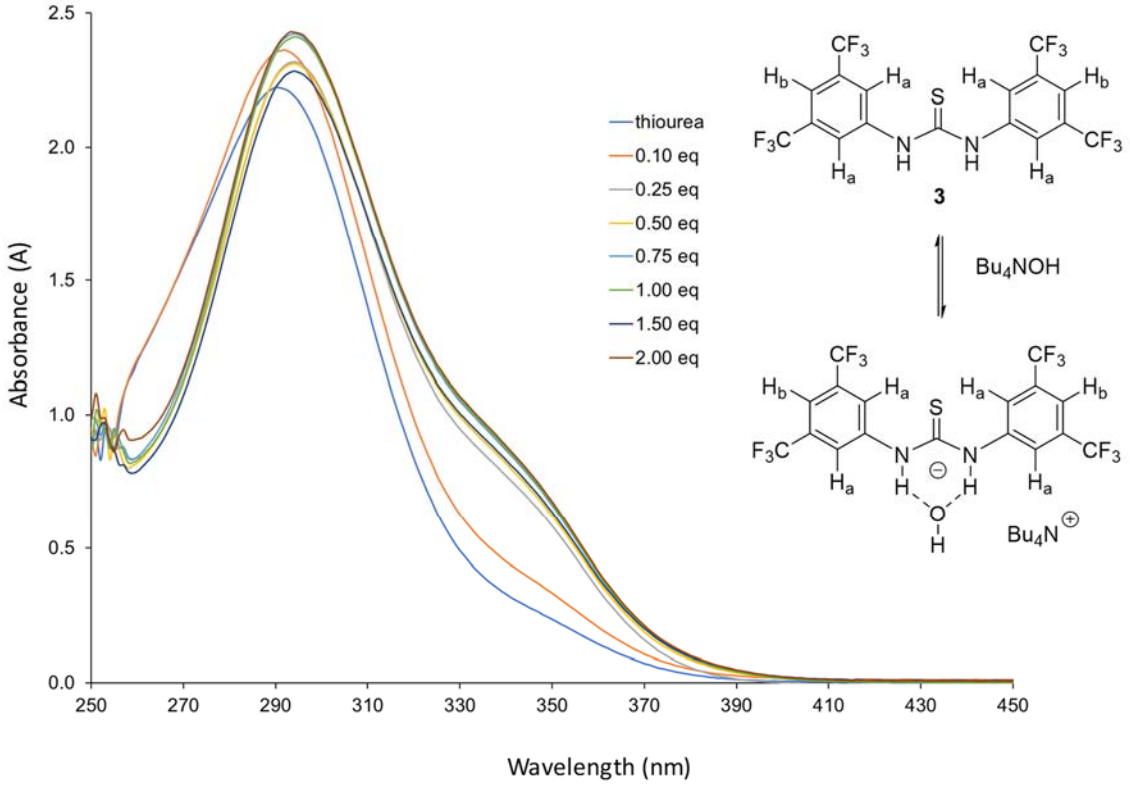


Figure S11. UV-VIS spectral titration of **3** with OH- (as its tetrabutylammonium salt) in DMSO solution, from which the association constant was determined,[3] log K = 5.50 ± 0.20

[3] (a) X. Baoa and Y. Zhou, *Sens. Actuators B*, **2010**, *147*, 434-441. (b) J. Bourson, J. Pouget and B. Valeur, *J. Phys. Chem.* **1993** *97*, 4552-4557.

pK_a Determination for squaramide 12

pK_a values for thioureas **3** (pK_a = 8.5), **9** (pK_a = 13.4) and **10** (pK_a = 10.7), and squaramide **11** (pK_a = 8.4) were taken from the literature.[4] pK_a for sqauaramide **12** was determined by ^{19}F-NMR titration in DMSO-d_6.

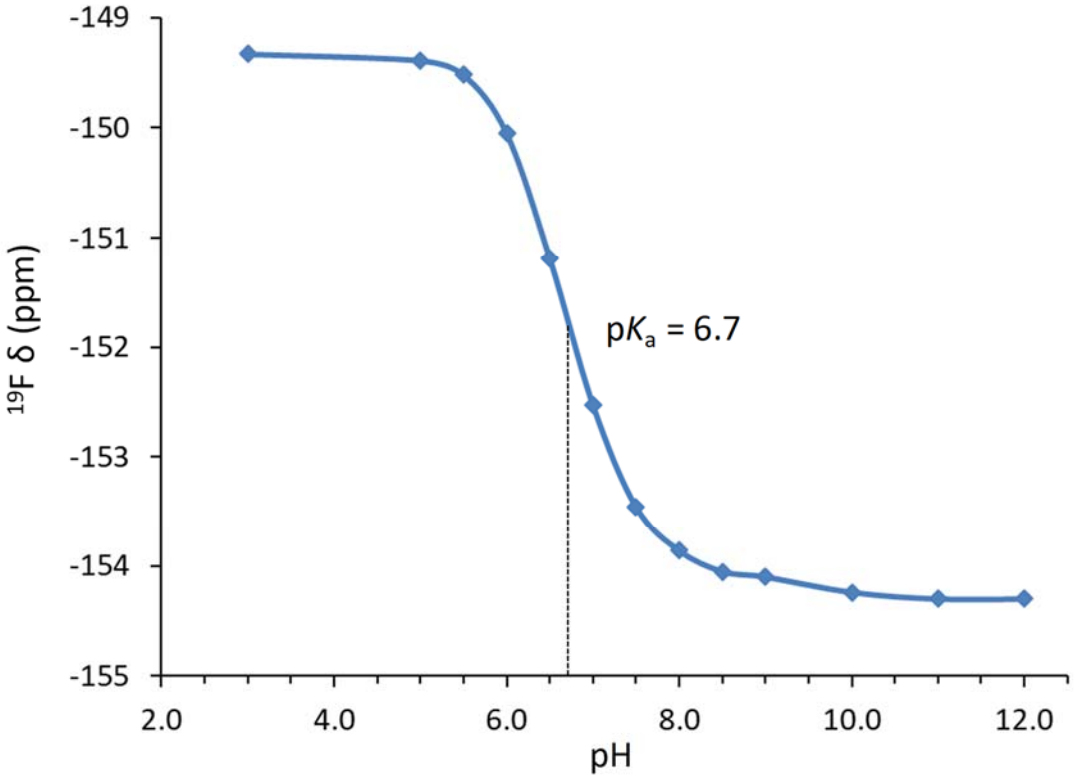


Figure S12. pK_a determination of squaramide **12** through ^{19}F-NMR titration in DMSO-d_6.

[4] Thioureas **3**, **9** and **10**: G. Jakab, C. Tancon, Z. Zhang, K. M. Lippert, P. R. Schreiner *Org. Lett.* **2012**, *14*, 1724-1727. Squaramide **11**: X. Ni, X. Li, Z. Wang, J.-P. Cheng *Org. Lett.* **2014**, *16*, 1786-1789.

Linear dependences of % of iminium at equilibrium

There is a linear correlation between % of iminium at equilibrium and pK_a of thiourea/squaramide responsible of anion recognition (Figure S13).

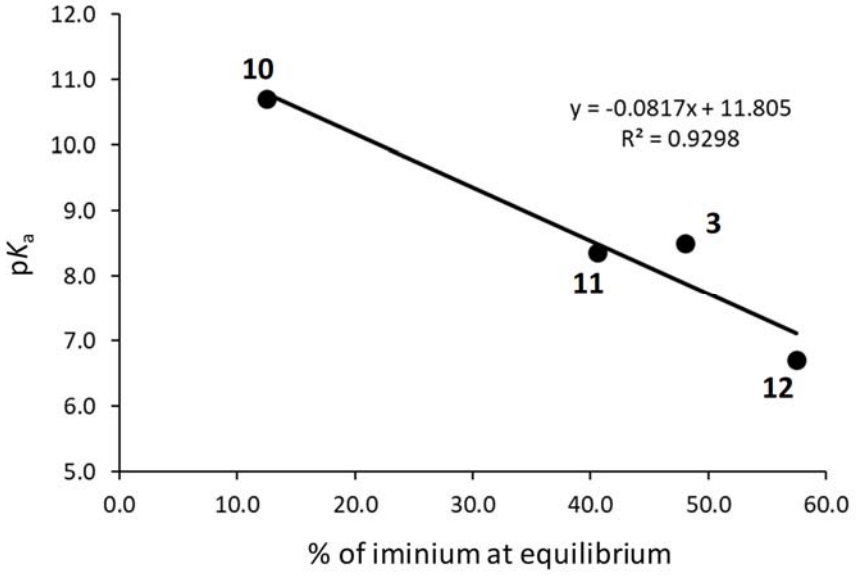
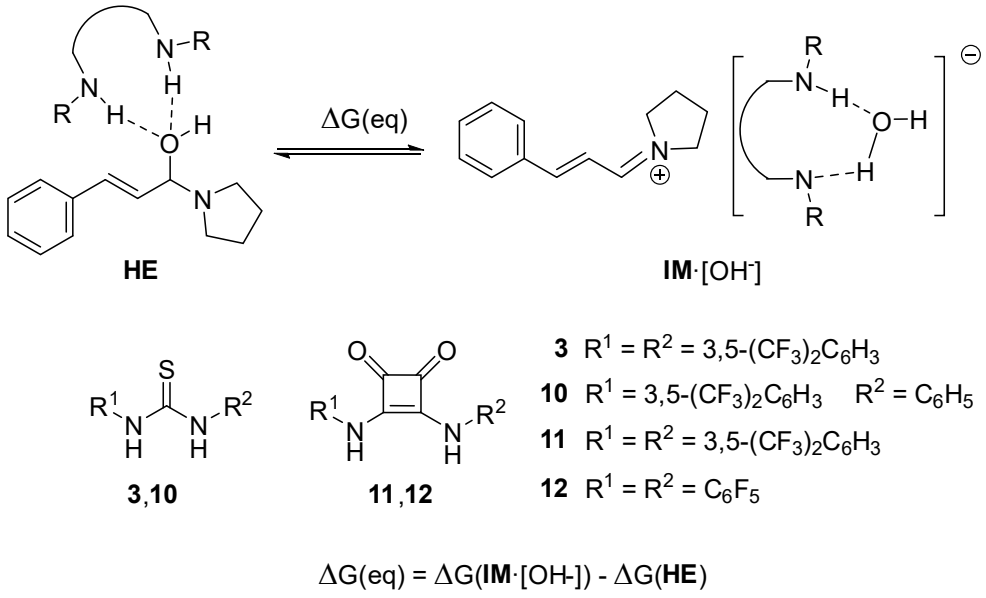


Figure S13. Linear relationship between pK_a of thioureas **3** and **10** and squaramides **11-12**, and % of iminium at equilibrium

Admittedly, the formation of iminium ion (**IM**) from aldehyde and catalyst takes place through the corresponding hemiaminal (**HE**) (Figure S14).



$$\Delta G(eq) = \Delta G(\mathbf{IM}\cdot[OH\text{-}]) - \Delta G(\mathbf{HE})$$

Figure S14. Equilibrium between iminium ions and hemiaminals

The % of iminium at equilibrium also correlates with the difference (ΔG(eq)) in free energy between the corresponding ion pair **IM**·[OH^-] and the precursor hemiaminal (**HE**).

Table S2. Calculated (B3LYP-D3BJ/def2SVP(CPCM=$CHCl_3$) absolute (hartrees) and relative (kcal/mol) for hemiaminals (**HE**) and iminium ions (**IM**·[OH^-]).

	G(**HE**)	G(**IM**·[OH^-])	ΔG(eq)
3	-2991.792270	-2991.809441	-10.8
9	-1644.606088	-1644.609912	-2.4
10	-2318.201578	-2318.212761	-7.0
11	-2858.239741	-2858.256310	-10.4
12	-2502.659909	-2502.678291	-11.9

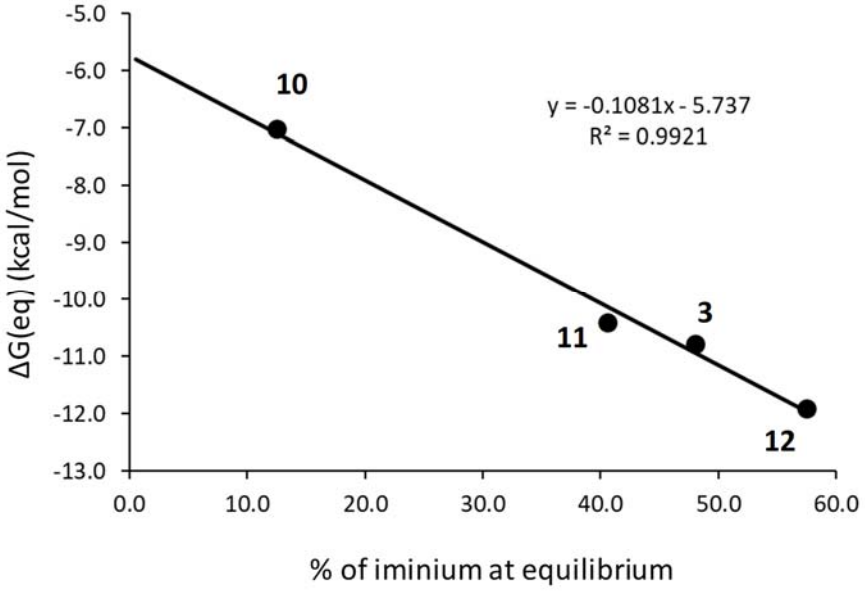


Figure S15. Linear relationship between relative stability of iminium ions of thioureas **3** and **10** and squaramides **11-12**, and % of iminium at equilibrium

According to the graphic illustrated in Figure S15, a difference higher than 5.7 kcal/mol is required for the formation of iminium ion (which is a thermodynamic process depending on the energy difference between **HE** and **IM**·[OH^-]). Since thiourea **9** leads to a difference of -2.4 kcal/mol the lack of reactivity experimentally observed with that thiourea is fully supported by calculations. On the contrary, thiourea **3** and squaramide **12** put into play 47% and 56% of iminium at equilibrium facilitating the reaction.

Theoretical Calculations

Computational Methods

All of the calculations were performed using the Gaussian09 program.[5] The B3LYP functional[6] was employed in geometry optimizations and frequency calculations, including the D3 dispersion correction of Grimme.[7] The electronic configuration of the molecular systems was described with the standard split-valence basis set def2SVP[8] Analytical second derivatives of the energy were calculated to classify the nature of every stationary point, to determine the harmonic vibrational frequencies, and to provide zero-point vibrational energy corrections. All calculations have been carried out considering solvent effects ($CHCl_3$) with the CPCM model.[9] The thermal and entropic contributions to the free energies were also obtained from the vibrational frequency calculations, using the unscaled frequencies. All discussions are based on values of free energies (G). However, several of the individual reactions involved on the study are bimolecular processes. In order to avoid errors due to entropic effects when comparing all stationery points in an only energy diagram, we used corrected free energy (G_{corr}) values following Morokuma's model[10] based on consideration of translational entropy.[11] All transition structures were characterized by one imaginary frequency. All the located TSs were confirmed to connect to reactants and products by intrinsic reaction coordinate (IRC) calculations.[12] The IRC paths were traced using the Hratchian-Schlegel algorithm.[13] Molecular graphics have been performed with CYLview 1.0 software.[14]

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[5] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J.; Gaussian, Inc., Wallingford CT,: 2009.

[6] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785-789.

[7] S. Grimme, S. Ehrlich, L. Goerigk, *J. Comput. Chem.* **2011**, *32*, 1456-1465.

[8] F. Weigend, R. Ahlrichs, *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297-3305.

[9] M. Cossi, N. Rega, G. Scalmani, V. Barone *J. Comput. Chem.* **2003**, *24*, 669-681.

[10] T. Kawatsu, M. Lundberg, K. Morokuma, *J. Chem. Theory Comput.* **2011**, *7*, 390-401.

[11] L.-L. Han, S.-J. Li, D.-C. Fang *Phys. Chem. Chem. Phys.* **2016**, *18*, 6182-6190

[12] (a) Fukui, K. *J. Phys. Chem.* **1970**, *74*, 4161-4163. (b) Fukui, K. *Acc. Chem. Res.* **1981**, *14*, 363-368.

[13] Hratchian, H. P.; Schlegel, H. B. *J. Phys. Chem. A* **2002**, *106*, 165-169.

[14] Legault, C. Y. *Université de Sherbrooke* **2009**, http://www.cylview.org.

Calculation Methodology

Catalyst **I** is known to operate according to a steric model,[15] particularly when it catalyzes Michael-type reactions.[16] Consequently, only the attack through the less hindered *Re* face of the iminium needs to be considered in agreement with previous calculations for other reactions. For unraveling the mechanism of the reaction and determining the diastereoselectivity of the reaction is not necessary to include chirality in the pyrrolidine. Just for illustrating the correct enantiomer that it is predicted we have chosen for our study the attack by the *Re* face of the iminium derived from pyrrolidine. According to the experimental observations the stepwise mechanism was considered. Phenyl rings were used in place of the aromatic rings except for thiourea, which was used as the real compound. We studied the catalytic cycle illustrated in the main text.

The formation of the iminium ion as the ion pair **IN0** can be considered a barrierless process that might be described by a typical reaction valley approach,[17] i.e. going downhill from **HE** to **IN0**. In principle, two diastereomeric hemiaminals should be considered for the real system. In the case of our model both hemiaminals are enantiomeric so, only one has been studied. In any case, since both of them converge to the same iminium ion, we have not considered relevant this point for the whole mechanistic study.

Starting from **EP** two attacks are possible considering *Re* and *Si* faces of the nitrone (as mentioned above, *Re* face of the iminium is fixed according to the less hindered face of the real catalyst **1**). Accordingly, two diastereomeric routes **a** and **b** were located from **EP** corresponding to those leading to products with configurations (2*S**,3*S**,4*R**,5*S**) and (2*R**,3*S**,4*R**,5*S**), respectively (Scheme S4). For **IN3a,b** the two possible hemiaminals have been calculated, only being considered the most stable one in each series.

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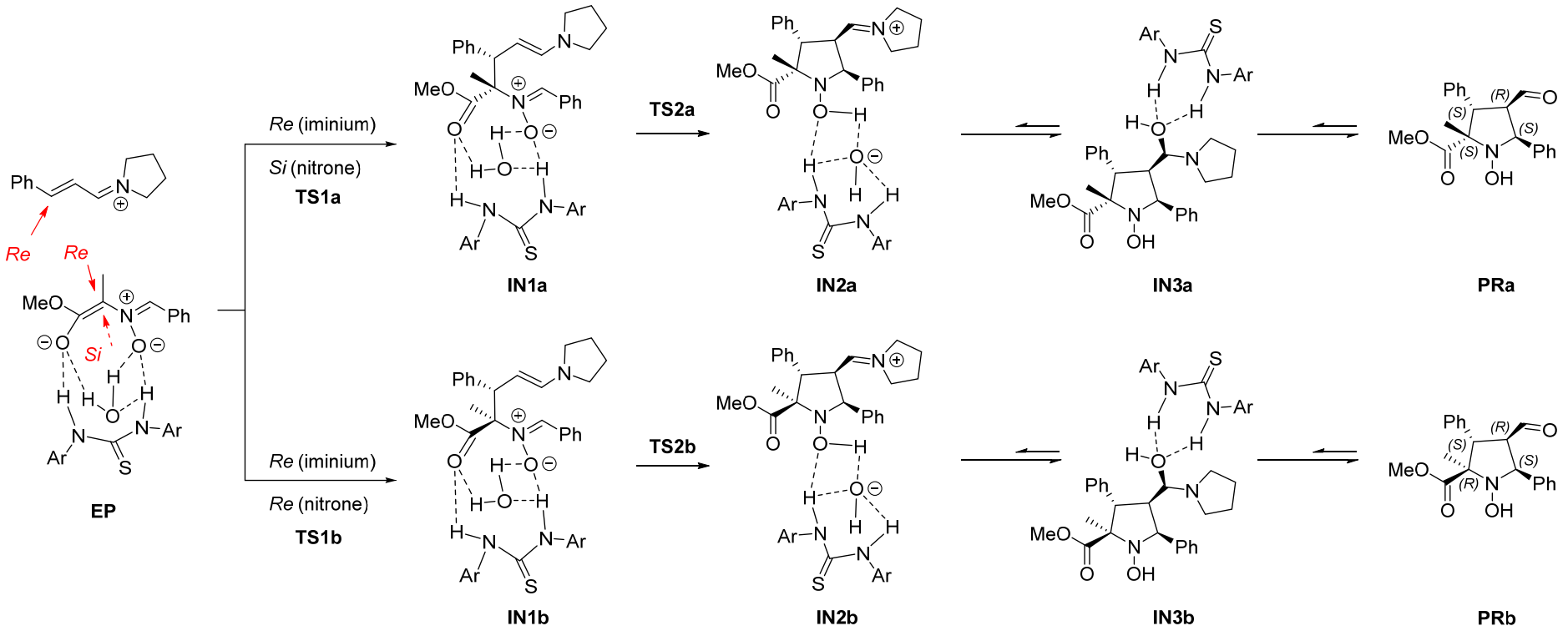
[15] (a) M. Marigo, T. C. Wabnitz, D. Fielenbach, K. A. Jorgensen *Angew. Chem. Int. Ed*. 2005, **44**, 794 (b) H. Gotoh, T. Hayashi, M. Shoji, *Angew. Chem. Int. Ed.* 2005, **44**, 4212. (c) Y. Hayashi, D. Okamura, T. Yamazaki, Y. Ameda. H. Gotoh, S. Tsuzuki, T. Uchimaru, D. Seebach, *Chem. Eur. J.,* 2014, **20**, 17077. For some reviews: (d) B. S. Donslund, T. K. Johansen, P. H. Poulsen, K. S. Halskov, K. A. Jorgensen, *Angew. Chem., Int. Ed.,* 2015, **54**, 13860. (e) S. Meninno, A. Lattanzi, *Chem. Commun.,* 2013, **49**, 3821. (f) K. L. Jensen, G. Dickmeiss, H. Jiang, L. Albrecht, K. A. Jorgensen, *Acc. Chem. Res.,* 2012, **45**, 248. (g) A. Mielgo, C. Palomo, *Chem. Asian J.,* 2008, **3**, 922.

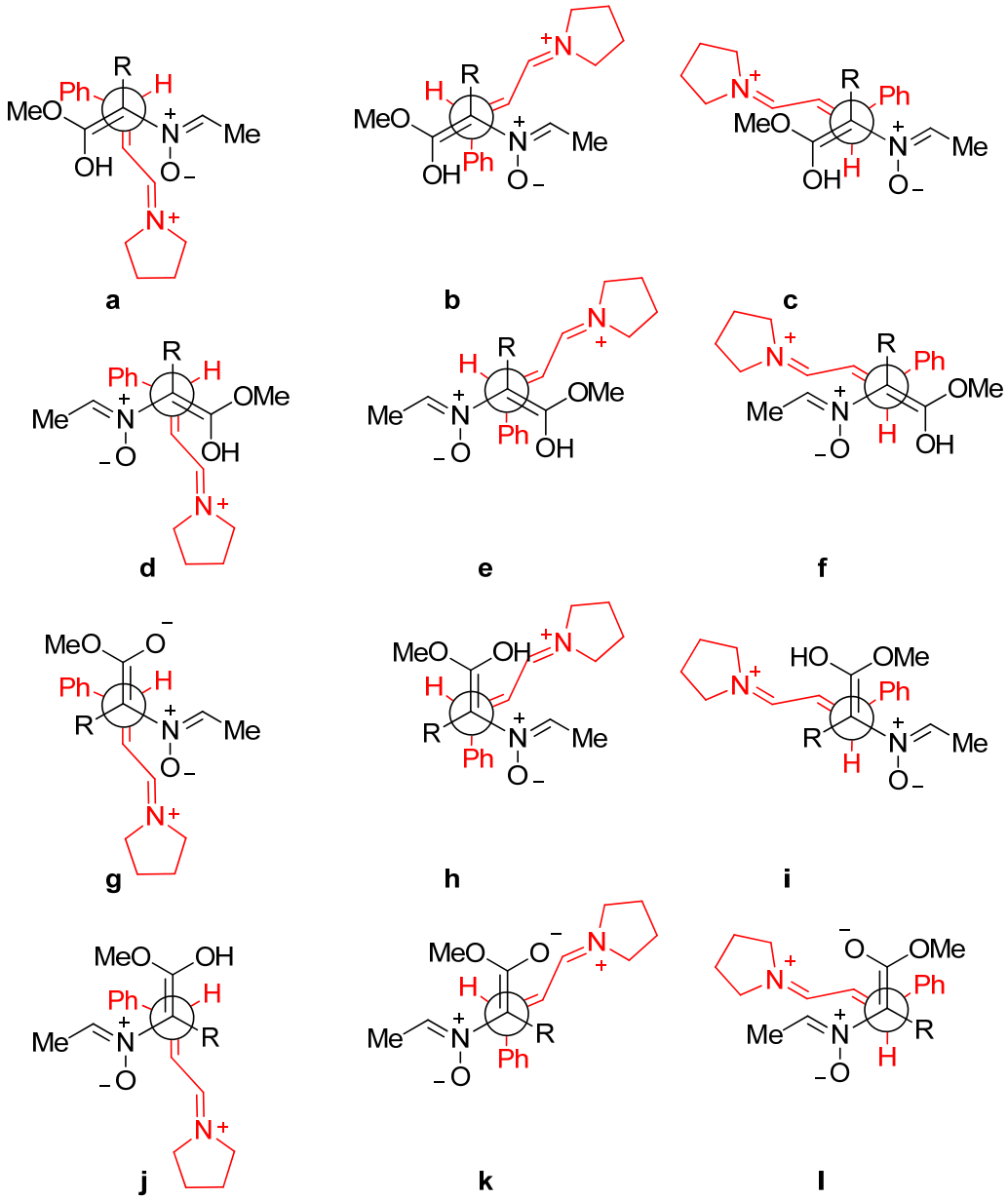
[16] (a) S. Bertelsen, M. Marigo, S. Brandes, P. Diner, K. A. Jørgensen, *J. Am. Chem. Soc*., **2006**, *128*, 12973. (b) S. Reboredo, E. Reyes, J. L. Vicario, D. Badia, L. Carrillo, A. Cozar, F. Cossio, *Chem. Eur. J.* **2012**, *18*, 7179.

[17] H. Joo. E. Kraka, W. Quapp, D. Cremer *Mol. Phys.***2007**, *105*, 2697-2717.



Scheme S4. Diastereotopic routes for the formation of **PRa** and **PRb**. Ar = 3,5-$(CF_3)_2C_6H_3$

Considering the *Re* face (less hindered in the real catalyst **1**) of the iminium (see above), the *Re* and *Si* faces of the nitrone and S/W conformation of the nitrone ylide we studied a total of 12 approaches for locating **TS1** (Scheme S5). The 12 approaches converged to 8 minima. The most stable one for *Si* and *Re* faces were identified as **TS1a** and **TS1b**, respectively.



Scheme S5. Approaches studied for locating **TS1a,b** ([**3**·**OH**]$^-$ is not showed for clarity)

Location of **TS2a,b** was carried out from **IN1a,b** considering the opposite *Si* face of the nitrone fragment and resulting in *Si-Si* and *Re-Si* attacks for **a** and **b** series, respectively. Although it is possible to consider two additional attacks, i.e.: *Si-Re* and *Re-Re*, they should involve a conformational change through an unfavored rotation of the nitrone fragment. In any case we have calculated these two additional attacks and are higher in energy, confirming that the second step is not the rate-limiting step.

Energy Data

Table S3. Calculated (B3LYP-D3BJ/def2SVP/CPCM=$CHCl_3$) absolute (hartrees) free energies of the stationary points corresponding to the reaction between aldehyde **AL** and nitrone **NI** catalyzed by pyrrolidine **PY** in the presence of thiourea **3**.[a]

	E_0	G	im. freq
3	-2356.774877	-2356.840337	
PY	-212.319500	-212.346680	
AL	-422.566476	-422.599124	
NI	-706.749132	-706.791764	
HE	-634.898462	-634.941575	
IN0	-2991.725717	-2991.807627	
EP	-3698.438790	-3698.537666	
TS1a	*-3698.429925*	*-3698.528776*	*-155.4*
IN1a	-3698.447447	-3698.551589	
TS2a	*-3698.432825*	*-3698.530866*	*-414.0*
IN2a	-3698.441433	-3698.542062	
IN3a	-3698.447636	-3698.545927	
PRa	-1129.286523	-1129.339634	
TS1b	*-3698.426956*	*-3698.523919*	*-141.8*
IN1b	-3698.451025	-3698.550044	
TS2b	*-3698.438021*	*-3698.534921*	*-403.2*
IN2b	-3698.446869	-3698.543923	
IN3b	-3698.447202	-3698.544606	
PRb	-1129.278159	-1129.328161	

[a] **a** and **b** series refers to final products with configurations (2*S**,3*S**,4*R**,5*S**) and (2*R**,3*S**,4*R**,5*S**), respectively

Transition Structures

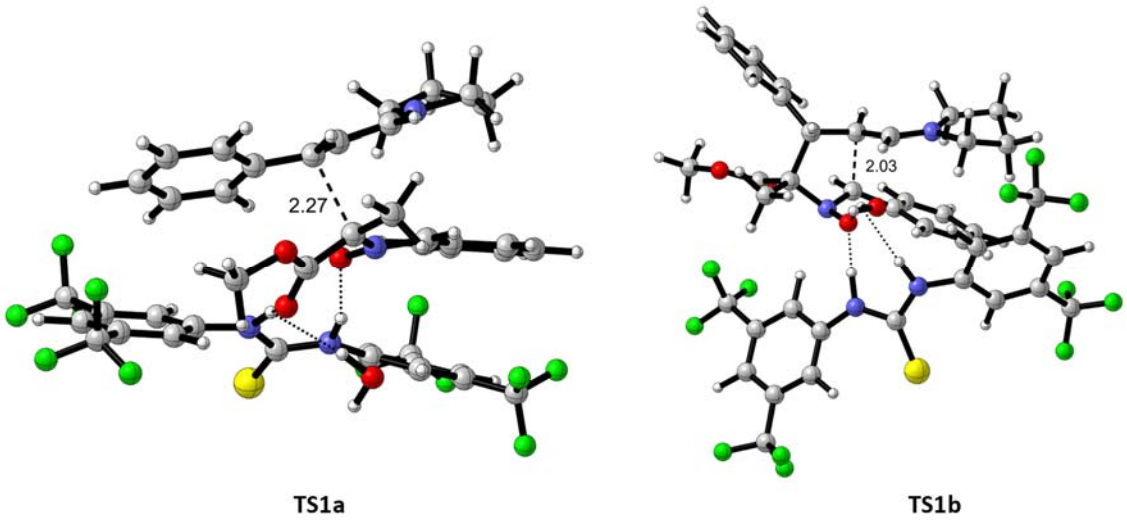


Figure S16. Transition structures for **a** series leading to products with (2*S**,3*S**,4*R**,5*S**) configuration

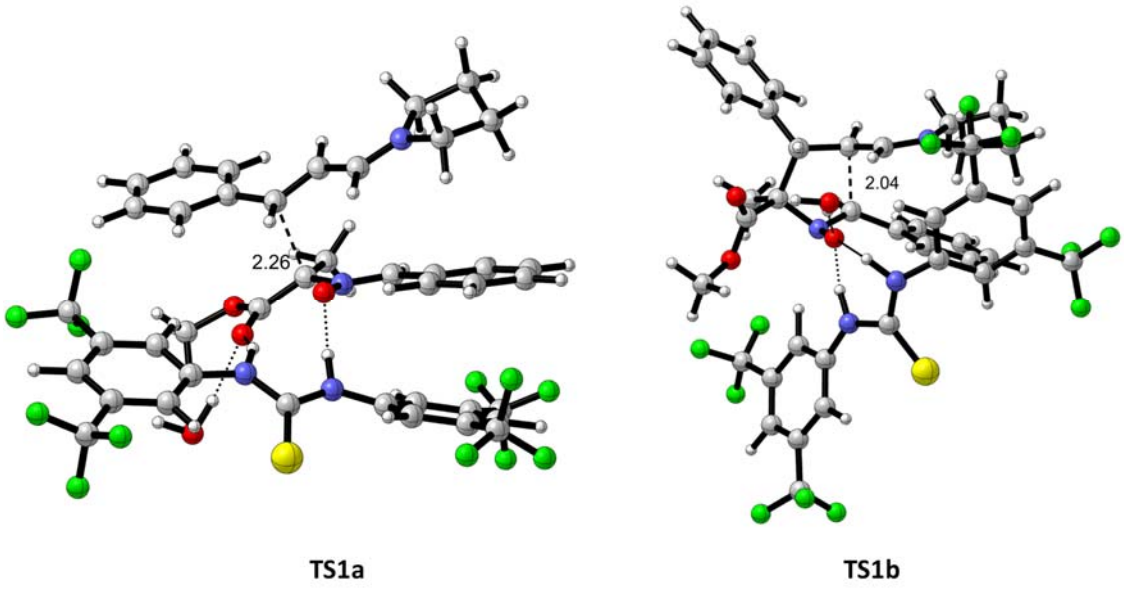


Figure S17. Transition structures for **b** series leading to products with (2*R**,3*S**,4*R**,5*S**) configuration

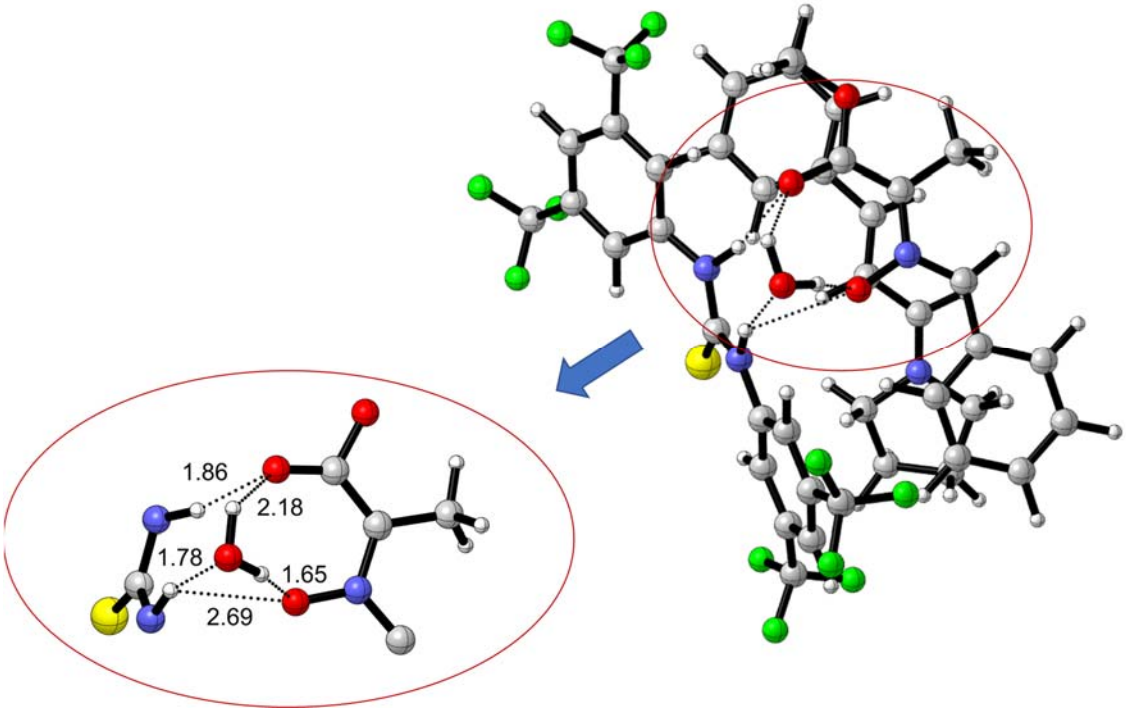


Figure S18. Encounter pair **EP** and detail of the H-bond network facilitating enolization of nitrone

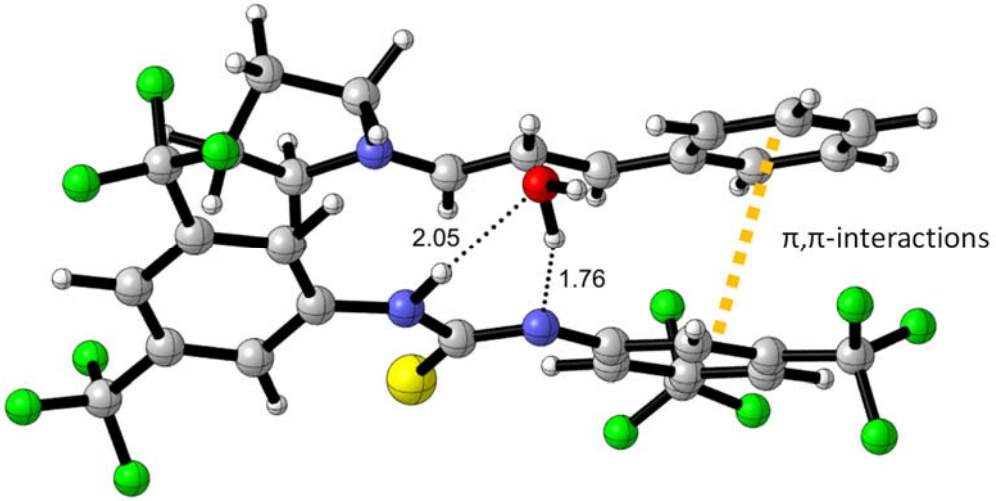
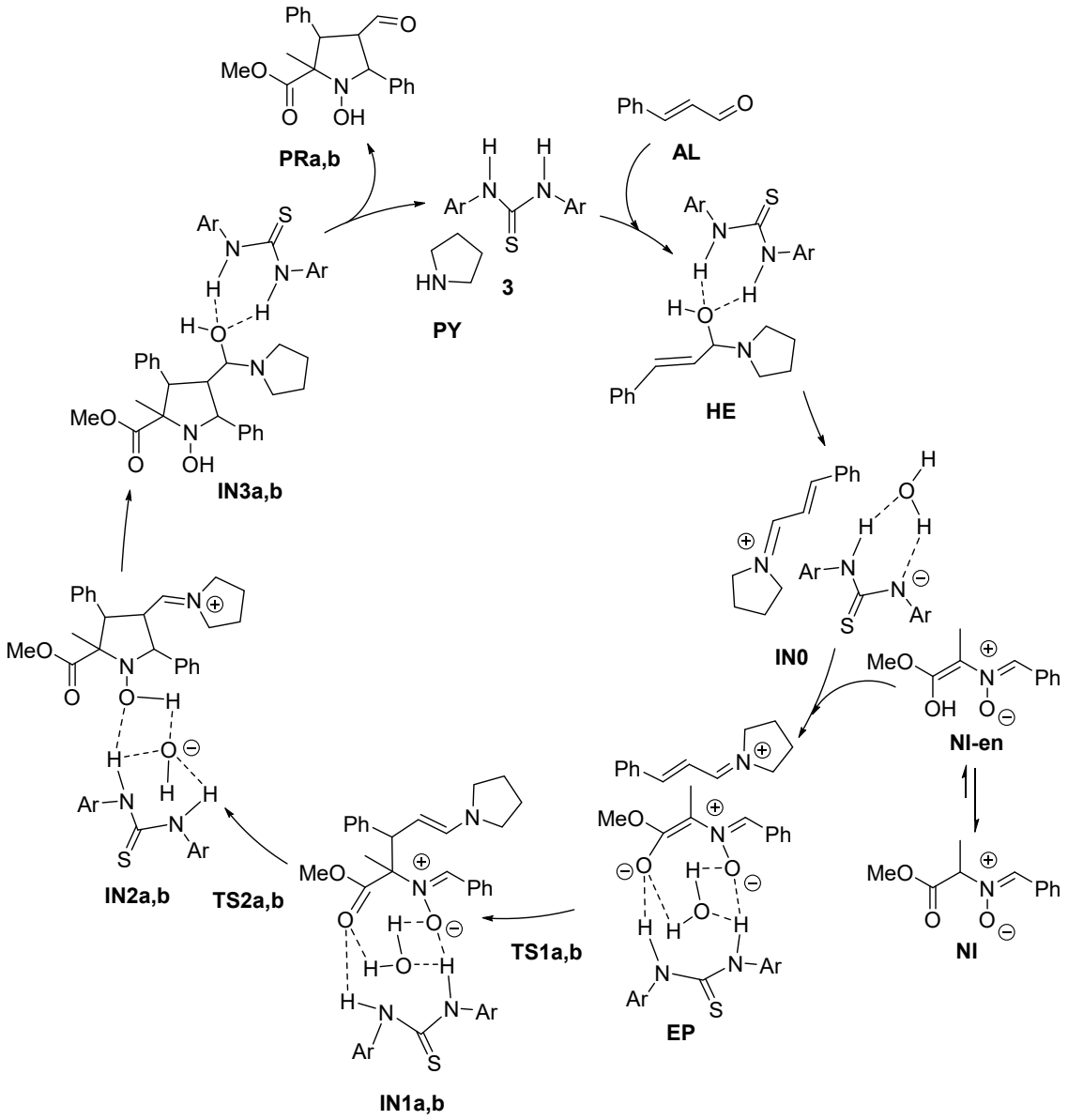


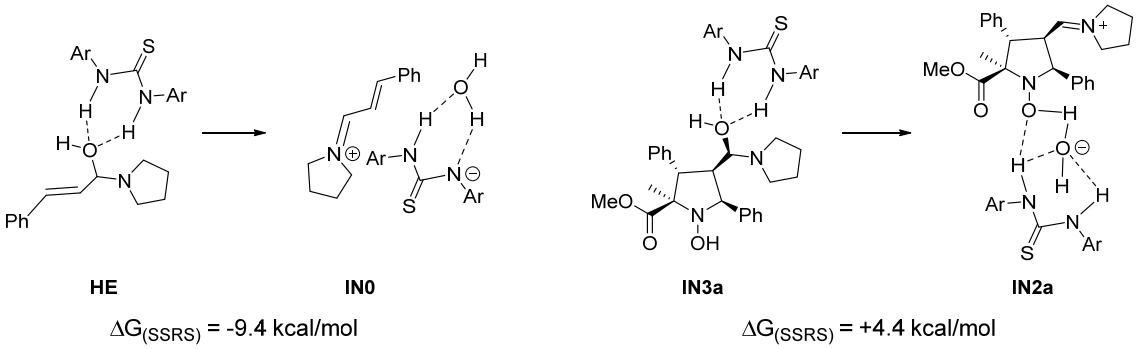
Figure S19. Ion pair formed by iminium ion and thiourea-OH complex (**IN0**). Favorable hydrophobic interactions between the phenyl group of the iminium and one of the aromatic rings of the thiourea are evidenced.

The Catalytic Cycle



Scheme S5. Catalytic cycle (for the different diastereomeric configurations of **IN1**, **IN2**, **IN3** and **PR** see Scheme S4). Ar = 3,5-$(CF_3)_2C_6H_3$

Notably, whereas the formation of iminium **IN0** from hemiaminal **HE** is favored by 9.4 kcal/mol, iminium **IN2a** is disfavored with respect to **IN3a** by 4.4 kcal/mol thus pushing forward the catalytic cycle (Scheme S6).



Scheme S6. Relative stability of iminium ions. Ar = 3,5-$(CF_3)_2C_6H_3$

The energy profiles for both diastereomeric routes are given in Figure S18. The first transition state in which the new stereogenic centers are generated is the rate-limiting step. The observed barriers for **TS1a** and **TS1b** predict the obtention of the final product with (2*S**,3*S**,4*R**,5*S**) configuration in agreement with the observed experimental results.

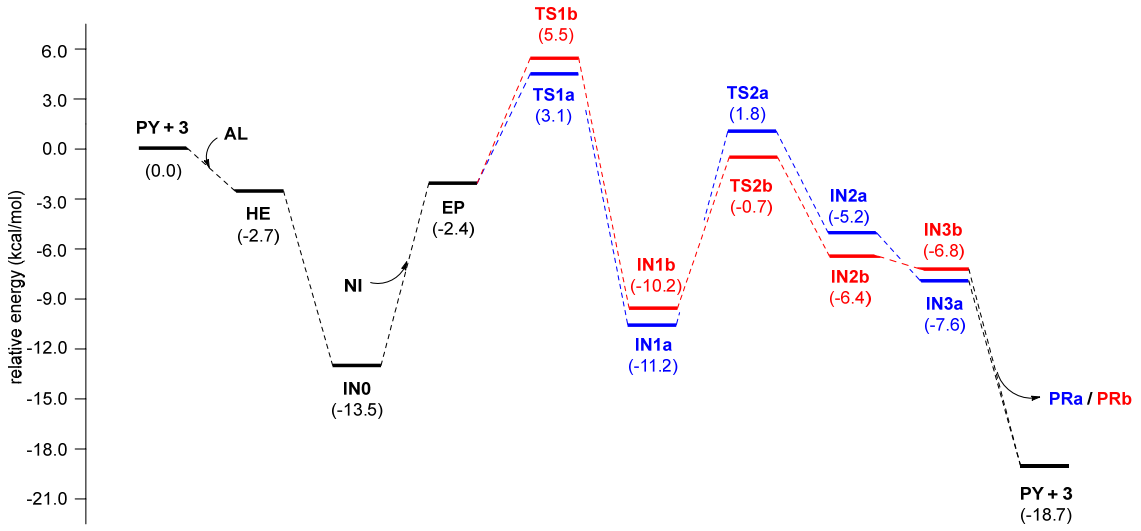


Figure S19. Energy profiles for **a** and **b** series corresponding to the catalytic cycle given in Scheme S5.

Cartesian Coordinates

AL

0 1

C	0.9693618866	-0.8597101493	-0.0324773763
H	0.9009848826	-1.9544652783	-0.0501198764
C	-0.1936092271	-0.1690536572	-0.0371477777
H	-0.2368458344	0.9236173053	-0.0209723442
C	-1.4759633325	-0.8705187434	-0.0646440652
H	-1.3930072393	-1.9886229382	-0.0807157789
C	2.3285304544	-0.3252243144	-0.0064878715
C	2.6031931542	1.0585575729	0.0181674642
C	3.4132293049	-1.2248908654	-0.0059129853
C	3.9166011199	1.5199147047	0.0424555805
H	1.7817095362	1.7770377122	0.0182816897
C	4.7291171203	-0.7616273067	0.0184422693
H	3.2138147846	-2.2993032231	-0.0248804688
C	4.9844835287	0.6124111600	0.0427002910
H	4.1132557463	2.5942333353	0.0613750383
H	5.5572977673	-1.4737820577	0.0185024931
H	6.0134439659	0.9788402016	0.0618051712
O	-2.5641373386	-0.3259598082	-0.0704804033

3

0 1

H	-1.0016700091	-1.6841058023	-1.0208298375
H	1.0069366847	-1.6098099229	-1.1263394753
C	-0.0008114992	-0.1459447923	-0.1261594486
S	-0.0089827566	1.1620871085	0.9155888052
C	-2.4828637426	-0.4614676346	-0.3360799945
C	-2.9539185858	0.8581847235	-0.2945265565
C	-3.3917037862	-1.5207893545	-0.2013559517
C	-4.3153359513	1.0983238527	-0.1019500542
C	-4.7505878784	-1.2627026875	-0.0198355453
C	-5.2253838420	0.0488966652	0.0393033160
C	2.4853747556	-0.4355864347	-0.3585636813
C	2.9581714483	0.8782697043	-0.2336482283
C	3.3932976340	-1.5022989277	-0.2921477322
C	4.3198902365	1.1034195033	-0.0245576439
C	4.7525109499	-1.2581953585	-0.0936330879
C	5.2285859055	0.0461523341	0.0504730346
N	-1.1333335637	-0.7839114335	-0.5675763184
N	1.1351552307	-0.7458839008	-0.6065062148
H	2.2652697589	1.7128562435	-0.2957045097
H	3.0344723478	-2.5278865694	-0.3934887164
H	6.2888481028	0.2354696062	0.2131572330
H	-3.0344512491	-2.5510929504	-0.2369658094
H	-2.2605760433	1.6870454679	-0.4089243105
H	-6.2857245501	0.2501168326	0.1879640872
C	5.7032657563	-2.4212513992	0.0345315014

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 C       4.8175457151    2.5256354037    0.0479645875
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 F       5.3075349821   -3.4735473461   -0.7035343144
 F       6.9466235871   -2.0962708758   -0.3560584772
 F       5.7911439446   -2.8491547515    1.3091419310
 F      -5.8802245910   -2.6829209736    1.4911895412
 F      -5.2688556060   -3.5393151741   -0.3983292874
 F      -6.9233941770   -2.1389558158   -0.3219719647
 F       5.9812812694    2.6170878545    0.7132458352
 F       5.0266728219    3.0361530268   -1.1820099212
 F       3.9352127447    3.3331965429    0.6597655818
 F      -5.0428363011    2.9444642976   -1.3814190283
 F      -5.9661922652    2.6601411634    0.5537114757
 F      -3.9222643801    3.3711646190    0.4171356968


EP

0 1
 C      -2.0749626656    3.3033715864   -1.0365700121
 C       0.2484216044    3.2969583078   -1.5438331910
 C       1.4145059562    2.5720195364   -1.9667128492
 N      -0.9369689749    2.6242689498   -1.2458400662
 O       2.4297186772    3.4222205378   -2.2860207255
 C       3.6731831467    2.8448985972   -2.6620690760
 H      -2.0183038405    4.3732866661   -1.2002056139
 H       3.5501091069    2.1205044809   -3.4794720189
 H       4.1501862951    2.3494209475   -1.8061525444
 H       4.3061006586    3.6779199658   -2.9923180255
 C      -3.3789762739    2.7684661119   -0.7225976022
 C      -4.4440390648    3.7069435333   -0.6822371233
 C      -3.6855843385    1.4183487432   -0.4285397654
 C      -5.7404374903    3.3211061665   -0.3589896517
 H      -4.2345192559    4.7562972451   -0.9058579106
 C      -4.9901692168    1.0413239291   -0.1076833193
 H      -2.8842219994    0.6889226906   -0.4552565506
 C      -6.0240711980    1.9803047492   -0.0650526199
 H      -6.5369995443    4.0687932369   -0.3345320276
 H      -5.1967755561   -0.0041763284    0.1227822865
 H      -7.0399247067    1.6729992453    0.1927870455
 O      -0.9206252848    1.3359291523   -1.0862454354
 O       1.5974220697    1.3513251326   -2.0746487969
 H      -0.3785558020   -1.2672290658   -1.5030495533
 H       1.3525296547   -0.2029624726   -1.0743066416
 C       0.4657840832   -1.4073305257    0.3291627544
 S       0.4556140073   -1.7607256955    1.9765385335
 C      -1.9179963064   -1.9100018627   -0.3507603074
 C      -2.5143234331   -2.2958672965    0.8612539818
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C	5.7211968233	-1.5478129917	-0.0046984114
N	-0.5792948298	-1.5563538980	-0.5257450071
N	1.5607934004	-0.8858779671	-0.3313416122
C	0.8804836463	3.1415332769	1.2056347729
H	0.6048585522	4.1808172216	1.0131913988
C	-0.1004947646	2.2917089063	1.6555536284
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C	-1.3995554201	2.7790908797	1.9184820319
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C	2.3028279166	2.8505923337	1.1443788793
C	2.8459854706	1.6227284817	1.5809140943
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C	5.0829649012	2.4146595939	1.0981908451
H	4.6280561292	0.4638437480	1.9120949358
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C	-2.2767747577	0.6725607464	2.8712276782
C	-3.6793633538	2.6673740586	2.8438443816
C	-3.3770068637	0.5332580978	3.9211255040
H	-1.2709615663	0.4442796750	3.2441088988
H	-2.4616246094	0.0345767804	1.9947953722
C	-4.4670521765	1.4787799442	3.4027059020
H	-3.5048271945	3.4396188466	3.6106227289
H	-3.7174097729	-0.5039629001	4.0256317898
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H	-5.1797807267	1.7895938131	4.1785964403
H	-5.0317136284	0.9919676749	2.5956803131
H	-4.1544983522	3.1350555246	1.9724744532
N	-2.3745326800	2.0830122094	2.4589786048
H	2.8228084024	-2.4107859463	1.5884601813
H	3.3713098961	0.0724686010	-1.8806292931
H	6.7968832103	-1.7043932572	0.0599056685
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H	-1.9117929063	-2.3500331540	1.7628839841
H	-5.7187452348	-2.8468089618	-0.2238198315
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H	-0.4376429115	5.1277971554	-2.5032717175
H	-0.2058110063	5.2707523634	-0.7517578762
H	1.2037001684	5.1845961286	-1.8283352117
C	6.0704162898	-0.0699506548	-2.0032618453
C	5.4194821861	-2.9008876167	2.0815570820
C	-4.9062365804	-2.0853043461	-2.7053377269
C	-4.5433693856	-2.9139385783	2.2054812256
F	5.4829592877	0.0963586122	-3.2026719876
F	6.4233725259	1.1655755683	-1.5761722322
F	7.2127239866	-0.7471811883	-2.2032299356

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 F      -5.8538942874   -3.0387419350   -2.7573020035
 F      -4.1777634167   -2.1754779427   -3.8293102058
 F      -5.5470405066   -0.8989071260   -2.7454787320
 F       6.6068925922   -3.4610514193    1.7942814951
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 F      -5.3481410931   -3.9862642234    2.1310065150
 F      -3.6644222395   -3.1316236783    3.1970505716
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 H      -0.6602788637    0.3984074218   -2.4196661610
 H       0.4846393766   -0.0777514951   -3.2860257432


HE

0 1
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 H       0.6617856733   -1.6838033829   -0.0634977043
 C      -1.0781920574   -0.6266918036   -0.5618475022
 H      -1.6480132056   -0.0667952711   -1.3087248317
 C       0.8697158110   -1.0292225812   -2.1124062616
 C       0.4342583332   -0.2465518991   -3.1983447928
 C       2.0382611687   -1.7975293951   -2.2687316464
 C       1.1375353095   -0.2474058865   -4.4013050167
 H      -0.4639506749    0.3667868965   -3.1028290750
 C       2.7411032210   -1.8012071078   -3.4740784262
 H       2.3859338696   -2.4132006972   -1.4353627378
 C       2.2908855593   -1.0281265014   -4.5468911291
 H       0.7835632610    0.3636709003   -5.2350643638
 H       3.6369135127   -2.4173518071   -3.5785878662
 H       2.8349935569   -1.0317424675   -5.4941216679
 C      -1.5005951619    1.5118729794    1.4835373544
 C      -3.4058214756    0.2603348662    2.2923903097
 C      -2.3507028410    2.4175721045    2.3748570310
 H      -1.1963967007    1.9916131032    0.5396973843
 H      -0.5705663985    1.2284095027    2.0205516930
 C      -3.0860051761    1.4055128779    3.2624559475
 H      -4.4143210504    0.3745749229    1.8549855640
 H      -1.7478604457    3.1426484899    2.9403634249
 H      -3.0703257083    2.9801621378    1.7574554833
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 H      -2.4132079519    1.0485033107    4.0584323656
 H      -3.3802151458   -0.7185355444    2.7957157331
 N      -2.3789948358    0.3631130591    1.2379259300
 C      -1.8173873703   -0.8342501363    0.7360020824
 H      -2.6392350757   -1.5504260725    0.5633527491
 O      -0.9798588187   -1.5477390106    1.6991319229
 H      -1.2556048246   -3.0730836781    2.5931151189
 H      -0.5931031119   -3.4198312347    0.8576542910
 C      -0.9084503292   -4.9993569270    2.1002758604
 S      -0.9241579834   -6.6502712641    2.3809853537
 C      -2.0485377361   -4.0588120512    4.1654140804
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 C      -3.4638154446   -3.8185428040    6.6016225303
 C       0.1615776869   -5.0221588910   -0.1768755883
 C       1.0857147605   -6.0720608745   -0.0859454130
 C      -0.1544469170   -4.4904873274   -1.4371352614
 C       1.6767135700   -6.5734452333   -1.2476657959
 C       0.4517373761   -4.9967350345   -2.5856361559
 C       1.3705124218   -6.0456373835   -2.5034903868
 N      -1.3795470741   -4.0309496735    2.9426681145
 N      -0.4265551592   -4.4227039337    0.9476153827
 H       1.3389274956   -6.4889063286    0.8854228405
 H      -0.8731030127   -3.6750459672   -1.5152877915
 H       1.8403351395   -6.4456743087   -3.4017974927
 H      -2.0452817683   -1.8995413735    4.1651624844
 H      -2.2090942691   -6.1901886579    4.4682447326
 H      -4.0176242511   -3.7307781464    7.5349773562
 C       0.0718490268   -4.4641775225   -3.9436440514
 C       2.7221060457   -7.6535016485   -1.1284807018
 C      -3.4240390665   -1.2992416665    6.3783188349
 C      -3.4951473053   -6.3127544641    6.8523371191
 F      -0.5609605471   -3.2827508502   -3.8714665645
 F       1.1493977206   -4.3027158156   -4.7331220367
 F      -0.7534497280   -5.3141278188   -4.5886952314
 F      -4.3547162754   -0.7277373499    5.5829155324
 F      -2.3561992451   -0.4753726337    6.3634646261
 F      -3.9151520041   -1.3011515068    7.6251247460
 F       2.7981149454   -8.4038256019   -2.2412088551
 F       3.9486922430   -7.1303062922   -0.9255820849
 F       2.4762361687   -8.4796521083   -0.0981461697
 F      -2.5198208244   -6.6484471233    7.7206119307
 F      -4.6175372493   -6.1448238793    7.5742202180
 F      -3.6857524960   -7.3734164176    6.0503078861
 H      -0.2065047642   -1.0054358143    1.9201369520


IN0

0 1
 C      -2.2321817759   -0.1469664624   -2.0684703733
 H      -2.4890221276    0.8824015986   -2.3344728052
 C      -0.9116164390   -0.4941083692   -2.0443435163
 H      -0.6018236734   -1.5073516490   -1.7877704080
 C       0.0833474013    0.4847536008   -2.3079017424
 H      -0.2105319644    1.5333197231   -2.4017755989
 C      -3.3548362905   -1.0206628705   -1.7905904628
 C      -3.1886383663   -2.3209445044   -1.2612481643
 C      -4.6603016941   -0.5442048783   -2.0311042107
 C      -4.2987482007   -3.1155714344   -1.0002755979
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 C      -5.7685555161   -1.3497399119   -1.7758786784
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H	-6.7743744648	-0.9675631463	-1.9609220942
H	-6.4577253947	-3.2625718924	-1.0444661467
C	1.9512785518	-1.1230372113	-2.4279458165
C	2.3738467065	1.2798136342	-2.6557546865
C	3.3807629895	-0.9005964083	-2.9273417166
H	1.3636738102	-1.8006885419	-3.0619323628
H	1.9115558843	-1.5045956454	-1.3981421463
C	3.7029504828	0.5391032104	-2.5028242649
H	2.2471112830	1.7065682883	-3.6633979639
H	4.0781921239	-1.6332681111	-2.5023589955
H	3.4104011103	-0.9945814415	-4.0241705480
H	4.4968835367	0.9969276558	-3.1076943470
H	4.0259964836	0.5675455139	-1.4553003449
H	2.2153463835	2.0651059835	-1.9025038514
N	1.3537981596	0.2277145675	-2.4562652855
H	-0.5400801755	-1.8612225105	0.6711368742
C	0.3779473123	0.4979682633	0.9411997372
S	0.6117382573	2.1557345893	0.5535683606
C	2.8433023871	-0.1996295675	0.9776030878
C	3.5270632397	1.0209857996	1.1352677053
C	3.6064362048	-1.3628940529	0.7344068300
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NI

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TS02a

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TS02b

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exchange demonstrating that both situations render 7a nucleophilic, and evidencing that additional favorable circumstances should be present when the ion pair 3·6 is present.

[29] a) P. Merino, T. Tejero, *Synlett* **2011**, 1965–1977. b) P. Merino, in *Science of Synthesis. C-1 Building Blocks in Organic Synthesis* (Ed.: P. W. N. M. v. Leeuwen), Georg Thieme Verlag, Stuttgart, **2014**, pp. 311–331.

[30] Catalyst **1** is known to operate according to a steric model, particularly when it catalyzes Michael-type reactions. Consequently, only the attack through the less hindered *Re* face of the iminium needs to be considered. For details and references see SI.

[31] Quantification of iminium ion at equilibrium has been made by NMR, which has recently been showed to be useful for this sort of studies (See ref. 9b). Attempts of quantification with more sensitive UV were also made but overlapping of bands does not allow accurate measurements.

[32] The iminium ion is, actually, in equilibrium with the substrates (aldehyde and catalyst) and the intermediate hemiaminal so, it is necessary to consider the thermodynamic (and not the kinetic) of the process. Admittedly, it is necessary to establish equilibrium conditions providing enough concentration of iminium to feed the reaction.

[33] T. Okino, H. Yasutaka, Y. Takemoto *J. Am. Chem. Soc.* **2003**, *125*, 12672–12673.

[34] X. Li, H. Deng, B. Zhang, J. Y. Li, L. Zhang, S. Z. Luo, J. P. Cheng *Chem. Eur. J.* **2010**, *16*, 450–455.

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Lithium Catalysis |*Hot Paper*|

Azomethine Ylides from Nitrones: Using Catalytic *n*BuLi for the Totally Stereoselective Synthesis of *trans*-2-Alkyl-3-oxazolines

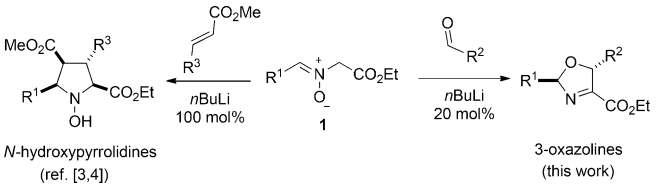
Veronica Juste-Navarro,[a] Ignacio Delso,[b] Tomás Tejero,[a] and Pedro Merino*[a]

Dedicated to Professor Miguel Yus for his contribution to the field of organolithium chemistry

Abstract: The cycloaddition of azomethine ylide *N*-oxides (nitrone ylides) with aldehydes provides 3-oxazolines in a completely stereoselective manner in the presence of a catalytic amount of *n*-butyllithium. The process involves an initial nucleophilic attack on the aldehyde, followed by intramolecular oxygen addition to the nitrone moiety and lithium-assisted elimination of water, regenerating the catalytic species. Various Li-based catalytic systems are possible and the in situ generated water is required for continuing the catalytic cycle. The best results are observed with 20 mol% of *n*-butyllithium, whereas the use of stoichiometric amounts inhibit the rate of catalysis. Experimental, spectroscopic, and computational mechanistic studies have provided evidence of lithium-ion catalysis and rationalized several competing catalytic pathways

The chemistry of azomethine ylides has been extensively studied in the past.[1] In particular, N-metalated azomethine ylides have received considerable attention because of their utility in asymmetric catalytic reactions.[2] We have reported the use of a novel class of azomethine ylides derived from nitrones **1** (azomethine ylide *N*-oxides or nitrone ylides) in a tandem Michael–Mannich reaction with α,β-unsaturated esters to provide *N*-hydroxypyrrolidines in excellent yields and complete stereoselectivity (Scheme 1).[3] The reaction required stoichiometric amounts of *n*BuLi to generate the ylide, and the lithium ion for activating the reagents in both steps.[4]

Organolithium compounds have been extensively employed as bases in stoichiometric amounts for metalation reactions,[5] but their use as catalysts, other than in polymerization reactions,[6] is an ongoing research challenge.[7] Although several catalytic processes involving lithium salts have already been



Scheme 1. Reactivity of *N*-(ethoxycarbonylmethyl) nitrone precursors (**1**) of nitrone ylides.

documented for lithium chloride,[8] lithium bromide,[9] lithium perchlorate[10] and, to a lesser extent, lithium hydroxide,[11] there is currently only one report dealing with the use of an organic alkali metal compound in catalytic reactions.[12] In continuation of our work on the reactivity of nitrone ylides with electrophiles, we have investigated the reaction with aldehydes and found that using catalytic amounts of *n*BuLi, 3-oxazolines can be obtained in good yields and in a completely selective fashion (Scheme 1).[13]

3-Oxazolines are heterocyclic systems of interest[14] yet difficult to prepare, and no methods are reported for the stereoselective synthesis of their 2,5-disubsutituted derivatives. In contrast to well-established methods for accessing 2-oxazolines,[15] the preparation of isomeric 3-oxazolines (2,5-dihydrooxazoles) have received far less attention.[16] Taking into account a retrosynthetic analysis considering the fragments that join to form the heterocyclic nucleus (Figure 1), all of these methods belong to the [C+OC$_2$N] approach. Very recently, Zhong and co-workers developed an acid-promoted formal [3+2] cycloaddition between donor–acceptor oxiranes and nitriles,[17] the only method representing a [COC+CN] approach.

Here, we report a novel and efficient catalytic stereospecific synthesis of *trans*-2-alkyl-5-substituted-3-oxazolines based on a [OC+CNC] approach (Figure 1). Various catalytic systems, all of them based on a lithium salt, are possible. Among them, *n*BuLi provided the best results acting as an efficient pre-catalyst. To the best of our knowledge, this is the first method that describes a catalytic synthesis of substituted 3-oxazolines in a completely stereoselective manner and uses aldehydes as

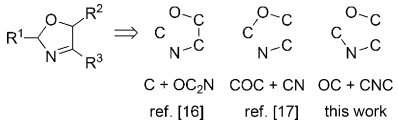


Figure 1. Retrosynthetic approaches for 3-oxazolines.

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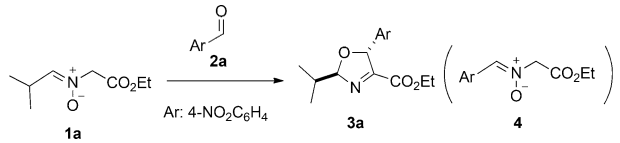
starting materials. A rationale based on DFT computational studies is provided to explain both the stereoselectivity and the catalytic cycles involved in the reaction.

The synthetic approach began with the preparation of novel *C*-alkyl nitrones **1** following the methodology previously reported by us.[18] Initially, we screened reaction conditions developed in our group for nitrone ylides.[3] Optimization studies are given in Table 1.

Table 1. Synthesis of 3-oxazolines **3**: Optimization of reaction conditions.



1a 3a 4

Entry	Base (equiv)	Li or Cu salt (equiv)	*T* [°C]	*t* [h]	Solvent	Yield [%][a]
1	Et_3N (1.0)	LiBr (1.0)	25	24	MeCN	80
2	Et_3N (1.0)	LiBr (1.0)	0	72	MeCN	72
3	Et_3N (1.0)	LiBr (1.0)	50	6	MeCN	70
4	Et_3N (1.0)	LiBr (1.0)	25	24	CH_2Cl_2	68
5	Et_3N (1.0)	LiBr (1.0)	25	24	DMSO	36
6	Et_3N (1.0)	CuBr (1.0)	25	24	MeCN	15[b]
7	Et_3N (1.0)	LiOAc (1.0)	25	24	MeCN	60
8	DBU (1.0)	LiBr (1.0)	25	24	MeCN	91
9	DABCO (1.0)	LiBr (1.0)	25	24	MeCN	94
10[b]	DABCO (1.0)	LiBr (1.0)	25	24	MeCN	10[c]
11	DABCO (1.0)	LiBr (0.5)	25	24	MeCN	88
12	DABCO (1.0)	LiBr (0.2)	25	24	MeCN	46
13	DABCO (0.5)	LiBr (1.0)	25	24	MeCN	90
14	DABCO (0.5)	LiBr (0.5)	25	24	MeCN	92
15	DABCO (0.2)	LiBr (0.2)	25	48	MeCN	30 (30)
16	LiOH (1.0)	–	25	12	MeCN	87 (8)
17[b]	LiOH (1.0)	–	25	12	MeCN	10[c]
18	LiOH (1.0)	–	25	12	EtOH	68
19	LiOH (0.5)	–	25	12	MeCN	80 (15)
20	LiOH (0.2)	–	25	96	MeCN	10 (50)
21	LiOH (0.1)	–	25	96	MeCN	n.r.[c]
22	*n*BuLi (1.0)	–	−80	24	THF	< 10[c]
23	*n*BuLi (1.0)	–	RT[d]	12	THF	74
24	*n*BuLi (1.0)	–	−40[d]	4	THF	40[c]
25	*n*BuLi (0.5)	–	−40[d]	4	THF	90
26	*n*BuLi (0.2)	–	−40[d]	4	THF	90[e]
27	*n*BuLi (0.1)	–	−40[d]	24	THF	68

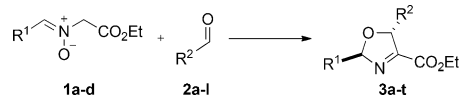
[a] Only the *trans*-isomer was obtained. When compound **4** was also obtained, the yield is given in brackets. [b] The reaction was conducted in the presence of 4 Å MS. [c] Starting materials were recovered. [d] *n*BuLi was added at −80 °C and after 5 min the reaction was warmed to the stated temperature. [e] An identical result was obtained by carrying out the reaction at −80 °C to RT.

The use of stoichiometric amounts of triethylamine and LiBr (Table 1, entry 1) led exclusively to *trans*-3-oxazoline **3a**, the elimination product of the initially expected *N*-hydroxypyrrolidine.[19] The reaction can be carried out at 0 or 50 °C for longer or shorter reaction times, respectively, with minimum loss of yield (entries 2 and 3). Both the use of solvents other than acetonitrile (entries 4 and 5), and lithium salts other than LiBr (entries 6 and 7) caused an evident decrease of the yield. Changing the base to DBU (entry 8) or DABCO (entry 9) improved the yield considerably to more than 90%. However, when the reaction was carried out in the presence of molecular sieves (entry 10), the reaction showed a conversion of only 10% after 24 h and the starting materials were recovered. We studied the possibility of using catalytic amounts of base and/or lithium salt (entries 11–15) and found that 50 mol% of both DABCO and LiBr led to the same result as that using stoichiometric amounts. Unfortunately, decreasing to 20 mol% led to a considerable loss of yield (30%) and formation of undesired nitrone **4** as a result of transoximation between the starting nitrone **1a** and aldehyde **2a**, through hydrolysis of the former. In this context, we did not observed cross-reactivity between **4** and **2a**. Next, we consider the possibility of integrating both base and lithium in the same species and found that LiOH promotes the reaction in 87% yield (entry 16) although 8% of **4** was obtained. Again, the presence of molecular sieves blocked the reaction (entry 17). To increase the solubility of LiOH, ethanol was tested as a solvent but lower yield was obtained (entry 18). The use of catalytic amounts led to either increased transoximation or no reaction (entries 19–21). When *n*BuLi was used at low temperature, the reaction did not progress after 24 h (entry 22), but slow warming of the reaction to ambient temperature over 12 h increased the yield to 74% (entry 23). In an attempt to adjust the reaction conditions, we checked the reaction after warming up to −40 °C over 4 h (entry 24). At this time, only a 40% yield was observed and starting materials were recovered indicating that the reaction had not finished. On the other hand, the use of substoichiometric amounts of *n*BuLi (entry 25) led to a clean reaction in a high yield under otherwise the same conditions, revealing a faster rate of the reaction. By decreasing *n*BuLi to 20 mol%, the same result was obtained (entry 25 versus 26) and no transoximation was observed. With lower amounts of *n*BuLi, the reaction required more time (entry 27), but still 68% yield was obtained. In all cases, the *trans*-isomer was the only observed product. The structure of compound **3a** was confirmed by X-ray crystallography.[20] At this point, it became evident that the process was catalytic involving a lithium species and that different mechanisms were occurring under stoichiometric and catalytic conditions.

The optimized reaction conditions (20 mol% BuLi; Table 1, entry 26) were applied to various nitrones and aldehydes (Table 2). For the purpose of comparison, the reactions were also carried out with 50 mol% DABCO/LiBr (Table 1, entry 14) and identical results were obtained. Thus, either set reaction of conditions could be used. The reaction proceeded smoothly for nitrones **1a–d** with both aliphatic and aromatic aldehydes. In the case of electron-rich aromatic aldehydes (Table 2, entries 4 and 5) and α,β-unsaturated aldehydes (Table 2, entries, 10, 11 and 17), additional reaction time was needed for achieving good yields. In the latter case, there was the possibility for 1,4-addition to occur but it was never observed.

Although *C*-alkyl nitrones afforded good reactivity, there still remained limitations on the substrate scope. When *C*-aryl nitrones were used, we did not observe any reactivity, supporting the well-known fact that *C*-aryl nitrones are less reactive than *C*-alkyl nitrones.[21] The lack of reactivity was also observed for heteroaryl nitrones (*C*-(2-pyridyl) and *C*-(2-furylyl)) and an α,β-

Table 2. Synthesis of 3-oxazolines **5**: scope of the reaction.[a]



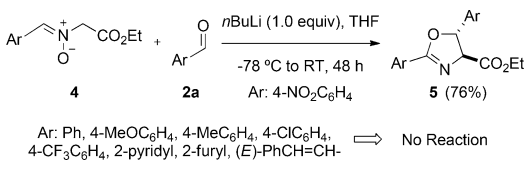
1a-d **2a-l** **3a-t**

Entry	R^1	R^2	1	2	3	Yield [%][b]
1	*i*Pr	4-$NO_2C_6H_4$	**1a**	**2a**	**3a**	90 (92)
2[c]	*i*Pr	4-$NO_2C_6H_4$	**1a**	**2a**	**3a**	74 (70)
3	*i*Pr	Ph	**1a**	**2b**	**3b**	89 (90)
4[d]	*i*Pr	4-MeC_6H_4	**1a**	**2c**	**3c**	78 (69)
5[e]	*i*Pr	4-$MeOC_6H_4$	**1a**	**2d**	**3d**	75 (64)
6	*i*Pr	*i*Pr	**1a**	**2e**	**3e**	86 (82)
7	*i*Pr	*i*Bu	**1a**	**2f**	**3f**	88 (89)
8	*i*Pr	cyclopentyl	**1a**	**2g**	**3g**	89 (85)
9	*i*Pr	$PhCH_2$	**1a**	**2h**	**3h**	93 (91)
10[d]	*i*Pr	(*E*)-MeCH=CH	**1a**	**2i**	**3i**	78 (71)
11[d]	*i*Pr	(*E*)-PhCH=CH	**1a**	**2j**	**3j**	69 (53)
12	*i*Bu	4-$NO_2C_6H_4$	**1b**	**2a**	**3k**	93 (90)
13	*i*Bu	Ph	**1b**	**2b**	**3l**	88 (85)
14	cyclohexyl	4-$NO_2C_6H_4$	**1c**	**2a**	**3m**	92 (90)
15	cyclohexyl	Ph	**1c**	**2b**	**3n**	90 (87)
16	cyclohexyl	*i*Pr	**1c**	**2e**	**3o**	78 (80)
17[d]	cyclohexyl	(*E*)-MeCH=CH	**1c**	**2i**	**3p**	72 (68)
18	cyclopentyl	4-$NO_2C_6H_4$	**1d**	**2a**	**3q**	92 (89)
19	cyclopentyl	Ph	**1d**	**2b**	**3r**	90 (86)
20	*i*Pr	2-piridyl	**1a**	**2k**	**3s**	86 (89)
21	*i*Pr	2-furyl	**1a**	**2l**	**3t**	92 (90)

[a] Reactions were run using nitrones **1** (0.5 mmol scale) and 1.0 equiv of aldehyde **2** in the stated solvent (0.5 M) unless otherwise indicated. Conditions A: 20 mol% *n*BuLi, THF, −80 to −40 °C, 4 h. Conditions B: 50 mol% DABCO, 50 mol% LiBr, MeCN, RT, 24 h. [b] Isolated yield after purification by column chromatography; values corresponding to conditions A (isolated yields for conditions B in brackets); only the *trans*-isomer was obtained. [c] 6.0 mmol (1.04 g nitrone) reaction scale. [d] 36 h reaction time. [e] 48 h reaction time.

unsaturated nitrone derived from cinnamalehyde. Indeed, only in the favorable case of nitrone **4** and aldehyde **2a** did we observe the formation of a product in good yield after 48 h (Scheme 2).[22] However, that product was confirmed to be the corresponding 2-oxazoline **5** by X-ray crystallography.[20] The formation of **5** is possibly a result of a double bond migration as a consequence of stabilization by conjugation with the aromatic ring.[23]

We also initiated preliminary studies on the asymmetric version of the reaction. Unfortunately, only negative results were obtained. Performing the standard reaction of **1a** and **2a** in the presence of 20 mol% (−)-sparteine provided the product in only 6% *ee*. The use of a chiral lithum alkoxide derived from (*R*)-BINOL (20 mol%) and *n*BuLi (20 mol%) afforded large amounts of transoximation (30% of **3a** and 45% of **4**), in a similar way to LiOH, and almost no chiral induction (10% *ee* for **3a**) was observed.



Scheme 2. Exceptional reaction of nitrone **4** with aldehyde **2a**.

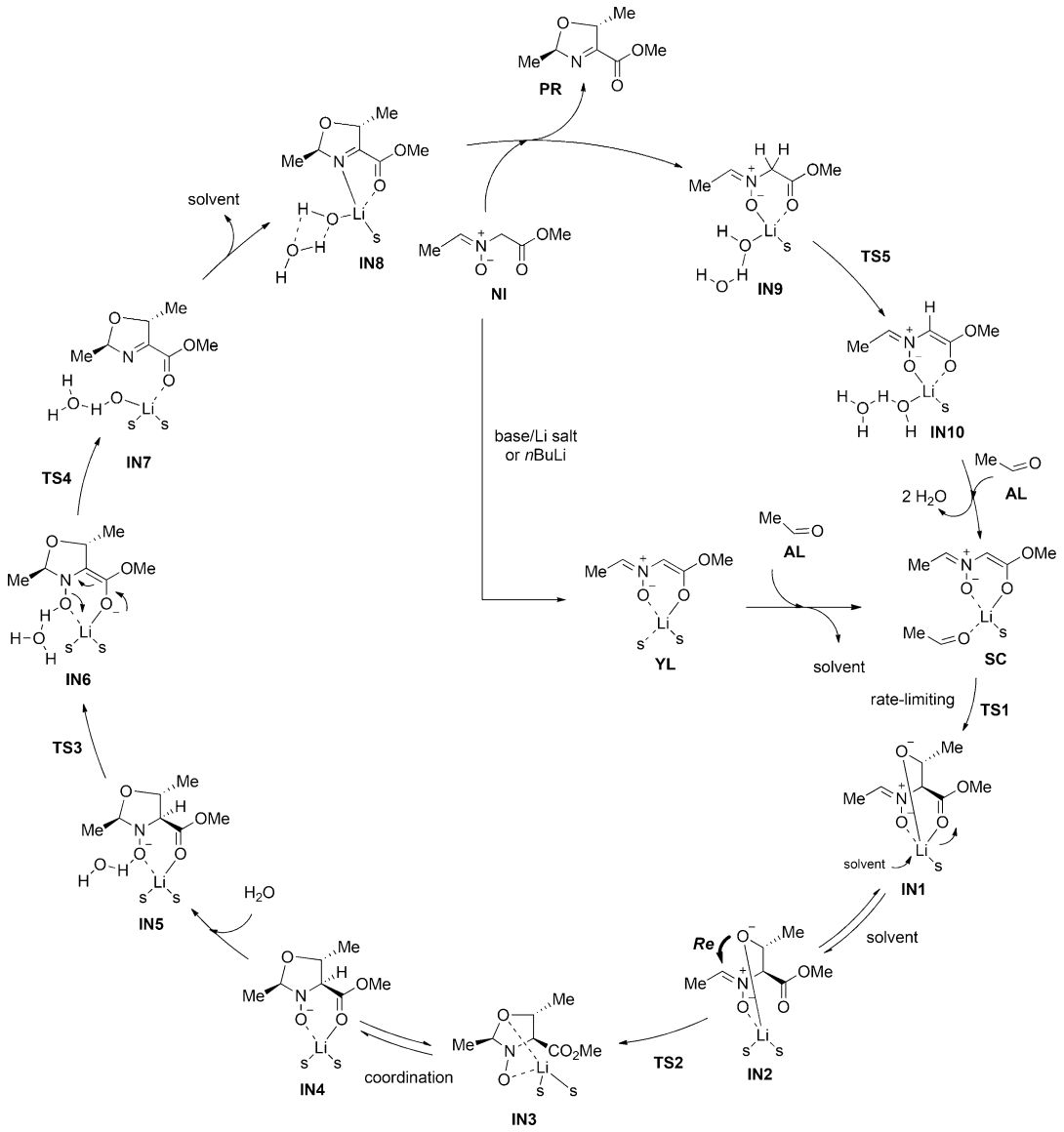
In our previous work with α,β-unsaturated esters and *C*-aryl nitrones like **4,** we demonstrated that the reaction was stepwise by isolating the initial Michael intermediate;[3] further computational studies[4] corroborated the mechanism providing the *N*-hydroxypyrrolidine as the final product of the reaction. However, for the reaction presented here between **1a** and **2a**, which can be conducted under catalytic conditions, any attempt of isolating either an intermediate or the *N*-hydroxypyrrolidine precursor from 3-oxazoline **3** failed. These observed differences, the fact that molecular sieves blocked the reaction demonstrating the need for water, and the observation that the reaction is faster with substoichiometric amounts of *n*BuLi prompted us to investigate the mechanism of the reaction both computationally and by use of NMR spectroscopy.

We modelled the reaction between nitrone **NI** and aldehyde **AL** catalyzed by *n*BuLi considering the formation of the corresponding nitrone ylide **YL** as the first step. Several approaches are possible for the reaction between **YL** and **AL**. A comprehensive study of all the possible pathways has been carried out at M06-2X/6-311+G(d,p)/PCM=THF level of theory using geometries optimized at M06-2X/6-31G(d)/PCM=THF level. Further discussion will only refer to the preferred pathway leading to the *trans*-isomer (for the complete computational analysis see the Supporting Information).

Once **YL** is formed, **AL** coordinates the lithium atom to form the starting complex **SC**, in which both reagents are activated. The catalytic cycle, illustrated in Scheme 3, starts from **SC,** the most stable intermediate in the cycle. The most favorable **TS1** leads to **IN1** with a barrier of $\Delta G = 5.0$ kcal mol^{-1}, which corresponds to the rate-limiting step. Further exchange of a solvent molecule is favored by 14.6 kcal mol^{-1} giving rise to **IN2**, which undergoes the preferred *Re* attack (**TS2** located 1.3 kcal mol^{-1} below the ground state) to generate **IN3**. Exchange of coordination in this intermediate forms **IN4** (7.3 kcal mol^{-1} more stable), which can then be transformed into **IN6** through a [1,3]-H shift.

The prototropy observed between **IN4** and **IN6** can take place via an intramolecular transition state (located 10.8 kcal mol^{-1} above the ground state, not shown in Scheme 3; see the Supporting Information) or the more stable **TS3** (located 14.2 kcal mol^{-1} below the ground state) after formation of **IN5**, involving a water molecule generated in the last step of the catalytic cycle. Under catalytic conditions, only the first round of the cycle takes place through the above-mentioned intramolecular transition state higher in energy, at which time water is produced and the catalytic cycle carries on through **IN5** and **TS3**.

In agreement with this hypothesis, the use of molecular sieves should drastically reduce the rate of the reaction, and indeed, this is observed experimentally. When equimolar amounts of base/LiBr are used, the reaction is completed in one round and in this case, the prototropy in **IN4** can be facilitated by the protonated base, also through a bimolecular process. In the case of using equimolar amounts of *n*BuLi, transformation of **IN4** should occur through the intramolecular transition state ([1,3]-H shift) higher in energy (see the Supporting



Scheme 3. Catalytic cycle for Li-catalyzed synthesis of 3-oxazolines.

Information). This justifies the reduced rate of the reaction observed with 1.0 equivalent of *n*BuLi. After formation of **IN6** from **IN5**, the reaction proceeds through **TS4** located at -21.6 kcal mol^{-1} below the ground state to form intermediate **IN7,** which, after releasing a solvent molecule, provides **IN8**.

Figure 2 illustrates the energy profile for the formation of the only observed *trans*-3-oxazoline **PR** and completion of the catalytic cycle. The driving force of the catalytic cycle illustrated in Scheme 2 is determined by the regeneration of **SC** from **IN8** (via **IN9, TS5**, and **IN10**) with concomitant release of the final product and two molecules of water (actually only one is produced per cycle). This final catalyst-turnover step involves a favored energy step ($\Delta G = -15.8$ kcal mol^{-1}) for the reaction of **1** (**NI**) with **2** (**AL**).

NMR experiments using 0.2 equivalents of *n*BuLi recording the complete reaction in real time showed the presence of the final product **3 a** without any addition of a proton source, confirming that an *N*-hydroxypyrrolidine could not be a real intermediate. However, when the reaction mixture was maintained at $-80\,^{\circ}$C both nitrone and aldehyde are consumed immediately giving rise to signals that are in agreement with the formation of **IN4** (see the Supporting Information). This intermediate was found to be stable at $-80\,^{\circ}$C for 4 h, and resulted in the formation of **3 a** after warming to $-40\,^{\circ}$C. Since the use of 1.0 equivalent of *n*BuLi does not allow the formation of water in the catalytic cycle, an alternative and more energetically favorable pathway must be occurring, which is indeed observed (see the Supporting Information). By using 0.2 equivalents of *n*BuLi, warming to $-40\,^{\circ}$C is sufficient for completing the reaction in 4 h. This demonstrates the faster pathway illustrated in Scheme 3, in which assistance of a water molecule renders the corresponding **TS3** lower in energy (in the alternative path where water is not involved, alternative **TS3'** is, indeed, 5.8 kcal mol^{-1} higher in energy). Thus, both computational and spectroscopic studies are in complete agreement with the experimental observations.

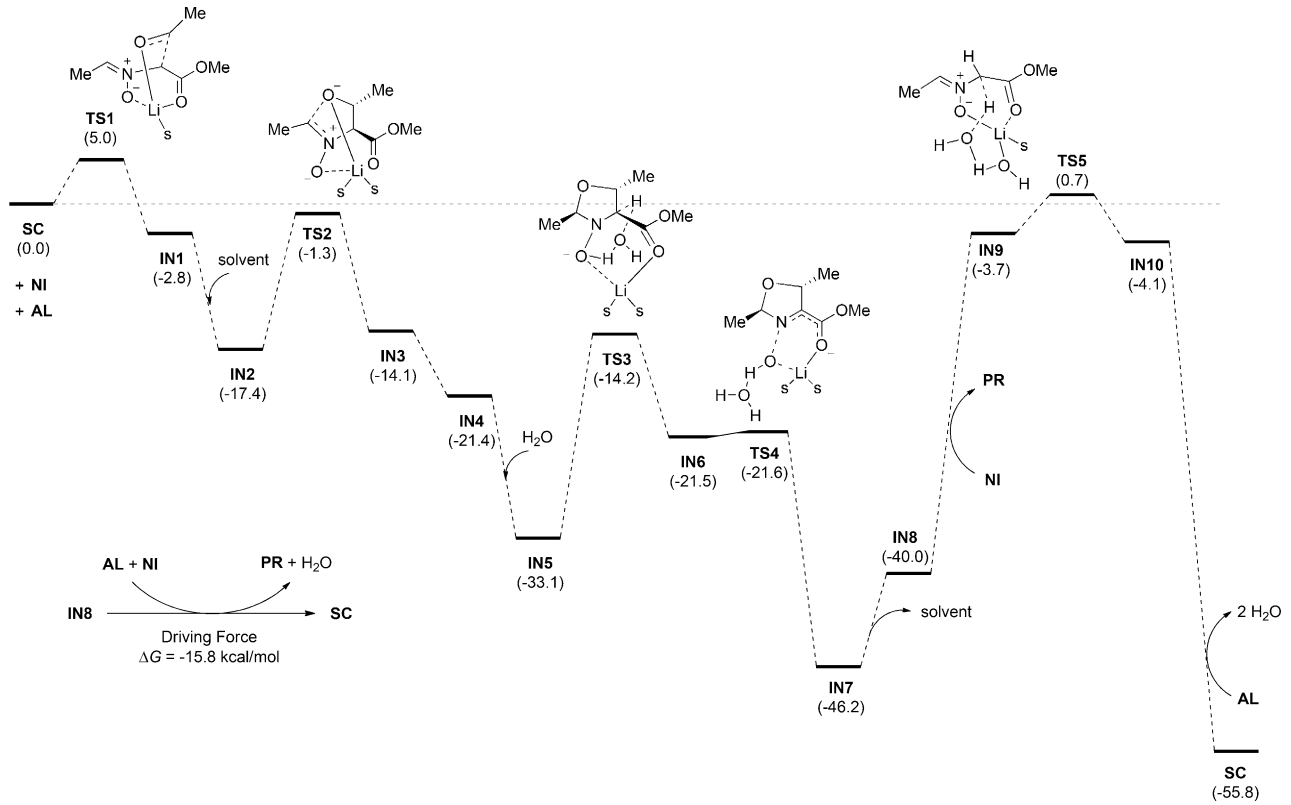


Figure 2. Energy surface for the reaction between **1** and **2** catalyzed by *n*BuLi. The most stable route corresponding to the formation of *trans*-**3** is shown.

In summary, a lithium-catalyzed route towards 3-oxazolines starting from novel azomethine ylide *N*-oxides (nitrone ylides) and aldehydes has been developed. Actually, lithium facilitates elimination of water, which serves to push the catalytic cycle forward. The combination of a base and a lithium salt or the use of *n*BuLi serves as a pre-catalyst to initiate the catalytic cycle, which is self-sufficient until starting materials are consumed. The only species formally regenerated in the catalytic cycle are the lithium atom, which must be solvated/coordinated throughout the entire cycle and the water, which might be considered to have an autocatalytic role. These results demonstrate that a lithium ion can act as a catalyst confirming previous computational results of Saa and Capo.[8e] Notably, an excess of water or the use of lithium salts like LiOH promote undesired nitrone hydrolysis leading to a transoximation, making the use of catalytic amounts of *n*BuLi a unique system for the progress of the reaction (using DABCO/LiBr is also possible but <50 mol% transoximation is also observed). The same problem of transoximation arises for the asymmetric version of the reaction when a chiral lithium alkoxide is used as the base. Both spectroscopic and computational studies are in agreement with the experimental observations, showing a faster reaction with substoichiometric amounts of *n*BuLi than with equimolar amounts. Also, these studies explain the necessity of water for the progress of the reaction at low temperature. Further endeavours directed towards other lithium-catalyzed reactions with nitrone ylides, including catalytic asymmetric versions of the reaction are currently in progress in our laboratories.

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Keywords: azomethine ylides · density functional calculations · lithium · nitrones · oxazolines

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[19] Apparently, compound **3 a** might be formed through dehydration of the corresponding *N*-hydroxypyrrolidine, which was the initially expected product in a similar way to the reaction between nitrone ylides and unsaturated esters (see ref. [3]). However, such a hydroxylamine is never formed (see below).

[20] CCDC 1444429 (**3 a**), and 1444430 (**3 f**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

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[22] Any other combination of nitrone and aldehyde gave no reaction, proving that both the aldehyde (for the first step) and the nitrone (for the second step) must be activated by the presence of electron-withdrawing groups.

[23] In addition to conjugation as a driving force, it should be noted that 2-oxazolines are more stable than 3-oxazolines.

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Azomethine Ylides from Nitrones: Using Catalytic *n*-BuLi for the Totally Stereoselective Synthesis of *trans*-2-Alkyl-3-Oxazolines

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Supporting Information

Theoretical Calculations

Computational Methods.

All of the calculations were performed using the Gaussian09 program.[1] Computations were done using the Thrular's functional M06-2X.[2] Standard basis sets 6-31G(d) and 6-311G(d,p) were employed and diffuse functions were added in 3-ζ calculations.[3] Geometry full optimizations were made at M06-2X/6-31G(d,p)/PCM=THF level and then single point calculations at M06-2X/6-311+G(d,p)/PCM=THF level were carried out in order to obtain more accurate values of the energies. This level of theory has been successfully employed in previous calculations with nitrone ylides.[4] All discussions are based on values of free energies (G). However, several of the individual reactions involved on the study are bimolecular processes (due, for instance, to coordination/decoordination of solvent molecules). In order to avoid errors due to entropic effects when comparing all stationery points in an only energy diagram, we used corrected free energy (G_{corr}) values following Sasaki's model.[5] Translational and rotational degrees of freedom in solution are highly suppressed owing to the interactions with solvent molecules and these interactions are not well-estimated by continuum solvent models like PCM; in consequence, thermodynamic corrections to potential energies calculated by using continuum solvation models overestimate the contributions of translational and rotational degrees of freedom to the entropy.[6] According to Sasaki's

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[1]Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knos-trans, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fos-trans, D. J. *Gaussian 09. Revision D1.*, Gaussian, Inc., Wallingford CT,: 2009.

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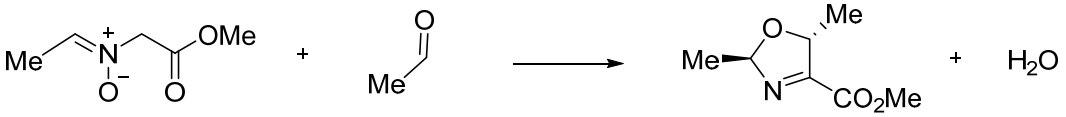
model only vibrational contributions to entropy must be considered calculating free energy as follows:

$$\Delta G_{corr} = \Delta H - T \cdot \Delta S_{vib}$$

It has been demonstrated that ΔG_{corr} is closer to the experimentally derived ΔG that the uncorrected calculated free energy.[6,7] The nature of stationary points was defined on the basis of calculations of normal vibrational frequencies (force constant Hessian matrix). The optimizations were carried out using the Berny analytical gradient optimization method.[8] Minimum energy pathways for the reactions studied were found by gradient descent of transition states in the forward and backward direction of the transition vector (IRC analysis),[9] using the second order González–Schlegel integration method.[10] The solvent effects modeled as a continuum model were considered for single points and full optimized highest level of theory employed using a relatively simple self-consistent reaction field (SCRF[11]) based on the polarizable continuum model (PCM) of Tomasi's group.[12] The electronic energies in solution were obtained by adding the total electrostatic energies obtained from the PCM calculations to the electronic energies in vacuo. The PCM and solvent = THF options were employed in the SCRF calculations. In addition, microsolvation of the lithium atom was considered by adding discrete molecules of dimethyl ether surrounding the lithium atom.[13] Molecular graphics have been performed with CYLview 1.0 software.[14] We use as models for the reaction nitrone **NI** and acetaldehyde **AL** to give 3-oxazoline **PR** (Scheme S1).



NI **AL** **PR**

Scheme S1. Model reaction

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Addition of Aldehyde to Nitrone Yide

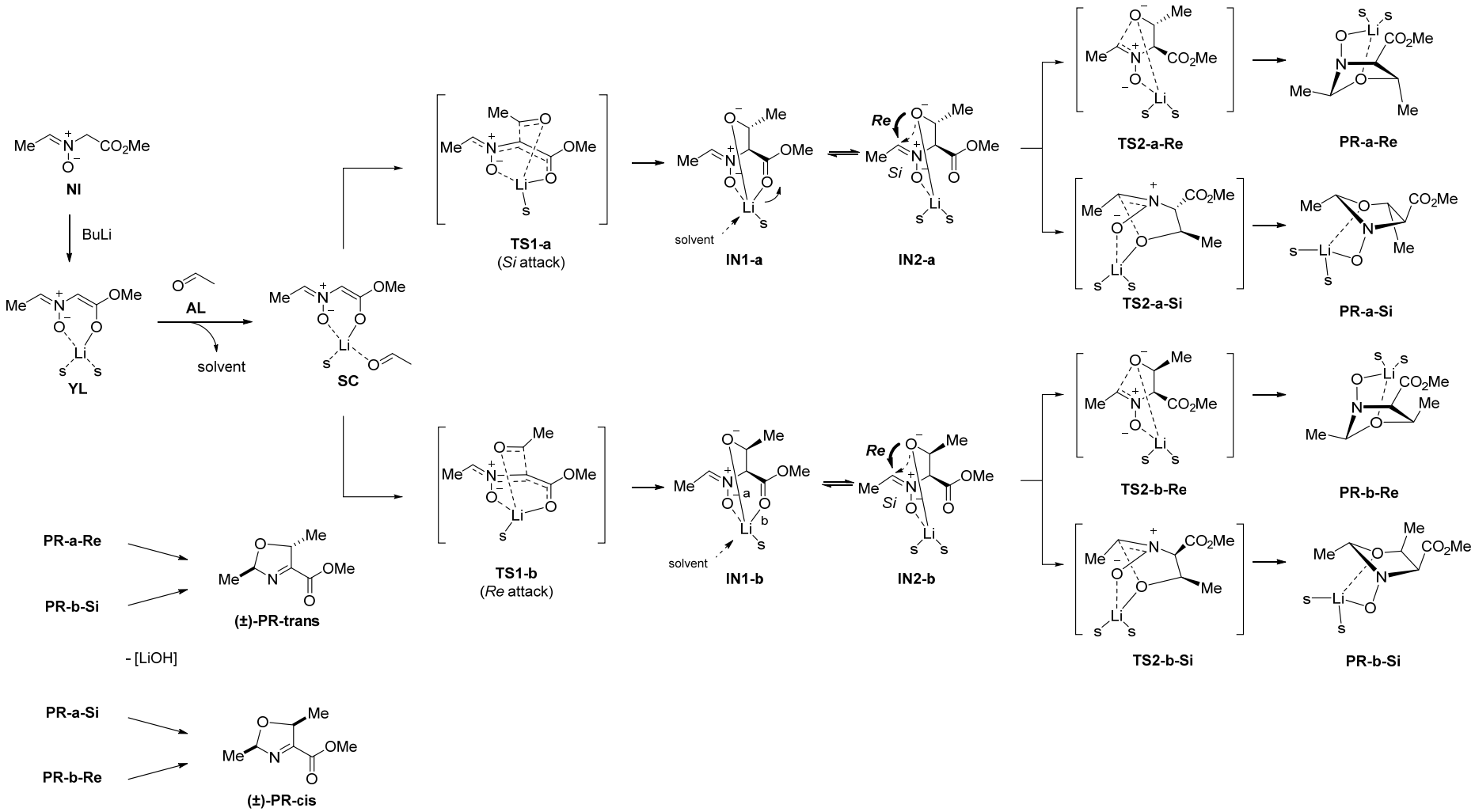
According to previous calculations with nitrone ylides[4] the first step of the reaction is the formation of the ylide **YL** by deprotonation of **NI** with *n*-BuLi followed by coordination of the aldehyde **AL** to form the starting complex **SC** (Scheme S2). This complex can evolve by two different pathways depending on the attacked face of the aldehyde. The corresponding transition structures **TS1-a** (*Si* atttack) and **TS1-b** (*Re*-attack) lead to intermediates **IN1-a** and **IN1-b**, which exchange a solvent molecule to form the more stable intermediates **IN2-a** and **IN2-b**.[4] These intermediates have enough flexibility to give two possible attacks by *Re* and *Si* faces of the nitrone (through **TS2-a-Re** and **TS2-a-Si** from **TS1-a**, and through **TS2-b-Re** and **TS2-b-Si** from **TS1-b**) leading to the corresponding cyclic products.[15] Table S1 collects energy values for all stationary points illustrated in Scheme S2. The energy diagram is given in Figure S1.

Table S1. Calculated (M06-2X/6-311+G(d,p)/PCM=THF//M06-2X/6-31G(d,p)/PCM=THF) absolute (hartrees) and relative (kcal/mol) energies of the stationary points corresponding to the reaction between nitrone ylide **YL** and acetaldehyde **AL**.

	E_0	ΔE_0[a]	G[b]	ΔG[a]	im. freq
AL	-153.754032		-153.750847		
YL	-792.994454		-793.009089		
SC	-791.826792	2.7	-791.842034	2.2	
TS1-a	-791.822845	5.2	-791.834036	7.2	-164.0
TS1-b	-791.820826	6.4	-791.832759	8.9	-160.9
IN1-a	-791.834782	-2.3	-791.846471	-0.6	
IN1-b	-791.833415	-1.5	-791.844866	0.4	
IN2-a	-946.765932	-10.9	-946.784201	-15.2	
IN2-b	-946.762965	-9.1	-946.779467	-12.3	-302.1
TS2-a-Re	-946.741928	4.1	-946.758536	0.9	-336.9
TS2-a-Si	-946.738278	6.4	-946.754428	3.5	-332.6
TS2-b-Re	-946.731067	10.9	-946.746983	8.1	-324.1
TS2-b-Si	-946.739056	5.9	-946.755488	2.8	
PR-a-Re	-946.76306	-9.1	-946.778872	-11.9	
PR-a-Si	-946.761098	-7.9	-946.777959	-11.3	
PR-b-Re	-946.75964	-7.0	-946.775658	-9.9	
PR-b-Si	-946.762761	-9.0	-946.779265	-12.1	

[a] Referred to reagents (**AL** + **YL**). A molecule of solvent (Me_2O: E_0 = -154.917396; G= -154.914378) has been included when necessary.

[15] Actually, intermediates **IN1d1** and **IN1d2** can also form the corresponding products through intramolecular *Re* attacks. However, the corresponding transition structures (not shown here) are higher in energy than **TS2** transition structures by more than 10 kcal/mol due to unfavourable strain exerted by coordination of lithium atom. Such strain is drastically reduced by formation of **IN2** intermediates.



Scheme S2. Reaction between **YL** and **AL**.

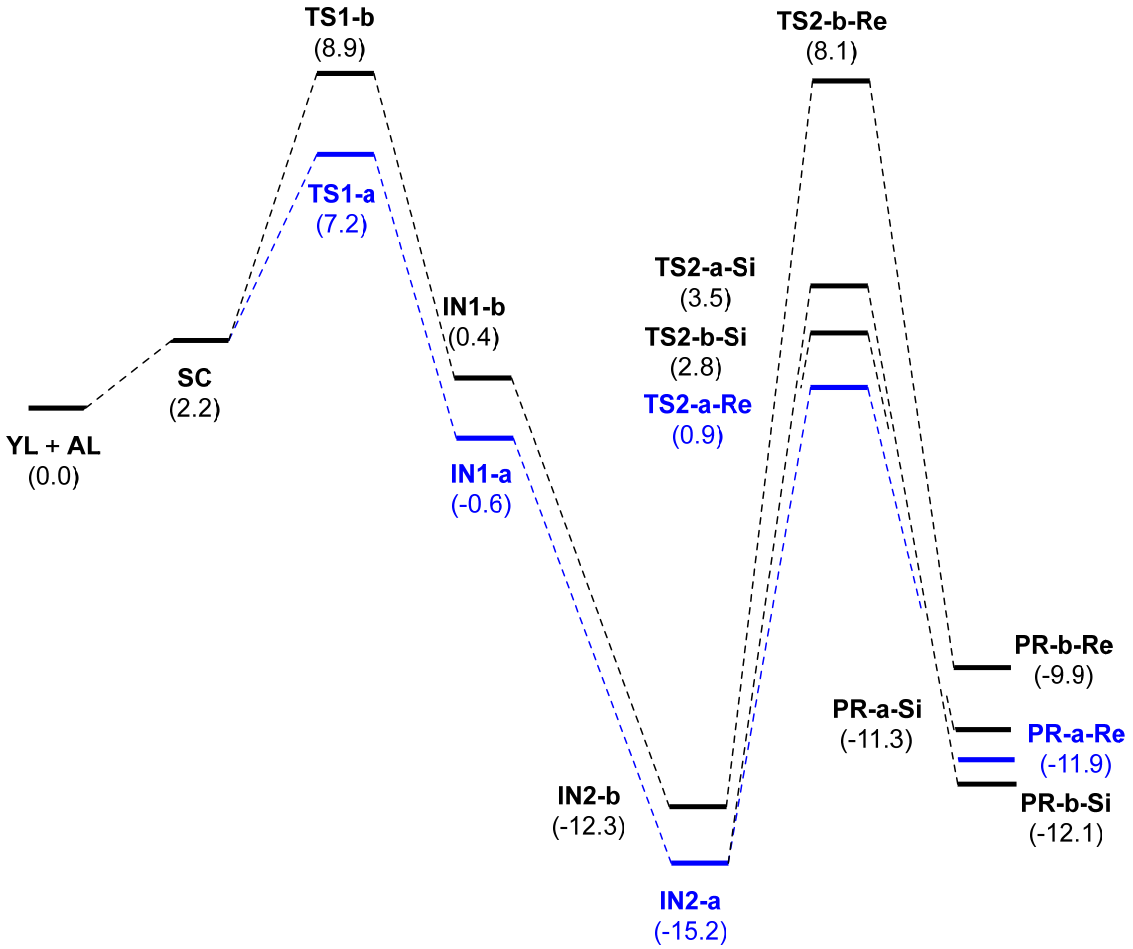


Figure S1. Energy diagram for the reaction between **YL** and **Al**. (see Scheme S2 and Table S1)

Further evolution of the intermediates to the final 3-oxazoline involves formal elimination of LiOH. Thus, compounds **PR-a-Re** and **PR-b-Si** converge to racemic **PR-trans** and compounds **PR-a-Si** and **PR-b-Re** converge to racemic **PR-cis** (Scheme S2). Further details on this transformation are given in the next subsection regarding the catalytic cycle The *cis/trans* selectivity should be evaluated by considering the energy differences illustrated in Figure S1. According the rate-limiting step (first step) the formation of **IN1-a** and then **IN2-a** is favoured. From the possible attacks in **IN2-a**, that by the *Re* face leading to *trans* isomer **PR-a-Re** through **TS2-a-Re** is also clearly favoured in good agreement with the experimental observations (only the *trans* isomer is obtained)

The geometries of optimized structures of transition structures are given in Figure S2

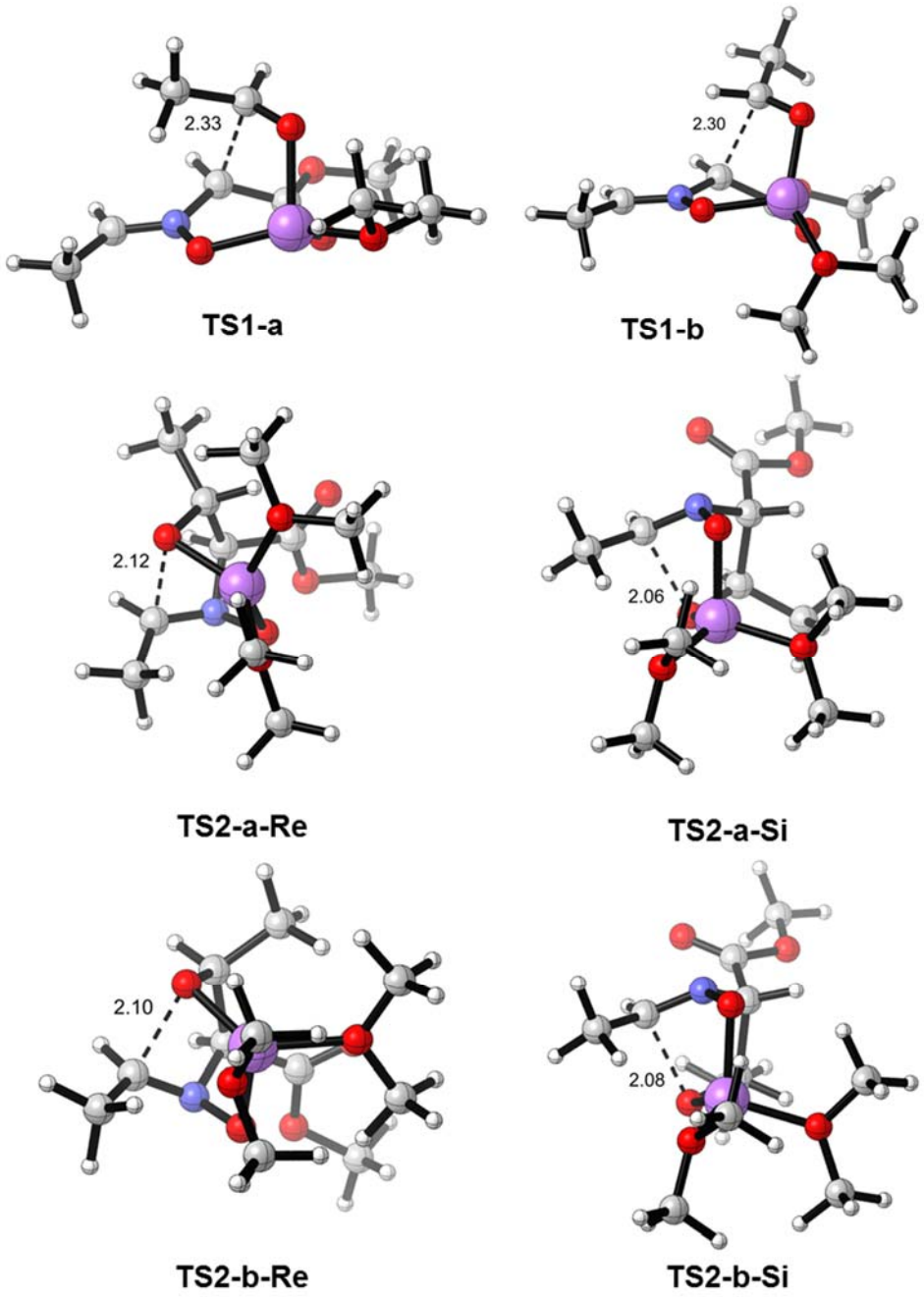


Figure S2. Optimized geometries of transition structures. Distances are given in angstrom

The Catalytic Cycle(s)

For the study of a representative catalytic cycle we chose the favoured route corresponding to the most stable **TS1-a** and **TS2-a-Re**.[16] The complete catalytic cycle including alternative pathways for stoichiometric reactions is illustrated in Figure S3.

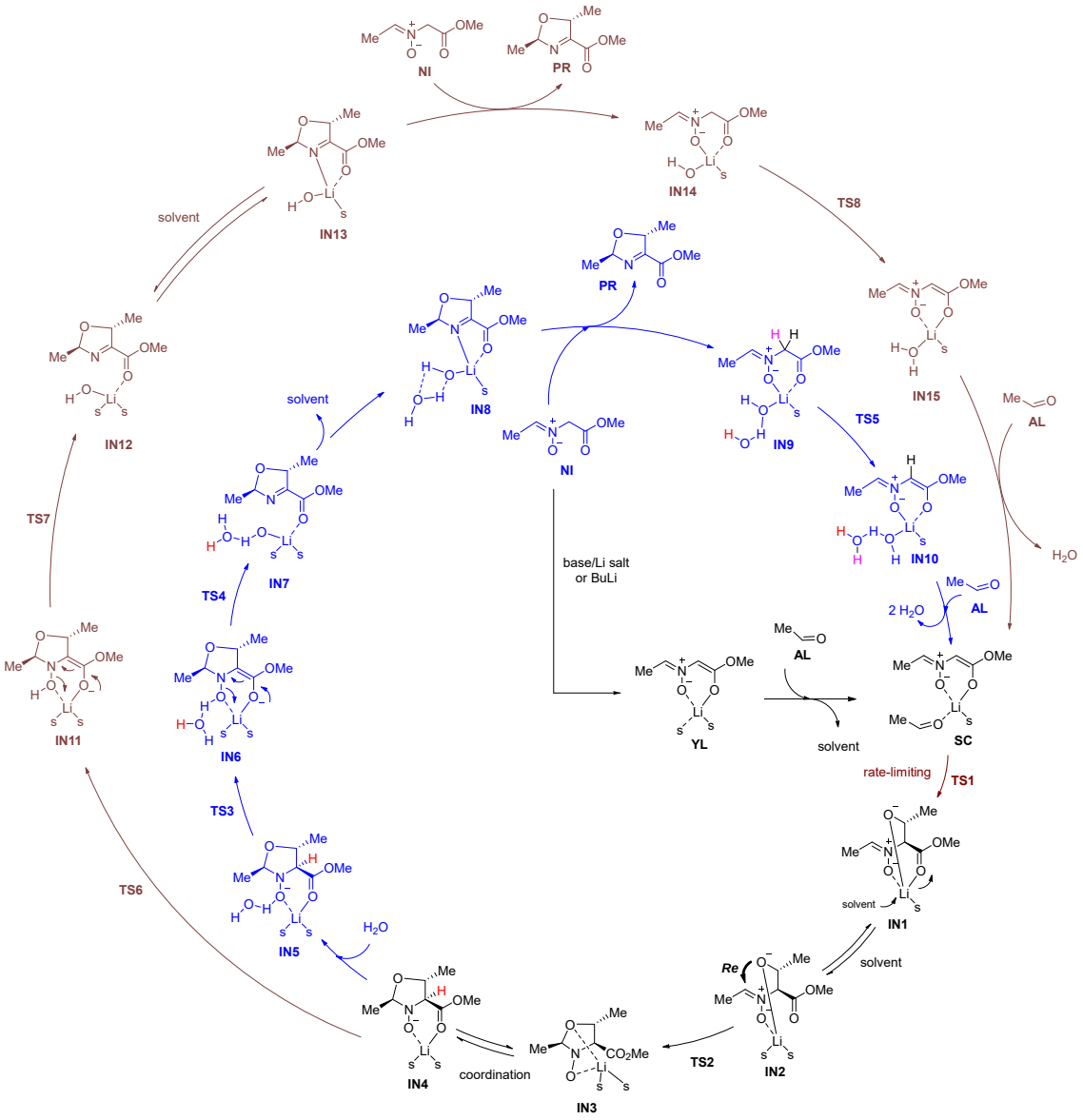


Figure S3. Catalytic cycles for the reaction between nitrone ylides and aldehydes. Blue path: catalytic amounts of *n*-BuLi. Red path: stoichiometric amounts of *n*-BuLi.

The reaction starts with the formation of the nitrone ylide **YL** by the action of the base. With 1.0 equiv. of *n*-BuLi all the nitrone **NI** is transformed into **YL** and once formed **IN4**

[16] The equivalence of stationary points defined above with that discussed in this section (the same given in the paper) is the following: **TS1-a** = **TS1**; **IN1-a** = **IN1**; **IN2-a** = **IN2**; **TS2-a-Re** = **TS2**; **PR-a-Re** = **IN3**

the reaction proceed through **TS6** (corresponding to an intramolecular 1,3-H shift) to give **IN11**. Regeneration of the activated complex **SC** takes place through intermediates **IN12**, **IN13**, **IN14** and **IN15.** In the transformation of **IN13** into **IN14** a unit of lithium hydroxyde is transferred from the product to the nitrone releasing the product of the reaction **PR**. Abstraction of the proton and coordination of the aldehyde liberates one molecule of water as a by-product of the reaction so, formally, it can be considered Li+ as the catalyst.

With catalytic amounts of *n*-BuLi the above illustrated process only takes place during the first round of the cycle. Then, the water molecule is available for assisting hydrogen migration in **IN4** by forming complex **IN5,** which is transformed into **IN6** through **TS3**, more stable than **TS6**. Regeneration of **SC** takes place through a similar pathway to that described above, in this case through intermediates **IN7**, **IN8**, **IN9** and **IN10** and finally releasing two water molecules (one regenerating that used in the formation of **IN5** and the other produced in the reaction). Table S2 collects all energy values for all the stationary points of the catalytic cycles illustrated in Figure S3. Optimized geometries of those stationary points are given in Figures S5-S8.

The energy profiles for both catalytic cycles (red:external and blu:internal) are depicted in Figure S4.Optimized geometries of stationery points are given in Figures S3-S5. A comparison between the two diagrams provides the rationalization for the observed experimental results. In the case of stoichiometric amounts of *n*-BuLi (external cycle) the rate limiting step of the process is **TS8**, whereas for catalytic amounts of *n*-BuLi (internal cycle) the rate-limiting step, lower in energy, is **TS1**. Consequently, the reaction with 1.0 equiv of *n*-BuLi is predicted to be slower than that using 0.2 equiv of *n*-BuLi.

Table S2. Calculated (M06-2X/6-311+G(d,p)/PCM=THF//M06-2X/6-31G(d,p)/PCM=THF) absolute (hartrees) and relative (kcal/mol) energies of the stationary points corresponding to the reaction between nitrone ylide **YL** and acetaldehyde **AL**.

	E_0	ΔE_0[a]	G[b]	ΔG[a]	im. freq
NI	-476.111148		-476.113358		
AL	-153.754032		-153.750847		
YL	-792.994454		-793.009091		
SC	-791.82679		-791.842028		
PR	-553.538118		-553.541497		
IN1	-791.834782	-5.0	-791.846471	-2.8	
IN2	-946.765932	-13.6	-946.784201	-17.4	
IN3	-946.76306	-11.8	-946.778872	-14.1	
IN4	-946.771829	-17.3	-946.790442	-21.4	
IN5	-1023.191662	-26.0	-1023.21148	-33.1	
IN6	-1023.174434	-15.1	-1023.19310	-21.6	
IN7	-1023.211712	-38.5	-1023.23242	-46.2	
IN8	-868.292348	-37.3	-868.308049	-40.0	
IN9	-790.888235	-2.0	-790.901824	-3.7	
IN10	-790.887132	-1.3	-790.902415	-4.1	
IN11	-946.763152	-11.9	-946.781614	-15.8	
IN12	-946.808325	-40.2	-946.827463	-44.6	
IN13	-791.879994	-33.4	-791.894264	-32.8	
IN14	-714.461270	11.0	-714.471357	13.9	
IN15	-714.477923	0.6	-714.488527	3.1	
TS1	-791.822845	2.5	-791.834036	5.0	-164.0
TS2	-946.741929	1.4	-946.758537	-1.3	-302.1
TS3	-1023.162917	-7.9	-1023.18131	-14.2	-1546.8
TS4	-1023.174774	-15.4	-1023.19310	-21.6	-371.4
TS5	-790.881127	2.4	-790.894816	0.7	-944.0
TS6	-946.723095	13.2	-946.739209	10.8	-1721.5
TS7	-946.759638	-9.7	-946.777070	-13.0	-364.4
TS8	-714.457144	13.6	-714.467629	16.2	-1115.9

[a] Referred to starting complex **SC**. Molecules of water (G_{corr} = -76.4023363) or dimethyl ether (G_{corr} = -154.914378) are used for compensating when necessary [b]Calculated considering exclusively vibrational entropy.

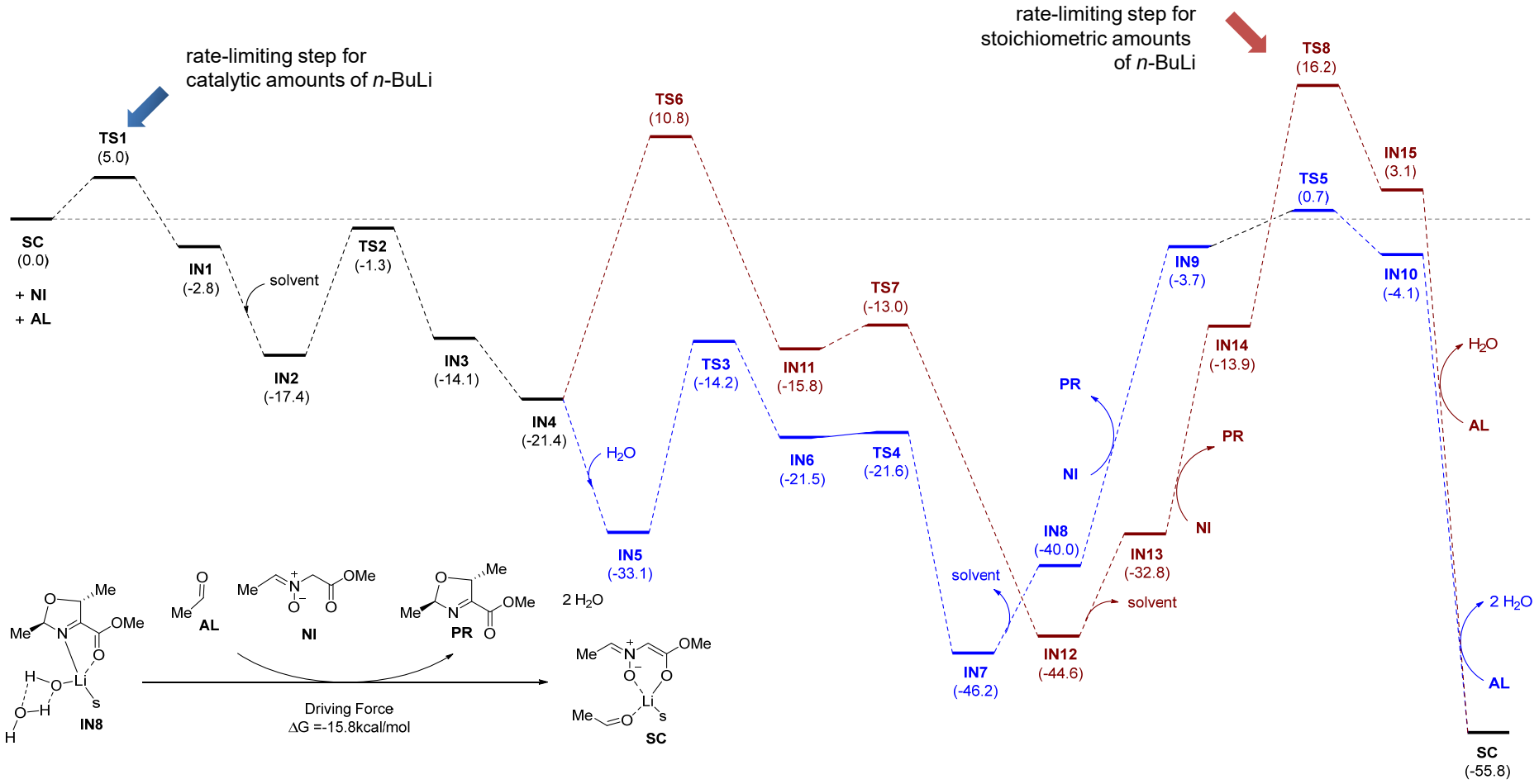


Figure S4. Energy profiles for the catalytic cycles illustrated in Figure S3.

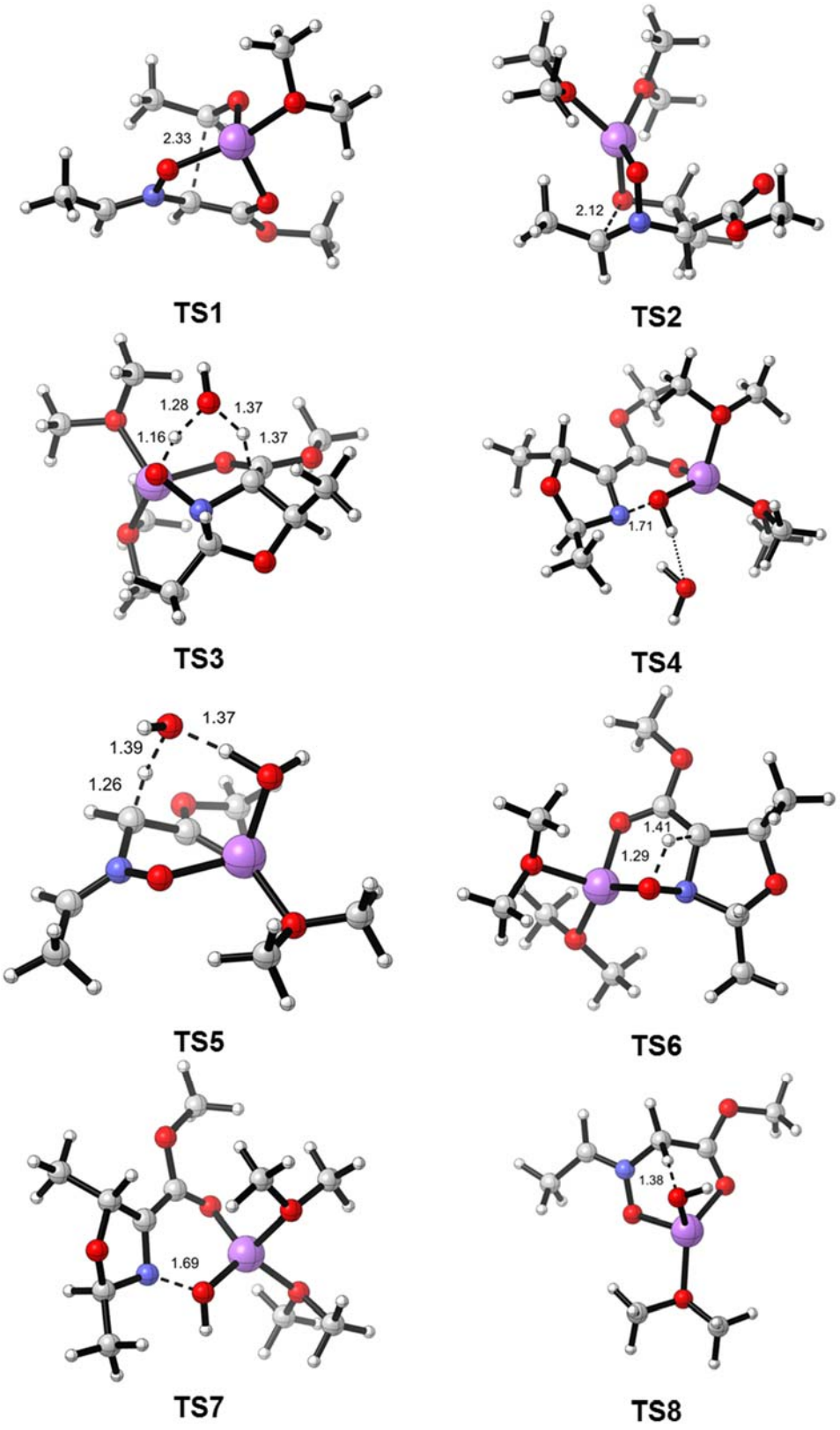


Figure S5. Optimized geometries of transition structures. Distances are given in angstrom

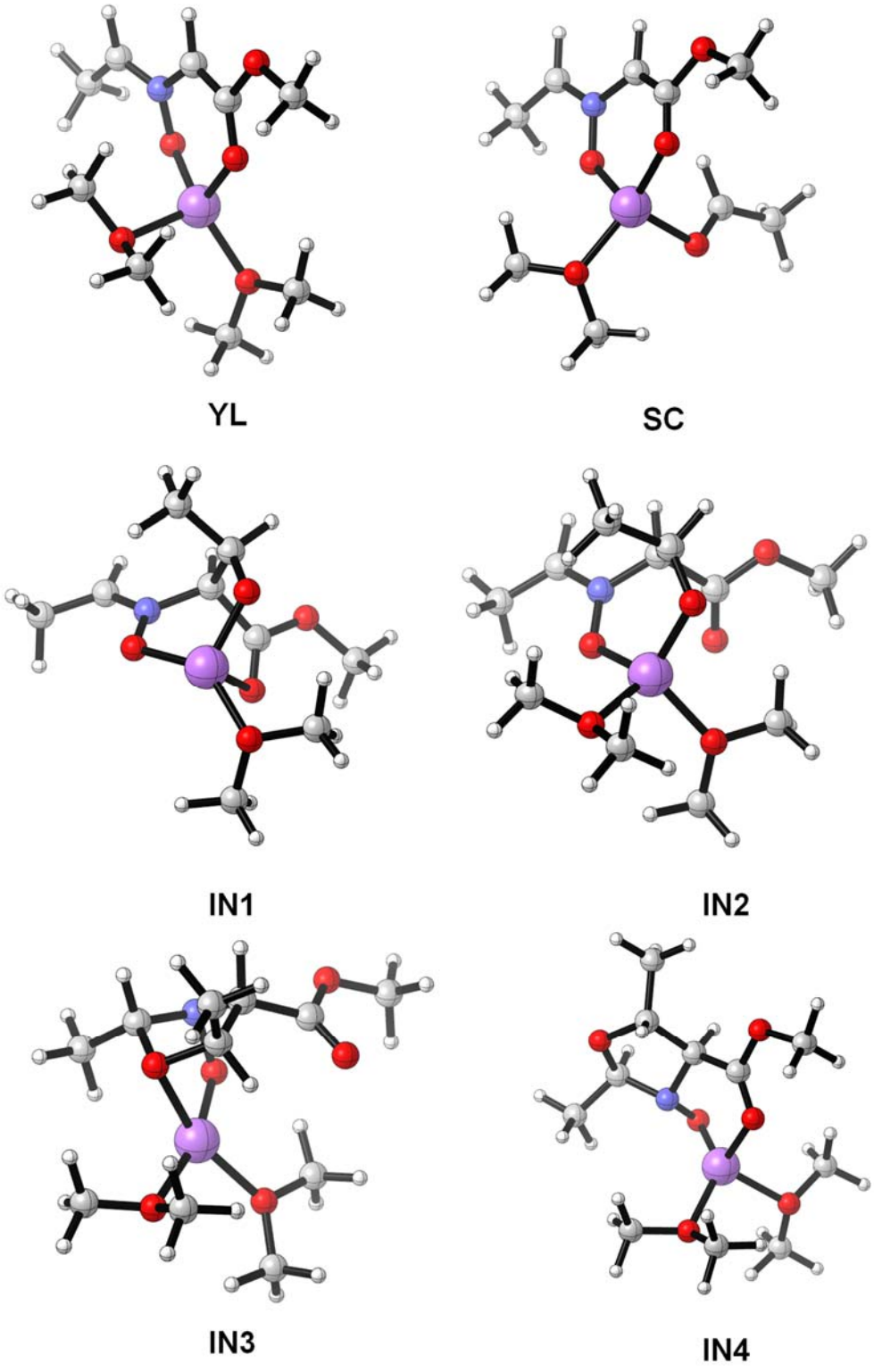


Figure S6. Optimized geometries of reactantans and intermediates **IN1**-**IN4**.

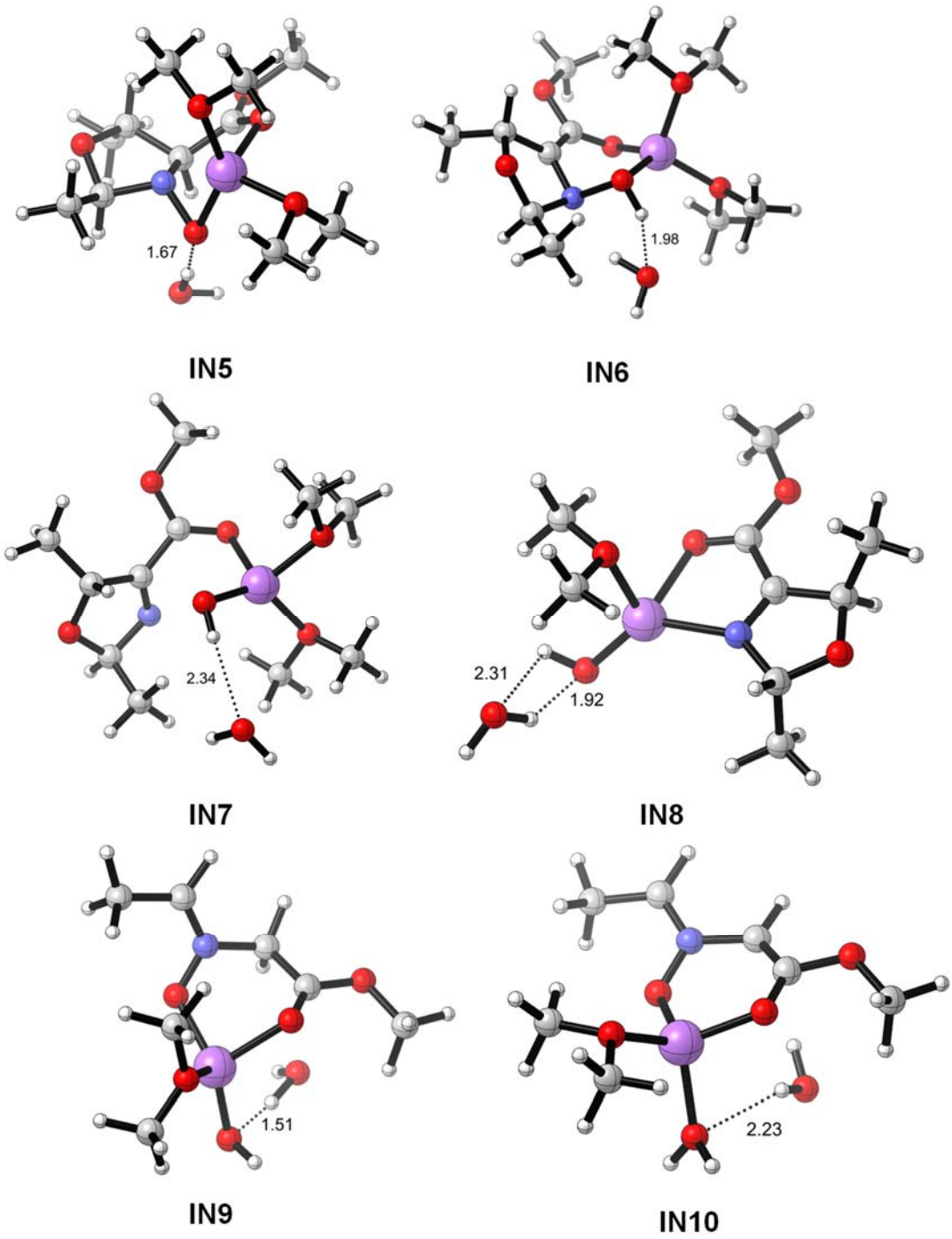


Figure S7. Optimized geometries of reactantans and intermediates **IN5-IN10**. Distances are given in angstrom

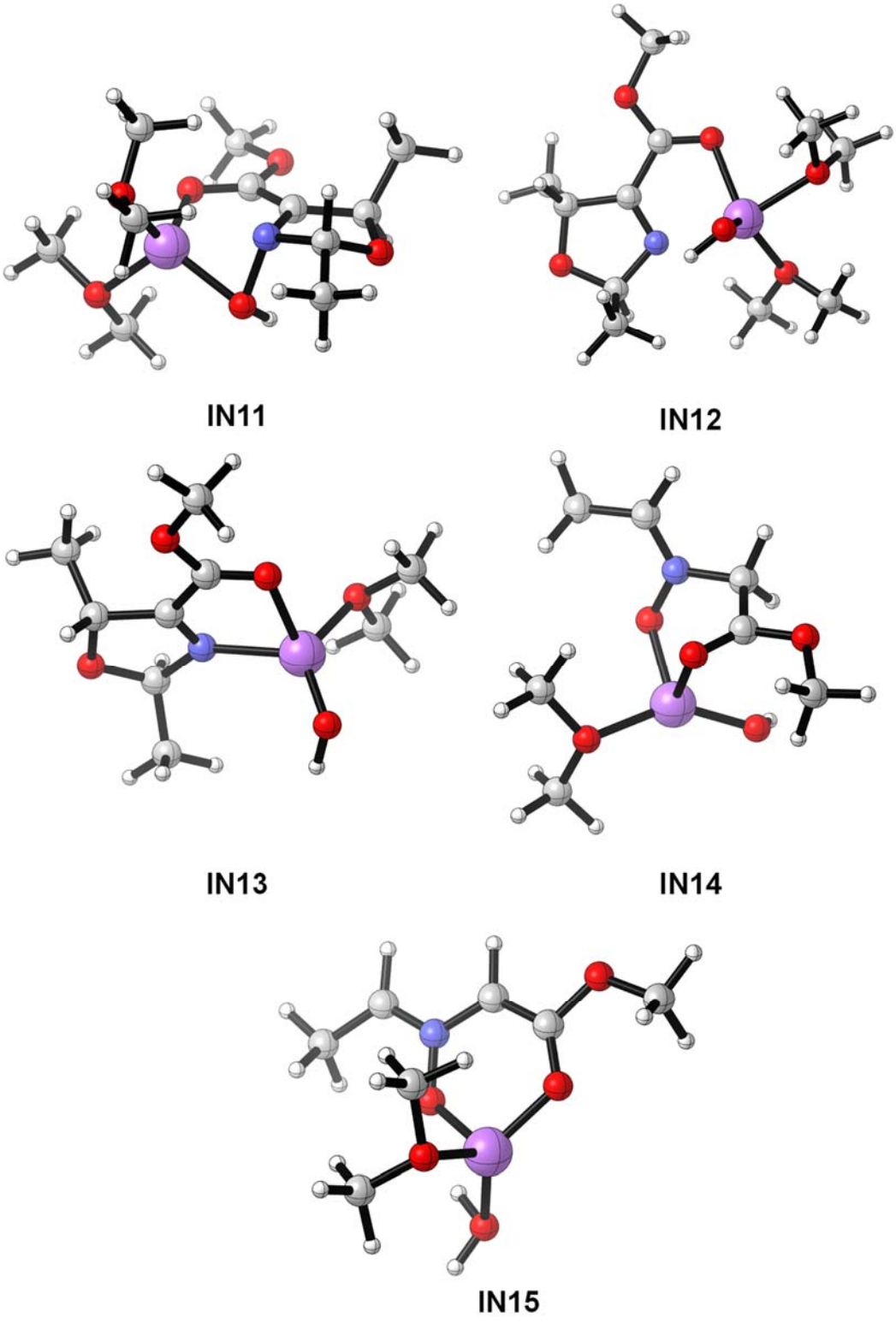


Figure S8. Optimized geometries of intermediates **IN11-IN15**

NMR Experiments

The reaction between **1a** and **2a** using 20 mol% of *n*-BuLi was monitored by NMR using THF-d_8 as a solvent (Figure S9). Trace A correspond to the mixture of nitrone and aldehyde before the addition of *n*-BuLi. Aromatic signals from aldehyde and azomethine signal of nitrone at 6.9 ppm disappear completely after the addition of 20 mol% of *n*-BuLi at -80 ºC. After 2 min (Trace B) some final product **3a** appears as indicated by the H_5 signal at 6.02 ppm. Also, two signals at 4.6 and 5.5 ppm can be observed. TOCSY experiments indicate that they correlate with C4 and C5 of the oxazoline ring, respectively so, they might correspond to intermediate **IN4**. In fact, the reaction does not progress at -80ºC after 4 h (Trace C) but after warming at -40ºC for additional 4 h signals at 4.6 and 5.5 ppm disappear and only the signals corresponding to compound **3a** (Trace D) are observed, evidencing the formation of the 3-oxazoline ring in the course of the reaction before quenching or participation of any external agent.

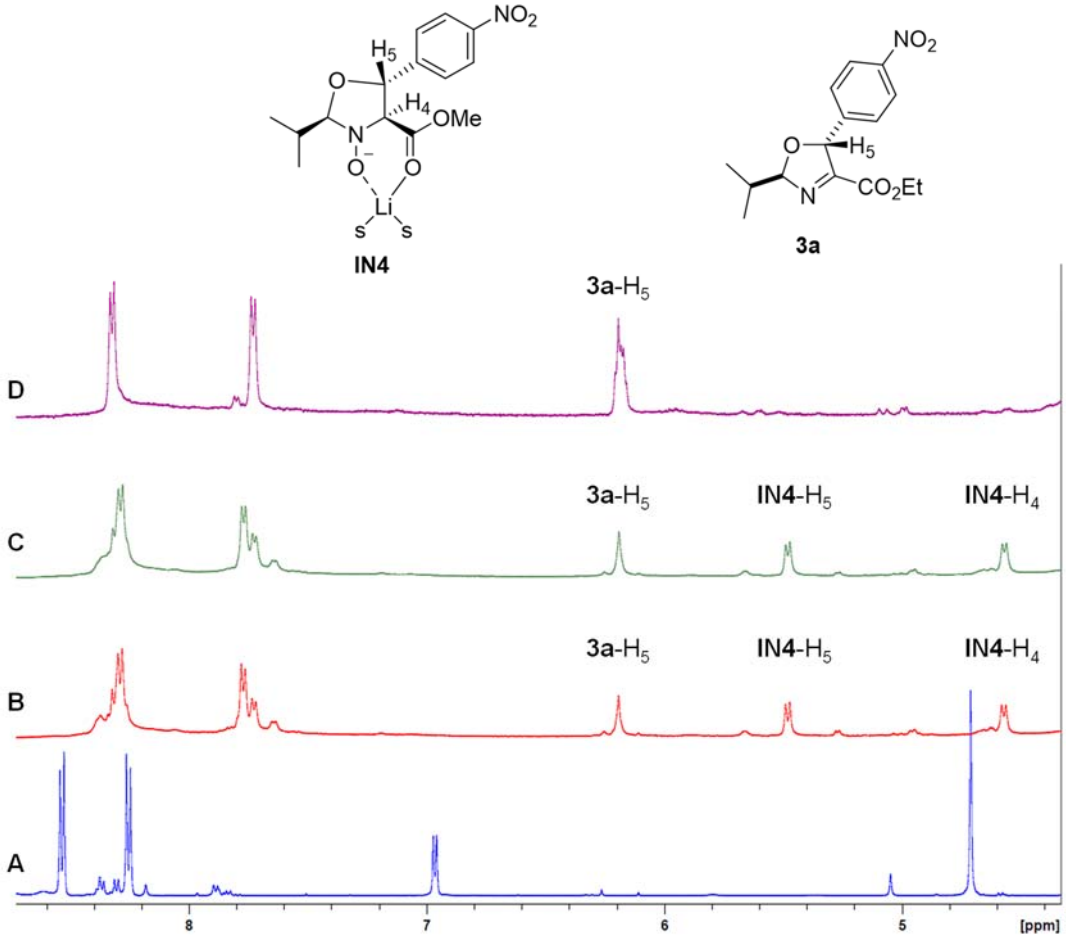
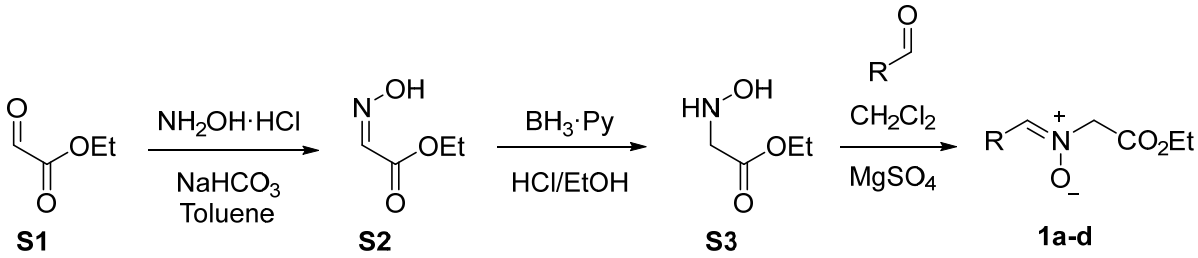


Figure S9. Monitoring of the reaction between **1a** and **2a** by NMR. Trace A: nitrone **1a** + aldehyde **2a**. Trace B: -80ºC; 2 min after the addition of 20 mol% of *n*-BuLi. Trace C: -80ºC, 4 h. Trace D: -40ºC, 4 h.

Experimental Procedures

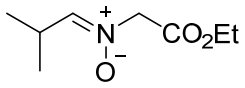
Synthesis of *C*-alkyl- *N*-(ethoxycarbonyl)methyl nitrones 1



Ethyl (Z)-2-(hydroxyimino)acetate S2. To a stirred solution of ethyl glyoxalate **S1** (8.5 mL, 42.9 mmol) in toluene (75 mL), hydroxylamine hydrochloride (3 g, 42.9 mmol) and sodium bicarbonate (7 g, 85.8 mmol) were added. The resulting suspension was stirred at ambient temperature for 16 h and then filtered. The filtrate is concentrated under reduced pressure and the crude product was dissolved in dichloromethane. The resulting solution was washed con brine. The organic layer was separated, dried over $MgSO_4$, filtered and evaporated under reduced pressure to give the pure oxime (4.5 g, 90%), which was used in the next step without further purification.

Ethyl hydroxyglycinate S3. To a well-stirred solution of oxime (2.70 g, 22.8 mmol) en EtOH (50 mL), cooled to 0 ºC, borane-pyridine complex (12 mL, 114 mmol) was added slowly. When the addition finished, 32 mL of 7N HCl/EtOH solution were added dropwise at which time the resulting mixture was stirred at ambient temperature for 3 h. The solvent was evaporated under reduced pressure without exceeding 40 ºC and the residue is dissolved in dichloromethane. Solid sodium carbonate was added until gas evolution stopped. The salts were filtered off and the filtrate was evaporated to yield the pure hydroxylamine (2.58 g, 95%), which was used in the next step without further purification.

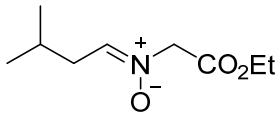
***C*-alkyl-*N*-(ethoxycarbonyl)methyl nitrones 1a-d**. To a well-stirred solution of hydroxylamine (2.58 g, 2.17 mmol) en dichloromethane (10 mL), magnesium sulfate (2.6 g, 21.7 mmol) and the corresponding aldehyde (2.17 mmol) were added and the resulting mixture was stirred at ambient temperature for 6 h. The solid was filtered off and the filtrate evaporated to yield the crude product which was purified by column chromatography (gradient Hexane/EtOAc 85:15 to EtOAc).



1a

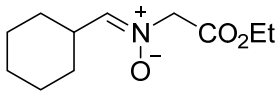
(*Z*)-2-ethoxy-N-(2-methylpropylidene)-2-oxoethanamine oxide 1a. yellow oil. (90%). ^{1}H NMR (acetone-d_6, 300 MHZ) δ 1,08 (d, 6H, *J*=6,8 Hz, (C*H*$_3$)$_2$-CH) 1,24 (t, 3H, *J*= 7,1 Hz, C*H*$_3$-CH$_2$), 3,07-2,94 (m, 1H, (CH$_3$)$_2$-C*H*), 4,18 (q, 2H,

J=7,1 Hz, CH_3-C*H*$_2$), 4,61(s, 2H, N-C*H*$_2$), 6,88 (d, 2H, *J*=6.8 Hz, C*H*=N). ^{13}C NMR (acetone-d_6, 75 MHz) δ 14.3 (*C*H_3-CH_2), 18.8 ((CH_3)$_2$-CH), 26.7 ((CH_3)$_2$-*C*H), 62.0 (CH_3-*C*H_2), 66.9 (N-*C*H_2), 146.6 (*C*H=N), 166.9 (*C*O). Anal Calcd. for $C_8H_{15}NO_3$: C, 55.47; H, 8.73; N, 8.09. Found C, 55.63; H, 8.65; N, 8.15



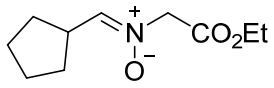
1b

(Z)-N-(2-ethoxy-2-oxoethyl)-3-methylbutan-1-imine oxide 1b. yellow oil. (88%). ^{1}H NMR ($CDCl_3$, 300 MHZ) δ 0.98 (d, 6H, *J*=6.7 Hz, (C*H*$_3$)$_2$-CH), 1.29 (t, 3H, *J*=7.2 Hz, C*H*$_3$-CH_2), 1.90-2.00 (m , 1H, (CH_3)$_2$- C*H*), 2.45 (t, 2H, *J*=6.5 Hz, C*H*$_2$-CH),4.25 (q, 2H, *J*=7.2 Hz, CH_3-C*H*$_2$), 4.57 (s, 2H, N-C*H*$_2$), 6.82 (t, 1H, *J*=6.0 Hz, C*H*=N). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0 (*C*H_3-CH_2), 22.5 ((*C*H_3)$_2$-CH), 26.0 ((CH_3)$_2$-*C*H), 35.6 (*C*H_2-CH), 62.2 (CH_3-*C*H_2), 66.3 (N-*C*H_2), 143.0 (*C*H=N), 165.5 (*C*O). Anal Calcd. for $C_9H_{17}NO_3$: C, 57.73; H, 9.15; N, 7.48. Found C, 57.59; H, 9.05; N, 7.36.



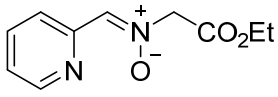
1c

(*Z*)-1-cyclohexyl-N-(2-ethoxy-2-oxoethyl)methanimine oxide 1c. white solid. (90%). mp 58-60ºC. ^{1}H NMR (CD_2Cl_2, 400 MHZ) δ 1.16-1.29 (m, 3H, C*H*$_2$ cy), 1.27 (t, 3H, *J*=7.1 Hz, CH_2-C*H*$_3$), 1.33-1.44 (m, 2H, C*H*$_2$ cy), 1.61-1.74 (m , 3H, C*H*$_2$ cy), 1.83-1.90 (m, 2H, C*H*$_2$ cy), 2.86-2.95 (m, 1H, C*H* cy), 4.22 (q, 2H, *J*=7.1 Hz, C*H*$_2$-CH_3), 4.45 (s, 2H, N-C*H*$_2$), 6.54 (d, 1H, *J*=7.3 Hz, C*H*=N). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.2 (*C*H_3-CH_2), 25.6 (*C*H_2 cy), 26.4 (*C*H_2 cy), 28.9 (*C*H_2 cy), 35.6 (*C*H cy), 62.4 (CH_3-*C*H_2), 67.0 (*C*H_2-N), 145.8 (*C*H=N), 166.2 (*C*O). Anal Calcd. for $C_{11}H_{19}NO_3$: C, 61.95; H, 8.98; N, 6.57. Found C, 61.88; H, 9.13; N, 6.74

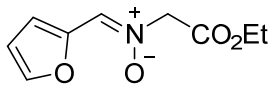


1d

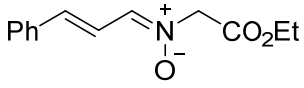
(*Z*)-1-cyclopentyl-N-(2-ethoxy-2-oxoethyl)methanimine oxide 1d. yellow oil. (90%). ^{1}H NMR (CD_2Cl_2, 400 MHZ) δ 1.28 (t, 3H, *J*= 7,1 Hz, CH_2-C*H*$_3$), 1.39-1.48 (m, 2H, C*H*$_2$ cy), 1.59-1.70 (m, 4H, C*H*$_2$ cy), 1.95-2.05 (m, 2H, C*H*$_2$ cy), 3.30-3.18 (m, 1H, C*H* cy), 4.22 (q, 2H, *J*=7.1 Hz, C*H*$_2$-CH_3), 4.46 (s, 2H, N-C*H*$_2$), 6.67 (d, 1H, *J*=7.2 Hz, N=C*H*). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.2 (CH_2-*C*H_3), 25.9 (*C*H_2 cy), 30.5 (*C*H_2 cy), 37.3 (*C*H cy), 62.4 (*C*H_2-CH_3), 66.7 (N-*C*H_2), 146.8 (N=*C*H), 166.2 (*C*O). Anal Calcd. for $C_{10}H_{17}NO_3$: C, 60.28; H, 8.60; N, 7.03. Found C, 60.37; H, 8.69; N, 6.91



(*Z*)-N-(2-ethoxy-2-oxoethyl)-1-(pyridin-2-yl)methanimine oxide1d. Yellow oil. (88%). ^{1}H NMR (CD_2Cl_2, 400 MHZ) δ 1.29 (t, 3H, *J*=7.1 Hz, C*H*$_3$), 4.26 (q, 2H, *J*=7.1 Hz, C*H*$_2$-CH$_3$), 4.75 (s, 2H, N-C*H*$_2$), 7.31 (ddd, 1H, *J*=7.6 Hz, *J*=4.8 Hz, *J*=0.9 Hz, *H*$_{Ar}$), 7.74 (s, 1H, C*H*=*N*), 7.80 (td, 1H, *J*=7.6 Hz, *J*=1.7 Hz, *H*$_{Ar}$), 8.63 (ddd, 1H, *J*=4.8 Hz, *J*=1.7 Hz, *J*=0.9 Hz, *H*$_{Ar}$), 9.08 (dt, 1H, *J*=7.6 Hz, *J*=0.9 Hz, *H*$_{Ar}$).. ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.2 (*C*H$_3$), 62.6 (*C*H$_2$-CH$_3$), 68.7 (*C*H$_2$), 123.8 (*C*H$_{Ar}$), 124.9 (*C*H$_{Ar}$), 137.0 (*C*H$_{Ar}$), 138.3 (*C*H=N), 149.6 (*C*$_{Ar}$), 150.1 (*C*H$_{Ar}$), 165.8 (*C*O). Anal Calcd. for $C_{10}H_{12}N_2O_3$: C, 57.69; H, 5.81; N, 13.45. Found C, 57.74; H, 5.67; N, 13.56.



(*Z*)-N-(2-ethoxy-2-oxoethyl)-1-(furan-2-yl)methanimine oxide. Transparent oil. (80%). ^{1}H NMR (CD_2Cl_2, 400 MHZ) δ 1.29 (t, 3H, J=7.1 Hz, CH3), 4.25 (q, 2H, J=7.1 Hz, CH2-CH3), 4.65 (s, 2H, N-CH2), 6.59 (ddd, 1H, J= 3.5 Hz, J= 1.8 Hz, J=0.7 Hz, HAr), 7.55 (dd, 1H, J= 1.8 Hz, J=0.7 Hz, HAr), 7.61 (s, 1H, CH=N), 7.75 (d, 1H, J= 3.5 Hz, CHAr). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.2 (*C*H$_3$), 62.6 (*C*H$_2$-CH$_3$), 66.9 (N-*C*H$_2$), 112.6 (*C*H$_{Ar}$), 115.9 (*C*H$_{Ar}$), 127.6 (*C*H=N), 144.5 (*C*H$_{Ar}$), 147.0 (*C*$_{Ar}$), 166.0 (*C*O). Anal Calcd. for $C_9H_{11}NO_4$: C, 54.82; H, 5.62; N, 7.10. Found C, 54.90; H, 5.73; N, 6.95.



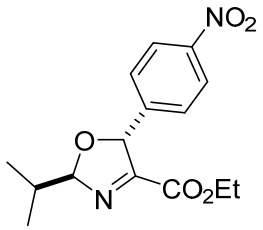
(1*Z*,2*E*)-N-(2-ethoxy-2-oxoethyl)-3-phenylprop-2-en-1-imine oxide. White solid; mp 70-72 ºC. (92%). ^{1}H NMR (CD_2Cl_2, 400 MHZ) δ 1.30 (t, 3H, *J*=7.1 Hz, C*H*$_3$), 4.26 (q, 2H, *J*=7.1 Hz, C*H*$_2$-CH$_3$), 4.59 (s, 2H, N-C*H*$_2$), 7.09 (d, 1H, J=15.8 Hz, C*H*=CH-CH), 7.27-7.46 (m, 5H, CH=C*H*-CH, C*H*=N, C*H*$_{Ar}$), 7.51-7.56 (m, 2H, C*H*$_{Ar}$). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.2 (*C*H$_3$), 62.6 (*C*H$_2$-CH$_3$), 66.7 (*C*H$_2$), 118.4 (CH=*C*H-CH), 127.7 (*C*H$_{Ar}$), 129.2 (*C*H$_{Ar}$), 129.7 (*C*H$_{Ar}$), 136.4 (*C*$_{Ar}$), 139.0 (*C*H=N), 139.2 (*C*H=CH-CH), 166.1 (*C*O). Anal Calcd. for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found C, 67.14; H, 6.53; N, 5.98.

Synthesis of 3-oxazolines 3a-r.

Method A. To a cooled (-80 ºC) solution of the corresponding nitrone (0.5 mmol) in anhydrous THF (5 mL), *n*-BuLi (63 μL of a 1.6M solution in hexanes, 0.1 mmol) was added. The resulting mixture was stirred at -80ºC for 15 min at which time a cooled (-80

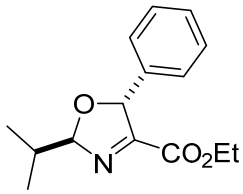
ºC) solution of aldehyde (0.5 mmol) in anhydrous THF (5 mL), was added via cannula. The reaction mixture was kept at -80ºC for additional 5 min and then placed in bath a -40 ºC for 4 hours. Ammonium chloride (1 mL) was added and the reaction mixture was warmed at ambient temperature, diluted with dichloromethane (15 mL) and treated with a saturated solution of ammonium chloride (10 mL). The organic layer was separated, dried over magnesium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography (gradient from hexane 100% to 7:3 hexane/EtOAc) to give the pure 3-oxazoline.

Method B. To a solution of the corresponding nitrone (0.5 mmol) in acetonitrile (5 mL), aldehyde (0.5 mmol), DABCO (28.04 mg, 0.25 mmol) and LiBr (21.7 mg, 0.25 mmol) were added. The resulting mixture was stirred at ambient temperature for 24 h at which time a saturated solution of ammonium chloride (10 mL) was added. The reaction mixture was diluted with dichloromethane (15 mL) and the organic layer was separated, dried over magnesium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography (gradient from hexane 100% to 7:3 hexane/EtOAc) to give the pure 3-oxazoline.

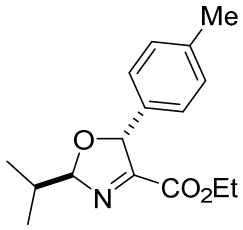


3a

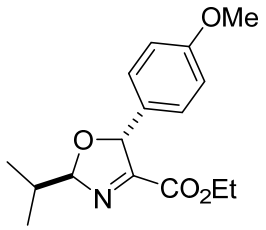
Ethyl (2R*,5R*)-2-isopropyl-5-(4-nitrophenyl)-2,5-dihydrooxazole-4-carboxylate 3a. white solid. mp 84-86 ºC. (90%, method A. 92%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.03 (d, 3H, *J*=6.8 Hz, C*H*$_3$), 1.05 (d, 3H, *J*=6.8 Hz, C*H*$_3$), 1.24 (t, 3H, *J*= 7.1 Hz, C*H*$_3$-CH$_2$), 2.20-2.08 (m, 1H, C*H*), 4.22 (dq, 1H, *J*=10.9 Hz, *J*=7.1 Hz, CH$_3$- C*H*$_2$), 4.22 (dq, 1H, *J*=10.9 Hz, *J*=7.1 Hz, CH$_3$- C*H*$_2$), 6.02 (d, 1H, *J*=6.6 Hz, *H*$_5$), 6.05 (dd, 1H, *J*=6.6 Hz, *J*=4.3 Hz, *H*$_2$), 7.55-7.51 (m, 2H, *H*$_{Ar}$), 8.22-8.18 (m, 2H, *H*$_{Ar}$). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.0 (*C*H$_3$-CH$_2$), 16.9 (*C*H$_3$-CH), 17.6 (*C*H$_3$-CH), 34.3 ((CH$_3$)$_2$-*C*H), 62.8 (CH$_3$-*C*H$_2$), 87.2 (*C*$_5$), 112.6 (*C*$_2$), 124.1 (*C*H$_{Ar}$), 128.5 (*C*H$_{Ar}$), 145.4 (*C*$_{Ar}$), 148.4 (*C*$_{Ar}$), 160.4 (*C*$_4$), 162.0 (*C*O). Anal Calcd. for $C_{15}H_{18}N_2O_5$: C, 58.82; H, 5.92; N, 9.15. Found C, 58.67; H, 6.11; N, 9.29



3b **Ethyl (2R*,5R*)-2-isopropyl-5-phenyl-2,5-dihydrooxazole-4-carboxylate 3b**. yellow oil. (89%, method A. 90%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.02 (d, 3H, *J*=6.9 Hz, C*H*$_3$-CH), 1.07 (d, 3H, *J*=6.9 Hz, C*H*$_3$-CH), 1.24 (t, 3H, *J*=6.9 Hz, C*H*$_3$-CH$_2$), 2.22-2.10 (m, 1H, C*H*), 4.23 (dq, 2H, *J*=10.9 Hz, *J*=6.9 Hz, CH$_3$-C*H*$_2$), 4.24 (dq, 2H, *J*=10.9 Hz, *J*=6.9 Hz, CH$_3$-C*H*$_2$), 5.94 (d, 1H, *J*=6.7 Hz, *H*$_5$), 6.00 (dd, 1H, *J*=6.7, *J*=4.5 Hz, *H*$_2$), 7.37-7.27 (m, 5H, *H*$_{Ar}$). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 13.9 (*C*H$_3$-CH$_2$), 16.6 (*C*H$_3$-CH), 17.7 (*C*H$_3$-CH), 33.8 (*C*H), 62.2 (CH$_3$-*C*H$_2$), 88.0 (*C*$_5$), 111.5 (*C*$_2$), 127.1 (*C*H$_{Ar}$), 127.8 (*C*H$_{Ar}$), 128.7 (*C*H$_{Ar}$), 137.5 (*C*$_{Ar}$), 160.5 (*C*$_4$), 163.1 (*C*O). Anal Calcd. for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found C, 68.83; H, 7.45; N, 5.48

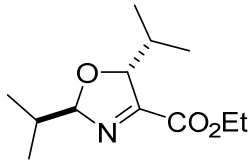


3c **Ethyl (2R*,5R*)-2-isopropyl-5-(p-tolyl)-2,5-dihydrooxazole-4-carboxylate 3c** yellow oil. (78%, method A. 69%, method B). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.01 (d, 3H, *J*=6.8 Hz, C*H*$_3$-CH), 1.03 (d, 3H, *J*=6.8 Hz, C*H*$_3$-CH), 1.23 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 2.06-2.13 (m, 1H, C*H*), 2.33 (s, 3H, CH$_3$-Ar), 4.20 (dq, 2H, *J*=10.9 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.21 (dq, 2H, *J*=10.9 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 5.87 (d, 1H, *J*=6.6 Hz, *H*$_5$), 5.92 (dd, 1H, *J*=6.6, *J*=4.7 Hz, *H*$_2$), 7.14-7.18 (m, 4H, *H*$_{Ar}$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0 (*C*H$_3$-CH$_2$), 17.0 (*C*H$_3$-CH), 17.6 (*C*H$_3$-CH), 21.3 (CH$_3$-Ar), 34.2 (*C*H), 62.4 (CH$_3$-*C*H$_2$), 88.1 (*C*$_5$), 111.6 (*C*$_2$), 127.4 (*C*H$_{Ar}$), 129.6 (*C*H$_{Ar}$), 135.3 (*C*$_{Ar}$), 139.0 (*C*$_{Ar}$), 160.9 (*C*$_4$), 163.4 (*C*O). Anal Calcd. for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found C, 69.86; H, 7.84; N, 4.96



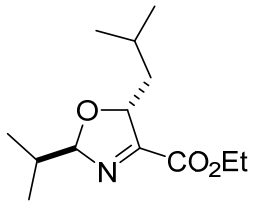
3d

Ethyl (2R*,5R*)-2-isopropyl-5-(4-methoxyphenyl)-2,5-dihydrooxazole-4-carboxylate 3d. yellow oil. (75%, method A. 64%, method B). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.00 (d, 3H, *J*=6.8 Hz, C*H*$_3$-CH), 1.03 (d, 3H, *J*=6.8 Hz, C*H*$_3$-CH), 1.23 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 2.04-2.12 (m, 1H, C*H*), 3.79 (s, 3H, CH$_3$-O), 4.19 (dq, 2H, *J*=9.6 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.20 (dq, 2H, *J*=9.6 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 5.89 (d, 1H, *J*=6.6 Hz, *H*$_5$), 5.91 (dd, 1H, *J*=6.6, *J*=4.7 Hz, *H*$_2$), 6.85-6.90 (m, 2H, *H*$_{Ar)}$, 7.16-7.21 (m, 2H, *H*$_{Ar}$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0 (*C*H$_3$-CH$_2$), 17.0 (*C*H$_3$-CH), 17.6 (*C*H$_3$-CH), 34.2 (*C*H), 55.6 (O-*C*H$_3$), 62.4 (CH$_3$-*C*H$_2$), 87.9 (*C*$_5$), 111.5 (*C*$_2$), 114.3 (*C*H$_{Ar}$), 128.8 (*C*H$_{Ar}$), 130.3 (*C*$_{Ar}$), 160.3 (*C*$_{Ar}$), 160.9 (*C*$_4$), 163.5 (*C*O). Anal Calcd. for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found C, 66.12; H, 7.18; N, 4.97



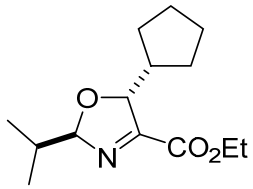
3e

Ethyl (2R*,5R*)-2,5-diisopropyl-2,5-dihydrooxazole-4-carboxylate 3e. oil. (86%, method A. 82%, method B). (78%, method A. 69%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 0.77 (d, 3H, *J*=7.0 Hz, C*H*$_3$-CH-C$_2$), 0.94 (d, 3H, *J*=6.9 Hz, C*H*$_3$-CH-C$_5$), 0 .95 (d, 3H, *J*=6.9 Hz, C*H*$_3$-CH-C$_5$), 1.02 (d, 3H, *J*=7.0 Hz, C*H*$_3$-CH-C$_2$), 1.35 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 1.98 (septd, 1H, *J*=7.0 Hz, *J*=4.7 Hz, C*H*-C$_2$), 2.16 (septd, 1H, *J*=6.9 Hz, *J*=2.5 Hz, C*H*-C$_5$), 4.32 (dq, 1H, *J*=11.6 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.33 (dq, 1H, *J*=11.6 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.90 (dd, 1H, *J*=7.0 Hz, *J*=2.5 Hz, *H*$_5$), 5.60 (dd, 1H, *J*=6.9 Hz, *J*=4.7 Hz, *H*$_2$). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.2 (*C*H$_3$-CH$_2$), 16.0 (*C*H$_3$-CH), 17.0 (*C*H$_3$-CH), 17.3 (*C*H$_3$-CH), 19.8 (*C*H$_3$-CH), 31.7 (CH$_3$-*C*H), 34.3 (CH$_3$-*C*H), 62.4 (CH$_3$-*C*H$_2$), 91.1 (*C*$_5$), 111.2 (*C*$_2$), 161.7 (*C*$_4$), 164.4 (*C*O). Anal Calcd. for $C_{12}H_{21}NO_3$: C, 63.41; H, 9.31; N, 6.16. Found C, 64.58; H, 9.45; N, 6.25



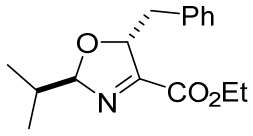
3f

Ethyl (2R*,5R*)-5-isobutyl-2-isopropyl-2,5-dihydrooxazole-4-carboxylate 3f. oil. (88%, method A. 89%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 0.92-0.97 (m, 12H, (CH_3)$_2$-CH-CH_2, (CH_3)$_2$-CH), 1.35 (t, 3H, *J*=7.1 Hz, CH_3-CH_2), 1.42-1.49 (m, 1H, CH_2), 1.56-1.62 (m, 1H, CH_2), 1.75-1.85 (m, 1H, (CH_3)$_2$-CH-CH_2), 1.93-2.02 (m, 1H, (CH_3)$_2$-CH), 4.32 (q, 2H, *J*=7.1 Hz, CH_3-CH_2), 5.02 (ddd, 1H, *J*=9.4 Hz *J*=6.5 Hz, *J*=2.9 Hz, H_5), 5.61 (dd, 1H, *J*=6.9 Hz, *J*=4.8 Hz, H_2). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.2 (CH_3-CH_2), 17.1 (CH_3-CH), 17.4 (CH_3-CH), 21.9 (CH_3-CH-CH_2), 23.6 (CH_3-CH-CH_2), 25.7 (CH-CH_2), 33.9 ((CH_3)$_2$-CH), 41.6 (CH_2), 62.3 (CH_3-CH_2), 84.9 (C_5), 109.8 (C_2), 161.4 (C_4), 165.4 (CO). Anal Calcd. for $C_{13}H_{23}NO_3$: C, 64.70; H, 9.61; N, 5.80. Found C, 64.63; H, 9.55; N, 5.65



3g

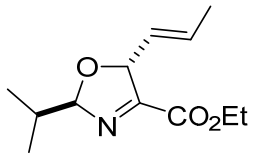
Ethyl (2R*,5R*)-5-cyclopentyl-2-isopropyl-2,5-dihydrooxazole-4-carboxylate 3g. oil. (89%, method A. 85%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.35 (t, 3H, *J*=7.1 Hz, CH_3-CH_2), 1.43-1.56 (m, 5H, $CH_{2\ cy}$), 1.59-1.74 (m, 3H, $CH_{2\ cy}$), 1.97 (septd, 1H, *J*=6.8 Hz, *J*=4.6 Hz, CH), 2.27-2.37 (m, 1H, CH_{cy}), 4.32 (dq, 1H, *J*=10.8 Hz, *J*=7.1 Hz, CH_3-CH_2), 4.33 (dq, 1H, *J*=10.8 Hz, *J*=7.1 Hz, CH_3-CH_2), 5.04 (dd, 1H, *J*=6.8 Hz, *J*=3.6 Hz, H_5), 5.62 (dd, 1H, *J*=6.8 Hz, *J*=4.6 Hz, H_2). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.2 (CH_3-CH_2), 17.0 (CH_3-CH), 17.3 (CH_3-CH), 25.9 ($CH_{2\ cy}$), 26.0 ($CH_{2\ cy}$), 26.8 ($CH_{2\ cy}$), 29.5 ($CH_{2\ cy}$), 34.3 (CH_{cy}), 42.8 (CH), 62.4 (CH_3-CH_2), 88.6 (C_5), 110.9 (C_2), 161.8 (C_4), 164.6 (CO). Anal Calcd. for $C_{14}H_{23}NO_3$: C, 66.37; H, 9.15; N, 5.53. Found C, 66.53; H, 9.35; N, 5.39



3h

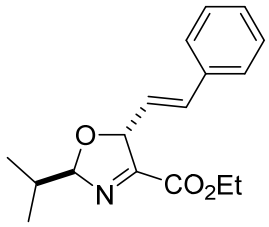
Ethyl (2R*,5R*)-5-benzyl-2-isopropyl-2,5-dihydrooxazole-4-carboxylate 3h. yellow oil. (93%, method A. 91%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 0.89 (d, 3H, *J*=6.8 Hz, CH_3-CH), 0.90 (d, 3H, *J*=6.8 Hz, CH_3-CH), 1.37 (t, 3H,

J=7.1 Hz, C*H*$_3$-CH$_2$), 1.88-2.00 (m, 1H, C*H*), 2.98 (dd, 1H, *J*=14.2 Hz, *J*= 5.9 Hz, CH$_2$-Ph), 3.15 (dd, 1H, *J*=14.2 Hz, *J*= 3.9 Hz, CH$_2$-Ph), 4.26-4.41 (m, 2H, CH$_3$-C*H*$_2$), 5.26 (ddd, 1H, *J*=6.7 Hz *J*=5.9 Hz, *J*=3.9 Hz, *H*$_5$), 5.36 (dd, 1H, *J*=6.7 Hz, *J*=4.7 Hz, *H*$_2$), 7.16-7.30 (m, 5H, *H*$_{Ar}$). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.2 (*C*H$_3$-CH$_2$), 17.0 (*C*H$_3$-CH), 17.3 (*C*H$_3$-CH), 33.9 (*C*H), 39.3 (*C*H$_2$-Ph), 62.5 (CH$_3$-*C*H$_2$), 86.8 (*C*$_5$), 110.5 (*C*$_2$), 127.0 (*C*H$_{Ar}$), 128.6 (*C*H$_{Ar}$), 129.9 (*C*H$_{Ar}$), 137.5 (*C*$_{Ar}$), 161.3 (*C*$_4$), 163.9 (*C*O). Anal Calcd. for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found C, 69.85; H, 7.75; N, 5.15



3i

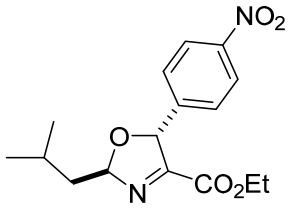
Ethyl (2R*,5R*)-2-isopropyl-5-((E)-prop-1-en-1-yl)-2,5-dihydrooxazole-4-carboxylate 3i. yellow oil. (78%, method A. 71%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 0.95 (d, 3H, *J*=6.8 Hz, C*H*$_3$-CH) , 0.97 (d, 3H, *J*=6.8 Hz, C*H*$_3$-CH), 1.33 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 1.71 (ddd, *J*=6.6 Hz, *J*=1.6 Hz, *J*=0.9 Hz, CH=CH-C*H*$_3$), 2.00 (septd, 1H, *J*= 6.8 Hz, *J*= 4.8 Hz, C*H*), 4.30 (dq, 1H, *J*= 10.9 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.31 (dq, 1H, *J*= 10.9 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 5.33-5.36 (m, 1H, *H*$_5$), 5.45 (ddq, 1H, *J*= 15.8 Hz, *J*=6.9 Hz, *J*=1.6 Hz, C$_5$-C*H*=CH), 5.66 (dd, 1H, *J*=6.3 Hz, *J*=4.8 Hz, H$_2$) , 5.85 (dqd, 1H, *J*=15.8 Hz, *J*=6.6 Hz, *J*=1.0 Hz, C$_5$-CH=C*H*). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.2 (*C*H$_3$-CH$_2$), 17.0 (*C*H$_3$-CH), 17.6 (*C*H$_3$-CH), 17.8 (*C*H$_3$-CH=CH), 33.9 (*C*H), 62.3 (CH$_3$-*C*H$_2$), 86.5 (*C*$_5$), 110.4 (*C*$_2$), 126.5 (C$_5$-CH=*C*H), 130.6 (C$_5$-*C*H=CH), 161.0 (*C*$_4$), 163.0 (*C*O). Anal Calcd. for $C_{12}H_{19}NO_3$: C, 63.98; H, 8.50; N, 6.22. Found C, 64.11; H, 8.42; N, 6.35



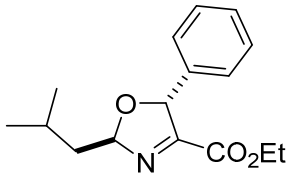
3j

Ethyl (2R*,5R*)-2-isopropyl-5-((E)-styryl)-2,5-dihydrooxazole-4-carboxylate 3j. yellow oil. (69%, method A. 53%, method B). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.00 (d, 3H, *J*=7.3 Hz, C*H*$_3$-CH) , 1.05 (d, 3H, *J*=7.3 Hz, C*H*$_3$-CH), 1.37 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 2.20-2.08 (m, 1H, C*H*), 4.37 (q, 2H, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 5.61 (td, 1H, *J*=6.4 Hz, *J*=1.0 Hz, *H*$_5$), 5.85 (dd, 1H, *J*=6.4 Hz, *J*=4.5 Hz, *H*$_2$), 6.20 (dd, 1H, *J*= 15.8 Hz, *J*=6.4 Hz, PhCH=C*H*) , 6.75 (dd, 1H, *J*=15.8 Hz, *J*=1.0 Hz, PhC*H*=CH), 7.39-7.27 (m, 5H, *H*$_{Ar}$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1 (*C*H$_3$-CH$_2$), 16.6 (*C*H$_3$-CH),

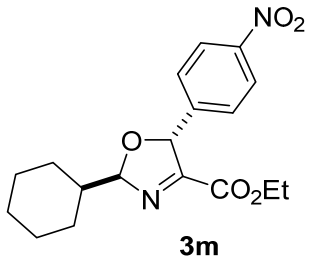
17.6 (*C*H$_3$-CH), 33.6 ((CH$_3$)$_2$-*C*H), 62.3 (CH$_3$-*C*H$_2$), 86.1 (*C*$_5$), 110.5 (*C*$_2$), 123.8 (PhCH=*C*H), 126.7 (*C*H$_{Ar}$), 128.1 (*C*H$_{Ar}$), 128.6 (*C*H$_{Ar}$), 133.2 (Ph*C*H=CH), 136.1 (*C*$_{Ar}$), 160.6 (*C*$_4$), 162.5 (*C*O). Anal Calcd. for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4.87. Found C, 71.23; H, 7.49; N, 4.62



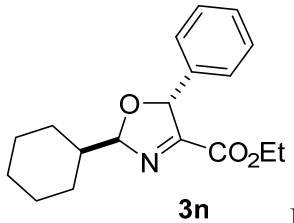
3k **Ethyl (2R*,5R*)-2-isobutyl-5-(4-nitrophenyl)-2,5-dihydrooxazole-4-carboxylate 3k**. yellow oil. (93%, method A. 90%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.02 (d, 3H, *J*=6.7 Hz, C*H*$_3$-CH), 1.03 (d, 3H, *J*=6.7 Hz, C*H*$_3$-CH), 1.24 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 1.61-1.69 (m, 1H, C*H*$_2$), 1.73-1.81 (m,1H, C*H*$_2$), 1.90-2.01 (m, 1H, CH$_3$-C*H*), 4.22 (dq, 1H, *J*=10.9 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.22 (dq, 1H, *J*=10.9 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 6.04 (d, 1H, *J*=6.4 Hz, *H*$_5$), 6.25 (ddd, 1H, *J*=7.2 Hz, *J*=6.4 Hz, *J*=5.5 Hz, *H*$_2$), 7.51-7.57 (m, 2H, *H*$_{Ar}$), 8.15-8.23 (m, 2H, *H*$_{Ar}$). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.0 (*C*H$_3$-CH$_2$), 22.6 (*C*H$_3$-CH), 23.1 (*C*H$_3$-CH), 25.2 ((CH$_3$)$_2$-*C*H), 44.9 (*C*H$_2$), 62.8 (CH$_3$-*C*H$_2$), 86.4 (*C*$_5$), 107.3 (*C*$_2$), 124.1 (*C*H$_{Ar}$), 128.5 (*C*H$_{Ar}$), 145.3 (*C*$_{Ar}$), 148.4 (*C*$_{Ar}$), 160.5 (*C*$_4$), 161.5 (*C*O). Anal Calcd. for $C_{16}H_{20}N_2O_5$: C, 59.99; H, 6.29; N, 8.74. Found C, 60.23; H, 6.19; N, 8.58



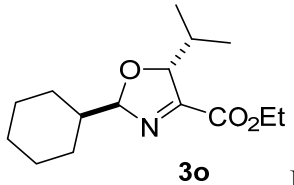
3l **Ethyl (2R*,5R*)-2-isobutyl-5-phenyl-2,5-dihydrooxazole-4-carboxylate 3l**. yellow oil. (88%, method A. 85%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.01 (d,3H, *J*=6.7 Hz, C*H*$_3$-CH), 1.02 (d, 3H, *J*=6.7 Hz, C*H*$_3$-CH), 1.22 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 1.62 (ddd, 1H, *J*=13.7 Hz, *J*=7.2 Hz, *J*= 6.5 Hz, C*H*$_2$), 1.75 (ddd, 1H, *J*=13.7 Hz, *J*=7.2 Hz, *J*=5.4 Hz, C*H*$_2$), 1.88-2.00 (m, 1H, (CH$_3$)$_2$-C*H*), 4.18 (dq, 1H, *J*=10.9 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.19 (dq, 1H, *J*=10.9 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 5.92 (d, 1H, *J*=6.4 Hz, *H*$_5$), 6.16 (ddd, 1H, *J*=7.2 Hz, *J*=6.4 Hz, *J*=5.4 Hz, *H*$_2$), 7.27-7.38 (m, 5H, *H*$_{Ar}$). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.0 (*C*H$_3$-CH$_2$), 22.6 (*C*H$_3$-CH), 23.2 (*C*H$_3$-CH), 25.2 ((CH$_3$)$_2$-*C*H), 45.0 (*C*H$_2$), 62.4 (CH$_3$-*C*H$_2$), 87.5 (*C*$_5$), 106.6 (*C*$_2$), 127.6 (*C*H$_{Ar}$), 128.9 (*C*H$_{Ar}$), 129.0 (*C*H$_{Ar}$), 138.2 (*C*$_{Ar}$), 160.9 (*C*$_4$), 162.7 (*C*O). Anal Calcd. for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found C, 69.94; H, 7.48; N, 4.86



3m **Ethyl (2R*,5R*)-2-cyclohexyl-5-(4-nitrophenyl)-2,5-dihydrooxazole-4-carboxylate 3m**. yellow oil. (92%, method A. 90%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.17-1.32 (m, 5H, C*H*$_2$ cy), 1.24 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 1.66-1.72 (m, 1H, C*H*$_2$ cy), 1.75-1.88 (m, 5H, C*H*$_2$ cy, C*H* cy), 4.21 (dq, 1H, *J*=10.9 Hz, *J*=7.1 Hz, CH$_3$-*C*H$_2$), 4.22 (dq, 1H, *J*=10.9 Hz, *J*=7.1 Hz, CH$_3$-*C*H$_2$), 5.99 (d, 1H, *J*=6.7 Hz, *H*$_5$), 6.02 (dd, 1H, *J*=6.7 Hz, *J*=4.3 Hz, *H*$_2$), 7.46-7.58 (m, 2H, *H*$_{Ar}$), 8.13-8.24 (m, 2H, *H*$_{Ar}$). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.0 (*C*H$_3$-CH$_2$), 26.2 (*C*H$_2$ cy), 26.3 (*C*H$_2$ cy), 26.7 (*C*H$_2$ cy), 27.6 (*C*H$_2$ cy), 28.4 (*C*H$_2$ cy), 43.9 (*C*H cy), 62.7 (CH$_3$-*C*H$_2$), 87.0 (*C*$_5$), 112.0 (*C*$_2$), 124.1 (*C*H$_{Ar}$), 128.5 (*C*H$_{Ar}$), 145.4 (*C*$_{Ar}$), 148.4 (*C*$_{Ar}$), 160.4 (*C*$_4$), 161.8 (*C*O). Anal Calcd. for $C_{18}H_{22}N_2O_5$: C, 62.42; H, 6.40; N, 8.09. Found C, 62.28; H, 6.59; N, 8.21

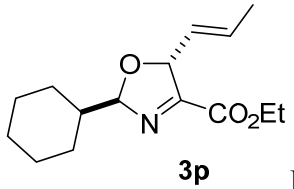


3n **Ethyl (2R*,5R*)-2-cyclohexyl-5-phenyl-2,5-dihydrooxazole-4-carboxylate 3n**. yellow oil. (90%, method A. 87%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.10-1.16 (m, 2H, C*H*$_{2\ cy}$), 1.13 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 1.17-1.20 (m, 3H, C*H*$_{2\ cy}$), 1.59-1.63 (m, 1H, C*H*$_{2\ cy}$), 1.65-1.78 (m, 5H, C*H*$_{2\ cy}$, C*H*$_{cy}$), 4.09 (dq, 1H, *J*=10.3 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.11(dq, 1H, *J*=10.3 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 5.79 (d, 1H, *J*=6.6 Hz, *H*$_5$), 5.85 (dd, 1H, *J*=6.6 Hz, *J*=4.5 Hz, *H*$_2$), 7.18-7.29 (m, 5H, *H*$_{Ar}$). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.0 (*C*H$_3$-CH$_2$), 26.2 (*C*H$_2$ cy), 26.3 (*C*H$_2$ cy), 26.7 (*C*H$_2$ cy), 27.6 (*C*H$_2$ cy), 28.4 (*C*H$_2$ cy), 43.9 (*C*H cy), 62.4 (CH$_3$-*C*H$_2$), 88.1 (*C*$_5$), 111.2 (*C*$_2$), 127.5 (*C*H$_{Ar}$), 128.9 (*C*H$_{Ar}$), 138.3 (*C*$_{Ar}$), 160.8 (*C*$_4$), 163.1 (*C*O). Anal Calcd. for $C_{18}H_{23}NO_3$: C, 71.73; H, 7.69; N, 4.65. Found C, 71.58; H, 7.93; N, 4.49

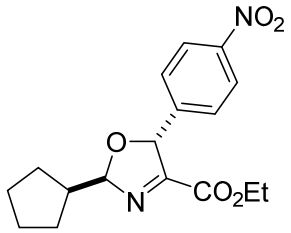


3o **Ethyl (2R*,5R*)-2-cyclohexyl-5-isopropyl-2,5-dihydrooxazole-4-carboxylate 3o.** yellow oil. (78%, method A. 80%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 0.75 (d, 3H, *J*=6.8 Hz, C*H*$_3$-CH), 1.01 (d, 3H, *J*=6.8 Hz,

C*H*$_3$-CH), 1.10-1.27 (m, 5H, C*H*$_{2\ cy}$), 1.35 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 1.63-1.77 (m, 6H, C*H*$_{2\ cy}$, C*H*$_{cy}$), 2.17 (septd, 1H, *J*=6.8 Hz, *J*=2.6 Hz, C*H*), 4.30 (dq, 1H, *J*=10.9 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.31 (dq, 1H, *J*=10.9 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.87 (dd, 1H, *J*=6.9 Hz, *J*=2.6 Hz, *H*$_5$), 5.58 (dd, 1H, *J*=6.9 Hz, *J*=4.4 Hz, *H*$_2$). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.2 (*C*H$_3$-CH$_2$), 15.9 (*C*H$_3$-CH), 19.8 (*C*H$_3$-CH), 26.2 (*C*H$_2$ cy), 26.3 (*C*H$_2$ cy), 26.8 (*C*H$_2$ cy), 27.7 (*C*H$_2$ cy), 28.1 (*C*H$_2$ cy), 31.7 (*C*H), 44.1 (*C*H cy), 62.3 (CH$_3$-*C*H$_2$), 90.9 (*C*$_5$), 110.6 (*C*$_2$), 161.7 (*C*$_4$), 164.1 (*C*O). Anal Calcd. for $C_{15}H_{25}NO_3$: C, 67.38; H, 9.43; N, 5.24. Found C, 67.24; H, 9.59; N, 5.35

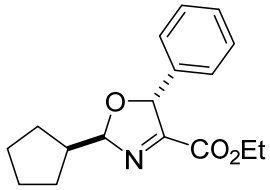


3p **Ethyl (2R*,5R*)-2-cyclohexyl-5-((E)-prop-1-en-1-yl)-2,5-dihydrooxazole-4-carboxylate 3p**. yellow oil. (72%, method A. 68%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.1-1.28 (m, 7H, CH$_{2\ cy}$), 1.33 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 1.65-1.68 (m, 1H, CH$_{2\ cy}$), 1.70 (ddd, *J*=6.6 Hz, *J*=1.6 Hz, *J*=0.8 Hz, CH=CH-C*H*$_3$), 1.73-1.81 (m, 3H, CH$_{2\ cy}$, CH$_{cy}$), 4.29 (dq, 1H, *J*= 10.9 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.30 (dq, 1H, *J*= 10.9 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 5.28-5.31 (m, 1H, *H*$_5$), 5.45 (ddq, 1H, *J*= 15.2 Hz, *J*=7.0 Hz, *J*=1.6 Hz, C$_5$-C*H*=CH), 5.64 (dd, 1H, *J*=6.3 Hz, *J*=4.7 Hz, H$_2$) , 5.84 (dqd, 1H, *J*=15.2 Hz, *J*=6.6 Hz, *J*=1.0 Hz, C$_5$-CH=C*H*). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.2 (*C*H$_3$-CH$_2$), 17.8 (*C*H$_3$-CH=CH), 26.2 (CH$_{2\ cy}$), 26.3 (CH$_{2\ cy}$), 26.7 (CH$_{2\ cy}$), 27.6 (CH$_{2\ cy}$), 28.4 (CH$_{2\ cy}$), 43.7 (*C*H$_{cy}$), 62.3 (CH$_3$-*C*H$_2$), 86.3 (*C*$_5$), 109.8 (*C*$_2$), 126.5 (C$_5$-CH=*C*H), 130.6 (C$_5$-*C*H=CH), 161.1 (*C*$_4$), 163.2 (*C*O). Anal Calcd. for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74; N, 5.28. Found C, 68.15; H, 8.90; N, 5.16

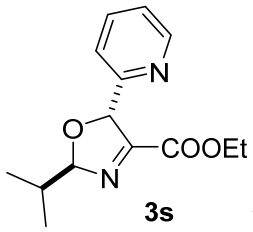


3q **Ethyl (2R*,5R*)-2-cyclopentyl-5-(4-nitrophenyl)-2,5-dihydrooxazole-4-carboxylate 3q**. yellow oil. (92%, method A. 89%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.24 (t, 3H, *J*=7,1 Hz, C*H*$_3$-CH$_2$), 1.48-1.68 (m, 6H, C*H*$_2$ cy), 1.75-1.86 (m, 2H, C*H*$_2$ cy), 2.27-2.37 (m, 1H, C*H* cy),4.21 (dq, 1H, J=10.9 Hz, J=7.1 Hz, CH$_3$-C*H*$_2$), 4.22 (dq, 2H, *J*= 10.9 Hz, *J*= 7.1 Hz, CH$_3$-C*H*$_2$), 6.04 (d, 1H, *J*=6.6 Hz, *H*$_5$), 6.12 (dd, 1H, *J*=6.6 Hz, *J*=6.6 Hz, *H*$_2$), 7.51-7.55 (m, 2H, *H*$_{Ar}$), 8.17-8.21 (m,2H,

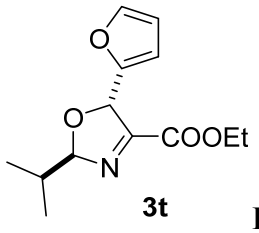
H_{Ar}). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.0 (CH_3-CH_2), 25.9 (CH_2 cy), 26.1 (CH_2 cy), 28.1 (CH_2 cy), 28.4 (CH_2 cy), 45.3 (CH cy), 62.7 (CH_3-CH_2), 86.9 (C_5), 111.5 (C_2), 124.1 (CH_{Ar}), 128.5 (CH_{Ar}), 145.4 (CH_{Ar}), 148.3 (CH_{Ar}), 160.5 (C_4), 161.8 (CO). Anal Calcd. for $C_{17}H_{20}N_2O_3$: C, 61.44; H, 6.07; N, 8.43. Found C, 61.58; H, 6.24; N, 8.37



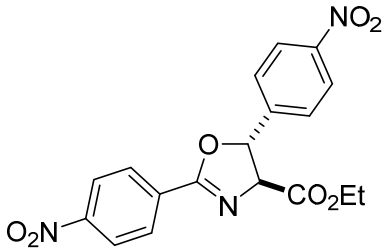
3r **Ethyl (2R*,5R*)-2-cyclopentyl-5-phenyl-2,5-dihydrooxazole-4-carboxylate 3r**. yellow oil. (90%, method A. 86%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.22 (t, 3H, J=7.1 Hz, CH_3-CH_2), 1.45-1.55 (m, 2H, CH_2 cy), 1.58-1.68 (m, 4H, CH_2 cy), 1.72-1.89 (m, 2H, CH_2 cy), 2.25-2.34 (m, 1H, CH cy), 4.19 (dq, 1H, J=10.9 Hz, J=7.1 Hz, CH_3-CH_2), 4.20 (dq, 1H, J=10.9 Hz, J=7.1 Hz, CH_3-CH_2), 5.92 (d, 1H, J=6.6 Hz, H_5), 6.03 (dd, 1H, J=6.6 Hz, J=6.4 Hz, H_2), 7.26-7.38 (m, 5H, H_{Ar}). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.0 (CH_3-CH_2), 26.0 (CH_2 cy), 26.1 (CH_2 cy), 28.1 (CH_2 cy), 28.4 (CH_2 cy), 45.3 (CH cy), 62.4 (CH_3-CH_2), 88.1 (C_5), 110.8 (C_2), 127.6 (CH_{Ar}), 128.9 (CH_{Ar}), 129.0 (CH_{Ar}), 138.4 (CH_{Ar}), 160.4 (C_4), 163.1 (CO). Anal Calcd. for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4.87. Found C, 70.94; H, 7.51; N, 4.95



3s **Ethyl (2R*,5R*)-2-isopropyl-5-(pyridin-2-yl)-2,5-dihydrooxazole-4-carboxylate 3s**. yellow oil. (86%, method A. 89%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.02 (d, 3H, J=6.8 Hz, CH_3-CH), 1.04 (d, 3H, J=6.8 Hz, CH_3-CH), 1.21 (t, 3H, J=7.1 Hz, CH_3-CH_2), 2.05-2.18 (m, 1H, CH), 4.18-4.24 (m, 2H, CH_3-CH_2), 5.88 (dd, 1H, J=6.3 Hz, J=4.8 Hz, H_2), 5.97 (d, 1H, J=6.3, H_5), 7.23-7.27 (m, 1H, H_{Ar}), 7.34-7.36 (m, 1H, H_{Ar}), 7.70-7.75 (m, 1H, H_{Ar}), 8.51-8.53 (m, 1H, H_{Ar}). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.0 (CH_3-CH_2), 17.1 (CH_3-CH), 17.6 (CH_3-CH), 33.9 (CH), 62.3 (CH_3-CH_2), 88.6 (C_5), 112.1 (C_2), 122.8 (CH_{Ar}), 123.8 (CH_{Ar}), 137.2 (CH_{Ar}), 150.0 (CH_{Ar}), 157.2 (C_{Ar}), 160.6 (C_4), 162.5 (CO). Anal Calcd. for $C_{14}H_{18}N_2O_3$: C, 64.11; H, 6.92; N, 10.68. Found C, 64.28; H, 7.13; N, 10.49



3t **Ethyl (2R*,5R*)-5-(furan-2-yl)-2-isopropyl-2,5-dihydrooxazole-4-carboxylate 3t**. transparent oil. (92%, method A. 90%, method B). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 0.99 (d, 3H, *J*=6.8 Hz, C*H*$_3$-CH), 1.02 (d, 3H, *J*=6.8 Hz, C*H*$_3$-CH), 1.26 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 2.01-2.16 (m, 1H, C*H*), 4.21-4.29 (m, 2H, CH$_3$-C*H*$_2$), 5.80 (dd, 1H, *J*=6.2 Hz, *J*=4.9 Hz, *H*$_2$), 5.95 (d, 1H, *J*=6.2, *H*$_5$), 6.36-6.39 (m, 2H, *H*$_{Ar}$), 7.39-7.40 (m, 1H, *H*$_{Ar}$). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.1 (*C*H$_3$-CH$_2$), 17.0 (*C*H$_3$-CH), 17.6 (*C*H$_3$-CH), 33.8 (*C*H), 62.5 (CH$_3$-*C*H$_2$), 80.6 (*C*$_5$), 109.4 (*C*H$_{Ar}$), 110.4 (*C*$_{Ar}$), 111.0 (*C*H$_{Ar}$), 111.0 (*C*$_2$), 143.5 (*C*H$_{Ar}$), 150.7 (*C*$_4$), 160.6 (*C*O). Anal Calcd. for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found C, 62.05; H, 6.75; N, 5.69



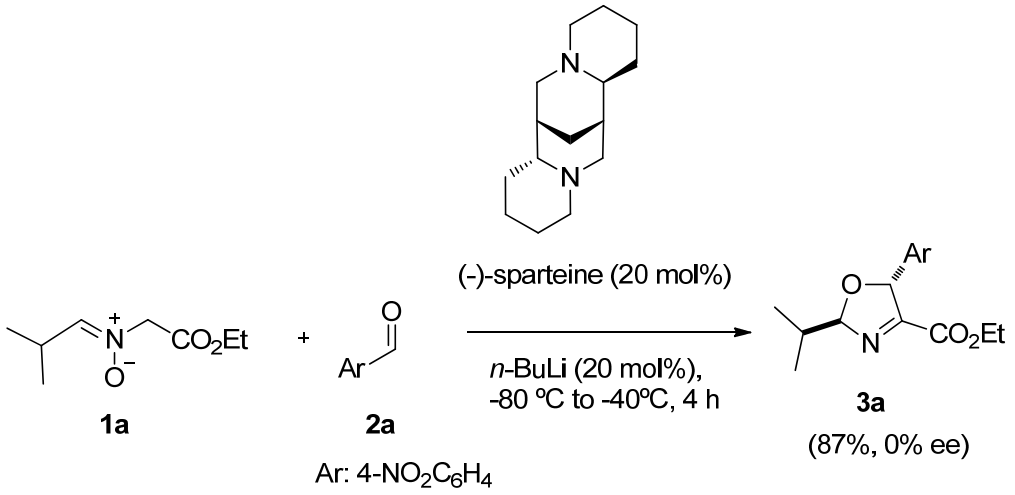
4 **Ethyl (4S*,5R*)-2,5-bis(4-nitrophenyl)-4,5-dihydrooxazole-4-carboxylate 4**. white solid. (76%). mp 90-92 ºC. ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.35 (t, 3H, *J*=7.1 Hz, C*H*$_3$-CH$_2$), 4.32 (dq, 1H, *J*=10.8 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.33 (dq, 1H, *J*=10.8 Hz, *J*=7.1 Hz, CH$_3$-C*H*$_2$), 4.82 (d, 1H, *J*=8.0 Hz, *H*$_4$), 6.05 (d, 1H, *J*=8.0 Hz, *H*$_5$), 7.62-7.57 (m, 2H, C*H*$_{Ar}$), 8.29-8.23 (m, 4H, *H*$_{Ar}$), 8.35-8.34 (m, 2H, *H*$_{Ar}$). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 14.3 (*C*H$_3$-CH$_2$), 62.8 (CH$_3$-*C*H$_2$), 77.5 (*C*$_4$), 83.1 (*C*$_5$), 124.1 (*C*H$_{Ar}$), 124.6 (*C*H$_{Ar}$), 126.8 (*C*H$_{Ar}$), 130.2 (*C*H$_{Ar}$), 132.8 (*C*$_{Ar}$), 146.6 (*C*$_{Ar}$), 148.6 (*C*$_{Ar}$), 150.5 (*C*$_{Ar}$), 163.6 (*C*$_2$), 170.1 (*C*O). Anal Calcd. for $C_{18}H_{15}N_3O_7$: C, 56.11; H, 3.92; N, 10.91. Found C, 56.27; H, 4.16; N, 10.78

Gram-scale Synthesis of 3-oxazoline 3a.

Method A. To a cooled (-80 ºC) solution of nitrone **1a** (1.03 g, 6 mmol) in anhydrous THF (50 mL), *n*-BuLi (0.8 mL of a 1.6M solution in hexanes, 1.28 mmol) was added dropwise during 30 minutes. The resulting mixture was stirred at -80ºC for 20 min at which time a cooled (-80 ºC) solution of aldehyde **2a** (0.91 g, 6 mmol) in anhydrous THF (30 mL), was added via cannula during a period of 15 min. The reaction mixture was kept at -80ºC for additional 5 min and then the cooler was programmed to warm up to -40 ºC. The reaction mixture was kept at -40 ºC for 4 hours. Ammonium chloride (10 mL) was added dropwise with vigorous stiring and the reaction mixture was warmed at ambient temperature, diluted with dichloromethane (150 mL) and treated with a saturated solution of ammonium chloride (100 mL). The organic layer was separated, dried over magnesium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography (gradient from hexane 100% to 7:3 hexane/EtOAc) to give 1.36 g (74%) of the pure 3-oxazoline **3a**.

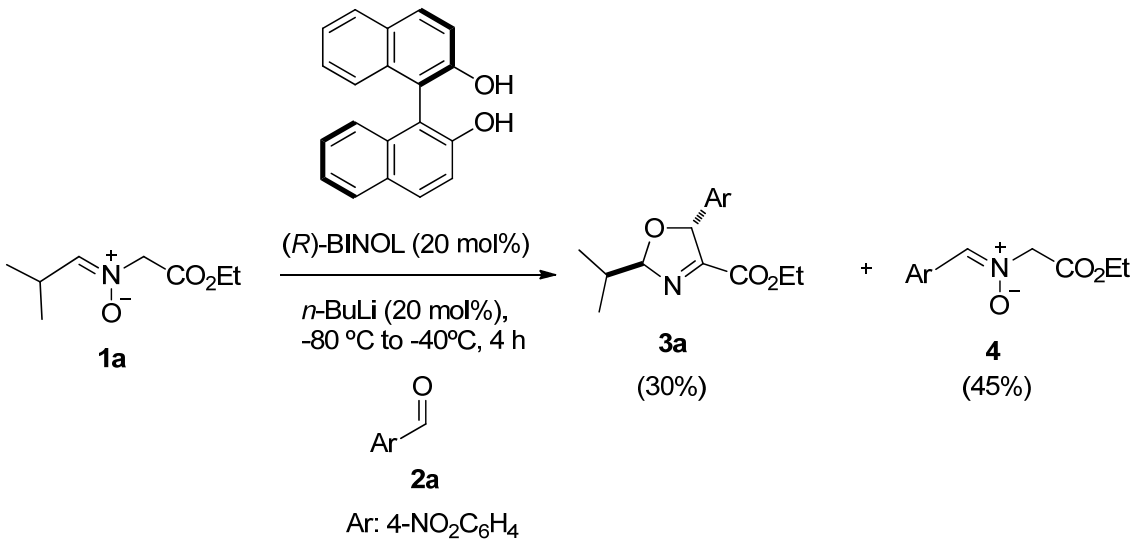
Method B. To a solution of nitrone **1a** (1.03 g, 6 mmol) in acetonitrile (40 mL), aldehyde **2a** (0.91 g, 6 mmol), DABCO (337 mg, 3 mmol) and LiBr (260 mg, 3 mmol) were added. The resulting mixture was stirred mechanically at ambient temperature for 24 h at which time a saturated solution of ammonium chloride (100 mL) was added. The reaction mixture was diluted with dichloromethane (150 mL) and the organic layer was separated, dried over magnesium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography (gradient from hexane 100% to 7:3 hexane/EtOAc) to give 1.29 g (70%) of the pure 3-oxazoline **3a**.

Addition in the presence of sparteine.

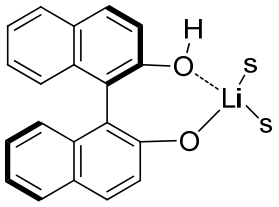


To a cooled (-80 ºC) solution of (-)-sparteine (29 mg, 0.12 mmol) in toluene (4 mL), *n*-BuLi (75 µL of a 1.6M solution in hexanes, 0.12 mmol) was added. The resulting mixture was stirred at -80ºC for 5 min and then was treated with a solution of nitrone **1a** (103 mg, 0.6 mmol) in toluene (4 mL). The resulting mixture was stirred at -80ºC for 15 min at which time a cooled (-80 ºC) solution of aldehyde **2a** (91 mg, 0.6 mmol) in toluene (2 mL), was added. The reaction mixture was kept at -80ºC for additional 5 min and then warmed to -40 ºC. The reaction mixture was kept at -40 ºC for 4 hours. Ammonium chloride (1 mL) was added and the reaction mixture was warmed at ambient temperature, diluted with dichloromethane (15 mL) and treated with a saturated solution of ammonium chloride (10 mL). The organic layer was separated, dried over magnesium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography (gradient from hexane 100% to 7:3 hexane/EtOAc) to give 160 mg (87%) of 3-oxazoline **3a**. The ee (6%) was determined by HPLC using a *Chiralpak IA* column [hexane/EtOAc (90:10)]; flow rate 1.0 mL/min; τ_{major}=5.37 min, τ_{minor}=4.77 min.

Addition catalyzed by a chiral alkoxide.



To a cooled (-80 ºC) solution of (*R*)-BINOL (34 mg, 0.12 mmol) in THF (4 mL), *n*-BuLi (75 µL of a 1.6M solution in hexanes, 0.12 mmol) was added. The resulting mixture was stirred at -80ºC for 5 min with the aim of preparing chiral lithium alkoxyde **LA**. The resultin solution was then treated with a solution of nitrone **1a** (103 mg, 0.6 mmol) in THF (4 mL). The resulting mixture was stirred at -80ºC for 15 min at which time a cooled (-80 ºC) solution of aldehyde **2a** (91 mg, 0.6 mmol) in THF (2 mL), was added. The reaction mixture was kept at -80ºC for additional 5 min and then warmed to -40 ºC. The reaction mixture was kept at -40 ºC for 4 hours. Ammonium chloride (1 mL) was added and the reaction mixture was warmed at ambient temperature, diluted with dichloromethane (15 mL) and treated with a saturated solution of ammonium chloride (10 mL). The organic layer was separated, dried over magnesium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography (gradient from hexane 100% to 7:3 hexane/EtOAc and then to 1:1 hexane/EtOAc) to give 55 mg (30%) of 3-oxazoline **3a** and 68 mg (45%) of nitrone **4**.

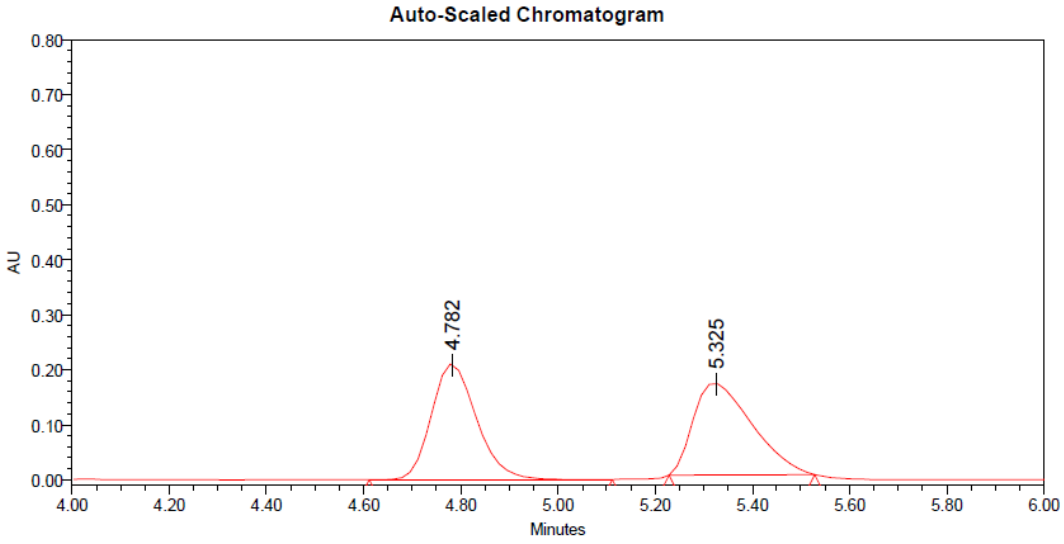


LA

The ee (10%) was determined by HPLC using a *Chiralpak IA* column [hexane/EtOAc (90:10)]; flow rate 1.0 mL/min; τ_{major}=5.32 min, τ_{minor}=4.83 min.

SAMPLE INFORMATION

Sample Name:	VJ-430	Acquired By:	asimetrica
Sample Type:	racemic	Date Acquired:	5/30/2016 4:47:20 PM
Vial:	19	Acq. Method Set:	IA_1_80A_20C
Injection #:	1	Date Processed:	5/30/2016 7:03:13 PM
Injection Volume:	5.00 ul	Processing Method	oks2
Run Time:	60.0 Minutes	Channel Name:	Wvln Ch1
Sample Set Name		Proc. Chnl. Descr.:	PDA 338.4 nm



Peak Results

	Name	RT	Area	Height	% Area
1		4.782	1355699	209947	49.26
2		5.325	1396692	166054	50.74

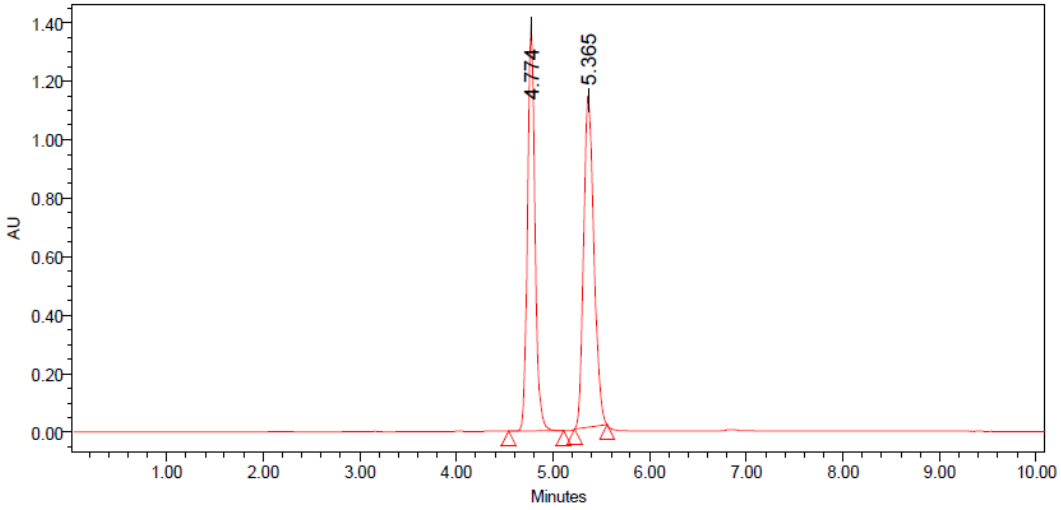
PDA Result Table

	Name	RT	Purity1 Angle	Purity1 Threshold	Match1 Spect. Name	Match1 Angle	Match1 Threshold
1		4.782					
2		5.325					

Figure S10. HPLC chromatogram (Chiralpak IA column; [hexane/EtOAc (90:10)]; flow rate 1.0 mL/min) corresponding to racemic **3a**.

SAMPLE INFORMATION

Sample Name:	VJ-433	Acquired By:	asimetrica
Sample Type:	(-)-sparteine-BuLi (20 mol%)	Date Acquired:	5/30/2016 5:40:01 PM
Vial:	20	Acq. Method Set:	IA_1_80A_20C
Injection #:	3	Date Processed:	5/30/2016 6:43:31 PM
Injection Volume:	2.00 ul	Processing Method	okq1
Run Time:	60.0 Minutes	Channel Name:	WvIn Ch2
Sample Set Name		Proc. Chnl. Descr.:	PDA 263.6 nm



Peak Results

	Name	RT	Area	Height	% Area
1		4.774	7419144	1372173	47.12
2		5.365	8326805	1133641	52.88

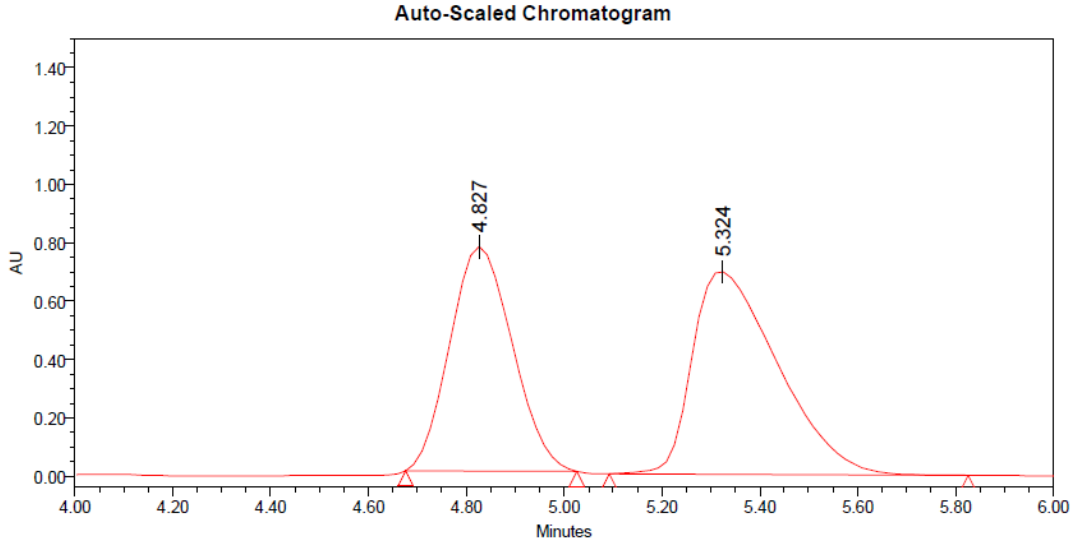
PDA Result Table

	Name	RT	Purity1 Angle	Purity1 Threshold	Match1 Spect. Name	Match1 Angle	Match1 Threshold
1		4.774					
2		5.365					

Figure S11. HPLC chromatogram (Chiralpak IA column; [hexane/EtOAc (90:10)]; flow rate 1.0 mL/min) corresponding to the reaction between **1a** and **2a** in the presence of (-)-sparteine (20 mol%).

SAMPLE INFORMATION

Sample Name:	VJ-426 B	Acquired By:	asimetrica
Sample Type:	(R)-BINOL-BuLi 20 mol%	Date Acquired:	5/30/2016 12:56:48 PM
Vial:	19	Acq. Method Set:	IA_1_80A_20C
Injection #:	2	Date Processed:	5/30/2016 6:54:09 PM
Injection Volume:	10.00 ul	Processing Method	v
Run Time:	60.0 Minutes	Channel Name:	WvIn Ch1
Sample Set Name		Proc. Chnl. Descr.:	PDA 313.5 nm



Peak Results

	Name	RT	Area	Height	% Area
1		4.827	6842194	769112	44.83
2		5.324	8421173	694854	55.17

PDA Result Table

	Name	RT	Purity1 Angle	Purity1 Threshold	Match1 Spect. Name	Match1 Angle	Match1 Threshold
1		4.827					
2		5.324					

Figure S12. HPLC chromatogram (Chiralpak IA column; [hexane/EtOAc (90:10)]; flow rate 1.0 mL/min) corresponding to the reaction between **1a** and **2a** in the presence of (*R*)BINOL (20 mol%).

X-ray structures

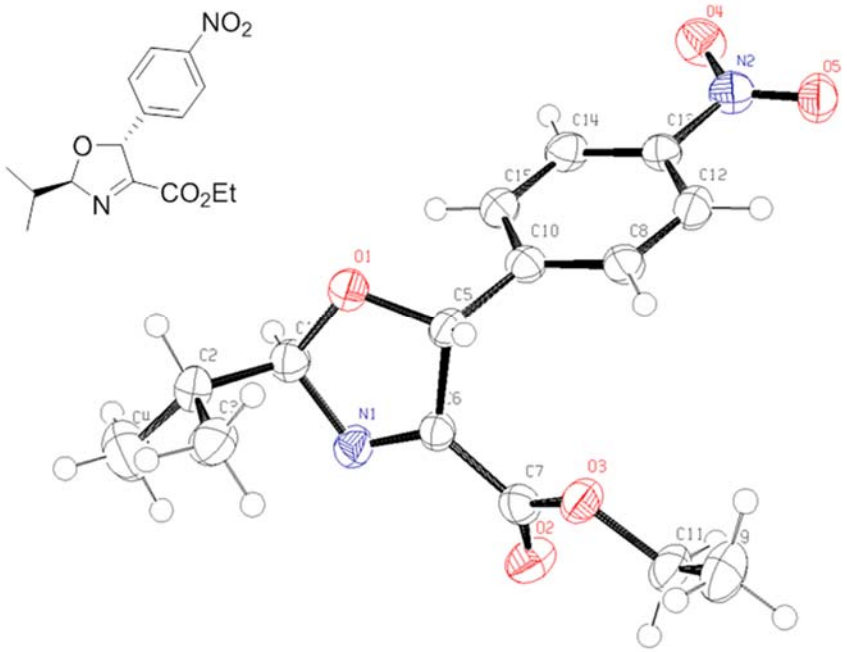


Figure S13. ORTEP representation of compound **3a**. Ellipsoids are represented at 50% probability level.

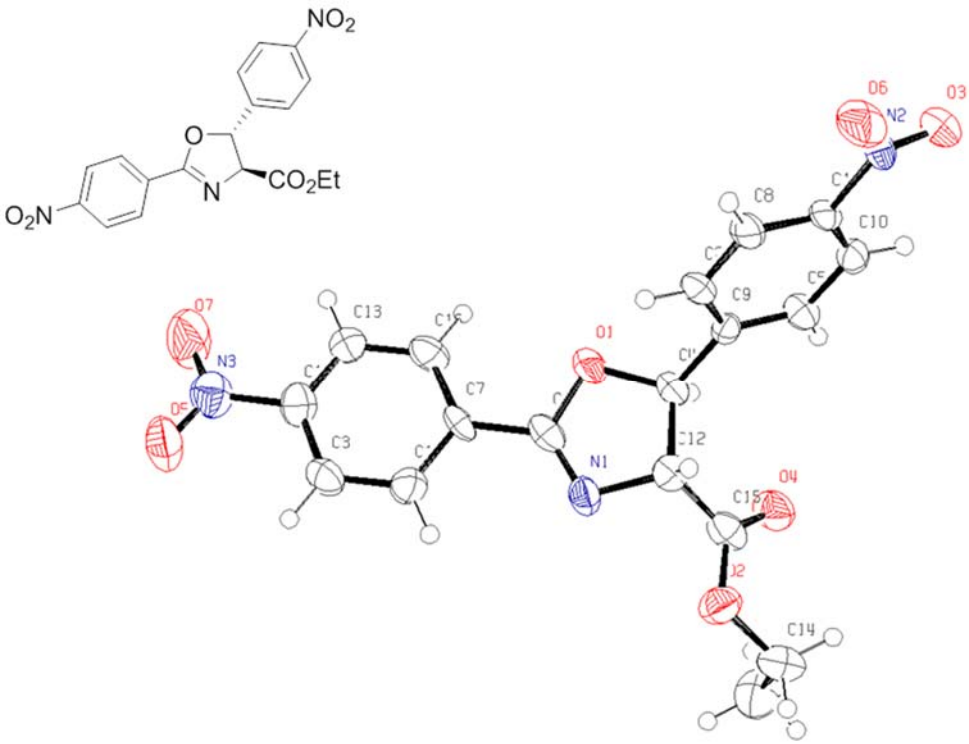
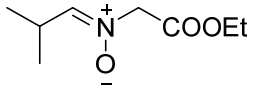


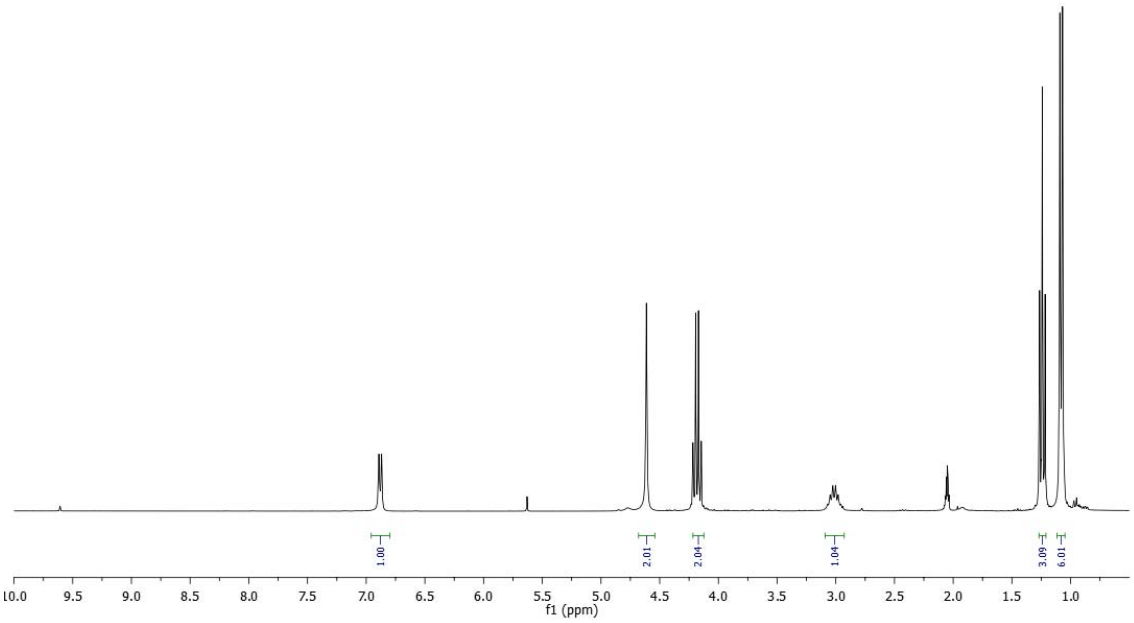
Figure S14. ORTEP representation of compound **4**. Ellipsoids are represented at 50% probability level

Copies of Spectra

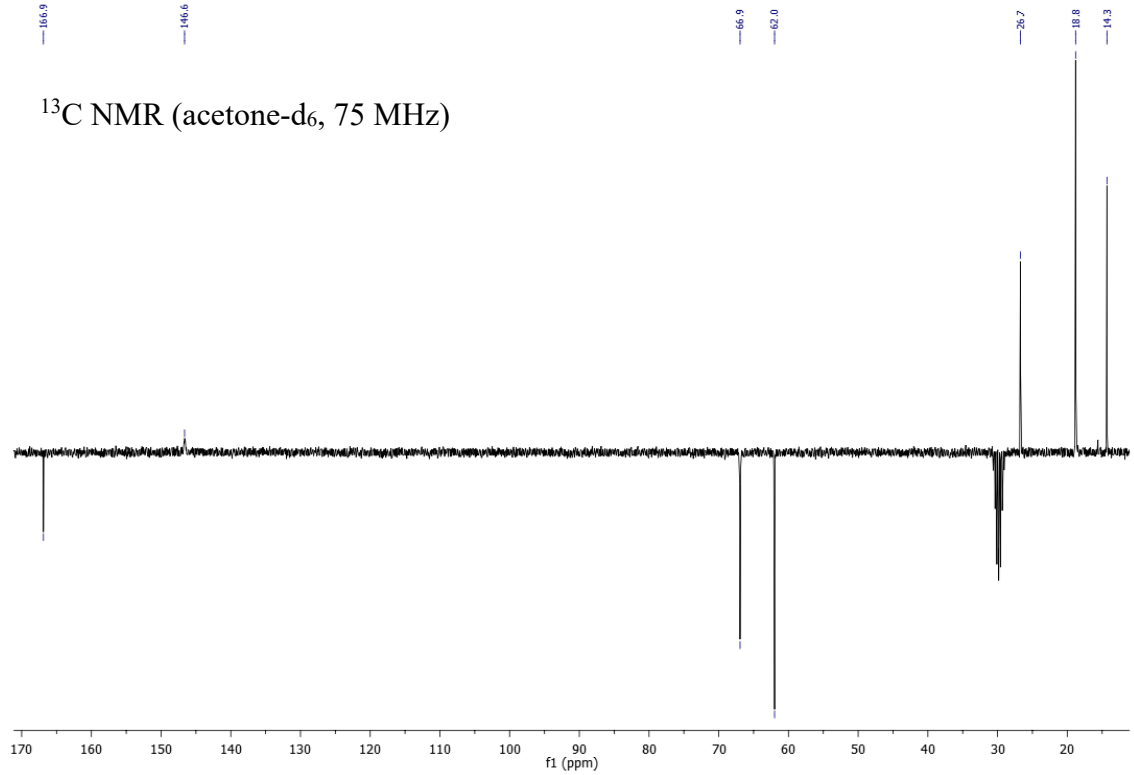


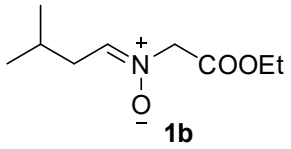
1a

^{1}H NMR (acetone-d_6, 300 MHz)



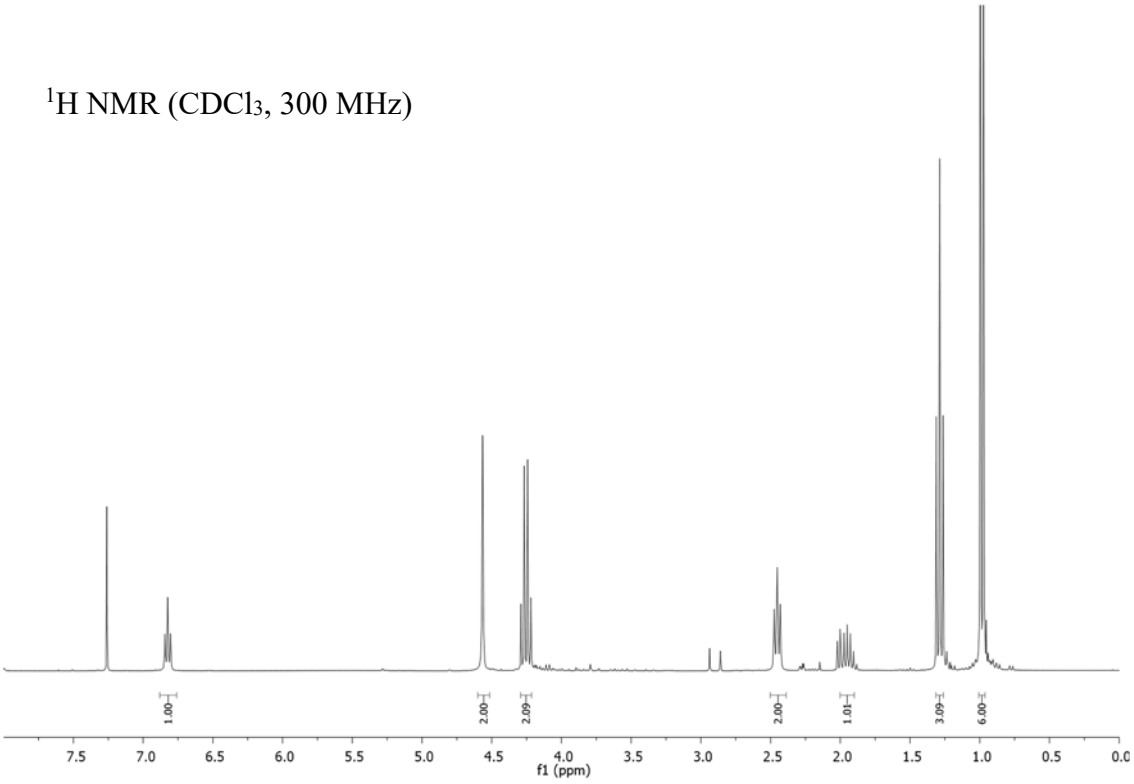
^{13}C NMR (acetone-d_6, 75 MHz)



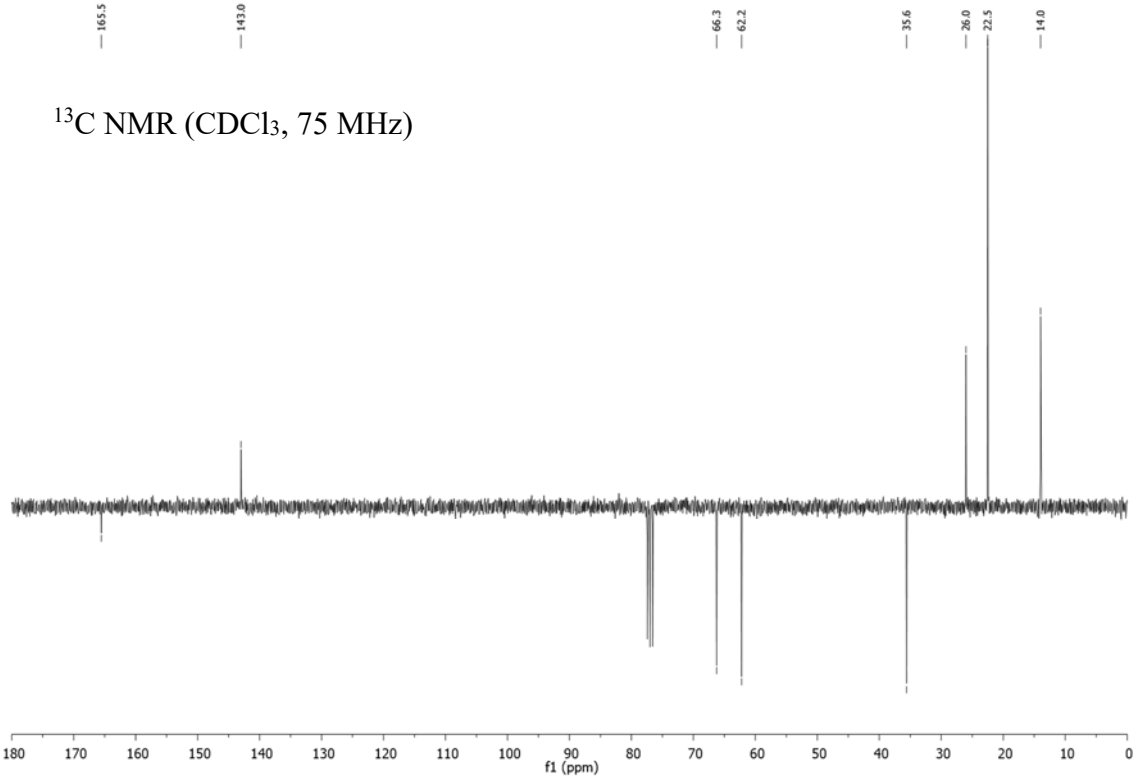


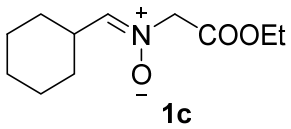
1b

^{1}H NMR ($CDCl_3$, 300 MHz)



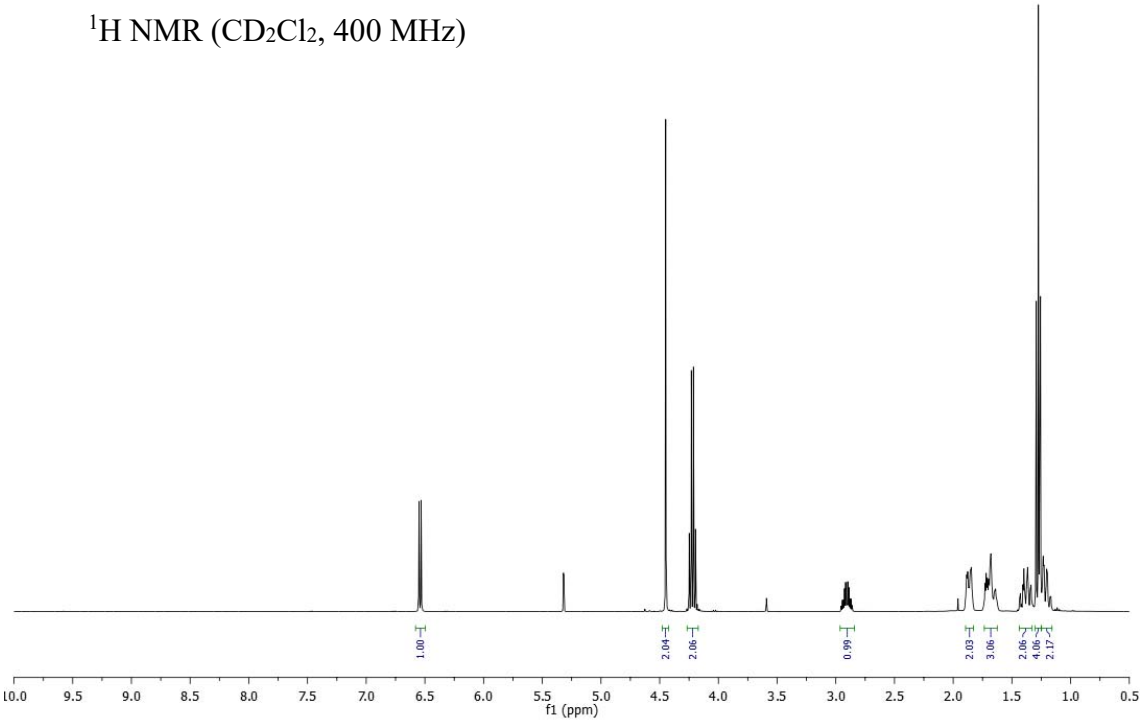
^{13}C NMR ($CDCl_3$, 75 MHz)



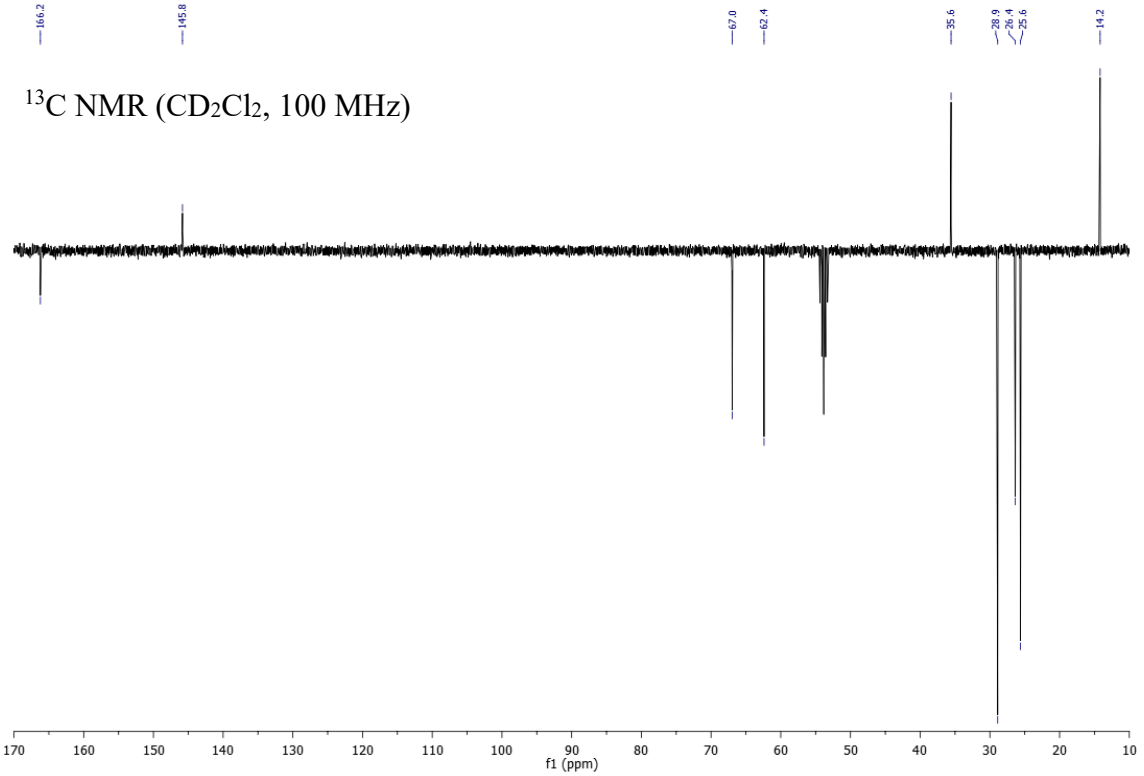


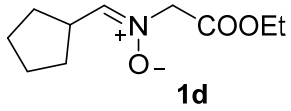
1c

^{1}H NMR (CD_2Cl_2, 400 MHz)



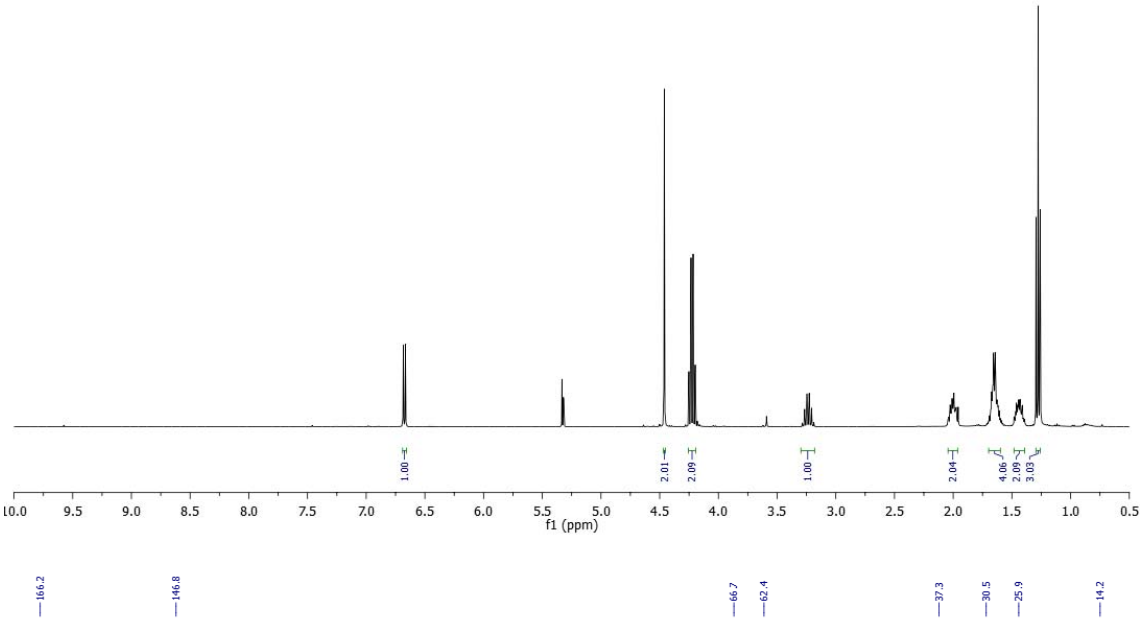
^{13}C NMR (CD_2Cl_2, 100 MHz)



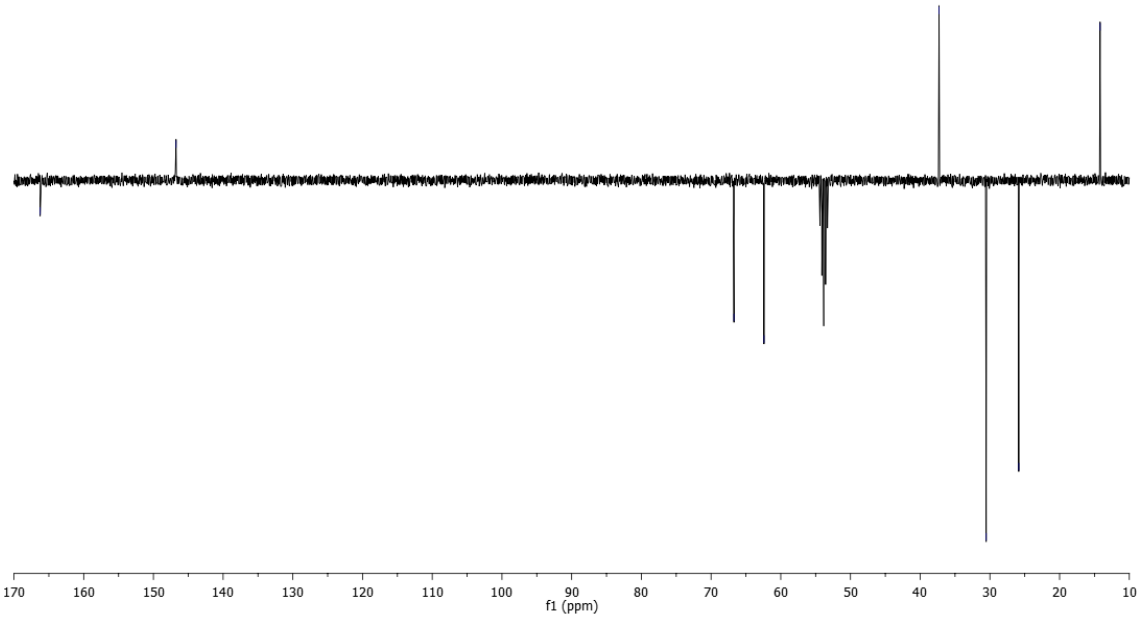


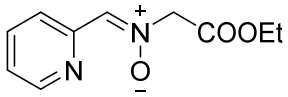
1d

^{1}H NMR (CD_2Cl_2, 400 MHz)

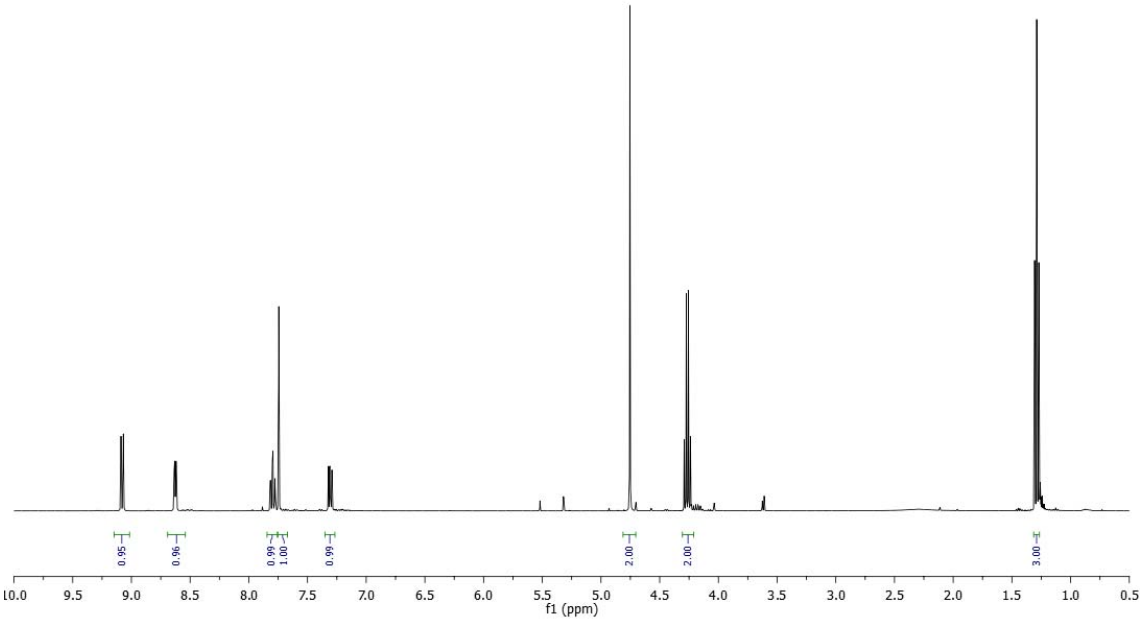


^{13}C NMR (CD_2Cl_2, 100 MHz)

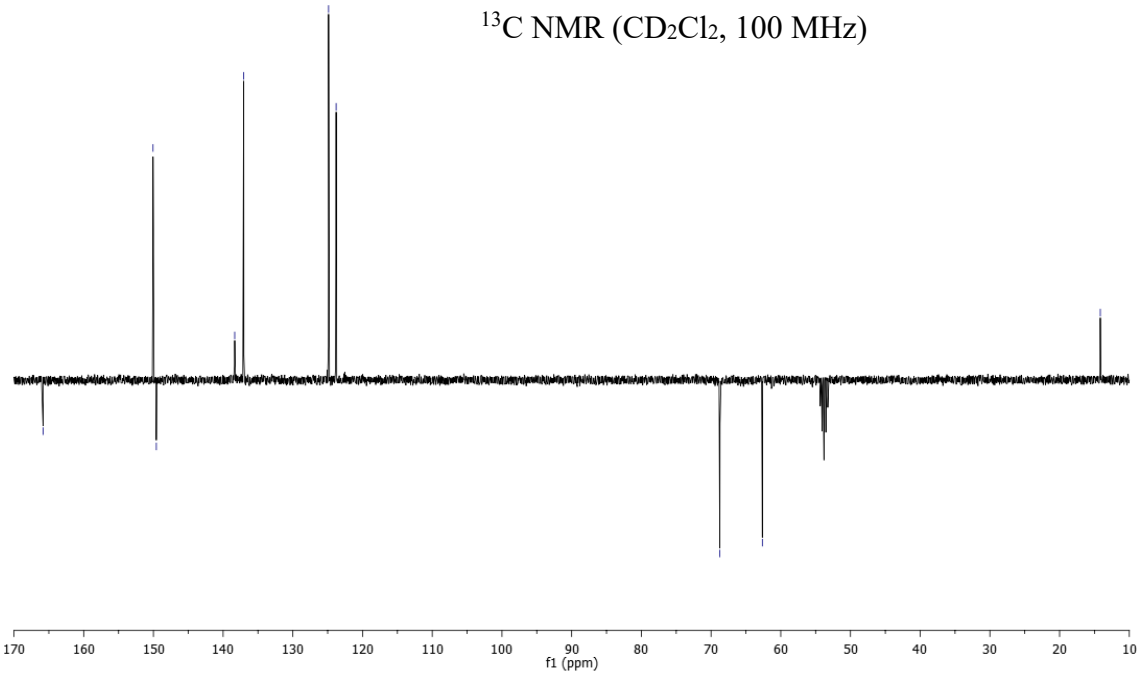


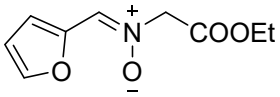


^{1}H NMR (CD_2Cl_2, 400 MHz)

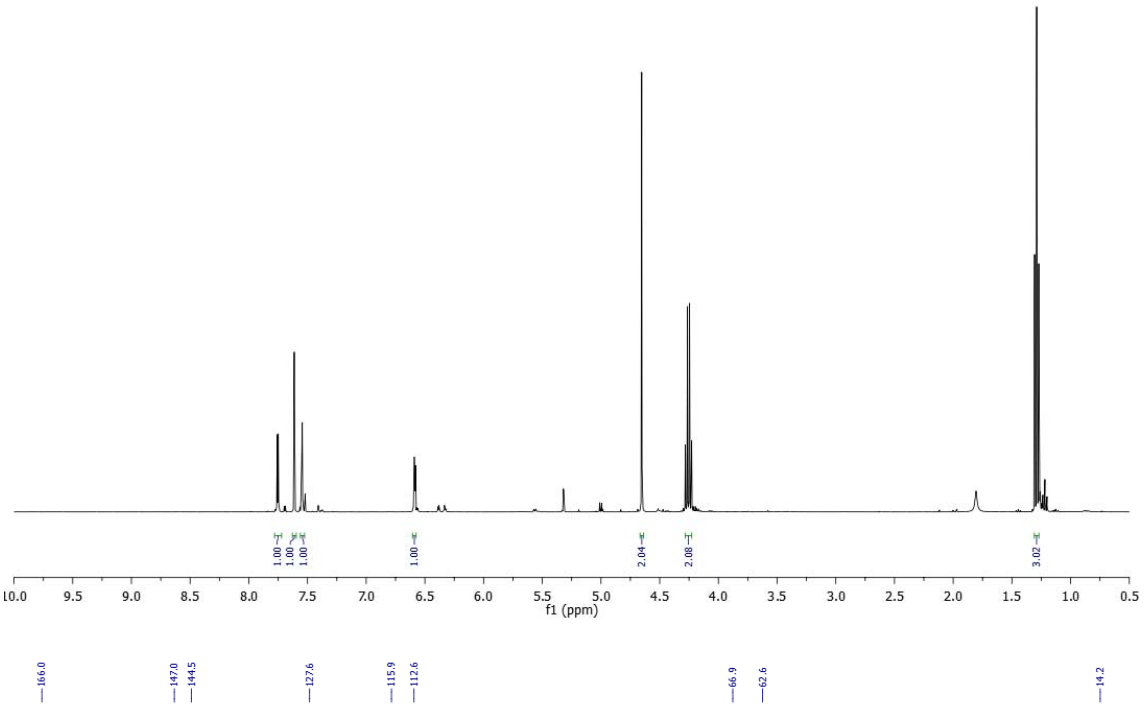


^{13}C NMR (CD_2Cl_2, 100 MHz)

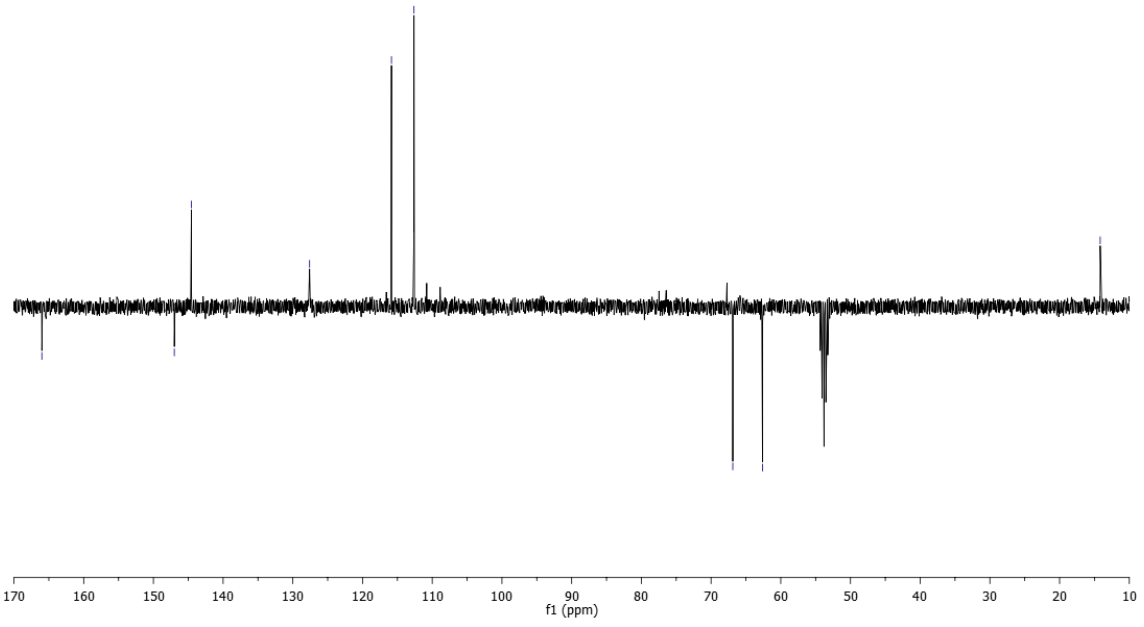


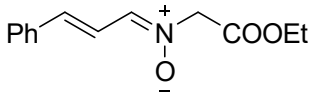


^{1}H NMR (CD_2Cl_2, 400 MHz)

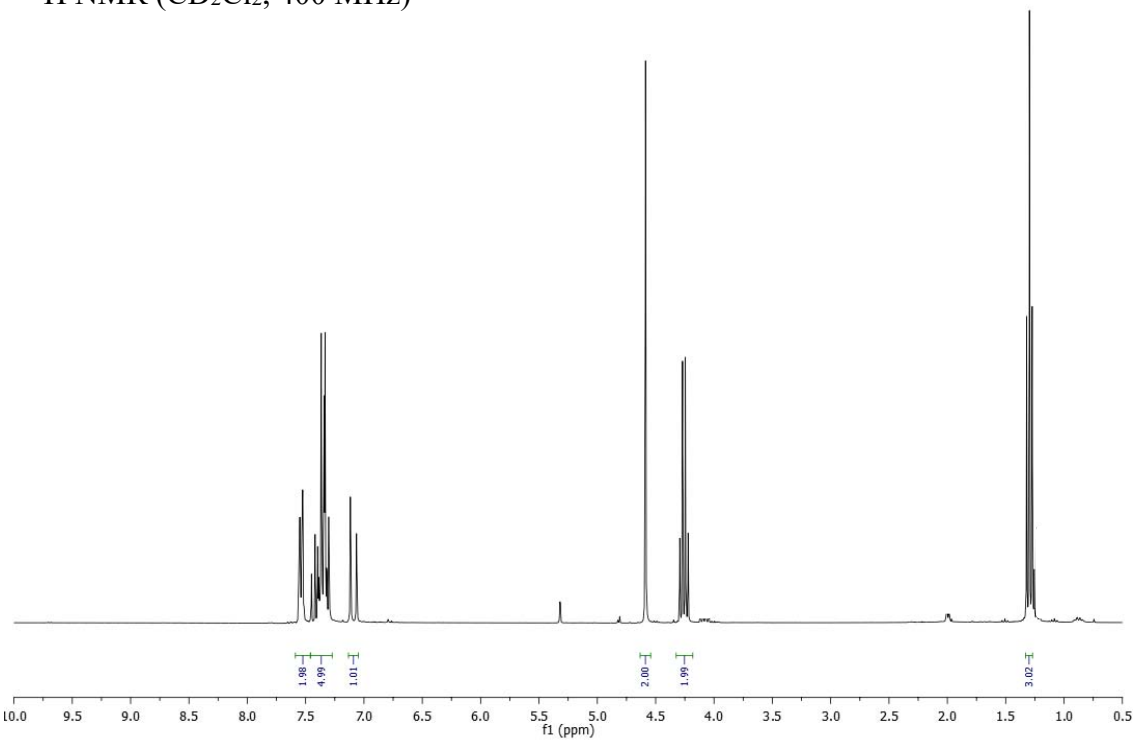


^{13}C NMR (CD_2Cl_2, 100 MHz)

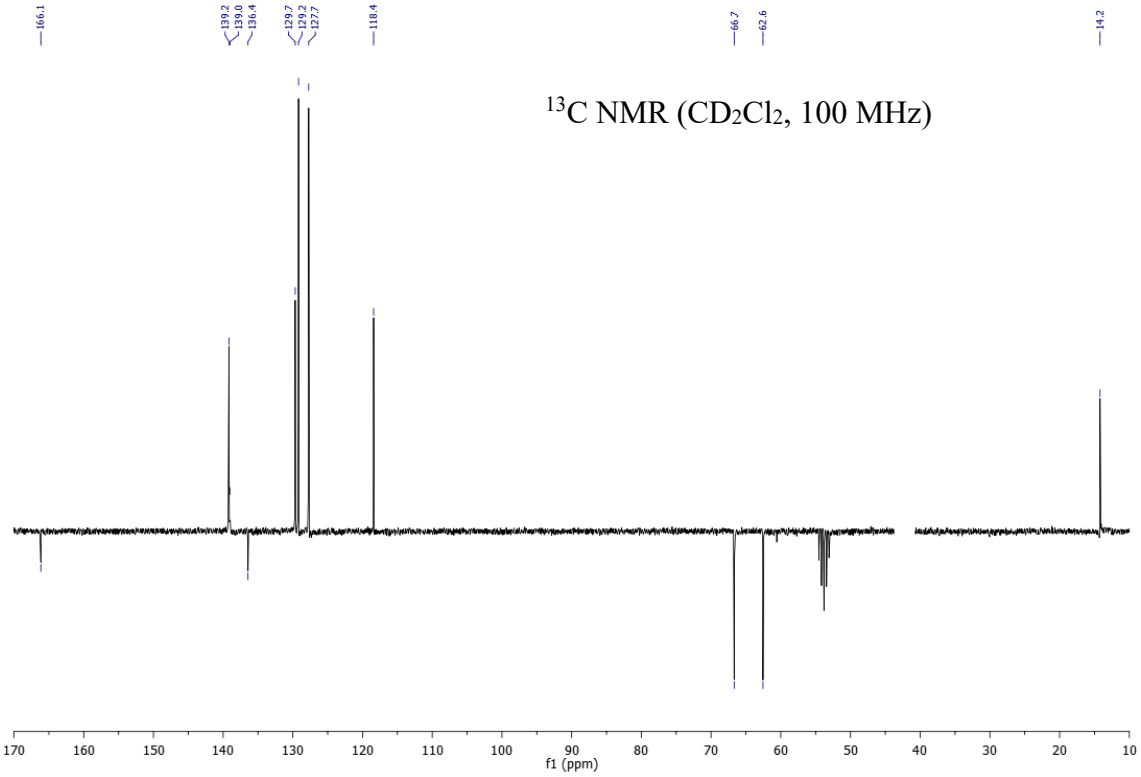


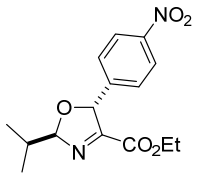


^{1}H NMR (CD_2Cl_2, 400 MHz)



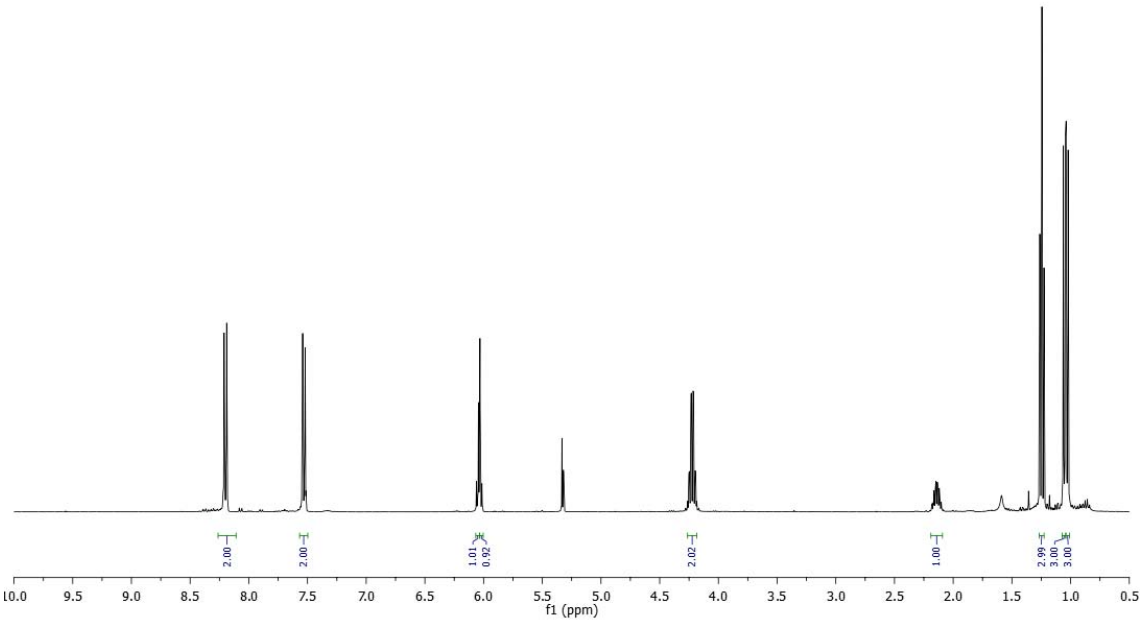
^{13}C NMR (CD_2Cl_2, 100 MHz)



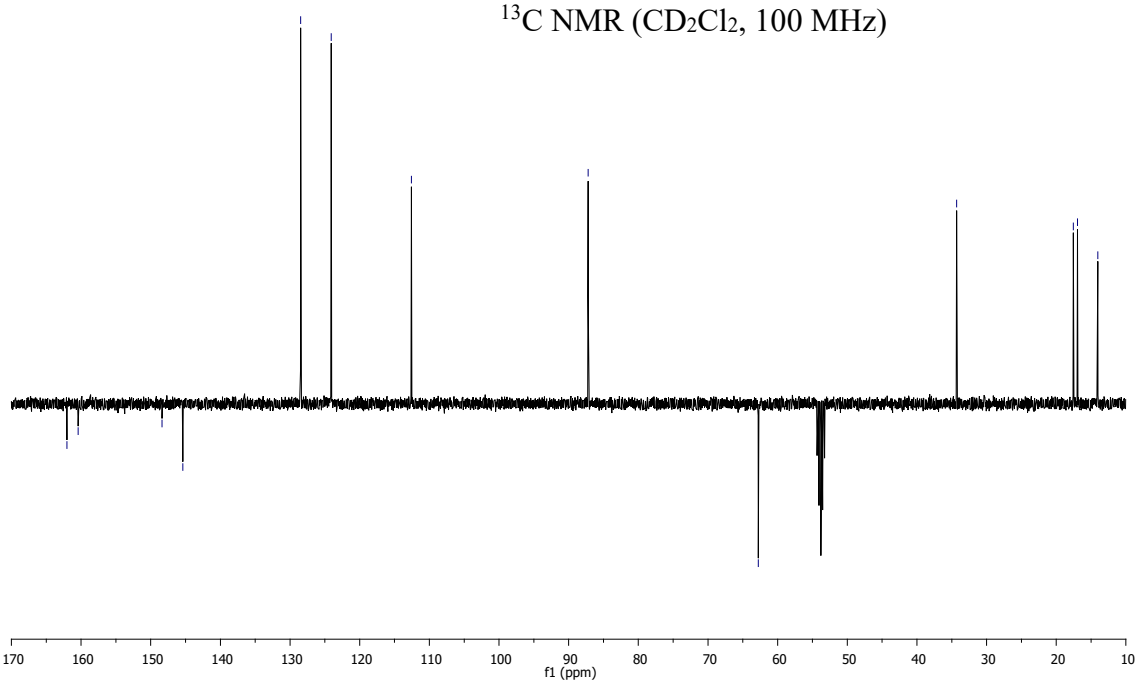


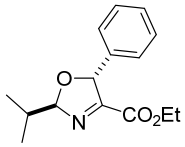
3a

^{1}H NMR (CD_2Cl_2, 400 MHz)



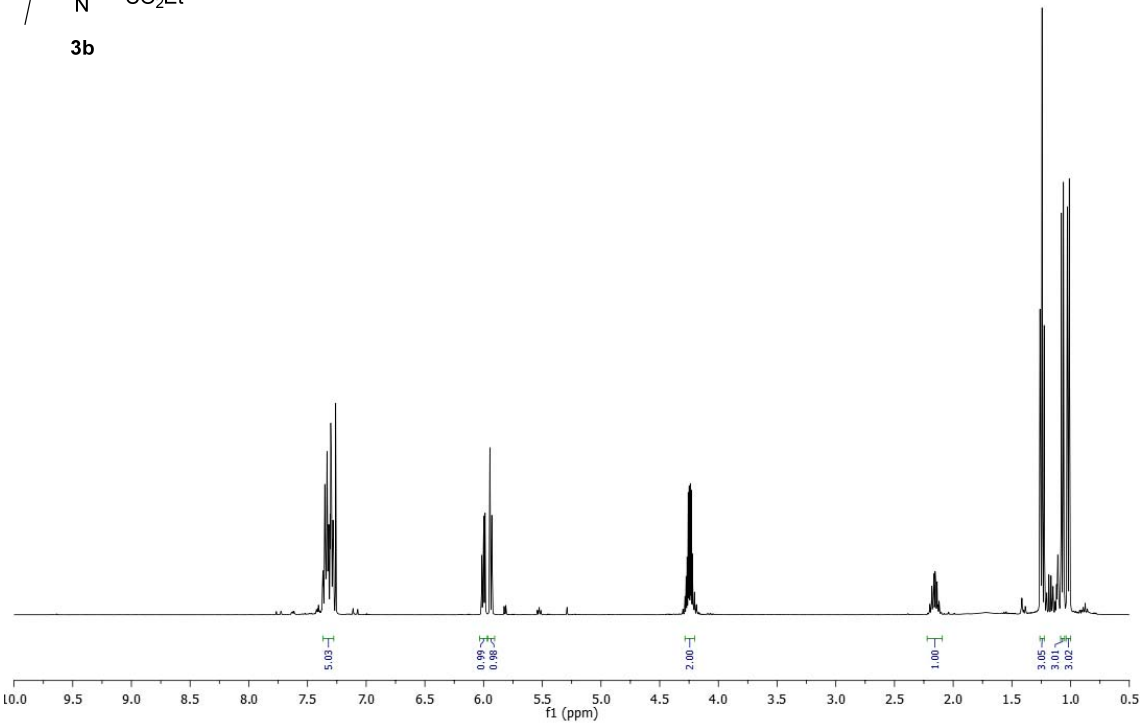
^{13}C NMR (CD_2Cl_2, 100 MHz)



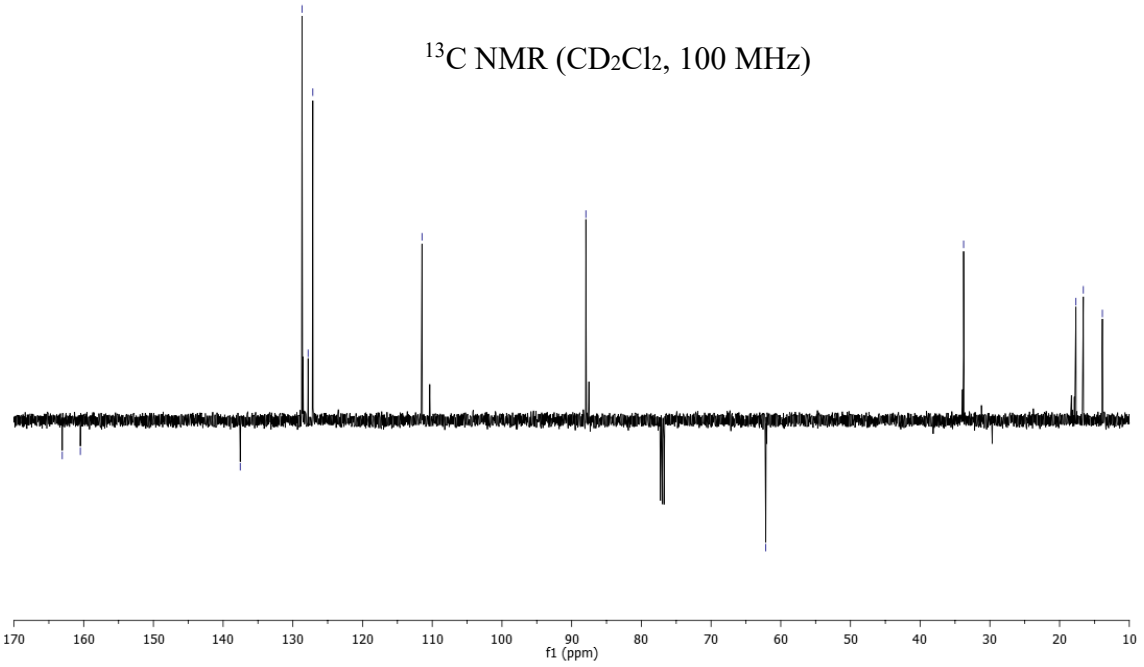


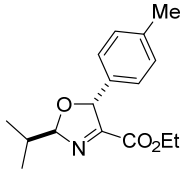
3b

^{1}H NMR (CD_2Cl_2, 400 MHz)



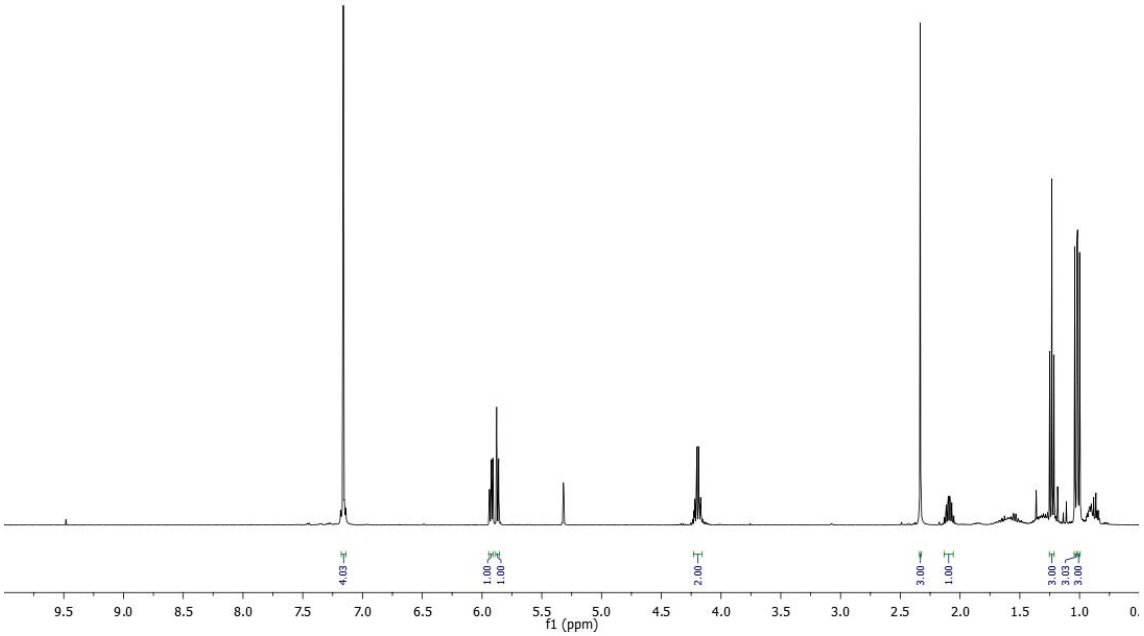
^{13}C NMR (CD_2Cl_2, 100 MHz)

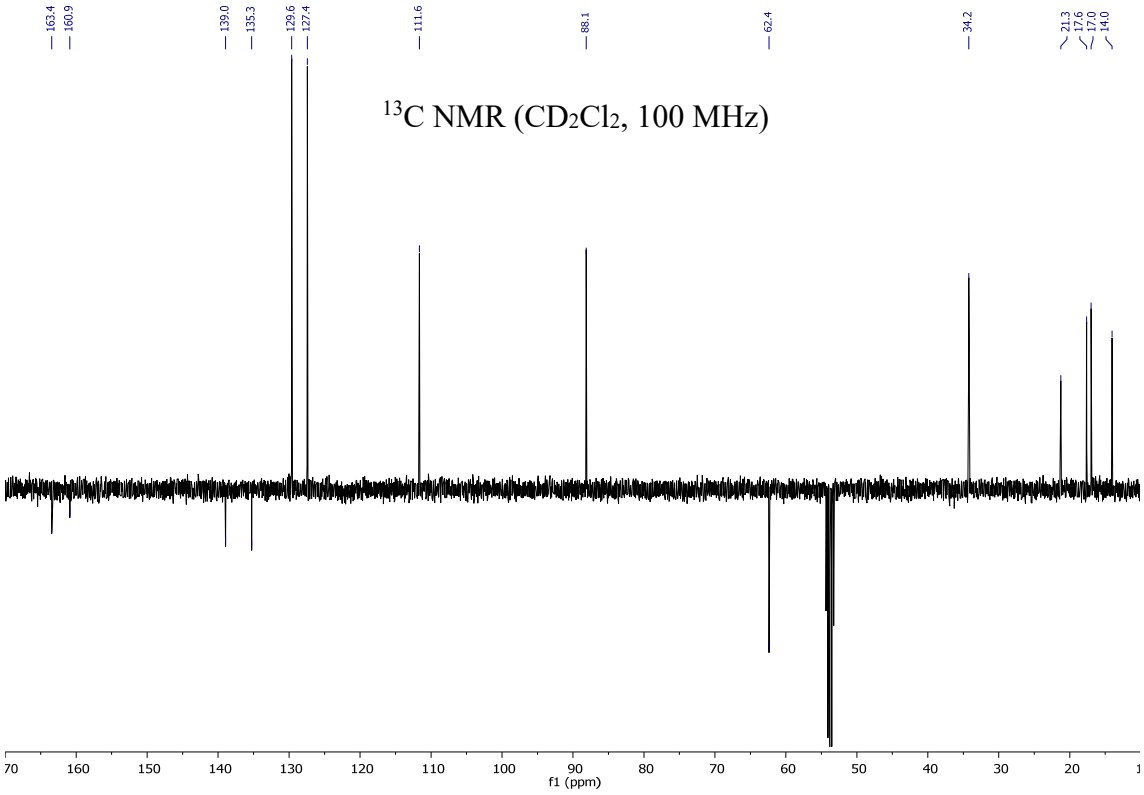




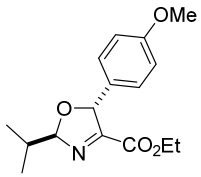
3c

^{1}H NMR (CD_2Cl_2, 400 MHz)



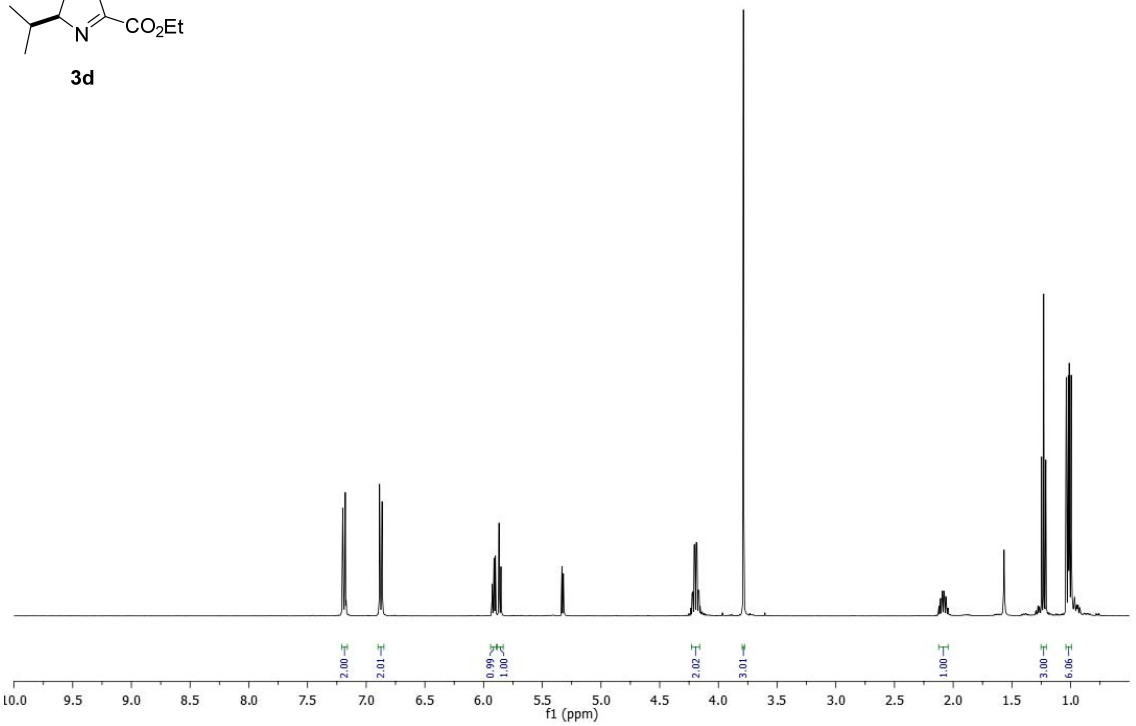


^{13}C NMR (CD_2Cl_2, 100 MHz)

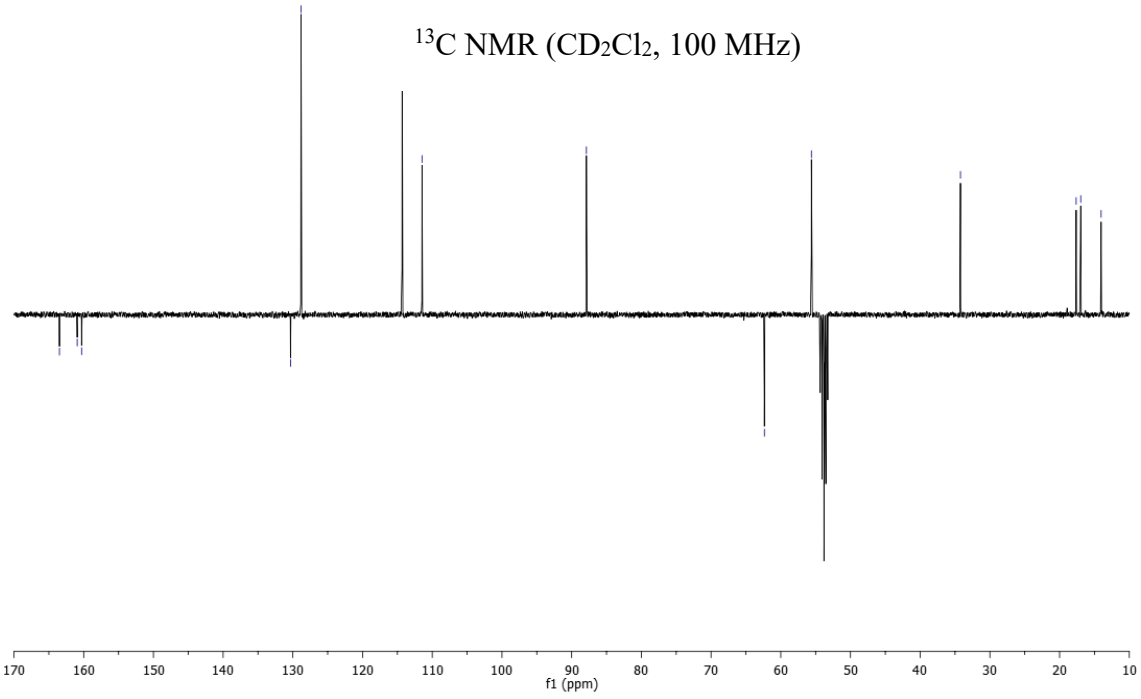


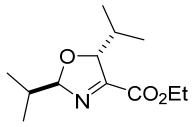
3d

^{1}H NMR (CD_2Cl_2, 400 MHz)



^{13}C NMR (CD_2Cl_2, 100 MHz)

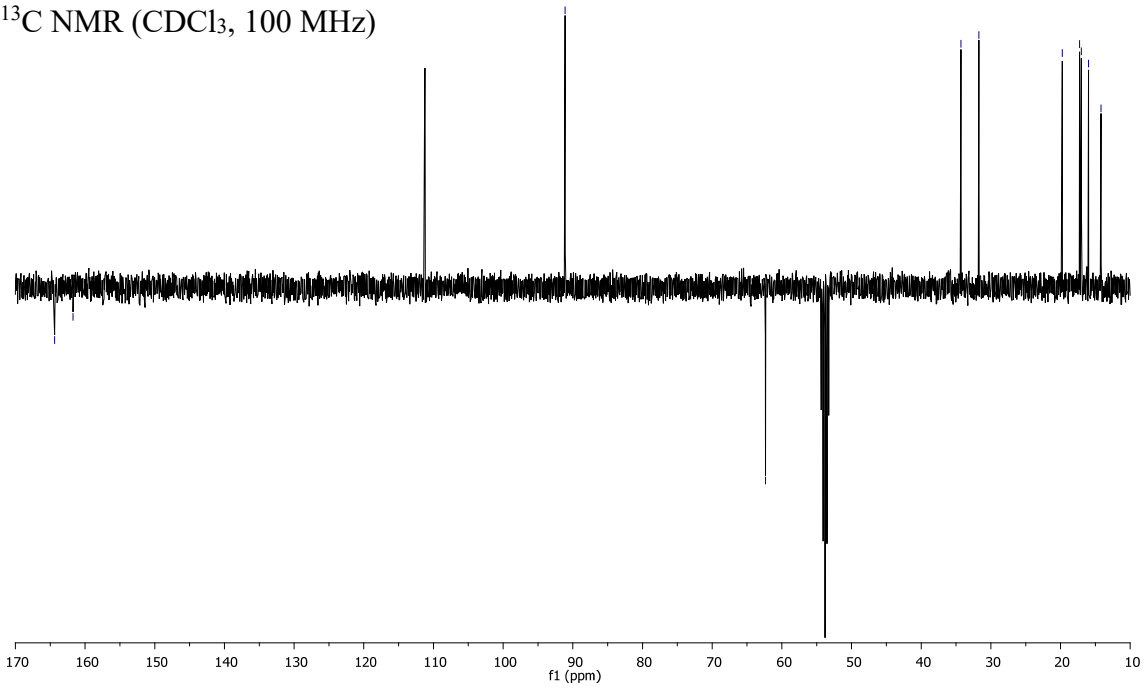


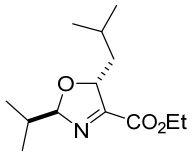


3e

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

^{13}C NMR ($CDCl_3$, 100 MHz)

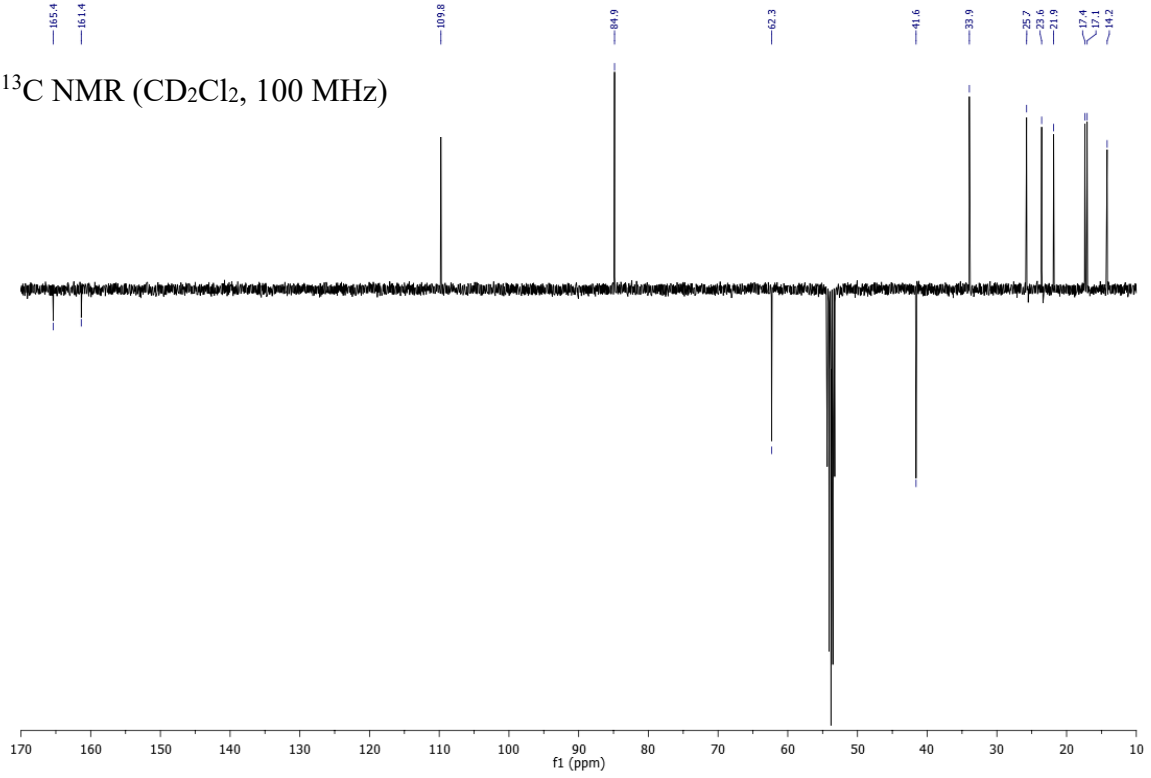


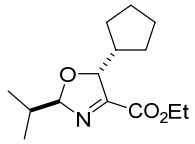


3f

^{1}H NMR (CD_2Cl_2, 400 MHz)

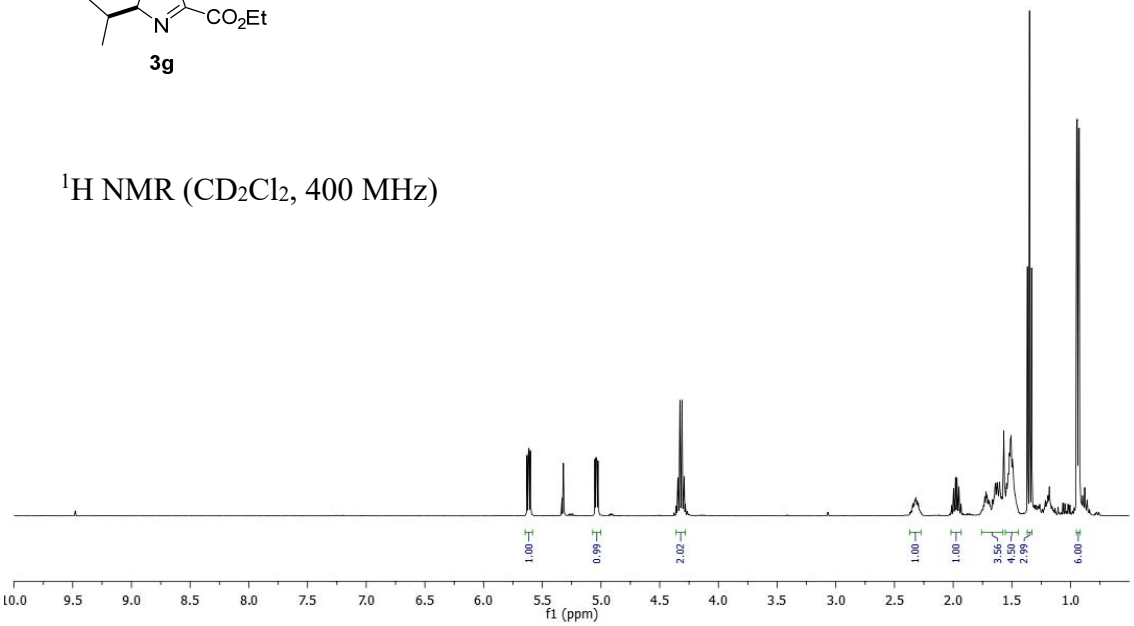
^{13}C NMR (CD_2Cl_2, 100 MHz)



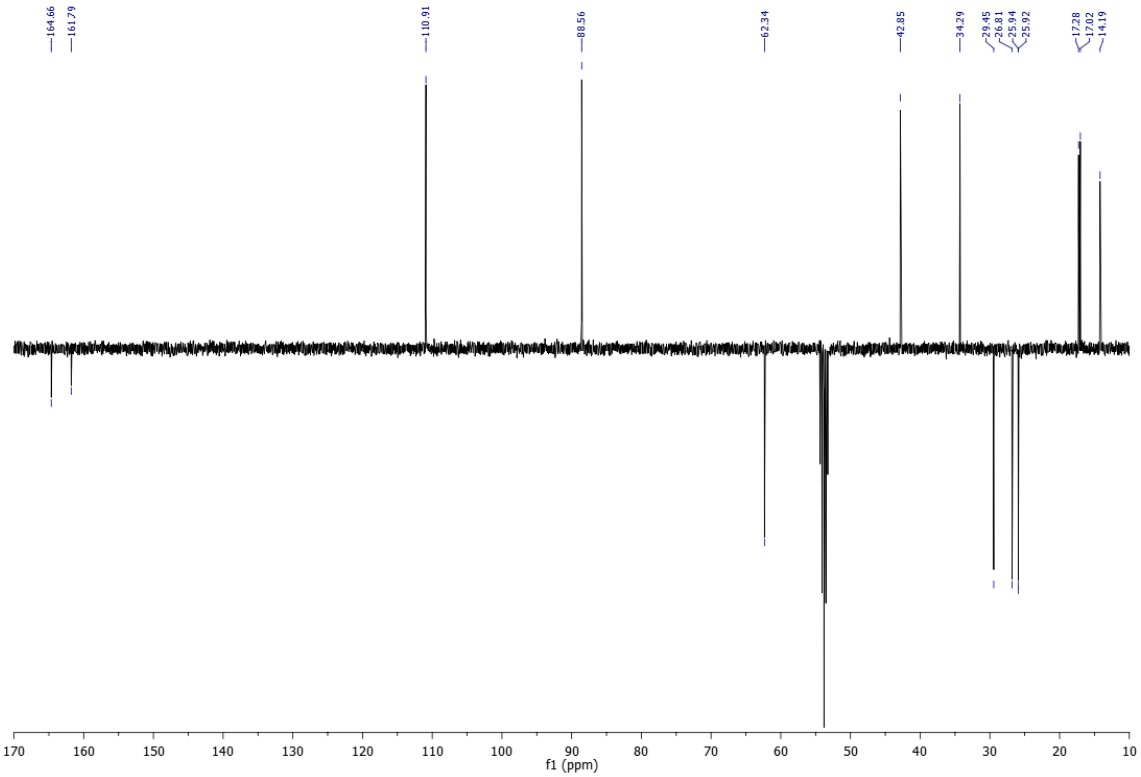


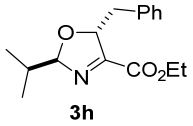
3g

^{1}H NMR (CD_2Cl_2, 400 MHz)



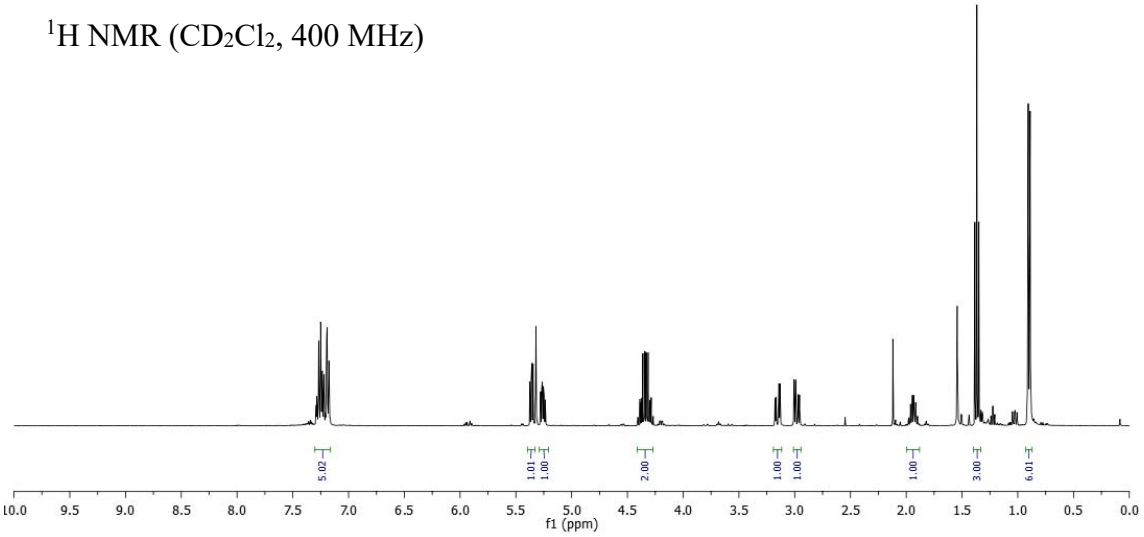
^{13}C NMR (CD_2Cl_2, 100 MHz)



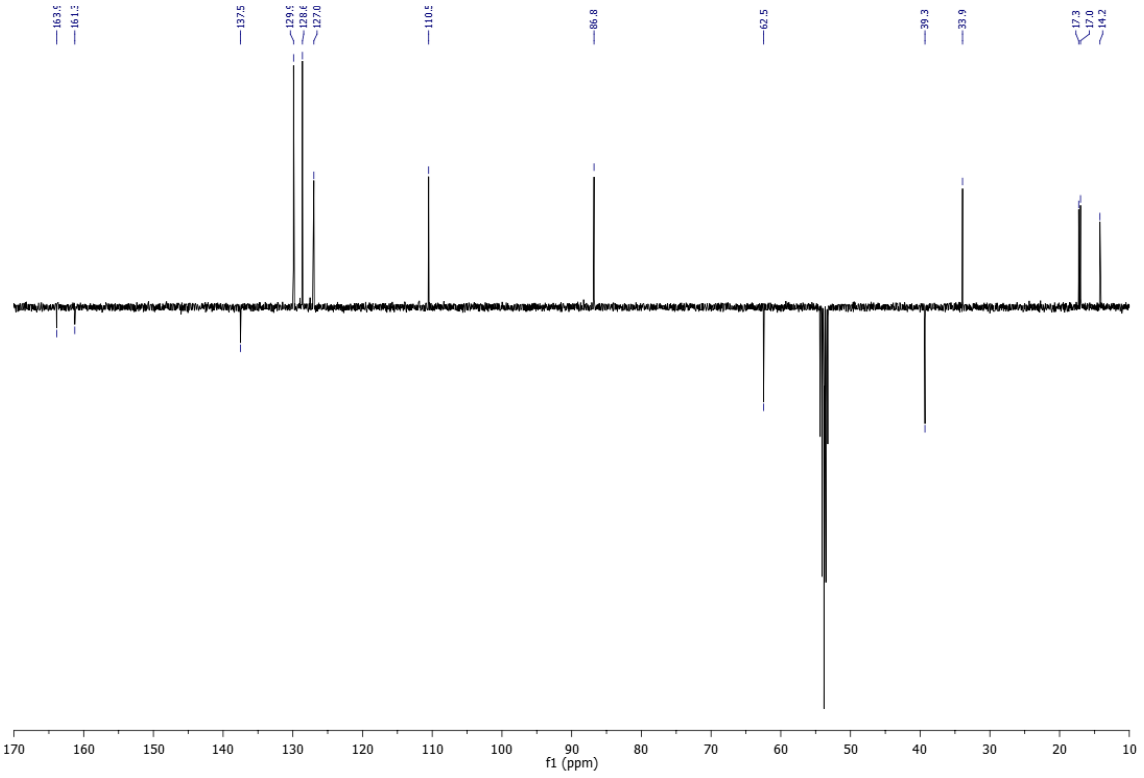


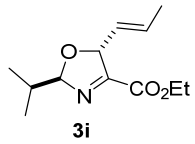
3h

^{1}H NMR (CD_2Cl_2, 400 MHz)



^{13}C NMR (CD_2Cl_2, 100 MHz)

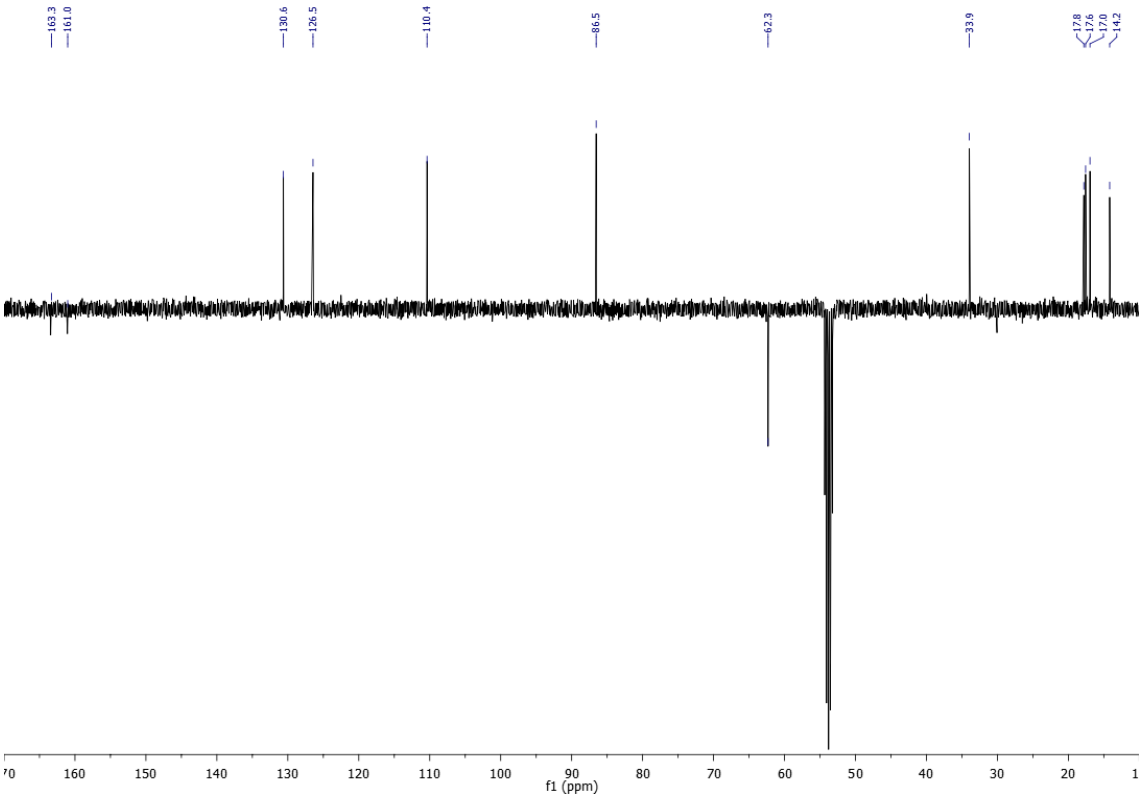


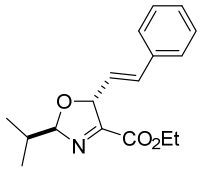


3i

^{1}H NMR (CD_2Cl_2, 400 MHz)

^{13}C NMR (CD_2Cl_2, 100 MHz)

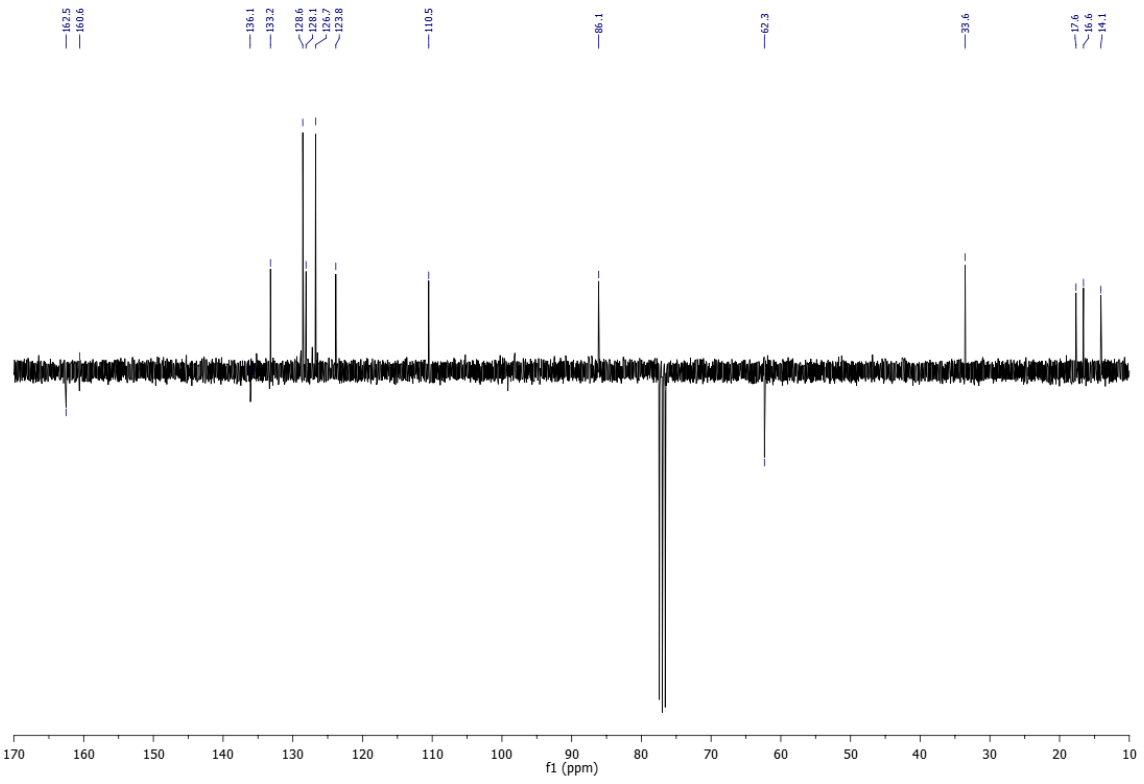


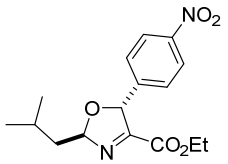


3j

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

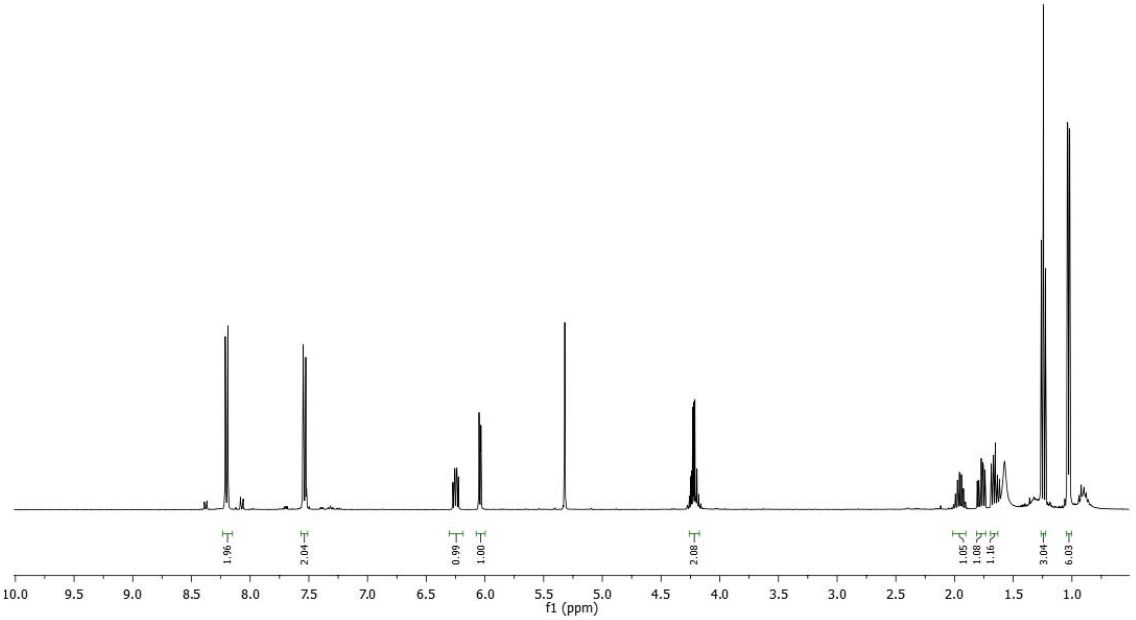
^{13}C NMR ($CDCl_3$, 100 MHz)



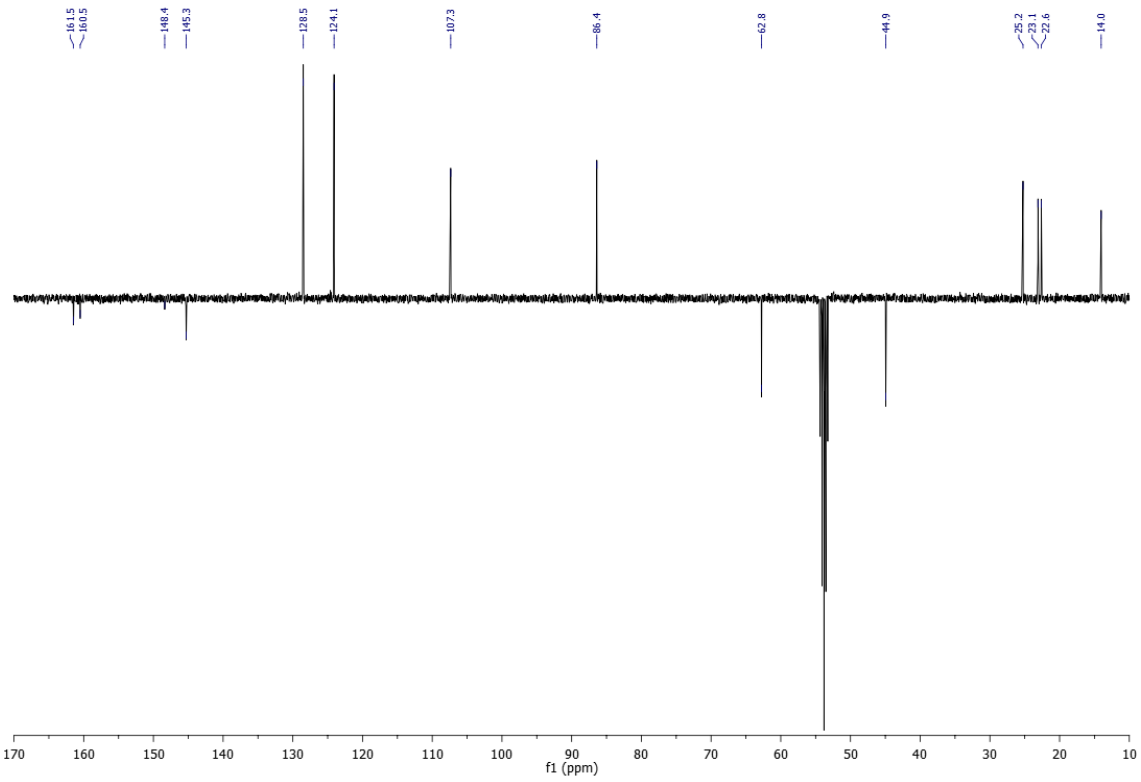


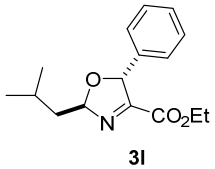
3k

^{1}H NMR (CD_2Cl_2, 400 MHz)



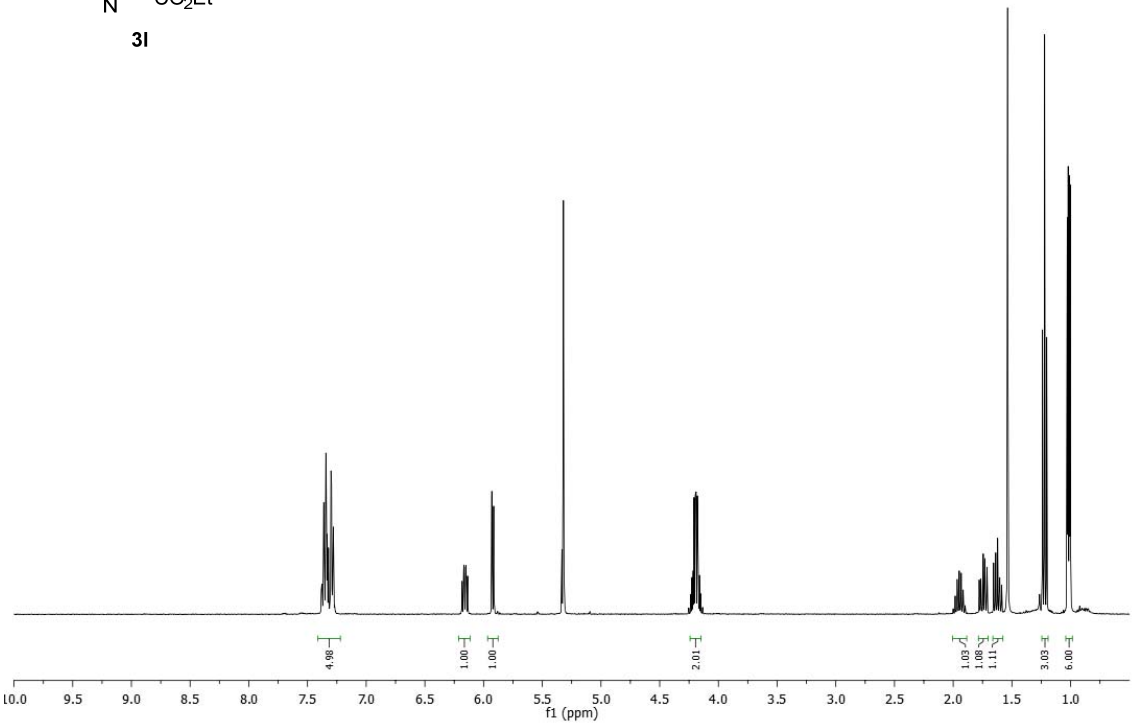
^{13}C NMR (CD_2Cl_2, 100 MHz)



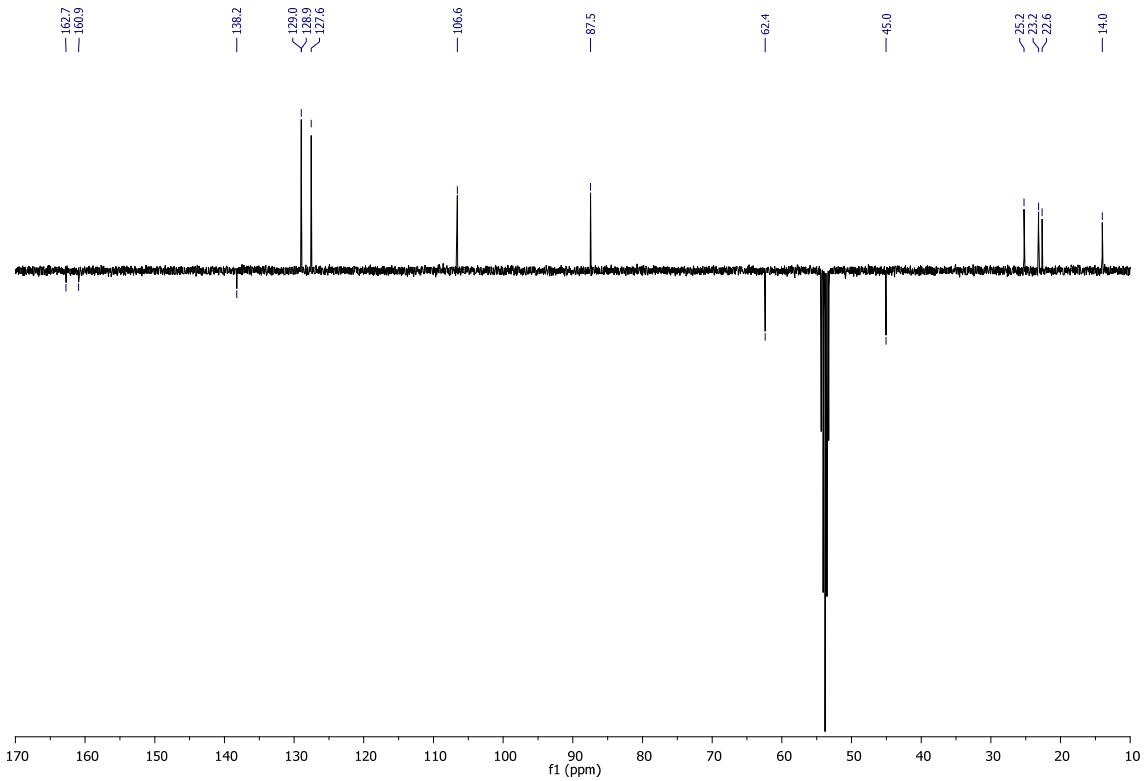


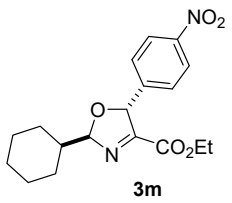
3l

^{1}H NMR (CD_2Cl_2, 400 MHz)



^{13}C NMR (CD_2Cl_2, 100 MHz)

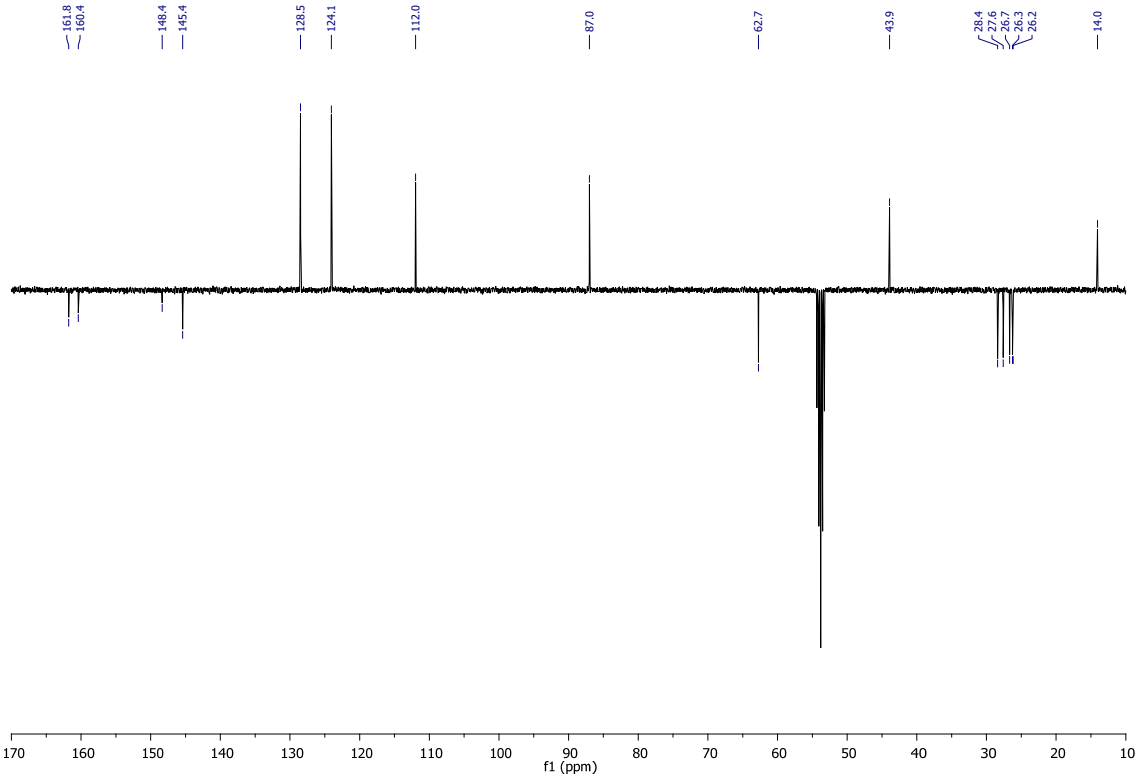


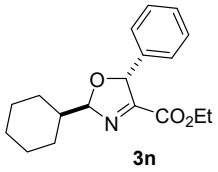


3m

^{1}H NMR (CD_2Cl_2, 400 MHz)

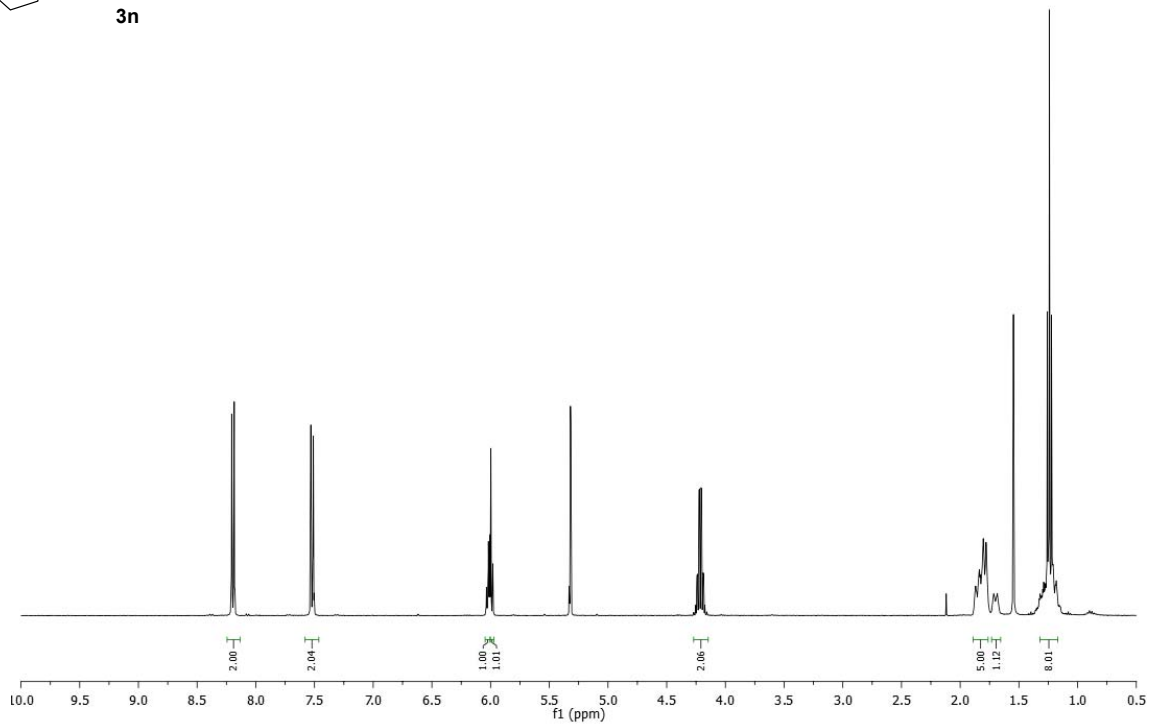
^{13}C NMR (CD_2Cl_2, 100 MHz)



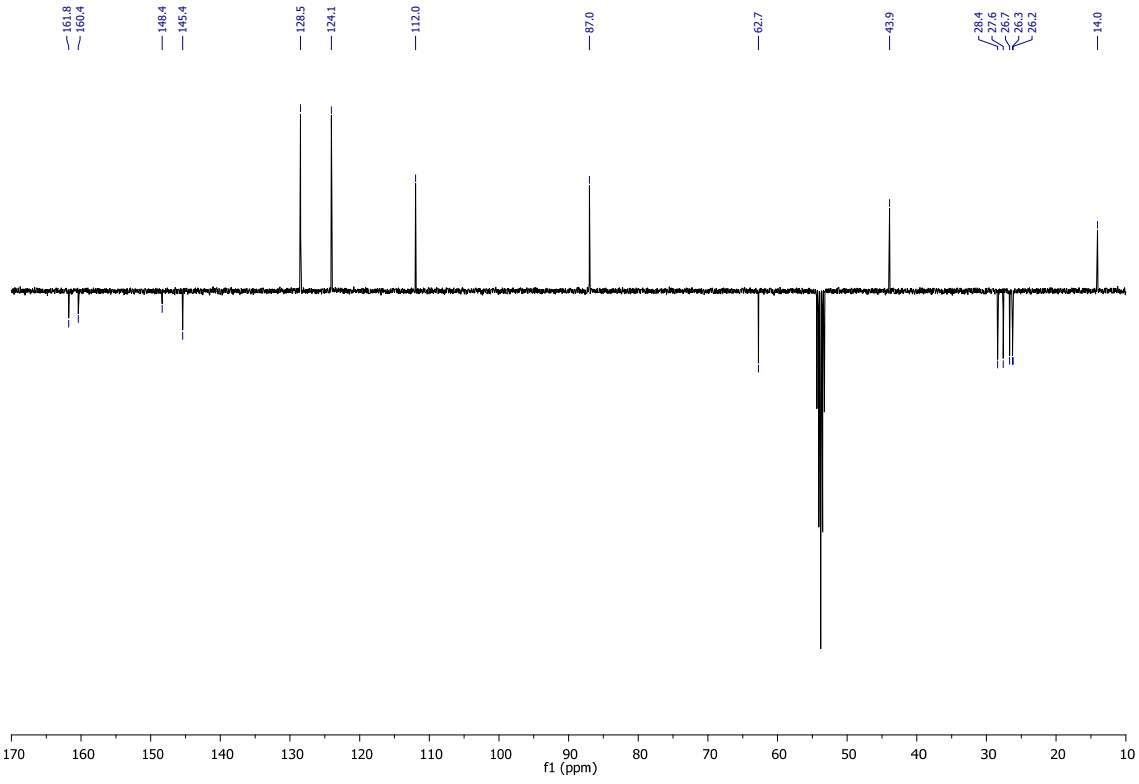


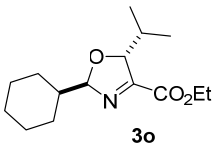
3n

^{1}H NMR (CD_2Cl_2, 400 MHz)



^{13}C NMR (CD_2Cl_2, 100 MHz)

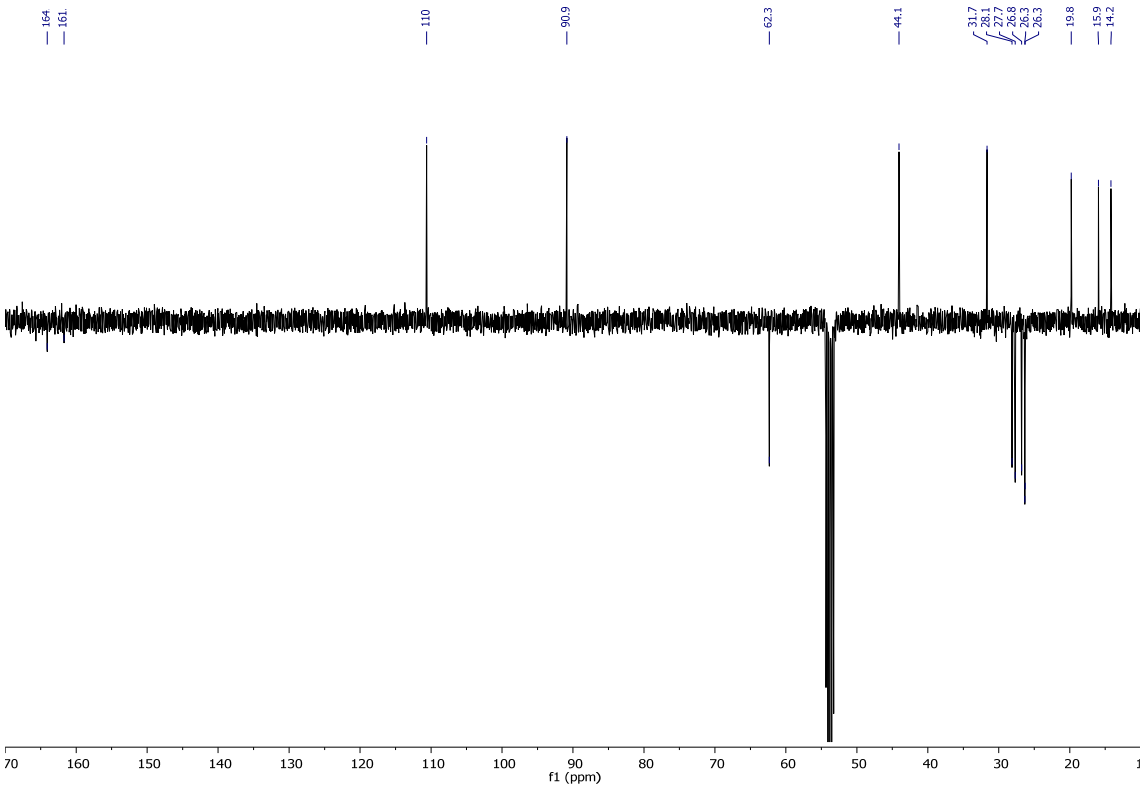


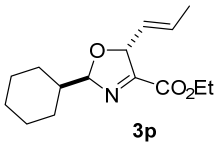


3o

^{1}H NMR (CD_2Cl_2, 400 MHz)

^{13}C NMR (CD_2Cl_2, 100 MHz)

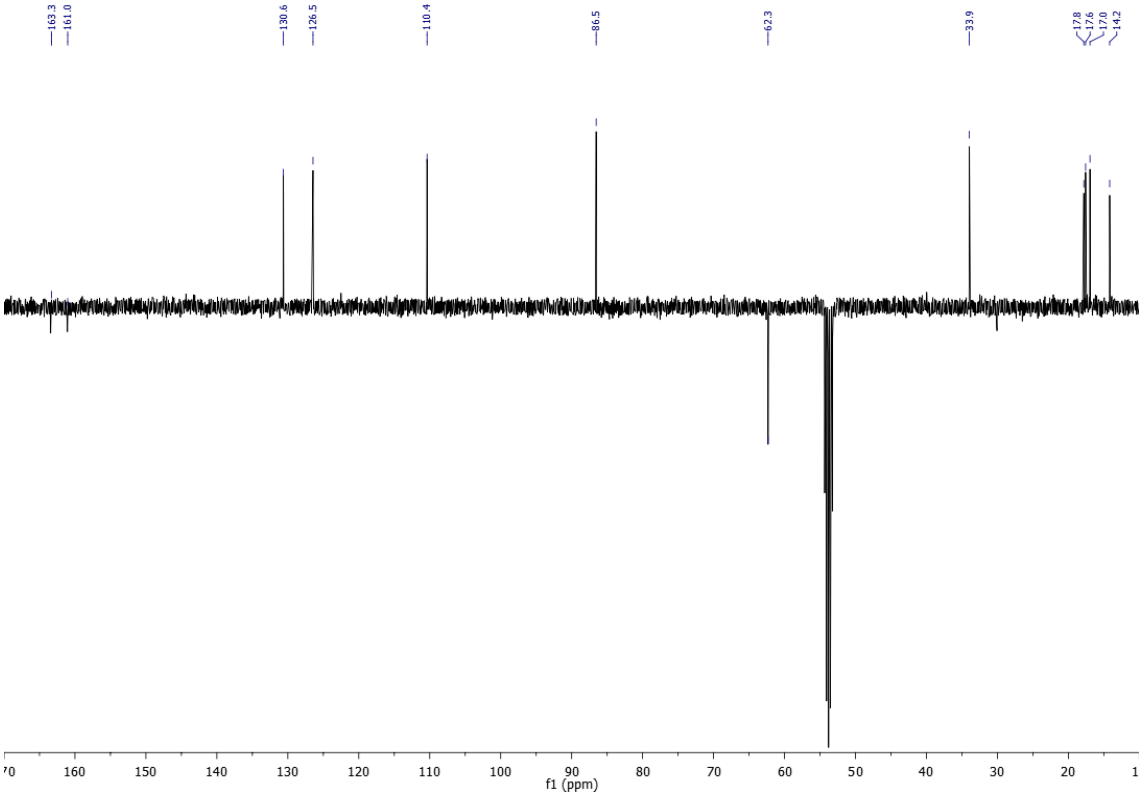


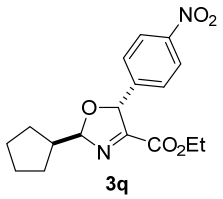


3p

^{1}H NMR (CD_2Cl_2, 400 MHz)

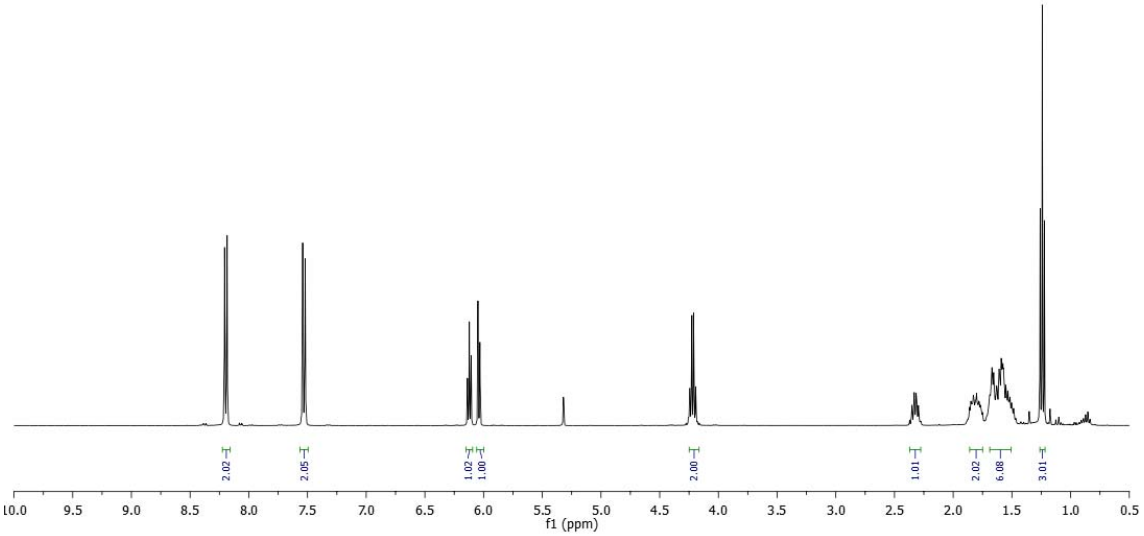
^{13}C NMR (CD_2Cl_2, 100 MHz)



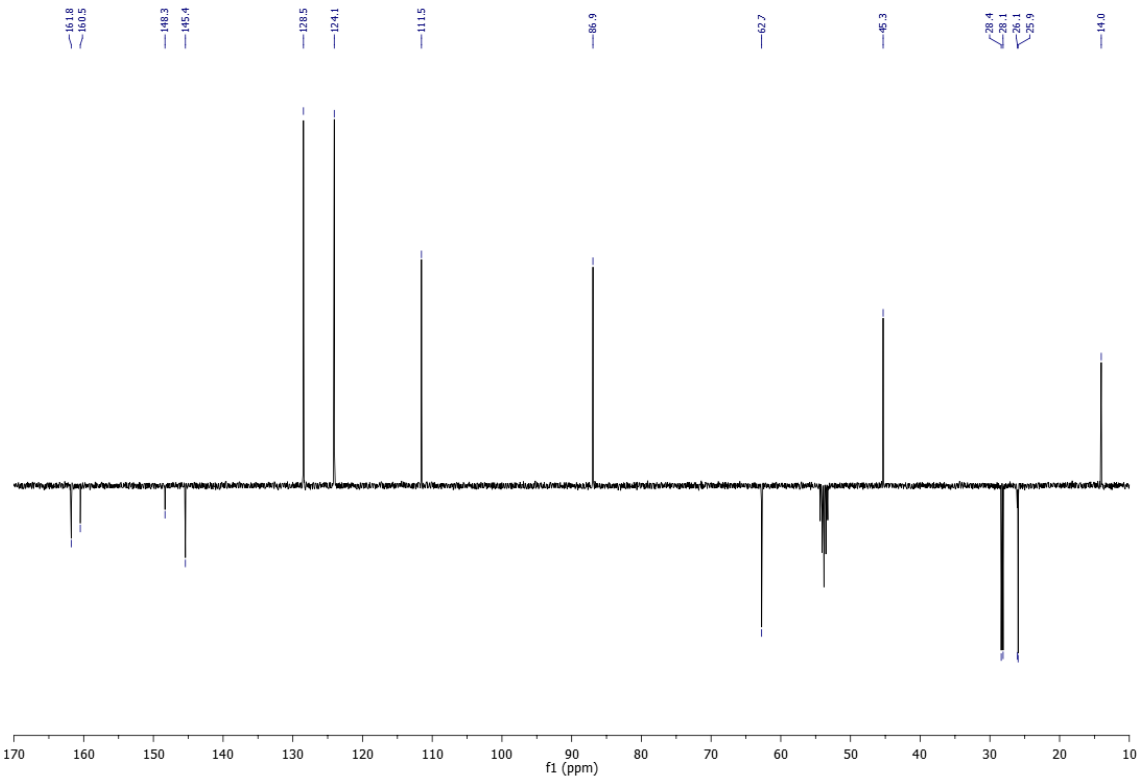


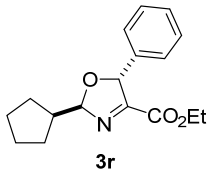
3q

^{1}H NMR (CD_2Cl_2, 400 MHz)



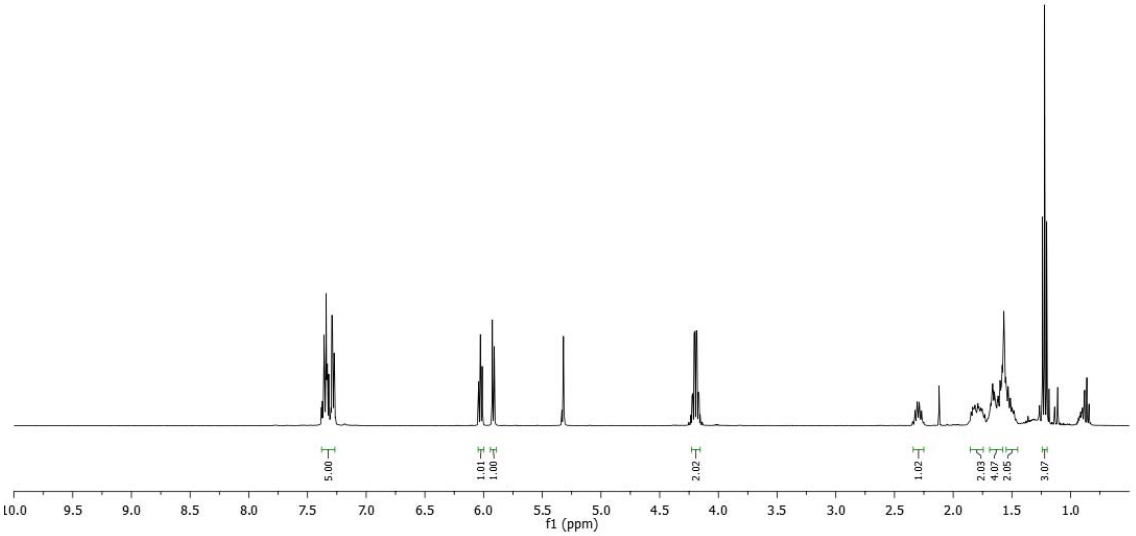
^{13}C NMR (CD_2Cl_2, 100 MHz)



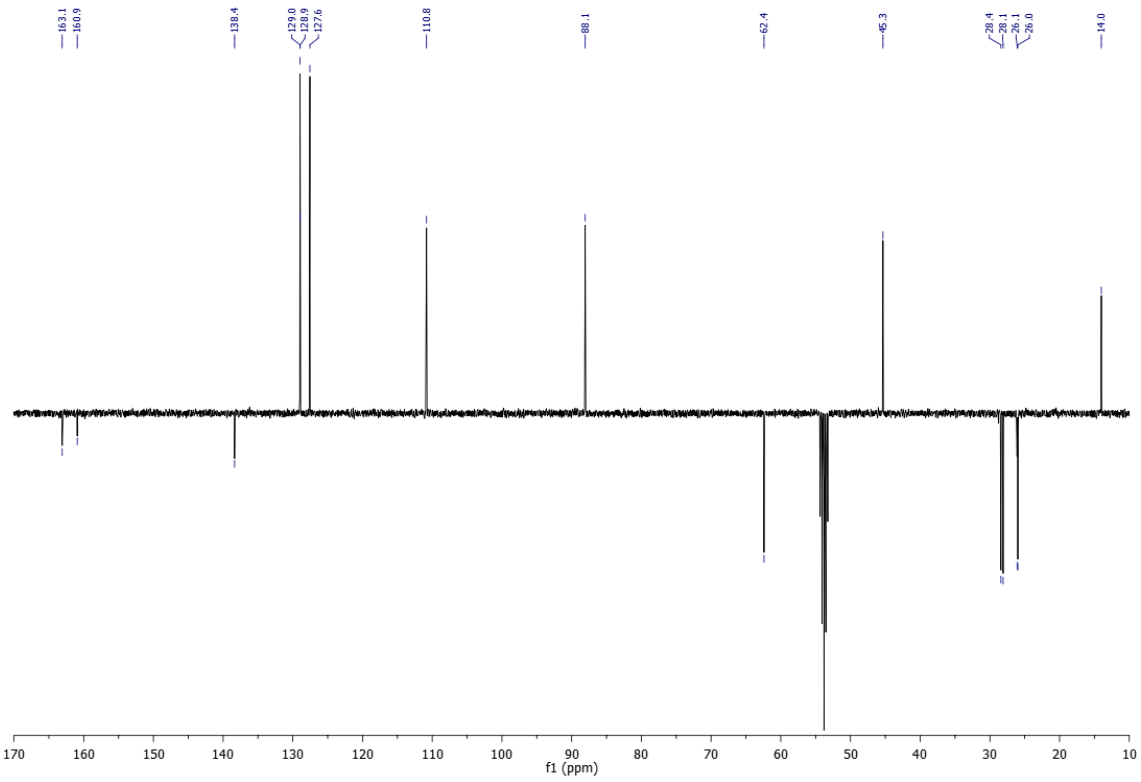


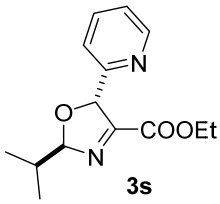
3r

^{1}H NMR (CD_2Cl_2, 400 MHz)



^{13}C NMR (CD_2Cl_2, 100 MHz)

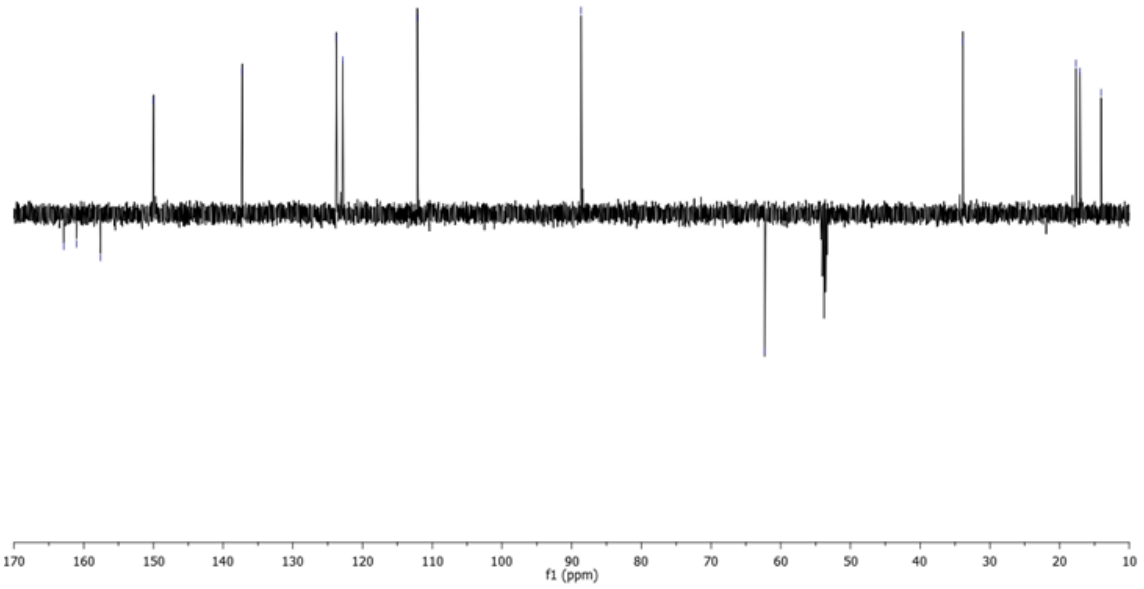


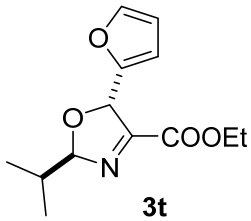


3s

^{1}H NMR (CD_2Cl_2, 400 MHz)

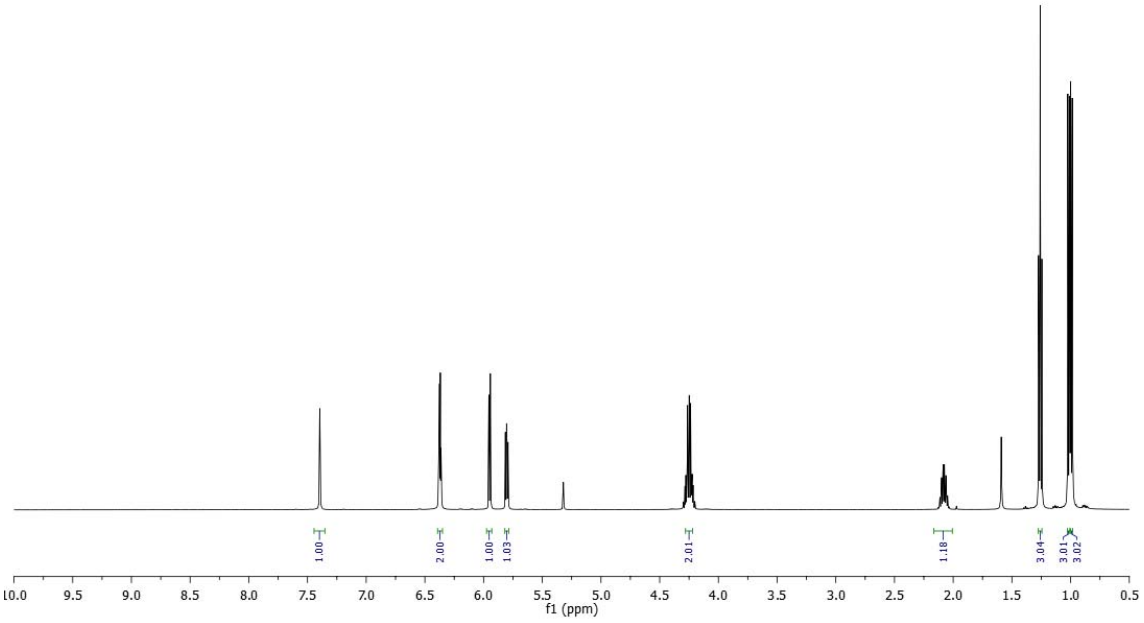
^{13}C NMR (CD_2Cr_2, 100 MHz)



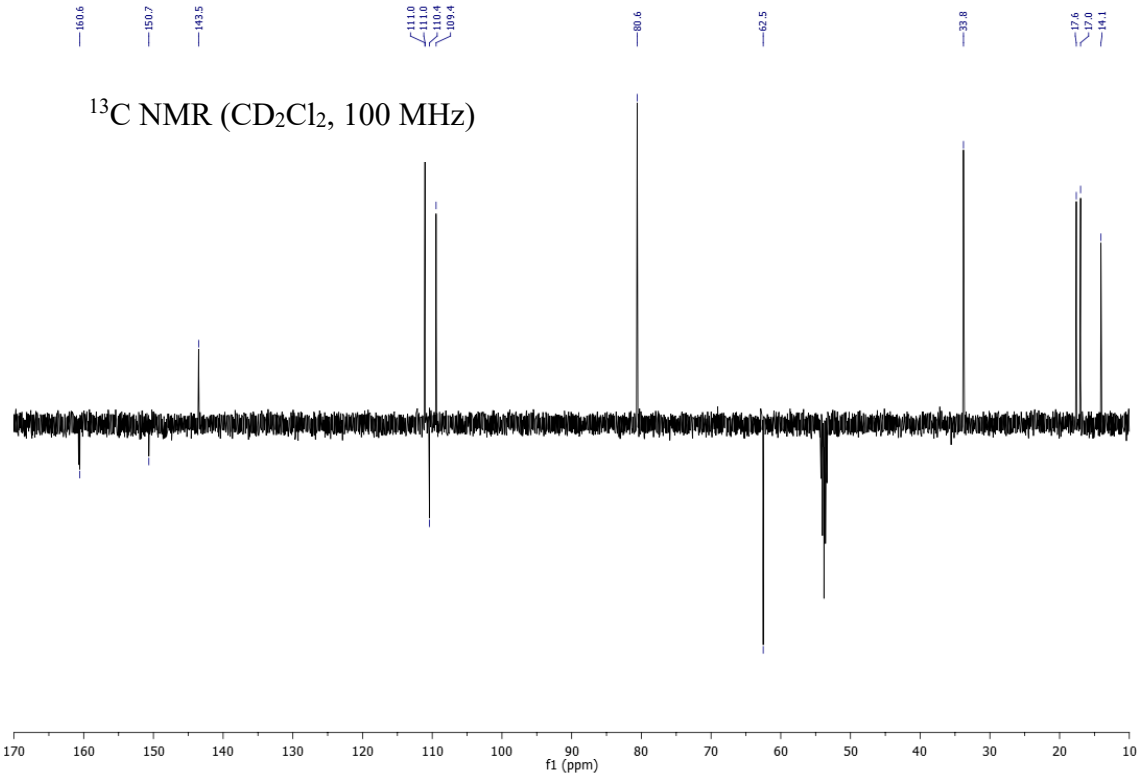


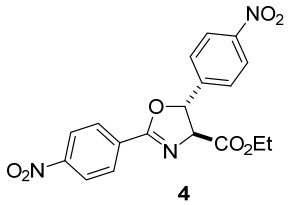
3t

^{1}H NMR (CD_2Cl_2, 400 MHz)



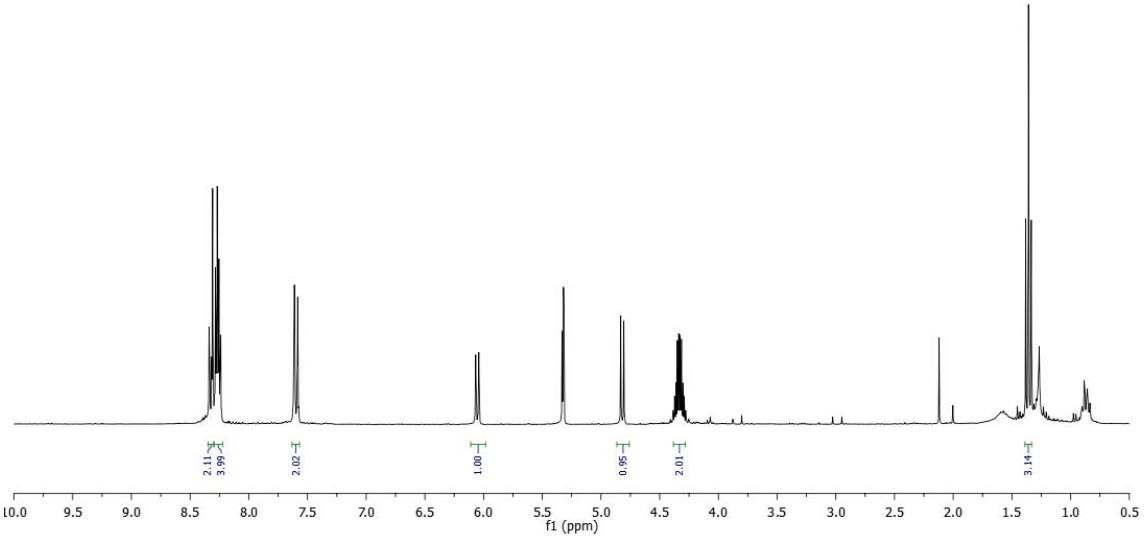
^{13}C NMR (CD_2Cl_2, 100 MHz)



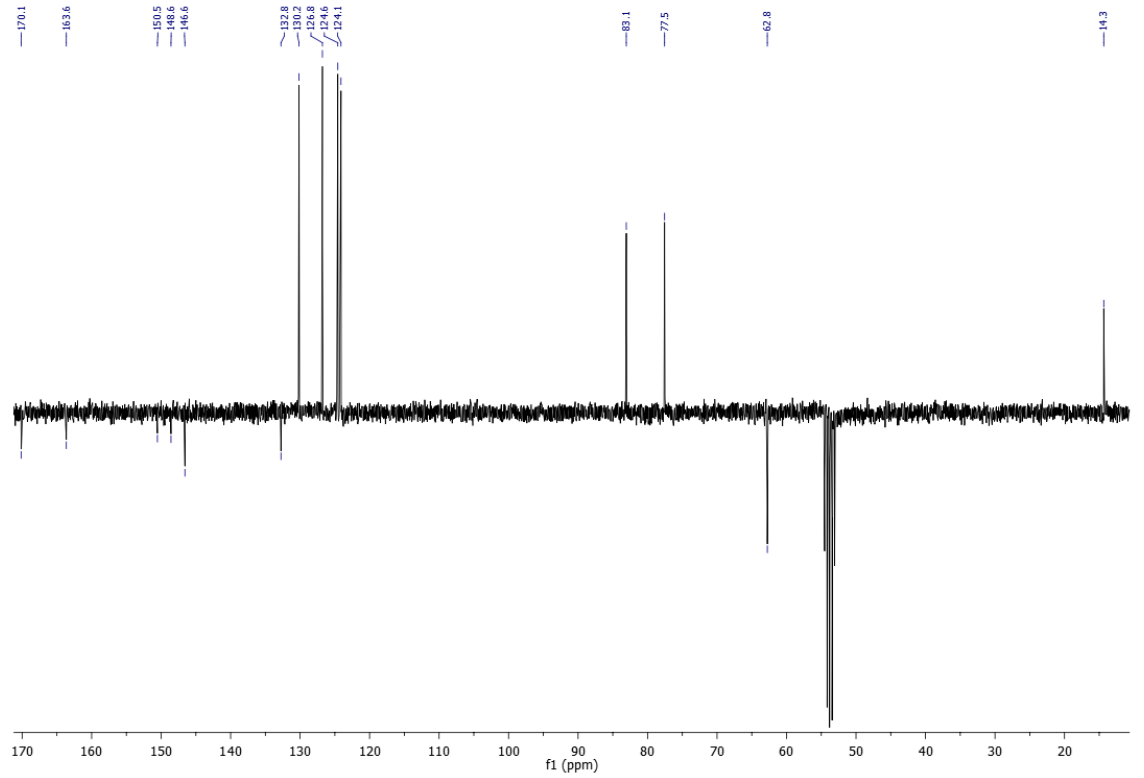


4

^{1}H NMR (CD_2Cl_2, 400 MHz)



^{13}C NMR (CD_2Cl_2, 100 MHz)



Cartesian Coordinates

AL

0 1

C	-1.0235672186	0.7022230038	-0.0192567765
H	-0.3723702290	-0.1537023300	-0.2265545534
H	-1.0344524363	1.3819327580	-0.8722768864
H	-2.0281553852	0.3039687306	0.1590581249
C	-0.5403926658	1.4135323945	1.2112373002
O	-0.2116620563	2.5770188176	1.2413762849
H	-0.4960682488	0.7984146955	2.1318955363

IN01

0 1

C	-1.1728931247	0.9765696756	0.0517206039
C	-0.8645397157	0.9533636149	1.6192022223
Li	0.3490071848	-1.2288582685	0.7352931857
C	-3.0831631725	-0.1317442304	-0.9072278299
C	0.1643747022	1.0402814373	-0.6407046311
N	-1.9172580073	-0.2284483148	-0.3557186097
O	0.8374024175	0.0841633121	-0.9674770741
O	0.5625784228	2.3024602591	-0.7676823382
O	-1.3963972482	-1.3812283955	-0.0678241626
C	1.8950896227	2.4839189332	-1.2637056113
C	-3.8518797008	-1.3626146728	-1.2205445906
H	-3.4493476647	0.8661711818	-1.1119265859
H	-1.7746897855	1.8481574582	-0.2091485201
H	1.9979076217	2.0217045512	-2.2467519545
H	2.0408477133	3.5600523536	-1.3262407801
H	2.6113326369	2.0387350288	-0.5706281139
H	-4.8138609612	-1.1136392918	-1.6673338401
H	-3.2832003152	-2.0000607054	-1.9062806282
H	-4.0098161195	-1.9458264230	-0.3064857242
O	2.1344654544	-2.0025512936	0.6327961642
C	3.0942306221	-1.0027447483	0.9434363709
C	2.4541425965	-2.6886054318	-0.5651008254
H	2.7050190370	-0.4397291635	1.7921318423
H	4.0549967807	-1.4681609749	1.1944210086
H	3.2226660394	-0.3285570324	0.0878039950
H	3.4274140899	-3.1853764222	-0.4729063008
H	1.6780449401	-3.4377005280	-0.7303840645
H	2.4760182489	-1.9877357228	-1.4084987579
O	0.1651472834	0.1325450158	1.9193758756
H	-0.6373122359	2.0260628239	1.8111664432
C	-2.1688826950	0.6216975168	2.3563057997
H	-1.9960677619	0.7215533842	3.4314981545
H	-2.9959403904	1.2845958016	2.0733188239
H	-2.4520913757	-0.4167247483	2.1503192632

IN02

0 1

C	1.7835367586	-0.5201996632	0.3687716680
C	1.0696478183	-0.2224814400	1.7441355195
Li	-0.9806884149	0.5233161363	0.2050063799
C	2.7583766077	1.1412644207	-1.0779621142
C	1.1425990101	-1.7386147540	-0.2612730961
N	1.6947810380	0.6253781336	-0.5554410476
O	0.5181352584	-1.7703546723	-1.2941117401
O	1.3871571606	-2.8112081570	0.4974080509
O	0.5218722840	1.1304199836	-0.7782696222
C	0.8399224033	-4.0425606593	0.0192096387
C	2.6456671674	2.3353328600	-1.9532459283

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 H      3.7026241479        0.6668899535       -0.8429006009
 H      2.8447022358       -0.7253672971        0.5334236535
 H     -0.2497717510       -3.9867826117       -0.0081448223
 H      1.2168119512       -4.2609896371       -0.9818863955
 H      1.1642666048       -4.8039763682        0.7259510708
 H      3.6271248566        2.6473250329       -2.3090169800
 H      1.9972159611        2.1176348906       -2.8088362518
 H      2.1757039346        3.1586819618       -1.4033655189
 O     -2.4397691681       -0.5712341782       -0.4431770897
 C     -2.4047390965       -1.9473850896       -0.1108146792
 C     -3.1984034273       -0.2991609362       -1.6024719264
 H     -1.7013534089       -2.0368788474        0.7196002215
 H     -3.4045999323       -2.2912609632        0.1847780000
 H     -2.0529706044       -2.5376964985       -0.9657891714
 H     -4.2362289814       -0.6320478733       -1.4717663667
 H     -3.1764420909        0.7815716136       -1.7544232490
 H     -2.7657647881       -0.8048465813       -2.4751079252
 C     -1.2636792205        3.3539366366        0.5927070073
 O     -2.0307228797        2.1931098359        0.3259292969
 C     -3.1457714858        2.0828608542        1.1930864784
 H     -0.9191387762        3.3543013768        1.6354623066
 H     -0.4029734504        3.3259608546       -0.0758513896
 H     -1.8606711247        4.2563952097        0.4105029030
 H     -2.8148519520        2.0374925359        2.2387460920
 H     -3.8186560453        2.9395051154        1.0627611745
 H     -3.6626441735        1.1577896349        0.9344851974
 O     -0.2788360957       -0.3133393034        1.6440997323
 H      1.5041458341       -1.0094472381        2.3980630462
 C      1.5720385275        1.1290015616        2.2731359213
 H      1.1456516103        1.2964181643        3.2666060777
 H      2.6658225001        1.1724635068        2.3518691414
 H      1.2297591973        1.9362454956        1.6145543374


IN03

0 1
 C     -1.6469562815       -0.3635136181        0.7682086377
 C     -0.4239317431        0.0487316768        1.6344637674
 C     -0.2626431035       -2.1095187693        0.8904853906
 C     -2.1458758657        0.7468462140       -0.1315366866
 N     -1.1875717279       -1.5005189790       -0.0493506443
 O     -1.7068217276        1.8751547351       -0.1589419747
 O     -3.1887949582        0.3495724052       -0.8633035980
 O     -0.4338415872       -0.9292598501       -1.1098467501
 C     -3.7070283384        1.3289808723       -1.7647767651
 C      0.6423475111       -3.1681647690        0.3138437624
 H     -0.8570496154       -2.5232434989        1.7192590428
 H     -2.4756614372       -0.6887070678        1.4120627062
 H     -4.0713699758        2.1993126480       -1.2146832630
 H     -2.9312395436        1.6456261424       -2.4655324939
 H     -4.5231211411        0.8420765488       -2.2952965738
 H      1.3314231080       -3.5306506248        1.0811367426
 H      0.0354064555       -4.0064205367       -0.0375560838
 H      1.2100772586       -2.7762448359       -0.5316361750
 H      0.0133870722        0.9817537722        1.2645339053
 O      0.5238591556       -1.0059898269        1.4045458337
 C     -0.7471422406        0.1801317023        3.1115893501
 H      0.1473244145        0.4399417180        3.6846401275
 H     -1.4962948989        0.9638925703        3.2641175231
 H     -1.1487697342       -0.7612546314        3.5014694237
 Li     1.1660848364       -0.2298095170       -0.5524524213
 C      3.6250706550       -1.1107084303        0.7991116825
 H      3.6446004097       -1.8487871691       -0.0044362778
 H      4.6519065178       -0.8790520947        1.1072954816
 H      3.0617576447       -1.5076237978        1.6515466934
 C      2.9227391315        1.0761395795        1.2684890276
 H      2.3752805405        0.7252913251        2.1527453209
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 H      3.9311650701        1.3903710444        1.5647086911
 H      2.3952255900        1.9217672617        0.8195838286
 C      2.5802648607        2.0273674532       -2.1021260226
 H      2.3543519052        3.0747829427       -1.8636363757
 H      3.3922789856        1.6665962259       -1.4707897734
 H      2.8767724586        1.9585216347       -3.1565265746
 C      0.3480572592        1.5442941181       -2.6755749005
 H      0.0111147007        2.5661478369       -2.4610242037
 H      0.6337716838        1.4694798925       -3.7326726880
 H     -0.4365611255        0.8267230366       -2.4343812874
 O      2.9919875651        0.0522894973        0.2908486105
 O      1.4558992451        1.2082361727       -1.8518170262


IN04

0 1
 C     -1.5843183150        0.3834142380       -0.4596591823
 C     -2.6070096592        0.9484472380        0.5463378352
 C     -2.0816104089       -1.2560395040        1.0077254612
 C     -0.5545870291        1.3784790785       -0.9320238016
 O      0.6505648545        1.2179260376       -0.8499489463
 O     -1.1084742645        2.4583710862       -1.4684956455
 O     -0.3959648718       -1.6435984072       -0.6124262674
 C     -0.2023695320        3.4488370053       -1.9754770352
 C     -1.6661194584       -2.1307710042        2.1624247404
 H     -2.7093068144       -1.8253980413        0.2946576741
 H      0.4314288926        3.8232776387       -1.1699484020
 H      0.4201500011        3.0167022093       -2.7609366527
 H     -0.8293329628        4.2436353988       -2.3733329006
 H     -2.5394682799       -2.5744591339        2.6478381176
 H     -1.0226828086       -2.9307276905        1.7865119550
 H     -1.1157923234       -1.5312197777        2.8928453364
 H     -2.1811539400        1.8001046018        1.0917151087
 O     -2.7832933853       -0.1197993498        1.4826905427
 C     -3.9303021425        1.3445564285       -0.0811416988
 H     -4.6268521788        1.6881305383        0.6881719847
 H     -3.7798828068        2.1507808346       -0.8054215200
 H     -4.3727759231        0.4864124751       -0.5967596083
 Li     1.1071576418       -0.6905168708       -0.3098381970
 C      3.1709050839        0.5736869475        1.1011582135
 H      2.5844578473        1.4690942952        1.3424928918
 H      4.0202715579        0.4979457475        1.7910637428
 H      3.5307575623        0.6362456824        0.0730554344
 C      1.8270864490       -0.7772133322        2.4839651195
 H      1.1689392598        0.0579102561        2.7561519443
 H      1.2490940166       -1.7014343585        2.4609129971
 H      2.6353699654       -0.8617788059        3.2207662305
 C      3.2479441114       -2.1602992620       -1.4357339457
 H      2.5871960322       -3.0341749121       -1.5105387059
 H      4.0622399099       -2.2602029256       -2.1637252691
 H      3.6559503775       -2.0957172940       -0.4261409733
 C      1.9288372392       -0.9468377815       -2.9558625132
 H      1.2193383690       -1.7762668057       -3.0629184292
 H      1.3969607513        0.0012385557       -3.0485804872
 H      2.7013144271       -1.0171277853       -3.7315147206
 O      2.5217091090       -0.9655352188       -1.6677015399
 O      2.3638823443       -0.5886514121        1.1871262531
 H     -2.1004192162       -0.0117192544       -1.3540336067
 N     -0.9490907425       -0.6985750555        0.2708841356


IN05

0 1
 C     -1.4023710640        0.2210194982       -0.3957795255
 C     -2.5565563331        0.0961628191        0.6274398697
 C     -1.4494667584       -1.9130011585        0.4127641424
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 C     -0.6413948859        1.5219812928       -0.3346240113
 O      0.5651194652        1.6053270221       -0.1812683185
 O     -1.4322041476        2.5764424584       -0.4833289065
 O      0.2904458589       -1.2932086953       -1.1087408283
 C     -0.7899061082        3.8589379960       -0.4448599634
 C     -0.7666419794       -2.9952487041        1.2079632306
 H     -1.9708036451       -2.3372780687       -0.4644143636
 H     -0.2941539463        3.9993434400        0.5172861756
 H     -0.0570977438        3.9339056758       -1.2499852499
 H     -1.5845894900        4.5894163497       -0.5781772487
 H     -1.4882680411       -3.7450235960        1.5419260421
 H     -0.0196213000       -3.4786823668        0.5735135913
 H     -0.2686660679       -2.5578221853        2.0784664155
 H     -2.4577031569        0.8394702373        1.4270485008
 O     -2.3561121218       -1.1905476213        1.2256427970
 C     -3.9281181541        0.1943332876       -0.0143913062
 H     -4.7103442233        0.0423877160        0.7335846605
 H     -4.0610718700        1.1809754977       -0.4693692485
 H     -4.0311454972       -0.5663852000       -0.7951135293
 Li     1.3836936208       -0.2610868903       -0.0087703040
 C      3.0896935588        0.6318178238        2.1710290429
 H      2.9518271114        1.6980217195        1.9465393500
 H      3.3835566875        0.5190840305        3.2217655345
 H      3.8664908369        0.2248919570        1.5231534917
 C      0.8267231131        0.3702418512        2.7245766373
 H      0.6680557490        1.4470033401        2.5766965689
 H     -0.0673408426       -0.1753950271        2.4183202446
 H      1.0468856887        0.1792684875        3.7821364118
 C      3.6471247816       -1.4142703881       -1.0589430762
 H      2.9203940346       -2.0663288309       -1.5586119483
 H      4.5835555289       -1.3937435714       -1.6288681743
 H      3.8418871512       -1.7883500959       -0.0513642629
 C      2.8323952859        0.4710281971       -2.1954023162
 H      2.0823809088       -0.1350586283       -2.7179783570
 H      2.4320407076        1.4687989581       -2.0120340042
 H      3.7466664717        0.5393929342       -2.7968170851
 O      3.1208795448       -0.1019868489       -0.9273776558
 O      1.8962543539       -0.0861872307        1.9118478135
 N     -0.5204070722       -0.8788435411       -0.0358755195
 H     -0.8140453441       -1.6210277679       -2.3207143508
 O     -1.5799832714       -1.7289539710       -2.9552925976
 H     -1.4297179486       -1.0400684457       -3.6173698083
 H     -1.7854234466        0.0937222435       -1.4209295608


IN06

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 C      1.4193080000       -0.2159700000       -0.3290960000
 C      2.7453350000       -0.3520670000        0.3866650000
 C      2.1900440000        1.8422030000        0.1051310000
 C      0.6239530000       -1.2035580000       -0.8582900000
 N      0.9632010000        1.1210430000       -0.2783210000
 O     -0.5710370000       -1.0714200000       -1.2728120000
 O      1.2057240000       -2.4496440000       -0.8619210000
 O     -0.0325230000        1.2466180000        0.8639010000
 C      0.4109130000       -3.5016460000       -1.3850870000
 C      1.9676760000        3.1576370000        0.8120910000
 H      2.7085420000        2.0012730000       -0.8533970000
 H     -0.4943110000       -3.6535660000       -0.7892230000
 H      0.1202370000       -3.3030950000       -2.4199070000
 H      1.0338810000       -4.3954970000       -1.3402400000
 H      2.9234210000        3.6721280000        0.9332040000
 H      1.2990540000        3.7913550000        0.2224870000
 H      1.5274640000        2.9844930000        1.7953150000
 H      2.7009220000       -1.0346540000        1.2471770000
 O      2.9396290000        0.9666080000        0.9219140000
 C      3.9142100000       -0.7509000000       -0.5082880000
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 H      4.8485490000       -0.7780710000        0.0611100000
 H      3.7291780000       -1.7402260000       -0.9355680000
 H      4.0209860000       -0.0356320000       -1.3304970000
 Li    -1.3090110000       -0.0741340000        0.1297710000
 C     -2.6740400000       -2.2041680000        1.3218210000
 H     -2.2838840000       -2.9300530000        0.5971100000
 H     -2.9886270000       -2.7309030000        2.2306250000
 H     -3.5210860000       -1.6724890000        0.8859640000
 C     -0.5149300000       -1.8132510000        2.1799790000
 H     -0.0630320000       -2.5173860000        1.4680350000
 H      0.1840130000       -0.9980470000        2.3731250000
 H     -0.7543030000       -2.3378710000        3.1127740000
 C     -3.5832760000        1.6700420000        0.4333500000
 H     -3.2036820000        2.6448250000        0.1086110000
 H     -4.6761500000        1.6465900000        0.3429940000
 H     -3.3020380000        1.4852470000        1.4726520000
 C     -3.3121930000        0.7666890000       -1.7279140000
 H     -2.9648400000        1.7367370000       -2.0971540000
 H     -2.7847070000       -0.0362940000       -2.2439600000
 H     -4.3937780000        0.6667230000       -1.8805310000
 O     -3.0049160000        0.6379250000       -0.3471150000
 O     -1.6887380000       -1.2327120000        1.6300730000
 H     -0.5037730000        2.0704550000        0.6156140000
 H     -0.7340070000        3.7142260000       -1.5155300000
 H     -0.2931270000        2.2425490000       -1.3221670000
 O     -1.0126680000        2.8776210000       -1.1169330000


IN07

0 1
 C      1.7740780000       -0.3319960000       -0.4280780000
 C      2.7781550000       -0.1326950000        0.6918780000
 C      2.6534540000        1.6349620000       -0.7820280000
 C      0.8307690000       -1.4887740000       -0.5557170000
 N      1.7404280000        0.6064890000       -1.2795010000
 O     -0.3357660000       -1.3912480000       -0.8841660000
 O      1.4231740000       -2.6427270000       -0.2909780000
 O     -0.1491110000        0.4022960000        1.4921710000
 C      0.6033580000       -3.8147810000       -0.4111890000
 C      1.8097930000        2.7688680000       -0.2124250000
 H      3.3174320000        1.9789110000       -1.5819230000
 H     -0.2179550000       -3.7664550000        0.3064690000
 H      0.2050680000       -3.8881370000       -1.4250950000
 H      1.2585460000       -4.6545860000       -0.1897720000
 H      2.4559000000        3.4931950000        0.2886970000
 H      1.2545080000        3.2729220000       -1.0077560000
 H      1.1085240000        2.3164710000        0.5018220000
 H      2.1961840000        0.0773460000        1.5983690000
 O      3.4503050000        1.0378730000        0.2303270000
 C      3.7969850000       -1.2390270000        0.9076580000
 H      4.5584100000       -0.8845010000        1.6083590000
 H      3.3254220000       -2.1312640000        1.3251840000
 H      4.2837670000       -1.5004500000       -0.0372390000
 Li    -1.3119730000       -0.0303740000        0.2280480000
 C     -3.3583930000       -1.8454420000       -0.6120860000
 H     -2.6465170000       -2.6316150000       -0.8937160000
 H     -4.3475710000       -2.2875700000       -0.4393610000
 H     -3.4153250000       -1.1051920000       -1.4124130000
 C     -2.7928440000       -2.0348250000        1.6635870000
 H     -2.0696600000       -2.8344040000        1.4554410000
 H     -2.4367050000       -1.4377250000        2.5027940000
 H     -3.7645610000       -2.4846860000        1.9074630000
 C     -3.4512270000        1.7806330000       -0.3730750000
 H     -3.1561840000        2.5119570000        0.3893470000
 H     -4.0540070000        2.2752830000       -1.1445540000
 H     -4.0236750000        0.9769930000        0.0911410000
 C     -1.4626860000        2.1535800000       -1.5696520000
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 H     -1.1943190000        2.9349070000       -0.8468260000
 H     -0.5586280000        1.6350960000       -1.8972180000
 H     -1.9740720000        2.6090700000       -2.4271590000
 O     -2.2986700000        1.1904740000       -0.9508170000
 O     -2.9119270000       -1.1681400000        0.5498190000
 H     -0.2462080000        3.6979800000        1.2630580000
 H     -1.6741030000        4.2077950000        1.4591360000
 O     -1.0663930000        3.5088750000        1.7427520000
 H     -0.4129020000        1.2621280000        1.8520090000
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IN08

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0 1
 C      1.4310010000       -0.2644600000       -0.1478340000
 C      2.7343800000       -0.9605510000        0.1729530000
 C      0.8702280000       -2.3670510000        0.2133770000
 C      1.2374390000        1.1676560000       -0.5552270000
 N      0.4124300000       -1.0179030000       -0.1053820000
 O      0.1817280000        1.5790550000       -0.9935820000
 O      2.3309100000        1.8859980000       -0.3915290000
 O     -2.8240170000       -0.2884240000       -1.5743530000
 C      2.2333330000        3.2817660000       -0.7181910000
 C      0.6077520000       -3.3043700000       -0.9550630000
 H      0.3606190000       -2.7077330000        1.1182140000
 H      1.7565370000        3.4022070000       -1.6941680000
 H      1.6469540000        3.7903040000        0.0509100000
 H      3.2554690000        3.6498860000       -0.7303670000
 H      1.0297900000       -4.2872070000       -0.7364520000
 H     -0.4684710000       -3.4053610000       -1.1167770000
 H      1.0719800000       -2.9154470000       -1.8684840000
 H      3.3642530000       -0.9948280000       -0.7285920000
 O      2.2663780000       -2.2682230000        0.4993830000
 C      3.5183200000       -0.3588510000        1.3303950000
 H      4.2953630000       -1.0637690000        1.6326170000
 H      3.9916030000        0.5759360000        1.0246840000
 H      2.8687170000       -0.1665790000        2.1892930000
 Li    -1.3464350000        0.1148490000       -0.6754330000
 C     -2.4231340000        2.3296730000        0.6301150000
 H     -3.3344880000        2.1175350000        0.0586400000
 H     -2.6778840000        2.9078650000        1.5263660000
 H     -1.7312010000        2.9066070000        0.0107670000
 C     -2.6061500000        0.3041210000        1.8023110000
 H     -3.4935210000       -0.0198510000        1.2421870000
 H     -2.0154600000       -0.5707760000        2.0813340000
 H     -2.9124020000        0.8482690000        2.7025100000
 O     -1.7701050000        1.1244230000        0.9945680000
 H     -4.2346180000       -1.2914380000       -0.7459100000
 H     -5.6967350000       -1.7248510000       -0.3806490000
 O     -4.9350660000       -1.2173370000       -0.0734310000
 H     -3.5418490000        0.2384870000       -1.1976130000
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IN09

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0 1
 Li    -0.7744815469       -0.8392562484       -0.3805502022
 C     -0.1826876719        2.9509165018       -0.5785437959
 C      1.6459884772        0.2086234094        0.3483383209
 N      0.1542274699        1.7365861538       -0.8595704968
 O      0.6999168191       -0.3133725327        0.9021196439
 O      2.9105624785       -0.0502841126        0.6102129623
 O     -0.6898154350        0.8613657438       -1.3136213428
 C      3.1408674823       -1.2225760935        1.4075965799
 C     -1.5855718575        3.3916189063       -0.7772024126
 H      0.6018480335        3.6097611600       -0.2273331099
 H      2.6772547447       -1.1088722845        2.3884998212
 H      2.7247108940       -2.0833841328        0.8815933772
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 H      4.2216508770       -1.3045384065        1.4995746885
 H     -1.7191046696        4.4183882812       -0.4391857057
 H     -1.8498576506        3.3194824293       -1.8383576998
 H     -2.2690221207        2.7292643765       -0.2375506069
 O     -2.2096851978       -0.7397289422        0.9302489672
 C     -2.4498099721        0.4682341496        1.6175118806
 C     -3.3618578915       -1.5490490195        0.8006690762
 H     -1.5121669910        1.0291578904        1.6114686348
 H     -3.2373766893        1.0502898830        1.1200951826
 H     -2.7548449713        0.2711158952        2.6533385707
 H     -4.1532103003       -1.0133118678        0.2605293000
 H     -3.0581956832       -2.4295115310        0.2330753713
 H     -3.7368530568       -1.8459122920        1.7881009556
 H      1.8248541794       -1.6429694857       -2.4374449653
 H     -0.5723870723       -3.1061371630       -0.2868303555
 O     -0.6135744542       -2.5086399480       -1.0473642835
 O      1.7609005843       -1.7023653752       -1.4742922409
 C      1.5385287101        1.2744692390       -0.7217849480
 H      1.8241886810        0.8063068690       -1.6657239250
 H      2.1990596885        2.1125642080       -0.4977291905
 H      0.8195364526       -2.1071541211       -1.3108385917


IN10

0 1
 C     -1.3719500000        1.4461700000       -0.3151590000
 Li     0.6758320000       -0.7748290000        0.2484600000
 C      0.3386320000        3.0856120000       -0.2250390000
 C     -1.6866340000        0.1323810000       -0.6330370000
 N     -0.0630230000        1.8674060000        0.0040110000
 O     -0.9702060000       -0.9014780000       -0.5741120000
 O     -2.9904890000        0.0034590000       -1.0203090000
 O      0.7482070000        1.0330060000        0.6202190000
 C     -3.4992390000       -1.3228620000       -1.0056460000
 C      1.6617420000        3.5535590000        0.2690370000
 H     -0.3524840000        3.7263150000       -0.7439850000
 H     -2.0745050000        2.2387050000       -0.5246840000
 H     -2.9844250000       -1.9557440000       -1.7325000000
 H     -3.3966200000       -1.7564760000       -0.0070260000
 H     -4.5540120000       -1.2372010000       -1.2693450000
 H      1.7785710000        4.6187150000        0.0708860000
 H      1.7607930000        3.3757980000        1.3461160000
 H      2.4829950000        3.0153390000       -0.2182880000
 O      2.3087920000       -1.2524950000       -0.7049870000
 C      3.4287170000       -0.4446380000       -0.3843310000
 C      2.6602940000       -2.6152400000       -0.8996710000
 H      3.0507070000        0.5649300000       -0.2538550000
 H      3.9031950000       -0.7958500000        0.5482660000
 H      4.1661960000       -0.4798210000       -1.1968030000
 H      3.1554210000       -3.0085800000       -0.0094160000
 H      1.7341510000       -3.1656110000       -1.0910620000
 H      3.3285890000       -2.7212570000       -1.7627230000
 H     -2.1099990000        0.2453580000        1.7951490000
 H      0.9324480000       -1.9068880000        2.6178300000
 H      0.3776190000       -2.9703690000        1.6350460000
 H     -1.5145060000       -1.1314960000        1.5972900000
 O      0.5255830000       -2.0196160000        1.7447340000
 O     -2.1793670000       -0.6645150000        2.1330450000


IN11

0 1
 C      1.2820012400        0.5324116567       -0.2028980604
 C      2.7274370682        0.6056955061       -0.6431933347
 C      2.0768555882       -1.5640265525       -0.3127725353
 C      0.3833009147        1.5318777155        0.1075853887
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 O     -0.8467320000        1.3653292585        0.3576644650
 O      0.9076083438        2.7963292445        0.0934680872
 O      0.0218756929       -1.0490763688       -1.4950732012
 C     -0.0144451623        3.8451086146        0.3474316979
 C      1.9821703161       -2.9225607720       -0.9621943678
 H      2.4031258964       -1.6531596100        0.7352799933
 H     -0.8271900128        3.8439488310       -0.3845610560
 H     -0.4440895561        3.7610766432        1.3493559719
 H      0.5572613171        4.7700491219        0.2664016346
 H      2.9512861506       -3.4217177425       -0.8888767281
 H      1.2312719073       -3.5365618931       -0.4591701815
 H      1.7104959369       -2.8176980850       -2.0129290433
 H      2.8839457015        1.2227747515       -1.5379218558
 O      2.9864462144       -0.7517083908       -1.0370550793
 C      3.6951611771        1.0564601200        0.4454727530
 H      4.7274374826        1.0458070851        0.0818252897
 H      3.4398752186        2.0724661938        0.7599645834
 H      3.6179282783        0.3982241985        1.3171906786
 Li    -1.3075629080       -0.4090674151       -0.1475210278
 C     -3.8606085837        0.5495462589       -0.0332375463
 H     -3.3932392612        1.4833886308        0.3019160815
 H     -4.8498701613        0.7581327519       -0.4578632844
 H     -3.9549586674       -0.1386332993        0.8075822115
 C     -2.8259501153        0.7454843002       -2.1309290686
 H     -2.3066812770        1.6636975476       -1.8282870362
 H     -2.2089784646        0.1850567409       -2.8350338602
 H     -3.7831887086        0.9973446681       -2.6028720243
 C     -1.3646418048       -2.7893284256        1.3748742997
 H     -0.2713213046       -2.8555825596        1.3094435786
 H     -1.7141776933       -3.3466189526        2.2524226216
 H     -1.8131753273       -3.2085659503        0.4723283814
 C     -1.1652627190       -0.7822706708        2.5718604119
 H     -0.0749333050       -0.7562848919        2.4448042817
 H     -1.5486831474        0.2374178040        2.5948743937
 H     -1.4223980860       -1.3076680973        3.4994734138
 O     -1.7674320211       -1.4330668948        1.4611855791
 O     -3.0370536009       -0.0870480271       -1.0009841950
 N      0.8220162309       -0.8047245395       -0.2292671189
 H      0.3904002122       -0.4102975041       -2.1354511926


IN12

0 1
 C     -1.5234729111        0.3142153684       -0.3650857389
 C     -2.9740512020        0.1137227140       -0.7323243957
 C     -1.6808353712       -1.8208121503       -0.8624693839
 C     -0.8763770993        1.5832550075        0.0951617667
 N     -0.8079073518       -0.7268015650       -0.4619870404
 O      0.3128064296        1.6688891052        0.3109516473
 O     -1.7511515024        2.5626888010        0.2505579411
 O      0.6144990716       -1.0532980440        2.3130904248
 C     -1.2130088733        3.8034378498        0.7369336485
 C     -1.6630365514       -2.9290377324        0.1735474048
 H     -1.3348800742       -2.1943736824       -1.8357510477
 H     -0.7249145395        3.6399195489        1.6989960133
 H     -0.4928982240        4.1993735157        0.0190870409
 H     -2.0645864487        4.4711480090        0.8405376077
 H     -2.3337658590       -3.7328312252       -0.1379562153
 H     -0.6507629660       -3.3276585513        0.2849783902
 H     -2.0035032975       -2.5336328888        1.1349645207
 H     -3.6276764026        0.3367745639        0.1209384499
 O     -2.9948998690       -1.2829369803       -1.0031600223
 C     -3.4052214971        0.9160483598       -1.9536489873
 H     -4.4151769798        0.6186940125       -2.2451216816
 H     -3.4033434441        1.9857338156       -1.7302151217
 H     -2.7272756700        0.7216100723       -2.7900983631
 Li     1.1297503166       -0.3368056159        0.7765932775
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 H     -0.0961015261       -1.6901027486        2.1582334549
 C      3.4052367653        1.5831415175        0.4675091654
 H      2.7615958738        2.4378261161        0.2208695776
 H      4.3523932083        1.9522573642        0.8832546854
 H      3.5994135771        0.9992780519       -0.4343451752
 C      2.4363533407        1.3777357318        2.5976687979
 H      1.8004012451        2.2514426363        2.3994084941
 H      1.8854847284        0.6495614720        3.1930975123
 H      3.3497047489        1.7040872823        3.1129286380
 C      3.2965014075       -1.9665162095       -0.0213654007
 H      2.8896875892       -2.9433725611        0.2709934481
 H      4.1466379753       -2.1175814783       -0.6992600175
 H      3.6147445040       -1.4195810183        0.8661031069
 C      1.7881179974       -1.8128642863       -1.8063947769
 H      1.2711834270       -2.7467129816       -1.5435341629
 H      1.0827309397       -1.1258943702       -2.2752133387
 H      2.5998347763       -2.0427630361       -2.5085634842
 O      2.2990967015       -1.1804445155       -0.6517488163
 O      2.7603930364        0.7256047252        1.3835551564


IN13

0 1
 C     -1.5755855146        0.1029761984       -0.4286287541
 C     -3.0764401008        0.2550043941       -0.4728580288
 C     -2.3508400612       -1.9570272073       -0.5034861746
 C     -0.5537258110        1.1960682459       -0.3370875226
 N     -1.1735566403       -1.0984645201       -0.4757525222
 O      0.6361127156        0.9668993212       -0.2779348010
 O     -1.1020512900        2.3950172746       -0.3135492206
 O      1.3525589547       -1.4513965493        1.7032648785
 C     -0.1861754425        3.4990035078       -0.1982291832
 C     -2.3171378568       -2.9572630511        0.6349393010
 H     -2.3667017546       -2.4688559361       -1.4755867051
 H      0.3836792562        3.4064291262        0.7271962718
 H      0.4912829841        3.5044679033       -1.0531967903
 H     -0.8066006142        4.3913155517       -0.1868770201
 H     -3.2340088703       -3.5508997691        0.6274718583
 H     -1.4585458299       -3.6248667202        0.5255175757
 H     -2.2409710810       -2.4239217911        1.5863398044
 H     -3.4440180111        0.8039069912        0.4021829956
 O     -3.4863705270       -1.1046310359       -0.3822631041
 C     -3.5702536489        0.9073698186       -1.7589472630
 H     -4.6614608904        0.8697851185       -1.7876215708
 H     -3.2519532154        1.9516254817       -1.8060687497
 H     -3.1776059796        0.3722191260       -2.6286874854
 Li     0.8996548424       -1.0771636524        0.0632779653
 C      3.1956579421       -0.7539257003       -1.5297223000
 H      3.8614113197       -1.2361391929       -0.8030072845
 H      3.6655921557       -0.7699280192       -2.5204575134
 H      3.0065648311        0.2763484989       -1.2261607794
 C      2.0617719673       -2.7778492078       -1.9261103678
 H      2.6943396182       -3.3120916460       -1.2059064683
 H      1.0571082476       -3.2049220155       -1.9186549748
 H      2.4931455744       -2.8754129670       -2.9295694700
 O      1.9397421570       -1.4123384726       -1.5705864949
 H      0.9696509836       -2.2666561940        2.0529902777


IN14

0 1
 Li    -0.5064615868       -0.8132125233       -0.0404629879
 C     -0.0280848539        3.0175908757       -0.6147344099
 C      1.6582560494        0.3420113665        0.6017846066
 N      0.1872105679        1.7512307633       -0.7432070354
 O      0.7673535610        0.2026689215        1.4144594972
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 O      2.8821881004       -0.1368166899        0.7193842966
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 C      3.0342946831       -1.1471171774        1.7267472276
 C     -1.4152523353        3.5385732098       -0.7058413356
 H      0.8358967203        3.6505643449       -0.4566807773
 H      2.8080391559       -0.7366988237        2.7121986174
 H      2.3594995700       -1.9698175272        1.4853292543
 H      4.0745904228       -1.4614752151        1.6713982634
 H     -1.4357642351        4.6148067186       -0.5390757317
 H     -1.8356986780        3.3135111909       -1.6923770971
 H     -2.0516596052        3.0369354749        0.0301591919
 O     -2.0837504128       -0.8964394914        1.1144551659
 C     -2.5428253129        0.3739989575        1.5393855941
 C     -3.1460071842       -1.7933630835        0.8501928635
 H     -1.6610883101        0.9994087059        1.6839684836
 H     -3.1928206352        0.8232729837        0.7776185851
 H     -3.0971823000        0.2794613803        2.4814670927
 H     -3.7912372540       -1.4061678638        0.0510258482
 H     -2.7024895675       -2.7394683250        0.5373748794
 H     -3.7479285091       -1.9509916064        1.7533931674
 O      0.8498249248       -1.8055138937       -0.6103601481
 C      1.5394866762        1.1887207609       -0.6528422388
 H      1.6877120492        0.5356068288       -1.5135446956
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 H      0.8260894412       -1.8400110226       -1.5771267379
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IN15

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0 1
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 Li    -0.5199151811       -1.2745228305        0.0813172899
 C     -0.4396015284        2.6270739228       -0.9124622888
 C      1.6494629349        0.1519252989        0.7842771513
 N     -0.0072489419        1.4693489250       -0.4956213397
 O      1.1527092135       -1.0033530560        0.7982315559
 O      2.8495649456        0.3496108674        1.4187871873
 O     -0.7214078082        0.4000044537       -0.7707520301
 C      3.4081880490       -0.7938690270        2.0454842724
 C     -1.7015154281        2.7237460105       -1.6929929419
 H      0.1682597013        3.4877609482       -0.6657384904
 H      1.7480670996        2.2465574887        0.3527938090
 H      2.7431477257       -1.1897760319        2.8178516916
 H      3.6130765726       -1.5851650015        1.3195071039
 H      4.3407615153       -0.4554907183        2.4981364234
 H     -1.8966717586        3.7631898986       -1.9607311638
 H     -1.6469589210        2.1261975512       -2.6106414767
 H     -2.5531274529        2.3415165758       -1.1176562315
 O     -1.9496328538       -1.1261123369        1.4312083386
 C     -1.5902356650       -0.0102379598        2.2343371398
 C     -3.2006920312       -0.9199928764        0.7952687922
 H     -0.5976871396       -0.2118749340        2.6388957722
 H     -1.5605664084        0.9018959375        1.6242191810
 H     -2.3121815936        0.1137804737        3.0505001744
 H     -3.1376009412       -0.0608725912        0.1153840014
 H     -3.4343787281       -1.8248863531        0.2316536358
 H     -3.9846361386       -0.7461467844        1.5420983604
 H     -0.9301408529       -1.1426313954       -2.0118646206
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 O     -0.9318474585       -2.0606481537       -1.6809101304
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NI

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0 1
 C     -3.1767399416       -0.8222818727       -0.1771719500
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 C      0.5598704711        3.4510052127        0.1970786185
 C     -3.1219727415       -2.2761076455       -0.4759966233
 H     -3.8090444703       -0.3862108383        0.5849839891
 H      0.4764634389        3.4861979645        1.2847172491
 H      1.3756902455        2.7835180127       -0.0848288237
 H      0.7192894137        4.4472243232       -0.2094903488
 H     -3.8023035962       -2.8324212164        0.1681872134
 H     -3.3824783061       -2.4546161911       -1.5252307953
 H     -2.0997800351       -2.6469550404       -0.3395844413
 C     -2.4036494844        1.4202498754       -0.5945530127
 H     -2.5495858729        1.9323713365       -1.5451503186
 H     -3.1946155863        1.6987116686        0.1059254871


PR

0 1
 C     -0.3243686601       -0.2841147727       -0.3266351891
 C     -1.3541044769       -1.3737285462       -0.1270899363
 C     -2.1982919442        0.7764054539        0.0819893099
 N     -0.7705577752        0.8942236446       -0.1897508447
 C     -3.0158278436        1.5838280405       -0.9072903790
 H     -2.3700233345        1.1328263890        1.1075945122
 H     -2.7705026604        2.6450860528       -0.8253969407
 H     -2.8006160157        1.2405438193       -1.9228475780
 H     -4.0800453201        1.4462832291       -0.7027333762
 O     -2.5439889105       -0.6051639198       -0.0158754891
 H     -1.4217482023       -2.0254004210       -1.0067172318
 C     -1.0977221814       -2.2035923454        1.1256039211
 H     -1.9327264896       -2.8886654468        1.2904678623
 H     -0.1789928172       -2.7842602122        1.0127592868
 H     -1.0041681855       -1.5496755517        1.9982961192
 C      1.1028310253       -0.6129613289       -0.6380264949
 O      1.4741688015       -1.7548482731       -0.7906411568
 O      1.8810122471        0.4576851094       -0.7290285576
 C      3.2549019339        0.1839201208       -1.0322358399
 H      3.3320302343       -0.3261725218       -1.9942707071
 H      3.7462255655        1.1535050117       -1.0691798895
 H      3.6927540094       -0.4426705316       -0.2528694010


SC

0 1
 C     -1.0520398872        1.1527942508       -1.1023205738
 C      1.9149005698       -1.0725667545       -1.6554632707
 Li     0.9378160400       -0.4088887733        0.7185045412
 C     -2.7610113204       -0.4639280413       -0.8297369393
 C      0.0970241958        1.7744594217       -0.6307109693
 N     -1.5351370166       -0.0736403504       -0.6162377420
 O      0.9596829823        1.3809913182        0.1944614251
 O      0.2643389792        3.0045993075       -1.2151993998
 O     -0.7246408759       -0.8720555866        0.0362081358
 C      1.4402107704        3.7065874688       -0.8460575032
 C     -3.2111033166       -1.8092316941       -0.3824730827
 H     -3.4060294220        0.2318381244       -1.3501761284
 H     -1.7192785027        1.6811734839       -1.7654013981
 H      1.4685036275        3.8986826454        0.2296191440
 H      2.3396817316        3.1515786935       -1.1272660831
 H      1.4029986961        4.6507808209       -1.3902964929
 H     -4.2361465976       -1.9899374227       -0.7096892418
 H     -2.5627317165       -2.5942734100       -0.7882512435
 H     -3.1699204619       -1.9011203697        0.7093356328
 O      1.0537887010       -1.5207136537        2.3132623590
 C     -0.1606547770       -2.0744018697        2.7915777454
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C	2.1446274085	-2.4104810836	2.4684879289
H	-0.9465156573	-1.3450924377	2.5991013549
H	-0.3943122925	-3.0034611426	2.2566862911
H	-0.0832772113	-2.2805712701	3.8658349713
H	1.9700280648	-3.3352843505	1.9044927936
H	3.0330730231	-1.9113626838	2.0815153280
H	2.2886613685	-2.6535968585	3.5280512925
O	2.2393053194	-1.2921978409	-0.5013902182
H	0.9844303862	-0.5122932187	-1.8588210543
C	2.7151178742	-1.5245913932	-2.8331157520
H	2.0931487305	-2.1655715987	-3.4671946236
H	2.9904666345	-0.6524470794	-3.4358748419
H	3.6086692321	-2.0611186711	-2.5121720452

TS1

0 1

C	2.0418798213	-0.6523500760	0.1373804622
C	0.3985927739	-0.1728724959	1.7197295671
Li	-0.6427922984	-0.2507635063	-0.8248546911
C	2.9777422614	1.3756559014	-0.6697096866
C	1.3519109390	-1.8107167013	-0.2984712693
N	1.9740524823	0.5509107745	-0.6114789554
O	0.3599826348	-1.8781510801	-1.0406540540
O	1.8162791928	-2.9237985326	0.3230222055
O	0.8338436719	0.8818361135	-1.1618558694
C	1.0329385940	-4.0985666205	0.1346690843
C	2.8200153594	2.7017942053	-1.3227368487
H	3.9063793041	1.0411977713	-0.2255806424
H	2.9748462061	-0.7879860937	0.6682529647
H	0.0038943535	-3.9326865677	0.4633188075
H	1.0283641514	-4.4001609443	-0.9153921422
H	1.5050938494	-4.8687253477	0.7436601533
H	3.7248968873	3.2967285177	-1.1939366960
H	2.6188541491	2.5911318235	-2.3945065710
H	1.9664765263	3.2413659409	-0.8968872350
O	-2.5372069411	-0.7310988649	-1.0929791907
C	-2.7450536231	-2.0578994087	-0.6277821533
C	-3.3954599818	0.1869570893	-0.4347396953
H	-2.0525455581	-2.7020212503	-1.1687963233
H	-2.5323917468	-2.1150232248	0.4466363072
H	-3.7799187379	-2.3648716534	-0.8217985406
H	-3.2040985042	0.1780722262	0.6448040343
H	-3.1827377104	1.1788736721	-0.8375042029
H	-4.4444355350	-0.0672470751	-0.6280788756
O	-0.6889977041	-0.3567061198	1.1433093151
H	0.8226432512	-0.9816590726	2.3383200368
C	0.9049631893	1.2163234814	2.0119586737
H	0.3435114499	1.6010255354	2.8723549986
H	1.9677471177	1.2197534970	2.2639072435
H	0.7126481749	1.8679200862	1.1548917890

TS2

0 1

C	-1.8692872961	0.0653525234	-0.7439941781
C	-0.8399938590	-1.0825533221	-1.1773526442
C	-0.4844734396	1.4822542551	-1.8492178479
C	-2.5570025644	-0.1800142557	0.5833445864
N	-1.0536902064	1.2526628865	-0.6868336918
O	-2.5228951933	-1.2209934190	1.1965802103
O	-3.2630263002	0.8839327388	0.9730802862
O	-0.2715222680	1.2988632559	0.4263904508
C	-3.9393717619	0.7416645164	2.2250840045
C	0.7293252518	2.3316818183	-1.9816010182
H	-1.1164750970	1.3202258805	-2.7162861428

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 H     -2.6405738169        0.1890096540       -1.5140383902
 H     -4.6605045340       -0.0768555455        2.1759718448
 H     -3.2189392355        0.5423070280        3.0209616547
 H     -4.4461796537        1.6892800980        2.3969292138
 H      1.0700558152        2.3337297946       -3.0177587468
 H      0.4910737068        3.3608435881       -1.6892562039
 H      1.5321419017        1.9765334460       -1.3329983345
 H     -0.5719616235       -1.5872746670       -0.2305685418
 O      0.2533866771       -0.4996396288       -1.7710224872
 C     -1.5623751609       -2.0854836668       -2.0733877248
 H     -0.9039707687       -2.9259603928       -2.3132582413
 H     -2.4621143267       -2.4787455328       -1.5857771704
 H     -1.8544039450       -1.6010519222       -3.0124088088
 Li     1.0919571741        0.0238236326       -0.1044096548
 C      2.5875700536        2.2936310143        1.1150147580
 H      1.5322955494        2.5656905021        1.0748178843
 H      2.9349756127        2.2544873189        2.1554163081
 H      3.1928832453        3.0247420374        0.5630744902
 C      4.0241861765        0.5387779504        0.4717549146
 H      4.6527881877        1.2096235363       -0.1269320044
 H      4.4408179868        0.4675334518        1.4851223504
 H      3.9972200653       -0.4521096305        0.0169929806
 C      1.7316117895       -2.8958878543       -0.2046798400
 H      0.9537653162       -3.5289289150        0.2420556349
 H      1.4520883899       -2.6291905637       -1.2245471047
 H      2.6855393965       -3.4383623473       -0.1982639901
 C      2.1998851746       -1.8679075616        1.8670196323
 H      1.4286597904       -2.4522448758        2.3841287197
 H      3.1640718462       -2.3858282383        1.9512937553
 H      2.2760596707       -0.8769557715        2.3191067365
 O      2.6927821996        1.0131837000        0.5154059980
 O      1.8557380732       -1.6795965167        0.5085923525
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TS3

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 C     -1.8390480018       -1.8694164750       -0.6662077015
 C     -0.7800657584        1.3698419171        0.4298943625
 O      0.4421278729        1.3420624298        0.5882555130
 O     -1.5318840890        2.3642604031        0.9121727753
 O      0.1191673833       -0.9038154955       -1.5780566509
 C     -0.8329485087        3.4043463987        1.6005812579
 C     -1.4141466559       -3.2638100793       -0.2802280877
 H     -2.1422402926       -1.8292872997       -1.7287642670
 H     -0.3033980980        3.0002282957        2.4656343442
 H     -0.1179163130        3.8883845620        0.9322091257
 H     -1.5963656709        4.1118806031        1.9190137451
 H     -2.2123973191       -3.9814126050       -0.4863357463
 H     -0.5286254516       -3.5449343080       -0.8564220110
 H     -1.1762184957       -3.2868579511        0.7868339110
 H     -3.1753006599        0.3831904296        1.0595394650
 O     -2.8781797883       -1.4280152671        0.1700160023
 C     -4.0187871215        0.4263642586       -0.9208354001
 H     -4.9968030197        0.0554612727       -0.6005776063
 H     -4.0569687717        1.5190276528       -0.9786150334
 H     -3.7971444306        0.0432243527       -1.9218319589
 Li     1.2718978505       -0.2794379961       -0.2050894186
 C      2.8487603449       -0.0368441531        2.0712040682
 H      2.0644625886        0.4886321282        2.6290149340
 H      3.5738953174       -0.4699876390        2.7702432599
 H      3.3477145198        0.6644152394        1.4005606676
 C      1.5738578089       -2.0159234128        2.0277176702
 H      0.7370408852       -1.5439264590        2.5581893065
 H      1.1887281822       -2.7635318319        1.3334185891
 H      2.2444986503       -2.4916738732        2.7529565120
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 C      3.8391008234       -0.1877090702       -1.5391710836
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 H      4.6632408349        0.4335876510       -1.9094883160
 H      4.1686532687       -0.7580624717       -0.6689880248
 C      2.2319008467        1.4096747953       -2.1752322705
 H      1.9172380573        0.7712717141       -3.0108181602
 H      1.3664596881        1.9403540437       -1.7729874851
 H      2.9821225897        2.1287722670       -2.5250694604
 O      2.7562841013        0.6234085545       -1.1195515744
 O      2.2824304071       -1.0558113999        1.2610237974
 N     -0.7738689082       -0.8746299840       -0.4575904069
 H     -0.3896296048       -0.2466025721       -2.3872519631
 O     -1.1507762633        0.5893408476       -2.9809058732
 H     -0.6074999356        1.3421944701       -3.2607416331
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TS4

0 1
 C     -1.4692727553        0.1968731041       -0.3583620927
 C     -2.7897638839        0.3467234386        0.3689351673
 C     -2.2197890592       -1.8451057695        0.0806911816
 C     -0.6442086590        1.2094240972       -0.8597700564
 N     -1.0249537948       -1.0916868159       -0.3370700464
 O      0.5538289417        1.0736647653       -1.2094417700
 O     -1.2356234771        2.4341186480       -0.8937355610
 O      0.0678633158       -1.2483125551        0.9676377139
 C     -0.4321839851        3.5006223184       -1.3846074328
 C     -1.9574320185       -3.1464811596        0.7997067737
 H     -2.7433499454       -2.0404981567       -0.8702134459
 H      0.4456324160        3.6546341870       -0.7510956926
 H     -0.1015350626        3.3018016165       -2.4067280030
 H     -1.0675374402        4.3853082418       -1.3609892527
 H     -2.8945280645       -3.6971880485        0.9099008343
 H     -1.2572385062       -3.7531061168        0.2179942891
 H     -1.5331808587       -2.9499199159        1.7846269929
 H     -2.7319716167        1.0231612011        1.2328979293
 O     -2.9856128947       -0.9752023271        0.8879885348
 C     -3.9551533443        0.7614405677       -0.5228056044
 H     -4.8891869632        0.7810753727        0.0466797649
 H     -3.7709929463        1.7566985116       -0.9365085404
 H     -4.0623303782        0.0565746853       -1.3539422057
 Li     1.2918672370       -0.0030100498        0.1970726693
 C      2.6481338383        2.2248903876        1.3088370156
 H      2.2463515969        2.9354583380        0.5751367935
 H      2.9559083431        2.7691840607        2.2096961506
 H      3.5026052329        1.7011477690        0.8781960063
 C      0.4992191552        1.8048077928        2.1794397333
 H      0.0394645553        2.5079776894        1.4706081035
 H     -0.1878406352        0.9784263860        2.3685697952
 H      0.7269699018        2.3310670123        3.1143220692
 C      3.5681941712       -1.6889386413        0.4326245645
 H      3.1533565367       -2.6460749920        0.0986969875
 H      4.6605784341       -1.6986719472        0.3323701707
 H      3.3016531606       -1.5091900075        1.4766081072
 C      3.3022141529       -0.7514976773       -1.7136454142
 H      2.9209758030       -1.7066353979       -2.0881335047
 H      2.7935856976        0.0725001670       -2.2156595078
 H      4.3843329513       -0.6816487510       -1.8796525544
 O      3.0160293242       -0.6276329835       -0.3284482042
 O      1.6805702541        1.2424031897        1.6310117149
 H      0.6954484955       -3.6031242580       -1.6975214677
 H      0.2747943666       -2.1895673475       -1.2277749036
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 O      0.9775194768       -2.8693184908       -1.1337303900
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TS5

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N	0.6027239407	1.6549747768	0.0495886041
O	0.7177391719	-1.0297995368	-0.9010043833
O	2.9444578616	-0.9236661801	-0.6902352730
O	-0.5837465467	1.1997051118	0.3351958535
C	3.0269136609	-2.1971285660	-1.3414864223
C	-0.4088259558	3.7423226265	-0.5912200191
H	1.7833376665	3.1582042546	-0.6187396709
H	2.4831269478	-2.9498632214	-0.7677864908
H	2.6110764483	-2.1331384682	-2.3483386469
H	4.0874627846	-2.4368482328	-1.3791729819
H	-1.1105214402	3.2937505258	-1.3028201043
H	-0.9487064593	3.8590357246	0.3549994796
H	-0.0968900972	4.7205259774	-0.9561792371
C	-3.1999594524	-2.1144852963	-0.6013247822
H	-3.6431352436	-2.2677862279	0.3902898619
H	-3.9828781704	-2.1949872054	-1.3651185303
H	-2.4360572185	-2.8725929861	-0.7817240401
C	-3.4660981862	0.2191407796	-0.4299904520
H	-3.9263378214	0.1111146795	0.5605571347
H	-2.8802701959	1.1379443926	-0.4644372666
H	-4.2521002900	0.2378475060	-1.1945873716
O	-2.5666937542	-0.8500208409	-0.6758450280
Li	-0.8521021424	-0.6646354753	0.2239823828
O	-0.7472405485	-1.5898345863	1.8412056063
H	-0.4429723083	-2.5044968380	1.7610398620
C	1.7316457525	0.7729520555	0.3389519303
H	2.6714298801	1.3142863424	0.2536289292
H	1.5224174316	0.3398497224	1.5085361253
O	1.1279649660	-0.2535633056	2.7074358010
H	0.6969857137	0.4659986571	3.1929150955
H	0.0843483426	-1.0286574568	2.2798342156

TS6

0 1

C	-1.4523439588	0.3747436696	-0.1683575614
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C	-1.8689134899	-1.8560631251	-0.4833817972
C	-0.7212644504	1.3743055103	0.5771137256
O	0.4917189193	1.3142049367	0.8179708376
O	-1.4494807294	2.4535696836	0.8959737595
O	-0.0235354918	-0.6755159769	-1.4575401180
C	-0.7321636902	3.5480602271	1.4692102326
C	-1.5711618482	-3.2556270301	-0.0053691465
H	-2.0602205774	-1.8369999652	-1.5692741539
H	-0.2843367605	3.2562913948	2.4213167776
H	0.0528716405	3.8873148692	0.7896908782
H	-1.4687259511	4.3348225645	1.6223530266
H	-2.4186809153	-3.9171415950	-0.2027814079
H	-0.6938808775	-3.6427131557	-0.5313757192
H	-1.3682276267	-3.2392812676	1.0690583471
H	-3.2807712753	0.5247236176	1.0220596304
O	-2.9631896745	-1.3275515873	0.2295134770
C	-3.8445247680	0.5544406568	-1.0538985162
H	-4.8840243832	0.2862907956	-0.8434876481
H	-3.7776238044	1.6410736206	-1.1670310211
H	-3.5408415682	0.0948206495	-1.9998065401
Li	1.2812756190	-0.1903222232	-0.1592258520
C	3.1100735697	-0.3395080137	1.9029645954
H	2.4143495325	0.0783637849	2.6406223730
H	3.9161670750	-0.8740640104	2.4192645647
H	3.5256324314	0.4662367836	1.2957003867

C	1.8226166317	-2.3013058455	1.7003412598
H	1.0777640501	-1.9374645370	2.4190064353
H	1.3287914607	-2.9202473607	0.9506813472
H	2.5842849852	-2.8882061086	2.2274823032
C	3.5478593828	-0.1519083624	-1.8560194614
H	2.9837966417	-0.7016298475	-2.6207160903
H	4.3704601910	0.3932288612	-2.3342701185
H	3.9451806166	-0.8529047562	-1.1202708089
C	2.0951071372	1.6898830636	-2.0274376816
H	1.4970576225	1.1814111289	-2.7941525399
H	1.4463388122	2.3160164888	-1.4126325855
H	2.8628564348	2.3077006320	-2.5089738195
O	2.6979857661	0.7433981112	-1.1602060156
O	2.4289424962	-1.2157479177	1.0180977565
H	-0.8118791677	0.3468032086	-1.4268104224
N	-0.7604888522	-0.9135572950	-0.2209092589

TS7

0 1

C	-1.4062736704	0.1435734370	-0.4037413930
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C	-2.2947448630	-1.8740197479	-0.1927633559
C	-0.5580882683	1.1629931747	-0.8406281405
N	-1.0733880263	-1.1697527238	-0.6140780002
O	0.5949492069	1.0130376580	-1.3192950140
O	-1.0590837586	2.4163150737	-0.6451926137
O	0.0799619938	-1.5842840713	0.5459051811
C	-0.2220521301	3.4905243194	-1.0536998435
C	-2.1151398341	-3.2879209990	0.3058221759
H	-2.9140810150	-1.8753642284	-1.1048269033
H	0.7241791446	3.4827103490	-0.5062515953
H	-0.0108883959	3.4370212385	-2.1243868645
H	-0.7760284975	4.4008736530	-0.8261122563
H	-3.0967760901	-3.7405943683	0.4649798831
H	-1.5774803282	-3.8840428419	-0.4370603141
H	-1.5643732372	-3.2884494234	1.2471760363
H	-2.4593256772	0.8223092513	1.3966126468
O	-2.9070593679	-1.0818979598	0.8069631949
C	-3.8442439685	0.9034252094	-0.2520648145
H	-4.7213782937	0.9070134764	0.4022437961
H	-3.6121605398	1.9320182713	-0.5404325470
H	-4.0821009082	0.3370974617	-1.1585807635
Li	1.3096819770	-0.2715182205	-0.0975987387
H	0.3941510004	-2.4365067682	0.1966545445
C	2.7792299957	1.7268094831	1.3242202762
H	2.3647090534	2.5772954693	0.7683879751
H	3.1531208637	2.0756691635	2.2941550469
H	3.5930468915	1.2809903962	0.7498038275
C	0.6640357279	1.1951976834	2.2168604189
H	0.1865389357	2.0244700167	1.6760065618
H	-0.0349505549	0.3605892306	2.2904828953
H	0.9596237518	1.5349543422	3.2168529265
C	3.7261449088	-1.7061326150	0.3058450376
H	3.3589367791	-2.7393302879	0.2603292857
H	4.8029997878	-1.6956737055	0.1008568042
H	3.5316216748	-1.2892901094	1.2957904824
C	3.1970846352	-1.3344720752	-1.9664406638
H	2.8253176461	-2.3609366062	-2.0770426136
H	2.6137813390	-0.6623772879	-2.5968199549
H	4.2533507046	-1.2979842127	-2.2566178289
O	3.0390854006	-0.8907544508	-0.6284647069
O	1.7970698101	0.7226116389	1.5043993339

TS8

0 1

C	-2.1184054473	-1.9798514912	-0.0076725745
C	-1.3040484730	1.4346011651	0.0248041478
N	-1.2591318321	-1.0157932419	0.0554728733
O	-0.2750614534	1.6850065522	-0.5889458493
O	-2.2902613543	2.3215815245	0.1580922438
O	-0.0880187835	-1.1133133101	-0.5017329373
C	-2.0527486440	3.6095716124	-0.4225742737
C	-1.7570919510	-3.2500874918	-0.6896076792
H	-3.0794816761	-1.8087224782	0.4598535403
H	-1.1551765005	4.0581608211	0.0076680259
H	-1.9320081695	3.5191570319	-1.5034754449
H	-2.9314563471	4.2051908728	-0.1840295099
H	-1.5847551557	-3.0789088392	-1.7580241897
H	-0.8216487613	-3.6427940873	-0.2767720320
H	-2.5501752083	-3.9880302354	-0.5691321459
C	3.9716239828	0.5094651788	-0.4058615668
H	4.2689920164	0.4890055830	0.6503514485
H	4.8007455600	0.1408624809	-1.0215700962
H	3.7281170930	1.5317007323	-0.6991077887
C	3.0275951994	-1.6408866036	-0.2691303403
H	3.3591963957	-1.7240184586	0.7734710367
H	2.0722505749	-2.1519135353	-0.3920581973
H	3.7851886842	-2.0823348787	-0.9278179131
O	2.8146605681	-0.2796795168	-0.6136646351
Li	1.0913563495	0.3077040744	0.0865567571
C	-1.5252055648	0.2029113638	0.8212517297
H	-2.5139654222	0.1600979057	1.2694803348
H	-0.5015713909	0.2541657287	1.5880005422
O	0.8361251798	0.2851079733	1.9315824785
H	0.9698615312	1.1467625672	2.3534090155

YL

0 1

C	-1.0736665915	1.3861454181	-0.7742804313
C	-2.5858601220	-0.3875542384	-1.1850921448
C	0.1698051865	1.8303108011	-0.3496921876
N	-1.3610639781	0.0517060415	-1.1051269405
O	1.2427273432	1.1989675618	-0.1661393382
O	0.1555119164	3.1785944565	-0.0958022942
O	-0.3788664913	-0.7742438581	-1.3821910576
C	1.3775465219	3.7301153618	0.3655004717
C	-2.8619670088	-1.7745850281	-1.6457577002
H	-3.3679690310	0.3171446674	-0.9342399961
H	-1.9155150819	2.0602286973	-0.7982644510
H	1.6911751422	3.2734627923	1.3087242689
H	2.1763156656	3.5996220439	-0.3702383614
H	1.1840683720	4.7927267070	0.5160669658
H	-3.9383117709	-1.9502746410	-1.6790234665
H	-2.4423770171	-1.9473218071	-2.6439680988
H	-2.4040265089	-2.5160763180	-0.9812079031
C	2.0160088809	-0.8854155271	2.0967704001
H	1.9387961965	0.2080445981	2.0490751724
H	1.8621613877	-1.2279869293	3.1273971484
H	3.0046417102	-1.1961835287	1.7552197209
C	-0.2641804473	-1.1973897021	1.6470247569
H	-0.4250899421	-1.5546154248	2.6716153261
H	-0.4587187880	-0.1168515172	1.5974203447
H	-0.9347431459	-1.7148280204	0.9601875847
C	4.1248457941	0.0289420041	-0.6670063764
H	4.6553454731	-0.1198840719	0.2830659642
H	4.8515592748	0.0197945972	-1.4881861413
H	3.5849761152	0.9755466635	-0.6441033949
C	3.7141792455	-2.2882177196	-0.8313631316
H	4.2092071466	-2.4792494196	0.1300120120
H	2.8969683300	-2.9978430315	-0.9672647059

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 H      4.4448599218       -2.4076542574       -1.6402279900
 O      1.0637117307       -1.4811022732        1.2310190296
 O      3.1566102066       -0.9885260627       -0.8541873442
 Li     1.2675683734       -0.6166280356       -0.5630896909


IN1b

0 1
 C      1.4726351065       -0.1664910680       -0.1123310033
 C      1.0433184438       -0.5931421706        1.3678898739
 Li    -0.9420311887        1.0136316447        0.5201727929
 C      2.8218103819        1.8211255124       -0.1290864116
 C      0.4135136455       -0.6322084926       -1.0767995954
 N      1.6380788454        1.3007655966       -0.1631008182
 O     -0.7321773212       -0.2262843546       -1.1086152696
 O      0.8484118823       -1.6433355544       -1.8249281664
 O      0.5704025030        2.0344629697       -0.1870898347
 C     -0.1399955518       -2.2698934474       -2.6527878188
 C      2.9738001185        3.2977749415       -0.0880682308
 H      3.6609510092        1.1369803940       -0.1342065548
 H      2.4289429378       -0.6199038677       -0.3744178047
 H     -0.9581649577       -2.6481699455       -2.0361855586
 H     -0.5305152675       -1.5545956451       -3.3785777573
 H      0.3733912417       -3.0865713169       -3.1554508819
 H      4.0258419719        3.5745191462       -0.0248723310
 H      2.5319519659        3.7486687714       -0.9836025998
 H      2.4316757285        3.7067699163        0.7712454301
 H      1.9489254998       -0.2986217122        1.9483991581
 O     -2.8863099455        0.6959347838        0.6391520244
 C     -3.0701556928       -0.6761496289        0.9596593494
 C     -3.7118989273        1.1058897659       -0.4340492887
 H     -2.2807930636       -0.9367691840        1.6653684032
 H     -4.0646542055       -0.8313087476        1.3955706310
 H     -2.9666786586       -1.2919530413        0.0564091340
 H     -4.7699928577        0.9630861993       -0.1820883689
 H     -3.5222024278        2.1658322508       -0.6107452683
 H     -3.4737544372        0.5331916954       -1.3394777220
 O     -0.0869286970        0.0060653140        1.7770904498
 C      0.9558700938       -2.1284117912        1.3937845985
 H      1.8592854098       -2.6222016242        1.0171504424
 H      0.7876209514       -2.4458276959        2.4266813539
 H      0.0940055332       -2.4613262238        0.8020639530


IN2b

0 1
 C     -1.5066361896       -0.9771440531        0.3390373229
 C     -0.6058416081       -0.8439291990        1.6341191230
 Li     1.0341112351        0.4020015390        0.0424674476
 C     -1.2164967410       -2.5102207752       -1.5012108376
 C     -1.9724120808        0.4045532223       -0.0695298920
 N     -0.7254664931       -1.5639063231       -0.7717079311
 O     -1.5573624053        1.0422788181       -1.0089849951
 O     -2.9170690511        0.8388080199        0.7652624945
 O      0.4726995143       -1.1078207670       -0.9673468161
 C     -3.3531696529        2.1849566063        0.5513344485
 C     -0.4057276947       -3.0957013449       -2.5989421471
 H     -2.2224714009       -2.8368213285       -1.2698220070
 H     -2.3707644200       -1.6232224793        0.5112443186
 H     -2.5179297341        2.8730747911        0.6975575627
 H     -3.7497191942        2.2996157795       -0.4591119419
 H     -4.1294094617        2.3644502689        1.2923598182
 H     -0.9662141692       -3.8705686426       -3.1210856629
 H     -0.1110508386       -2.3137081987       -3.3071220705
 H      0.5199137702       -3.5215814053       -2.1964995904
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 O      1.3113779339        2.0880527254       -0.8945330797
 C      0.6447268860        3.2259064212       -0.3802861824
 C      1.2207734502        2.0012078291       -2.3052886388
 H      0.7236691402        3.1795683162        0.7076340764
 H      1.1209853572        4.1438680746       -0.7480147683
 H     -0.4110733544        3.2117370158       -0.6732197358
 H      1.7109065874        2.8649360310       -2.7720257626
 H      1.7309978406        1.0836645431       -2.6038138887
 H      0.1714974291        1.9551067260       -2.6168580908
 C      2.9001087501       -1.2235782248        1.1574214420
 O      2.9381470466        0.0015497974        0.4407032489
 C      3.3680013315        1.0680937408        1.2709808259
 H      2.2424359706       -1.1217792556        2.0291236127
 H      2.4921208721       -1.9753328626        0.4803502752
 H      3.9105936293       -1.5087096287        1.4770894497
 H      2.6686232259        1.1930762009        2.1079714675
 H      4.3759116298        0.8708991522        1.6575328196
 H      3.3760084642        1.9700488569        0.6579265656
 O      0.1324952842        0.2931836008        1.6045681405
 C     -1.4989826736       -0.9456337343        2.8780209616
 H     -2.1858205342       -0.0962471707        2.9215124515
 H     -2.0778573936       -1.8766802754        2.9055648642
 H     -0.8547329889       -0.9104817508        3.7615698327
 H      0.0104205919       -1.7747000567        1.6068671986
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PR-a-Si

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0 1
 C      1.8210796970        0.7213855134       -0.6406162211
 C      0.9422718788        0.7905273942       -1.9258812668
 C      0.1263094838        2.1746068874       -0.3416154066
 C      3.0843207368        1.5523878554       -0.7432673533
 N      0.9828692857        1.2980391978        0.4461493474
 O      3.2143666250        2.5541965471       -1.4121506826
 O      4.0474436048        1.0727043915        0.0496890093
 O      0.1833154254        0.2383683650        0.9465477789
 C      5.2492660870        1.8464530455        0.0893697958
 H      0.7580885652        2.9732129417       -0.7550219455
 H      2.0779752018       -0.2958607482       -0.3451689563
 H      5.0364630399        2.8580945985        0.4404336222
 H      5.7001077448        1.8975940542       -0.9038565094
 H      5.9104586411        1.3319508491        0.7839678954
 H      1.3836465371        1.5152793868       -2.6204945197
 O     -0.2992282032        1.3431134117       -1.4518408576
 Li    -1.0961652436       -0.1758350814       -0.2922569241
 C     -4.2362108114        0.0041747673       -0.1921657437
 H     -4.1334016064        0.2852795398       -1.2412891326
 H     -4.8807788918        0.7284034760        0.3205888094
 H     -4.6913229667       -0.9924831775       -0.1212588008
 C     -2.9363020152       -0.3574198340        1.7465455386
 H     -3.3017002739       -1.3850083621        1.8756712239
 H     -3.5732158177        0.3248717389        2.3230840380
 H     -1.9004776249       -0.2753039250        2.0850586939
 C     -2.2670270042       -2.8948791347       -0.6994004842
 H     -1.9646738338       -3.8934262119       -1.0383289004
 H     -2.7254638299       -2.3526960203       -1.5290063296
 H     -2.9960238468       -3.0009729151        0.1158424461
 C     -0.4427386534       -2.7661237755        0.7960244264
 H      0.0012649996       -3.7131638127        0.4653235911
 H     -1.1245987750       -2.9631607275        1.6342274682
 H      0.3238813538       -2.0532330062        1.1022265639
 O     -2.9426229790        0.0047598088        0.3755068721
 O     -1.1442097890       -2.1519147009       -0.2741092908
 C     -1.0544766428        2.7604808281        0.3893982387
 H     -0.6839849318        3.3471735809        1.2340450799
 H     -1.6120589539        3.4238267331       -0.2772059195
 H     -1.7191189040        1.9819307452        0.7630900195
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 C      0.7083395246       -0.5340610348       -2.6206299086
 H      0.0126167314       -0.4142288926       -3.4567453198
 H      1.6561464989       -0.9104486299       -3.0176525159
 H      0.3110897259       -1.2833973774       -1.9278883098
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PR-b-Re

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0 1
 C      1.7580544347        0.5194665260        0.7281292247
 C      0.7746789086        0.5348395530        1.9555961076
 C      0.3456306879        2.2611102054        0.5452779352
 C      2.0913679635       -0.8127711180        0.0876274396
 N      1.1214366671        1.3721097021       -0.3021592572
 O      1.6919714679       -1.9040035371        0.4218825090
 O      2.9793054266       -0.6356033323       -0.8983178786
 O      0.2133947882        0.5254279335       -0.9980267510
 C      3.3428541638       -1.8195848133       -1.6063980073
 C     -0.6824516370        3.1039231386       -0.1674945648
 H      1.0546955315        2.9001933335        1.0946770315
 H      2.7060864399        0.9800989551        1.0308275910
 H      3.8193962369       -2.5371616977       -0.9347312256
 H      2.4591393440       -2.2797123392       -2.0545680755
 H      4.0390988624       -1.5012615185       -2.3803268556
 H     -1.1768129635        3.7698938630        0.5449936576
 H     -0.1796135830        3.7109316382       -0.9244884215
 H     -1.4314506816        2.4811318050       -0.6594722376
 H      1.2888354924        1.0586370308        2.7726966956
 O     -0.2911040781        1.3856384523        1.5037924822
 C      0.1759529433       -0.7478745251        2.5027509470
 H      0.9596861867       -1.3969002889        2.8981737932
 H     -0.5128867845       -0.4921296584        3.3143721180
 H     -0.3577316067       -1.3137167066        1.7349264168
 Li    -1.1923174538        0.1340238183        0.0933659905
 C     -3.9685061303        0.4931644358       -0.7059870084
 H     -3.5399352889       -0.2725409325       -1.3546507459
 H     -4.9311470936        0.1478409961       -0.3087747050
 H     -4.1231635270        1.4177384789       -1.2763667767
 C     -3.4834093541        1.7106766323        1.2512032773
 H     -3.6587072709        2.6563042367        0.7223080462
 H     -4.4114208103        1.3973265732        1.7449625526
 H     -2.6895672826        1.8441431547        1.9862042287
 C     -0.9021255738       -2.3476149550       -1.3339584067
 H     -1.5438956937       -2.6774666408       -2.1610985699
 H     -0.1618762058       -1.6240748810       -1.6766218302
 H     -0.3992670951       -3.2152927314       -0.8910709547
 C     -2.6677726884       -2.4989788110        0.2322342285
 H     -3.3586096266       -2.8793855562       -0.5315089695
 H     -2.2032152837       -3.3473971693        0.7504057735
 H     -3.2164655521       -1.8832090602        0.9476789326
 O     -3.0475768613        0.7105258180        0.3479554429
 O     -1.6817509792       -1.6767511683       -0.3555700703
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PR-b-Si

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0 1
 C      1.6820180746        0.7437203586        0.1030862269
 C      0.7621768802        0.3001493990       -1.1015524127
 C     -0.0486922593        2.1649579779       -0.0256447434
 C      2.8913970774        1.5210423022       -0.3756148405
 N      0.8138762046        1.5534034214        0.9668601125
 O      2.9621882211        2.7186239746       -0.5244325896
 O      3.9009512955        0.6871572243       -0.6680603476
 O      0.0379222946        0.6310940037        1.7229375626
 C      5.0622991896        1.3075086533       -1.2271497842
 H      0.5610742111        2.8587860918       -0.6163704785
 H      2.0276534566       -0.1174474123        0.6740813468
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 H      5.4761515303        2.0365890289       -0.5283060481
 H      4.8058330030        1.8101118716       -2.1626614259
 H      5.7724115238        0.5027595440       -1.4068789059
 H      0.4984823177       -0.7572321191       -0.9975211520
 O     -0.4409646096        1.0567306215       -0.8903271131
 Li    -1.2358526094       -0.0746431047        0.6175388259
 C     -3.7118552448        0.8385596661       -0.7838763003
 H     -2.9049976541        1.2523558412       -1.3891977364
 H     -4.2297715974        1.6456611581       -0.2505152120
 H     -4.4288963950        0.3100255102       -1.4239897103
 C     -4.0662079817       -0.6943890861        0.9755013567
 H     -4.7960587296       -1.2537790728        0.3772066844
 H     -4.5922256494        0.0477841435        1.5879470592
 H     -3.5163345645       -1.3829117281        1.6197251929
 C     -1.6352197503       -2.8803714954       -0.3537008521
 H     -0.9280958727       -3.1459962526       -1.1503439610
 H     -2.4919857441       -2.3577896656       -0.7818522221
 H     -1.9695913577       -3.7960106655        0.1490351072
 C      0.1319097912       -2.5391789474        1.1793799689
 H      0.8723367628       -2.8071679726        0.4131558231
 H     -0.1236412169       -3.4340623318        1.7595062207
 H      0.5312323779       -1.7547854753        1.8237061563
 O     -3.1182019919       -0.0636627153        0.1328837373
 O     -1.0306193618       -1.9978521853        0.5716221168
 C     -1.2749379481        2.8607036107        0.5116408842
 H     -0.9584850415        3.6367604520        1.2130182604
 H     -1.8270310126        3.3321189254       -0.3057804707
 H     -1.9344162152        2.1672749189        1.0375008165
 C      1.3214037096        0.5618189048       -2.4901631878
 H      2.2351276900       -0.0183633096       -2.6507143921
 H      0.5886921329        0.2750888856       -3.2483288471
 H      1.5576451929        1.6234256703       -2.6194835861
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TS1-b

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0 1
 C      1.8770996746        0.5695416847       -0.4865064101
 C      1.1885239248        0.4865319997        1.7115469389
 Li    -0.7696637751       -0.3741668672        0.1069142128
 C      1.2631591223        2.6465756615       -1.4652905889
 C      1.6673902896       -0.8195070748       -0.6700867468
 N      0.9093169758        1.5084383315       -0.9472151690
 O      0.5870062358       -1.4134556099       -0.8017835562
 O      2.8233541053       -1.5184685740       -0.5332889277
 O     -0.3583882952        1.2478593495       -0.7563441665
 C      2.6743959641       -2.9341230806       -0.4614033513
 C      0.2360069915        3.6657273830       -1.8046732306
 H      2.3223789136        2.7951286695       -1.6304172655
 H      2.8938427614        0.9368010612       -0.5274852890
 H      2.0311376851       -3.2125053207        0.3769543490
 H      2.2470864561       -3.3282276690       -1.3861282415
 H      3.6789713612       -3.3289320033       -0.3139483995
 H      0.7124371113        4.5866943641       -2.1422220840
 H     -0.4299249673        3.3002402669       -2.5946163159
 H     -0.3946553387        3.8783554963       -0.9345362327
 H      0.9752913957        1.5576159261        1.5560889098
 O     -2.3457612549       -1.2161038089       -0.6832673824
 C     -2.4058917889       -2.6037217674       -0.3928711670
 C     -2.2992826339       -0.9774422025       -2.0836963091
 H     -2.4438857665       -2.7086398179        0.6926523059
 H     -3.3065069135       -3.0456383061       -0.8349984615
 H     -1.5153567720       -3.1119367340       -0.7823534284
 H     -3.2170170469       -1.3457599766       -2.5573549589
 H     -2.2066278004        0.0997841955       -2.2221134159
 H     -1.4267721291       -1.4768124096       -2.5214769590
 O      0.2419568009       -0.3231620900        1.7609609914
 C      2.5179768212        0.1475026927        2.3371690610
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 H      3.2842085634        0.8793015853        2.0744925280
 H      2.3939561552        0.1407850566        3.4268385795
 H      2.8372111733       -0.8494644116        2.0219221811
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TS2-a-Si

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0 1
 C     -1.6205968076       -0.1379602584       -0.3064763277
 C     -1.1466849236       -0.3344410097        1.2419504121
 C     -0.7323592812        1.9214761787        0.1015106712
 C     -3.1028915330        0.1187057174       -0.3488501022
 N     -0.8188446623        0.9617155282       -0.8002255468
 O     -3.6451075571        1.1923628880       -0.4736208378
 O     -3.7674336187       -1.0274902559       -0.1502846366
 O      0.3505403293        0.5548187598       -1.3872472350
 C     -5.1906460229       -0.9039237121       -0.0652843116
 H     -1.6572456757        2.1371856666        0.6277654880
 H     -1.3787059599       -1.0146689141       -0.9091326610
 H     -5.5893333908       -0.4829549947       -0.9900345625
 H     -5.4641992136       -0.2600368297        0.7729206330
 H     -5.5667319381       -1.9133665213        0.0887953321
 H     -2.0214538451       -0.0700137516        1.8685043001
 O     -0.1009753560        0.5213717460        1.4744849048
 Li     1.2881997365        0.0844863157        0.2122004713
 C      3.9865782542        1.0126711234        1.3166562662
 H      3.4454842112        1.0538418033        2.2630094942
 H      4.6401379757        1.8889865440        1.2283969896
 H      4.6010831853        0.1034852135        1.2818243055
 C      3.6043896537        0.9235848389       -1.0097502102
 H      4.1909669026        0.0001399843       -1.1095139984
 H      4.2560839267        1.7869610071       -1.1912862917
 H      2.7781669662        0.9195039592       -1.7242463022
 C      3.0240450013       -2.3489201039        0.4361045420
 H      2.8127682257       -3.4255398568        0.4481912143
 H      2.9866570186       -1.9603672100        1.4561853058
 H      4.0264878469       -2.1871170335        0.0161818522
 C      1.9603346088       -2.0946308462       -1.6585706117
 H      1.6761719634       -3.1538237688       -1.6970567079
 H      2.9249013233       -1.9637183275       -2.1673735180
 H      1.1981555002       -1.4725914074       -2.1291940898
 O      3.0243747886        1.0067431453        0.2807020141
 O      2.0488092648       -1.6573643568       -0.3141033572
 C      0.3233340803        2.9674782309        0.0495756479
 H      0.1379012150        3.6183689736       -0.8127580944
 H      0.2849622812        3.5751677034        0.9548549225
 H      1.3136478020        2.5253062132       -0.0597335266
 C     -0.8236983947       -1.8073016930        1.4737933312
 H     -0.5574187943       -1.9758221934        2.5217451765
 H     -1.6902990062       -2.4319715841        1.2300104962
 H      0.0188389192       -2.1138129113        0.8441421584
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TS2-b-Re

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 C      1.7503302469        1.0261984088        0.5586827097
 C      0.8380102402        1.0178582967        1.8955561421
 C      0.2090659370        2.6178385008       -0.0165451660
 C      2.3126275708       -0.2718150790       -0.0051114561
 N      0.8799476885        1.5855984969       -0.4723039841
 O      2.1291200986       -1.3913967146        0.4056842170
 O      3.1120792034       -0.0005709409       -1.0459514184
 O      0.1843731187        0.6430736076       -1.1708356044
 C      3.6407210042       -1.1463063855       -1.7150368250
 C     -1.0225208602        3.1155095376       -0.6855301199
 H      0.7710173968        3.2806794277        0.6365527185
 H      2.5990874567        1.7003062546        0.7152050735
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H	4.2680227699	-1.7293688696	-1.0373005567
H	2.8265099629	-1.7753833176	-2.0822112746
H	4.2299151573	-0.7612232546	-2.5452859537
H	-1.4092211392	3.9878660922	-0.1573231955
H	-0.7868779114	3.4018561715	-1.7164593721
H	-1.7851294817	2.3353442555	-0.7156511356
H	1.3072837655	1.7954159183	2.5299242011
O	-0.4437968933	1.3887228635	1.5556429249
C	0.8843538628	-0.2861624648	2.6888991615
H	1.9112886326	-0.5788334891	2.9303194327
H	0.3355815181	-0.1365603168	3.6240312376
H	0.4245455160	-1.1002198257	2.1268696124
Li	-1.0340092748	0.1467225424	0.2234806850
C	-3.9119002298	-0.3049305112	0.1793574412
H	-3.8590698353	0.0309208638	1.2163989874
H	-4.8858164084	-0.0329075281	-0.2456331079
H	-3.7913603935	-1.3955852188	0.1361277675
C	-2.8241824351	-0.0585134132	-1.8892999329
H	-2.7229677375	-1.1495126233	-1.9668652295
H	-3.7390669419	0.2571758667	-2.4055519643
H	-1.9487865930	0.4231208232	-2.3284587120
C	-1.4690492552	-2.7130775098	1.2019092572
H	-0.6136446265	-3.2699480510	1.6060220273
H	-1.9306980592	-2.1270812986	1.9995033761
H	-2.2015608215	-3.4241931512	0.7976713701
C	-0.4182524000	-2.4653593781	-0.8899851511
H	0.4362442486	-3.0546164541	-0.5392527311
H	-1.1369013803	-3.1214442584	-1.3995642824
H	-0.0658398030	-1.6815077494	-1.5619985408
O	-2.8667355785	0.3355626575	-0.5271871661
O	-1.0455603362	-1.8117797818	0.2005545377

TS2-b-Si

0 1

C	1.4949489146	0.1795539126	-0.3971385984
C	0.8774713330	0.4311917548	1.1193575037
C	0.6304804222	-1.9136702052	-0.0506965983
C	2.9765796096	-0.0988229342	-0.3789932895
N	0.7070703299	-0.9170839084	-0.9093330122
O	3.5071392820	-1.1806316548	-0.2628526188
O	3.6635154083	1.0481900809	-0.4612875548
O	-0.4546408112	-0.5032683182	-1.4981437679
C	5.0825331579	0.9182962811	-0.3326451327
H	1.5507573486	-2.1422107900	0.4734962314
H	1.3059471750	1.0414479413	-1.0351533631
H	5.4768585621	0.2778124084	-1.1235981947
H	5.3329974419	0.4878031016	0.6396953101
H	5.4820115564	1.9266372859	-0.4200719065
H	0.4005695373	1.4211939690	1.0368766055
O	-0.0393509727	-0.5518175209	1.3717120597
Li	-1.4074817742	-0.1199956294	0.1216735059
C	-4.1159043687	-0.9399028744	1.1283848283
H	-3.5606957883	-1.2316638467	2.0208278499
H	-4.9001644835	-1.6784497979	0.9242455223
H	-4.5802763432	0.0421862774	1.2860551194
C	-3.7900681653	-0.4725304783	-1.1602220569
H	-4.2408124363	0.5226355717	-1.0465535415
H	-4.5624638316	-1.1865205463	-1.4703415889
H	-2.9943553204	-0.4356356609	-1.9073680790
C	-2.7589903664	2.4537007342	0.7938935231
H	-2.3760448692	3.4626286767	0.9912282798
H	-2.8027549002	1.8924430751	1.7294667740
H	-3.7667367739	2.5329069811	0.3631483310
C	-1.7352635580	2.3902919411	-1.3330562148
H	-1.2732594333	3.3771612109	-1.2046936092
H	-2.7086301853	2.5124637702	-1.8273099545

H	-1.0919028098	1.7378640505	-1.9246870428
O	-3.1935621070	-0.8889657635	0.0562305307
O	-1.8956654798	1.7542470759	-0.0775582020
C	-0.4346748979	-2.9484213742	-0.1378812672
H	-0.4100743843	-3.5771122076	0.7535521423
H	-1.4207940808	-2.4951717345	-0.2477081977
H	-0.2519799943	-3.5828974798	-1.0129163661
C	1.9831244275	0.4872526000	2.1725660427
H	2.5135609239	-0.4710032595	2.2198875747
H	2.7094342808	1.2802852284	1.9646665525
H	1.5354554241	0.6742360559	3.1522728705