Supporting Information

(3*S*,4*R*)-3,4-Dihydroxy-*N*-alkyl-L-homoprolines: Synthesis and Computational Mechanistic Studies

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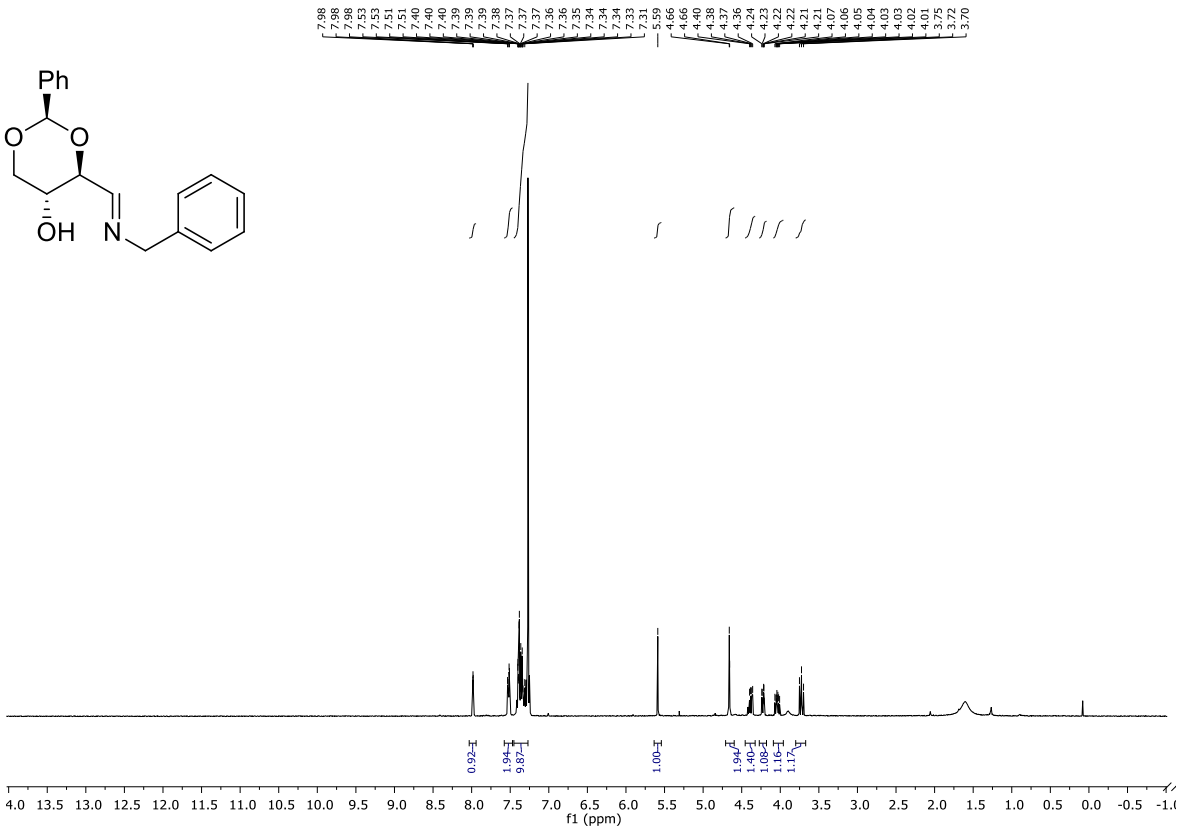
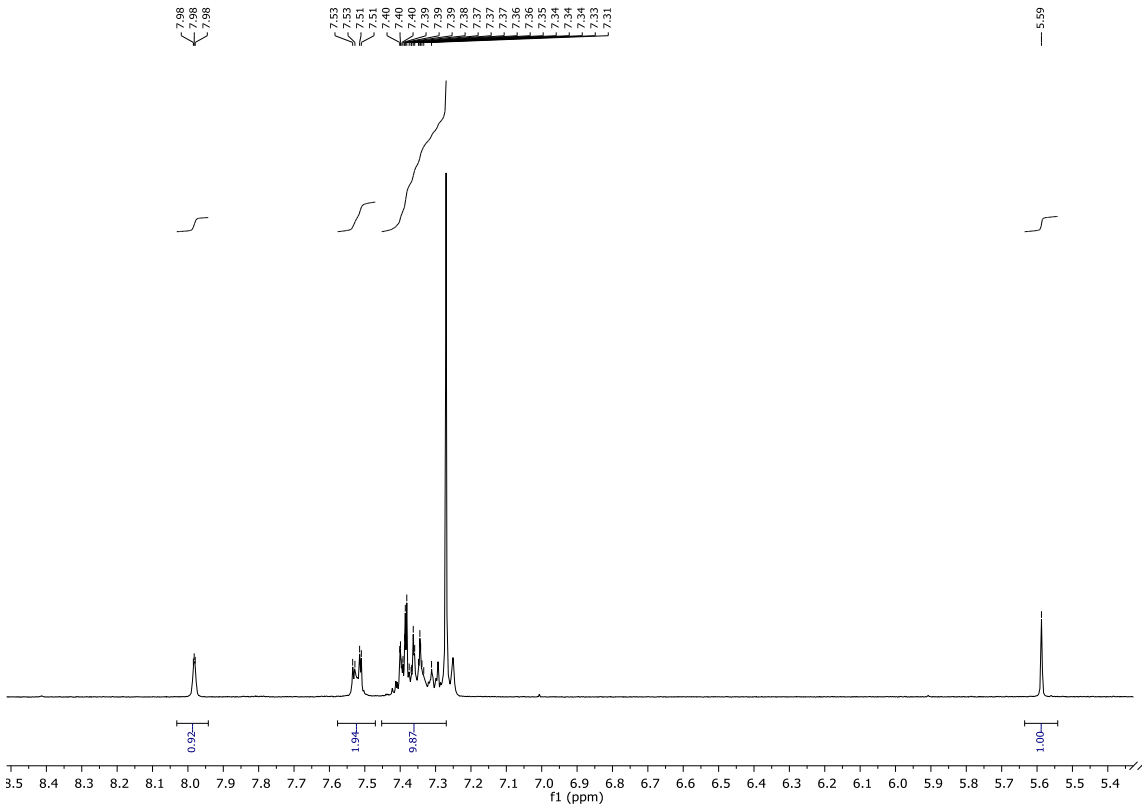
[‡] The first authors
[*]corresponding authors: mja@quimica.uminho.pt, nunoscerqueira@med.up.pt

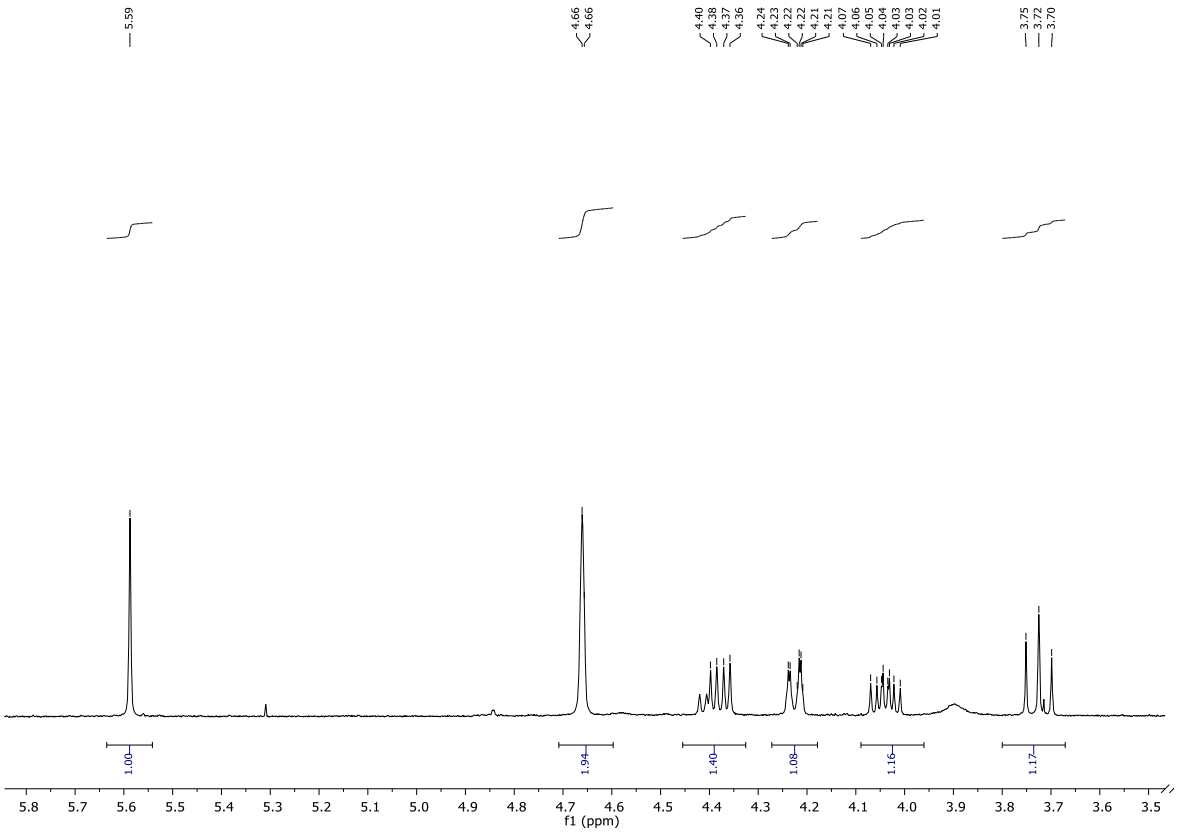
Table of Contents

1. NMR Spectra

1.1. ^{1}H NMR of compound **5a**



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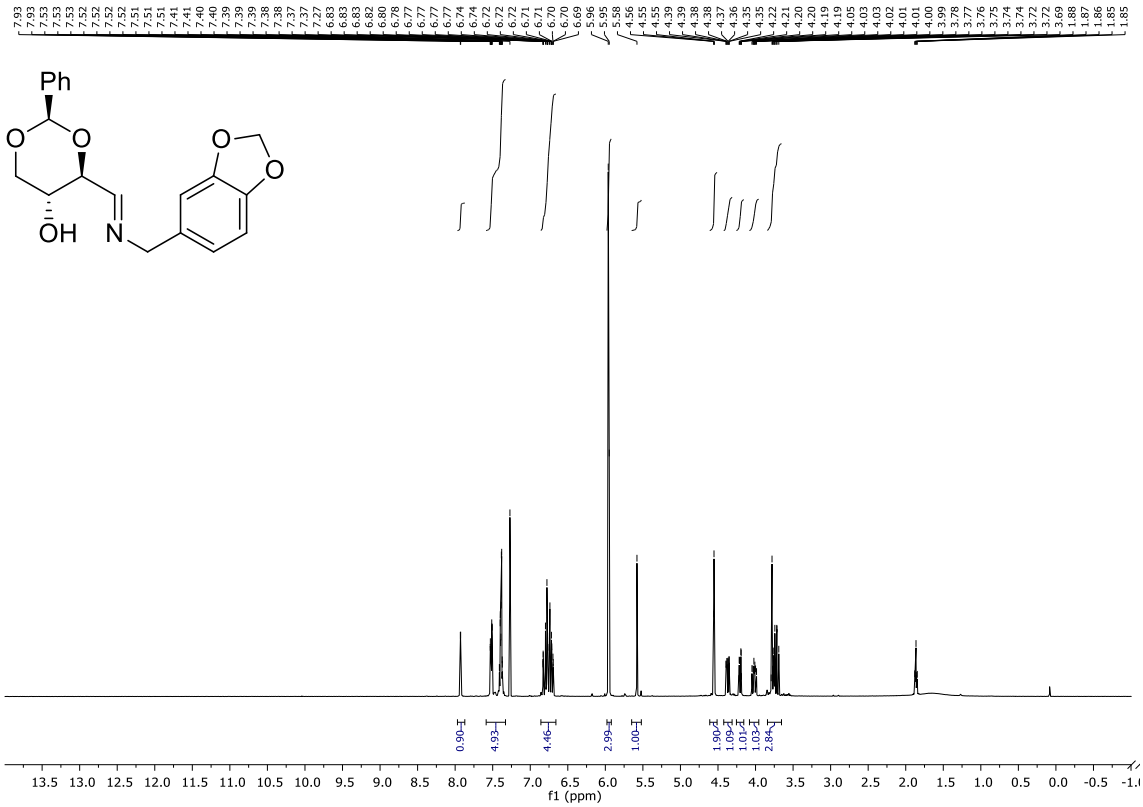
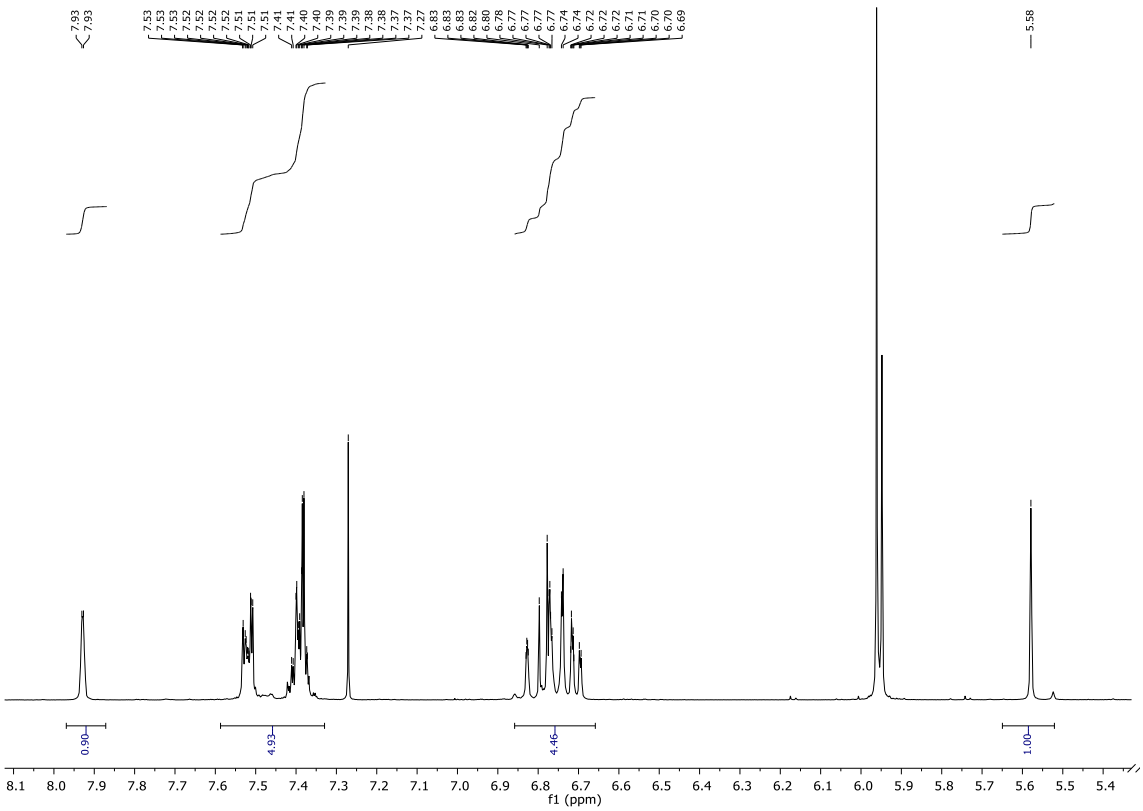
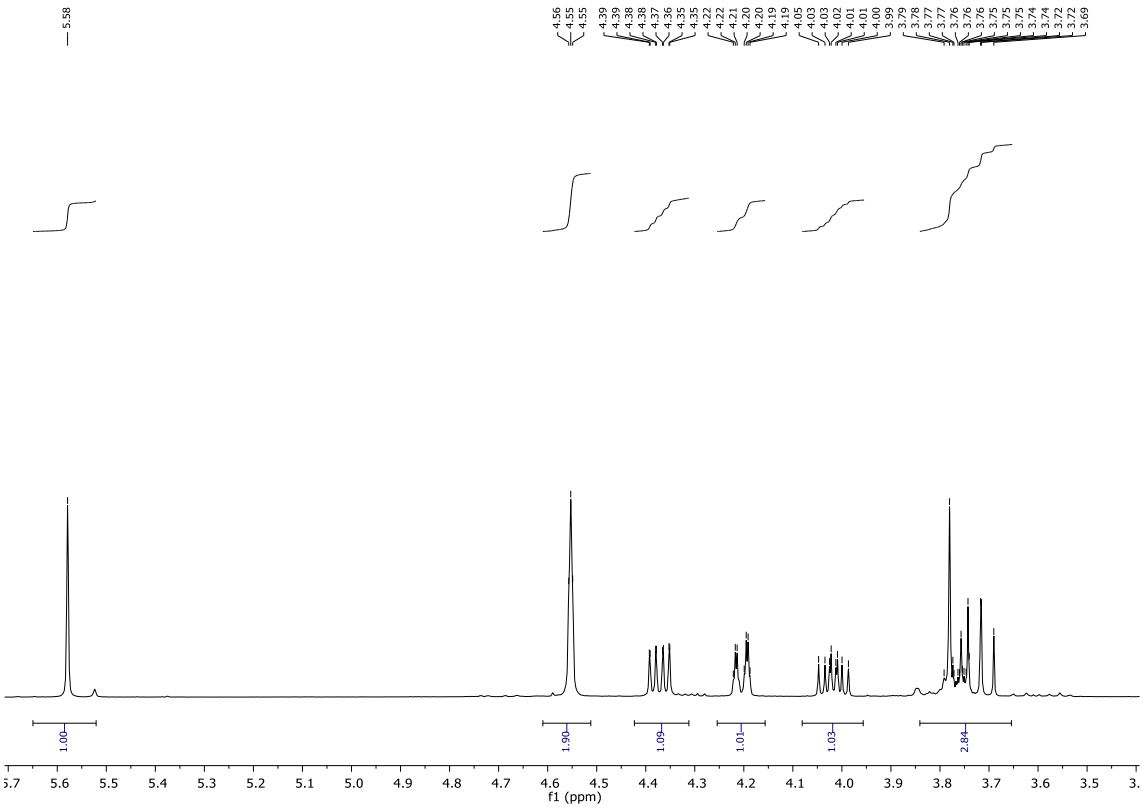
4.21
4.07
4.06
4.05
4.04
4.03
4.03
4.02
4.01
3.75
3.72
3.70
1.00
1.94
1.40
1.08
1.16
1.17
5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5
f1 (ppm)

1.2. ^{1}H NMR of compound **5b**



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4.22
4.21
4.20
4.20
4.19
4.18
4.05
4.03
4.03
4.02
4.01
4.01
4.00
3.99
3.79
3.78
3.77
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3.72
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1.09
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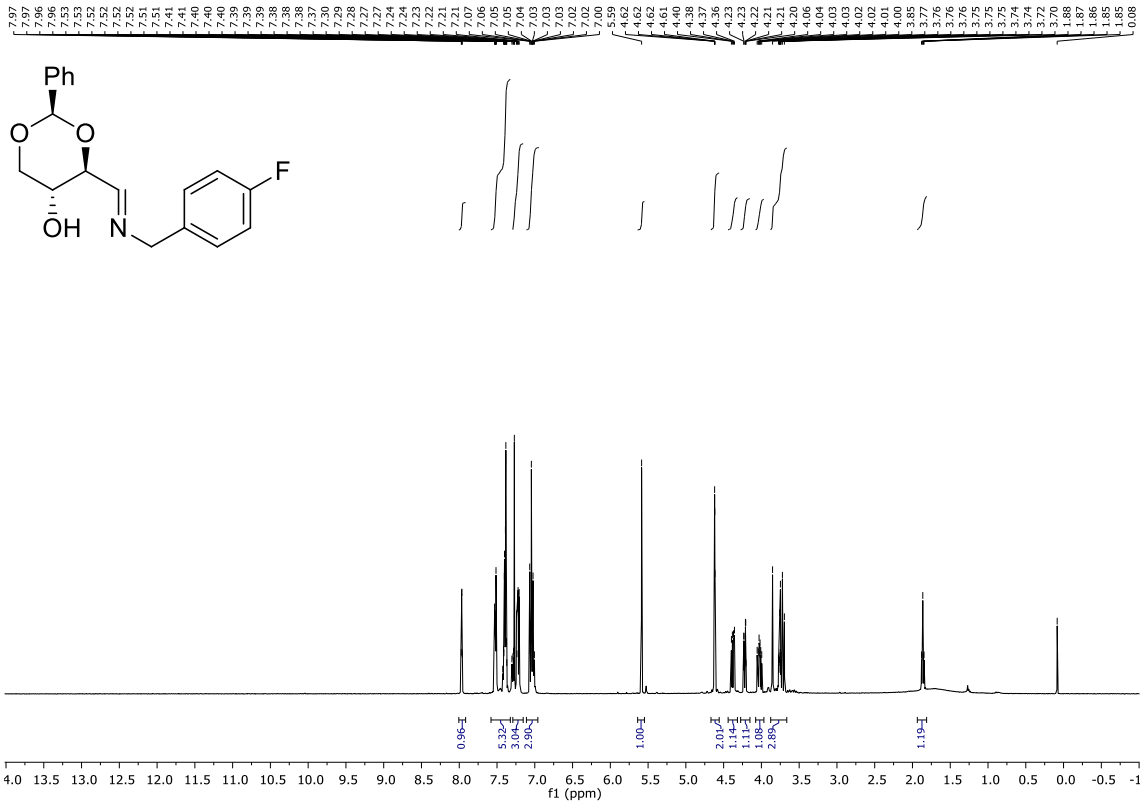
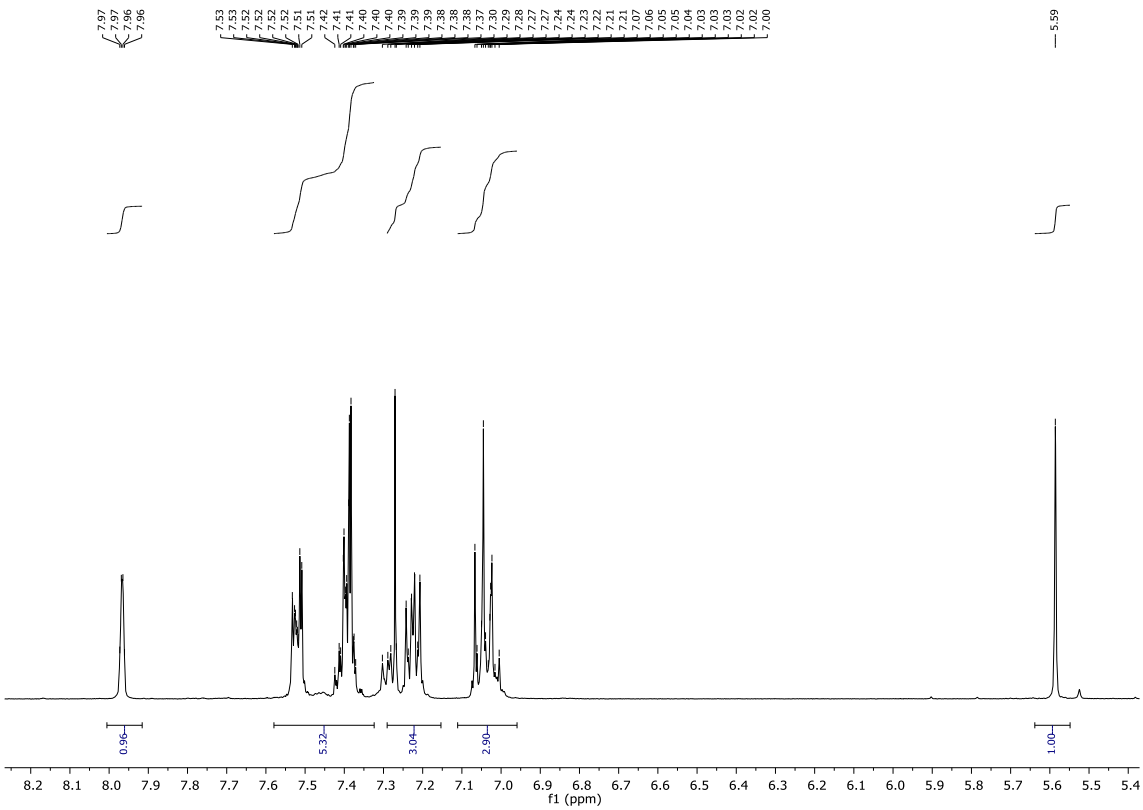
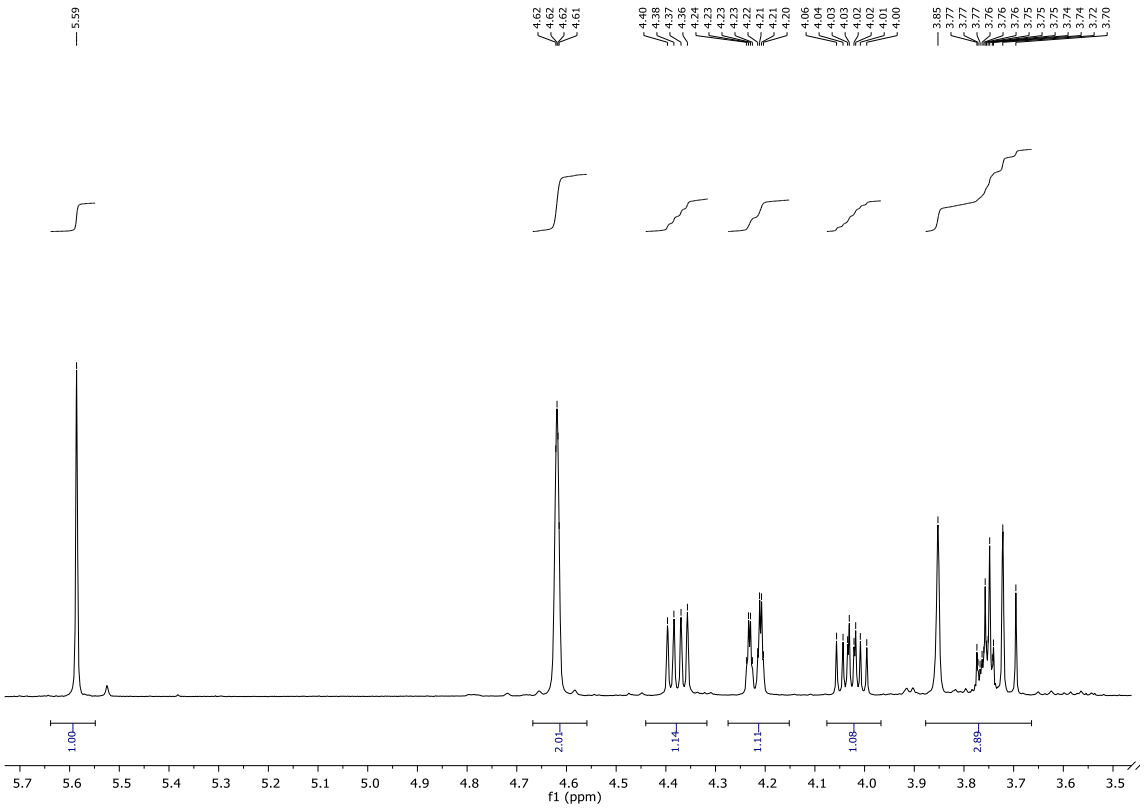
5.6
5.5
5.4
5.3
5.2
5.1
5.0
4.9
4.8
4.7
4.6
4.5
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.
f1 (ppm)

1.3. ^{1}H NMR of compound **5c**



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4.23
4.22
4.21
4.21
4.20
4.06
4.04
4.03
4.03
4.02
4.02
4.01
4.00
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3.77
3.77
3.76
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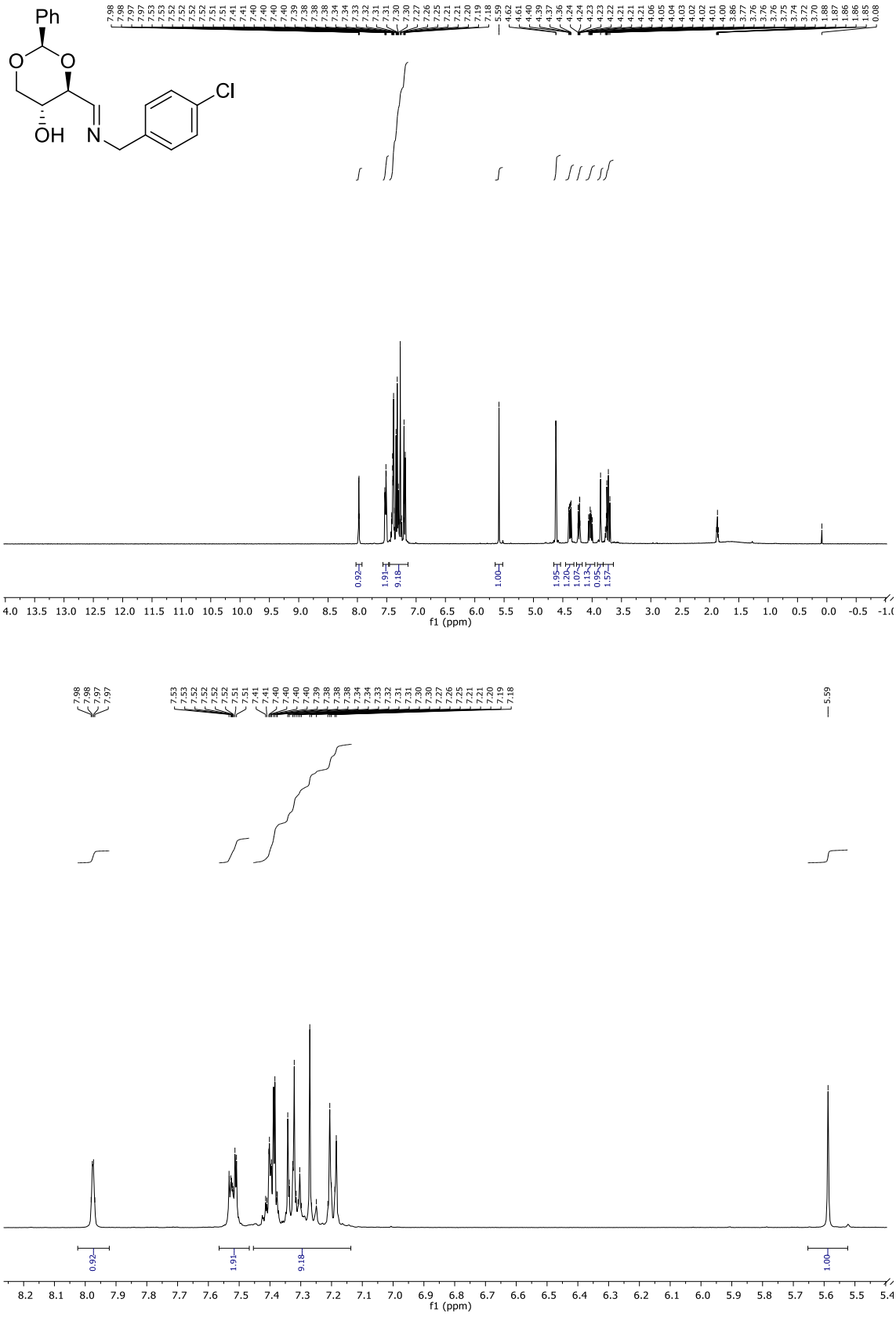
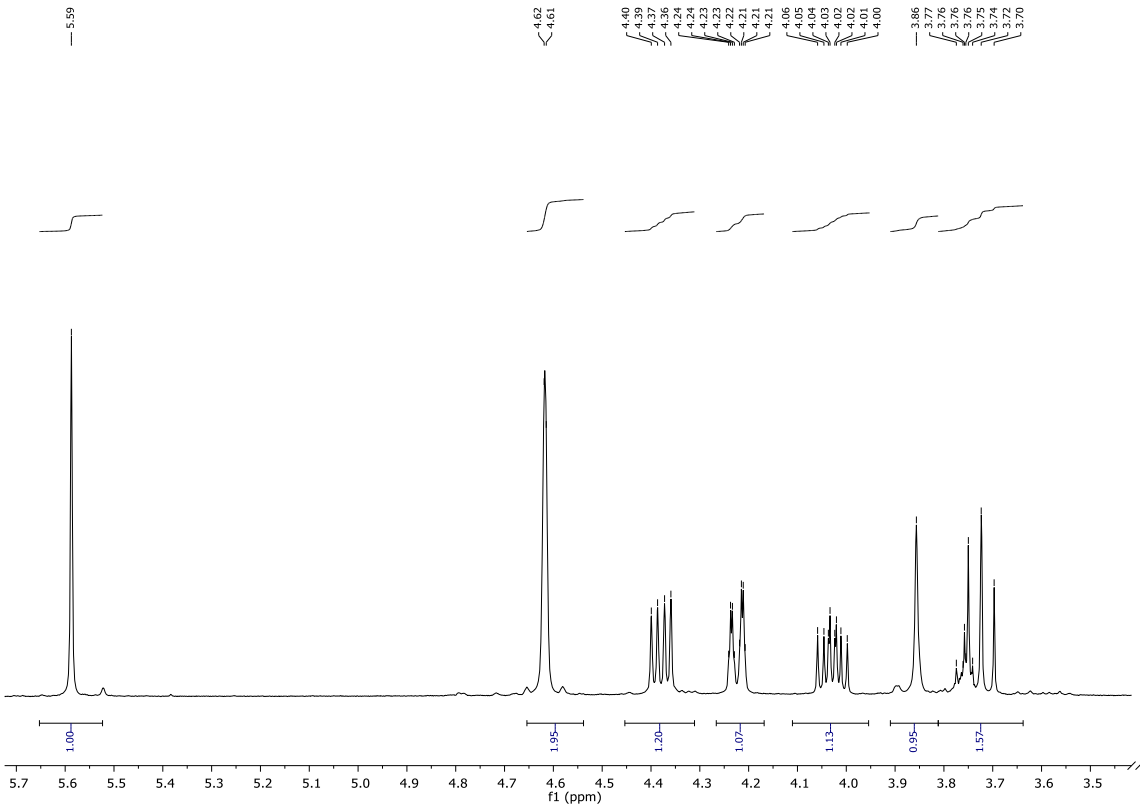
2.01
1.14
1.11
1.08
2.89
5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5
f1 (ppm)

1.4. ^{1}H NMR of compound **5d**

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4.62
4.61
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4.36
4.24
4.24
4.23
4.23
4.22
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4.21
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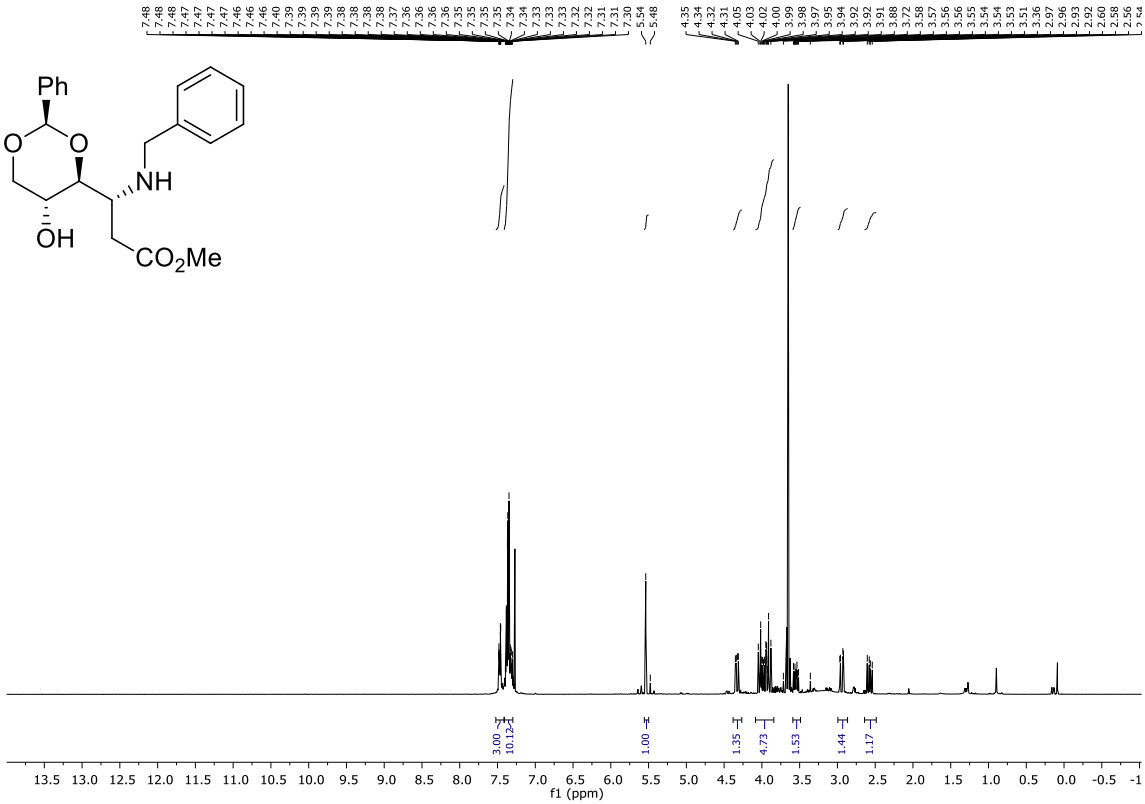
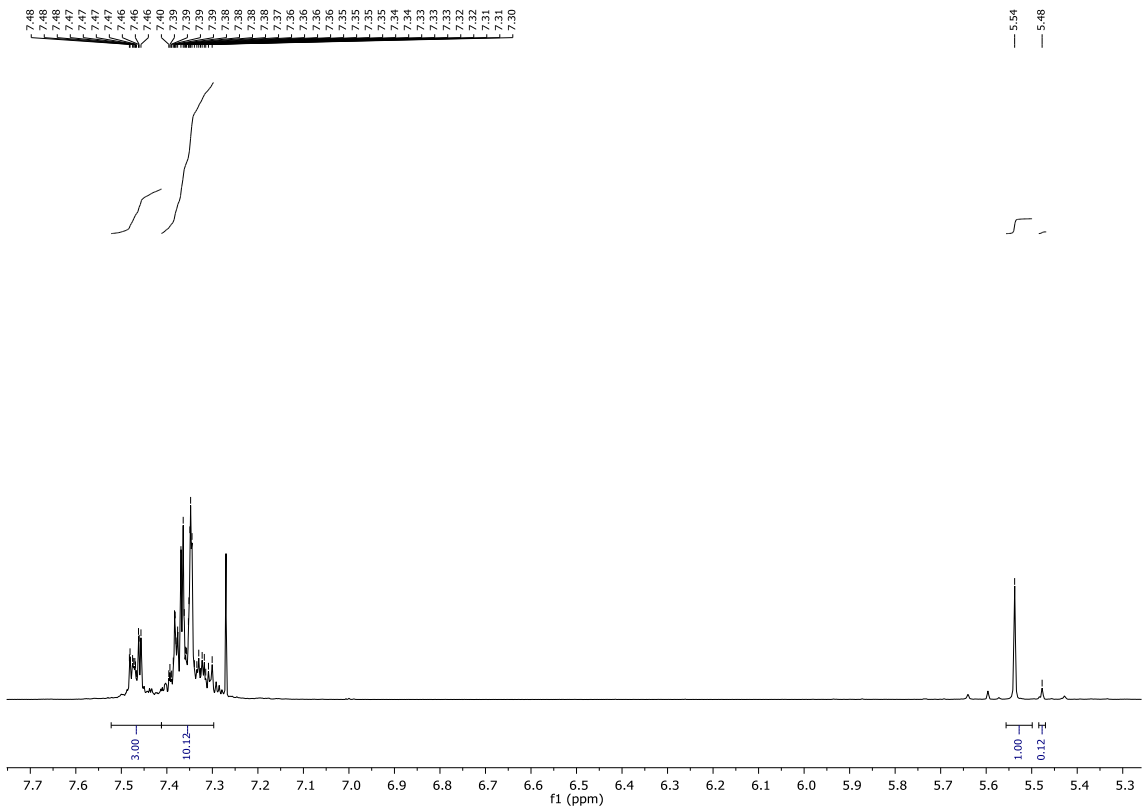
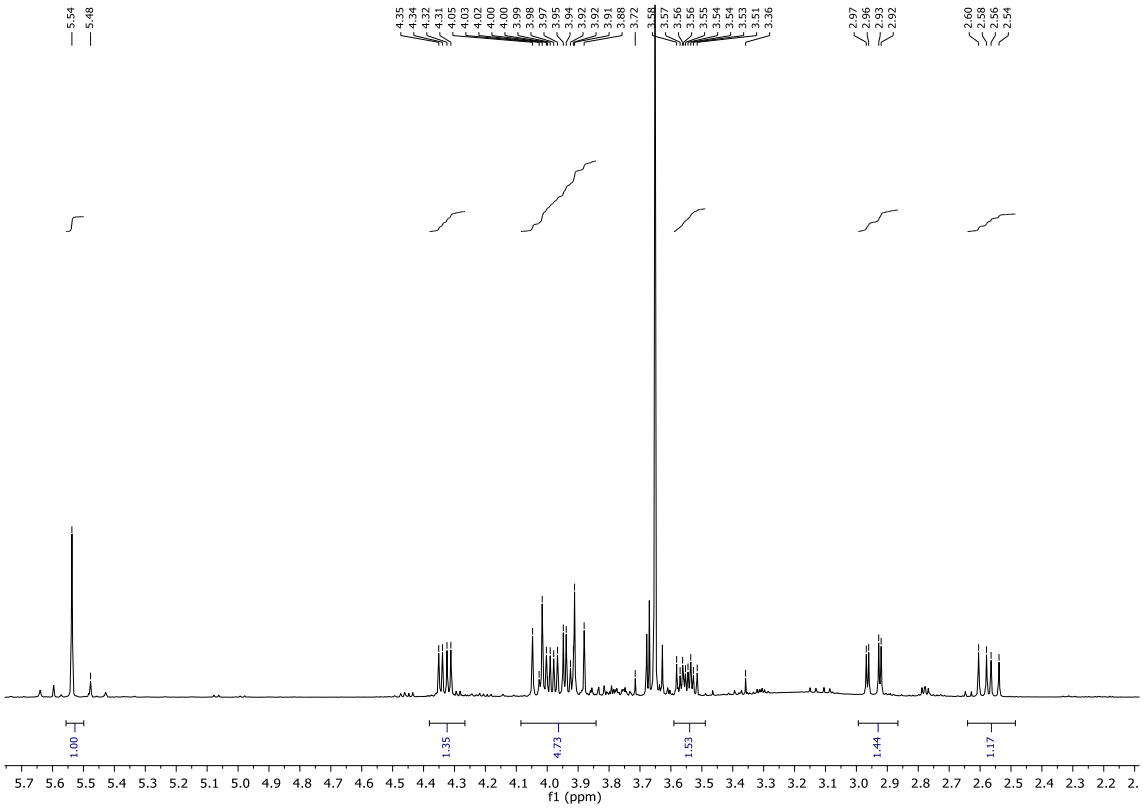
4.00
3.86
3.77
3.76
3.76
3.76
3.75
3.74
3.72
3.70
1.00
1.95
1.20
1.07
1.13
0.95
1.57
5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5
f1 (ppm)

1.5. ^{1}H and ^{13}C NMR of compound **6a**



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4.32
4.31
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4.02
4.00
4.00
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3.95
3.94
3.92
3.92
3.91
3.88
3.72
3.58
3.57
3.56
3.56
3.55
3.54
3.54
3.53
3.51
3.36
2.97
2.96
2.93
2.92
2.60
2.58
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1.00
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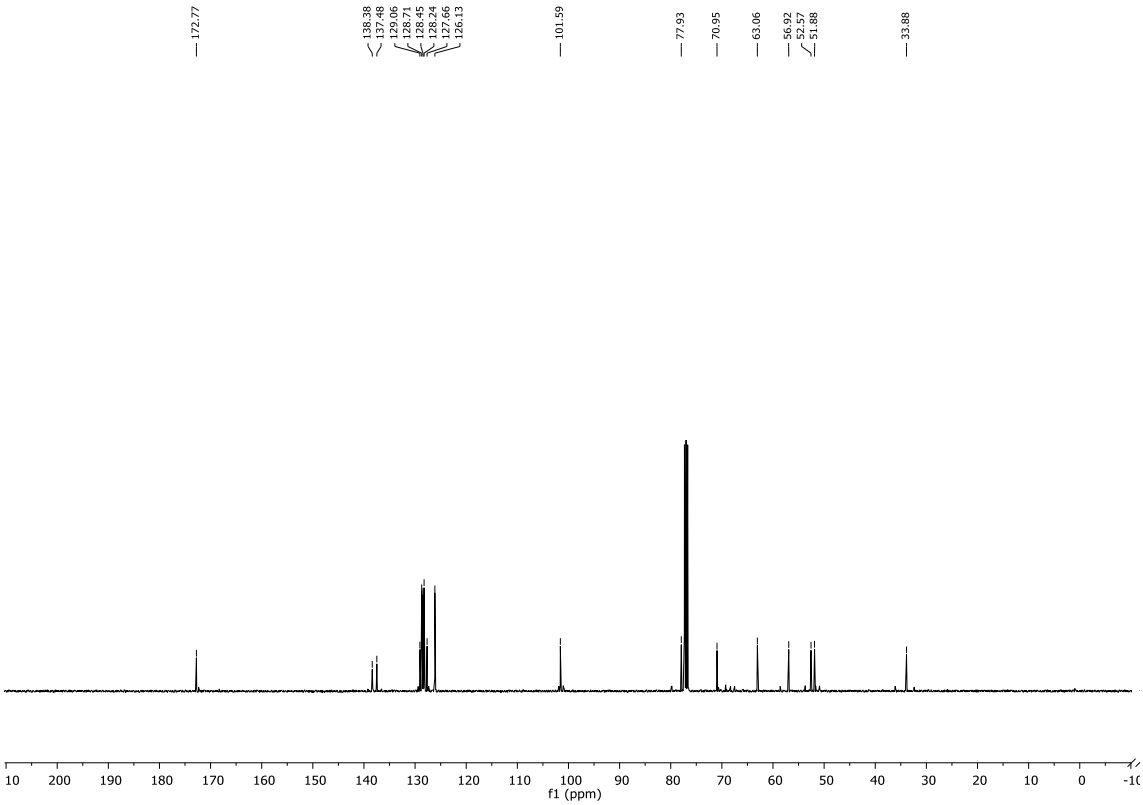
1.53
1.44
1.17
f1 (ppm)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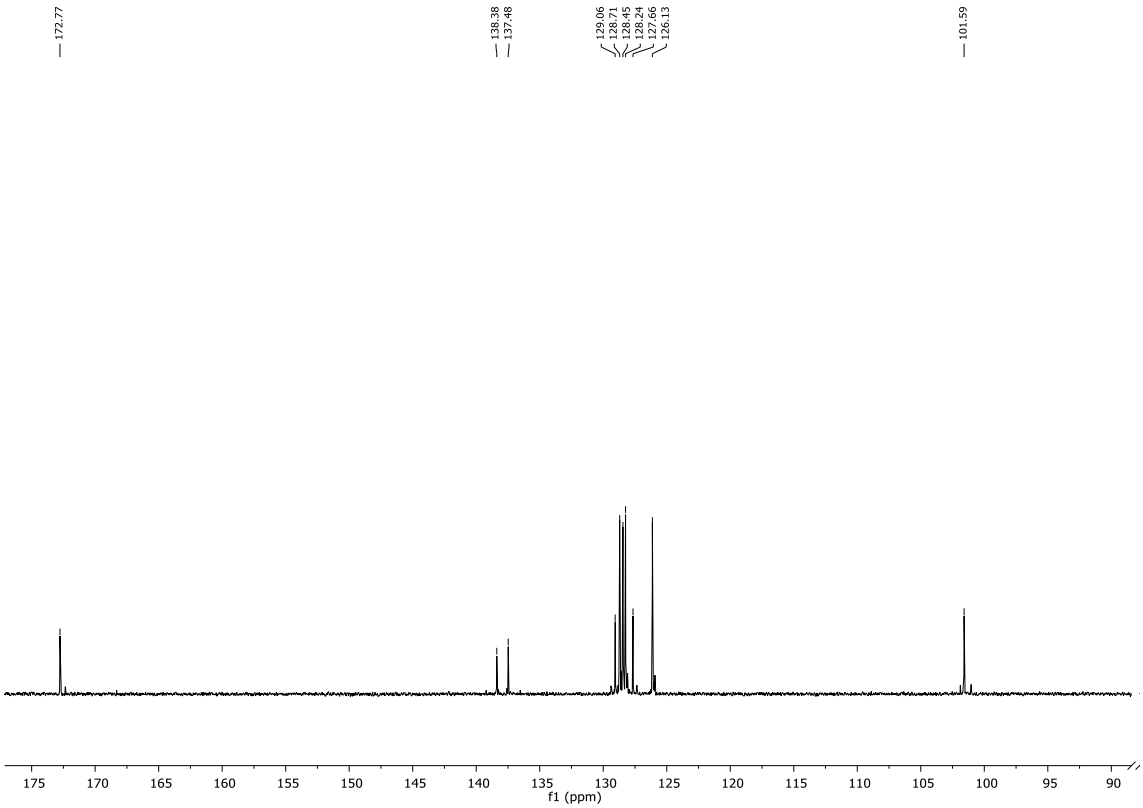
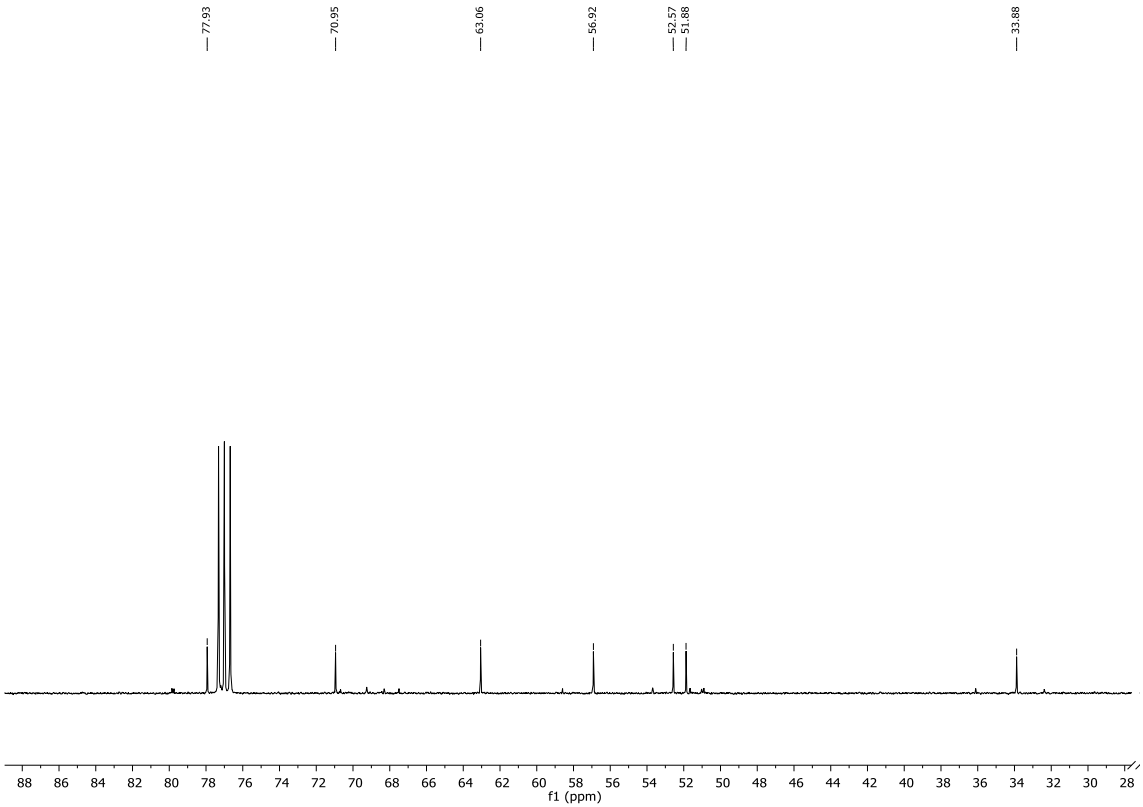
51.88
33.88
f1 (ppm)


172.77
138.38
137.48
129.06
128.71
128.45
128.24
127.66
126.13
101.59
175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90
f1 (ppm)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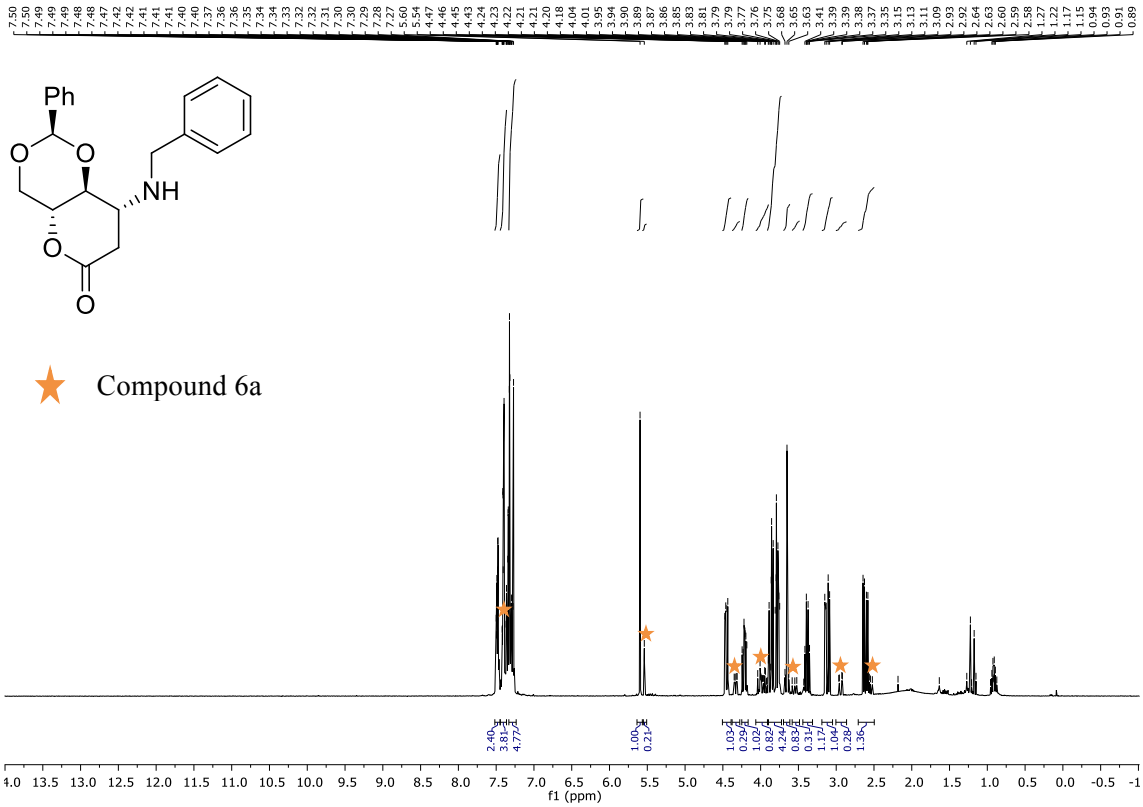
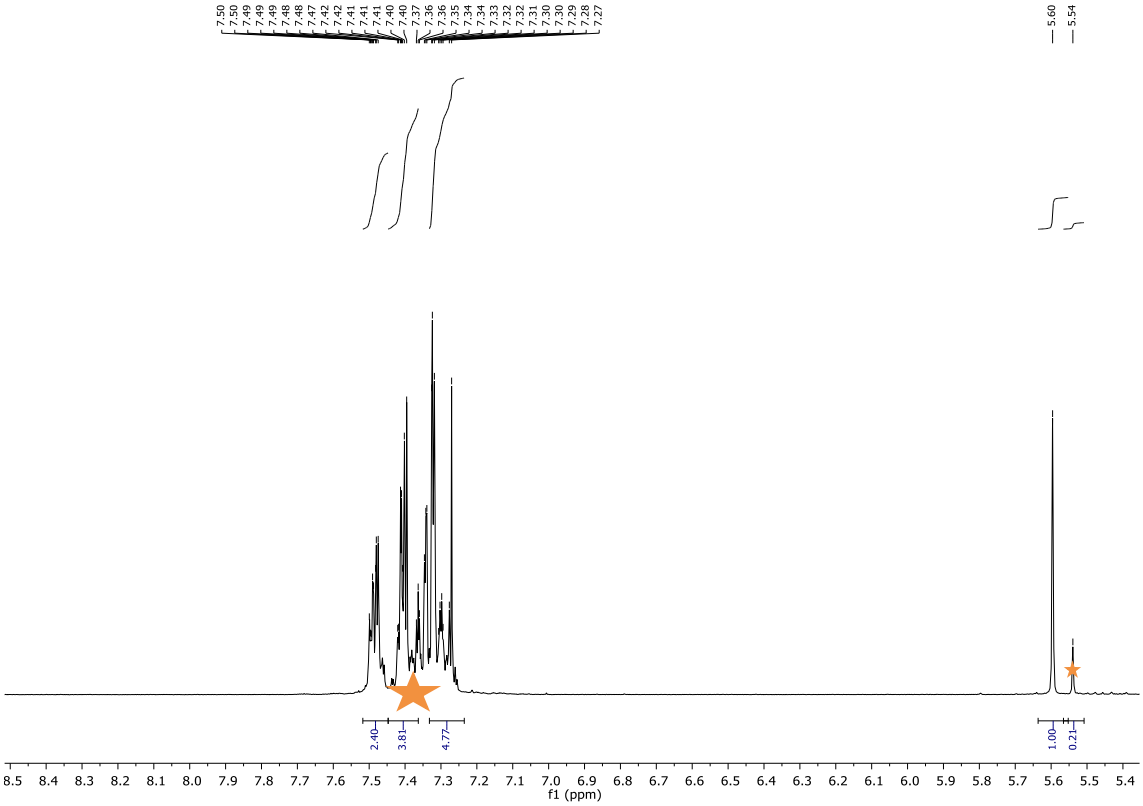
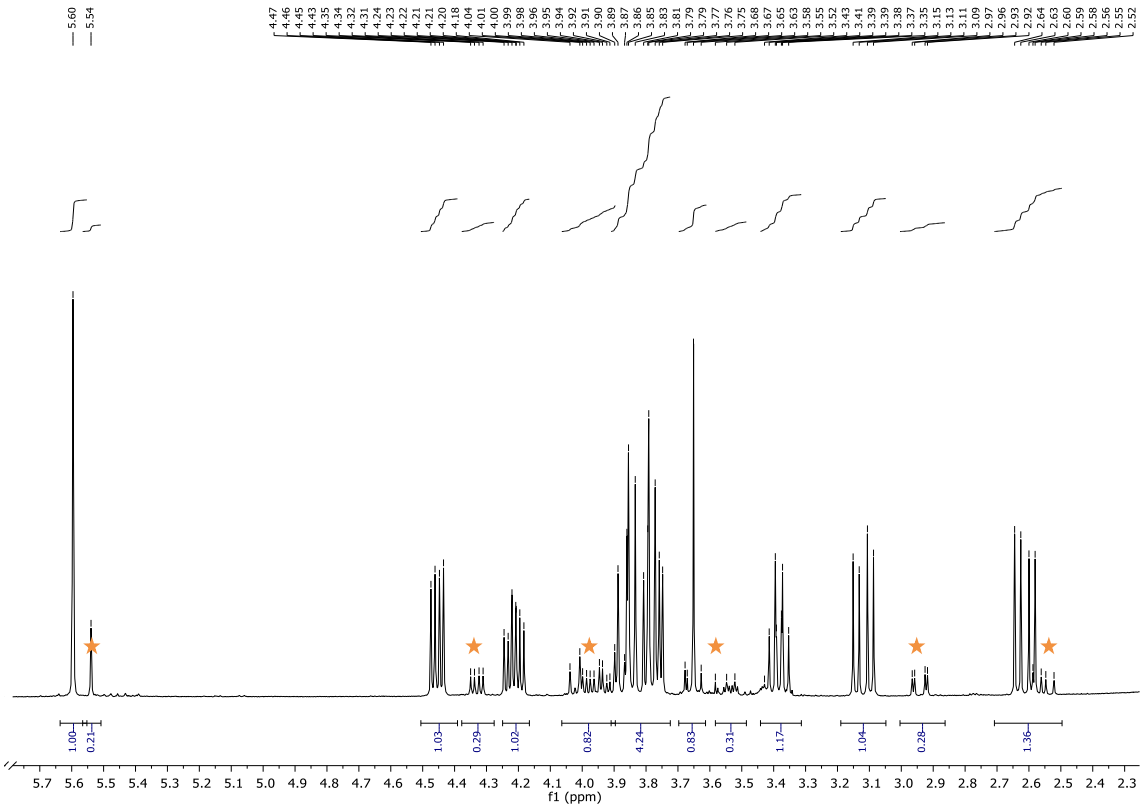
63.06
56.92
52.57
51.88
33.88
88 86 84 82 80 78 76 74 72 70 68 66 64 62 60 58 56 54 52 50 48 46 44 42 40 38 36 34 32 30 28
f1 (ppm)

1.6. ^{1}H and ^{13}C NMR of compound **7a**



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5.54
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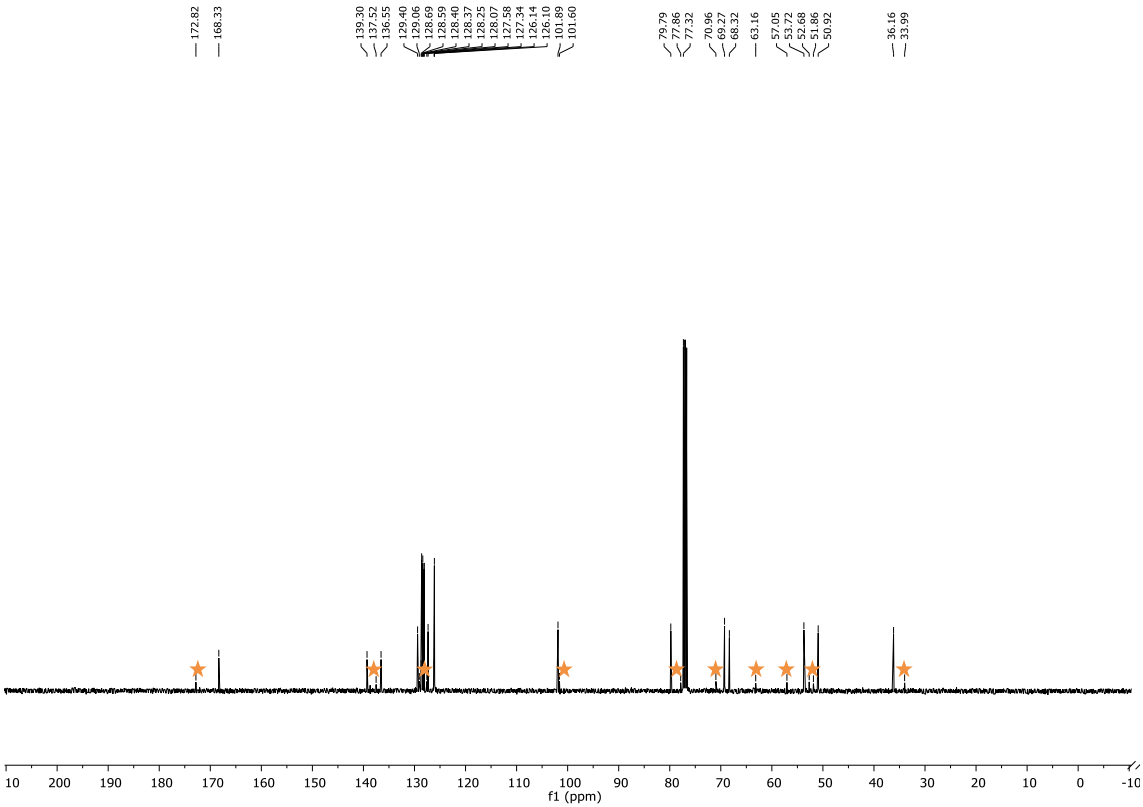
0.21
1.03
0.29
1.02
0.82
4.24
0.83
0.31
1.17
1.04
0.28
1.36
f1 (ppm)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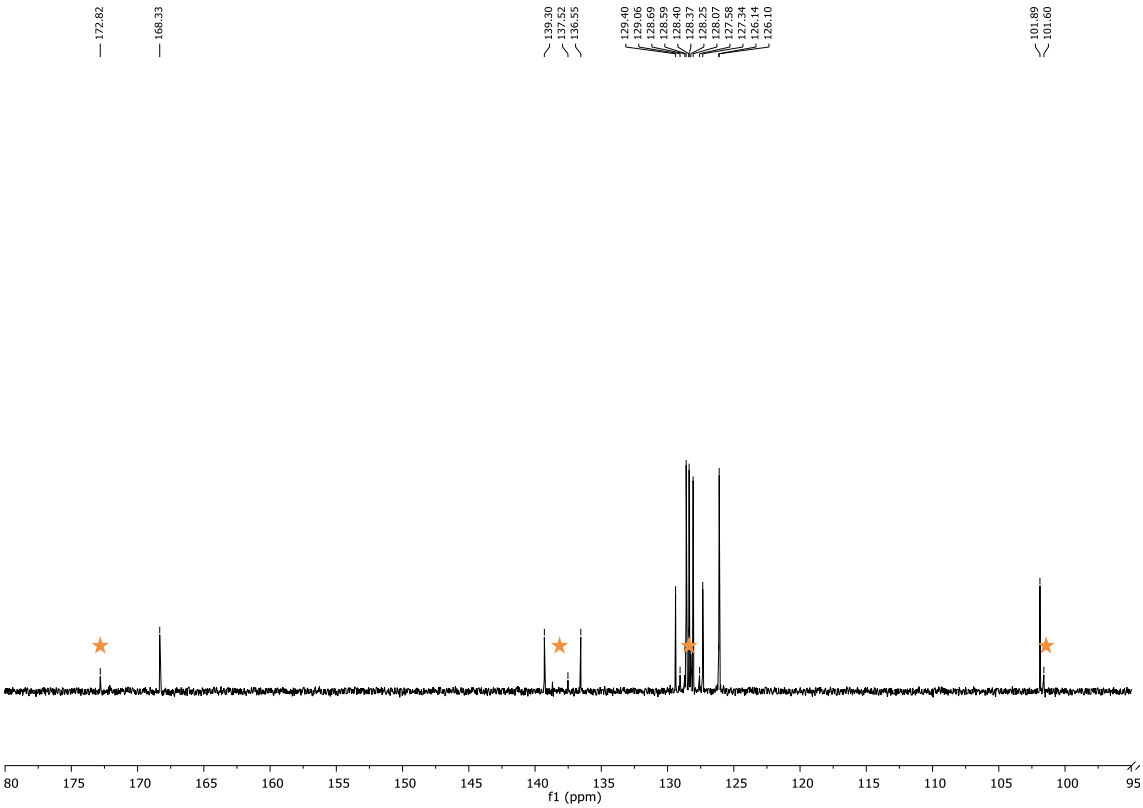
137.52
136.55
129.40
129.06
128.69
128.59
128.40
128.37
128.25
128.07
127.58
127.34
126.14
126.10
101.89
101.60
79.79
77.86
77.32
70.96
69.27
68.32
63.16
57.05
53.72
52.68
51.86
50.92
36.16
33.99
f1 (ppm)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139.30
137.52
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128.25
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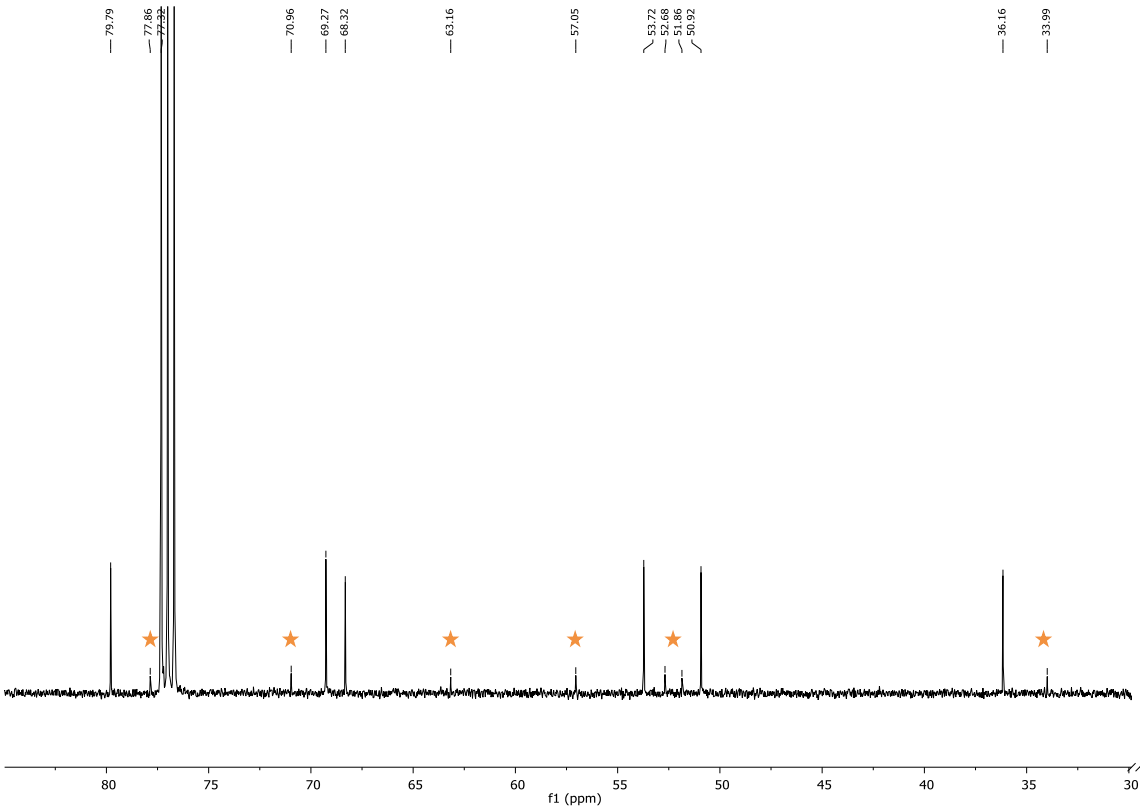
127.58
127.34
126.14
126.10
101.89
101.60
80
175
170
165
160
155
150
145
140
135
130
125
120
115
110
105
100
95
f1 (ppm)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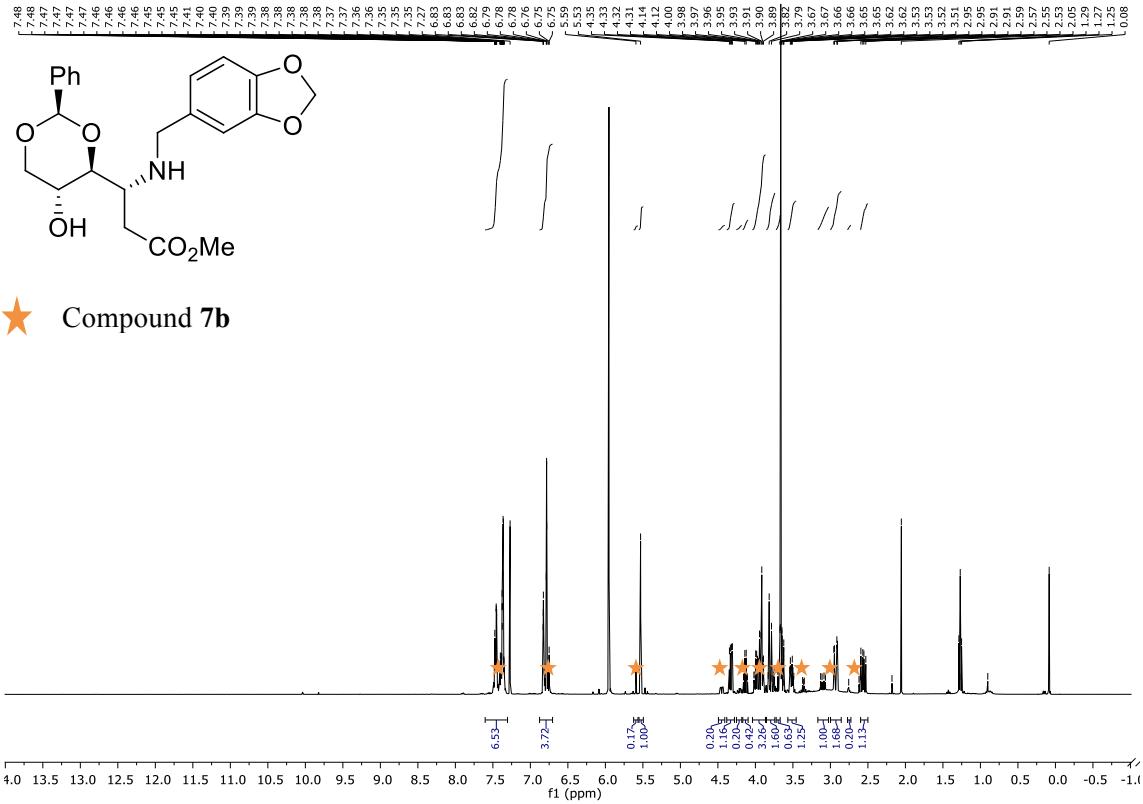
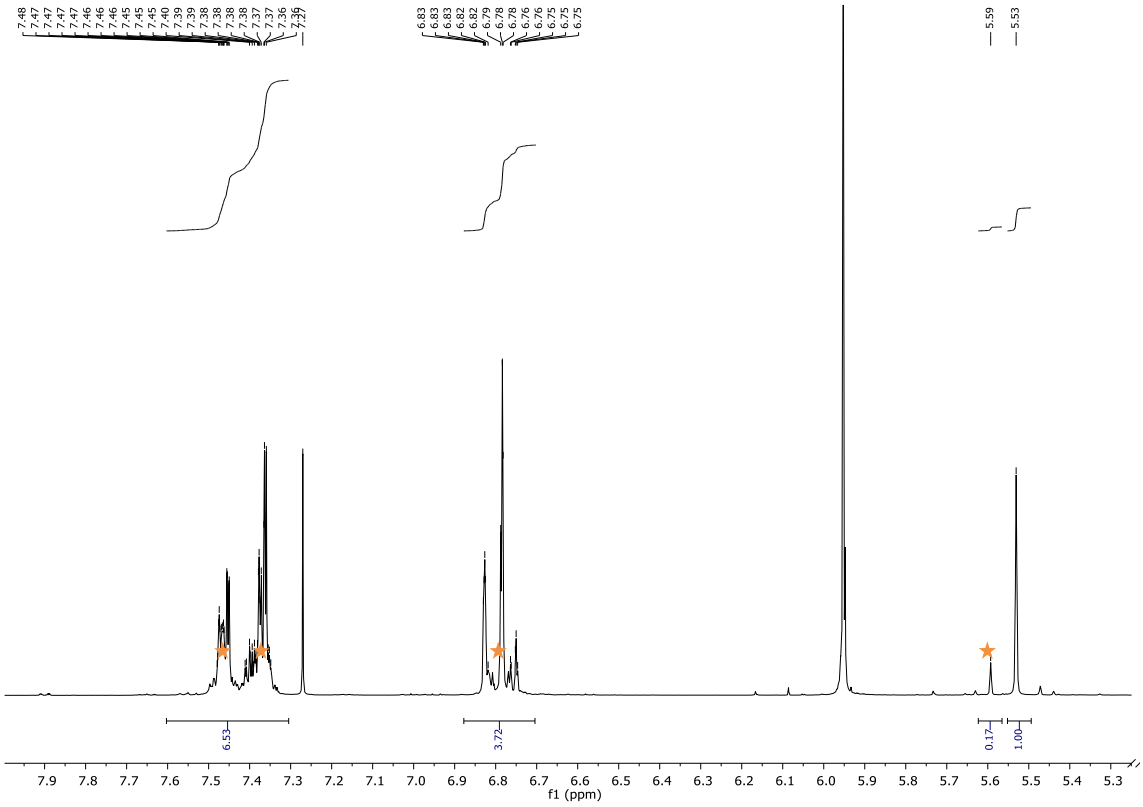
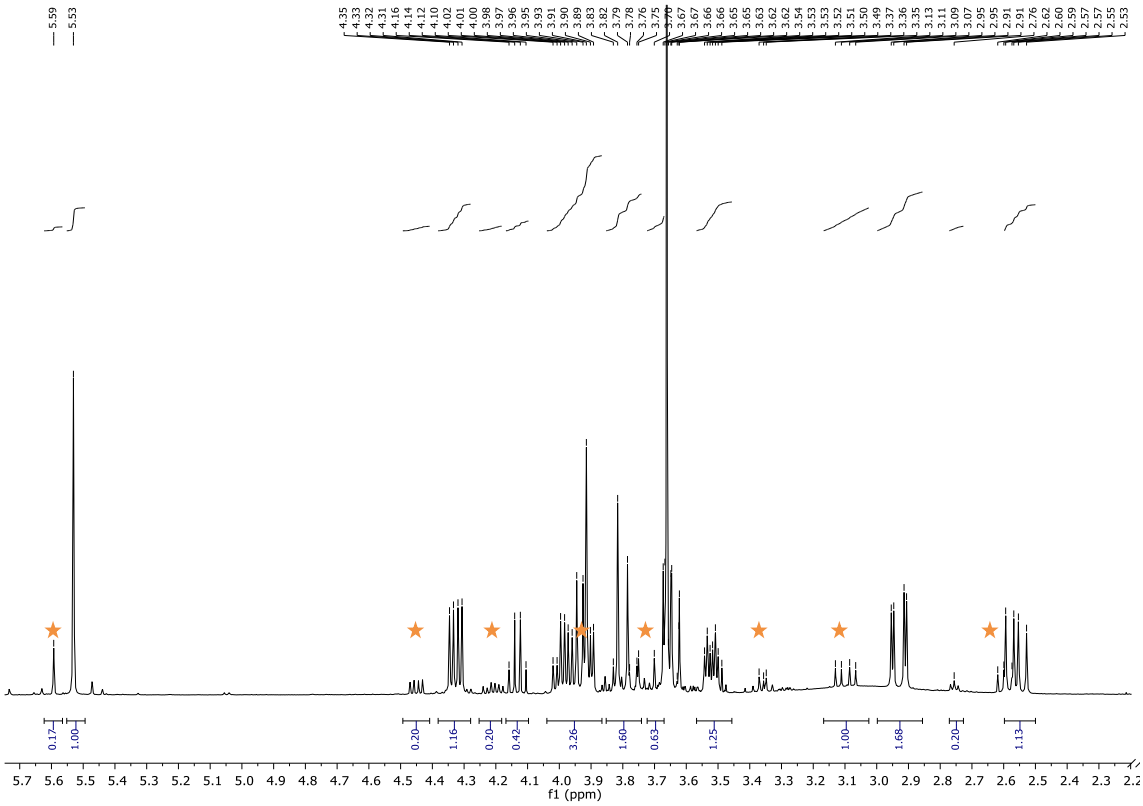
52.68
51.86
50.92
36.16
33.99
80
75
70
65
60
55
50
45
40
35
30
f1 (ppm)

1.7. ^{1}H and ^{13}C NMR of compound **6b**



★ Compound **7b**

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5.53
4.35 4.33 4.32 4.31 4.16 4.14 4.12 4.10 4.02 4.01 4.00 3.98 3.97 3.96 3.95 3.93 3.91 3.90 3.89 3.83 3.82 3.79 3.78 3.76 3.75 3.70 3.67 3.67 3.66 3.66 3.65 3.65 3.63 3.62 3.62 3.54 3.53 3.53 3.52 3.51 3.50 3.49 3.37 3.36 3.35 3.13 3.11 3.09 3.07 2.97 2.95 2.91 2.91 2.76 2.62 2.60 2.59 2.57 2.57 2.55 2.53
0.17
1.00
0.20
1.16
0.20
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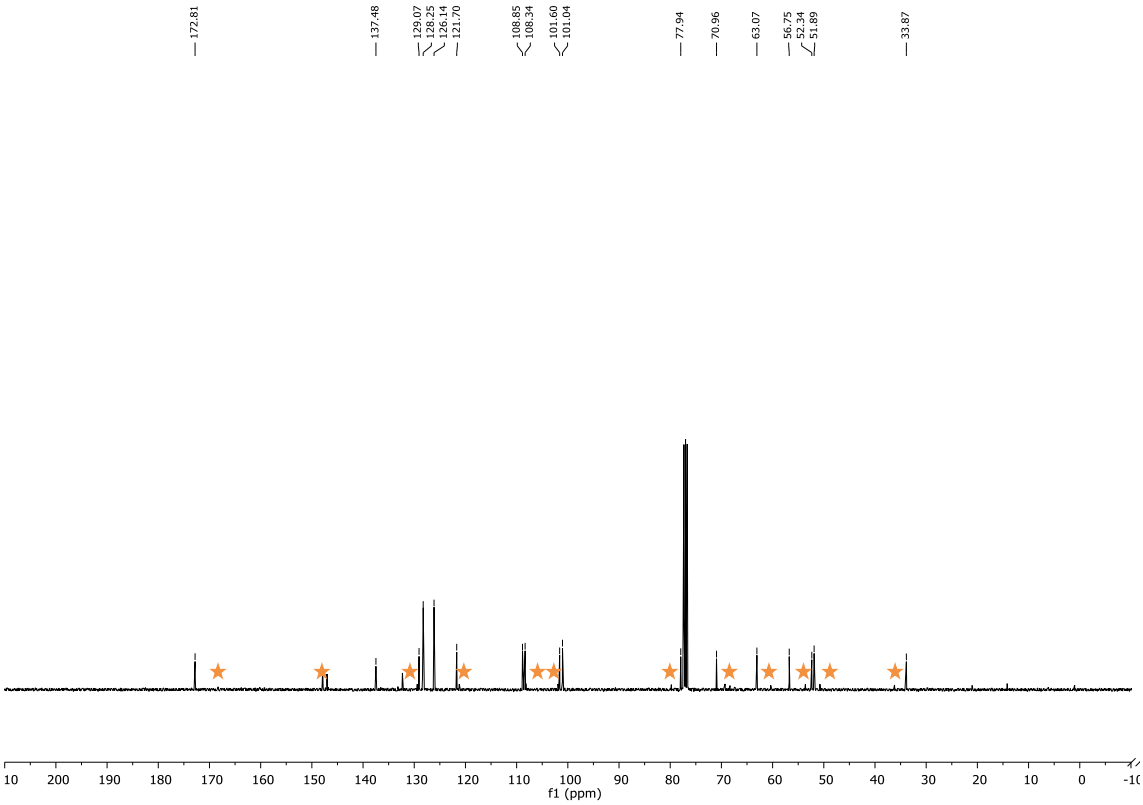
3.26
1.60
0.63
1.25
1.00
1.68
0.20
1.13
f1 (ppm)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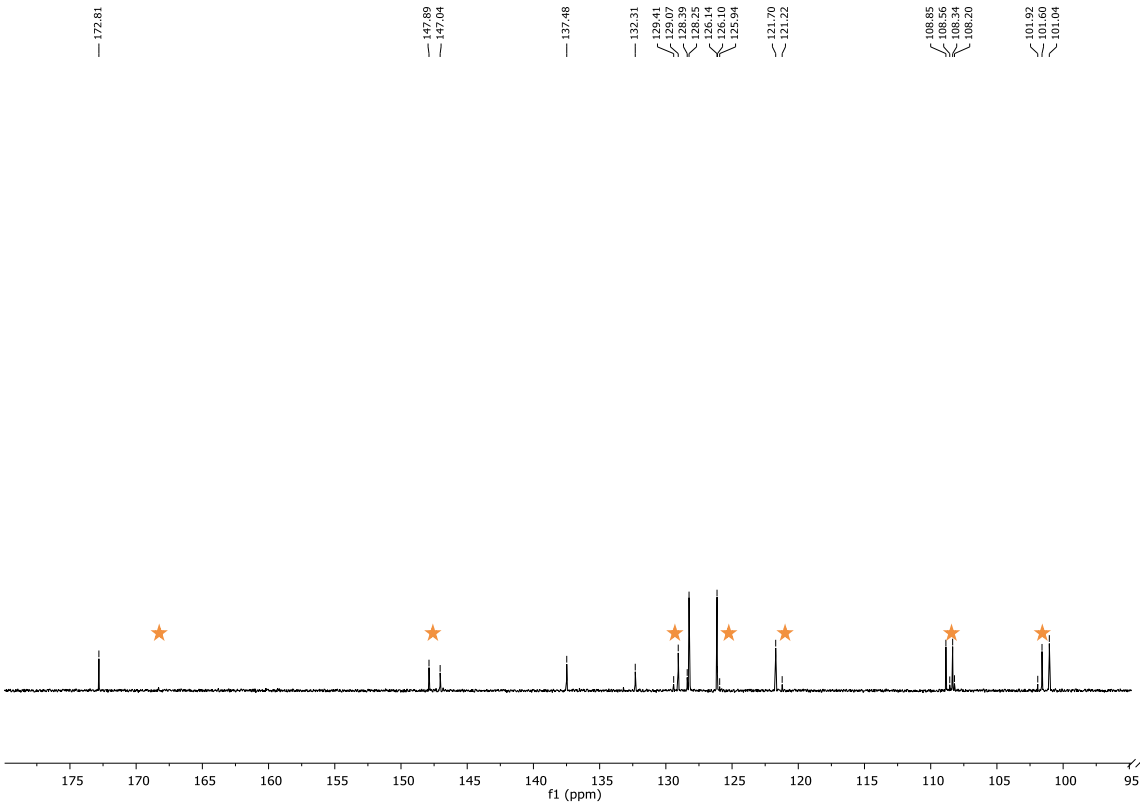
52.34
51.69
33.87
f1 (ppm)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121.70
121.22
108.85
108.56
108.34
108.20
101.92
101.60
101.04
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145
140
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120
115
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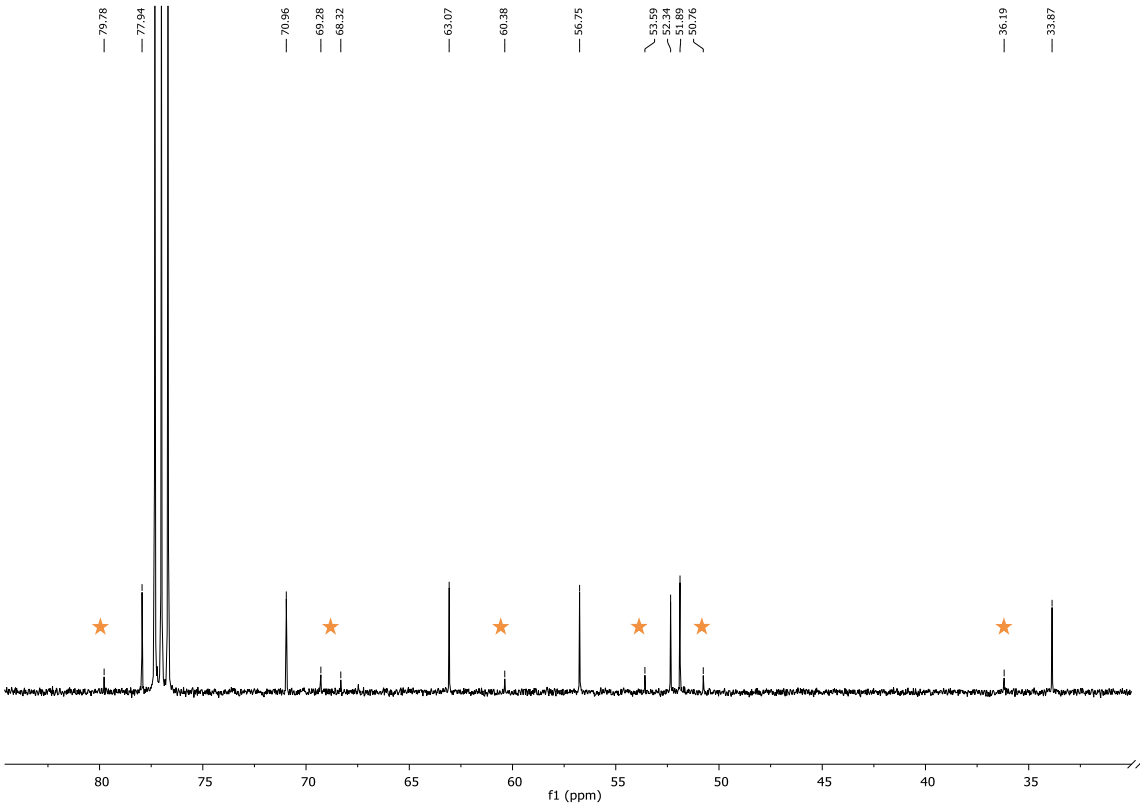
105
100
95
f1 (ppm)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68.32
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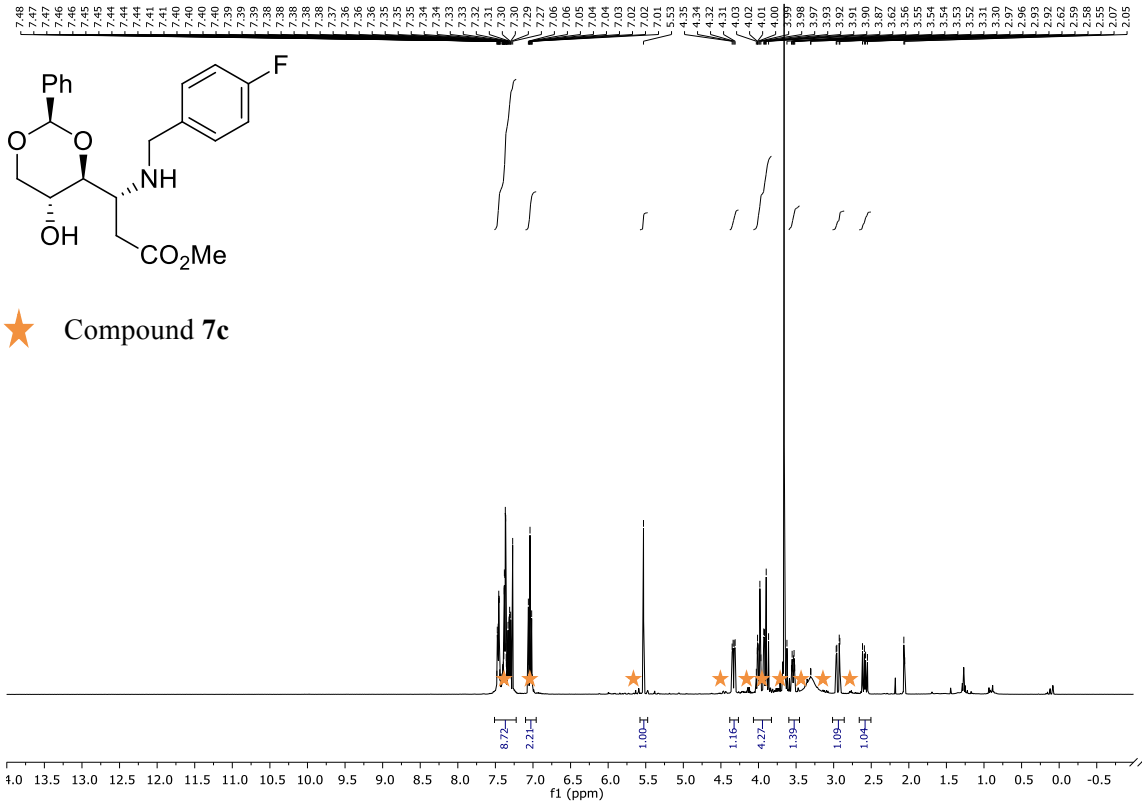
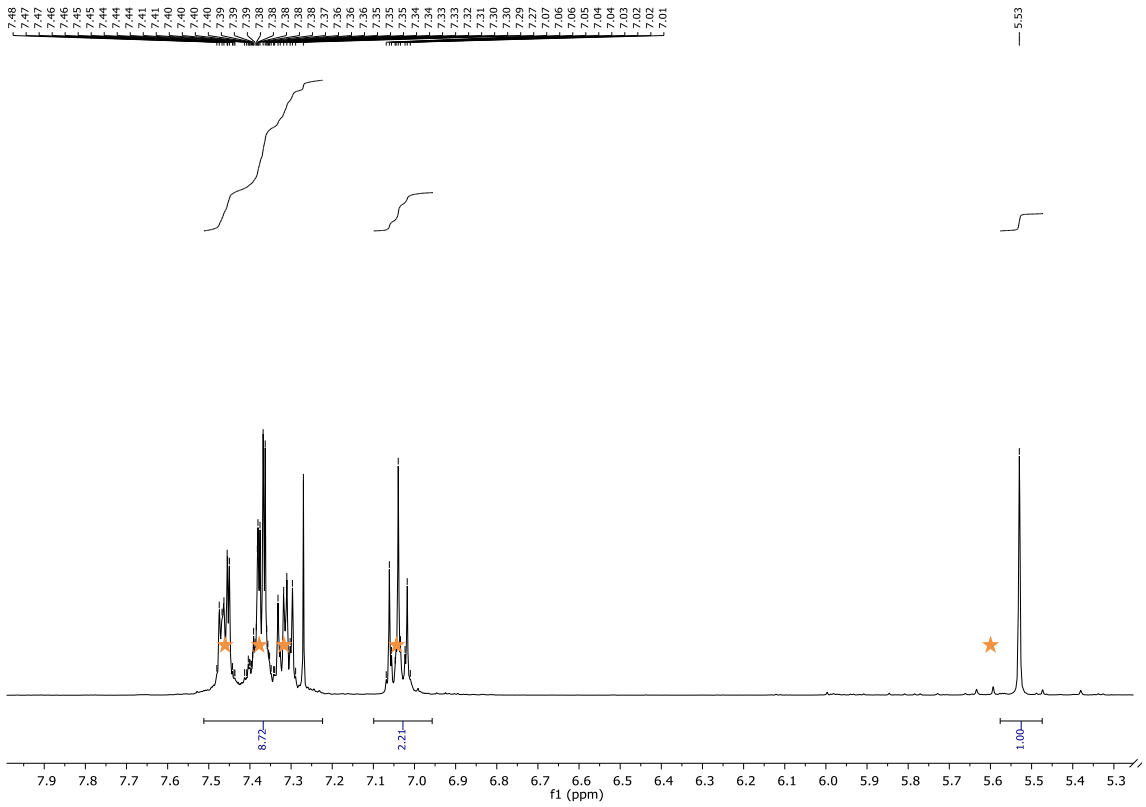
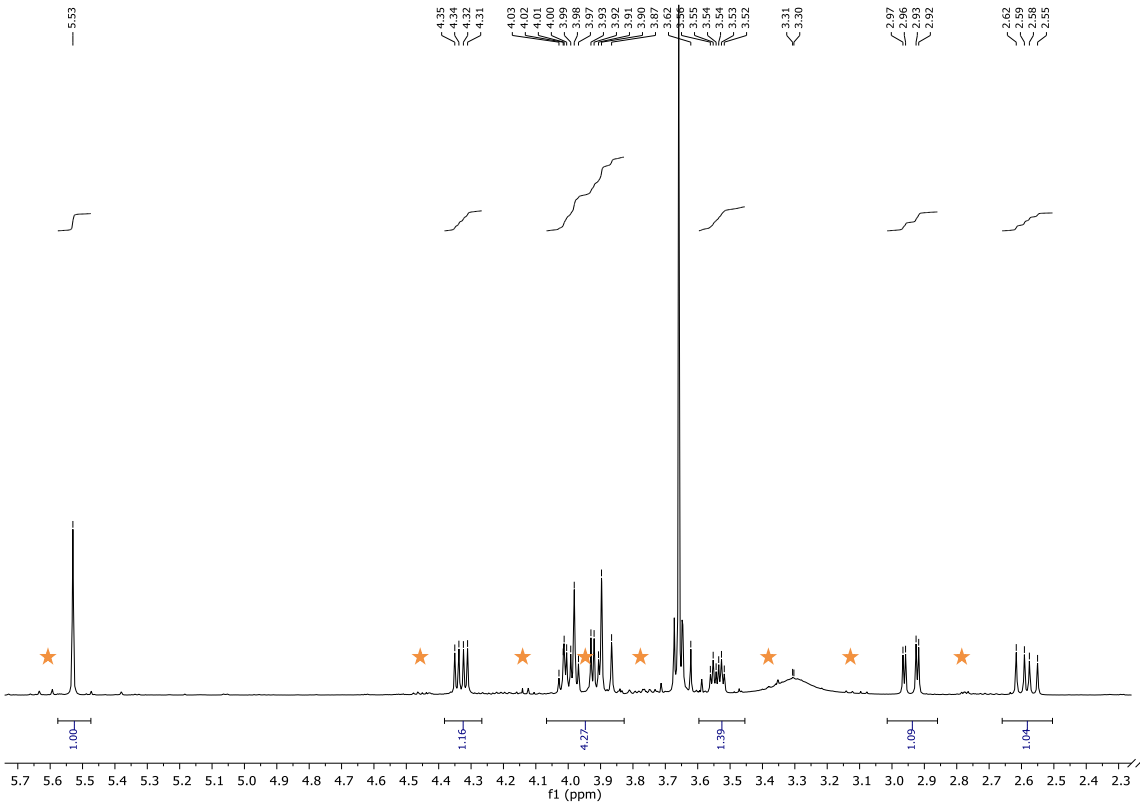
56.75
53.59
52.34
51.89
50.76
36.19
33.87
80
75
70
65
60
55
50
45
40
35
f1 (ppm)

1.8. ^{1}H and ^{13}C NMR of compound **6c**



★ Compound **7c**

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3.92
3.91
3.90
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3.54
3.54
3.53
3.52
3.31
3.30
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2.96
2.93
2.92
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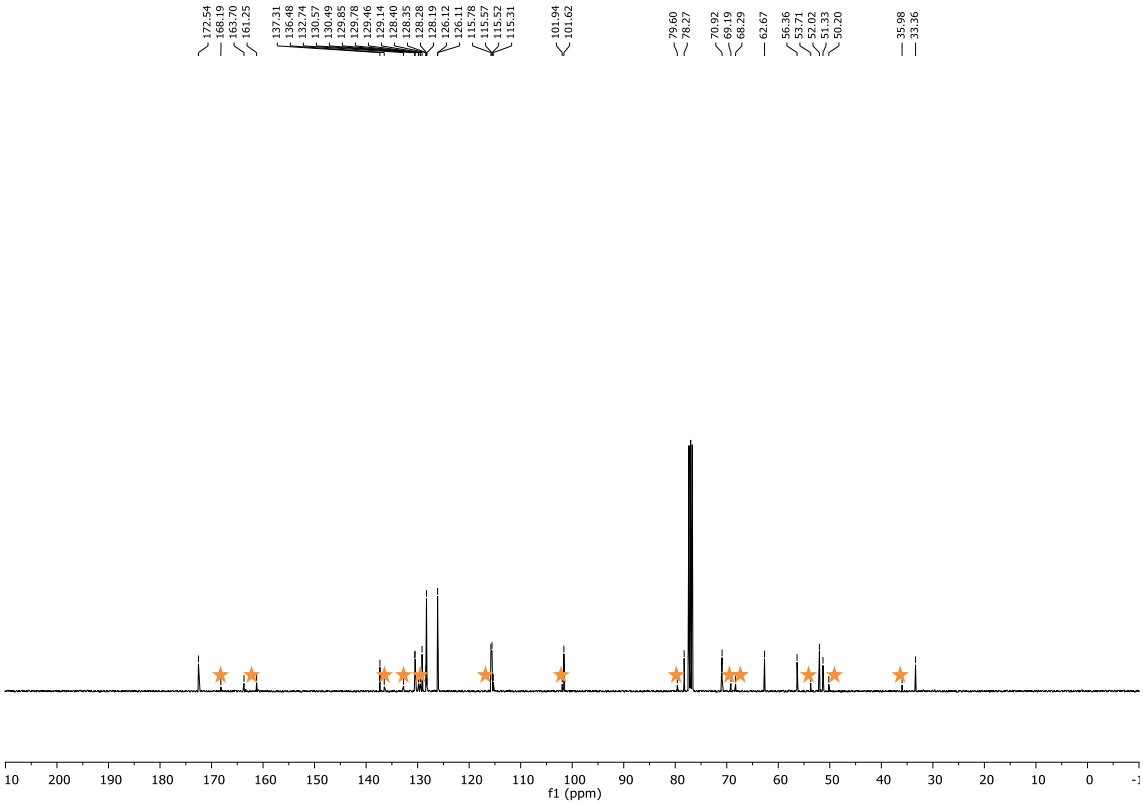
1.39
1.09
1.04
f1 (ppm)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129.46
129.14
128.40
128.35
128.28
128.19
126.12
126.11
115.78
115.57
115.52
115.31
101.94
101.62
79.60
78.27
70.92
69.19
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62.67
56.36
53.71
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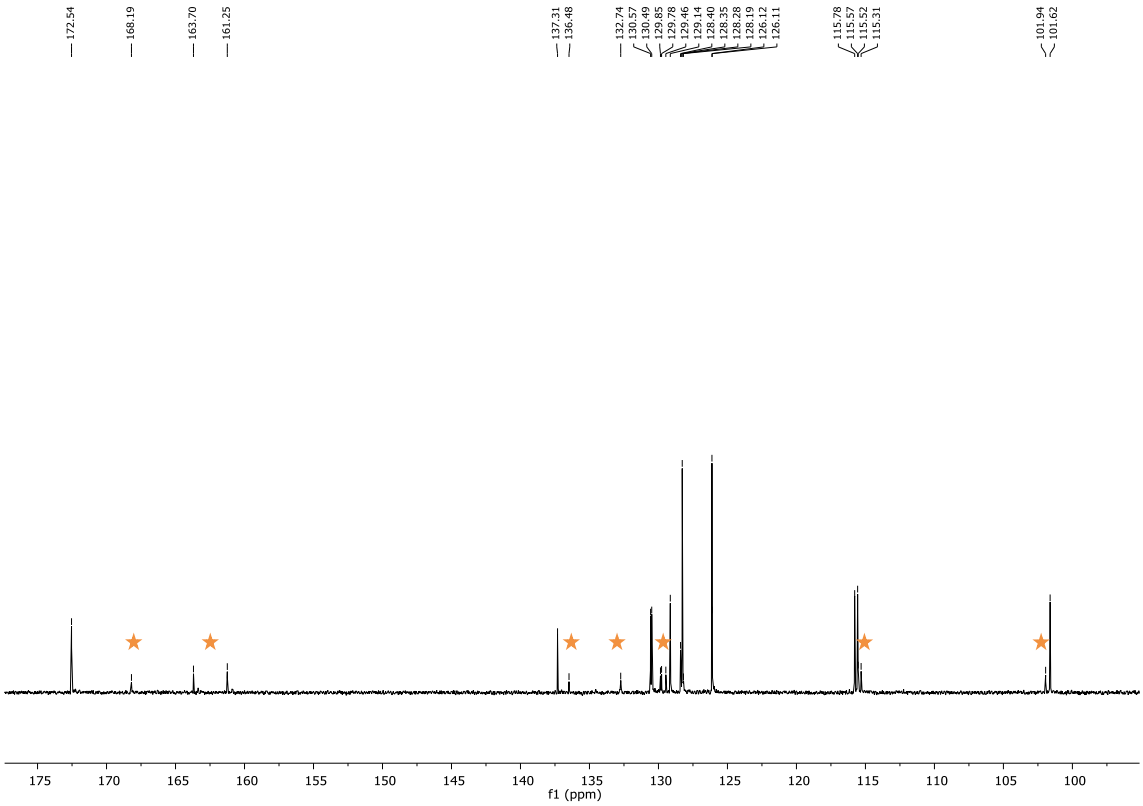
51.33
50.20
35.98
33.36
f1 (ppm)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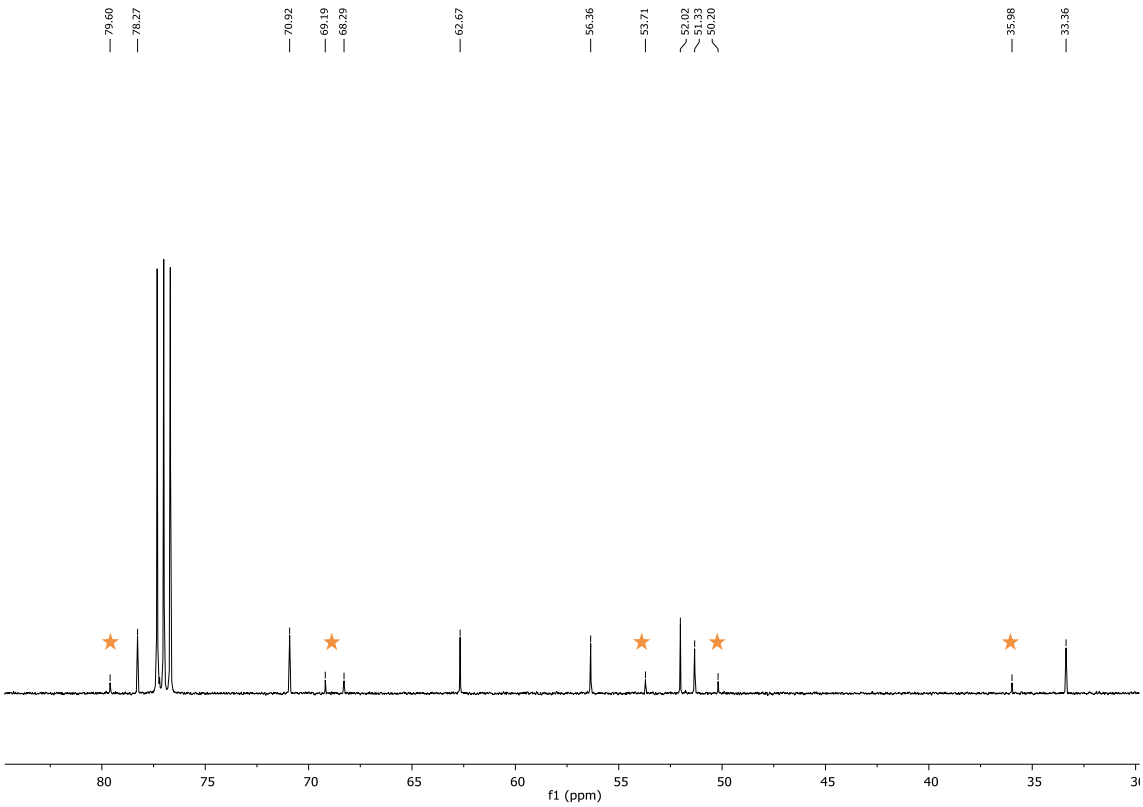
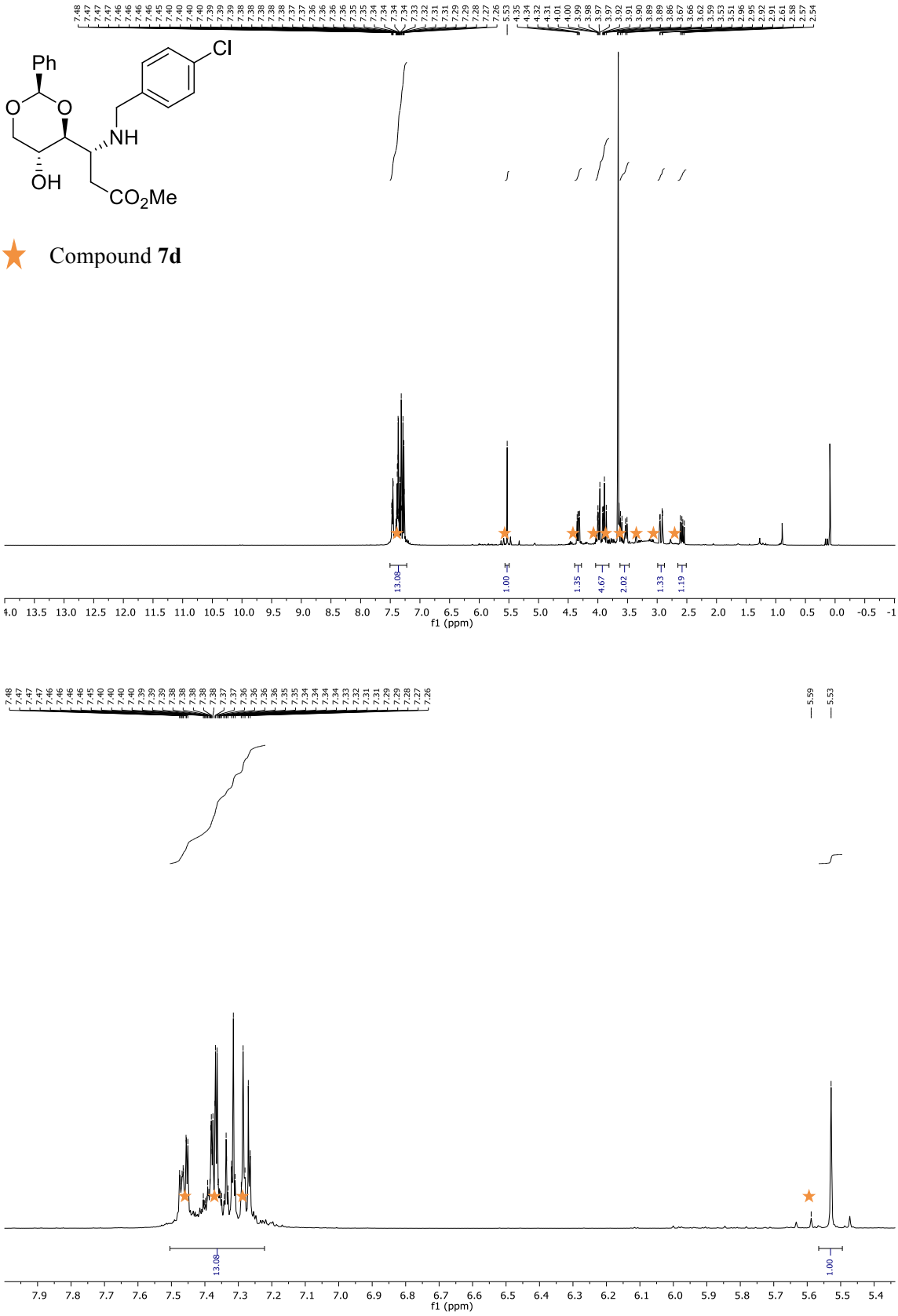
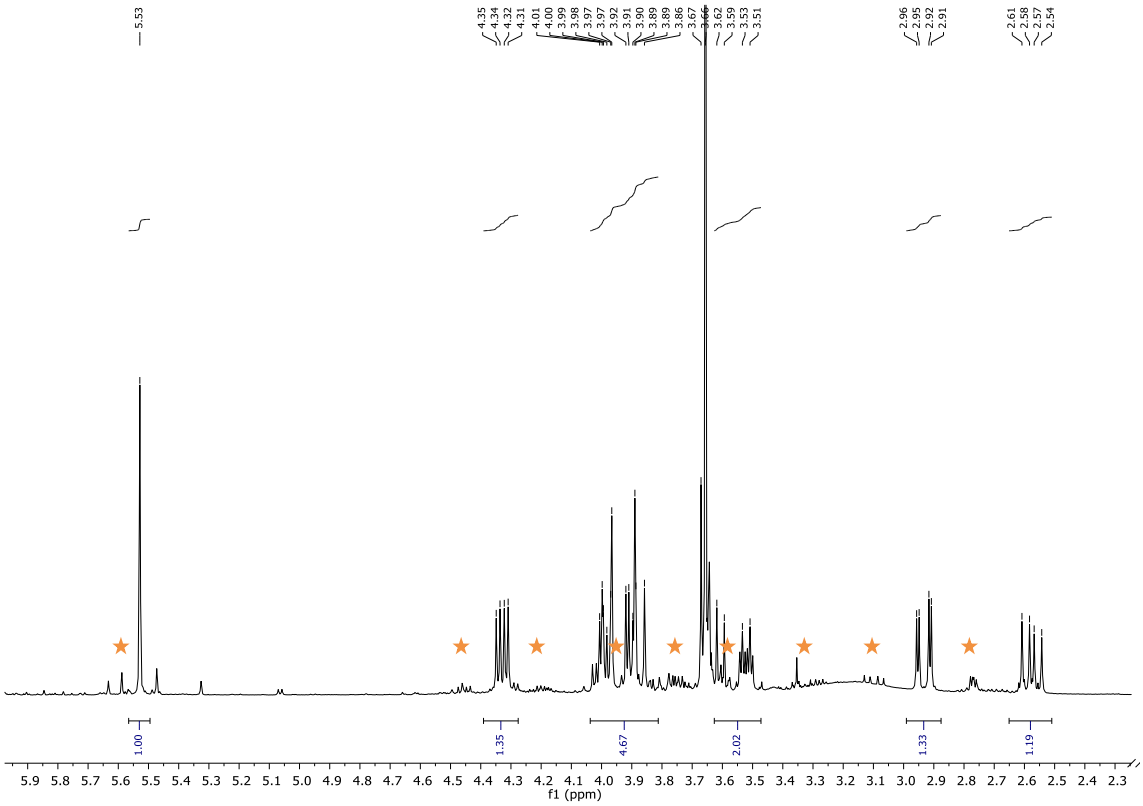
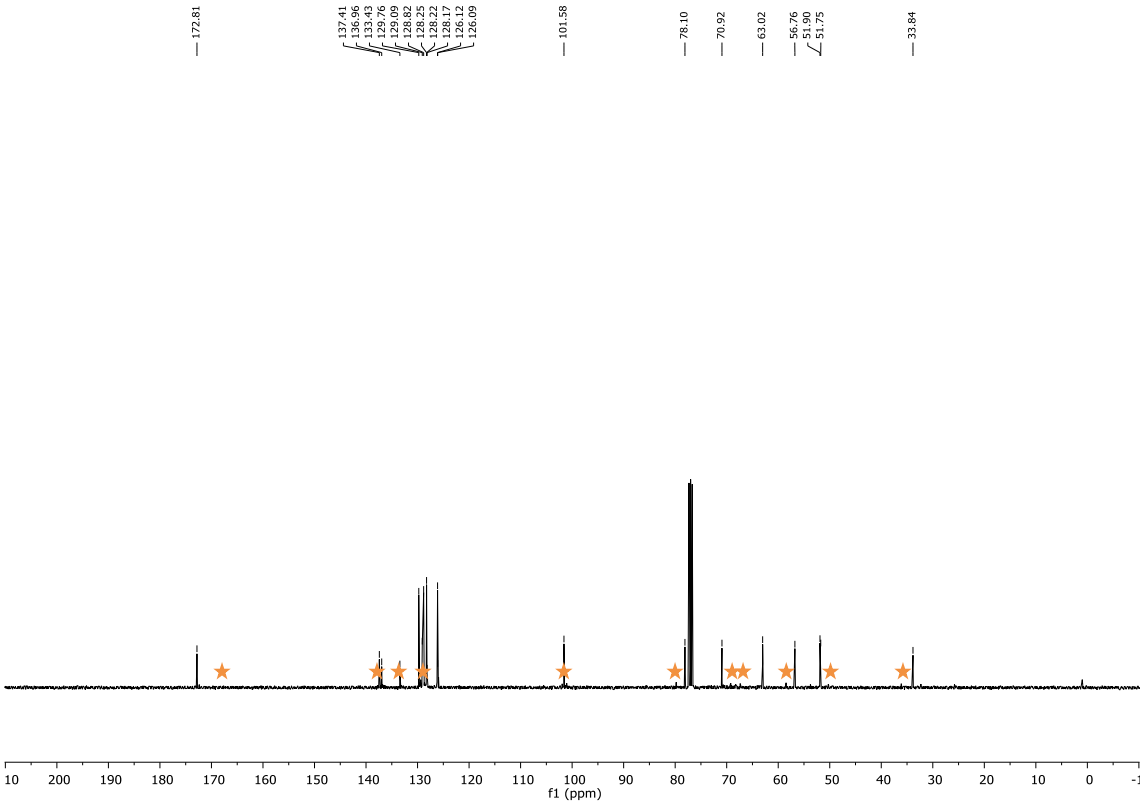
128.40
128.35
128.28
128.19
126.12
126.11
115.78
115.57
115.52
115.31
101.94
101.62
175
170
165
160
155
150
145
140
135
130
125
120
115
110
105
100
f1 (ppm)

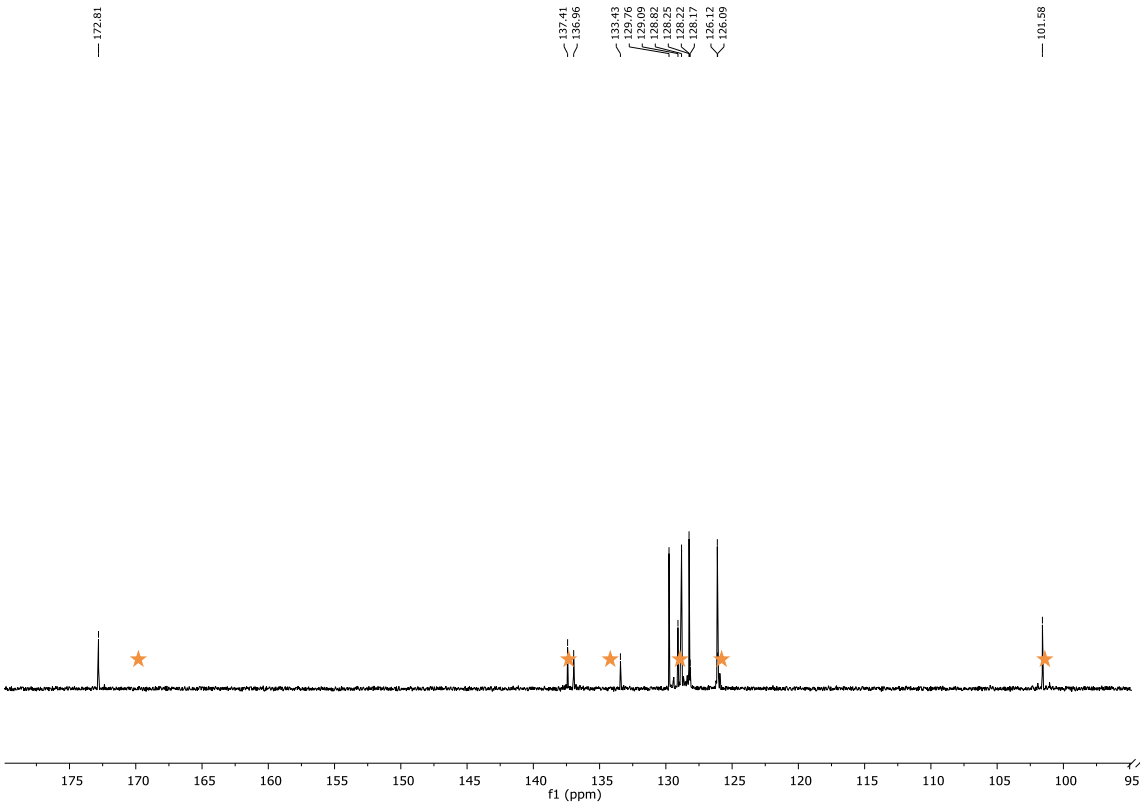

79.60
78.27
70.92
69.19
68.29
62.67
56.36
53.71
52.02
51.33
50.20
35.98
33.36
80
75
70
65
60
55
50
45
40
35
f1 (ppm)

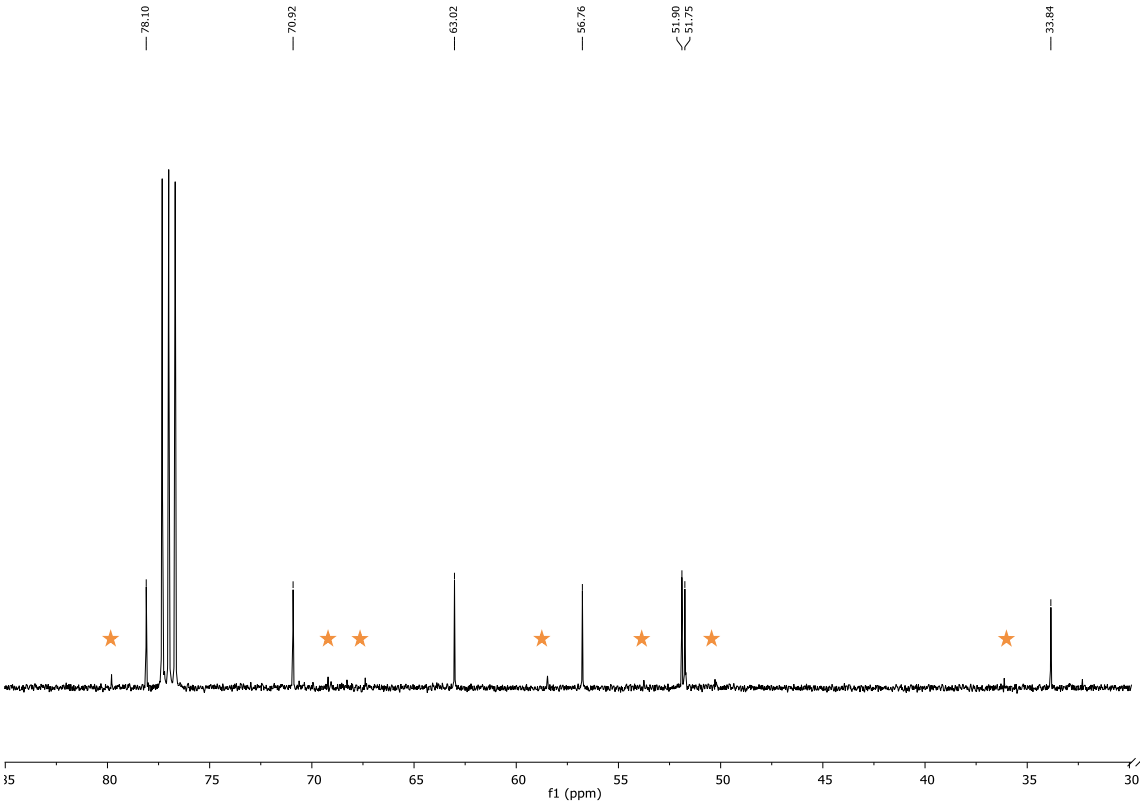
1.9. ^{1}H and ^{13}C NMR of compound **6d**



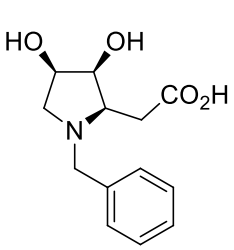

5.53
4.35
4.34
4.32
4.31
4.01
4.00
3.99
3.98
3.97
3.97
3.92
3.91
3.90
3.89
3.89
3.86
3.67
3.66
3.62
3.59
3.53
3.51
2.96
2.95
2.92
2.91
2.61
2.58
2.57
2.54
1.00
1.35
4.67
2.02
1.33
1.19
f1 (ppm)


172.81
137.41
136.96
133.43
129.76
129.09
128.82
128.25
128.22
128.17
126.12
126.09
101.58
78.10
70.92
63.02
56.76
51.90
51.75
33.84
f1 (ppm)

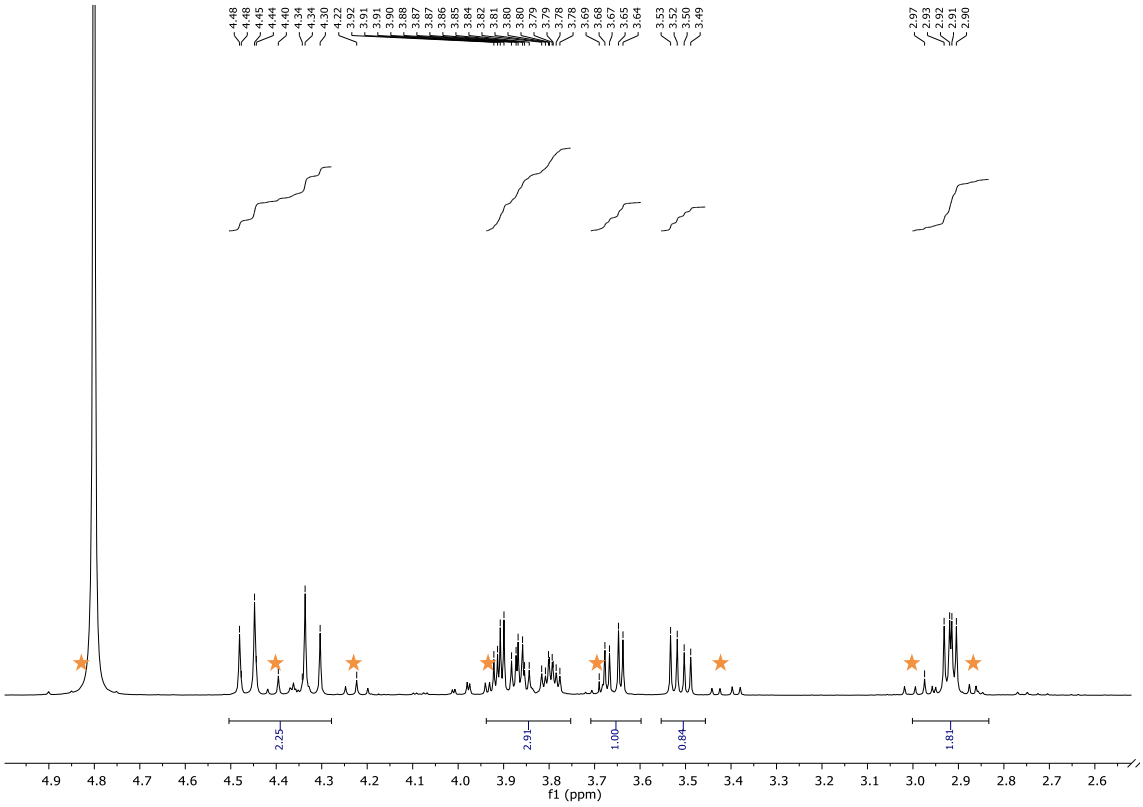

172.81
137.41
136.96
133.43
129.76
129.09
128.82
128.25
128.22
128.17
126.12
126.09
101.58
175
170
165
160
155
150
145
140
135
130
125
120
115
110
105
100
95
f1 (ppm)

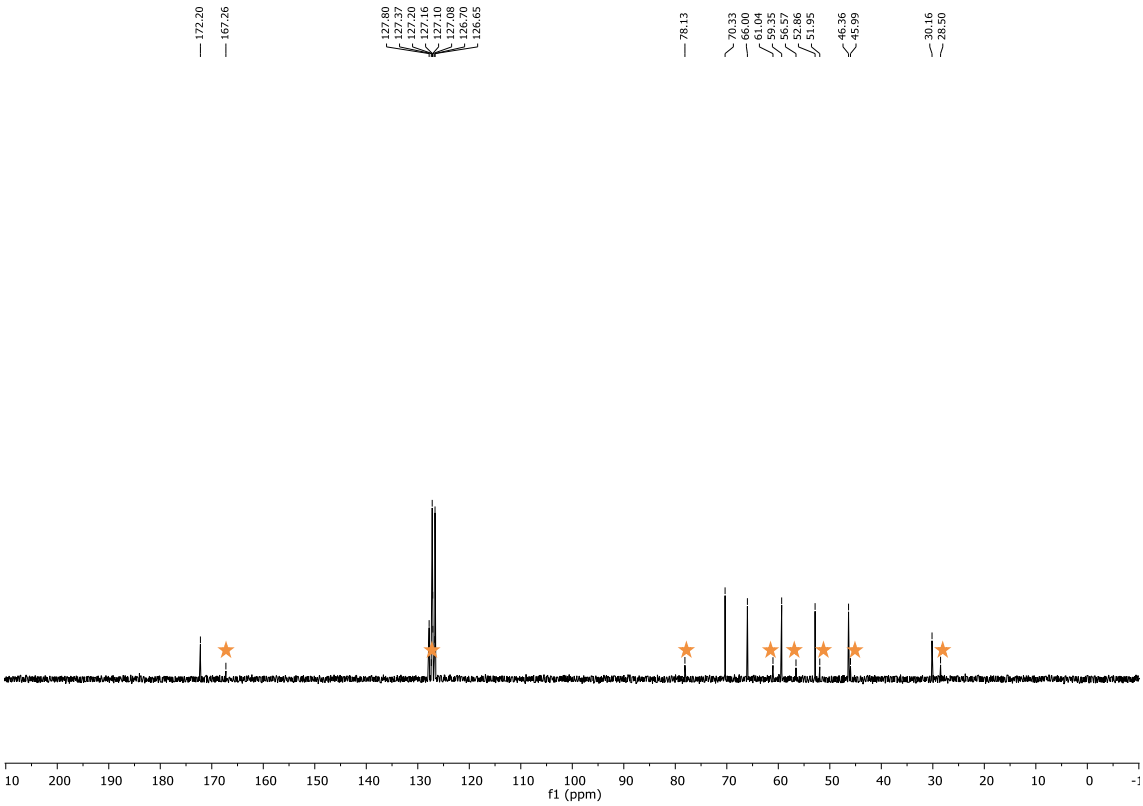

78.10
70.92
63.02
56.76
51.90
51.75
33.84
80
75
70
65
60
55
50
45
40
35
30
f1 (ppm)

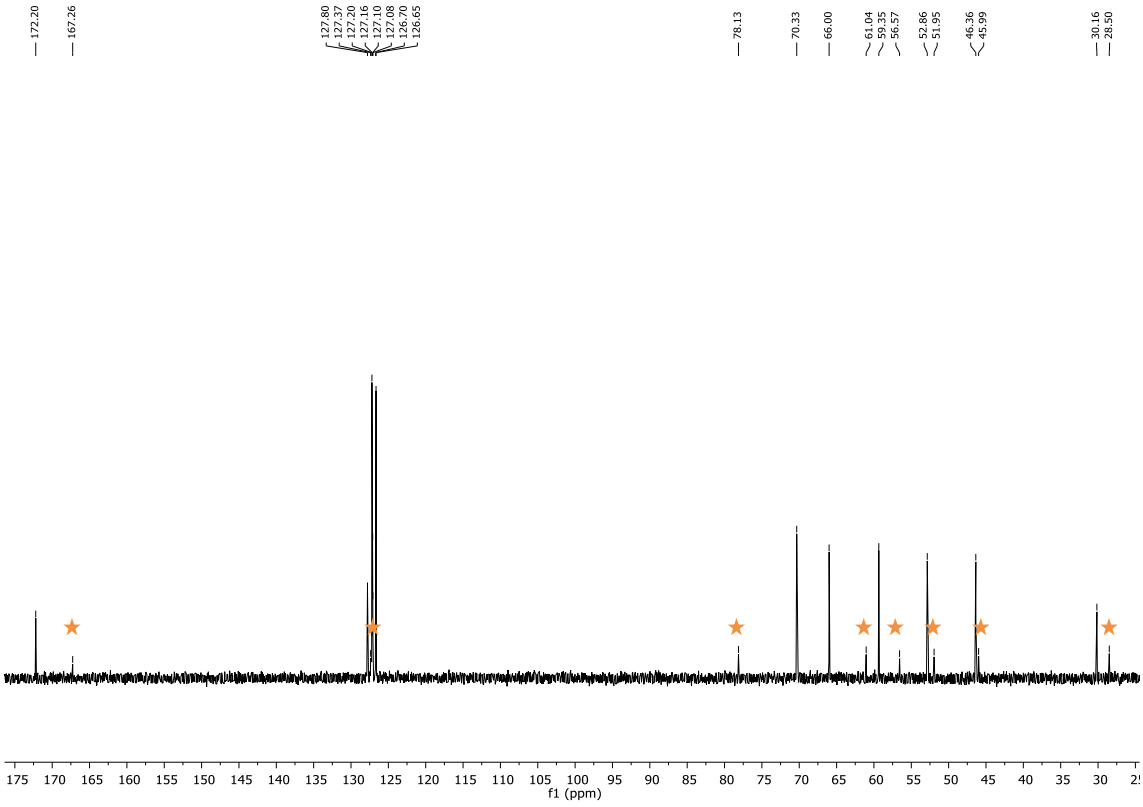
1.10. ^{1}H and ^{13}C NMR of compound **8a**



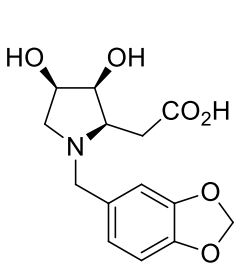
★ Compound **13a**



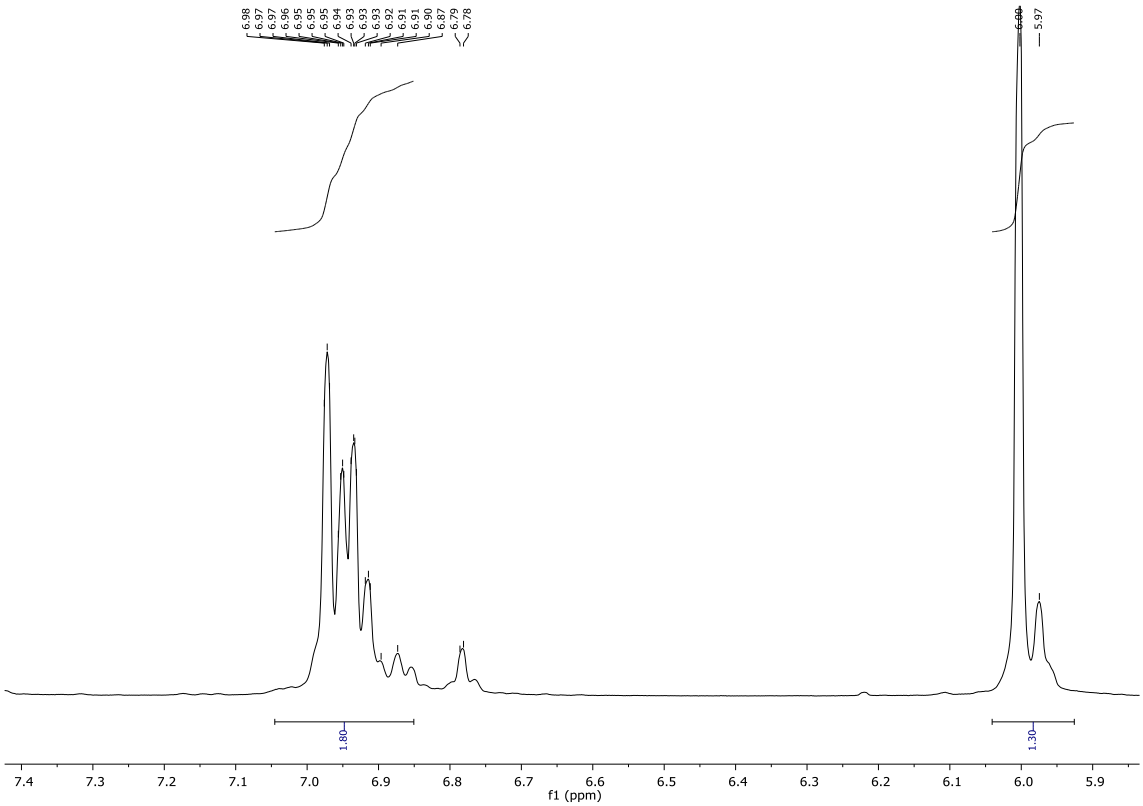

172.20
167.26
127.80
127.37
127.20
127.16
127.10
127.08
126.70
126.65
78.13
70.33
66.00
61.04
59.35
56.57
52.86
51.95
46.36
45.99
30.16
28.50
f1 (ppm)

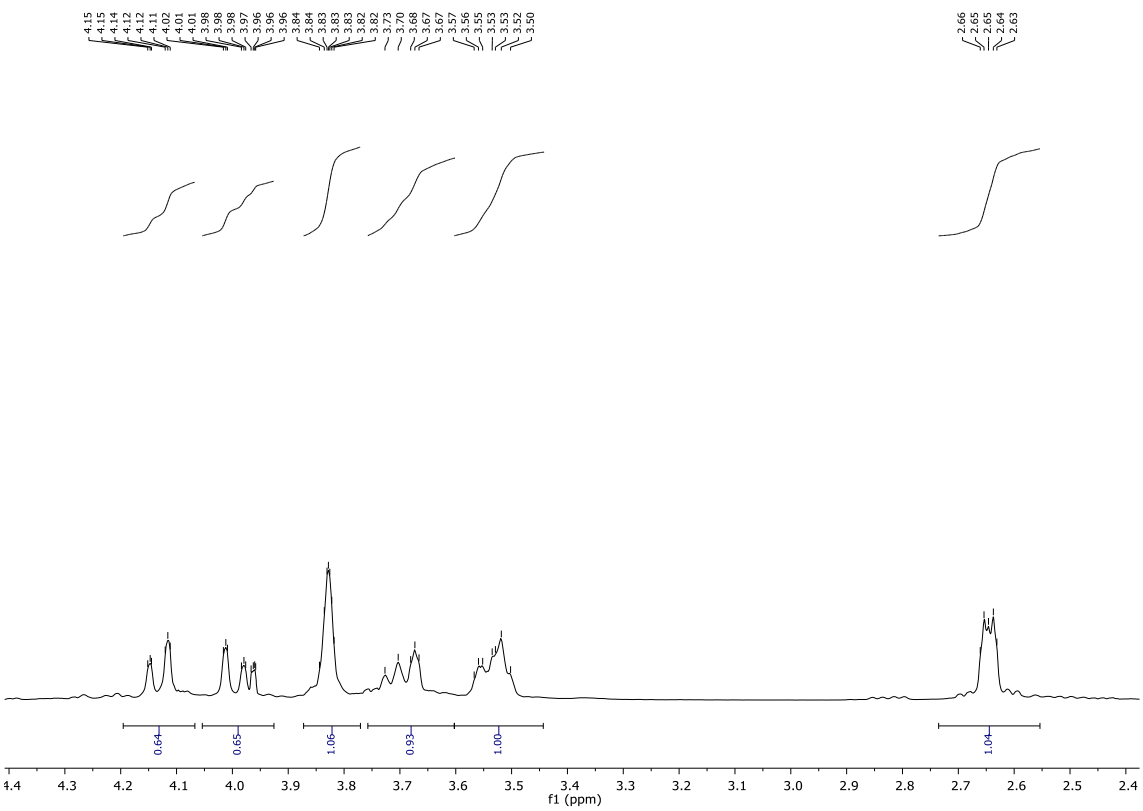

172.20
167.26
127.80
127.37
127.20
127.16
127.10
127.08
126.70
126.65
78.13
70.33
66.00
61.04
59.35
56.57
52.86
51.95
46.36
45.99
30.16
28.50
f1 (ppm)

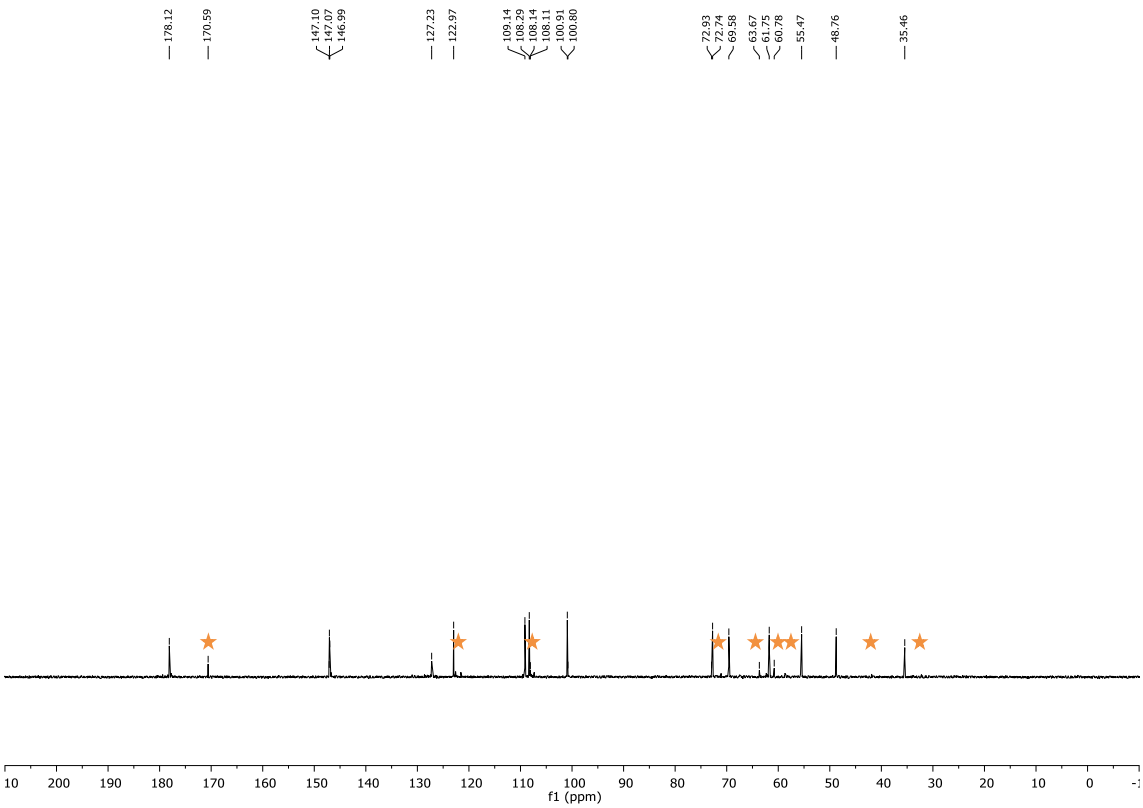
1.11. ^{1}H and ^{13}C NMR of compound **8b**

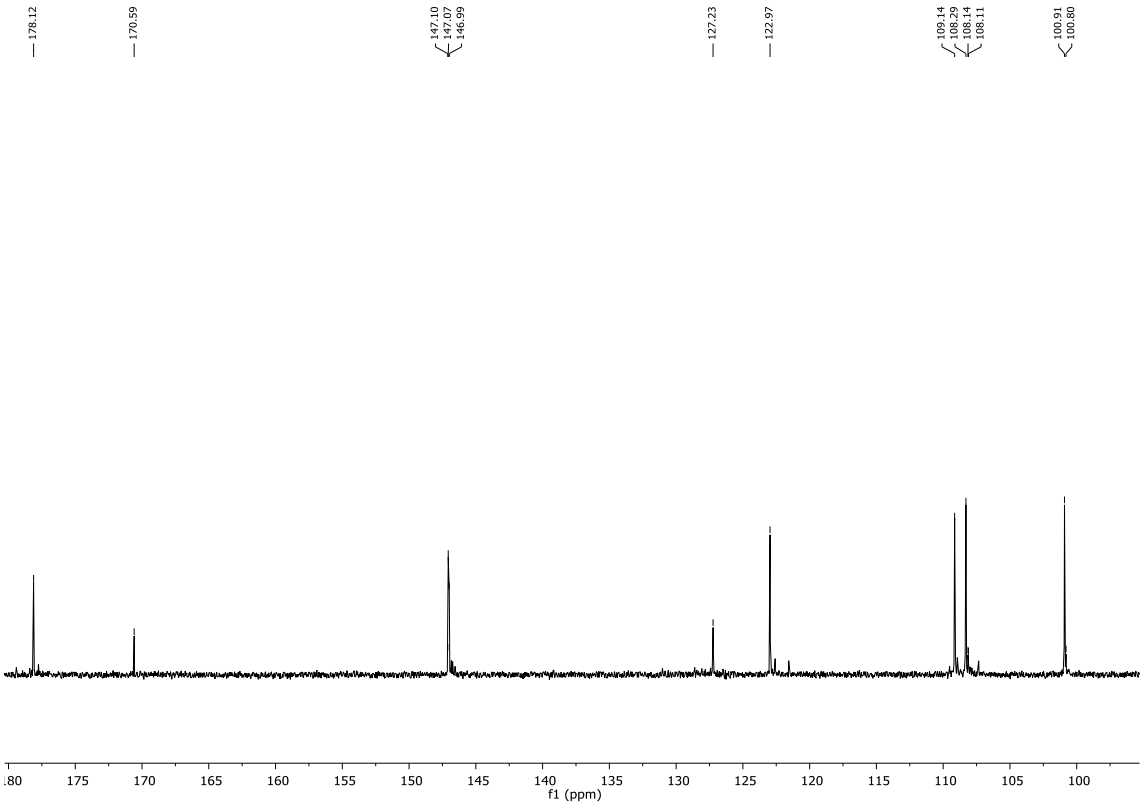


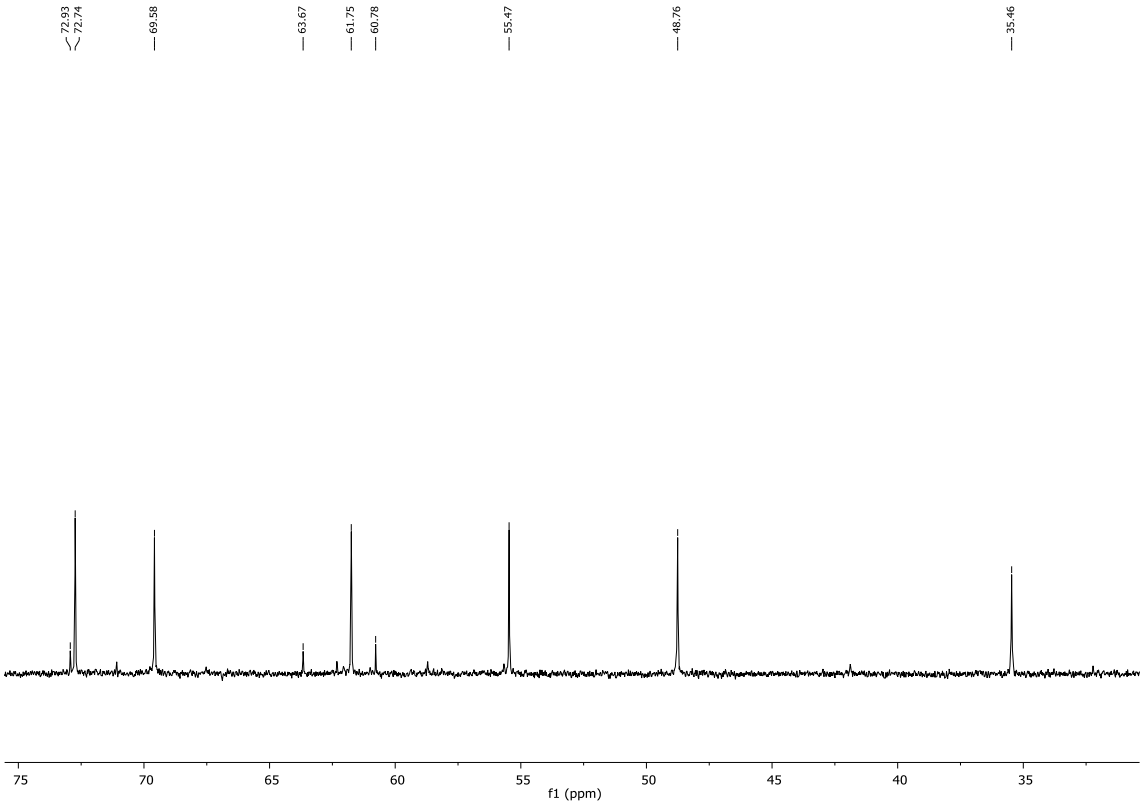
★ Compound **13b**



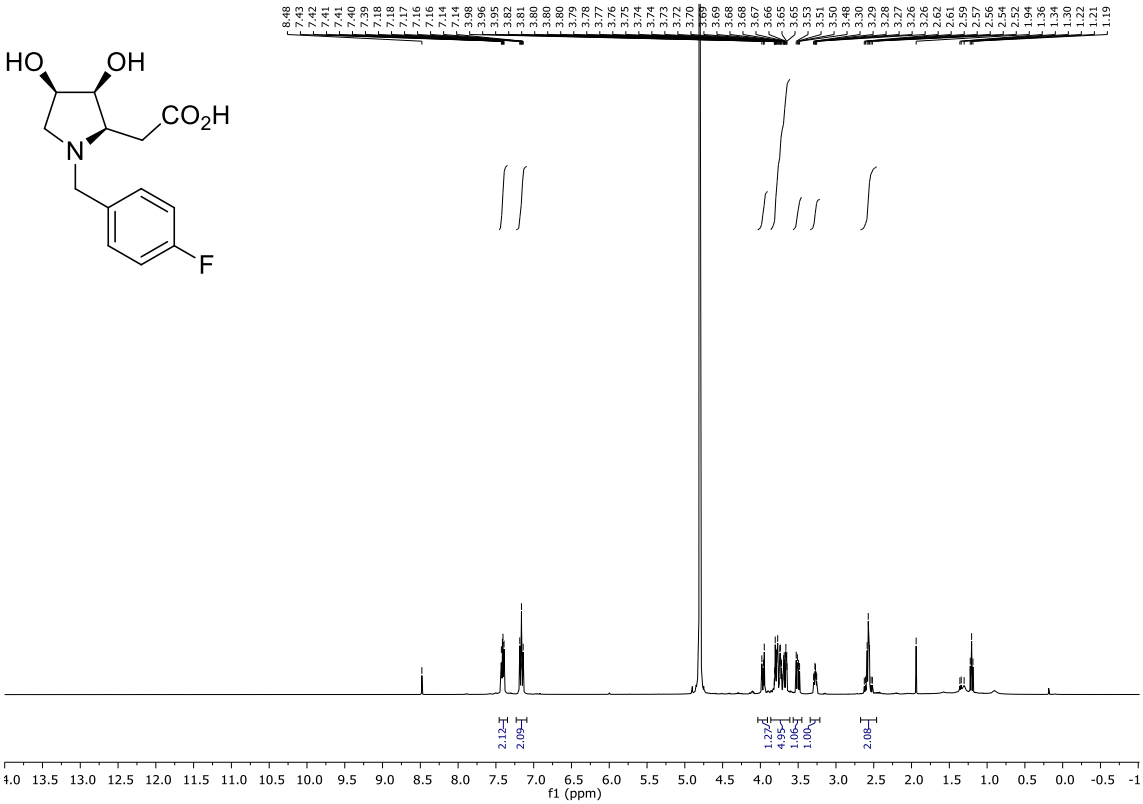

4.15
4.15
4.14
4.12
4.12
4.11
4.02
4.01
4.01
3.98
3.98
3.97
3.96
3.96
3.96
3.84
3.84
3.83
3.83
3.82
3.82
3.73
3.70
3.68
3.67
3.67
3.57
3.56
3.55
3.53
3.53
3.52
3.50
2.66
2.65
2.65
2.64
2.63
0.64
0.65
1.06
0.93
1.00
1.04
f1 (ppm)

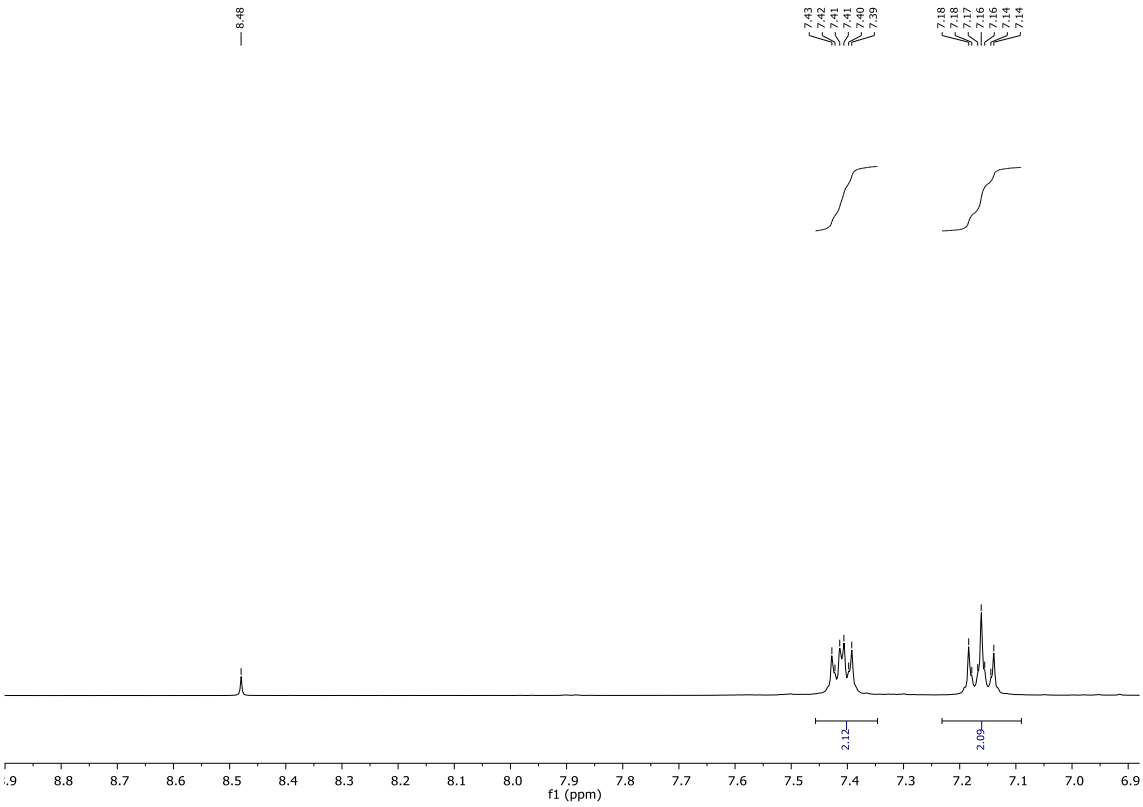

178.12
170.59
147.10
147.07
146.99
127.23
122.97
109.14
108.29
108.14
108.11
100.91
100.80
72.93
72.74
69.58
63.67
61.75
60.78
55.47
48.76
35.46
f1 (ppm)

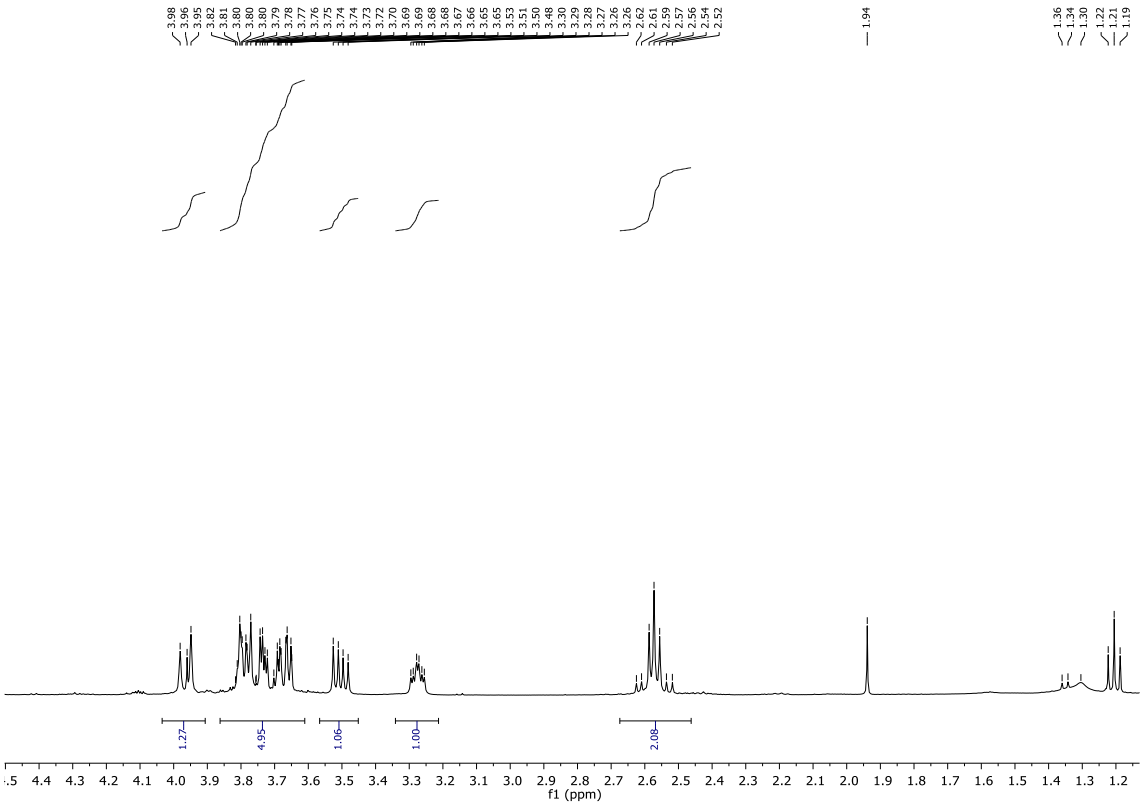

178.12
170.59
147.10
147.07
146.99
127.23
122.97
109.14
109.29
108.14
108.11
100.91
100.80
f1 (ppm)

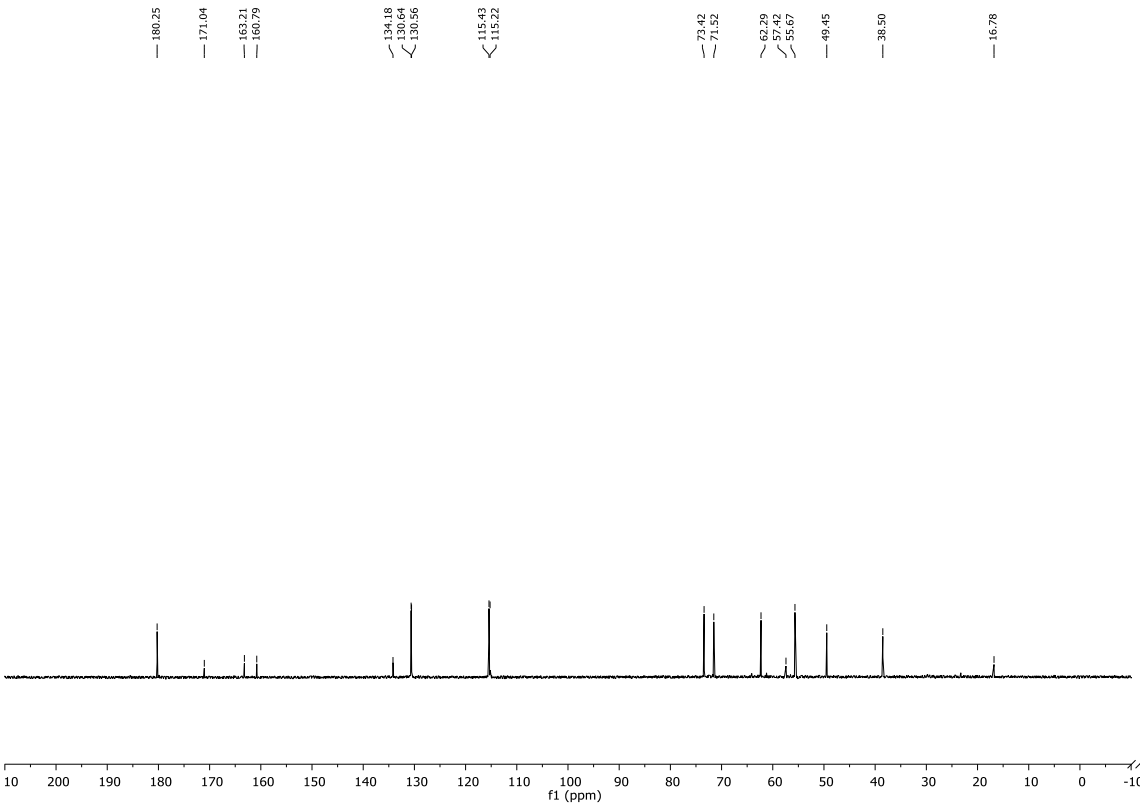

72.93
72.74
69.58
63.67
61.75
60.78
55.47
48.76
35.46
f1 (ppm)

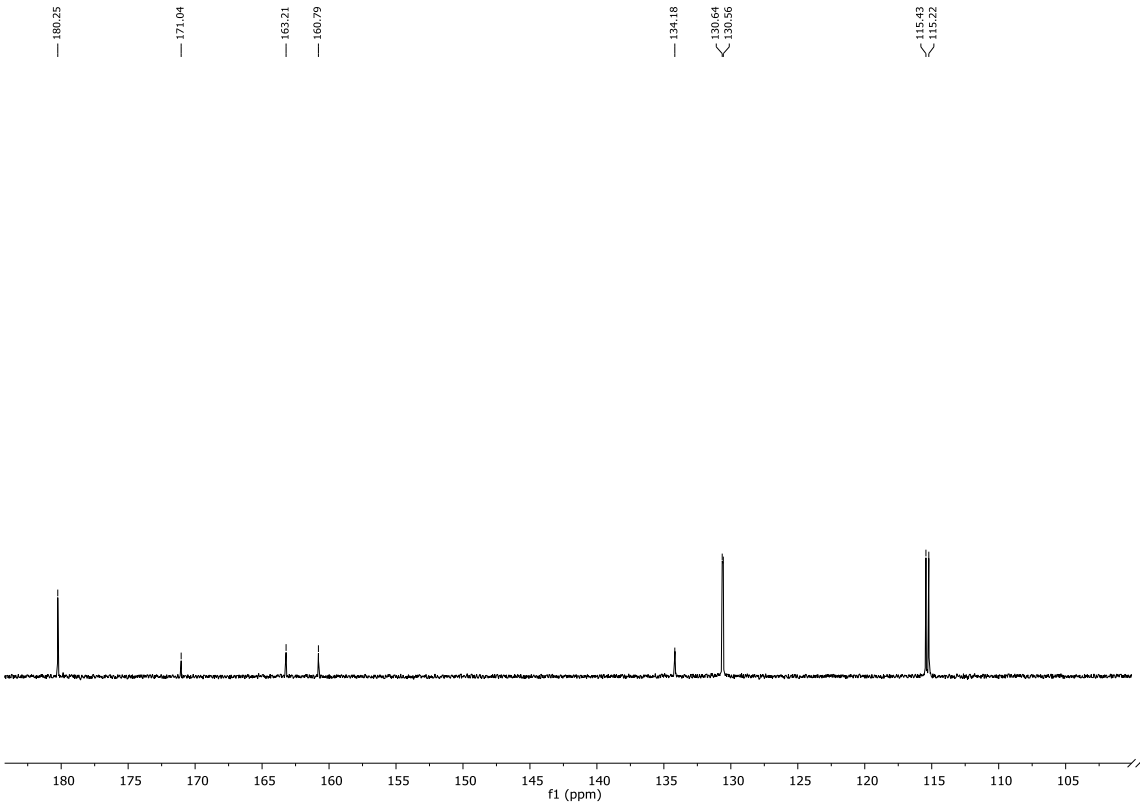
1.12. ^{1}H and ^{13}C NMR of compound **8c**

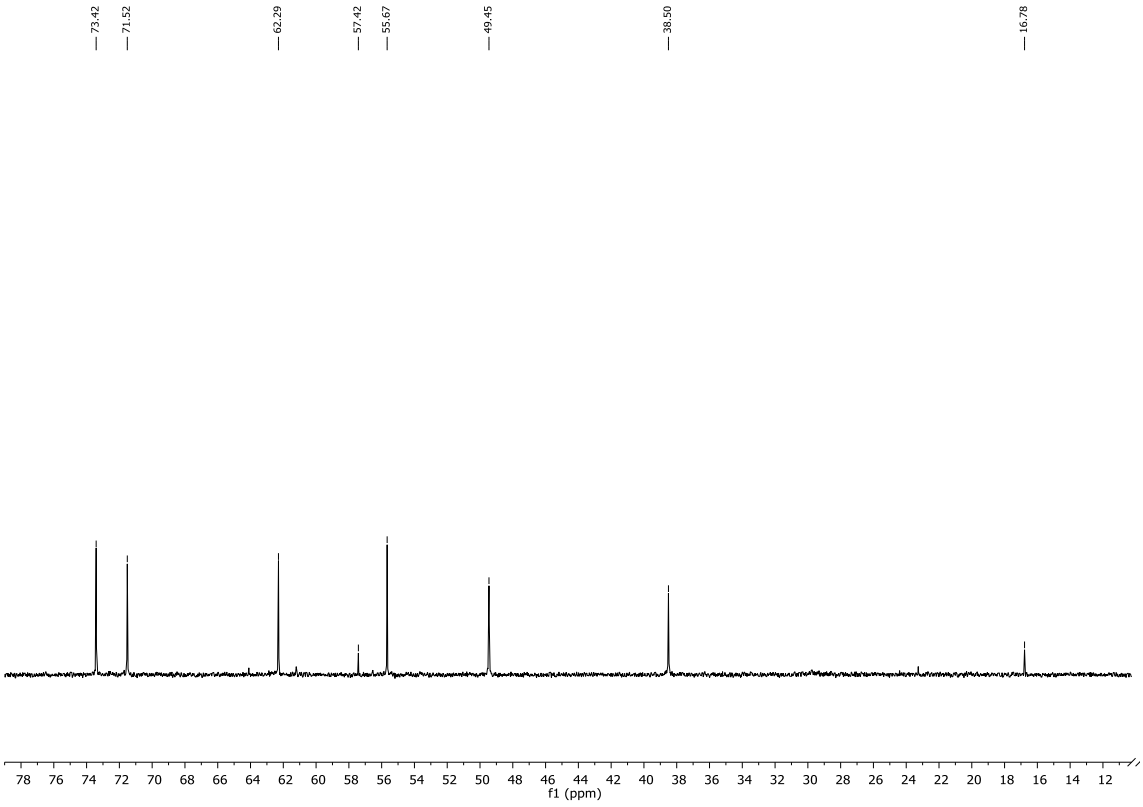




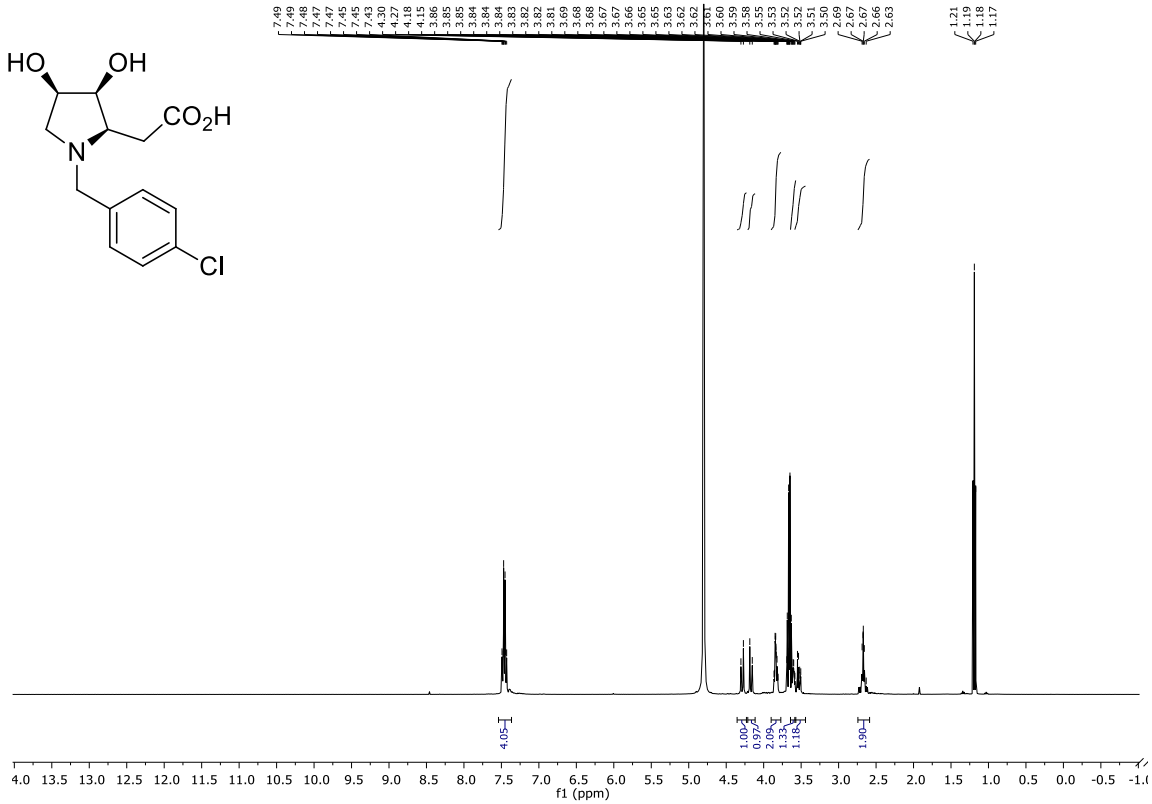

3.98
3.96
3.95
3.82
3.81
3.80
3.80
3.80
3.79
3.78
3.77
3.76
3.75
3.74
3.74
3.73
3.72
3.70
3.69
3.69
3.68
3.68
3.67
3.66
3.65
3.65
3.53
3.51
3.50
3.48
3.30
3.29
3.28
3.27
3.26
3.26
2.62
2.61
2.59
2.57
2.56
2.54
2.52
1.94
1.36
1.34
1.30
1.22
1.21
1.19
1.27
4.95
1.06
1.00
2.08
f1 (ppm)

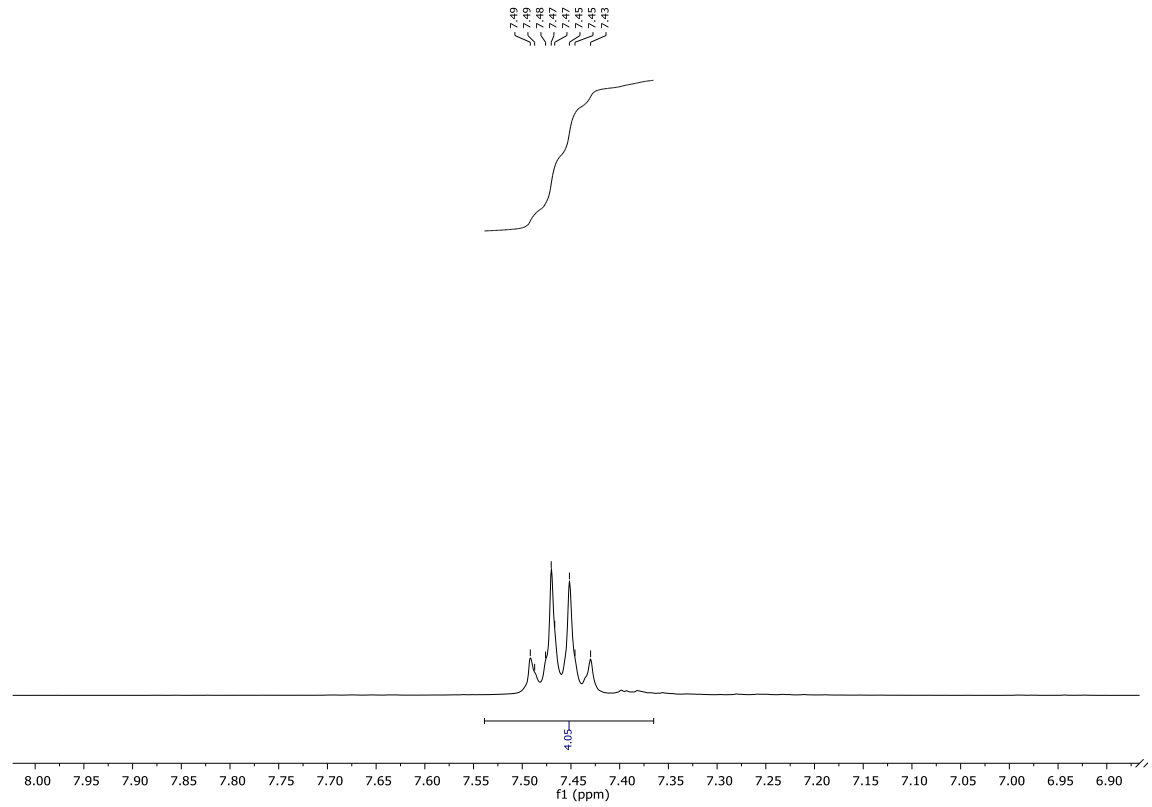

180.25
171.04
163.21
160.79
134.18
130.64
130.56
115.43
115.22
73.42
71.52
62.29
57.42
55.67
49.45
38.50
16.78
f1 (ppm)

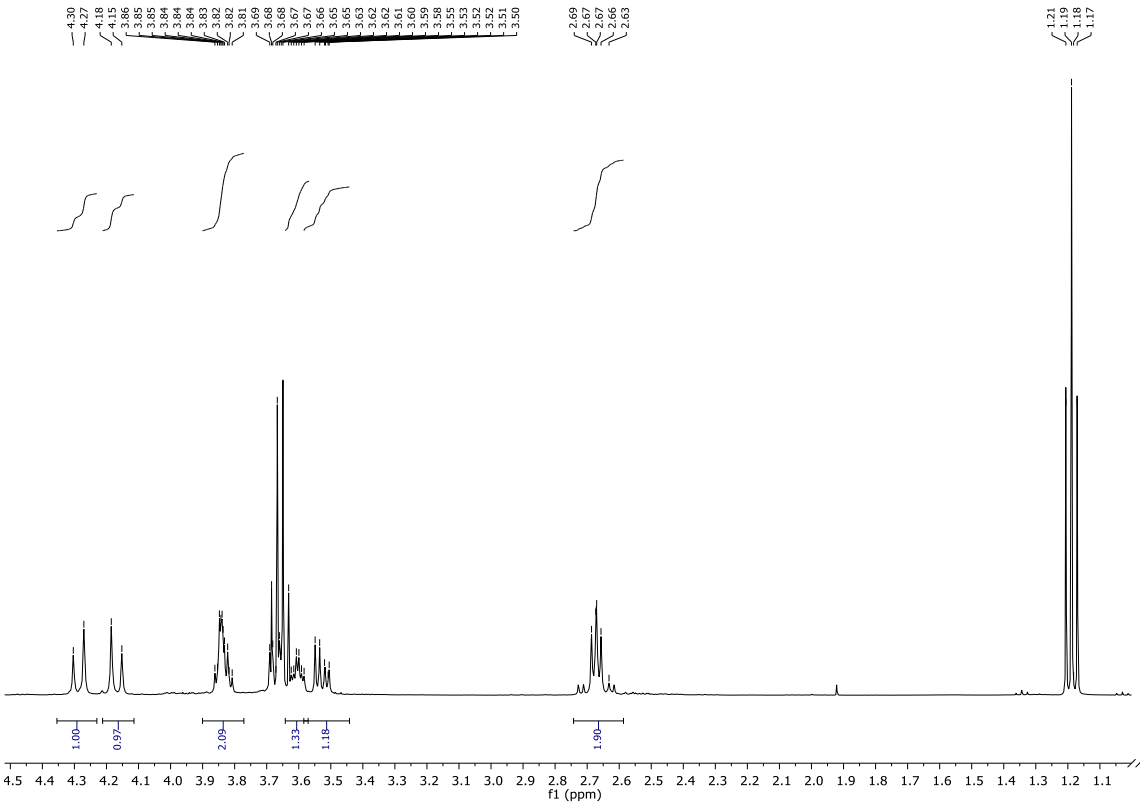

180.25
171.04
163.21
160.79
134.18
130.64
130.56
115.43
115.22
180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105
f1 (ppm)

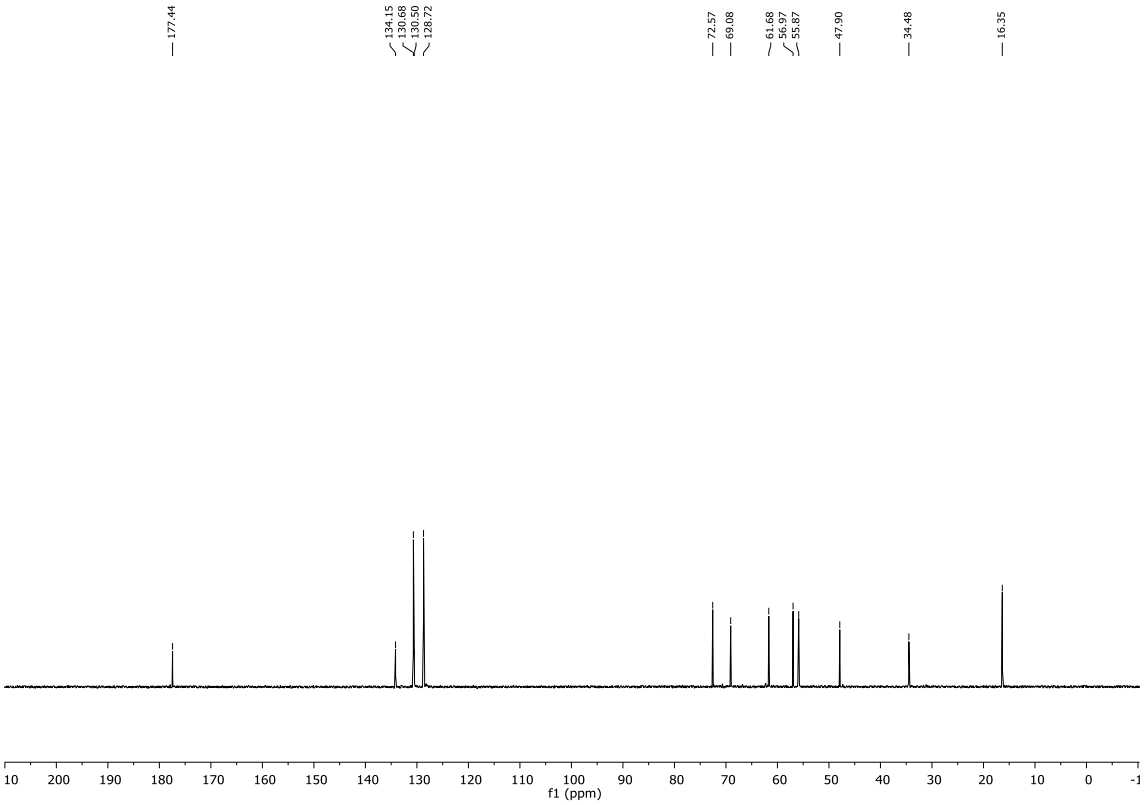

73.42
71.52
62.29
57.42
55.67
49.45
38.50
16.78
78 76 74 72 70 68 66 64 62 60 58 56 54 52 50 48 46 44 42 40 38 36 34 32 30 28 26 24 22 20 18 16 14 12
f1 (ppm)

1.13. ^{1}H and ^{13}C NMR of compound **8d**

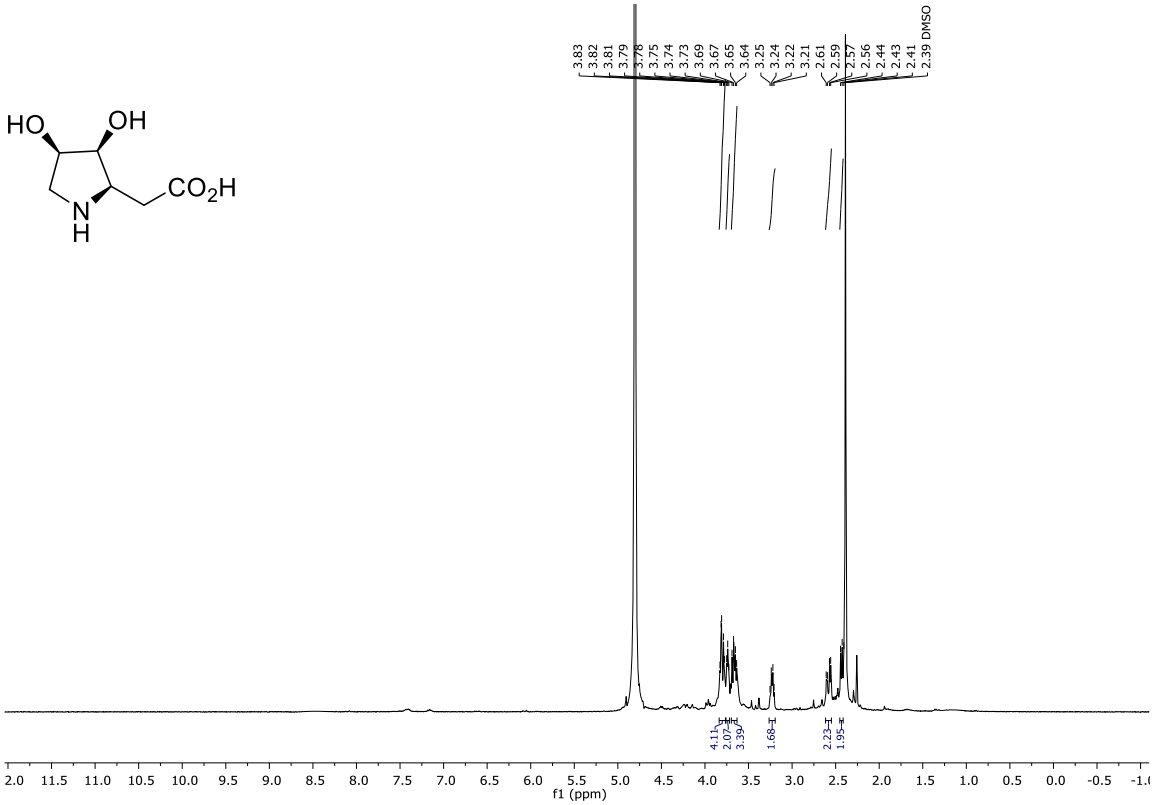


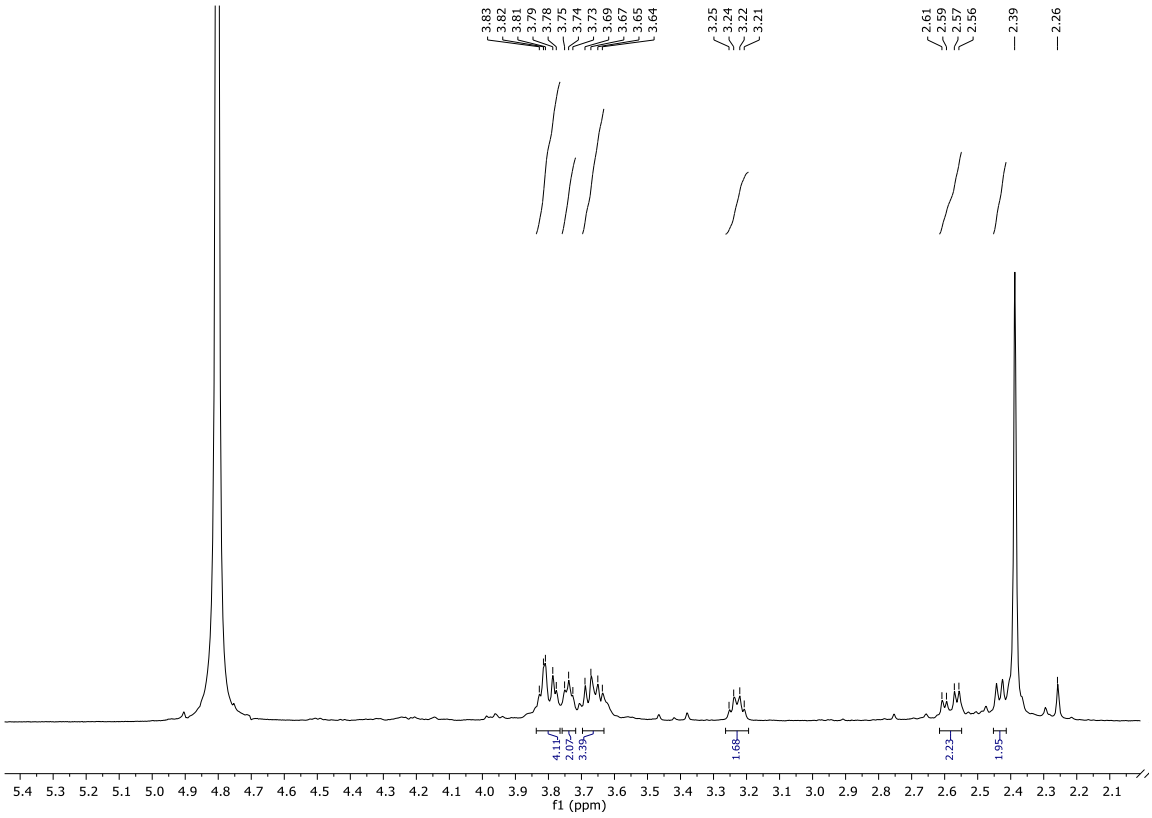


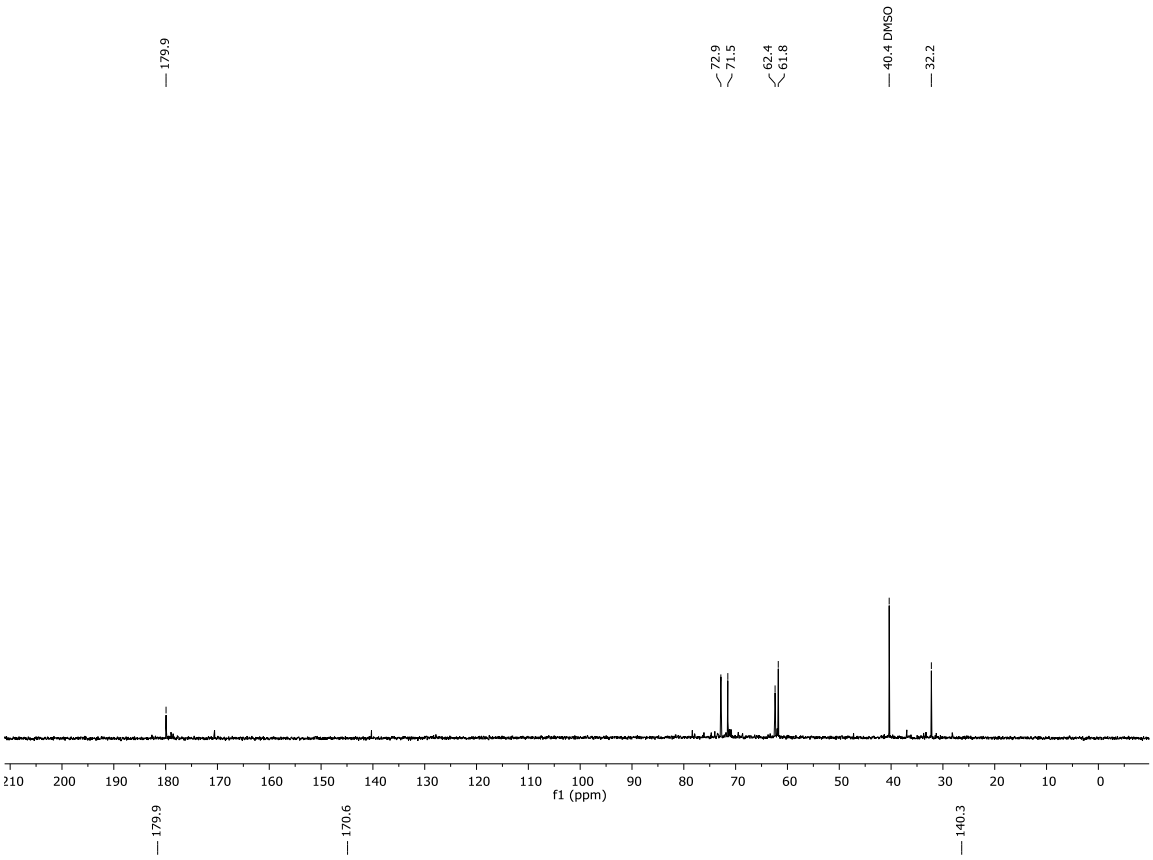

4.30
4.27
4.18
4.15
3.86
3.85
3.85
3.84
3.84
3.84
3.83
3.82
3.82
3.81
3.69
3.68
3.68
3.67
3.67
3.66
3.65
3.65
3.63
3.62
3.62
3.61
3.60
3.59
3.58
3.55
3.53
3.52
3.51
3.50
2.69
2.67
2.67
2.66
2.63
1.21
1.19
1.18
1.17
1.00
0.97
2.09
1.33
1.18
1.90
f1 (ppm)

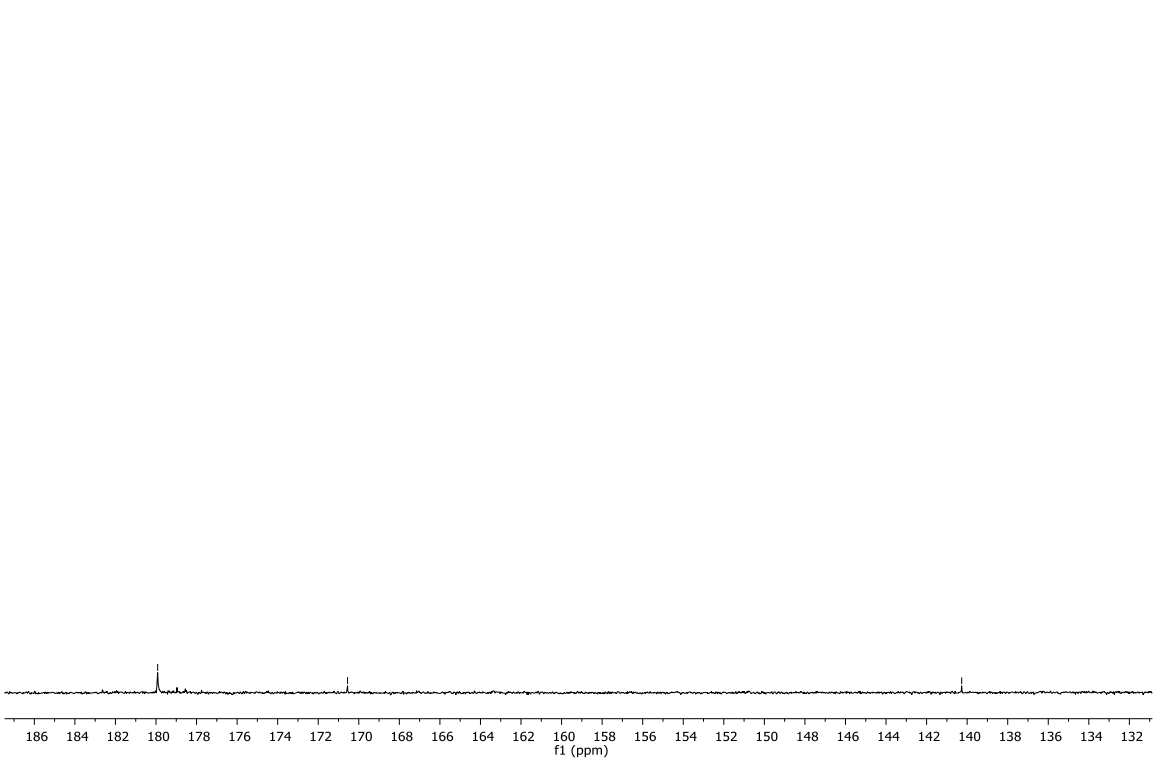

177.44
134.15
130.68
130.50
128.72
72.57
69.08
61.68
56.97
55.87
47.90
34.48
16.35
f1 (ppm)

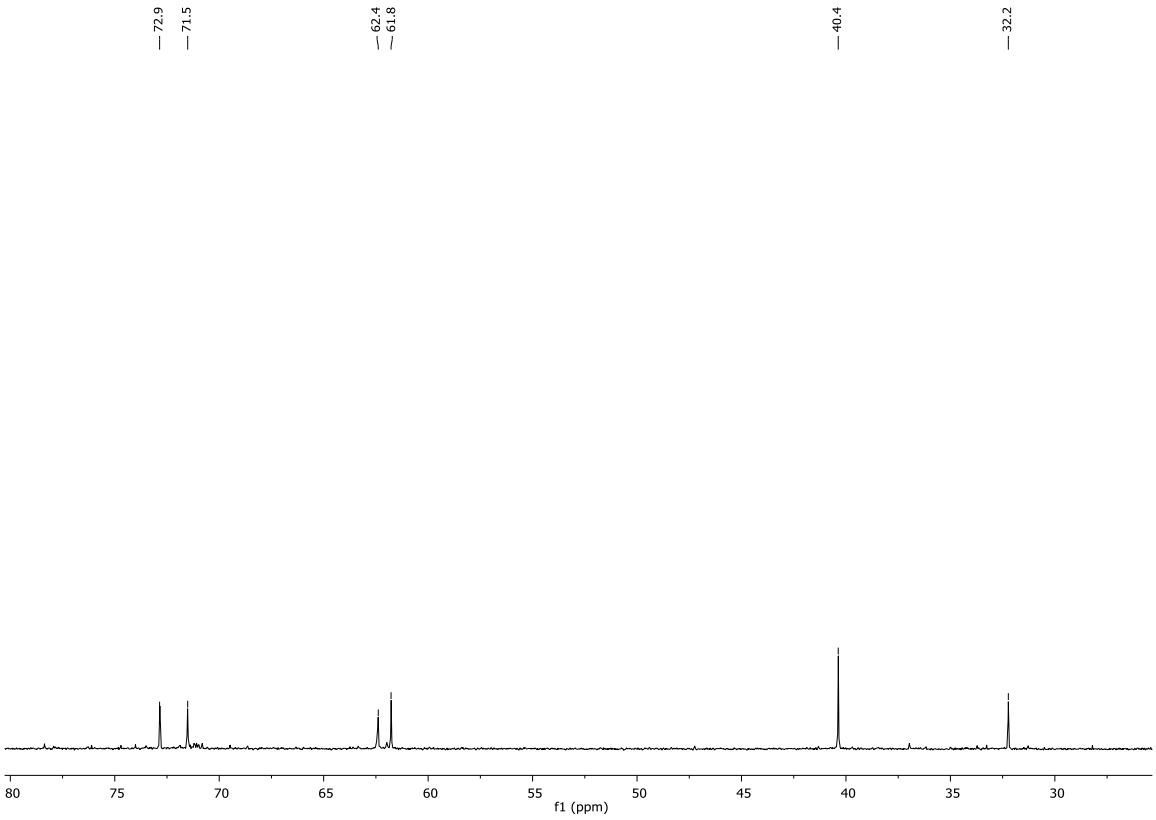
1.14. ^{1}H and ^{13}C NMR of compound **8e**





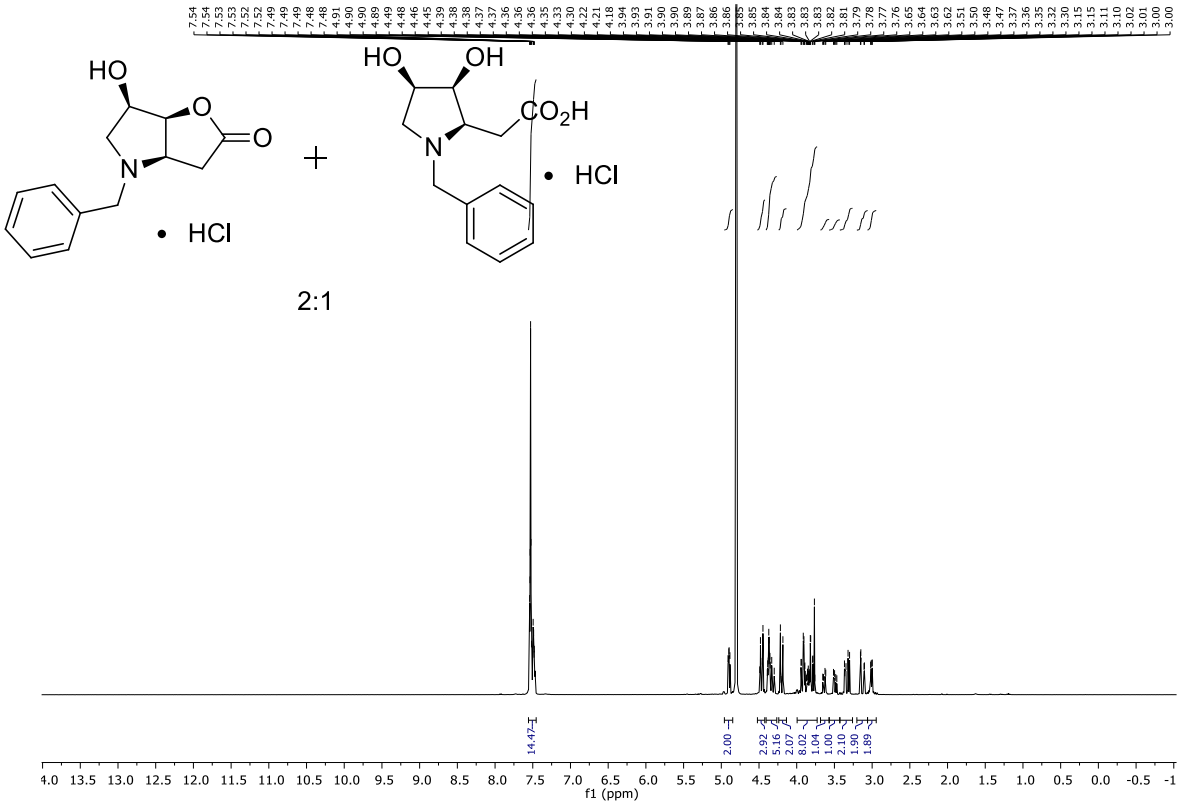

179.9
72.9
71.5
62.4
61.8
40.4 DMSO
32.2
f1 (ppm)

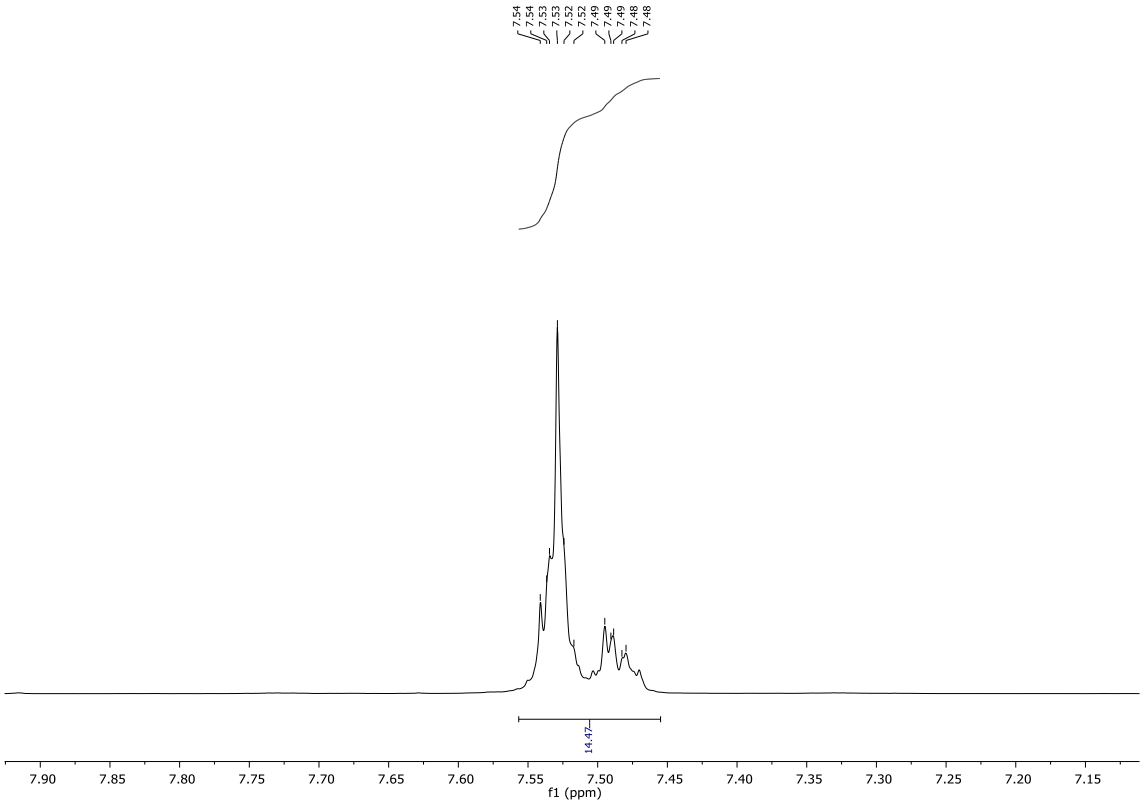

179.9
170.6
140.3
f1 (ppm)

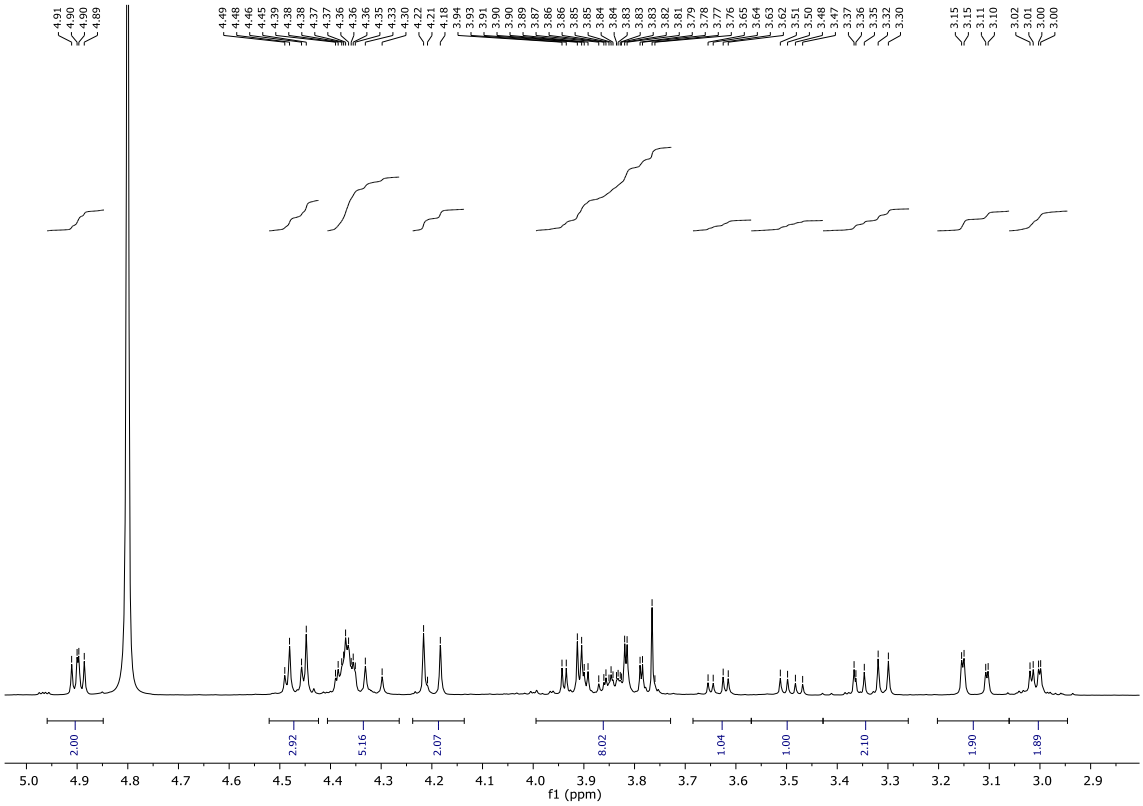

72.9
71.5
62.4
61.8
40.4
32.2
80
75
70
65
60
55
50
45
40
35
30
f1 (ppm)

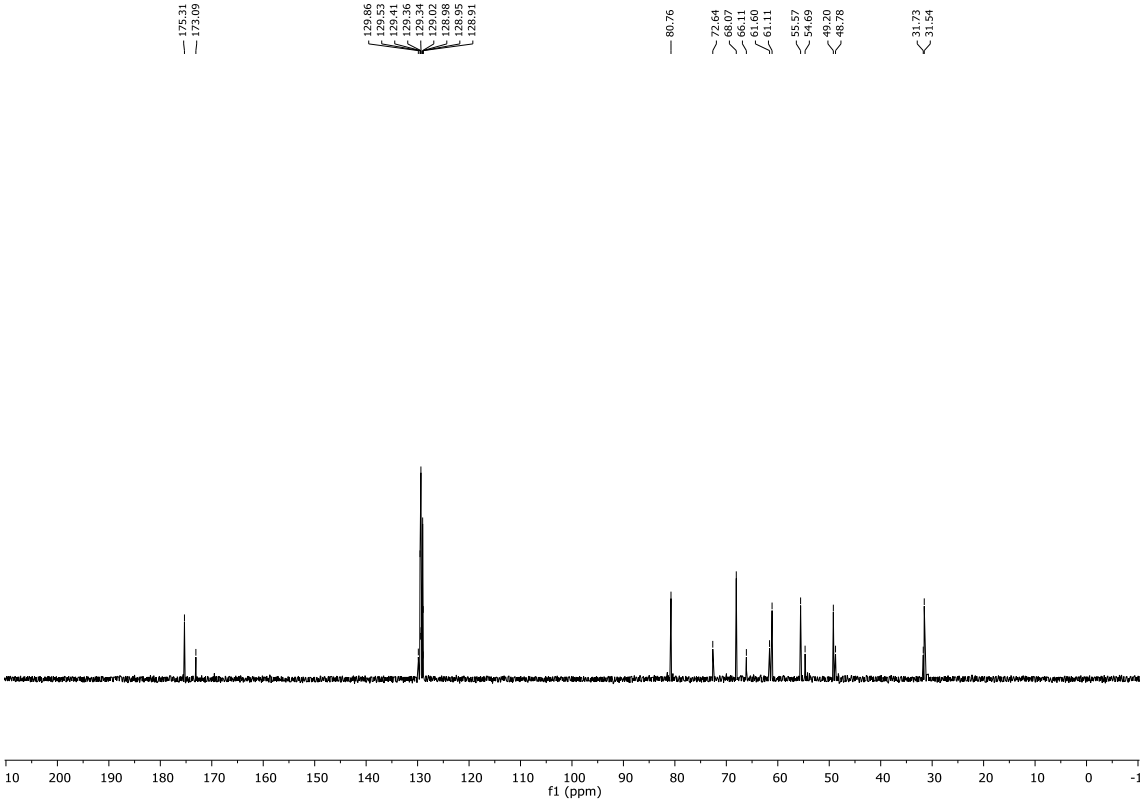
1.15. ^{1}H and ^{13}C NMR of compound **13a-8a**

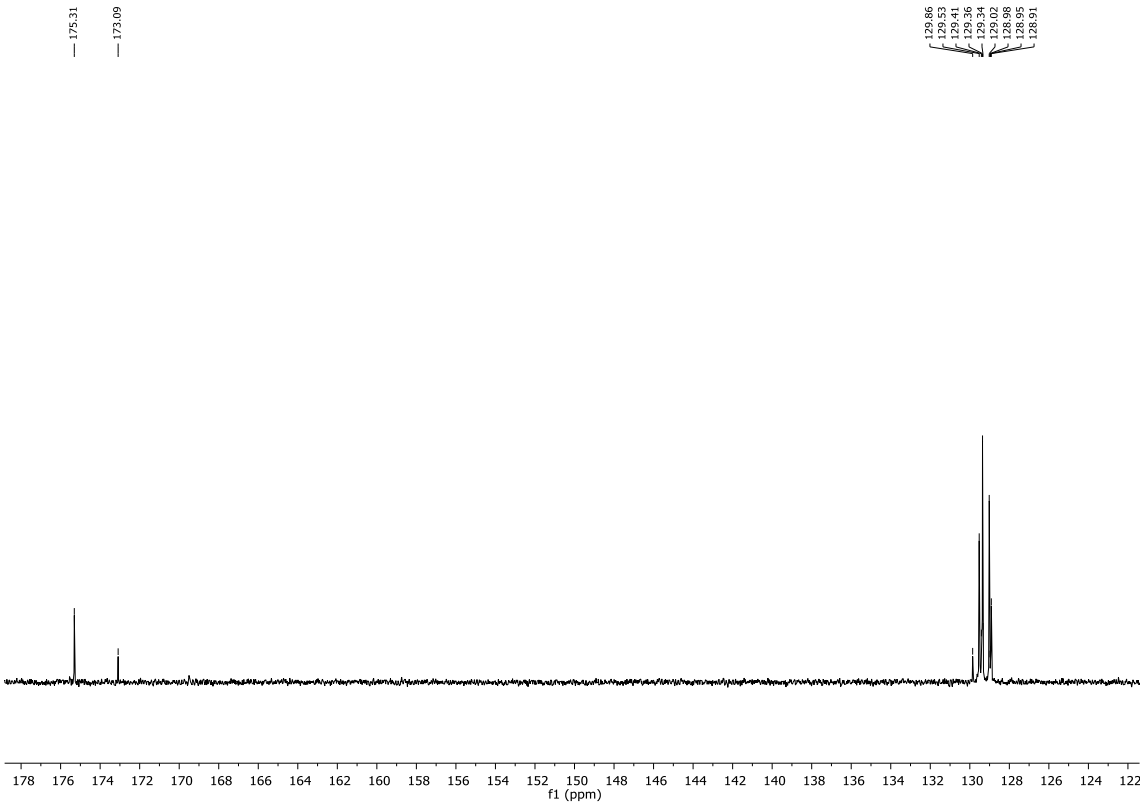
- **HCl**

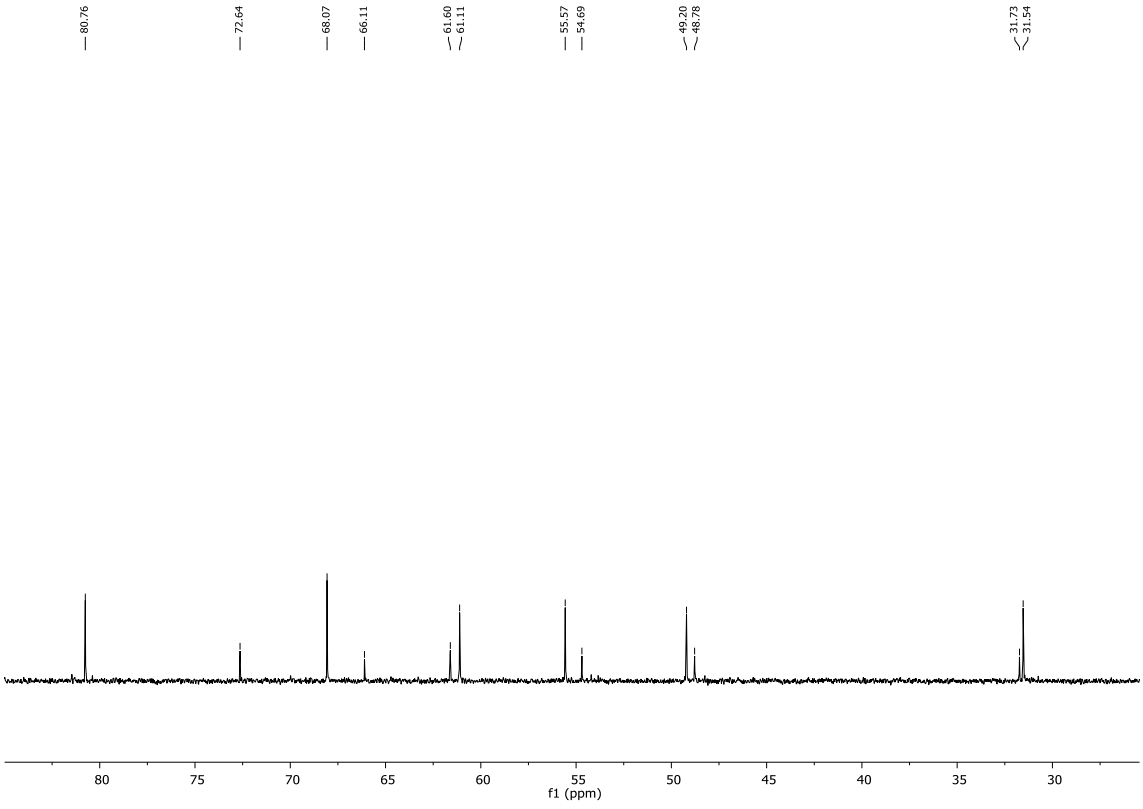




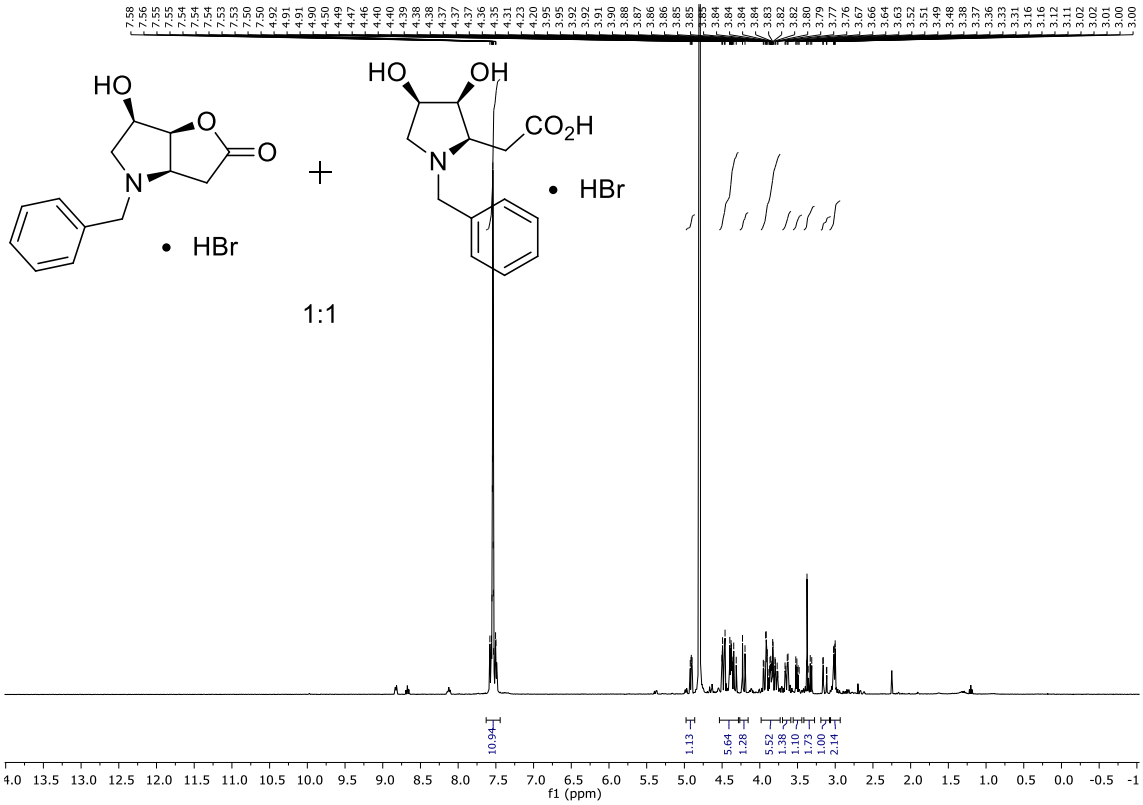

4.91
4.90
4.90
4.89
4.49
4.48
4.46
4.45
4.39
4.38
4.38
4.37
4.37
4.36
4.36
4.36
4.35
4.33
4.30
4.22
4.21
4.18
3.94
3.93
3.91
3.90
3.90
3.89
3.87
3.86
3.86
3.85
3.85
3.84
3.84
3.83
3.83
3.83
3.82
3.81
3.79
3.78
3.77
3.76
3.65
3.64
3.63
3.62
3.51
3.50
3.48
3.47
3.37
3.36
3.35
3.32
3.30
3.15
3.15
3.11
3.10
3.02
3.01
3.00
3.00
2.00
2.92
5.16
2.07
8.02
1.04
1.00
2.10
1.90
1.89
5.0
4.9
4.8
4.7
4.6
4.5
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
f1 (ppm)

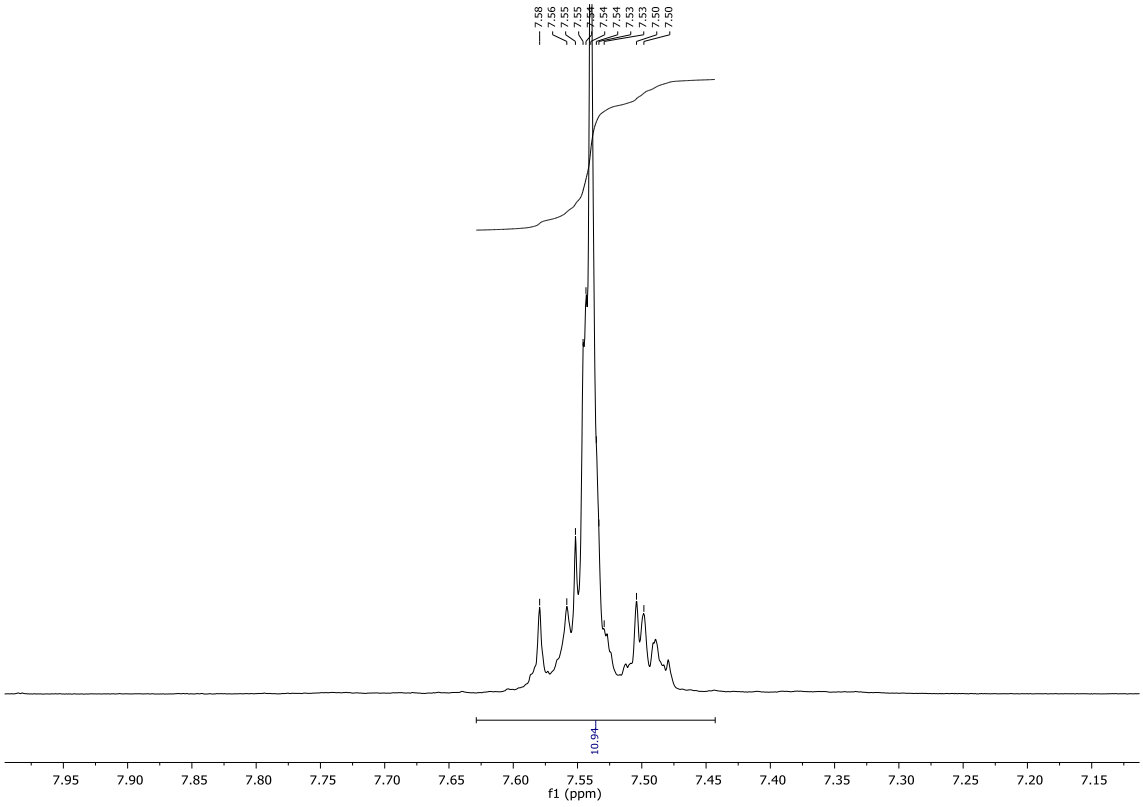

175.31
173.09
129.86
129.53
129.41
129.36
129.34
129.02
128.98
128.95
128.91
80.76
72.64
68.07
66.11
61.60
61.11
55.57
54.69
49.20
48.78
31.73
31.54
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

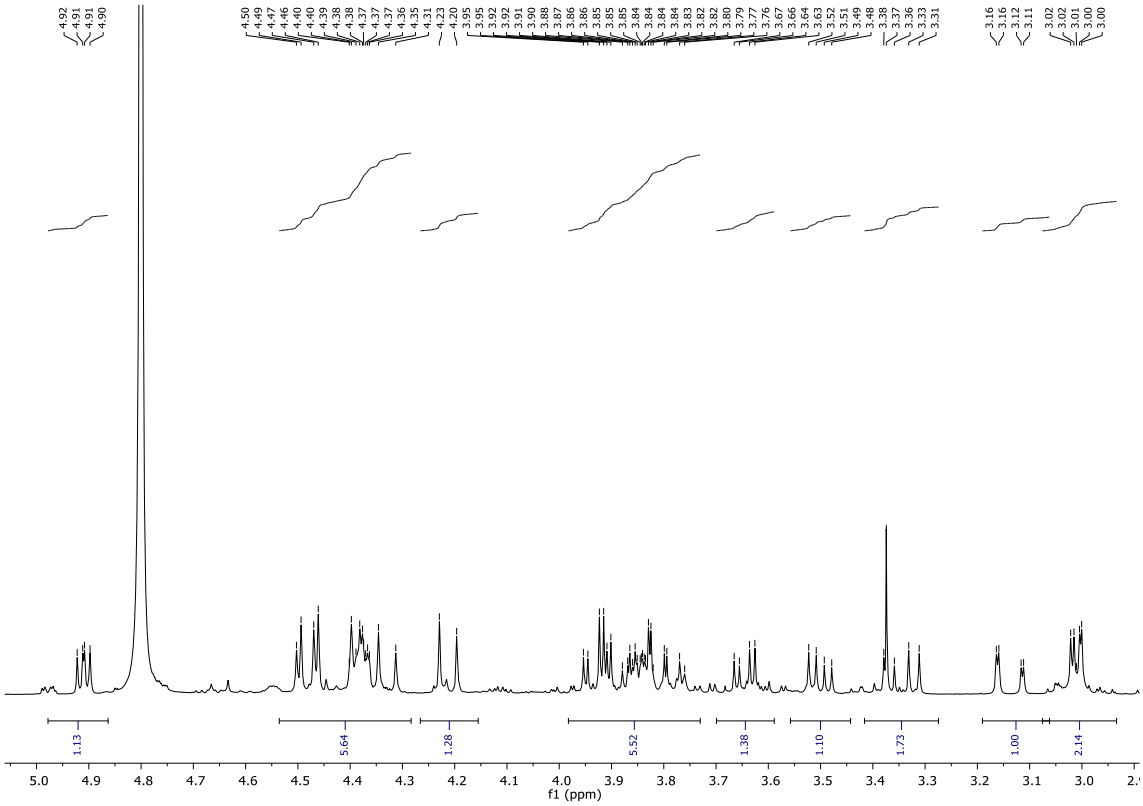

175.31
173.09
129.86
129.53
129.41
129.36
129.34
129.02
128.98
128.95
128.91
178 176 174 172 170 168 166 164 162 160 158 156 154 152 150 148 146 144 142 140 138 136 134 132 130 128 126 124 122
f1 (ppm)

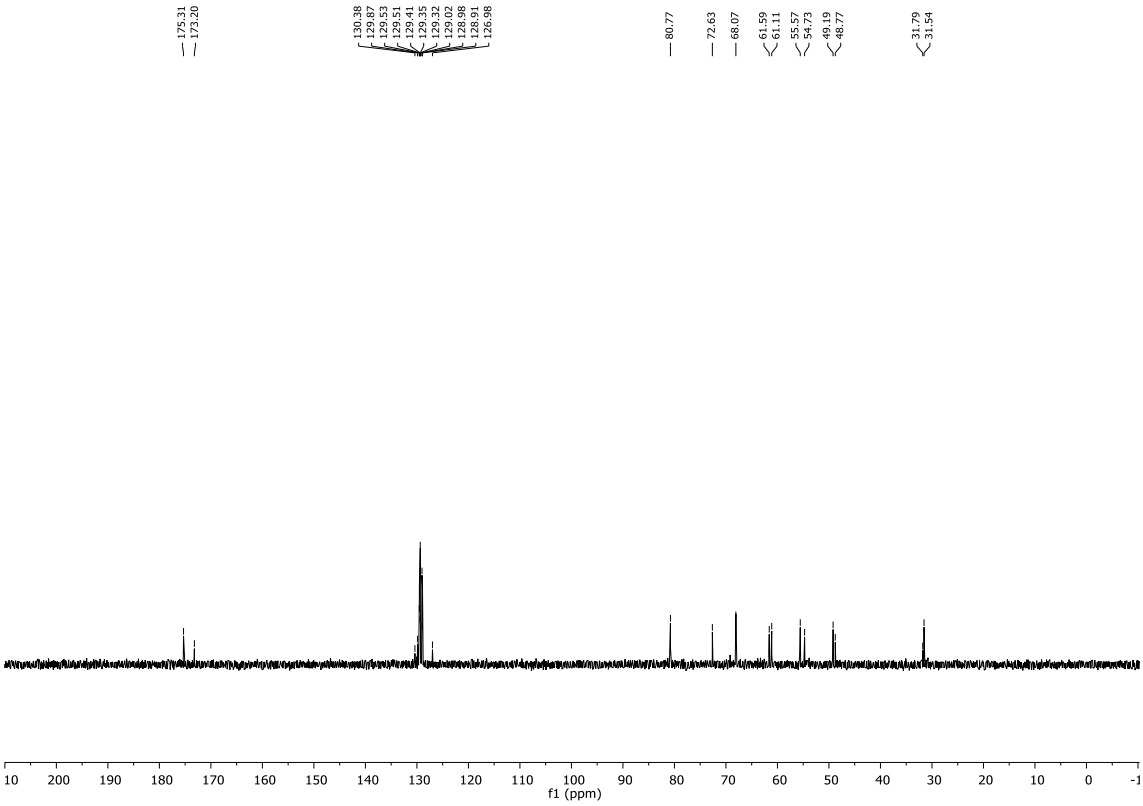

80.76
72.64
68.07
66.11
61.60
61.11
55.57
54.69
49.20
48.78
31.73
31.54
80 75 70 65 60 55 50 45 40 35 30
f1 (ppm)

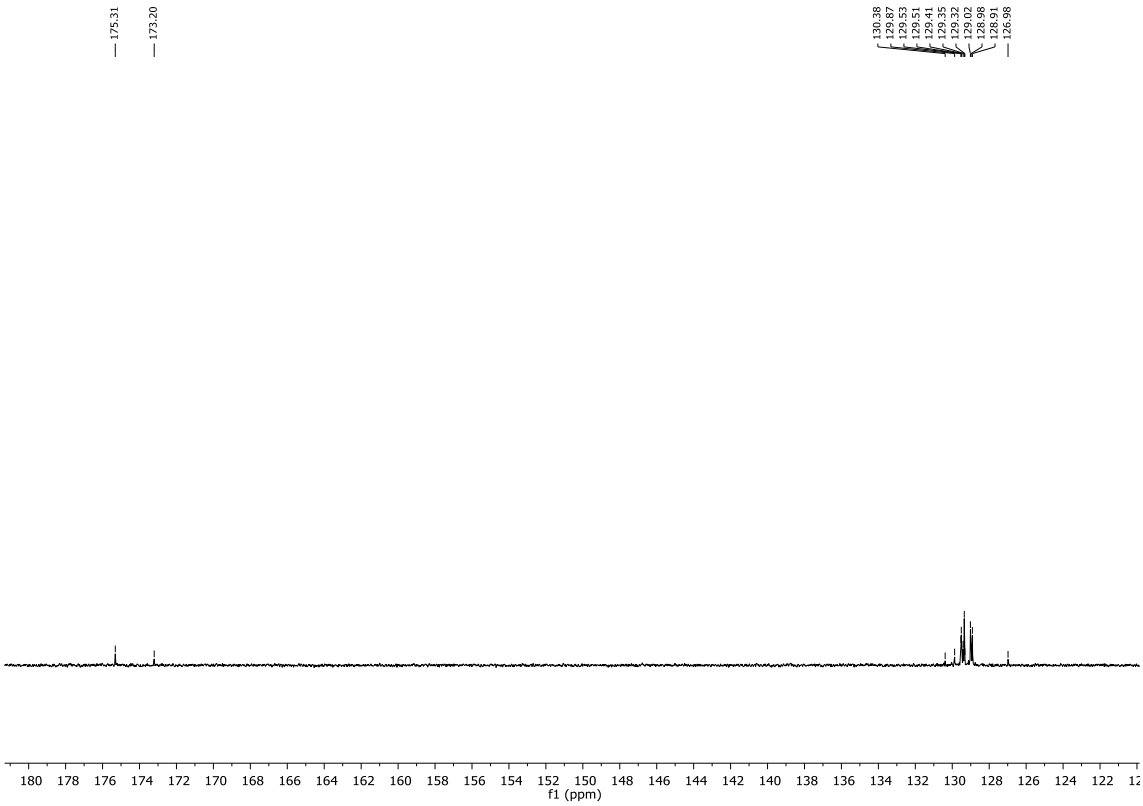
- **HBr**

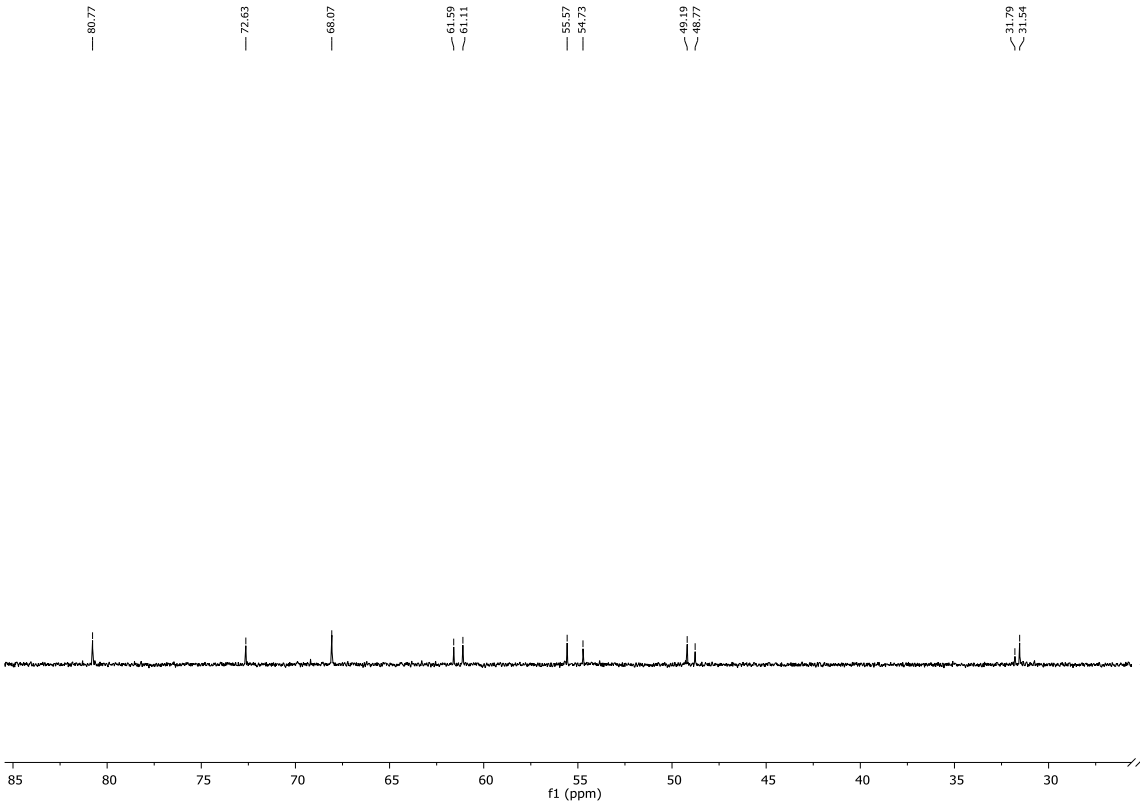

HO
O
O
N
• HBr
+
HO
OH
CO2H
N
• HBr
1:1
10.94
1.13
5.64
1.28
5.52
1.38
1.10
1.73
1.00
2.14
f1 (ppm)


10.94
f1 (ppm)

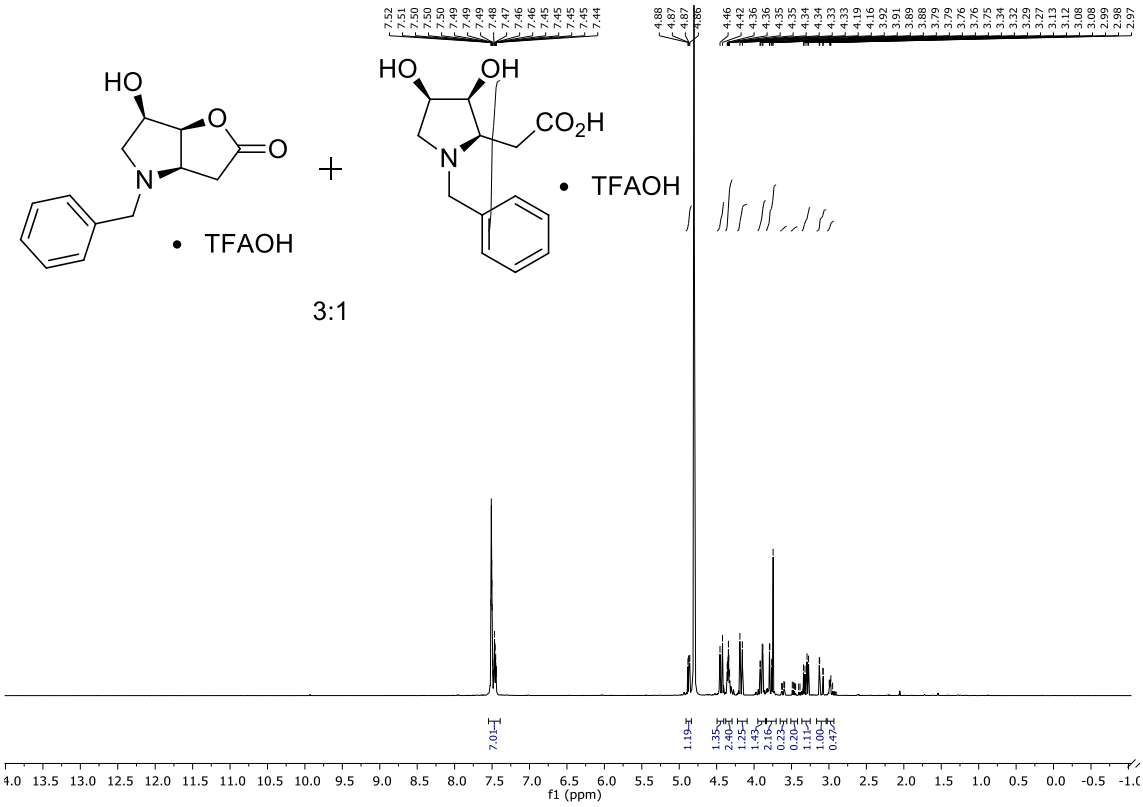

4.92 4.91 4.91 4.90
4.50 4.49 4.47 4.46 4.40 4.40 4.39 4.38 4.37 4.37 4.37 4.36 4.35 4.31 4.23 4.20 3.95 3.95 3.92 3.92 3.91 3.91 3.88 3.87 3.86 3.86 3.85 3.85 3.85 3.84 3.84 3.84 3.84 3.83 3.82 3.80 3.79 3.77 3.76 3.67 3.66 3.64 3.63 3.52 3.51 3.49 3.48 3.38 3.37 3.36 3.33 3.31
3.16 3.16 3.12 3.11 3.02 3.02 3.01 3.00 3.00
1.13 5.64 1.28 5.52 1.38 1.10 1.73 1.00 2.14
f1 (ppm)

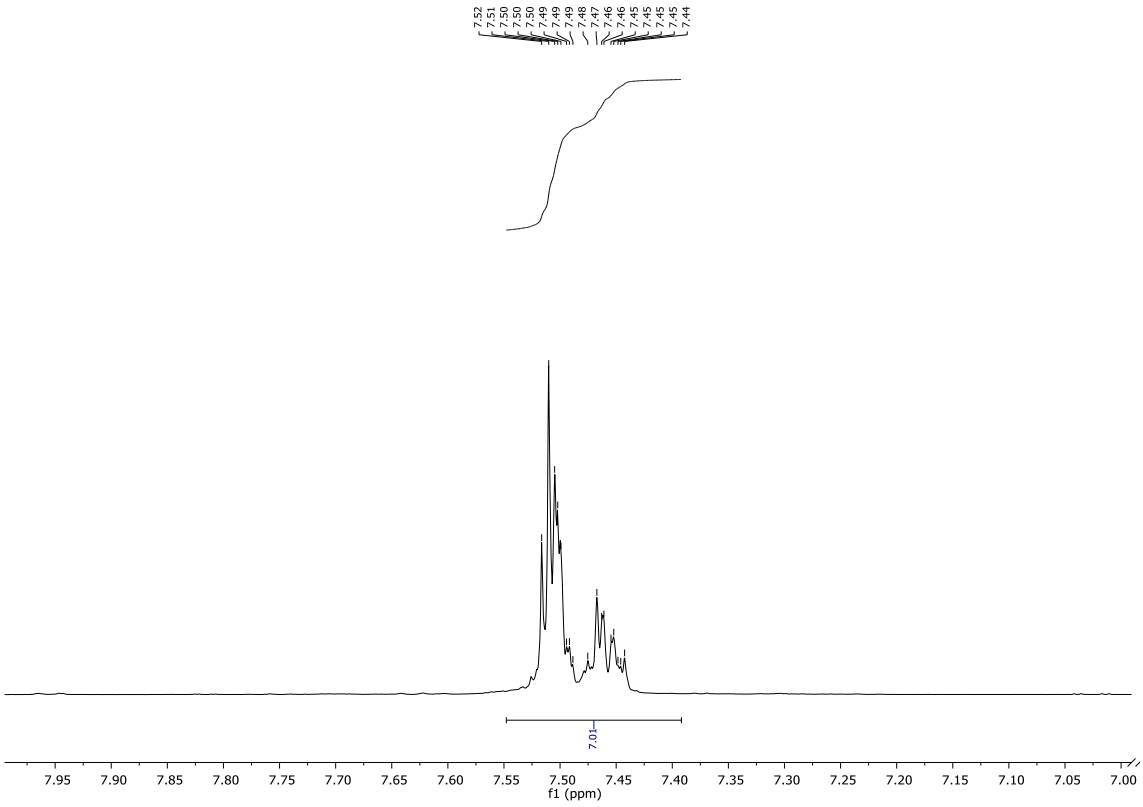

175.31 173.20
130.38 129.87 129.53 129.51 129.41 129.35 129.22 129.02 128.98 128.91 126.98
80.77 72.63 68.07 61.59 61.11 55.57 54.73 49.19 48.77 31.79 31.54
f1 (ppm)

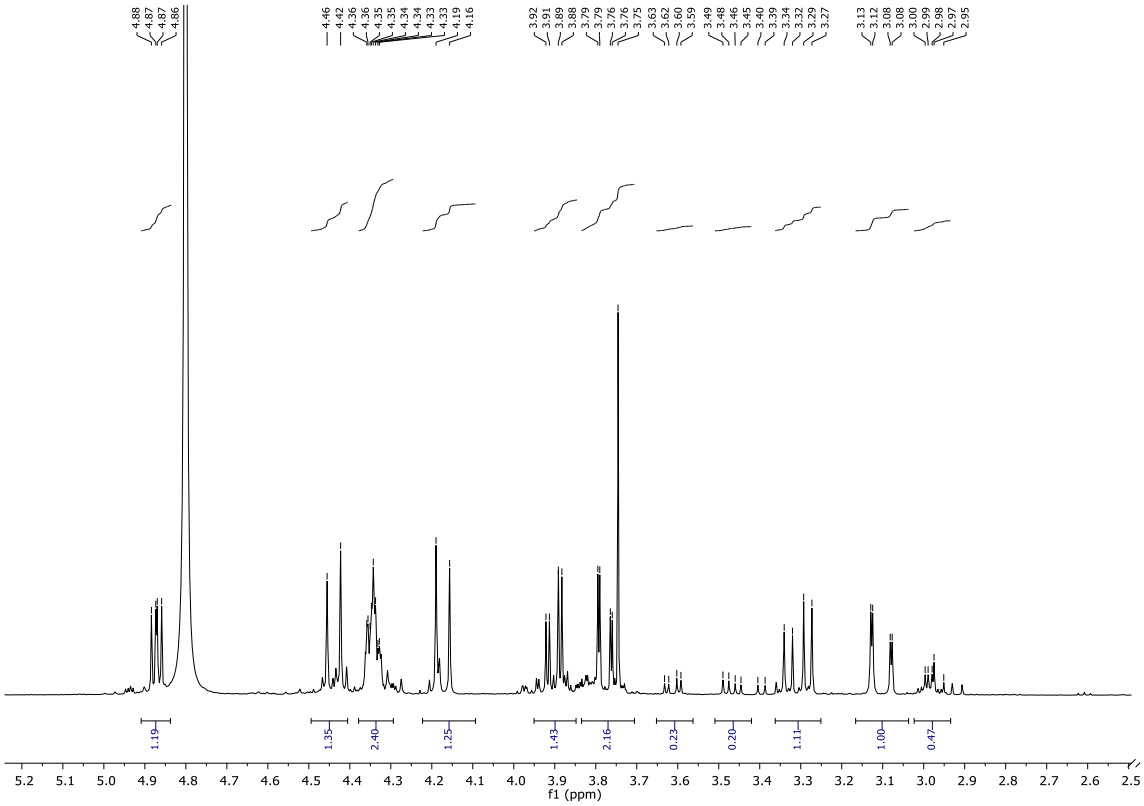

175.31
173.20
130.38
129.87
129.53
129.51
129.41
129.35
129.32
129.02
128.98
128.91
126.98
180 178 176 174 172 170 168 166 164 162 160 158 156 154 152 150 148 146 144 142 140 138 136 134 132 130 128 126 124 122
f1 (ppm)

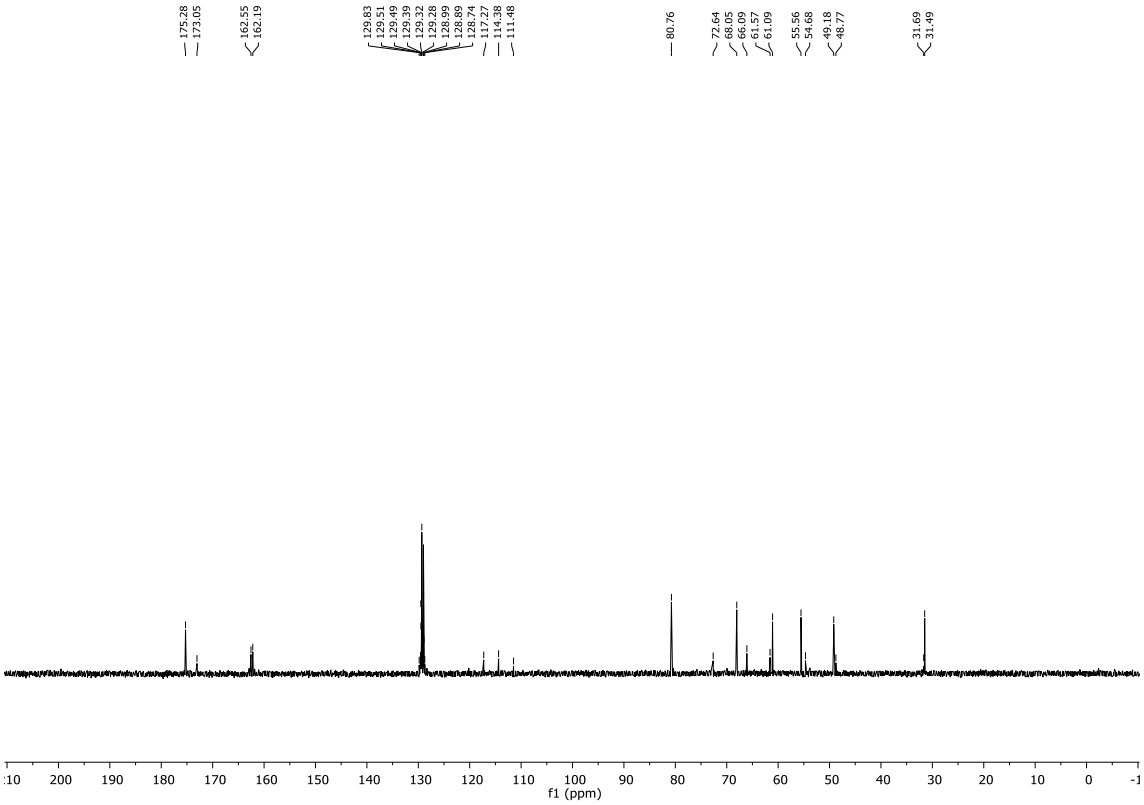

80.77
72.63
68.07
61.59
61.11
55.57
54.73
49.19
48.77
31.79
31.54
85 80 75 70 65 60 55 50 45 40 35 30
f1 (ppm)

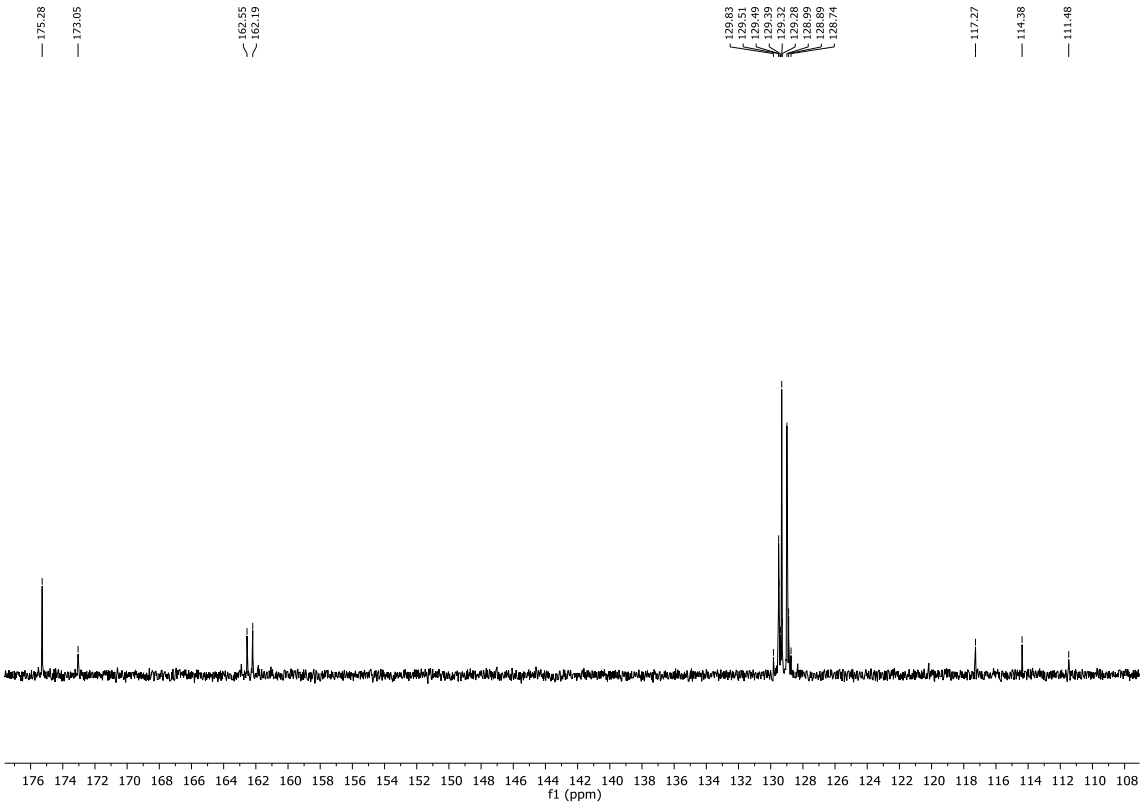
- **TFAOH**

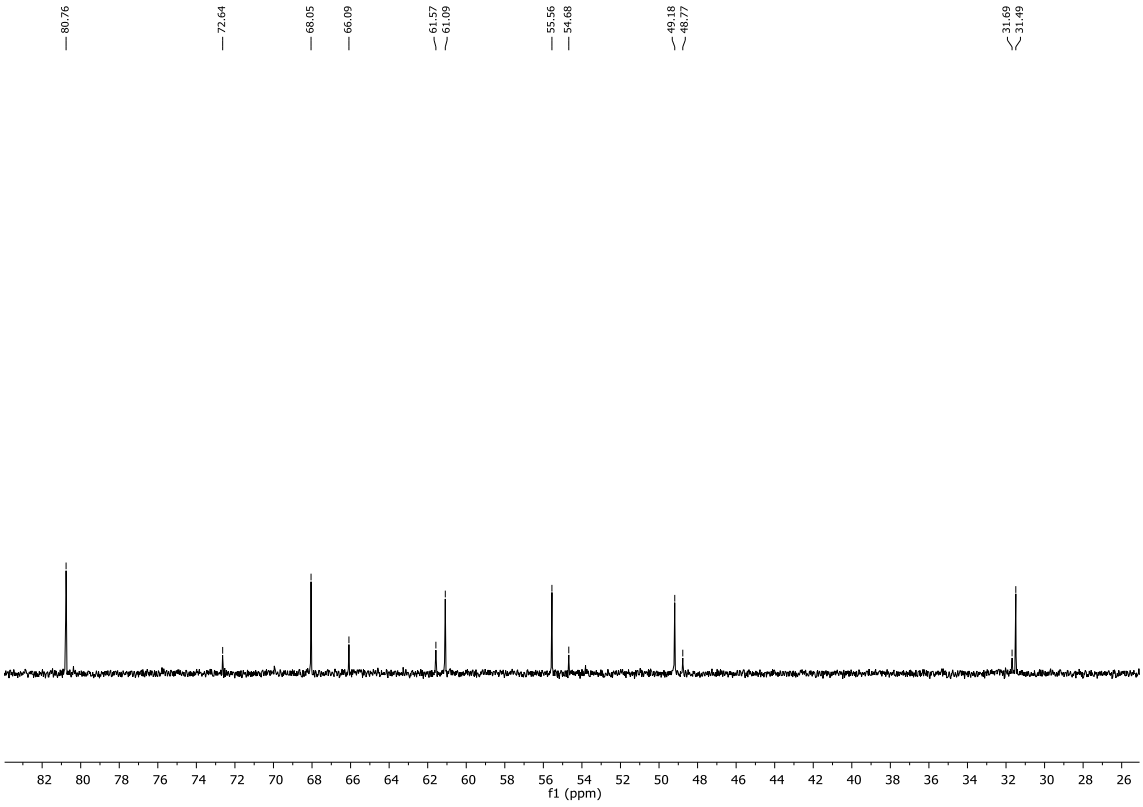





4.88
4.87
4.87
4.86
4.46
4.42
4.36
4.36
4.35
4.34
4.34
4.33
4.19
4.16
3.92
3.91
3.89
3.88
3.79
3.79
3.76
3.76
3.75
3.63
3.62
3.60
3.59
3.49
3.48
3.46
3.45
3.40
3.39
3.34
3.32
3.29
3.27
3.13
3.12
3.08
3.08
3.00
2.99
2.98
2.97
2.95
1.19
1.35
2.40
1.25
1.43
2.16
0.23
0.20
1.11
1.00
0.47
5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5
f1 (ppm)


175.28
173.05
162.55
162.19
129.83
129.51
129.49
129.39
129.32
129.28
128.99
128.89
128.74
117.27
114.38
111.48
80.76
72.64
68.05
66.09
61.57
61.09
55.56
54.68
49.18
48.77
31.69
31.49
:10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)


175.28
173.05
162.55
162.19
129.83
129.51
129.49
129.39
129.32
129.28
128.99
128.89
128.74
117.27
114.38
111.48
176 174 172 170 168 166 164 162 160 158 156 154 152 150 148 146 144 142 140 138 136 134 132 130 128 126 124 122 120 118 116 114 112 110 108
f1 (ppm)


80.76
72.64
68.05
66.09
61.57
61.09
55.56
54.68
49.18
48.77
31.69
31.49
82 80 78 76 74 72 70 68 66 64 62 60 58 56 54 52 50 48 46 44 42 40 38 36 34 32 30 28 26
f1 (ppm)