Supporting information

Forming Spirocyclohexadienone-oxocarbenium Cation Species in the Biomimetic Synthesis of Amomols

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Table of contents

General Synthetic Information

All reagents were used as purchased from commercial suppliers. Solvent were purified by conventional methods prior to use. For reactions performed under anhydrous conditions, glassware was oven-dried and reactions were performed under argon atmosphere. Reactions were monitored by thin-layer chromatography with 0.20 mm pre-coated silica gel plates ($60F_{254}$). Detection was monitored by UV absorbance (254 nm) or by reaction with cerium/molybdenum solution [phosphomolybdic acid (25 g), cerium sulfate (10 g), concd. H_2SO_4 (80 mL), H_2O (1 L)]. Flash column chromatography was performed on silica gel 0.04-0.063mm (230-400 mesh).

^1H and ^{13}C NMR spectra were recorded at room temperature in deuterated solvents with spectrometer at 400 MHz for ^1H and 100 MHz for ^{13}C. Chemical shifts δ are given relative to TMS as internal standard or relative to the solvent [^1H: $\delta(CDCl_3)$ = 7.24 ppm, ^{13}C: $\delta(CDCl_3)$ = 77.23 ppm]. Optical rotations data was reported follows: [ ]^{temperature}D (concentration c = g/100 mL, solvent). Mass spectra (low resolution) were recorded with ESI ionization. High resolution mass spectra were carried out on (MALDI) spectrometer.

In vitro antimalarial activity against *Plasmodium falciparum*

Drug effects on *in vitro P.falciparum*[1] growth was measured in microtiter plates according to Desjardins and co-workers[2] The final volume in each well was 200 µL consisting of 50 µL of complete medium **CM**[3] without (controls) or with drug and 150 µL of *P. falciparum*-infected erythrocyte suspension (1.5% final hematocrite and 0.6% parasitemia).

Drug (previously dissolved in DMSO) were diluted in culture medium so that final DMSO concentration never exceeded 0.25%.

After 48 h incubation at 37°C, 30 µL of complete medium containing 0.6µCi [^{3}H]-hypoxanthine were added to each well. After 18 h at 37°C, cells lyzed using an automatic cell harvester and the parasite macromolecules, including radioactive nucleic acids, were retained onto glass fiber filters. The filters were counted for radioactivity, after adding scintillation cocktail, in a liquid scintillation spectrometer.

Radioactivity background was obtained from incubation of non-infected erythrocytes under the same condition, and deduced.

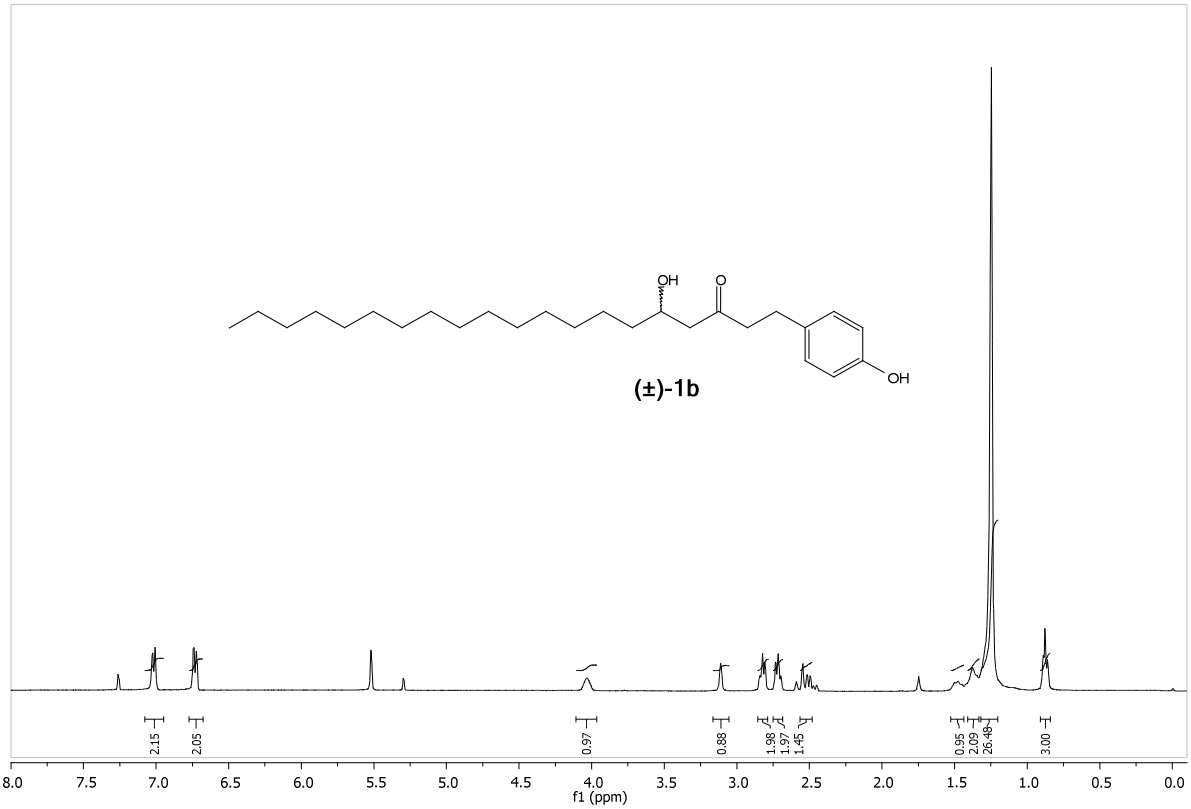
Parasitic viability was expressed as IC_{50} which is the drug concentration leading to 50% parasite growth inhibition.

IC_{50} values represent the mean of at least two independent experiments carried out in triplicate.

[1] *P. falciparum* strain = 3D7

[2] Desjardin, R. E.; Canfield, C. J.; Haynes, J. D.; Chulay, J. D.; Quantitative assessment of antimalarial activity *in vitro* by a semiautomated microdilution technique. *Antimicrob. Agents Chemoth*. **1979**, *16*, 710-718.

[3] RPMI 1640 + 10% AB human serum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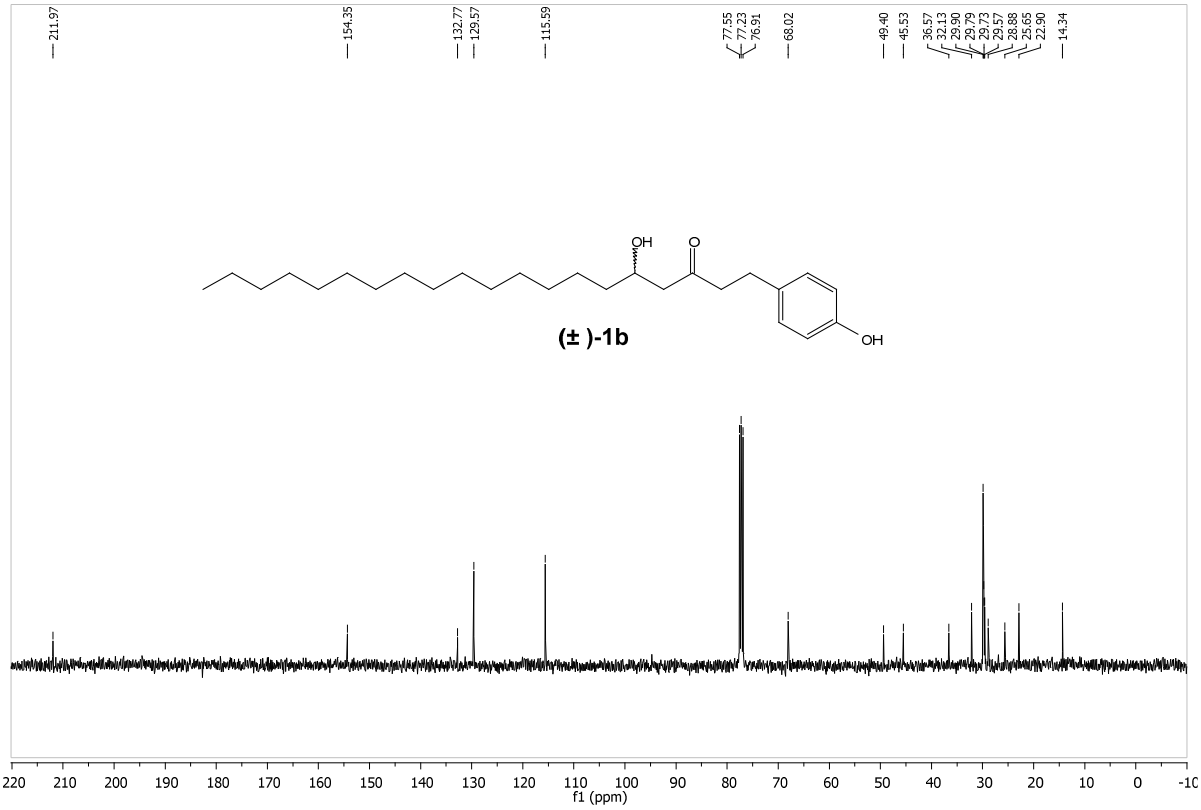
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OH
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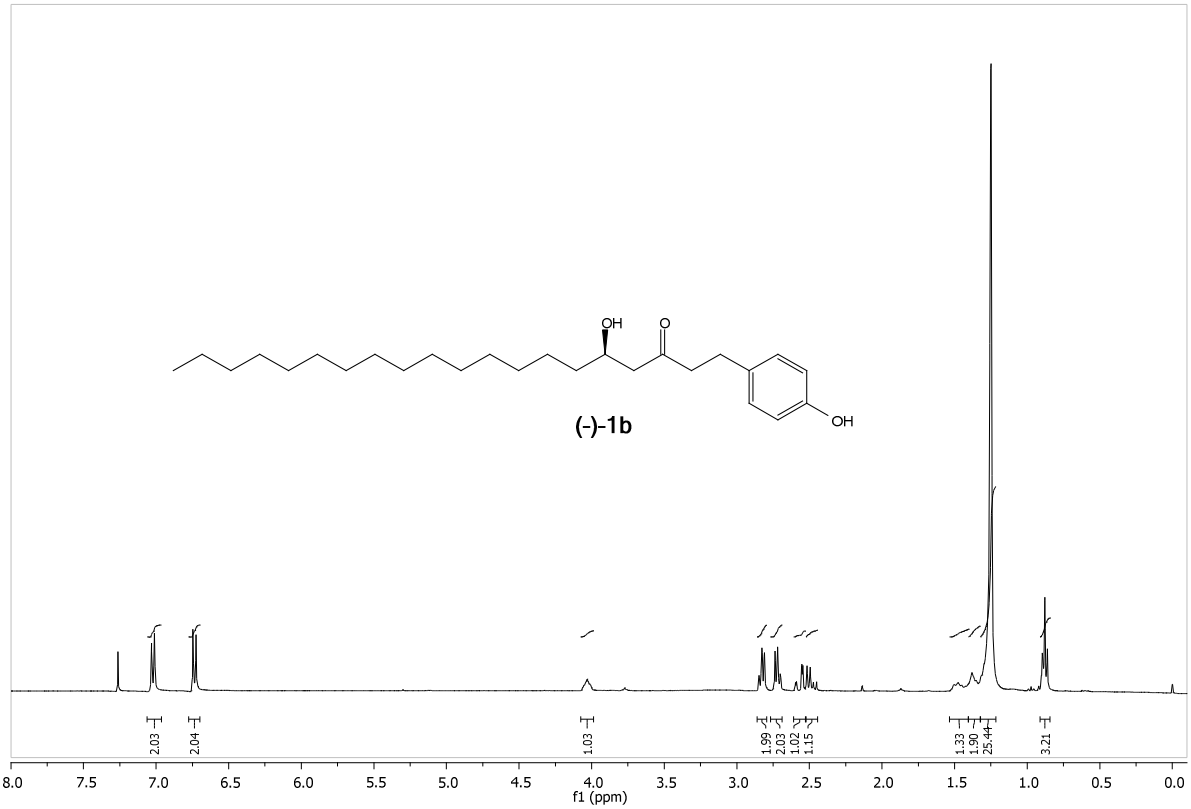
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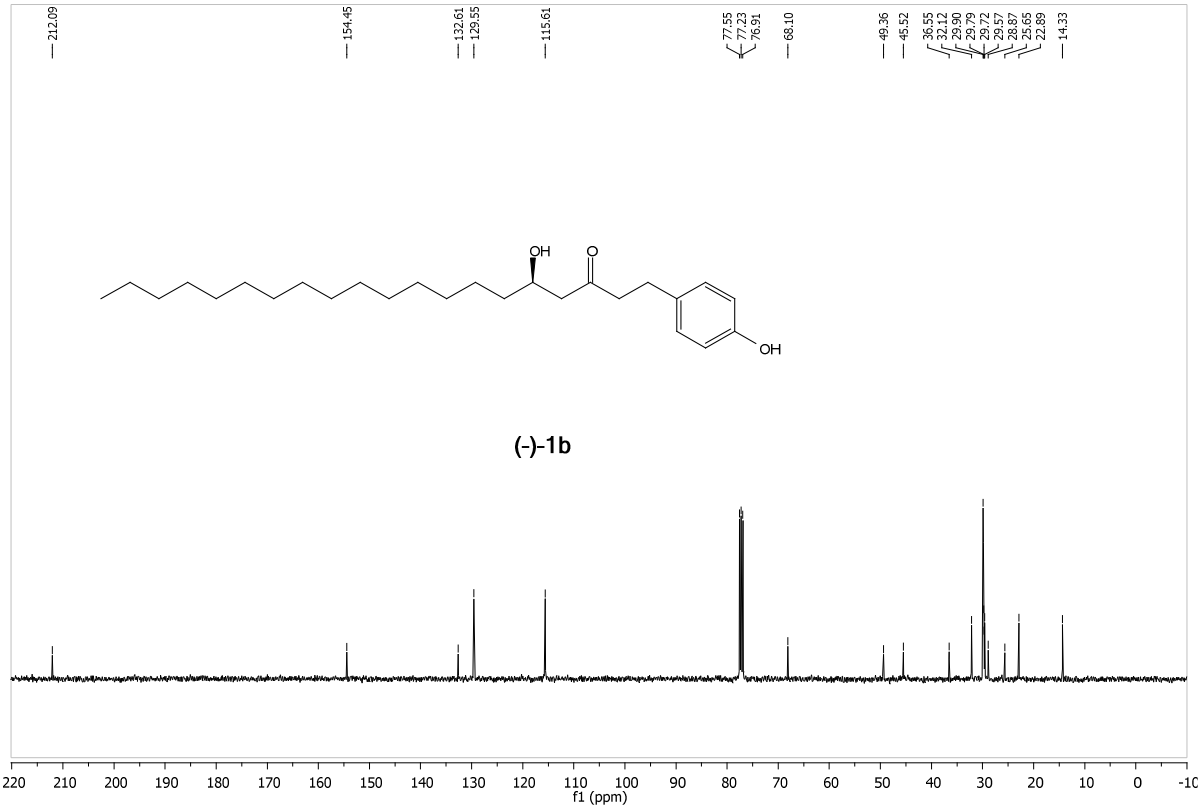
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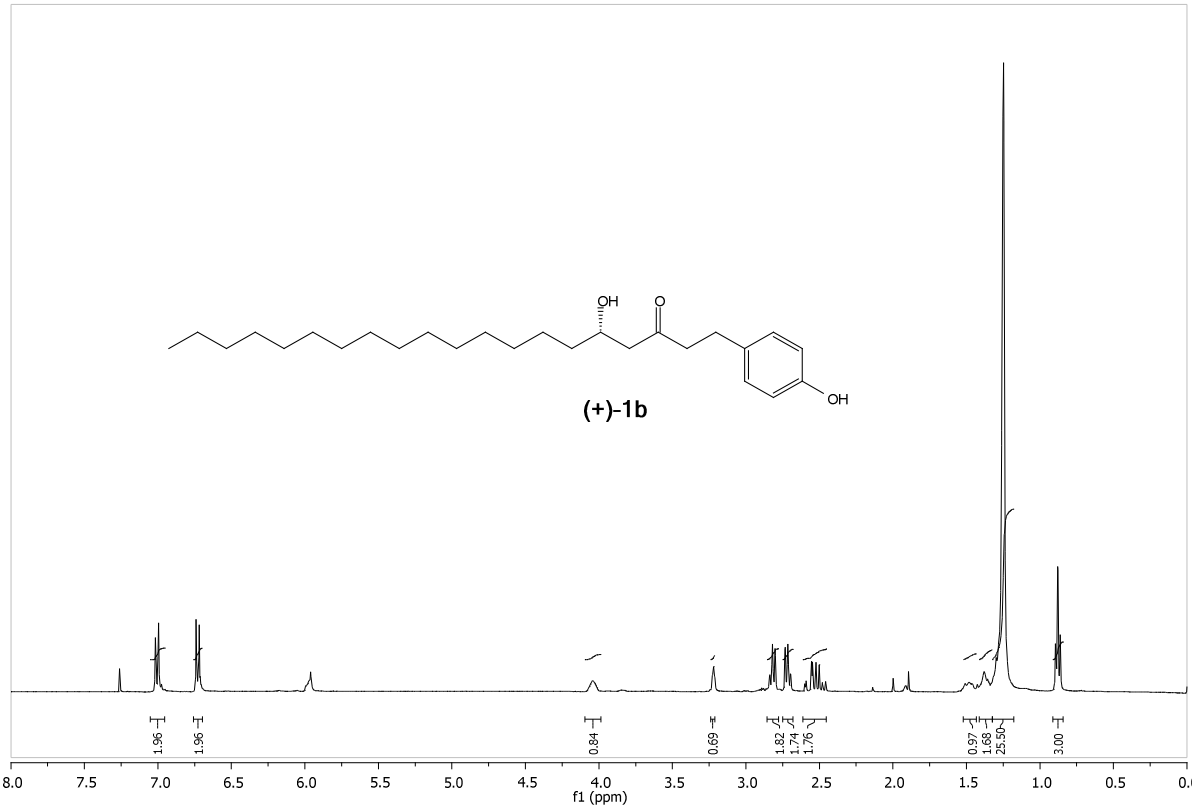
f1 (ppm)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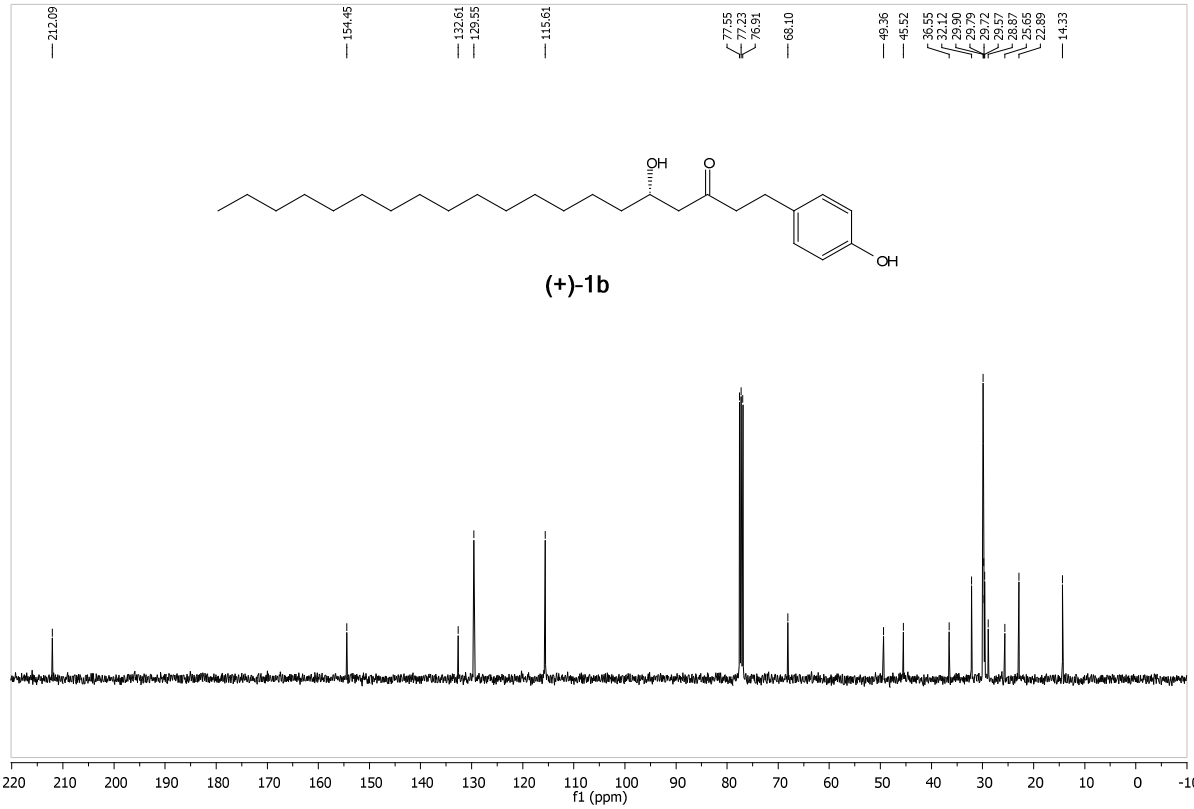
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32.12
29.90
29.79
29.72
29.57
28.87
25.65
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OH
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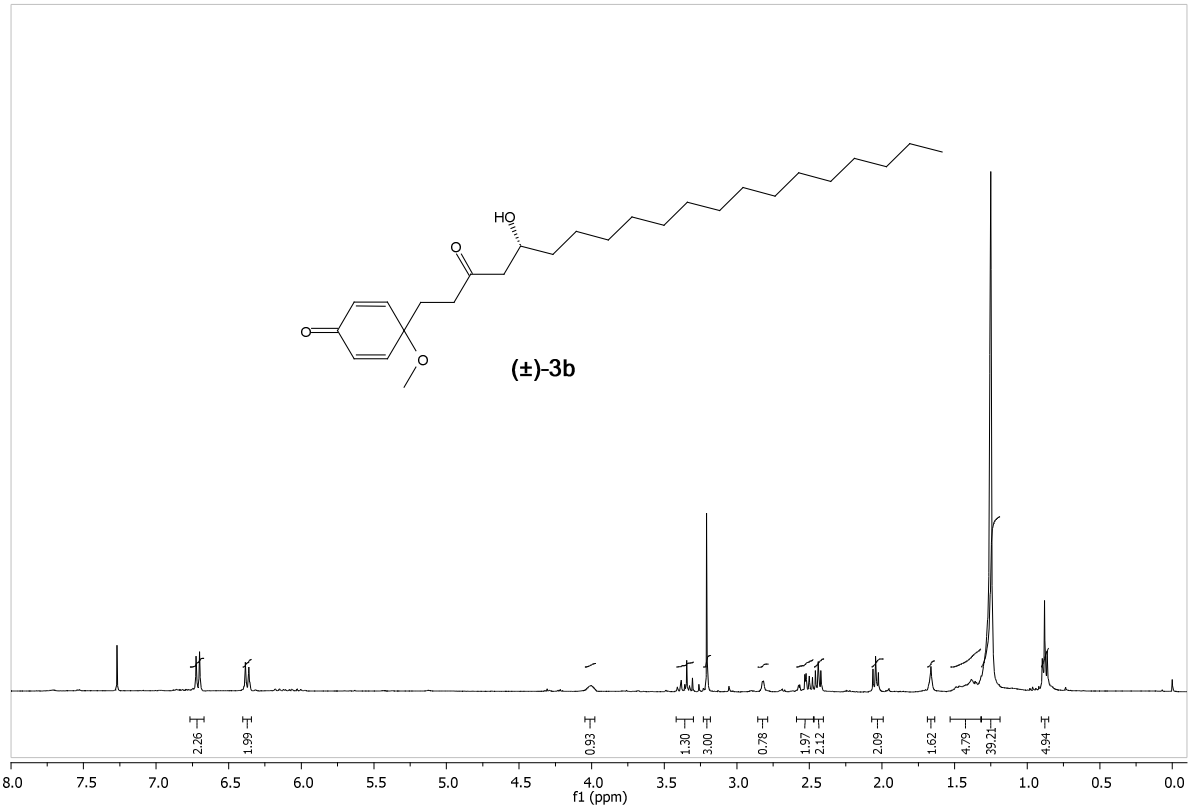
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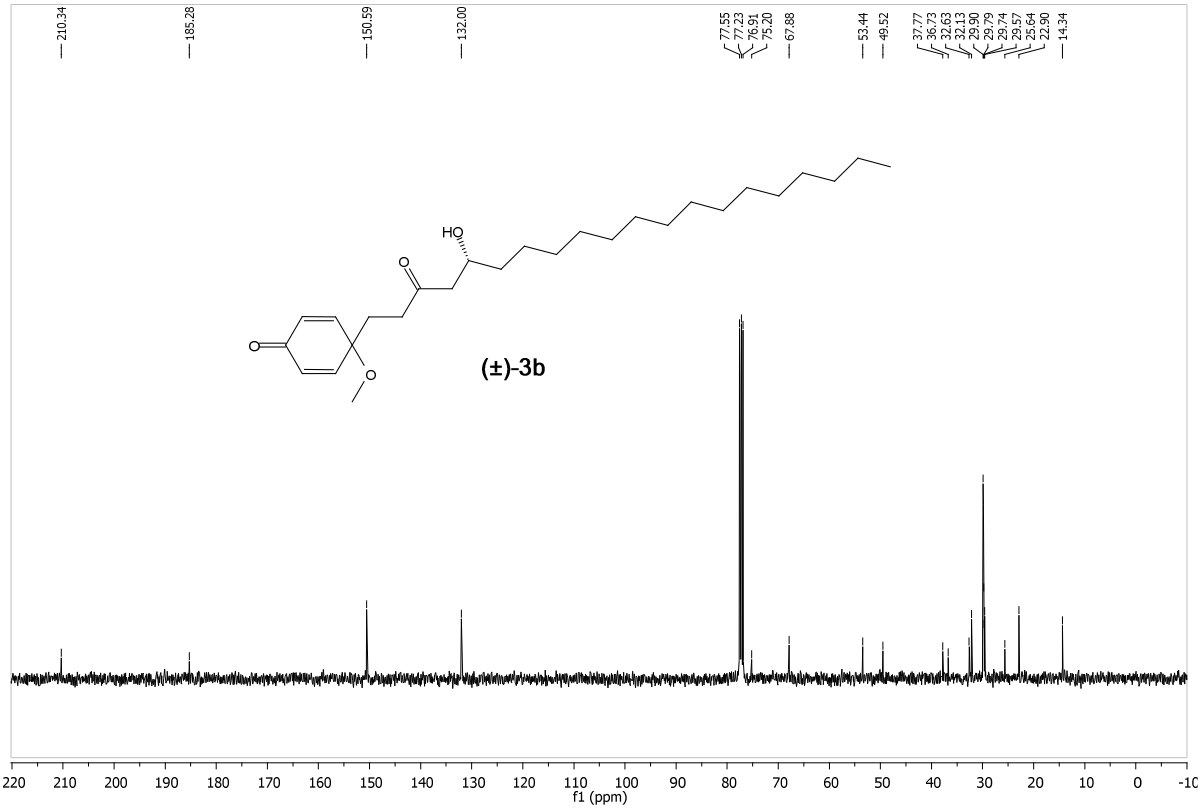
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25.64
22.90
14.34
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O
O
O
(±)-3b
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210
200
190
180
170
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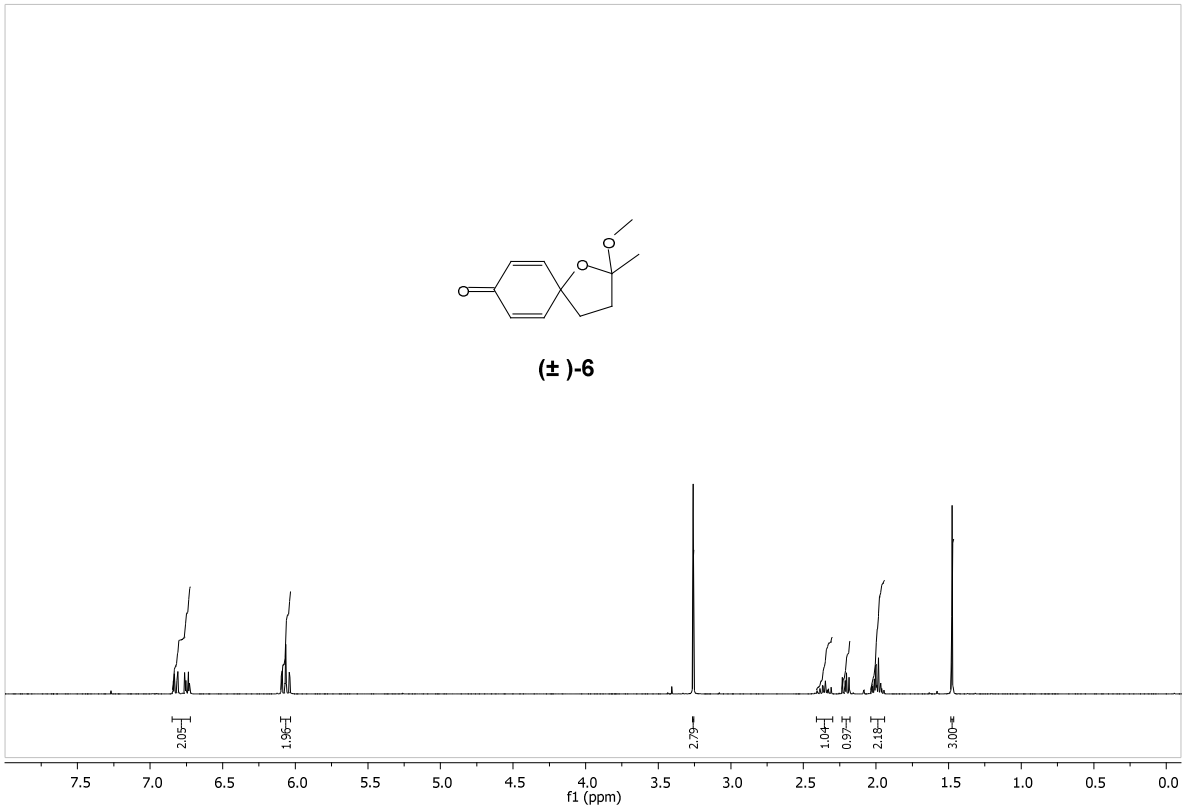
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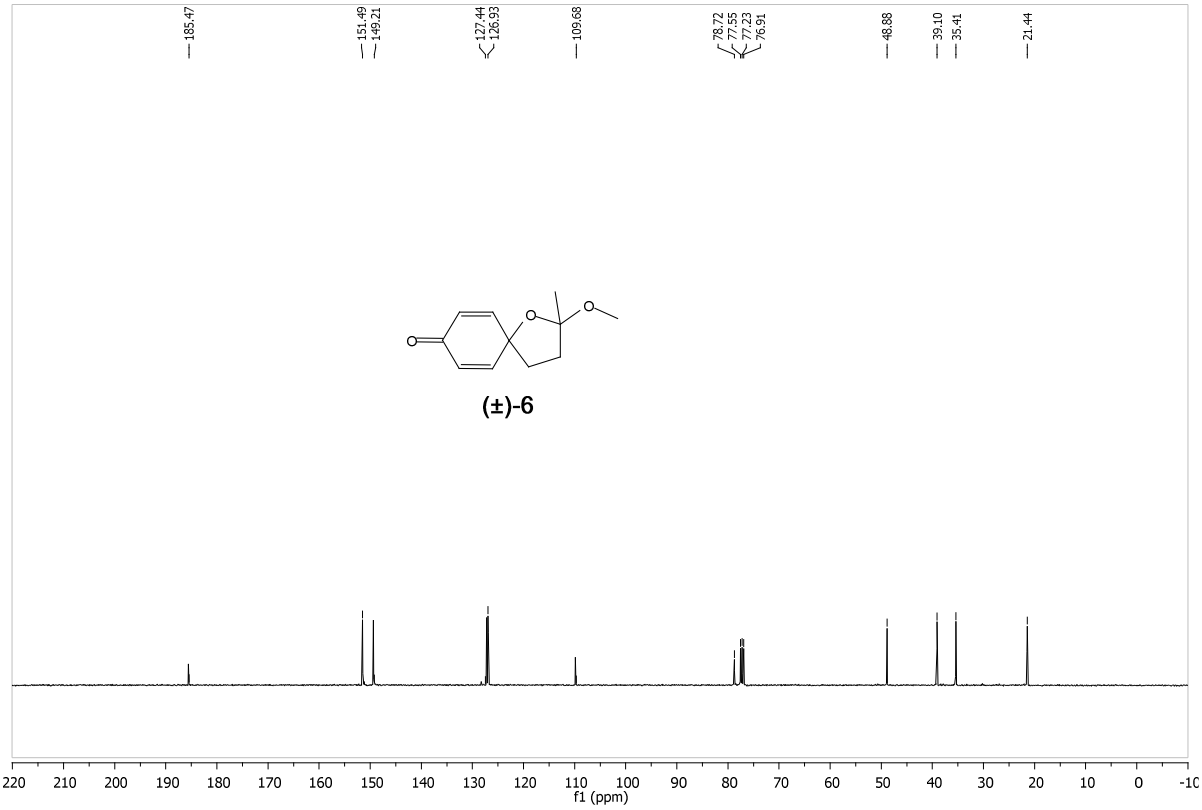
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210
200
190
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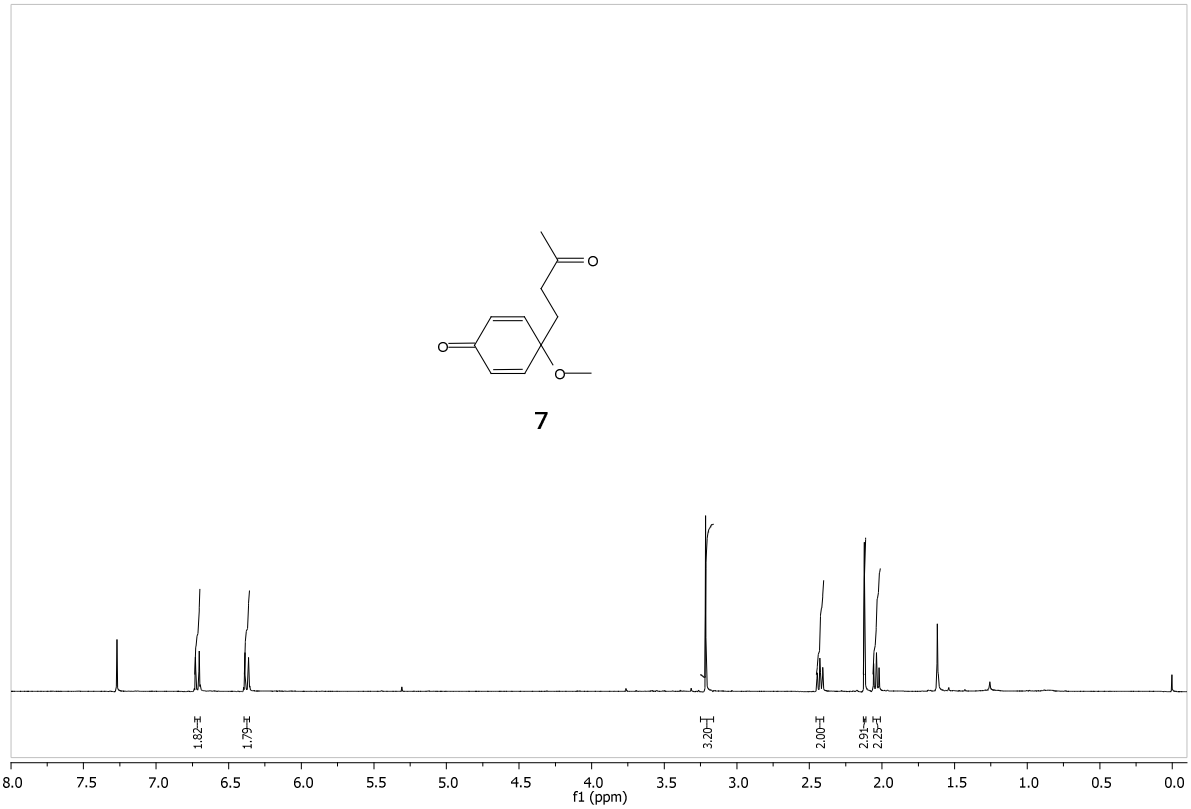
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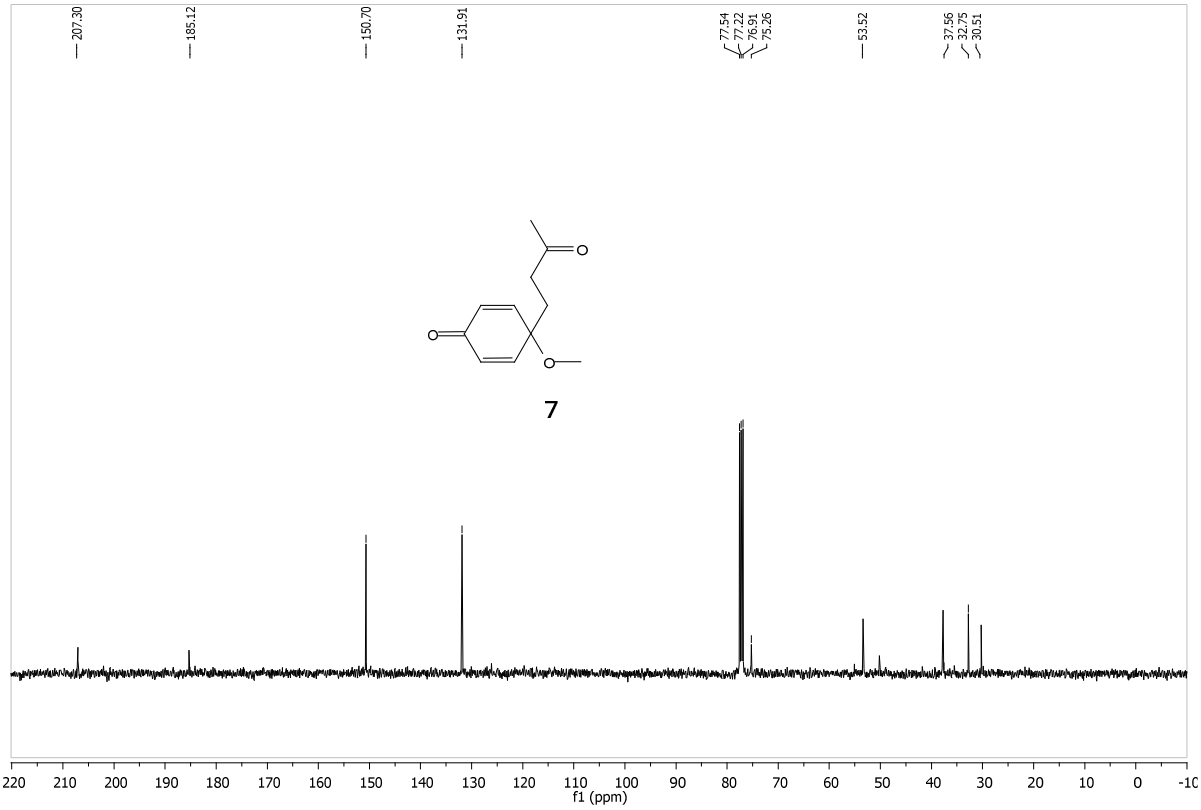
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f1 (ppm)

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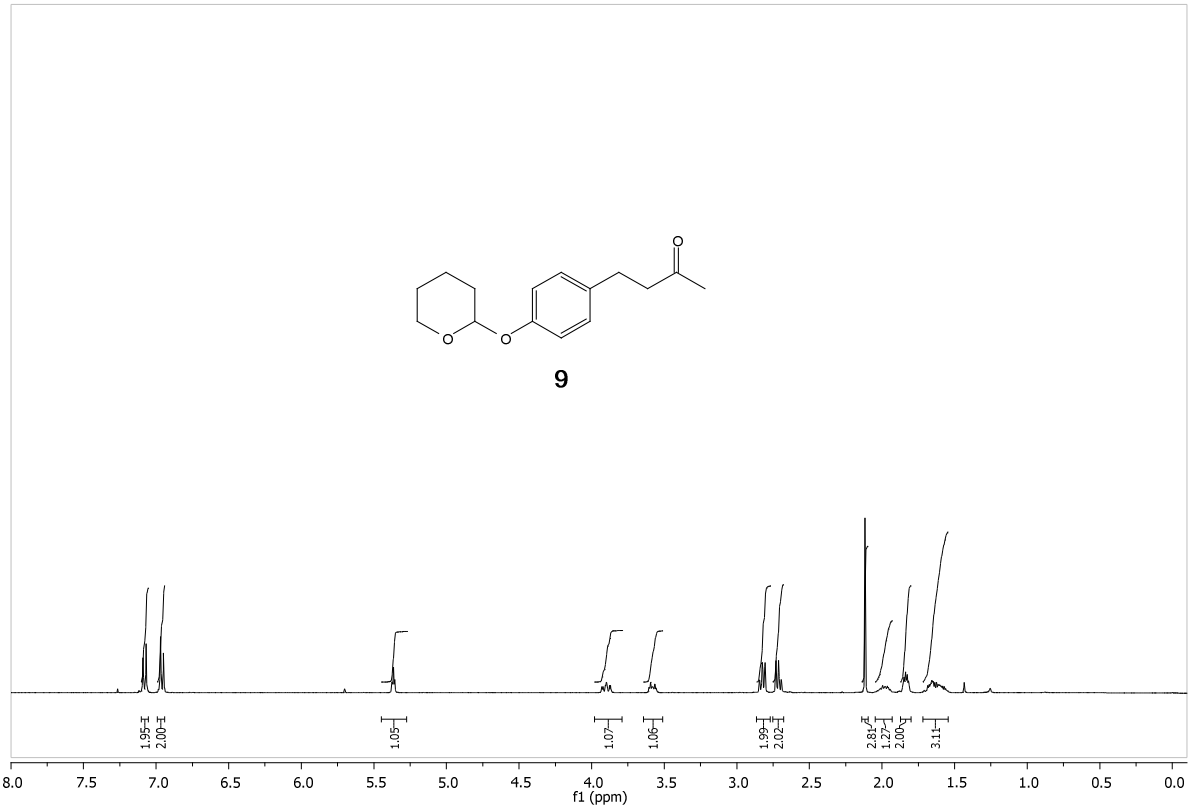
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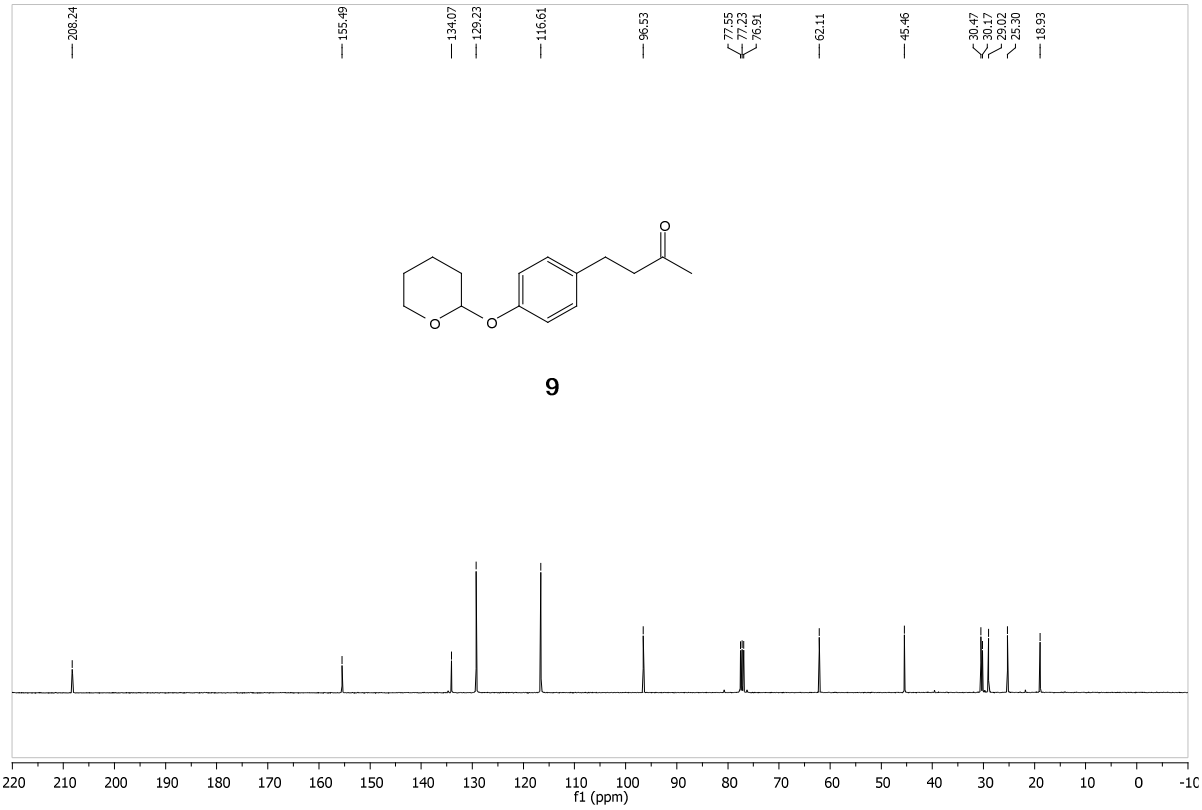
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f1 (ppm)

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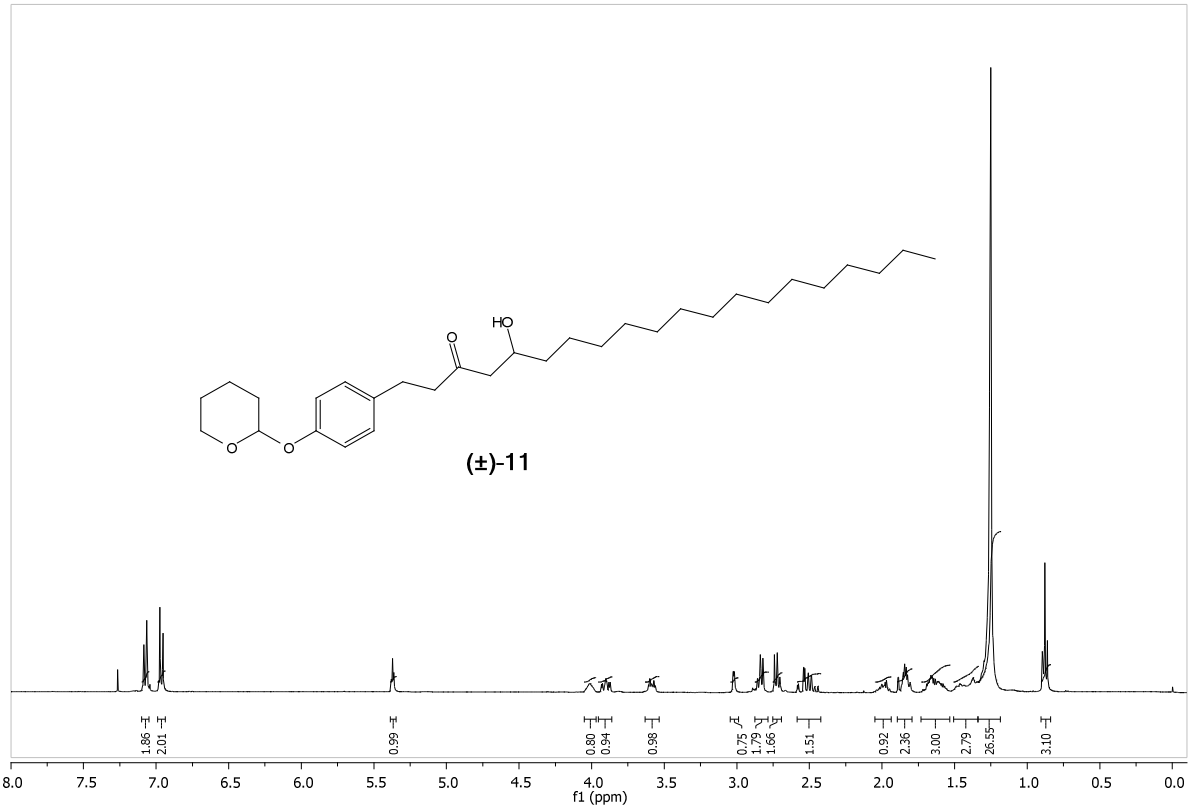
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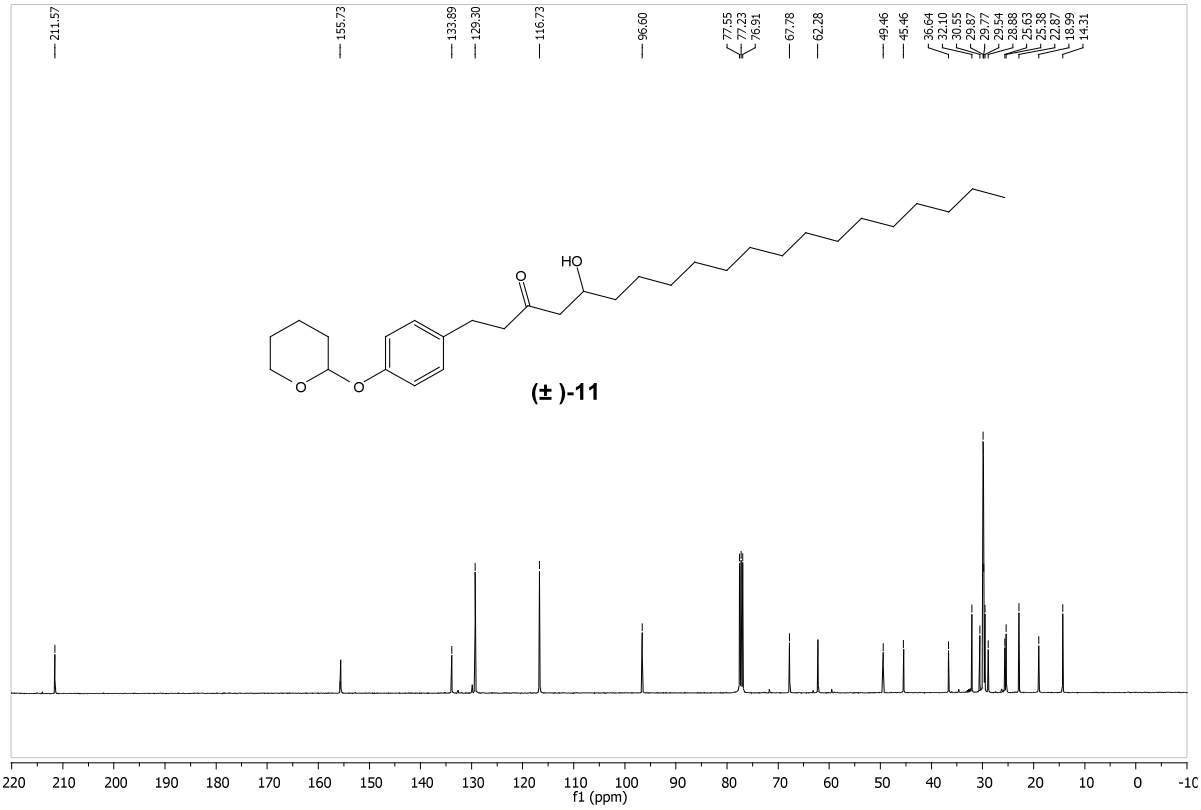
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29.77
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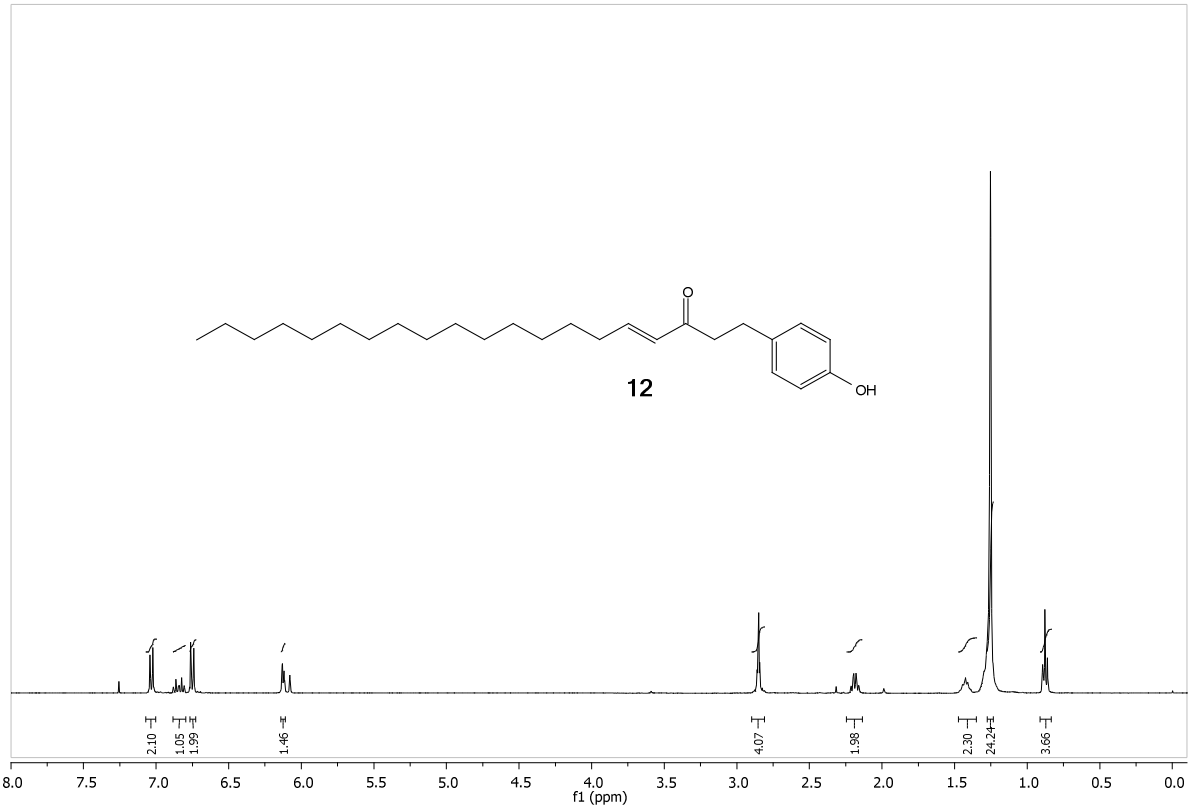
HO
O
O
O
(±)-11
f1 (ppm)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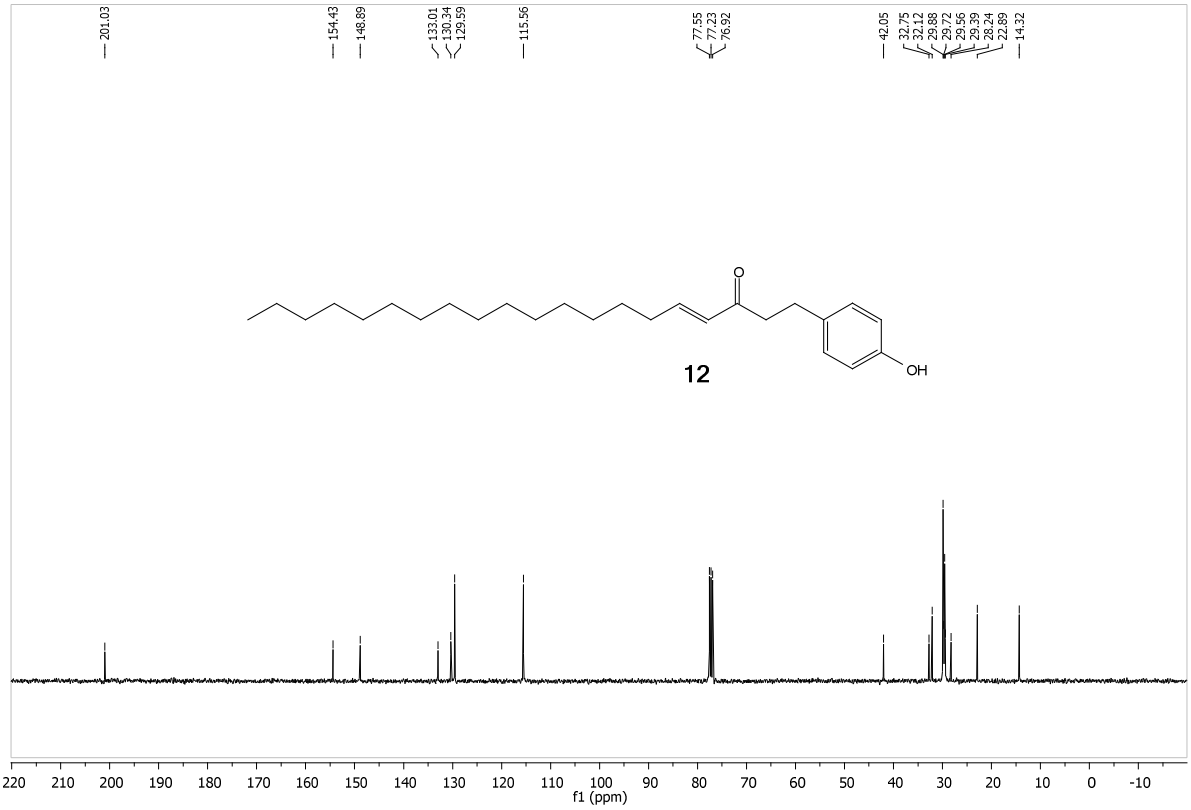
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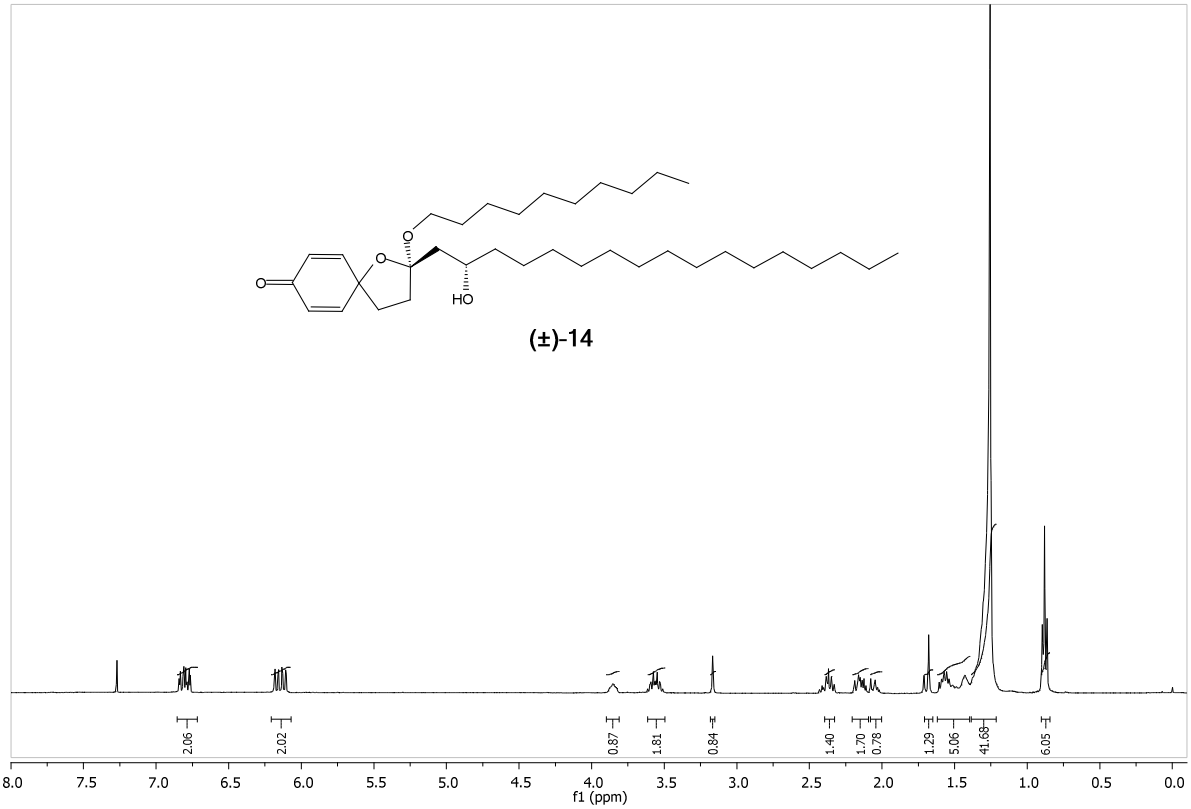
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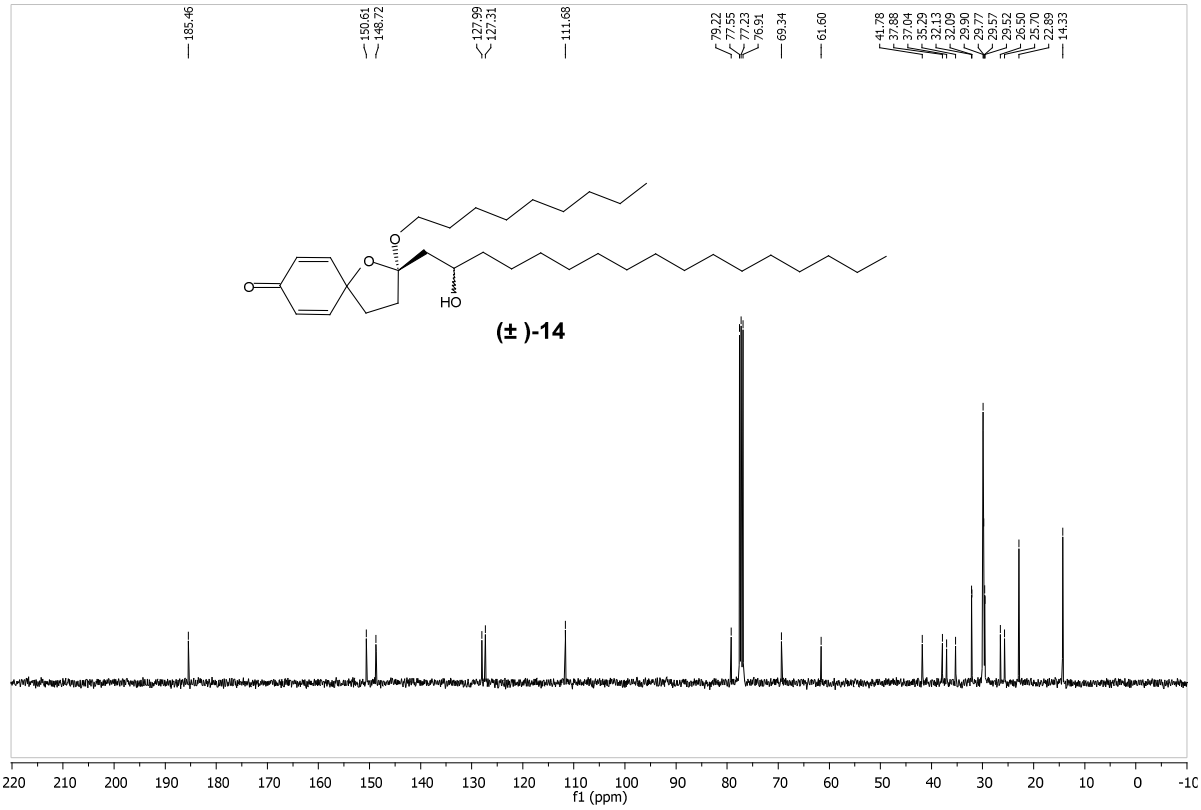
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14.33
O
O
HO
(±)-14
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200
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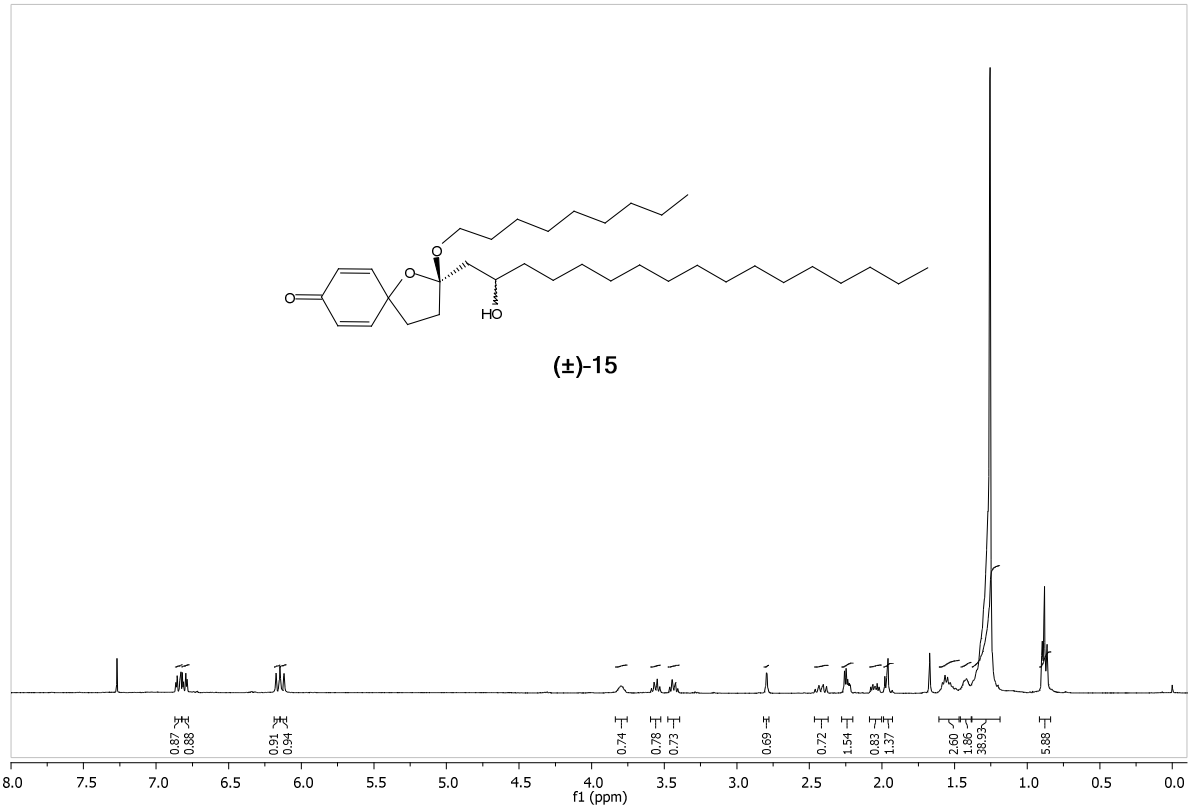
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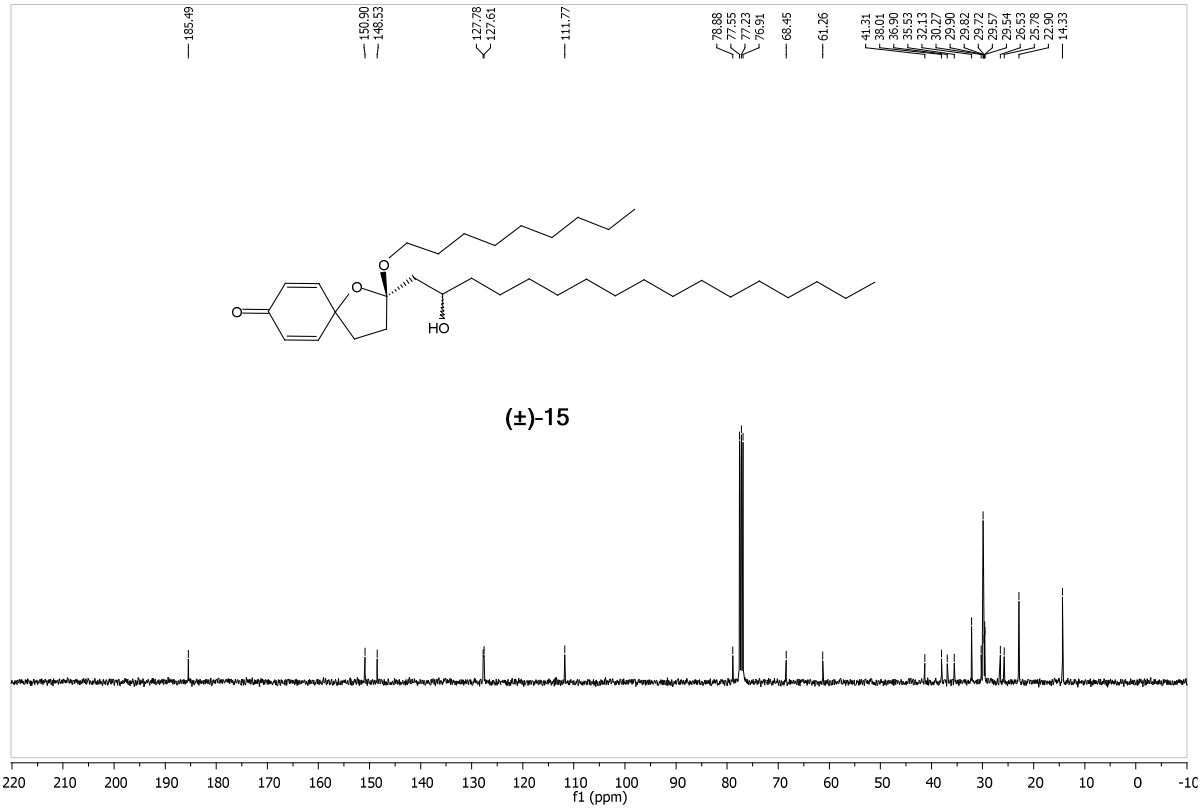
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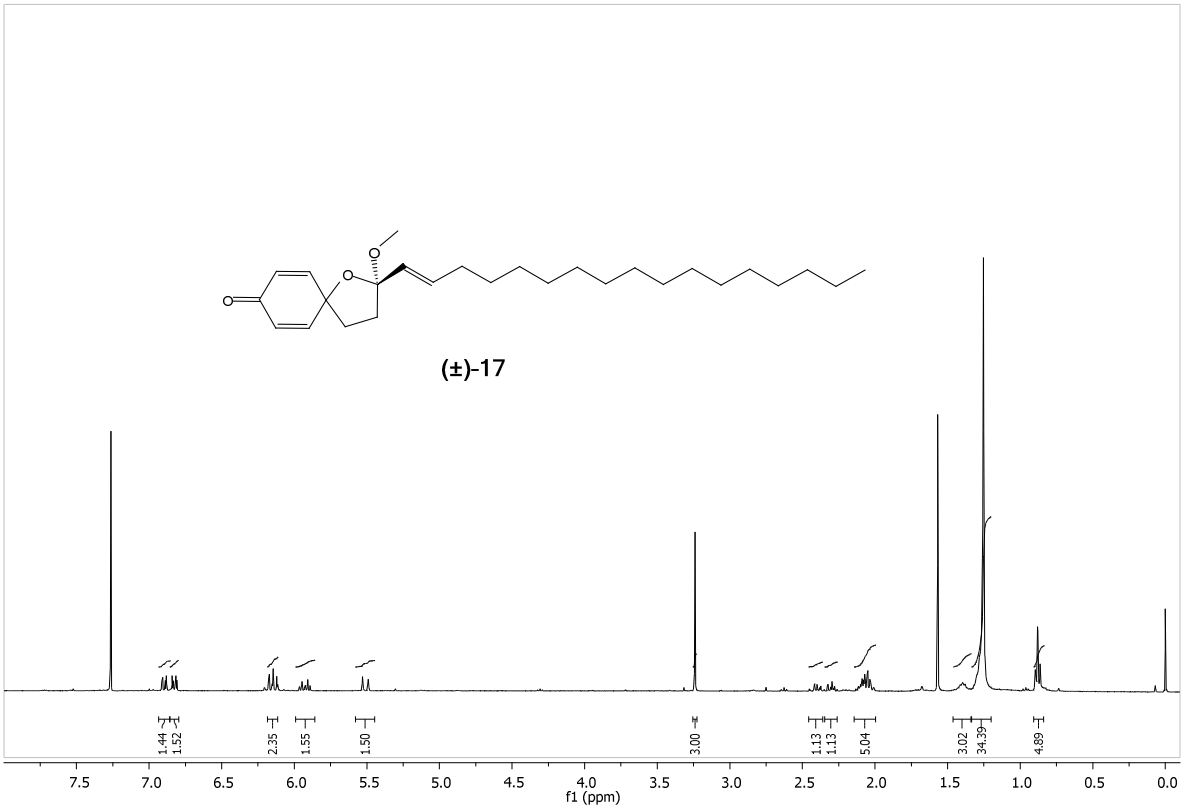
O
O
HO
(±)-15
f1 (ppm)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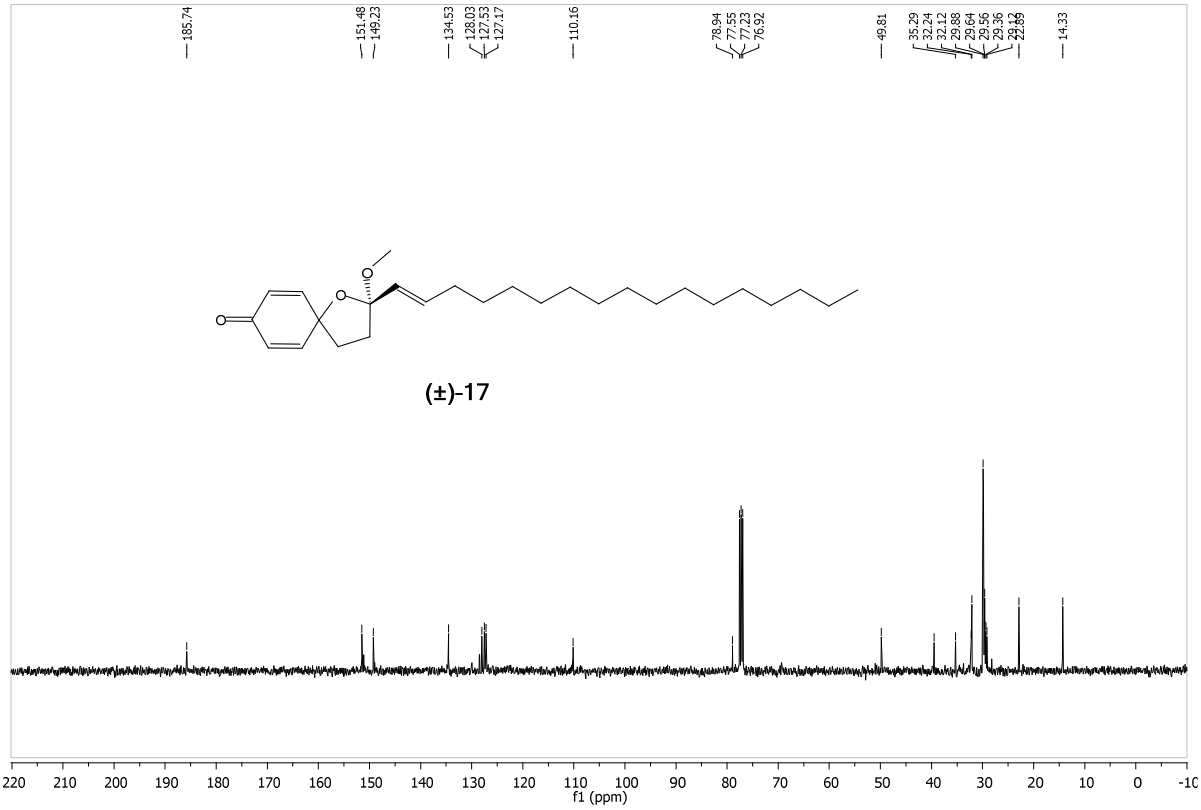
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35.29
32.24
32.12
29.88
29.64
29.56
29.36
29.12
22.89
14.33
(±)-17
220
210
200
190
180
170
160
150
140
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120
110
100
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80
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40
30
20
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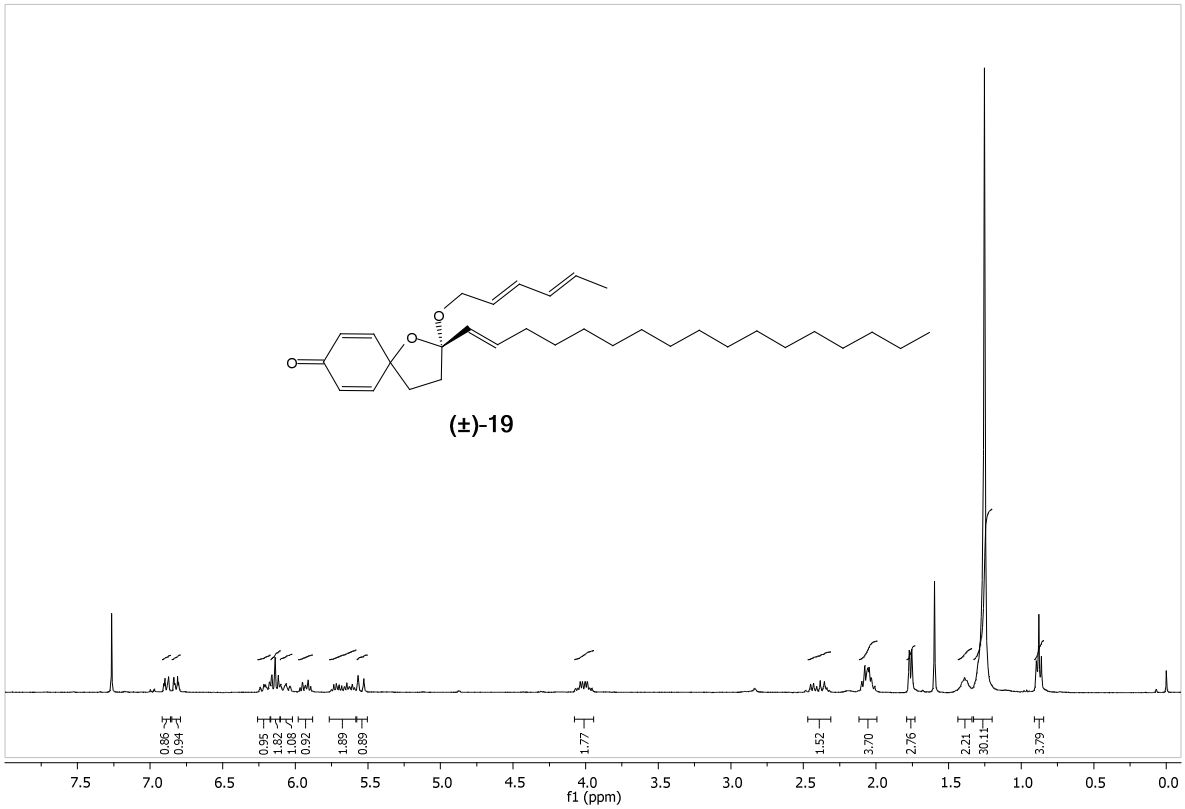
0
-10
f1 (ppm)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3.79
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6.0
5.5
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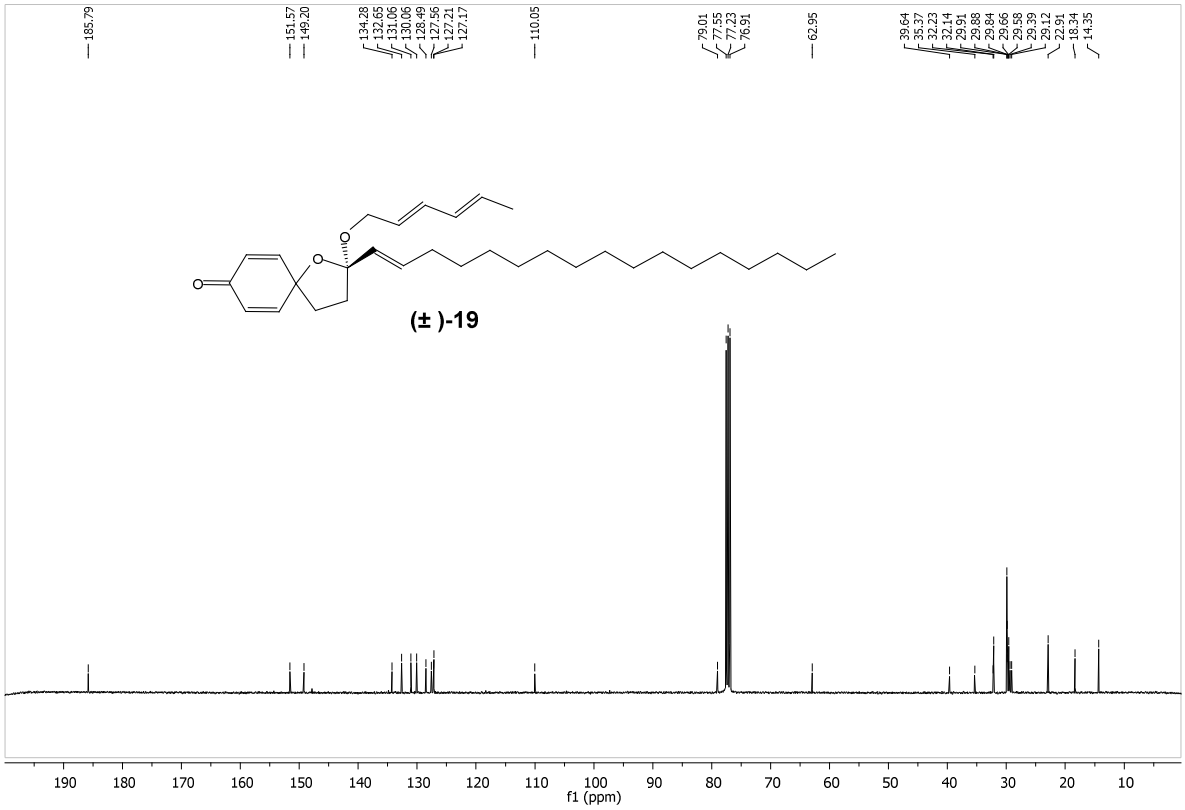
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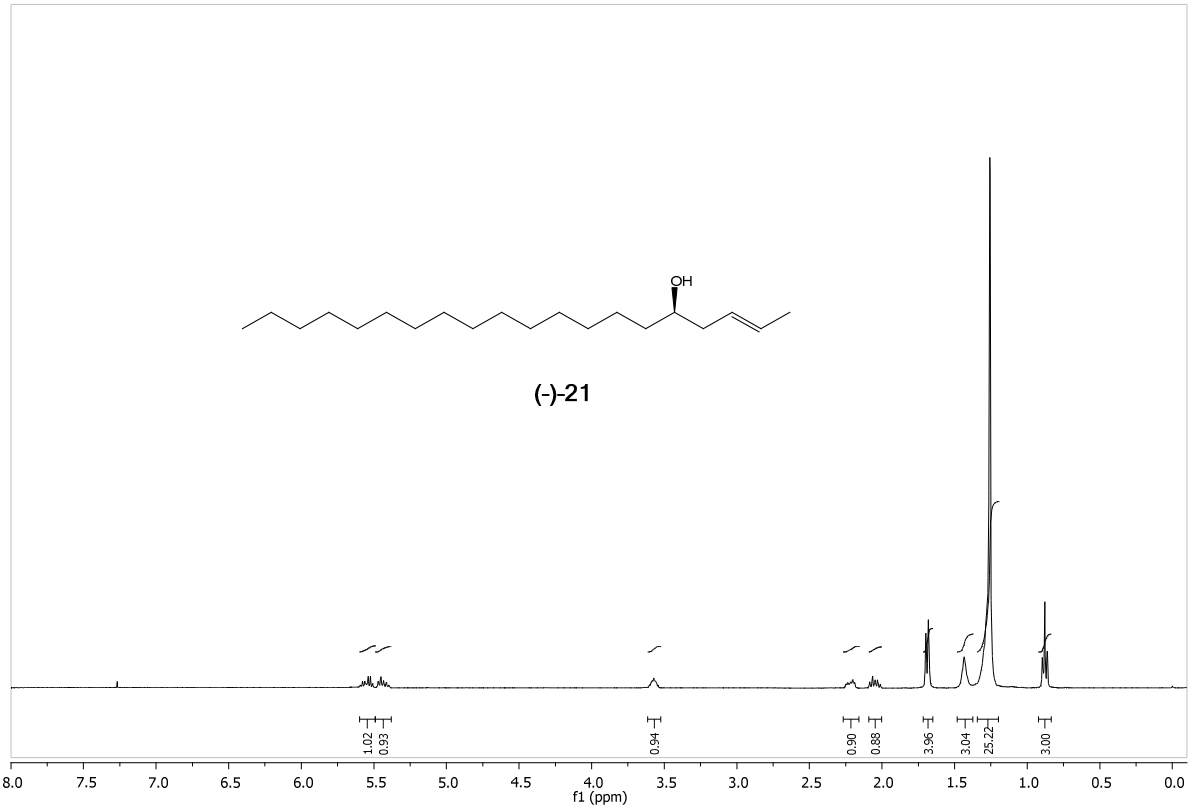
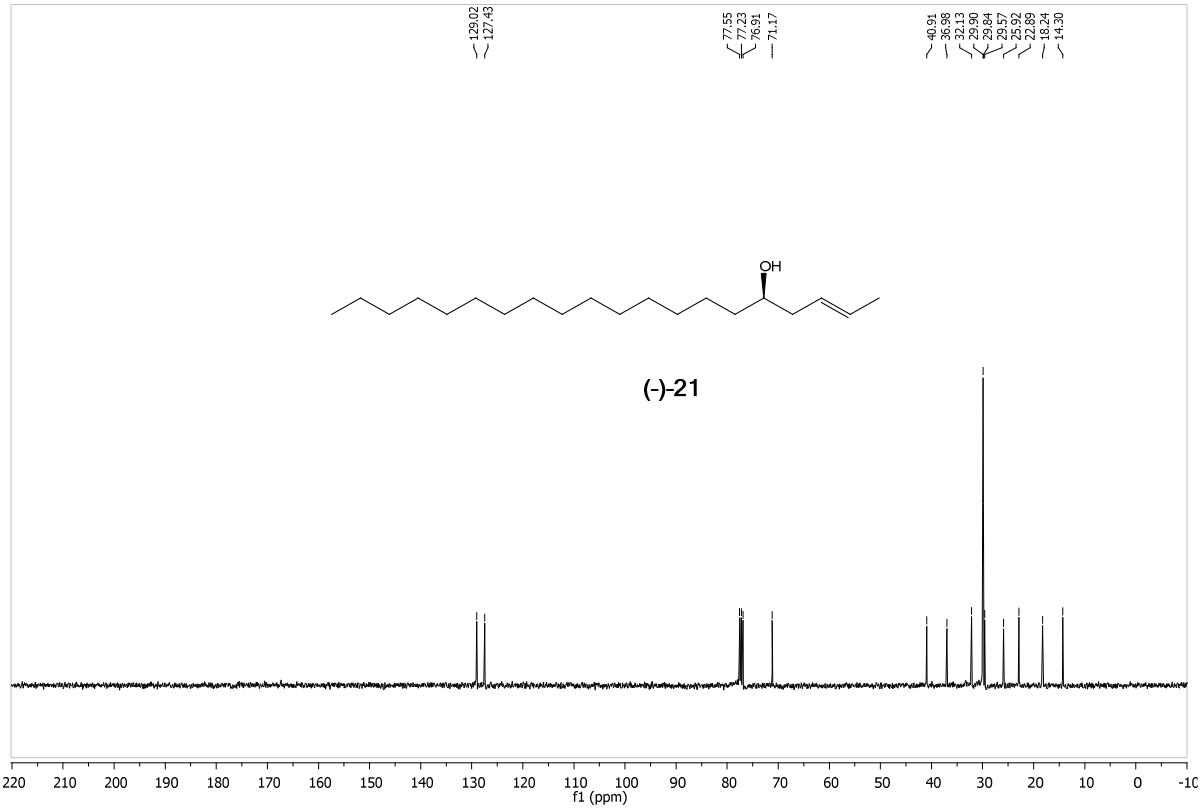
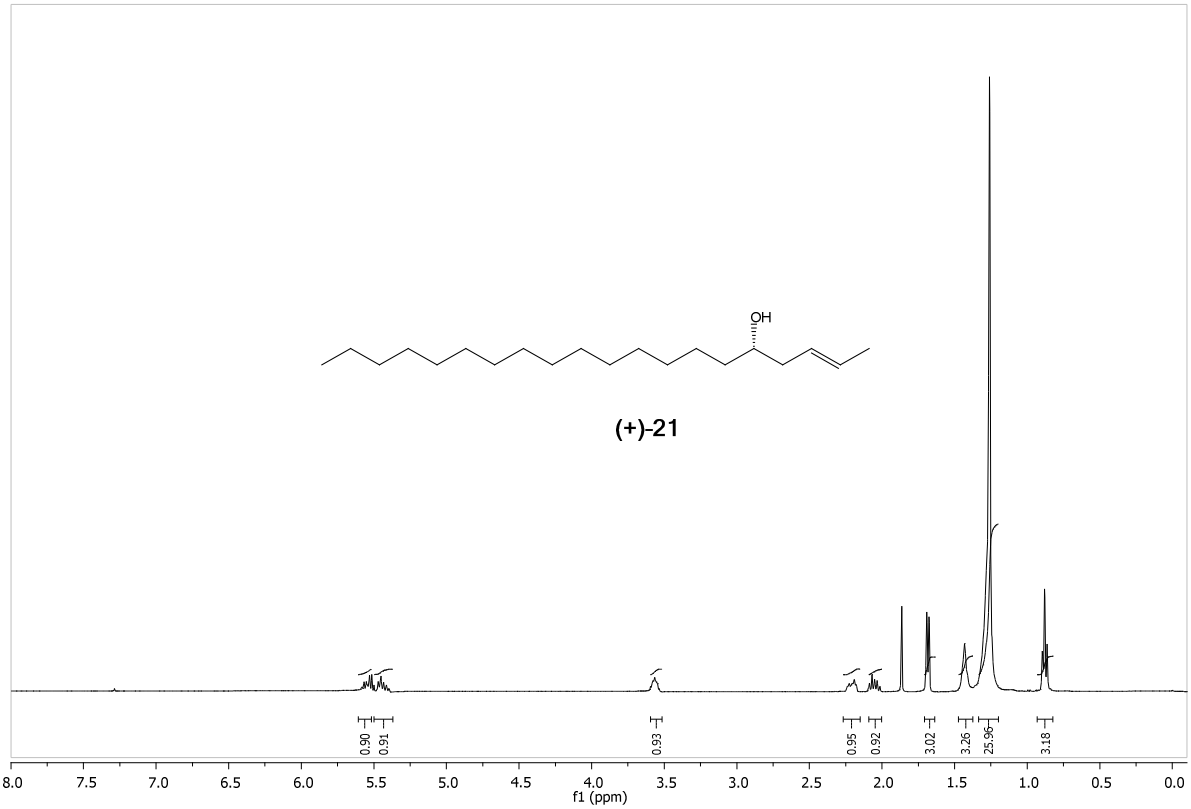
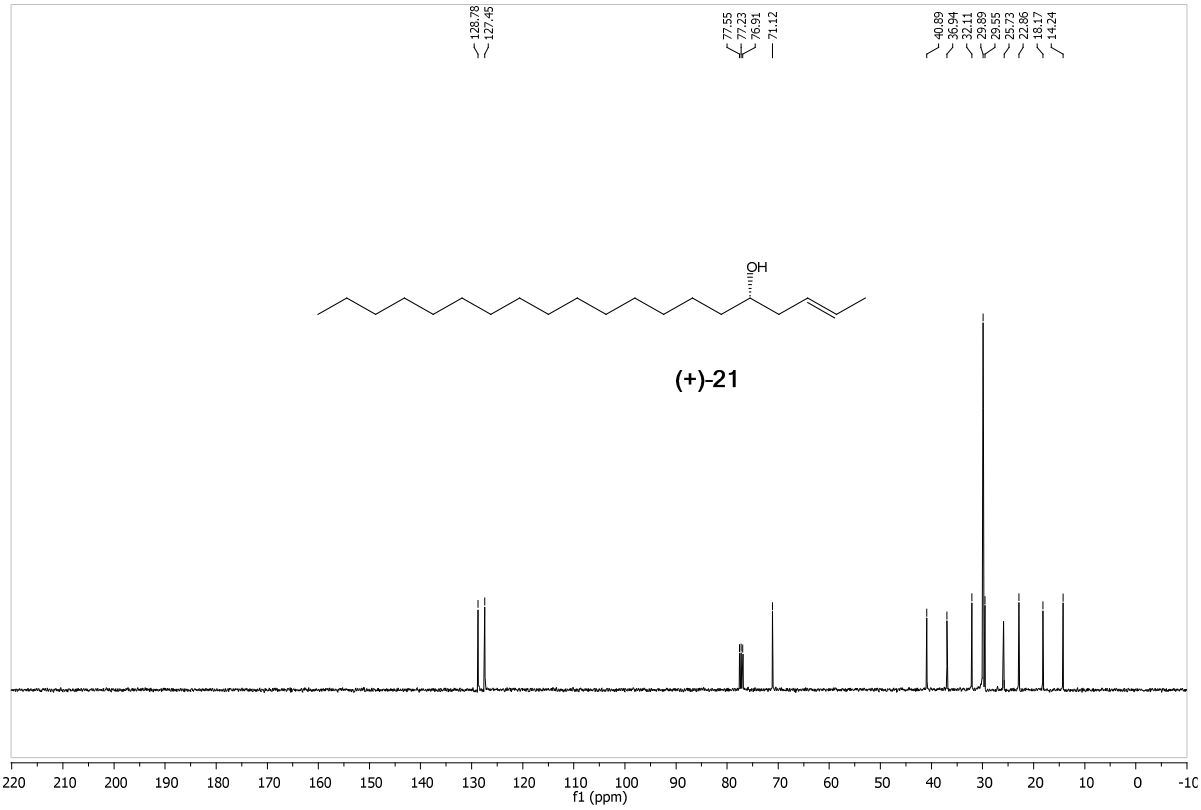
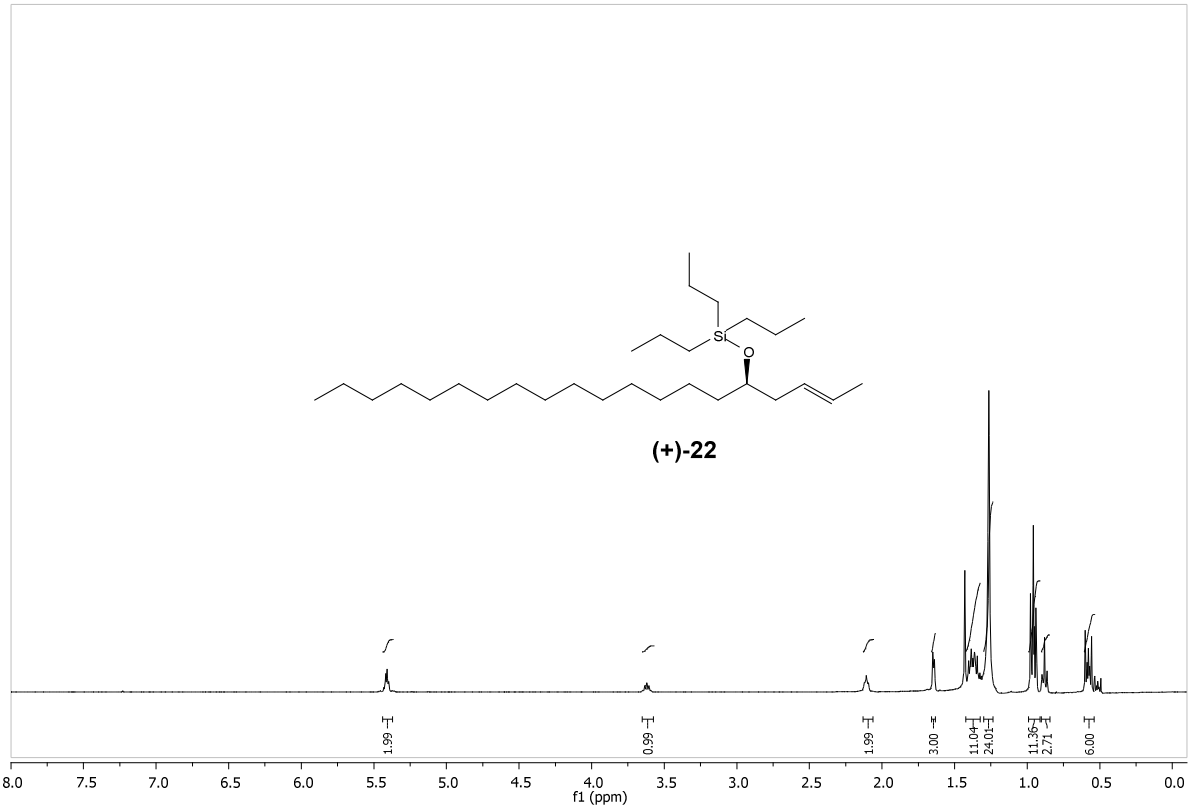
127.17
110.05
79.01
77.55
77.23
76.91
62.95
39.64
35.37
32.23
32.14
29.91
29.88
29.84
29.66
29.58
29.39
29.12
22.91
18.34
14.35
(±)-19
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

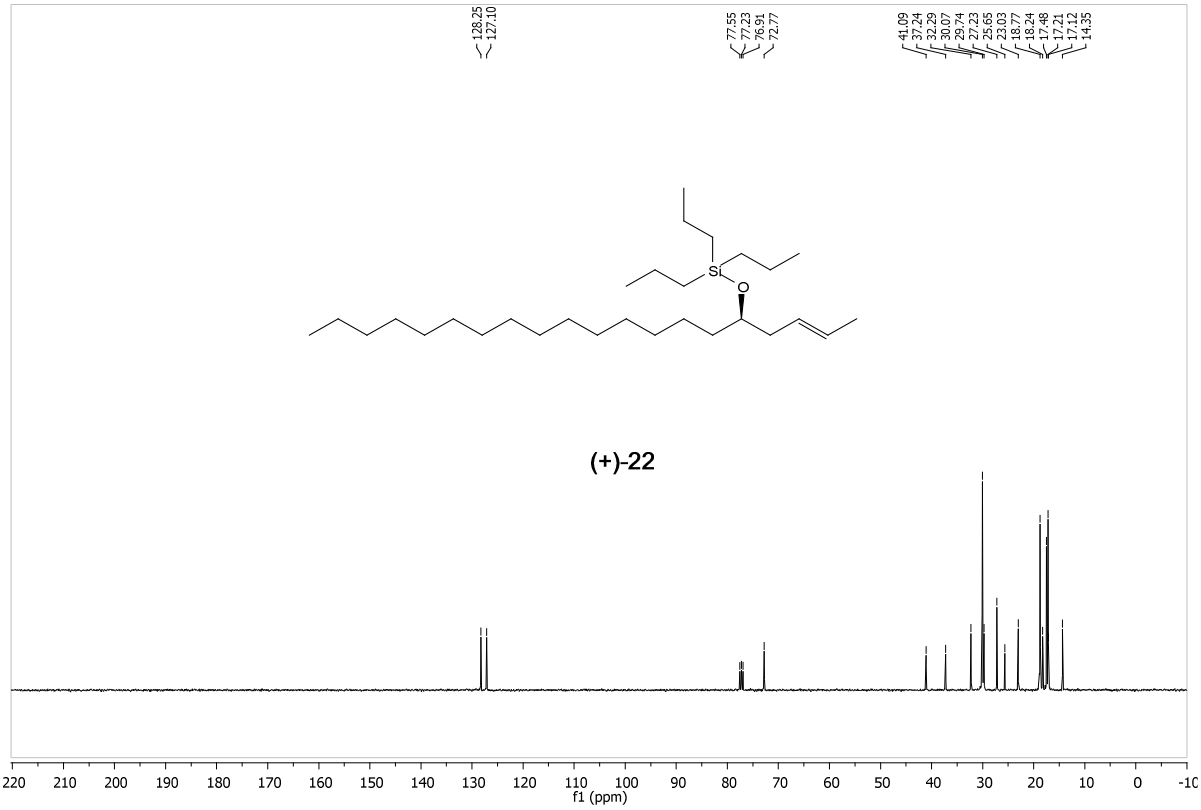

OH
(-)-21
1.02
0.93
0.94
0.90
0.88
3.96
3.04
25.22
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

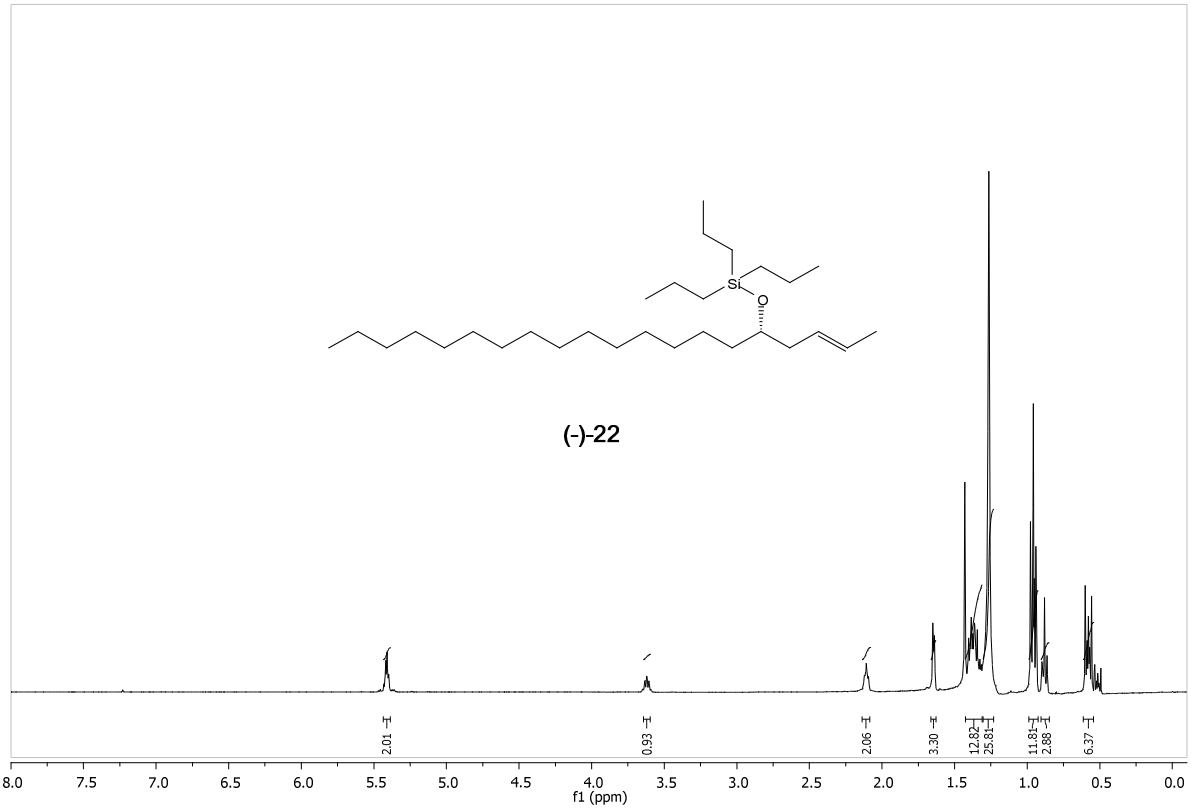

129.02
127.43
77.55
77.23
76.91
71.17
40.91
36.98
32.13
29.90
29.84
29.57
25.92
22.89
18.24
14.30
OH
(-)-21
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

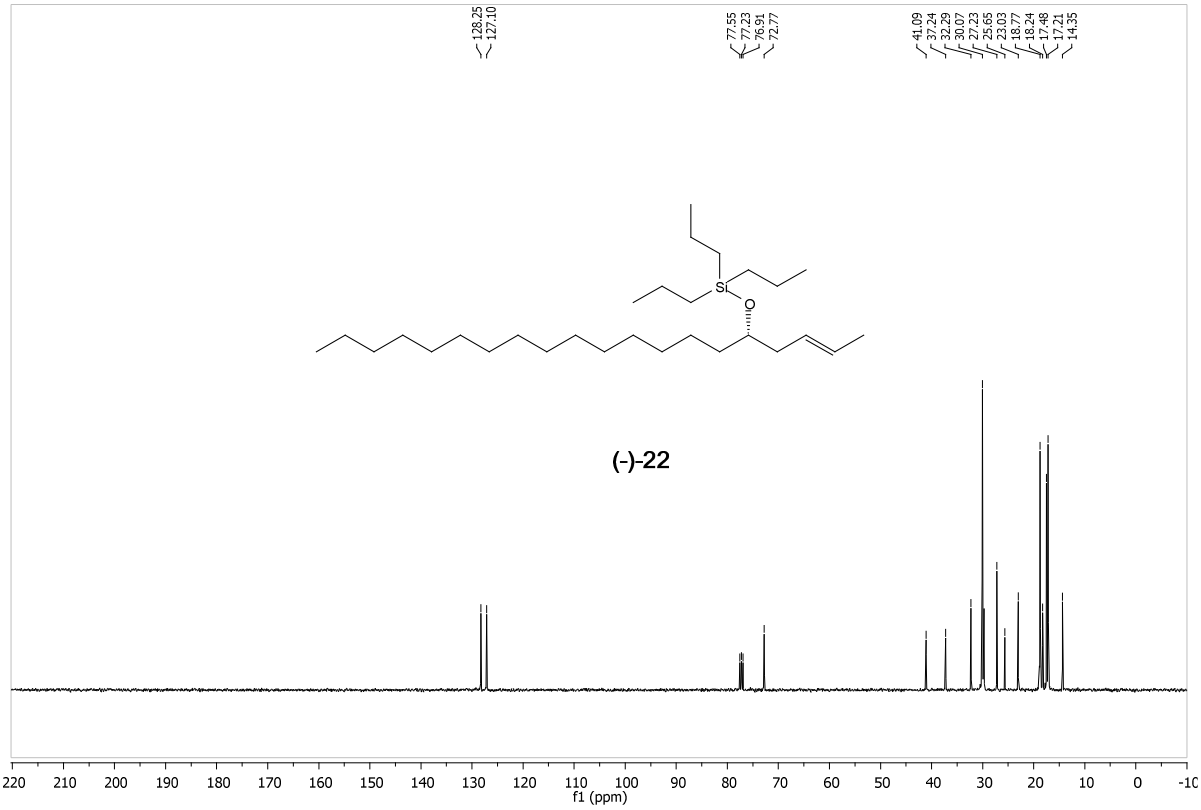

OH
(+)-21
0.90
0.91
0.93
0.95
0.92
3.02
3.26
25.96
3.18
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

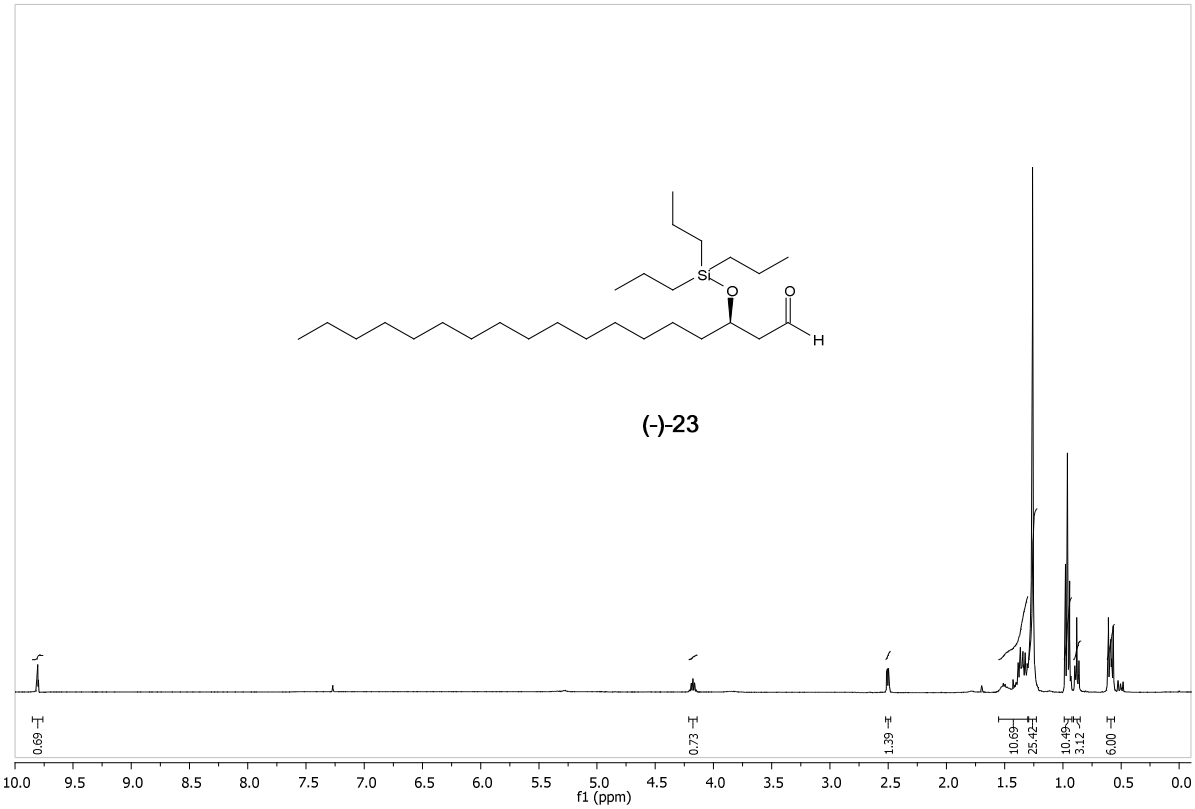

128.78
127.45
77.55
77.23
76.91
71.12
40.89
36.94
32.11
29.89
29.55
25.73
22.86
18.17
14.24
OH
(+)-21
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Si
O
(+)-22
1.99
0.99
1.99
3.00
11.04
24.01
11.36
2.71
6.00
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 1.0 0.5 0.0
f1 (ppm)

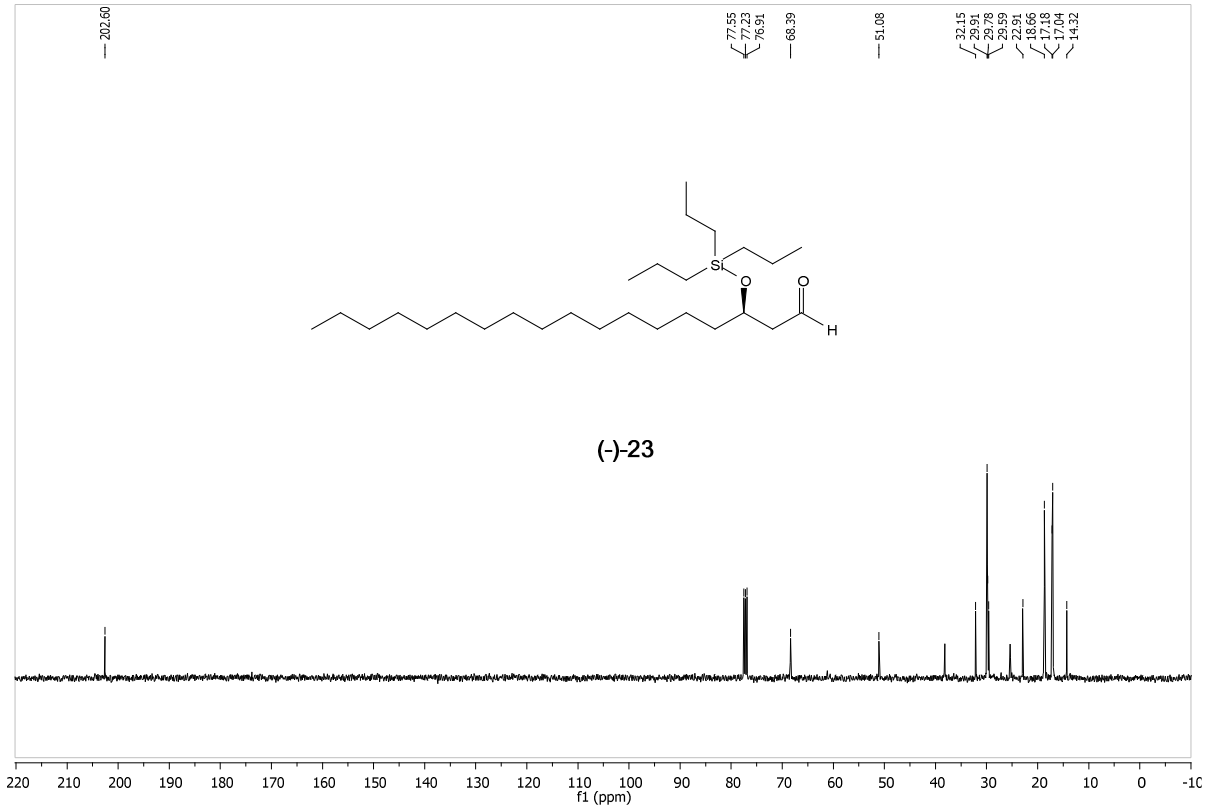

128.25
127.10
77.55
77.23
76.91
72.77
41.09
37.24
32.29
30.07
29.74
27.23
25.65
23.03
18.77
18.24
17.48
17.21
17.12
14.35
Si
O
(+)-22
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Si
O
(-)-22
2.01
0.93
2.06
3.30
12.82
25.81
11.81
2.88
6.37
f1 (ppm)

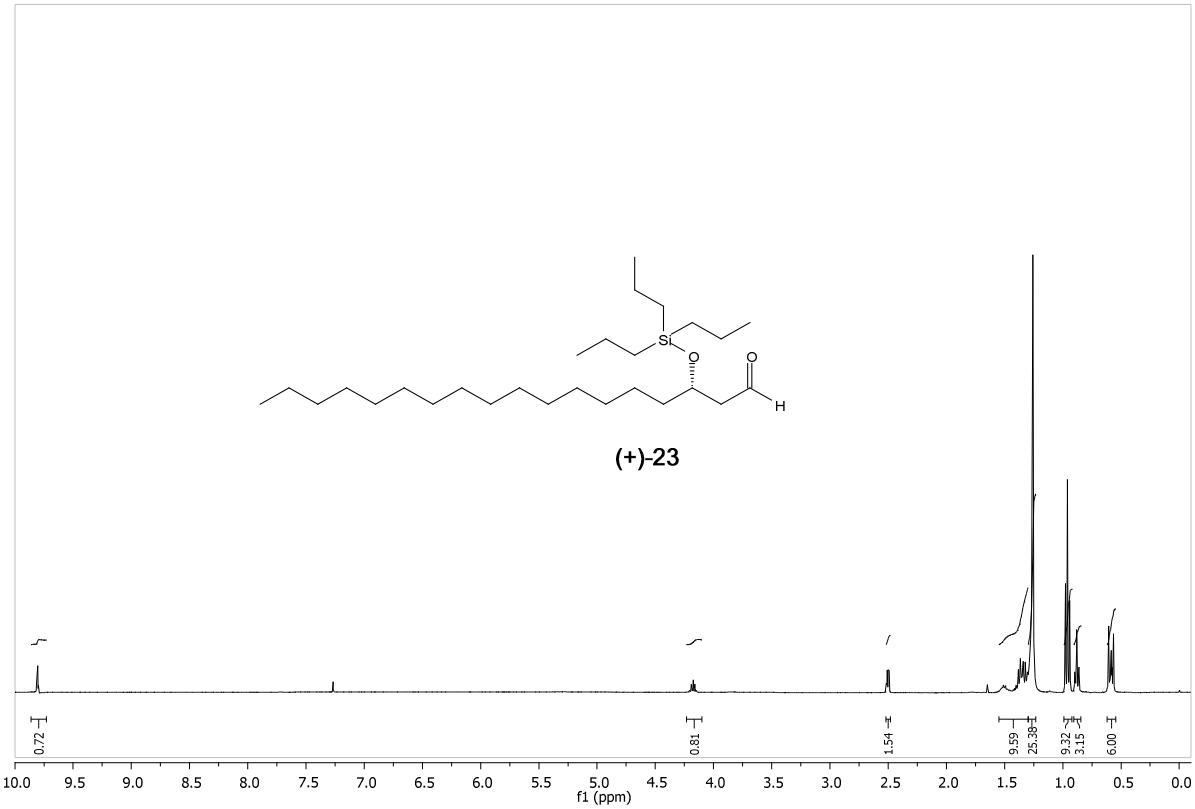

128.25
127.10
77.55
77.23
76.91
72.77
41.09
37.24
32.29
30.07
27.23
25.65
23.03
18.77
18.24
17.48
17.21
14.35
Si
O
(-)-22
f1 (ppm)


Si
O
O
H
0.69
0.73
1.39
10.69
25.42
10.49
3.12
6.00
f1 (ppm)

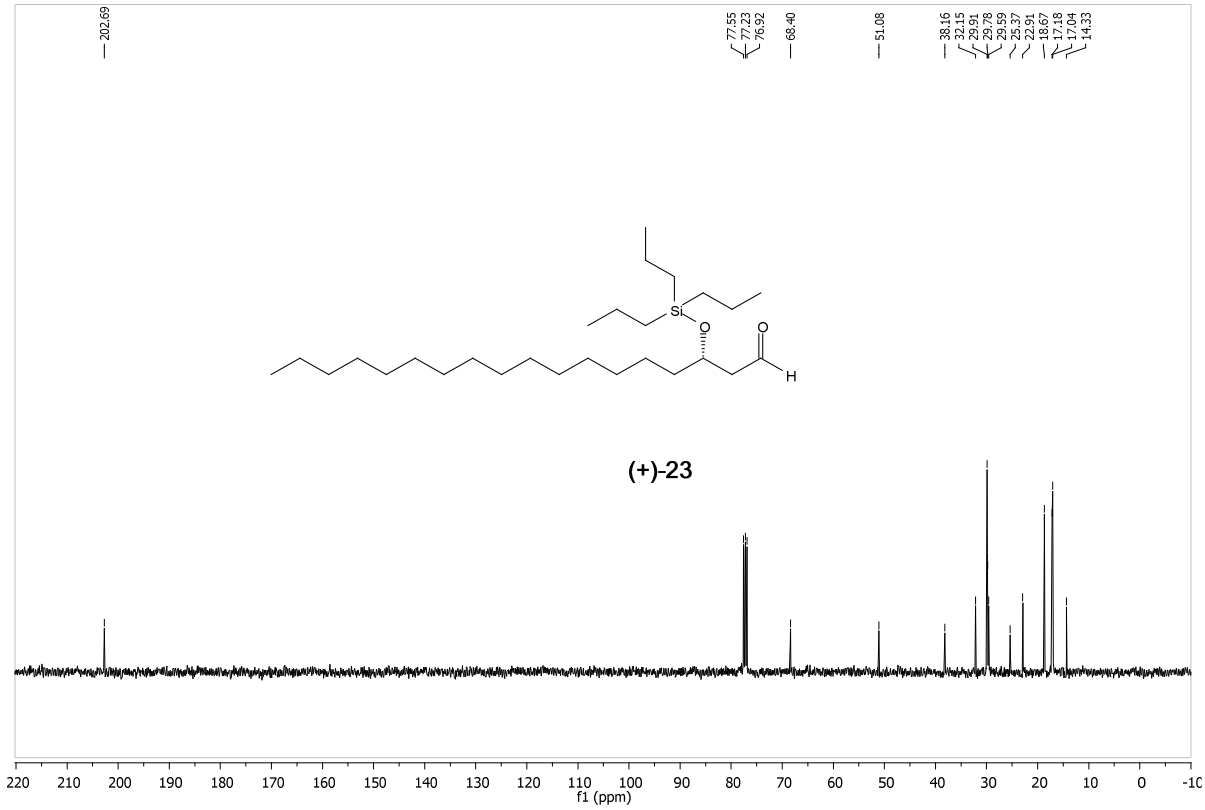
(-)-23


202.60
77.55
77.23
76.91
68.39
51.08
32.15
29.91
29.78
29.59
22.91
18.66
17.18
17.04
14.32
Si
O
O
H
f1 (ppm)

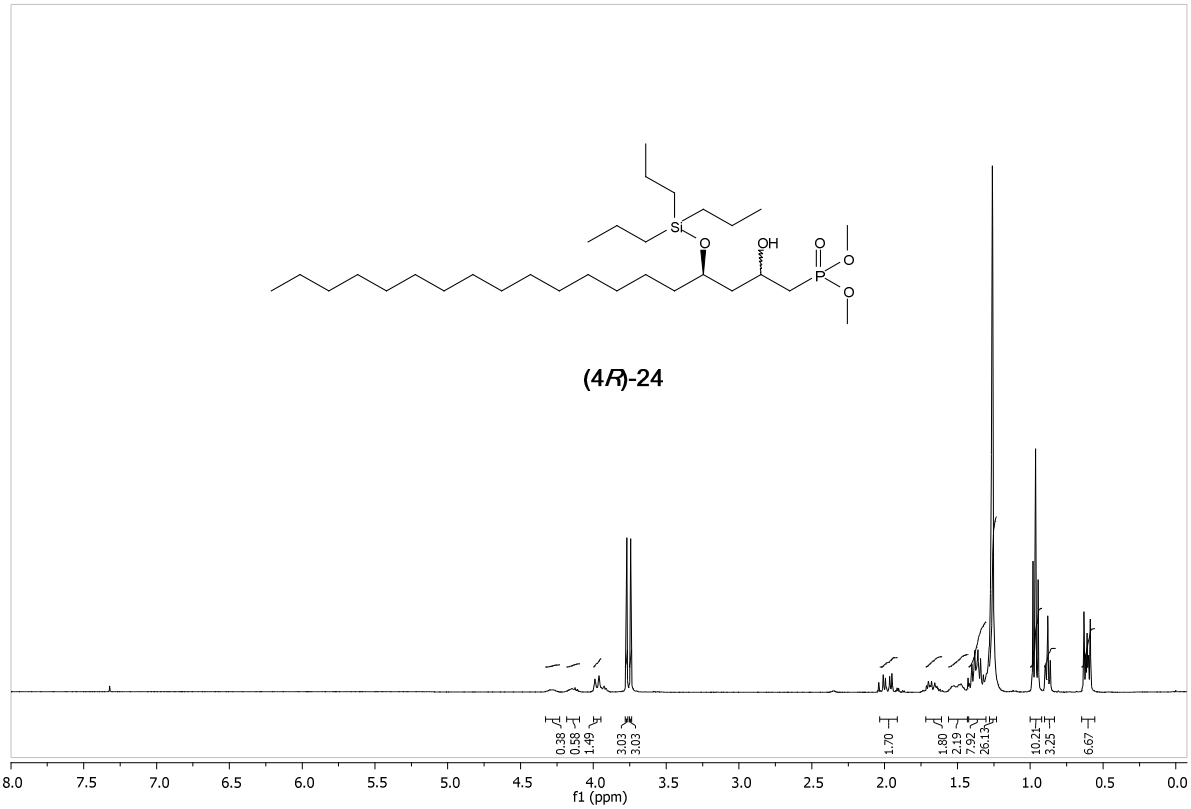
(-)-23


Si
O
O
H
0.72
0.81
1.54
9.59
25.38
9.32
3.15
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 0.5 0.0
f1 (ppm)

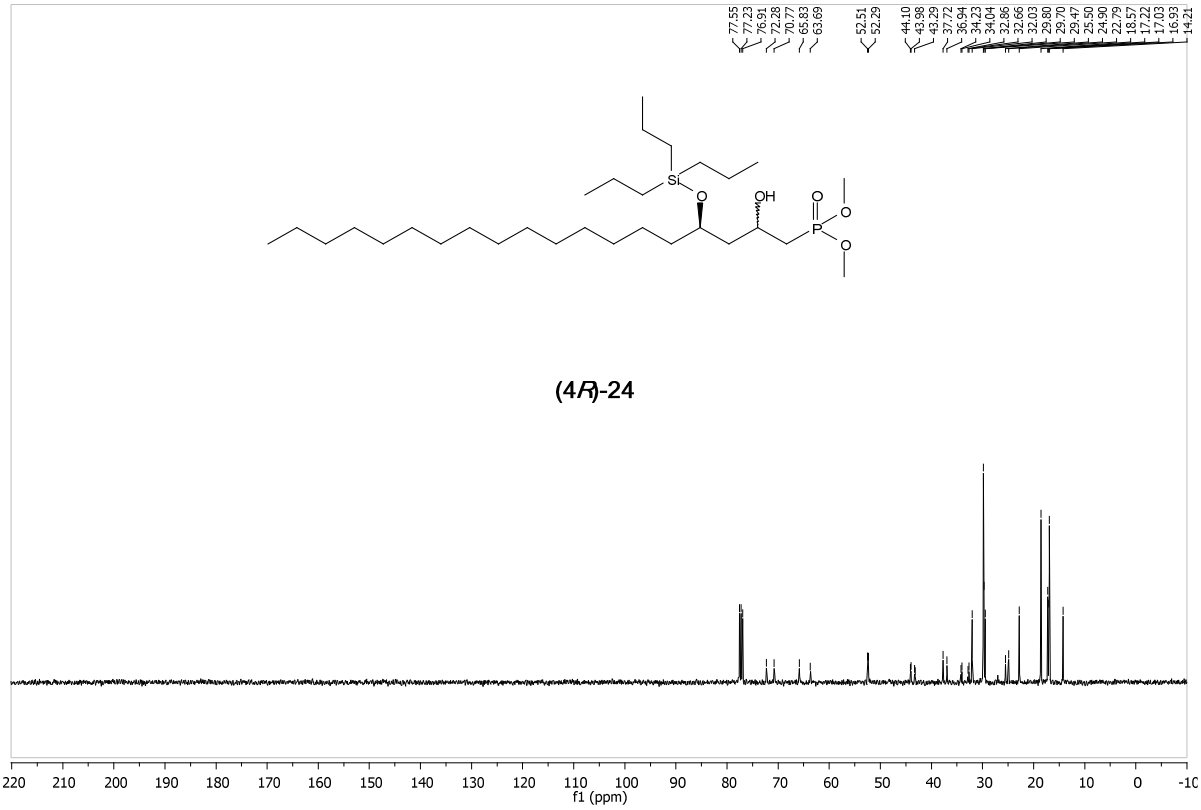
(+)-23


202.69
77.55
77.23
76.92
68.40
51.08
38.16
32.15
29.91
29.78
29.59
25.37
22.91
18.67
17.18
17.04
14.33
Si
O
O
H
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

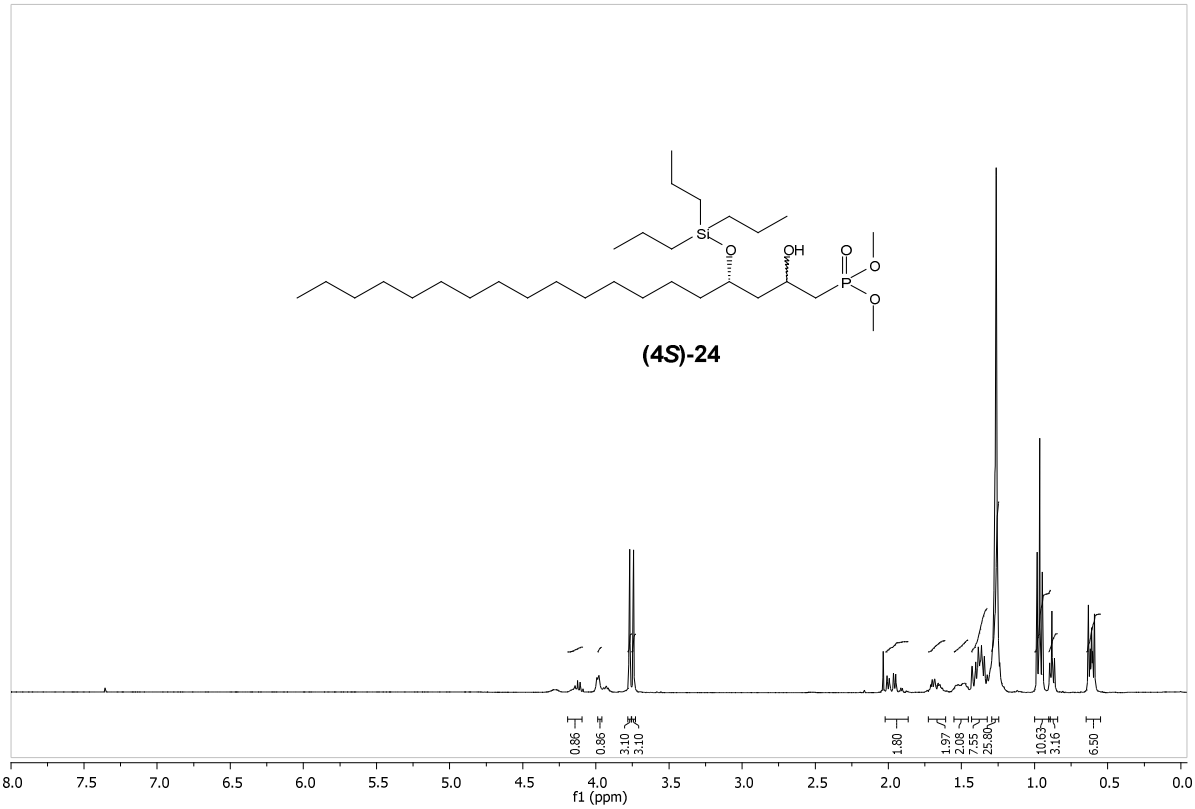
(+)-23


Si
O
OH
O
P
O
O
0.38
0.58
1.49
3.03
3.03
1.70
1.80
2.19
7.92
26.13
10.21
3.25
6.67
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)

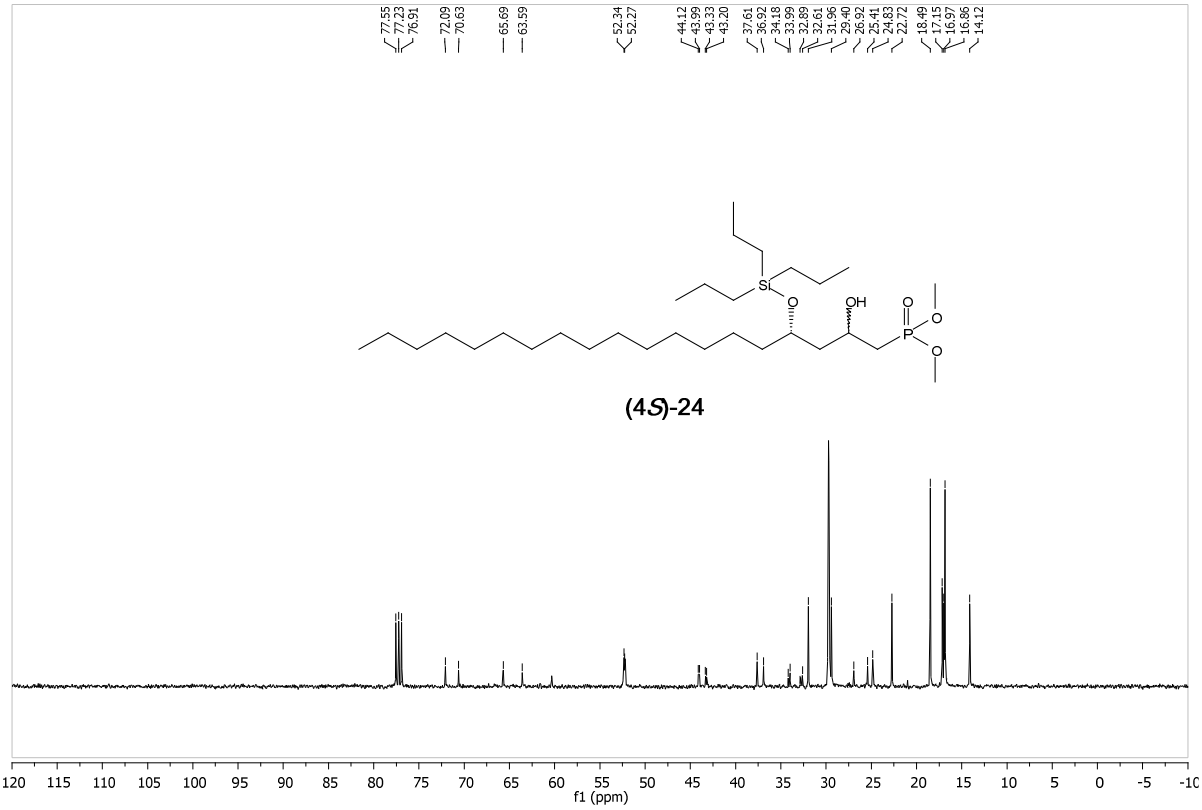
(4*R*)-24


77.55
77.23
76.91
72.28
70.77
65.83
63.69
52.51
52.29
44.10
43.98
43.29
37.72
36.94
34.23
34.04
32.86
32.66
32.03
29.80
29.70
29.47
25.50
24.90
22.79
18.57
17.22
17.03
16.93
14.21
Si
O
OH
O
P
O
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

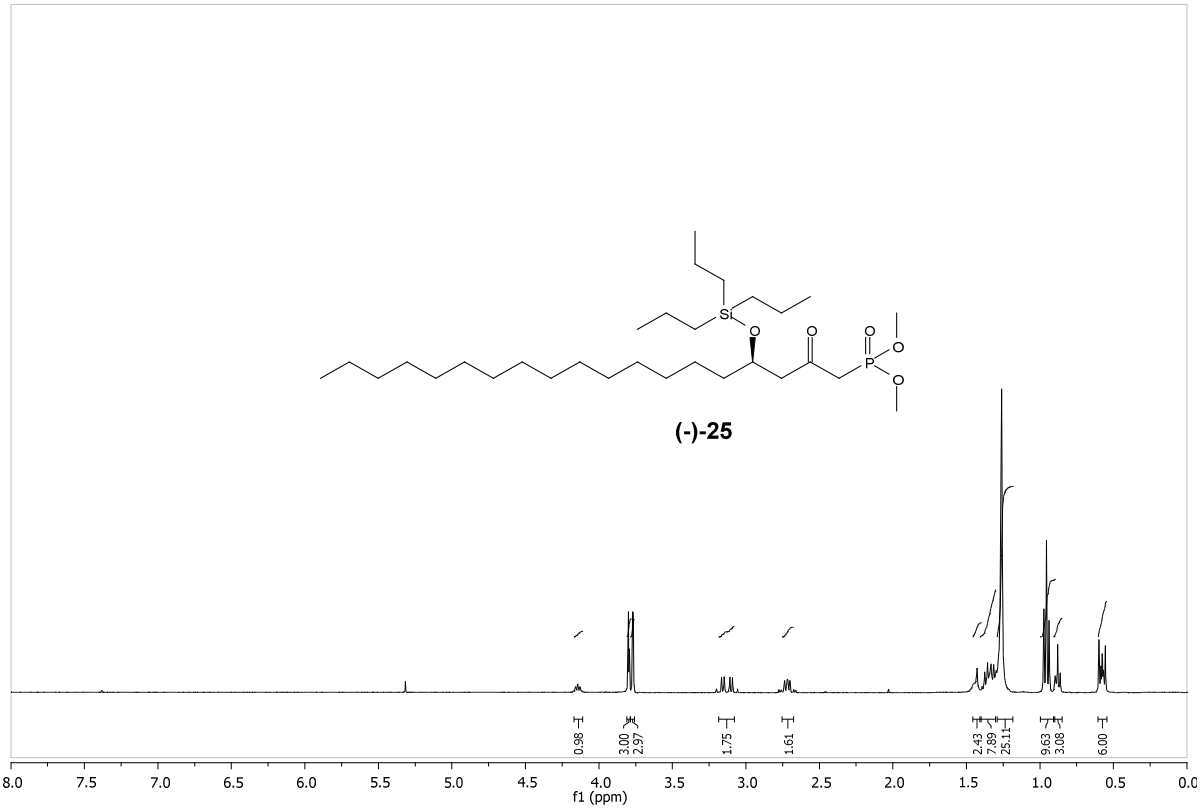
(4*R*)-24

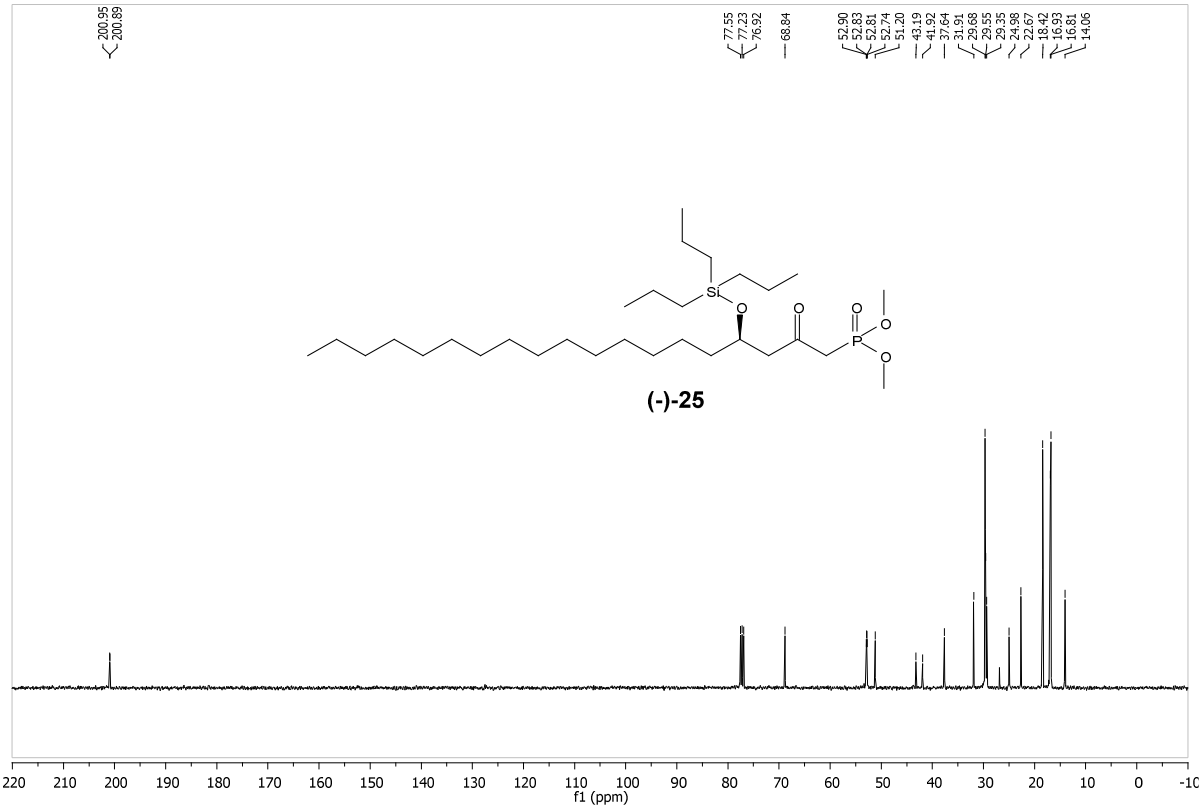

Si
O
OH
O
O
P
O
0.86
0.86
3.10
3.10
1.80
1.97
2.08
7.55
25.80
10.63
3.16
6.50
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

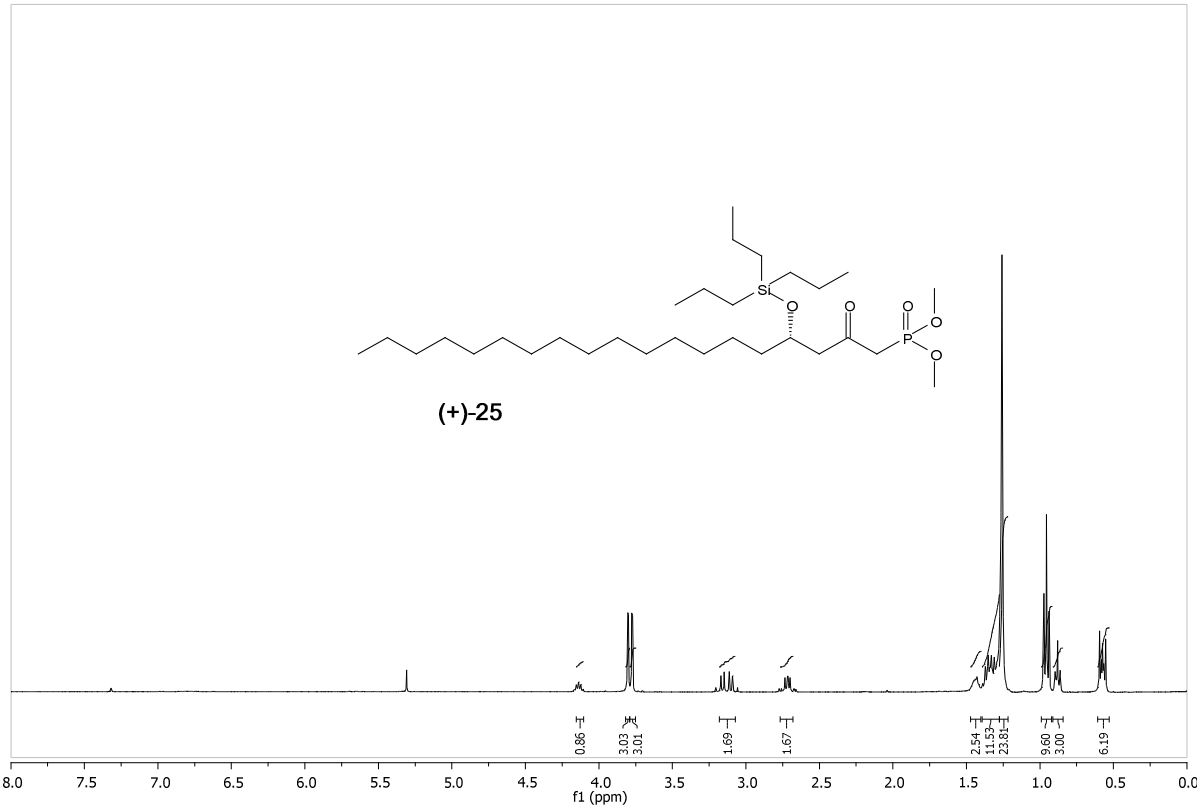
(4*S*)-24

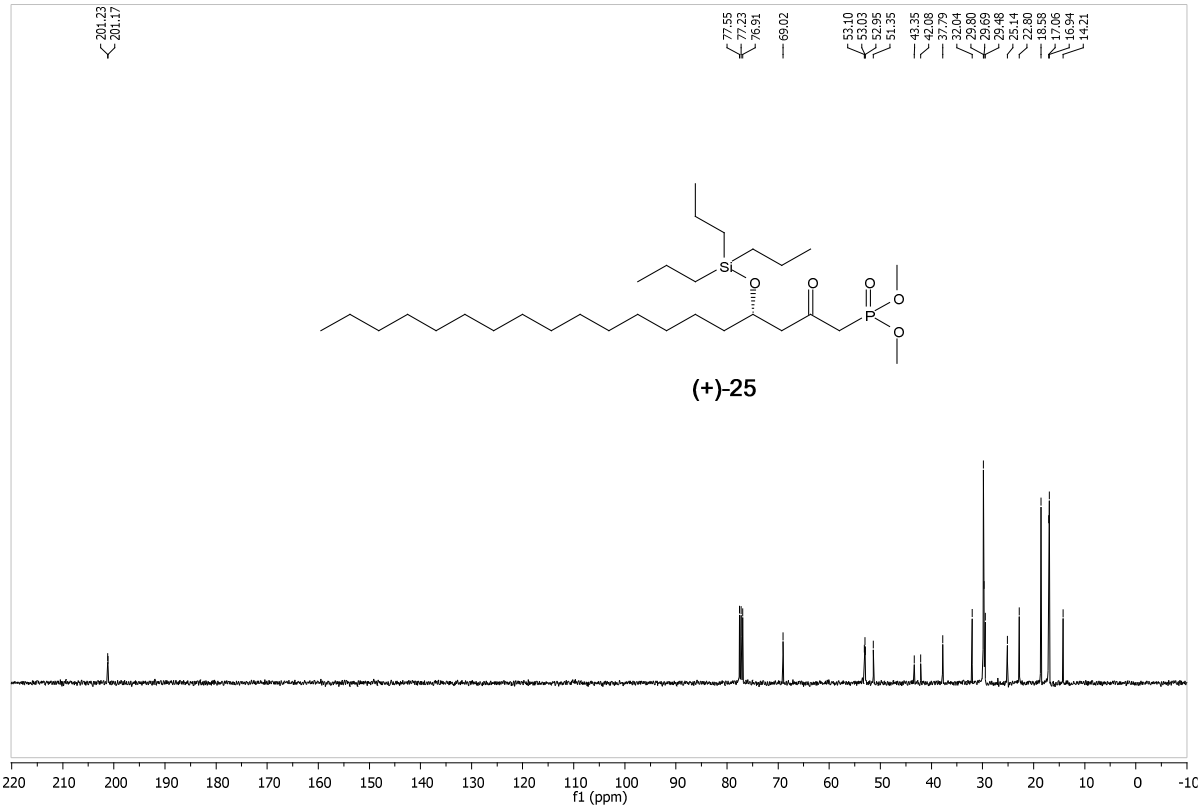

77.55
77.23
76.91
72.09
70.63
65.69
63.59
52.34
52.27
44.12
43.99
43.33
43.20
37.61
36.92
34.18
33.99
32.89
32.61
31.96
29.40
26.92
25.41
24.83
22.72
18.49
17.15
16.97
16.86
14.12
Si
O
OH
O
O
P
O
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
f1 (ppm)

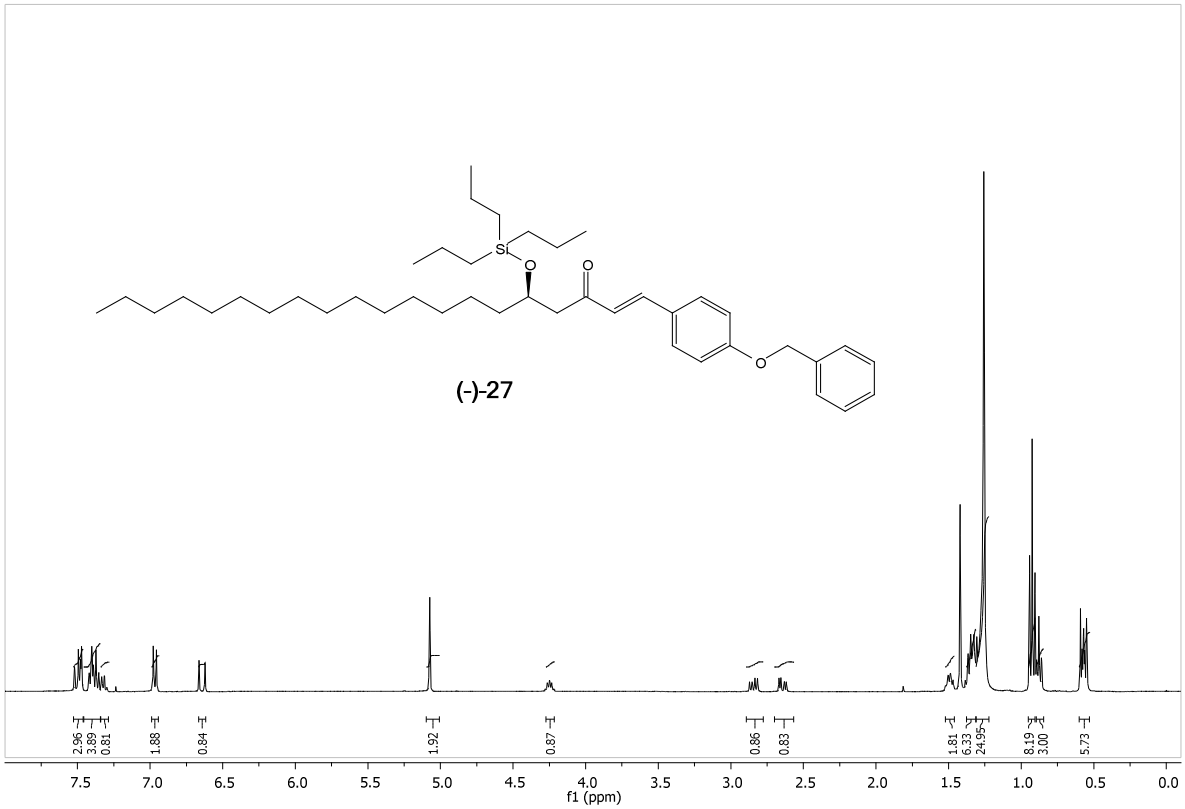
(4*S*)-24

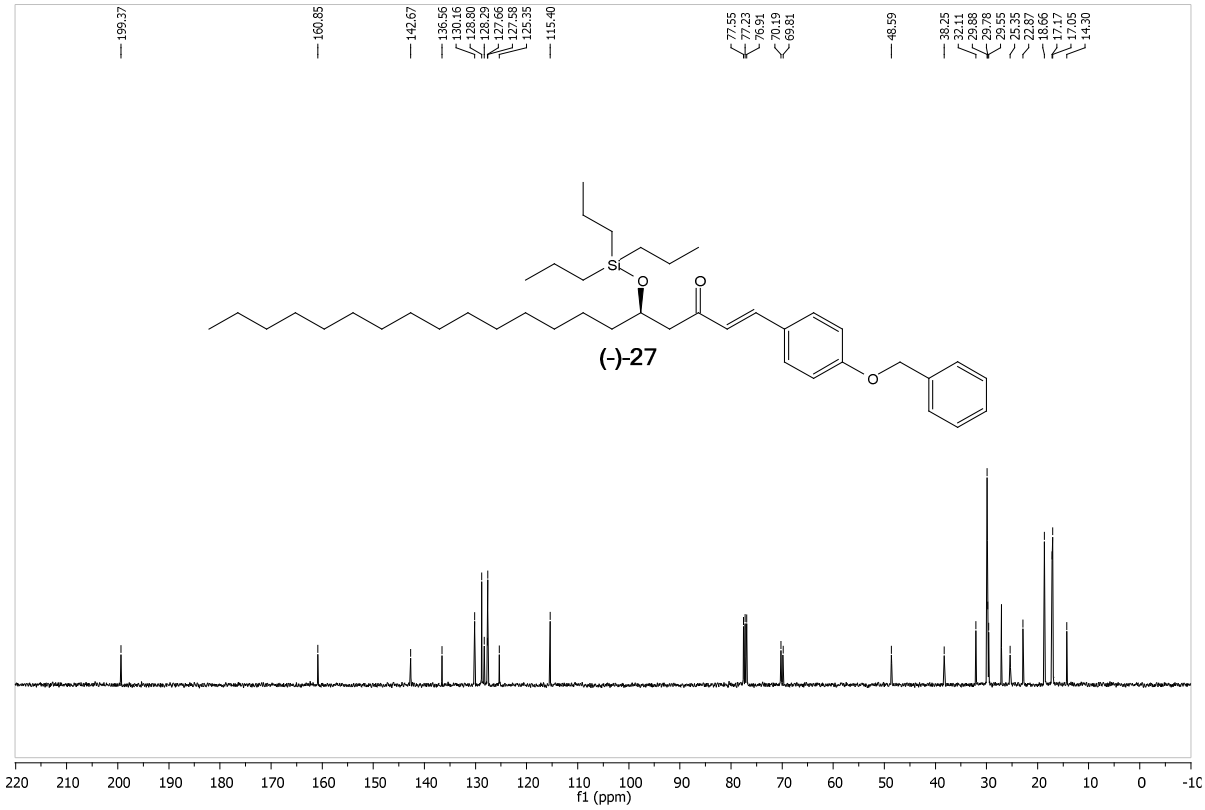

(-)-25
0.98
3.00
2.97
1.75
1.61
2.43
7.89
25.11
9.63
3.08
6.00
f1 (ppm)

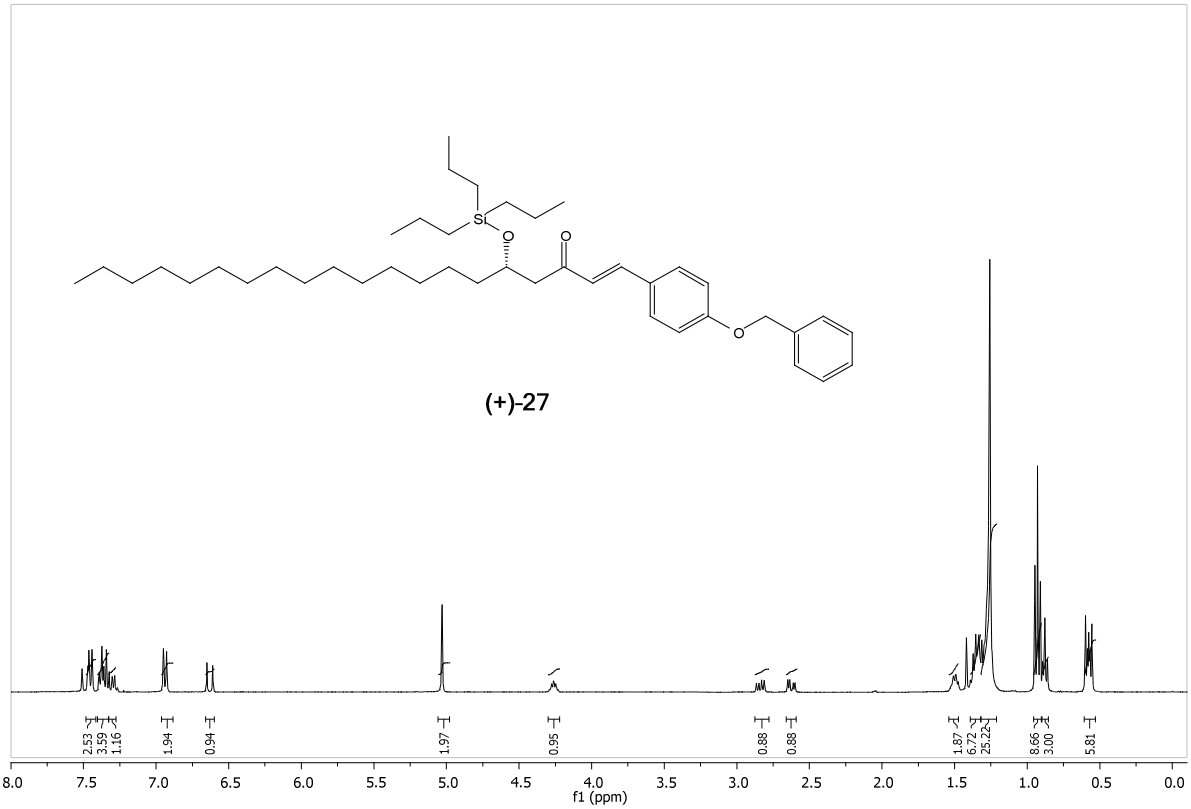

200.95
200.89
77.55
77.23
76.92
68.84
52.90
52.83
52.81
52.74
51.20
43.19
41.92
37.64
31.91
29.68
29.55
29.35
24.98
22.67
18.42
16.93
16.81
14.06
(-)-25
f1 (ppm)

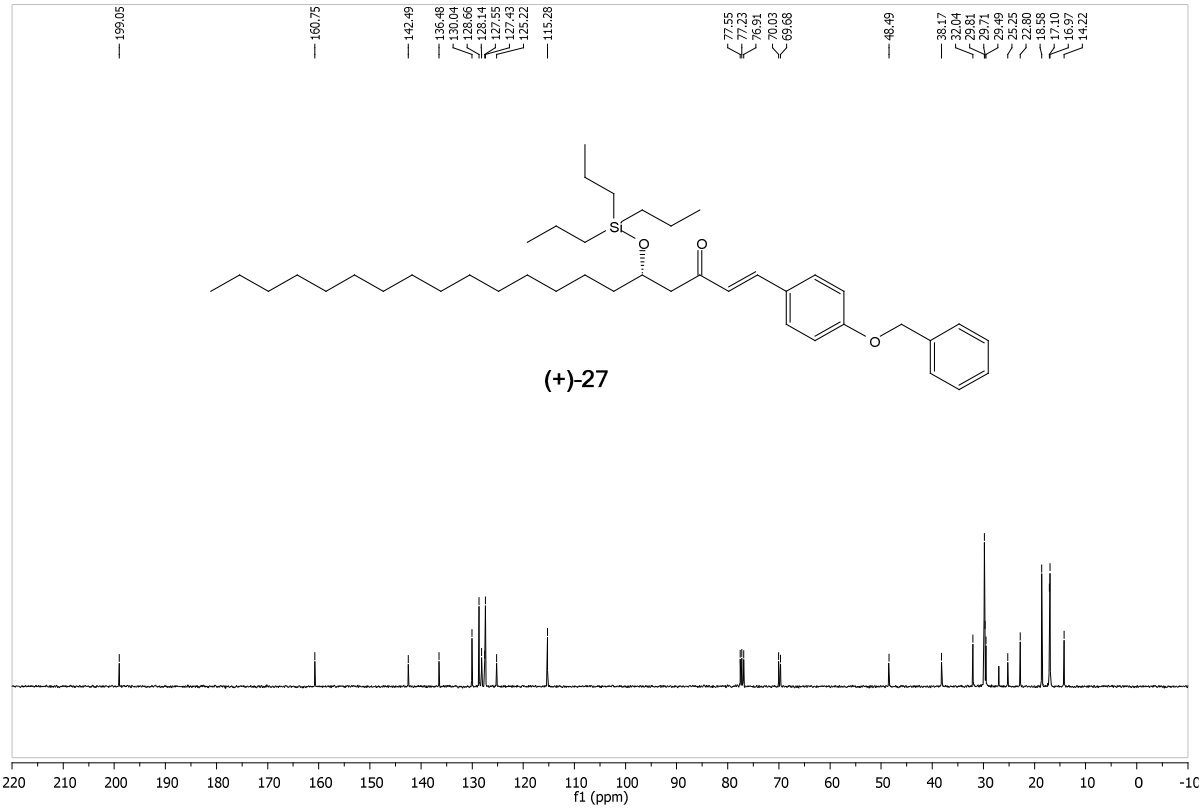

(+)-25
0.86
3.03
3.01
1.69
1.67
2.54
11.55
23.81
9.60
3.00
6.19
f1 (ppm)

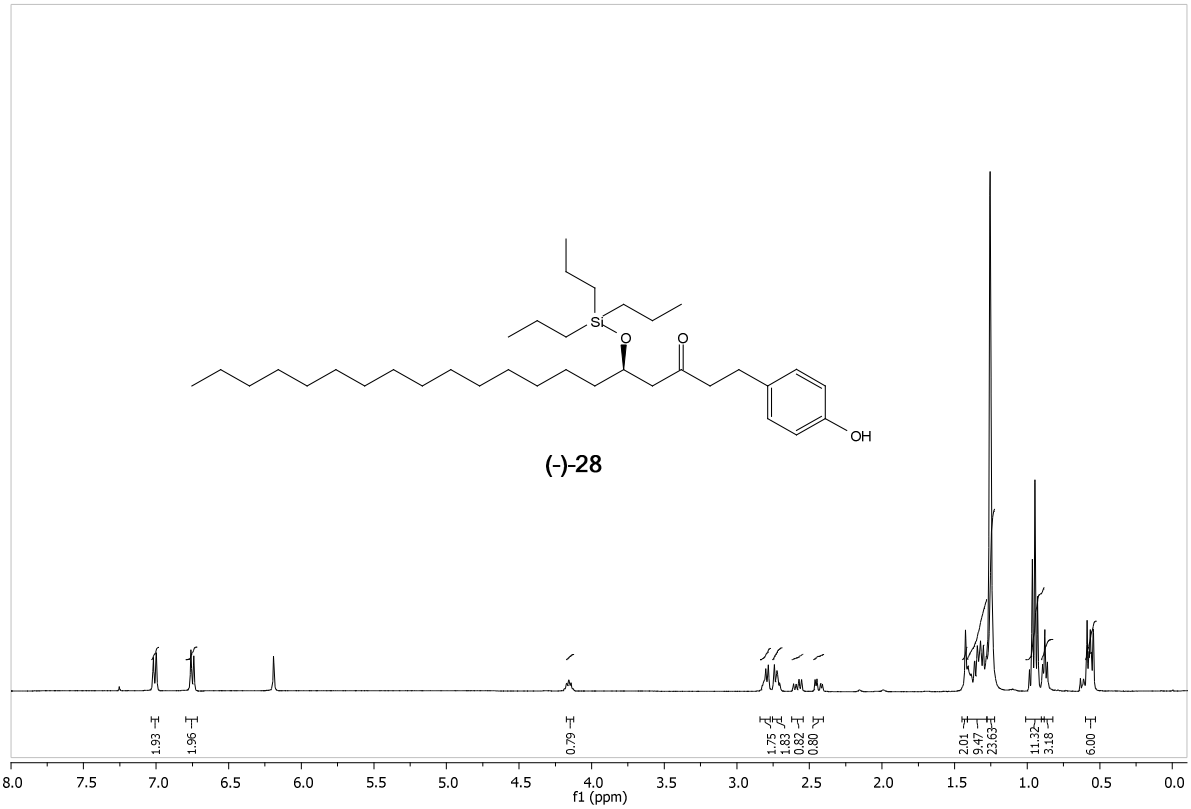

201.23
201.17
77.55
77.23
76.91
69.02
53.10
53.03
52.95
51.35
43.35
42.08
37.79
32.04
29.80
29.69
29.48
25.14
22.80
18.58
17.06
16.94
14.21
(+)-25
f1 (ppm)


(-)-27
2.96
3.89
0.81
1.88
0.84
1.92
0.87
0.86
0.83
1.81
6.33
24.95
8.19
3.00
5.73
f1 (ppm)

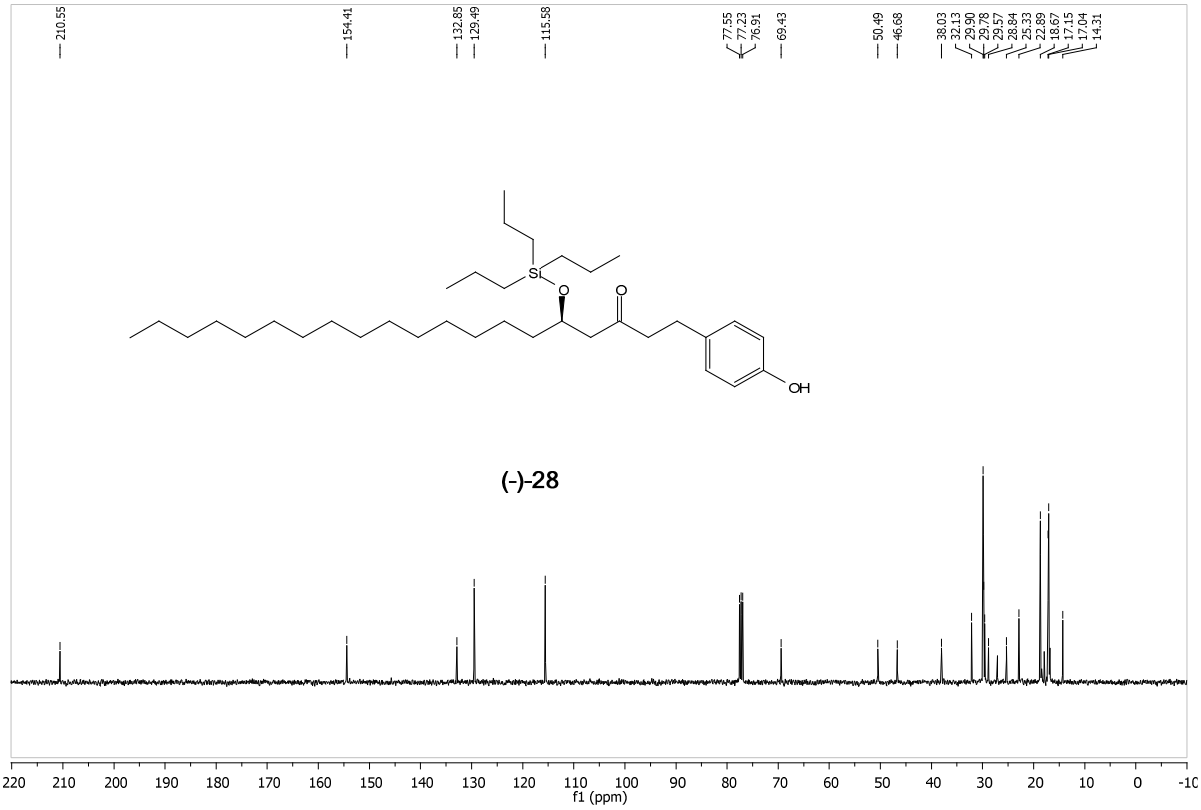

(-)-27
199.37
160.85
142.67
136.56
130.16
128.80
128.29
127.66
127.58
125.35
115.40
77.55
77.23
76.91
70.19
69.81
48.59
38.25
32.11
29.88
29.78
29.55
25.35
22.87
18.66
17.17
17.05
14.30
f1 (ppm)


Si
O
O
O
(+)-27
2.53
3.59
1.16
1.94
0.94
1.97
0.95
0.88
0.88
1.87
6.72
25.26
8.66
3.00
5.81
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)

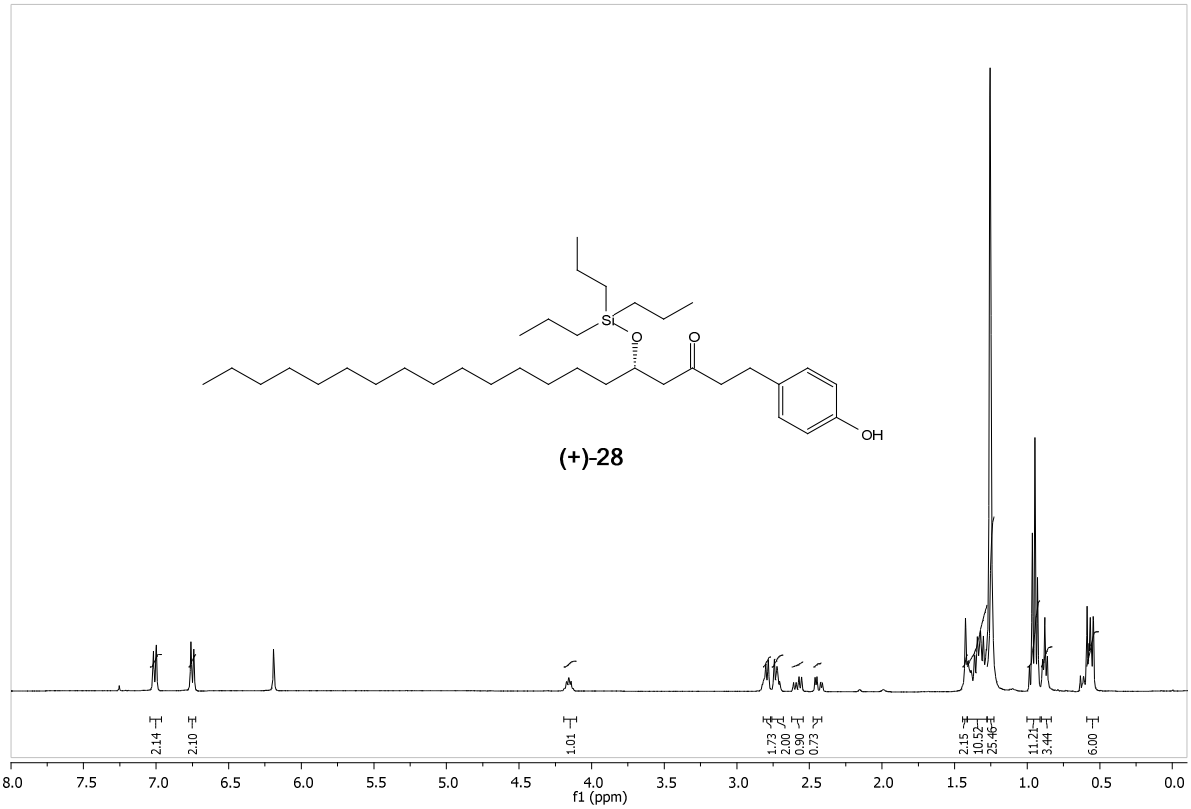

199.05
160.75
142.49
136.48
130.04
128.66
128.14
127.55
127.43
125.22
115.28
77.55
77.23
76.91
70.03
69.68
48.49
38.17
32.04
29.81
29.71
29.49
25.25
22.80
18.58
17.10
16.97
14.22
Si
O
O
O
(+)-27
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Si
O
O
OH
1.93
1.96
0.79
1.75
1.83
0.82
0.80
2.01
9.47
23.63
11.32
3.18
6.00
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 1.0 0.5 0.0
f1 (ppm)

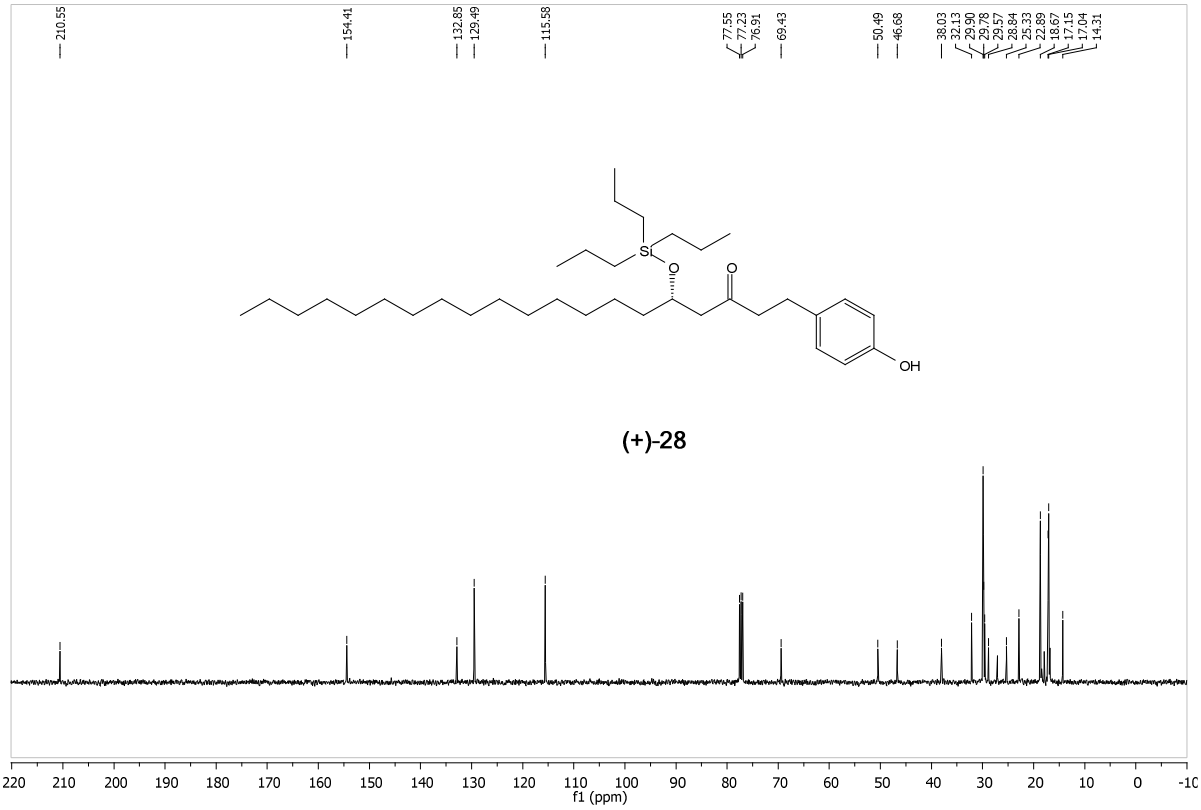
(-)-28


210.55
154.41
132.85
129.49
115.58
77.55
77.23
76.91
69.43
50.49
46.68
38.03
32.13
29.90
29.78
29.57
28.84
25.33
22.89
18.67
17.15
17.04
14.31
Si
O
O
OH
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

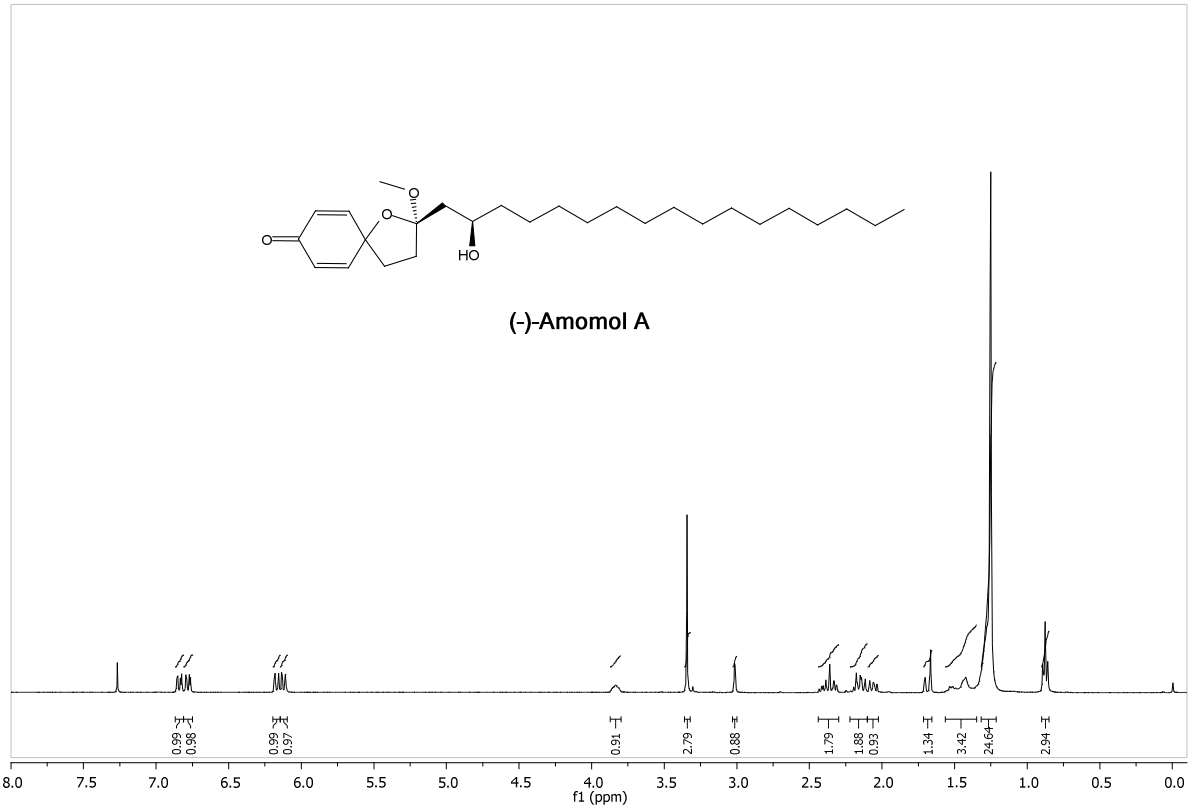
(-)-28

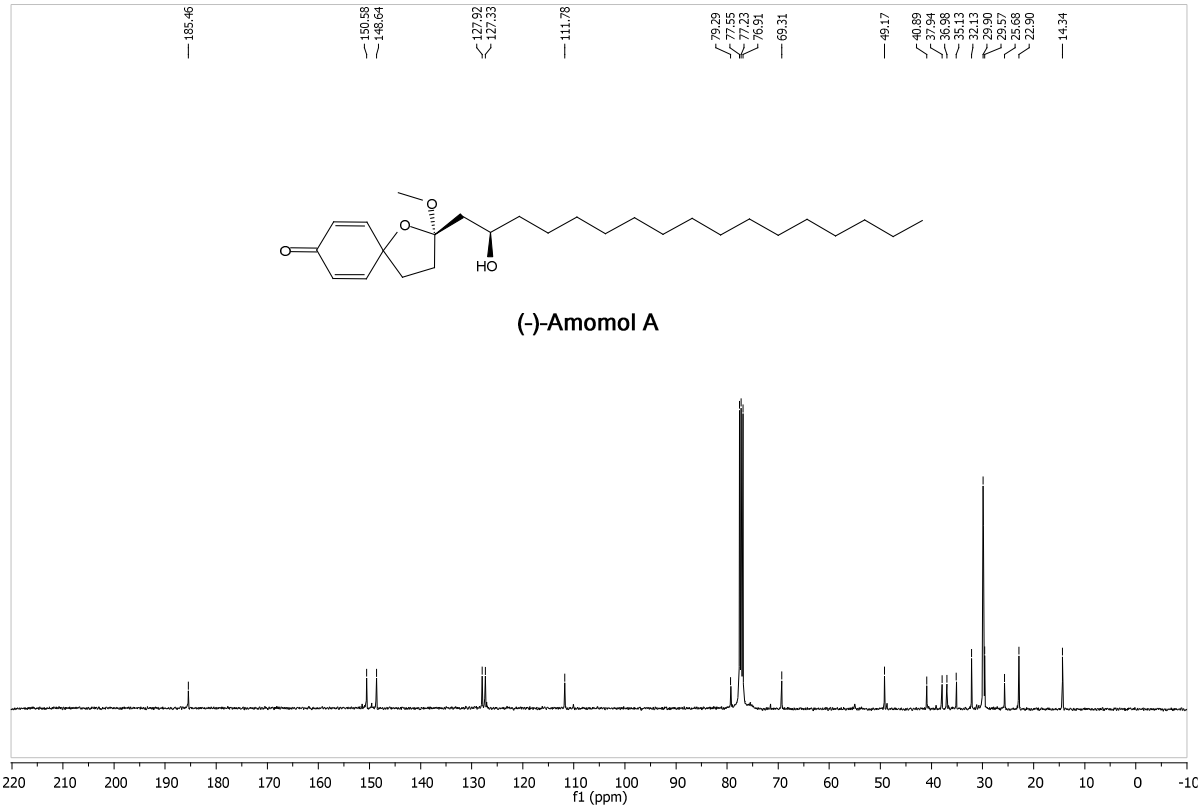

Si
O
O
OH
2.14
2.10
1.01
1.73
2.00
0.90
0.73
2.15
10.52
25.46
11.21
3.44
6.00
f1 (ppm)

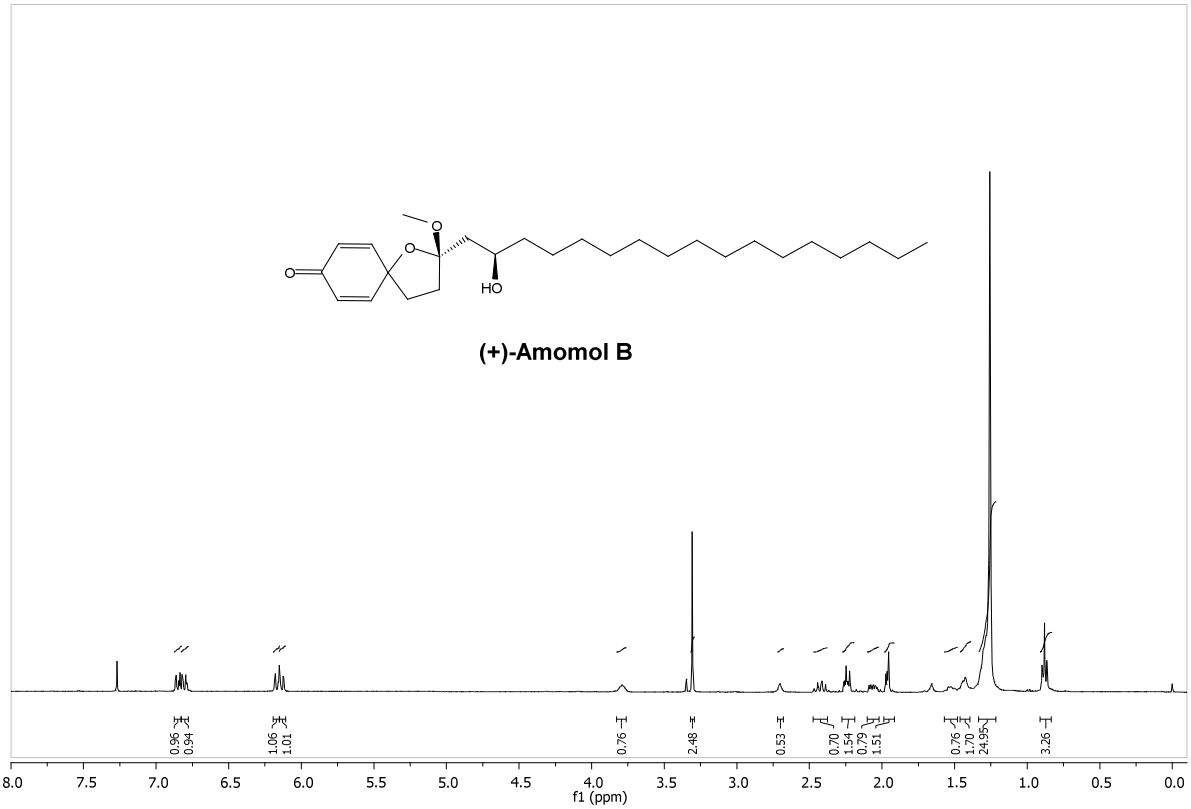
(+)-28

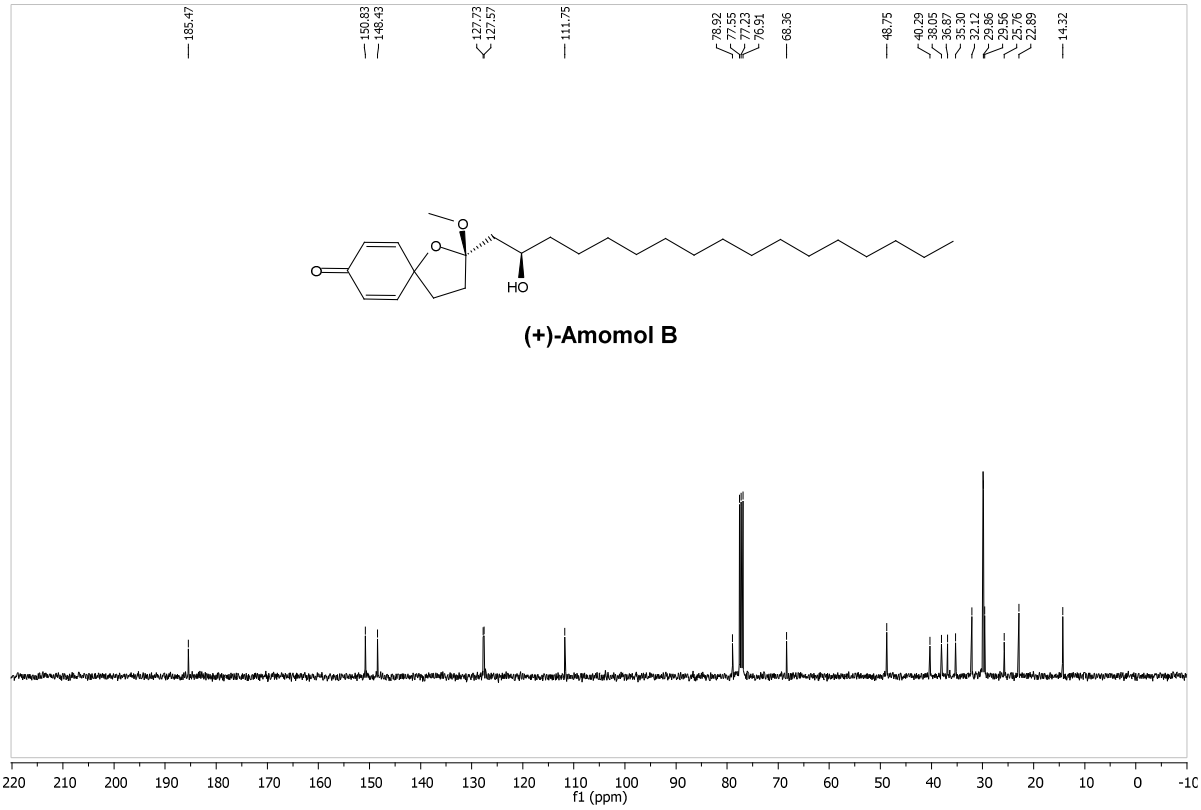

210.55
154.41
132.85
129.49
115.58
77.55
77.23
76.91
69.43
50.49
46.68
38.03
32.13
29.90
29.78
29.57
28.84
25.33
22.89
18.67
17.15
17.04
14.31
Si
O
O
OH
f1 (ppm)

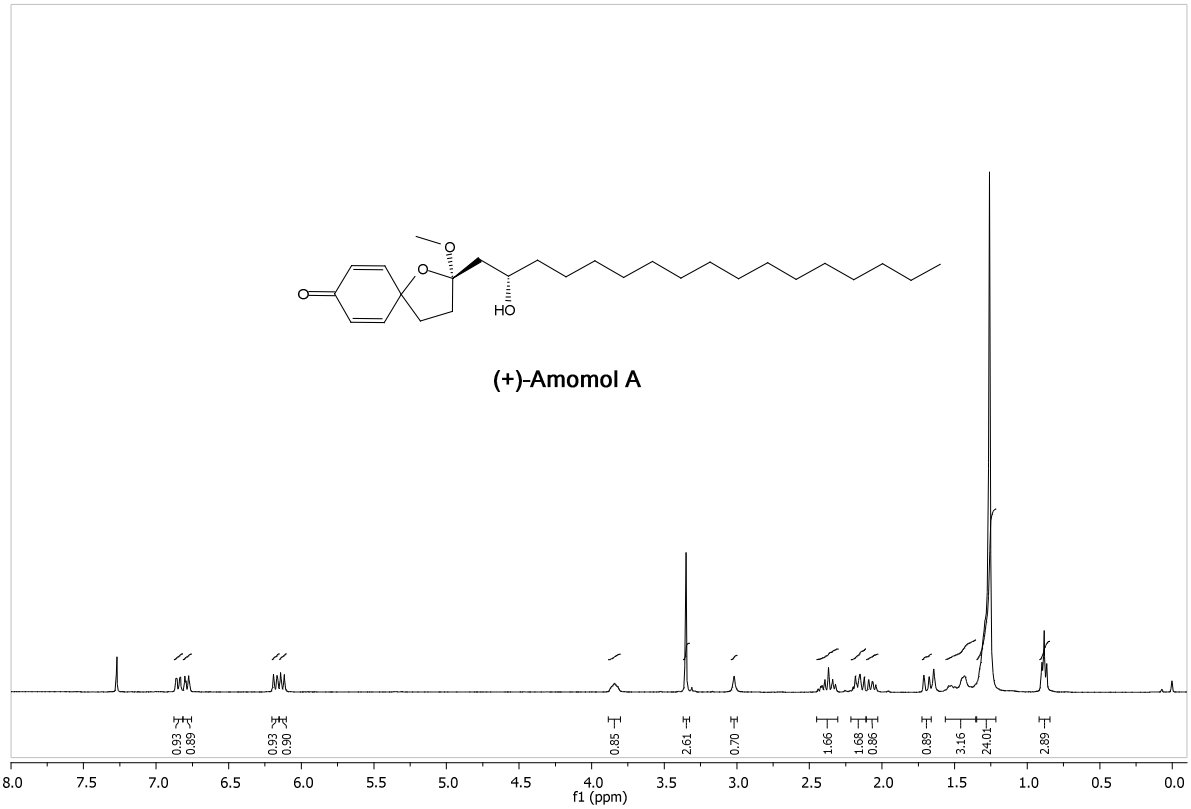
(+)-28

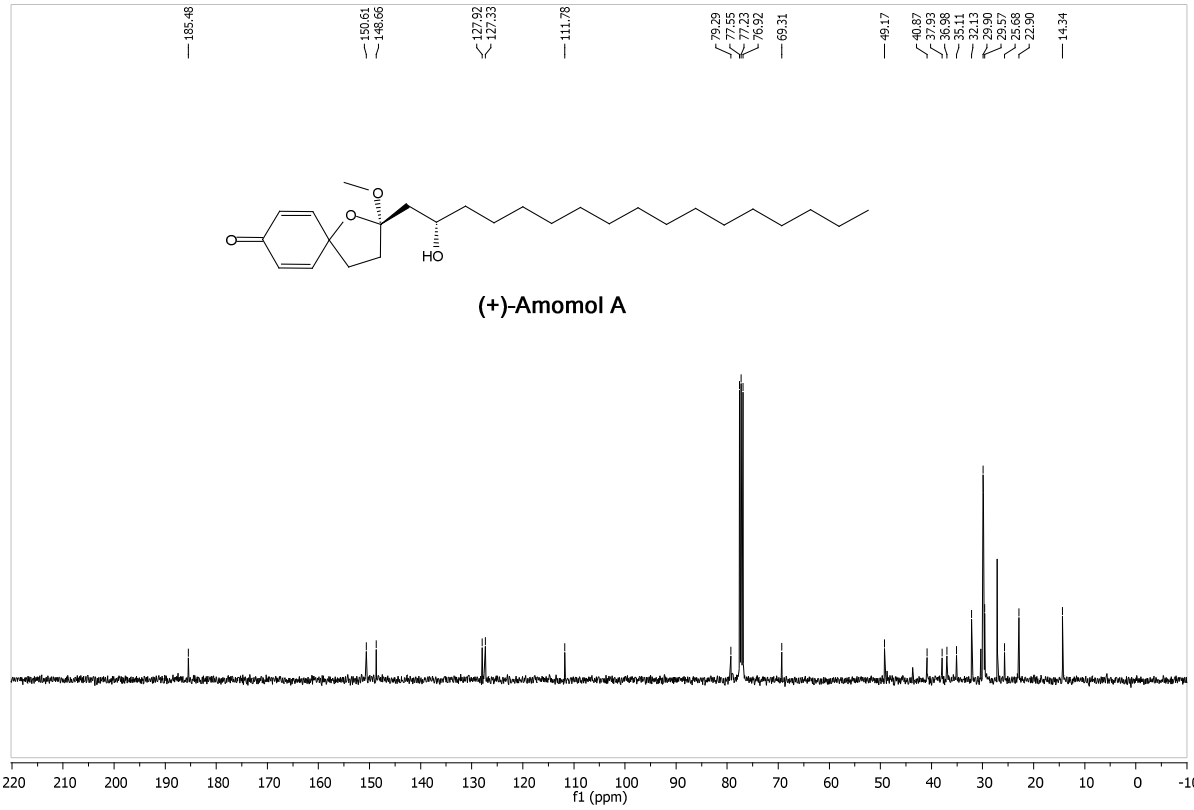

(-)-Amomol A
0.99
0.98
0.99
0.97
0.91
2.79
0.88
1.79
1.88
0.93
1.34
3.42
24.64
2.94
f1 (ppm)

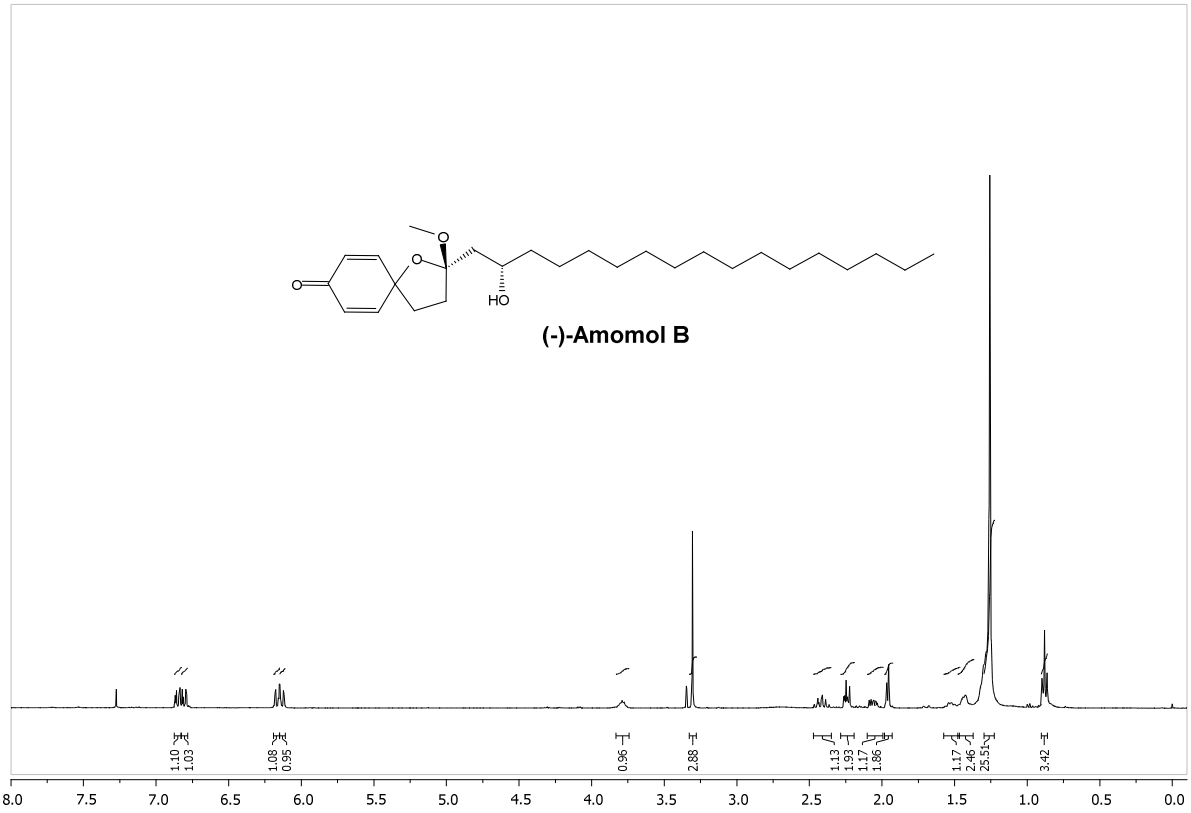

185.46
150.58
148.64
127.92
127.33
111.78
79.29
77.55
77.23
76.91
69.31
49.17
40.89
37.94
36.98
35.13
32.13
29.90
29.57
25.68
22.90
14.34
(-)-Amomol A
f1 (ppm)

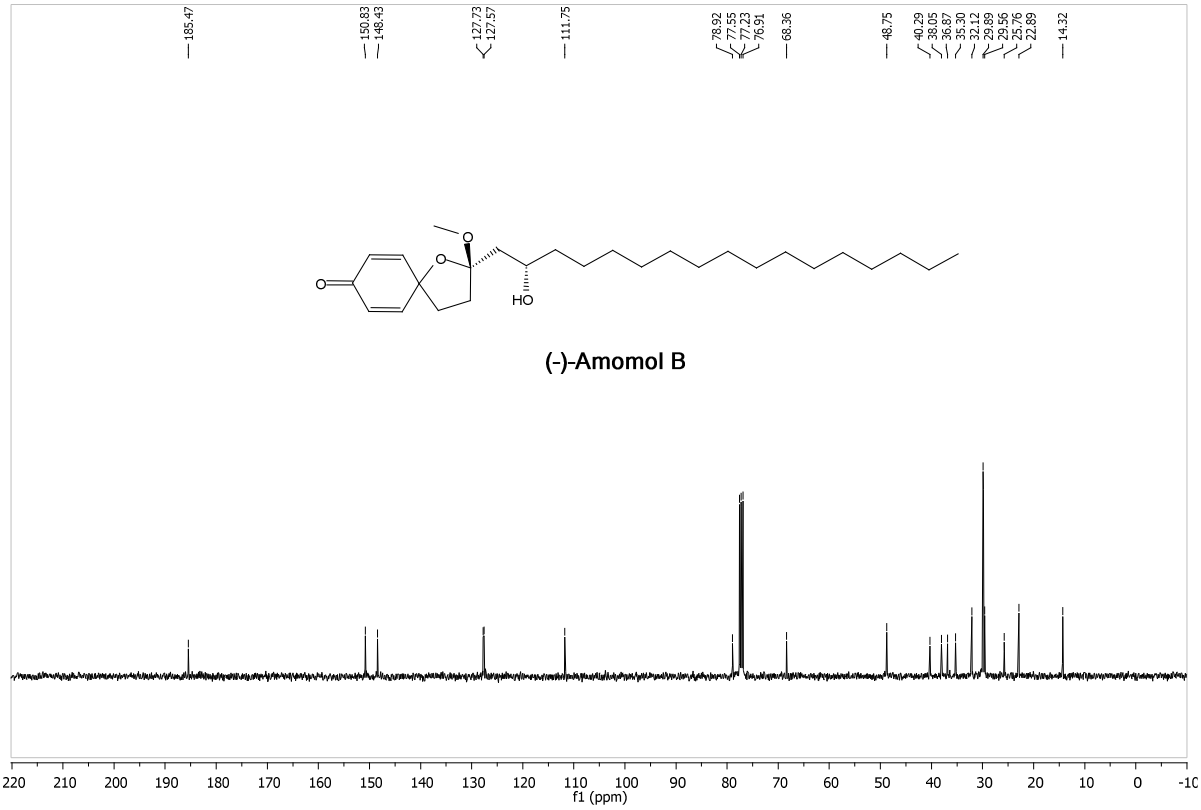

O
O
HO
(+)-Amomol B
0.96
0.94
1.06
1.01
0.76
2.48
0.53
0.70
1.54
0.79
1.51
0.76
1.70
24.95
3.26
f1 (ppm)


185.47
150.83
148.43
127.73
127.57
111.75
78.92
77.55
77.23
76.91
68.36
48.75
40.29
38.05
36.87
35.30
32.12
29.86
29.56
25.76
22.89
14.32
O
O
HO
(+)-Amomol B
f1 (ppm)


(+)-Amomol A
0.93
0.89
0.93
0.90
0.85
2.61
0.70
1.66
1.68
0.86
0.89
3.16
24.01
2.89
f1 (ppm)


185.48
150.61
148.66
127.92
127.33
111.78
79.29
77.55
77.23
76.92
69.31
49.17
40.87
37.93
36.98
35.11
32.13
29.90
29.57
25.68
22.90
14.34
(+)-Amomol A
f1 (ppm)


(-)-Amomol B
1.10
1.03
1.08
0.95
0.96
2.88
1.13
1.93
1.17
1.86
1.17
2.46
25.51
3.42
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


185.47
150.83
148.43
127.73
127.57
111.75
78.92
77.55
77.23
76.91
68.36
48.75
40.29
38.05
36.87
35.30
32.12
29.89
29.56
25.76
22.89
14.32
(-)-Amomol B
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)