Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.
This journal is © The Royal Society of Chemistry 2014

Supporting Information

Evaluation of the Effect of Fluorination on the Property of Monofluorinated Dimyristoylphosphatidylcholines

Marie-Claude Gagnon,[a,b] Bianka Turgeon,[a,b] Jean-Daniel Savoie,[a,b] Jean-François Parent,[a,b] Michèle Auger[b,*] and Jean-François Paquin[a,*]

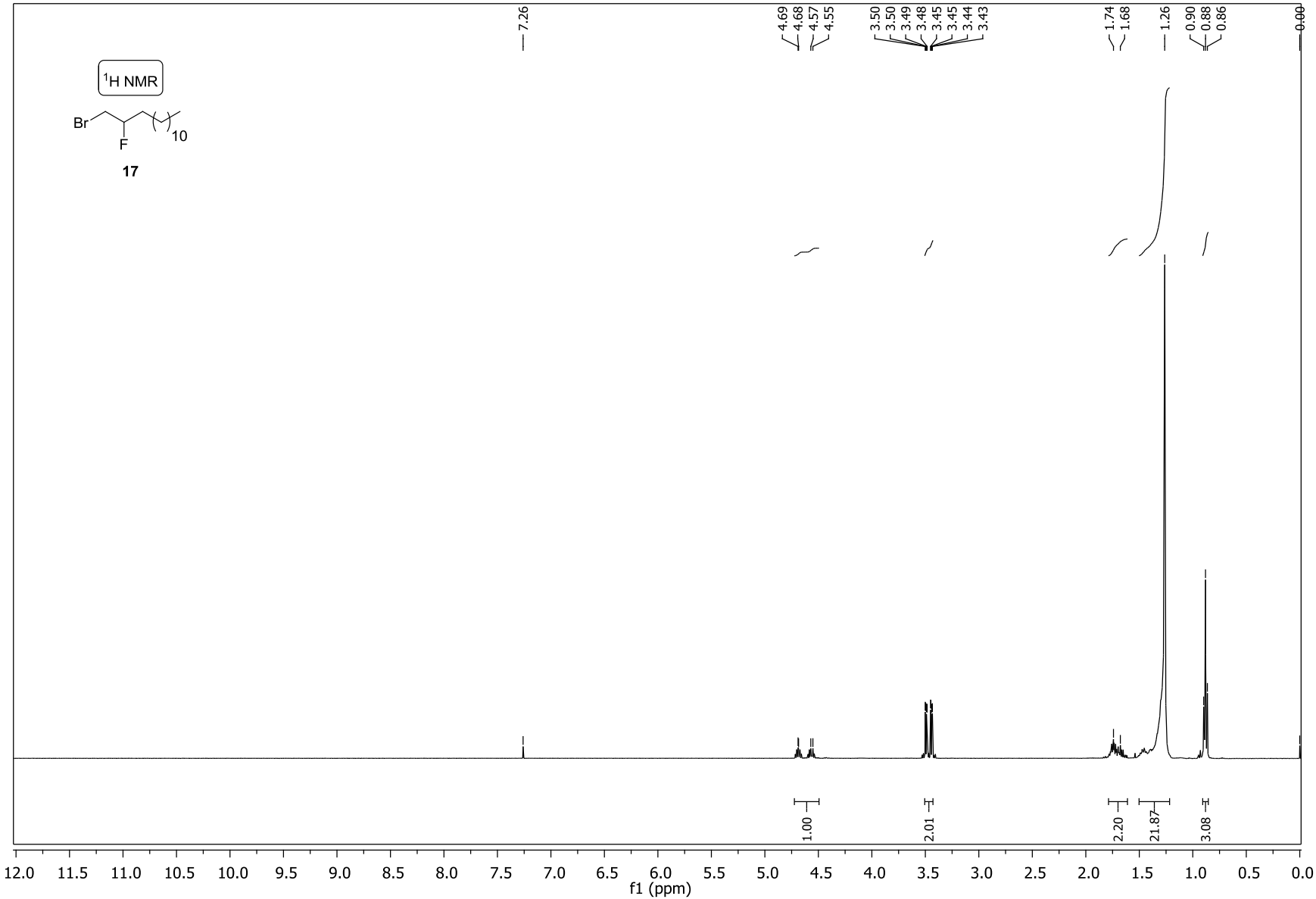
[a]Canada Research Chair in Organic and Medicinal Chemistry, PROTEO, Département de chimie, Université Laval, 1045 avenue de la Médecine, Québec, QC, Canada G1V 0A6

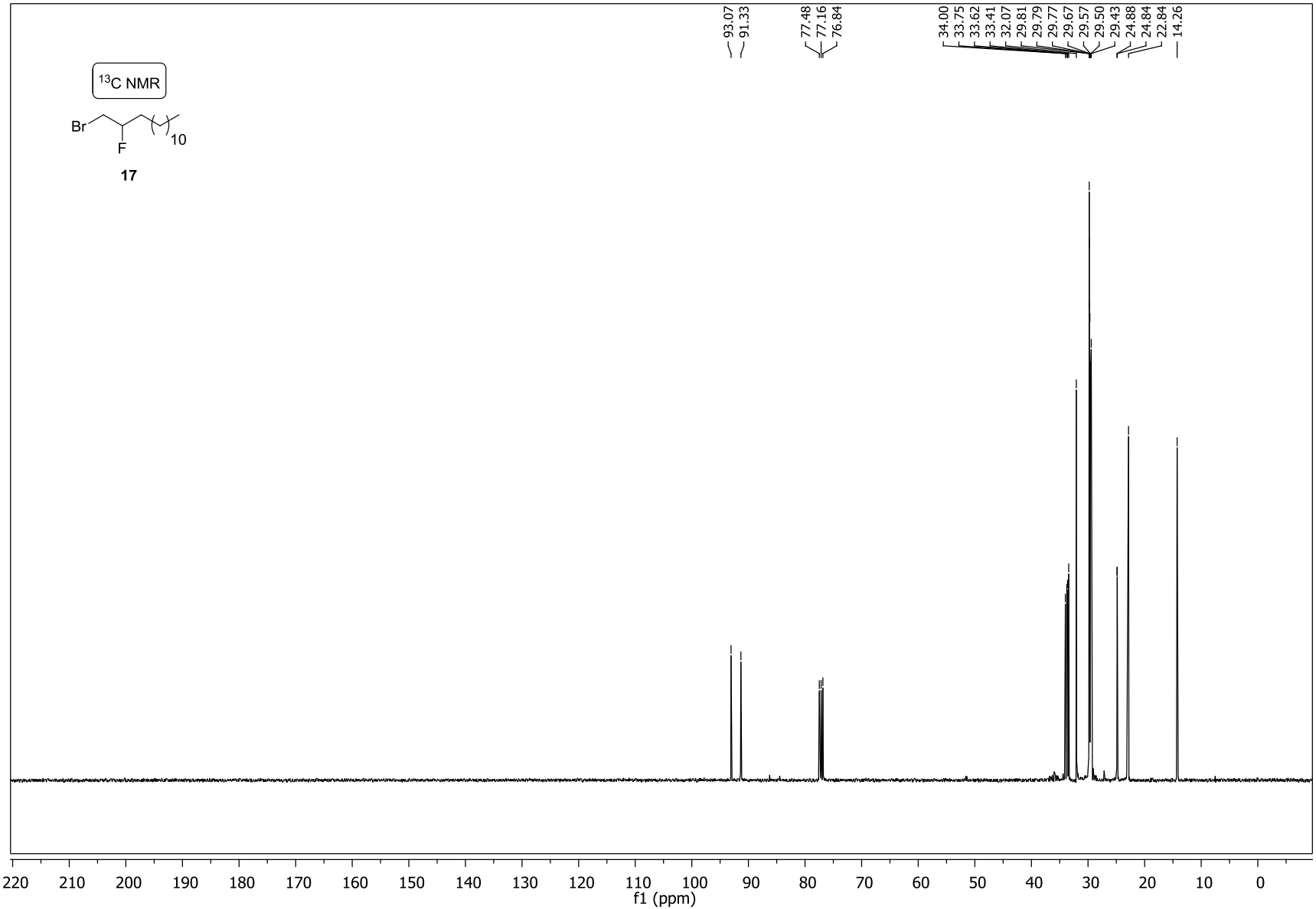
[b]PROTEO, CERMA, Département de chimie, Université Laval, 1045 avenue de la Médecine, Québec, QC, Canada G1V 0A6

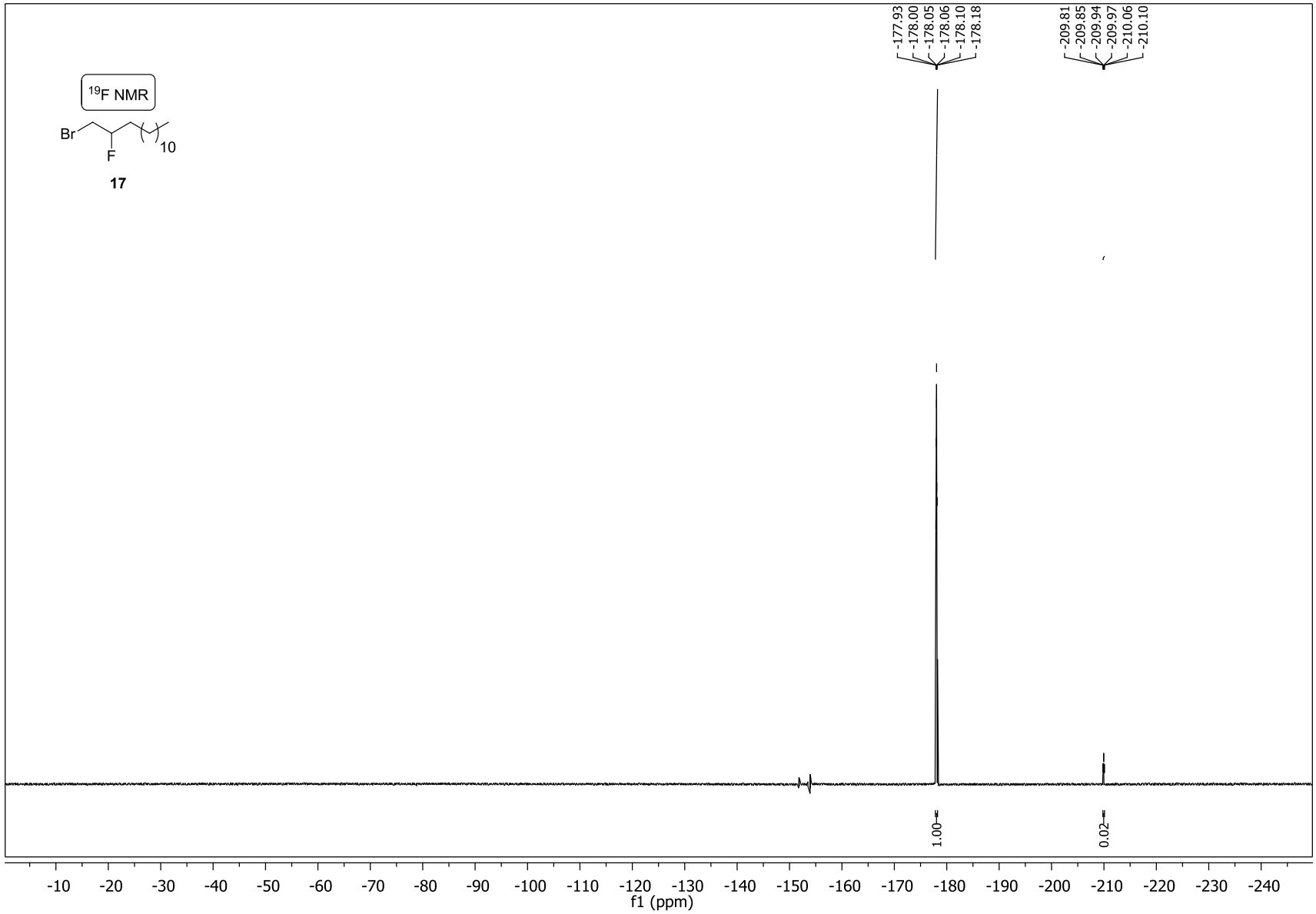
michele.auger@chm.ulaval.ca

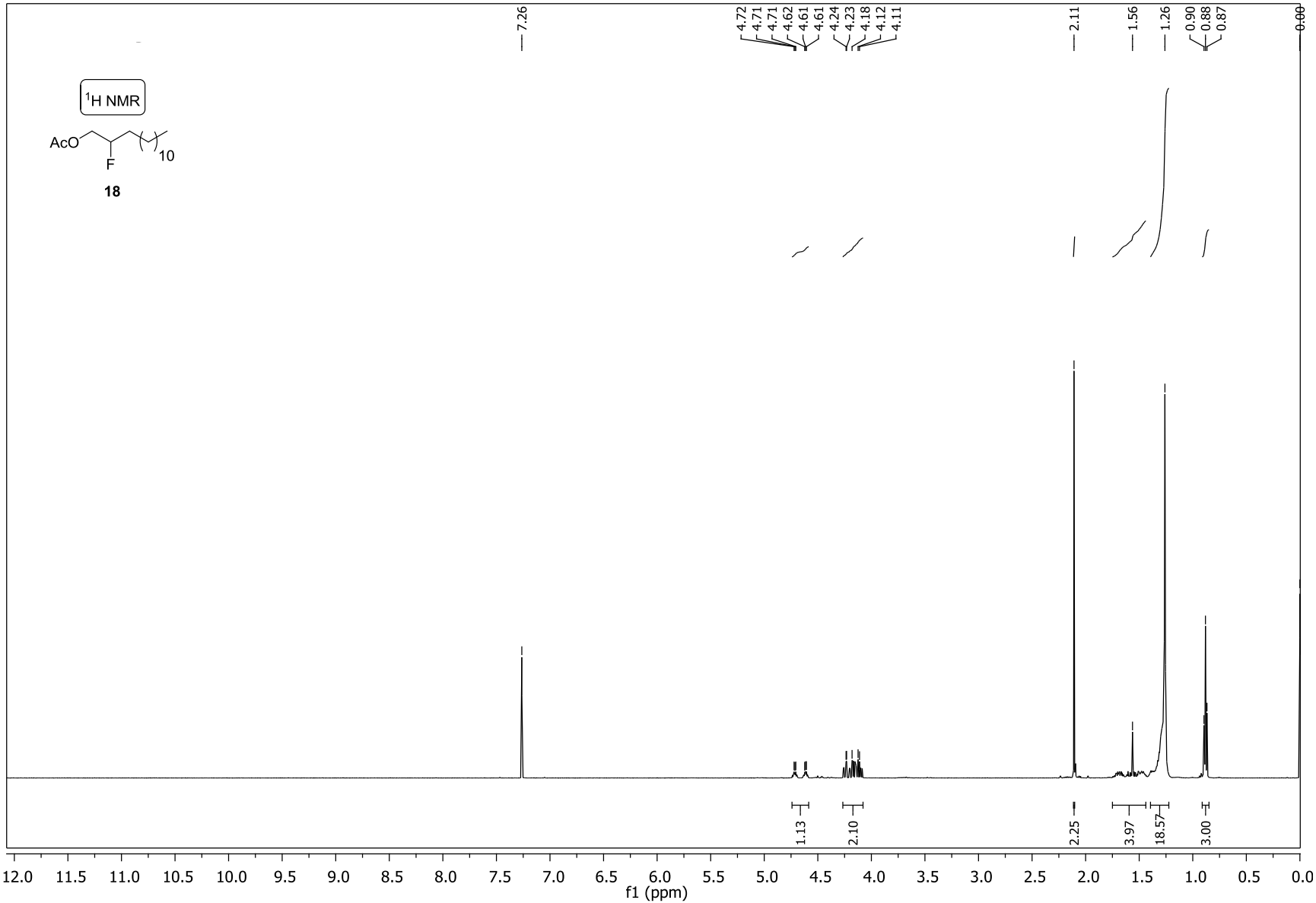
jean-francois.paquin@chm.ulaval.ca

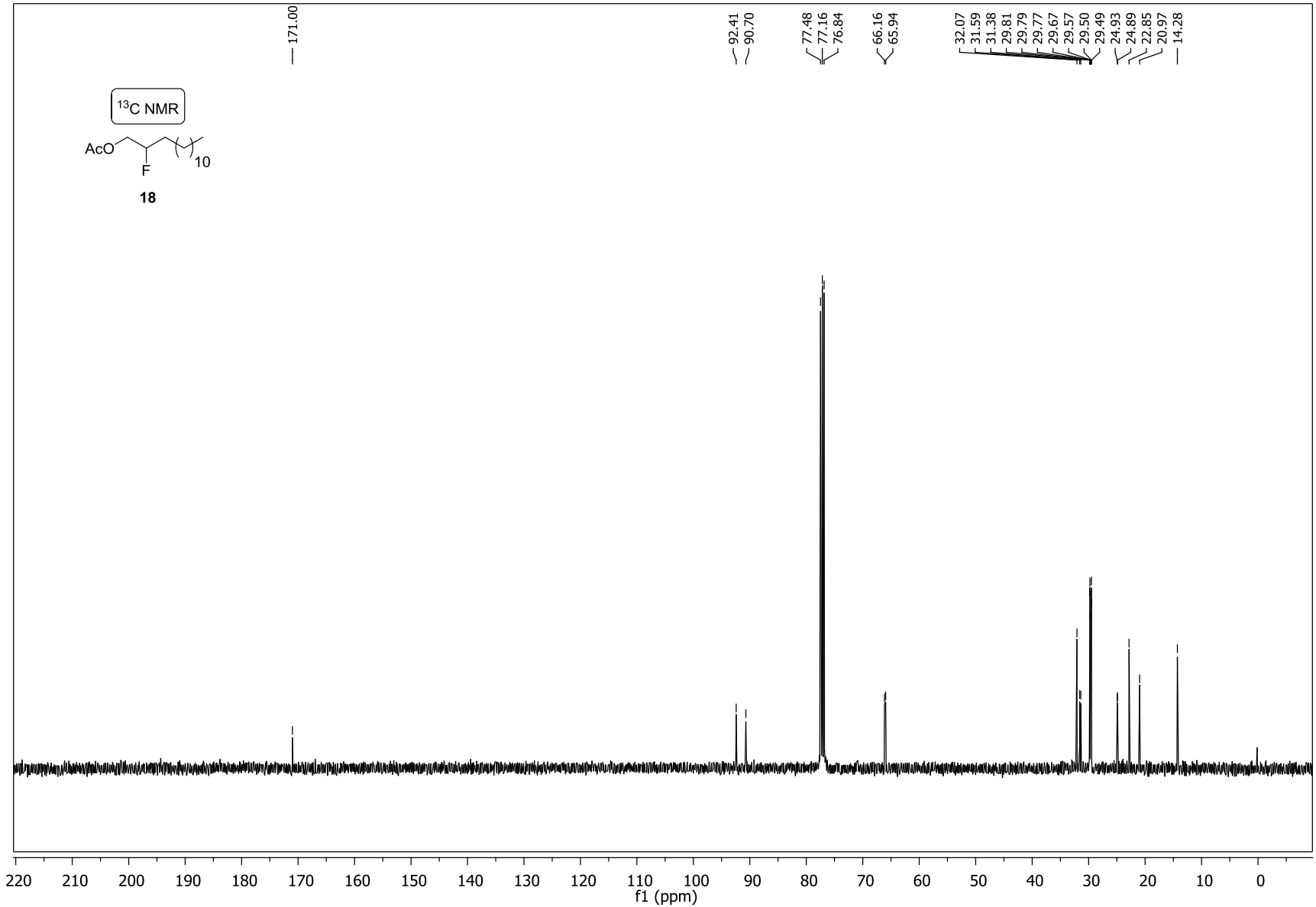
Table of contents

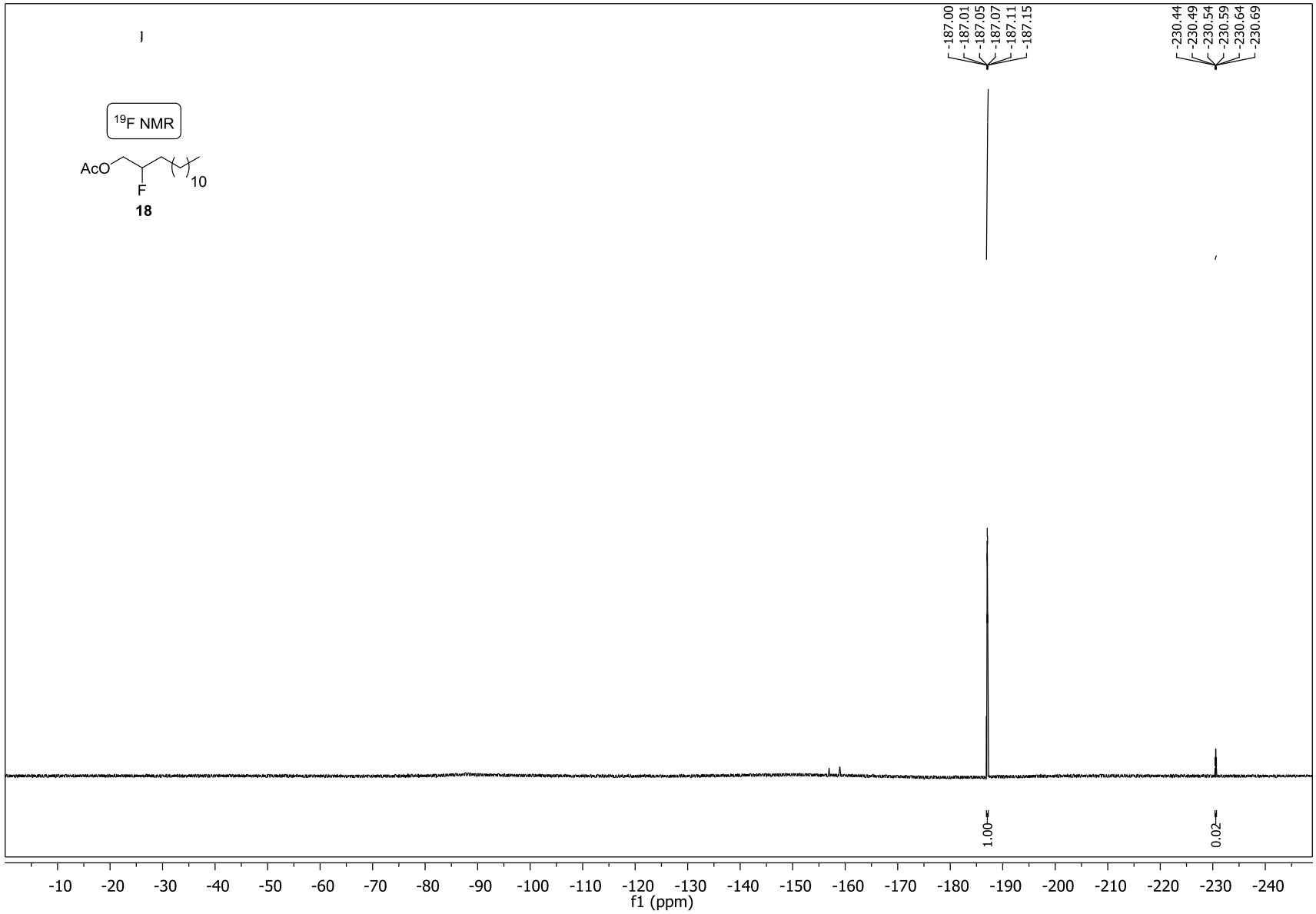

7.26
4.69
4.68
4.57
4.55
3.50
3.50
3.49
3.48
3.45
3.45
3.44
3.43
1.74
1.68
1.26
0.90
0.88
0.86
0.00
1H NMR
Br
F
10
17
1.00
2.01
2.20
21.87
3.08
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

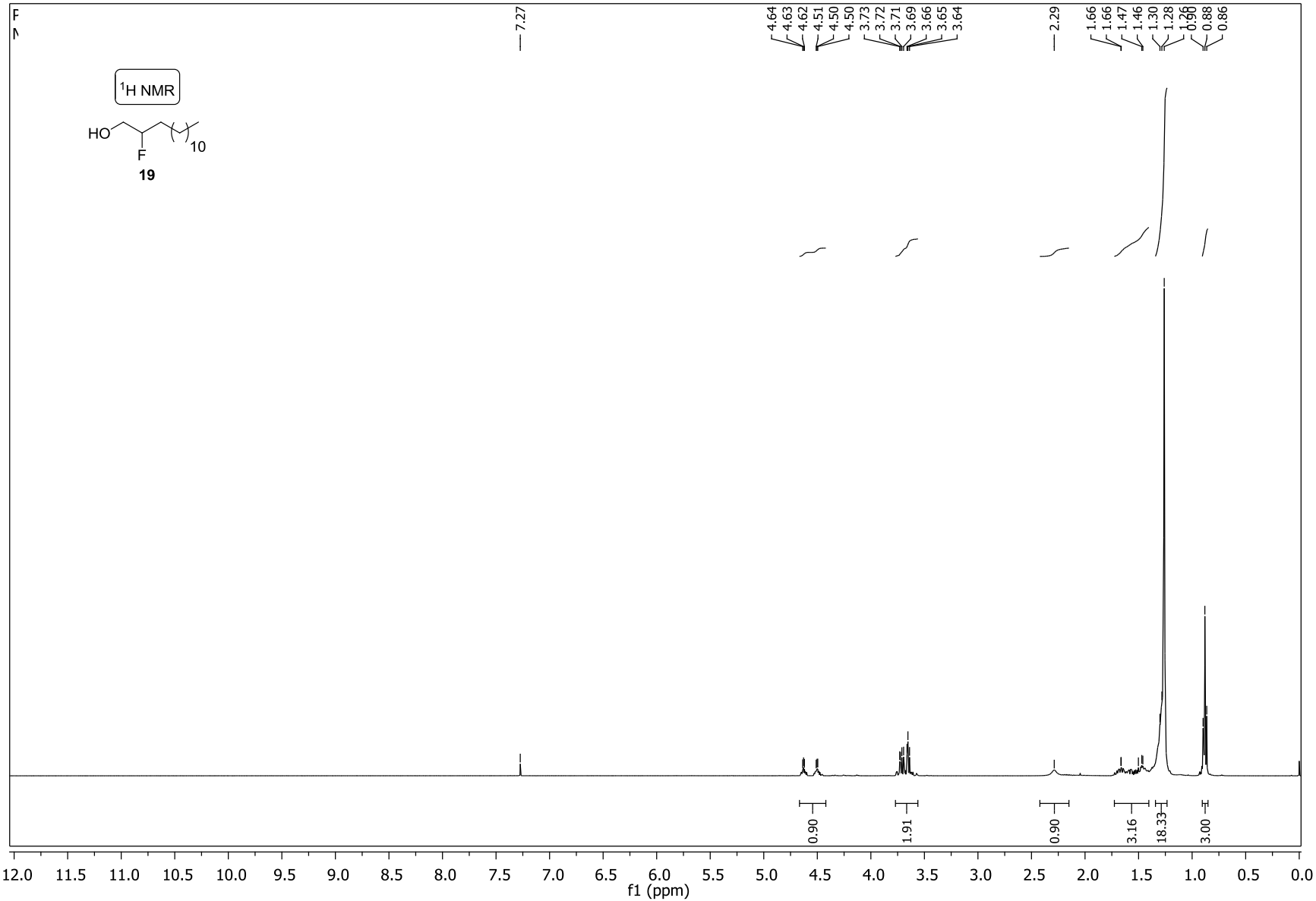

93.07
91.33
77.48
77.16
76.84
34.00
33.75
33.62
33.41
32.07
29.81
29.79
29.77
29.67
29.57
29.50
29.43
24.88
24.84
22.84
14.26
13C NMR
Br
F
10
17
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

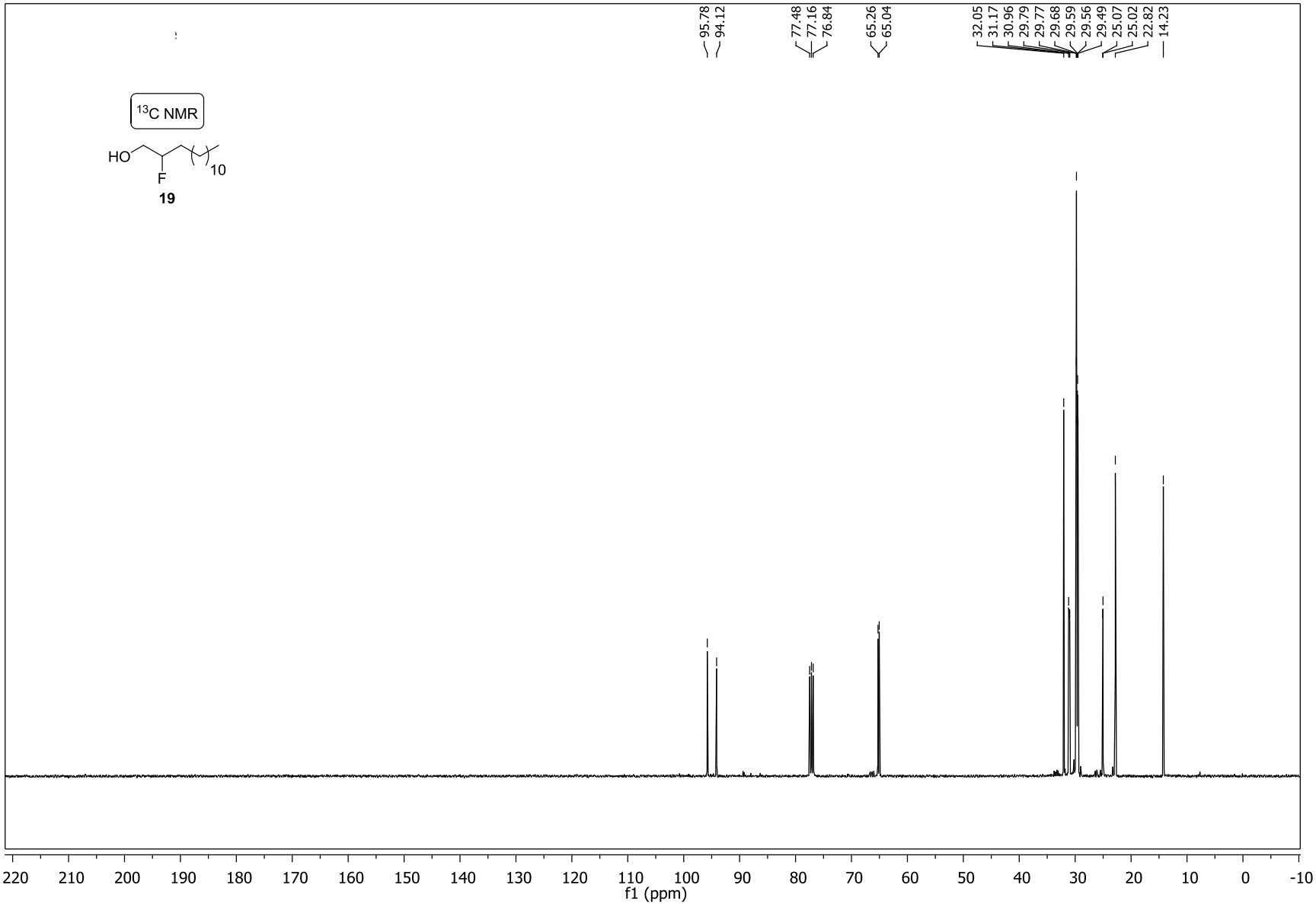

-177.93
-178.00
-178.05
-178.06
-178.10
-178.18
-209.81
-209.85
-209.94
-209.97
-210.06
-210.10
19F NMR
Br
F
10
17
1.00
0.02
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

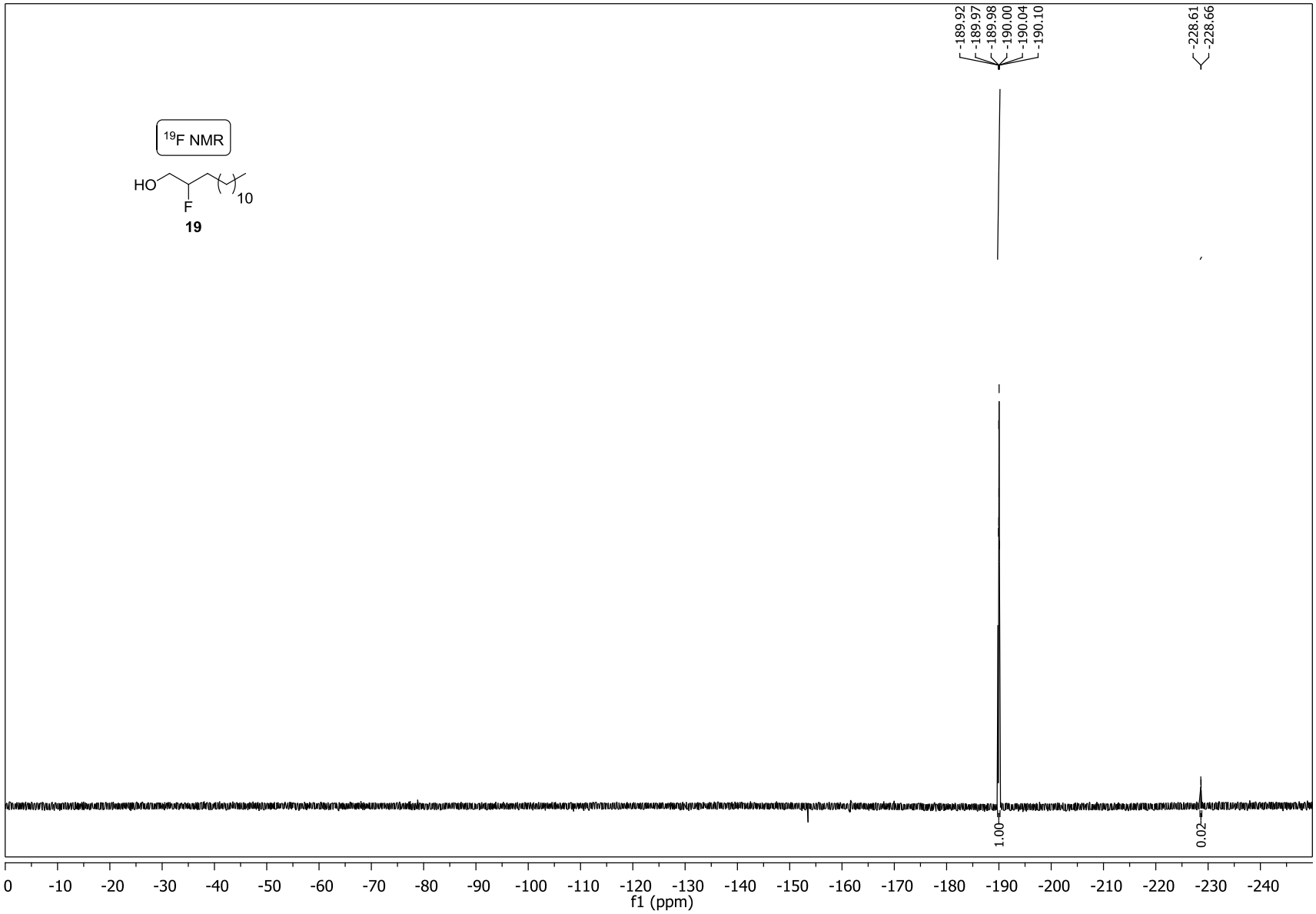

7.26
4.72
4.71
4.71
4.62
4.61
4.61
4.24
4.23
4.18
4.12
4.11
2.11
1.56
1.26
0.90
0.88
0.87
0.00
1H NMR
AcO
F
10
18
1.13
2.10
2.25
3.97
18.57
3.00
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

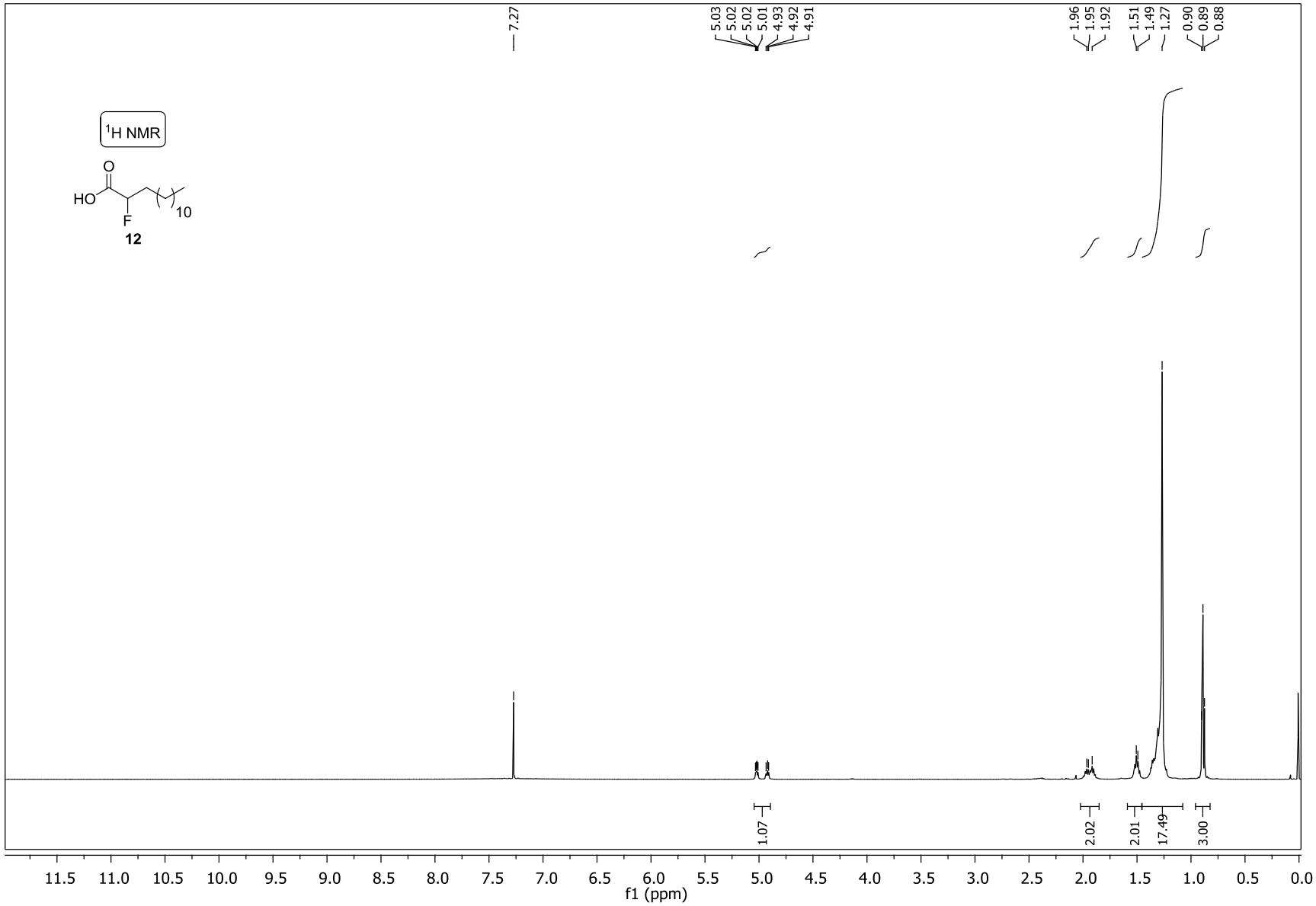

171.00
92.41
90.70
77.48
77.16
76.84
66.16
65.94
32.07
31.59
31.38
29.81
29.79
29.77
29.67
29.57
29.50
29.49
24.93
24.89
22.85
20.97
14.28
13C NMR
AcO
F
10
18
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

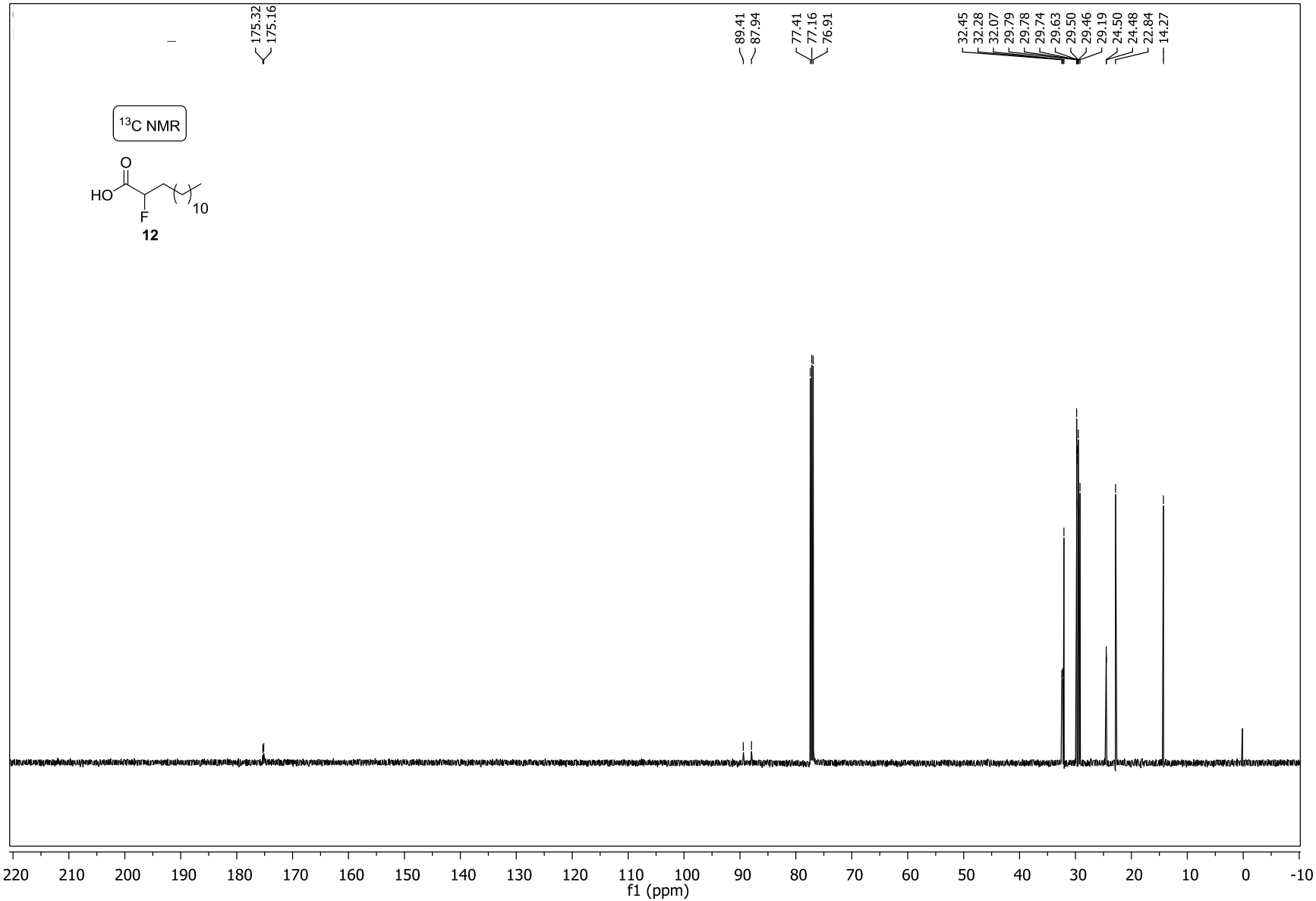

-187.00
-187.01
-187.05
-187.07
-187.11
-187.15
-230.44
-230.49
-230.54
-230.59
-230.64
-230.69
^{19}F NMR
AcO
F
10
18
1.00
0.02
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

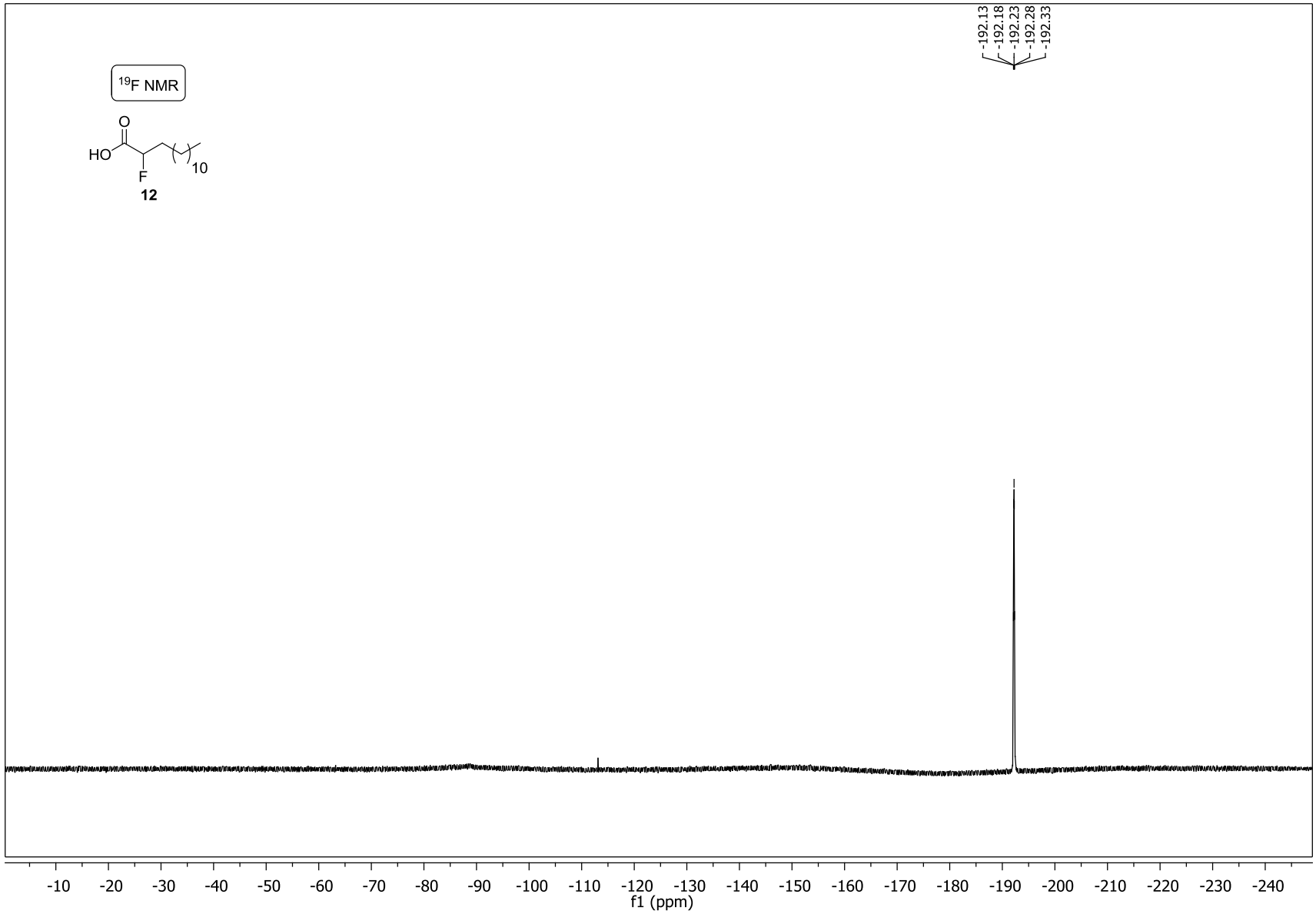

^{1}H NMR
HO
F
10
19
7.27
4.64
4.63
4.62
4.51
4.50
4.50
3.73
3.72
3.71
3.69
3.66
3.65
3.64
2.29
1.66
1.66
1.47
1.46
1.30
1.28
0.88
0.86
0.90
1.91
0.90
3.16
18.33
3.00
f1 (ppm)

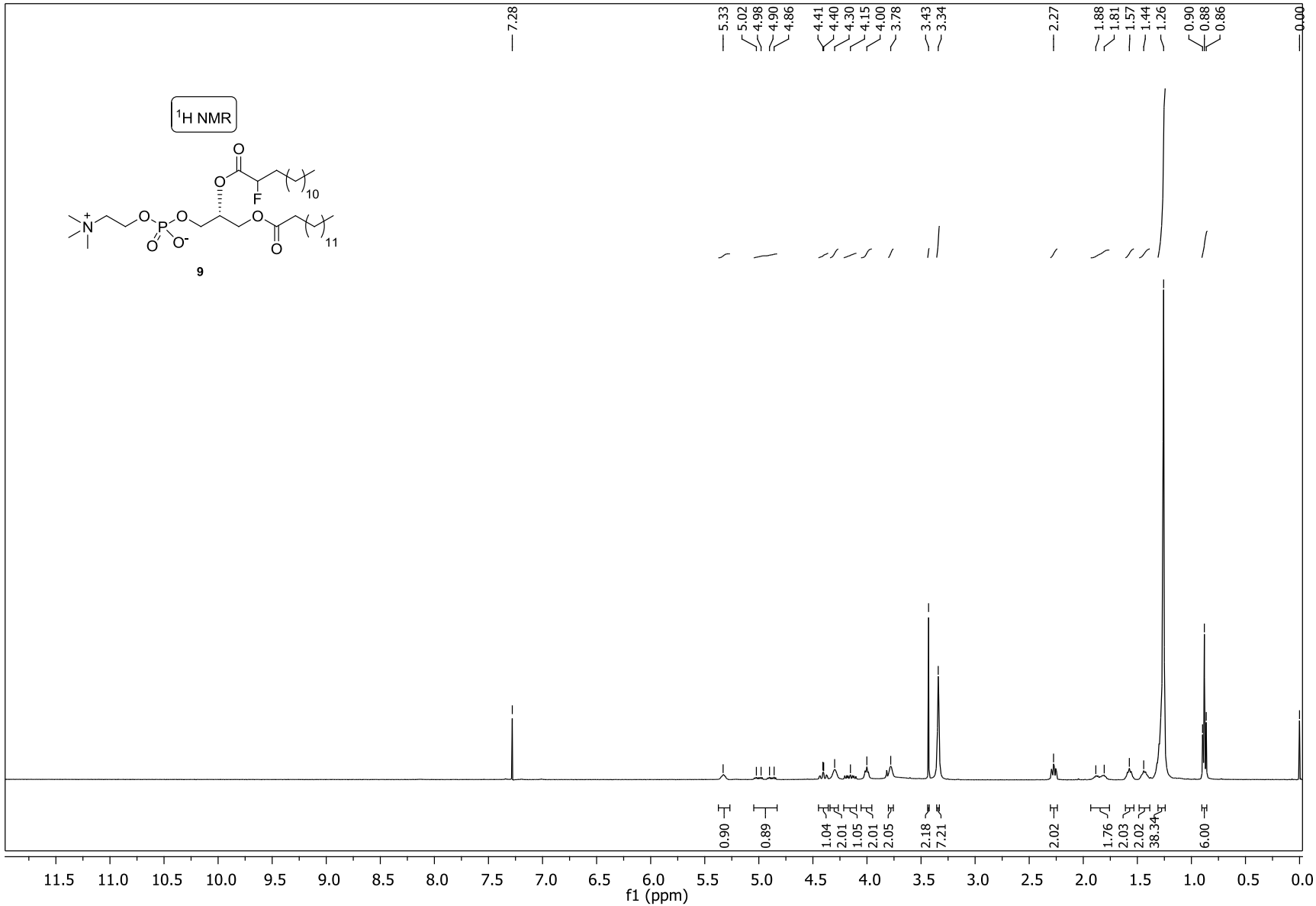

95.78
94.12
77.48
77.16
76.84
65.26
65.04
32.05
31.17
30.96
29.79
29.77
29.68
29.59
29.56
29.49
25.07
25.02
22.82
14.23
13C NMR
HO
F
10
19
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

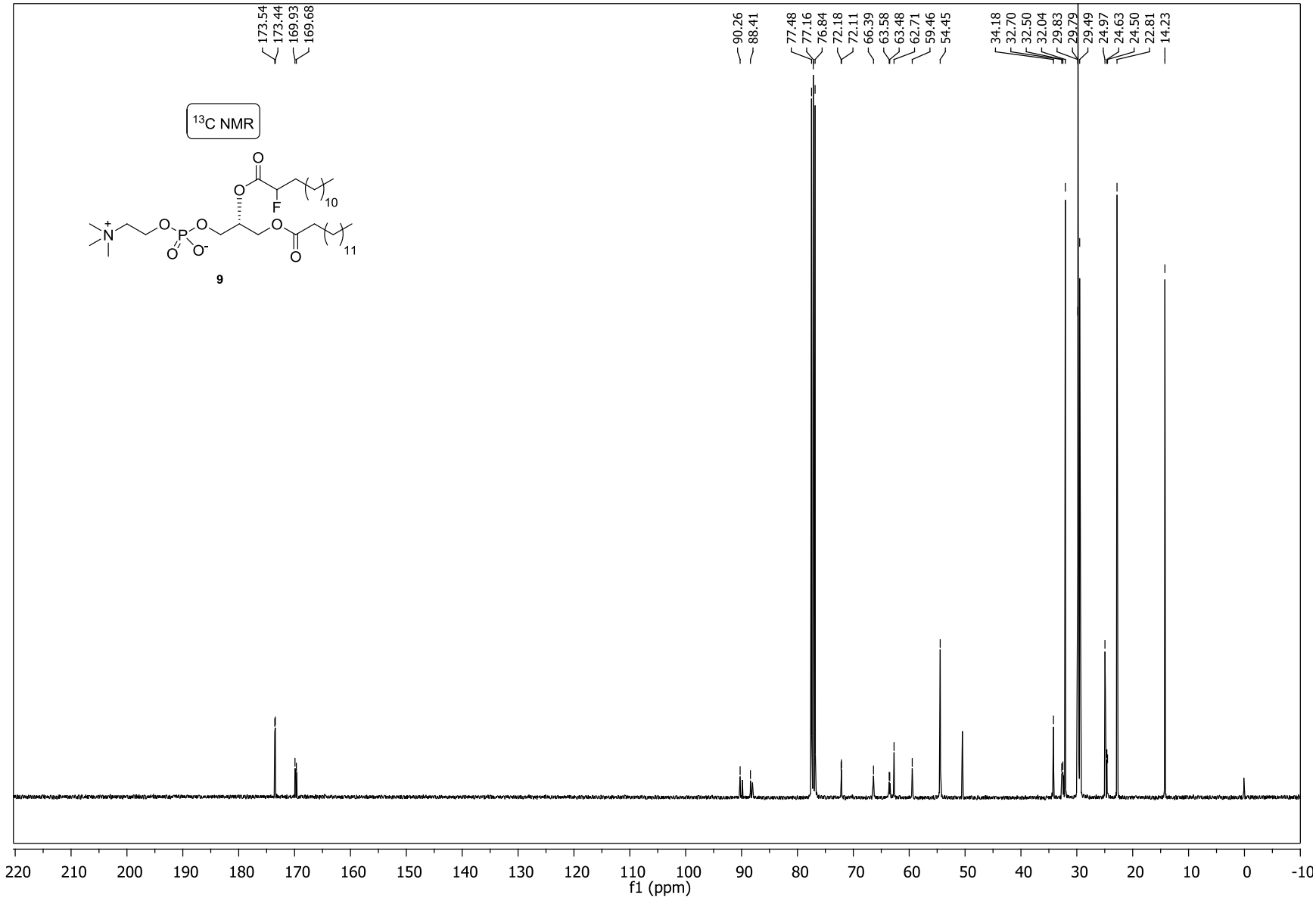

-189.92
-189.97
-189.98
-190.00
-190.04
-190.10
-228.61
-228.66
^{19}F NMR
HO
F
10
19
1.00
0.02
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

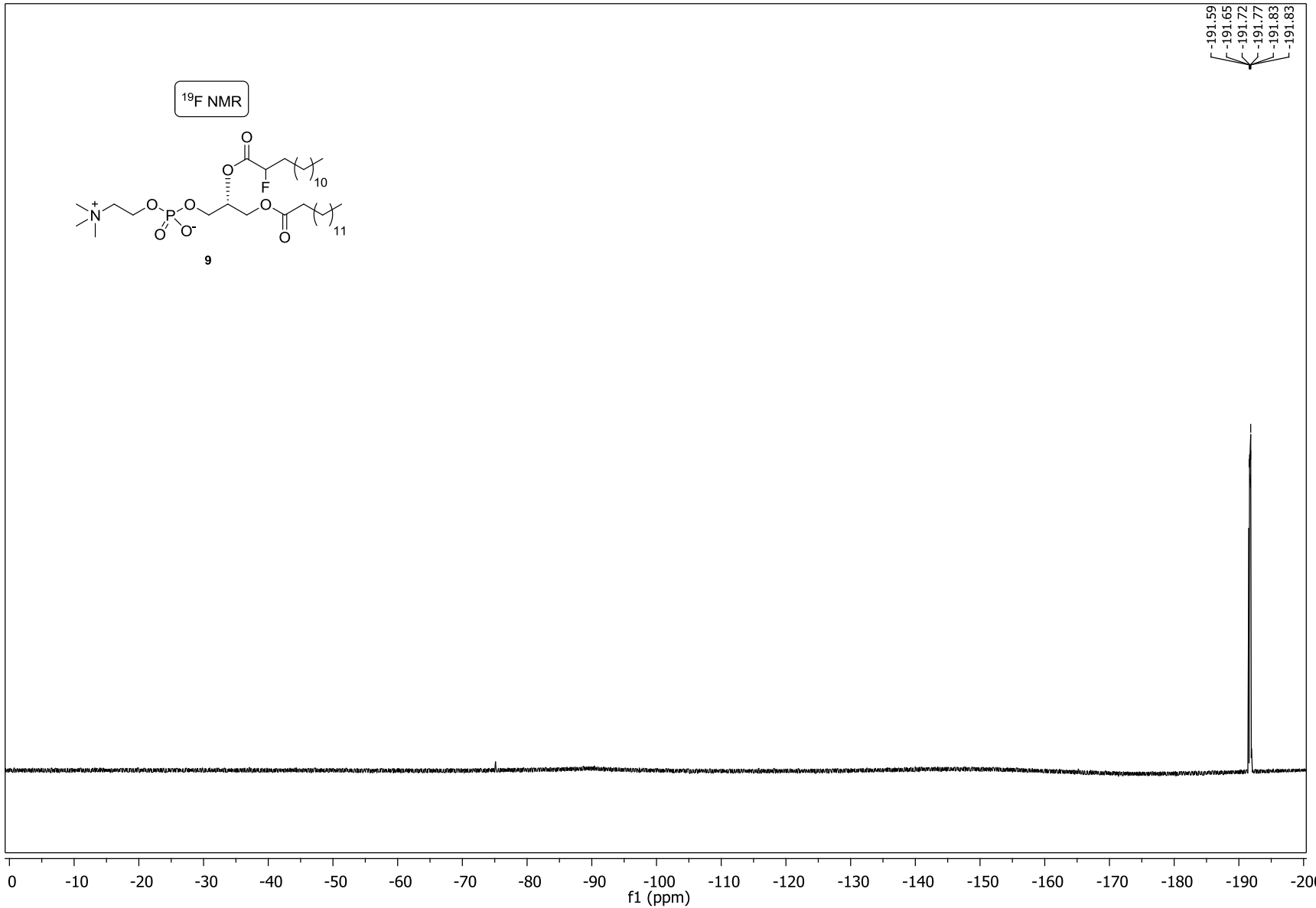

7.27
5.03
5.02
5.02
5.01
4.93
4.92
4.91
1.96
1.95
1.92
1.51
1.49
1.27
0.90
0.89
0.88
^{1}H NMR
HO
O
F
10
12
1.07
2.02
2.01
17.49
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

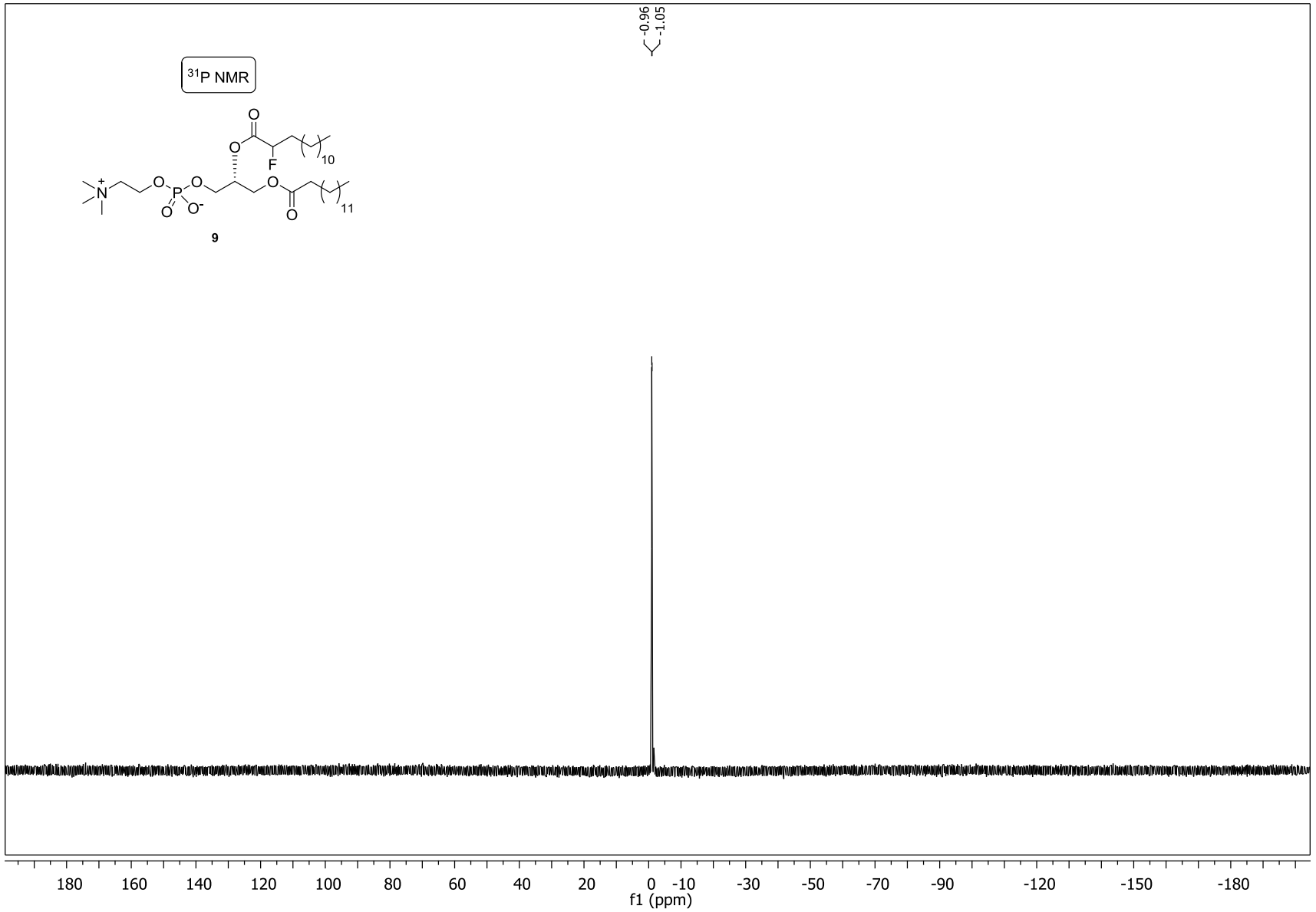

175.32
175.16
89.41
87.94
77.41
77.16
76.91
32.45
32.28
32.07
29.79
29.78
29.74
29.63
29.50
29.46
29.19
24.50
24.48
22.84
14.27
13C NMR
HO
O
F
10
12
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

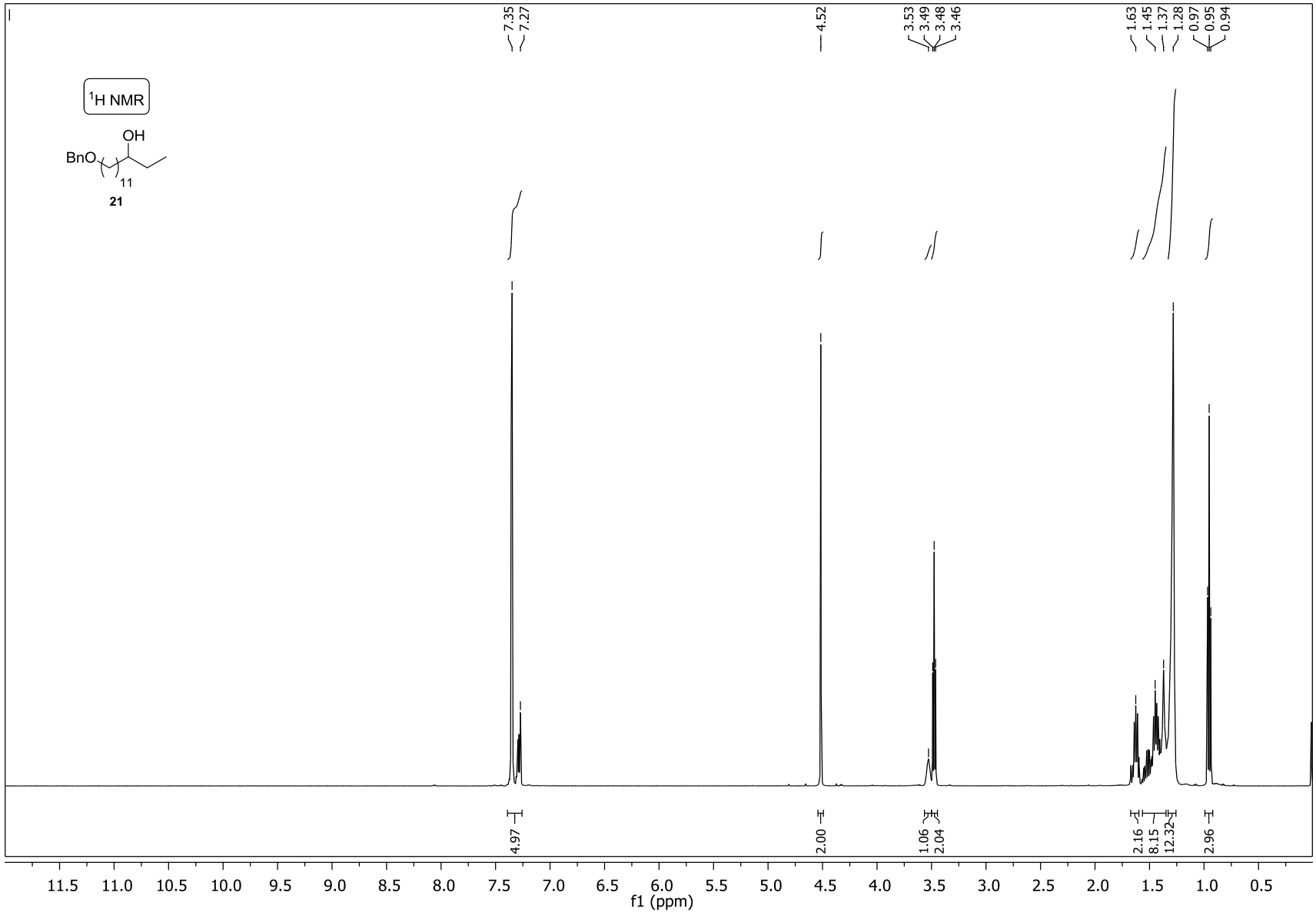

-192.13
-192.18
-192.23
-192.28
-192.33
19F NMR
O
HO
F
10
12
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

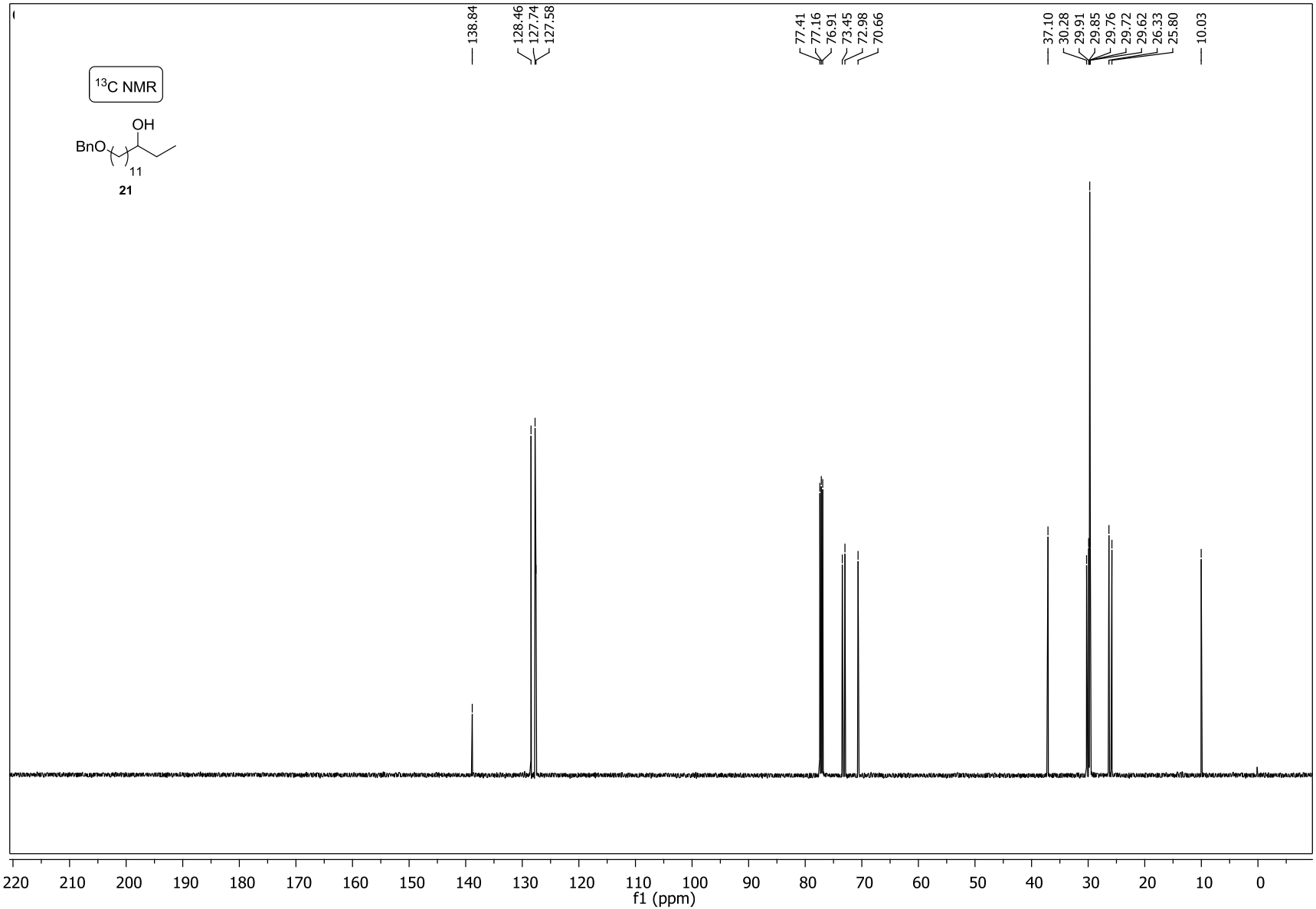

1H NMR
9
f1 (ppm)

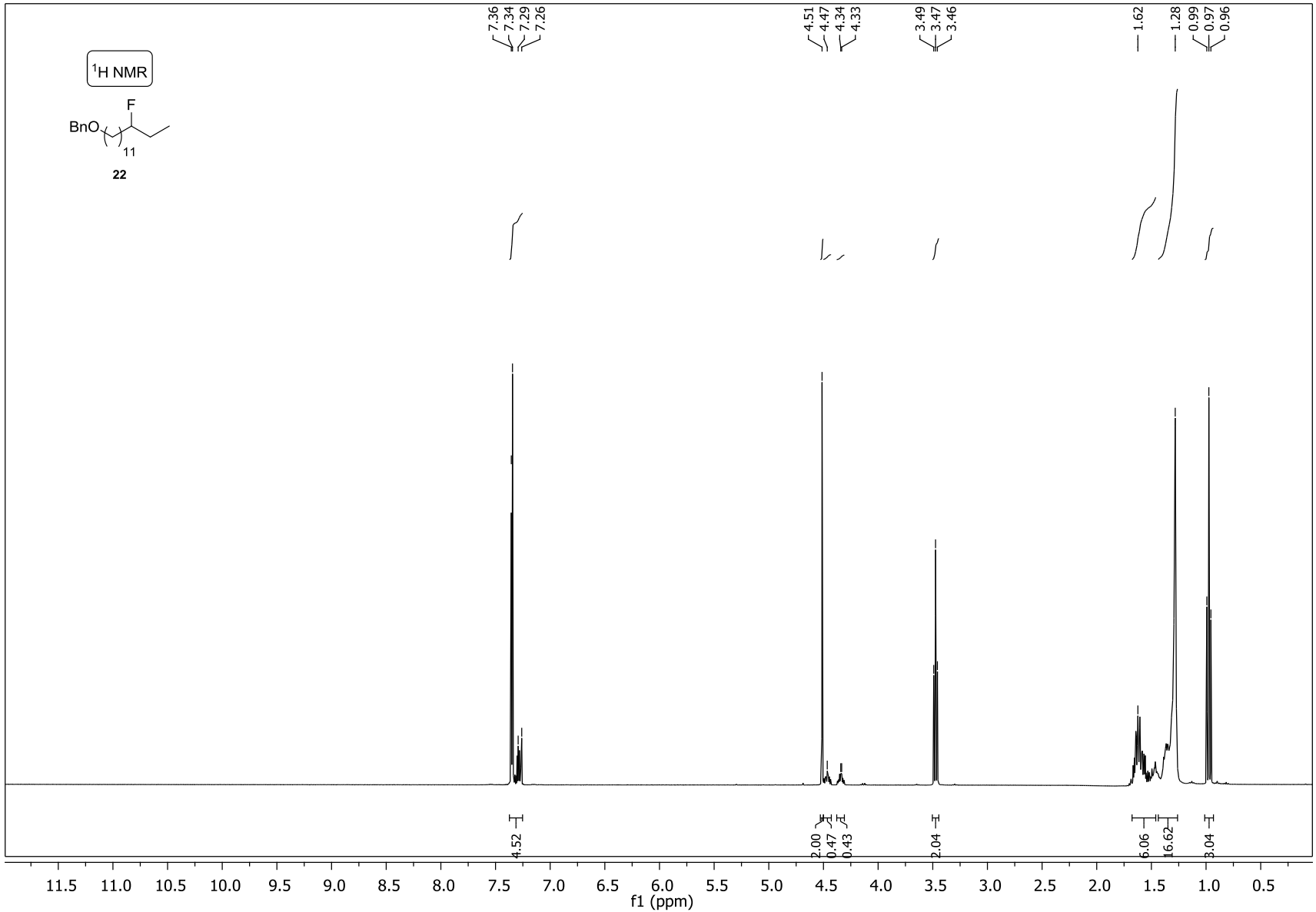

173.54
173.44
169.93
169.68
90.26
88.41
77.48
77.16
76.84
72.18
72.11
66.39
63.58
63.48
62.71
59.46
54.45
34.18
32.70
32.50
32.04
29.83
29.79
29.49
24.97
24.63
24.50
22.81
14.23
13C NMR
9
f1 (ppm)

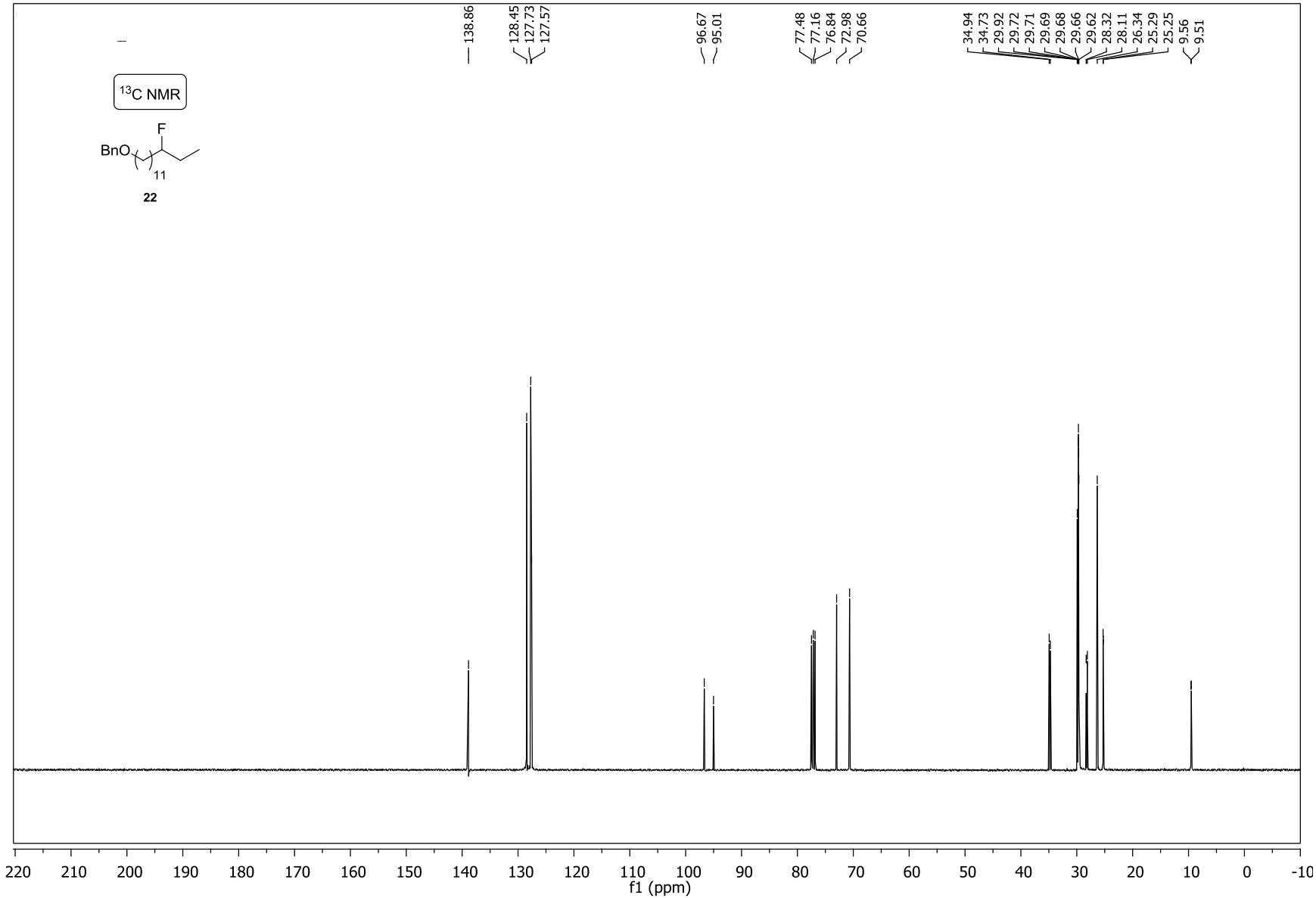

-191.59
-191.65
-191.72
-191.77
-191.83
-191.83
^{19}F NMR
9
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

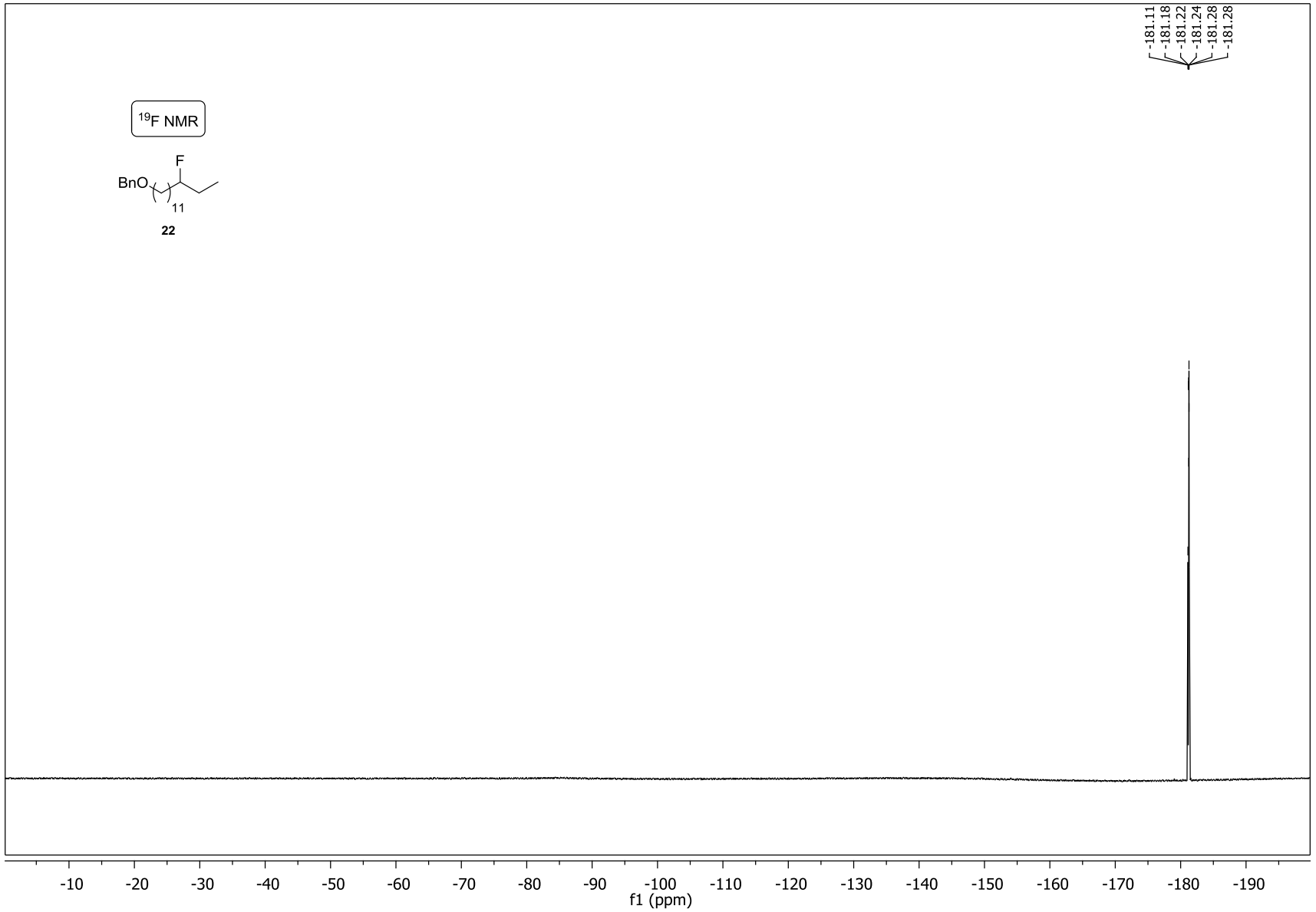

-0.96
-1.05
31P NMR
9
180
160
140
120
100
80
60
40
20
0
-10
-30
-50
-70
-90
-120
-150
-180
f1 (ppm)

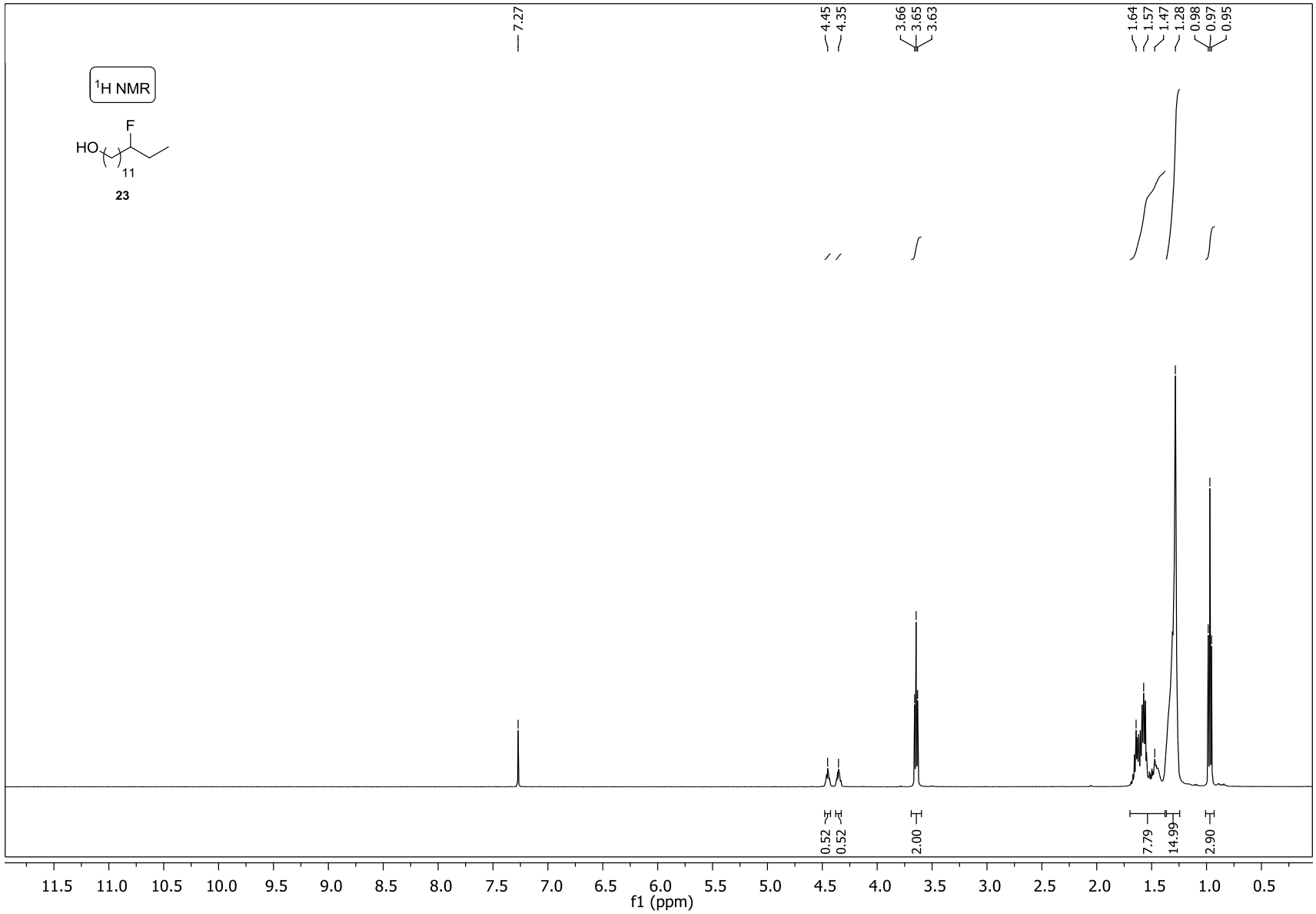

7.35
7.27
4.52
3.53
3.49
3.48
3.46
1.63
1.45
1.37
1.28
0.97
0.95
0.94
^{1}H NMR
OH
BnO
11
21
4.97
2.00
1.06
2.04
2.16
8.15
12.32
2.96
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

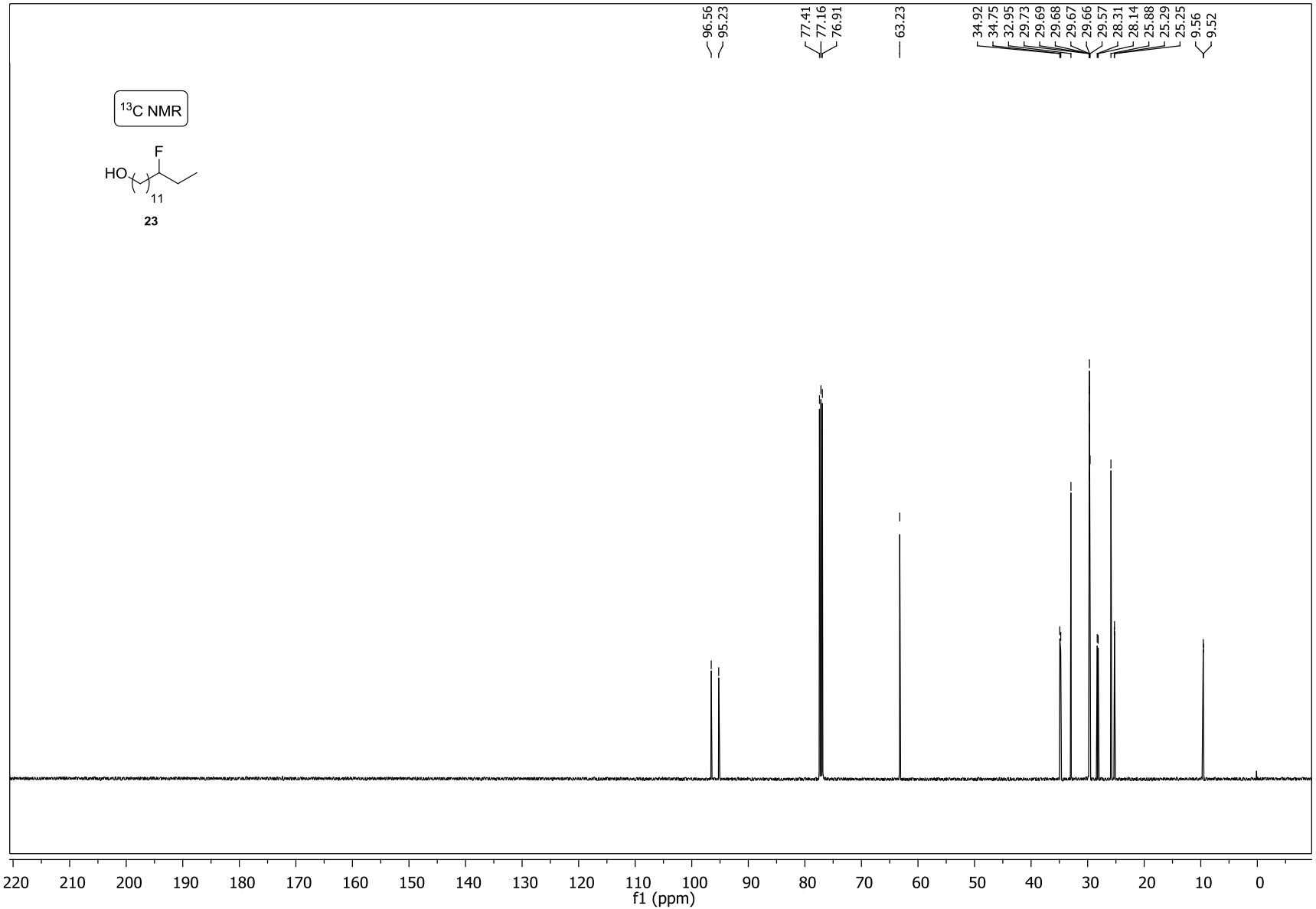

138.84
128.46
127.74
127.58
77.41
77.16
76.91
73.45
72.98
70.66
37.10
30.28
29.91
29.85
29.76
29.72
29.62
26.33
25.80
10.03
13C NMR
OH
BnO
11
21
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

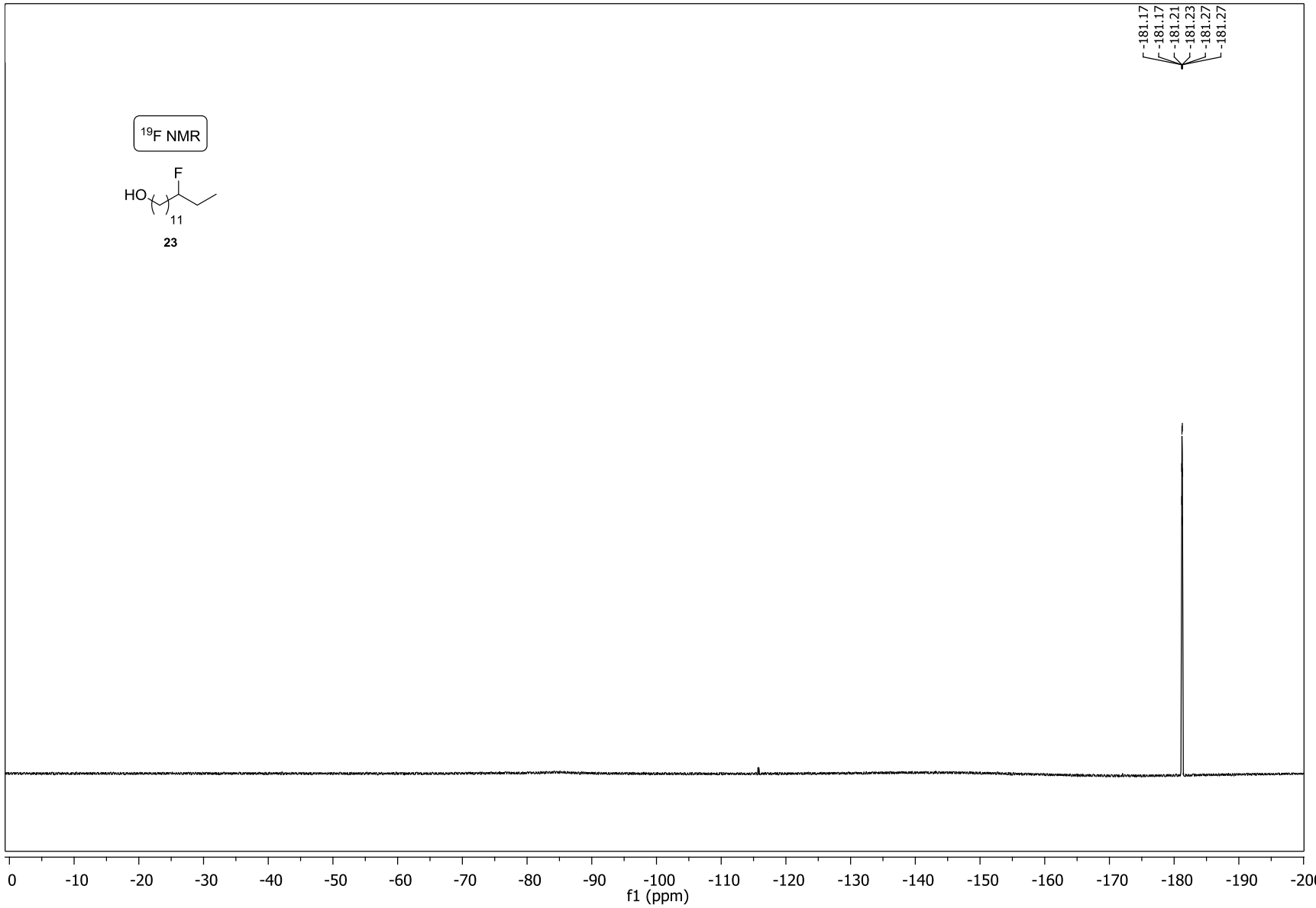

7.36
7.34
7.29
7.26
4.51
4.47
4.34
4.33
3.49
3.47
3.46
1.62
1.28
0.99
0.97
0.96
1H NMR
F
BnO
11
22
4.52
2.00
0.47
0.43
2.04
6.06
16.62
3.04
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

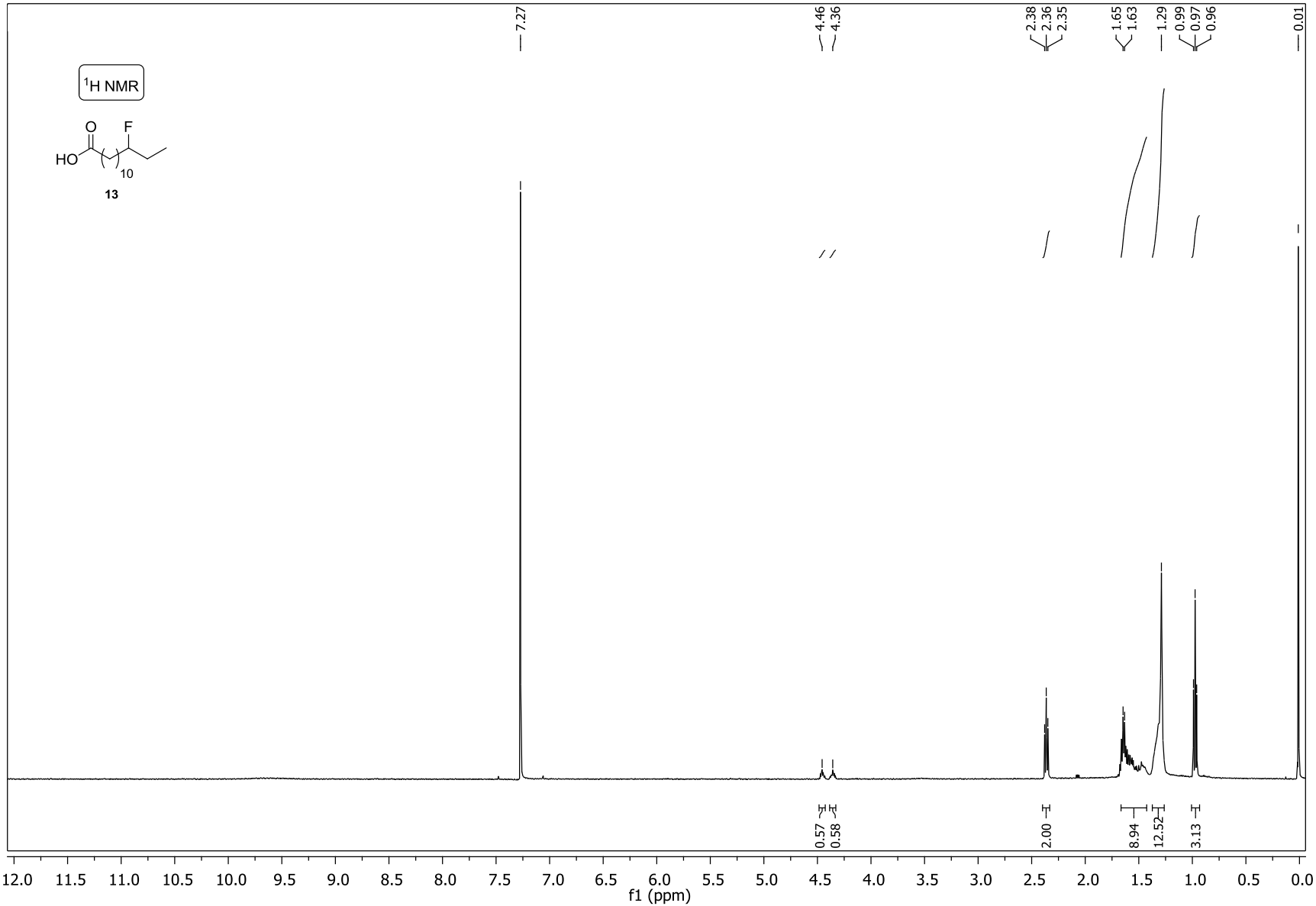

138.86
128.45
127.73
127.57
96.67
95.01
77.48
77.16
76.84
72.98
70.66
34.94
34.73
29.92
29.72
29.71
29.69
29.68
29.66
29.62
28.32
28.11
26.34
25.29
25.25
9.56
9.51
13C NMR
F
BnO
11
22
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

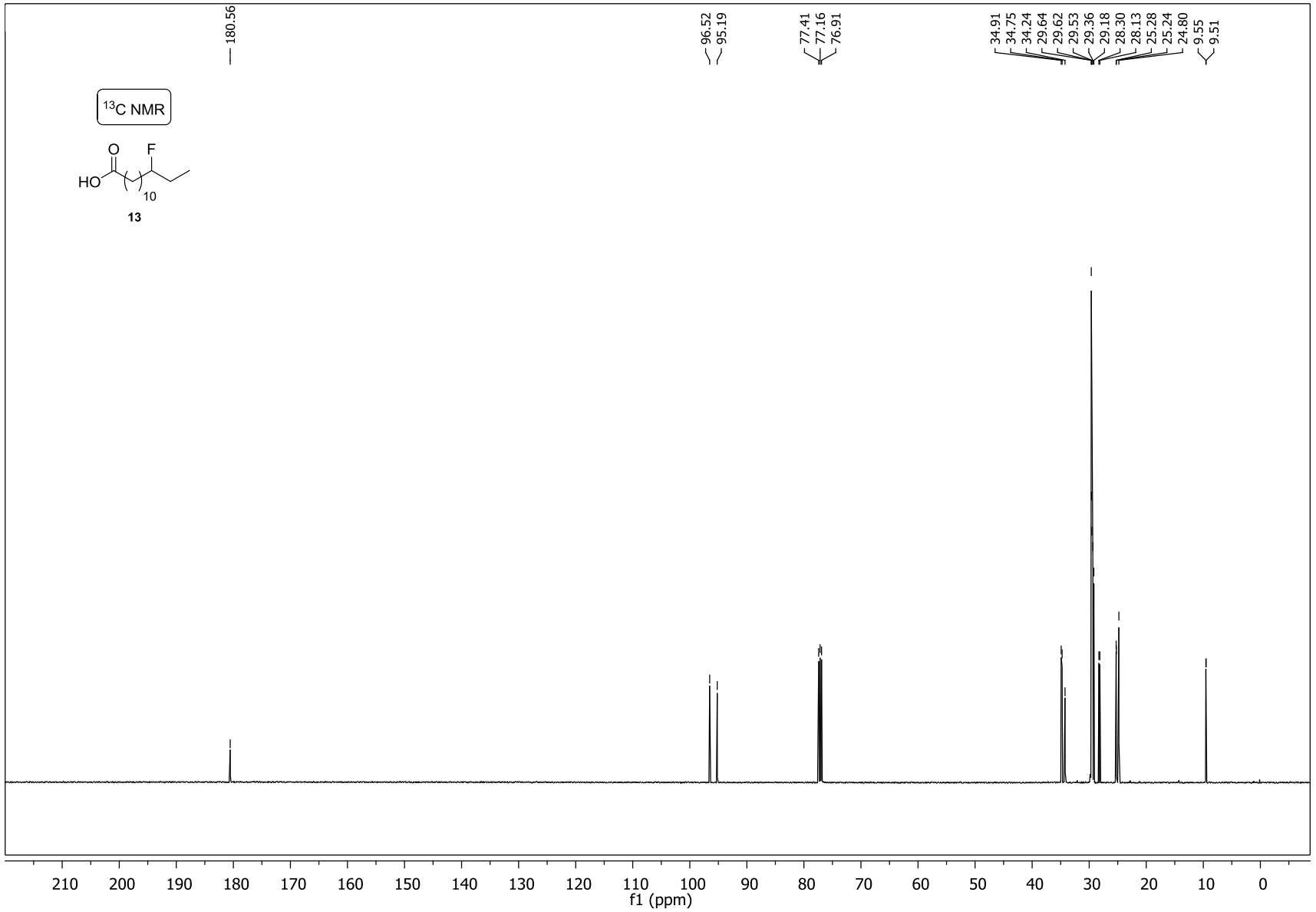

-181.11
-181.18
-181.22
-181.24
-181.28
-181.28
19F NMR
F
BnO
11
22
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

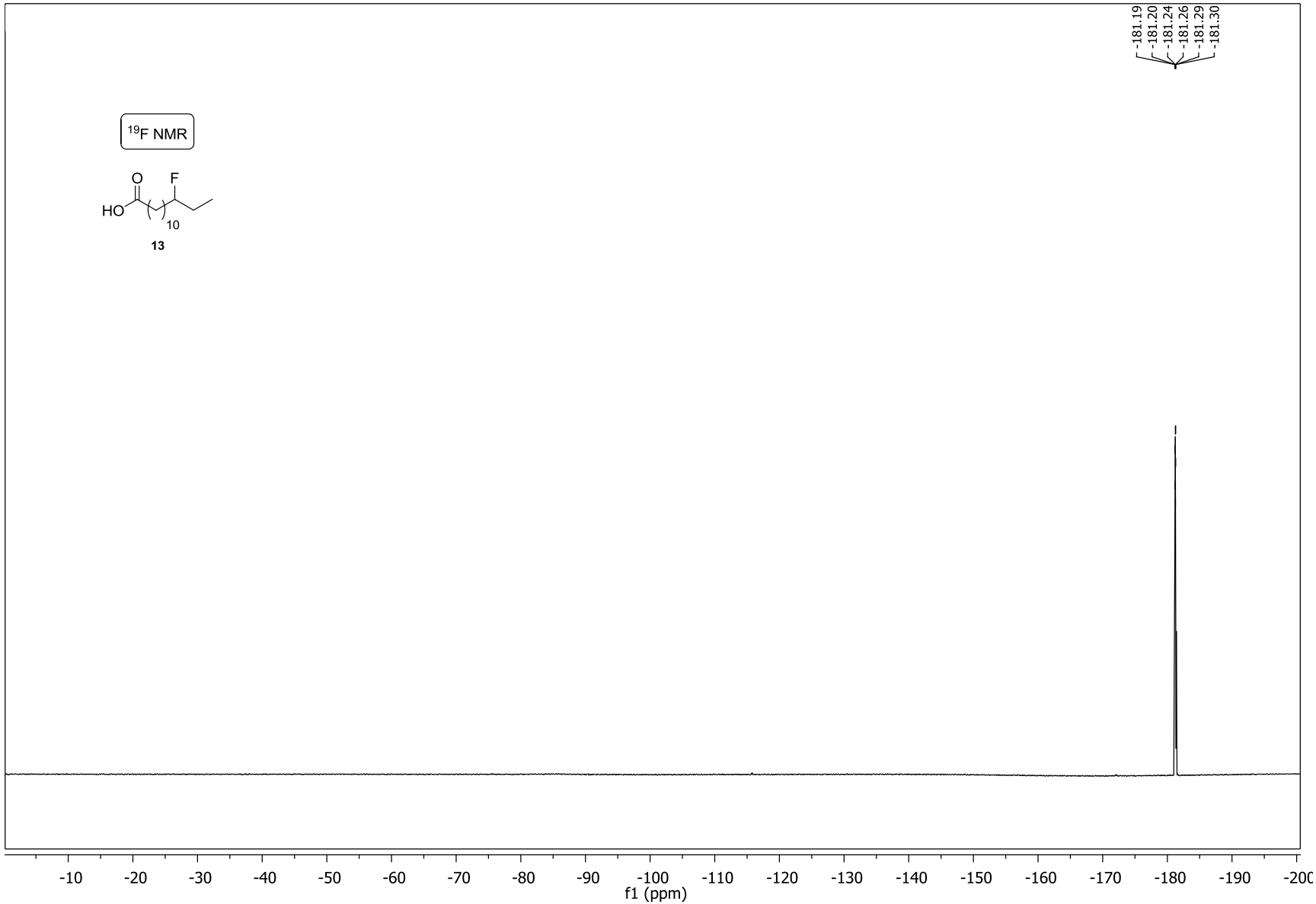

7.27
4.45
4.35
3.66
3.65
3.63
1.64
1.57
1.47
1.28
0.98
0.97
0.95
^{1}H NMR
F
HO
11
23
0.52
0.52
2.00
7.79
14.99
2.90
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

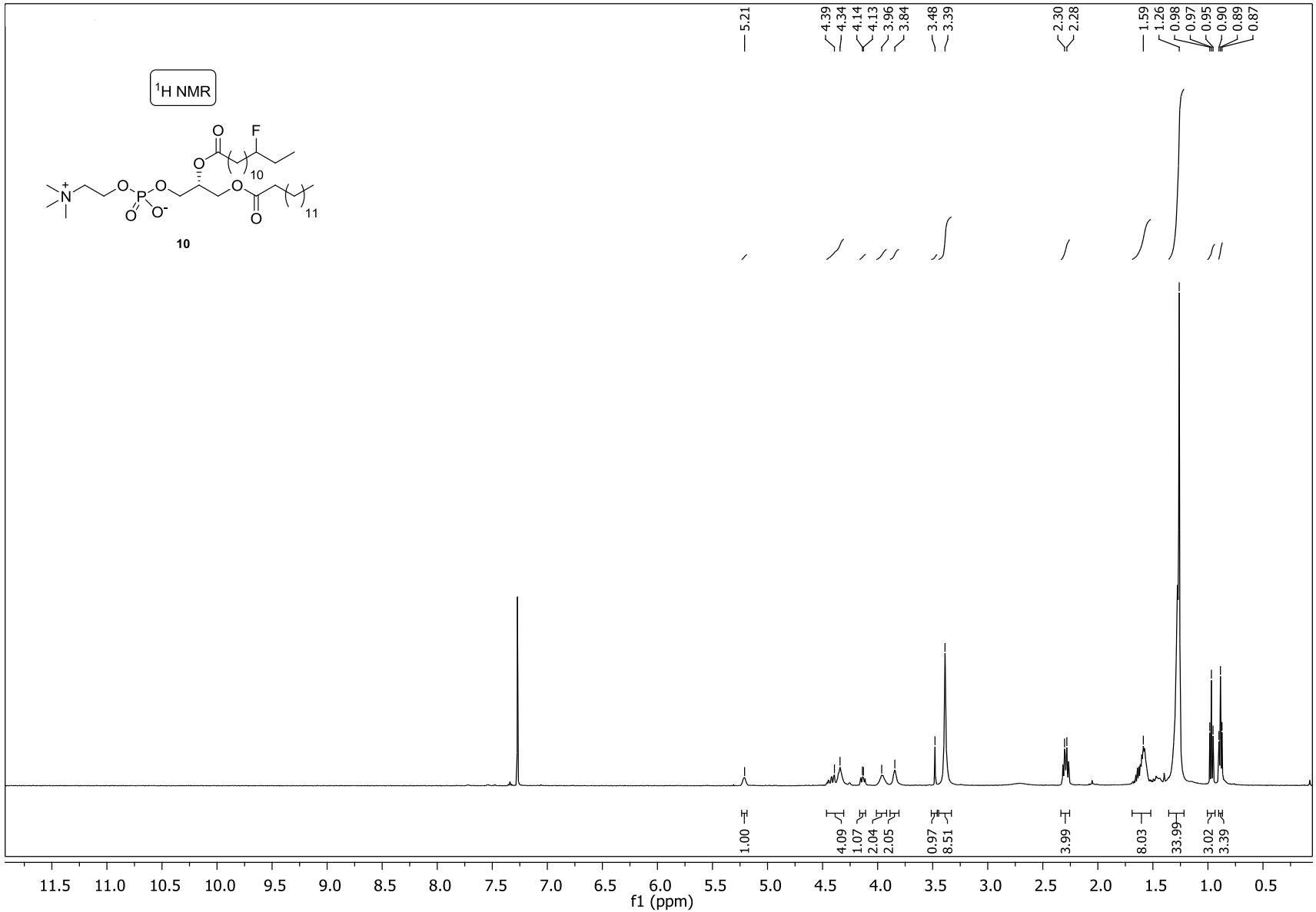

96.56
95.23
77.41
77.16
76.91
63.23
34.92
34.75
32.95
29.73
29.69
29.68
29.67
29.66
29.57
28.31
28.14
25.88
25.29
25.25
9.56
9.52
13C NMR
F
HO
11
23
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

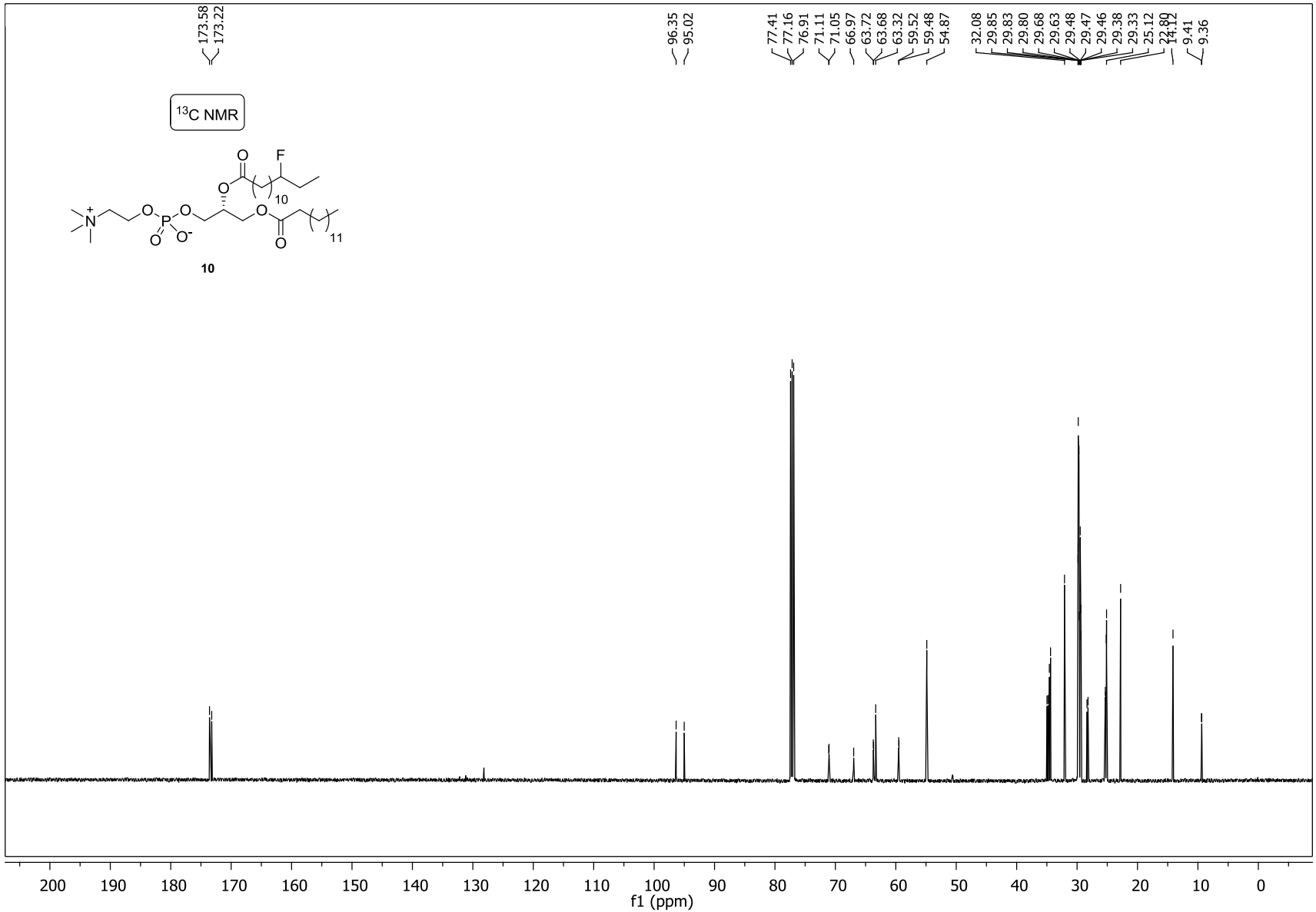

-181.17
-181.17
-181.21
-181.23
-181.27
-181.27
^{19}F NMR
F
HO
11
23
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

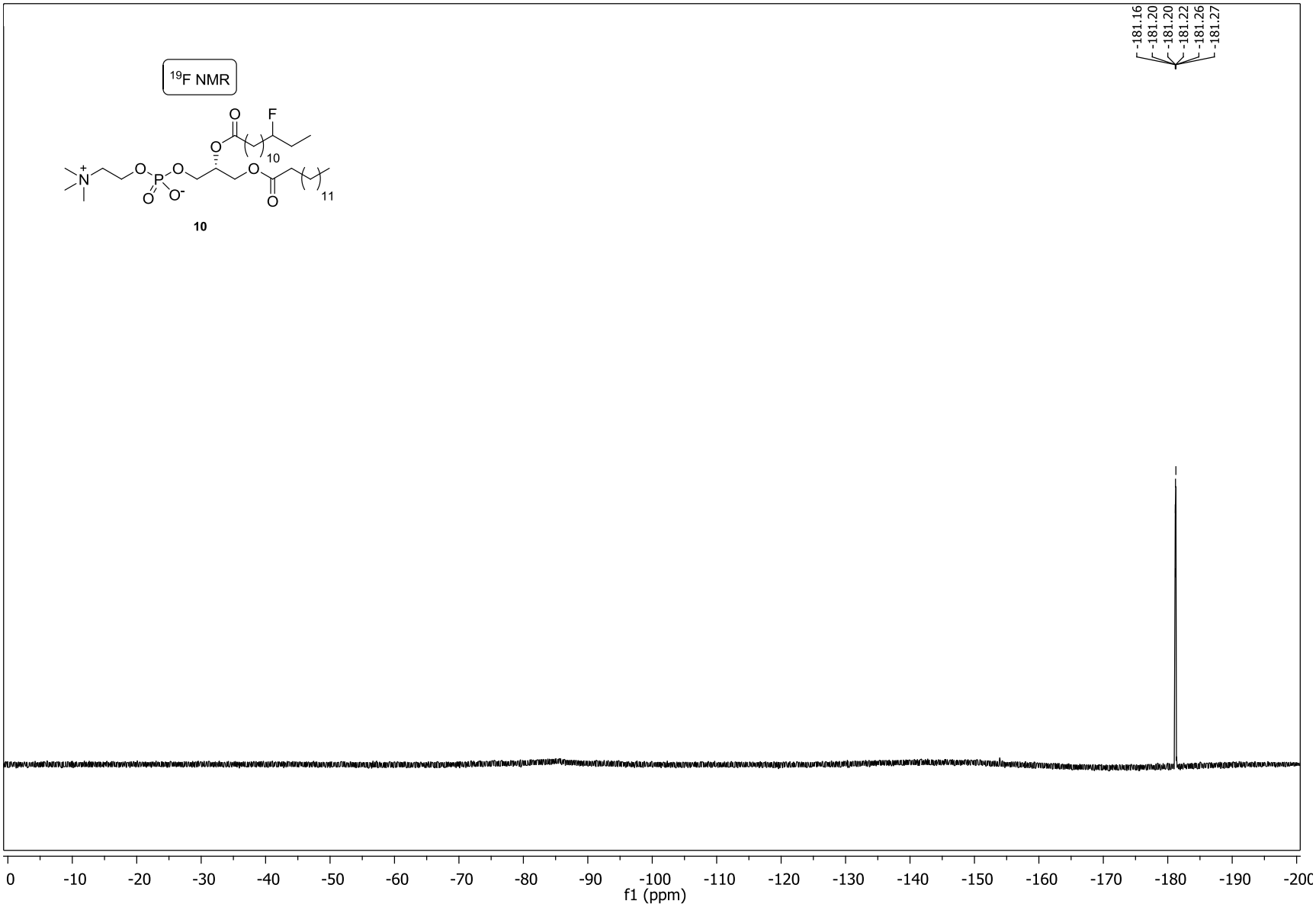

7.27
4.46
4.36
2.38
2.36
2.35
1.65
1.63
1.29
0.99
0.97
0.96
0.01
^{1}H NMR
O
F
HO
10
13
0.57
0.58
2.00
8.94
12.52
3.13
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

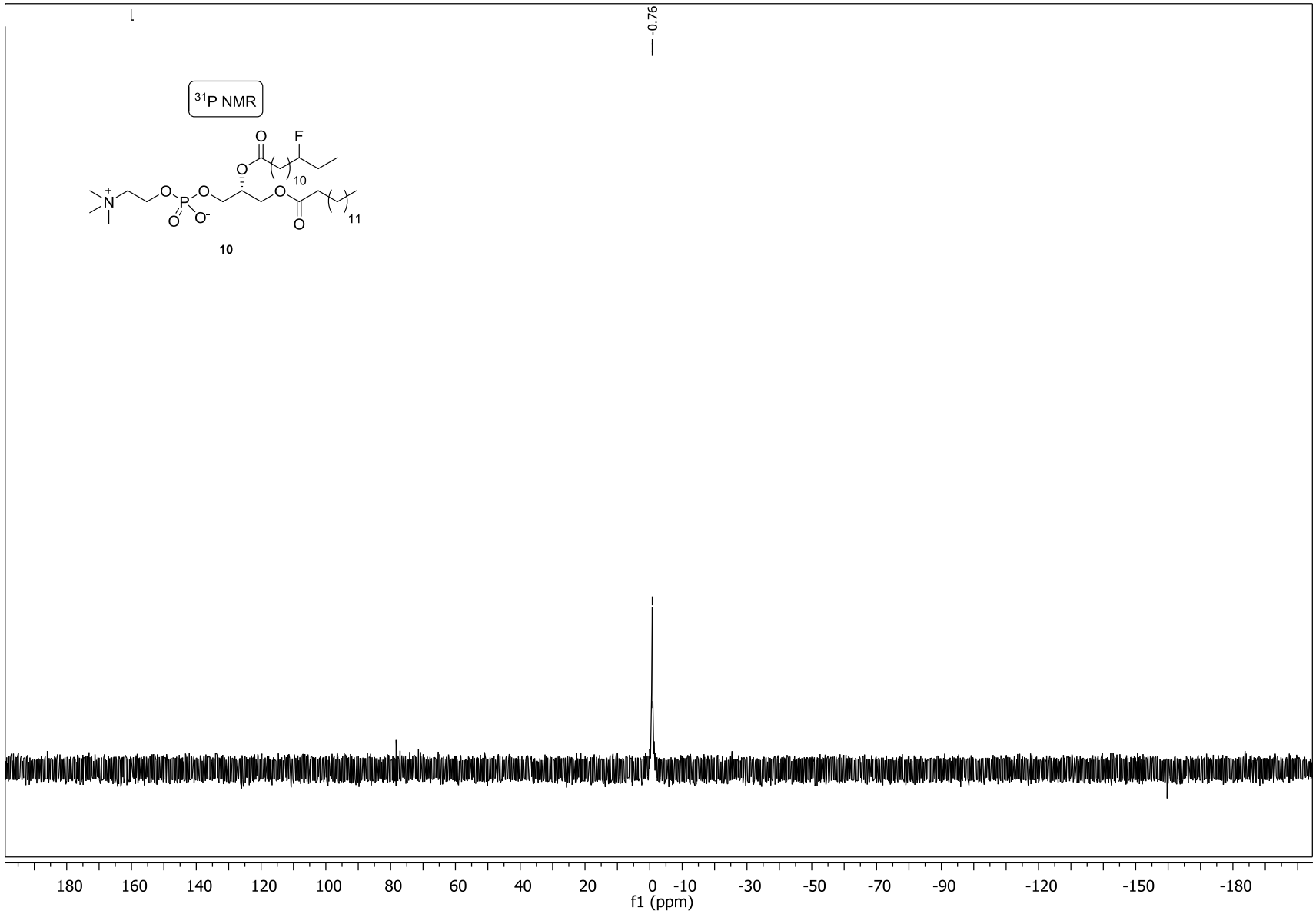

180.56
96.52
95.19
77.41
77.16
76.91
34.91
34.75
34.24
29.64
29.62
29.53
29.36
29.18
28.30
28.13
25.28
25.24
24.80
9.55
9.51
13C NMR
O
F
HO
10
13
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

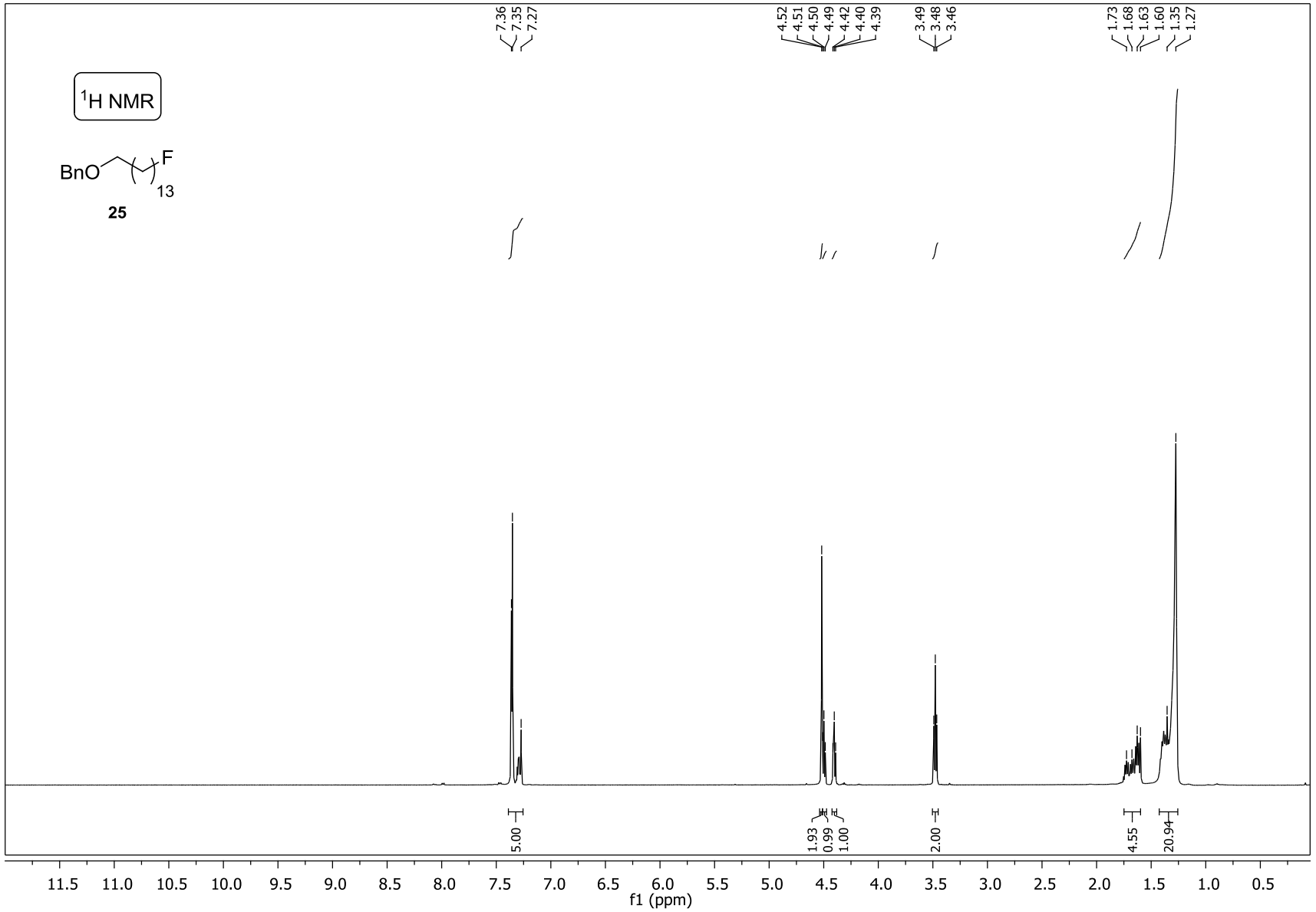

-181.19
-181.20
-181.24
-181.26
-181.29
-181.30
^{19}F NMR
O
F
HO
10
13
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

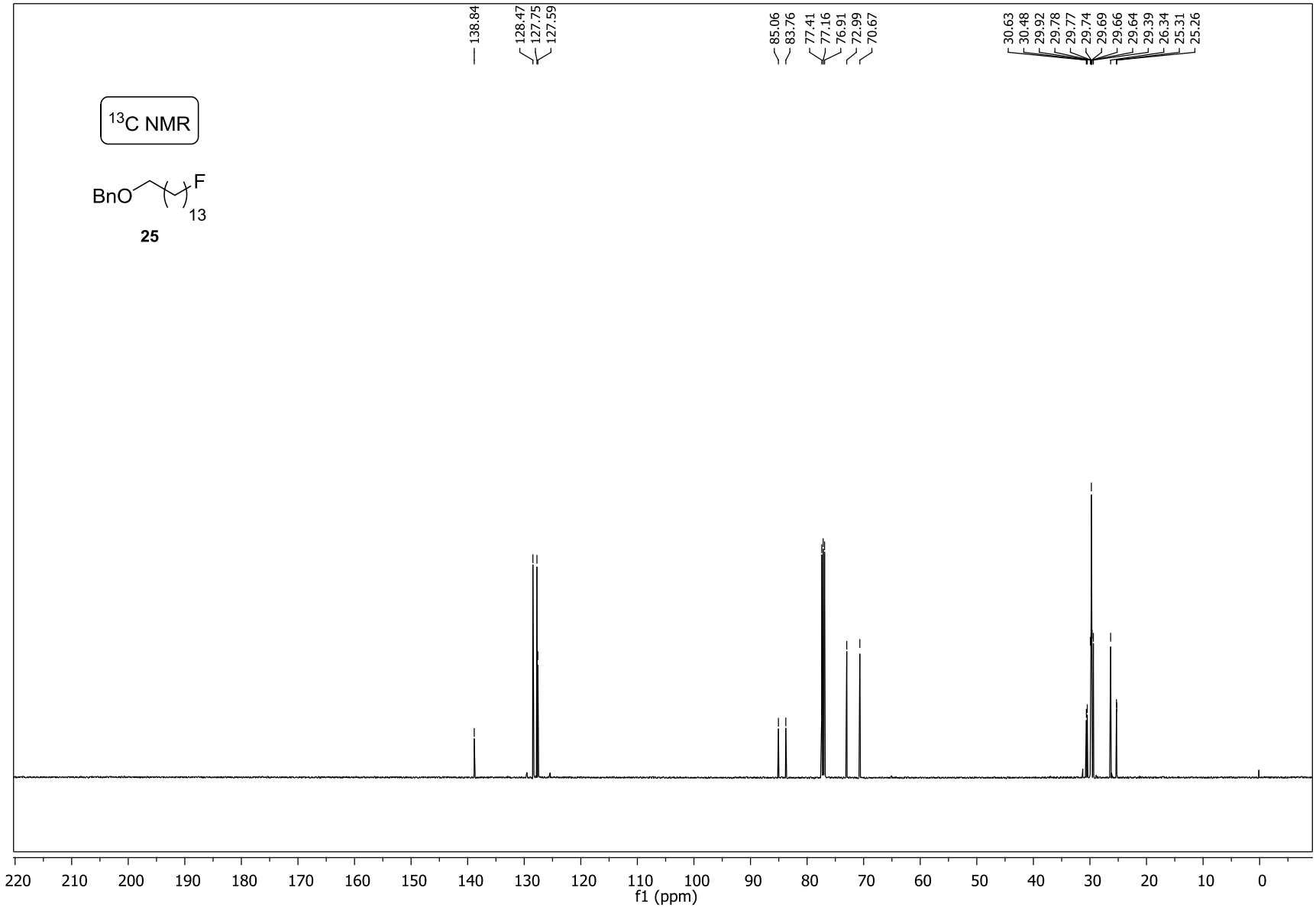

1H NMR
10
5.21
4.39
4.34
4.14
4.13
3.96
3.84
3.48
3.39
2.30
2.28
1.59
1.26
0.98
0.97
0.95
0.90
0.89
0.87
1.00
4.09
1.07
2.04
2.05
0.97
8.51
3.99
8.03
33.99
3.02
3.39
f1 (ppm)

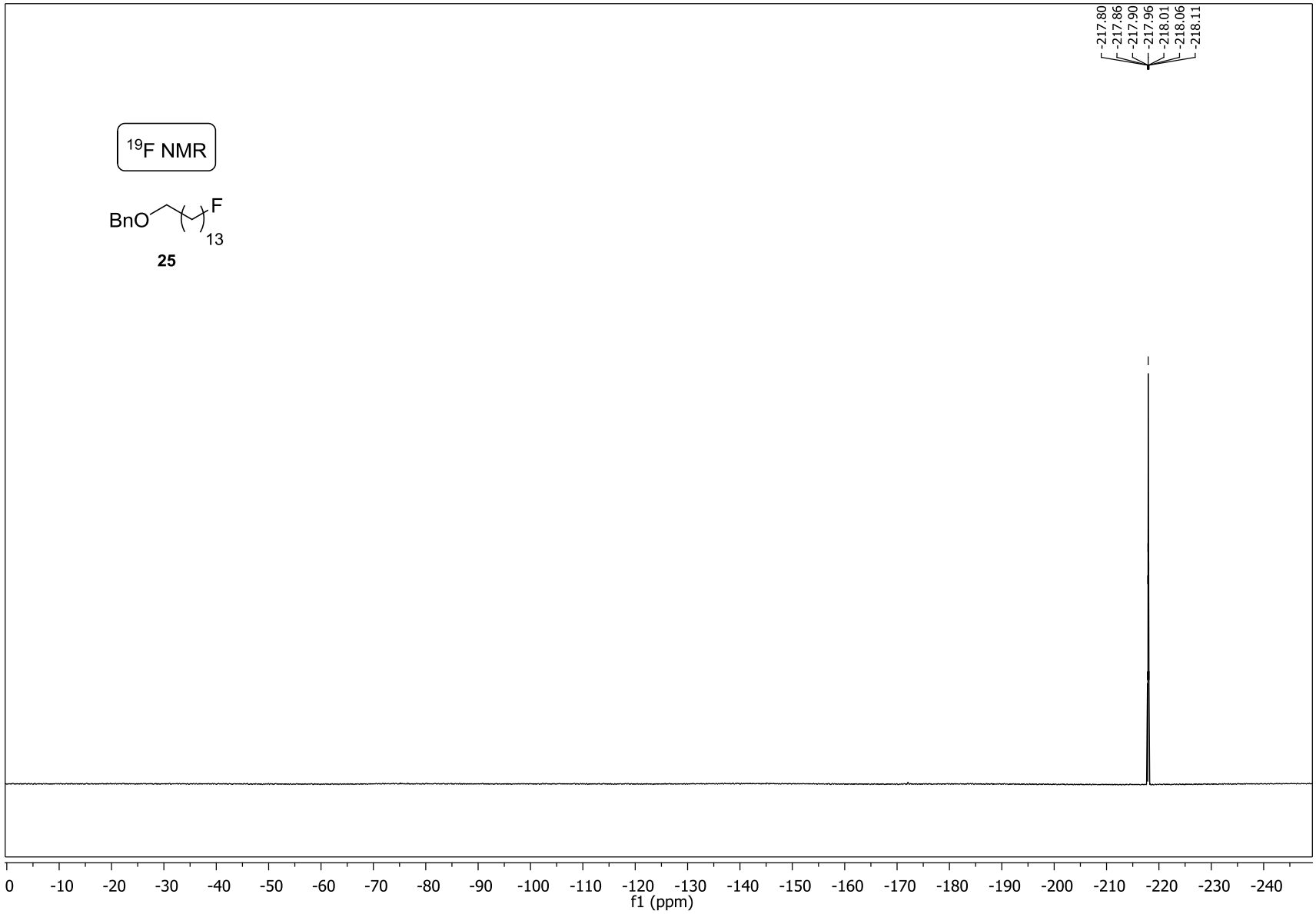

173.58
173.22
96.35
95.02
77.41
77.16
76.91
71.11
71.05
66.97
63.72
63.68
63.32
59.52
59.48
54.87
32.08
29.85
29.83
29.80
29.68
29.63
29.48
29.47
29.46
29.38
29.33
25.12
22.80
14.12
9.41
9.36
13C NMR
O
F
O
10
O
O
P
O
O
O
O
11
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

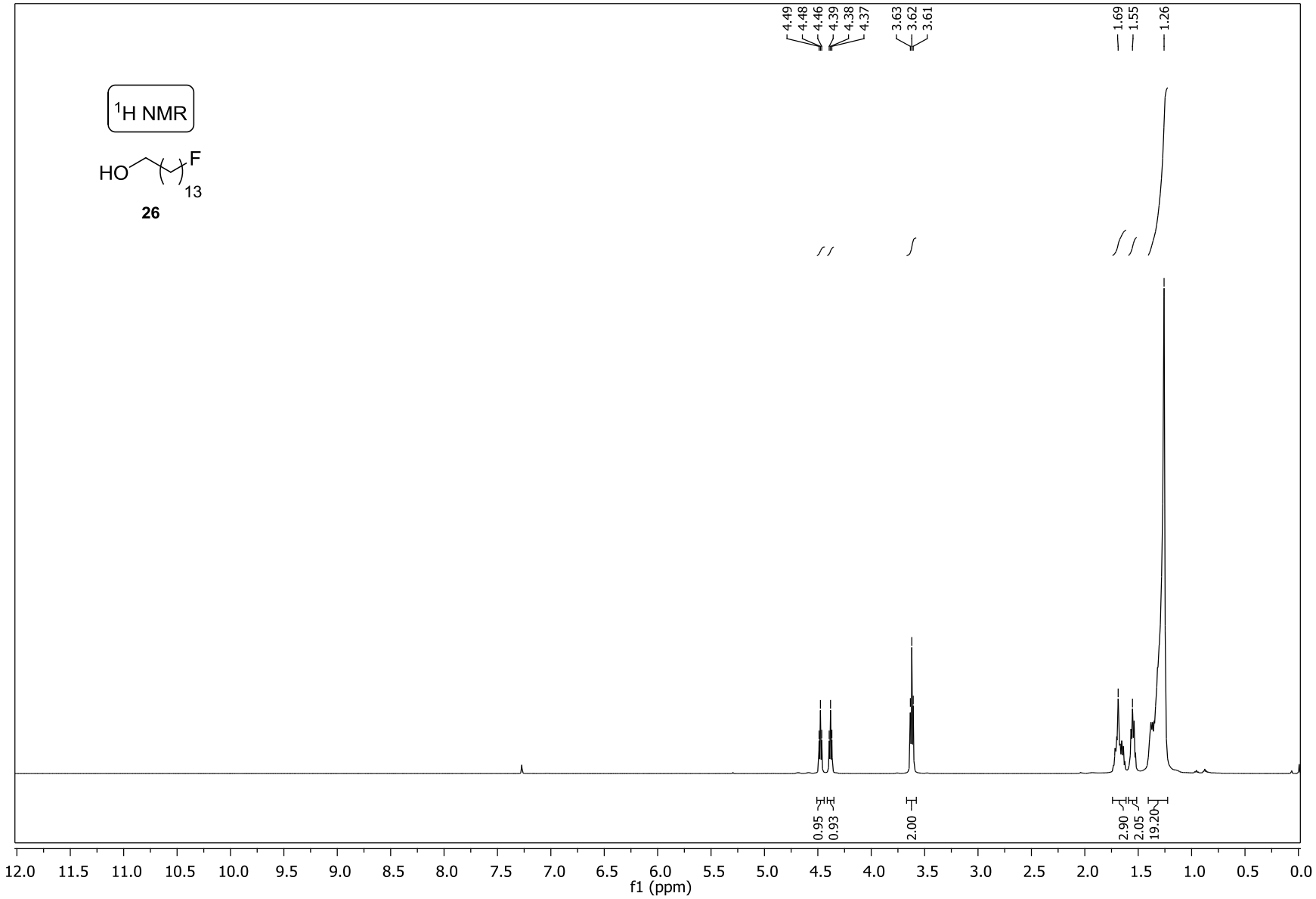

-181.16
-181.20
-181.20
-181.22
-181.26
-181.27
19F NMR
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

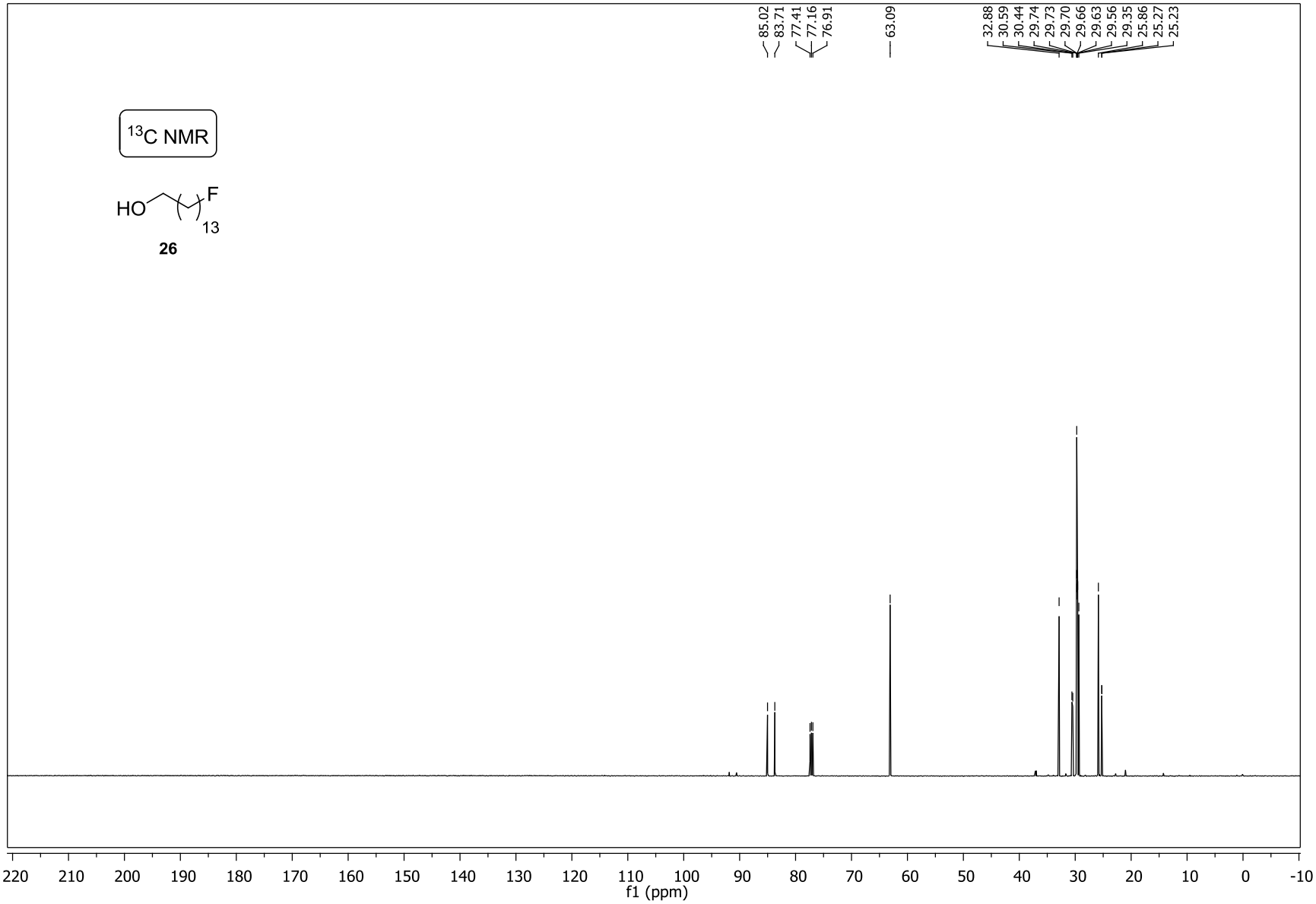

-0.76
31P NMR
10
180
160
140
120
100
80
60
40
20
0
-10
-30
-50
-70
-90
-120
-150
-180
f1 (ppm)

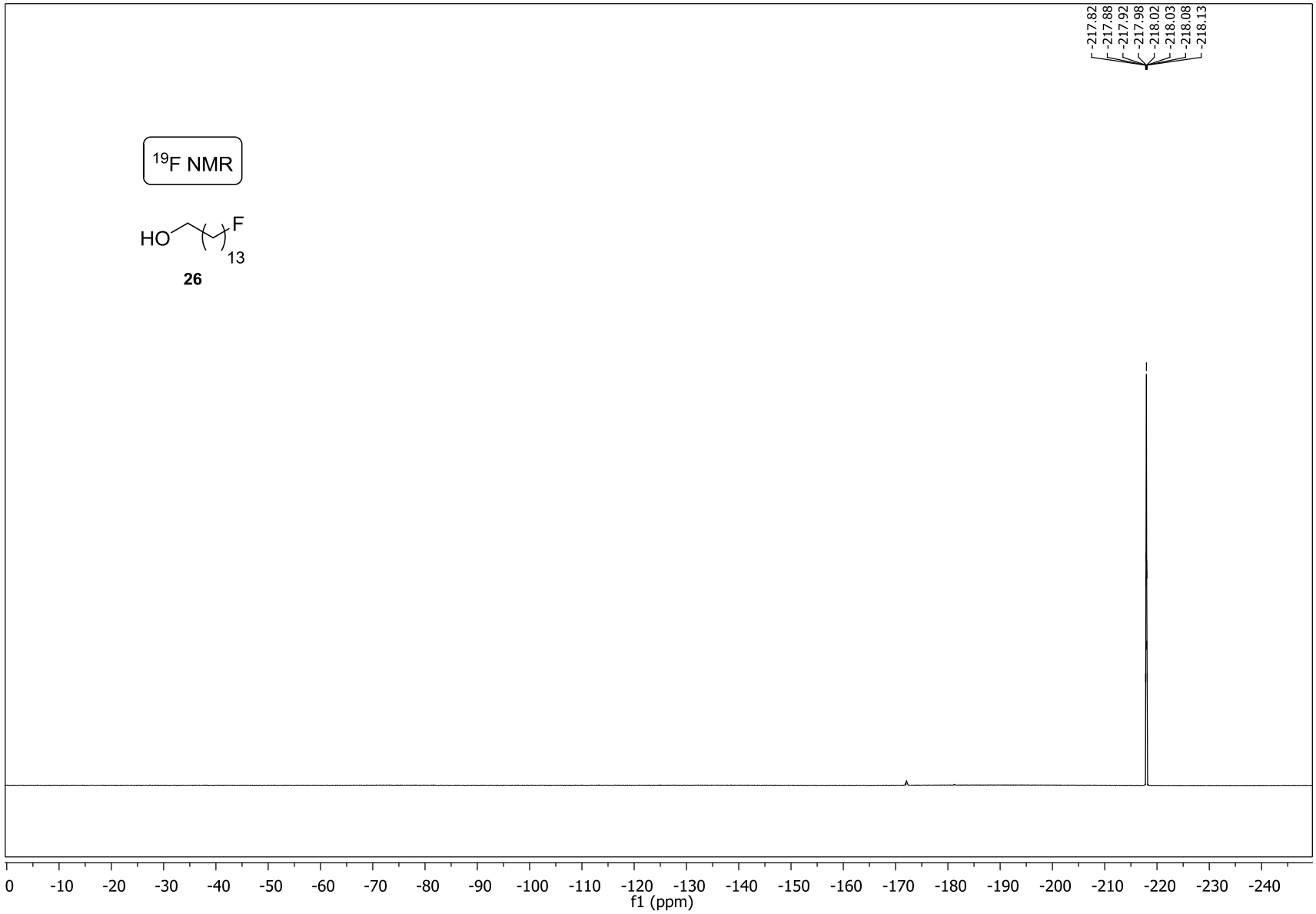

7.36
7.35
7.27
4.52
4.51
4.50
4.49
4.42
4.40
4.39
3.49
3.48
3.46
1.73
1.68
1.63
1.60
1.35
1.27
^{1}H NMR
BnO
F
13
25
5.00
1.93
0.99
1.00
2.00
4.55
20.94
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

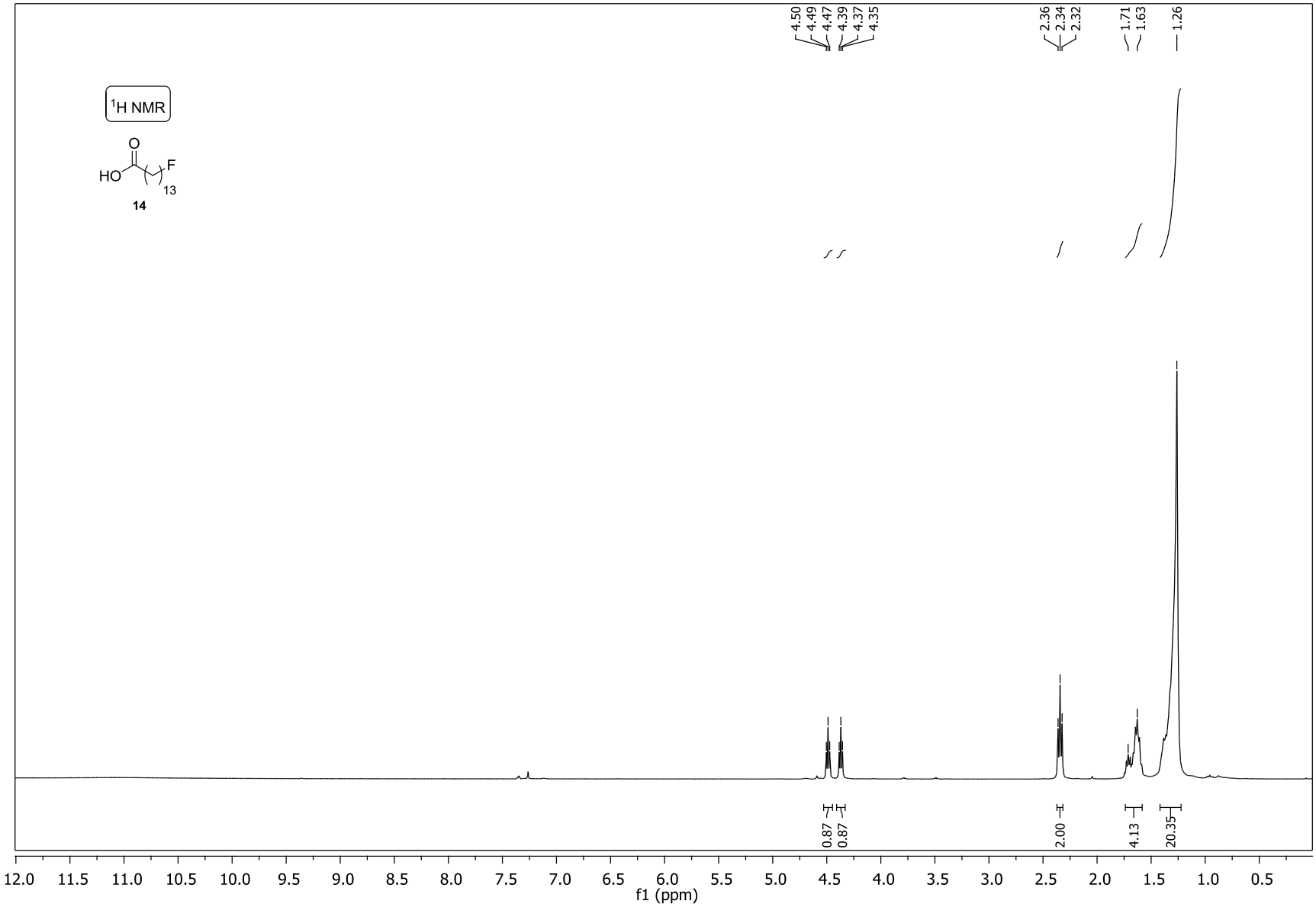

138.84
128.47
127.75
127.59
85.06
83.76
77.41
77.16
76.91
72.99
70.67
30.63
30.48
29.92
29.78
29.77
29.74
29.69
29.66
29.64
29.39
26.34
25.31
25.26
13C NMR
BnO
F
13
25
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

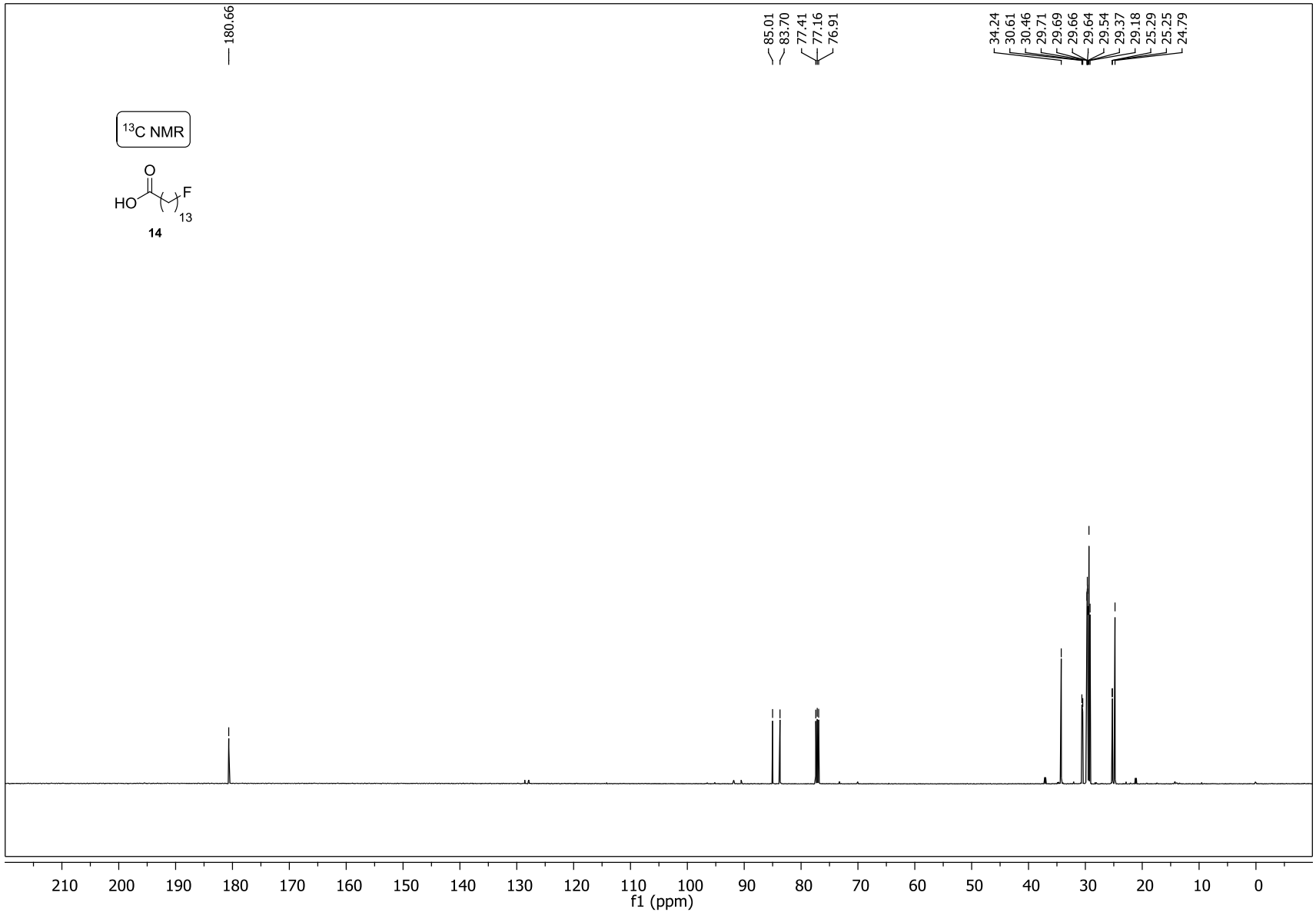

-217.80
-217.86
-217.90
-217.96
-218.01
-218.06
-218.11
19F NMR
BnO
F
13
25
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
f1 (ppm)

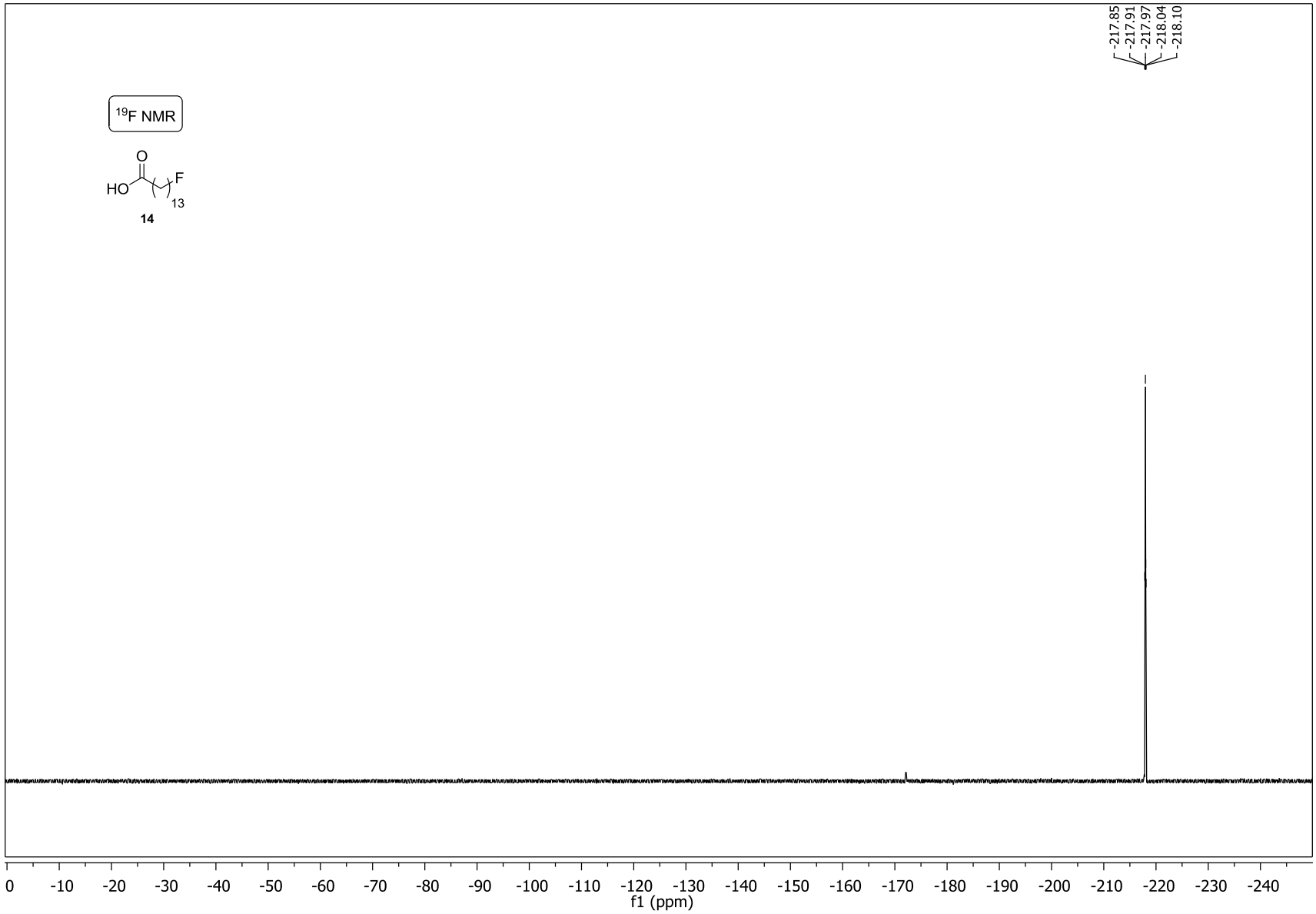

4.49
4.48
4.46
4.39
4.38
4.37
3.63
3.62
3.61
1.69
1.55
1.26
^{1}H NMR
HO
F
13
26
0.95
0.93
2.00
2.90
2.05
19.20
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

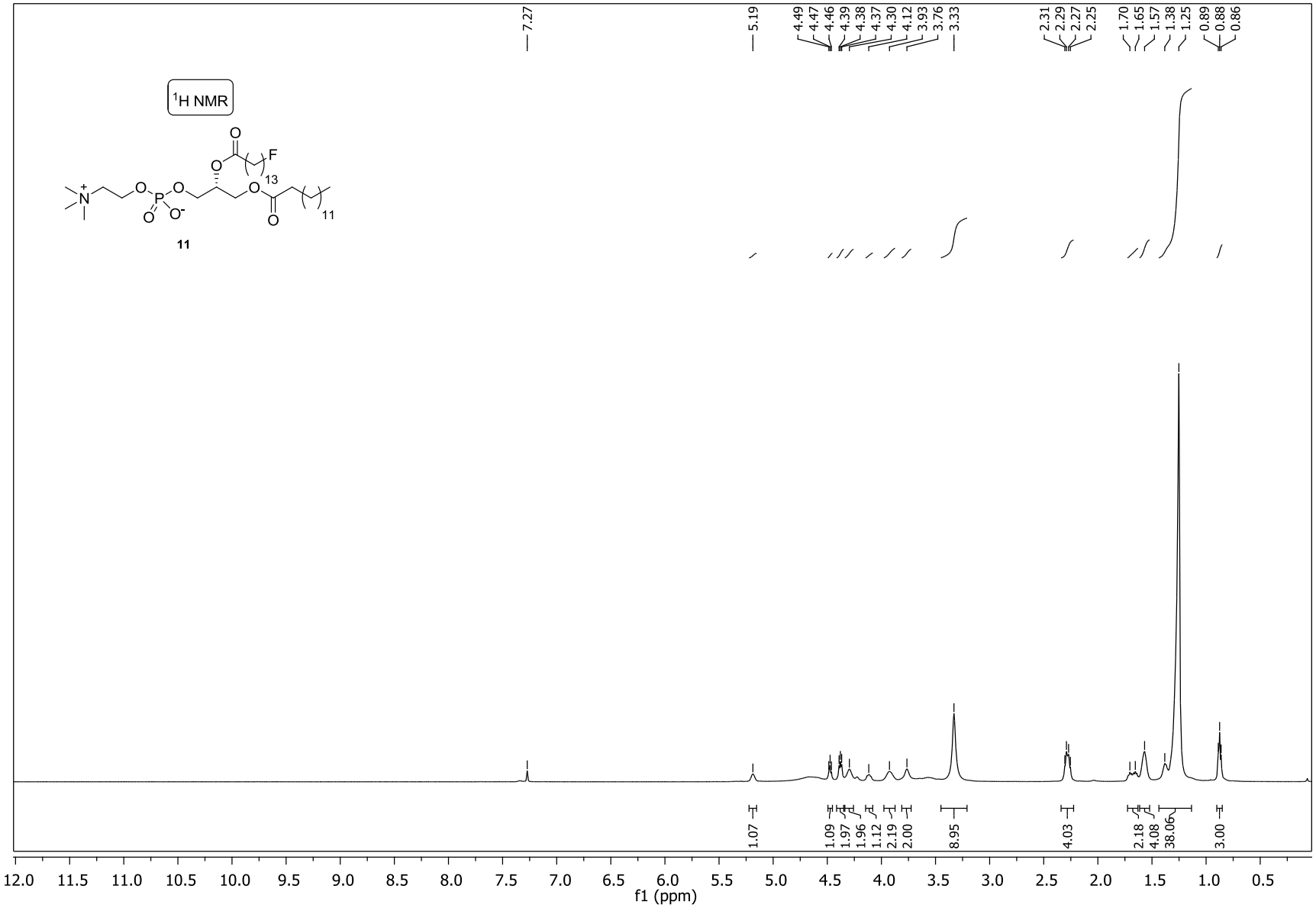

85.02
83.71
77.41
77.16
76.91
63.09
32.88
30.59
30.44
29.74
29.73
29.70
29.66
29.63
29.56
29.35
25.86
25.27
25.23
13C NMR
HO
F
13
26
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

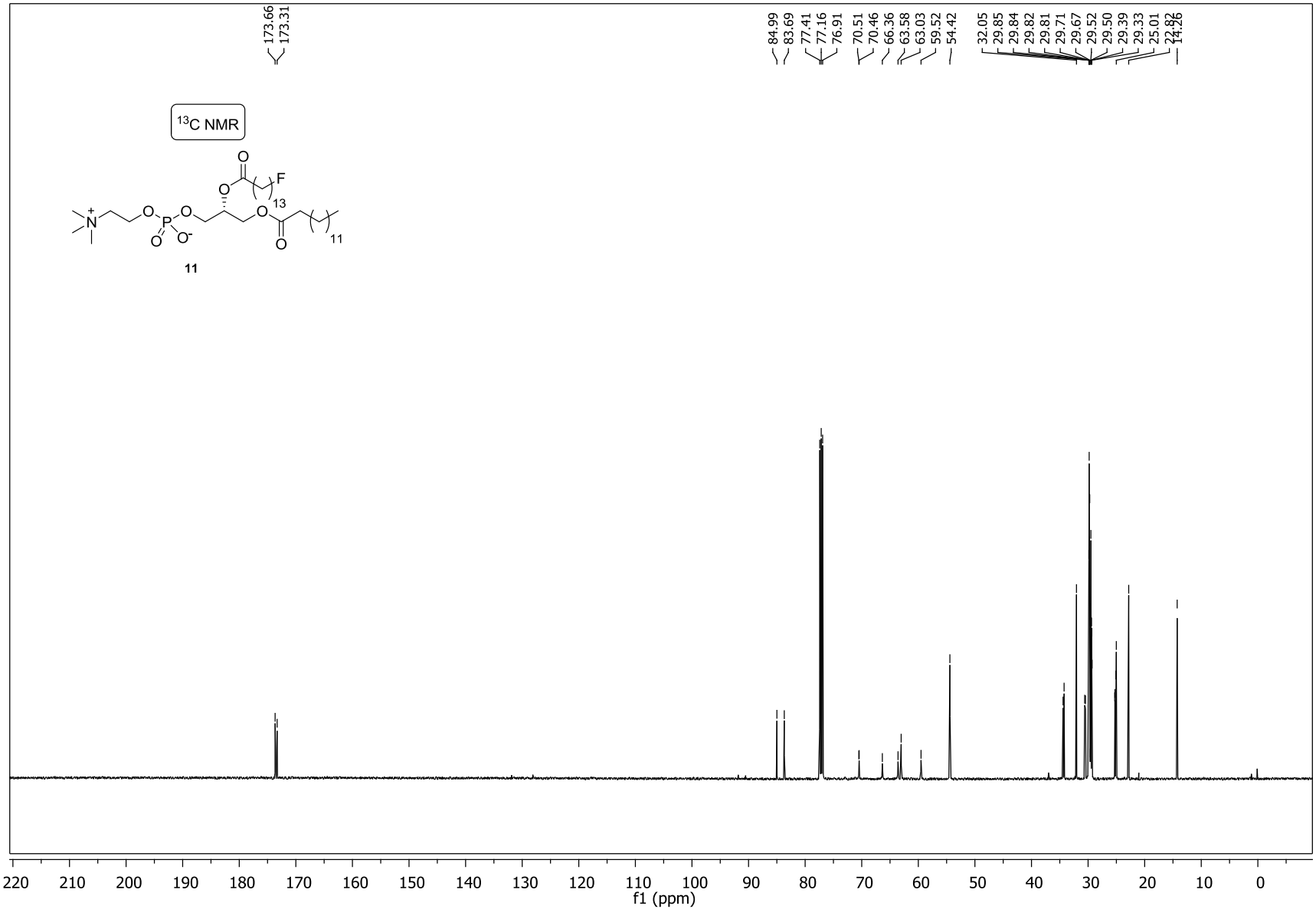

-217.82
-217.88
-217.92
-217.98
-218.02
-218.03
-218.08
-218.13
19F NMR
HO
F
13
26
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
f1 (ppm)

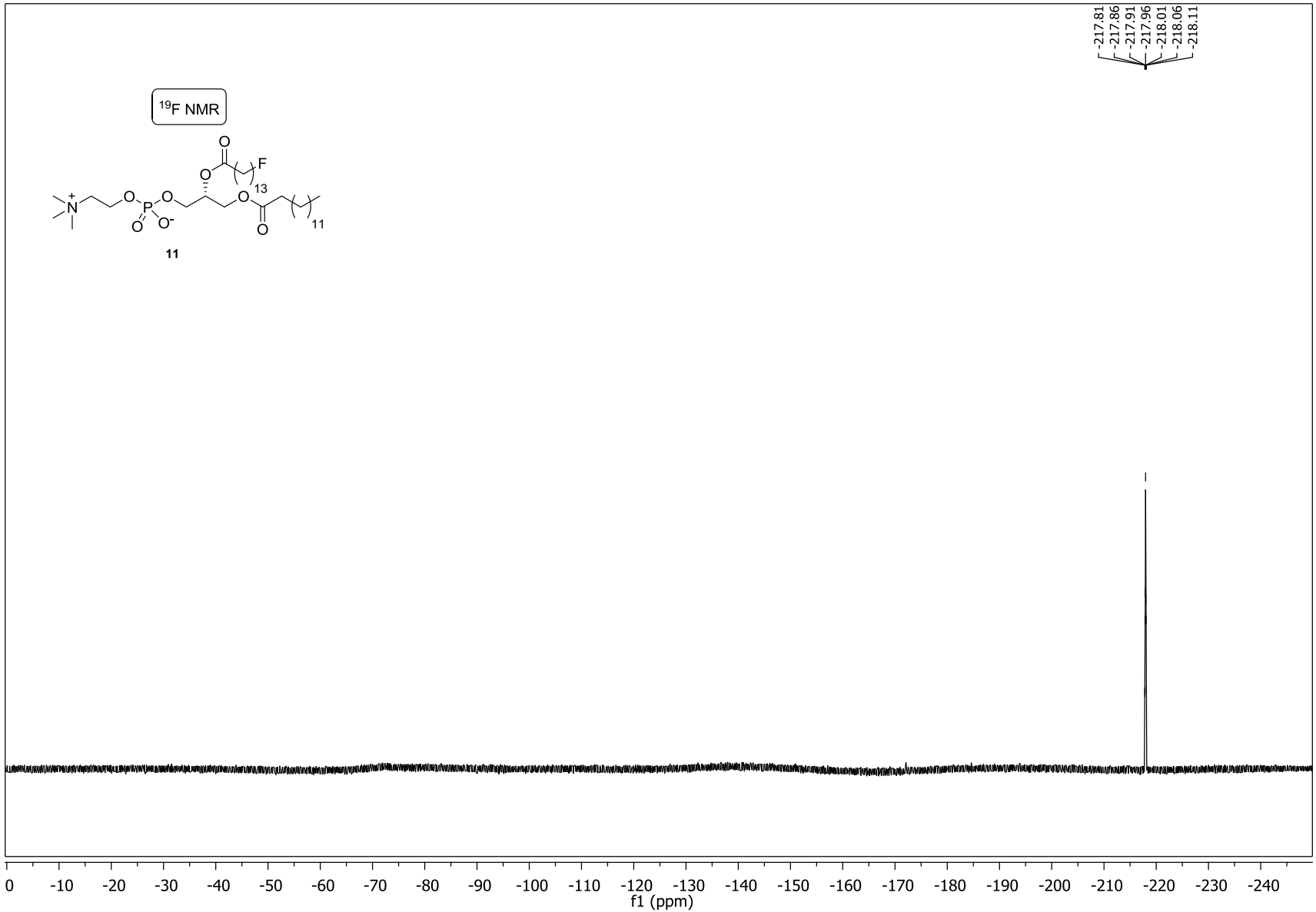

4.50
4.49
4.47
4.39
4.37
4.35
2.36
2.34
2.32
1.71
1.63
1.26
^{1}H NMR
O
HO
F
13
14
0.87
0.87
2.00
4.13
20.35
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

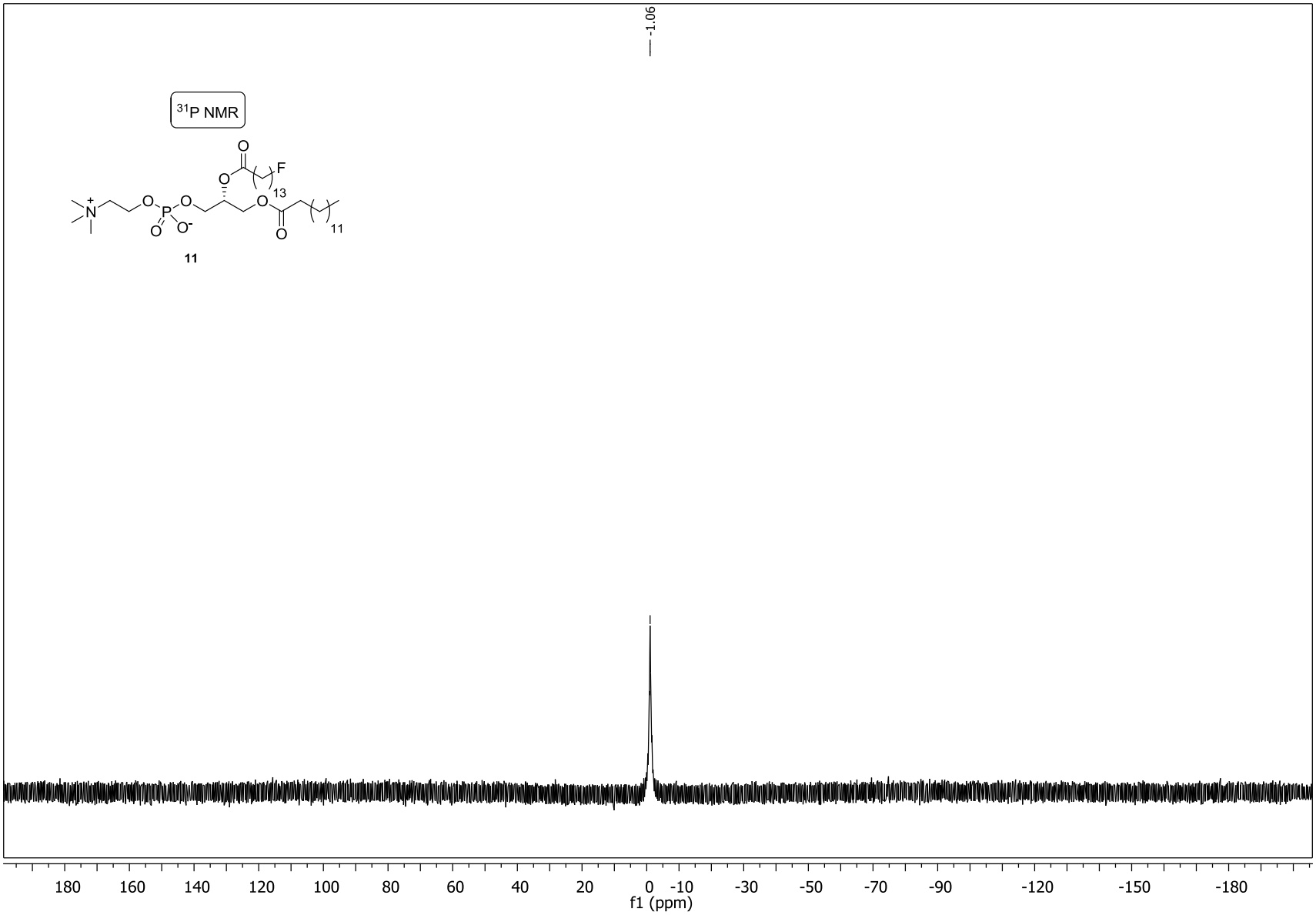

180.66
85.01
83.70
77.41
77.16
76.91
34.24
30.61
30.46
29.71
29.69
29.66
29.64
29.54
29.37
29.18
25.29
25.25
24.79
13C NMR
HO
O
F
13
14
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-217.85
-217.91
-217.97
-218.04
-218.10
^{19}F NMR
O
HO
F
13
14
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
f1 (ppm)


1H NMR
11
7.27
5.19
4.49
4.47
4.46
4.39
4.38
4.37
4.30
4.12
3.93
3.76
3.33
2.31
2.29
2.27
2.25
1.70
1.65
1.57
1.38
1.25
0.89
0.88
0.86
1.07
1.09
1.97
1.96
1.12
2.19
2.00
8.95
4.03
2.18
4.08
38.06
3.00
f1 (ppm)


173.66
173.31
84.99
83.69
77.41
77.16
76.91
70.51
70.46
66.36
63.58
63.03
59.52
54.42
32.05
29.85
29.84
29.82
29.81
29.71
29.67
29.52
29.50
29.39
29.33
25.01
22.82
14.26
13C NMR
11
f1 (ppm)


-217.81
-217.86
-217.91
-217.96
-218.01
-218.06
-218.11
19F NMR
11
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)


-1.06
31P NMR
11
180
160
140
120
100
80
60
40
20
0
-10
-30
-50
-70
-90
-120
-150
-180
f1 (ppm)

Fourier-transformed Infrared

Sample preparation

The fluorinated lipids were dissolved in chloroform at a concentration known precisely (the source of pure DMPC is also in a solution of chloroform, at a concentration of 25 mg/mL). The lipid multilamellar vesicles were prepared by measuring the necessary volume of the two lipids solutions (fluorinated DMPC and pure DMPC) and combining them before reducing the solvent volume with a stream of nitrogen or argon. The samples are placed in a lyophilizer for at least one night to remove all traces of residual organic solvent. A solution of deuterated water with 0.1 molar of HEPES buffer (2-[4-(2-hydroxyethyl)piperazin-1-yl]ethanesulfonic acid) is added to the samples to obtain a lipid concentration of 2% w/v. Then the samples underwent five thaw (heating 5 minutes at 50°C)/vortex shaking (10 secondes)/freezes (liquid N_2) cycles. After the last cycle, the sample is allowed to cool to room temperature 5 minutes. Table 1 shows the different amounts of lipids and HEPES buffer used for the measurements.

Table 1: Necessary amounts of lipids and buffer for the preparation of FTIR samples

Fluorinated lipid ratio (%)	Fluorinated lipid mass (mg)	Pure DMPC mass (mg)	HEPES buffer volume (µL)
100	1,6	-	40
50	0,8	0.8	40
25	0,4	1.2	40
10	0,2	1.4	50
5	0,2	3.8	100
2,5	0,2	7.8	200

Experiments

Infrared spectra were recorded with a Nicolet Magna 550 Fourier transform spectrometer (Thermo-Nicolet, Madison, WI, USA) equipped with a narrow band mercury–cadmium–telluride (MCT) detector and a germanium-coated KBr beam splitter. Ten microliters of the sample were placed between CaF_2 windows separated by a 6µm Mylar spacer. A total of 128 interferograms were acquired with a resolution of 2 cm^{-1} in the spectral range of 4000–650 cm^{-1} at various temperatures ranging from 10 to 70 °C and controlled by a home-made device. The spectra were

corrected for the water vapor and CaF_2 contribution by subtraction of a reference spectrum. The data were processed with the software Grams 386 (Galactic Industries Corporation, Salem, MA, USA). The spectral is baseline-corrected using a cubic function. The methylene symmetric stretching frequency was obtained from the center of gravity calculated at the top 10% of the band. The informations obtained can then be transposed in graph using the Excel software (Microsoft, Redmond, WA). The transition temperatures and the cooperativity indices have been calculated from a custom algorithm in the Matlab program.

Figure 1 shows the type of spectra obtained with these experiments and describe the bands of interest; the CH_2 stretching bands.

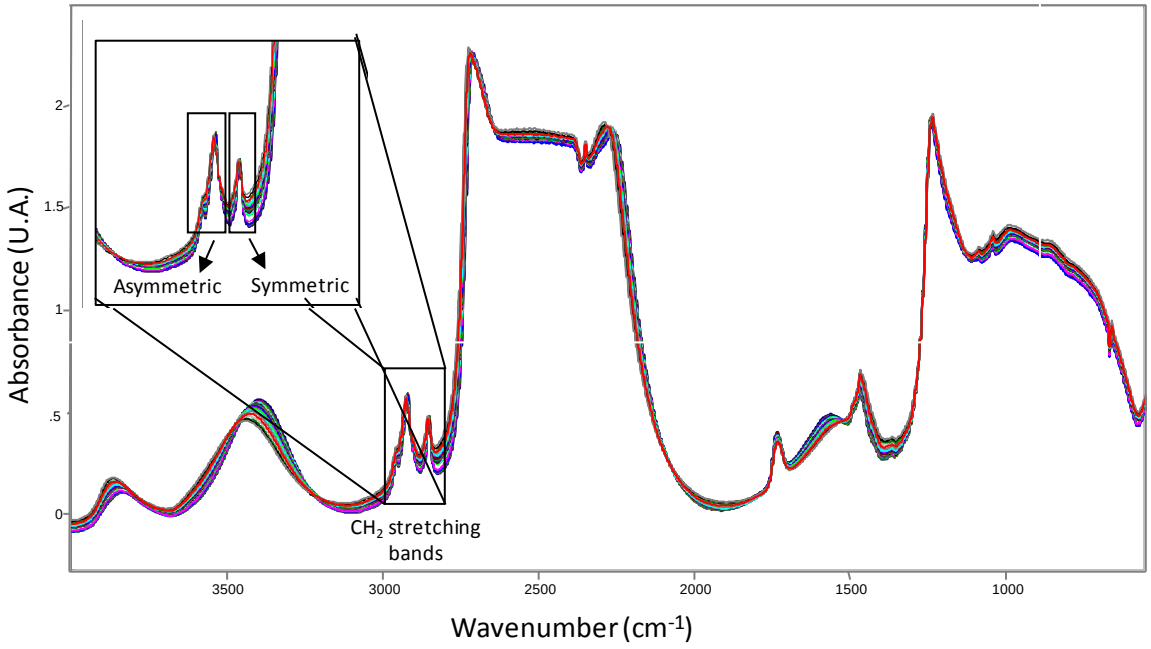


Fig.1 FTIR spectra of 7F-DMPC (10 to 70 °C)