Domino Michael-Aldol Annulation for the Stereocontrolled Synthesis of Bicyclo[3.3.1]nonane and Bicyclo[3.2.1]octane Derivatives

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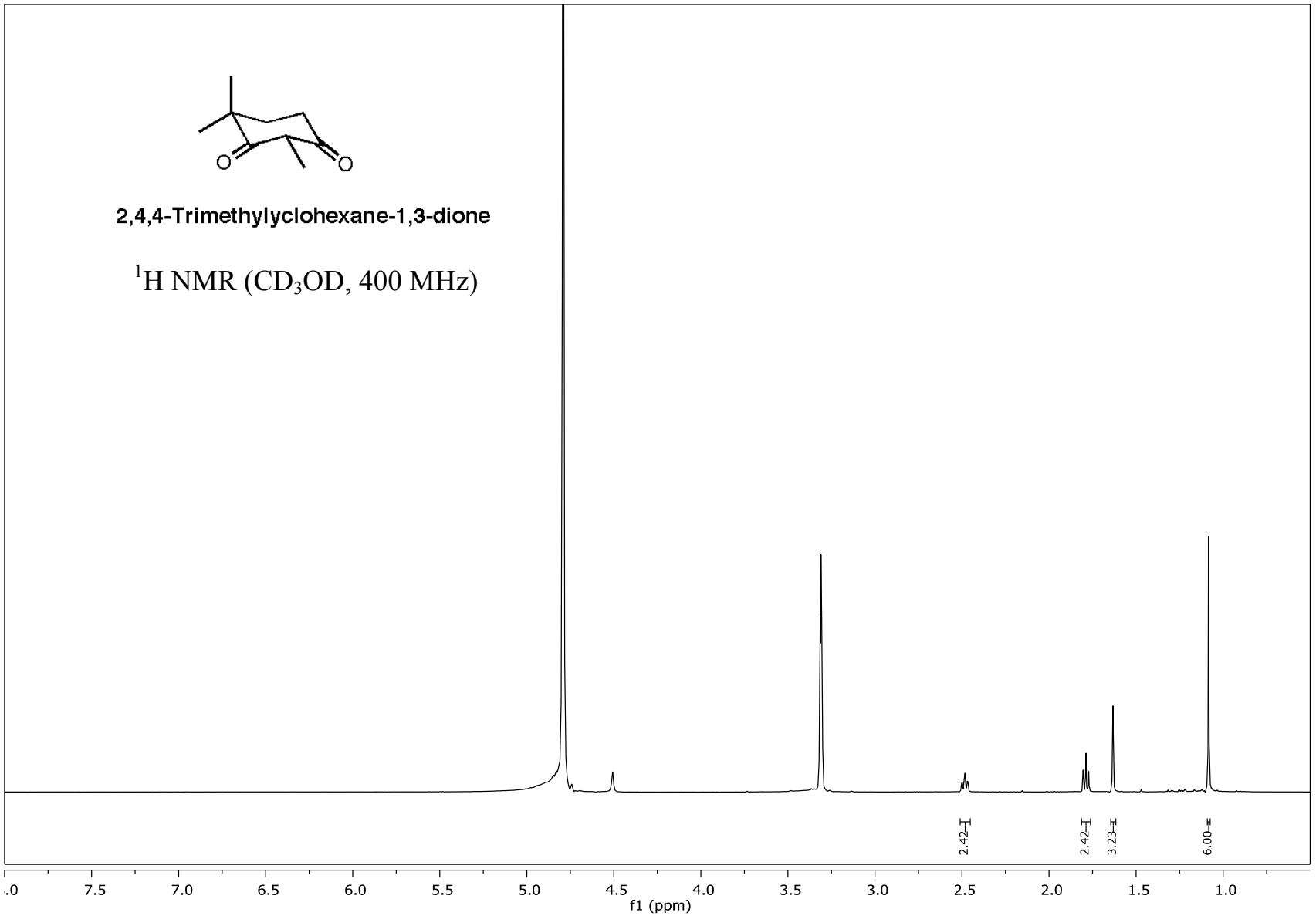
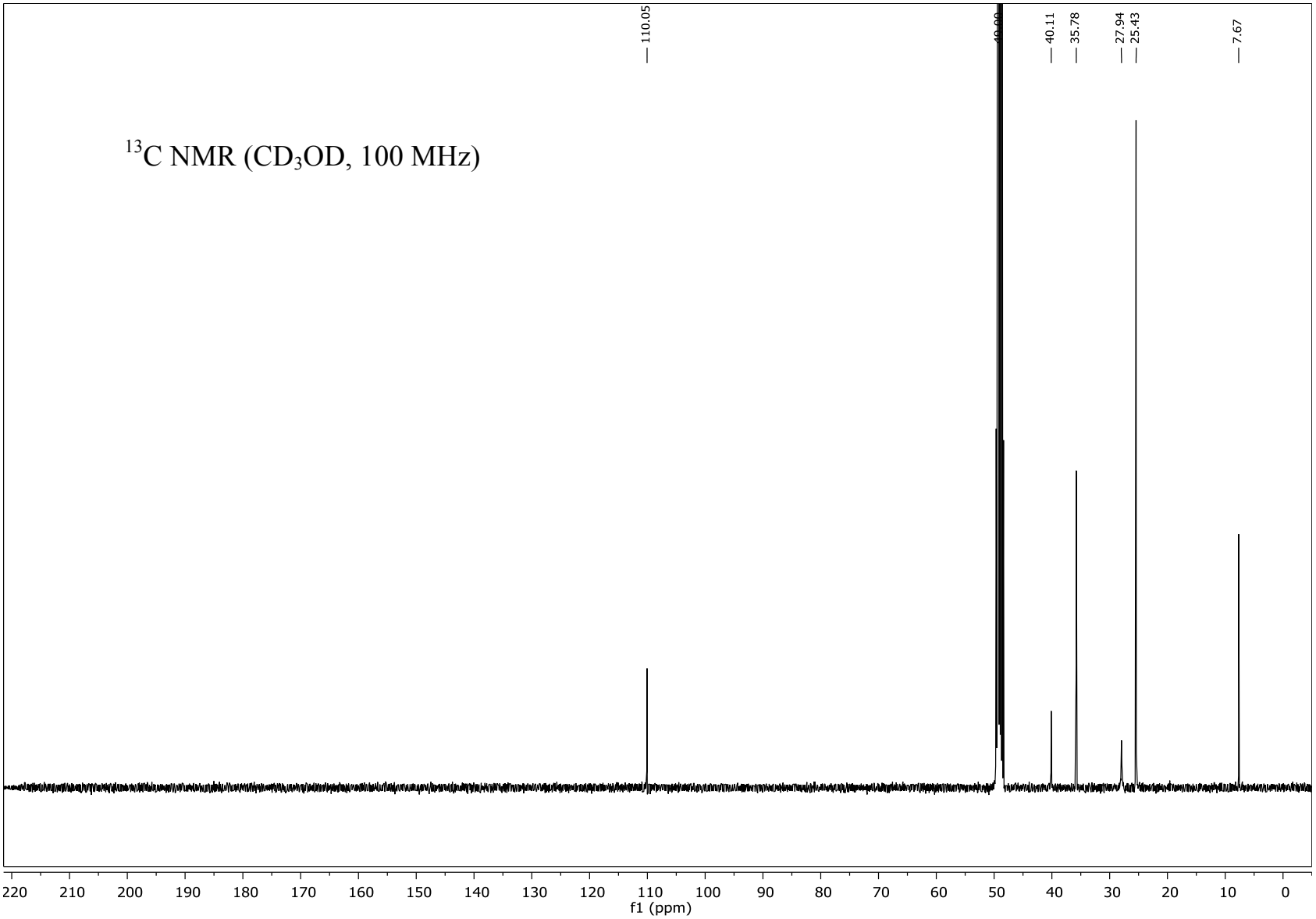
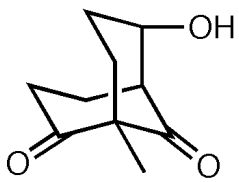
1. ^{1}H and ^{13}C NMR spectra

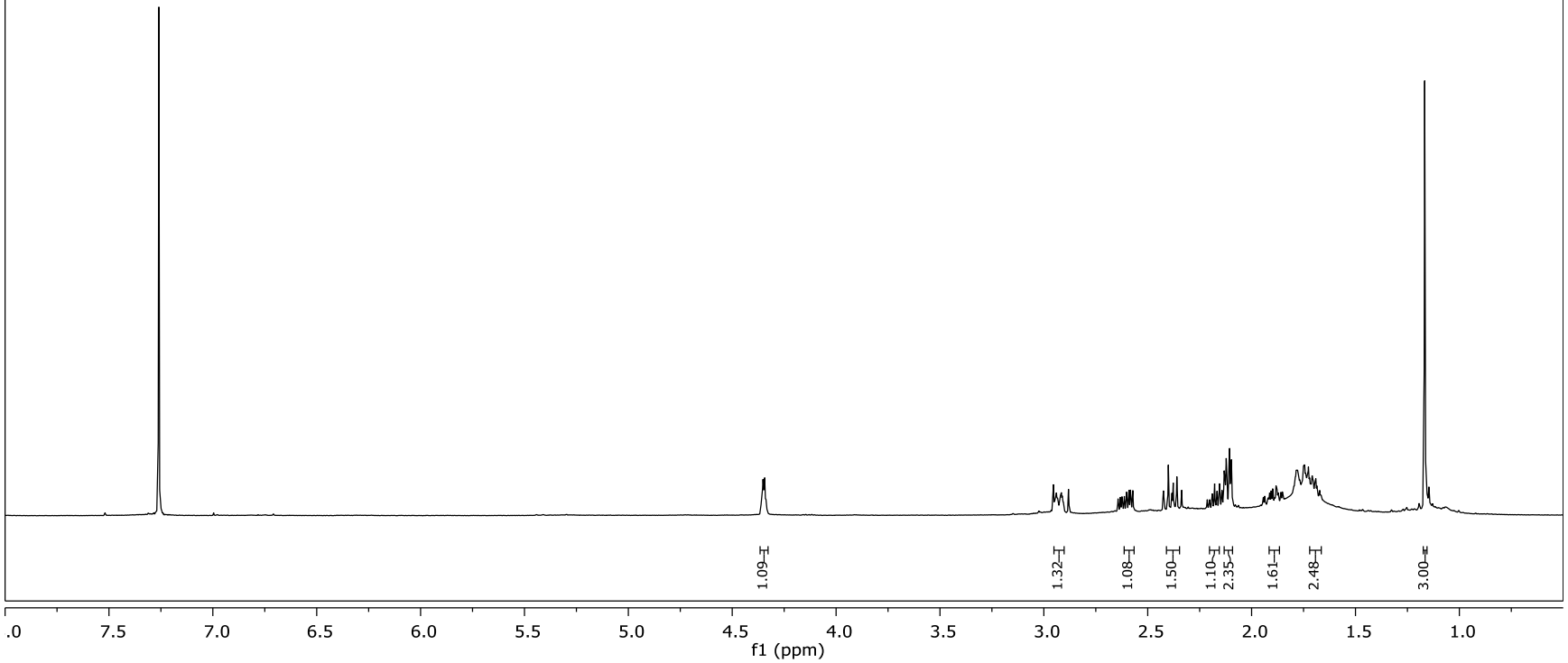

2,4,4-Trimethylyclohexane-1,3-dione
^{1}H NMR (CD_3OD, 400 MHz)
2.42
2.42
3.23
6.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


^{13}C NMR (CD_3OD, 100 MHz)
110.05
40.11
35.78
27.94
25.43
7.67
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)



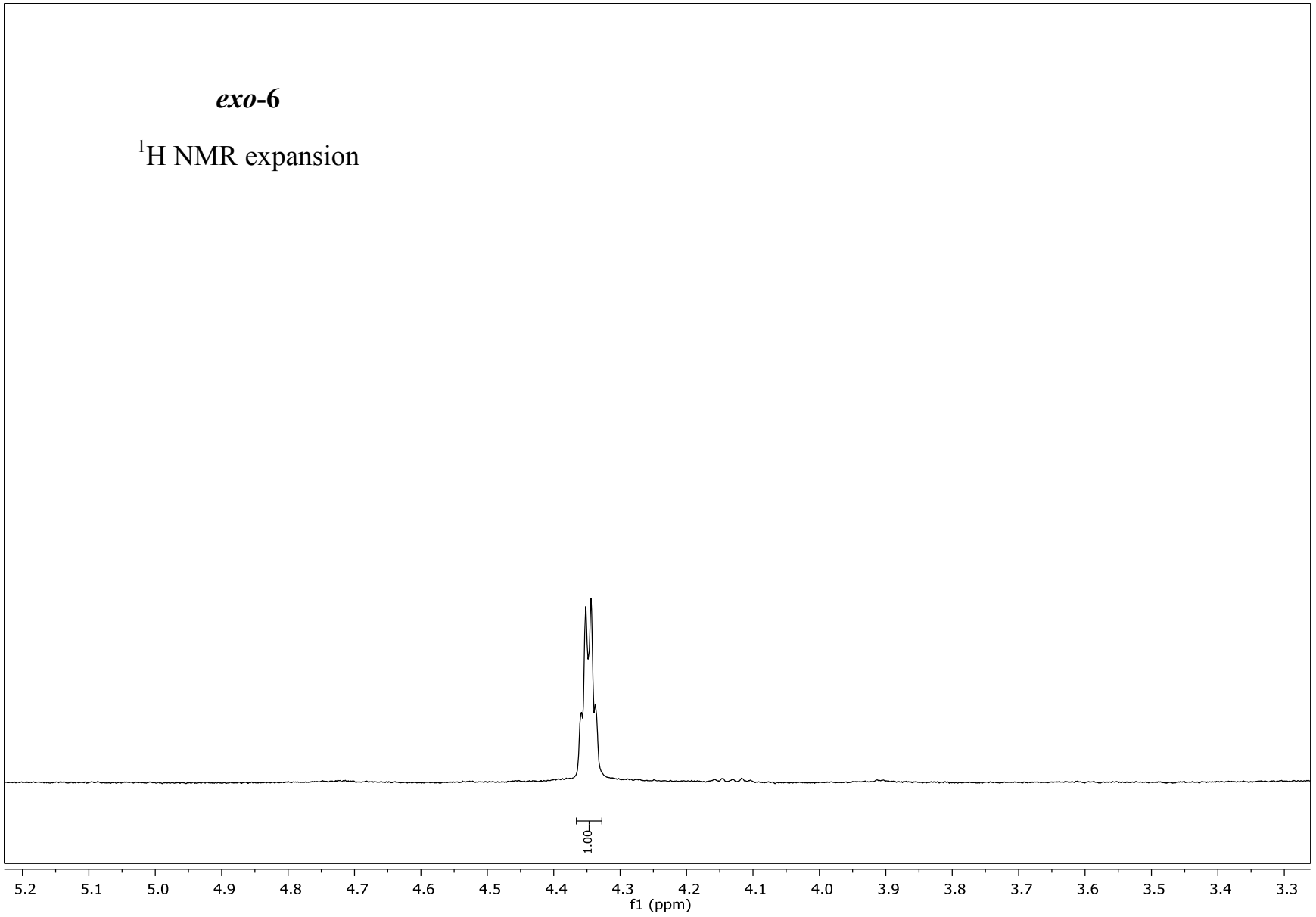
exo-**6**

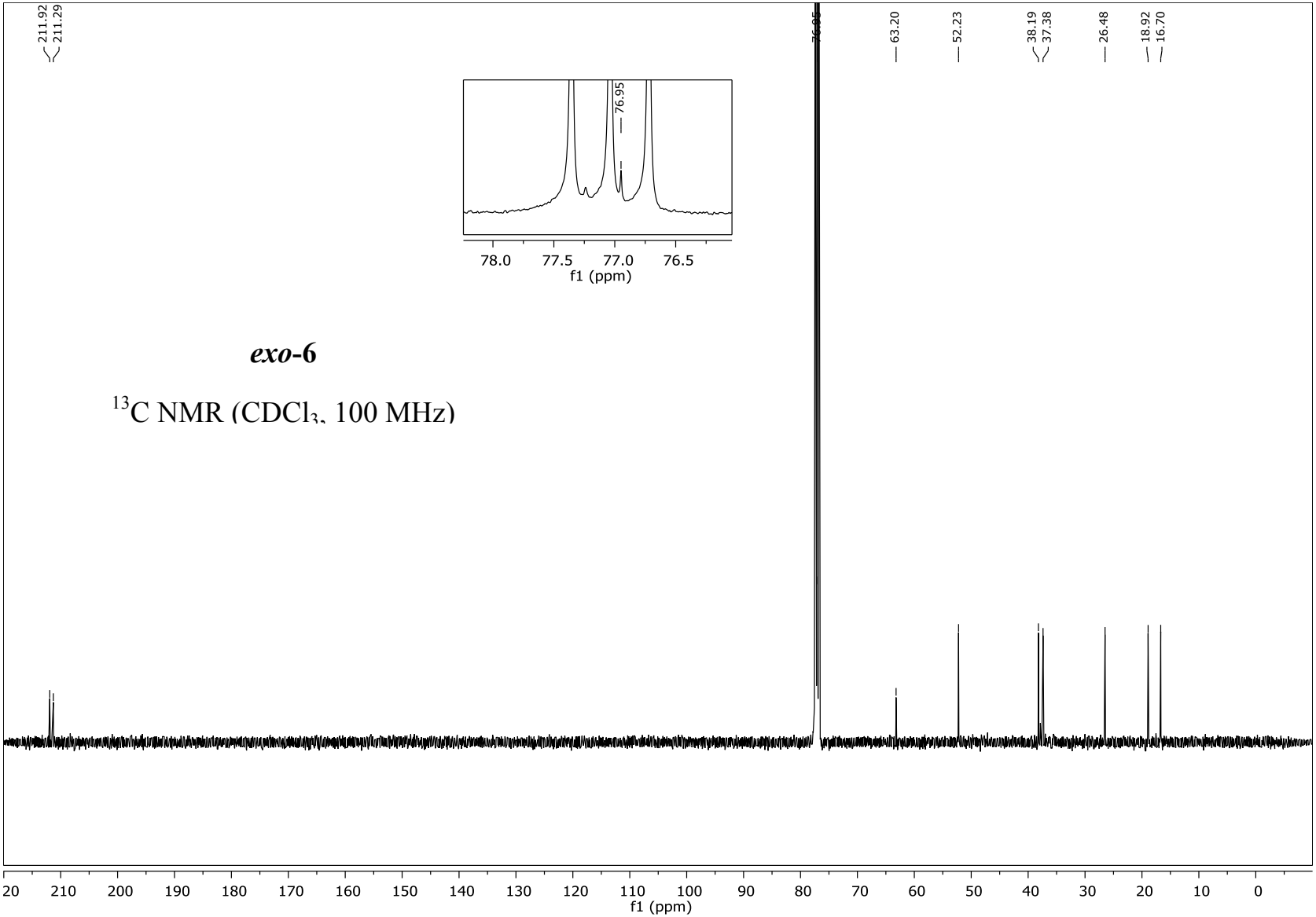
^{1}H NMR ($CDCl_3$, 400 MHz)



***exo*-6**

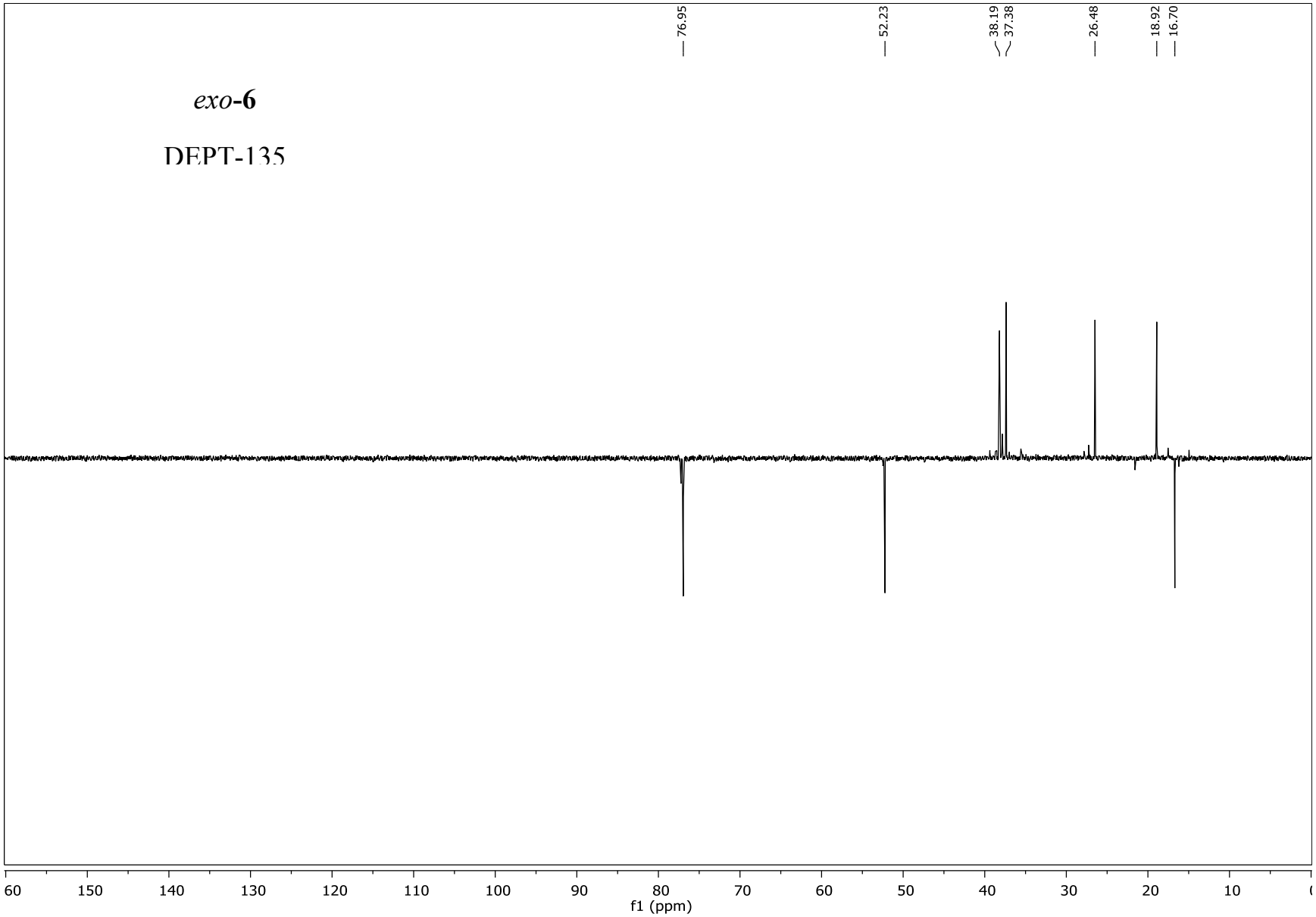
^{1}H NMR expansion





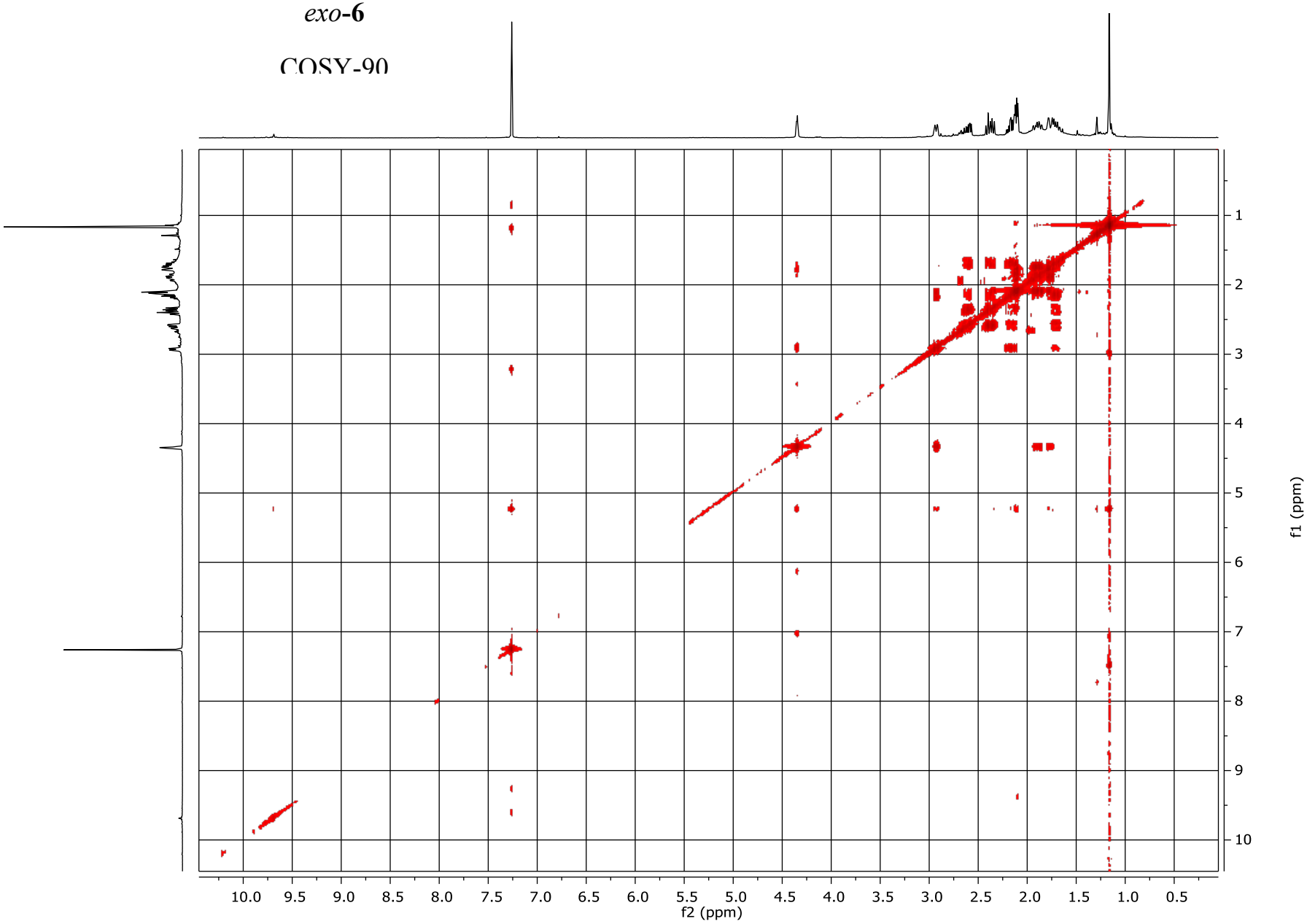
***exo*-6**

^{13}C NMR ($CDCl_3$, 100 MHz)


76.95
52.23
38.19
37.38
26.48
18.92
16.70
exo-6
DEPT-135
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

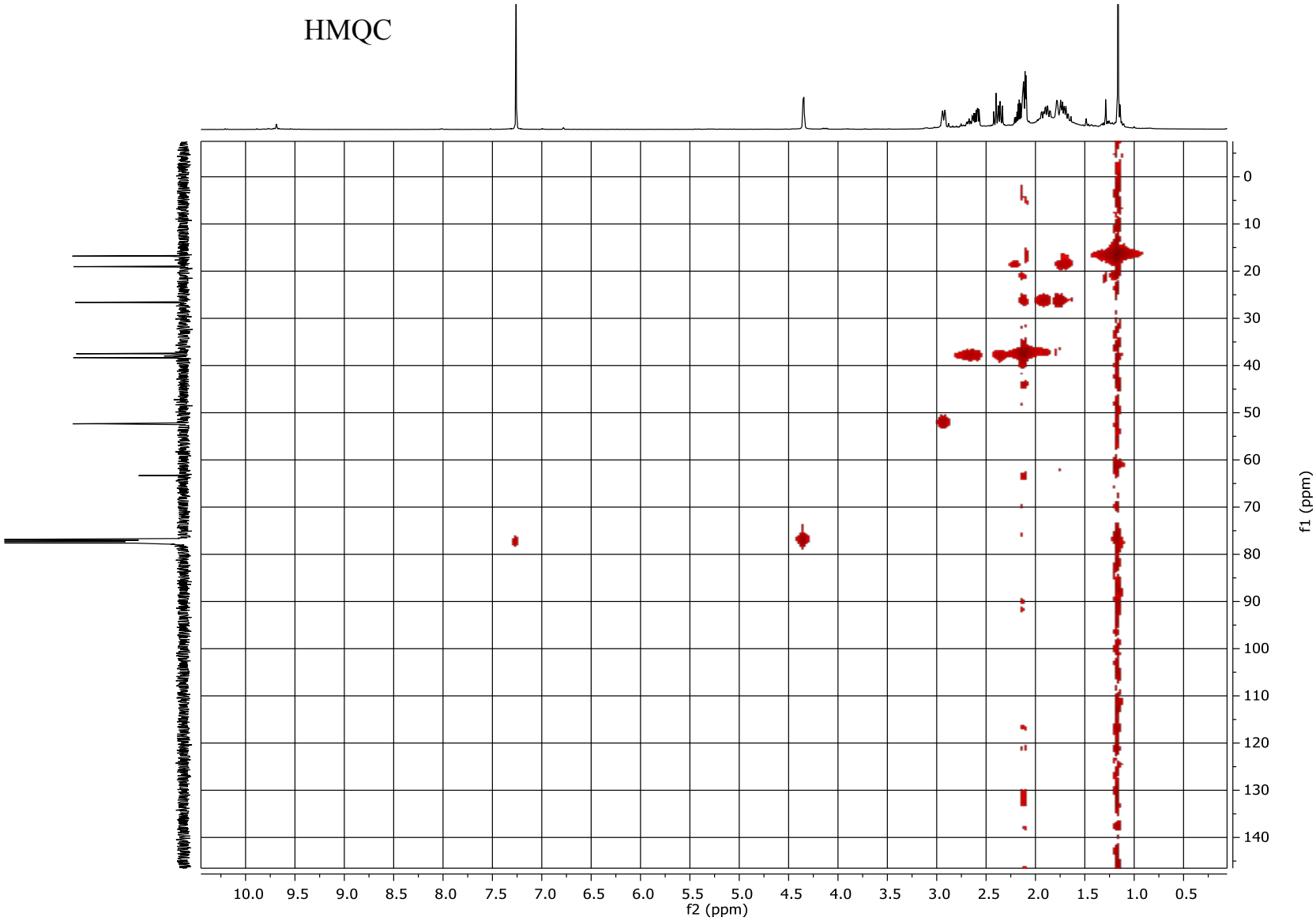
exo-**6**

COSY-90


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
f2 (ppm)
1
2
3
4
5
6
7
8
9
10
f1 (ppm)

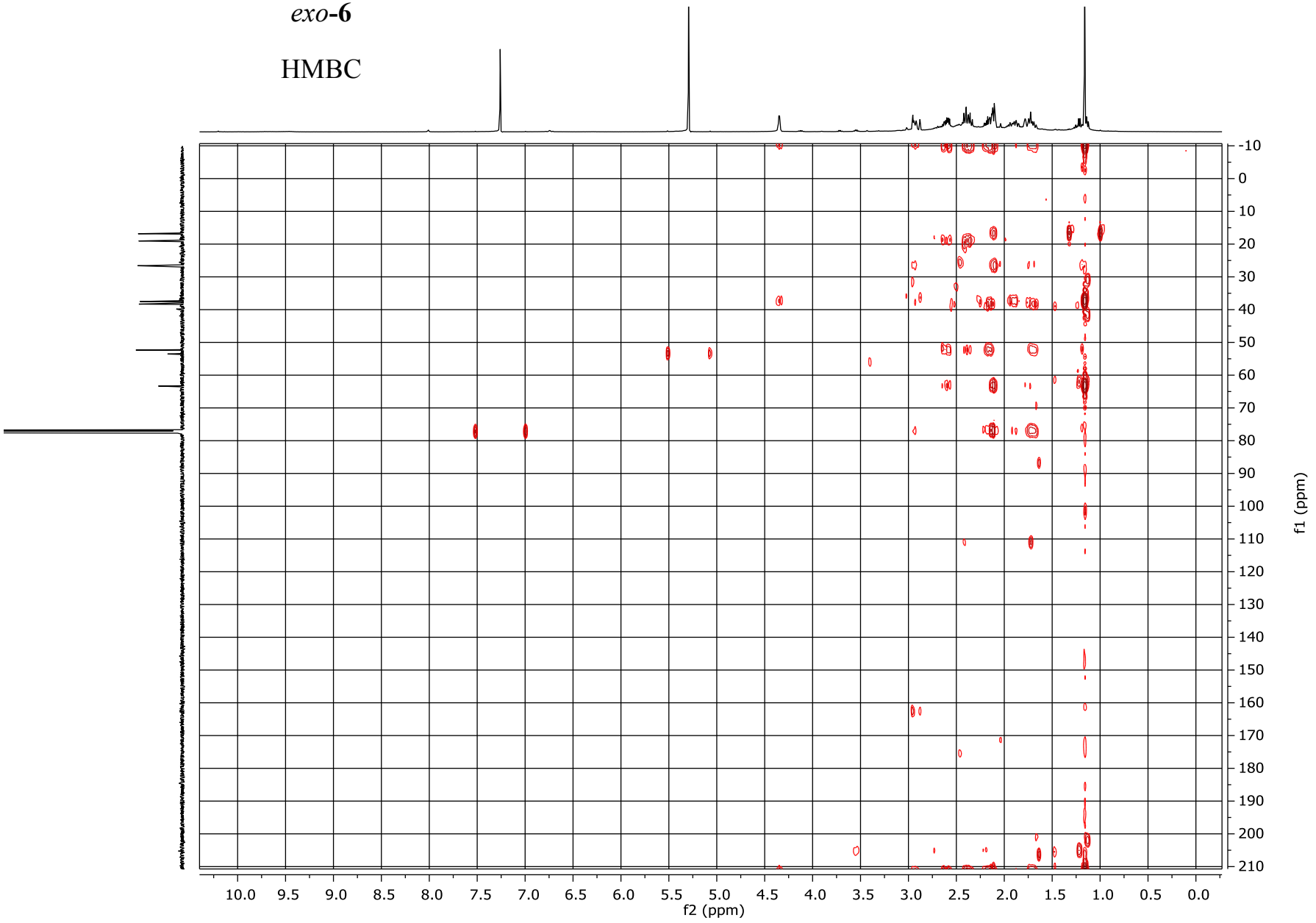
exo-**6**

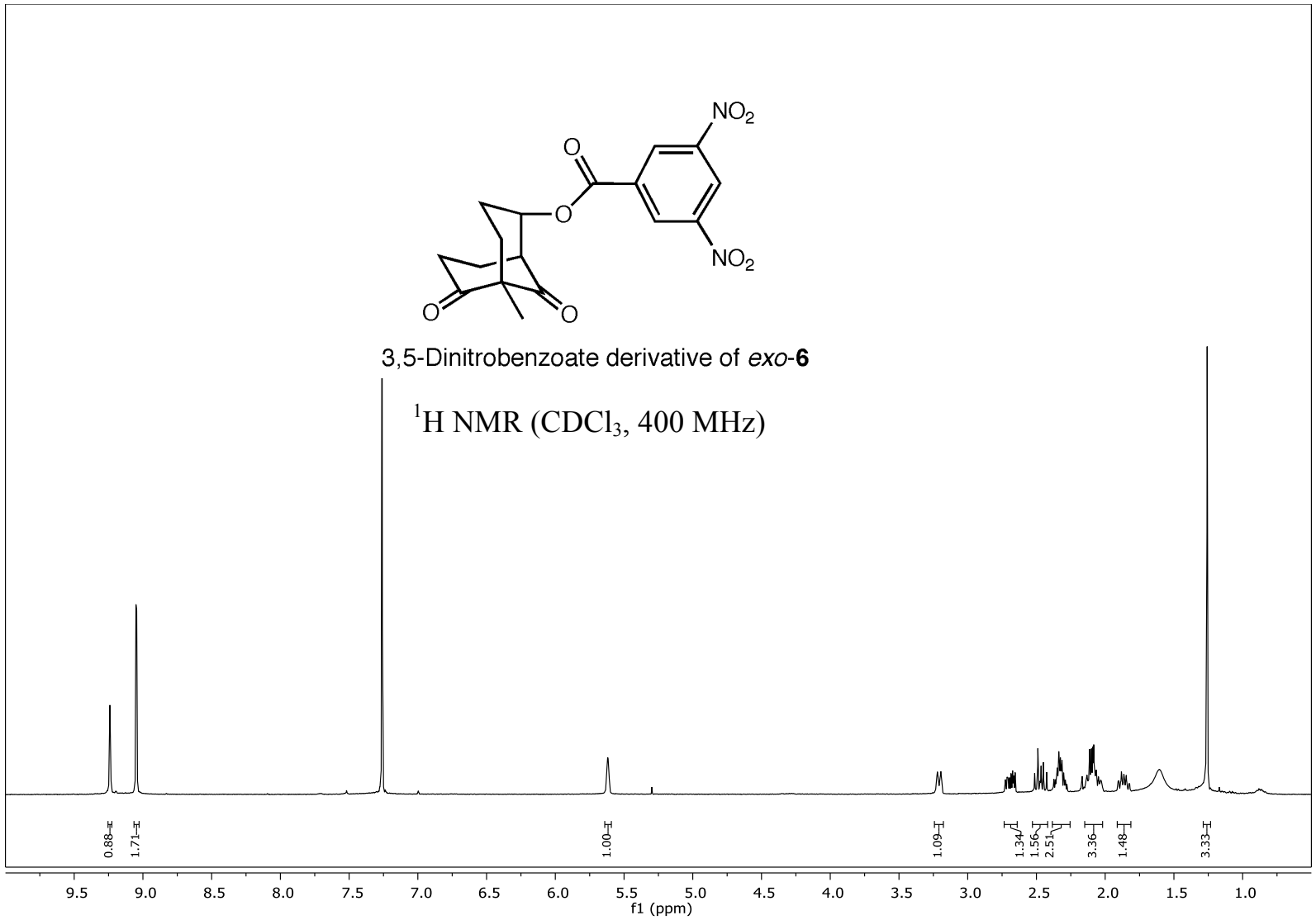
HMQC

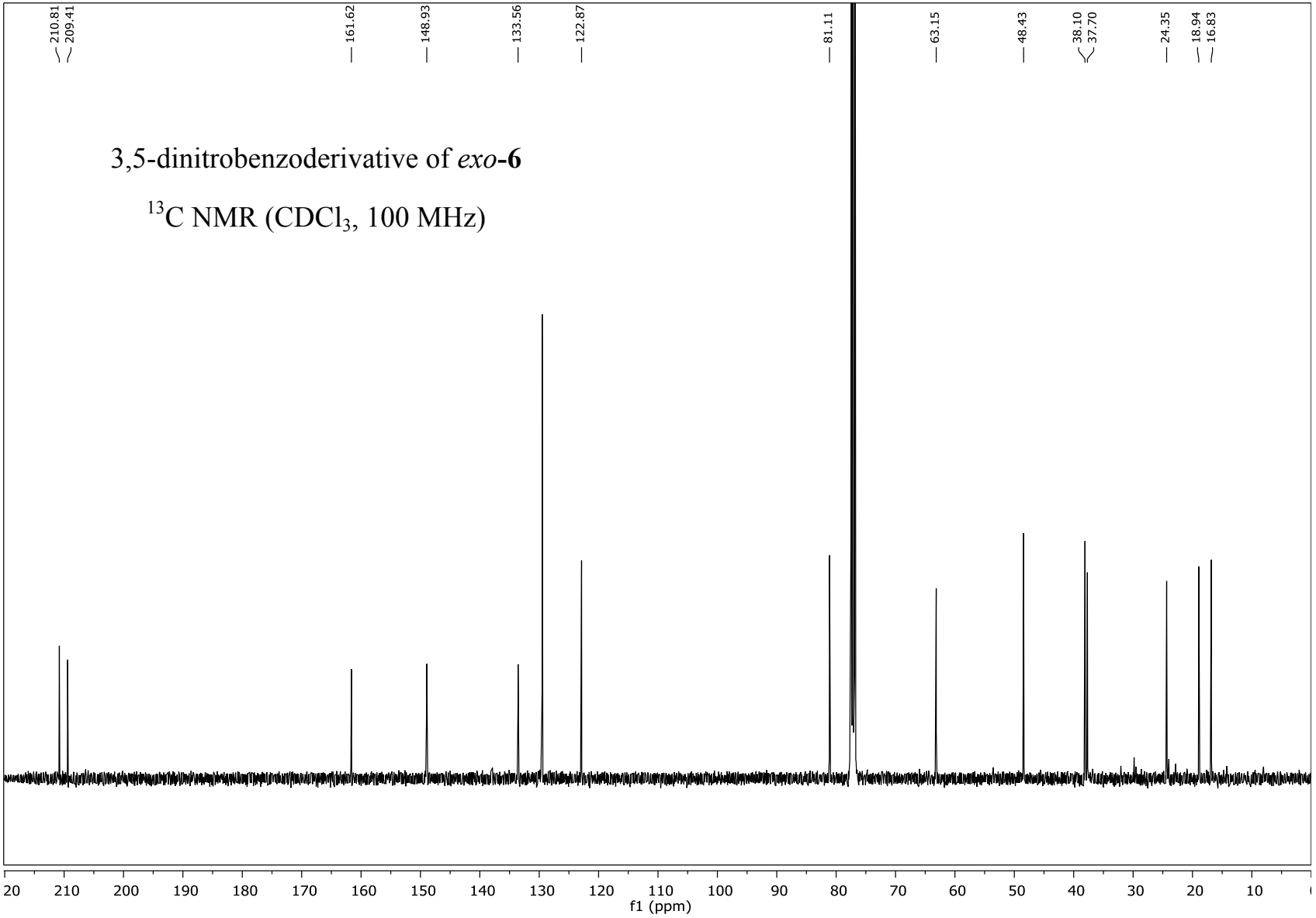

10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)

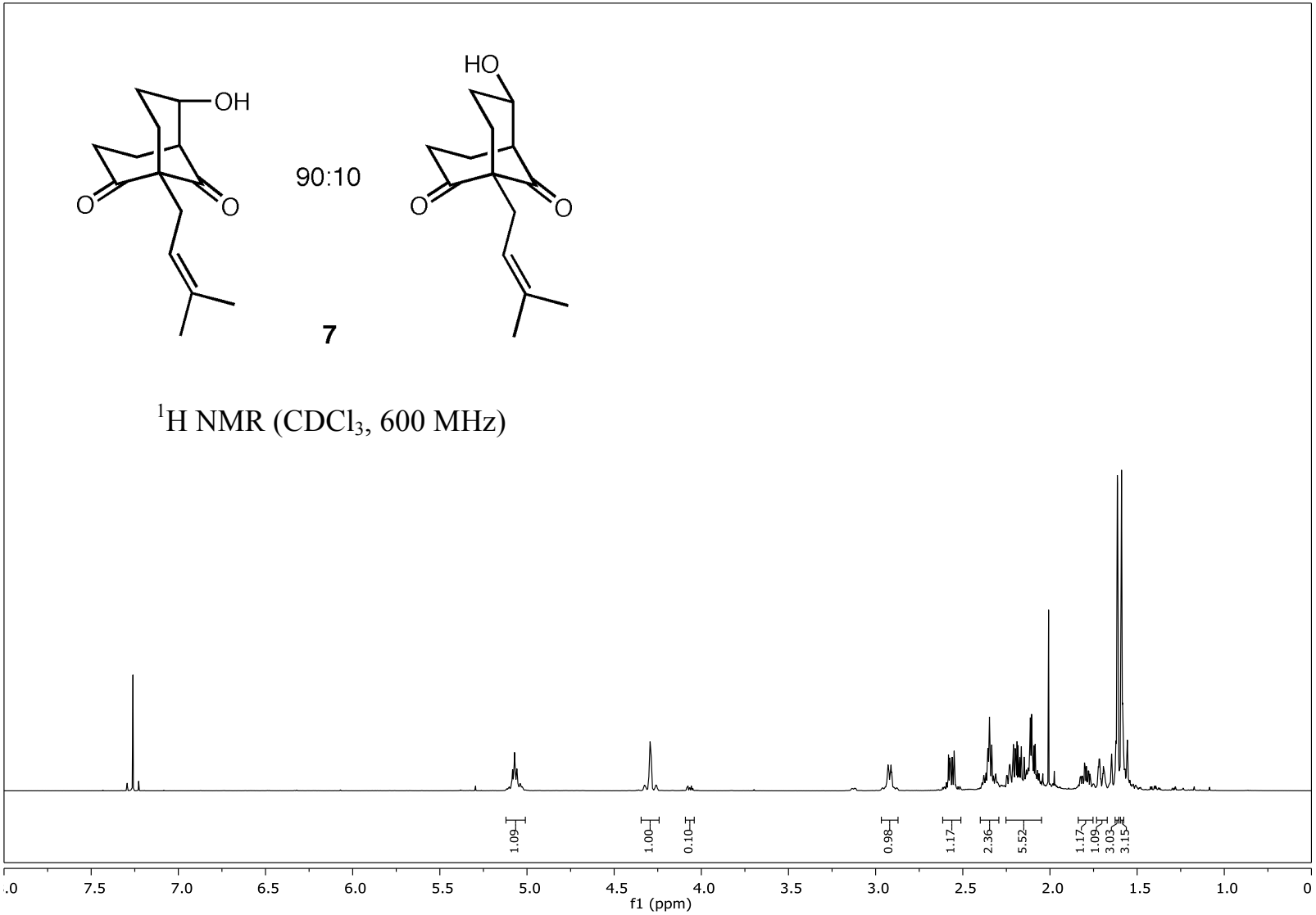
exo-**6**

HMBC



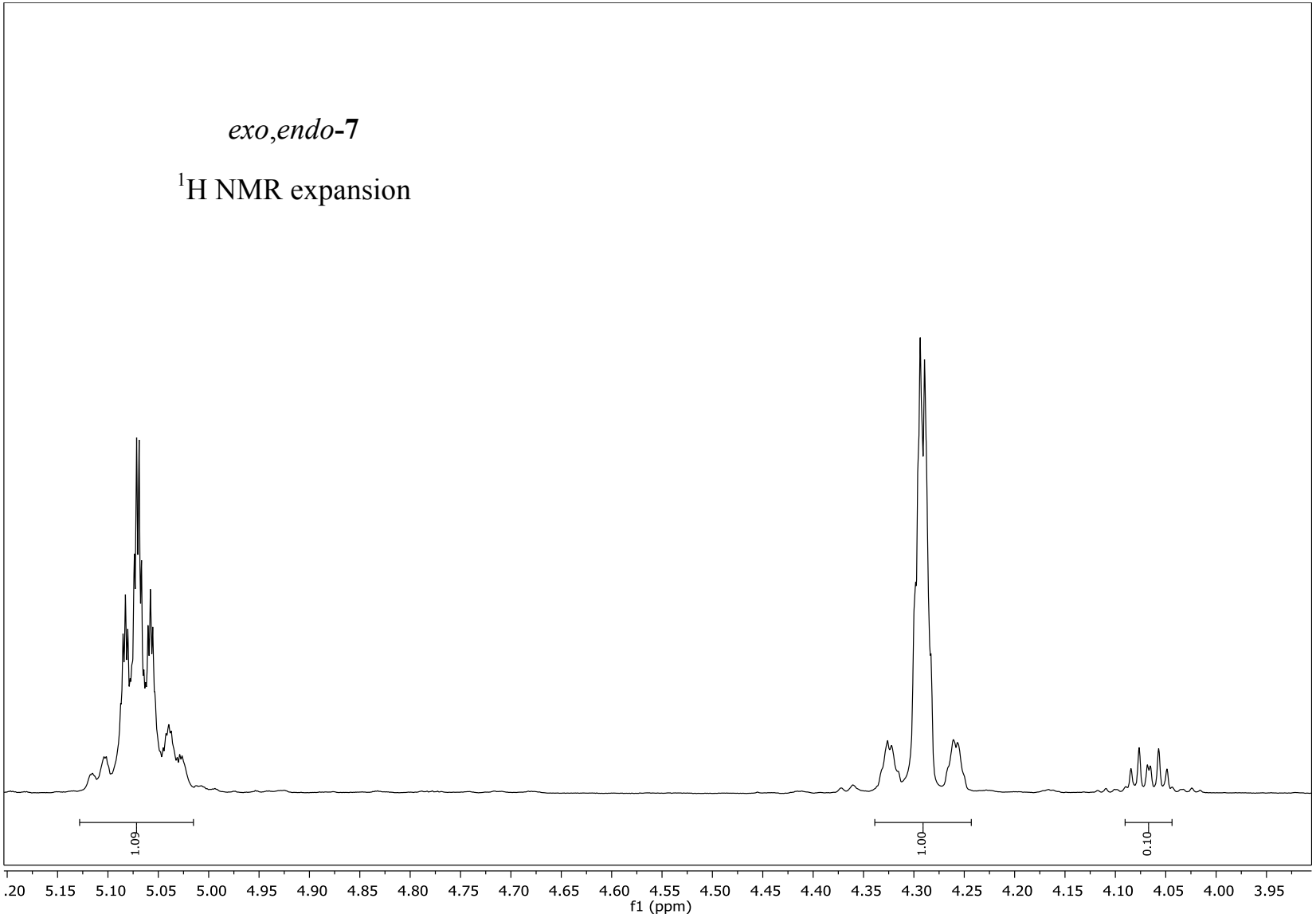

NO2
NO2
O
O
O
O
3,5-Dinitrobenzoate derivative of exo-6
1H NMR (CDCl3, 400 MHz)
0.88
1.71
1.00
1.09
1.34
1.56
2.51
3.36
1.48
3.33
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


210.81
209.41
161.62
148.93
133.56
122.87
81.11
63.15
48.43
38.10
37.70
24.35
18.94
16.83
3,5-dinitrobenzoderivative of *exo*-**6**
^{13}C NMR ($CDCl_3$, 100 MHz)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


OH
O
O
90:10
HO
O
O
7
1H NMR (CDCl3, 600 MHz)
1.09
1.00
0.10
0.98
1.17
2.36
5.52
1.17
1.09
3.03
3.15
.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
f1 (ppm)

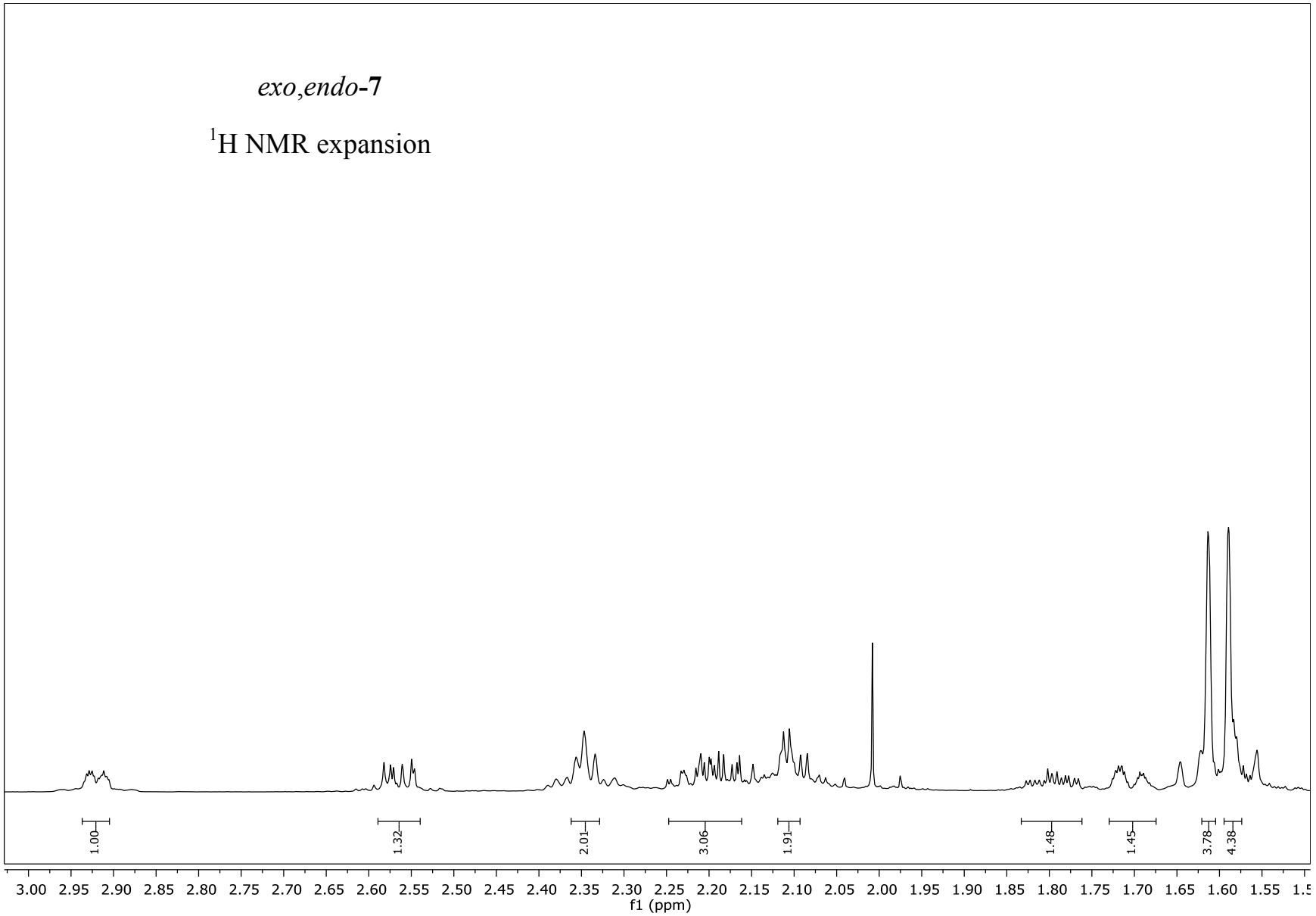
exo,*endo*-**7**

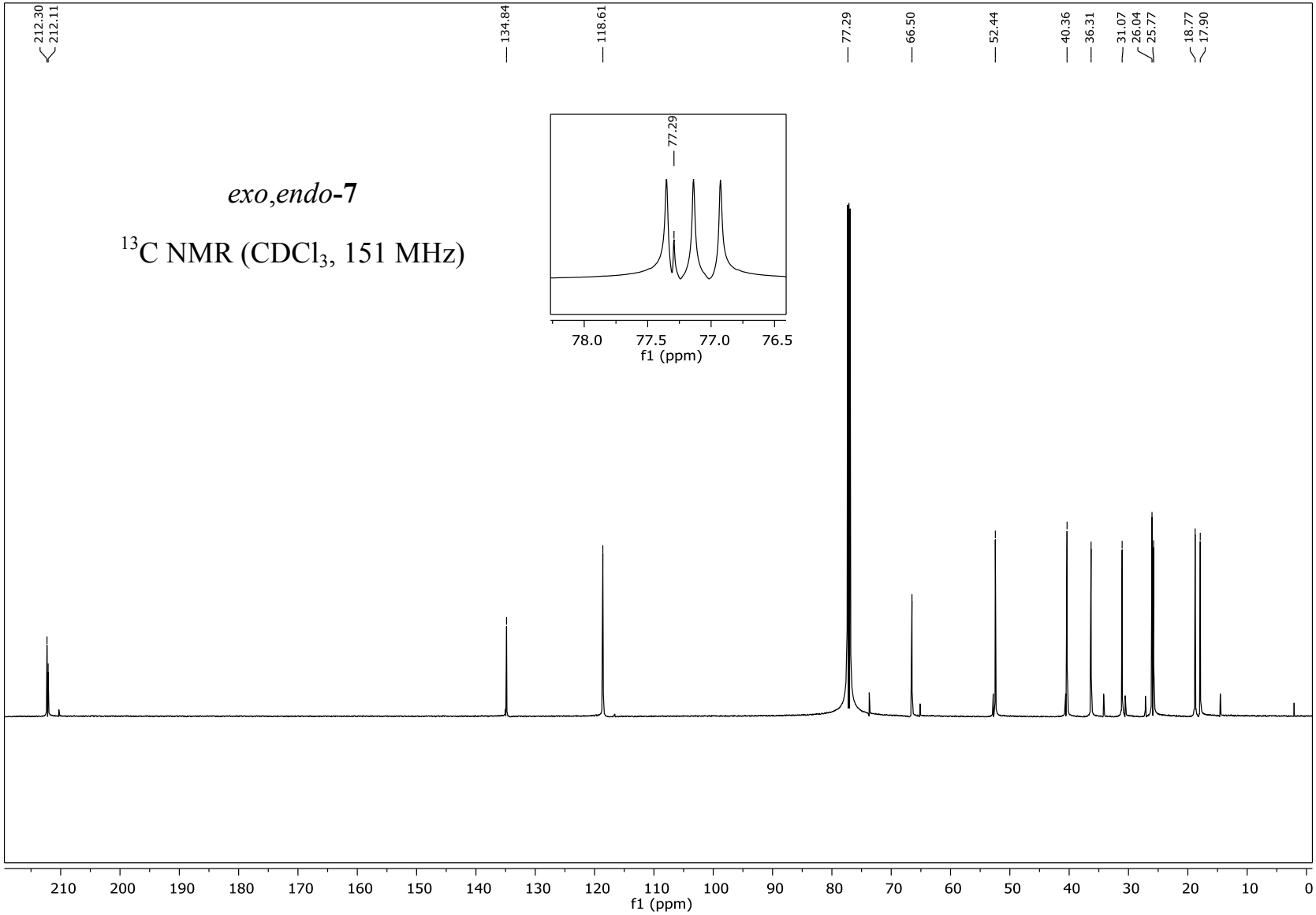
^{1}H NMR expansion

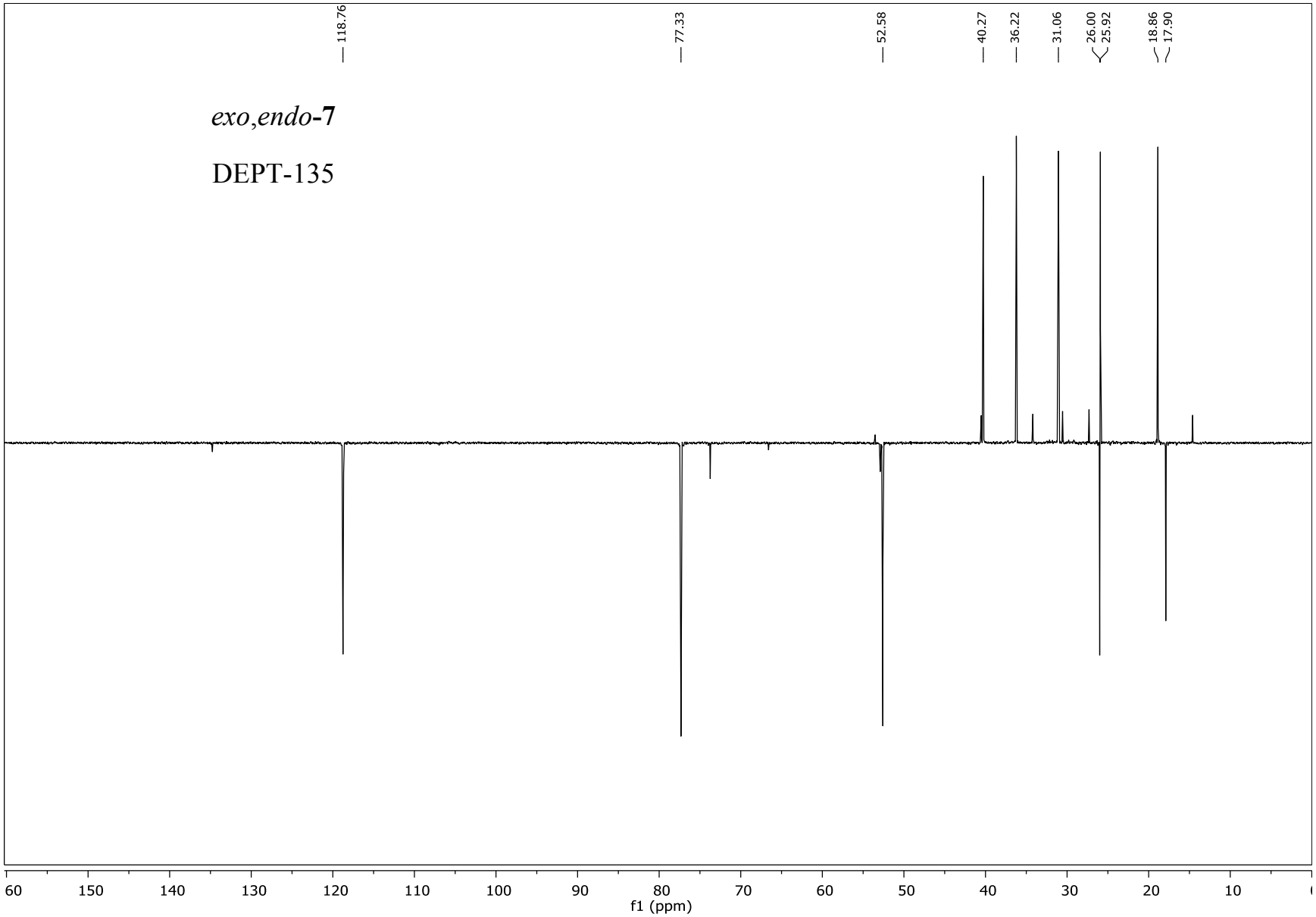


exo,*endo*-**7**

^{1}H NMR expansion

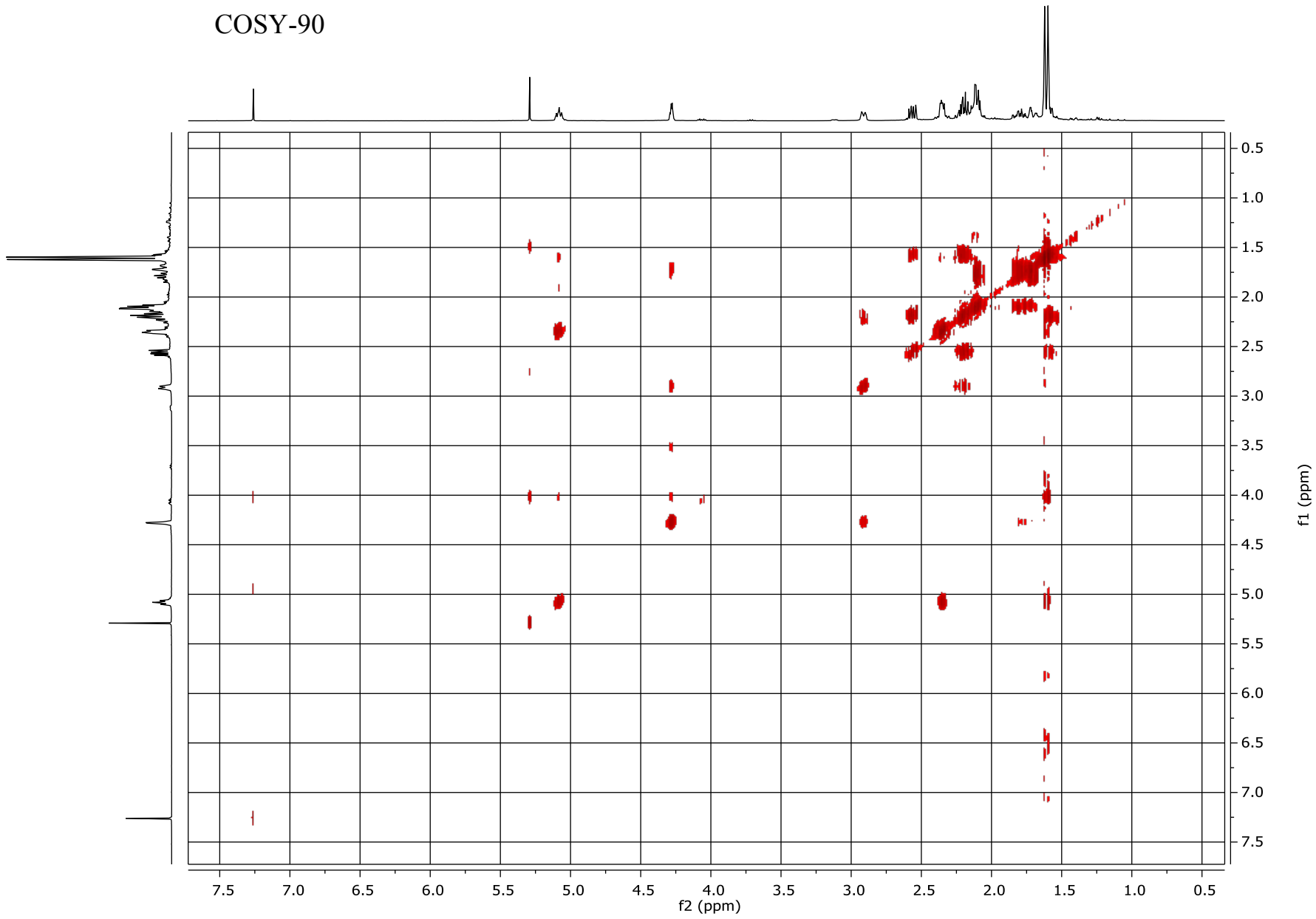



212.30
212.11
134.84
118.61
77.29
66.50
52.44
40.36
36.31
31.07
26.04
25.77
18.77
17.90
exo,endo-**7**
^{13}C NMR ($CDCl_3$, 151 MHz)
77.29
78.0
77.5
77.0
76.5
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


118.76
77.33
52.58
40.27
36.22
31.06
26.00
25.92
18.86
17.90
exo,endo-7
DEPT-135
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

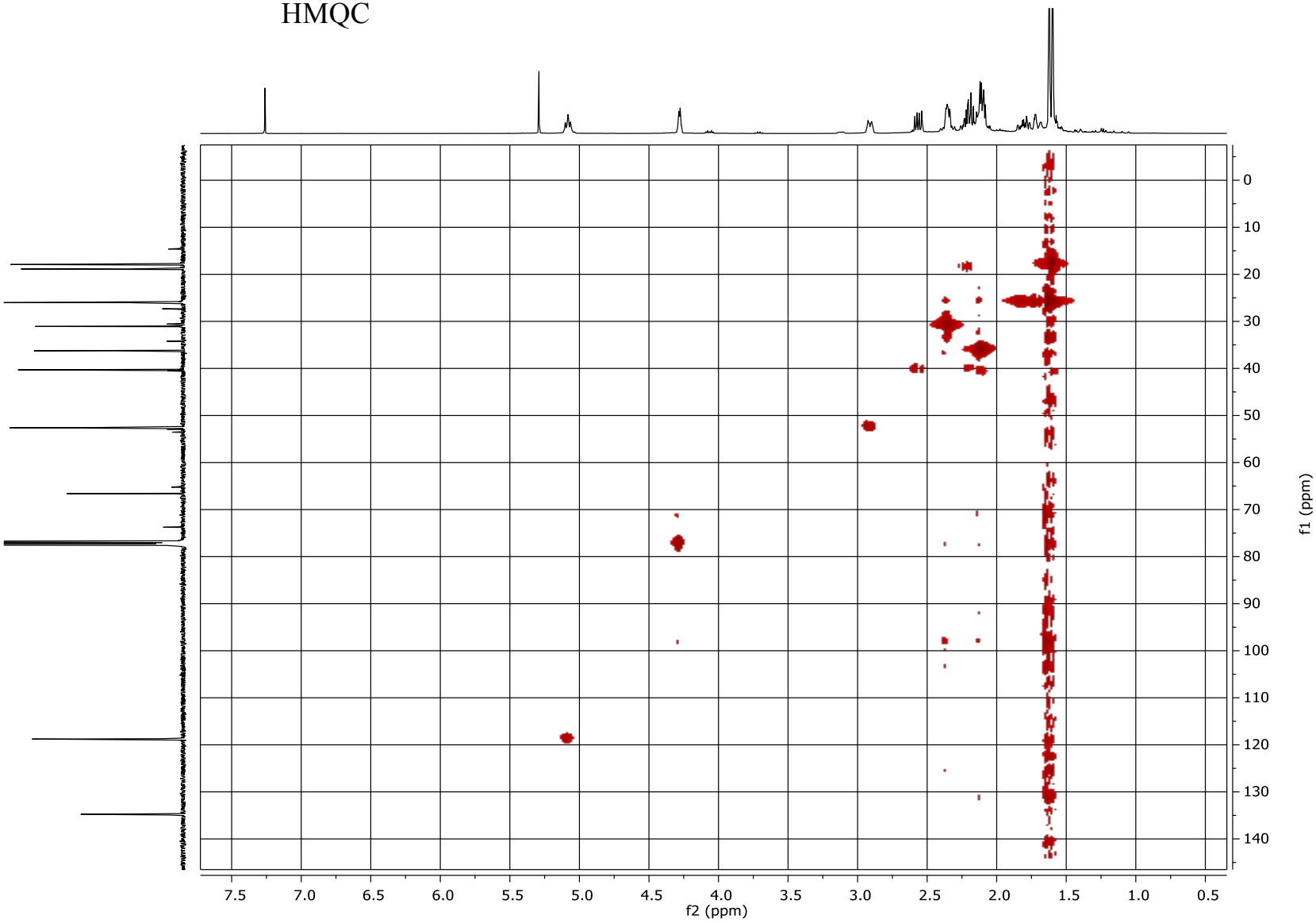
exo,endo-**7**

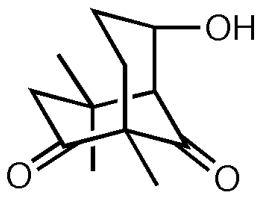
COSY-90



exo,endo-**7**

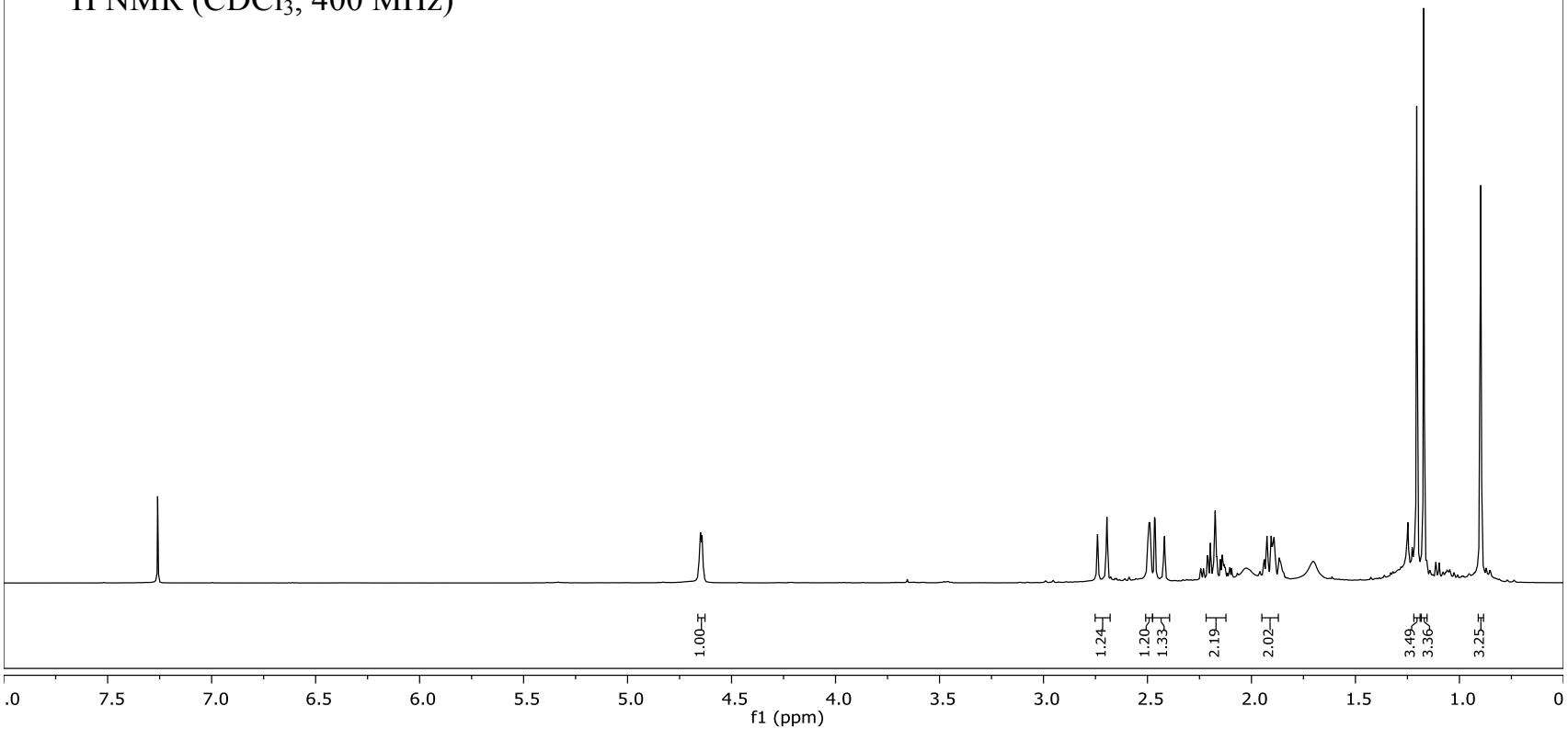
HMQC

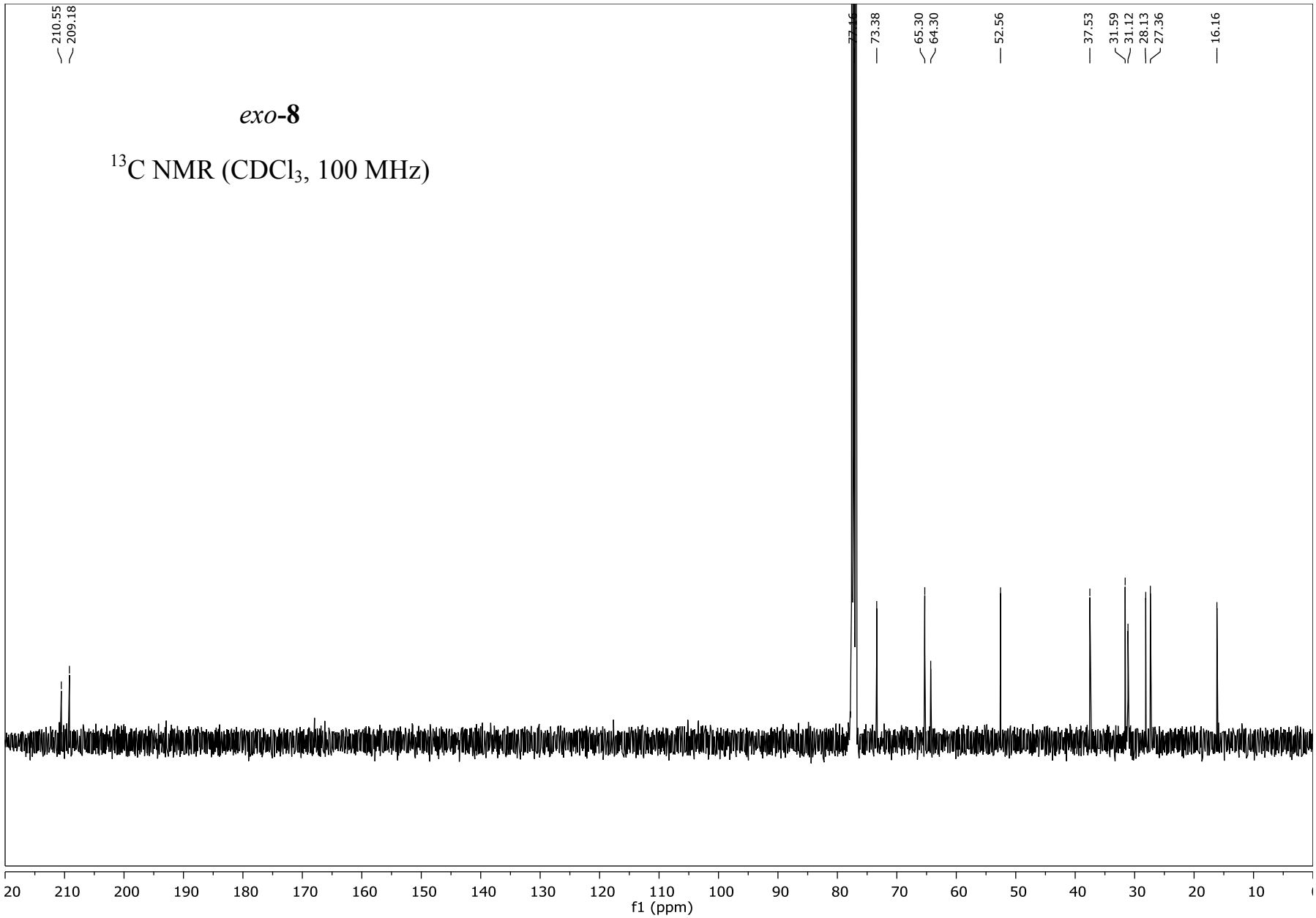


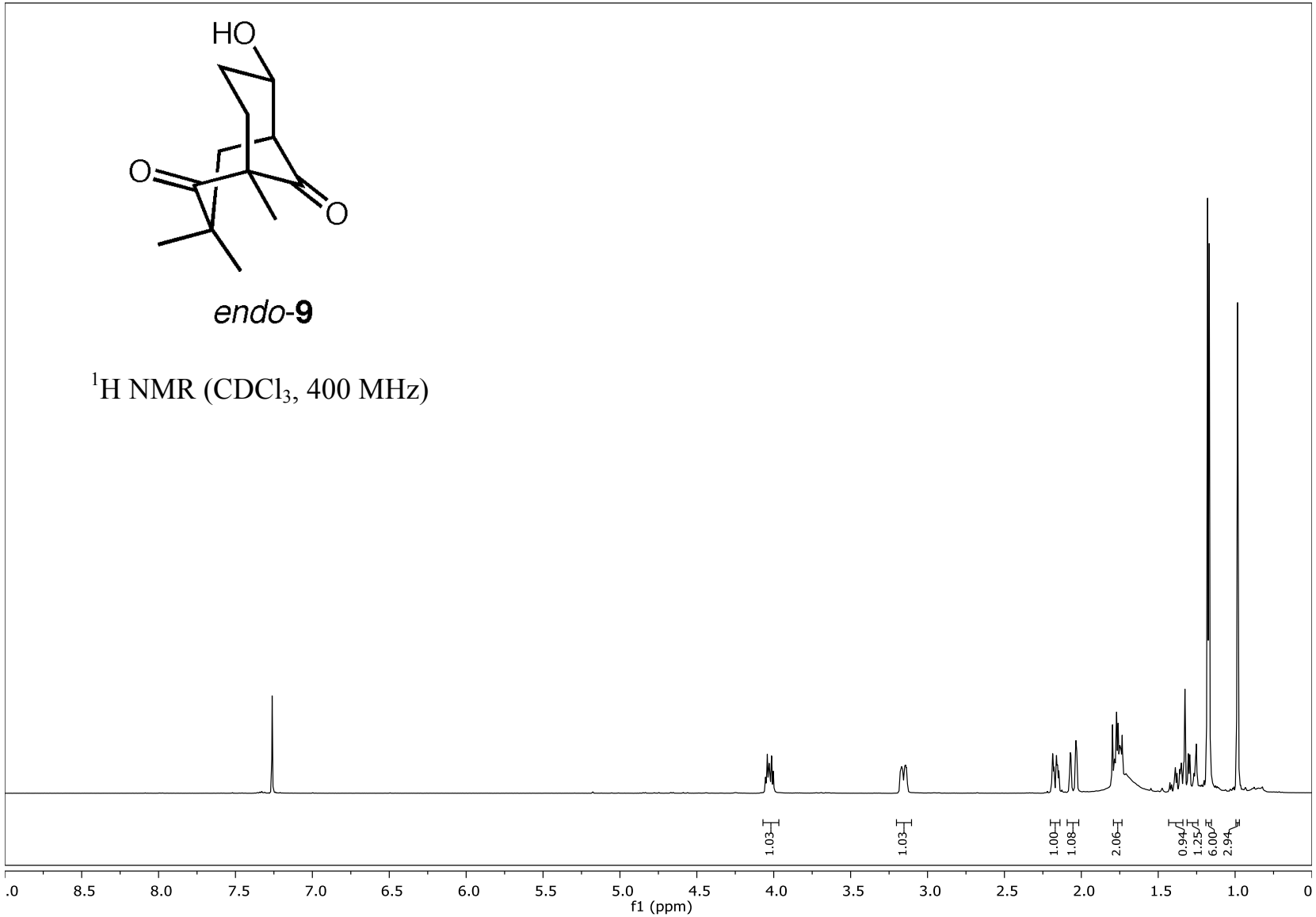


***exo*-8**

^{1}H NMR ($CDCl_3$, 400 MHz)

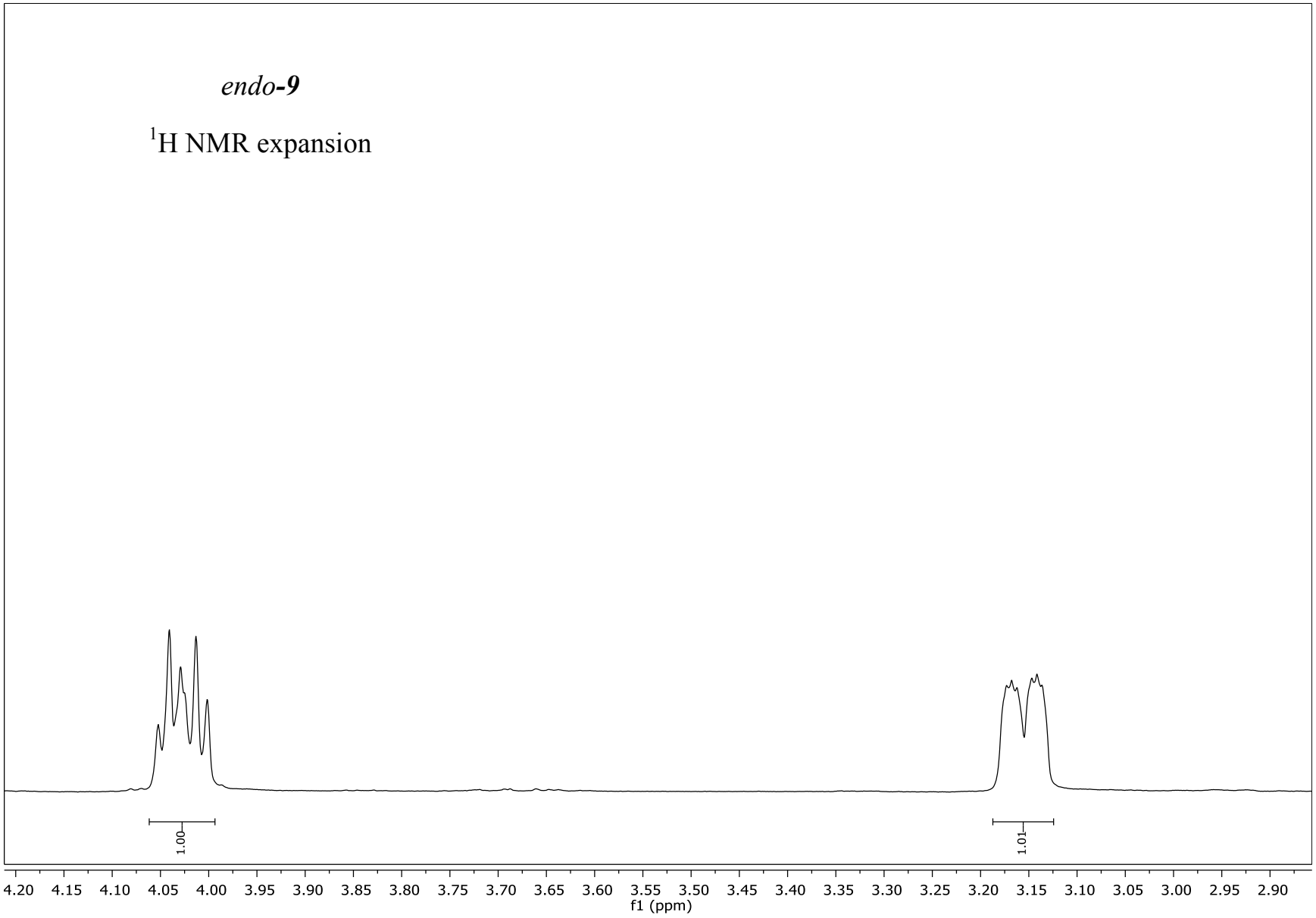



210.55
209.18
77.16
73.38
65.30
64.30
52.56
37.53
31.59
31.12
28.13
27.36
16.16
exo-8
13C NMR (CDCl3, 100 MHz)
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


HO
O
O
endo-9
1H NMR (CDCl3, 400 MHz)
1.03
1.03
1.00
1.08
2.06
0.94
1.25
6.00
2.94
.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
f1 (ppm)

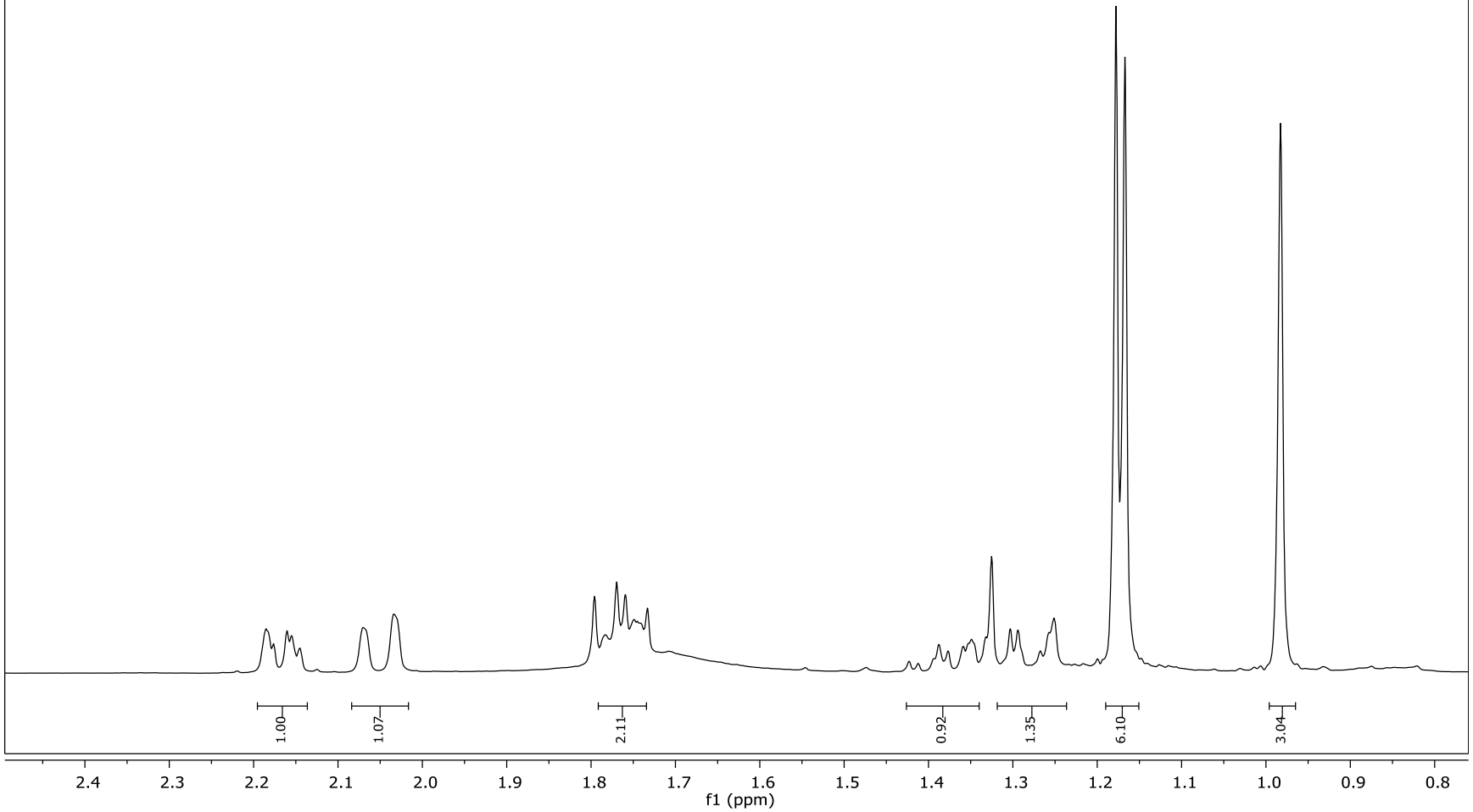
*endo-**9***

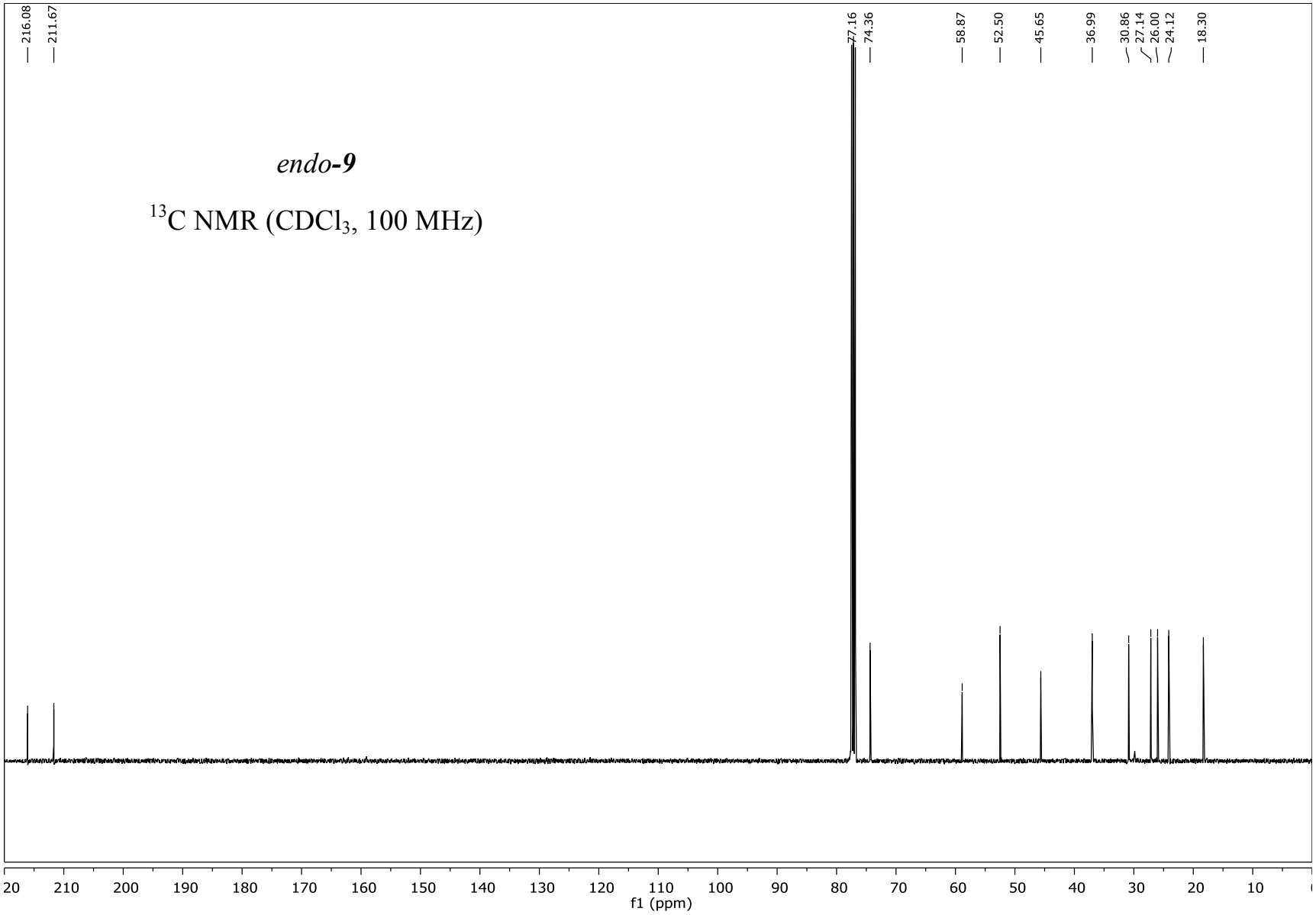
^{1}H NMR expansion

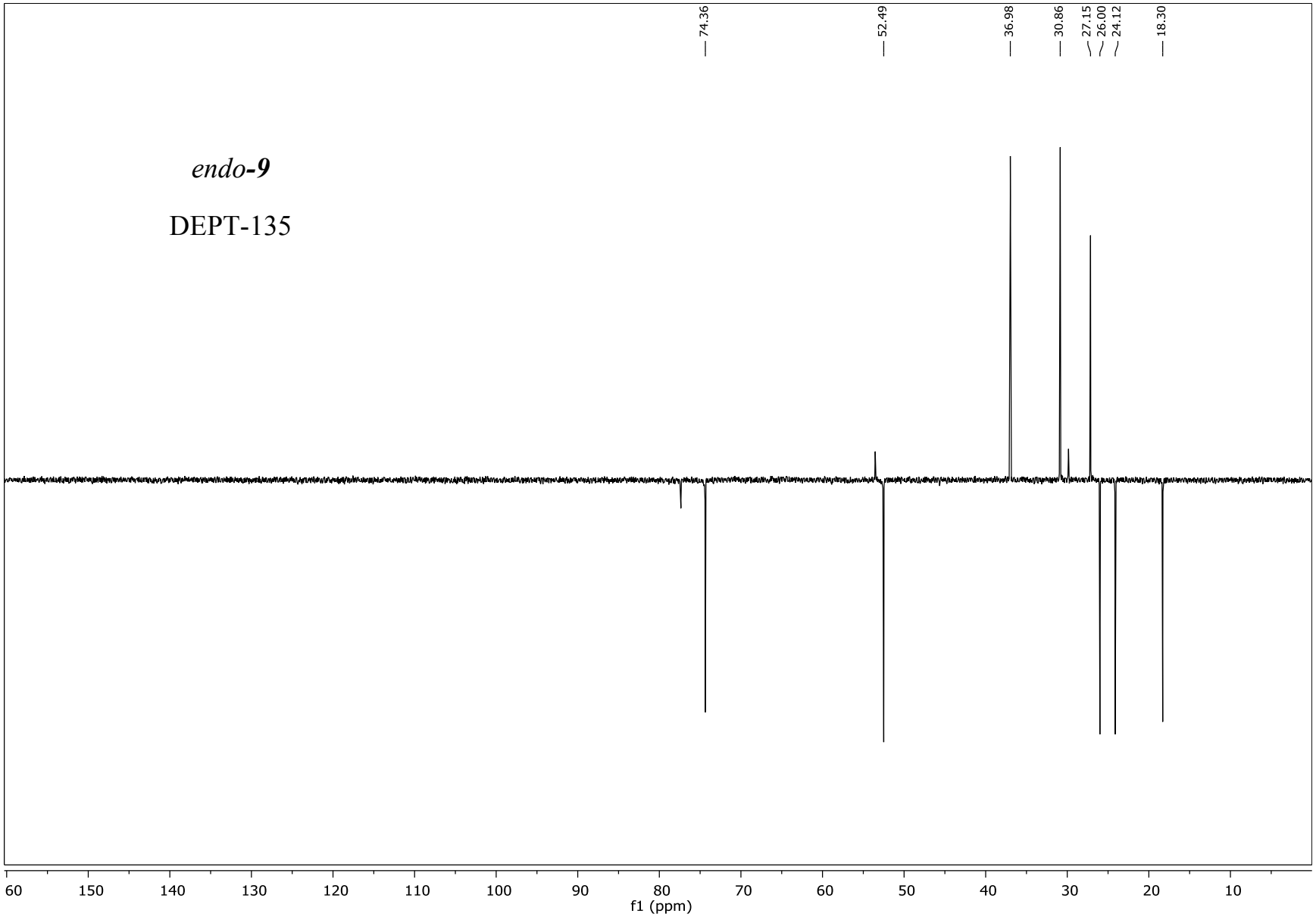


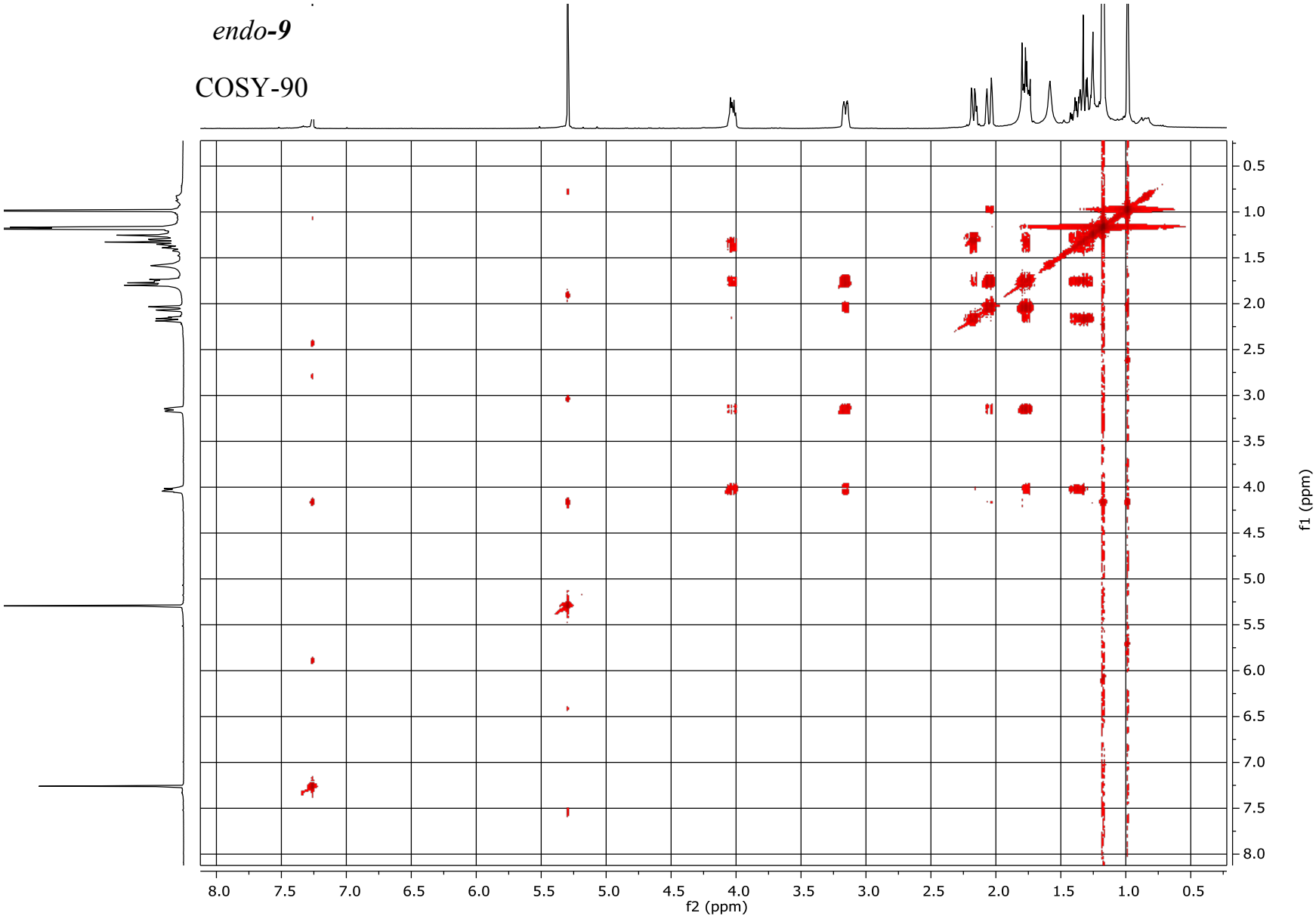
*endo-**9***

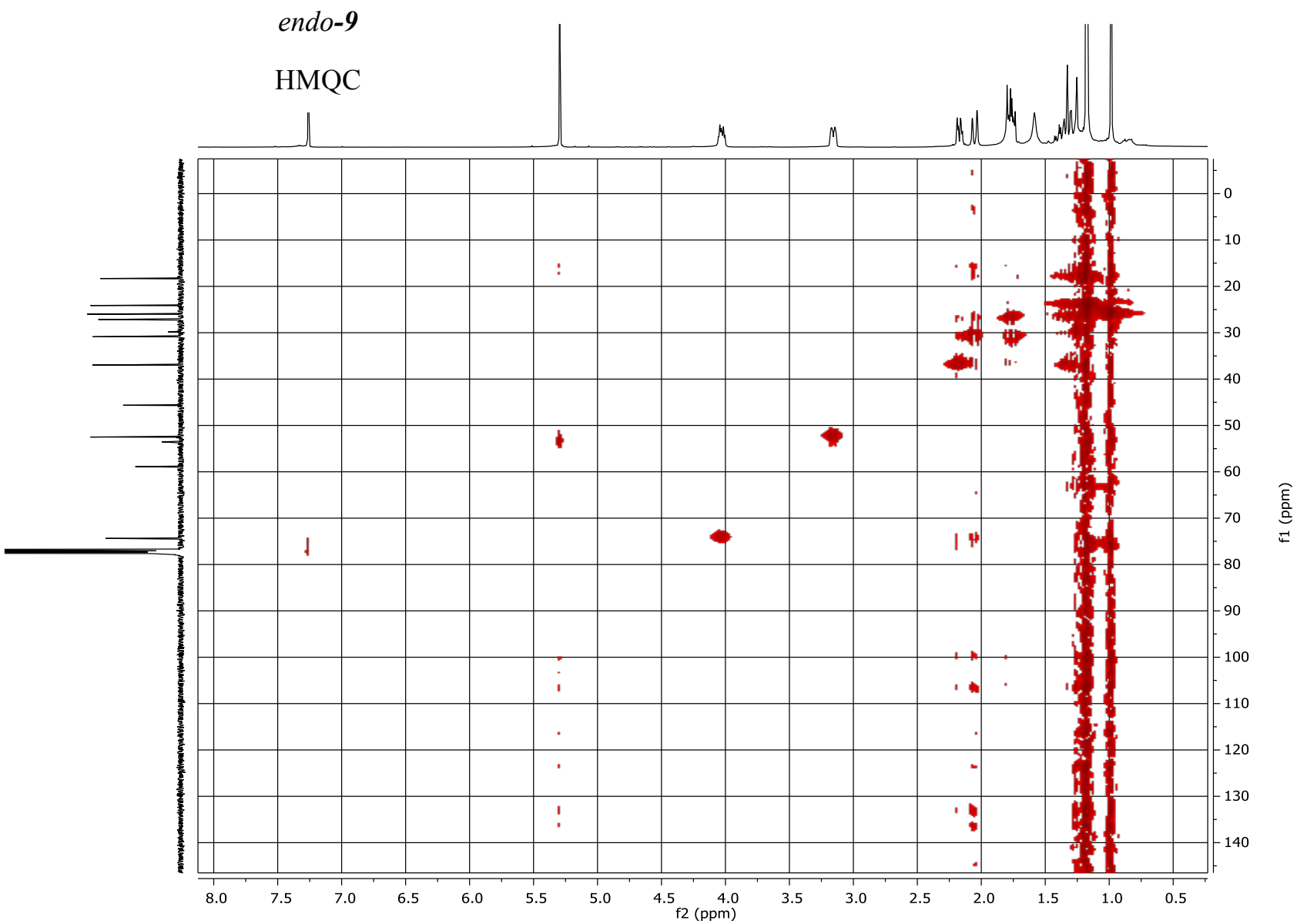
^{1}H NMR expansion

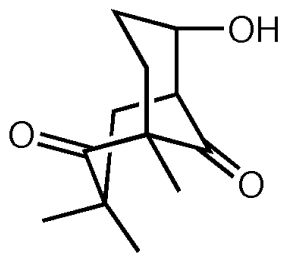



216.08
211.67
77.16
74.36
58.87
52.50
45.65
36.99
30.86
27.14
26.00
24.12
18.30
endo-9
13C NMR (CDCl3, 100 MHz)
f1 (ppm)


74.36
52.49
36.98
30.86
27.15
26.00
24.12
18.30
*endo-**9***
DEPT-135
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

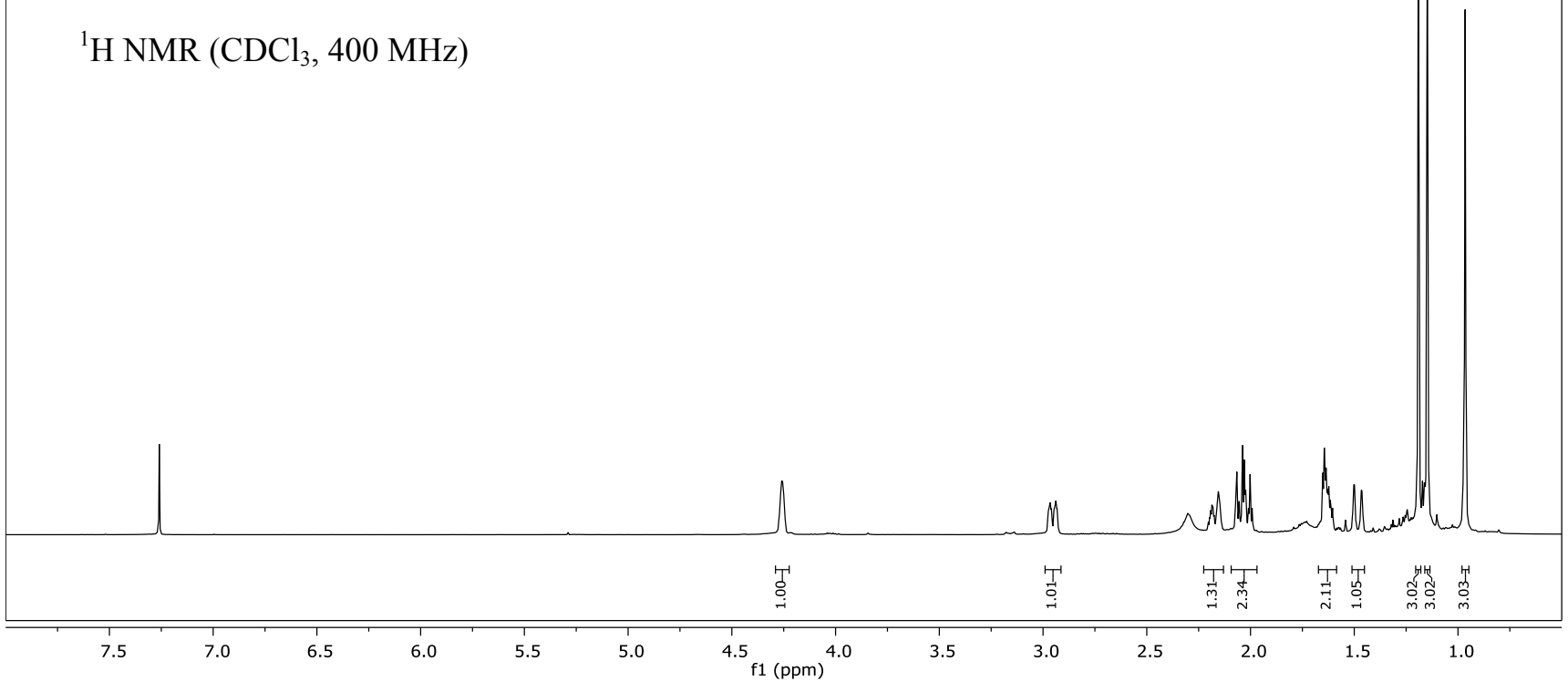

endo-9
COSY-90
f2 (ppm)
f1 (ppm)


endo-9
HMQC
f2 (ppm)
f1 (ppm)



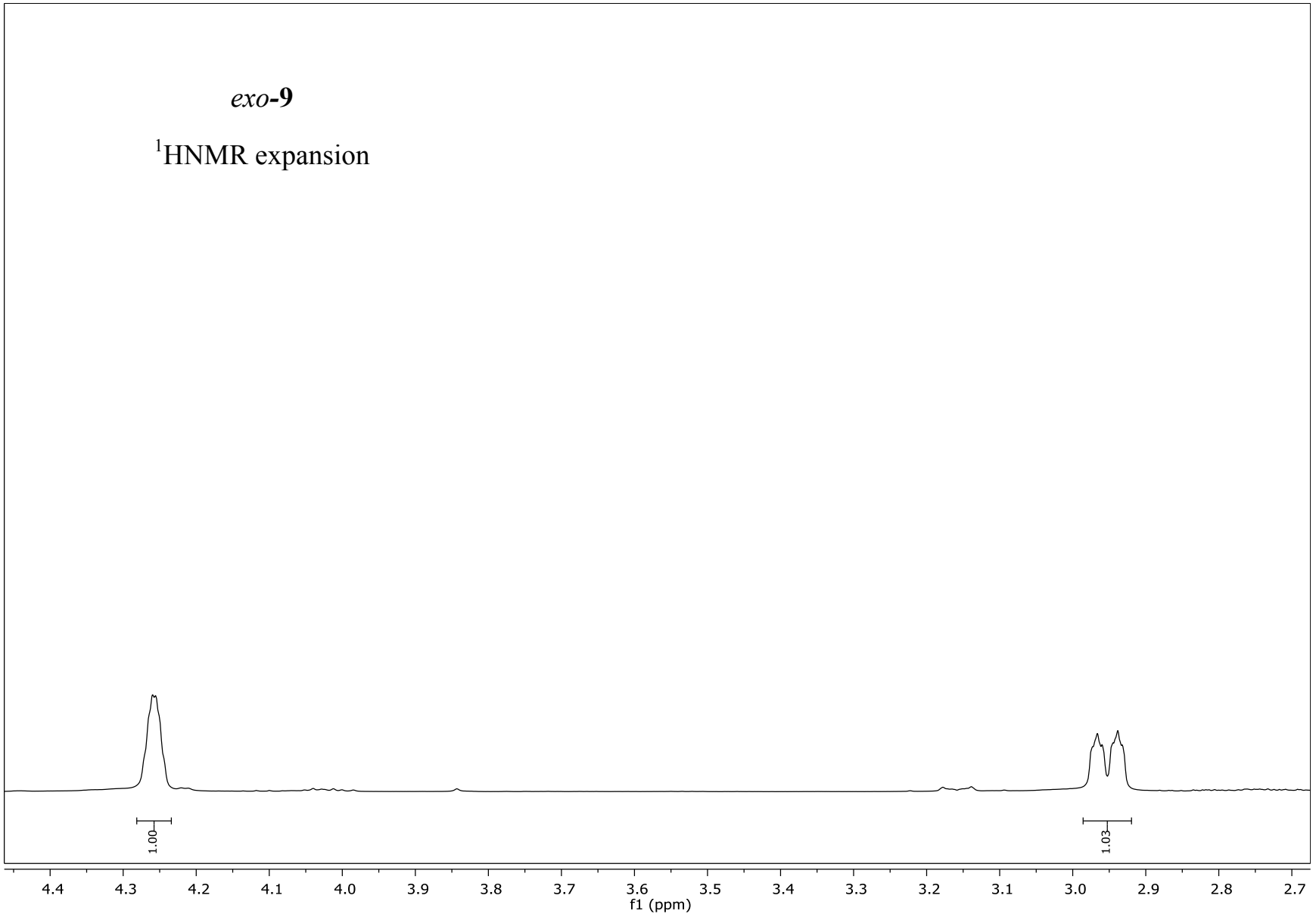
exo-**9**

^{1}H NMR ($CDCl_3$, 400 MHz)



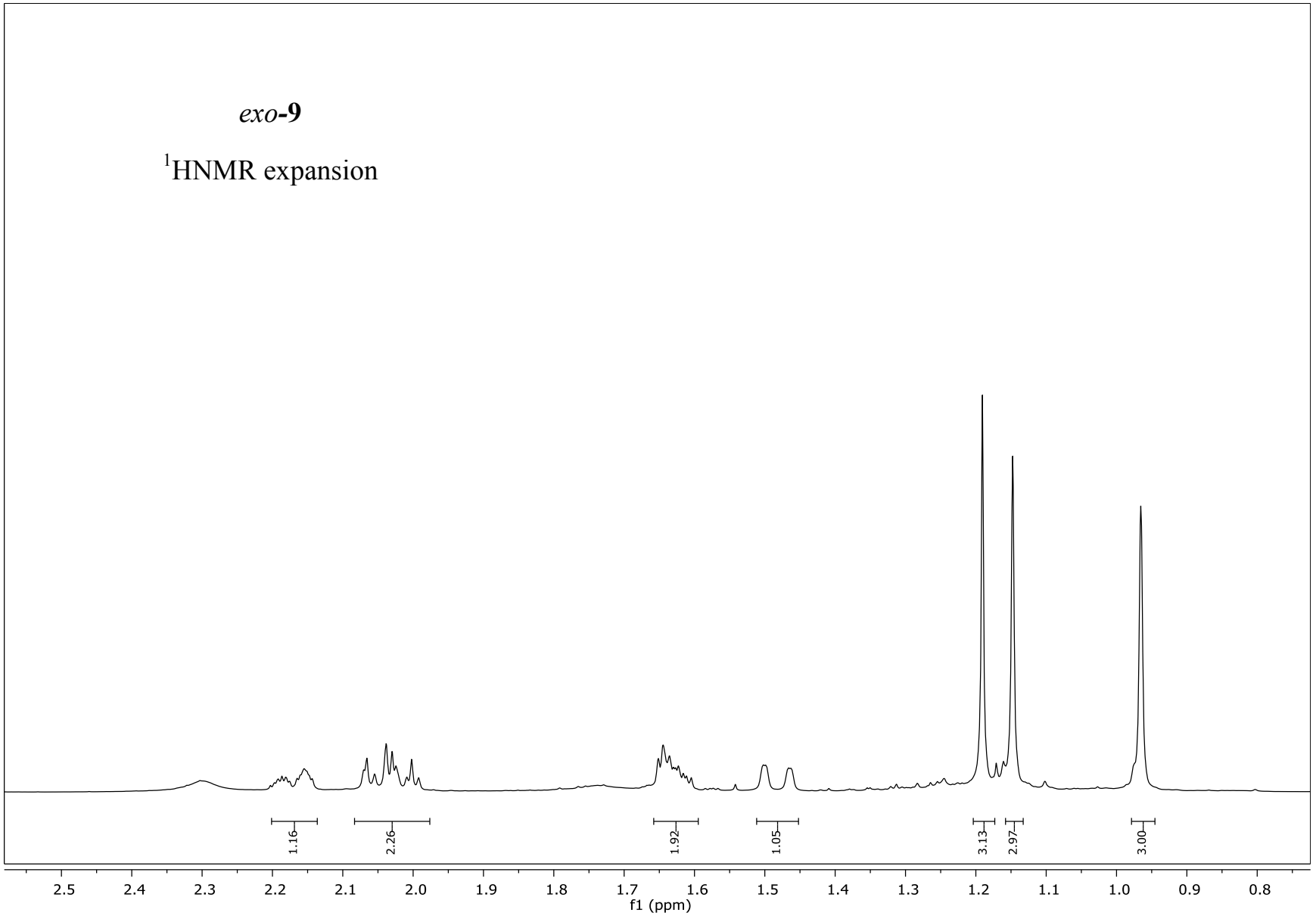
exo-**9**

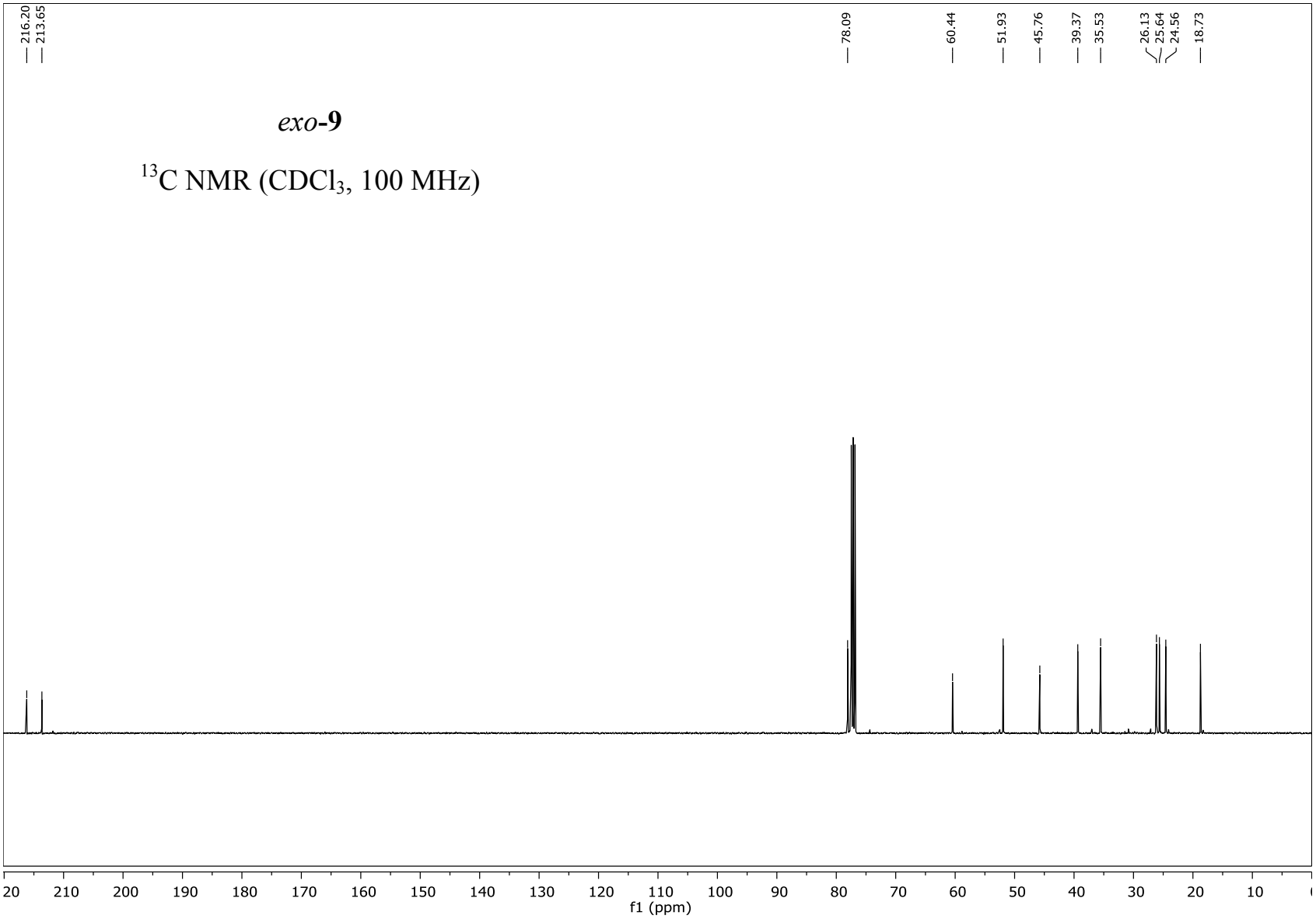
^{1}HNMR expansion

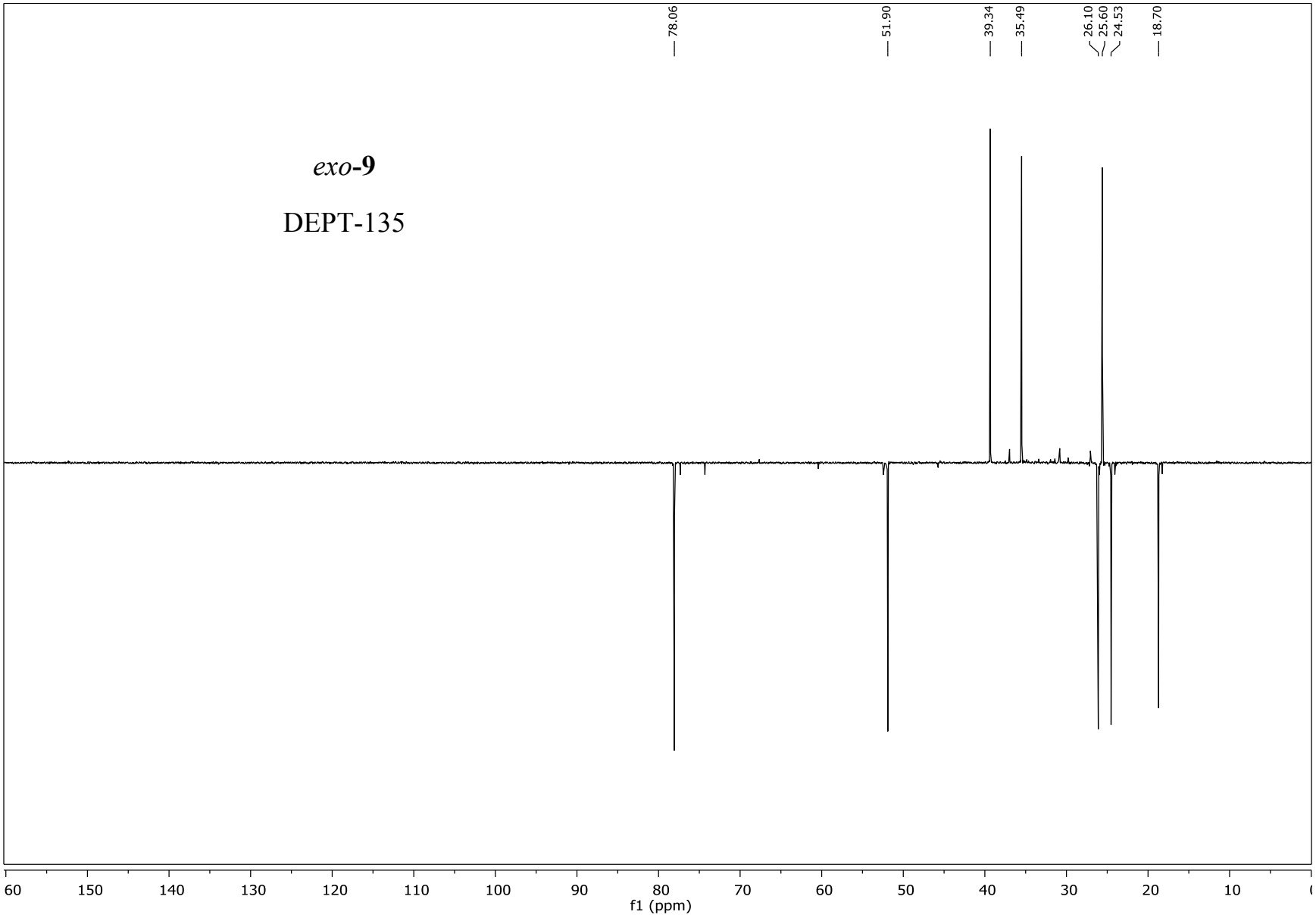


exo-**9**

^{1}HNMR expansion

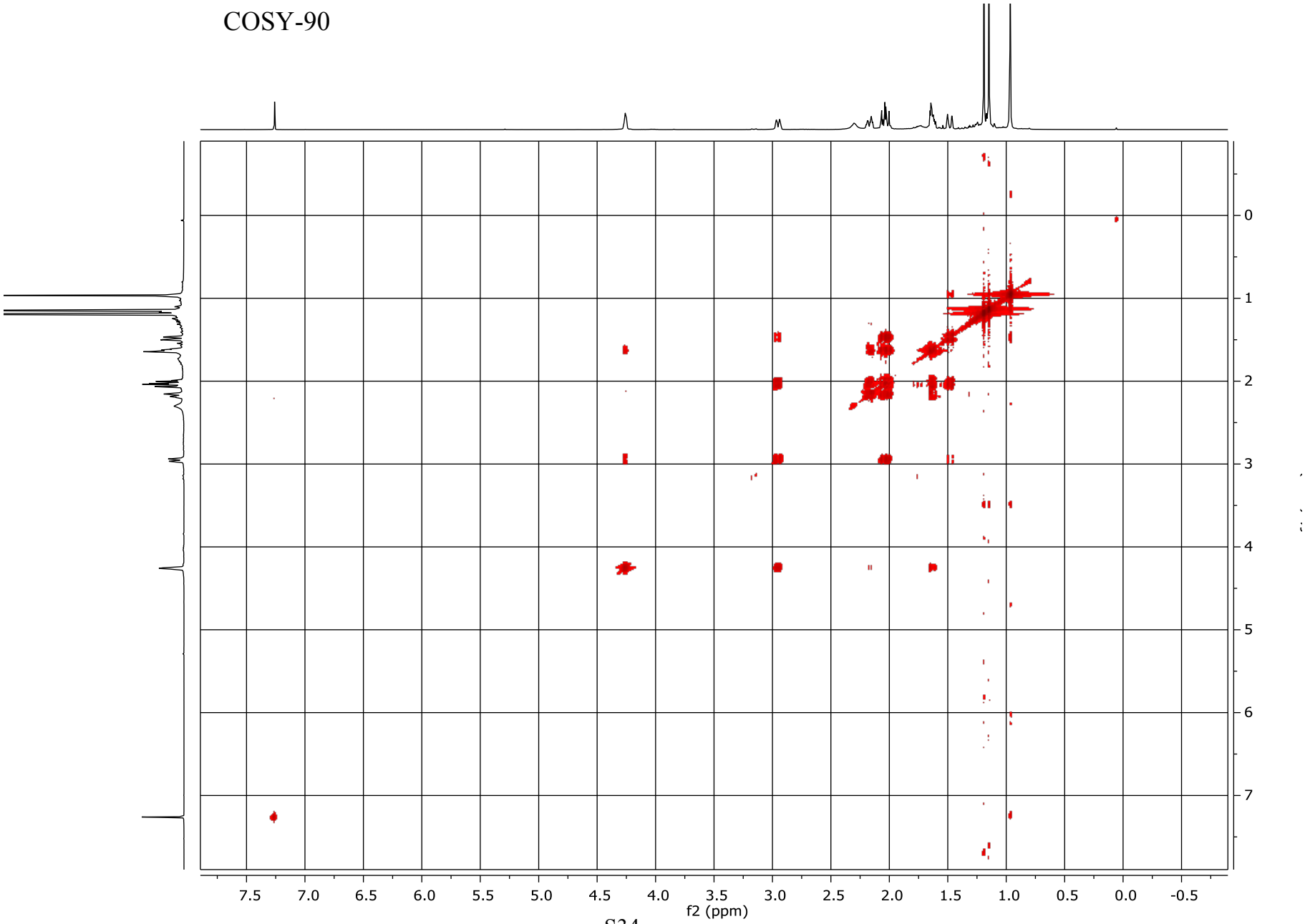


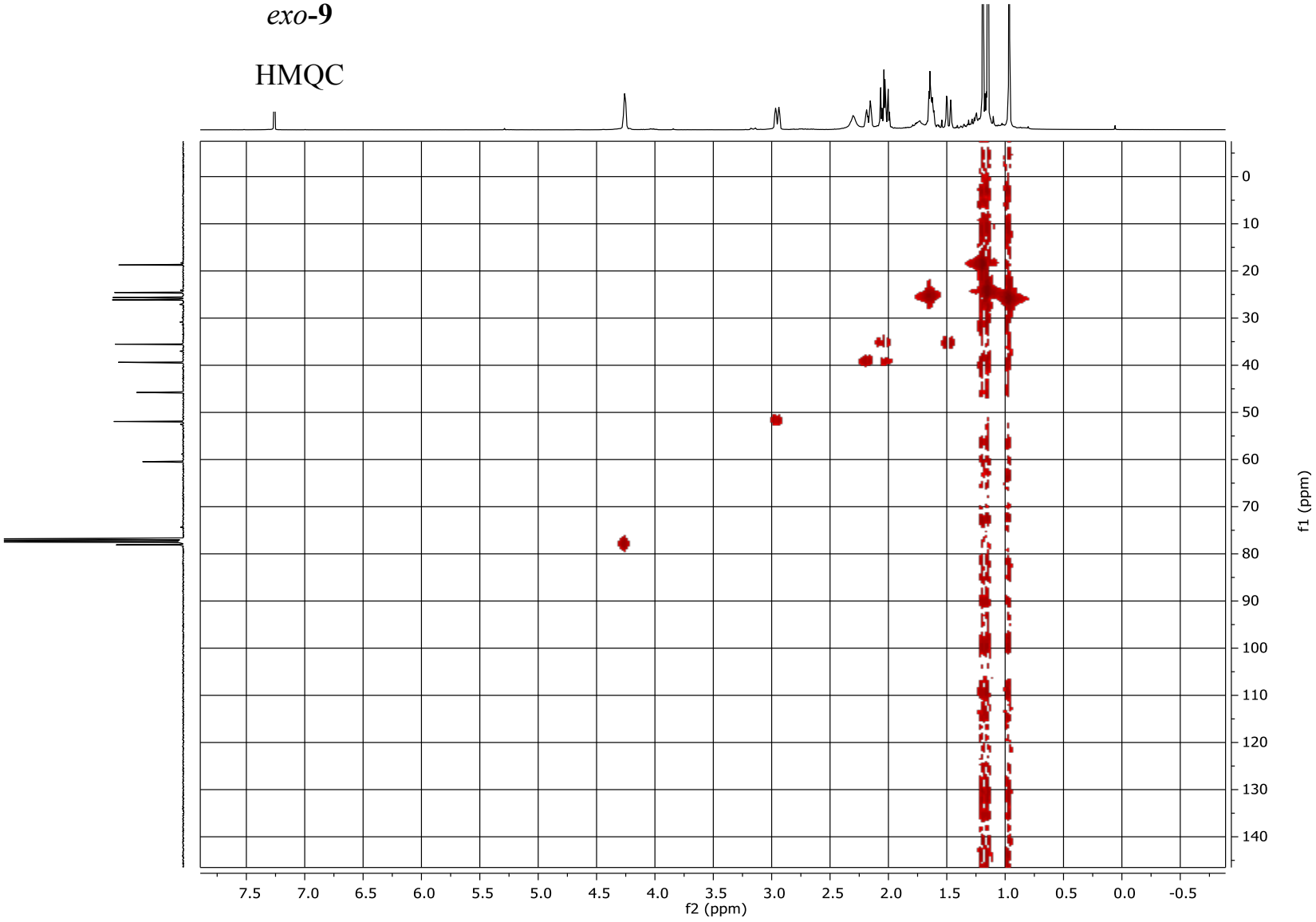

216.20
213.65
78.09
60.44
51.93
45.76
39.37
35.53
26.13
25.64
24.56
18.73
exo-9
13C NMR (CDCl3, 100 MHz)
f1 (ppm)

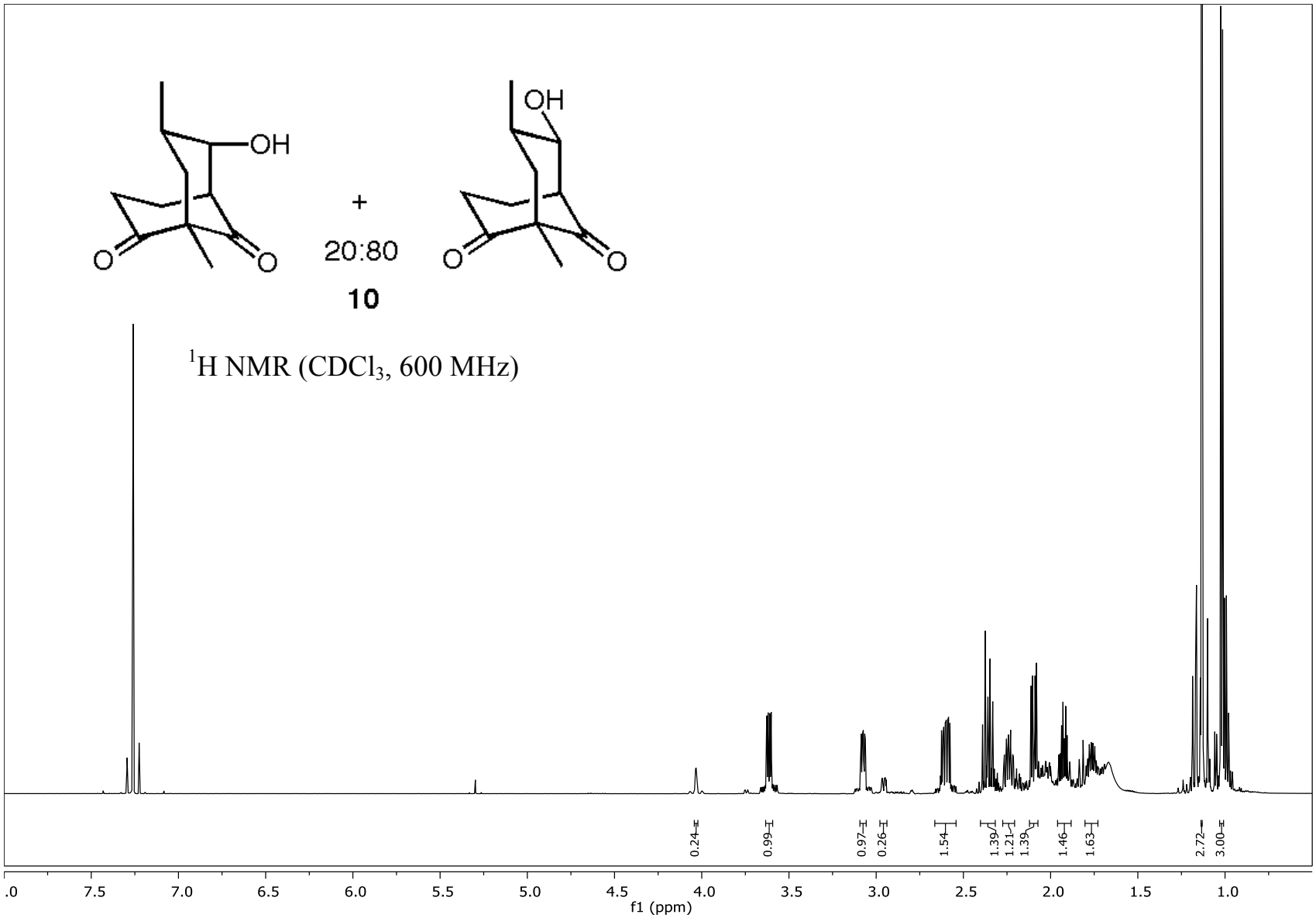

78.06
51.90
39.34
35.49
26.10
25.60
24.53
18.70
exo-**9**
DEPT-135
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

exo-**9**

COSY-90

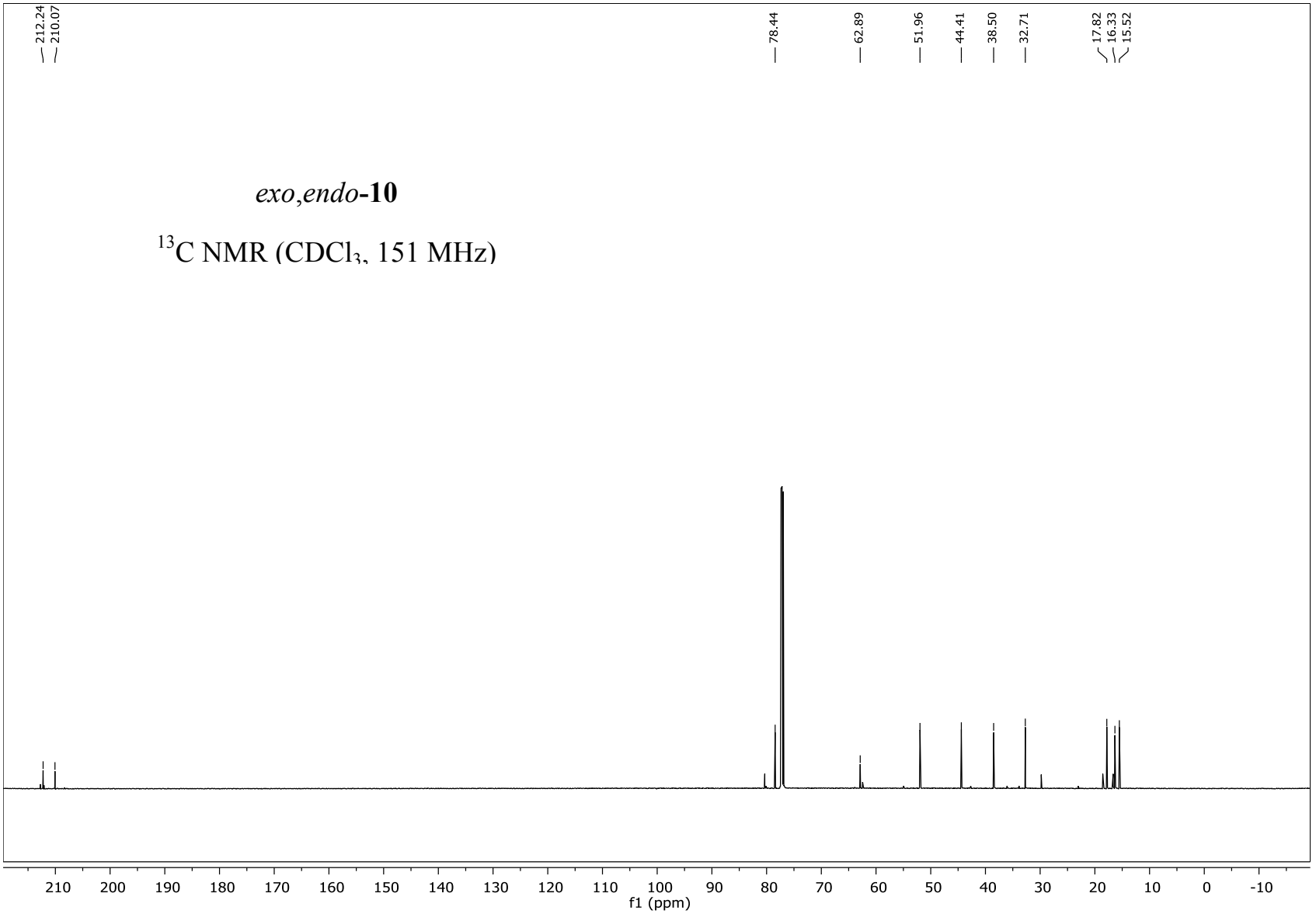


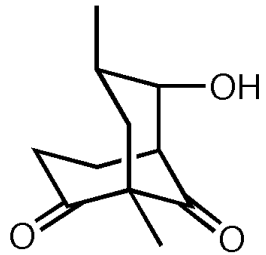

exo-**9**
HMQC
f2 (ppm)
f1 (ppm)


OH
+
20:80
OH
O
O
O
O
10
^{1}H NMR ($CDCl_3$, 600 MHz)
0.24
0.99
0.97
0.26
1.54
1.39
1.21
1.39
1.46
1.63
2.72
3.00
.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)

exo,endo-**10**

^{13}C NMR ($CDCl_3$, 151 MHz)



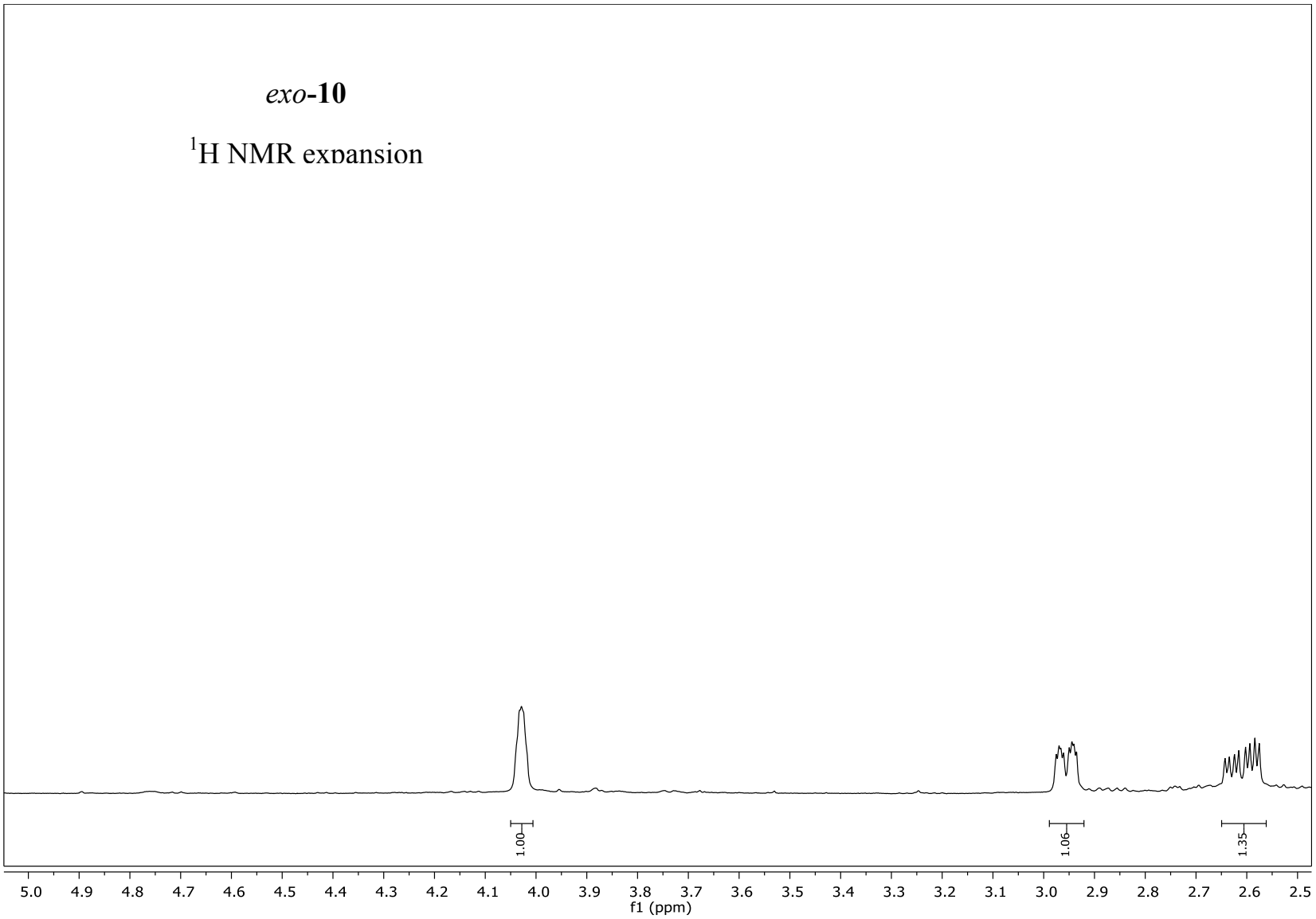


exo-**10**

^{1}H NMR ($CDCl_3$, 400 MHz)

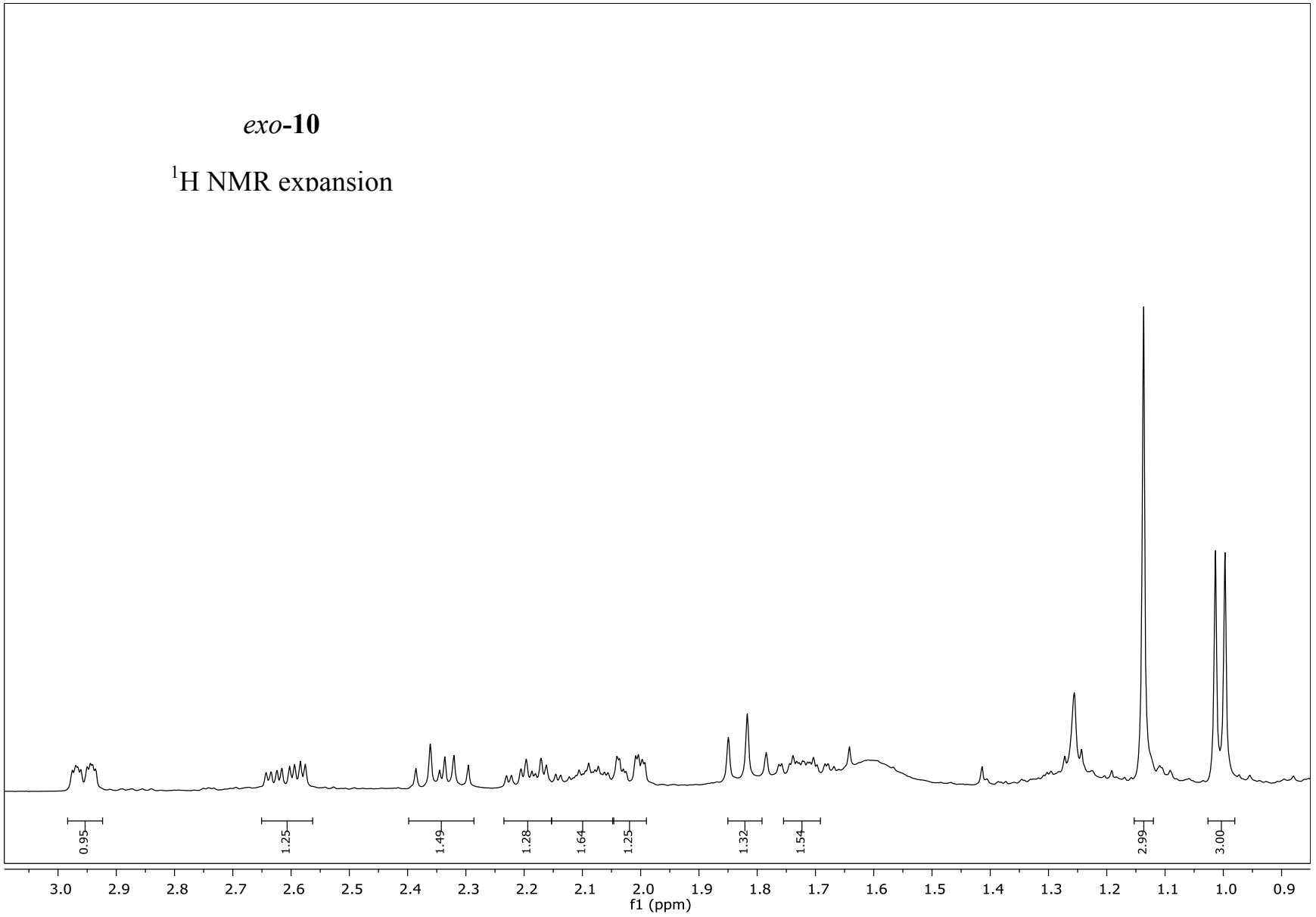
exo-**10**

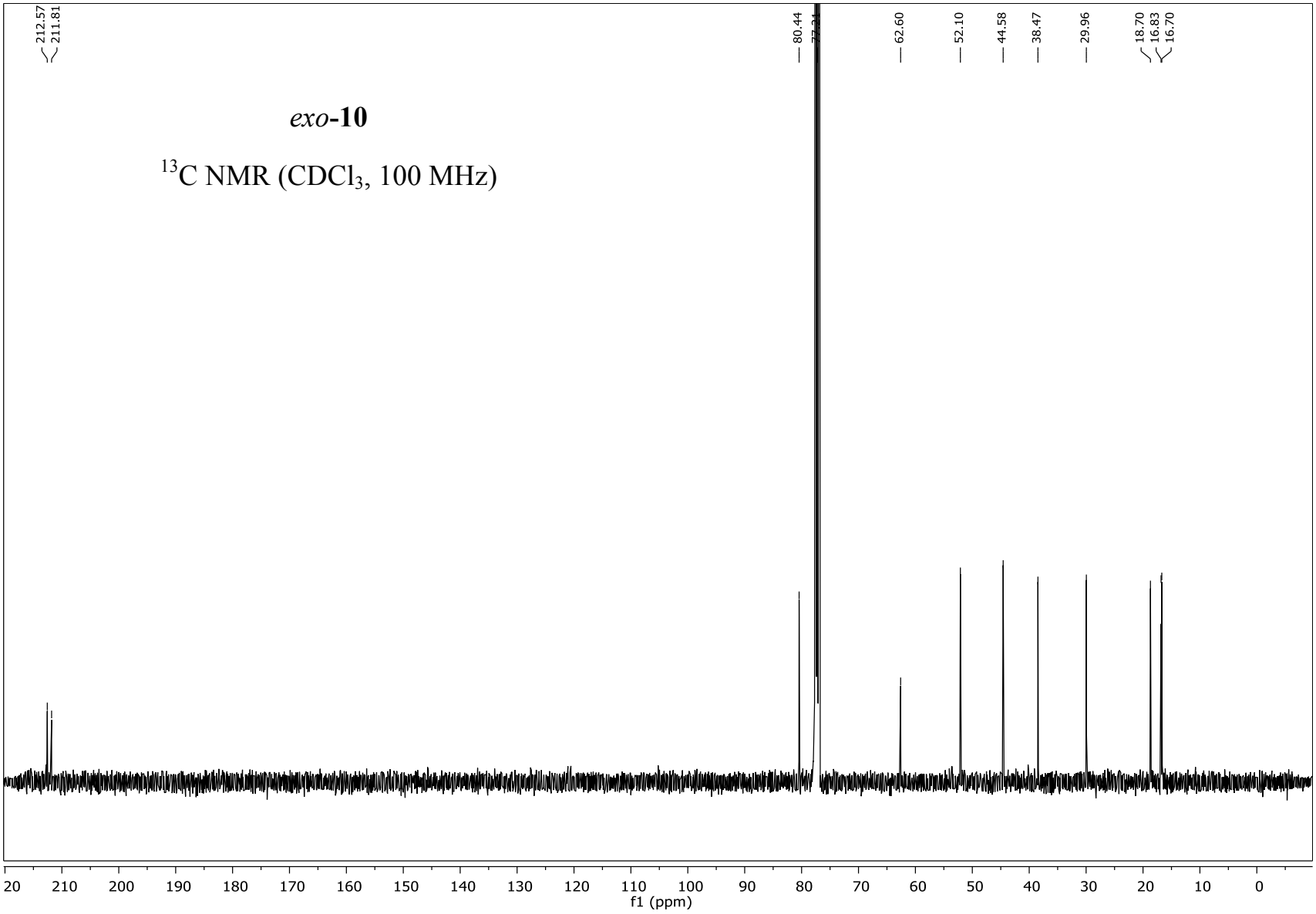
^{1}H NMR expansion

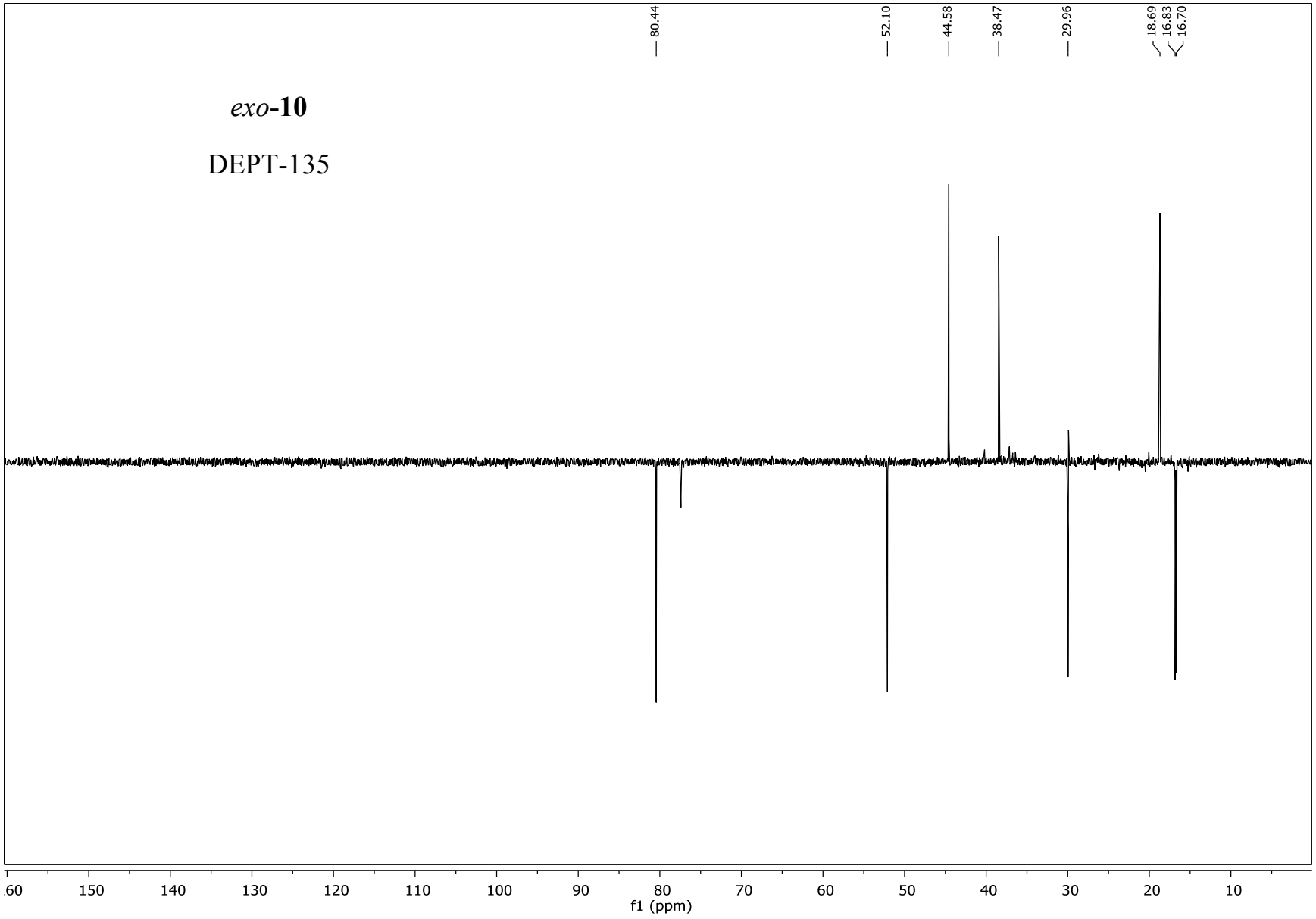


exo-**10**

^{1}H NMR expansion

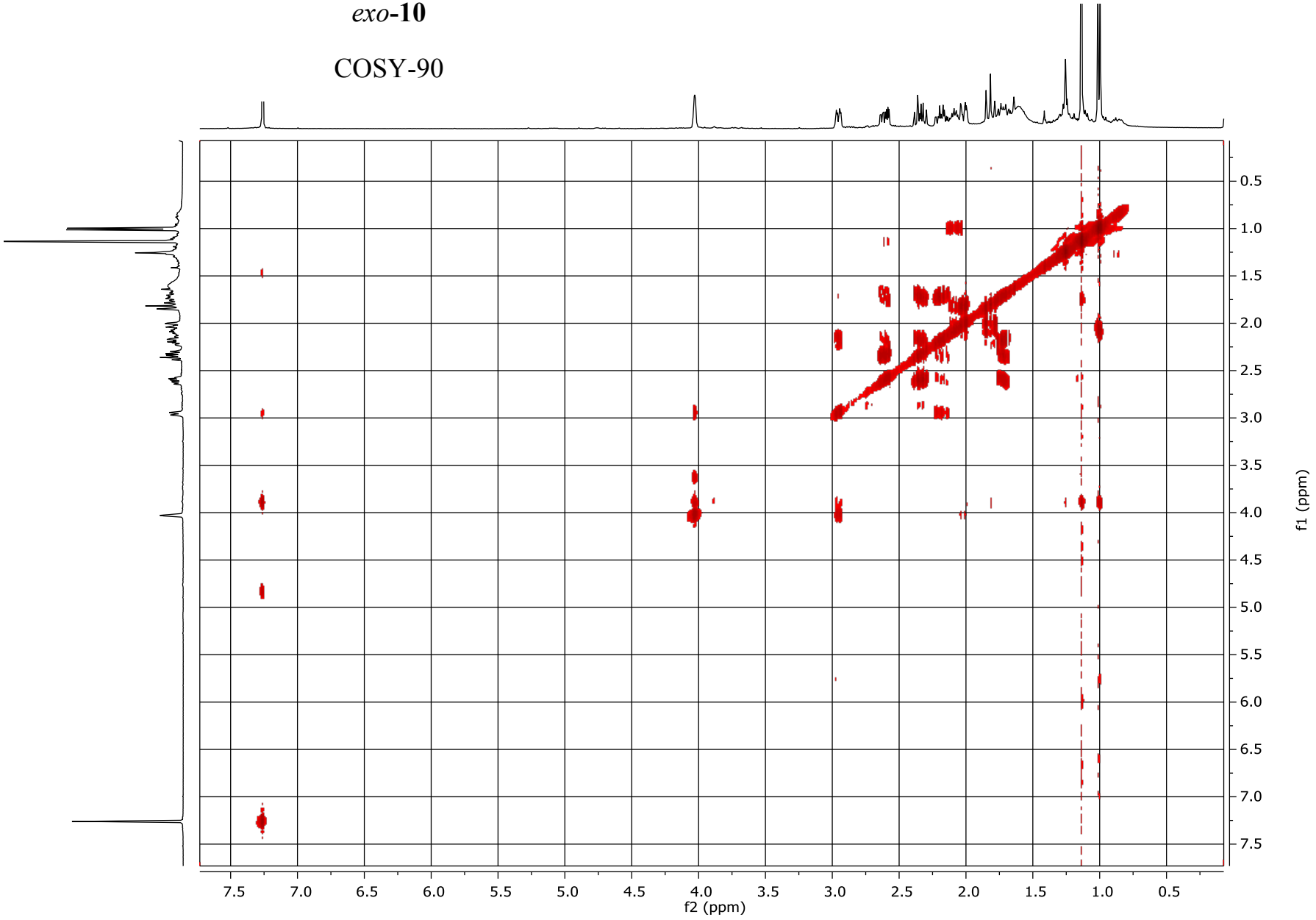



212.57
211.81
80.44
77.31
62.60
52.10
44.58
38.47
29.96
18.70
16.83
16.70
exo-**10**
^{13}C NMR ($CDCl_3$, 100 MHz)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


80.44
52.10
44.58
38.47
29.96
18.69
16.83
16.70
exo-10
DEPT-135
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

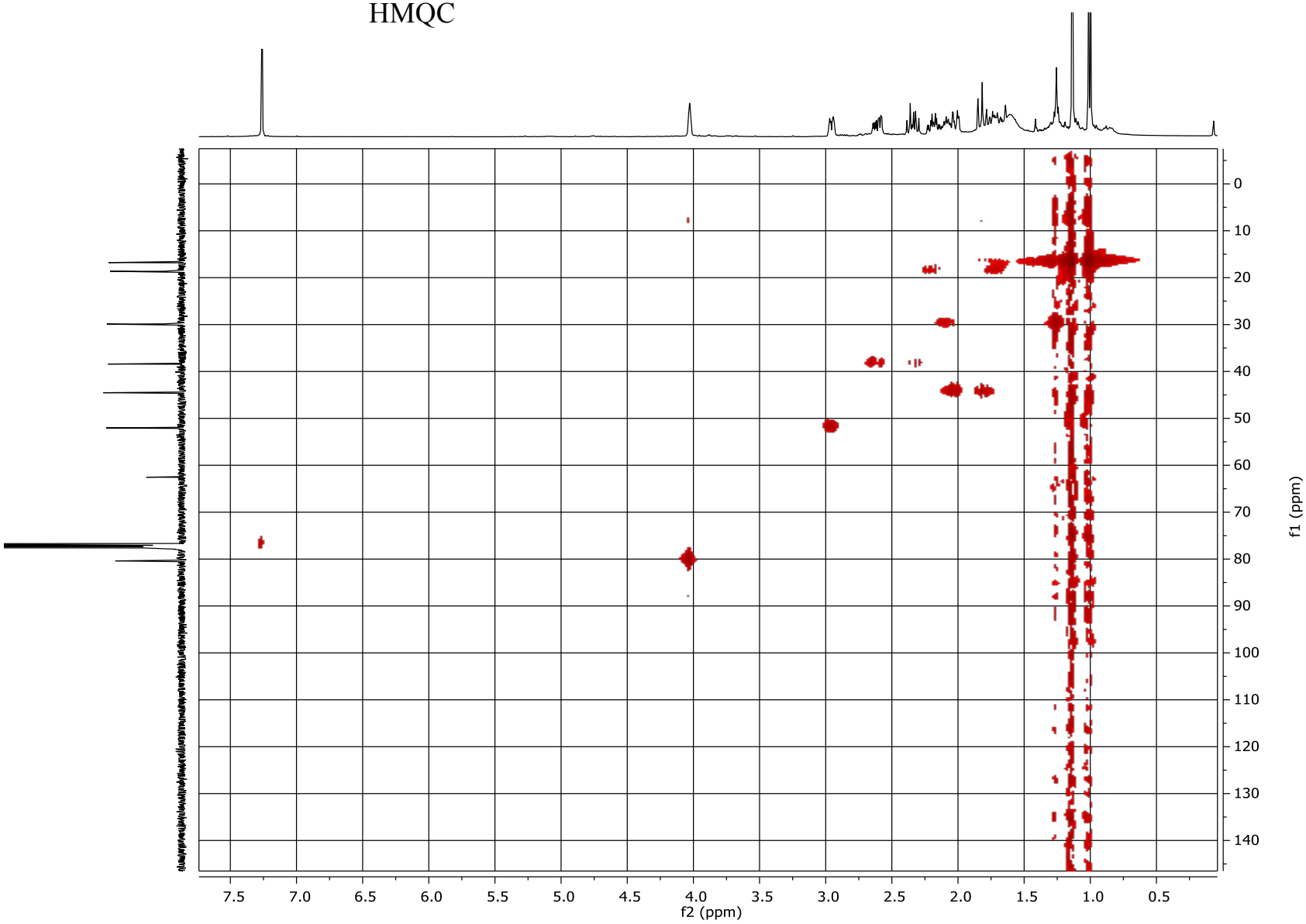
exo-**10**

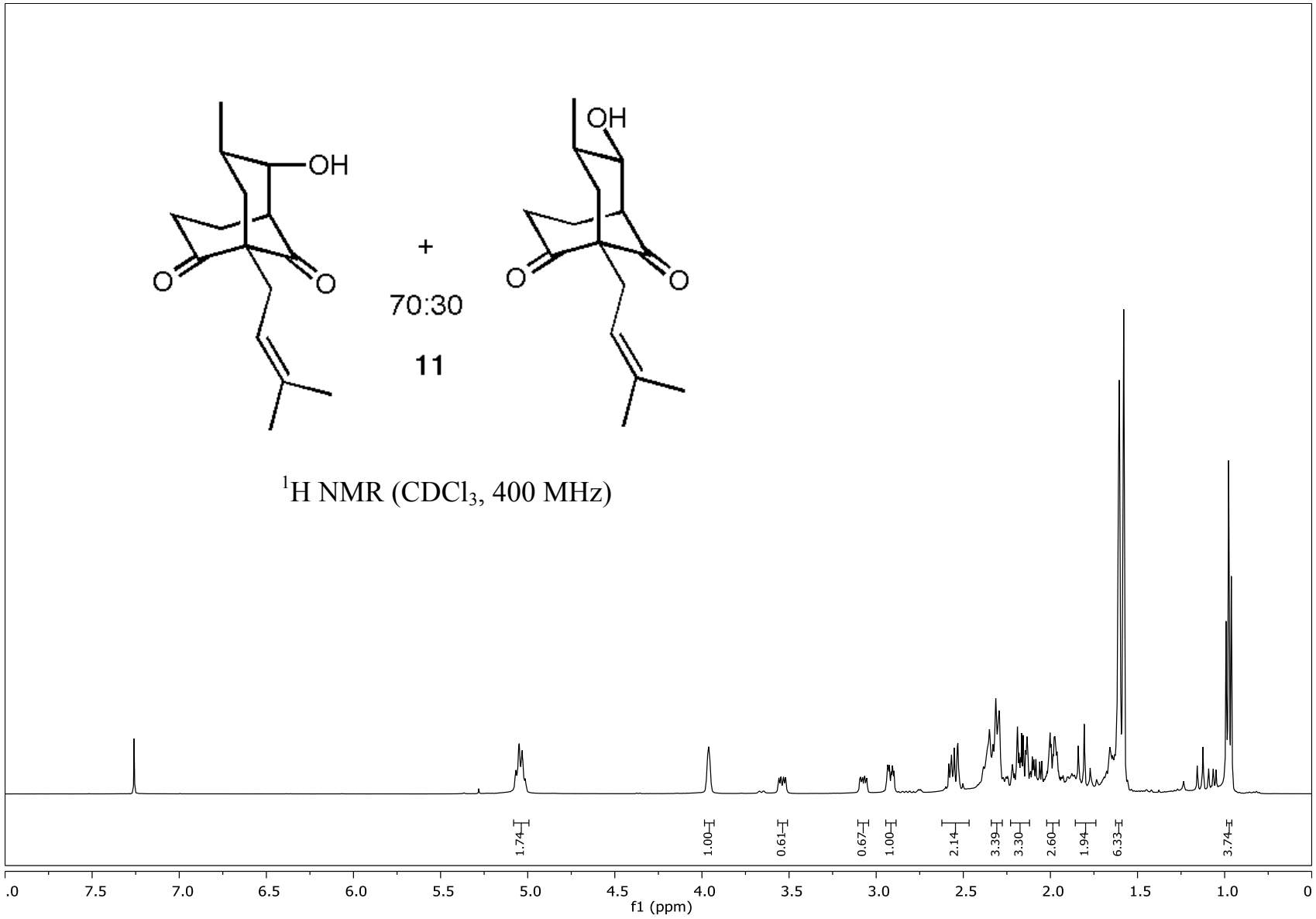
COSY-90



exo-**10**

HMQC

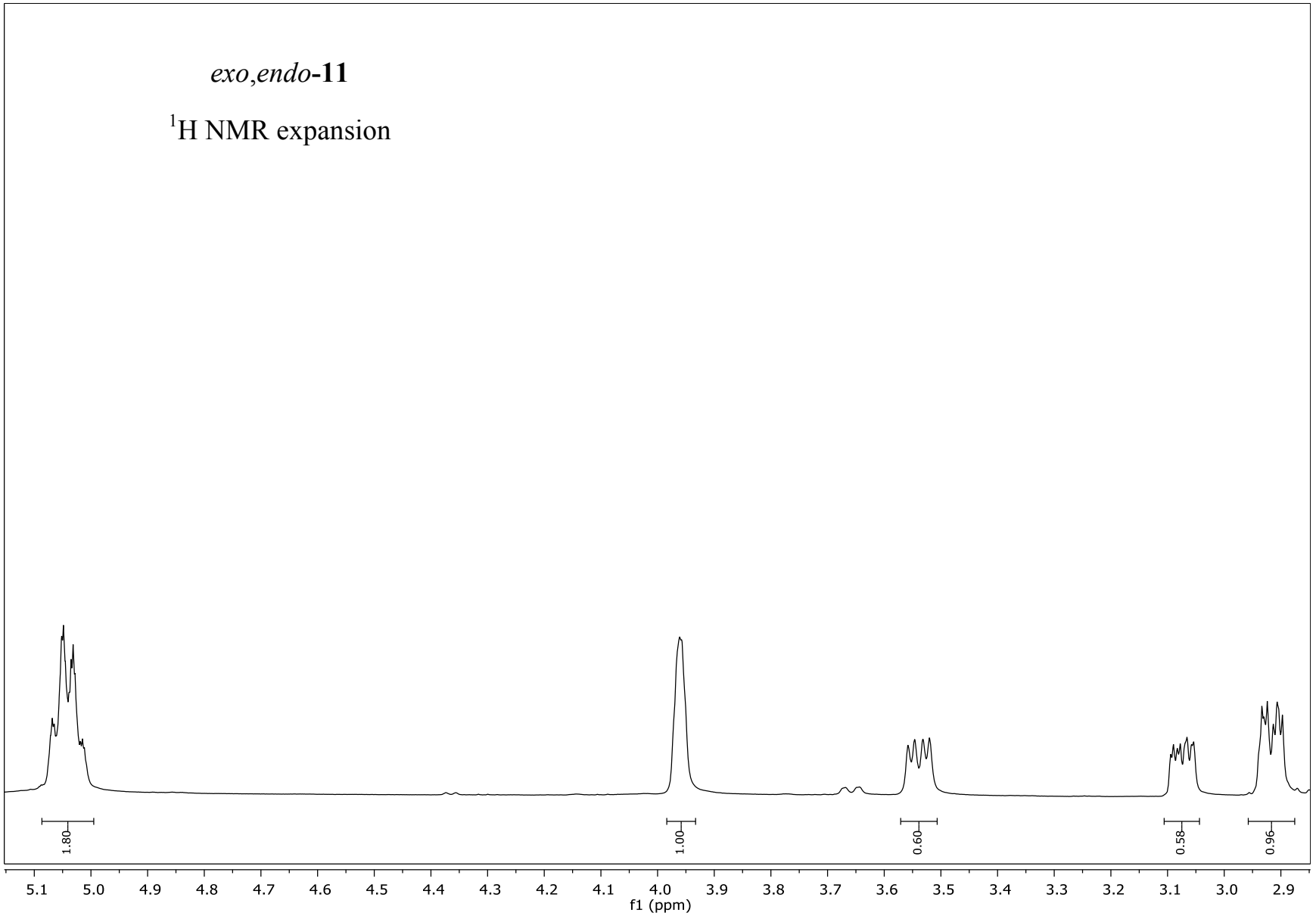

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)



^{1}H NMR ($CDCl_3$, 400 MHz)

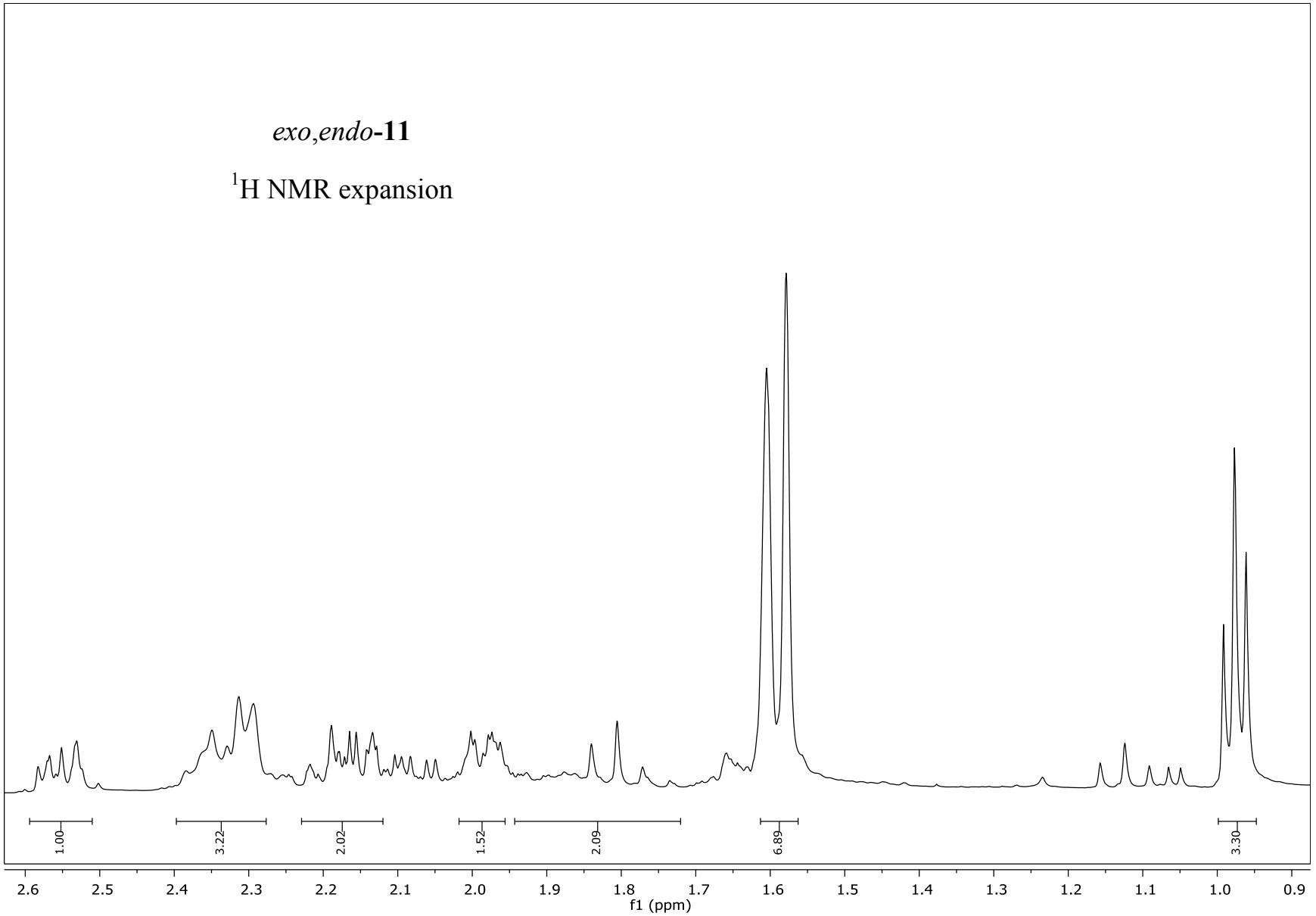
exo,endo-**11**

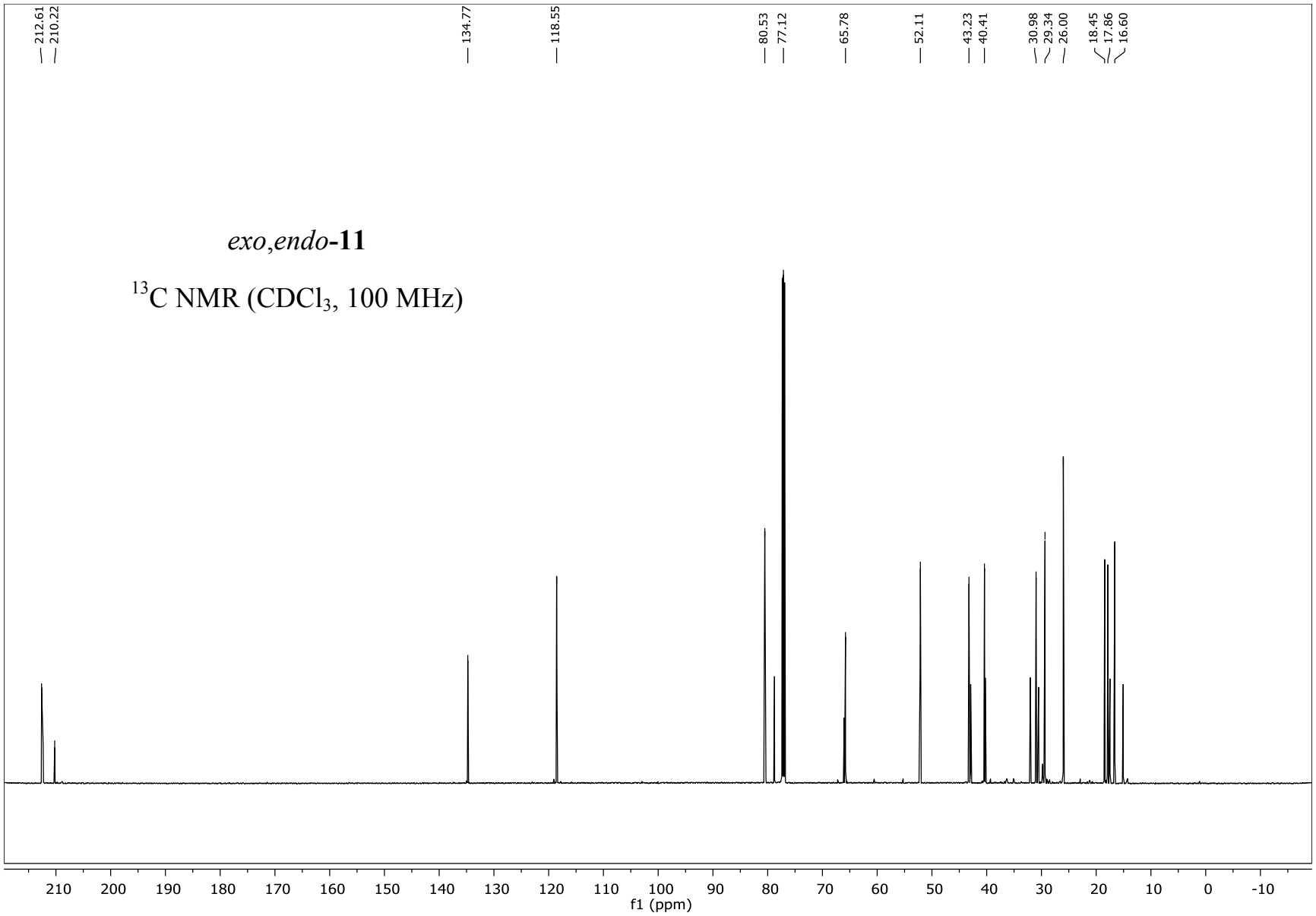
^{1}H NMR expansion

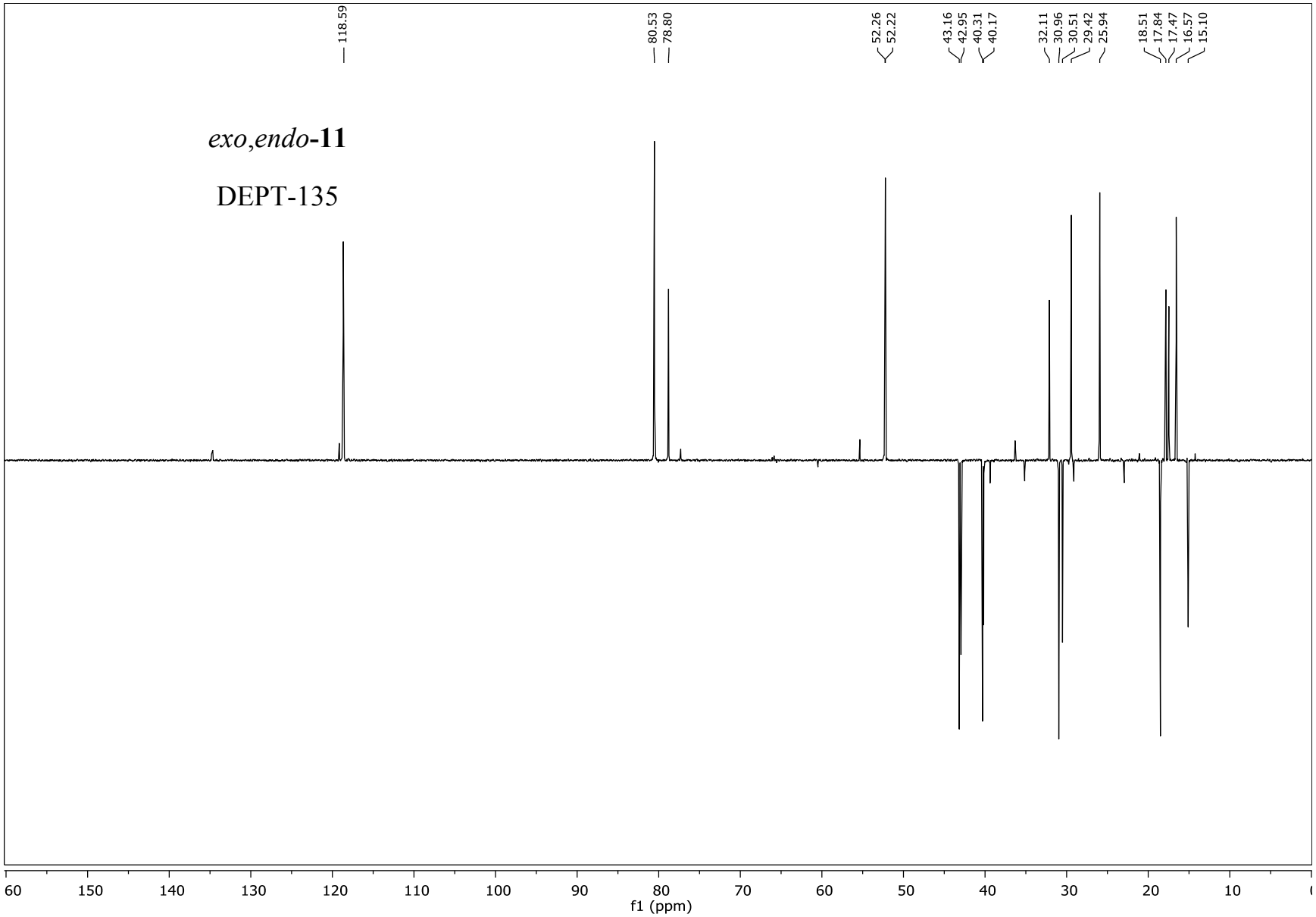


exo,endo-**11**

^{1}H NMR expansion

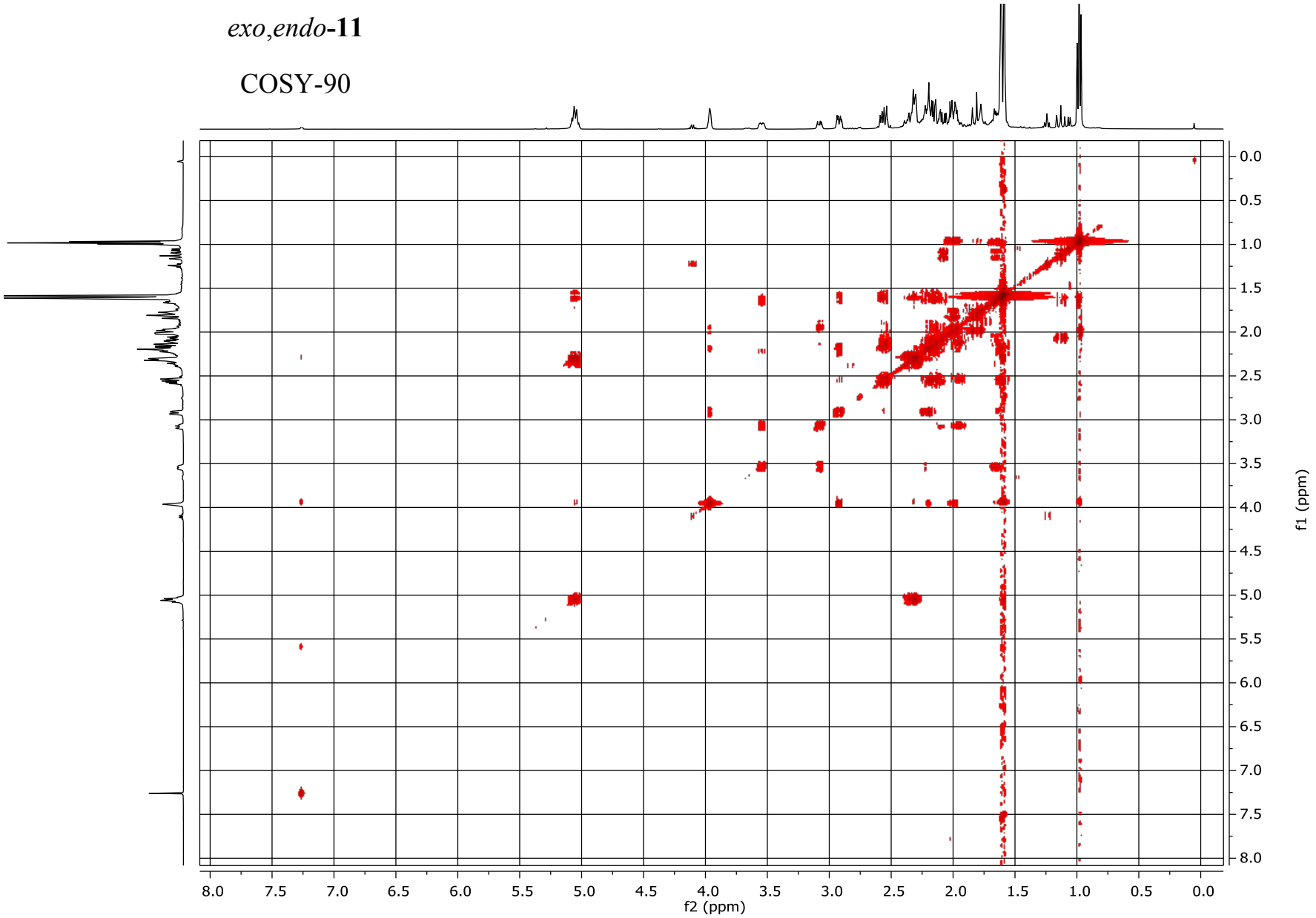



212.61
210.22
134.77
118.55
80.53
77.12
65.78
52.11
43.23
40.41
30.98
29.34
26.00
18.45
17.86
16.60
exo,*endo*-**11**
^{13}C NMR ($CDCl_3$, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


118.59
80.53
78.80
52.26
52.22
43.16
42.95
40.31
40.17
32.11
30.96
30.51
29.42
25.94
18.51
17.84
17.47
16.57
15.10
exo,endo-11
DEPT-135
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

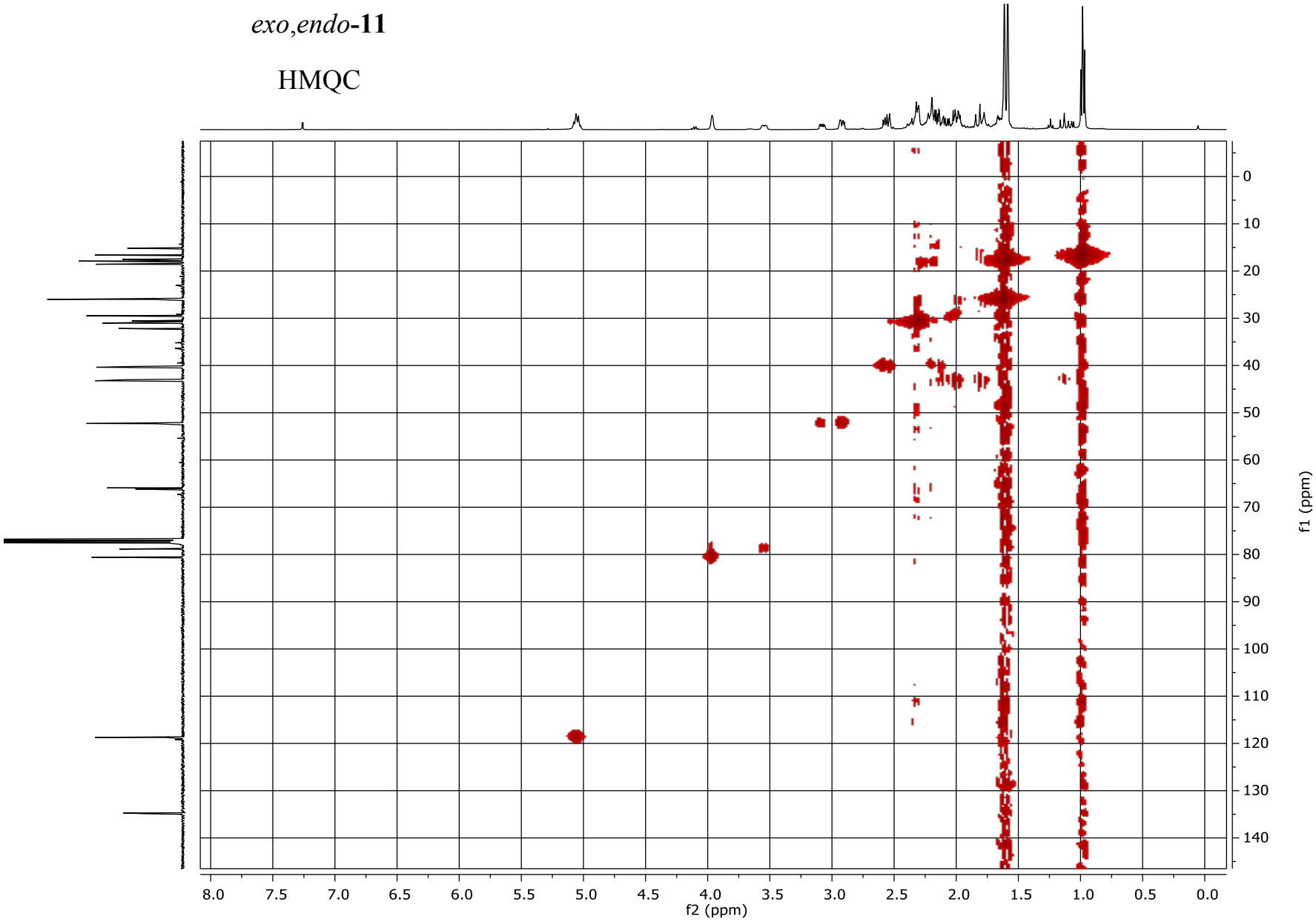
exo,endo-**11**

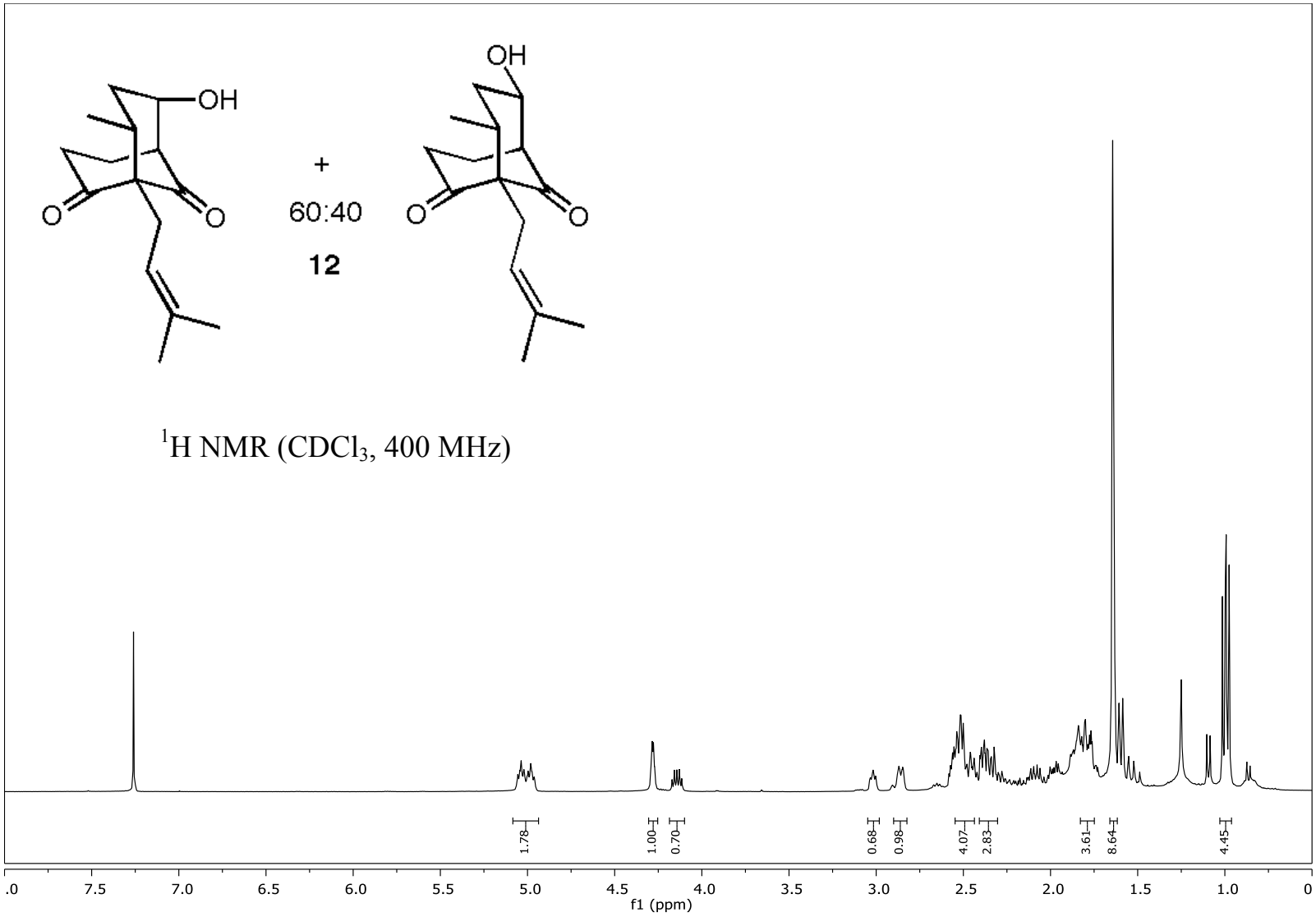
COSY-90

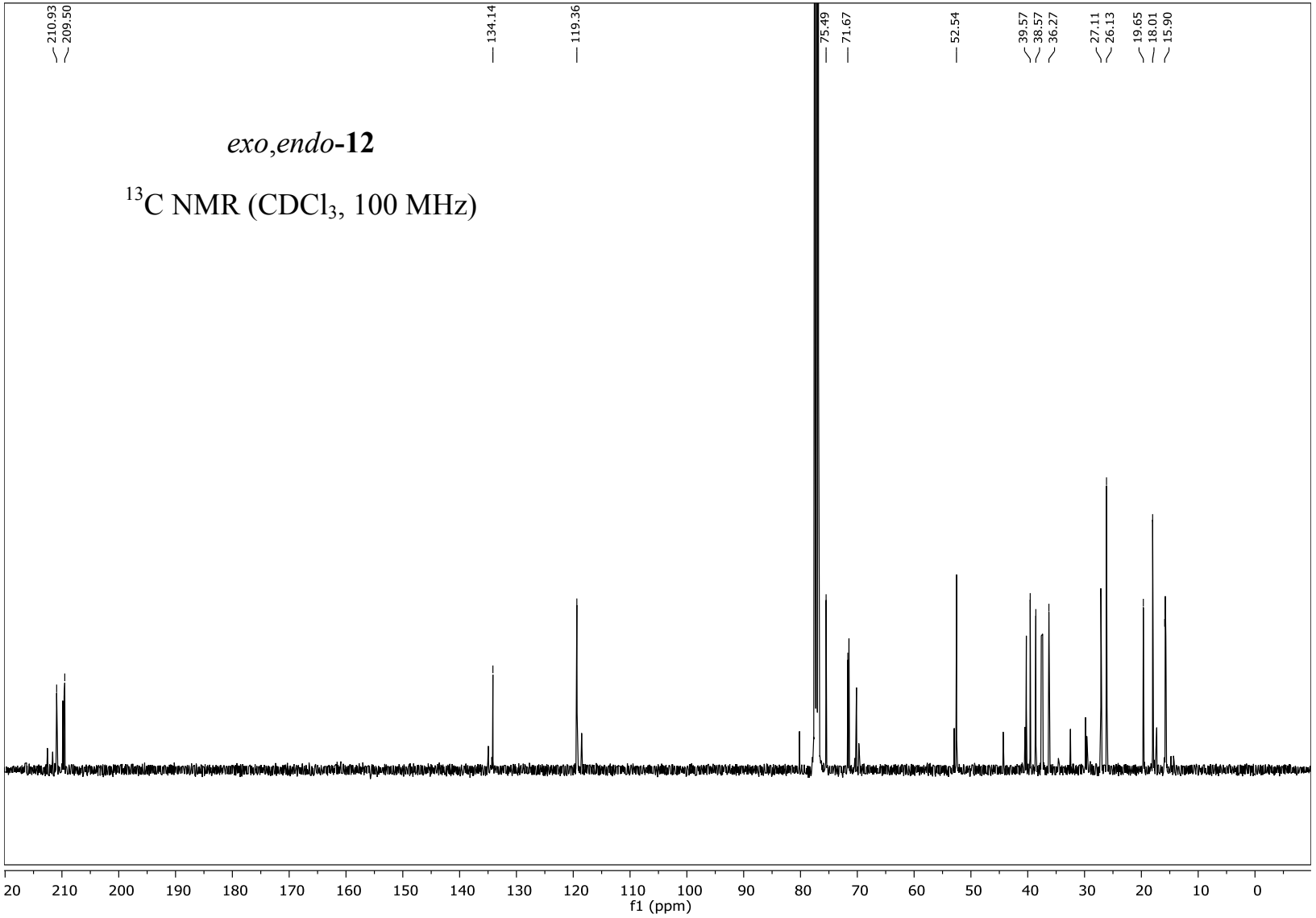


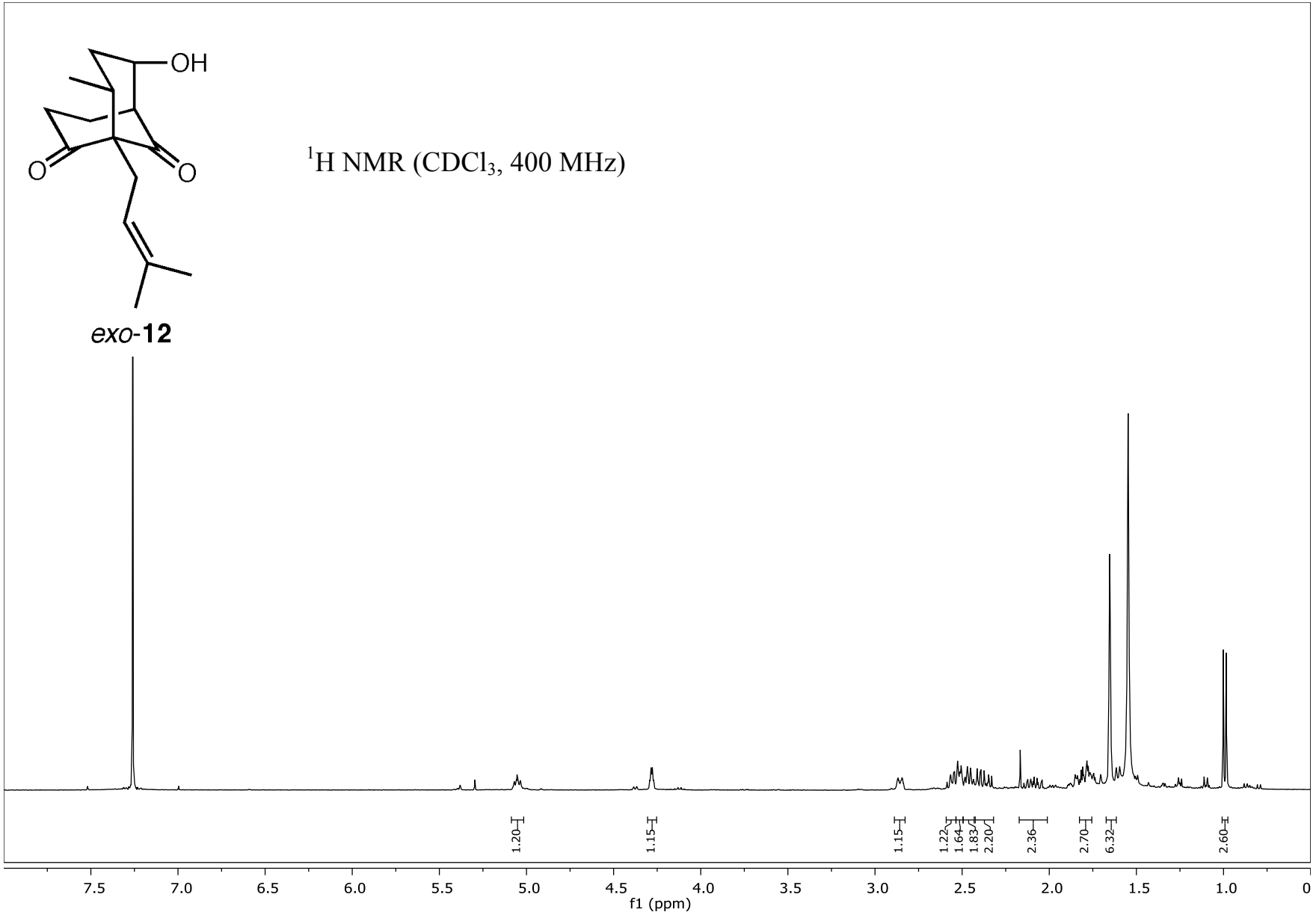
exo,endo-**11**

HMQC



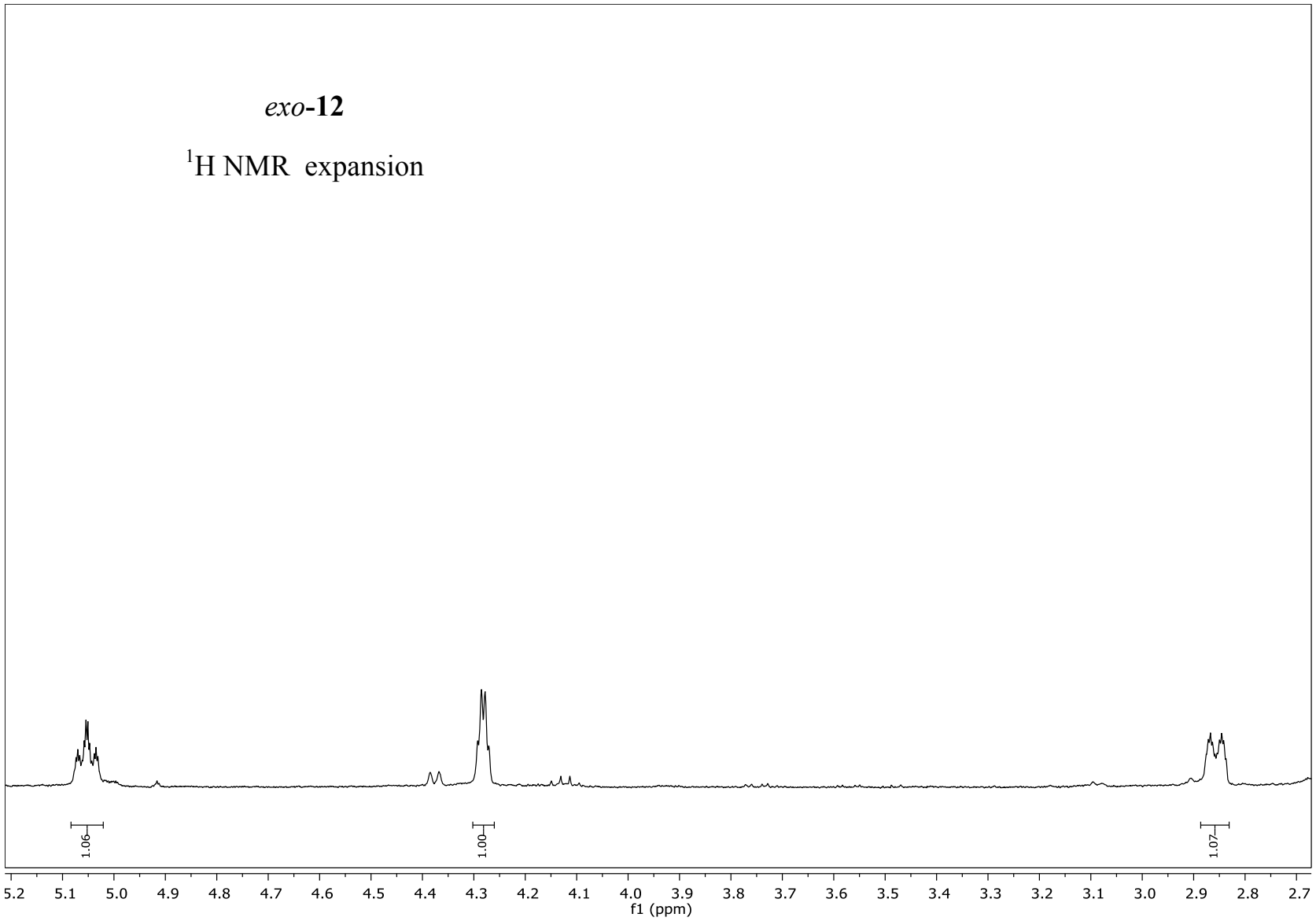

OH
O
O
+
60:40
12
OH
O
O
^{1}H NMR ($CDCl_3$, 400 MHz)
1.78
1.00
0.70
0.68
0.98
4.07
2.83
3.61
8.64
4.45
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0
f1 (ppm)

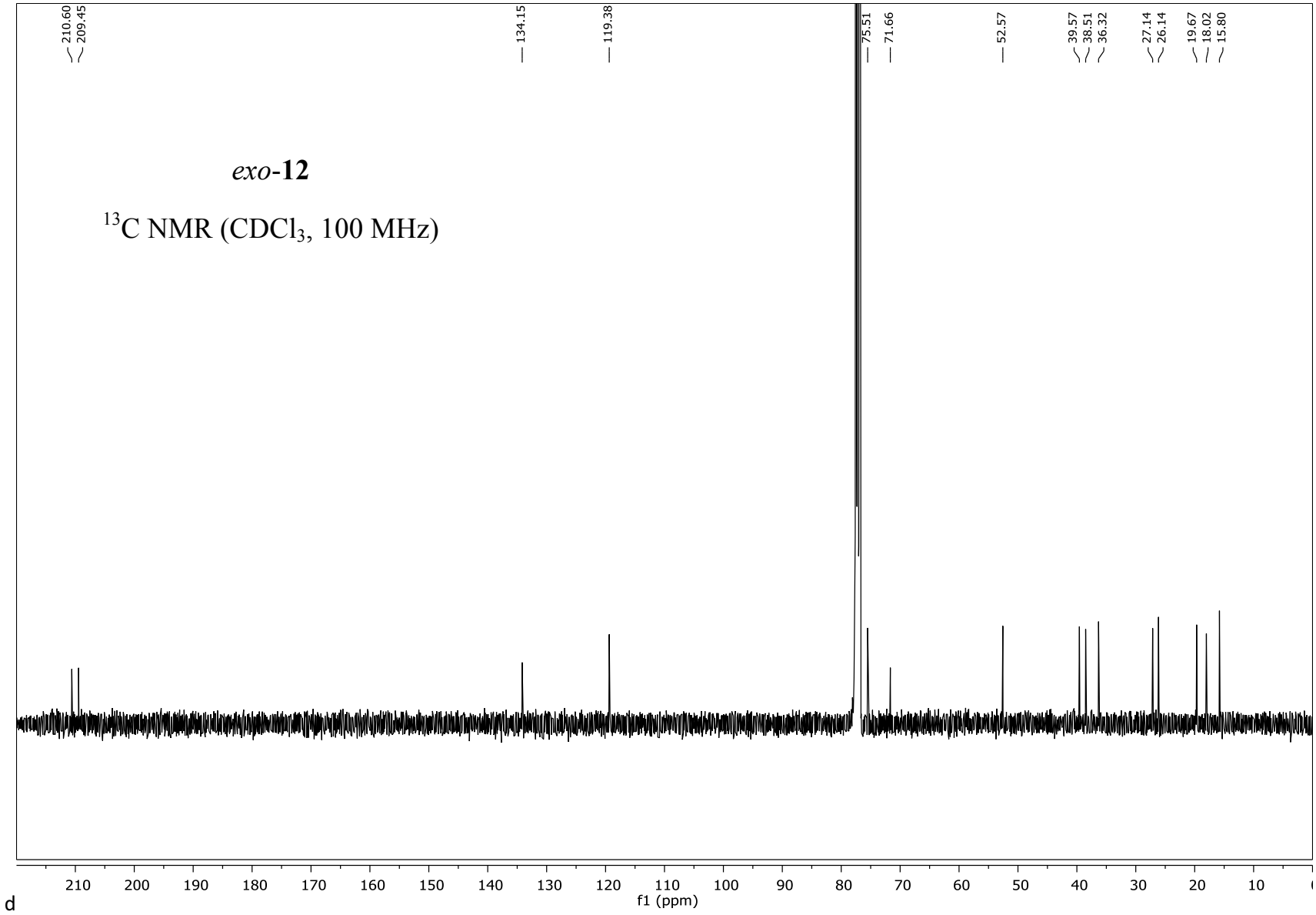

210.93
209.50
134.14
119.36
75.49
71.67
52.54
39.57
38.57
36.27
27.11
26.13
19.65
18.01
15.90
exo,*endo*-**12**
^{13}C NMR ($CDCl_3$, 100 MHz)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

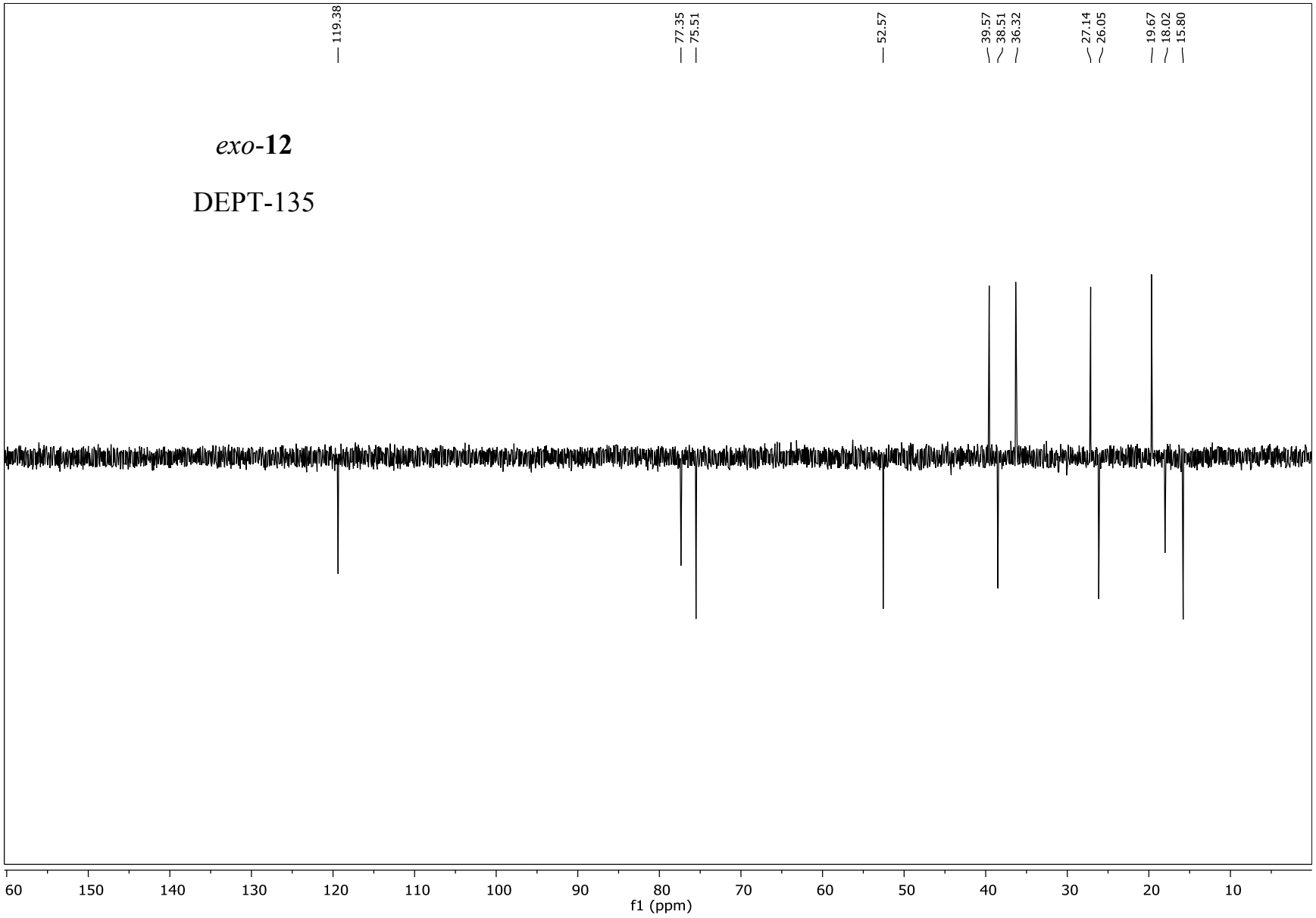

OH
O
O
exo-12
1H NMR (CDCl3, 400 MHz)
1.20
1.15
1.15
1.22
1.64
1.83
2.20
2.36
2.70
6.32
2.60
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0
f1 (ppm)

exo-**12**

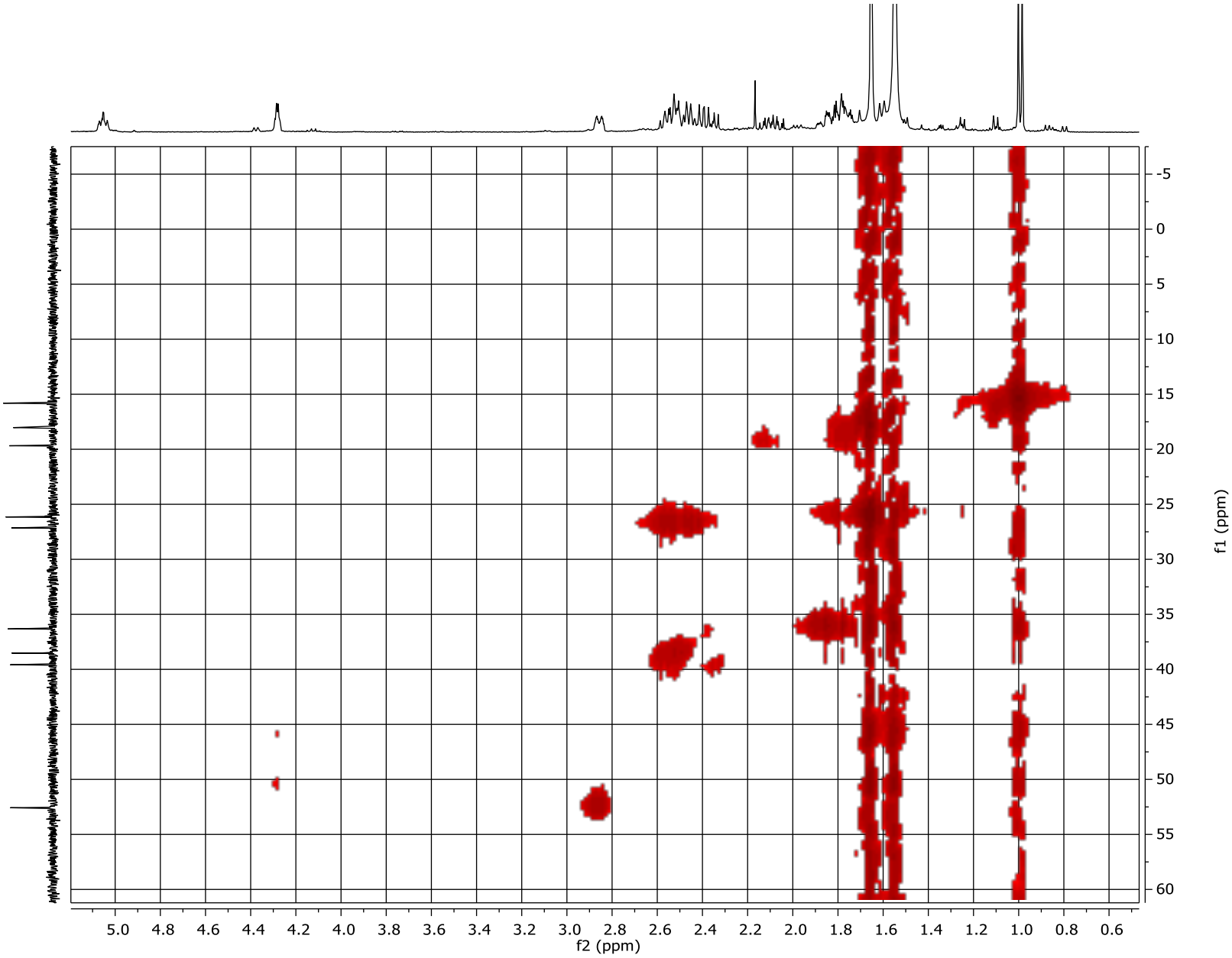
^{1}H NMR expansion



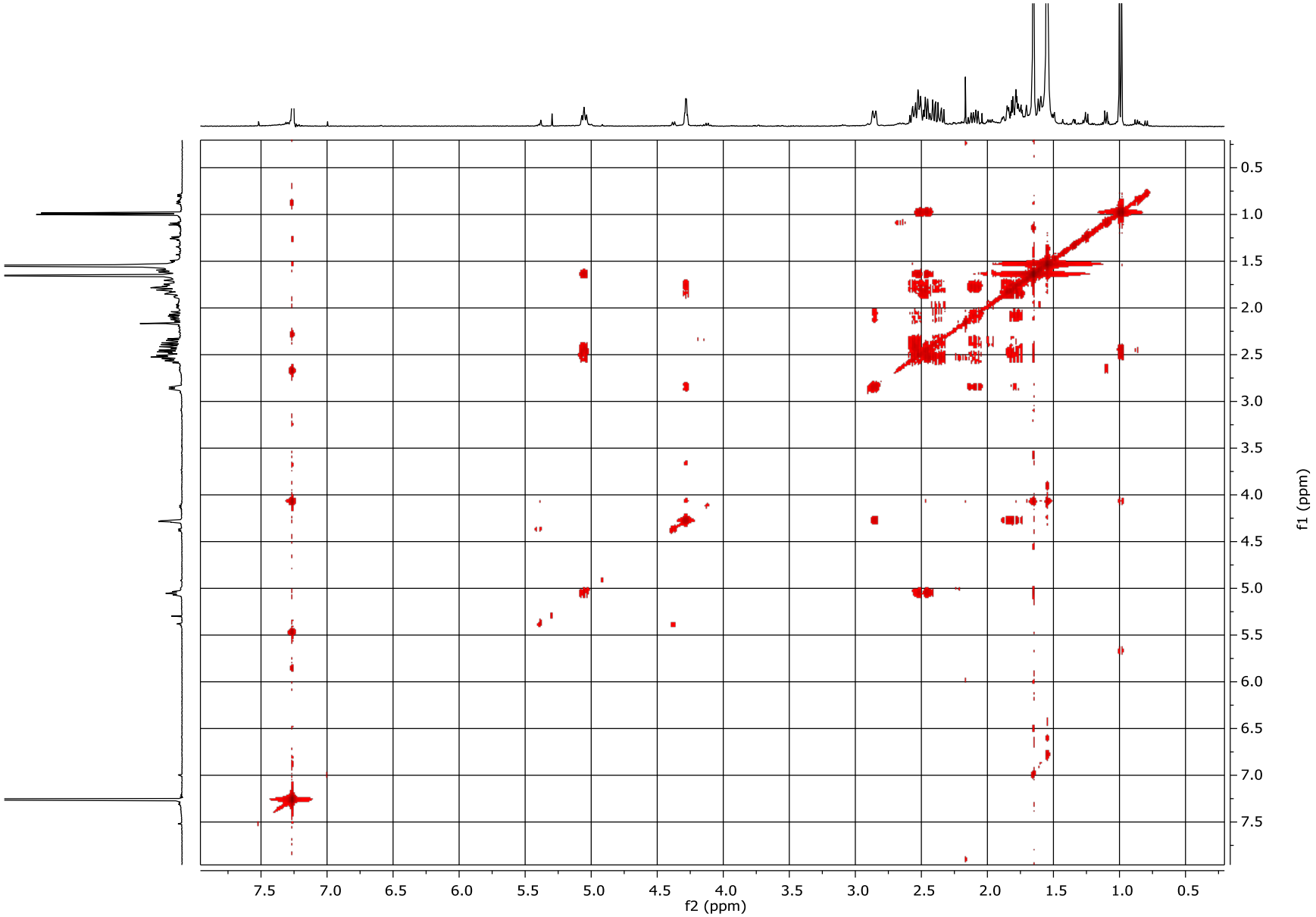

210.60
209.45
134.15
119.38
75.51
71.66
52.57
39.57
38.51
36.32
27.14
26.14
19.67
18.02
15.80
exo-**12**
^{13}C NMR ($CDCl_3$, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)
d


119.38
77.35
75.51
52.57
39.57
38.51
36.32
27.14
26.05
19.67
18.02
15.80
exo-12
DEPT-135
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

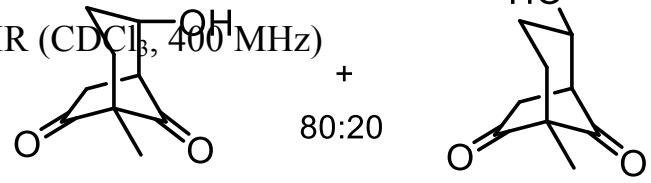
HMQC



COSY-90


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
f2 (ppm)
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
f1 (ppm)

^{1}H NMR ($CDCl_3$, 400 MHz)



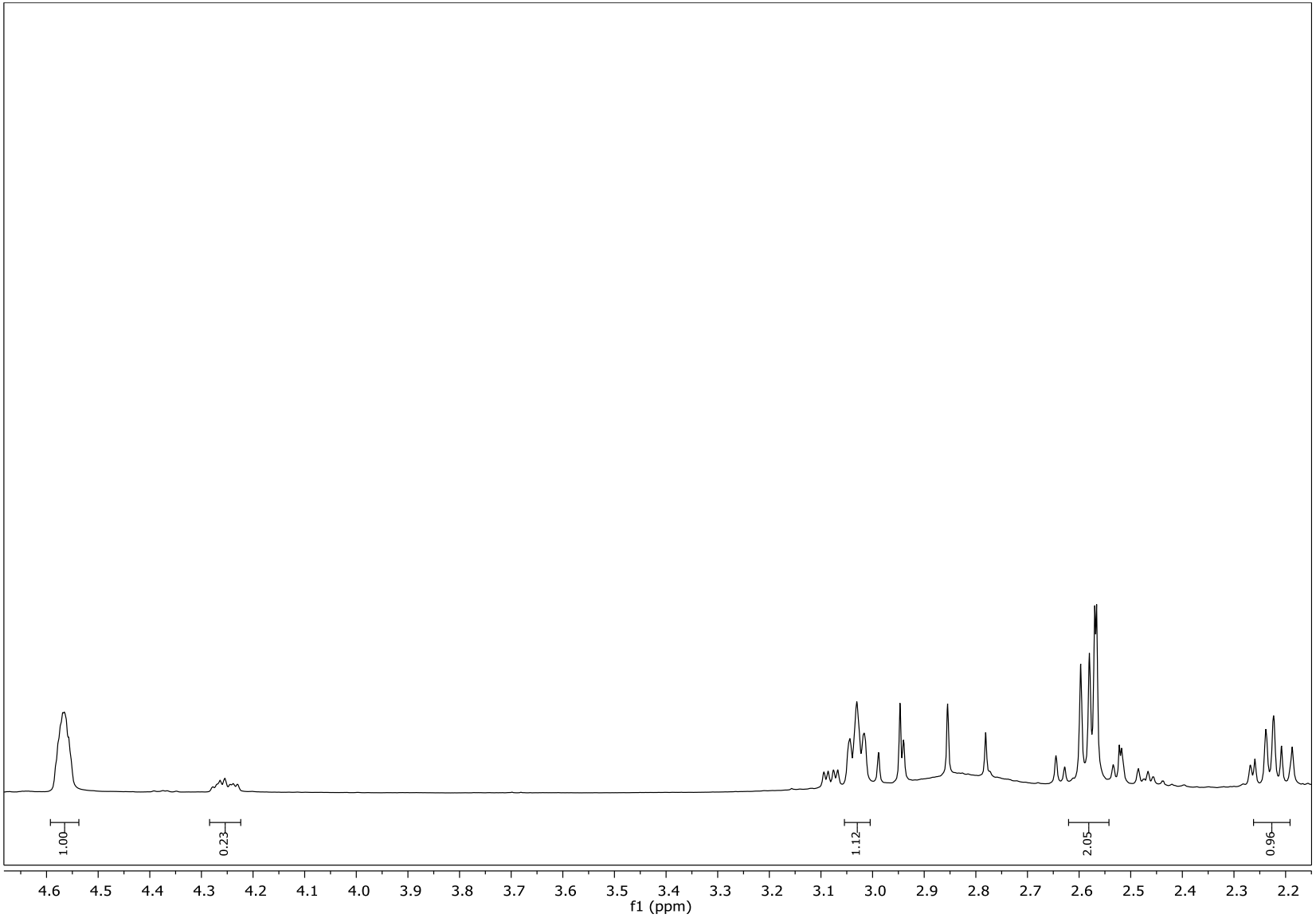
+

80:20

13

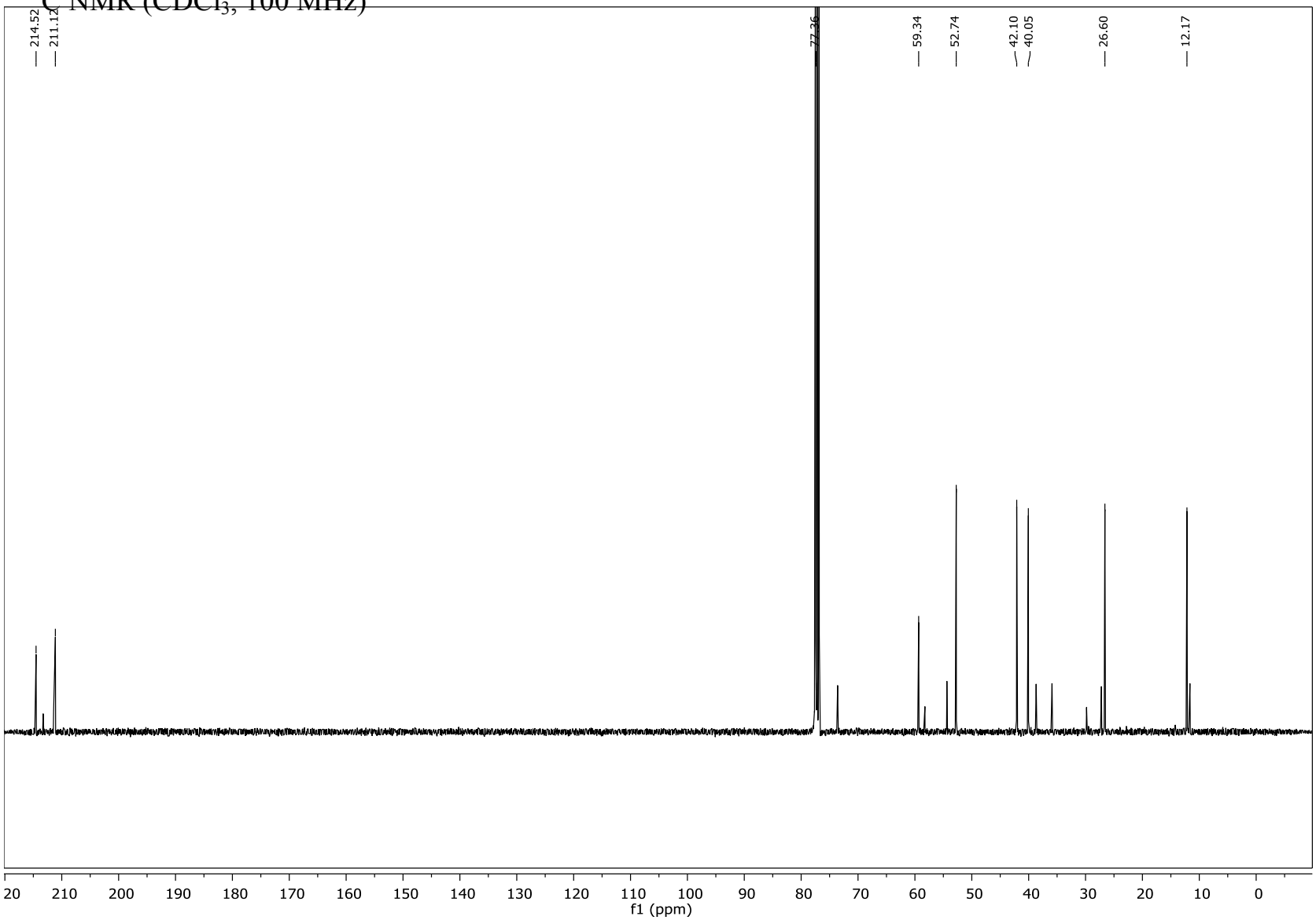
exo,*endo*-**13**

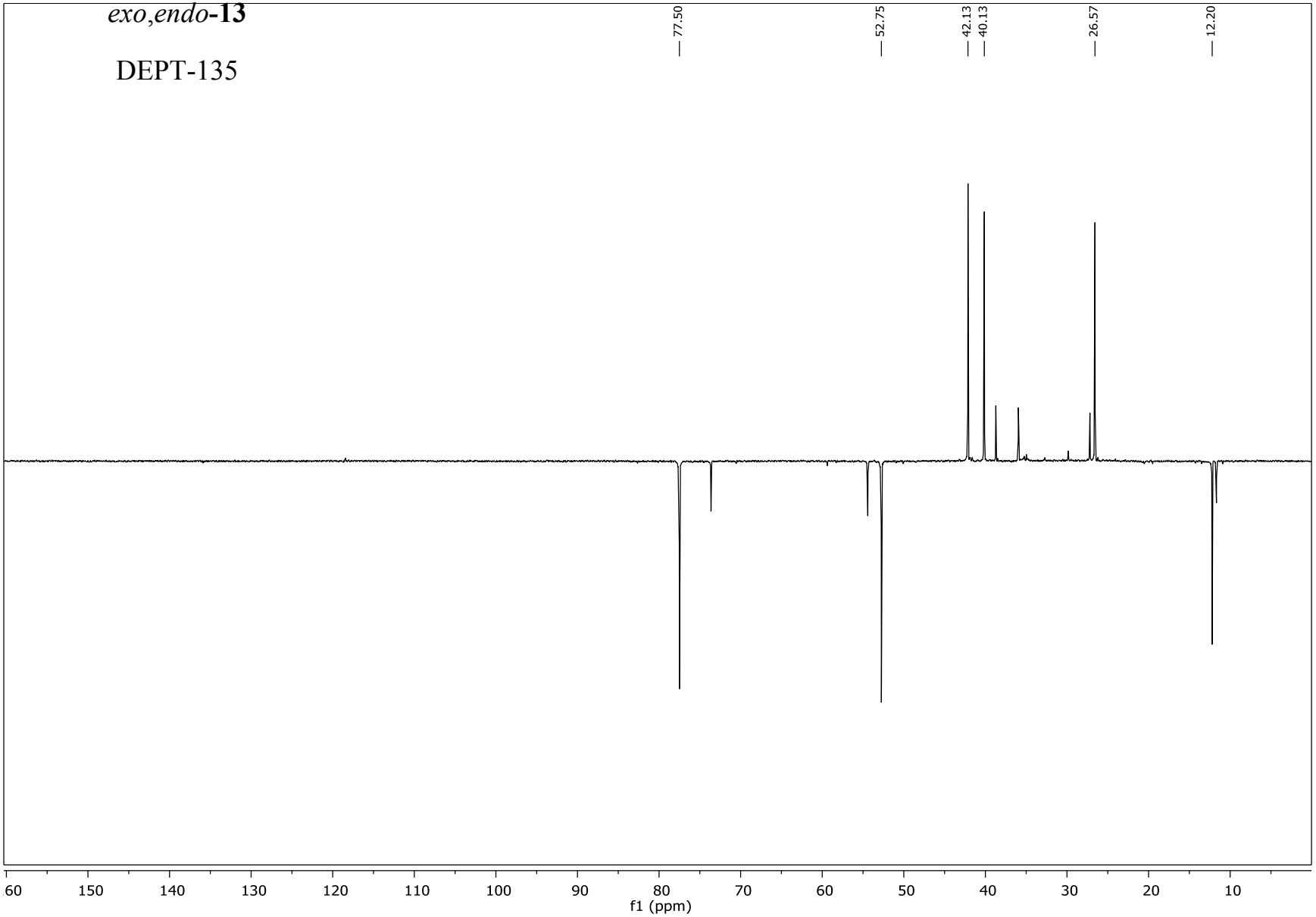
^{1}H NMR expansion



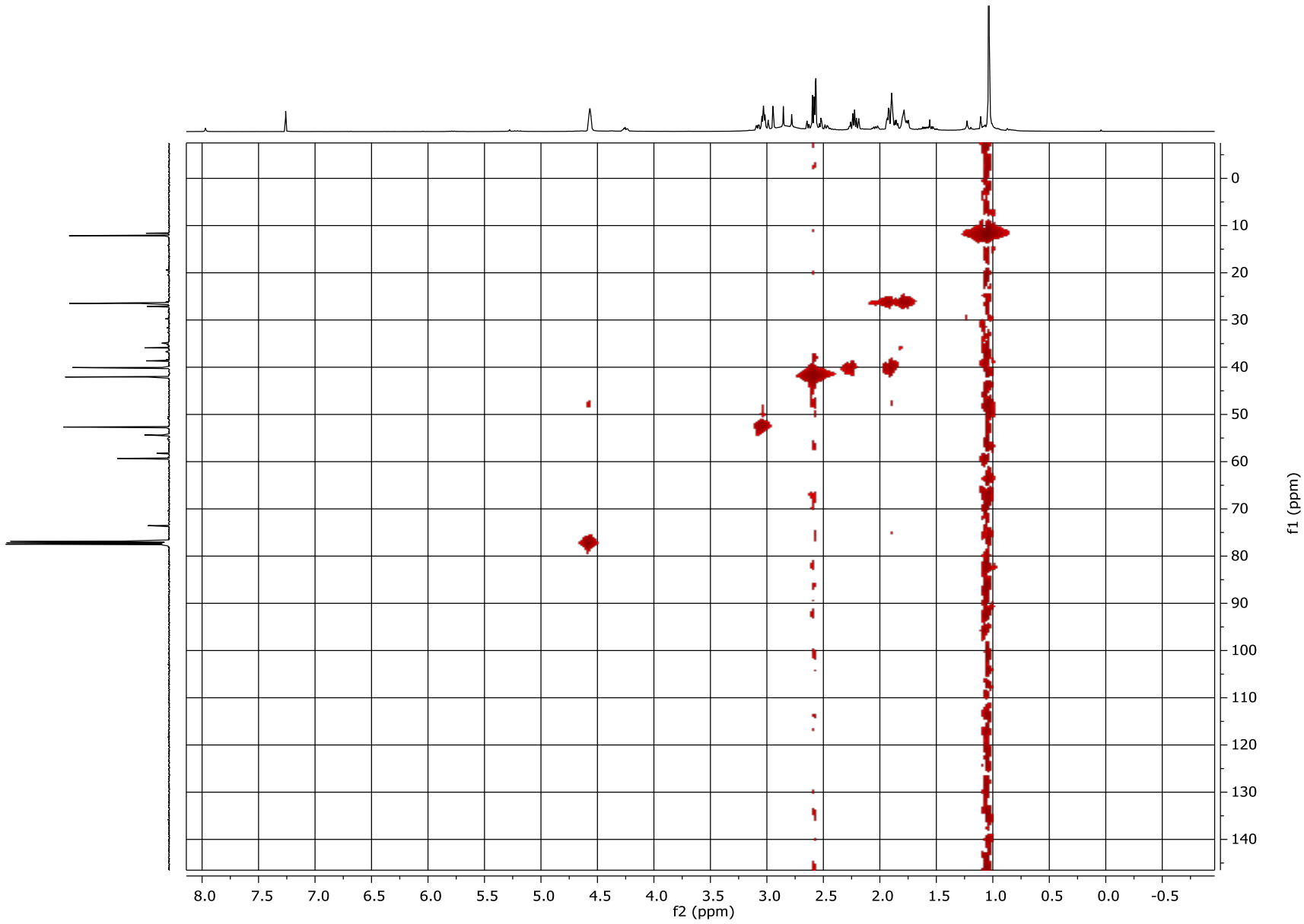
exo,endo-**13**

^{13}C NMR ($CDCl_3$, 100 MHz)

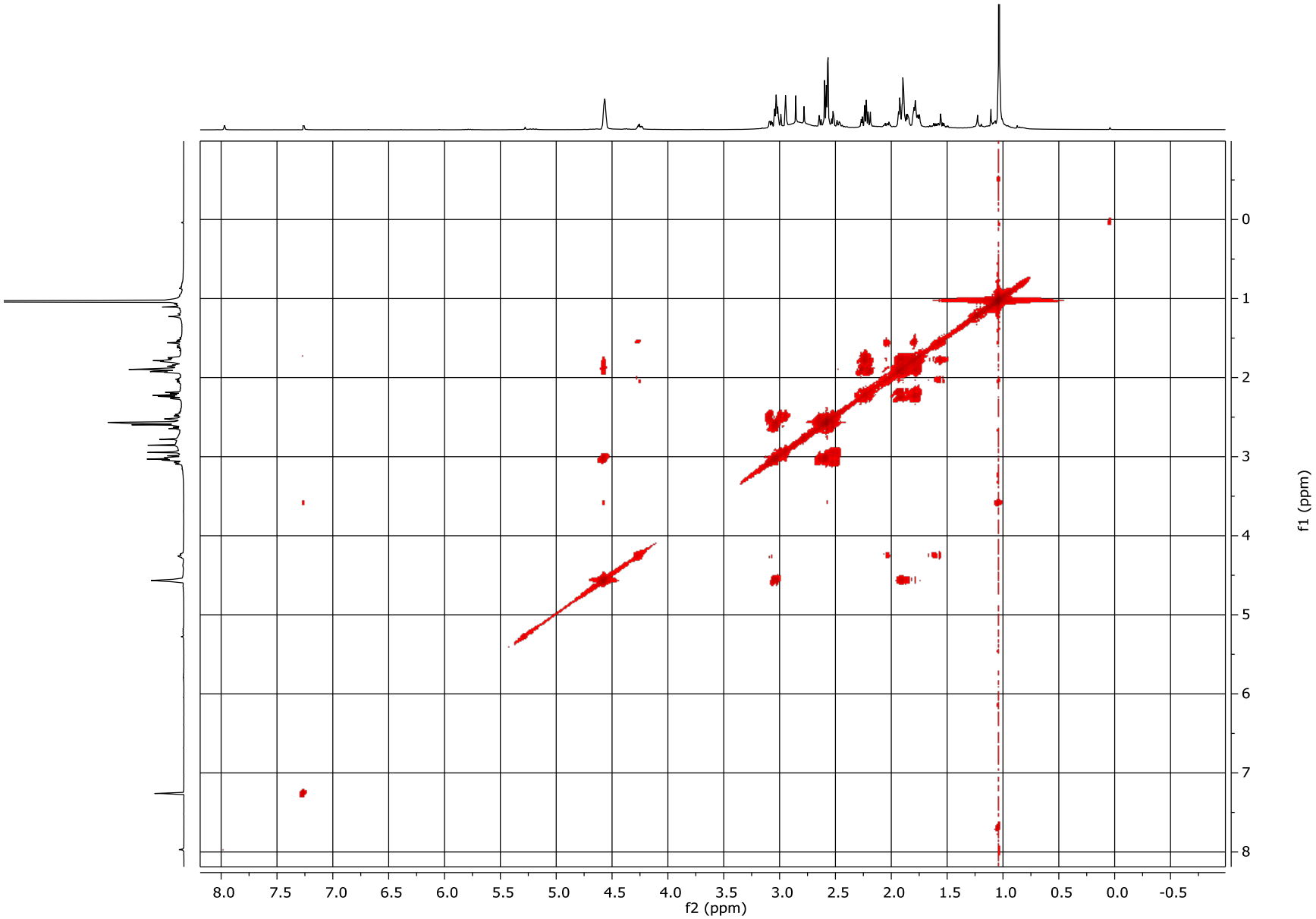


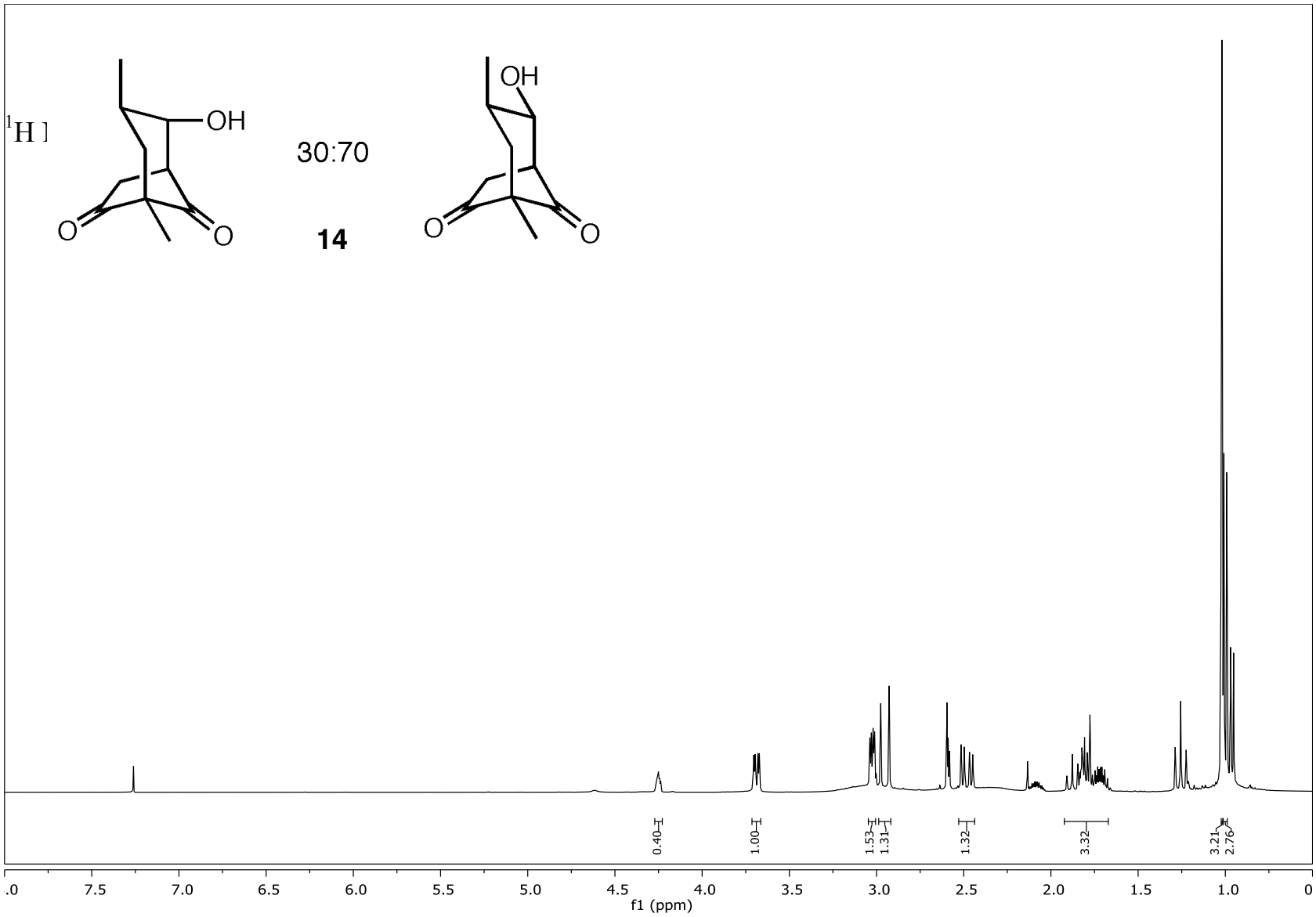

exo,*endo*-**13**
DEPT-135
77.50
52.75
42.13
40.13
26.57
12.20
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

HMQC


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
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)

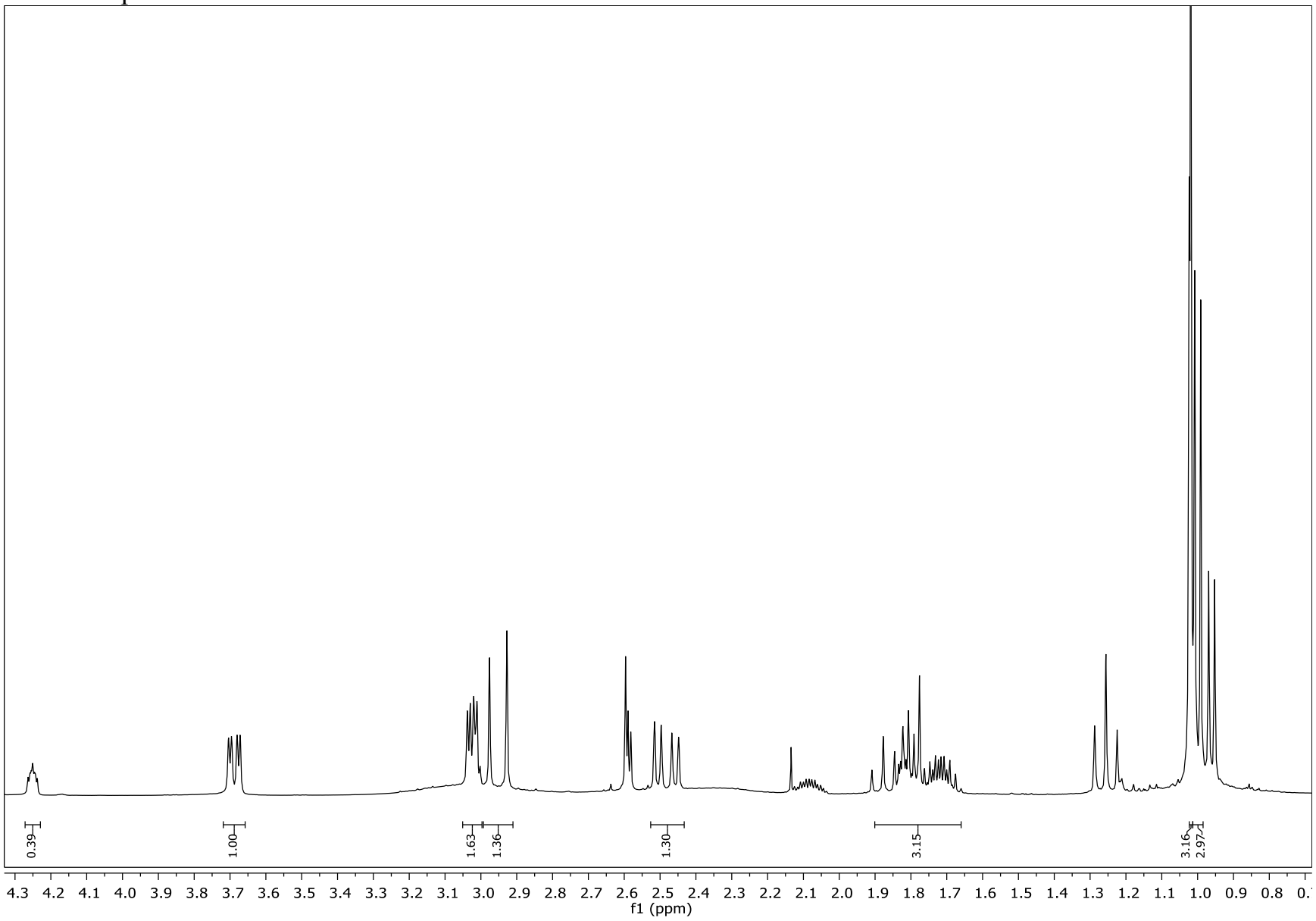
COSY-90


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
f2 (ppm)
0
1
2
3
4
5
6
7
8
f1 (ppm)


[1H]
OH
O
O
30:70
14
OH
O
O
0.40
1.00
1.53
1.31
1.32
3.32
3.21
2.76
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
f1 (ppm)

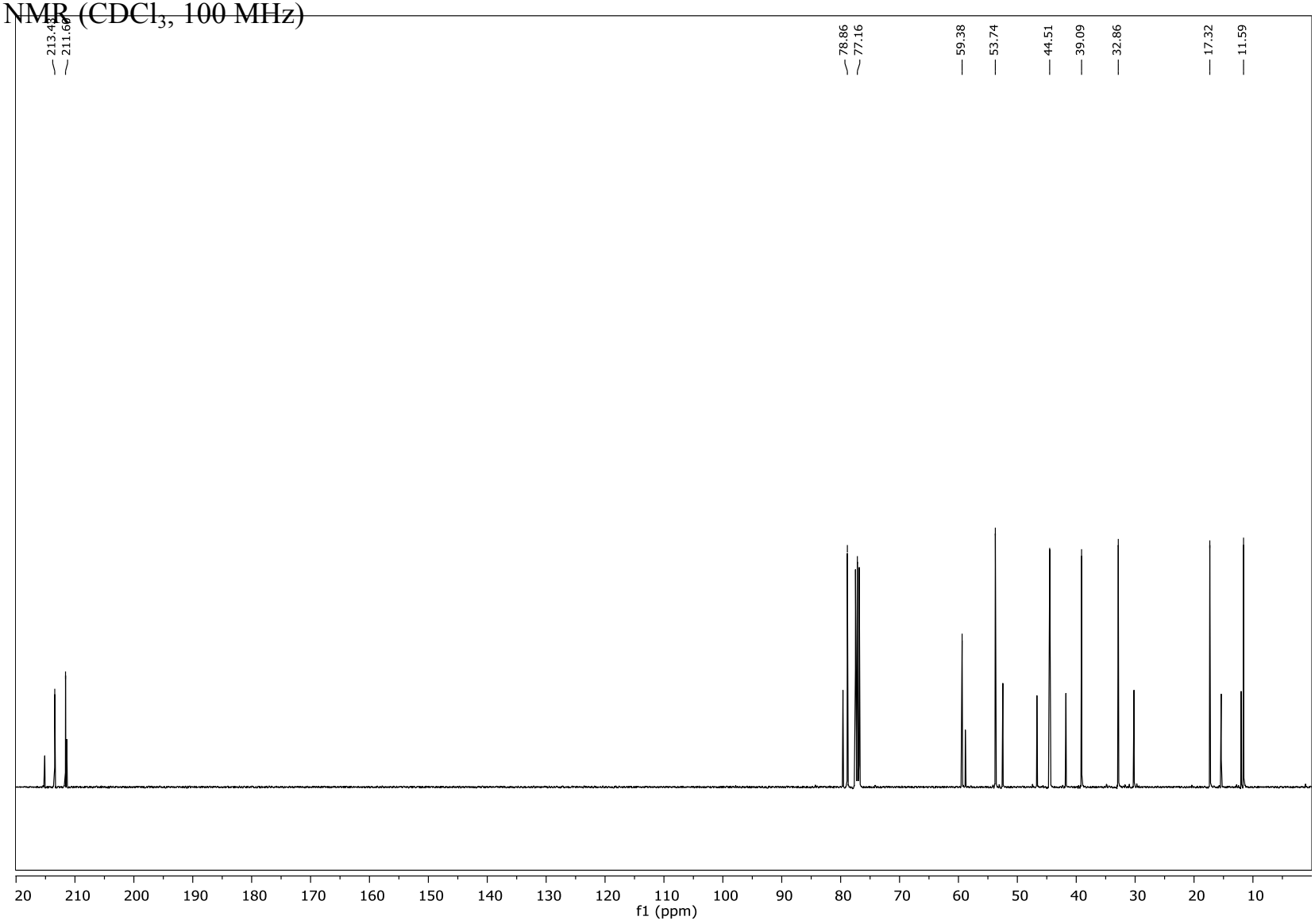
endo, *exo*-**14**

^{1}H NMR expansion



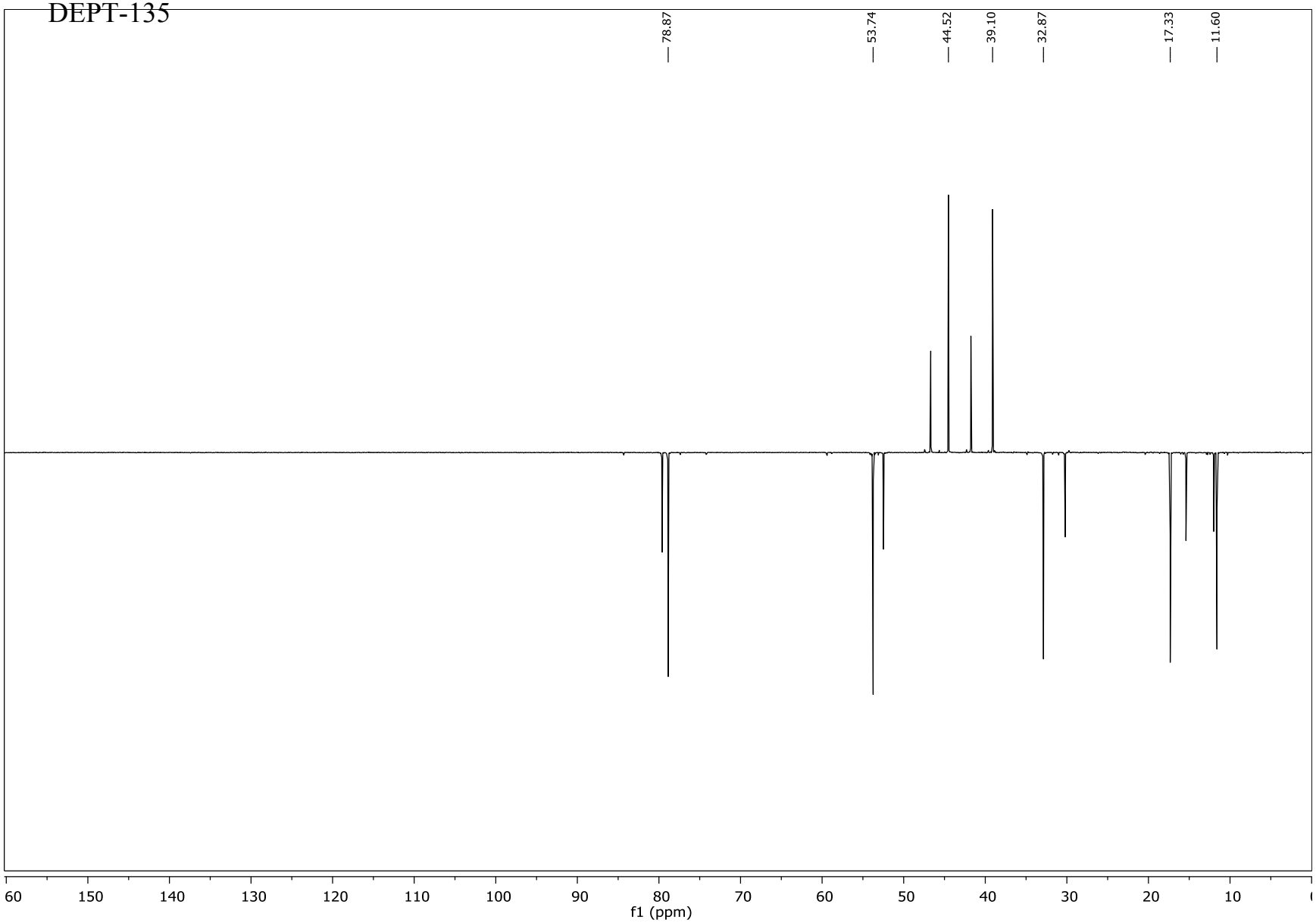
endo, *exo*-**14**

^{13}C NMR ($CDCl_3$, 100 MHz)

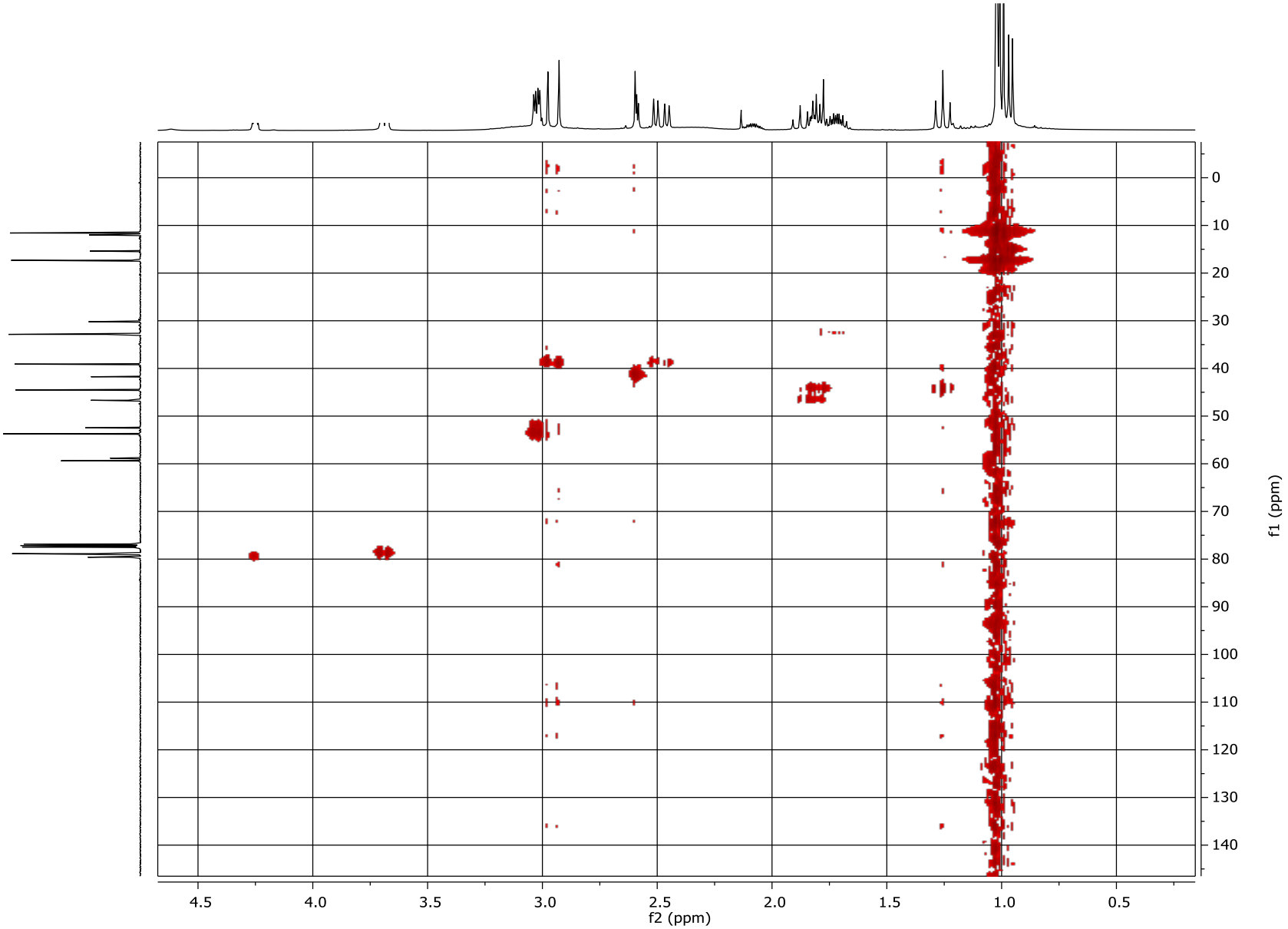


endo, *exo*-**14**

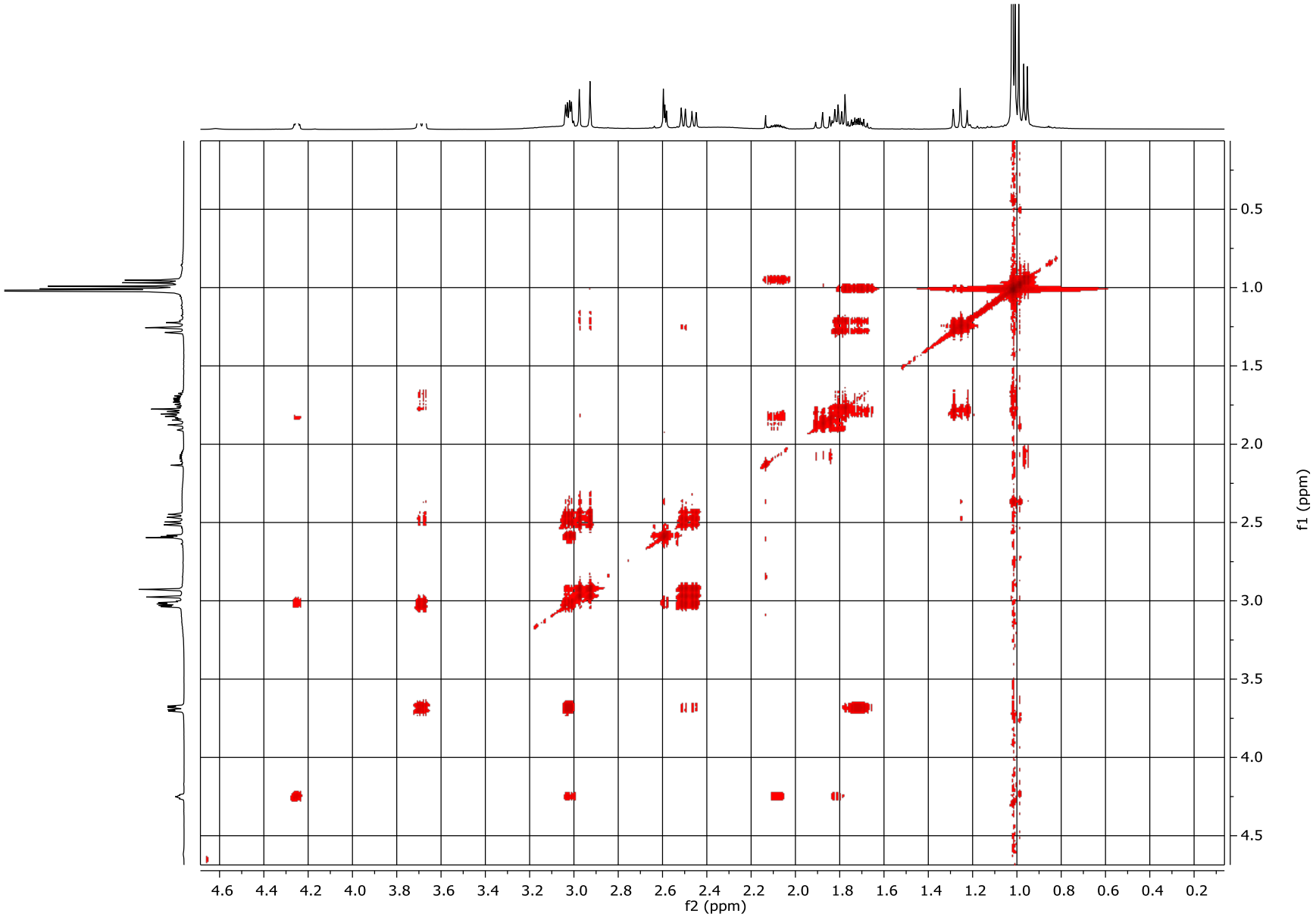
DEPT-135

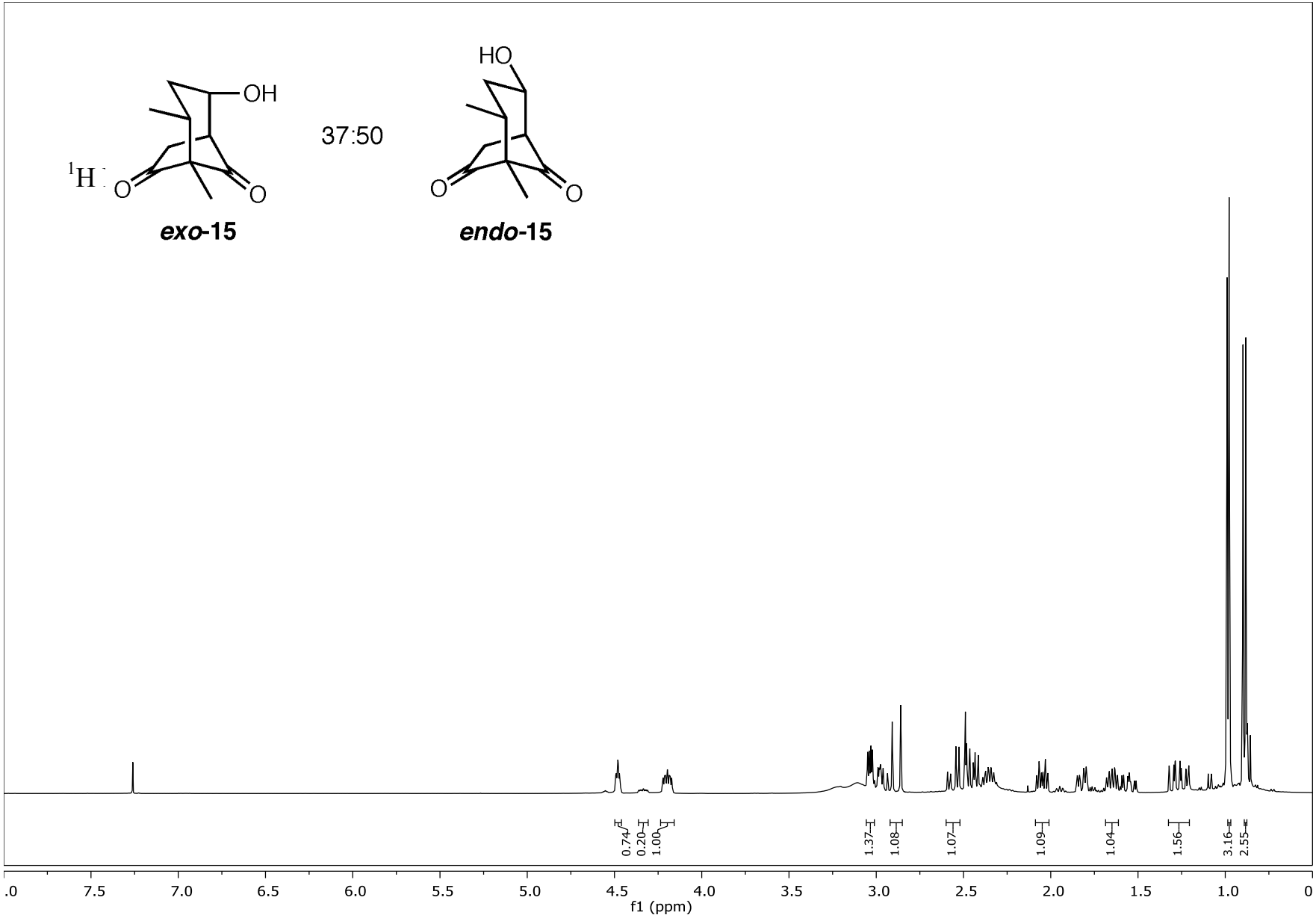


HMQC


4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)

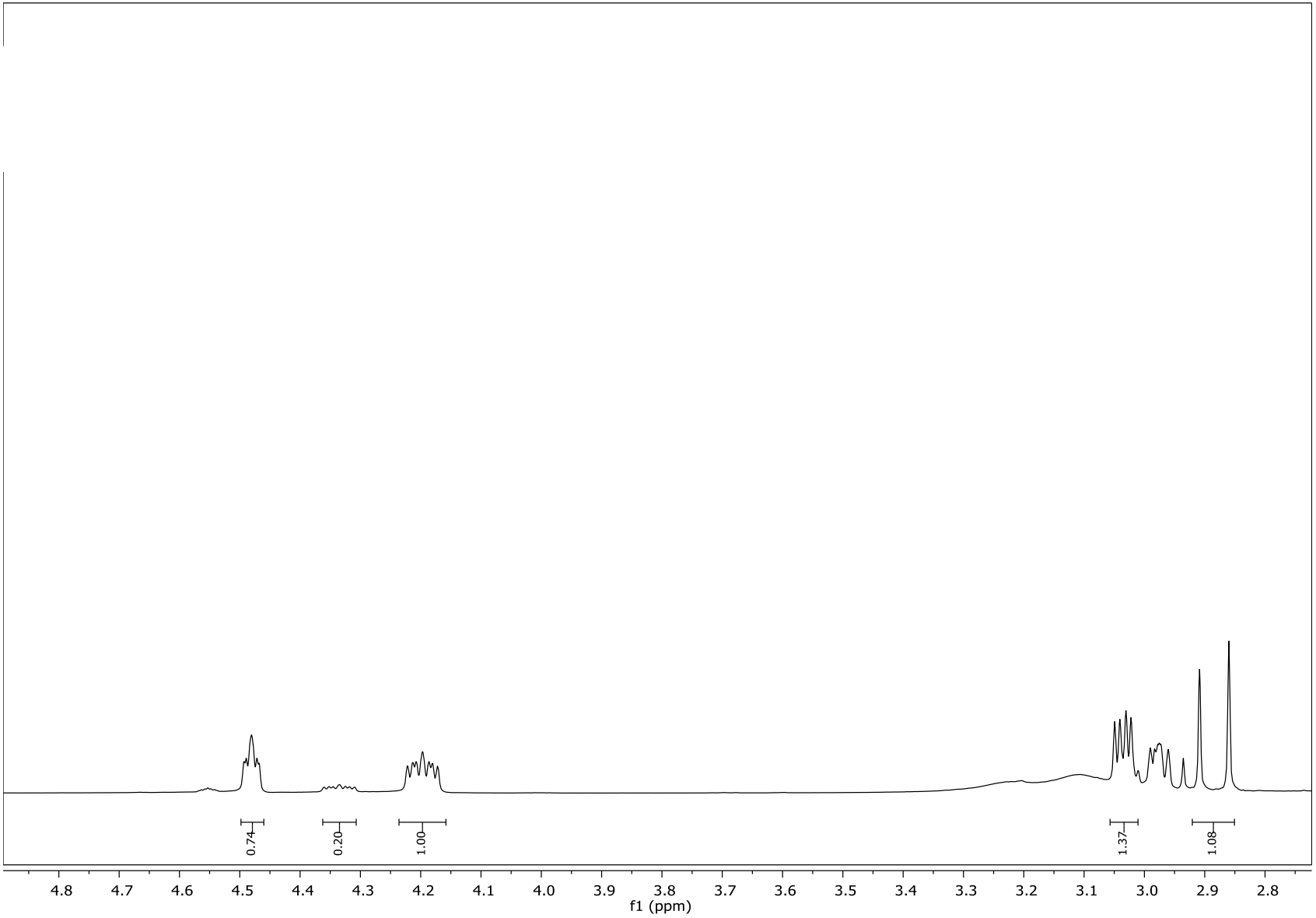
COSY-90


4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
f2 (ppm)
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
f1 (ppm)


OH
O
O
37:50
HO
O
O
exo-15
endo-15
0.74
0.20
1.00
1.37
1.08
1.07
1.09
1.04
1.56
3.16
2.55
.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
f1 (ppm)

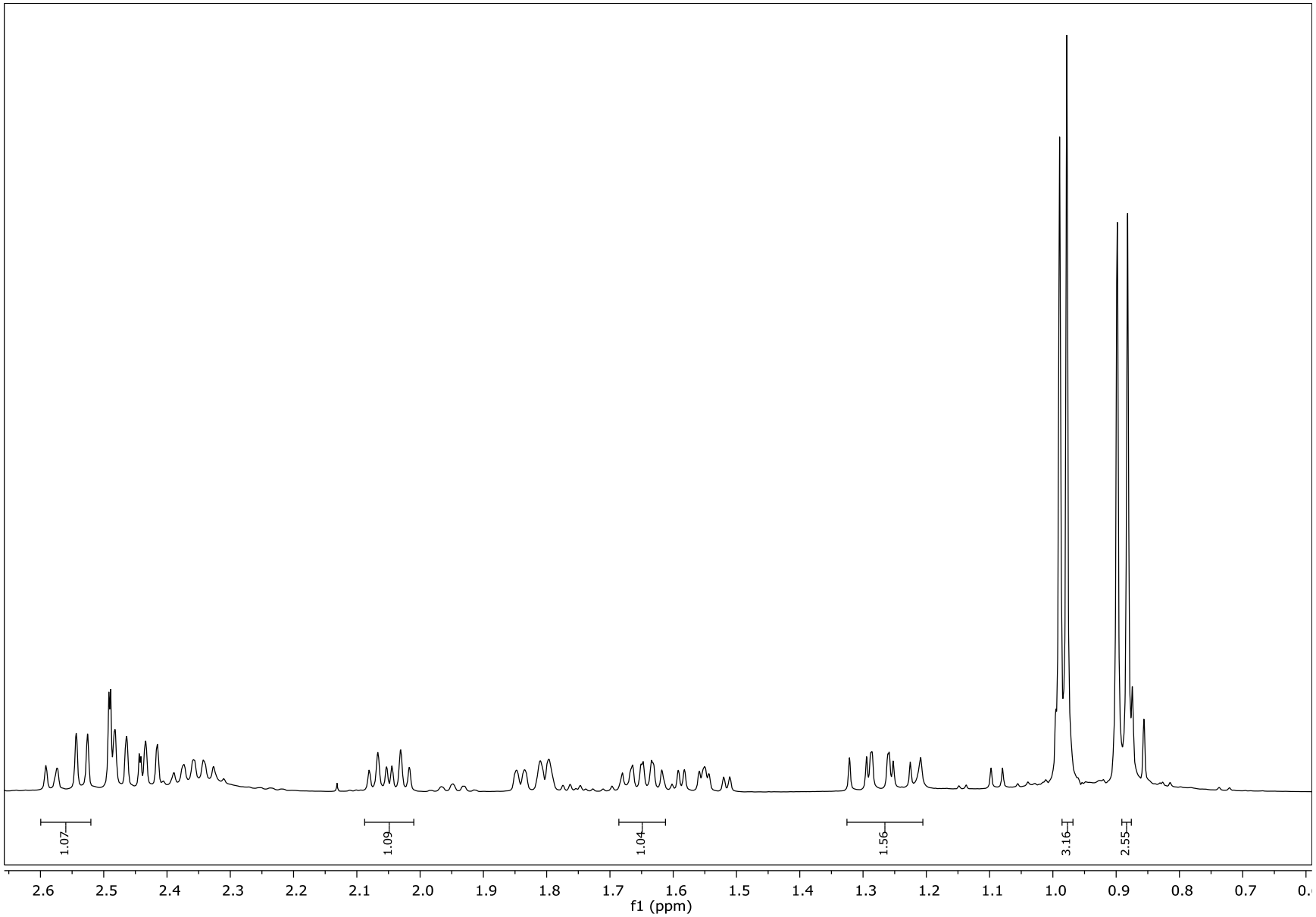
endo,exo-**15**

^{1}H NMR expansion



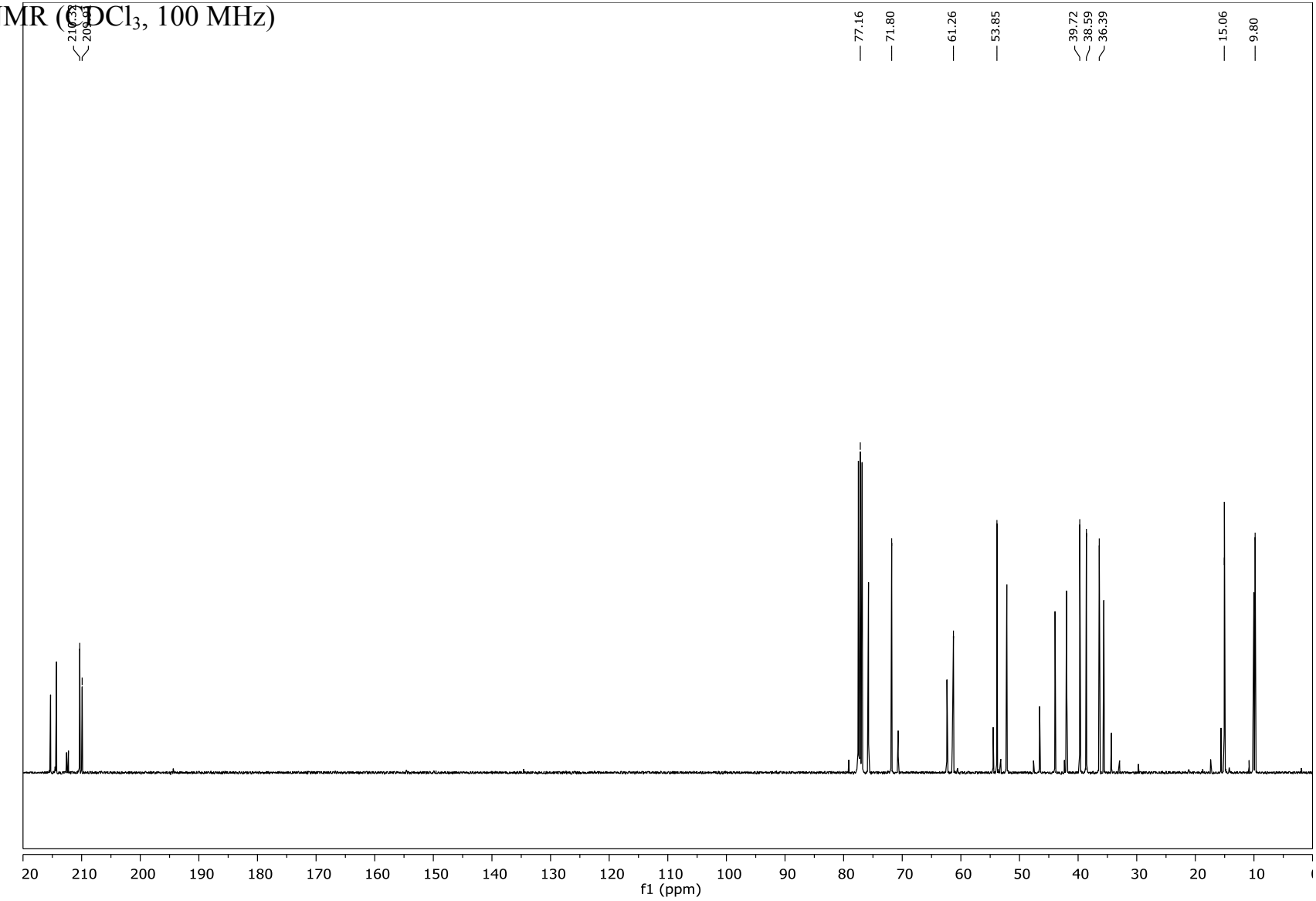
endo, *exo*-**15**

^{1}H NMR expansion

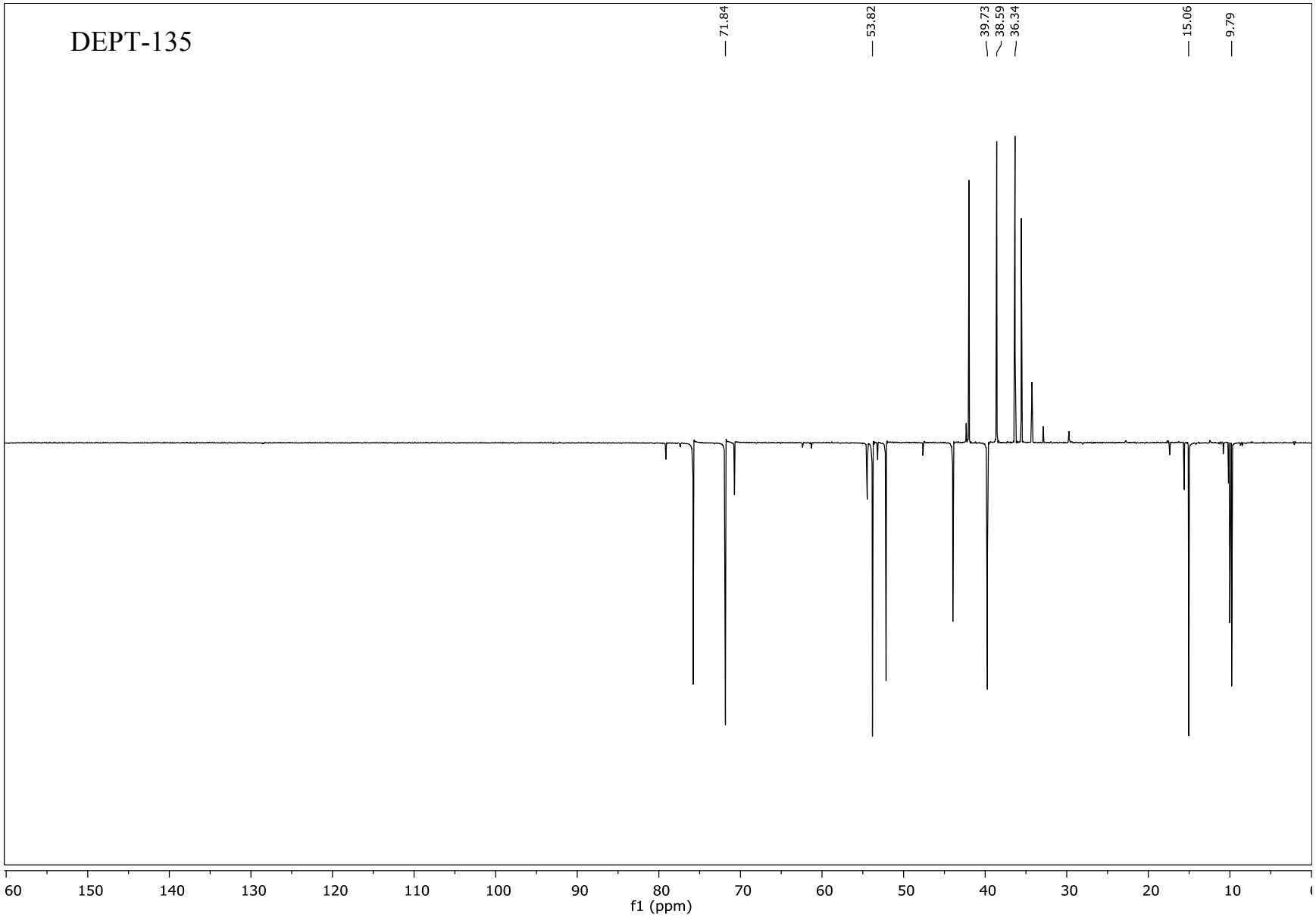


endo, *exo*-**15**

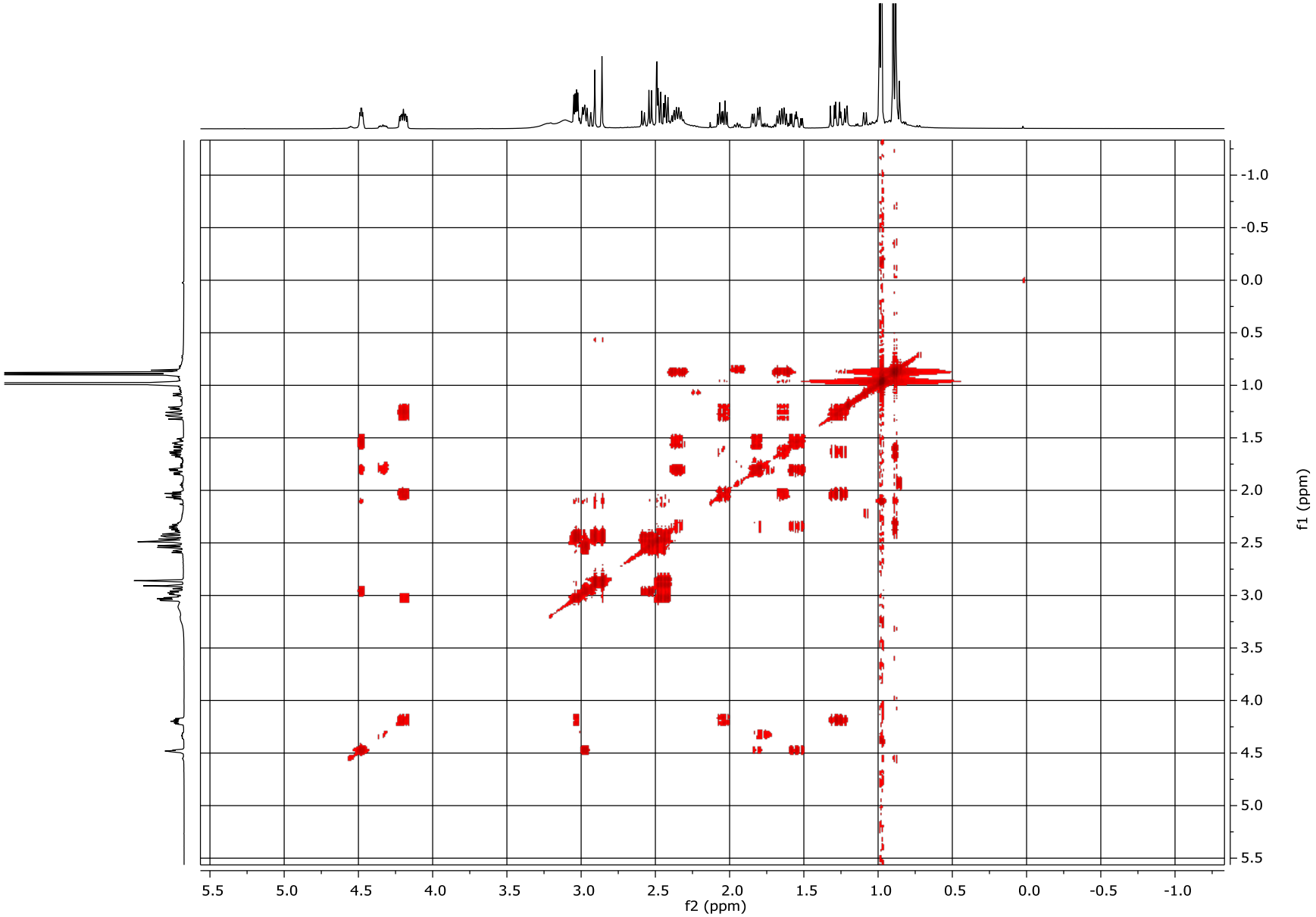
^{13}C NMR ($CDCl_3$, 100 MHz)

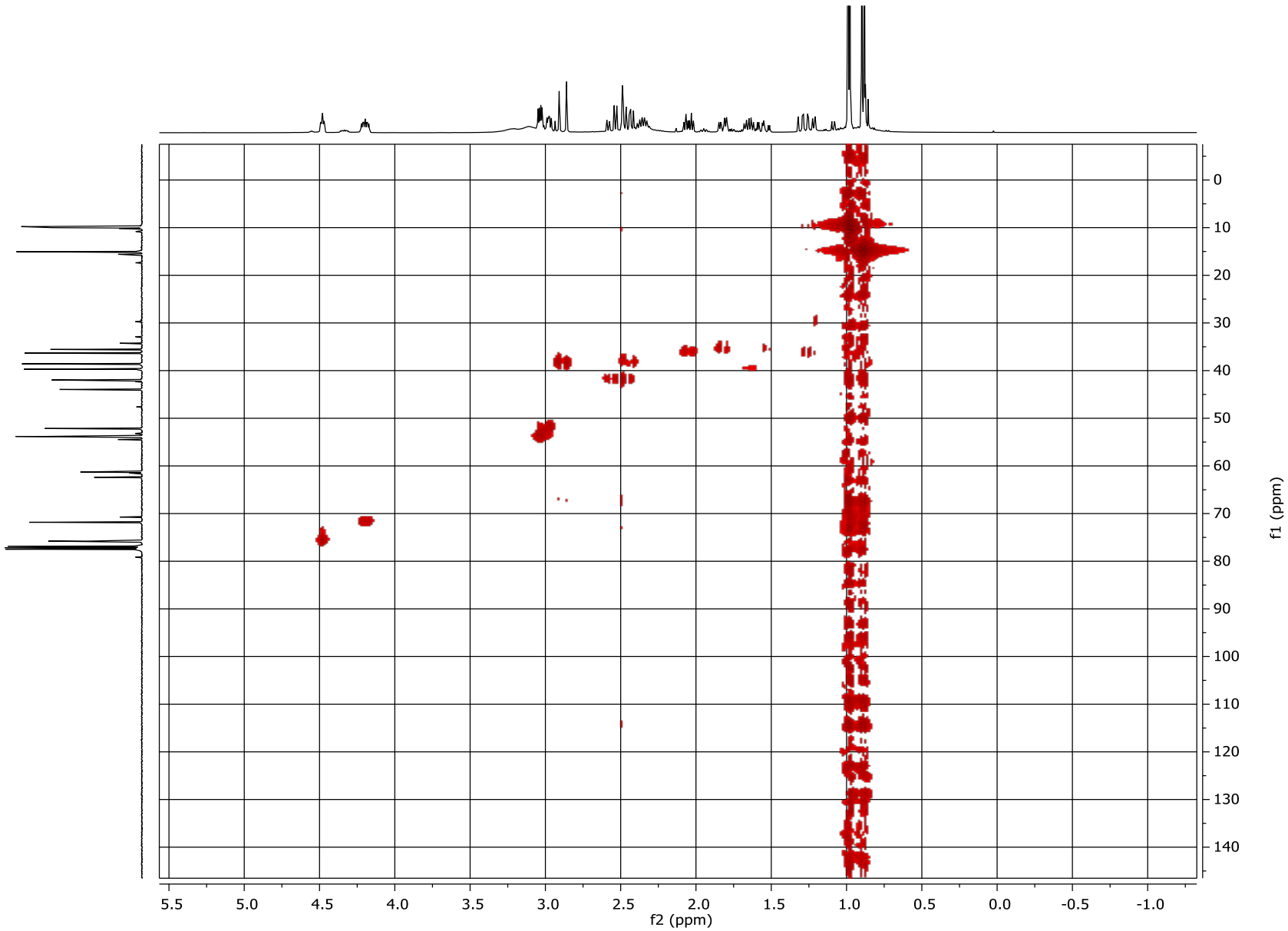


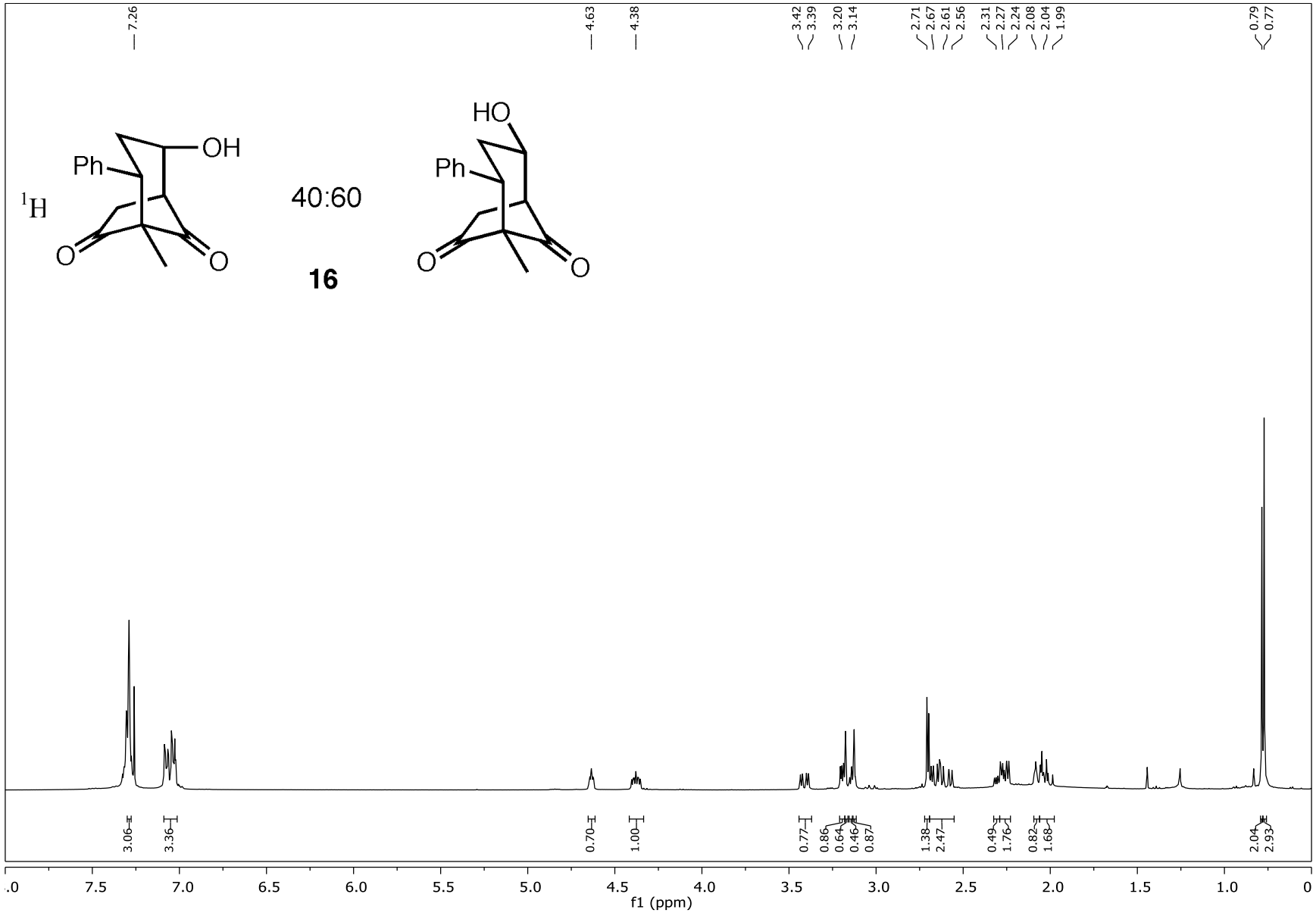
endo, *exo*-**15**


DEPT-135
71.84
53.82
39.73
38.59
36.34
15.06
9.79
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

COSY-90

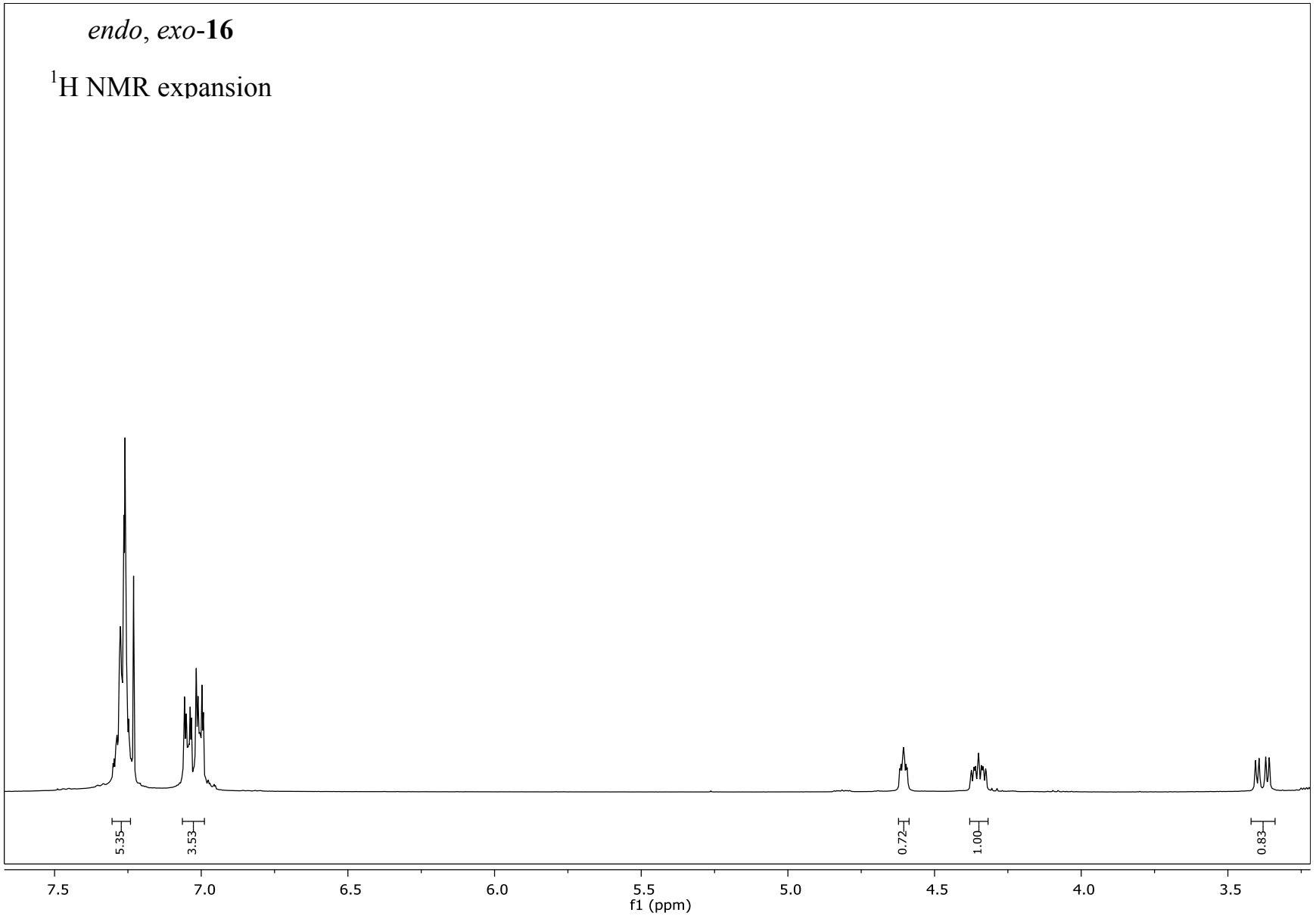

5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f2 (ppm)
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
f1 (ppm)


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
-1.0
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)


7.26
4.63
4.38
3.42
3.39
3.20
3.14
2.71
2.67
2.61
2.56
2.31
2.27
2.24
2.08
2.04
1.99
0.79
0.77
OH
Ph
O
O
^{1}H
40:60
HO
Ph
O
O
16
3.06
3.36
0.70
1.00
0.77
0.86
0.64
0.46
0.87
1.38
2.47
0.49
1.76
0.82
1.68
2.04
2.93
f1 (ppm)

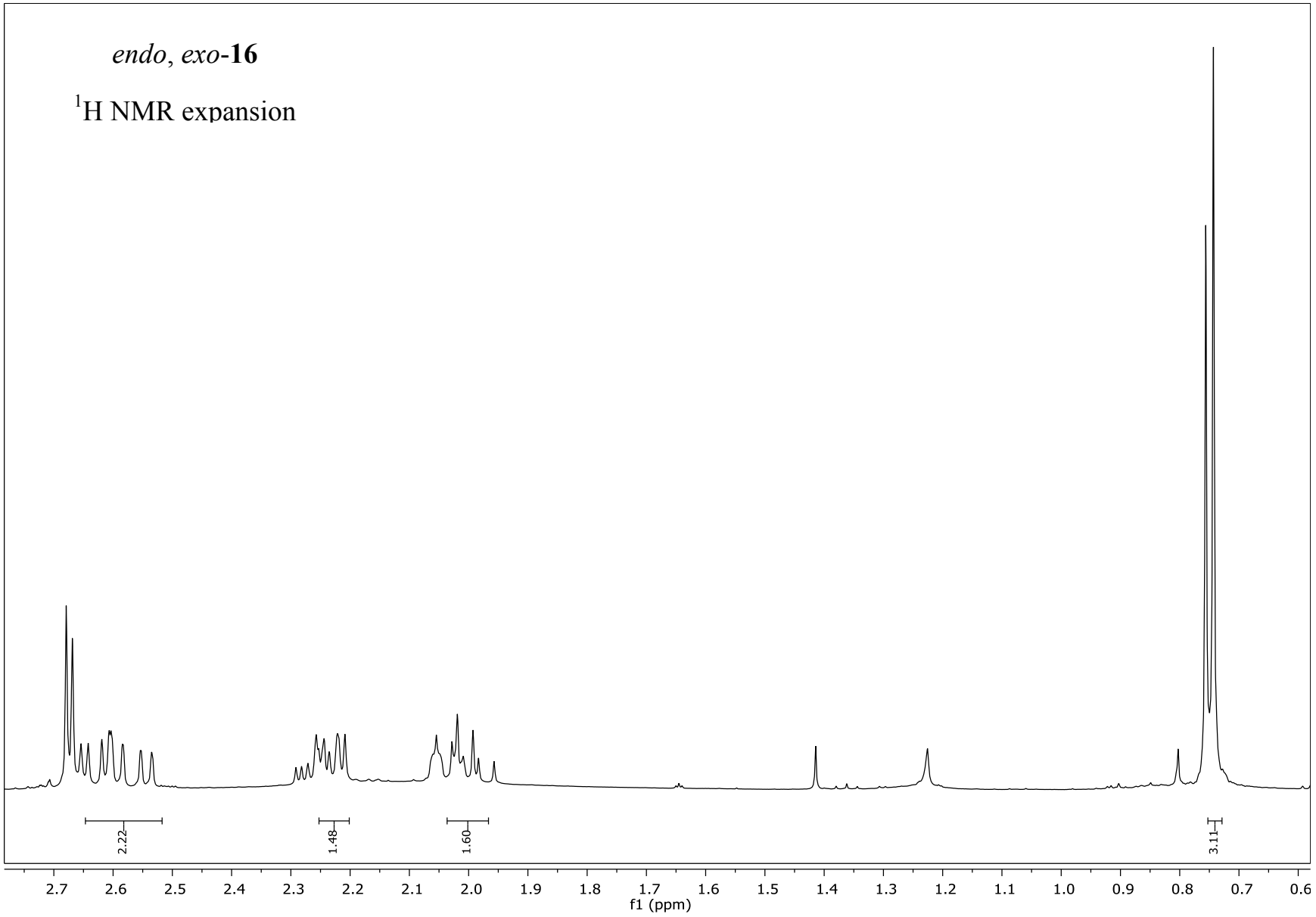
endo, *exo*-**16**

^{1}H NMR expansion



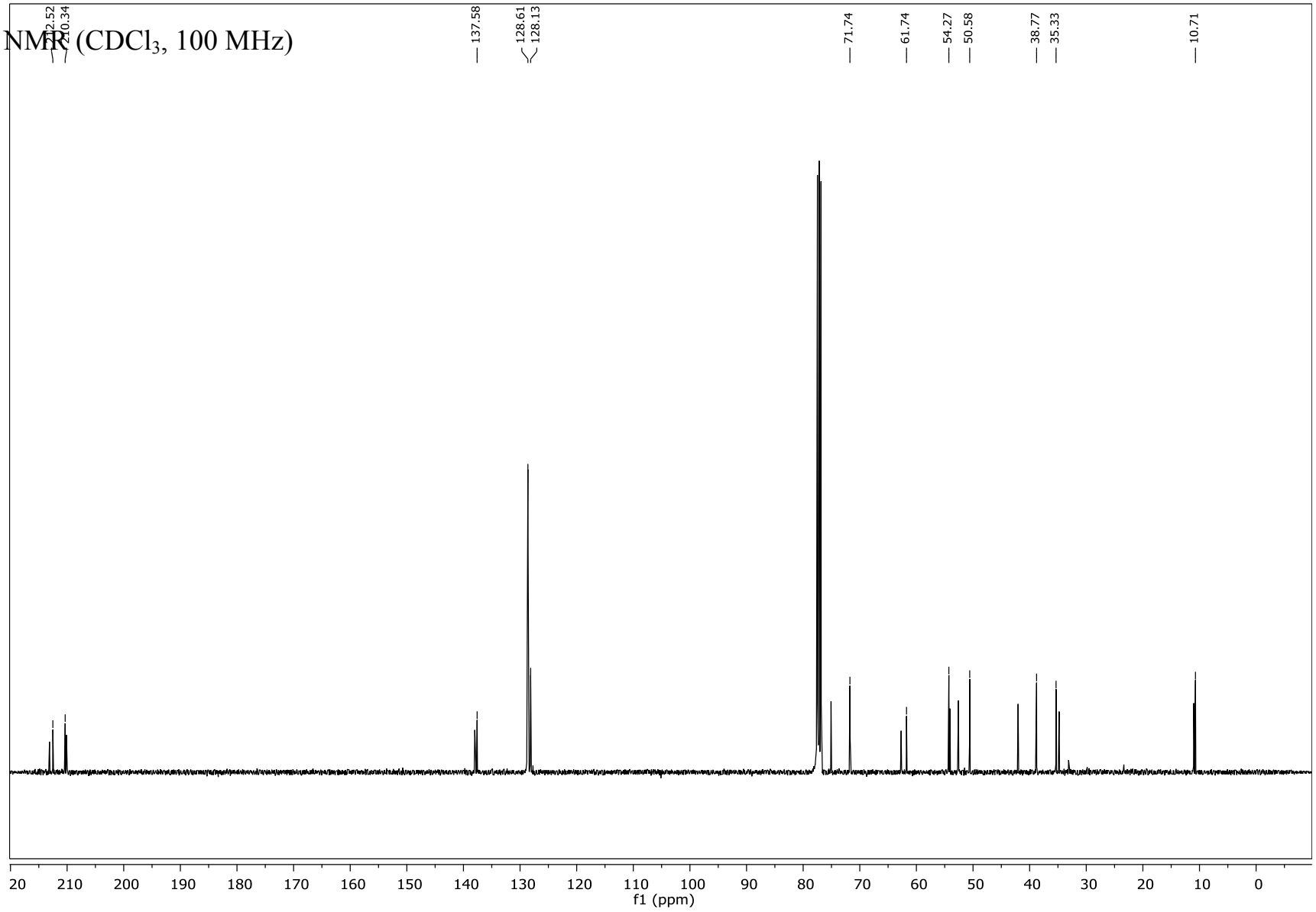
endo, *exo*-**16**

^{1}H NMR expansion

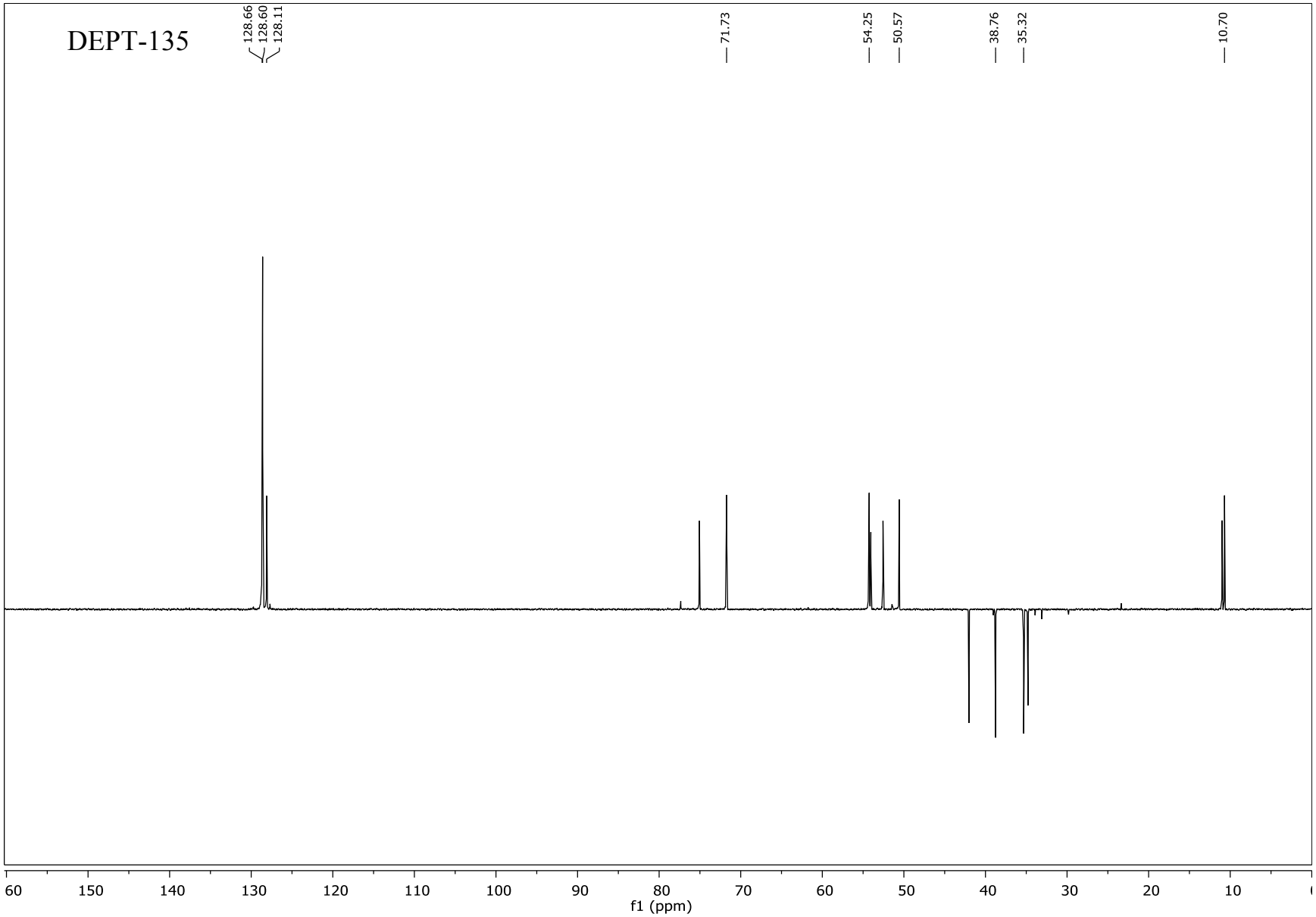


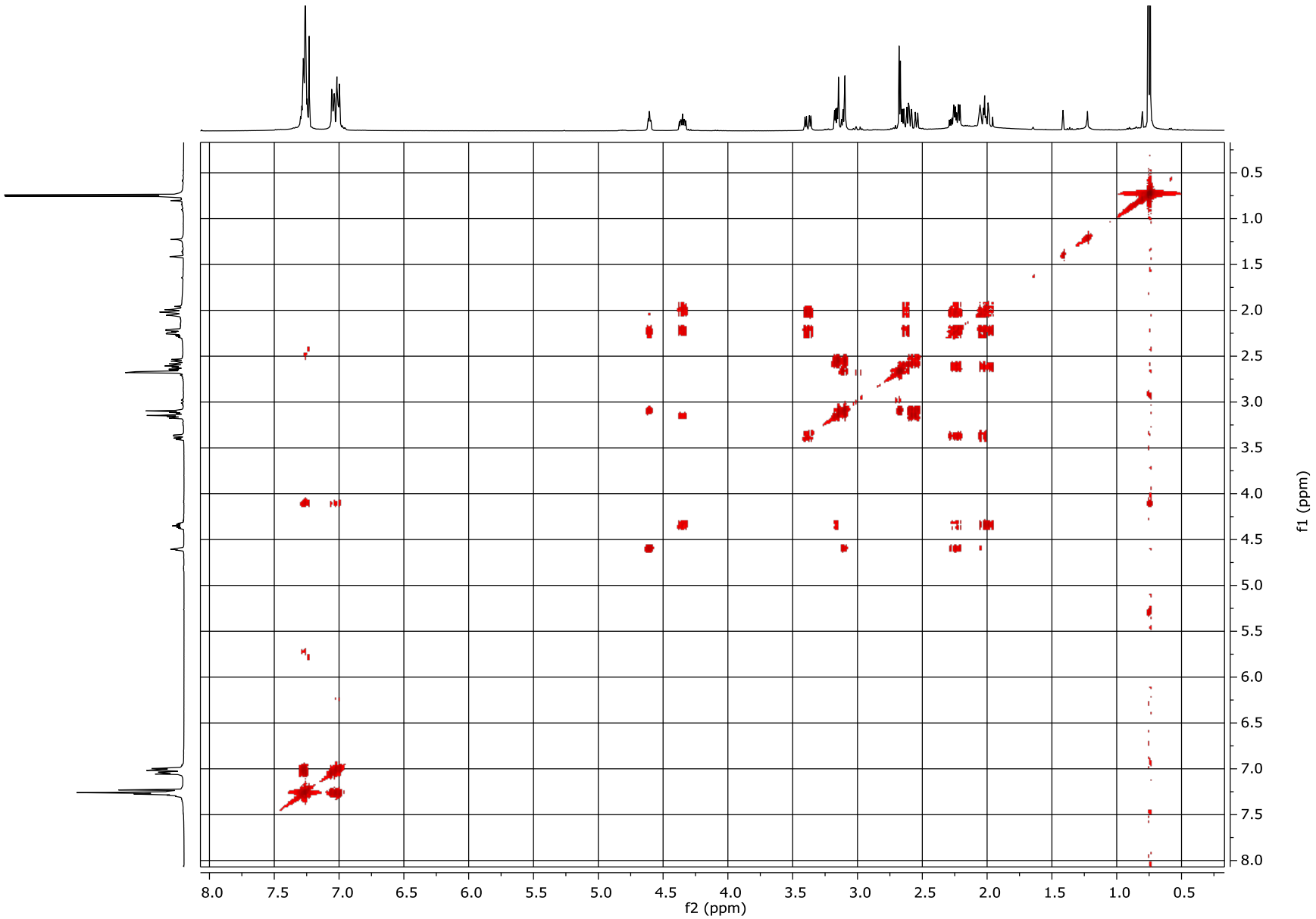
endo, *exo*-**16**

^{13}C NMR ($CDCl_3$, 100 MHz)

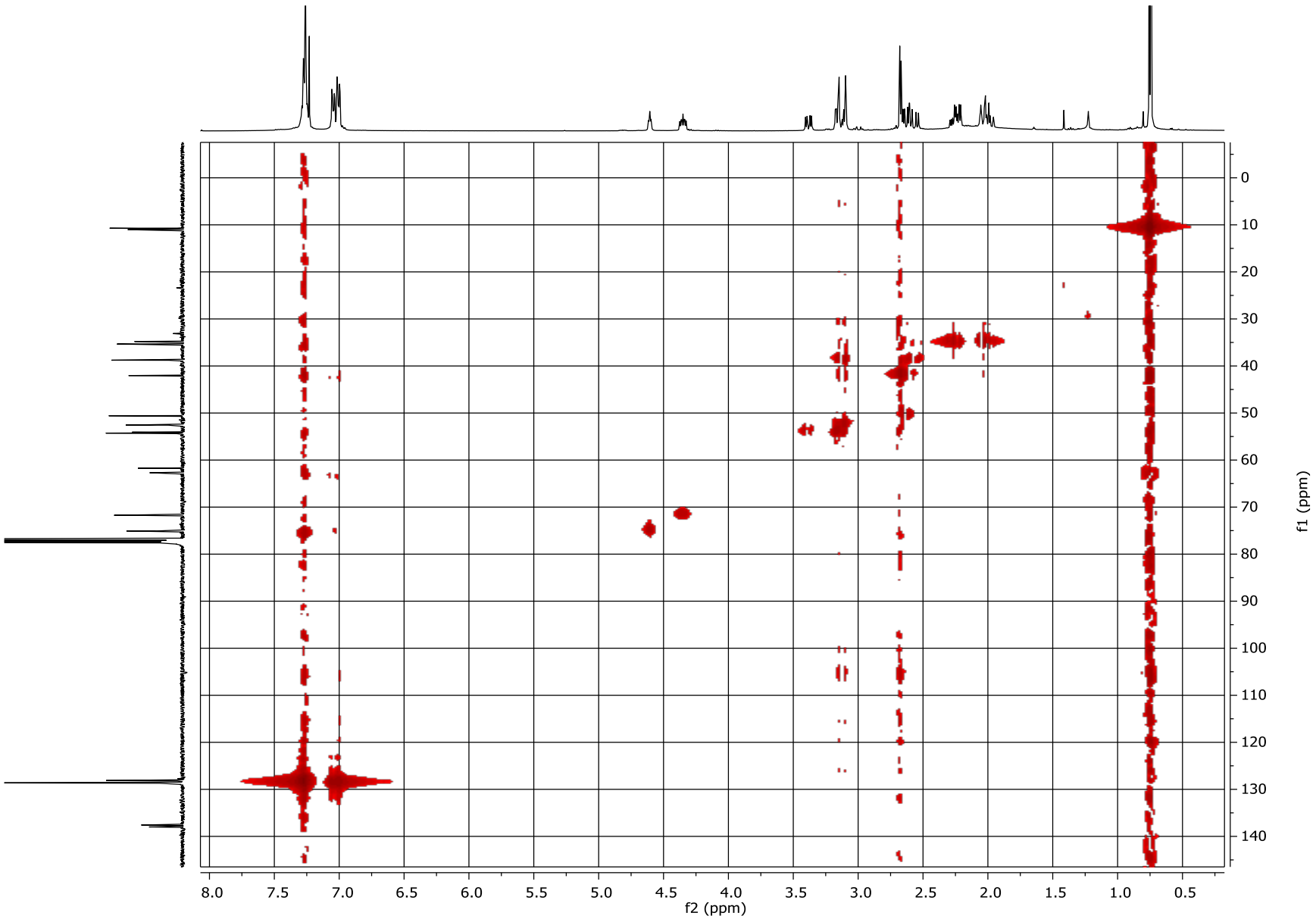


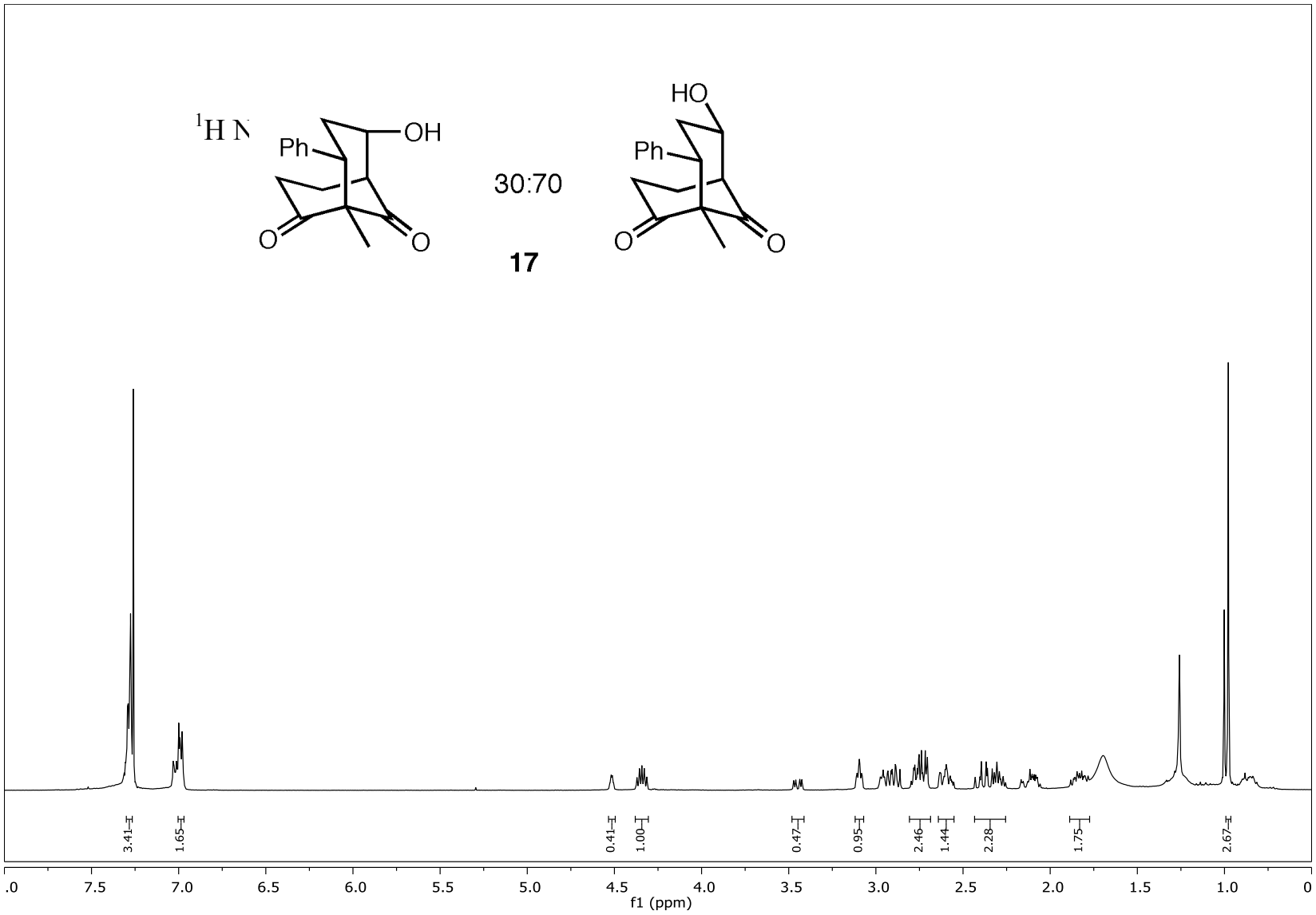
endo, *exo*-**16**


DEPT-135
128.66
128.60
128.11
71.73
54.25
50.57
38.76
35.32
10.70
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


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
f2 (ppm)
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
f1 (ppm)

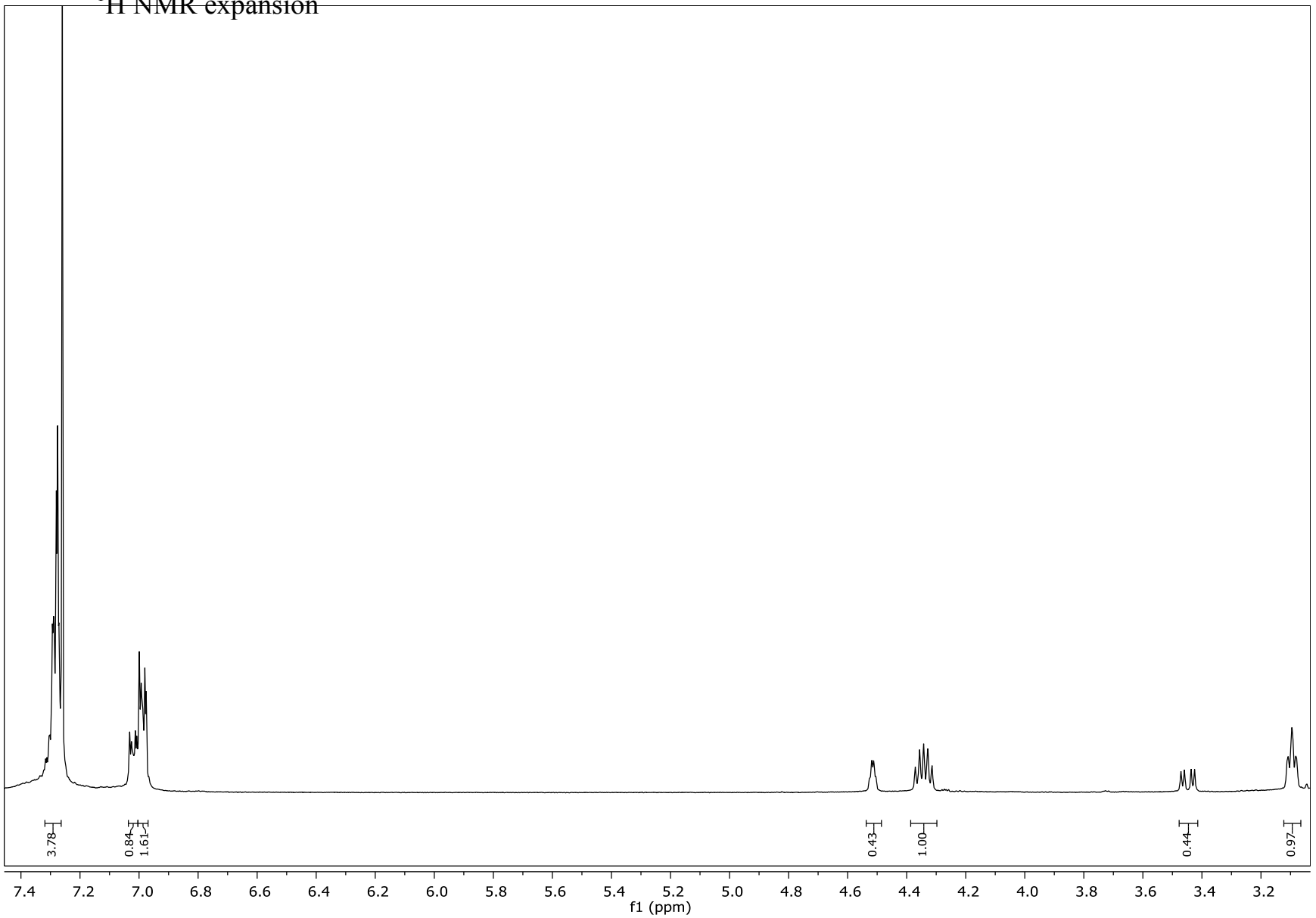
HMQC


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
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)


1H N
Ph
OH
O
O
30:70
17
HO
Ph
O
O
3.41
1.65
0.41
1.00
0.47
0.95
2.46
1.44
2.28
1.75
2.67
.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
f1 (ppm)

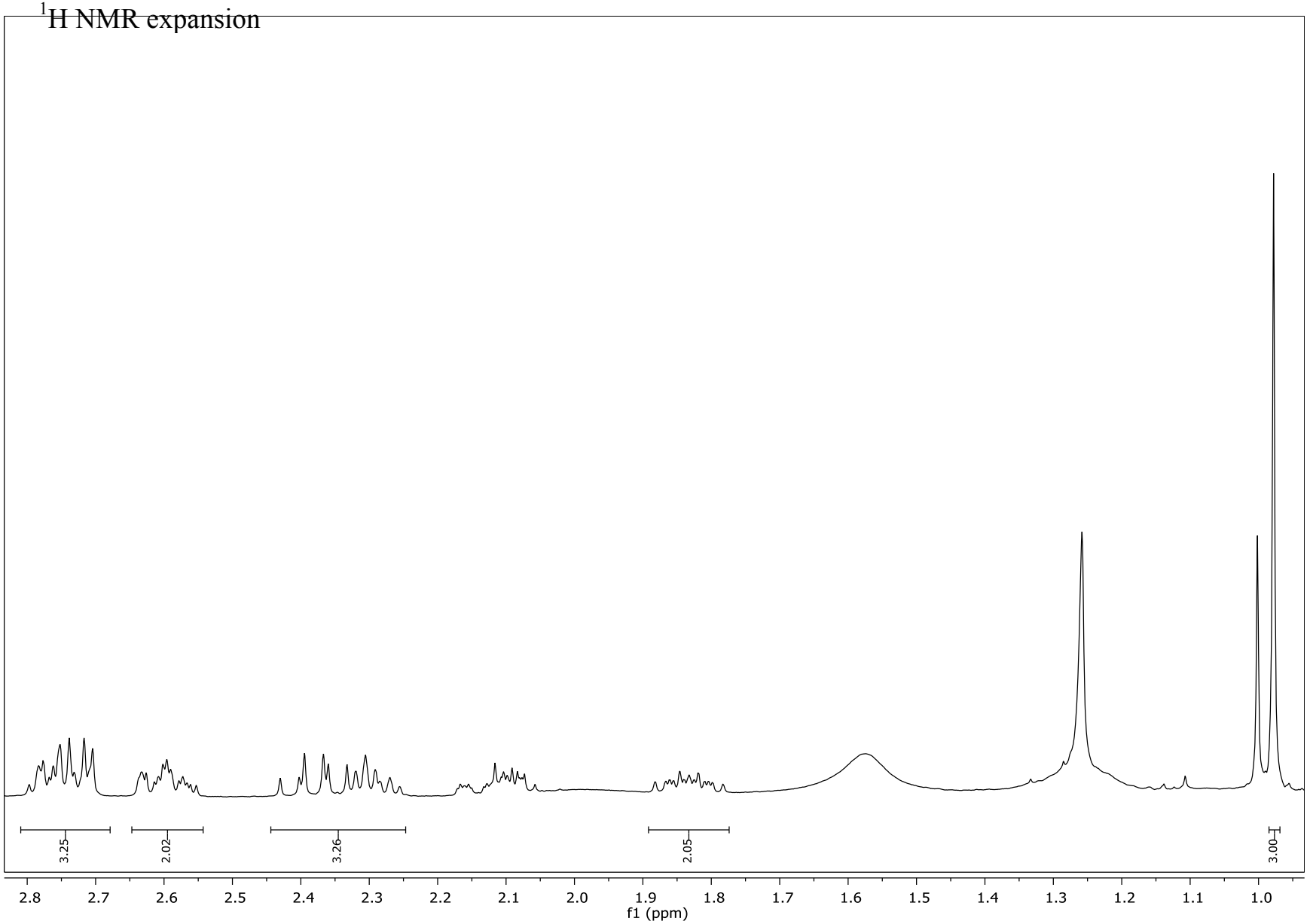
endo, *exo*-**17**

^{1}H NMR expansion



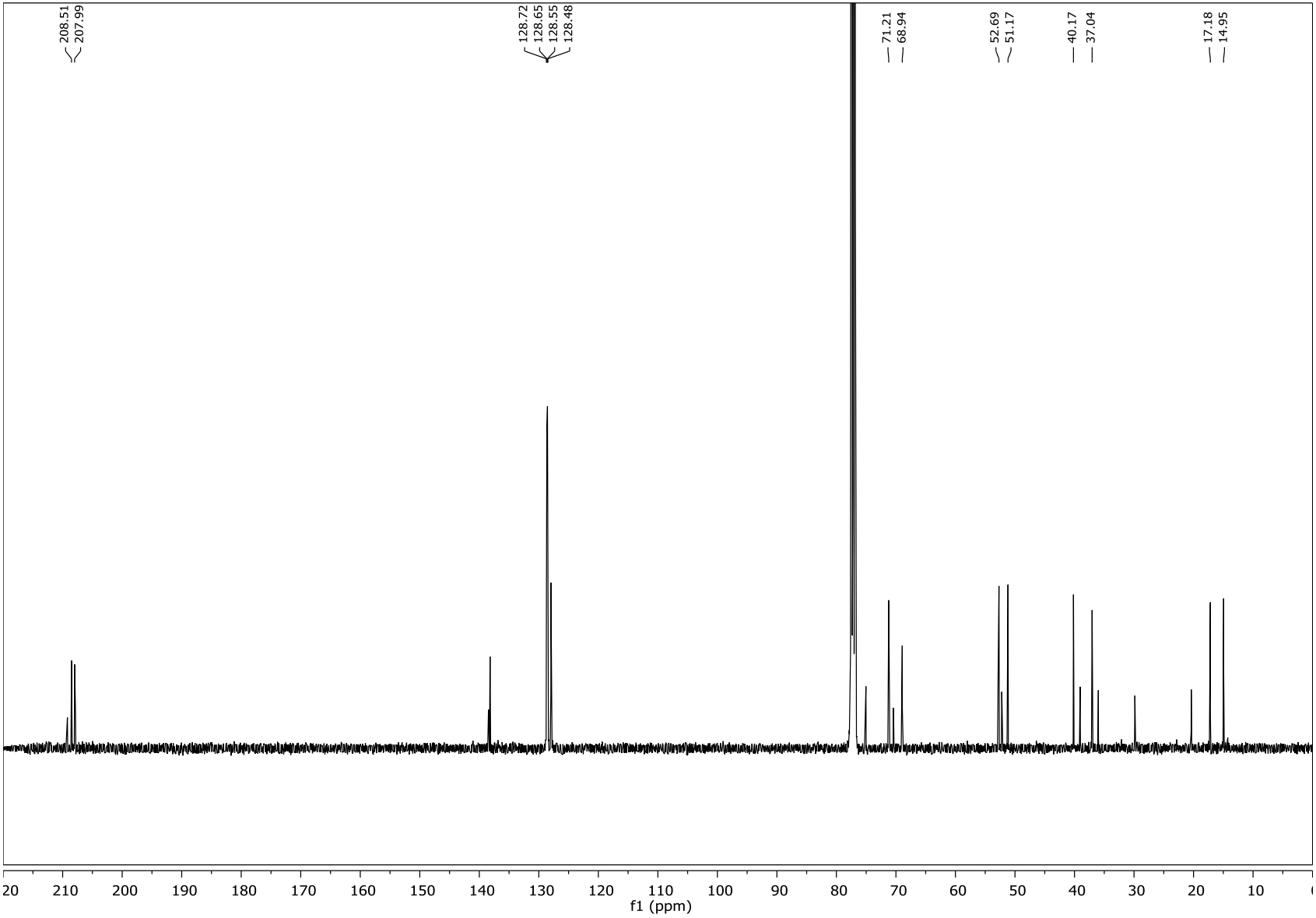
endo, *exo*-**17**

^{1}H NMR expansion



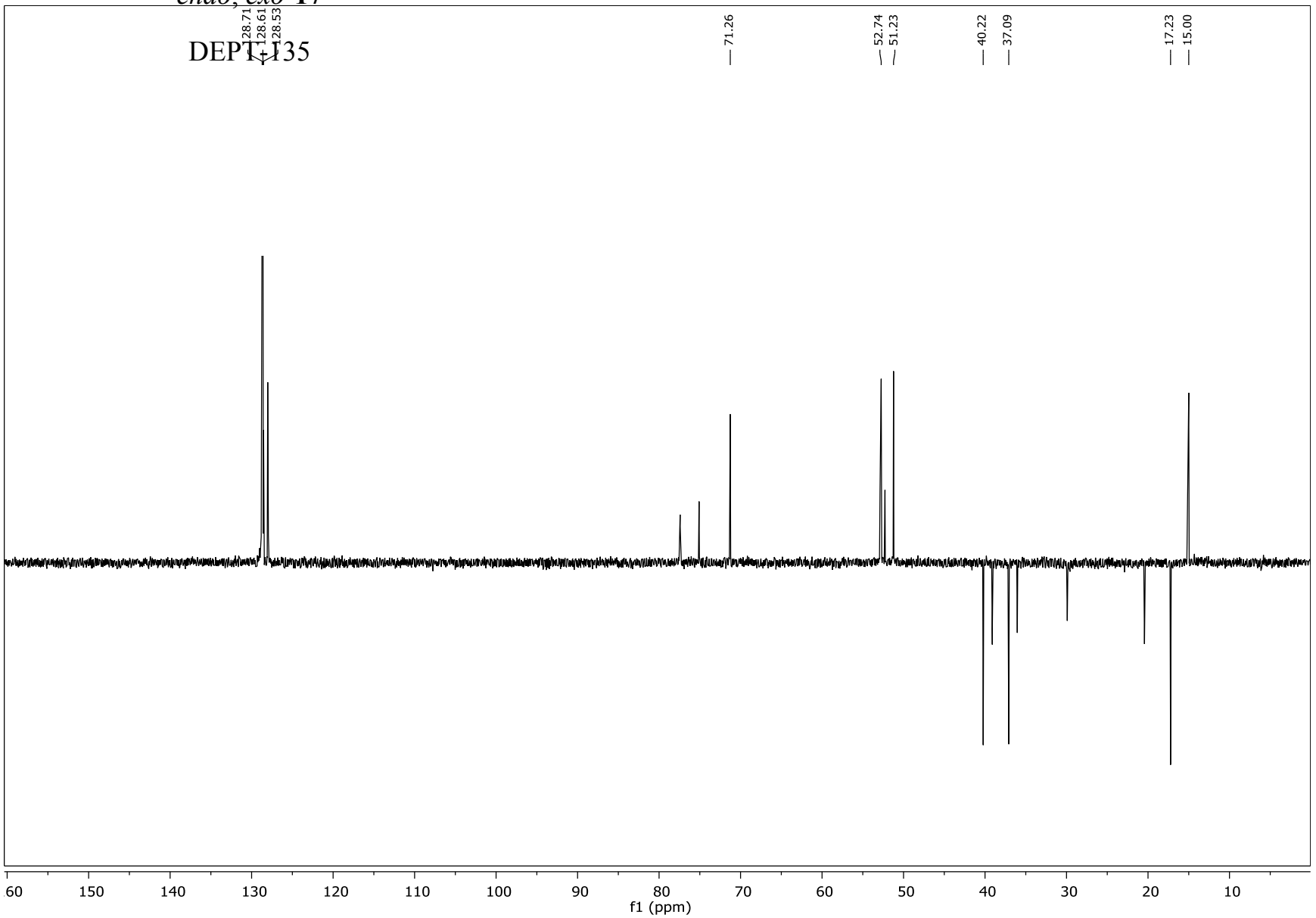
endo, *exo*-**17**

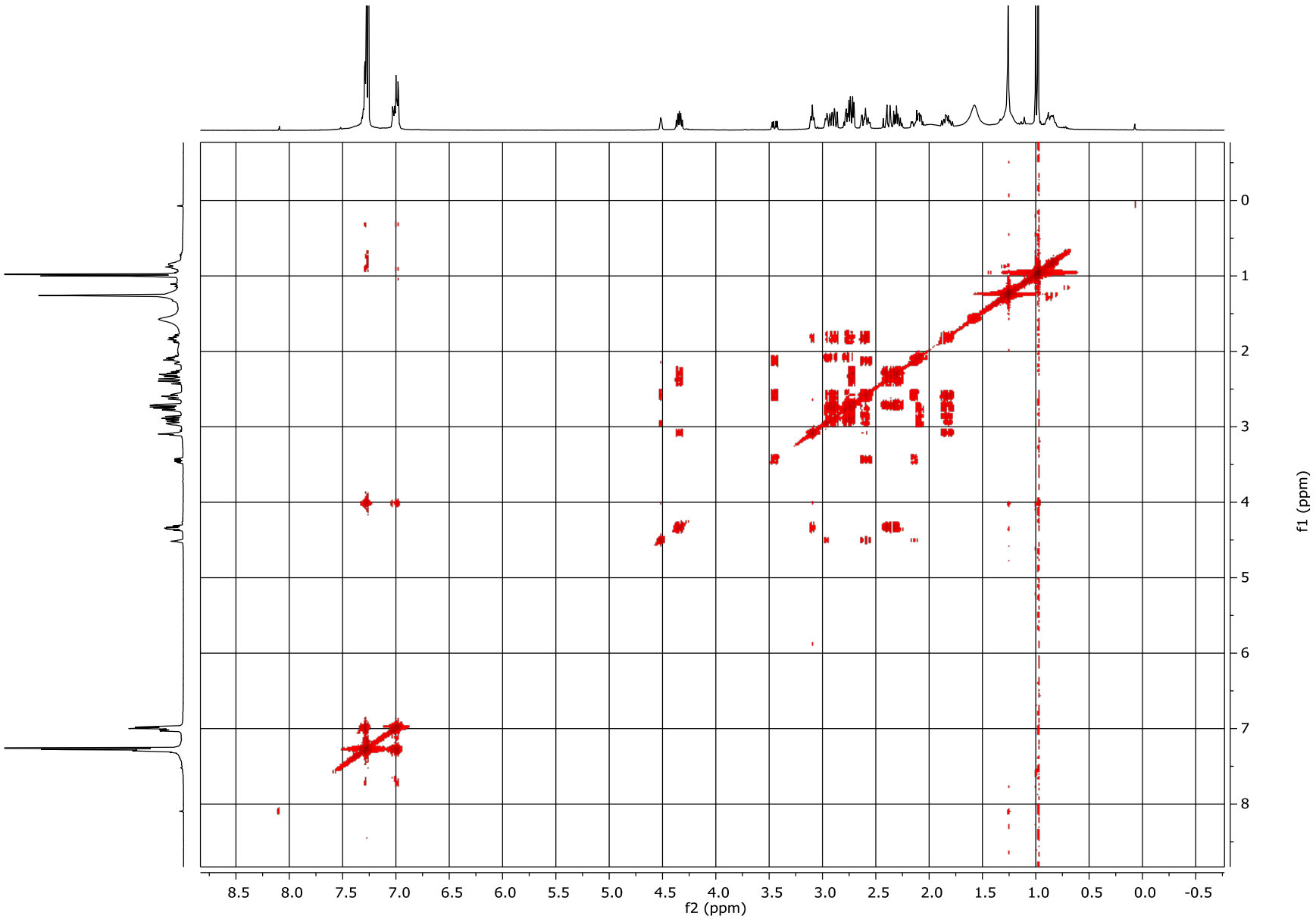
^{13}C NMR ($CDCl_3$, 100 MHz)

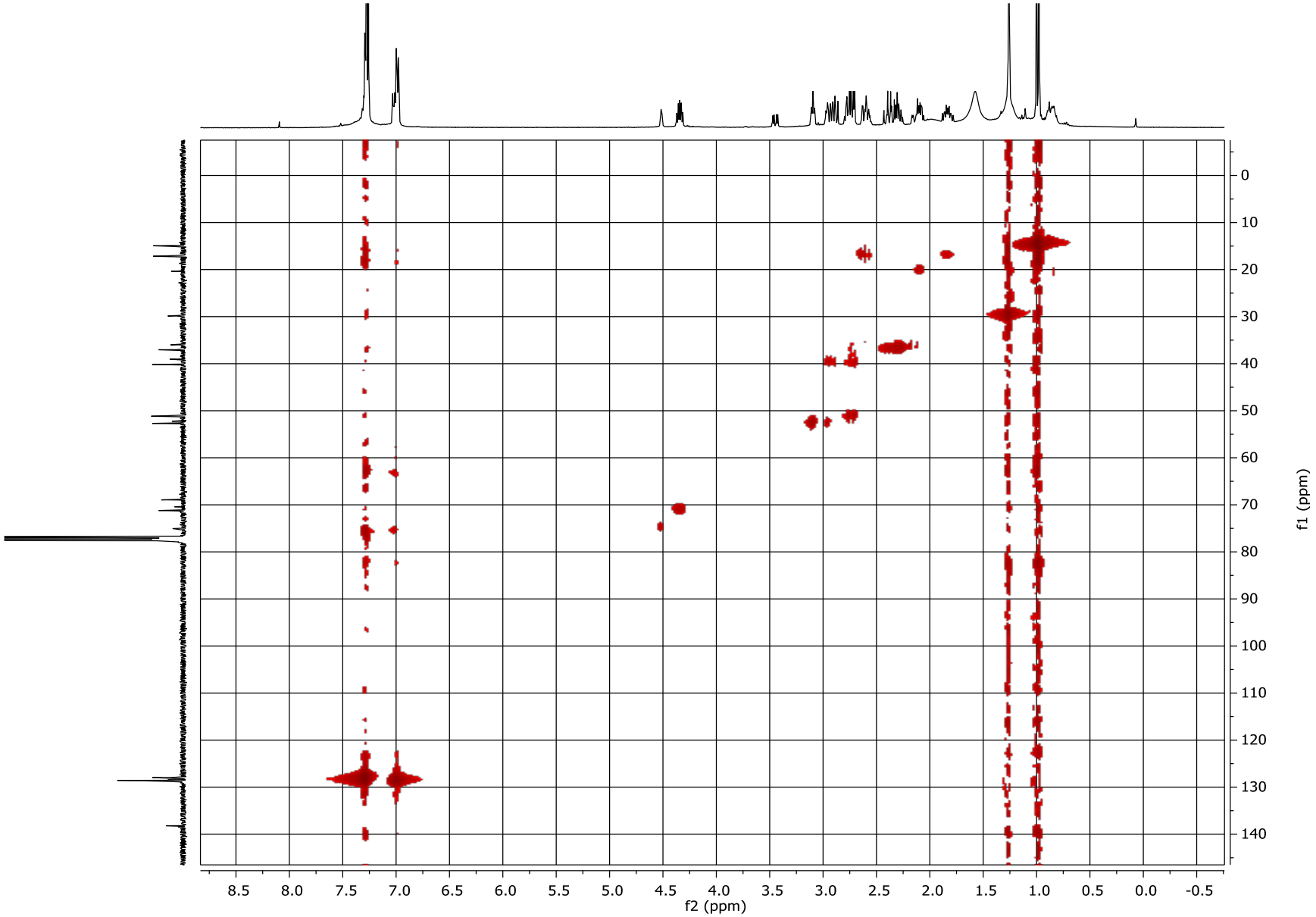


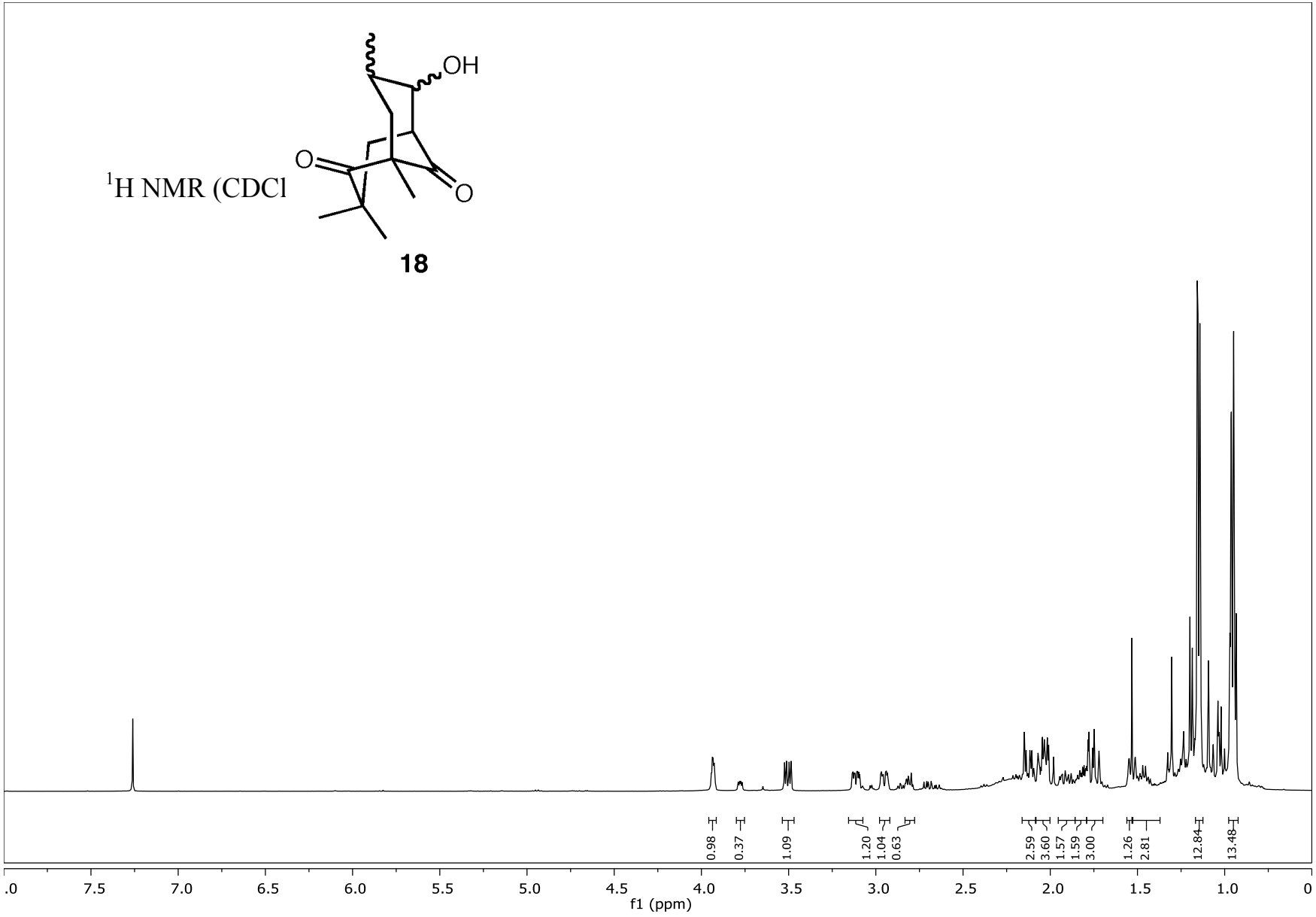
endo, *exo*-**17**

DEPT-135




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
f2 (ppm)
0
1
2
3
4
5
6
7
8
f1 (ppm)

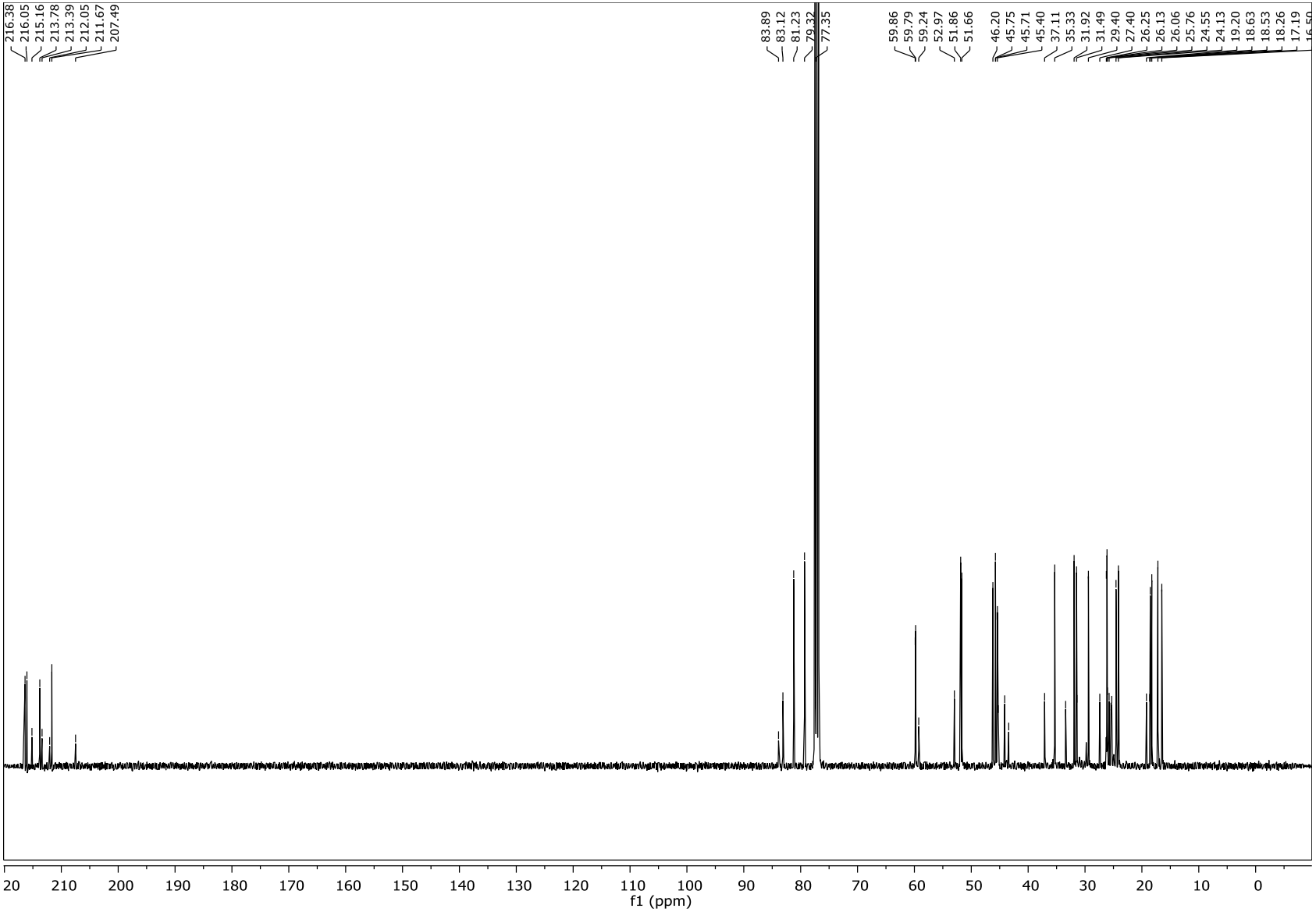

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)

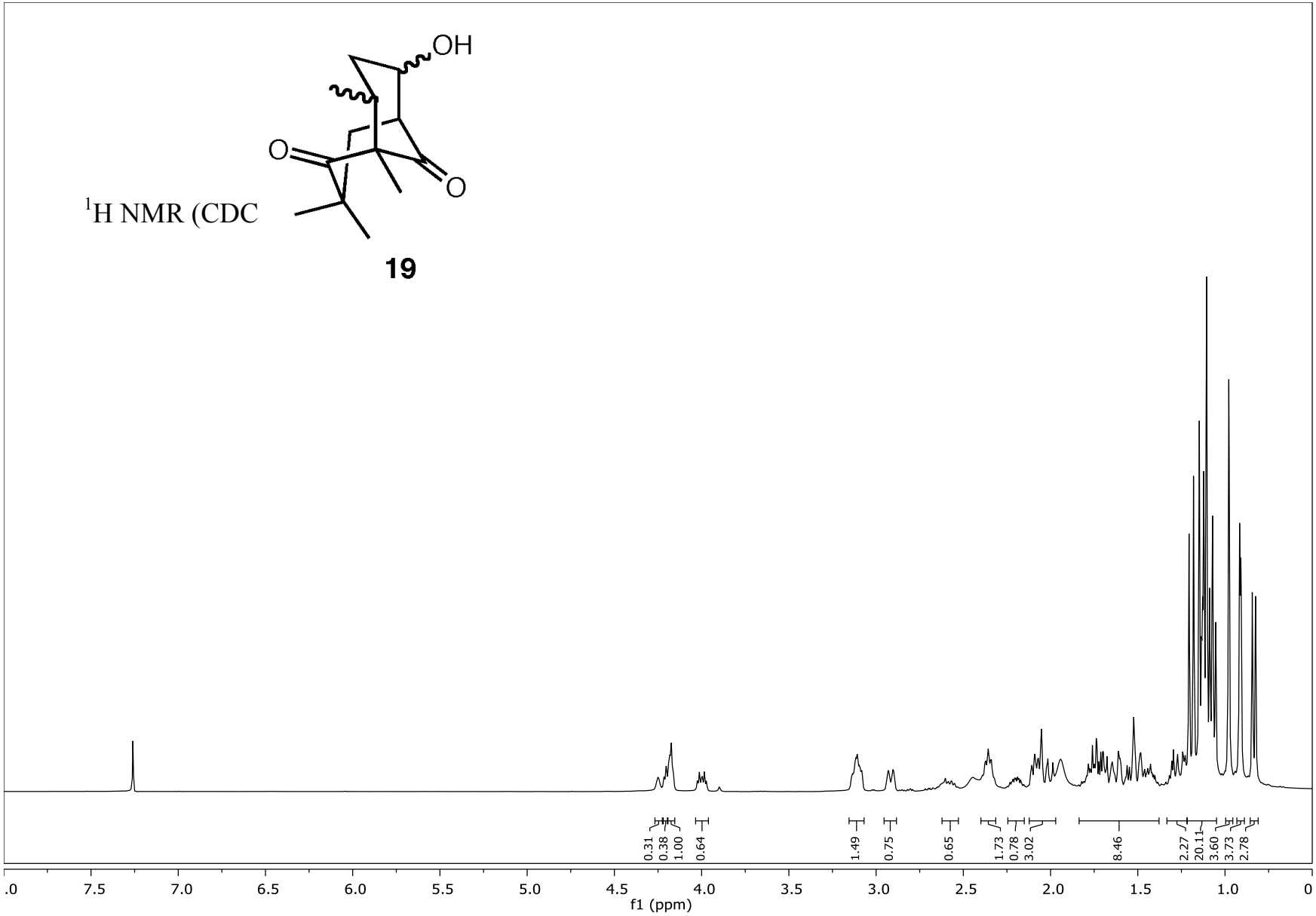

OH
O
O
18
0.98
0.37
1.09
1.20
1.04
0.63
2.59
3.60
1.57
1.59
3.00
1.26
2.81
12.84
13.48
f1 (ppm)

^{1}H NMR (CDCl

18

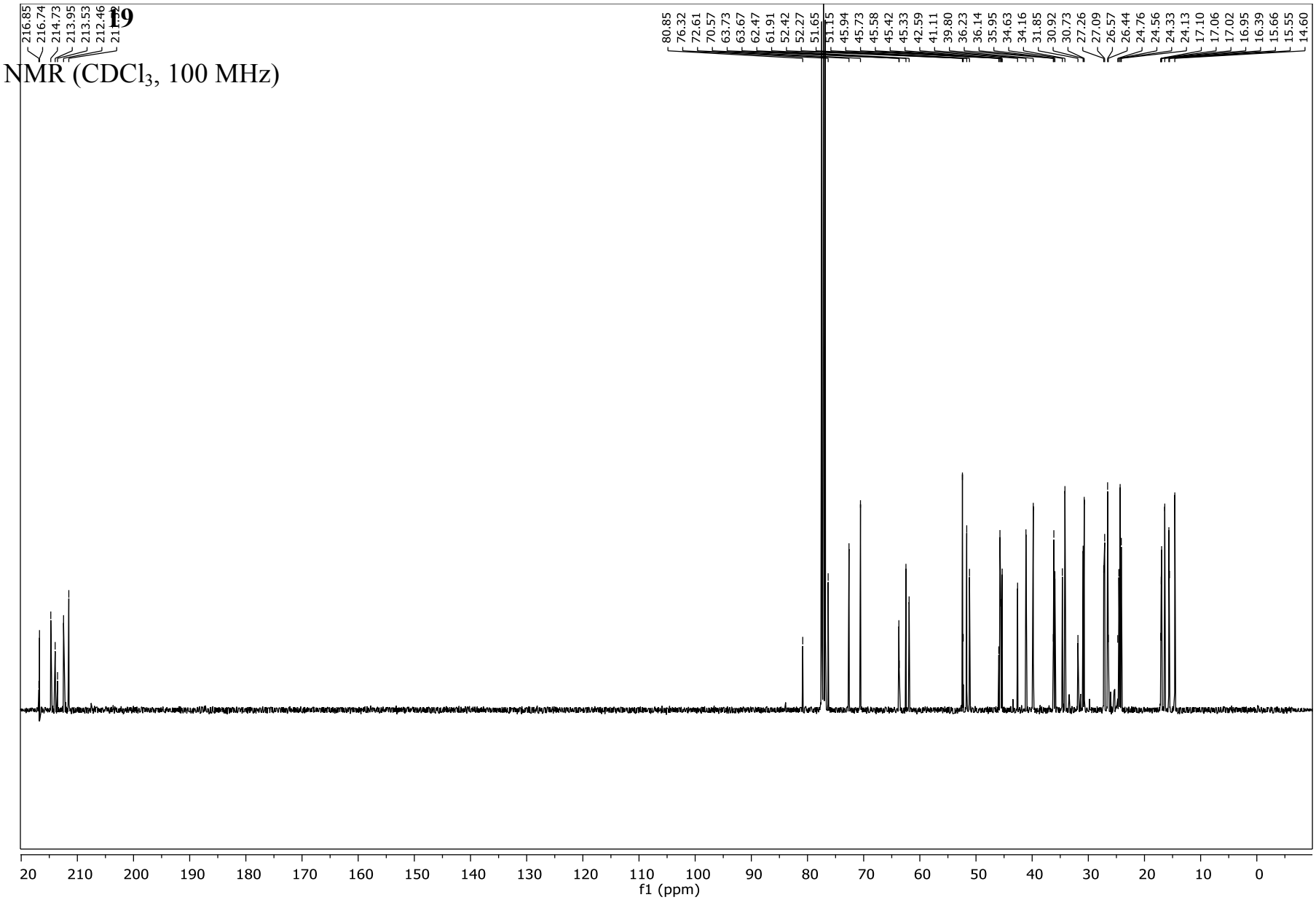
^{13}C NMR ($CDCl_3$, 100 MHz)

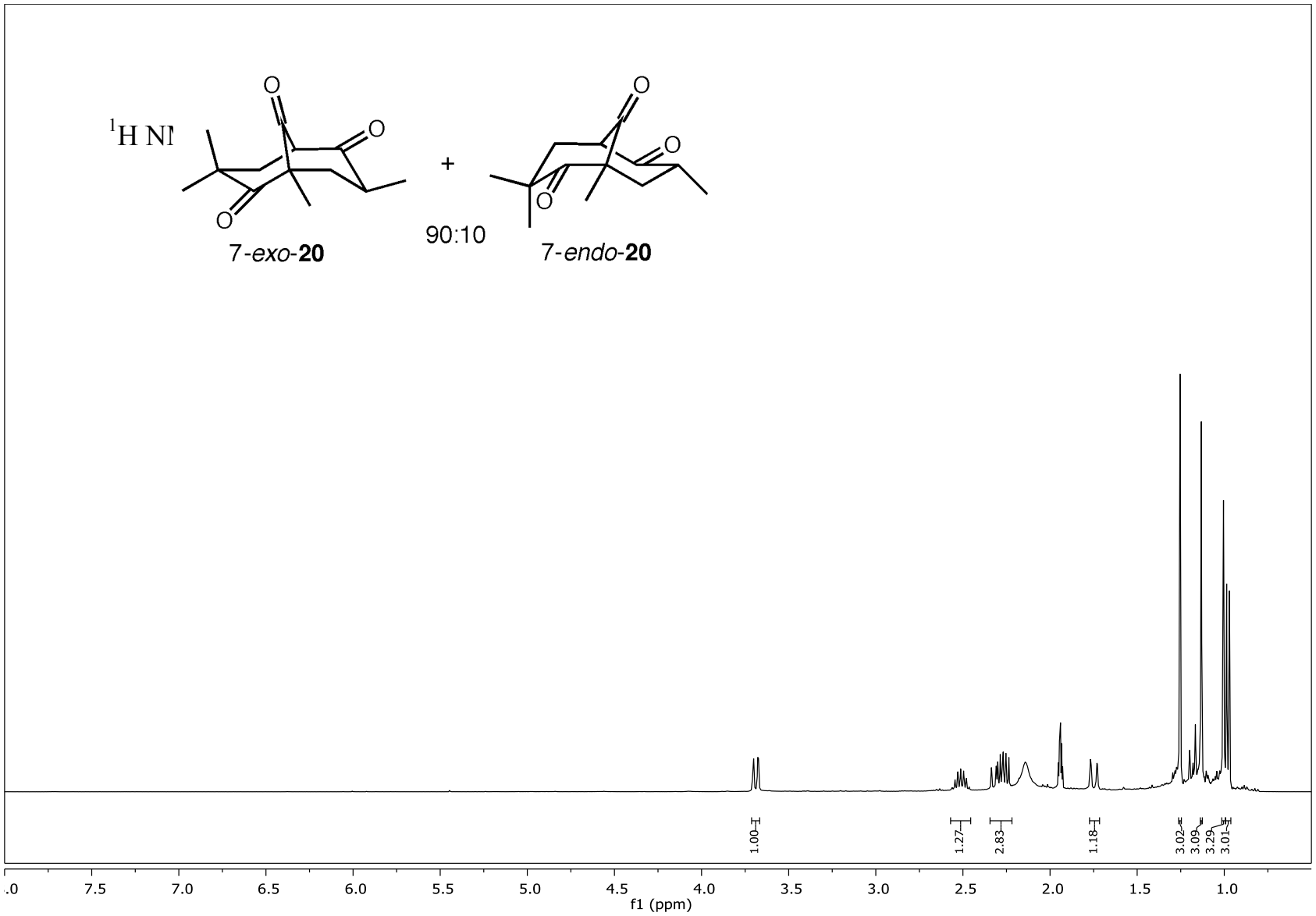



OH
O
O
19
^{1}H NMR (CDC
0.31
0.38
1.00
0.64
1.49
0.75
0.65
1.73
0.78
3.02
8.46
2.27
20.11
3.60
3.73
2.78
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0
f1 (ppm)

f9

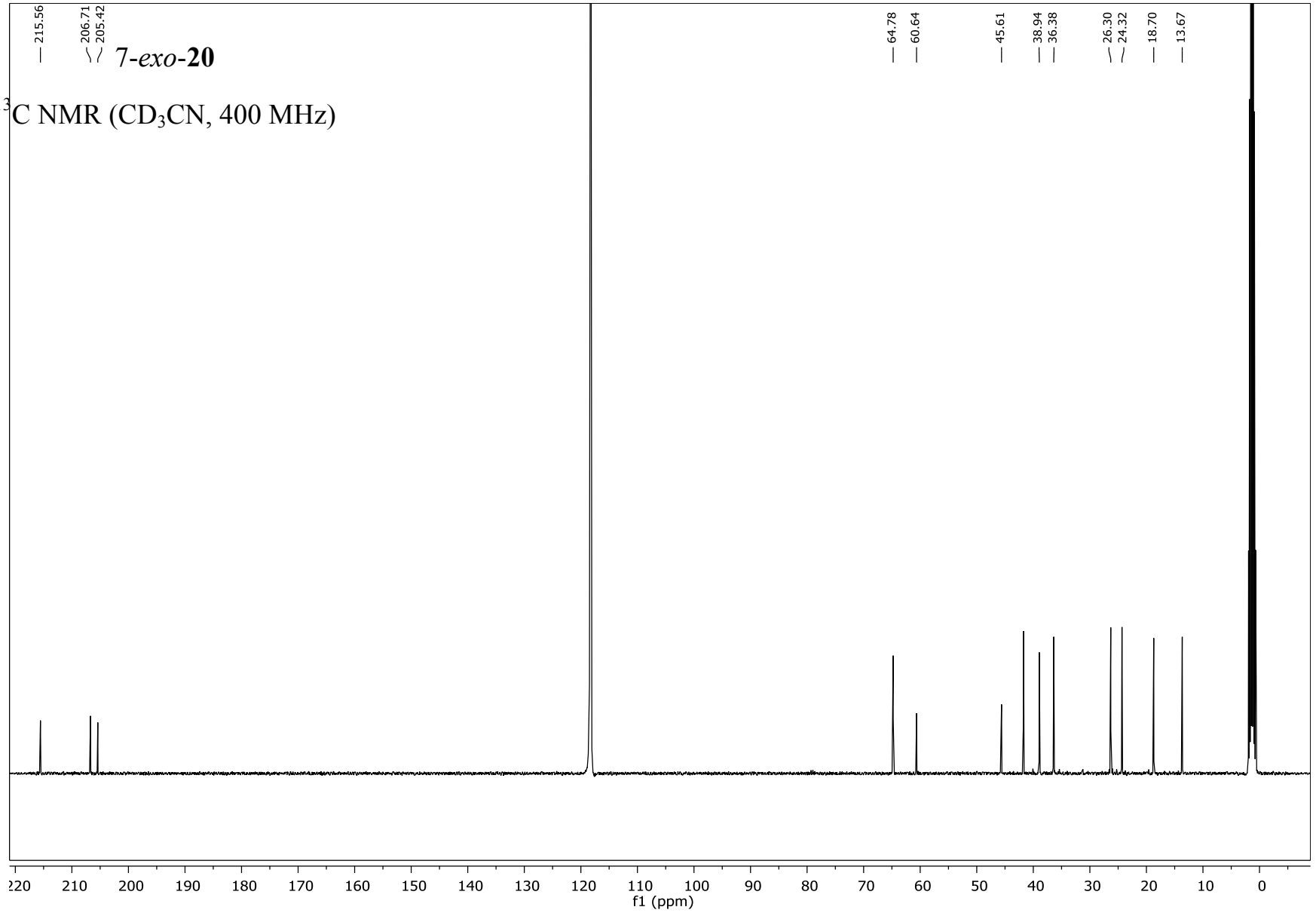
^{13}C NMR ($CDCl_3$, 100 MHz)




1H NM
O
O
O
O
+
O
O
O
90:10
7-exo-20
7-endo-20
1.00
1.27
2.83
1.18
3.02
3.09
3.29
3.01
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)

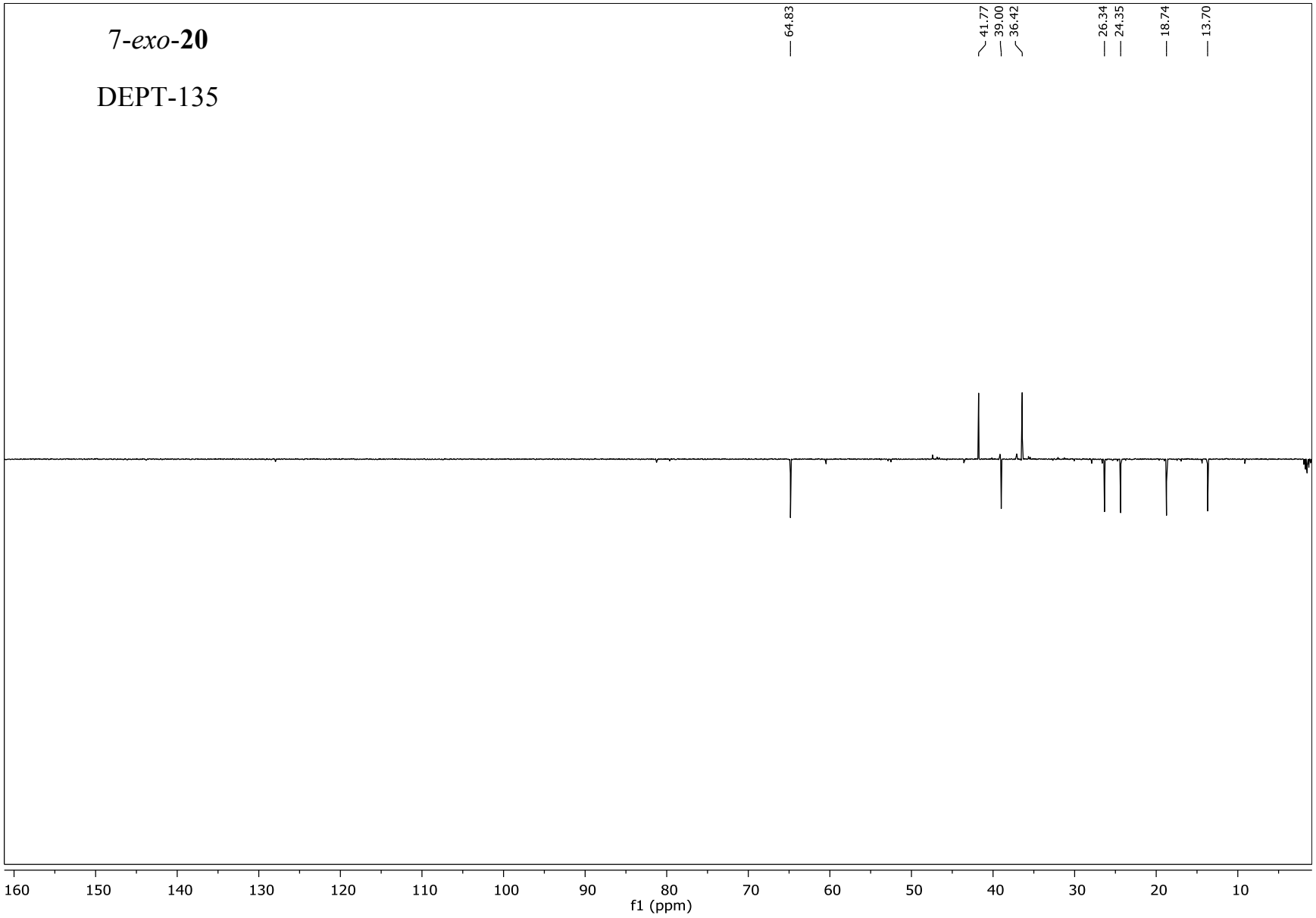
7-*exo*-**20**

^{13}C NMR (CD_3CN, 400 MHz)

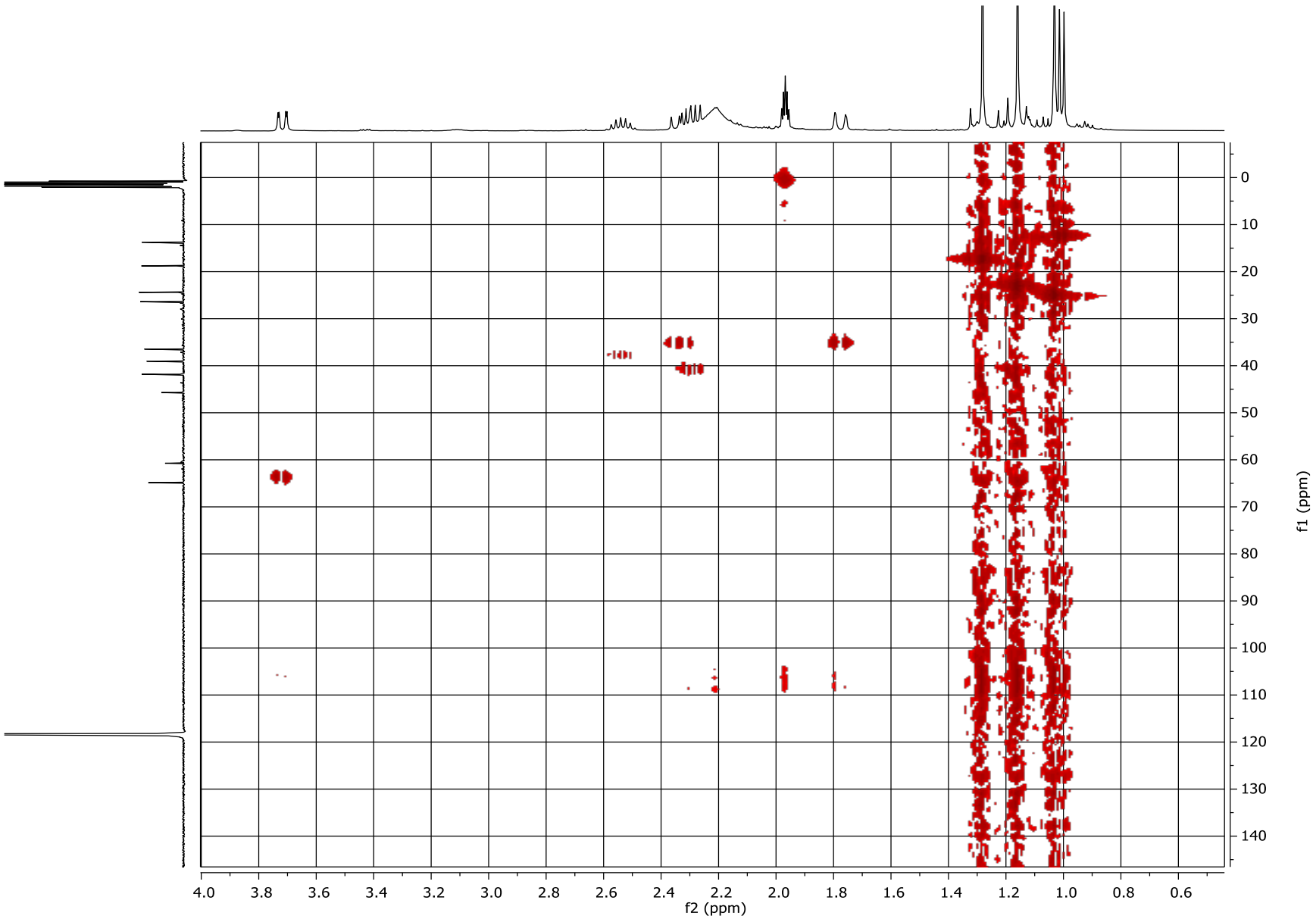


7-*exo*-**20**

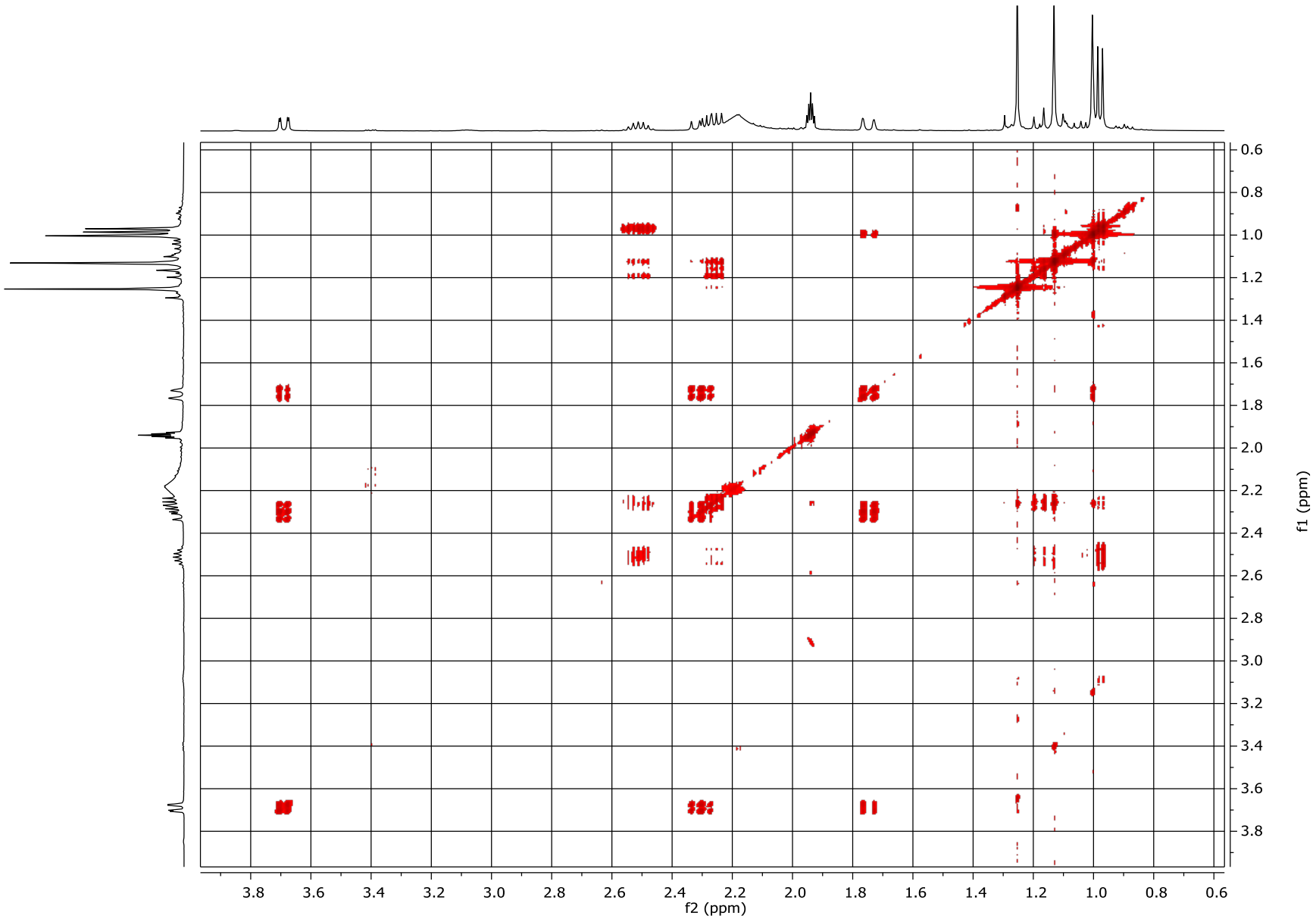
DEPT-135

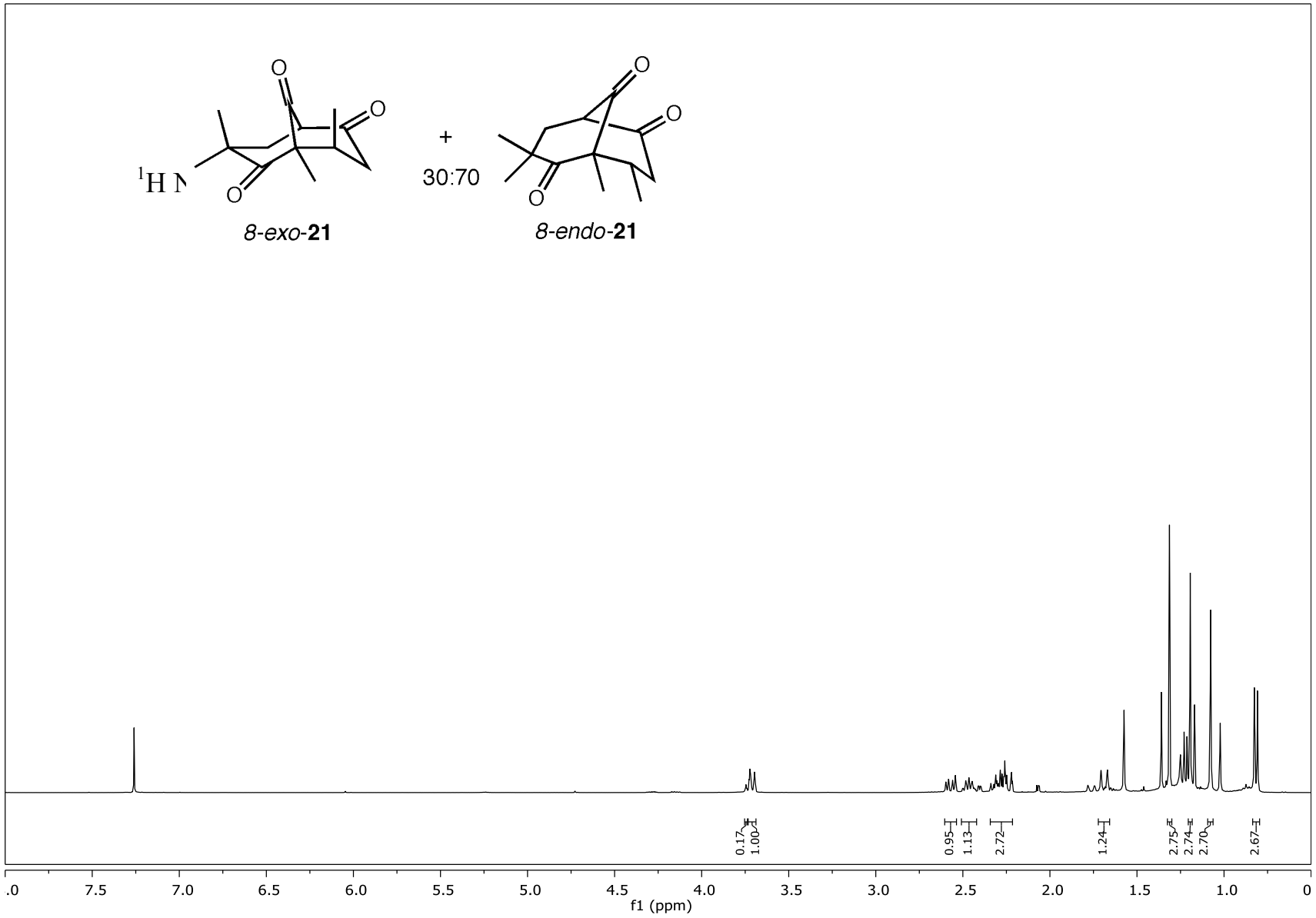


HMQC


4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)

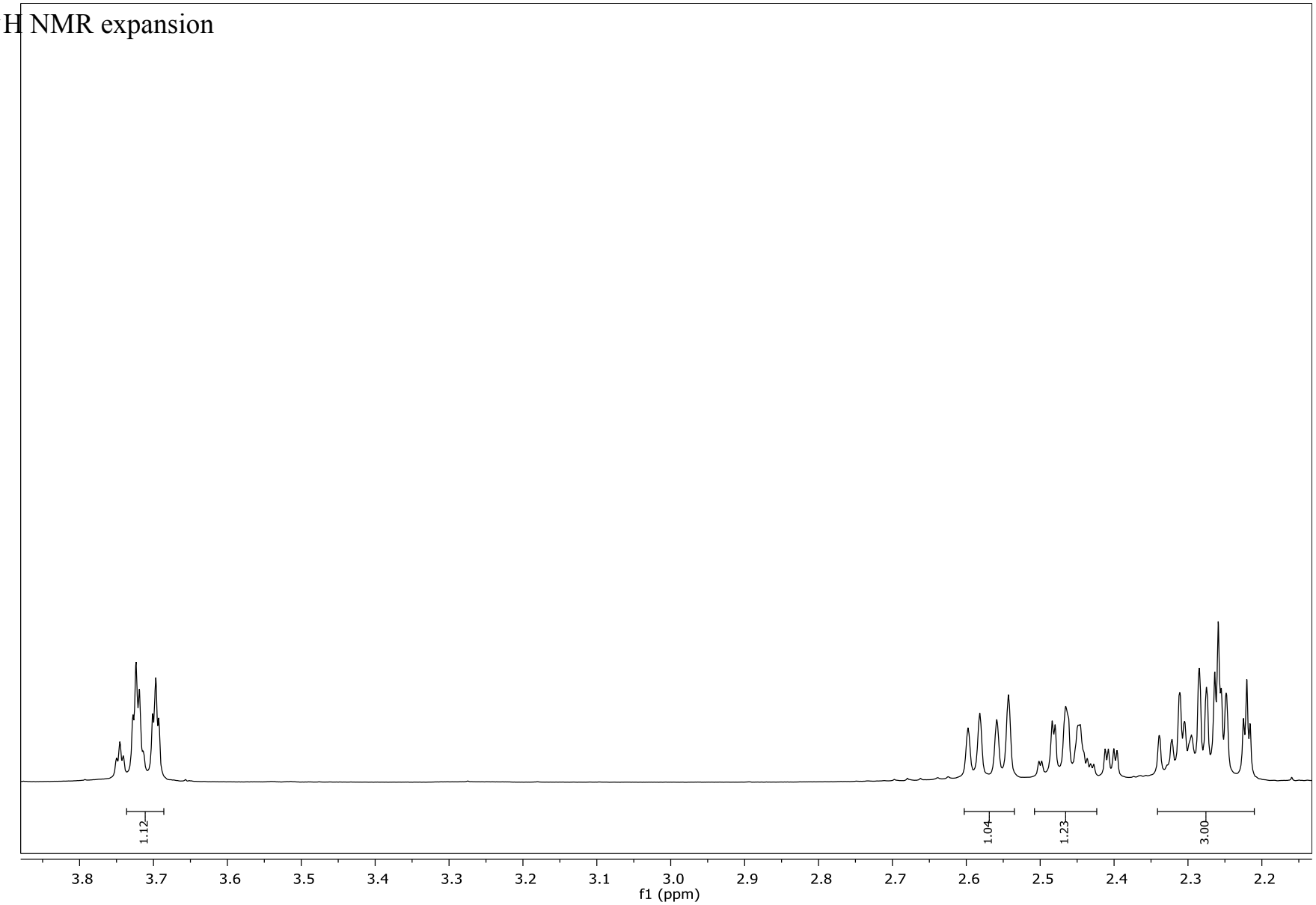
COSY-90




O
O
O
+
30:70
O
O
O
8-exo-21
8-endo-21
0.17
1.00
0.95
1.13
2.72
1.24
2.75
2.74
2.70
2.67
.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
f1 (ppm)

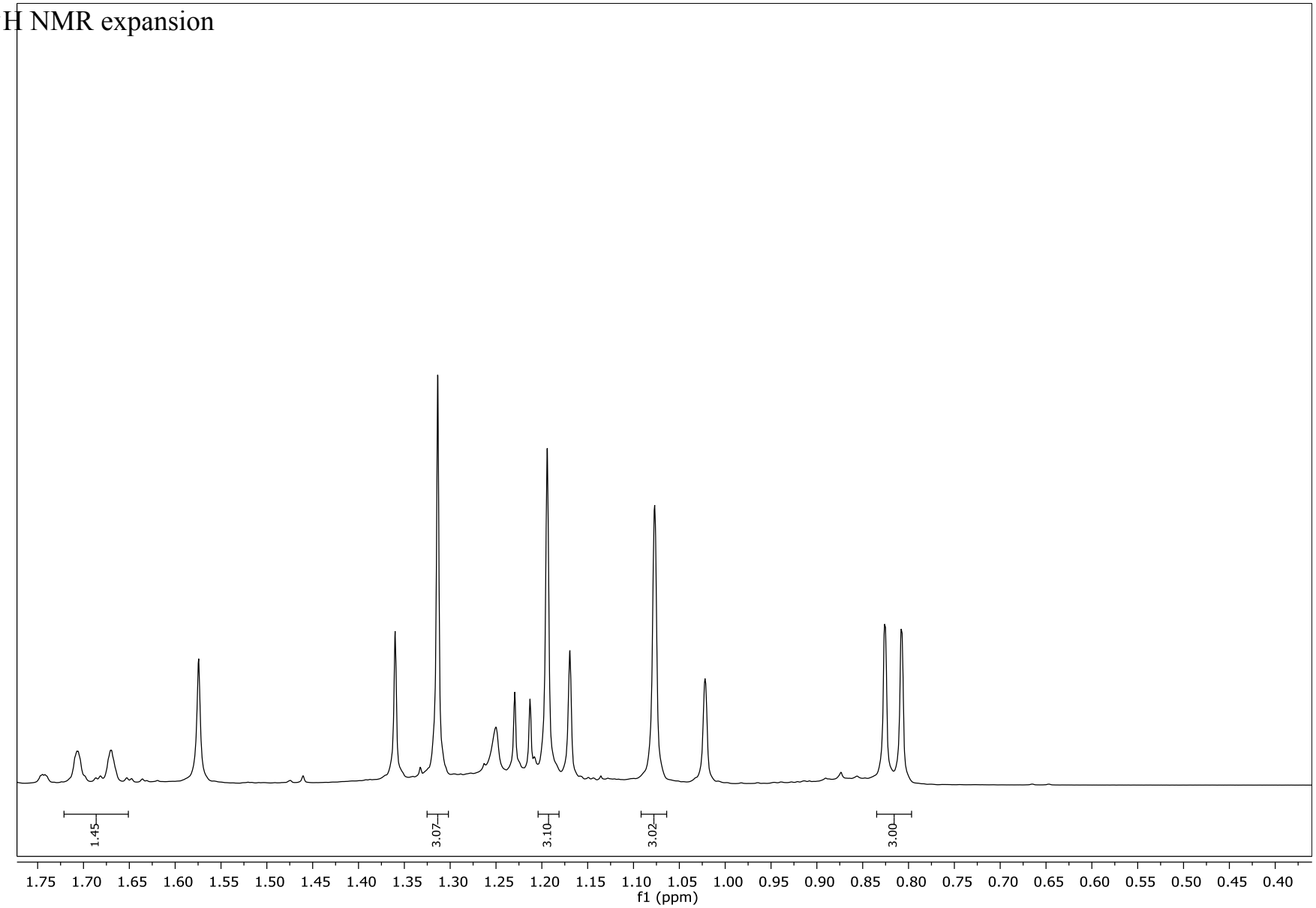
8-*exo*-**21,** 8-*endo*-**21**

^{1}H NMR expansion



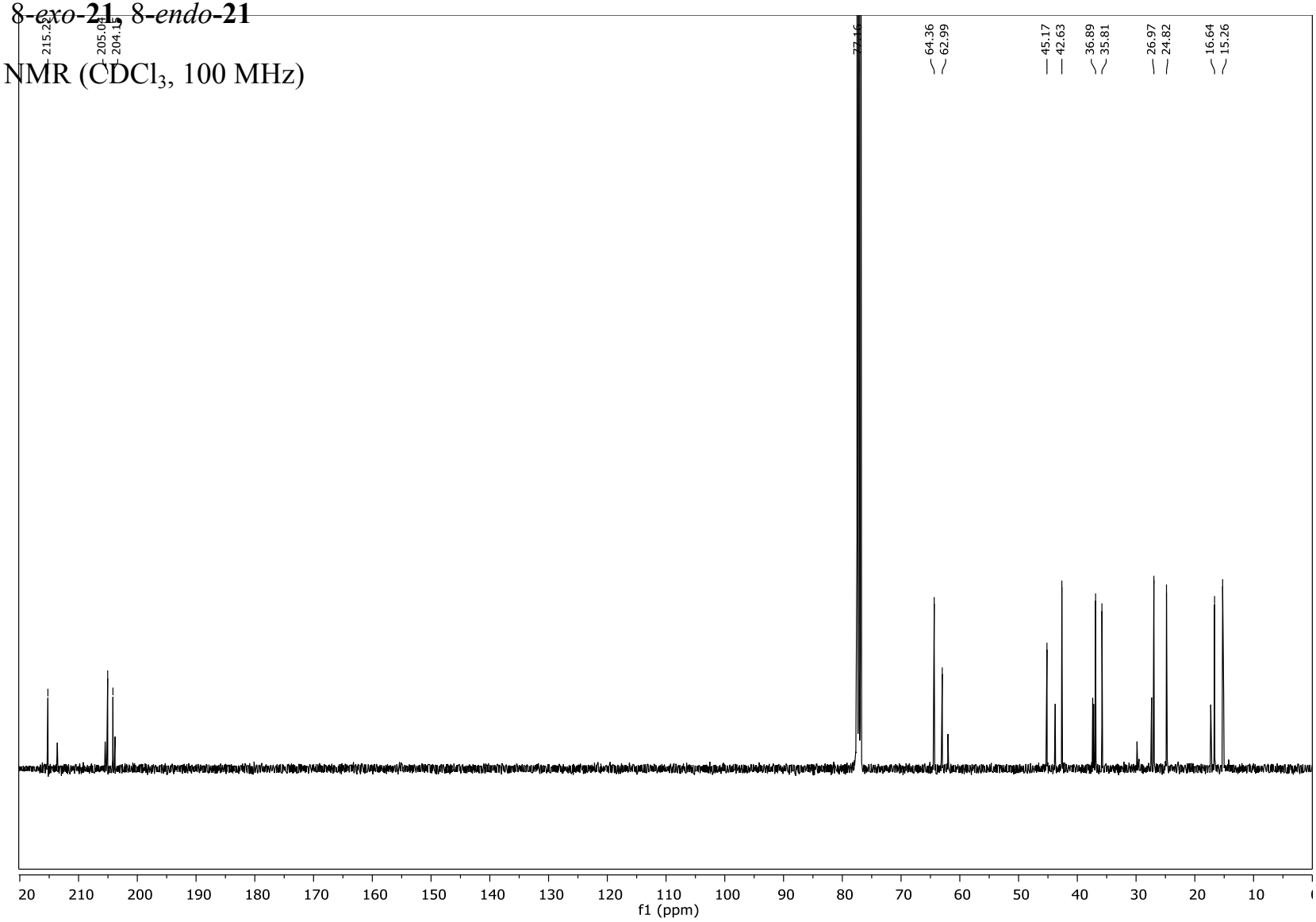
8-*exo*-**21,** 8-*endo*-**21**

^{1}H NMR expansion

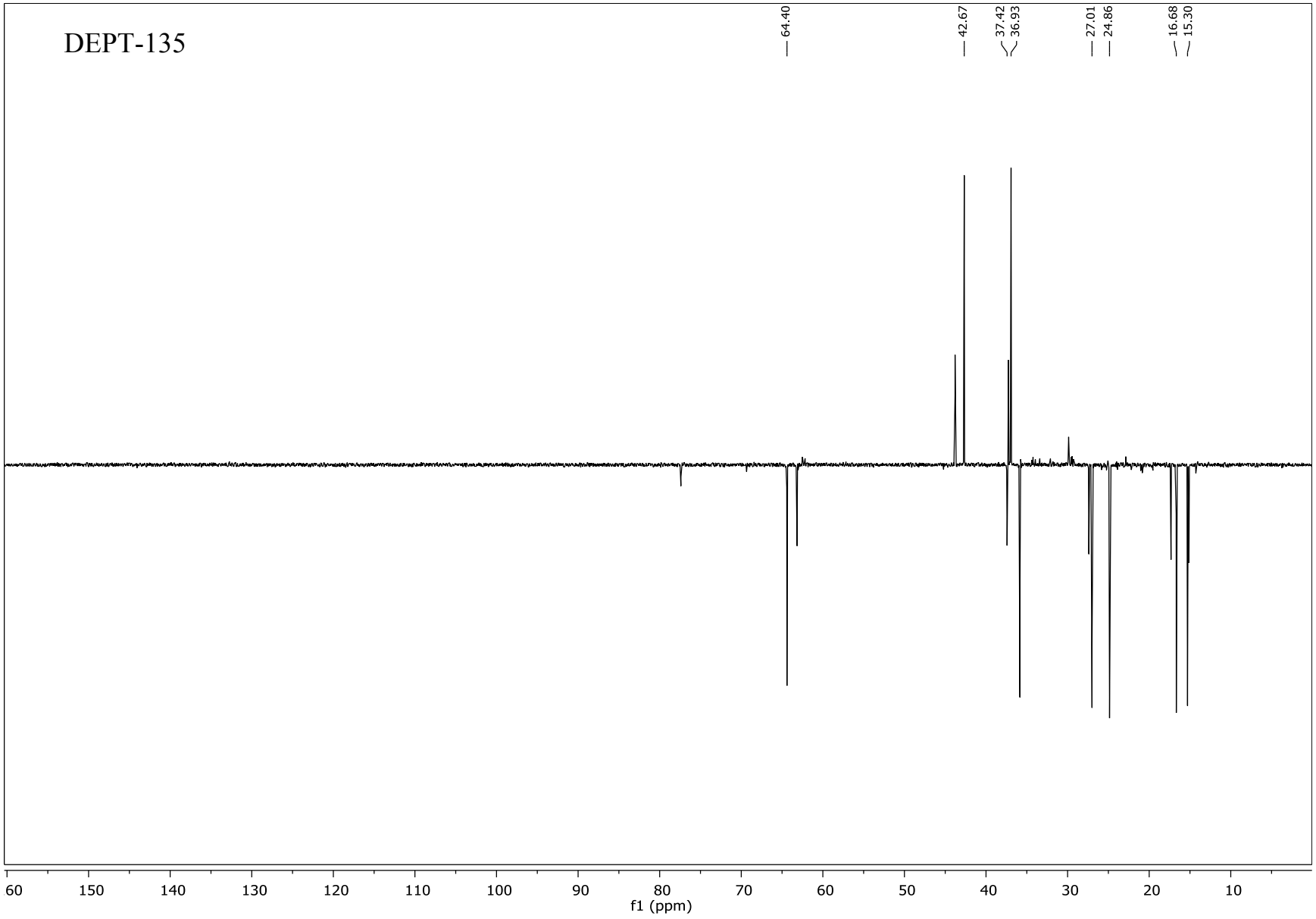


8-*exo*-**21**, 8-*endo*-**21**

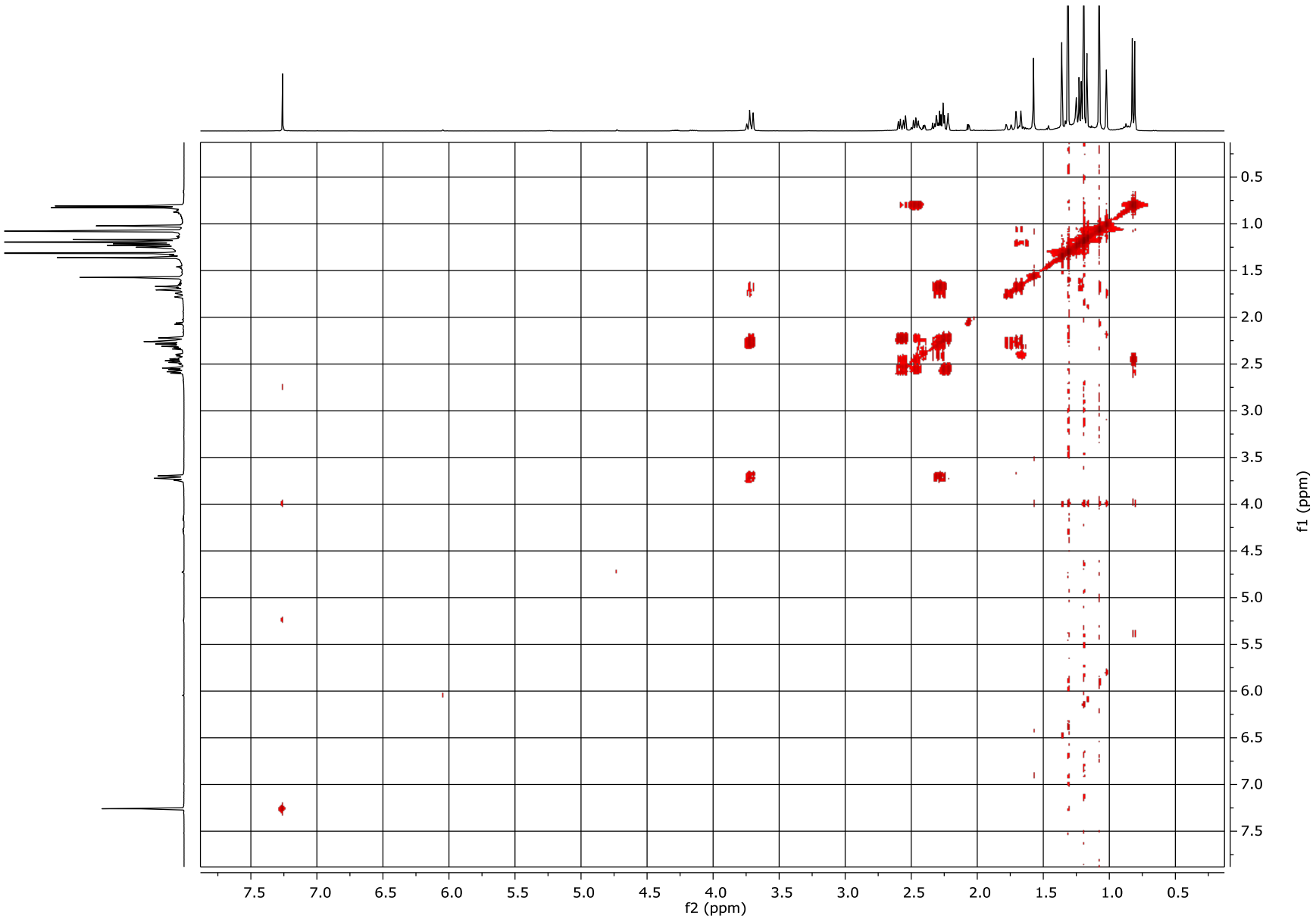
^{13}C NMR ($CDCl_3$, 100 MHz)



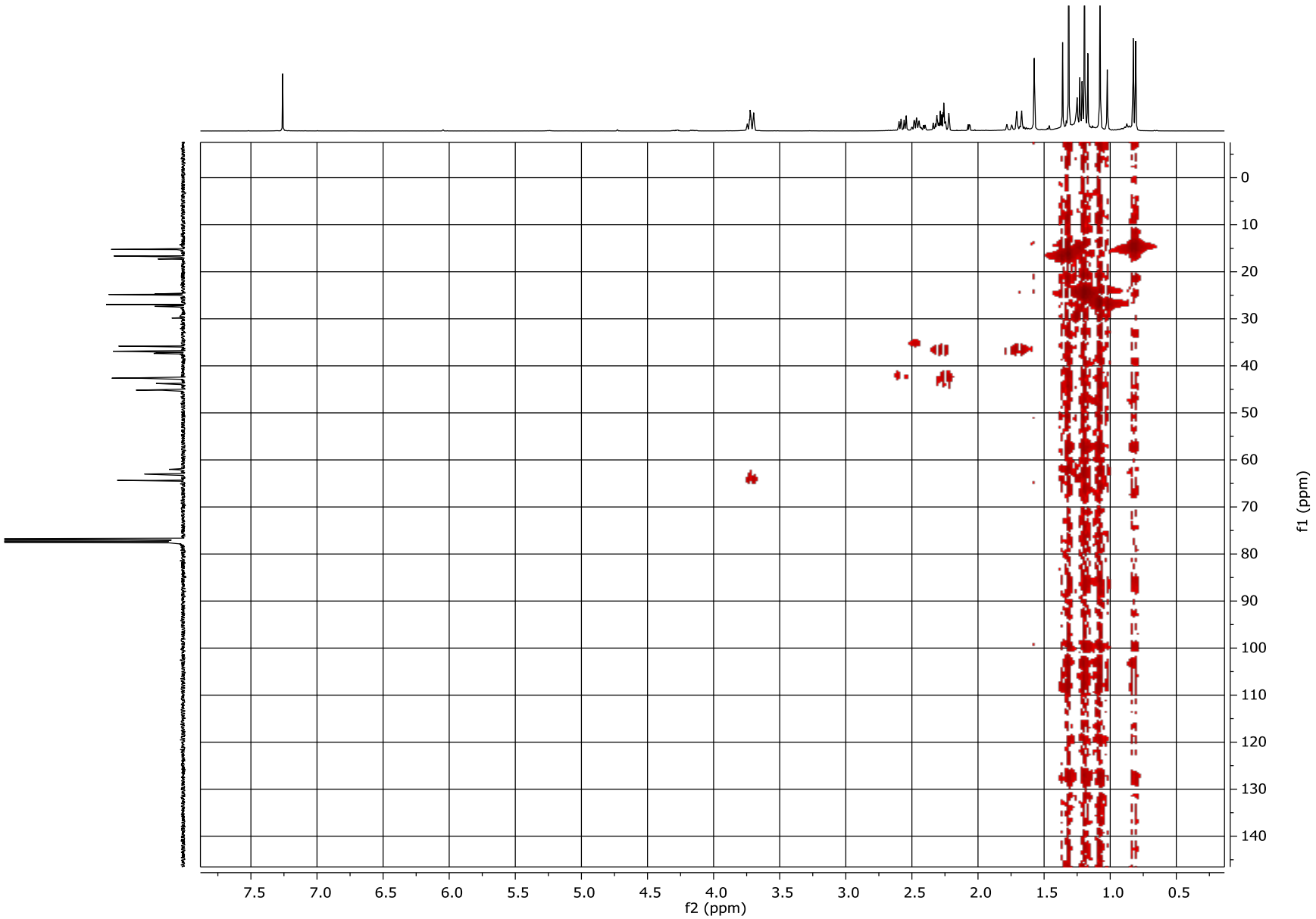
8-*exo*-**21,** 8-*endo*-**21**



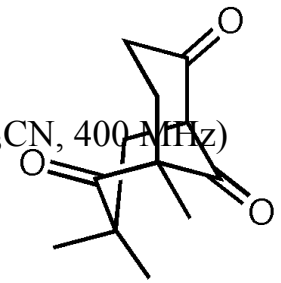
COSY-90


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
f2 (ppm)
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
f1 (ppm)

HMQC


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
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)

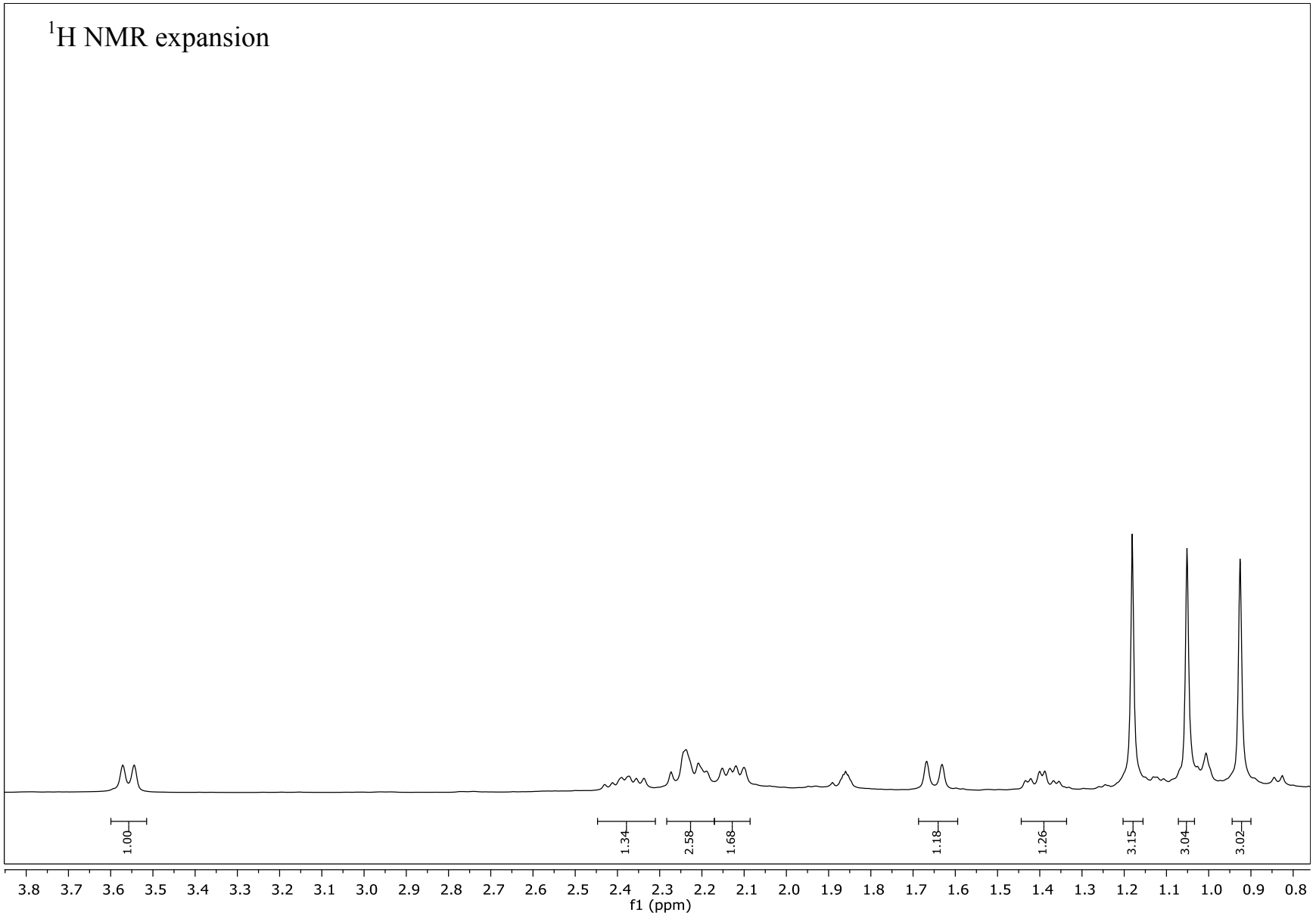
^{1}H NMR (CD_3CN, 400 MHz)



22

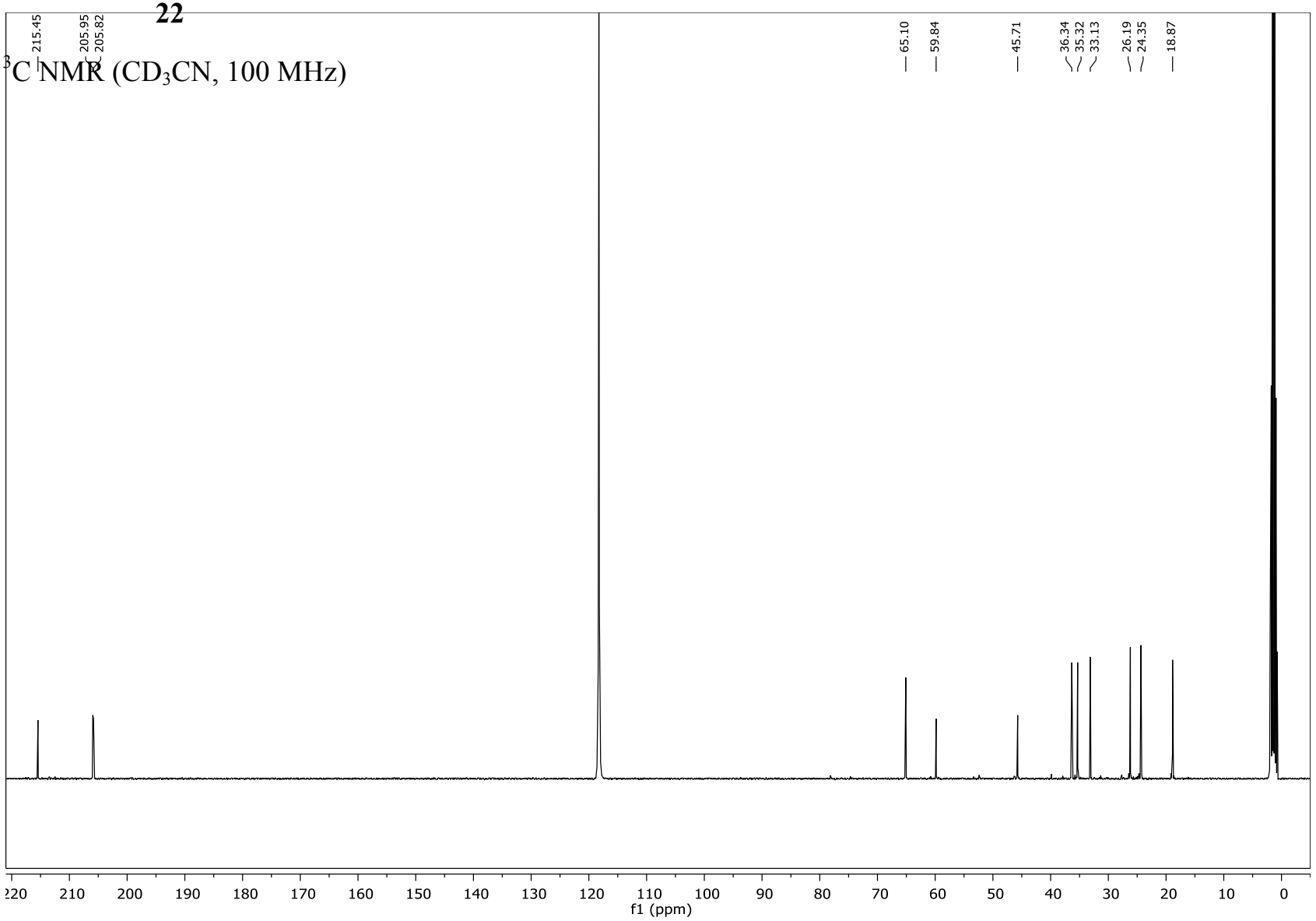
22

^{1}H NMR expansion



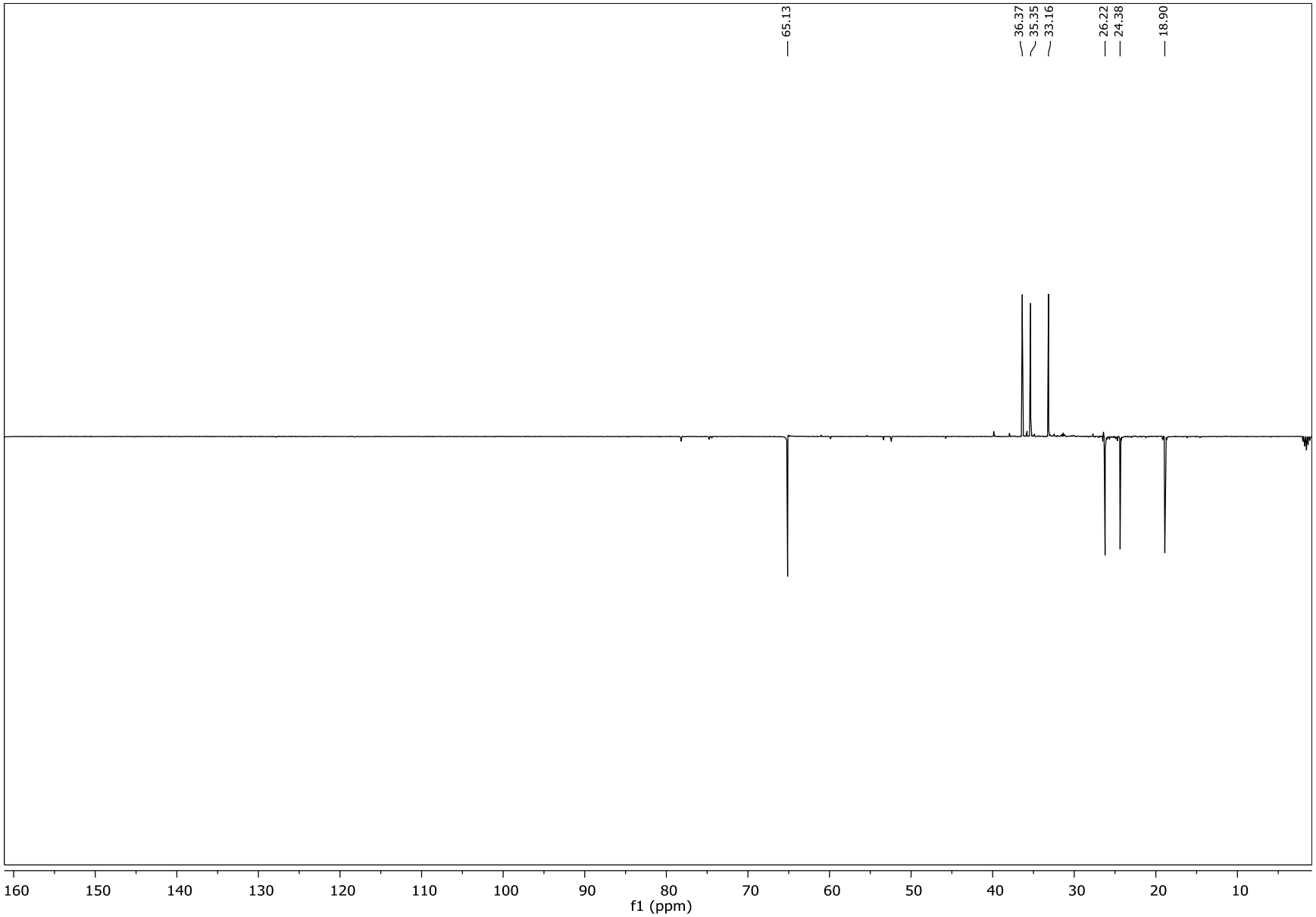
22

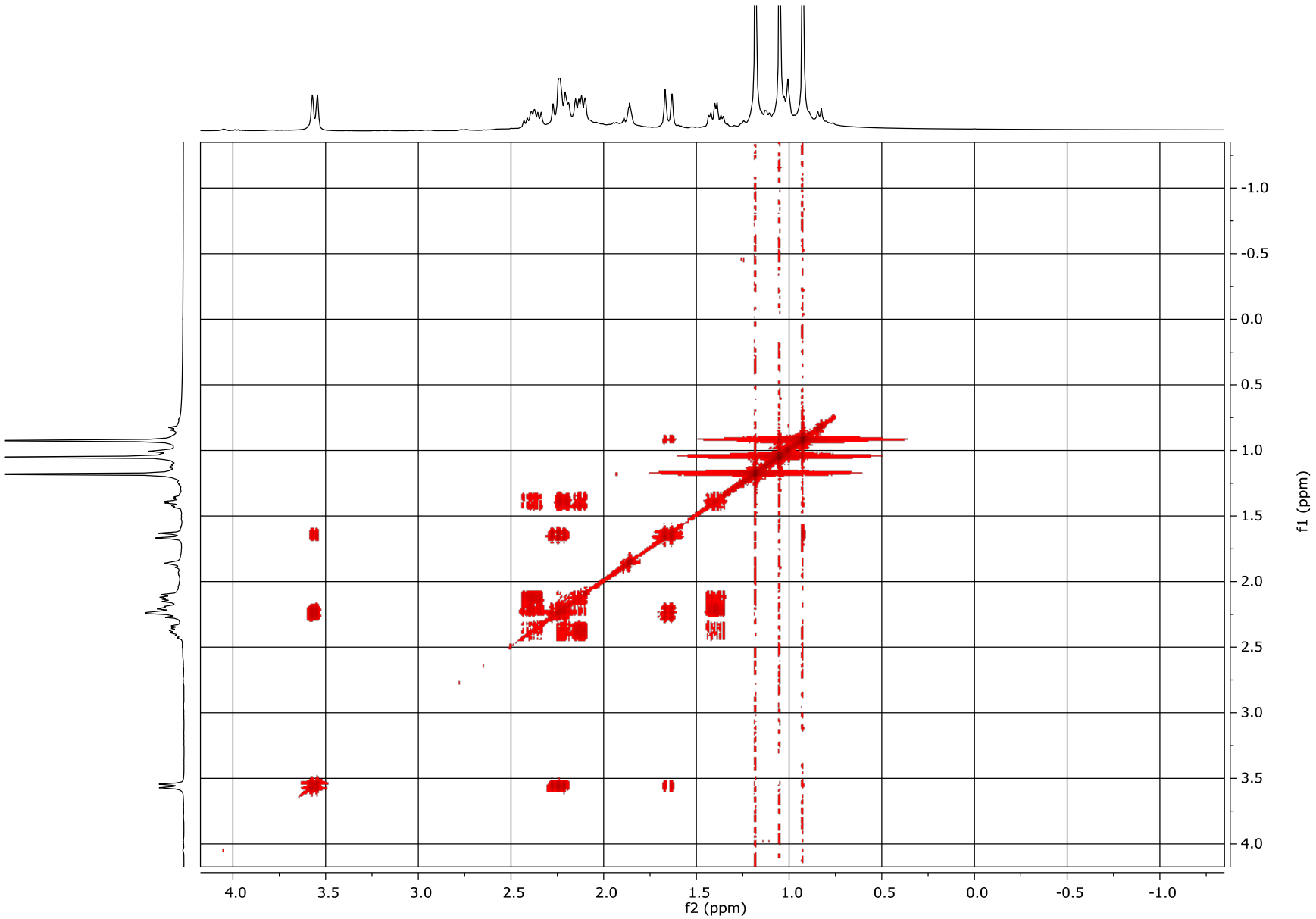
^{13}C NMR (CD_3CN, 100 MHz)

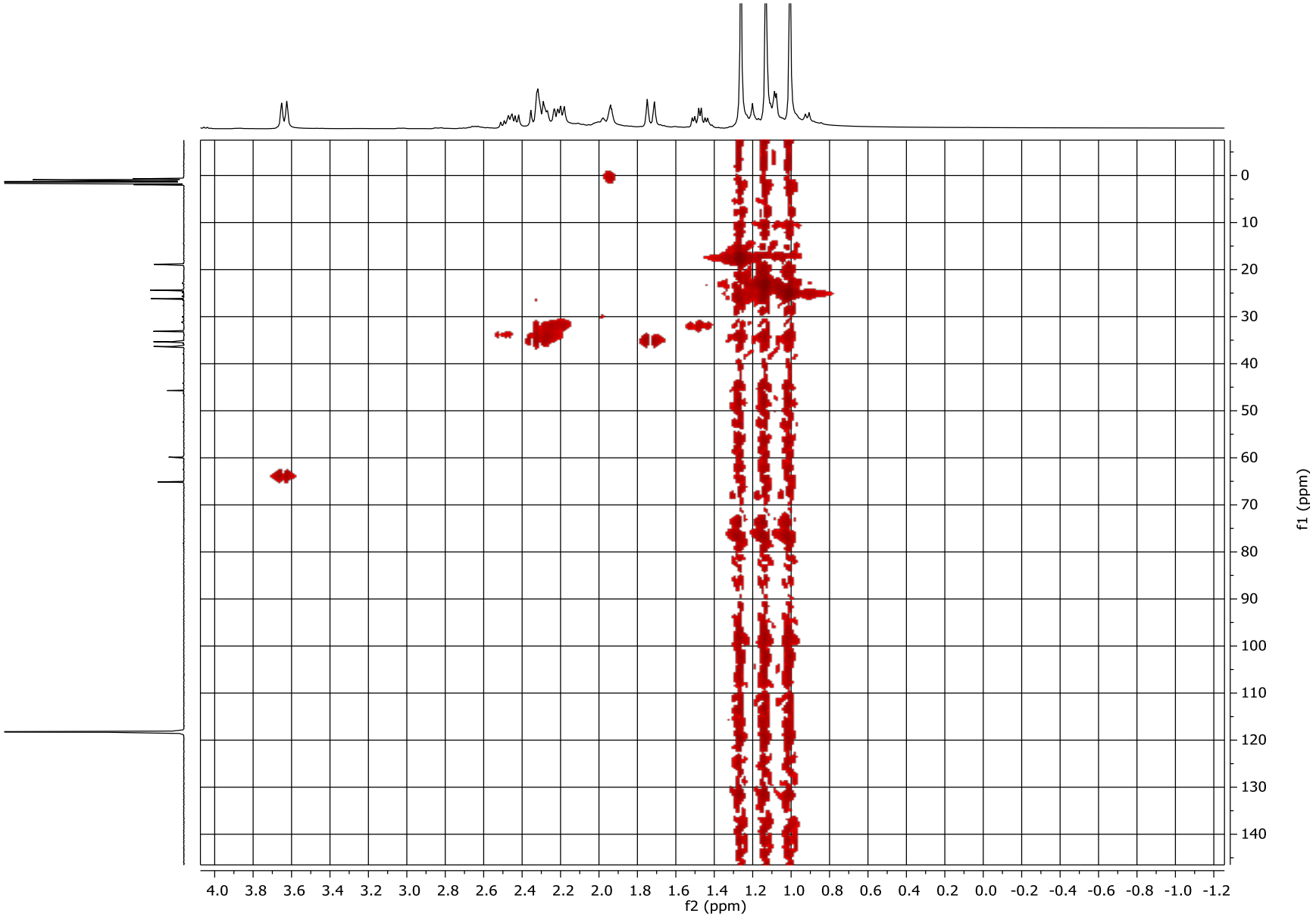


22

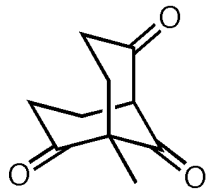
DEPT-135


65.13
36.37
35.35
33.16
26.22
24.38
18.90
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f2 (ppm)
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
f1 (ppm)


4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2 0.0 -0.2 -0.4 -0.6 -0.8 -1.0 -1.2
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140
f1 (ppm)

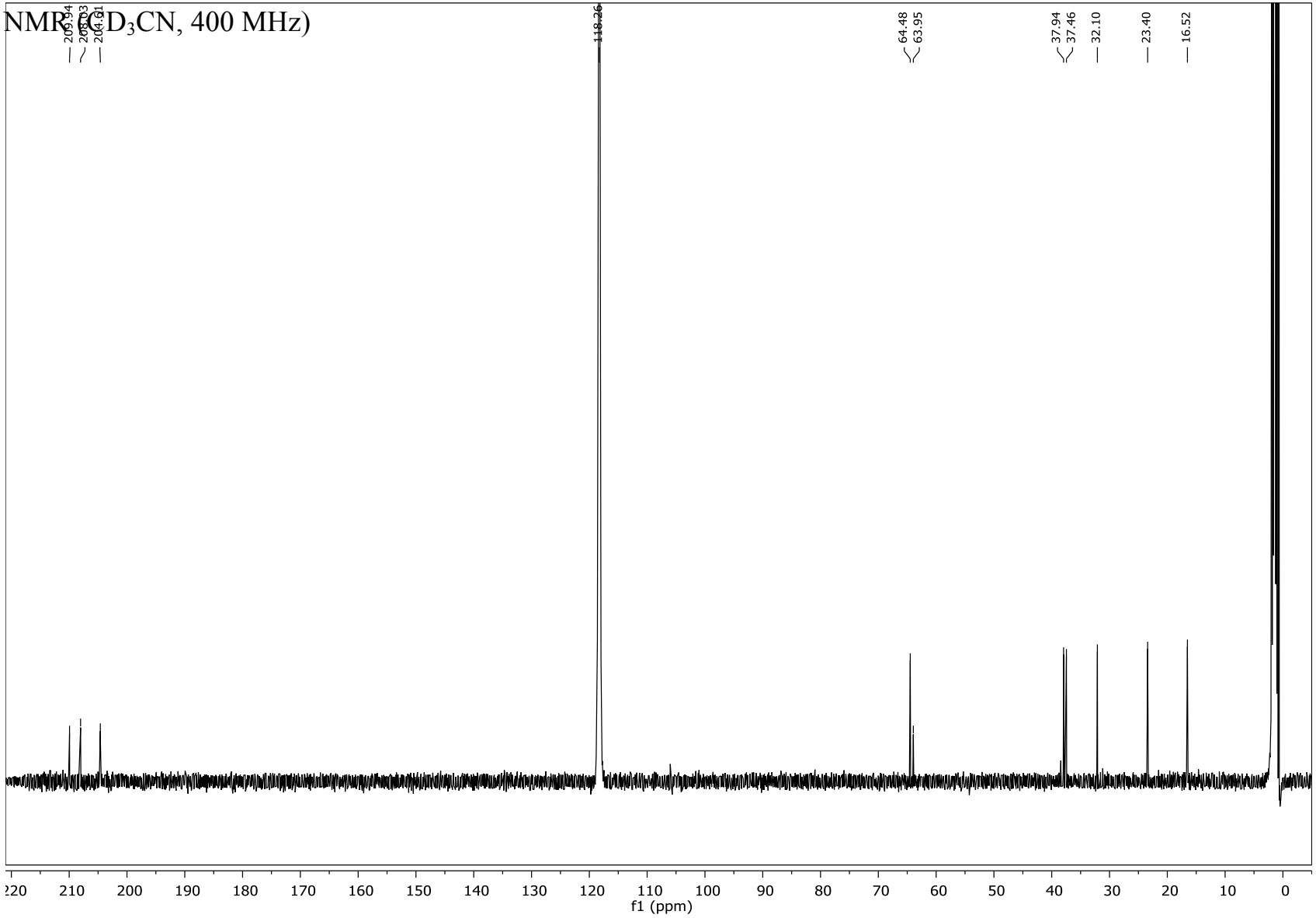
^{1}H NMR (CD_3CN, 4



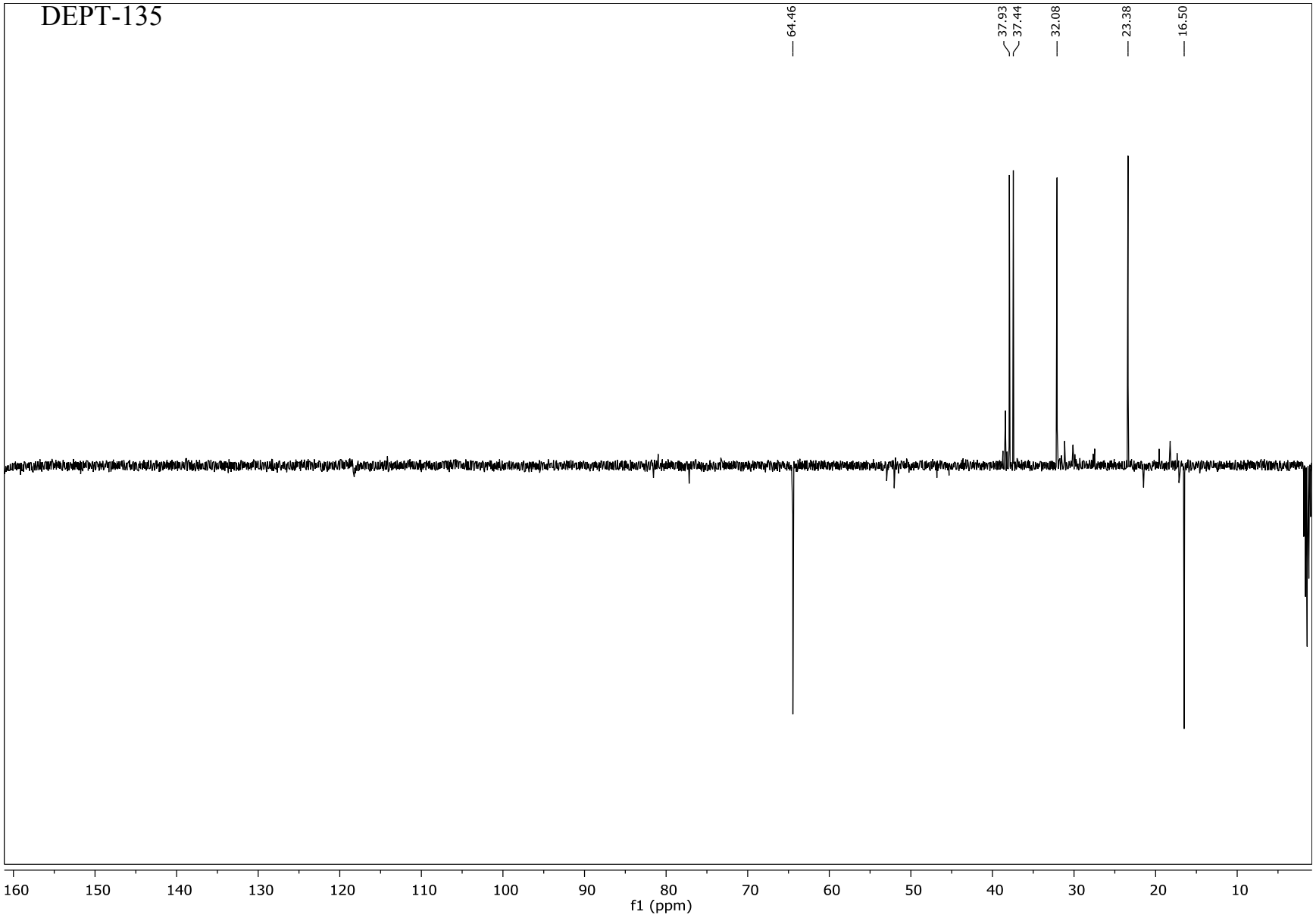
23

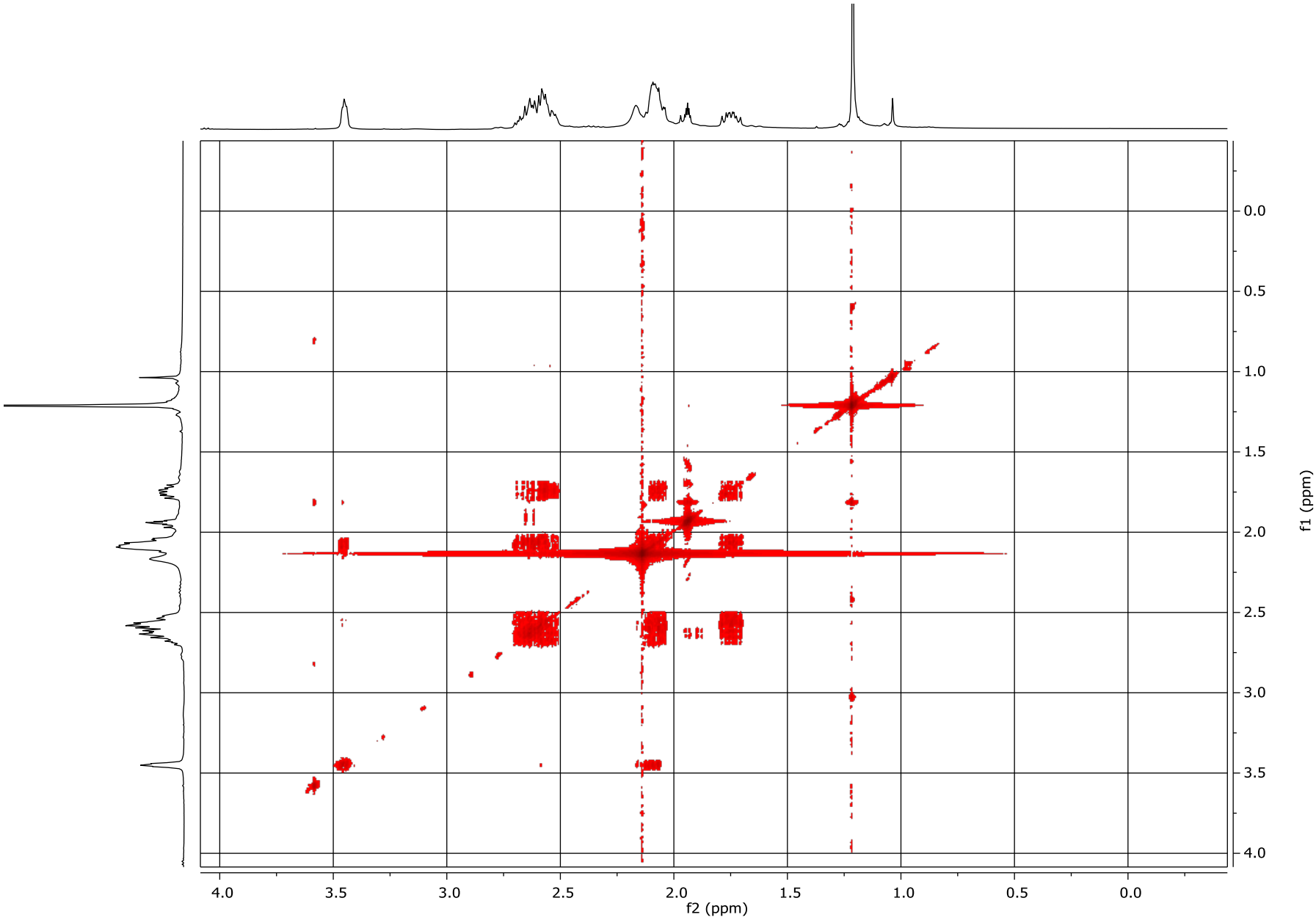
23

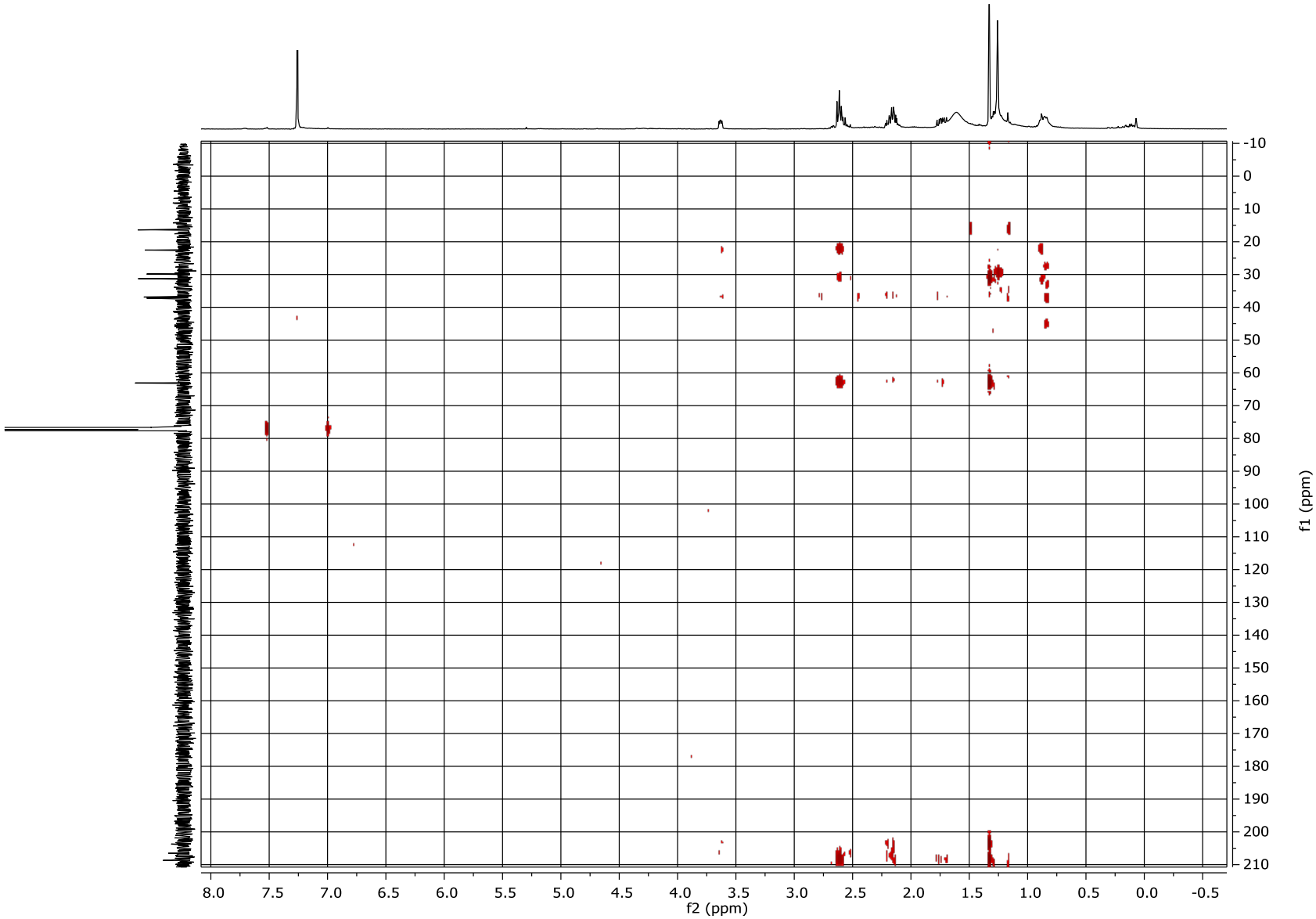
^{13}C NMR (CD_3CN, 400 MHz)



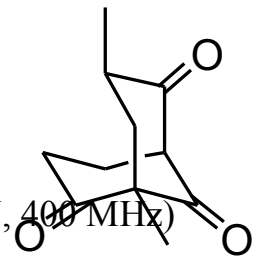
23


DEPT-135
64.46
37.93
37.44
32.08
23.38
16.50
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
f1 (ppm)


f2 (ppm)
f1 (ppm)

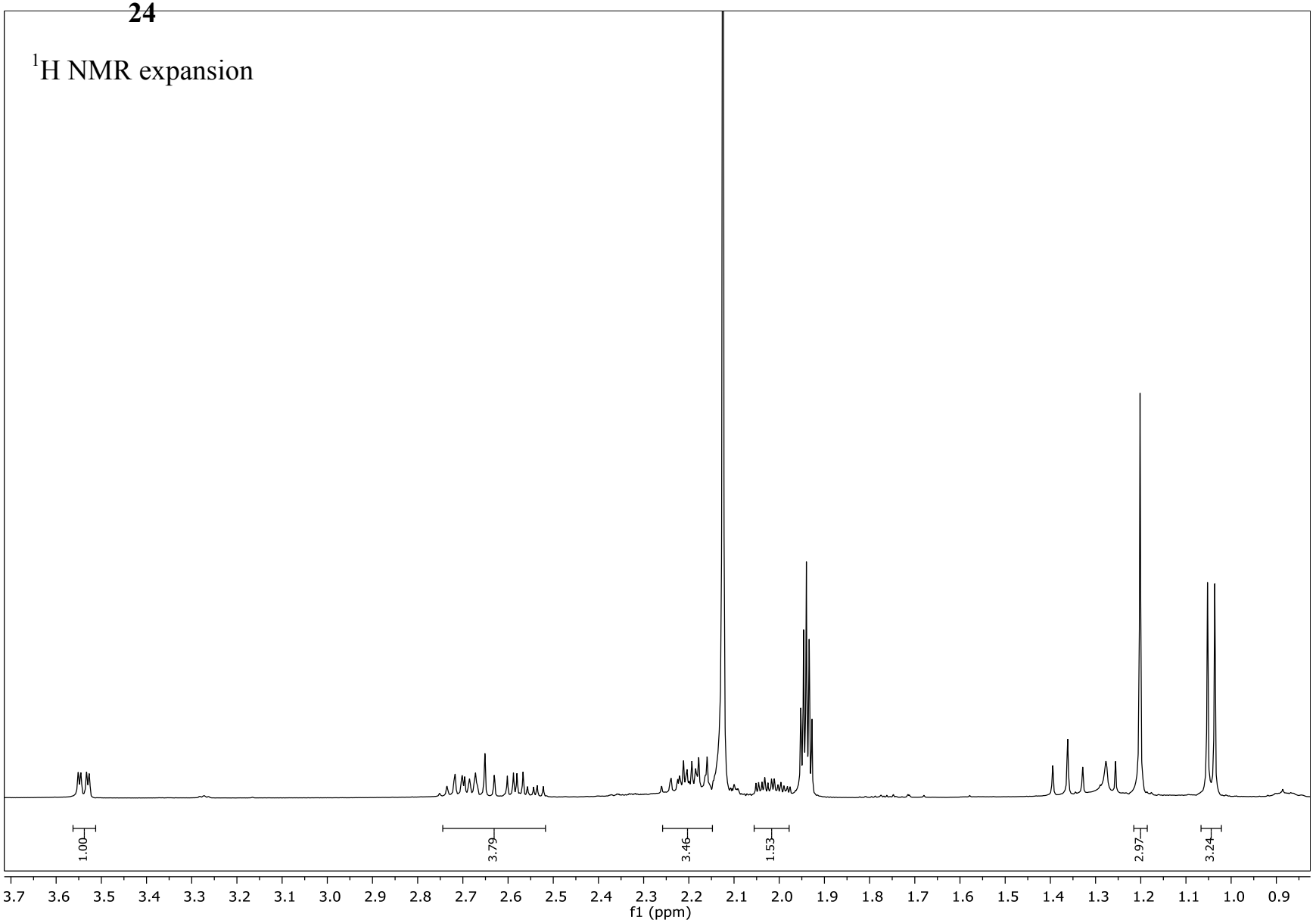
^{1}H NMR (CD_3CN, 400 MHz)



24

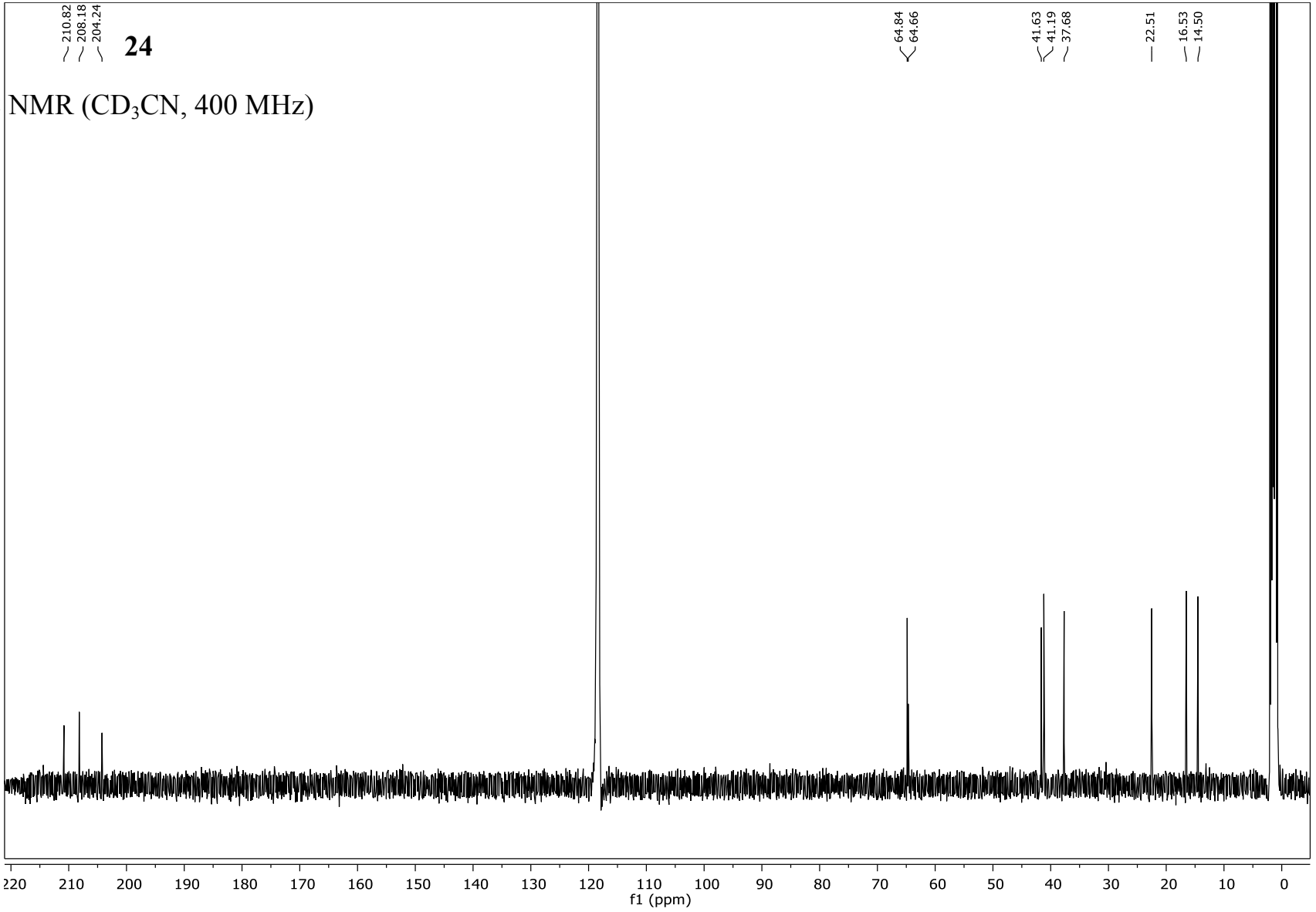
24

^{1}H NMR expansion

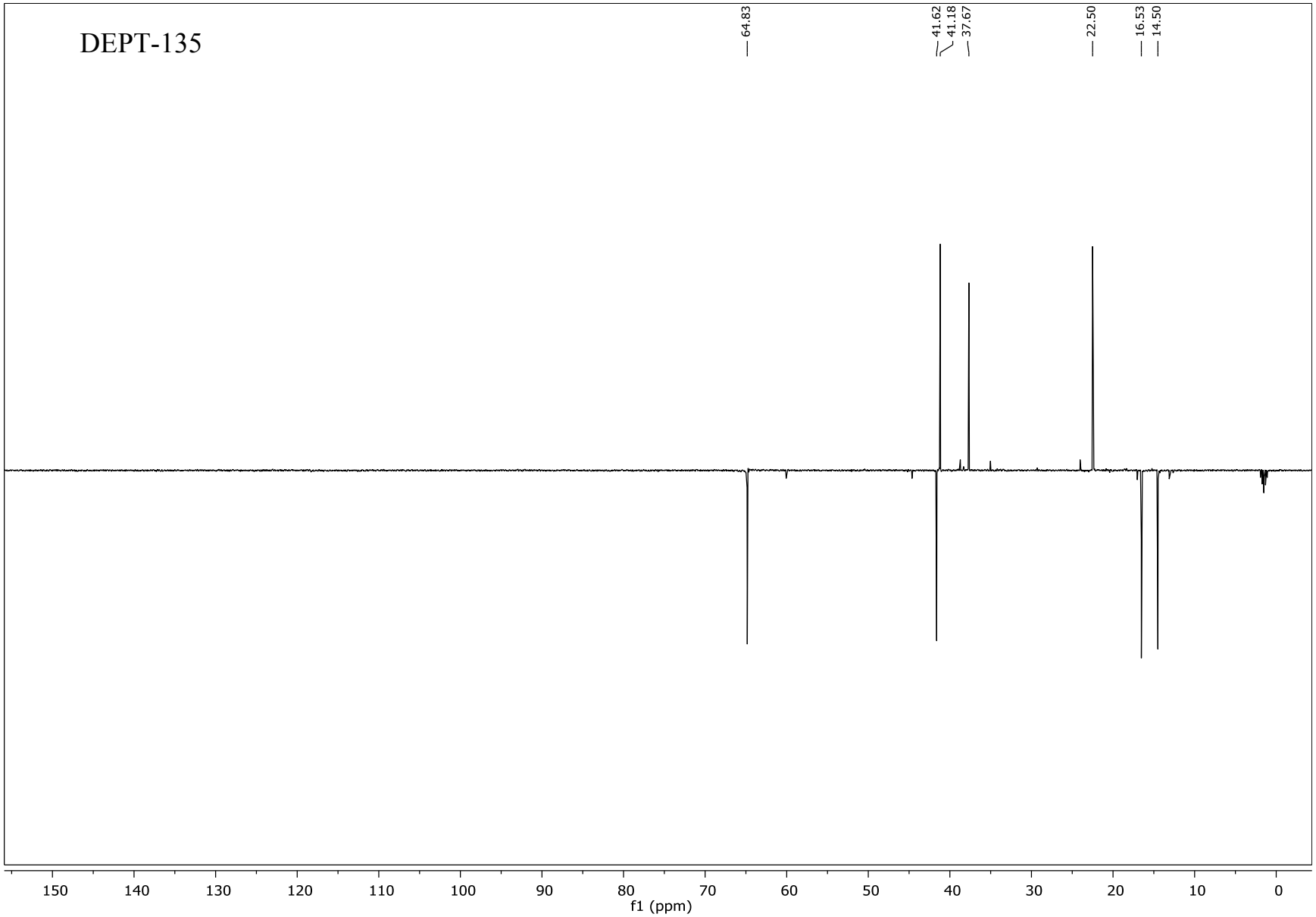


24

^{13}C NMR (CD_3CN, 400 MHz)



24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37.67
22.50
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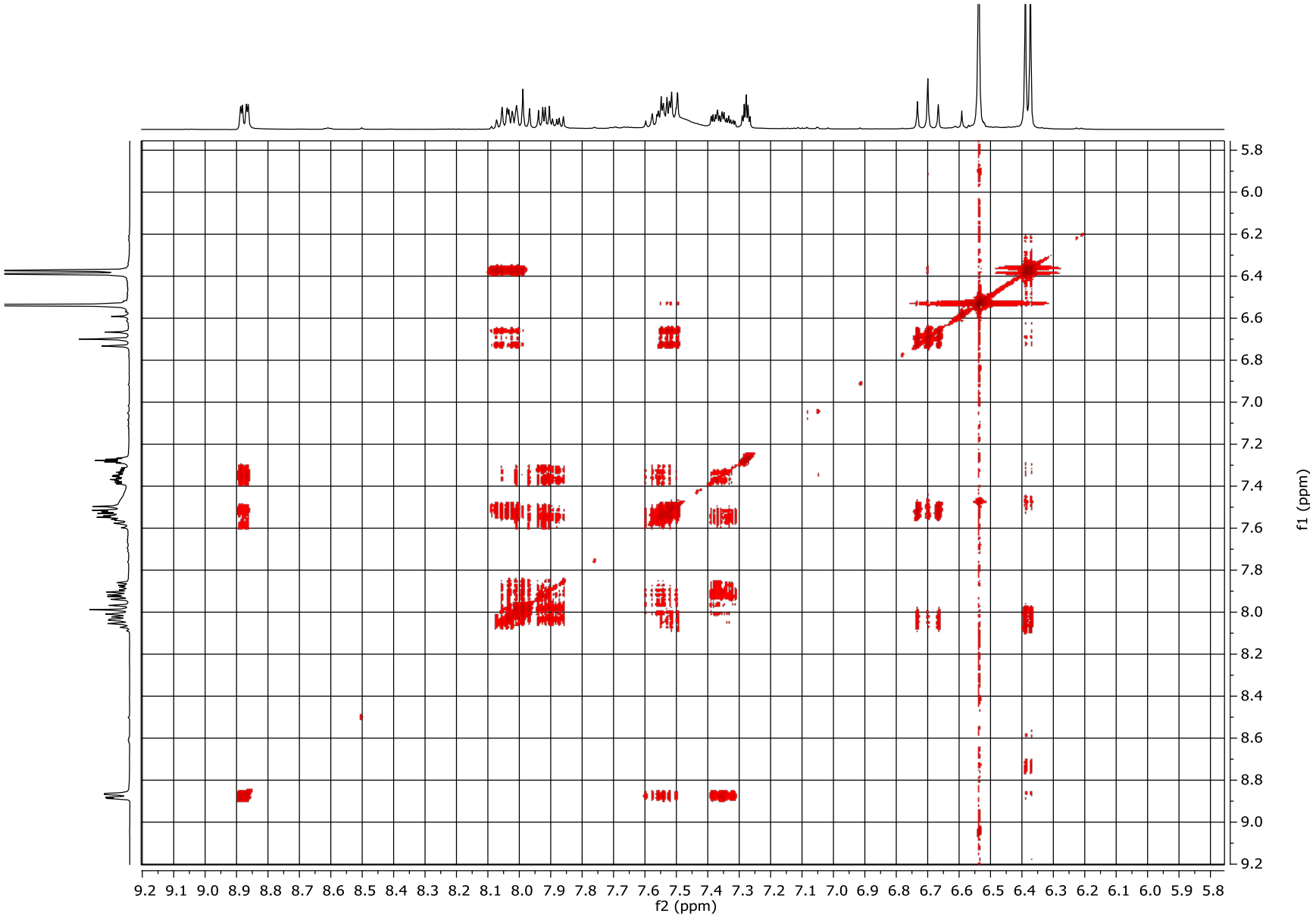
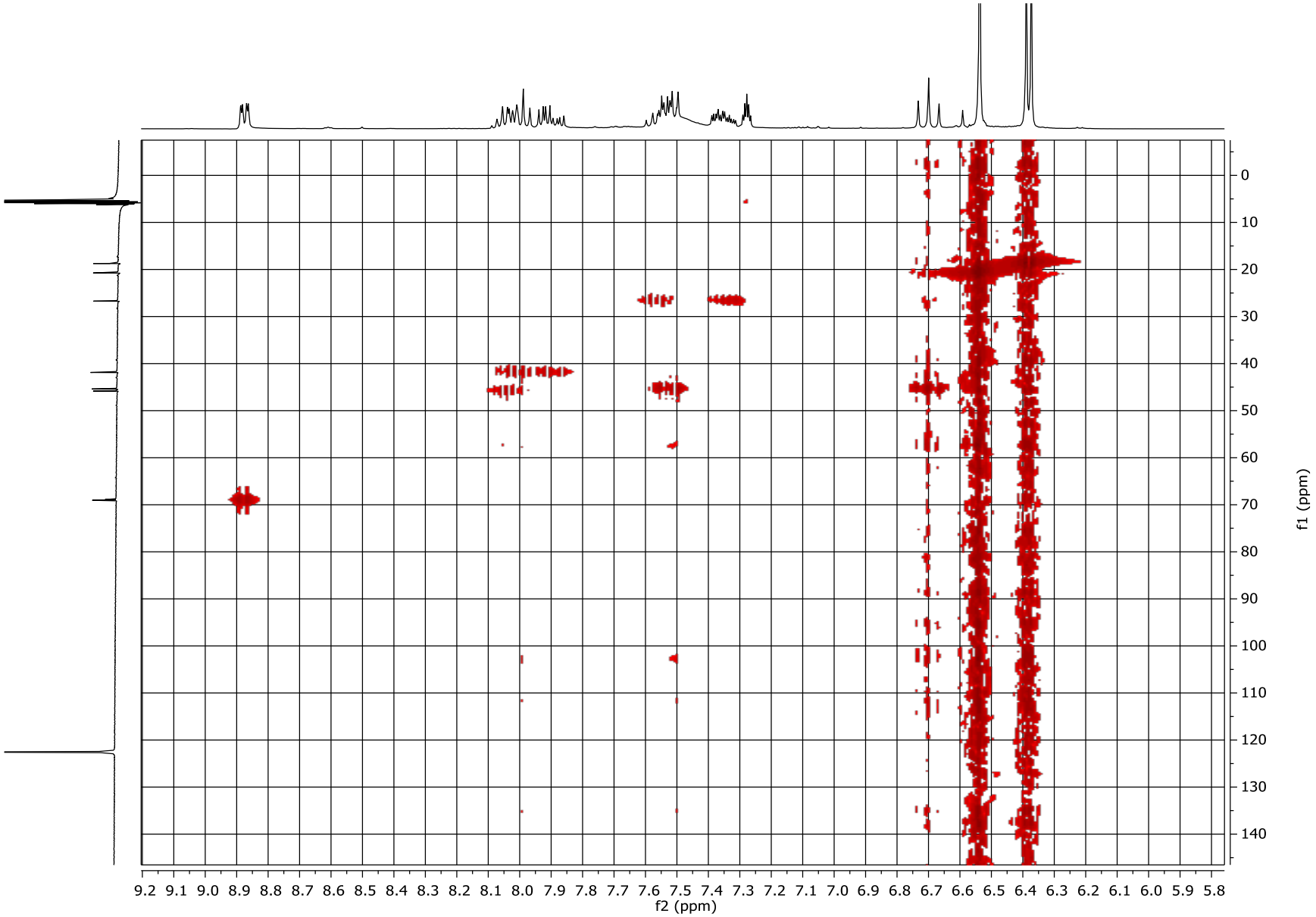
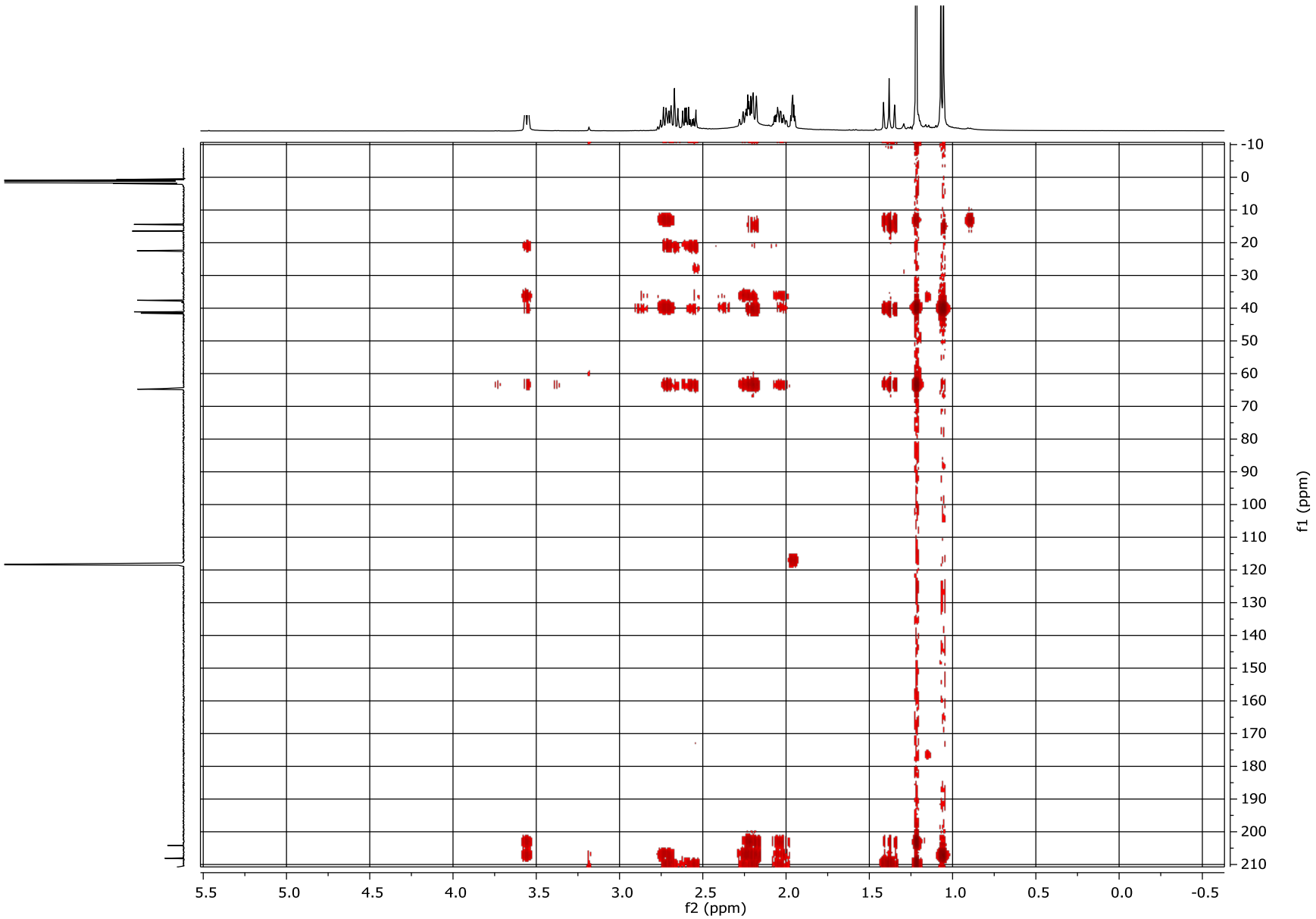
14.50
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.2 9.1 9.0 8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8
f2 (ppm)
5.8 6.0 6.2 6.4 6.6 6.8 7.0 7.2 7.4 7.6 7.8 8.0 8.2 8.4 8.6 8.8 9.0 9.2
f1 (ppm)

HMQC

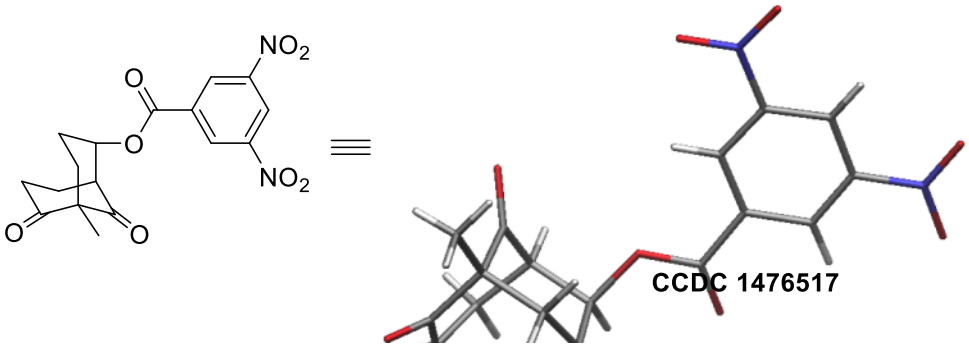

9.2 9.1 9.0 8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140
f1 (ppm)

HMBC


-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
f1 (ppm)
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
f2 (ppm)

2. X-ray crystallographic data

3,5-dinitrobenzoate ester of *exo*-ketol **6**:



An X-ray quality crystal was obtained by slow diffusion of dichloromethane into a nearly sat. solution in hexane.

A colorless block-like specimen of $C_{17}H_{16}N_2O_8$, approximate dimensions 0.220 mm x 0.400 mm x 0.420 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

The total exposure time was 1.02 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 24863 reflections to a maximum θ angle of 36.39° (0.60 Å resolution), of which 7597 were independent (average redundancy 3.273, completeness = 99.8%, R_{int} = 4.59%, R_{sig} = 4.71%) and 6529 (85.94%) were greater than $2\sigma(F^2)$. The final cell constants of a = 10.6964(11) Å, b = 25.365(3) Å, c = 6.2244(6) Å, volume = 1688.8(3) $Å^3$, are based upon the refinement of the XYZ-centroids of 4917 reflections above 20 σ(I) with 4.981° < 2θ < 67.90°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.861. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9520 and 0.9740.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P n a 21, with Z = 4 for the formula unit, $C_{17}H_{16}N_2O_8$. The final anisotropic full-matrix least-squares refinement on F^2 with 245 variables converged at R1 = 4.46%, for the observed data and wR2 = 10.94% for all data. The goodness-of-fit was 1.009. The largest peak in the final difference electron density synthesis was 0.453 $e^-/Å^3$ and the largest hole was -0.241 $e^-/Å^3$ with an RMS deviation of 0.058 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.480 g/cm^3 and F(000), 784 e^-.

Crystal data, data collection and structure refinement.

Identification code	ices15	
Chemical formula	$C_{17}H_{16}N_2O_8$	
Formula weight	376.32 g/mol	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.220 x 0.400 x 0.420 mm	
Crystal habit	colorless block	
Crystal system	orthorhombic	
Space group	P n a 21	
Unit cell dimensions	a = 10.6964(11) Å	α = 90°
	b = 25.365(3) Å	β = 90°
	c = 6.2244(6) Å	γ = 90°
Volume	1688.8(3) $Å^3$	
Z	4	
Density (calculated)	1.480 g/cm^3	
Absorption coefficient	0.120 mm^{-1}	
F(000)	784	
Theta range for data collection	2.49 to 36.39°	
Index ranges	-17<=h<=17, -42<=k<=40, -10<=l<=9	
Reflections collected	24863	
Independent reflections	7597 [R(int) = 0.0459]	
Coverage of independent reflections	99.8%	
Absorption correction	Multi-Scan	
Max. and min. transmission	0.9740 and 0.9520	
Structure solution technique	direct methods	
Structure solution program	XT, VERSION 2014/4	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)	
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	7597 / 1 / 245	
Goodness-of-fit on F2	1.009	

Final R indices	6529 data; I>2σ(I)	R1 = 0.0446, wR2 = 0.1037
	all data	R1 = 0.0542, wR2 = 0.1094
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0599P)^2]$ where $P=(F_o^2+2F_c^2)/3$	
Largest diff. peak and hole	0.453 and -0.241 eÅ^{-3}	
R.M.S. deviation from mean	0.058 eÅ^{-3}	

Table S1. Bond lengths (Å).

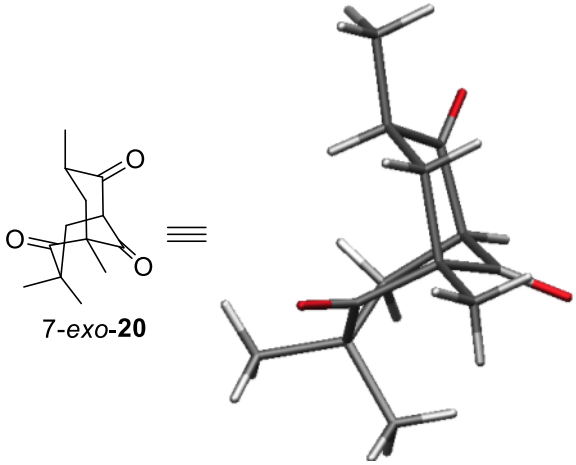
C1-C2	1.3913(19)	C1-C6	1.392(2)
C2-C3	1.382(2)	C2-N1	1.477(2)
C3-C4	1.387(2)	C4-C5	1.3846(19)
C4-N2	1.471(2)	C5-C6	1.396(2)
C6-C7	1.4942(18)	C7-O5	1.2117(17)
C7-O6	1.3371(18)	C8-O6	1.4717(17)
C8-C14	1.522(2)	C8-C9	1.524(2)
C9-C10	1.513(2)	C9-C15	1.545(2)
C10-O7	1.2156(18)	C10-C11	1.525(2)
C11-C12	1.523(2)	C11-C17	1.545(2)
C11-C13	1.559(3)	C13-C14	1.529(2)
C15-C16	1.539(2)	C16-C17	1.512(2)
C17-O8	1.2144(19)	N1-O1	1.224(2)
N1-O2	1.2250(18)	N2-O4	1.2288(19)
N2-O3	1.2325(16)		

Table S2. Bond angles (°).

C2-C1-C6	118.14(14)	C3-C2-C1	123.37(14)
C3-C2-N1	118.36(13)	C1-C2-N1	118.27(15)
C2-C3-C4	116.32(13)	C5-C4-C3	123.15(15)
C5-C4-N2	118.34(14)	C3-C4-N2	118.51(12)
C4-C5-C6	118.44(14)	C1-C6-C5	120.57(12)
C1-C6-C7	121.53(13)	C5-C6-C7	117.89(12)
O5-C7-O6	125.12(13)	O5-C7-C6	123.28(14)
O6-C7-C6	111.60(12)	O6-C8-C14	107.96(12)
O6-C8-C9	104.62(12)	C14-C8-C9	113.86(12)
C10-C9-C8	109.63(13)	C10-C9-C15	108.87(12)
C8-C9-C15	113.04(12)	O7-C10-C9	123.62(13)
O7-C10-C11	122.72(13)	C9-C10-C11	113.65(12)

C12-C11-C10	112.20(13)	C12-C11-C17	110.79(13)
C10-C11-C17	108.69(13)	C12-C11-C13	109.74(15)
C10-C11-C13	106.98(13)	C17-C11-C13	108.29(13)
C14-C13-C11	114.75(14)	C8-C14-C13	112.22(13)
C16-C15-C9	115.38(12)	C17-C16-C15	117.49(12)
O8-C17-C16	120.78(14)	O8-C17-C11	119.44(14)
C16-C17-C11	119.65(12)	O1-N1-O2	124.56(14)
O1-N1-C2	117.86(13)	O2-N1-C2	117.58(15)
O4-N2-O3	123.93(15)	O4-N2-C4	117.75(12)
O3-N2-C4	118.33(13)	C7-O6-C8	116.95(11)

Triketone 7-*exo*-**20**:



An X-ray quality crystal was obtained by slow diffusion of dichloromethane into a nearly sat. solution of 7-*exo*-**20** in hexane.

A colorless block-like specimen of $C_{13}H_{18}O_3$, approximate dimensions 0.100 mm x 0.220 mm x 0.420 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

The total exposure time was 0.99 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 21935 reflections to a maximum θ angle of 29.70° (0.72 Å resolution), of which 6533 were independent (average redundancy 3.358, completeness = 99.2%, R_{int} = 8.68%, R_{sig} = 9.08%) and 4743 (72.60%) were greater than $2\sigma(F^2)$. The final cell constants of a = 12.6185(16) Å, b = 6.4539(8) Å, c = 28.975(4) Å, β = 100.150(2)°, volume = 2322.8(5) $Å^3$, are

based upon the refinement of the XYZ-centroids of 4832 reflections above 20 σ(I) with 5.713° < 2θ < 59.23°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.815. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9640 and 0.9910.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21/n 1, with Z = 8 for the formula unit, $C_{13}H_{18}O_3$. The final anisotropic full-matrix least-squares refinement on F^2 with 297 variables converged at R1 = 6.23%, for the observed data and wR2 = 17.86% for all data. The goodness-of-fit was 1.029. The largest peak in the final difference electron density synthesis was 0.447 $e^-/Å^3$ and the largest hole was -0.329 $e^-/Å^3$ with an RMS deviation of 0.073 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.271 g/cm^3 and F(000), 960 e^-.

Crystal data, data collection and structure refinement for 7-*exo*-**20**:

Identification code	ices7	
Chemical formula	$C_{13}H_{18}O_3$	
Formula weight	222.27 g/mol	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.100 x 0.220 x 0.420 mm	
Crystal habit	colorless block	
Crystal system	monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 12.6185(16) Å	α = 90°
	b = 6.4539(8) Å	β = 100.150(2)°
	c = 28.975(4) Å	γ = 90°
Volume	2322.8(5) $Å^3$	
Z	8	
Density (calculated)	1.271 g/cm^3	
Absorption coefficient	0.089 mm^{-1}	
F(000)	960	
Theta range for data collection	1.43 to 29.70°	
Index ranges	-17<=h<=13, -8<=k<=8, -40<=l<=40	

Reflections collected	21935		
Independent reflections	6533 [R(int) = 0.0868]		
Coverage of independent reflections	99.2%		
Absorption correction	Multi-Scan		
Max. and min. transmission	0.9910 and 0.9640		
Structure solution technique	direct methods		
Structure solution program	XS, VERSION 2013/1		
Refinement method	Full-matrix least-squares on F2		
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)		
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$		
Data / restraints / parameters	6533 / 0 / 297		
Goodness-of-fit on F2	1.029		
Δ/σmax	0.001		
Final R indices	4743 data; I>2σ(I)	R1 = 0.0623, wR2 = 0.1622	
	all data	R1 = 0.0846, wR2 = 0.1786	
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0843P)^2+0.3771P]$ where $P=(F_o^2+2F_c^2)/3$		
Largest diff. peak and hole	0.447 and -0.329 eÅ^{-3}		
R.M.S. deviation from mean	0.073 eÅ^{-3}		

Table S3. Bond lengths (Å).

C1-O1	1.2128(16)	C1-C2	1.523(2)
C1-C8	1.5468(19)	C2-C11	1.530(2)

C2-C10	1.543(2)	C2-C3	1.5487(18)
C3-C4	1.5669(19)	C4-C9	1.5140(19)
C4-C5	1.5314(19)	C5-O2	1.2099(16)
C5-C6	1.5146(19)	C6-C12	1.522(2)
C6-C7	1.5395(19)	C7-C8	1.5506(19)
C8-C9	1.5187(19)	C8-C13	1.5267(19)
C9-O3	1.2113(17)	C14-O4	1.2083(17)
C14-C15	1.525(2)	C14-C21	1.547(2)
C15-C24	1.526(2)	C15-C23	1.546(2)
C15-C16	1.5481(19)	C16-C17	1.5617(19)
C17-C22	1.5122(18)	C17-C18	1.5314(19)
C18-O5	1.2106(16)	C18-C19	1.5158(19)
C19-C25	1.523(2)	C19-C20	1.5367(19)
C20-C21	1.5529(19)	C21-C22	1.5145(19)
C21-C26	1.5277(19)	C22-O6	1.2121(17)

Table S4. Bond angles (°).

O1-C1-C2	123.11(13)	O1-C1-C8	119.31(13)
C2-C1-C8	117.56(11)	C1-C2-C11	111.24(12)
C1-C2-C10	106.98(11)	C11-C2-C10	109.45(12)
C1-C2-C3	109.71(11)	C11-C2-C3	108.84(12)
C10-C2-C3	110.61(11)	C2-C3-C4	115.91(11)
C9-C4-C5	109.28(11)	C9-C4-C3	110.18(10)
C5-C4-C3	108.76(11)	O2-C5-C6	124.09(13)
O2-C5-C4	120.25(12)	C6-C5-C4	115.65(11)
C5-C6-C12	112.53(11)	C5-C6-C7	109.74(11)
C12-C6-C7	112.36(12)	C6-C7-C8	113.88(11)
C9-C8-C13	112.28(12)	C9-C8-C1	110.24(11)
C13-C8-C1	110.30(11)	C9-C8-C7	105.43(10)
C13-C8-C7	110.70(12)	C1-C8-C7	107.69(11)
O3-C9-C4	123.46(13)	O3-C9-C8	124.35(13)
C4-C9-C8	112.15(11)	O4-C14-C15	122.52(13)
O4-C14-C21	119.45(13)	C15-C14-C21	117.98(11)
C14-C15-C24	110.86(12)	C14-C15-C23	106.69(12)
C24-C15-C23	109.59(12)	C14-C15-C16	110.95(11)
C24-C15-C16	108.53(12)	C23-C15-C16	110.22(11)
C15-C16-C17	116.38(11)	C22-C17-C18	109.57(11)

C22-C17-C16	110.16(11)	C18-C17-C16	108.54(11)
O5-C18-C19	123.96(13)	O5-C18-C17	120.39(12)
C19-C18-C17	115.61(11)	C18-C19-C25	112.58(11)
C18-C19-C20	109.54(11)	C25-C19-C20	112.40(12)
C19-C20-C21	113.93(11)	C22-C21-C26	112.48(12)
C22-C21-C14	110.29(11)	C26-C21-C14	110.51(11)
C22-C21-C20	105.63(10)	C26-C21-C20	110.30(12)
C14-C21-C20	107.39(11)	O6-C22-C17	123.41(13)
O6-C22-C21	124.10(13)	C17-C22-C21	112.47(11)

3. Conformational analysis

Computational experiments were performed using the Schrödinger software package. Minimization and conformational analyses were performed with MacroModel using the OPLS3 force field. The results obtained is Table S5 were confirmed by quantum mechanics calculations in Table S6-S8 using Jaguar and the B3LYP 6-31g** hybrid functional.

Table S5: OPLS3-GB/SA conformational energies (kJ/mol)

Compound	7-*exo*-**20**	8-*endo*-**21**	**22**	*endo*-**9**	*exo*-**9**
Boat-Chair	0	0	0	0	0
Chair-Boat	16.2	-	10.0	35.6	28.4
Twistboat-Twistboat	23.9	27.7	19.2	34.2	33.1
Boat-Boat	27.4	-	21.0	-	-
Twistboat-Twistboat2	-	-	-	41.3	-
Chair-Chair	-	-	-	-	-

- Conformation not found during conformational search

Table S6: B3LYP 6-31g** gas phase conformational energies (kJ/mol)

Compound	7-*exo*-**20**	8-*endo*-**21**	**22**	*endo*-**9**	*exo*-**9**
Boat-Chair	0	0	0	0	0
Chair-Boat	20.1	15.0‡	12.3	32.6	29.1
Twistboat-Twistboat	20.7	18.8	13.7	23.0	24.4
Boat-Boat	*	*	*	*	*
Twistboat-Twistboat2	17.1	13.4	9.7	21.4	19.2
Chair-Chair	†	†	†	†	†

† Conformation minimized to Boat-Chair
* Conformation minimized to Twistboat-Twistboat2.
‡ Conformation minimized to Twistchair-Twistboat.

Table S7: B3LYP 6-31g** PBF/Water conformational energies (kJ/mol)

Compound	7-*exo*-**20**	8-*endo*-**21**	**22**	*endo*-**9**	*exo*-**9**
Boat-Chair	0	0	0	0	0
Chair-Boat	20.5	16.1‡	11.8	34.7	28.6
Twistboat-Twistboat	19.4	18.3	11.4	22.9	22.2
Boat-Boat	*	*	*	*	*
Twistboat-Twistboat2	20.9	16.6	12.8	26.5	25.9
Chair-Chair	†	†	†	†	†

† Conformation minimized to Boat-Chair
* Conformation minimized to Twistboat-Twistboat2.
‡ Conformation minimized to Twistchair-Twistboat.

Table S8: B3LYP 6-31g** PBF/Acetonitrile conformational energies (kJ/mol)

Compound	7-*exo*-**20**	8-*endo*-**21**	**22**	*endo*-**9**	*exo*-**9**
Boat-Chair	0	0	0	0	0
Chair-Boat	20.7	16.6‡	12.0	33.4	28.4
Twistboat-Twistboat	19.2	18.6	11.4	23.0	22.3
Boat-Boat	*	*	*	*	*
Twistboat-Twistboat2	17.3	16.7	12.6	24.8	18.8
Chair-Chair	†	†	†	†	†

† Conformation minimized to Boat-Chair
* Conformation minimized to Twistboat-Twistboat2.
‡ Conformation minimized to Twistchair-Twistboat.