SUPPORTING INFORMATION

Synthesis and Activity of a Novel Autotaxin Inhibitor-Icodextrin Conjugate

Natalie Fisher,[a,b] Michael G. Edwards,[b] Ryan Hemming,[c] Steven M. Allin,[c] John D. Wallis,[c] Philip C. Bulman Page,[d] Michael J. Mckenzie,[e] Stefanie M Jones,[a] Mark R. J. Elsegood,[f] John King-Underwood[g] and Alan Richardson[a*]

[a] School of Pharmacy, Keele University, Keele, ST5 5BG, UK

[b] Keele Molecular Chemistry Group, Lennard-Jones Laboratories, School of Chemical and Physical Sciences, Keele University, Keele, ST5 5BG, UK

[c] School of Science and Technology, Nottingham Trent University, Nottingham NG11 8NS, UK

[d] School of Chemistry, University of East Anglia, Norwich NR4 7TJ

[e] Charnwood Molecular Ltd., The Heritage Building, Prince William Road, Loughborough LE11 5DA, UK

[f] Department of Chemistry, Loughborough University, Loughborough, LE11 3TU, UK

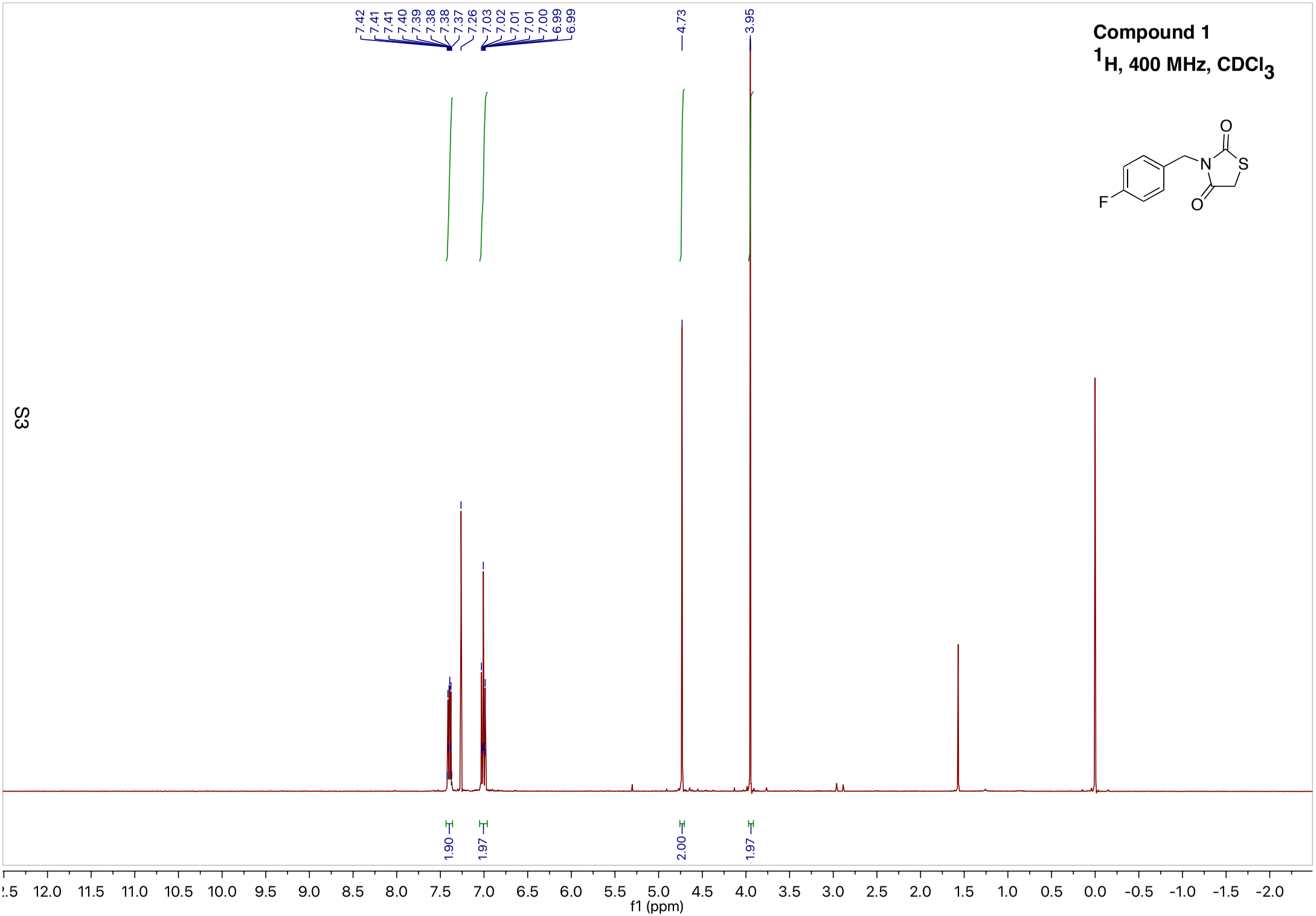
[g] Computational Chemistry Resource, Old Cottage Hospital, Ledbury, HR8 1ED, UK

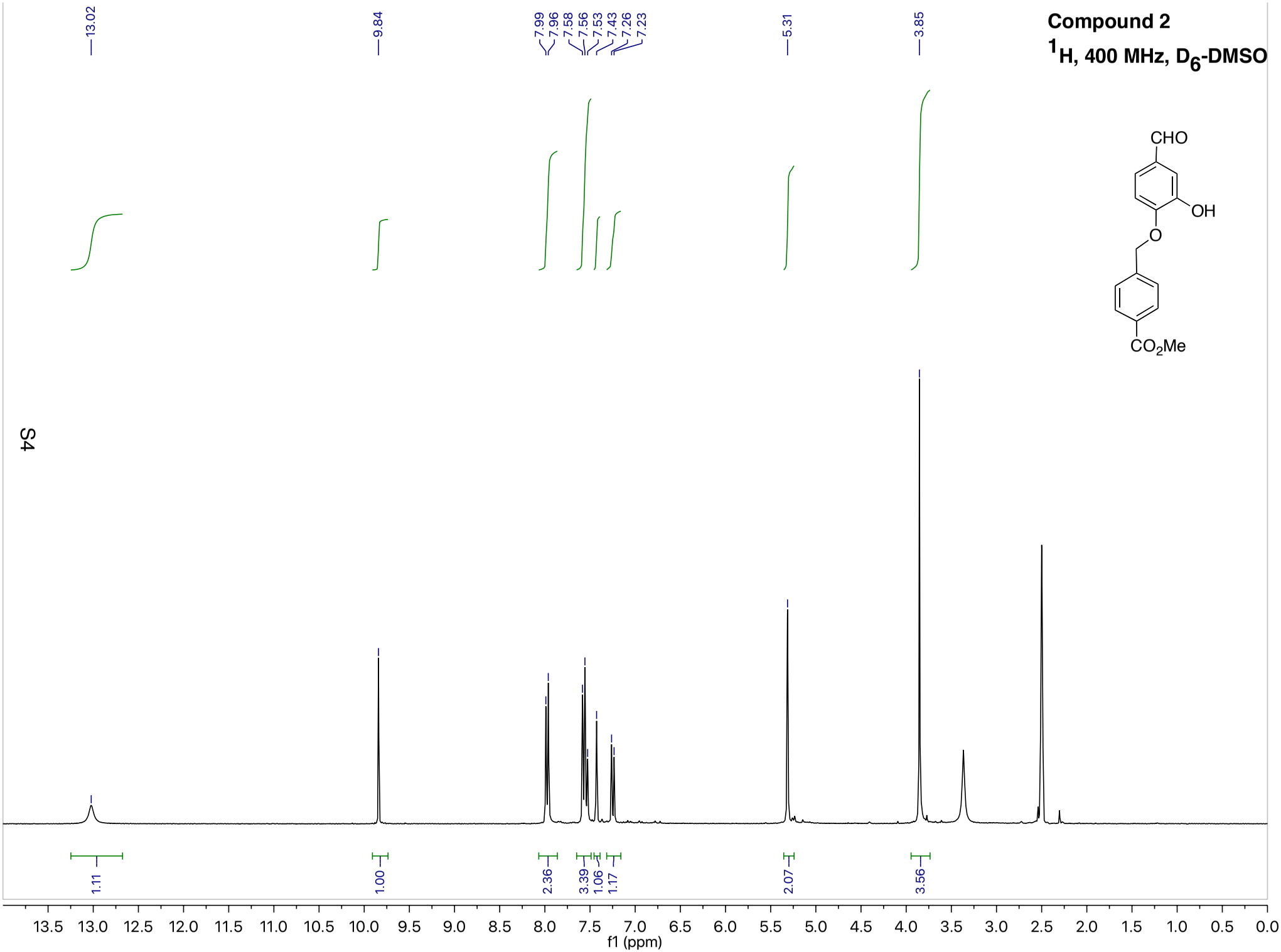
*Corresponding author: a.richardson1@keele.ac.uk

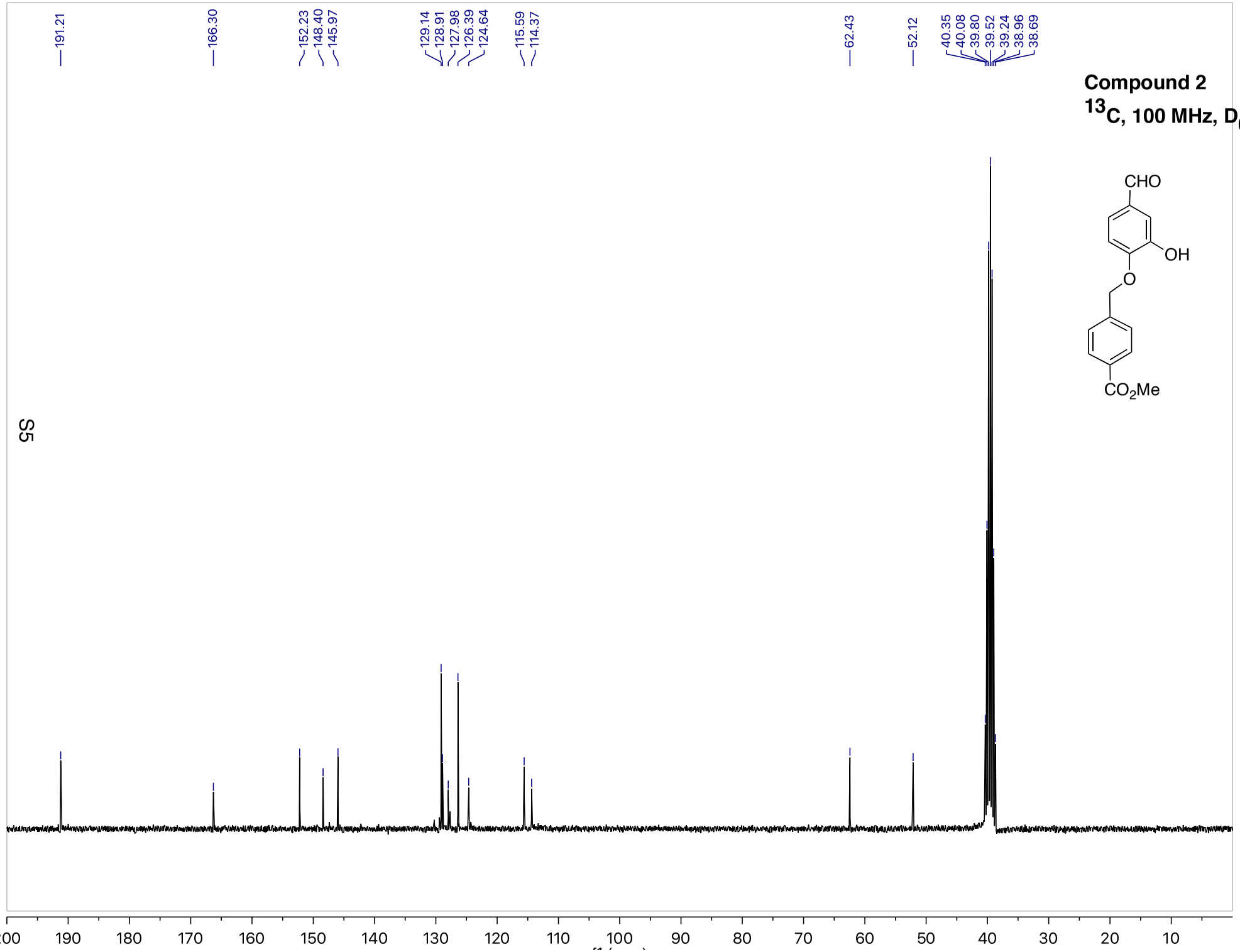
ORCHID

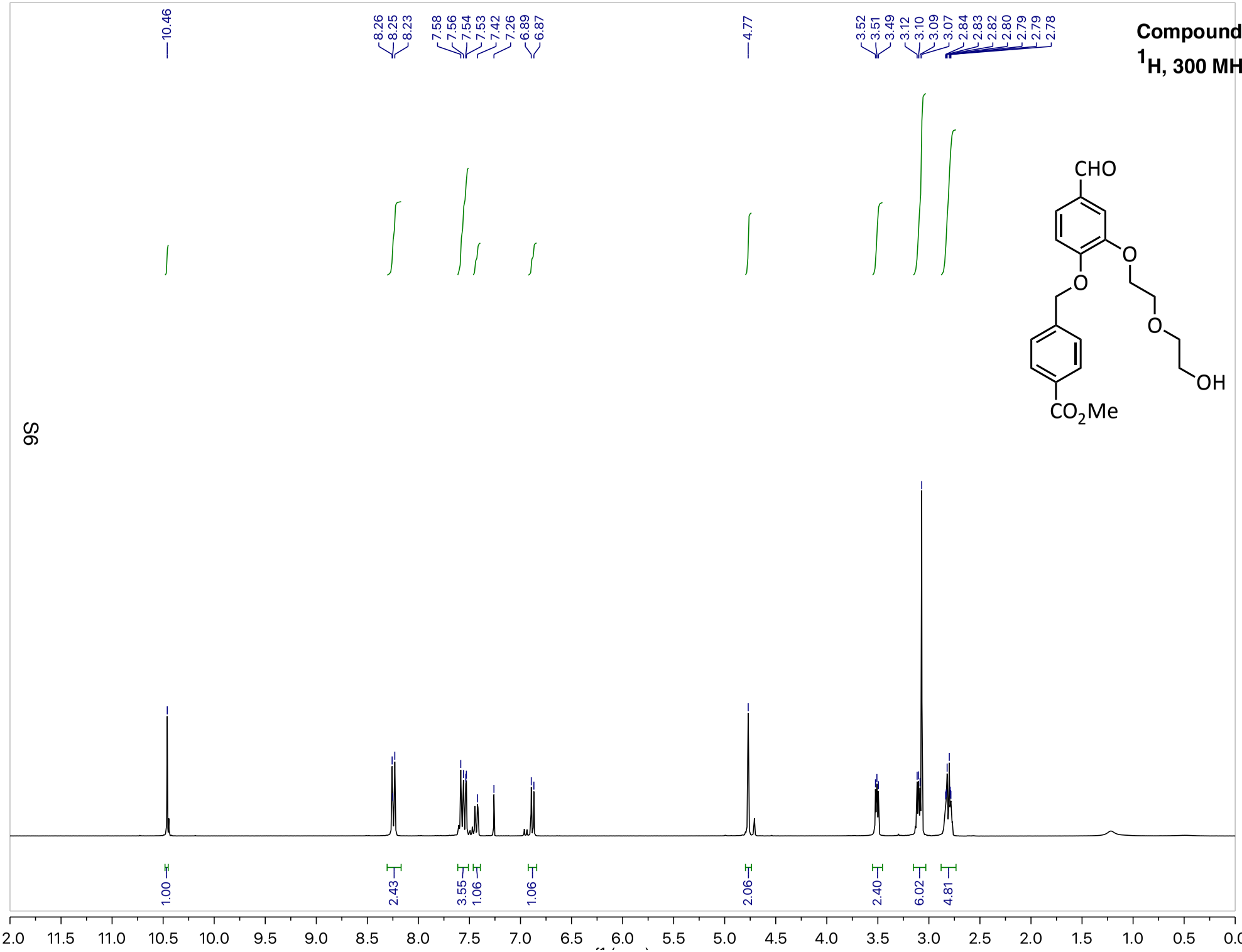
Alan Richardson 0000-0003-1825-3375

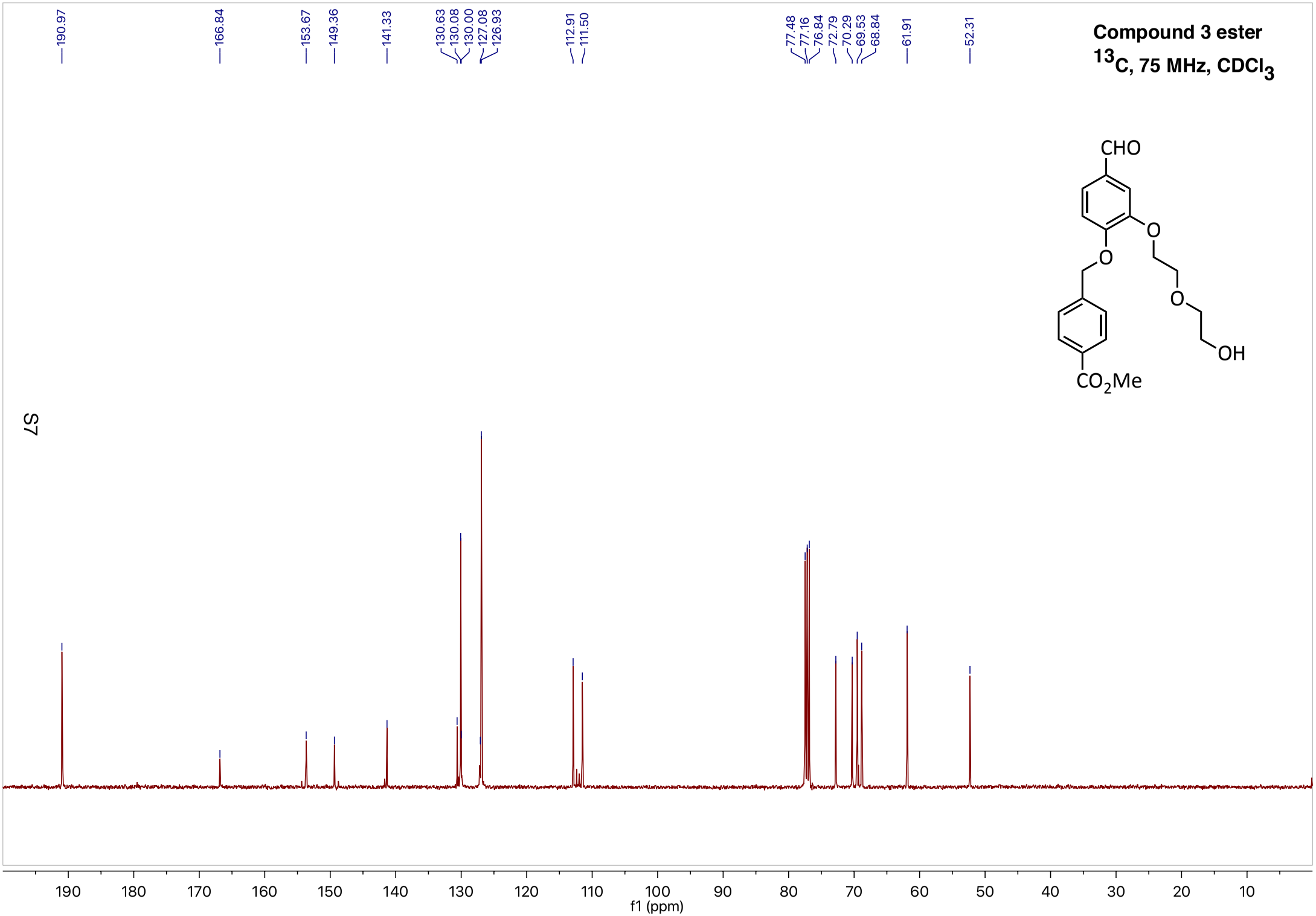
Table of Contents

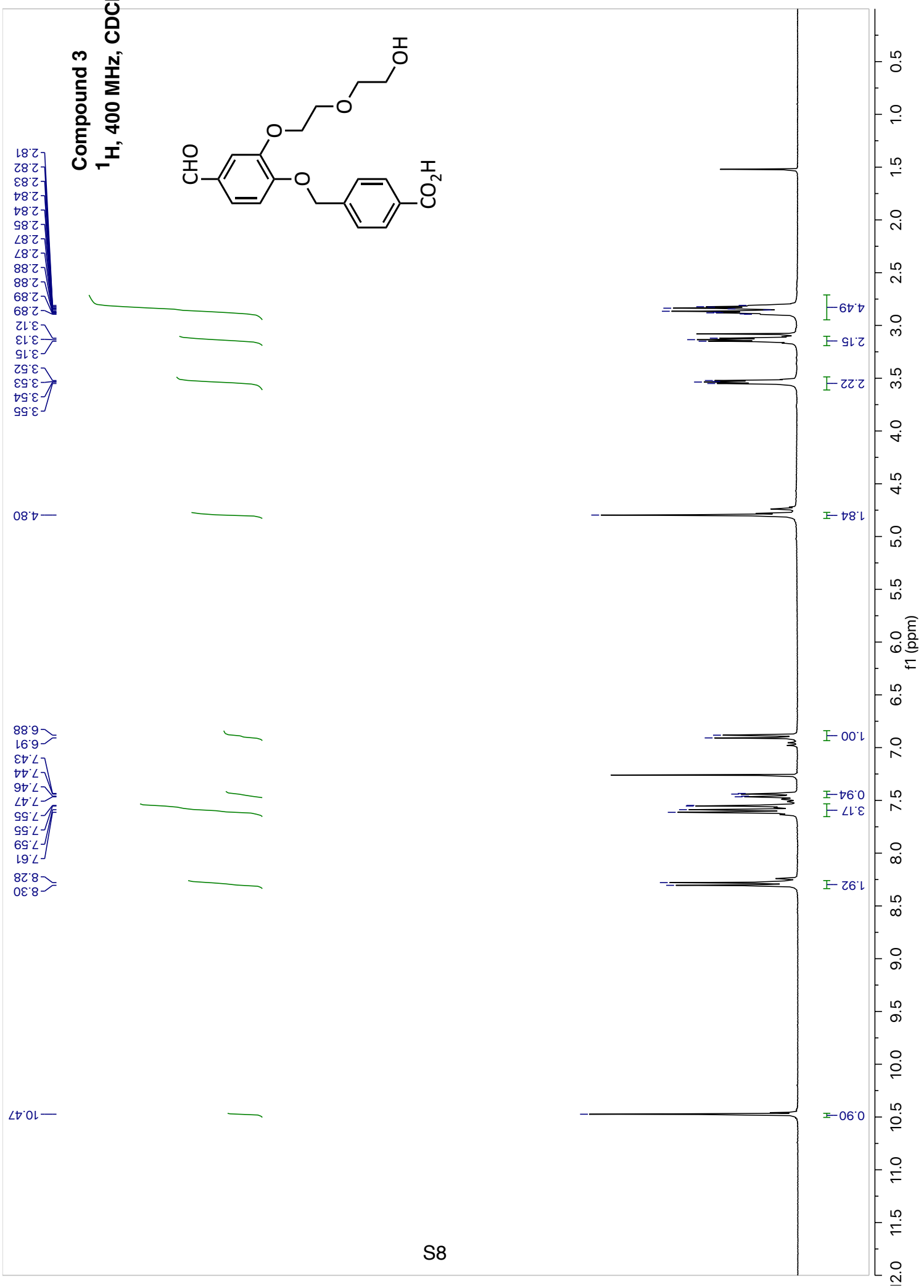

7.42
7.41
7.41
7.40
7.39
7.38
7.38
7.37
7.26
7.03
7.02
7.01
7.01
7.00
6.99
6.99
4.73
3.95
Compound 1
1H, 400 MHz, CDCl3
O
N
S
O
F
S3
1.90
1.97
2.00
1.97
f1 (ppm)

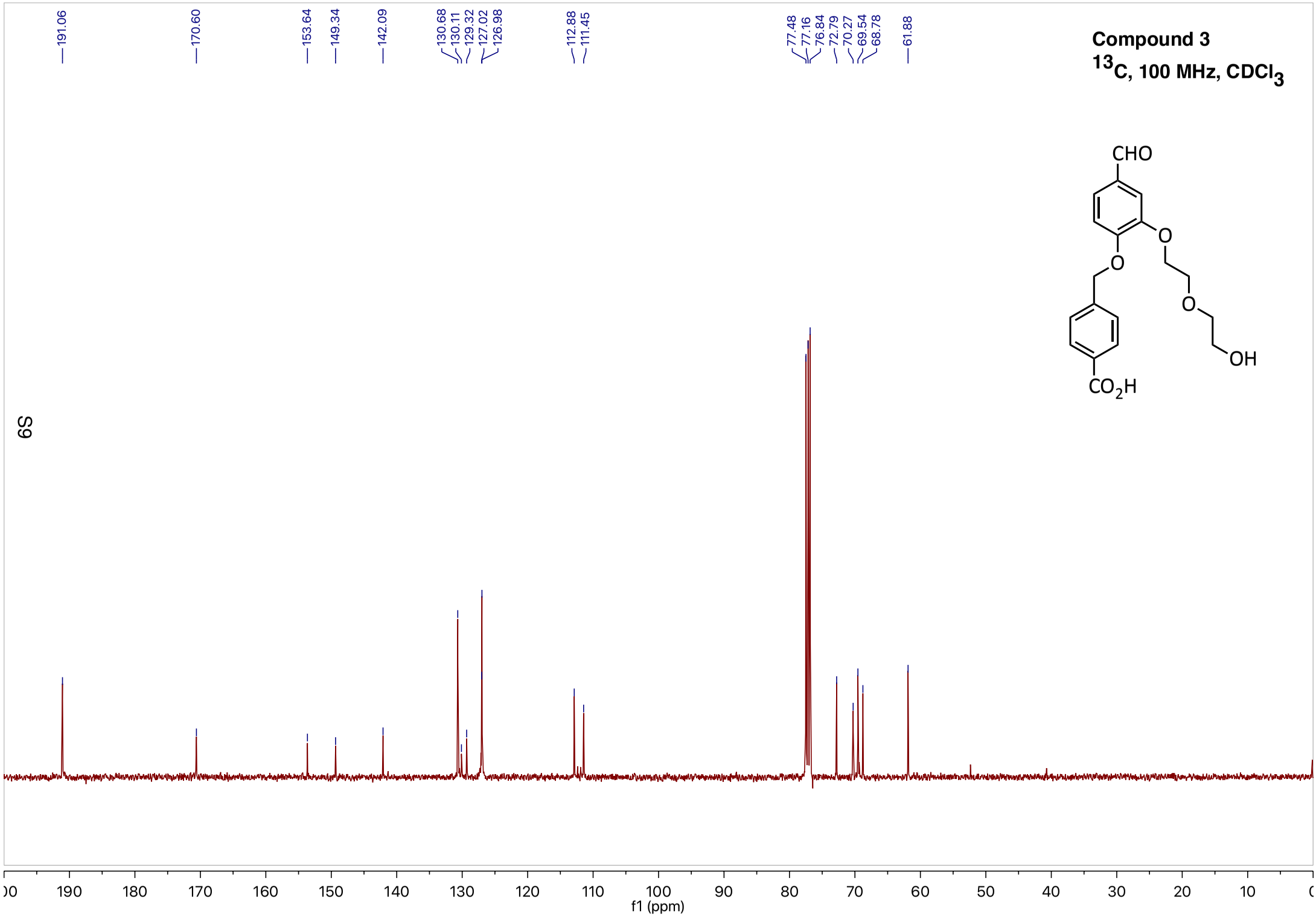

13.02
9.84
7.99
7.96
7.58
7.56
7.53
7.43
7.26
7.23
5.31
3.85
Compound 2
1H, 400 MHz, D6-DMSO
CHO
OH
O
CO2Me
1.11
1.00
2.36
3.39
1.06
1.17
2.07
3.56
f1 (ppm)

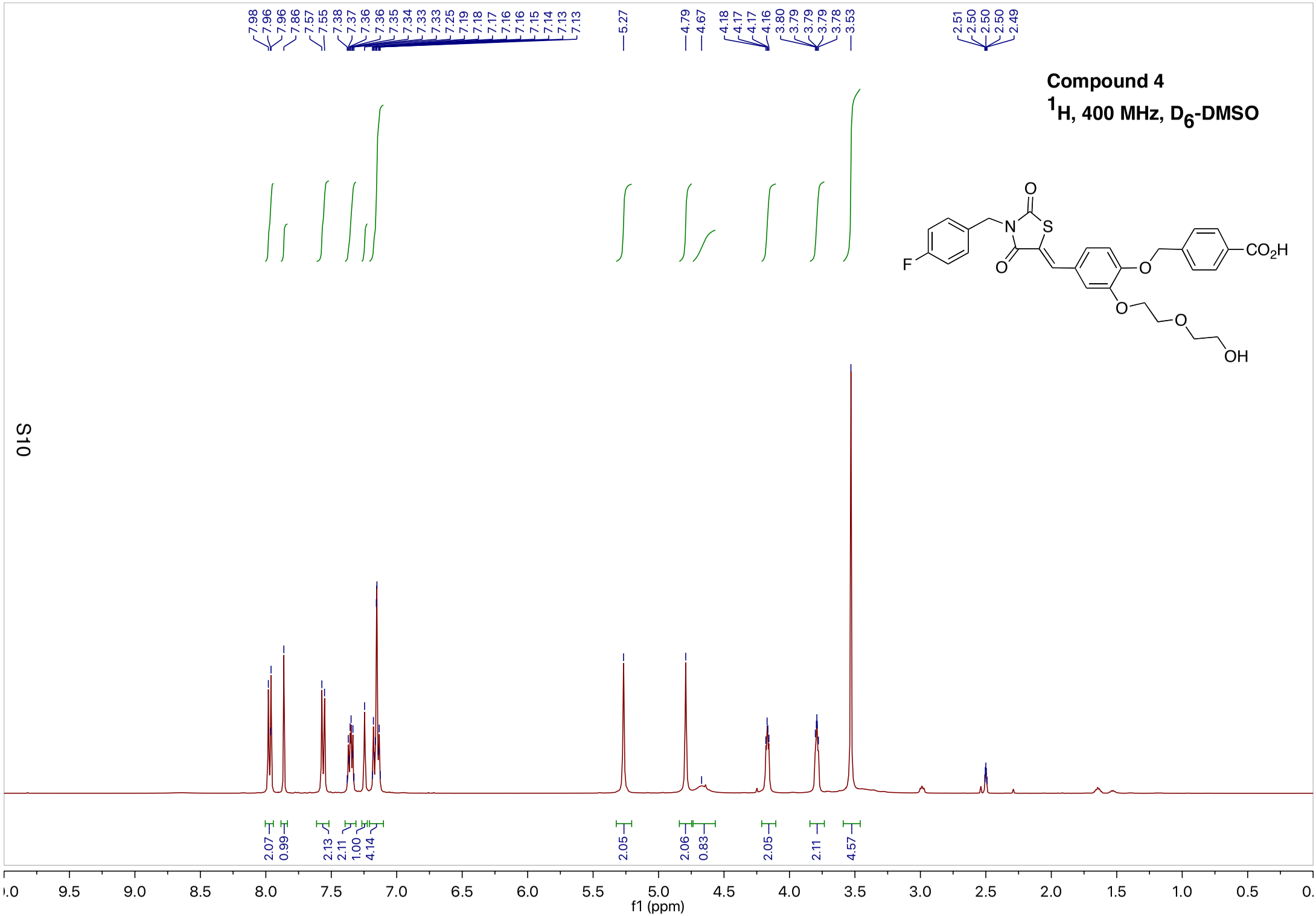

191.21
166.30
152.23
148.40
145.97
129.14
128.91
127.98
126.39
124.64
115.59
114.37
62.43
52.12
40.35
40.08
39.80
39.52
39.24
38.96
38.69
Compound 2
13C, 100 MHz, D6-DMSO
CHO
OH
O
CO2Me
S5
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

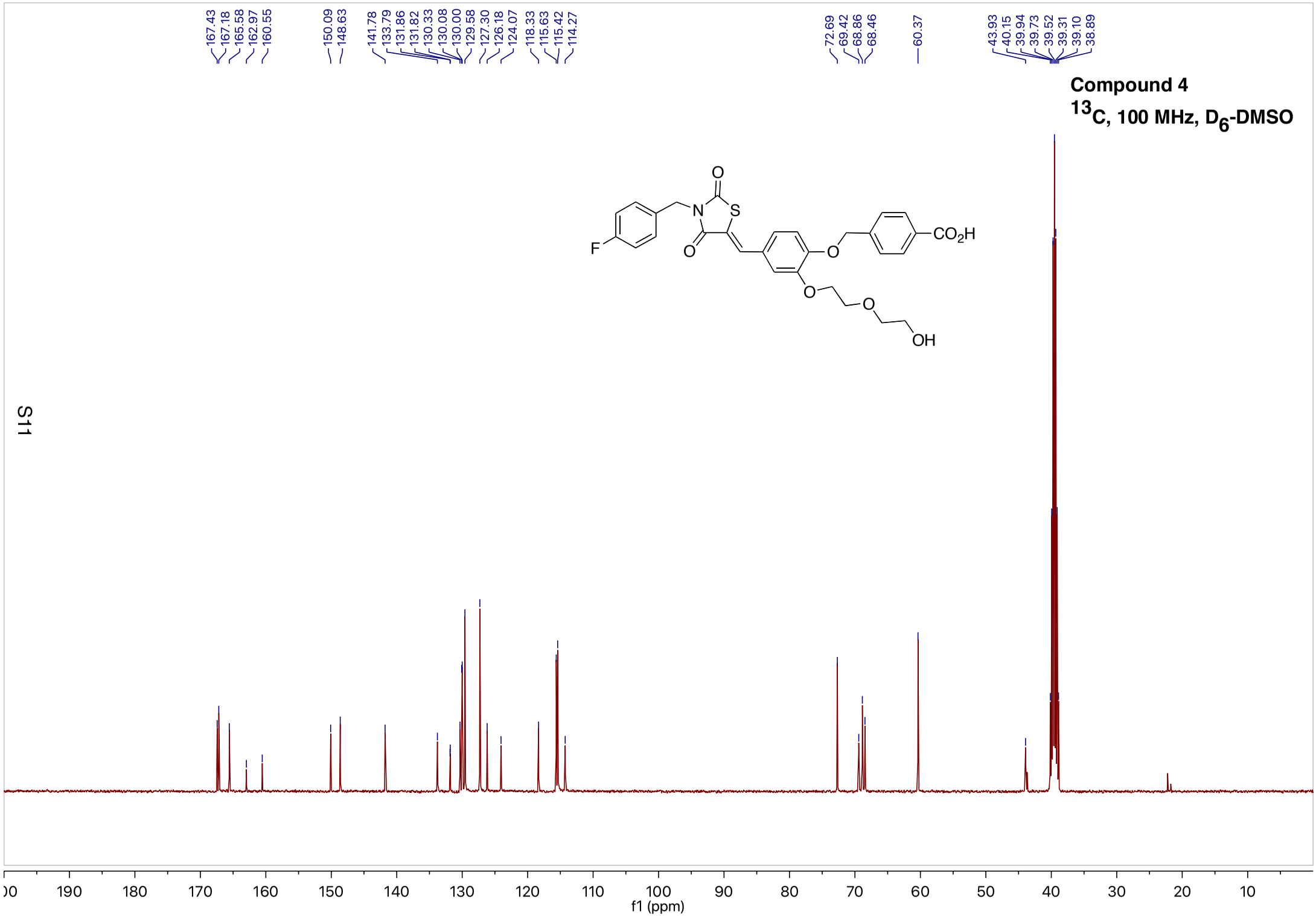

Compound 3 ester
1H, 300 MHz, CDCl3
10.46
8.26
8.25
8.23
7.58
7.56
7.54
7.53
7.42
7.26
6.89
6.87
4.77
3.52
3.51
3.49
3.12
3.10
3.09
3.07
2.84
2.83
2.82
2.80
2.79
2.79
2.78
CHO
O
O
O
OH
CO2Me
1.00
2.43
3.55
1.06
1.06
2.06
2.40
6.02
4.81
2.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


190.97
166.84
153.67
149.36
141.33
130.63
130.08
130.00
127.08
126.93
112.91
111.50
77.48
77.16
76.84
72.79
70.29
69.53
68.84
61.91
52.31
Compound 3 ester
13C, 75 MHz, CDCl3
CHO
O
O
O
OH
CO2Me
S7
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

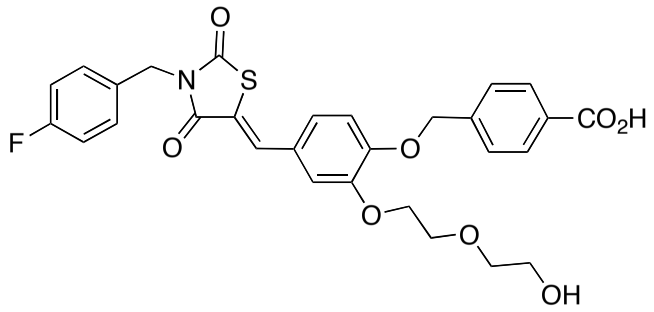

Compound 3
^{1}H, 400 MHz, CDCl$_3$
CHO
O
O
O
OH
CO$_2$H
2.81
2.82
2.83
2.84
2.84
2.85
2.87
2.87
2.88
2.88
2.89
2.89
3.12
3.13
3.15
3.52
3.53
3.54
3.55
4.80
6.88
6.91
7.43
7.44
7.46
7.47
7.55
7.55
7.59
7.61
8.28
8.30
10.47
4.49
2.15
2.22
1.84
1.00
0.94
3.17
1.92
0.90
f1 (ppm)

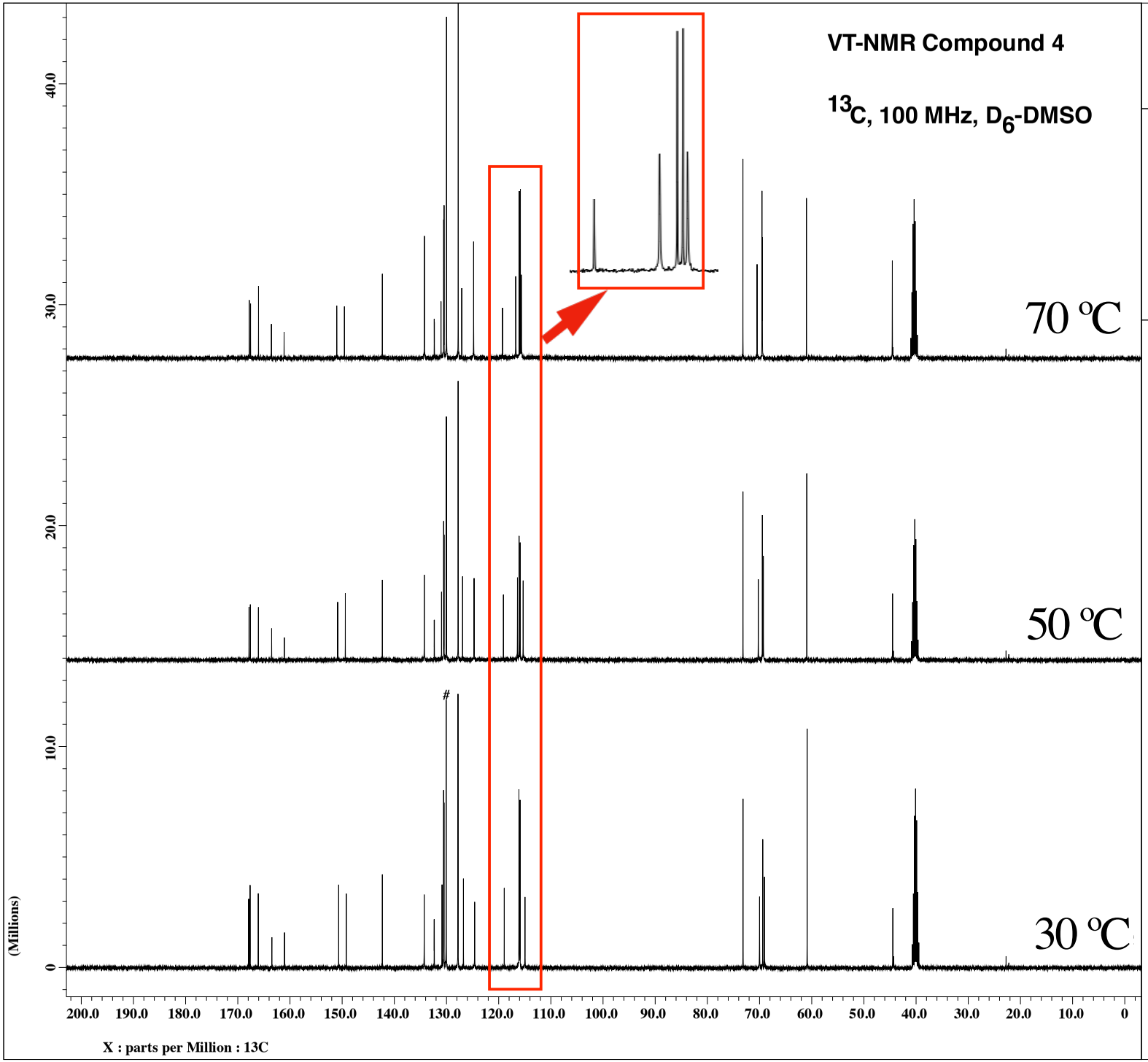

191.06
170.60
153.64
149.34
142.09
130.68
130.11
129.32
127.02
126.98
112.88
111.45
77.48
77.16
76.84
72.79
70.27
69.54
68.78
61.88
Compound 3
13C, 100 MHz, CDCl3
CHO
O
O
O
OH
CO2H
S9
f1 (ppm)


7.98
7.96
7.96
7.86
7.57
7.55
7.38
7.37
7.36
7.36
7.35
7.34
7.33
7.33
7.25
7.19
7.18
7.17
7.16
7.16
7.15
7.14
7.13
7.13
5.27
4.79
4.67
4.18
4.17
4.17
4.16
3.80
3.79
3.79
3.79
3.78
3.53
2.51
2.50
2.50
2.50
2.49
Compound 4
1H, 400 MHz, D6-DMSO
S10
2.07
0.99
2.13
2.11
1.00
4.14
2.05
2.06
0.83
2.05
2.11
4.57
f1 (ppm)


167.43
167.18
165.58
162.97
160.55
150.09
148.63
141.78
133.79
131.86
131.82
130.33
130.08
130.00
129.58
127.30
126.18
124.07
118.33
115.63
115.42
114.27
72.69
69.42
68.86
68.46
60.37
43.93
40.15
39.94
39.73
39.52
39.31
39.10
38.89
Compound 4
13C, 100 MHz, D6-DMSO
S11
f1 (ppm)

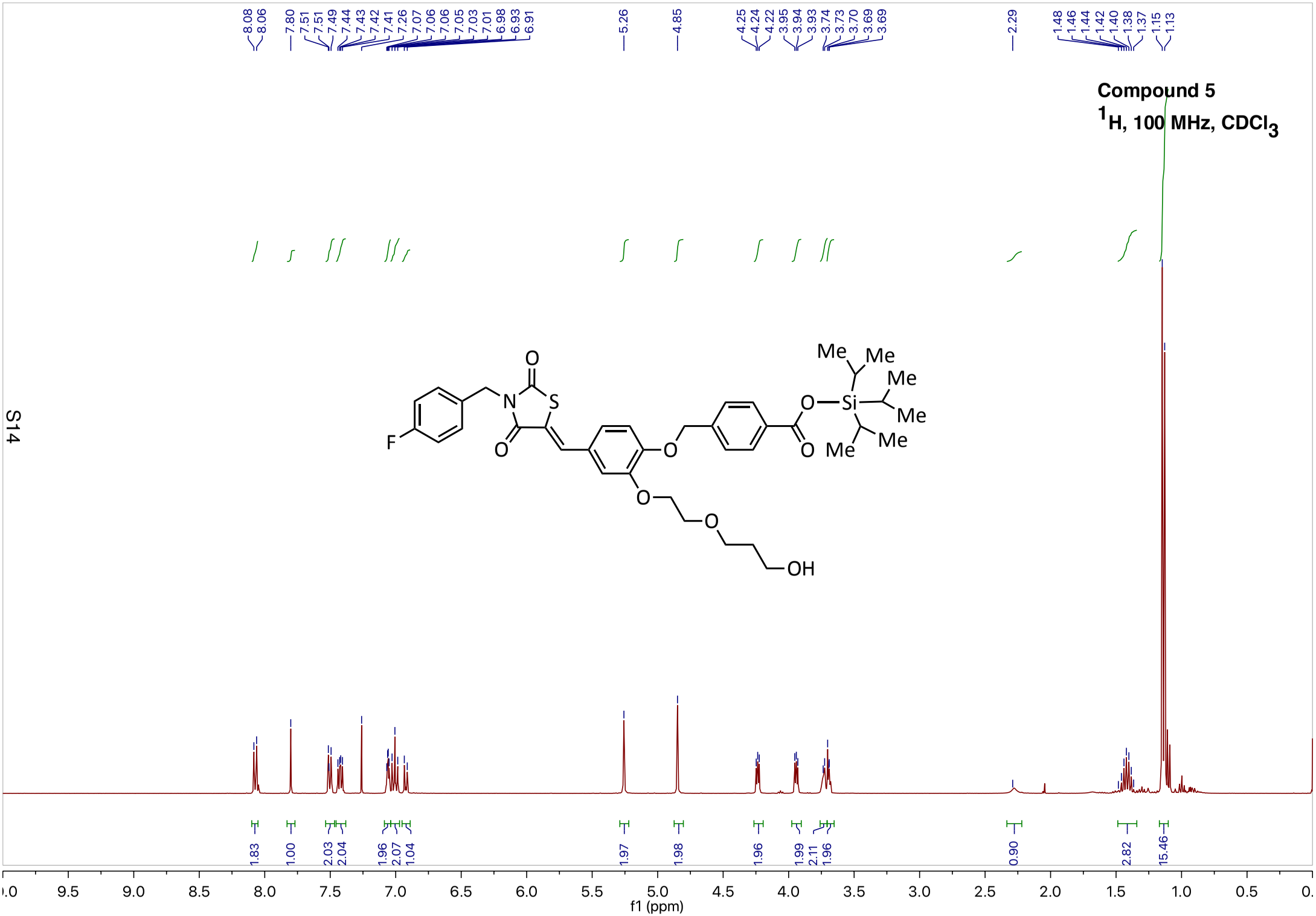
Compound 4
^{13}C expansion

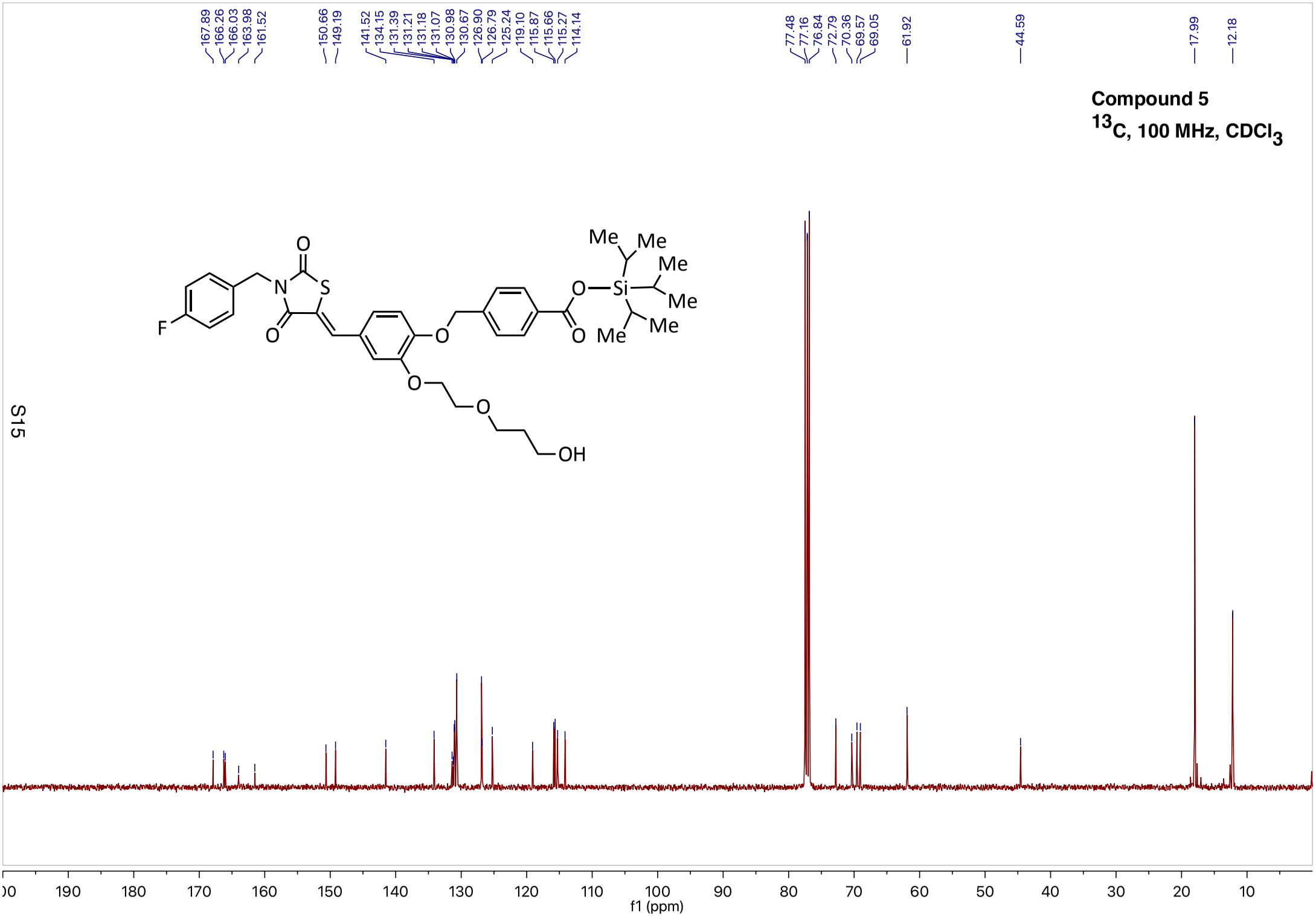




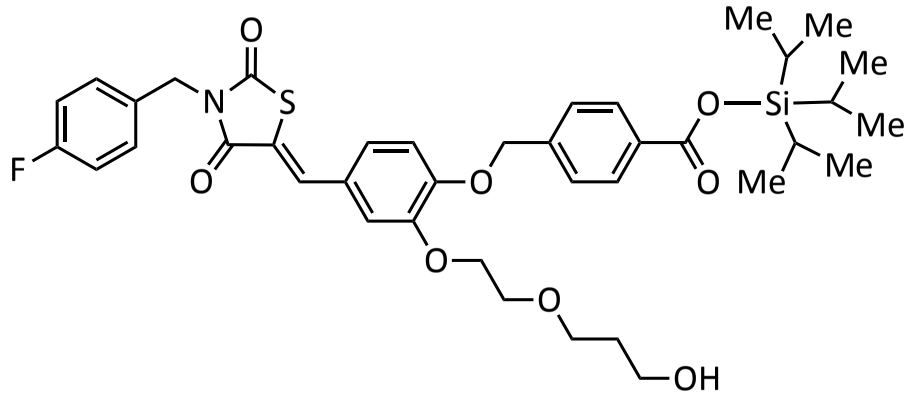

```
---- PROCESSING PARAMETERS ----
dc_balance : 0 : FALSE
sexp : 1.0[Hz] : 0.0[s]
trapezoid3 : 0[%] : 80[%] : 100[%]
zerofill : 1
fft : 1 : TRUE : TRUE
machinephase
ppm
peak_pick : 0[Hz] : 50[Hz] : Peaks : 0[H
```

```
Filename          = sma-cpd4-2.jdf
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#607536
Solvent           = DMSO-D6
Creation_time     = 27-SEP-2017 16:23:32
Revision_time     = 28-SEP-2017 08:35:07
Current_time      = 28-SEP-2017 08:35:32

Comment           = Single Pulse with Bro
Data_format       = 1D COMPLEX
Dim_size          = 32768
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 400A
Spectrometer      = DELTA_NMR

Field_strength    = 9.389766[T] (400[MHz]
X_acq_duration    = 1.3008896[s]
X_domain          = 13C
X_freq            = 100.52530333[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 0.76870474[Hz]
X_sweep           = 25.18891688[kHz]
Irr_domain        = 1H
Irr_freq          = 399.78219838[MHz]
Irr_offset        = 5[ppm]
Clipped           = TRUE
Mod_return        = 2
Scans             = 714
Total_scans       = 714

X_90_width        = 14[us]
X_acq_time        = 1.3008896[s]
X_angle           = 60[deg]
X_pulse           = 9.33333333[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 30
Relaxation_delay  = 1[s]
Temp_get          = 30[dC]
Unblank_time      = 2[us]
```


Compound 5
1H, 100 MHz, CDCl3
8.08
8.06
7.80
7.51
7.51
7.49
7.44
7.43
7.42
7.41
7.26
7.07
7.06
7.06
7.05
7.03
7.01
6.98
6.93
6.91
5.26
4.85
4.25
4.24
4.22
3.95
3.94
3.93
3.74
3.73
3.70
3.69
3.69
2.29
1.48
1.46
1.44
1.42
1.40
1.38
1.37
1.15
1.13
F
N
S
O
O
O
O
O
O
Si
Me
Me
Me
Me
Me
Me
O
O
OH
1.83
1.00
2.03
2.04
1.96
2.07
1.04
1.97
1.98
1.96
1.99
2.11
1.96
0.90
2.82
15.46
f1 (ppm)


167.89
166.26
166.03
163.98
161.52
150.66
149.19
141.52
134.15
131.39
131.21
131.18
131.07
130.98
130.67
126.90
126.79
125.24
119.10
115.87
115.66
115.27
114.14
77.48
77.16
76.84
72.79
70.36
69.57
69.05
61.92
44.59
17.99
12.18
Compound 5
13C, 100 MHz, CDCl3
S15
f1 (ppm)

Compound 5
^{13}C expansion

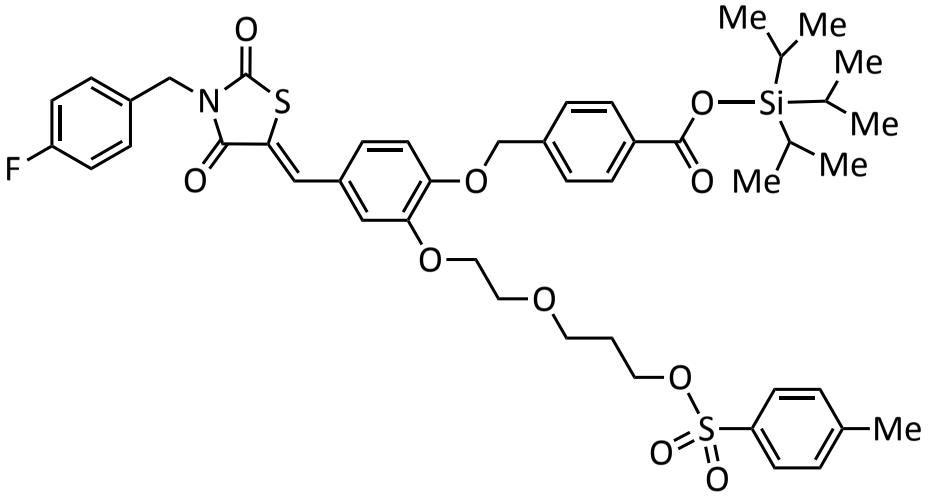


167.89
166.26
166.03
163.98
161.52
150.66
149.19
141.52
134.15
131.39
131.21
131.18
131.07
130.98
130.67
126.90
126.79
125.24
119.10
115.87
115.66
115.27
114.14

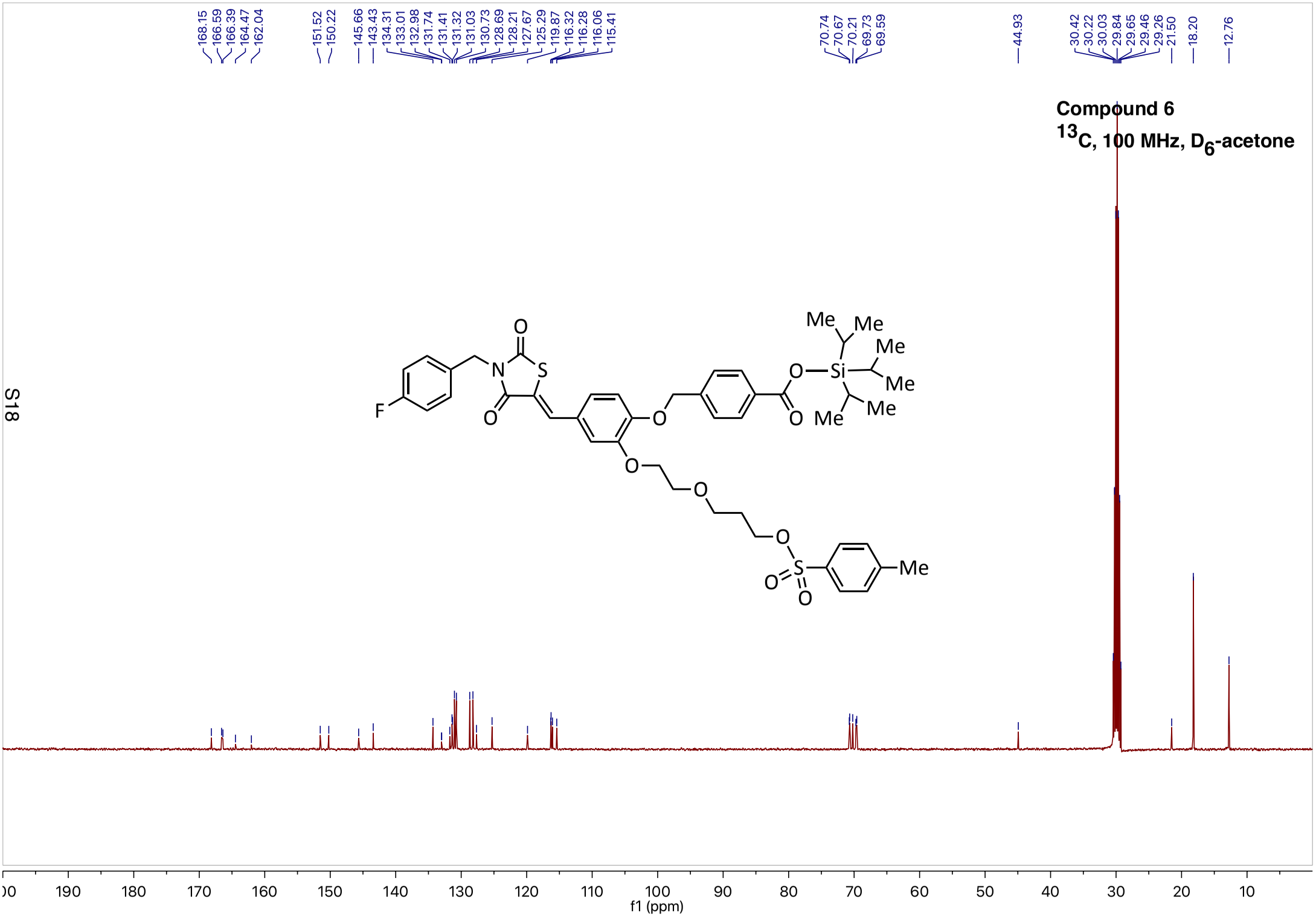
170 165 160 155 150 145 140 135 130 125 120 115
f1 (ppm)

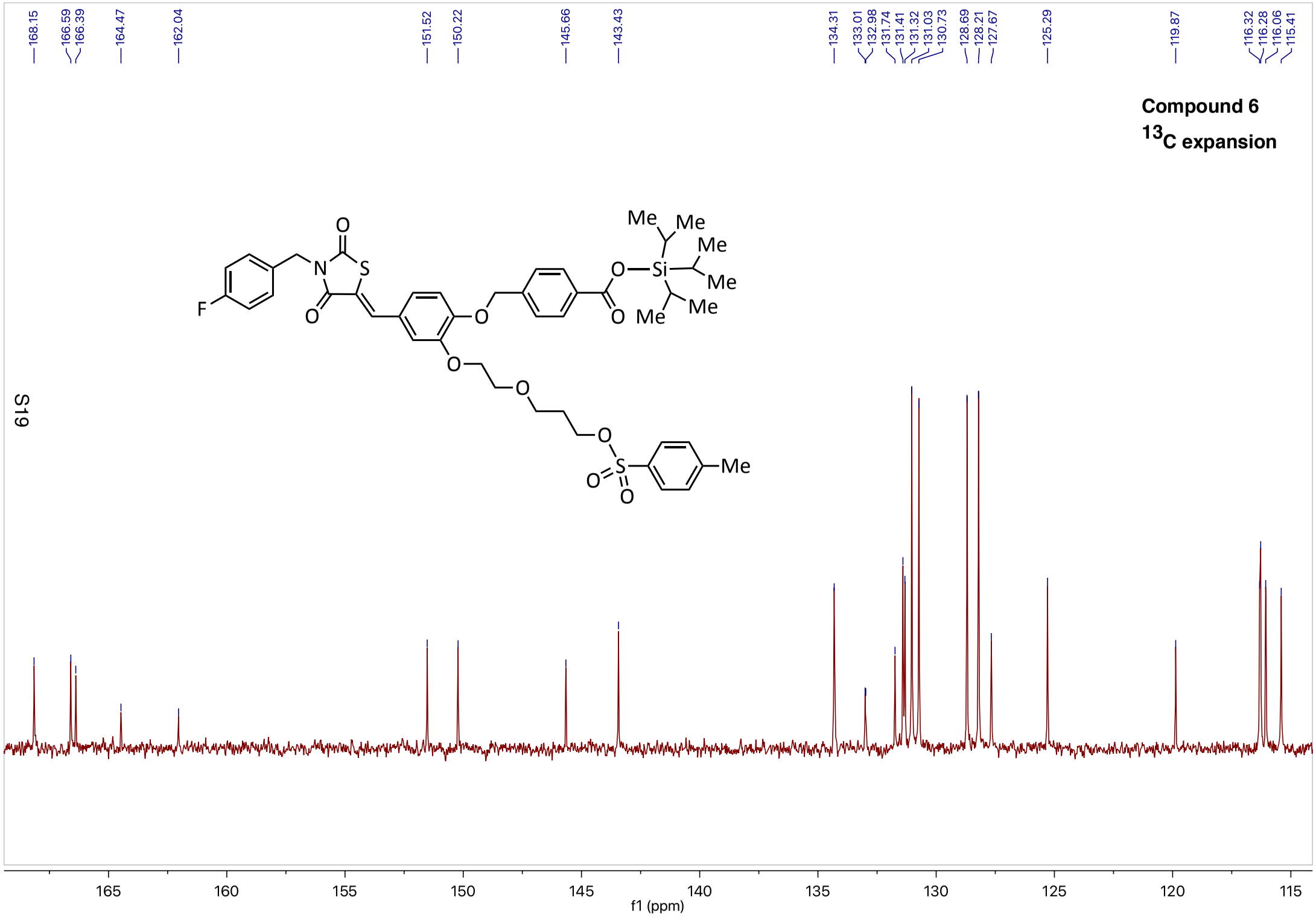
Compound 6

^{1}H, 400 MHz, D$_6$-acetone



f1 (ppm)


168.15
166.59
166.39
164.47
162.04
151.52
150.22
145.66
143.43
134.31
133.01
132.98
131.74
131.41
131.32
131.03
130.73
128.69
128.21
127.67
125.29
119.87
116.32
116.28
116.06
115.41
70.74
70.67
70.21
69.73
69.59
44.93
30.42
30.22
30.03
29.84
29.65
29.46
29.26
21.50
18.20
12.76
Compound 6
13C, 100 MHz, D6-acetone
F
N
S
O
Si
Me
f1 (ppm)


168.15
166.59
166.39
164.47
162.04
151.52
150.22
145.66
143.43
134.31
133.01
132.98
131.74
131.41
131.32
131.03
130.73
128.69
128.21
127.67
125.29
119.87
116.32
116.28
116.06
115.41
Compound 6
13C expansion
S19
F
O
N
S
O
O
O
O
O
Si
Me
Me
Me
Me
Me
Me
O
O
O
O
S
O
O
Me
165
160
155
150
145
140
135
130
125
120
115
f1 (ppm)