Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Syntheses and *in vitro* biological evaluation of new S1PR1 ligands and PET studies of four F-18 labeled radiotracers in the brain of nonhuman primate

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[b]*Departments of Neurology, Neuroscience, Physical Therapy and Occupational Therapy, Washington University School of Medicine, St. Louis, MO 63110, United States.*
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Contents of Supporting Information

1. MicroPET Study for [^{18}F]6 in the Brain of Nonhuman Primate

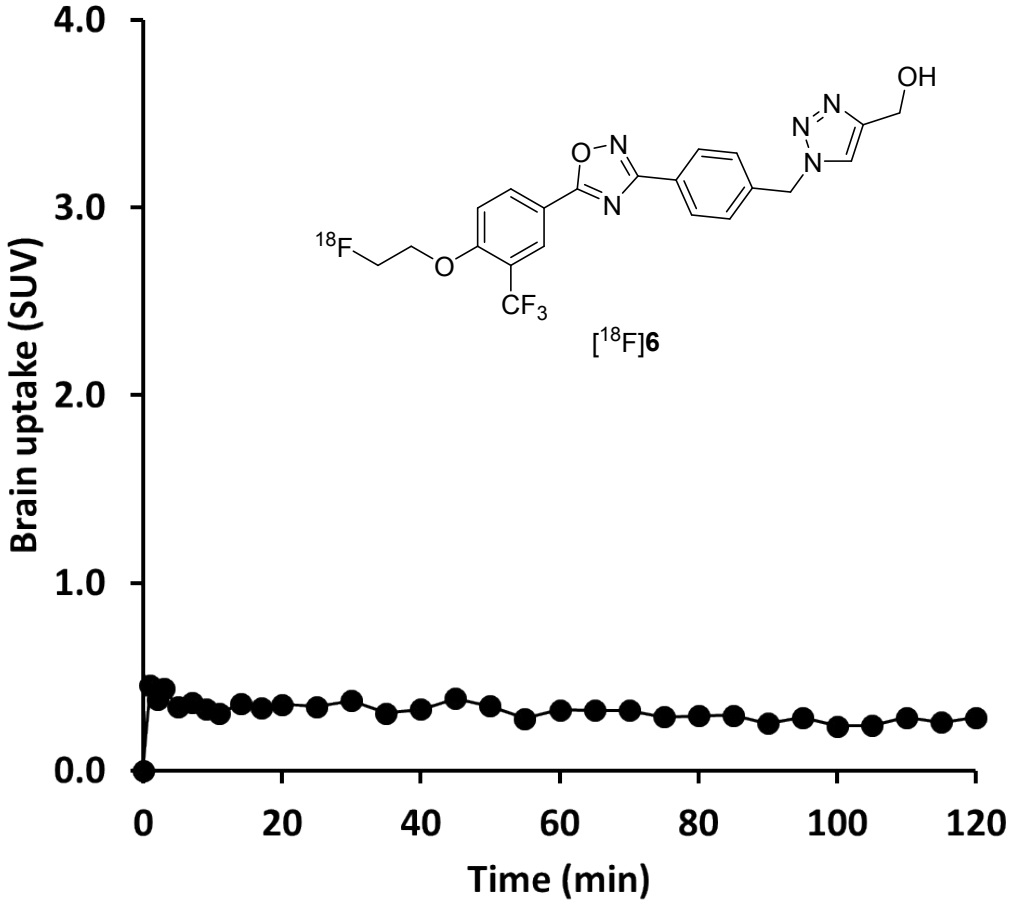
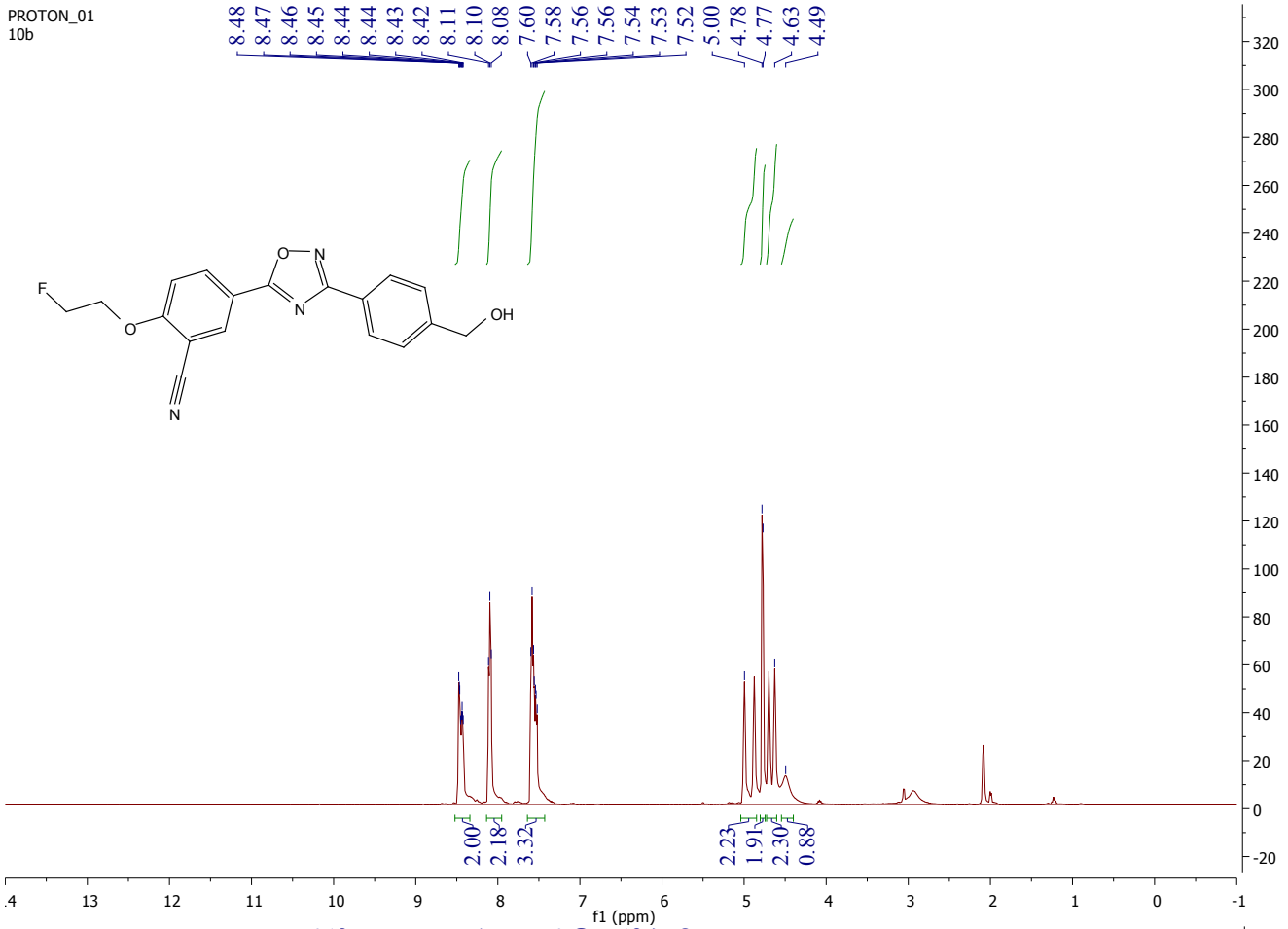


Figure S1. Representative time-activity curves of microPET studies for [^{18}F]**6** in the brain of nonhuman primates. Male macaques (9-10 kg) received i.v. injection of ~0.35 GBq of [^{18}F]**6**, and underwent a 2 h dynamic PET scan using microPET Focus 220. PET data was corrected, reconstructed, and co-registered with MRI images for quantitative analysis. The ROI (the global brain) was identified on the MRI and transformed to the reconstructed PET images to obtain time-activity curves. Activity measures were standardized to body weight and the dose of radioactivity injected to yield standardized uptake values (SUVs). The low brain uptake indicated that [^{18}F]**6** cannot enter the NHP brain, which limited its application in imaging brain S1PR1 *in vivo*.

2. ^{1}H NMR and ^{13}C NMR spectra for new compounds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4.63
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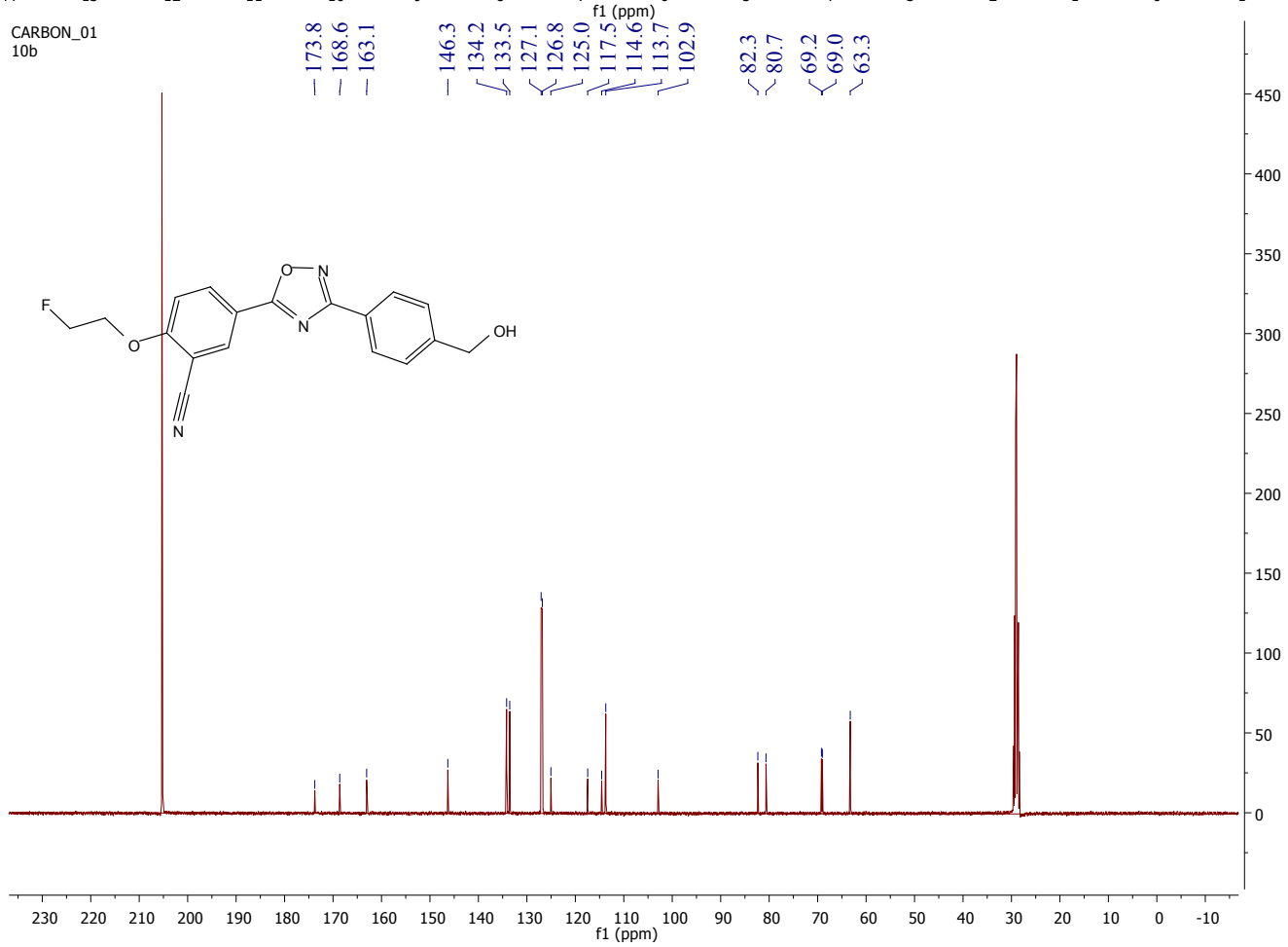
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OH
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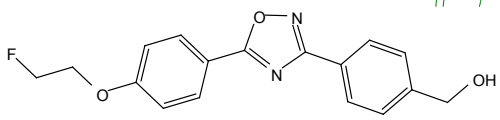

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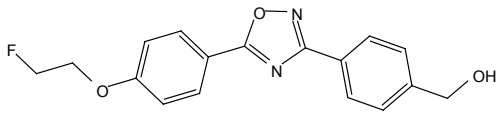

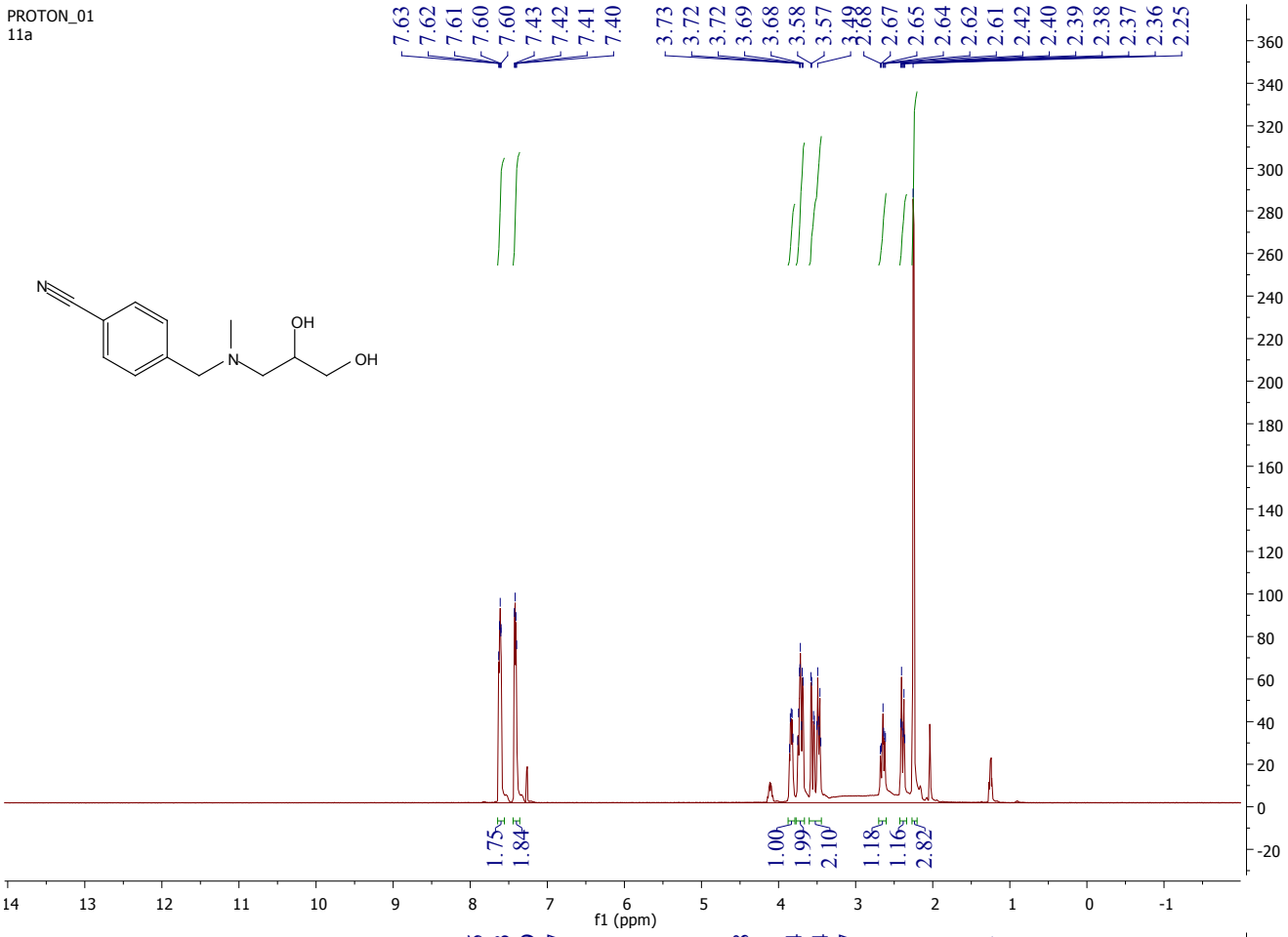
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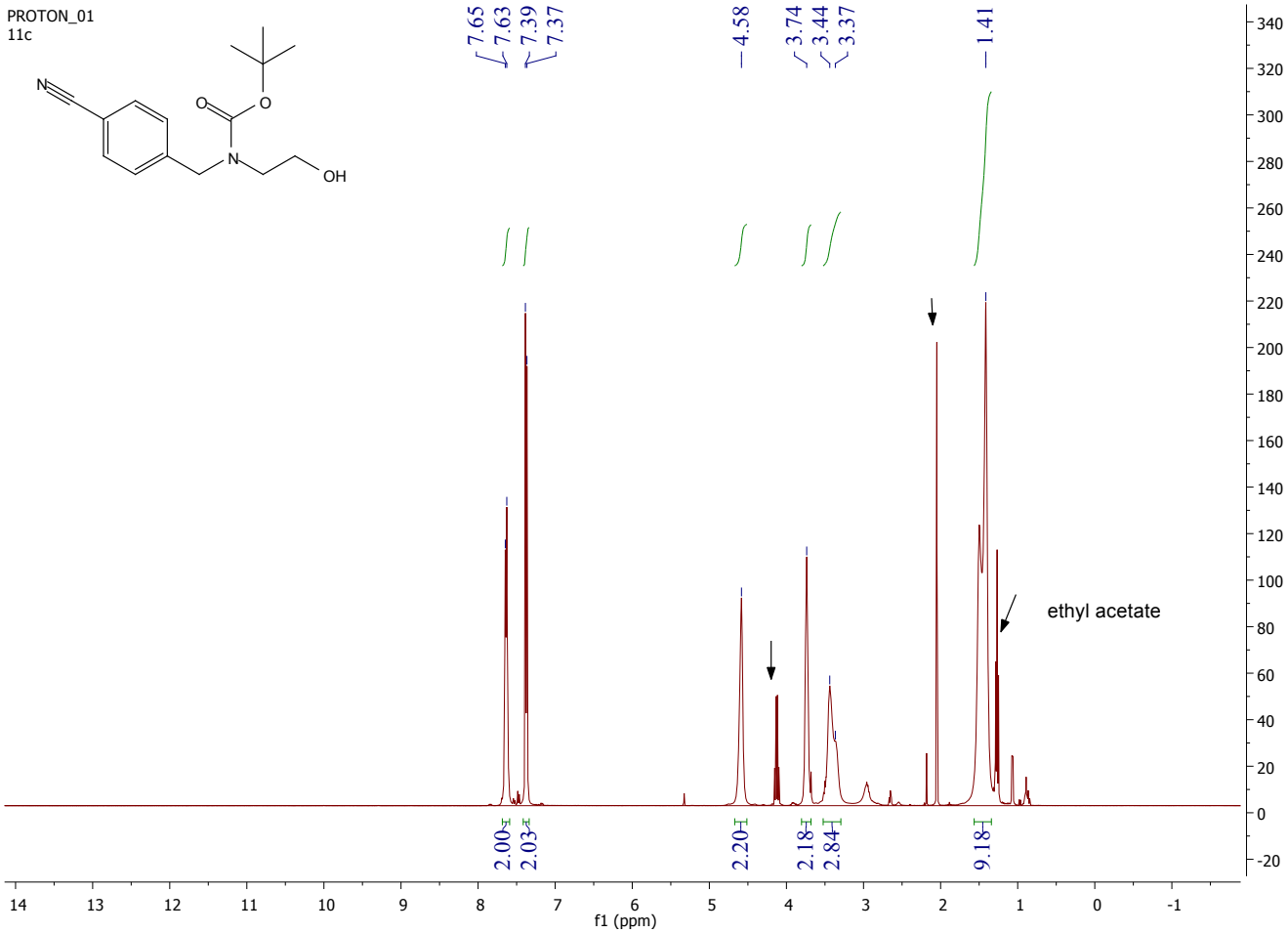
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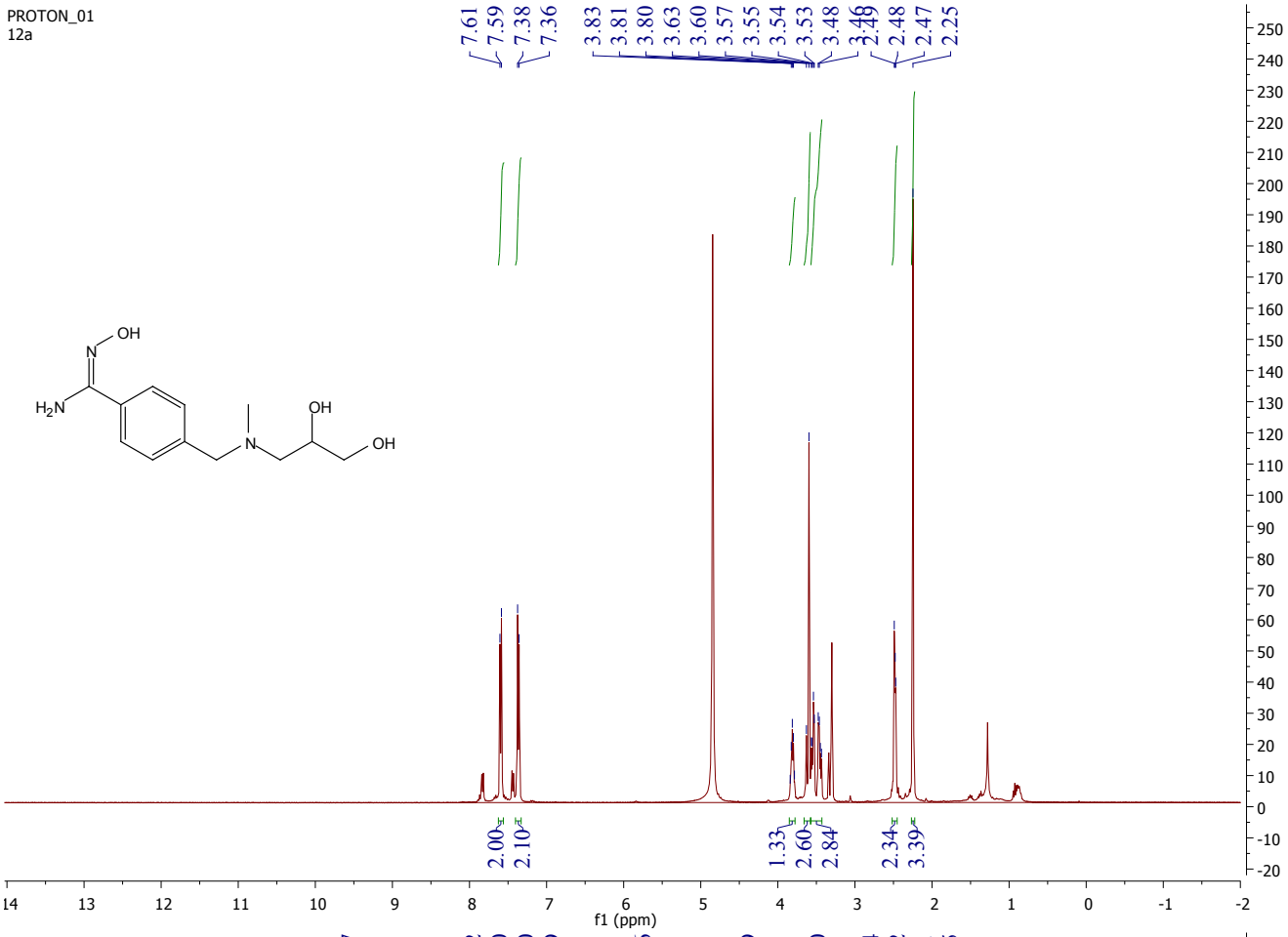
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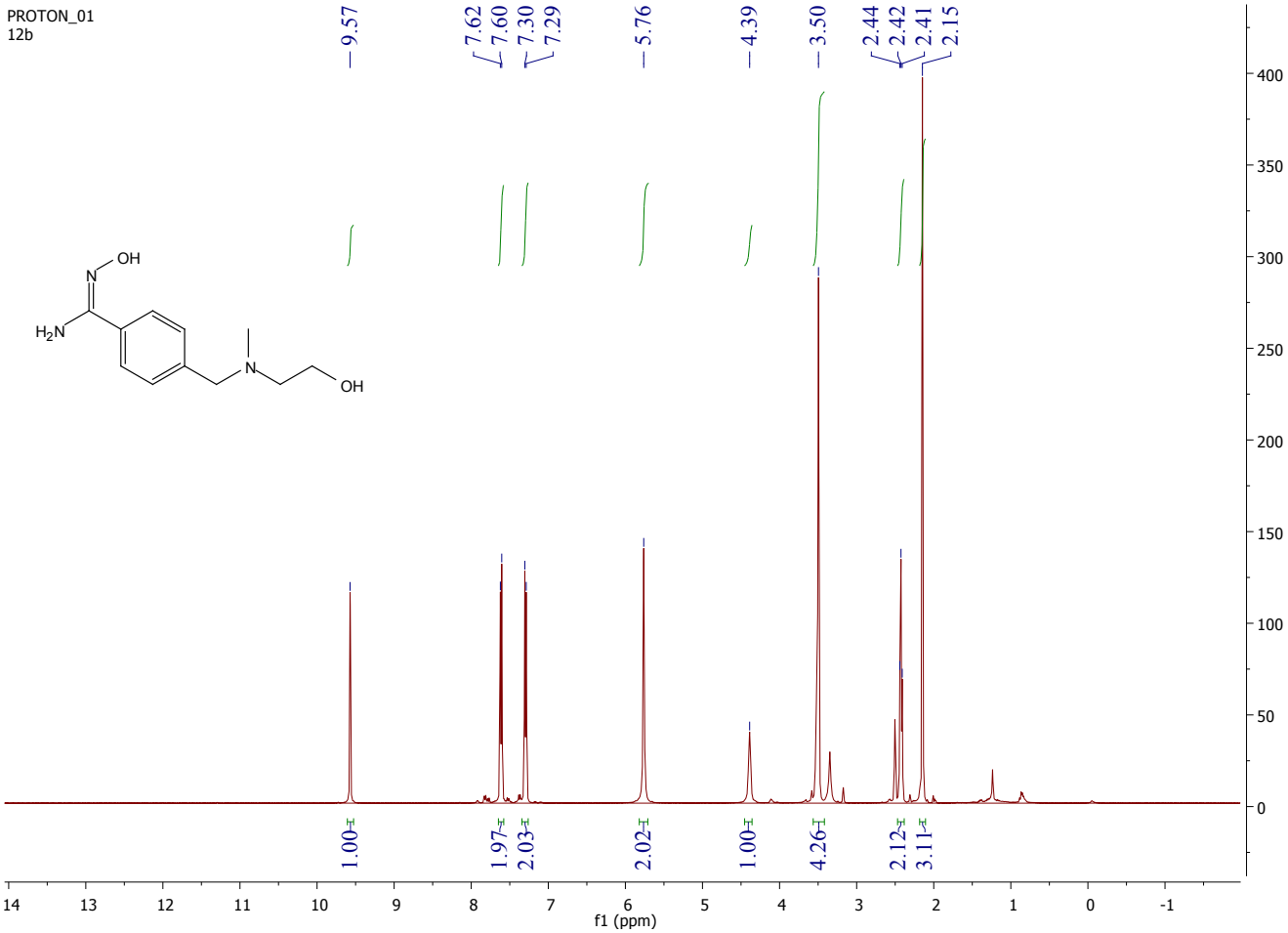
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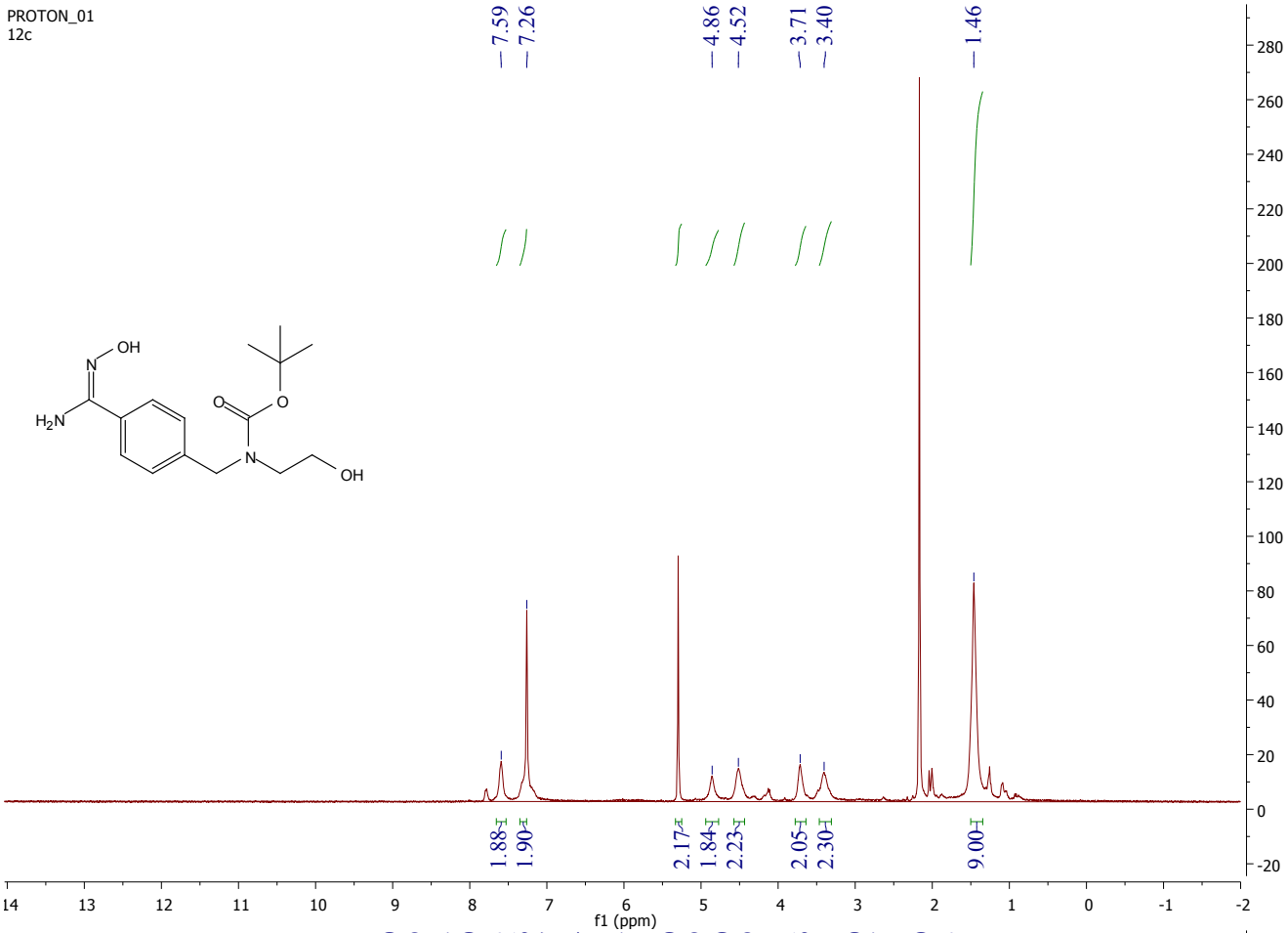
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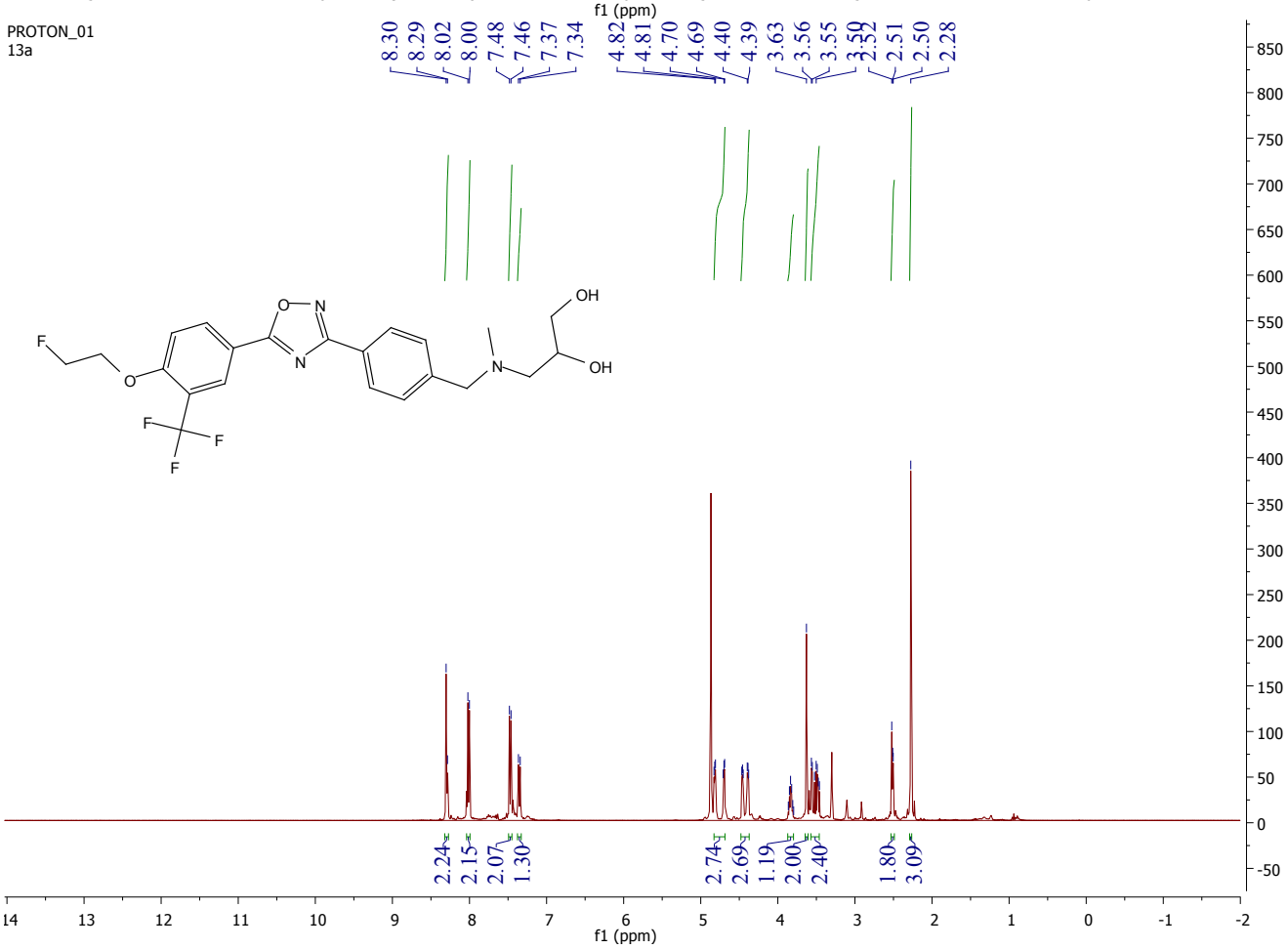
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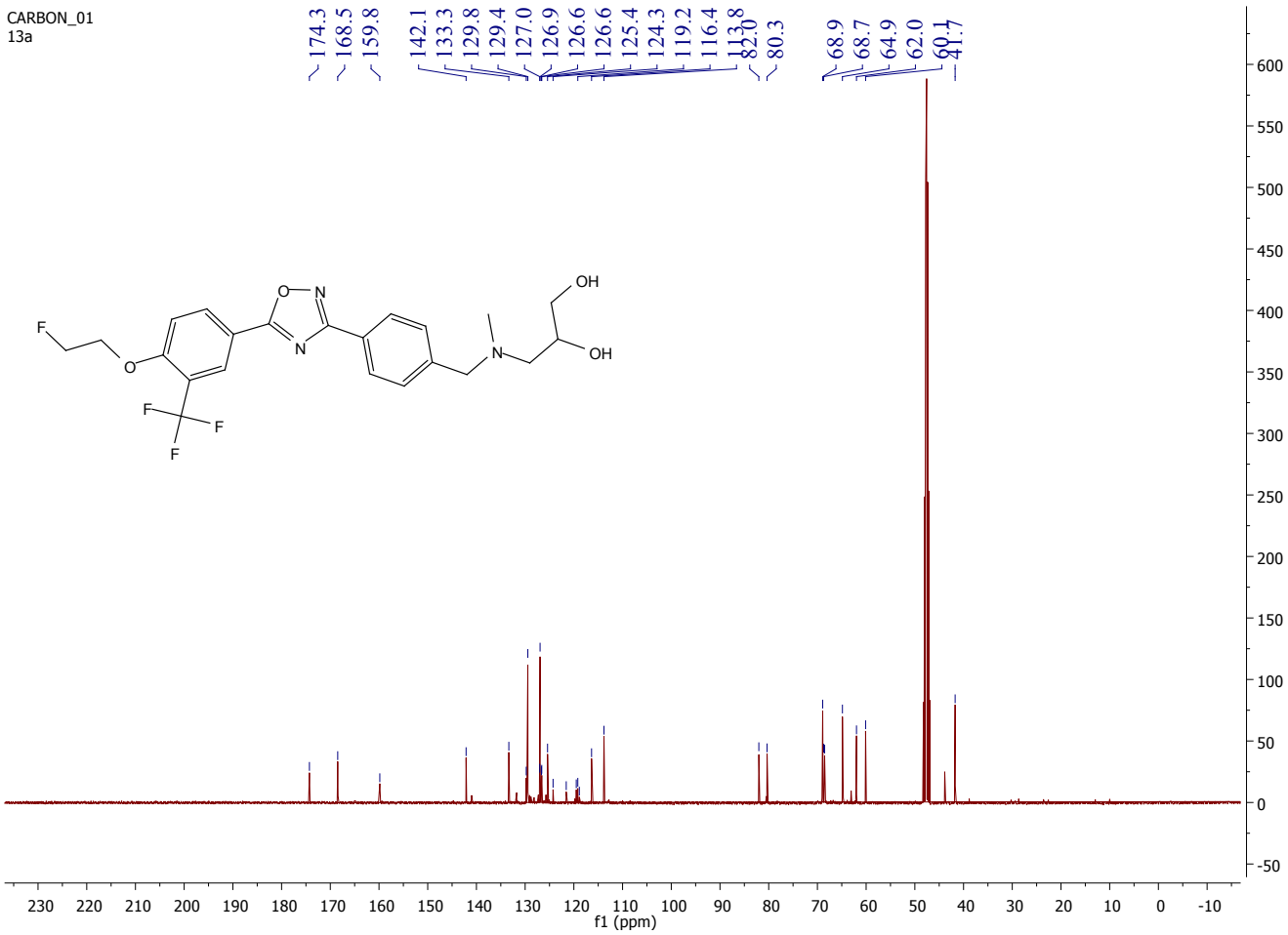
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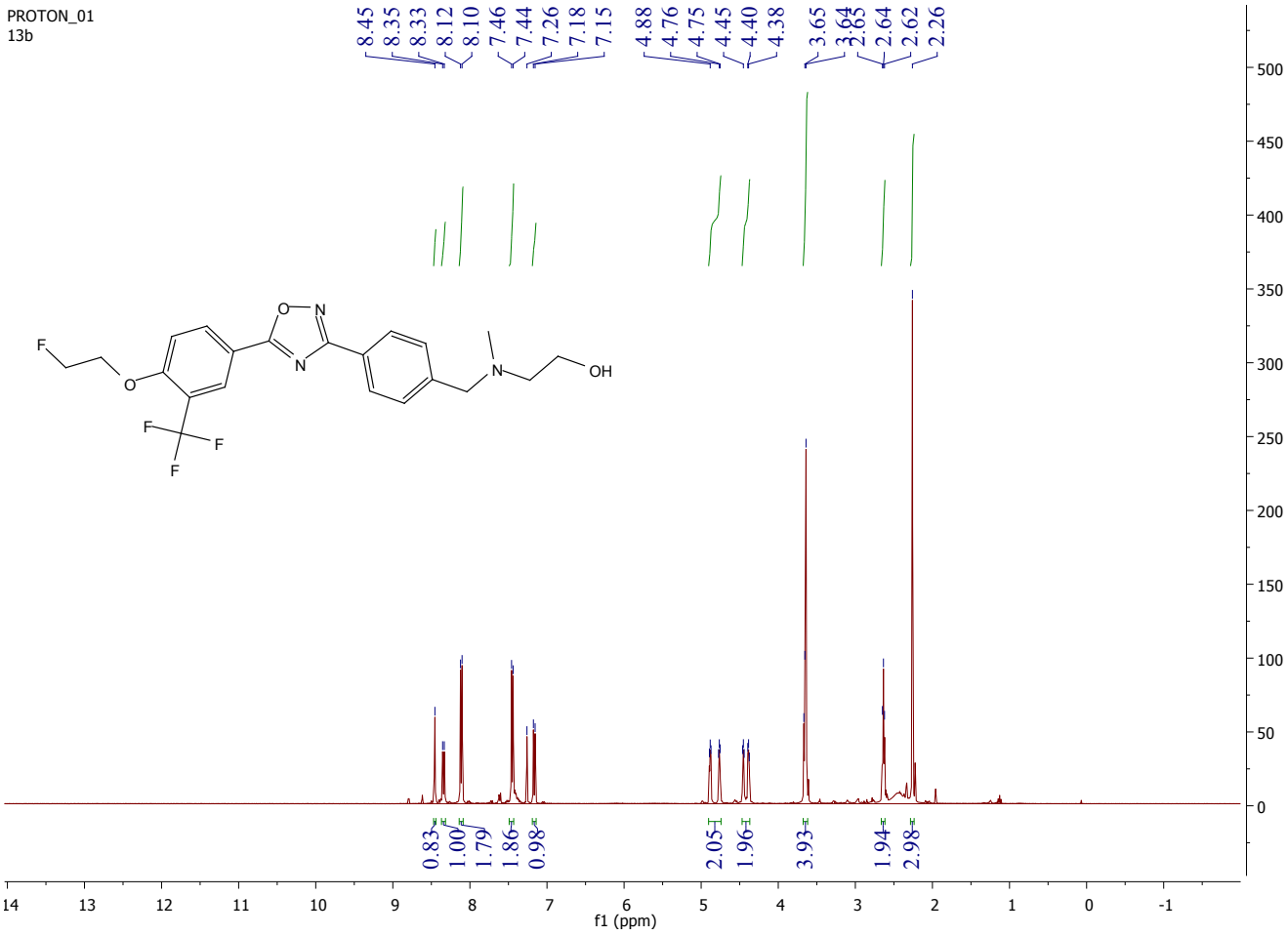
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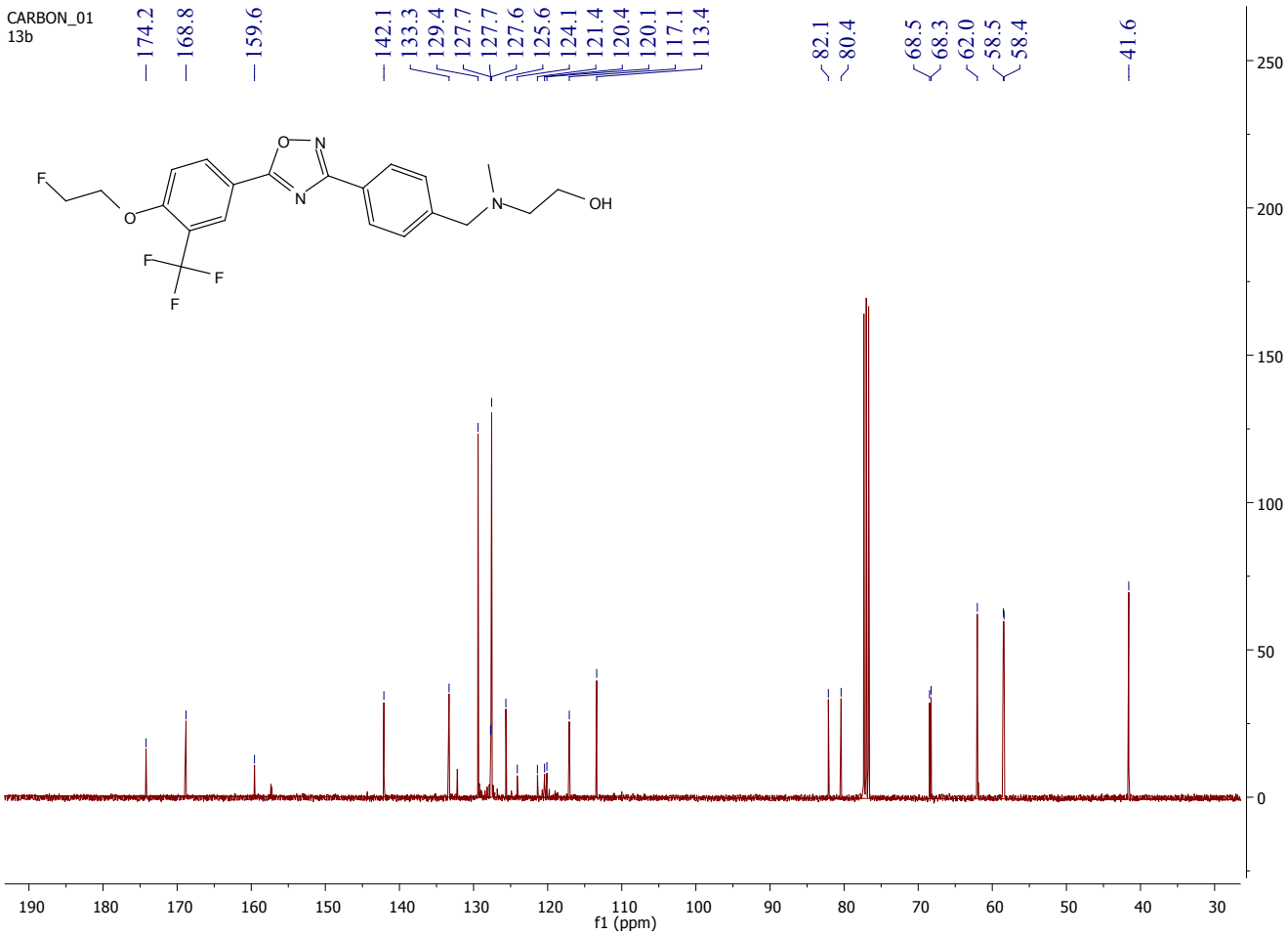
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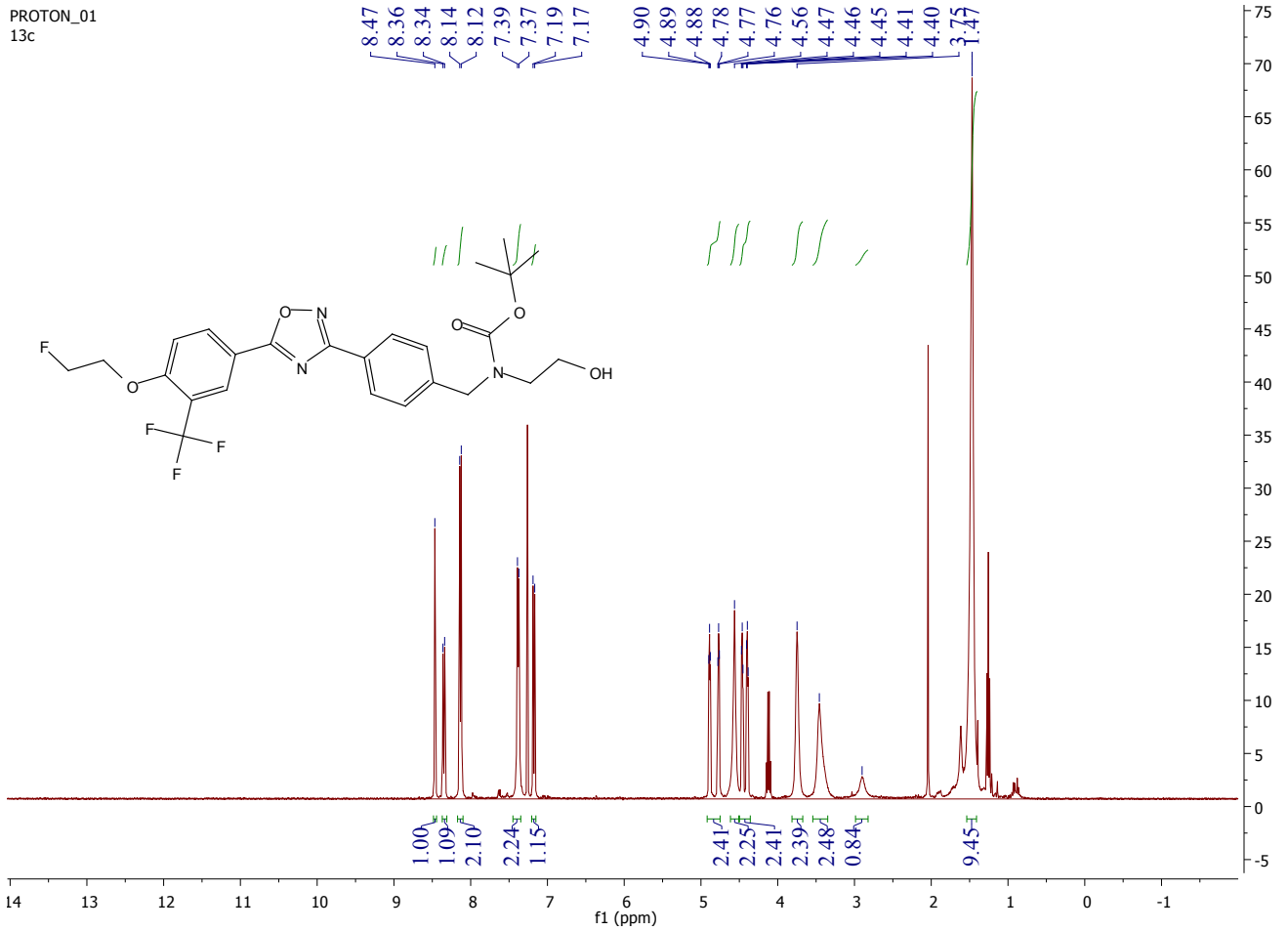
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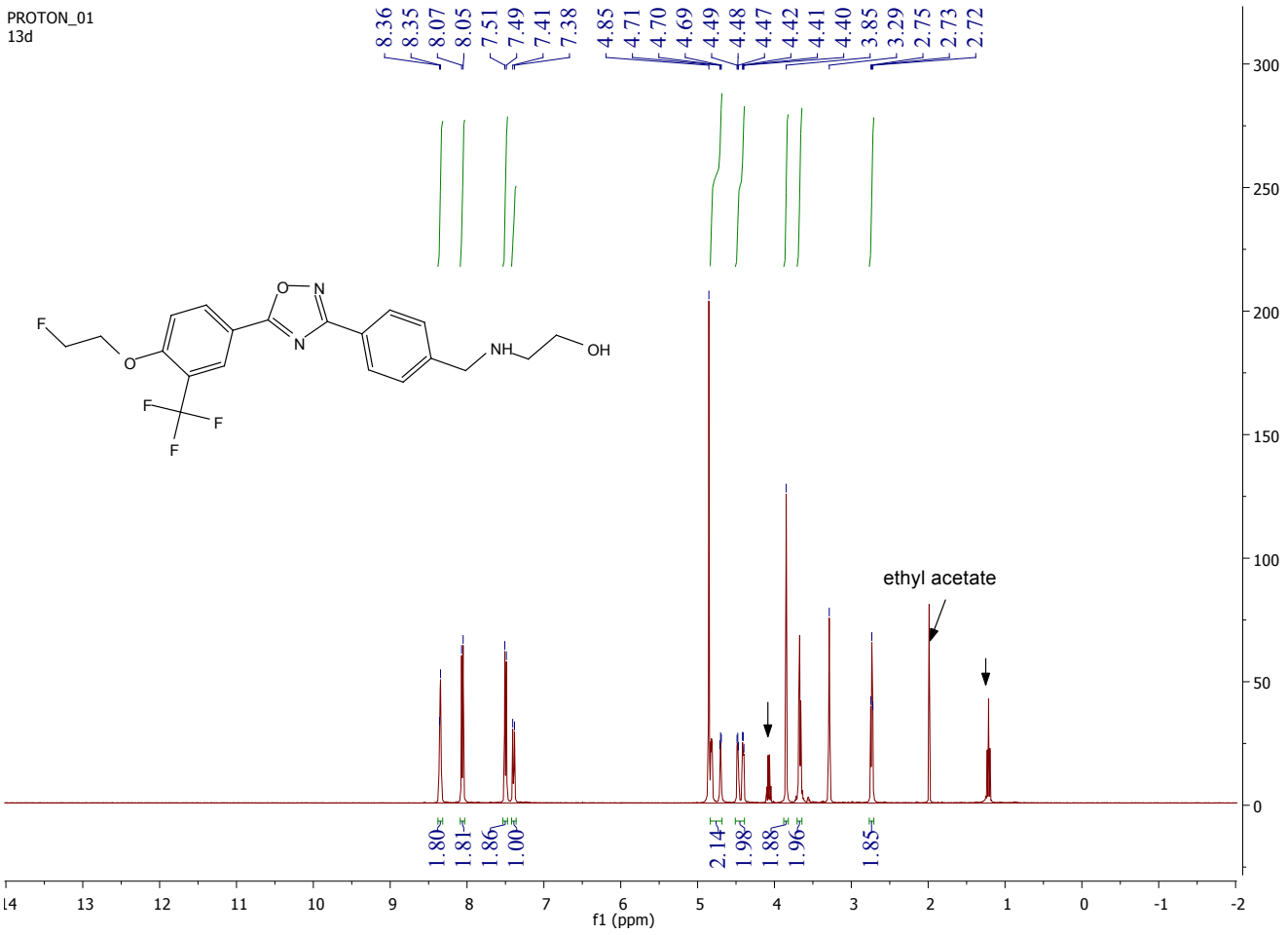
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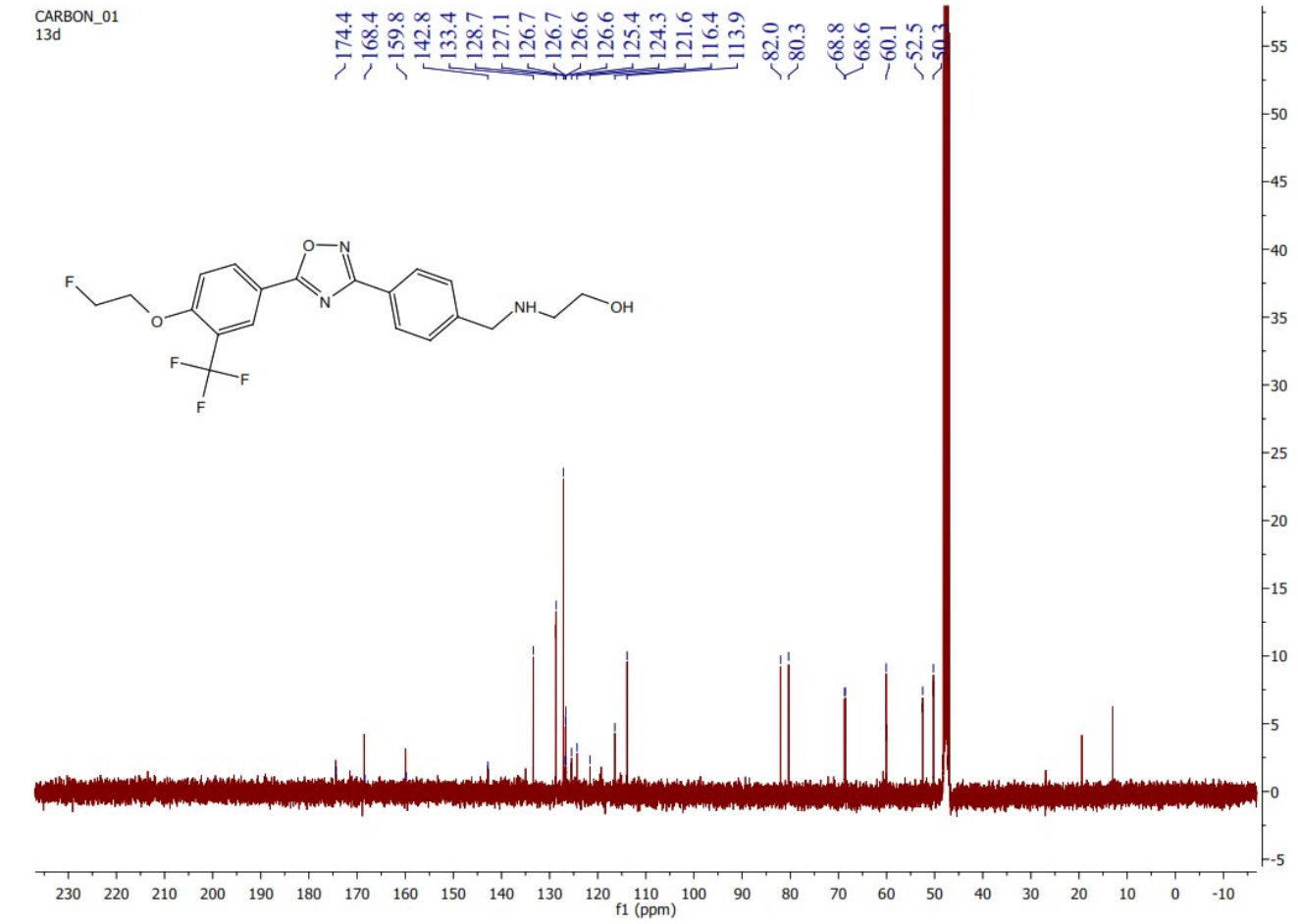
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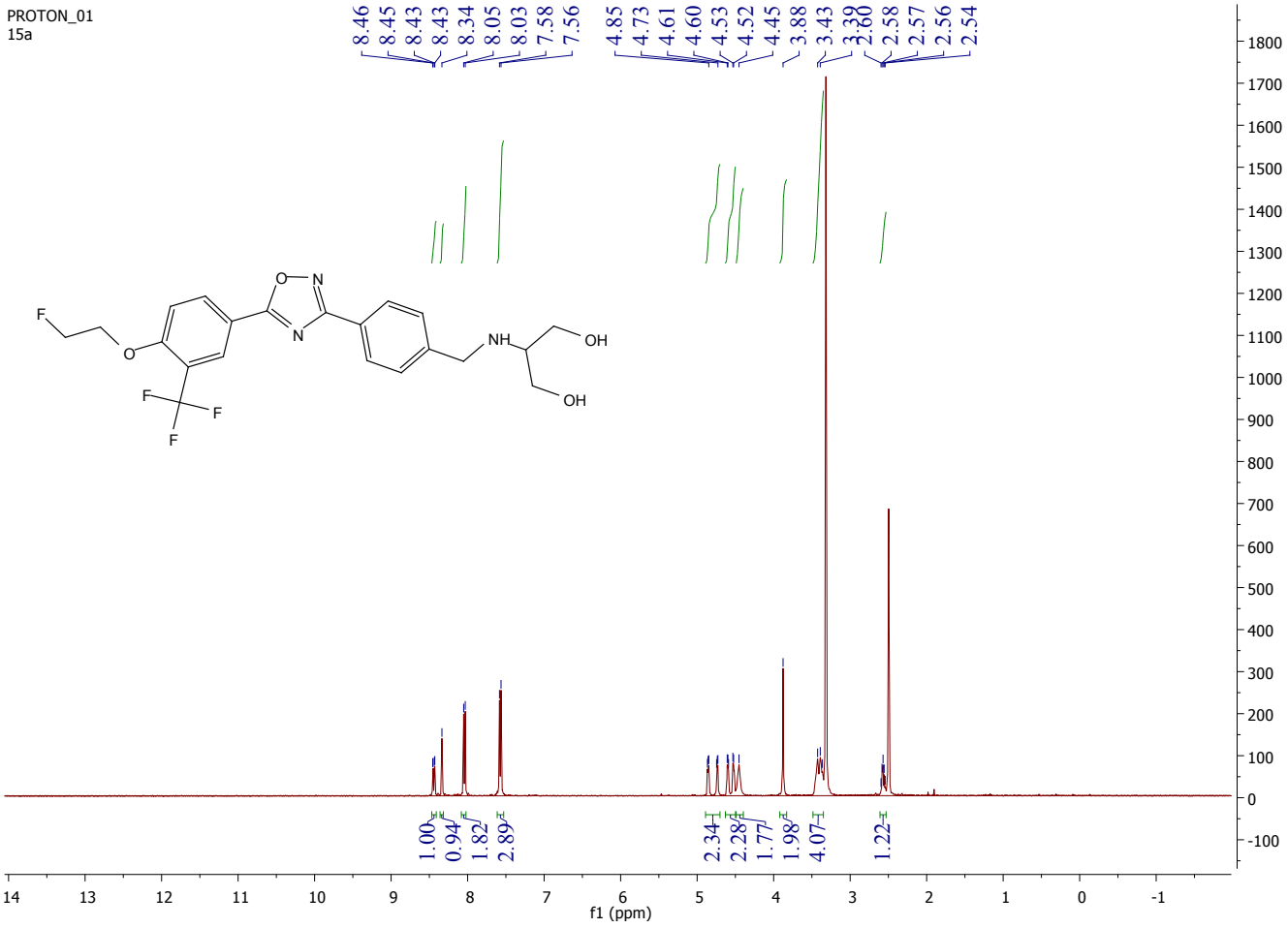
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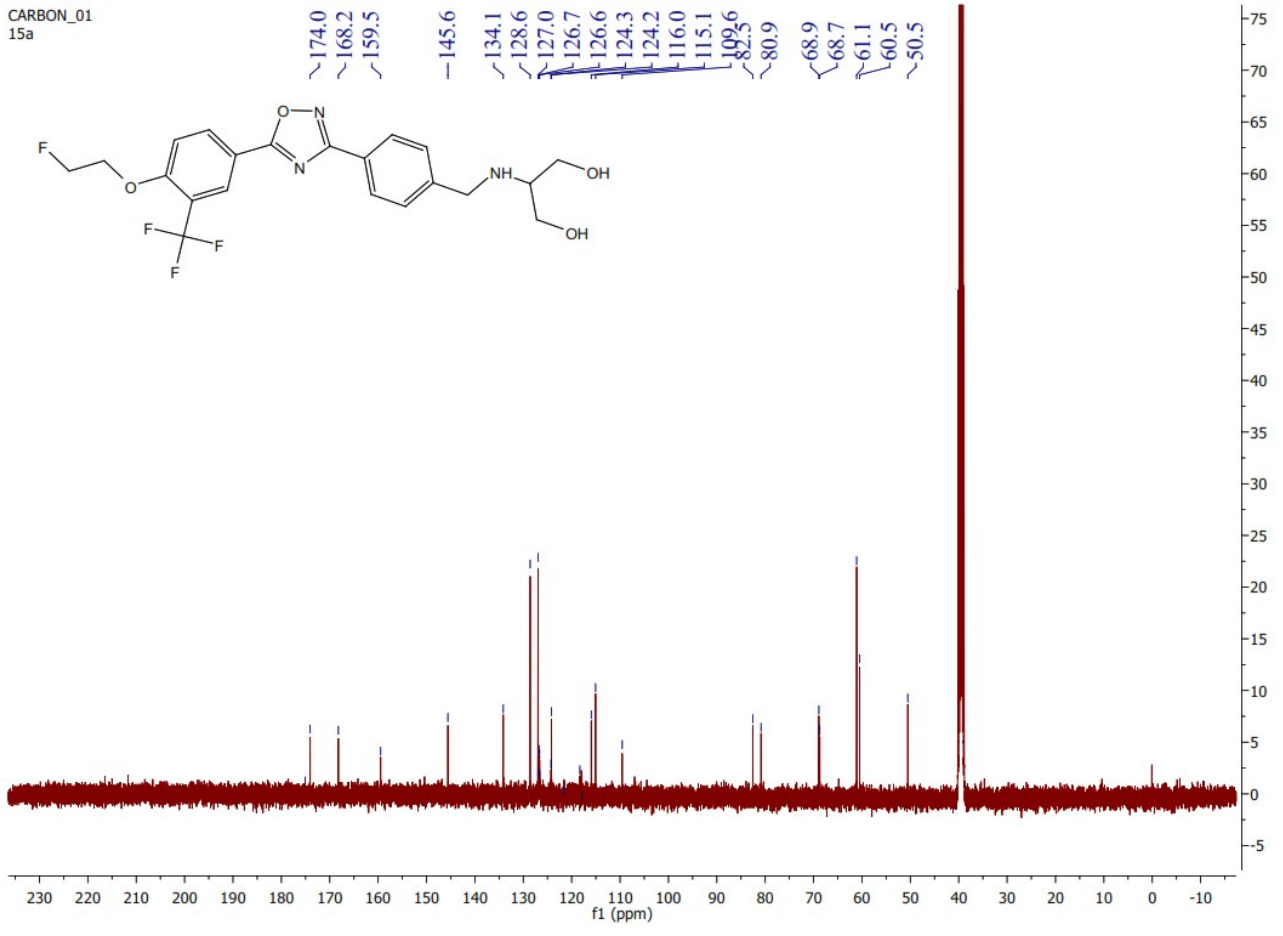
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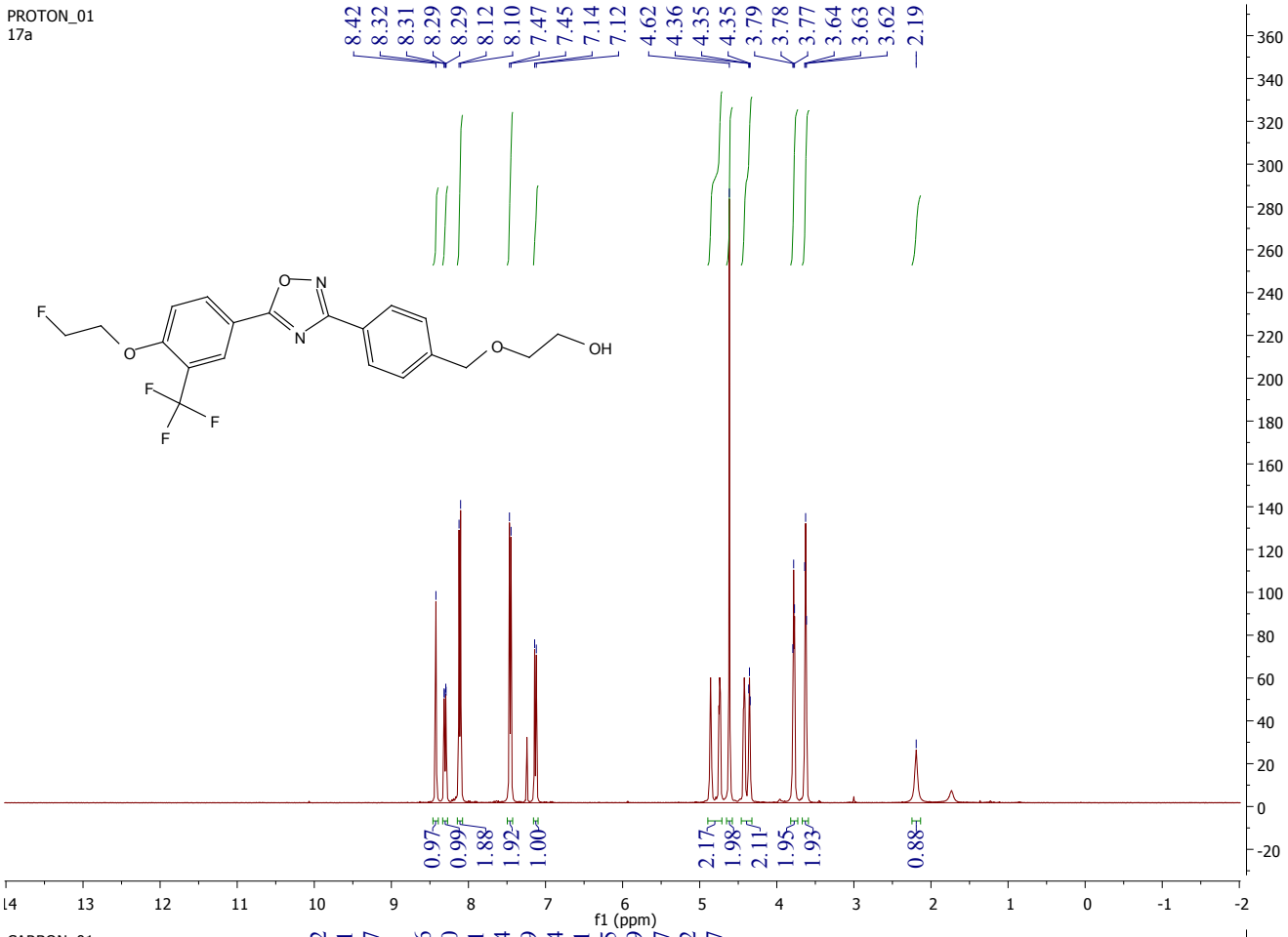
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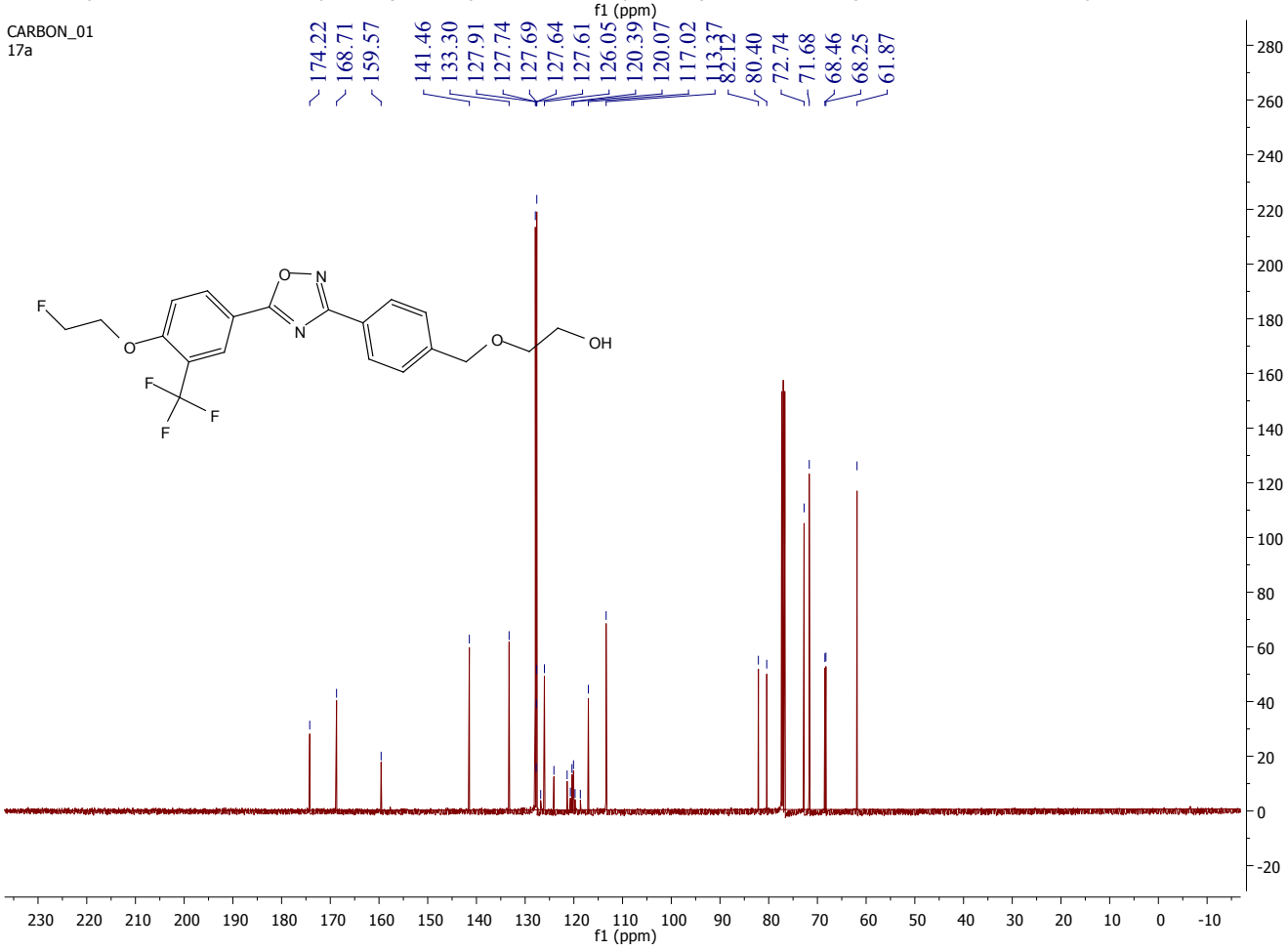
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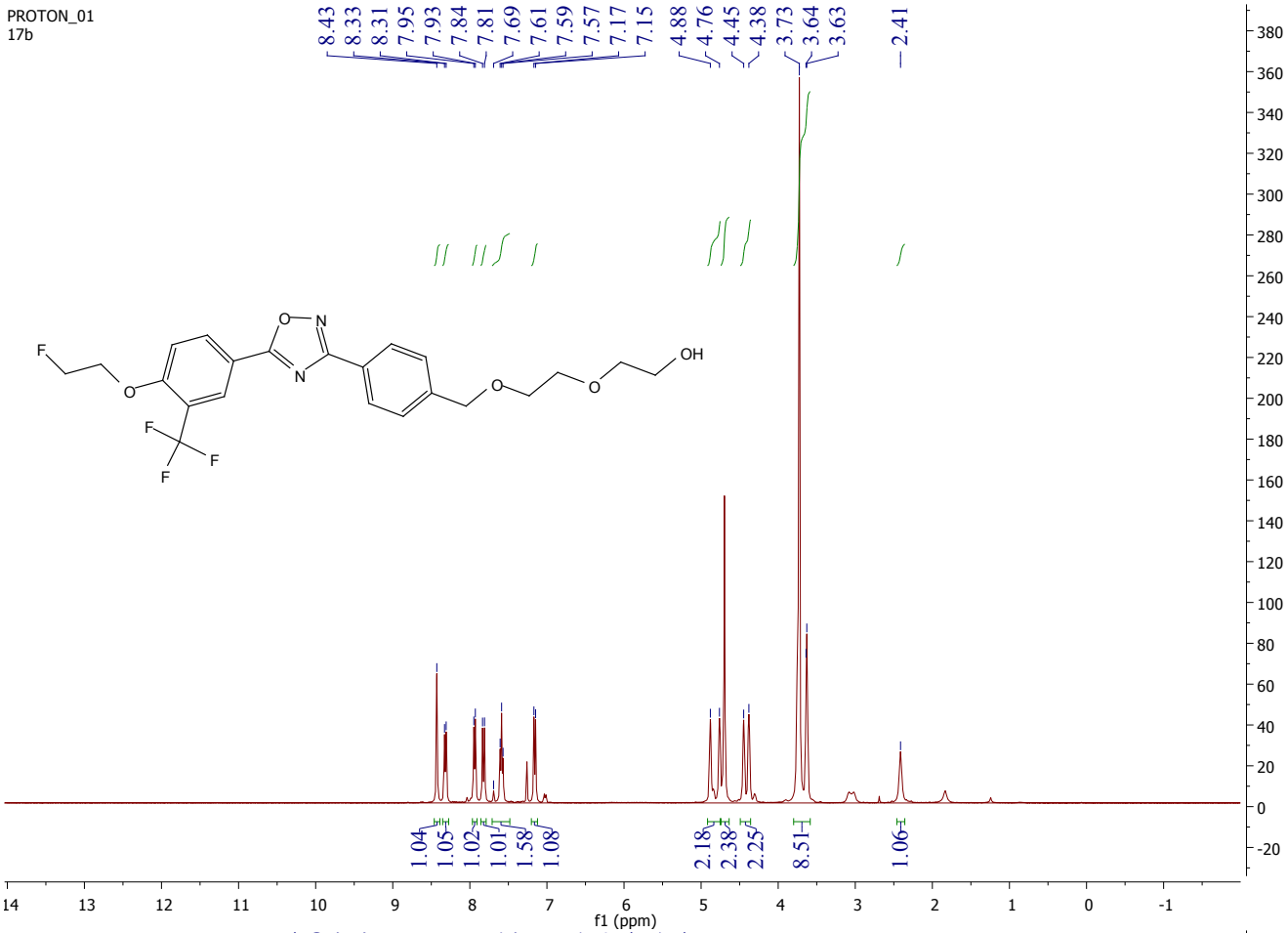
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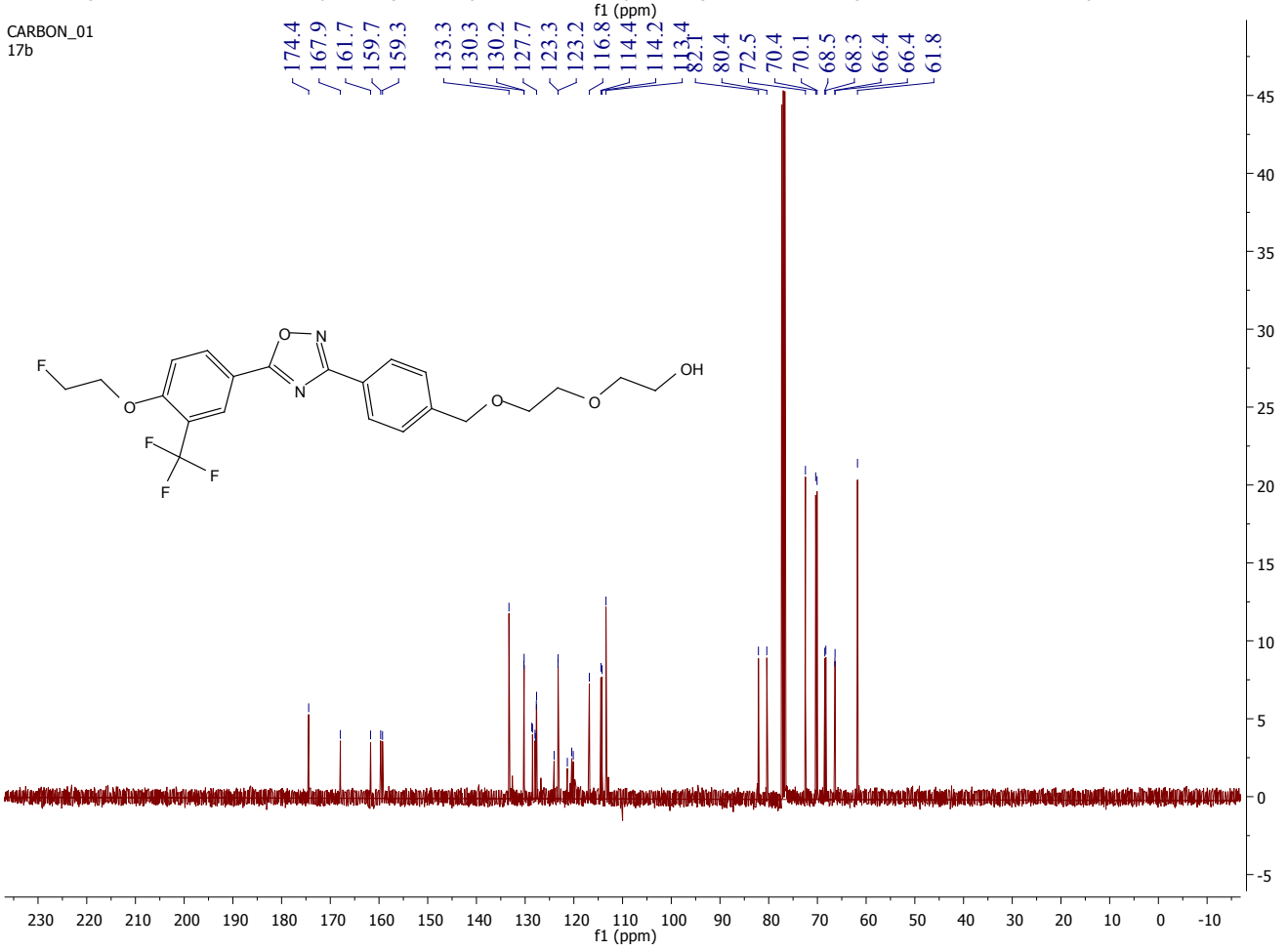
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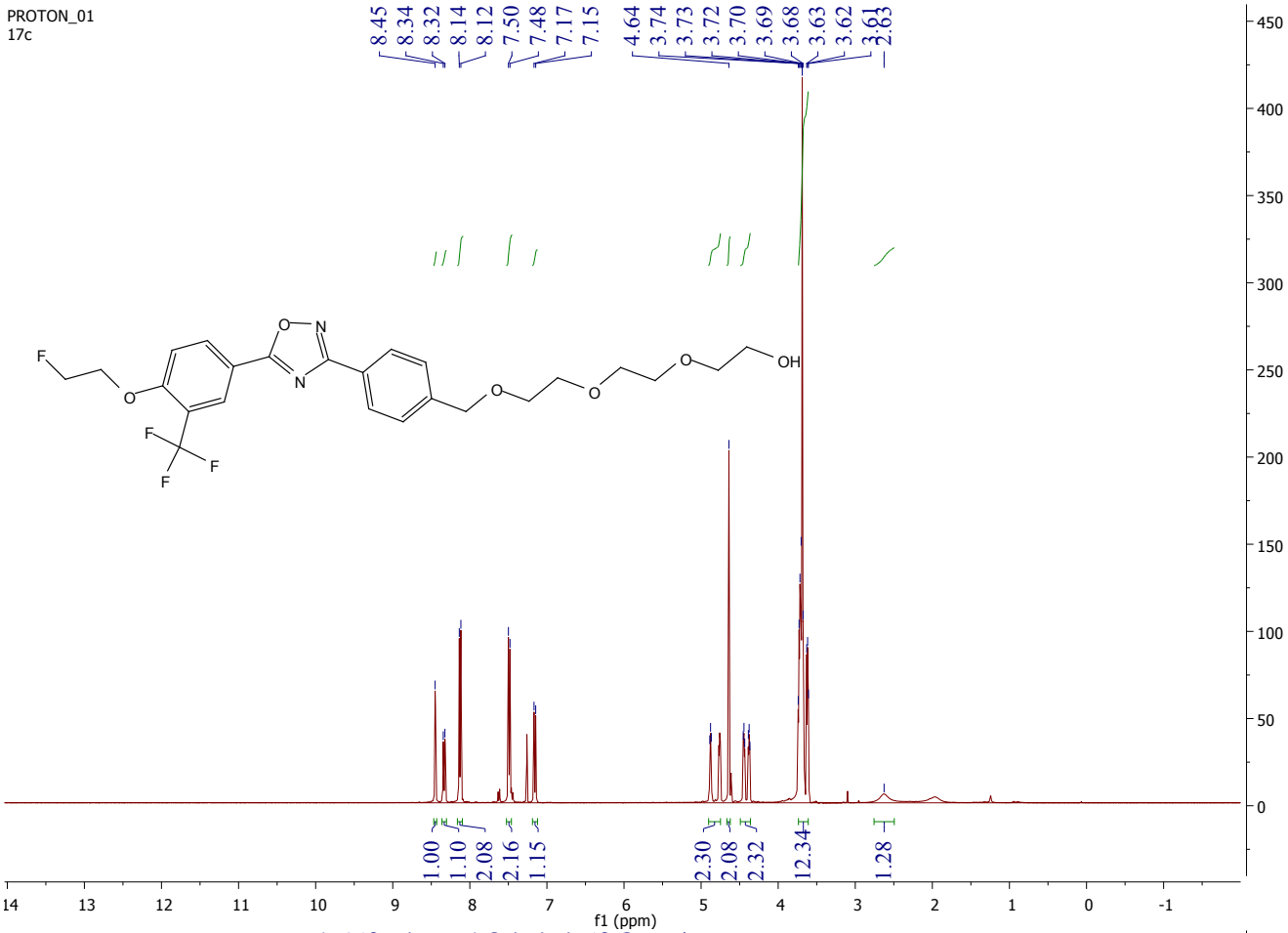
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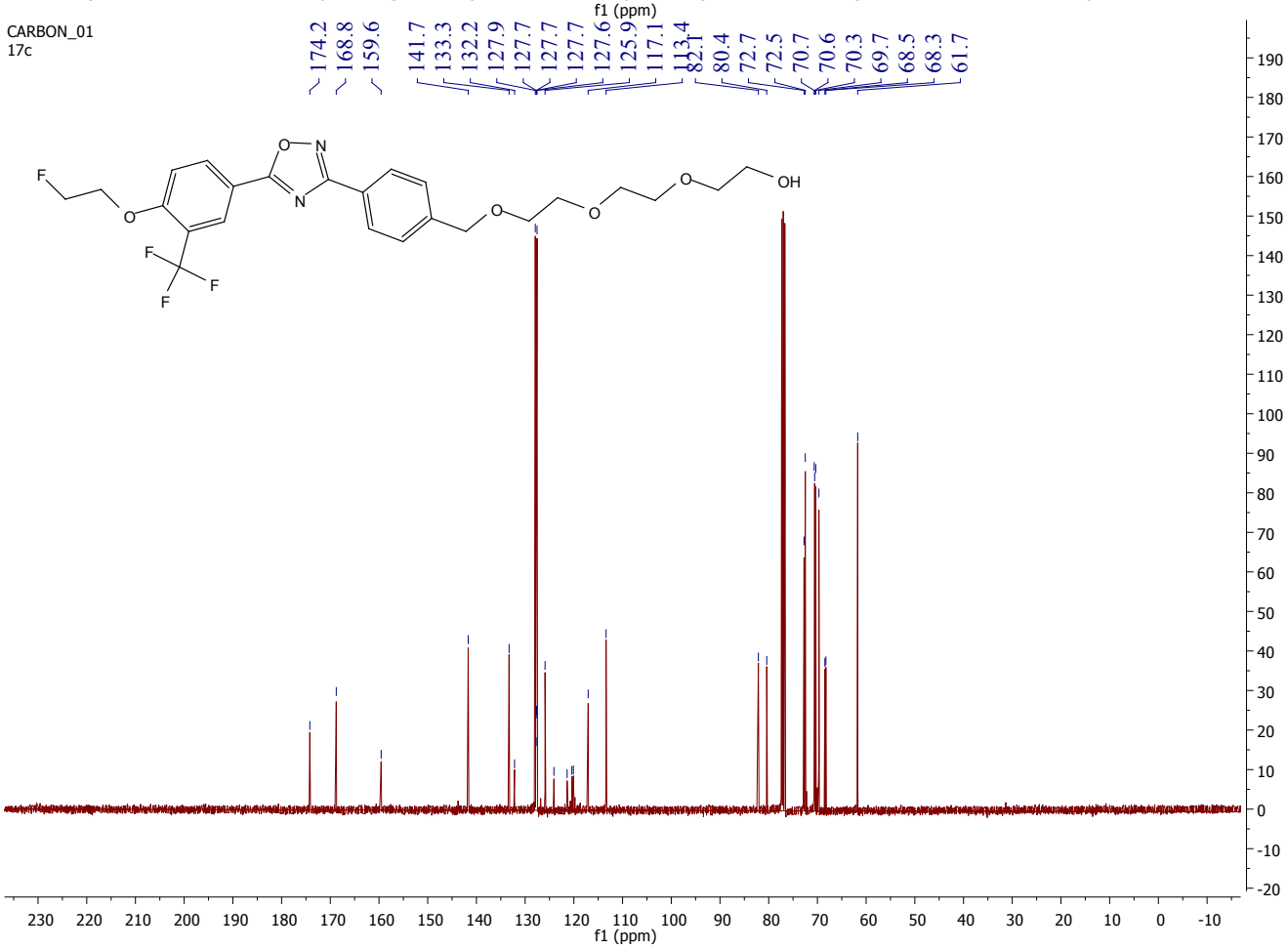
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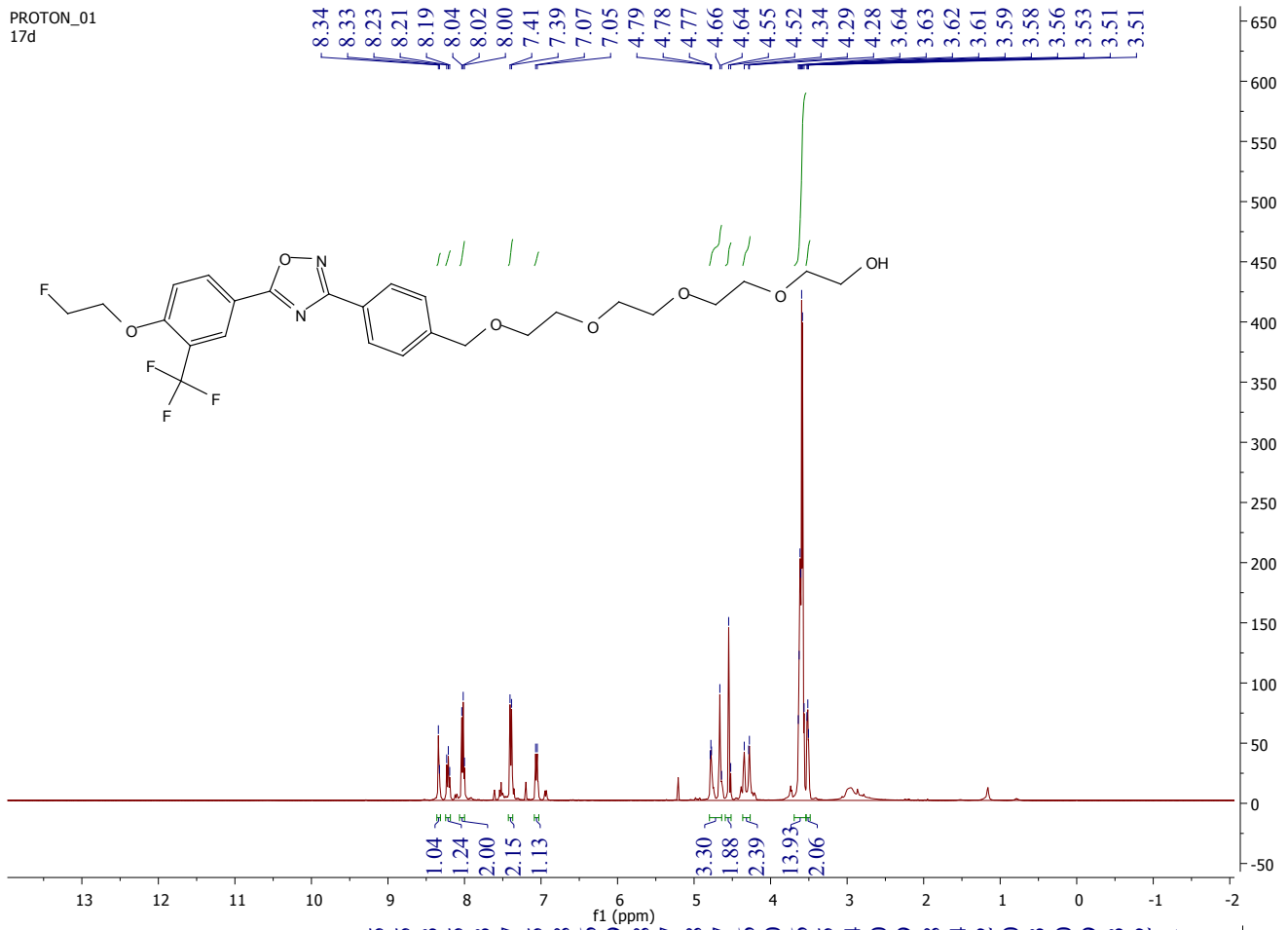
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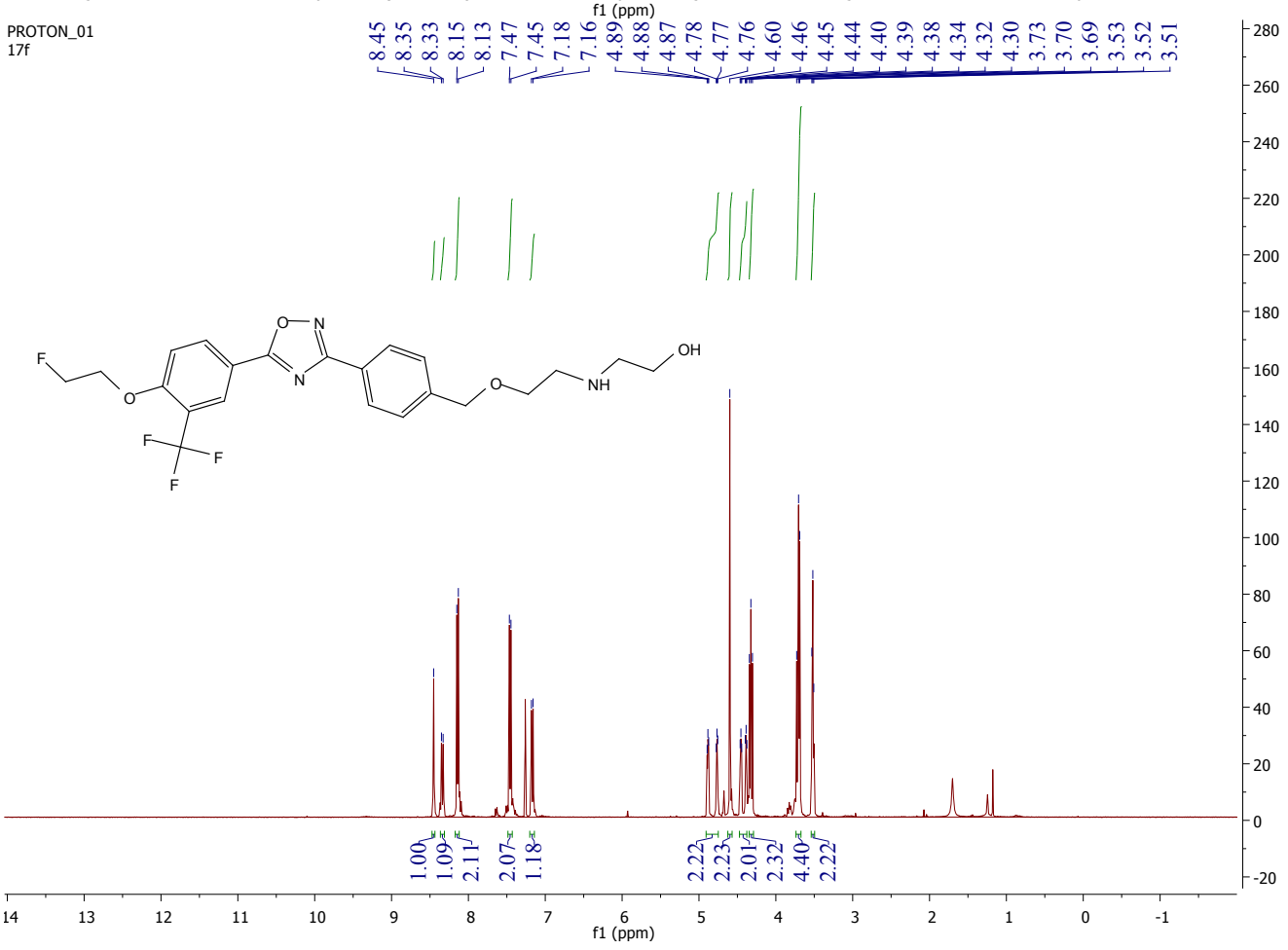
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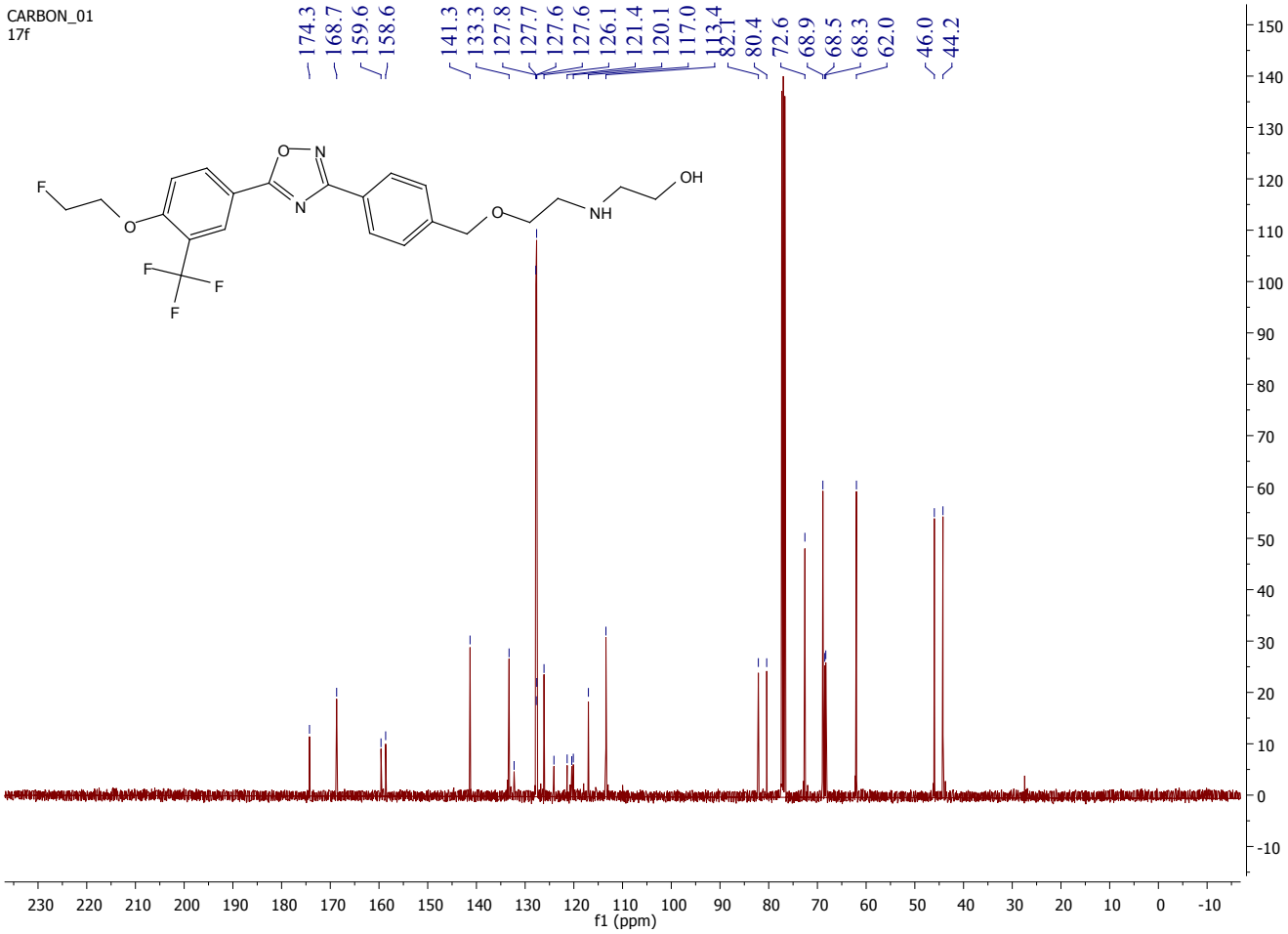
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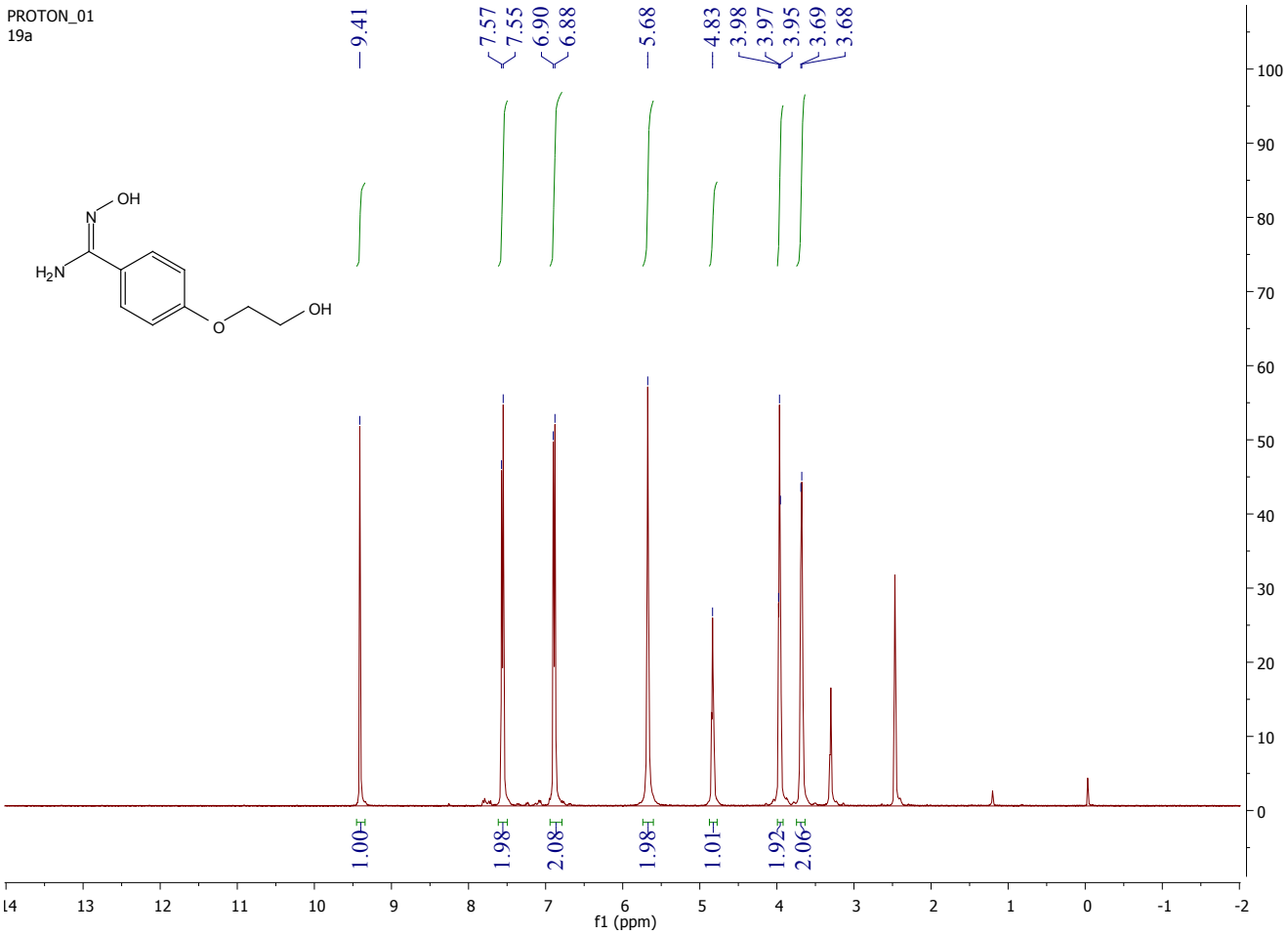
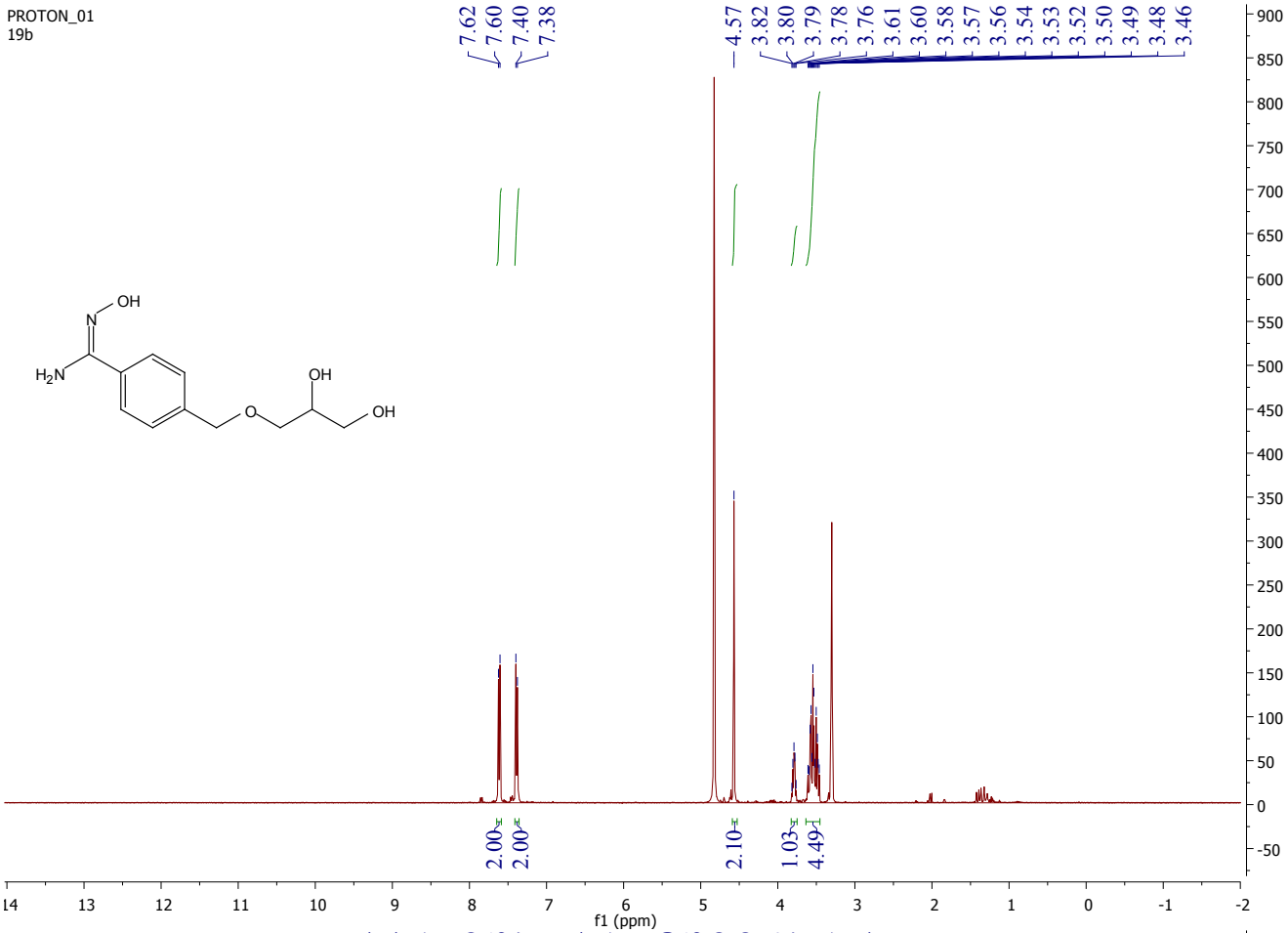
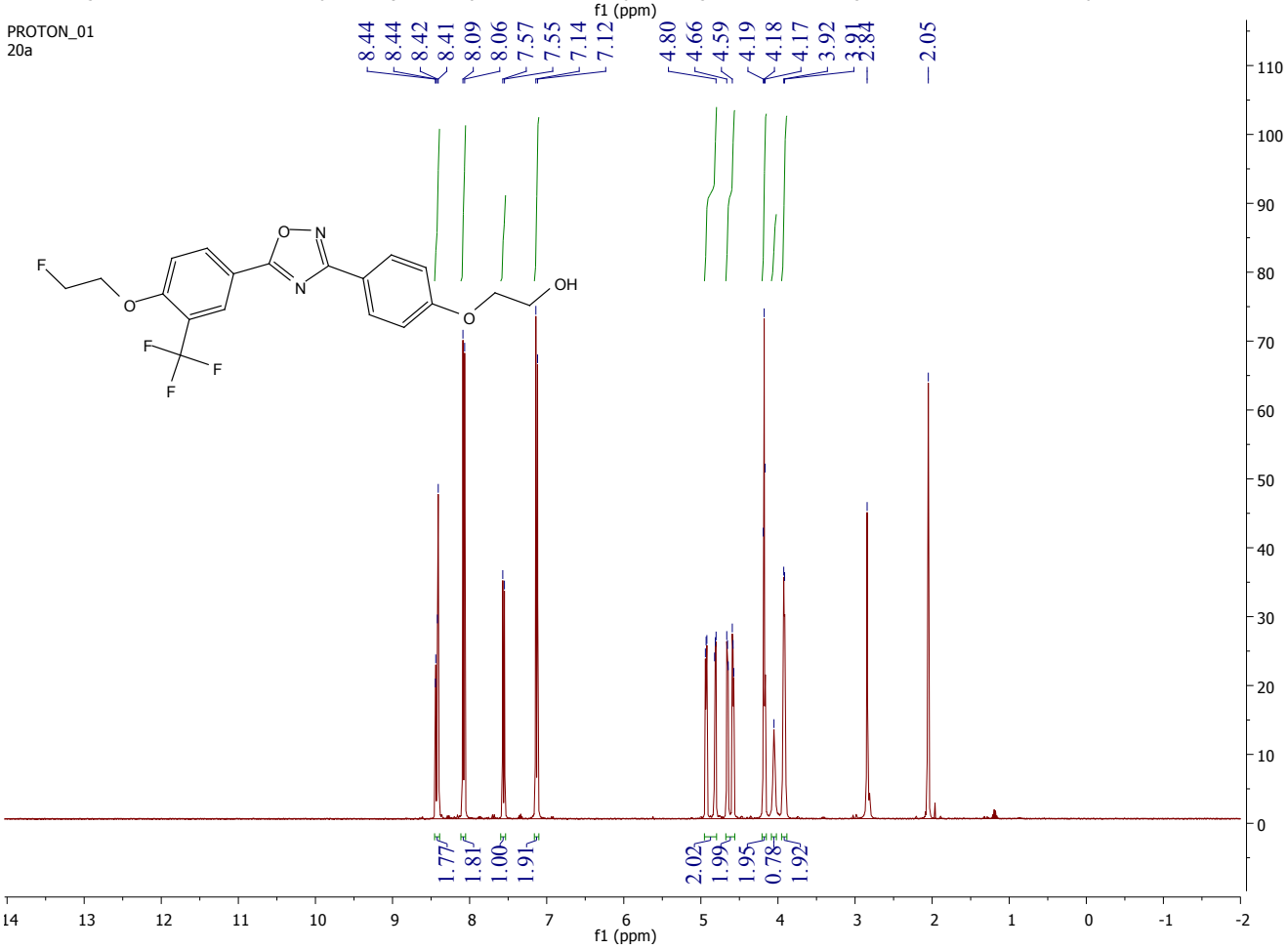
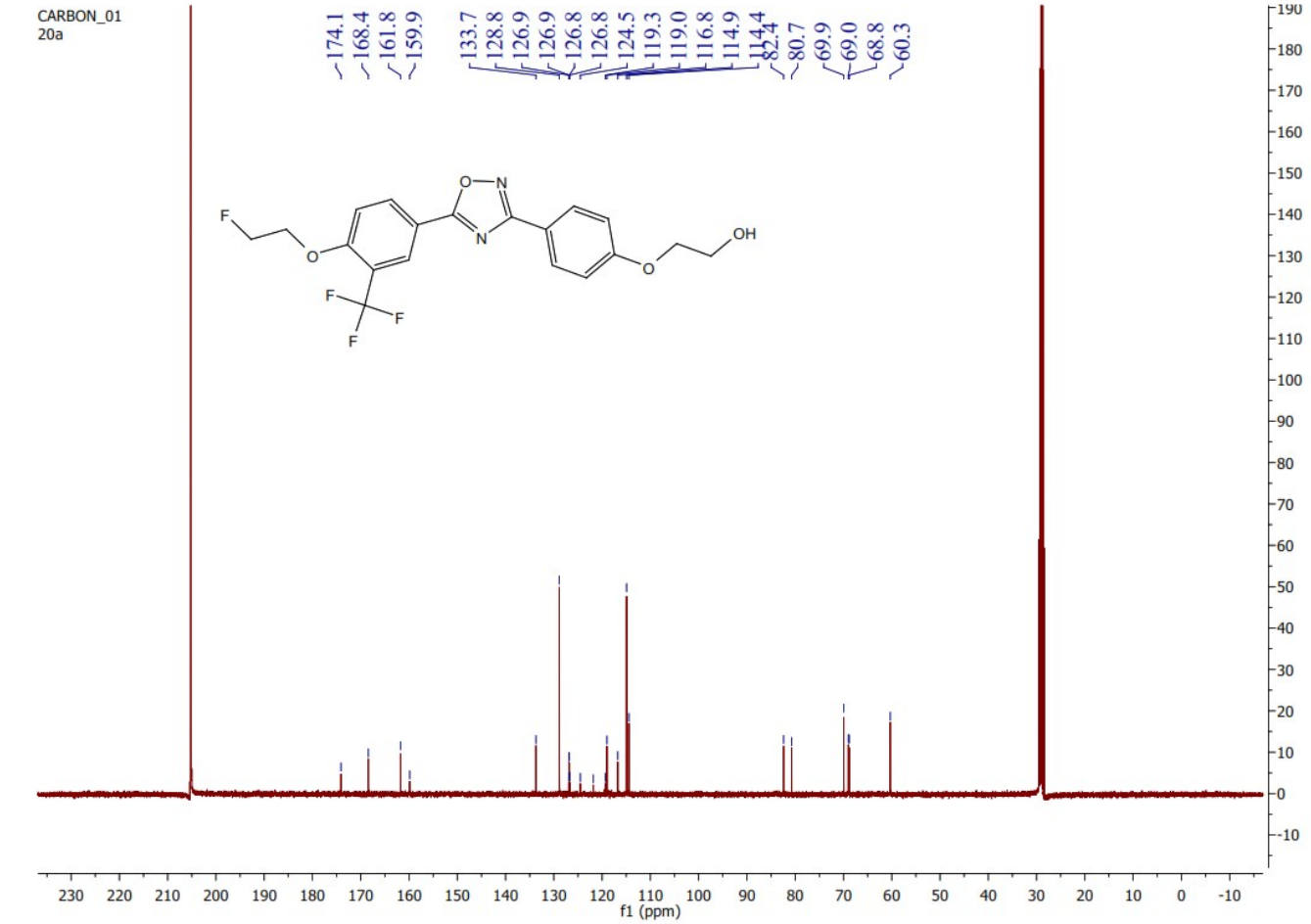
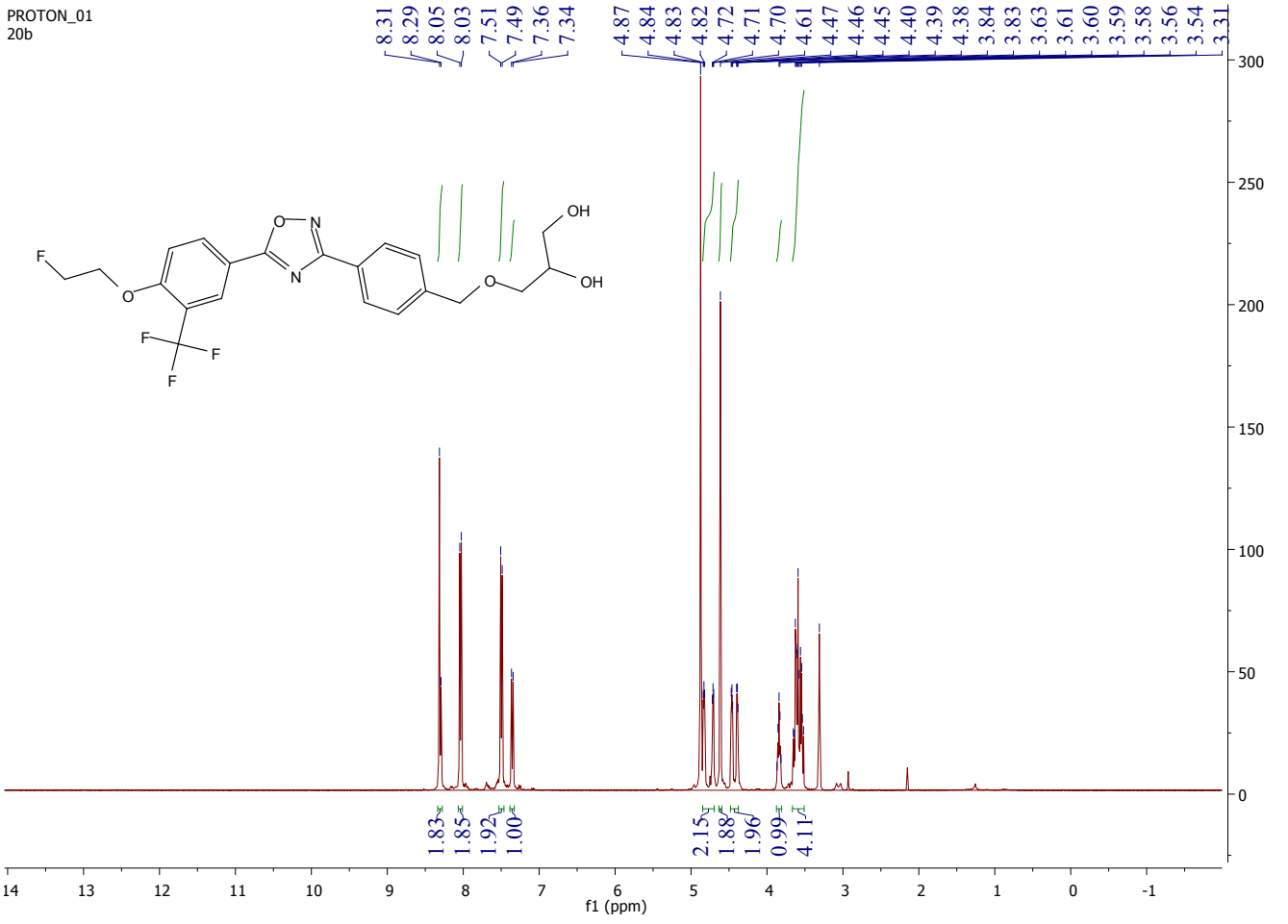
44.2
f1 (ppm)

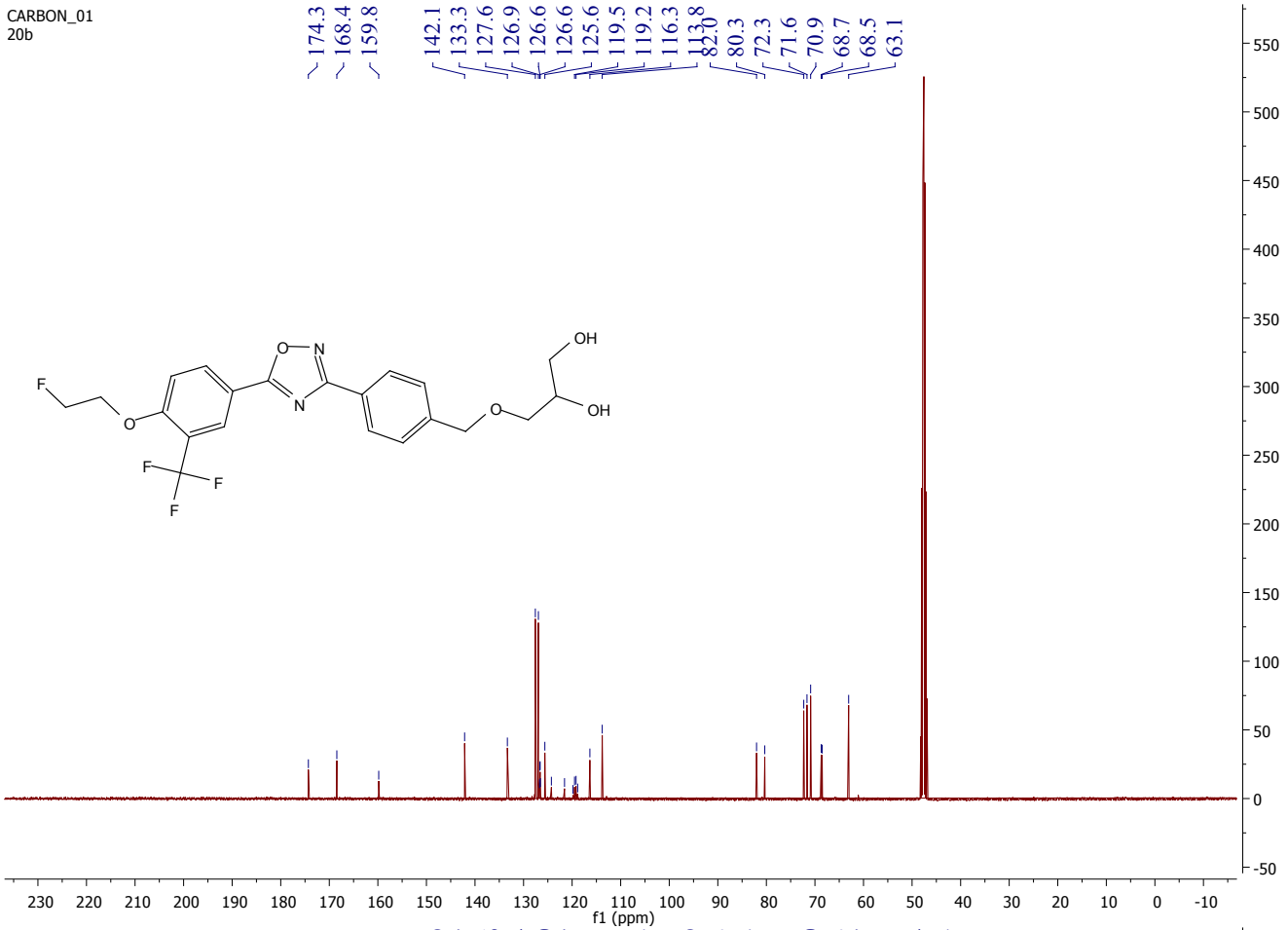

PROTON_01
19a
9.41
7.57
7.55
6.90
6.88
5.68
4.83
3.98
3.97
3.95
3.69
3.68
1.00
1.98
2.08
1.98
1.01
1.92
2.06
f1 (ppm)

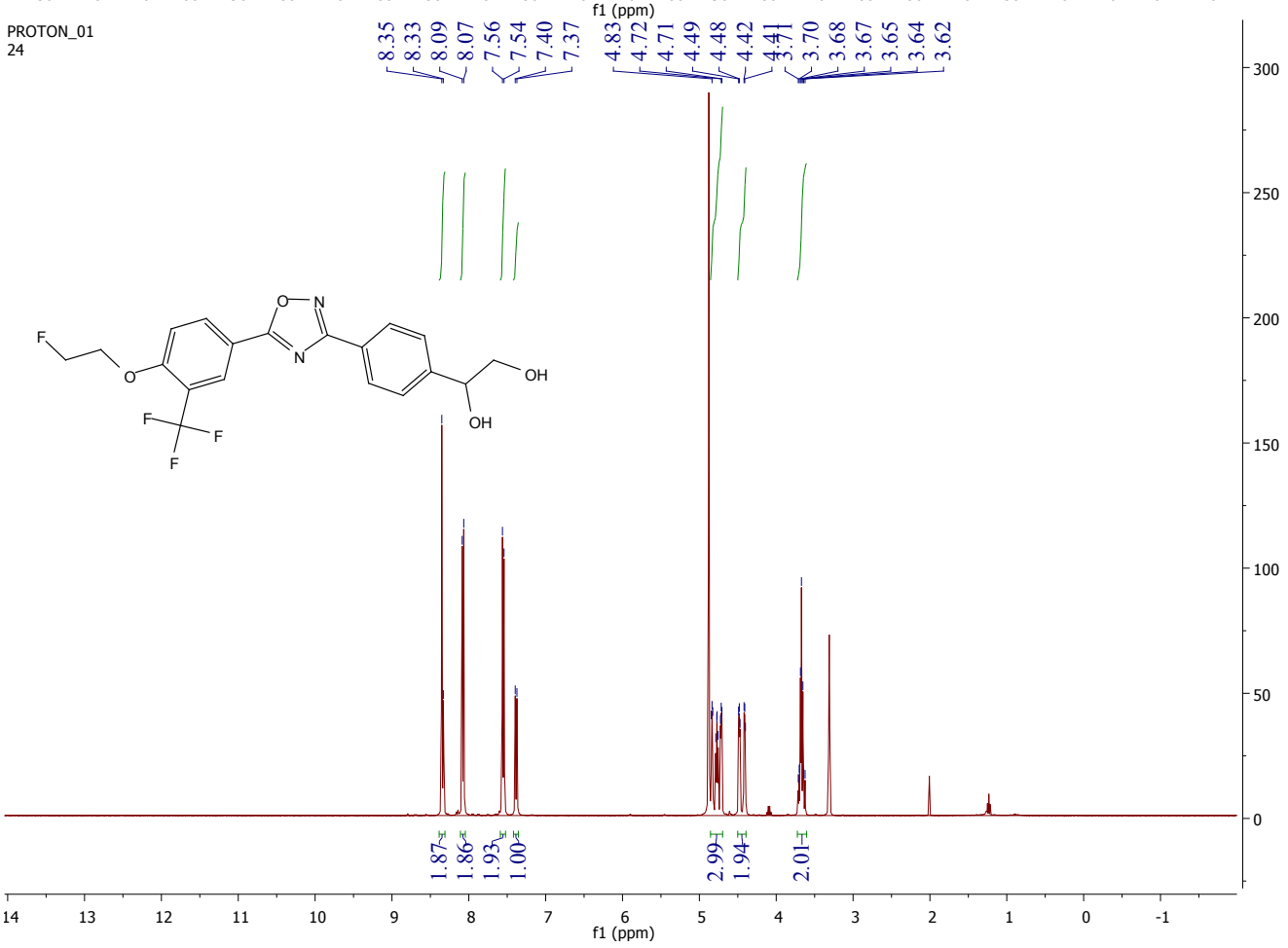

PROTON_01
19b
7.62
7.60
7.40
7.38
4.57
3.82
3.80
3.79
3.78
3.76
3.61
3.60
3.58
3.57
3.56
3.54
3.53
3.52
3.50
3.49
3.48
3.46
OH
N
H2N
OH
O
OH
2.00
2.00
2.10
1.03
4.49
f1 (ppm)

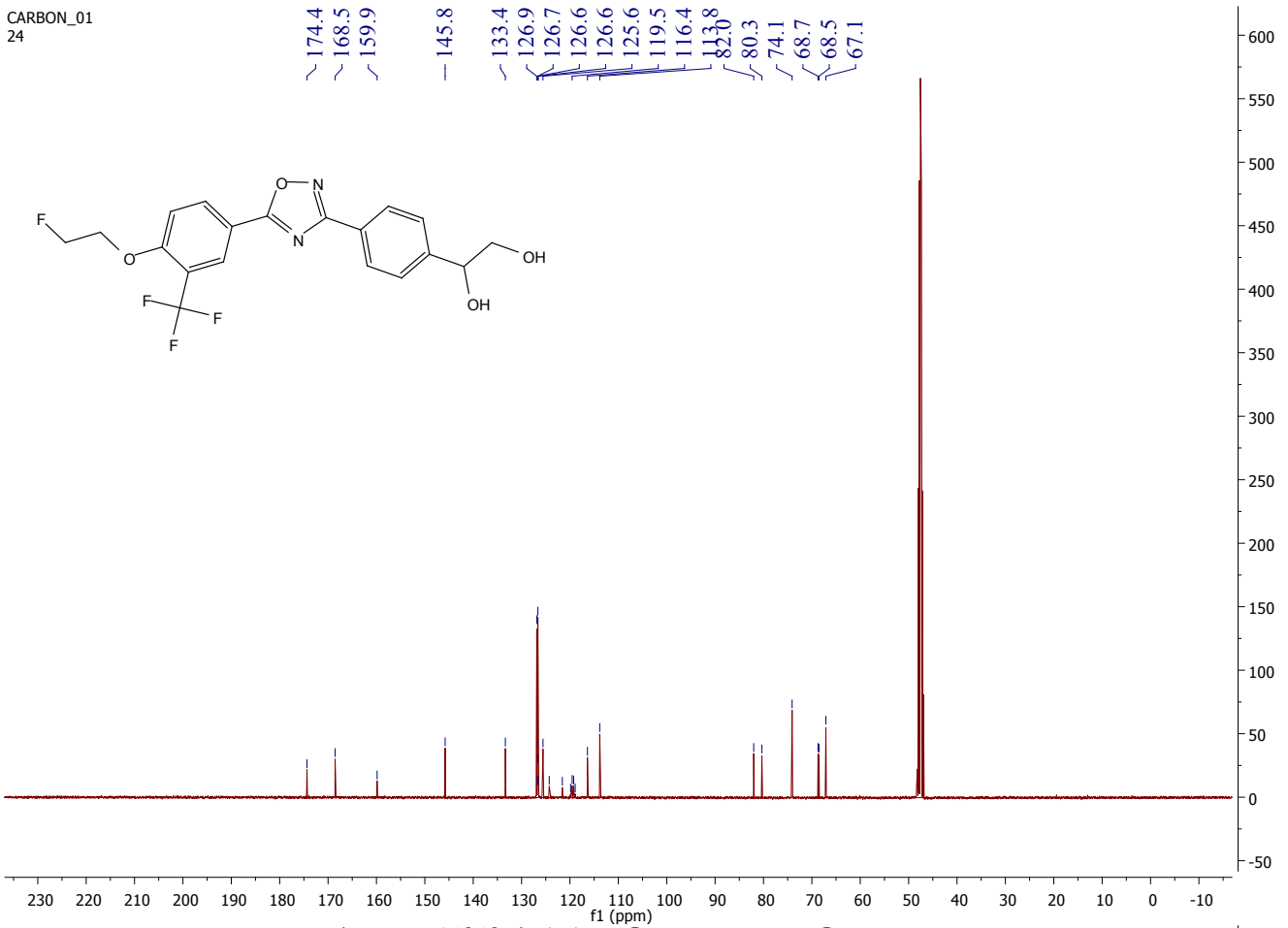

PROTON_01
20a
8.44
8.44
8.42
8.41
8.09
8.06
7.57
7.55
7.14
7.12
4.80
4.66
4.59
4.19
4.18
4.17
3.92
3.91
2.84
2.05
F
O
O
N
N
F
F
F
OH
1.77
1.81
1.00
1.91
2.02
1.99
1.95
0.78
1.92
f1 (ppm)

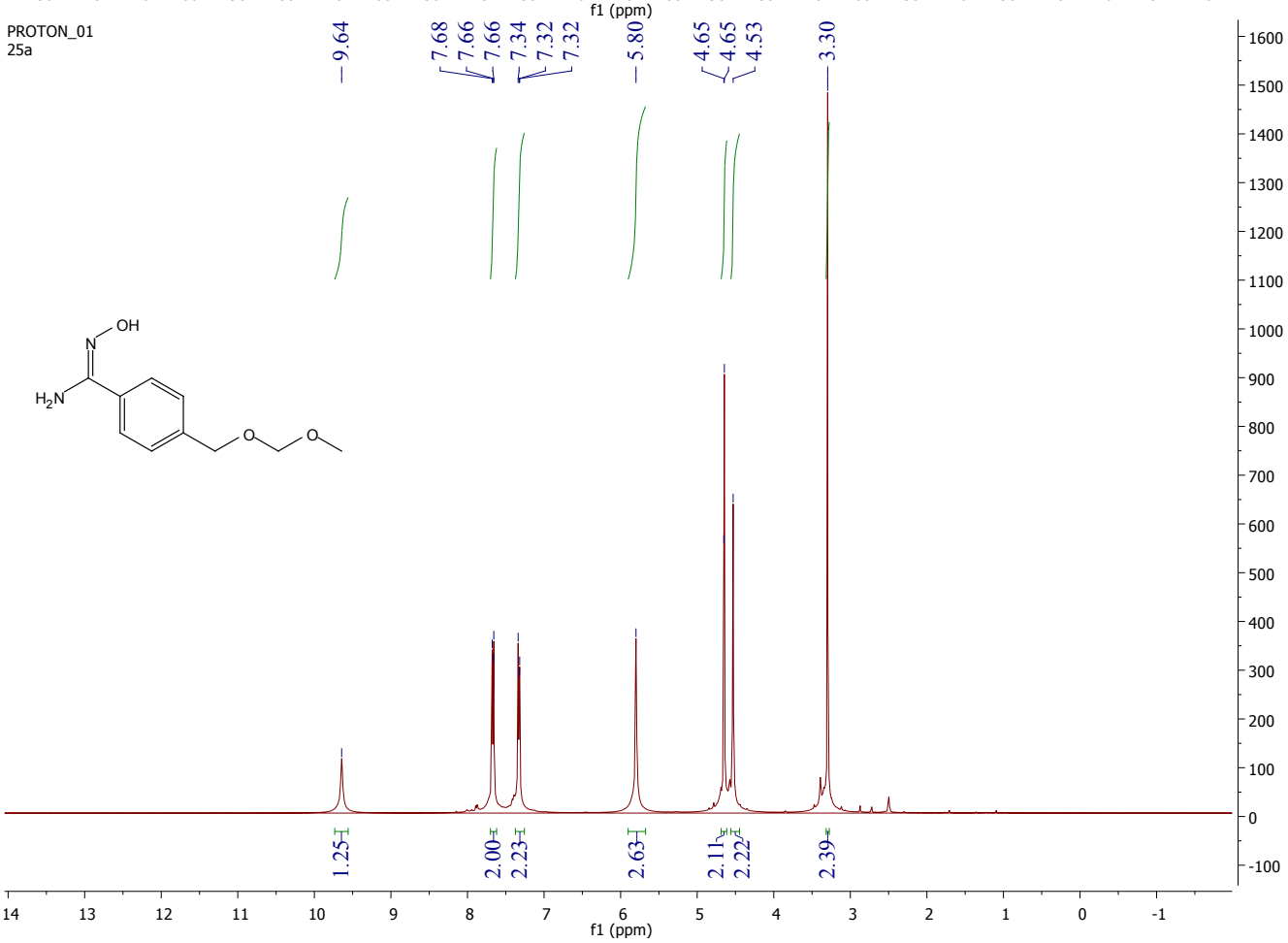

CARBON_01
20a
174.1
168.4
161.8
159.9
133.7
128.8
126.9
126.9
126.8
126.8
124.5
119.3
119.0
116.8
114.9
114.4
82.4
80.7
69.9
69.0
68.8
60.3
F
O
N
O
N
O
OH
F
F
F
f1 (ppm)

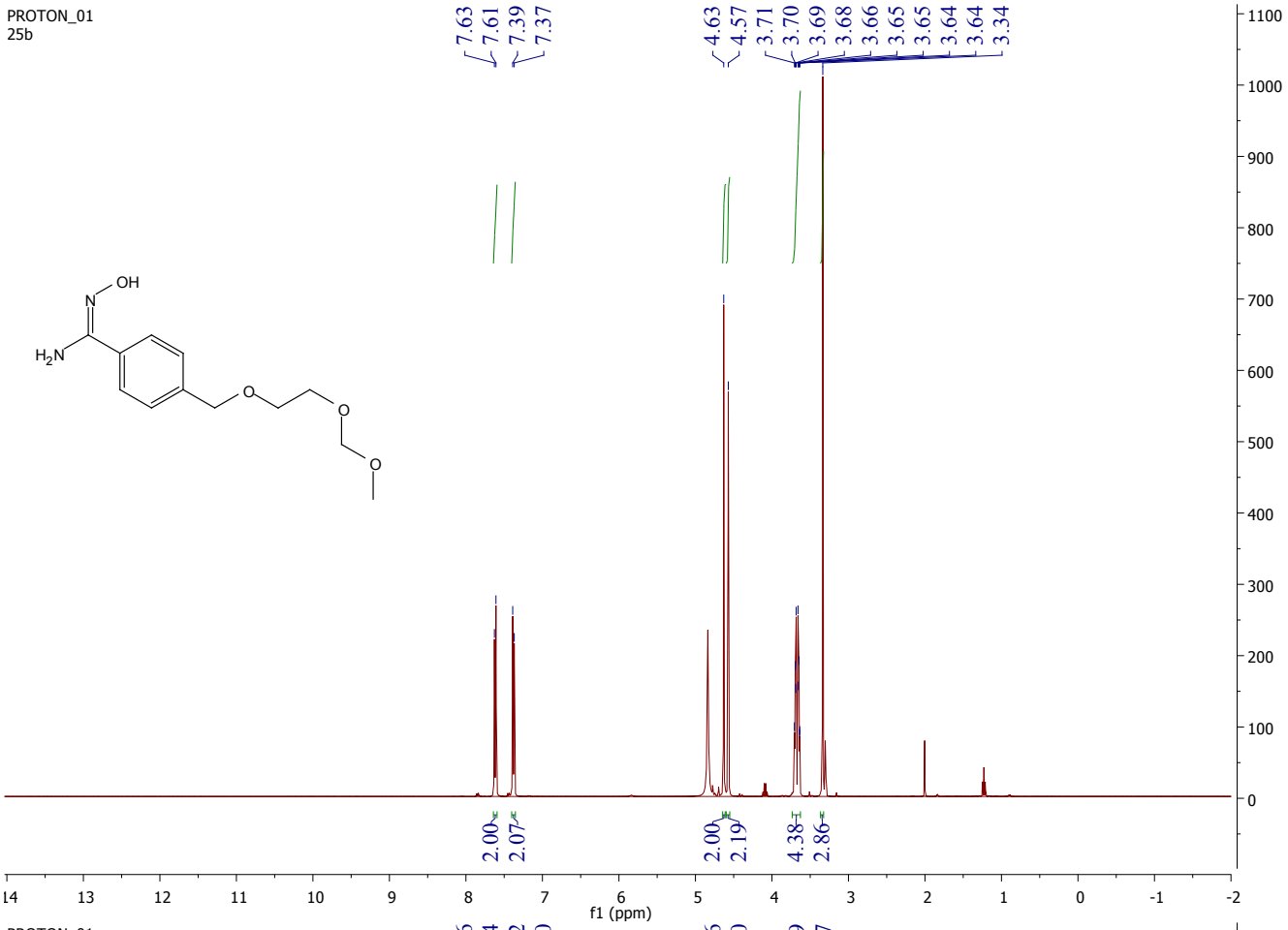

PROTON_01
20b
8.31
8.29
8.05
8.03
7.51
7.49
7.36
7.34
4.87
4.84
4.83
4.82
4.72
4.71
4.70
4.61
4.47
4.46
4.45
4.40
4.39
4.38
3.84
3.83
3.63
3.61
3.60
3.59
3.58
3.56
3.54
3.31
F
O
O
N
O
OH
OH
F
F
F
1.83
1.85
1.92
1.00
2.15
1.88
1.96
0.99
4.11
f1 (ppm)

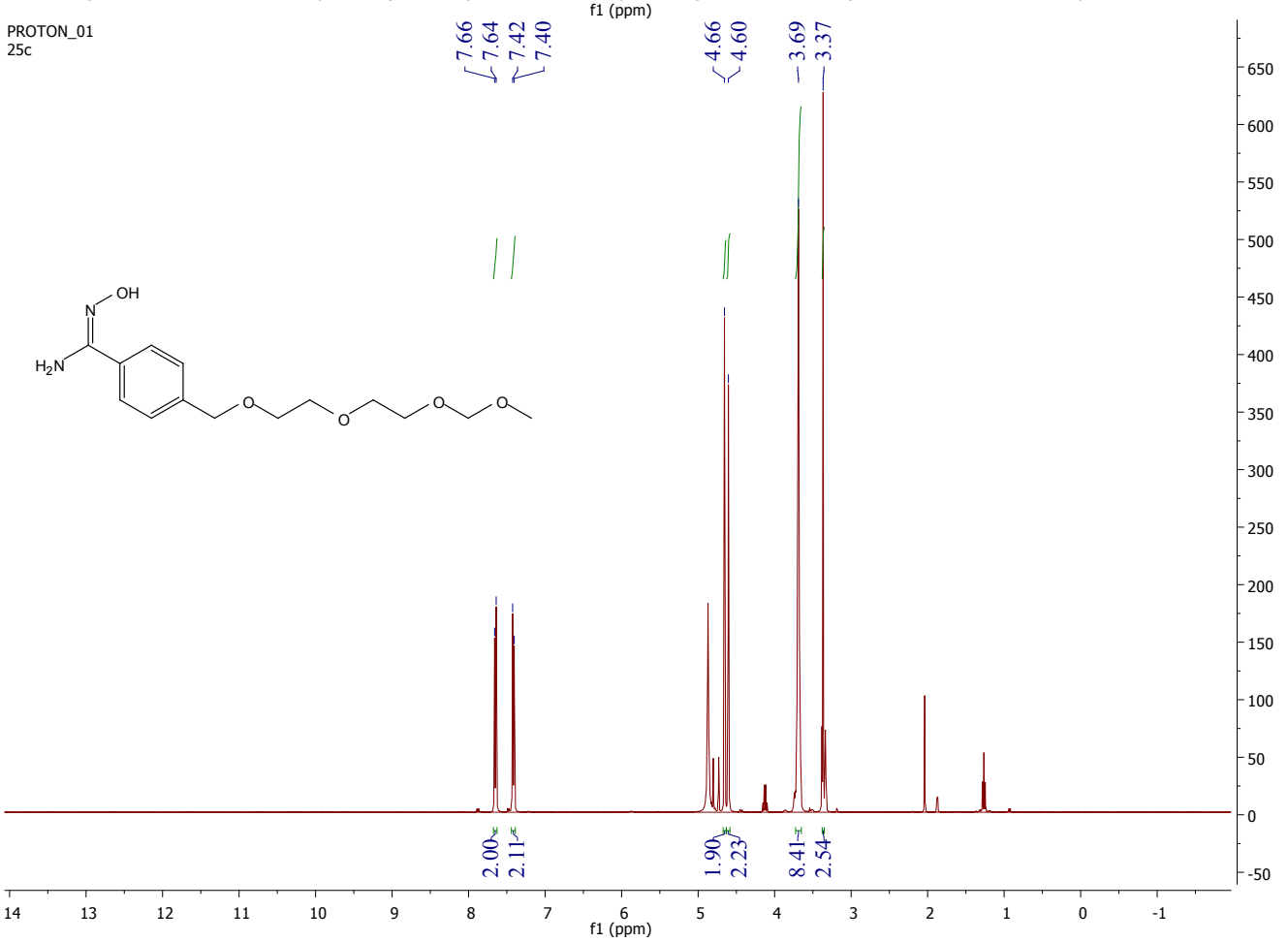

CARBON_01
20b
174.3
168.4
159.8
142.1
133.3
127.6
126.9
126.6
126.6
125.6
119.5
119.2
116.3
113.8
82.0
80.3
72.3
71.6
70.9
68.7
68.5
63.1
f1 (ppm)

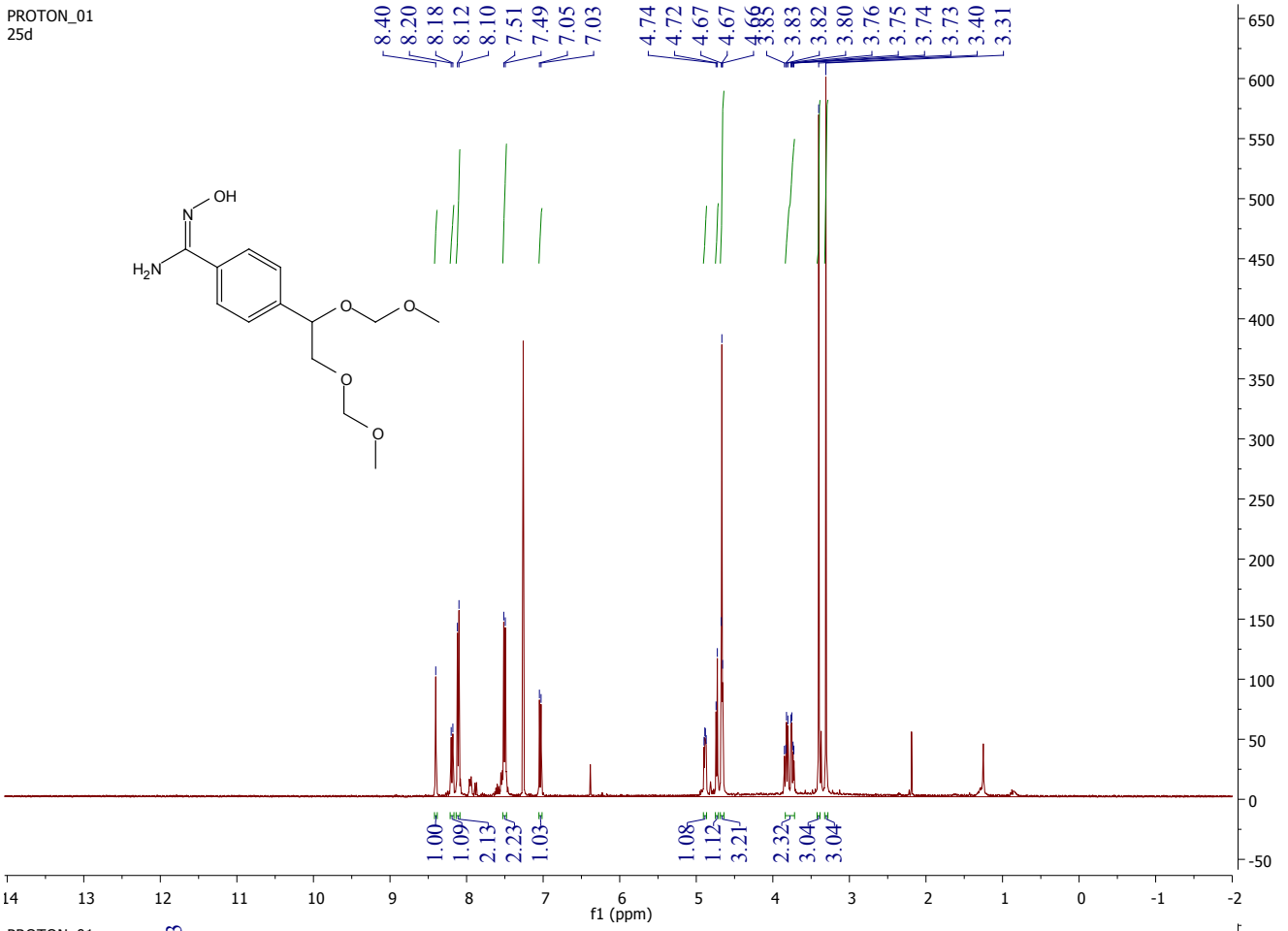

PROTON_01
24
8.35
8.33
8.09
8.07
7.56
7.54
7.40
7.37
4.83
4.72
4.71
4.49
4.48
4.42
4.41
3.71
3.70
3.68
3.67
3.65
3.64
3.62
1.87
1.86
1.93
1.00
2.99
1.94
2.01
f1 (ppm)

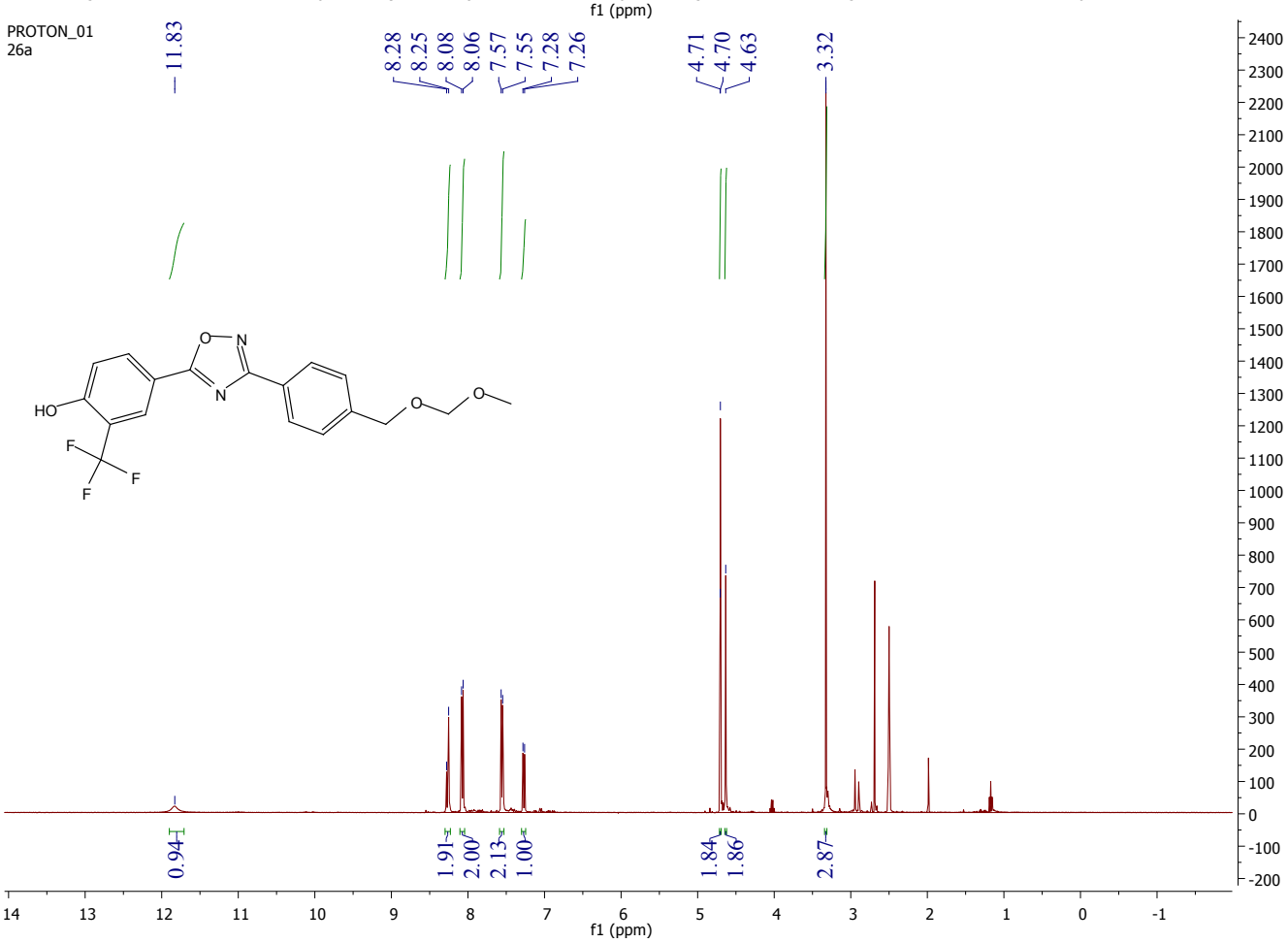

CARBON_01
24
174.4
168.5
159.9
145.8
133.4
126.9
126.7
126.6
126.6
125.6
119.5
116.4
113.8
82.0
80.3
74.1
68.7
68.5
67.1
F
O
O
N
N
F
F
F
OH
OH
f1 (ppm)

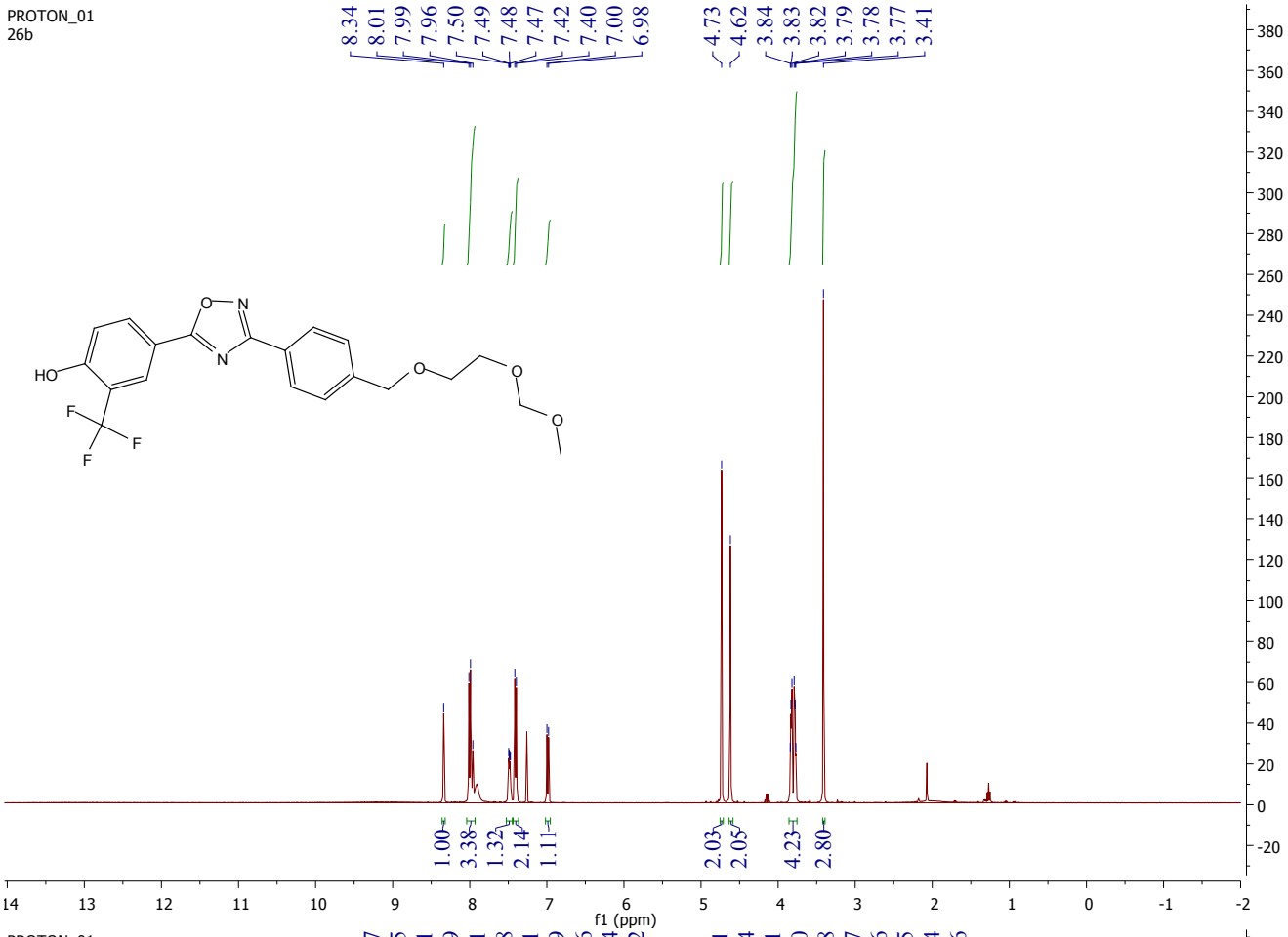

PROTON_01
25a
9.64
7.68
7.66
7.66
7.34
7.32
7.32
5.80
4.65
4.65
4.53
3.30
OH
N
H2N
O
O
1.25
2.00
2.23
2.63
2.11
2.22
2.39
f1 (ppm)

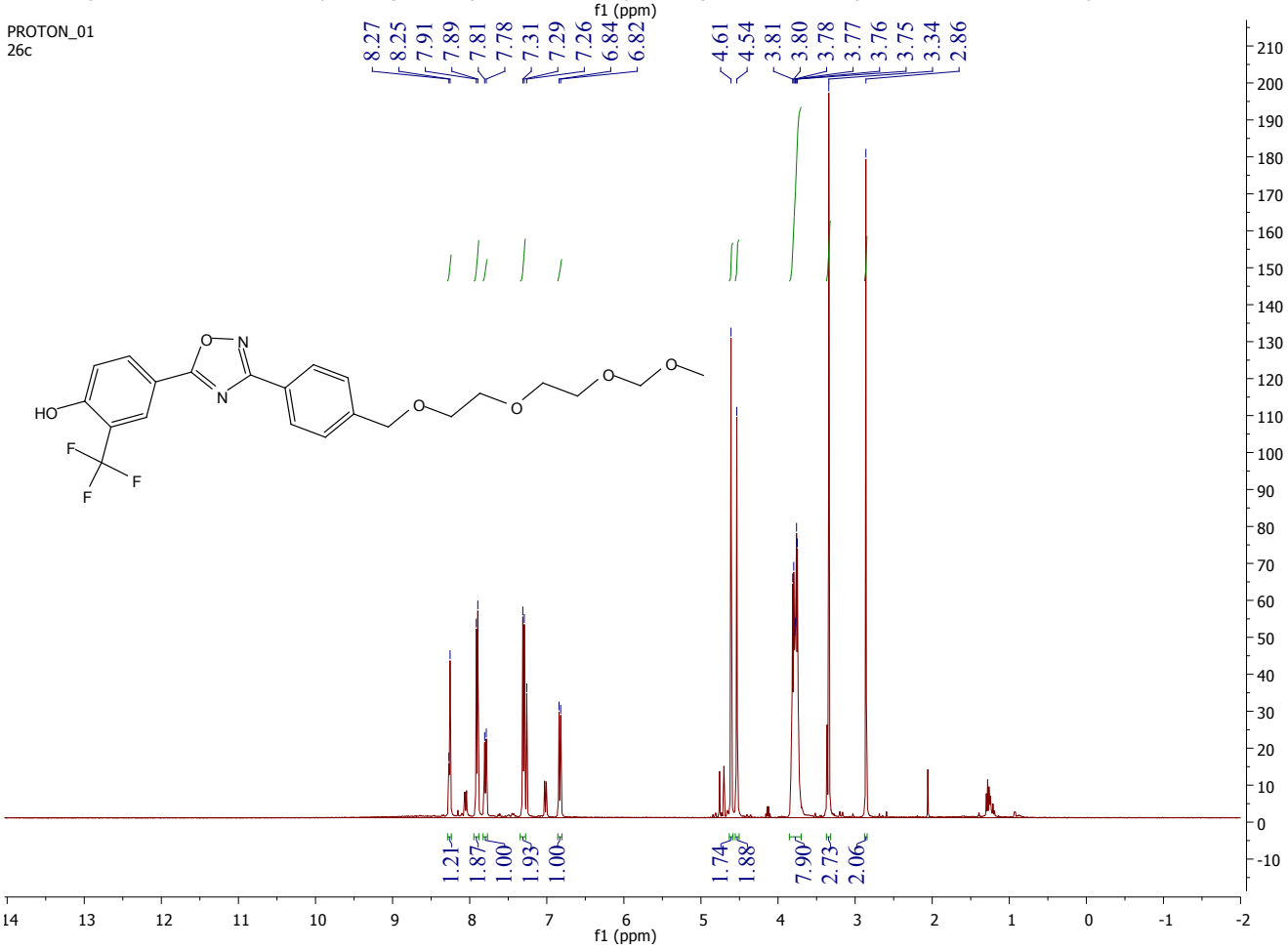

PROTON_01
25b
7.63
7.61
7.39
7.37
4.63
4.57
3.71
3.70
3.69
3.68
3.66
3.65
3.65
3.64
3.64
3.34
OH
N
H2N
O
O
O
2.00
2.07
2.00
2.19
4.38
2.86
f1 (ppm)

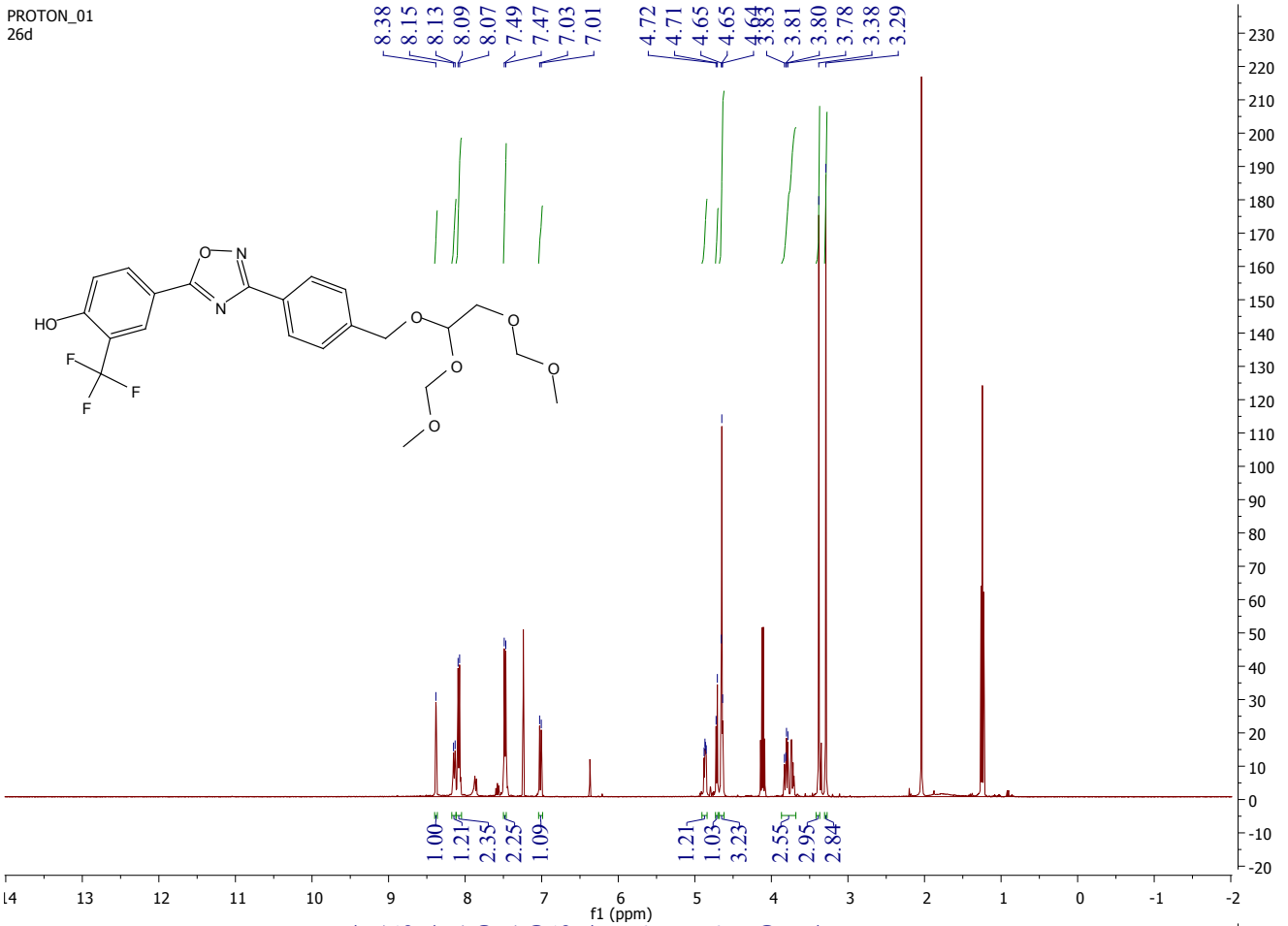

PROTON_01
25c
7.66
7.64
7.42
7.40
4.66
4.60
3.69
3.37
OH
N
H2N
O
O
O
O
2.00
2.11
1.90
2.23
8.41
2.54
f1 (ppm)

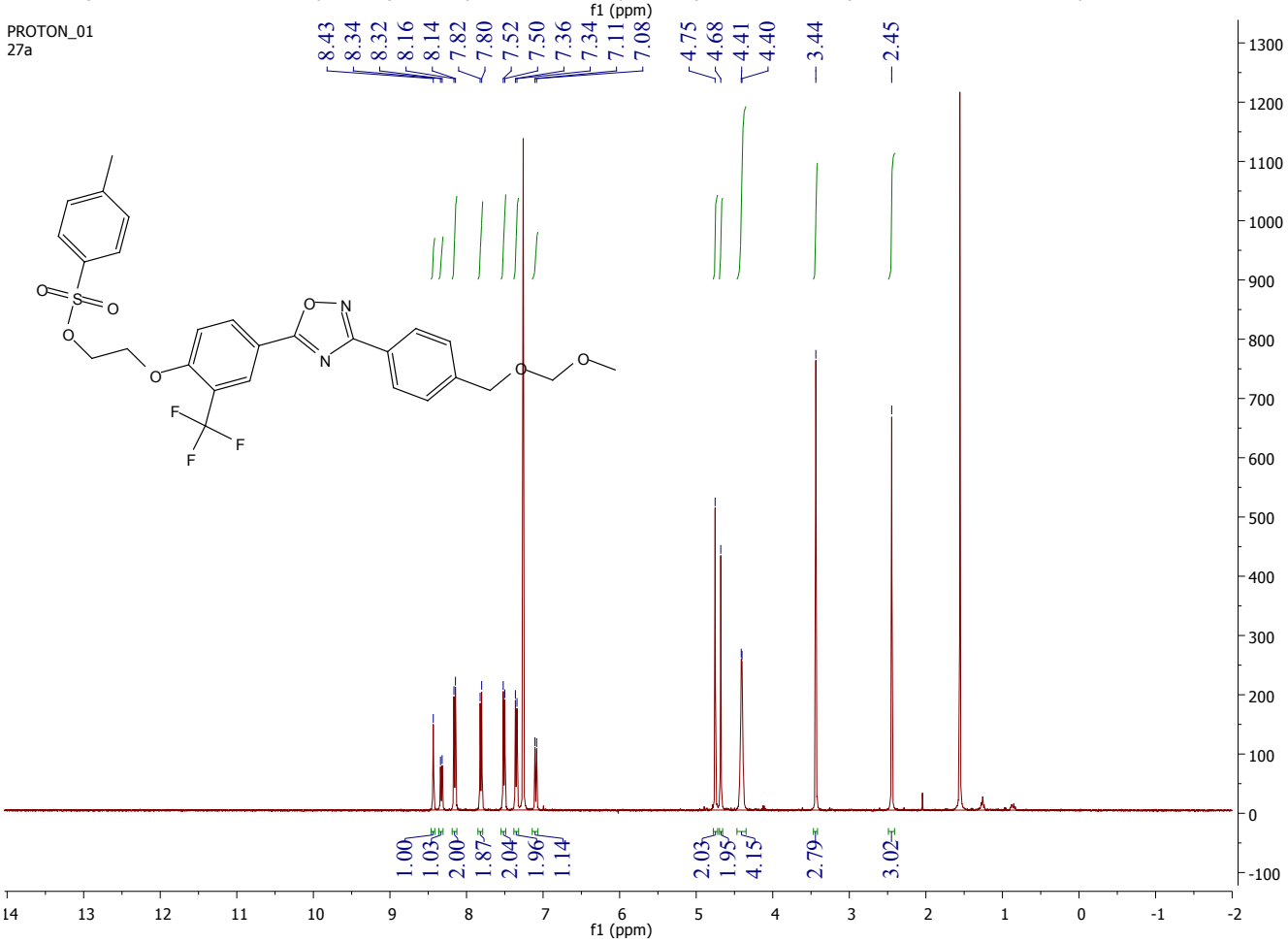

PROTON_01
25d
8.40
8.20
8.18
8.12
8.10
7.51
7.49
7.05
7.03
4.74
4.72
4.67
4.67
4.66
3.85
3.83
3.82
3.80
3.76
3.75
3.74
3.73
3.40
3.31
OH
N
H2N
O
O
O
O
1.00
1.09
2.13
2.23
1.03
1.08
1.12
3.21
2.32
3.04
3.04
f1 (ppm)

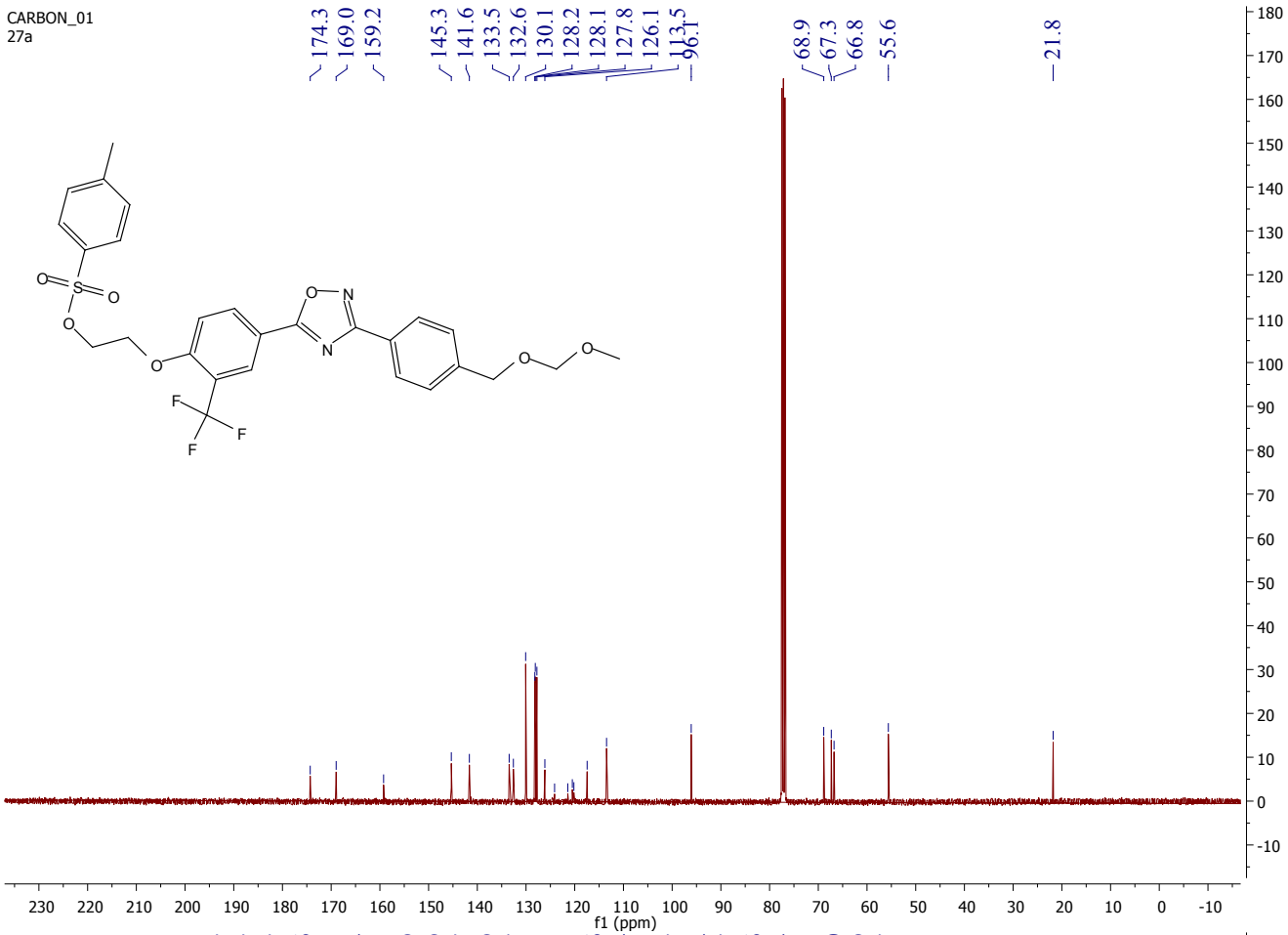

PROTON_01
26a
11.83
8.28
8.25
8.08
8.06
7.57
7.55
7.28
7.26
4.71
4.70
4.63
3.32
HO
O
N
N
O
O
F
F
F
0.94
1.91
2.00
2.13
1.00
1.84
1.86
2.87
f1 (ppm)

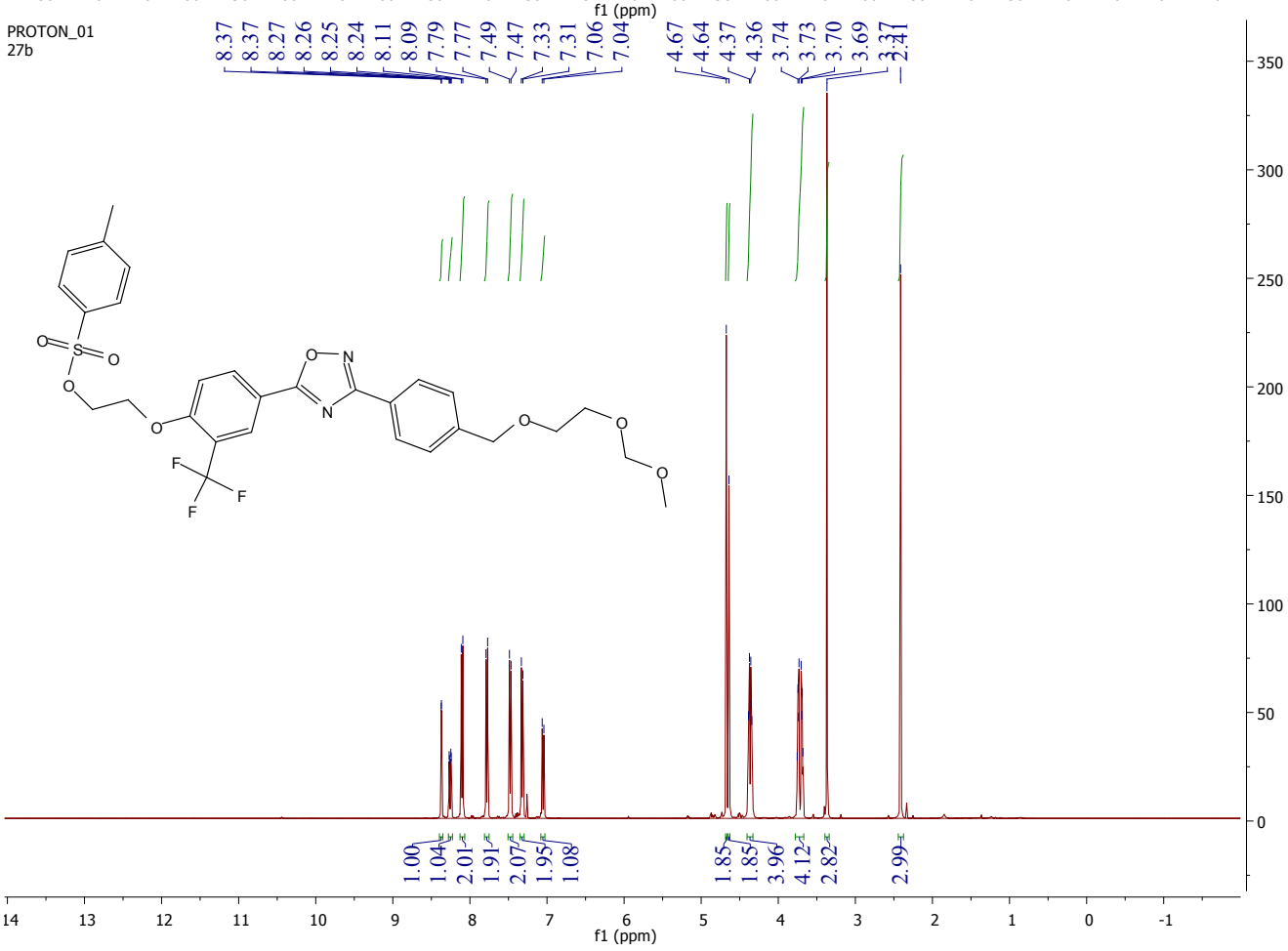

PROTON_01
26b
8.34
8.01
7.99
7.96
7.50
7.49
7.48
7.47
7.42
7.40
7.00
6.98
4.73
4.62
3.84
3.83
3.82
3.79
3.78
3.77
3.41
1.00
3.38
1.32
2.14
1.11
2.03
2.05
4.23
2.80
f1 (ppm)


PROTON_01
26c
8.27
8.25
7.91
7.89
7.81
7.78
7.31
7.29
7.26
6.84
6.82
4.61
4.54
3.81
3.80
3.78
3.77
3.76
3.75
3.34
2.86
1.21
1.87
1.00
1.93
1.00
1.74
1.88
7.90
2.73
2.06
f1 (ppm)


PROTON_01
26d
8.38
8.15
8.13
8.09
8.07
7.49
7.47
7.03
7.01
4.72
4.71
4.65
4.65
4.64
4.63
3.81
3.80
3.78
3.38
3.29
HO
O
N
N
O
O
O
O
O
O
F
F
F
1.00
1.21
2.35
2.25
1.09
1.21
1.03
3.23
2.55
2.95
2.84
f1 (ppm)


PROTON_01
27a
8.43
8.34
8.32
8.16
8.14
7.82
7.80
7.52
7.50
7.36
7.34
7.11
7.08
4.75
4.68
4.41
4.40
3.44
2.45
O
S
O
O
O
O
N
N
O
O
F
F
F
1.00
1.03
2.00
1.87
2.04
1.96
1.14
2.03
1.95
4.15
2.79
3.02
f1 (ppm)


CARBON_01
27a
174.3
169.0
159.2
145.3
141.6
133.5
132.6
130.1
128.2
128.1
127.8
126.1
113.5
96.1
68.9
67.3
66.8
55.6
21.8
f1 (ppm)


PROTON_01
27b
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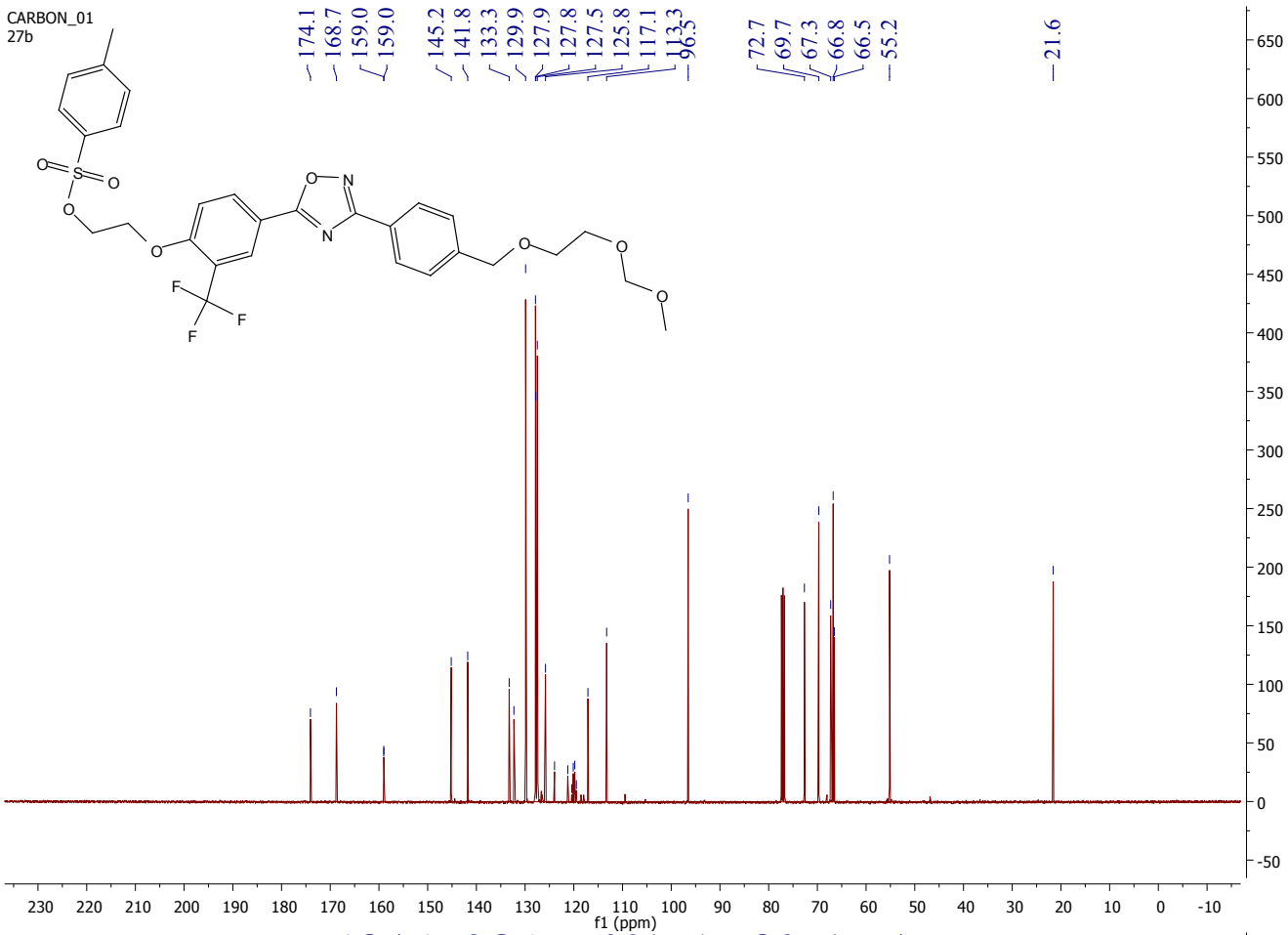
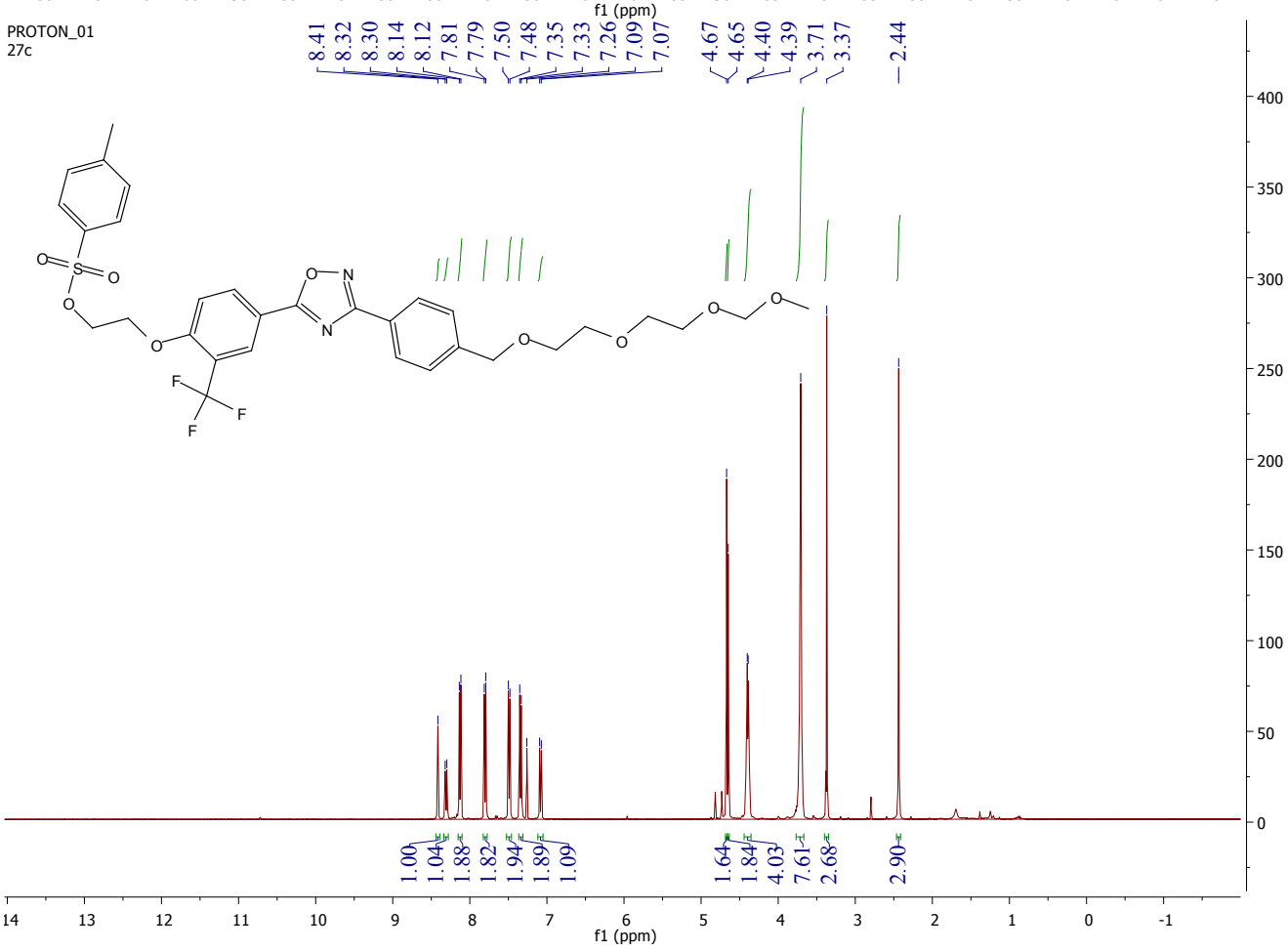
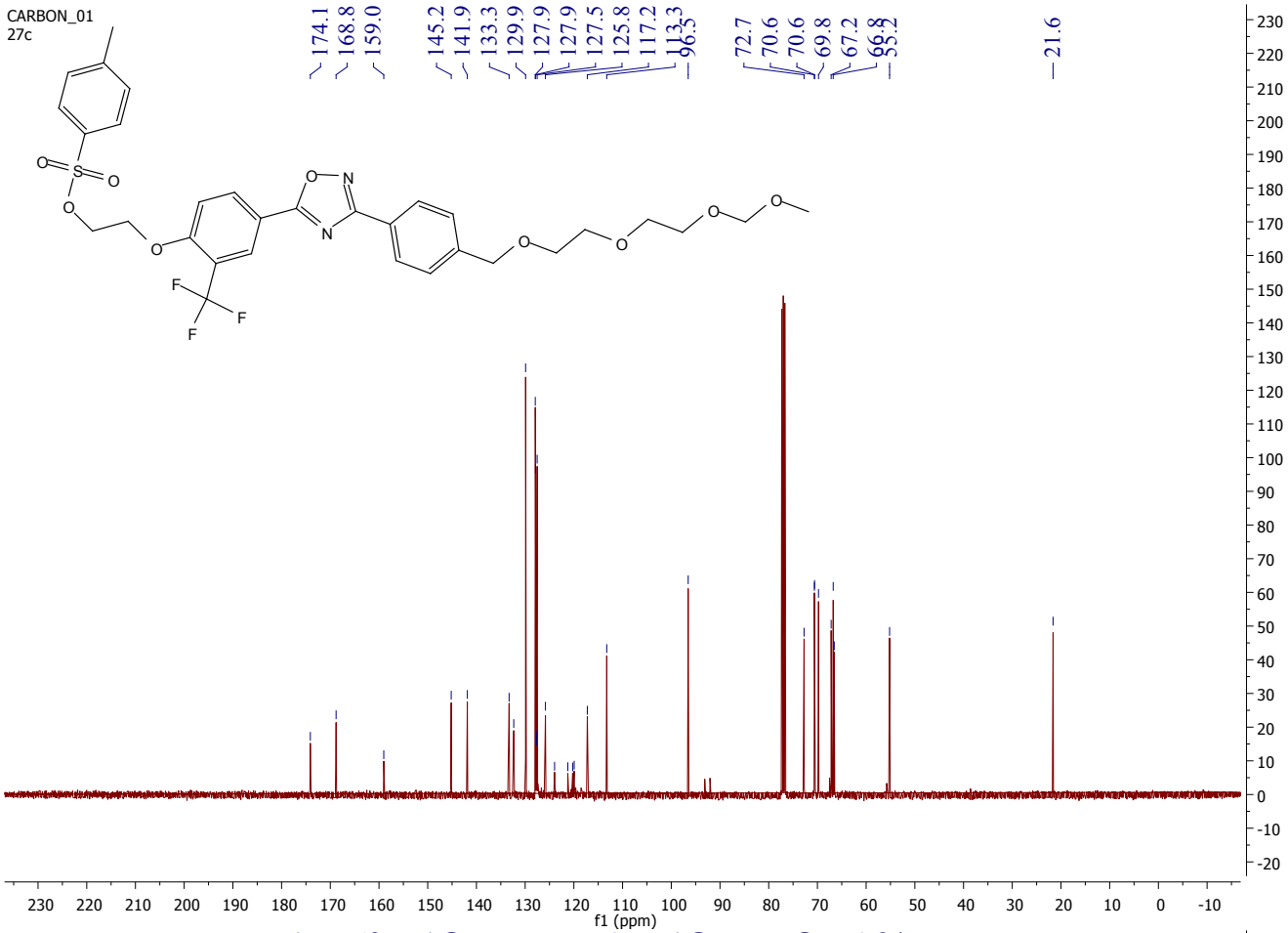
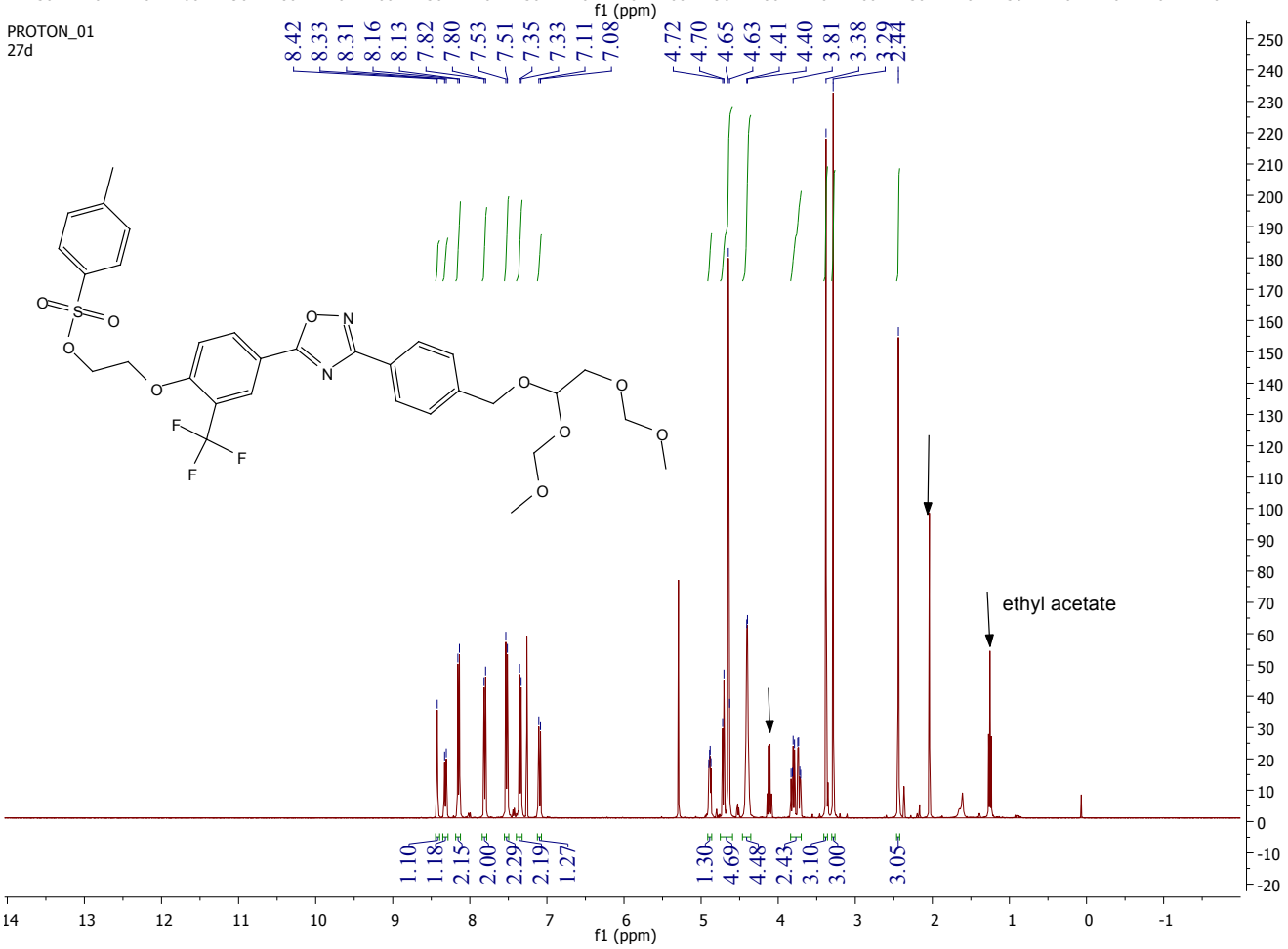
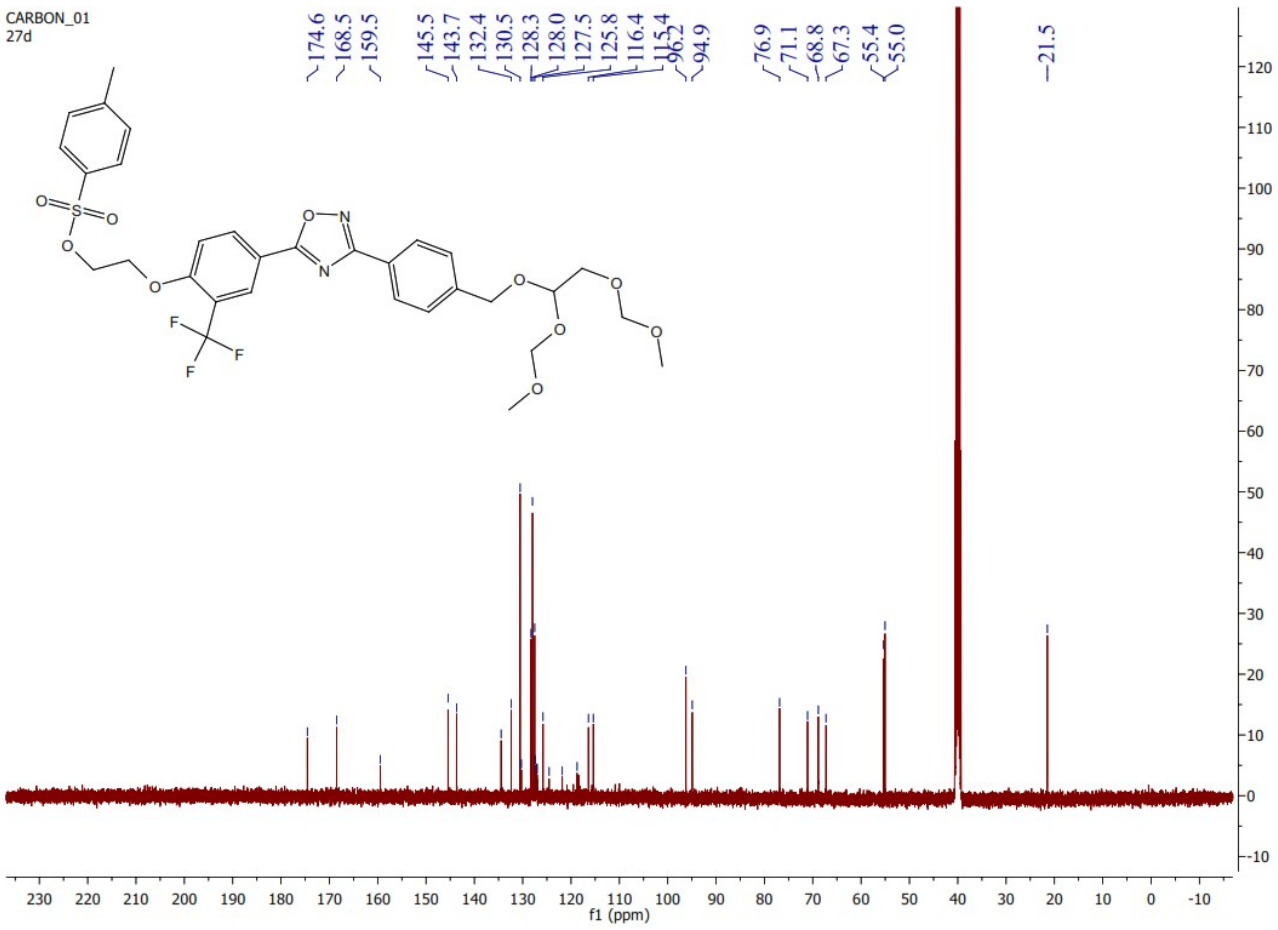
8.37
8.27
8.26
8.25
8.24
8.11
8.09
7.79
7.77
7.49
7.47
7.33
7.31
7.06
7.04
4.67
4.64
4.37
4.36
3.74
3.73
3.70
3.69
3.37
2.41
1.00
1.04
2.01
1.91
2.07
1.95
1.08
1.85
1.85
3.96
4.12
2.82
2.99
f1 (ppm)


CARBON_01
27b
174.1
168.7
159.0
159.0
145.2
141.8
133.3
129.9
127.9
127.8
127.5
125.8
117.1
113.3
96.5
72.7
69.7
67.3
66.8
66.5
55.2
21.6
f1 (ppm)


PROTON_01
27c
8.41
8.32
8.30
8.14
8.12
7.81
7.79
7.50
7.48
7.35
7.33
7.26
7.09
7.07
4.67
4.65
4.40
4.39
3.71
3.37
2.44
1.00
1.04
1.88
1.82
1.94
1.89
1.09
1.64
1.84
4.03
7.61
2.68
2.90
f1 (ppm)


CARBON_01
27c
174.1
168.8
159.0
145.2
141.9
133.3
129.9
127.9
127.9
127.5
125.8
117.2
113.3
96.5
72.7
70.6
70.6
69.8
67.2
66.8
55.2
21.6
f1 (ppm)


PROTON_01
27d
8.42
8.33
8.31
8.16
8.13
7.82
7.80
7.53
7.51
7.35
7.33
7.11
7.08
4.72
4.70
4.65
4.63
4.41
4.40
3.81
3.38
3.29
2.44
ethyl acetate
1.10
1.18
2.15
2.00
2.29
2.19
1.27
1.30
4.69
4.48
2.43
3.10
3.00
3.05
f1 (ppm)


CARBON_01
27d
174.6
168.5
159.5
145.5
143.7
132.4
130.5
128.3
128.0
127.5
125.8
116.4
115.4
96.2
94.9
76.9
71.1
68.8
67.3
55.4
55.0
21.5
f1 (ppm)