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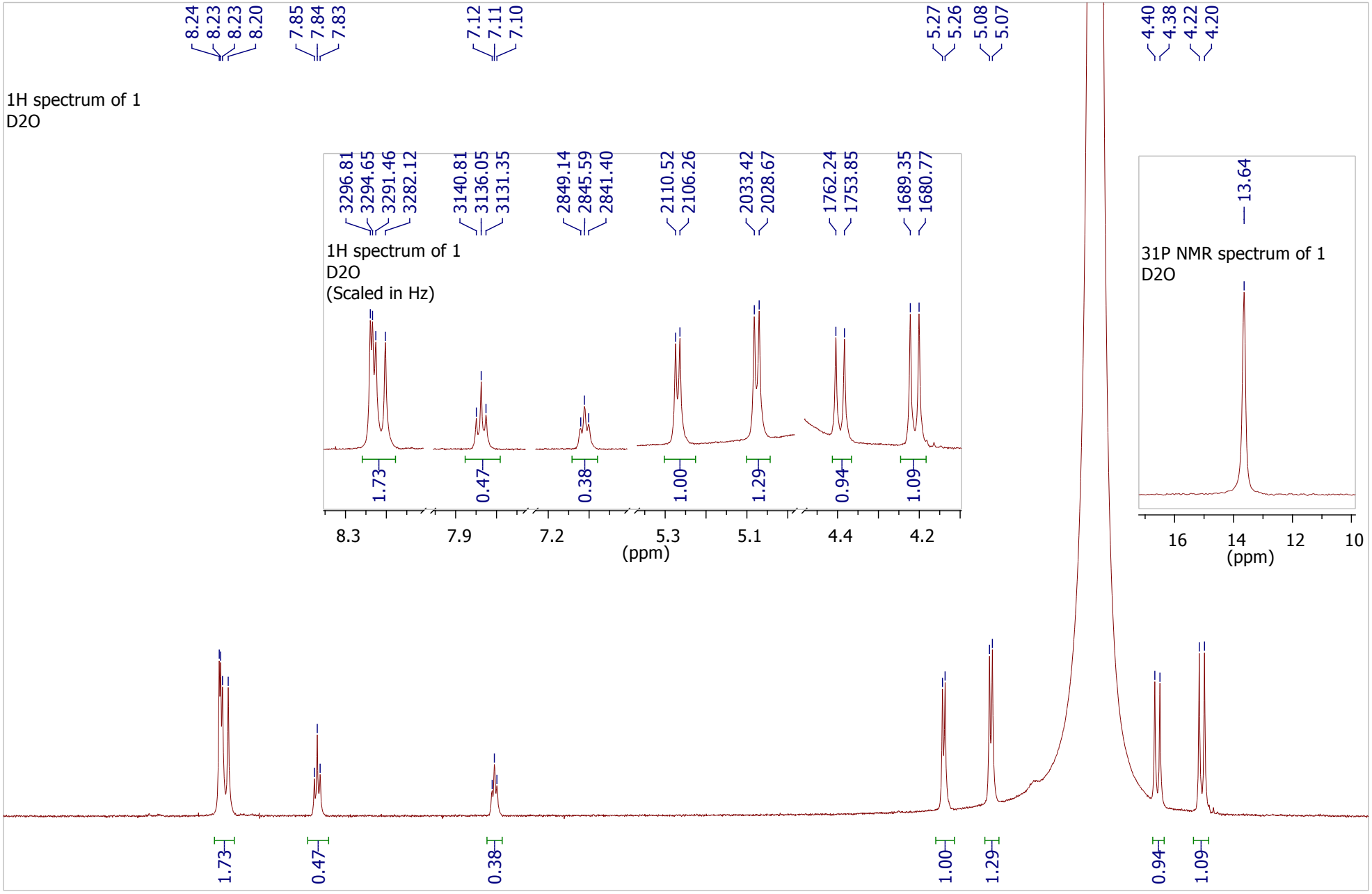
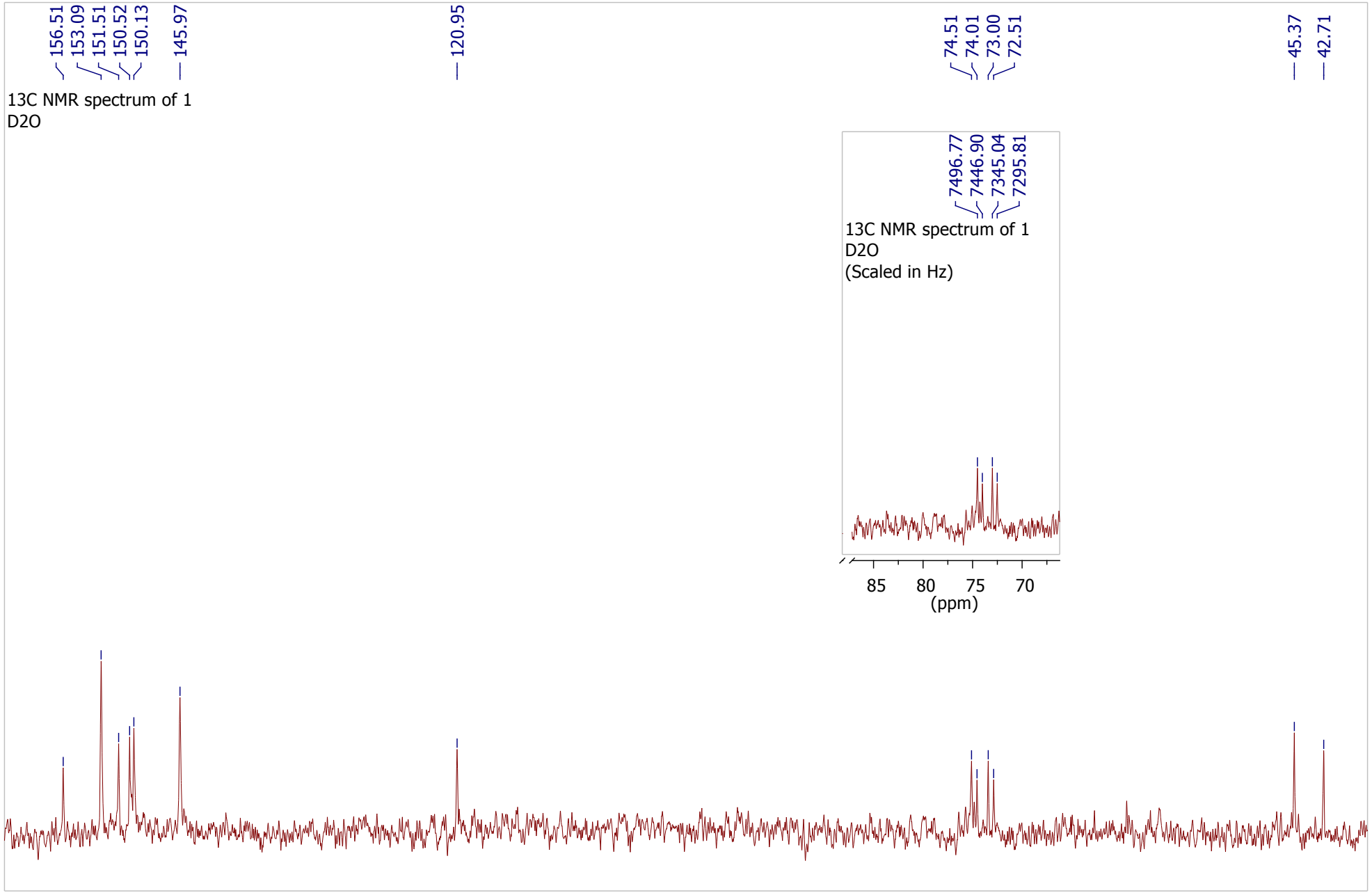
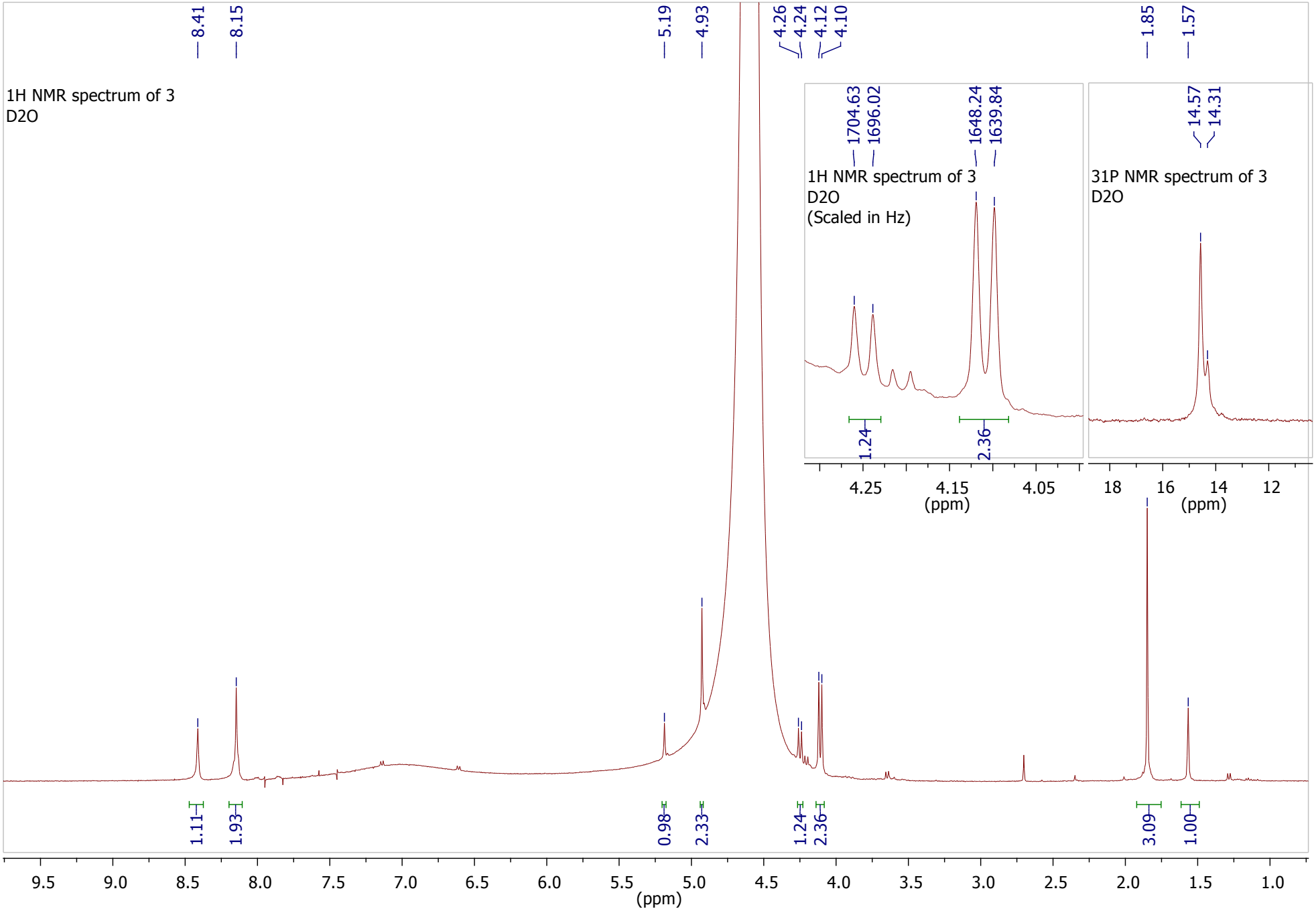
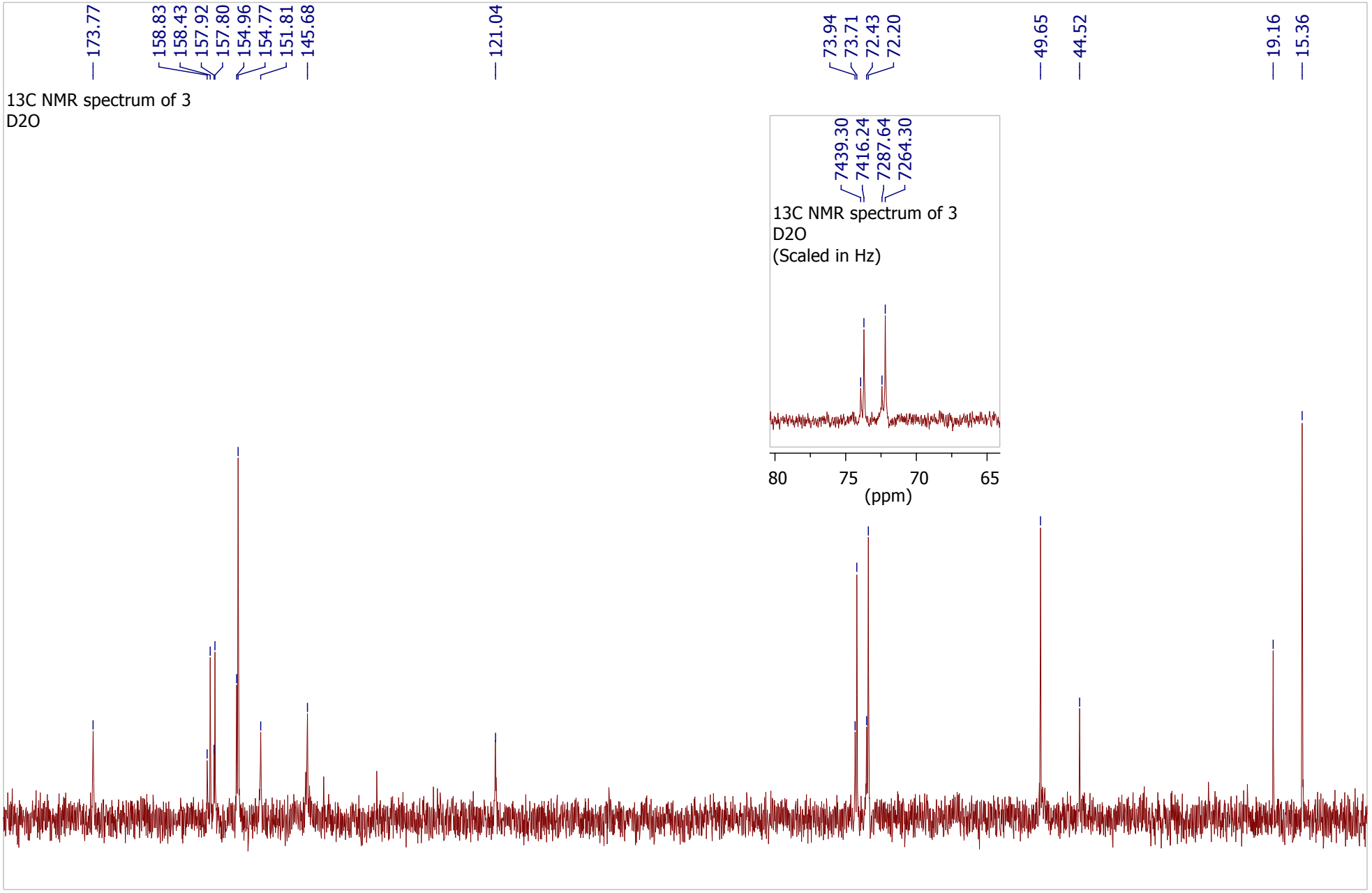
Supplementary Information

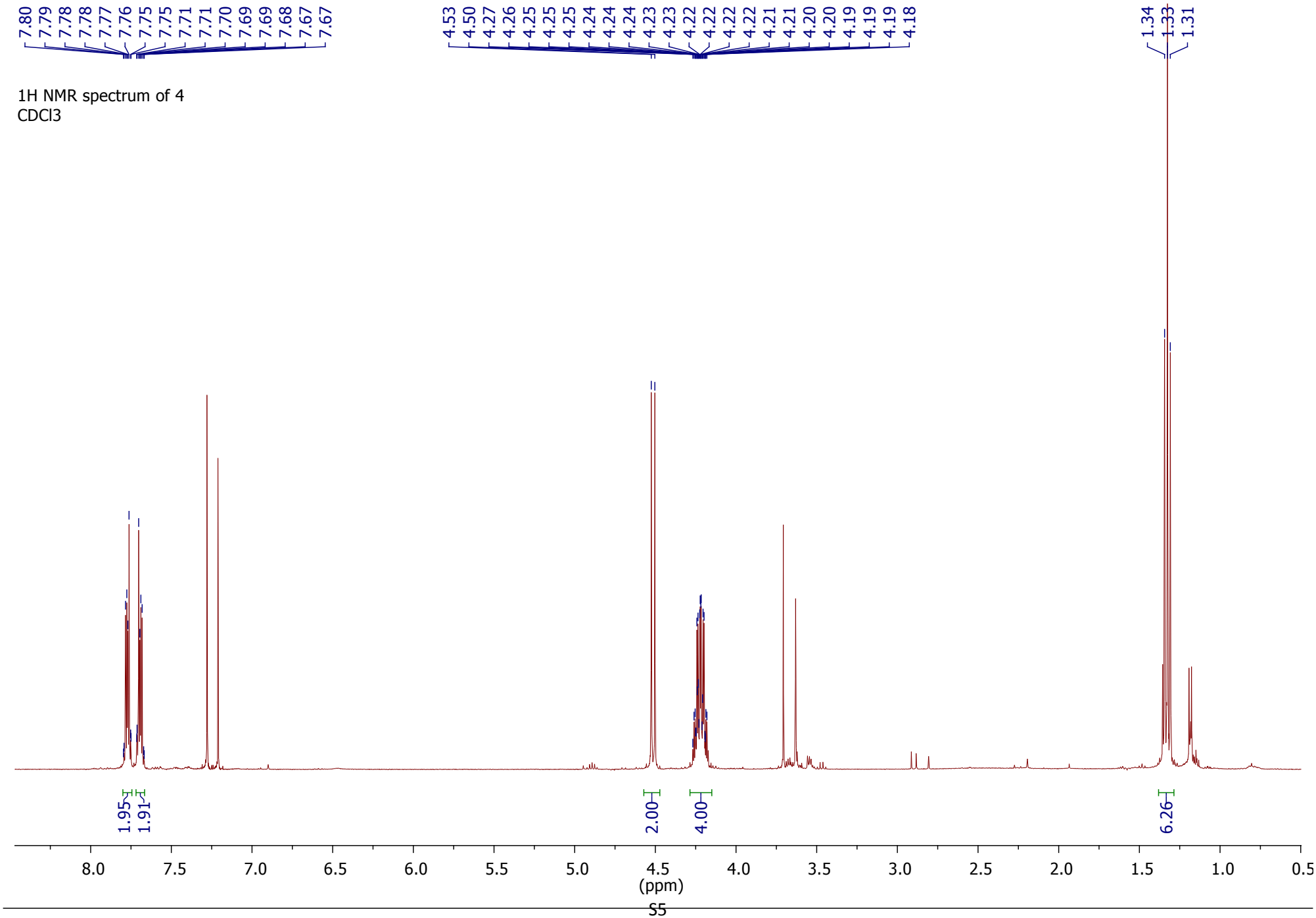
for P.N. Solyev, M.V. Jasko, M.K. Kukhanova, A.A. Kleymenova, S.N. Kochetkov. Versatile synthesis of oxime-containing acyclic nucleoside phosphonates – synthetic solutions and antiviral activity.

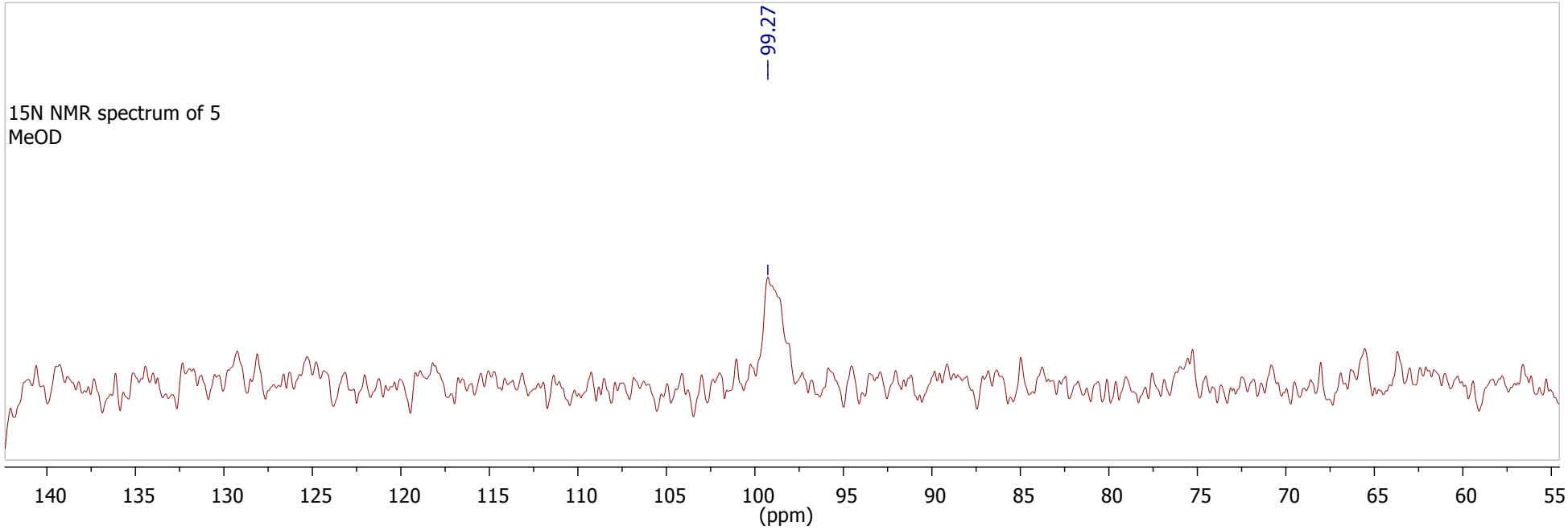

1H spectrum of 1
D2O
8.24
8.23
8.23
8.20
7.85
7.84
7.83
7.12
7.11
7.10
5.27
5.26
5.08
5.07
4.40
4.38
4.22
4.20
1.73
0.47
0.38
1.00
1.29
0.94
1.09
9.0 8.8 8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6
(ppm)
1H spectrum of 1
D2O
(Scaled in Hz)
3296.81
3294.65
3291.46
3282.12
3140.81
3136.05
3131.35
2849.14
2845.59
2841.40
2110.52
2106.26
2033.42
2028.67
1762.24
1753.85
1689.35
1680.77
1.73
0.47
0.38
1.00
1.29
0.94
1.09
8.3 7.9 7.2 5.3 5.1 4.4 4.2
(ppm)
31P NMR spectrum of 1
D2O
13.64
16 14 12 10
(ppm)

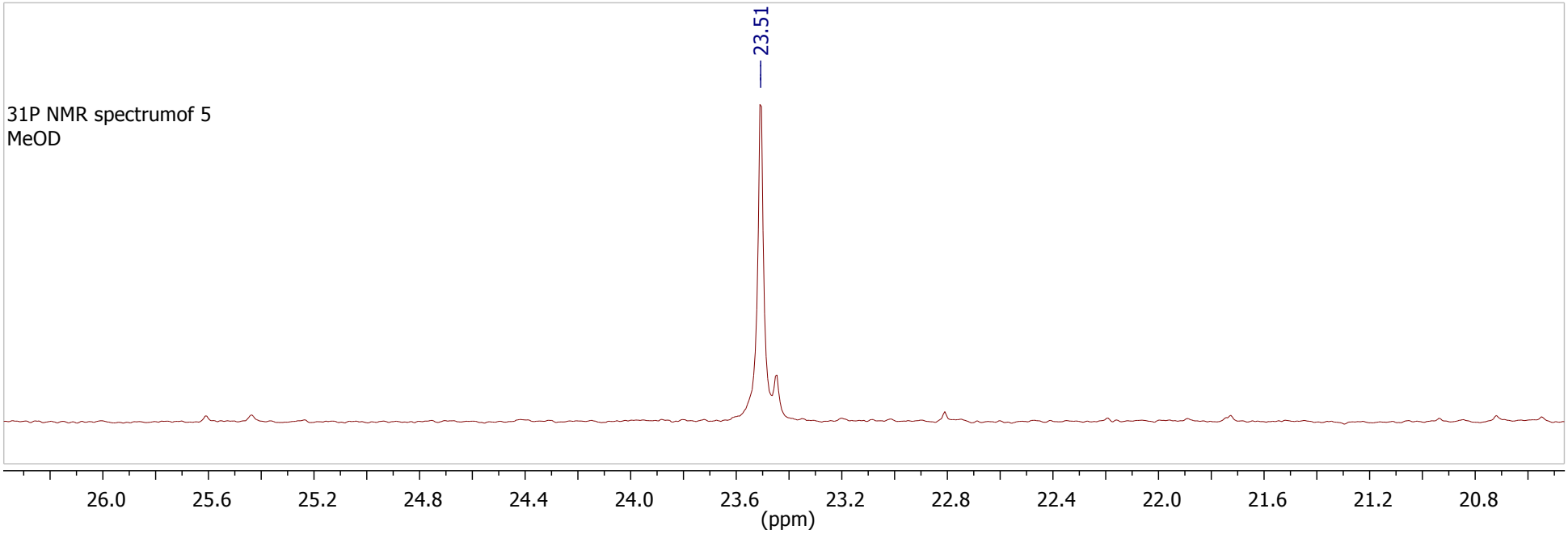

156.51
153.09
151.51
150.52
150.13
145.97
120.95
74.51
74.01
73.00
72.51
45.37
42.71
13C NMR spectrum of 1
D2O
7496.77
7446.90
7345.04
7295.81
13C NMR spectrum of 1
D2O
(Scaled in Hz)
85
80
75
70
(ppm)
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
(ppm)

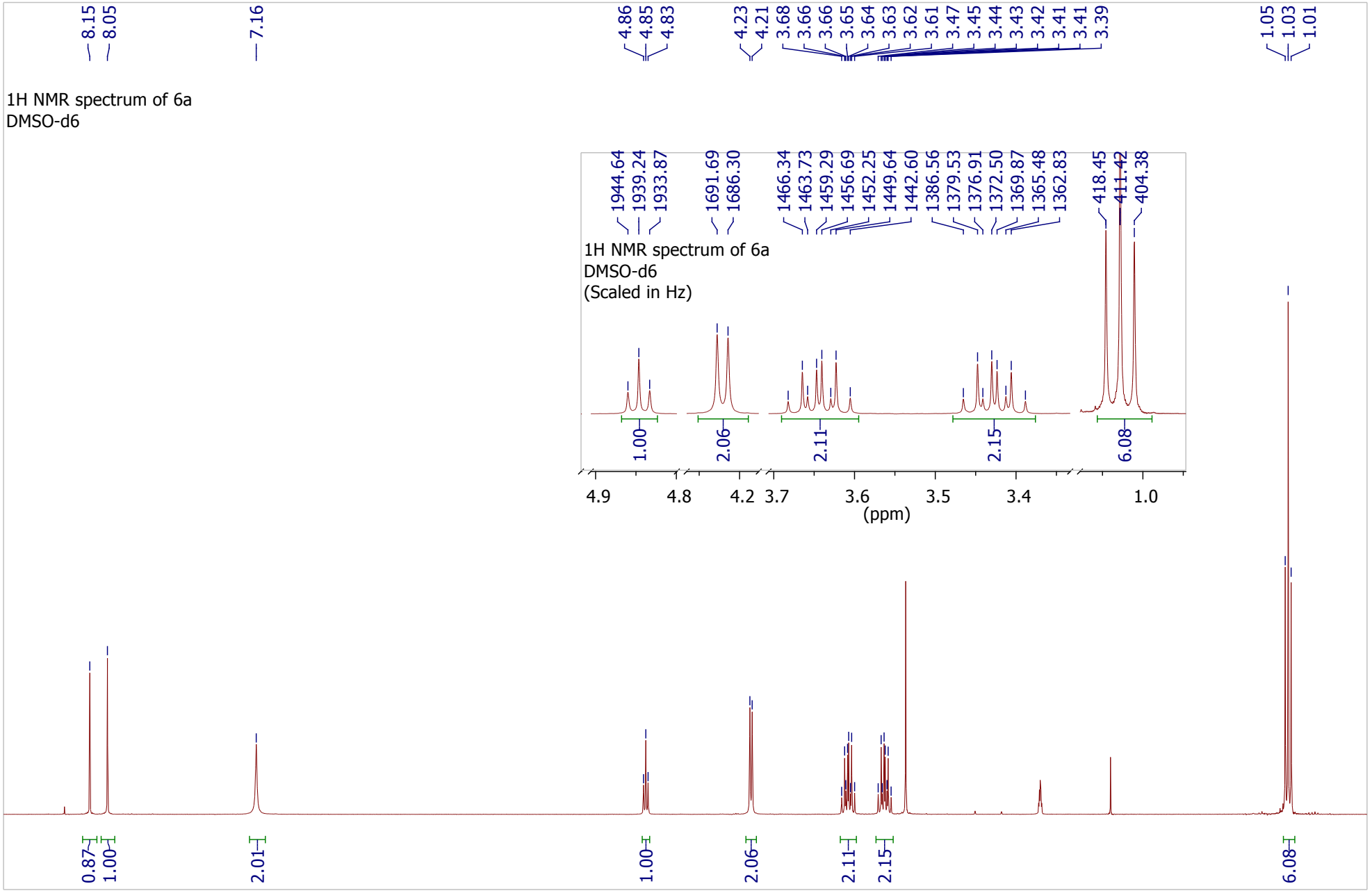

1H NMR spectrum of 3
D2O
8.41
8.15
5.19
4.93
4.26
4.24
4.12
4.10
1.85
1.57
1.11
1.93
0.98
2.33
1.24
2.36
3.09
1.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
(ppm)
1704.63
1696.02
1648.24
1639.84
1H NMR spectrum of 3
D2O
(Scaled in Hz)
1.24
2.36
4.25
4.15
4.05
(ppm)
14.57
14.31
31P NMR spectrum of 3
D2O
18
16
14
12
(ppm)

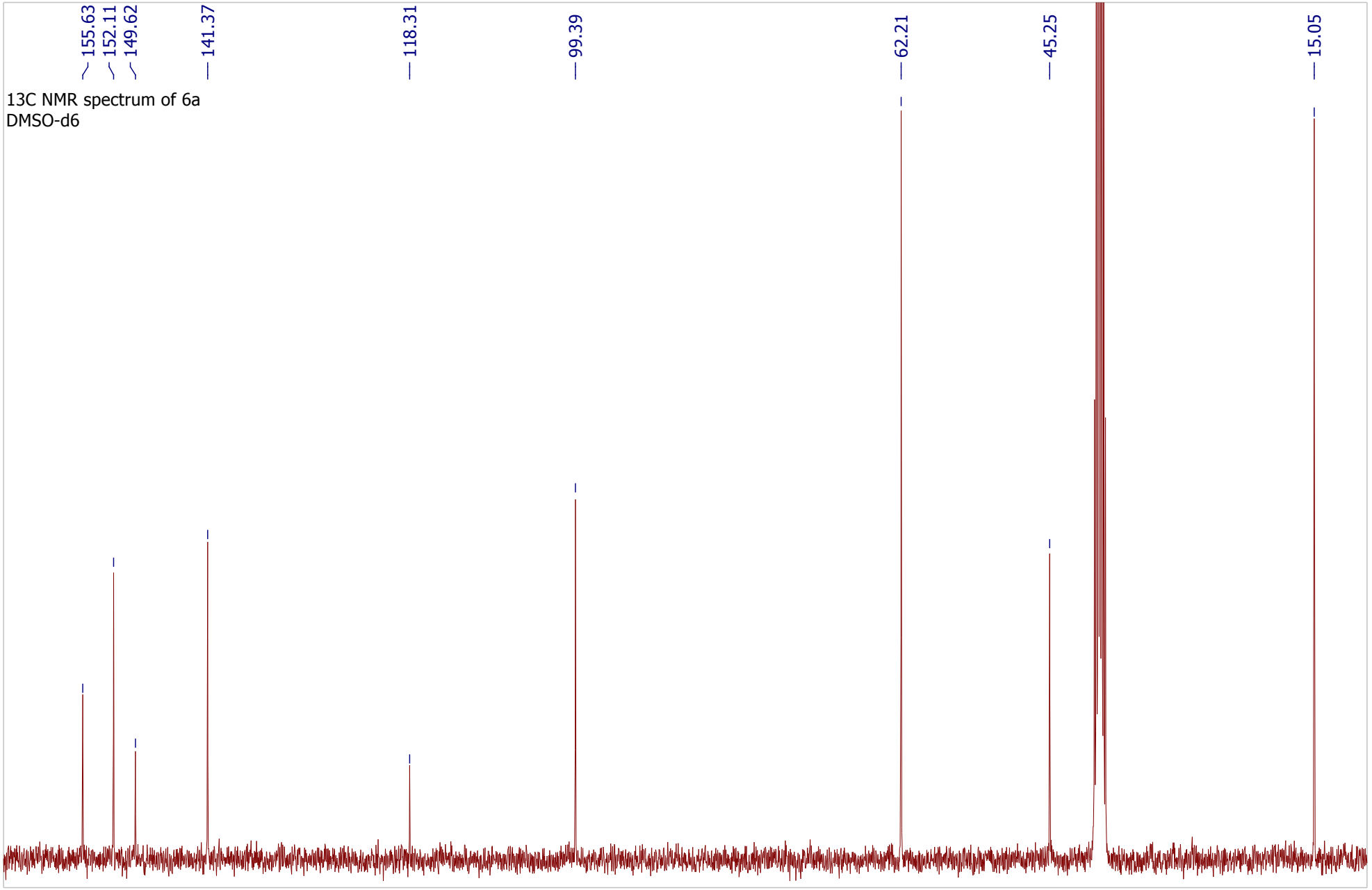

173.77
158.83
158.43
157.92
157.80
154.96
154.77
151.81
145.68
121.04
73.94
73.71
72.43
72.20
49.65
44.52
19.16
15.36
13C NMR spectrum of 3
D2O
7439.30
7416.24
7287.64
7264.30
13C NMR spectrum of 3
D2O
(Scaled in Hz)
80
75
70
65
(ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

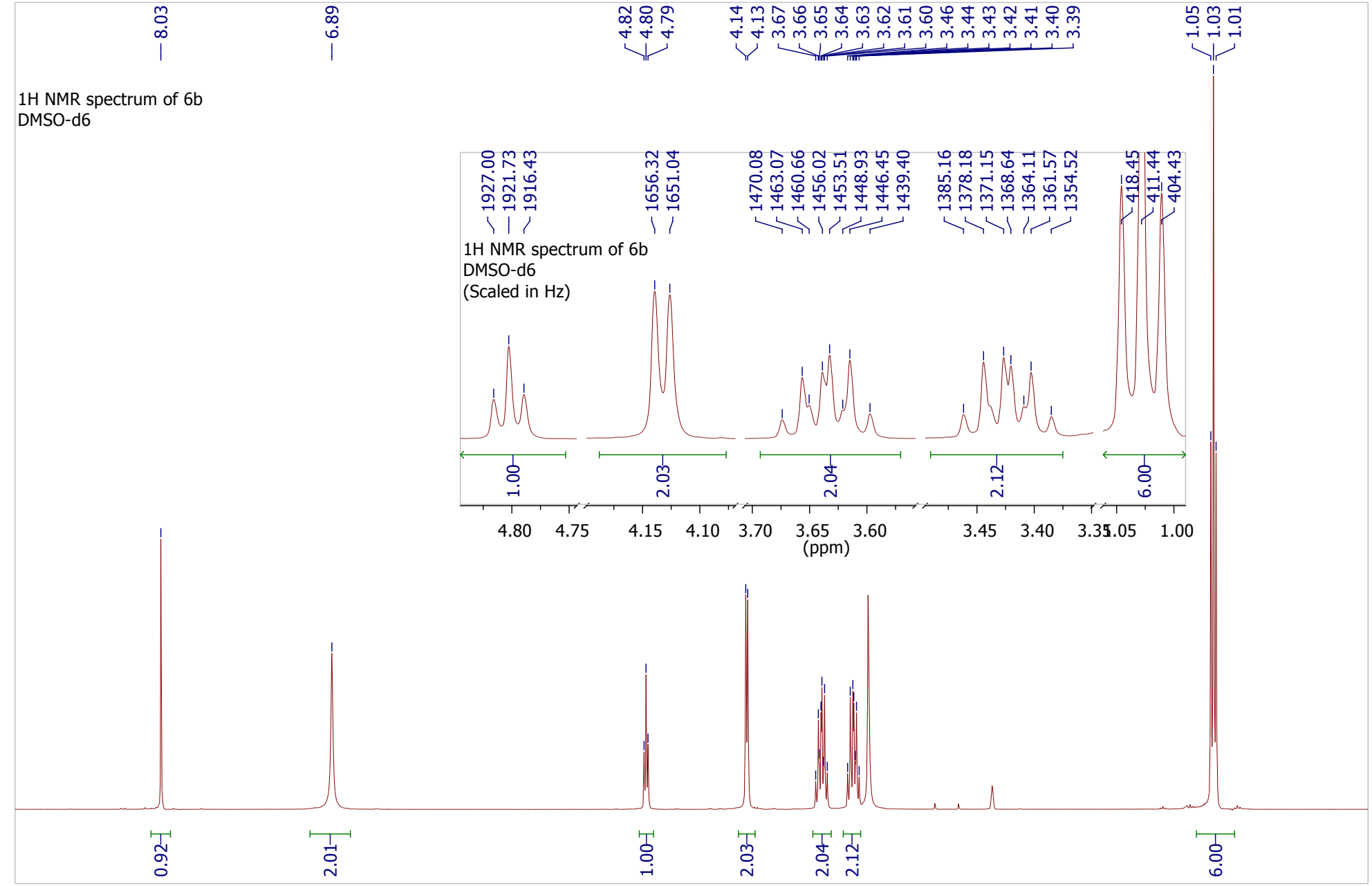

7.80
7.79
7.78
7.78
7.77
7.76
7.75
7.75
7.71
7.71
7.70
7.69
7.69
7.68
7.67
7.67
4.53
4.50
4.27
4.26
4.25
4.25
4.25
4.24
4.24
4.24
4.23
4.23
4.22
4.22
4.22
4.22
4.21
4.21
4.20
4.20
4.19
4.19
4.19
4.18
1.34
1.33
1.31
1H NMR spectrum of 4
CDCl3
1.95
1.91
2.00
4.00
6.26
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
(ppm)

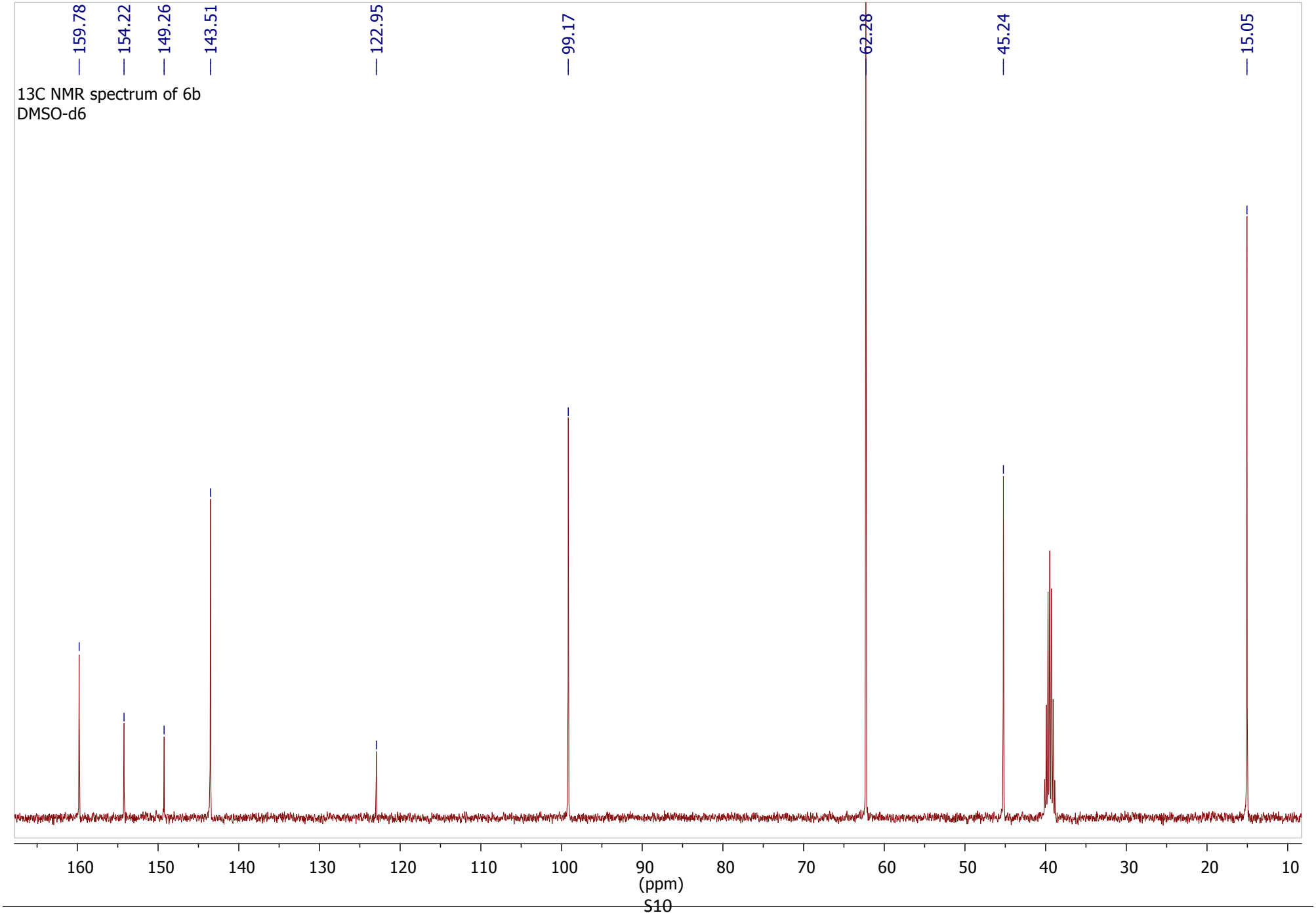

99.27
15N NMR spectrum of 5
MeOD
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
(ppm)

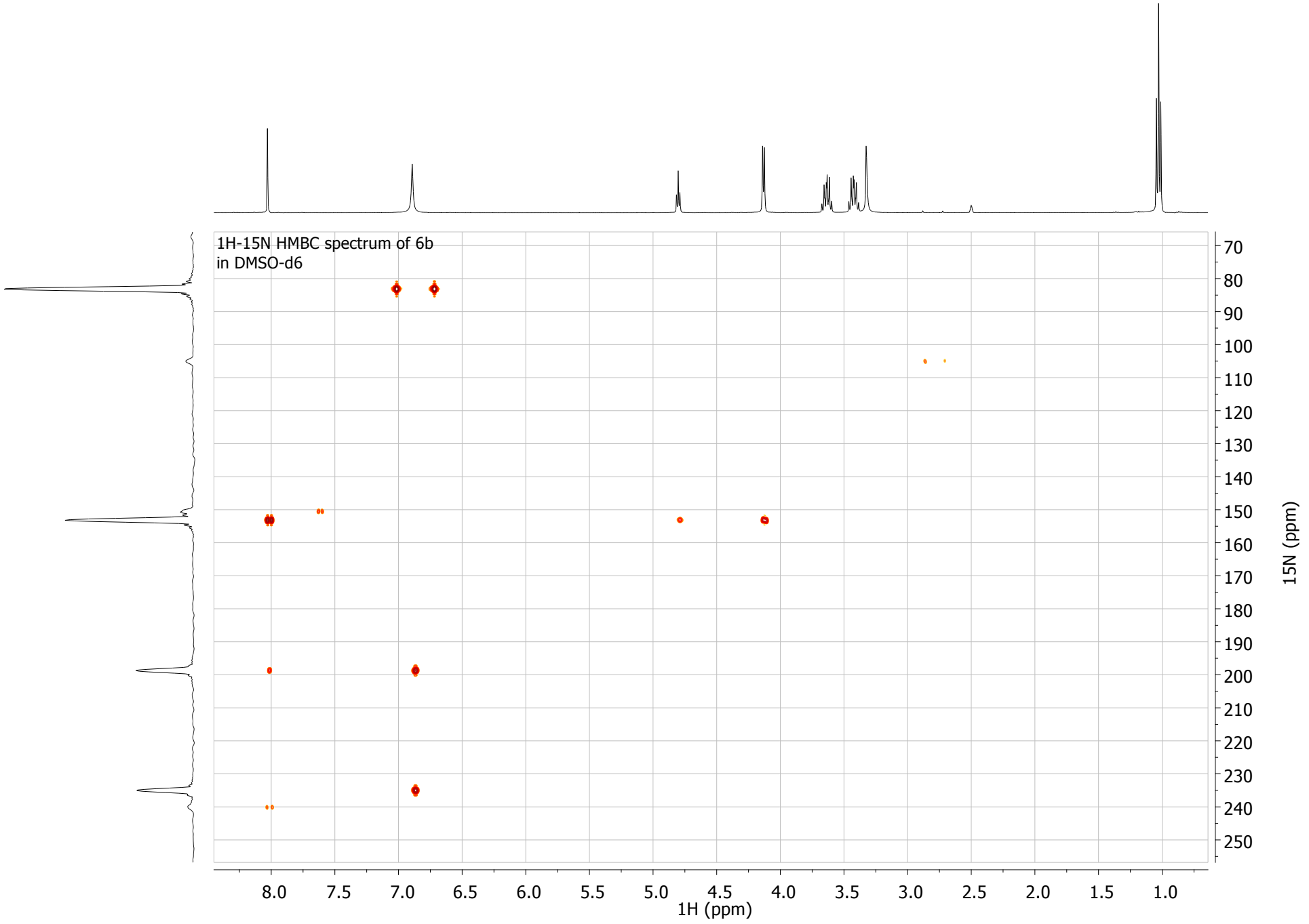

23.51
31P NMR spectrumof 5
MeOD
26.0
25.6
25.2
24.8
24.4
24.0
23.6
23.2
22.8
22.4
22.0
21.6
21.2
20.8
(ppm)

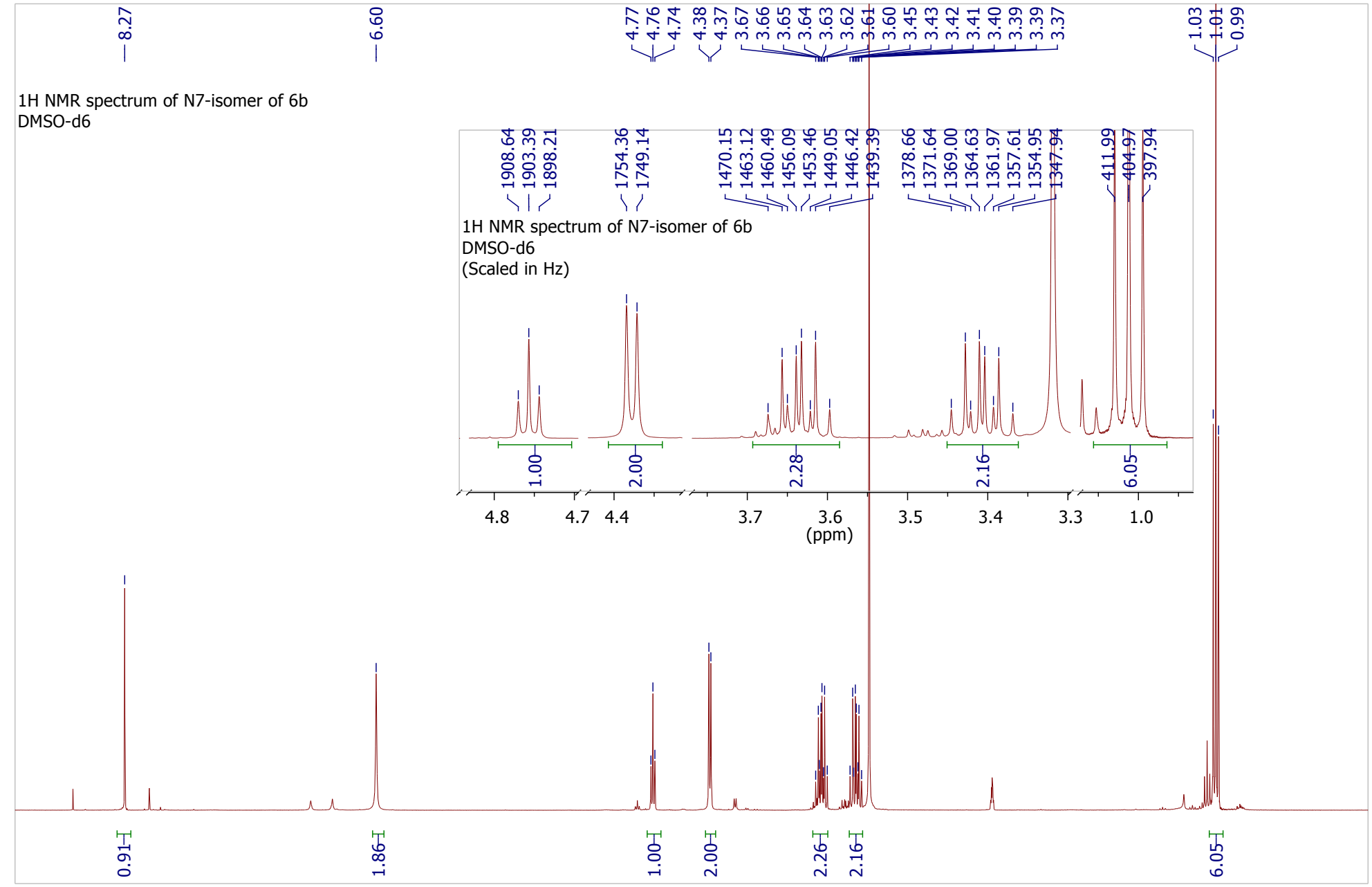

8.15
8.05
7.16
4.86
4.85
4.83
4.23
4.21
3.68
3.66
3.66
3.65
3.64
3.63
3.62
3.61
3.47
3.45
3.44
3.43
3.42
3.41
3.41
3.39
1.05
1.03
1.01
1H NMR spectrum of 6a
DMSO-d6
1944.64
1939.24
1933.87
1691.69
1686.30
1466.34
1463.73
1459.29
1456.69
1452.25
1449.64
1442.60
1386.56
1379.53
1376.91
1372.50
1369.87
1365.48
1362.83
418.45
411.42
404.38
1H NMR spectrum of 6a
DMSO-d6
(Scaled in Hz)
1.00
2.06
2.11
2.15
6.08
4.9
4.8
4.2
3.7
3.6
3.5
3.4
1.0
(ppm)
0.87
1.00
2.01
1.00
2.06
2.11
2.15
6.08
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
(ppm)

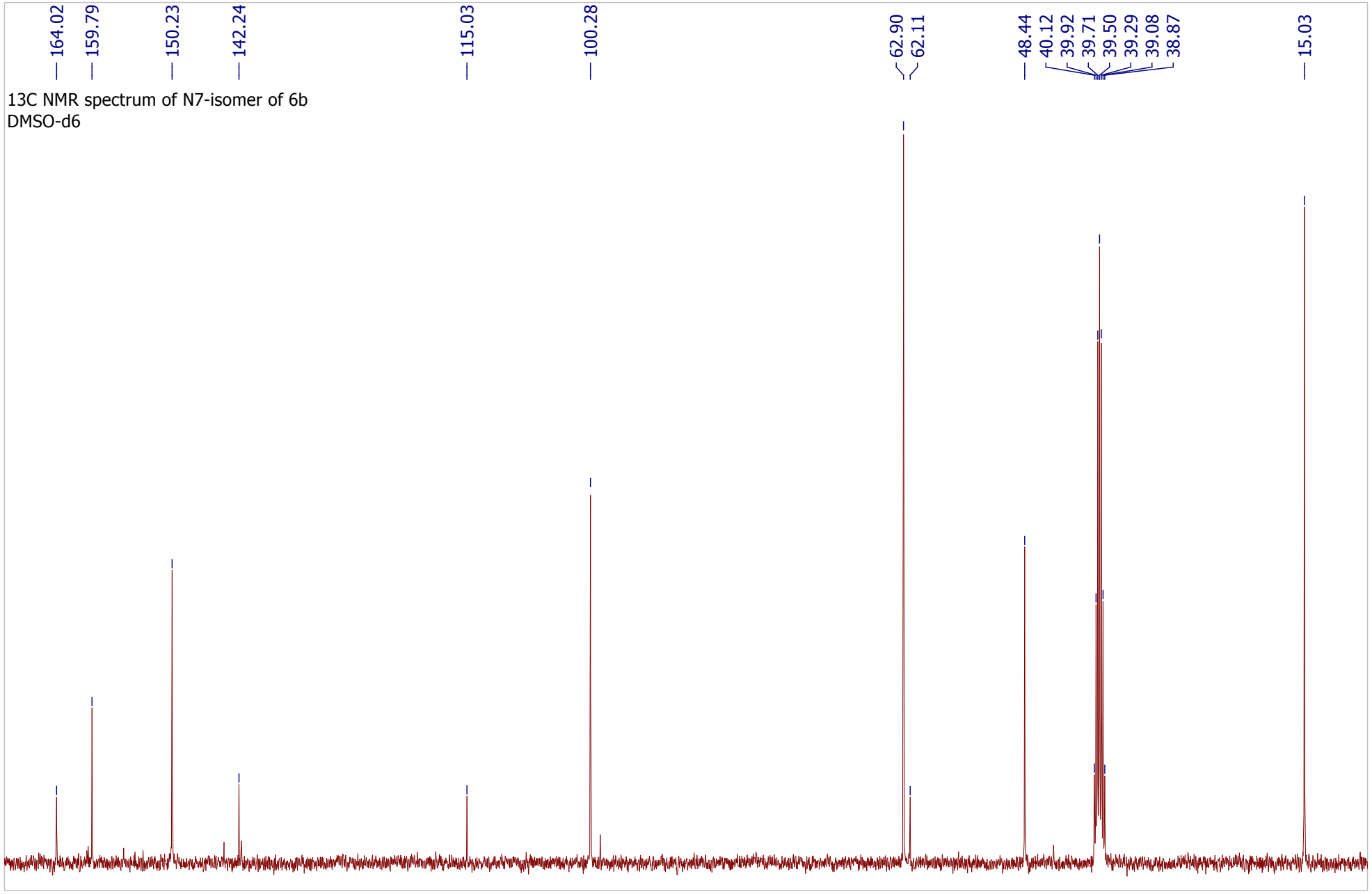

155.63
152.11
149.62
141.37
118.31
99.39
62.21
45.25
15.05
13C NMR spectrum of 6a
DMSO-d6
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

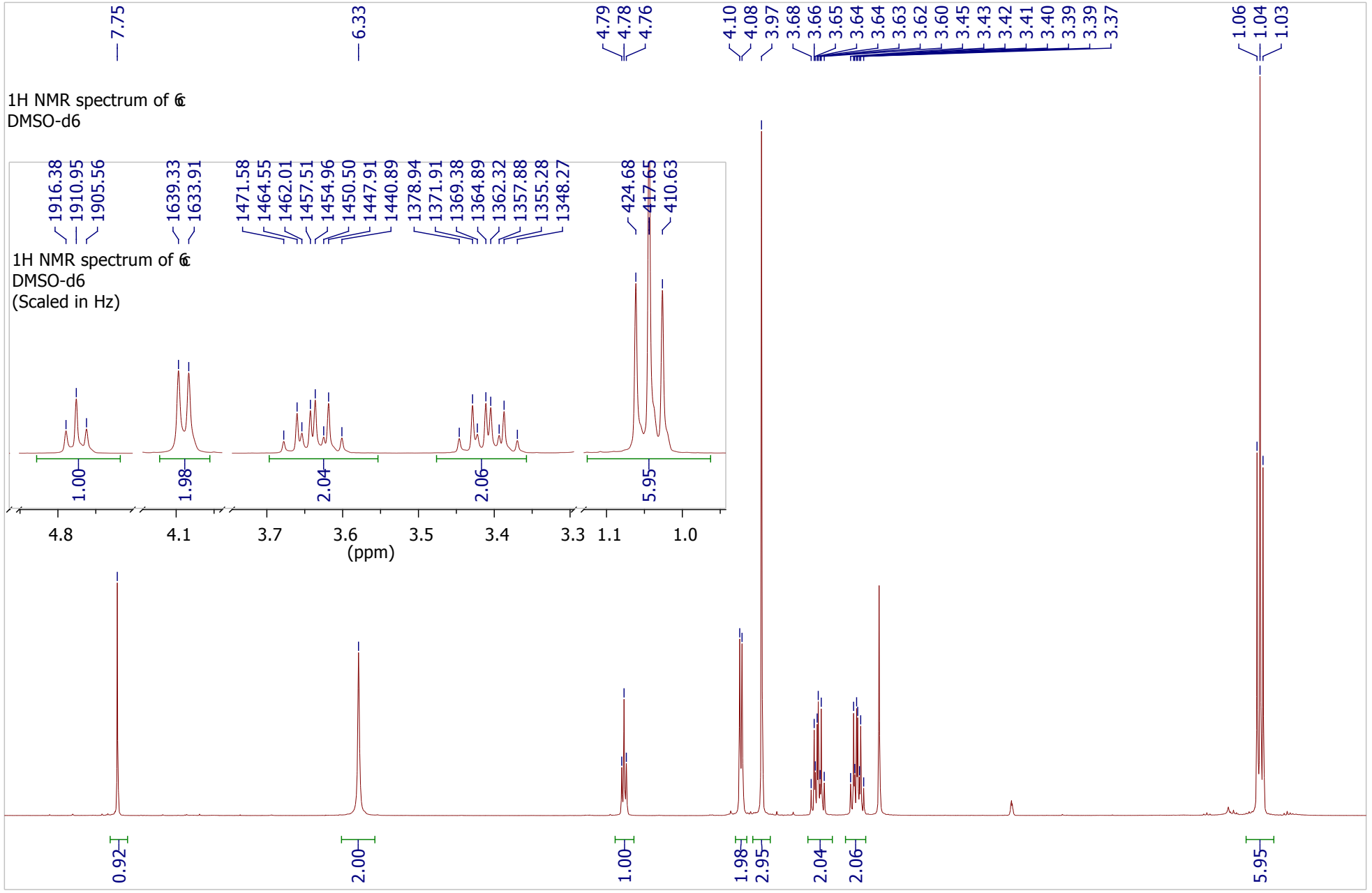

1H NMR spectrum of 6b
DMSO-d6
8.03
6.89
4.82
4.80
4.79
4.14
4.13
3.67
3.66
3.65
3.64
3.63
3.62
3.61
3.60
3.46
3.44
3.43
3.42
3.41
3.40
3.39
1.05
1.03
1.01
1927.00
1921.73
1916.43
1656.32
1651.04
1470.08
1463.07
1460.66
1456.02
1453.51
1448.93
1446.45
1439.40
1385.16
1378.18
1371.15
1368.64
1364.11
1361.57
1354.52
418.45
411.44
404.43
1H NMR spectrum of 6b
DMSO-d6
(Scaled in Hz)
1.00
2.03
2.04
2.12
6.00
4.80
4.75
4.15
4.10
3.70
3.65
3.60
3.45
3.40
3.35
1.05
1.00
(ppm)
0.92
2.01
1.00
2.03
2.04
2.12
6.00
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
(ppm)

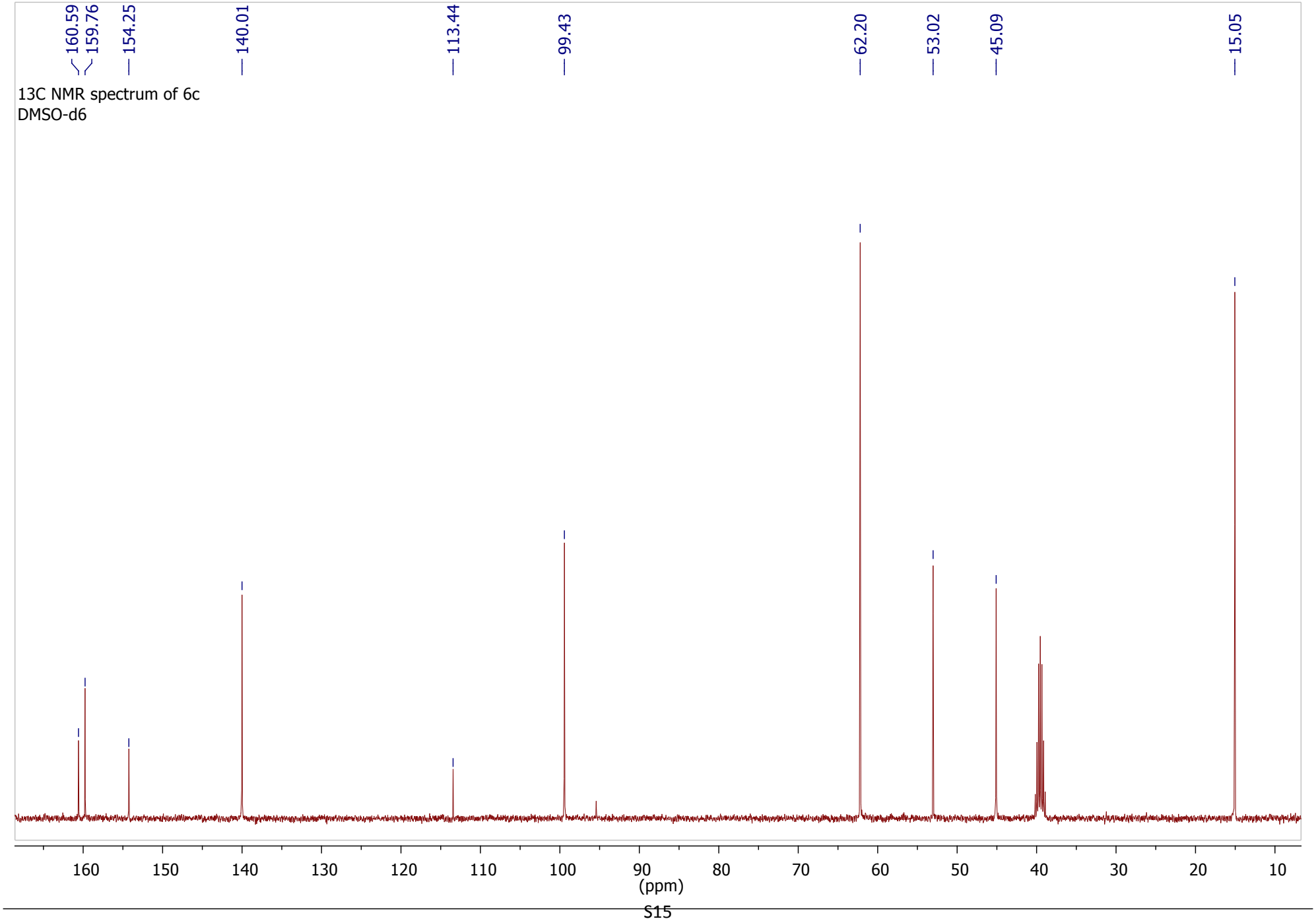

159.78
154.22
149.26
143.51
122.95
99.17
62.28
45.24
15.05
13C NMR spectrum of 6b
DMSO-d6
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

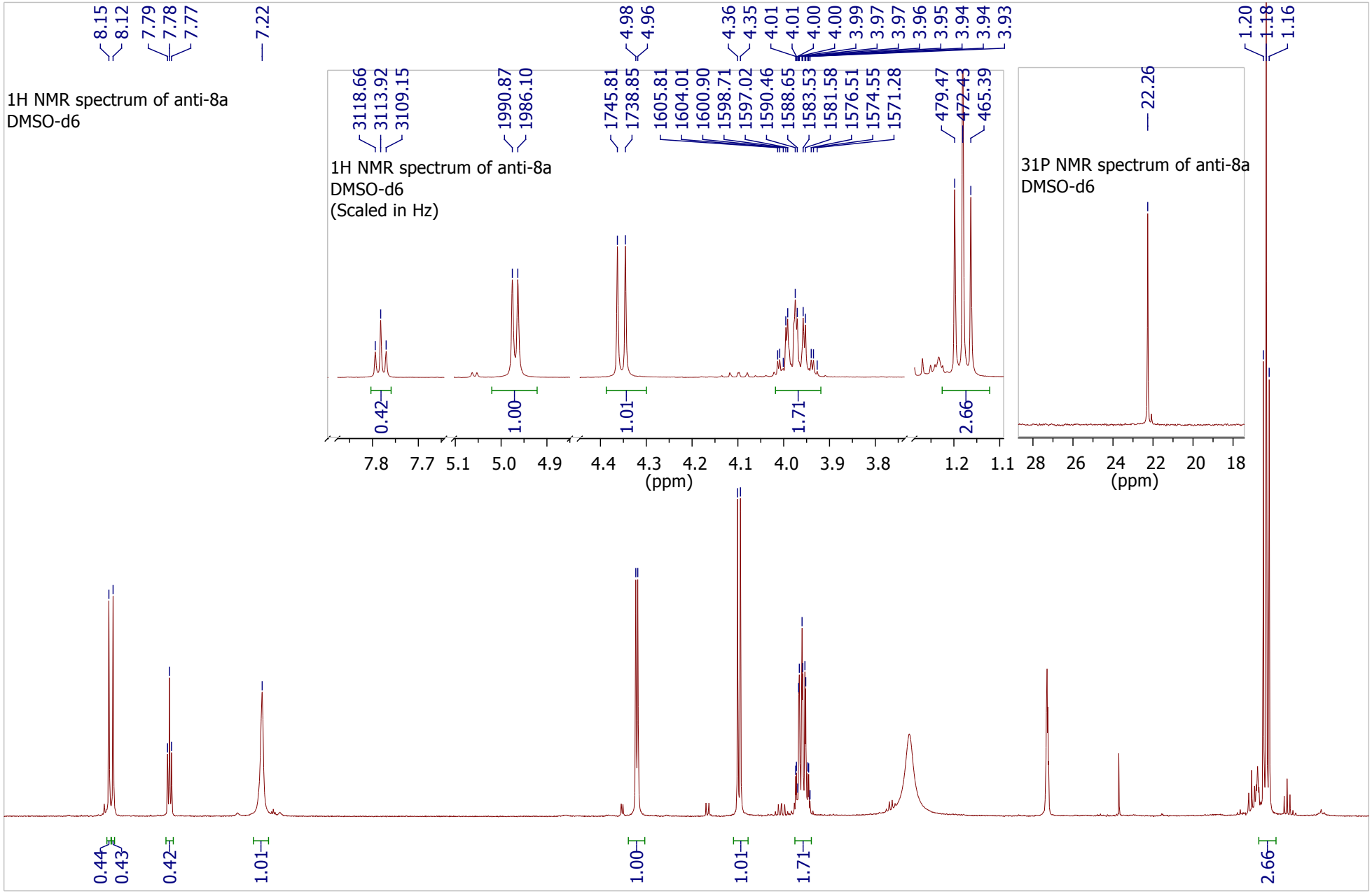

1H-15N HMBC spectrum of 6b
in DMSO-d6
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
1H (ppm)
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
240
250
15N (ppm)

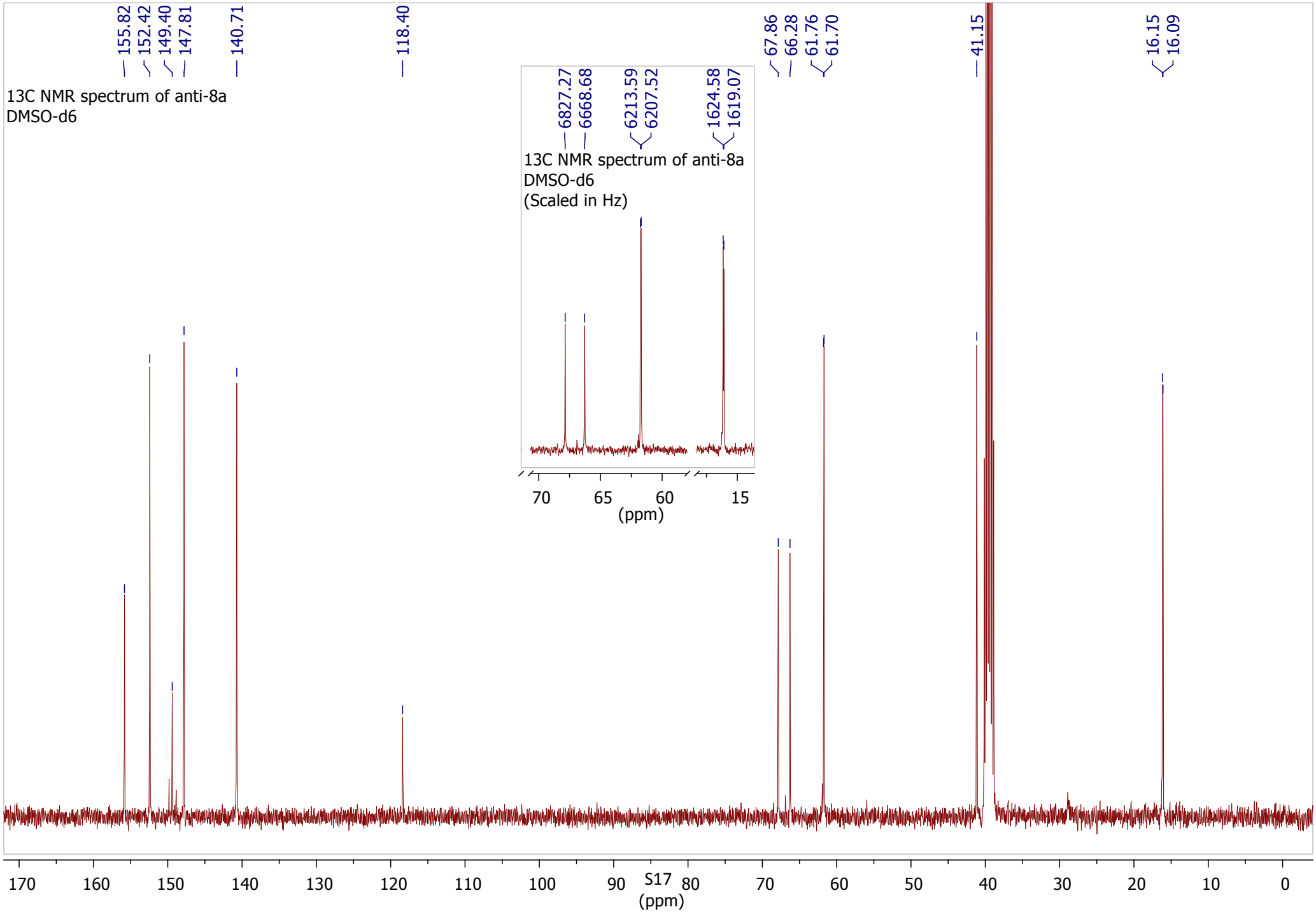

1H NMR spectrum of N7-isomer of 6b
DMSO-d6
8.27
6.60
4.77
4.76
4.74
4.38
4.37
3.67
3.66
3.65
3.64
3.63
3.62
3.61
3.60
3.45
3.43
3.42
3.41
3.40
3.39
3.39
3.37
1.03
1.01
0.99
1908.64
1903.39
1898.21
1754.36
1749.14
1470.15
1463.12
1460.49
1456.09
1453.46
1449.05
1446.42
1439.39
1378.66
1371.64
1369.00
1364.63
1361.97
1357.61
1354.95
1347.94
411.99
404.97
397.94
1H NMR spectrum of N7-isomer of 6b
DMSO-d6
(Scaled in Hz)
1.00
2.00
2.28
2.16
6.05
4.8
4.7
4.4
3.7
3.6
3.5
3.4
3.3
1.0
(ppm)
0.91
1.86
1.00
2.00
2.26
2.16
6.05
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
(ppm)

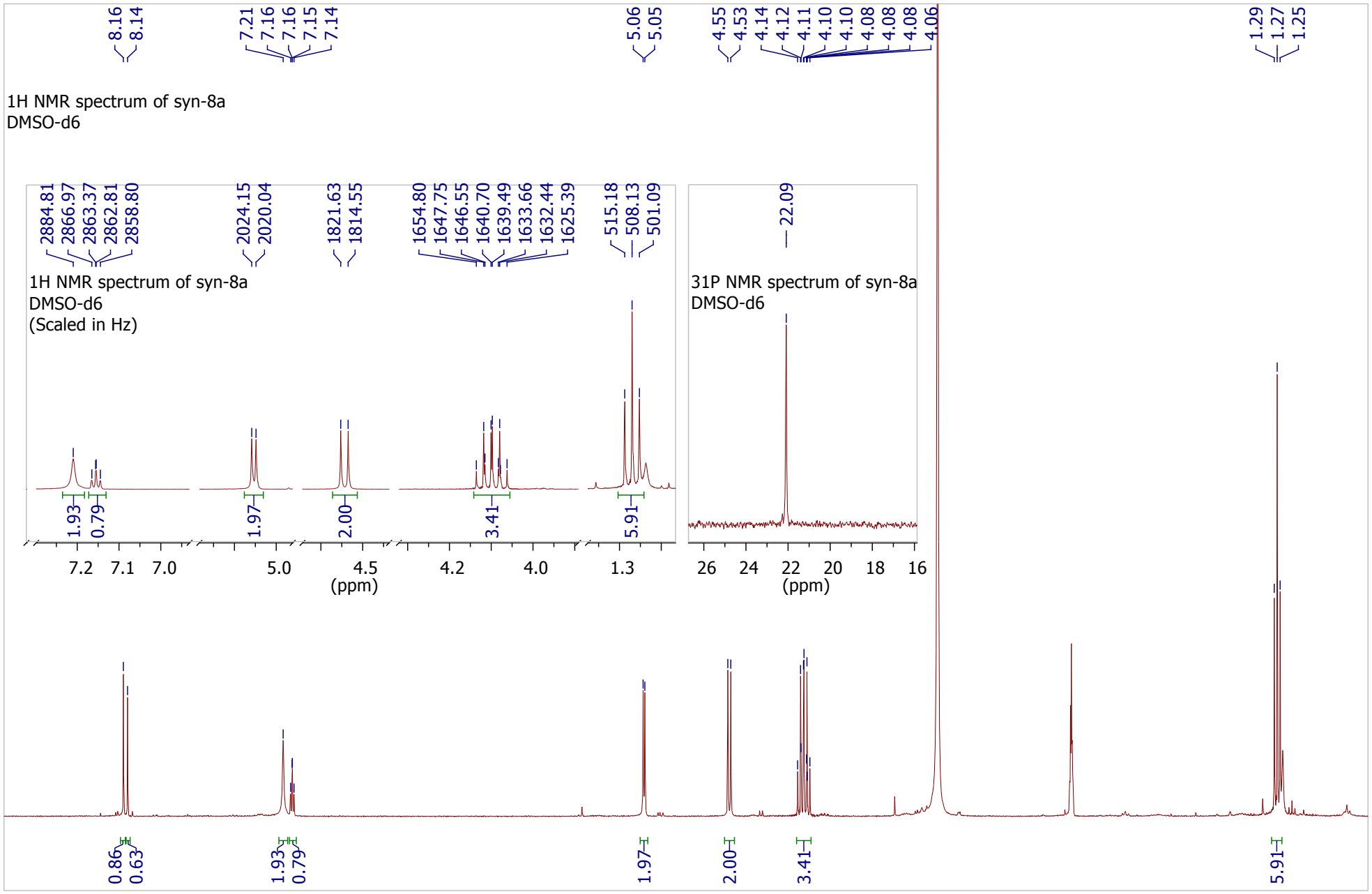

164.02
159.79
150.23
142.24
115.03
100.28
62.90
62.11
48.44
40.12
39.92
39.71
39.50
39.29
39.08
38.87
15.03
13C NMR spectrum of N7-isomer of 6b
DMSO-d6
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

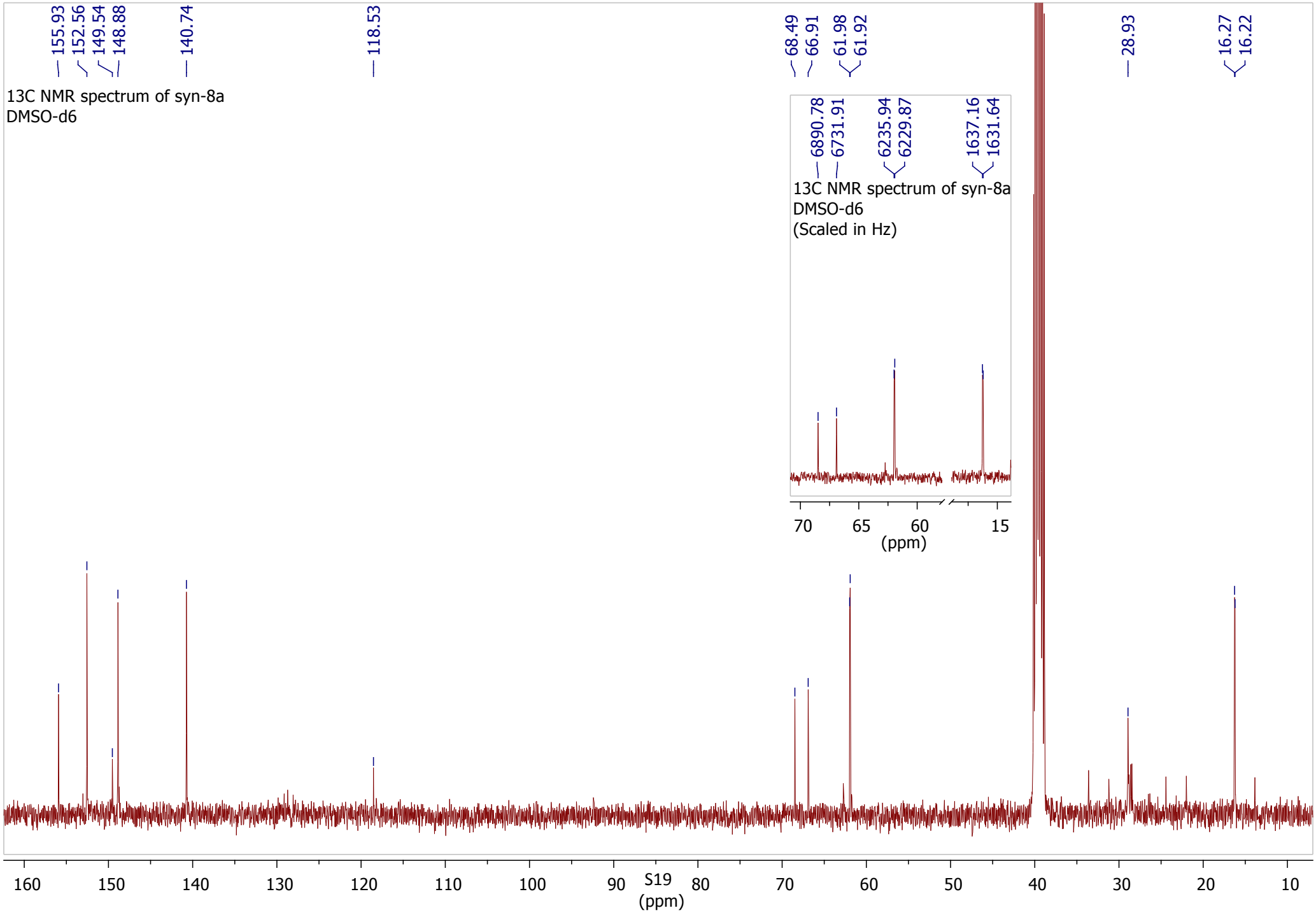

1H NMR spectrum of 6c
DMSO-d6
7.75
6.33
4.79
4.78
4.76
4.10
4.08
3.97
3.68
3.66
3.65
3.64
3.64
3.63
3.62
3.60
3.45
3.43
3.42
3.41
3.40
3.39
3.39
3.37
1.06
1.04
1.03
1916.38
1910.95
1905.56
1639.33
1633.91
1471.58
1464.55
1462.01
1457.51
1454.96
1450.50
1447.91
1440.89
1378.94
1371.91
1369.38
1364.89
1362.32
1357.88
1355.28
1348.27
424.68
417.65
410.63
1H NMR spectrum of 6c
DMSO-d6
(Scaled in Hz)
1.00
1.98
2.04
2.06
5.95
4.8
4.1
3.7
3.6
3.5
3.4
3.3
1.1
1.0
(ppm)
0.92
2.00
1.00
1.98
2.95
2.04
2.06
5.95
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
(ppm)

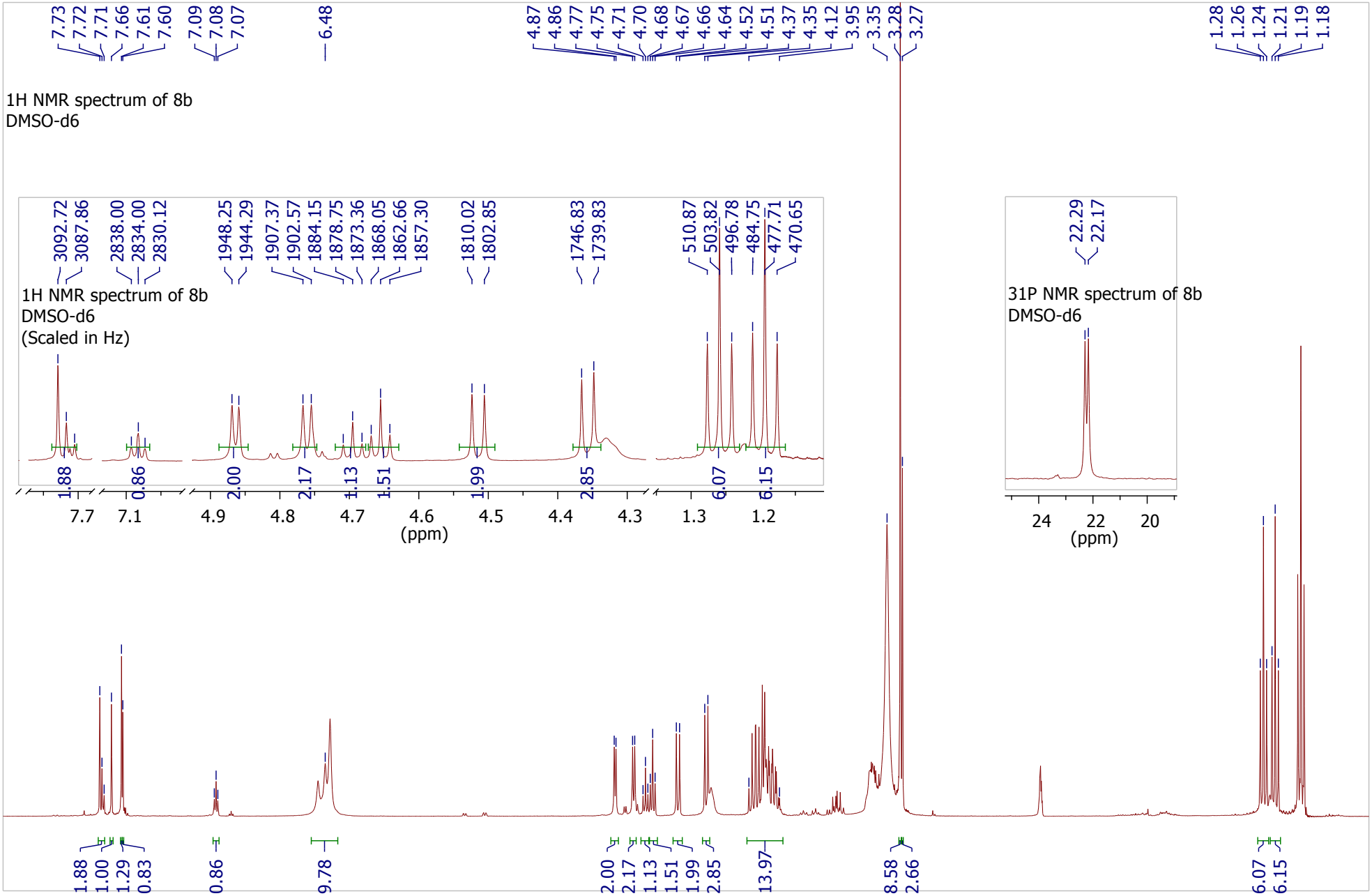

160.59
159.76
154.25
140.01
113.44
99.43
62.20
53.02
45.09
15.05
13C NMR spectrum of 6c
DMSO-d6
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

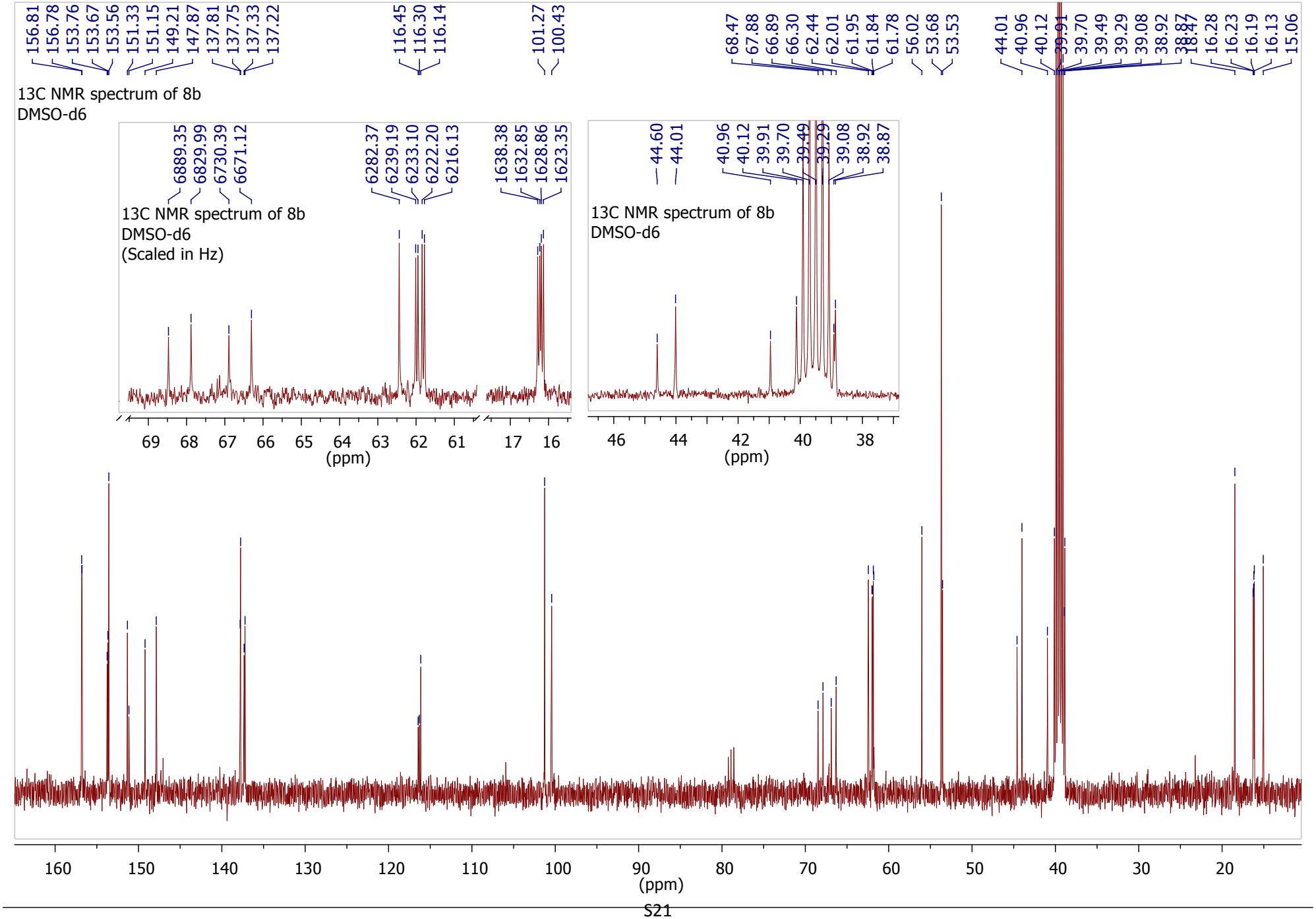

1H NMR spectrum of anti-8a
DMSO-d6
8.15
8.12
7.79
7.78
7.77
7.22
4.98
4.96
4.36
4.35
4.01
4.01
4.00
4.00
3.99
3.97
3.97
3.96
3.95
3.94
3.94
3.93
1.20
1.18
1.16
3118.66
3113.92
3109.15
1990.87
1986.10
1745.81
1738.85
1605.81
1604.01
1600.90
1598.71
1597.02
1590.46
1588.65
1583.53
1581.58
1576.51
1574.55
1571.28
479.47
472.43
465.39
1H NMR spectrum of anti-8a
DMSO-d6
(Scaled in Hz)
0.42
1.00
1.01
1.71
2.66
7.8
7.7
5.1
5.0
4.9
4.4
4.3
4.2
4.1
4.0
3.9
3.8
1.2
1.1
(ppm)
22.26
31P NMR spectrum of anti-8a
DMSO-d6
28
26
24
22
20
18
(ppm)
0.44
0.43
0.42
1.01
1.00
1.01
1.71
2.66
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
(ppm)

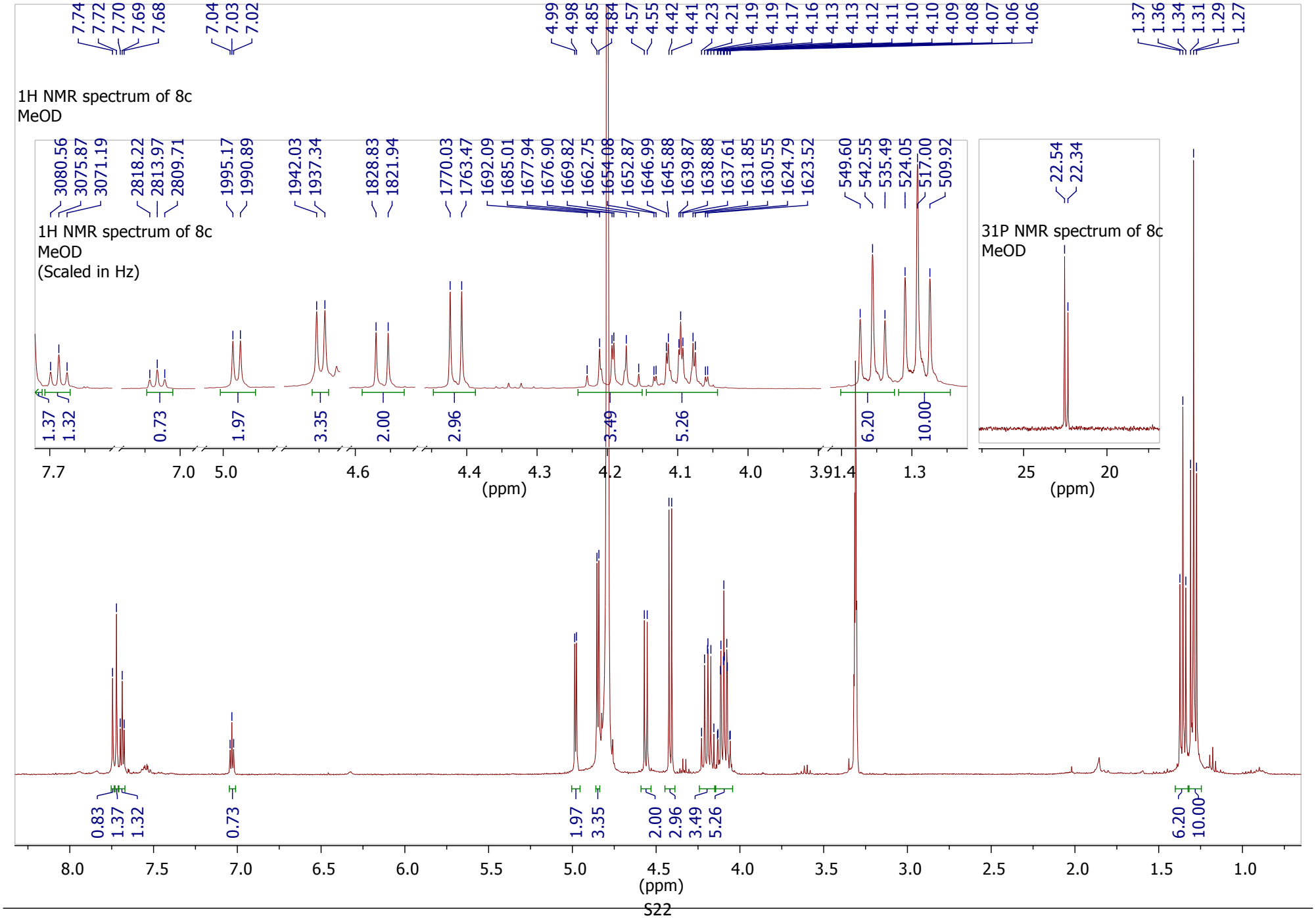

155.82
152.42
149.40
147.81
140.71
118.40
67.86
66.28
61.76
61.70
41.15
16.15
16.09
13C NMR spectrum of anti-8a
DMSO-d6
6827.27
6668.68
6213.59
6207.52
1624.58
1619.07
13C NMR spectrum of anti-8a
DMSO-d6
(Scaled in Hz)
70
65
60
15
(ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

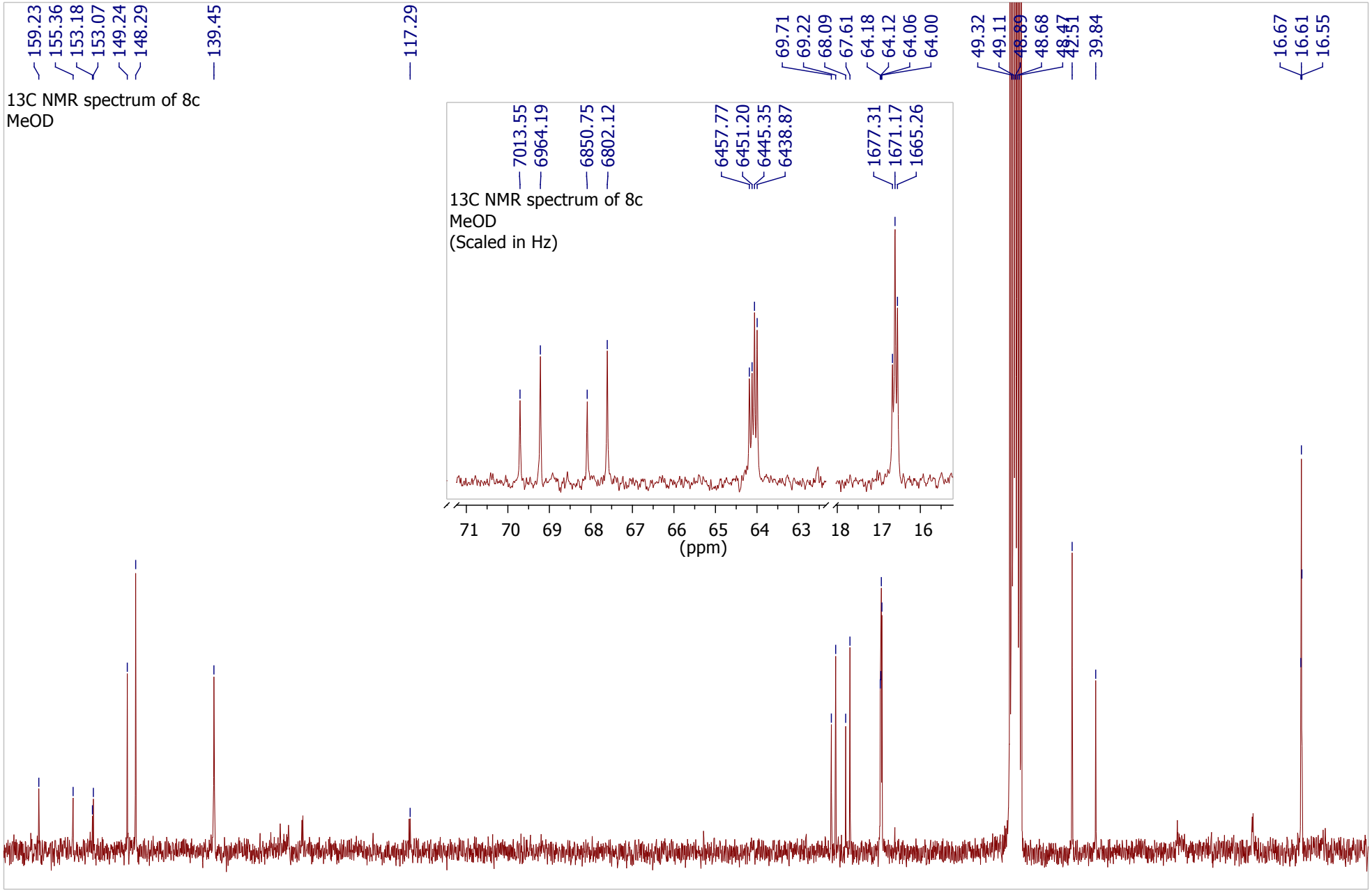

1H NMR spectrum of syn-8a
DMSO-d6
1H NMR spectrum of syn-8a
DMSO-d6
(Scaled in Hz)
31P NMR spectrum of syn-8a
DMSO-d6
(ppm)

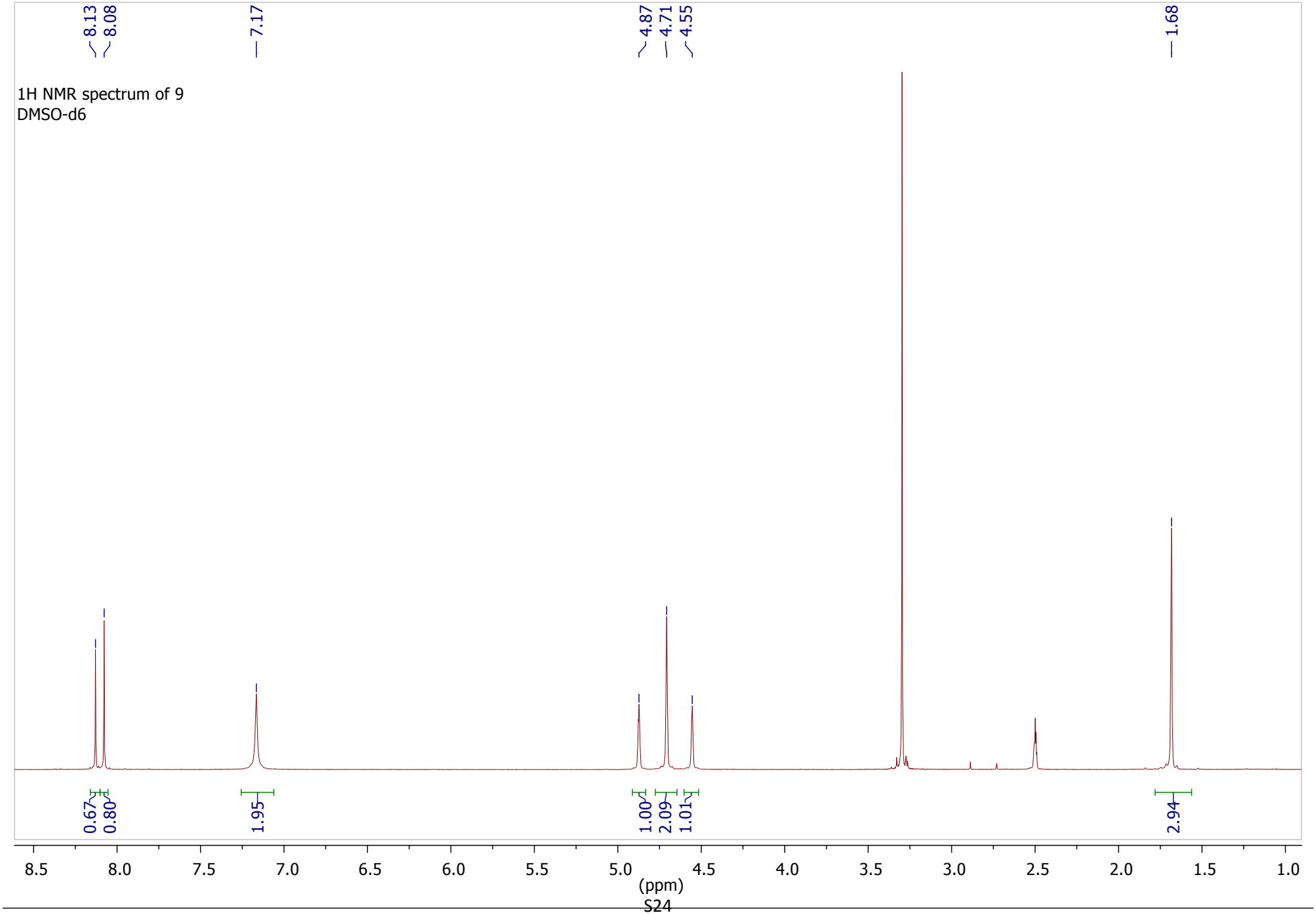

155.93
152.56
149.54
148.88
140.74
118.53
68.49
66.91
61.98
61.92
28.93
16.27
16.22
13C NMR spectrum of syn-8a
DMSO-d6
6890.78
6731.91
6235.94
6229.87
1637.16
1631.64
13C NMR spectrum of syn-8a
DMSO-d6
(Scaled in Hz)
70
65
60
15
(ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

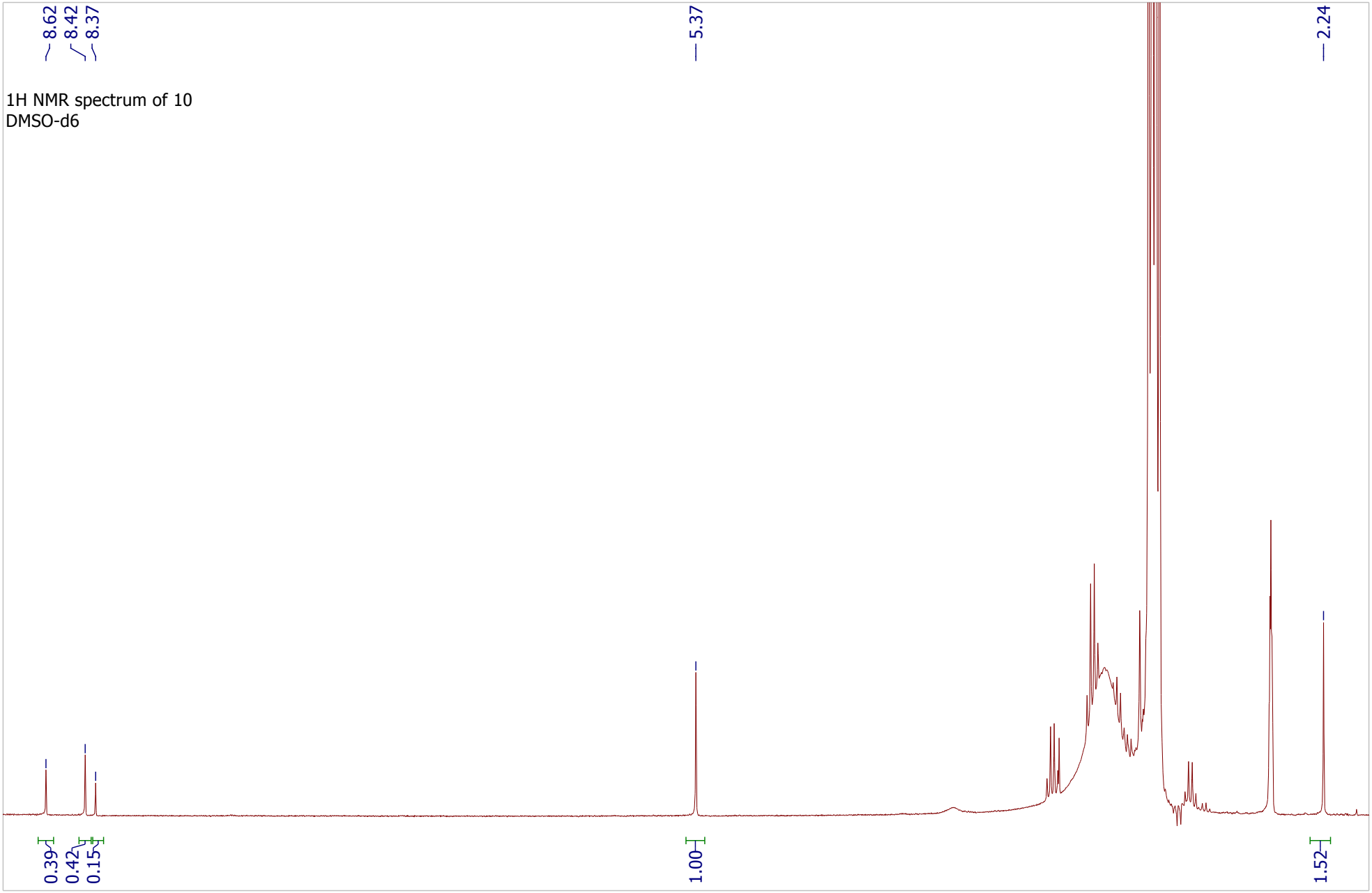

1H NMR spectrum of 8b
DMSO-d6
1H NMR spectrum of 8b
DMSO-d6
(Scaled in Hz)
31P NMR spectrum of 8b
DMSO-d6
(ppm)

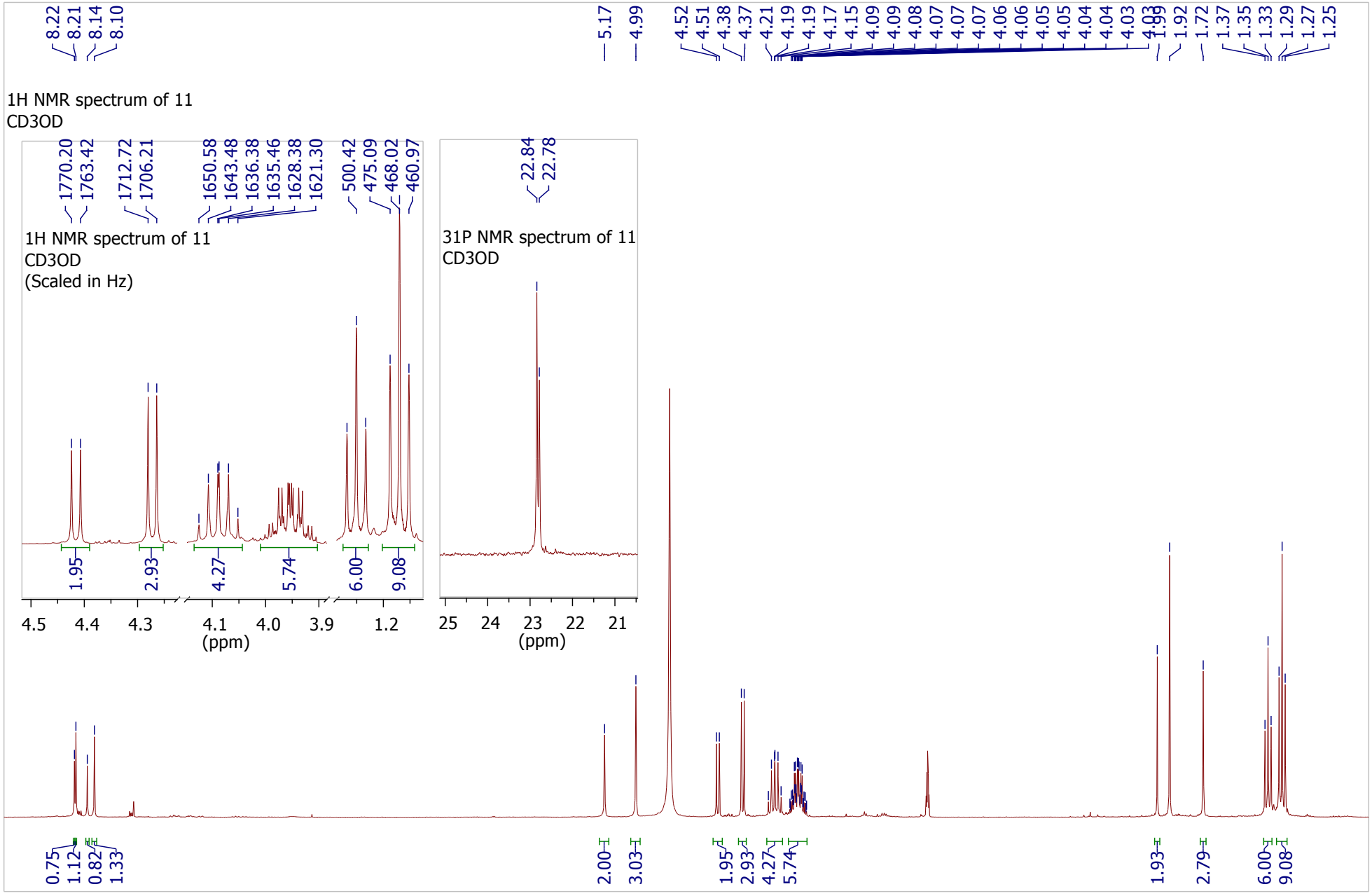

156.81
156.78
153.76
153.67
153.56
151.33
151.15
149.21
147.87
137.81
137.75
137.33
137.22
116.45
116.30
116.14
101.27
100.43
68.47
67.88
66.89
66.30
62.44
62.01
61.95
61.84
61.78
56.02
53.68
53.53
44.01
40.96
40.12
39.91
39.70
39.49
39.29
39.08
38.92
38.87
16.28
16.23
16.19
16.13
15.06
13C NMR spectrum of 8b
DMSO-d6
6889.35
6829.99
6730.39
6671.12
6282.37
6239.19
6233.10
6222.20
6216.13
1638.38
1632.85
1628.86
1623.35
13C NMR spectrum of 8b
DMSO-d6
(Scaled in Hz)
69 68 67 66 65 64 63 62 61 17 16
(ppm)
44.60
44.01
40.96
40.12
39.91
39.70
39.49
39.29
39.08
38.92
38.87
13C NMR spectrum of 8b
DMSO-d6
46 44 42 40 38
(ppm)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
(ppm)

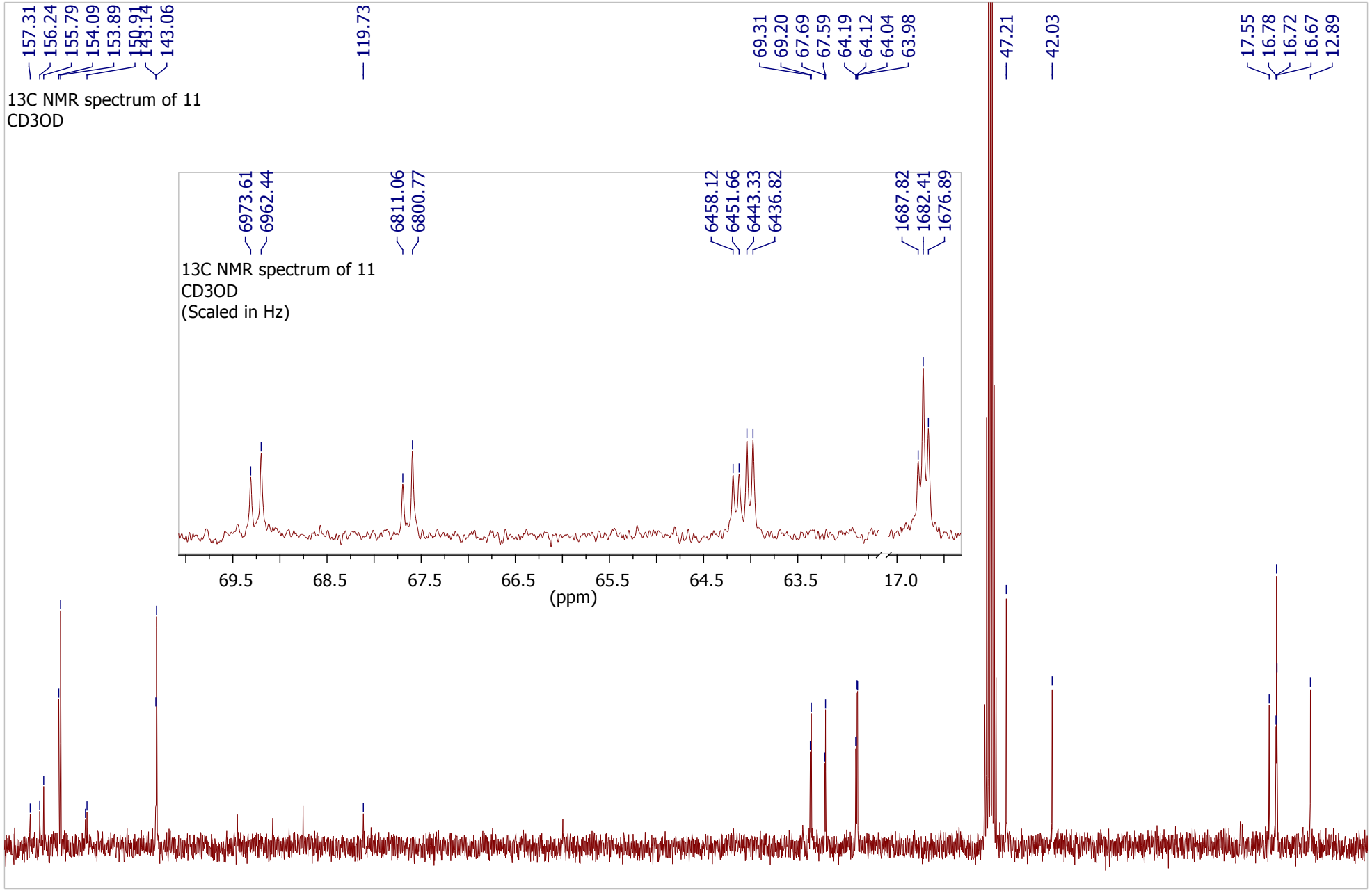

1H NMR spectrum of 8c
MeOD
1H NMR spectrum of 8c
MeOD
(Scaled in Hz)
31P NMR spectrum of 8c
MeOD
(ppm)
(ppm)


159.23
155.36
153.18
153.07
149.24
148.29
139.45
117.29
69.71
69.22
68.09
67.61
64.18
64.12
64.06
64.00
49.32
49.11
48.89
48.68
48.47
42.51
39.84
16.67
16.61
16.55
13C NMR spectrum of 8c
MeOD
7013.55
6964.19
6850.75
6802.12
6457.77
6451.20
6445.35
6438.87
1677.31
1671.17
1665.26
13C NMR spectrum of 8c
MeOD
(Scaled in Hz)
71 70 69 68 67 66 65 64 63 18 17 16
(ppm)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)


8.13
8.08
7.17
4.87
4.71
4.55
1.68
1H NMR spectrum of 9
DMSO-d6
0.67
0.80
1.95
1.00
2.09
1.01
2.94
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
(ppm)


8.62
8.42
8.37
5.37
2.24
1H NMR spectrum of 10
DMSO-d6
0.39
0.42
0.15
1.00
1.52
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
(ppm)


1H NMR spectrum of 11
CD3OD
1H NMR spectrum of 11
CD3OD
(Scaled in Hz)
31P NMR spectrum of 11
CD3OD
(ppm)
(ppm)


157.31
156.24
155.79
154.09
153.89
150.91
143.14
143.06
119.73
69.31
69.20
67.69
67.59
64.19
64.12
64.04
63.98
47.21
42.03
17.55
16.78
16.72
16.67
12.89
13C NMR spectrum of 11
CD3OD
6973.61
6962.44
6811.06
6800.77
6458.12
6451.66
6443.33
6436.82
1687.82
1682.41
1676.89
13C NMR spectrum of 11
CD3OD
(Scaled in Hz)
69.5
68.5
67.5
66.5
65.5
64.5
63.5
17.0
(ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

TLC development of diethyl aminooxymethylphosphonate 5
in ninhydrin and Dragendorff reagent

Product **5** appeared to be invisible under typical 254 nm or blacklight (365 nm) lamps, and iodine treatment doesn't develop it either. On the other hand, ninhydrin is used as a TLC staining reagent of amino group due to the formation of the bright purple Ruhemann colouring. It is known that ninhydrin reveals hydrazine through yellow colour while hydroxylamine gives no colour [J.M. Bremner. *Analyst*, 1954, **79**: 198-201]. However, the situation is different for aminooxy derivatives; besides, it is neither described in previous articles nor in the patents that could be found on this topic [M. Joullié, T. R. Thompson and N. H. Nemeroff. Tetrahedron, 1991, **47**, 8791]. We have observed that aminooxy group of **5** reacting with a nynhidrin solution results in a white to pale yellow colouring that we attribute to the nynhidrin oxime formation. Herein, a convenient procedure to observe **5** is proposed: after eluting in a chamber dip the TLC plate into aq. ammonia solution (25 %), allow it to nearly evaporate and then, after spraying ninhydrin solution over the plate while heating, the white spot of aminooxy product will develop on the pink background.

In addition, we also tried the Dragendorff reagent, which forms $RONH_3^+[BiI_4]^-$ complex salt, developing red-brown spots on the orange background on a TLC plate [Z. Jia and C. Tian. *Desalination*, 2009, **247**, 423]. It can also develop the final product of this synthesis – oximes of aminooxymethylphosphonate – but the layout of red-brown spots depends on heating and may not be that bright on the orange background.