Supporting Information

Synthesis of Ring-Fused, *N*-Substituted 4-Quinolinones Using pK_a-Guided, Base-Promoted Annulations with Isatoic Anhydrides: Total Synthesis of Penicinotam

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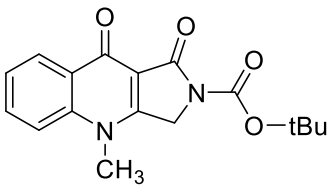
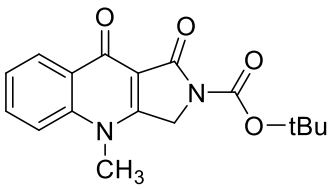
1H NMR (DMSO-d6, 400 MHz)



27a

13C NMR (DMSO-d6, 101 MHz)



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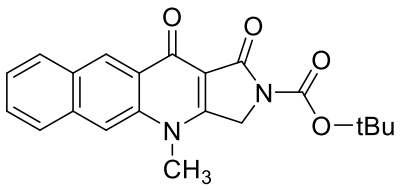

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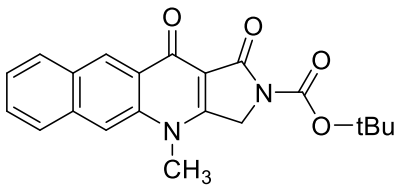

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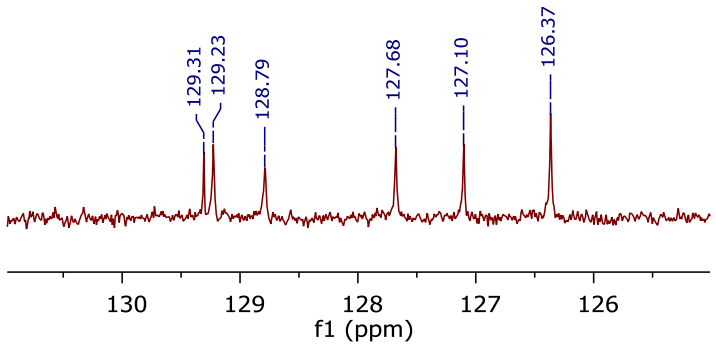

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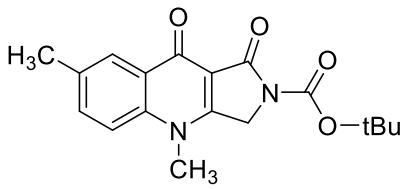

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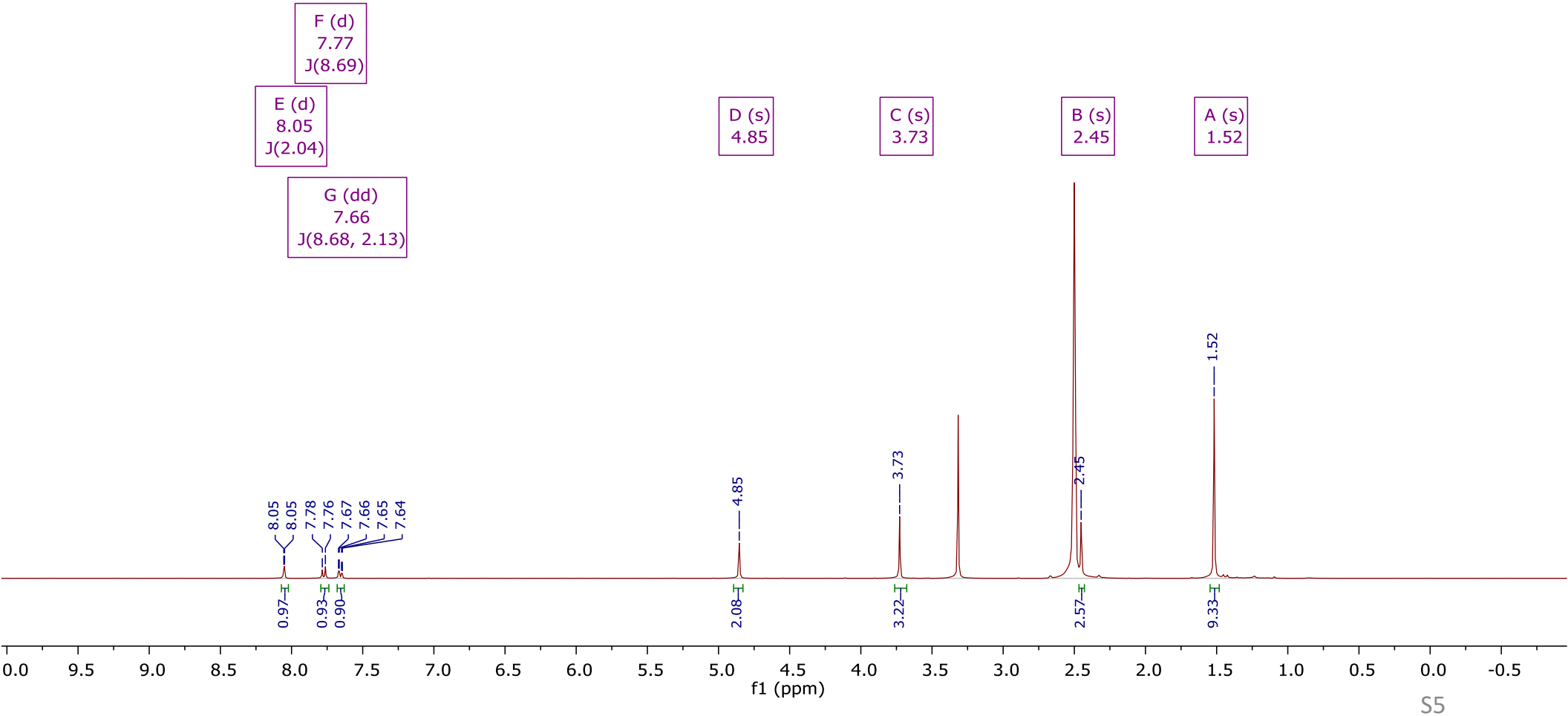
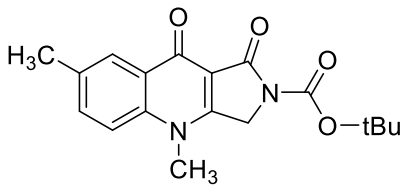


13C NMR (DMSO-d6, 101 MHz)



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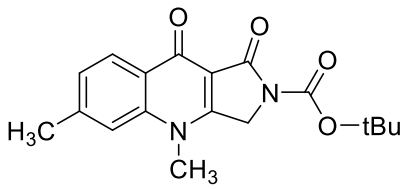

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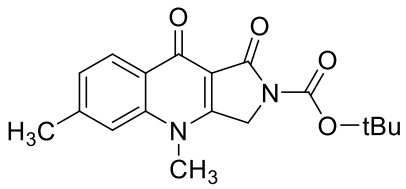

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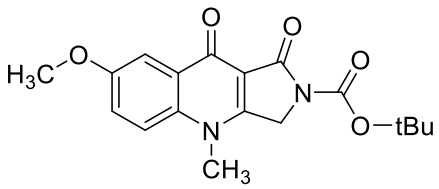

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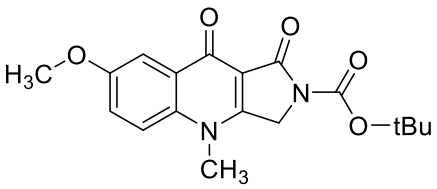

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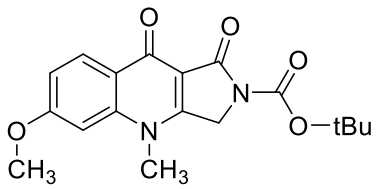

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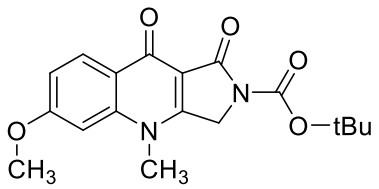

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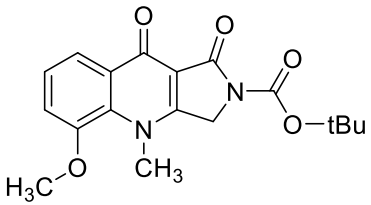

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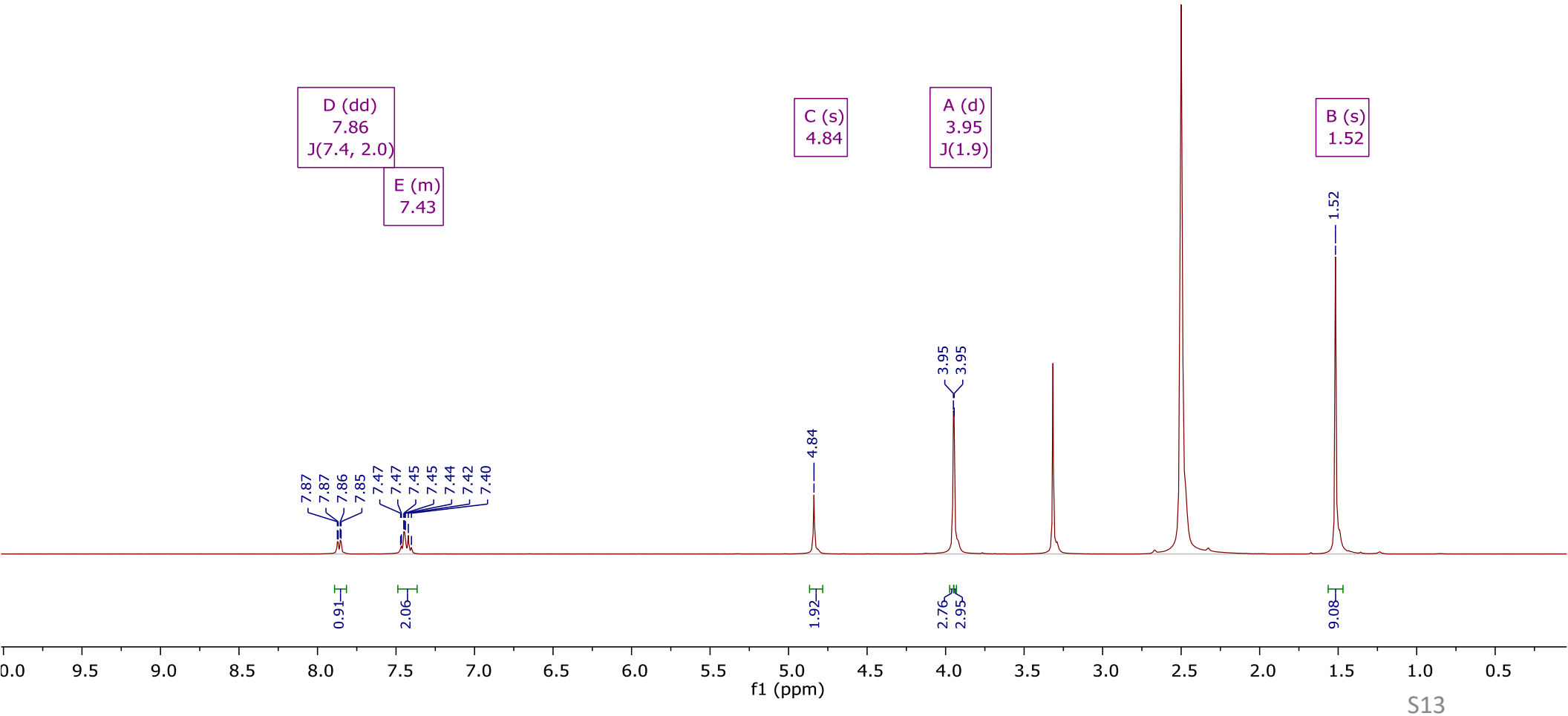

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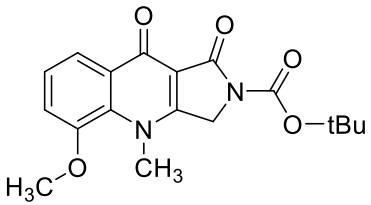

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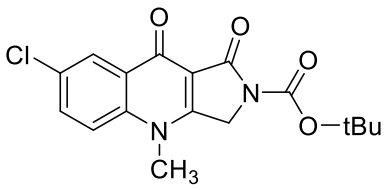

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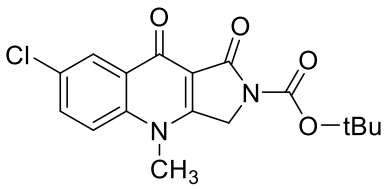

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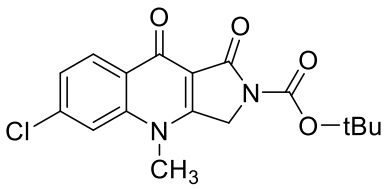

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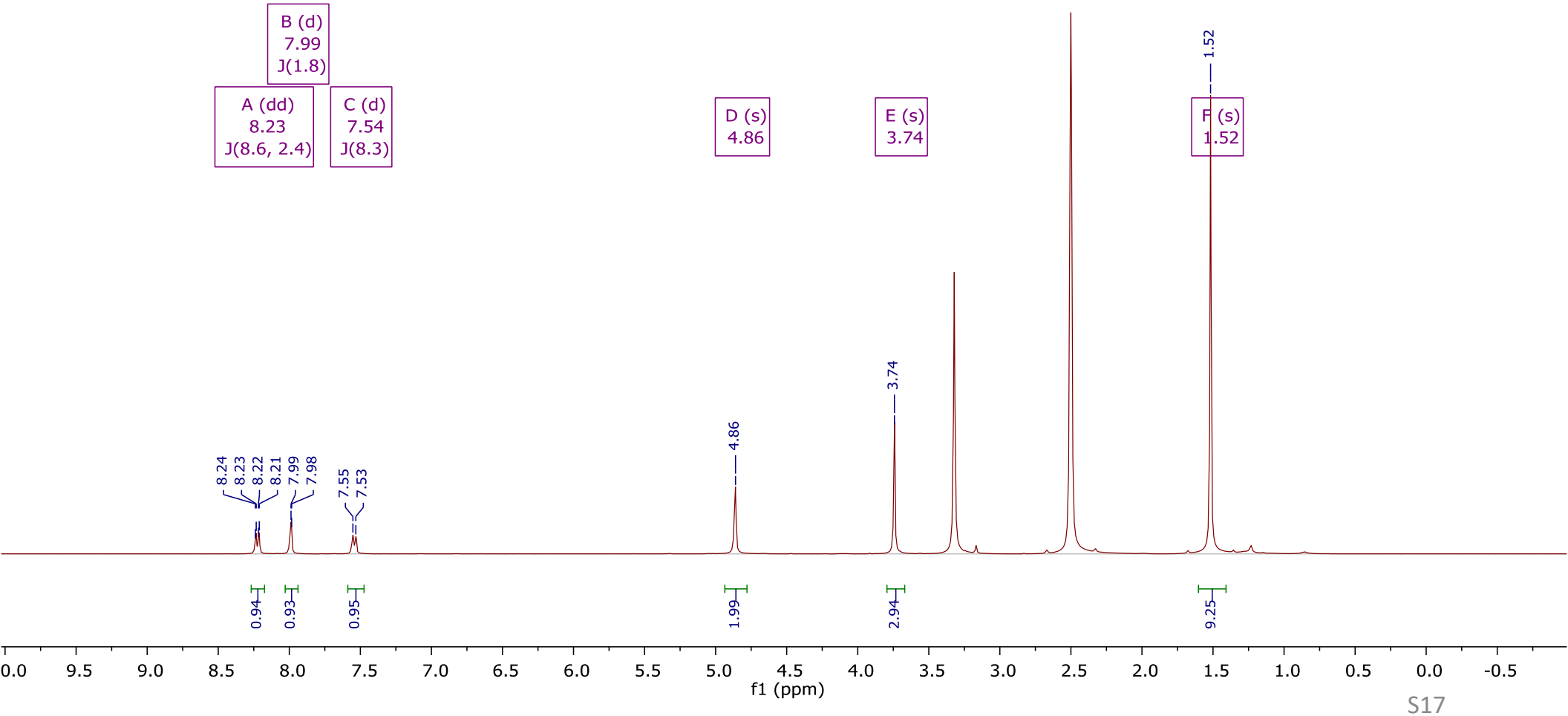

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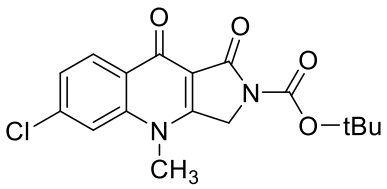

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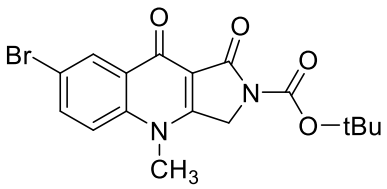

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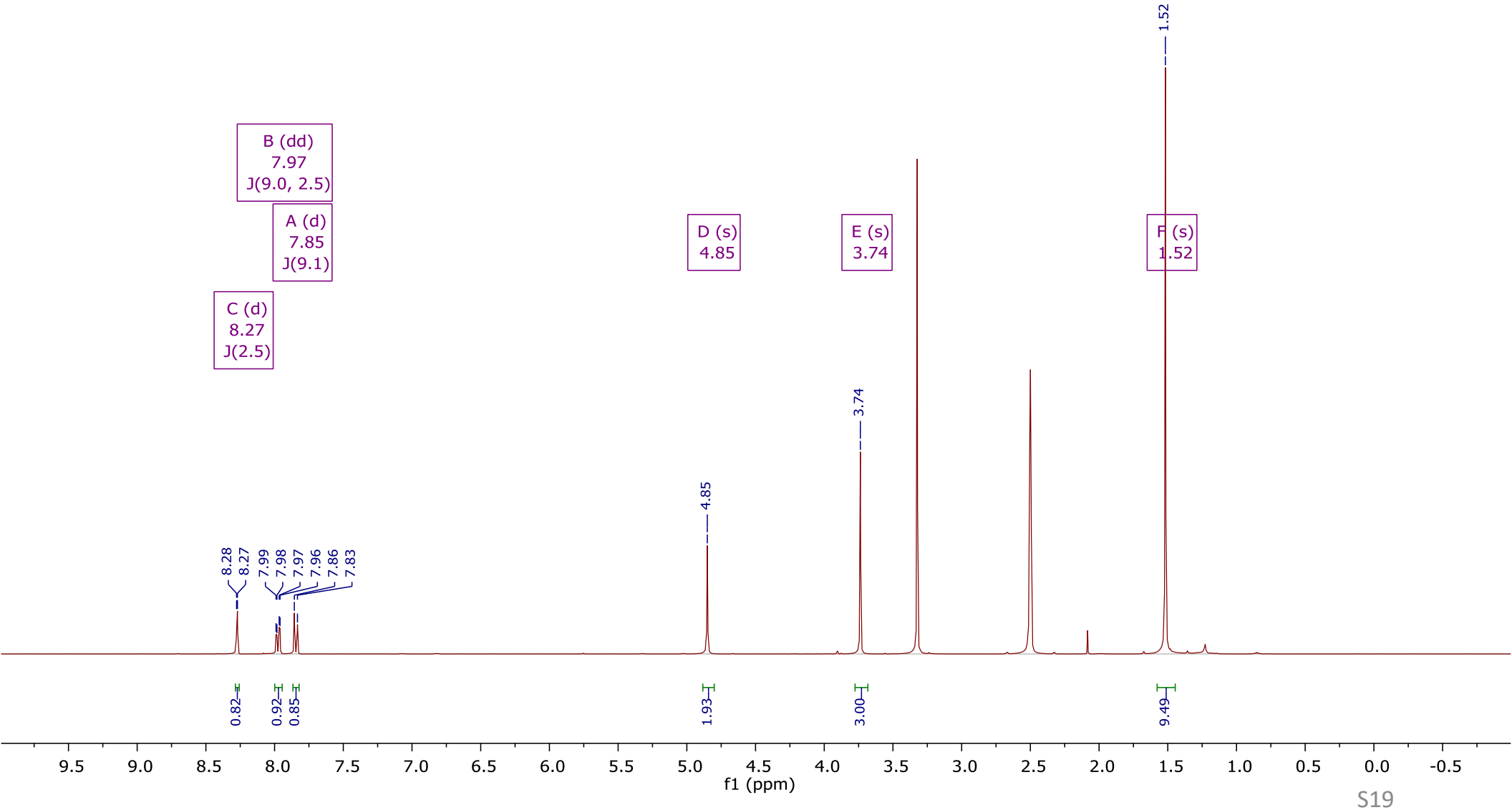

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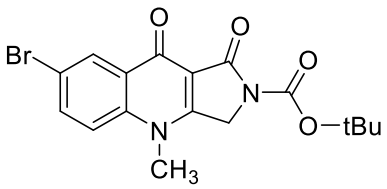

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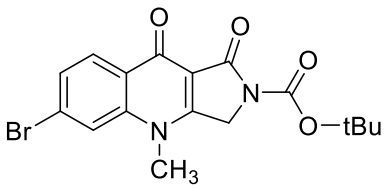

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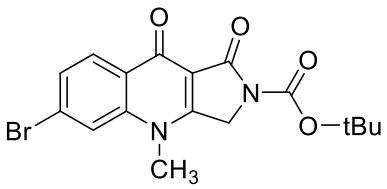

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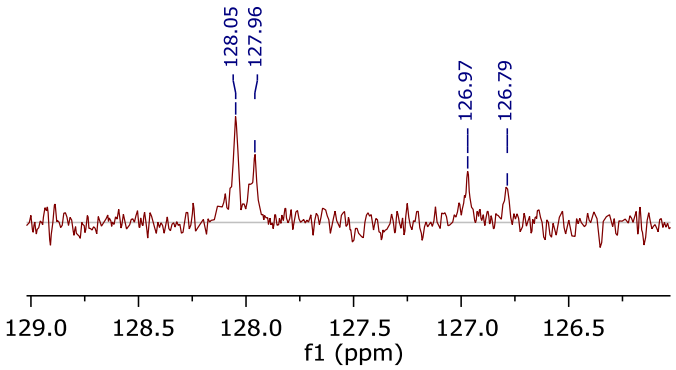

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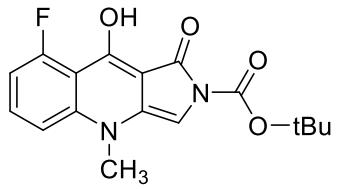
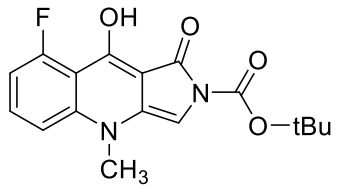


27m

19F NMR (DMSO-d6, 376 MHz)



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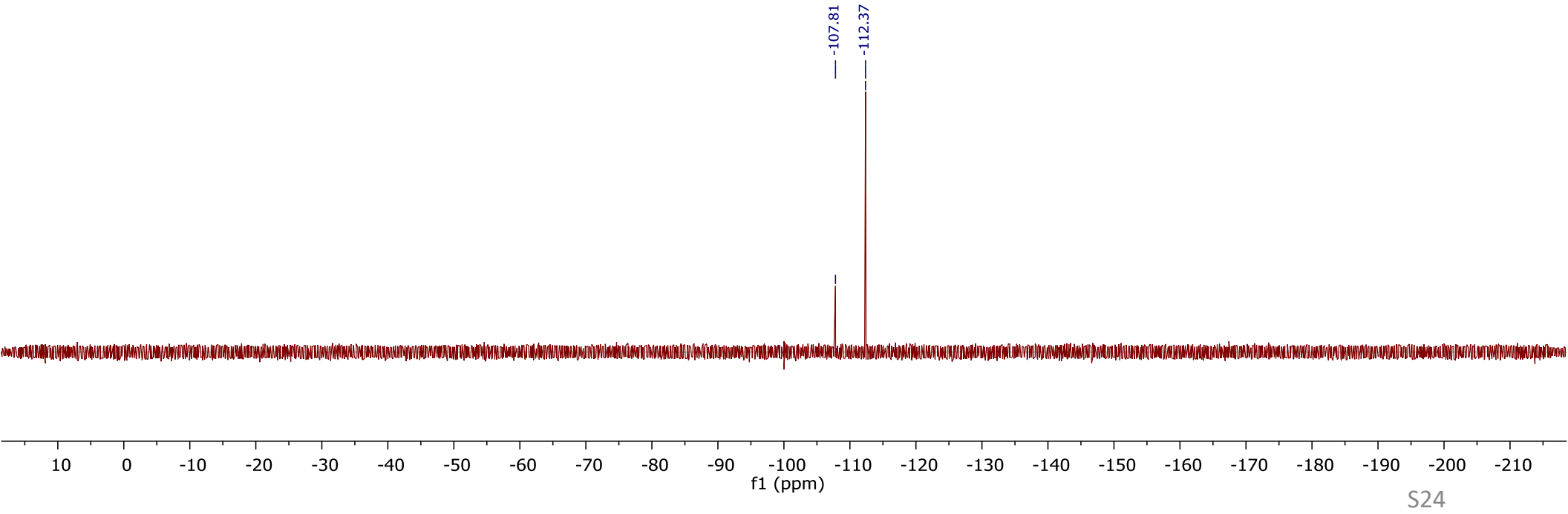
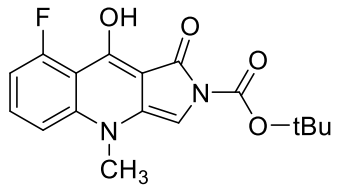
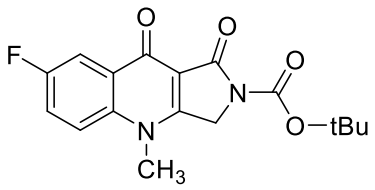


13C NMR (DMSO-d6, 101 MHz)



27m

1H NMR (DMSO-d6, 400 MHz)



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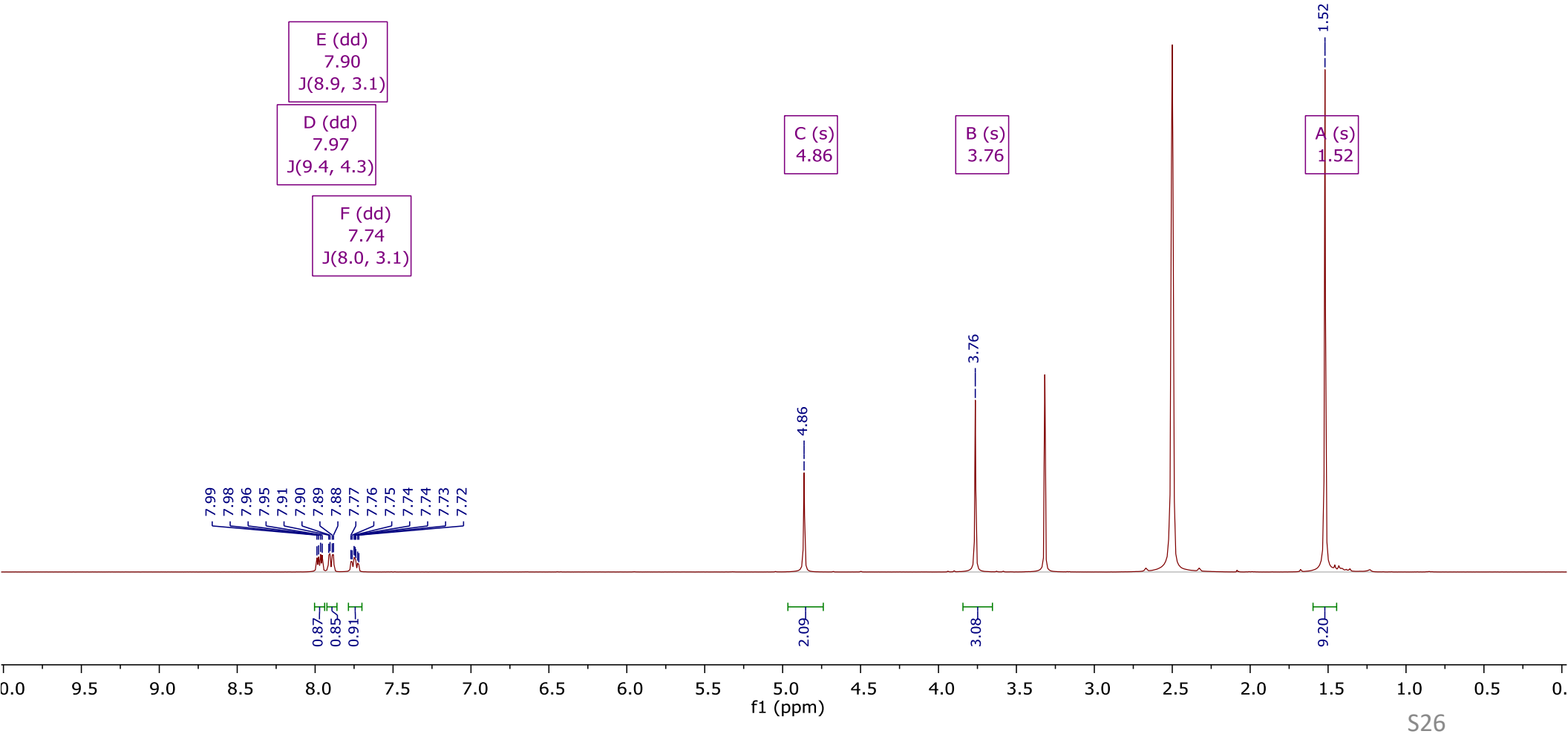
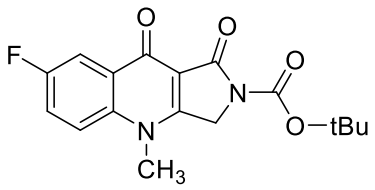


19F NMR (DMSO-d6, 376 MHz)



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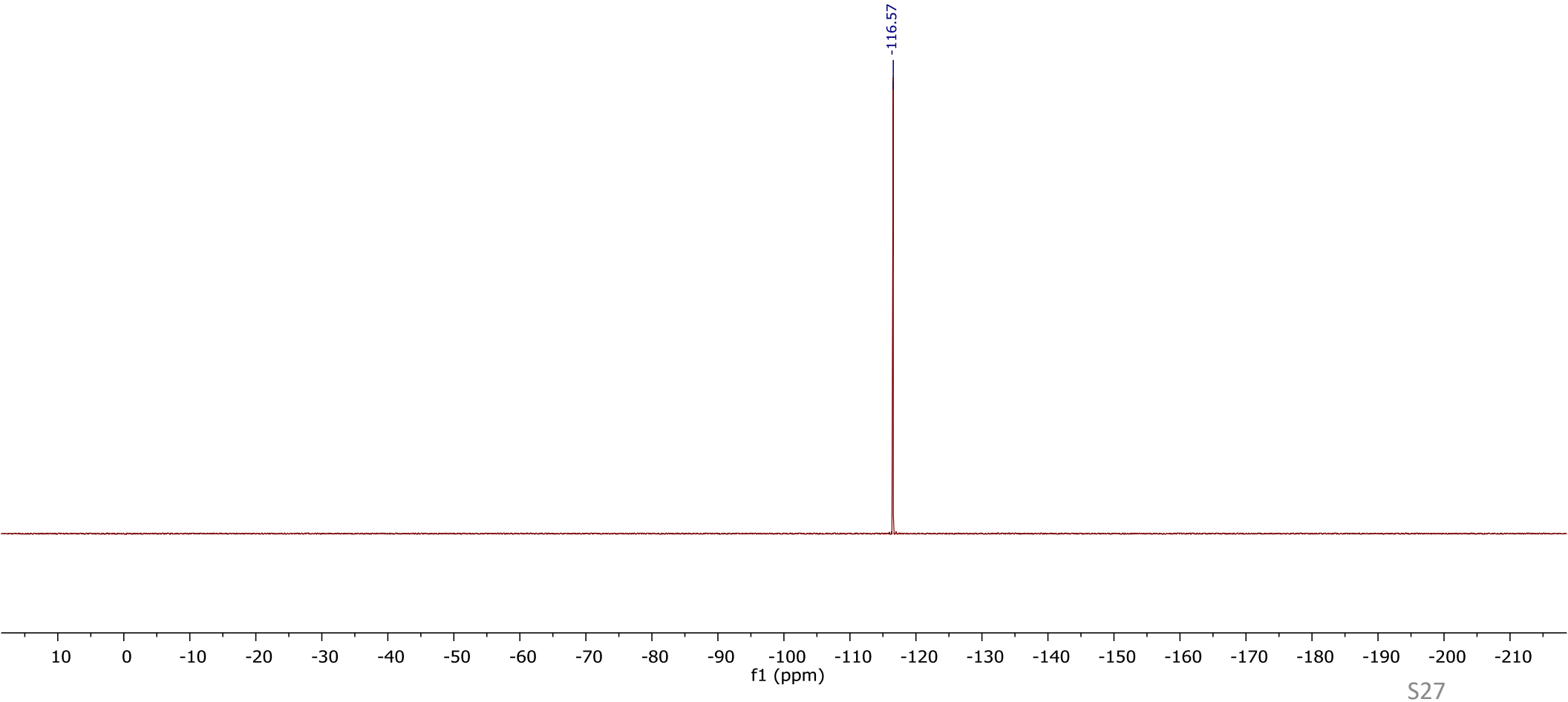

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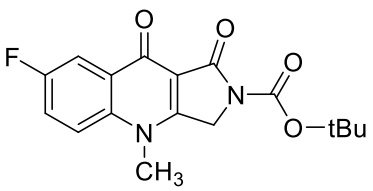

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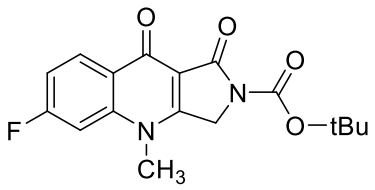

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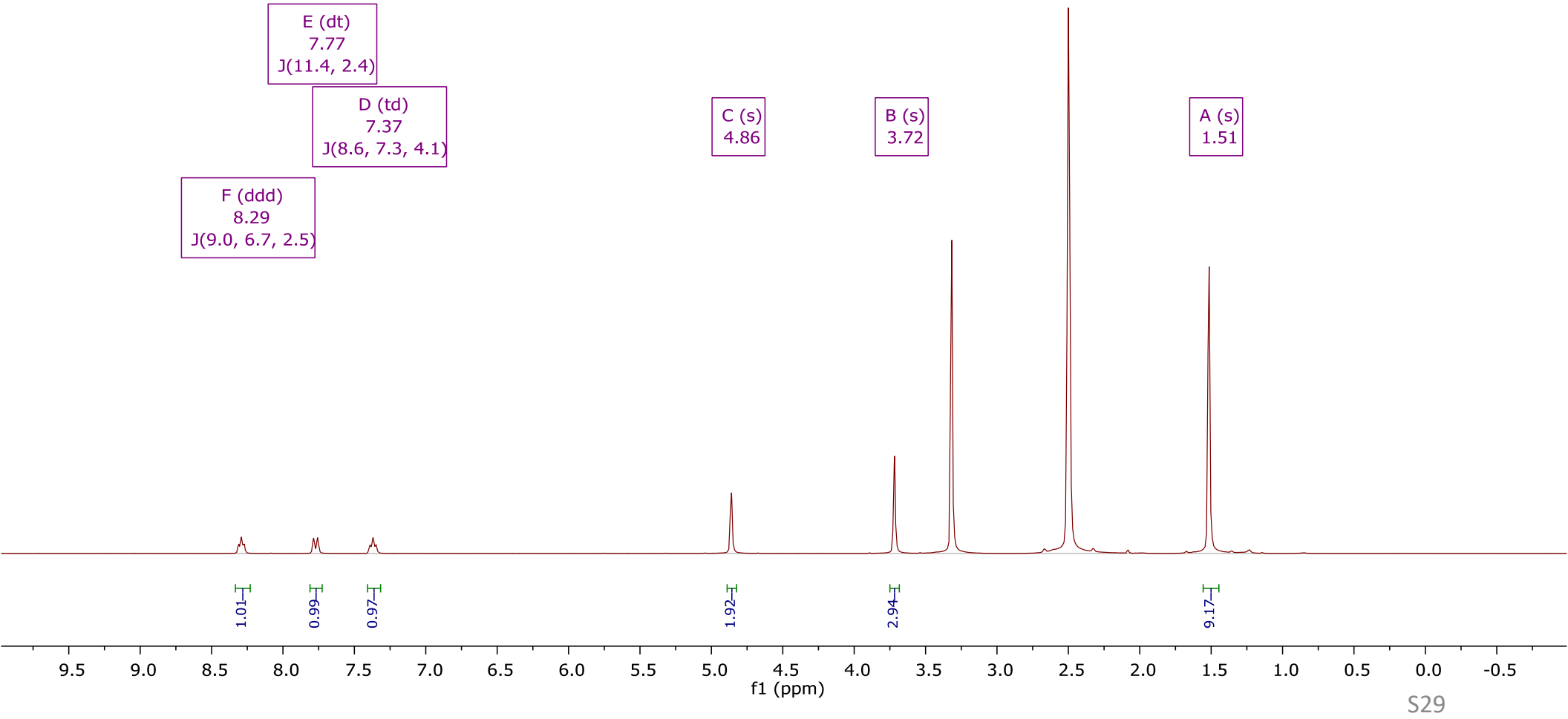

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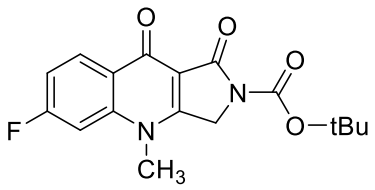

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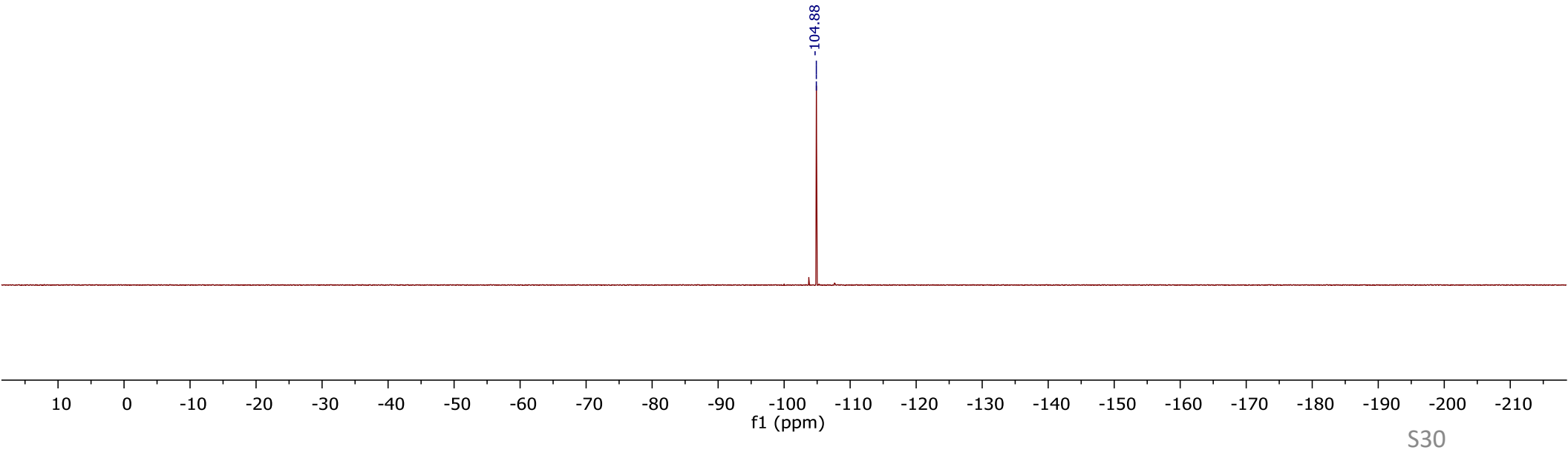

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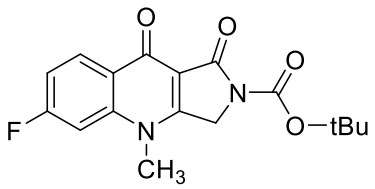


27o

F (d)
164.70
J(249.28)

D (d)
142.48
J(11.94)

C (d)
129.15
J(11.00)

B (d)
113.02
J(23.06)

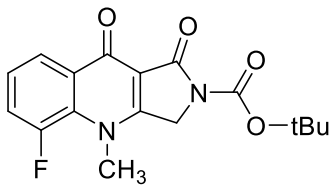
A (d)
103.83
J(27.23)

170.71
165.94
163.46
162.76
161.44
149.34
142.54
142.42
129.20
129.09
124.73
113.14
112.91
108.44
103.96
103.69
81.79
46.63
35.22
27.80

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

1H NMR (DMSO-d6, 400 MHz)



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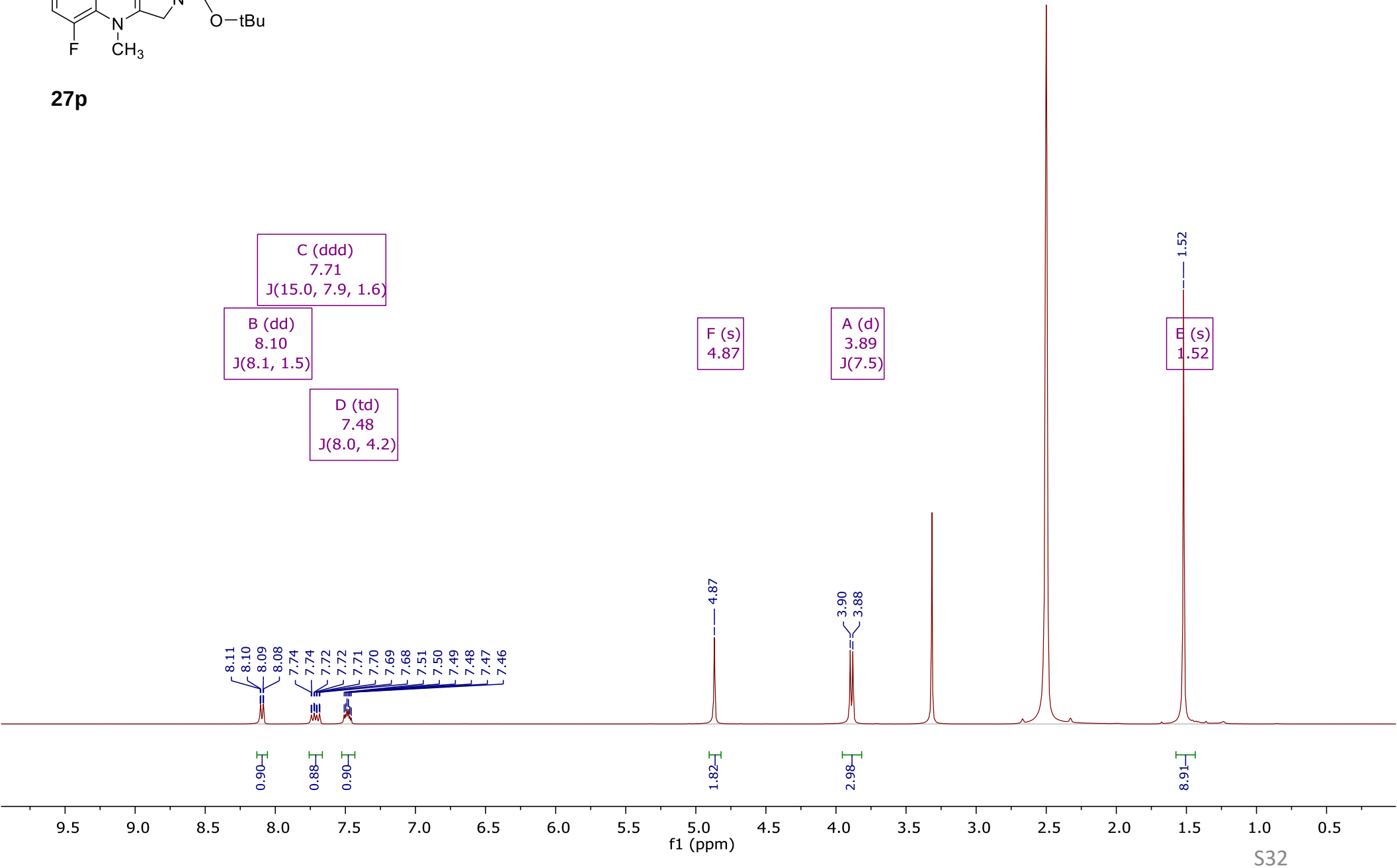

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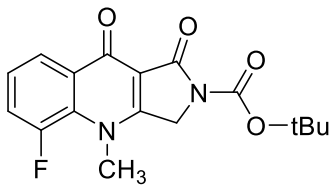

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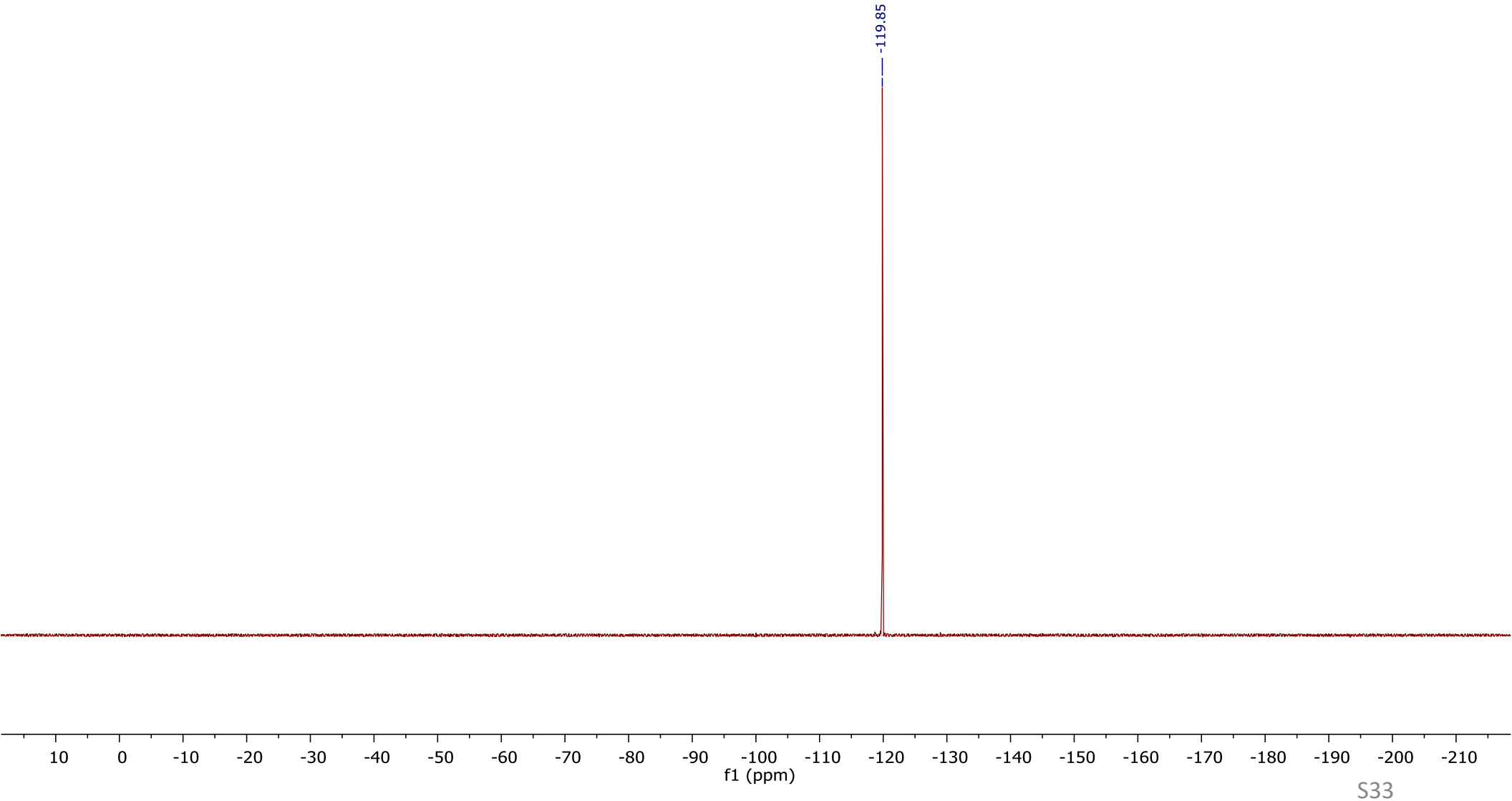

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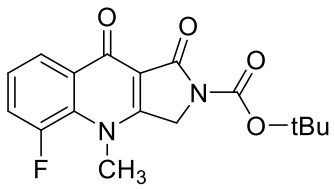

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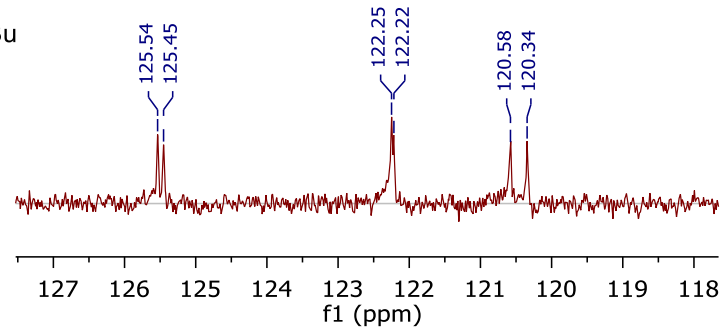


A (d)
170.19
J(2.46)

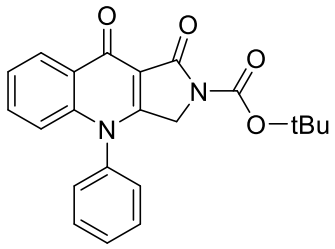
E (d)
152.29
J(248.84)

C (d)
120.46
J(23.53)

B (d)
122.23
J(3.32)

D (d)
125.49
J(8.44)

1H NMR (DMSO-d6, 400 MHz)



27q

A (d)
8.31
J(7.15)

C (d)
7.52
J(8.90)

B (m)
7.68

D (d)
6.85
J(7.24)

F (s)
4.28

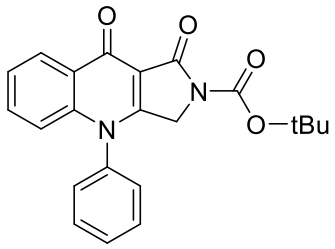
E (s)
1.43

8.32
8.30
8.29
7.76
7.74
7.74
7.68
7.65
7.64
6.87
6.86
6.84
6.84
4.28
1.43

0.96
6.23
0.99
0.98
1.91
8.94

0.0 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 -0.5
f1 (ppm)

13C NMR (DMSO-d6, 101 MHz)



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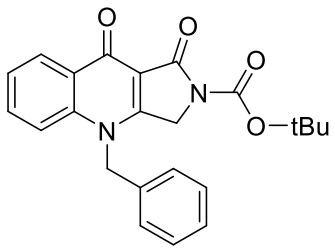

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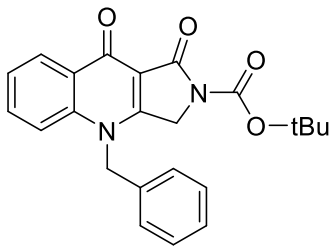
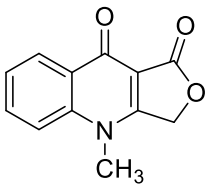
13C NMR (DMSO-d6, 101 MHz)

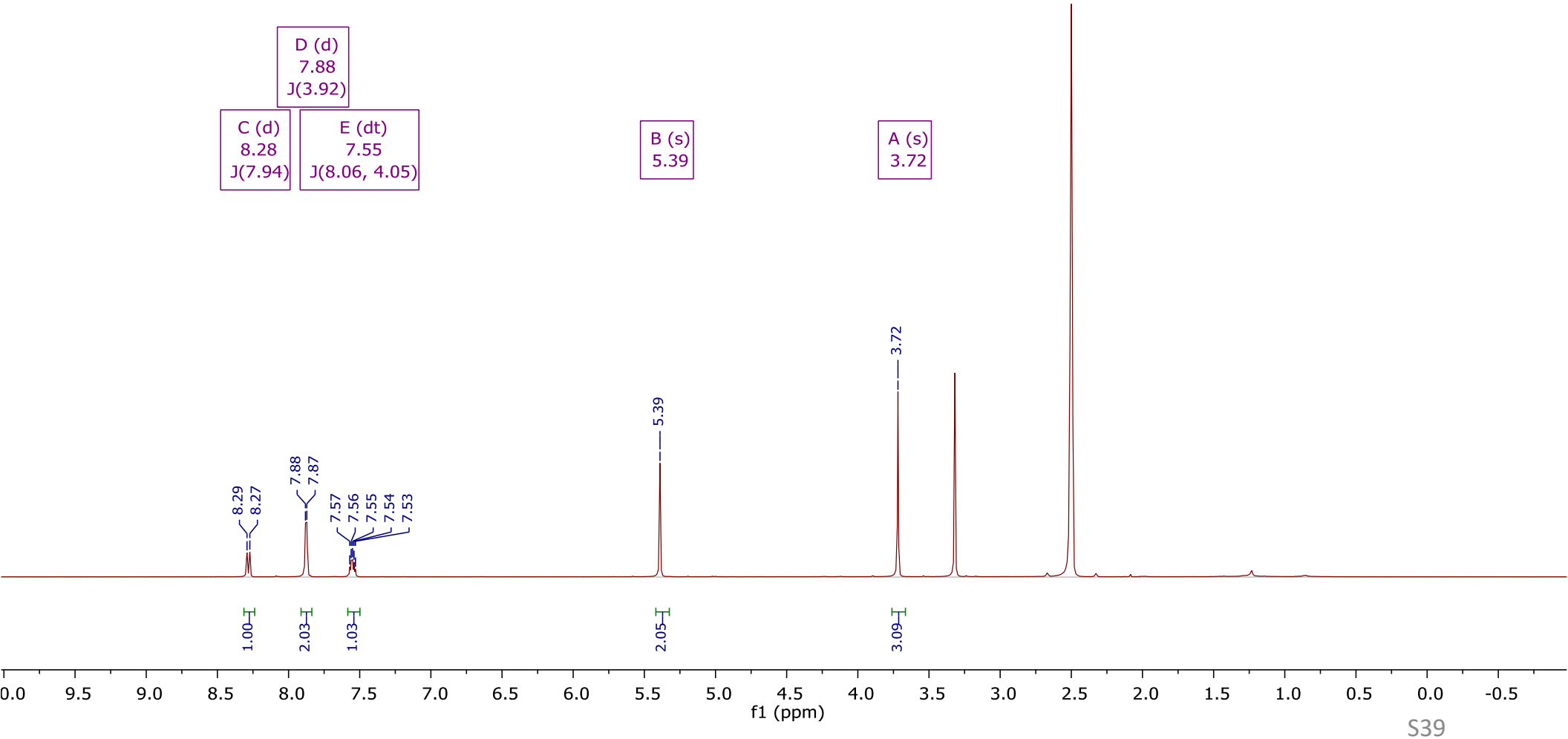


27r

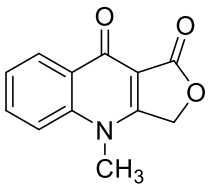
1H NMR (DMSO-d6, 400 MHz)



33

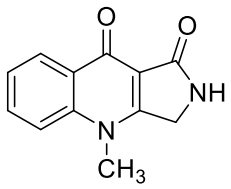


13C NMR (DMSO-d6, 101 MHz)



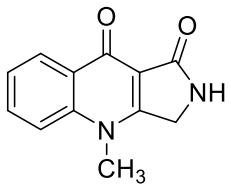
33

1H NMR (DMSO-d6, 400 MHz)



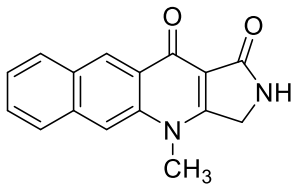
28a

13C NMR (DMSO-d6, 101 MHz)



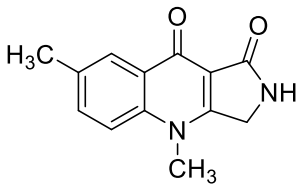
28a

1H NMR (DMSO-d6, 400 MHz)

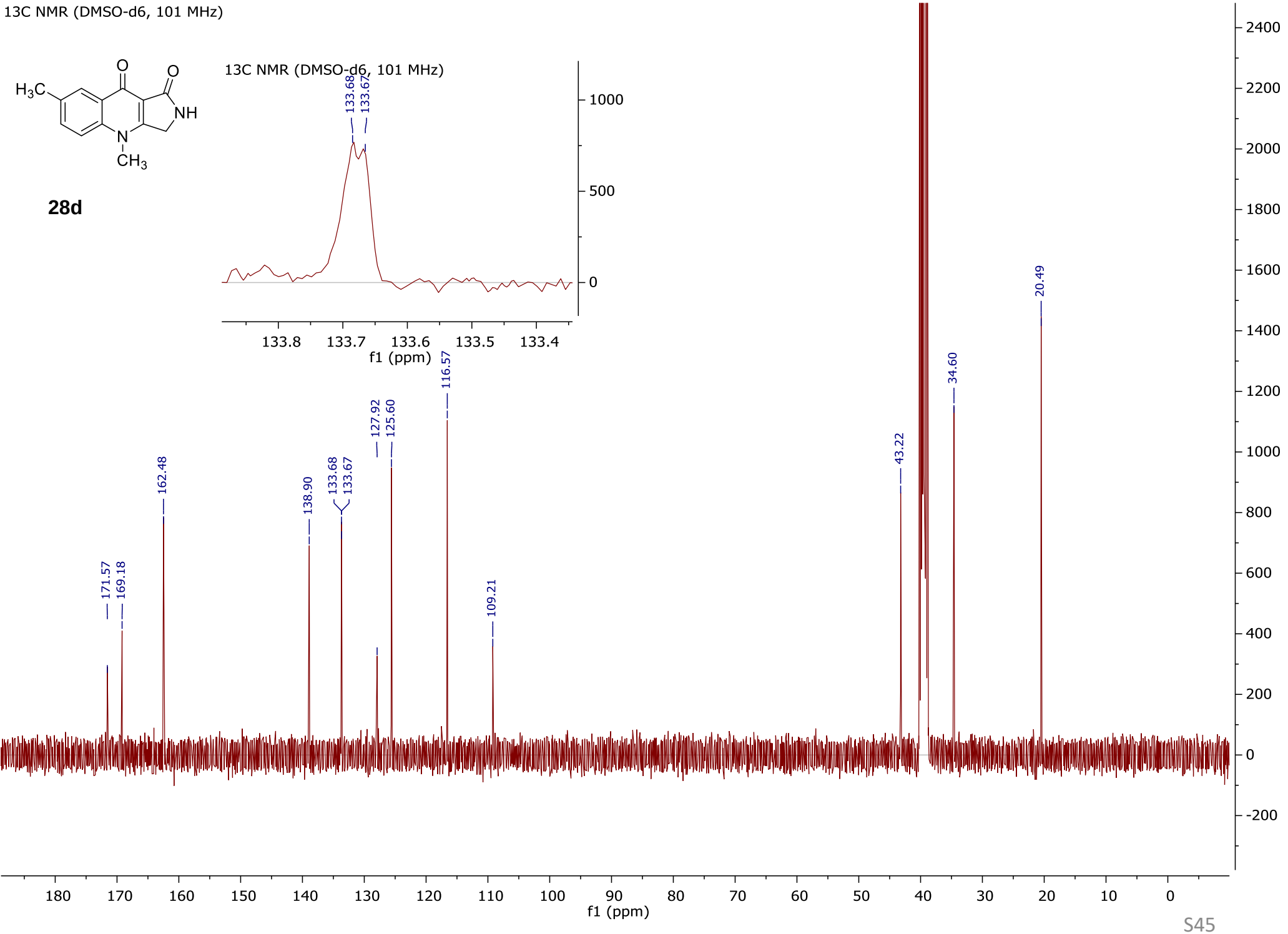


28b

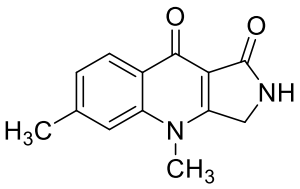
1H NMR (DMSO-d6, 400 MHz)



28d

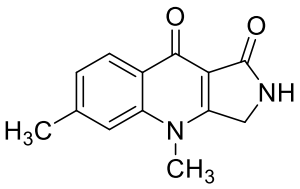

13C NMR (DMSO-d6, 101 MHz)
O
O
H3C
NH
N
CH3
28d
13C NMR (DMSO-d6, 101 MHz)
133.68
133.67
1000
500
0
133.8
133.7
133.6
133.5
133.4
f1 (ppm)
171.57
169.18
162.48
138.90
133.68
133.67
127.92
125.60
116.57
109.21
43.22
34.60
20.49
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

1H NMR (DMSO-d6, 400 MHz)

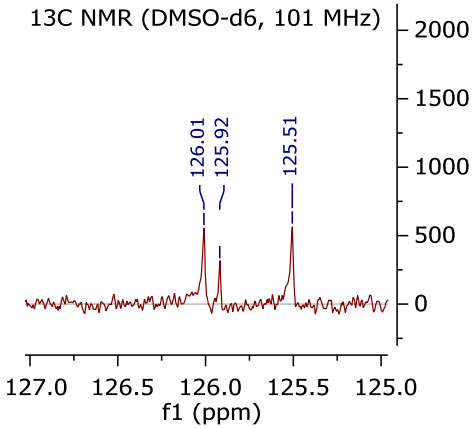


28e

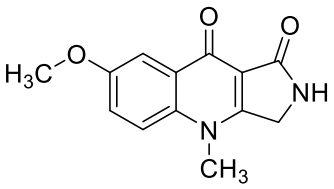
13C NMR (DMSO-d6, 101 MHz)



28e

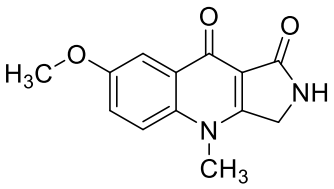


1H NMR (DMSO-d6, 400 MHz)



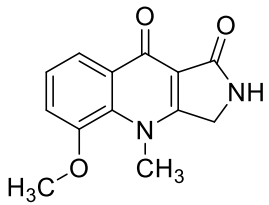
28f

13C NMR (DMSO-d6, 101 MHz)



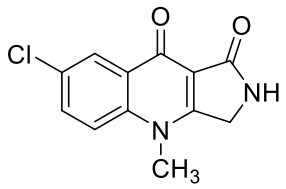
28f

1H NMR (DMSO-d6, 400 MHz)



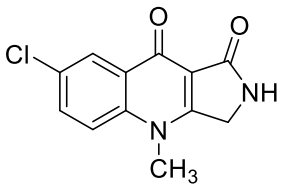
28h

1H NMR (DMSO-d6, 400 MHz)



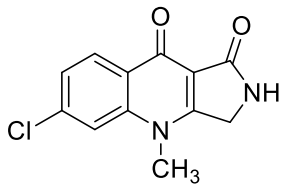
28i

13C NMR (DMSO-d6, 101 MHz)

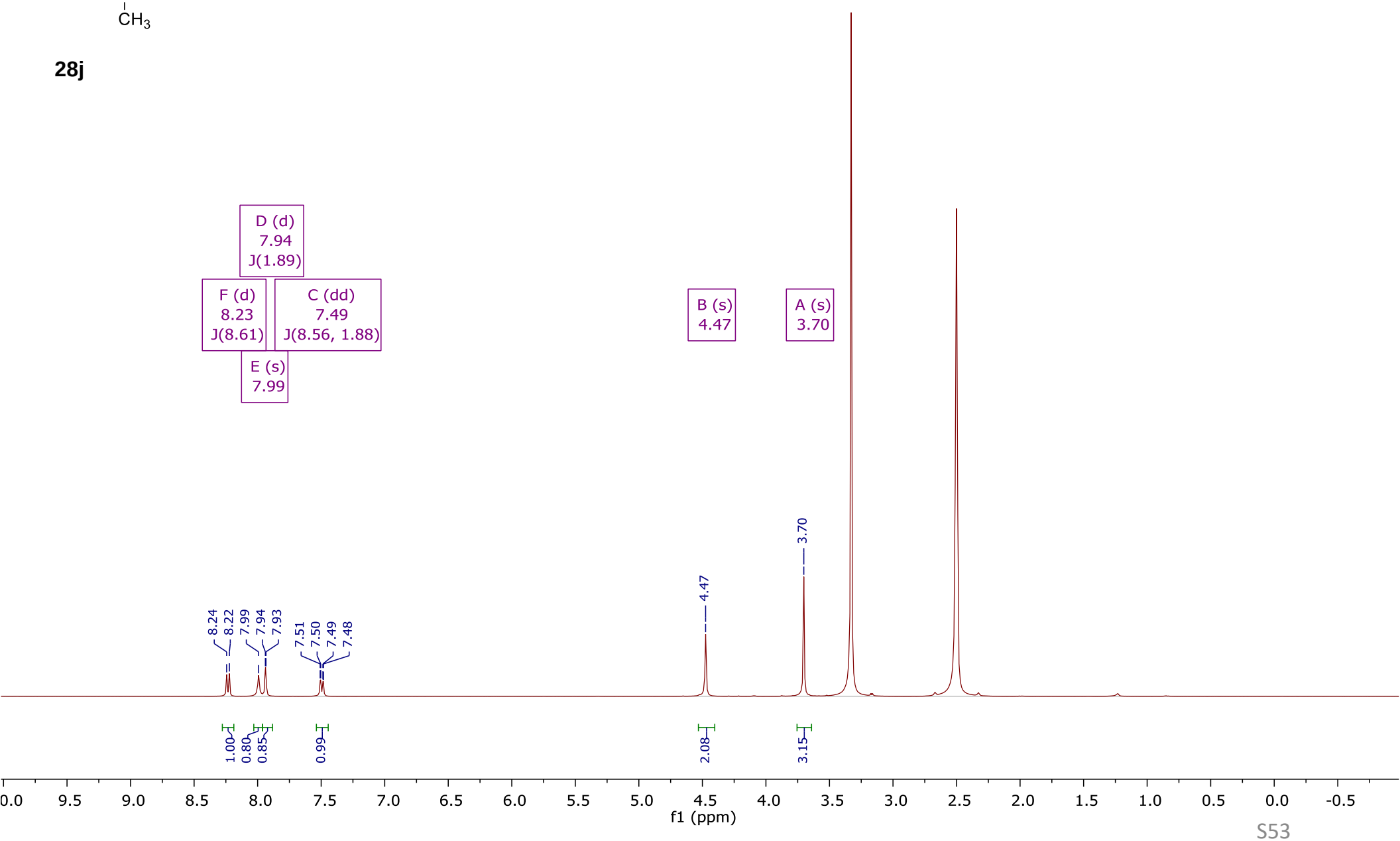


28i

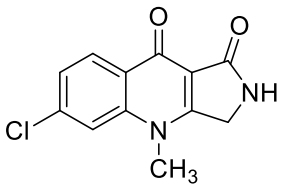
1H NMR (DMSO-d6, 400 MHz)



28j

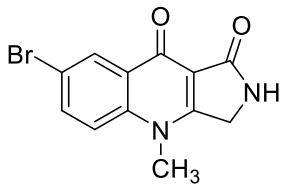


13C NMR (DMSO-d6, 101 MHz)



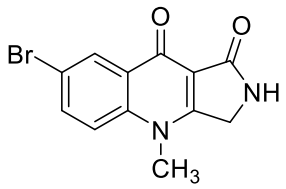
28j

1H NMR (DMSO-d6, 400 MHz)



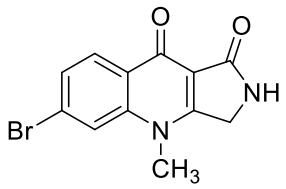
28k

13C NMR (DMSO-d6, 101 MHz)



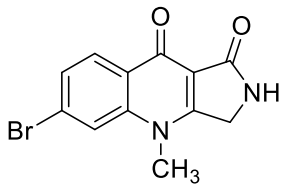
28k

1H NMR (DMSO-d6, 400 MHz)



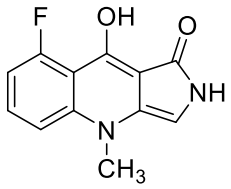
28l

13C NMR (DMSO-d6, 101 MHz)



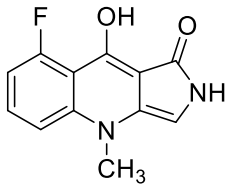
28l

1H NMR (DMSO-d6, 400 MHz)

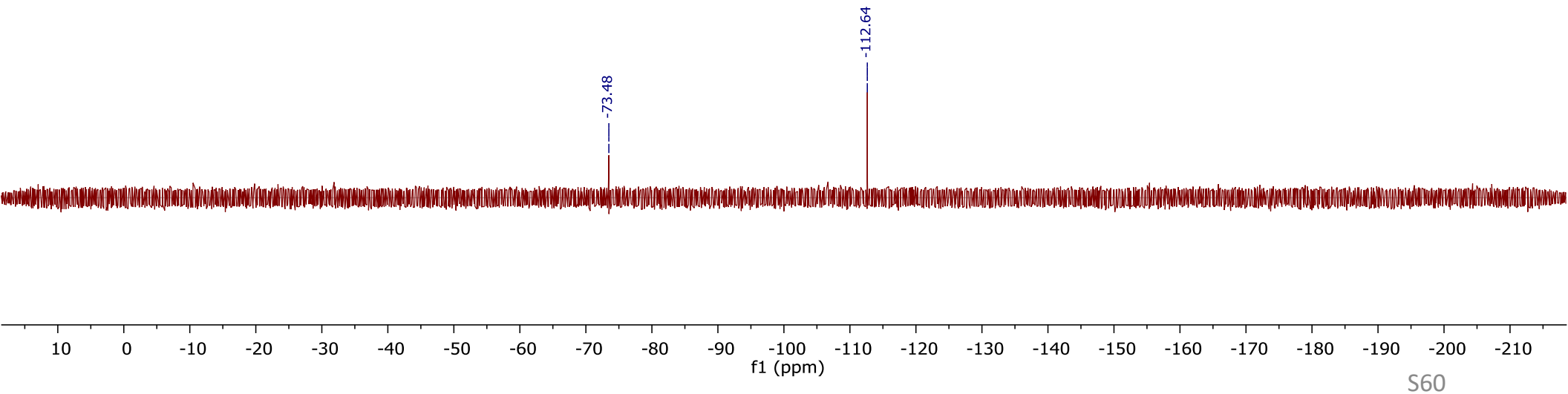


28m

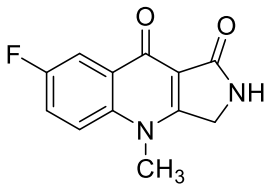
19F NMR (DMSO-d6, 376 MHz)



28m

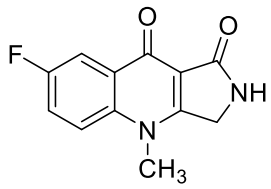


1H NMR (DMSO-d6, 400 MHz)



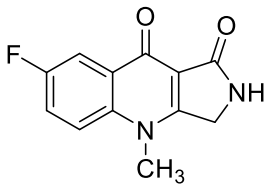
28n

19F NMR (DMSO-d6, 376 MHz)



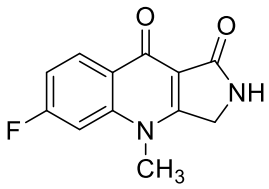
28n

13C NMR (DMSO-d6, 101 MHz)



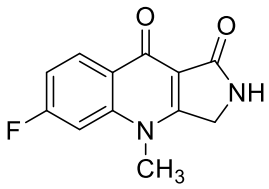
28n

1H NMR (DMSO-d6, 400 MHz)

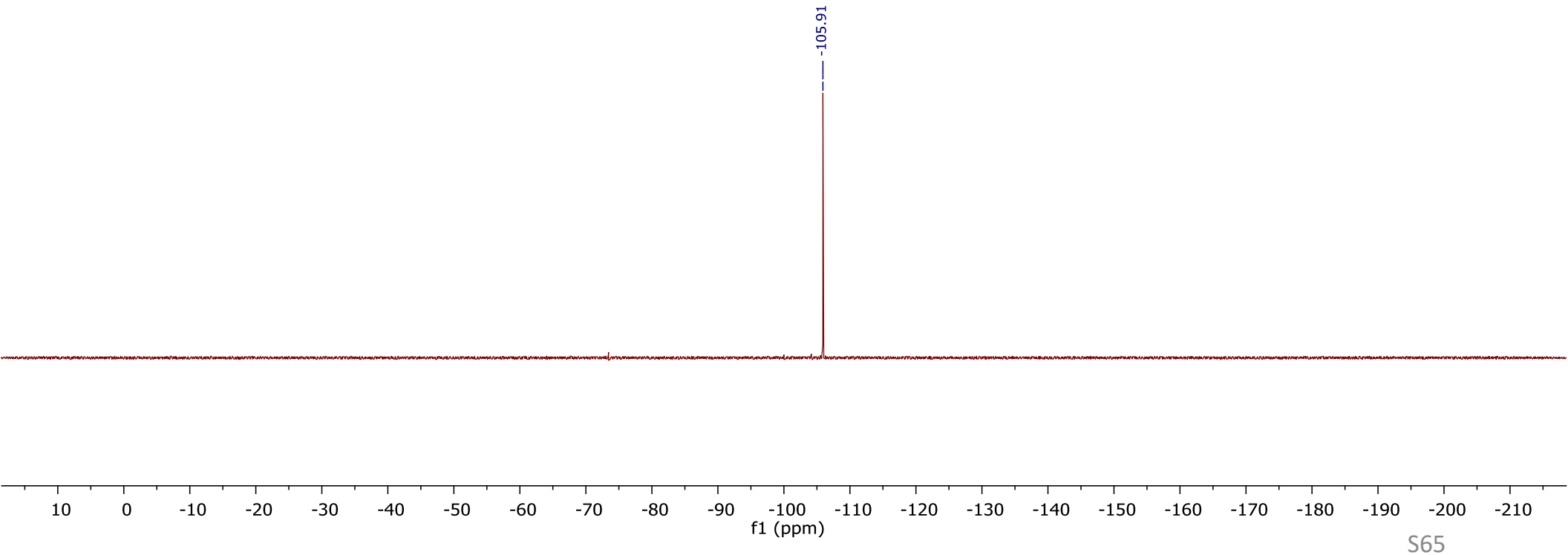


28o

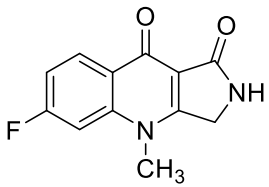
19F NMR (DMSO-d6, 376 MHz)



28o



13C NMR (DMSO-d6, 101 MHz)



28o

D (d)
164.51
J(248.32)

C (d)
129.18
J(10.64)

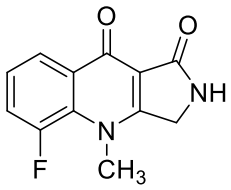
B (d)
112.41
J(23.16)

A (d)
103.35
J(26.89)

170.96
168.79
165.74
163.75
163.27
142.65
129.24
129.13
124.94
112.53
112.30
109.85
103.48
103.21
43.34
34.95

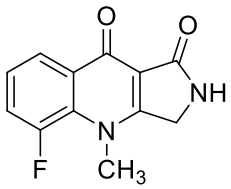
f1 (ppm)

1H NMR (DMSO-d6, 400 MHz)

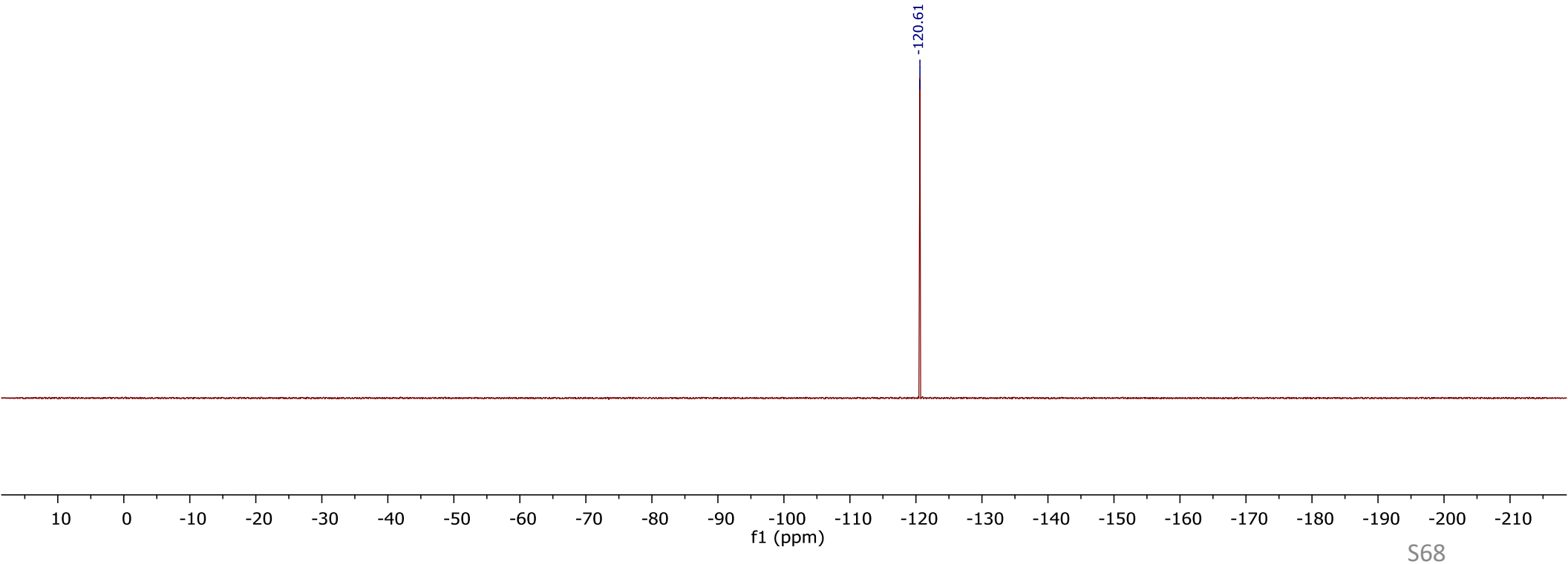


28p

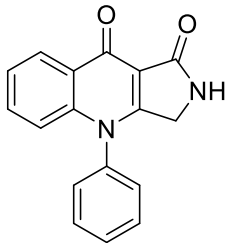
19F NMR (DMSO-d6, 376 MHz)



28p

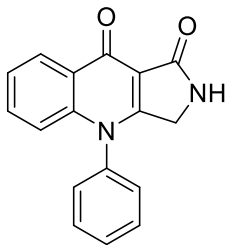


1H NMR (DMSO-d6, 400 MHz)



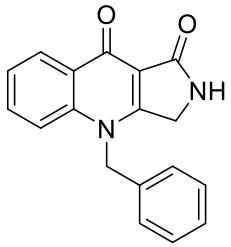
28q

13C NMR (DMSO-d6, 101 MHz)



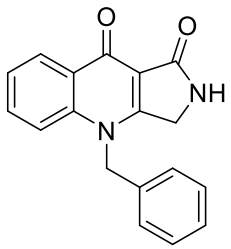
28q

1H NMR (DMSO-d6, 400 MHz)



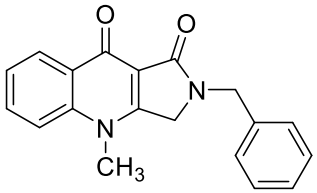
28r

13C NMR (DMSO-d6, 101 MHz)



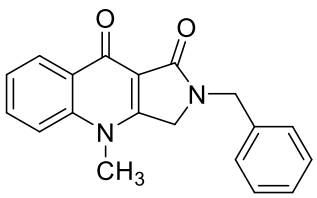
28r

1H NMR (DMSO-d6, 400 MHz)



29a

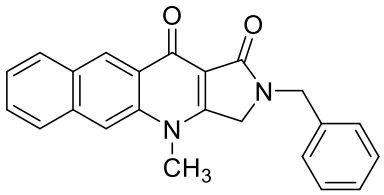
13C NMR (DMSO-d6, 101 MHz)



29a

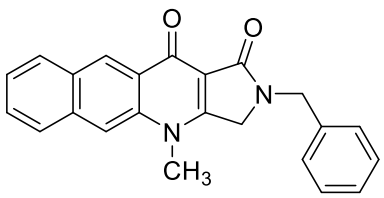
171.66
166.70
161.38
141.07
138.18
133.00
129.10
128.52
128.07
127.71
126.50
124.72
117.14
109.48
47.99
44.90
40.68 DMSO
40.63 DMSO
40.47 DMSO
40.42 DMSO
40.26 DMSO
40.21 DMSO
40.00 DMSO
39.79 DMSO
39.59 DMSO
39.38 DMSO
35.34

1H NMR (DMSO-d6, 400 MHz)



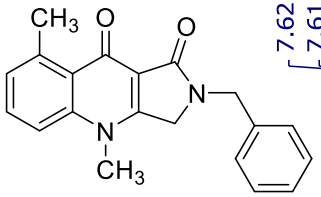
29b

13C NMR (DMSO-d6, 101 MHz)

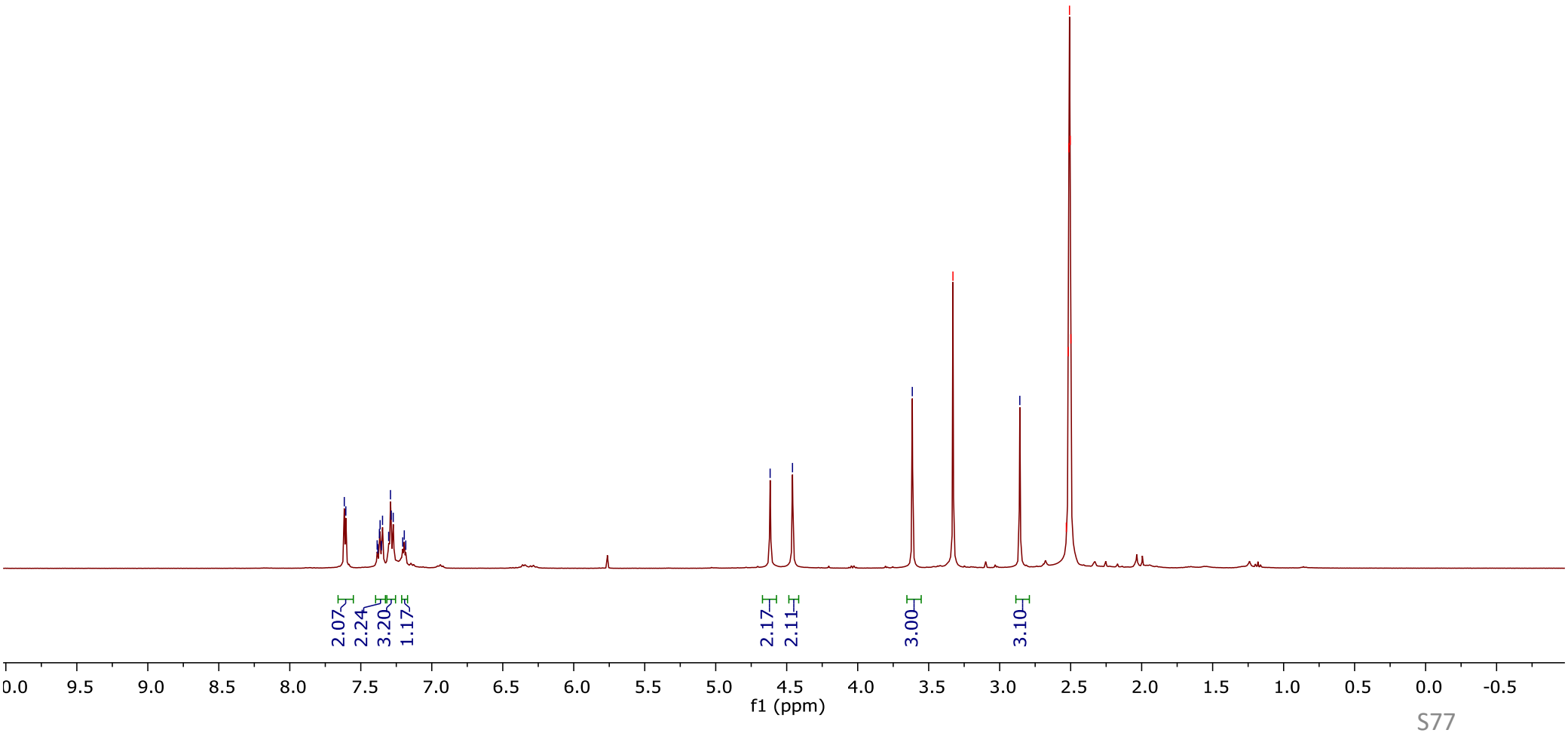


29b

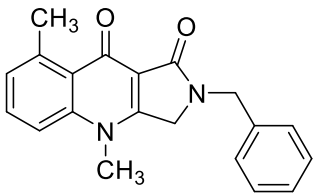
1H NMR (DMSO-d6, 400 MHz)



29c

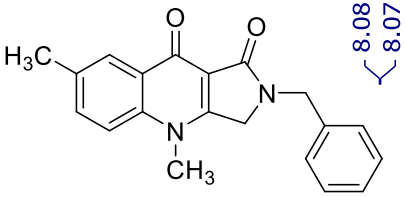


13C NMR (DMSO-d6, 101 MHz)



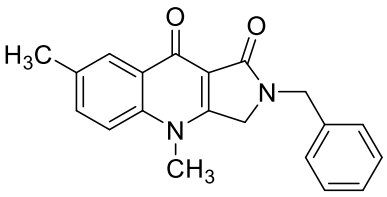
29c

1H NMR (DMSO-d6, 400 MHz)



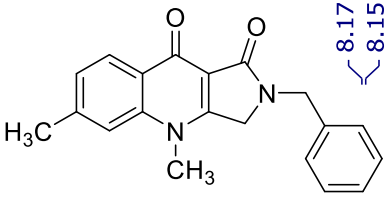
29d

13C NMR (DMSO-d6, 101 MHz)



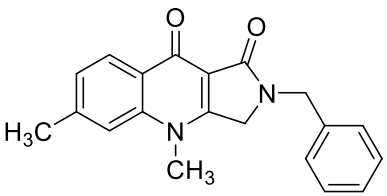
29d

1H NMR (DMSO-d6, 400 MHz)



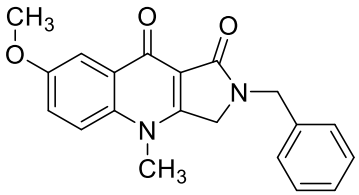
29e

13C NMR (DMSO-d6, 101 MHz)



29e

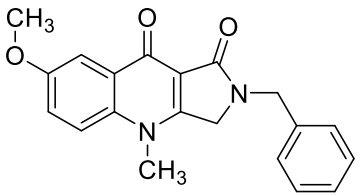
1H NMR (DMSO-d6, 400 MHz)



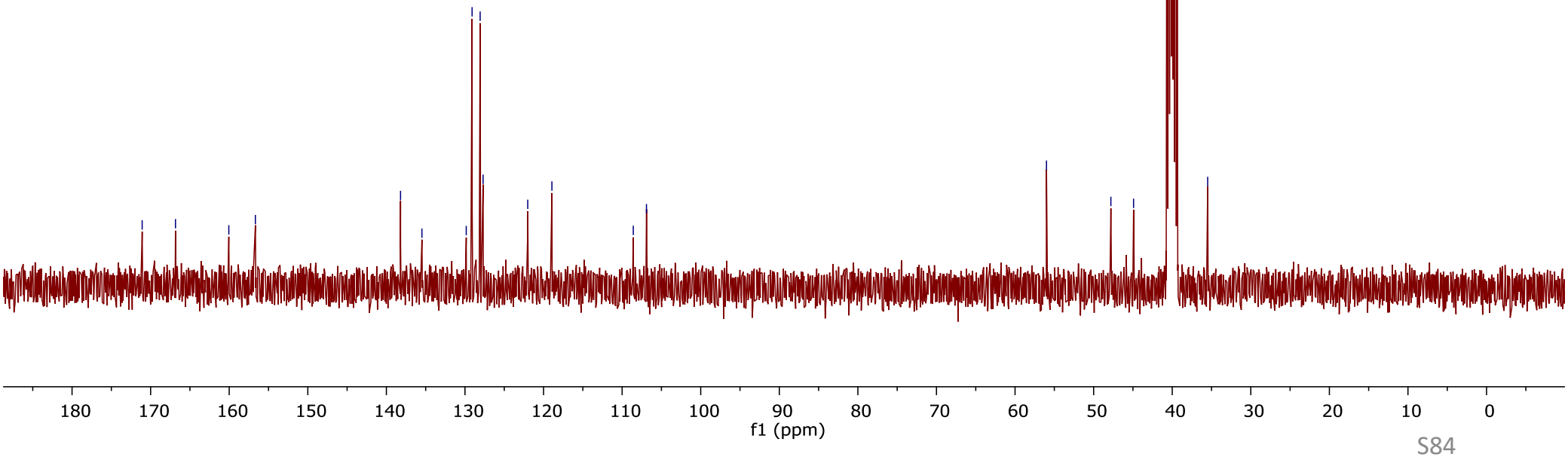
29f

13C NMR (DMSO-d6, 101 MHz)

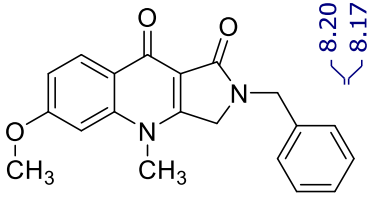
171.08
166.84
160.05
156.67
138.20
135.48
129.84
129.09
128.07
127.70
122.01
118.94
108.58
106.90
56.00
47.80
44.92
40.68 DMSO
40.63 DMSO
40.47 DMSO
40.42 DMSO
40.26 DMSO
40.21 DMSO
40.00 DMSO
39.79 DMSO
39.58 DMSO
39.37 DMSO
35.49



29f



1H NMR (DMSO-d6, 400 MHz)



29g

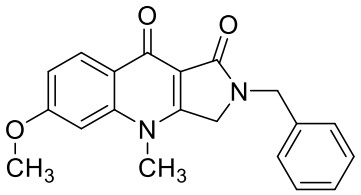
8.20 8.17 7.39 7.39 7.38 7.37 7.37 7.37 7.36 7.36 7.35 7.31 7.30 7.30 7.29 7.28 7.28 7.27 7.13 7.13 7.09 7.08 7.07 7.06 4.62 4.48 3.94 3.65 3.34 HDO 2.53 DMSO 2.53 DMSO 2.52 DMSO 2.51 DMSO 2.51 DMSO 2.50 DMSO 2.50 DMSO

1.02 5.00 2.04 2.16 2.05 3.05 3.00

0.0 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 -0.5

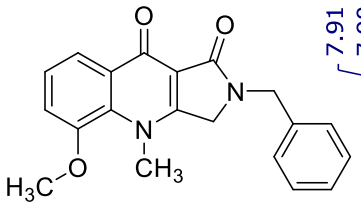
f1 (ppm)

13C NMR (DMSO-d6, 101 MHz)



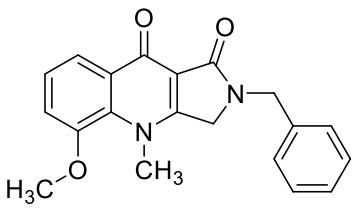
29g

1H NMR (DMSO-d6, 400 MHz)



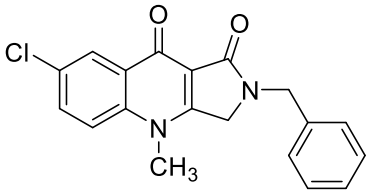
29h

13C NMR (DMSO-d6, 101 MHz)



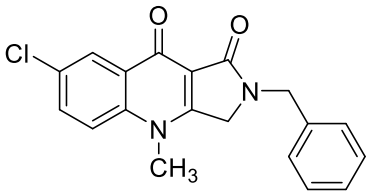
29h

1H NMR (DMSO-d6, 400 MHz)



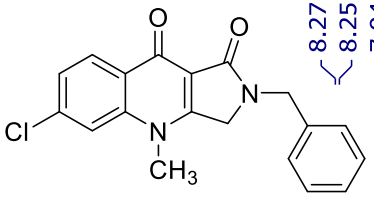
29i

13C NMR (DMSO-d6, 101 MHz)



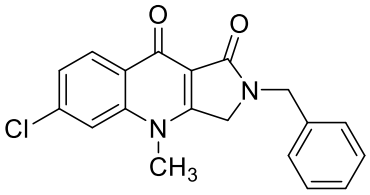
29i

1H NMR (DMSO-d6, 400 MHz)



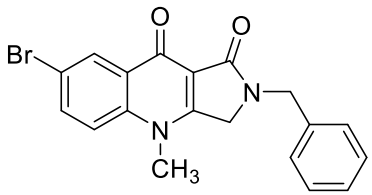
29j

13C NMR (DMSO-d6, 101 MHz)



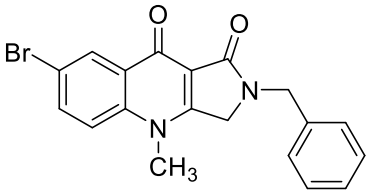
29j

1H NMR (DMSO-d6, 400 MHz)



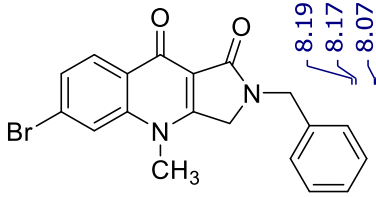
29k

13C NMR (DMSO-d6, 101 MHz)



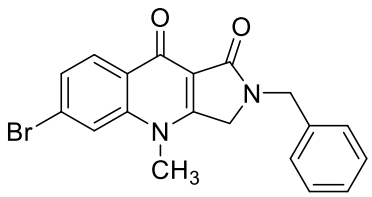
29k

1H NMR (DMSO-d6, 400 MHz)



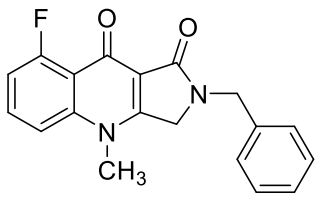
29l

13C NMR (DMSO-d6, 101 MHz)



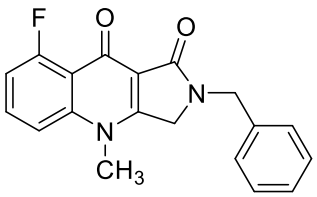
29l

1H NMR (DMSO-d6, 400 MHz)



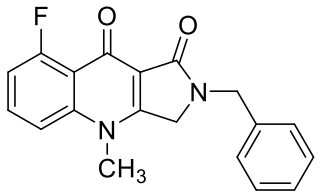
29m

19F NMR (DMSO-d6, 376 MHz)



29m

13C NMR (DMSO-d6, 101 MHz)



29m

170.73
166.39
163.42
161.11
143.34
143.30
138.12
133.60
133.49
129.09
128.07
127.72
118.04
117.97
113.20
113.16
111.76
111.55
110.56
47.81
44.87
40.62 DMSO
40.42 DMSO
40.21 DMSO
40.00 DMSO
39.79 DMSO
39.58 DMSO
39.37 DMSO
36.20

A (d)
162.13
J(260.48)

C (d)
143.32
J(3.68)

B (d)
133.55
J(11.29)

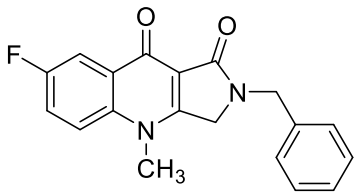
D (d)
118.01
J(7.35)

E (d)
113.18
J(4.03)

F (d)
111.65
J(21.00)

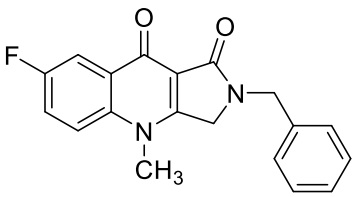
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1H NMR (DMSO-d6, 400 MHz)



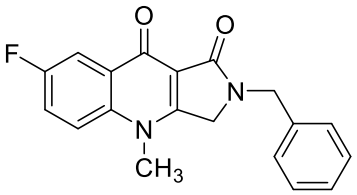
29n

19F NMR (DMSO-d6, 376 MHz)



29n

13C NMR (DMSO-d6, 101 MHz)



29n

170.72 170.69 166.52 161.39 160.67 158.24

138.09 137.81 130.18 130.12 129.10 128.07 127.73 121.21 120.96 120.22 120.14 111.12 110.89 109.02

47.99 44.91 40.68 DMSO 40.63 DMSO 40.47 DMSO 40.42 DMSO 40.26 DMSO 40.21 DMSO 40.00 DMSO 39.79 DMSO 39.58 DMSO 39.37 DMSO 35.75

B (d) 170.71 J(2.36)

A (d) 159.46 J(244.01)

F (d) 130.15 J(6.55)

D (d) 120.18 J(8.14)

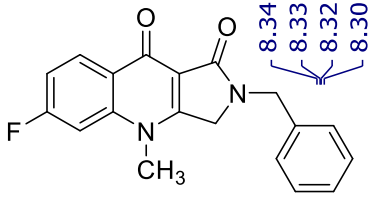
C (d) 111.00 J(22.62)

E (d) 121.09 J(24.33)

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

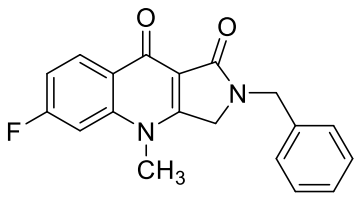
f1 (ppm)

1H NMR (DMSO-d6, 400 MHz)



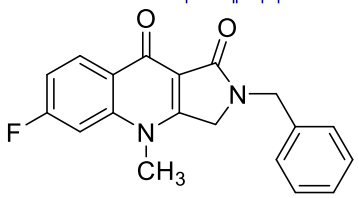
29o

19F NMR (DMSO-d6, 376 MHz)



29o

13C NMR (DMSO-d6, 101 MHz)



29o

170.98 166.48 166.17 163.71 162.16

142.91 142.79 138.11 129.65 129.54 129.10 128.91 128.06 127.72 125.43 125.42 113.07 112.84 109.87 104.01 103.74

48.02 44.90 40.68 DMSO 40.63 DMSO 40.47 DMSO 40.42 DMSO 40.26 DMSO 40.21 DMSO 40.00 DMSO 39.79 DMSO 39.59 DMSO 39.38 DMSO 35.68

A (d) 164.94 J(248.19)

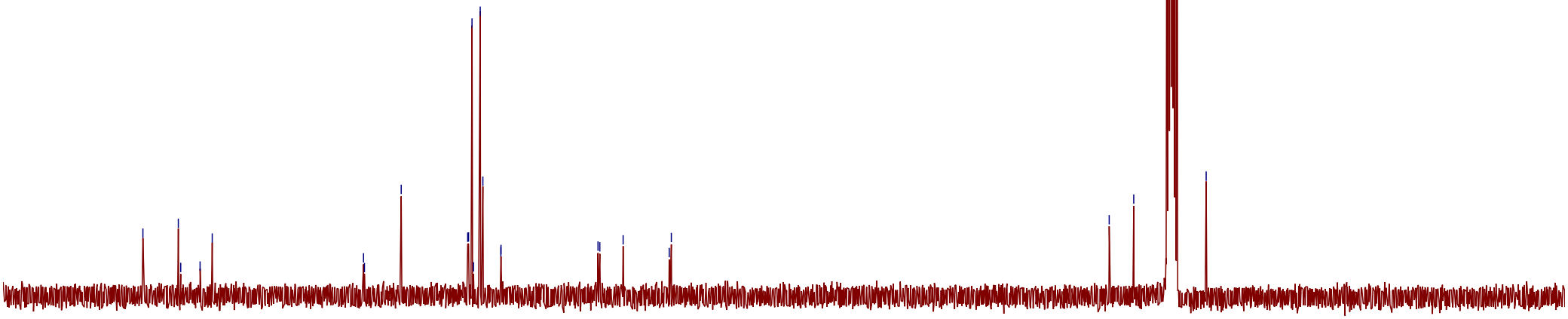
E (d) 142.85 J(12.00)

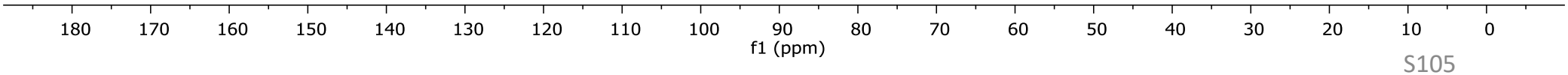
D (d) 129.60 J(10.96)

F (d) 125.42 J(1.46)

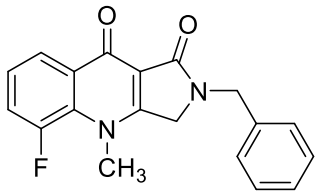
C (d) 112.95 J(23.11)

B (d) 103.87 J(27.16)



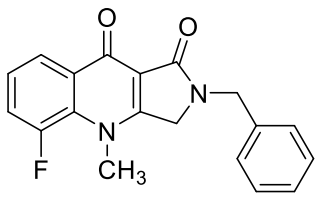


1H NMR (DMSO-d6, 400 MHz)



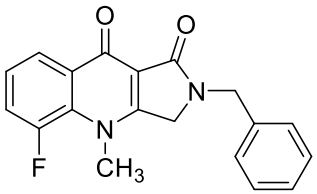
29p

19F NMR (DMSO-d6, 376 MHz)



29p

13C NMR (DMSO-d6, 101 MHz)



29p

170.41
170.38
166.26
162.65
153.96
151.49
138.04
131.47
130.40
130.33
129.10
128.12
127.75
125.29
125.21
122.70
122.66
120.41
120.18
109.73

48.28
44.90
40.68 DMSO
40.63 DMSO
40.47 DMSO
40.42 DMSO
40.26 DMSO
40.21 DMSO
40.00 DMSO
39.79 DMSO
39.58 DMSO
39.38 DMSO

A (d)
170.40
J(2.39)

B (d)
152.73
J(248.52)

C (d)
130.36
J(6.51)

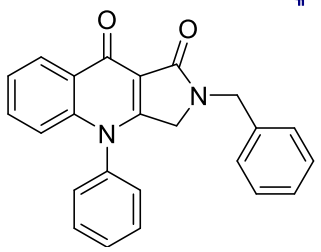
D (d)
125.25
J(8.29)

E (d)
122.68
J(3.47)

F (d)
120.30
J(23.06)

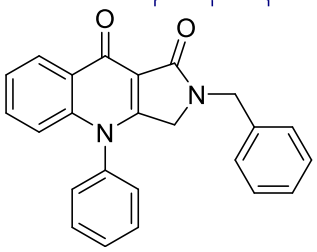
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1H NMR (DMSO-d6, 400 MHz)



29q

13C NMR (DMSO-d6, 101 MHz)

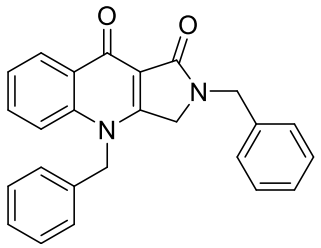


29q

172.00
166.50
161.10
142.08
138.11
136.83
133.02
131.24
130.94
129.01
128.79
128.07
127.65
126.44
124.91
117.80
109.79
47.98
44.79
40.68 DMSO
40.63 DMSO
40.47 DMSO
40.42 DMSO
40.26 DMSO
40.21 DMSO
40.00 DMSO
39.80 DMSO
39.58 DMSO
39.38 DMSO

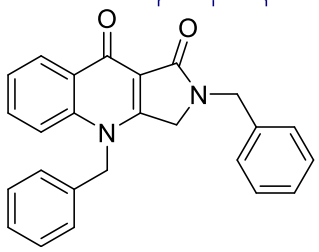
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1H NMR (DMSO-d6, 400 MHz)



29r

13C NMR (DMSO-d6, 101 MHz)

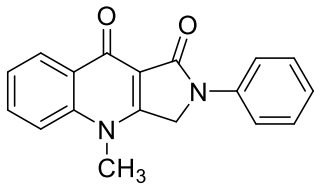


29r

171.85
166.59
161.51
140.41
138.09
135.54
133.06
129.44
129.08
128.92
128.83
128.07
127.69
126.73
126.29
124.88
117.74
109.99
50.68
48.06
44.90
40.67 DMSO
40.62 DMSO
40.46 DMSO
40.41 DMSO
40.25 DMSO
40.20 DMSO
39.99 DMSO
39.78 DMSO
39.57 DMSO
39.37 DMSO

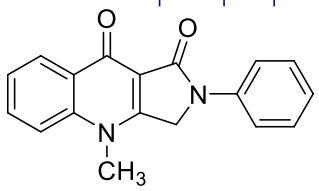
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1H NMR (DMSO-d6, 400 MHz)



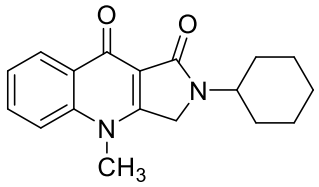
30

13C NMR (DMSO-d6, 101 MHz)



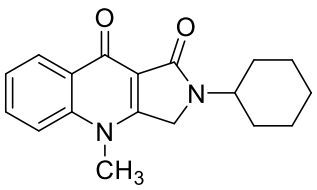
30

1H NMR (DMSO-d6, 400 MHz)



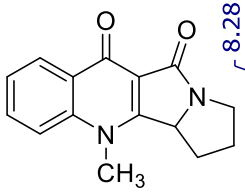
31

13C NMR (DMSO-d6, 101 MHz)



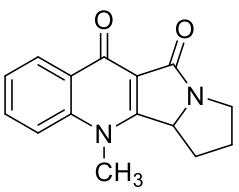
31

1H NMR (DMSO-d6, 400 MHz)



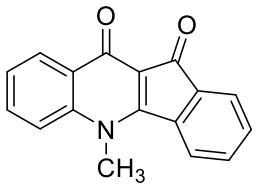
32

13C NMR (DMSO-d6, 101 MHz)



32

1H NMR (DMSO-d6, 400 MHz)



34

D (ddd)
7.83
J(8.71, 7.04, 1.68)

B (d)
8.20
J(7.43)

A (dd)
8.27
J(7.89, 1.63)

F (t)
7.54
J(7.48)

G (s)
4.30

C (d)
8.05
J(8.62)

E (m)
7.67

8.28 8.27 8.26 8.25 8.21 8.19 8.07 8.04 7.86 7.85 7.84 7.83 7.83 7.82 7.81 7.71 7.71 7.70 7.70 7.69 7.68 7.67 7.66 7.66 7.65 7.56 7.54 7.52

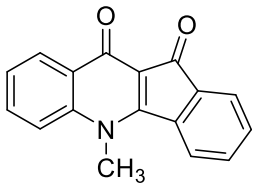
4.30

0.96 0.97 0.93 0.99 2.92 0.97 3.00

0.0 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 -0.5

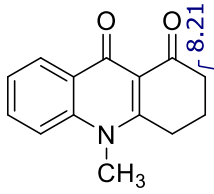
f1 (ppm)

13C NMR (DMSO-d6, 101 MHz)



34

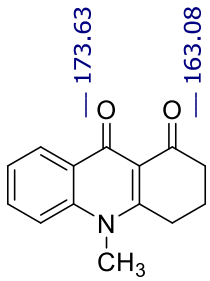
1H NMR (DMSO-d6, 400 MHz)



35

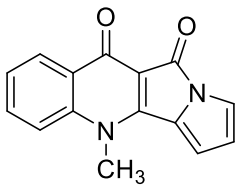
f1 (ppm)

13C NMR (DMSO-d6, 101 MHz)



35

1H NMR (DMSO-d6, 400 MHz)



3

8.21 8.19 7.92 7.90 7.80 7.79 7.77 7.51 7.49 7.48 7.48 7.12 7.11 6.44 6.43 6.43 3.99 3.31 HDO 2.50 DMSO 2.49 DMSO 2.49 DMSO 2.48 DMSO

B (d) 7.91 J(8.53)

E (d) 7.11 J(3.31)

A (d) 8.20 J(7.92)

D (m) 7.50

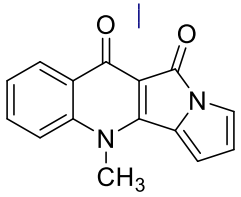
F (d) 6.44 J(3.23)

C (t) 7.79 J(7.82)

1.06 1.05 1.03 2.01 1.03 1.01 3.00

f1 (ppm)

13C NMR (DMSO-d6, 101 MHz)



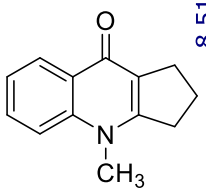
3

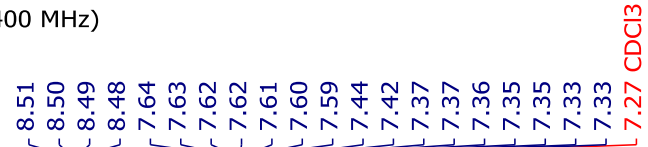
169.90
159.59
153.75
140.36
132.73
128.65
125.93
125.59
125.53
120.20
117.81
116.65
116.61
104.26

40.12 DMSO
40.07 DMSO
39.91 DMSO
39.86 DMSO
39.70 DMSO
39.65 DMSO
39.44 DMSO
39.24 DMSO
39.03 DMSO
38.82 DMSO
36.66

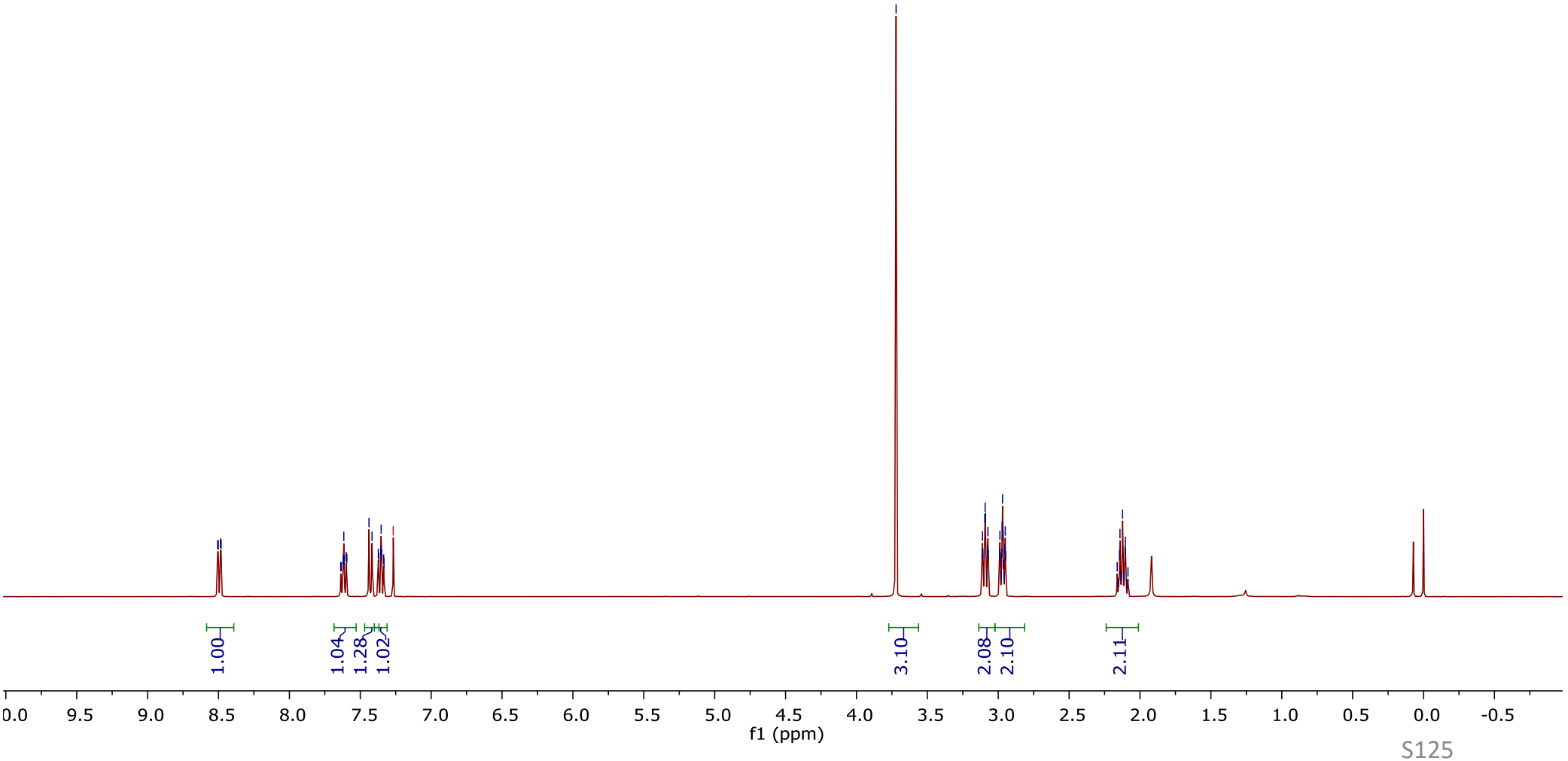
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1H NMR (CDCl3, 400 MHz)

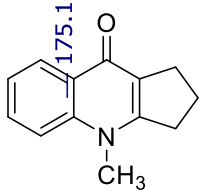




24a

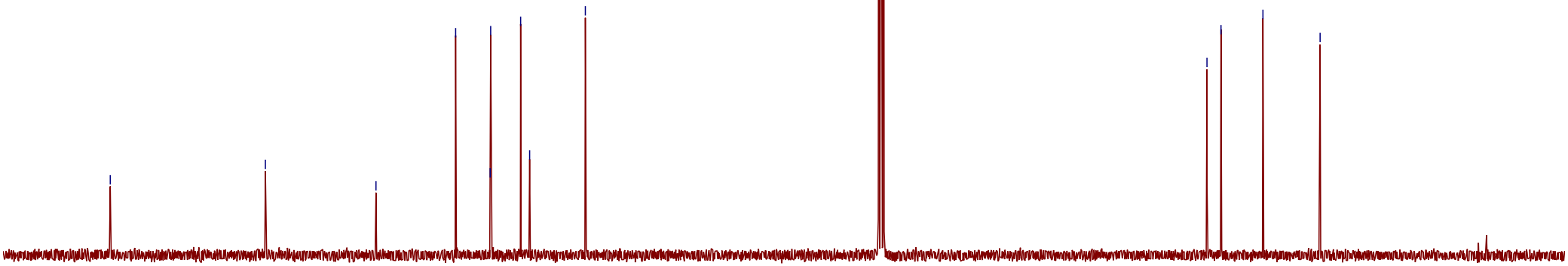


13C (CDCl3, 101 MHz)



175.14 155.40 141.32 131.19 126.79 126.73 122.92 121.77 114.68 77.35 CDCl3 77.04 CDCl3 76.72 CDCl3 35.58 33.79 28.45 21.18

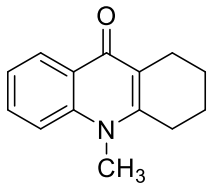
24a



180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

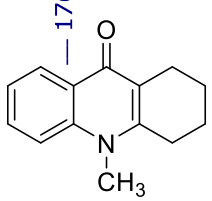
f1 (ppm)

1H NMR (CDCl3, 500 MHz)



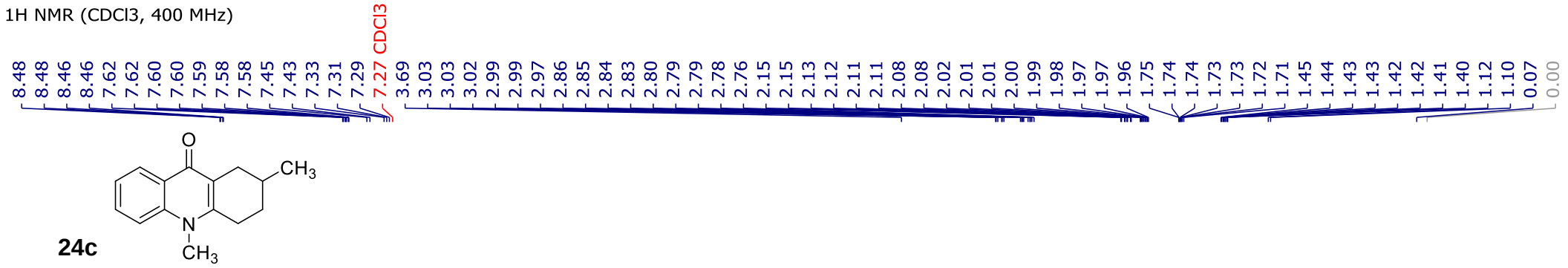
24b

13C NMR (CDCl3, 126 MHz)

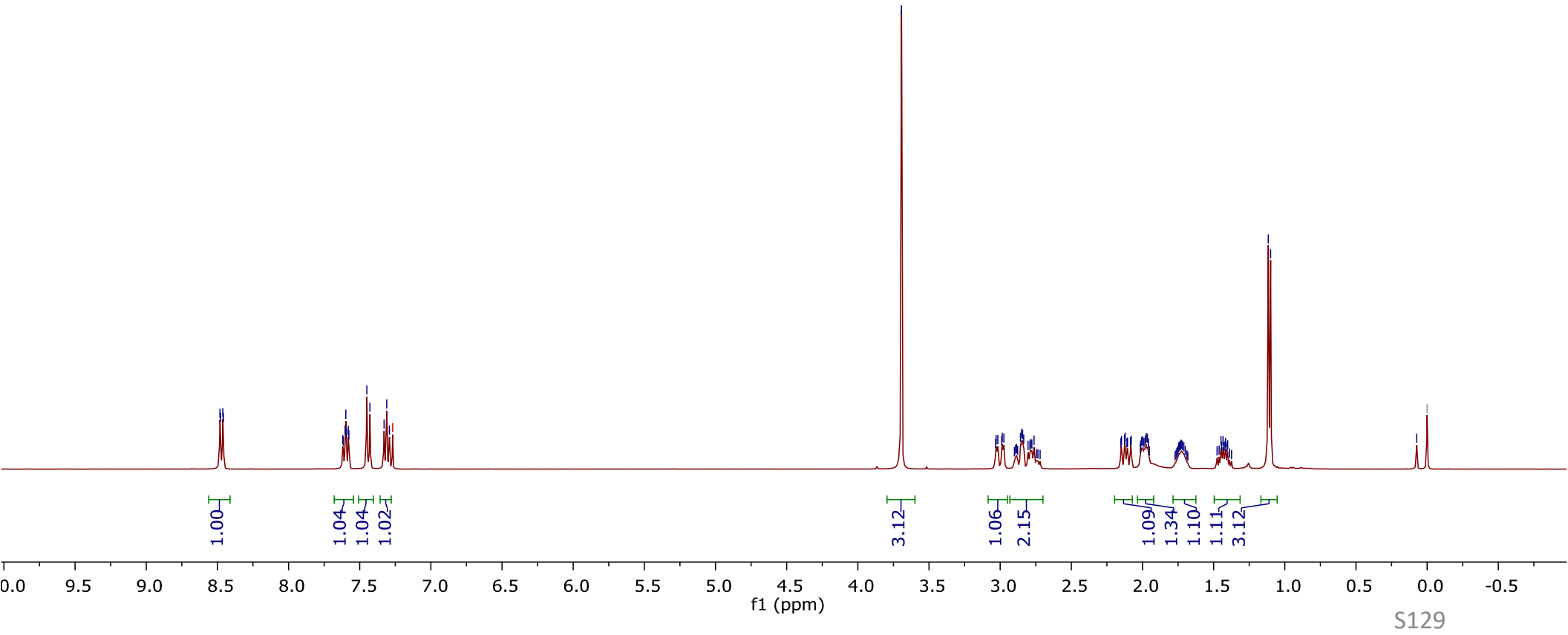


24b

1H NMR (CDCl3, 400 MHz)



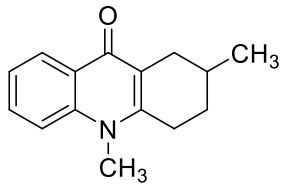
24c

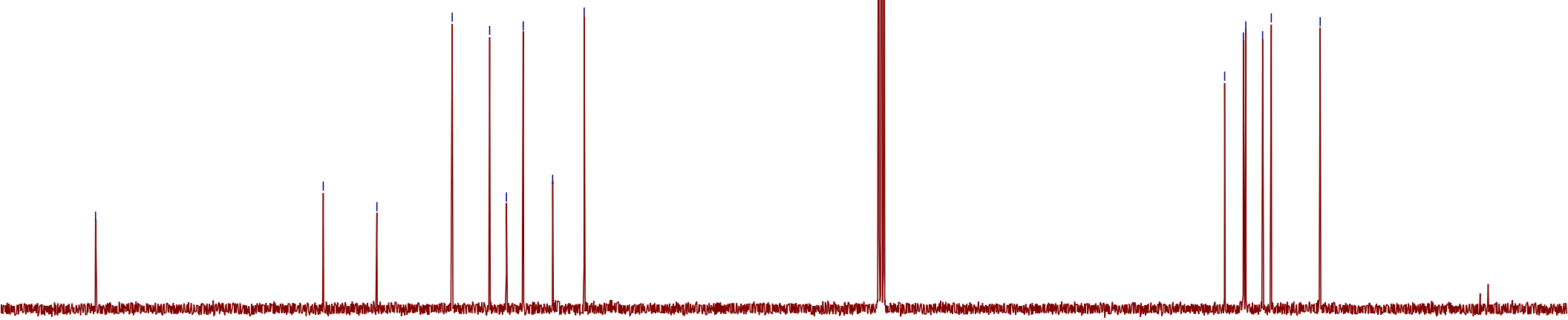


13C (CDCl3, 101 MHz)

176.79
147.89
141.08
131.52
126.76
124.63
122.50
118.76
114.76
77.36 CDCl3
77.04 CDCl3
76.72 CDCl3
33.46
31.09
30.78
28.64
27.54
21.33

24c

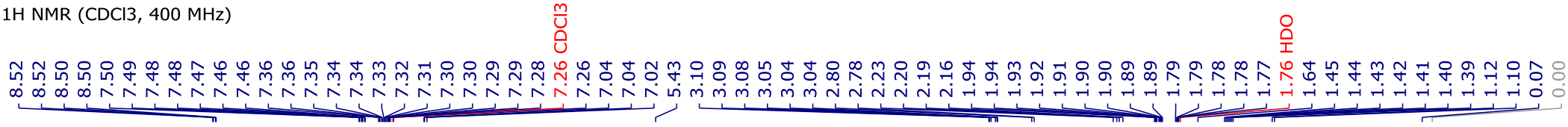




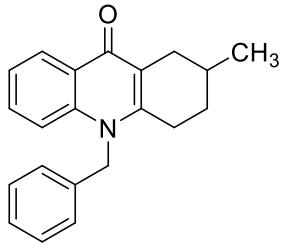
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

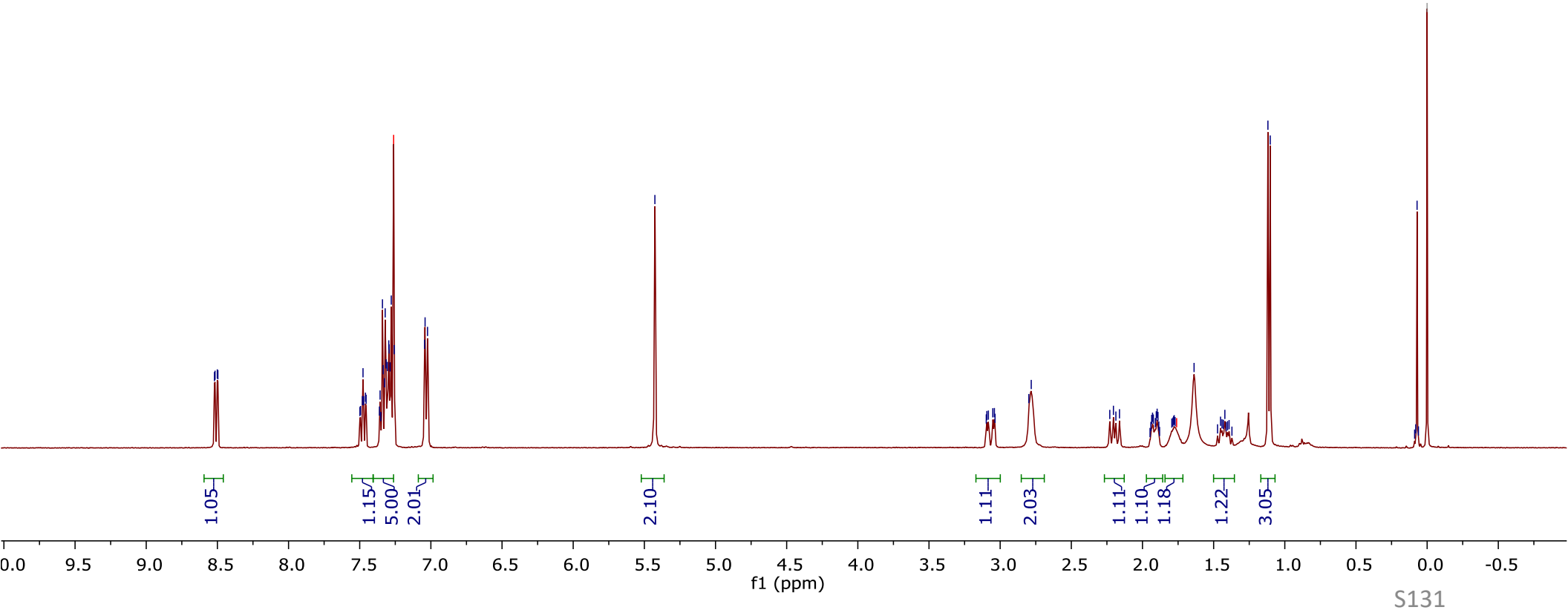
f1 (ppm)

1H NMR (CDCl3, 400 MHz)



24d

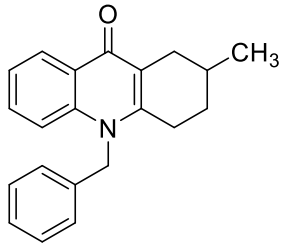




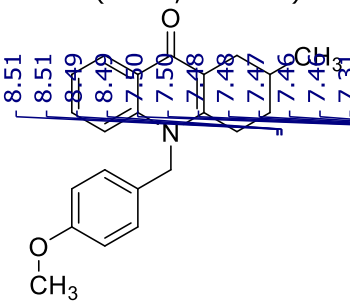
13C NMR (CDCl3, 126 MHz)

177.10
148.07
140.94
135.92
131.79
129.29
127.79
126.84
125.33
124.86
122.76
118.97
115.69
77.38 CDCl3
77.13 CDCl3
76.87 CDCl3
49.39
31.18
30.78
27.89
27.70
21.41

24d



1H NMR (CDCl3, 400 MHz)

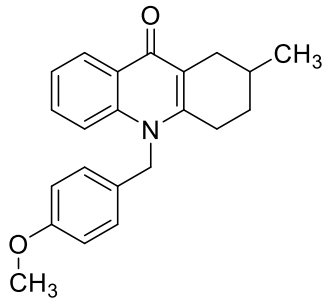


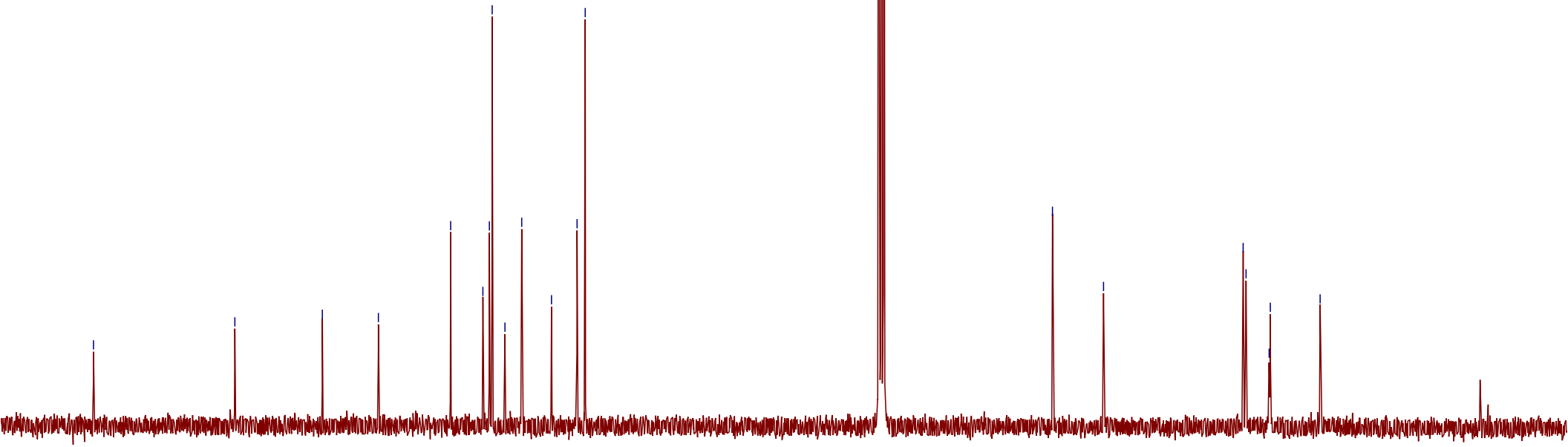
24e

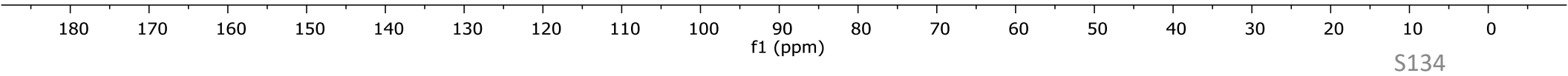
13C (CDCl3, 101 MHz)

177.05
159.11
148.00
140.89
131.71
127.62
126.80
126.44
124.82
122.69
118.91
115.66
114.63
77.35 CDCl3
77.03 CDCl3
76.71 CDCl3
55.32
48.84
31.11
30.74
27.81
27.66
21.34

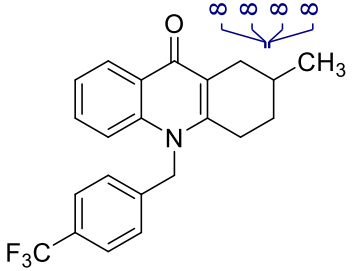
24e



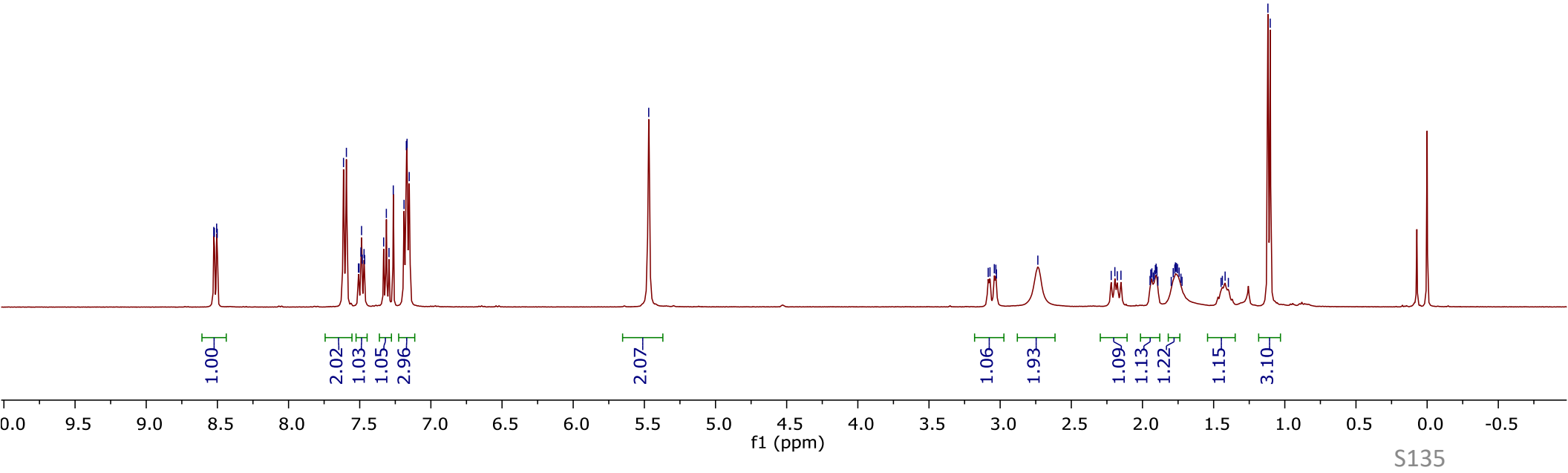




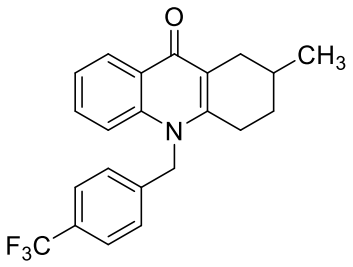
1H NMR (CDCl3, 400 MHz)



24f

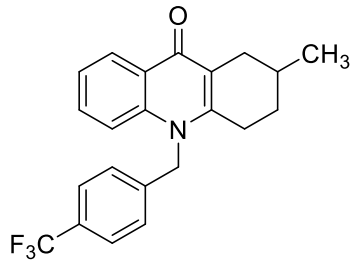


19F NMR (CDCl3, 376 MHz)

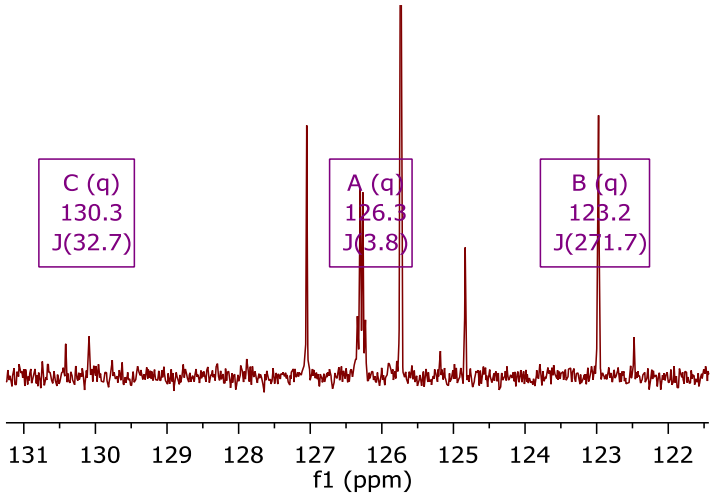


24f

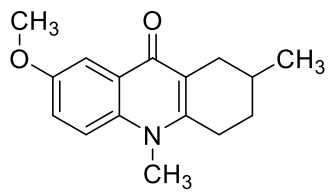
13C (CDCl3, 101 MHz)



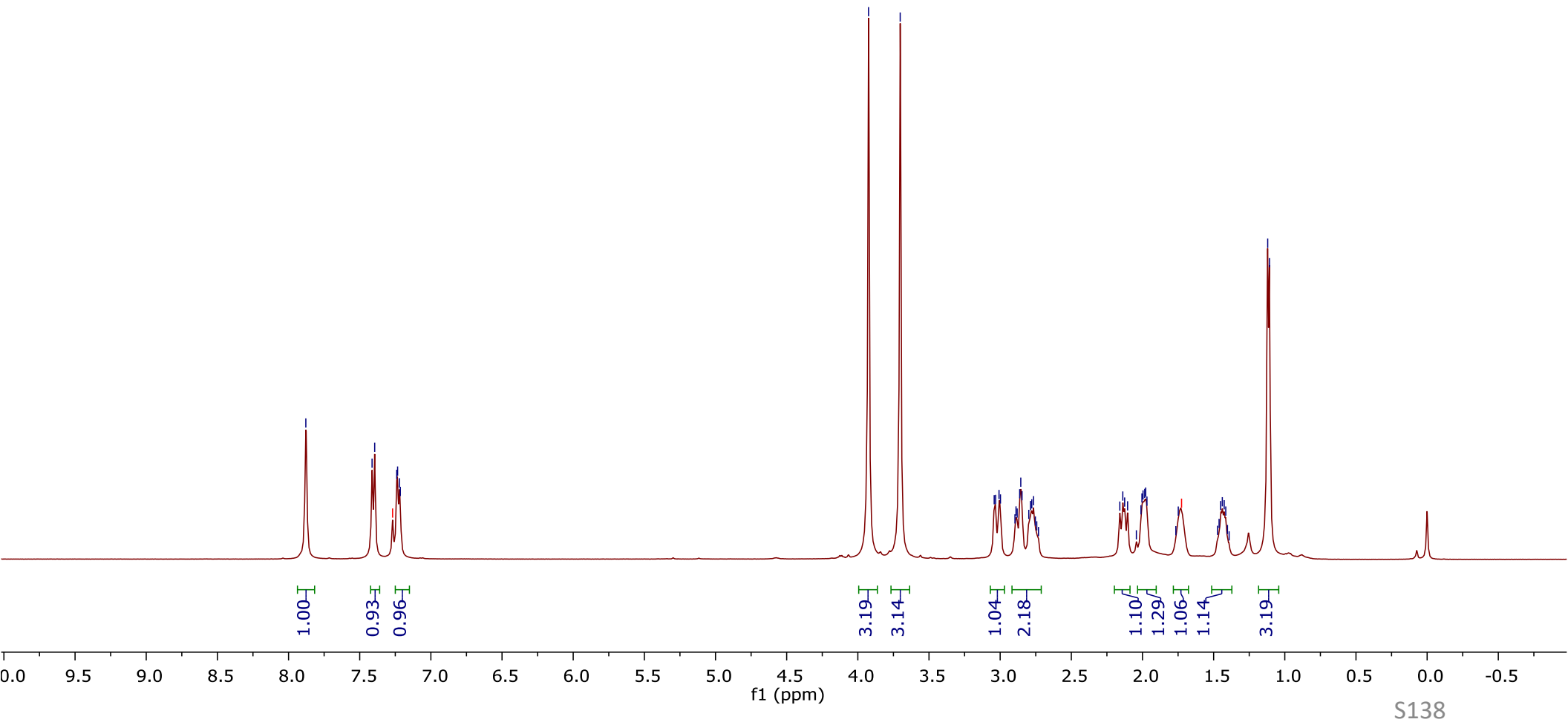
24f



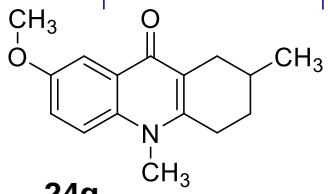
1H NMR (CDCl3, 500 MHz)



24g



13C NMR (CDCl3, 126 MHz)

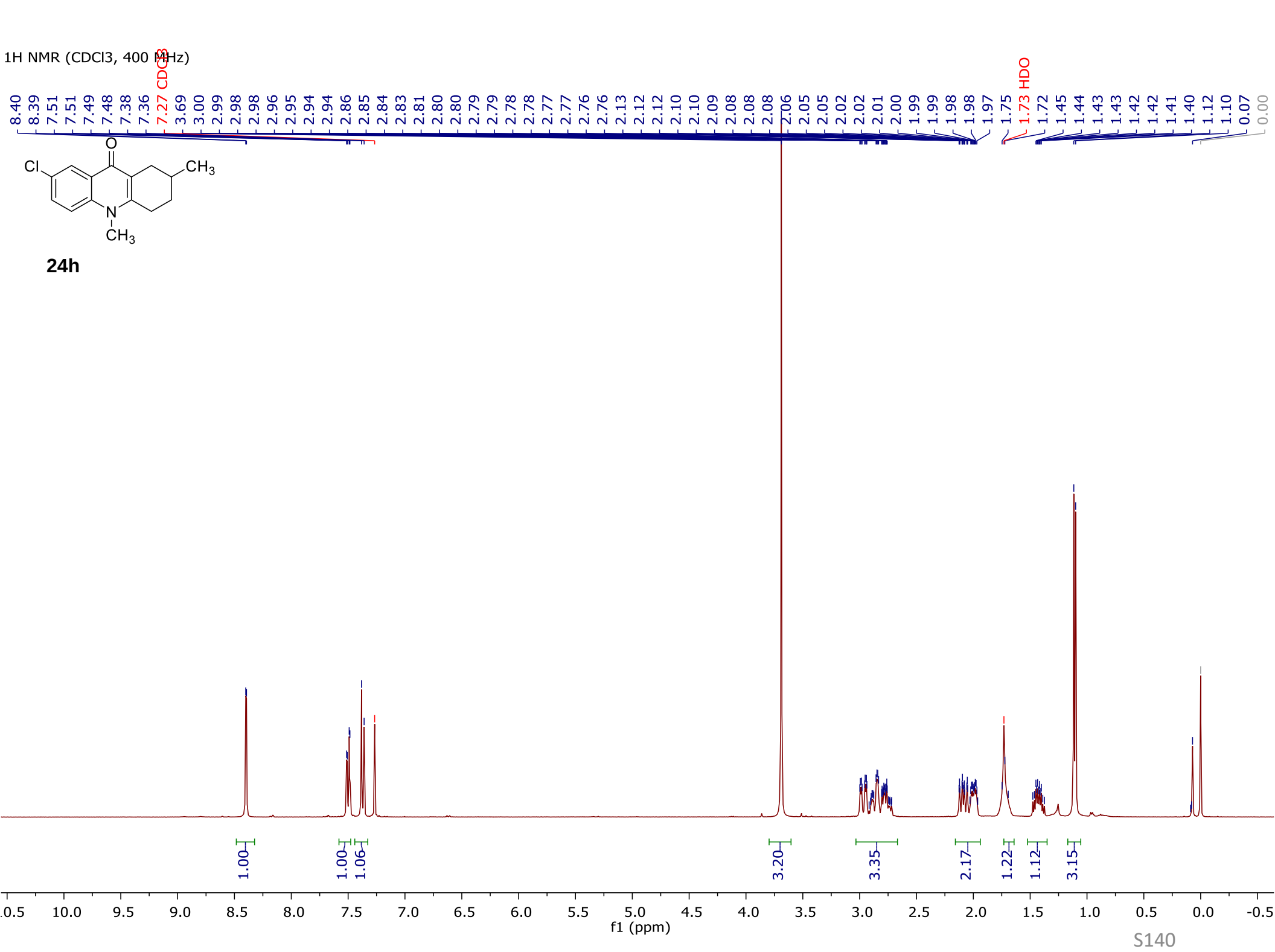


24g

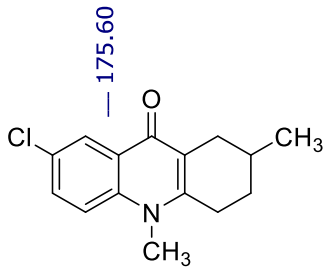
176.02 155.38 147.15 135.90 125.63 122.18 117.80 116.64 105.54 77.40 CDCl3 77.15 CDCl3 76.89 CDCl3 55.77 33.63 31.29 30.84 28.54 27.63 21.44

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)


1H NMR (CDCl3, 400 MHz)
7.27 CDCl3
1.73 HDO
8.40 8.39 7.51 7.51 7.49 7.48 7.38 7.36 3.69 3.00 2.99 2.98 2.98 2.96 2.95 2.94 2.94 2.86 2.85 2.84 2.83 2.81 2.80 2.80 2.79 2.79 2.78 2.78 2.77 2.77 2.76 2.76 2.13 2.12 2.12 2.10 2.10 2.09 2.08 2.08 2.08 2.06 2.05 2.05 2.02 2.02 2.01 2.00 1.99 1.99 1.98 1.98 1.97 1.75 1.72 1.45 1.44 1.43 1.43 1.42 1.42 1.41 1.40 1.12 1.10 0.07 0.00
Cl
O
CH3
N
CH3
24h
1.00
1.00
1.06
3.20
3.35
2.17
1.22
1.12
3.15
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 -0.5
f1 (ppm)

13C (CDCl3, 101 MHz)

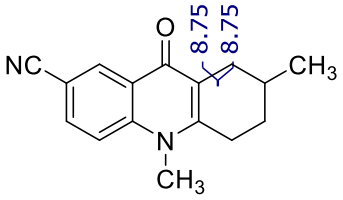


24h

175.60
148.20
139.45
131.65
128.58
125.88
125.51
119.24
116.67
77.35 CDCl3
77.03 CDCl3
76.71 CDCl3
33.68
31.09
30.69
28.62
27.43
21.29

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

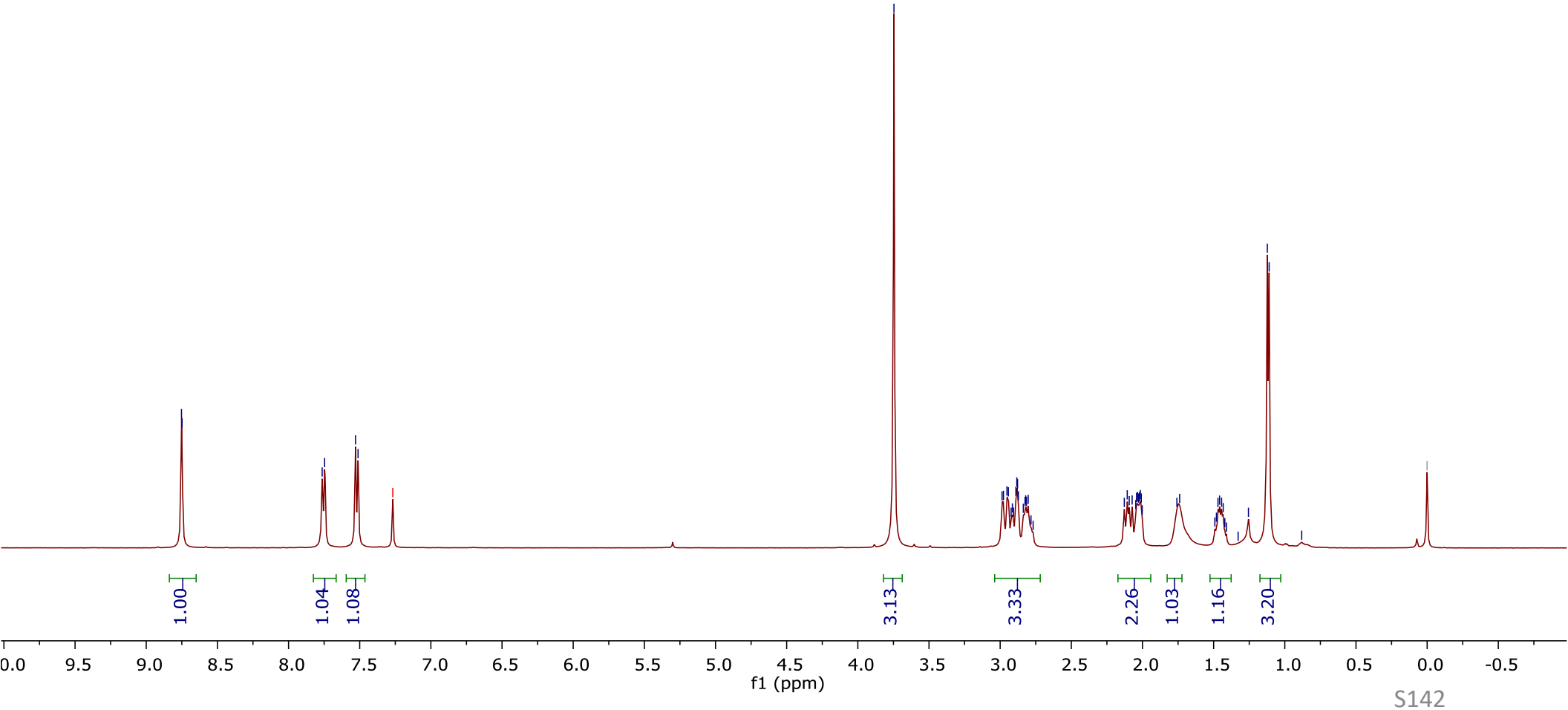
1H NMR (CDCl3, 500 MHz)



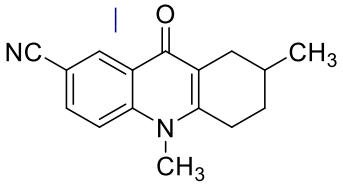
8.75 8.75 7.76 7.75 7.53 7.51 7.27 CDCl3

3.75 2.99 2.98 2.95 2.94 2.92 2.91 2.91 2.89 2.88 2.88 2.87 2.84 2.83 2.82 2.82 2.80 2.78 2.77 2.13 2.11 2.09 2.07 2.05 2.04 2.04 2.03 2.02 2.01 2.01 2.00 1.76 1.74 1.49 1.48 1.47 1.46 1.44 1.43 1.42 1.41 1.33 1.26 1.12 1.11 0.88 0.00

24i

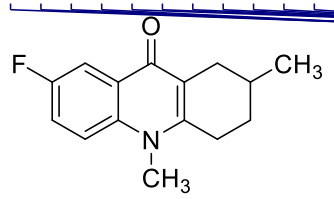


13C NMR (CDCl3, 126 MHz)



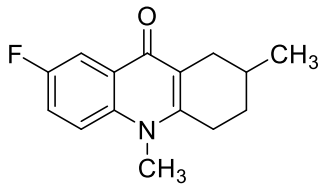
24i

1H NMR (CDCl3, 400 MHz)

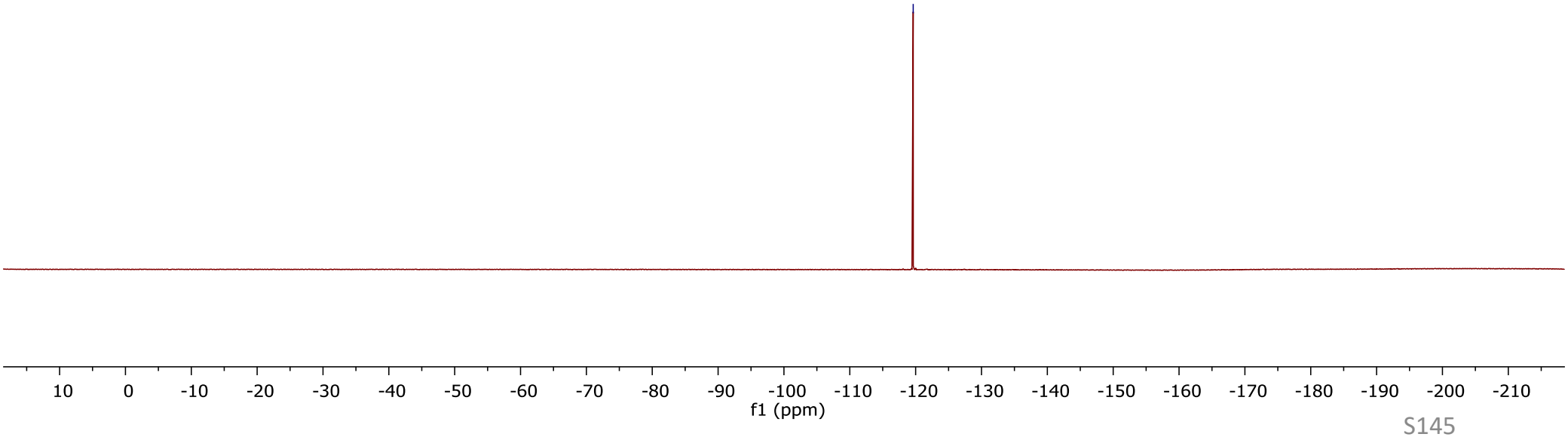


24j

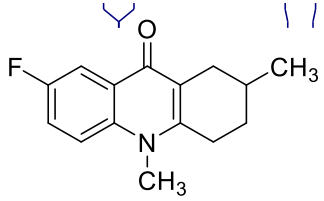
19F NMR (CDCl3, 376 MHz)



24j



13C (CDCl3, 101 MHz)



24j

175.96
175.94
159.74
157.32
148.04
137.68
137.67
125.95
125.88
120.12
119.87
118.31
117.03
116.96
111.14
110.92
77.34 CDCl3
77.03 CDCl3
76.71 CDCl3
33.80
31.08
30.73
28.61
27.47
21.29

A (d)
175.95
J(2.73)

B (d)
158.53
J(243.94)

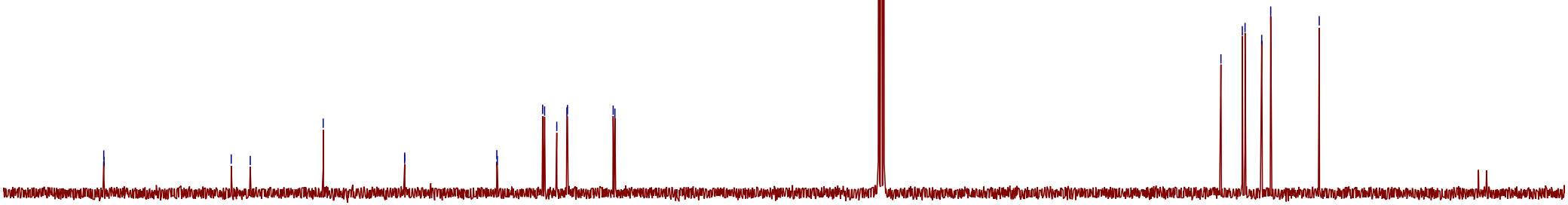
C (d)
137.68
J(0.99)

D (d)
125.91
J(6.78)

E (d)
119.99
J(24.98)

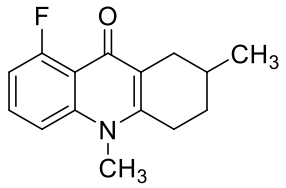
F (d)
116.99
J(7.63)

G (d)
111.03
J(22.18)



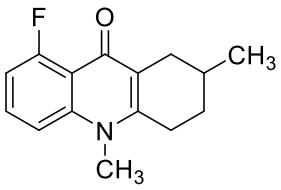
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1H NMR (CDCl3, 400 MHz)



24k

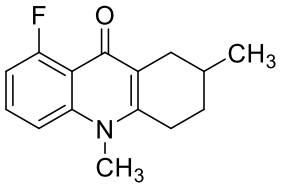
19F NMR (CDCl3, 376 MHz)



24k

13C (CDCl3, 101 MHz)

175.83
175.81
163.48
160.87
147.01
143.35
143.31
131.48
131.37
120.61
114.83
114.75
110.56
110.51
109.13
108.92
77.34 CDCl3
77.02 CDCl3
76.71 CDCl3
34.31
30.74
30.71
28.56
27.48
21.30



24k

A (d)
175.82
J(1.35)

F (d)
162.18
J(262.72)

G (d)
143.33
J(4.04)

D (d)
131.43
J(11.28)

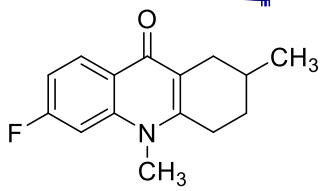
C (d)
110.53
J(4.64)

B (d)
109.02
J(21.69)

E (d)
114.79
J(7.48)

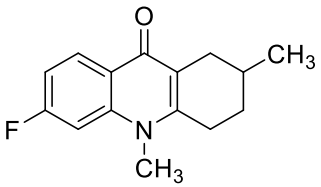
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1H NMR (CDCl3, 400 MHz)



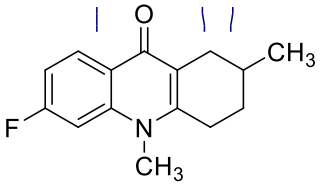
24l

19F NMR (CDCl3, 376 MHz)



24l

13C (CDCl3, 101 MHz)



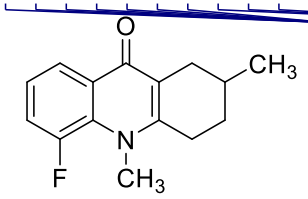
24l

176.21
166.07
163.59
148.24
148.22
142.50
142.39
129.76
129.65
121.39
121.37
119.10
111.33
111.10
101.04
100.78
77.36 CDCl3
77.04 CDCl3
76.72 CDCl3
33.68
30.92
30.67
28.62
27.46
21.27

A (d) 164.83 J(249.53)
B (d) 148.23 J(1.50)
C (d) 142.45 J(11.23)
D (d) 129.71 J(10.64)
G (d) 121.38 J(1.47)
F (d) 111.22 J(22.99)
E (d) 100.91 J(26.67)

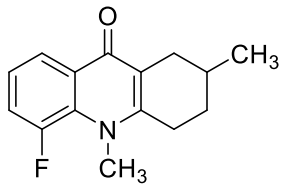
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1H NMR (CDCl3, 400 MHz)

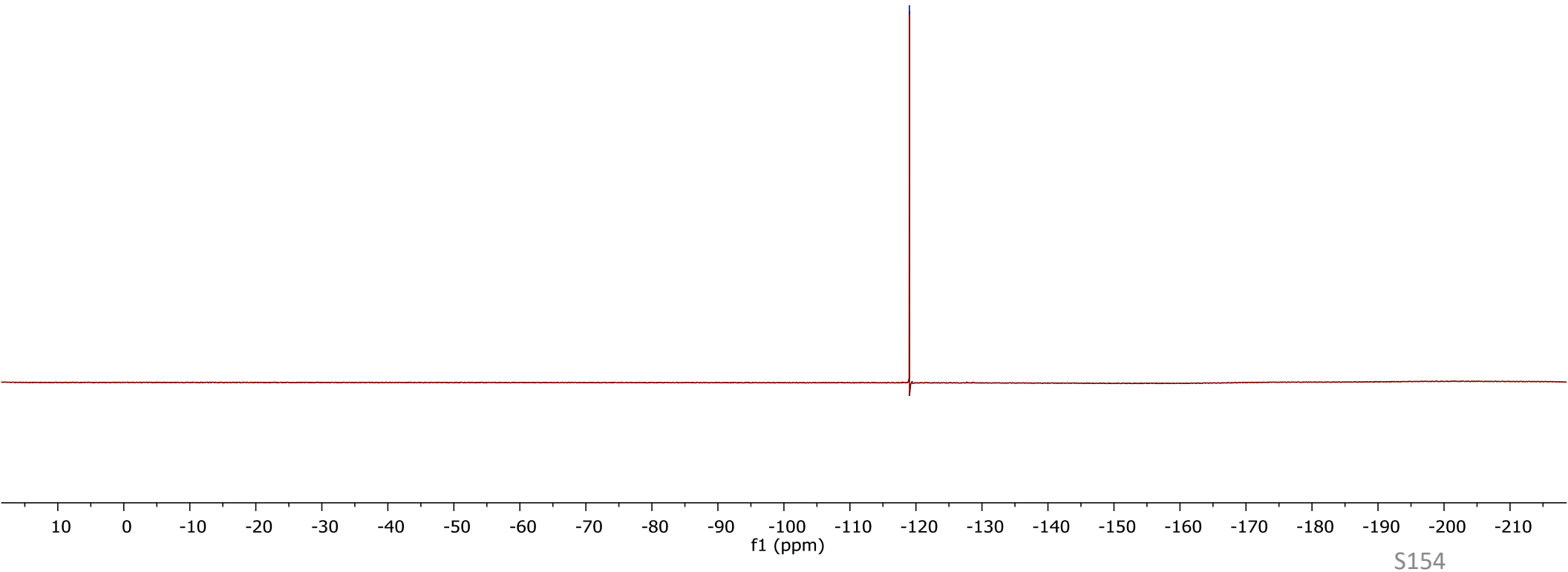


24m

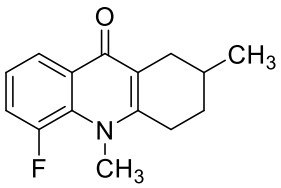
19F NMR (CDCl3, 376 MHz)



24m



13C (CDCl3, 101 MHz)



24m

175.90
175.88
153.23
150.77
149.88
131.63
131.58
127.61
122.59
122.51
122.44
122.41
119.16
118.28
118.05
77.34 CDCl3
77.02 CDCl3
76.71 CDCl3
37.87
37.69
30.86
30.66
28.47
27.54
21.37

$CDCl_3$

A (d)
175.89
J(2.35)

B (d)
152.00
J(247.51)

C (d)
131.61
J(5.67)

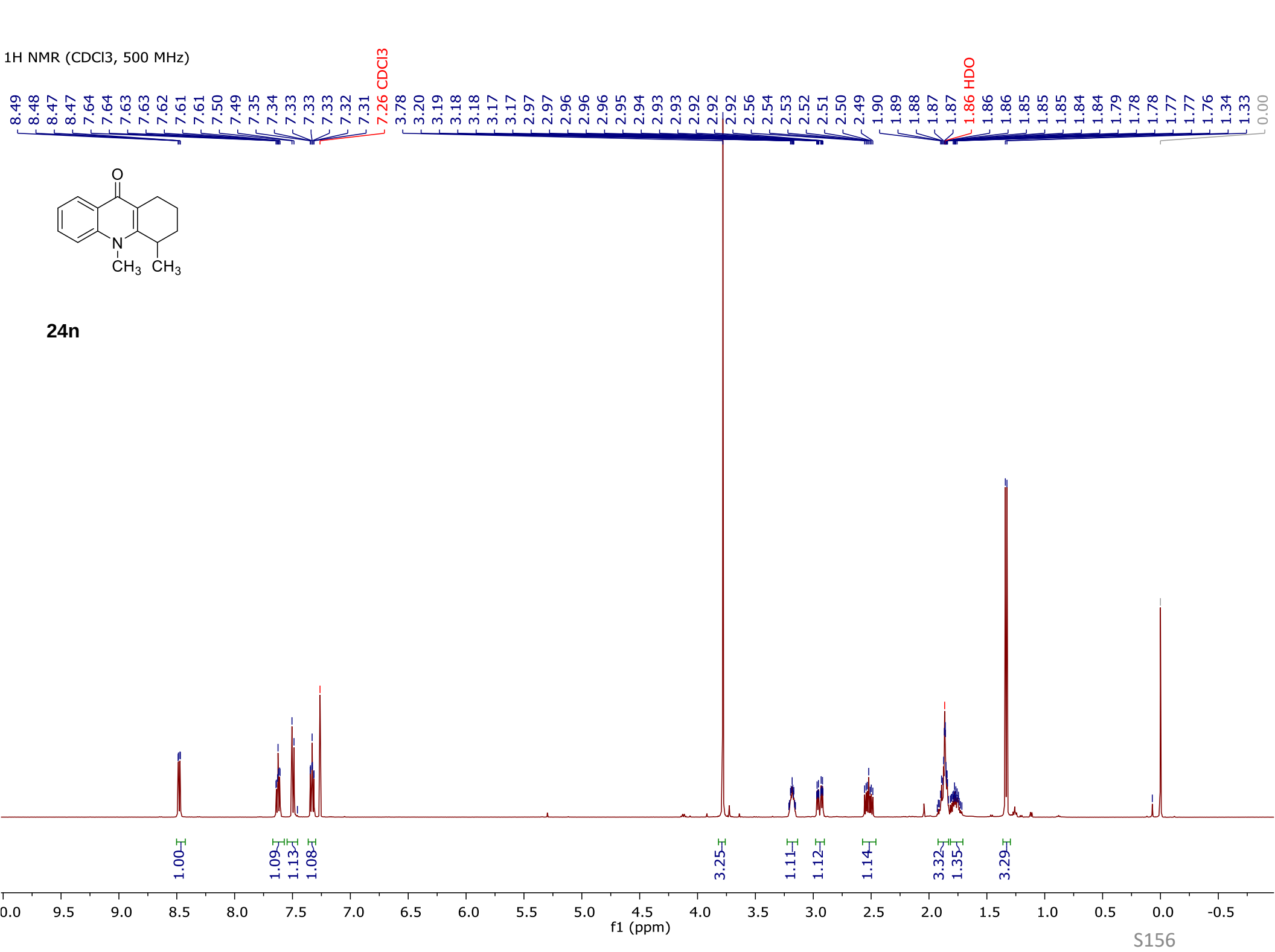
D (d)
122.55
J(8.22)

E (d)
122.43
J(3.57)

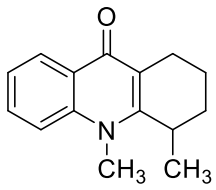
F (d)
118.17
J(23.41)

G (d)
37.78
J(17.63)

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

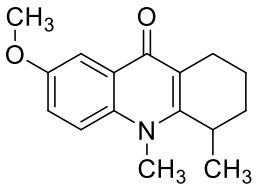

1H NMR (CDCl3, 500 MHz)
7.26 CDCl3
1.86 HDO
O
N
CH3
CH3
24n
1.00
1.09
1.13
1.08
3.25
1.11
1.12
1.14
3.32
1.35
3.29
f1 (ppm)

13C NMR (CDCl3, 126 MHz)

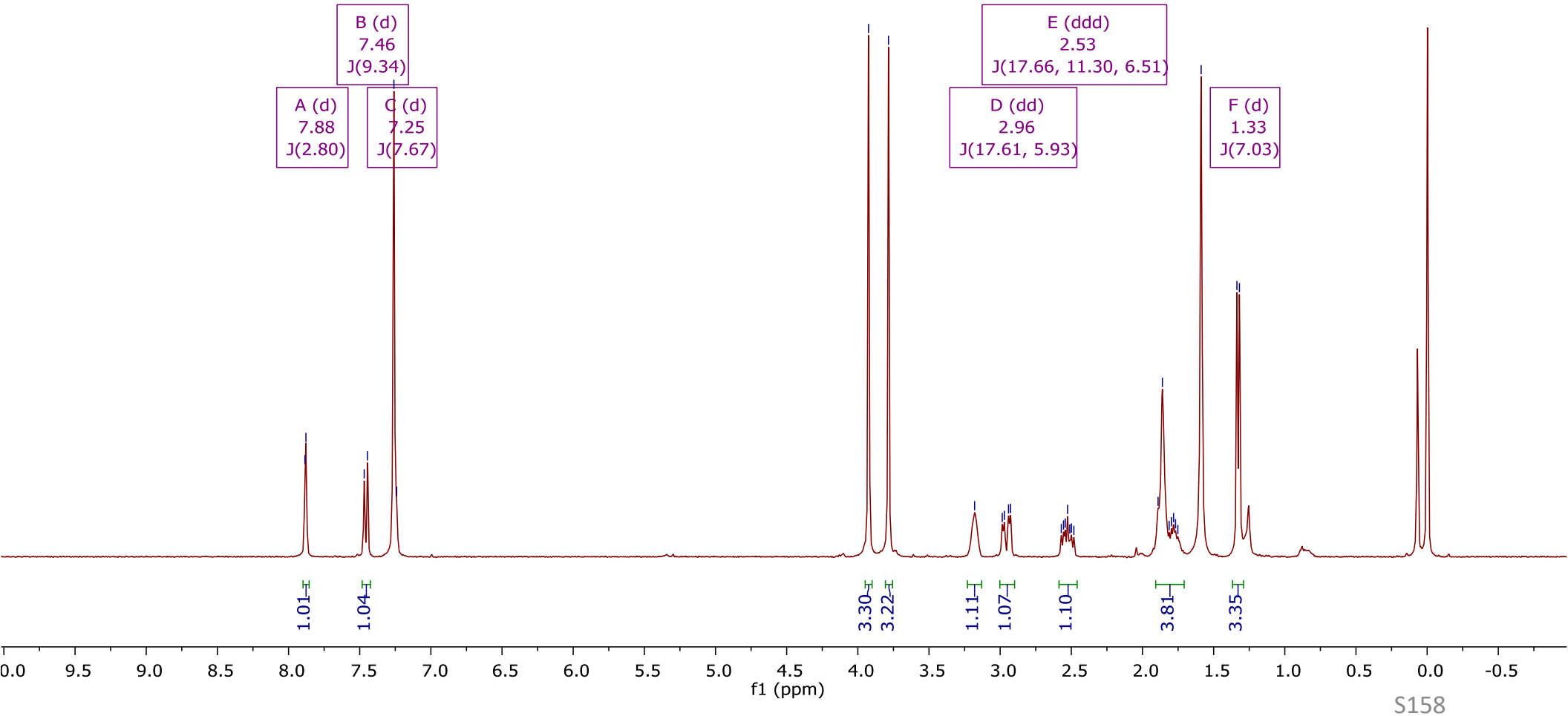


24n

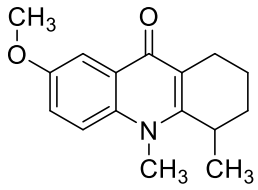
1H NMR (CDCl3, 400 MHz)



24o

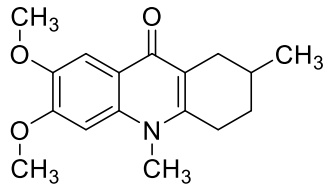


13C (CDCl3, 101 MHz)

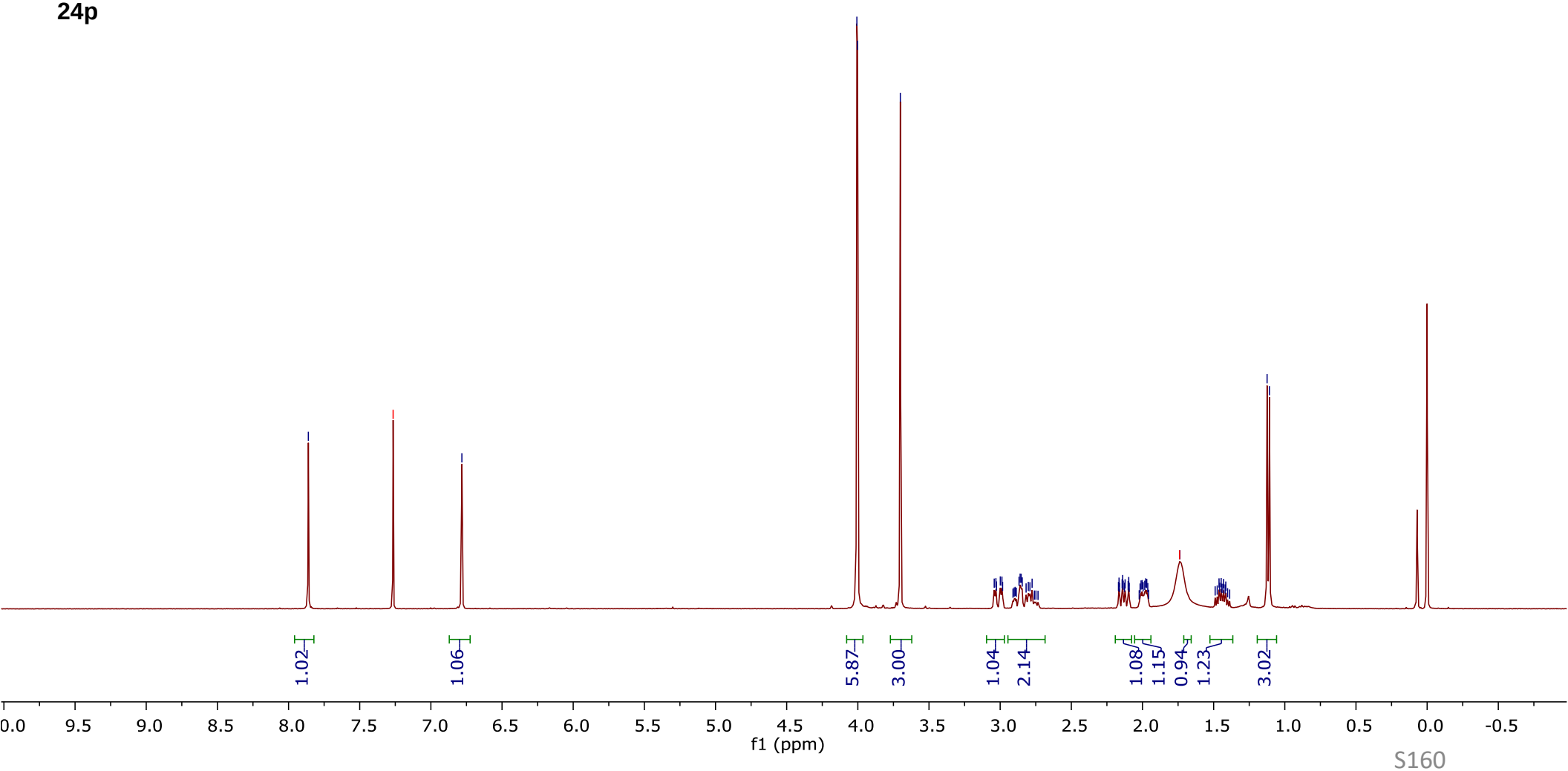


24o

1H NMR (CDCl3, 400 MHz)

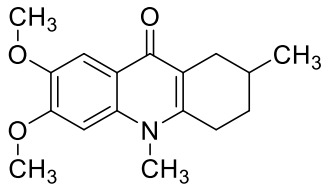


24p



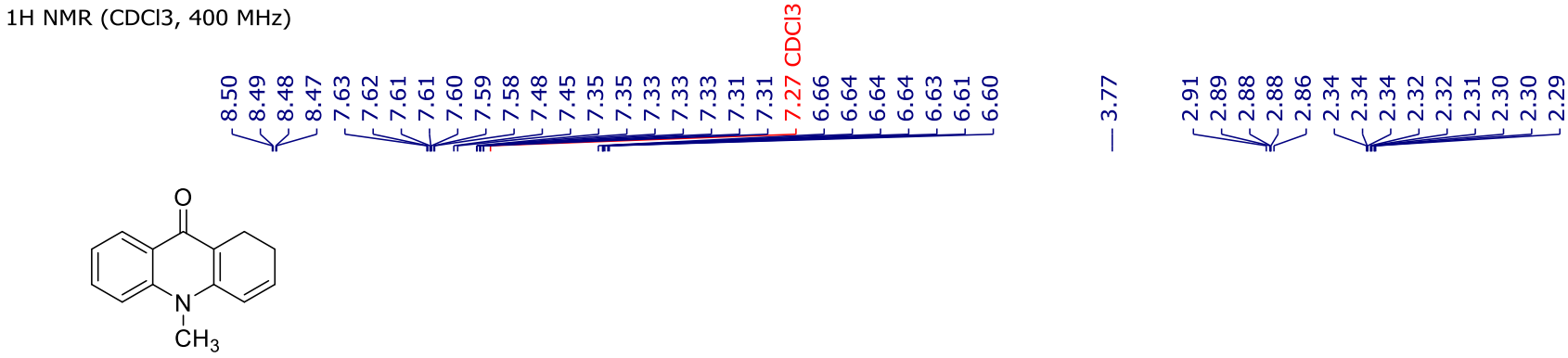
13C (CDCl3, 101 MHz)

175.59
152.98
146.50
146.25
136.82
118.92
118.07
106.07
96.53
77.34 CDCl3
77.02 CDCl3
76.71 CDCl3
56.18
56.08
33.73
31.17
30.87
28.60
27.63
21.36

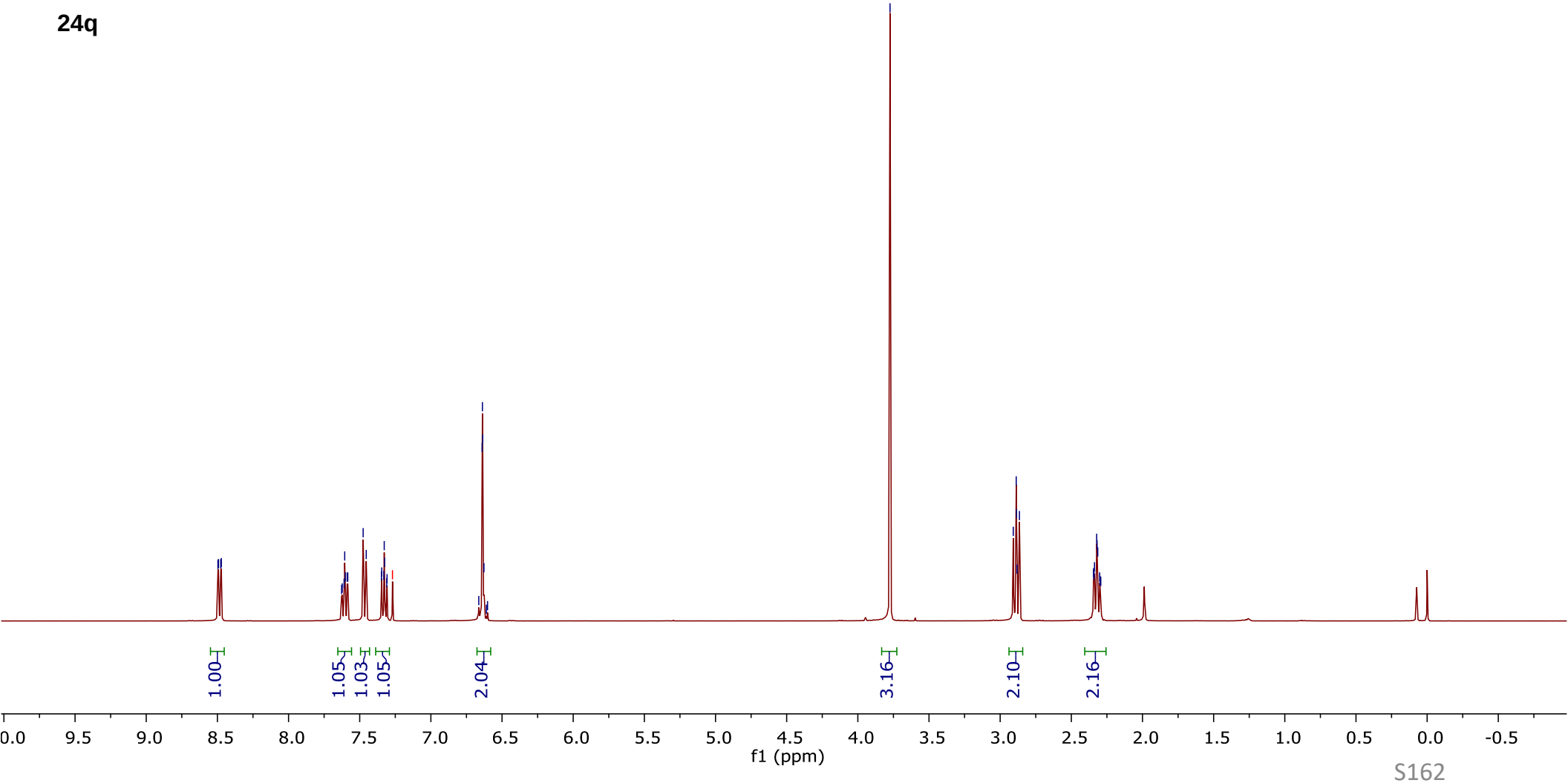


24p

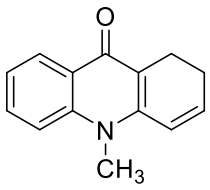
1H NMR (CDCl3, 400 MHz)



24q

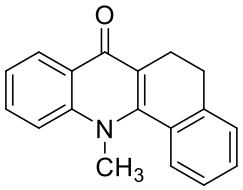


13C (CDCl3, 101 MHz)

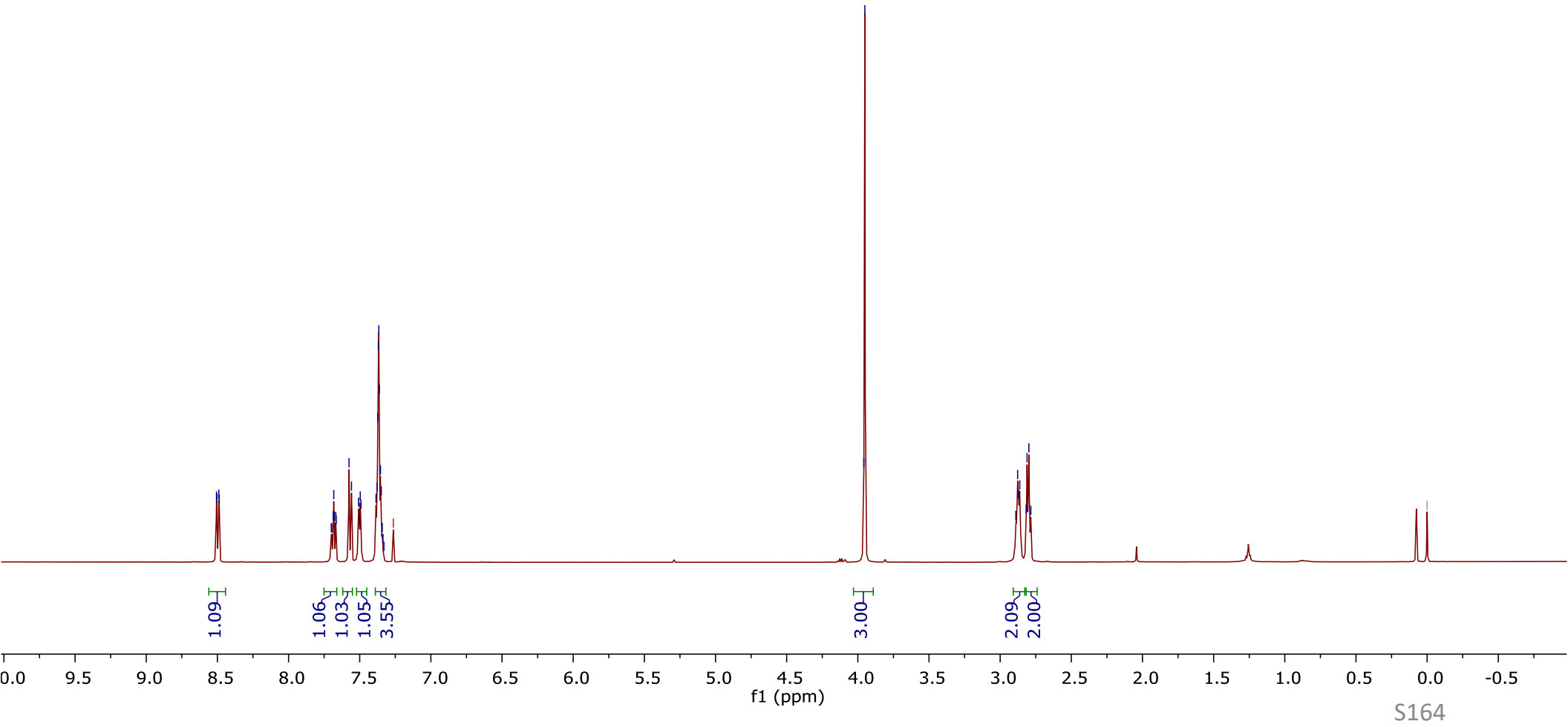


24q

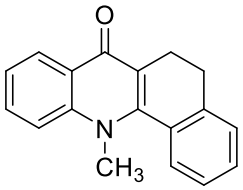
1H NMR (CDCl3, 500 MHz)



24r

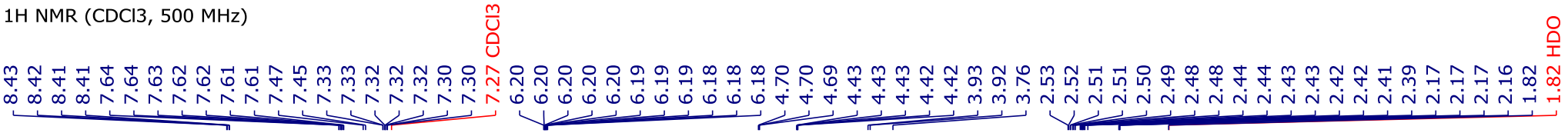


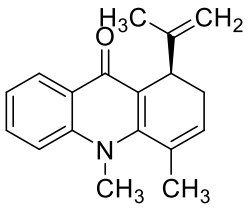
13C NMR (CDCl3, 126 MHz)



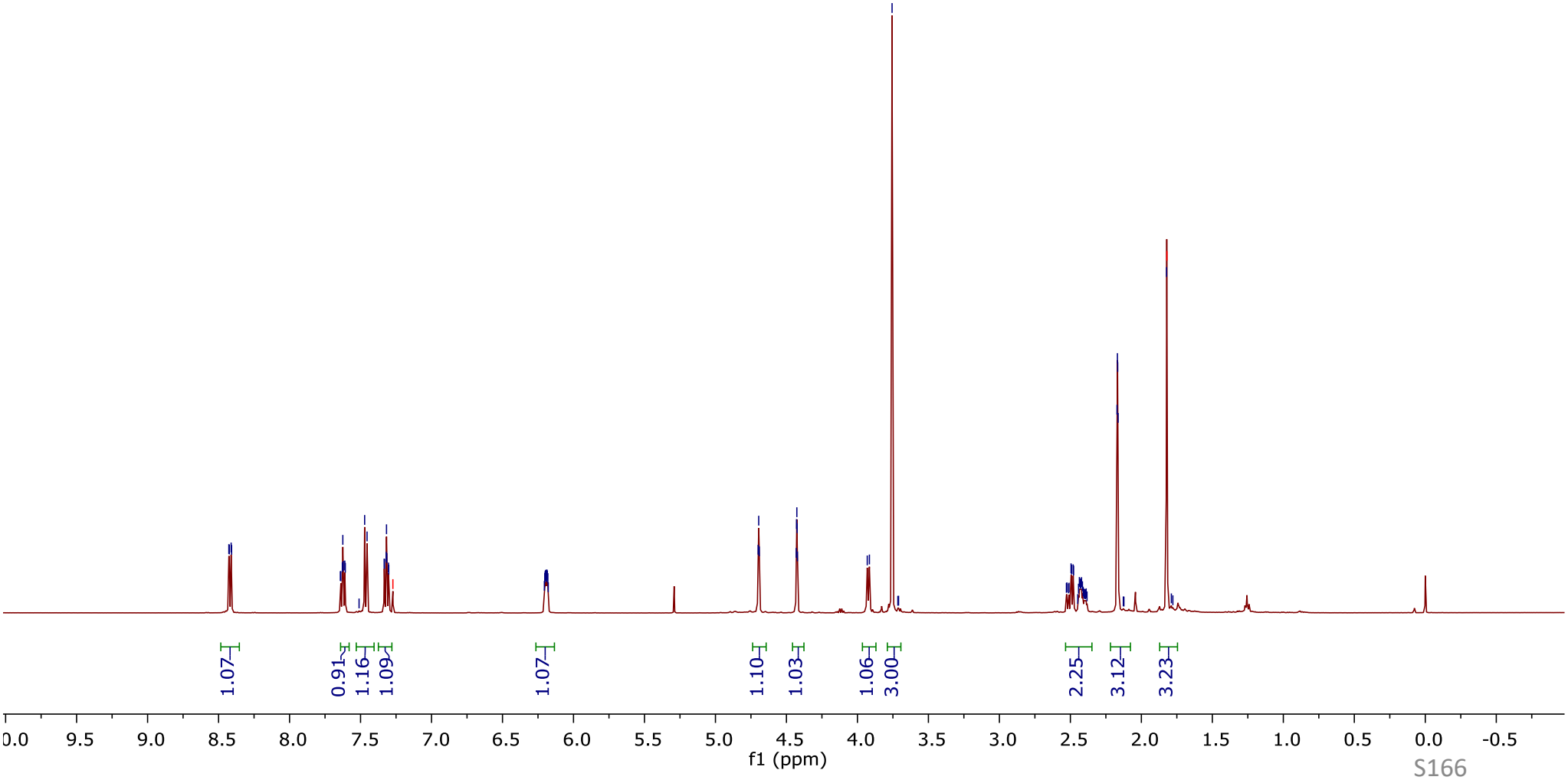
24r

1H NMR (CDCl3, 500 MHz)

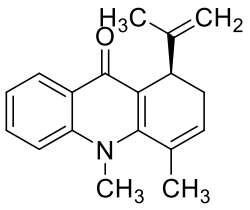




24s

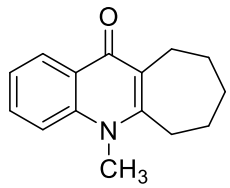


13C NMR (CDCl3, 126 MHz)

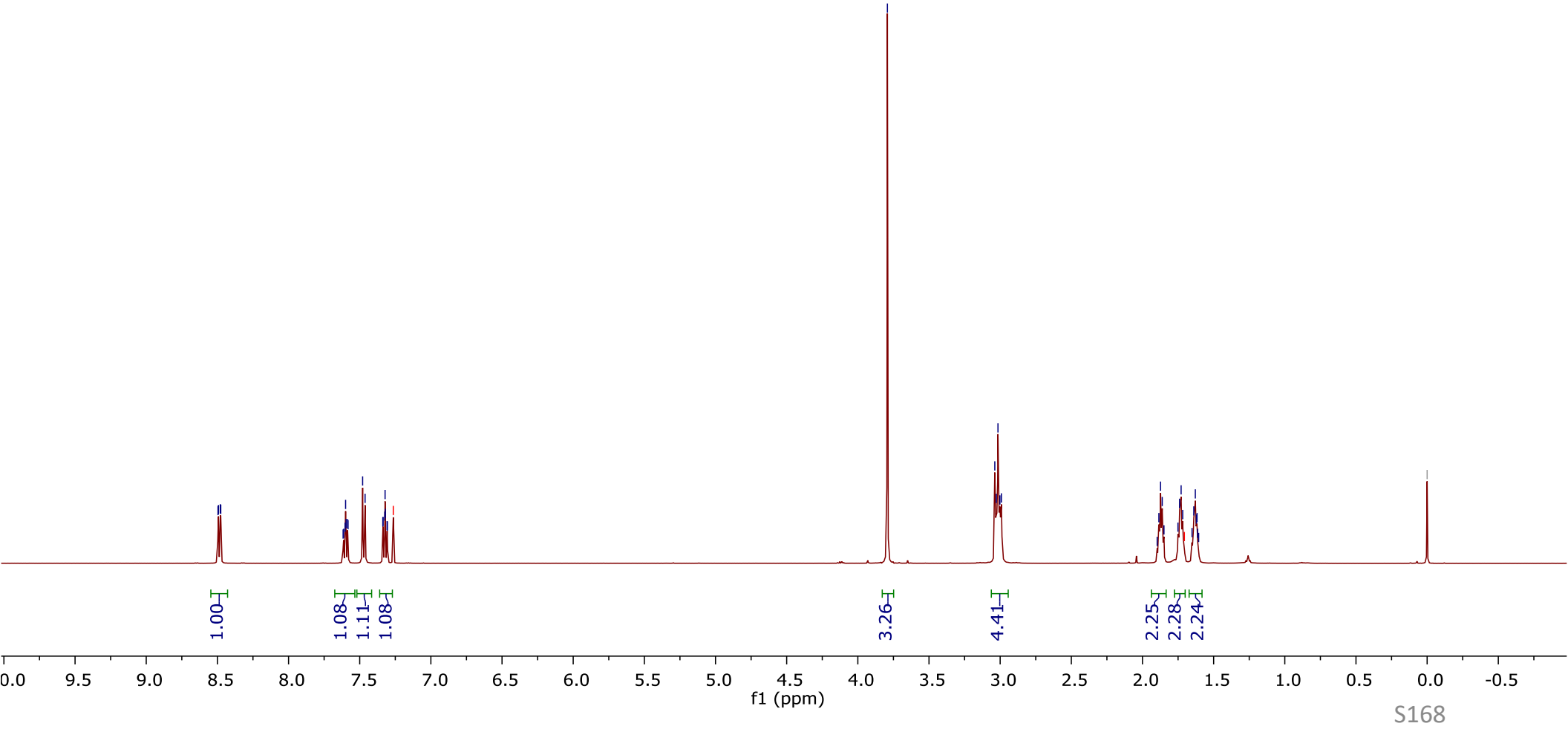


24s

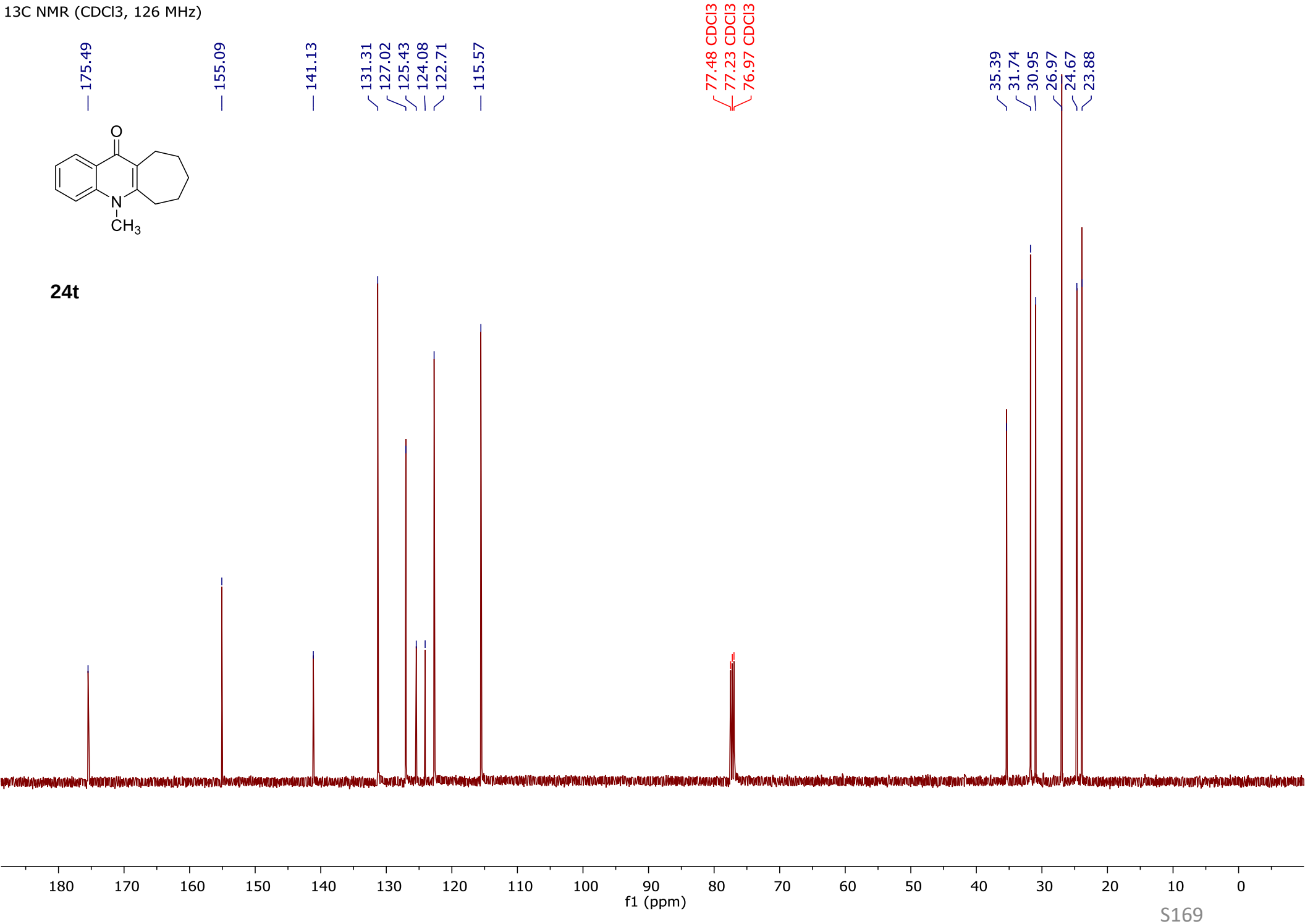
1H NMR (CDCl3, 500 MHz)



24t



13C NMR (CDCl3, 126 MHz)

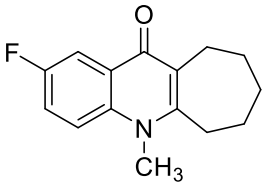


1H NMR (CDCl3, 500 MHz)

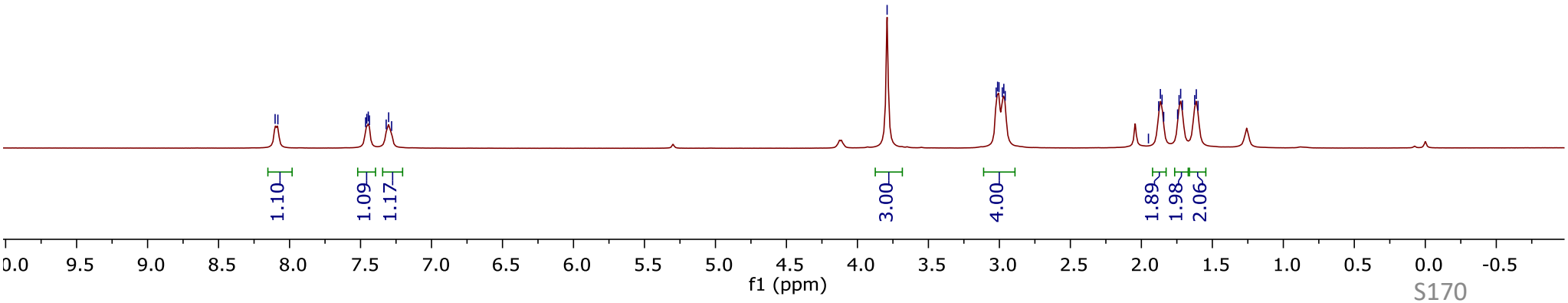
8.10 8.08 7.46 7.46 7.45 7.44 7.32 7.30 7.28

3.79

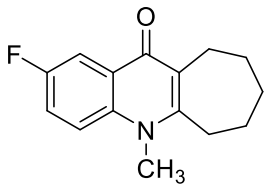
3.02 3.01 3.00 2.98 2.97 2.96 1.95 1.88 1.87 1.85 1.84 1.74 1.73 1.72 1.71 1.62 1.61 1.60



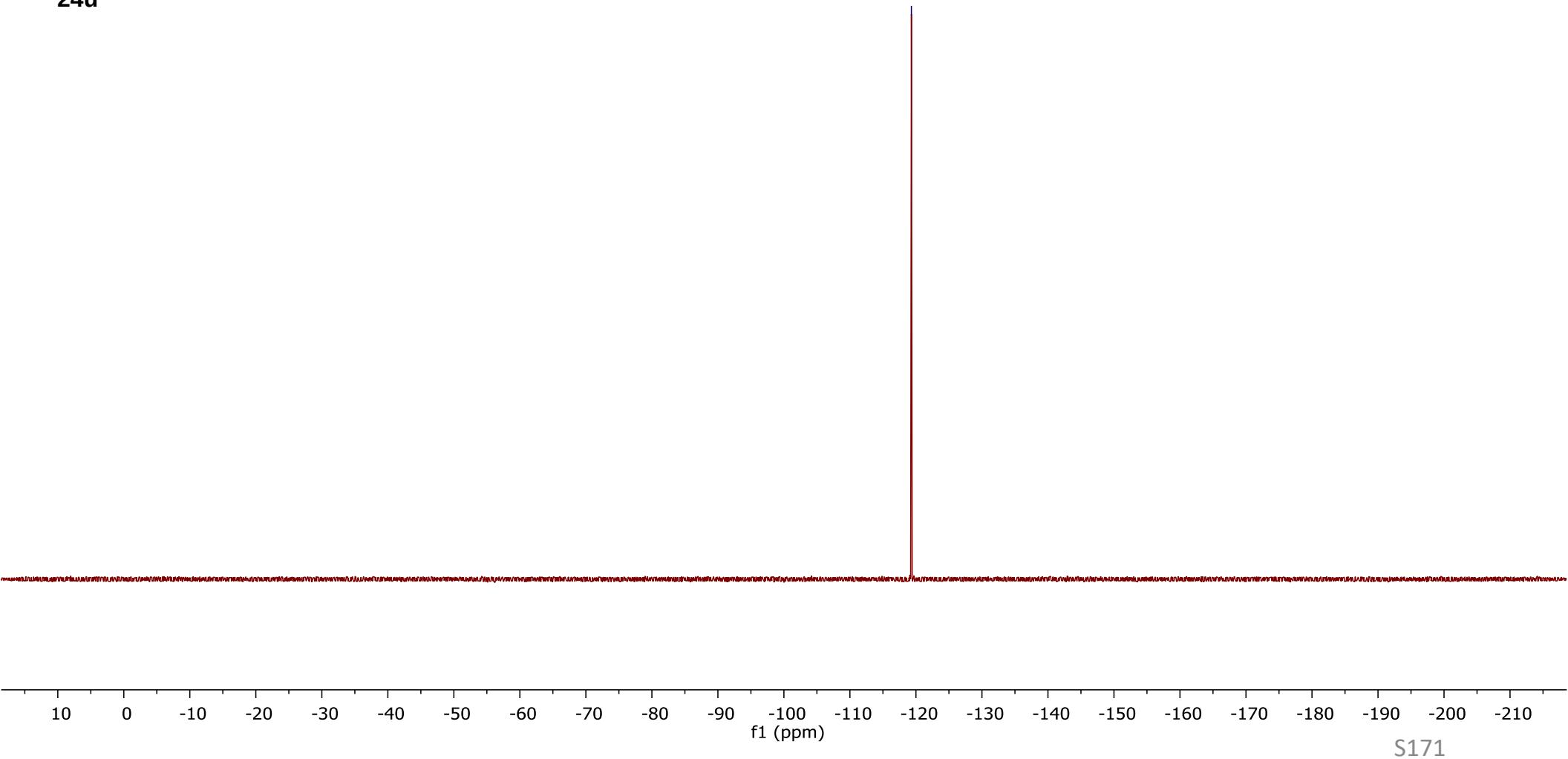
24u



19F NMR (CDCl3, 376 MHz)

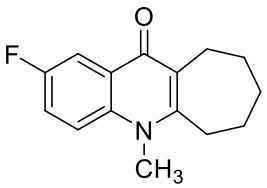


24u



13C NMR (CDCl3, 126 MHz)

174.73
174.71
159.71
157.76
155.25
137.75
126.92
126.86
123.71
119.87
119.67
117.83
117.77
111.53
111.35
77.37 CDCl3
77.12 CDCl3
76.87 CDCl3
60.45
35.77
31.72
31.01
26.97
26.94
24.69
23.97
21.12
14.27



24u

A (d)
174.72
J(3.04)

B (d)
158.73
J(244.13)

C (d)
126.89
J(6.70)

D (d)
119.77
J(24.99)

E (d)
117.80
J(7.65)

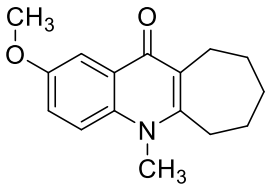
F (d)
111.44
J(22.12)

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

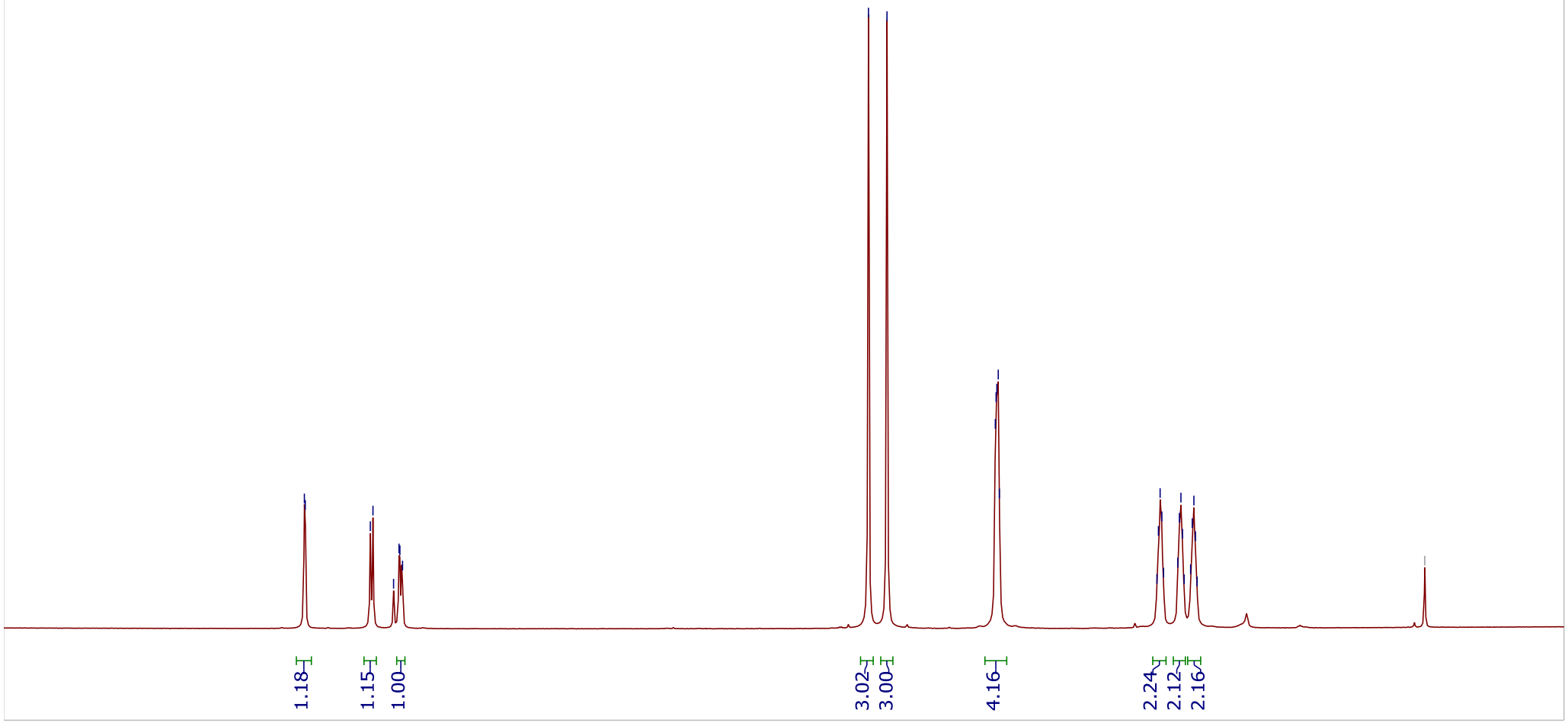
f1 (ppm)

1H NMR (CDCl3, 500 MHz)

7.90 7.89 7.43 7.41 7.27 7.23 7.23 7.21 3.92 3.79 3.03 3.02 3.02 3.01 3.00 1.89 1.88 1.87 1.85 1.84 1.74 1.73 1.72 1.71 1.70 1.65 1.64 1.63 1.62 1.60 0.00

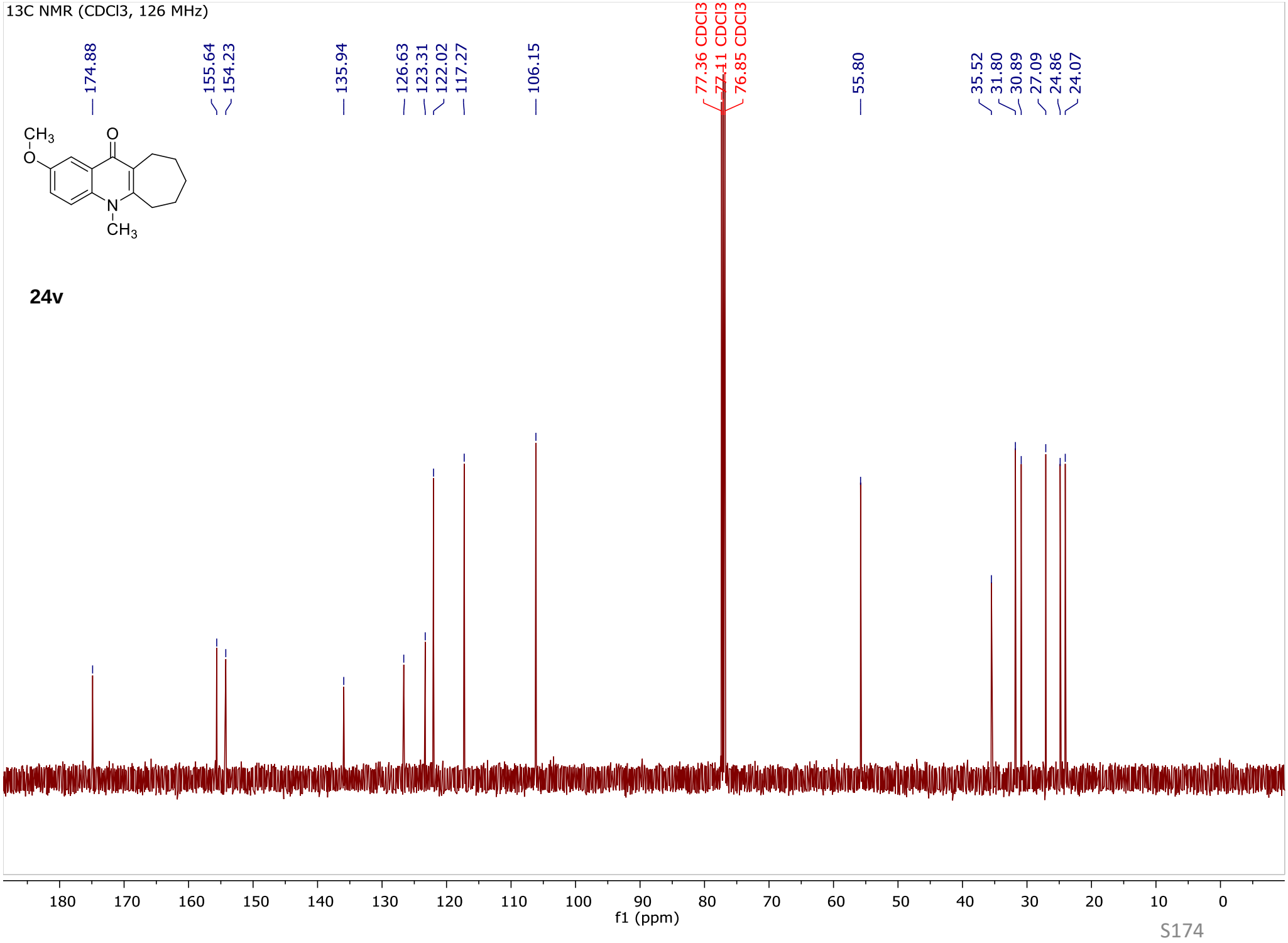


24v

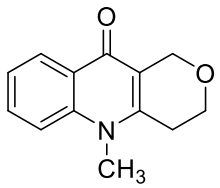


1.18 1.15 1.00 3.02 3.00 4.16 2.24 2.12 2.16

f1 (ppm)

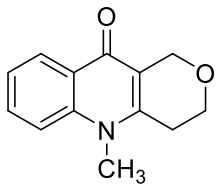

13C NMR (CDCl3, 126 MHz)
174.88
155.64
154.23
135.94
126.63
123.31
122.02
117.27
106.15
77.36 CDCl3
77.11 CDCl3
76.85 CDCl3
55.80
35.52
31.80
30.89
27.09
24.86
24.07
CH3
O
O
N
CH3
24v
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

1H NMR (CDCl3, 400 MHz)

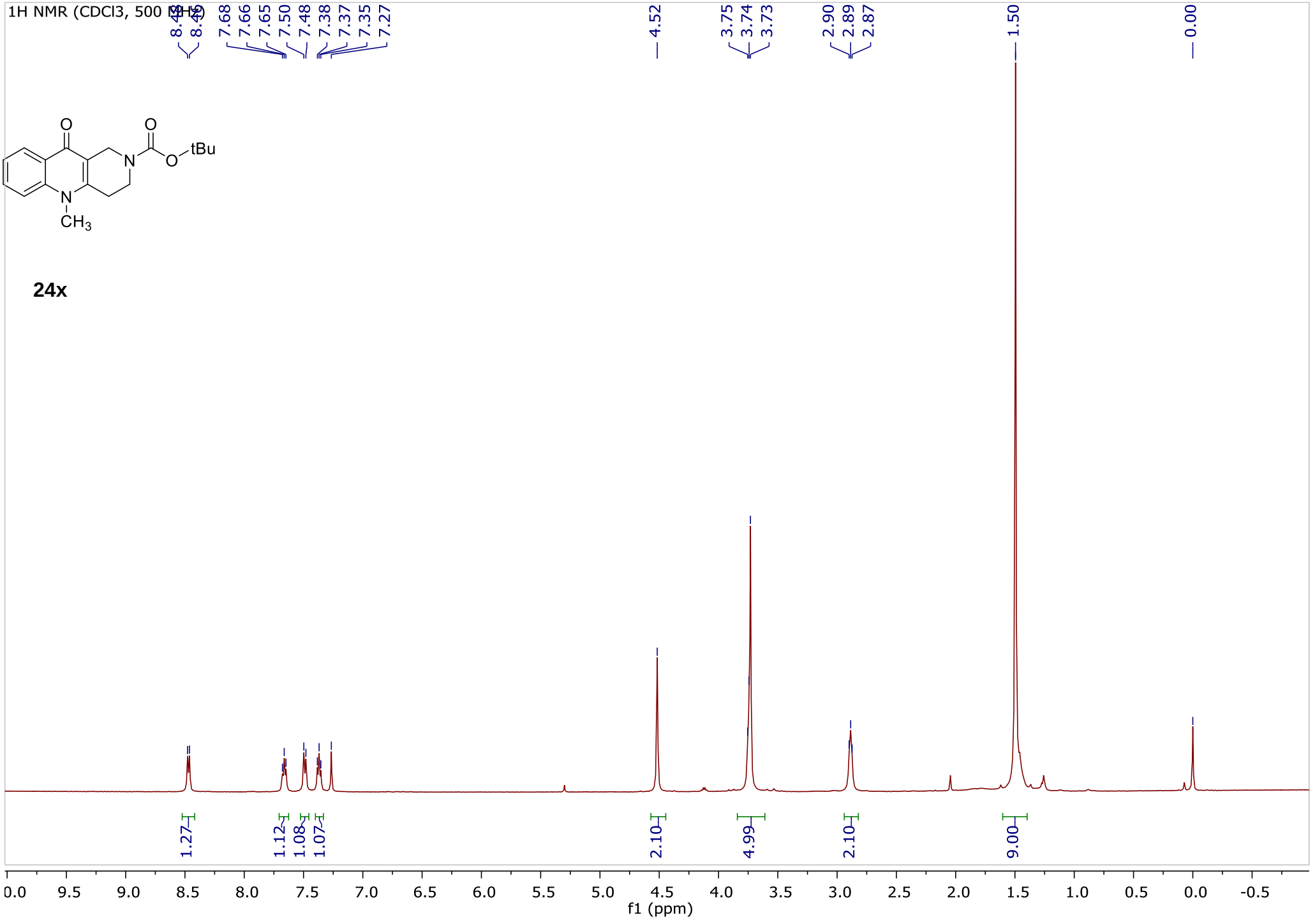


24w

13C (CDCl3, 101 MHz)

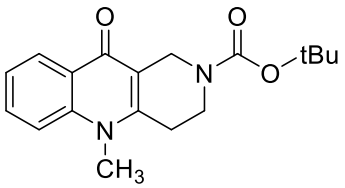


24w

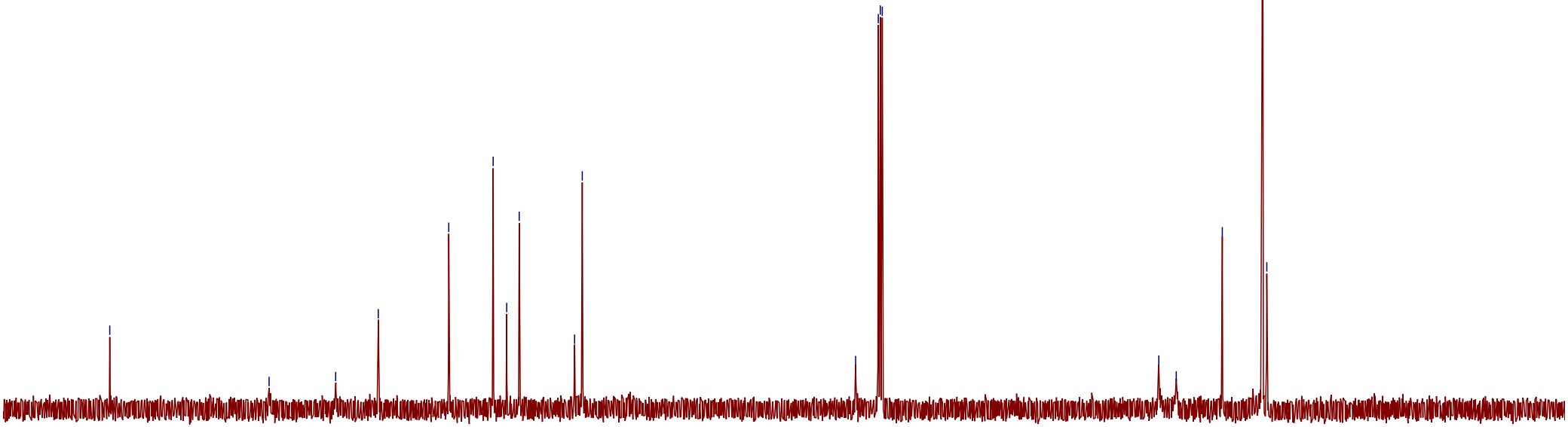

1H NMR (CDCl3, 500 MHz)
8.48
8.47
7.68
7.66
7.65
7.50
7.48
7.38
7.37
7.35
7.27
4.52
3.75
3.74
3.73
2.90
2.89
2.87
1.50
0.00
O
O
tBu
N
O
N
CH3
24x
1.27
1.12
1.08
1.07
2.10
4.99
2.10
9.00
f1 (ppm)

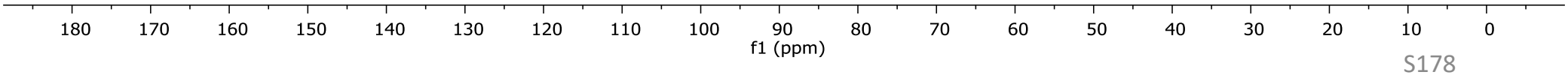
13C NMR (CDCl3, 126 MHz)

175.20
154.93
146.46
141.03
132.06
126.41
124.69
123.10
116.05
115.07
80.29
77.40
77.15
76.89
41.71
39.49
33.63
28.54
27.96

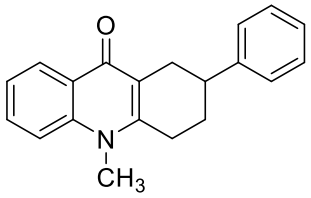


24x



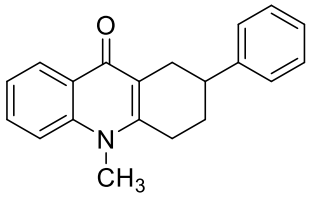


1H NMR (CDCl3, 500 MHz)



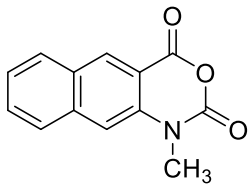
24y

13C NMR (CDCl3, 126 MHz)



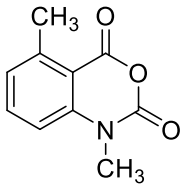
24y

^{1}H NMR (DMSO-d_6, 400 MHz)



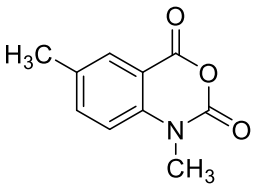
9b

^{1}H NMR (DMSO-d_6, 400 MHz)



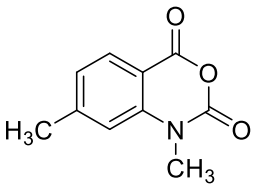
9c

^{1}H NMR (DMSO-d_6, 400 MHz)



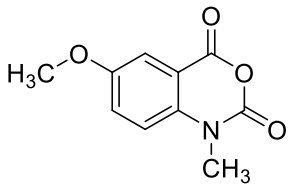
9d

^{1}H NMR (DMSO-d_6, 400 MHz)



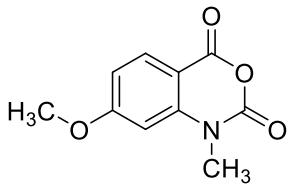
9e

^{1}H NMR (DMSO-d_6, 400 MHz)



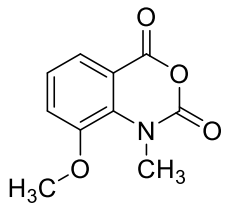
9f

^{1}H NMR (DMSO-d_6, 400 MHz)



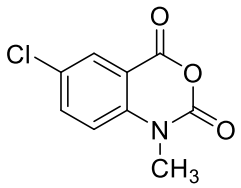
9g

^{1}H NMR (DMSO-d_6, 400 MHz)

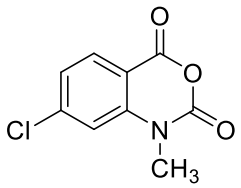


9h

^{1}H NMR (DMSO-d_6, 400 MHz)



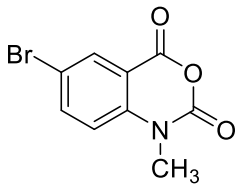
9i


O
O
Cl
N
O
CH3

9j

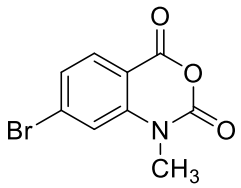
B (d)
7.59
J(1.8)
A (d)
8.00
J(8.4)
C (dd)
7.39
J(8.4, 1.8)
D (s)
3.46
8.01
7.99
7.59
7.58
7.40
7.40
7.38
7.37
0.96
0.98
0.97
3.09
f1 (ppm)

^{1}H NMR (DMSO-d_6, 400 MHz)



9k

^{1}H NMR (DMSO-d_6, 400 MHz)



9l

B (d)
7.71
J(1.7)

A (d)
7.90
J(8.3)

C (dd)
7.52
J(8.3, 1.5)

D (s)
3.46

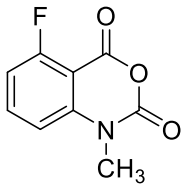
7.91
7.89
7.71
7.70
7.54
7.53
7.53
7.52
7.51

3.46

0.98
1.01
1.02
3.00

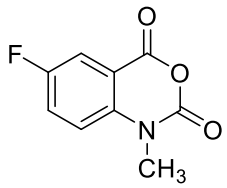
f1 (ppm)

^{1}H NMR (DMSO-d_6, 400 MHz)



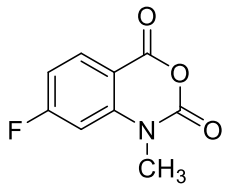
9m

^{1}H NMR (DMSO-d_6, 400 MHz)



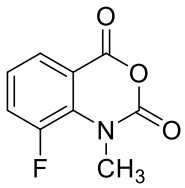
9n

^{1}H NMR (DMSO-d_6, 400 MHz)



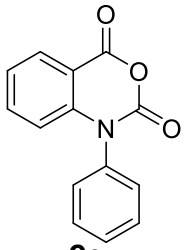
9o

^{1}H NMR (DMSO-d_6, 400 MHz)



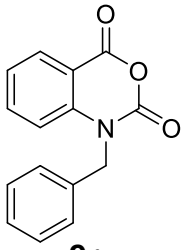
9p

^{1}H NMR (DMSO-d_6, 400 MHz)

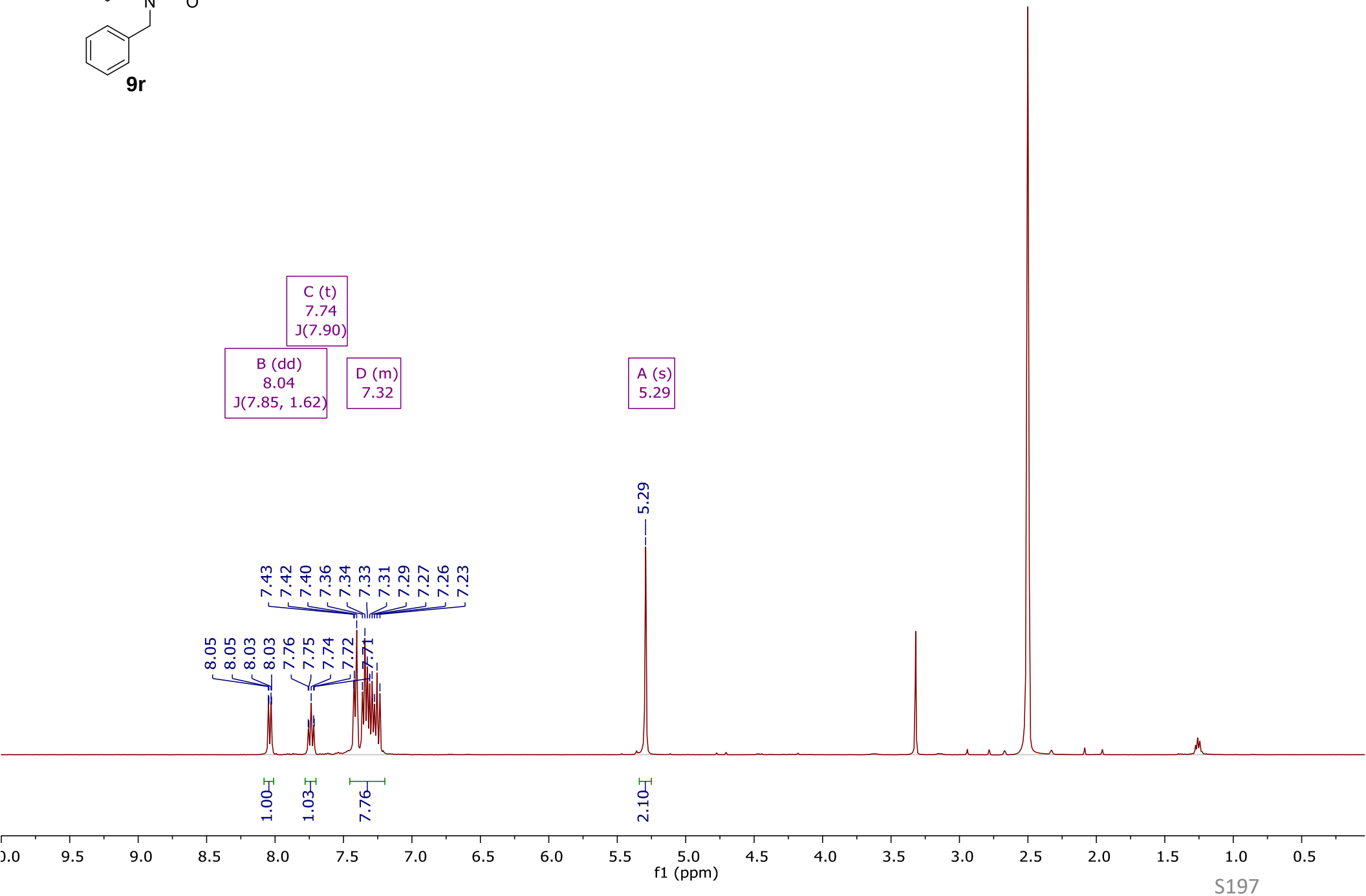


9q

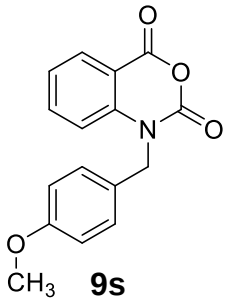
^{1}H NMR (DMSO-d_6, 400 MHz)



9r

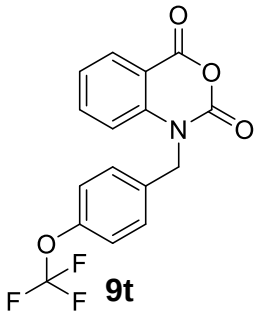


^{1}H NMR (DMSO-d_6, 400 MHz)



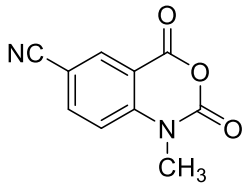
9s

^{1}H NMR (DMSO-d_6, 400 MHz)



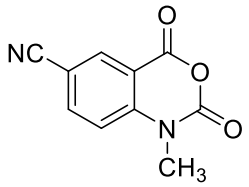
9t

1H NMR (DMSO-d6, 400 MHz)



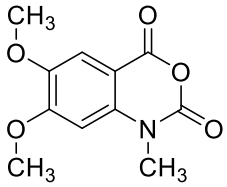
9u

13C NMR (DMSO-d6, 101 MHz)



9u

^{1}H NMR (DMSO-d_6, 400 MHz)



9v

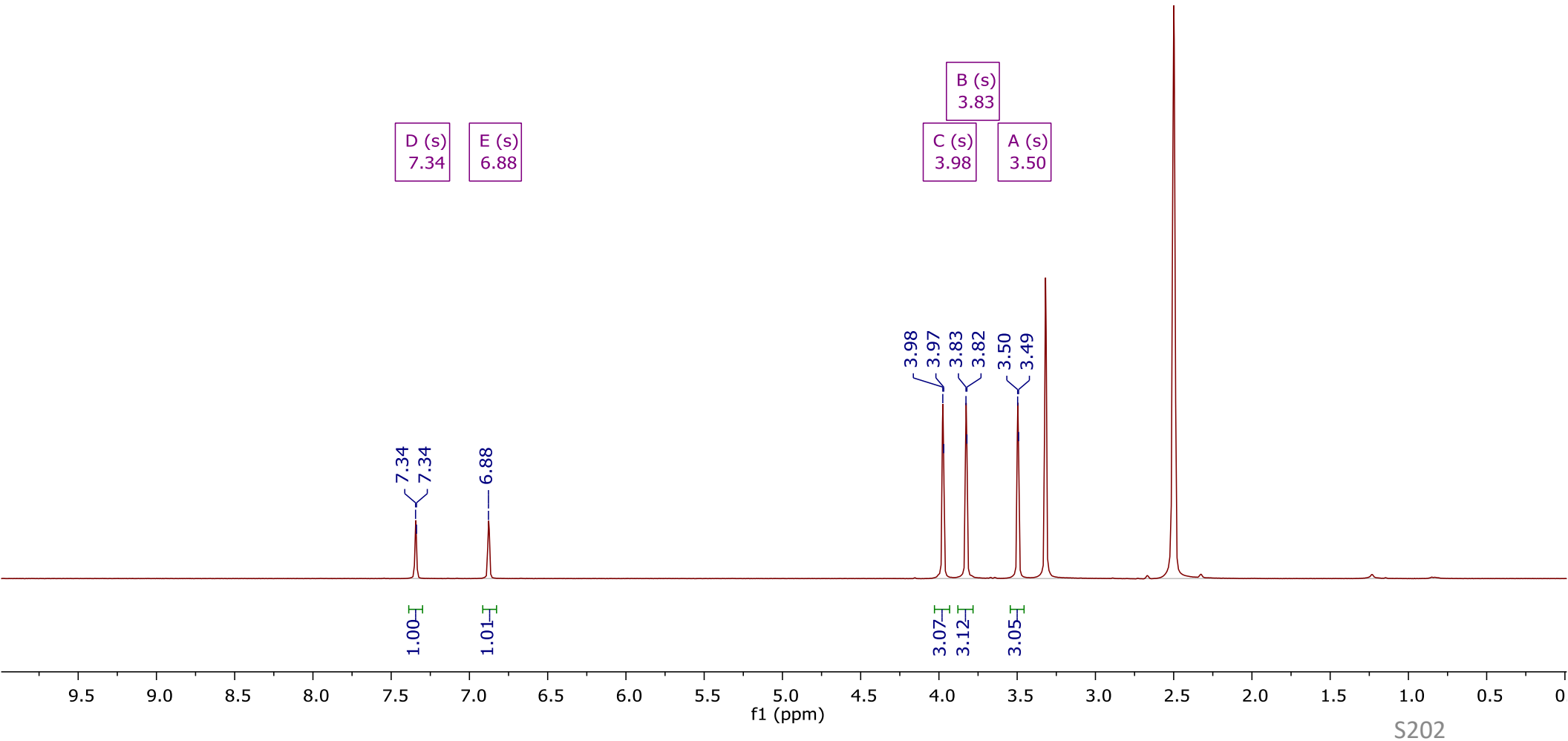
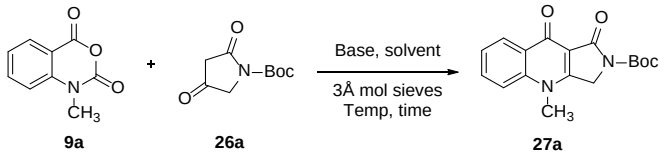


Table S1. Selected experiments in the optimization of annulation between **9a** and **26a**.

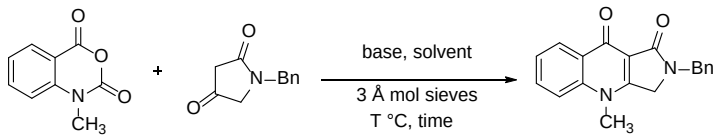


9a **26a** **27a**

	Entry	26a Equiv.	Base ID	Base Equiv.	Solvent	Temp (°C)	Time	Yield 27a
Base screening	**1**	0.9	DBU	1.2	CH_2Cl_2	25	14 h	ND
	2	0.9	DMAP	1.2	CH_2Cl_2	25	14 h	ND
	3	0.9	NaOEt	1.2	CH_2Cl_2	25	14 h	ND
	4	0.9	K_2CO_3	1.2	CH_2Cl_2	25	14 h	ND
	5	0.9	iPr_2NEt	1.2	CH_2Cl_2	25	14 h	ND
	6	0.9	Et_3N	1.2	CH_2Cl_2	25	14 h	ND
Solvent screening	**7**	1	DBU	1.2	CH_2Cl_2	25	15 h	ND
	8	1	DBU	1.2	THF	25	15 h	ND
	9	1	DBU	1.2	Et_2O	25	15 h	ND
	10	1	DBU	1.2	CH_3CN	25	15 h	ND
	11	1	DBU	1.2	DMSO	25	15 h	ND
	12	1	DBU	1.2	DMF	25	15 h	ND
	13	1	DBU	1.2	$PhCH_3$	25	15 h	ND
	14	1	K_2CO_3	1.2	CH_2Cl_2	25	15 h	ND
	15	1	K_2CO_3	1.2	THF	25	15 h	ND
	16	1	K_2CO_3	1.2	Et_2O	25	15 h	ND
	17	1	K_2CO_3	1.2	CH_3CN	25	15 h	ND
	18	1	K_2CO_3	1.2	DMSO	25	15 h	ND
	19	1	K_2CO_3	1.2	DMF	25	15 h	ND
	20	1	K_2CO_3	1.2	$PhCH_3$	25	15 h	ND
	21	1	NEt_3	1.2	CH_2Cl_2	25	15 h	ND
	22	1	NEt_3	1.2	THF	25	15 h	ND
	23	1	NEt_3	1.2	Et_2O	25	15 h	ND
	24	1	NEt_3	1.2	CH_3CN	25	15 h	ND
	25	1	NEt_3	1.2	DMSO	25	15 h	Trace (MS)
	26	1	NEt_3	1.2	DMF	25	15 h	Trace (MS)
	27	1	NEt_3	1.2	$PhCH_3$	25	15 h	ND
Optimization	**28**	3	NEt_3	1.2	DMSO	100	3 h	19%[a]
	29	3	NEt_3	4.0	DMSO	25	240 h	43%[a]
	30	3	NEt_3	4.0	EtOAc	25	96 h	34%[a]
	31	3	NEt_3	4.0	DMF	25	96 h	51%[a]
	32	3	NEt_3	4.0	Dioxane	25	96 h	62%[a]
	33	3	NEt_3	4.0	CH_3CN	25	96 h	61%[a]
	34	1.5	NEt_3	4.0	Dioxane	65	18 h	17%[a]
	35	1.5	NEt_3	4.0	CH_3CN	65	18 h	52%[a]
	36	0.5	NEt_3	4.0	CH_3CN	85	17 h	32%[a]
	37	2.5	NEt_3	0.7	CH_3CN	85	17 h	50%[a]
	38	2.3	TMG	4.0	CH_3CN	45	18 h	ND
	39	2.8	NEt_3	12mol%	CH_3CN	45	18 h	ND
	40	1.9	DMAP	12mol%	CH_3CN	45	18 h	ND
	41	1.9	NEt_3/DMAP	12mol% each	CH_3CN	45	18 h	ND
	42	2.5	NEt_3	4.0	CH_3CN	85	13 h	75%[a, b]
	43	2.5	NEt_3	4.0	CH_3CN	85	13 h	35%[c]
	44	3	NEt_3	4.0	CH_3CN	100[d]	1 h	33%
	45	2.9	NEt_3	4.0	CH_3CN	85[d]	3 h	47%

[a]Isolated yields. DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene. DMAP = 4-Dimethylaminopyridine. TMG = Tetramethylguanidine. [b]Average of three independent experiments. [c]Reaction was run without molecular sieves. [d]Heated by microwave irradiation. ND = **27a** not detected (TLC and/or MS).

Table S2. Selected experiments in the optimization of annulation between **9a** and **26b**.

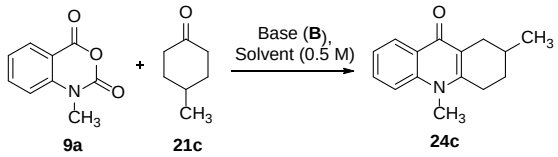


9a **26b** **29a**

entry	**26b** equiv.[a]	base name	base equiv.[a]	solvent	T °C	time	yield[b] **29a**%
1	2.5	NEt_3	2.5	CH_3CN	85	13 h	trace[c]
2	2.5	DBU	4.0	CH_3CN	85	13 h	31
3	1.2	DBU	4.0	CH_3CN	85	13 h	39
4	2.5	DBU	2.0	CH_3CN	85	13 h	47
5	1.2	DBU	2.0	CH_3CN	85	2h	60
6	0.75	DBU	2.0	CH_3CN	85	2h	68
7	0.5	DBU	2.0	CH_3CN	50	2 h	77
8	0.5	DBU	2.0	CH_3CN[d]	50	2 h	79

[a] Relative to **9a** (1.0 equiv). [b] Isolated yields unless otherwise noted. [c] LCMS analysis. [d] 0.05 M concentration

Table S3. Selected experiments in the optimization of annulation between **9a** and **21c**.



Entry	Base (B)	Ketone (21c)/ Base (B) equivalents[a]	Solvent	Reaction temp when base added	Reaction temp after base addition	Reaction time	Yield[b]
1	KHMDS	1.4/1.7	THF	-20 °C	RT	12h	17%
2	KHMDS	1.4/1.7	Et_2O	-20 °C	RT	12h	28%
3	KHMDS	1.4/1.7	Toluene	-20 °C	RT	12h	59%
4	KHMDS	1.4/1.7	Toluene	0 °C	RT	12h	50%
5	KHMDS	2.5/2.7	Toluene	0 °C	110 °C	12h	63%
6	NaHMDS	2.5/2.7	Toluene	0 °C	110 °C	12h	65%
7	LiHMDS	2.5/2.7	Toluene	0 °C	110 °C	12h	84%
8	LiHMDS	1.3/1.4	Toluene	0 °C	110 °C	4h	56%
9	LiHMDS	1.3/1.4	Toluene	0 °C	RT	4h	51%
10	LiHMDS	2.5/2.7	Toluene	0 °C	110 °C	2h	88%
11	LiHMDS	2.5/2.7	Toluene	0 °C	60 °C	2h	78%
12	LiHMDS	2.5/2.7	Toluene	0 °C	RT	2h	75%
13	LiHMDS	2.1/2.3	Toluene	0 °C	80 °C	2h	84%

[a]Relative to anhydride **9a** (1.0 equiv.). [b]Isolated yields; RT = room temperature

Figure S1. In the presence of DBU, but not Et_3N, the ^1H resonance of methylene C3 in **27a** is susceptible to deprotonation with concomitant formation of degradation product(s).

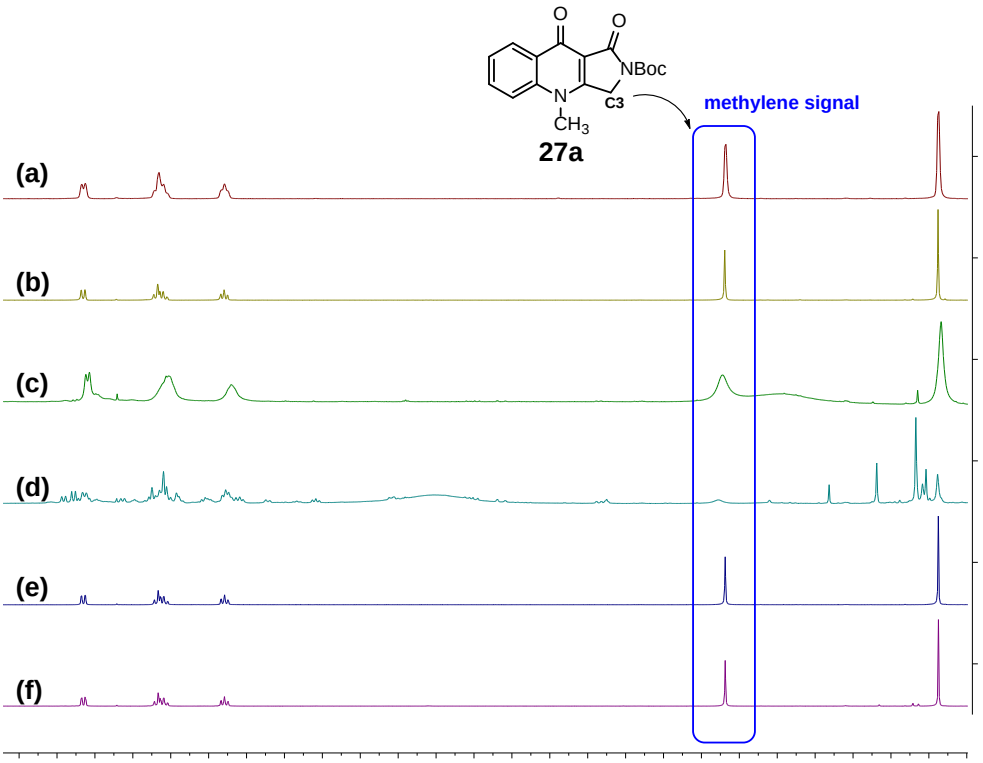


Figure S1. Analysis of the C3 methylene resonance in aligned ^1H NMR spectra (DMSO-d6) of **27a**: (a) rt, no base, t = 10 min; (b) 85 °C, no base, t = 16 h; (c) rt, DBU added, t = 10 min; (d) 85 °C, DBU added, t = 16 h; (e) rt, NEt_3 added, t = 10 min; (f) 85 °C, NEt_3 added, t = 16 h.