BEILSTEIN JOURNAL OF ORGANIC CHEMISTRY

Supporting Information

for

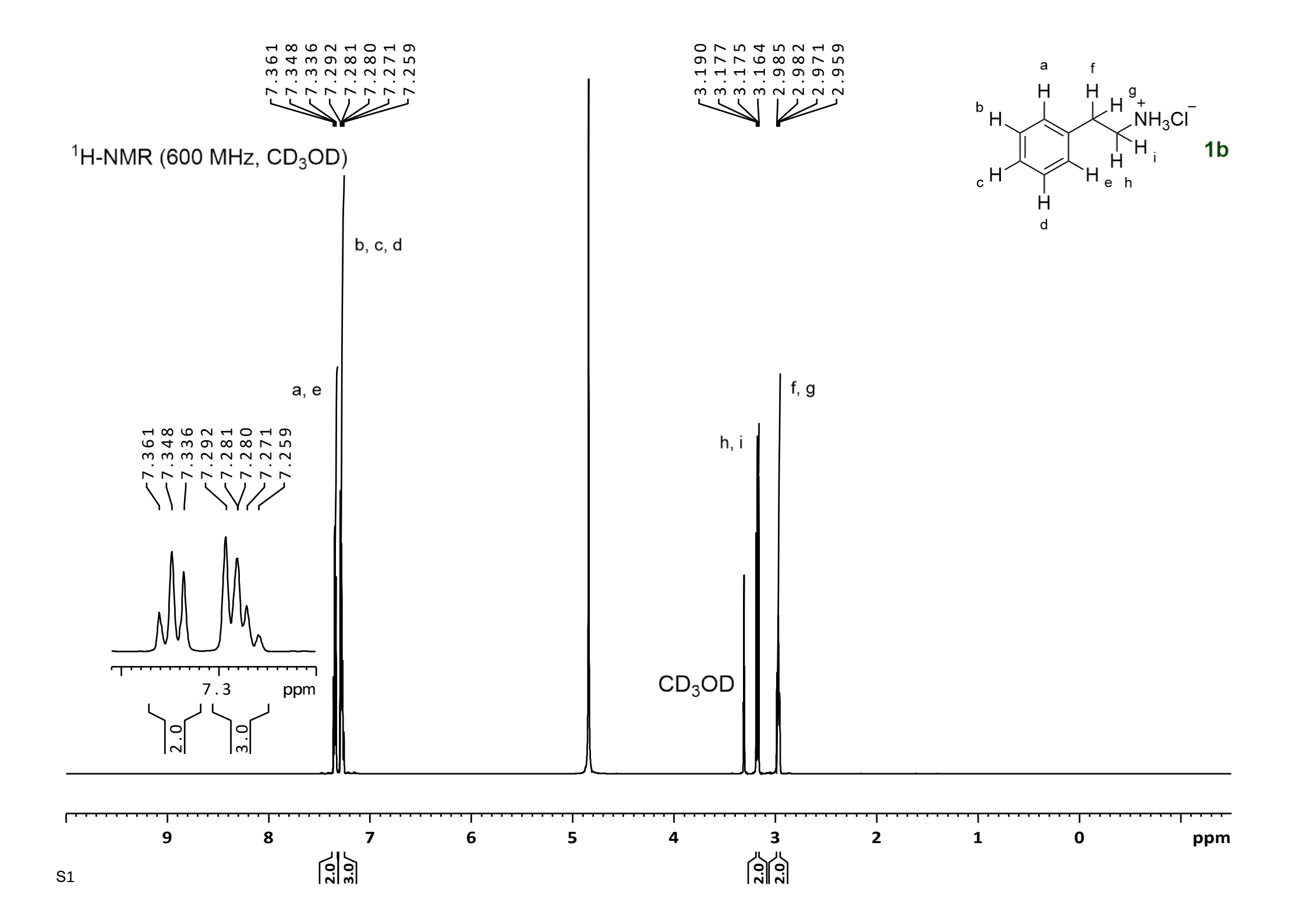
Facile one-pot reduction of β-nitrostyrenes to phenethylamines using sodium borohydride and copper(II) chloride

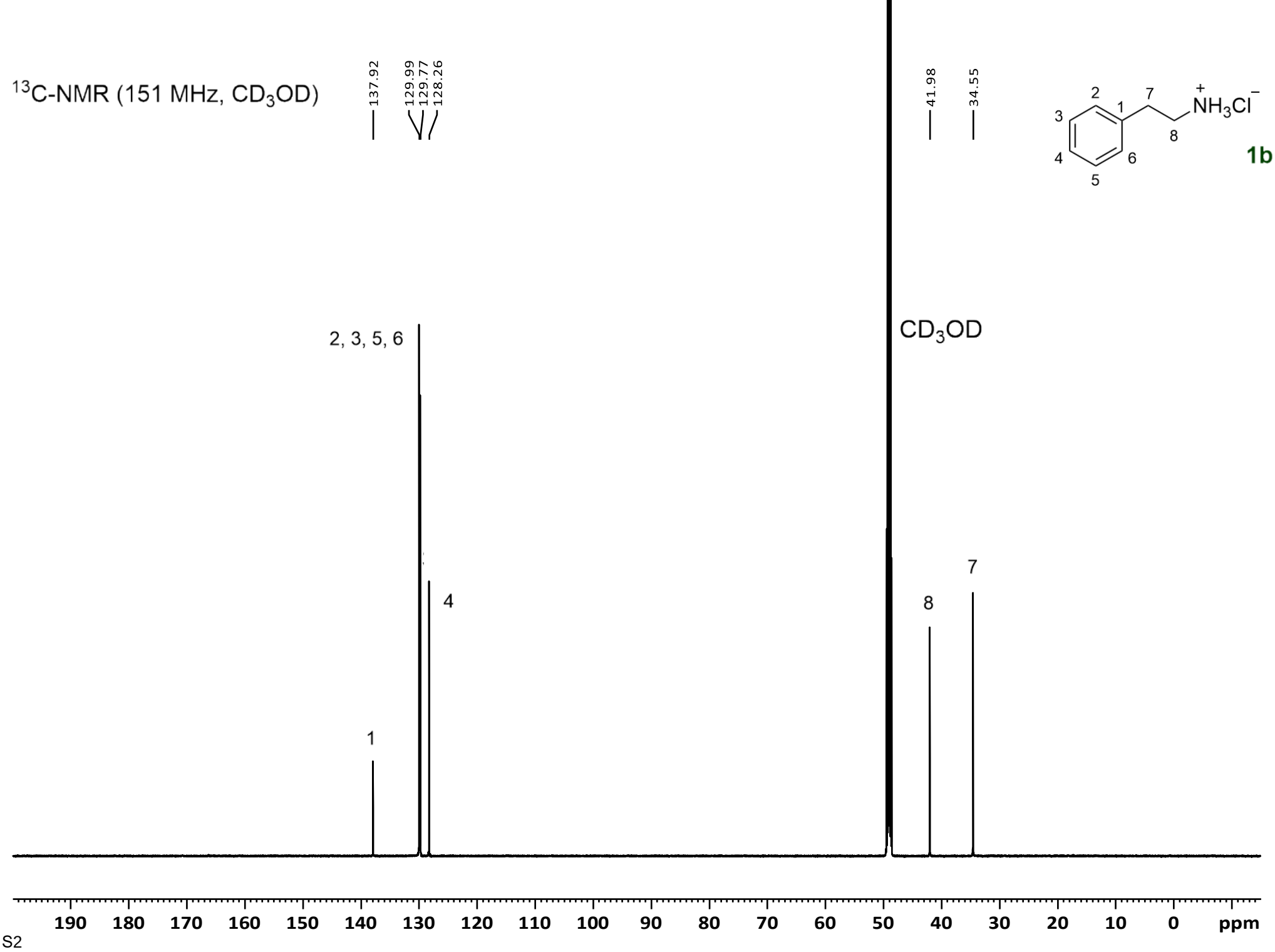
Laura D'Andrea and Simon Jademyr

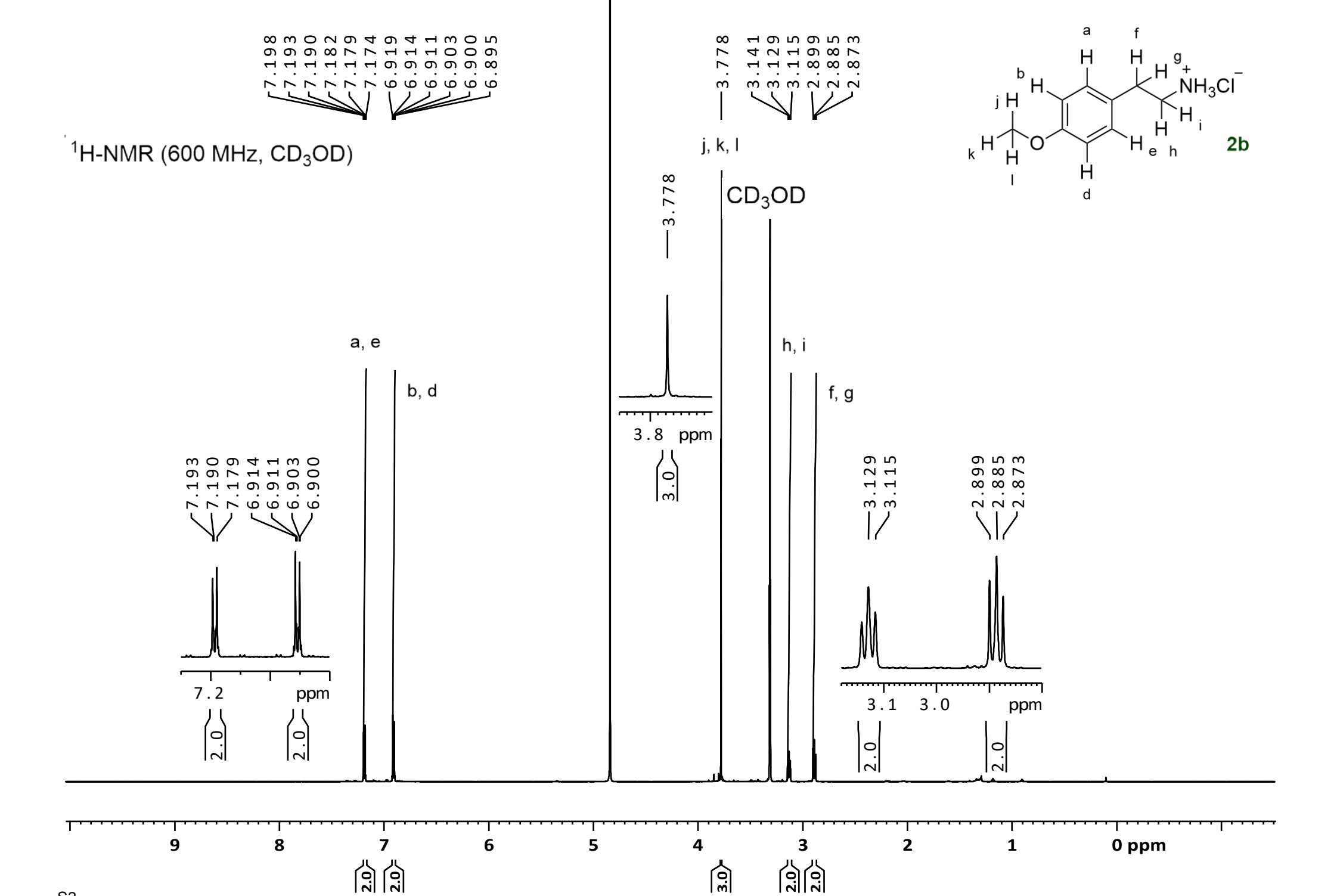
Beilstein J. Org. Chem. **2025,** *21,* 39–46. doi:10.3762/bjoc.21.4

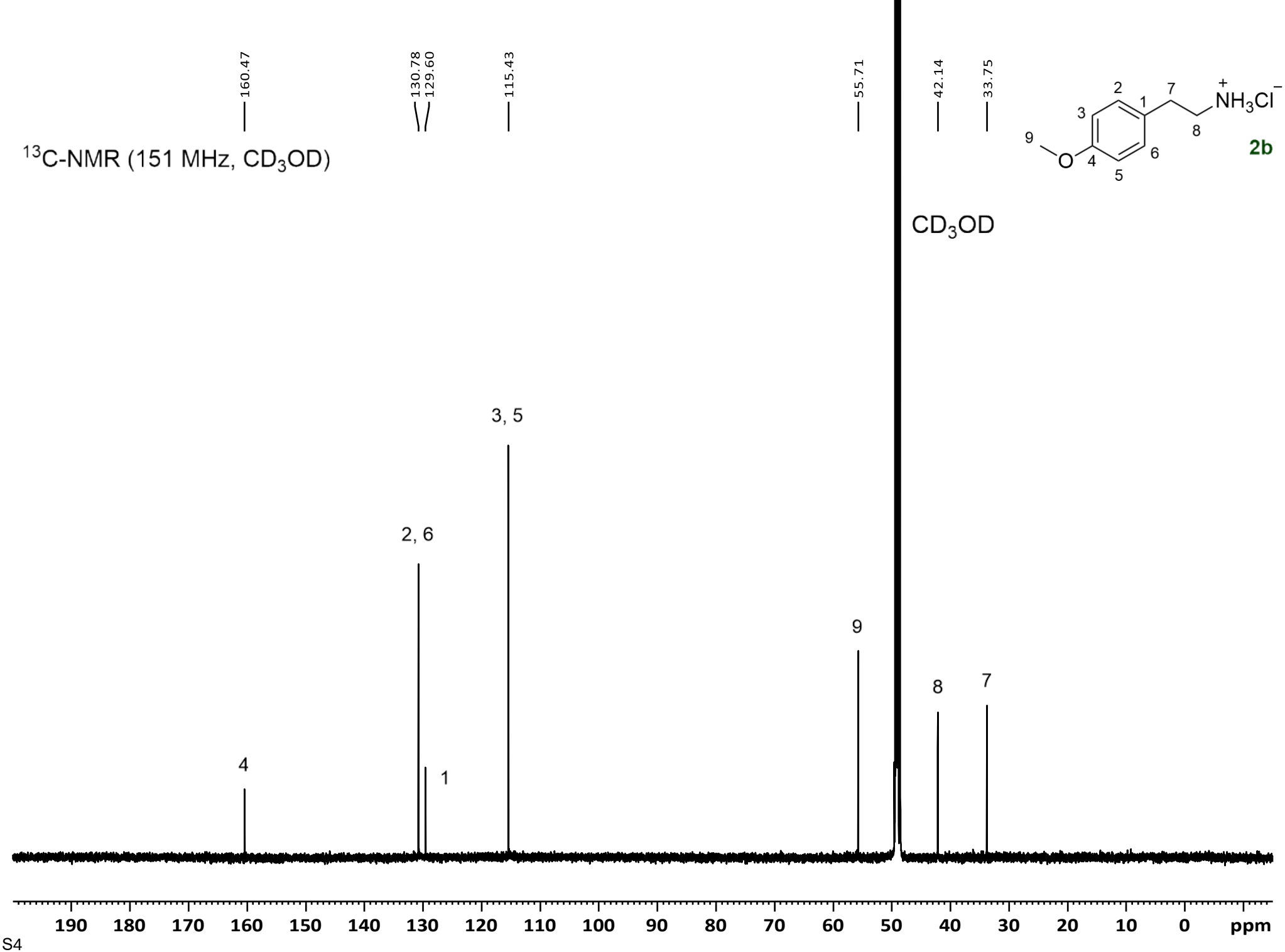
^{1}H and ^{13}C NMR spectra of the synthesized compounds, the optimization table, and ESI-MS spectra for the synthesis of 4b

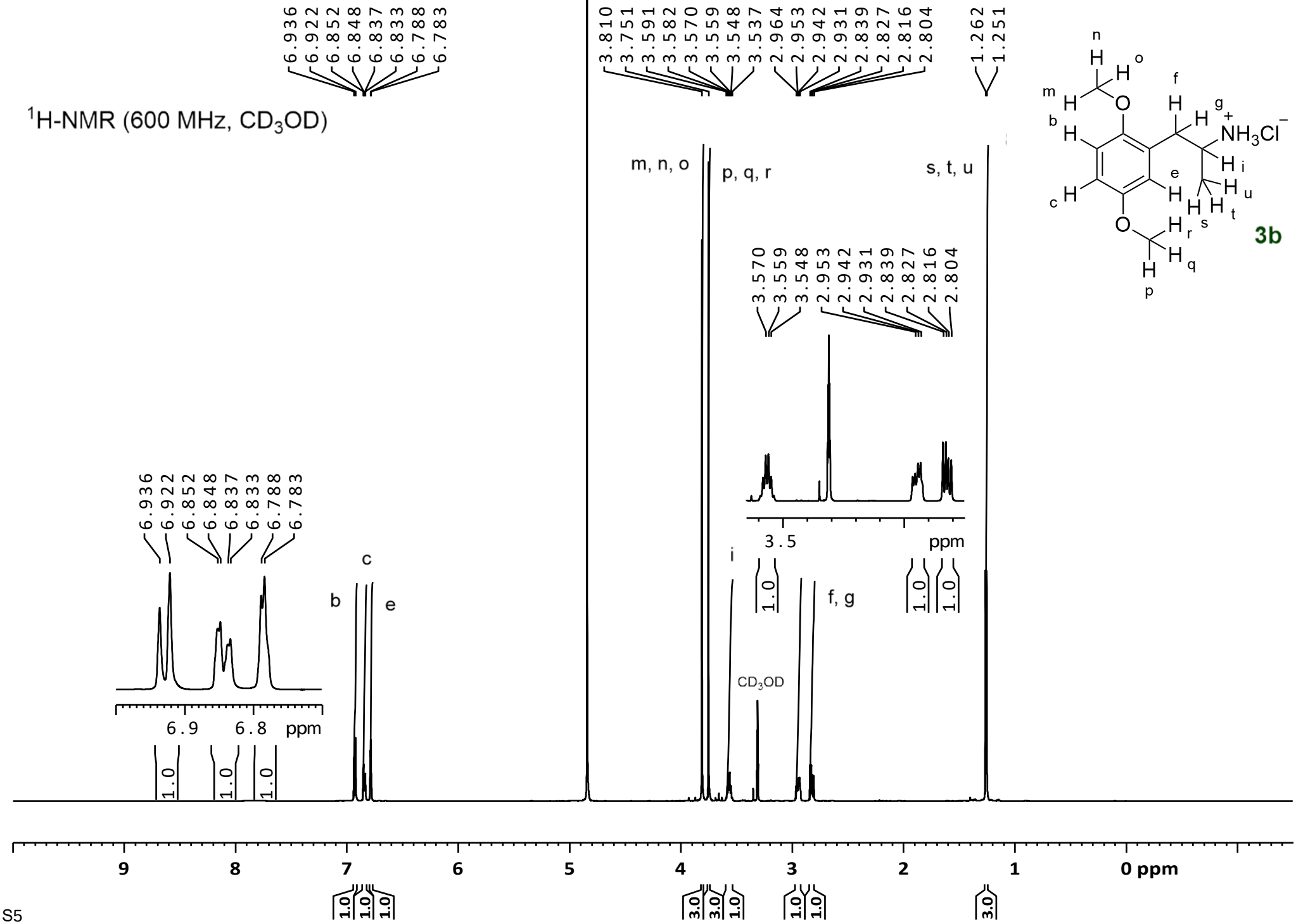
Table of Contents

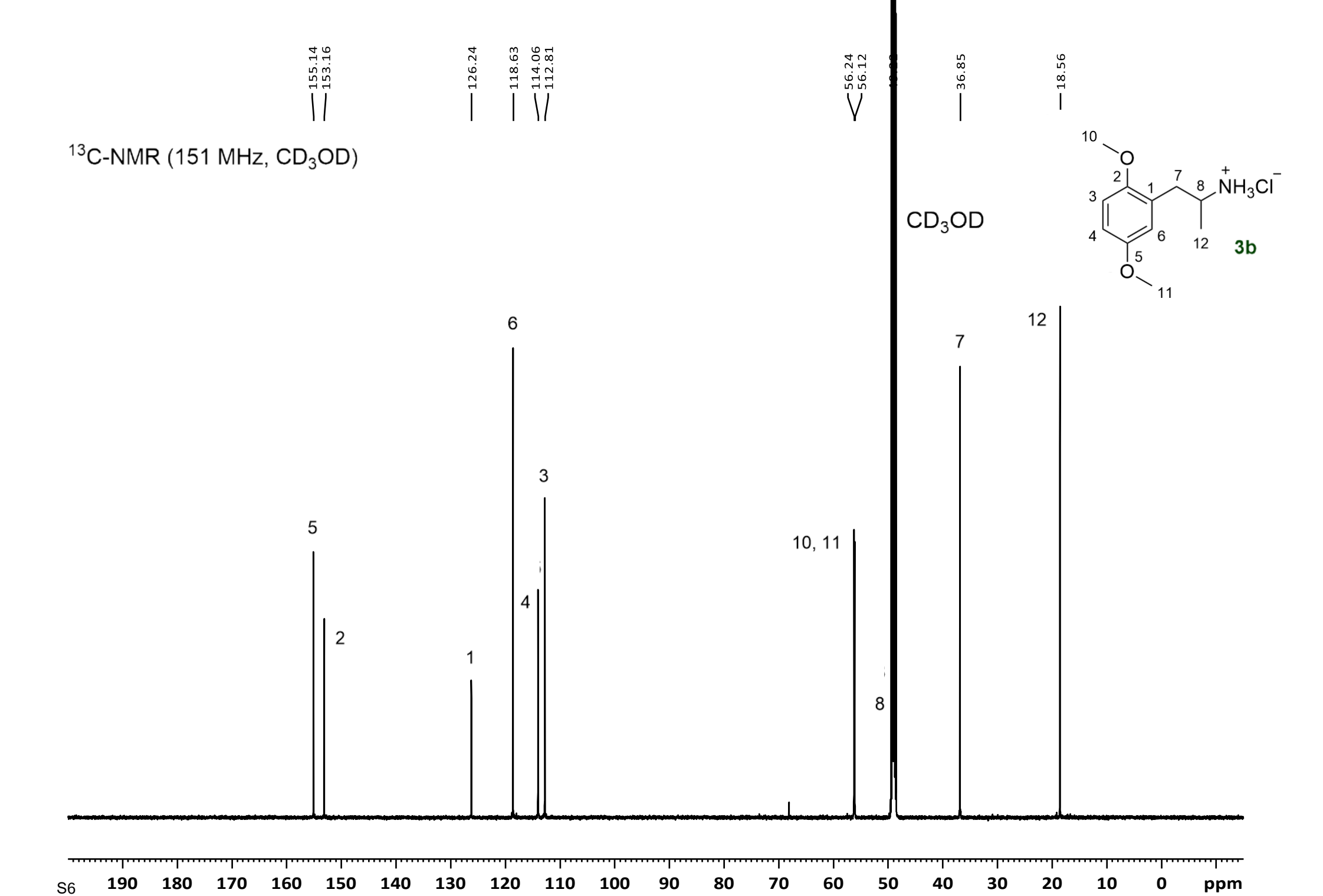

7.361
7.348
7.336
7.292
7.281
7.280
7.271
7.259
3.190
3.177
3.175
3.164
2.985
2.982
2.971
2.959
1H-NMR (600 MHz, CD3OD)
b, c, d
a, e
h, i
f, g
CD3OD
7.3
ppm
2.0
3.0
1b
9
8
7
6
5
4
3
2
1
0
ppm

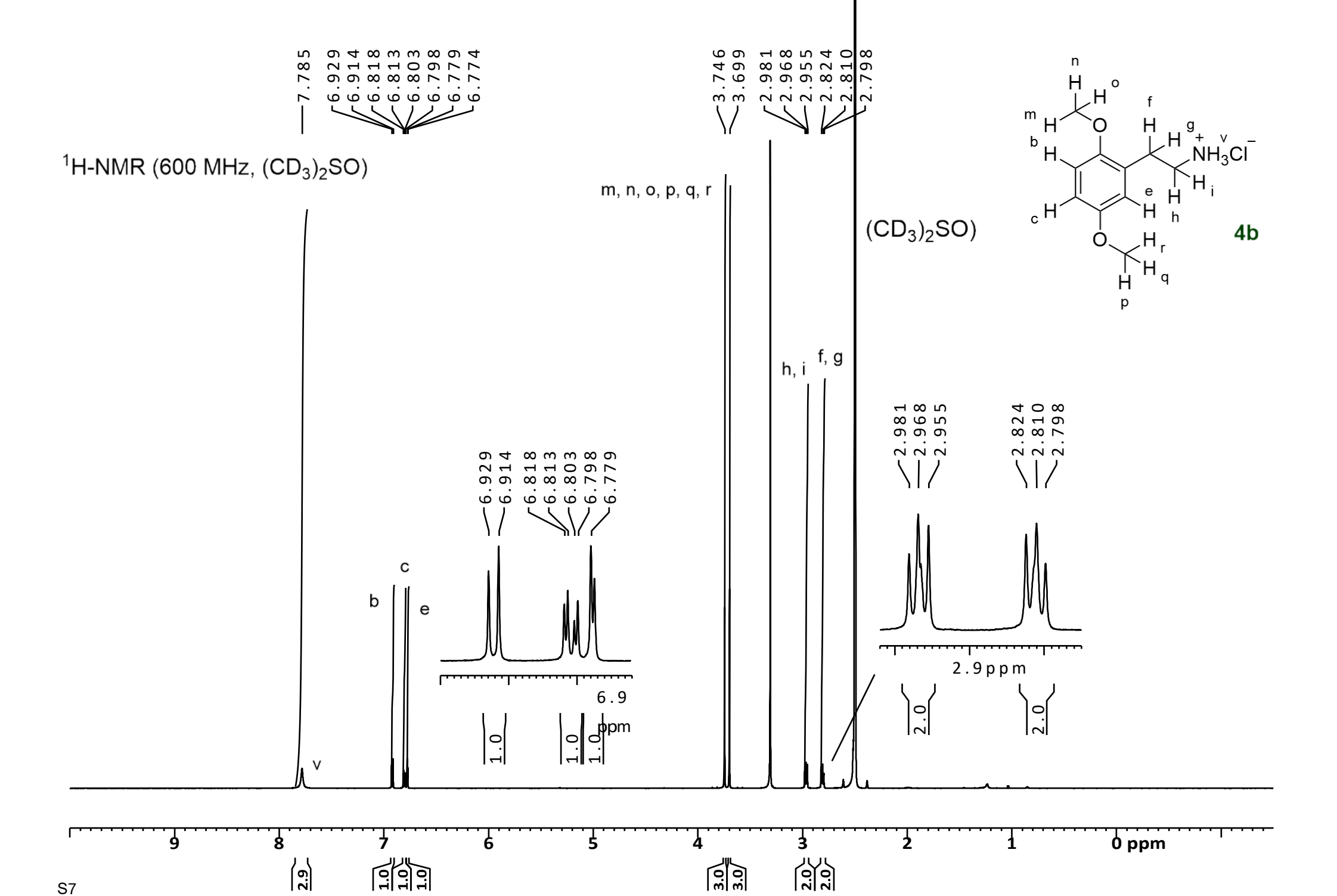

^{13}C-NMR (151 MHz, CD_3OD)
137.92
129.99
129.77
128.26
41.98
34.55
NH_3Cl^-
1b
2, 3, 5, 6
CD_3OD
1
4
8
7
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

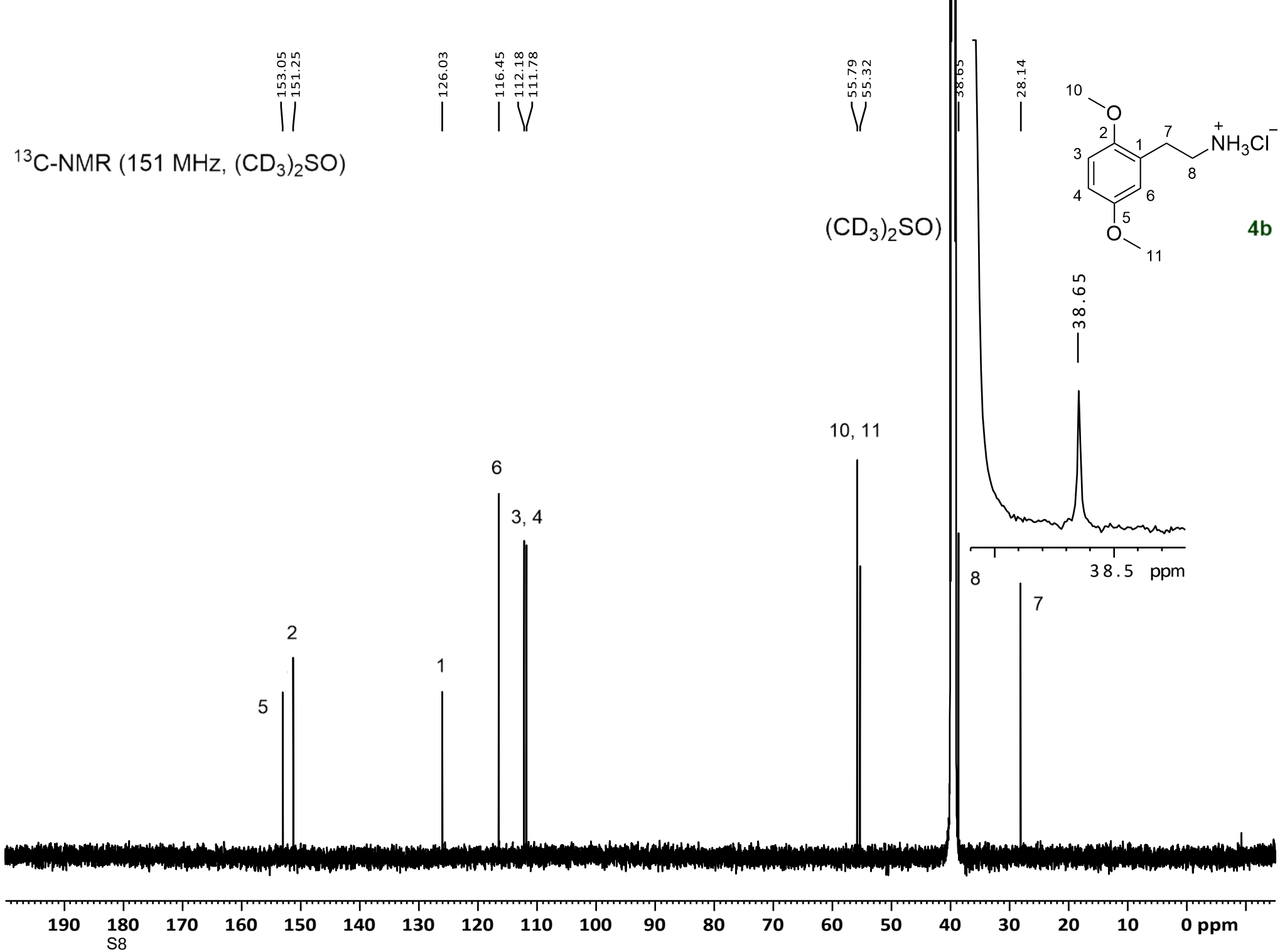

7.198
7.193
7.190
7.182
7.179
7.174
6.919
6.914
6.911
6.903
6.900
6.895
3.778
3.141
3.129
3.115
2.899
2.885
2.873
^{1}H-NMR (600 MHz, CD_3OD)
a, e
b, d
j, k, l
CD_3OD
h, i
f, g
3.8 ppm
7.2 ppm
3.1 3.0 ppm
2.0
3.0
9 8 7 6 5 4 3 2 1 0 ppm
NH_3Cl^-
2b

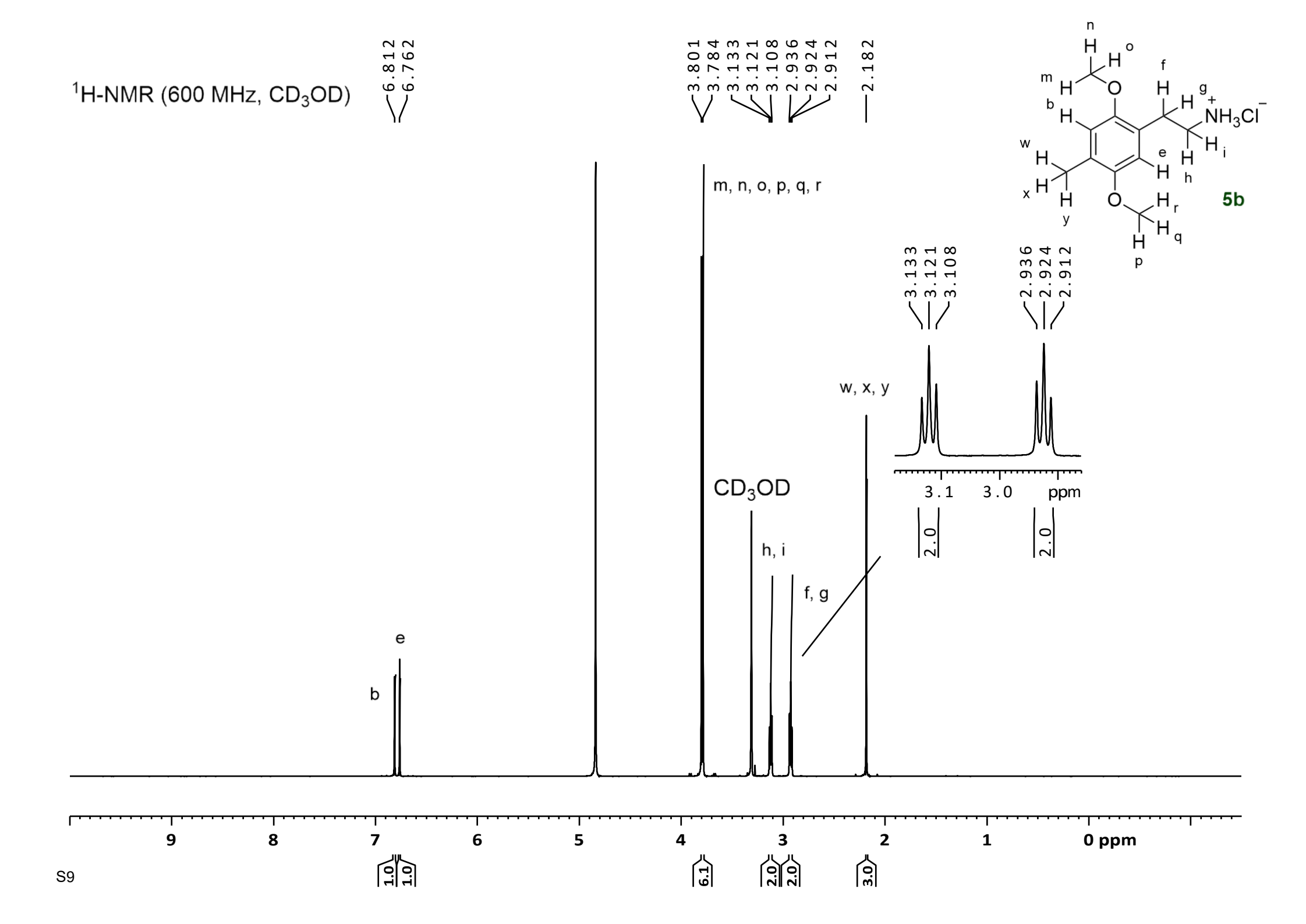

160.47
130.78
129.60
115.43
55.71
42.14
33.75
^{13}C-NMR (151 MHz, CD_3OD)
CD_3OD
2b
4
2, 6
1
3, 5
9
8
7
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

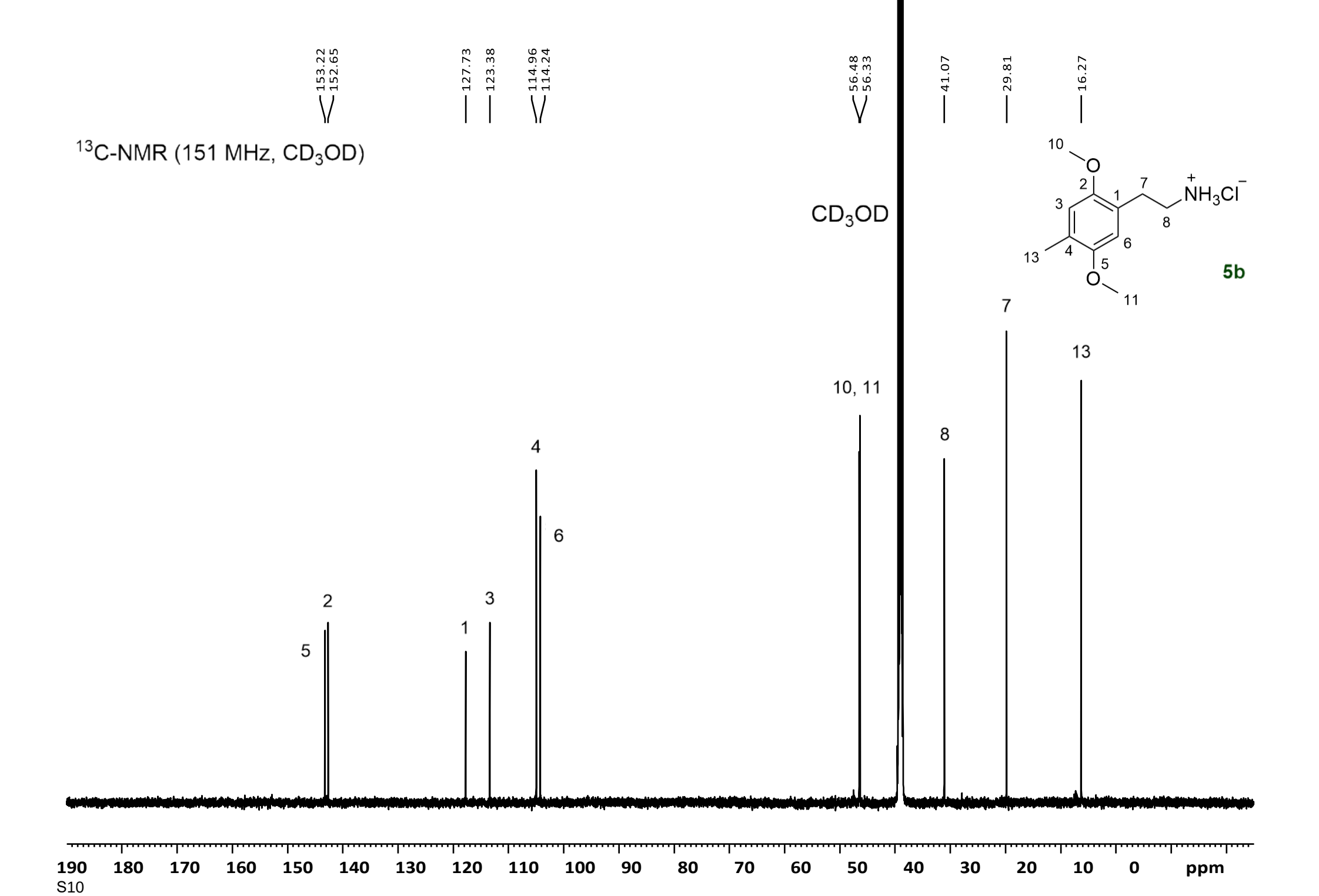

6.936
6.922
6.852
6.848
6.837
6.833
6.788
6.783
3.810
3.751
3.591
3.582
3.570
3.559
3.548
3.537
2.964
2.953
2.942
2.931
2.839
2.827
2.816
2.804
1.262
1.251
1H-NMR (600 MHz, CD3OD)
m, n, o
p, q, r
s, t, u
b
c
e
i
f, g
CD3OD
6.9
6.8
ppm
3.5
ppm
1.0
3.0
9
8
7
6
5
4
3
2
1
0 ppm
NH3Cl
3b

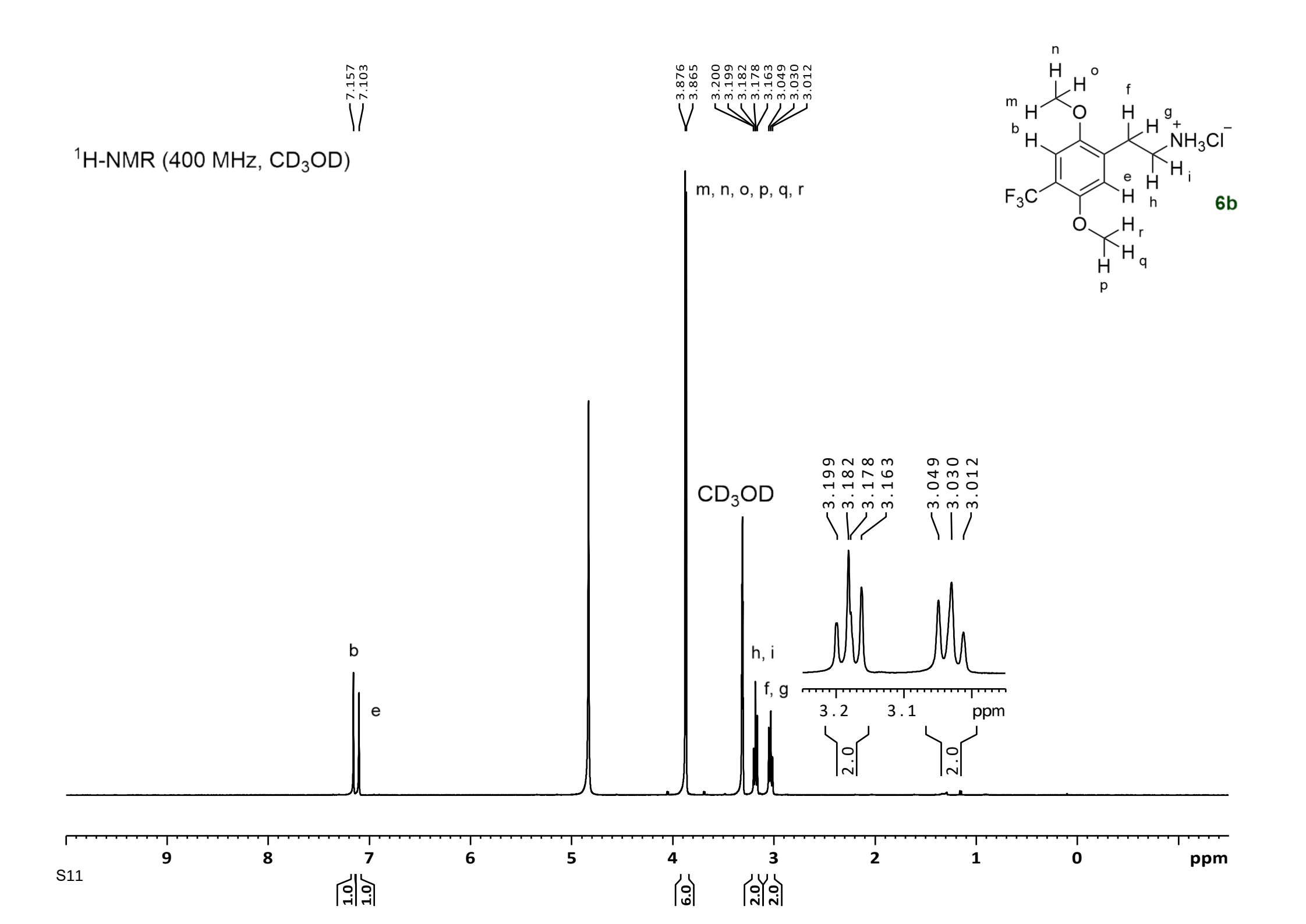

155.14
153.16
126.24
118.63
114.06
112.81
56.24
56.12
36.85
18.56
13C-NMR (151 MHz, CD3OD)
CD3OD
3b
5
2
1
6
4
3
10, 11
8
7
12
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

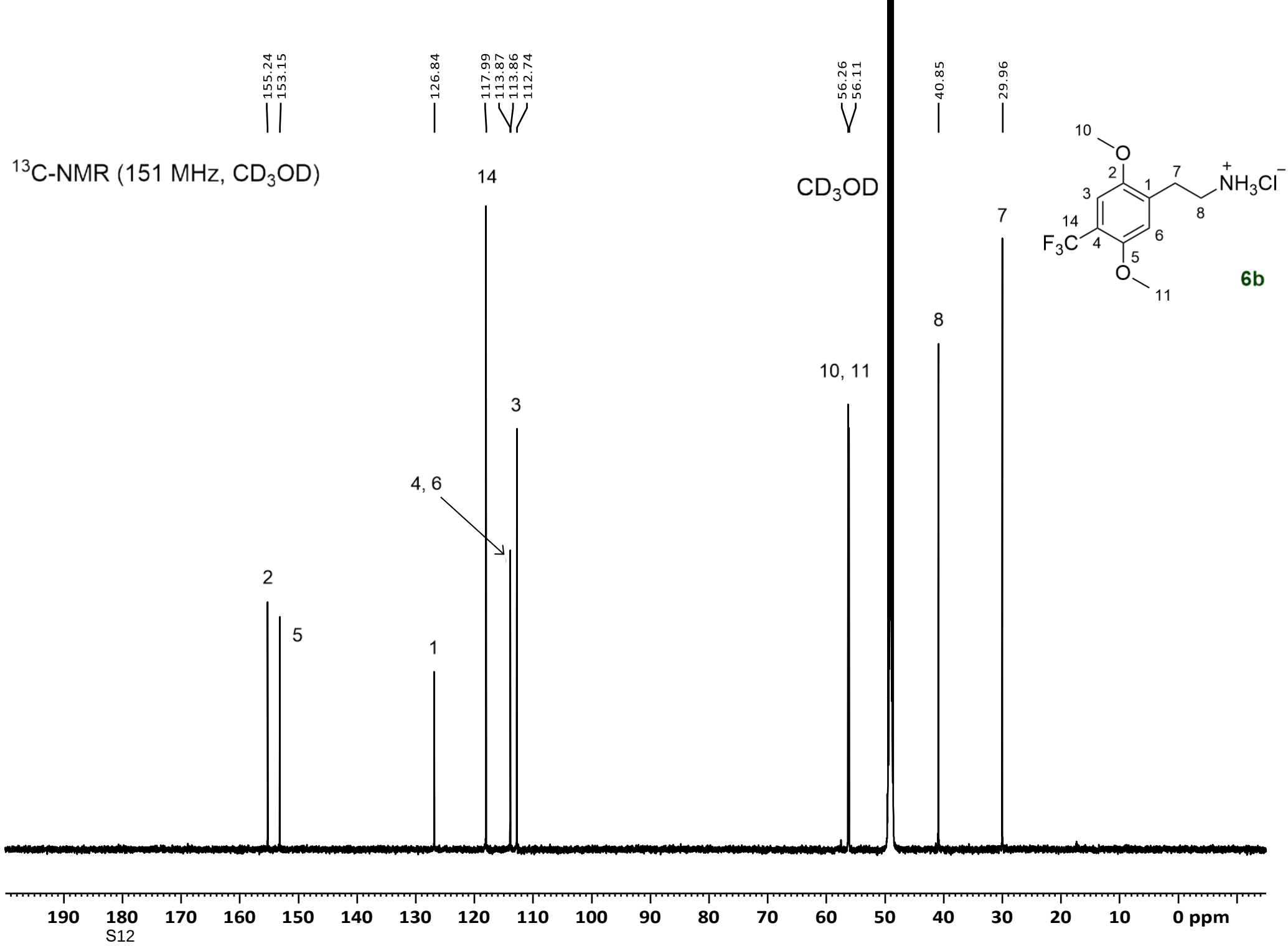

7.785
6.929
6.914
6.818
6.813
6.803
6.798
6.779
6.774
3.746
3.699
2.981
2.968
2.955
2.824
2.810
2.798
1H-NMR (600 MHz, (CD3)2SO)
m, n, o, p, q, r
(CD3)2SO)
h, i
f, g
b
c
e
v
6.9 ppm
2.9 ppm
1.0
2.0
3.0
2.9
0 ppm
4b

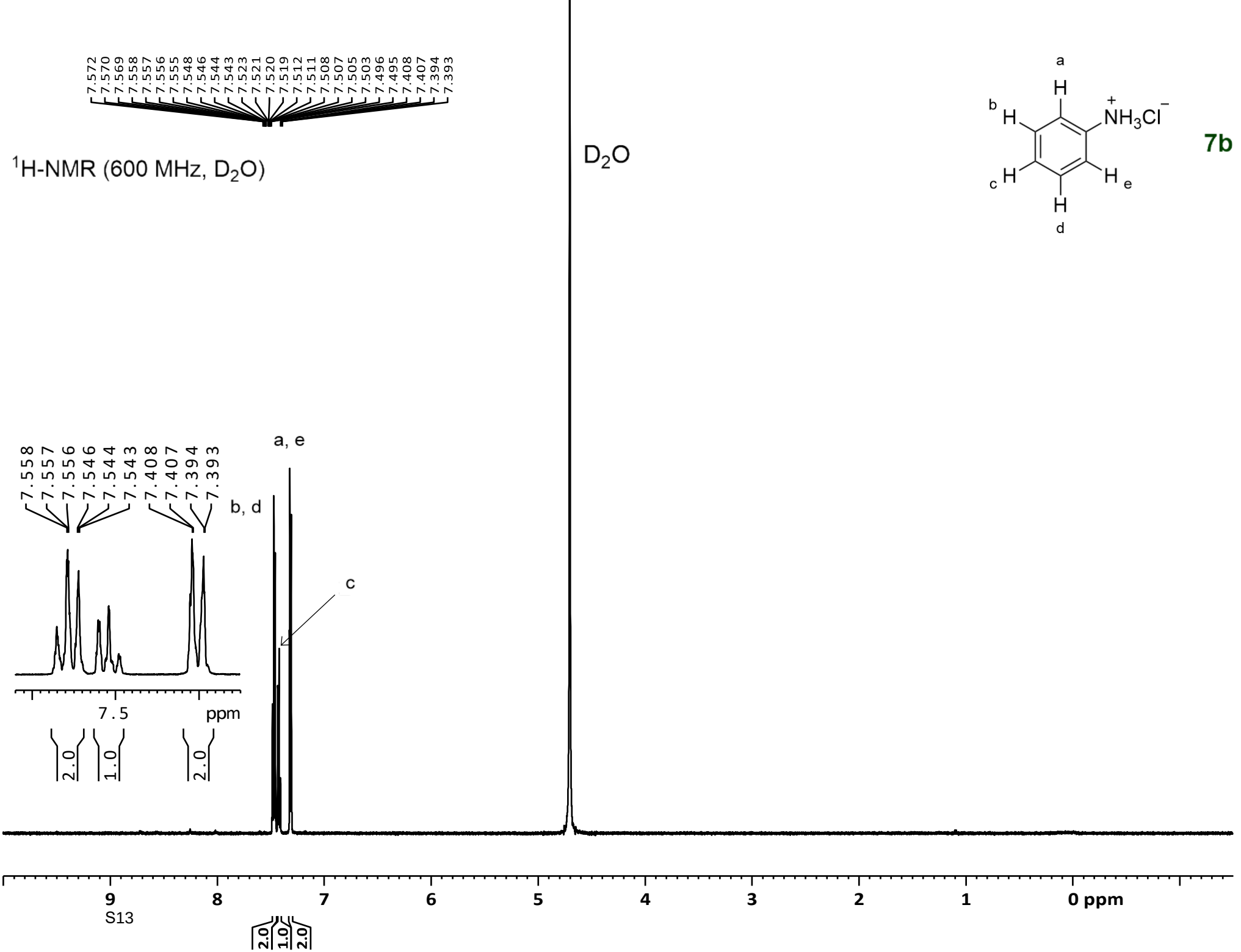

153.05
151.25
126.03
116.45
112.18
111.78
55.79
55.32
38.65
28.14
^{13}C-NMR (151 MHz, $(CD_3)_2SO$)
$(CD_3)_2SO$)
10, 11
6
3, 4
2
5
1
8
7
38.65
38.5 ppm
4b
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


^{1}H-NMR (600 MHz, CD_3OD)
6.812
6.762
3.801
3.784
3.133
3.121
3.108
2.936
2.924
2.912
2.182
m, n, o, p, q, r
w, x, y
CD_3OD
h, i
f, g
e
b
5b
3.1
3.0
ppm
2.0
2.0
9
8
7
6
5
4
3
2
1
0 ppm
1.0
1.0
6.1
2.0
2.0
3.0


153.22
152.65
127.73
123.38
114.96
114.24
56.48
56.33
41.07
29.81
16.27
13C-NMR (151 MHz, CD3OD)
CD3OD
10
O
2
1
7
+
NH3Cl−
3
8
6
13
4
5
O
11
5b
7
13
10, 11
8
4
6
2
3
1
5
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

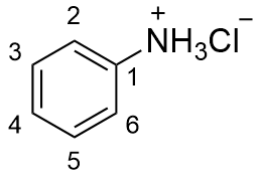

7.157
7.103
3.876
3.865
3.200
3.199
3.182
3.178
3.163
3.049
3.030
3.012
^{1}H-NMR (400 MHz, CD_3OD)
m, n, o, p, q, r
CD_3OD
b
e
h, i
f, g
3.199
3.182
3.178
3.163
3.049
3.030
3.012
3.2
3.1
ppm
2.0
2.0
6b
9
8
7
6
5
4
3
2
1
0
ppm
1.0
1.0
6.0
2.0
2.0


155.24
153.15
126.84
117.99
113.87
113.86
112.74
56.26
56.11
40.85
29.96
^{13}C-NMR (151 MHz, CD_3OD)
CD_3OD
14
7
10, 11
8
3
4, 6
2
5
1
10
O
2
1
7
NH_3Cl^-
3
8
14
6
F_3C
4
5
O
11
6b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

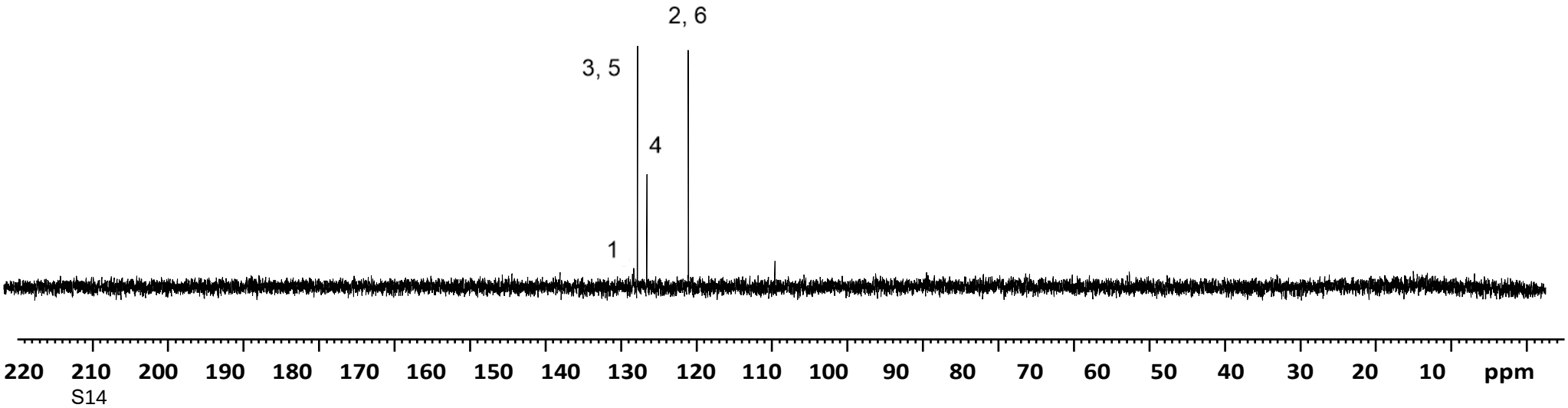

7.572
7.570
7.569
7.558
7.557
7.556
7.555
7.548
7.546
7.544
7.543
7.523
7.521
7.520
7.519
7.512
7.511
7.508
7.507
7.505
7.503
7.496
7.495
7.408
7.407
7.394
7.393
^{1}H-NMR (600 MHz, D_2O)
D_2O
a
b
c
d
e
NH_3Cl^-
7b
7.558
7.557
7.556
7.546
7.544
7.543
7.408
7.407
7.394
7.393
b, d
a, e
c
7.5
ppm
2.0
1.0
2.0
9
8
7
6
5
4
3
2
1
0 ppm
2.0
1.0
2.0

^{13}C-NMR (151 MHz, D_2O)

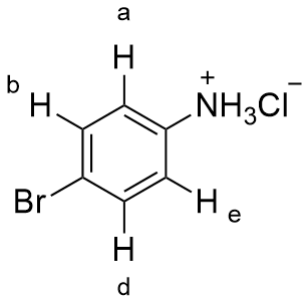
130.64
130.07
128.67
122.50



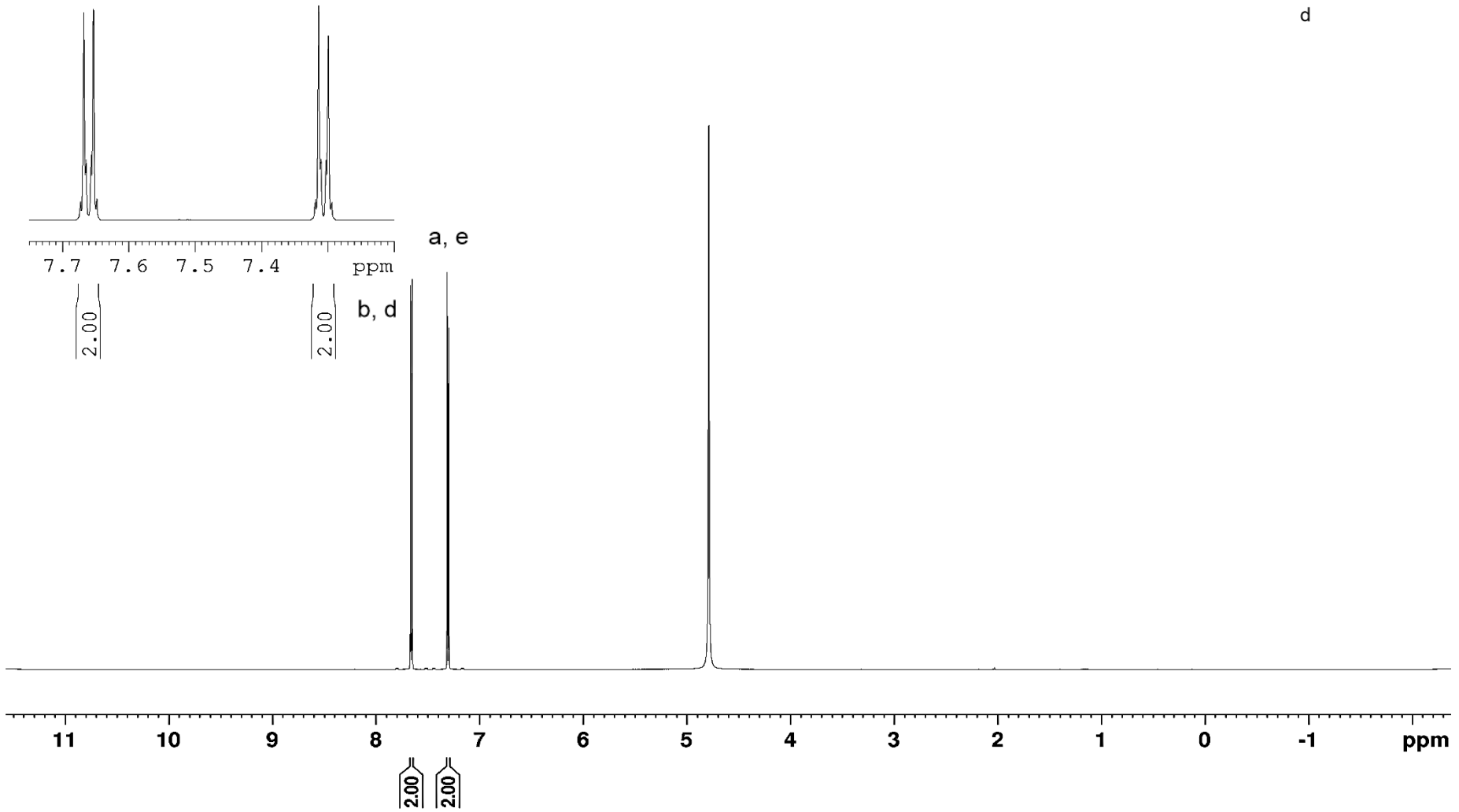
7b



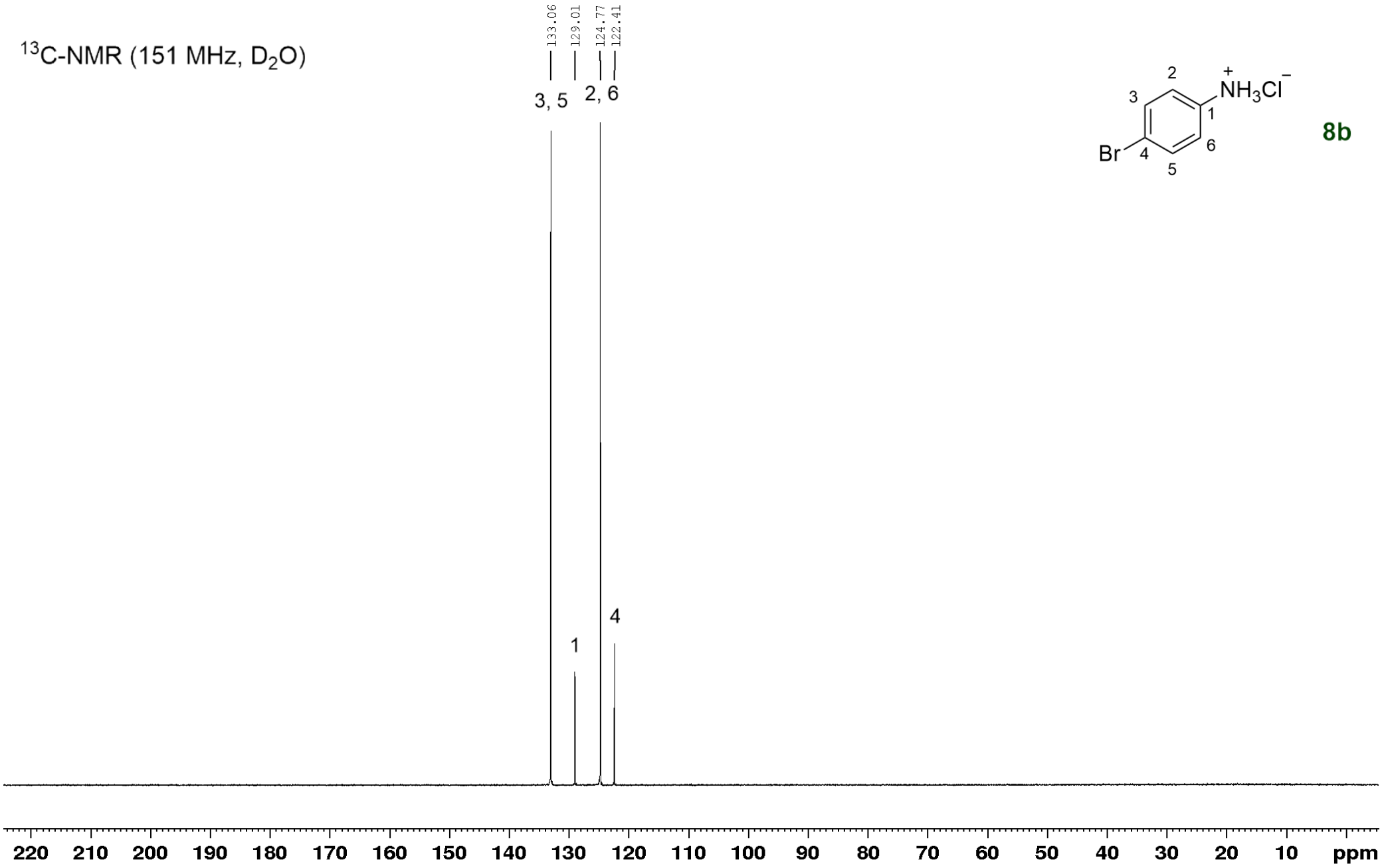
^{1}H-NMR (600 MHz, D_2O)



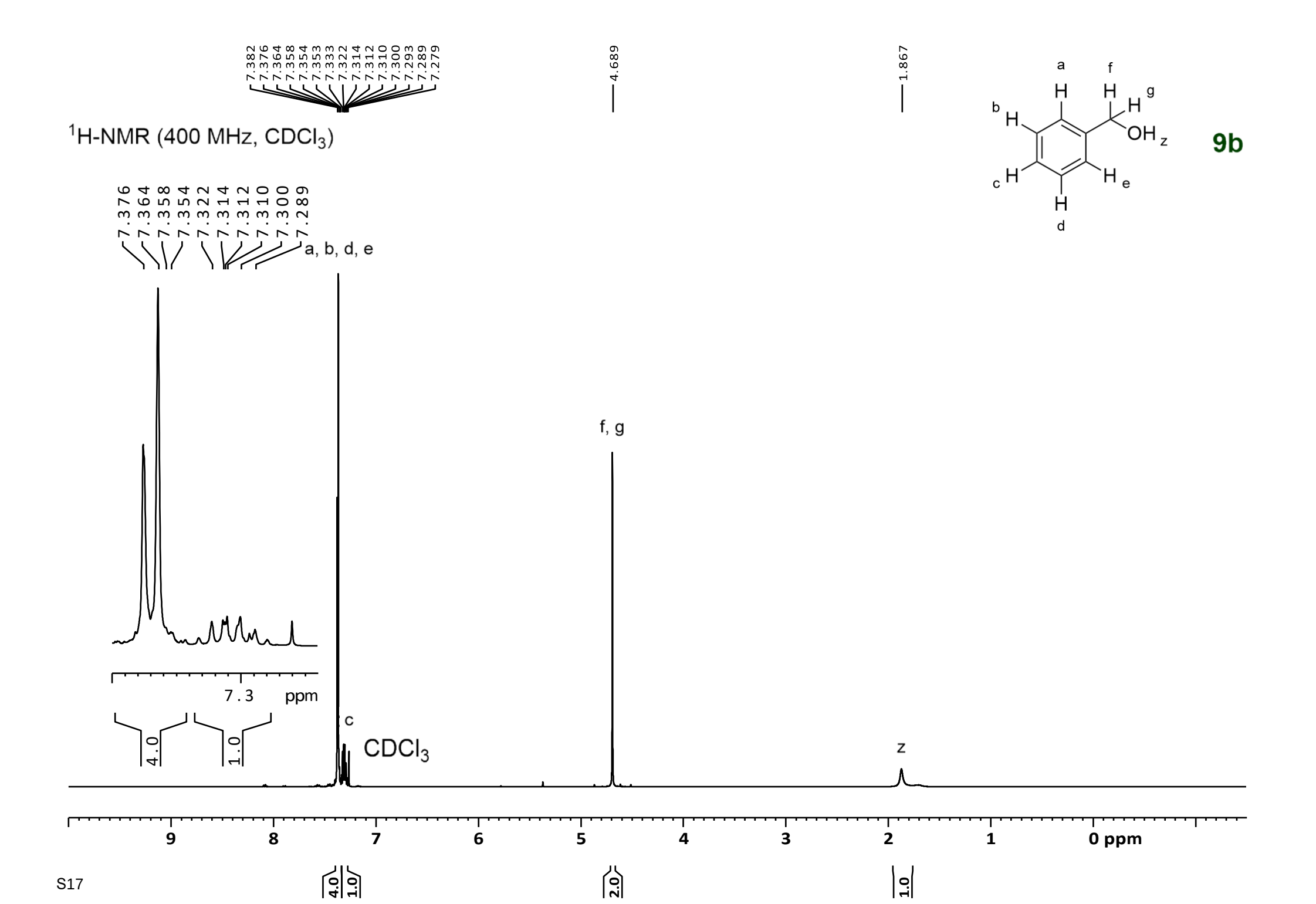
8b



^{13}C-NMR (151 MHz, D_2O)



8b


7.382
7.376
7.364
7.358
7.354
7.353
7.333
7.322
7.314
7.312
7.310
7.300
7.293
7.289
7.279
4.689
1.867
1H-NMR (400 MHz, CDCl3)
a
f
b
g
OH
z
c
e
d
9b
7.376
7.364
7.358
7.354
7.322
7.314
7.312
7.310
7.300
7.289
a, b, d, e
7.3
ppm
4.0
1.0
c
CDCl3
f, g
z
9
8
7
6
5
4
3
2
1
0 ppm
4.0
1.0
2.0
1.0

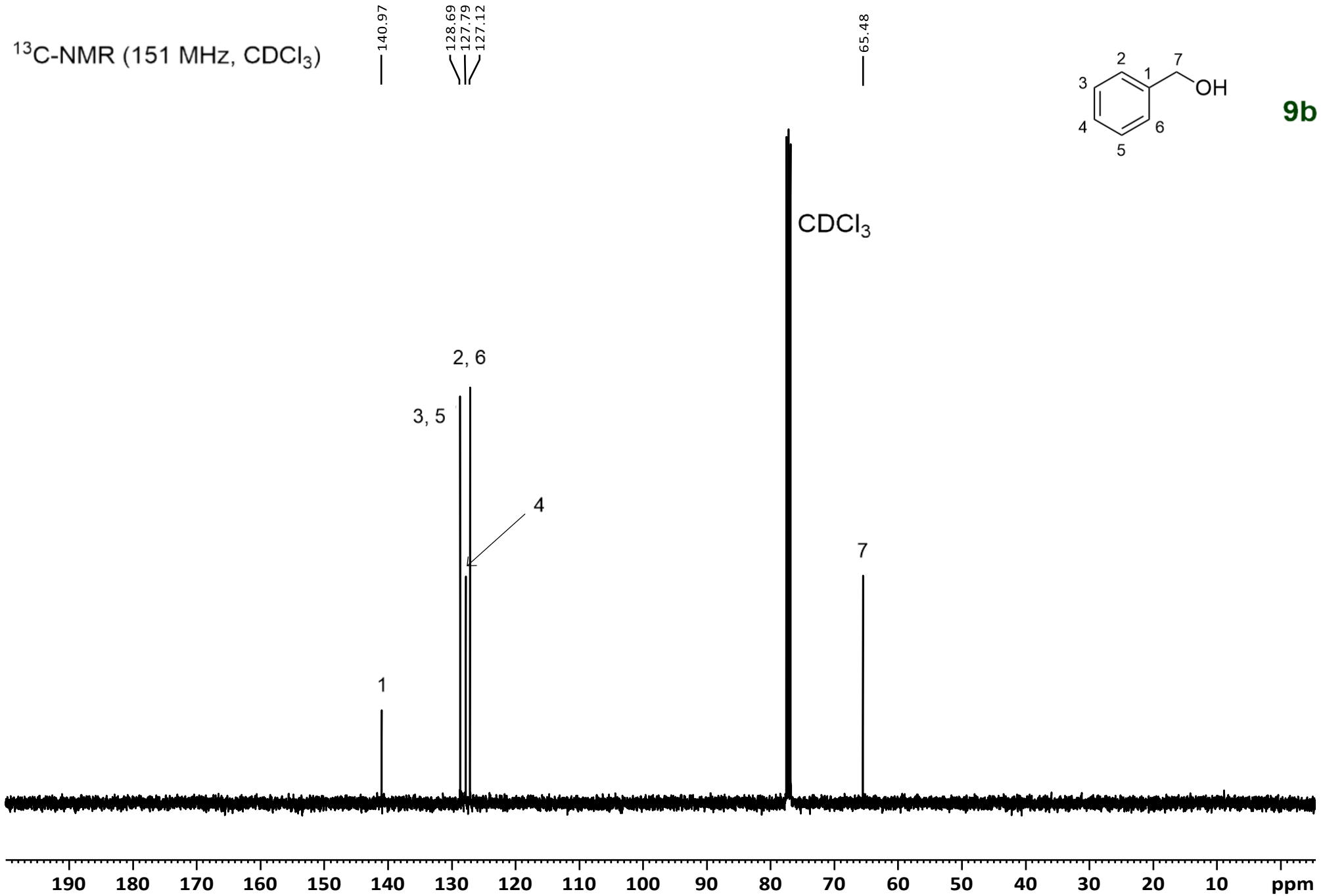

^{13}C-NMR (151 MHz, $CDCl_3$)
140.97
128.69
127.79
127.12
65.48
2
1
7
3
OH
4
6
5
9b
$CDCl_3$
2, 6
3, 5
4
7
1
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

Table S1: All the parameters tested during the optimization process are listed, with their corresponding isolated product yields. Methanol, 2-propanol, and water were independently evaluated as reaction solvents. In each case, the extraction process turned out to be troublesome and the product could not be isolated.

	Assessed parameters	Time (min.)	Temperature (°C)	Yield (%)
Time test	$CuCl_2$ 0,1 eq	10	80	82
	$CuCl_2$ 0,1 eq	15	80	82
	$CuCl_2$ 0,1 eq	30	80	65
	$CuCl_2$ 0,1 eq	60	80	60
	$CuCl_2$ 0,1 eq	80	80	57
	$CuCl_2$ 0,1 eq	90	80	48
Reagents test	$CuCl_2$ 0,05 eq	10	80	73
	$CuCl_2$ 0,05 eq	30	80	56
	$NaBH_4$ 3 eq.	10	80	59
	$CuCl_2$ 0,1 eq / 10 min. stirring prior to $CuCl_2$ addition	10	80	82
	$CuCl_2$ 0,05 eq / 15 min. stirring prior to $CuCl_2$ addition	10	80	71
	$CuCl_2$ 0,025 eq / 15 min. stirring prior to $CuCl_2$ addition	30	80	42
	$CuCl_2$ 0,05 eq / $NaBH_4$ and nitrostyrene order switched	10	80	68
	$CuCl_2$ 0,1 eq / $CuCl_2$ addition between $NaBH_4$ split in two portions	80	80	48
	$CuCl_2$ 0,1 eq / DETA addition	10	80	80
	$CuCl_2$ 0,05 eq / DETA addition in NaOH solution	10	80	70
	$CuCl_2$ 0,05 eq / DETA addition in NaOH solution	90	80	41
Temp. test	CuCl2 0,1 eq	15	60	64
	$CuCl_2$ 0,1 eq	10	110	82,6
	$CuCl_2$ 0,1 eq	o.n.	rt	79
Solvents	MeOH	15	80	-
	2-PrOH	15	80	-
	H_2O	15	80	-

Figure S1: ESI/MS spectrum of the crude mixture for the synthesis of **4b** after 15 minutes of stirring at 80 ˚C. The major peaks relate to the target product ($[M+H]^+$ *m/z* = 182,2) and the fragment with mass $[M+H]^+$ *m/z* = 165,0 originated from α-cleavage of **4b** [1].

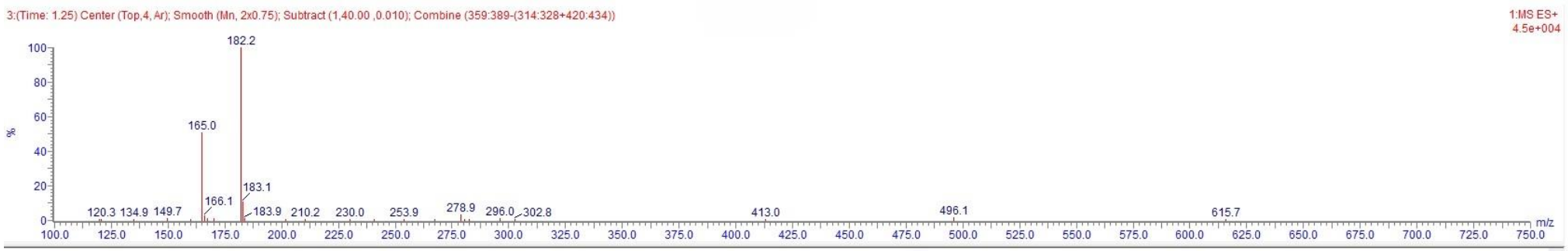


Figure S2: ESI/MS spectrum of the crude mixture for the synthesis of **4b** after 30 minutes of stirring at 80 ˚C.

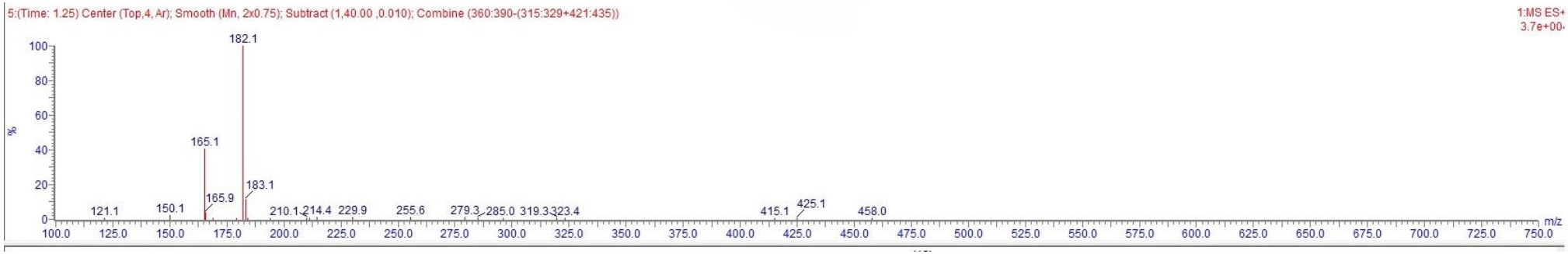


Figure S3: ESI/MS spectrum of the crude mixture for the synthesis of **4b** after 45 minutes of stirring at 80 ˚C. New structures with higher molecular masses emerge, while the concentration of **4b** decreases. The peaks with masses > 500 might indicate the formation of trimeric products.

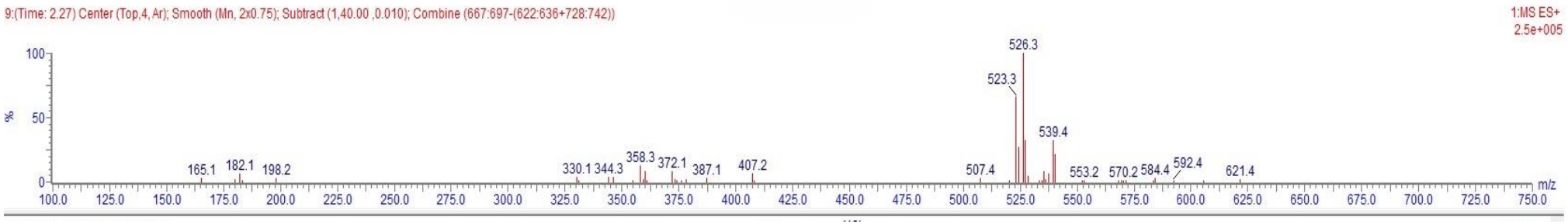


Figure S4: ESI/MS spectrum of the crude mixture for the synthesis of **4b** after 60 minutes of stirring at 80 ˚C. The peak with $[M+H]^+$ *m/z* = 151,0 is associated to the fragment originated from β-cleavage of **4b** [1]. The peak with $[M+H]^+$ *m/z* = 362,2 might be resulting from the formation of *N,N*-bis(2,5-dimethoxyphenethyl)hydroxylamine as an intermediate species.

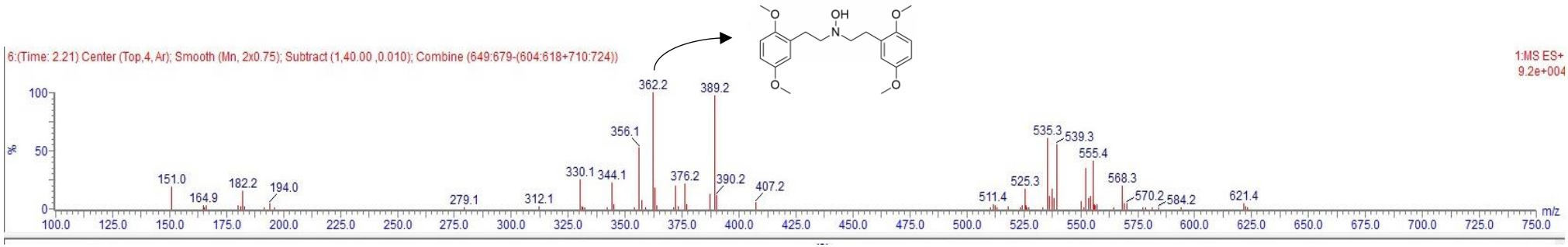


Figure S5: ESI/MS spectrum of the crude mixture for the synthesis of **4b** after 75 minutes of stirring at 80 ˚C.

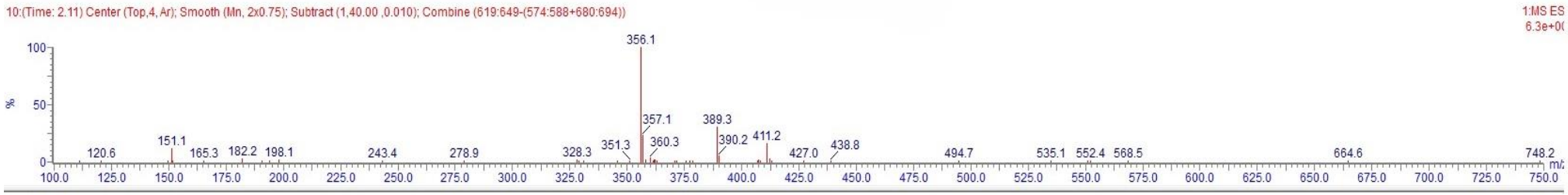
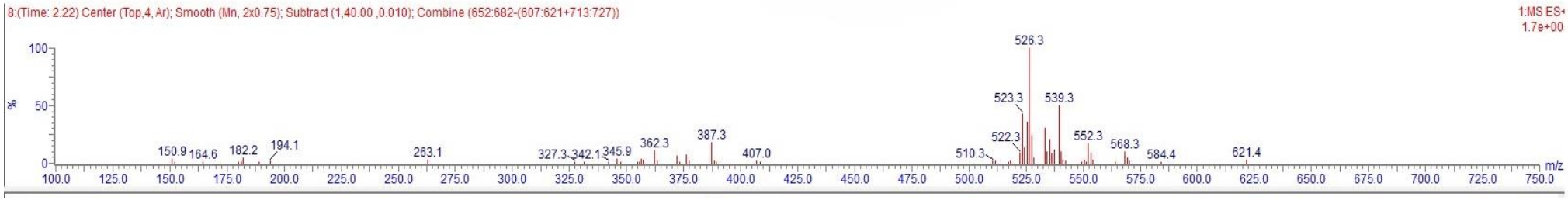


Figure S6: ESI/MS spectrum of the crude mixture for the synthesis of **4b** after 90 minutes of stirring at 80 ˚C.



References

[1] Chen, B.H.; Liu, J.T.; Chen, H.M.; Chen, W.X.; Lin, C.H. *Applied Sciences* **2018**, *8*(7), p.1022.