

Supporting Information

A new convenient synthetic route towards 2-(hetero)aryl-substituted thieno[3,2-*b*]indoles using Fischer indolization

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General information

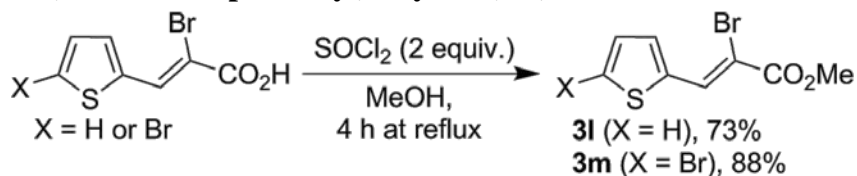
The purity of the obtained compounds was evaluated by GC-MS analysis, performed on an Agilent GC 7890A MS 5975C Inert XL EI/CI GC-MS spectrometer. All used solvents were dried and distilled per standard procedures. Bromine, triethylamine and thionyl chloride were obtained from commercial sources and used as received. 2-Bromo-3-(thiophen-2-yl)acrylic and 2-bromo-3-(5-bromothiophen-2-yl)acrylic acids were prepared from 3-(thiophen-2-yl)acrylic acid according to the previously described procedures.¹ Diethyl 3,3'-(1,4-phenylene)diacrylate and 3,3'-(thiophene-2,5-diyl)diacrylate were prepared by esterification of corresponding diacrylic acids according to the previously described procedure.² Silica gel 0.040–0.063 mm (230–400 mesh) was used to purify compounds.

General procedure for preparation of methyl α -bromocinnamates (3a-k)

<div><div><div>Ar</div><div><div><div></div><div></div></div></div><div><div>CO₂Me</div></div></div><div><div>1. Br₂ (1.04 equiv) / CHCl₃, 2 h at rt</div><div>2. Et₃N (2 equiv) / CHCl₃, 2 h at reflux</div></div><div><div>Ar</div><div><div><div></div><div></div></div></div><div><div>CO₂Me</div></div><div>Br</div></div><div>3a-k</div></div>		
methyl α -bromocinnamate 3	Ar	yield (%)
3a	phenyl	87
3b	4-fluorophenyl	87
3c	4-bromophenyl	88
3d	4-methoxyphenyl	98
3e	4-hexyloxyphenyl	94
3f	3,4,5-trimethoxyphenyl	95
3g	2-fluorophenyl	97
3h	2-chlorophenyl	98
3i	2-bromophenyl	97
3j	2-methoxyphenyl	91
3k	1-naphthyl	96

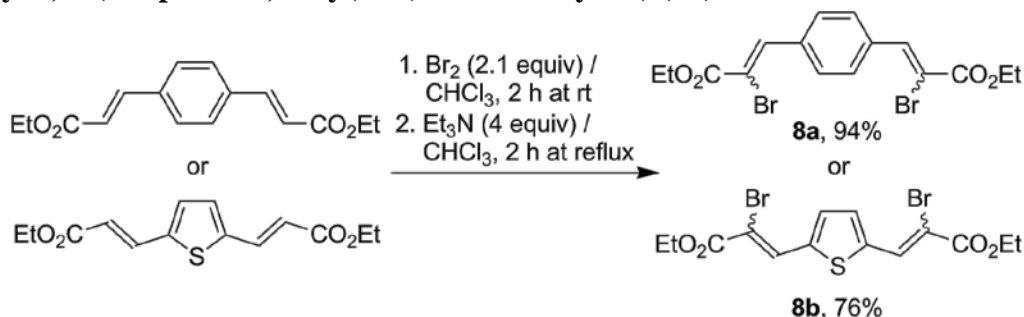
Br₂ (3.2 ml, 62.4 mmol) in dry CHCl₃ (20 ml) was added dropwise to methyl ester of appropriate cinnamic acid (60 mmol) in dry CHCl₃ (80 ml) at 0 °C during 20 min with continuous stirring, and the resulting solution was stirred for another 2 h at room temperature. After that, the reaction mixture was cooled to 0 °C and dropwise treated with Et₃N (16.8 ml, 120 mmol) at this temperature. The obtained dark-brown solution was stirred and heated at reflux for 2 h, then it was poured into ice-cold water (100 ml) with conc. HCl (6 ml), and this biphasic system was intensively shaken several times. The organic layer was separated, washed with water (4×50 ml), dried with CaCl₂ and eluted through a short silica gel plug (2 cm×4 cm) with CHCl₃ (2×20 ml). The filtrate was concentrated under reduced pressure and the residual oil was dried at 60 °C in vacuum (11 mbar) to give methyl α -bromocinnamate **3** (mixture of Z-E stereoisomers according to GC-MS analysis). All the substances **3** prepared in this manner were pure enough to be used in the next step without further purification.

General procedure for preparation of methyl 2-bromo-3-(thiophen-2-yl)acrylate (3l**) and methyl 2-bromo-3-(5-bromothiophen-2-yl)acrylate (**3m**)**



SOCl₂ (8.7 ml, 120 mmol) was added dropwise to a stirred suspension of 2-bromo-3-(thiophen-2-yl)acrylic acid (14 g, 60 mmol) or 2-bromo-3-(5-bromothiophen-2-yl)acrylic acid (18.72 g, 60 mmol) in dry MeOH (100 ml) at 0 °C during 30 min, and the obtained solution was stirred and heated at reflux for 4 h (CAUTION: significant SO₂ evolution). After this time, in the case of compound **3l**, the reaction mixture was concentrated in vacuum and the residue was treated with benzene (100 ml) and water (100 ml). The organic layer was separated, washed with saturated aqueous NaHCO₃ solution (2×25 ml), water (50 ml) and dried with CaCl₂. Benzene was removed under reduced pressure and the residue was additionally dried at 60 °C in vacuum (11 mbar) to afford pure ester **3l** (10.82 g, 73%) as the light-yellow oil. In the case of compound **3m**, the reaction mixture was cooled in an ice bath and the formed crystals were filtered, washed with cold MeOH (2×10 ml) and dried at room temperature to give pure ester **3m** (17.21 g, 88%).

General procedure for preparation of diethyl 3,3'-(1,4-phenylene)bis(2-bromoacrylate) (8a**) and diethyl 3,3'-(thiophene-2,5-diyl)bis(2-bromoacrylate) (**8b**)**



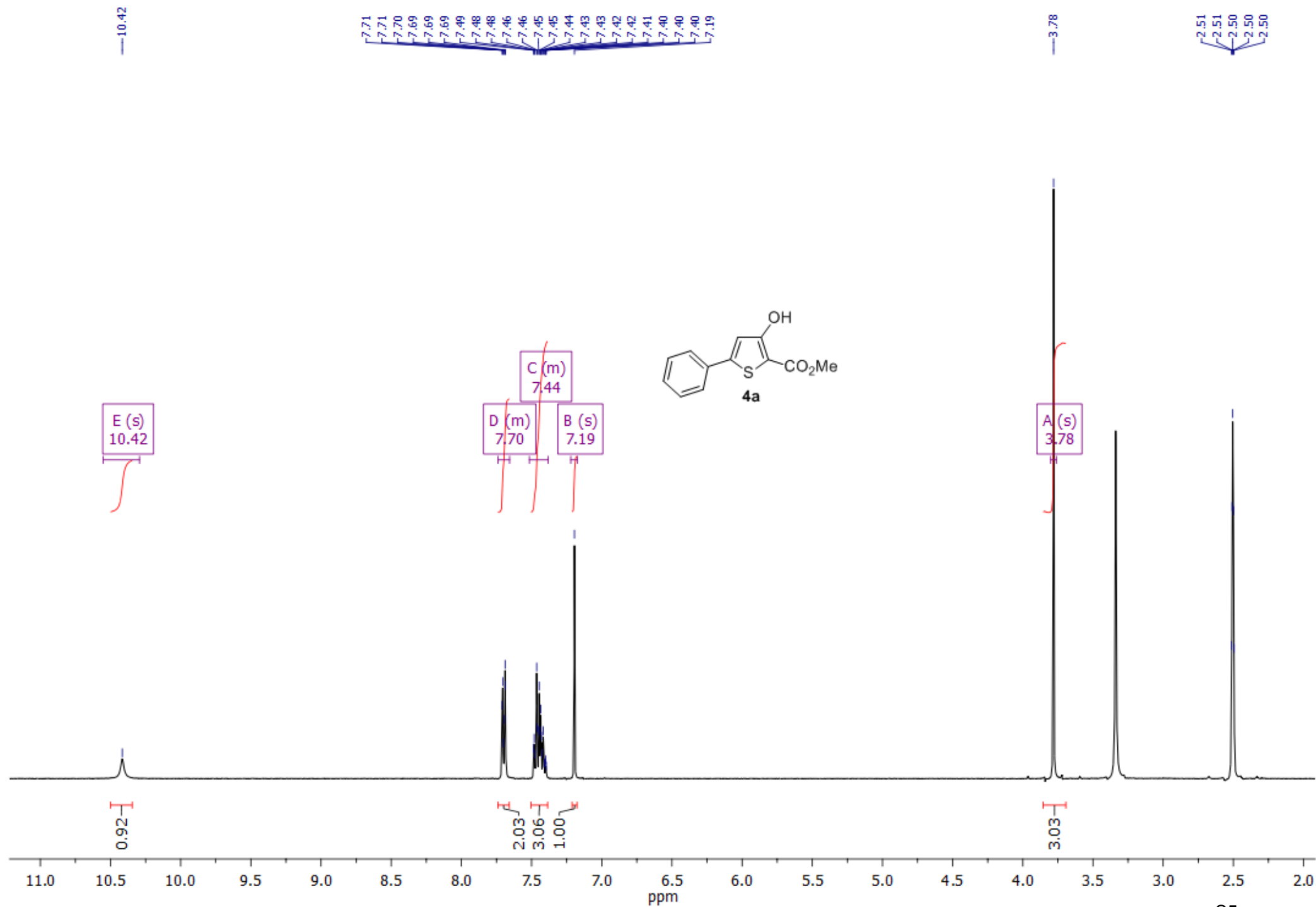
Br₂ (2.2 ml, 43 mmol) in dry CHCl₃ (25 ml) was added dropwise to a stirred solution of diethyl 3,3'-(1,4-phenylene)diacrylate (5.62 g, 20.5 mmol) or diethyl 3,3'-(thiophene-2,5-diyl)diacrylate (5.75 g, 20.5 mmol) in dry CHCl₃ (50 ml) at 0 °C during 15 min, and stirring was continued for another 2 h at room temperature. Then, the mixture was cooled to 0 °C and dropwise treated with Et₃N (11.4 ml, 82 mmol) at this temperature. The obtained dark-brown solution was stirred and heated at reflux for 2 h, then it was poured into ice-cold water (75 ml) with conc. HCl (5 ml), and this biphasic system was intensively shaken several times. The CHCl₃ layer was separated, washed with water (4×30 ml), dried with CaCl₂ and eluted through a short silica gel plug (2 cm×4 cm) with CHCl₃ (25 ml). The filtrate was concentrated under reduced pressure and the residual oil was dried at 60 °C in vacuum (11 mbar) to yield diethyl 3,3'-(1,4-phenylene)bis(2-bromoacrylate) **8a** (8.33 g, 94%) or diethyl 3,3'-(thiophene-2,5-diyl)bis(2-bromoacrylate) **8b** (7.6 g, 76%).

(thiophene-2,5-diyl)bis(2-bromoacrylate) **8b** (6.83 g, 76%), both **8a** and **8b** as mixture of (E,E)-(Z,E)-(Z,Z) stereoisomers according to GC-MS analysis. The obtained diesters were pure enough to be used in the next step without further purification.

References

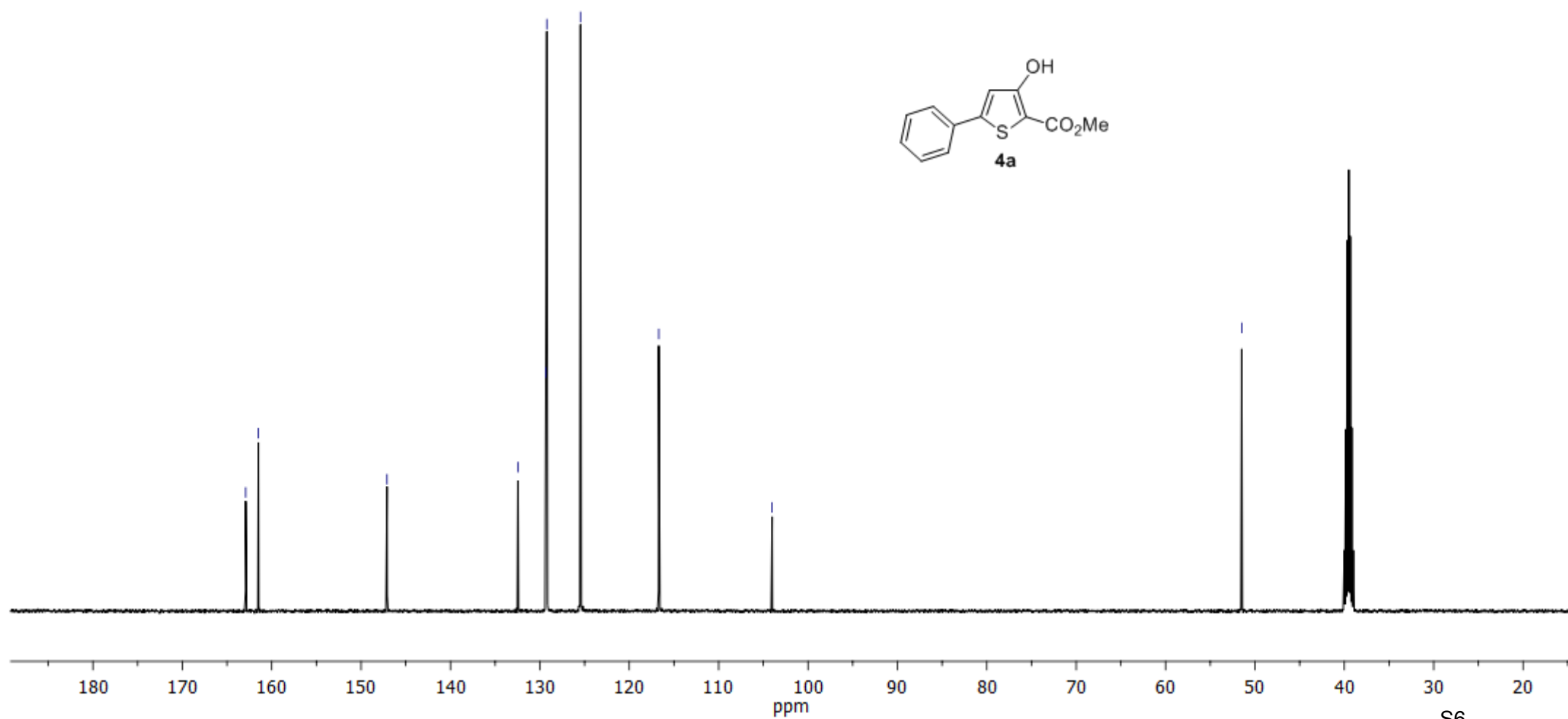
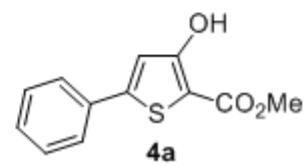
1. H. Keskin, R. E. Miller and F. F. Nord, *J. Org. Chem.*, 1951, **16**, 199.
2. H. Pohl, *J. fur Prakt. Chemier Prakt. Chemie*, 1934, **141**, 44.

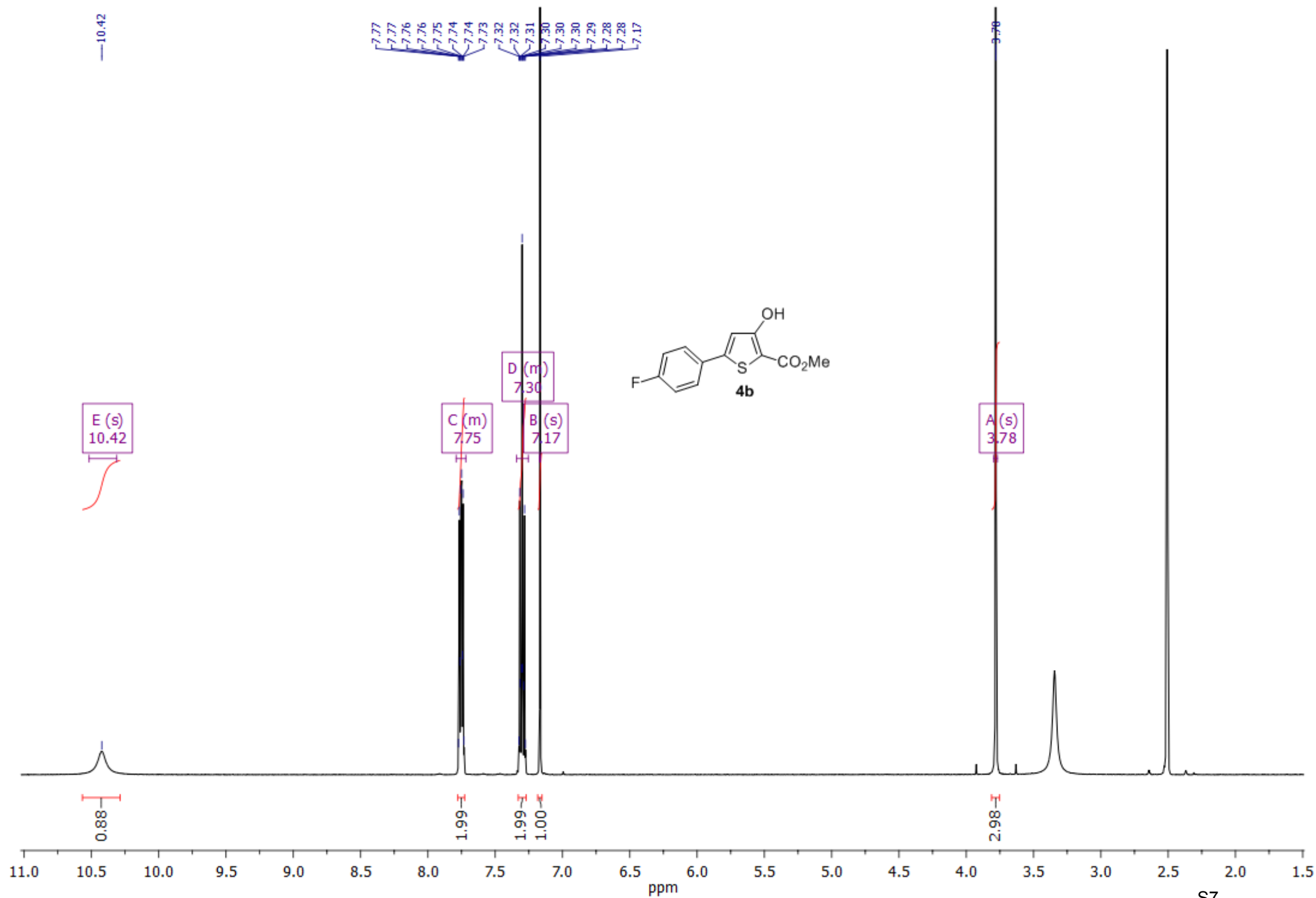
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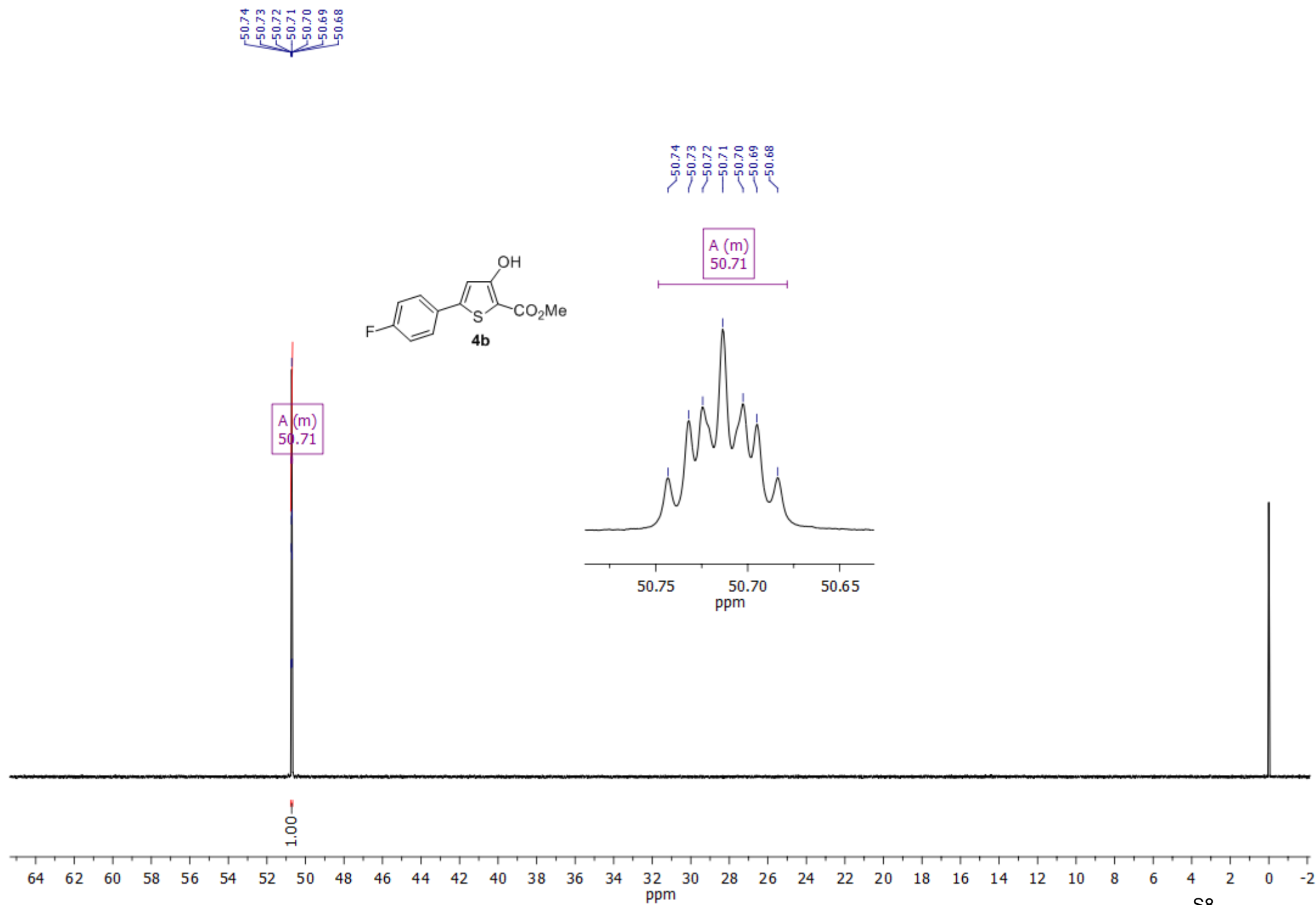


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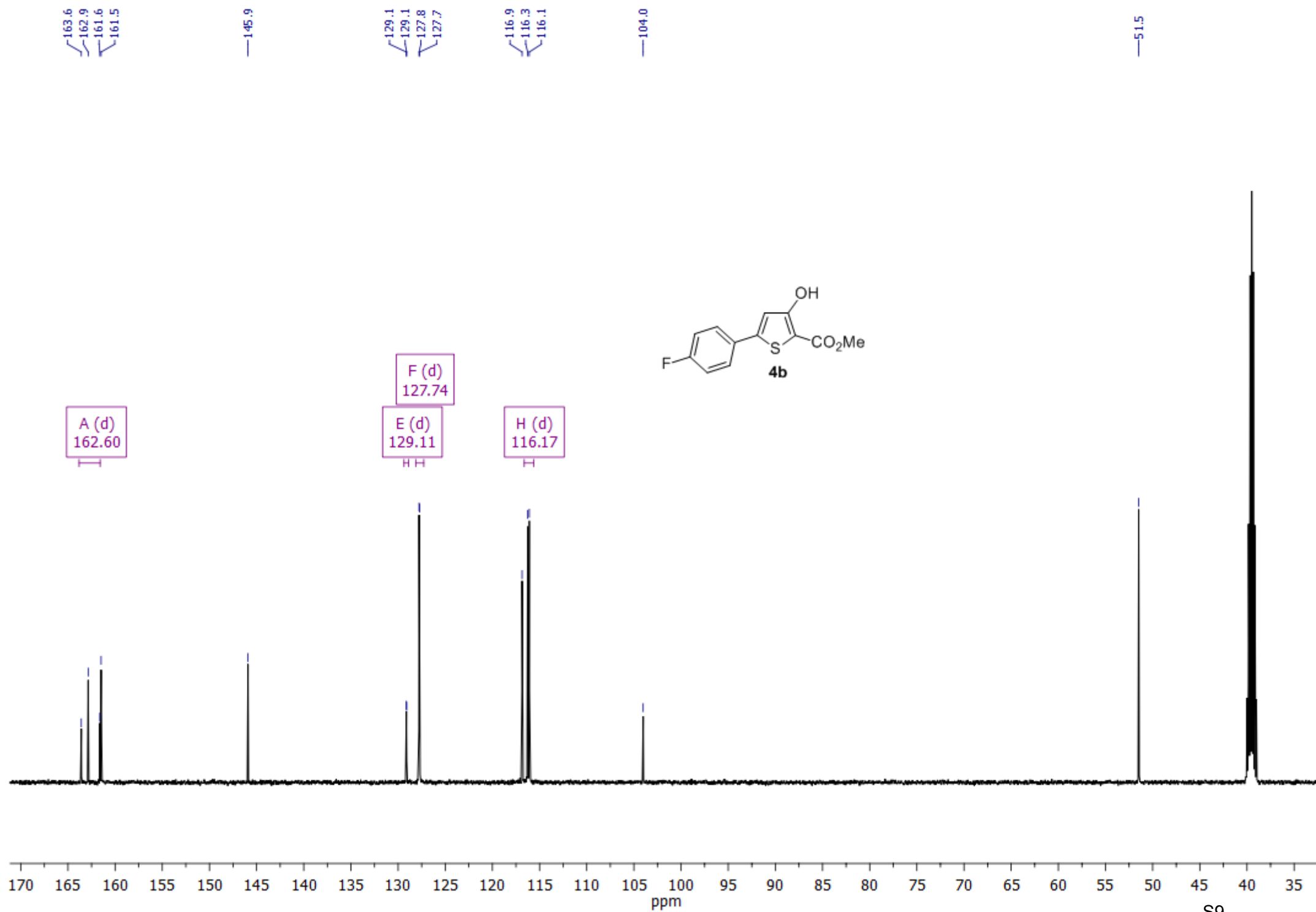
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161.5
147.1
132.4
129.3
129.2
125.5
116.7
104.0
51.5



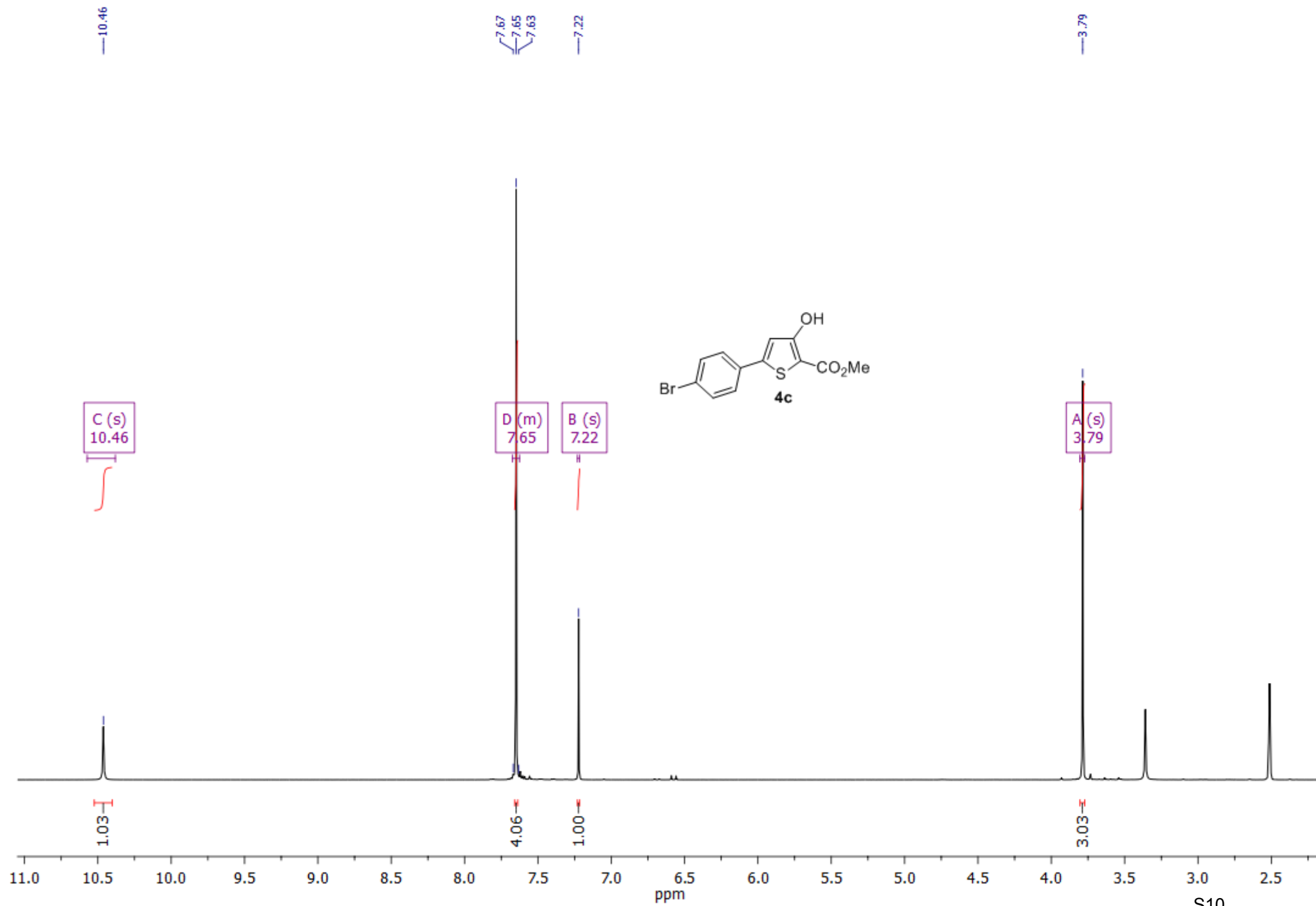


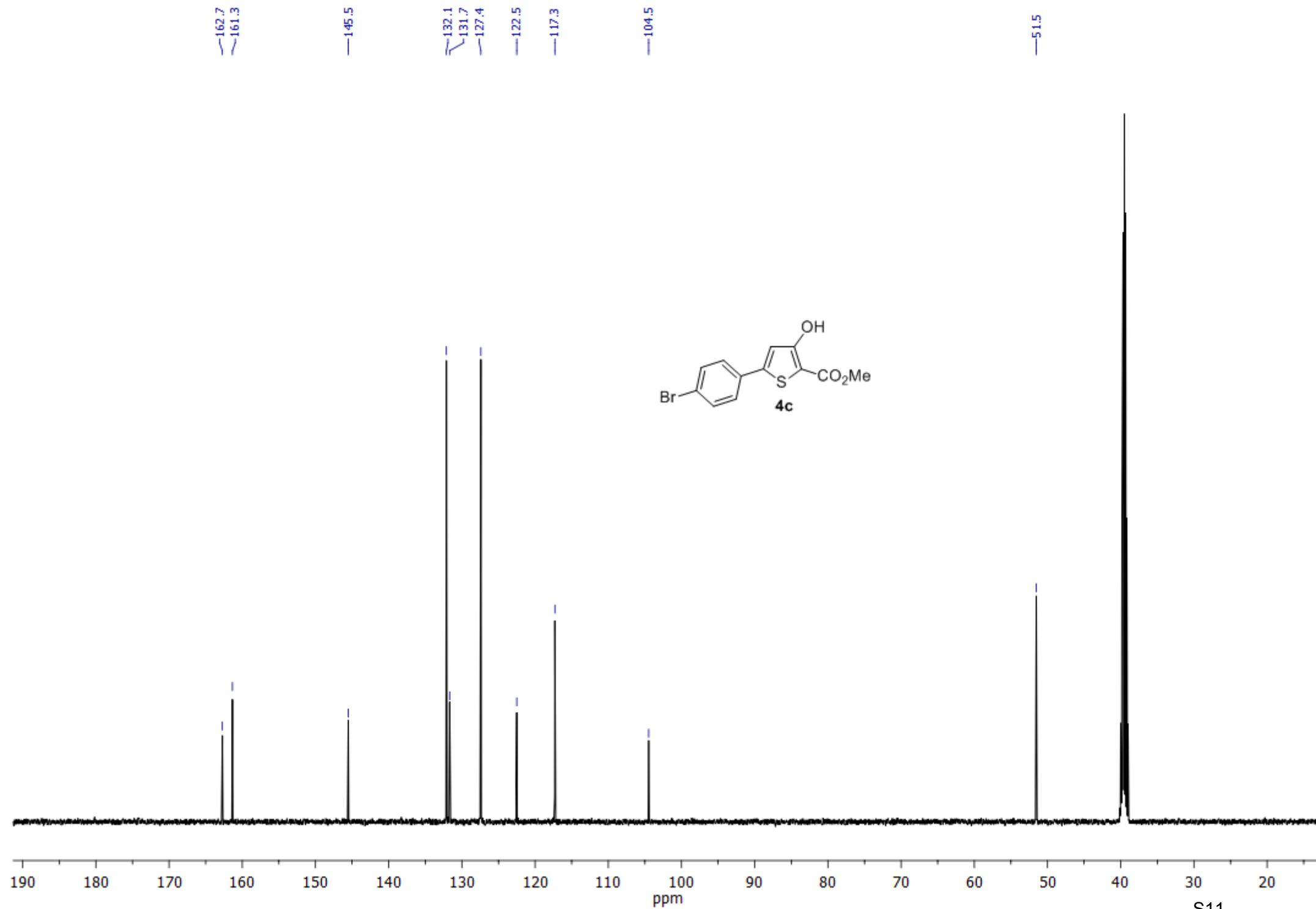


¹³C NMR (solvent: DMSO-*d*₆)

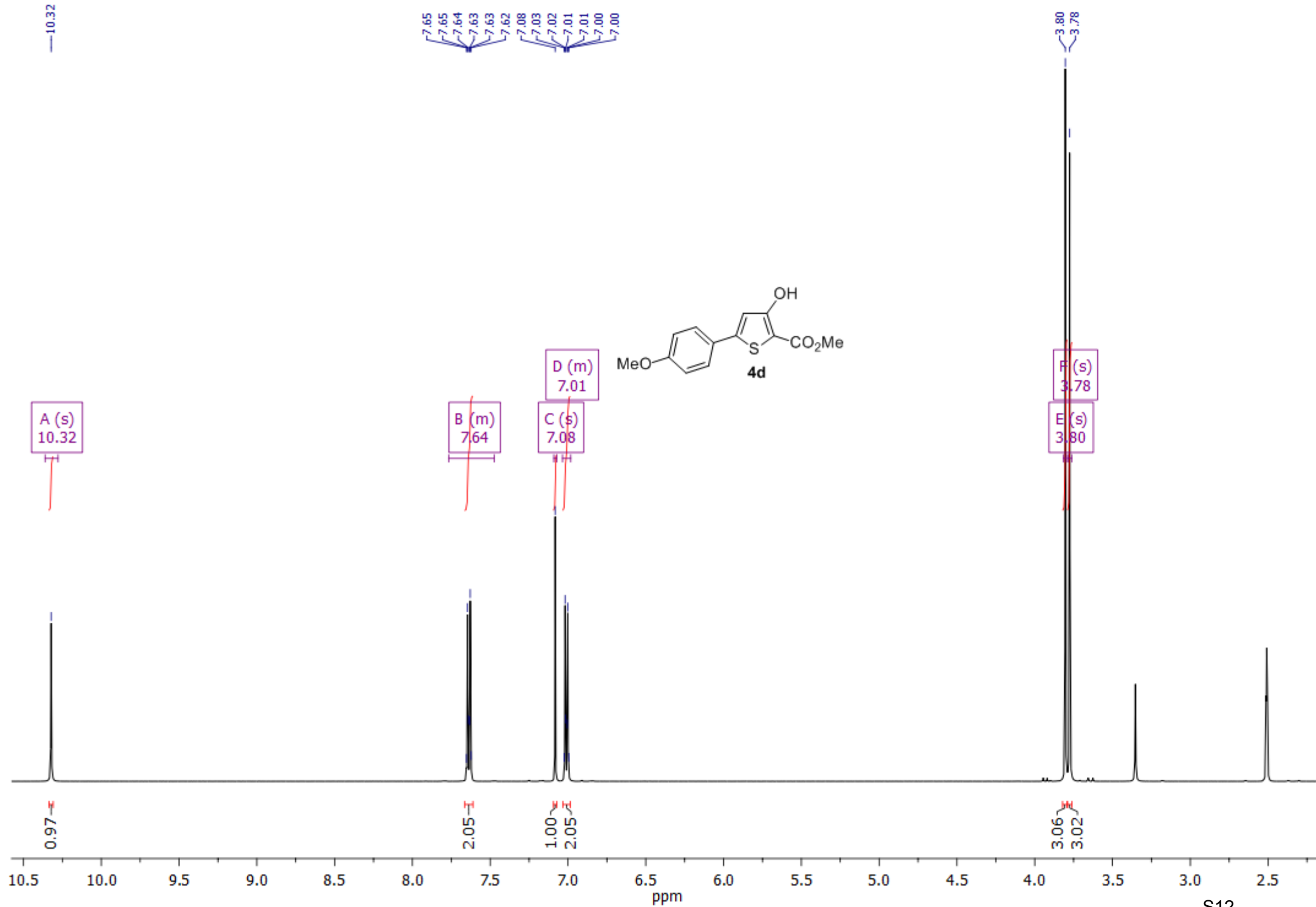


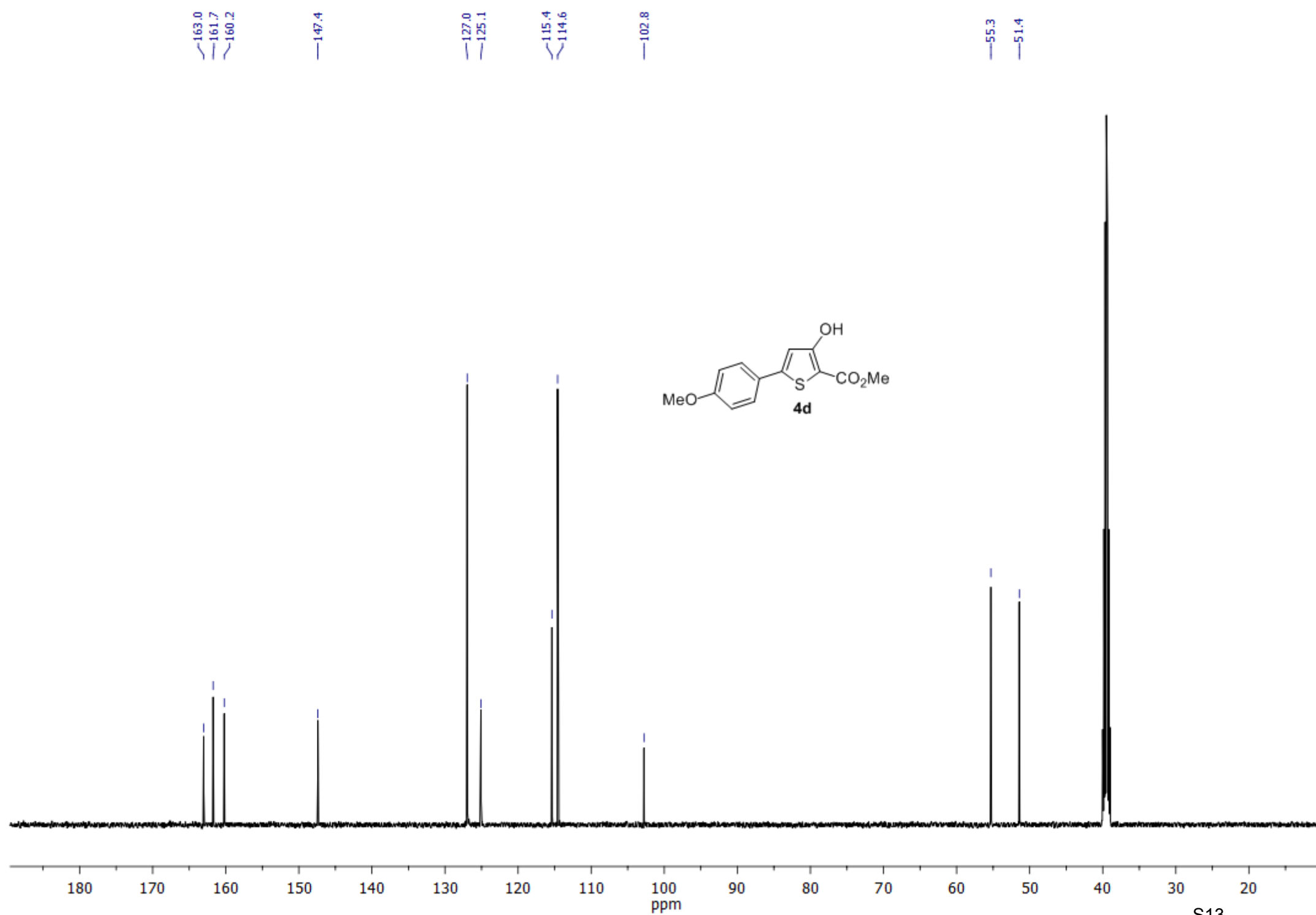
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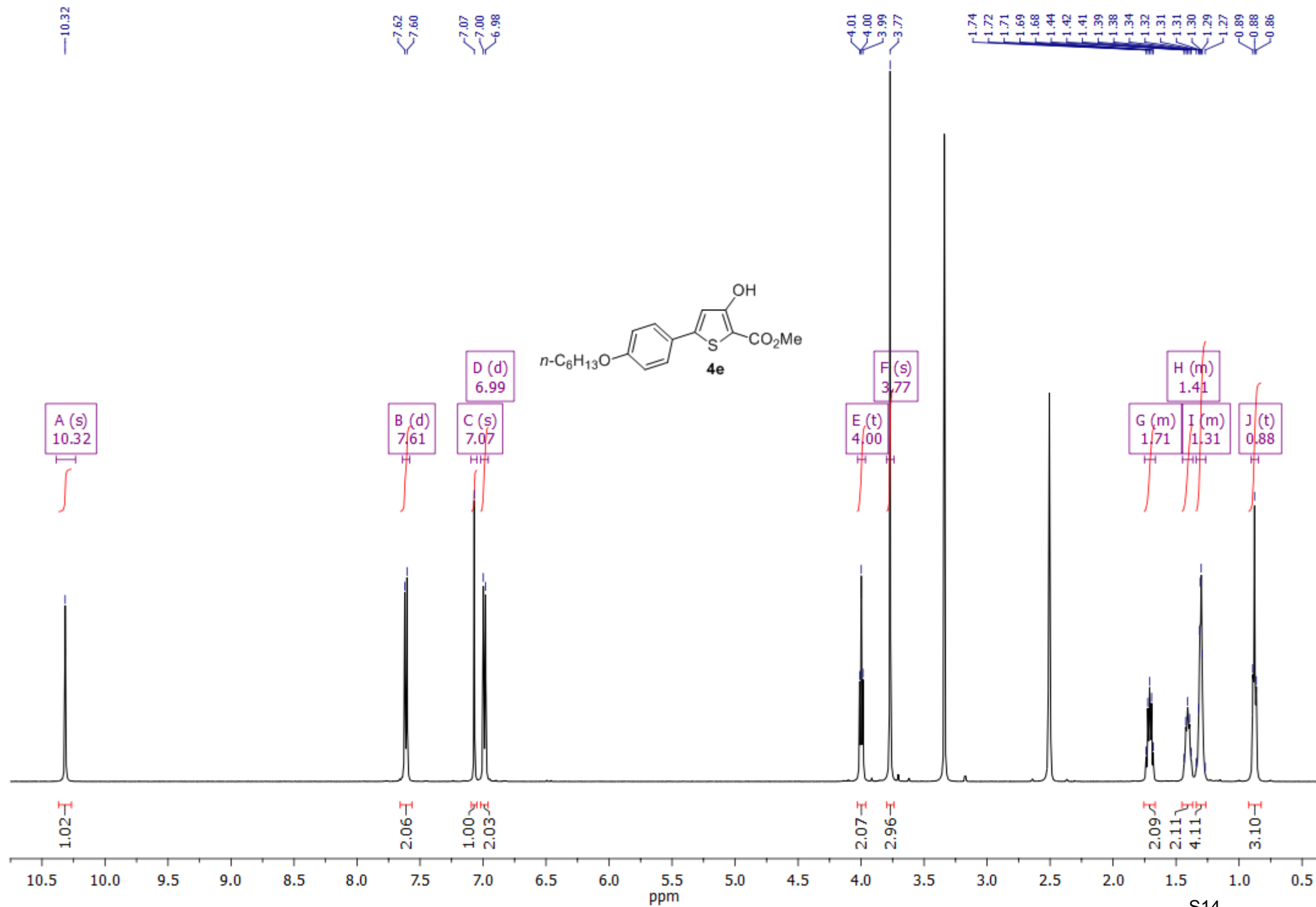


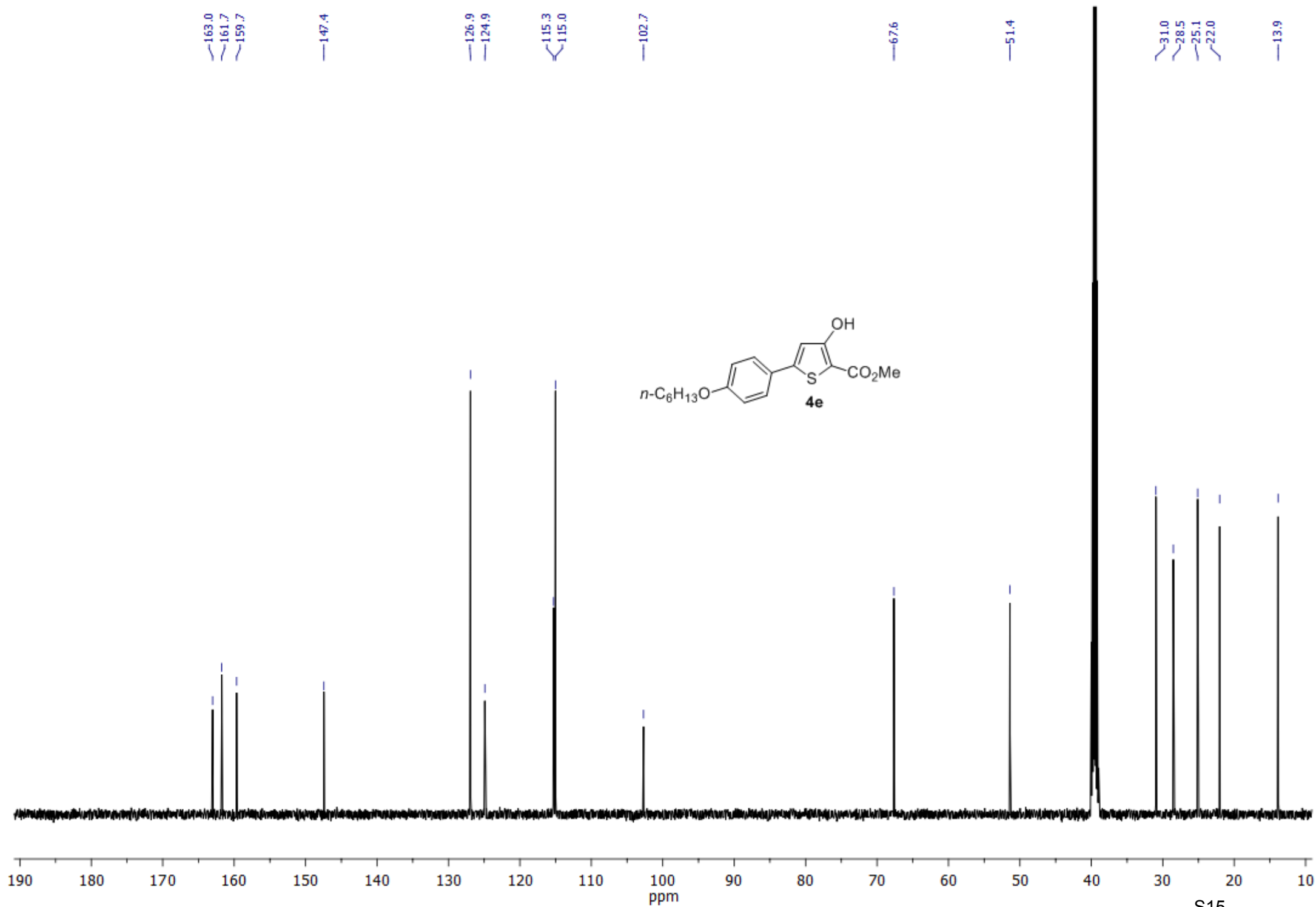
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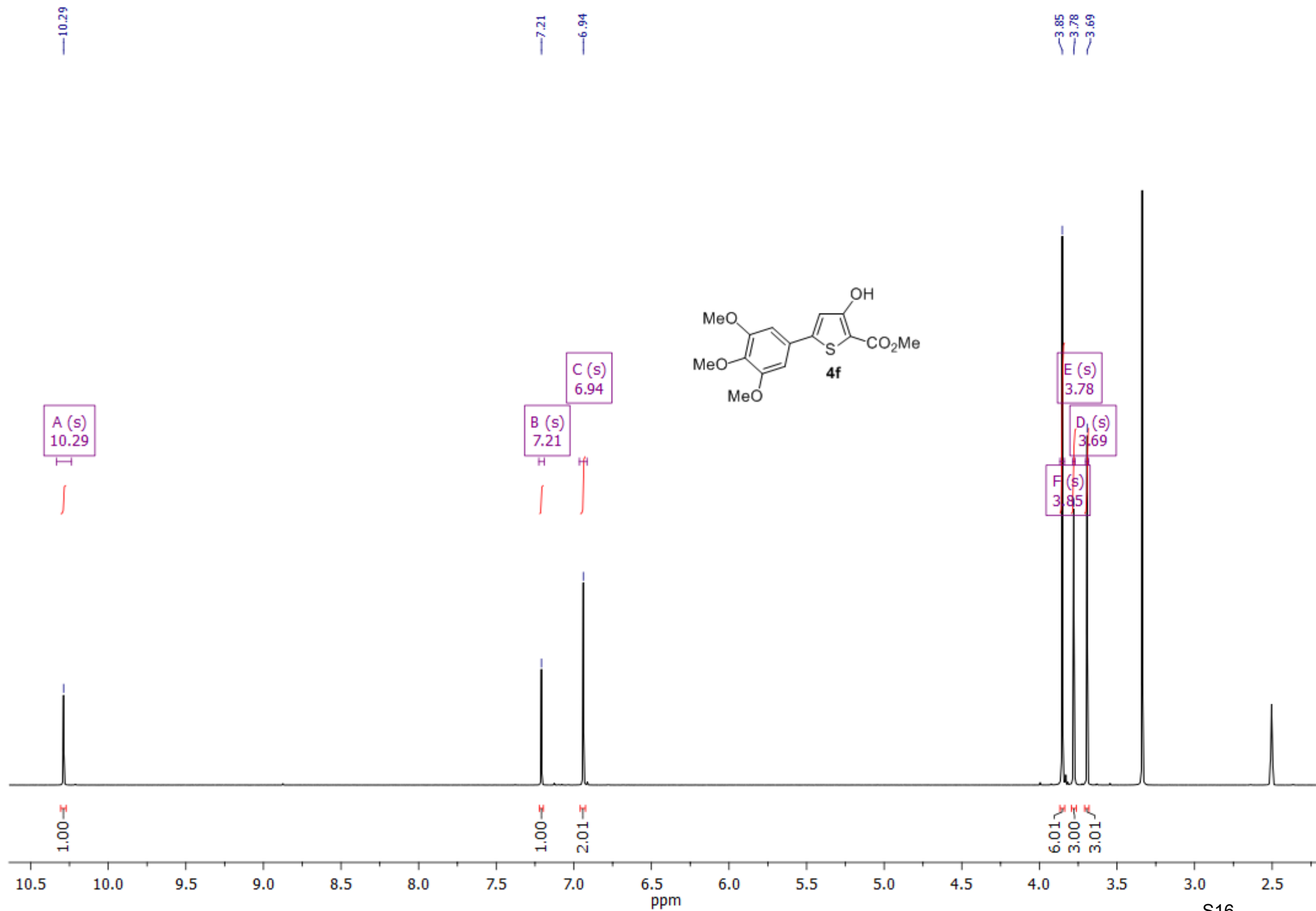


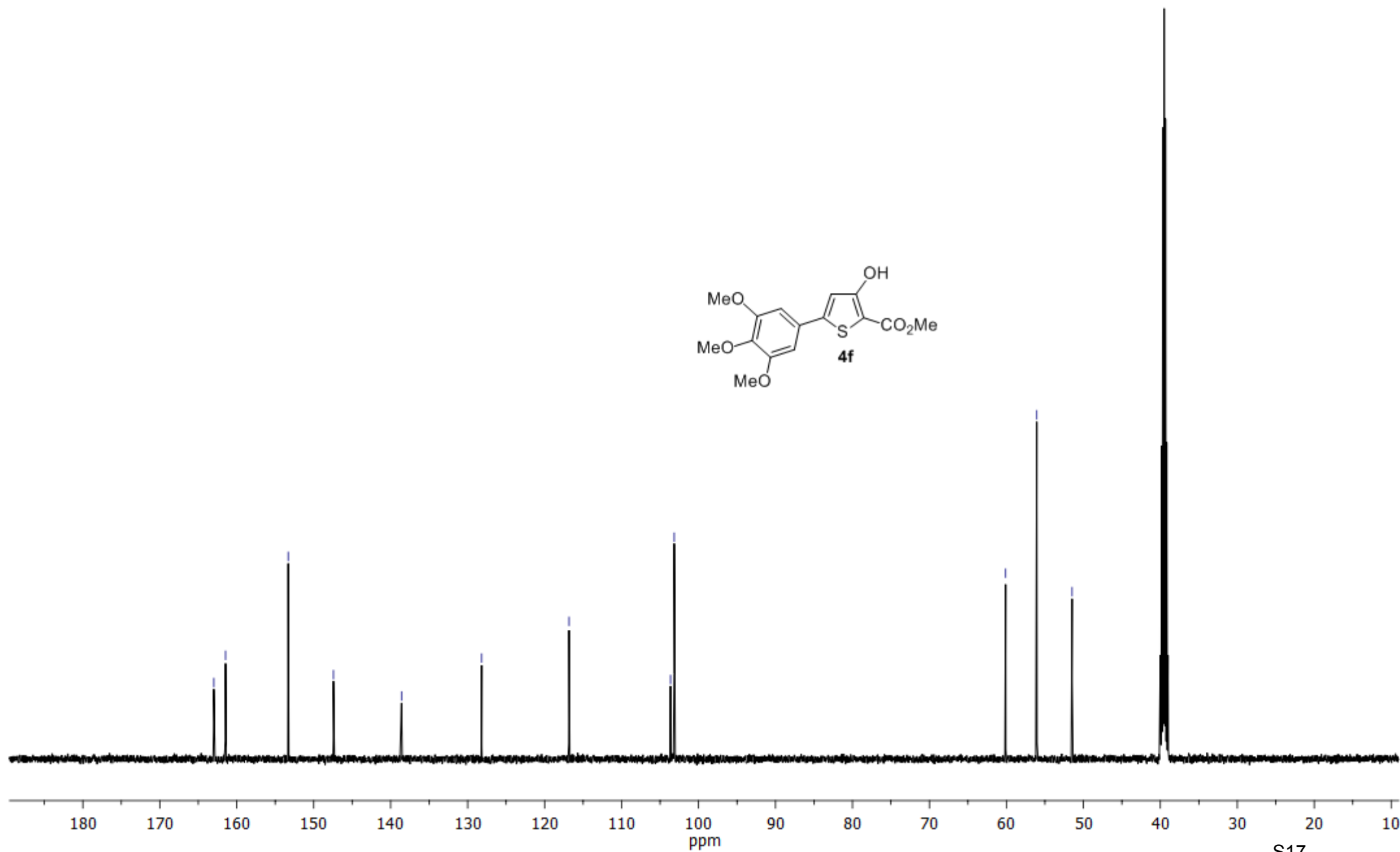
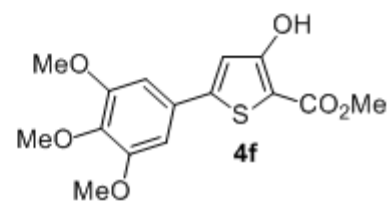
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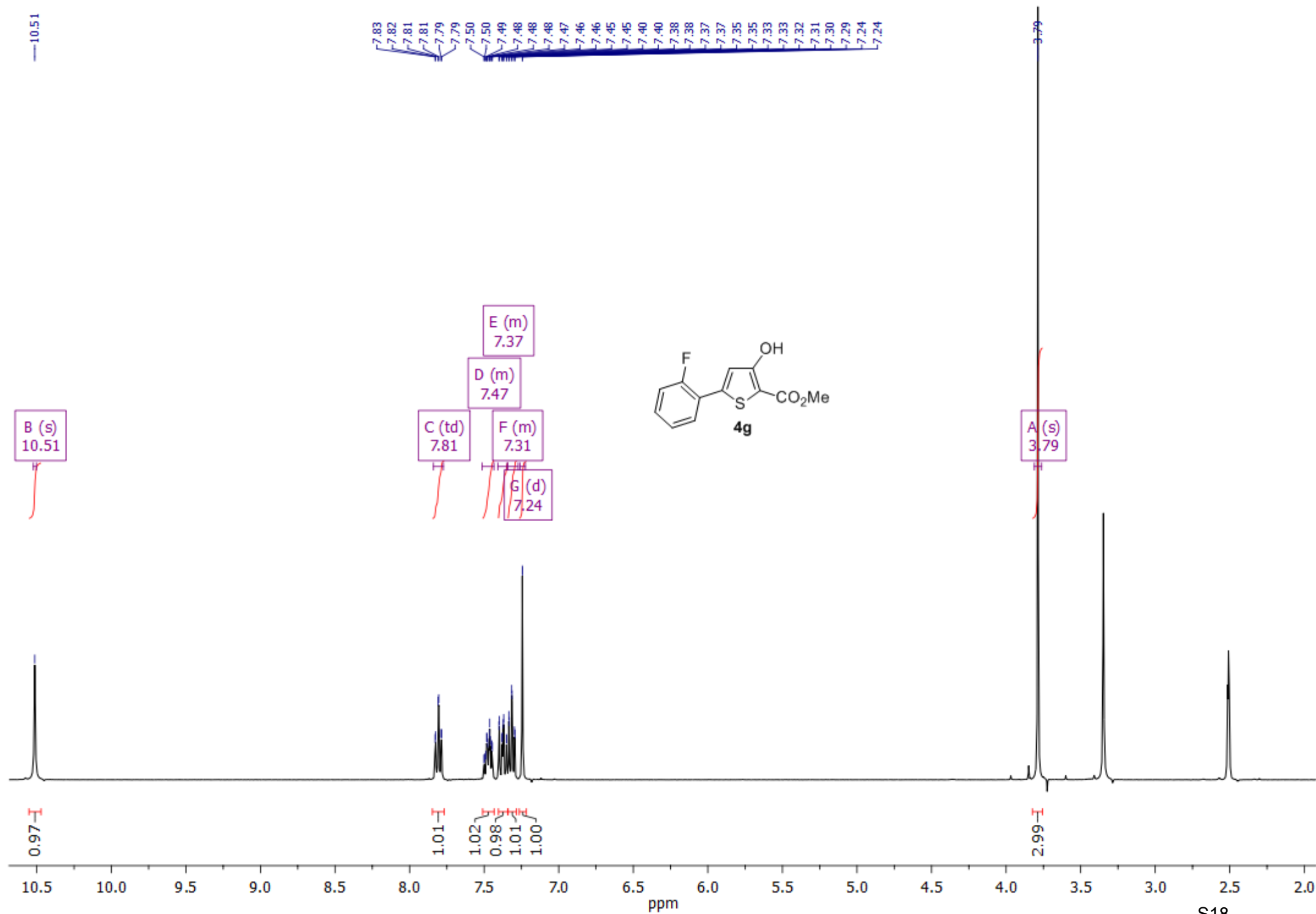




¹H NMR (solvent: DMSO-*d*₆)



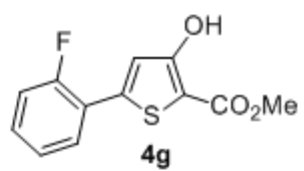




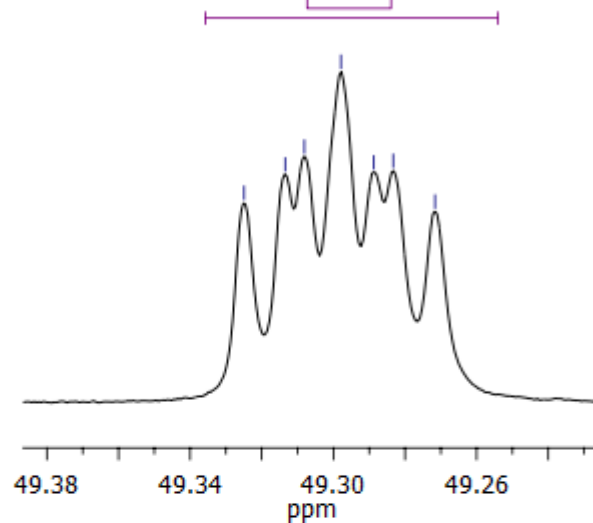
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49.31
49.31
49.30
49.29
49.28
49.27

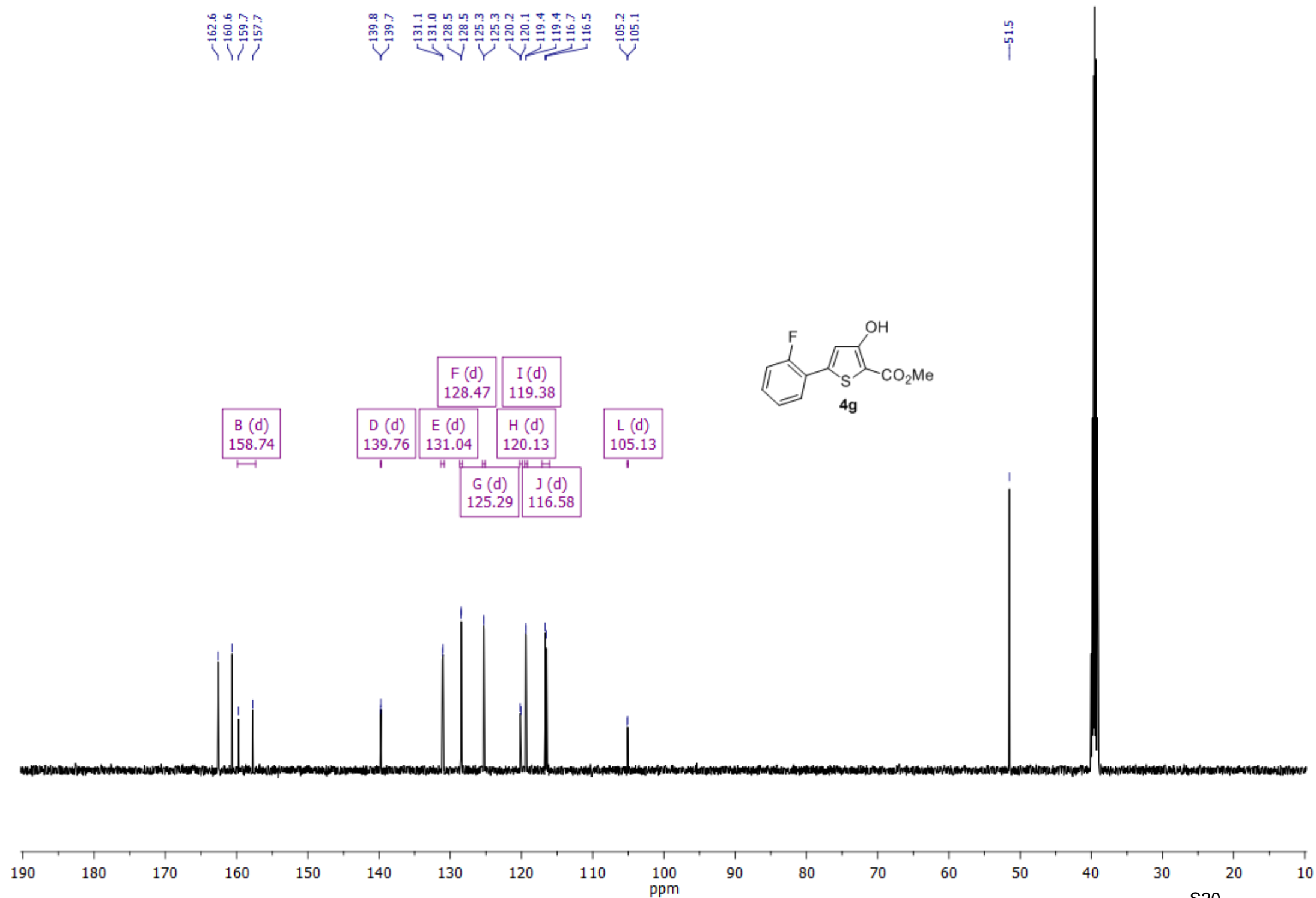
49.32
49.31
49.31
49.30
49.29
49.28
49.27

A (m)
49.30

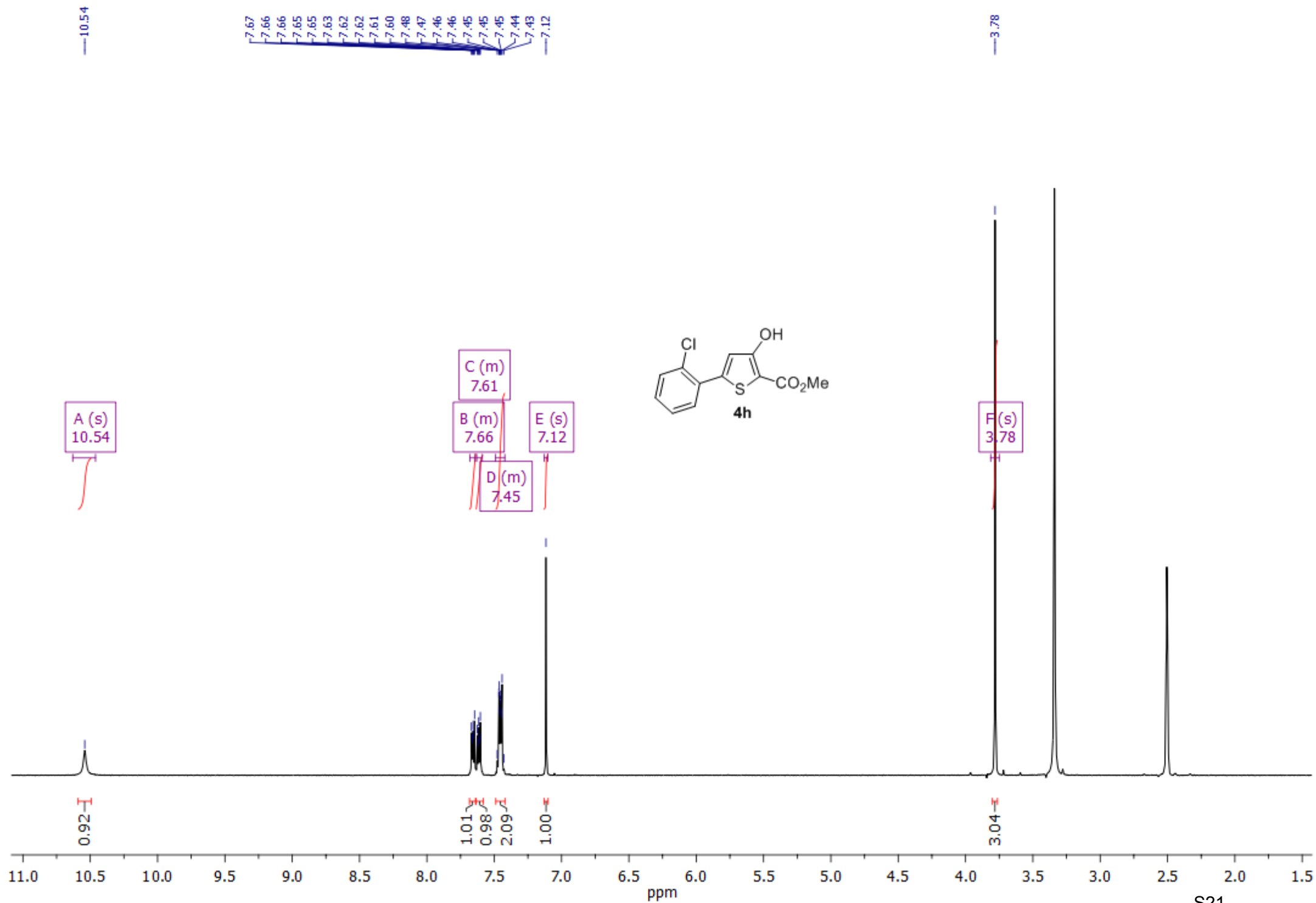


A (m)
49.30





¹H NMR (solvent: DMSO-*d*₆)



¹³C NMR (solvent: DMSO-*d*₆)

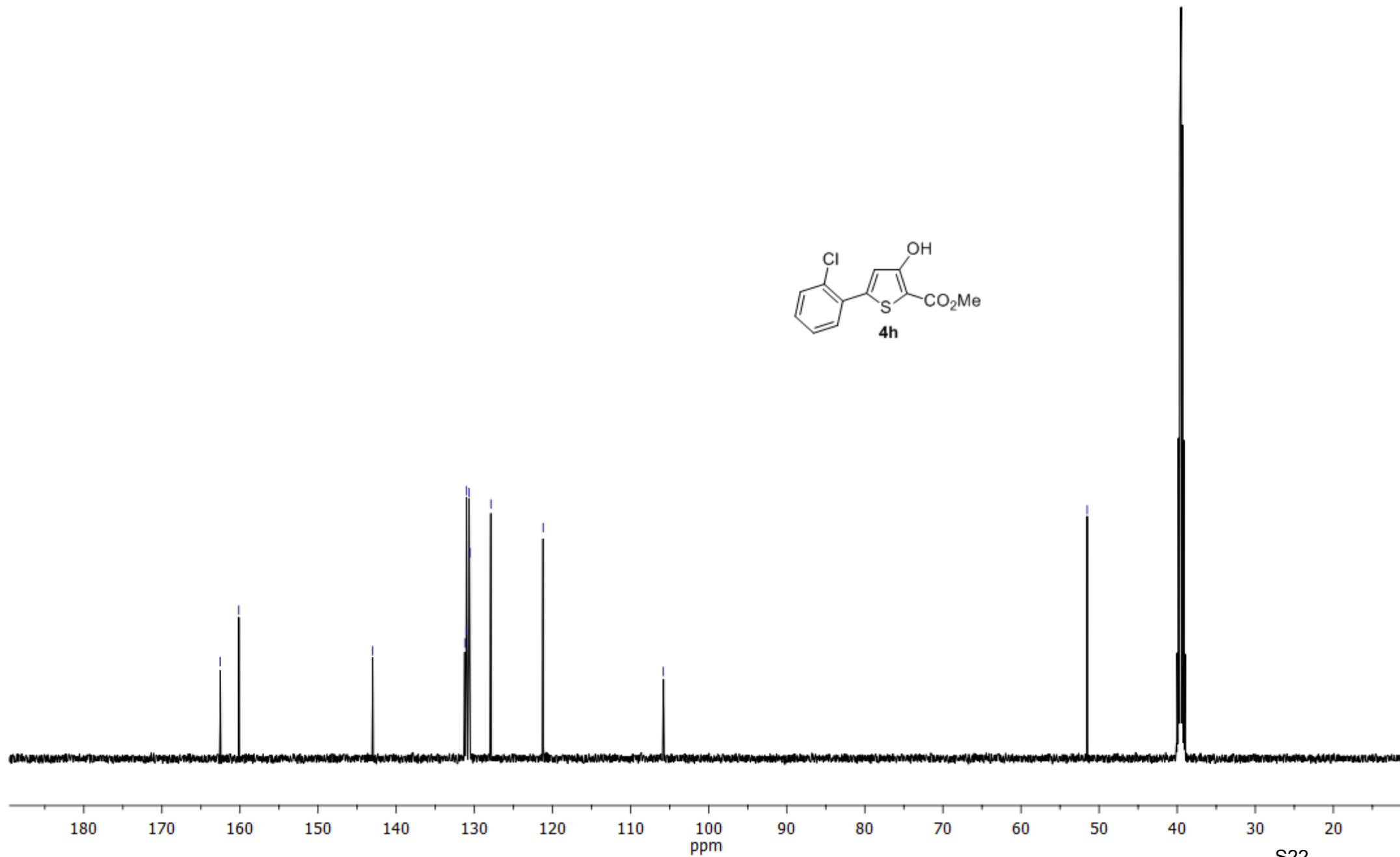
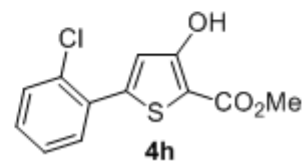
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—160.2

—143.0

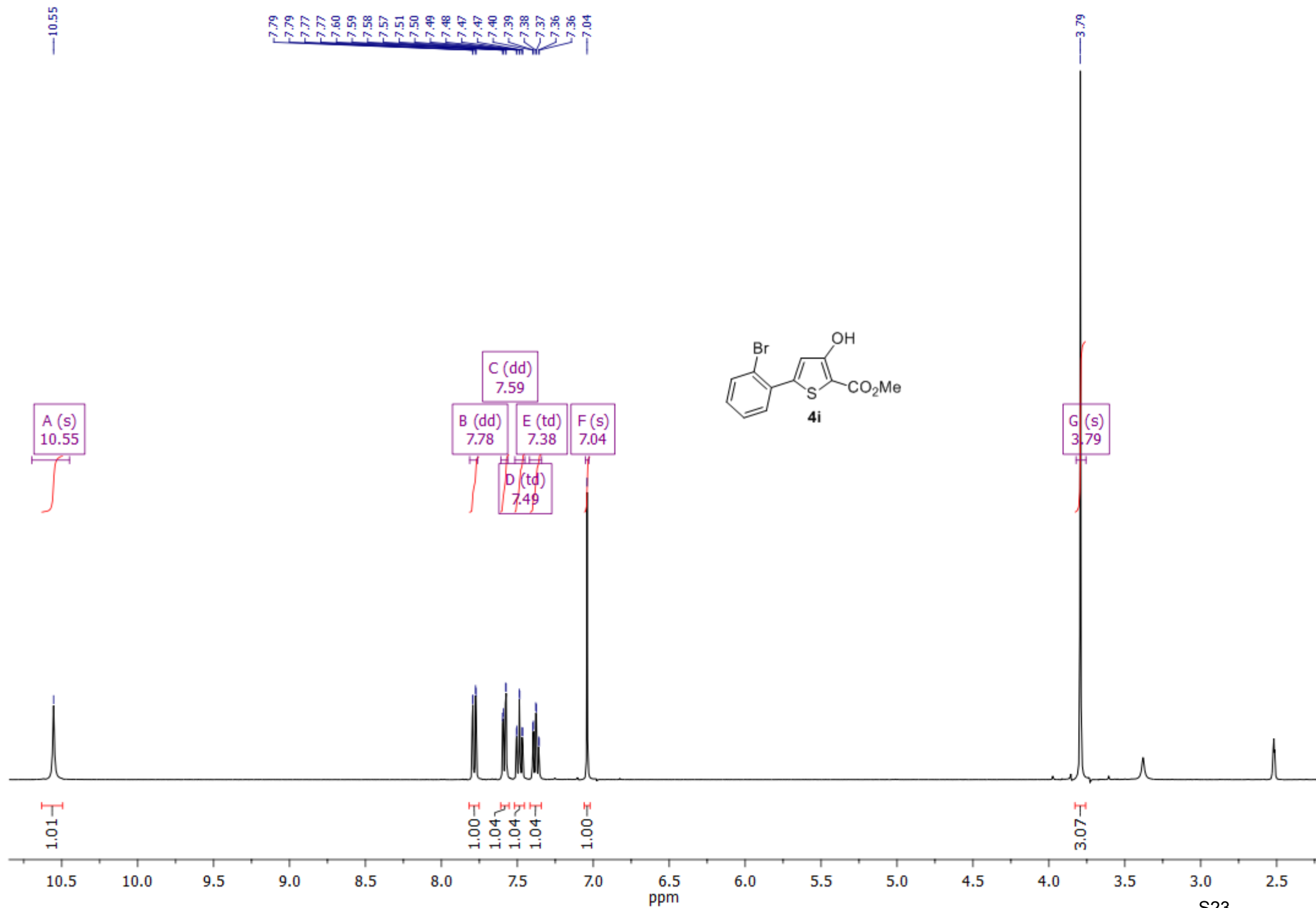
—131.2
—131.0
—131.0
—130.7
—130.6
—127.9
—121.2

—105.8

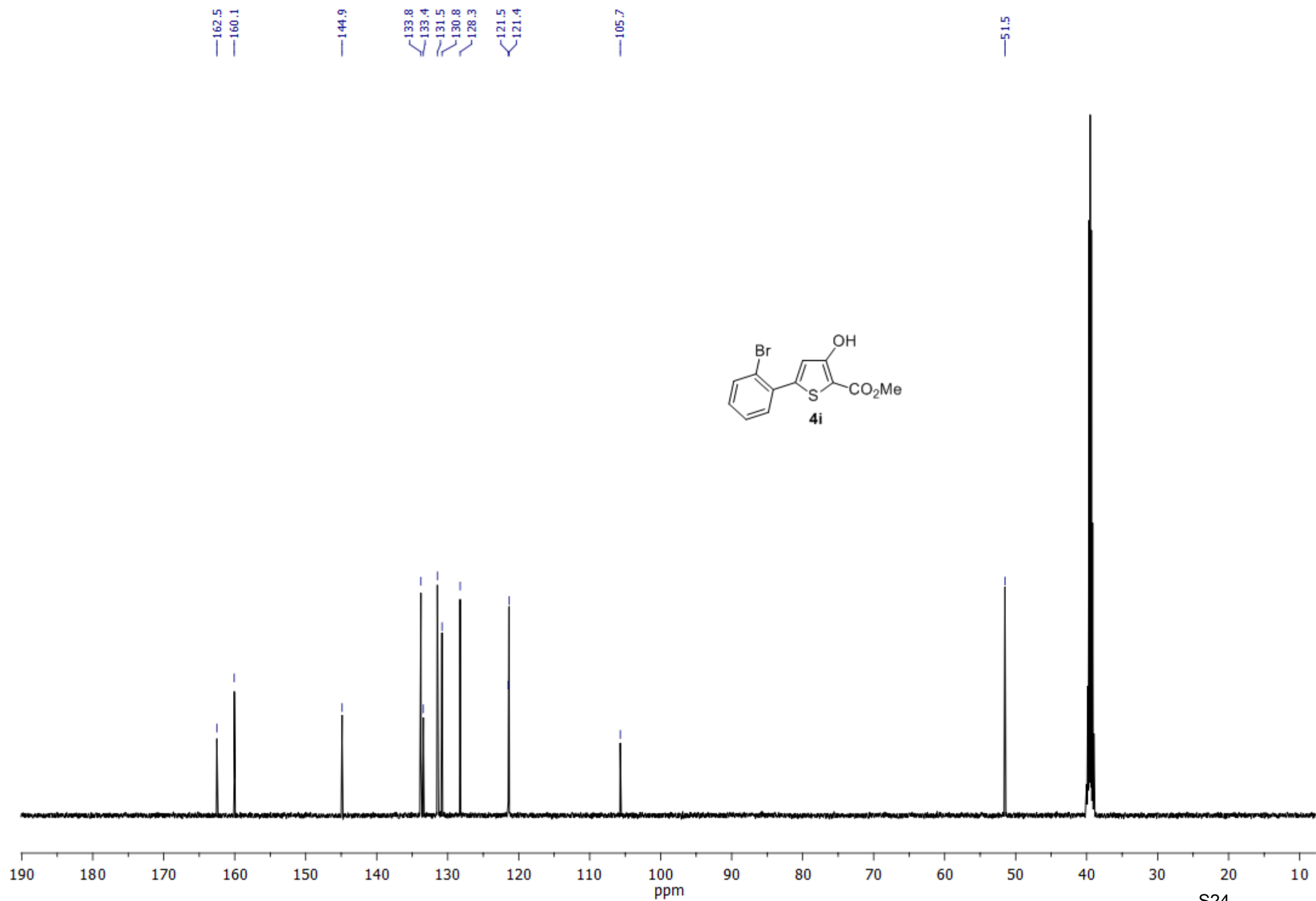
—51.5



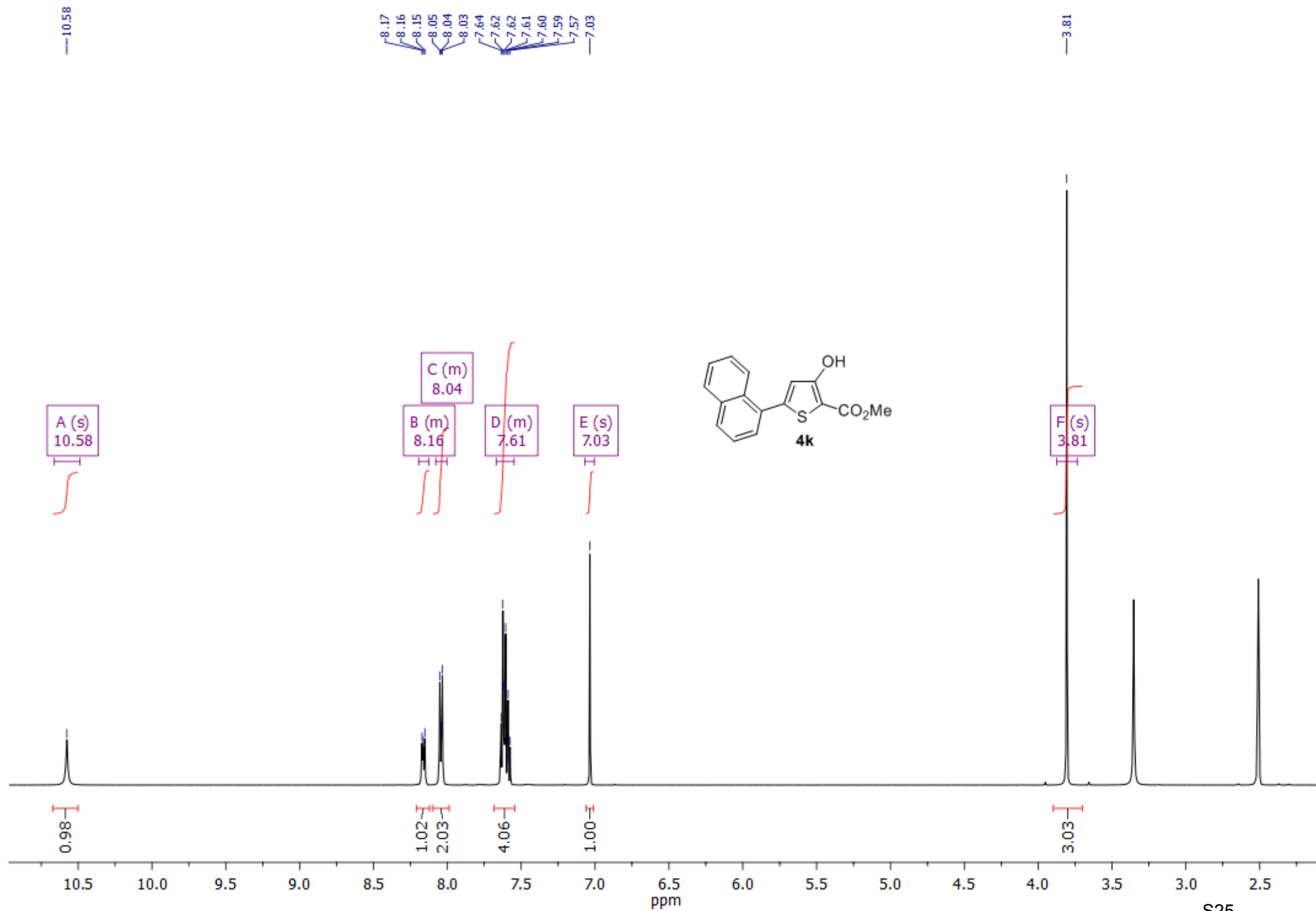
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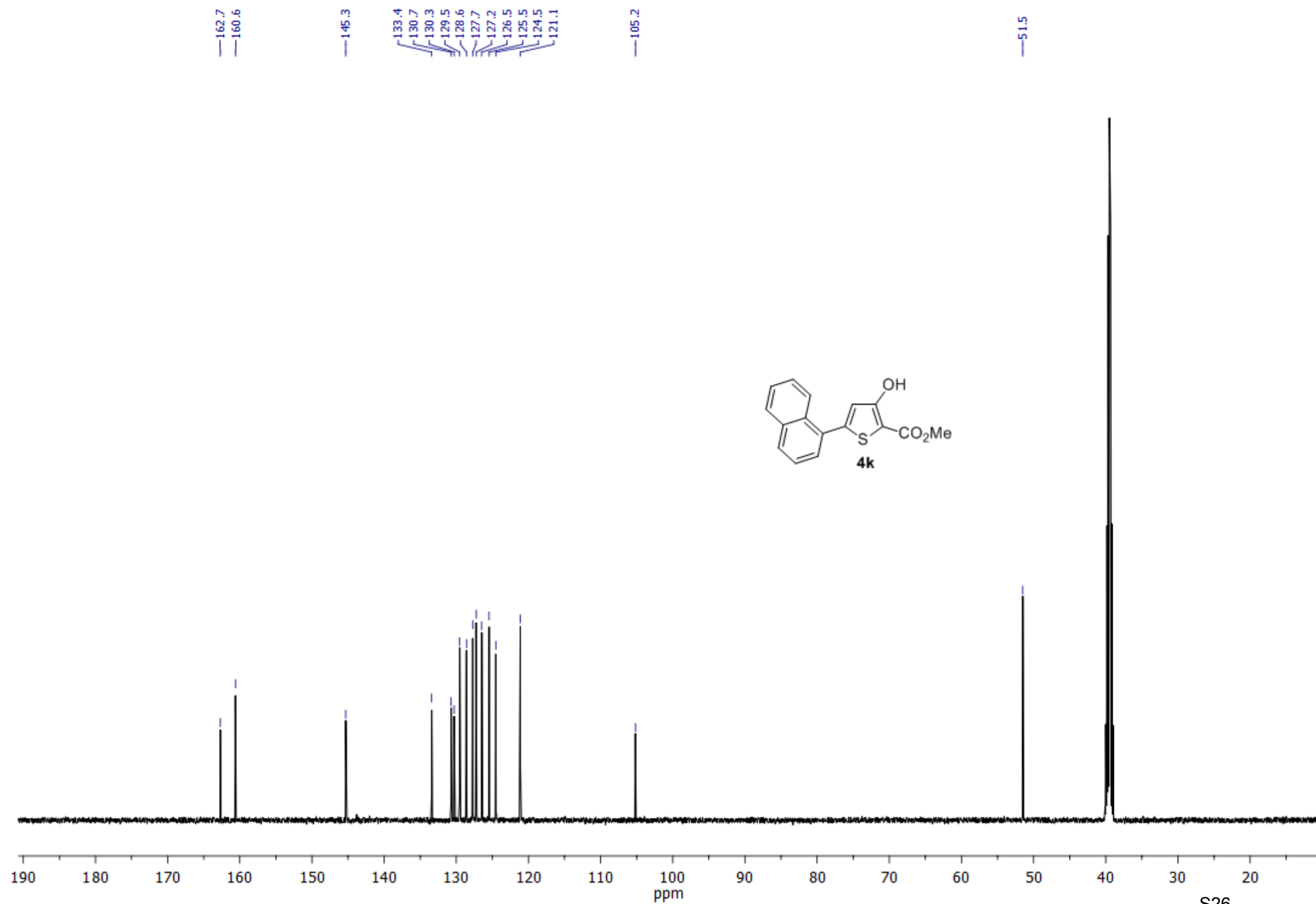


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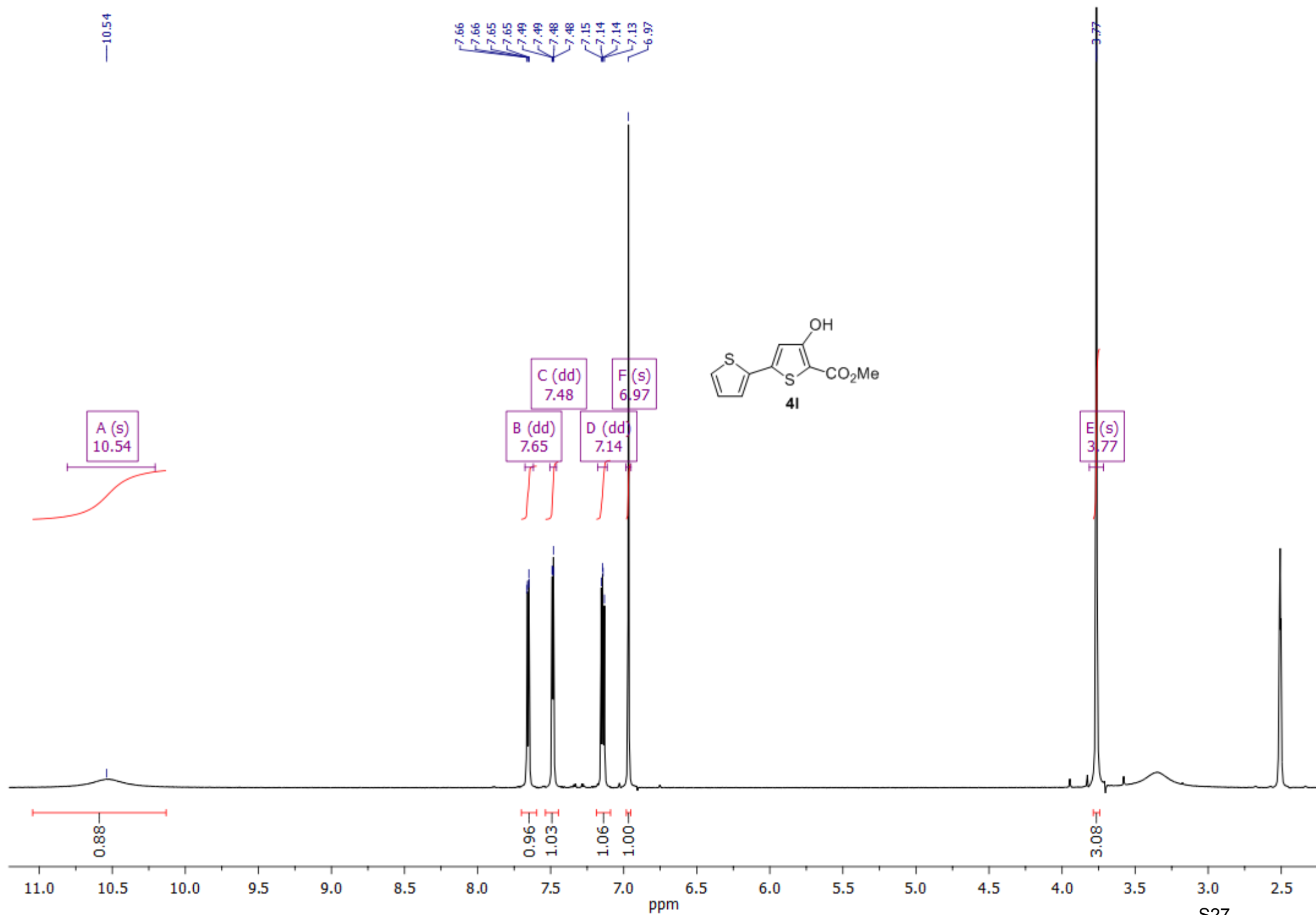


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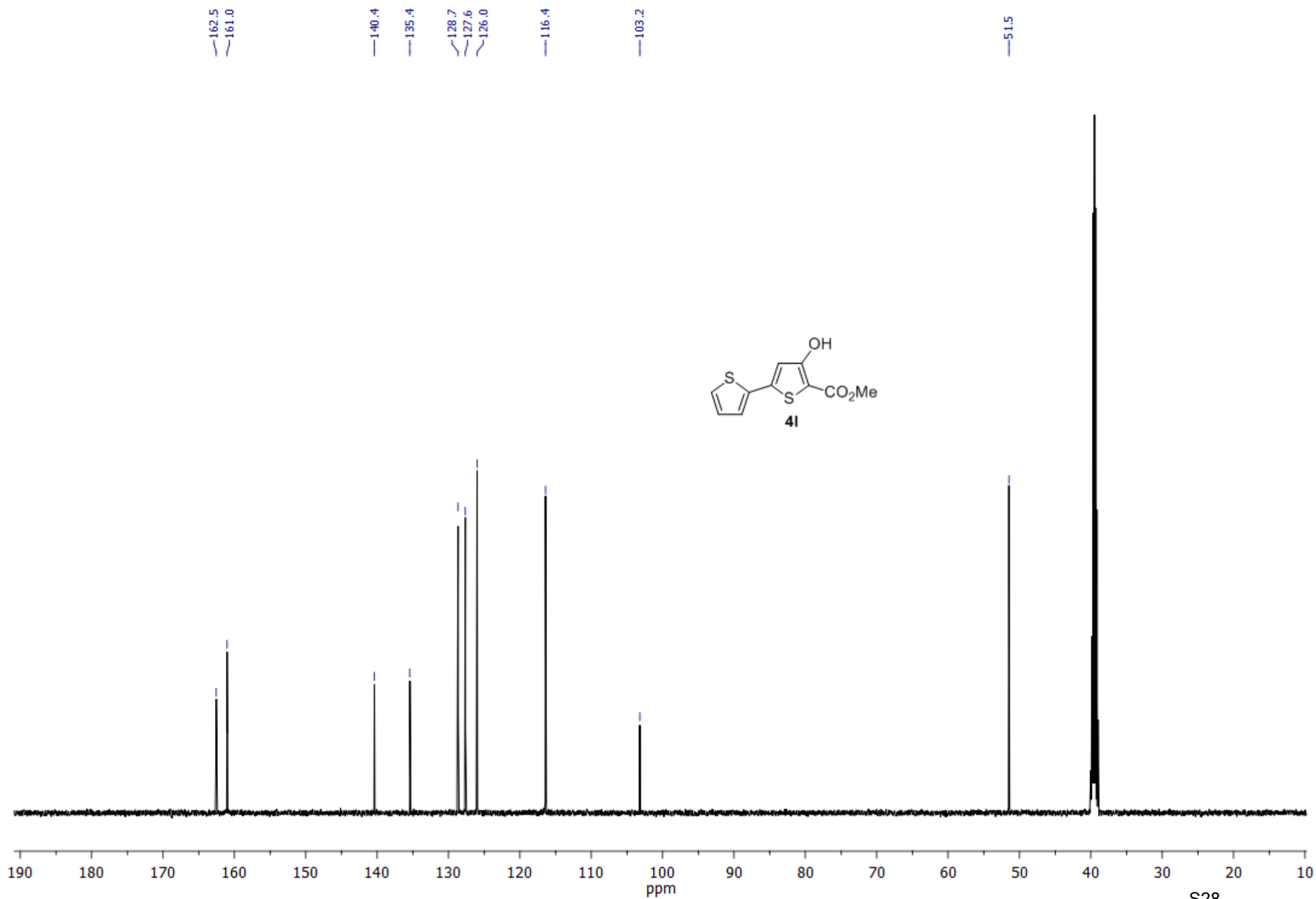




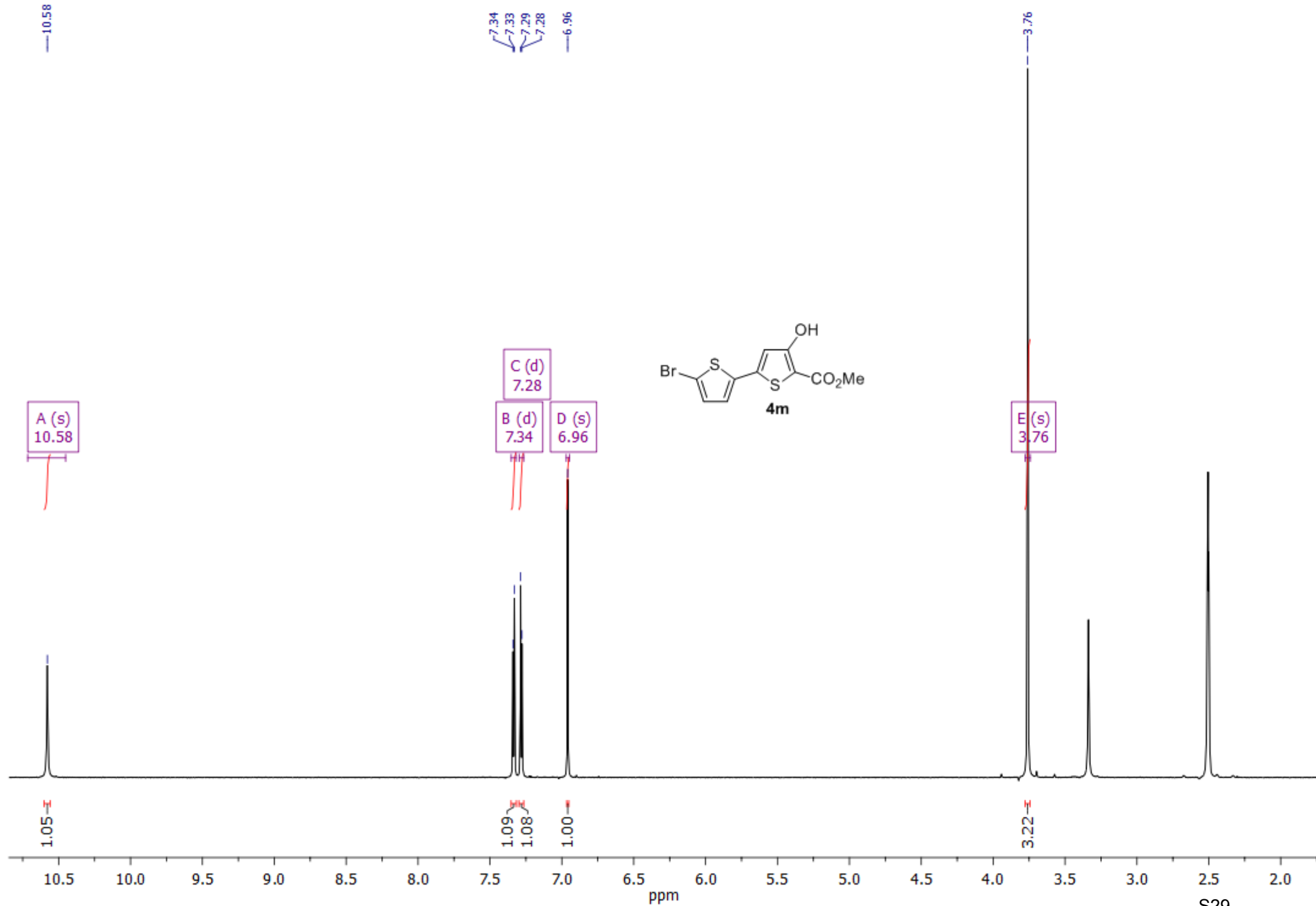
¹H NMR (solvent: DMSO-*d*₆)



¹³C NMR (solvent: DMSO-*d*₆)

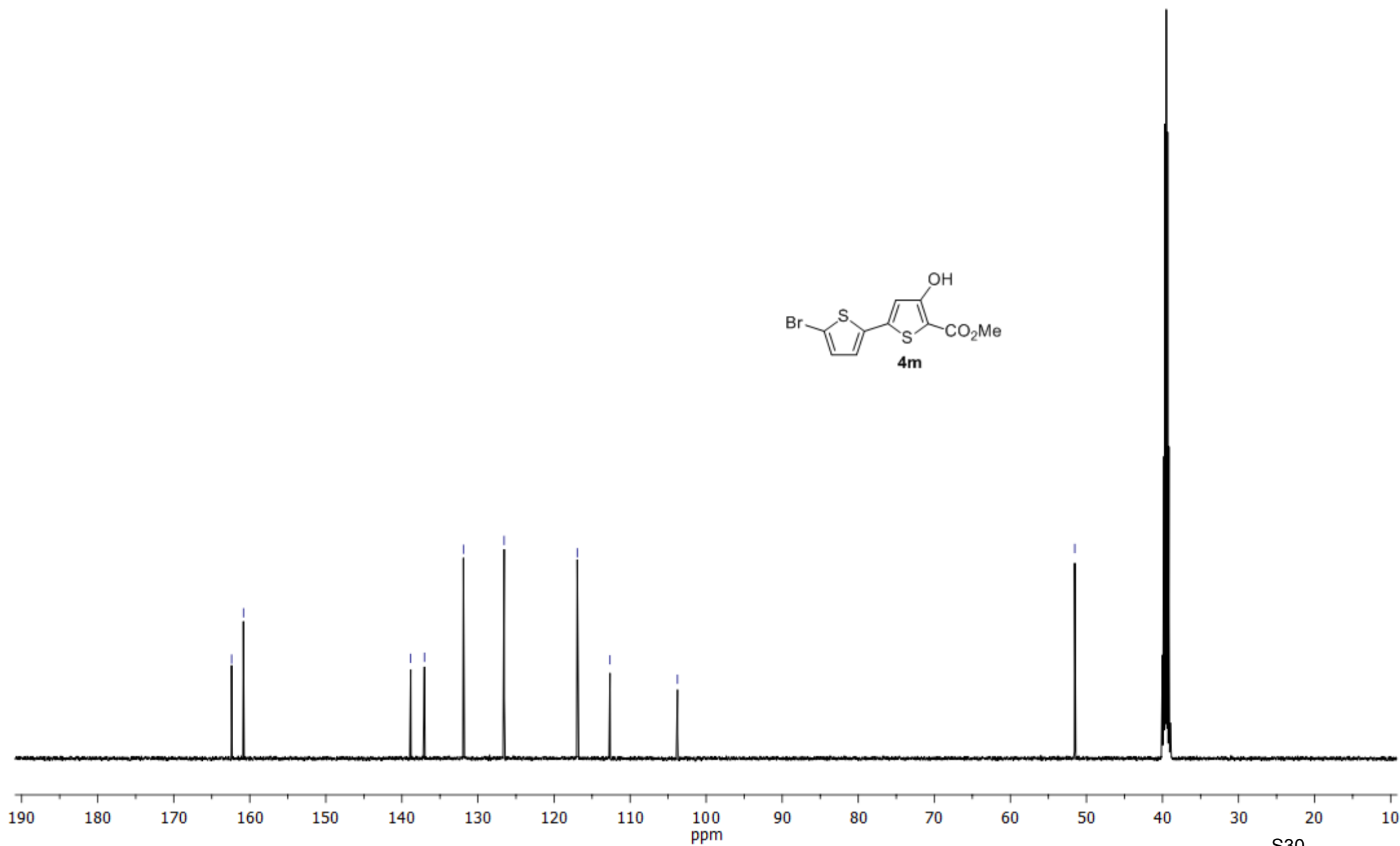
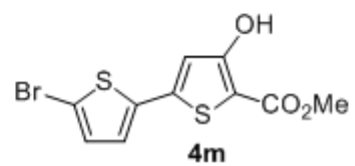


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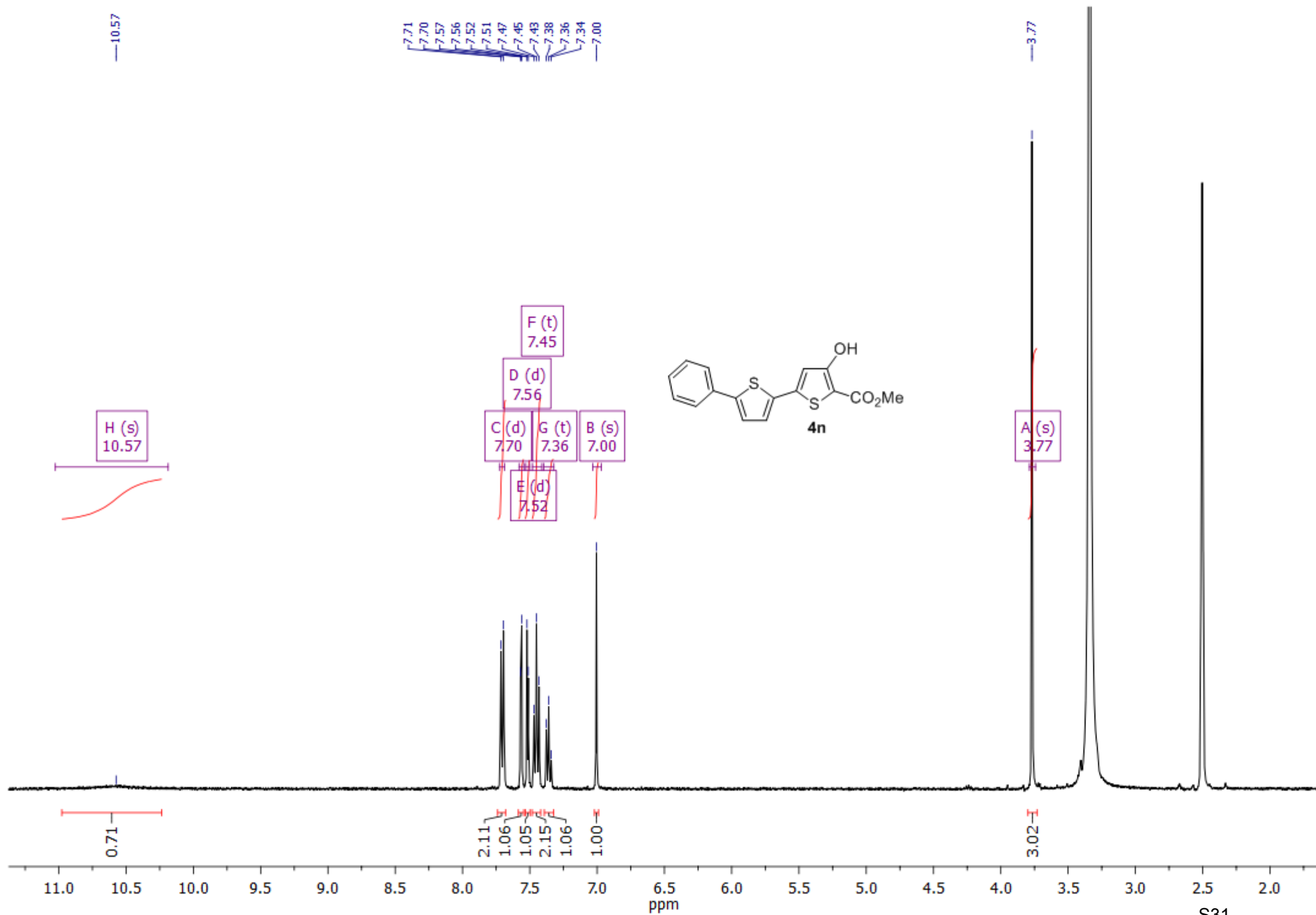


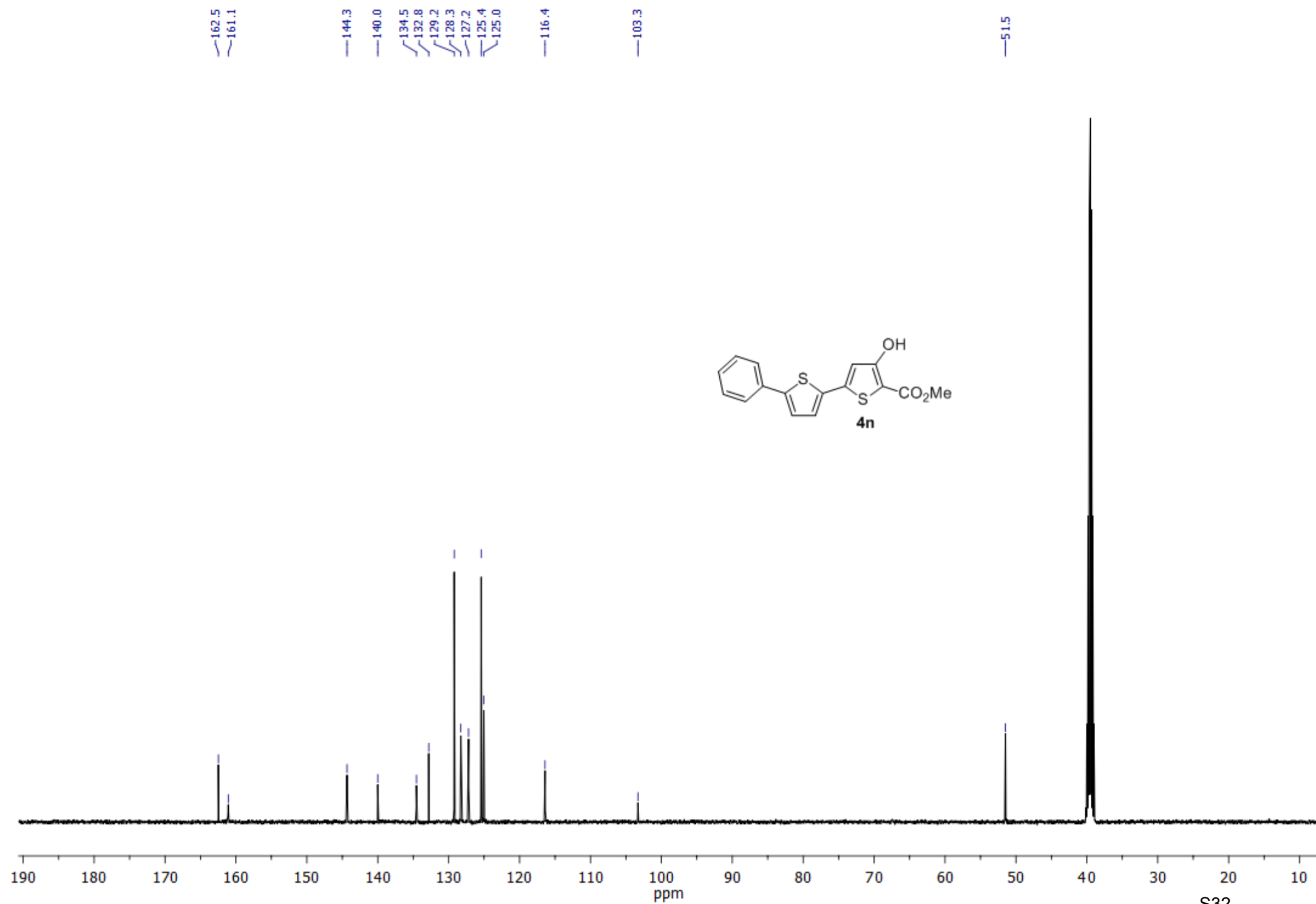
¹³C NMR (solvent: DMSO-*d*₆)

162.4
160.8
138.8
137.0
131.9
126.6
116.9
112.6
103.8
51.5



¹H NMR (solvent: DMSO-*d*₆)



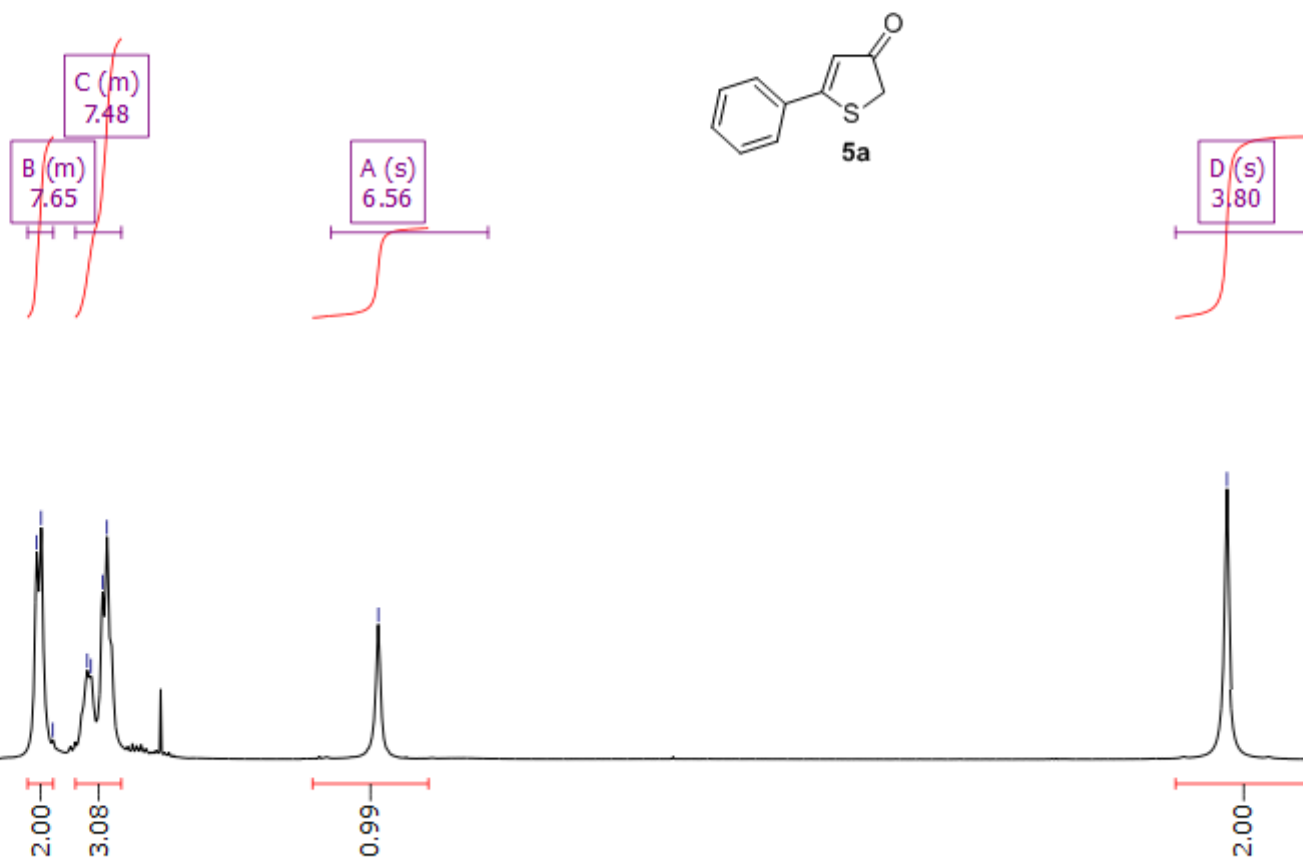


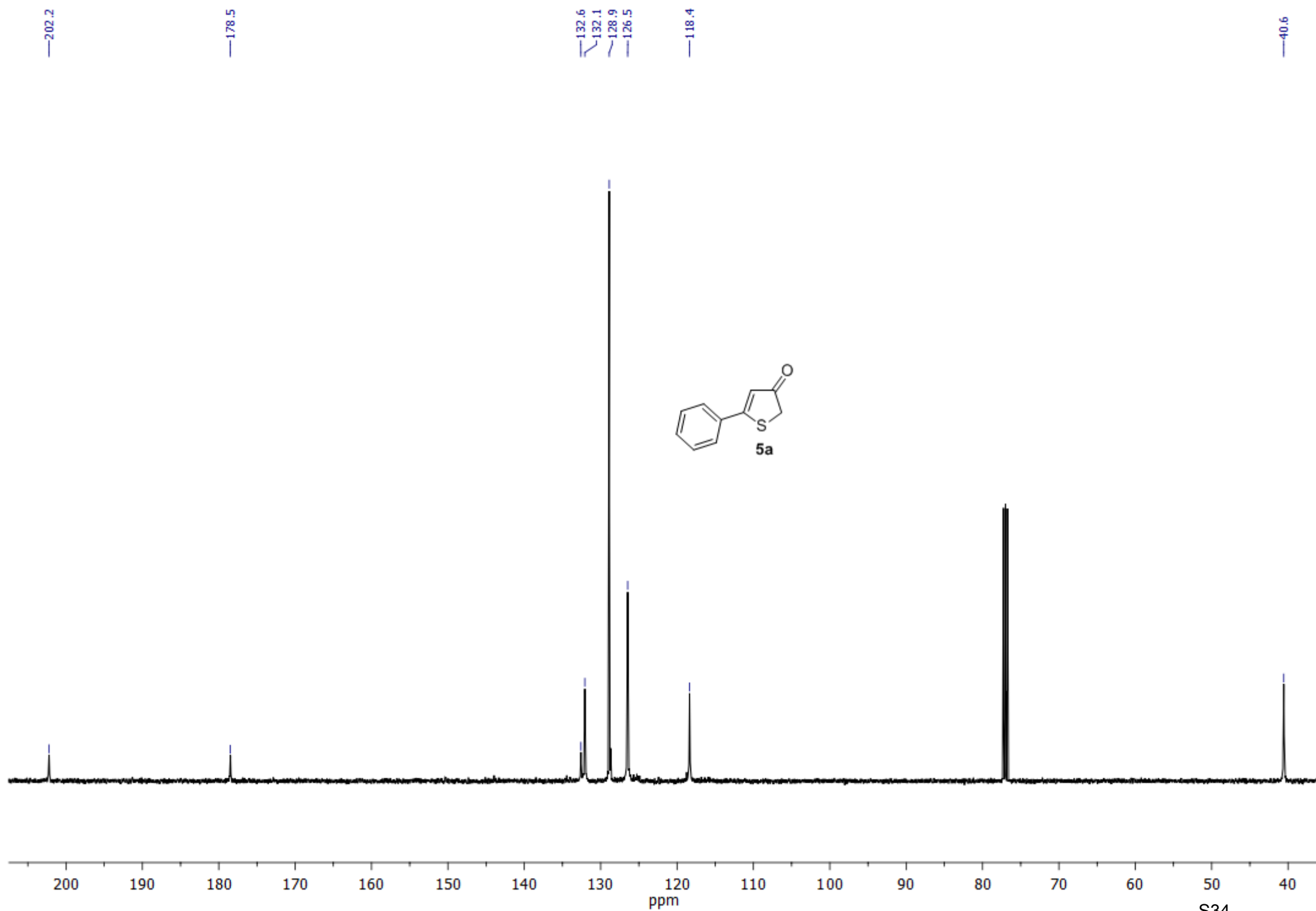
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7.67
7.66
7.62
7.51
7.50
7.46
7.44

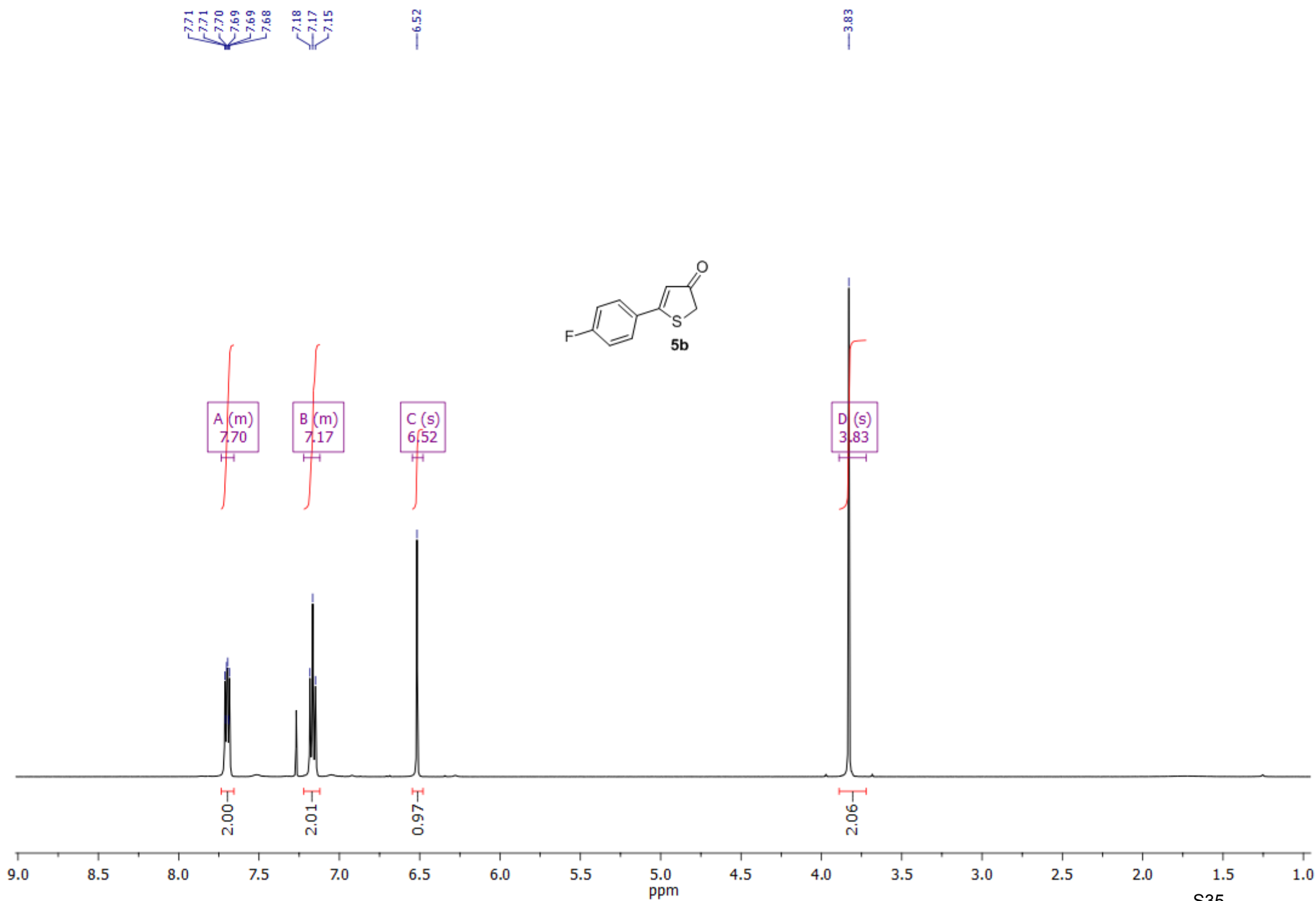
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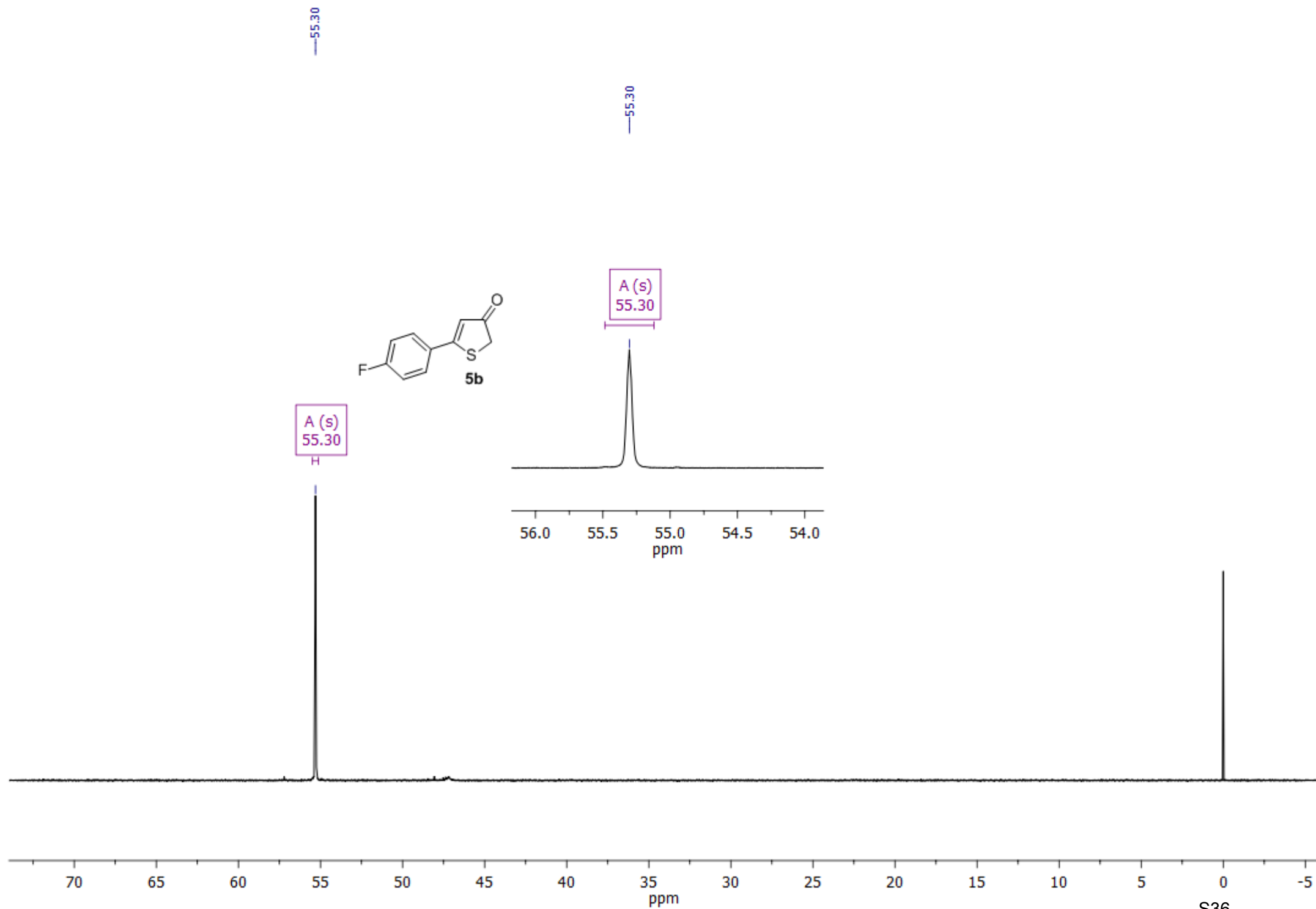
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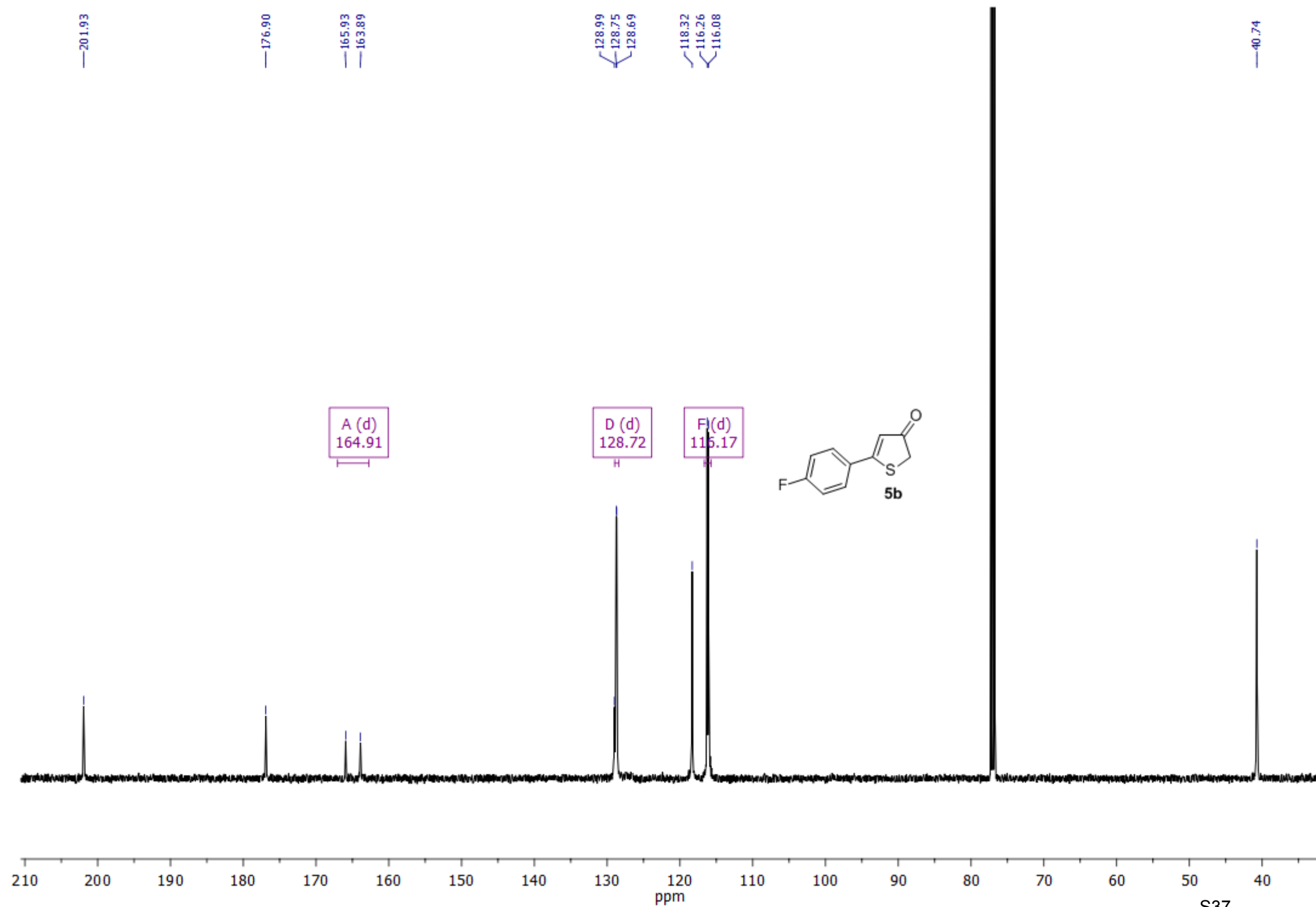




¹H NMR (solvent: CDCl₃)







¹H NMR (solvent: CDCl₃)

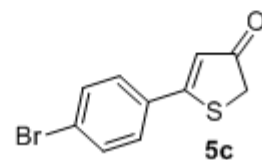
7.62
7.60
7.55
7.54

6.55

3.82

B (d)
7.55
A (d)
7.61
HH

C (s)
6.55

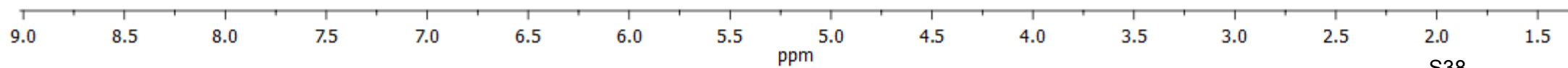


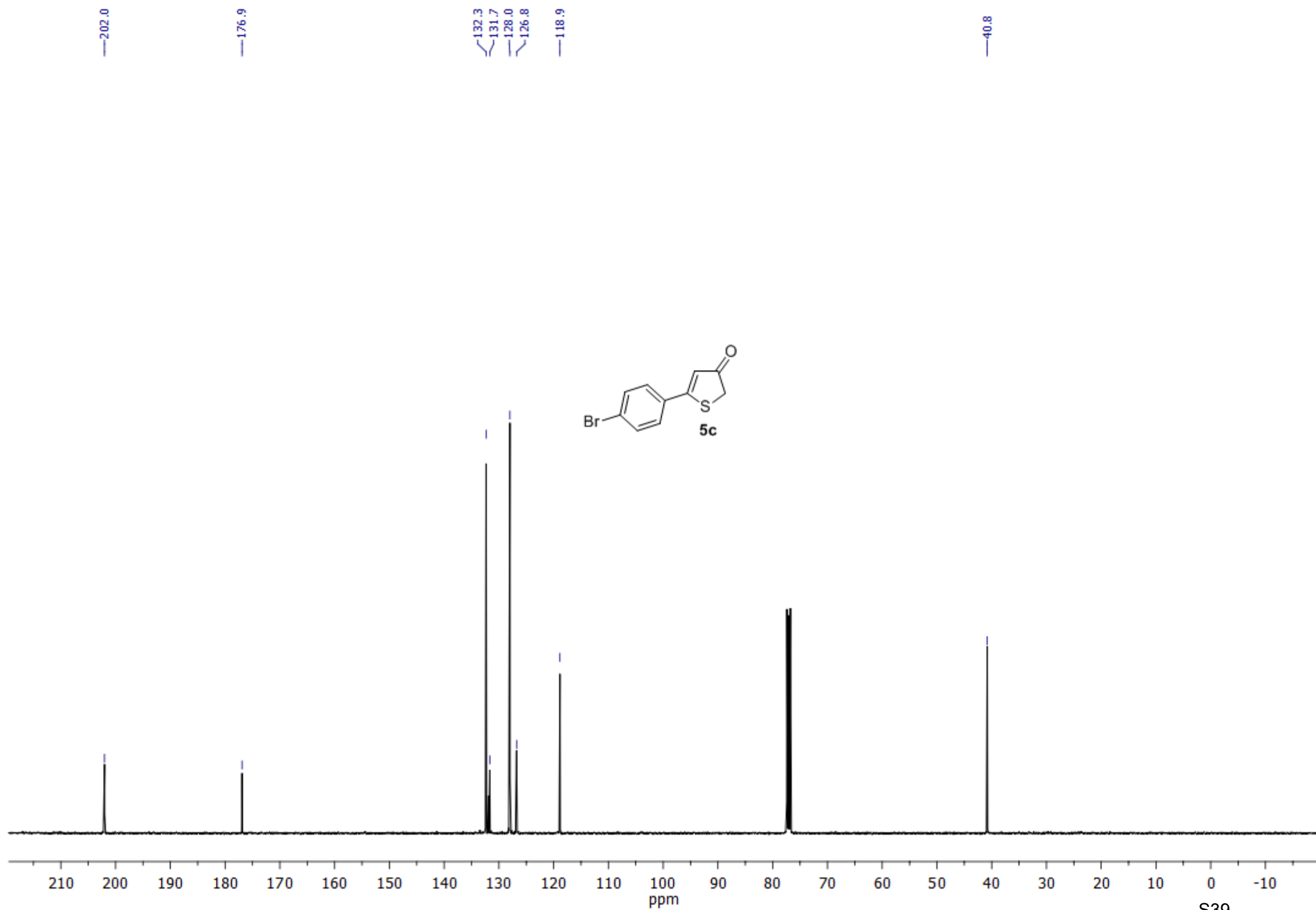
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4.11

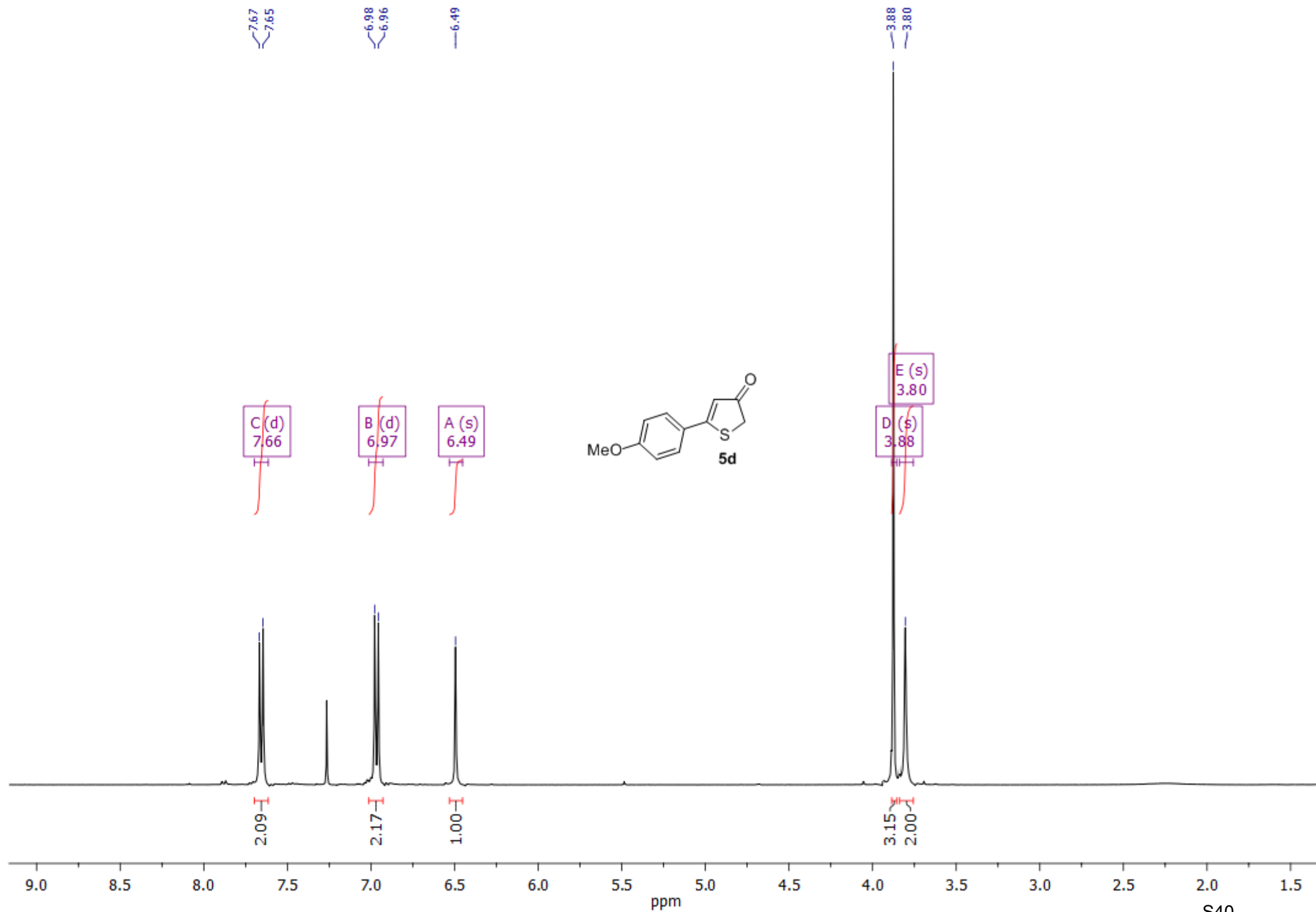
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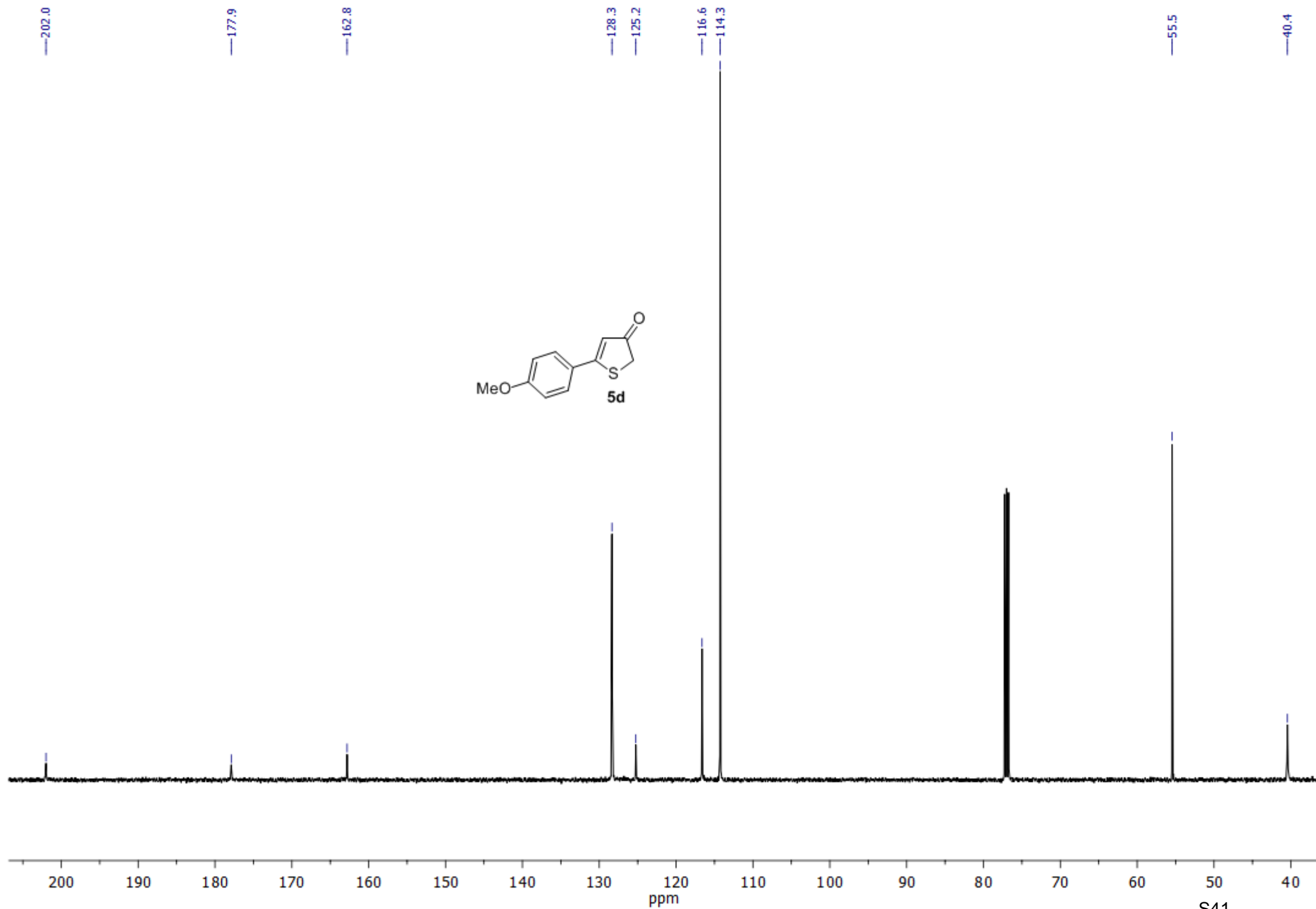
2.02





¹H NMR (solvent: CDCl₃)





¹H NMR (solvent: CDCl₃)

7.66
7.65
7.65
7.63
7.63
7.62

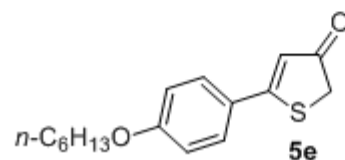
6.97
6.96
6.95
6.94
6.94
6.93

6.49

4.03
4.02
4.00
3.80

1.84
1.82
1.81
1.79
1.77

1.47
1.36
1.35
1.34
1.33
0.91
0.89



C (m)
7.64

B (m)
6.95

A (s)
6.49

D (t)
4.02

E (s)
3.80

F (m)
1.81

G (m)
1.47

H (m)
1.35

I (t)
0.91

2.03

2.05

1.00

2.12

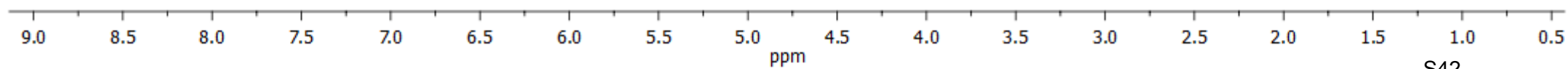
1.94

2.20

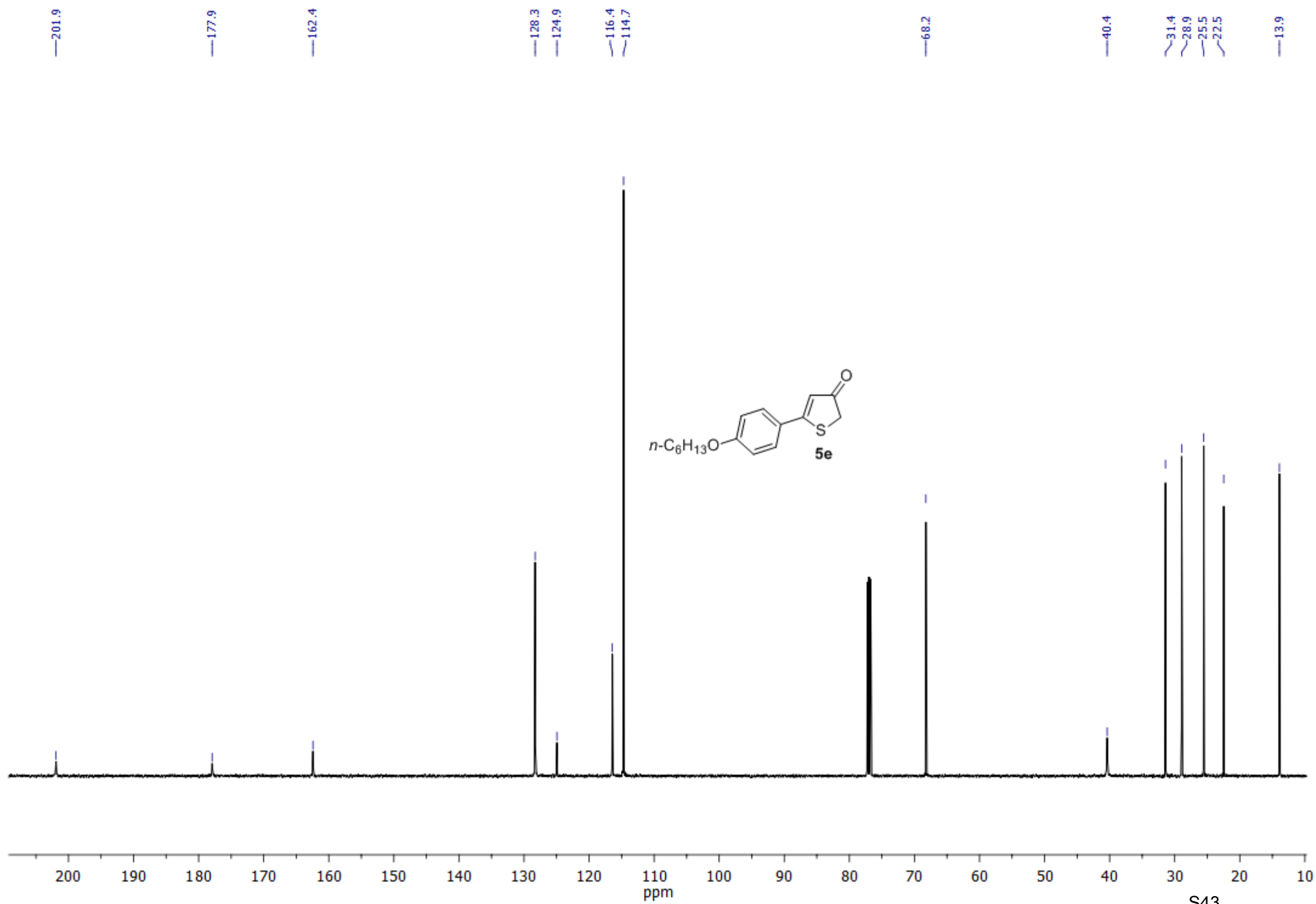
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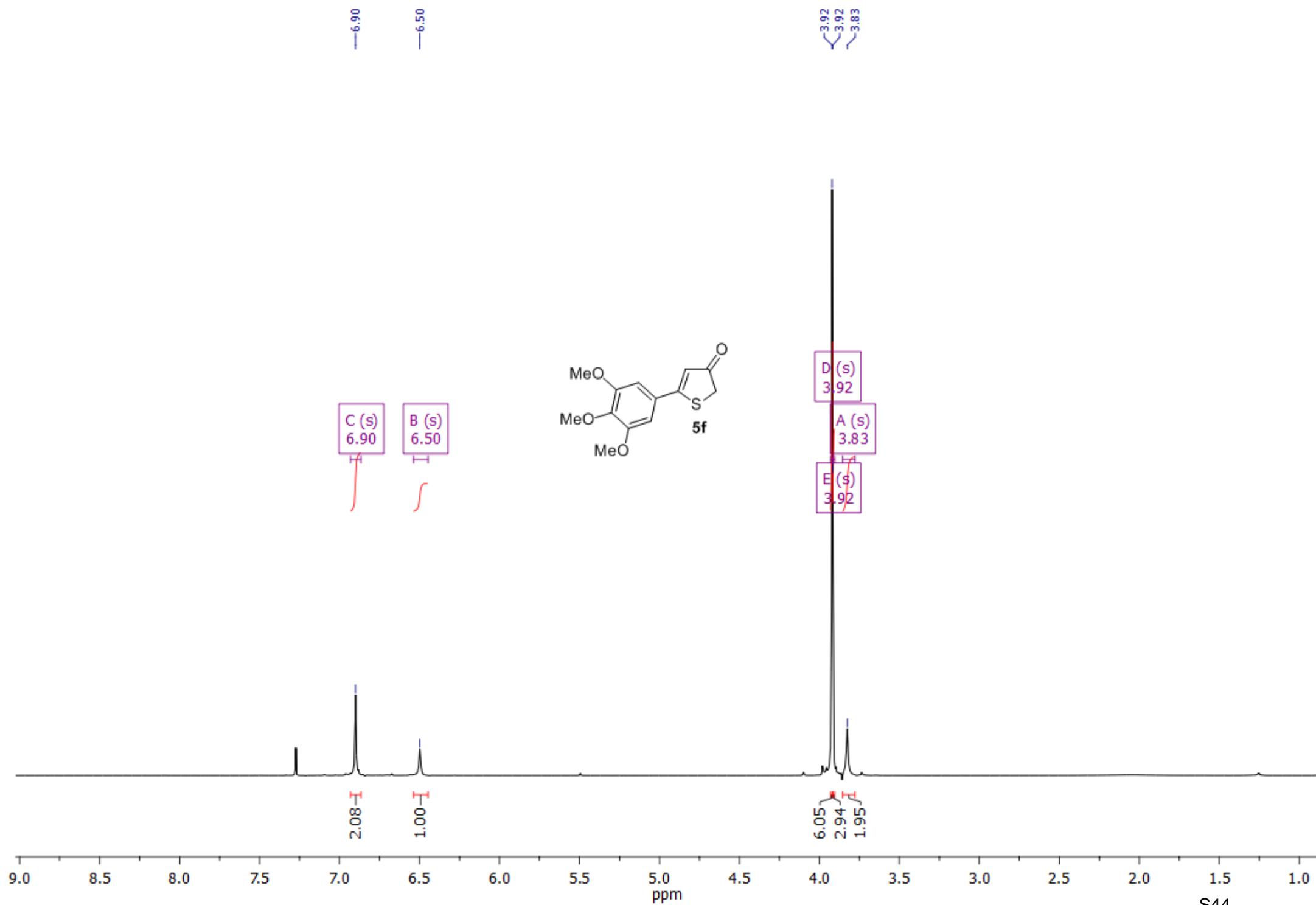
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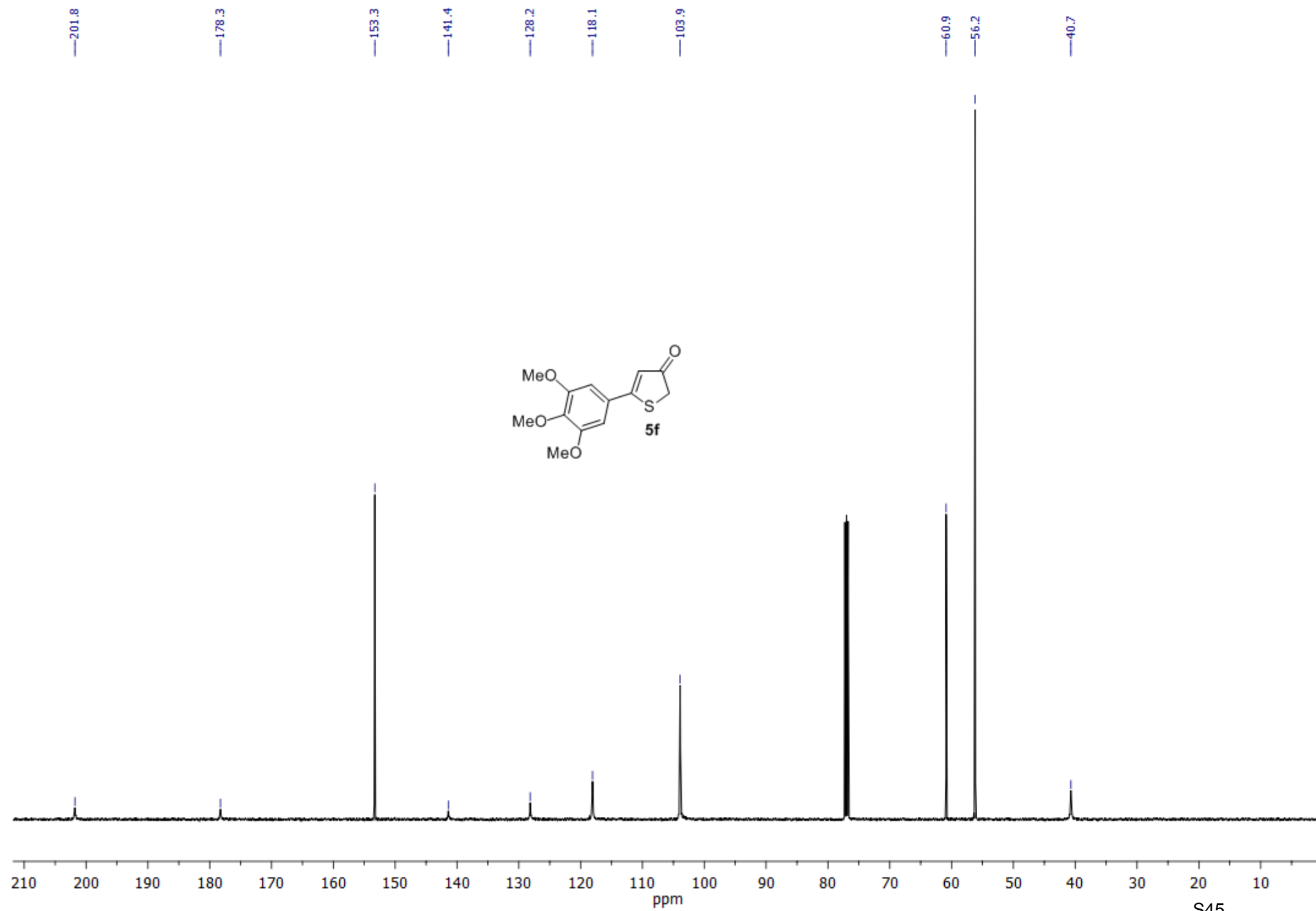
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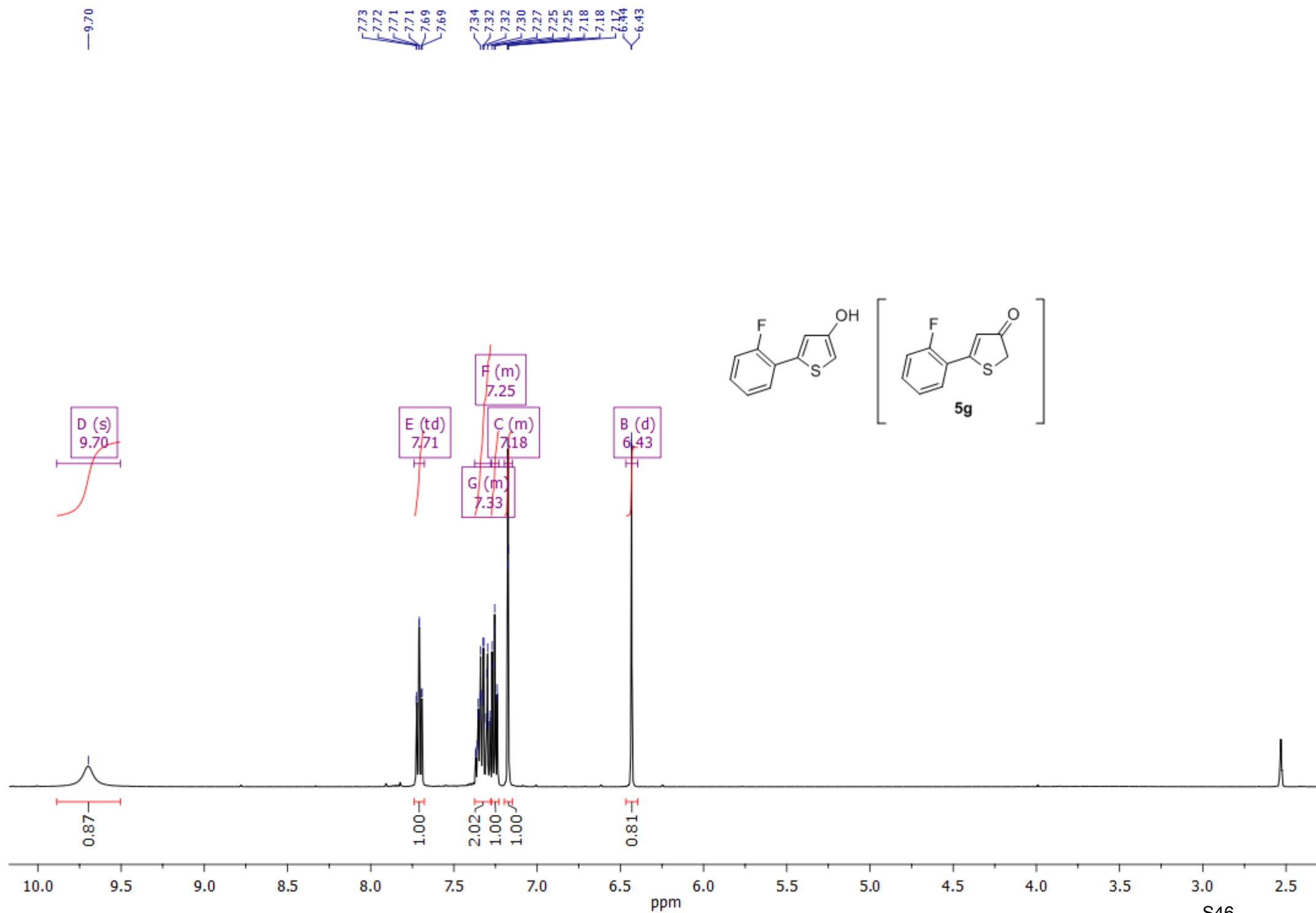
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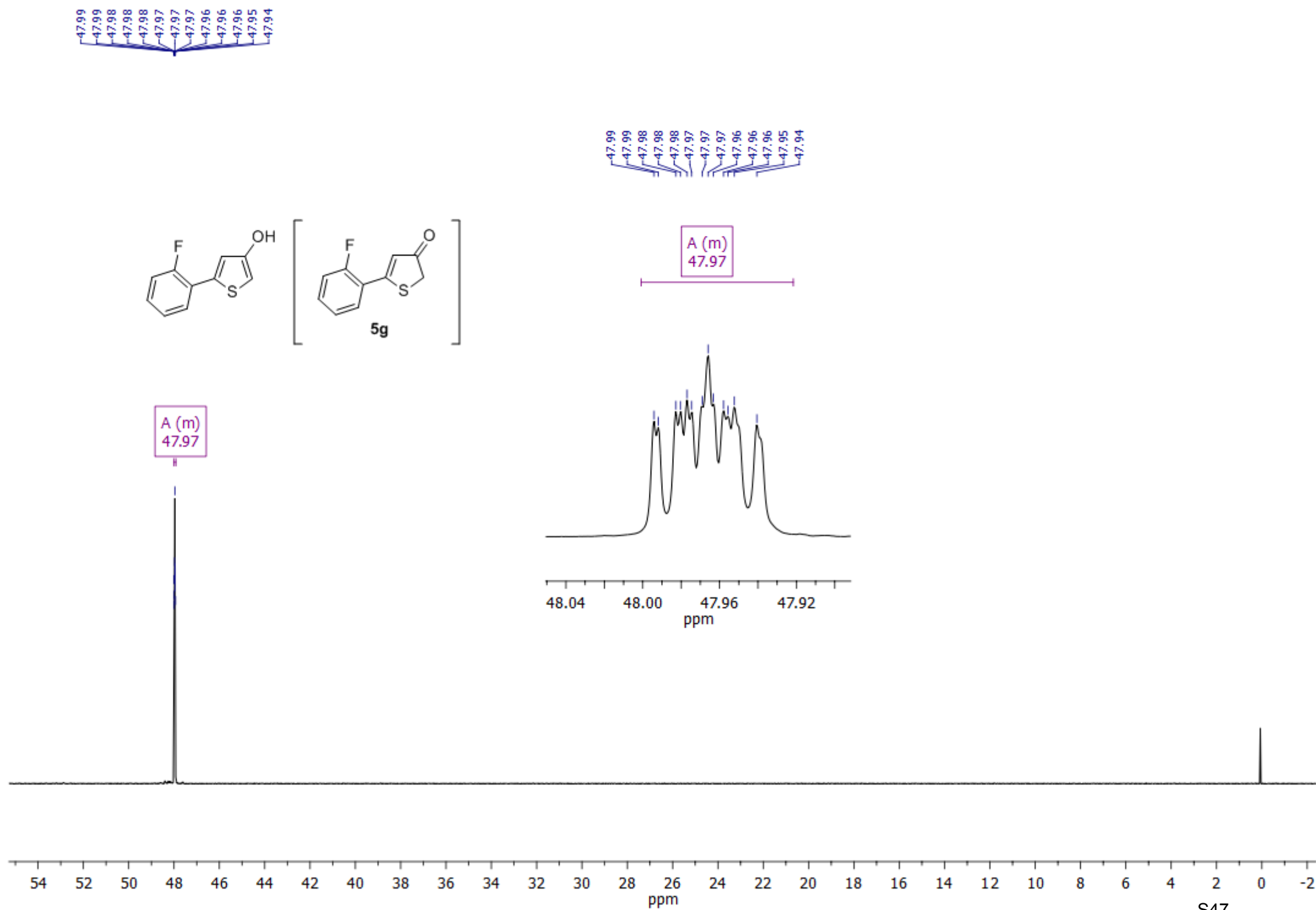




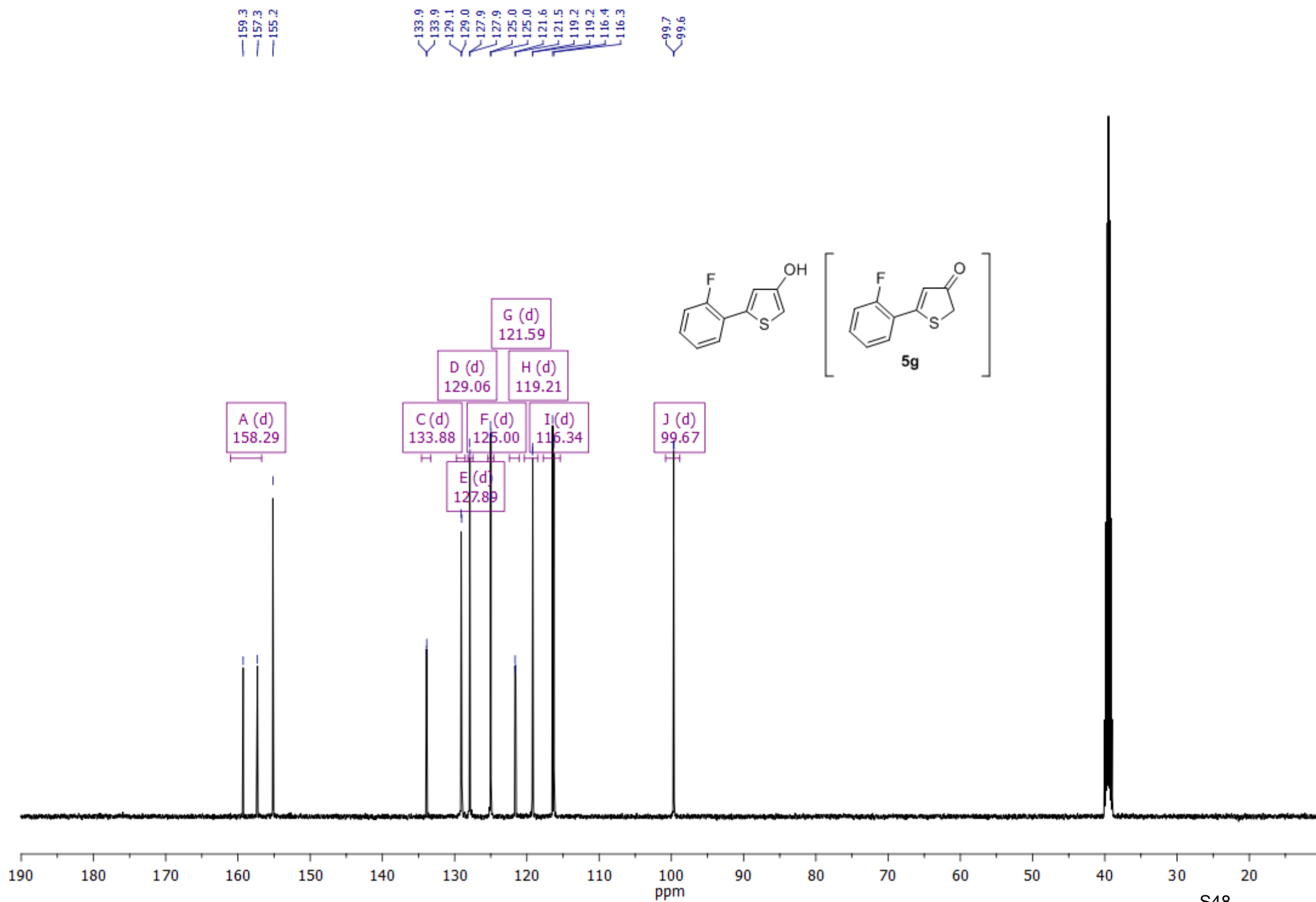
¹H NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **5g**



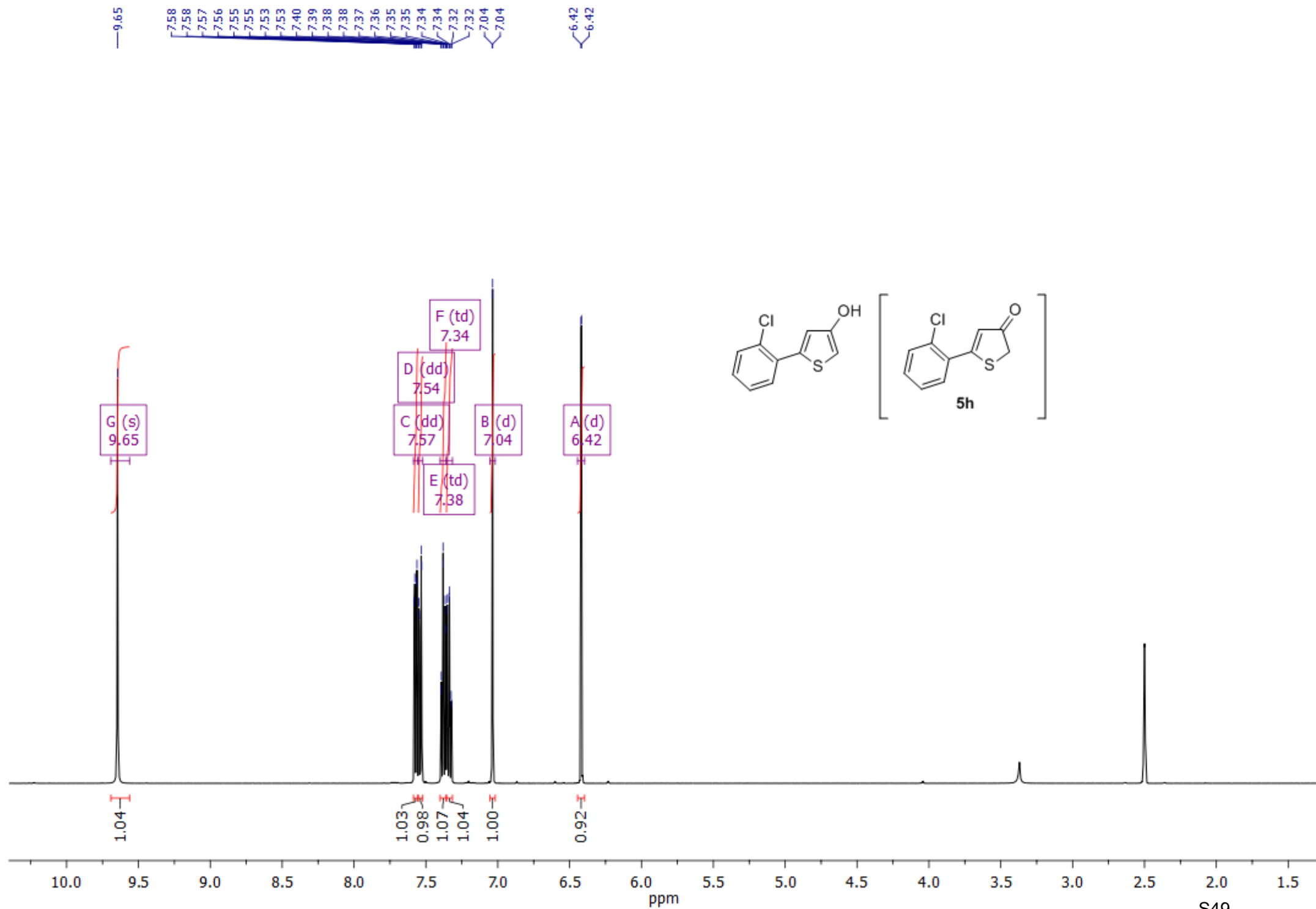
¹⁹F NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **5g**



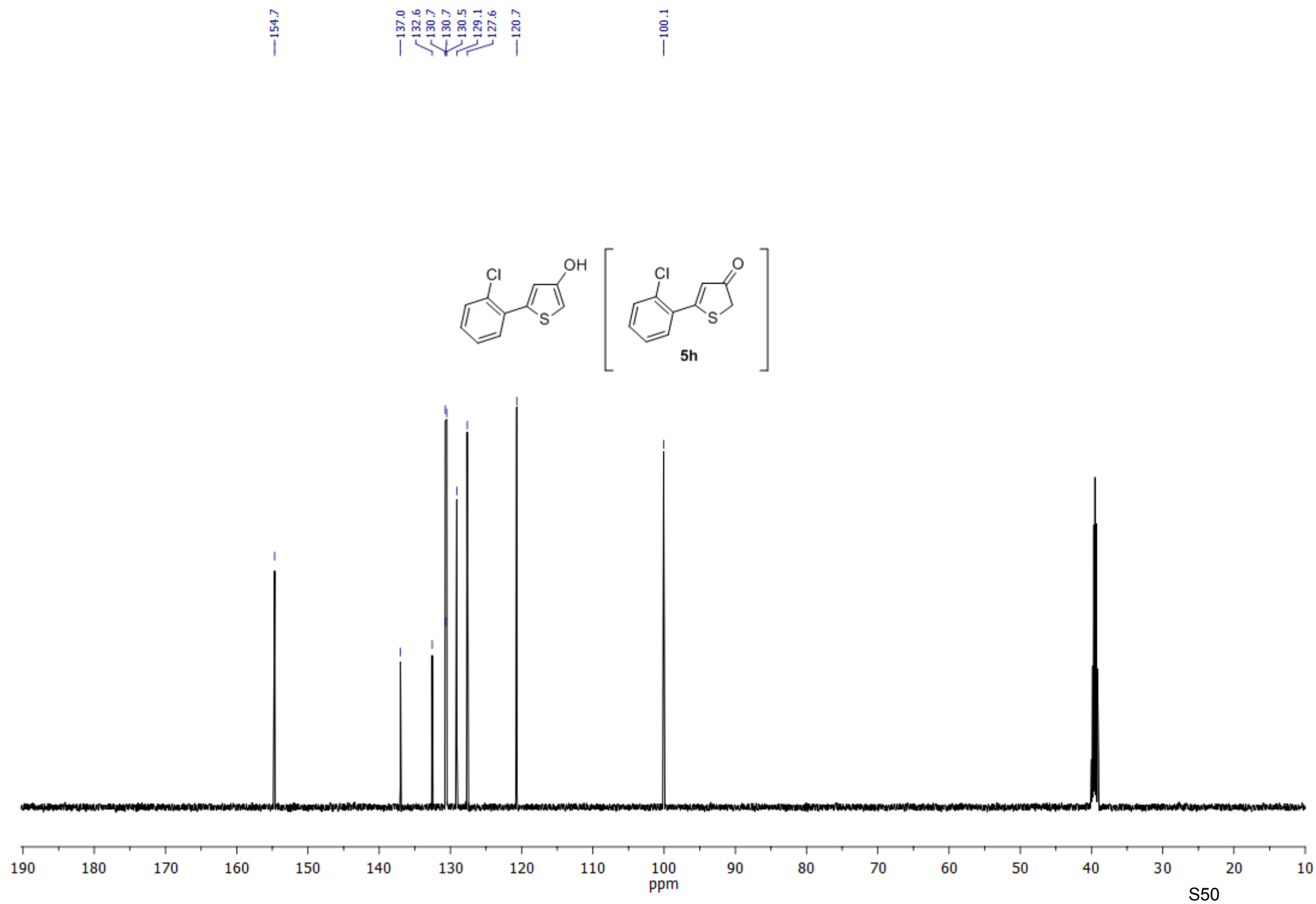
¹³C NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **5g**



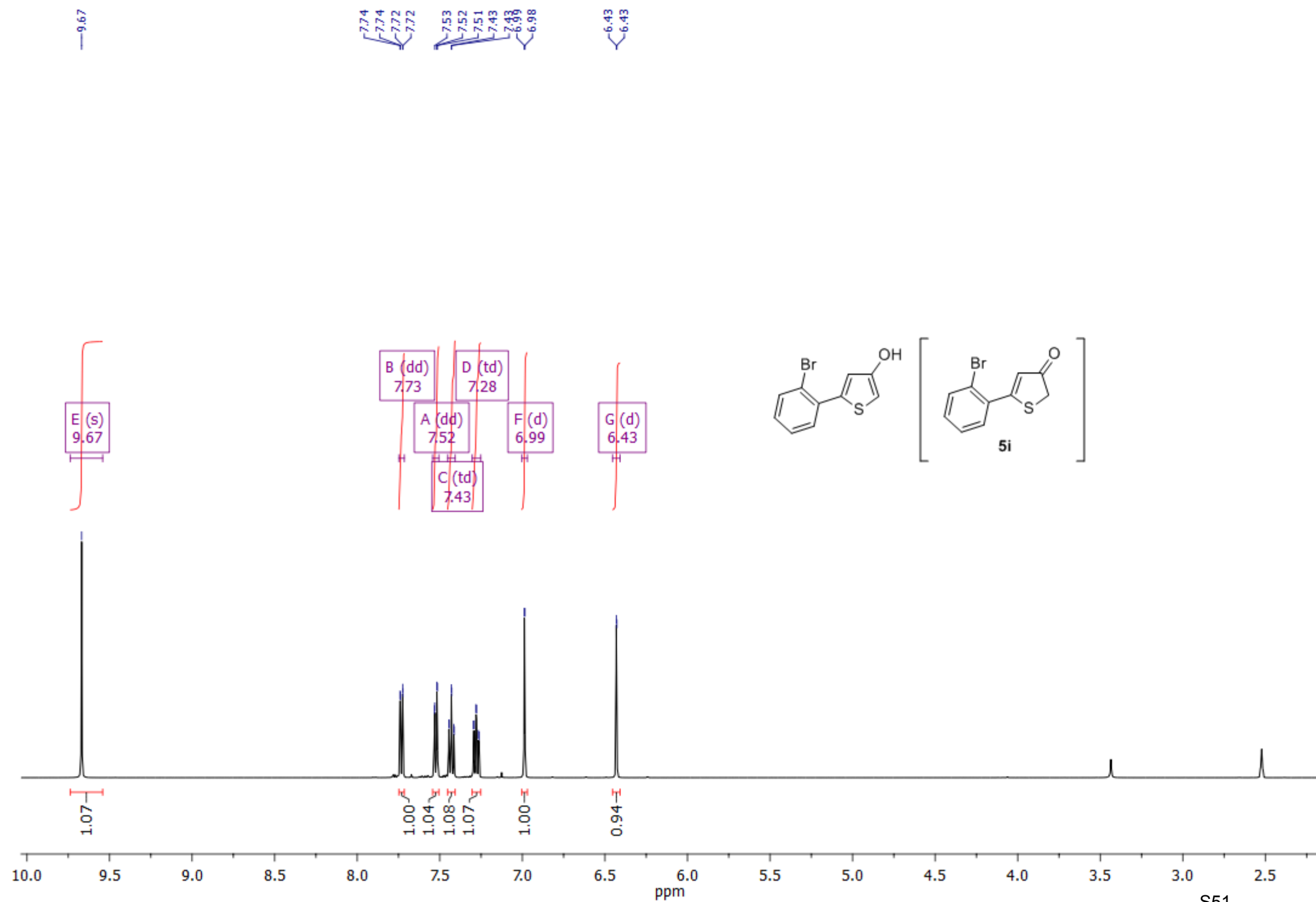
¹H NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **5h**



^{13}C NMR (solvent: $\text{DMSO-}d_6$), enol (3-hydroxythiophene) form of compound **5h**

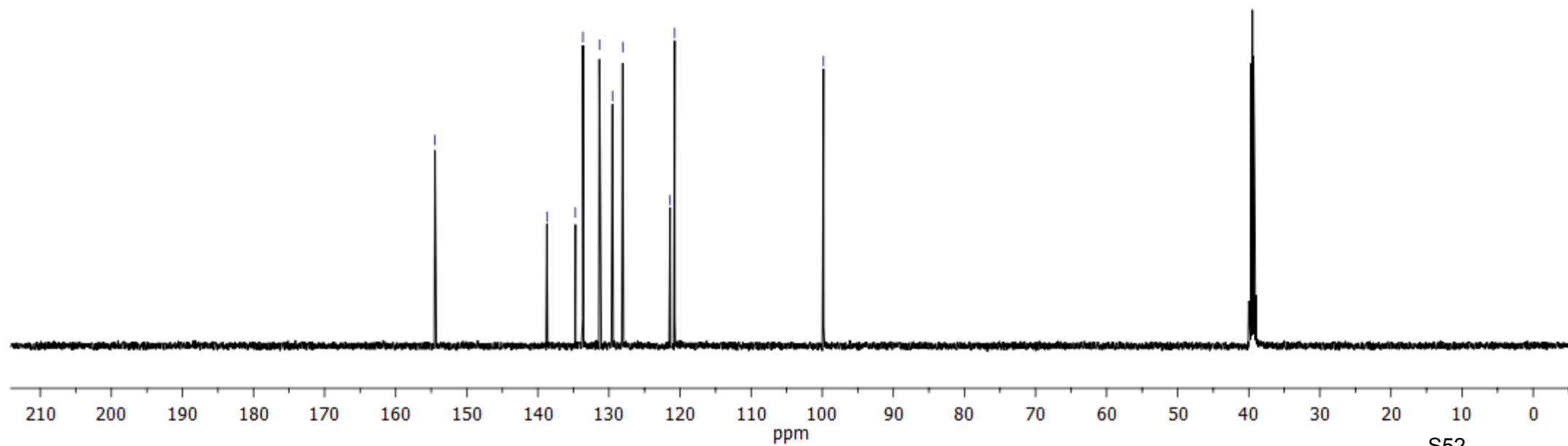
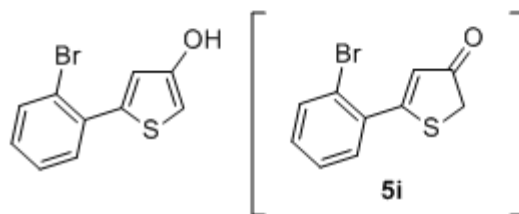


¹H NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **5i**

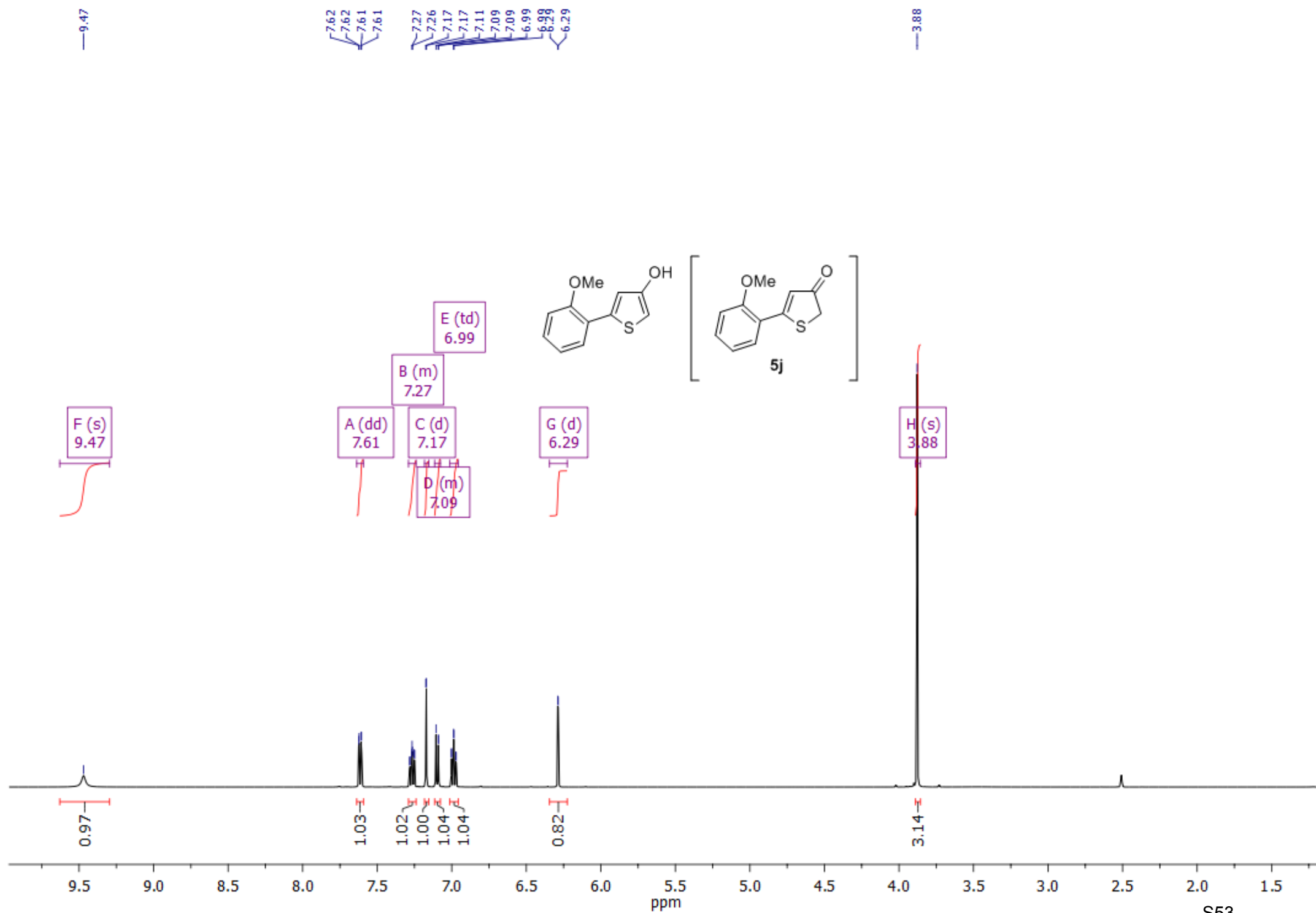


¹³C NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **5i**

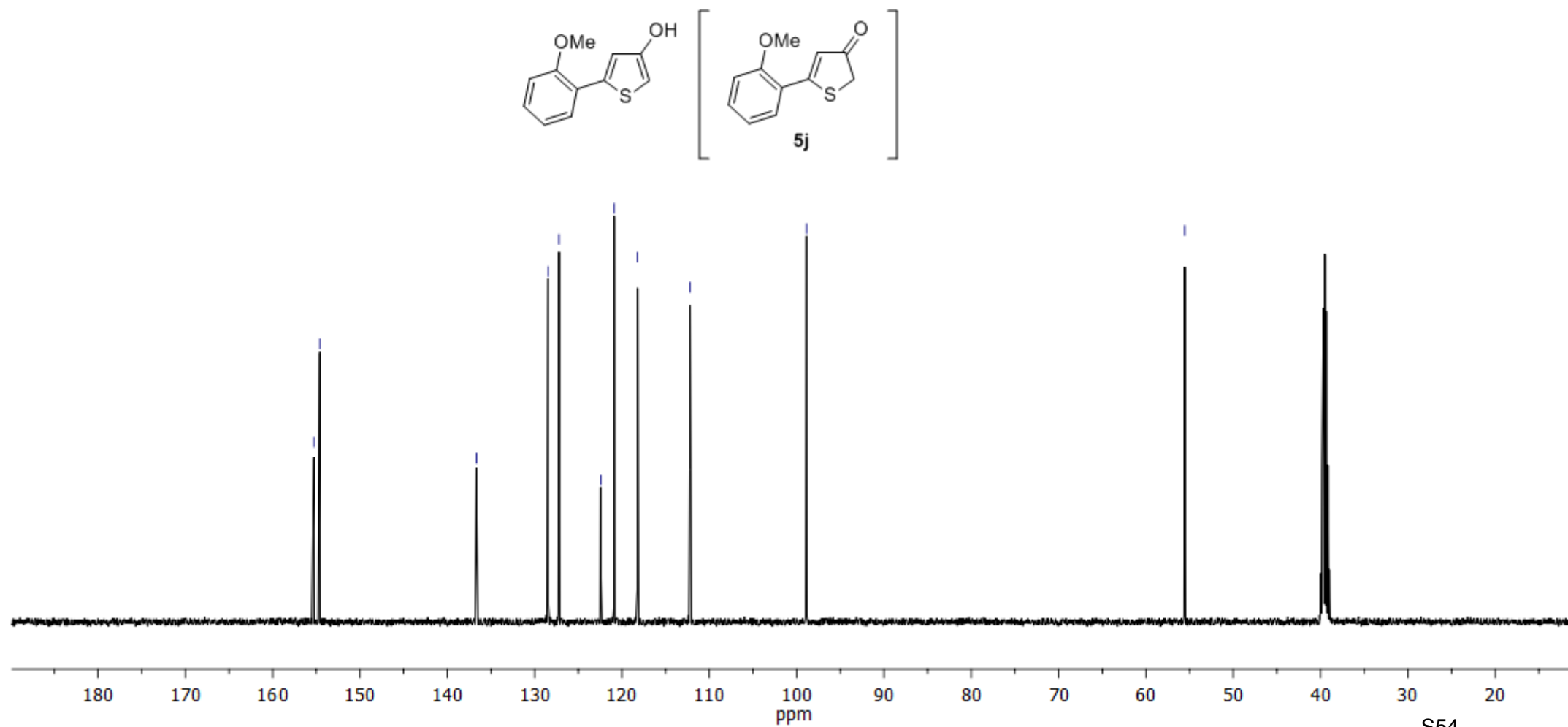
154.5
138.7
134.7
133.7
131.3
129.5
128.1
121.4
120.8
99.8



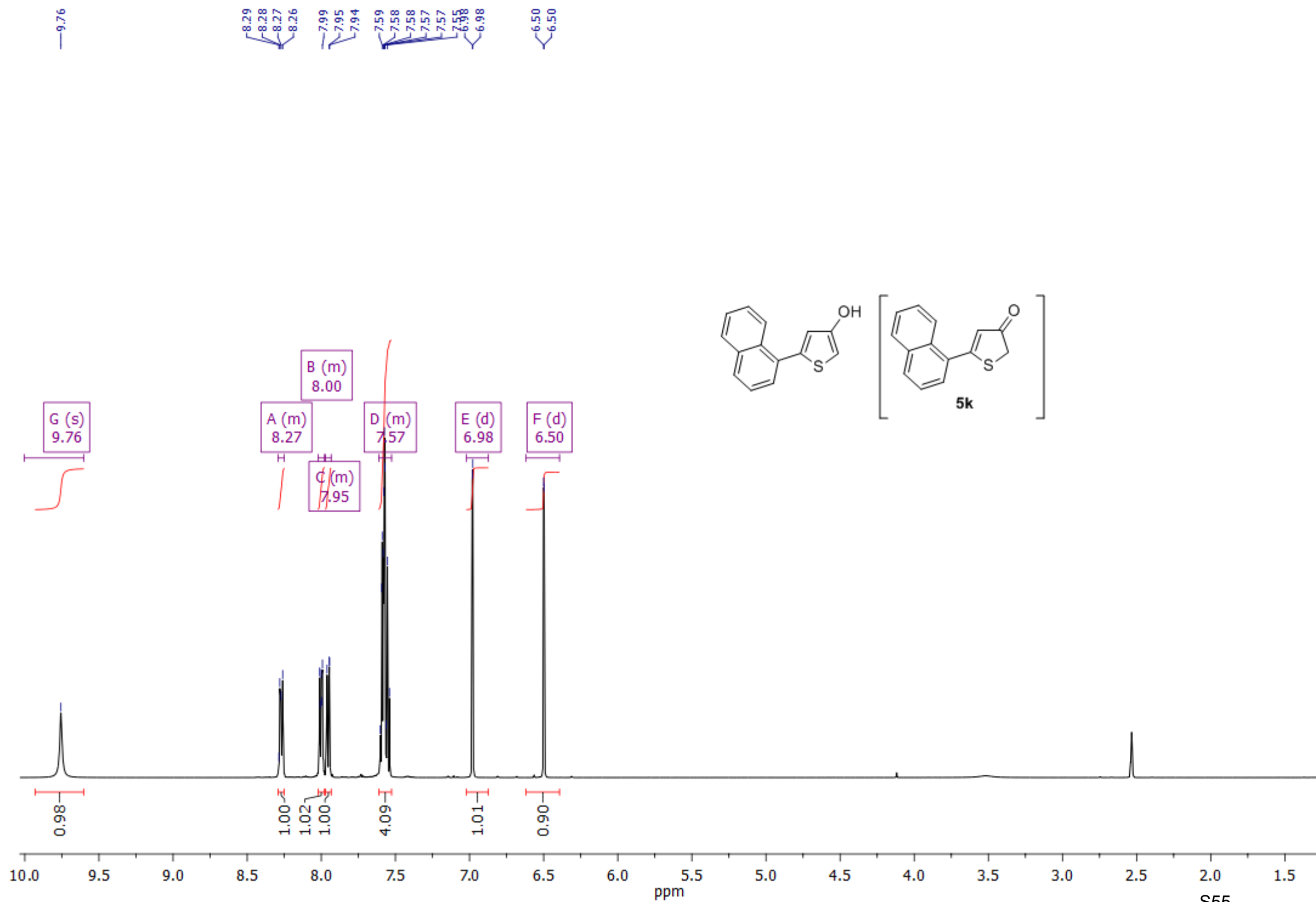
¹H NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **5j**



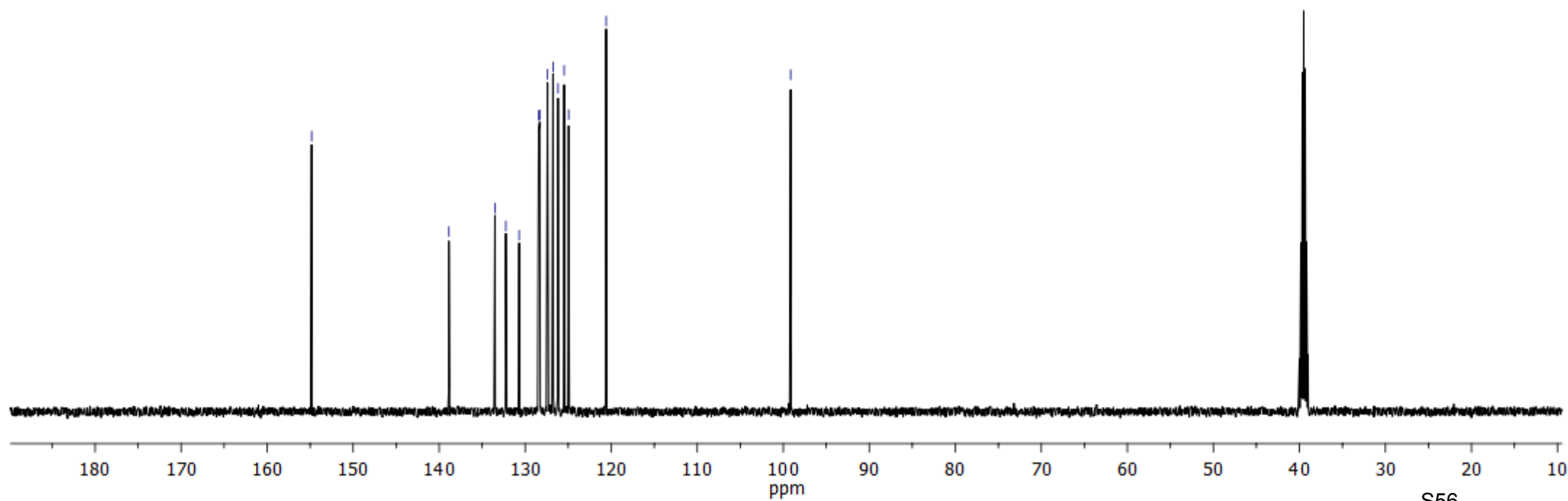
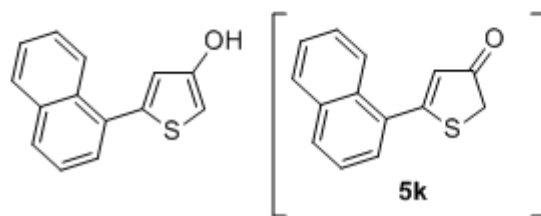
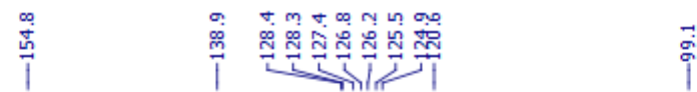
¹³C NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **5j**



¹H NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **5k**



^{13}C NMR (solvent: $\text{DMSO-}d_6$), enol (3-hydroxythiophene) form of compound **5k**



¹H NMR (solvent: CDCl₃)

7.58
7.57
7.56
7.55

7.15
7.14
7.13

6.41

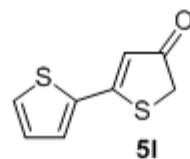
3.82

D (m)
7.57

C (m)
7.14

B (s)
6.41

A (s)
3.82



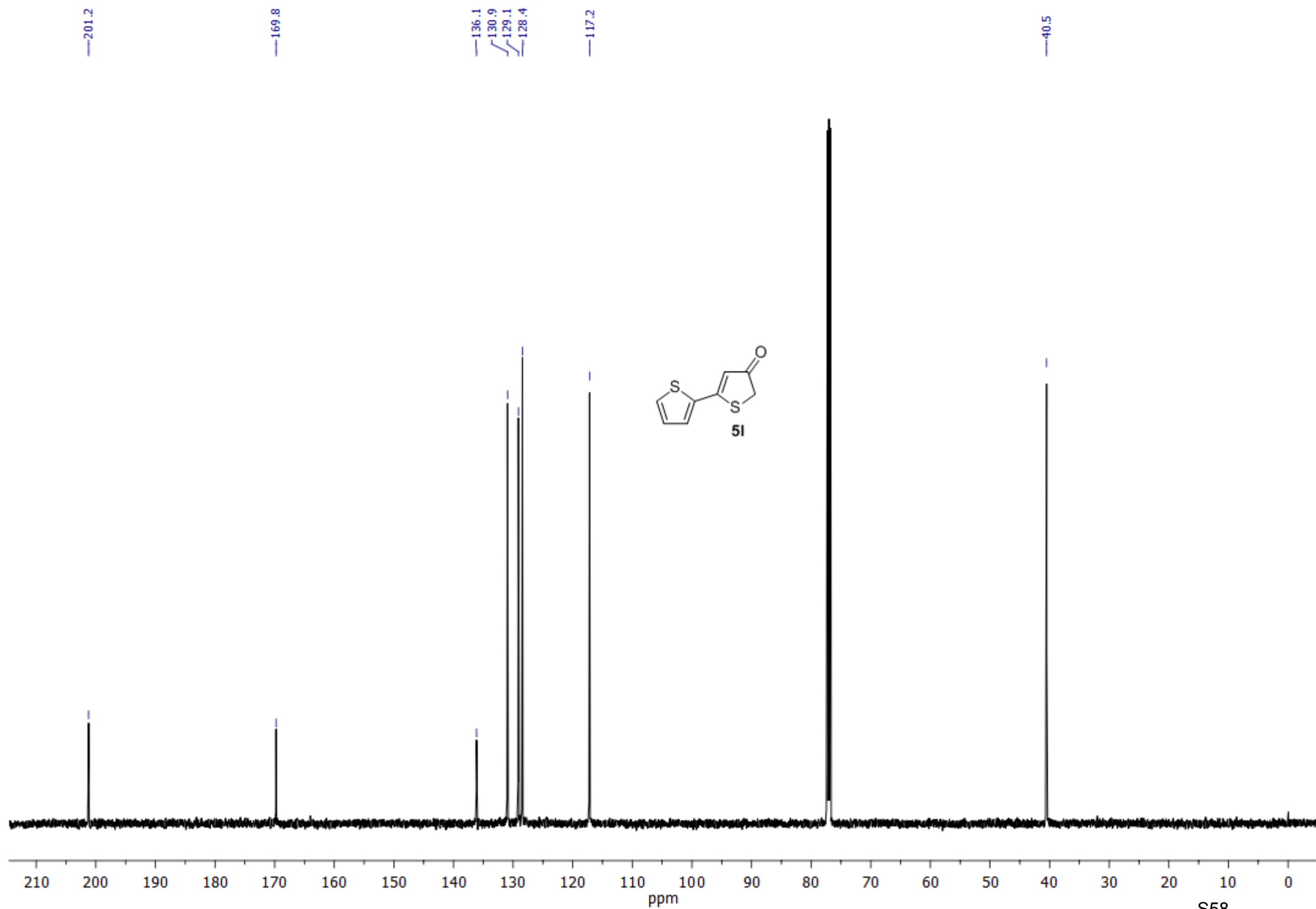
2.00

1.04

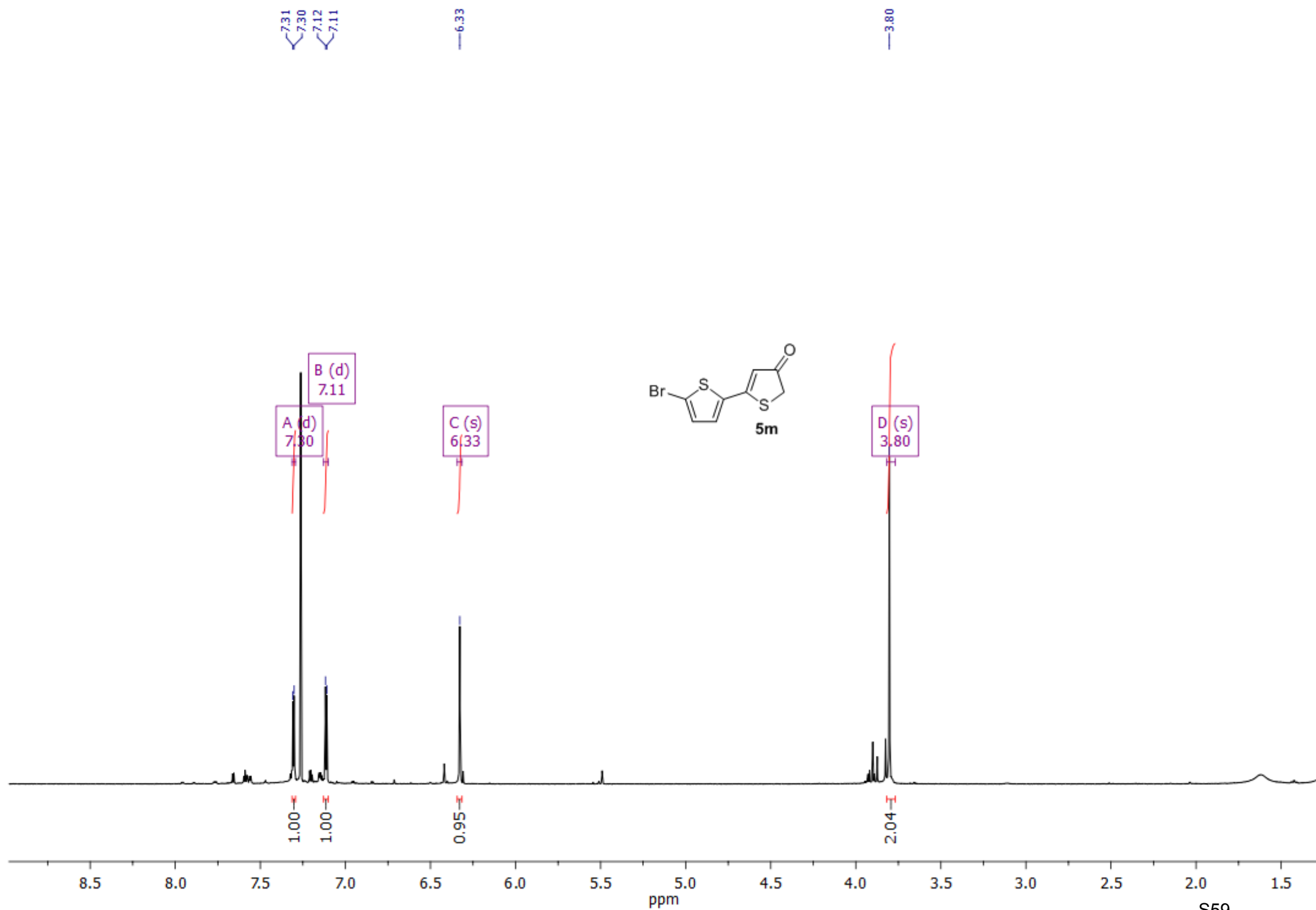
0.92

2.04

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
ppm



¹H NMR (solvent: CDCl₃), crude compound **5m**



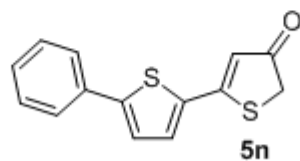
¹H NMR (solvent: CDCl₃)

7.65
7.65
7.63
7.54
7.53
7.45
7.44
7.43
7.43
7.41
7.40
7.39
7.38
7.37
7.36
7.35
7.34
7.33
6.42
3.83

B (m)
7.64
A (d)
7.53
C (m)
7.43
G (m)
7.37
F (d)
7.34

E (s)
6.42

D (s)
3.83

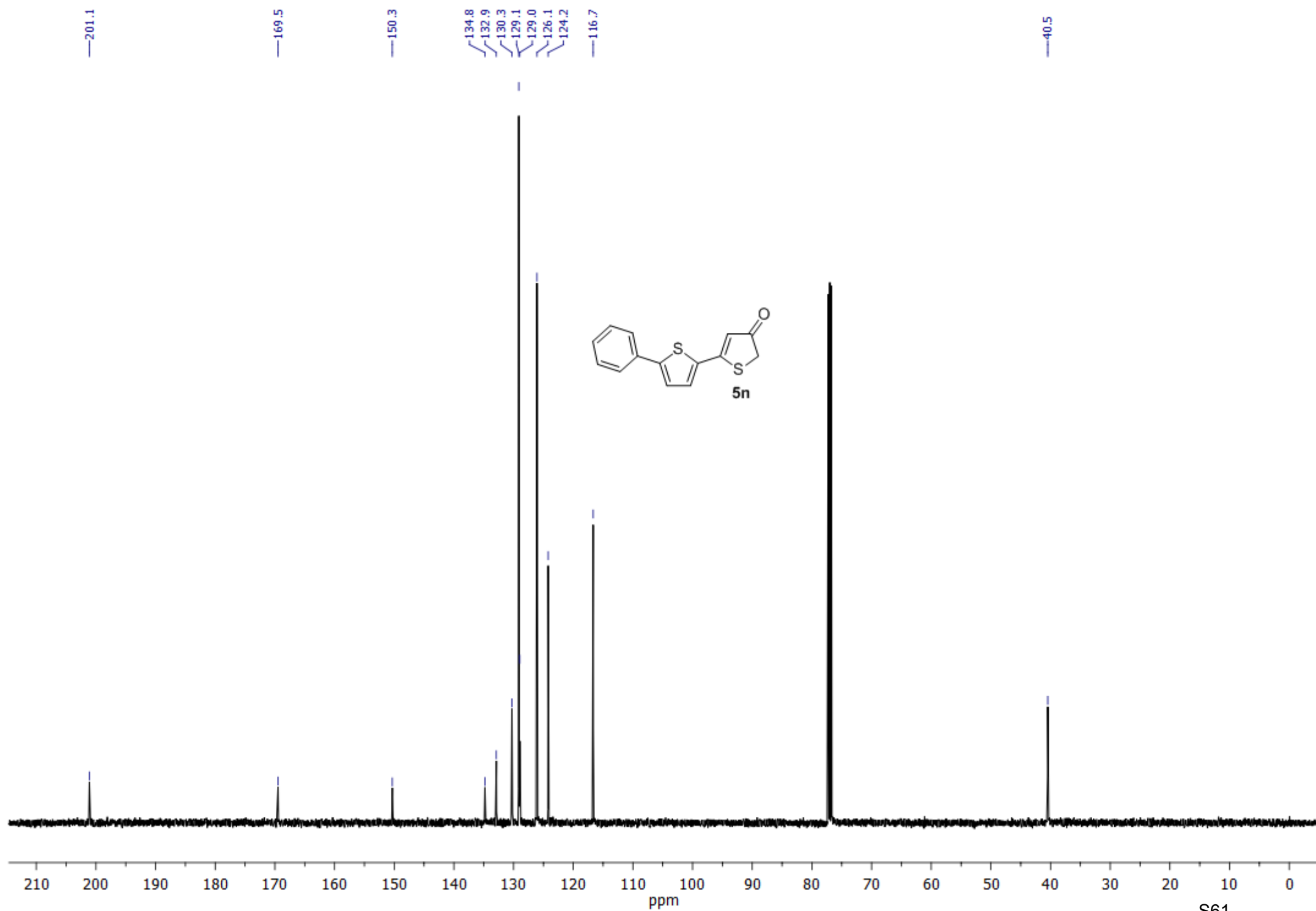


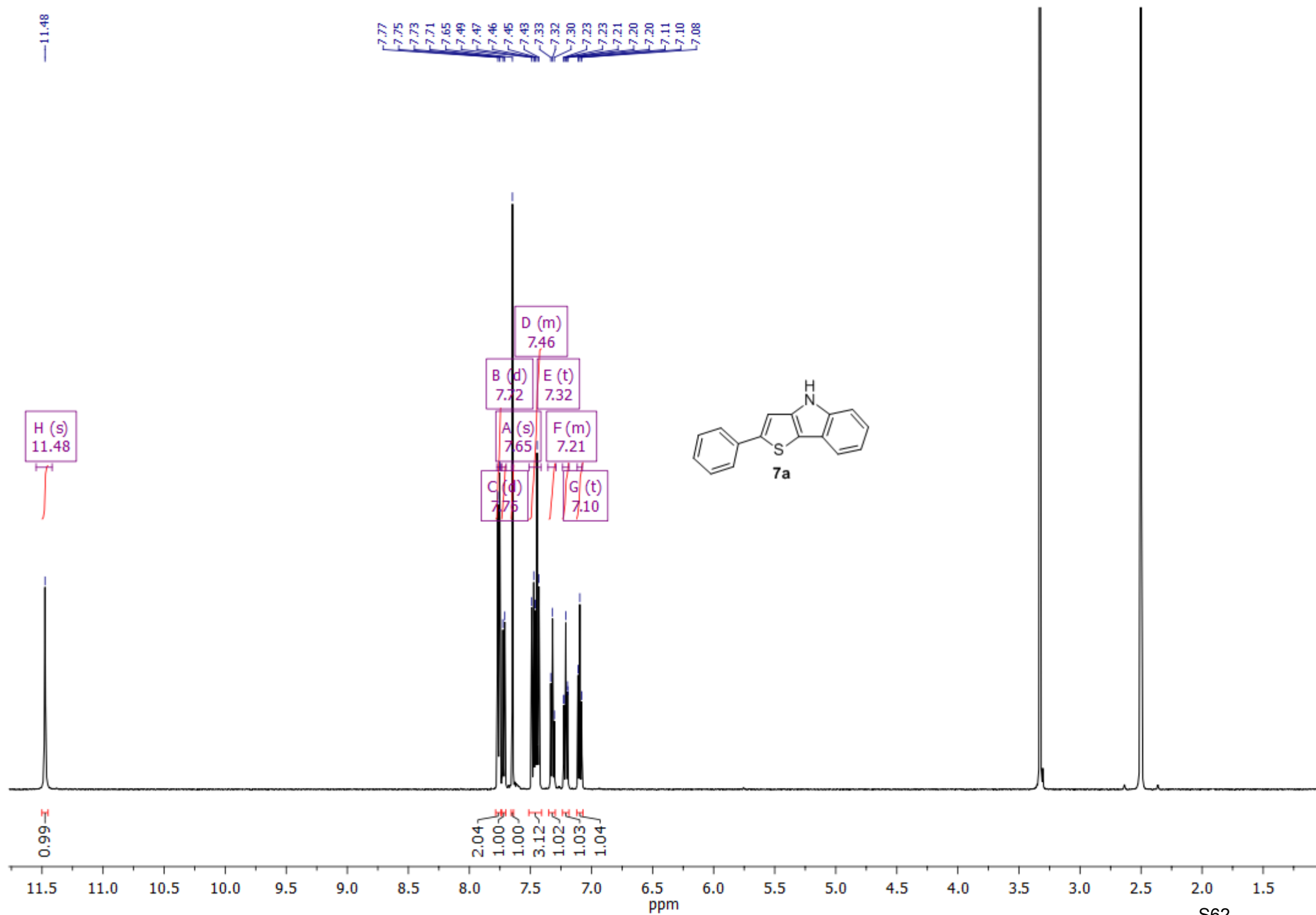
2.05
1.00
2.14
1.02
1.01

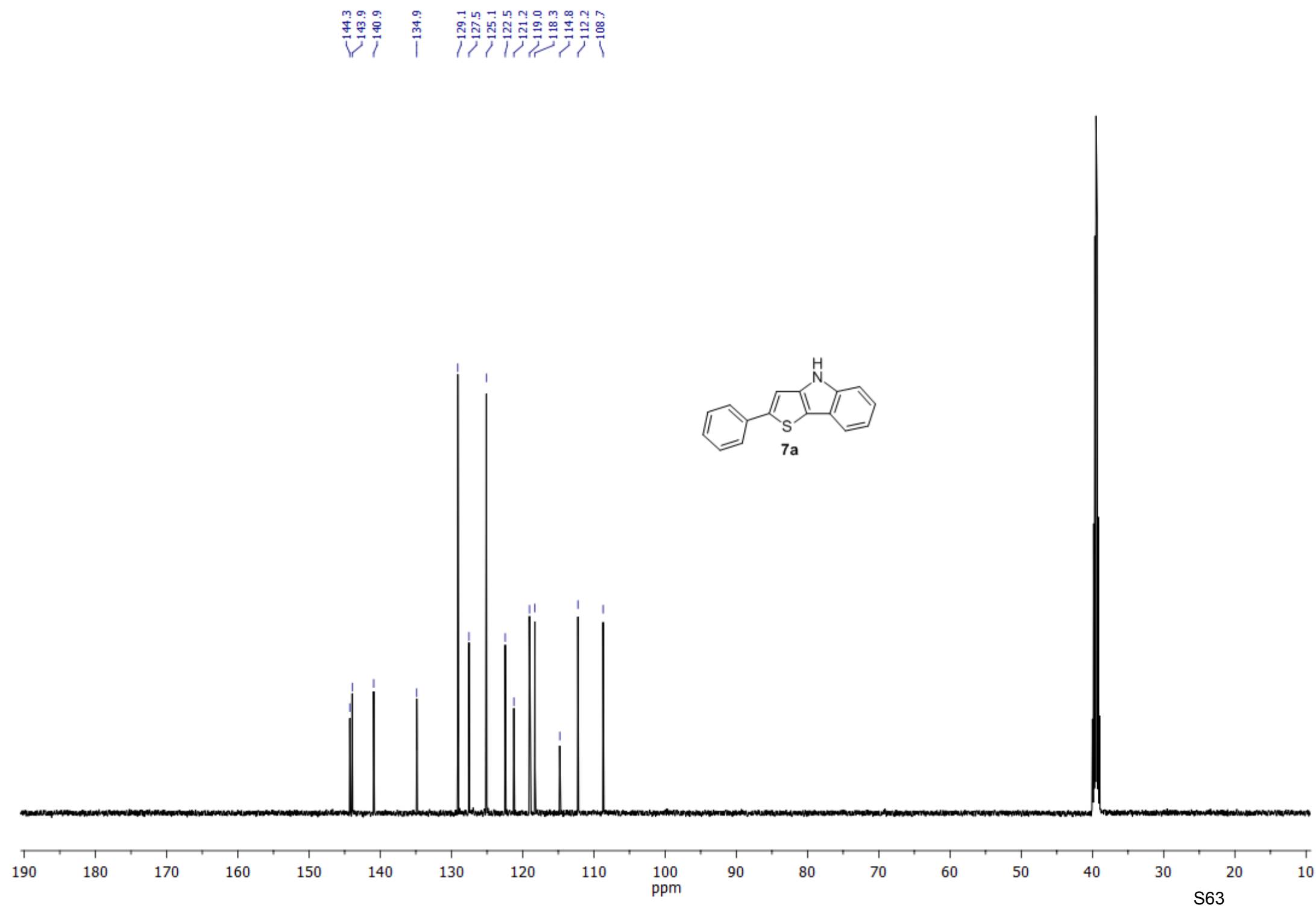
0.96

1.93

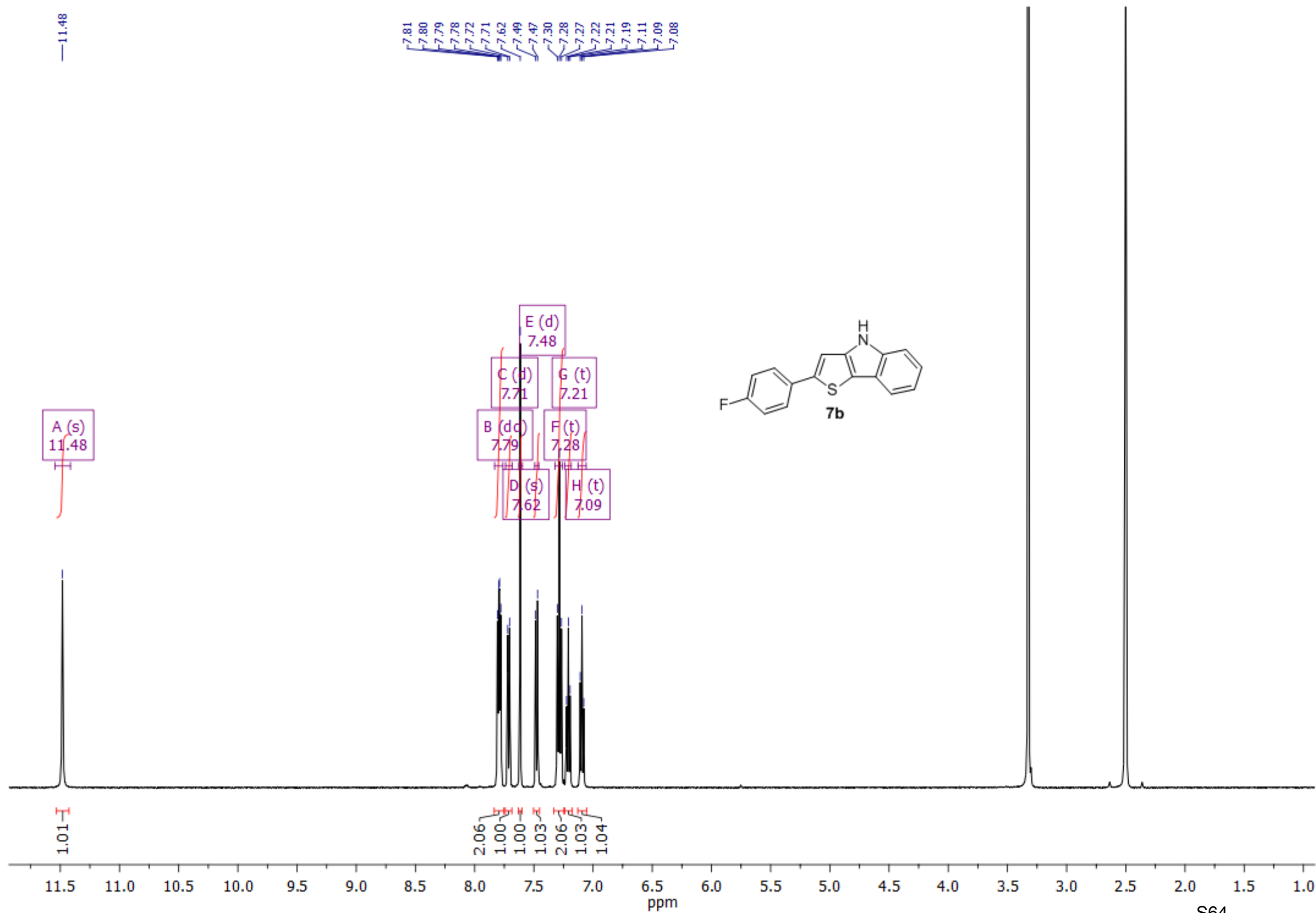
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
ppm



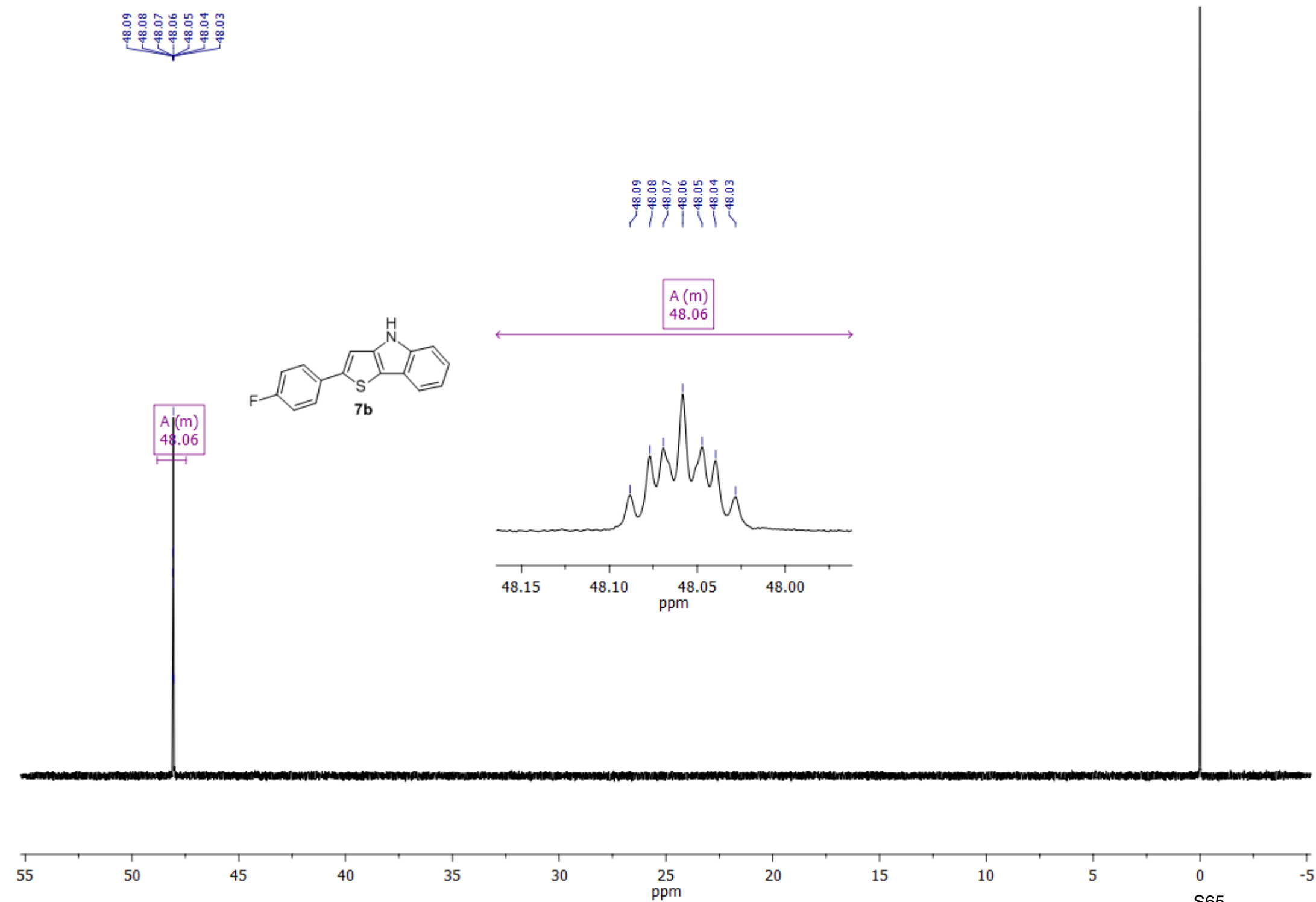


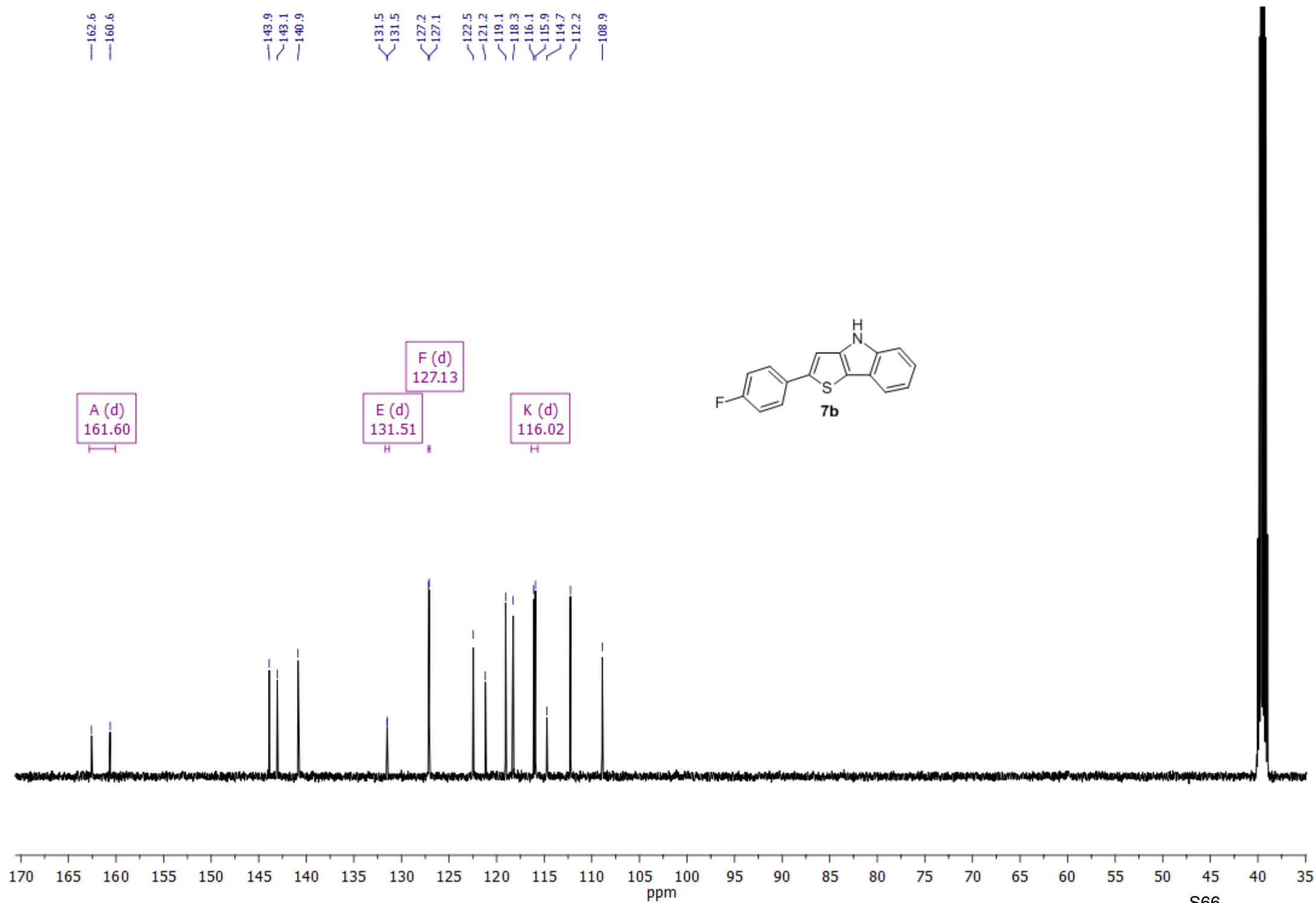


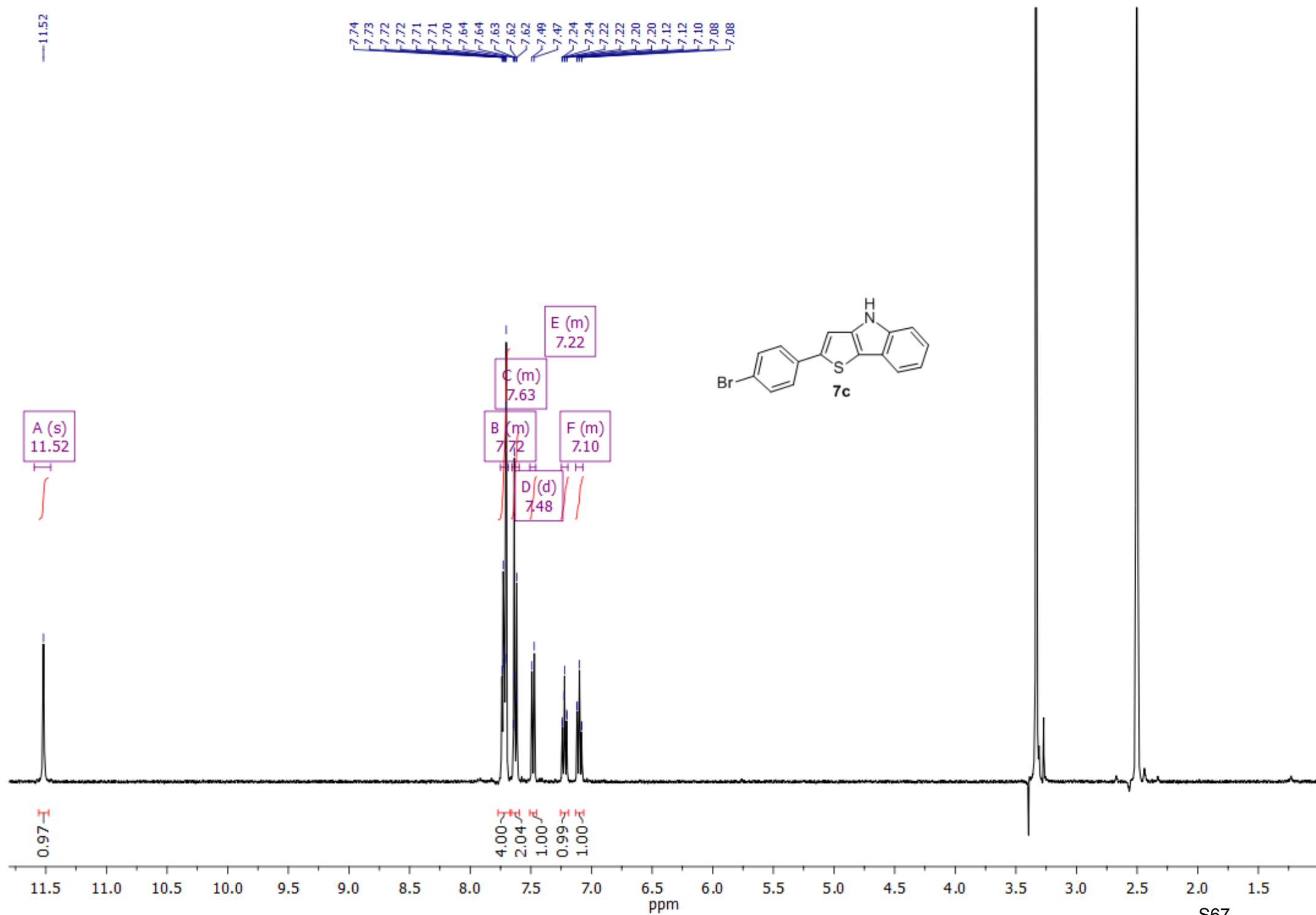
¹H NMR (solvent: DMSO-*d*₆)



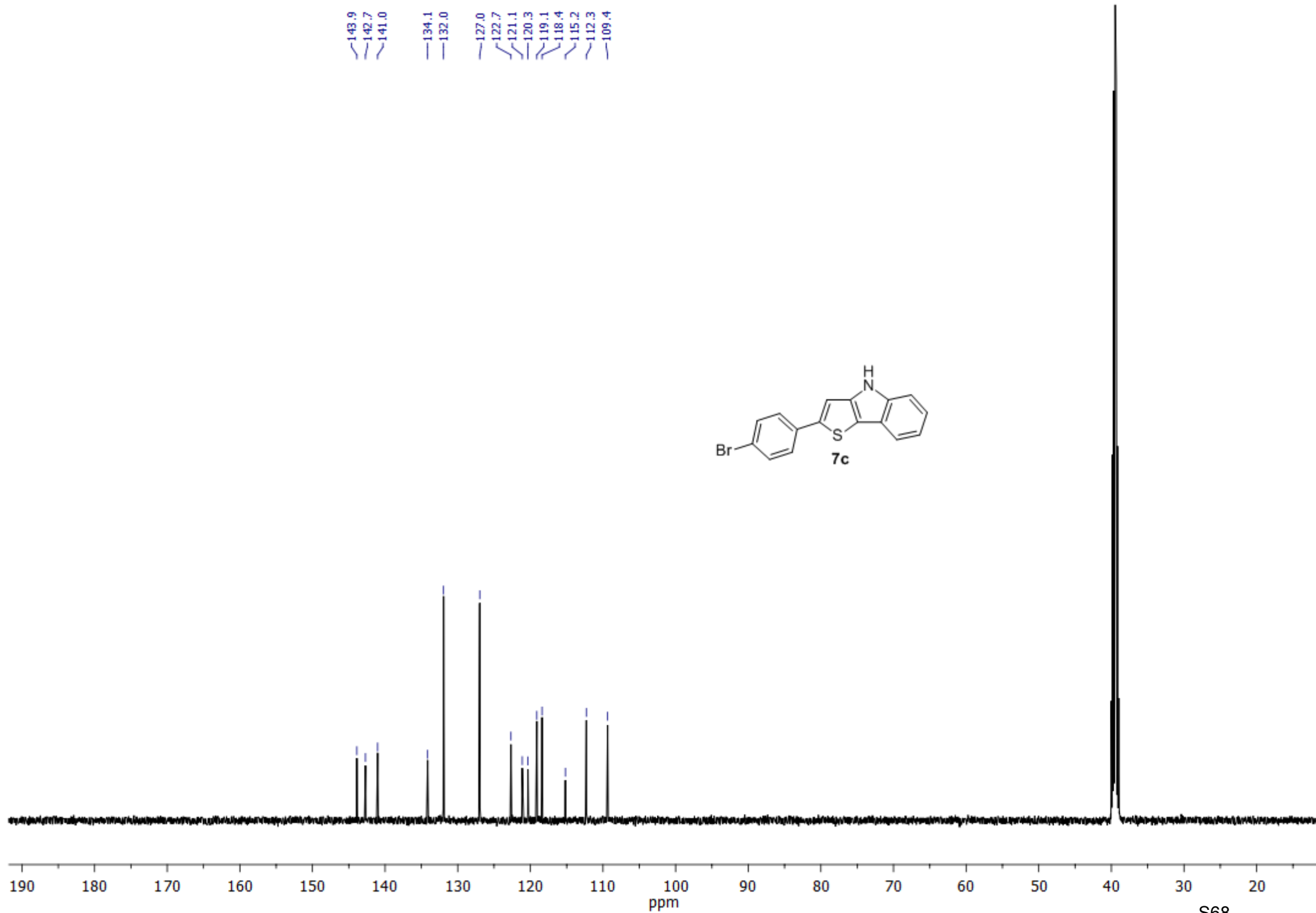
¹⁹F NMR (solvent: DMSO-*d*₆)



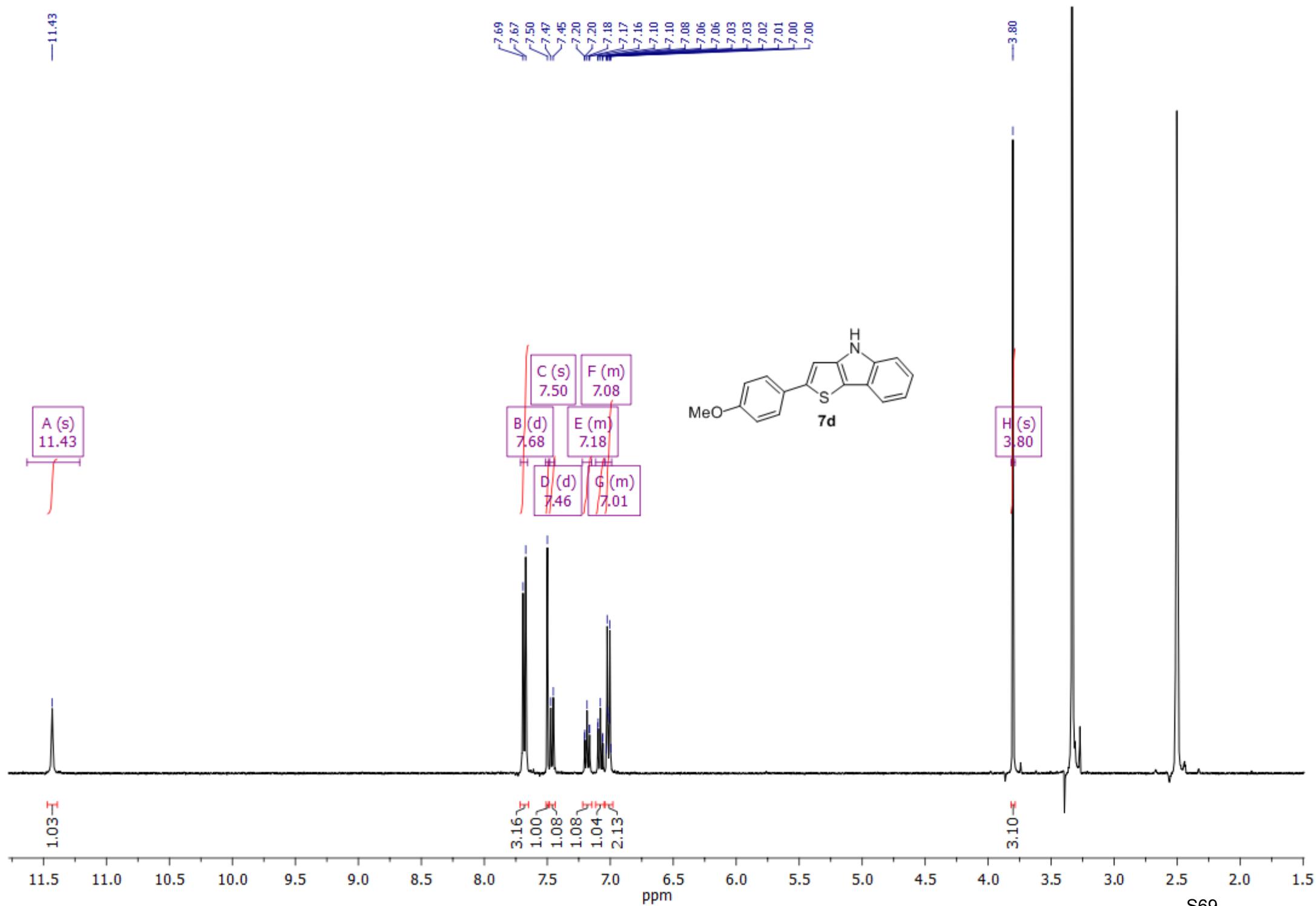


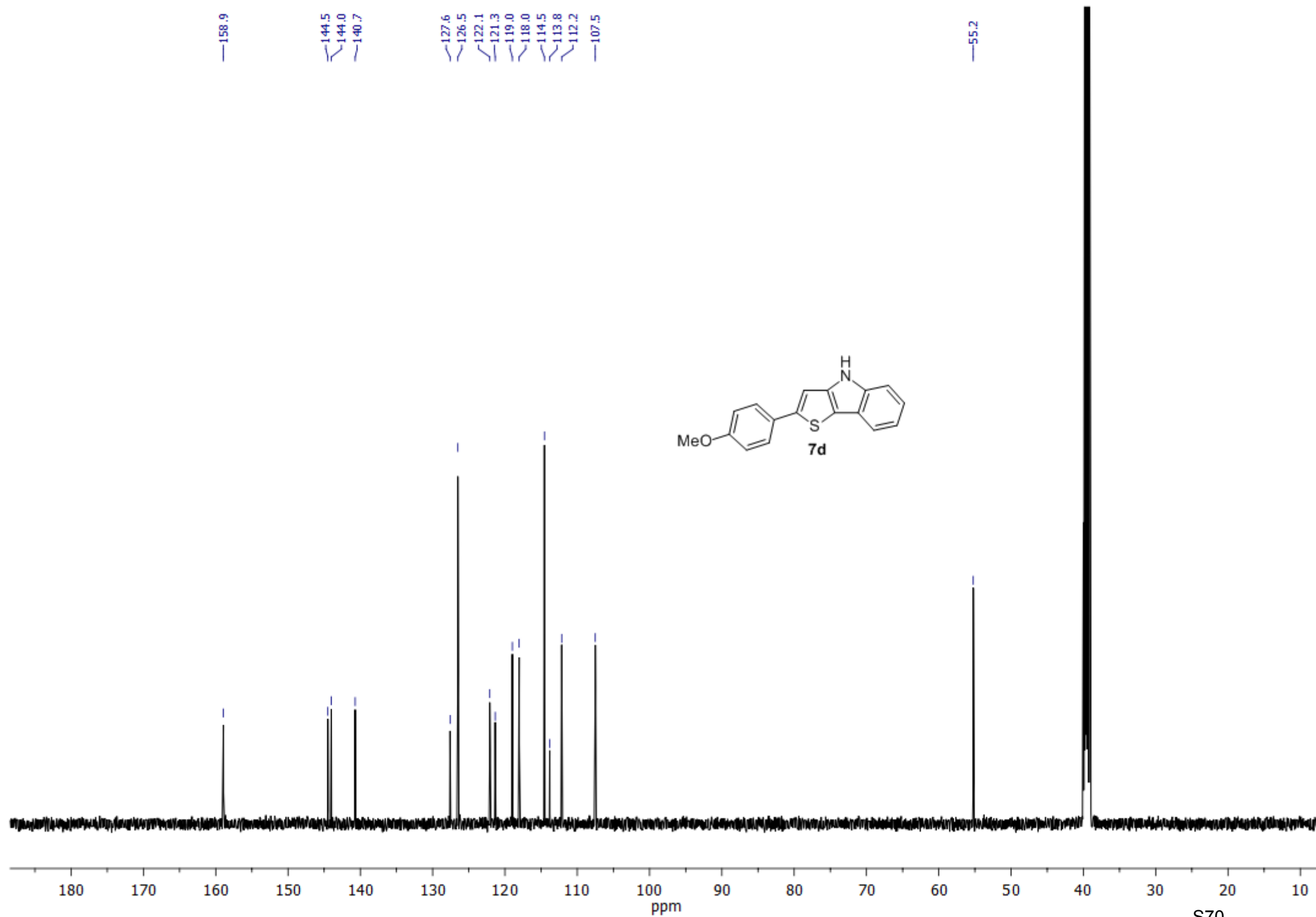


¹³C NMR (solvent: DMSO-*d*₆)

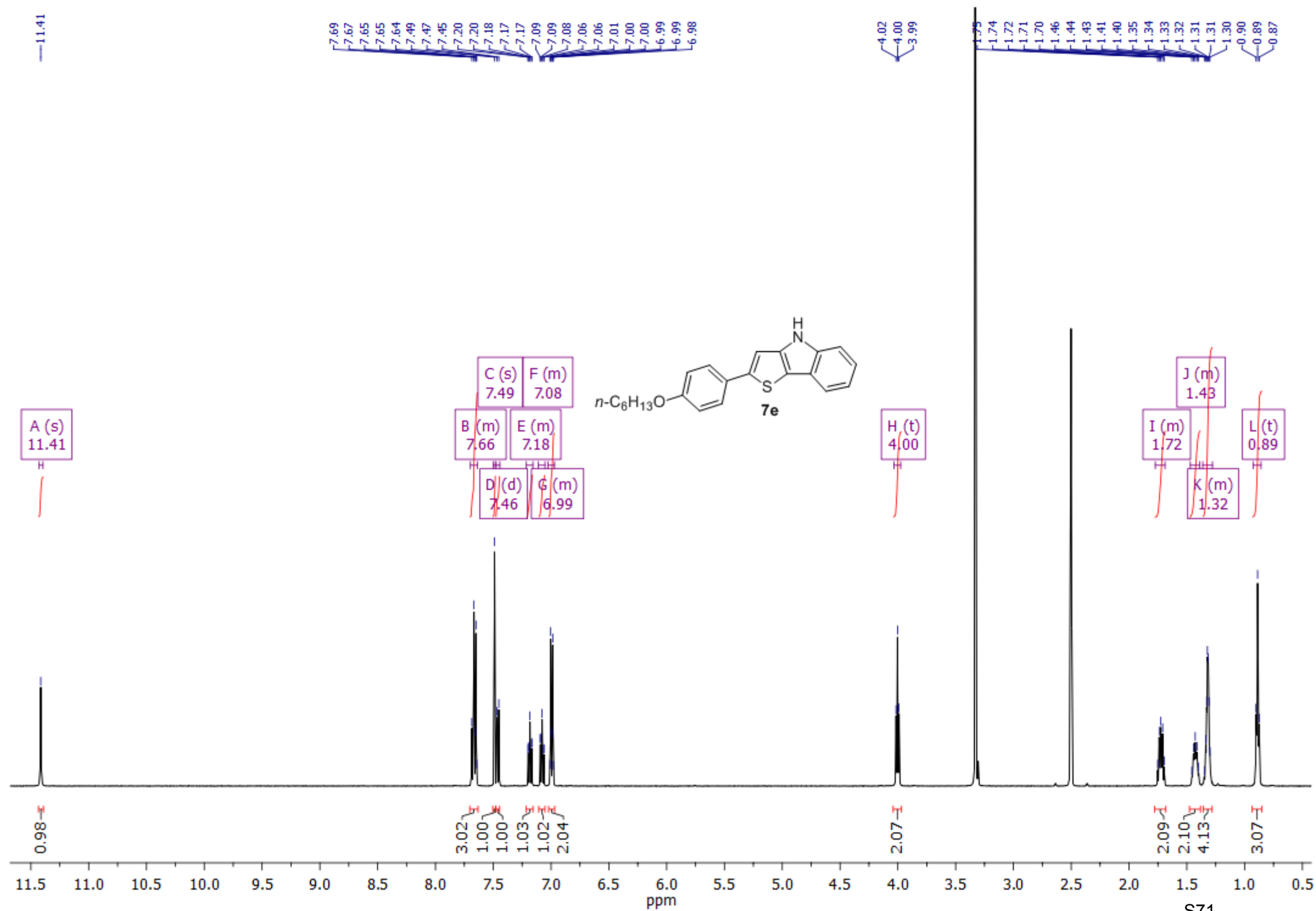


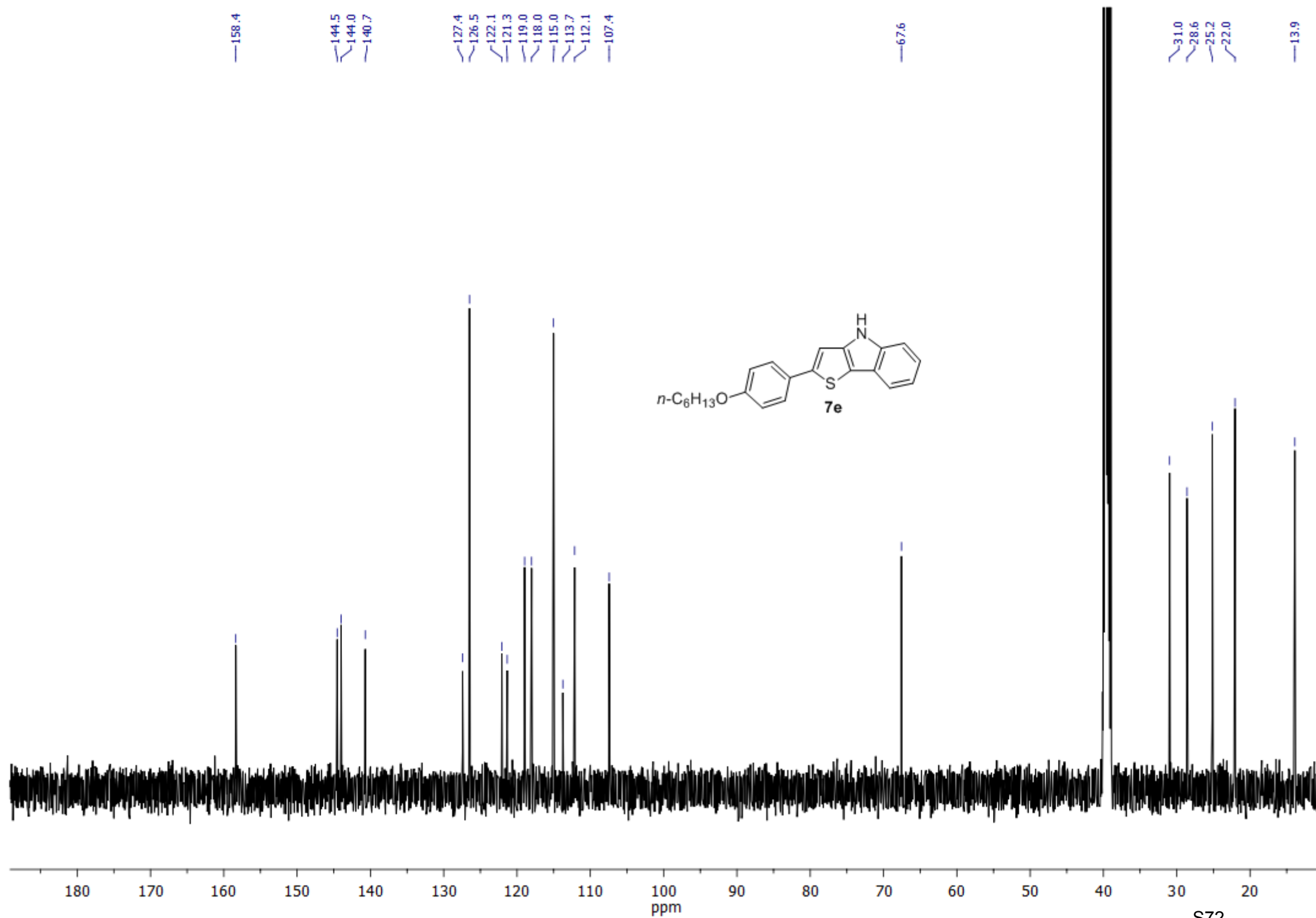
¹H NMR (solvent: DMSO-*d*₆)



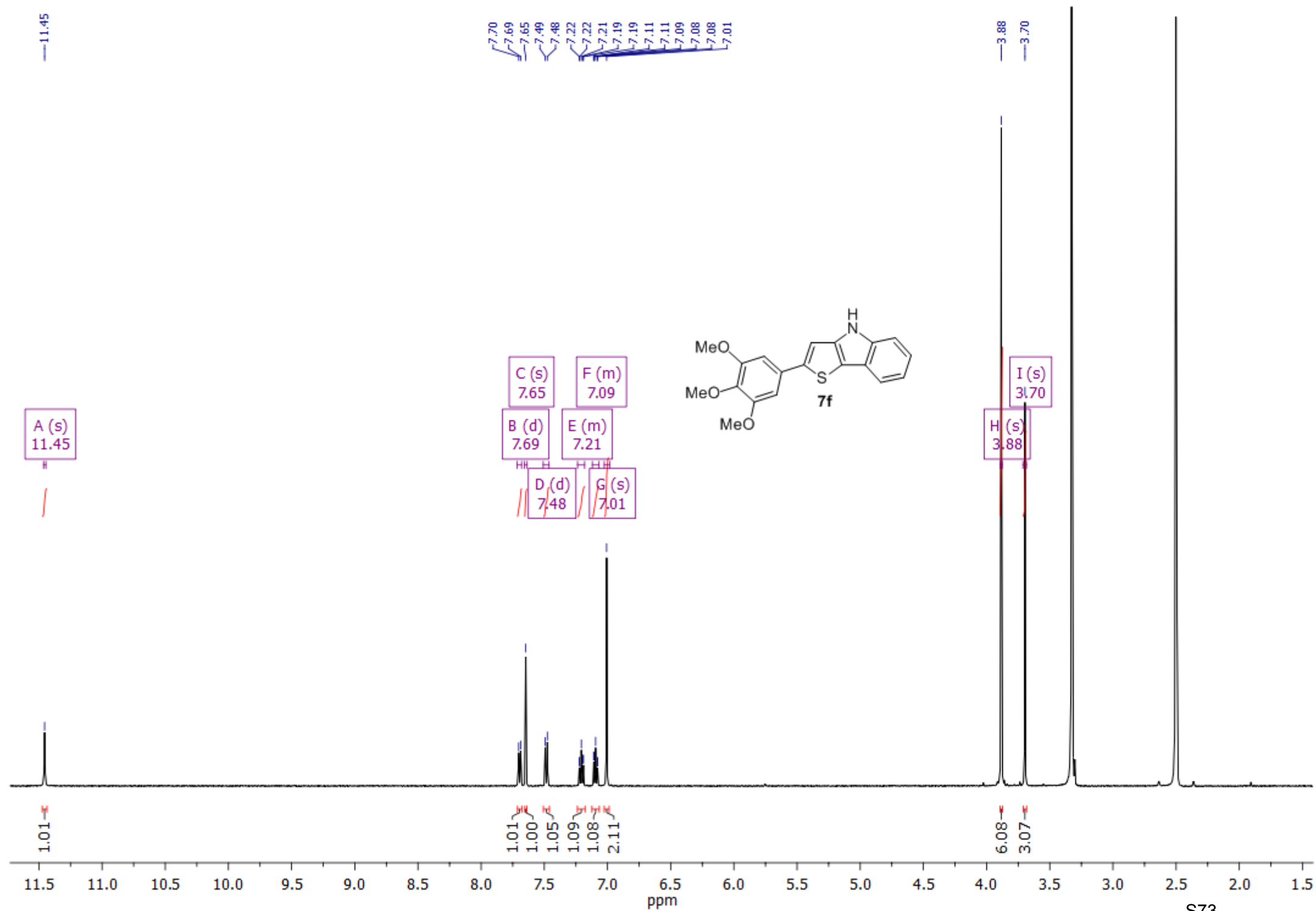


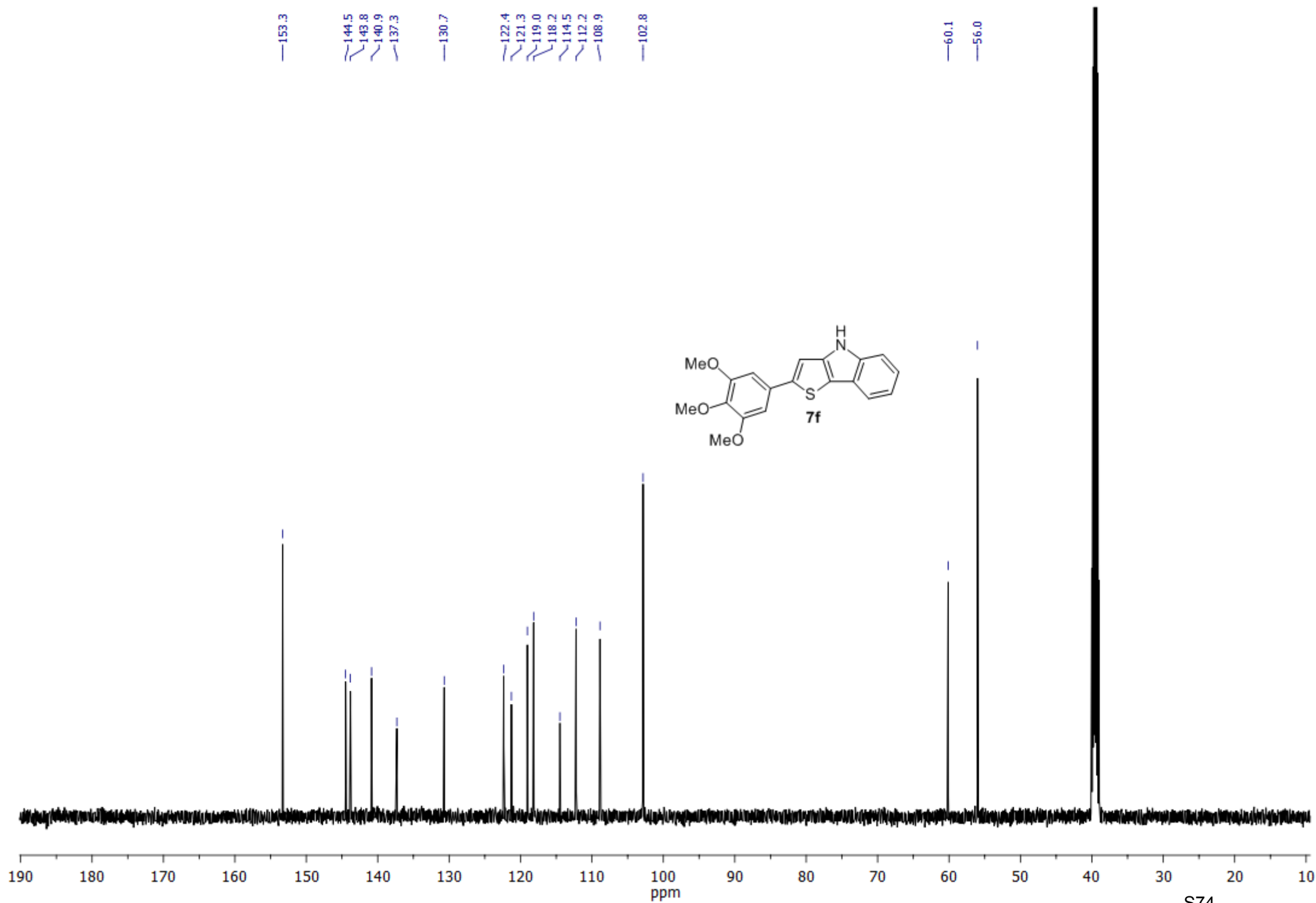
¹H NMR (solvent: DMSO-*d*₆)

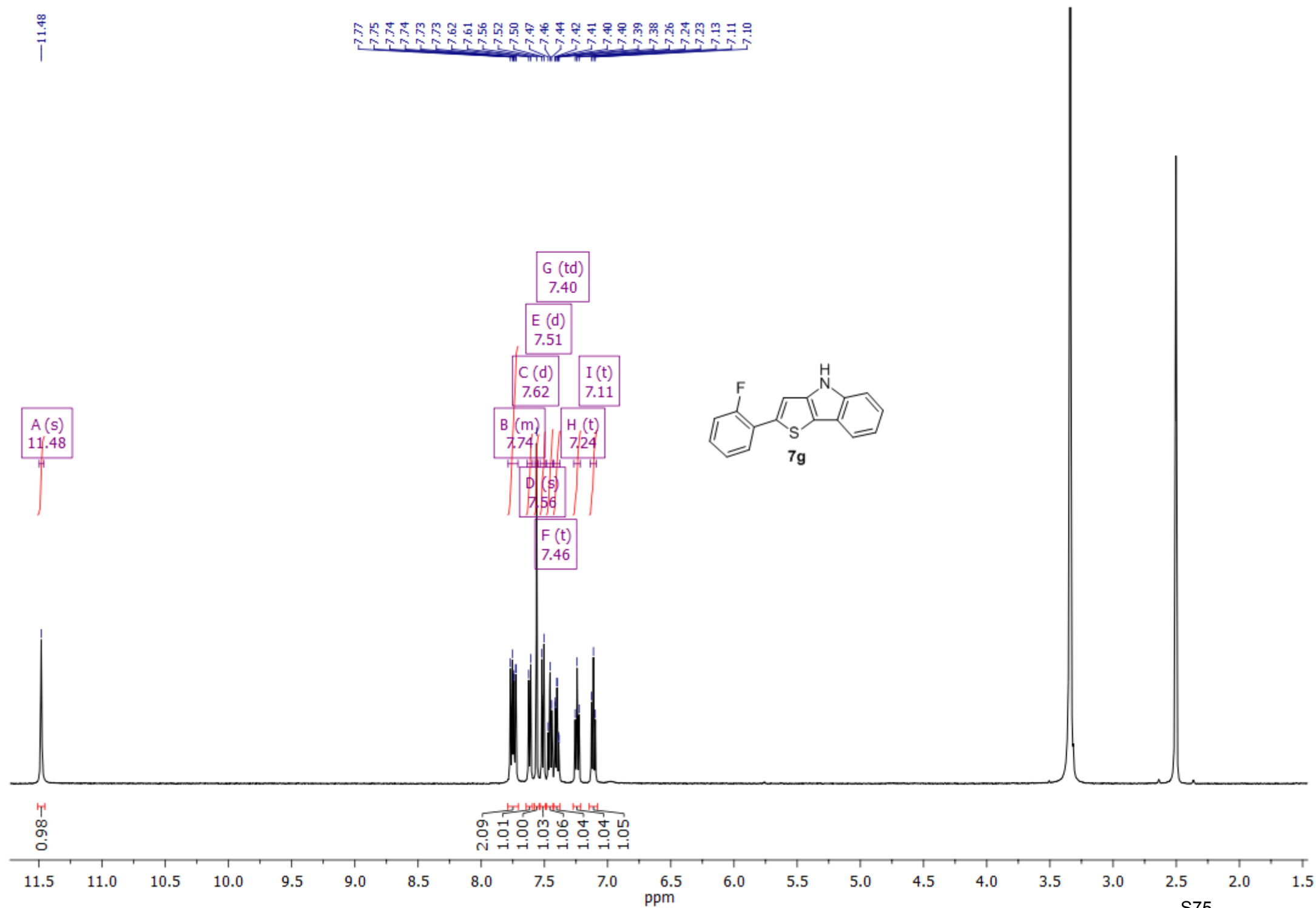




¹H NMR (solvent: DMSO-*d*₆)





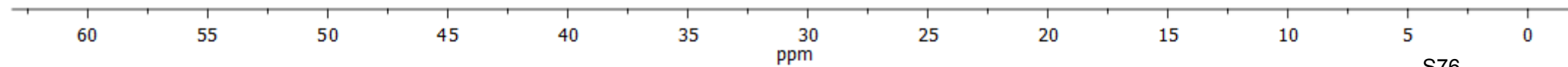
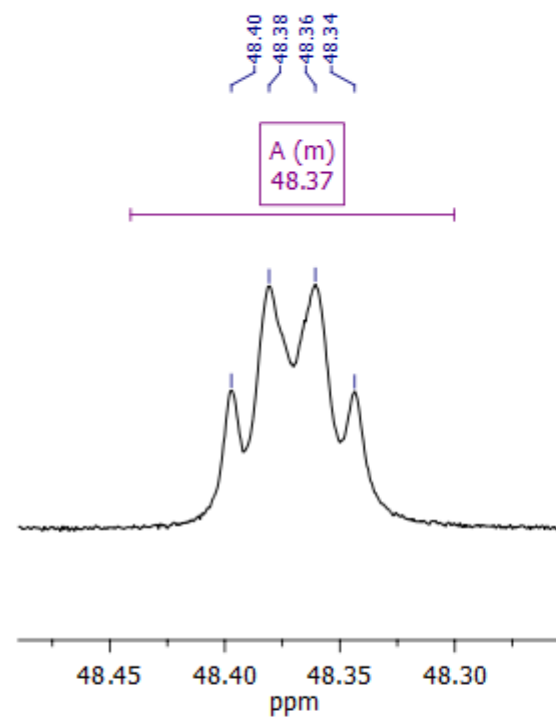
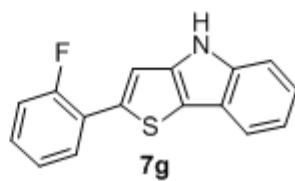


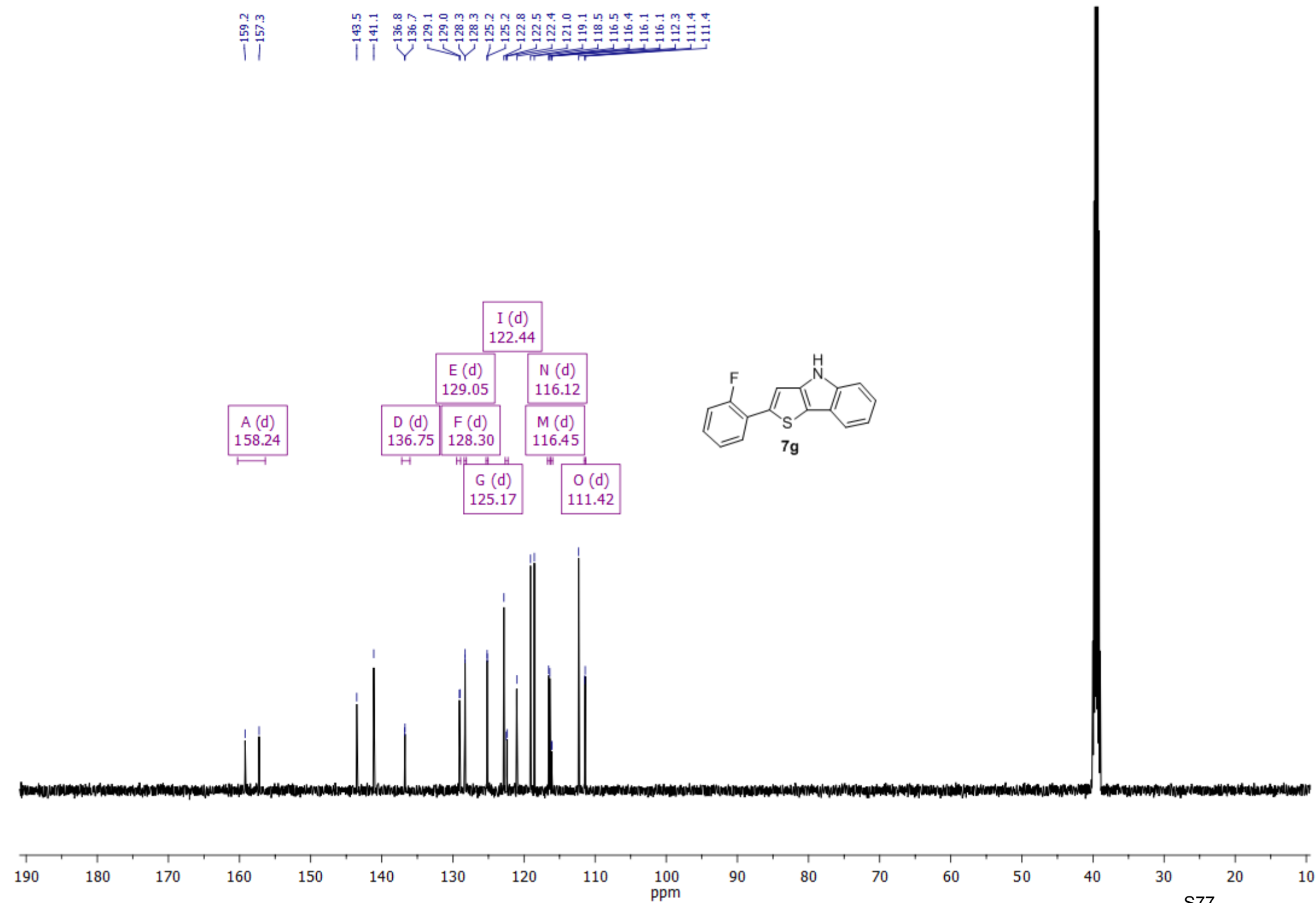
48.40
48.38
48.36
48.34

48.40
48.38
48.36
48.34

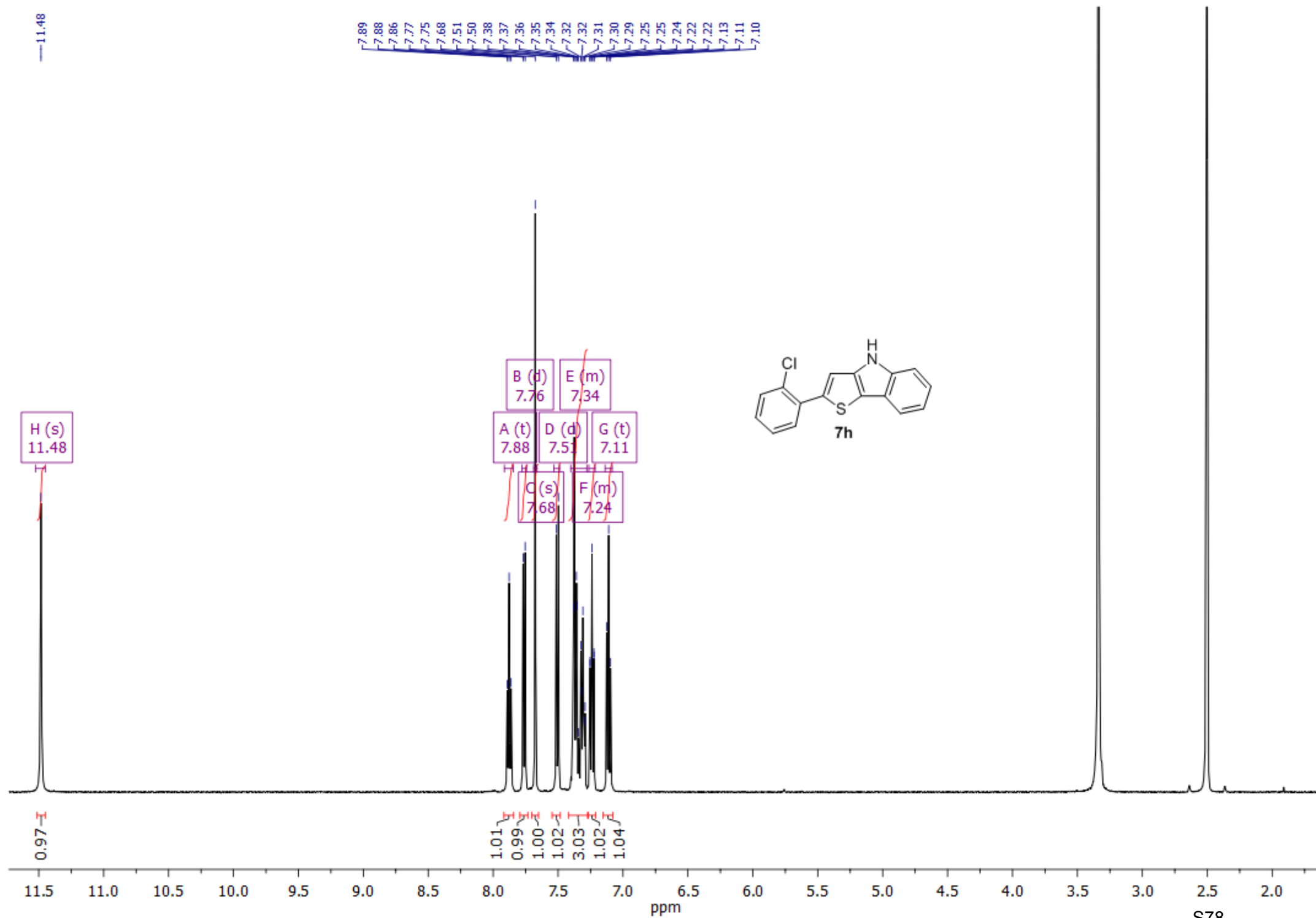
A (m)
48.37

A (m)
48.37

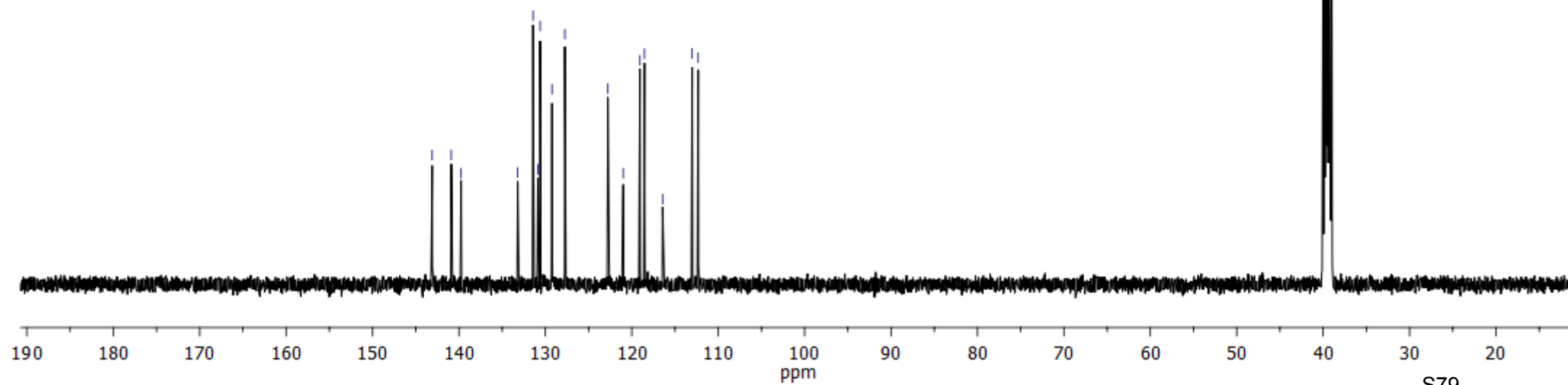
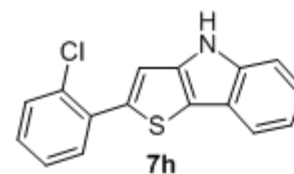




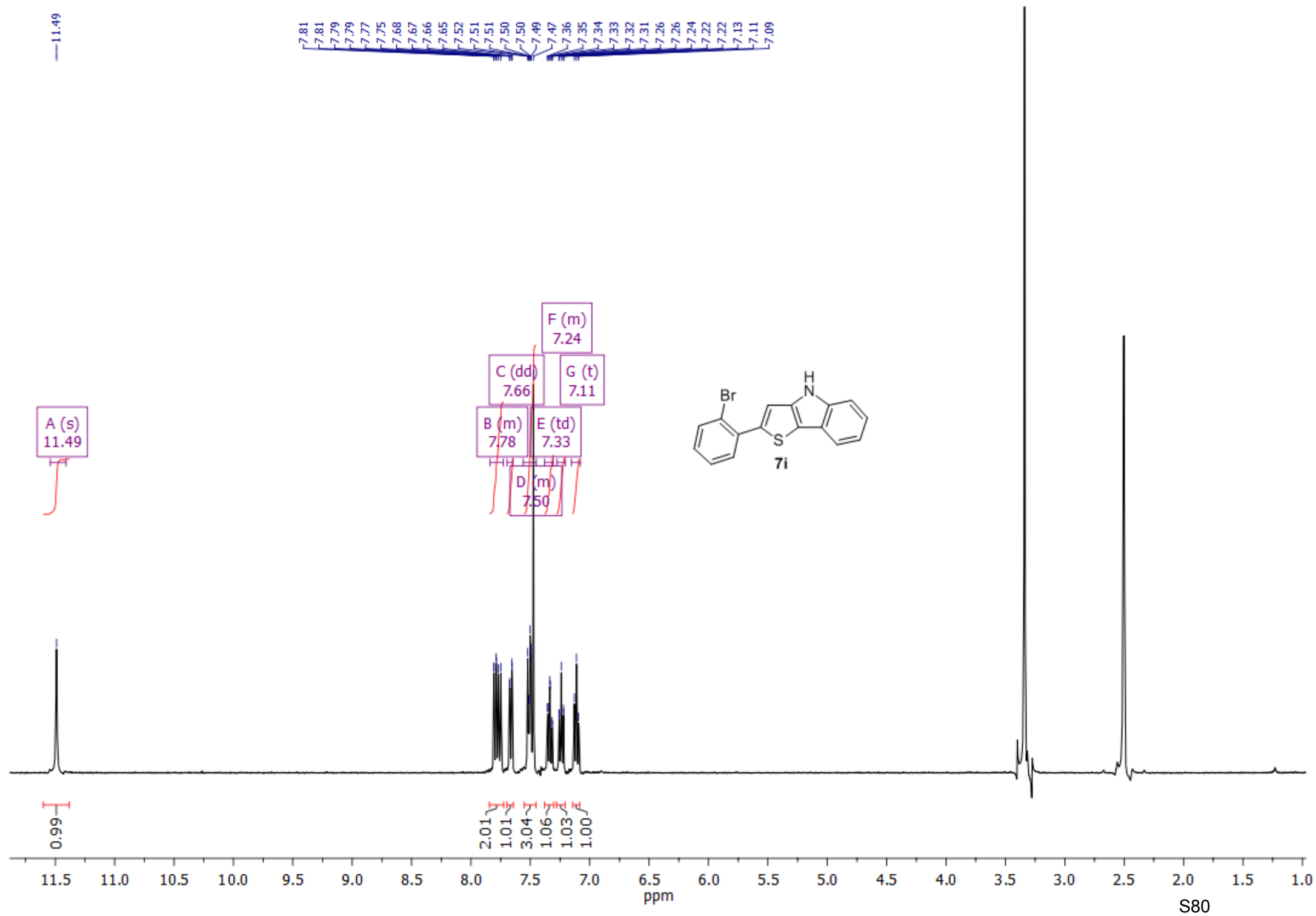
¹H NMR (solvent: DMSO-*d*₆)



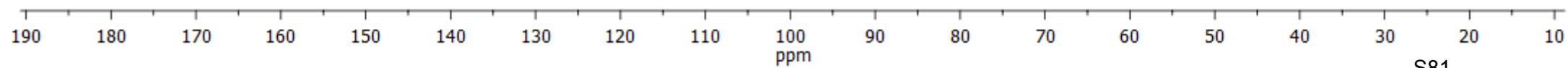
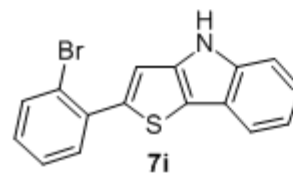
143.1
140.9
139.8
133.2
131.4
130.9
130.6
129.2
127.7
122.8
121.0
119.1
118.5
116.4
113.0
112.3



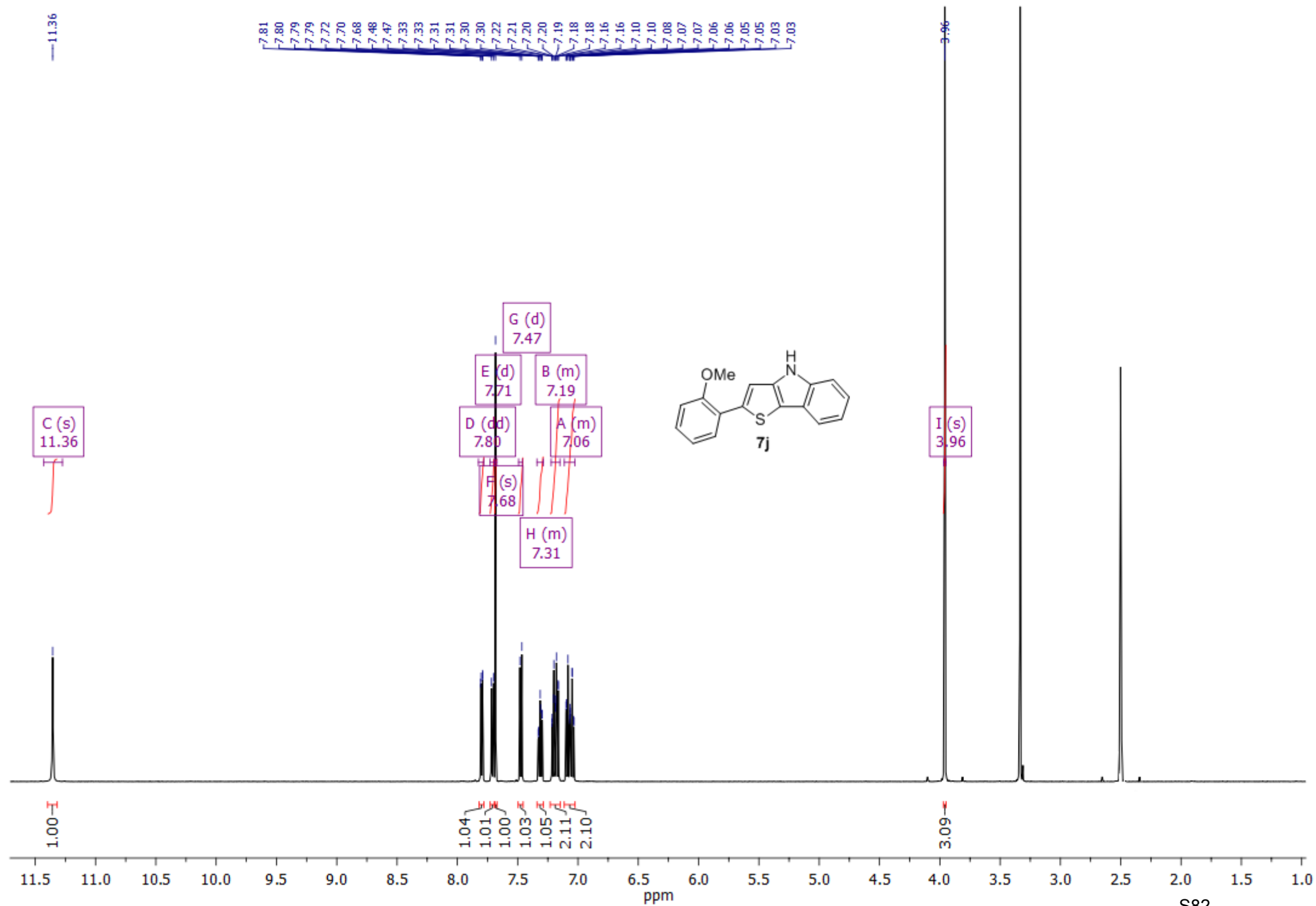
¹H NMR (solvent: DMSO-*d*₆)



143.0
141.5
140.8
135.3
133.7
132.0
129.7
128.1
122.7
121.8
121.0
119.1
118.5
116.3
113.1
112.3

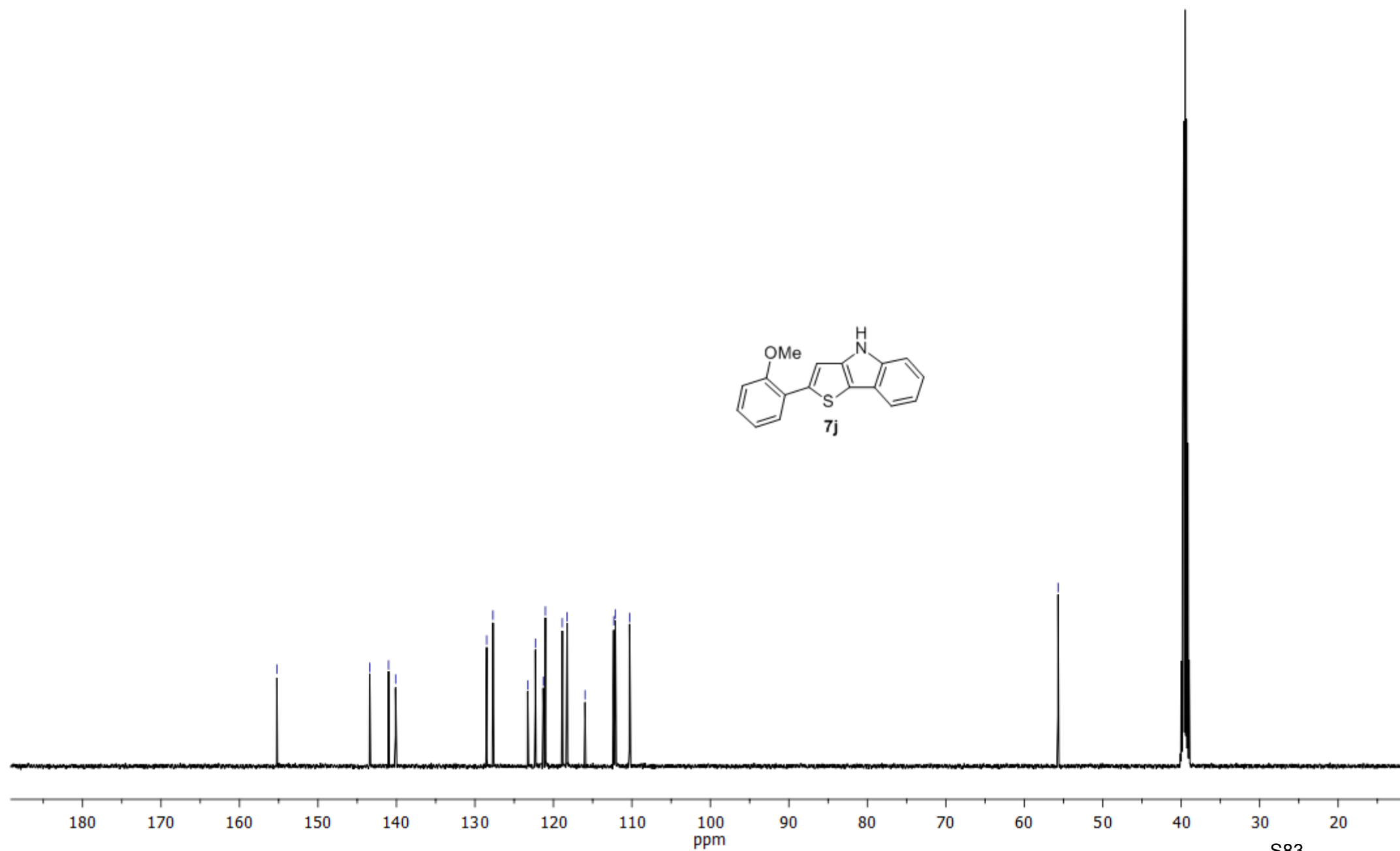
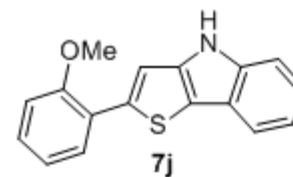


¹H NMR (solvent: DMSO-*d*₆)

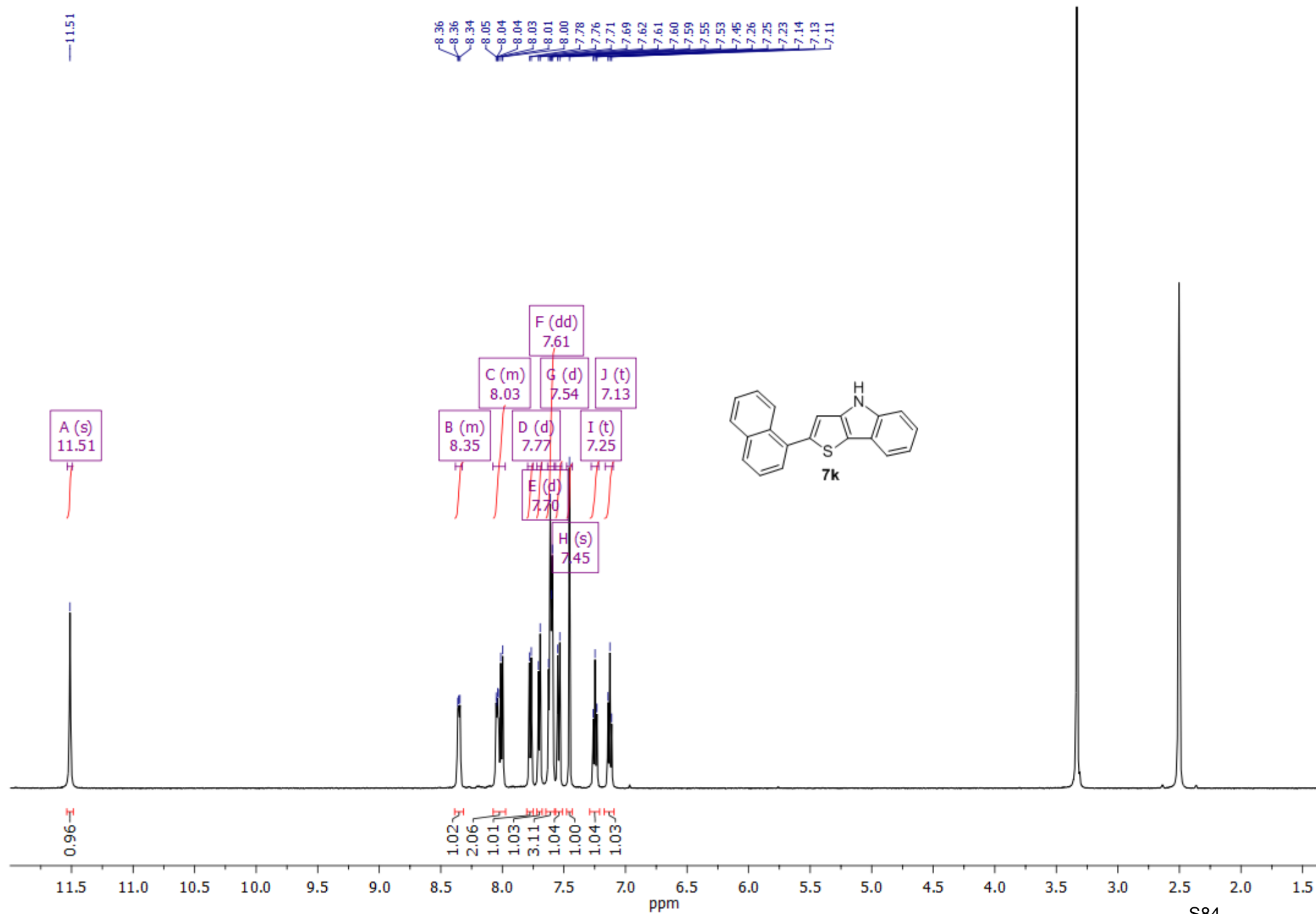


155.2
143.4
141.0
140.1
128.5
127.7
123.3
122.3
121.3
121.0
118.9
118.3
116.0
112.3
112.1
110.3

55.7

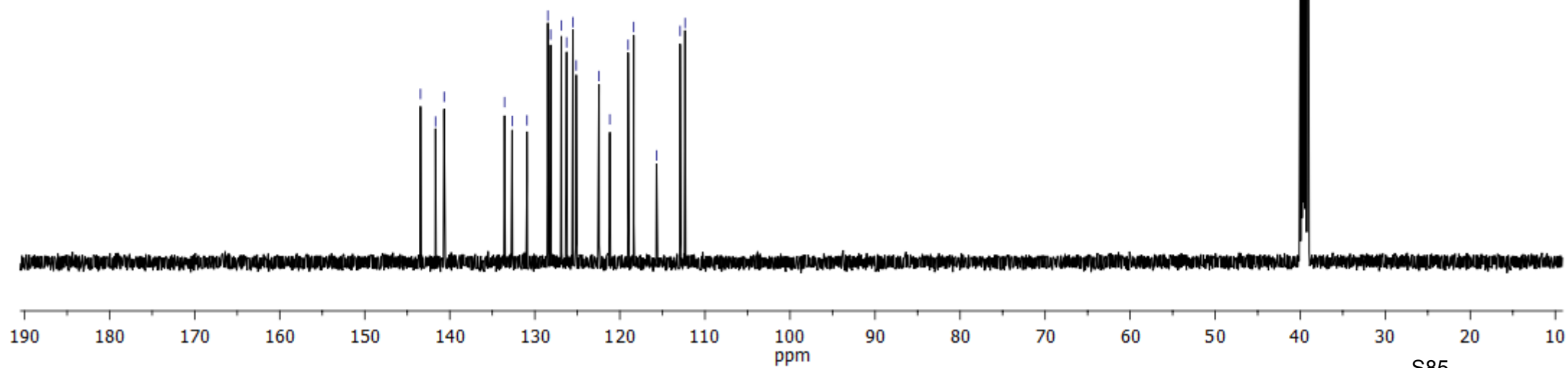
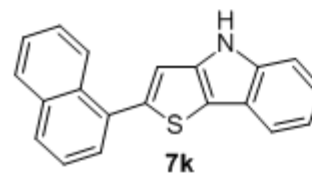


¹H NMR (solvent: DMSO-*d*₆)

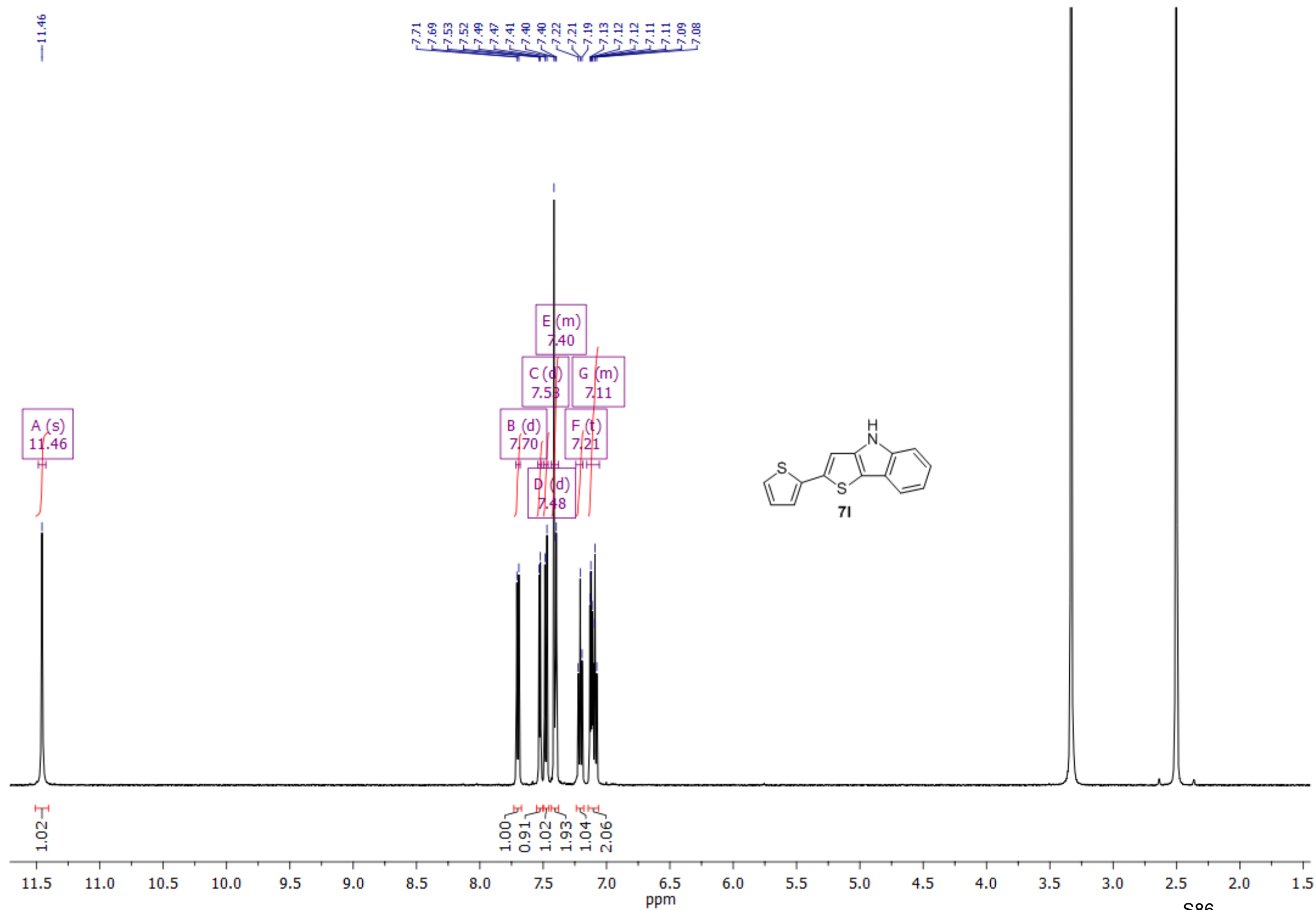


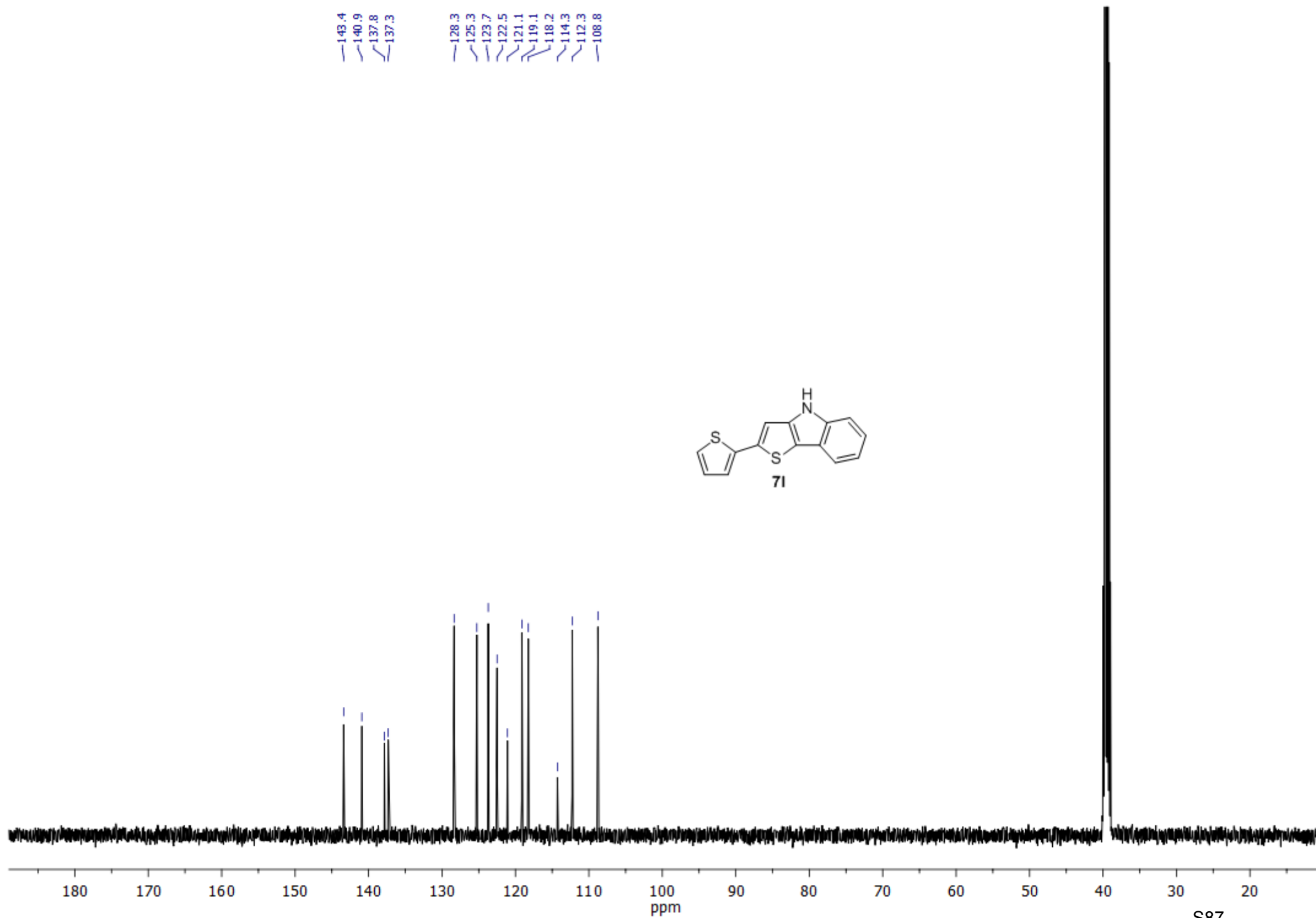
^{13}C NMR (solvent: $\text{DMSO-}d_6$)

143.4
141.7
140.7
133.6
132.7
130.9
128.5
128.1
126.9
126.3
125.5
125.1
122.5
121.2
119.0
118.4
115.7
112.9
112.3

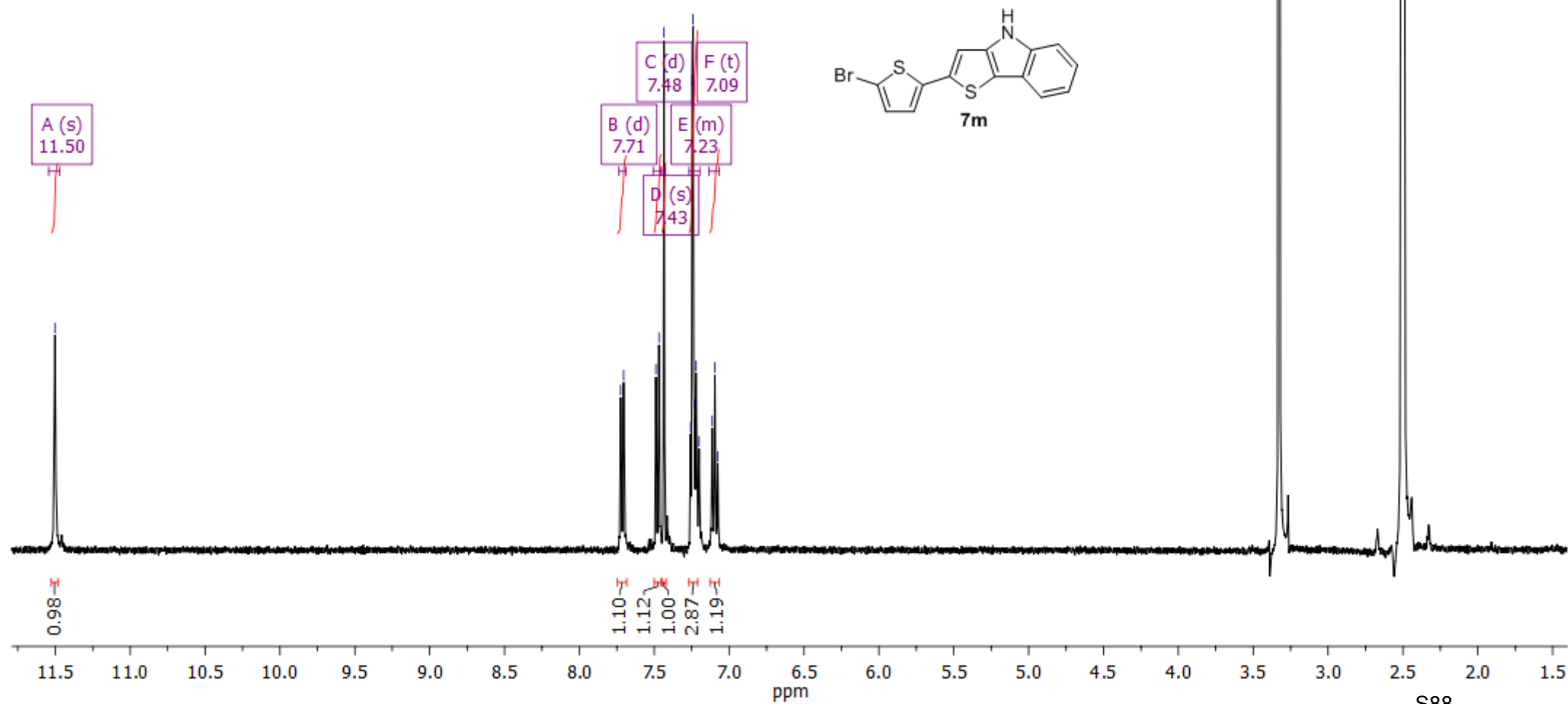


¹H NMR (solvent: DMSO-*d*₆)

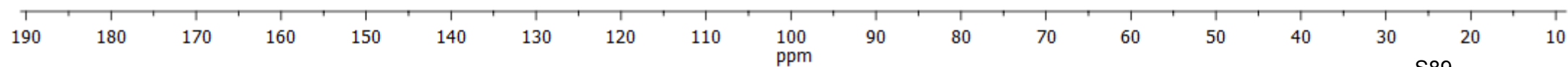
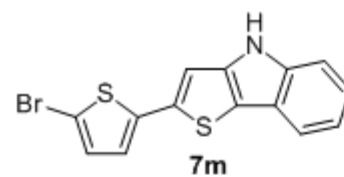




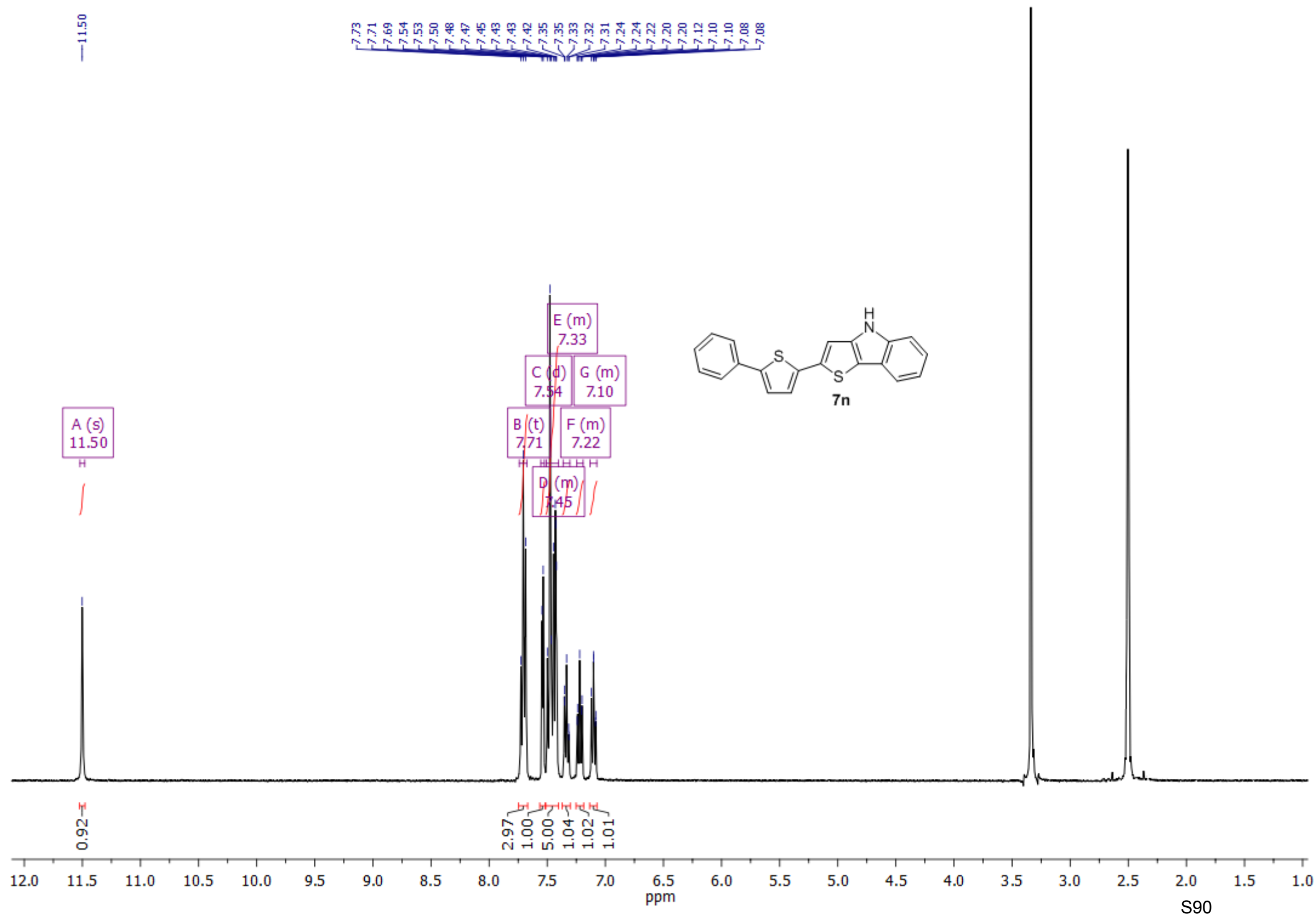
¹H NMR (solvent: DMSO-*d*₆)



143.3
141.1
139.6
135.8
131.6
124.2
122.8
121.0
119.2
118.4
114.7
112.3
109.9
109.4

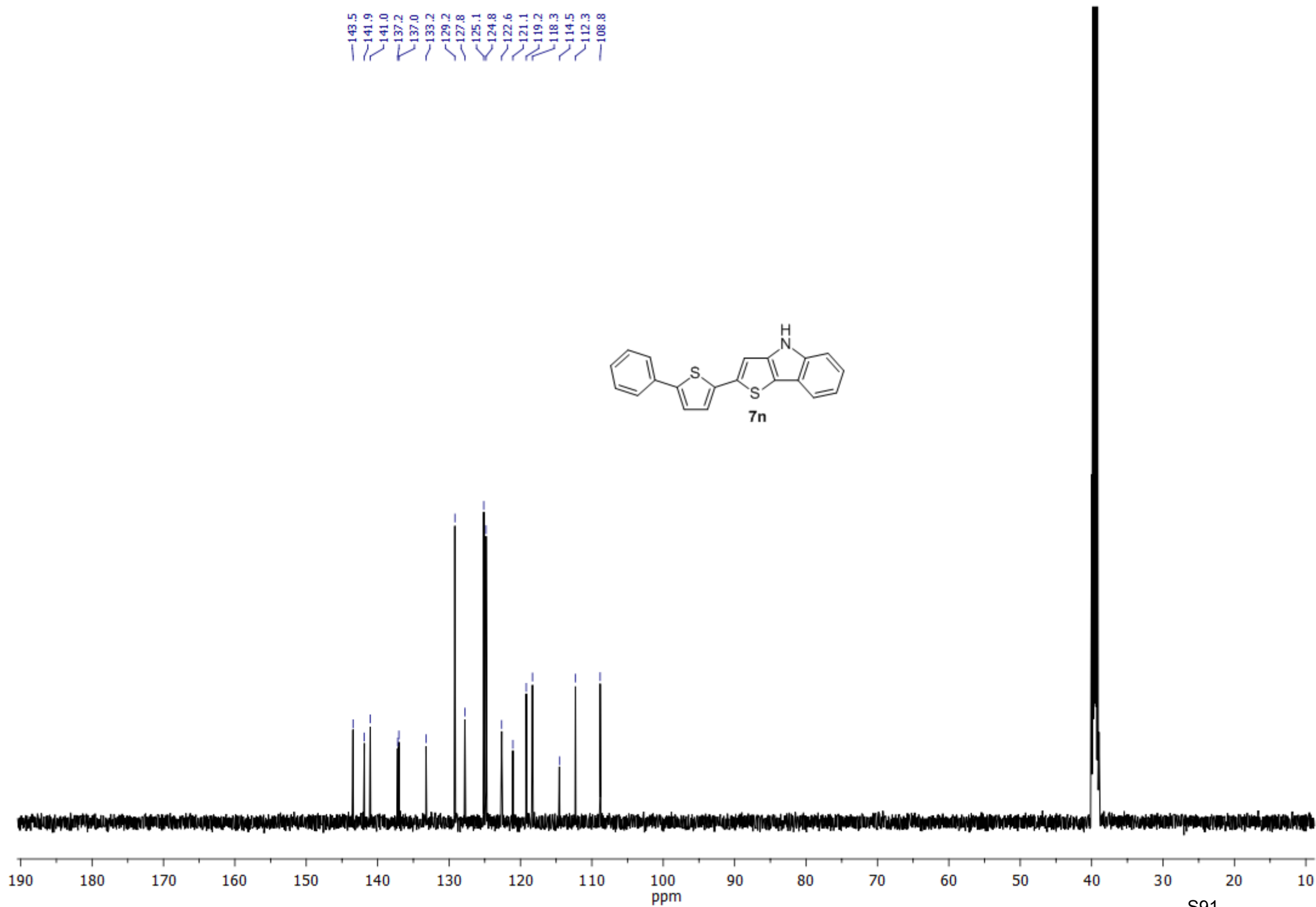
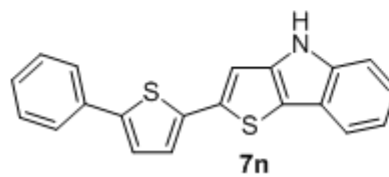


¹H NMR (solvent: DMSO-*d*₆)

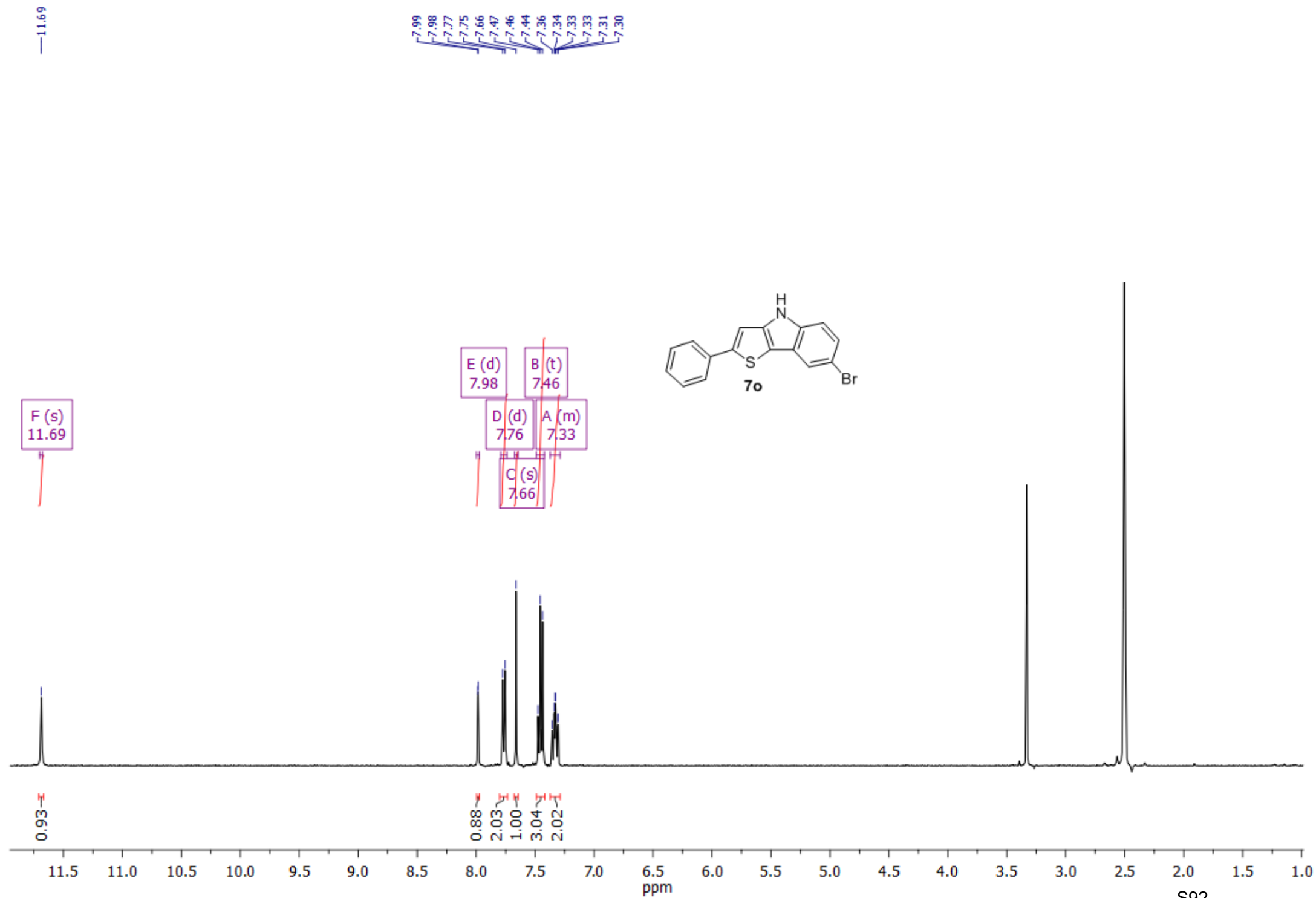


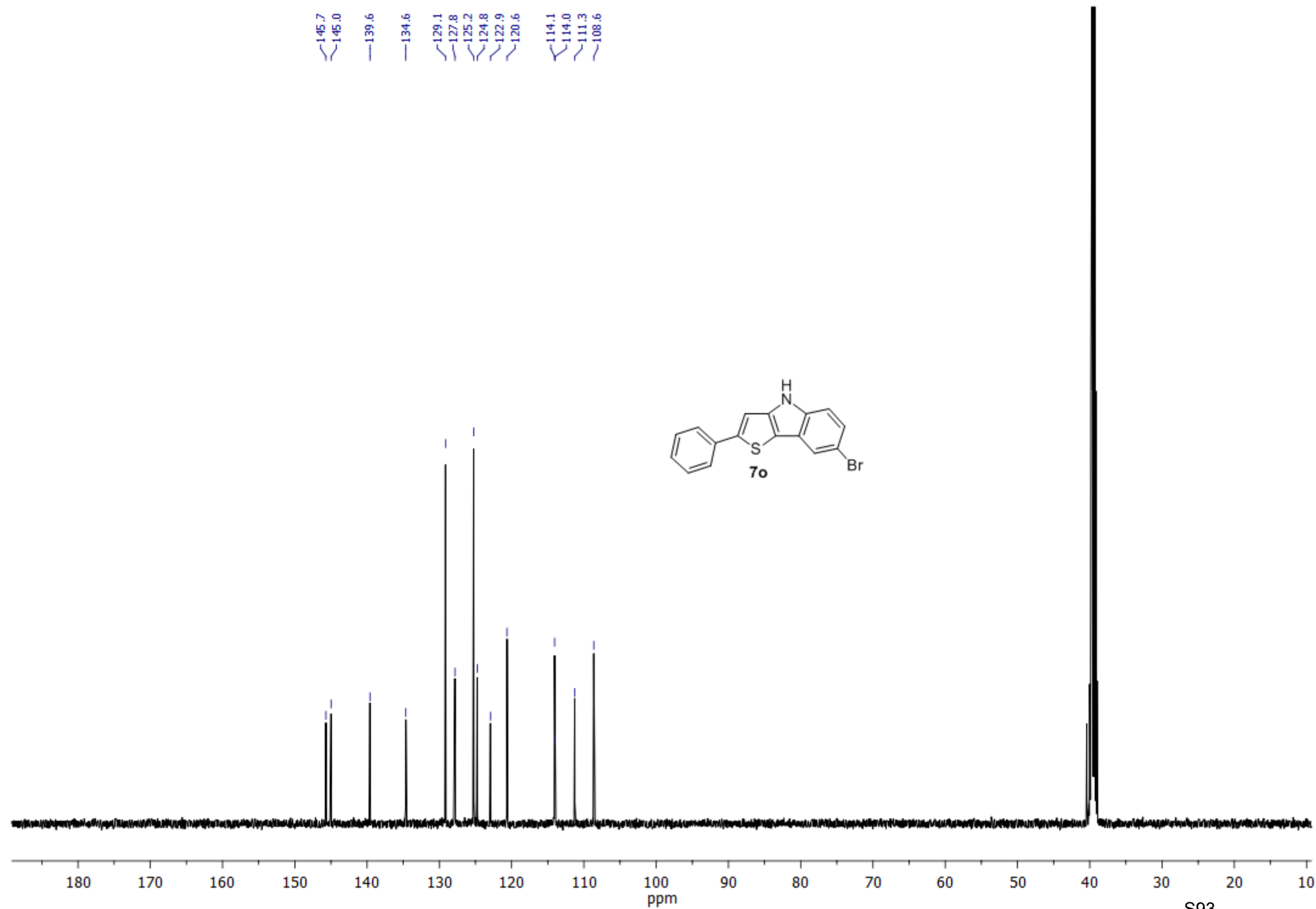
¹³C NMR (solvent: DMSO-*d*₆)

143.5
141.9
141.0
137.2
137.0
133.2
129.2
127.8
125.1
124.8
122.6
121.1
119.2
118.3
114.5
112.3
108.8

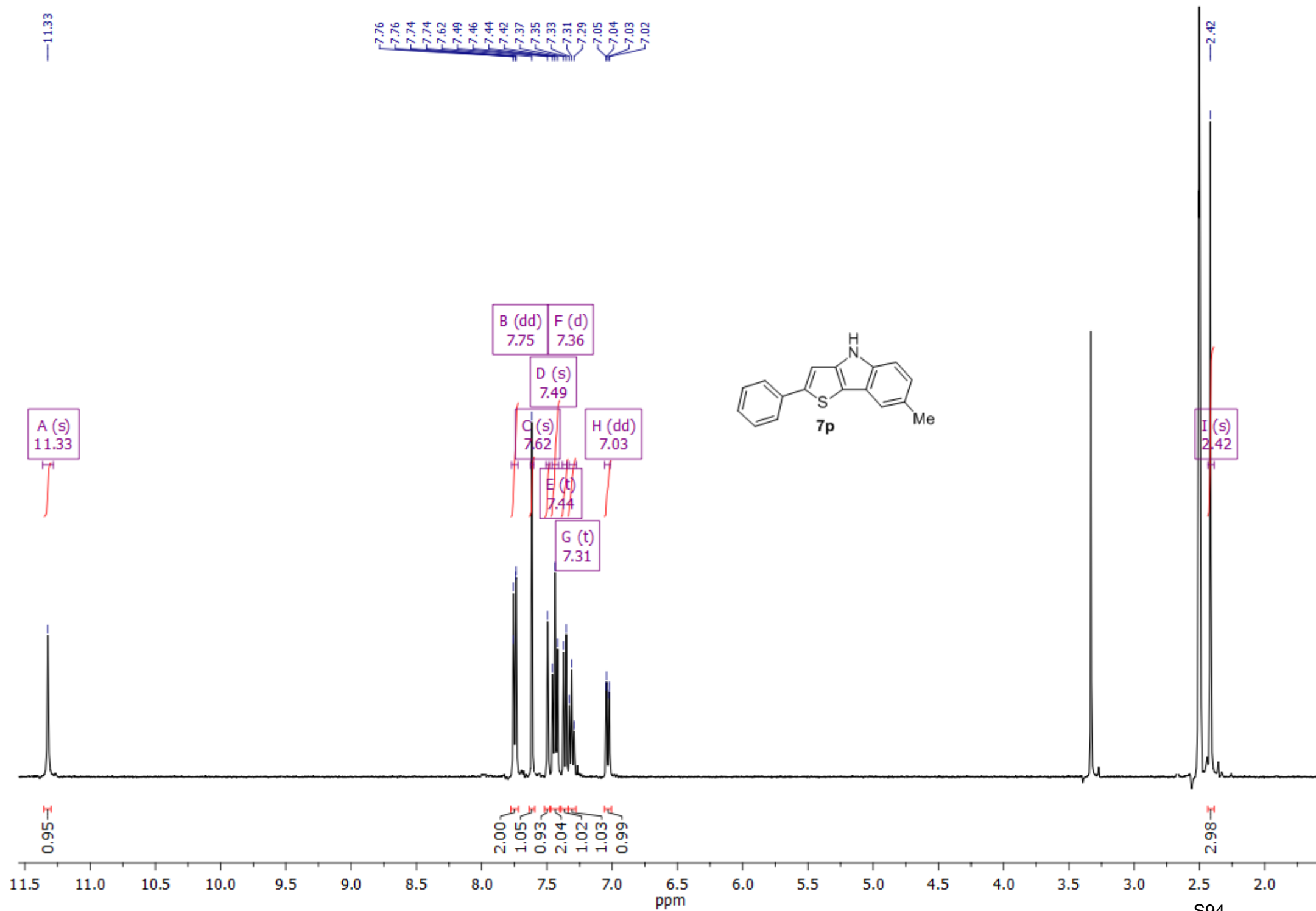


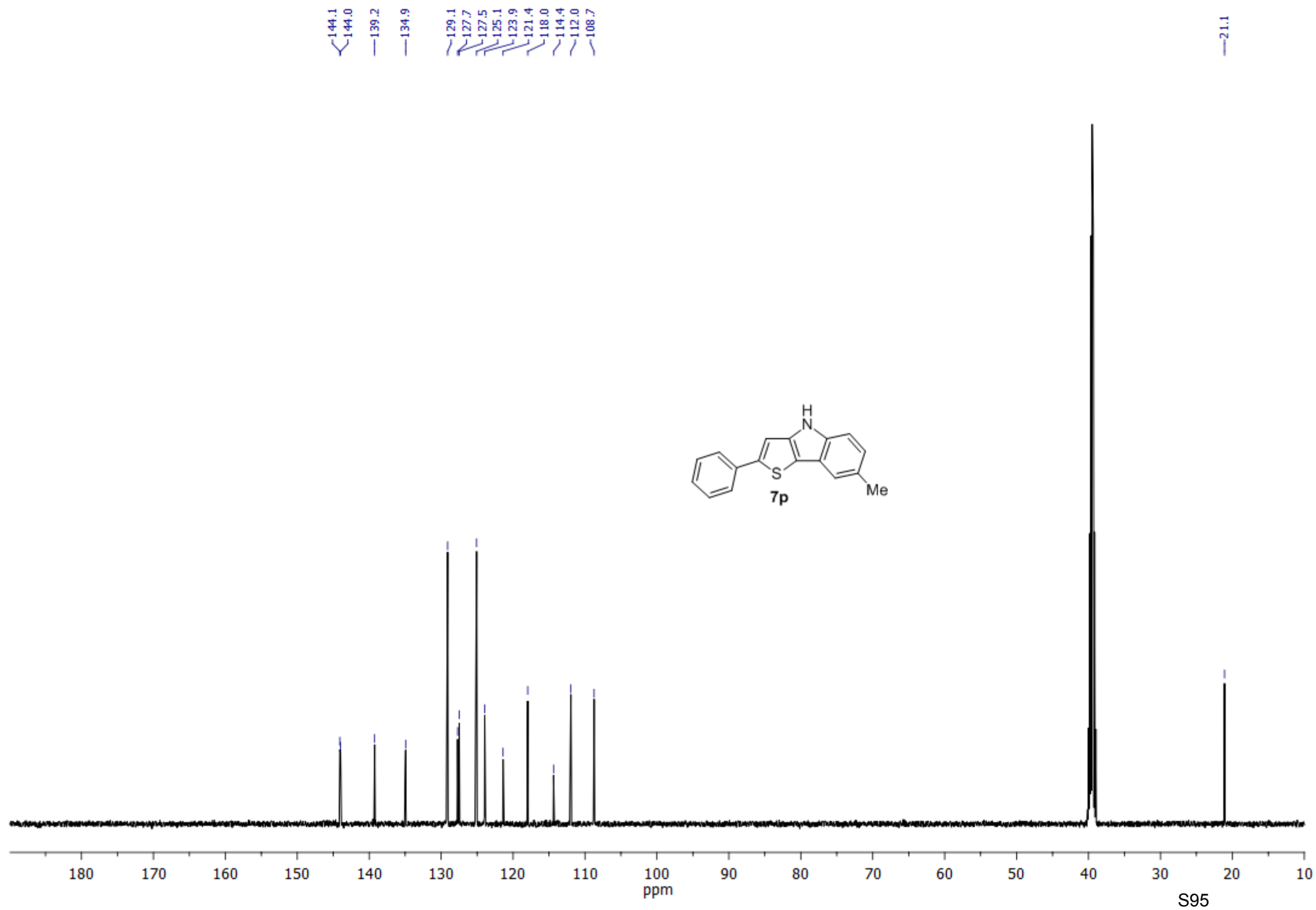
¹H NMR (solvent: DMSO-*d*₆)



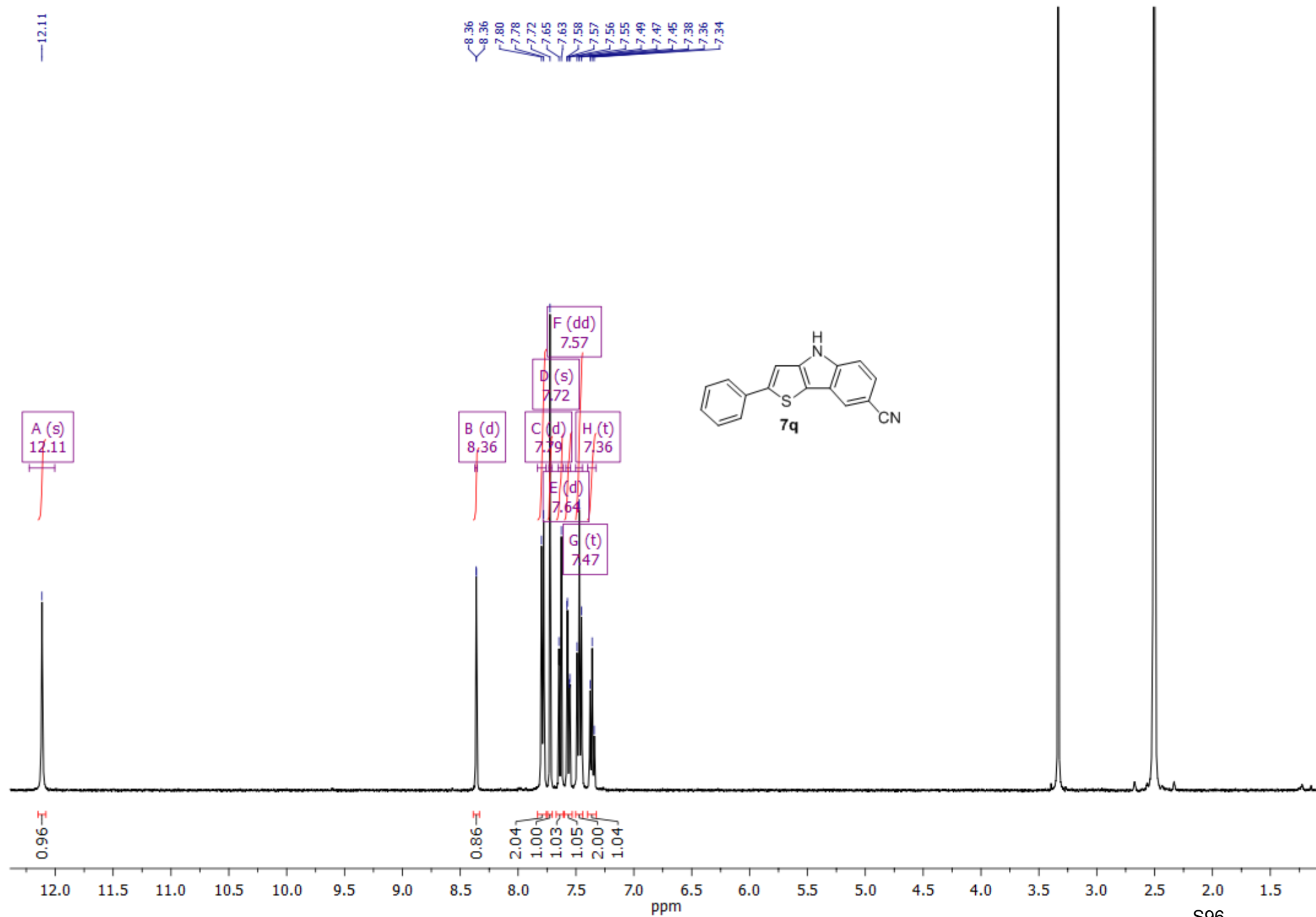


¹H NMR (solvent: DMSO-*d*₆)

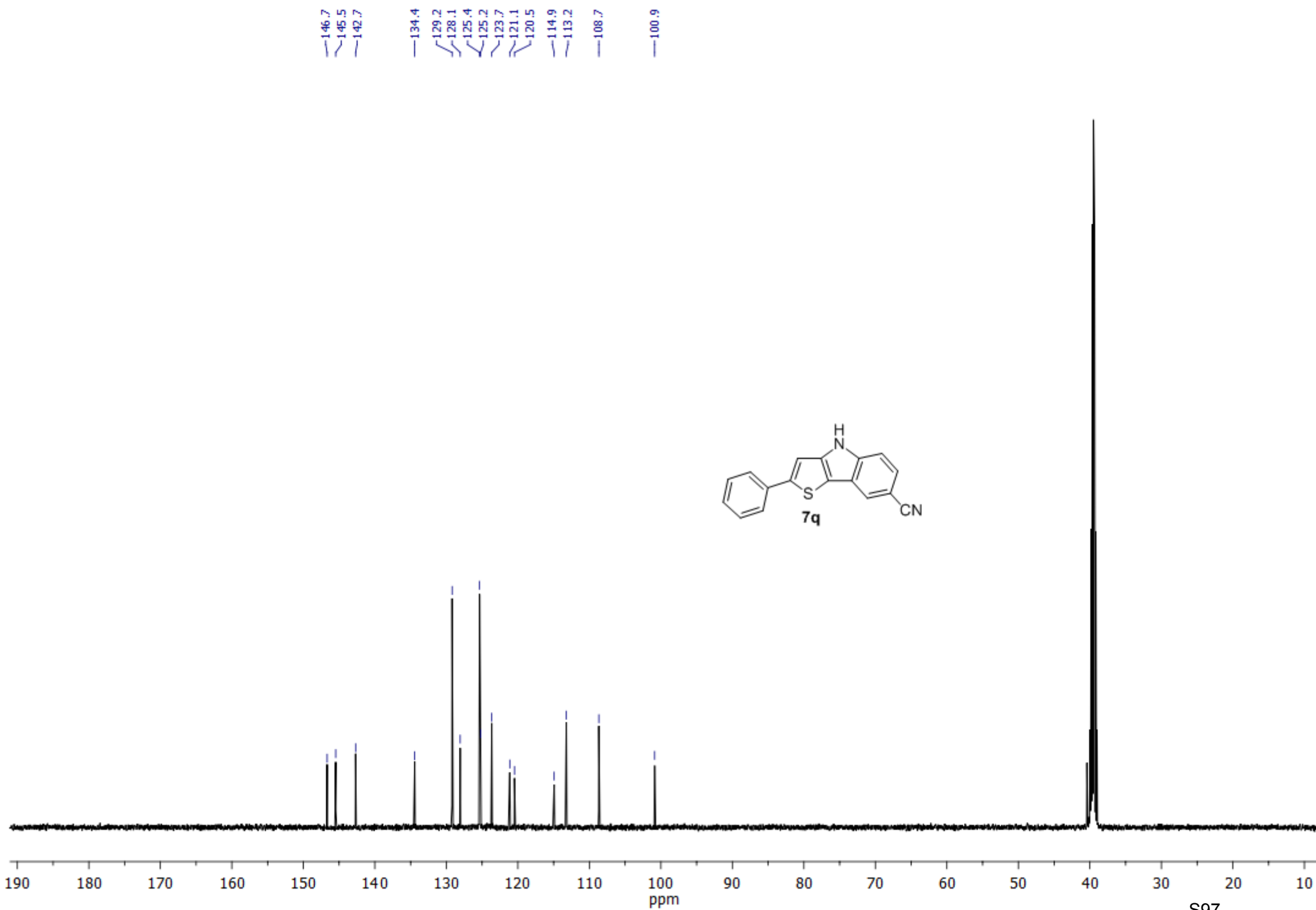




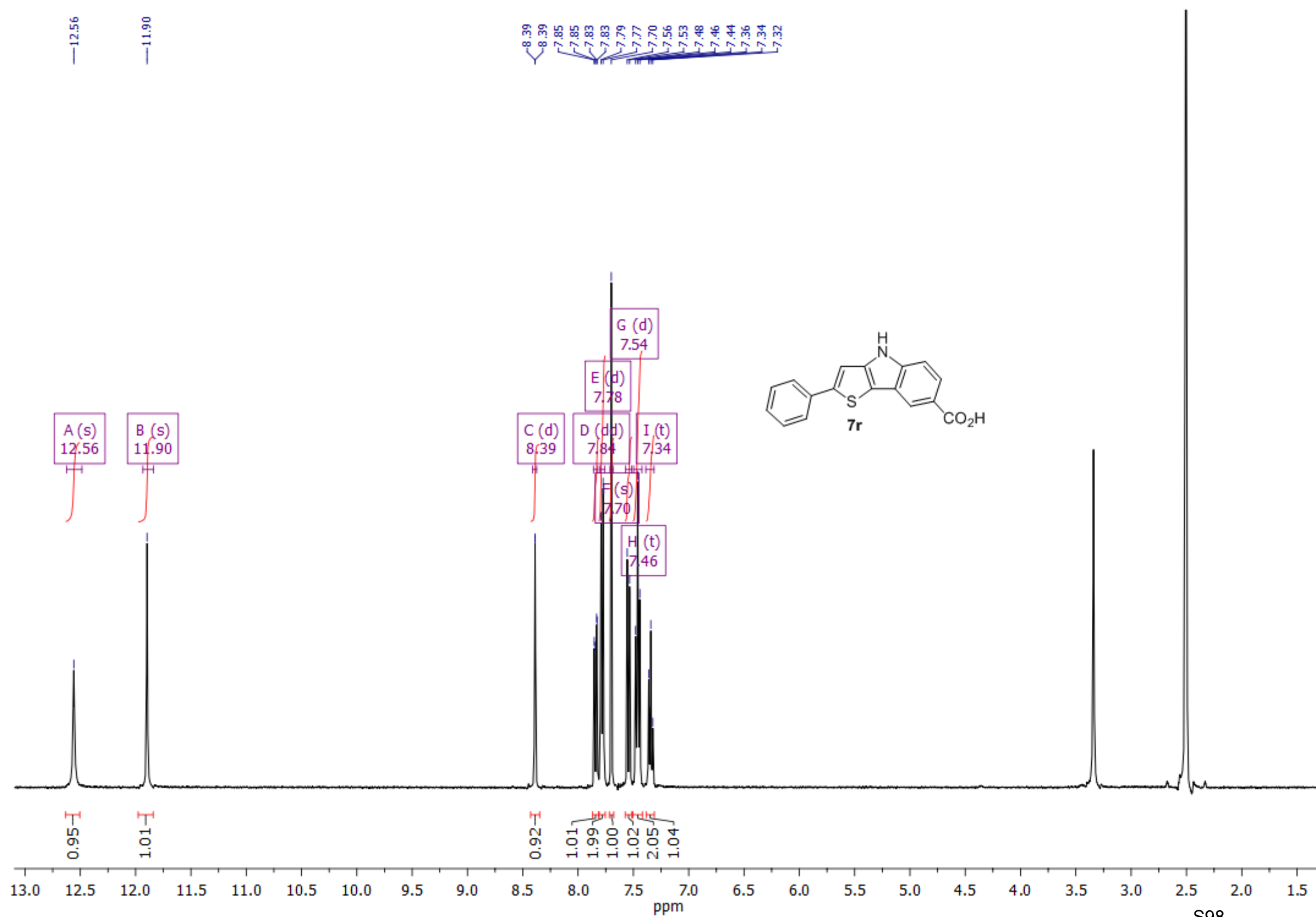
¹H NMR (solvent: DMSO-*d*₆)



¹³C NMR (solvent: DMSO-*d*₆)

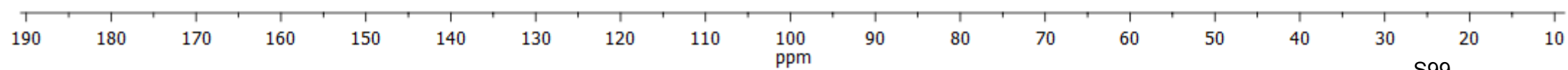
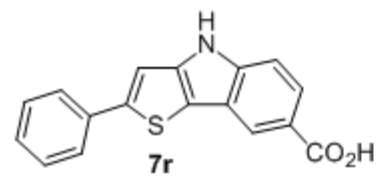


¹H NMR (solvent: DMSO-*d*₆)

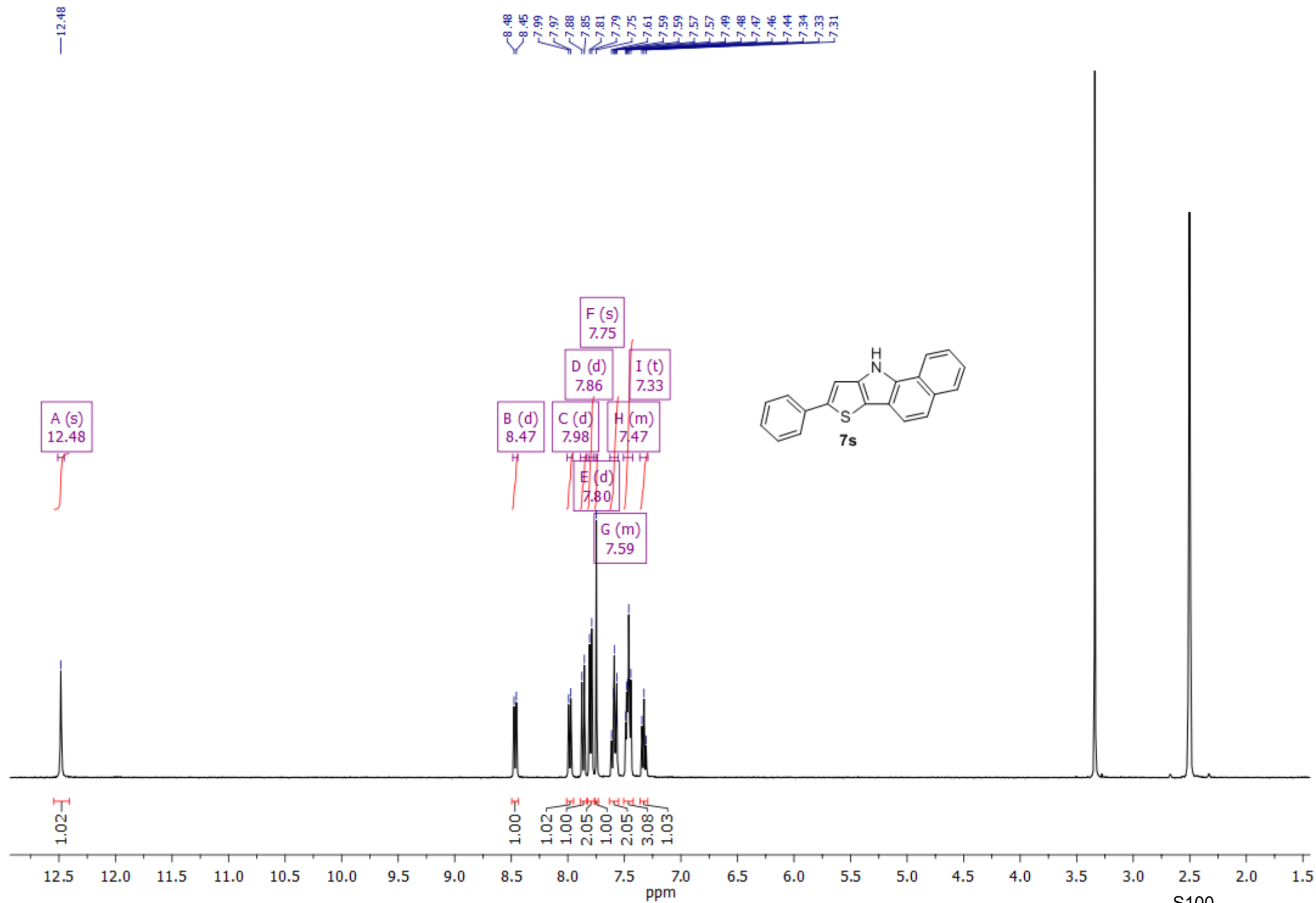


^{13}C NMR (solvent: $\text{DMSO-}d_6$)

168.0
145.5
145.0
143.4
134.6
129.2
127.8
125.3
123.7
121.5
120.8
120.6
115.5
111.9
108.8

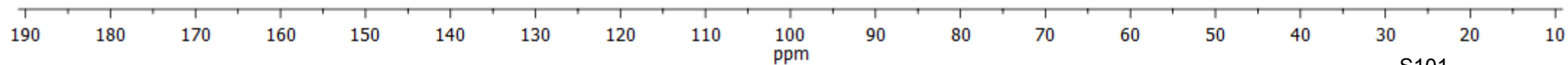
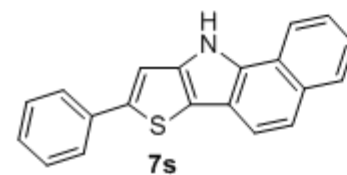


¹H NMR (solvent: DMSO-*d*₆)

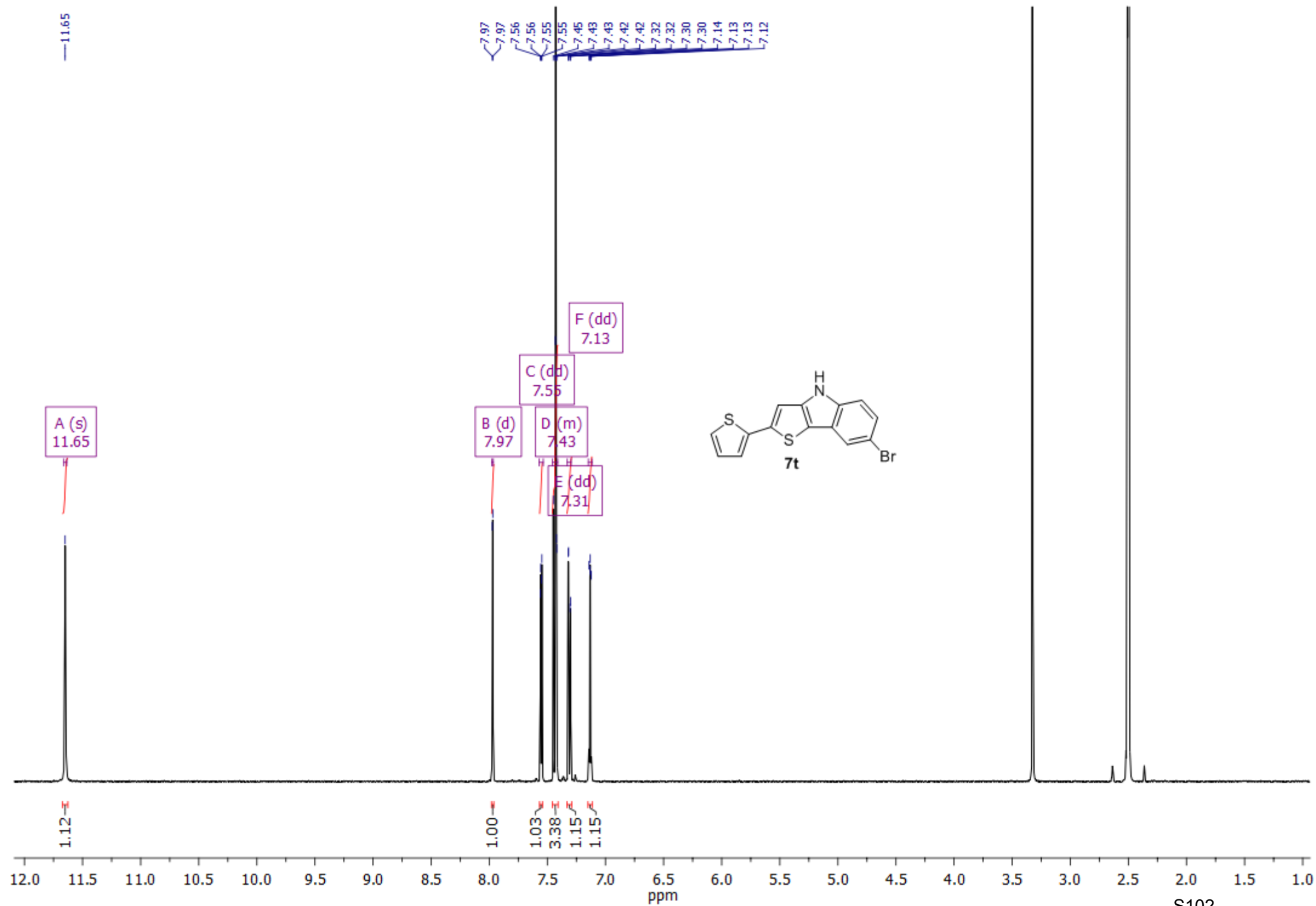


¹³C NMR (solvent: DMSO-*d*₆)

143.4
142.6
135.5
135.0
130.1
129.1
128.5
127.4
125.6
125.1
124.2
121.1
119.9
108.9

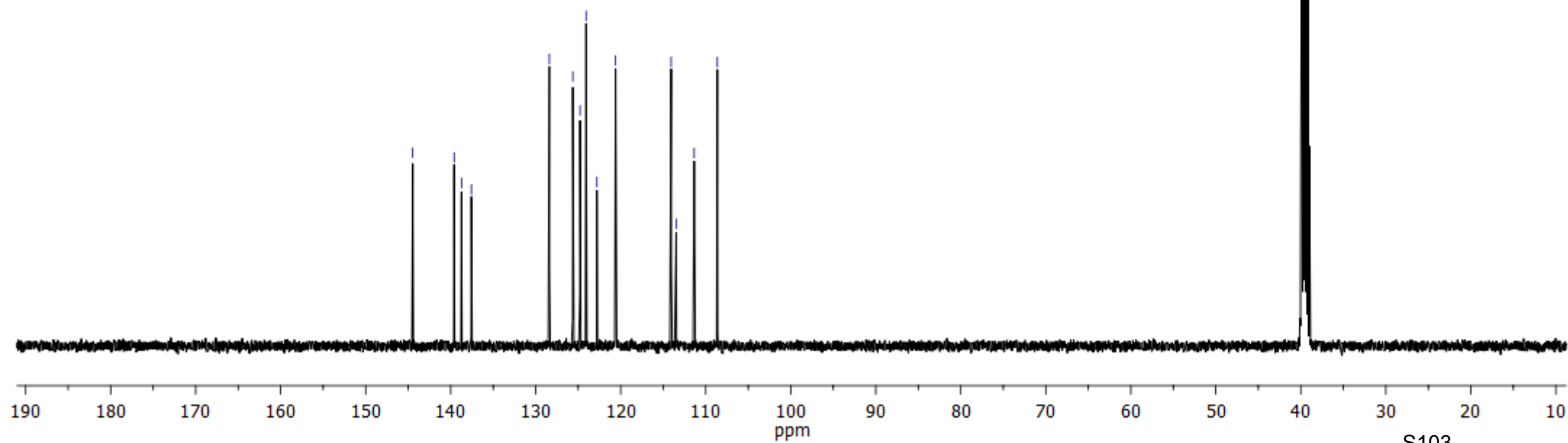
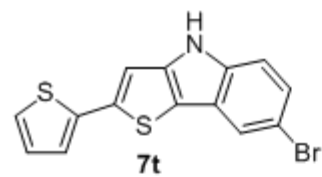


¹H NMR (solvent: DMSO-*d*₆)

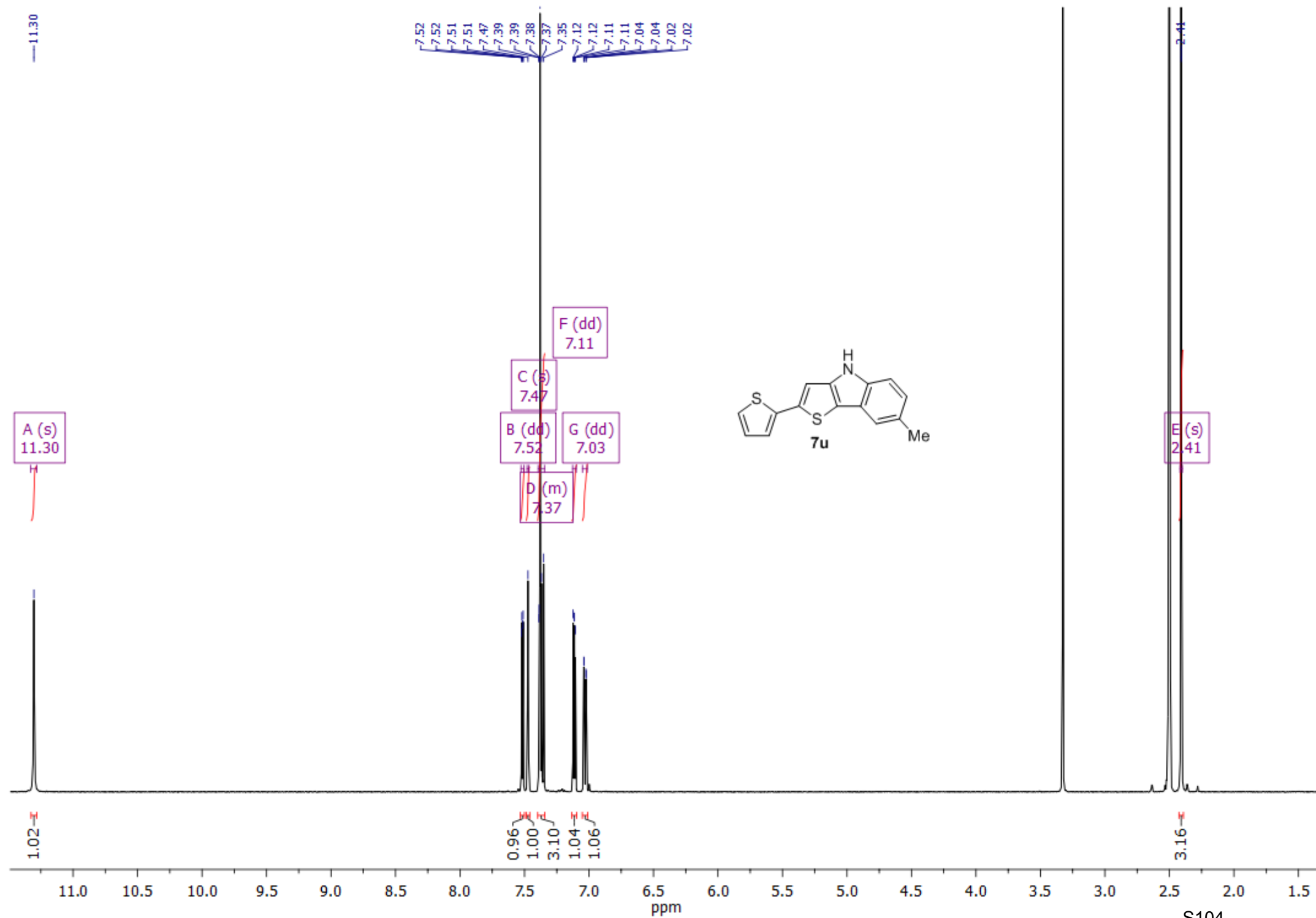


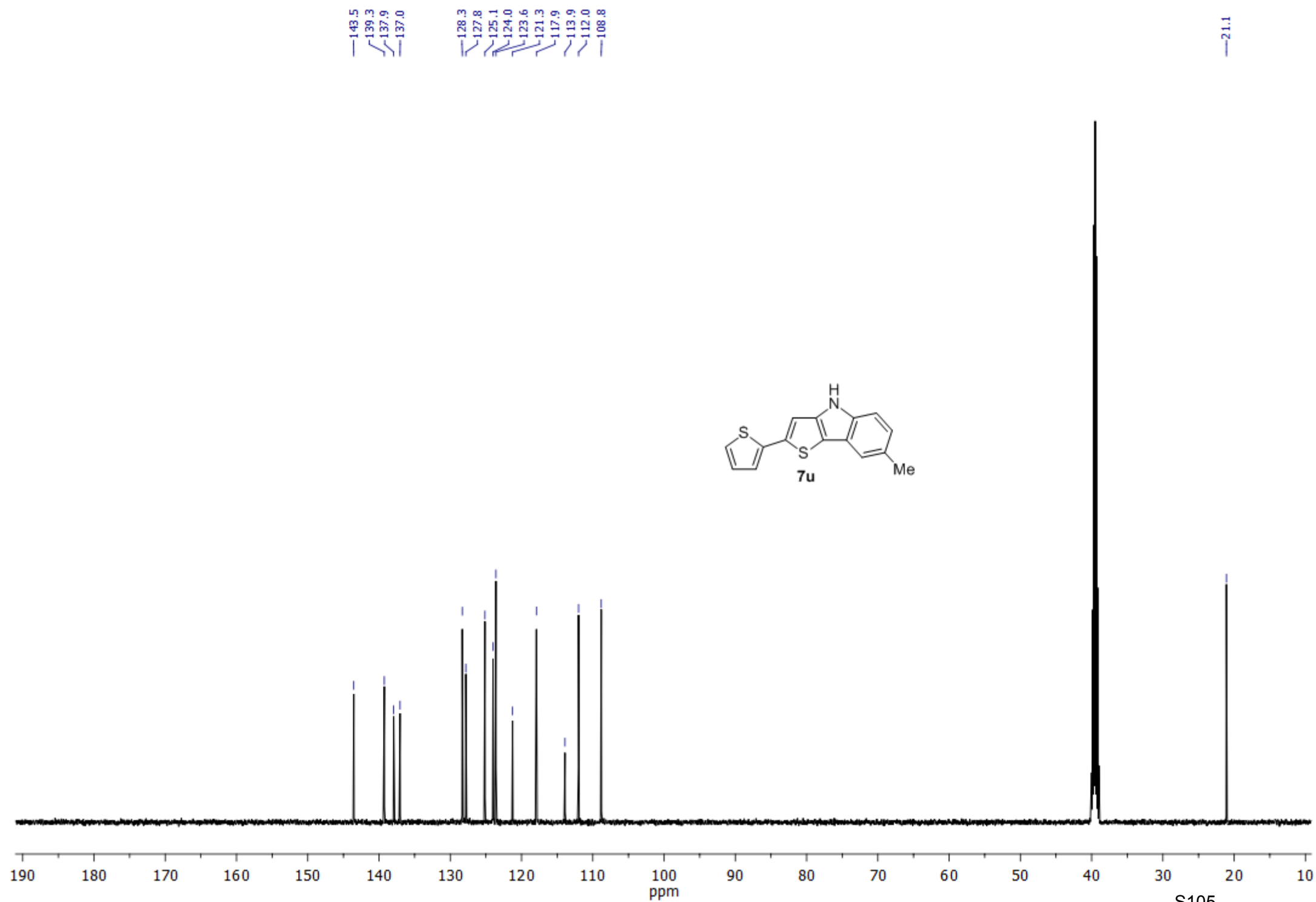
^{13}C NMR (solvent: $\text{DMSO-}d_6$)

144.5
139.6
138.7
137.6
128.4
125.6
124.8
124.1
122.8
120.6
114.1
113.5
111.4
108.6

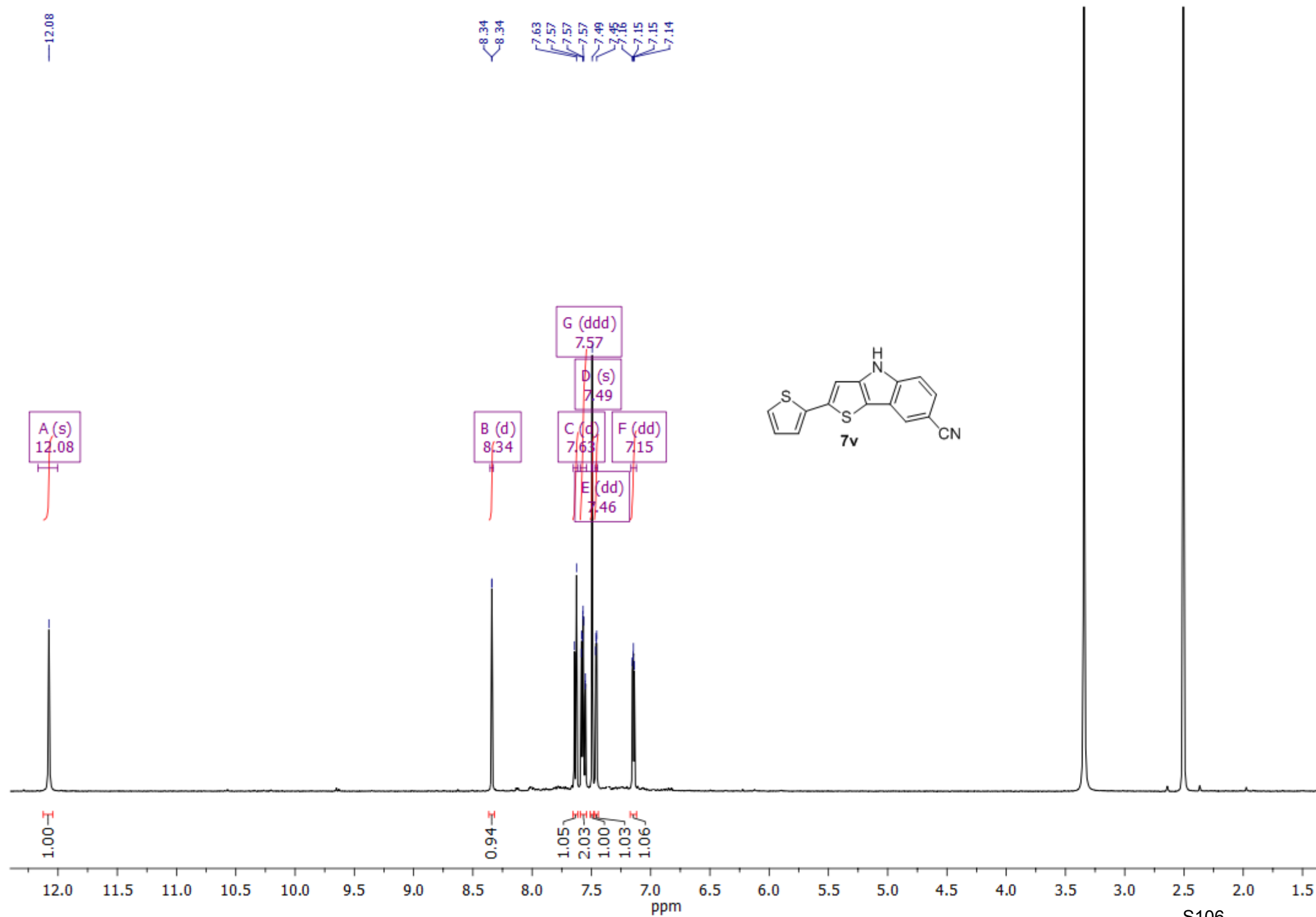


¹H NMR (solvent: DMSO-*d*₆)



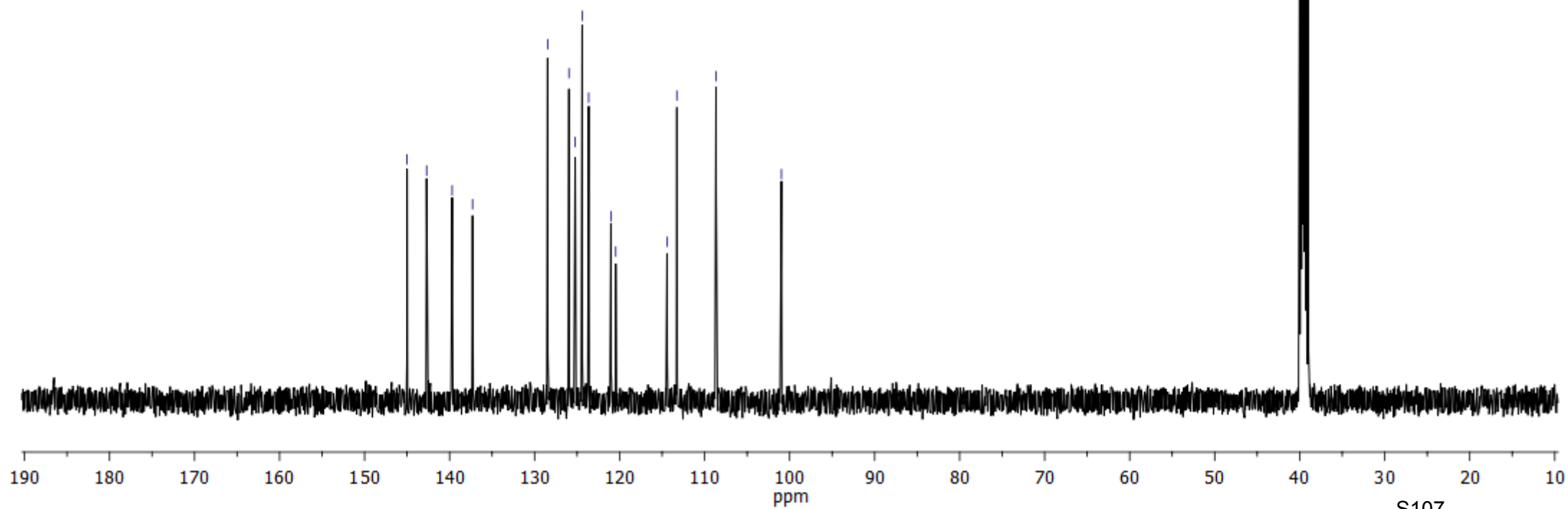
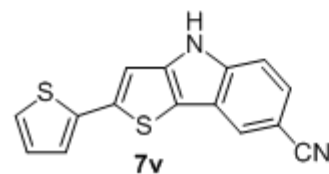


¹H NMR (solvent: DMSO-*d*₆)

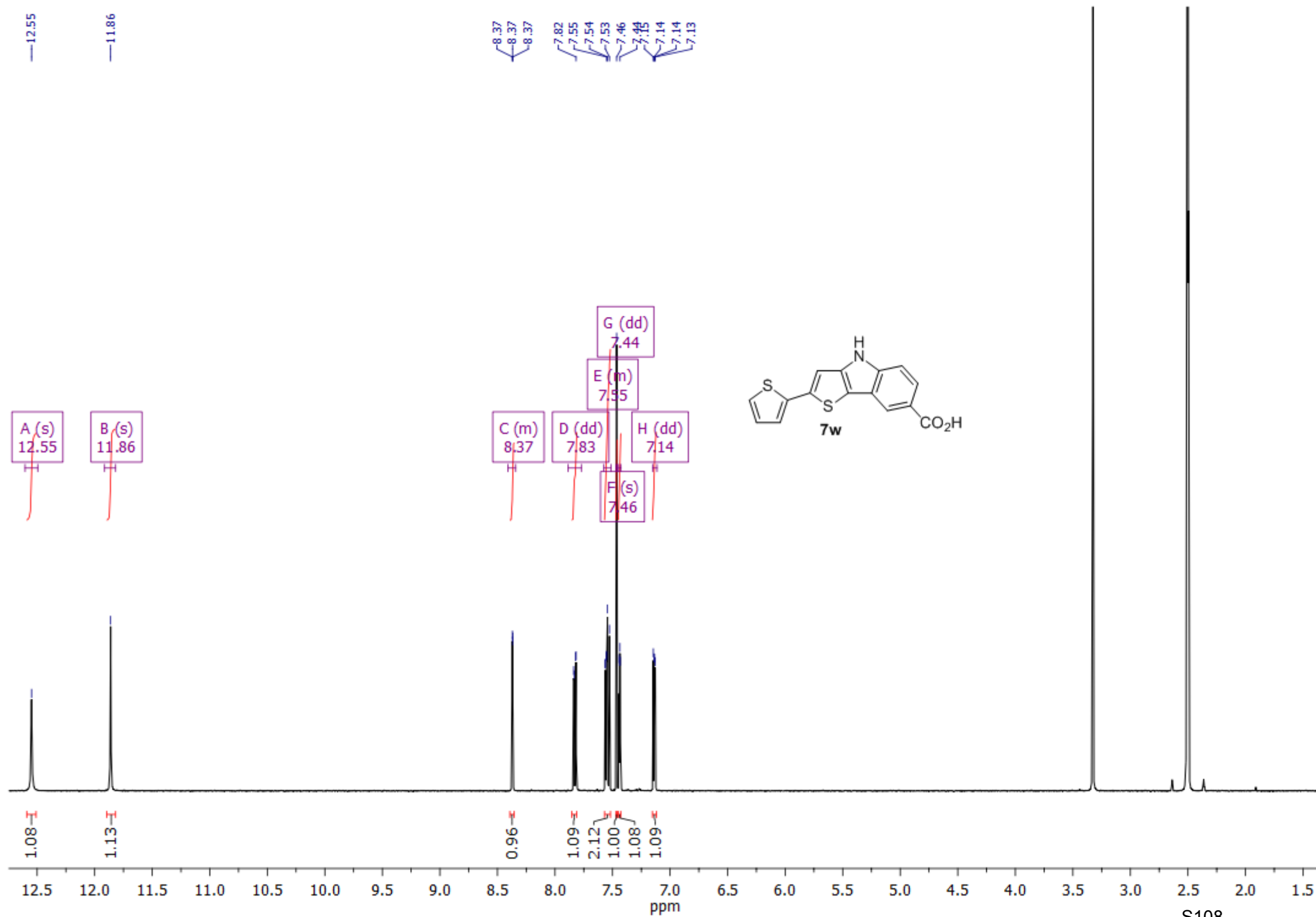


¹³C NMR (solvent: DMSO-*d*₆)

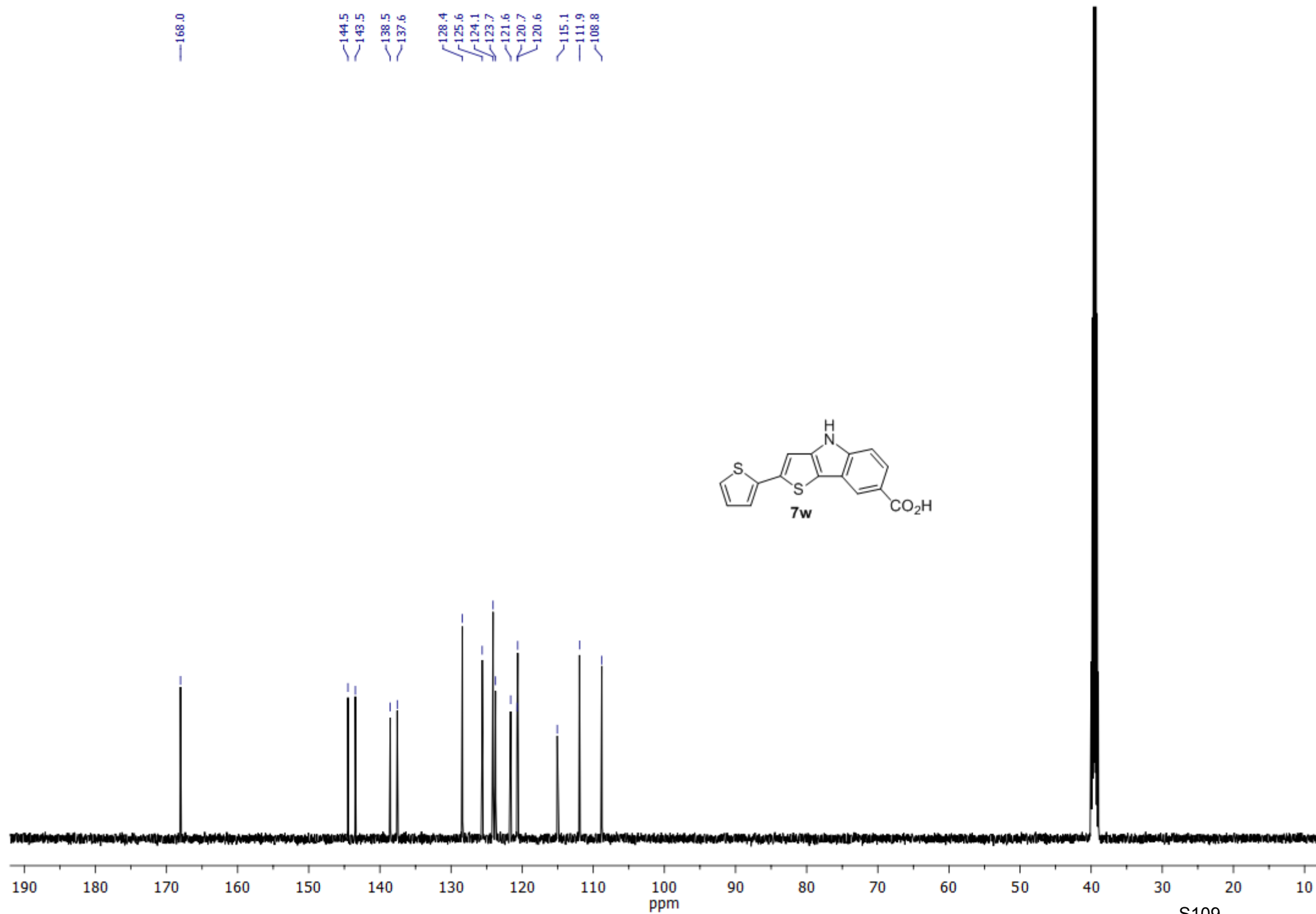
145.0
142.7
139.7
137.3
128.5
126.0
125.2
124.4
123.6
121.0
120.5
114.4
113.3
108.7
101.0



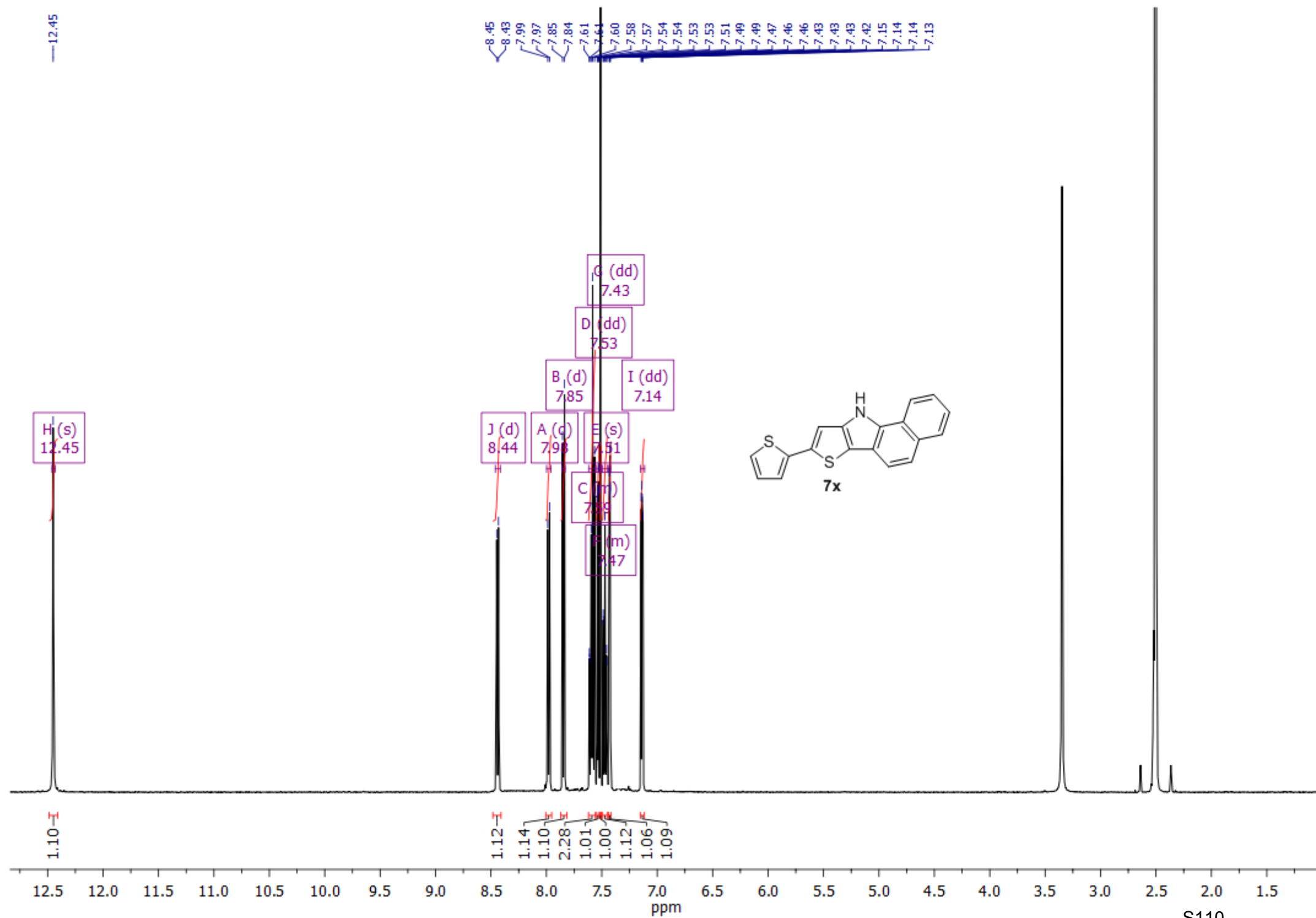
¹H NMR (solvent: DMSO-*d*₆)



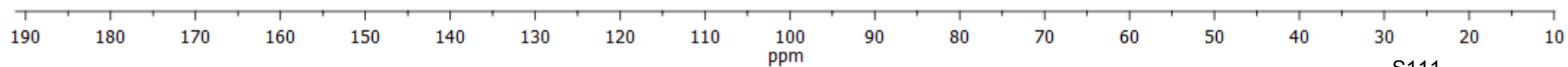
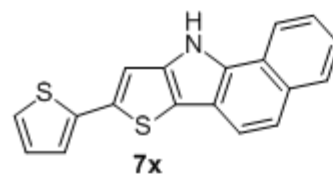
¹³C NMR (solvent: DMSO-*d*₆)



¹H NMR (solvent: DMSO-*d*₆)



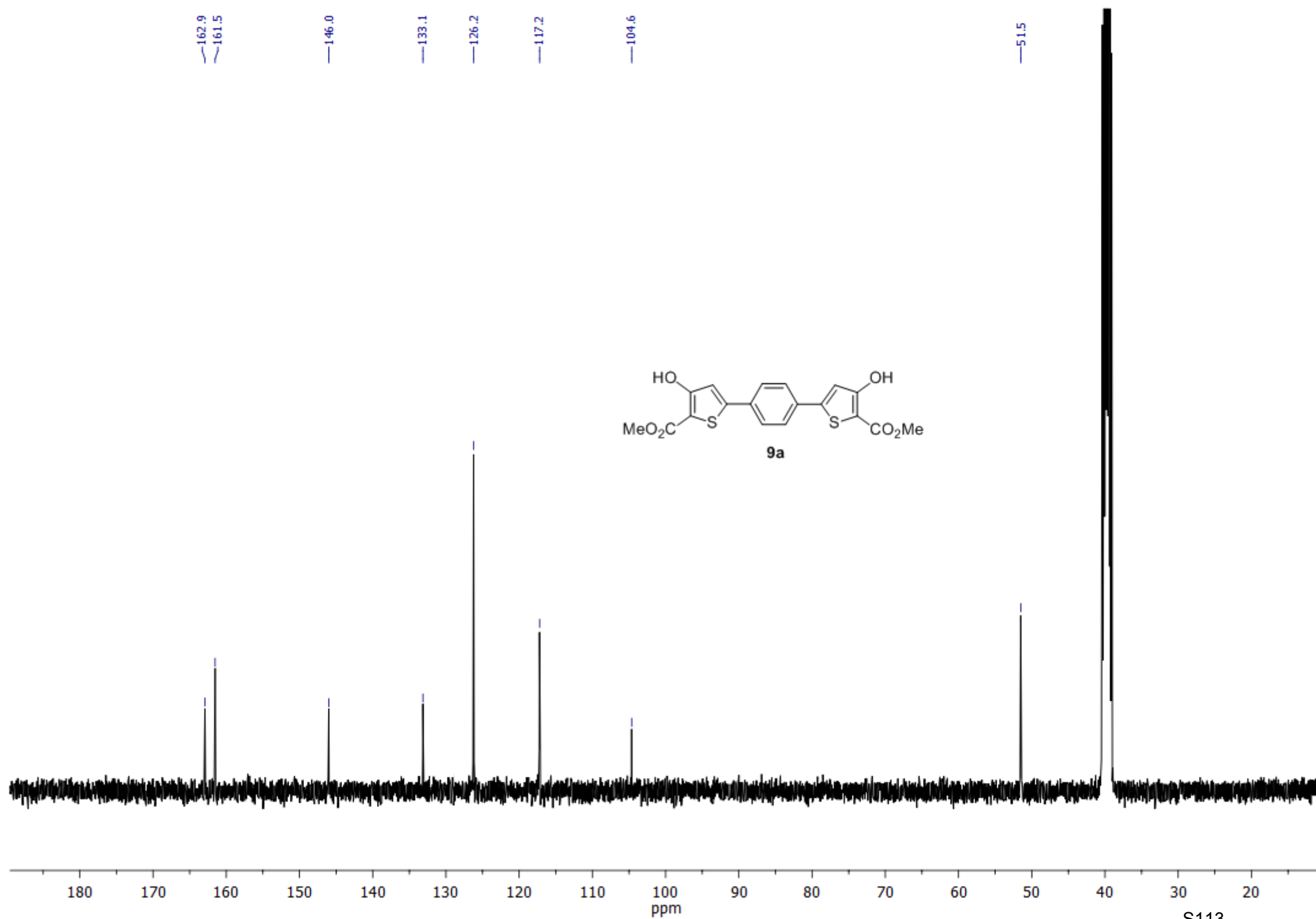
142.0
138.0
136.5
135.5
130.1
128.6
128.3
125.6
125.1
124.2
123.7
121.0
120.0
118.5
108.7



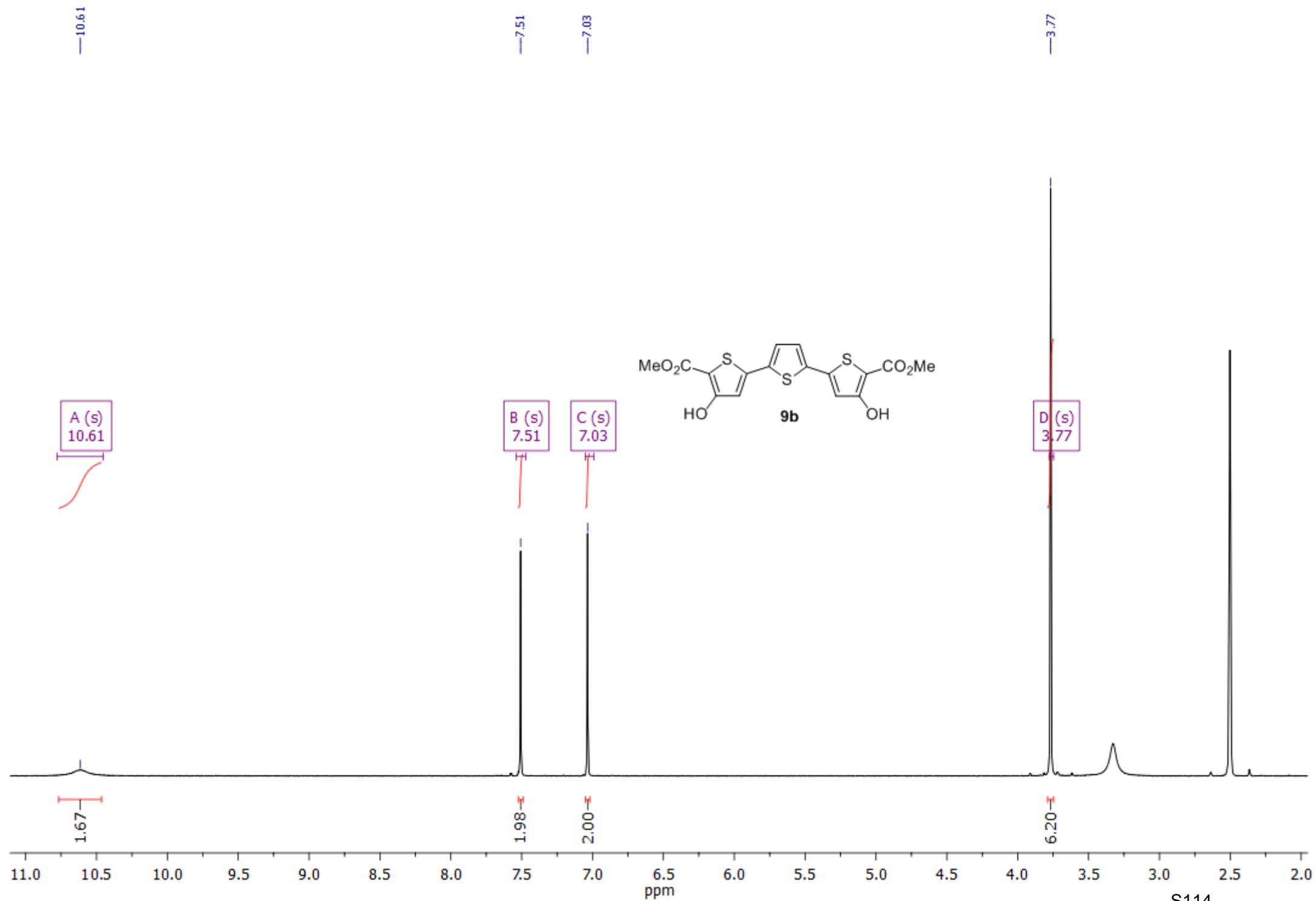
¹H NMR (solvent: DMSO-*d*₆)



¹³C NMR (solvent: DMSO-*d*₆)



¹H NMR (solvent: DMSO-*d*₆)



^{13}C NMR (solvent: $\text{DMSO-}d_6$)

162.6
161.1

139.2

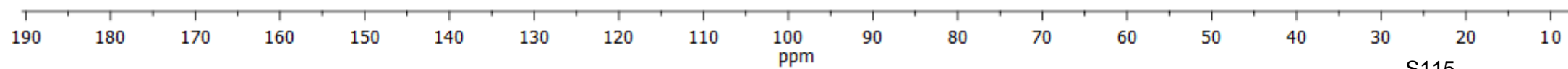
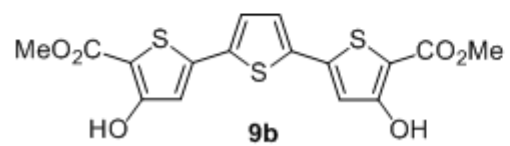
136.1

127.1

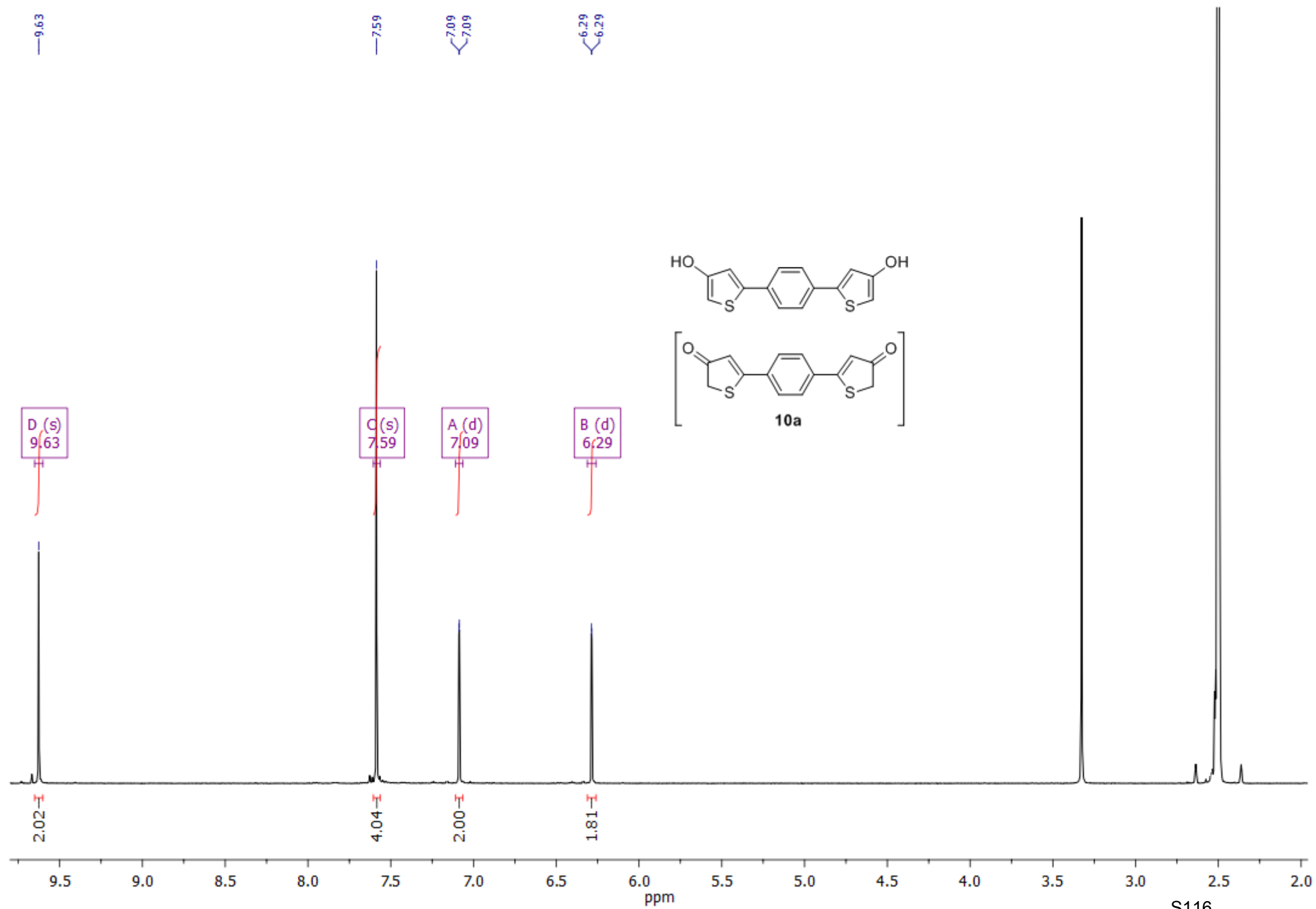
117.1

104.1

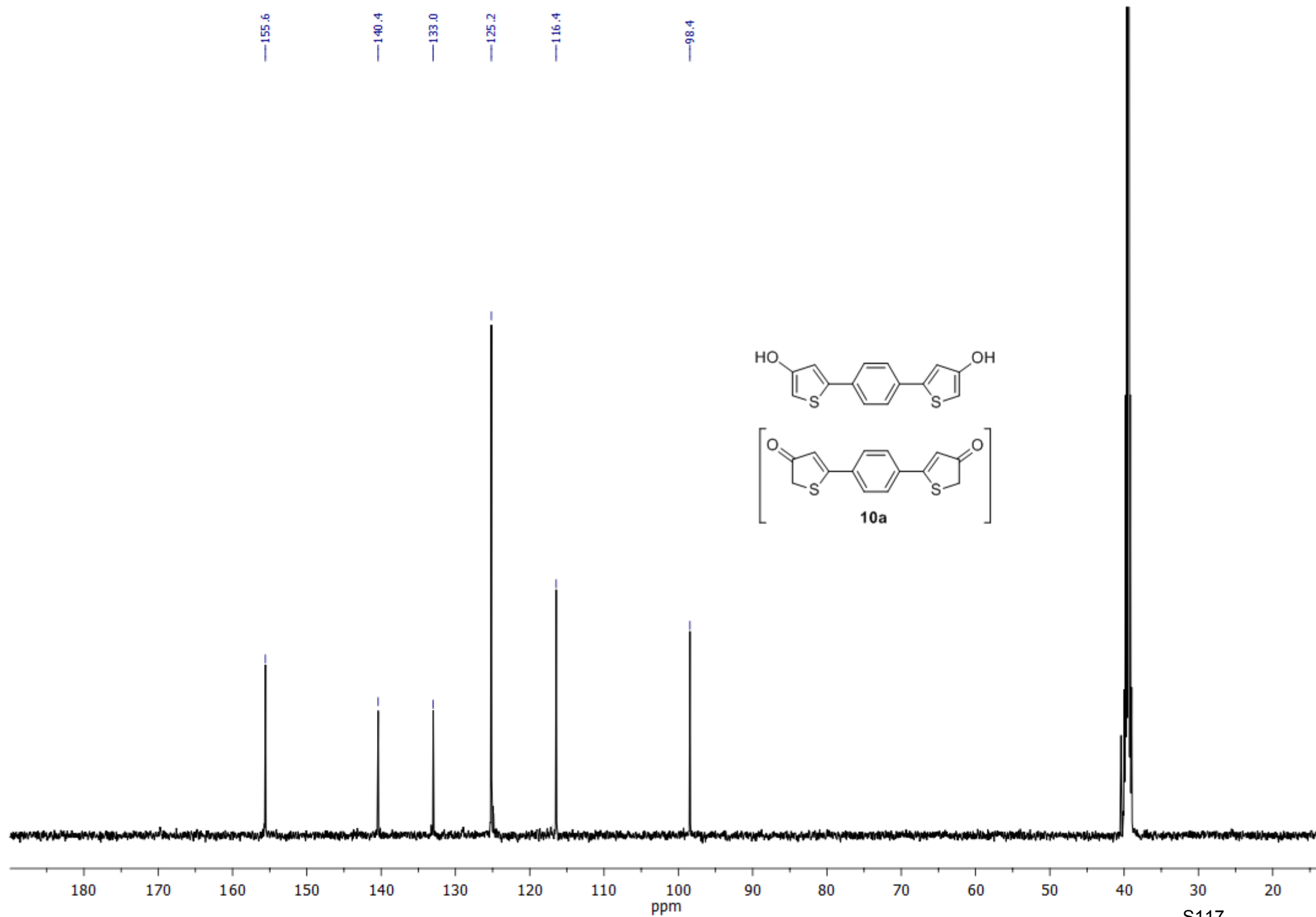
51.5



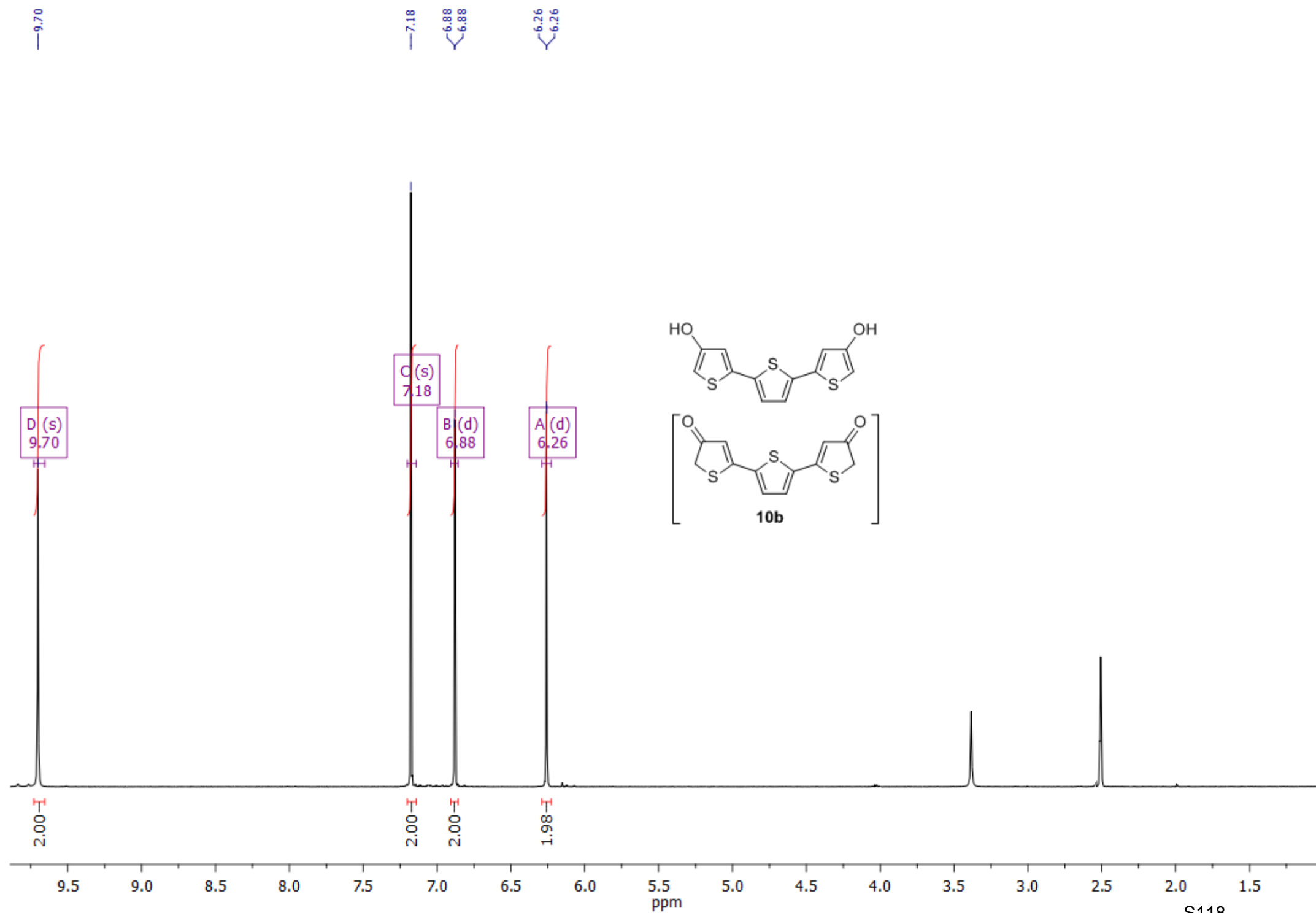
¹H NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **10a**



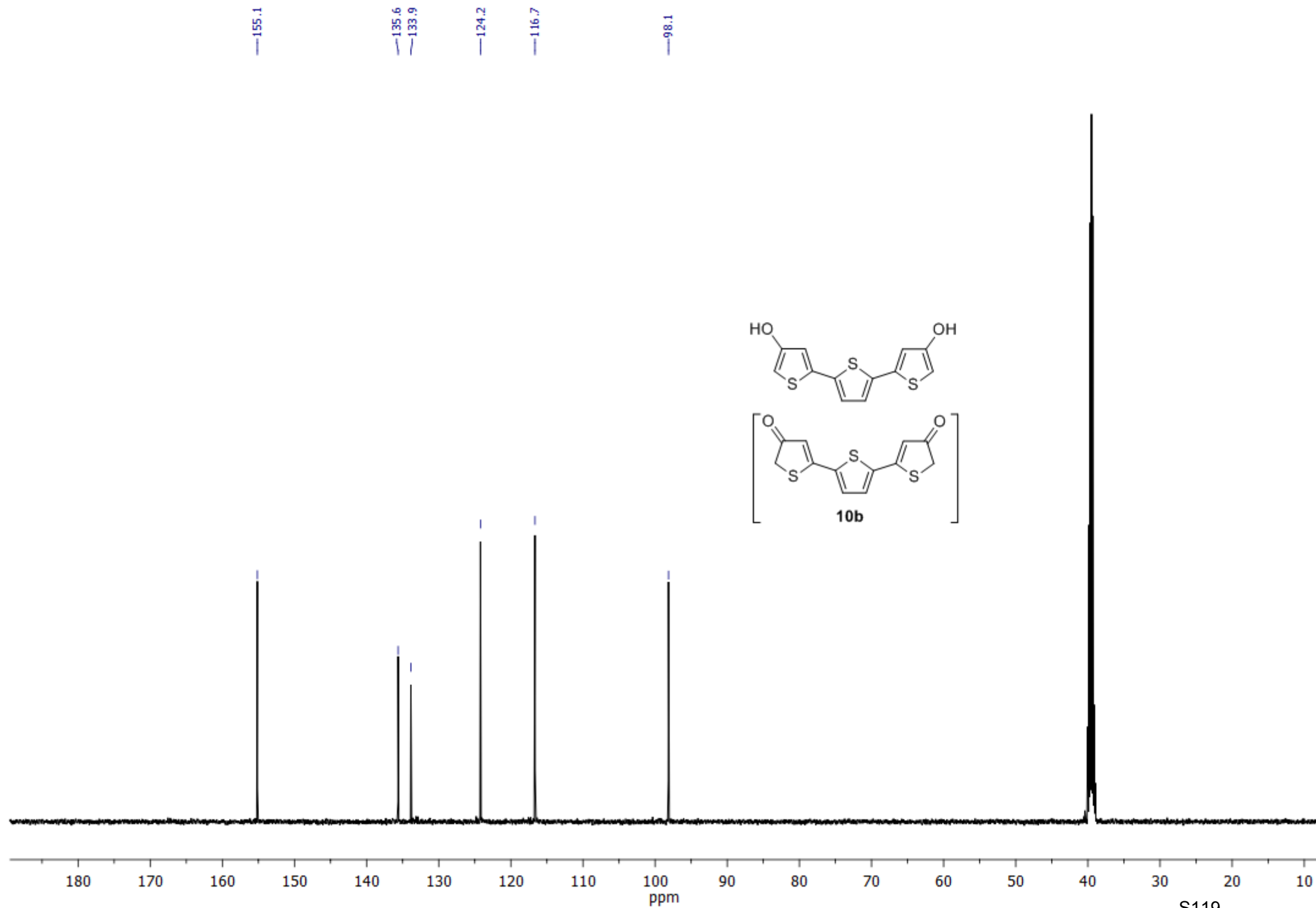
¹³C NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **10a**

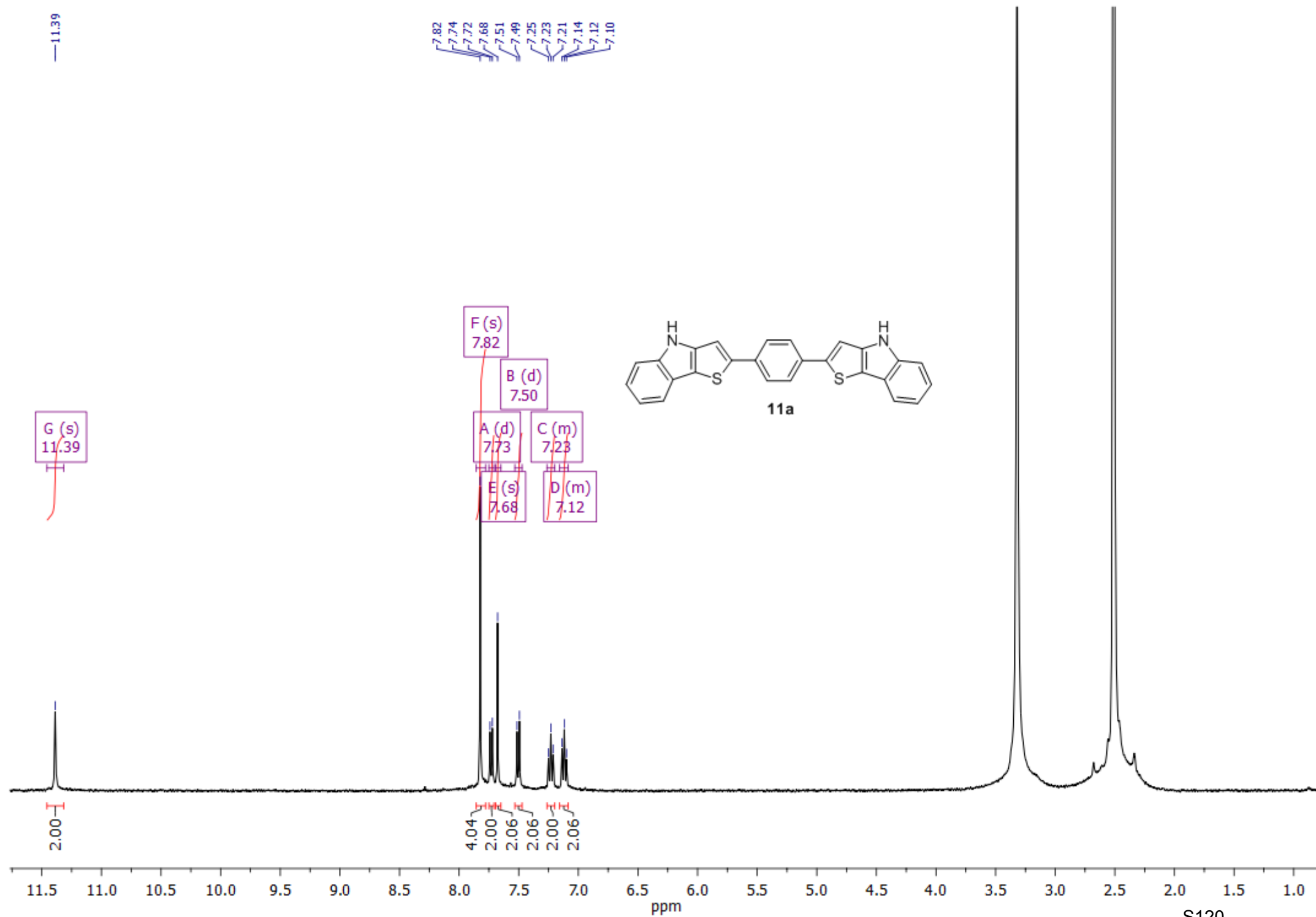


¹H NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **10b**



¹³C NMR (solvent: DMSO-*d*₆), enol (3-hydroxythiophene) form of compound **10b**





¹H NMR (solvent: DMSO-*d*₆)

