Supporting Information

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

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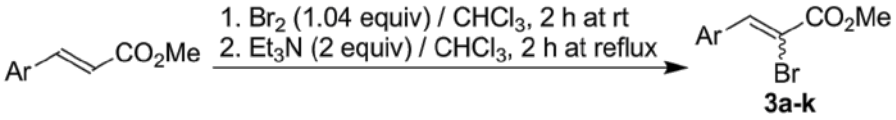
Table of content

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)

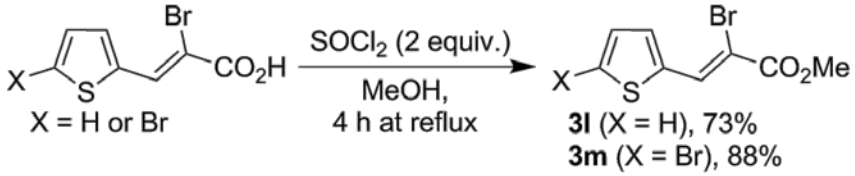


3a-k

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

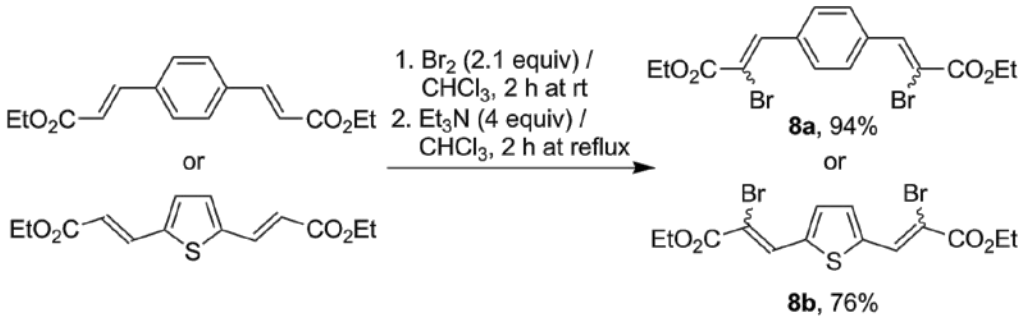
Br_2 (3.2 ml, 62.4 mmol) in dry $CHCl_3$ (20 ml) was added dropwise to methyl ester of appropriate cinnamic acid (60 mmol) in dry $CHCl_3$ (80 ml) at 0 °C during 20 min with continuous stirring, and the resulting solution was stirred for another 2 h at room temperature. After that, the reaction mixture was cooled to 0 °C and dropwise treated with Et_3N (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 shacked several times. The organic layer was separated, washed with water (4×50 ml), dried with $CaCl_2$ and eluted through a short silica gel plug (2 cm×4 cm) with $CHCl_3$ (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)



$SOCl_2$ (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 SO_2 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 $NaHCO_3$ solution (2×25 ml), water (50 ml) and dried with $CaCl_2$. 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)



Br_2 (2.2 ml, 43 mmol) in dry $CHCl_3$ (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 $CHCl_3$ (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 Et_3N (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 shacked several times. The $CHCl_3$ layer was separated, washed with water (4×30 ml), dried with $CaCl_2$ and eluted through a short silica gel plug (2 cm×4 cm) with $CHCl_3$ (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'-

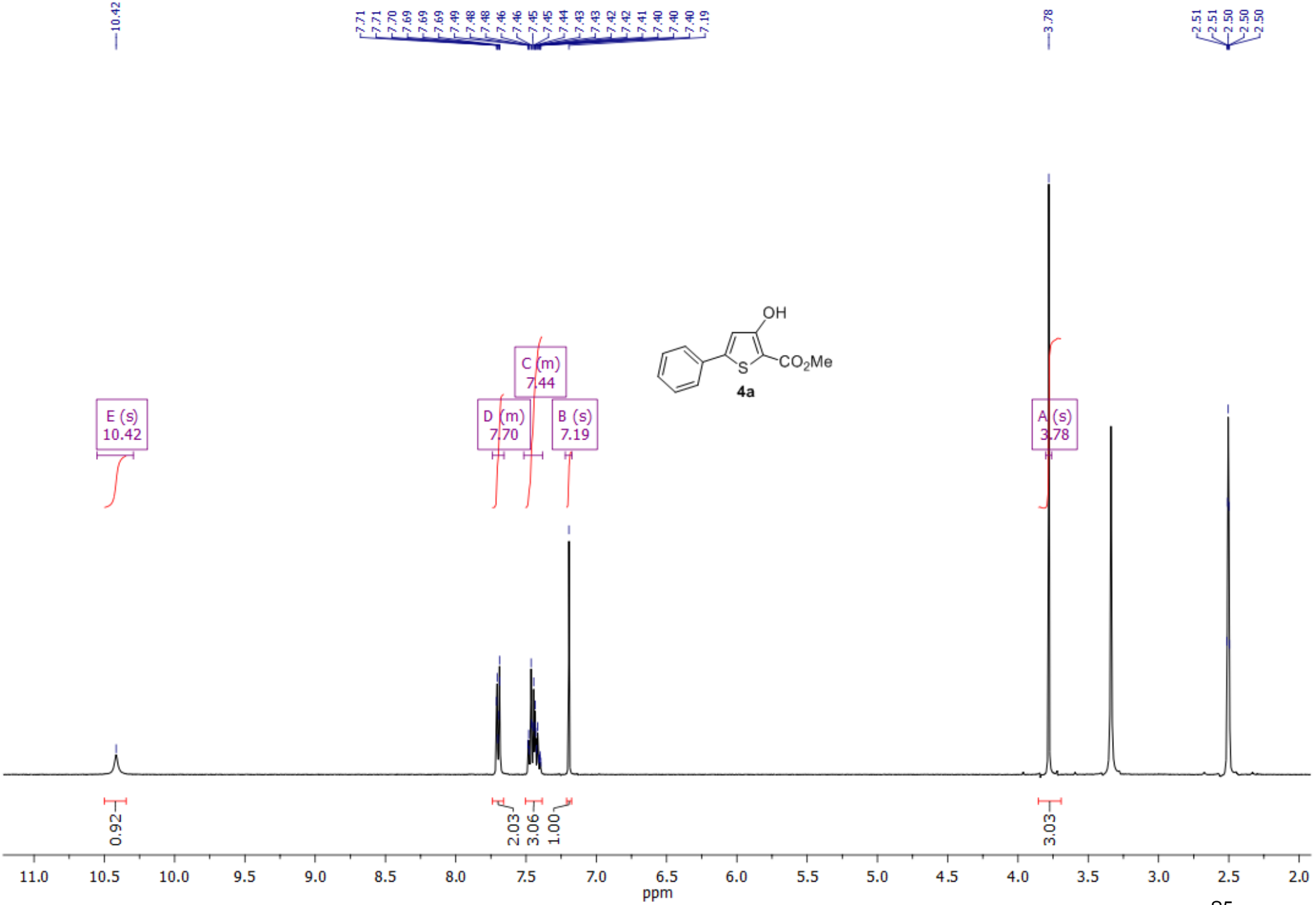
(thiophene-2,5-diyl)bis(2-bromoacrylate) **8b** (6.83 g, 76%), both **8a** and **8b** as mixture of (E,E)-(Z,E)-(Z,Z) stereoisomers according to GC-MS analysis. The obtained diesters were pure enough to be used in the next step without further purification.

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.

Copies of ^{1}H, ^{19}F and ^{13}C NMR spectra of new compounds

^{1}H NMR (solvent: DMSO-d_6)



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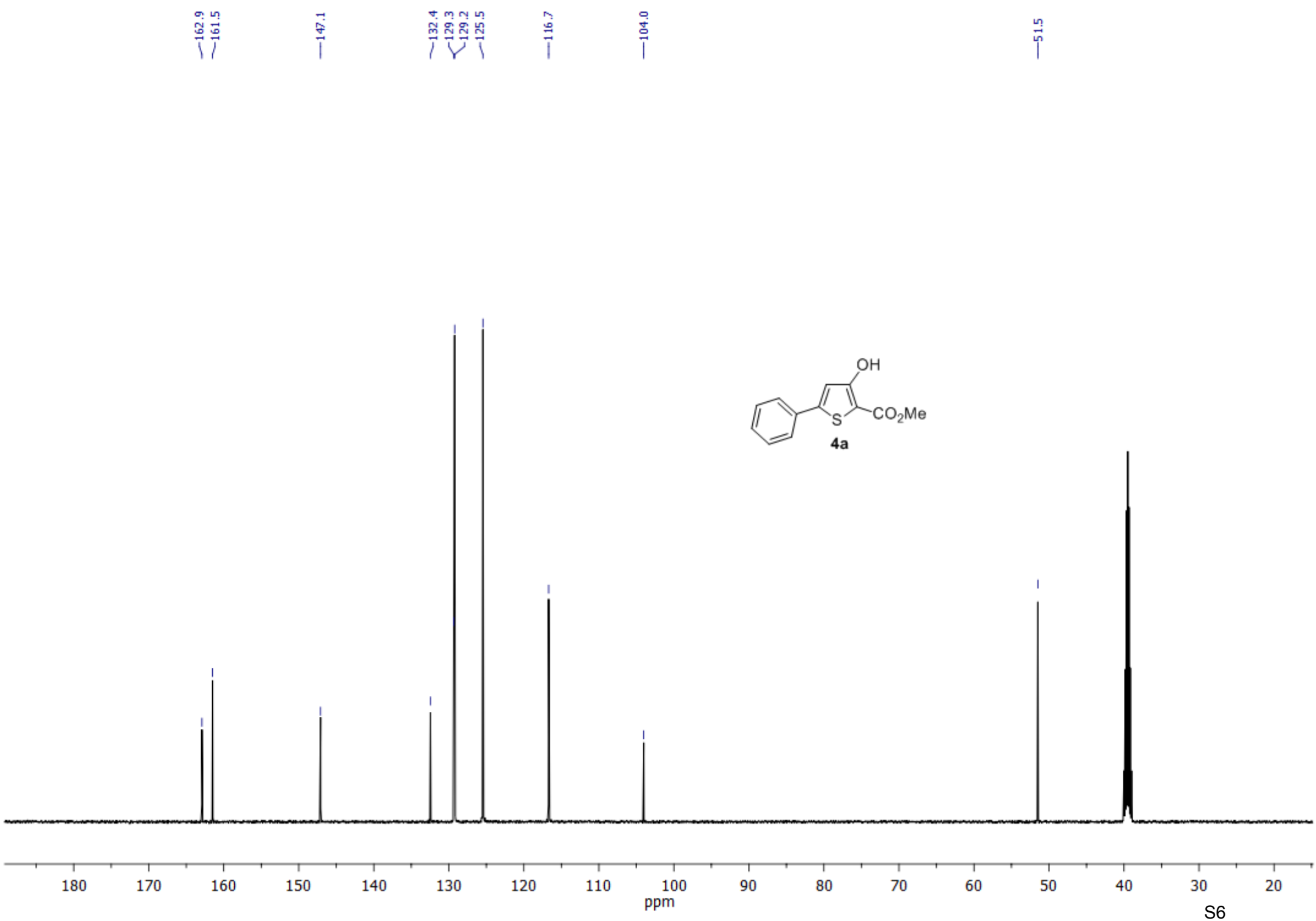

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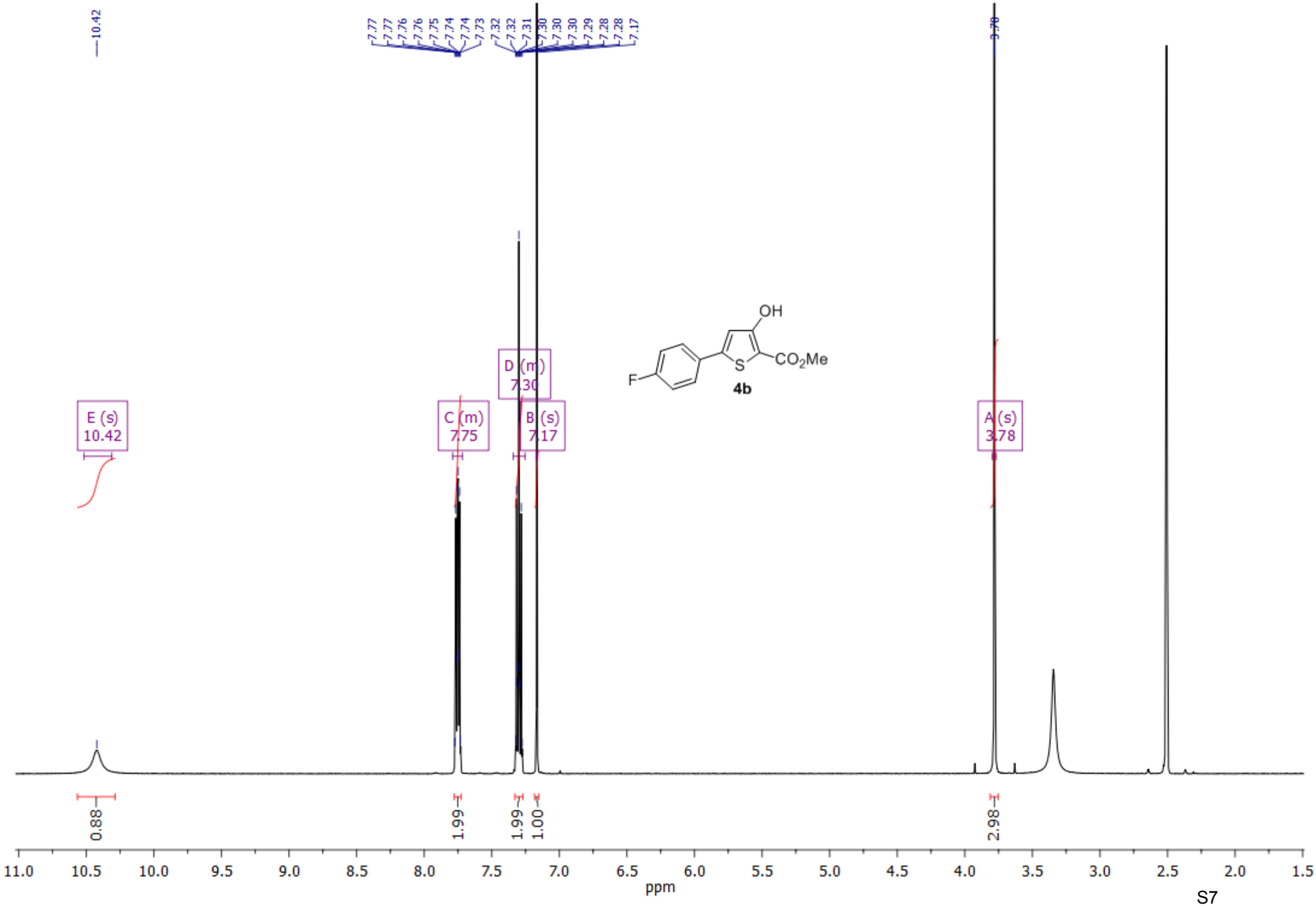

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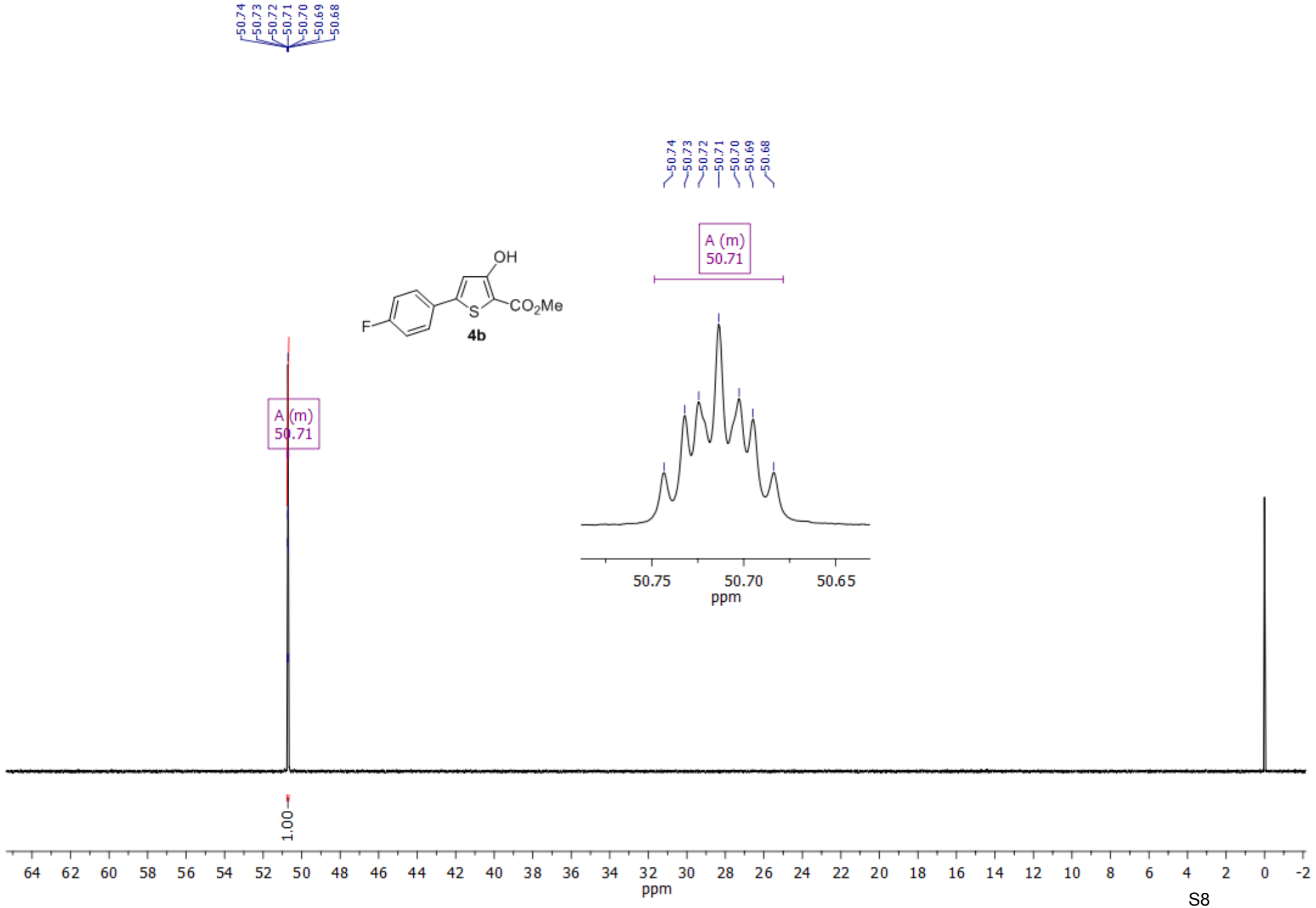

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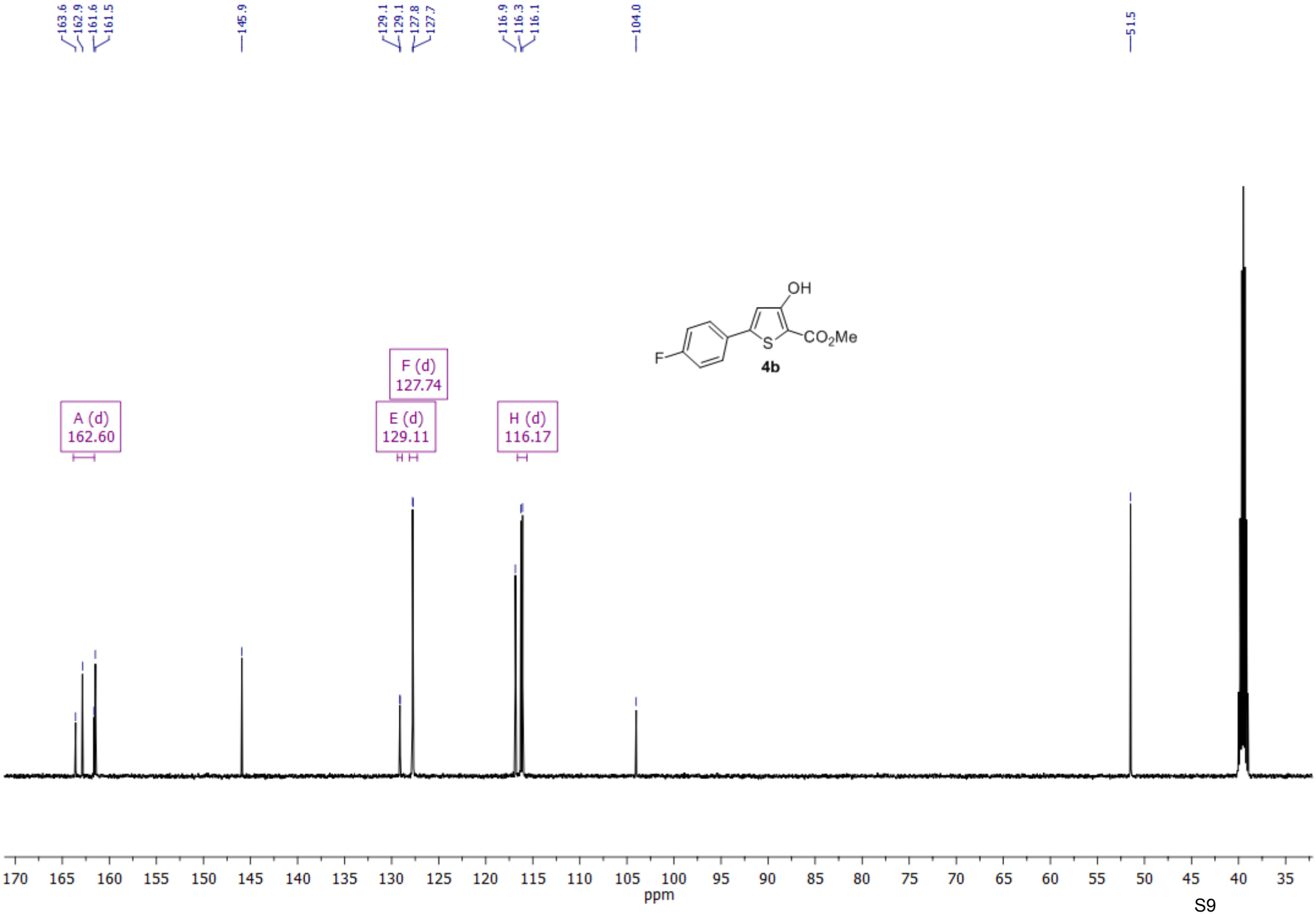

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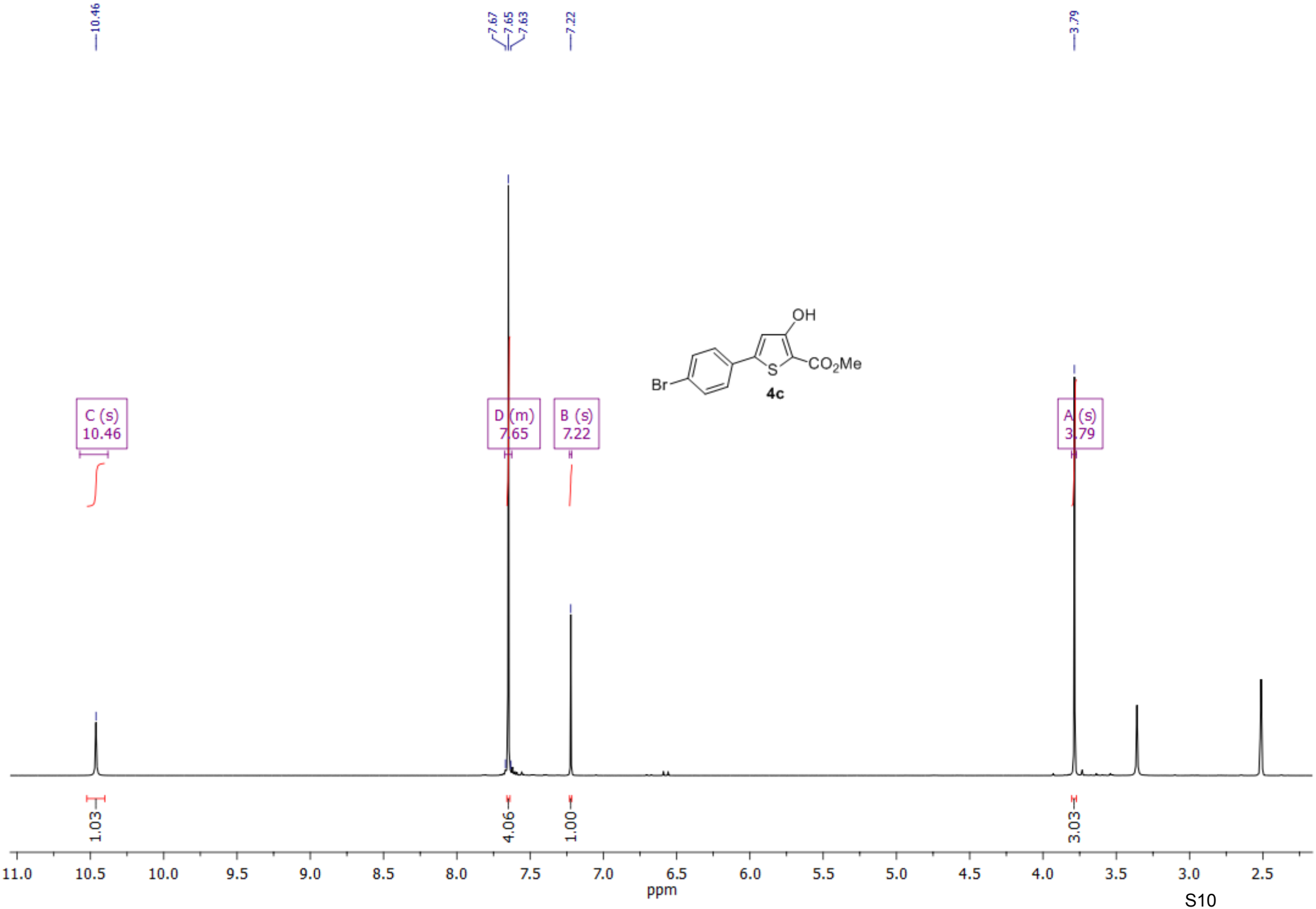

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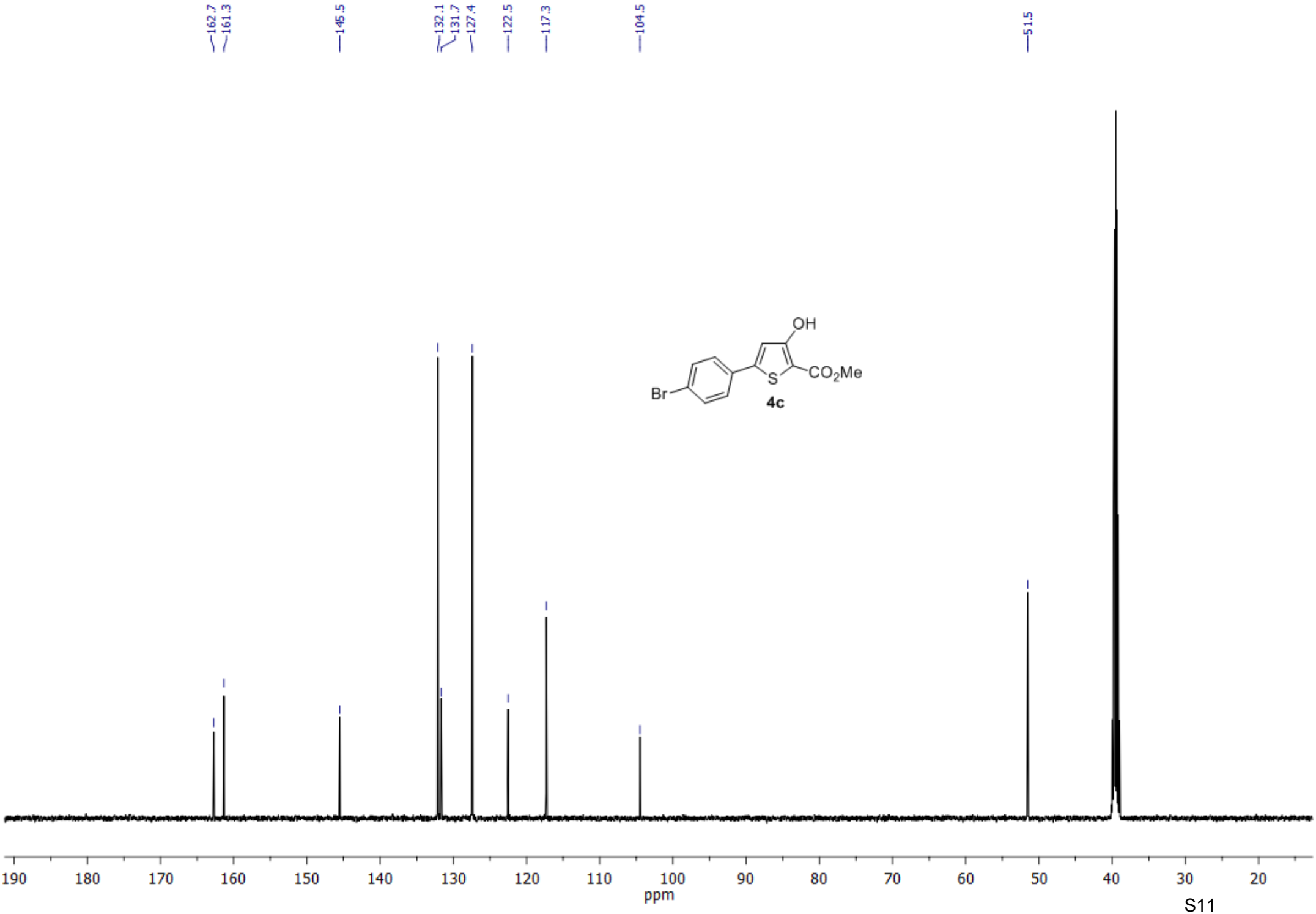

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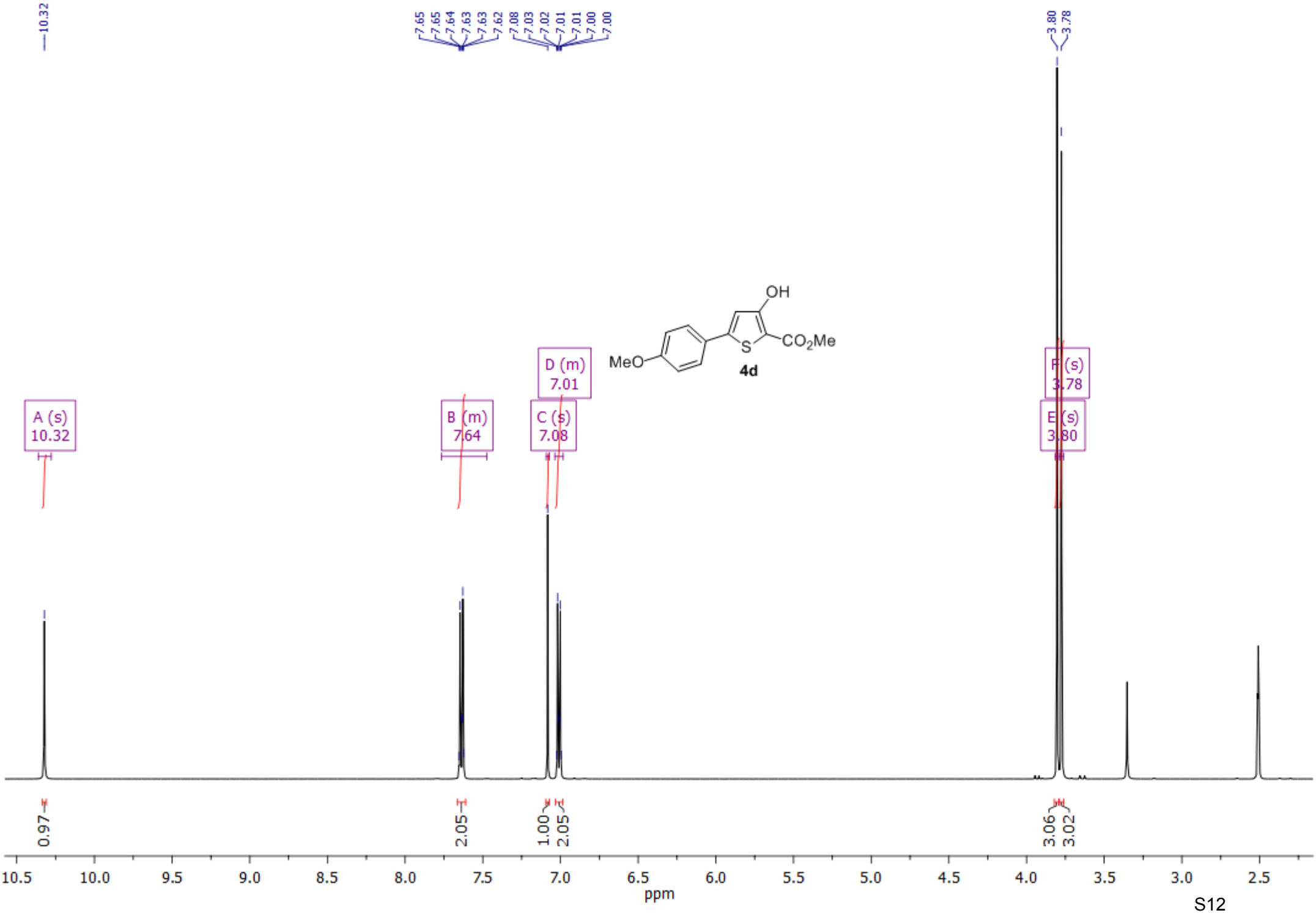

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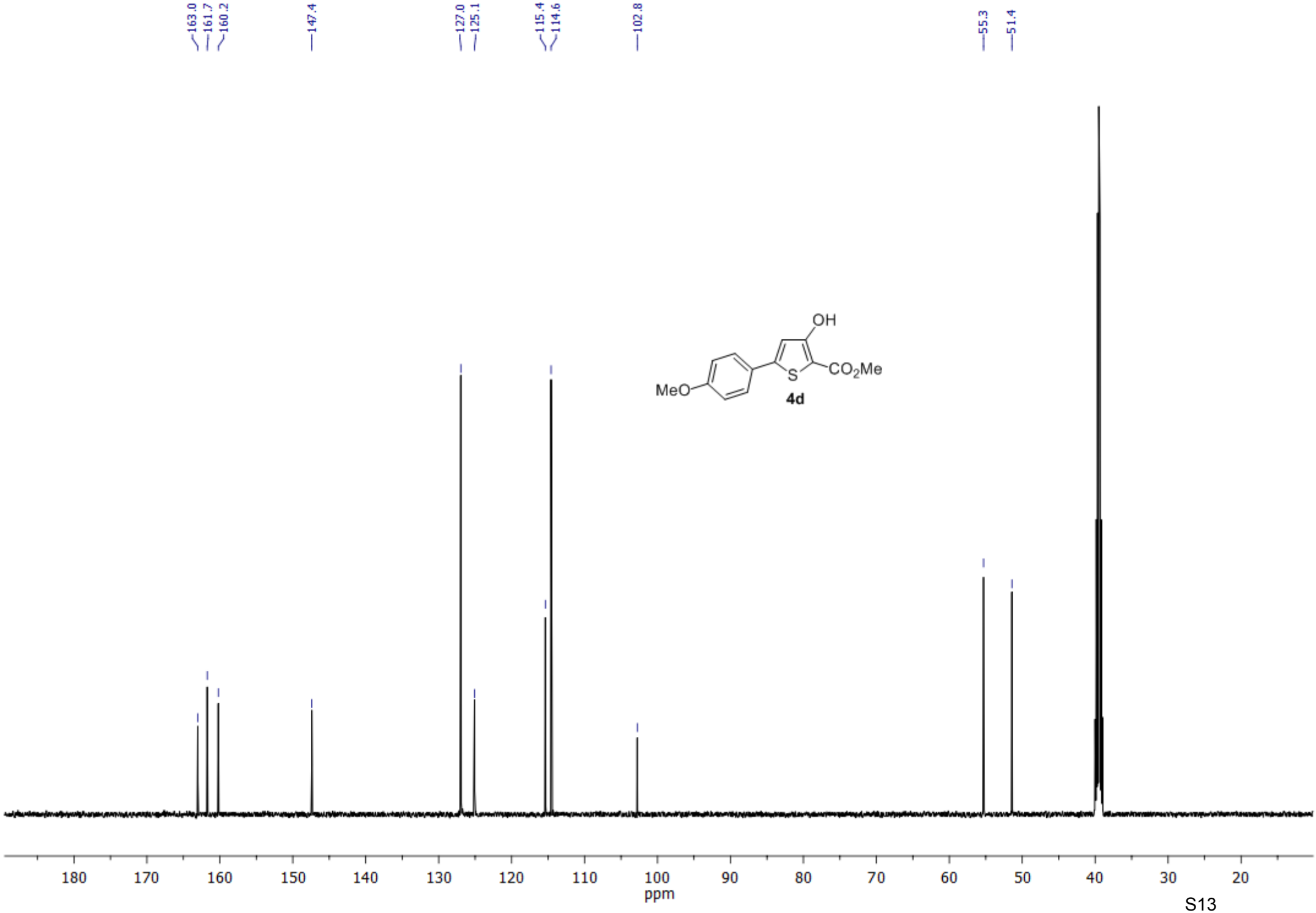

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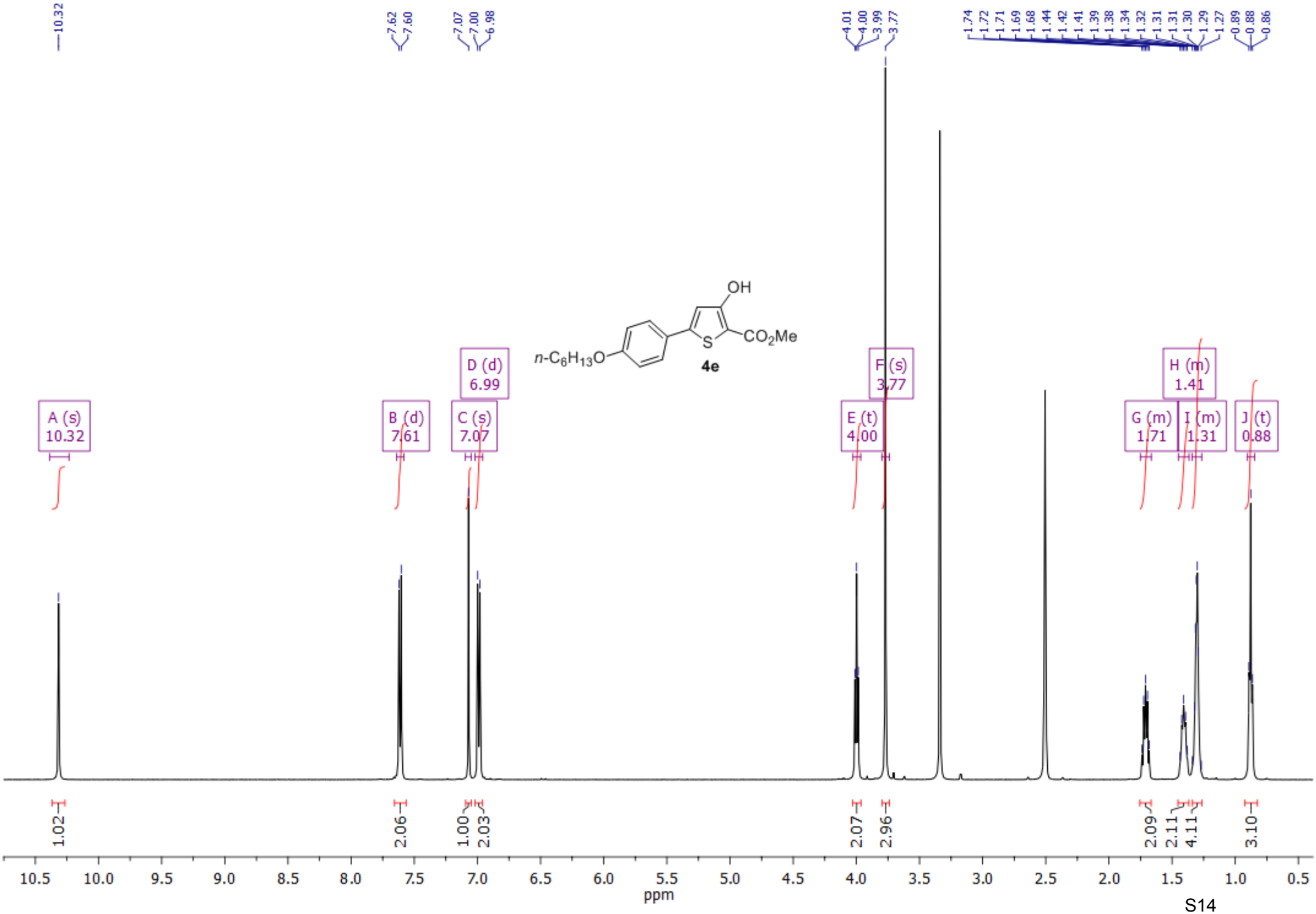

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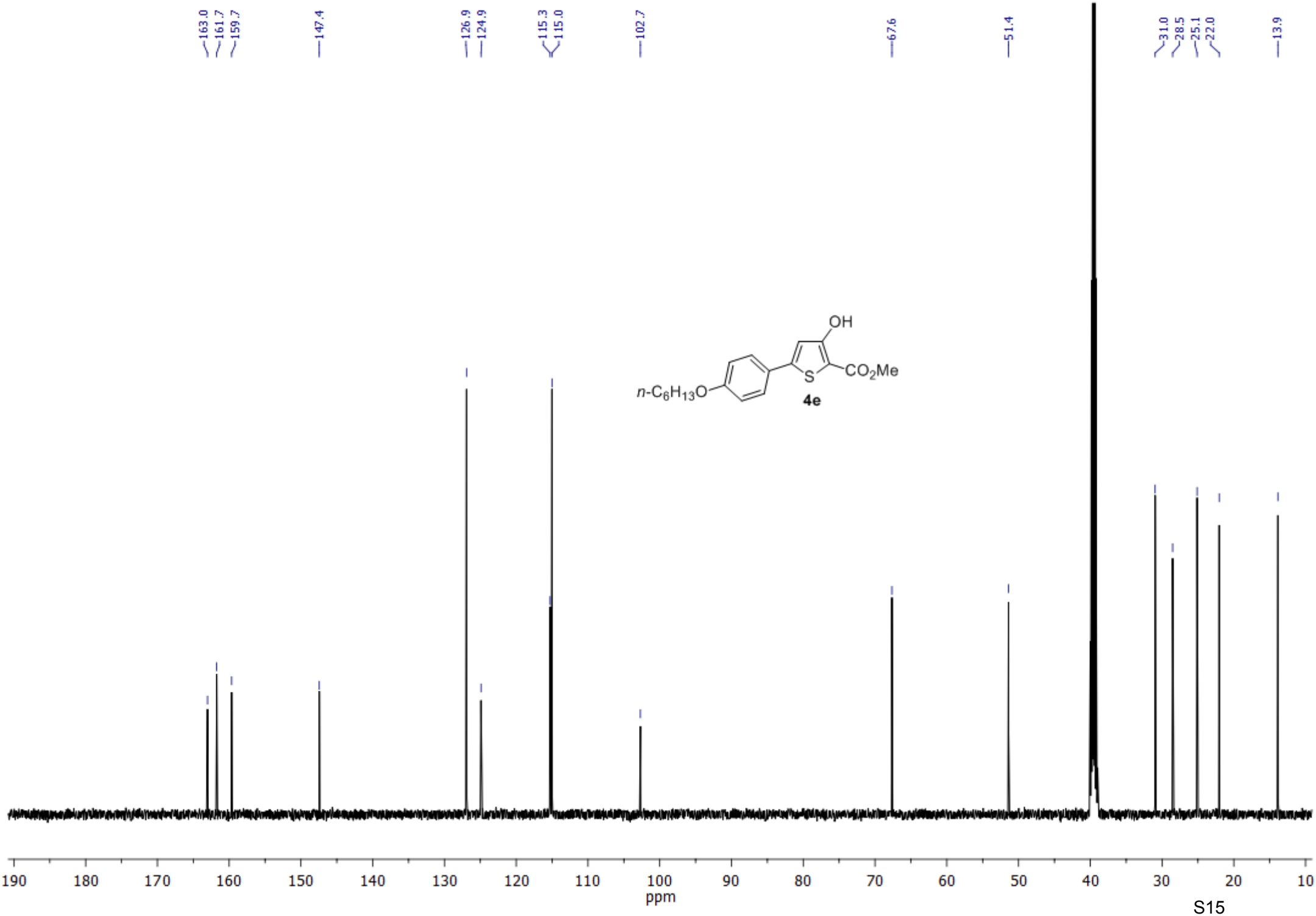

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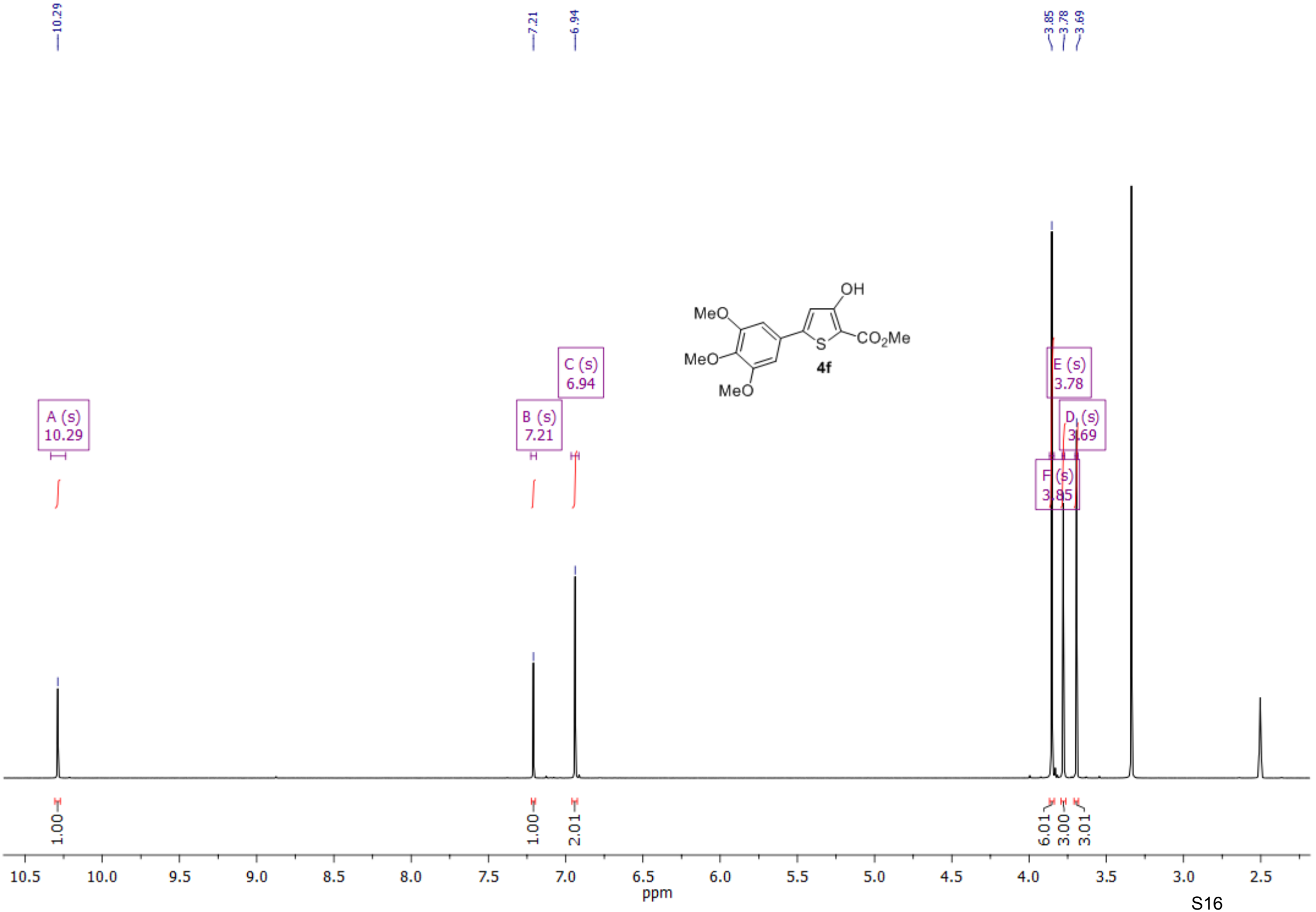

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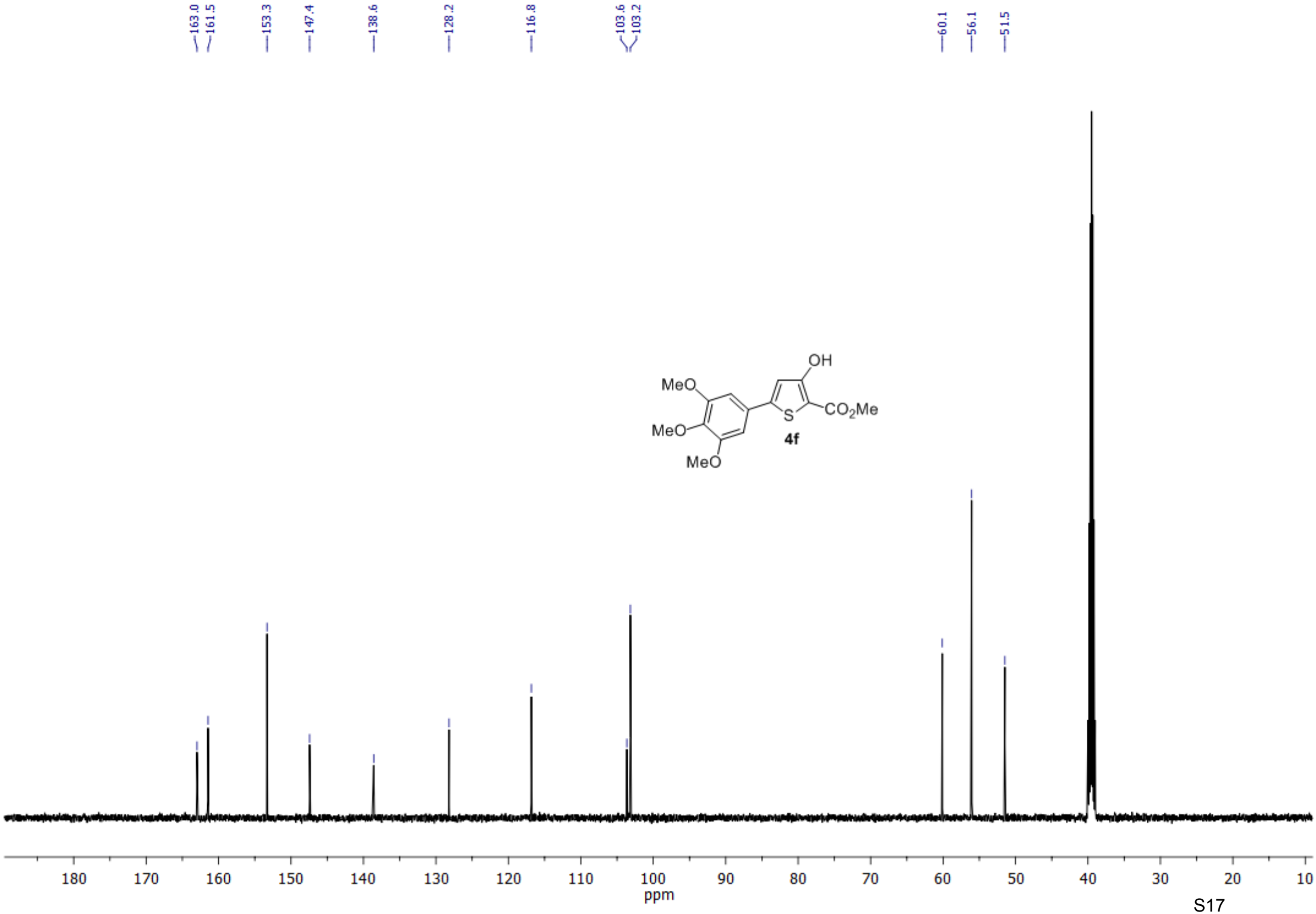

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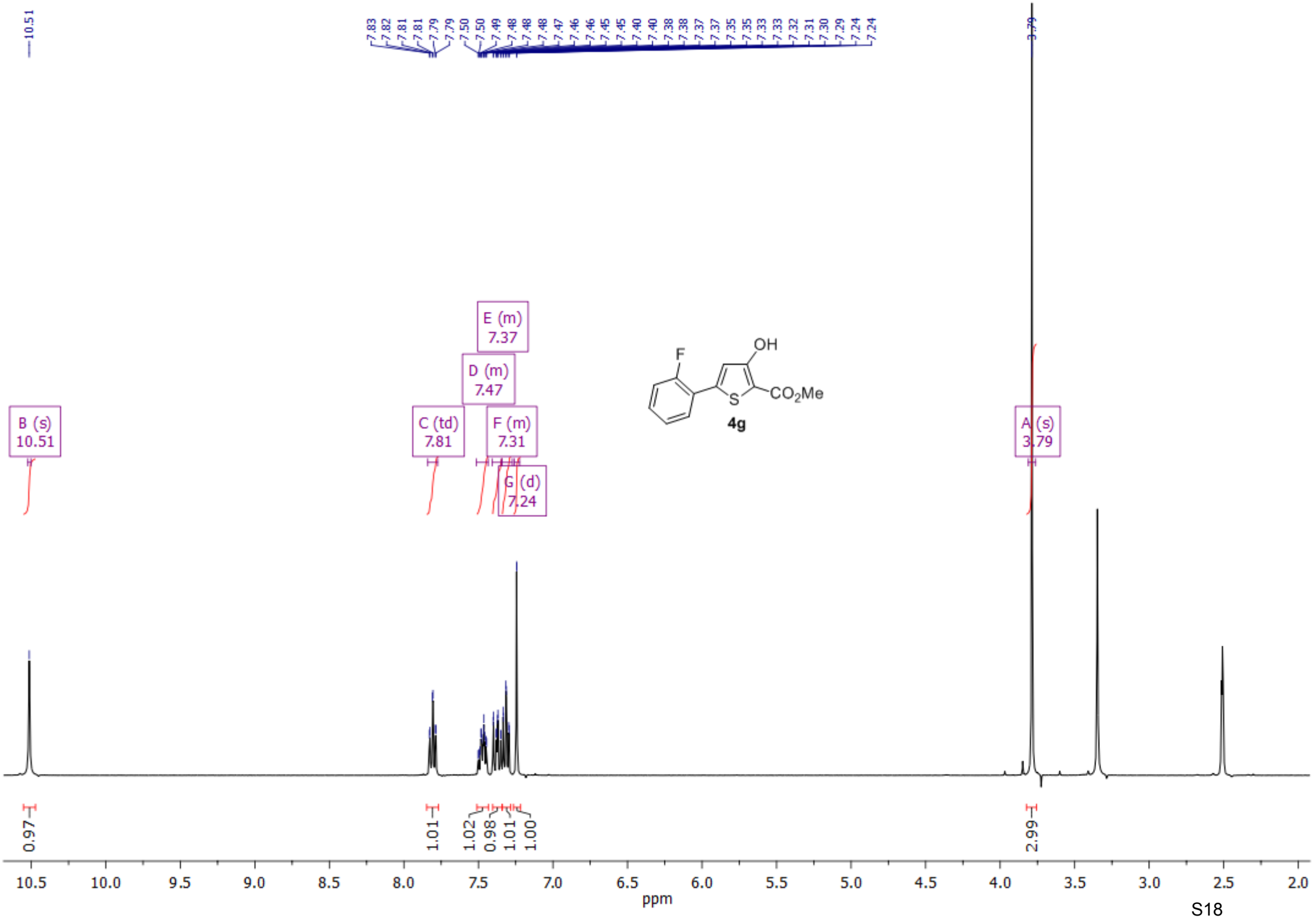

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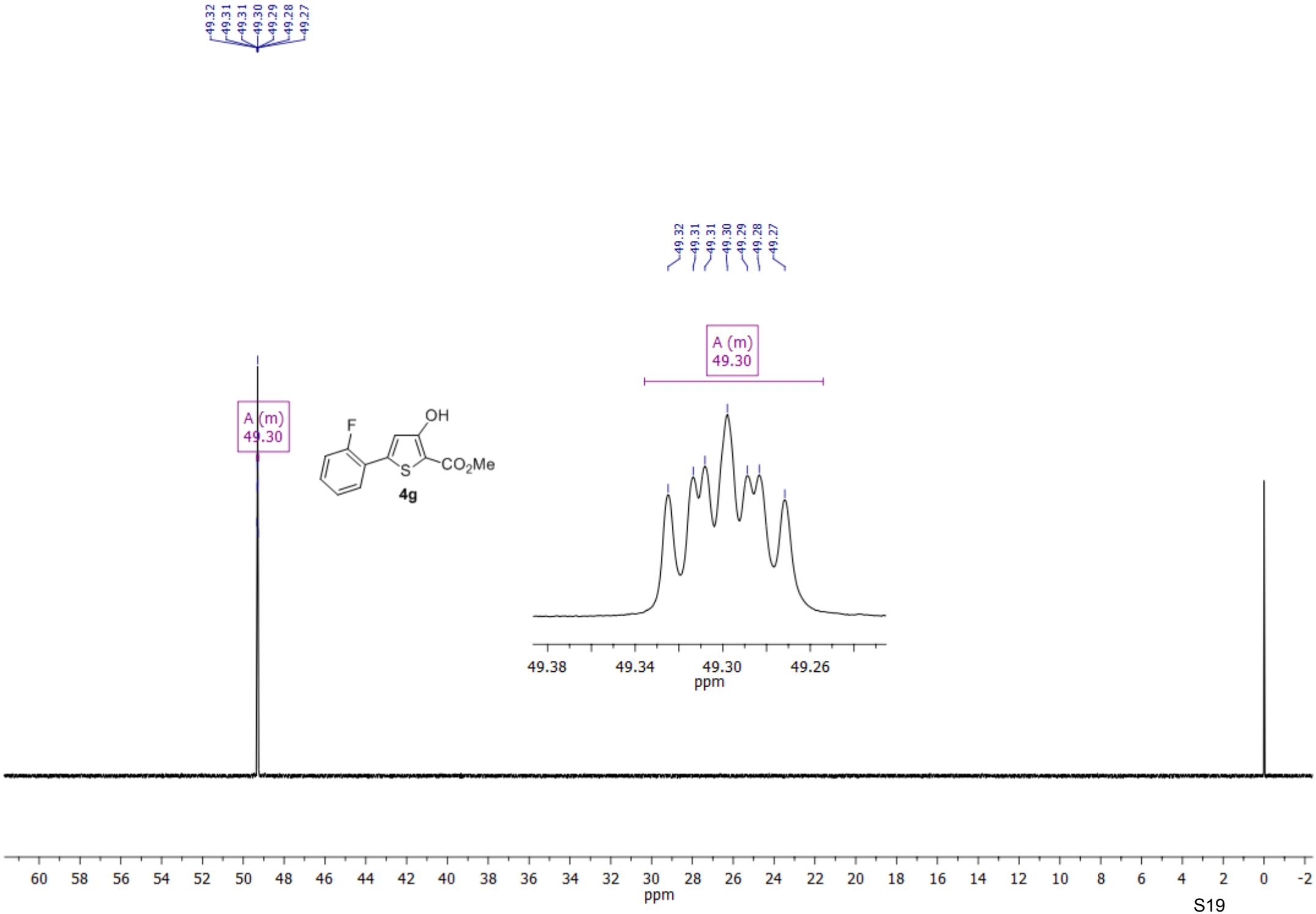

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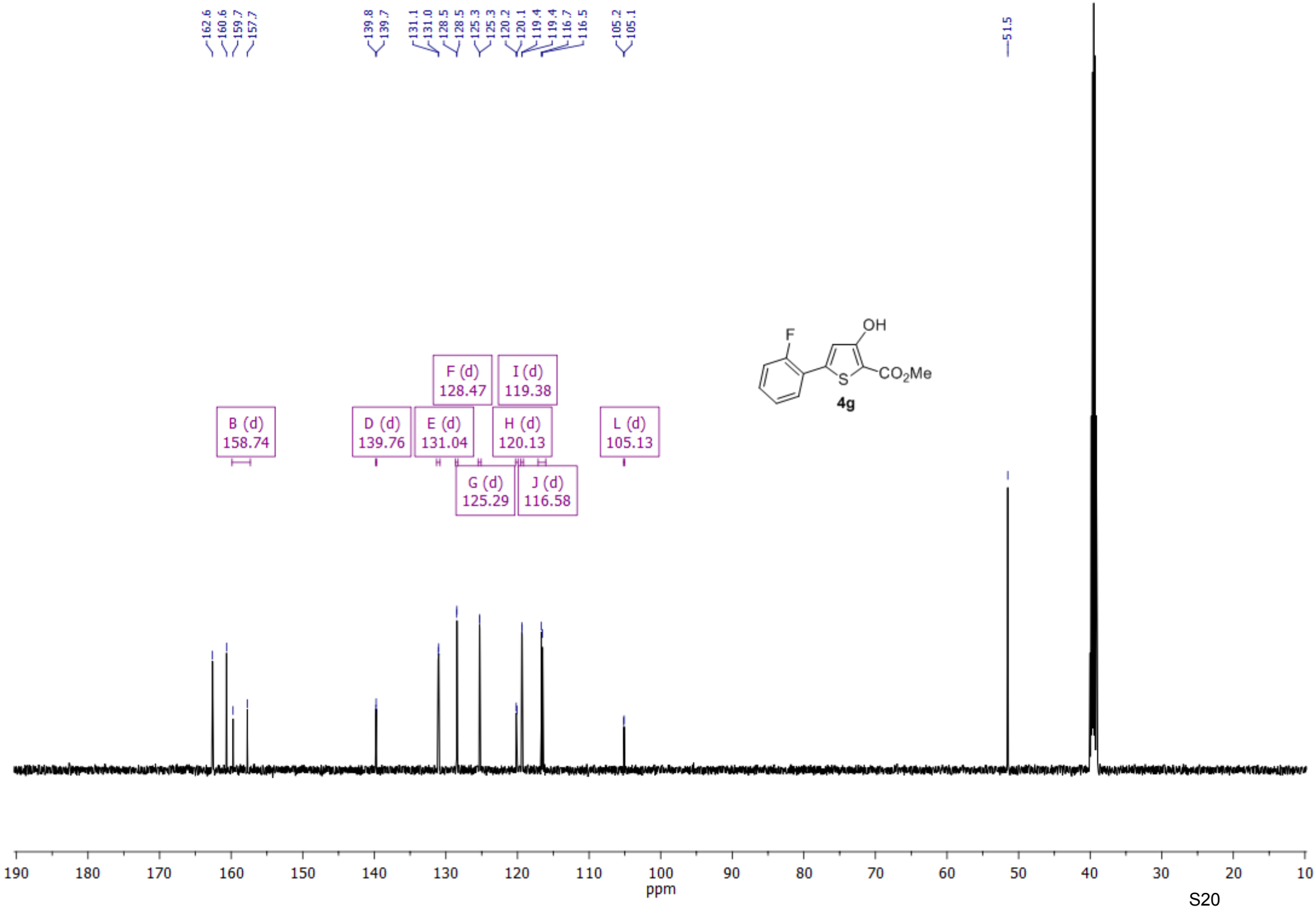

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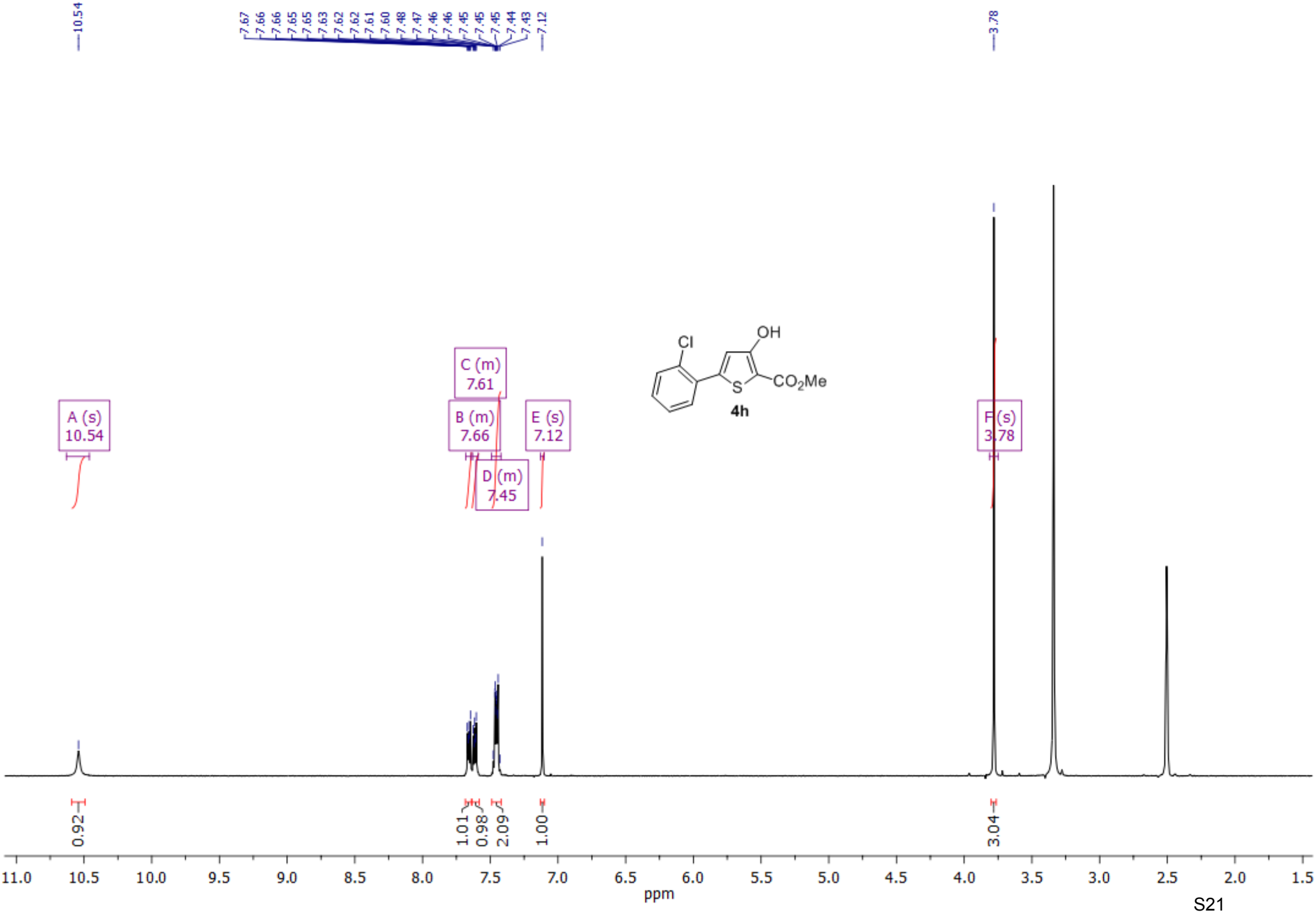

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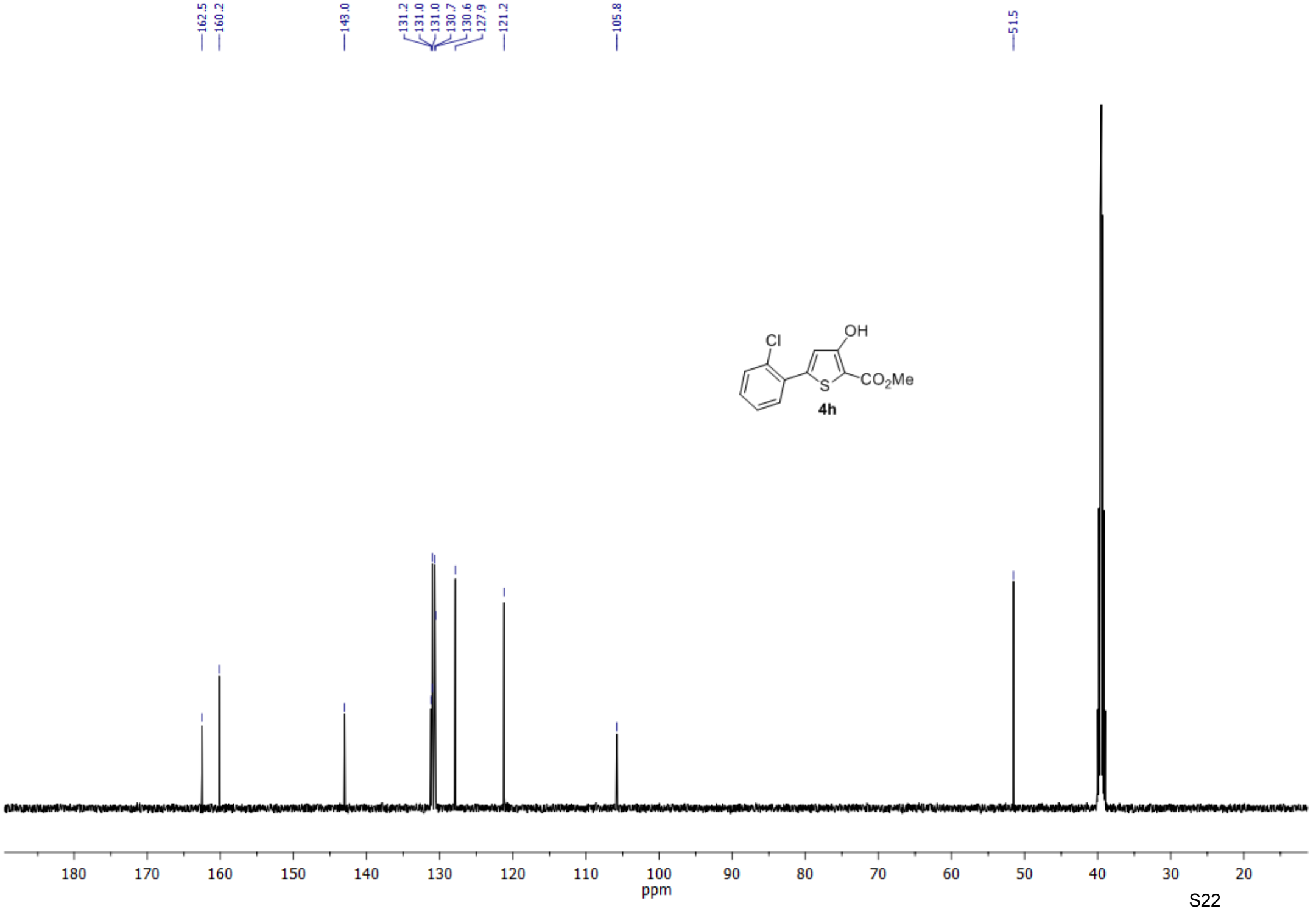

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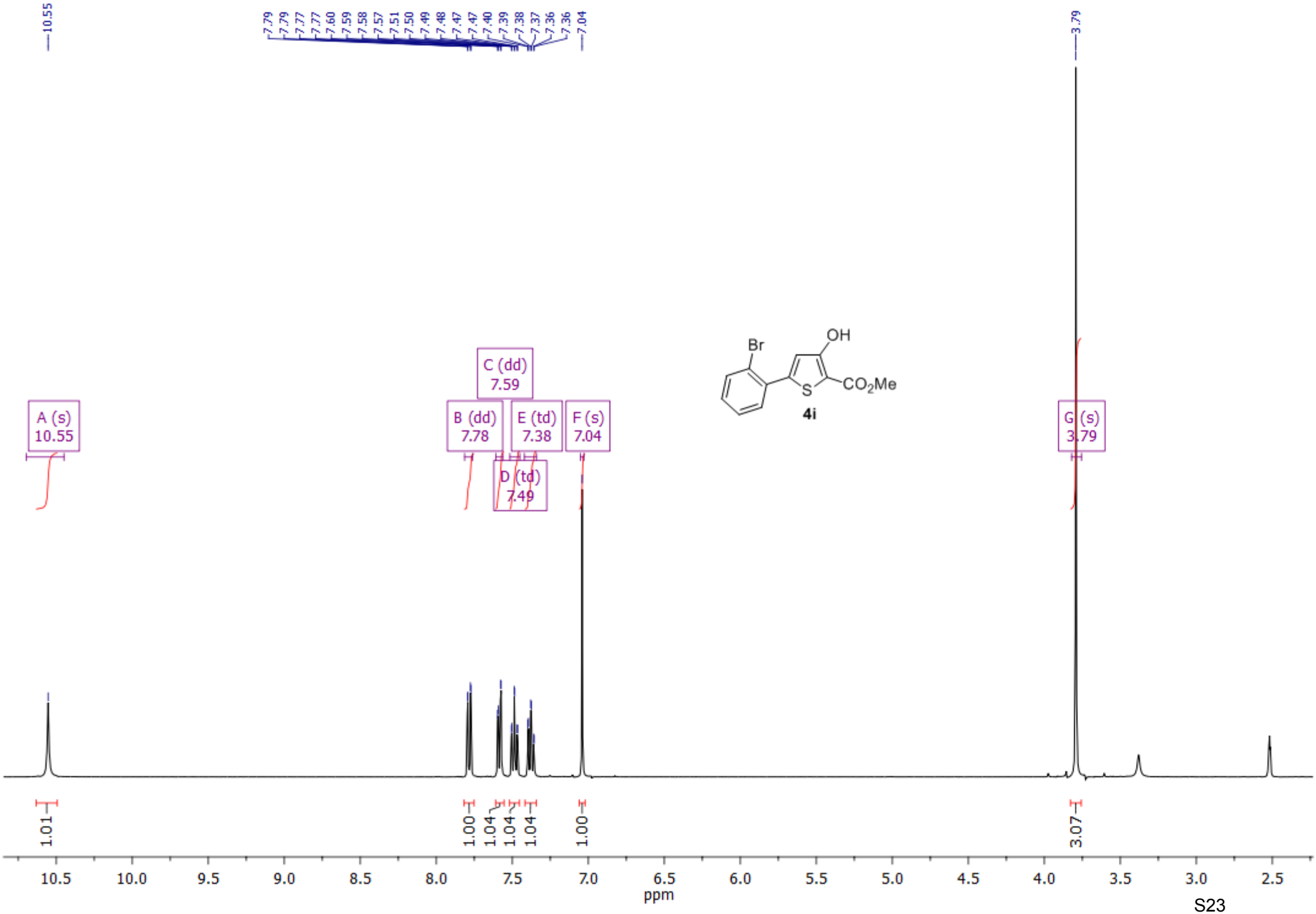

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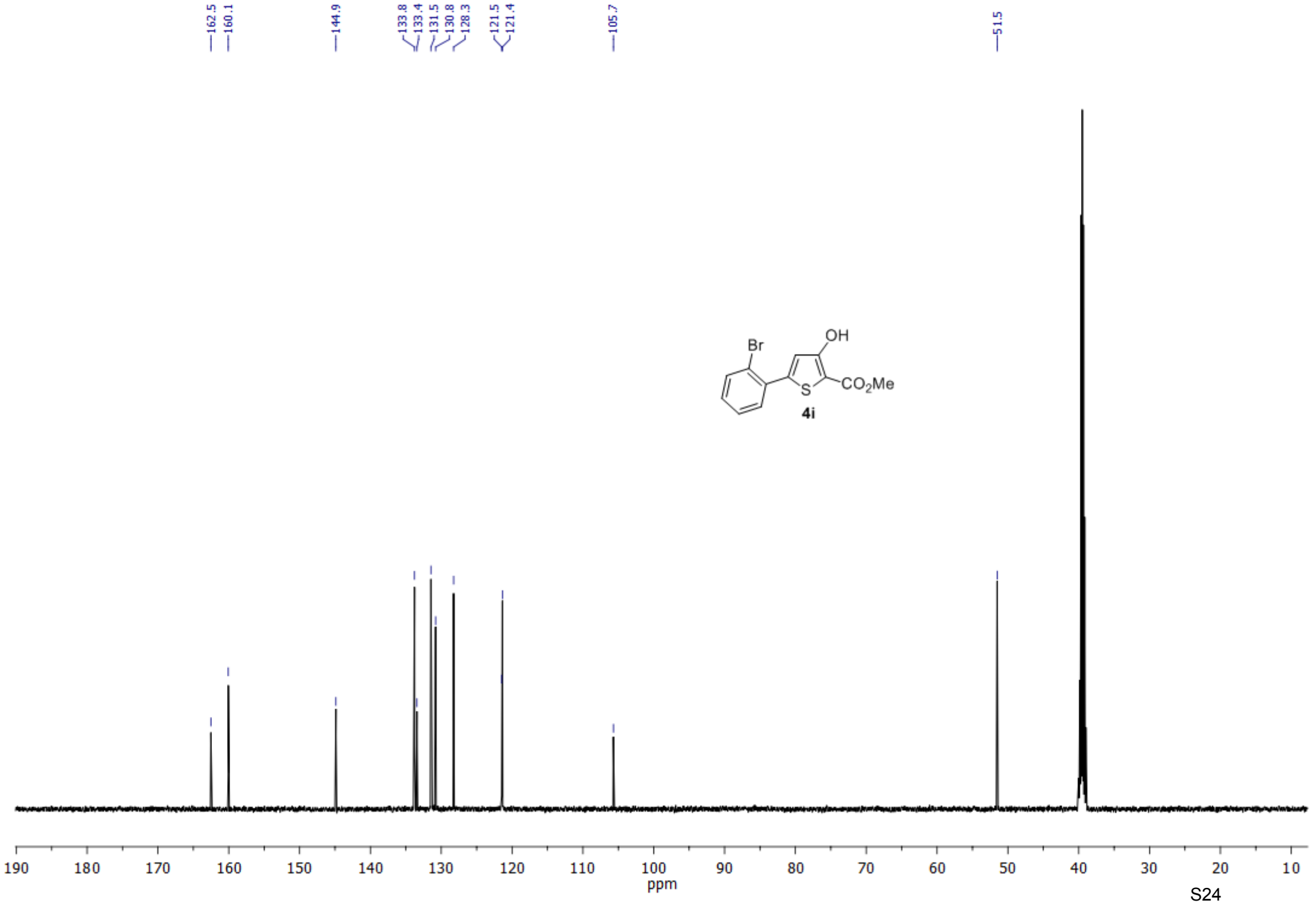

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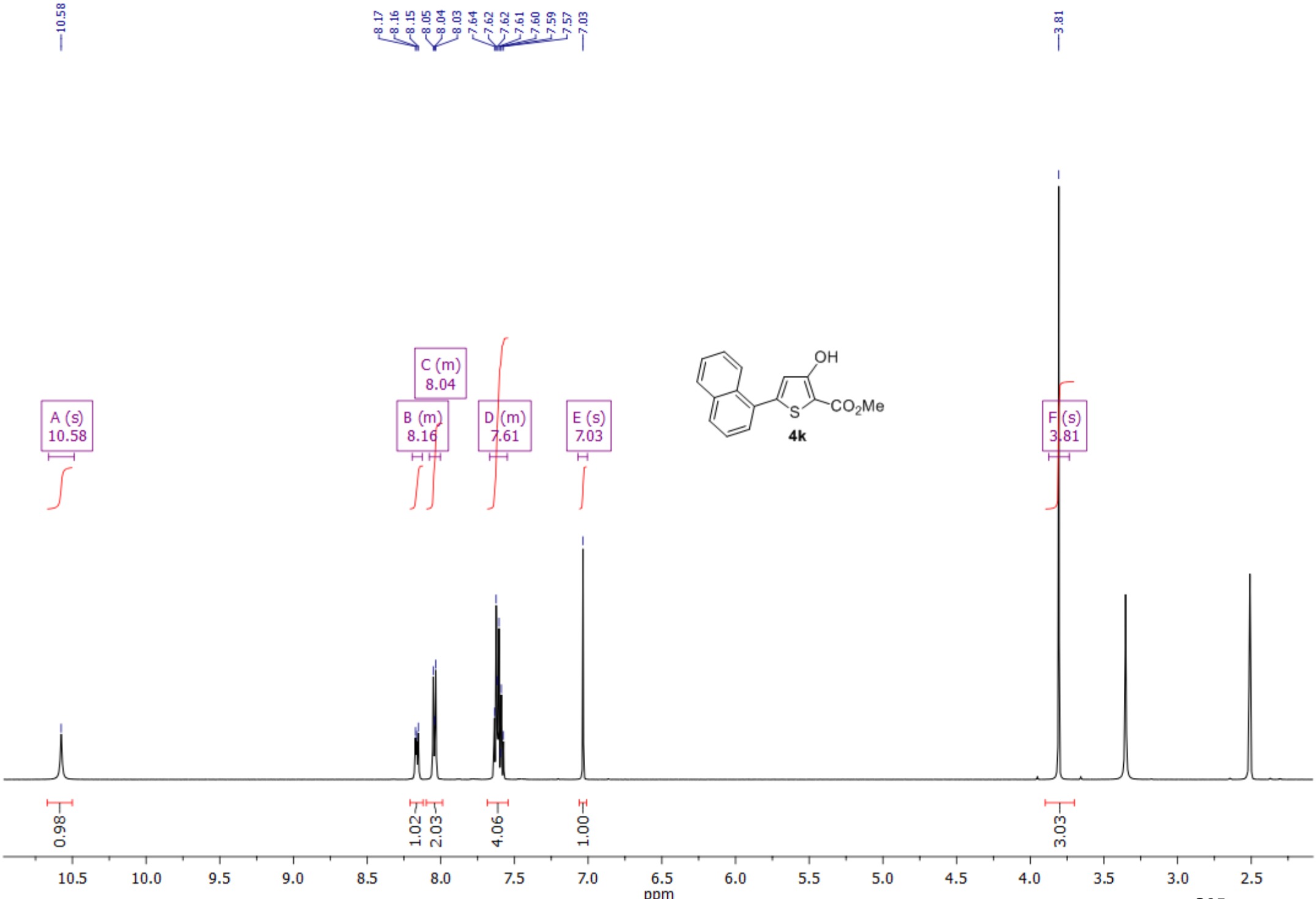

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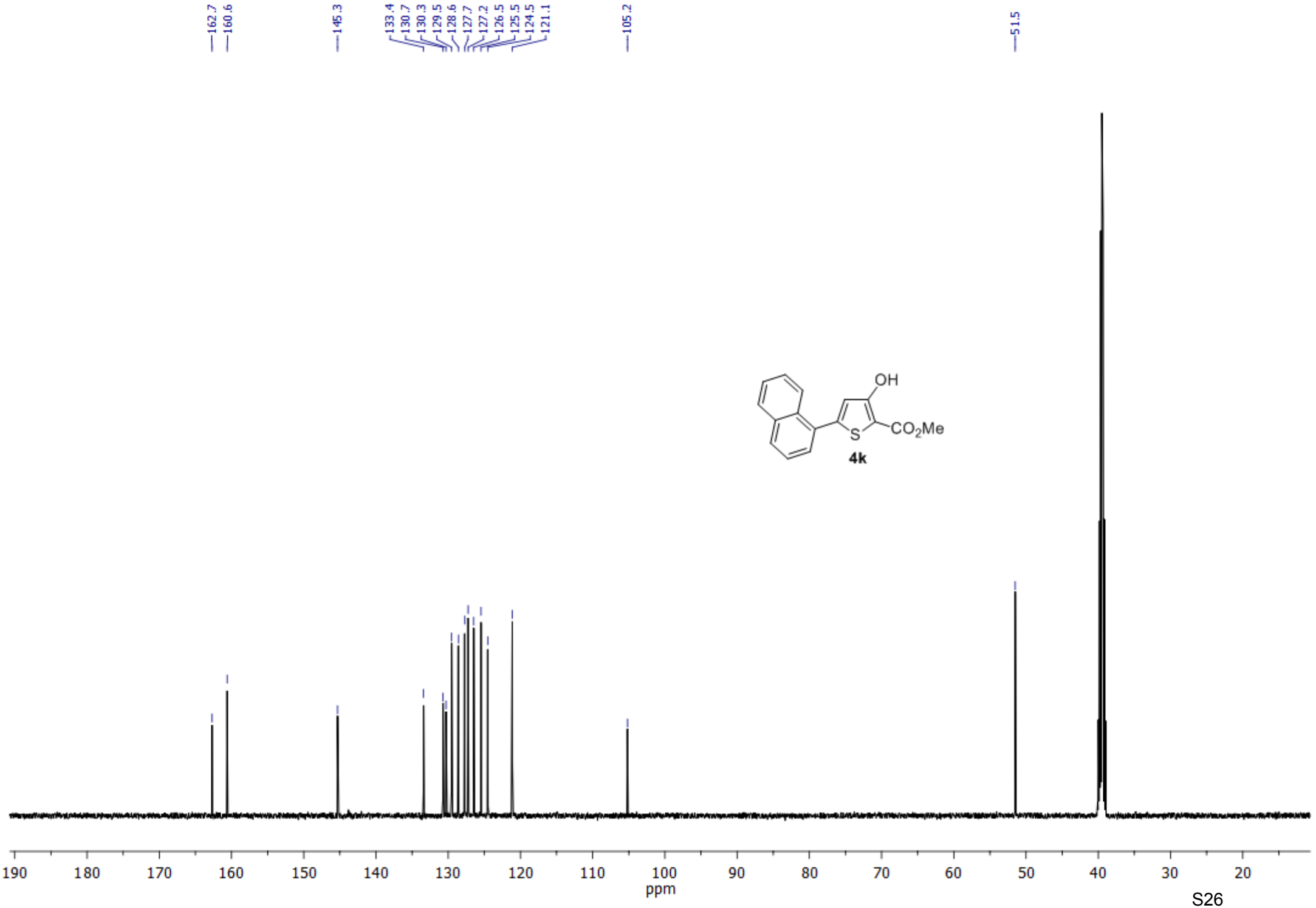

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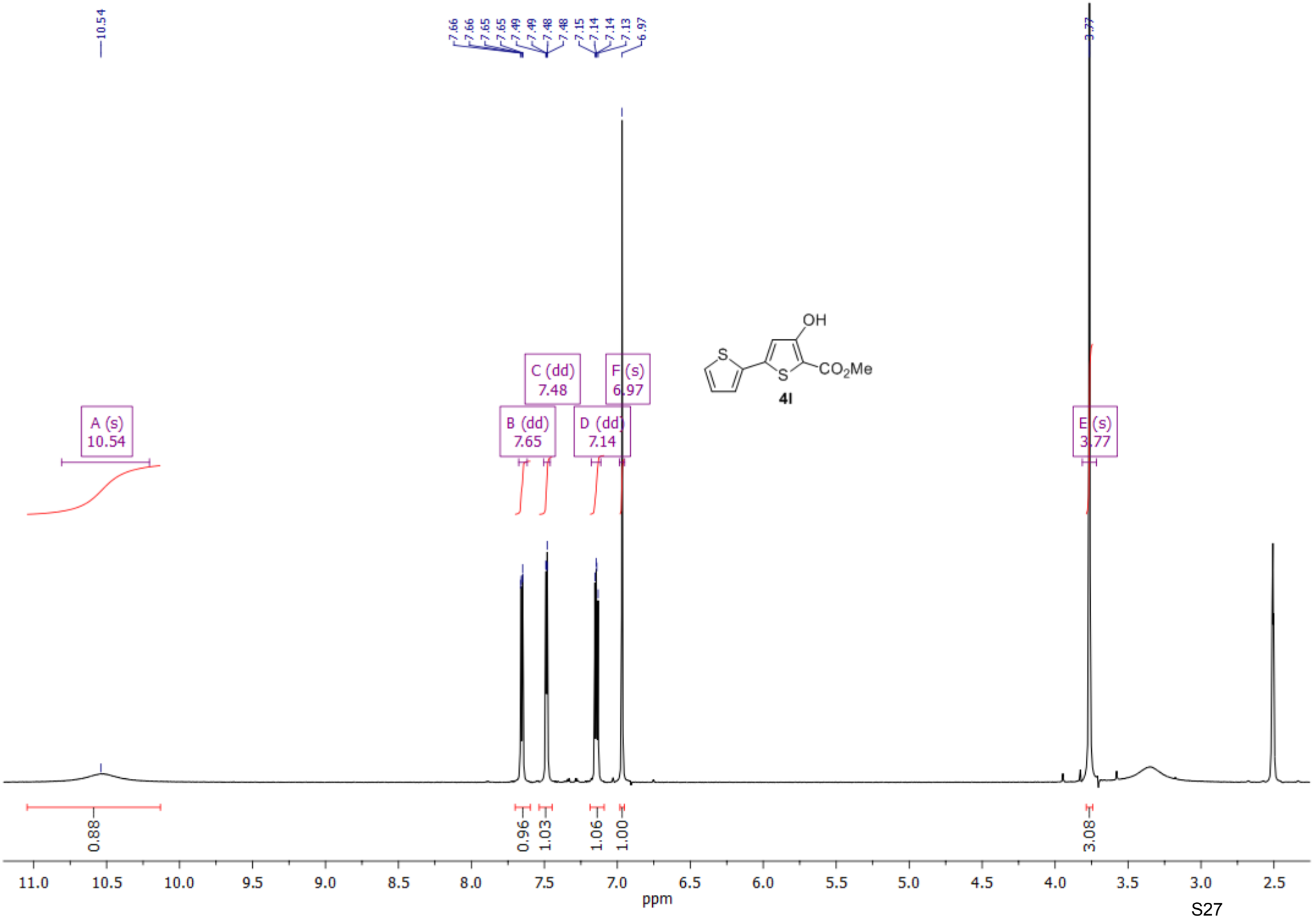

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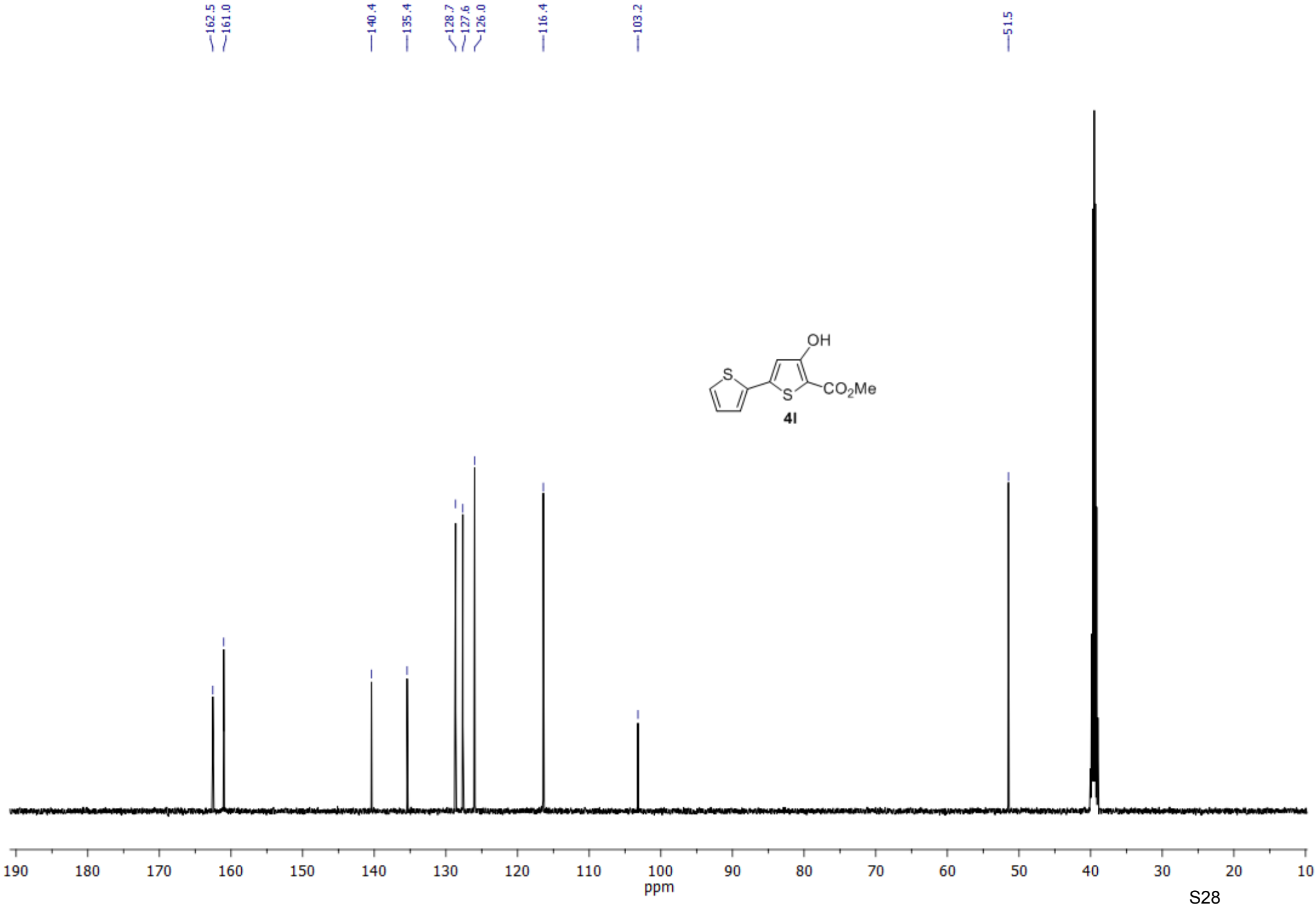

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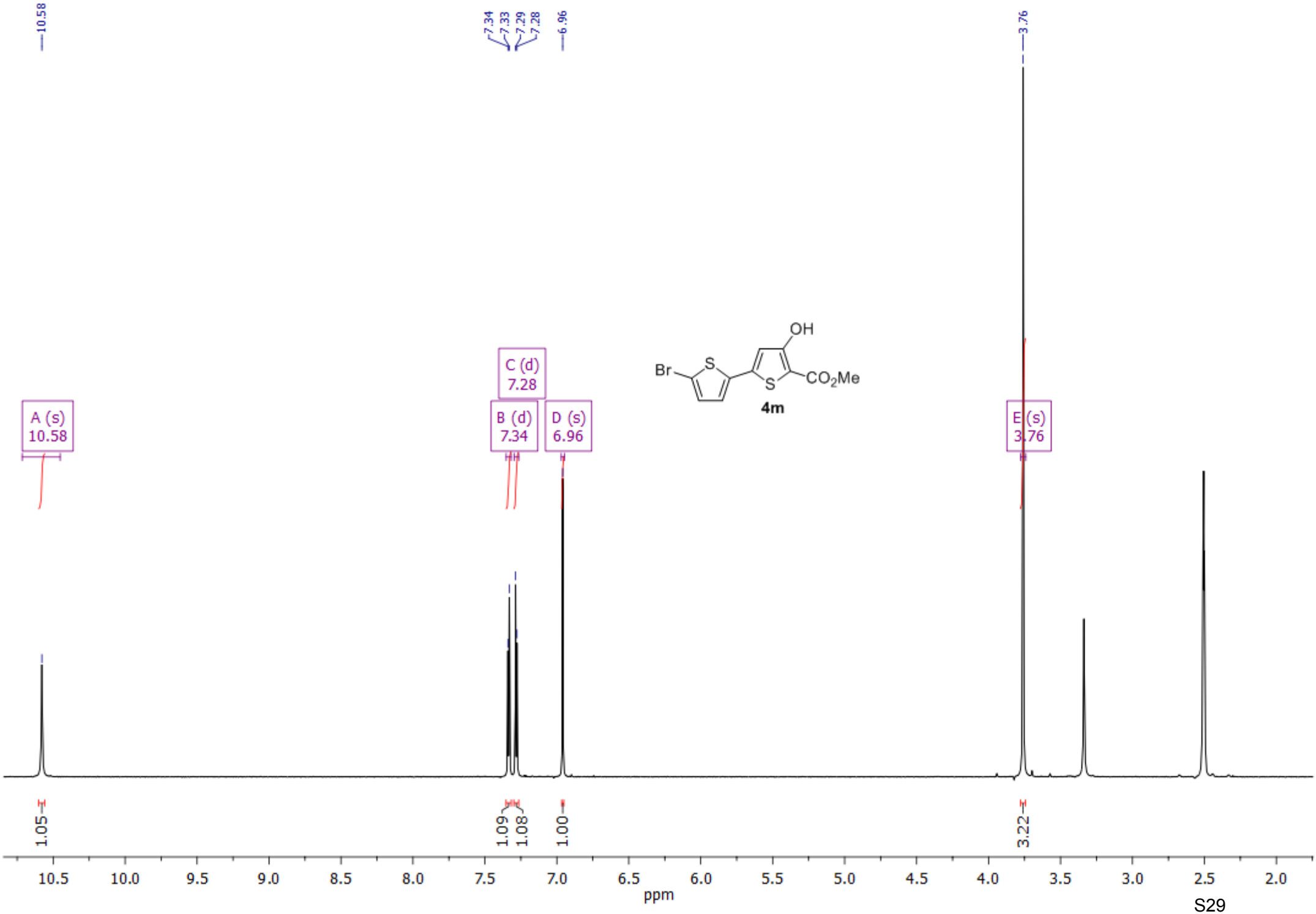

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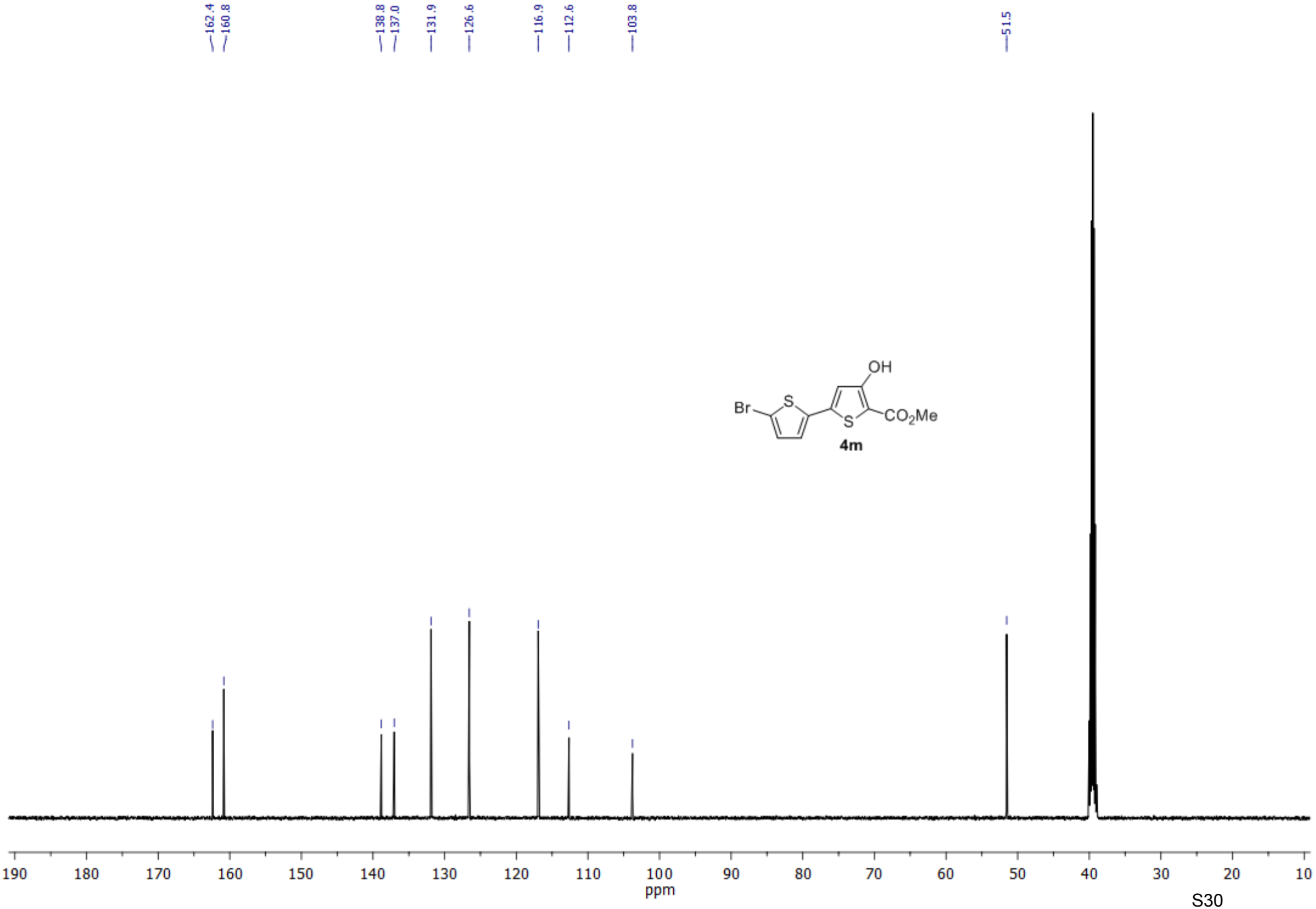

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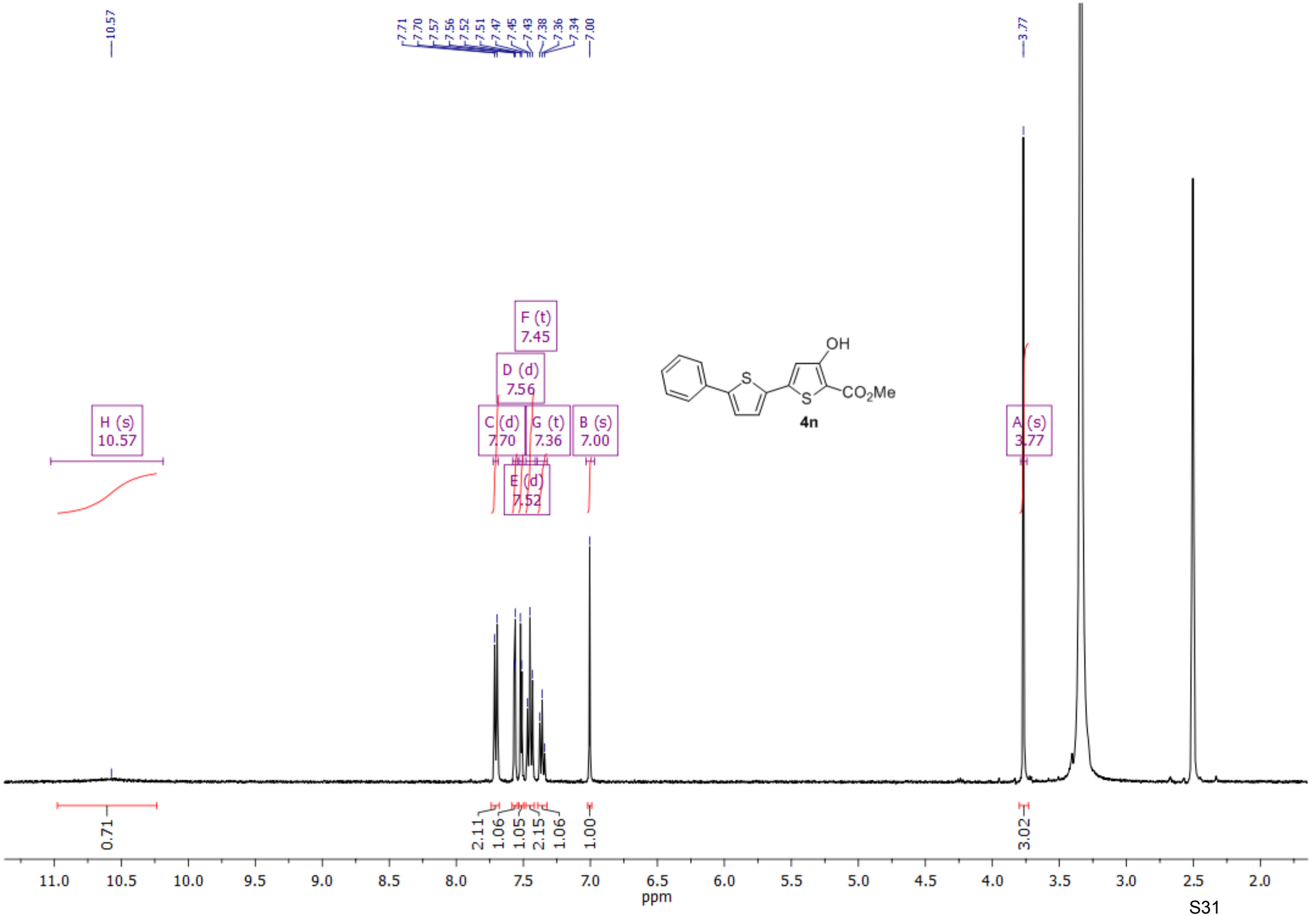

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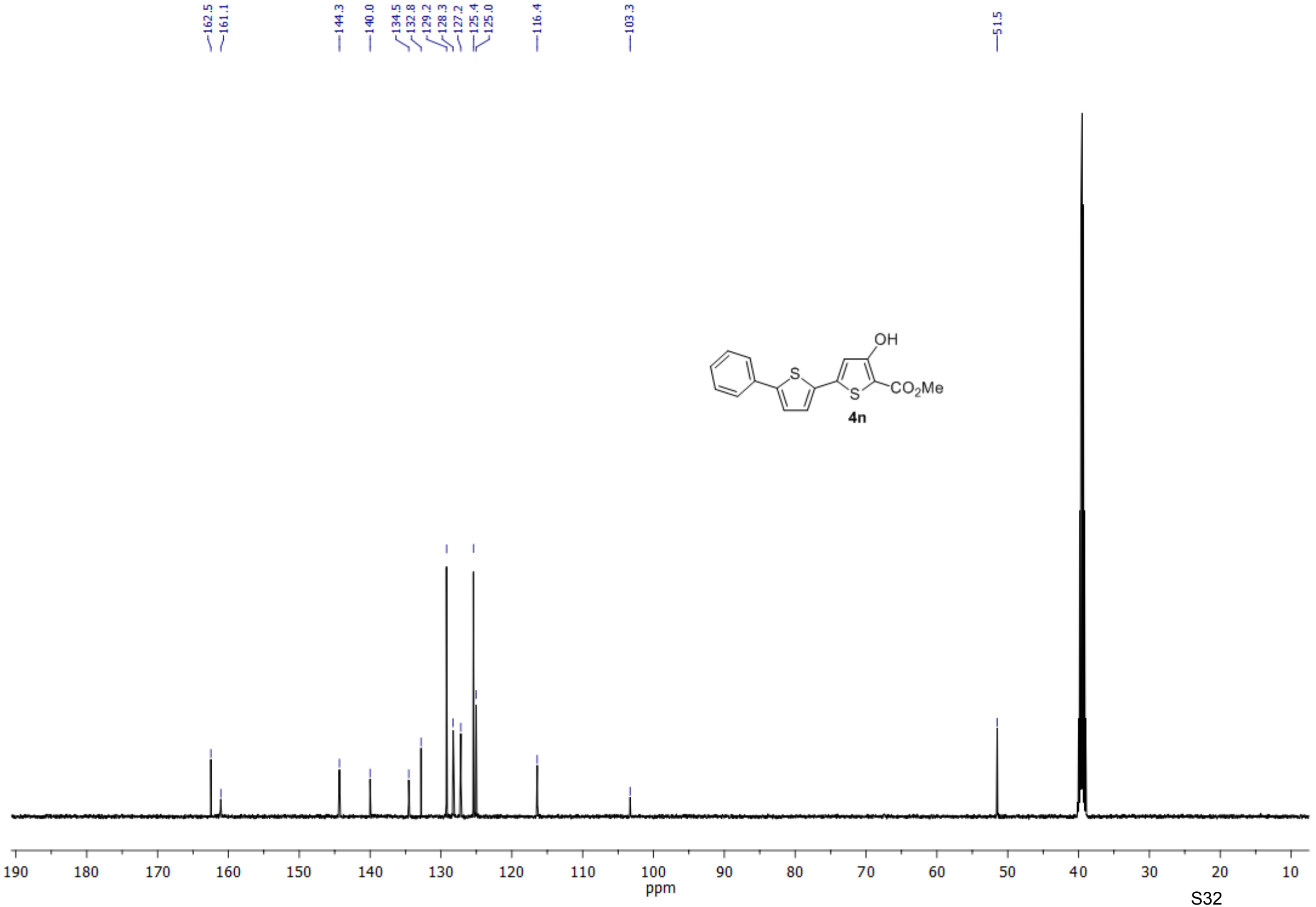

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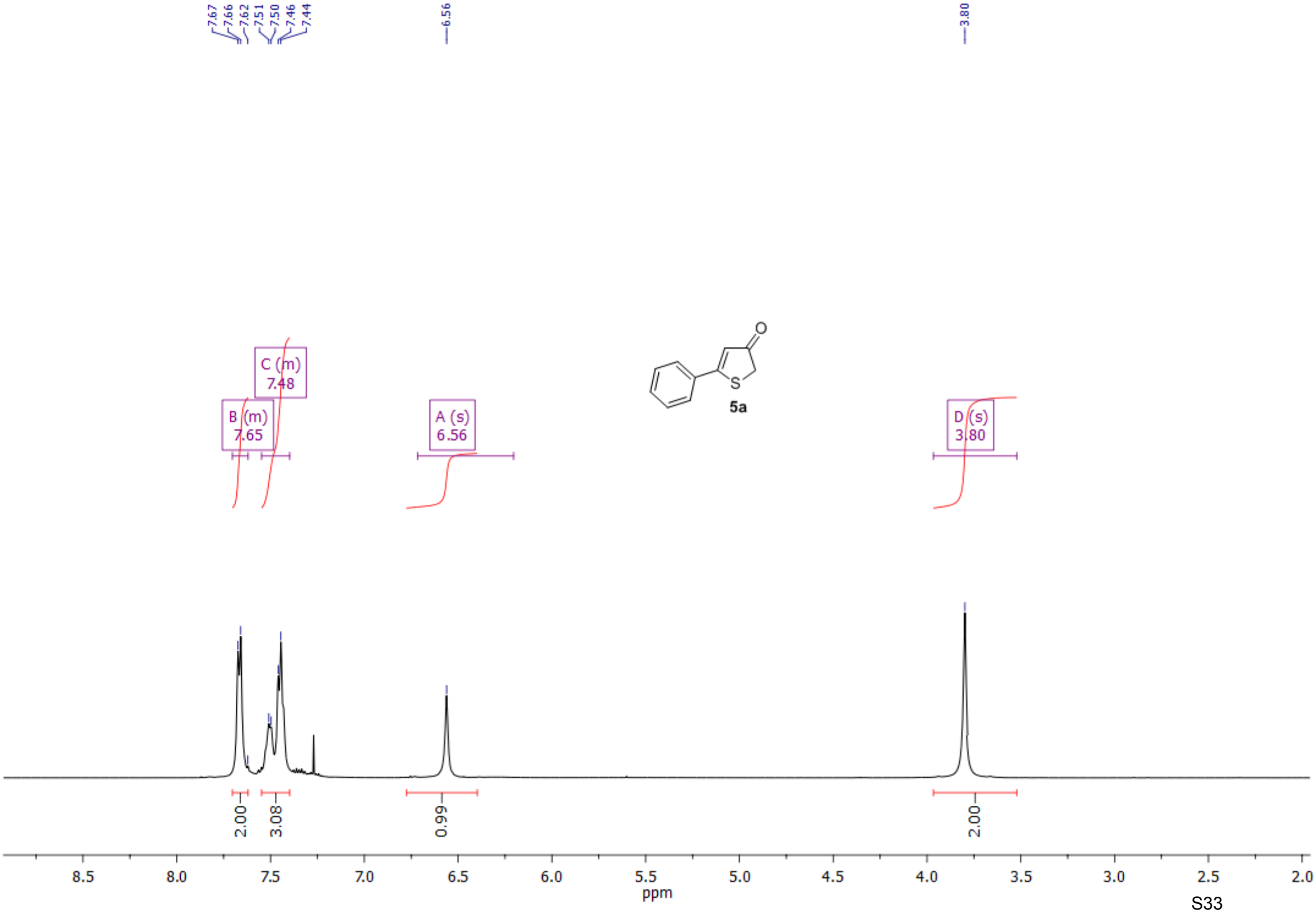

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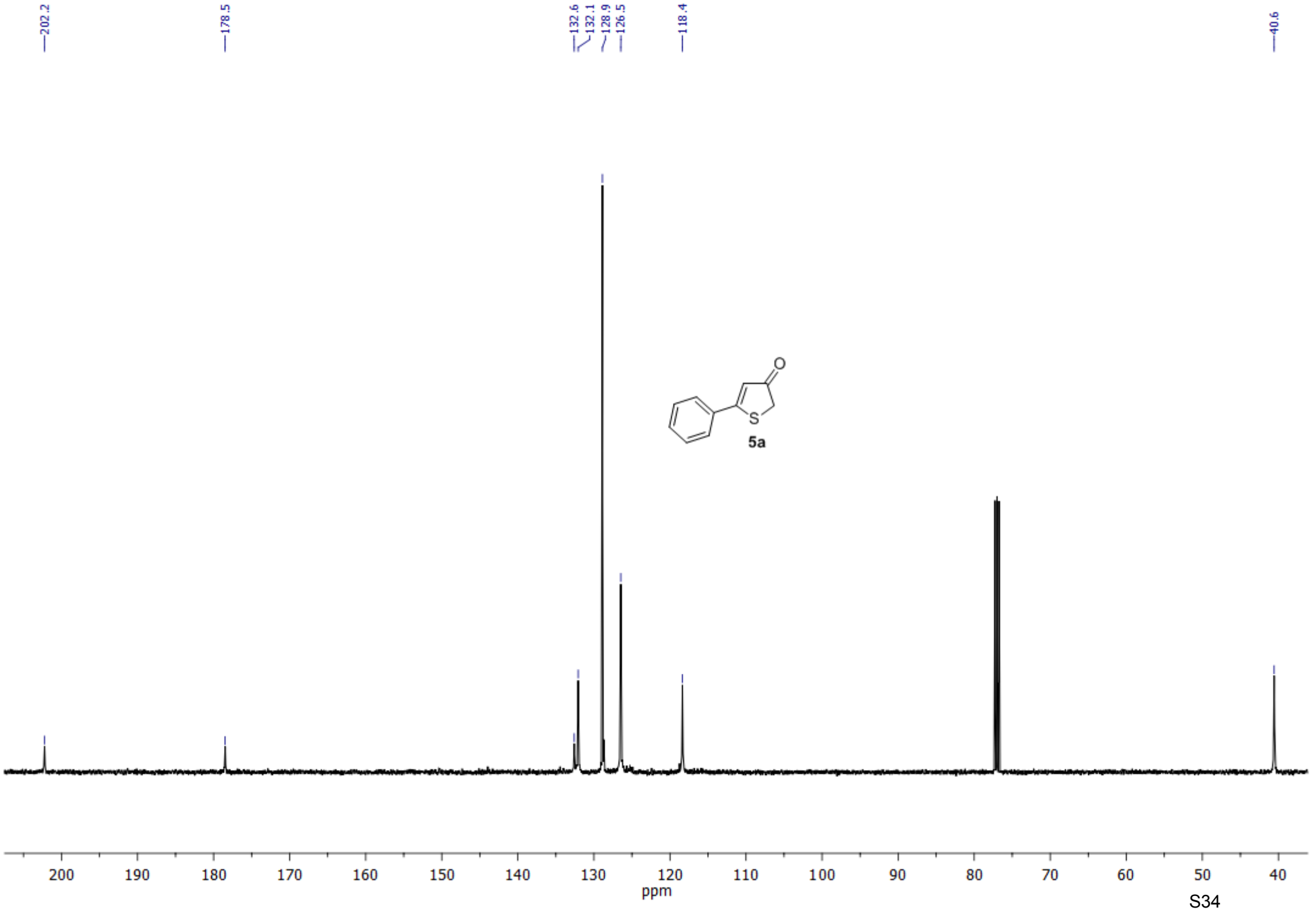

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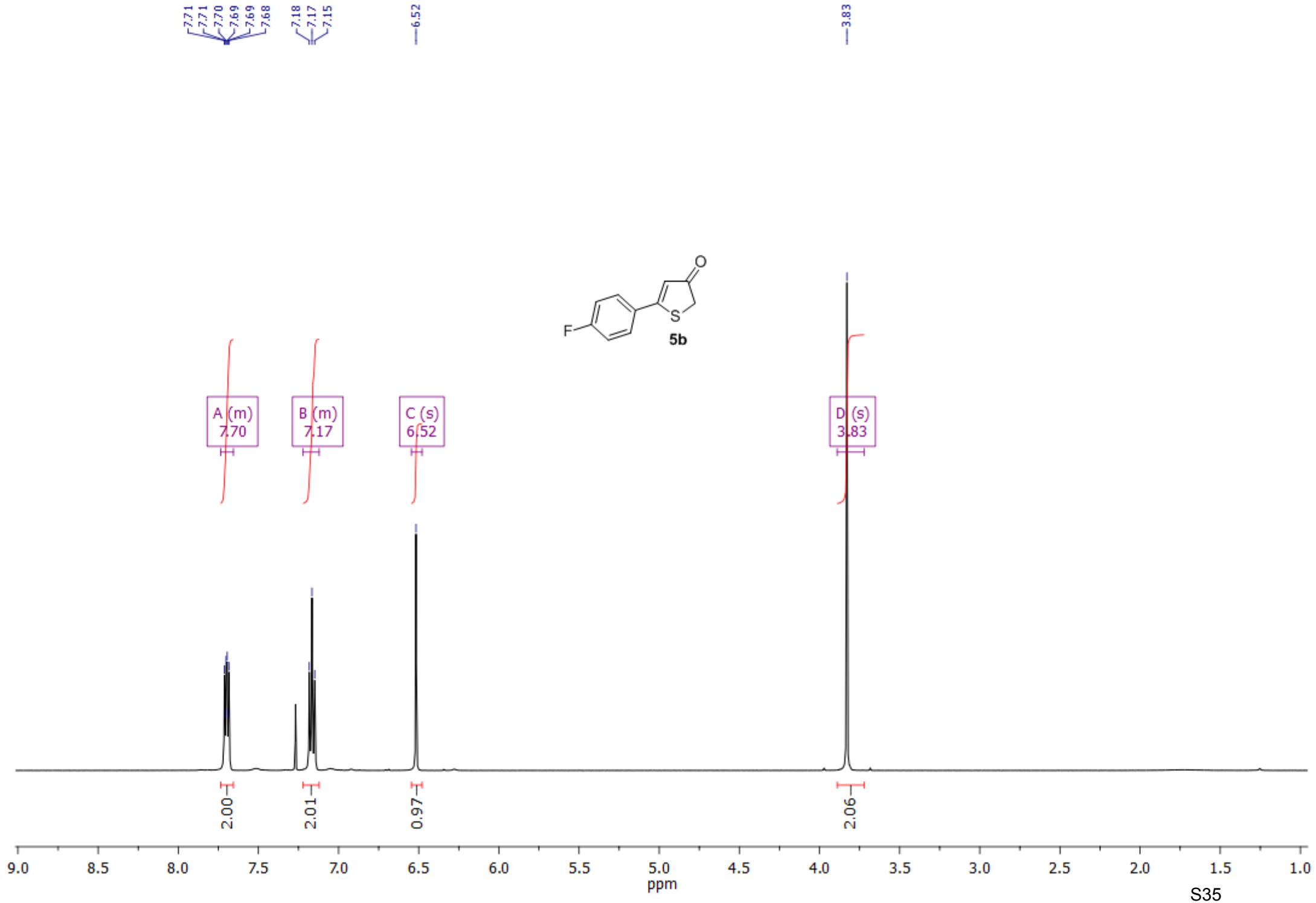

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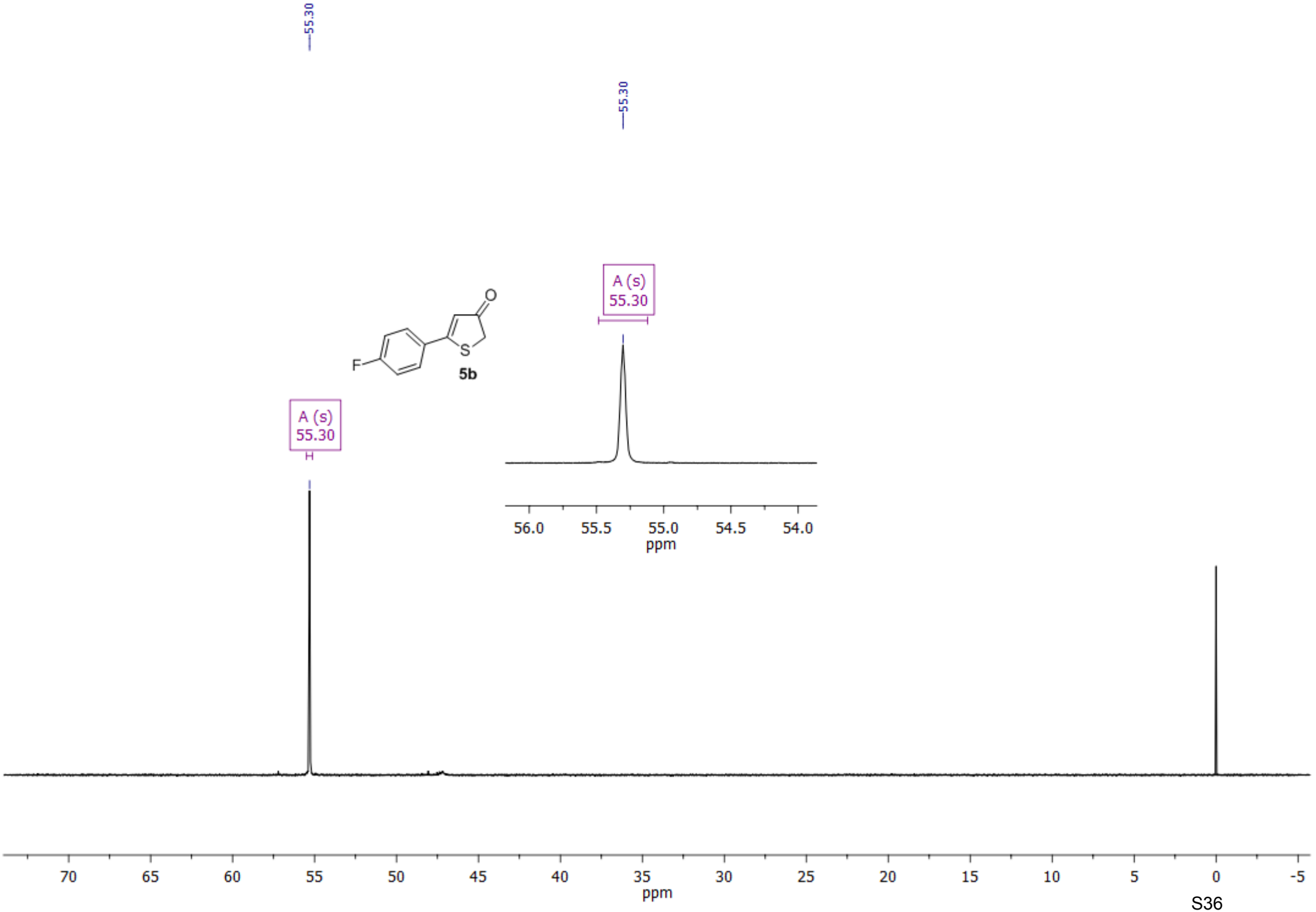

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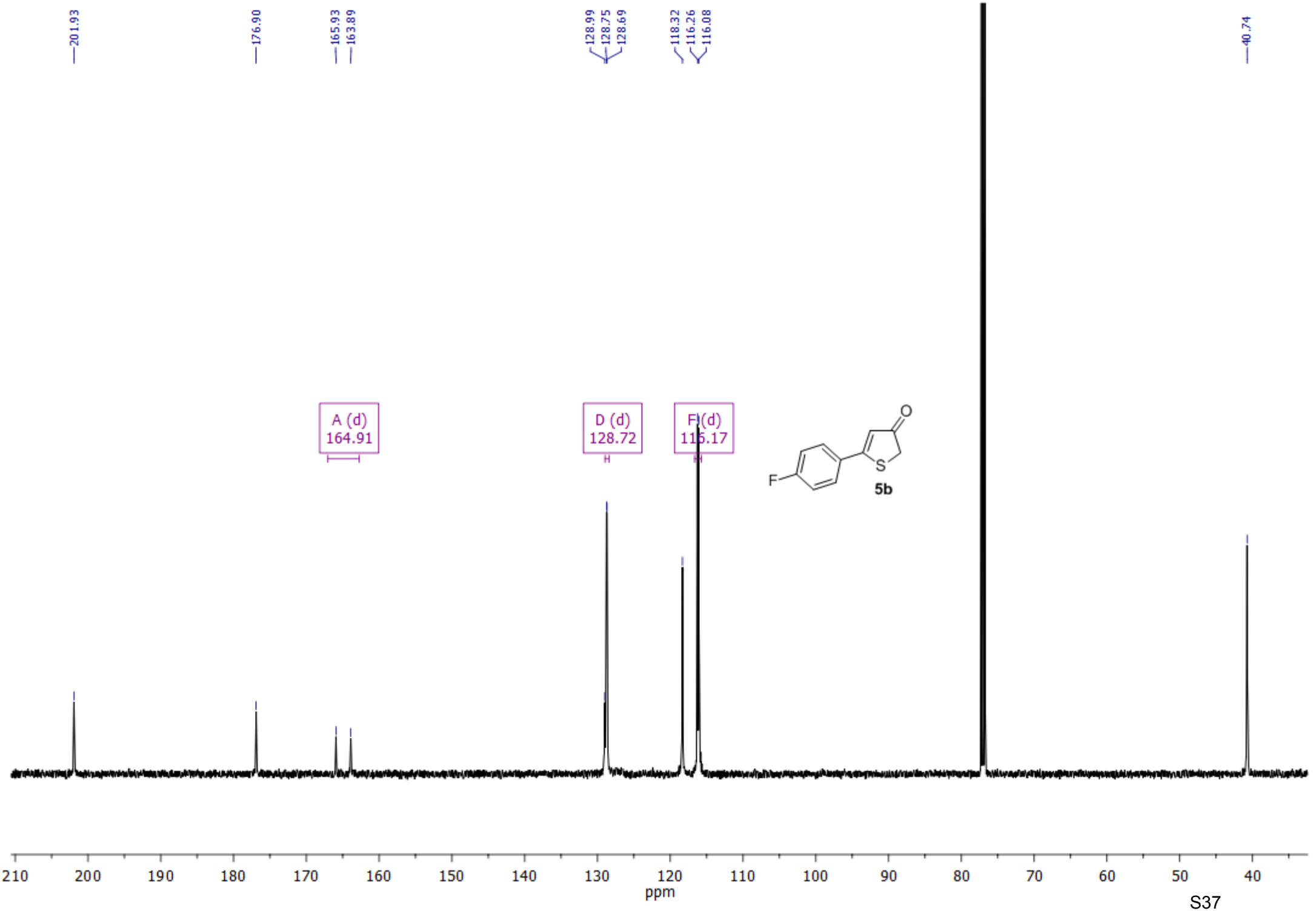

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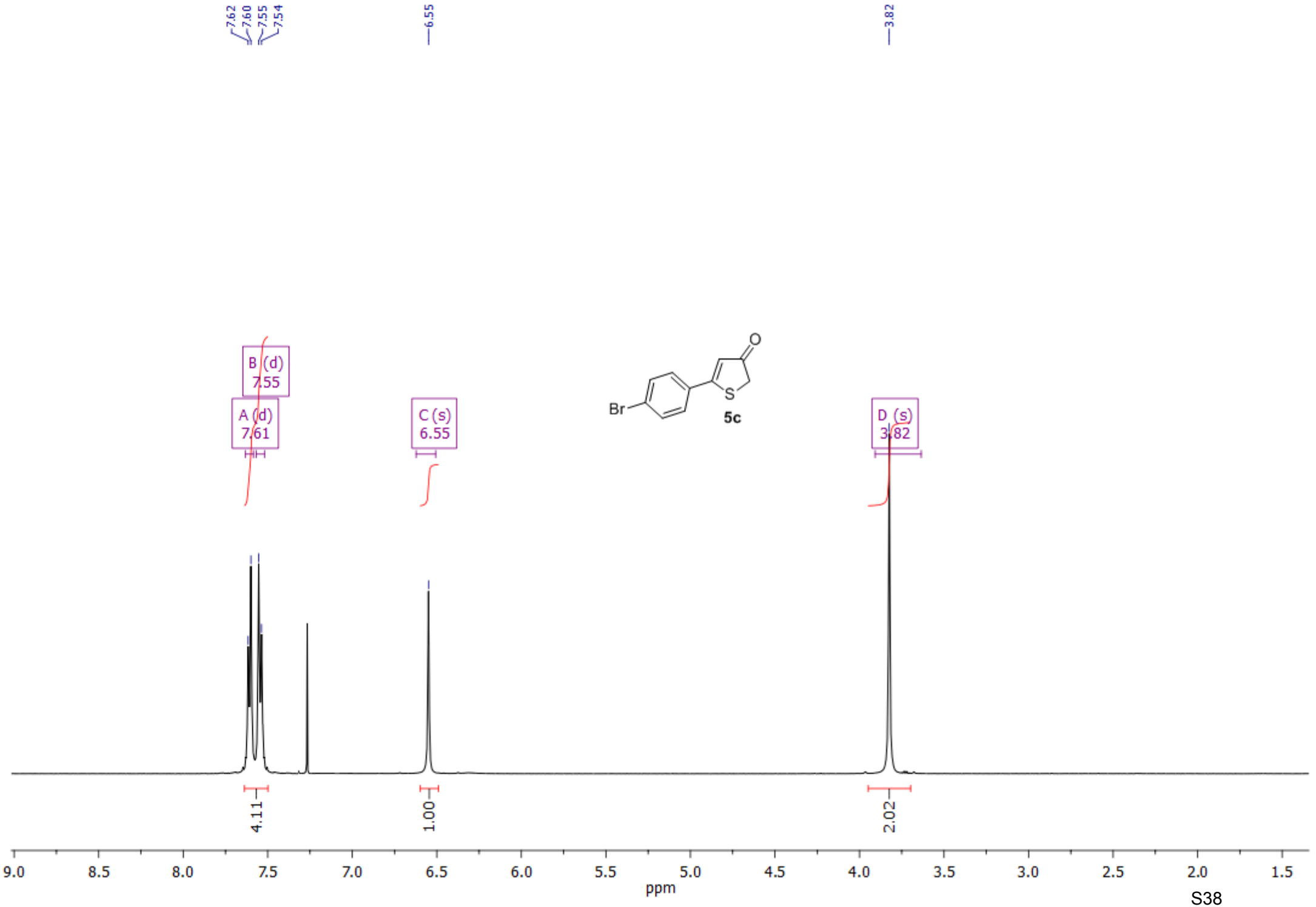

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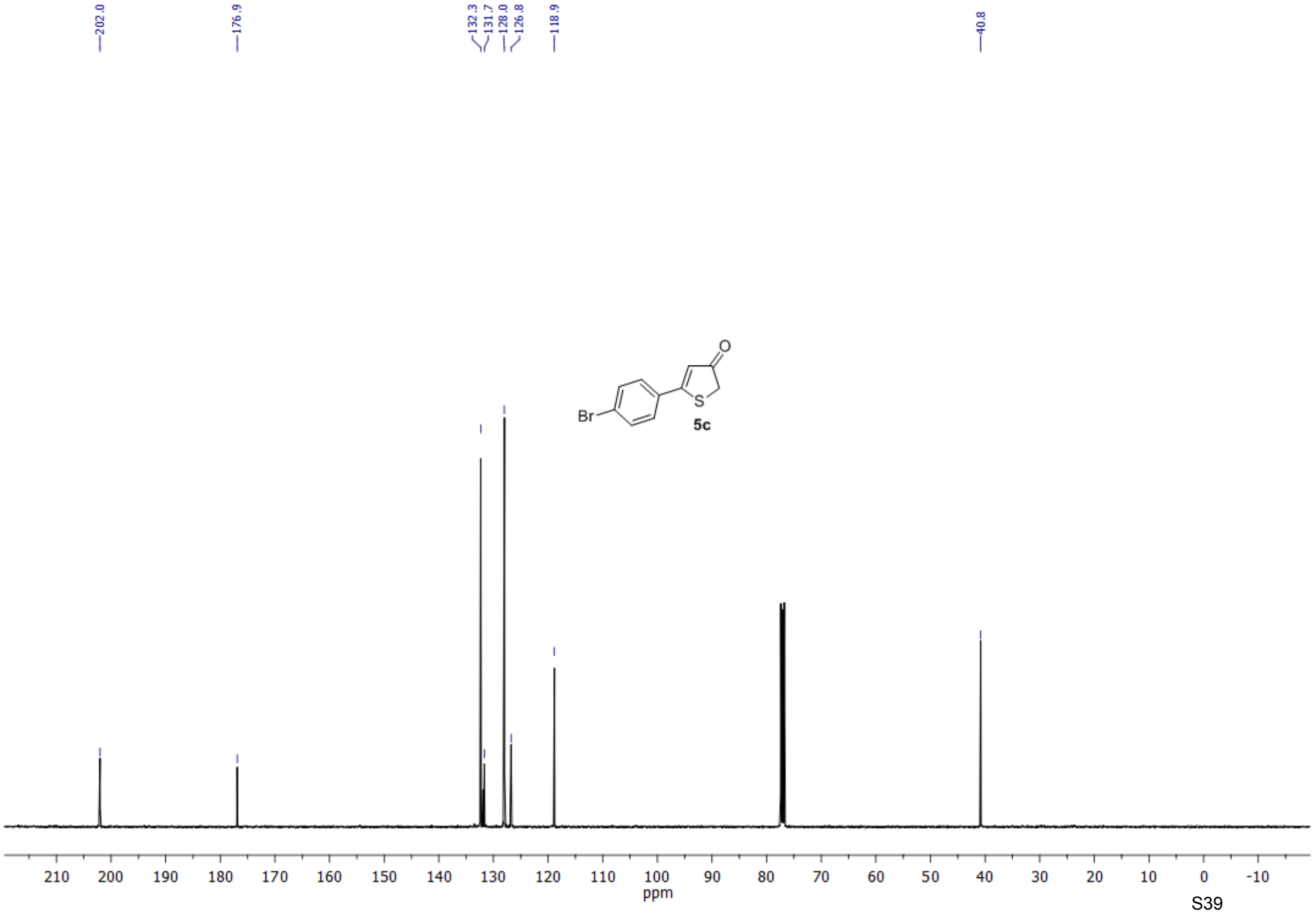

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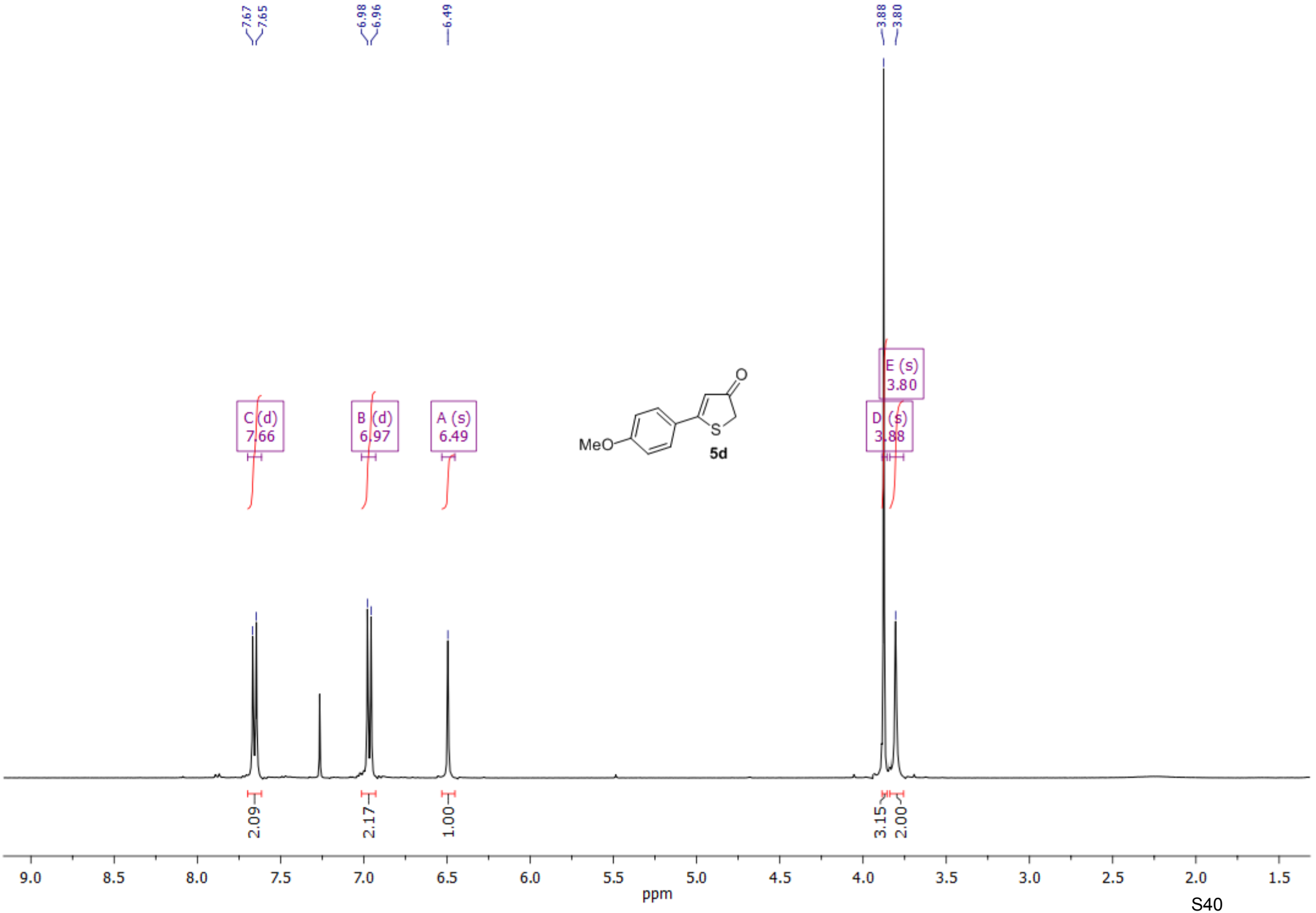

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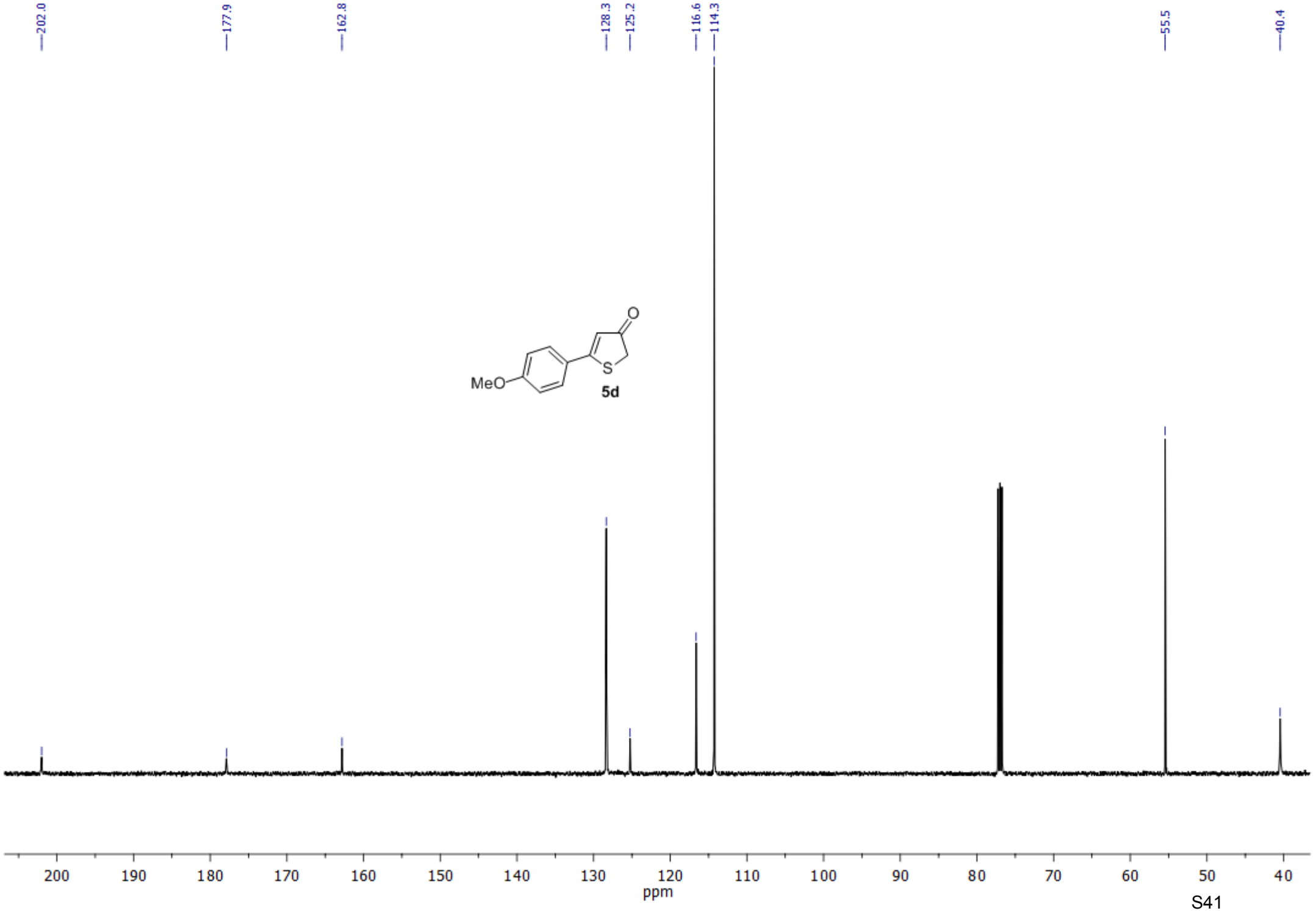

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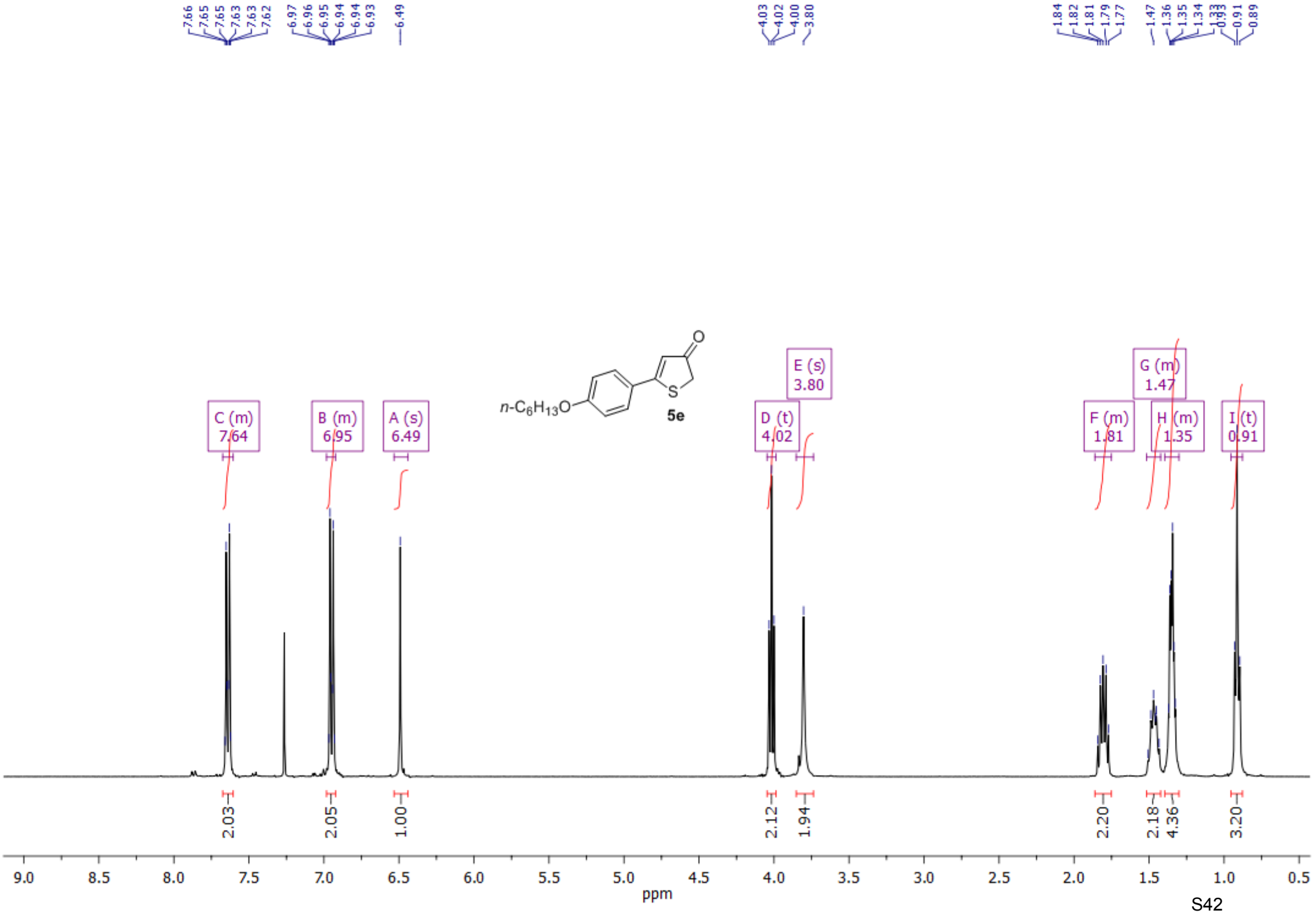

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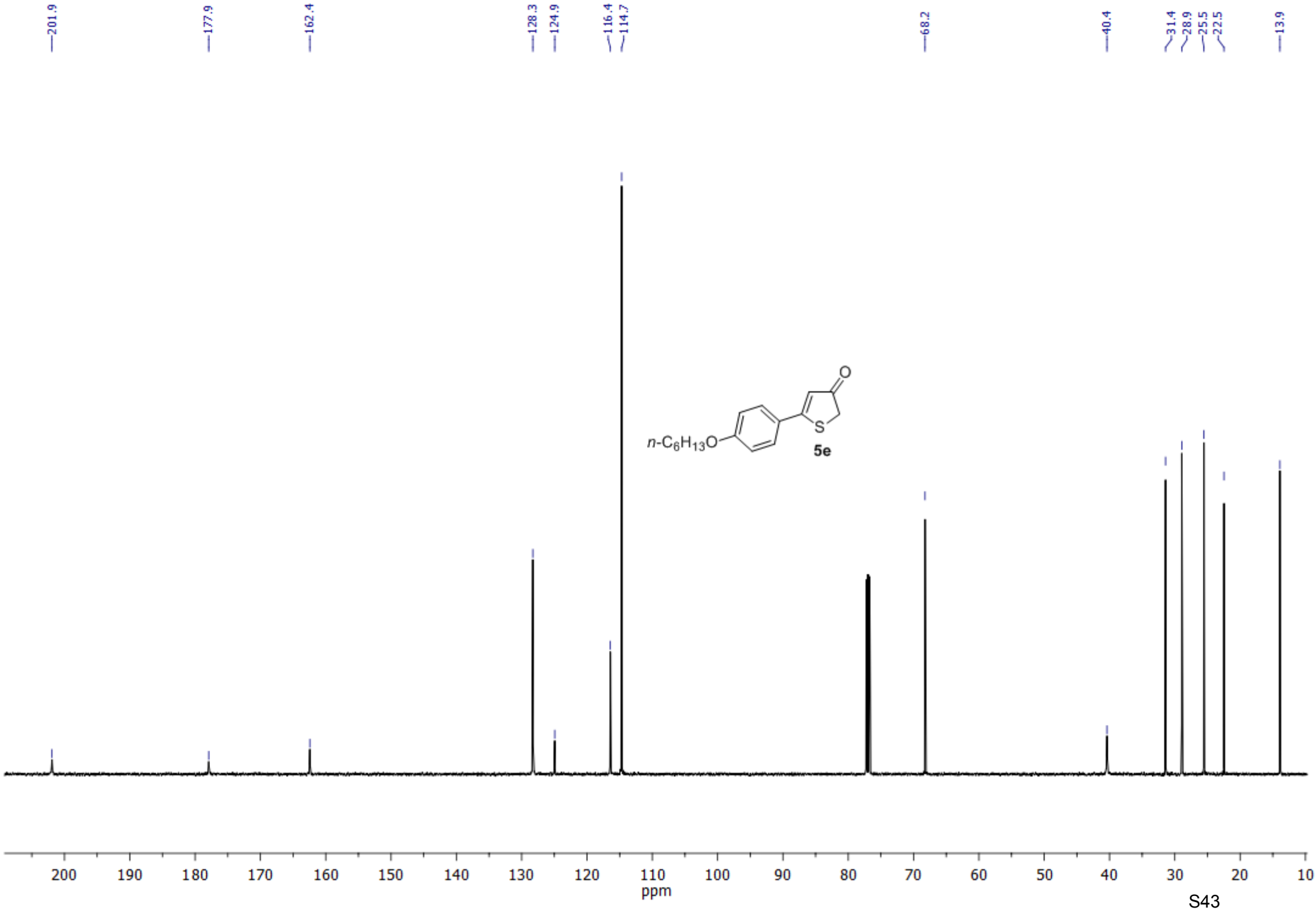

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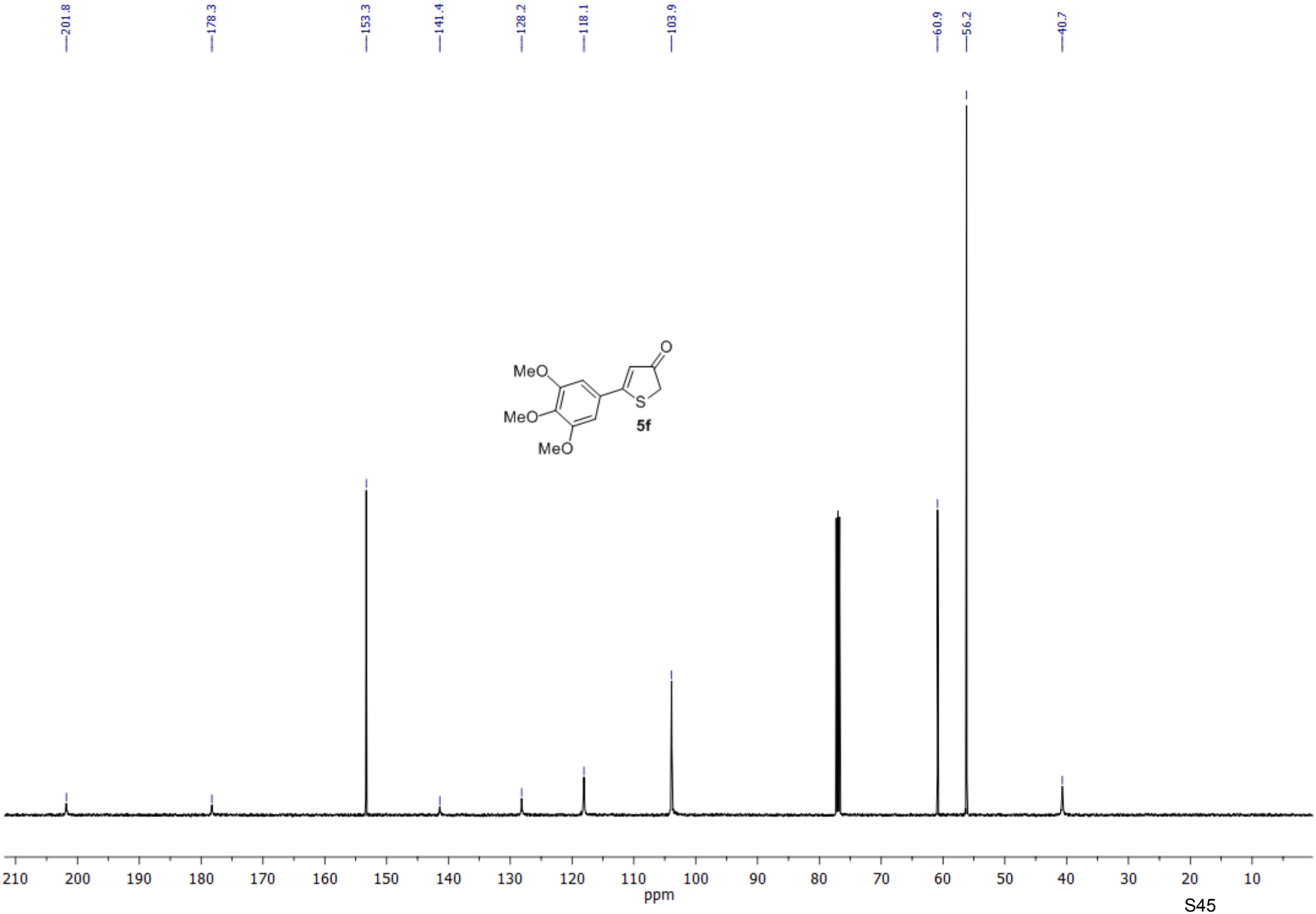

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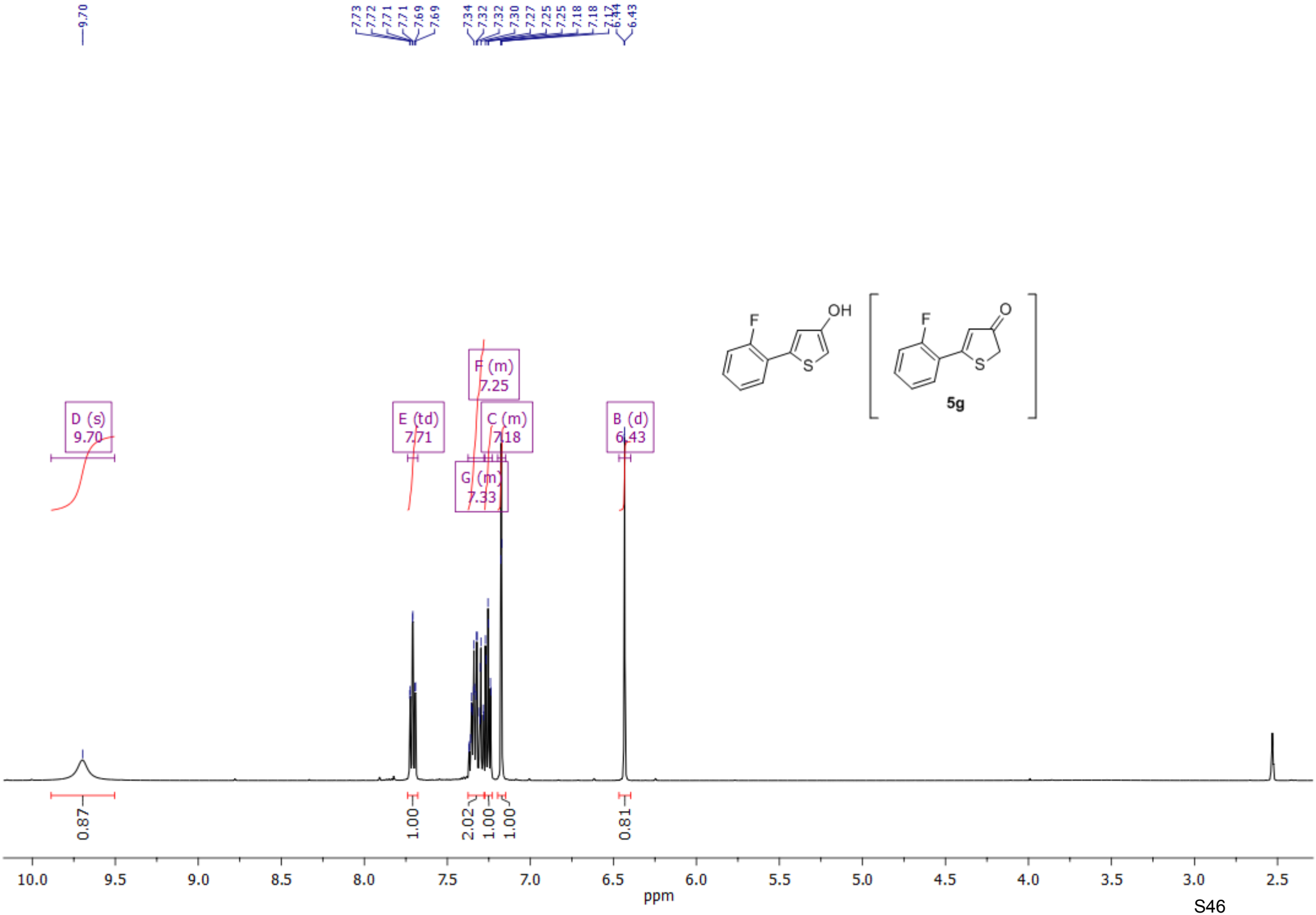

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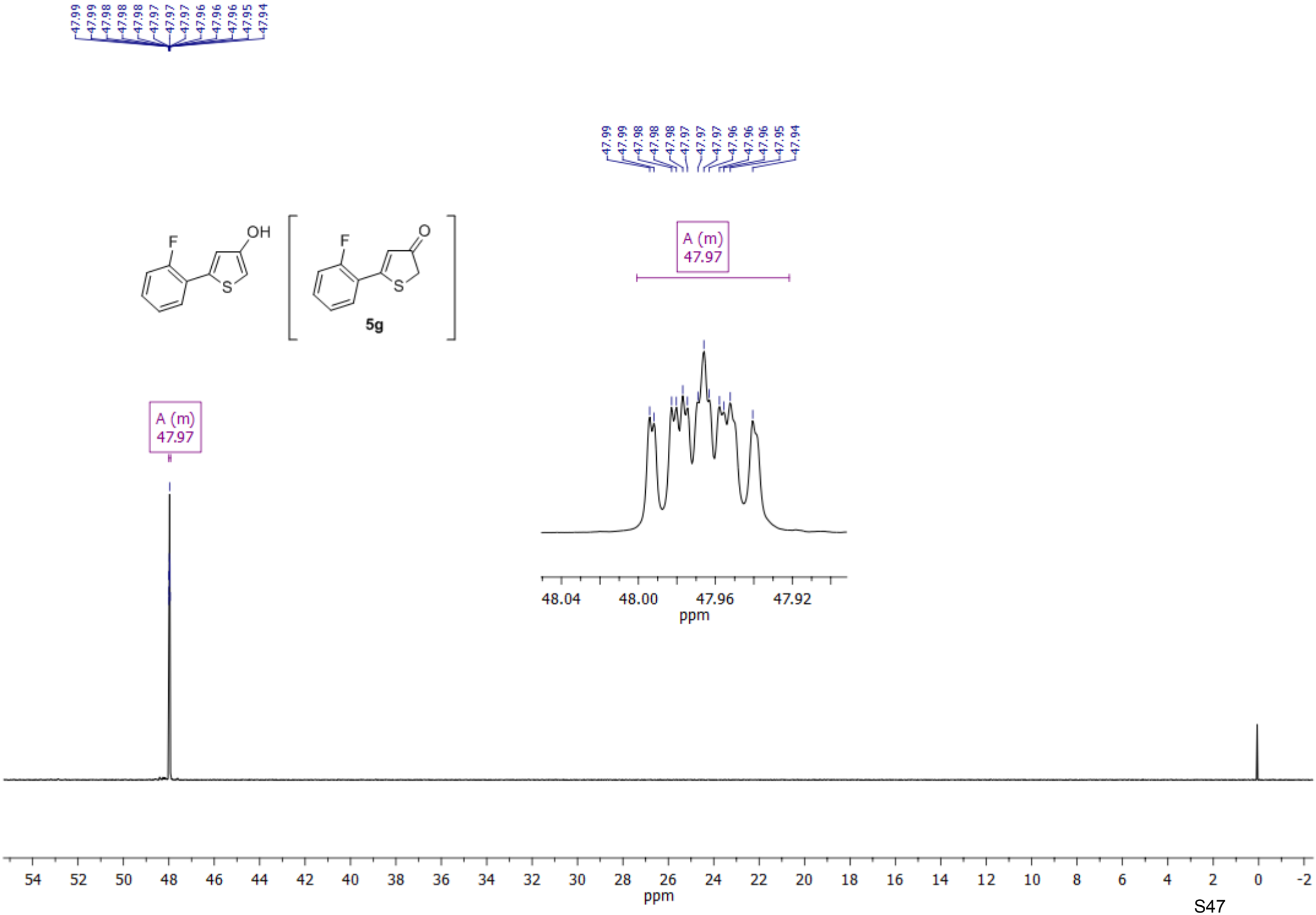
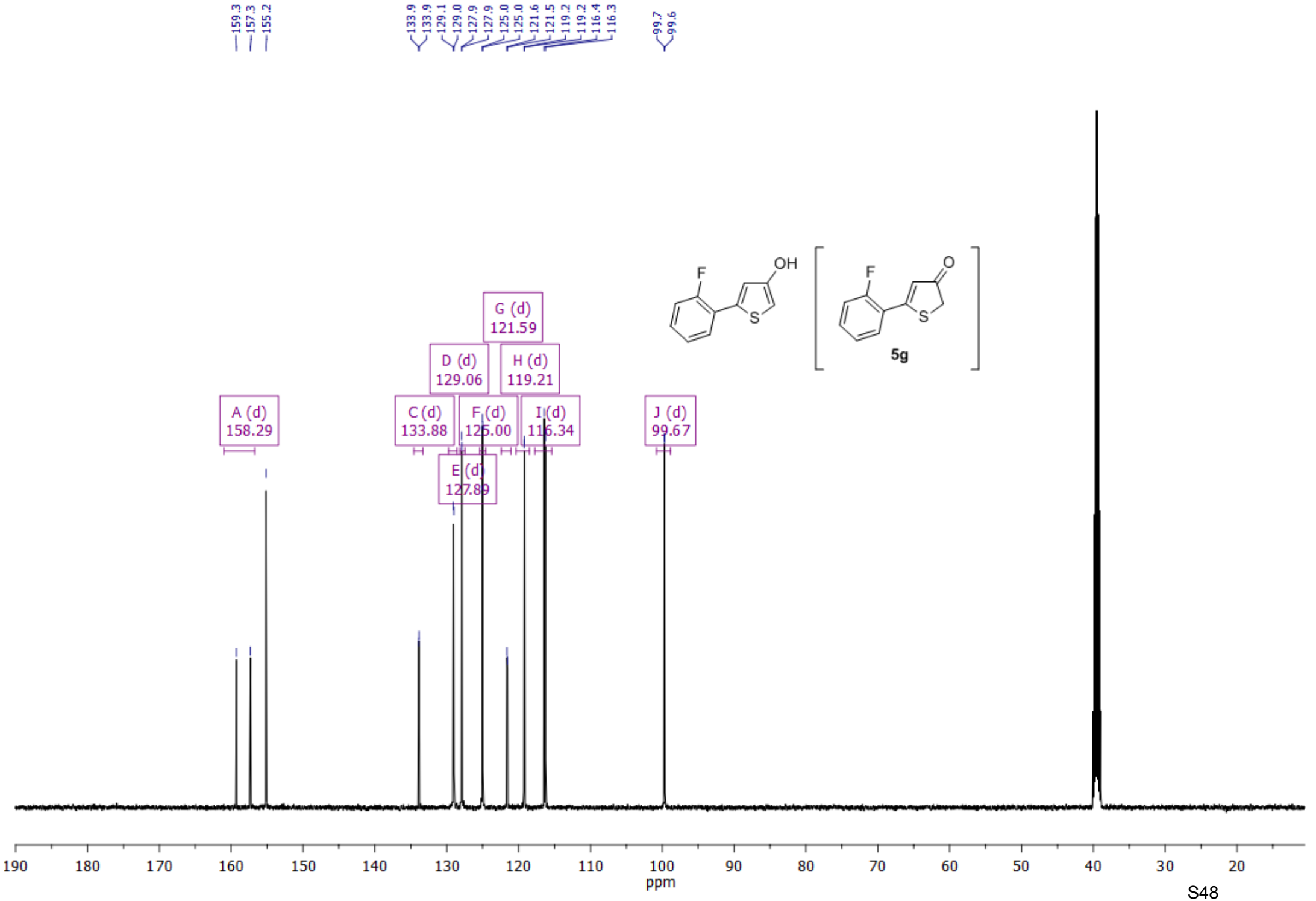
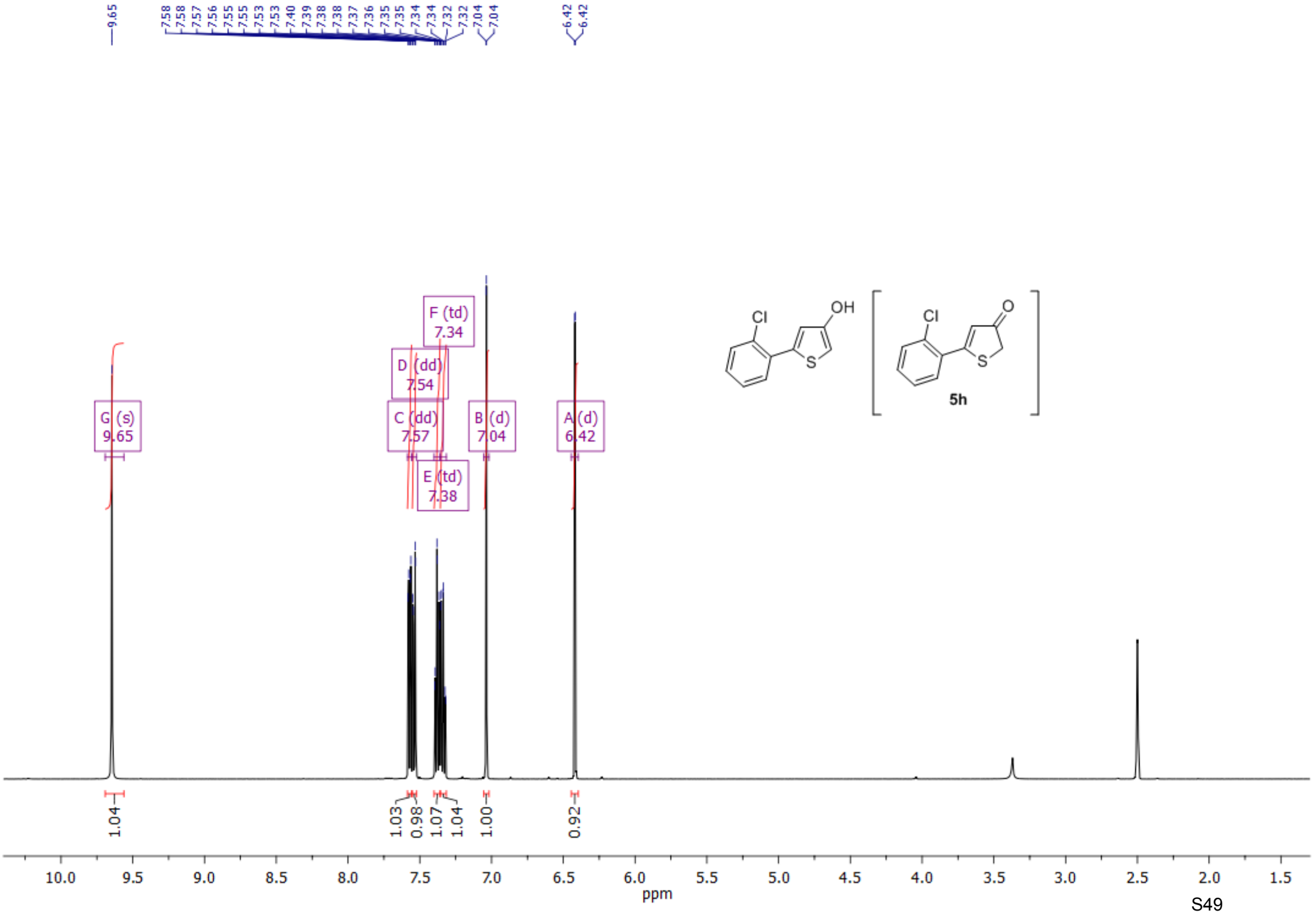


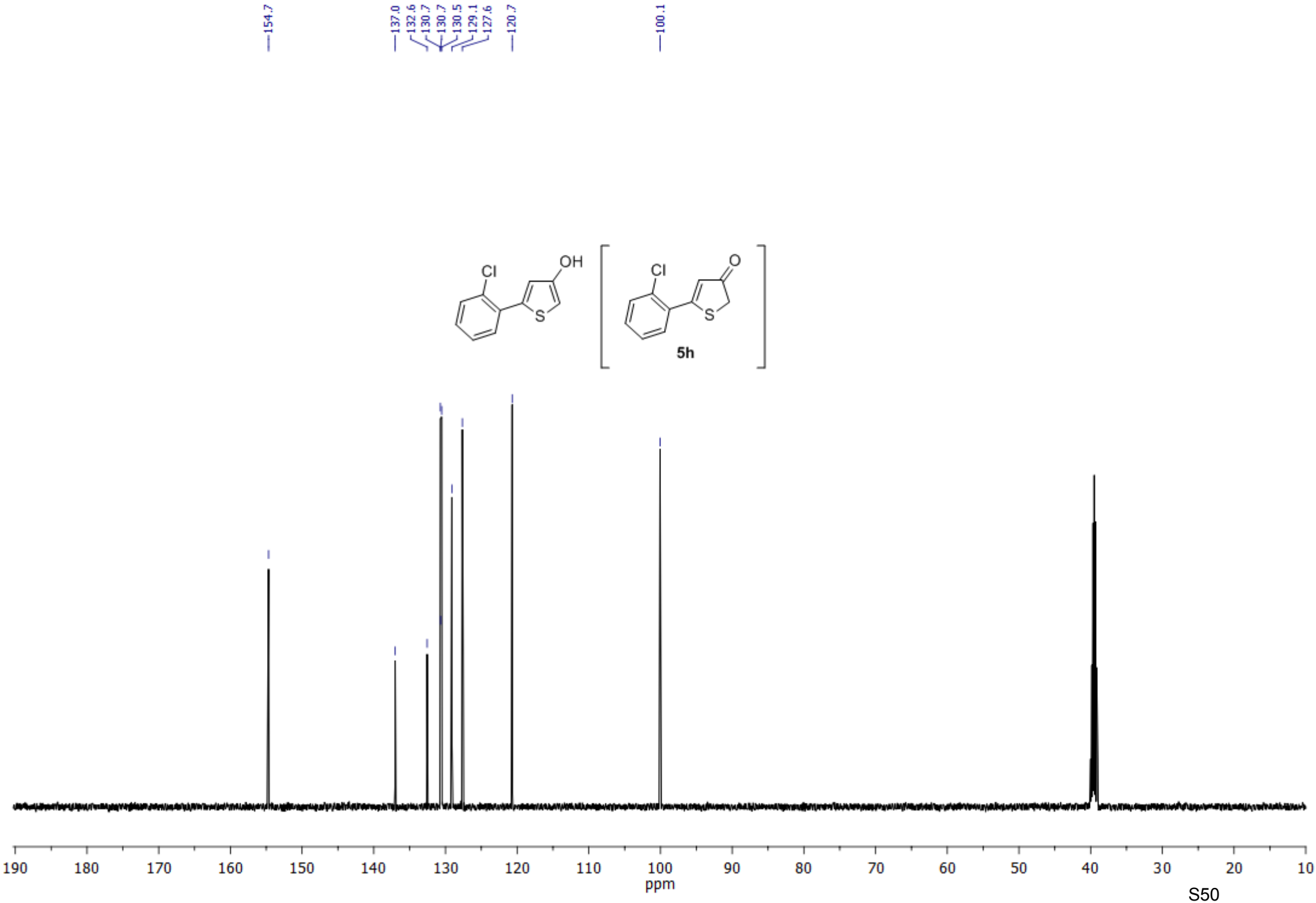
^{13}C NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **5g**



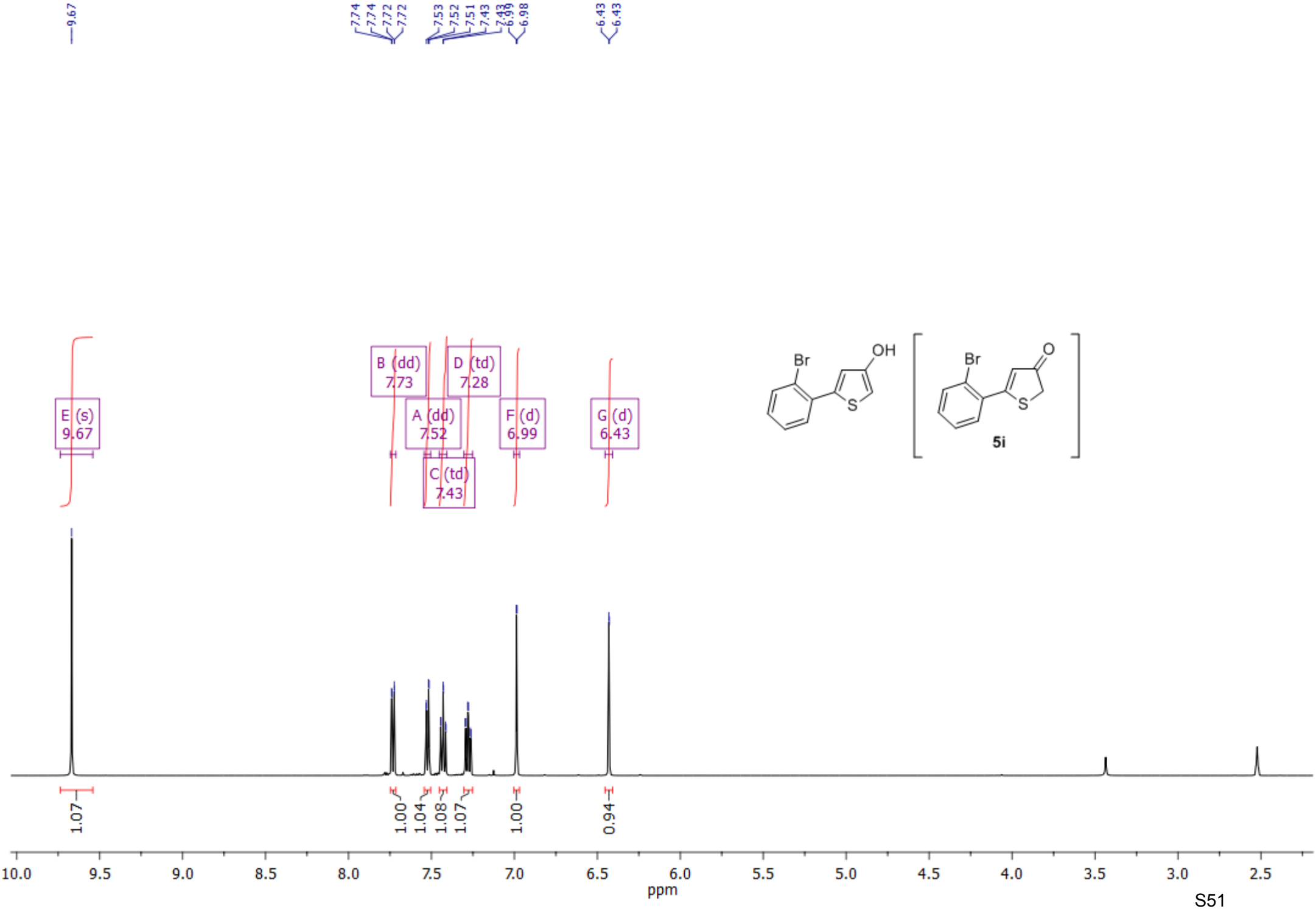
^{1}H NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **5h**



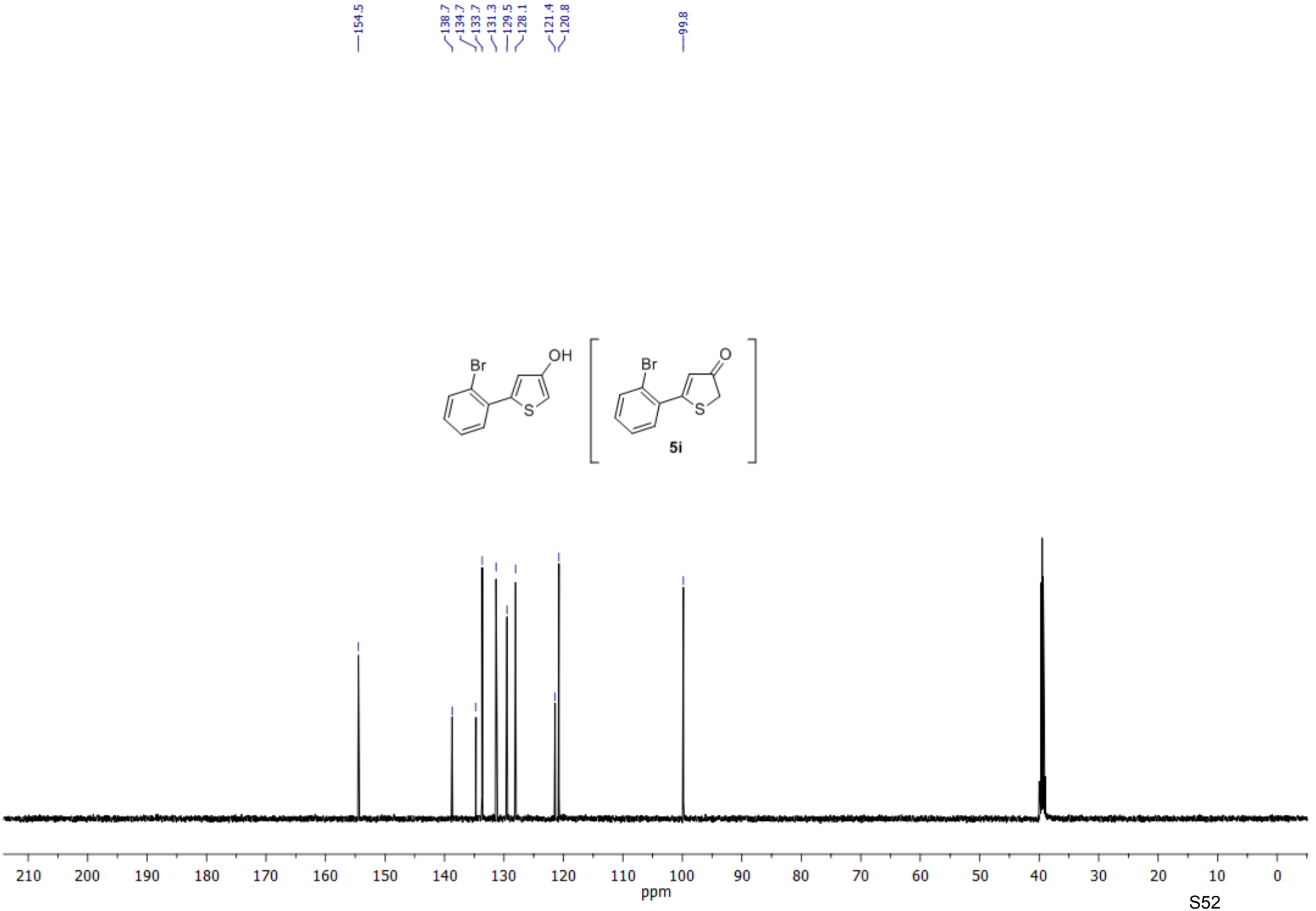
^{13}C NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **5h**



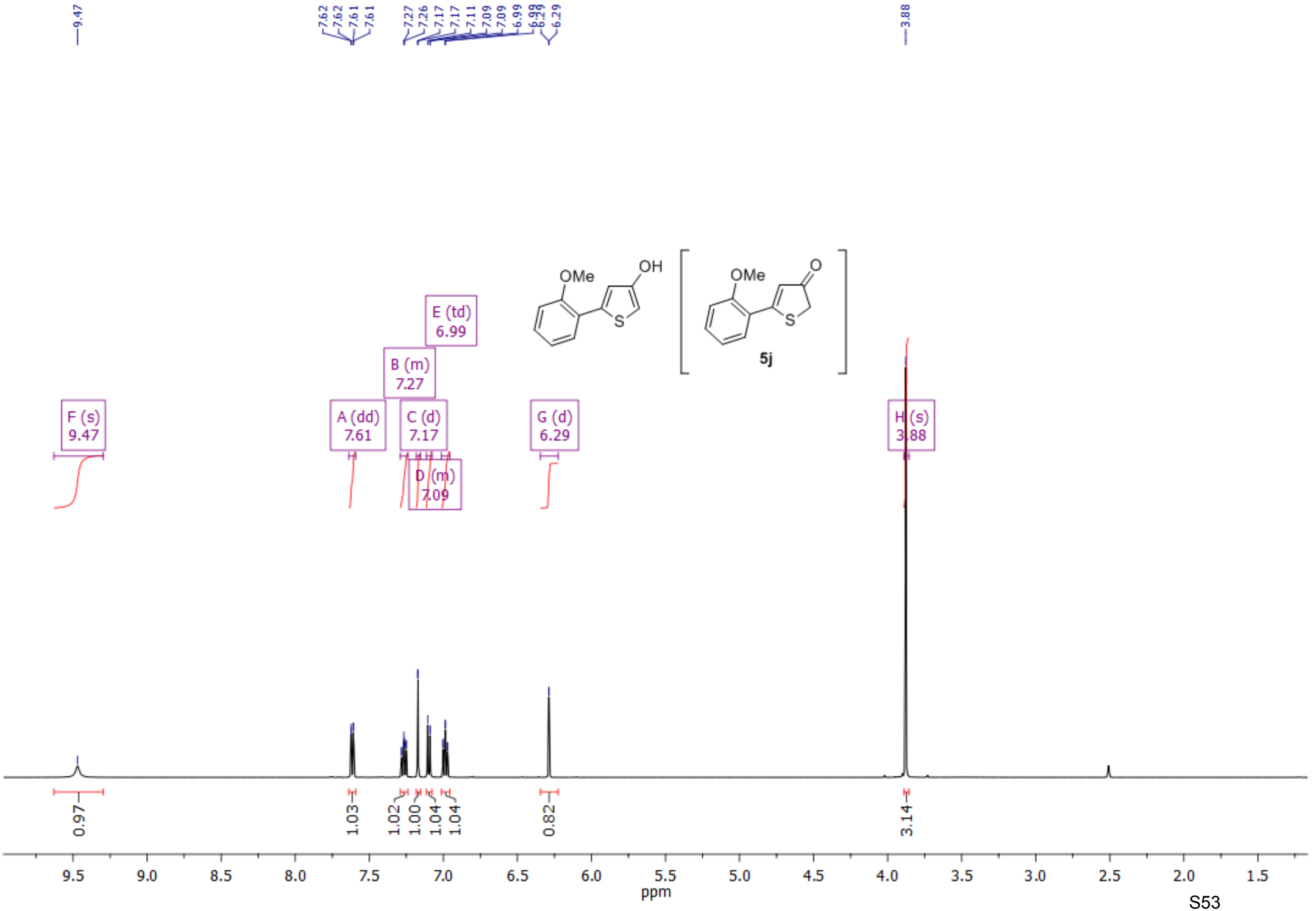
^{1}H NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **5i**



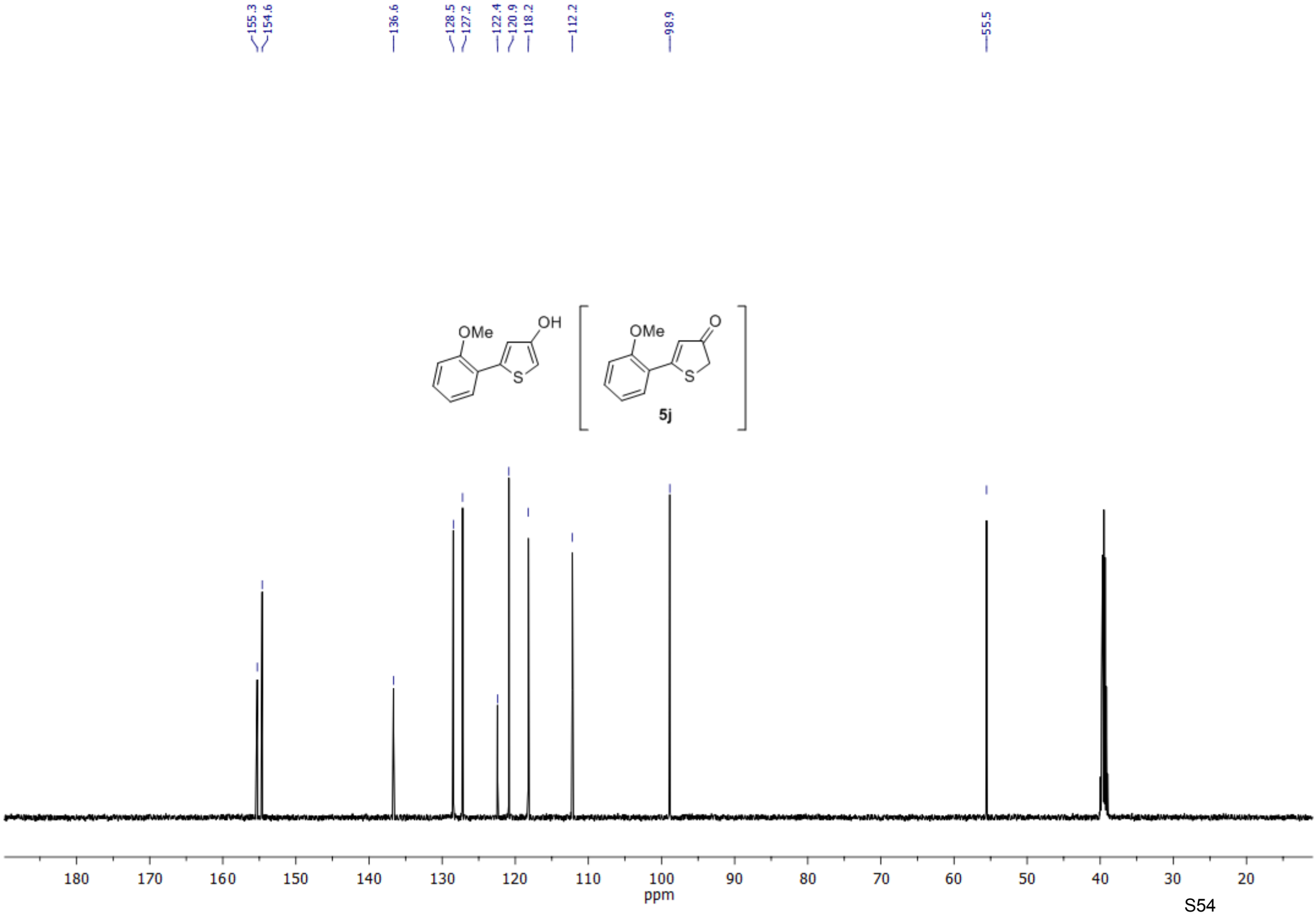
^{13}C NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **5i**



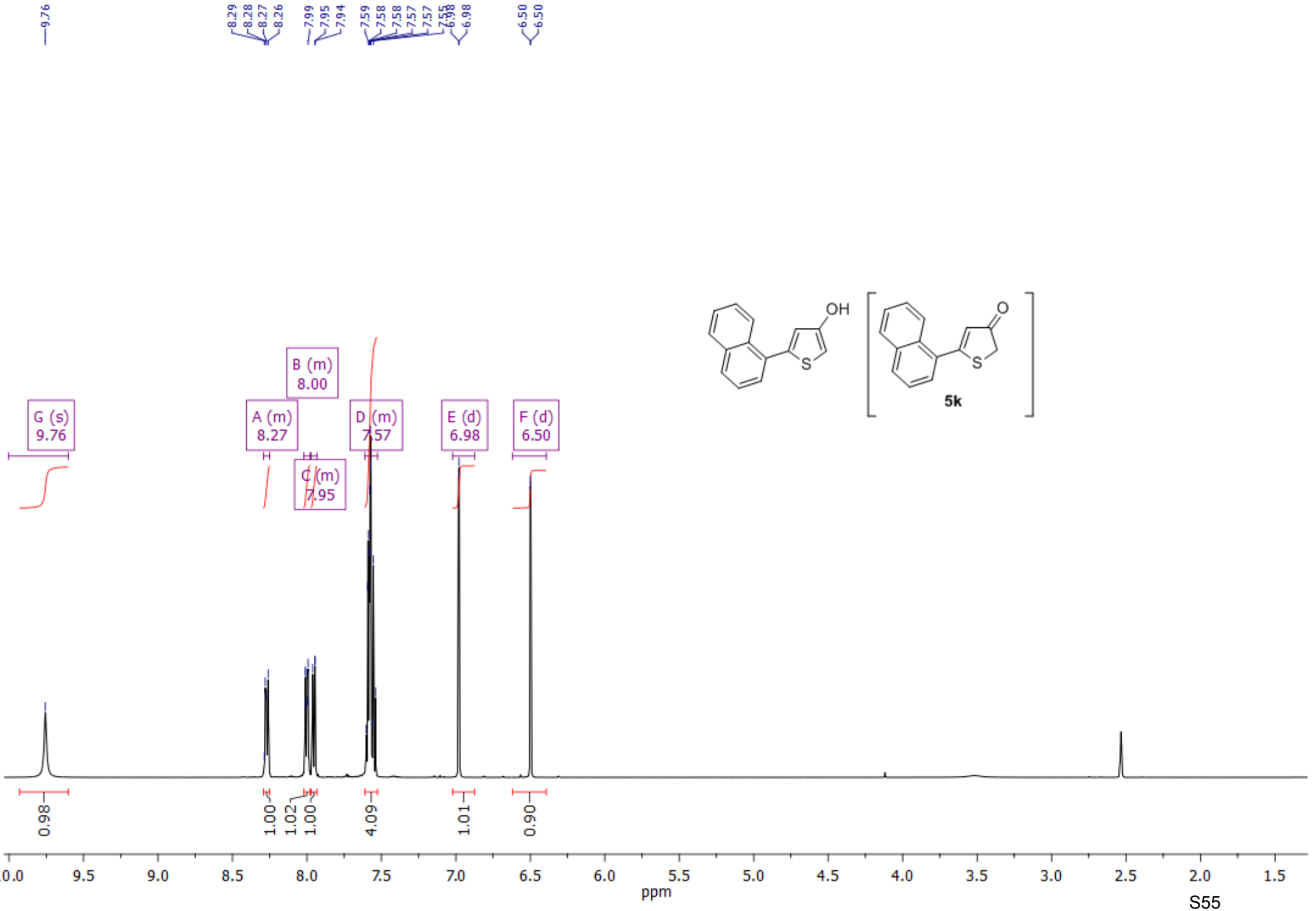
^{1}H NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **5j**



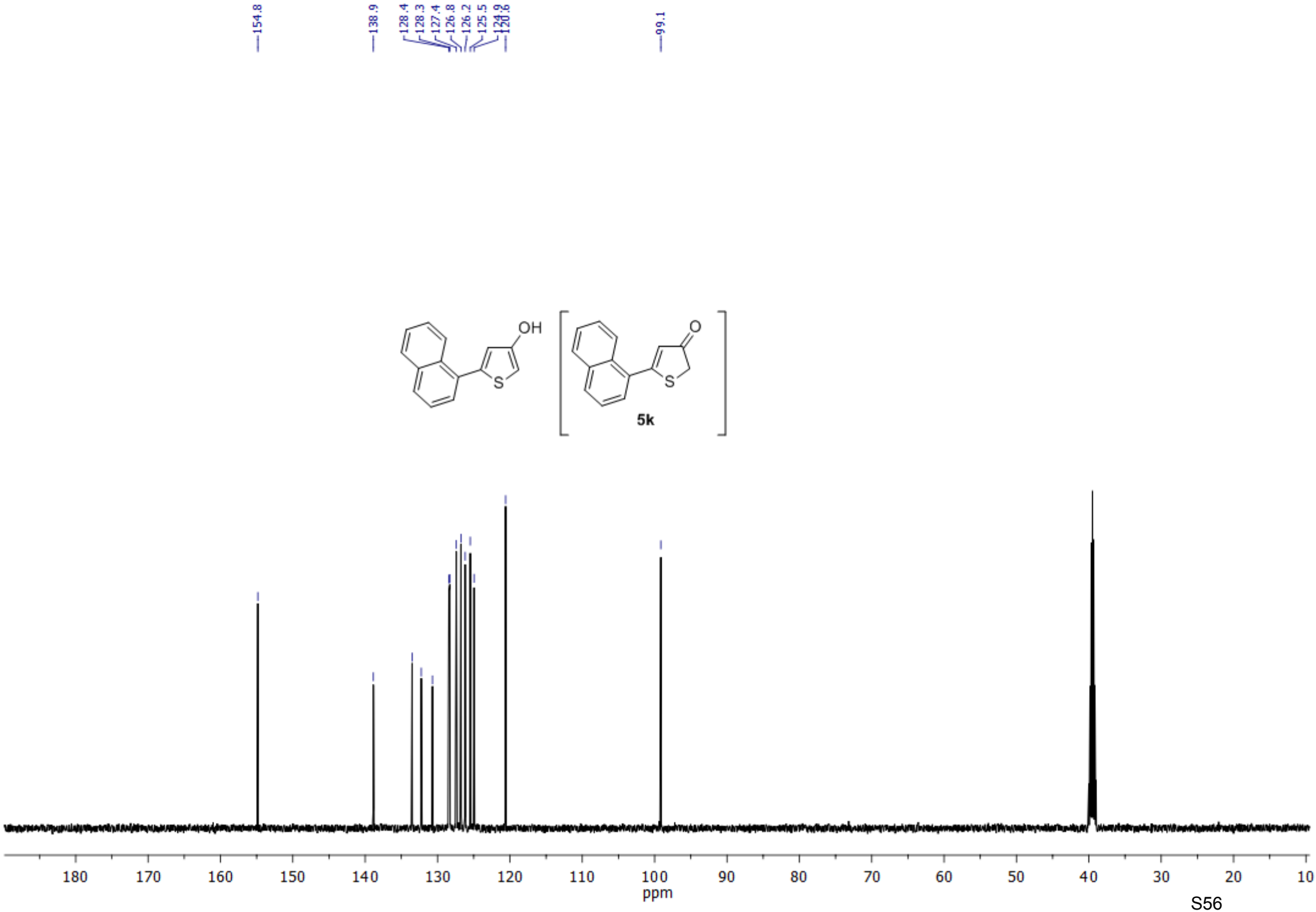
^{13}C NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **5j**



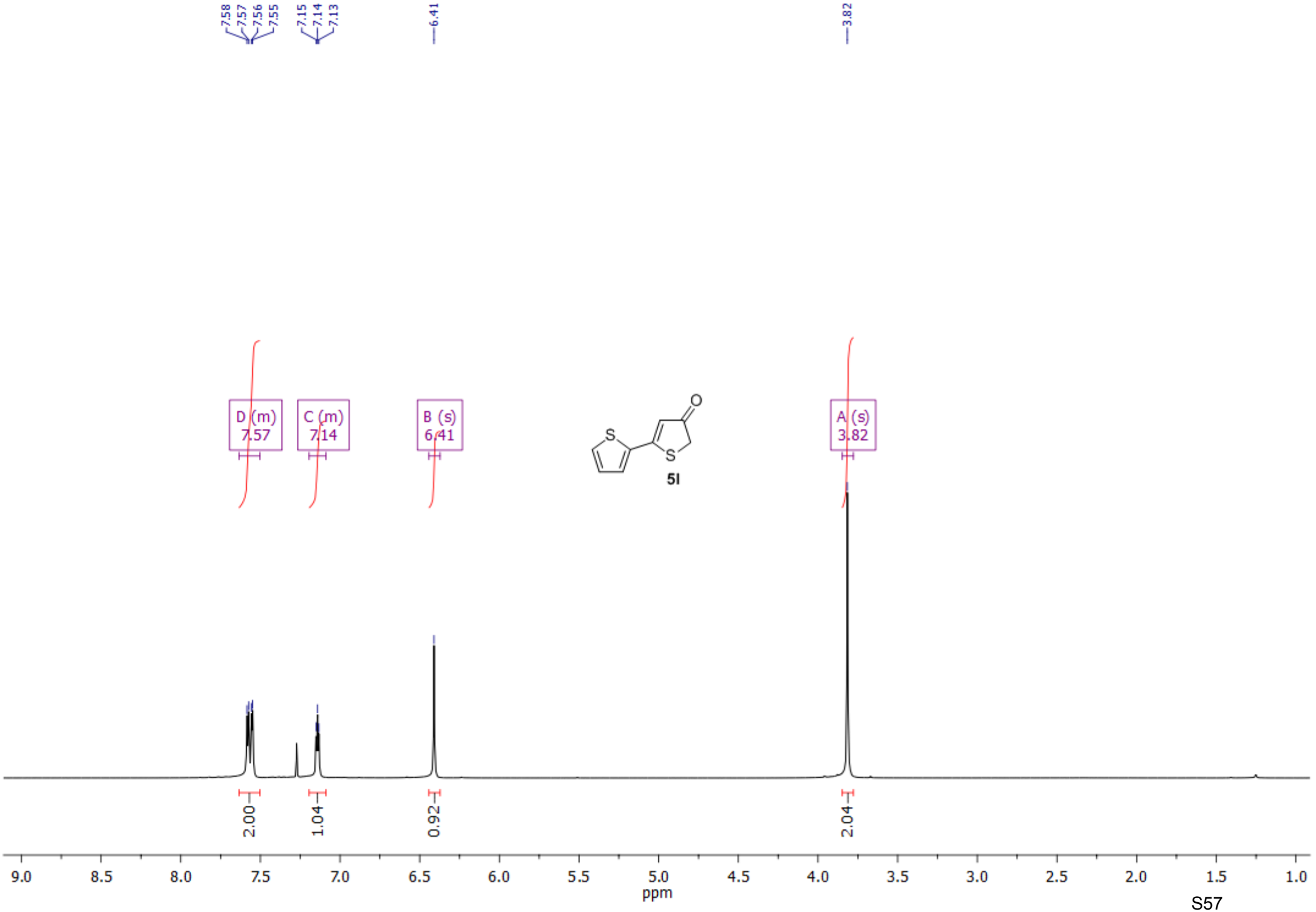
^{1}H NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **5k**



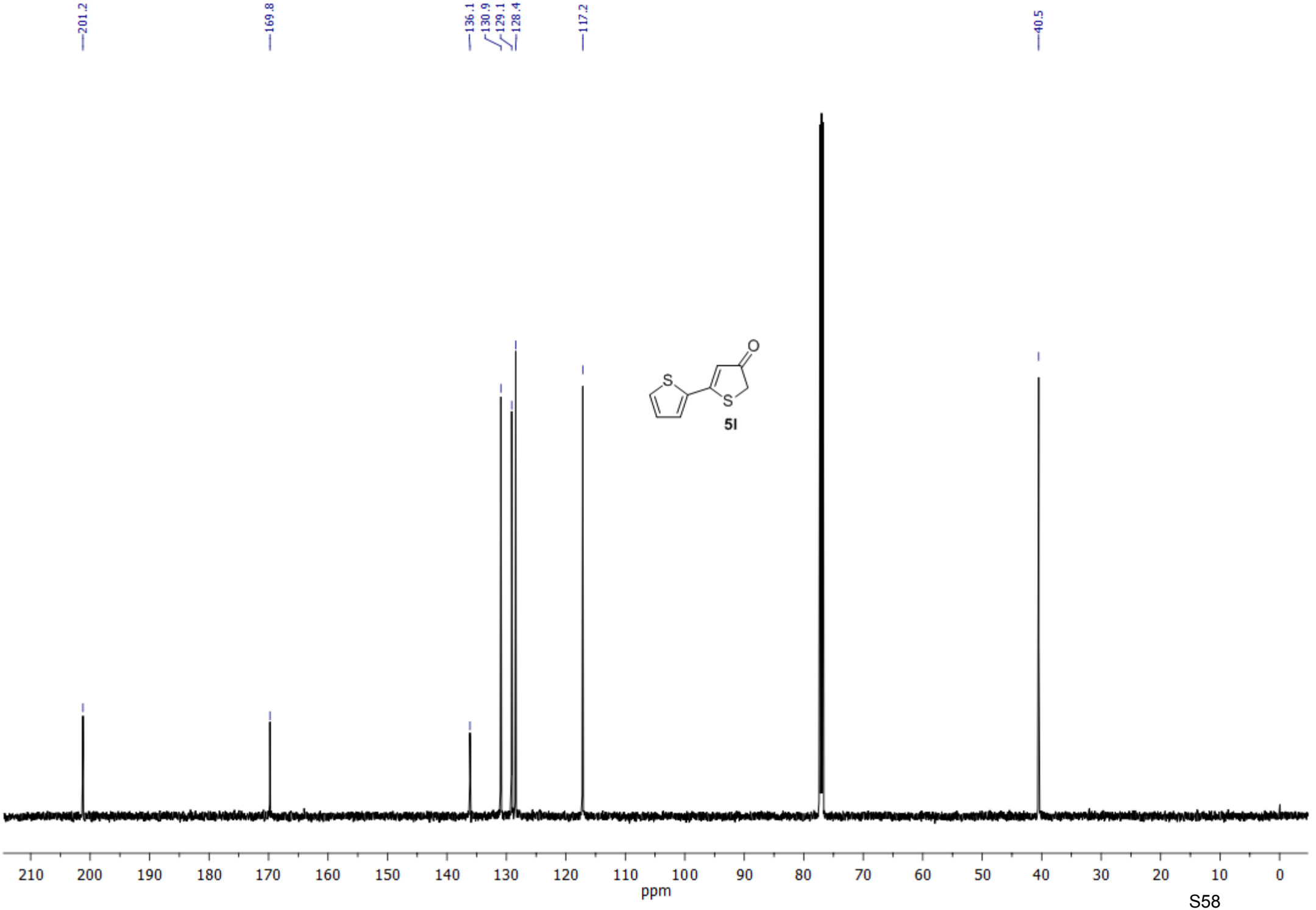
^{13}C NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **5k**



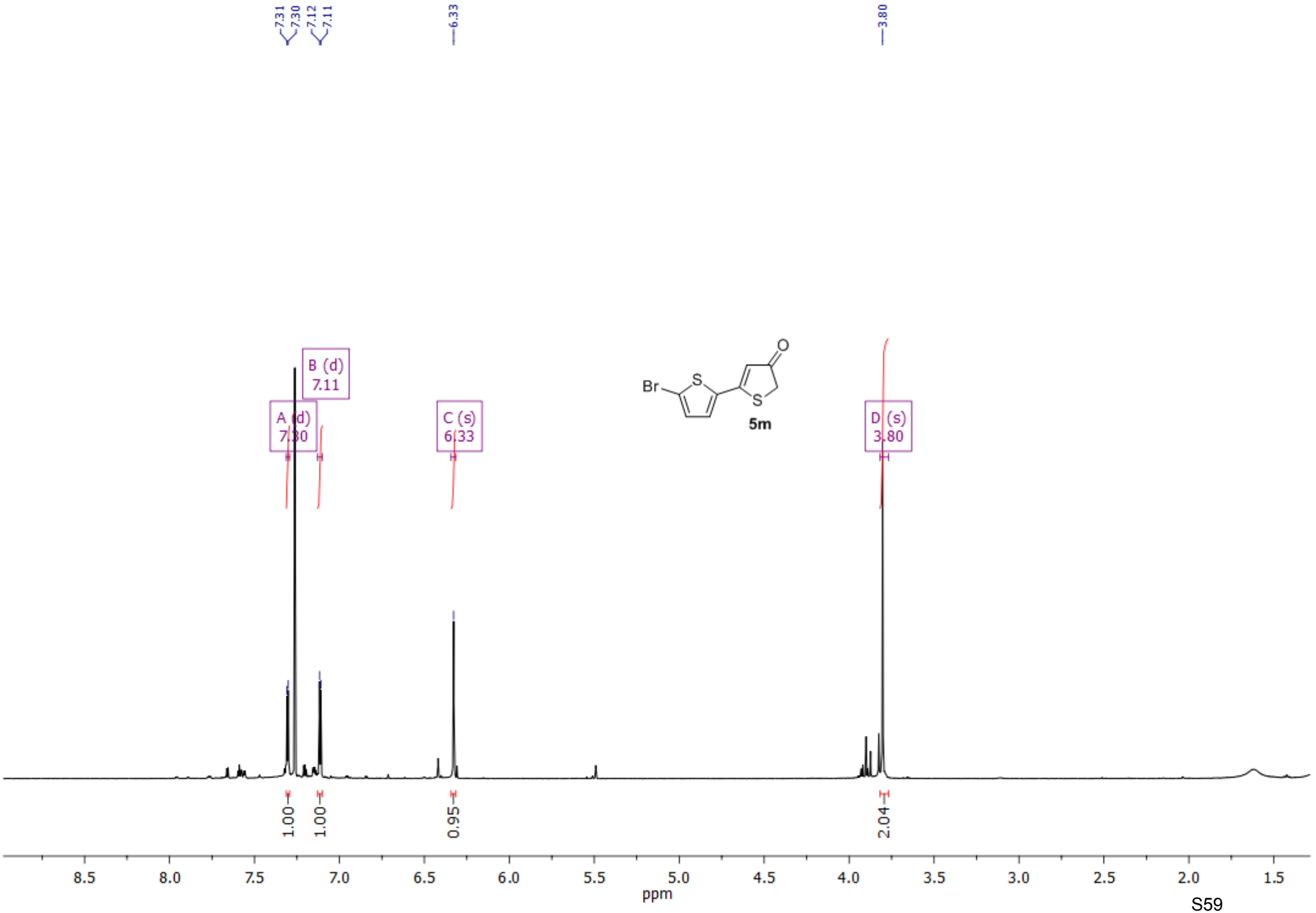
^{1}H NMR (solvent: $CDCl_3$)



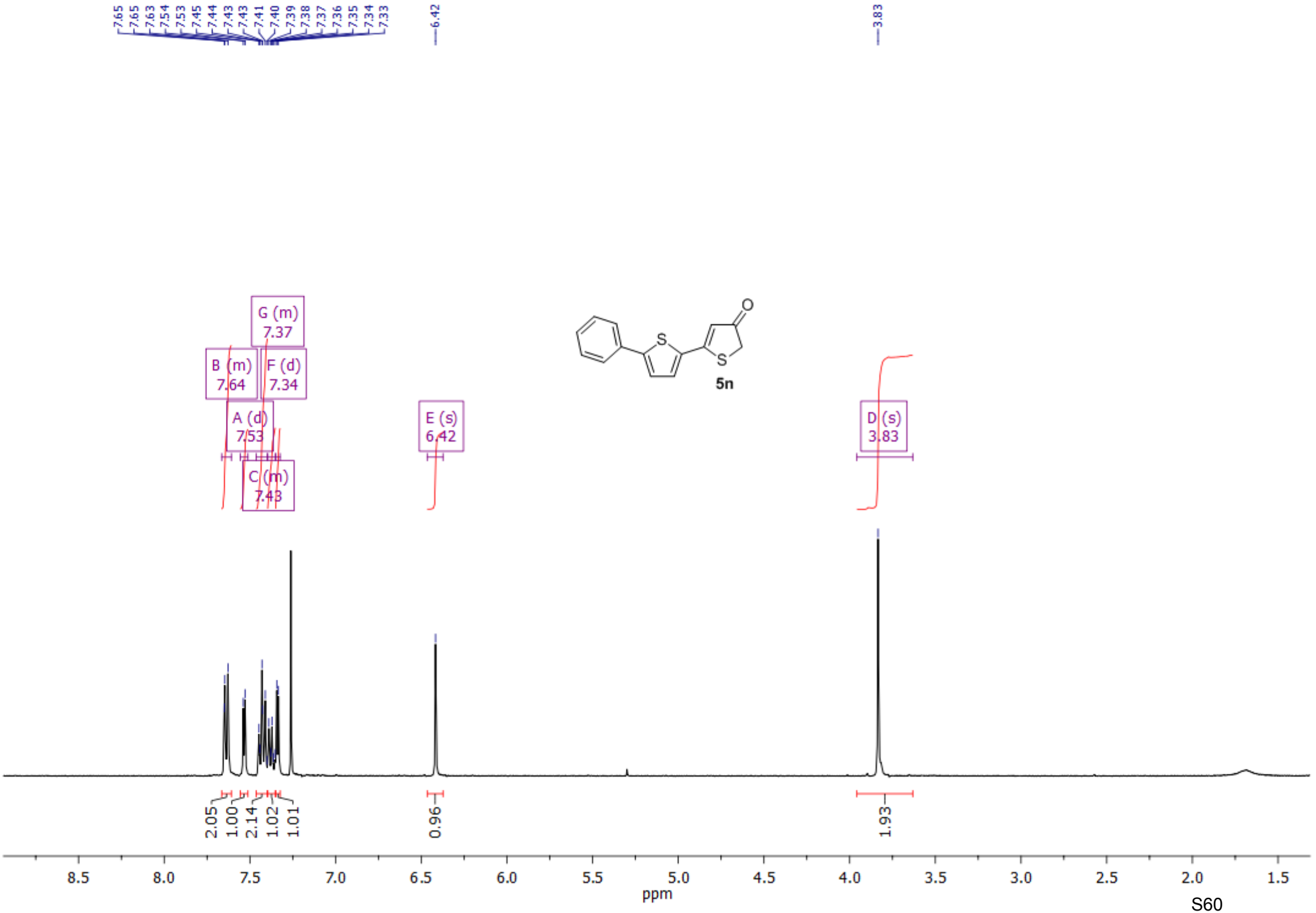
^{13}C NMR (solvent: $CDCl_3$)



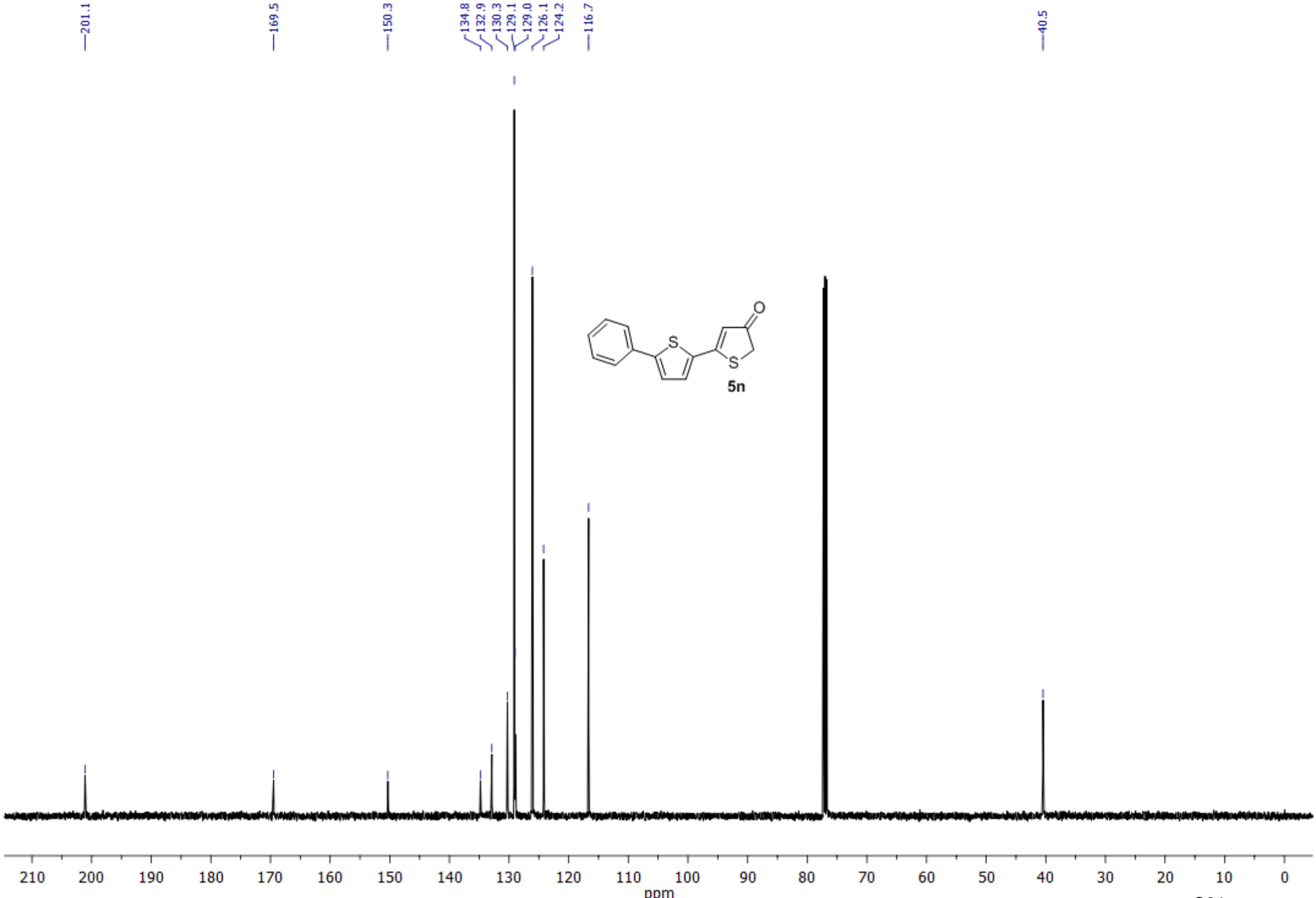
^{1}H NMR (solvent: $CDCl_3$), crude compound **5m**



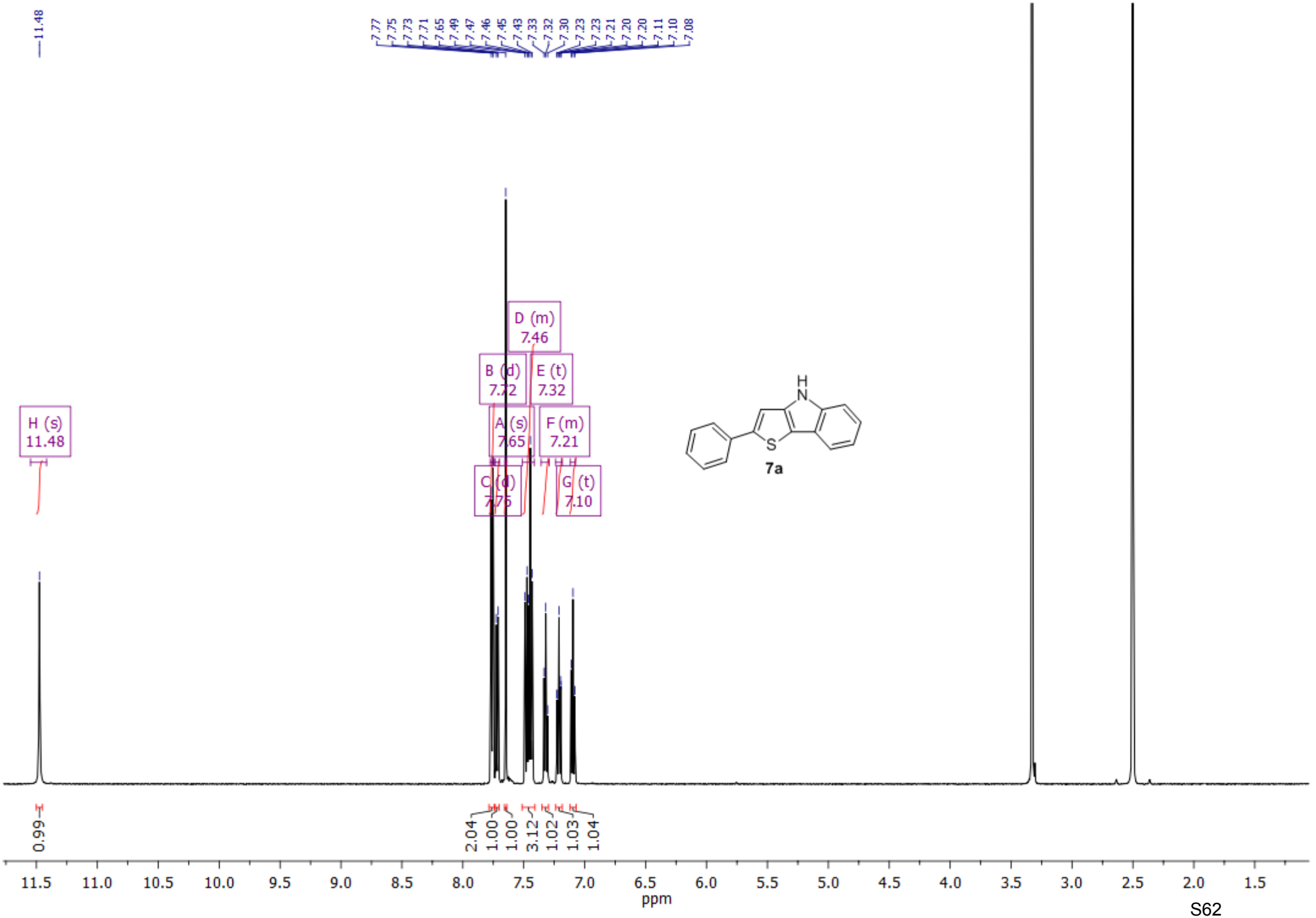
^{1}H NMR (solvent: $CDCl_3$)



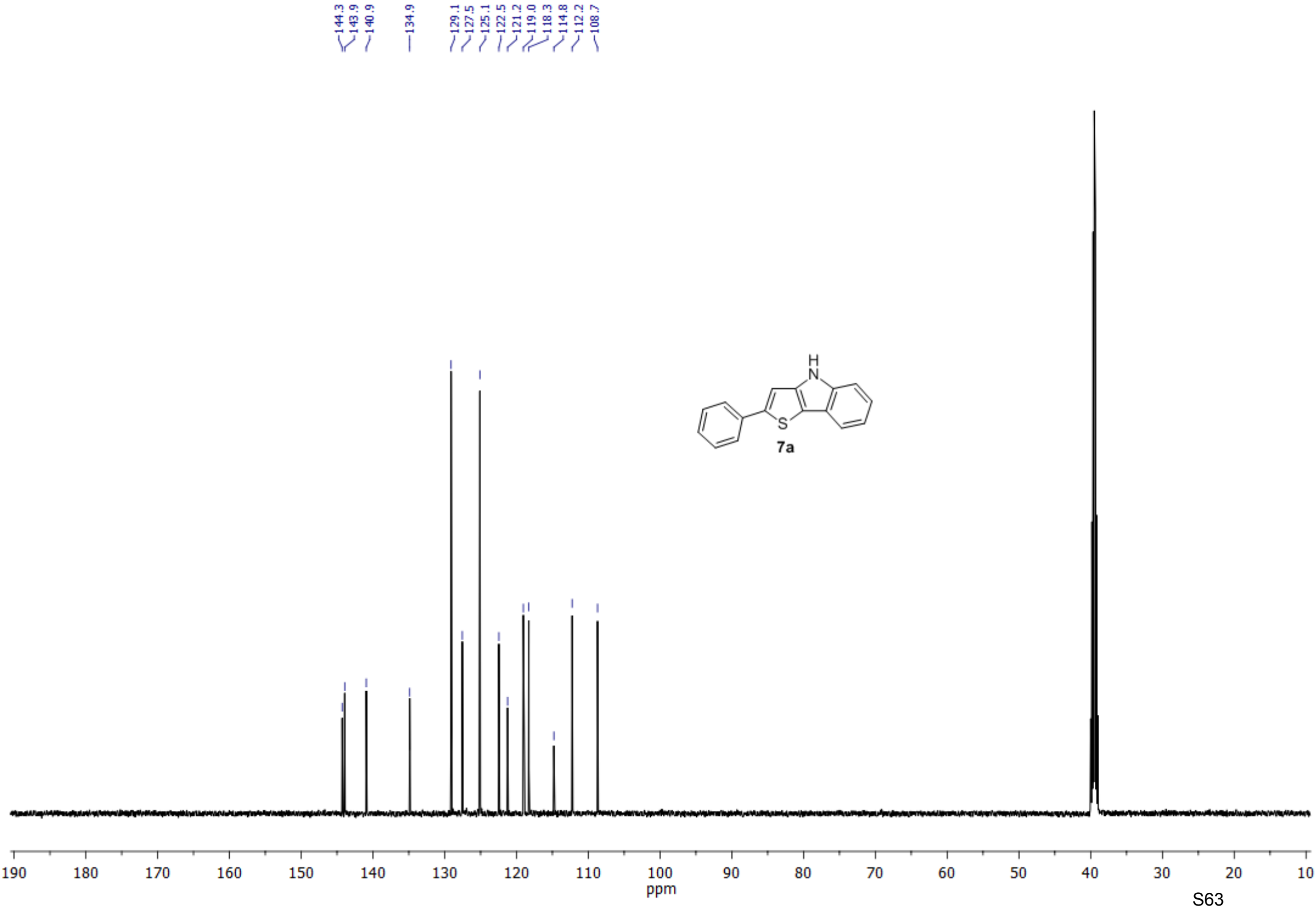
^{13}C NMR (solvent: $CDCl_3$)



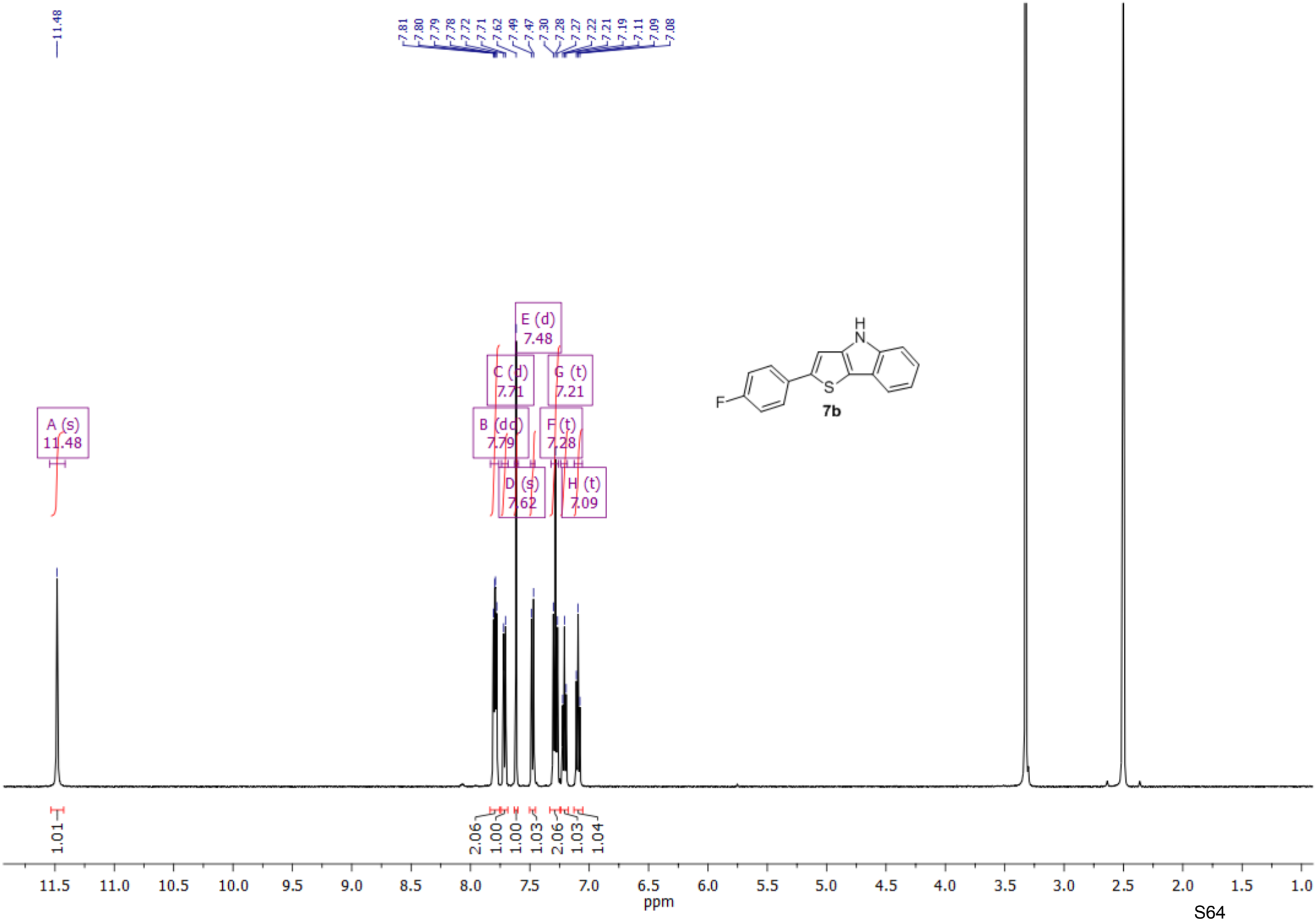
^{1}H NMR (solvent: DMSO-d_6)



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

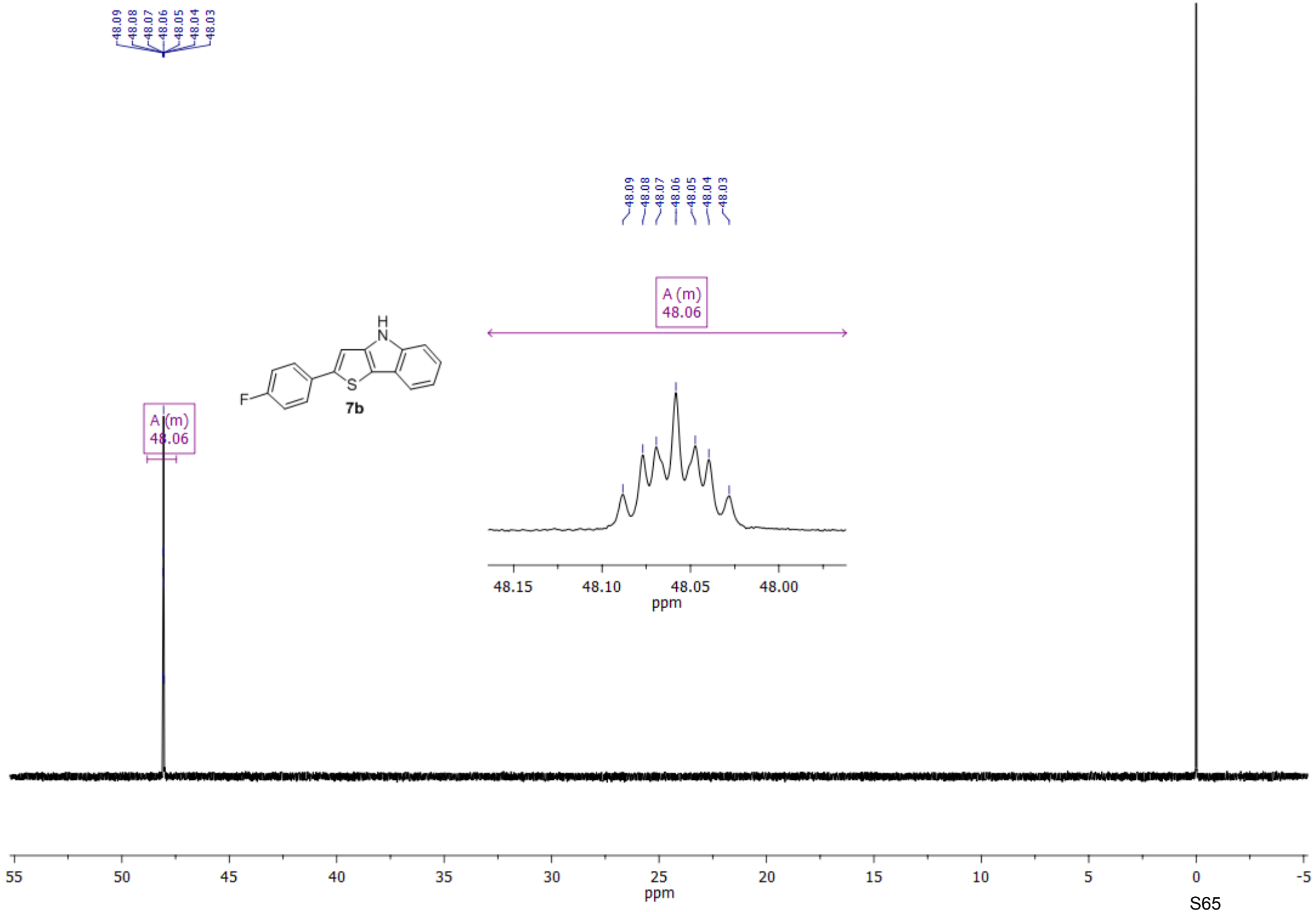


^{1}H NMR (solvent: DMSO-d_6)

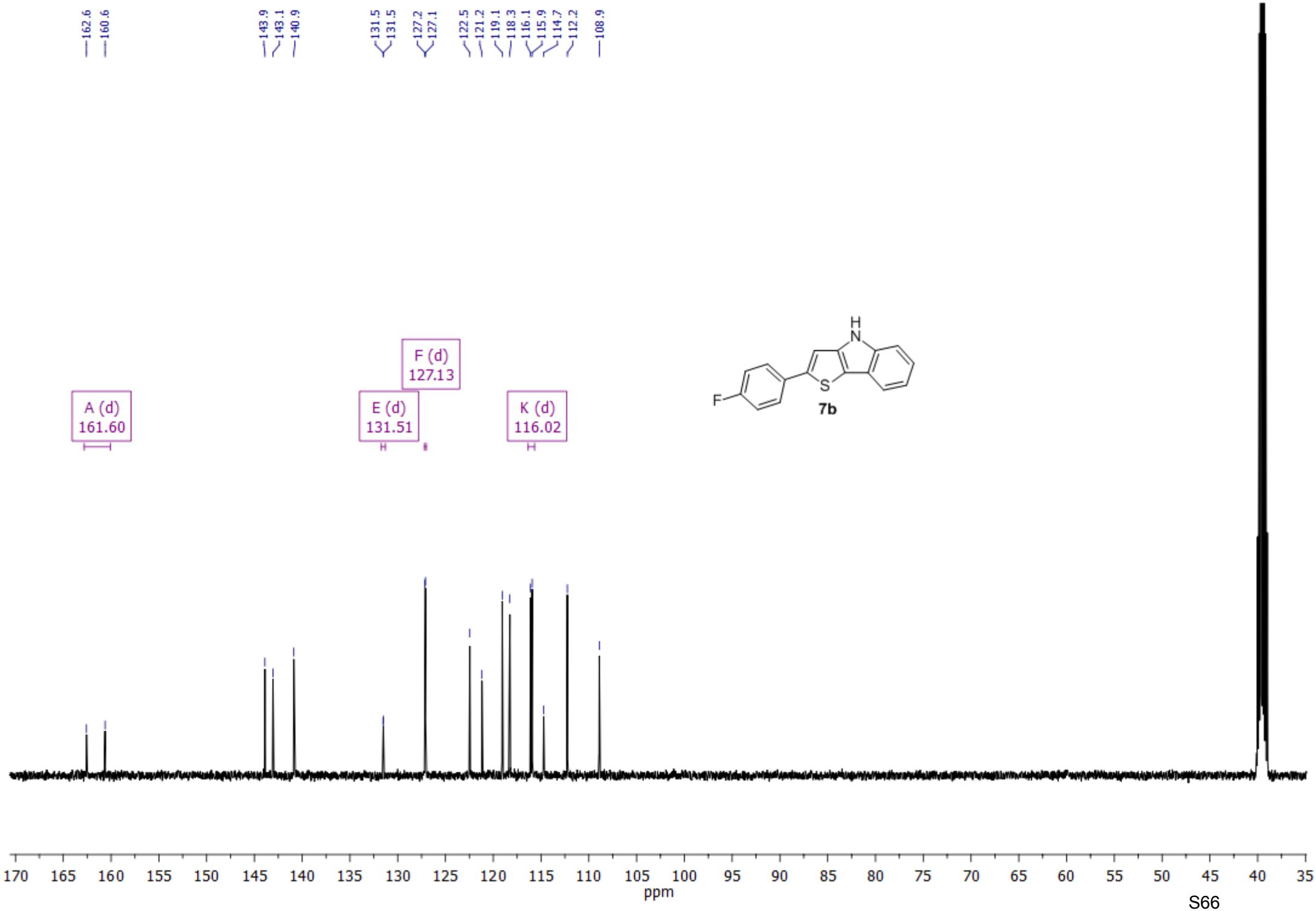


7b

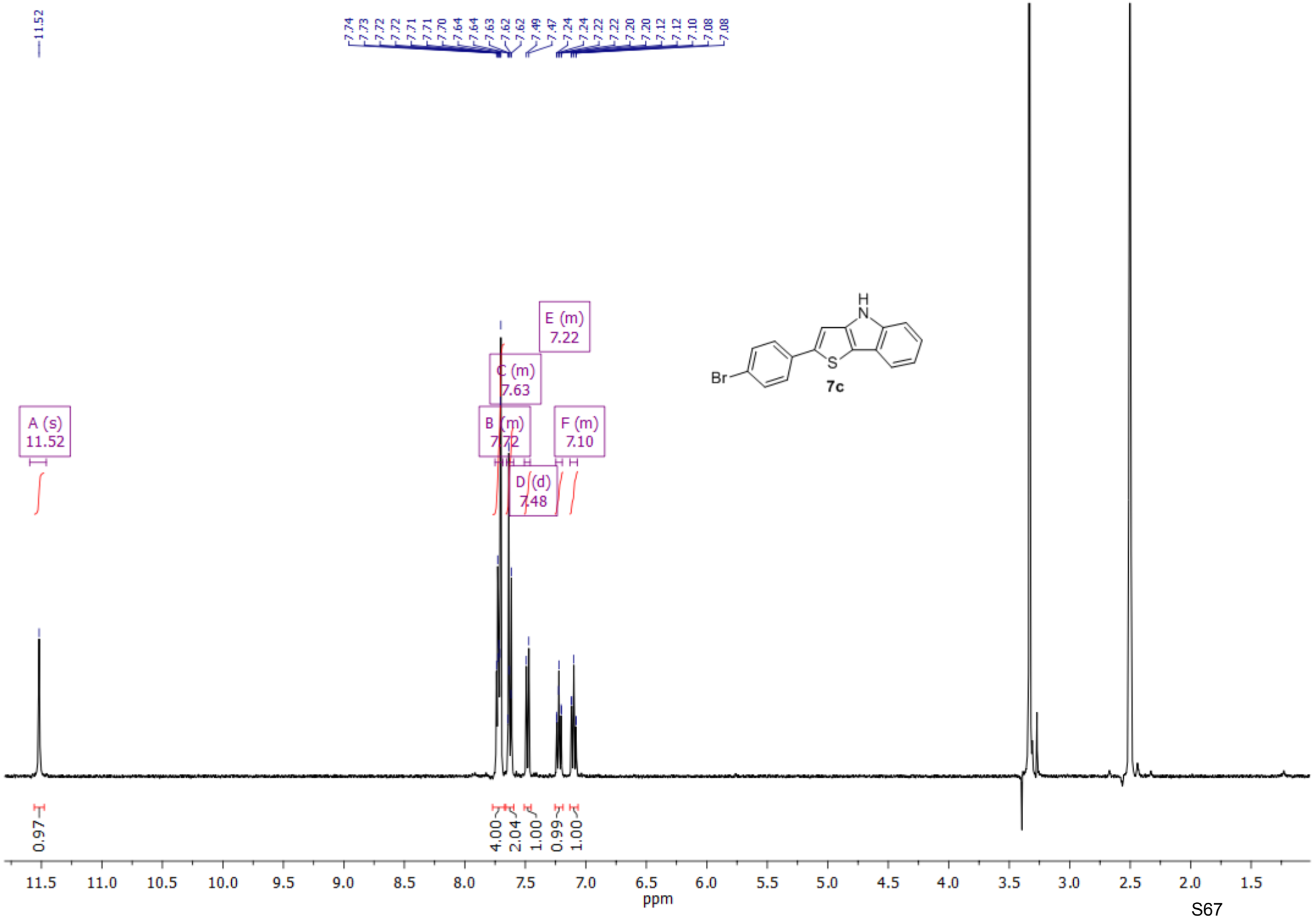
^{19}F NMR (solvent: DMSO-d_6)



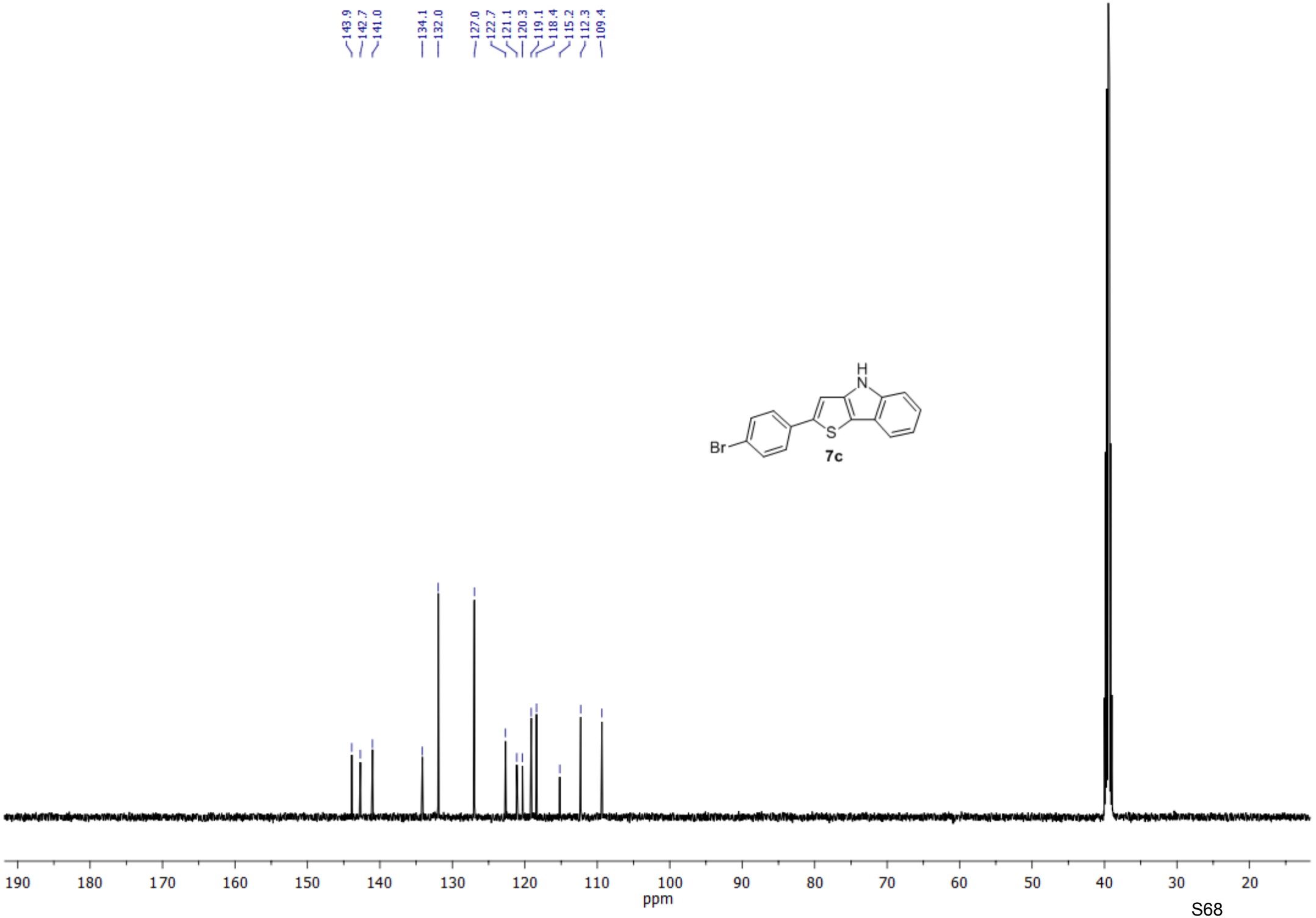
^{13}C NMR (solvent: DMSO-d_6)



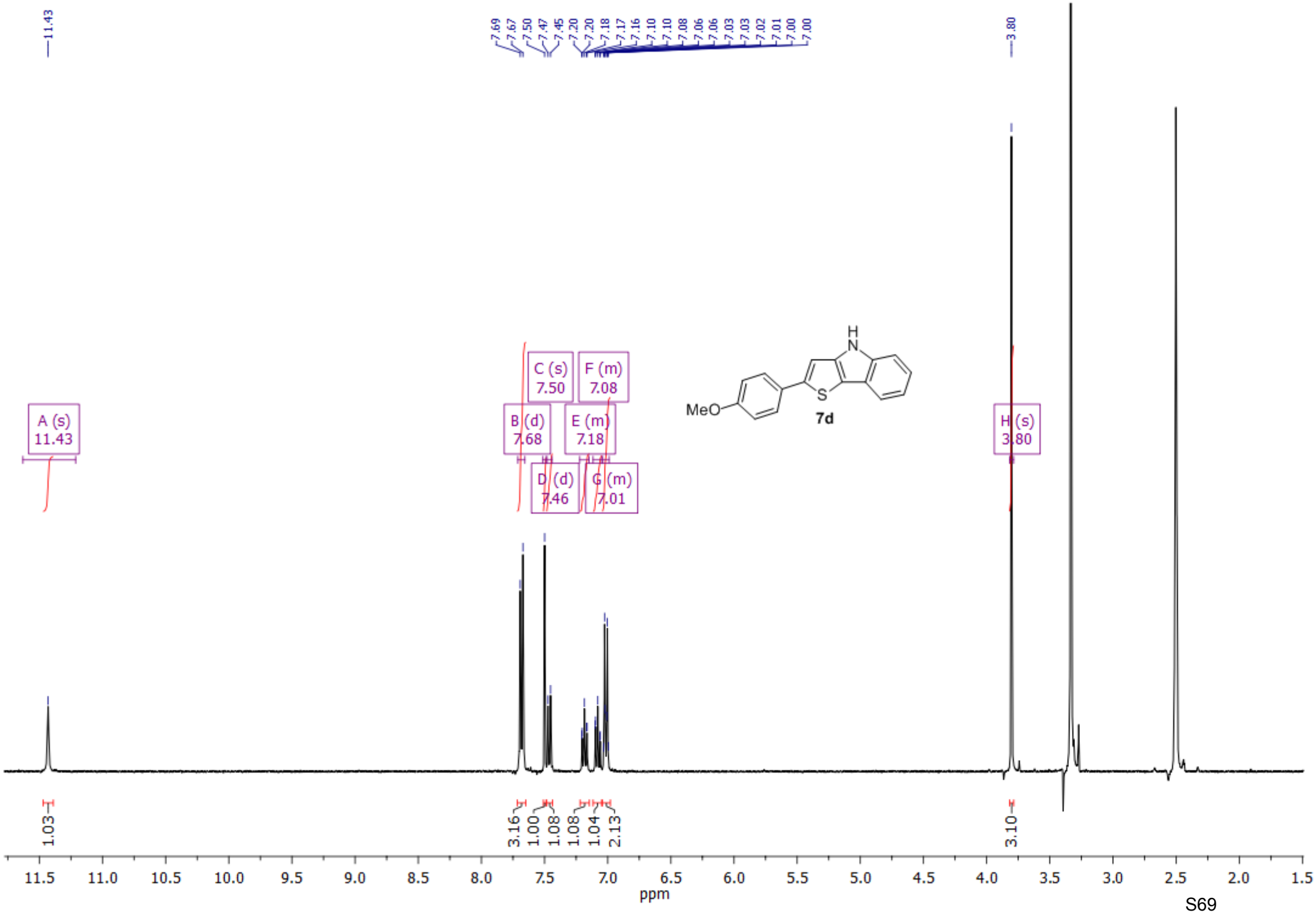
^{1}H NMR (solvent: DMSO-d_6)



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



^{1}H NMR (solvent: DMSO-d_6)



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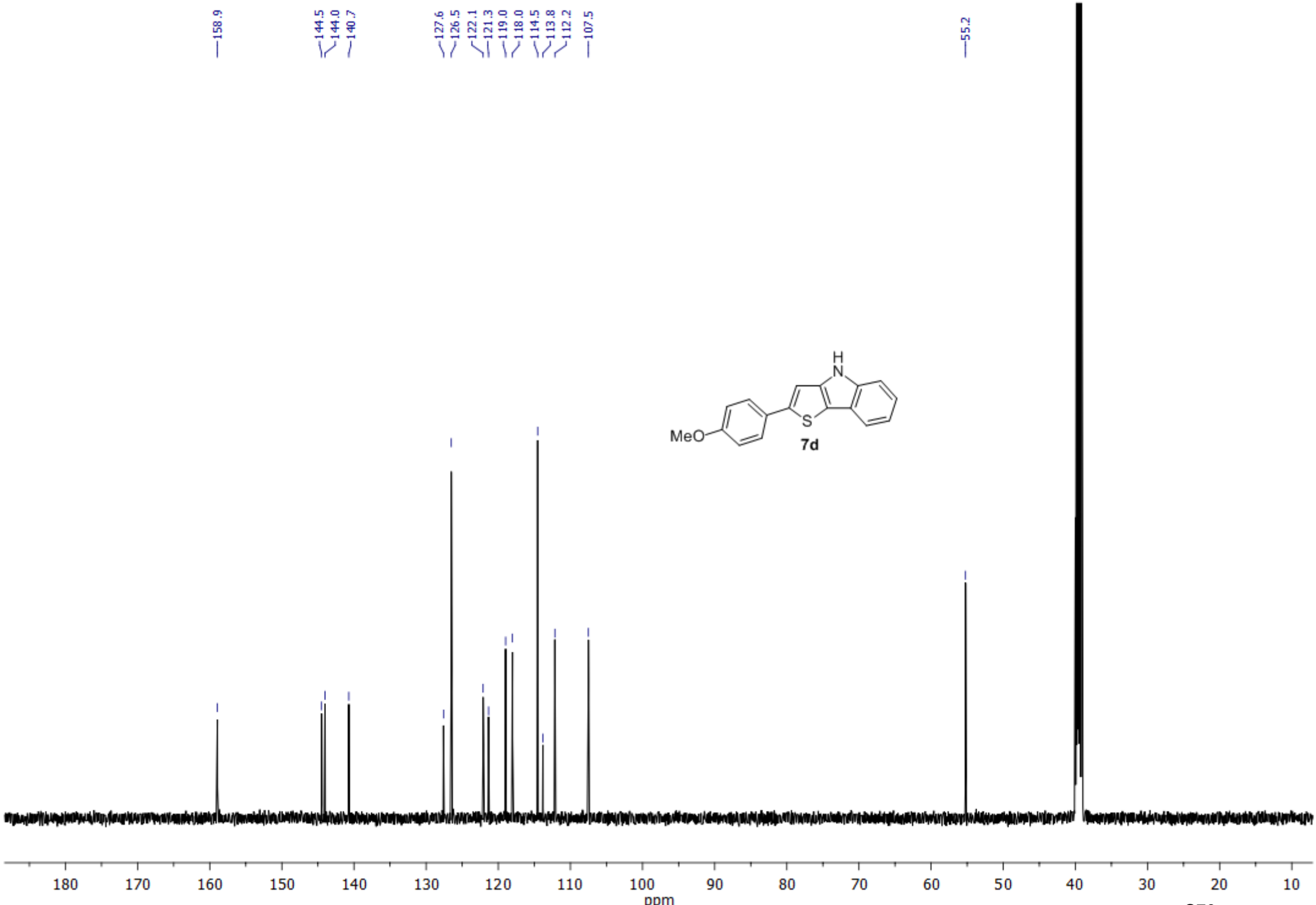
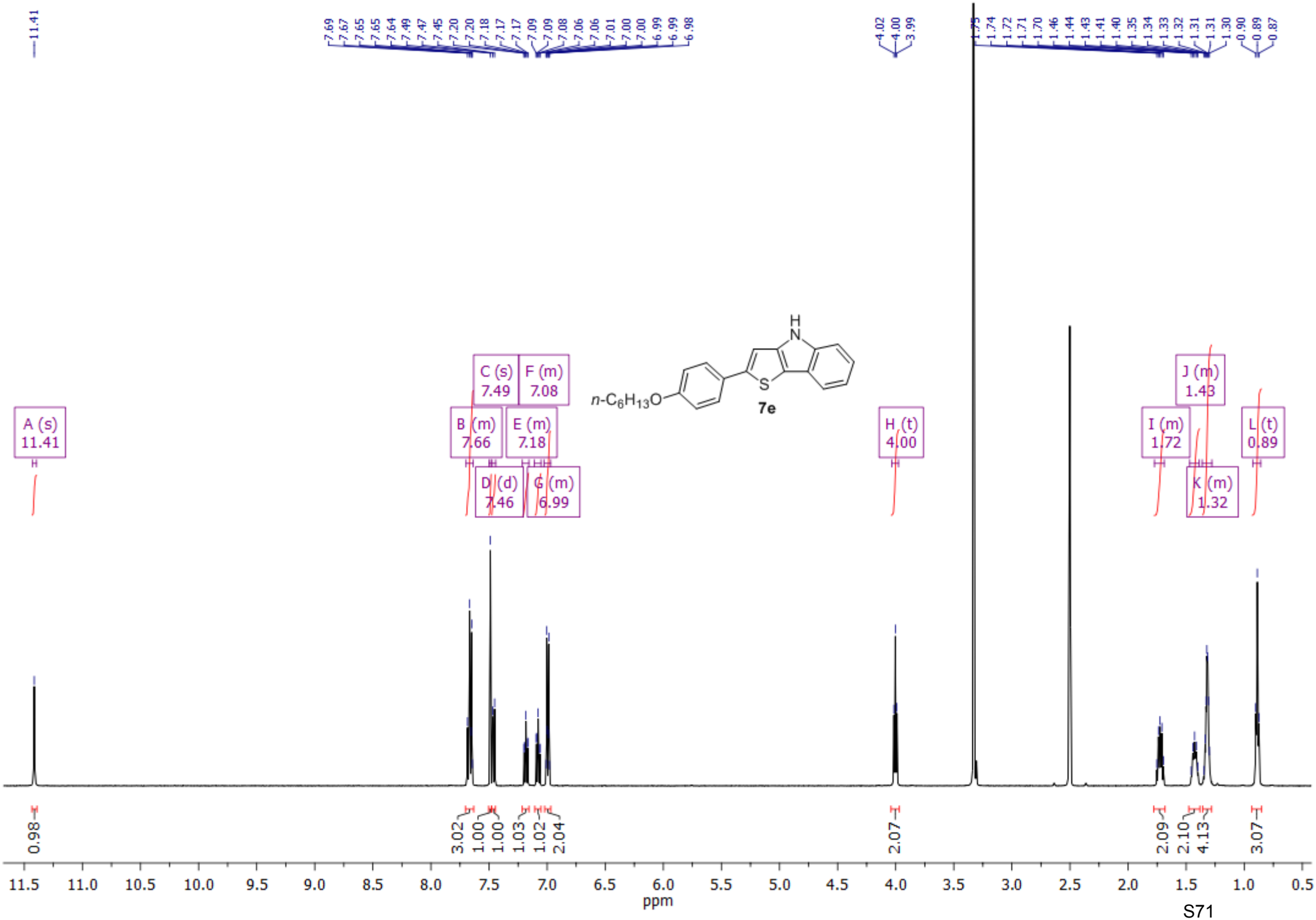


^{1}H NMR (solvent: DMSO-d_6)



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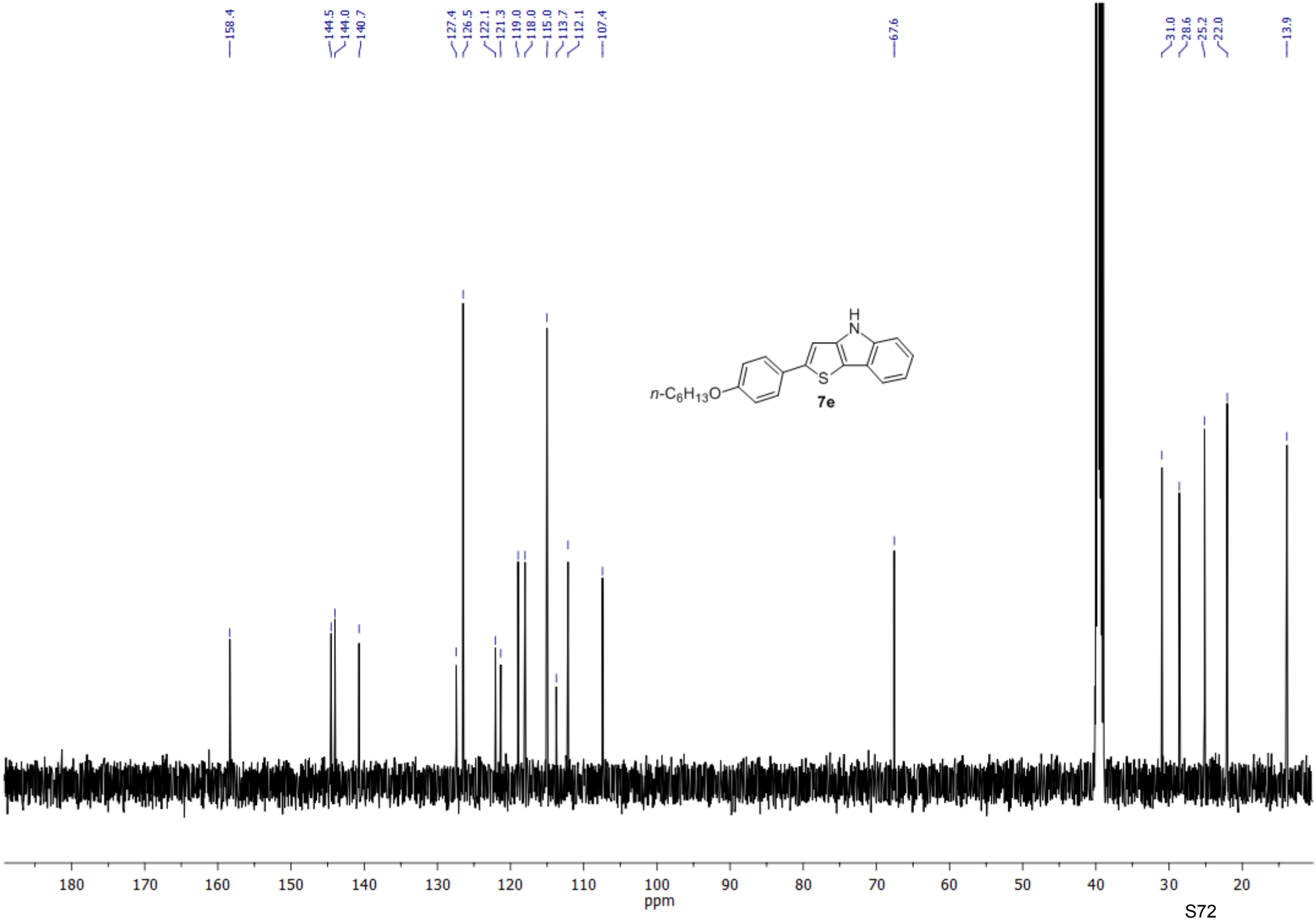

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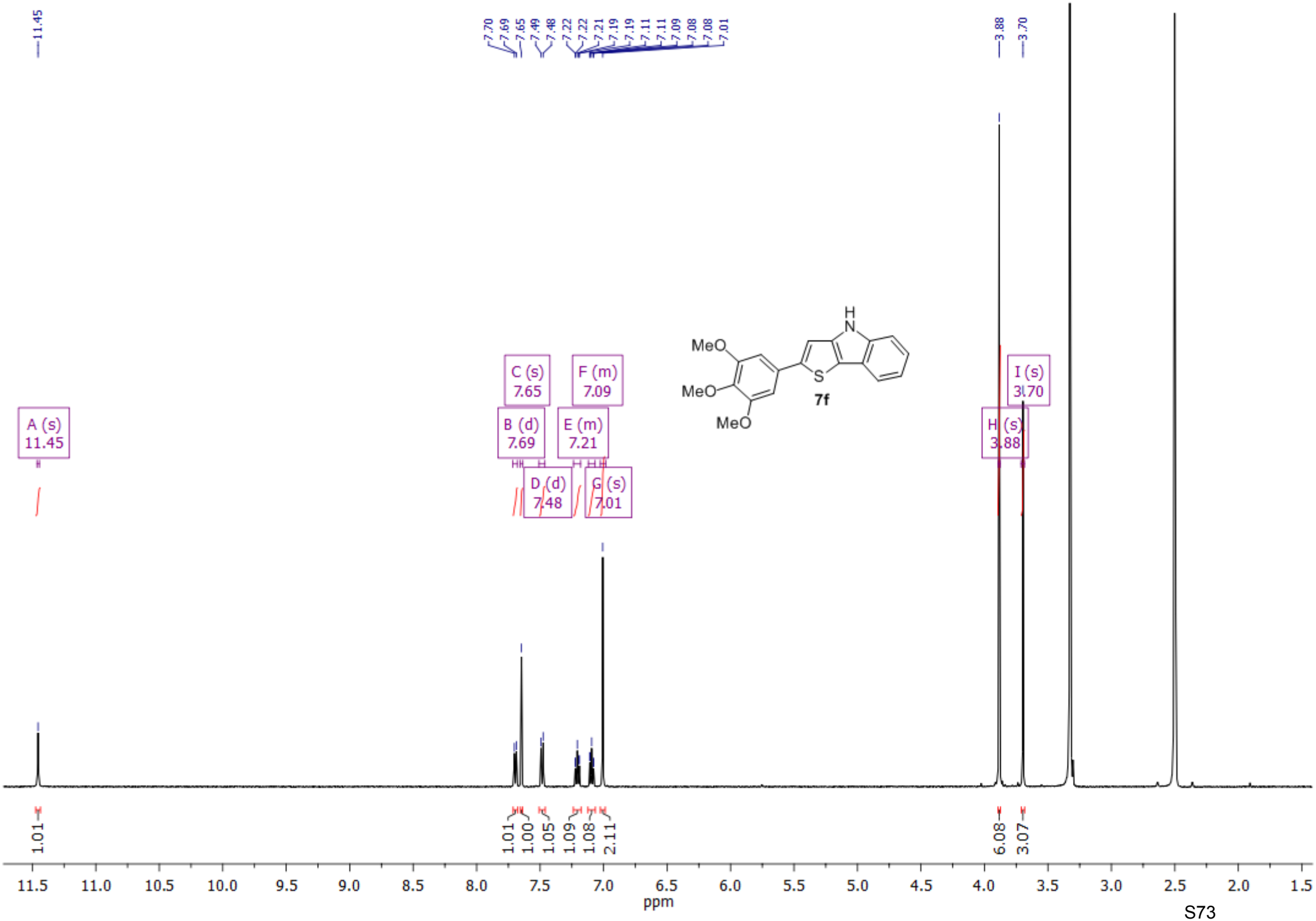

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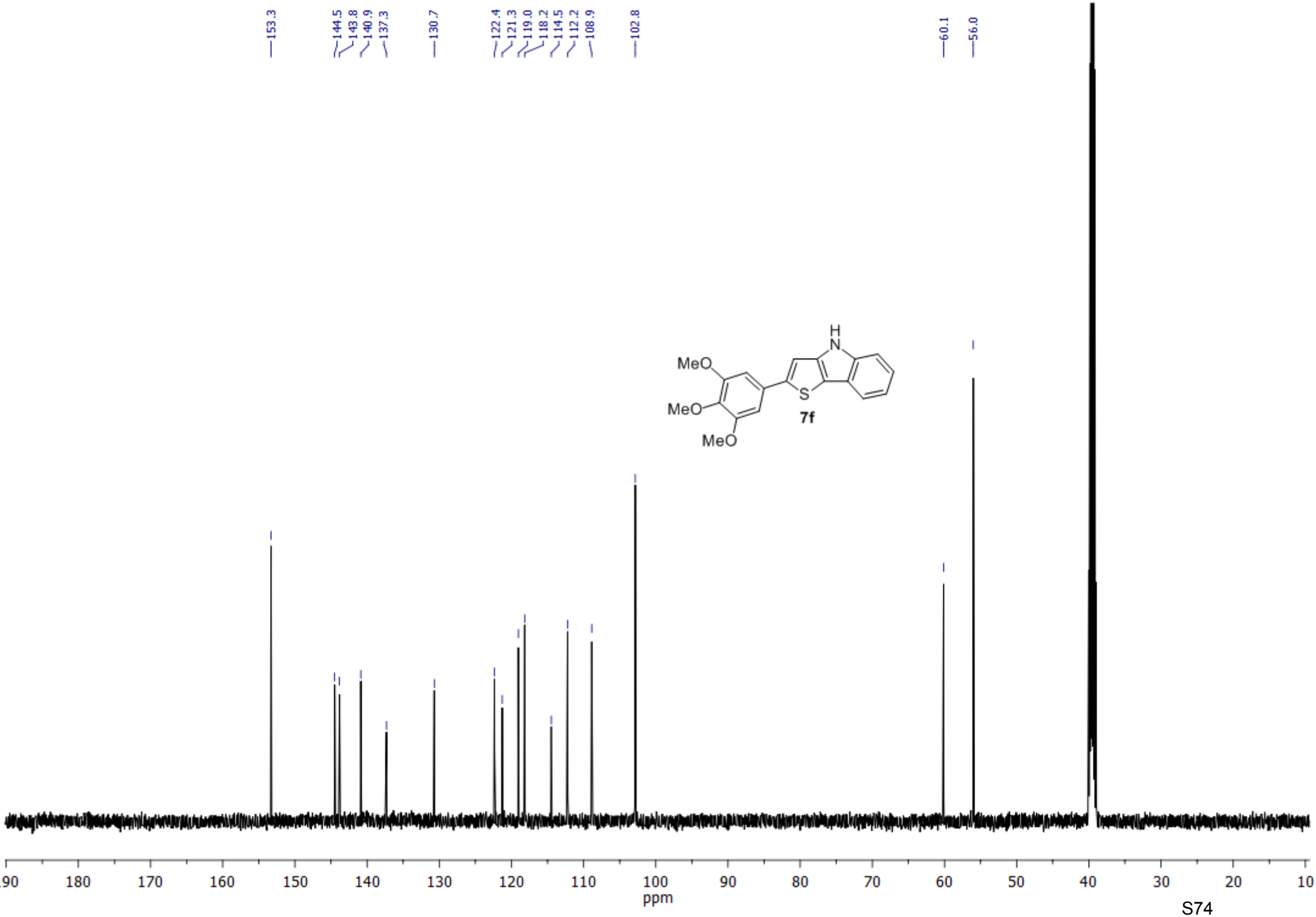
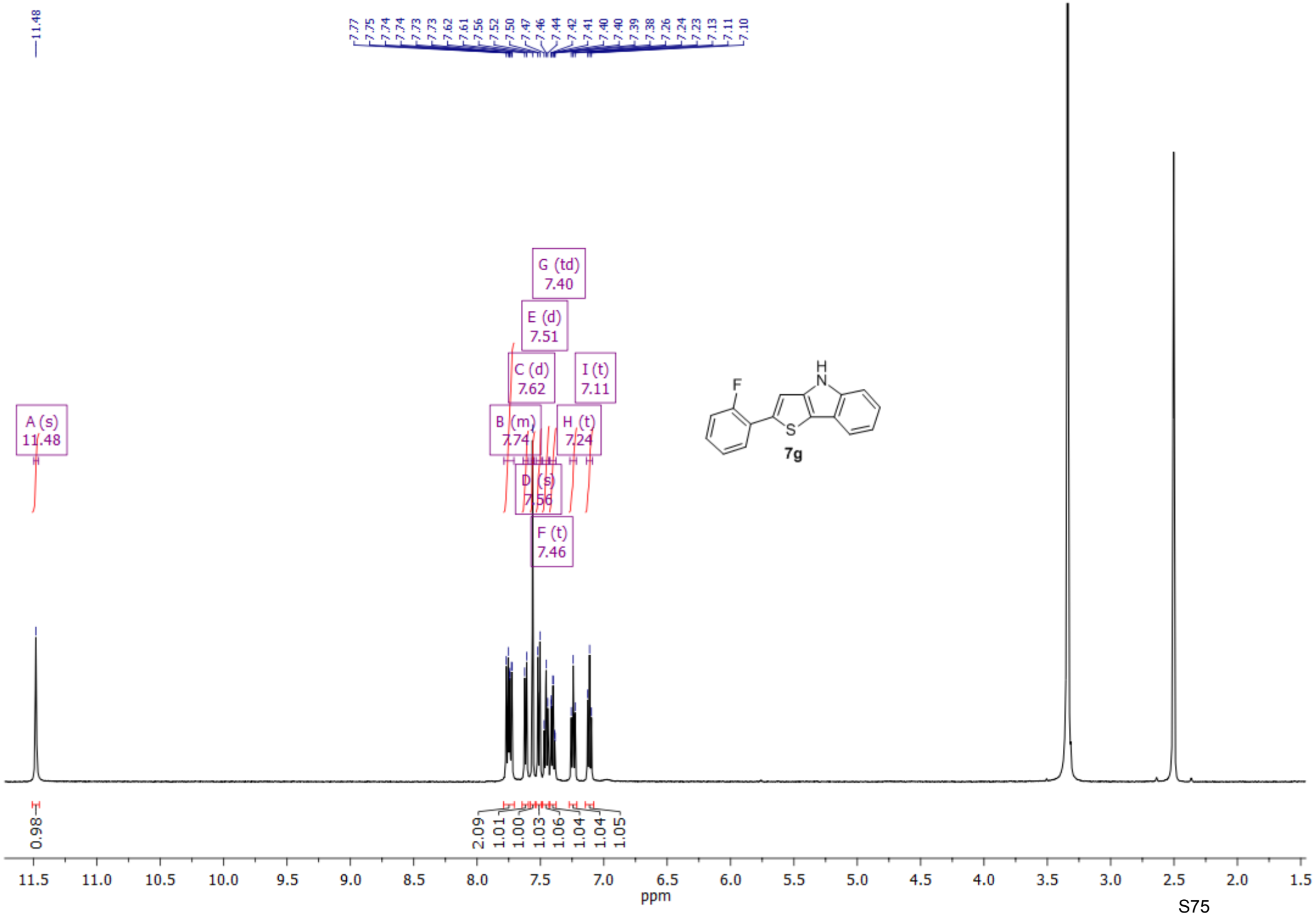
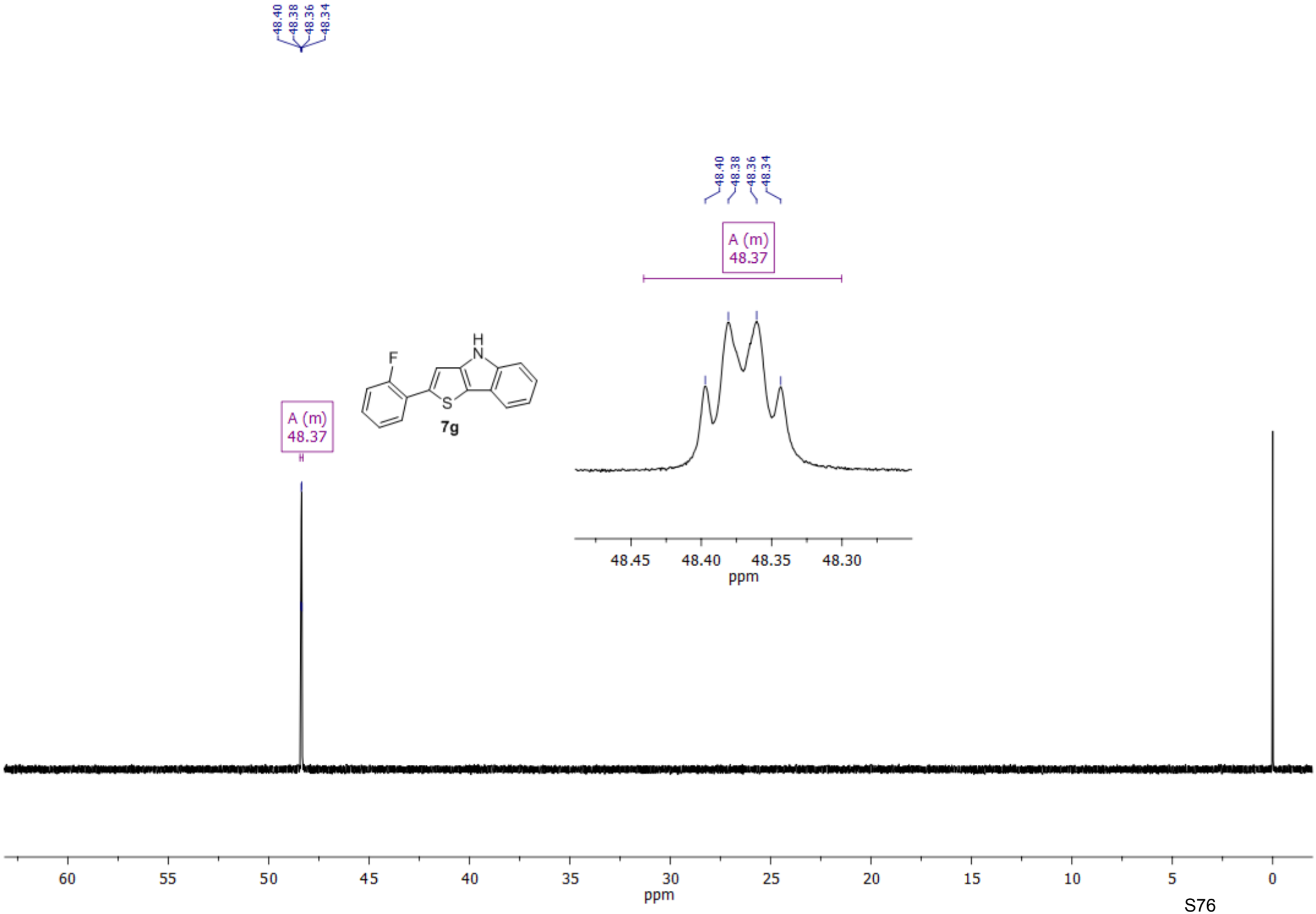


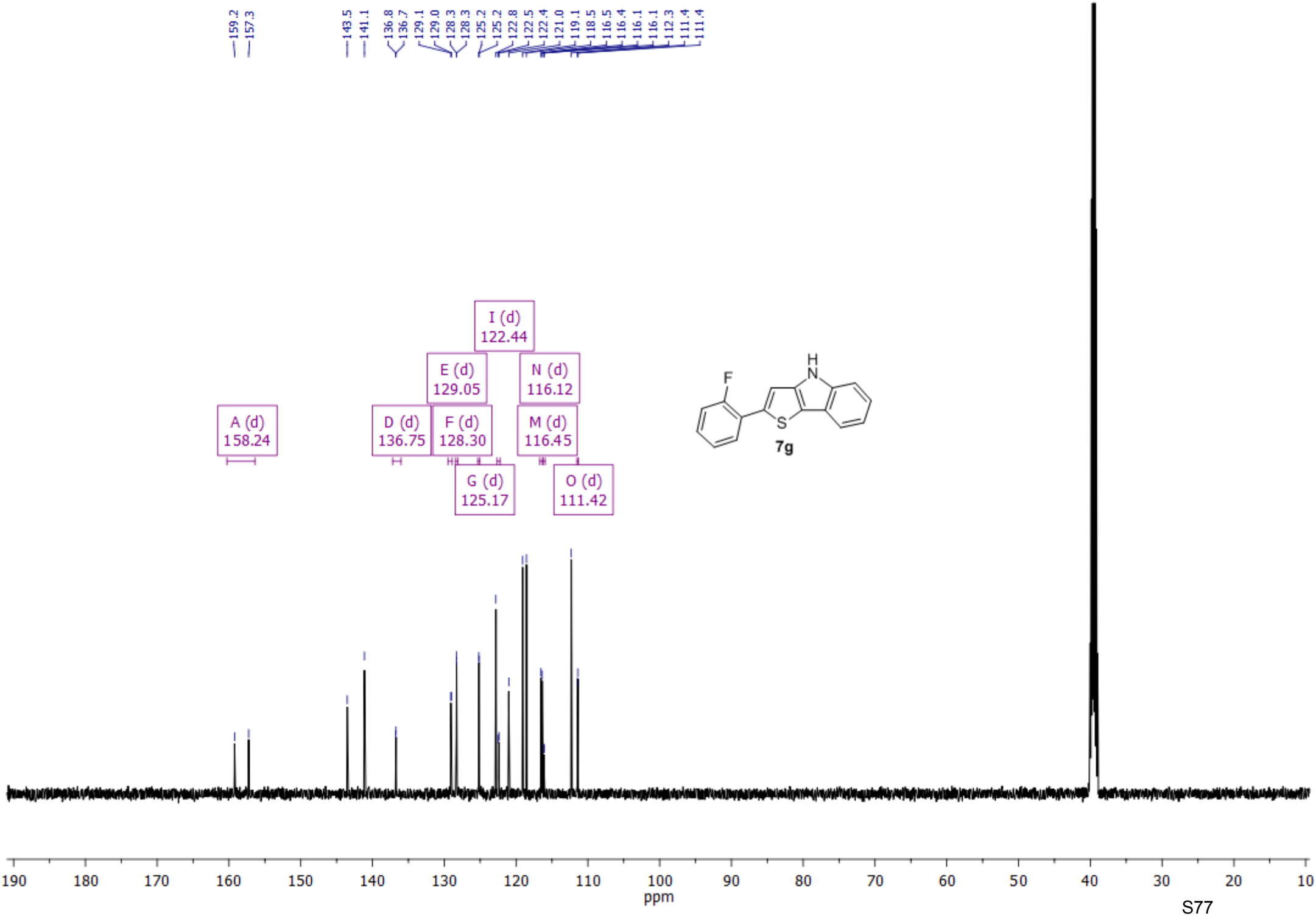
^{1}H NMR (solvent: DMSO-d_6)



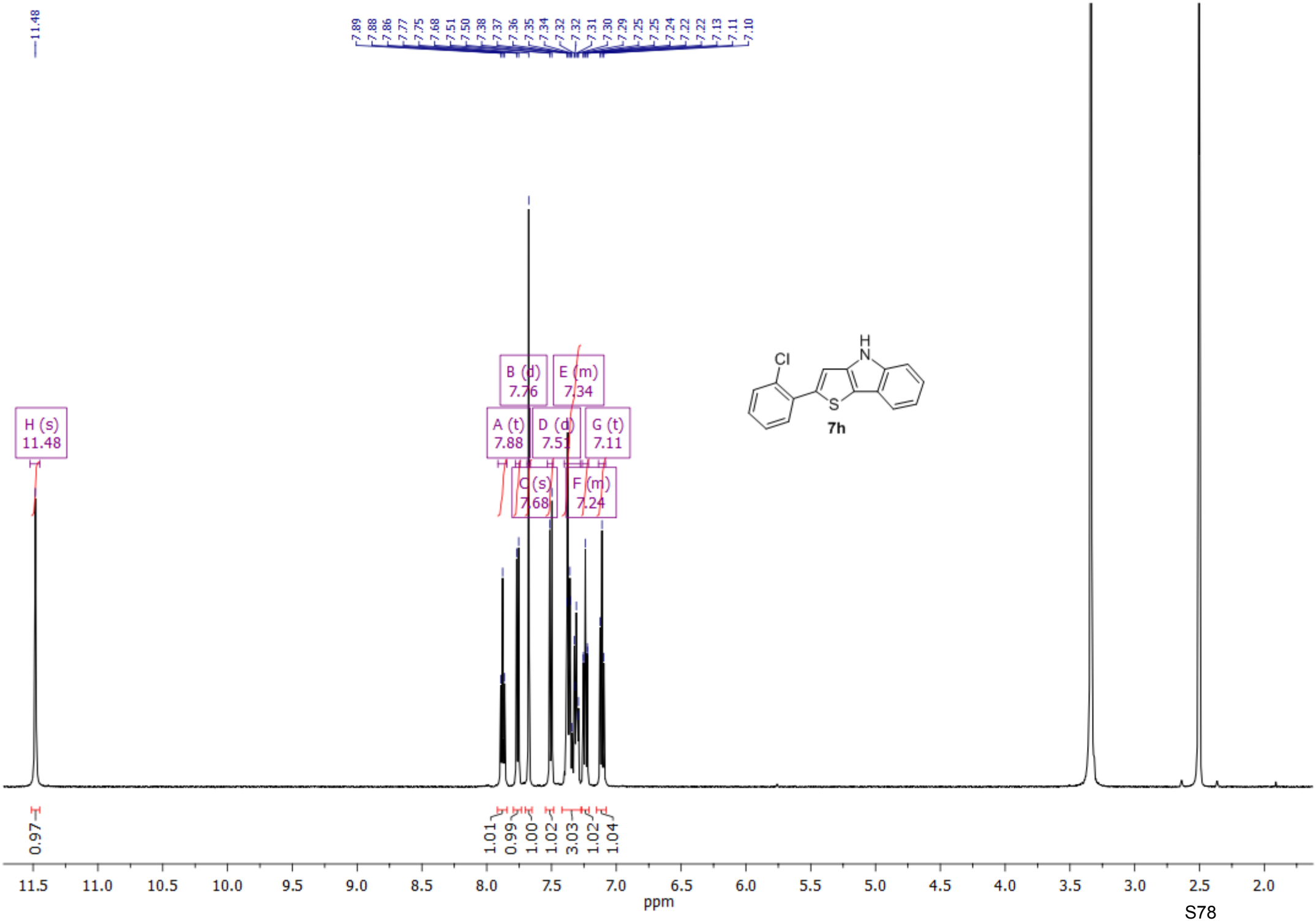
^{19}F NMR (solvent: DMSO-d_6)



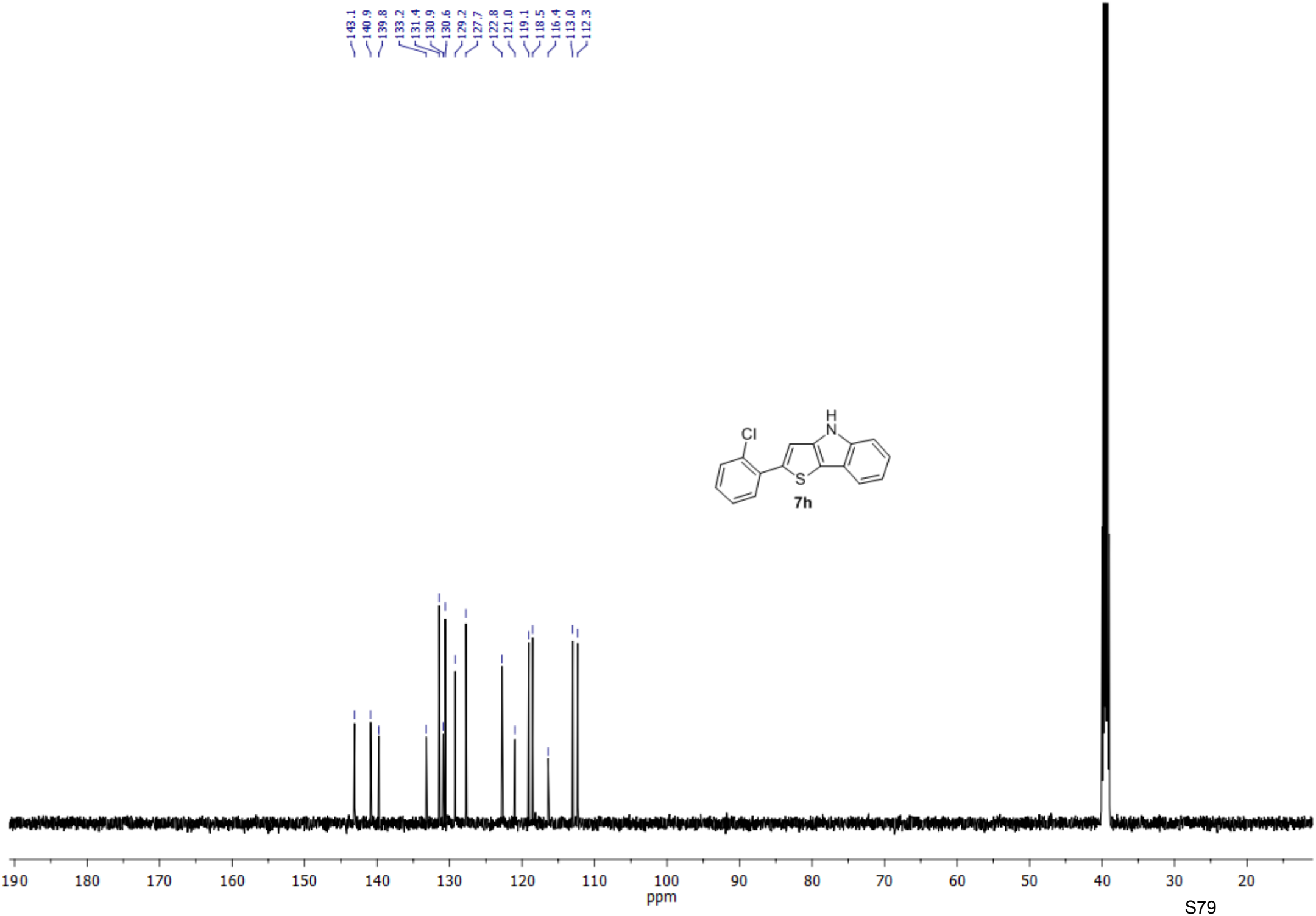
^{13}C NMR (solvent: DMSO-d_6)



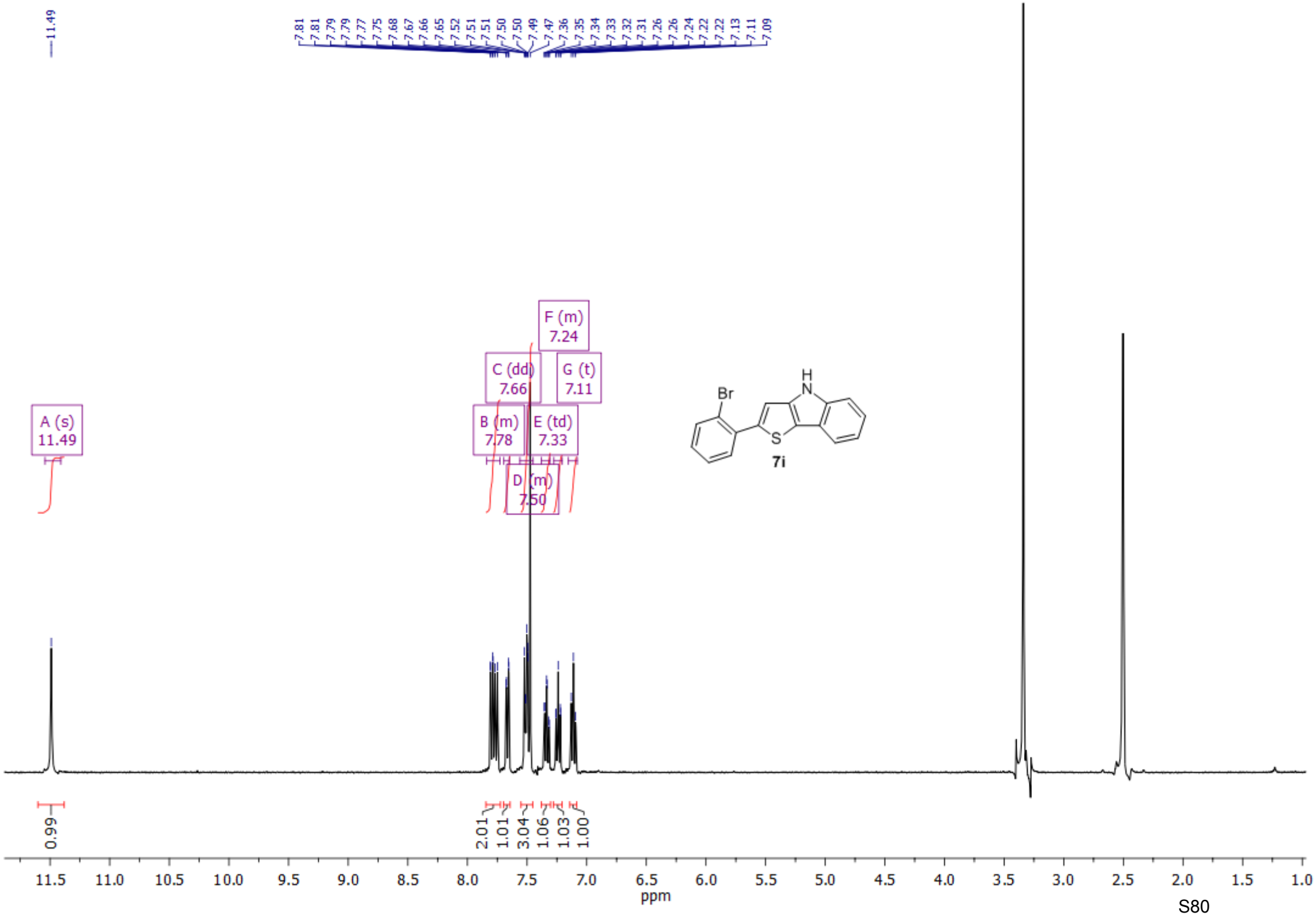
^{1}H NMR (solvent: DMSO-d_6)



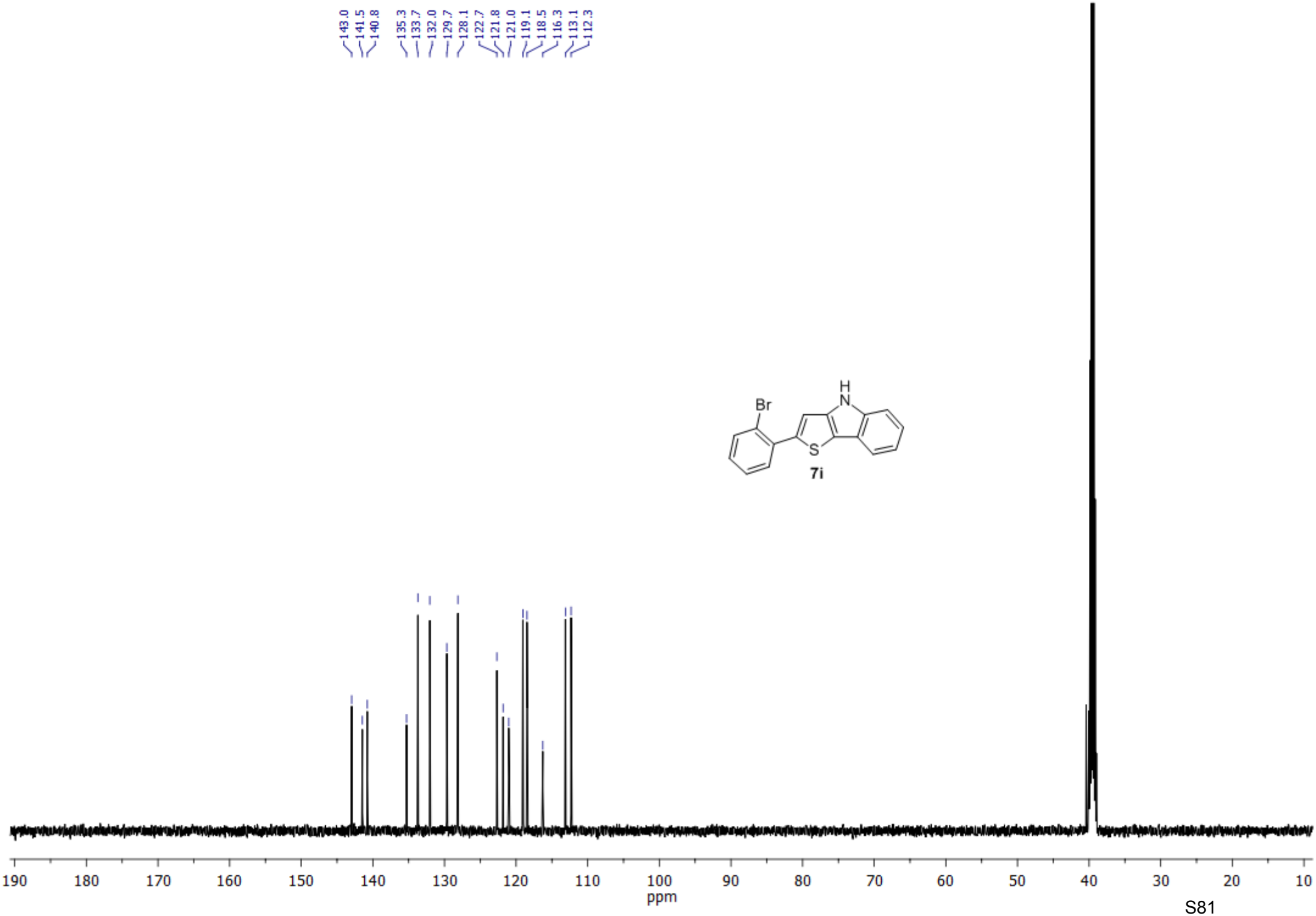
^{13}C NMR (solvent: DMSO-d_6)



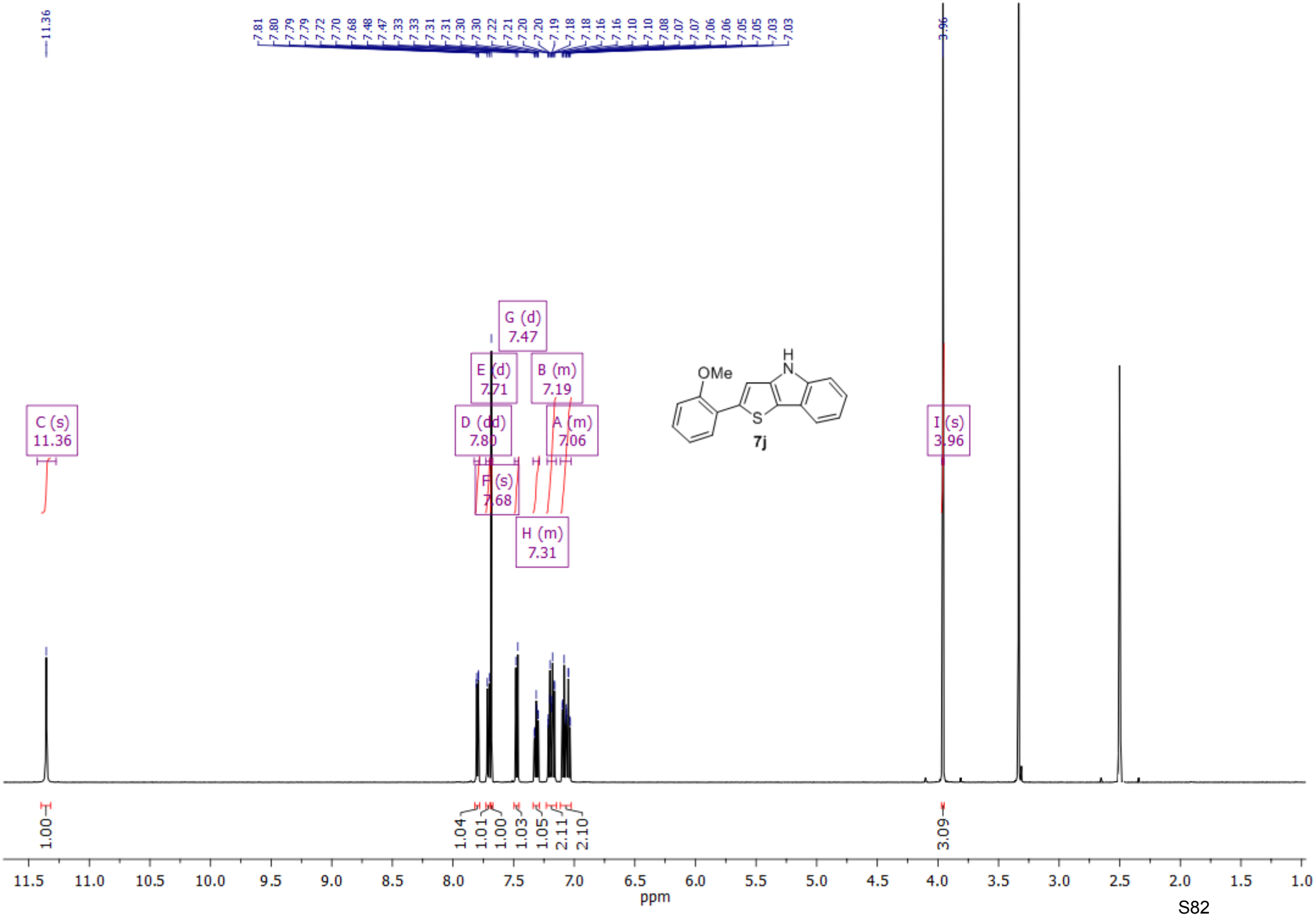
^{1}H NMR (solvent: DMSO-d_6)



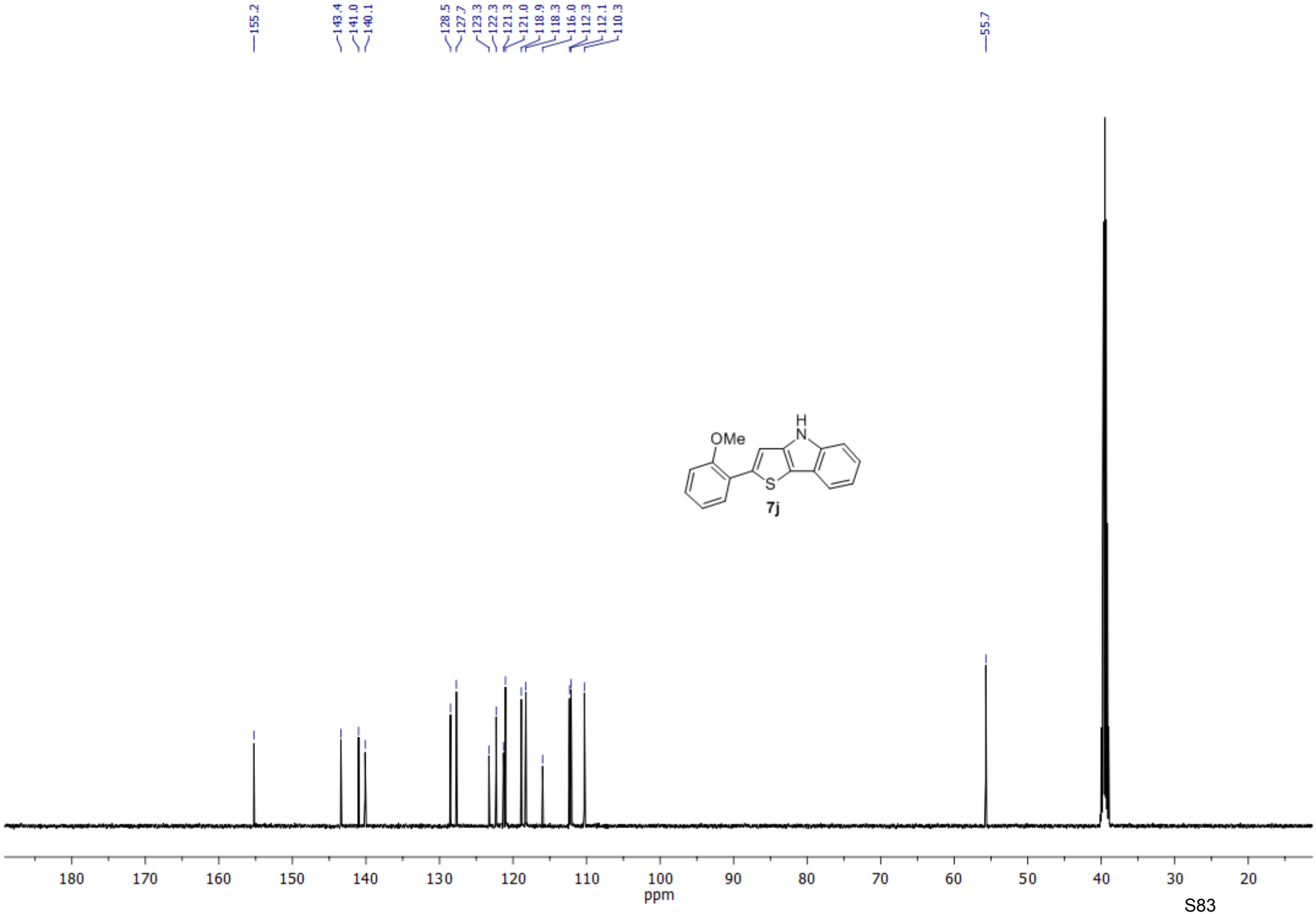
^{13}C NMR (solvent: DMSO-d_6)



^{1}H NMR (solvent: DMSO-d_6)



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



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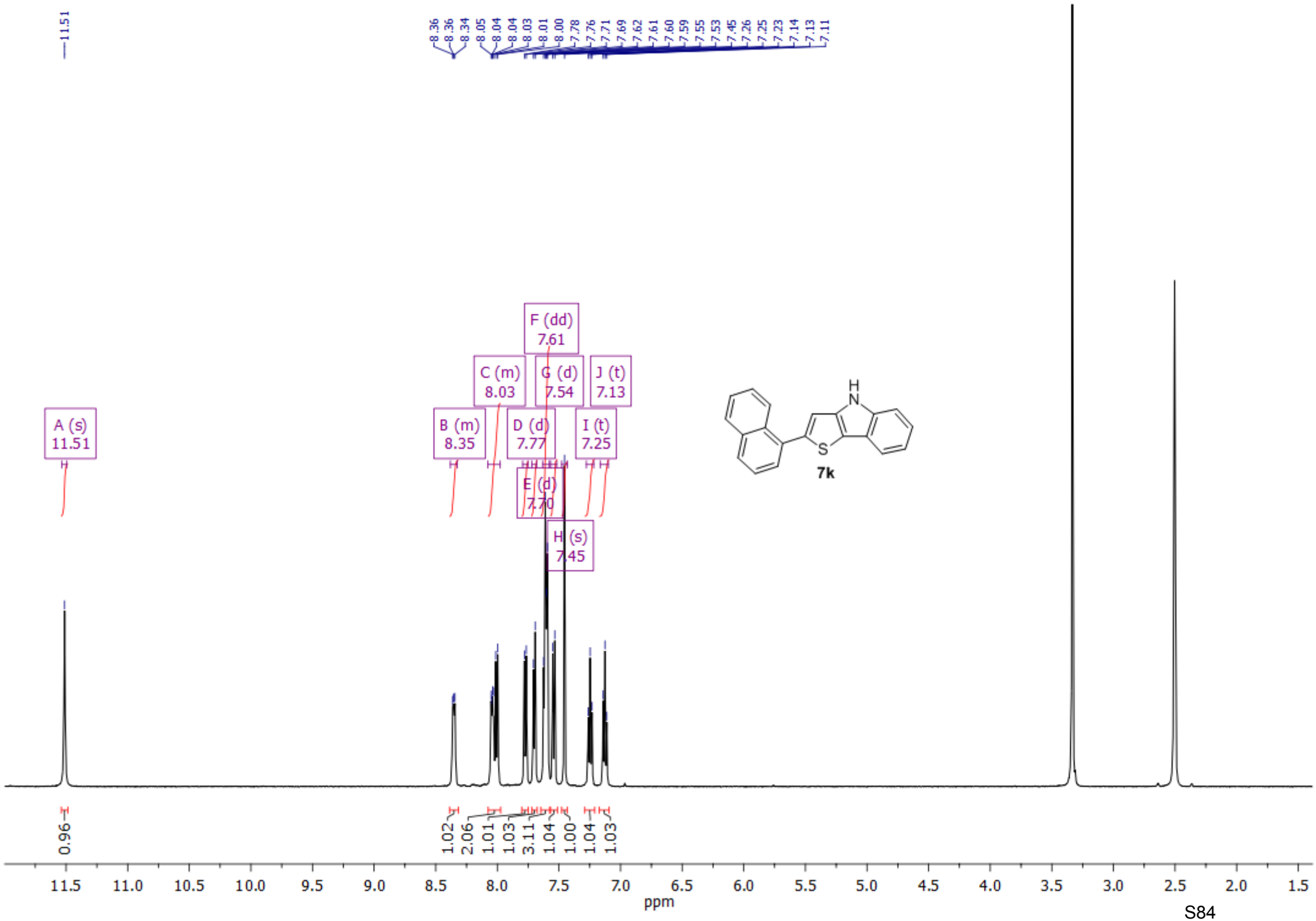

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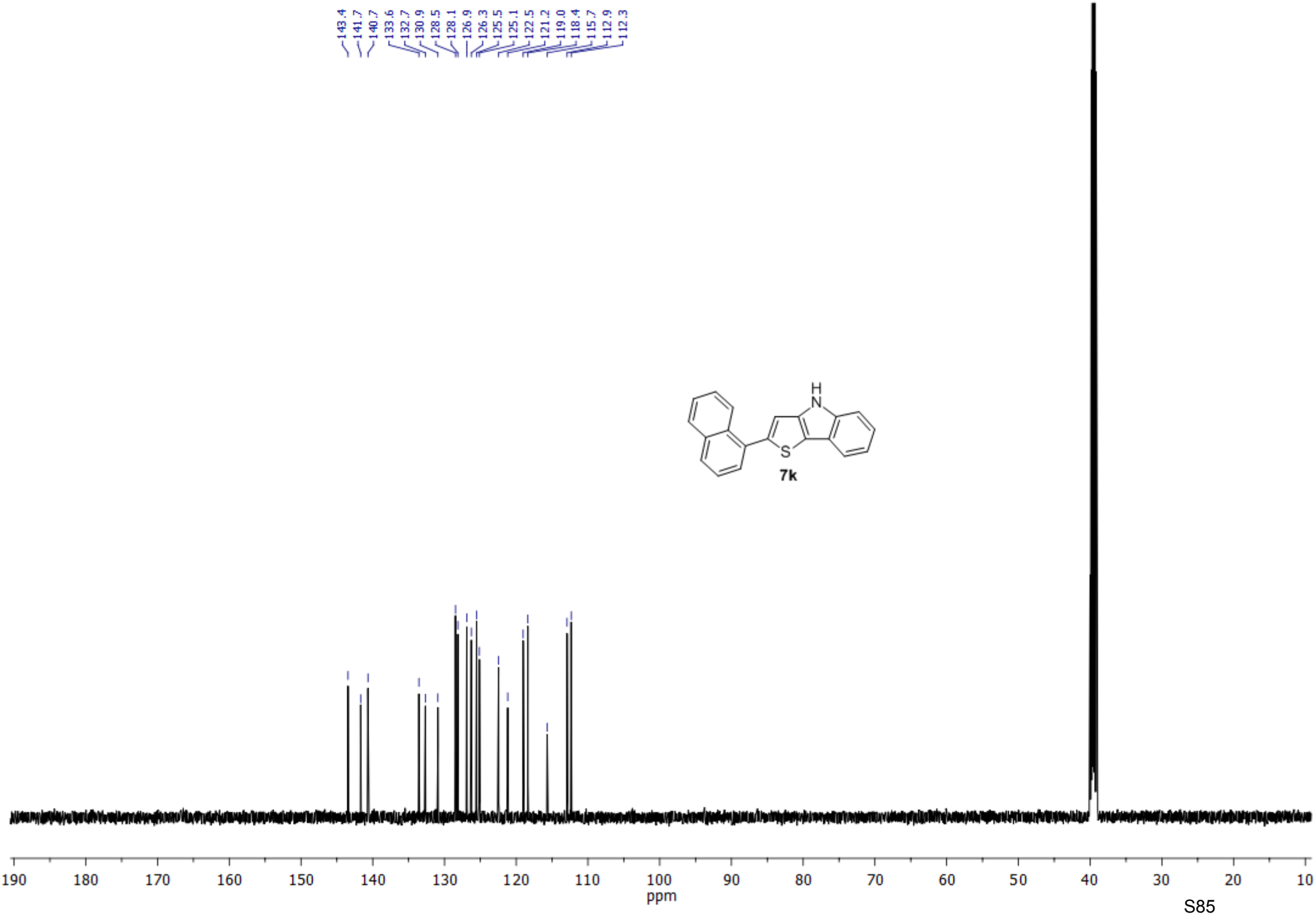
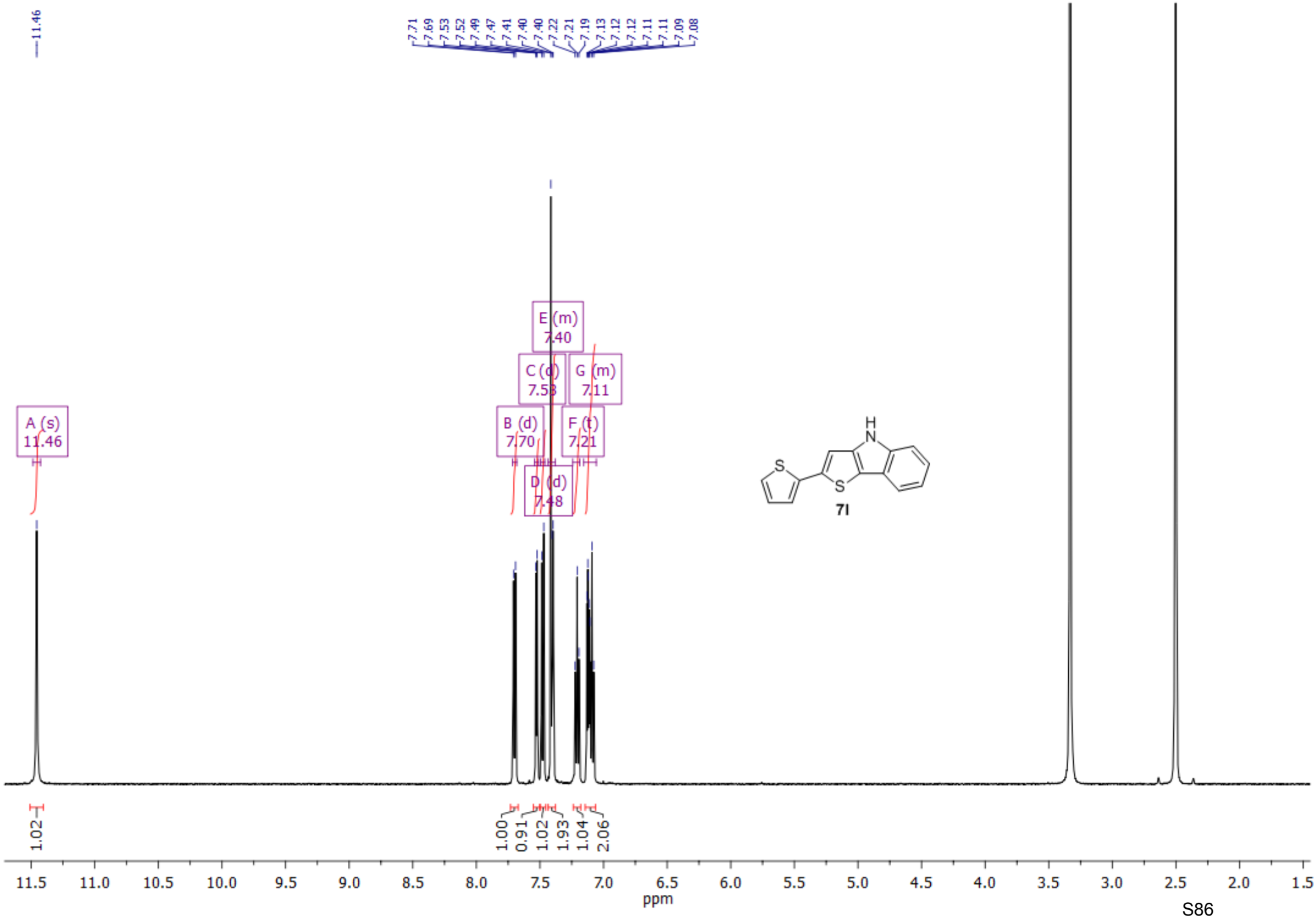


^{1}H NMR (solvent: DMSO-d_6)



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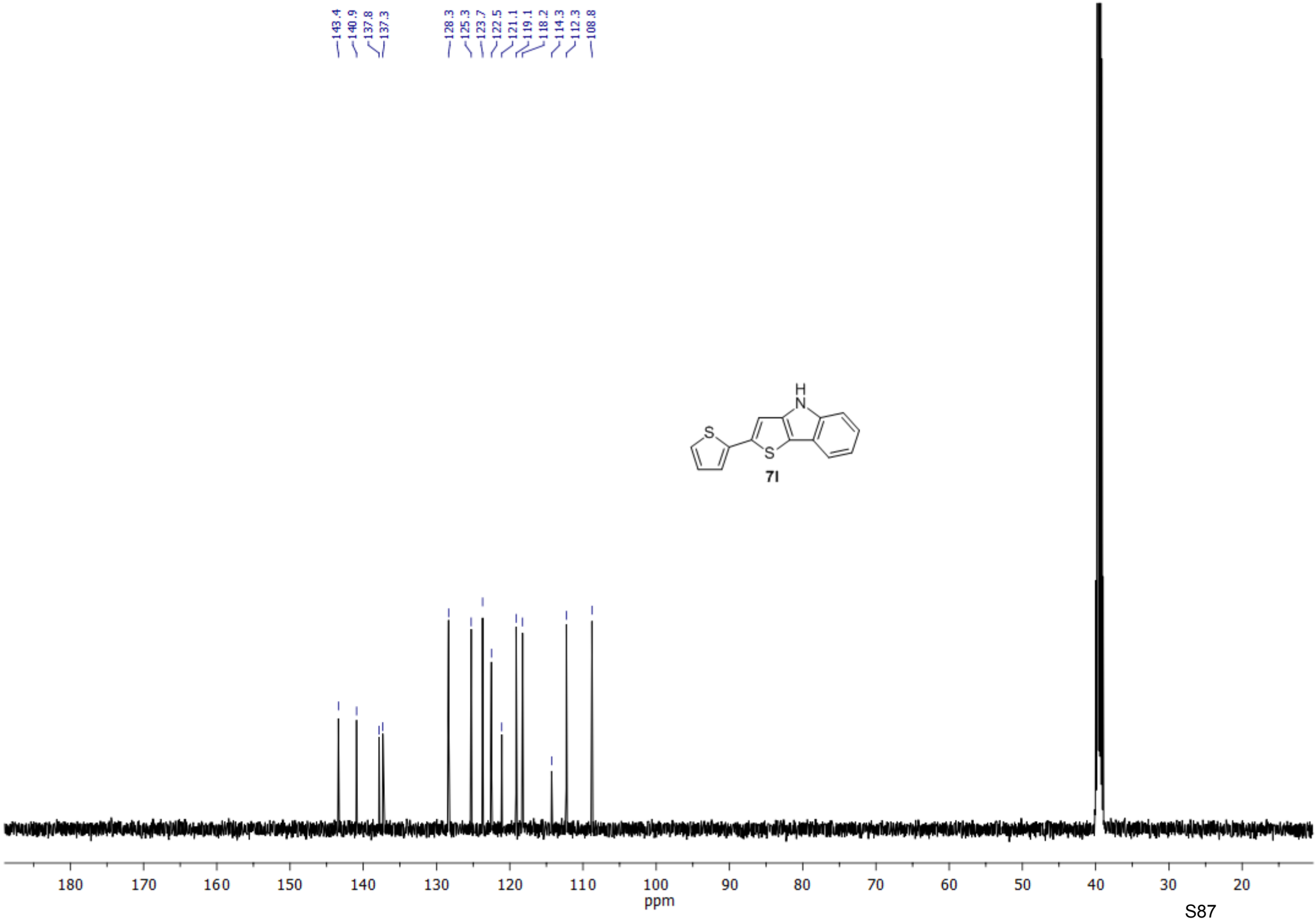
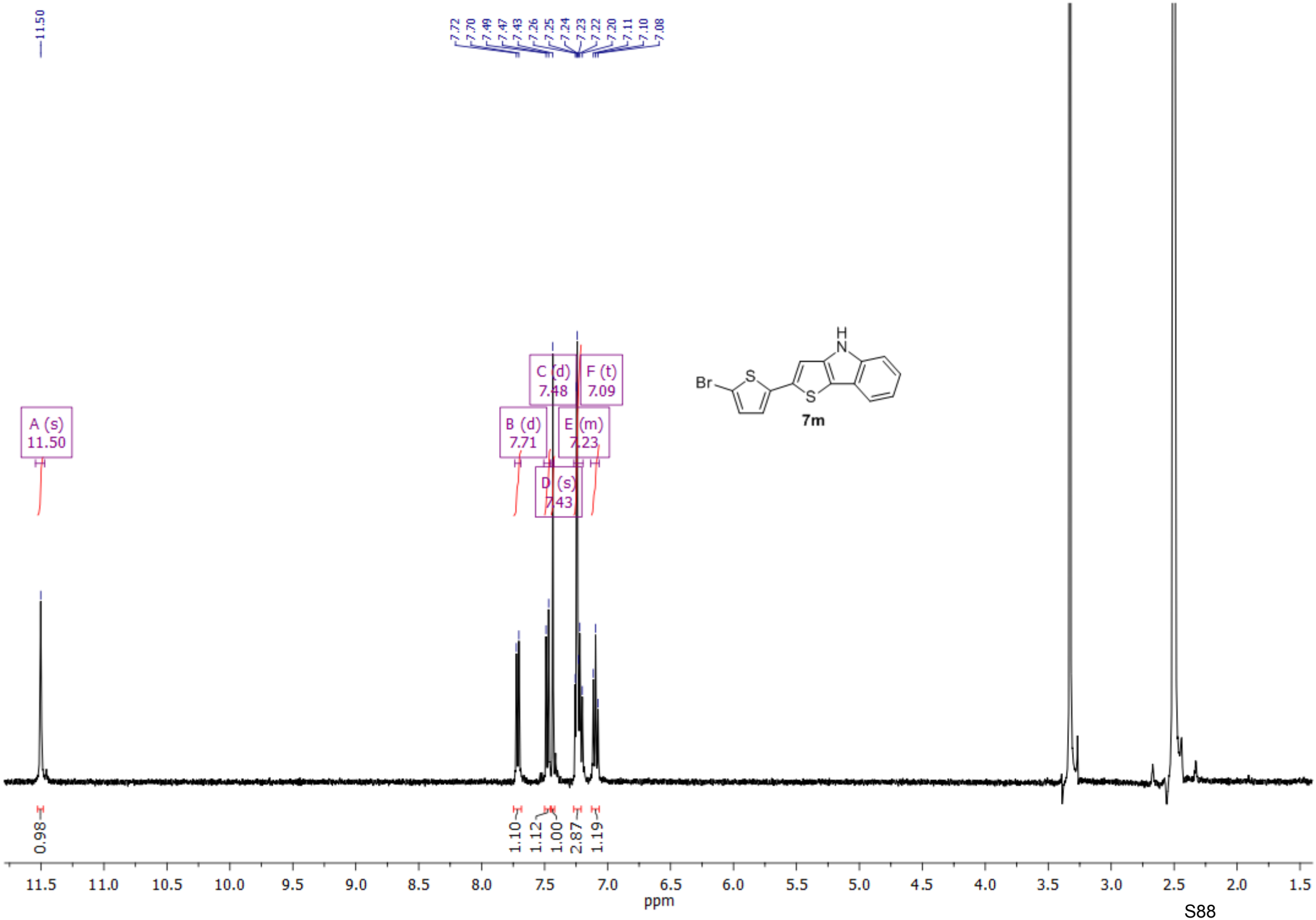
^{13}C NMR (solvent: DMSO-d_6)



^{1}H NMR (solvent: DMSO-d_6)



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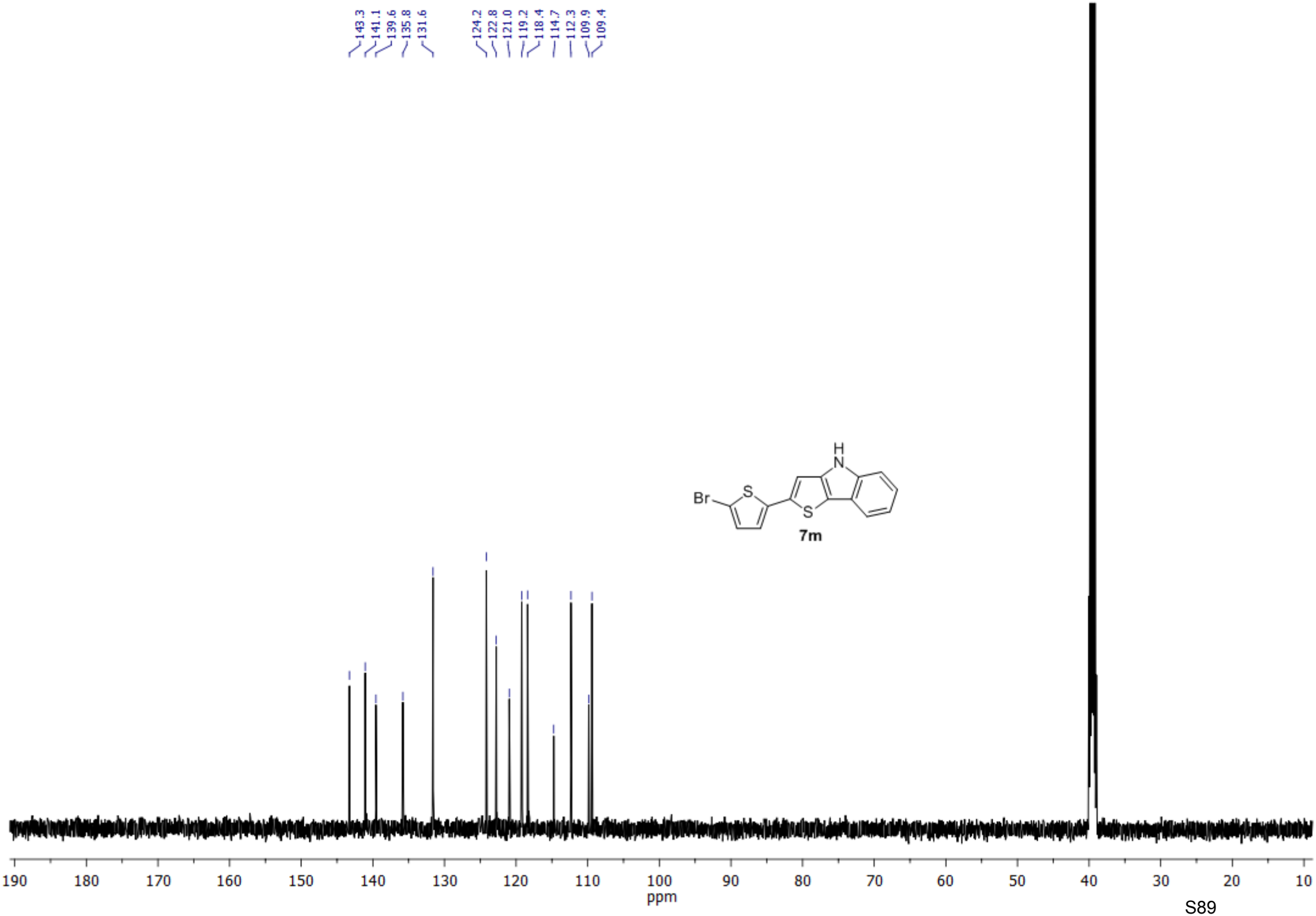

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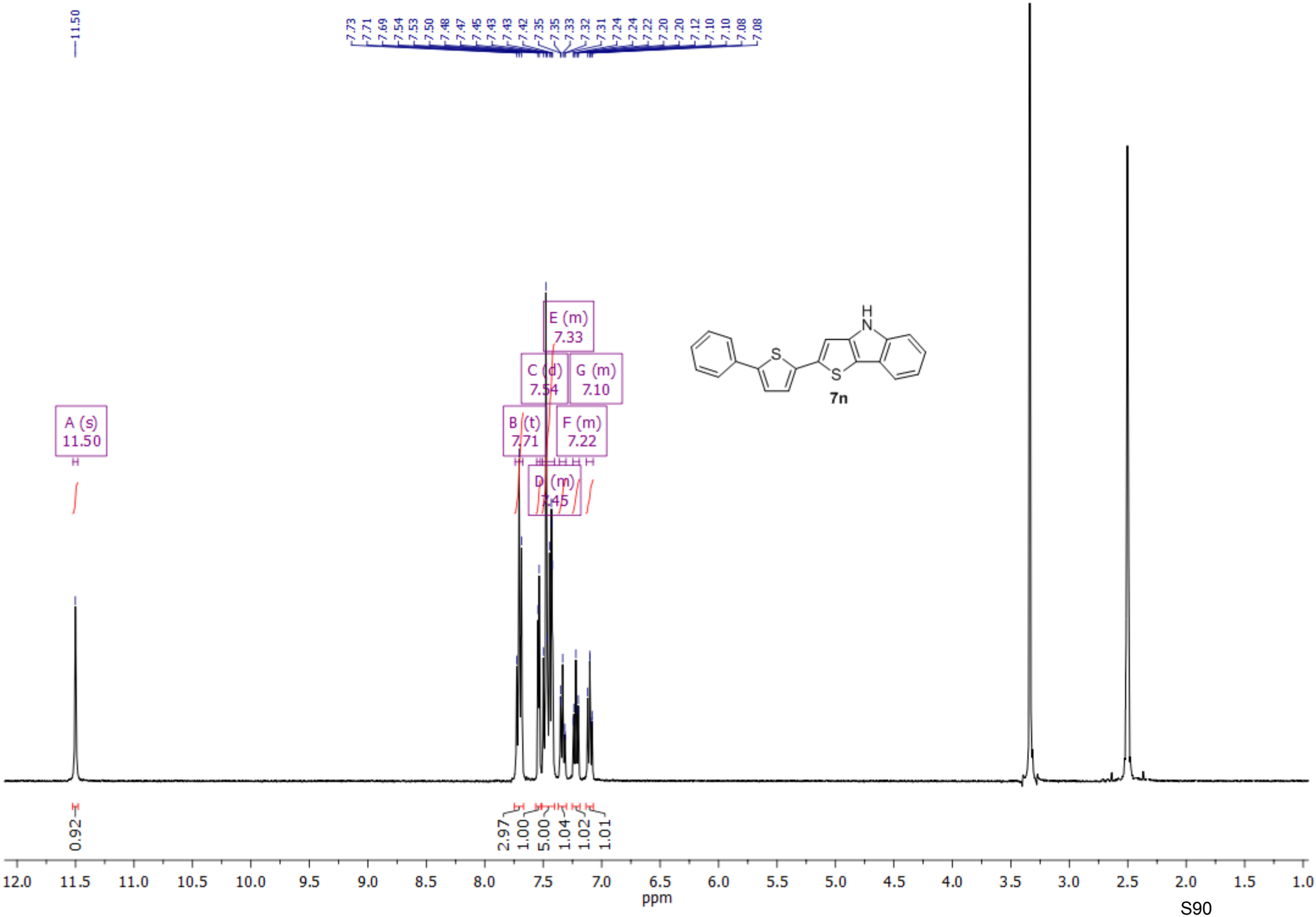

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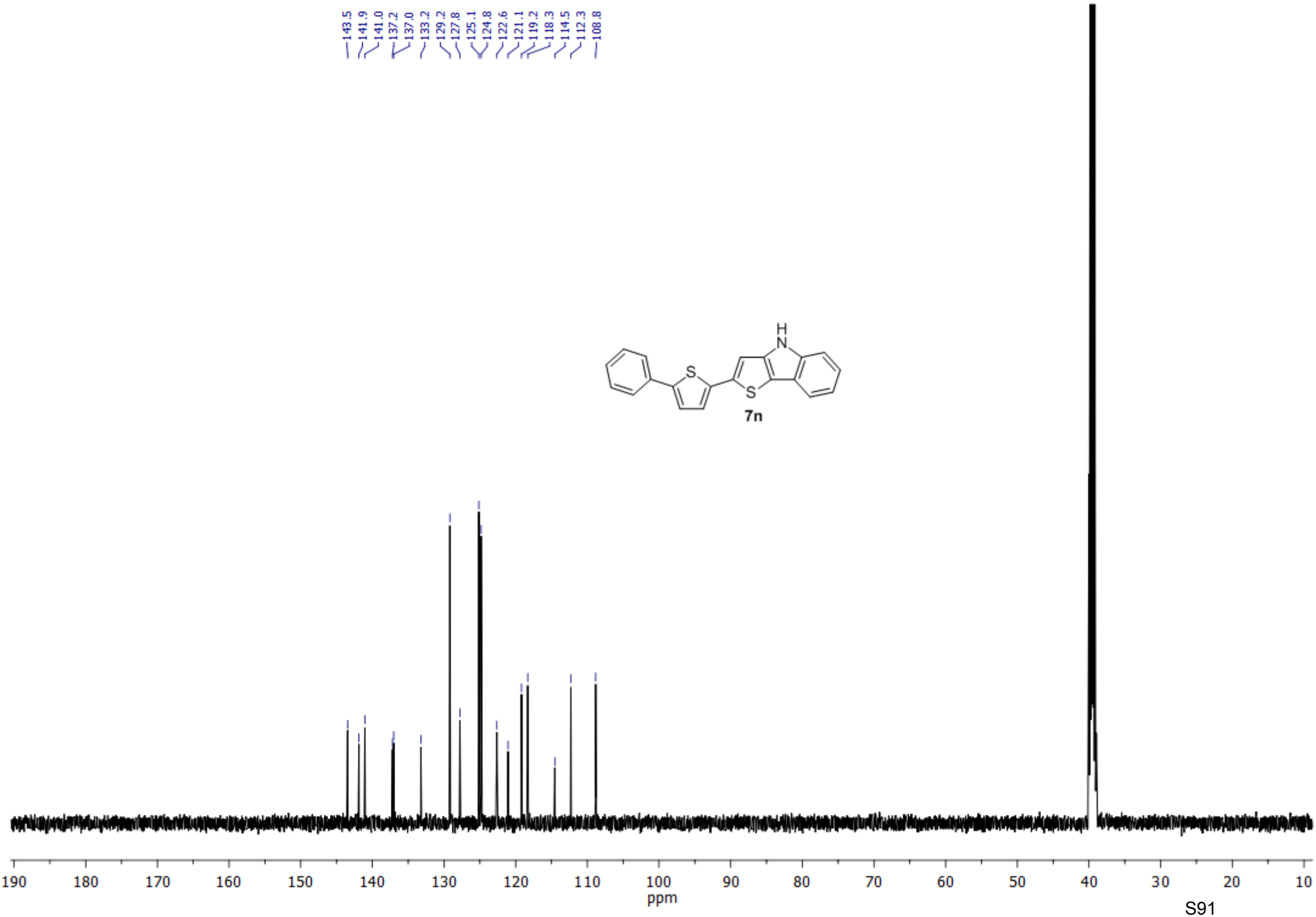

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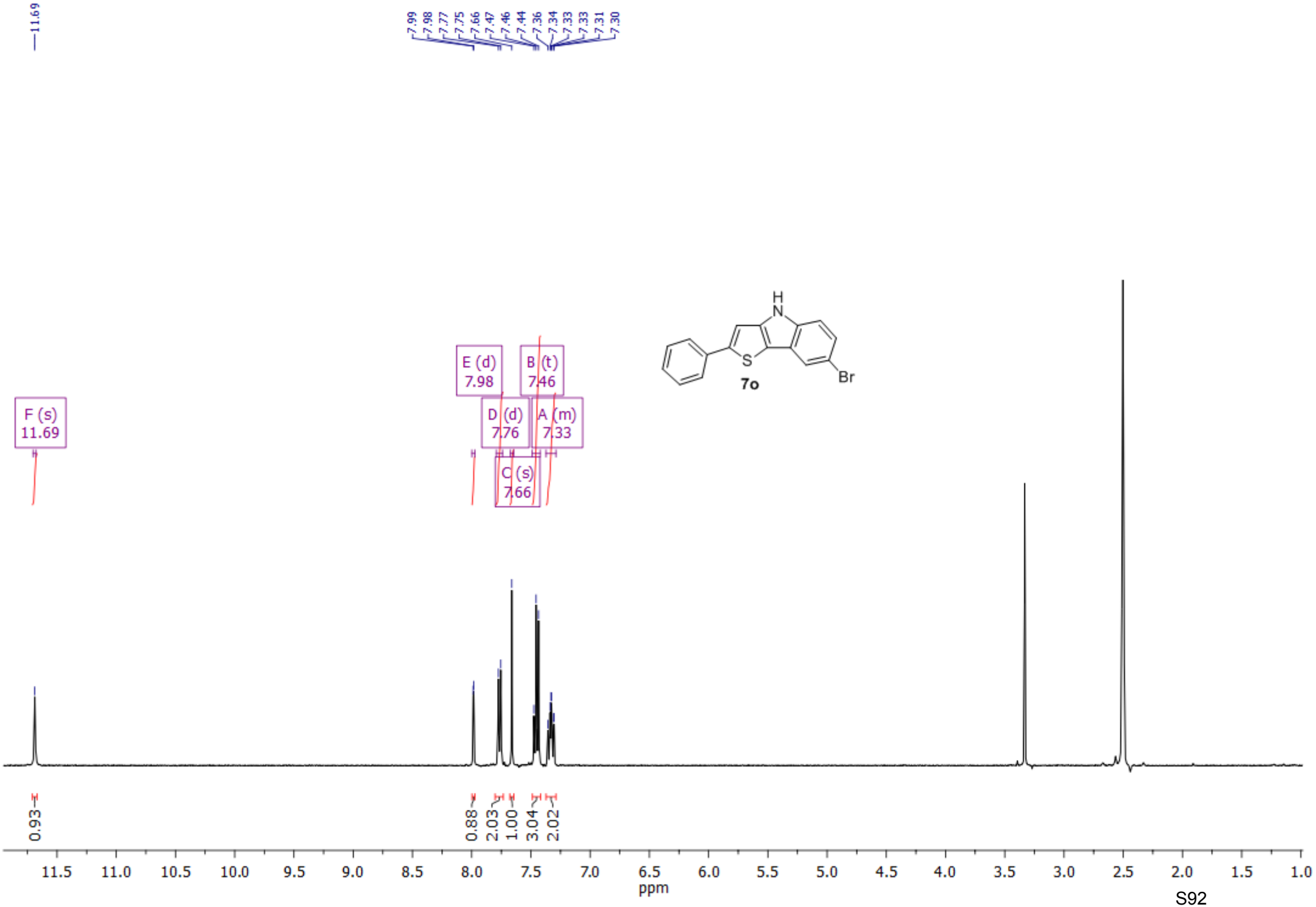

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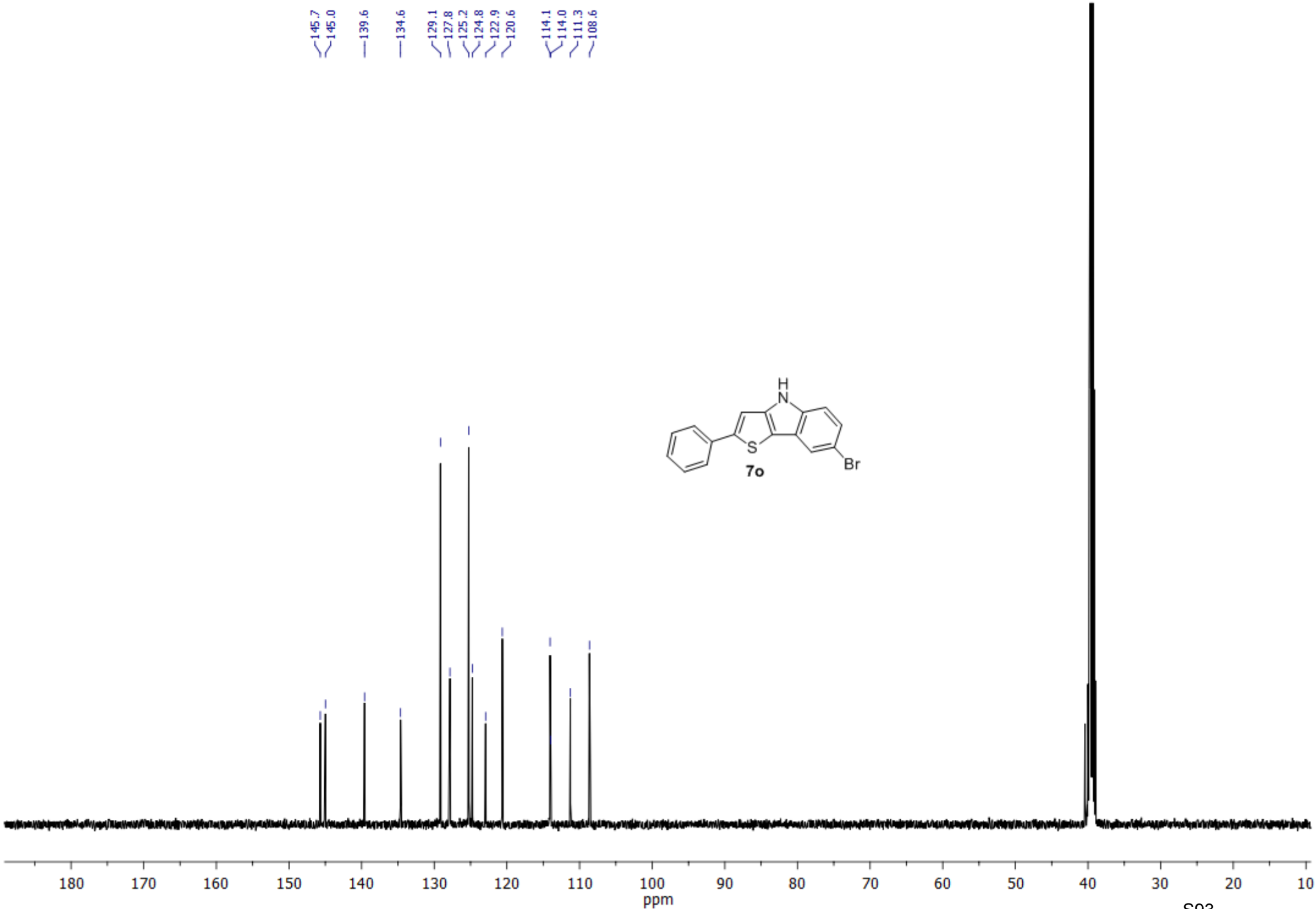

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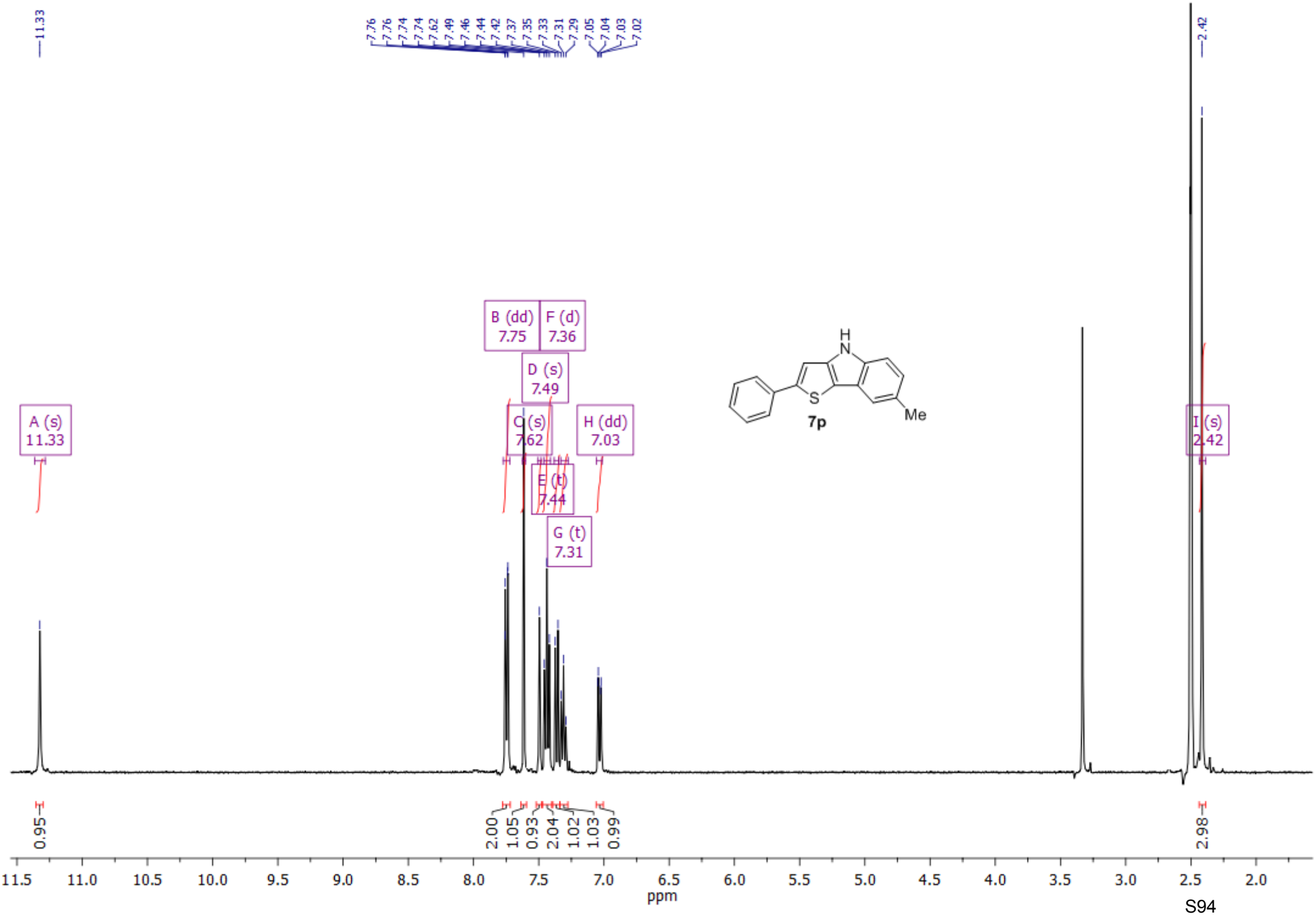

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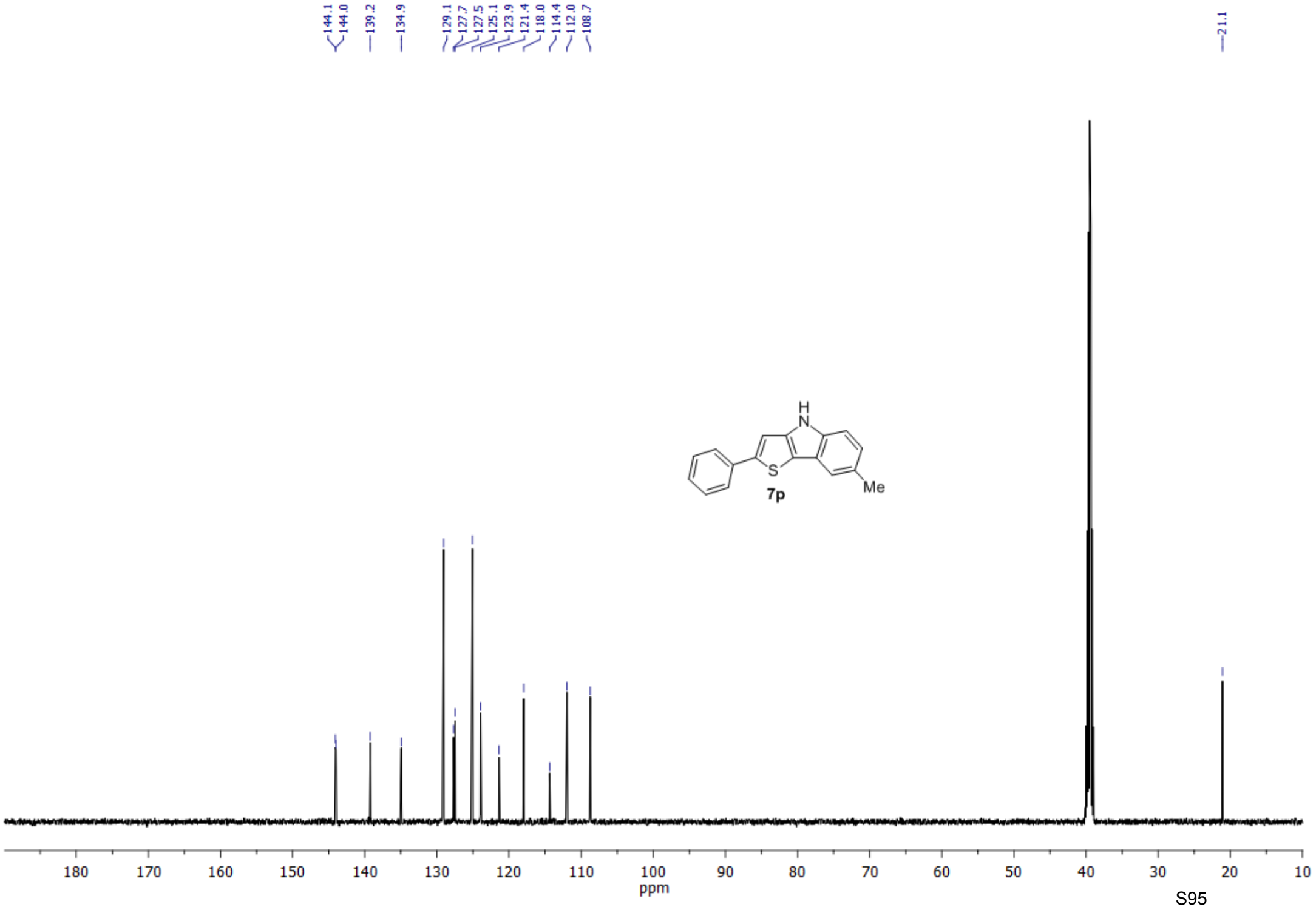

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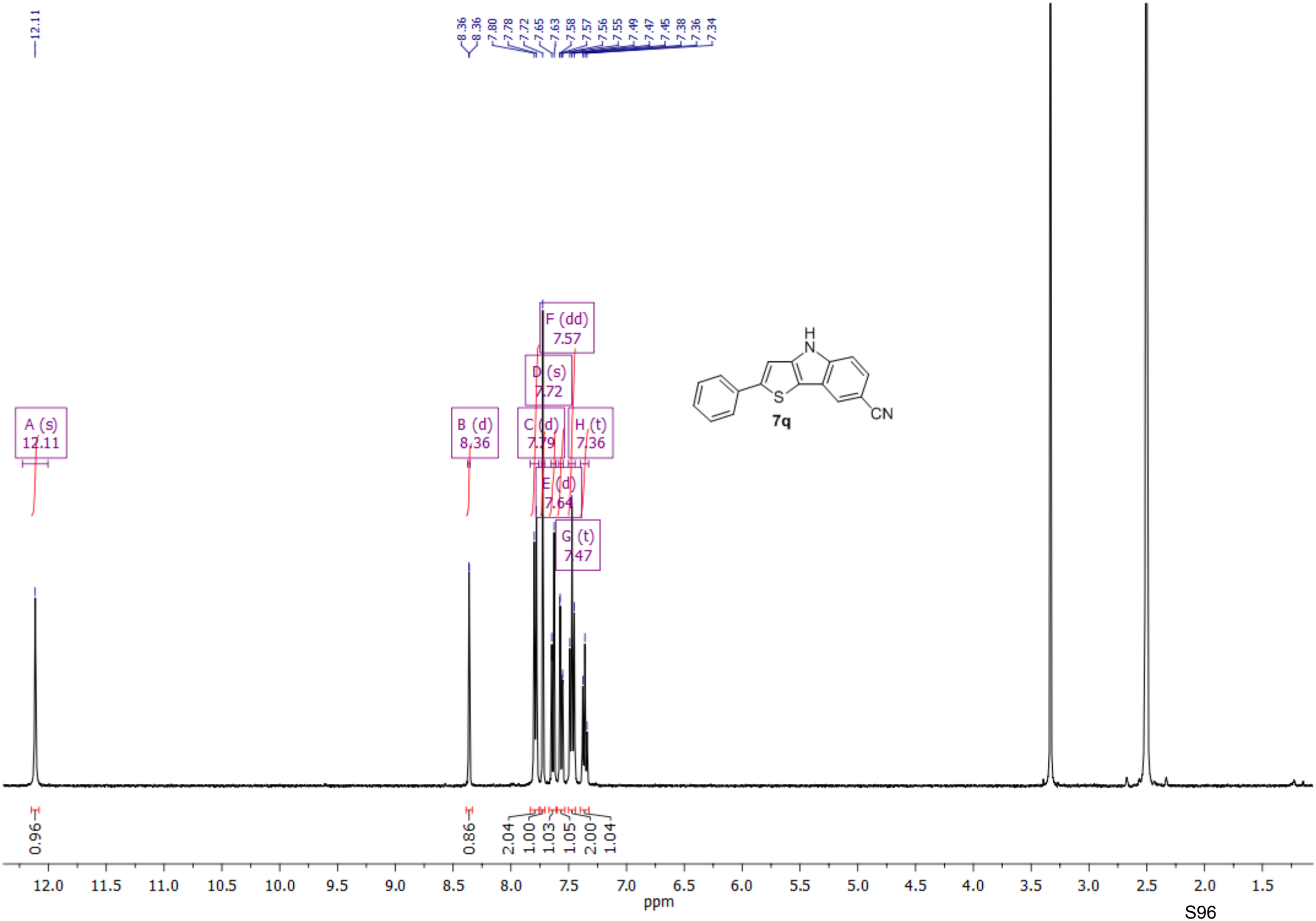

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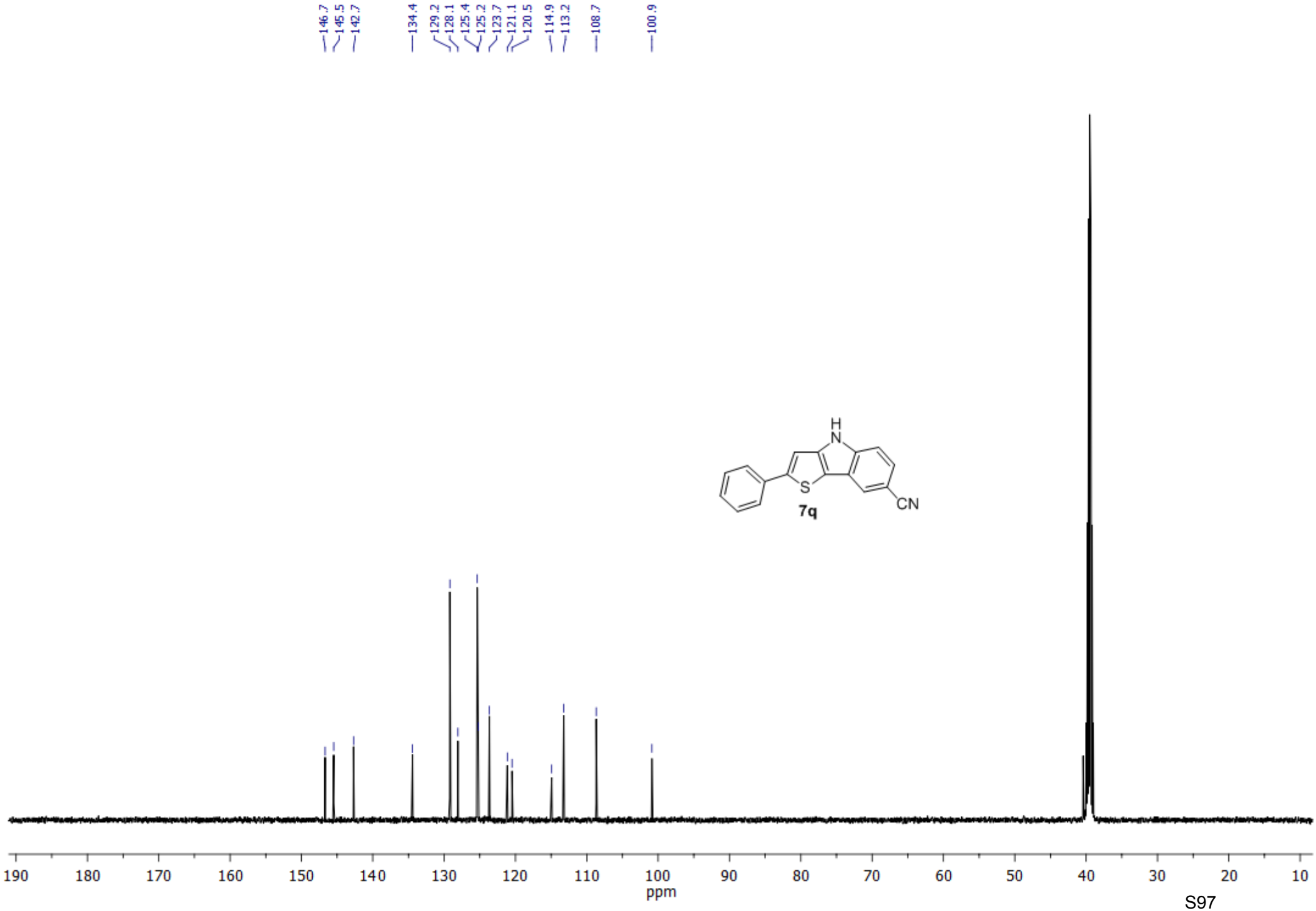

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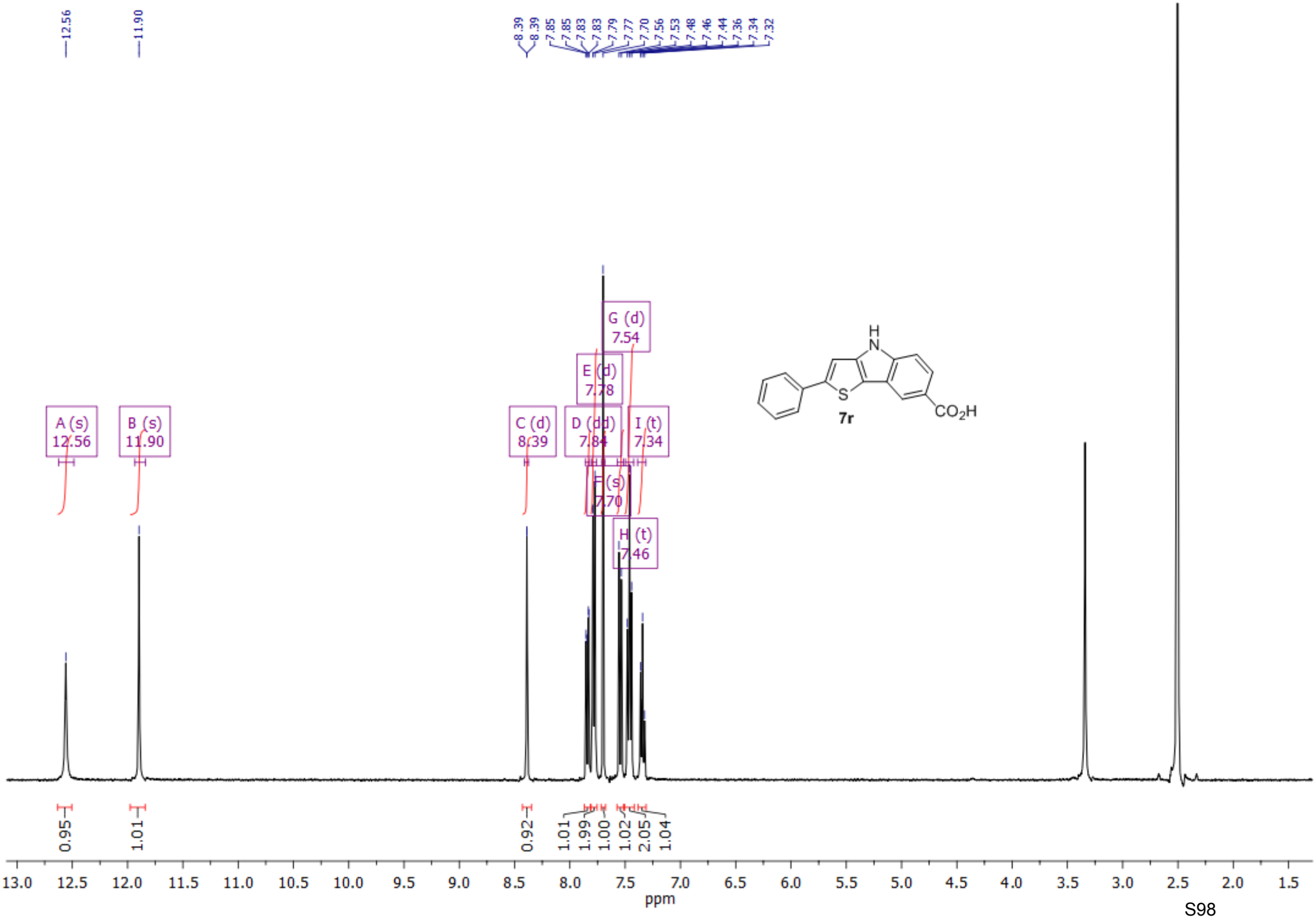
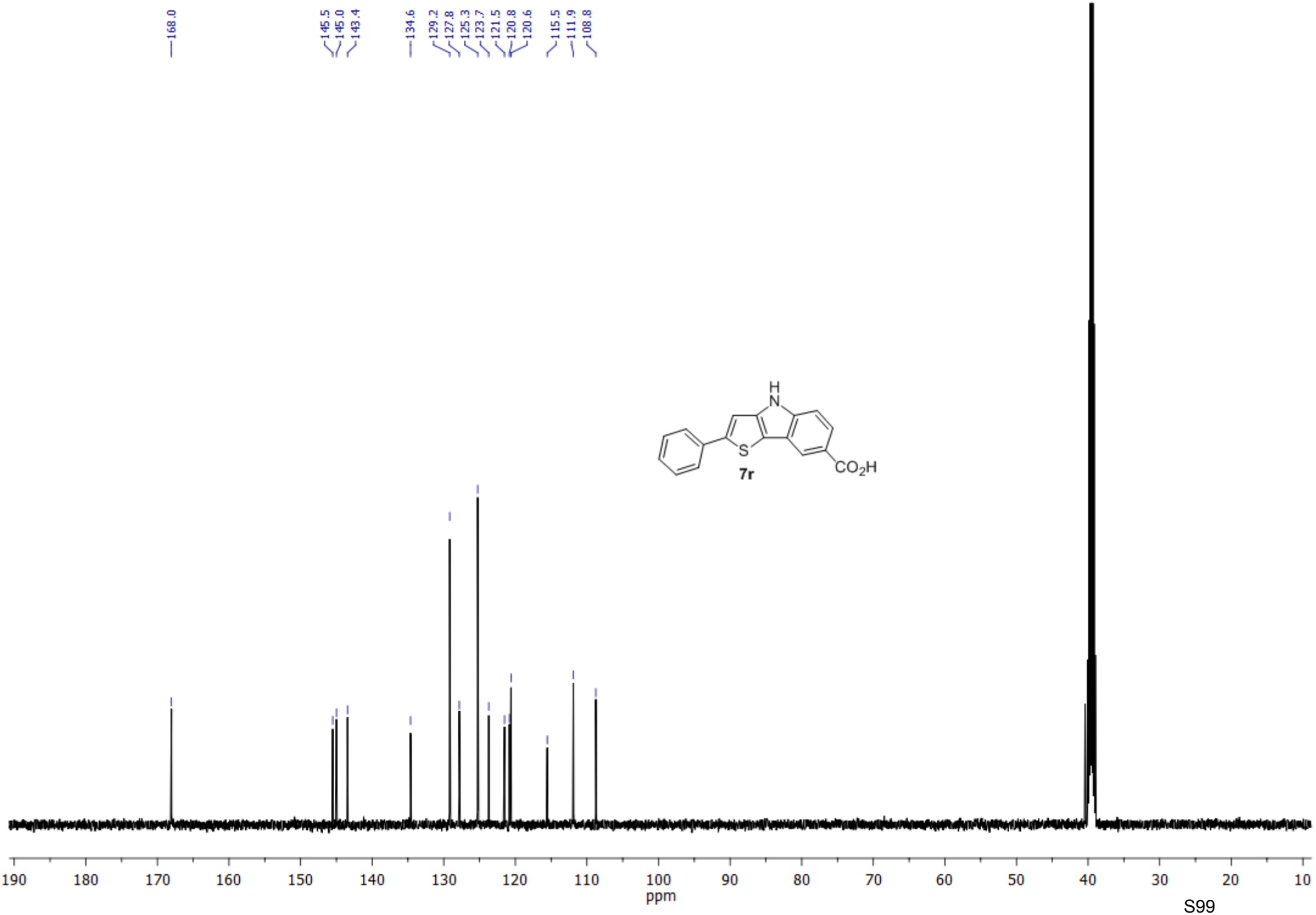


^{13}C NMR (solvent: DMSO-d_6)



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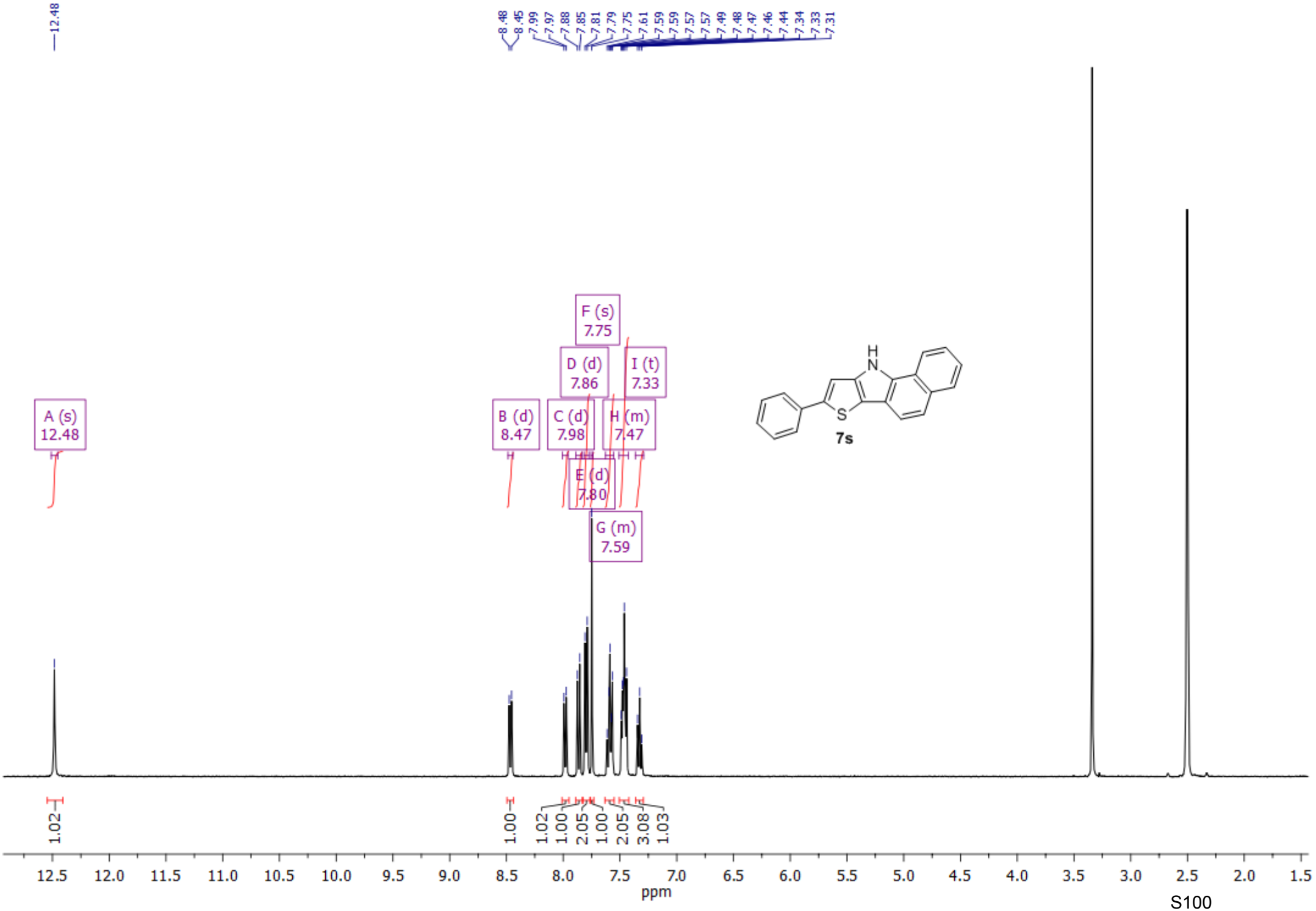

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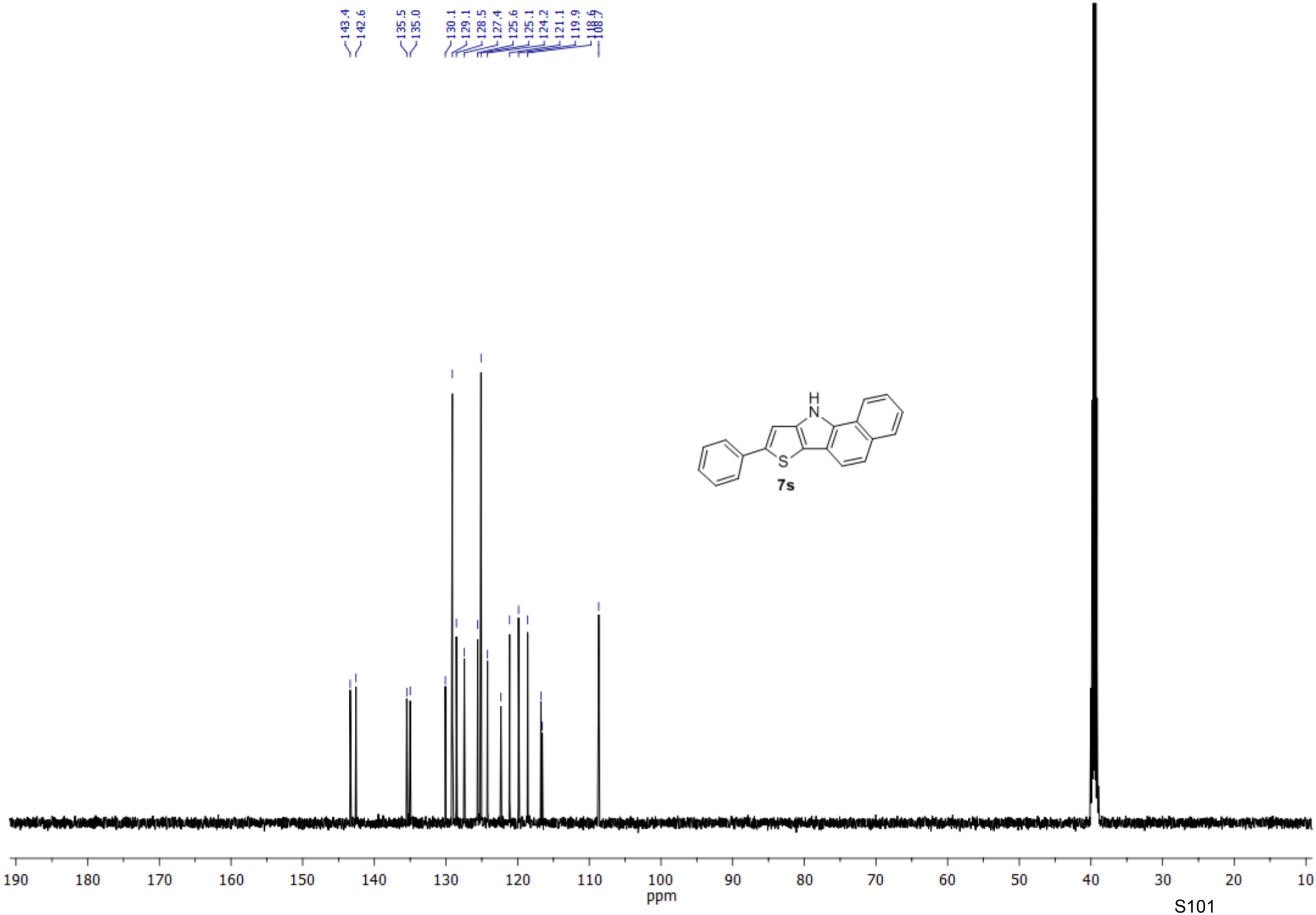

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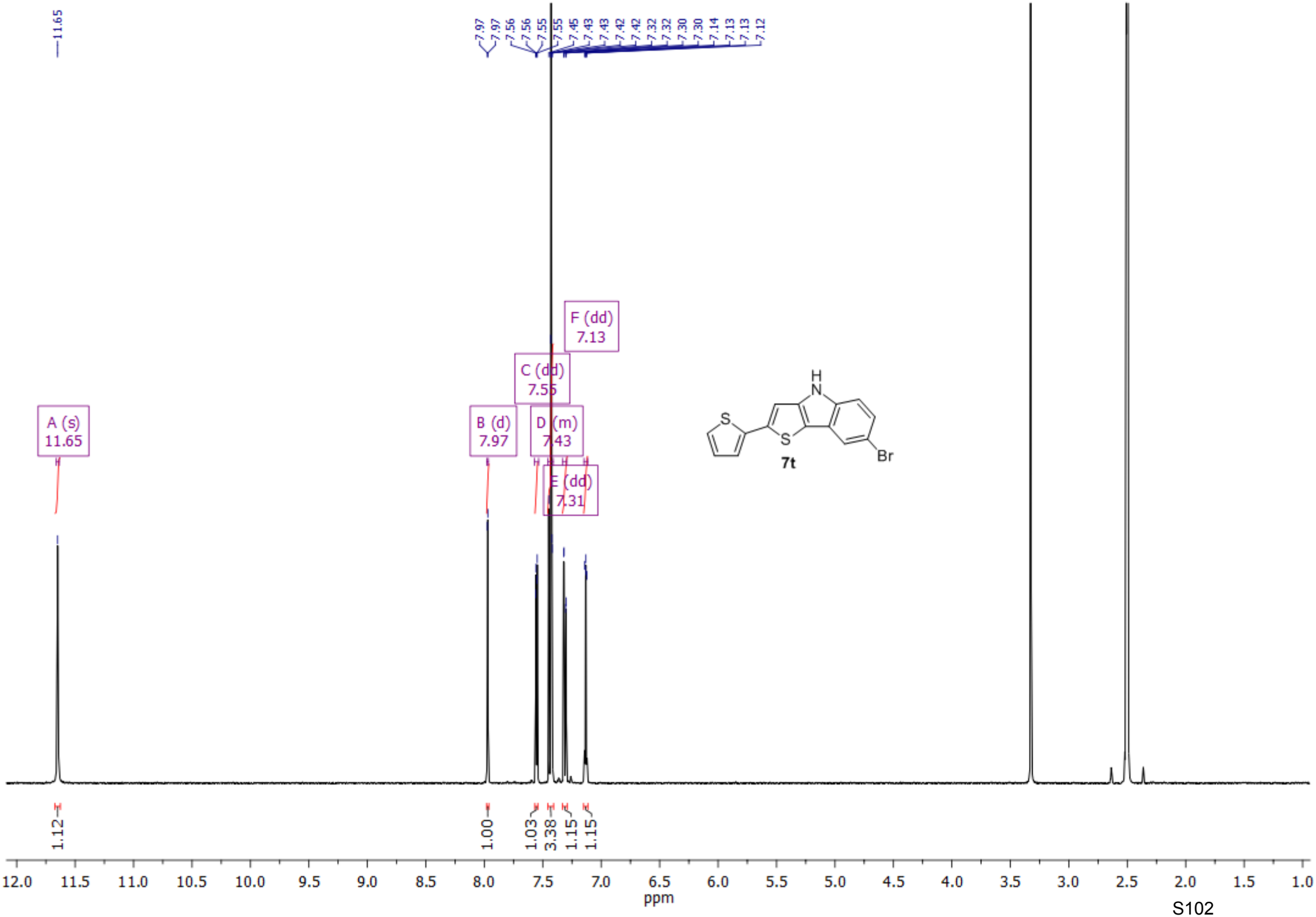
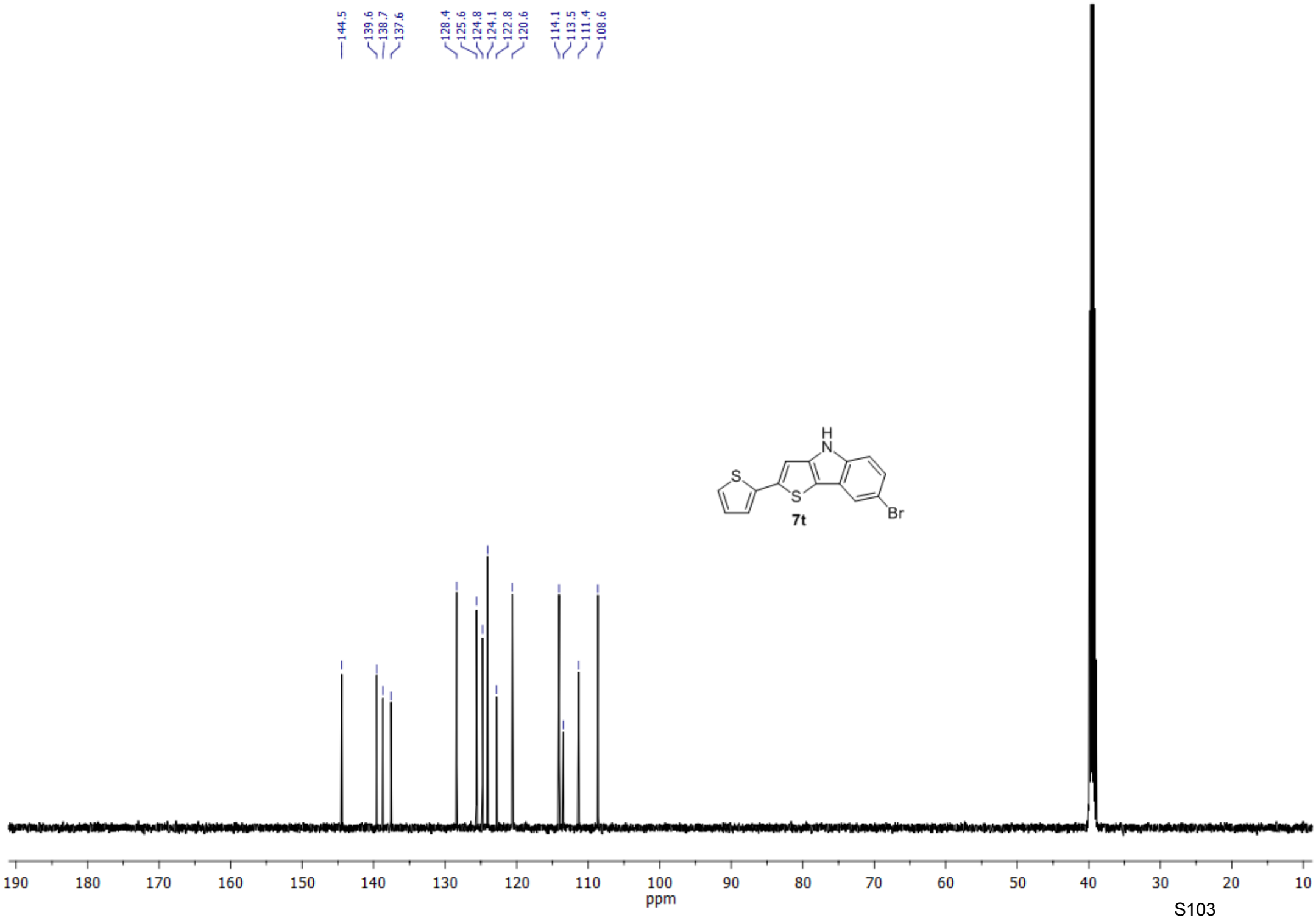
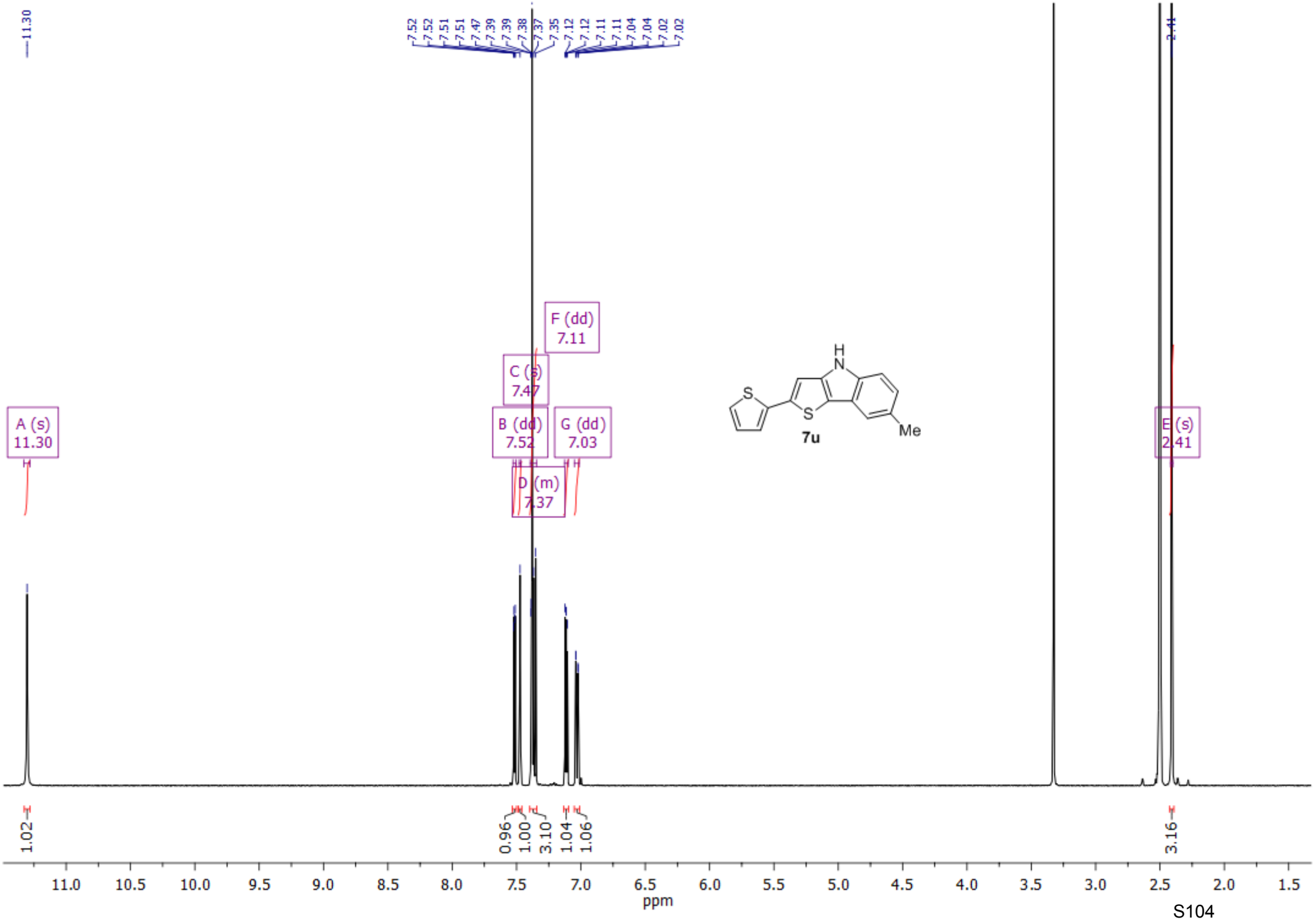


7t

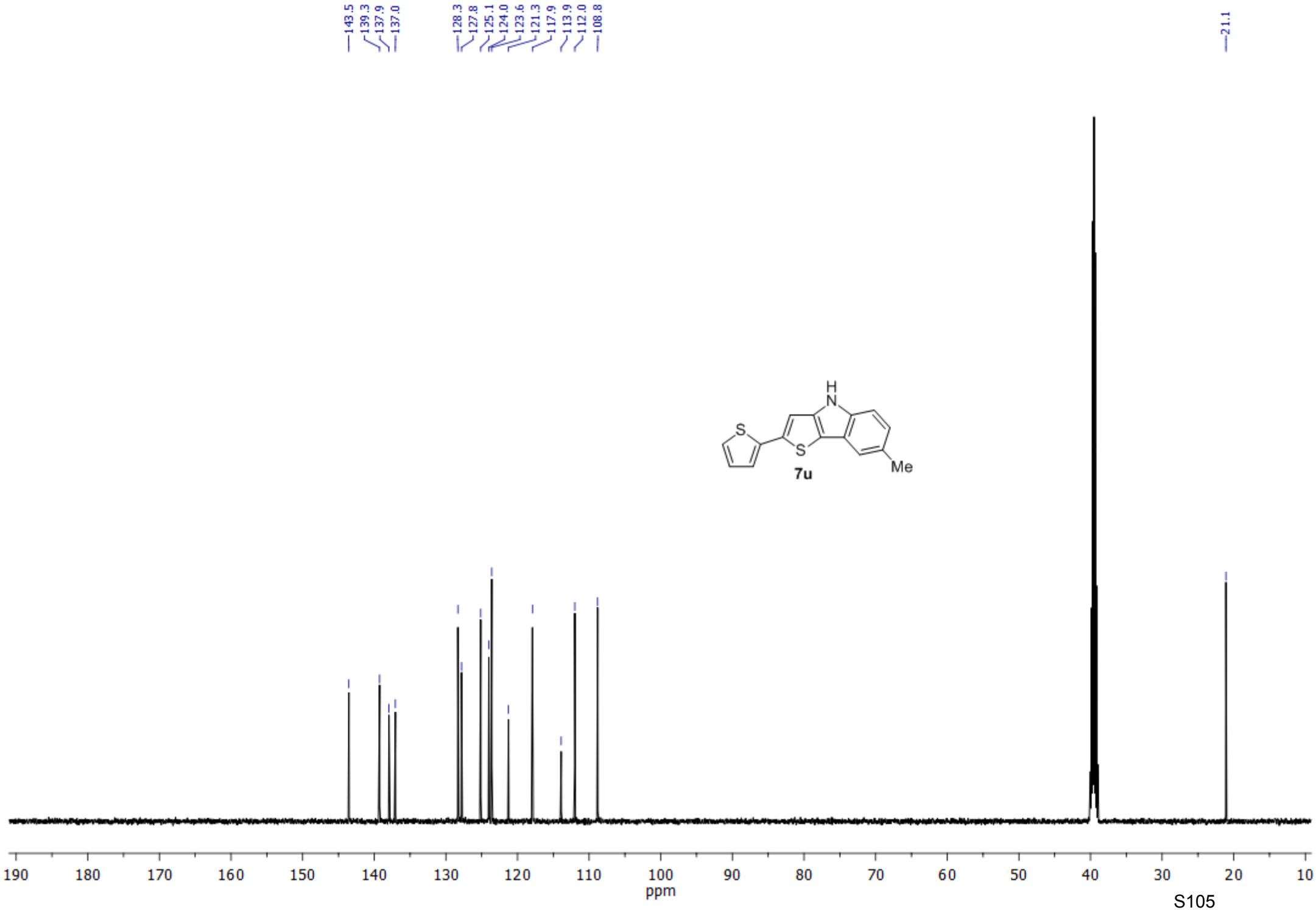
^{13}C NMR (solvent: DMSO-d_6)



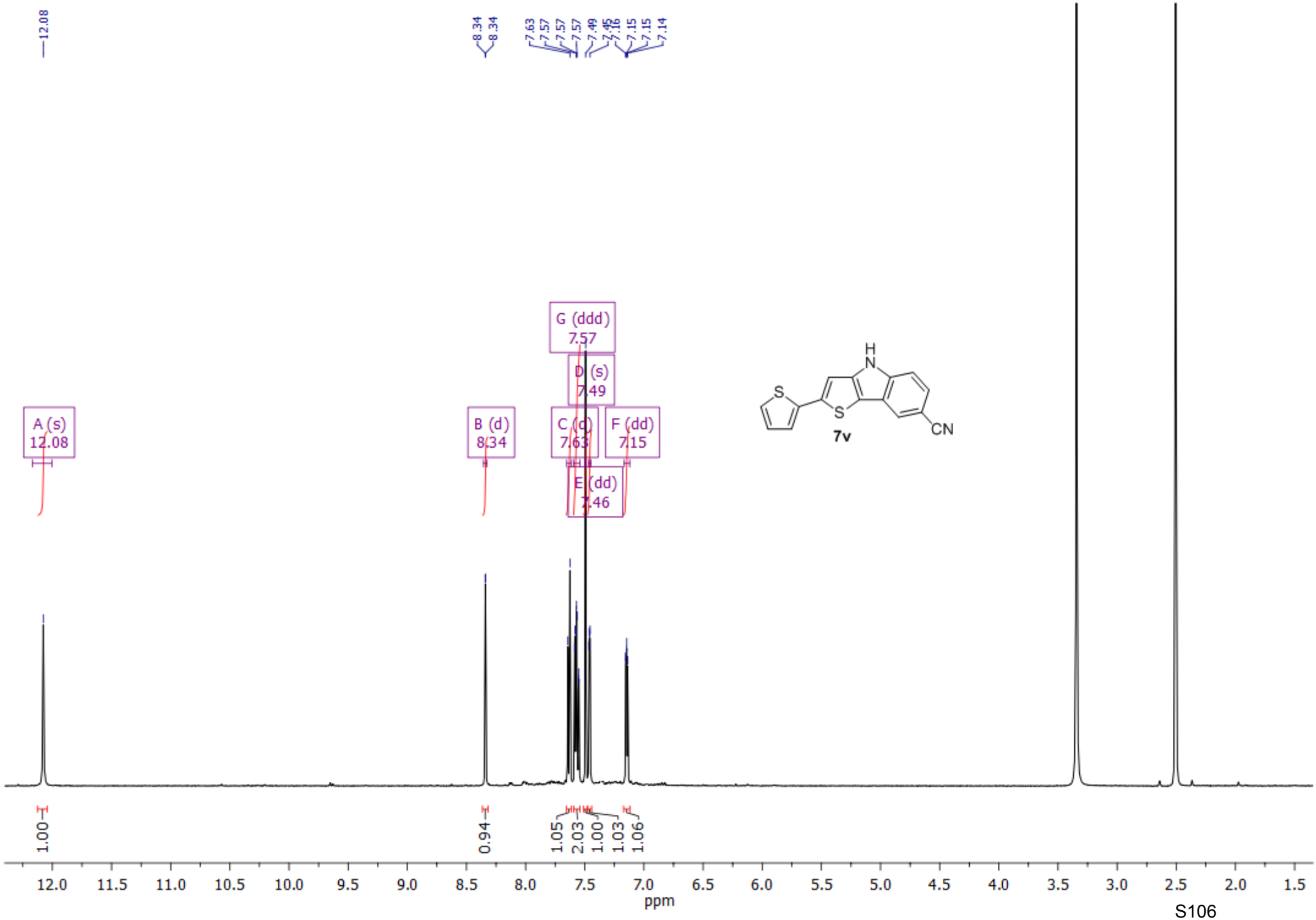
^{1}H NMR (solvent: DMSO-d_6)



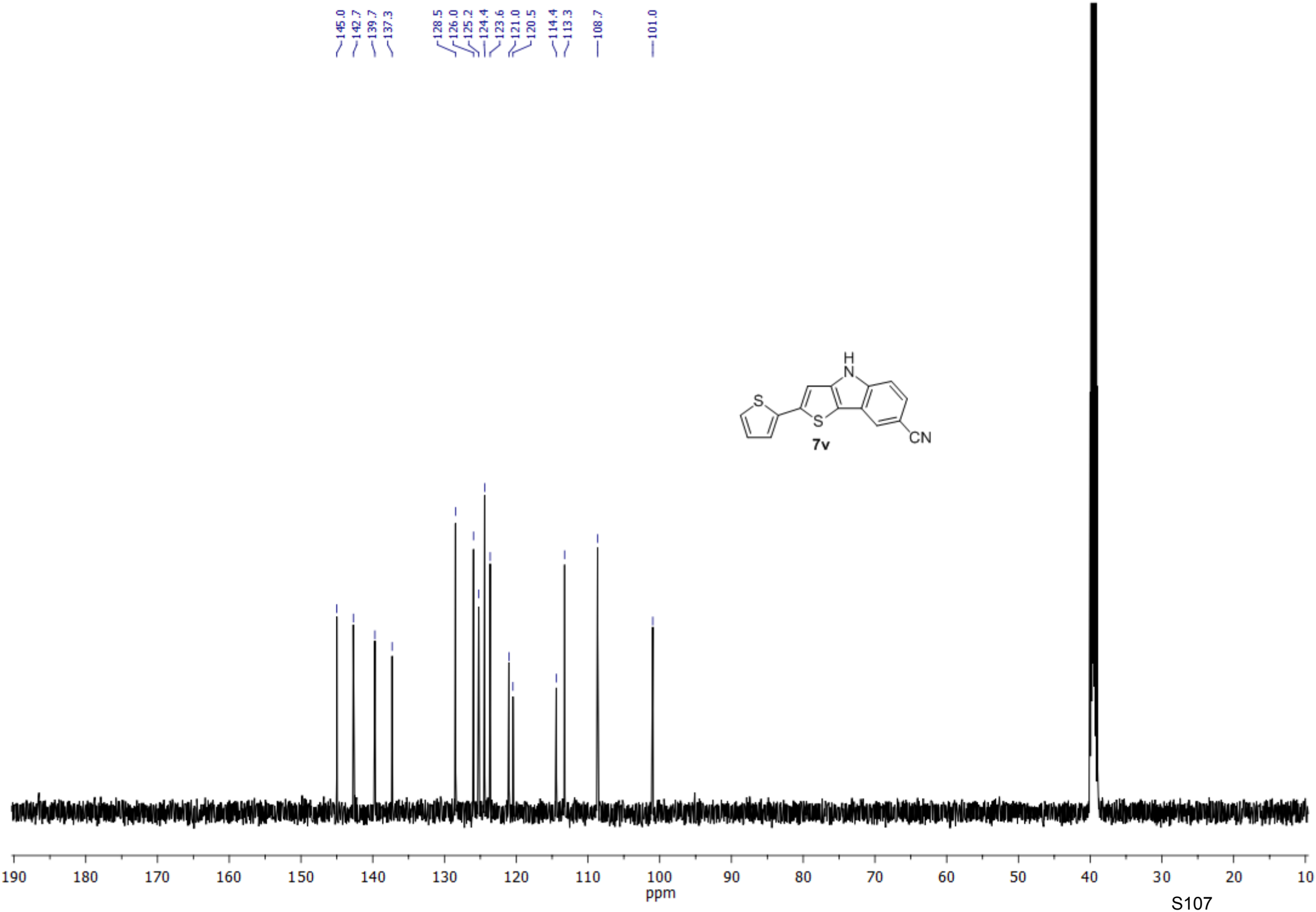
^{13}C NMR (solvent: DMSO-d_6)



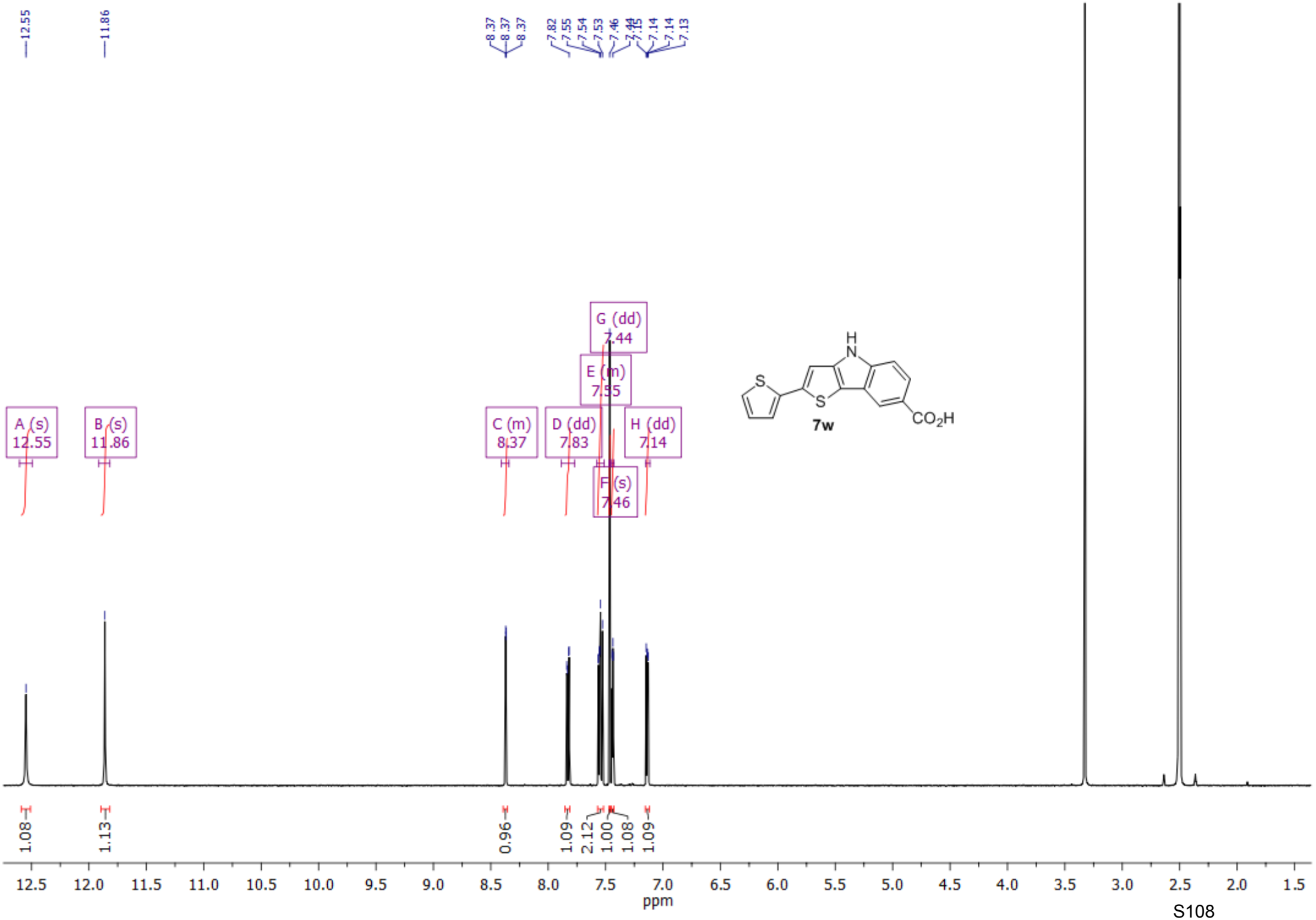
^{1}H NMR (solvent: DMSO-d_6)



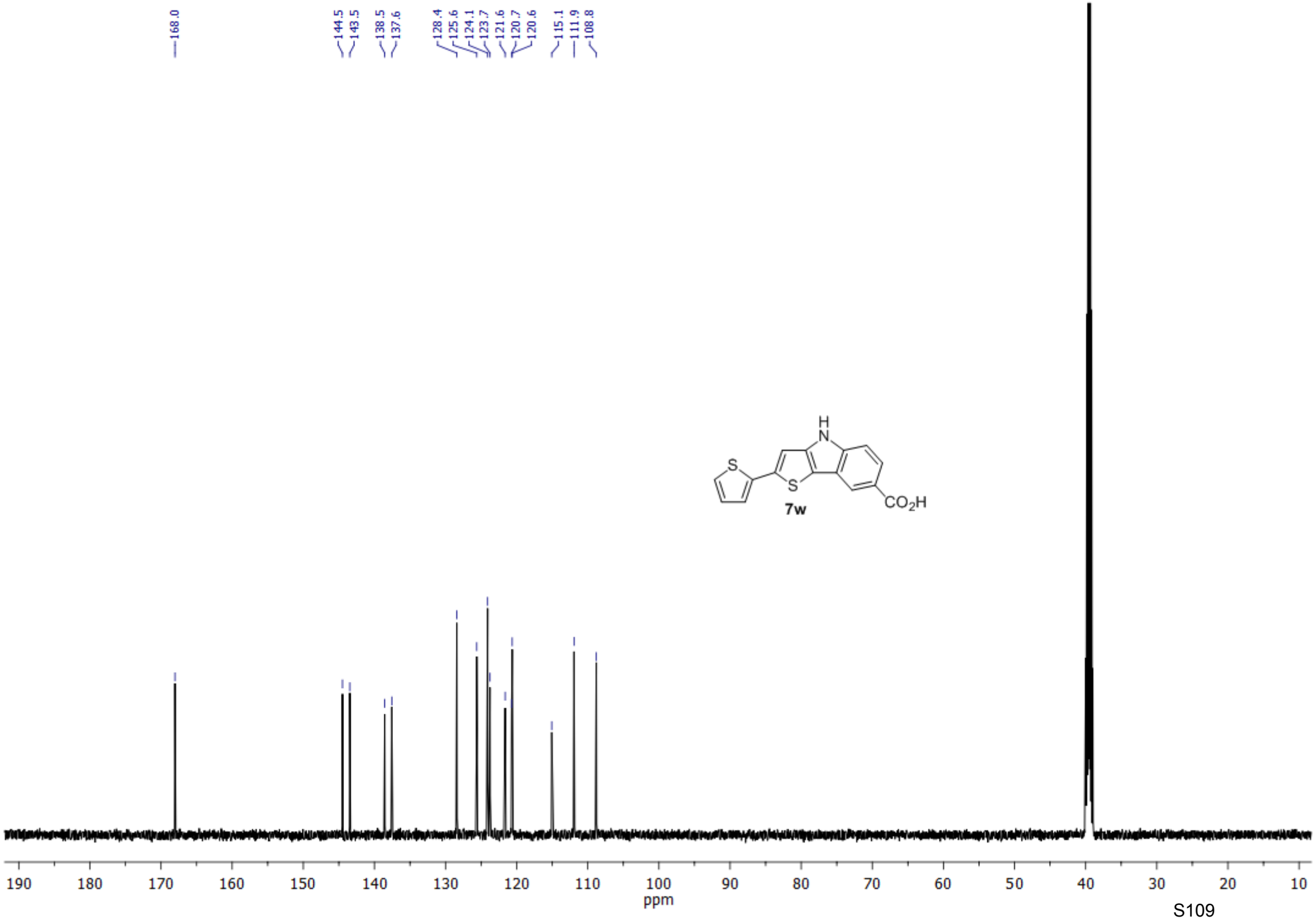
^{13}C NMR (solvent: DMSO-d_6)



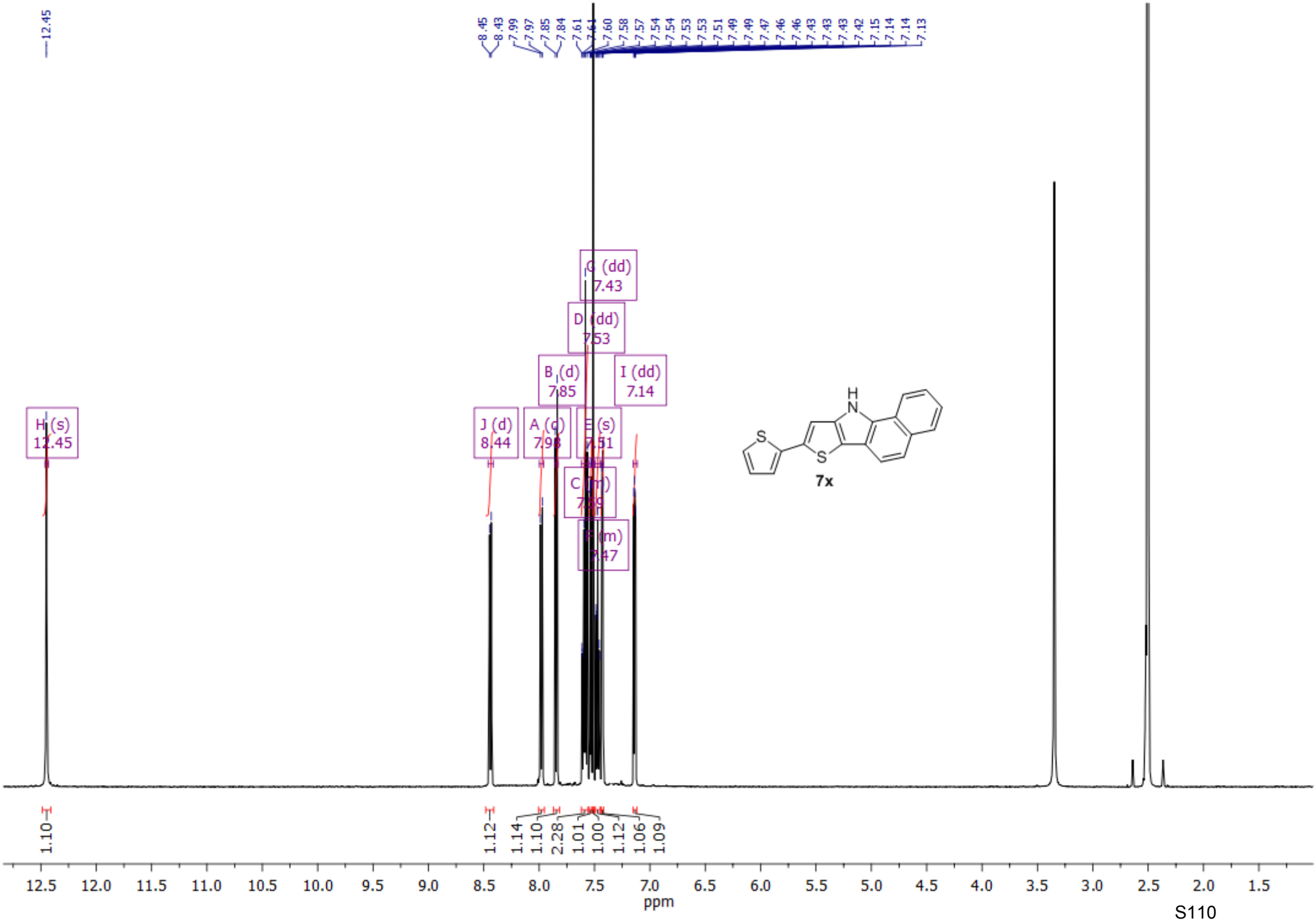
^{1}H NMR (solvent: DMSO-d_6)



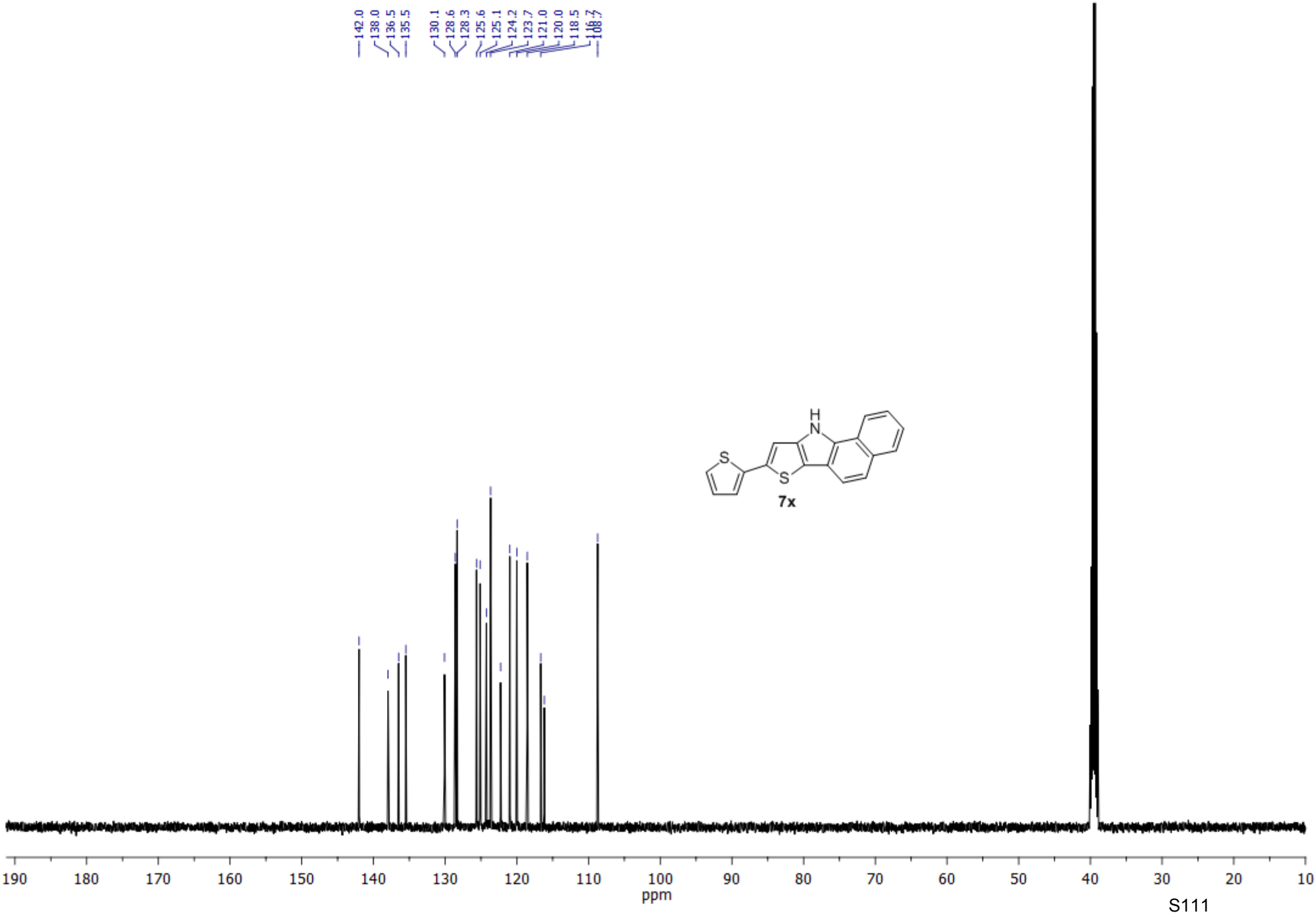
^{13}C NMR (solvent: DMSO-d_6)



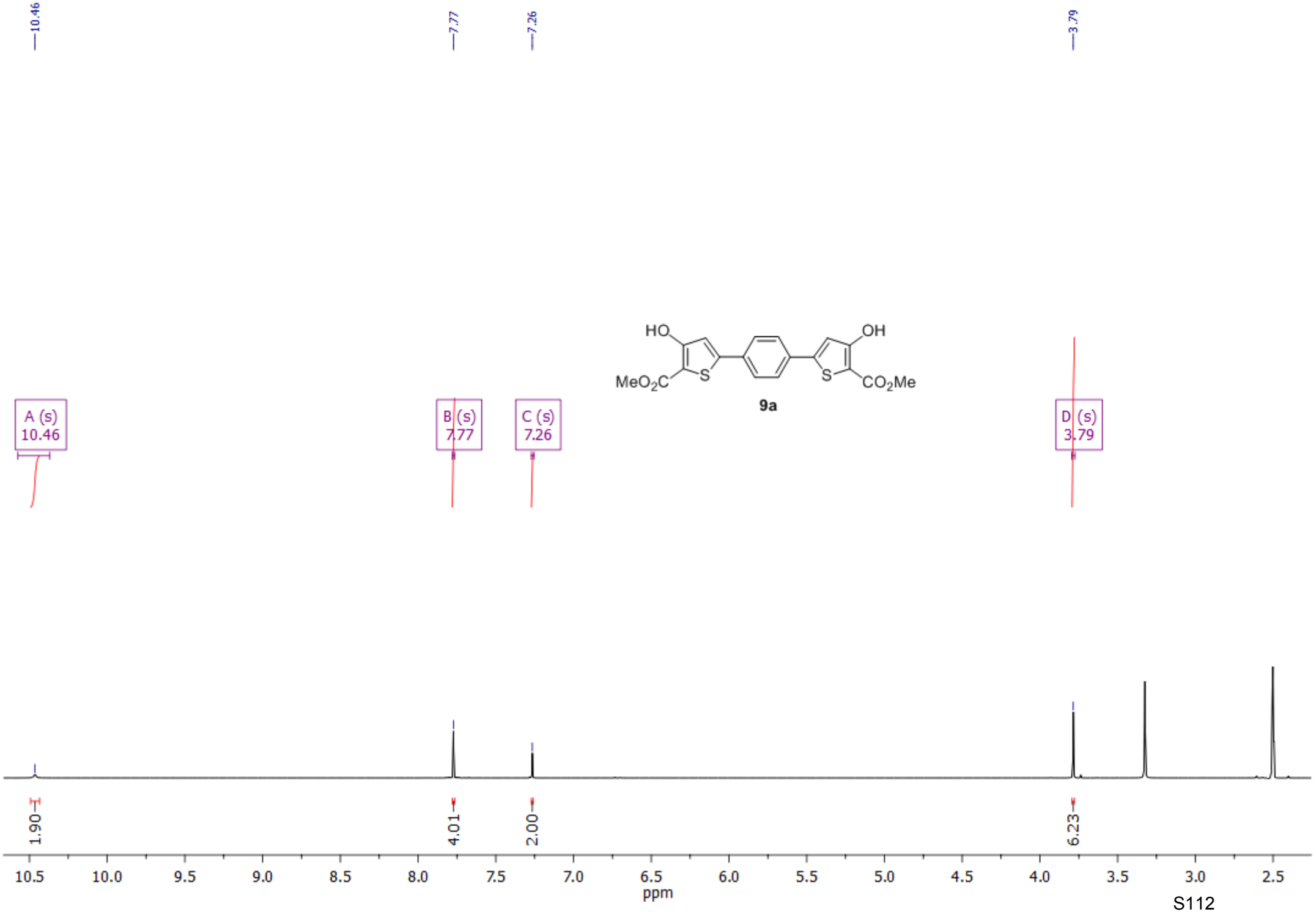
^{1}H NMR (solvent: DMSO-d_6)



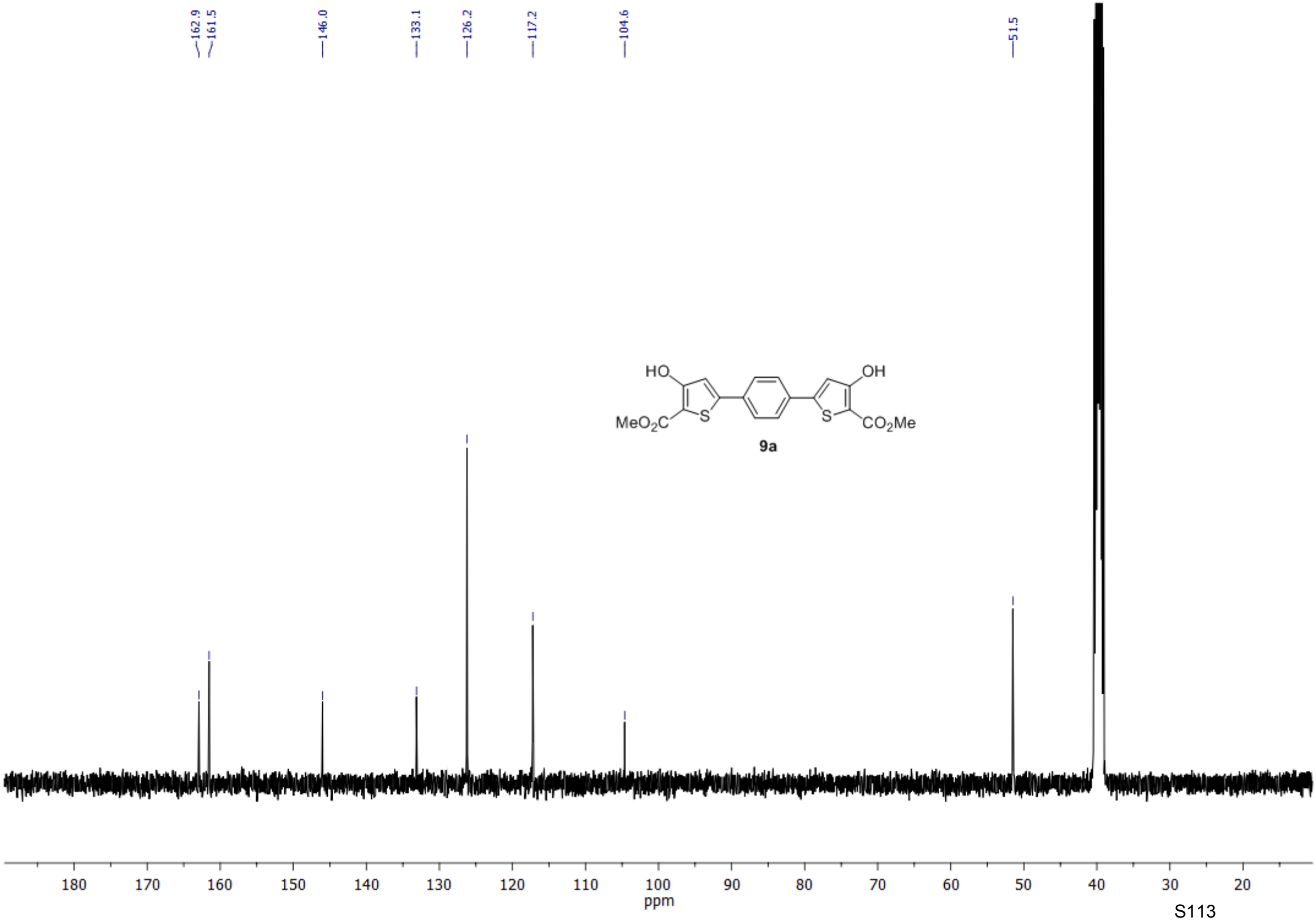
^{13}C NMR (solvent: DMSO-d_6)



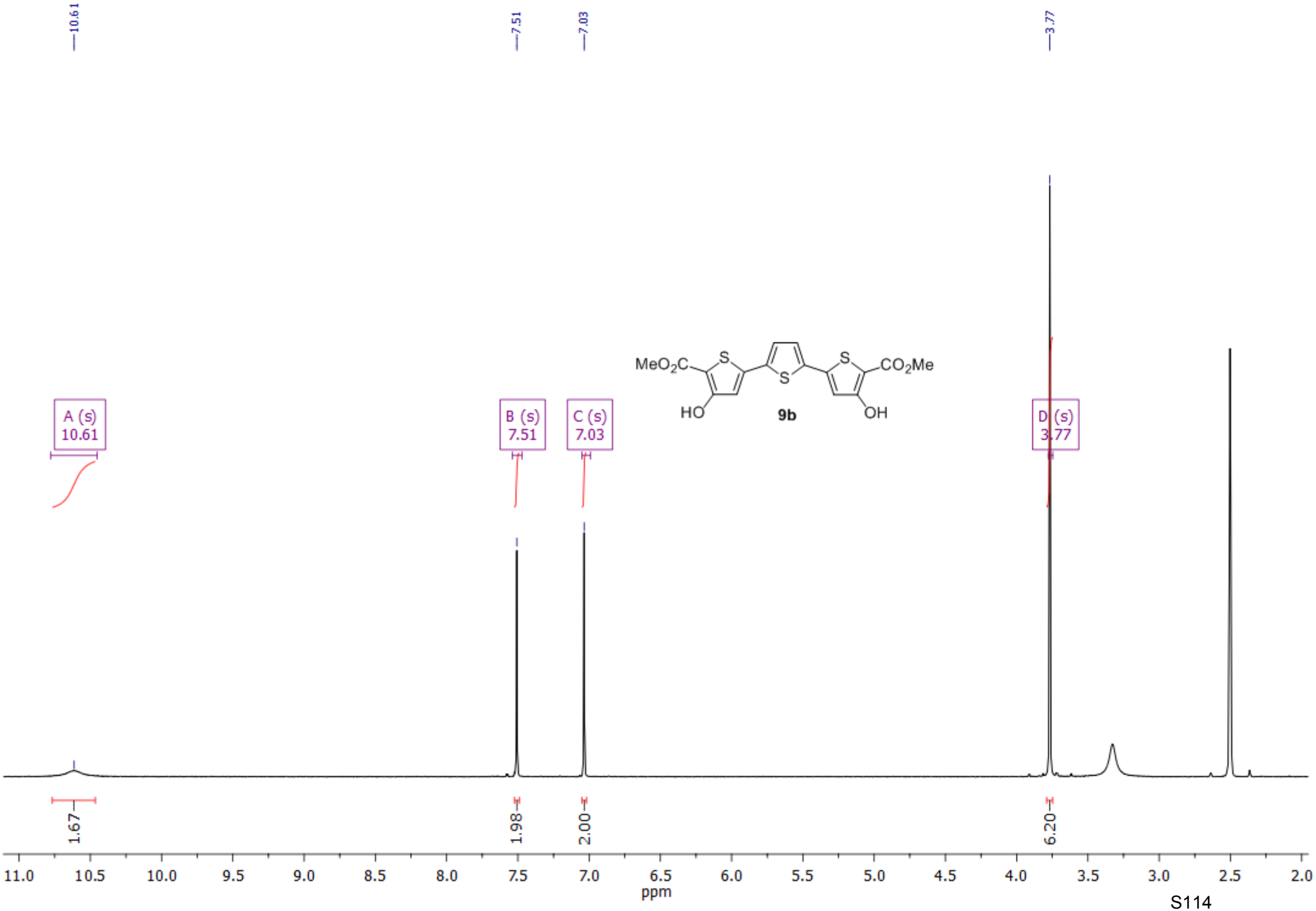
^{1}H NMR (solvent: DMSO-d_6)



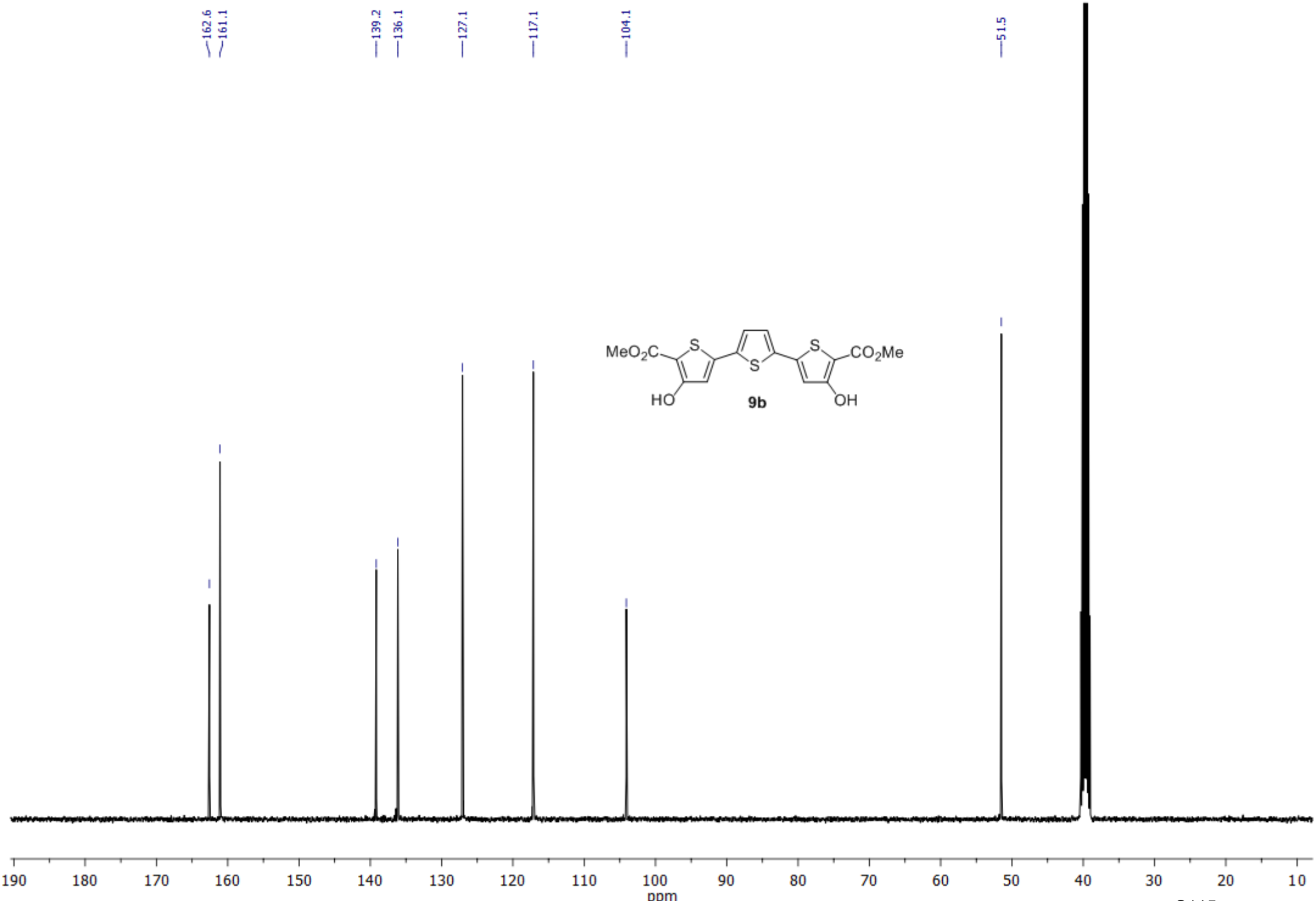
^{13}C NMR (solvent: DMSO-d_6)



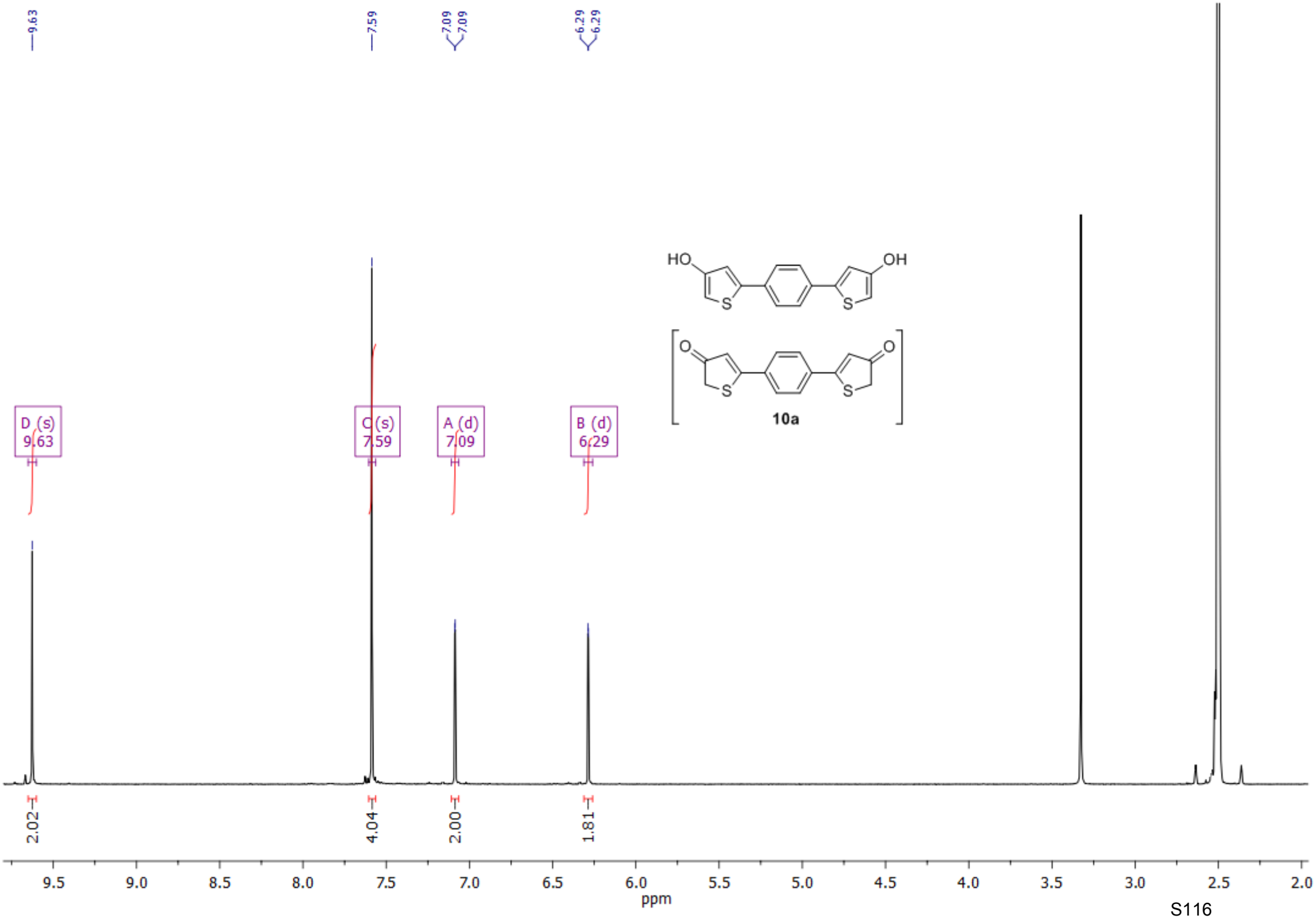
^{1}H NMR (solvent: DMSO-d_6)



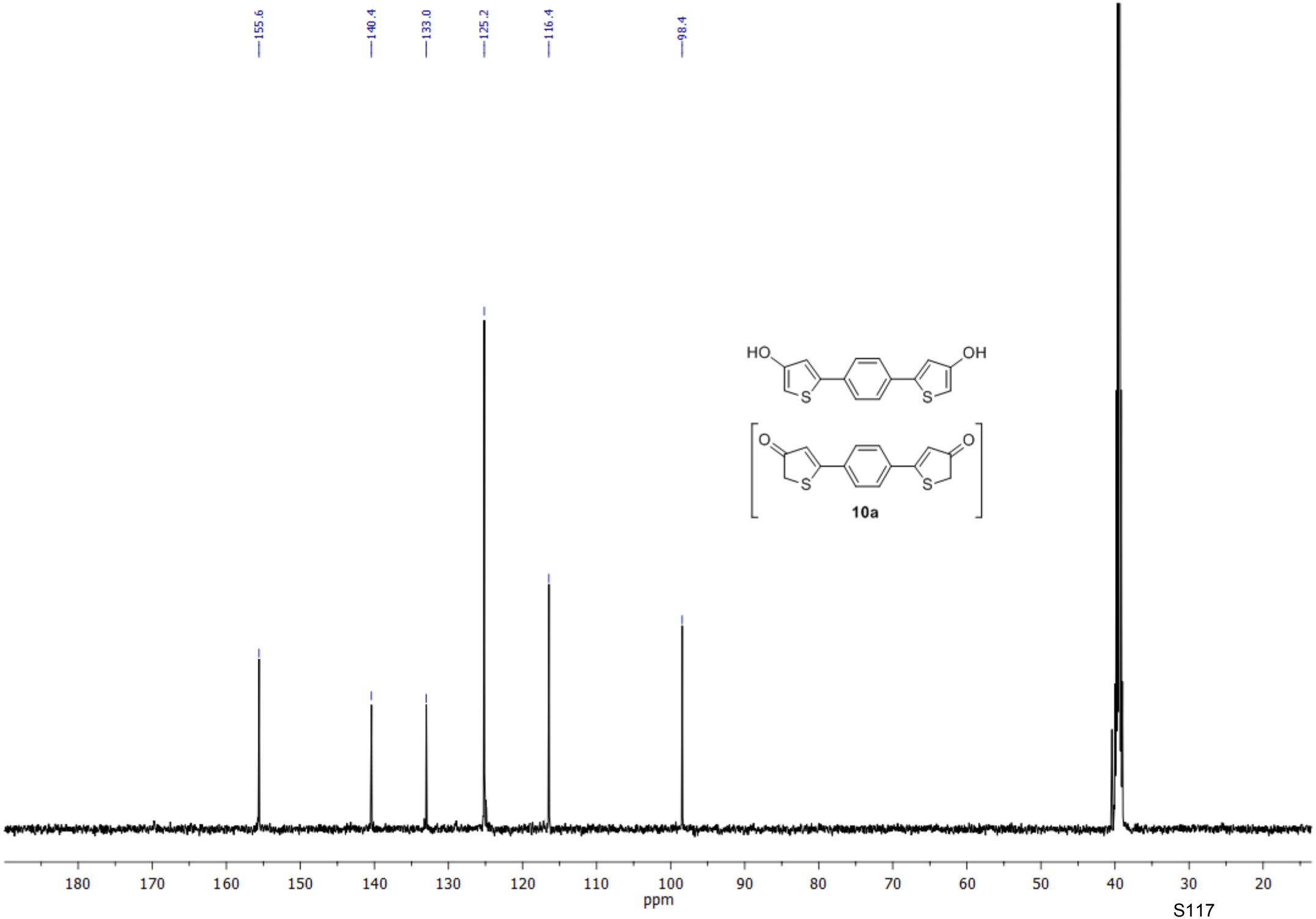
^{13}C NMR (solvent: DMSO-d_6)



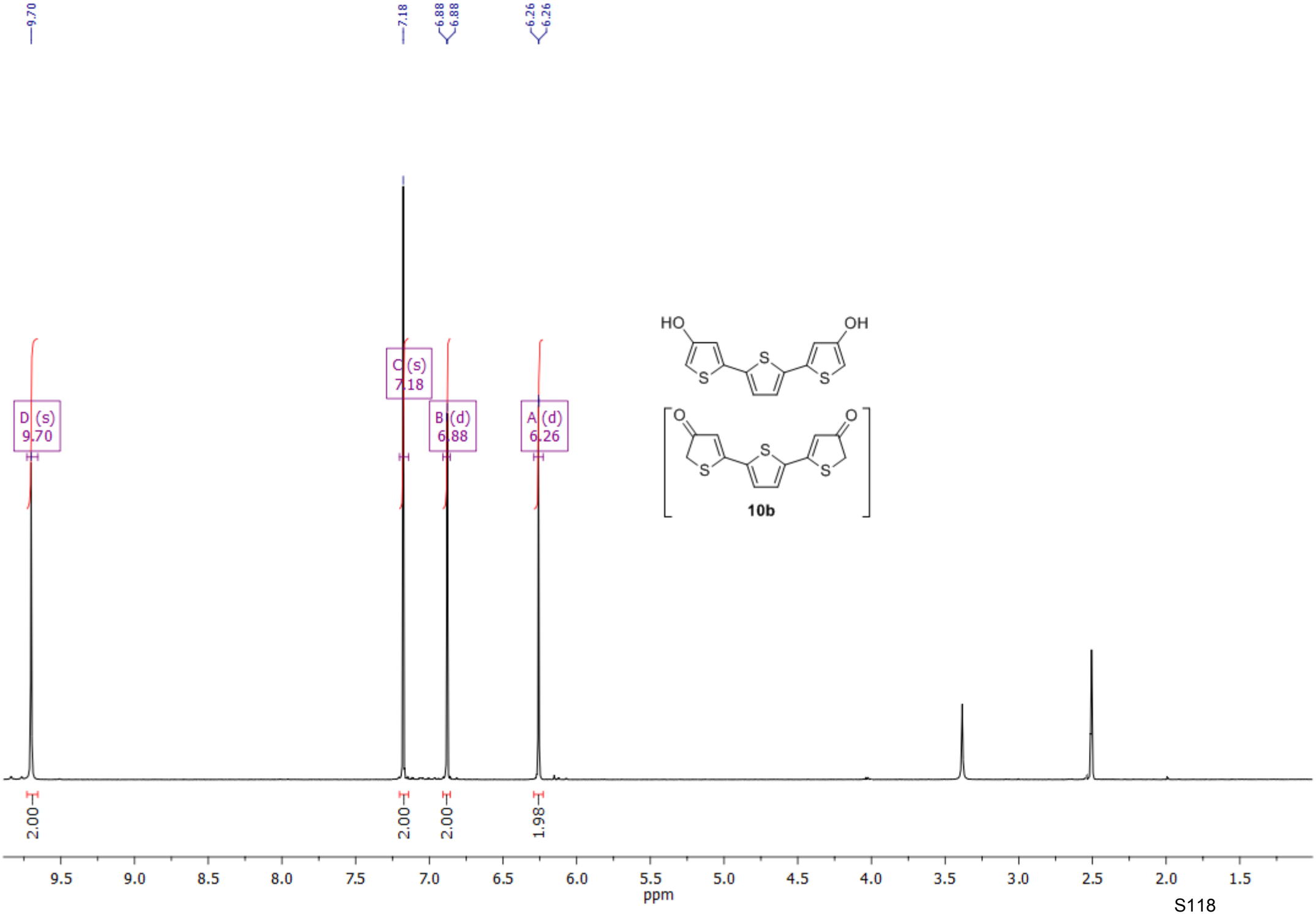
^{1}H NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **10a**



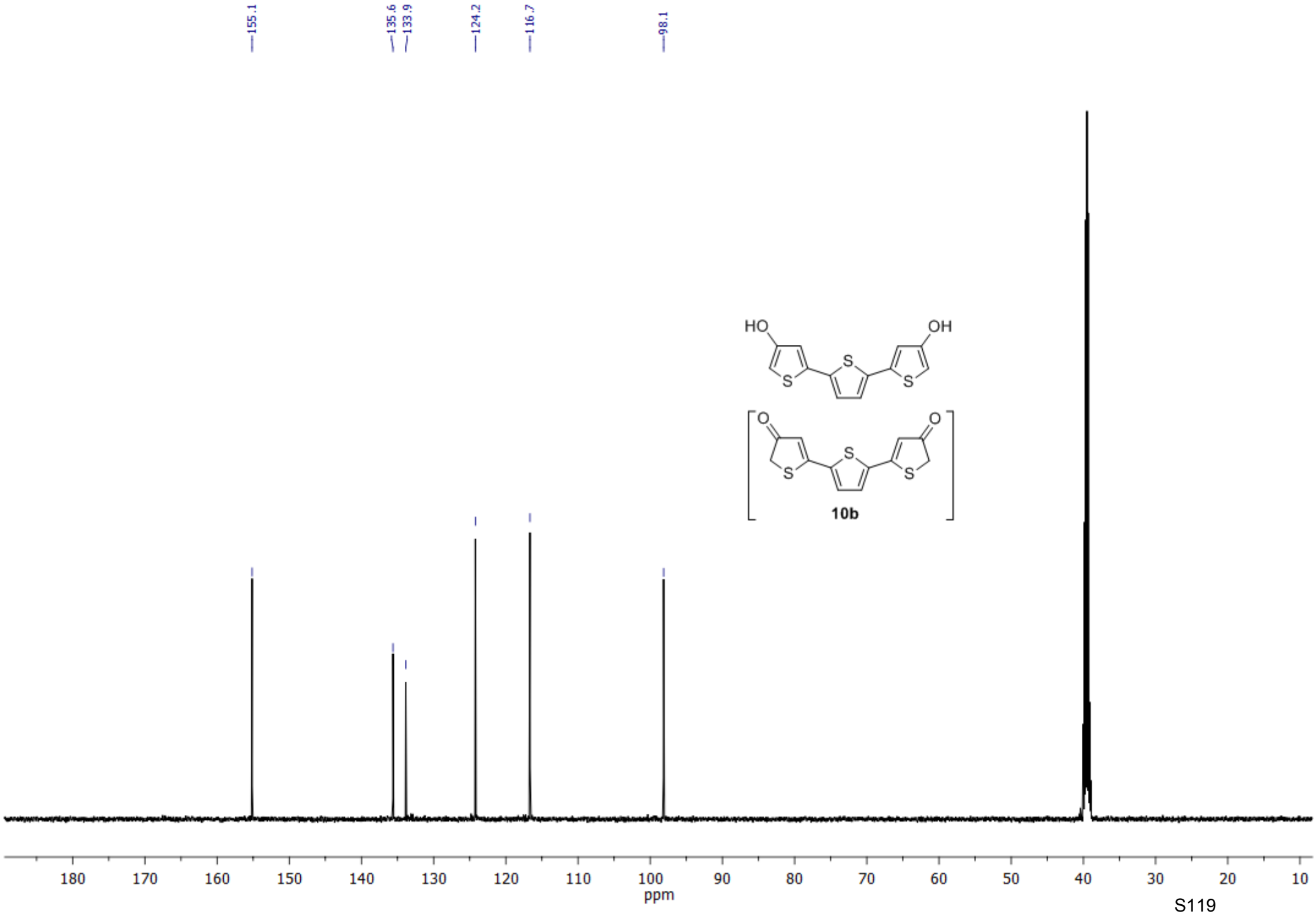
^{13}C NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **10a**



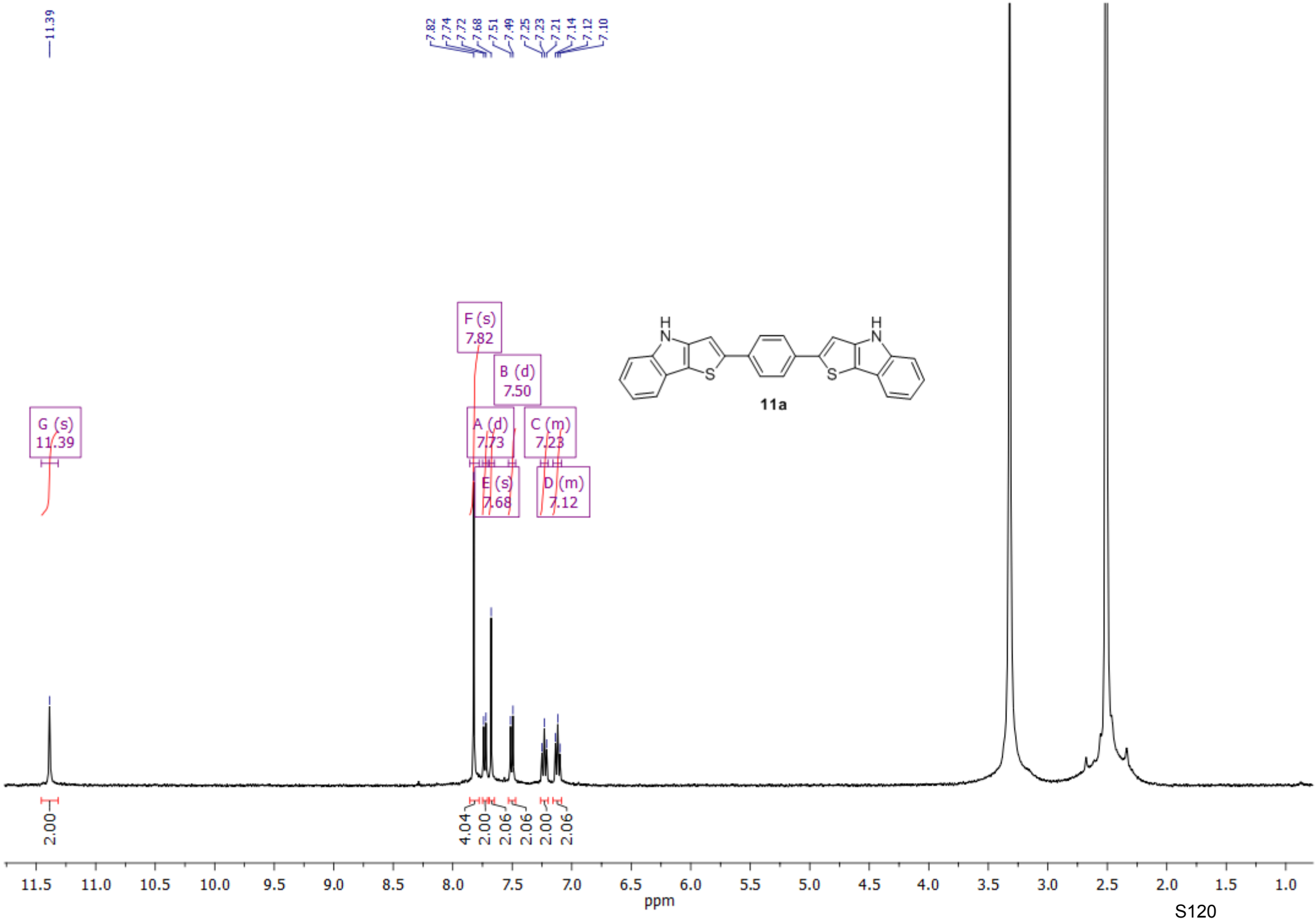
^{1}H NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **10b**



^{13}C NMR (solvent: DMSO-d_6), enol (3-hydroxythiophene) form of compound **10b**



^{1}H NMR (solvent: DMSO-d_6)



^{1}H NMR (solvent: DMSO-d_6)