

# SUPPORTING INFORMATION

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Rapid access to amino-substituted quinoline,  
(di)benzofuran and carbazole heterocycles through  
an aminobenzannulation reaction.

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## General methods:

### General procedure for Sonogashira coupling:

CuI (2.5 mol %), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (5 mol %), the appropriate aryl-halide (1 mmol), were suspended in anhydrous DMF (1 mL per mmol) and Et<sub>3</sub>N (0.6 mL per mmol) under argon. Then was added the appropriate acetylene (1.2 equiv.) was added. The mixture was stirred overnight at room temperature and then the slurry was diluted in EtOAc. Filtration on celite, evaporation of Et<sub>3</sub>N, DMF and EtOAc under reduced pressure and purification by flash chromatography on silica gel (using cyclohexane/ EtOAc mixtures) afforded the desired product. [For the benzofuran series the reaction is performed in dimethylacetamide (DMA) instead of DMF].<sup>1</sup>

### General procedure for Grignard reaction:

The appropriate aldehyde (1 mmol) was diluted in dry THF (5.0 mL) under stirring and cooled at 0-5°C under argon and methylmagnesium bromide (3M in Et<sub>2</sub>O, 1.3 equiv) was added dropwise to the solution. After 1 hour the reaction was quenched by addition of a saturated solution of NH<sub>4</sub>Cl. Dilution in EtOAc and washing with water and brine afforded the desired methyl-alcohol, used without further purification.

### General procedure for oxidation reaction mediated by TPAP/NMO system:

The appropriate methyl-alcohol (1 mmol) was stirred with N-methylmorpholine oxide (2 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (5 mL) under argon at 0°C. Tetrapropylammonium perruthenate (0.05 mmol) was added. After 20 min, the reaction media was filtered through silica gel eluting with EtOAc. Evaporation of solvents under reduced pressure and purification by flash chromatography on silica gel (using cyclohexane/EtOAc mixtures) afforded the desired methyl ketone.

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<sup>1</sup> In this case dimethylacetamide (DMA) was used instead of DMF to avoid partial reduction of the triple-bond.

General procedures for aminobenzannulation reaction:

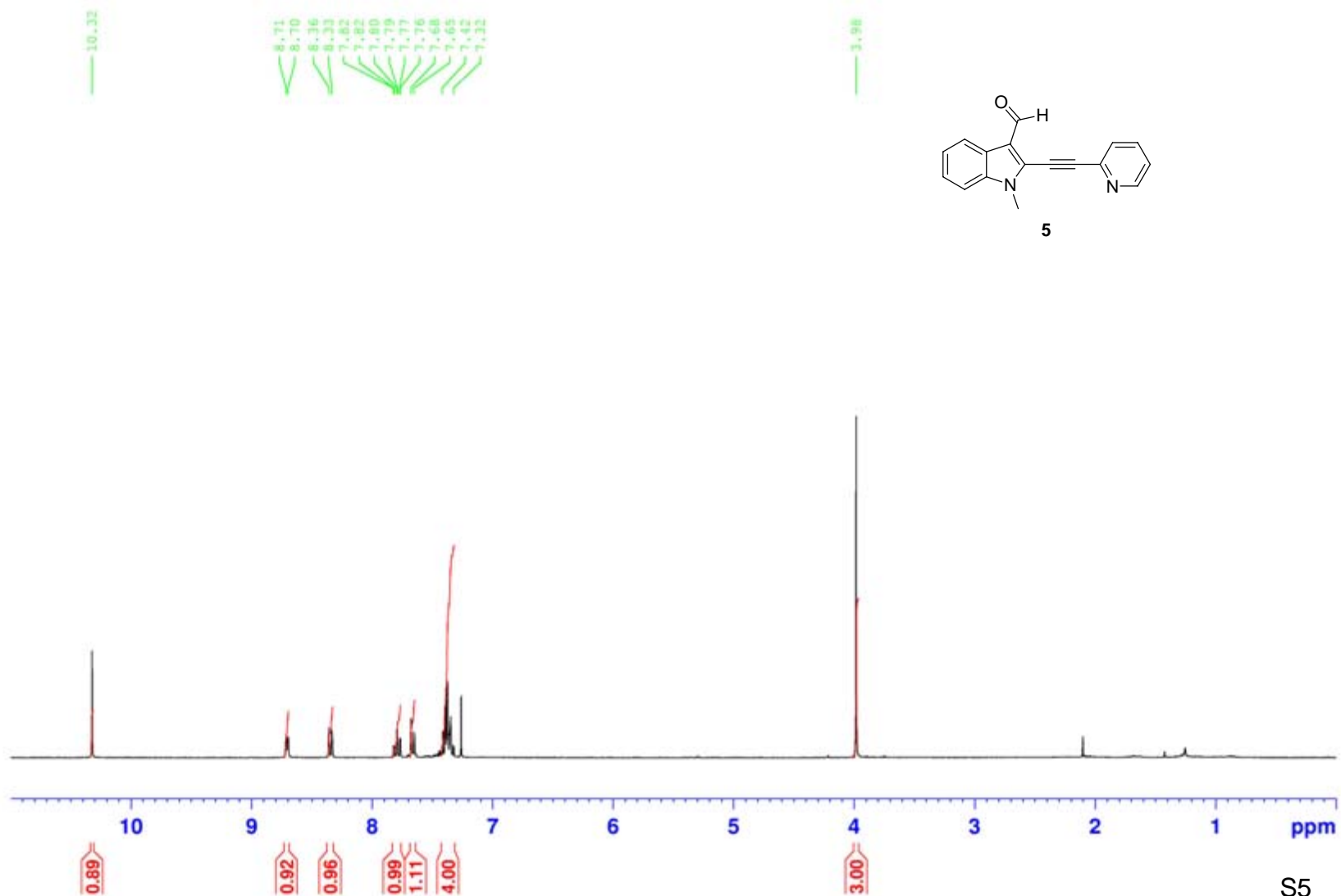
- Method A: To a solution of starting material (1 mmol) in dry dichloromethane (5 mL) under argon was added successively activated molecular sieves (4 Å, pulver < 5µ, 6 weight equiv.) and amine (3 equiv.). The mixture was stirred overnight at room temperature. Filtration through celite, evaporation of solvent and purification by flash chromatography on silica gel (using cyclohexane/EtOAc mixtures) afforded the desired products.
- Method B: To a solution of starting material (1 mmol) in dry dichloroethane (5 mL) under argon was added successively activated molecular sieves (4 Å, pulver < 5µ, 6 weight equiv.) and amine (3-6 equiv.). The mixture was stirred at reflux until completion (3 hours-2 days). Filtration through celite, evaporation of solvent and purification by flash chromatography on silica gel (using cyclohexane/EtOAc mixtures) afforded the desired products.
- Method C: starting material (1 mmol) was stirred in the appropriate amine (5 mL), with molecular sieves (4 Å, pulver < 5µ, 6 weight equiv.) at reflux until completion. Filtration through celite, dilution in EtOAc, washing evaporation of solvent and purification by flash chromatography on silica gel (using cyclohexane/EtOAc mixtures) afforded the desired products.

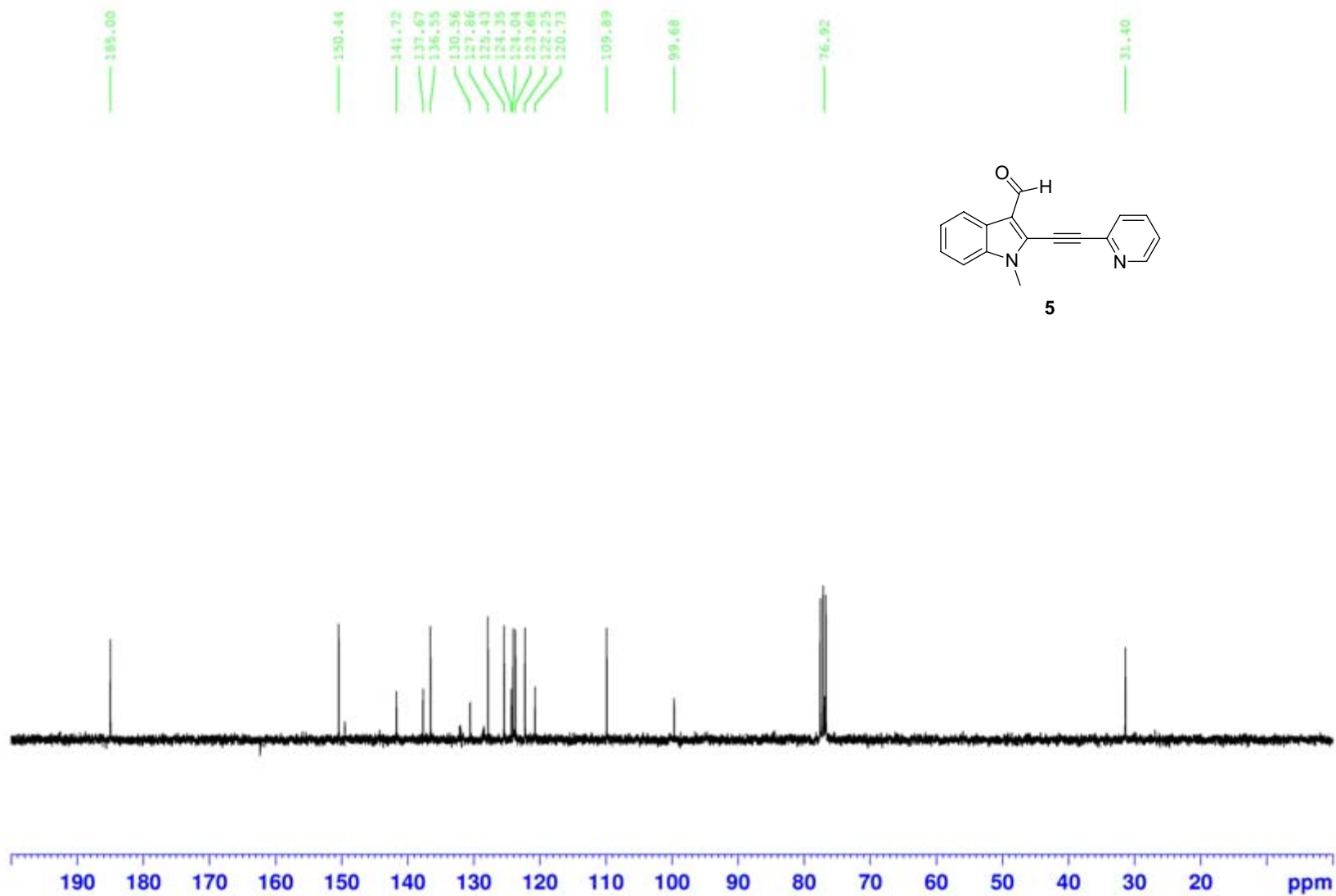
Procedure for removal of palladium residue:<sup>2</sup>

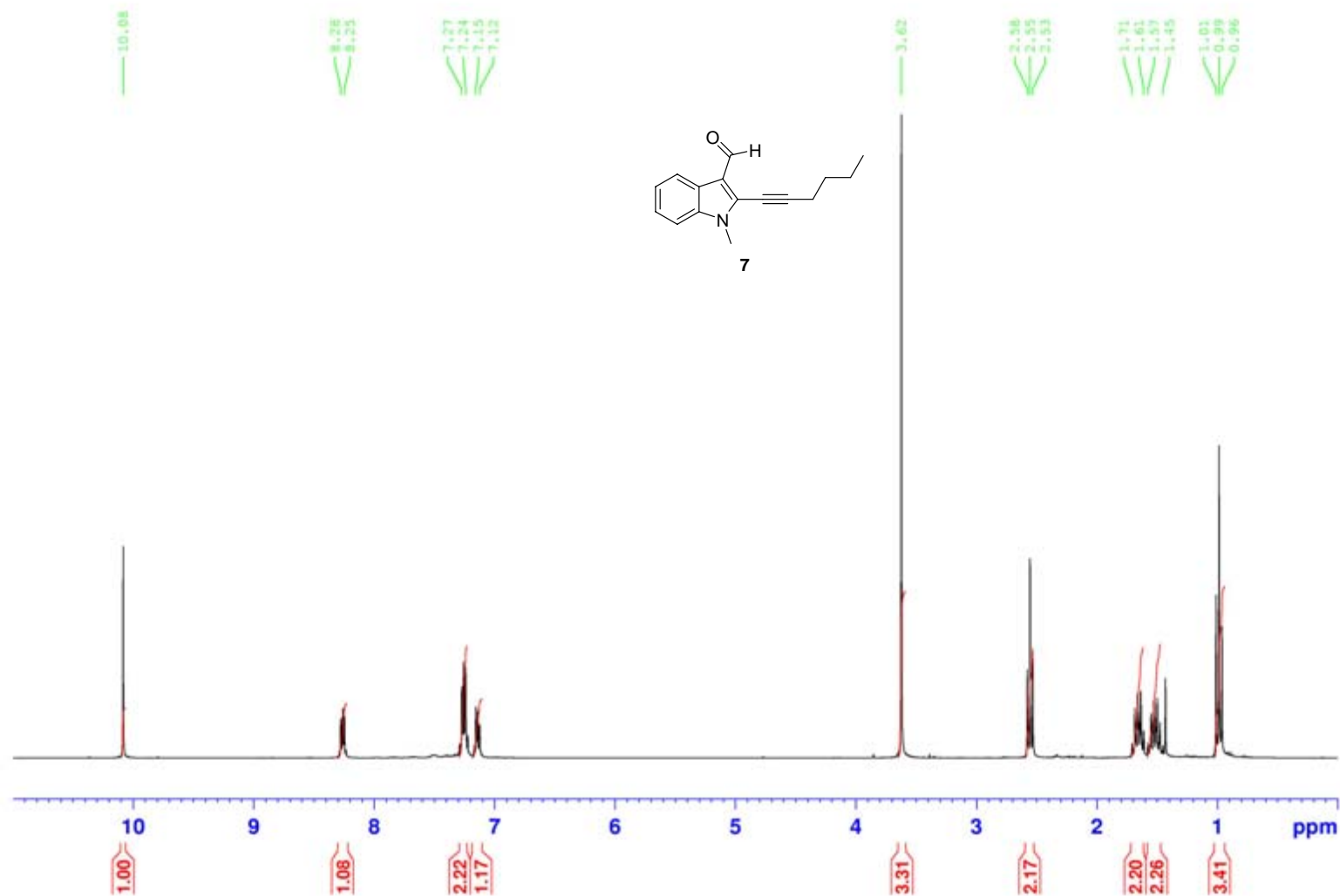
Compound **19** (26 mg, 0.074 mmol) was re-crystallized in cyclohexane and hot filtration allowed removal of some small red particles. Then, the resulting white powder was stirred with 500 mg of tris(2-aminoethyl)amine polystyrene in toluene during 48 hours and filtrated through celite. The residue was then submitted to the aminobenzannulation reaction (method **B**) with a new glassware and stir bar in 1 mL of DCE with 100 mg of 4Å powdered molecular sieves and pyrrolidine (25 µL). After purification, this reaction afforded 25 mg (0.062 mmol) of the desired product **48bis** with a yield of 84% (from **19**).

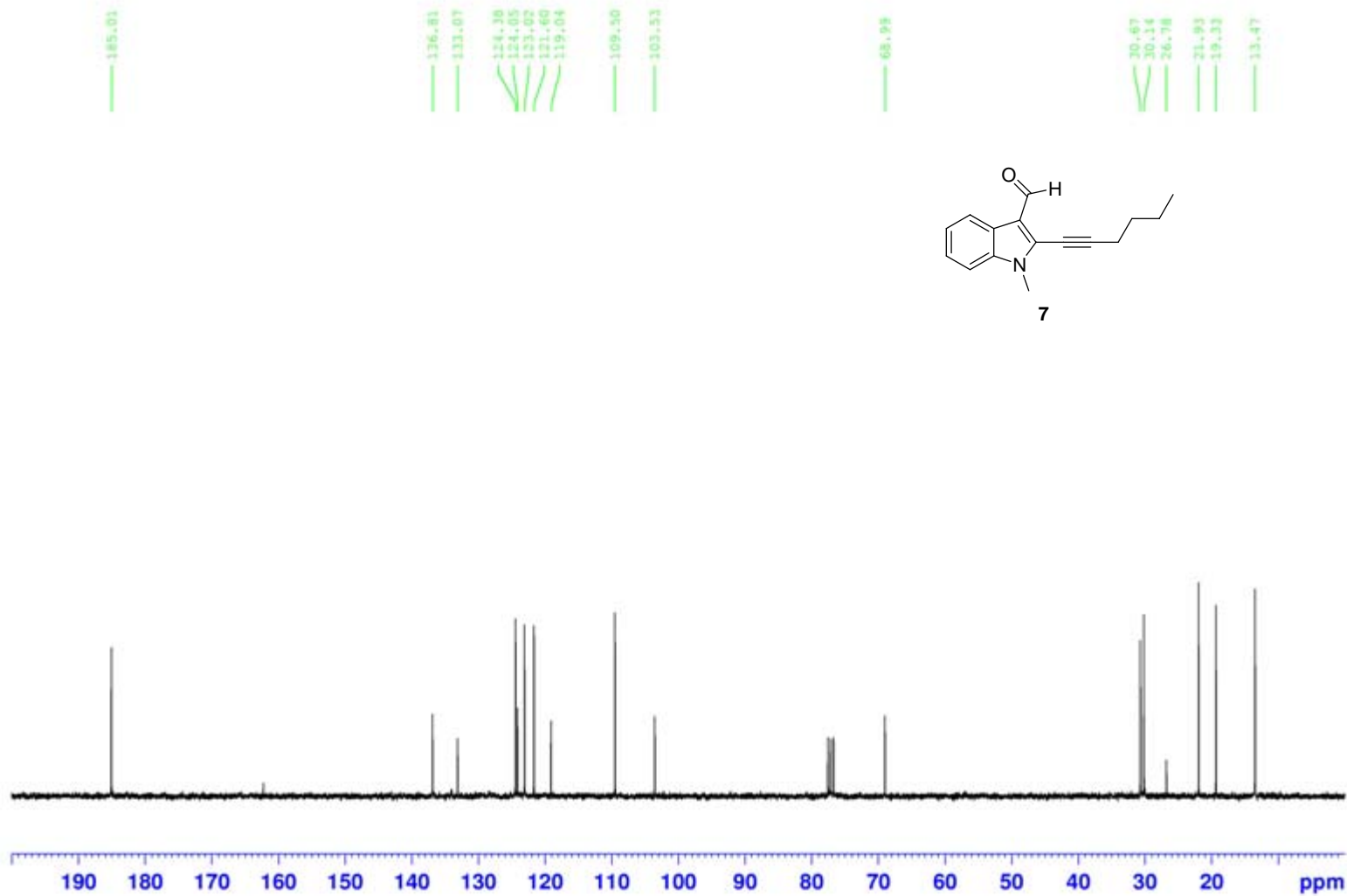
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<sup>2</sup> Urawa, Y.; Miyazawa, M.; Ozeki, N.; Ogura, K. *Org. Process Res. Dev.* **2003**, 7, 191.

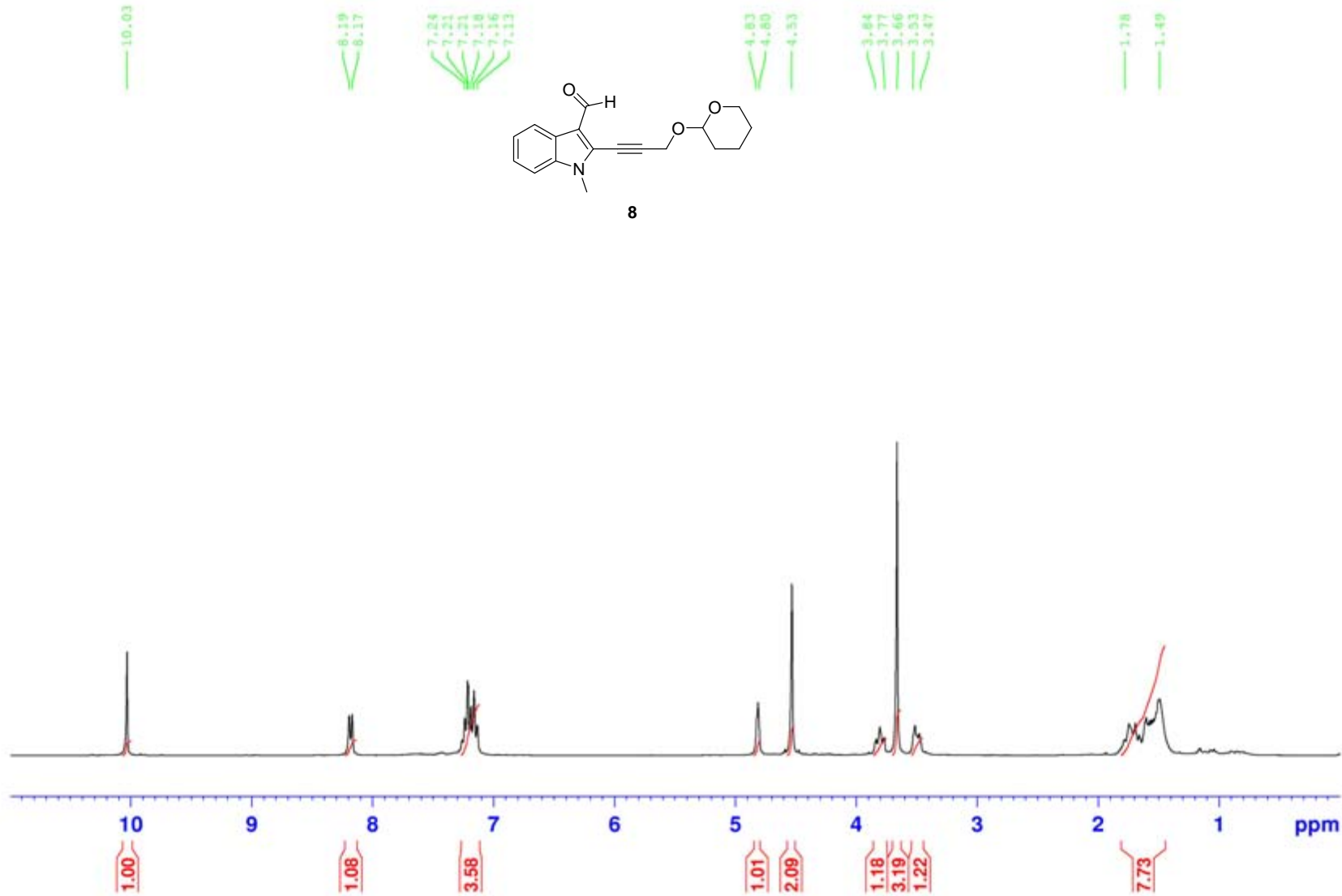


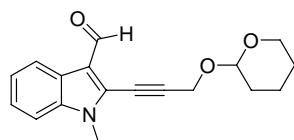




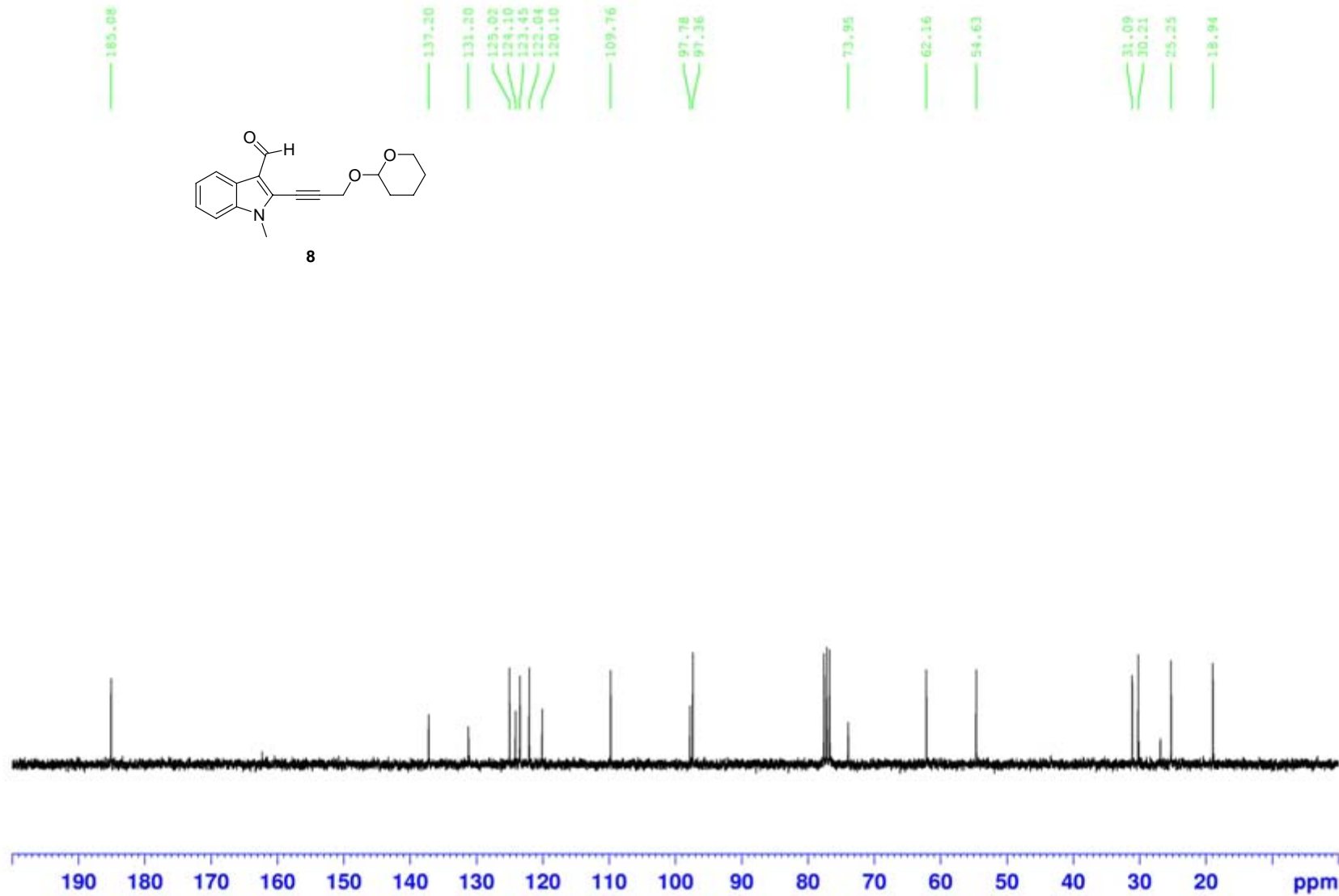


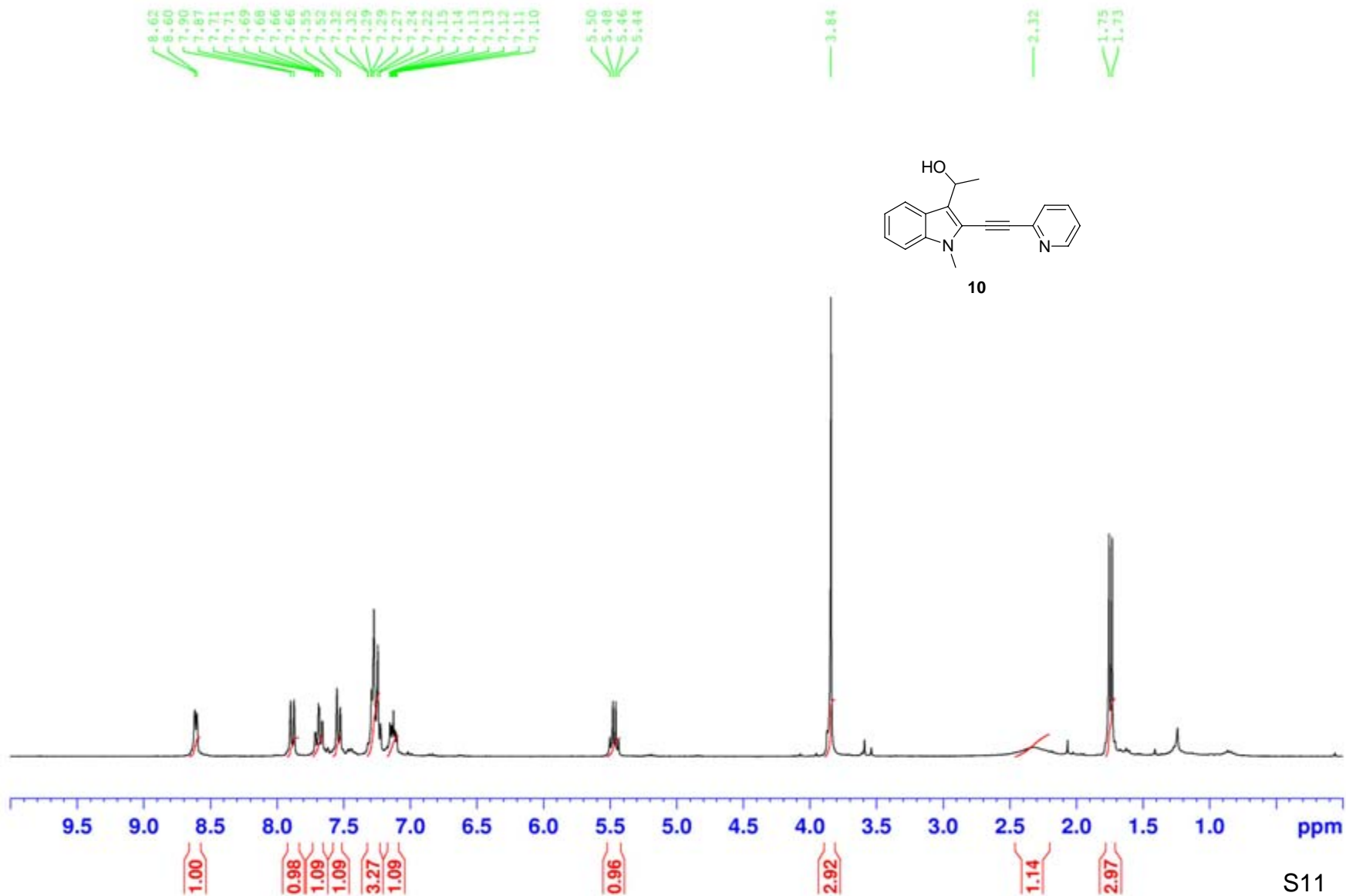


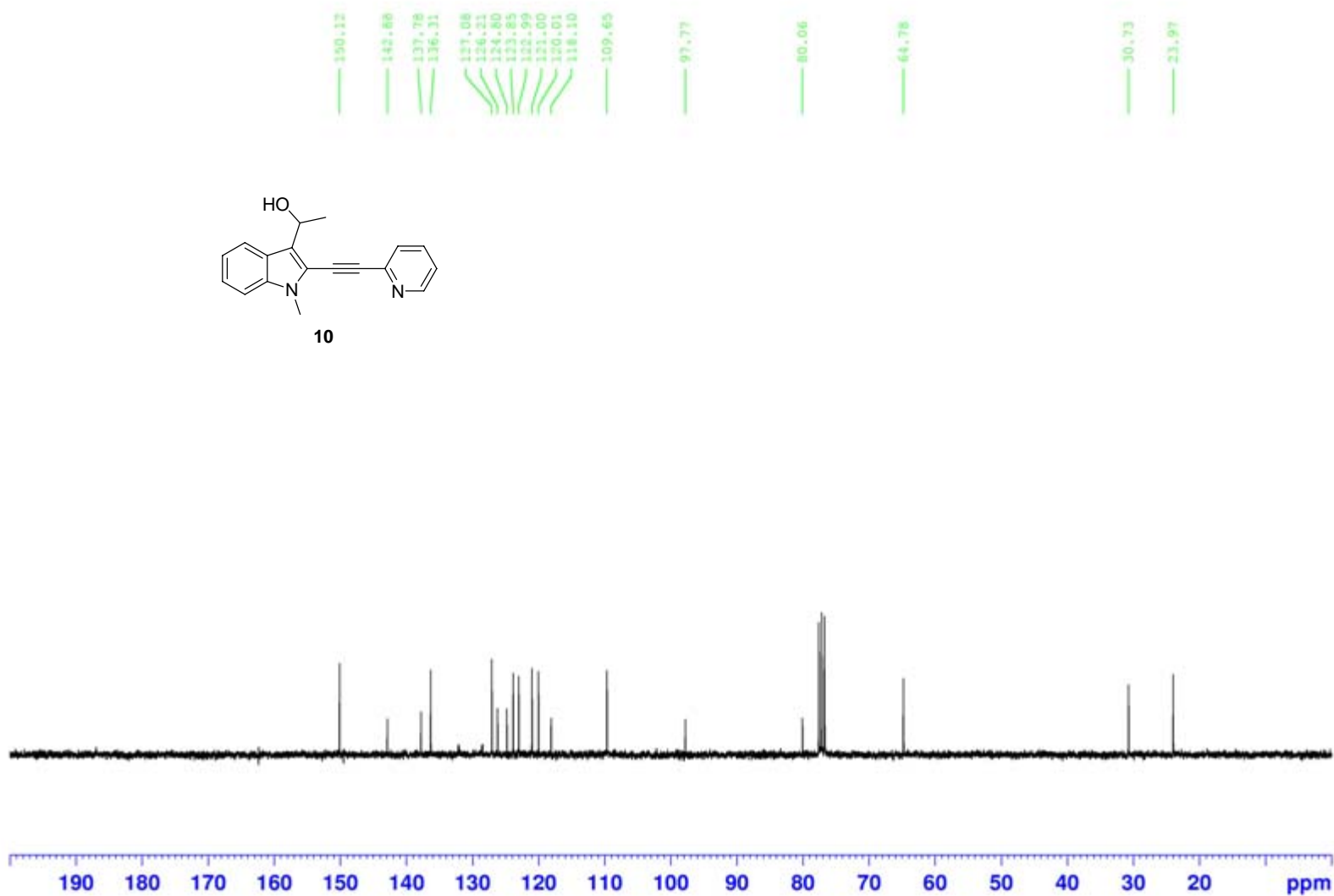
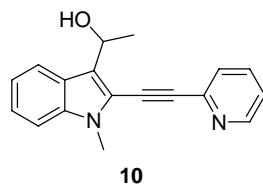


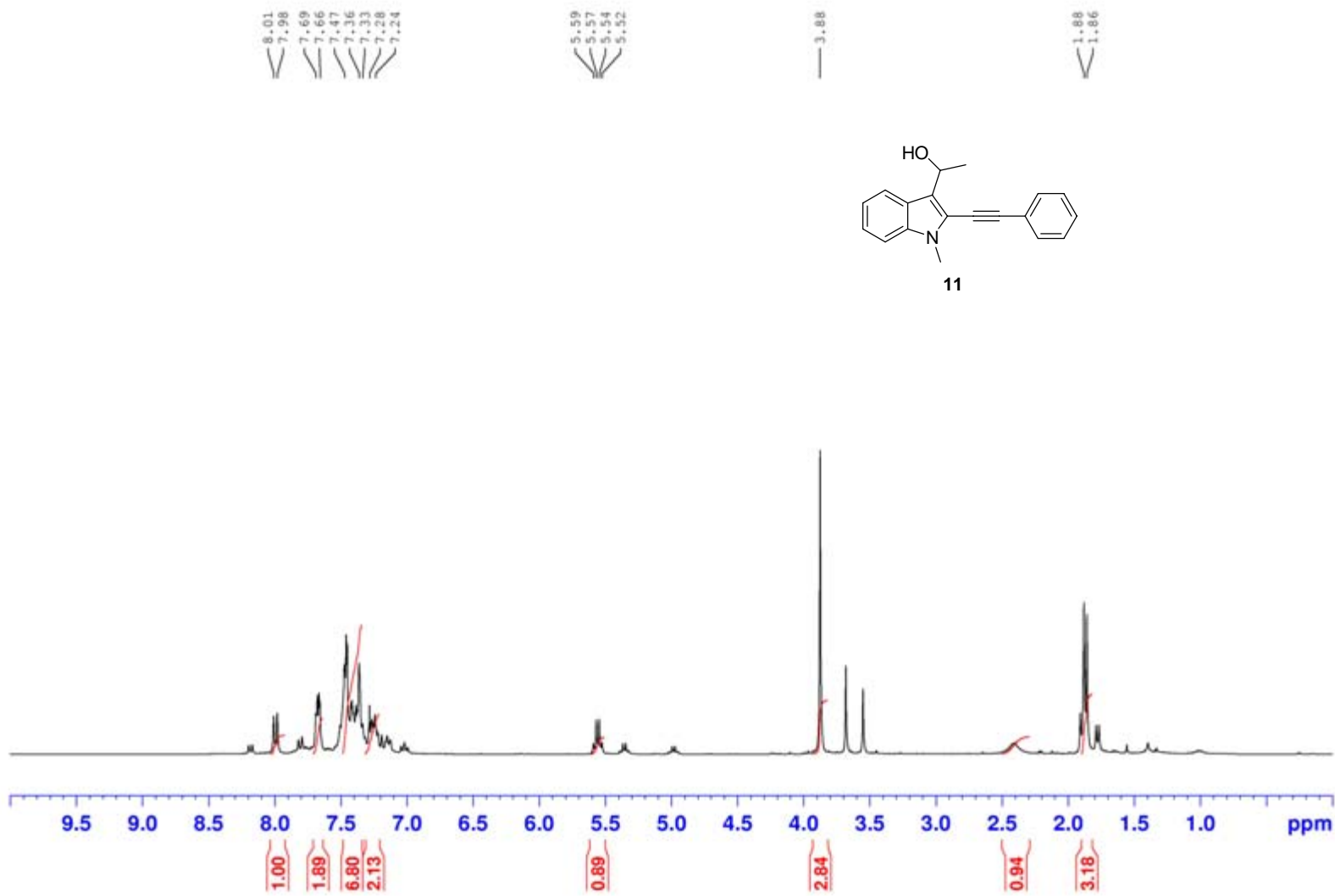


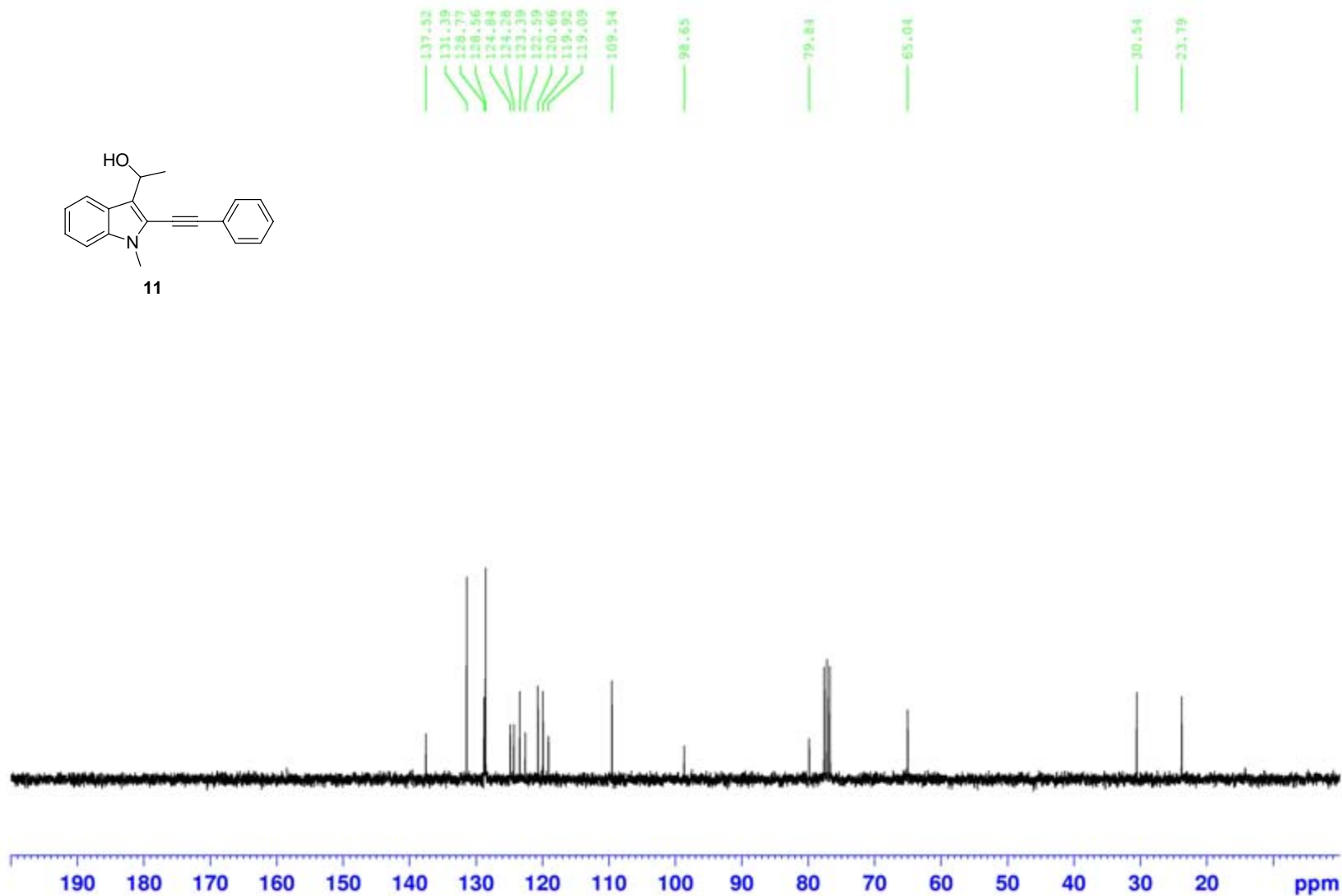
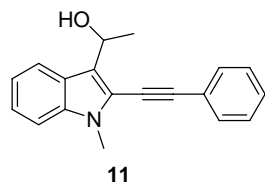
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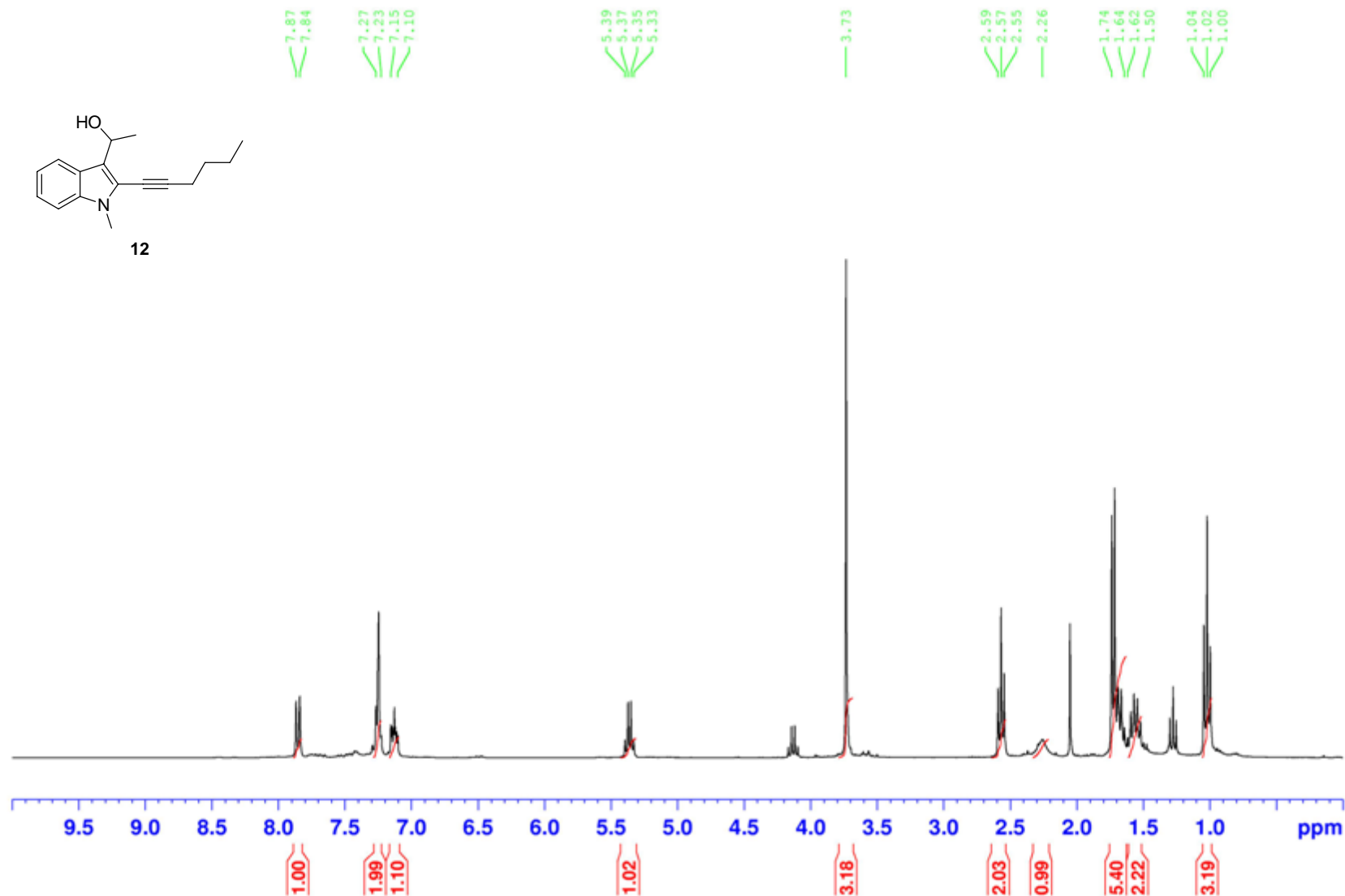
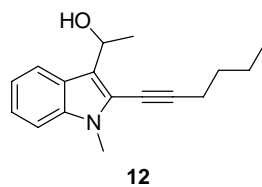


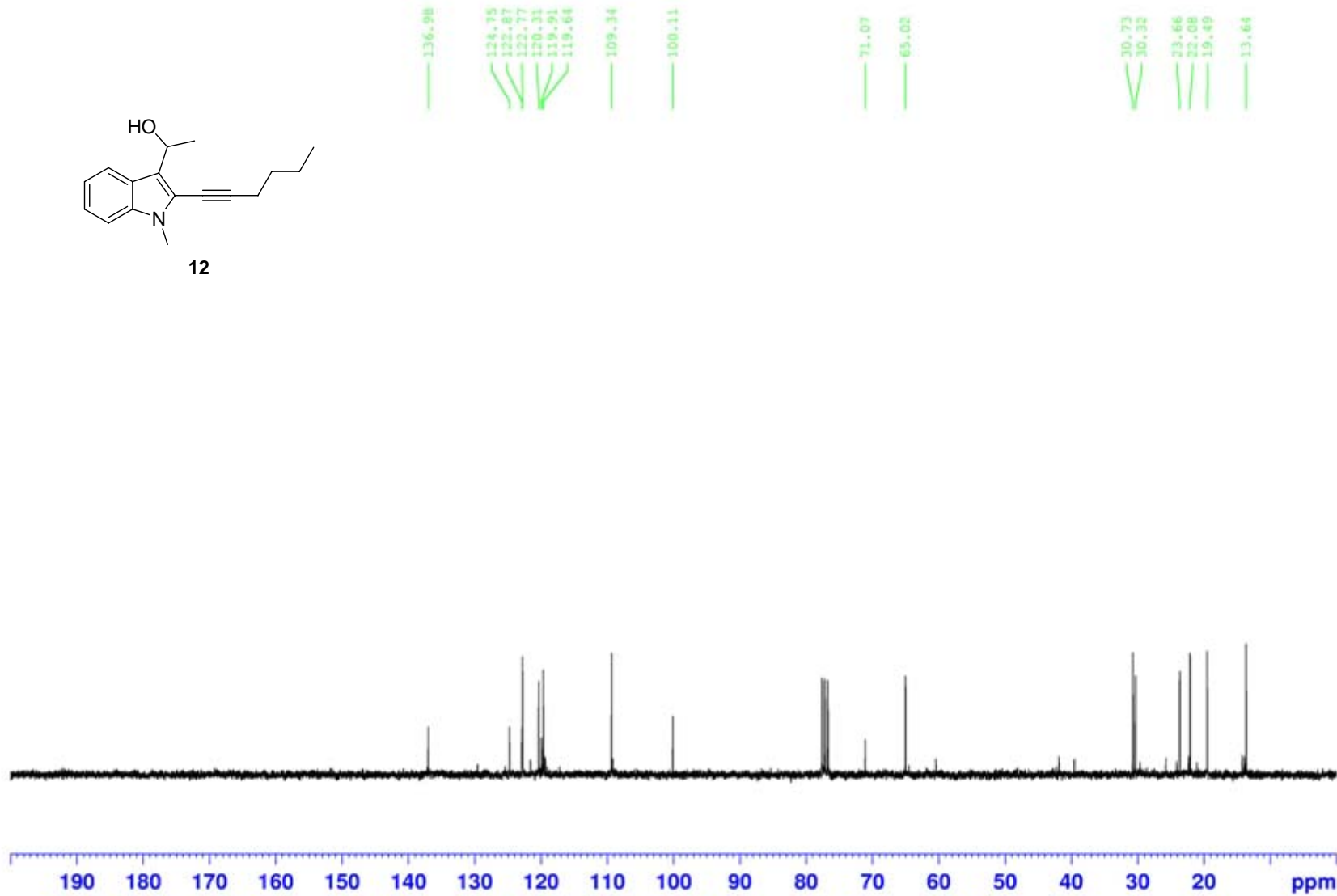
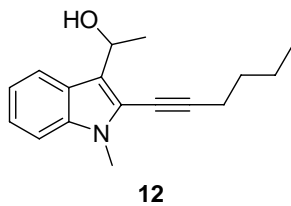




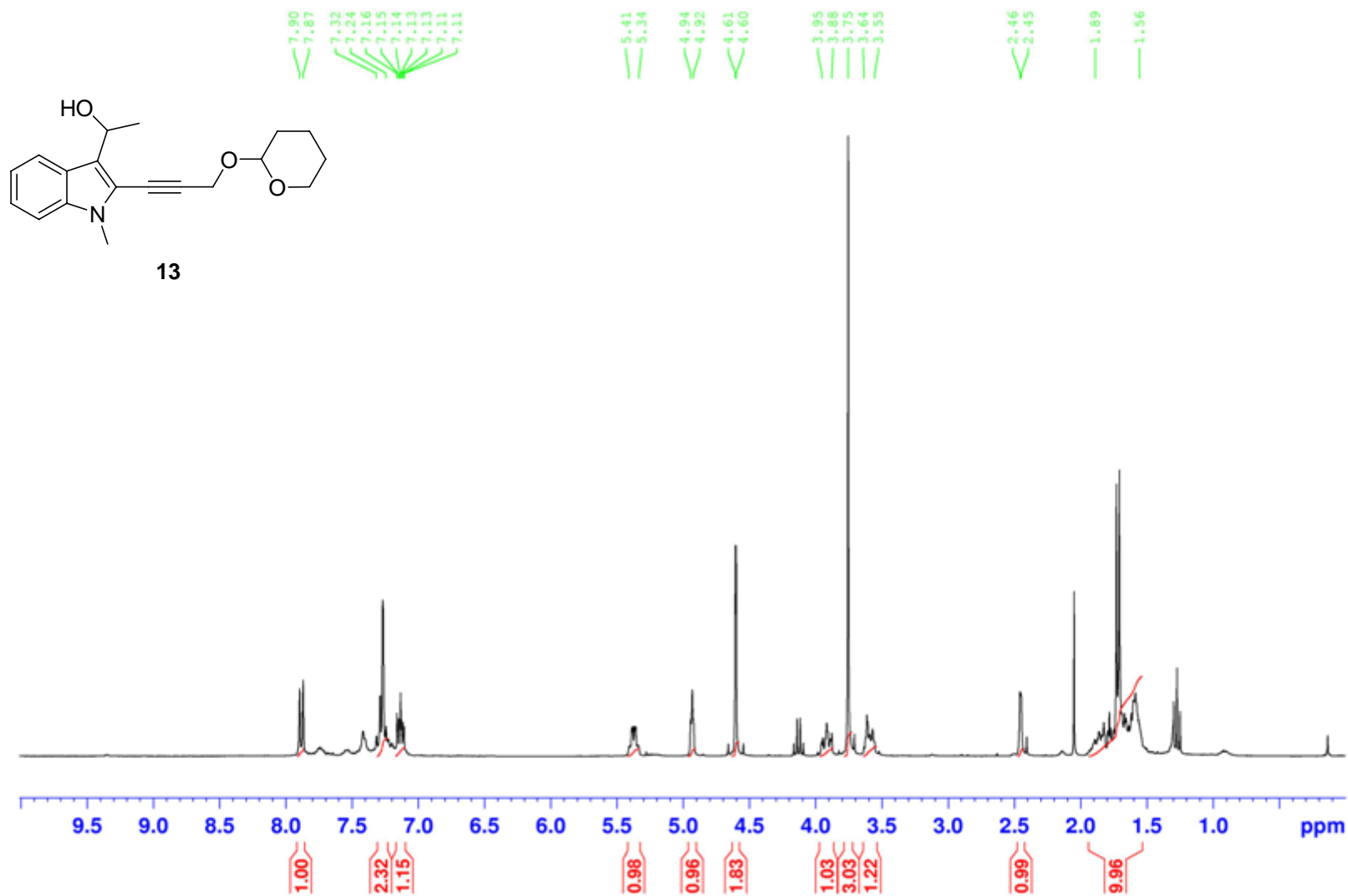


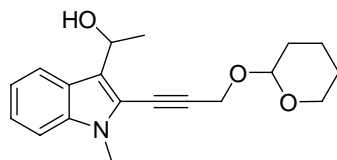












13

137.29

124.78

124.56

123.36

120.73

119.79

118.37

109.48

97.06

94.79

76.37

64.79

62.10

54.89

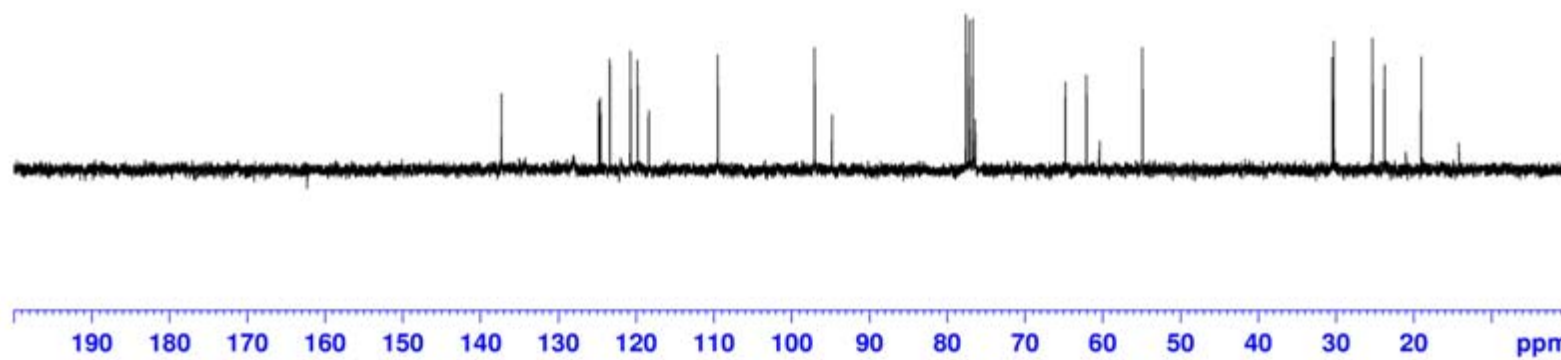
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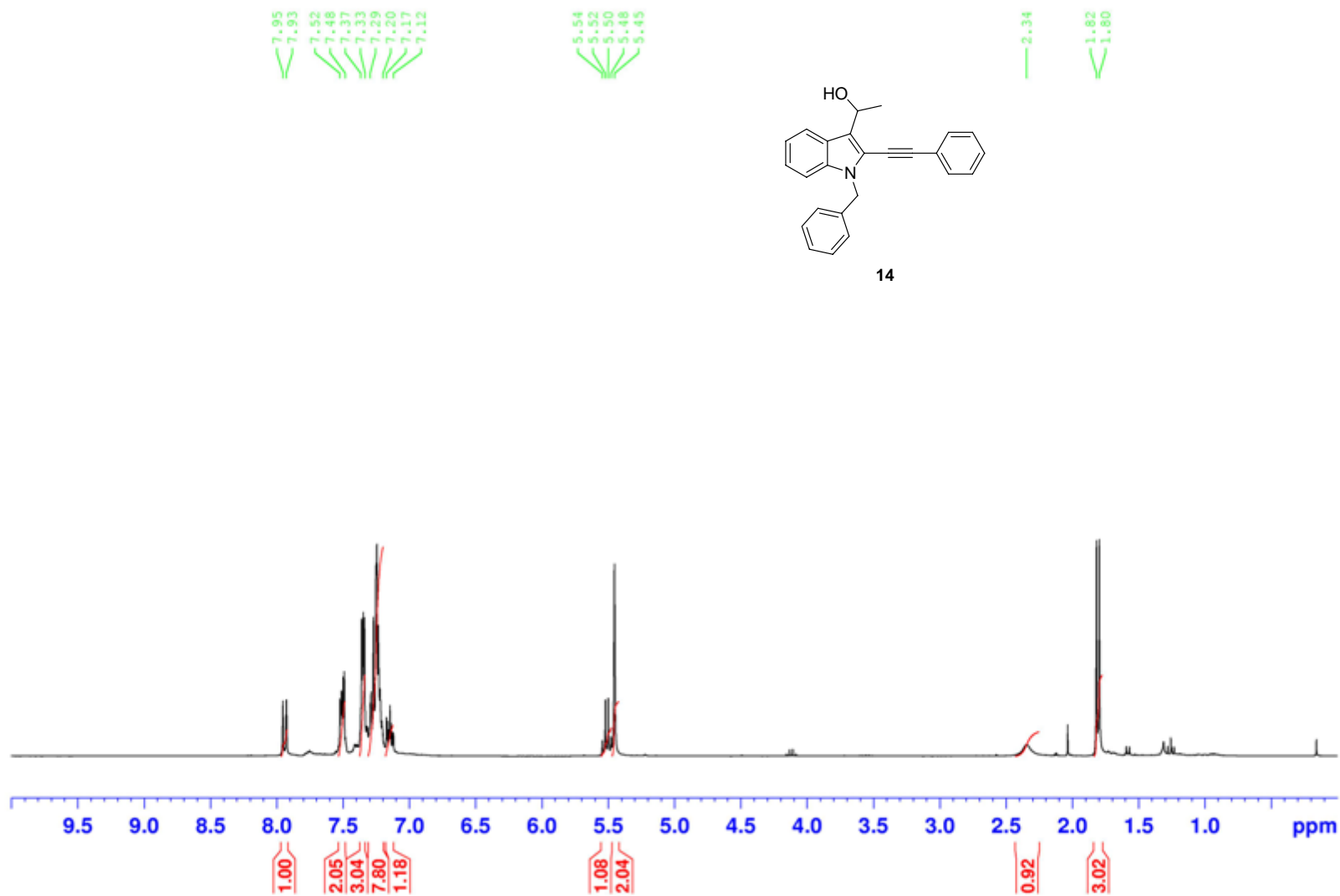
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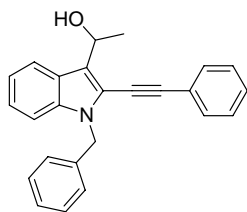
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23.76

19.02







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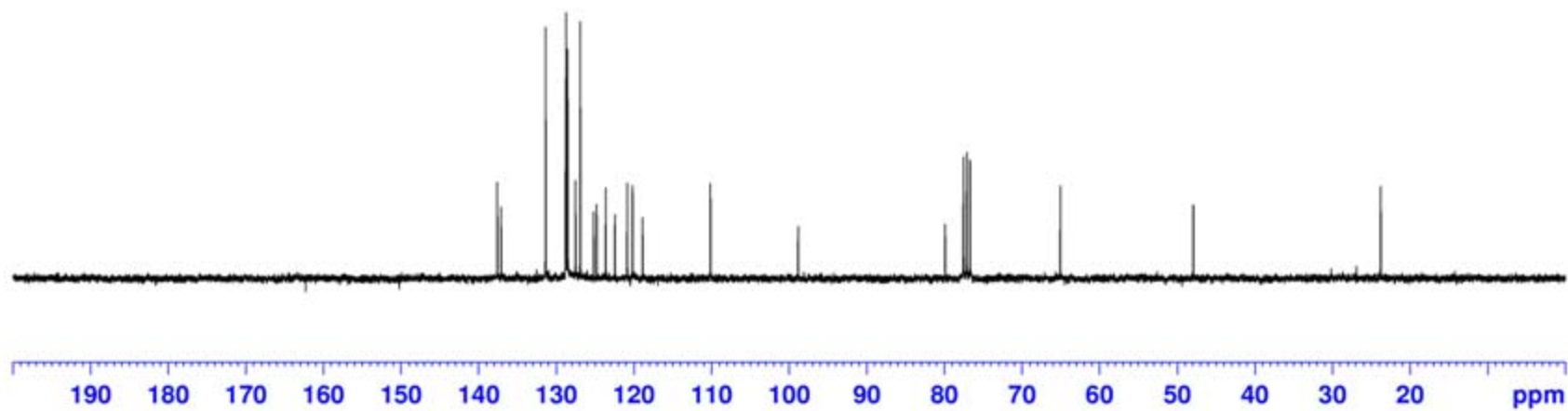
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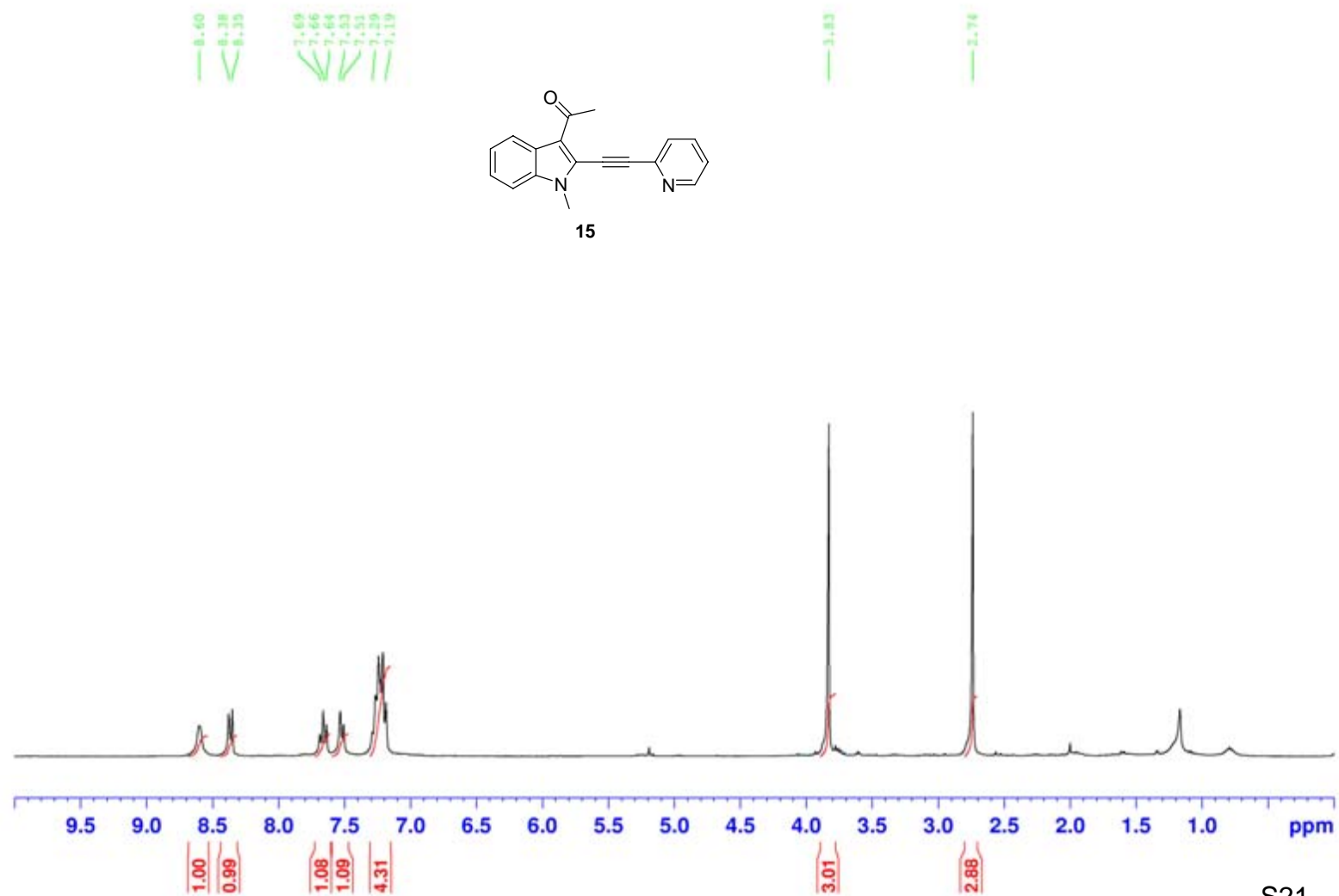
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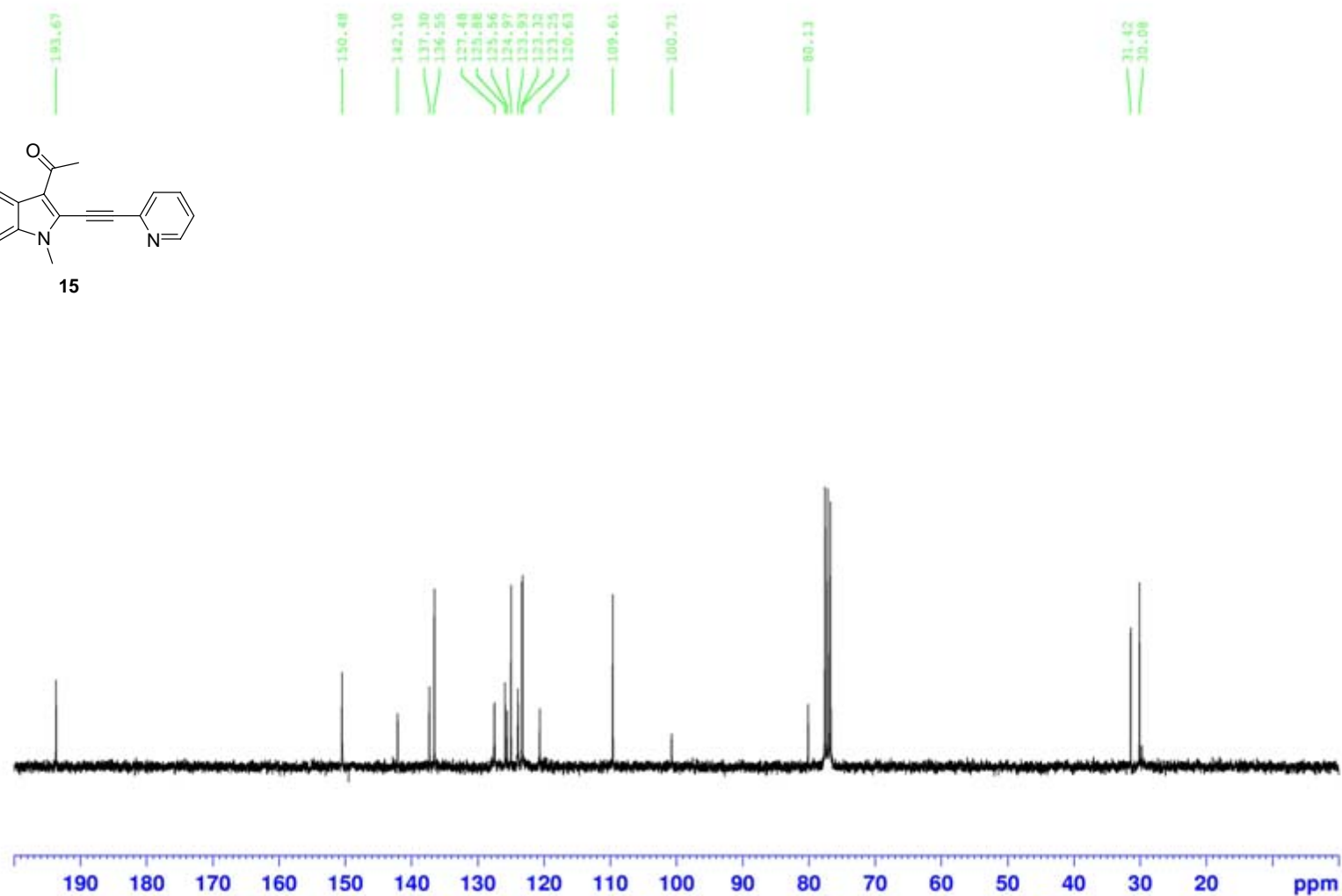
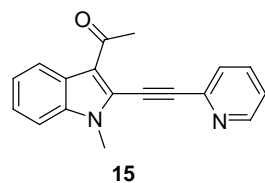
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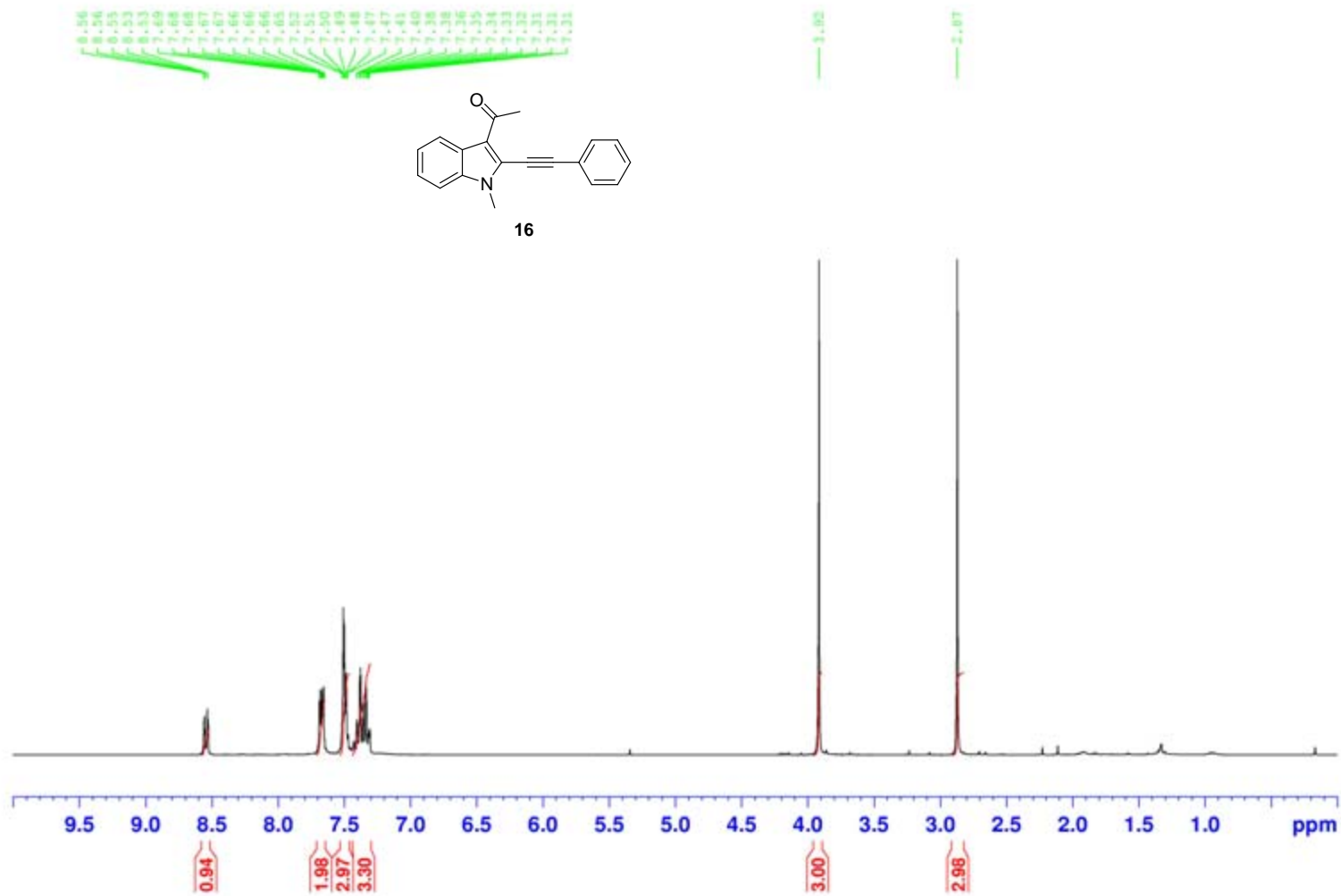
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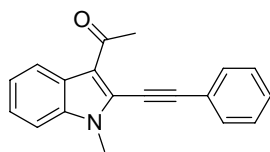
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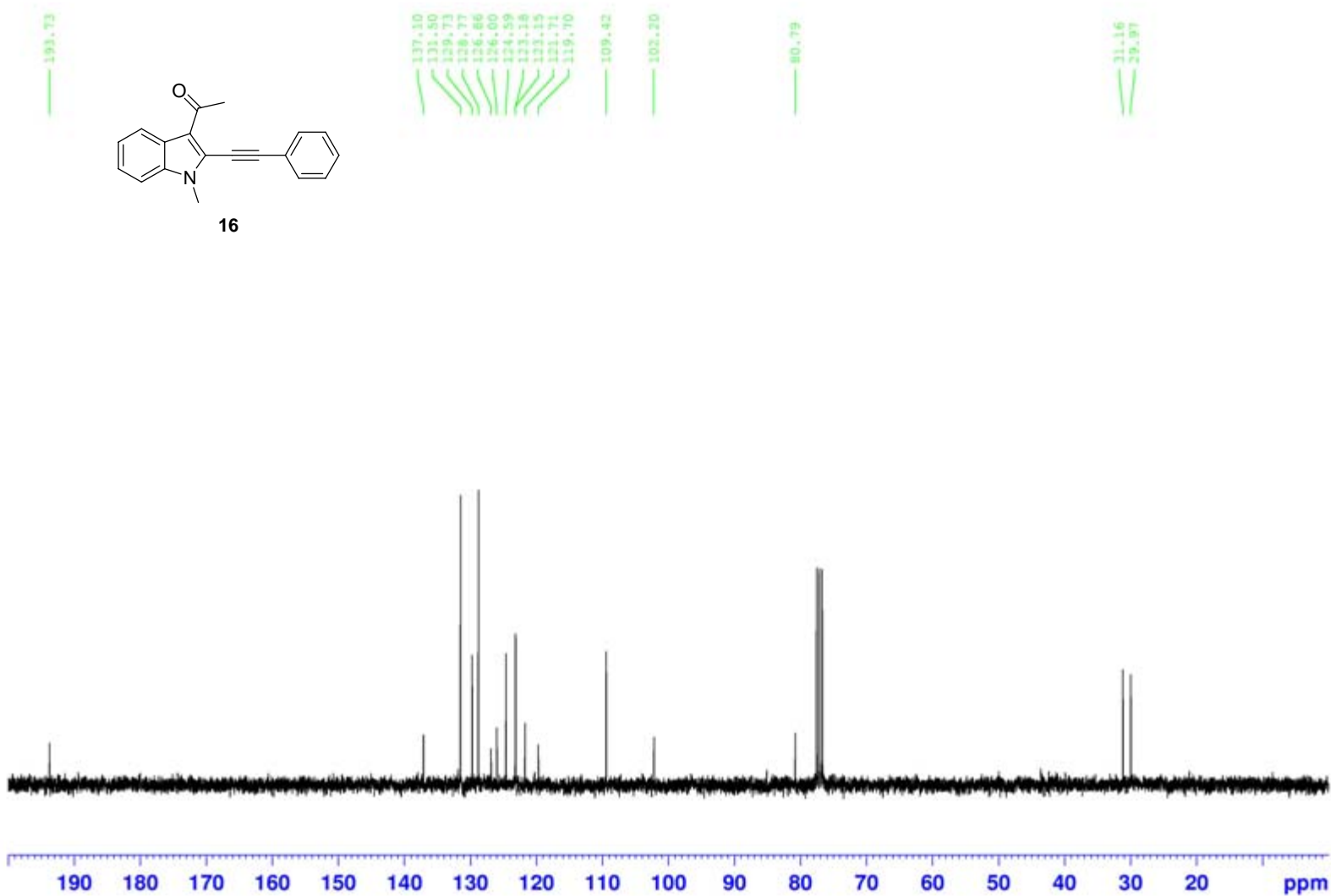




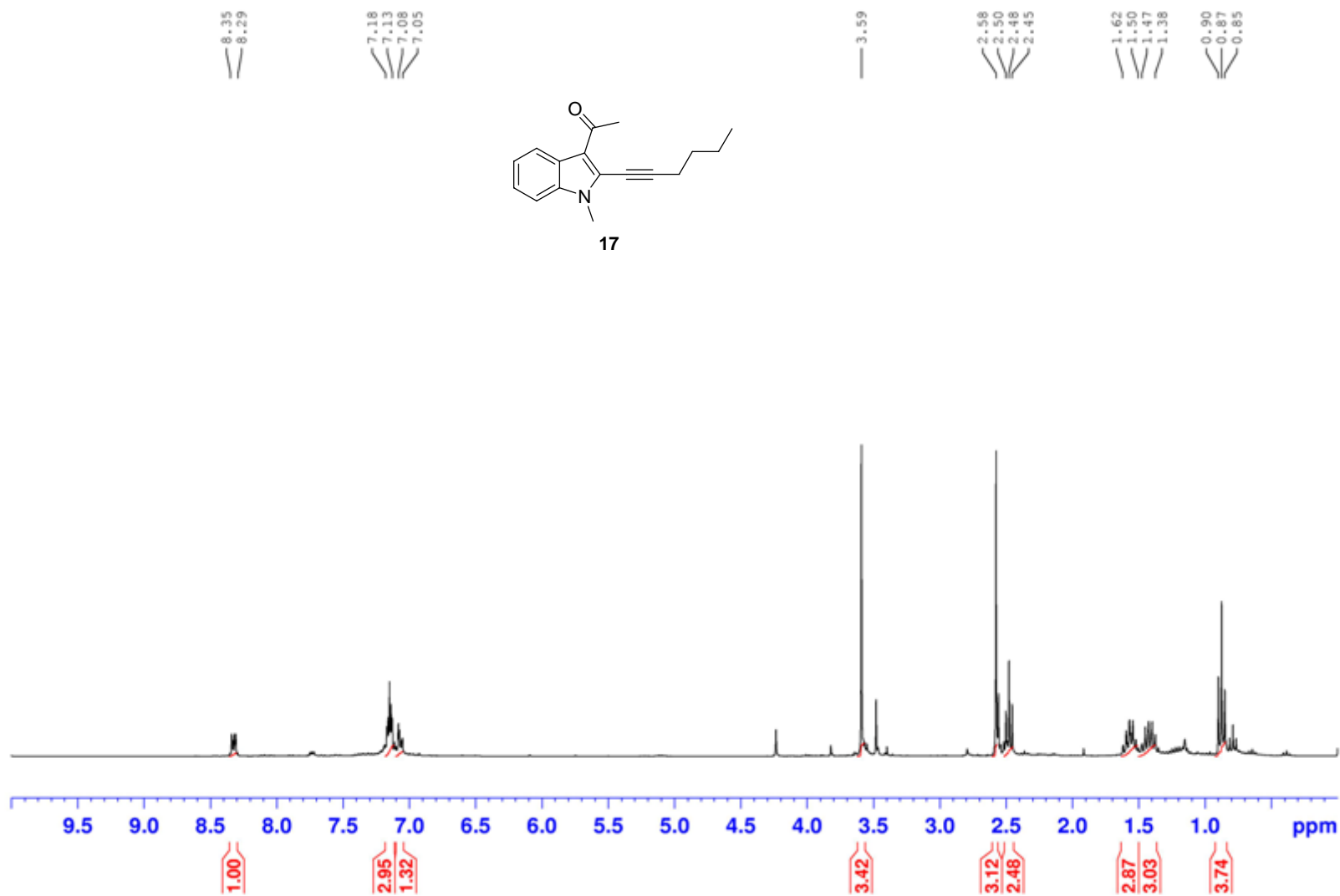


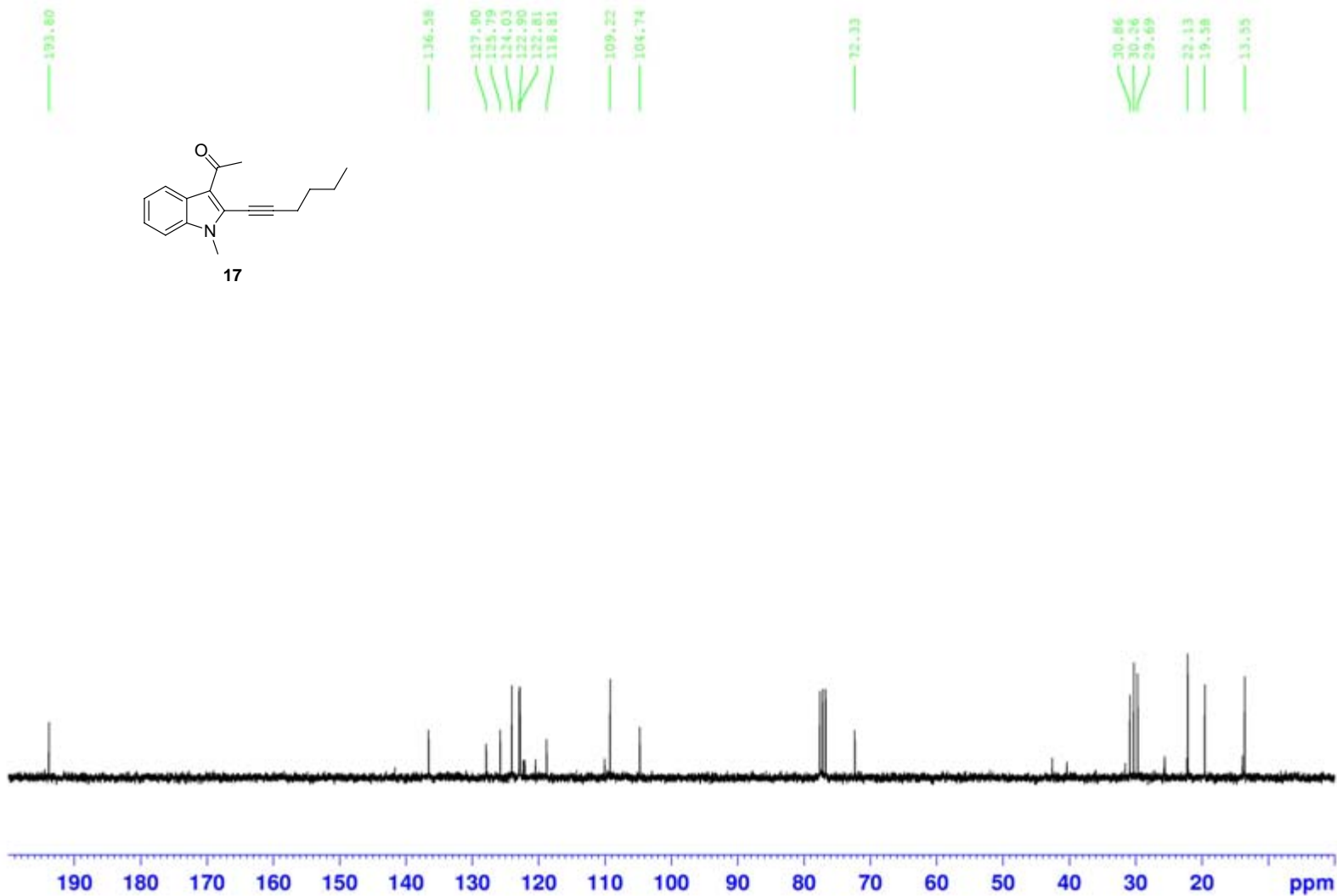


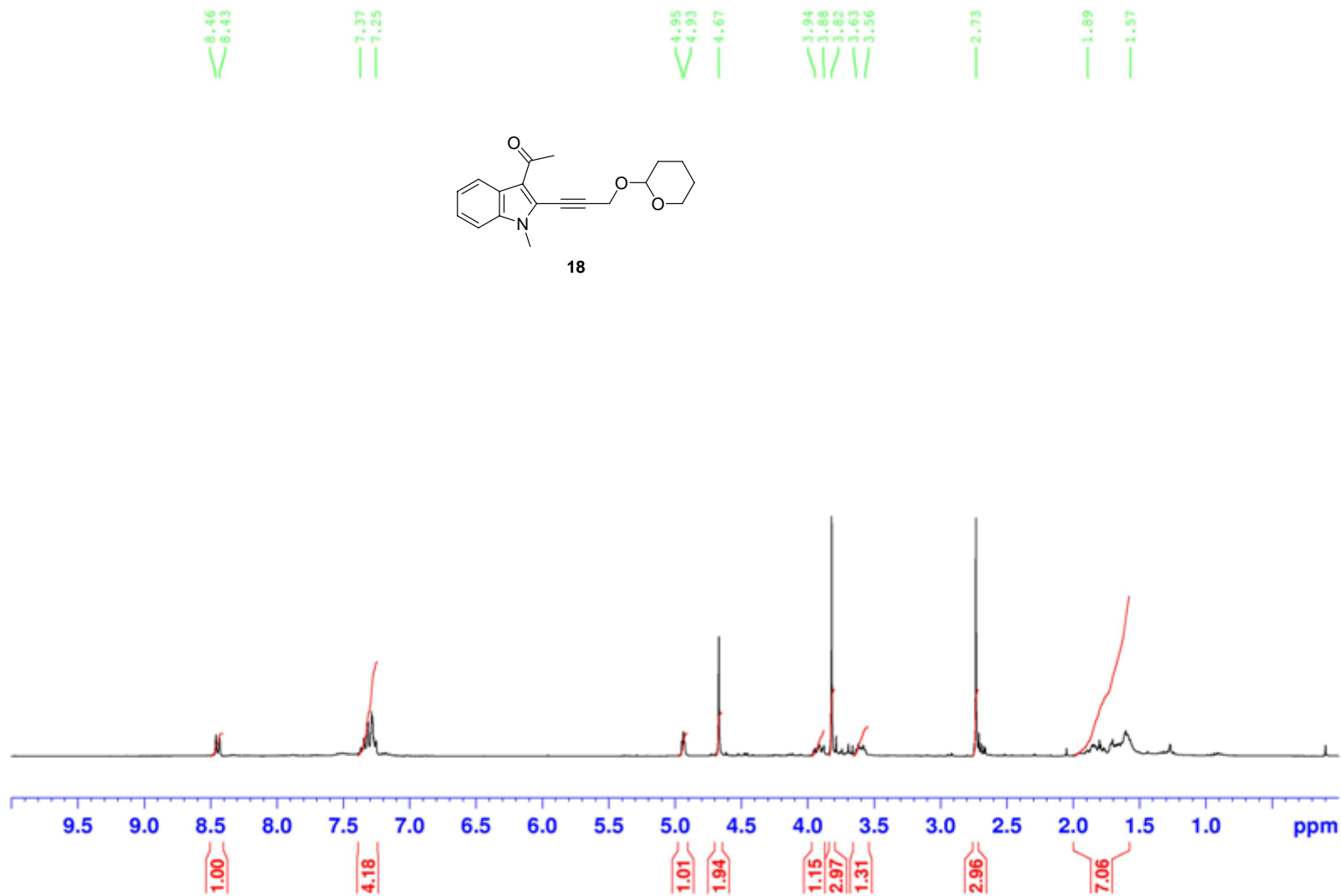
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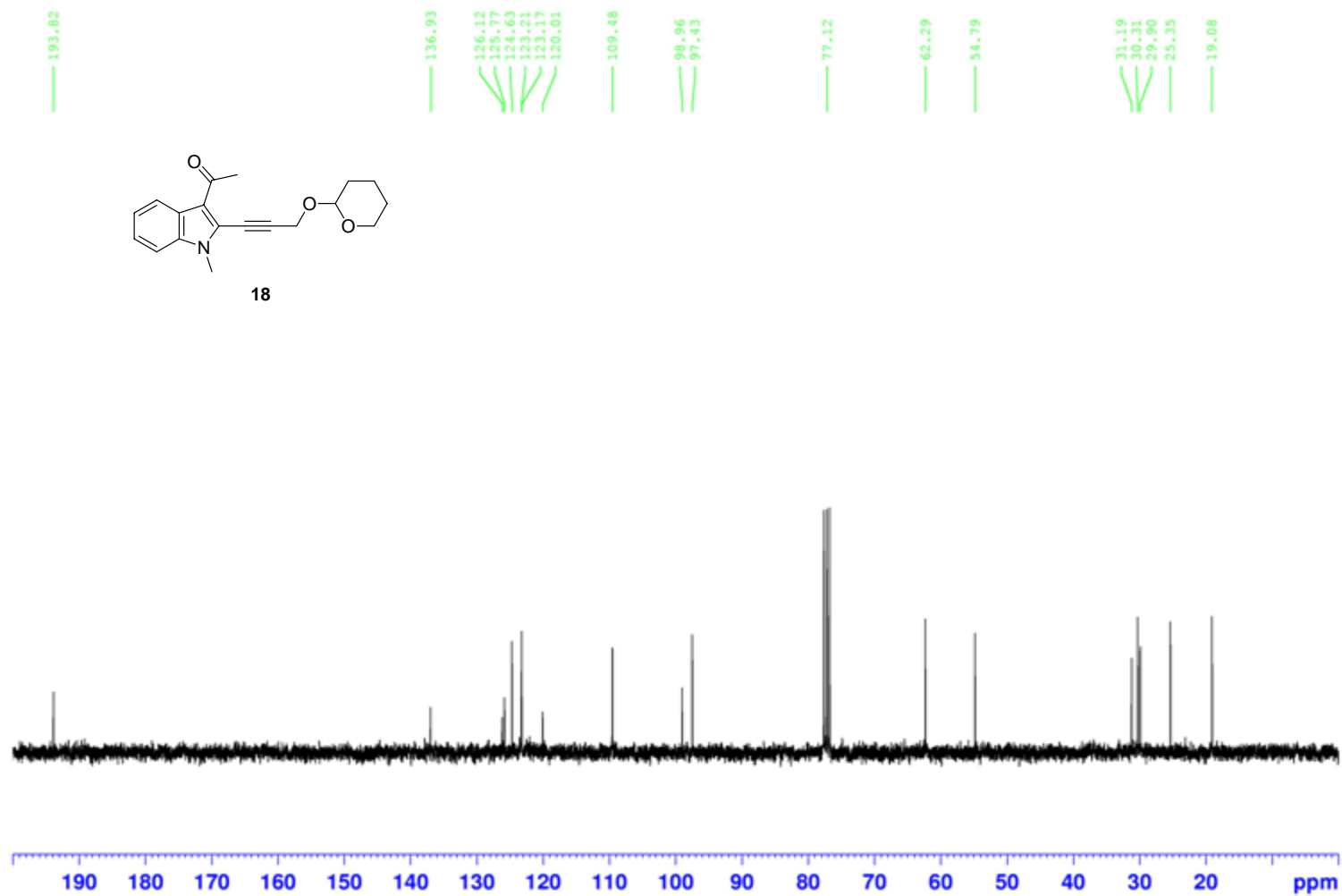


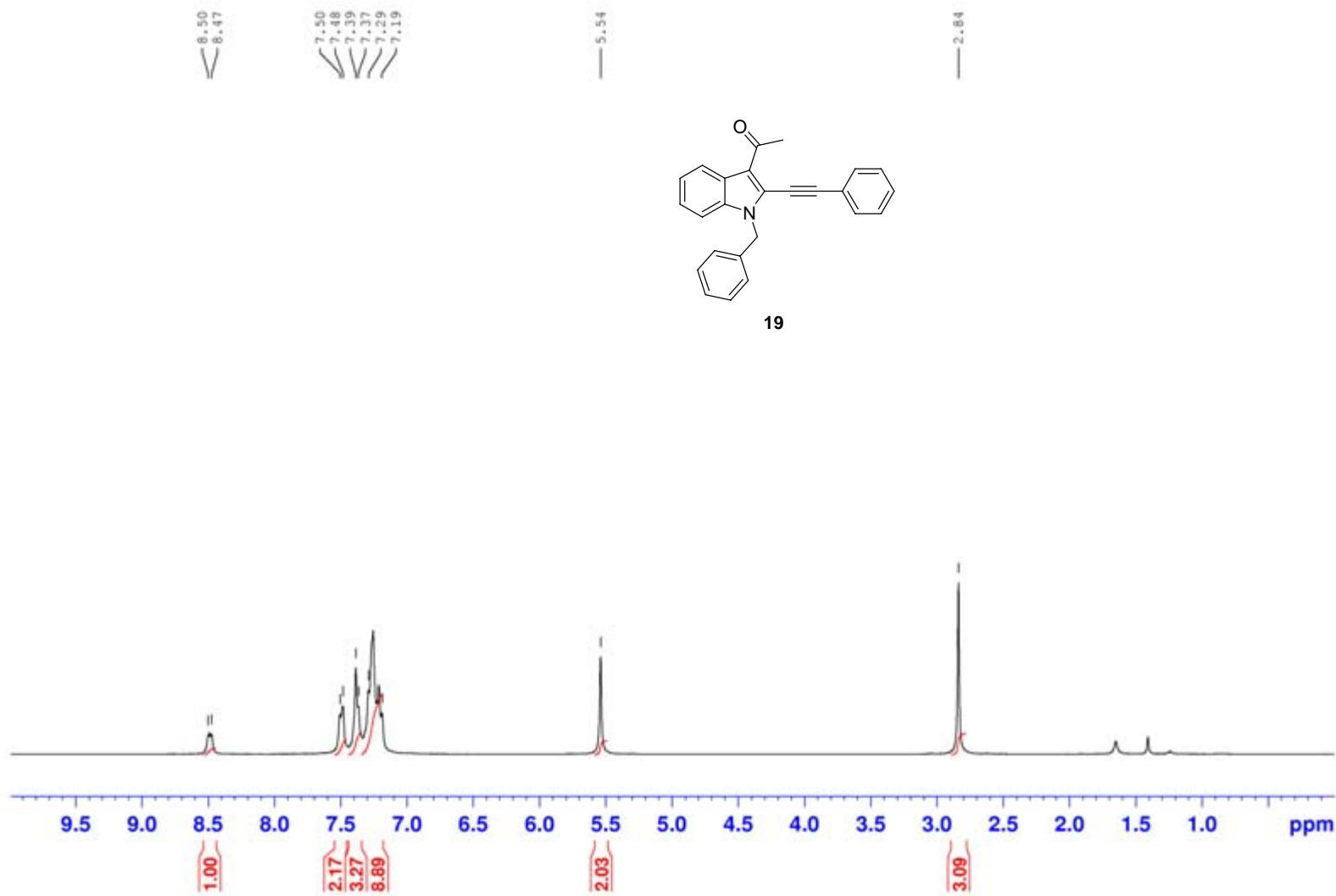


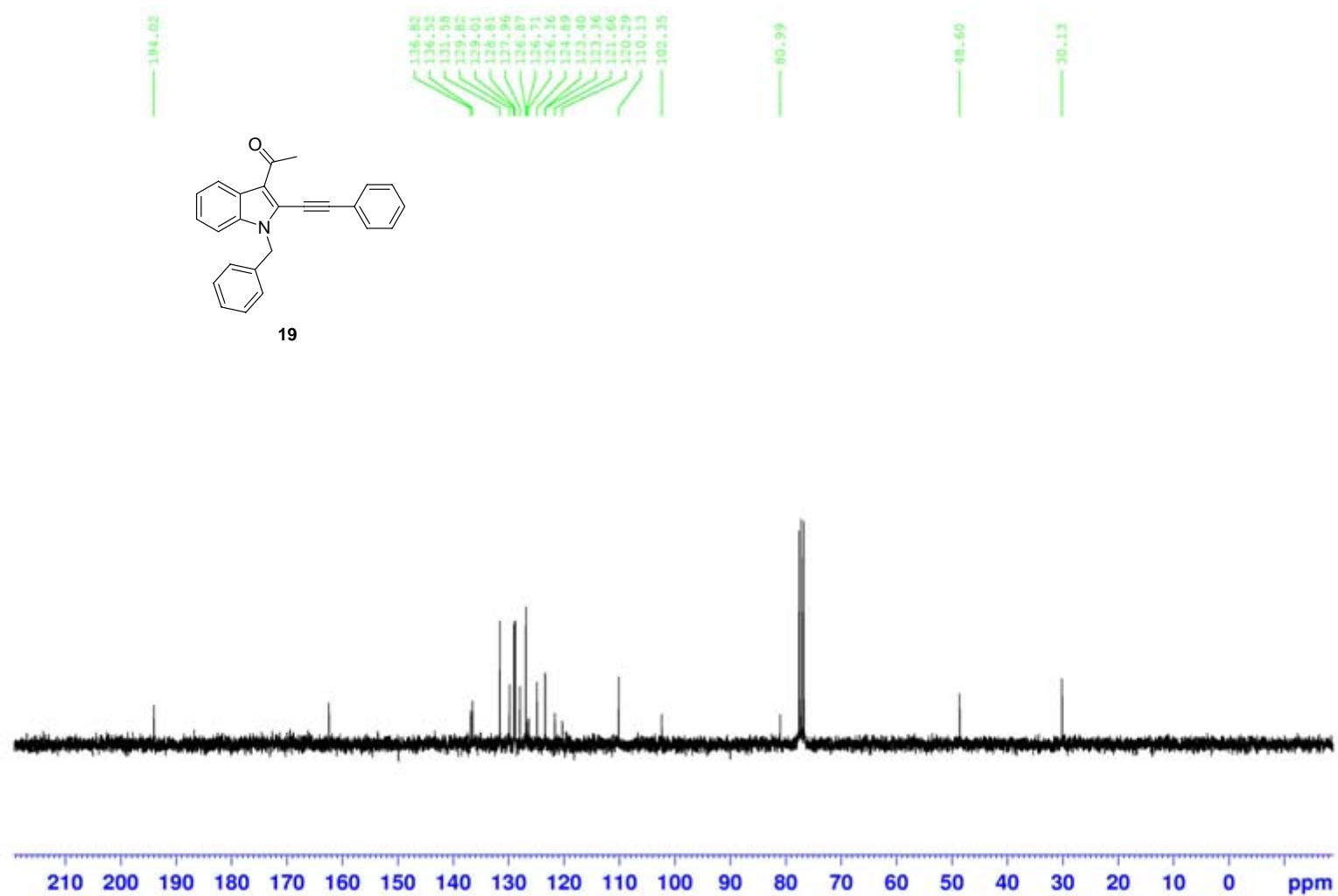


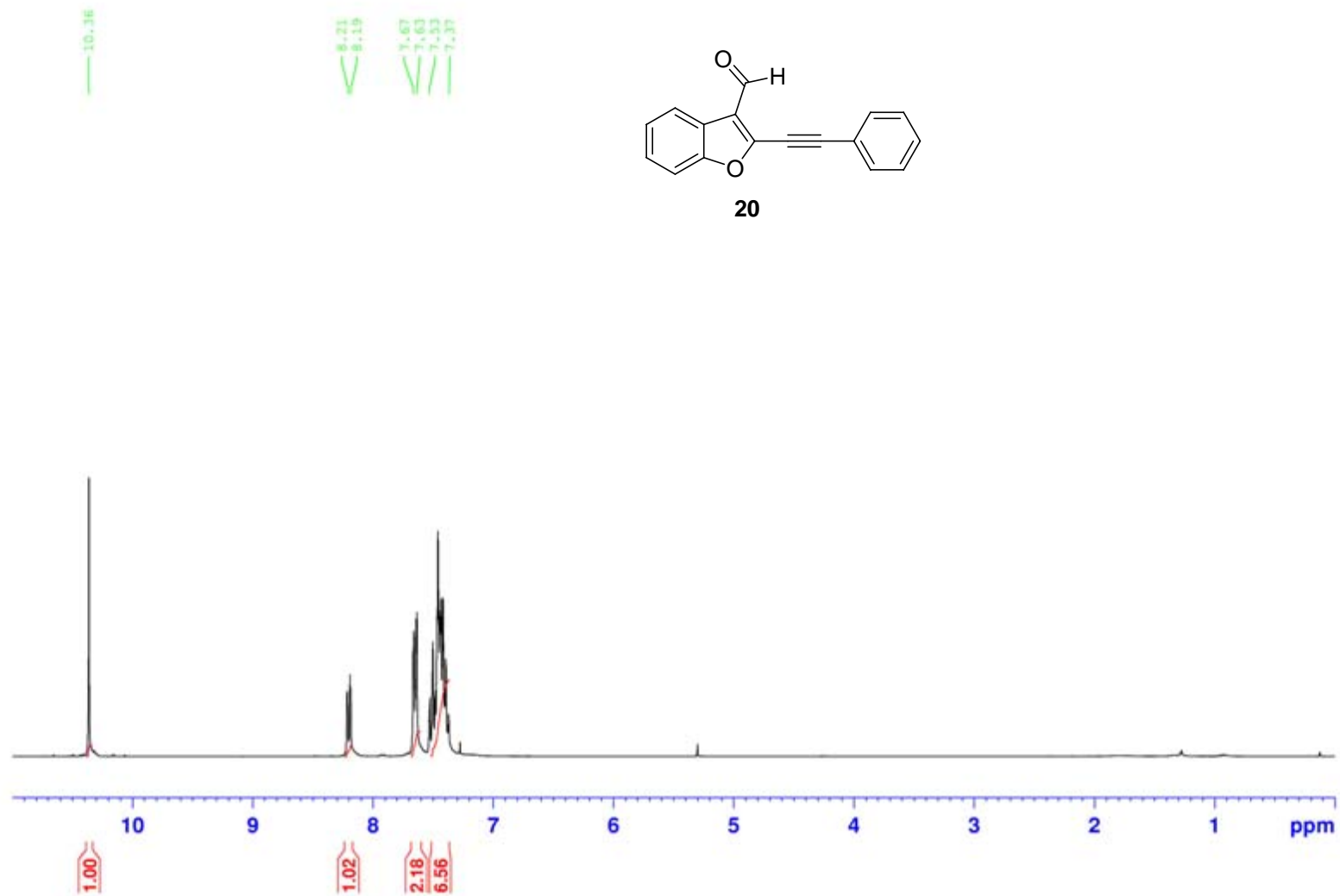
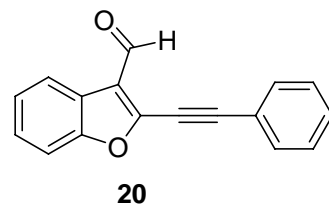


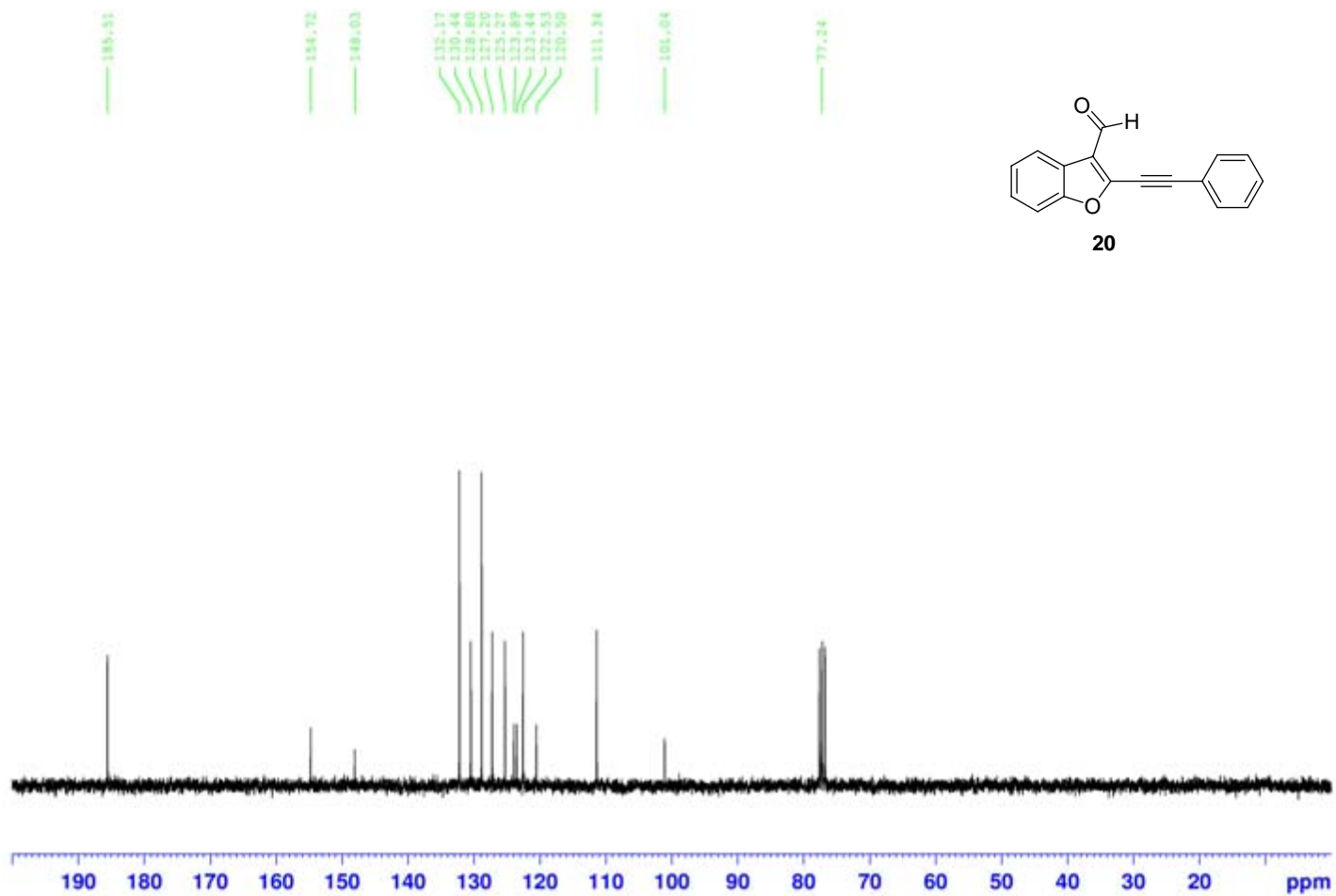




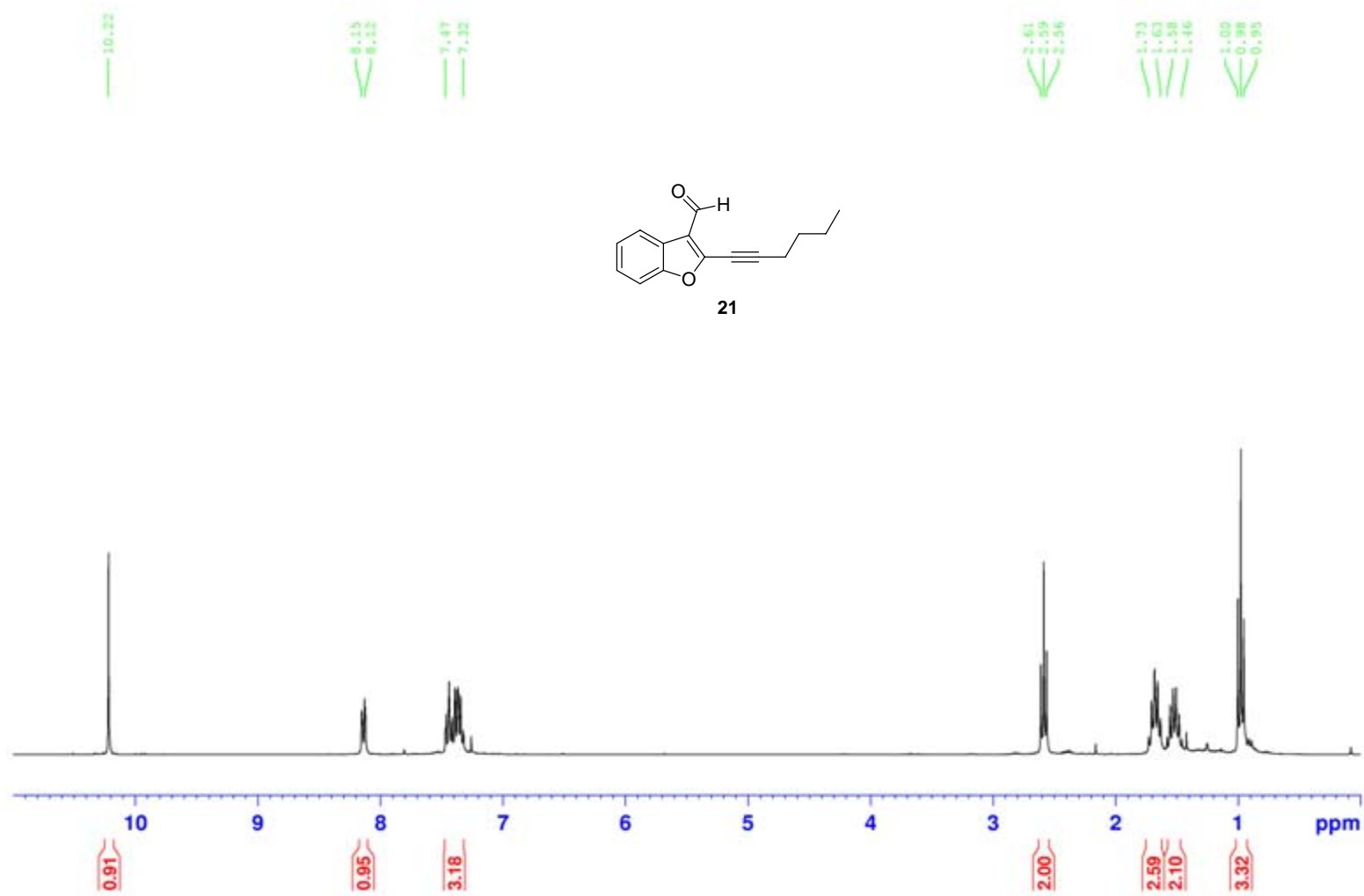


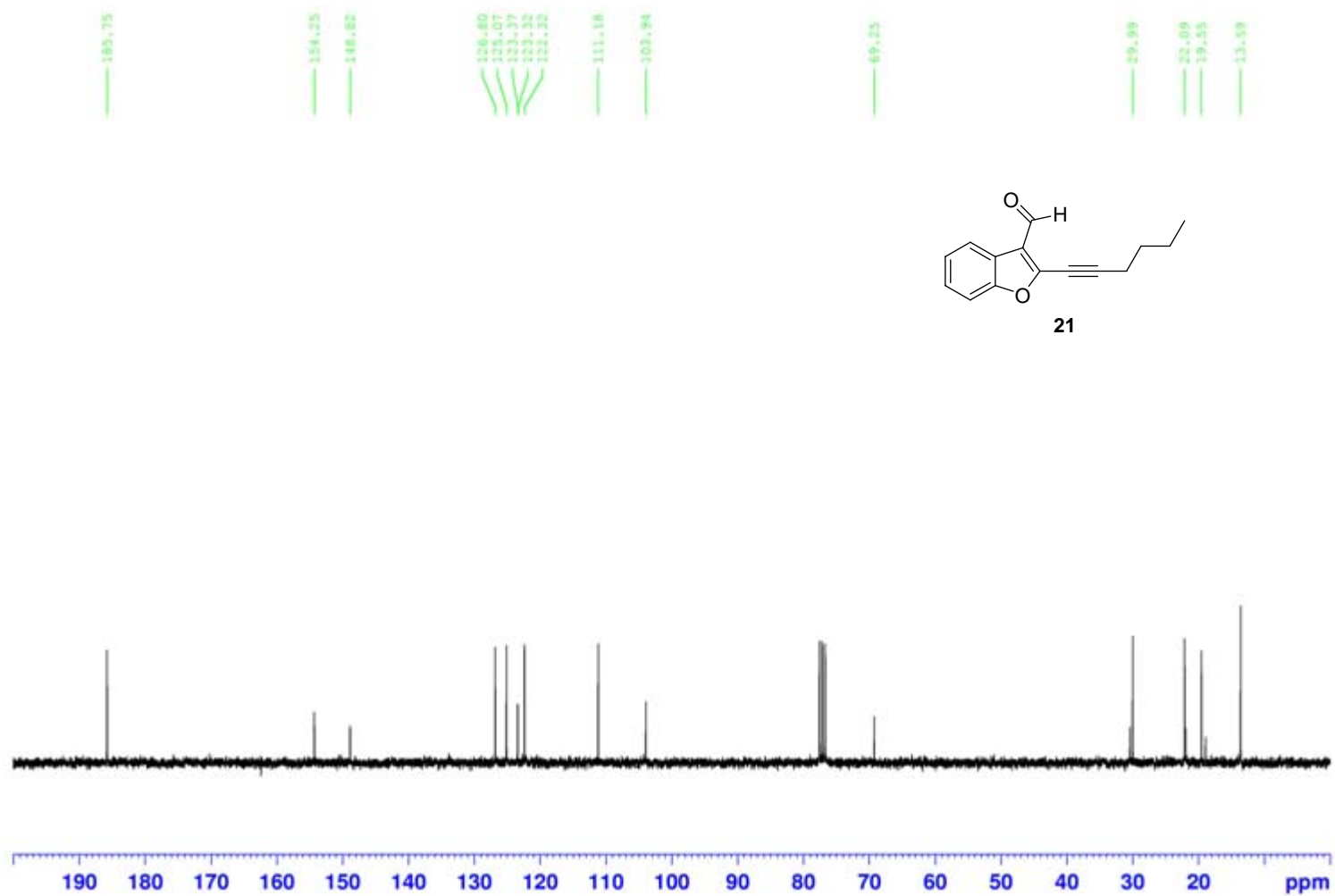


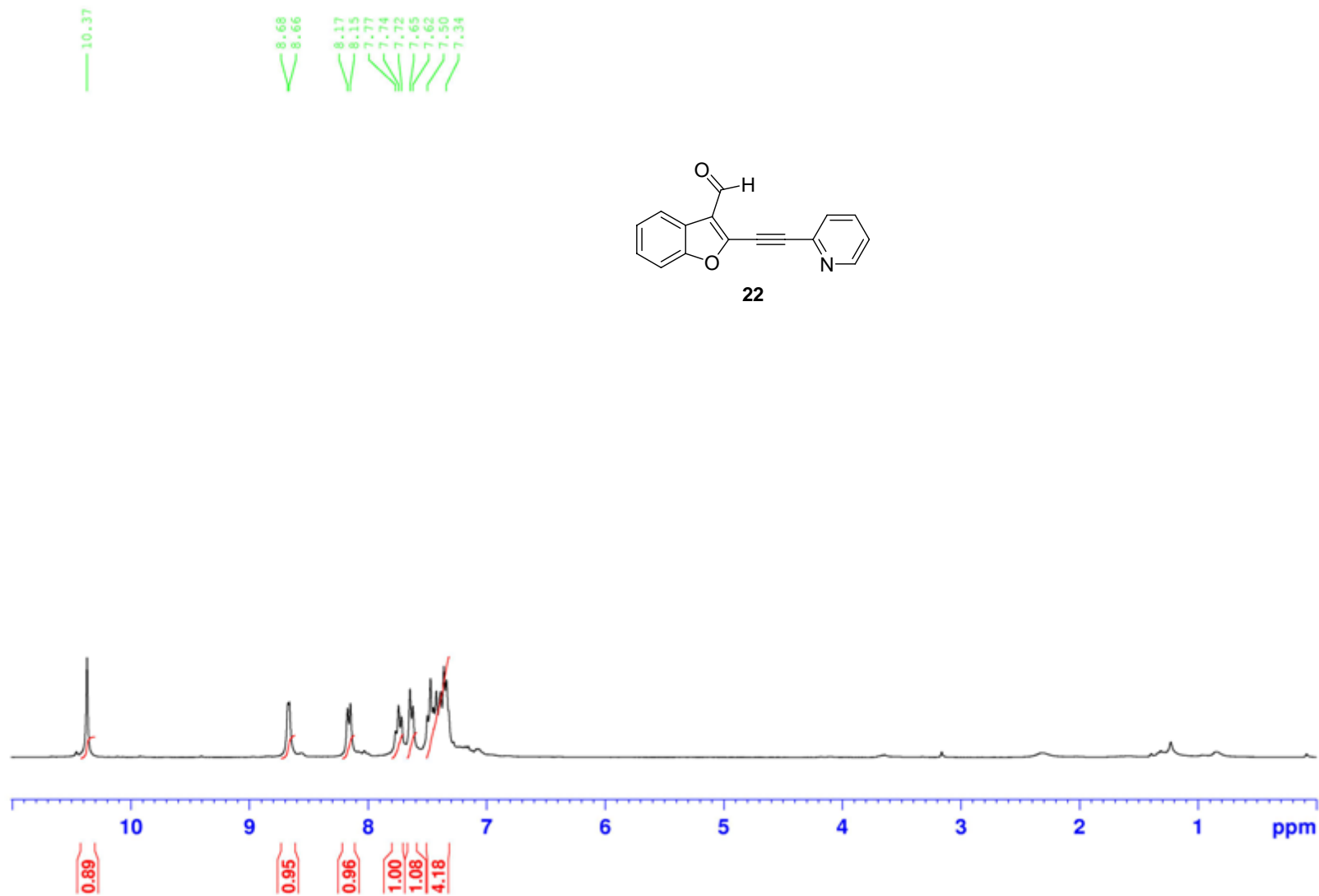


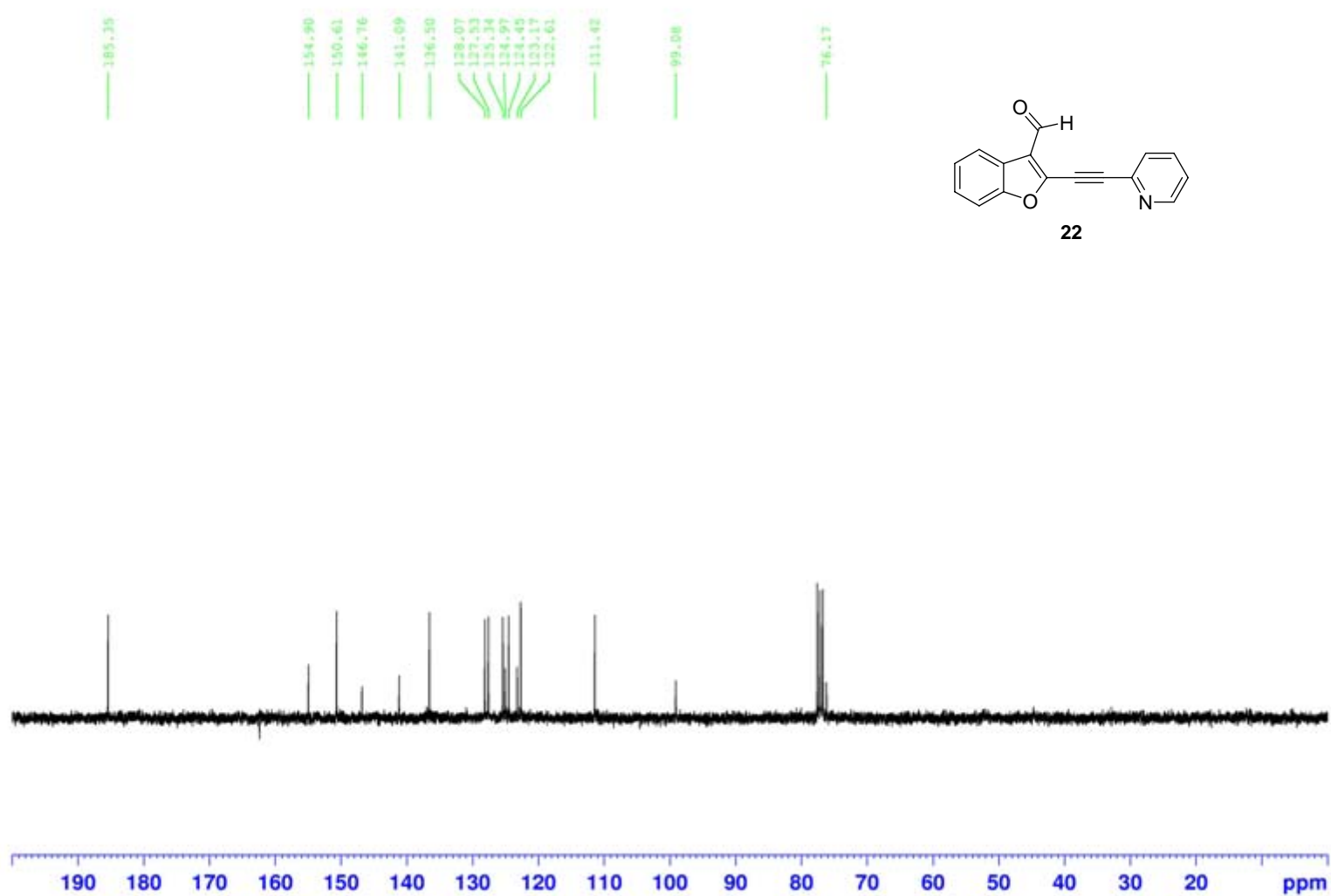


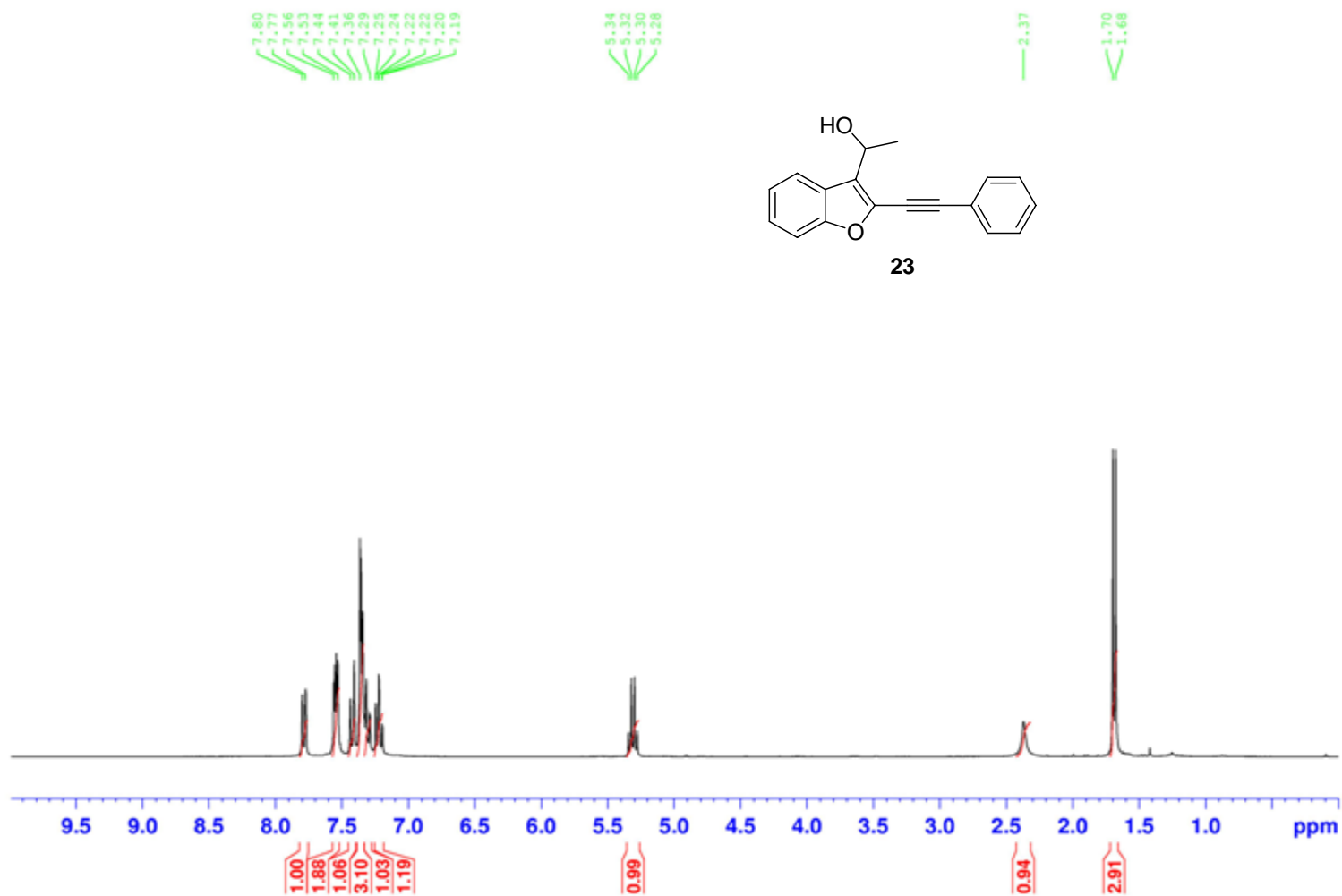


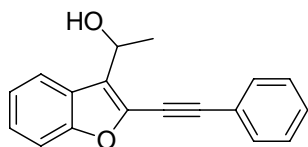




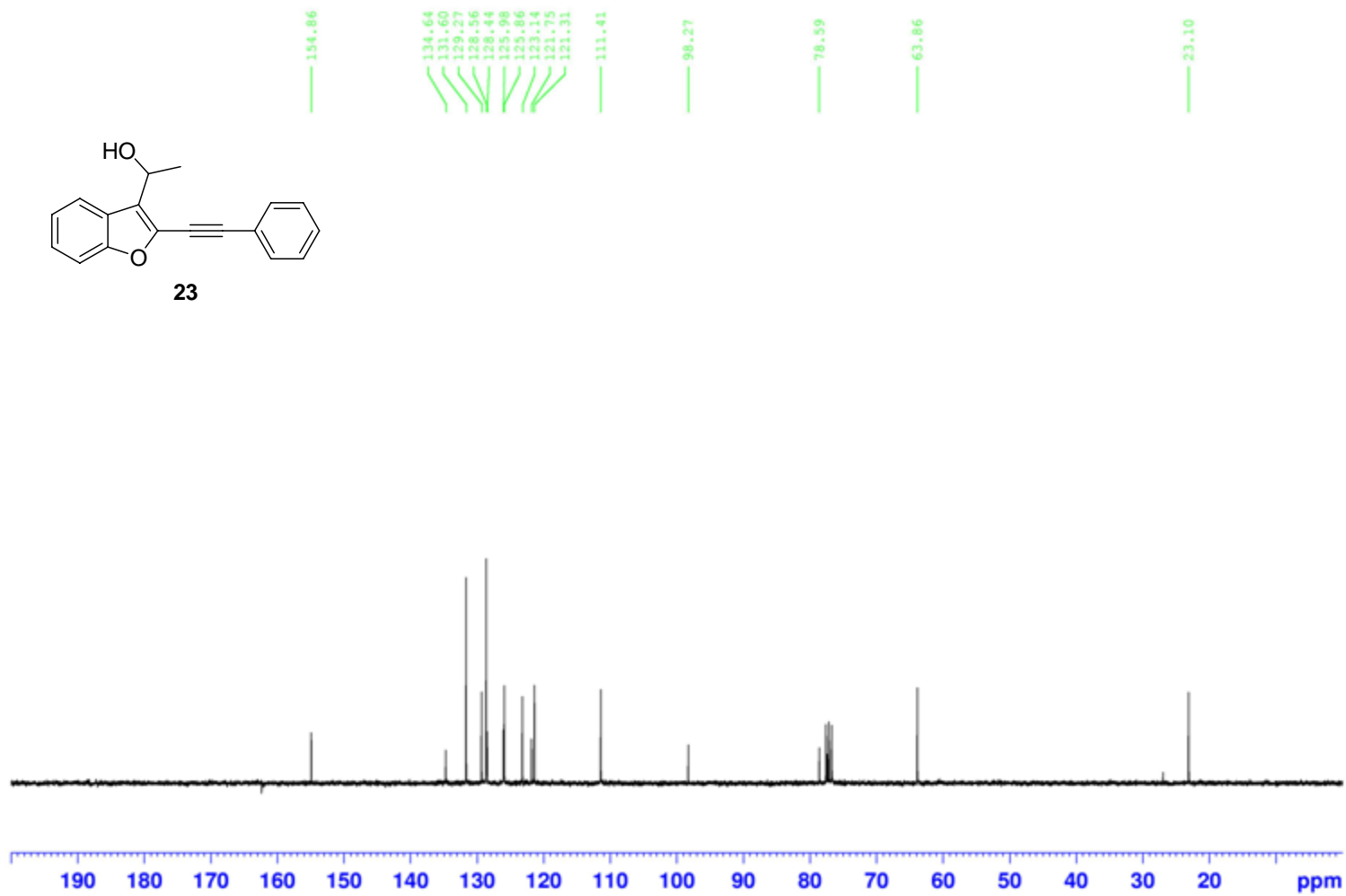


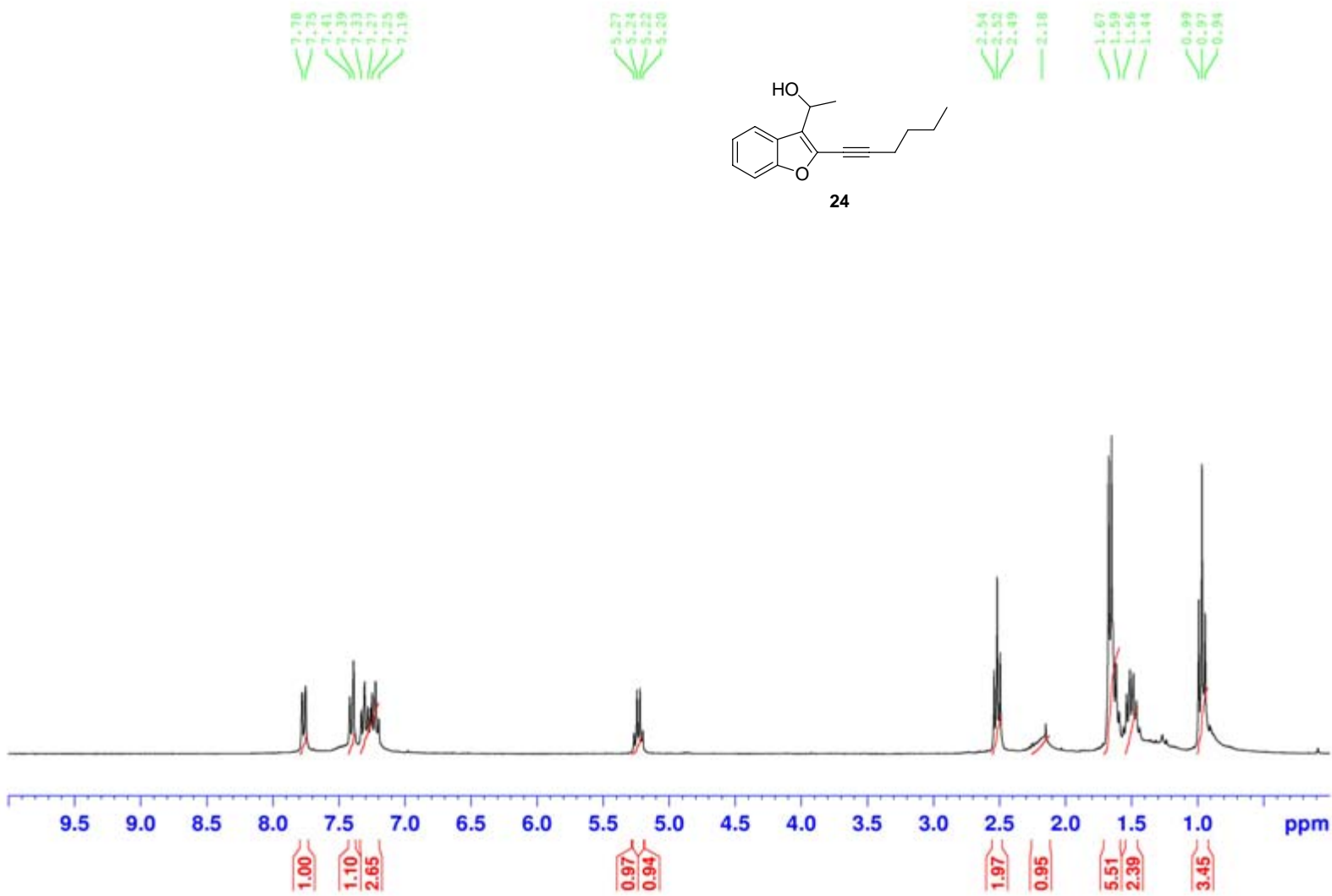


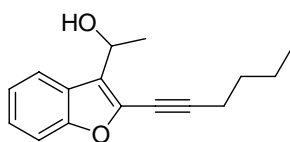




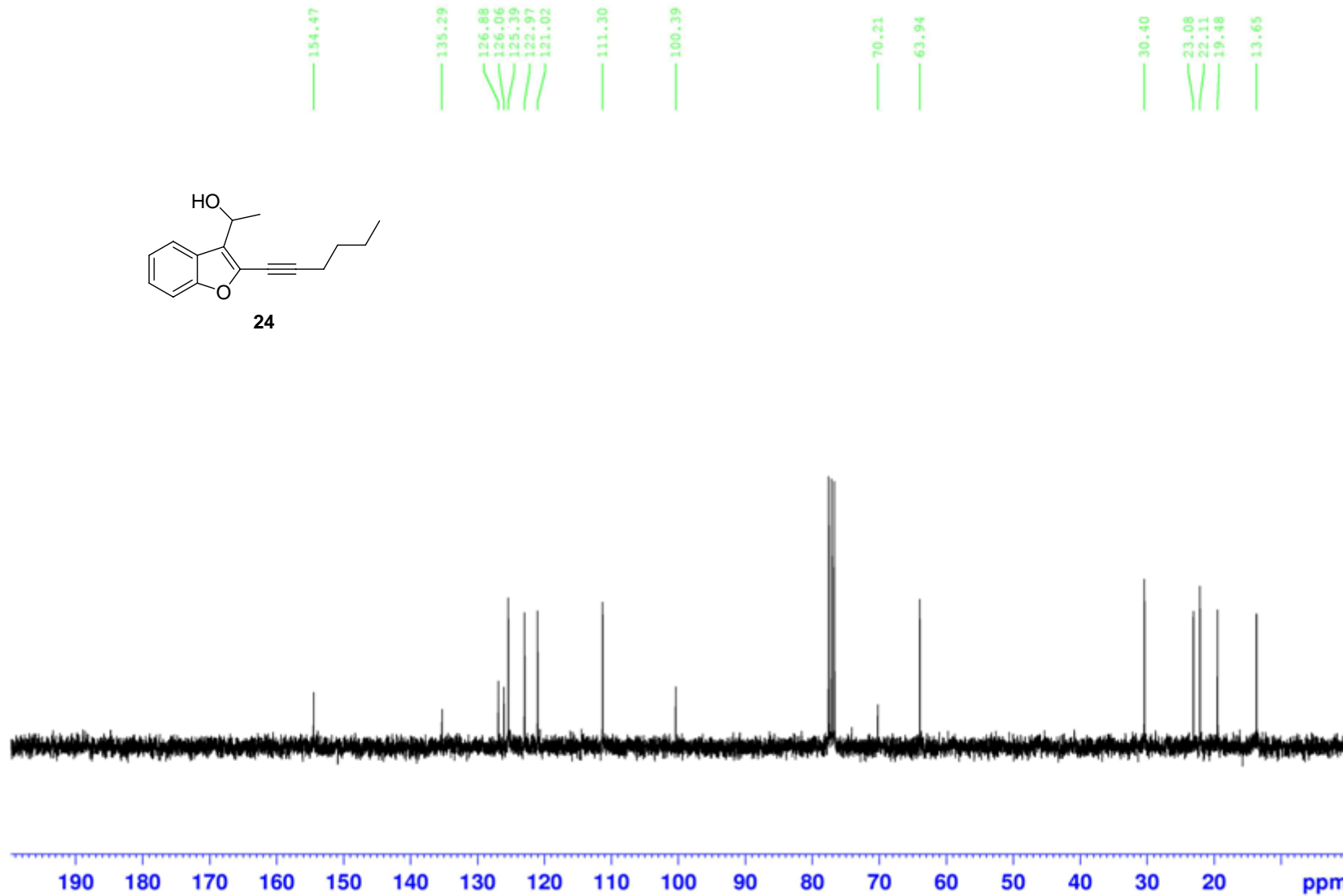
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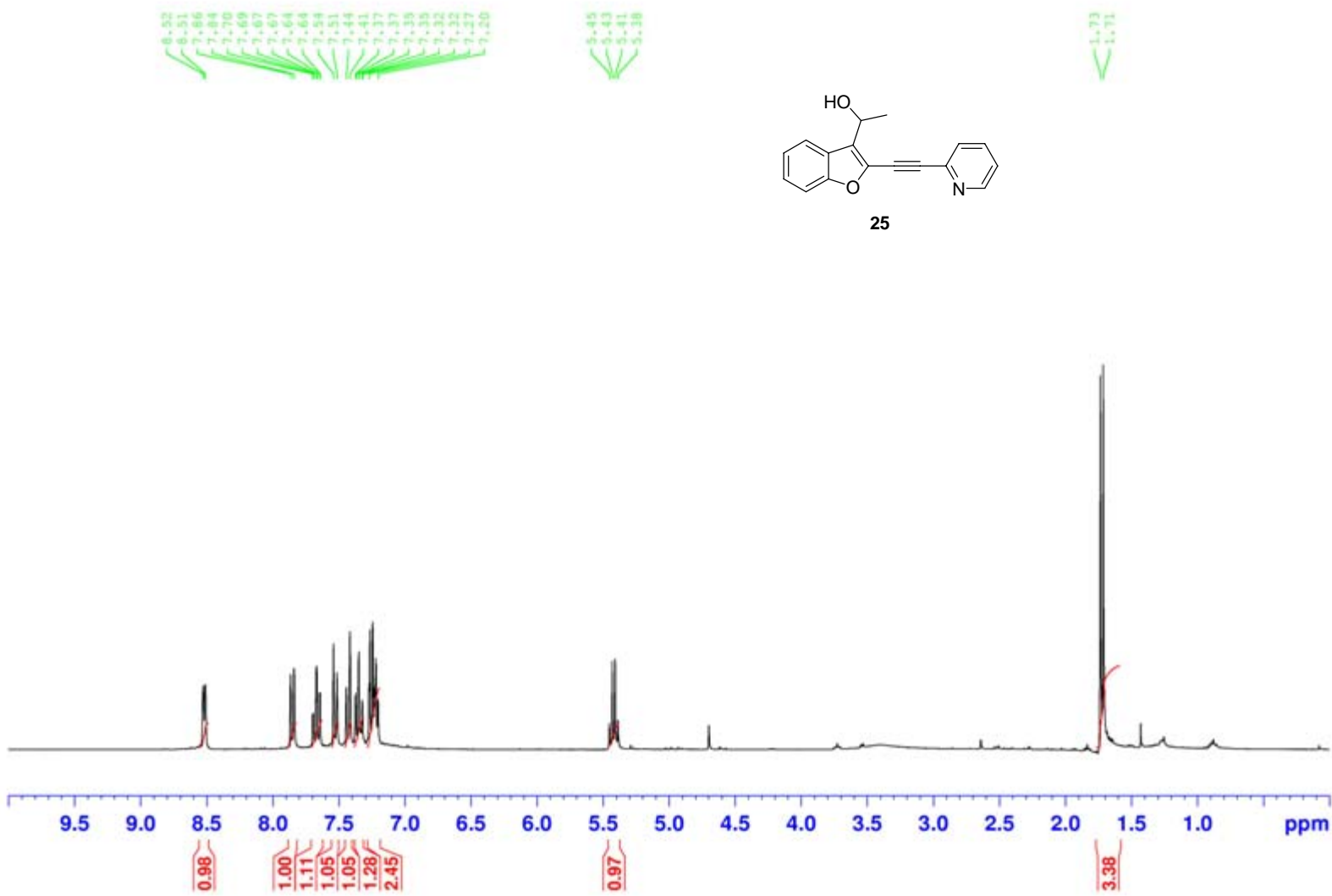


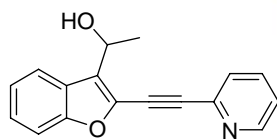


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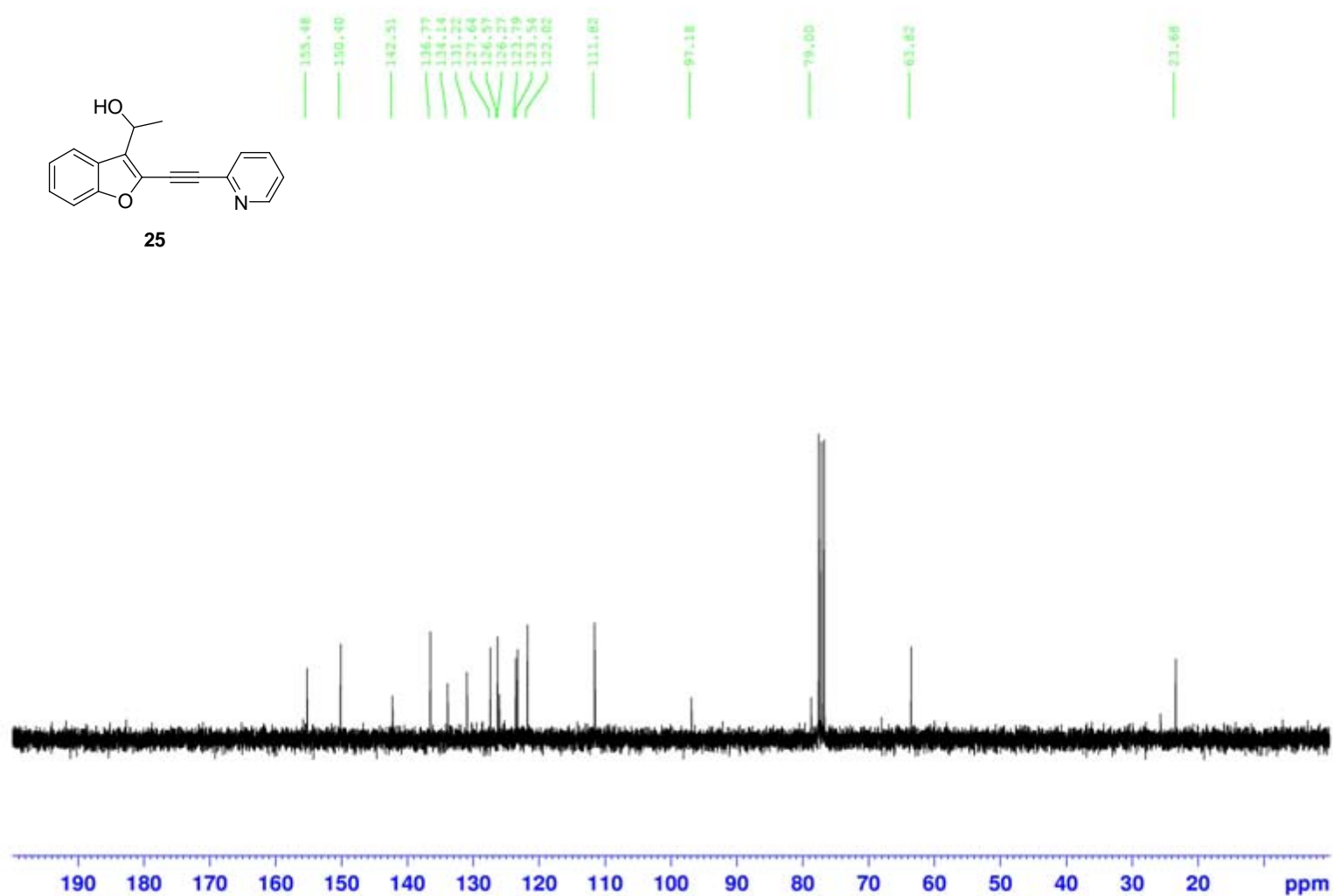


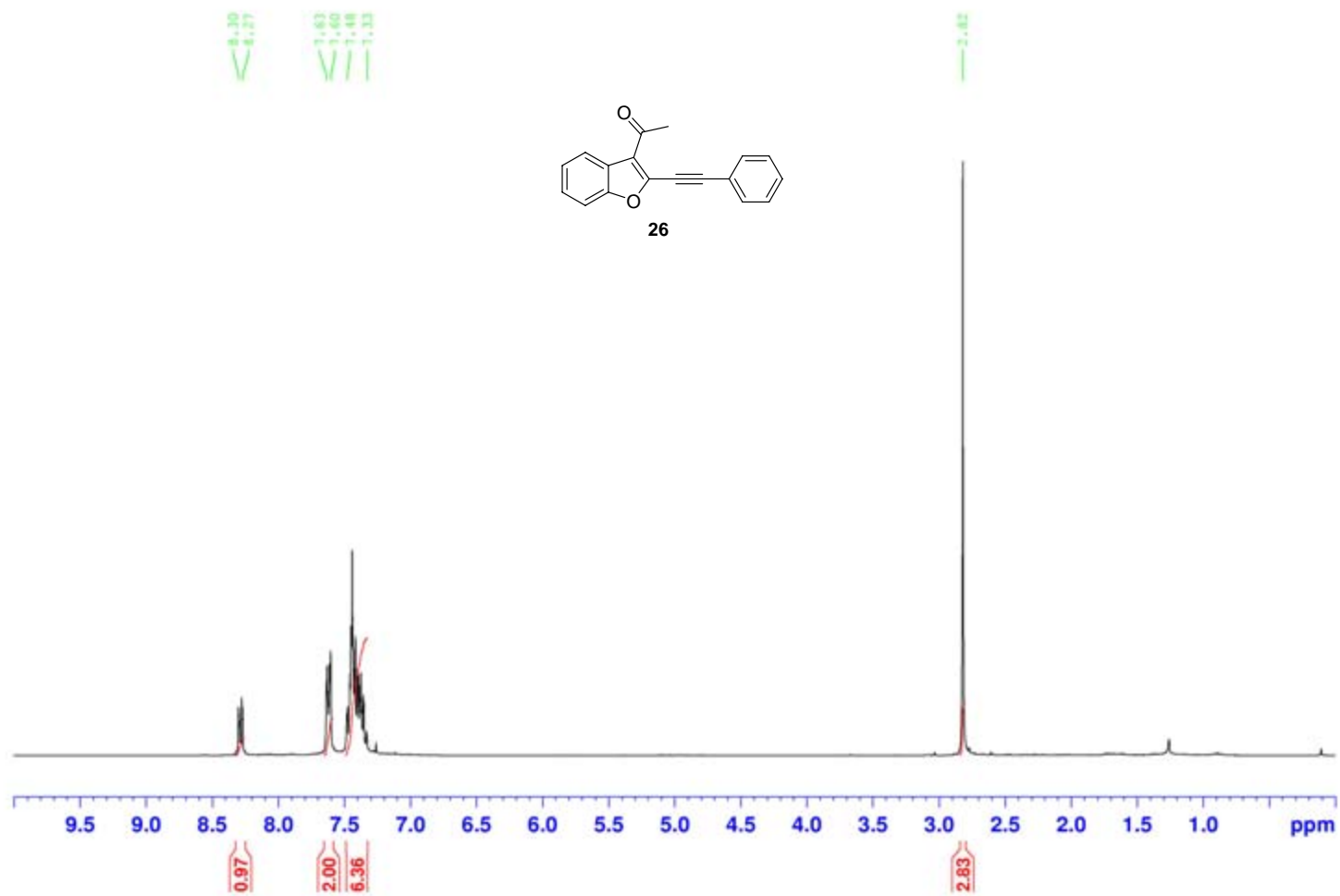




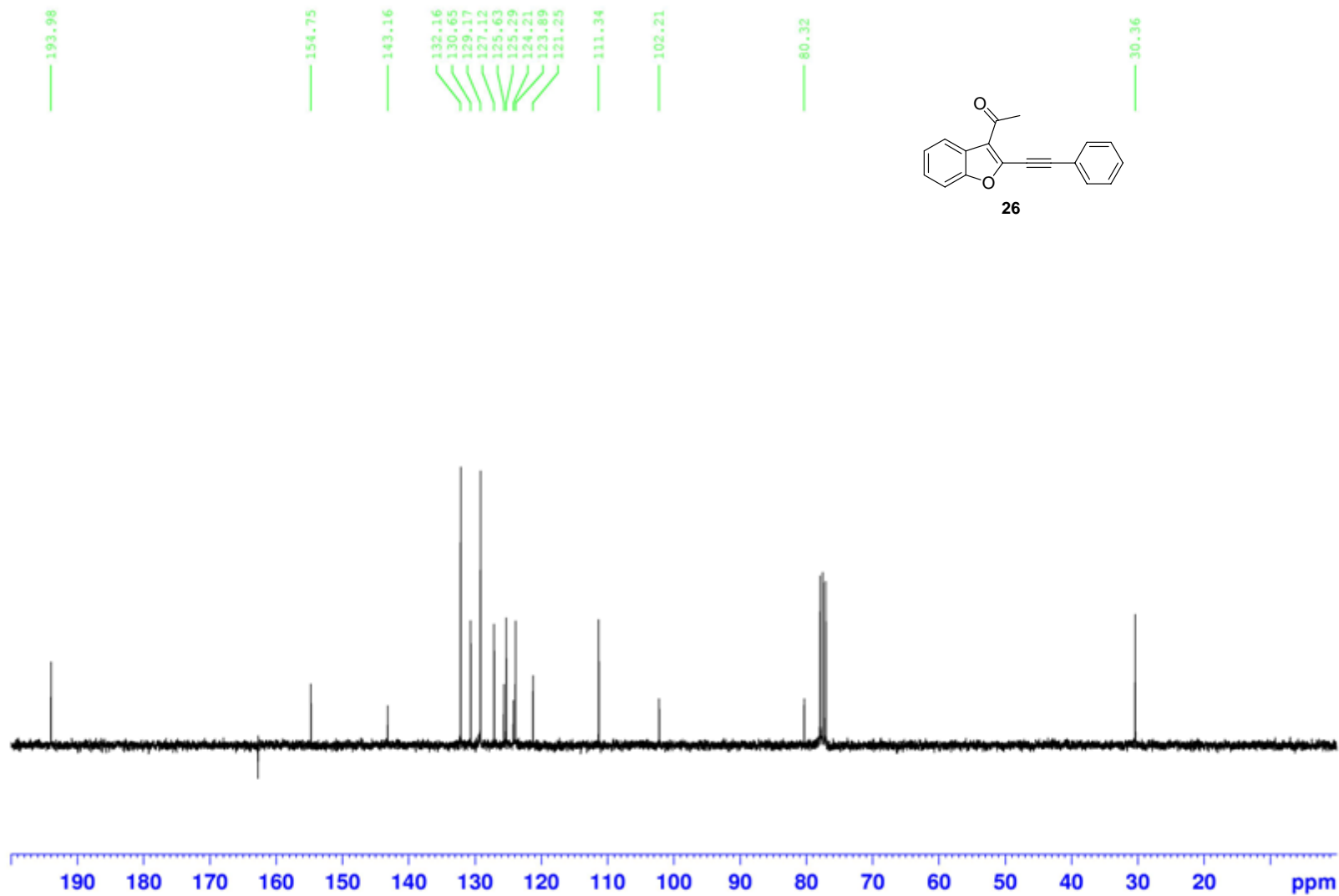


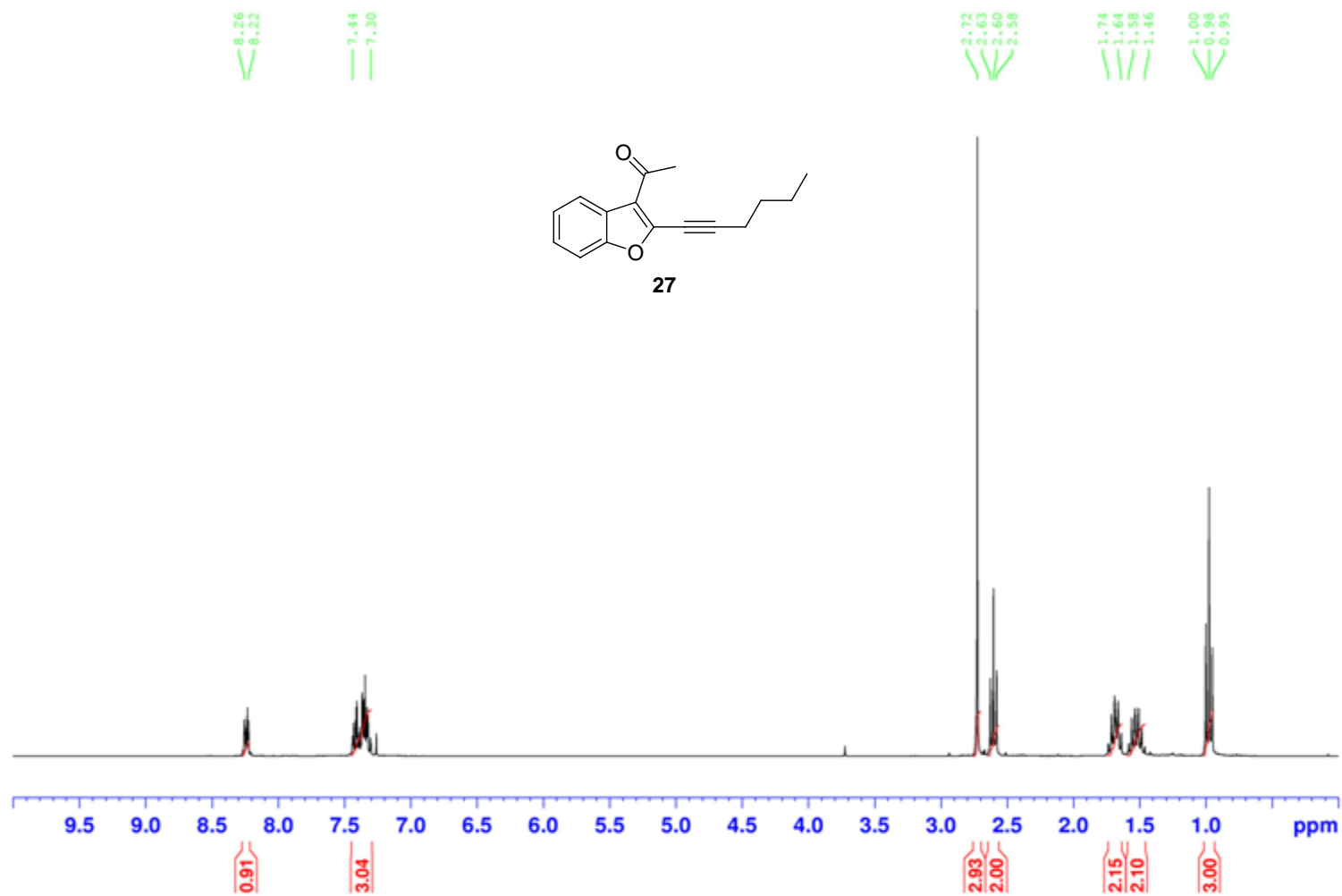
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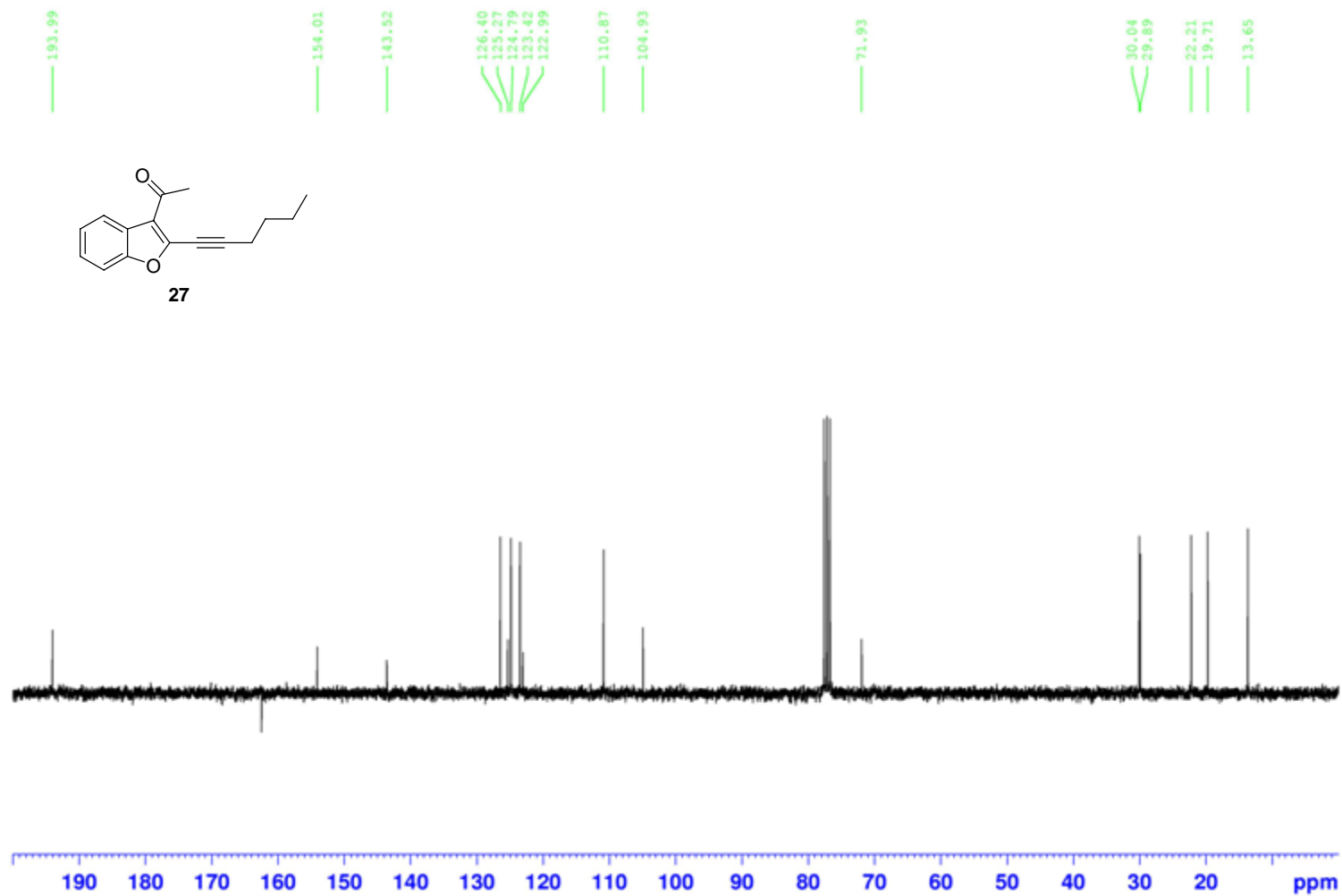


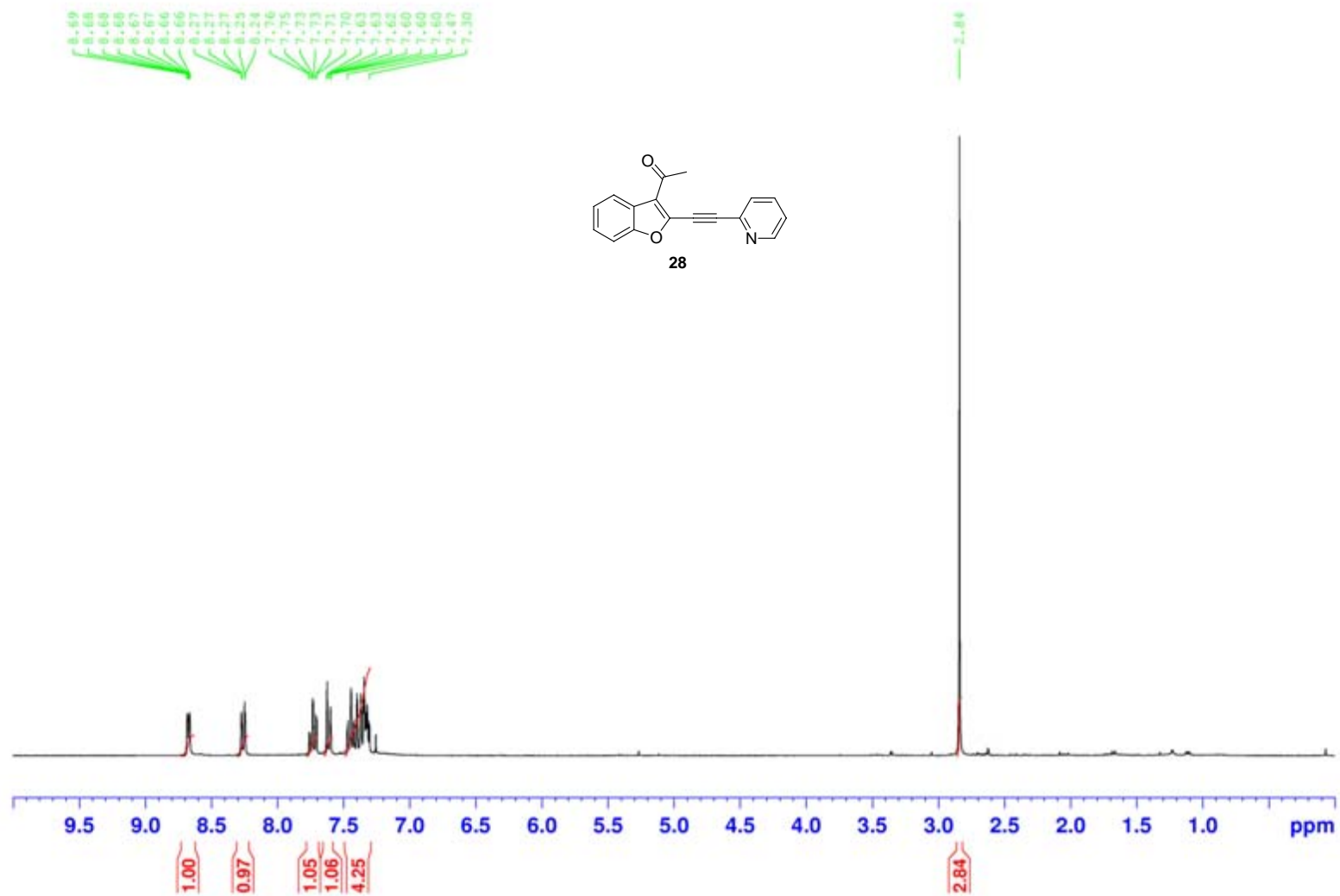


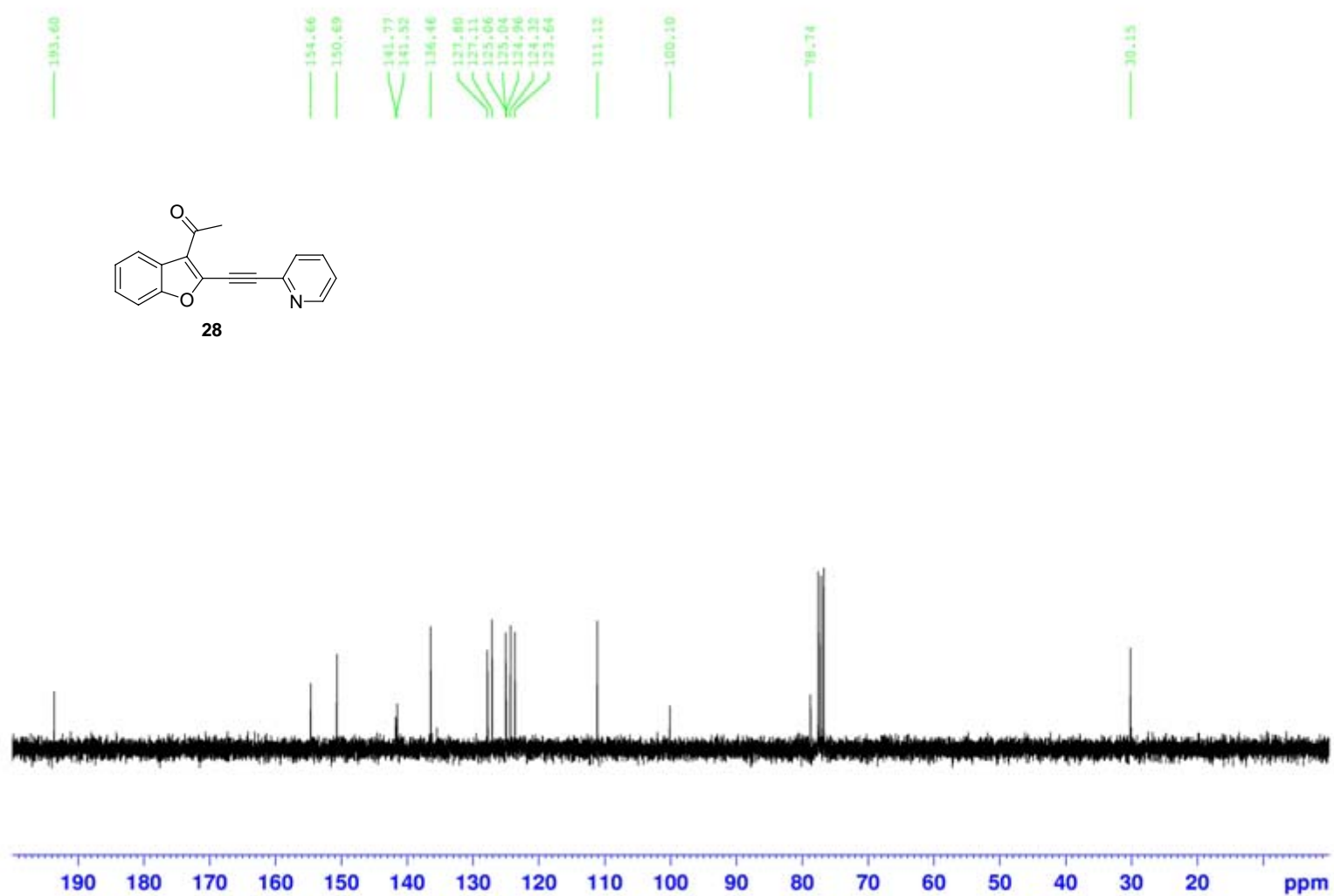
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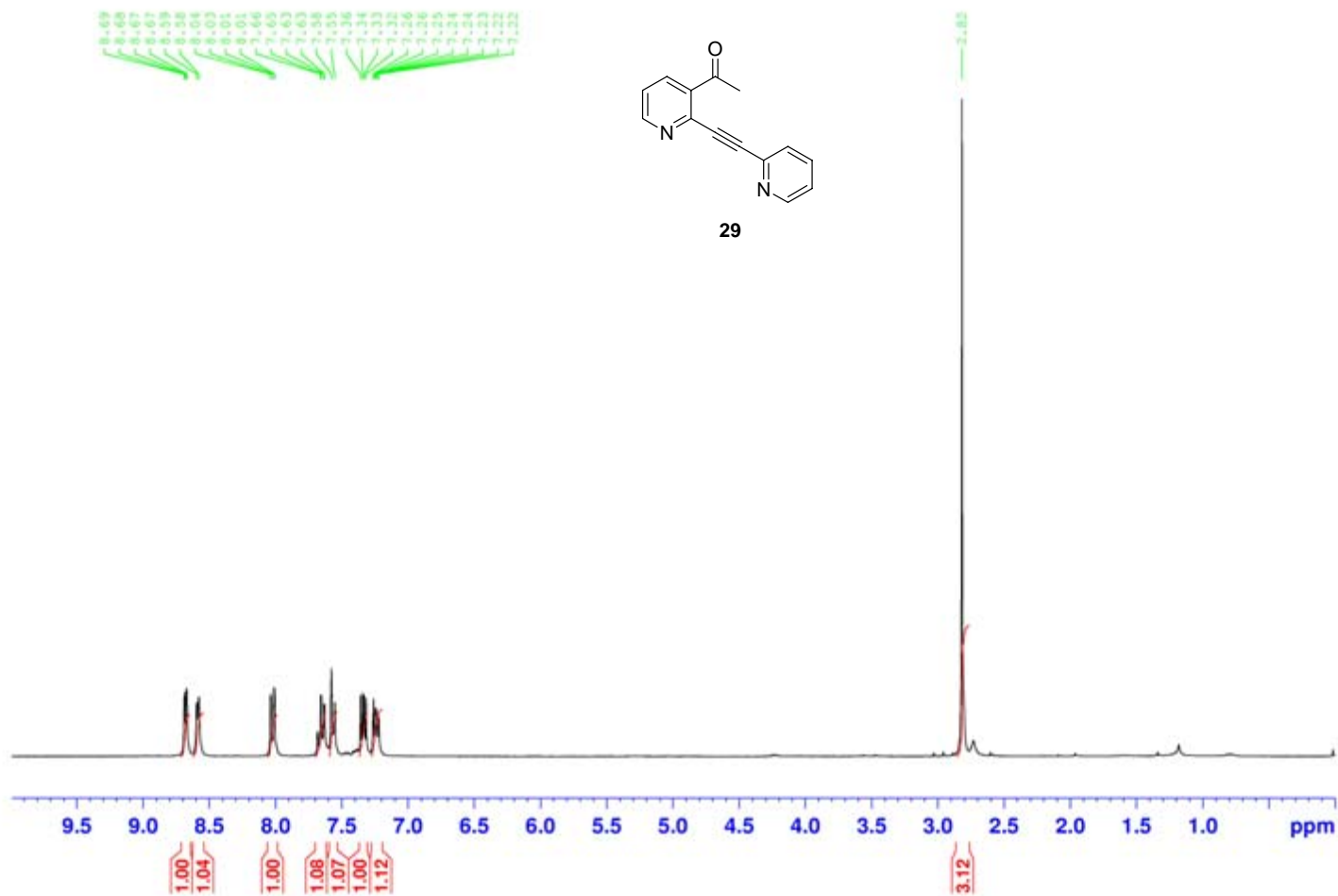


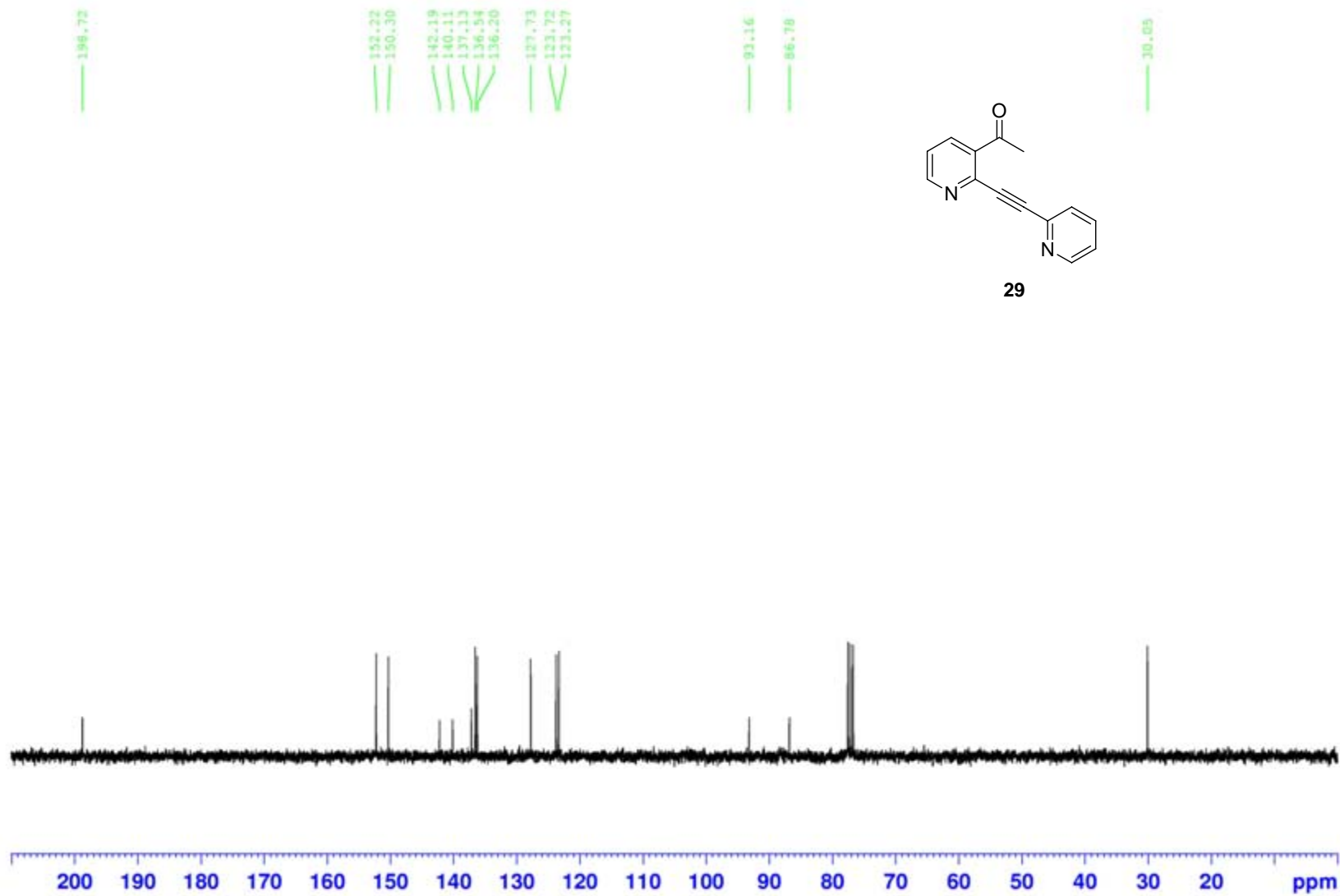


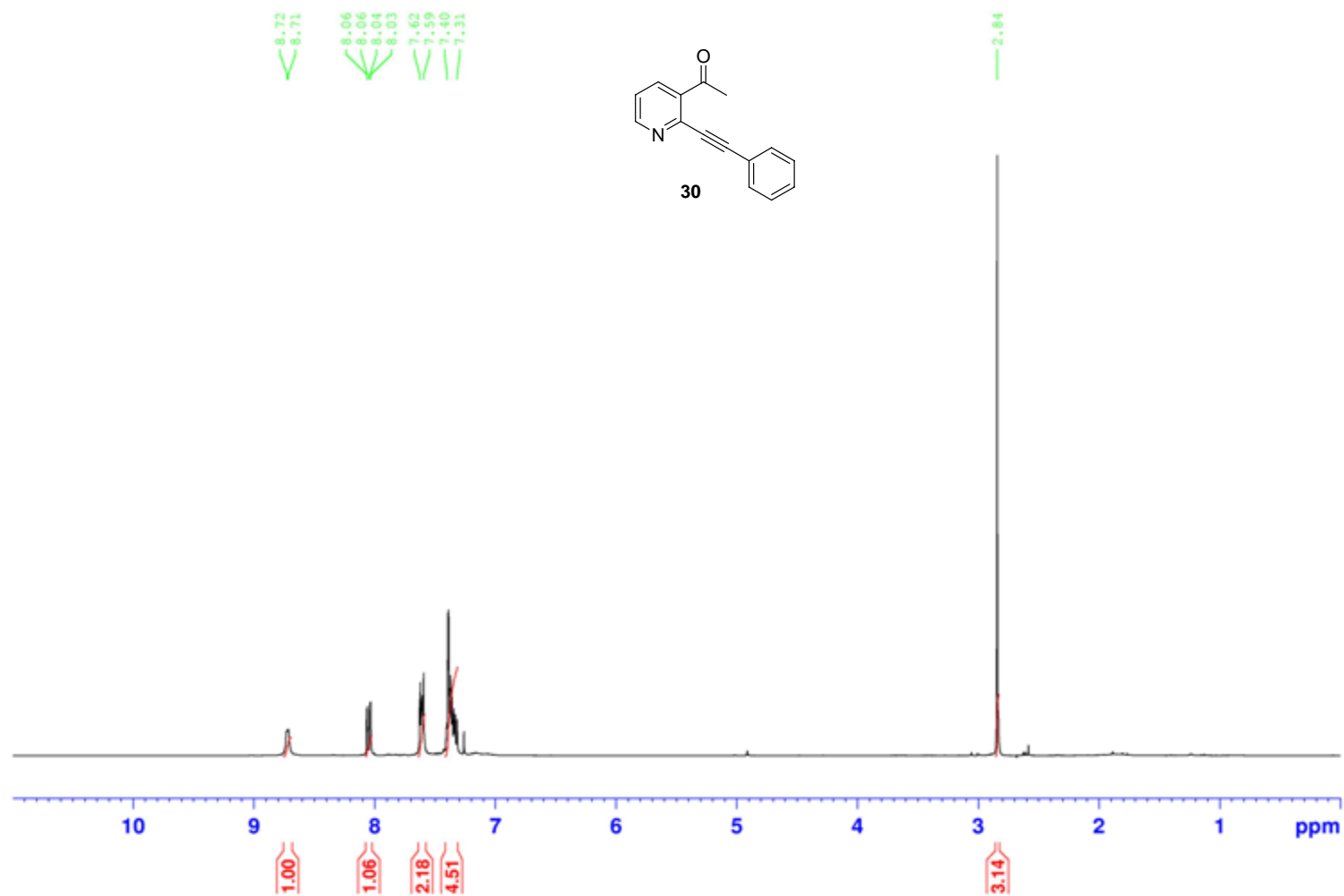


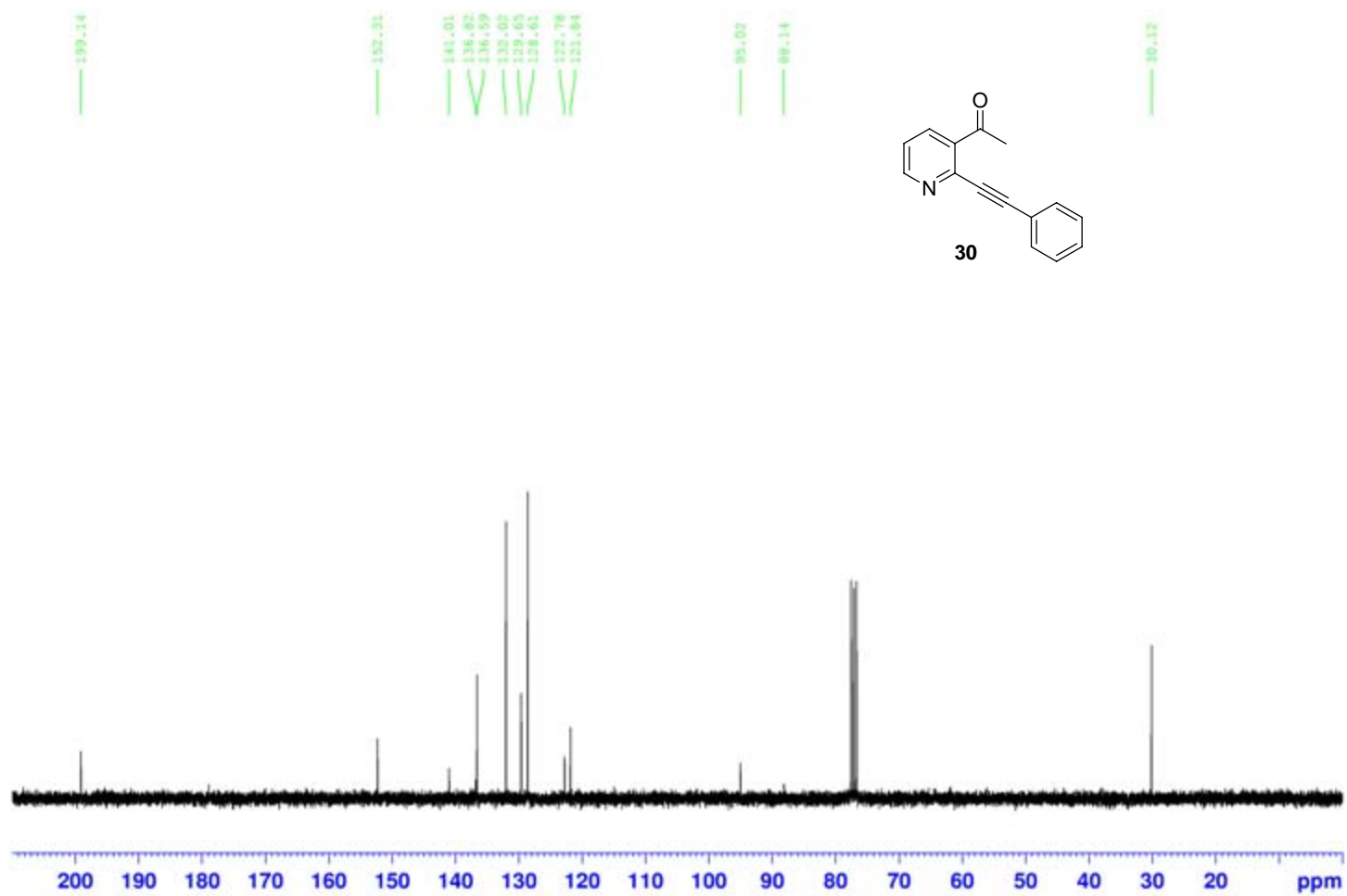


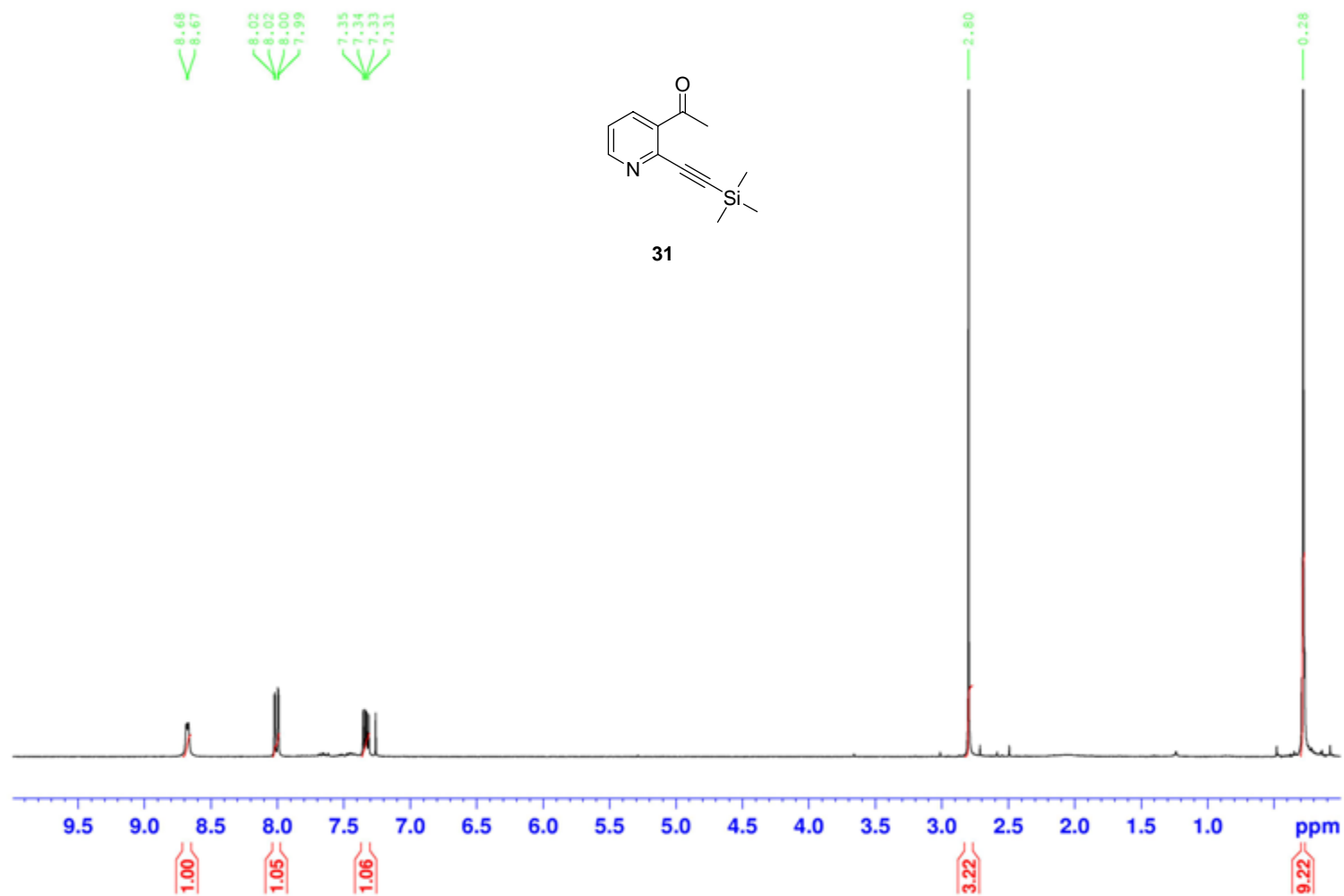


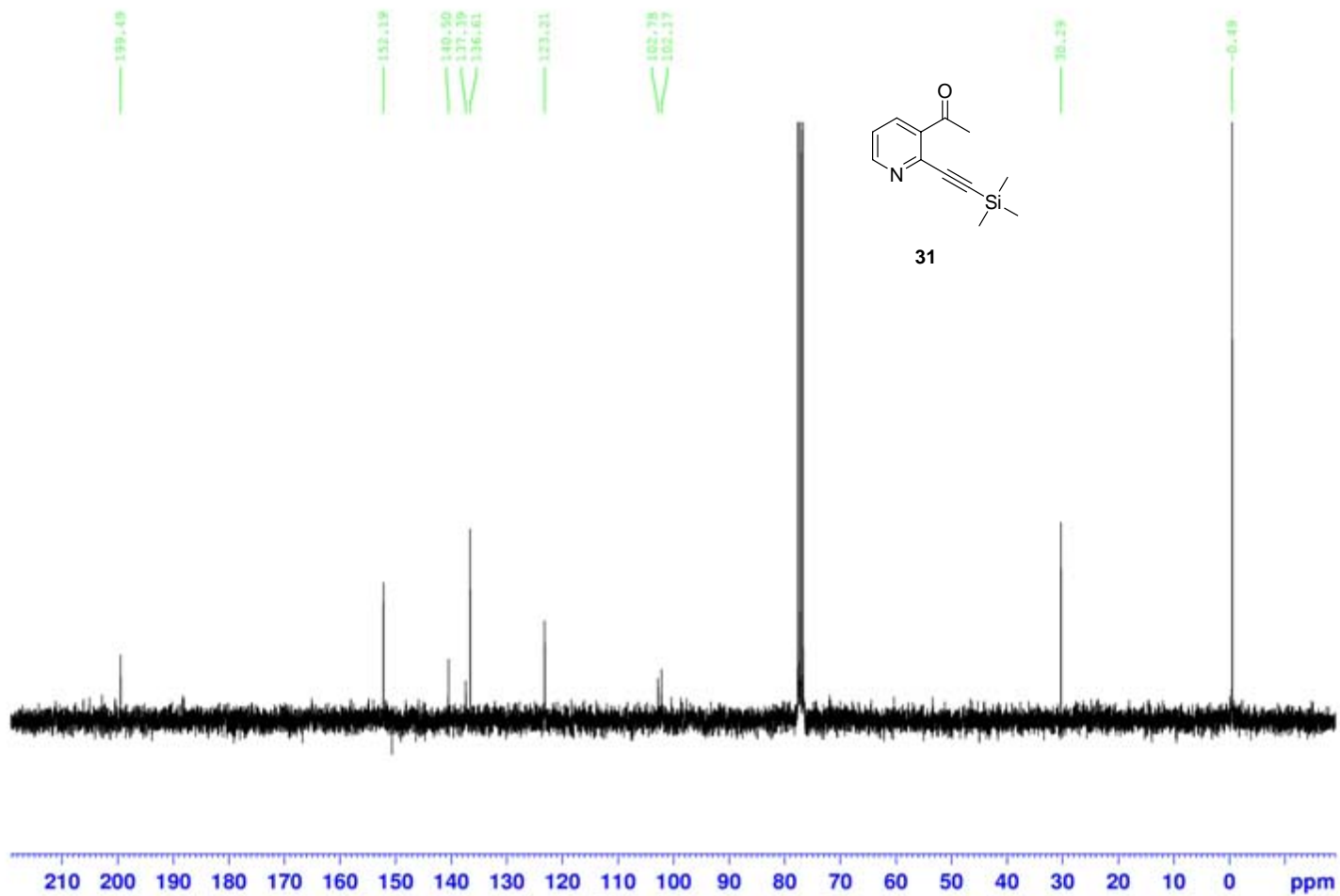


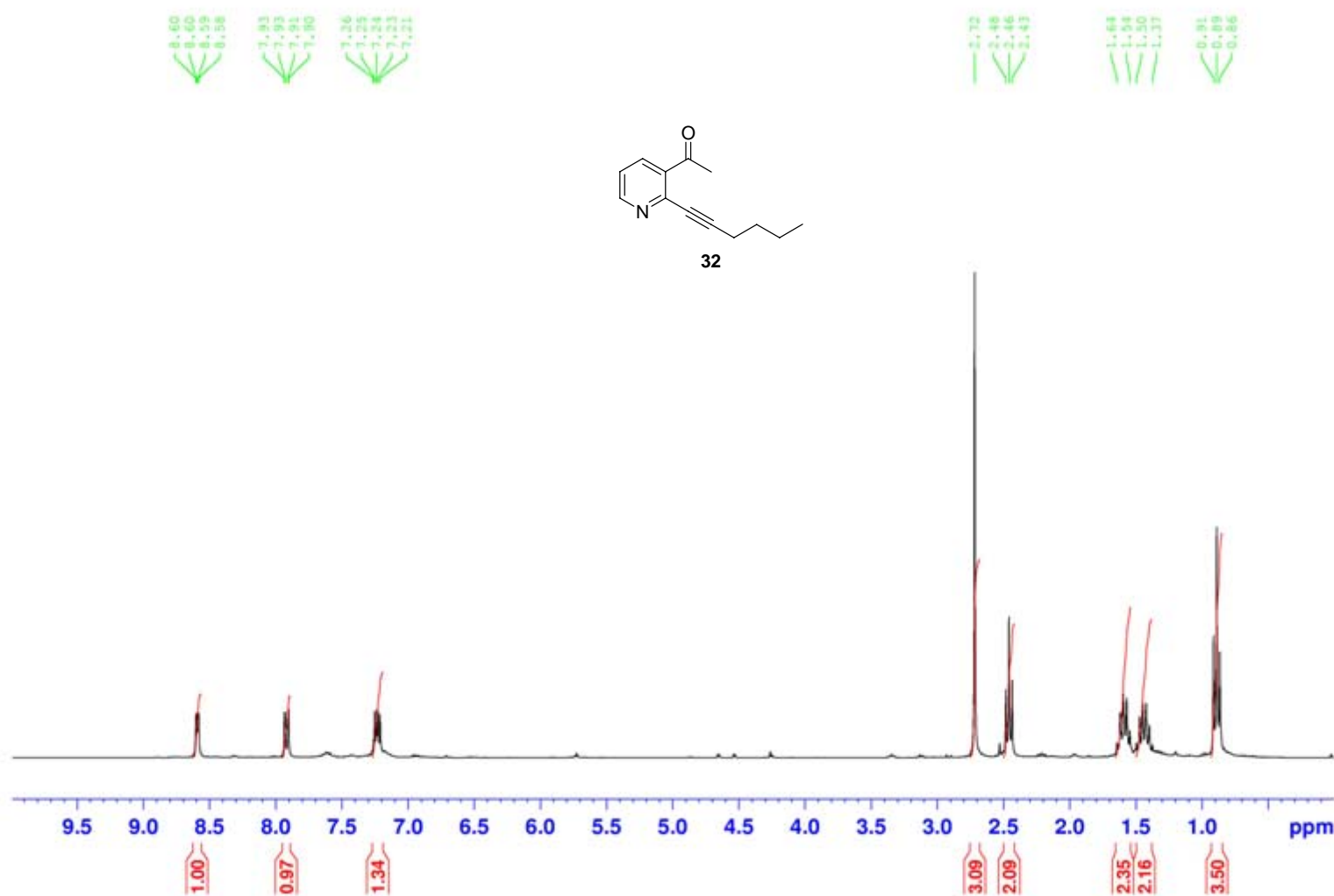


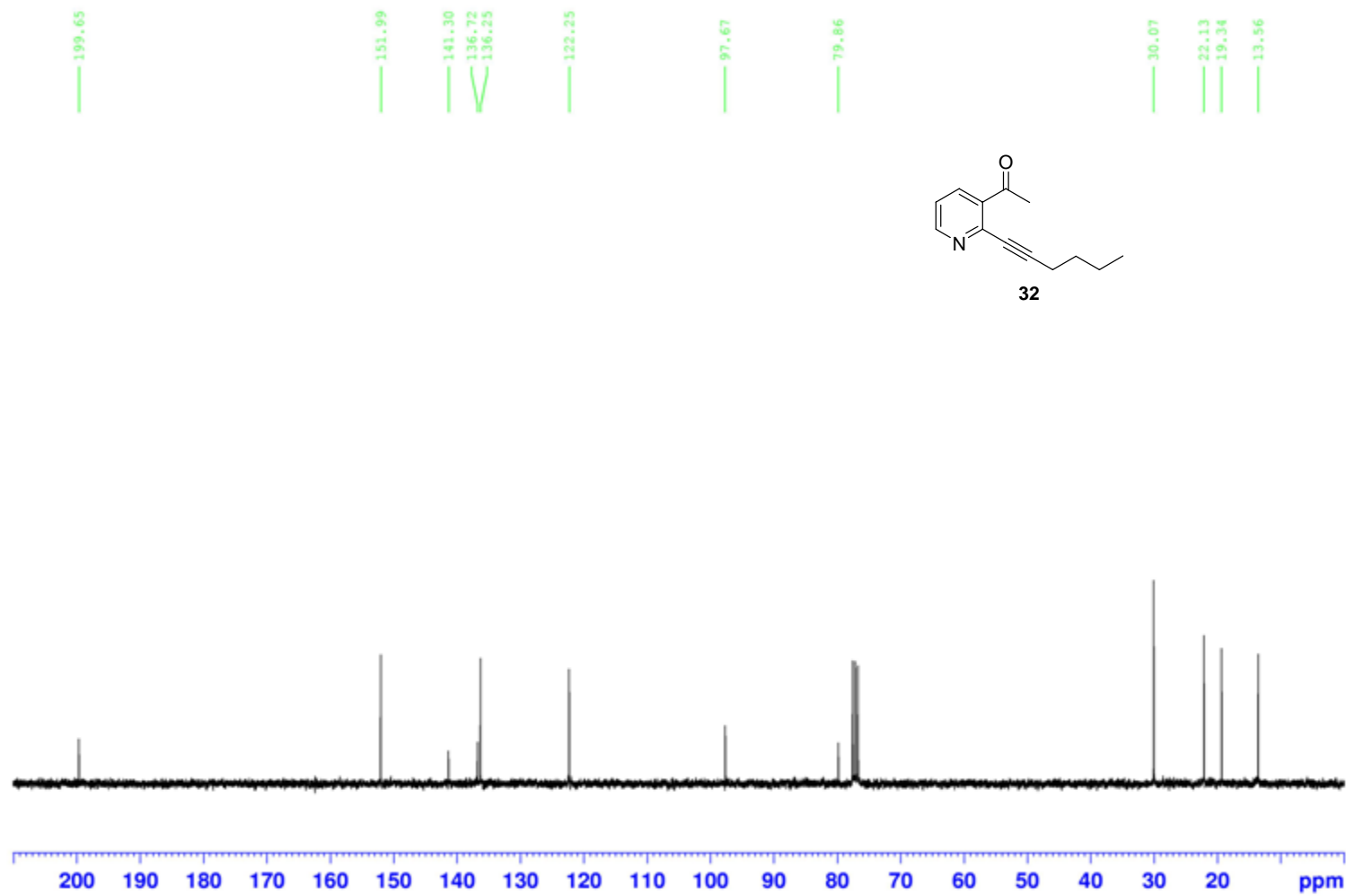




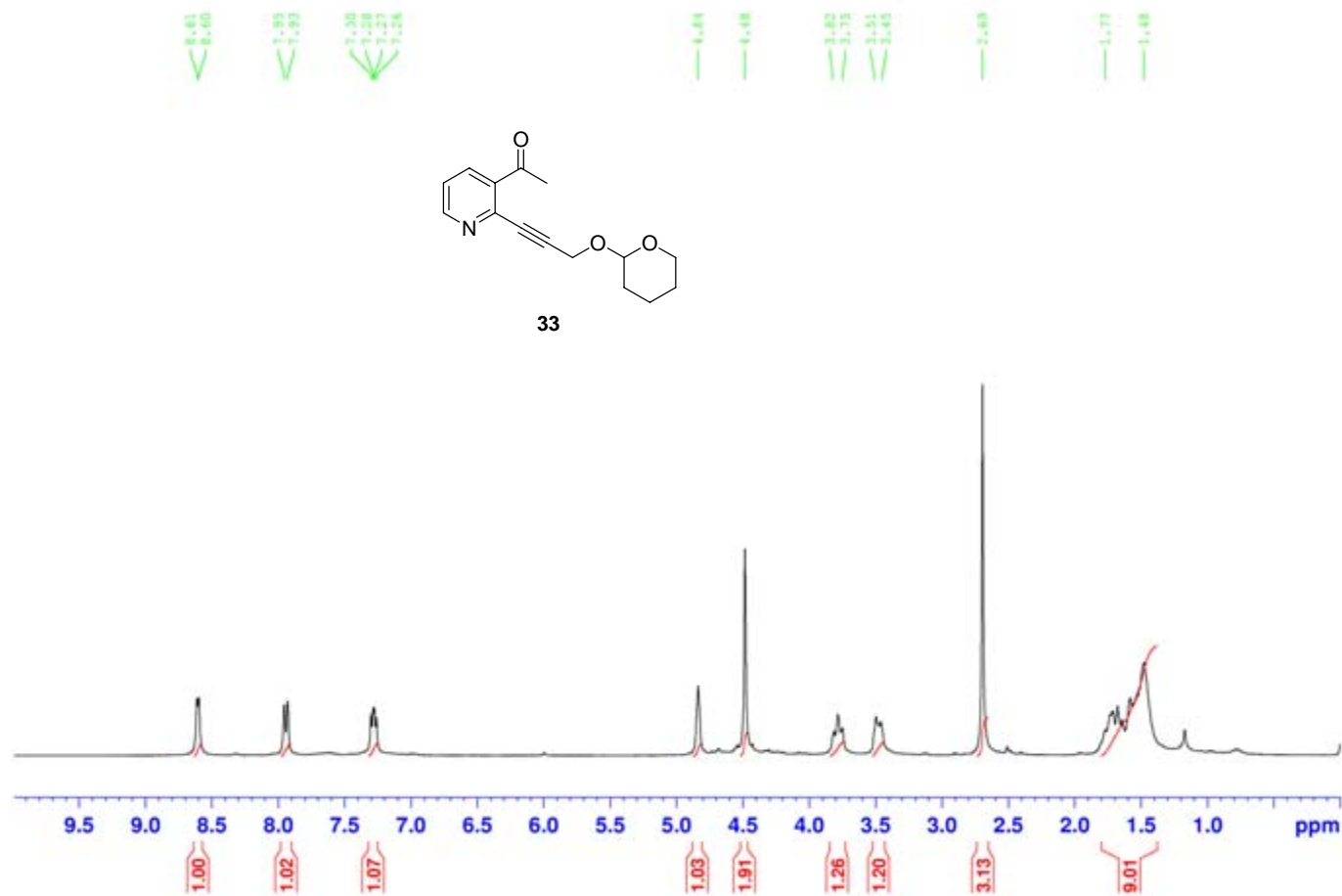


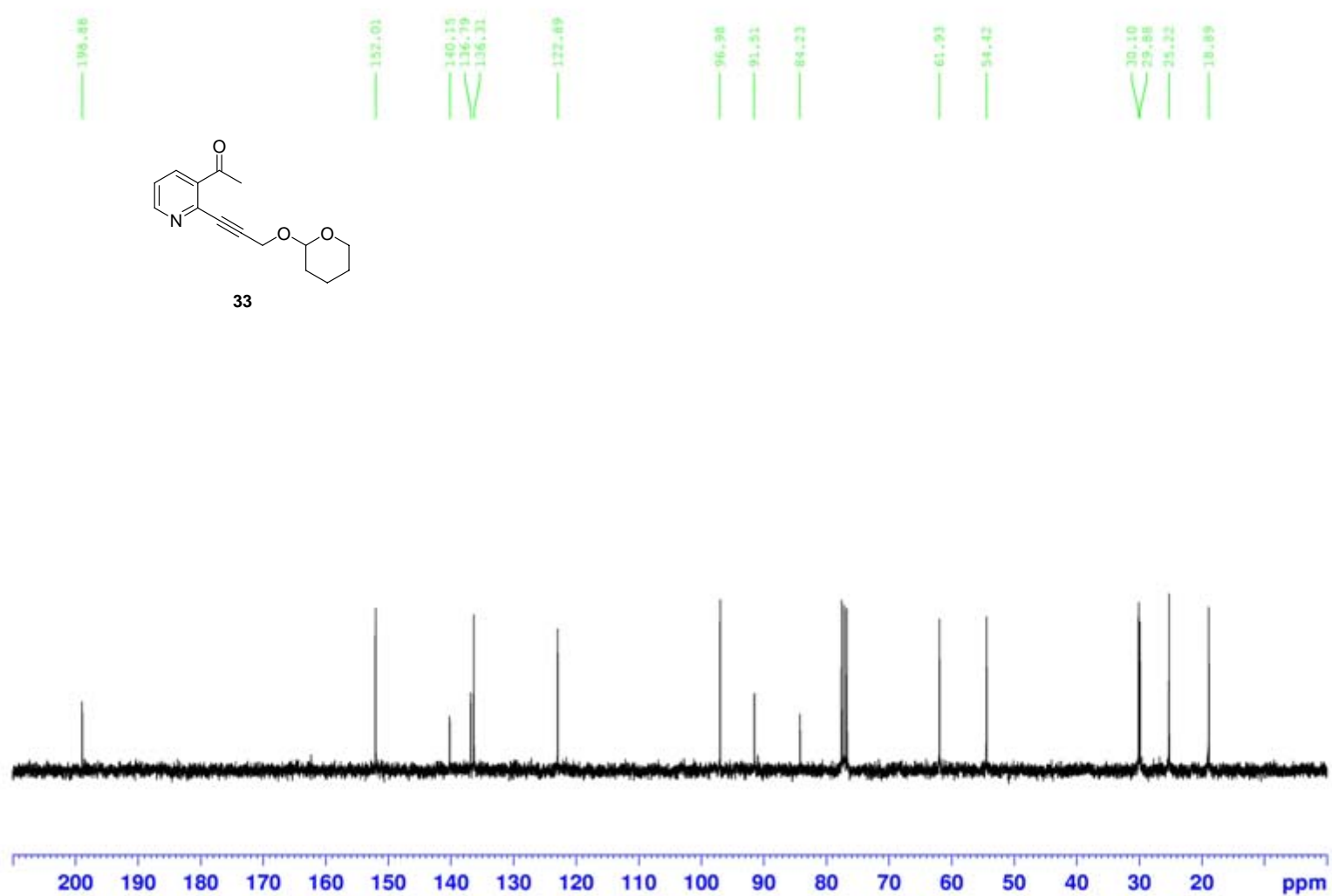


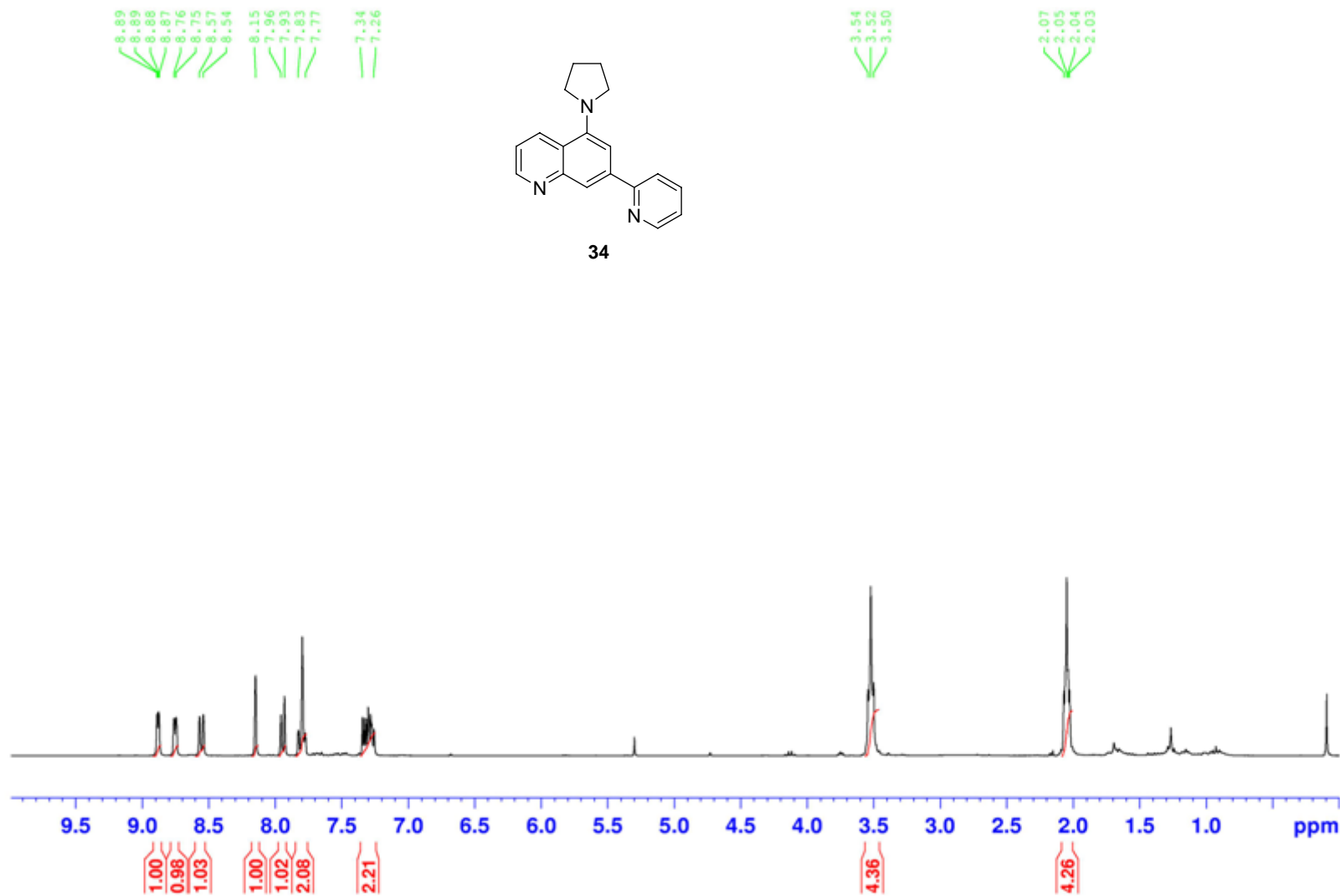


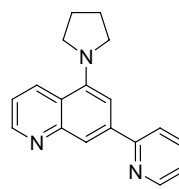




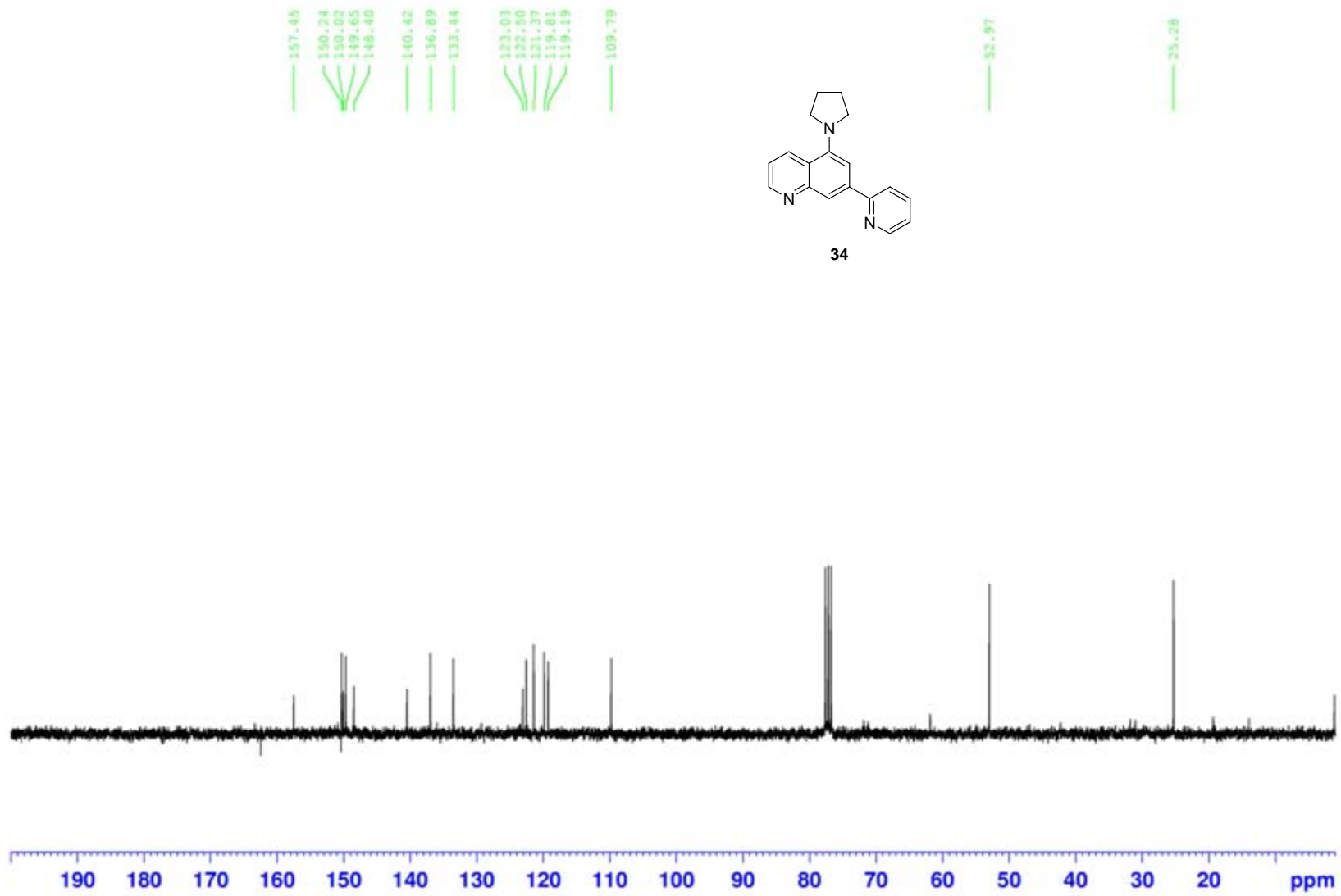


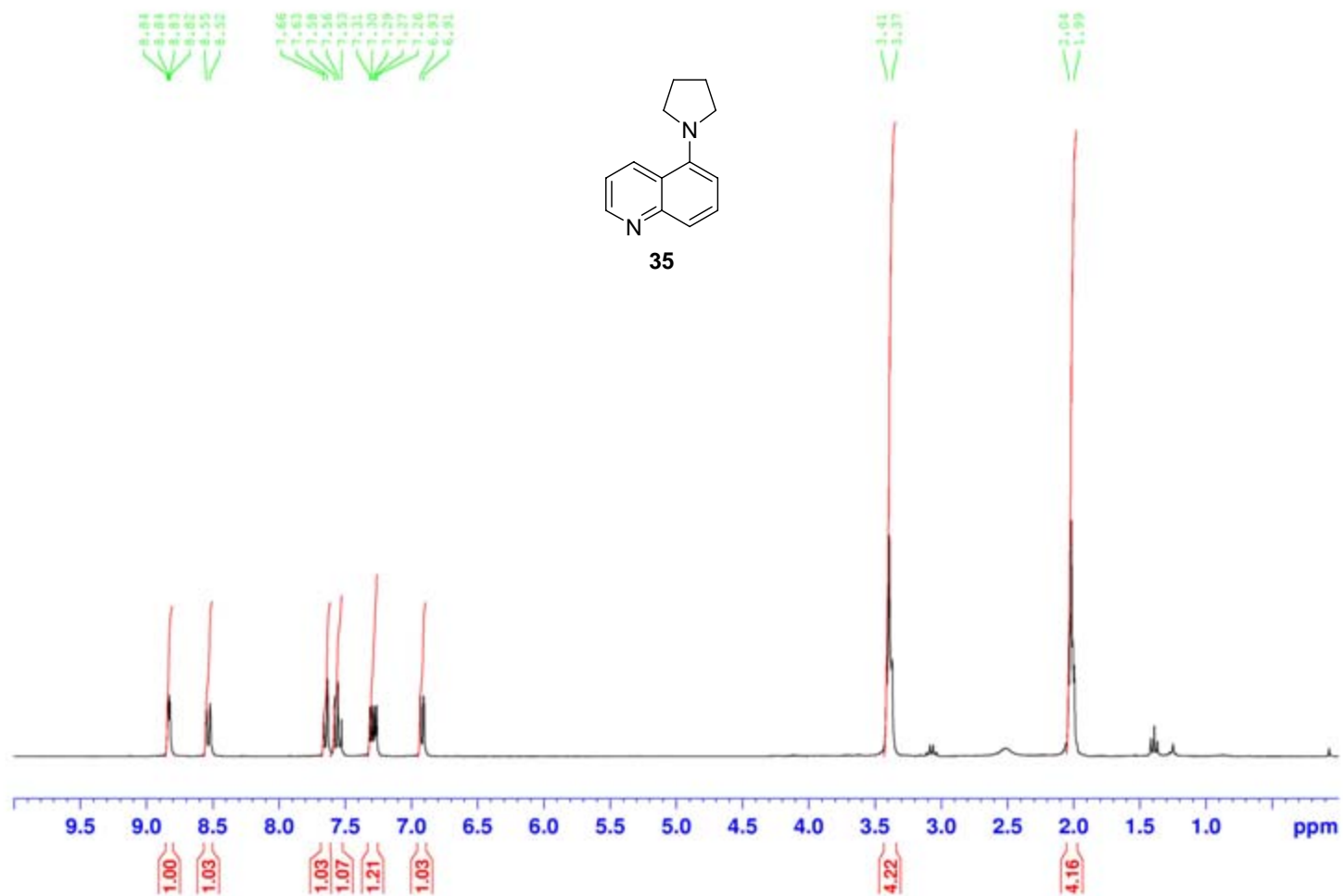


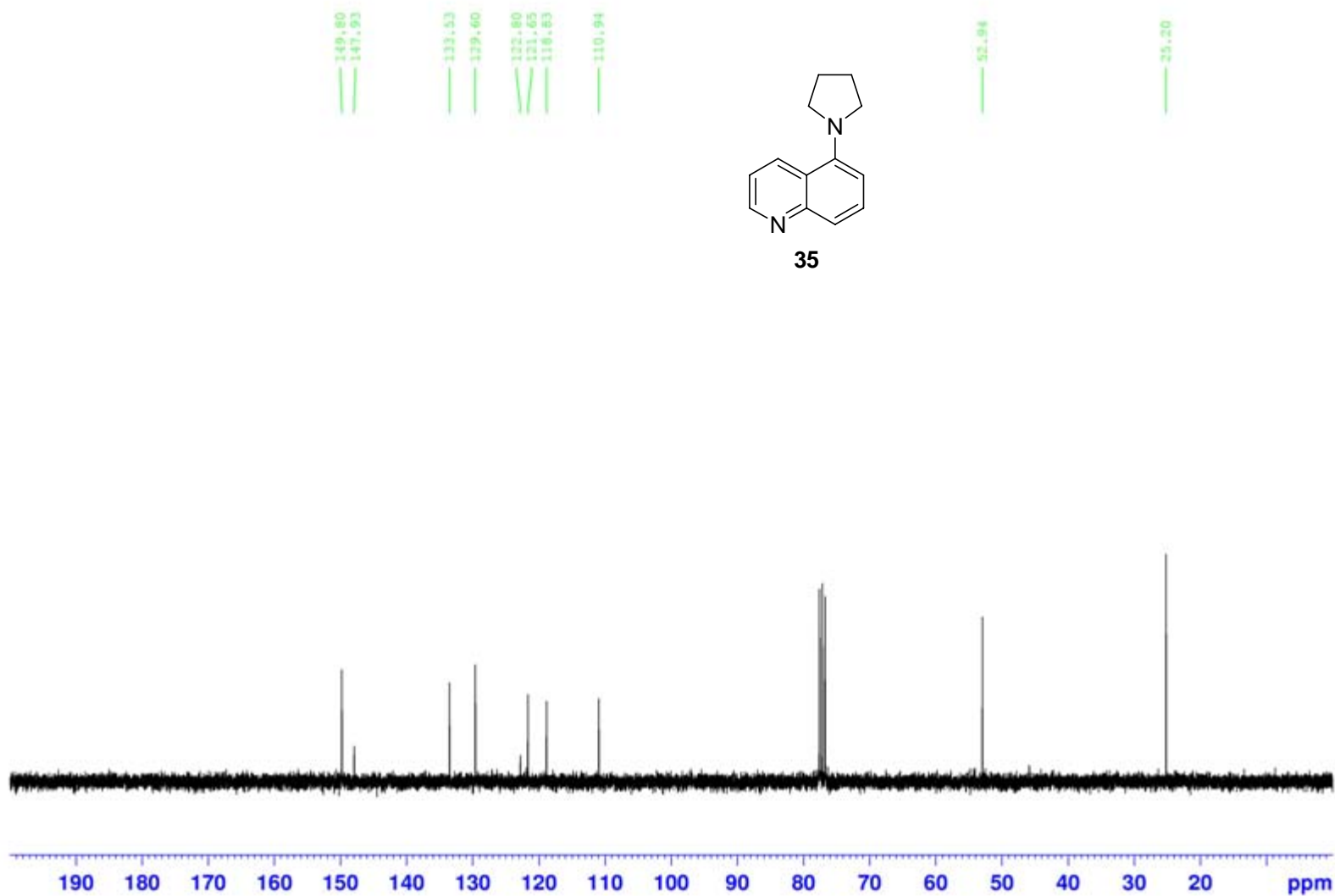
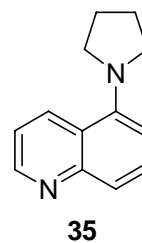


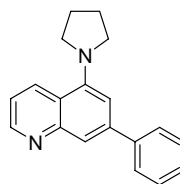


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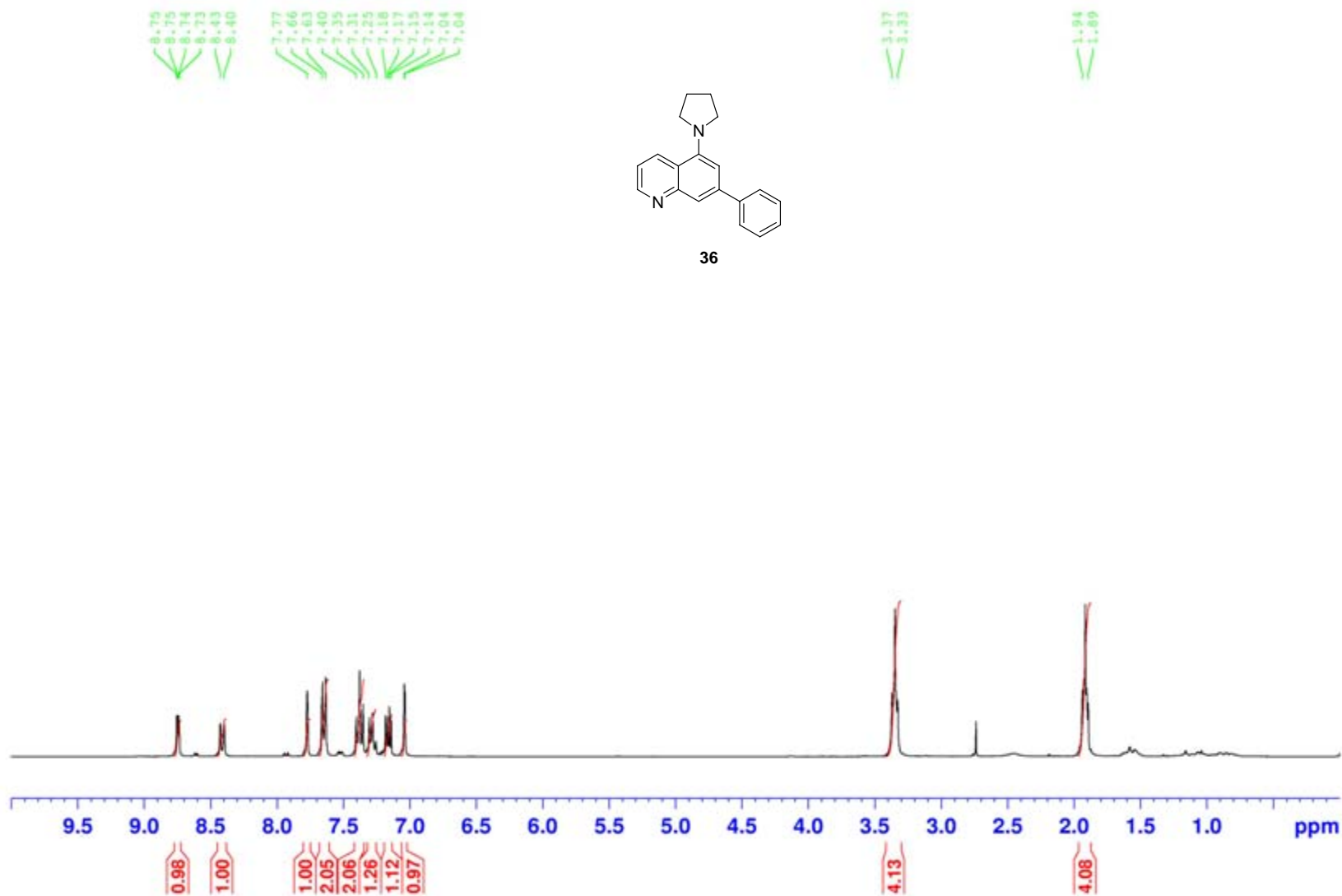


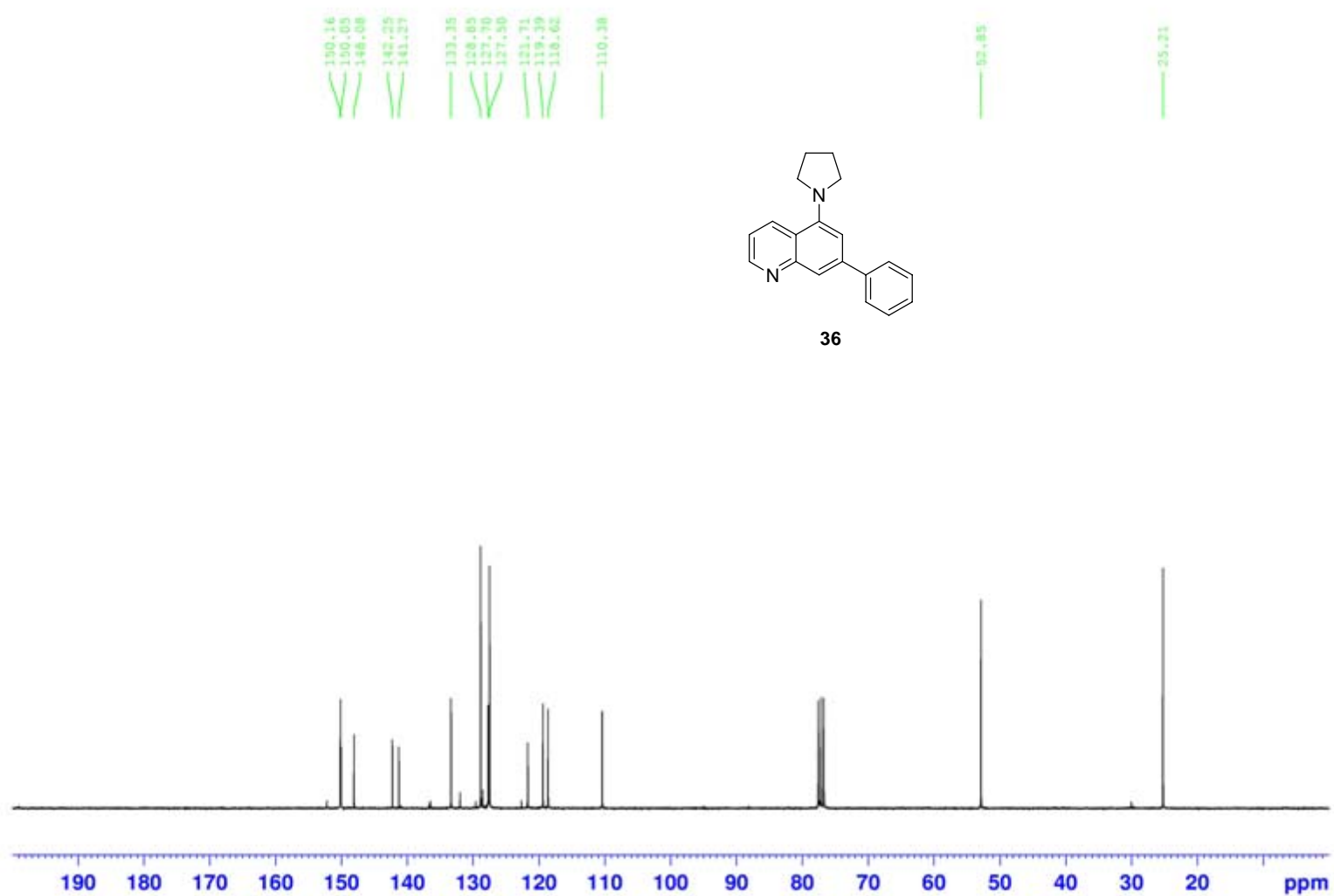




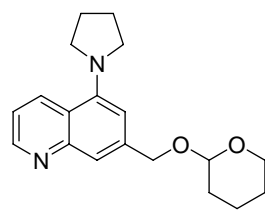


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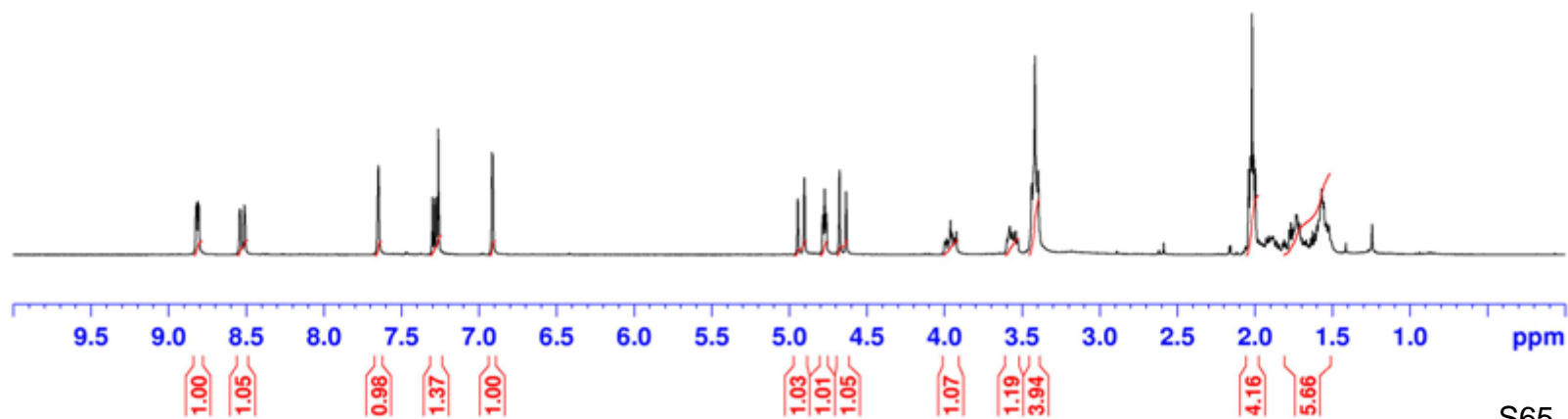


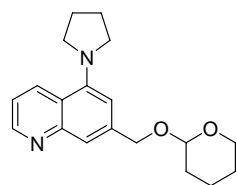




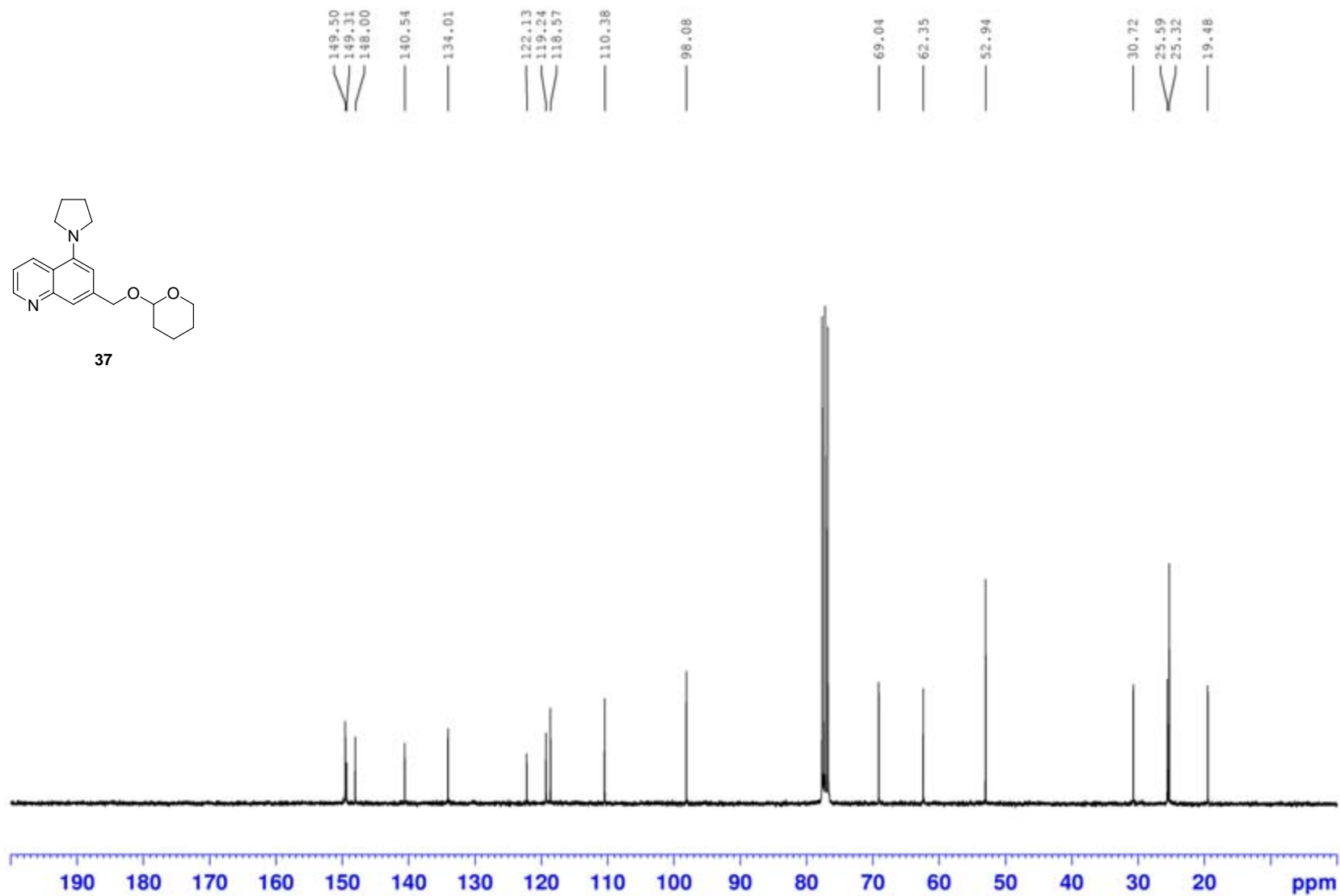


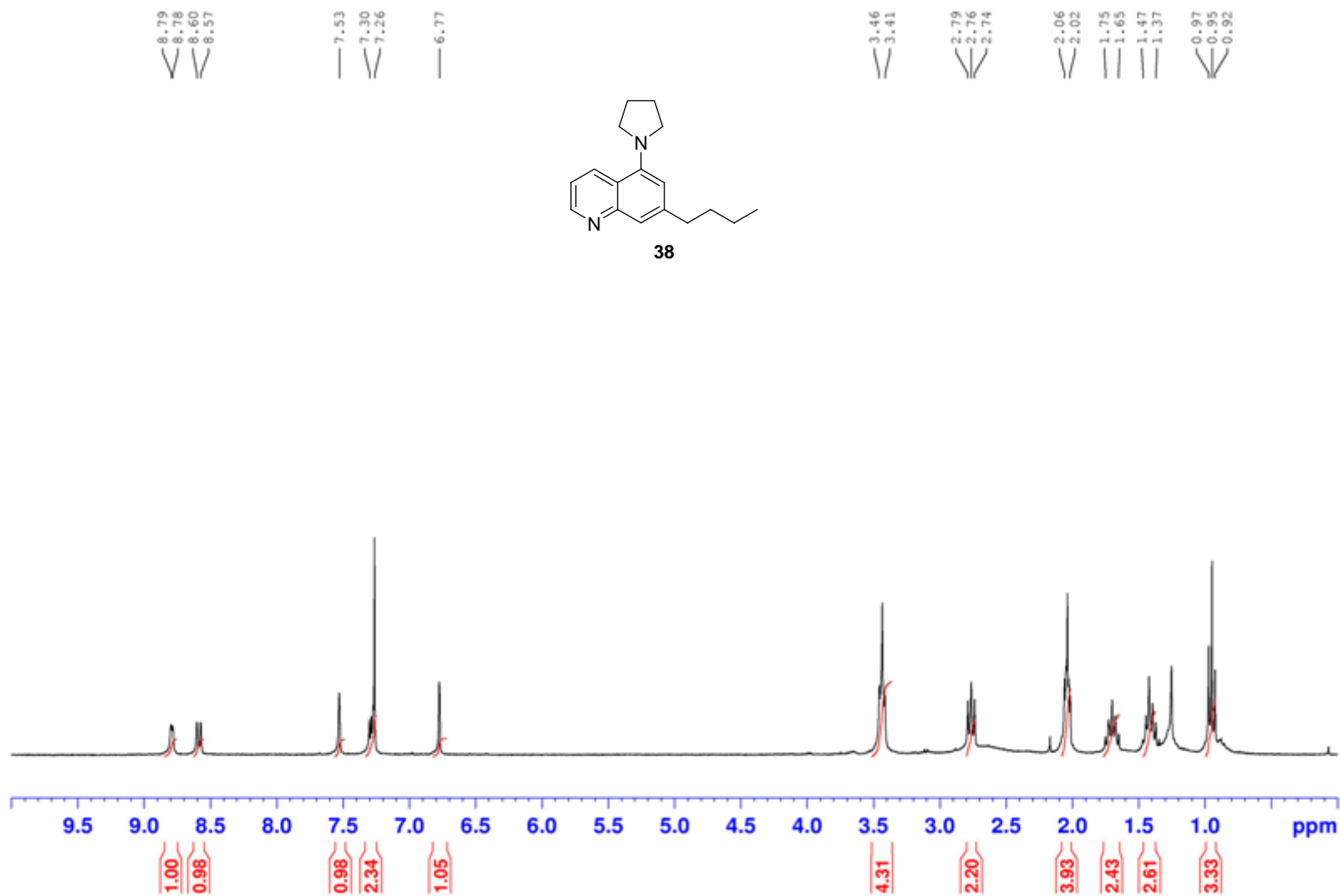
37

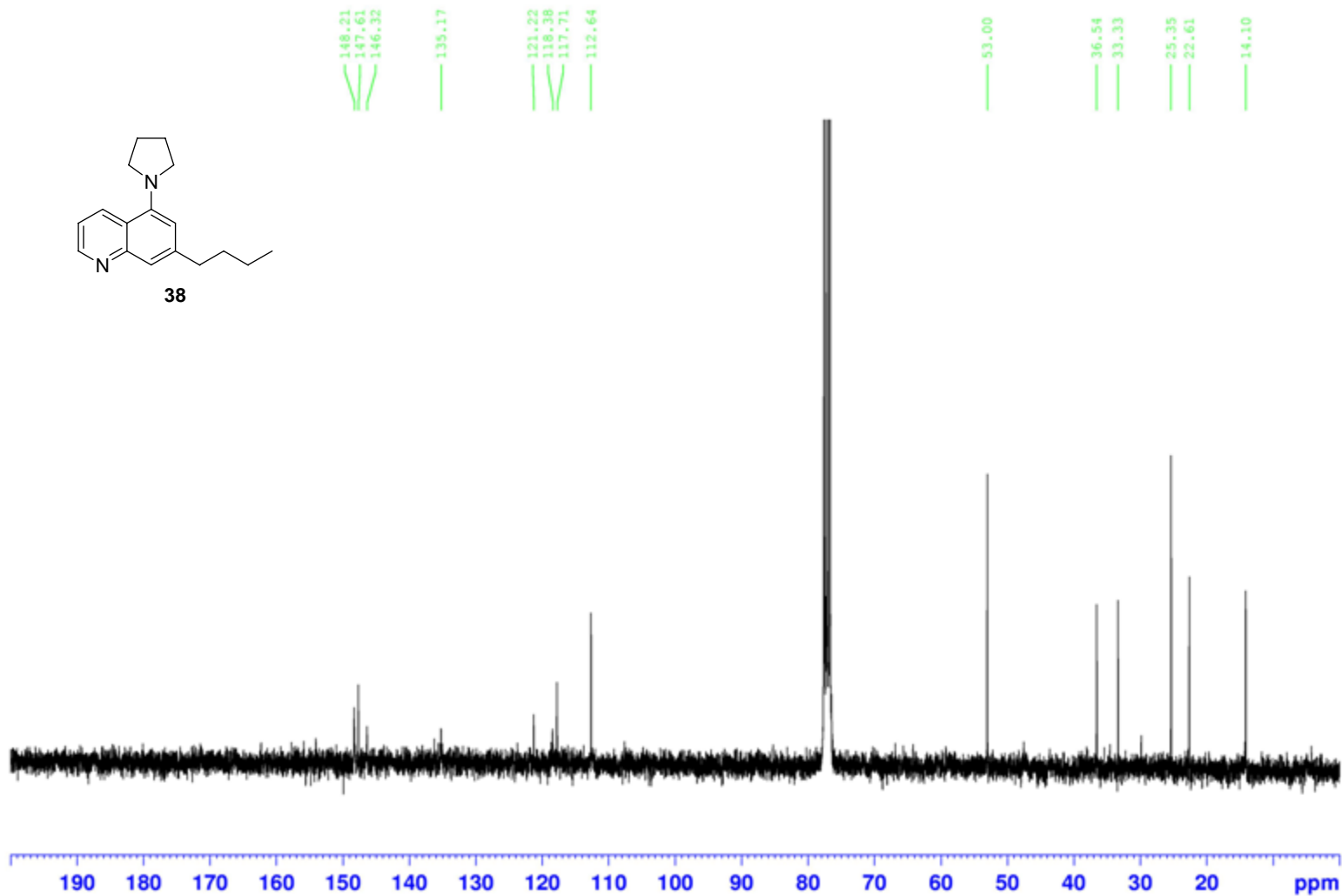


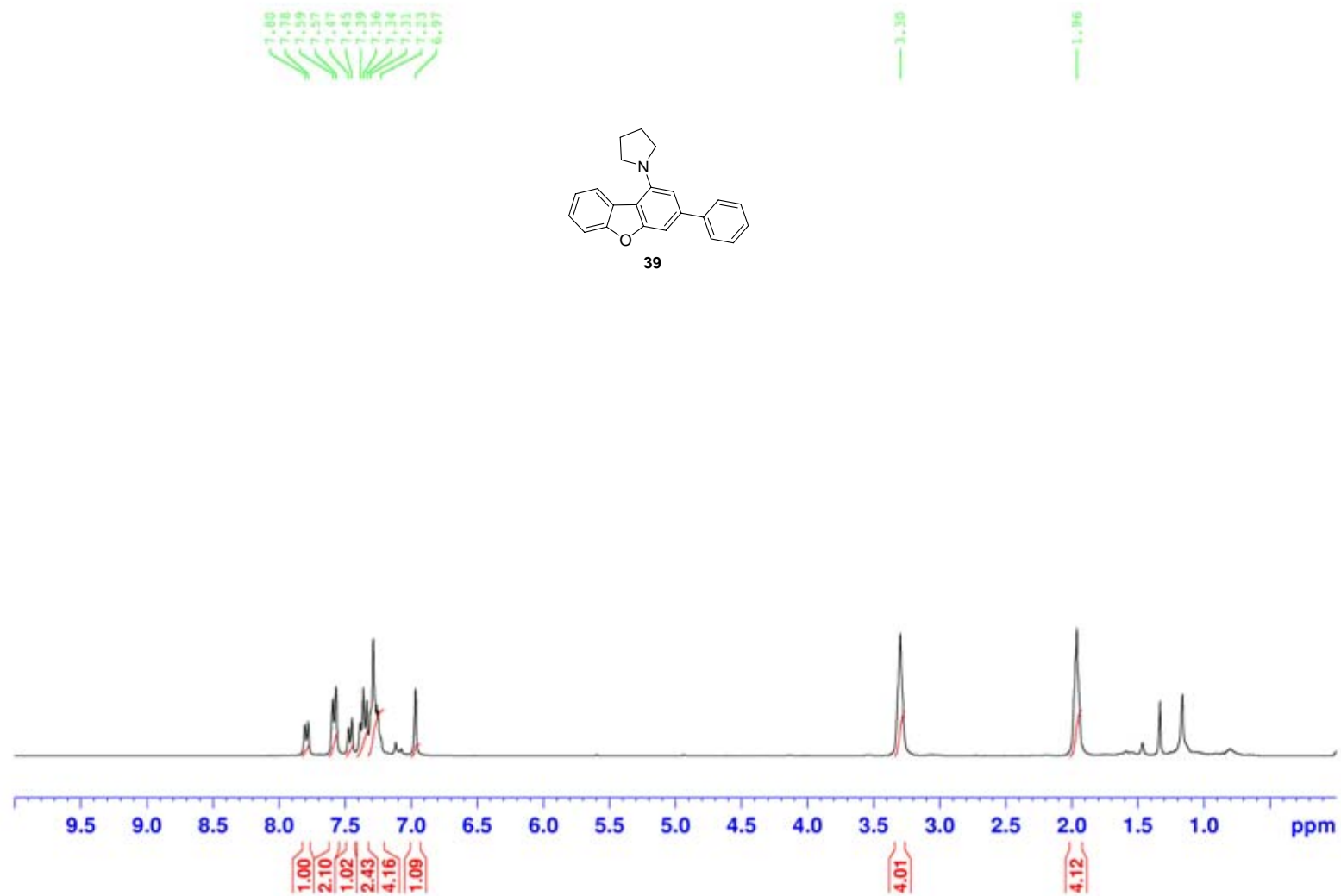


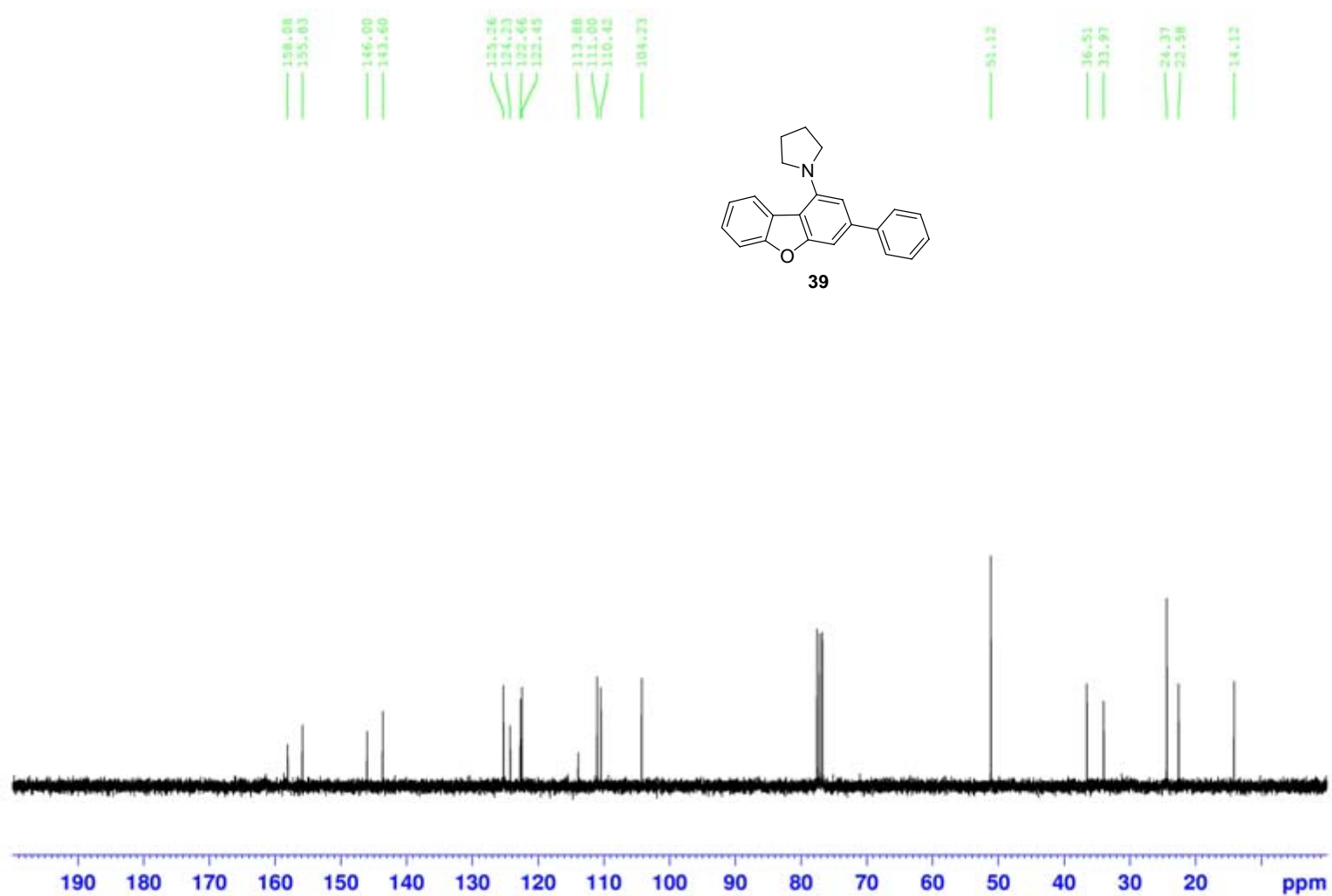
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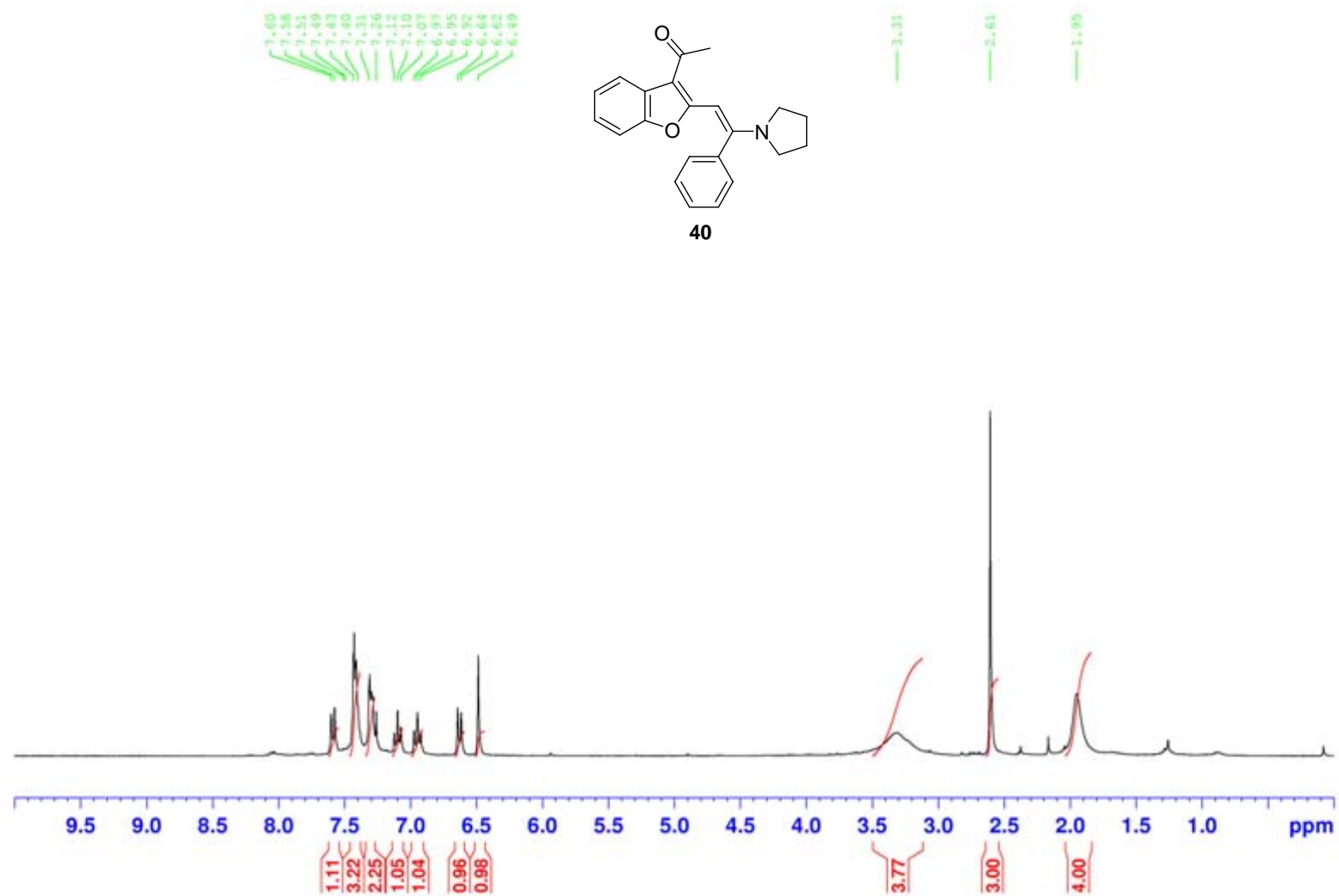


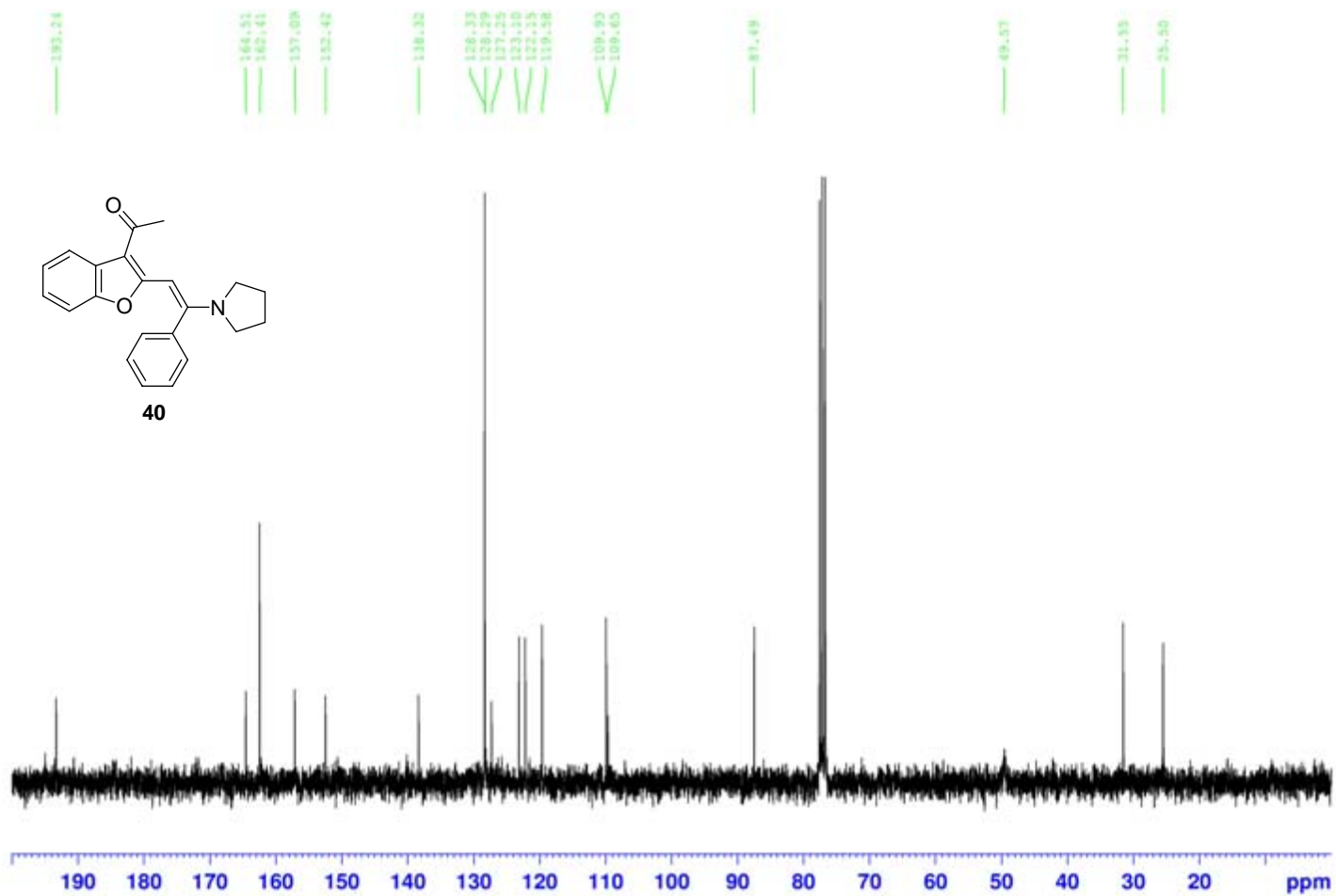




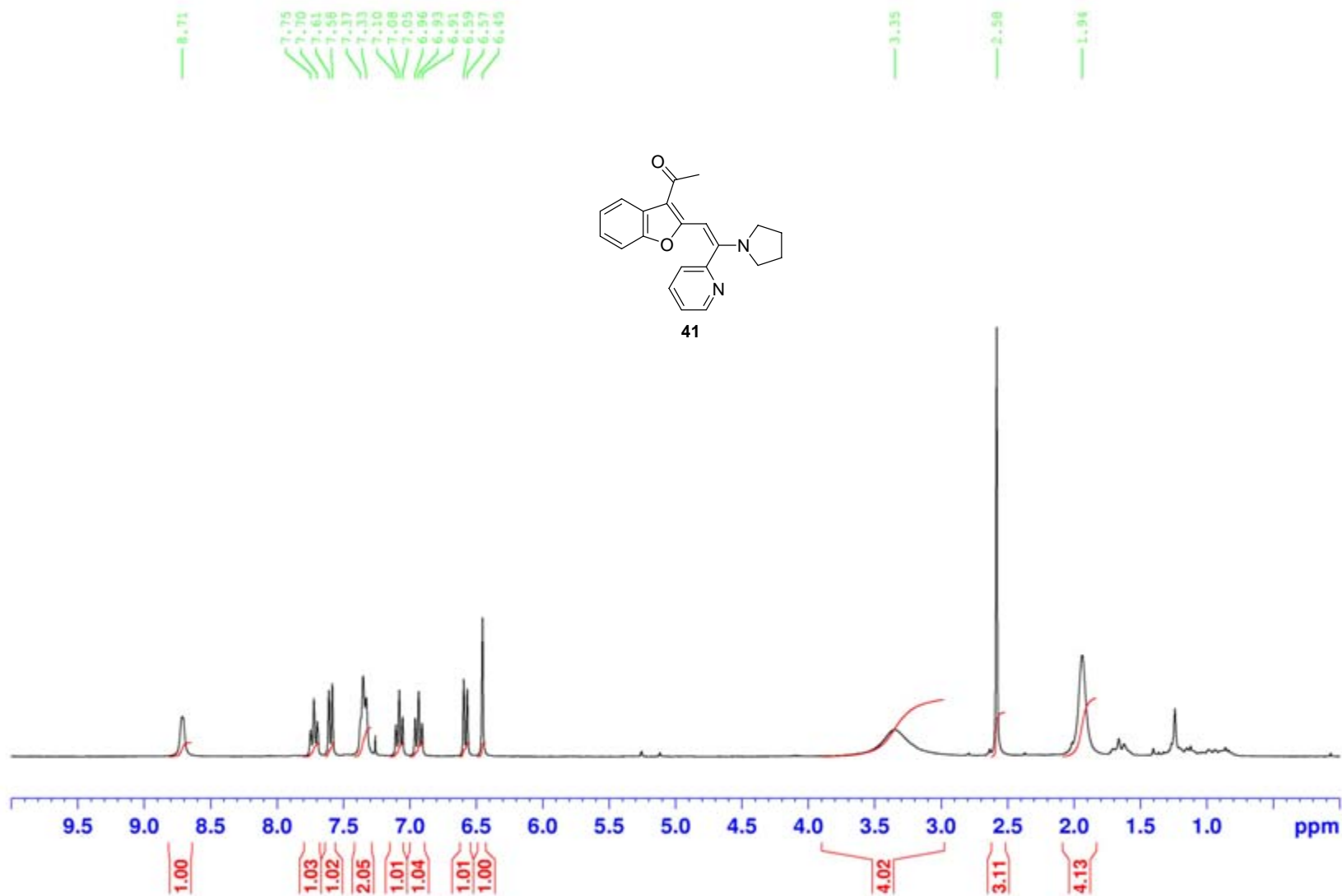


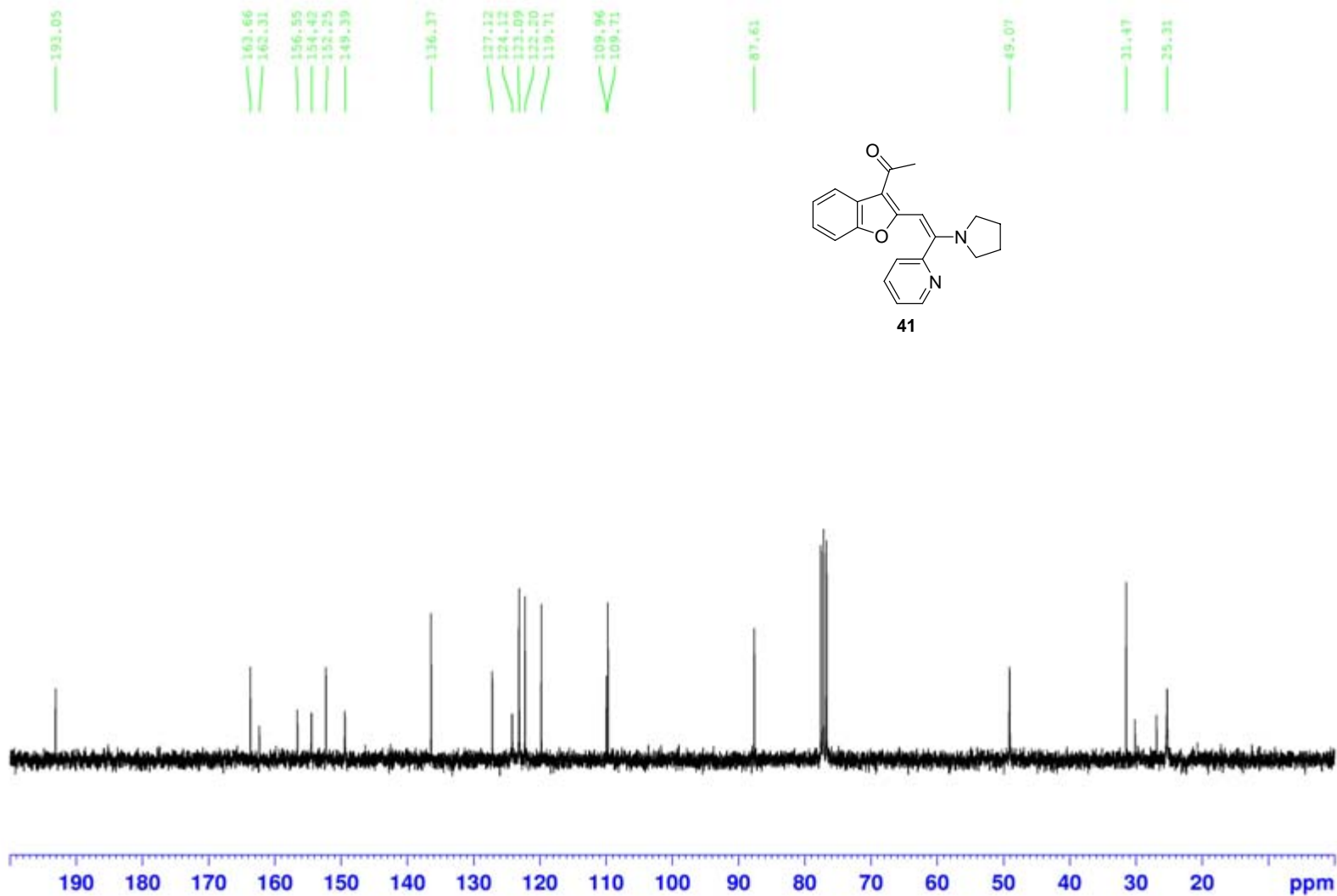


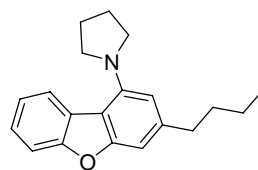




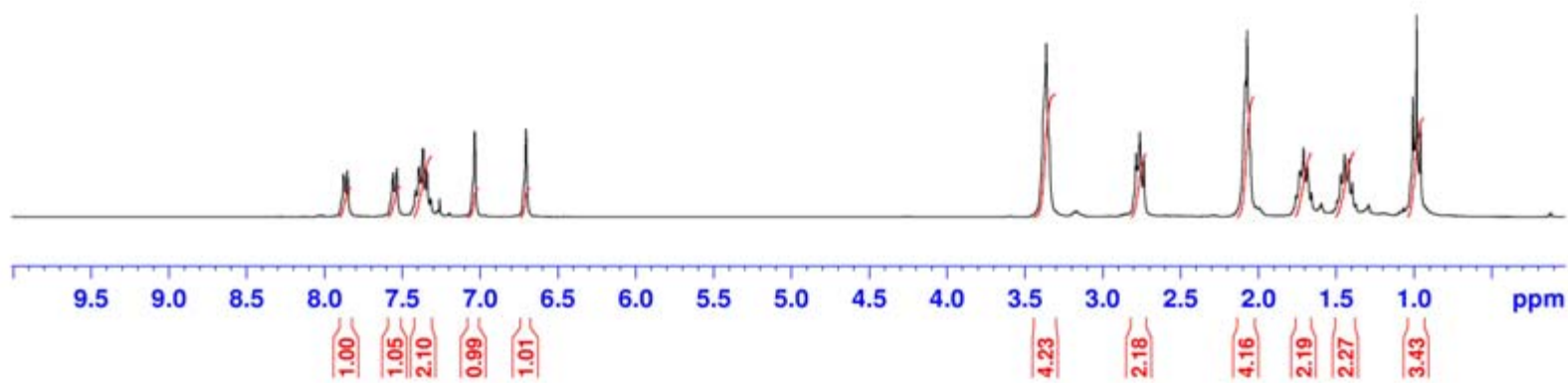


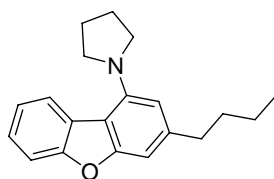




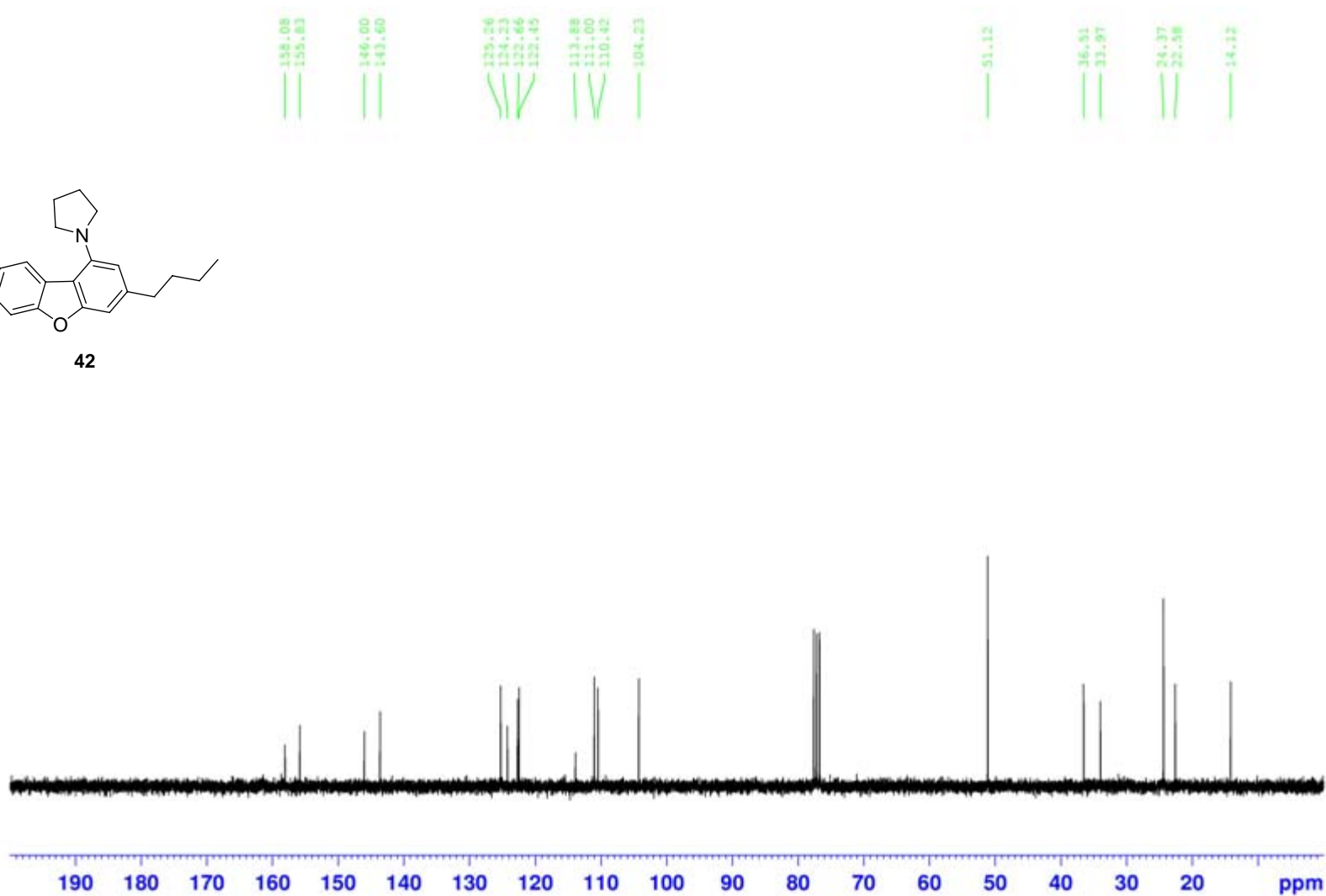


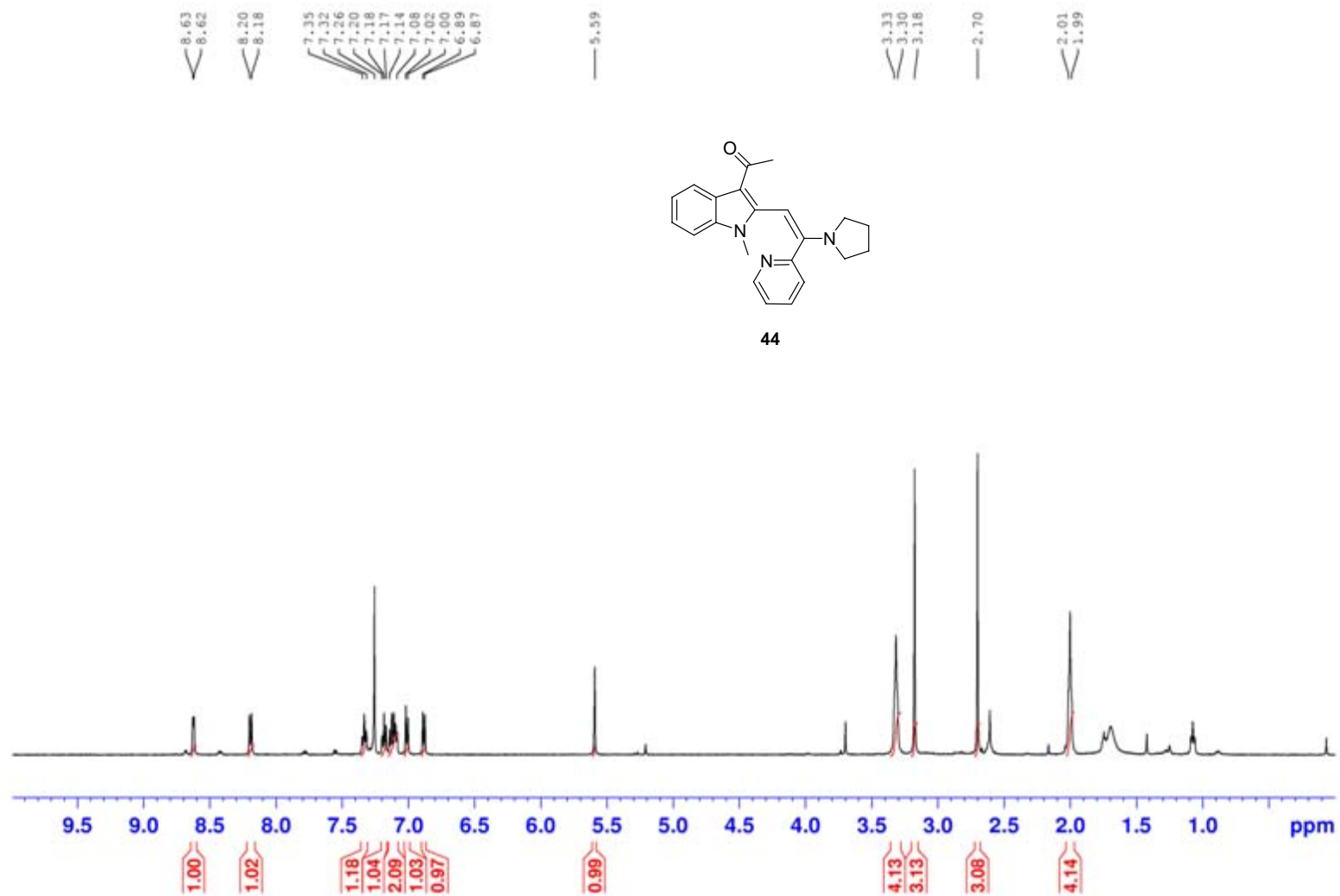
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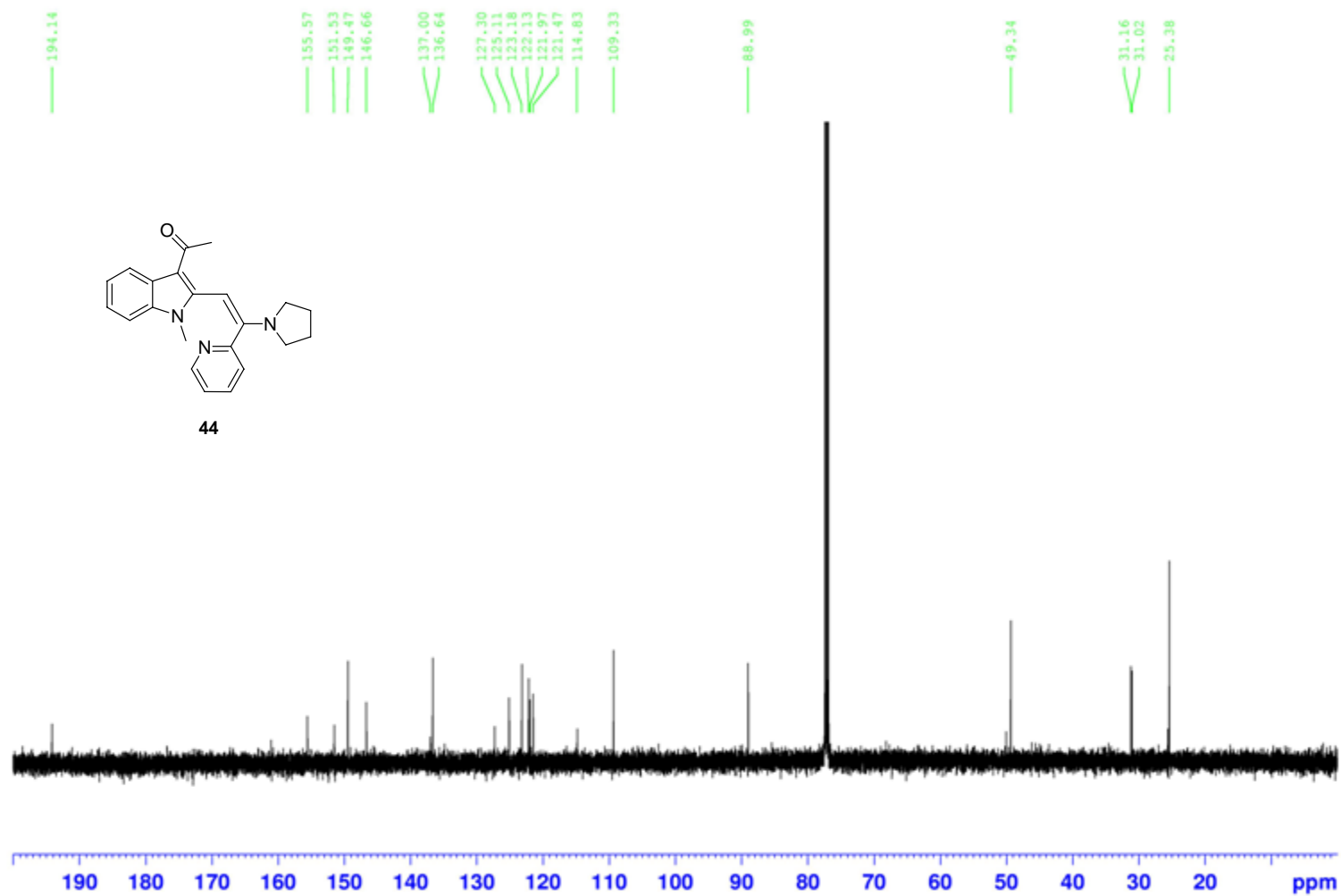


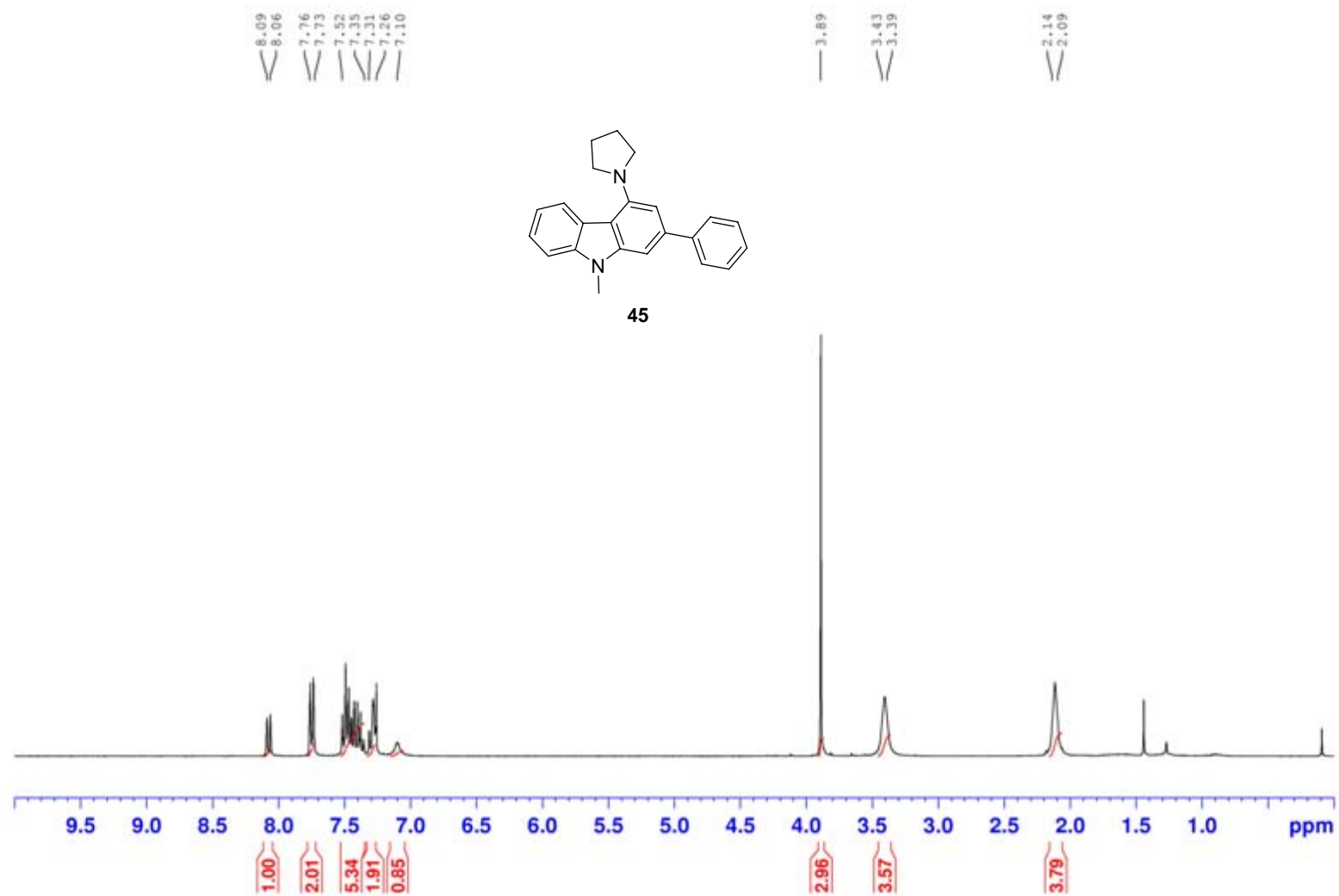


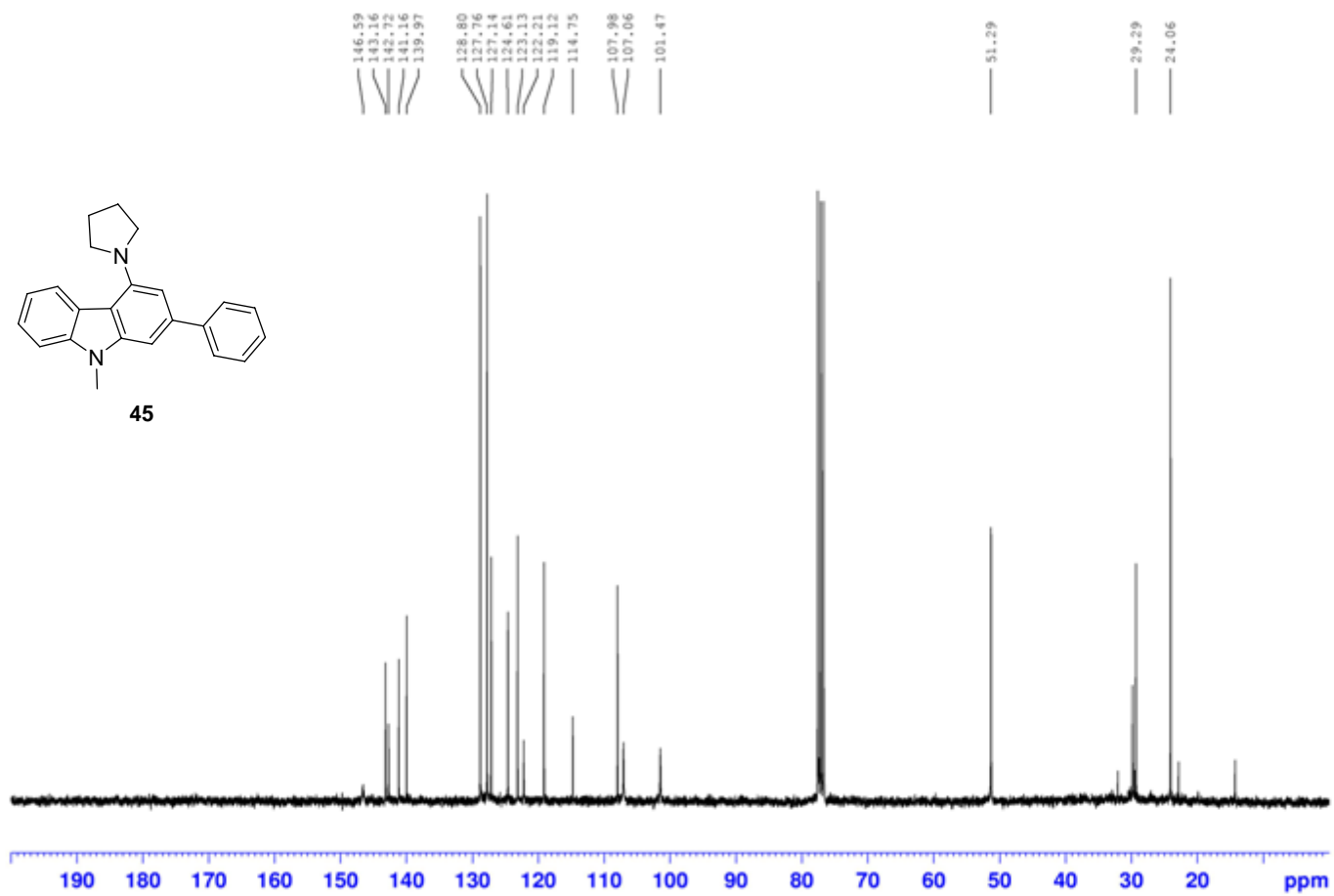
42



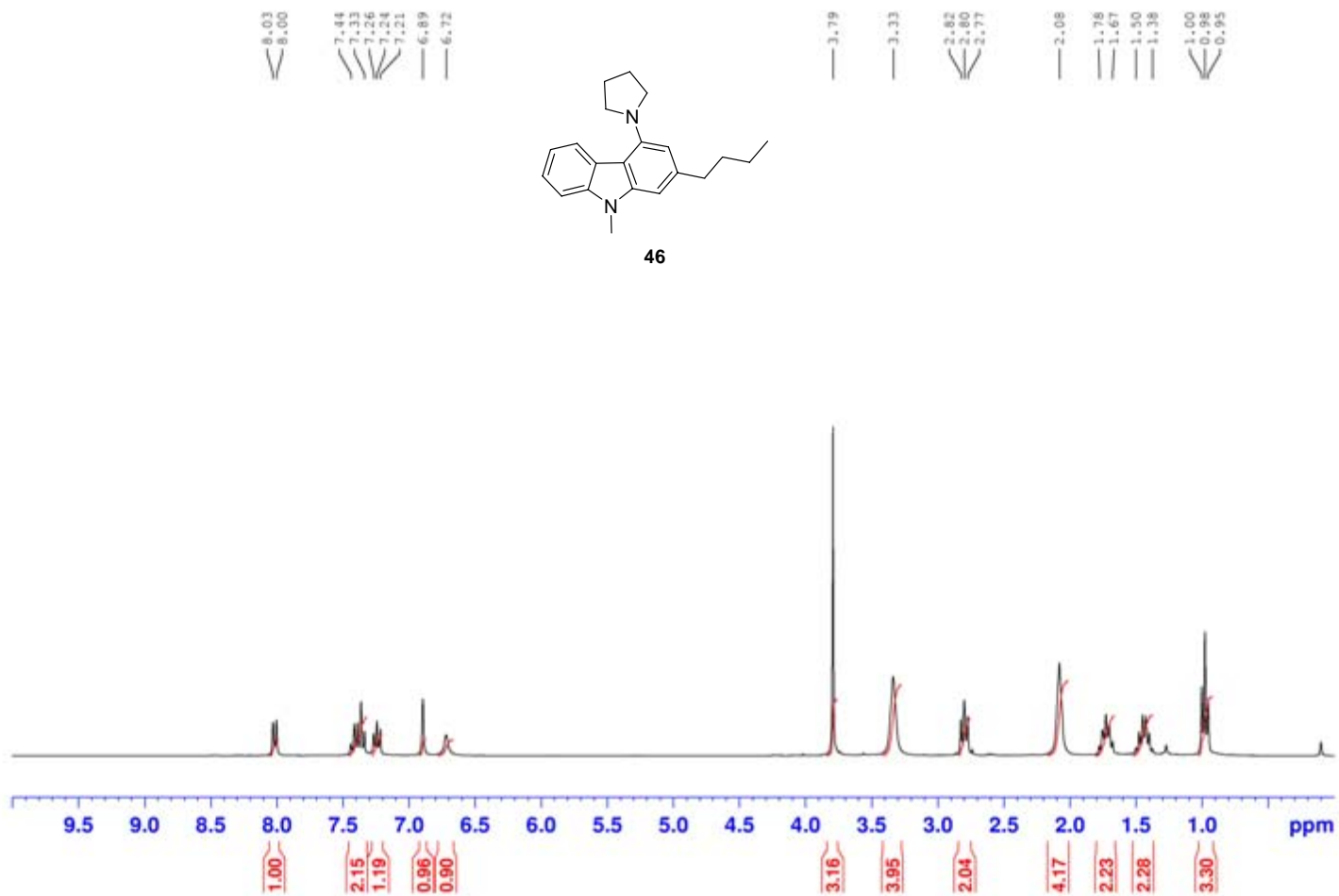


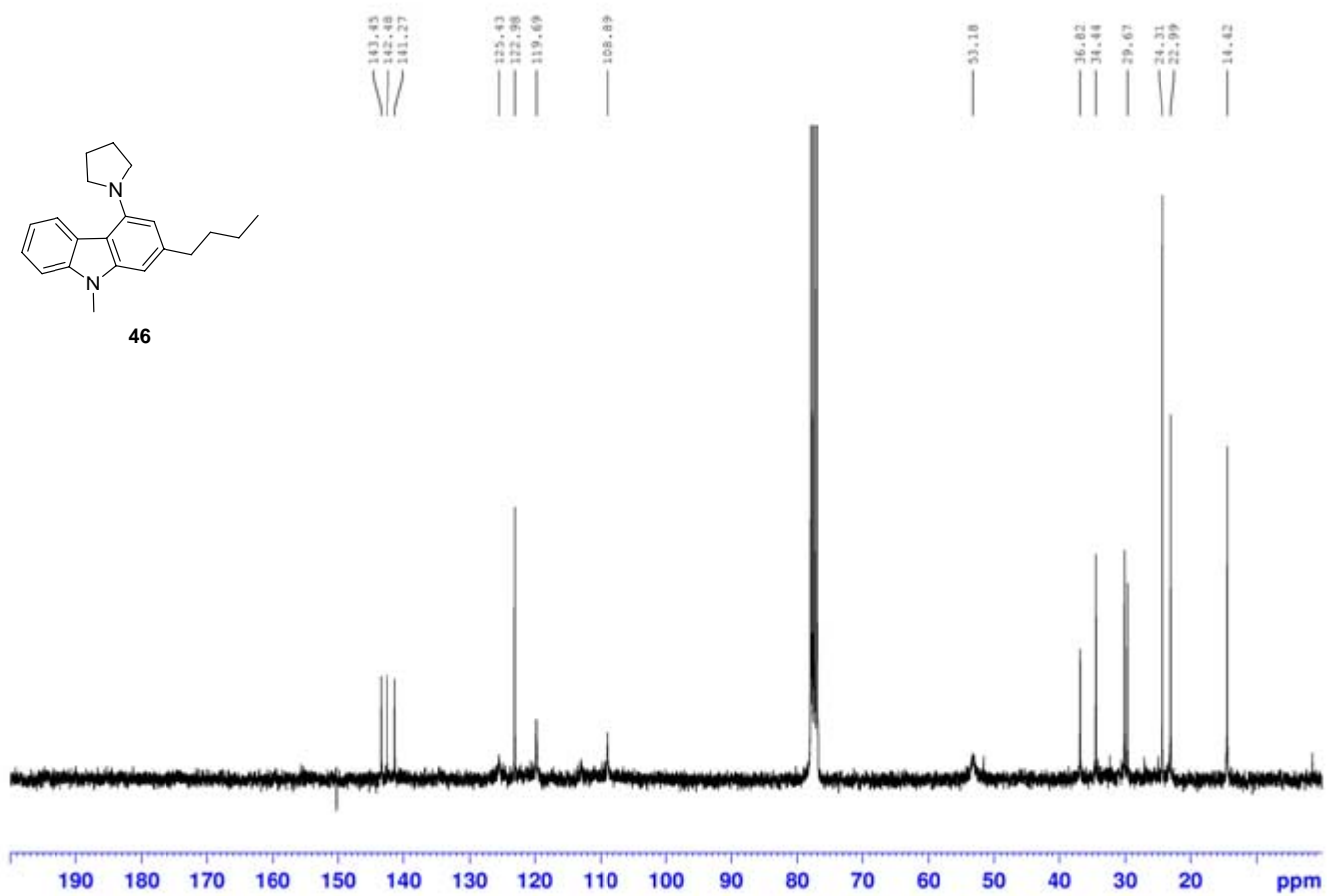


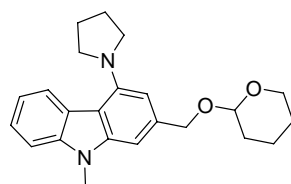




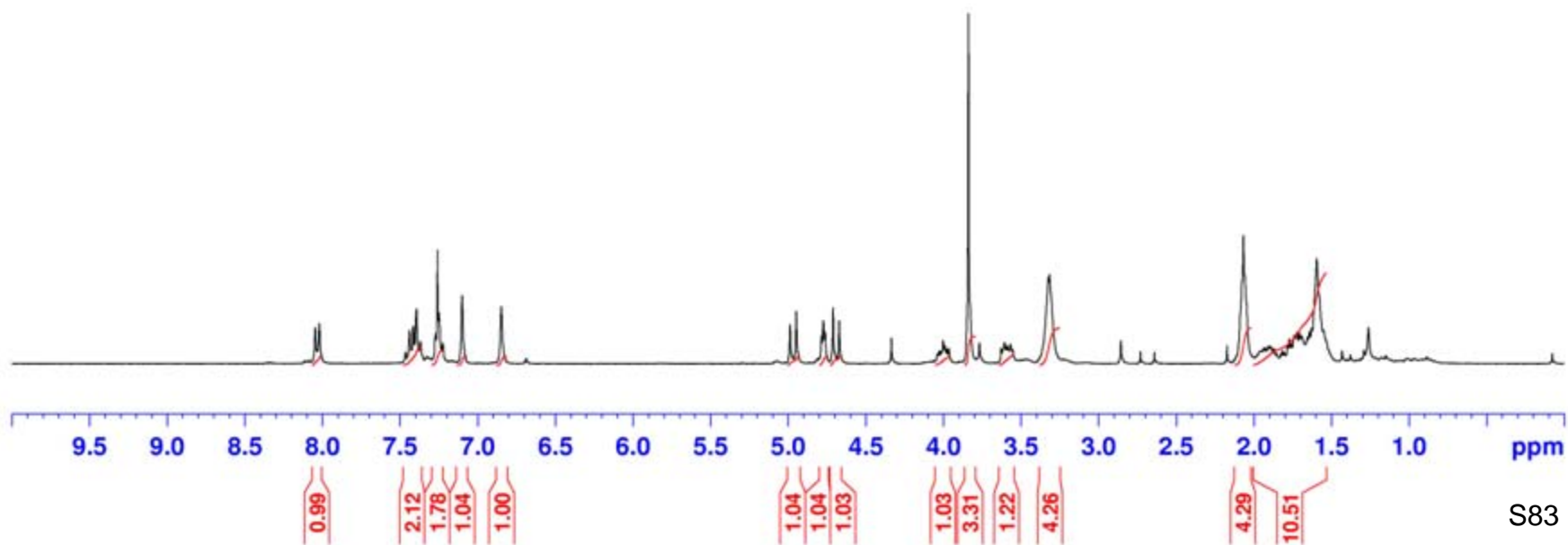


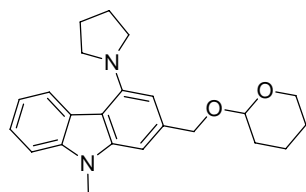




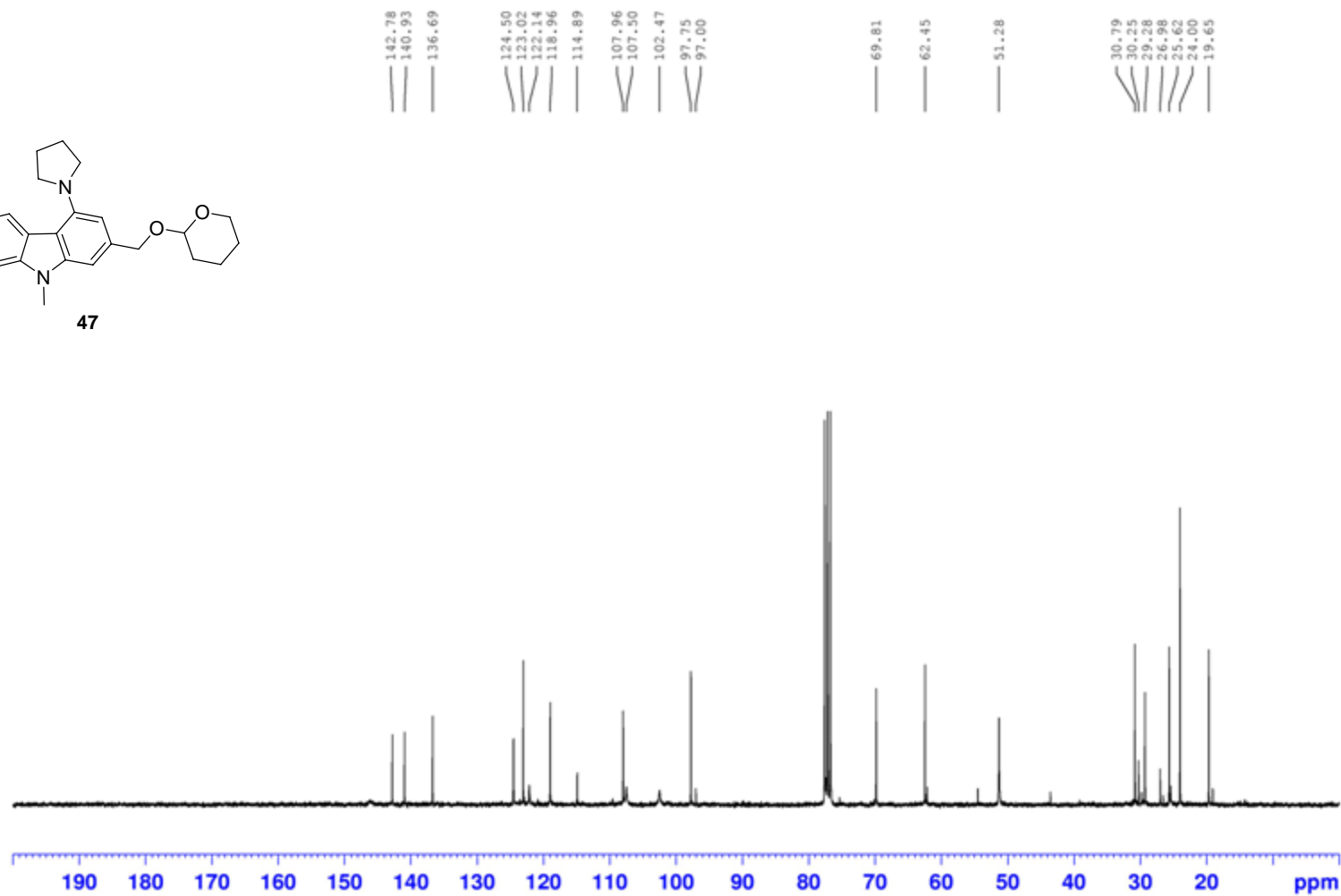


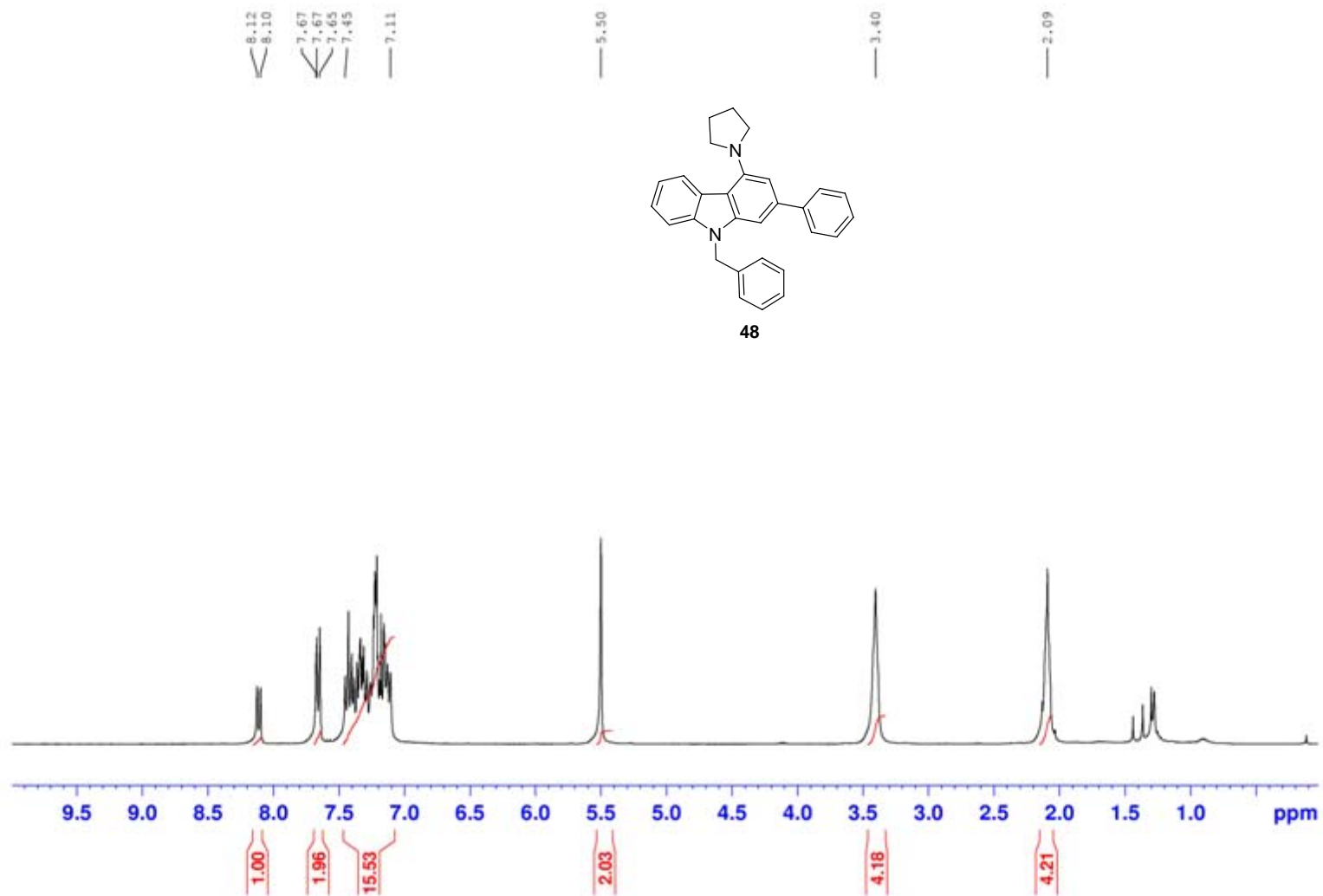
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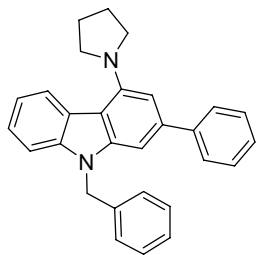




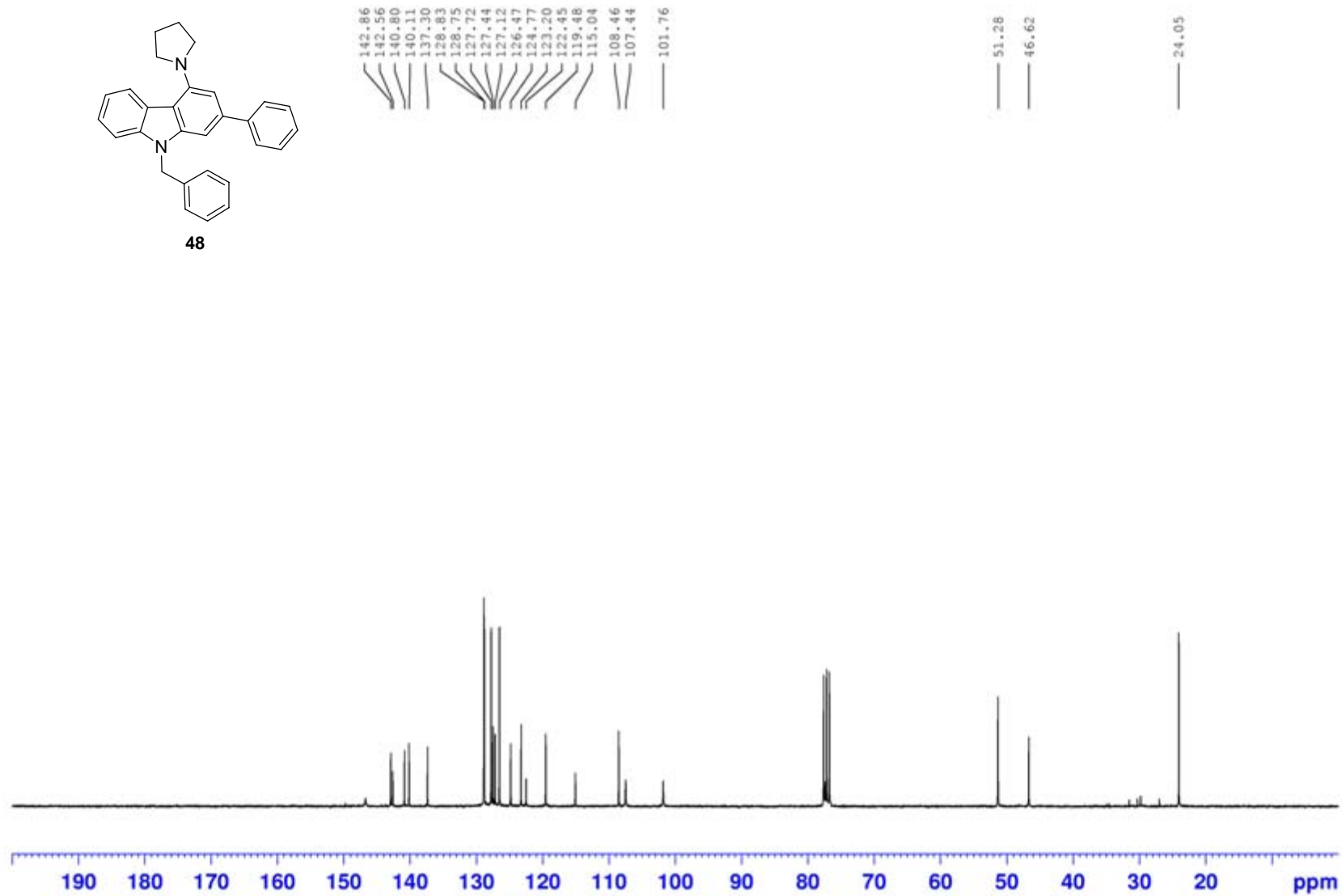
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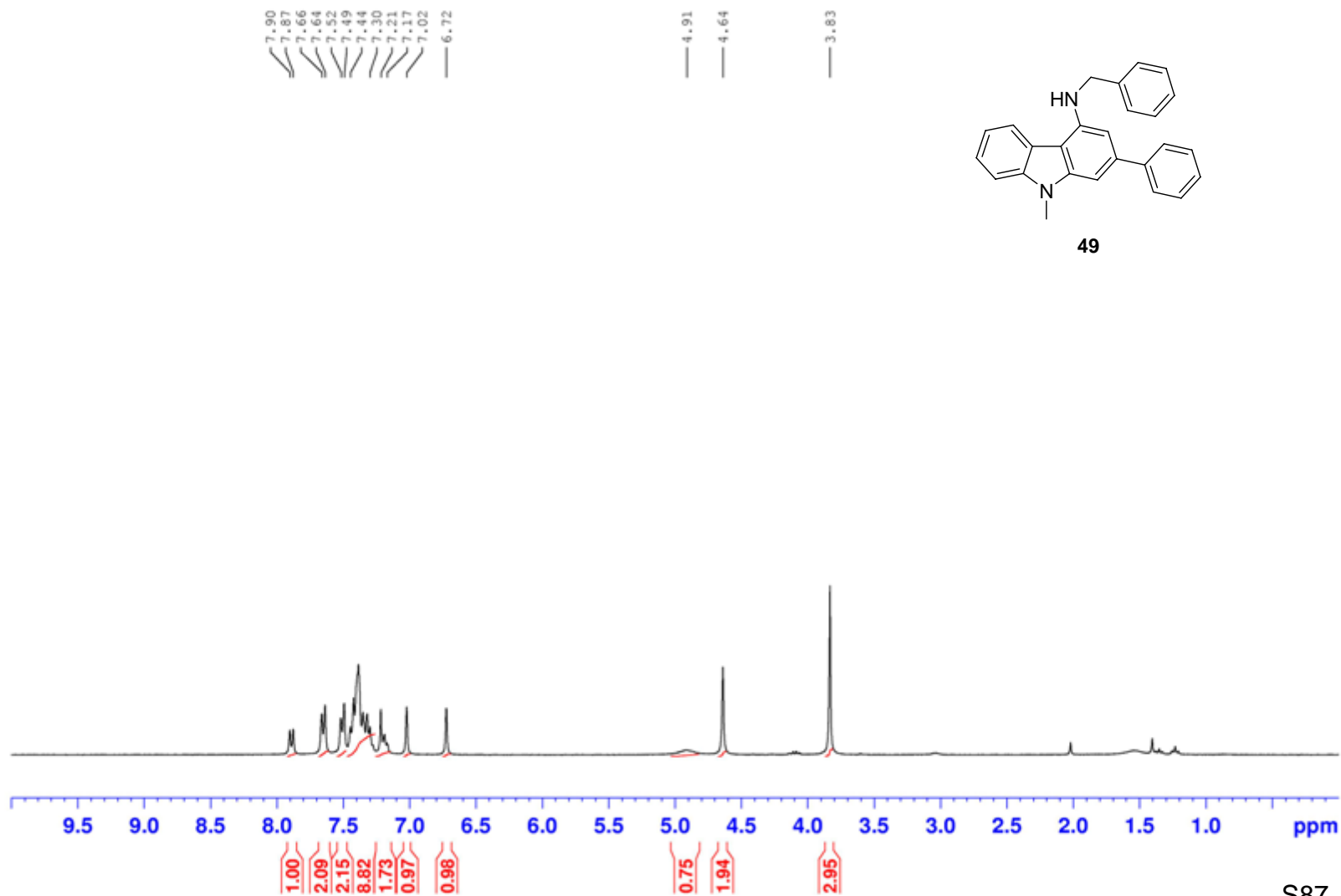


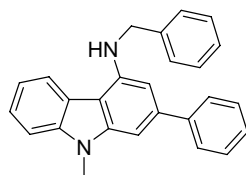




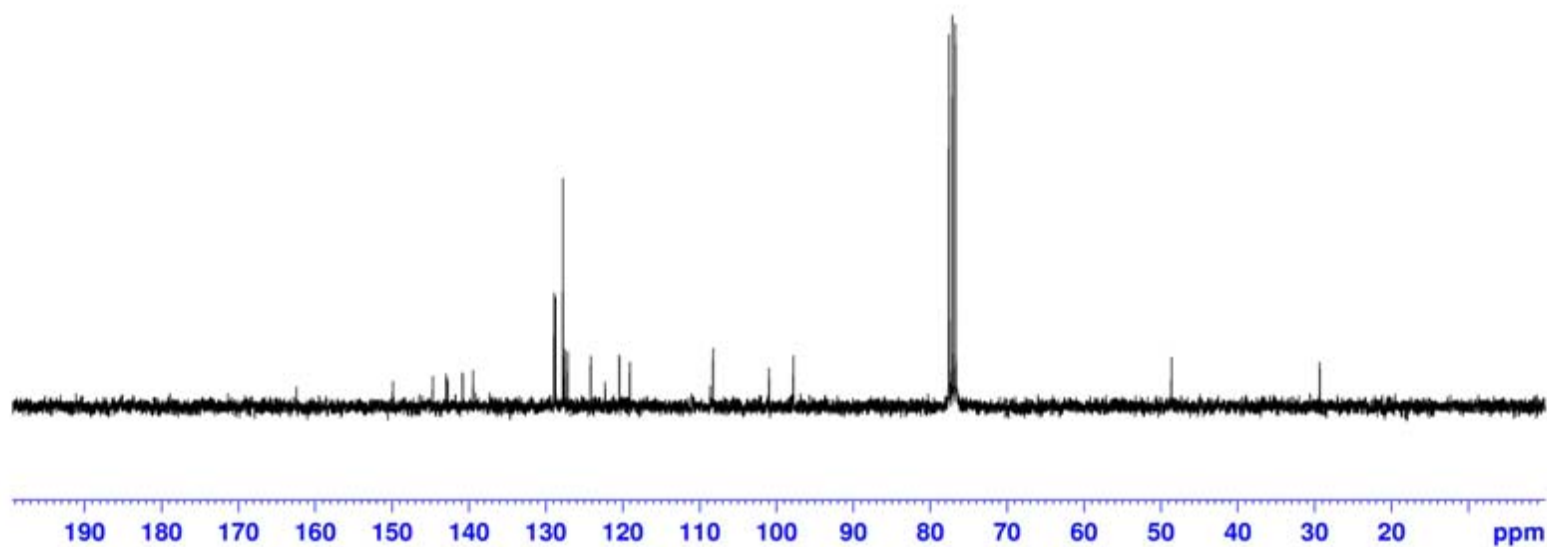
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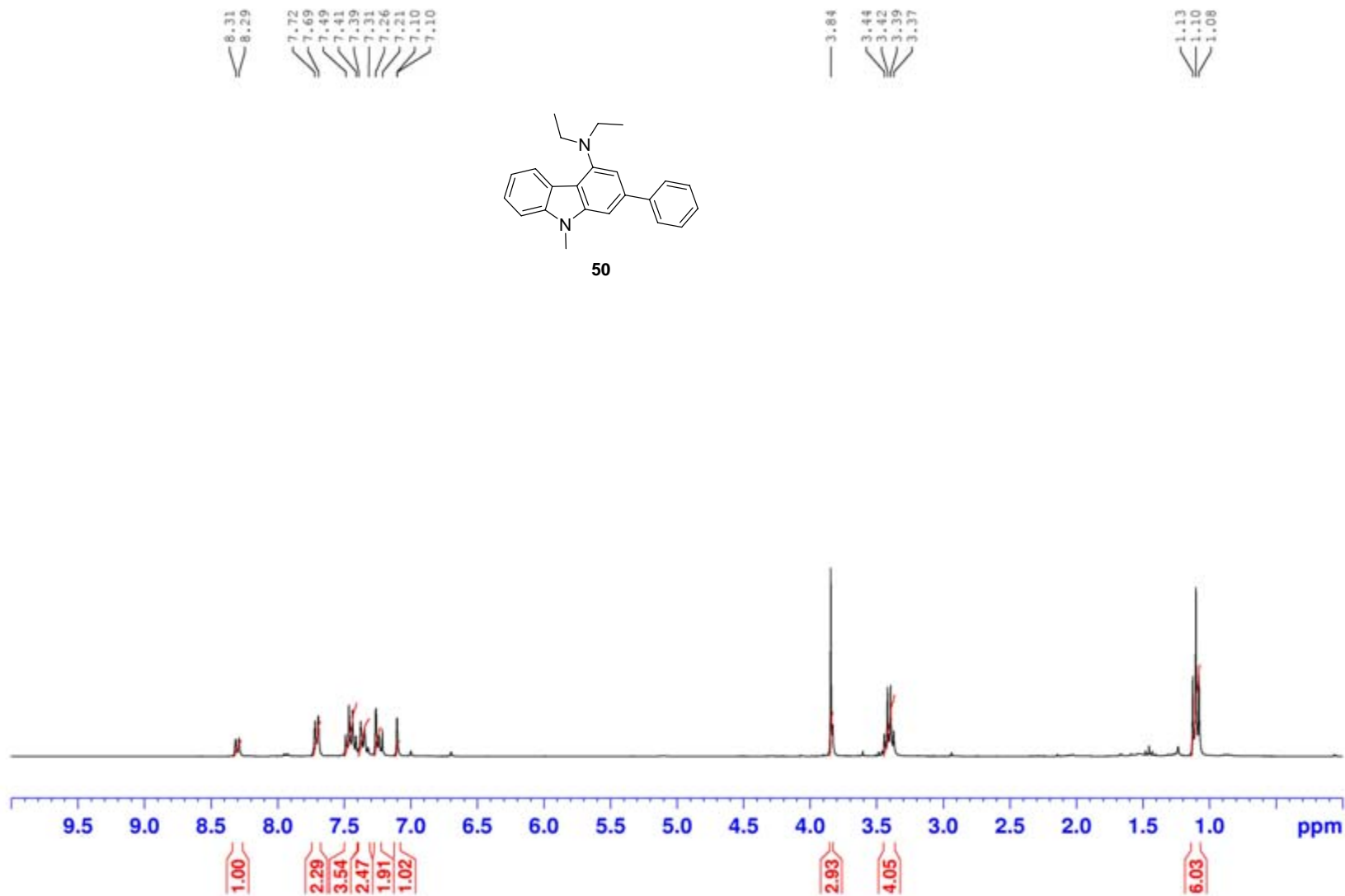


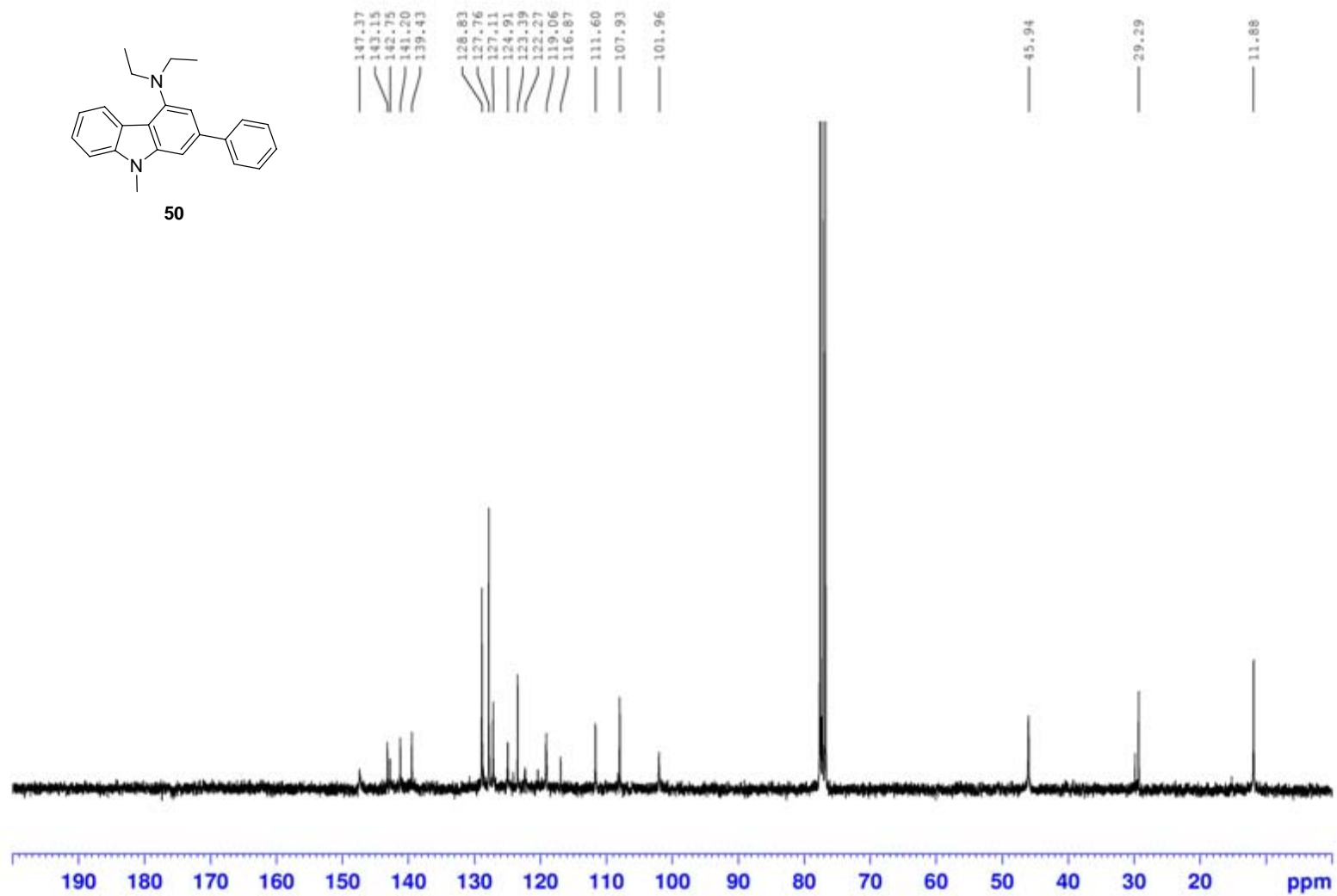
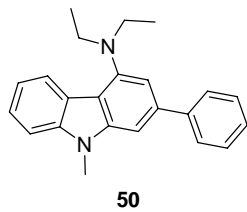


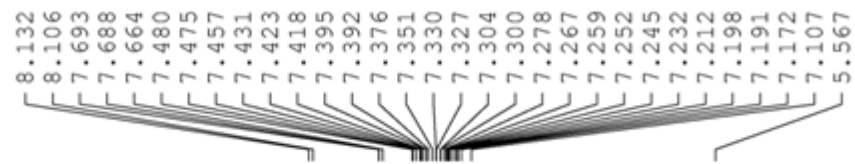
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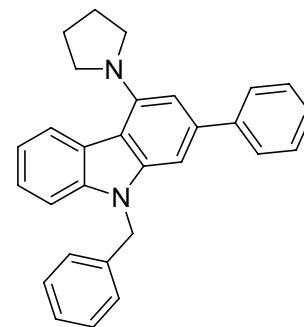






— 3.423

— 2.124



**48 bis**

