

# Development of conjugate addition of lithium dialkylcuprates to thiochromones: synthesis of 2-alkylthiochroman-4-ones and additional synthetic applications

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## Supporting Information

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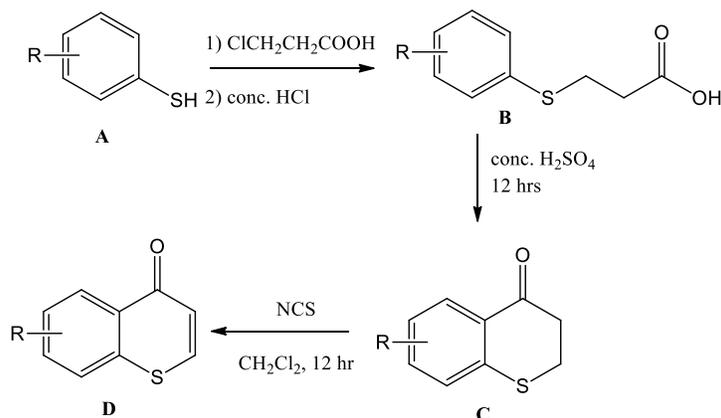
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#### <sup>1</sup>H, <sup>13</sup>C-NMR, and <sup>19</sup>F spectra:

<sup>1</sup>H, and <sup>13</sup>C-NMR spectra for compounds: **4Aa**, **4Ba**, **4Ca**, **4Da**, **4Ea**, **4Fa**, **4Ga**, **4Ha**, **4Ia**, **4Ja**, **5**, **6**, **7**, and **8** ..... S4 - S19 and S21- S32

<sup>19</sup>F-NMR spectra for compounds: **4Ha** ..... S20

## Preparation of starting materials – thiochromones:



Synthesis of starting materials - thiochromones

Thiochromones **D** were prepared according to procedures reported in literature. [1,2]

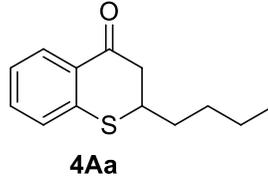
Thiophenols **A** were purchased from Fisher Scientific. To a 250 mL flask with a stirrer bar, was added 1M NaOH (25 mL), 1M Na<sub>2</sub>CO<sub>3</sub> (25 mL). To this, thiophenols **A** (50 mmol) was added as ethanol solution (30 mL) followed by the addition of 3-chloropropanoic acid (5.5 g, 151 mmol) in 20 mL water. The resultant reaction mixture was stirred at room temperature for 1 h, and then it was heated to reflux. When the reaction was completed as indicated by TLC monitor, the reaction mixture was cooled down to room temperature, then ethanol was evaporated under vacuum and then it was acidified to pH 1-2 with conc. HCl (18%). The solution was extracted with DCM for three times (3 X 30 mL) and the combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated under vacuum. The crude product was then purified by flash column chromatography (EtOAc/hexanes, 5% to 25%) to give 3-(phenylthio)propanoic acid **B** in 72- 85% yield.

3-(phenylthio)propanoic acids **B** was added slowly to a 100 mL flask filled with 25 mL conc. H<sub>2</sub>SO<sub>4</sub> at 0 °C. Then the resultant mixture was warmed up to room temperature and stirred at room temperature for about 12 hrs. When the reaction is finished as indicated by TLC monitoring, the reaction mixture was poured onto ice and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3X 30 mL) upon warming up to room temperature. The organic layers were combined and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. It was then filtered, and concentrated under vacuum. The crude product was purified by flash column chromatography (EtOAc/hexanes, 10%) to afford thiochroman-4-one **C** in 60-80% yield.

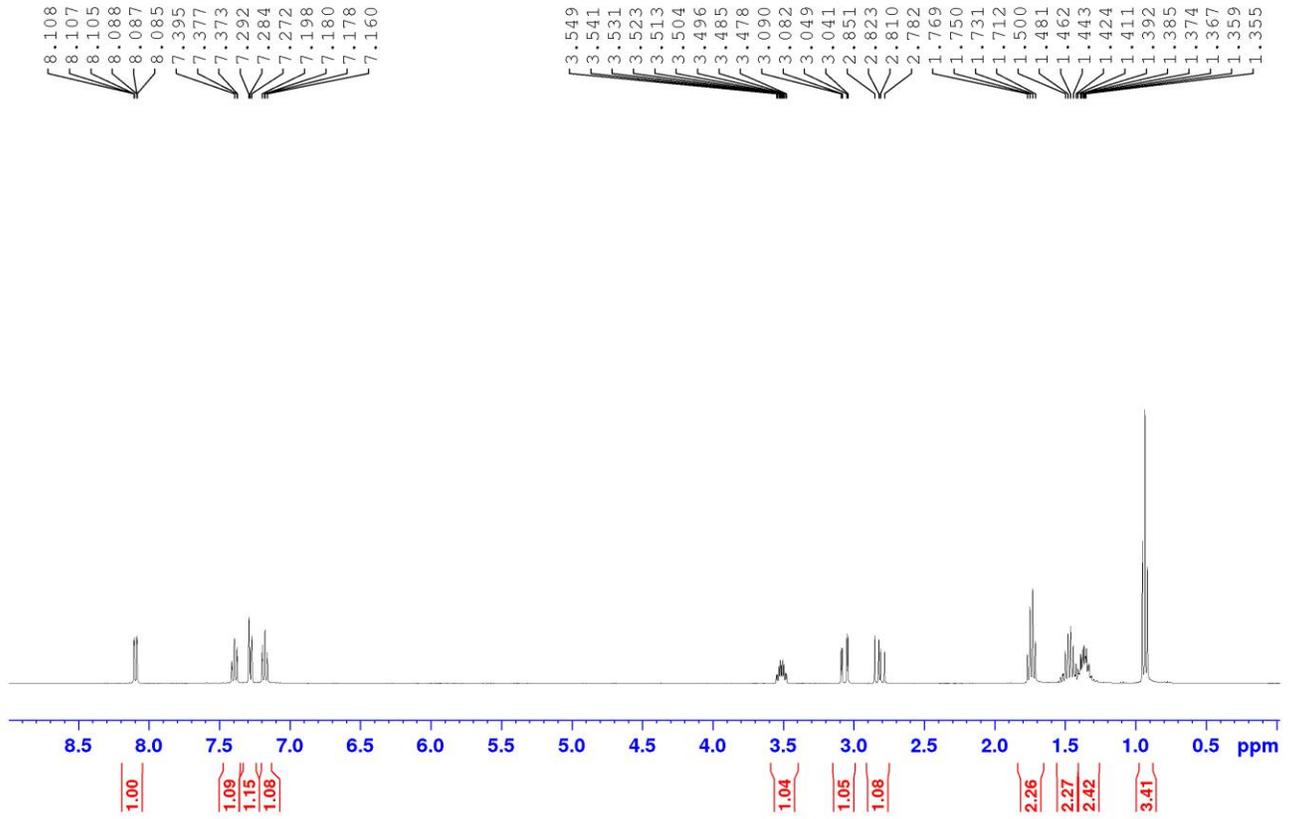
To a cool solution (ice bath) of **C** (10 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (30 ml) was added *N*-chlorosuccinimide (NCS) (10.5 mmol, 1.05 equivalent) in one portion. The resultant mixture was then warmed up to room temperature and stirred overnight for about 12 hours. It was quenched with water (30 ml) and the organic layer was separated. The aqueous layer was extracted with DCM (2 X 30 mL). The organic layers were combined and dried (Na<sub>2</sub>SO<sub>4</sub>). It was then filtered, concentrated under vacuum to give crude product. The crude product was then purified by flash column chromatography (EtOAc/hexanes, 5-10%) to give thiochromone **D** in 50-70% yield.

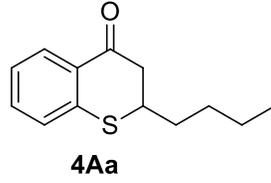
## References:

1. Giles, P. R.; Marson, C. M. *Aust. J. Chem.* **1992**, 45, 439–443.
2. Jia, W.; Liu, Y.-J.; Li, W.; Liu, Y.; Zhang, D.-J.; Zhang, P.; Gong, P. *Bioorg. Med. Chem.* **2009**, 17, 4569–4574.

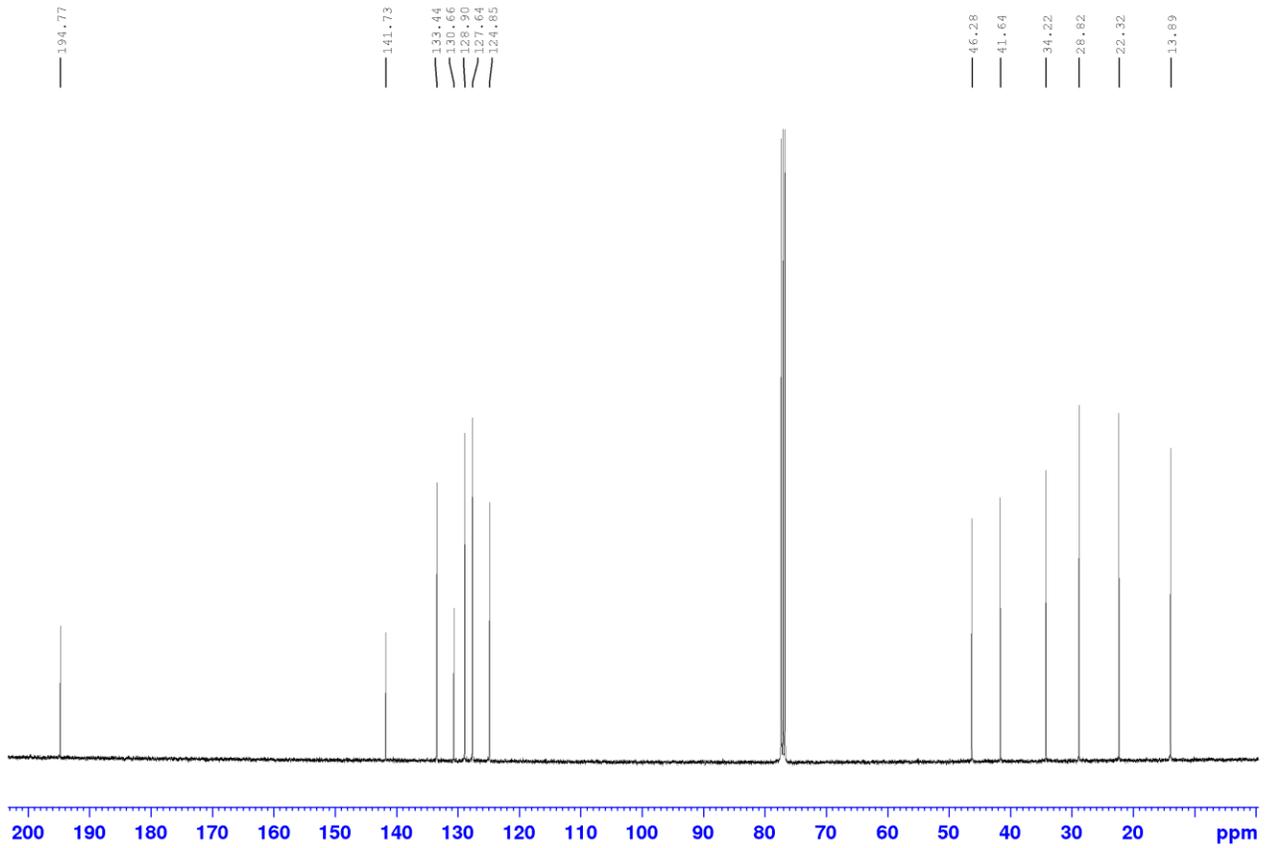


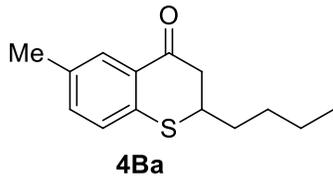
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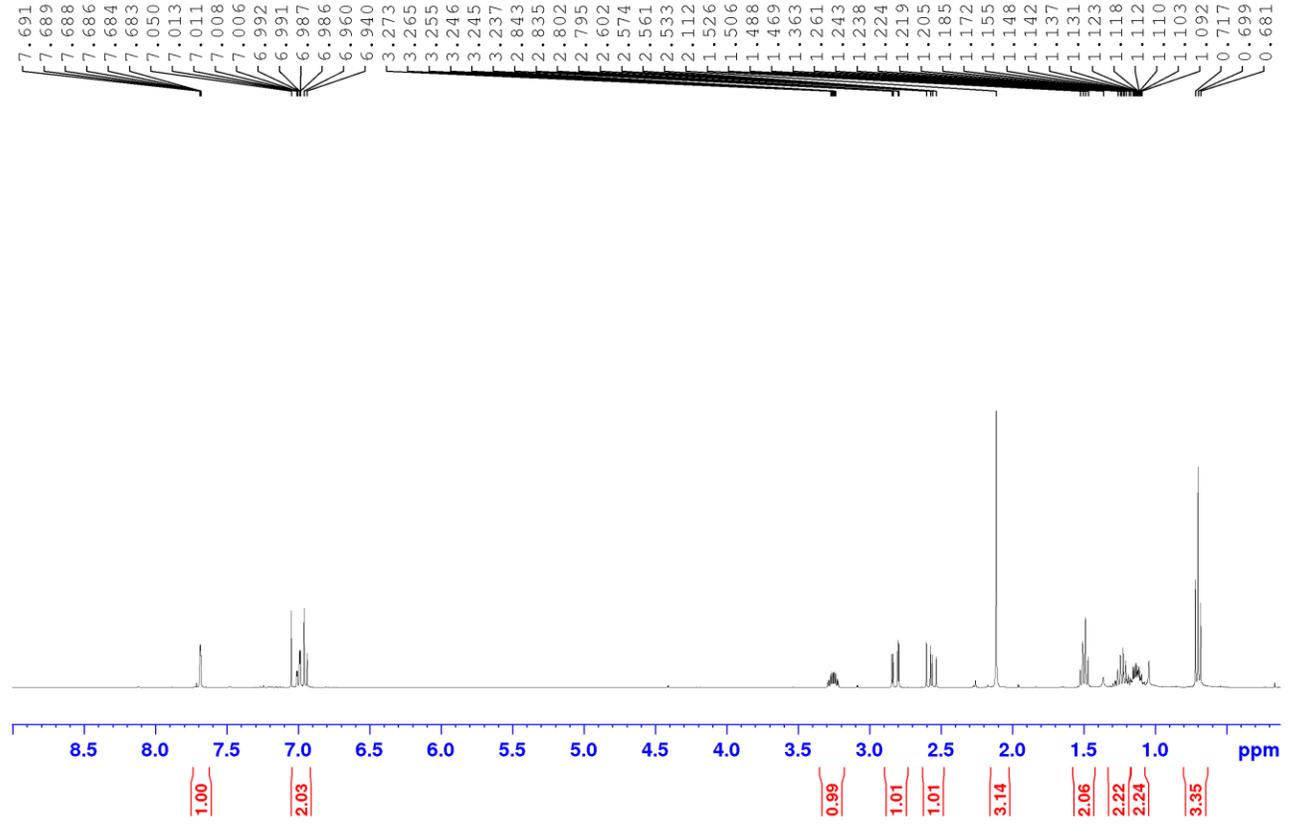


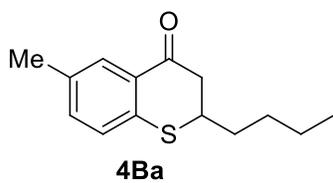
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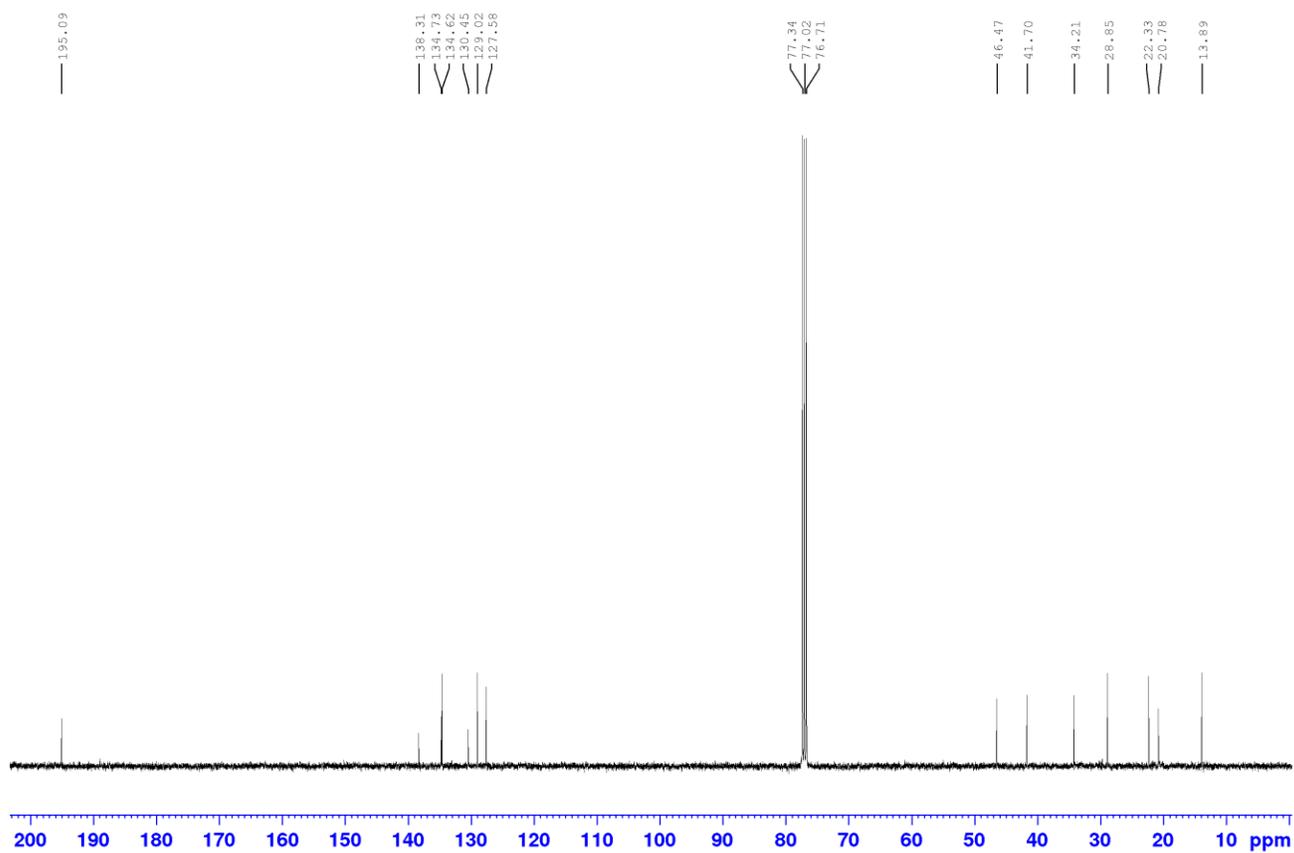


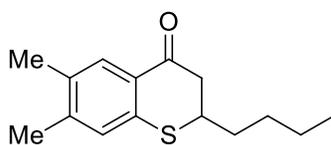
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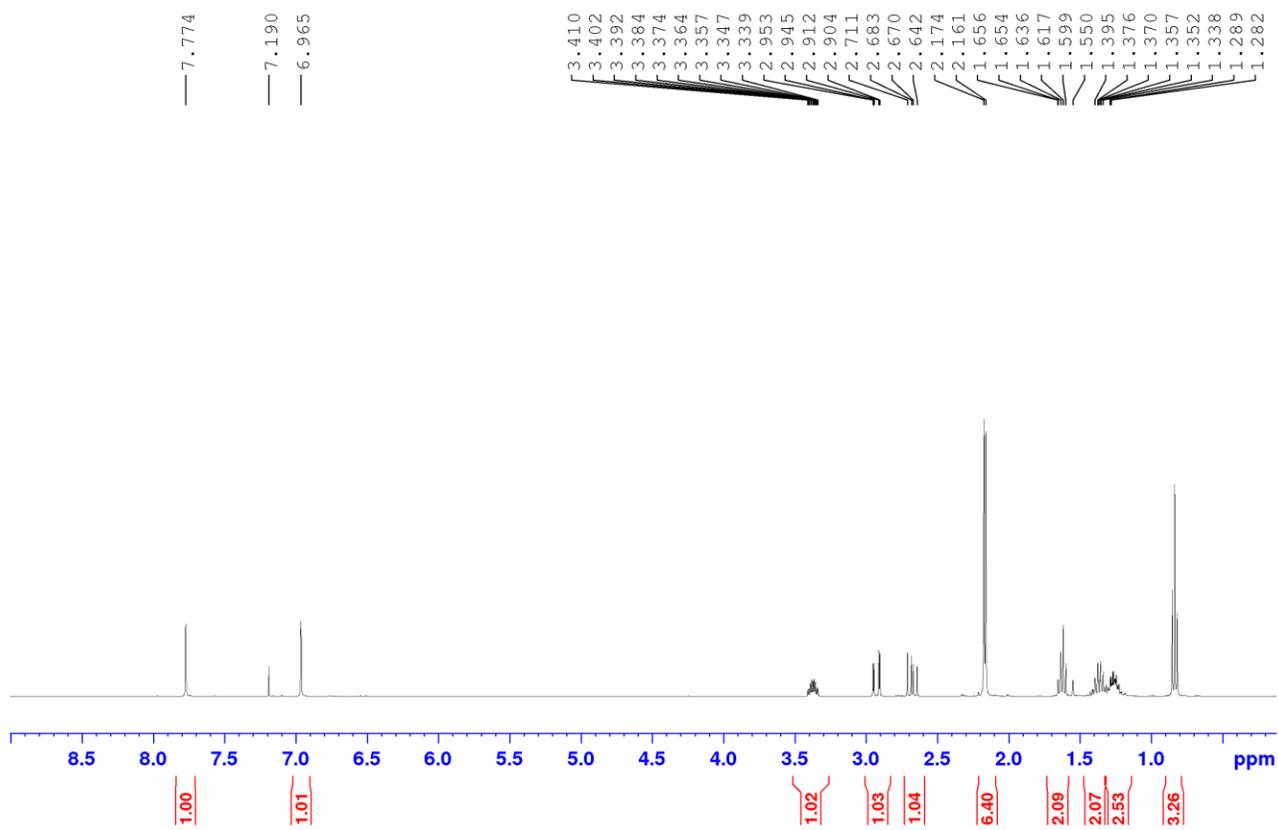
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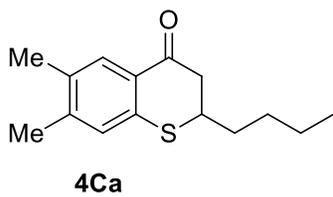




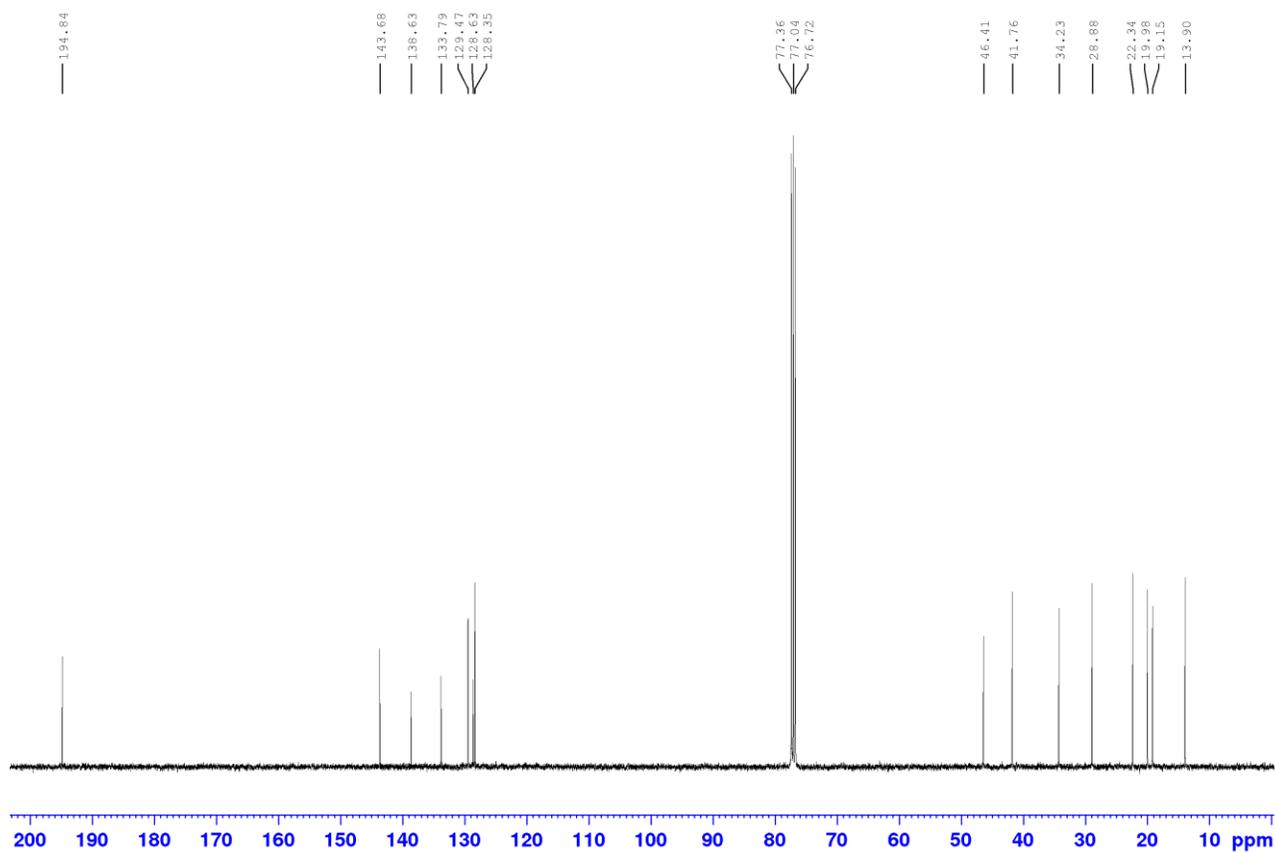
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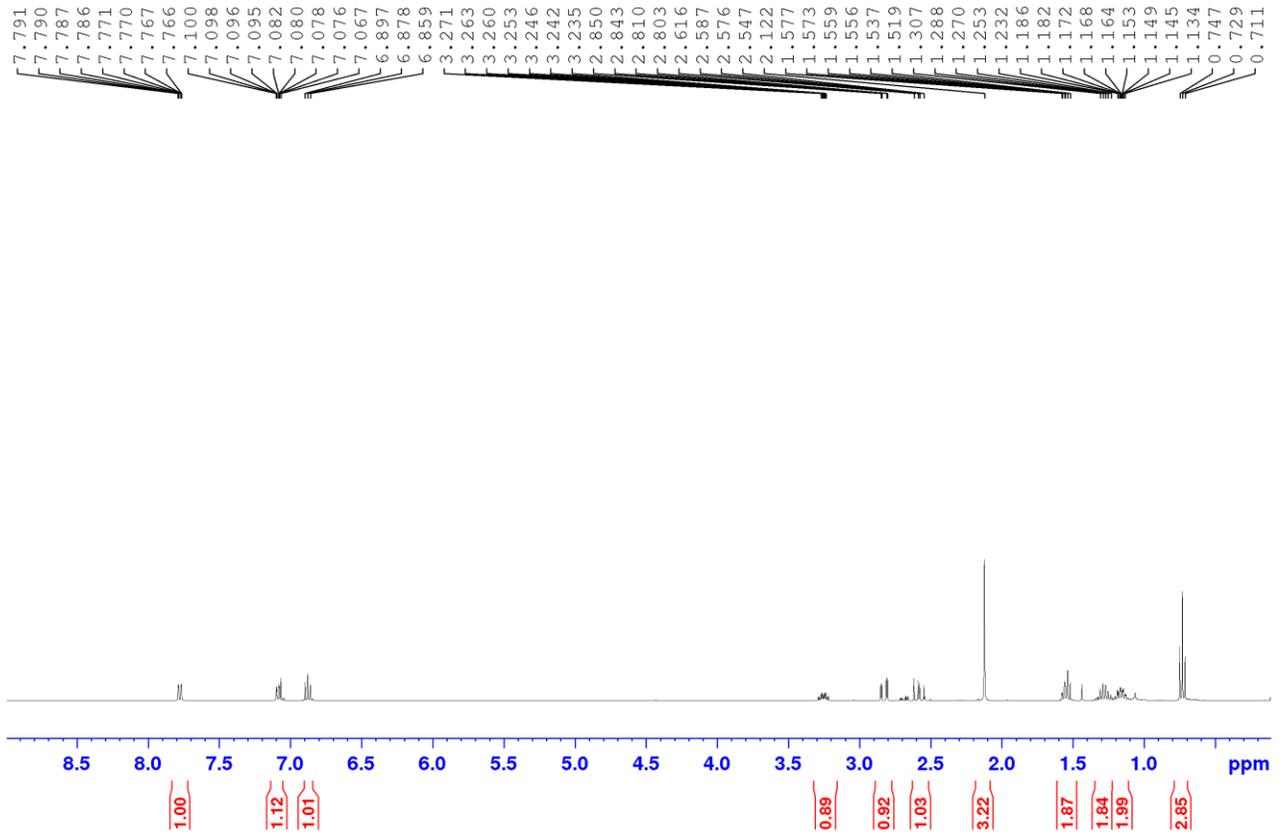
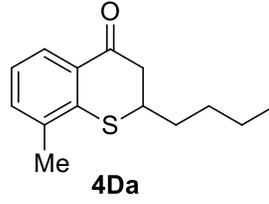
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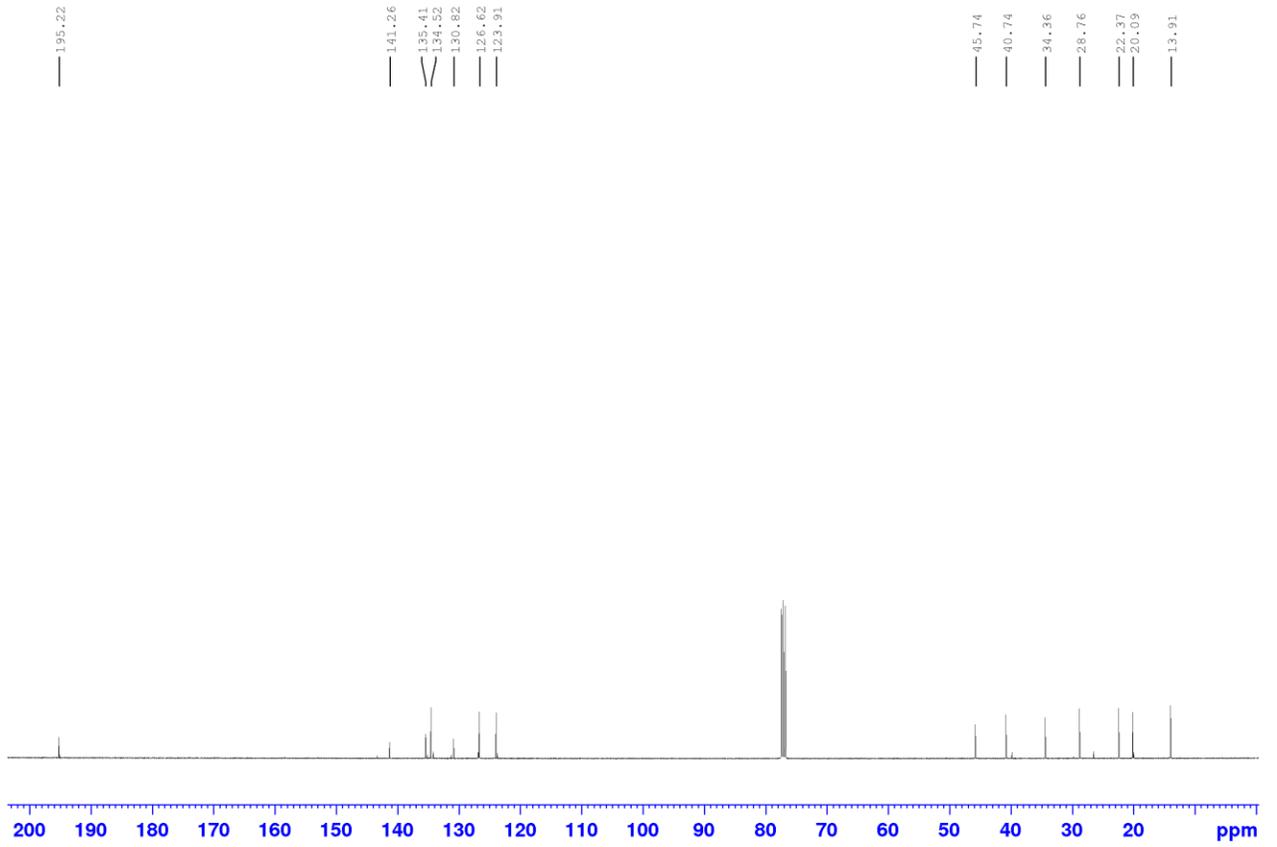
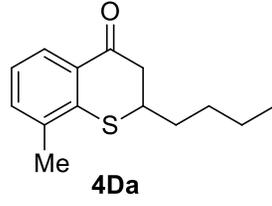


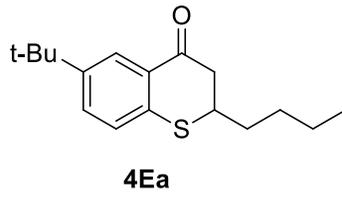


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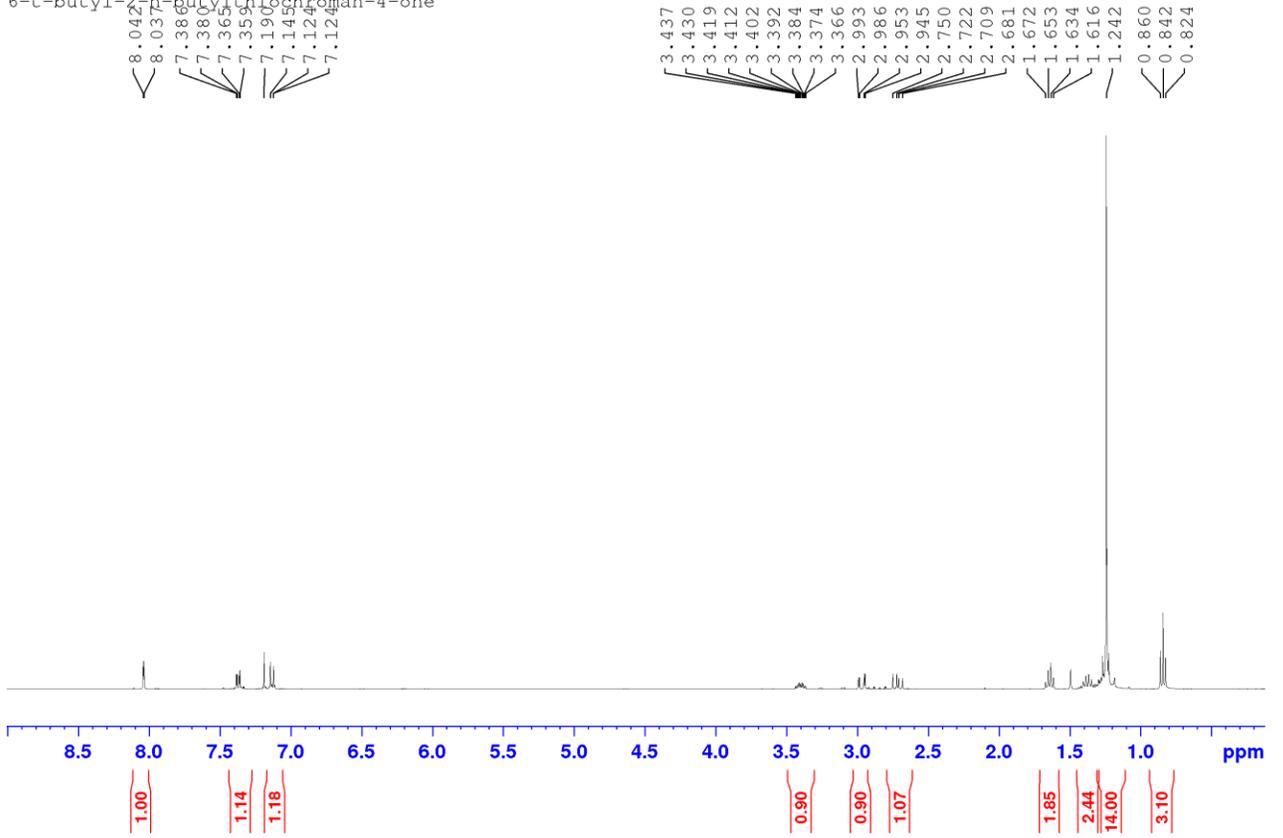


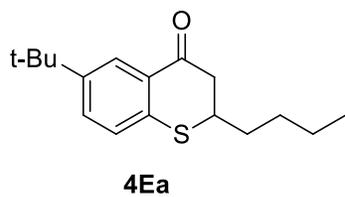




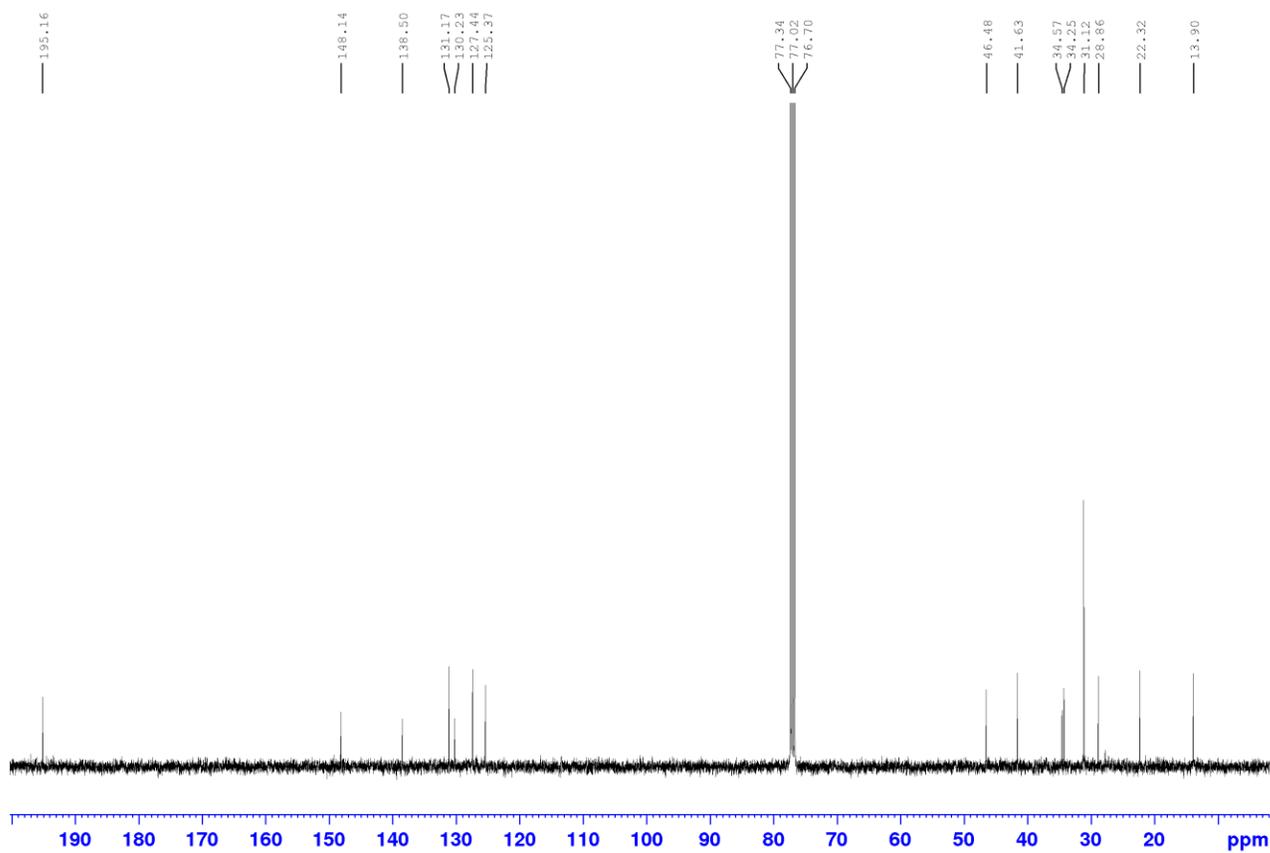


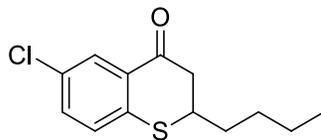
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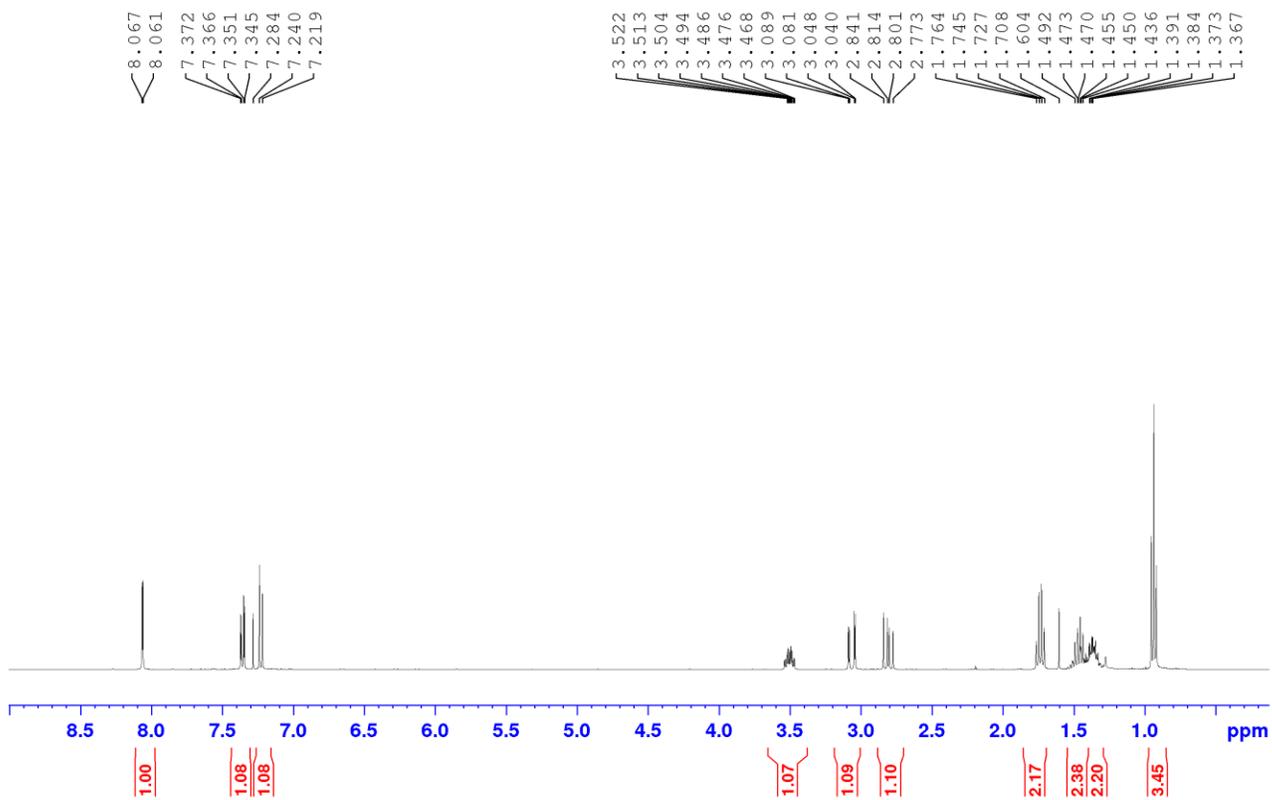
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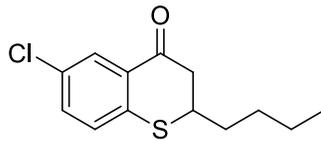




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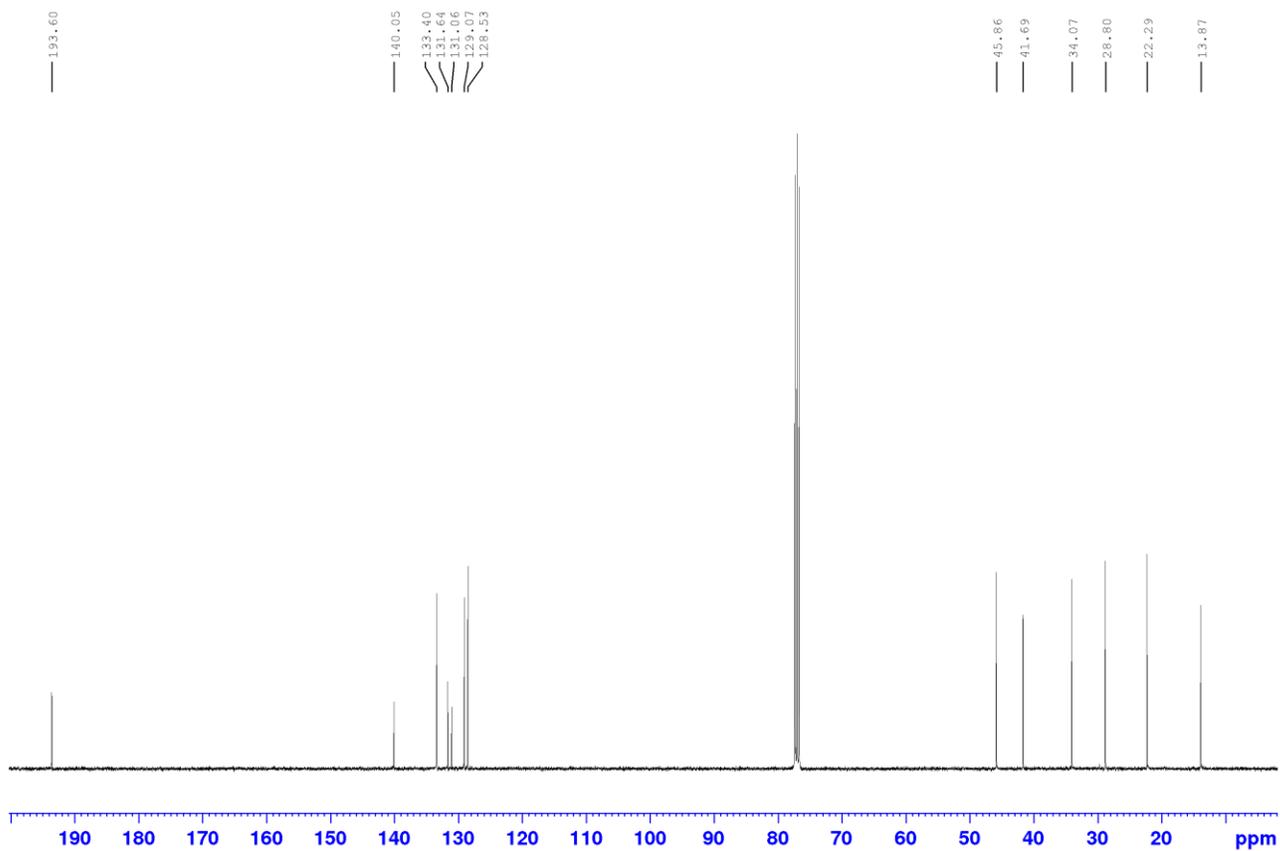
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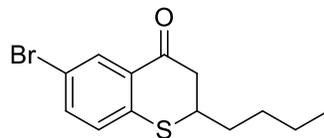




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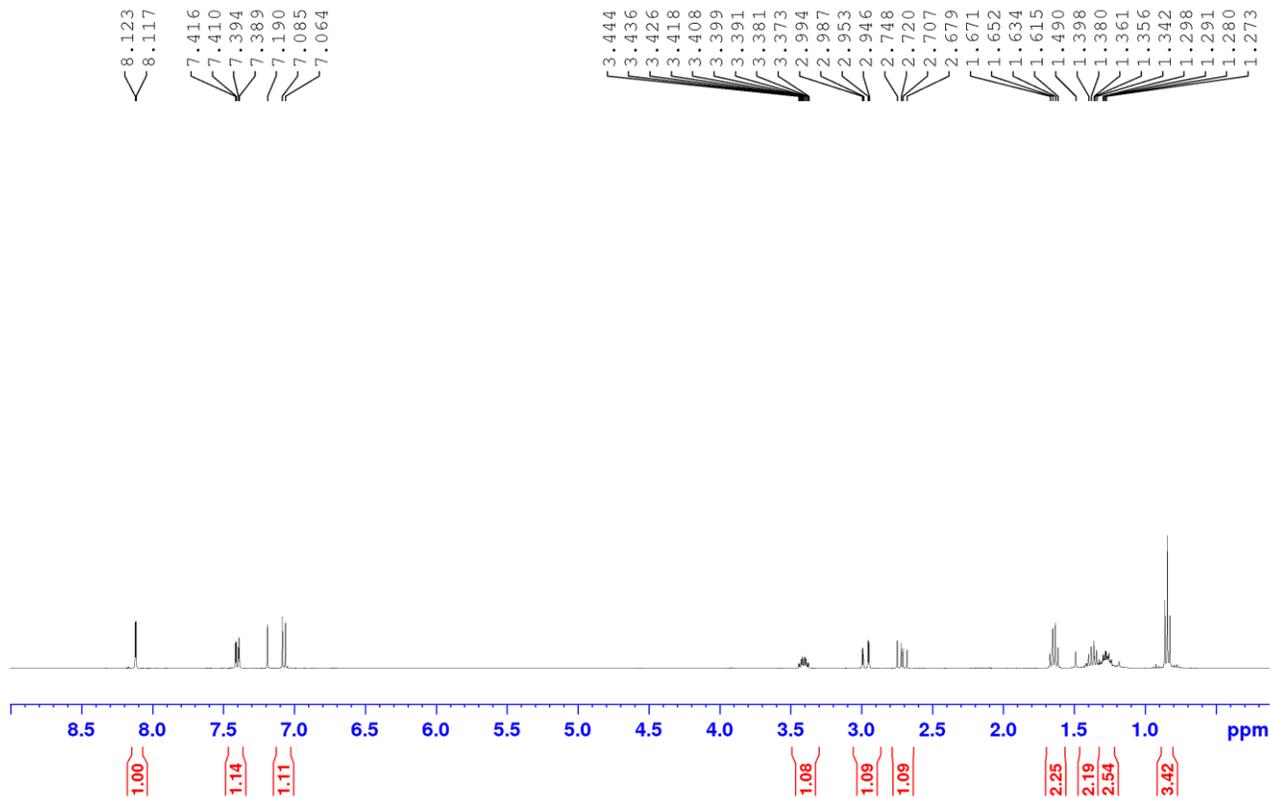
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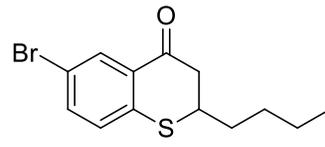




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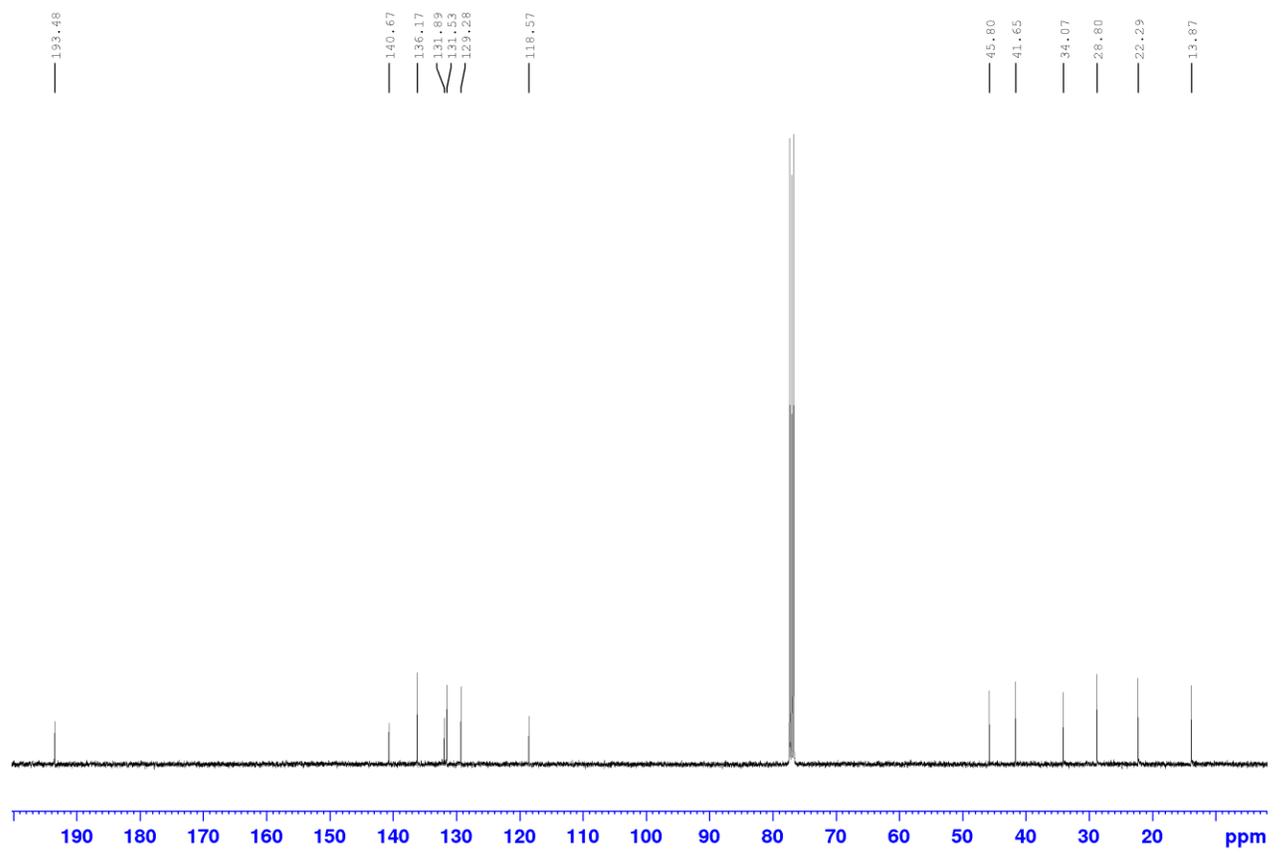
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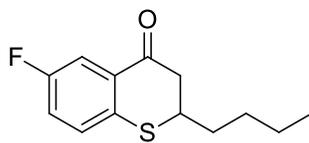




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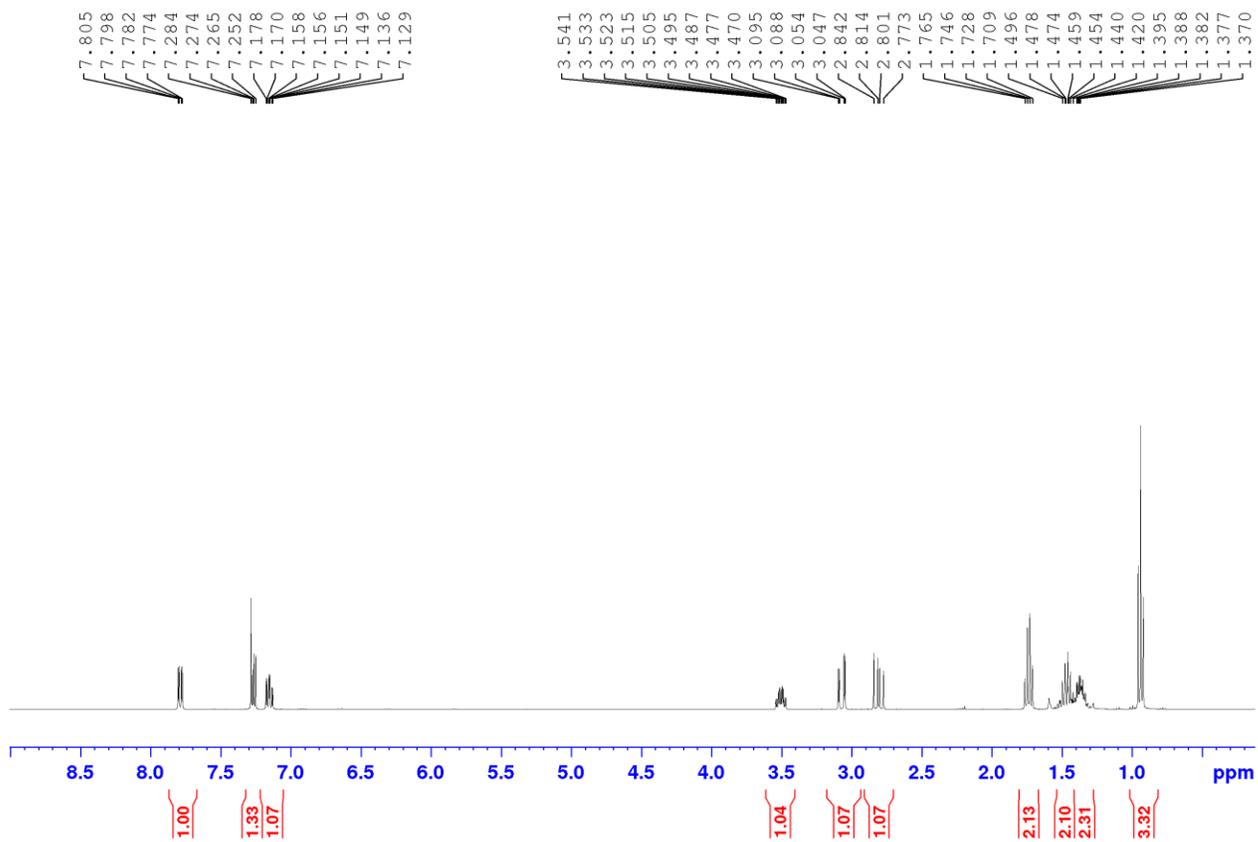
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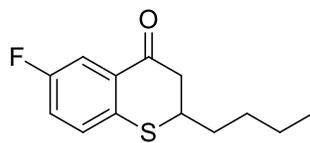




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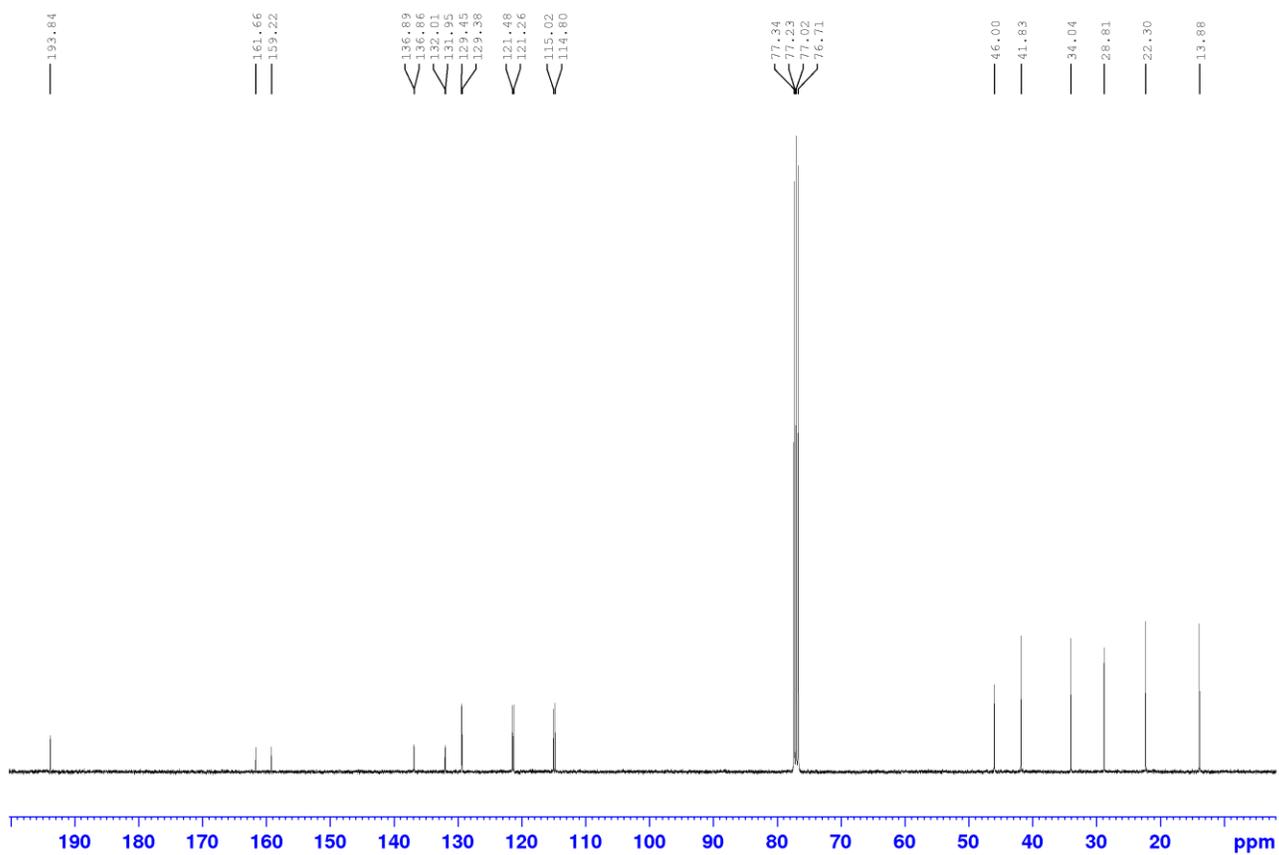
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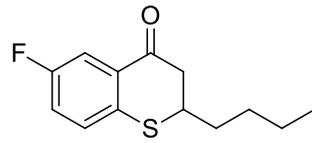




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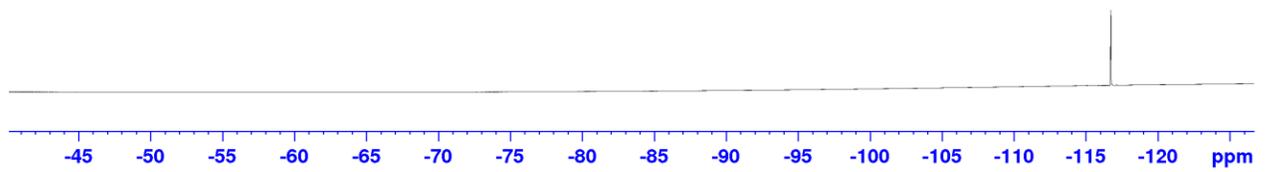


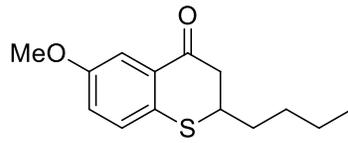


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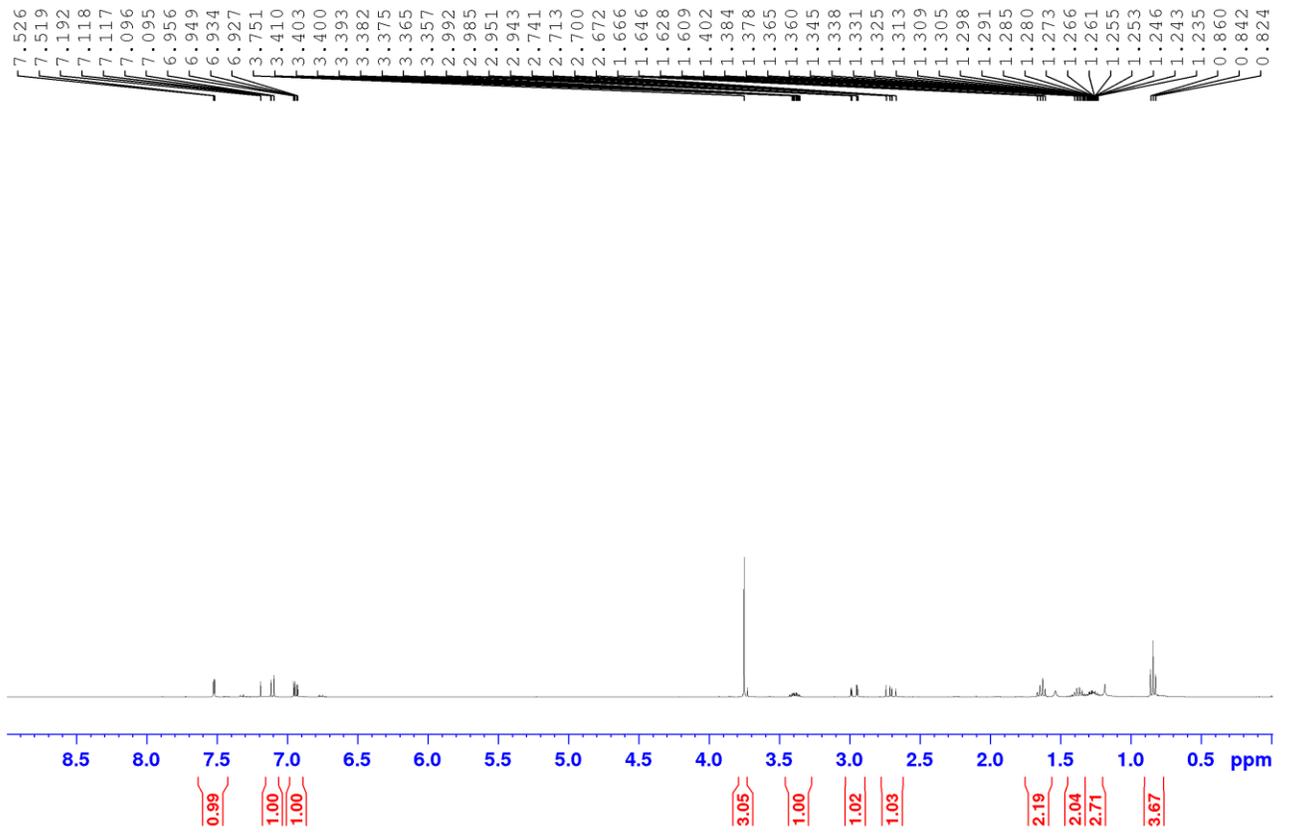
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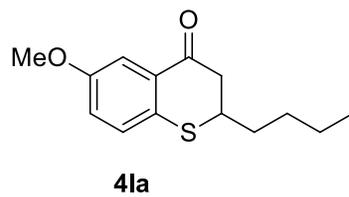




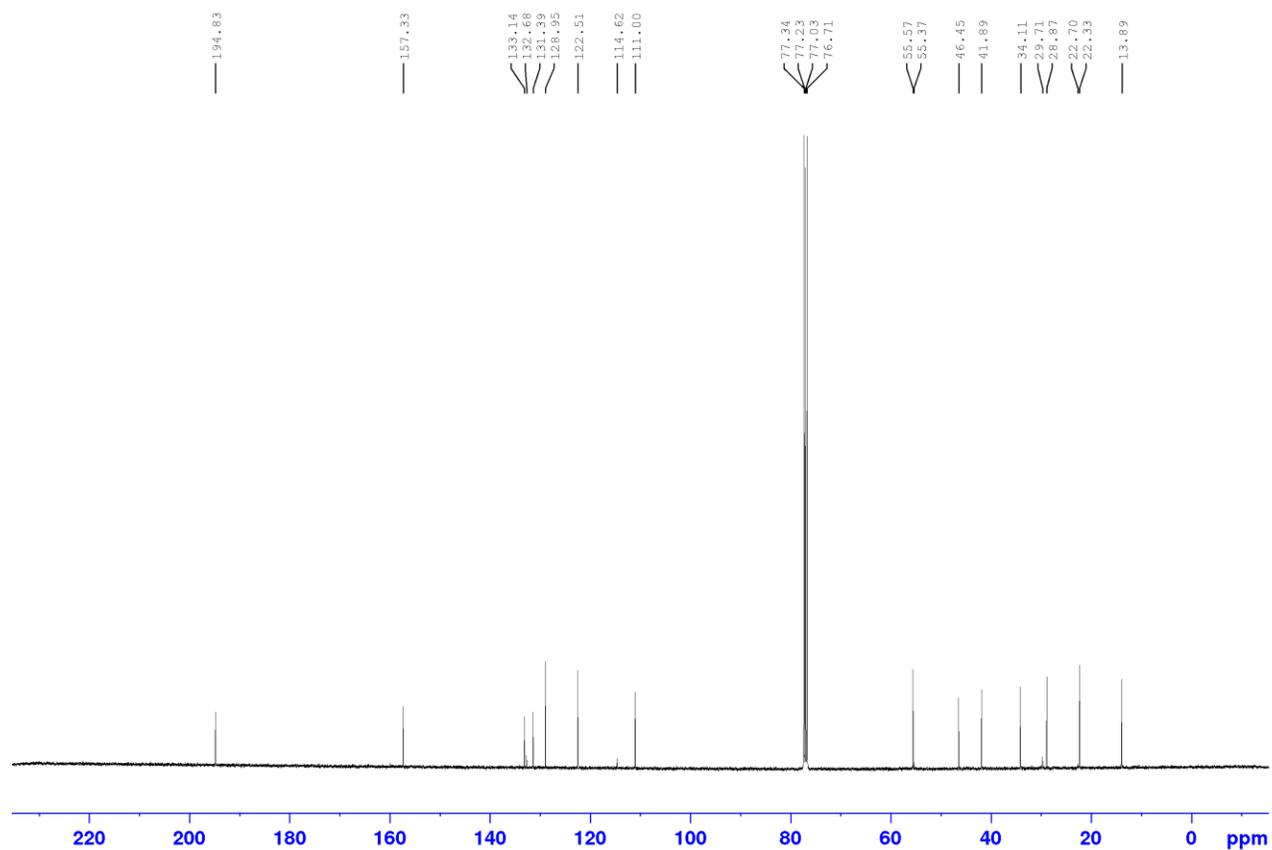
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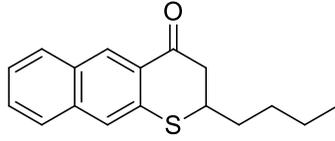
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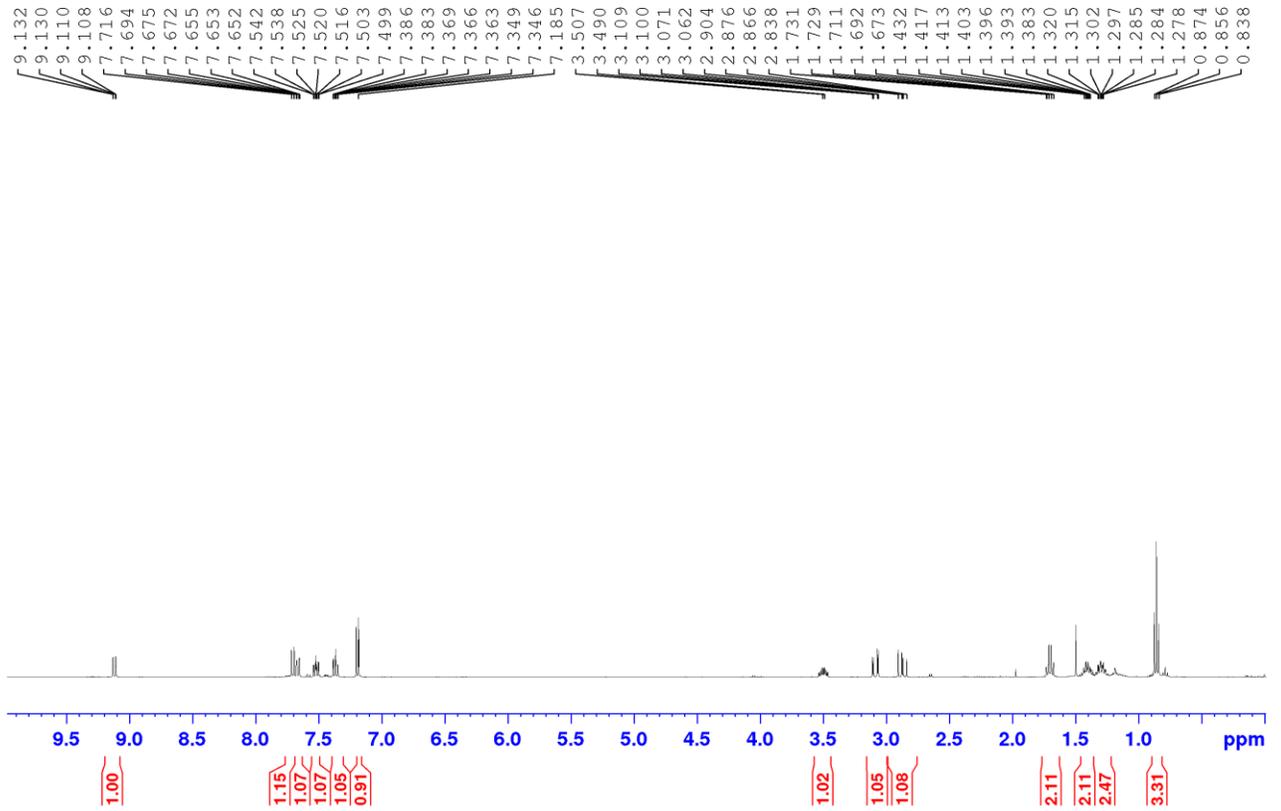


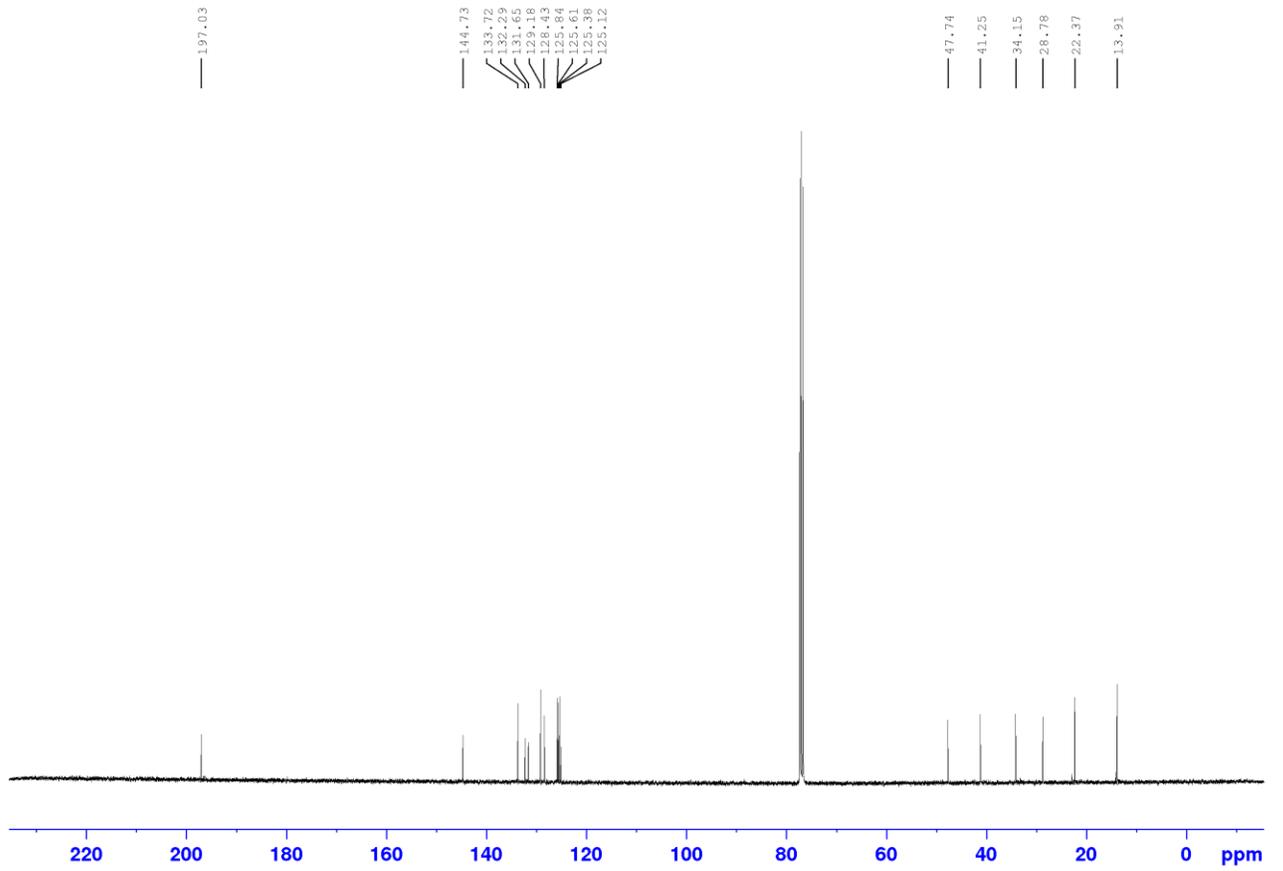
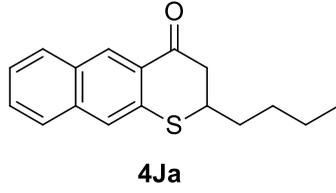
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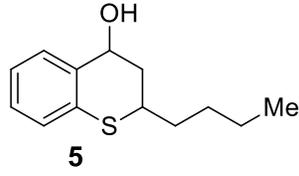




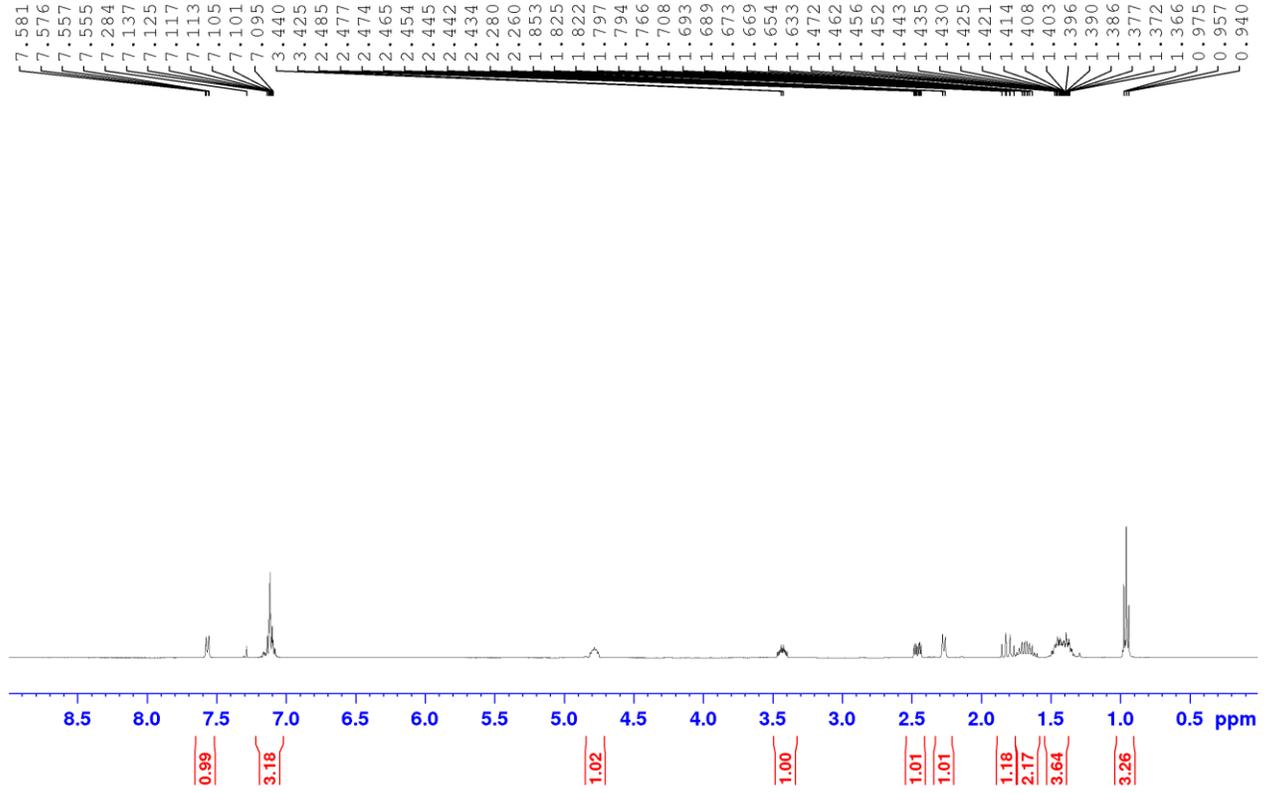
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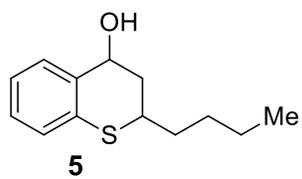




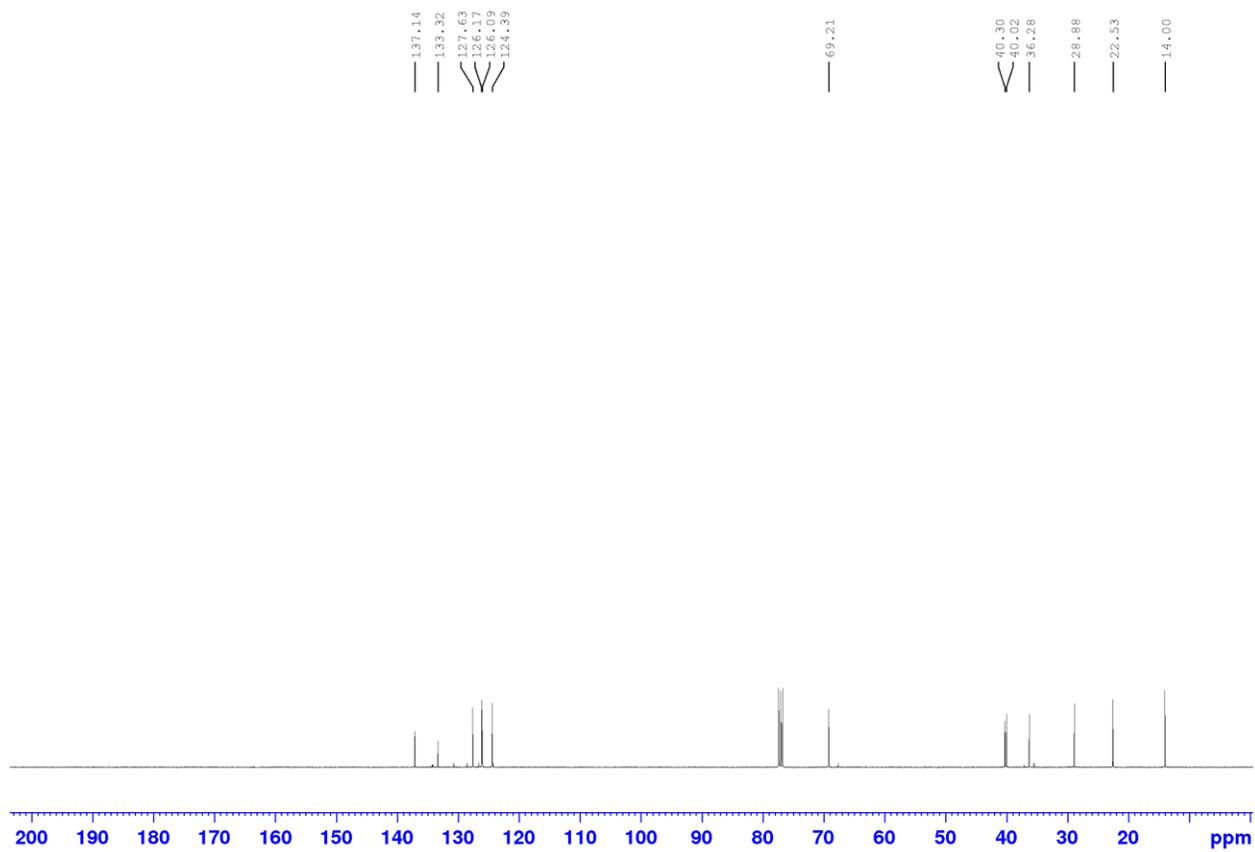


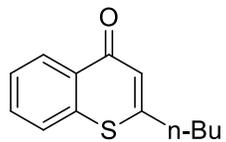
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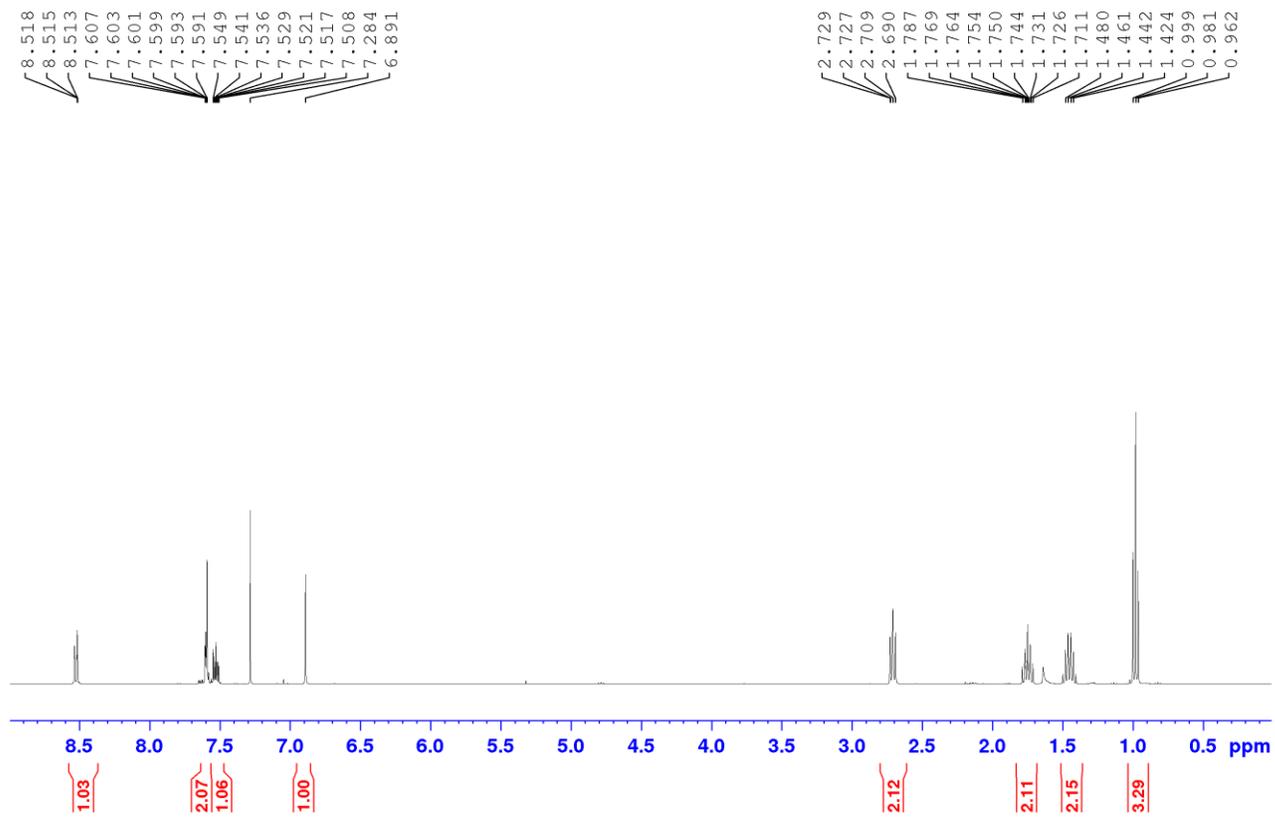
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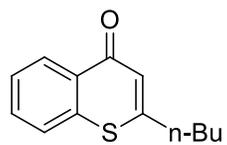




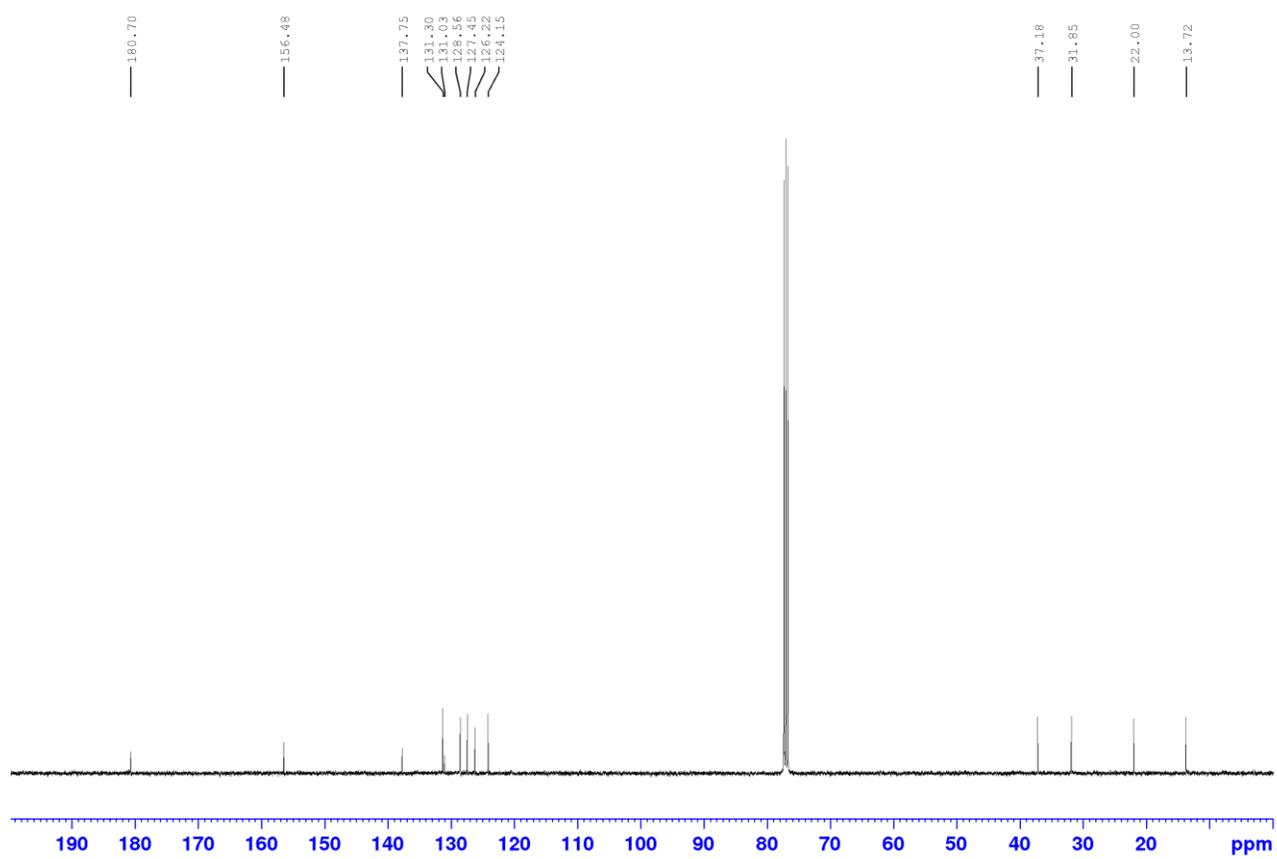
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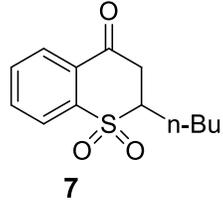
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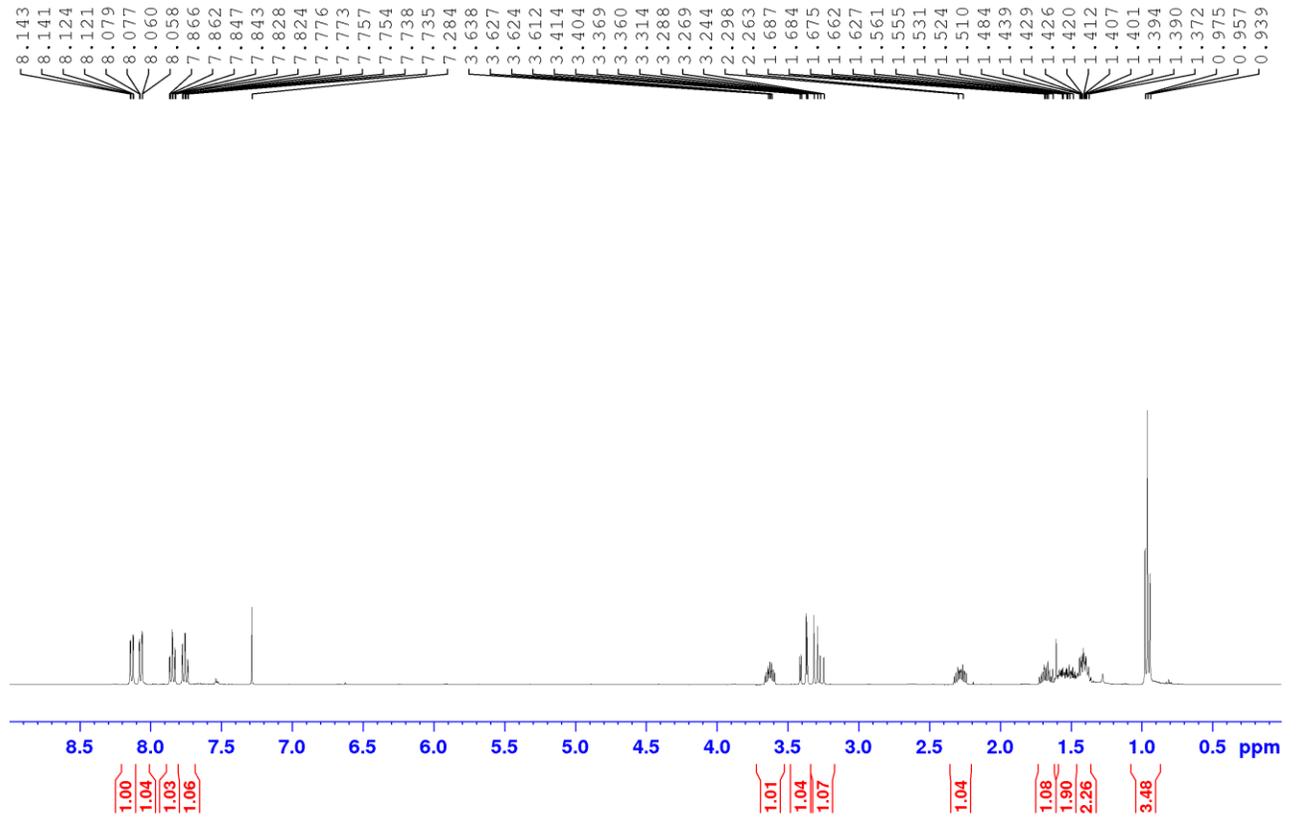


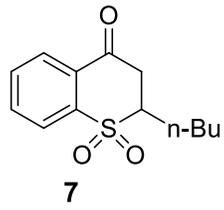
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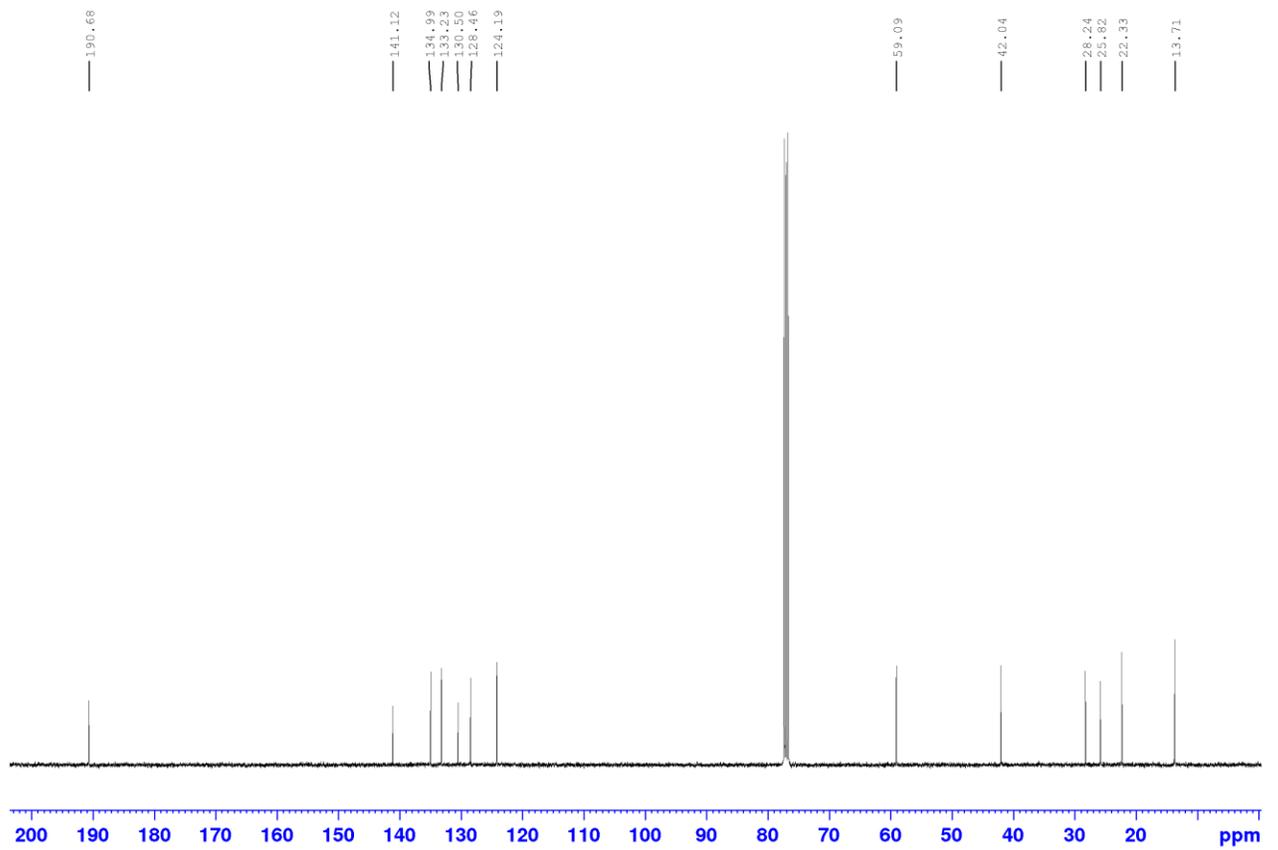


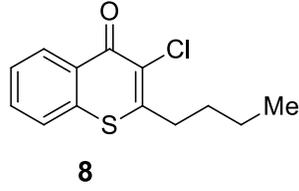
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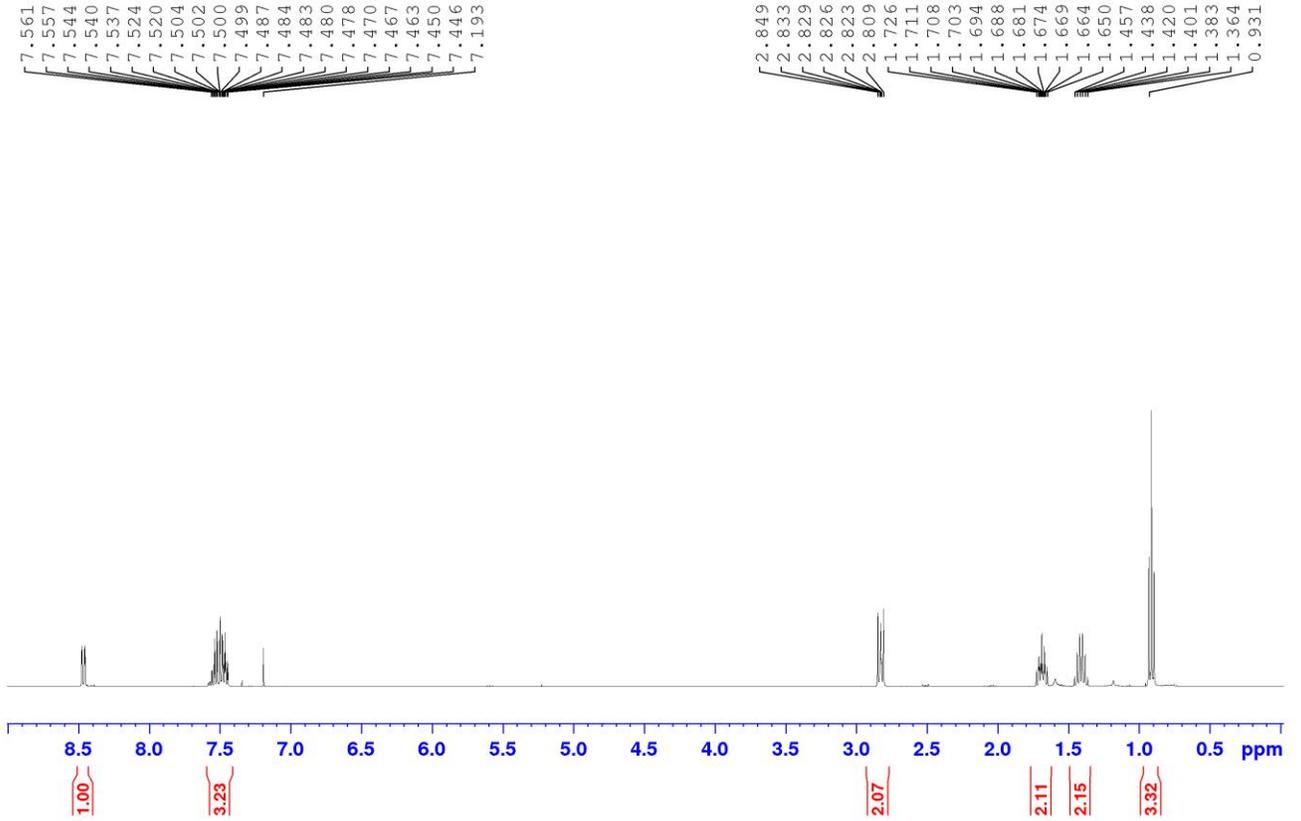


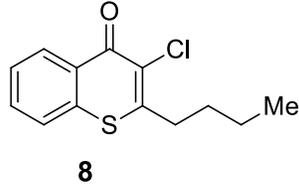
II-6pure





3-chloro-2-n-butyl-4H-thiochromen-4-one





3-chloro-2-n-butyl-4H-thiochromen-4-one

