

## “Supplementary Materials”

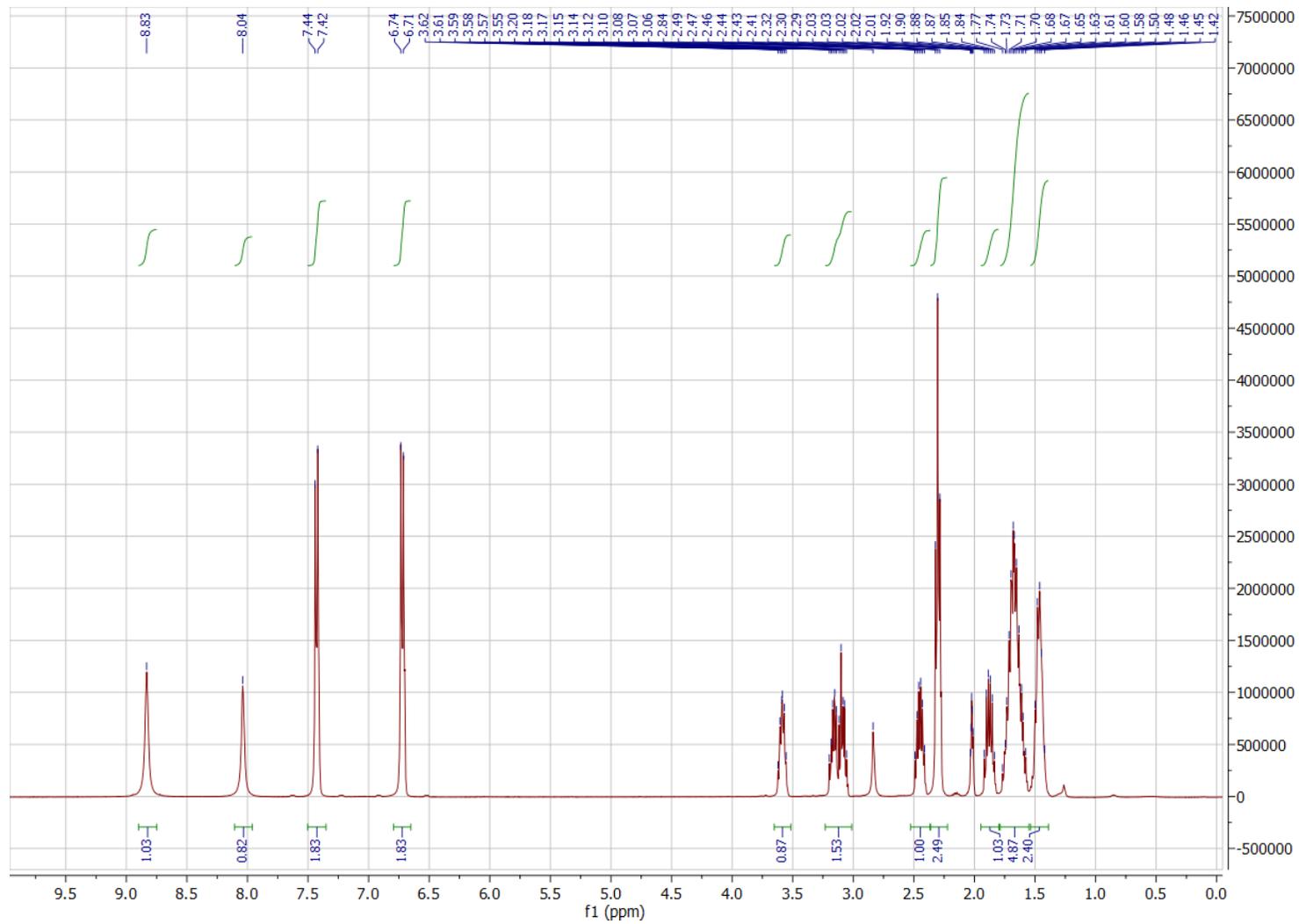
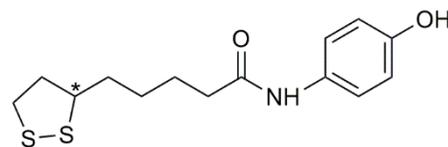
# Lipoic/capsaicin-related amides. Synthesis and biological characterization of new TRPV1 agonists endowed with protective properties against oxidative stress

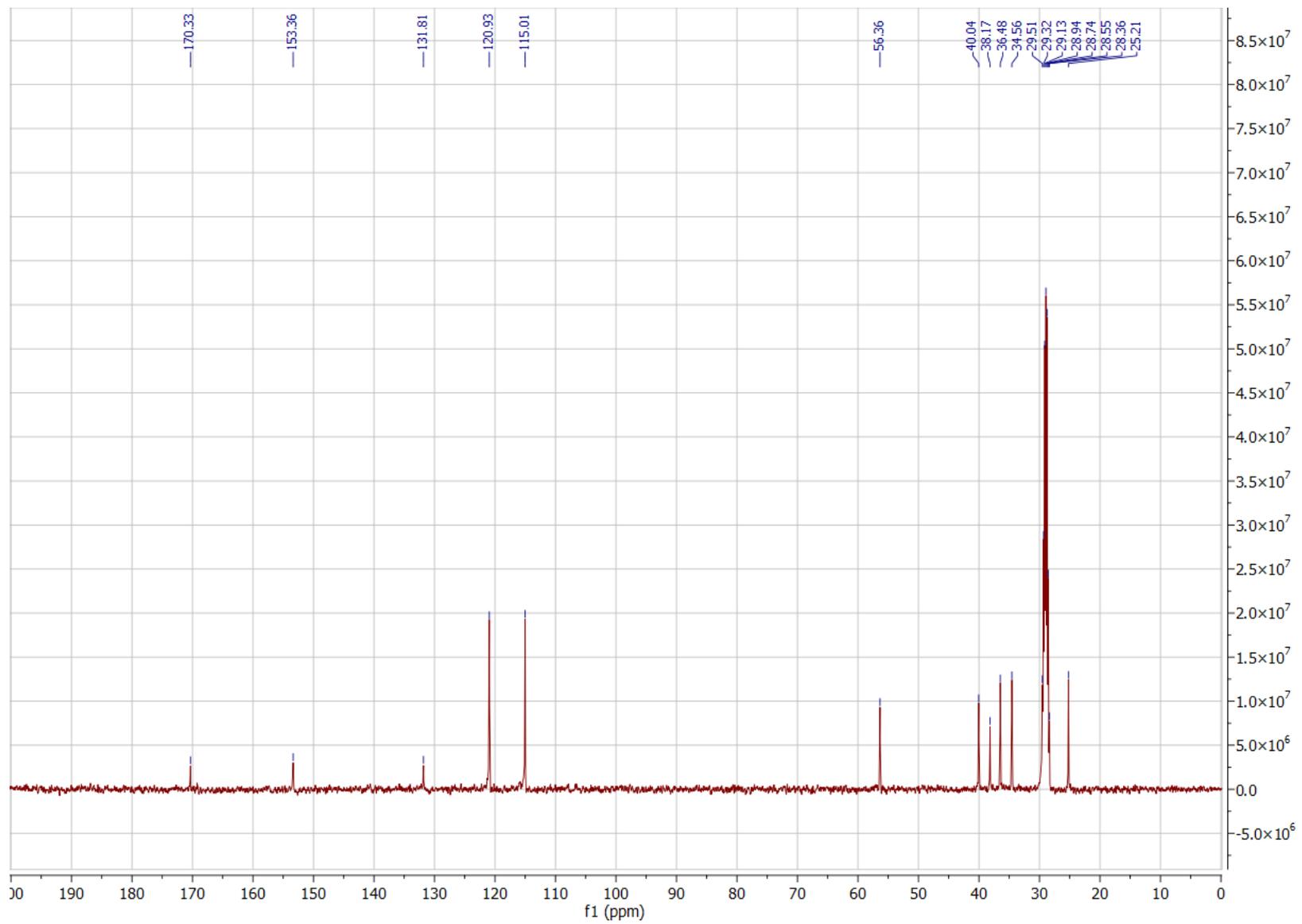
Antonella Brizzi <sup>1,\*</sup>,<sup>†</sup>, **Samuele Maramai** <sup>1,†</sup>, Francesca Aiello <sup>2</sup> Maria Camilla Baratto <sup>1</sup>, Federico Corelli <sup>1</sup>, Claudia Mugnaini <sup>1</sup>, Marco Paolino <sup>1</sup>, Francesco Scorzelli <sup>3</sup>, Carlo Aldinucci <sup>4</sup>, Luciano De Petrocellis <sup>5</sup>, Cinzia Signorini <sup>4</sup> and Federica Pessina <sup>4,\*</sup>

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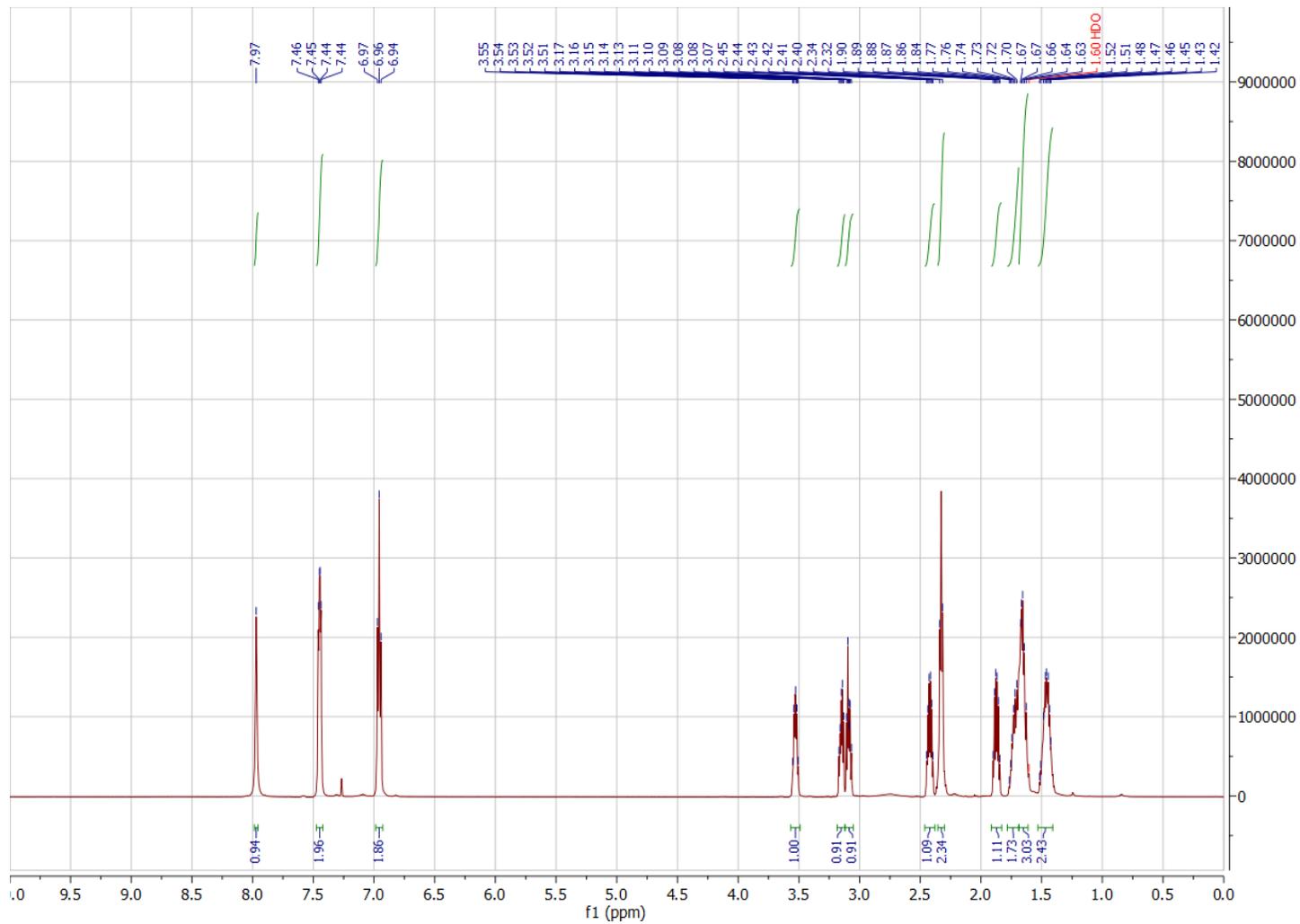
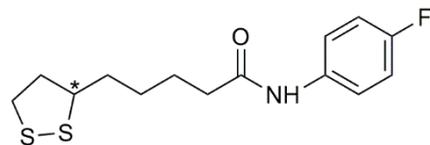
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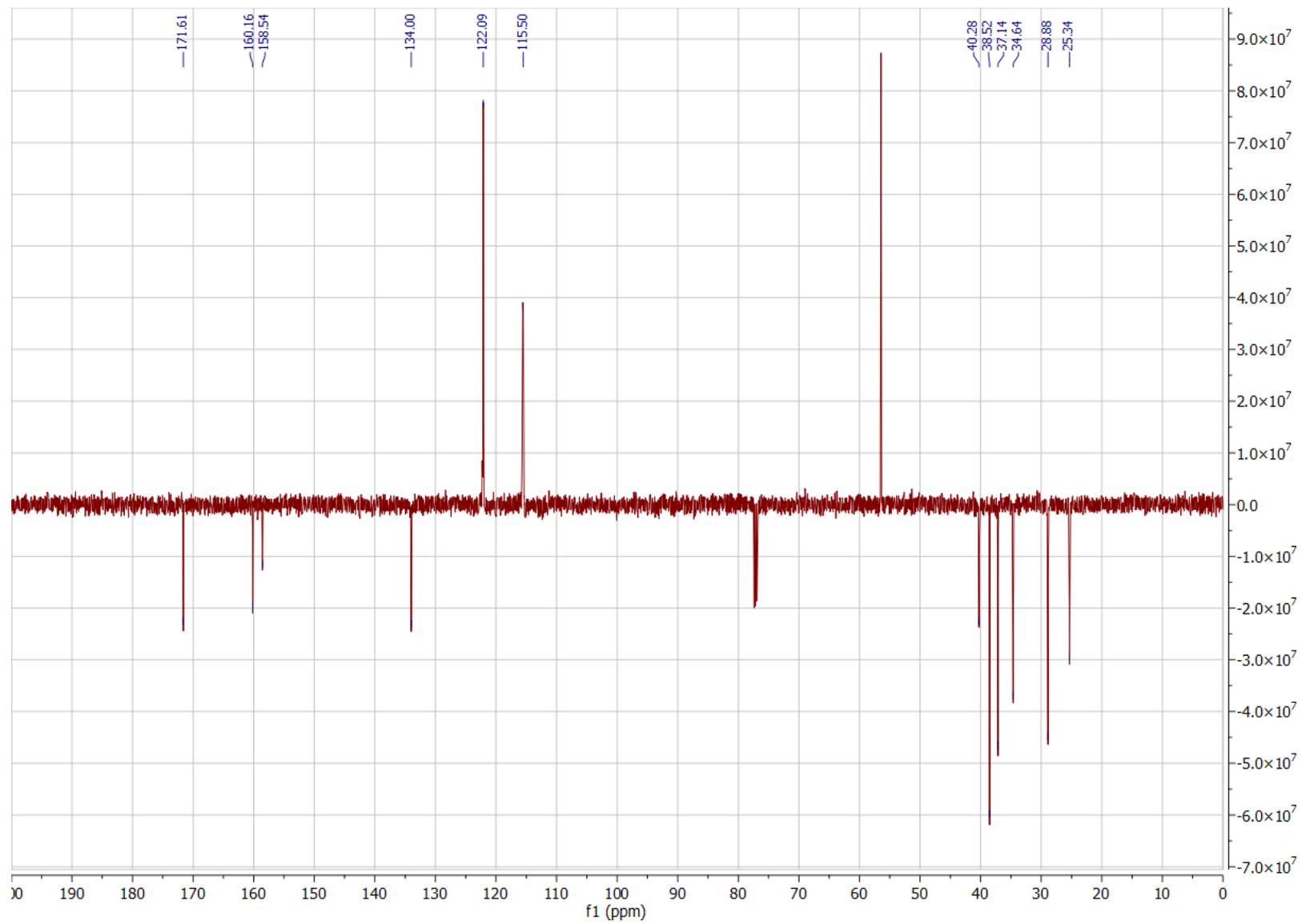
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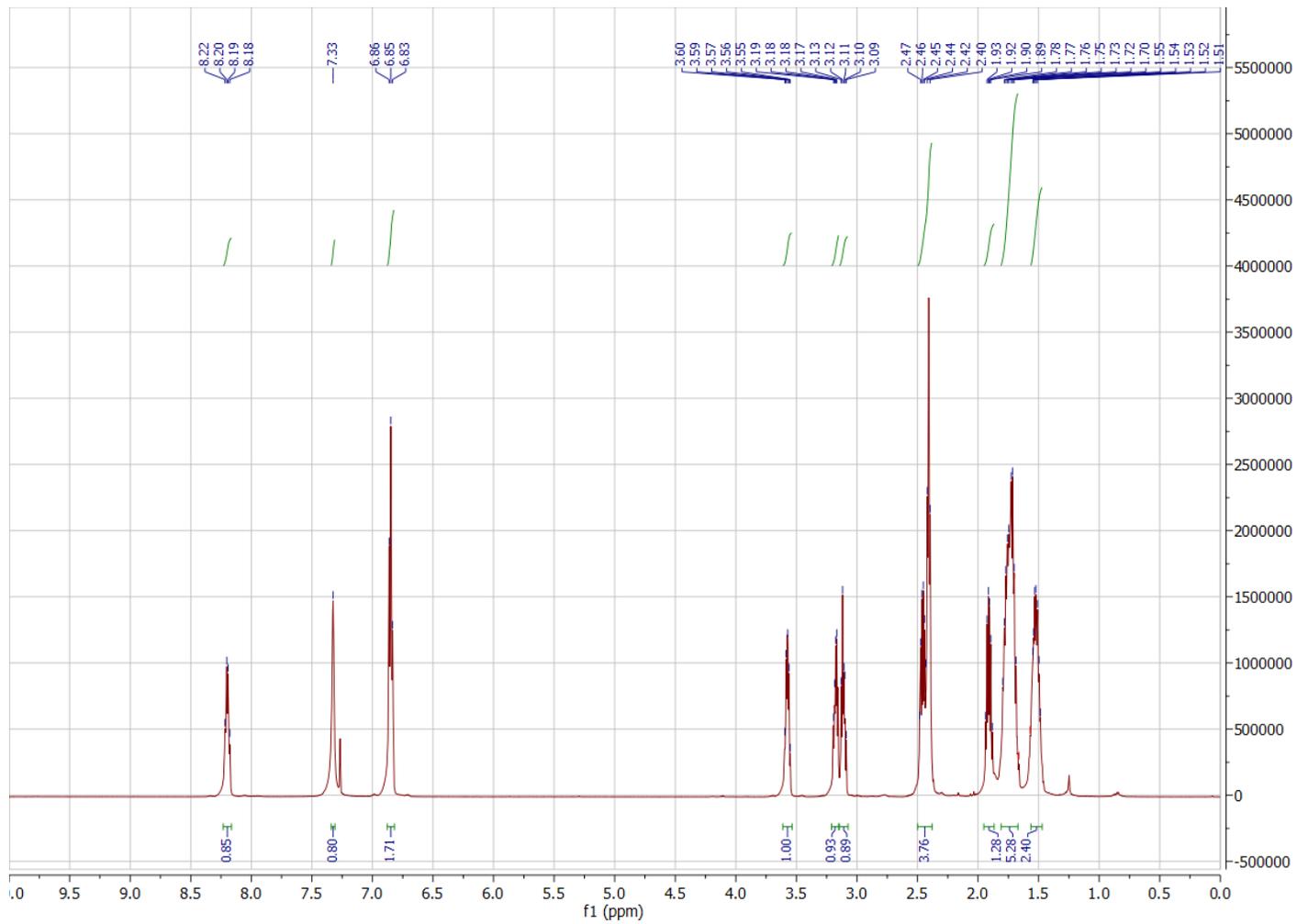
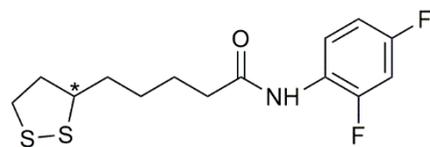


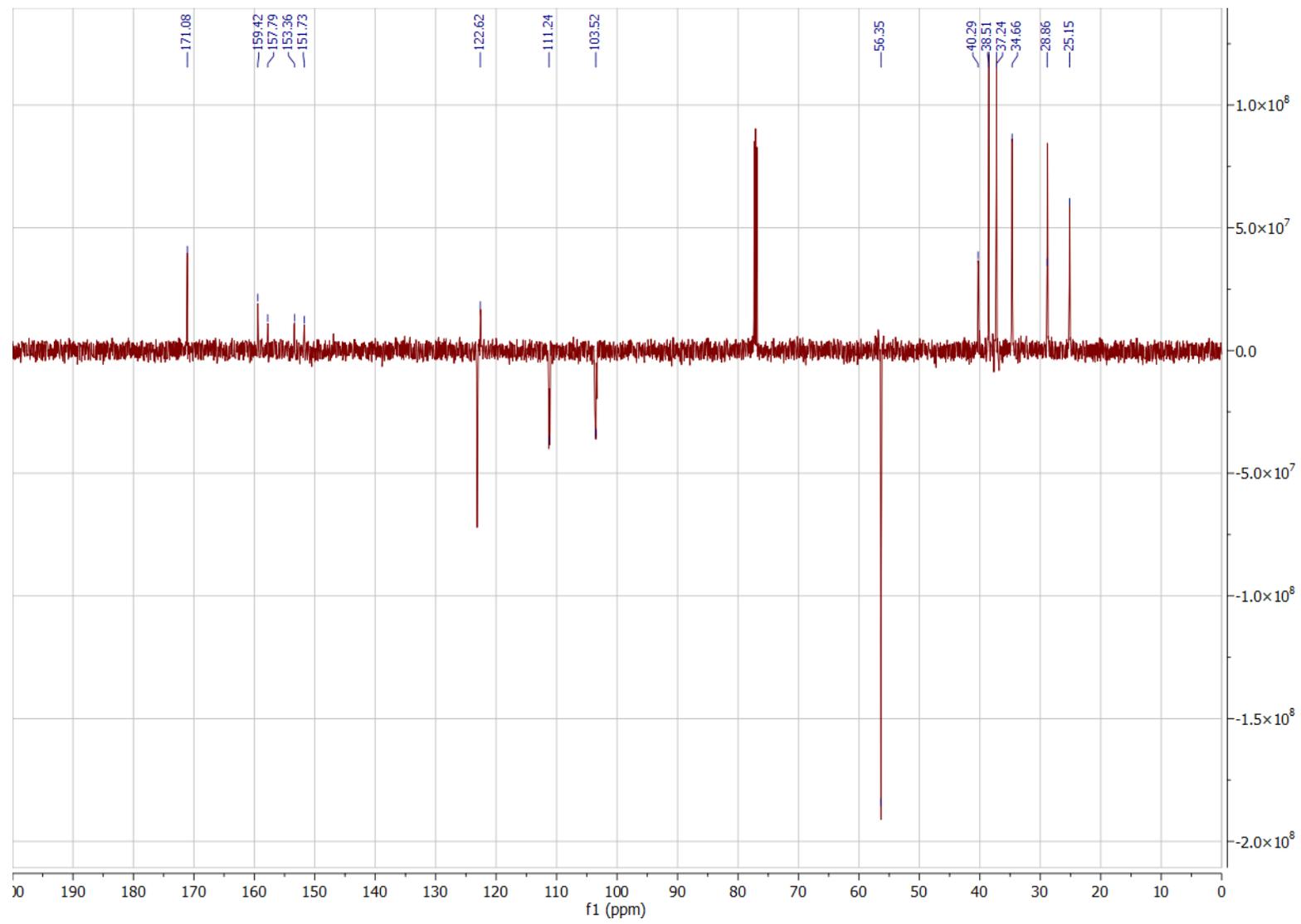
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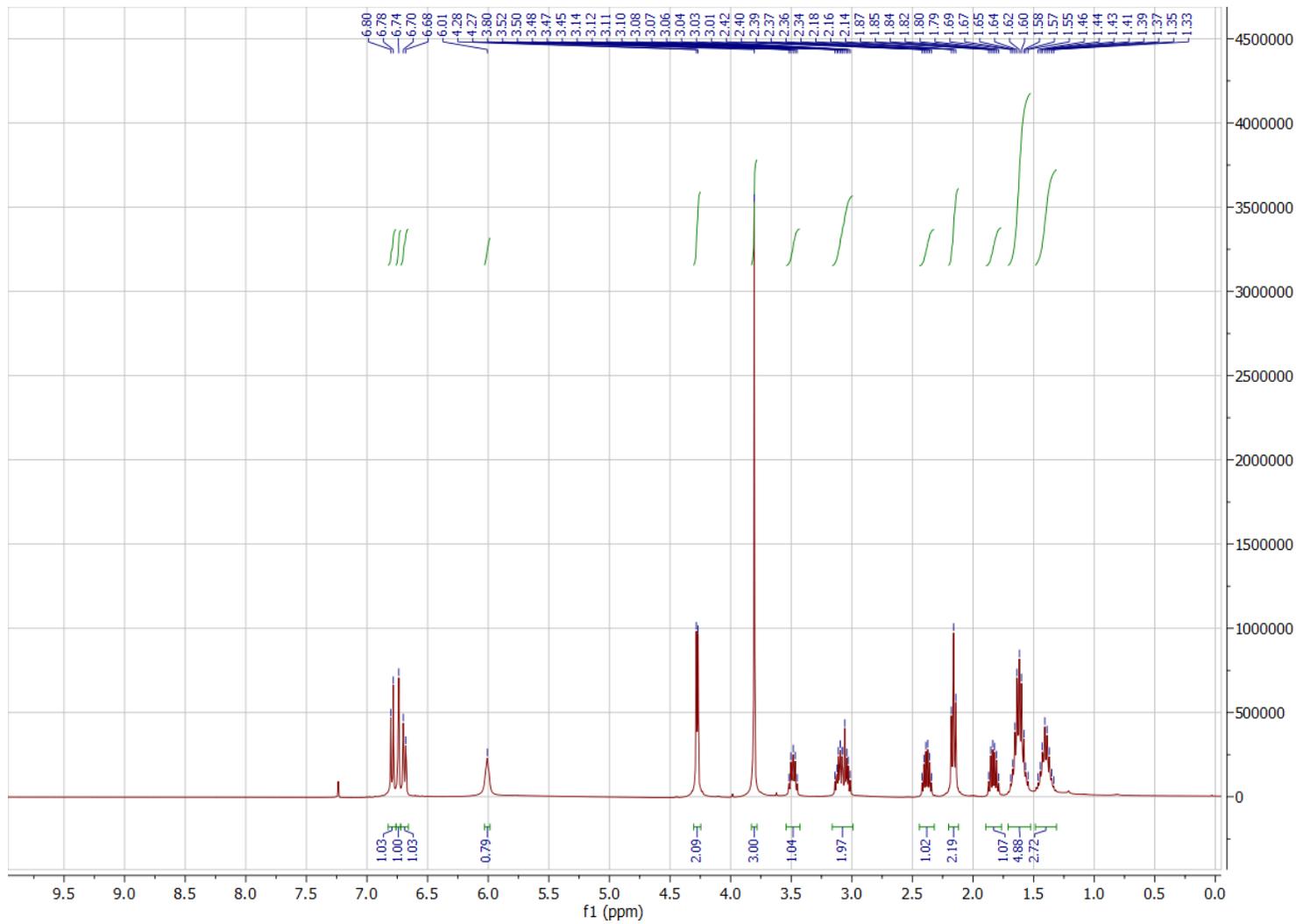
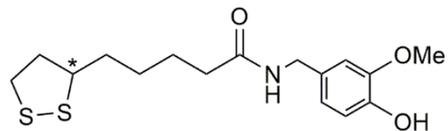


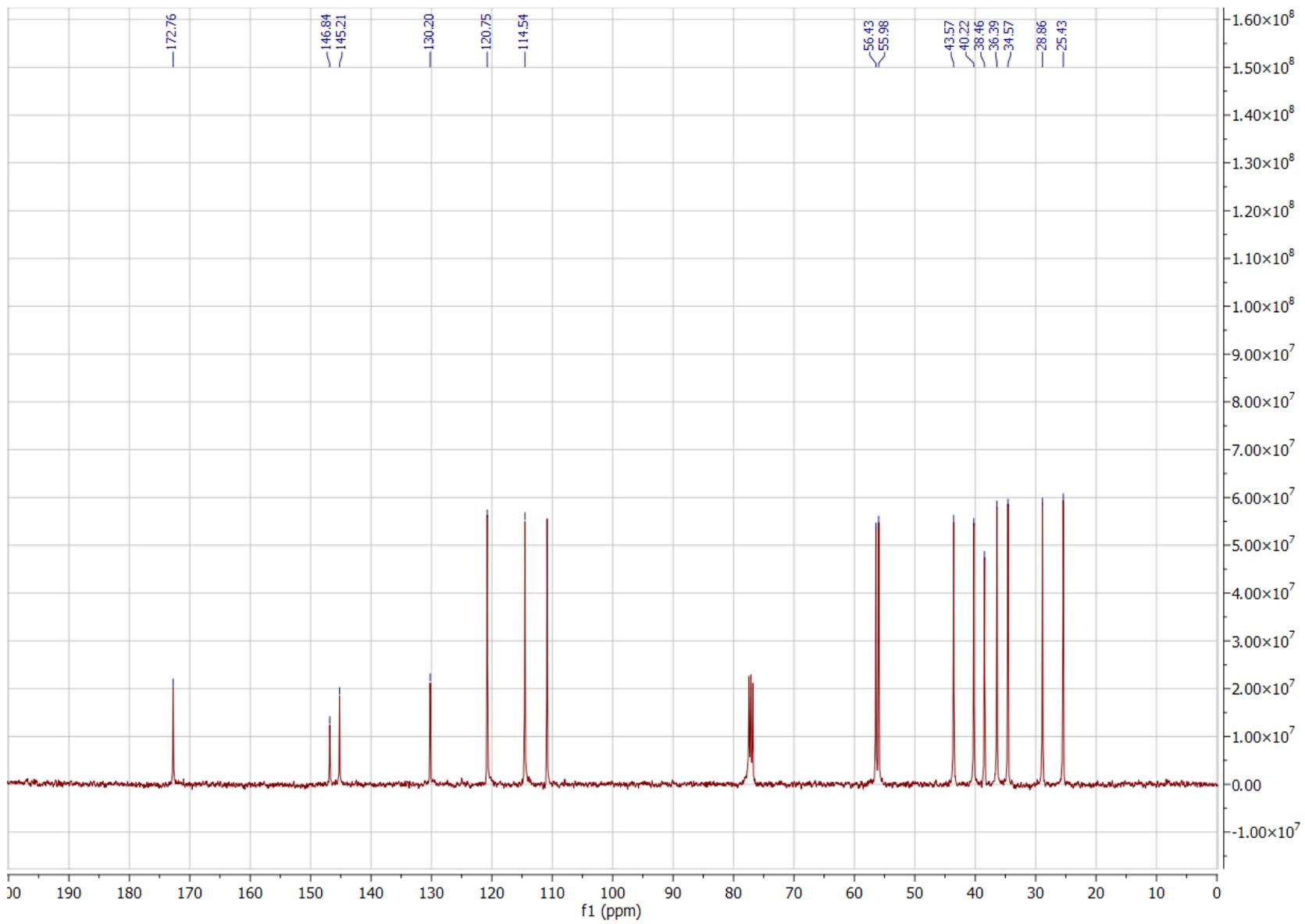
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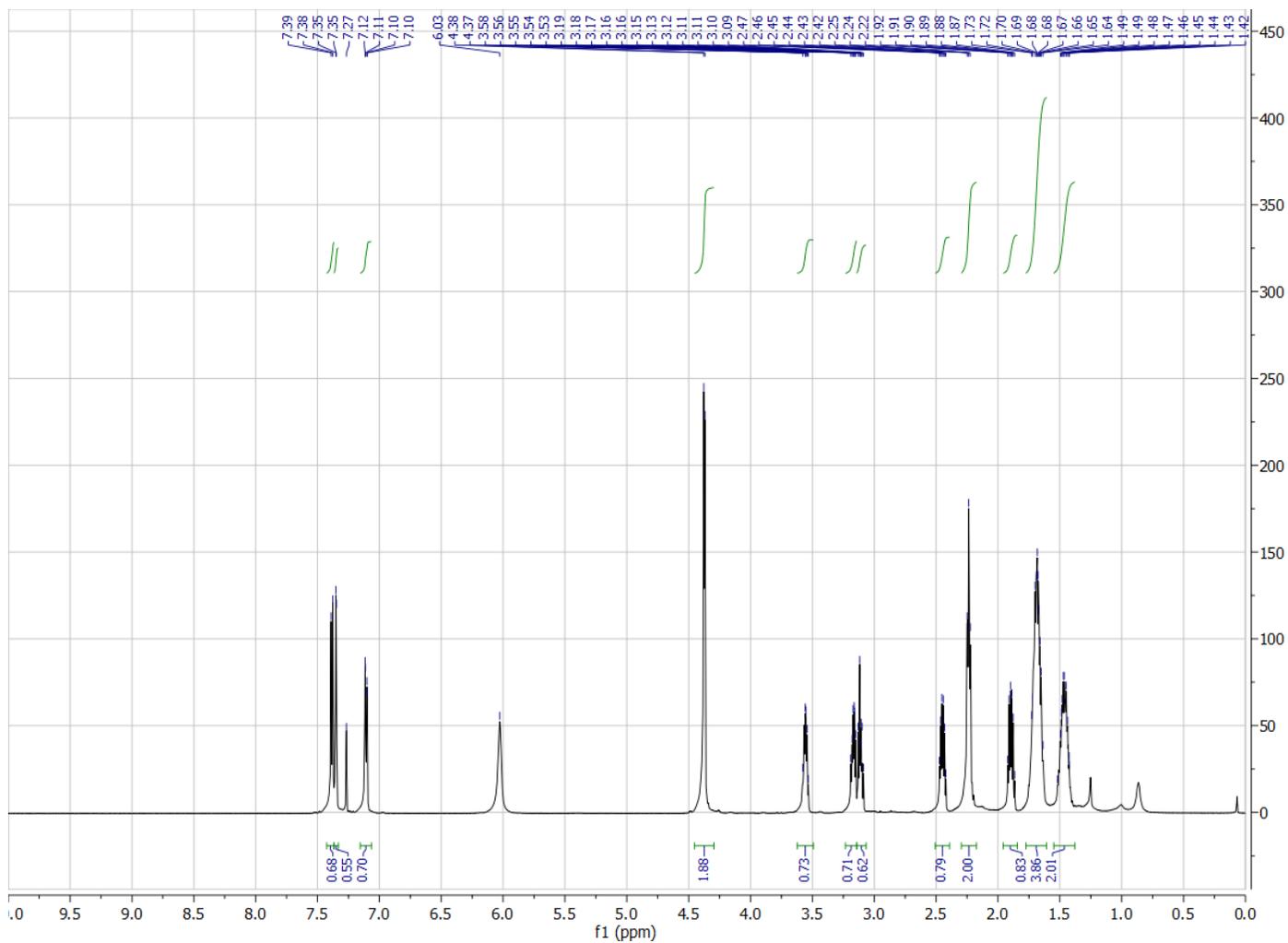
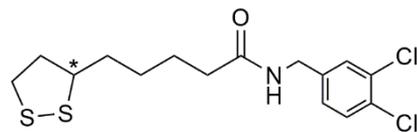


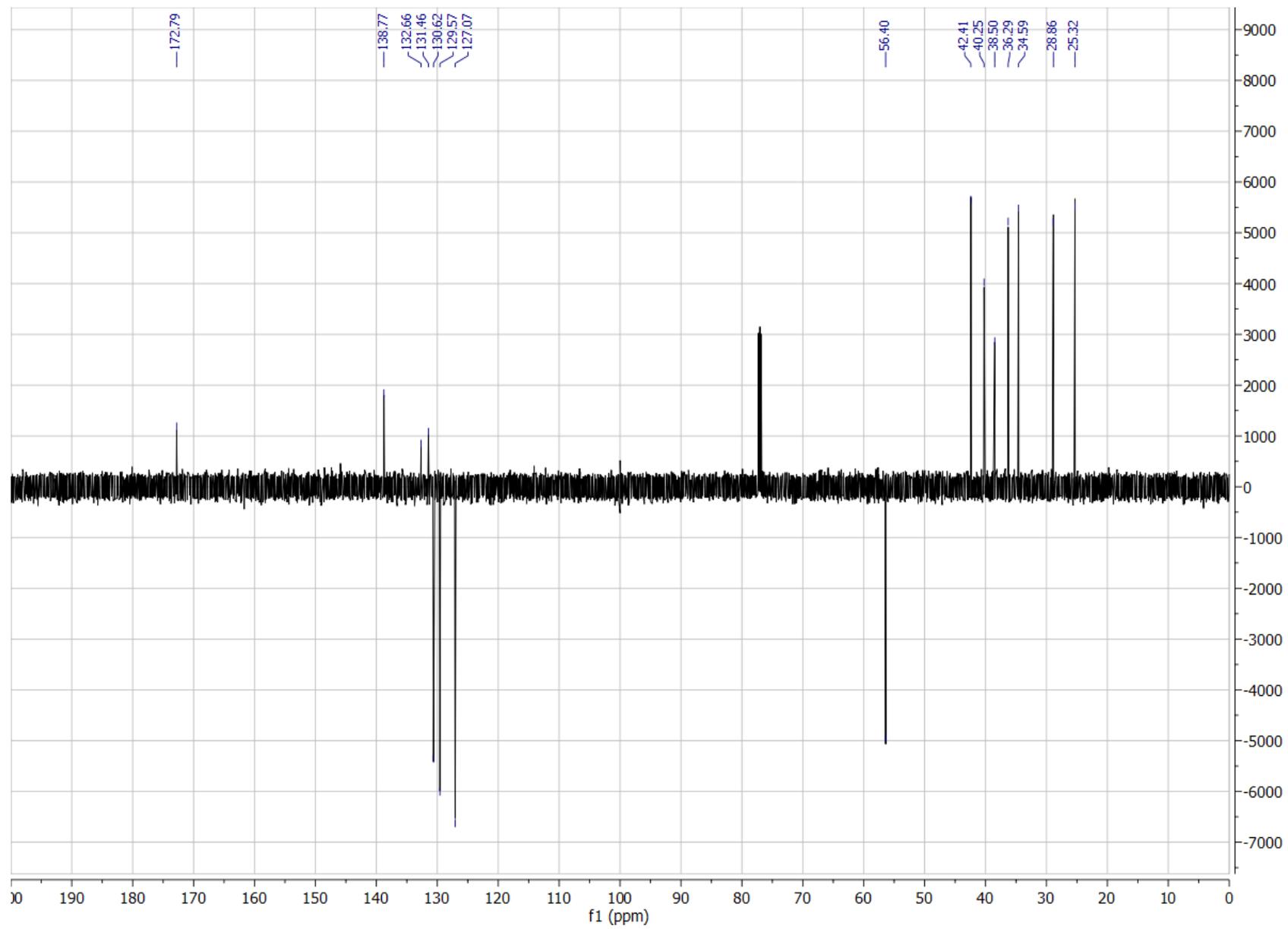
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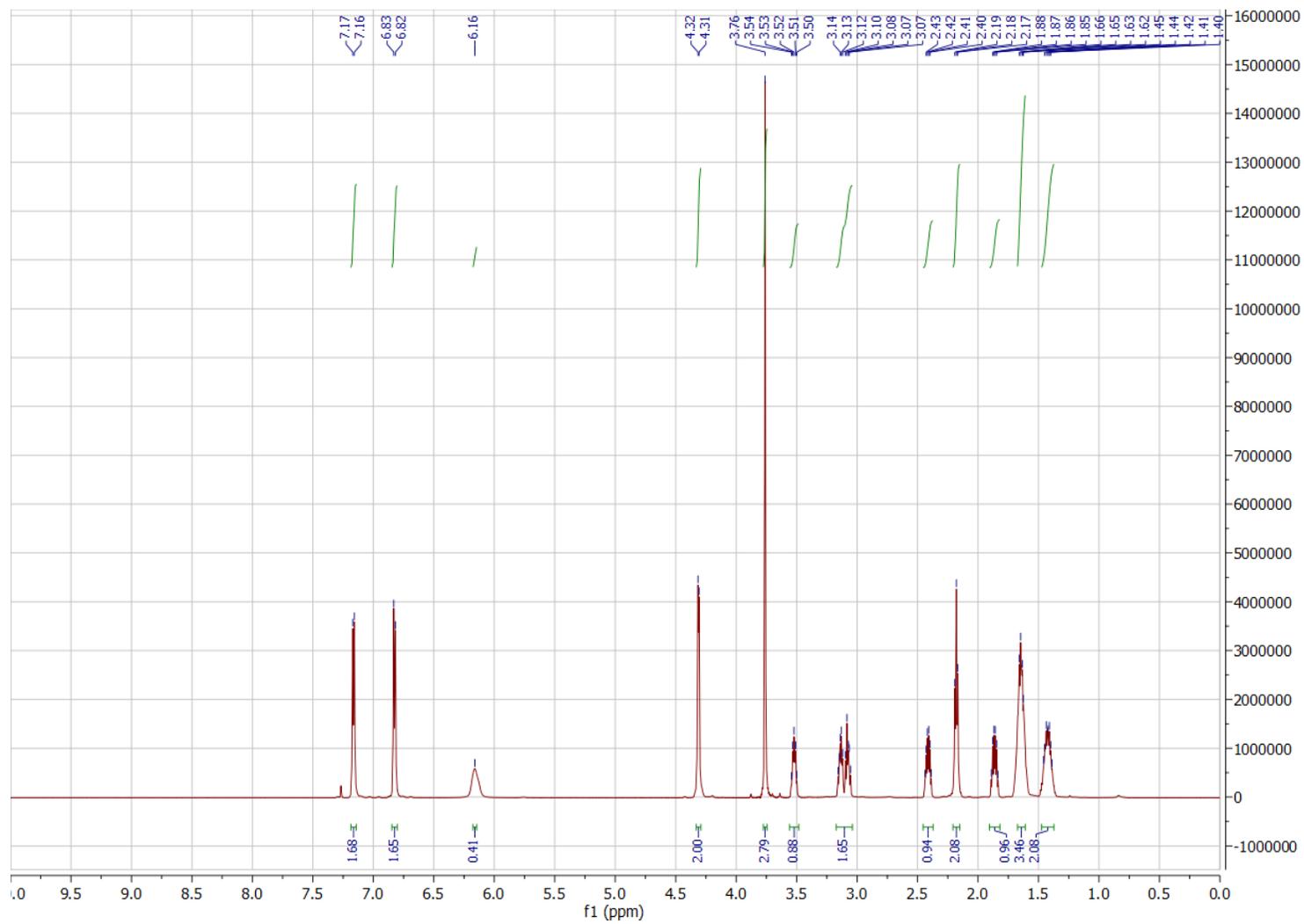
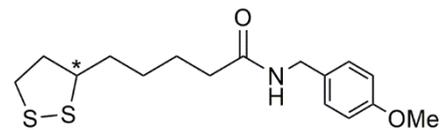


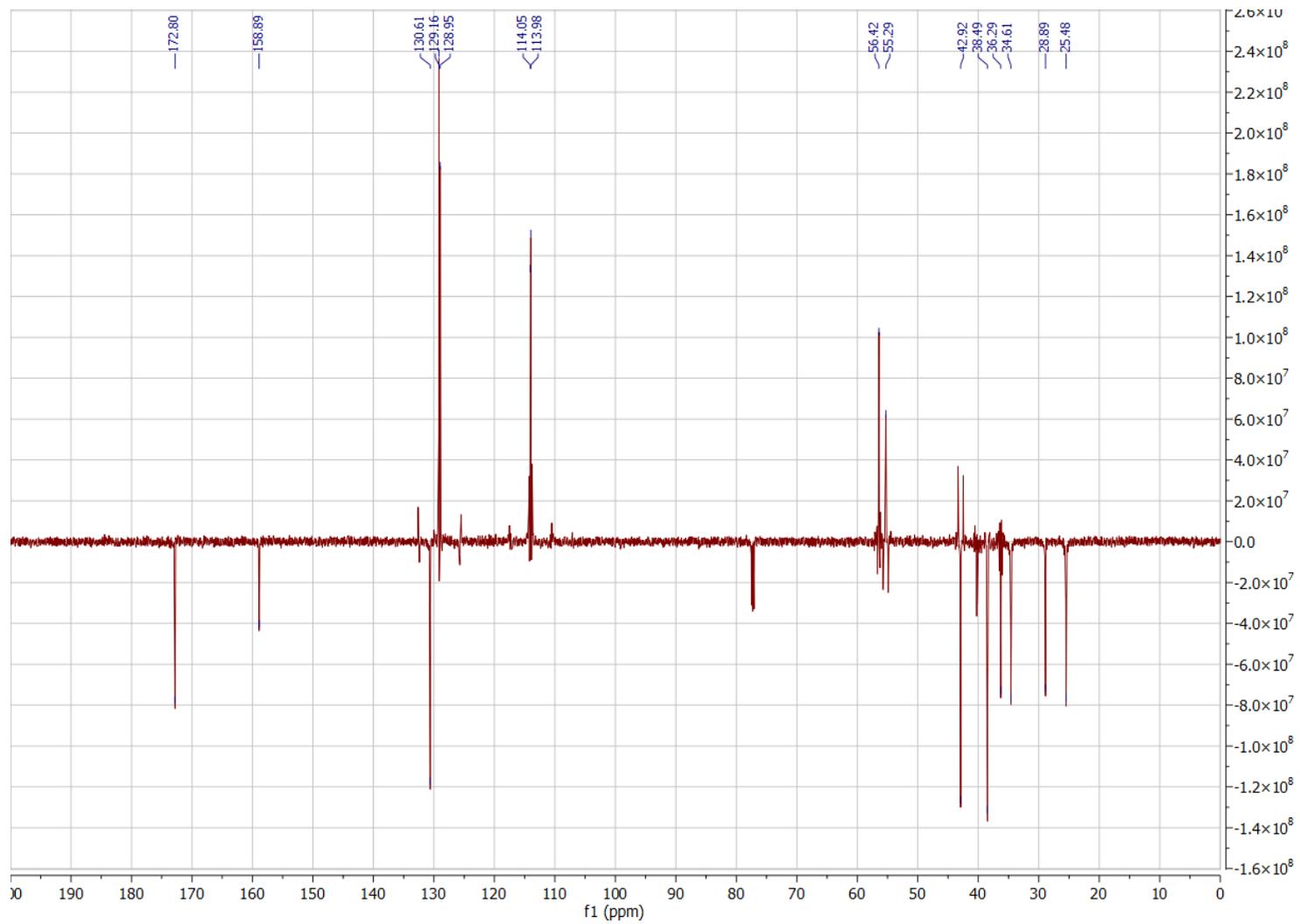
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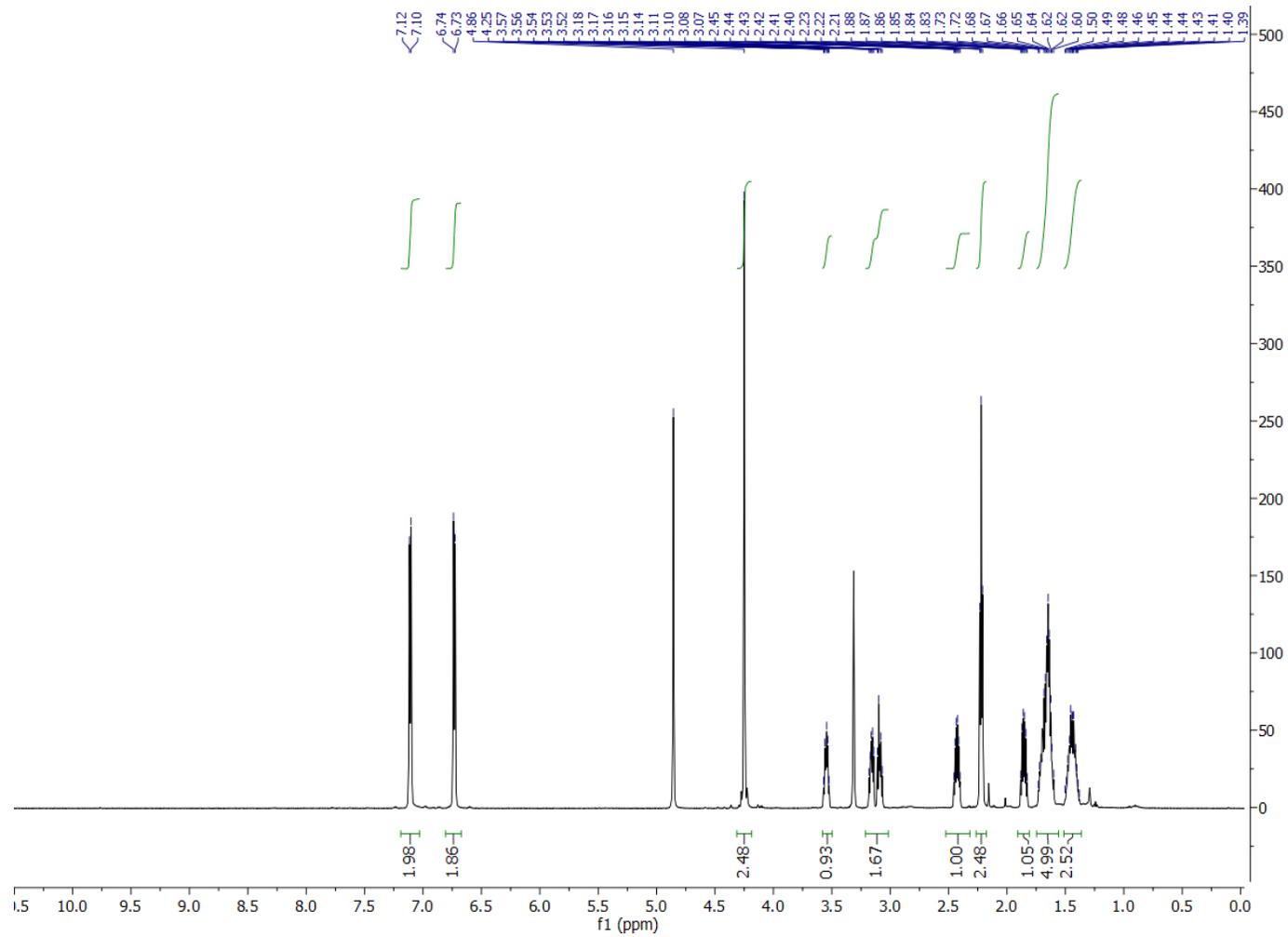
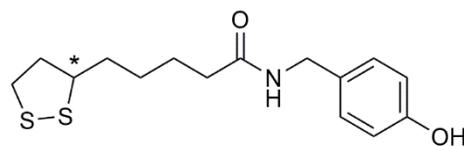


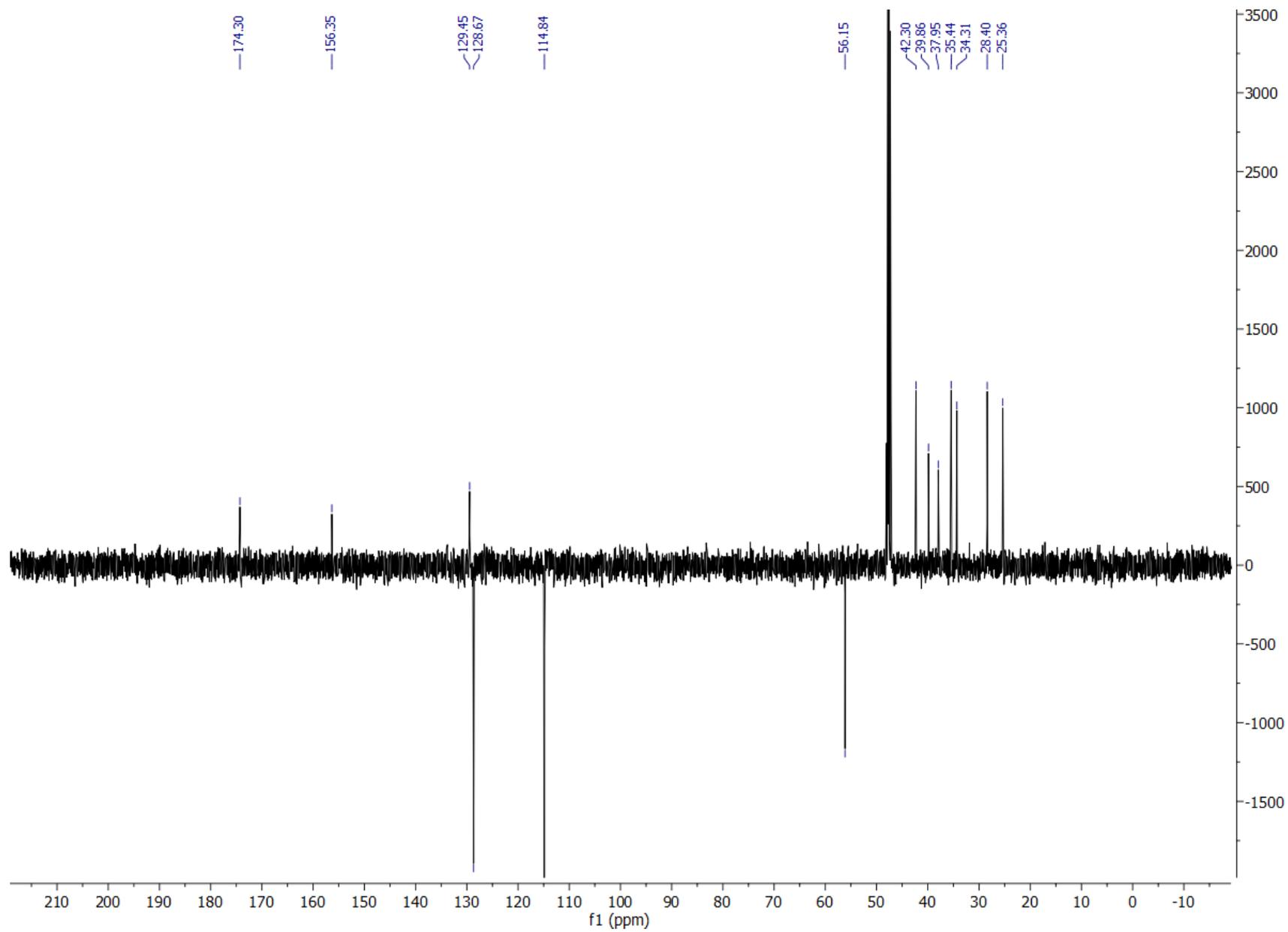
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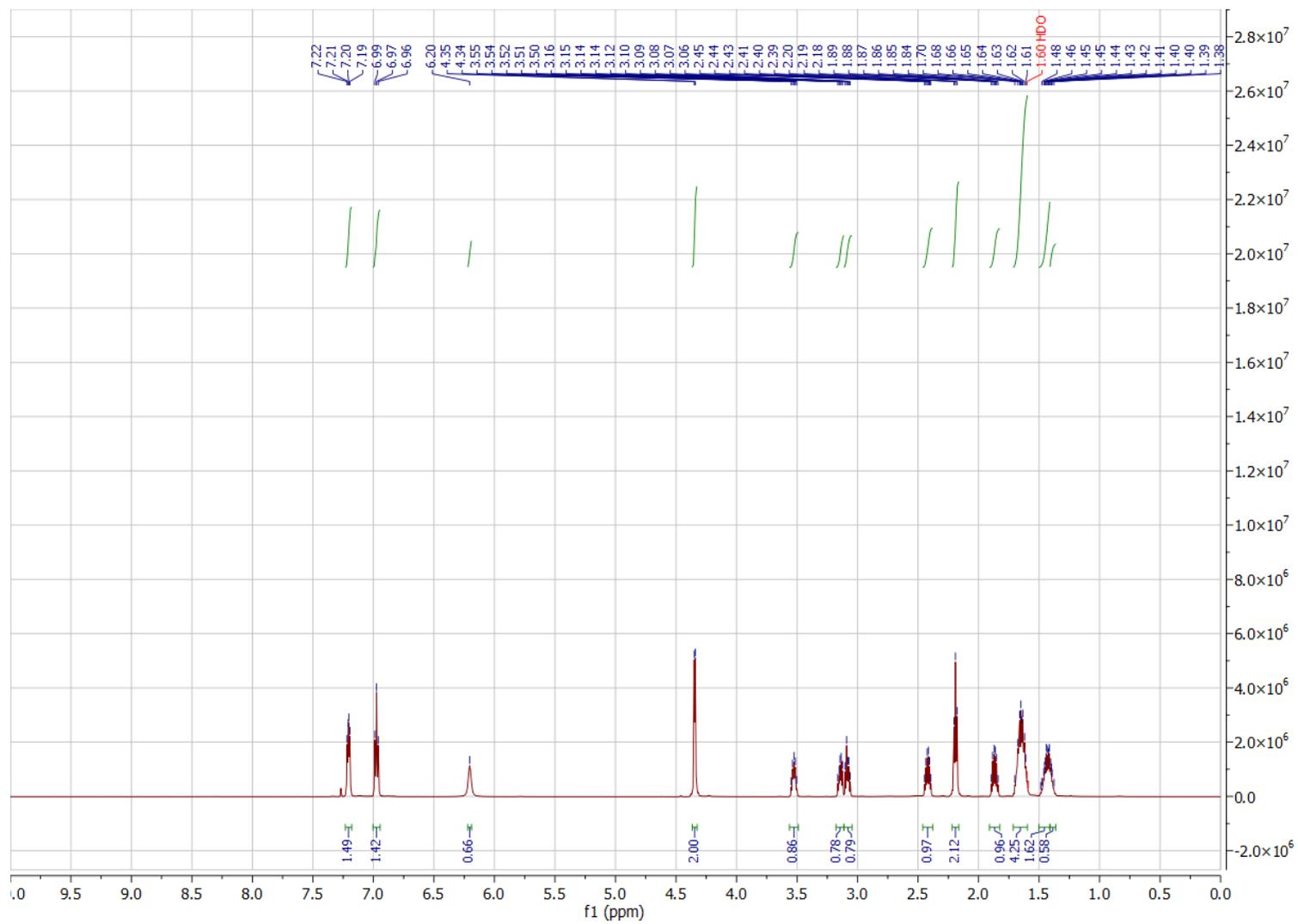
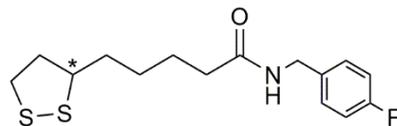


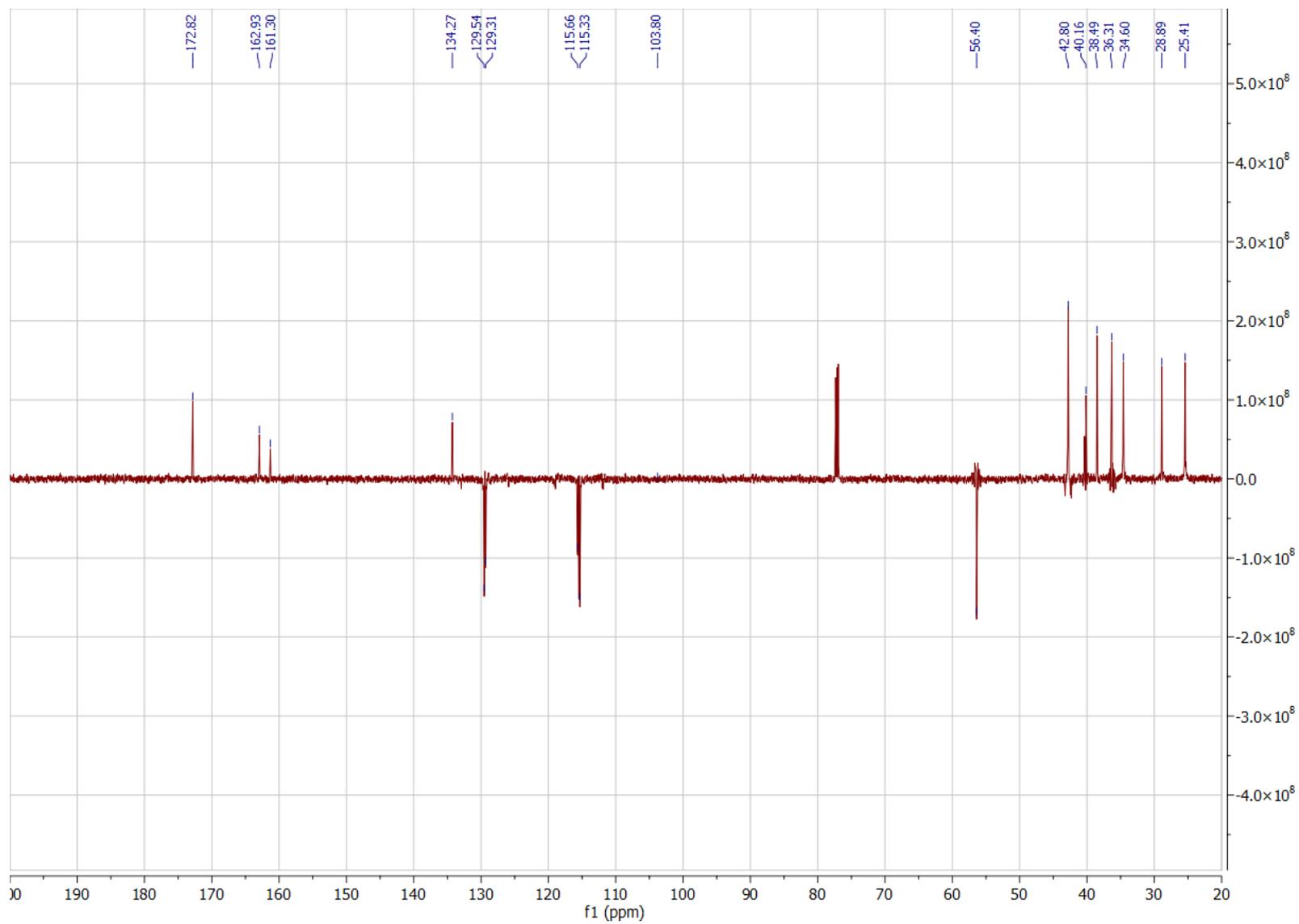
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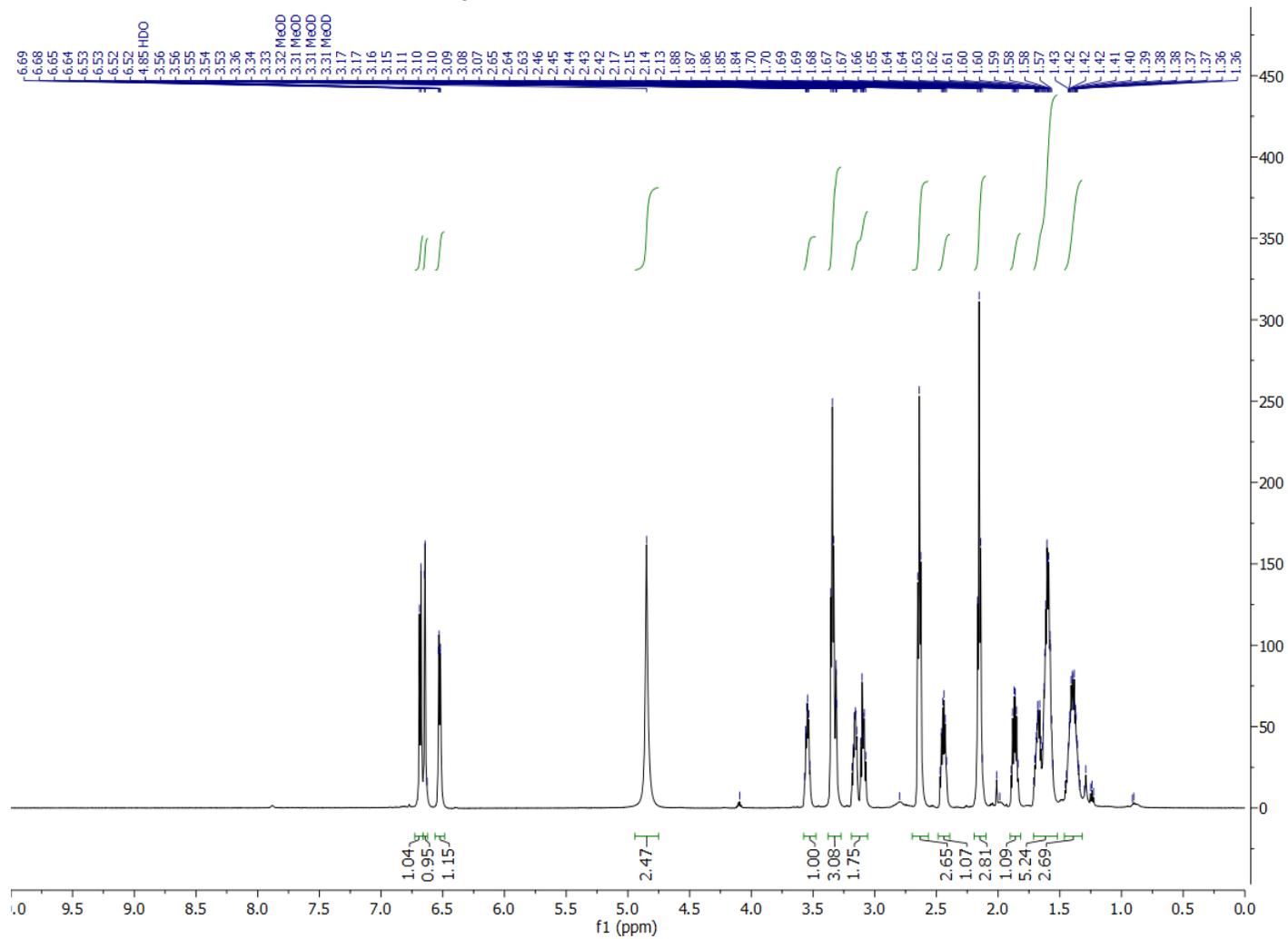
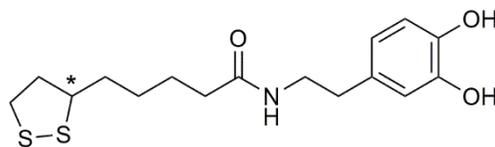


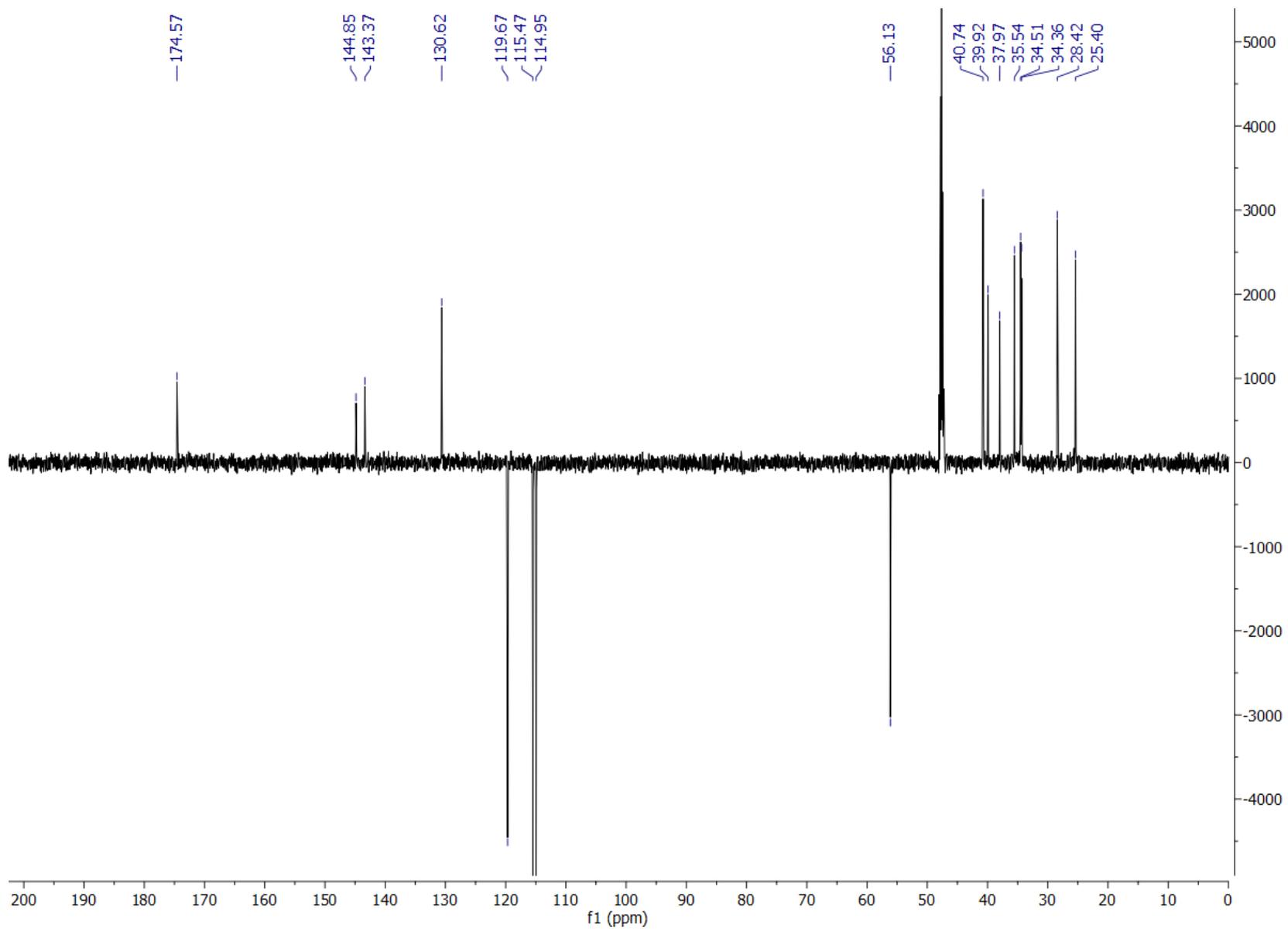
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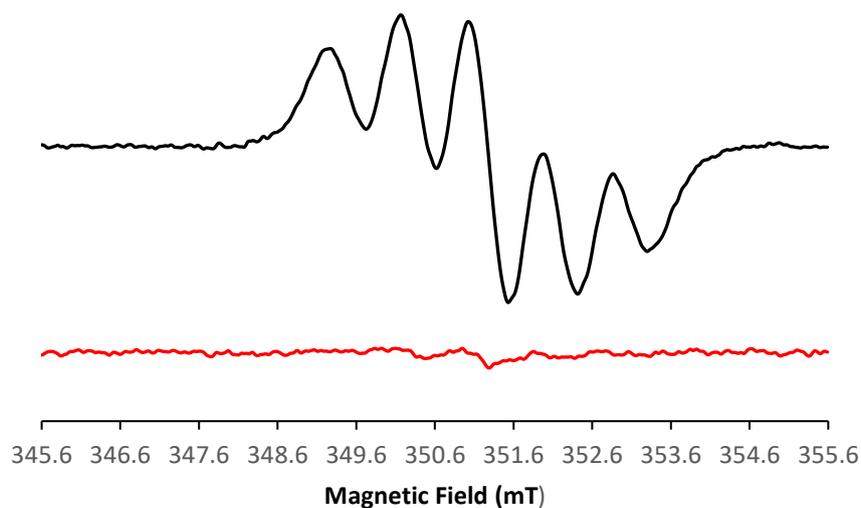


# Compound 9





**Figure S20. Scavenger activity of capsaicin through the DPPH assay using EPR spectroscopy**



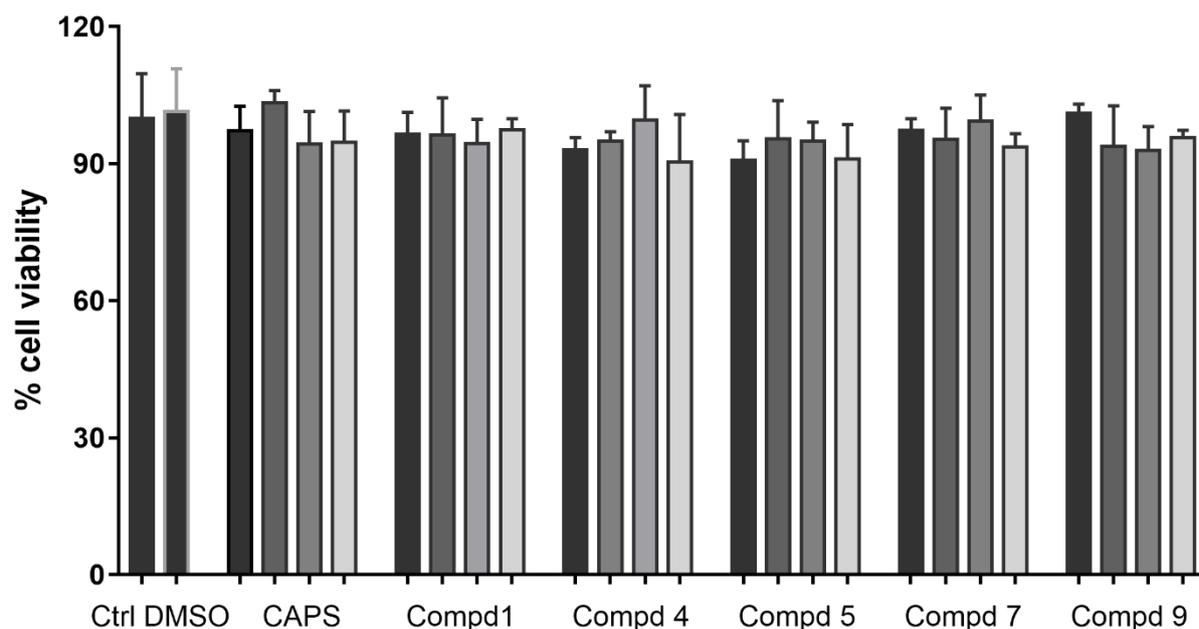
*Room temperature (298K) EPR spectra at X-band of DPPH radical before (black line) and after the addition of capsaicin (red line) with 20 minutes of incubation. Experimental conditions:  $\nu=9.869\text{GHz}$  microwave frequency, 2mW microwave power, 0.1mT modulation amplitude.*

The solutions were prepared in acetonitrile with a final concentration of 0.1mM of DPPH and 2.2mM of capsaicin.

Room temperature EPR spectra of DPPH radical before (black line) and after the addition of capsaicin (red line). The EPR spectrum of the radical in the presence of the antioxidant shows a strong reduction of the intensity within 20 minutes of incubation time as performed for the other antioxidants.

The calculated value of the R scavenger ratio percentage is 93% for capsaicin.

Figure S21. Cell viability of capsaicin (caps) and tested **lipoic** amides **1**, **4-5**, **7** and **9**



Cell viability expressed as percentage calculated by division of the absorbance values obtained after 48 h of capsaicin or compounds, *i.e.* **1**, **4-5**, **7** and **9**, incubation at increasing concentration (0.1, 1, 3, 10 μM) by those obtained without substances. Each point represents the mean  $\pm$  SEM of five independent experiments. No significant differences were measured (ANOVA with post-test).