

Supplementary Material

Environmentally benign synthesis of unsymmetrical bis-1,2,4-triazolopyridazines using iodobenzene diacetate as an oxidant

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General procedure for one-pot synthesis of unsymmetrical bis-1,2,4-triazolo-[4,3-*b*][3',4'-*f*]pyridazine (4a-m)

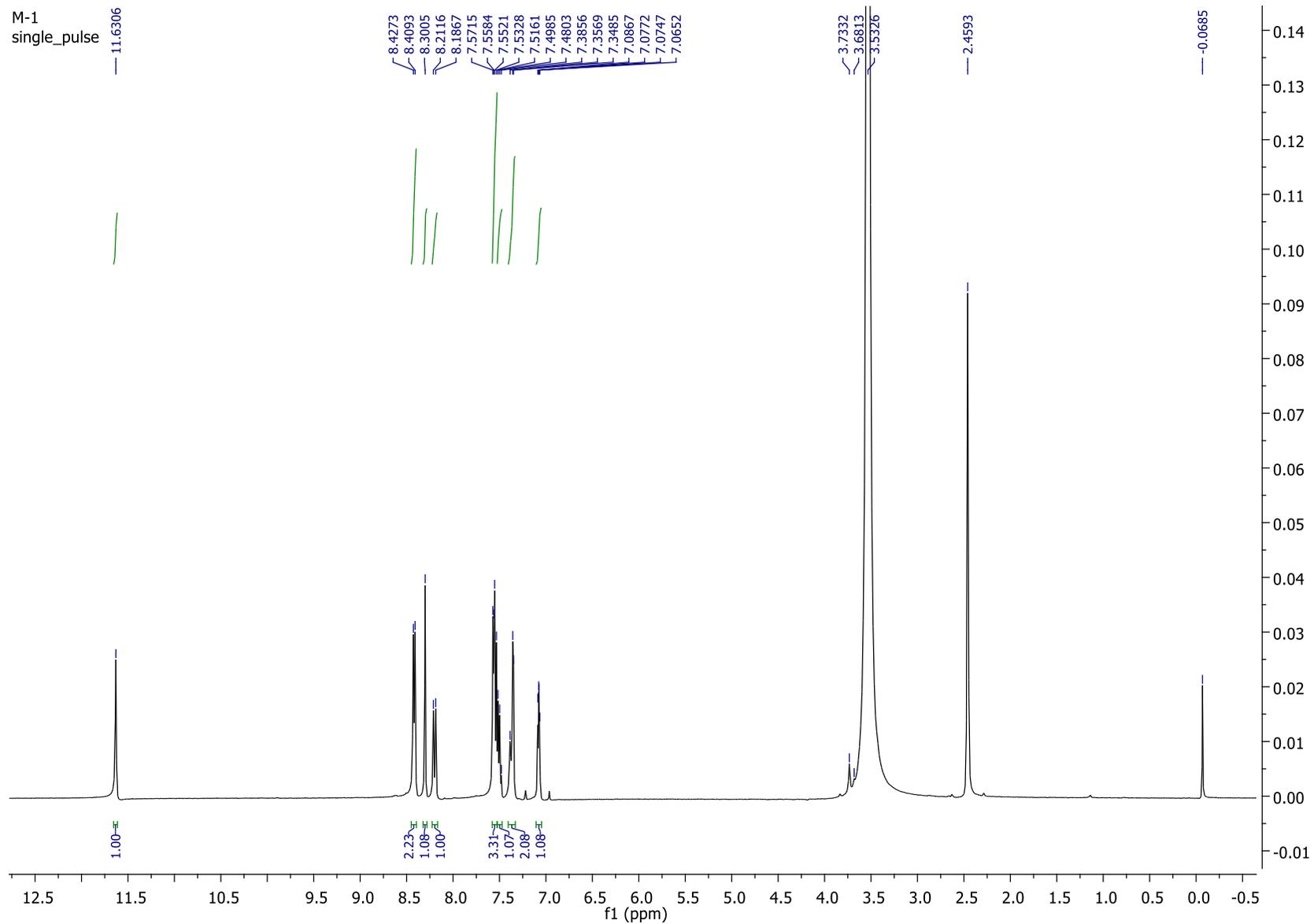
An equimolar mixture of 6-hydrazino-3-aryl/heteroaryl-1,2,4-triazolo[4,3-*b*]pyridazine (**2**) (2.0 mmol) and the appropriate aldehyde (2.0 mmol) was ground in a mortar and pestle for 15–20 minutes at room temperature, resulting in the formation of the corresponding 6-arylidenehydrazino-3-aryl-1,2,4-triazolo[4,3-*b*]pyridazine (**3**). Upon completion of the reaction, as indicated by TLC, IBD (2.2 mmol, 1.1 equiv) was added, and the mixture was ground thoroughly for an additional 1 h. The solid that precipitated after trituration with petroleum ether was filtered and recrystallized from ethanol to afford the corresponding unsymmetrical bis-1,2,4-triazolo[4,3-*b*][3',4'-*f*]pyridazine derivatives (**4a–m**).

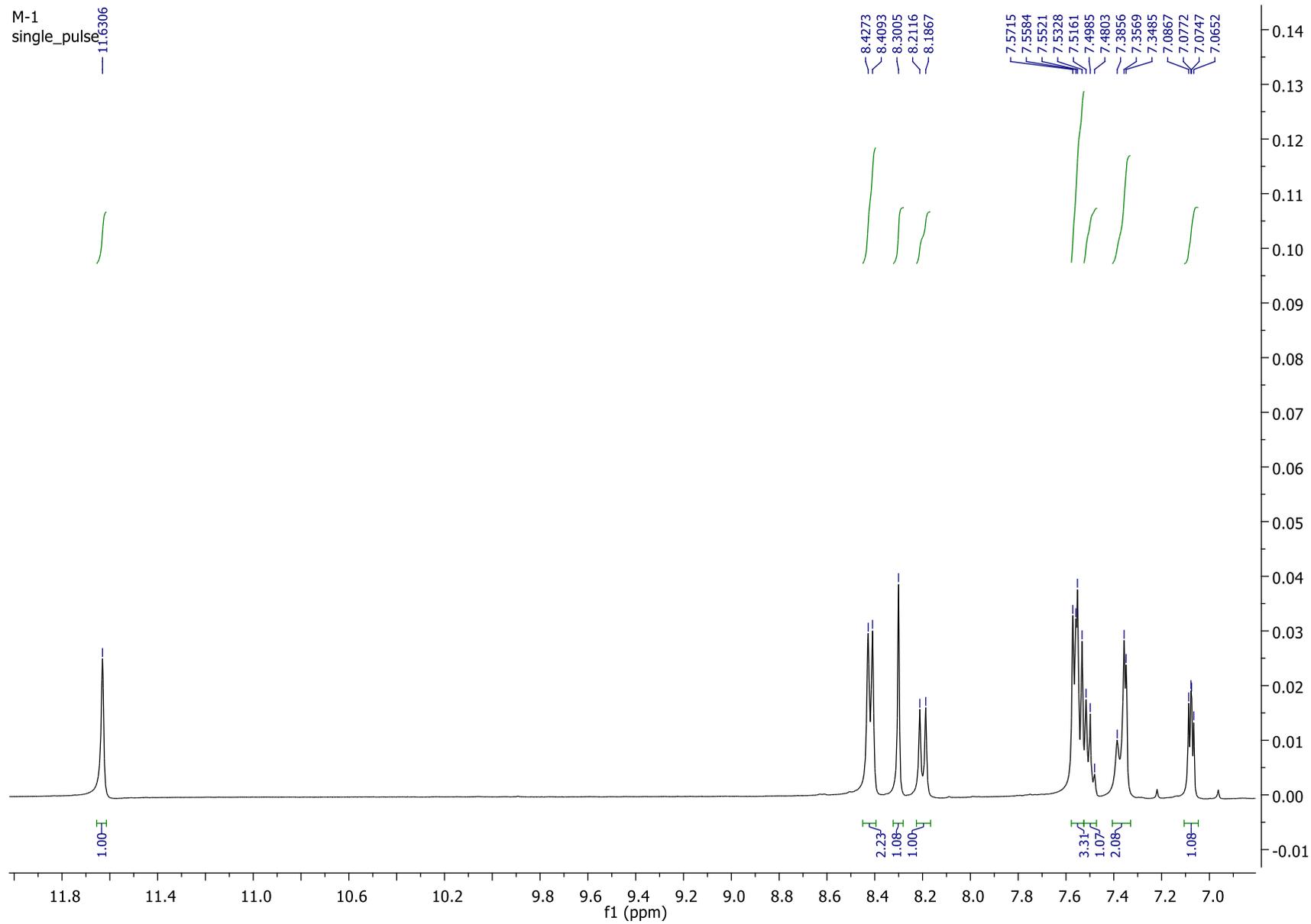
Cytotoxicity Viability Assay

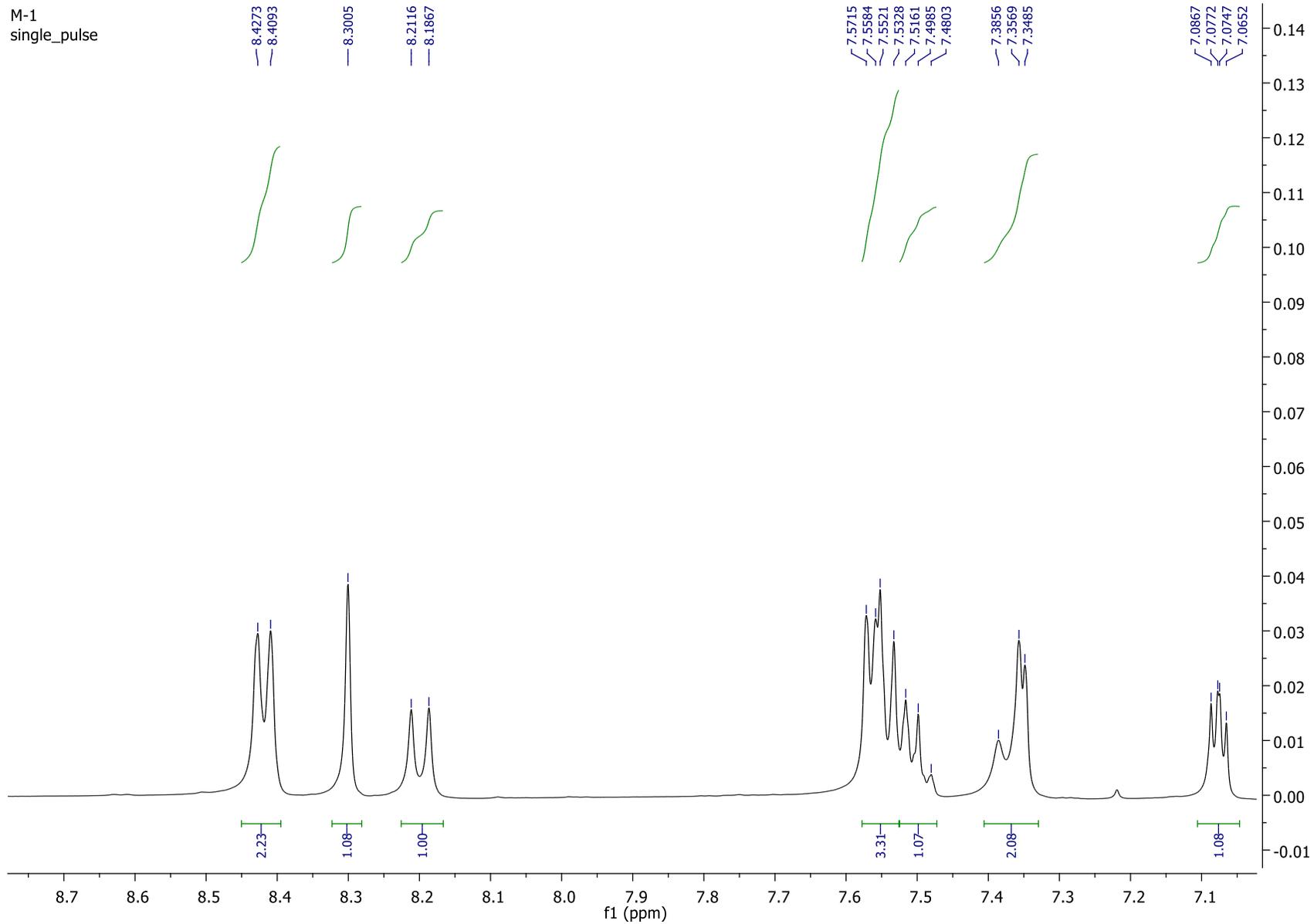
Cells were seeded at a density of 50,000 per mL into a 96-well plate and treated with various compounds at a final concentration of 10 μ M. The cells were then incubated for 48 h. An MTT cell proliferation kit from ATCC (#30-1010K) was used to assess cell viability. At the end of incubation, 10 μ L of MTT reagent was added to each well, and the cells were placed back in the incubator for 4 h. Subsequently, 100 μ L of detergent (from the kit) was added, and absorbance at 570 nm wavelength was recorded using a BioTek Synergy 2 spectrophotometer. Data was calculated as the percentage of cell survival using the following formula:

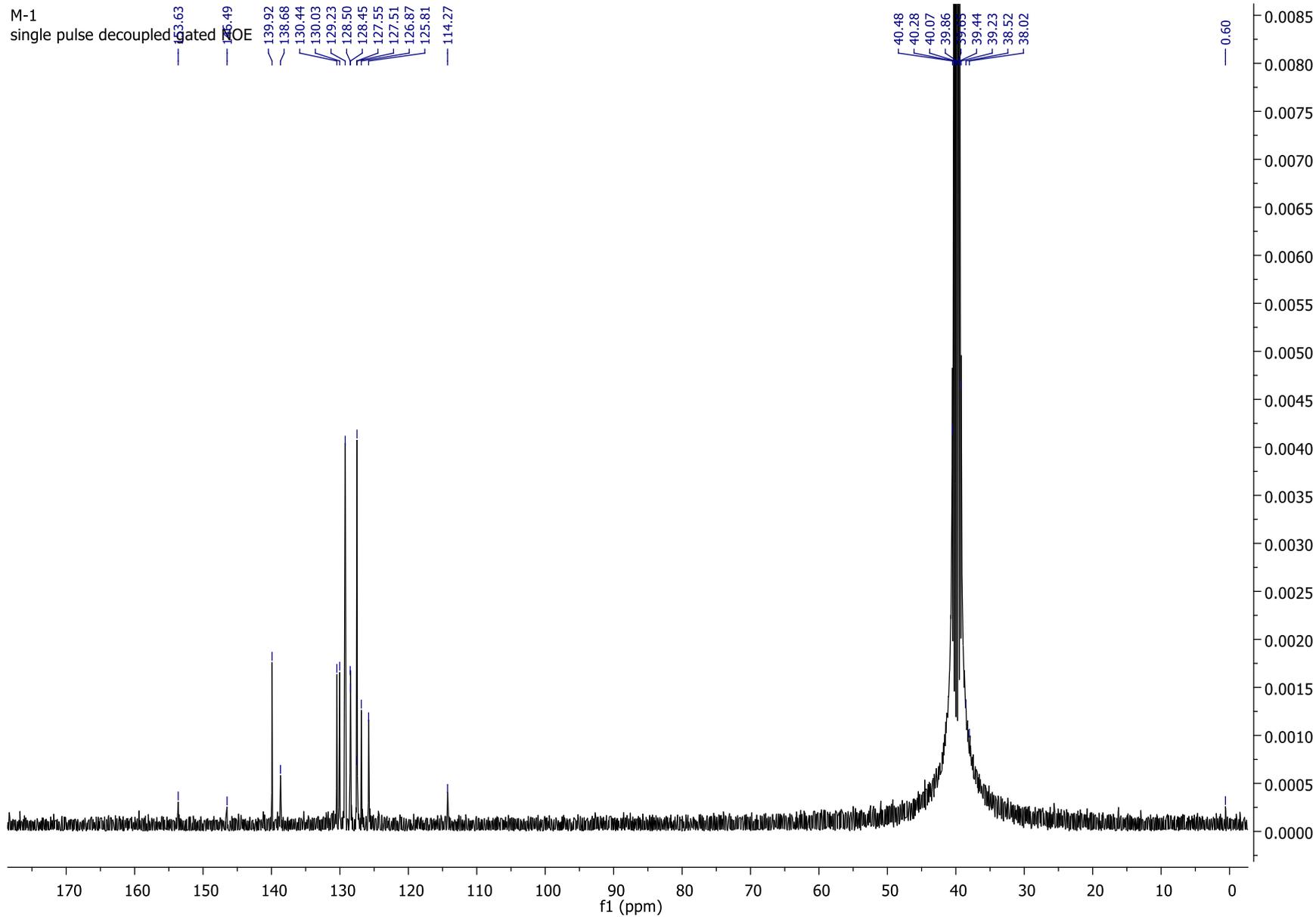
$$\% \text{ Cell survival} = (100/A_t * A_s)$$

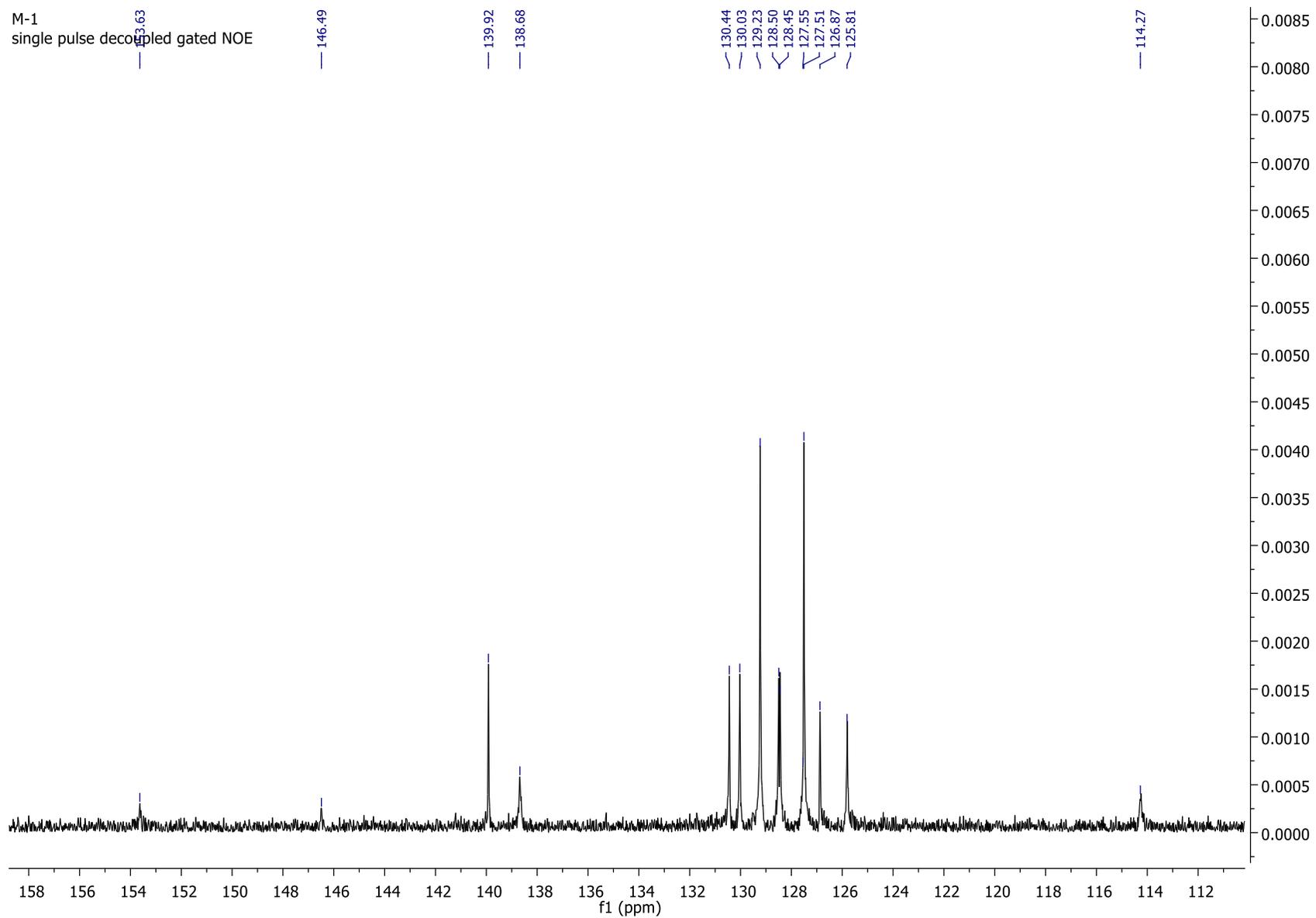
Where A_t and A_s are the absorbance of wells treated with test compounds and solvent control, respectively.

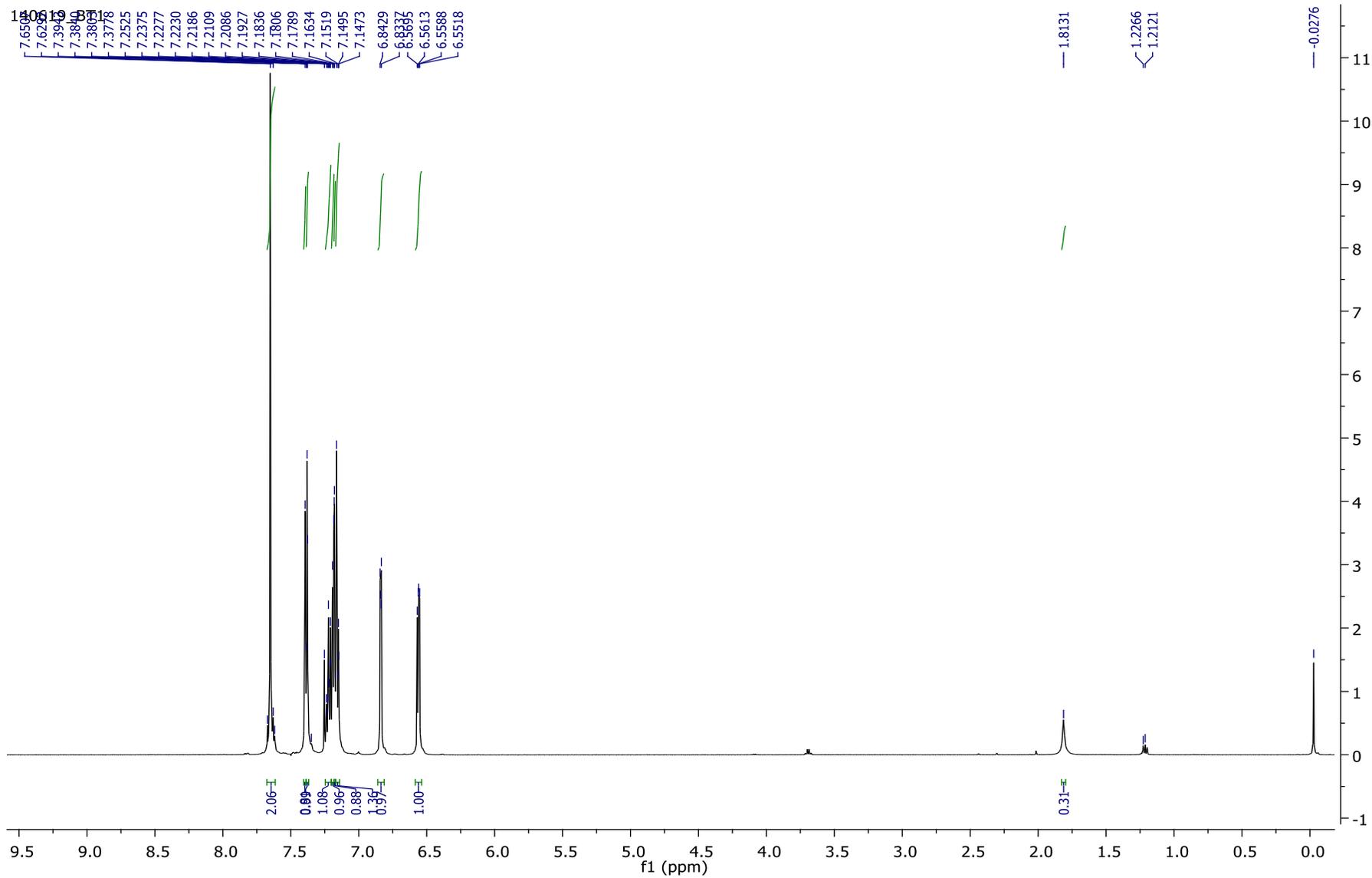


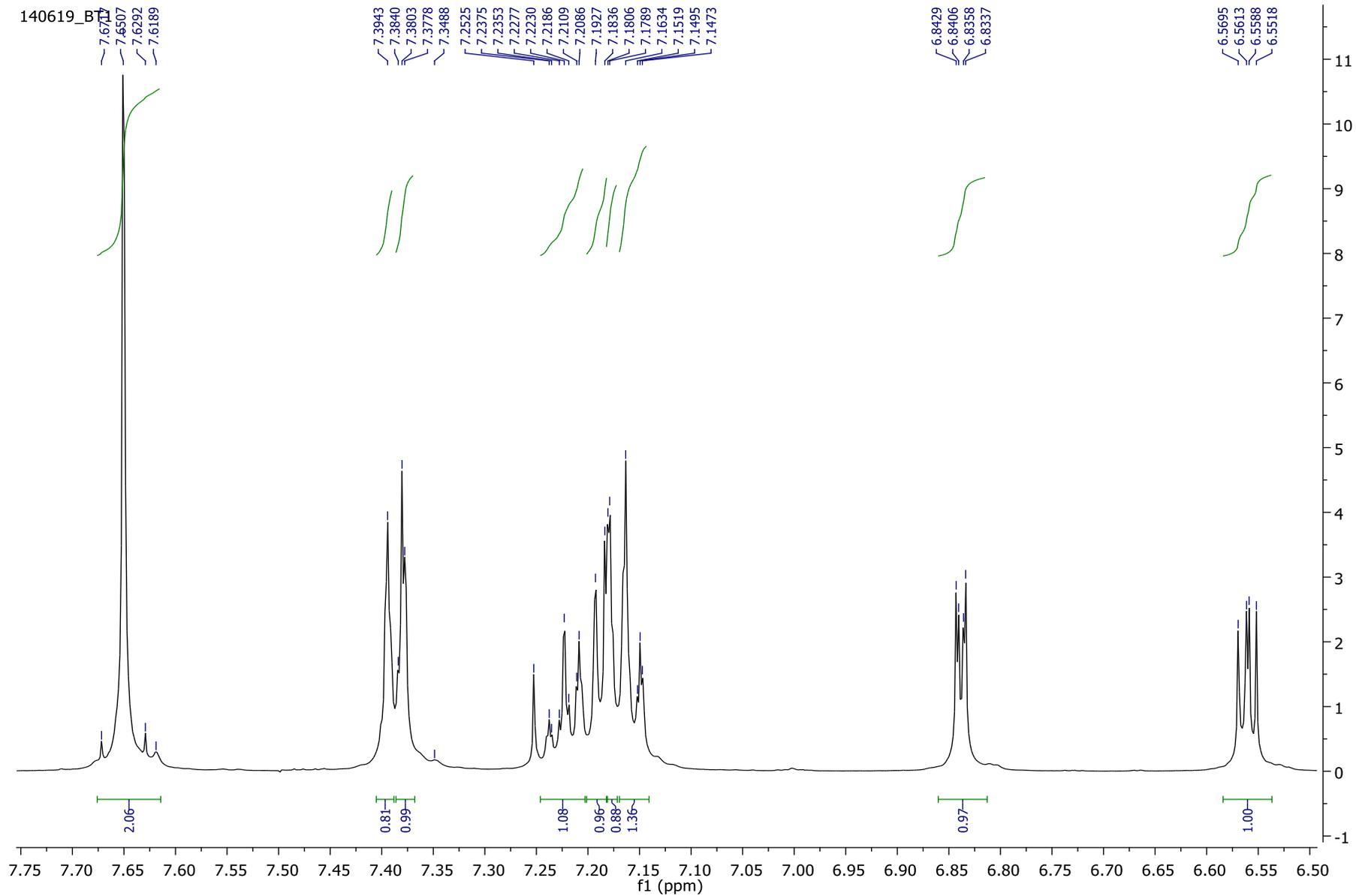




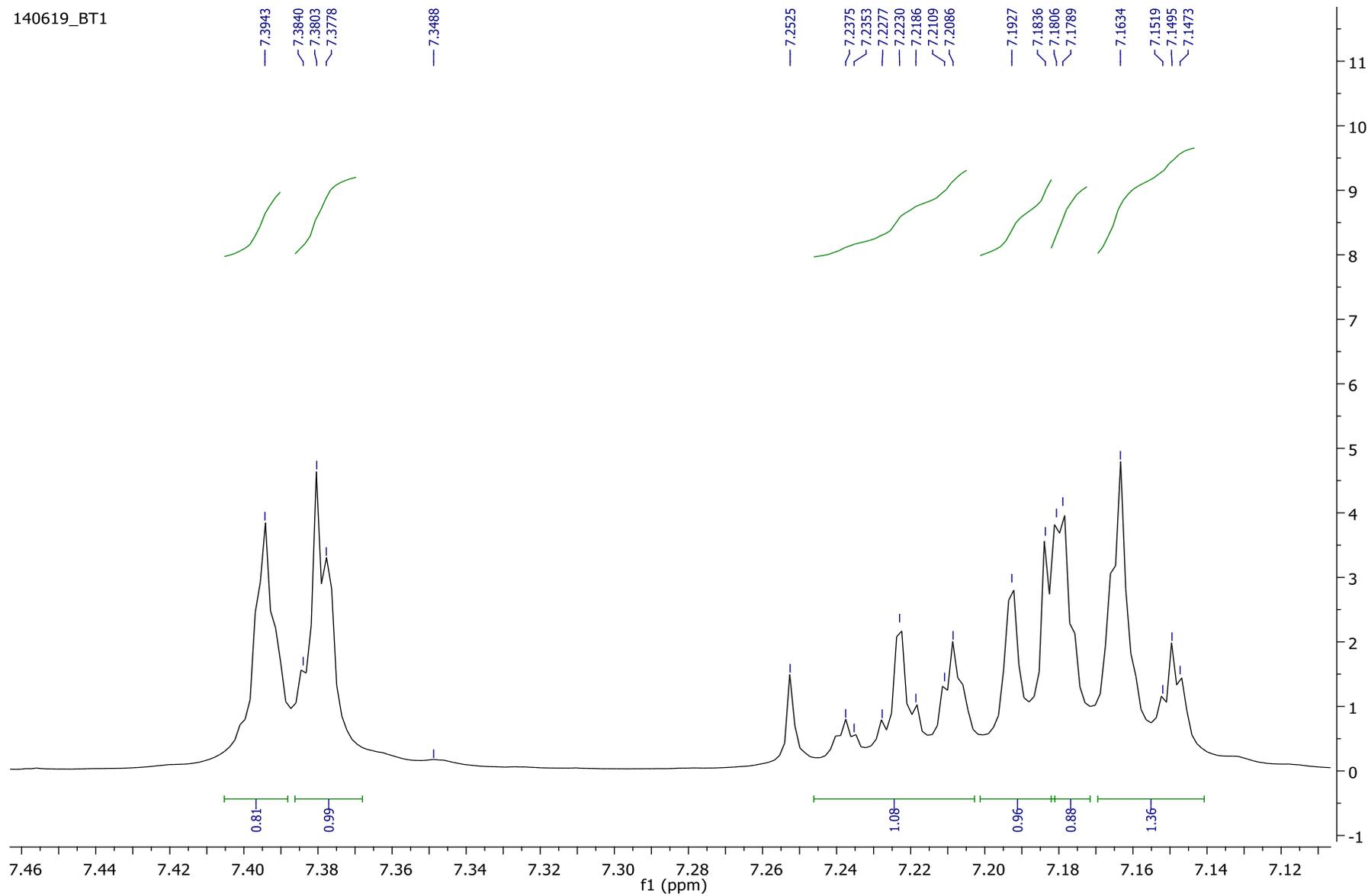




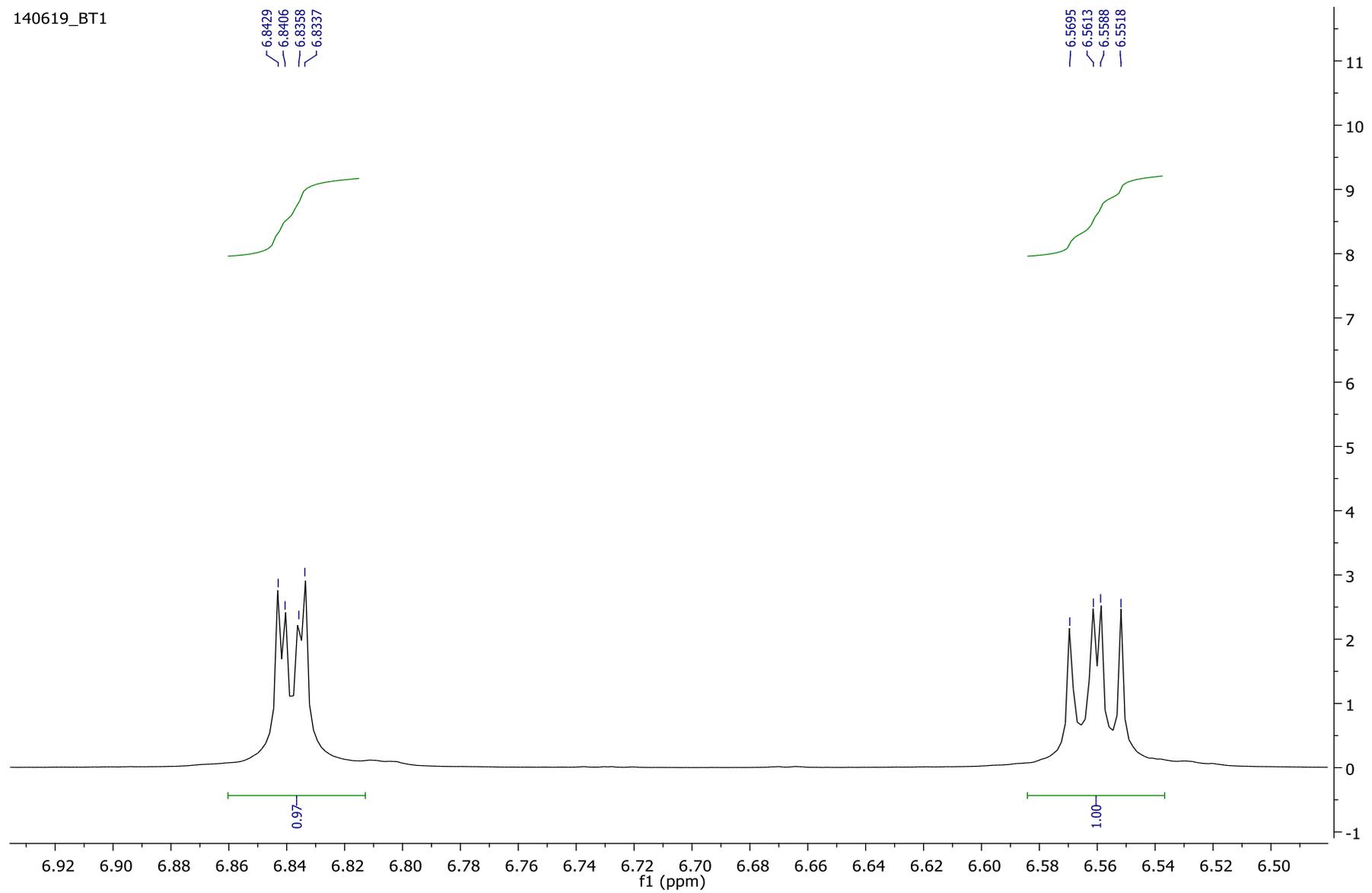




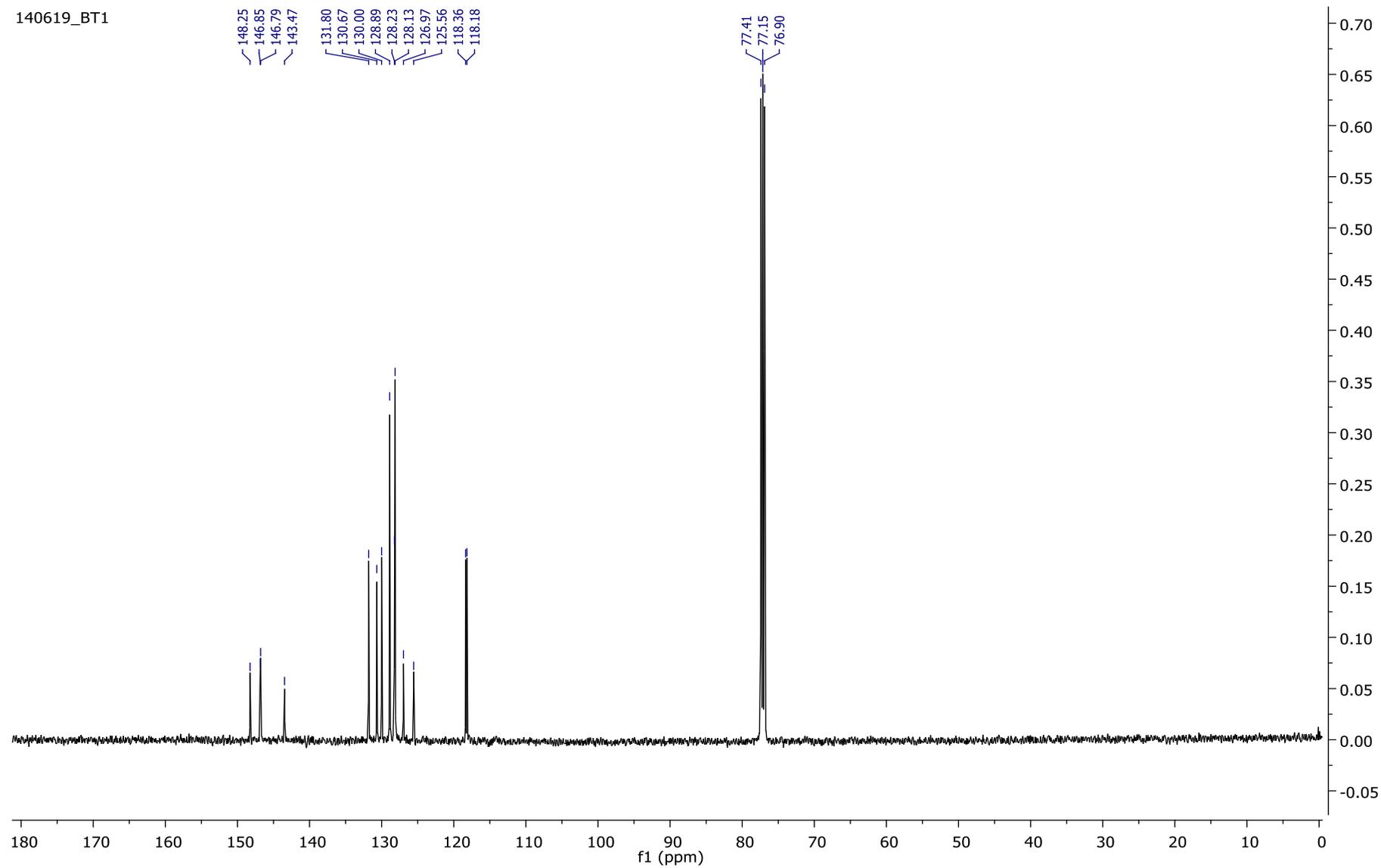
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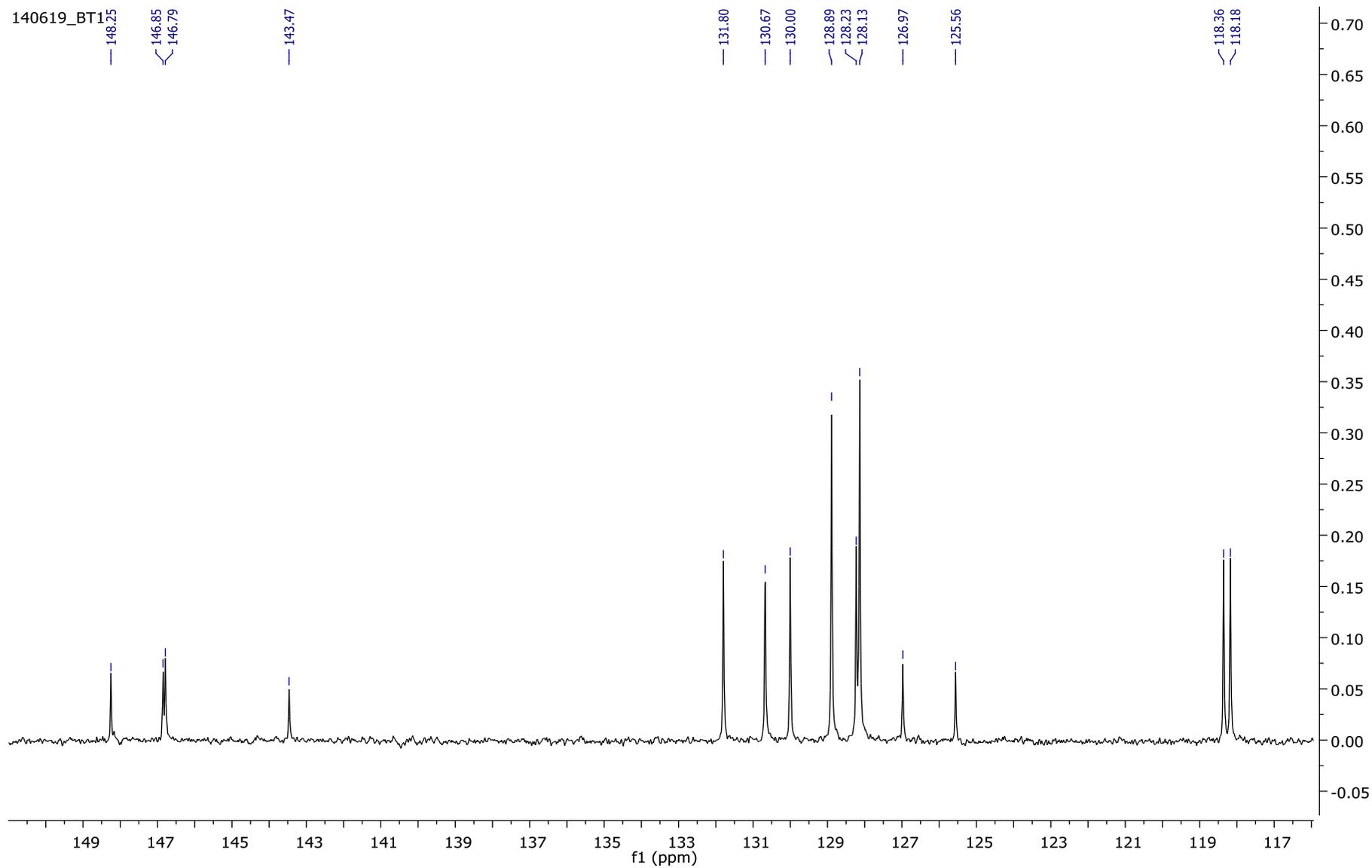


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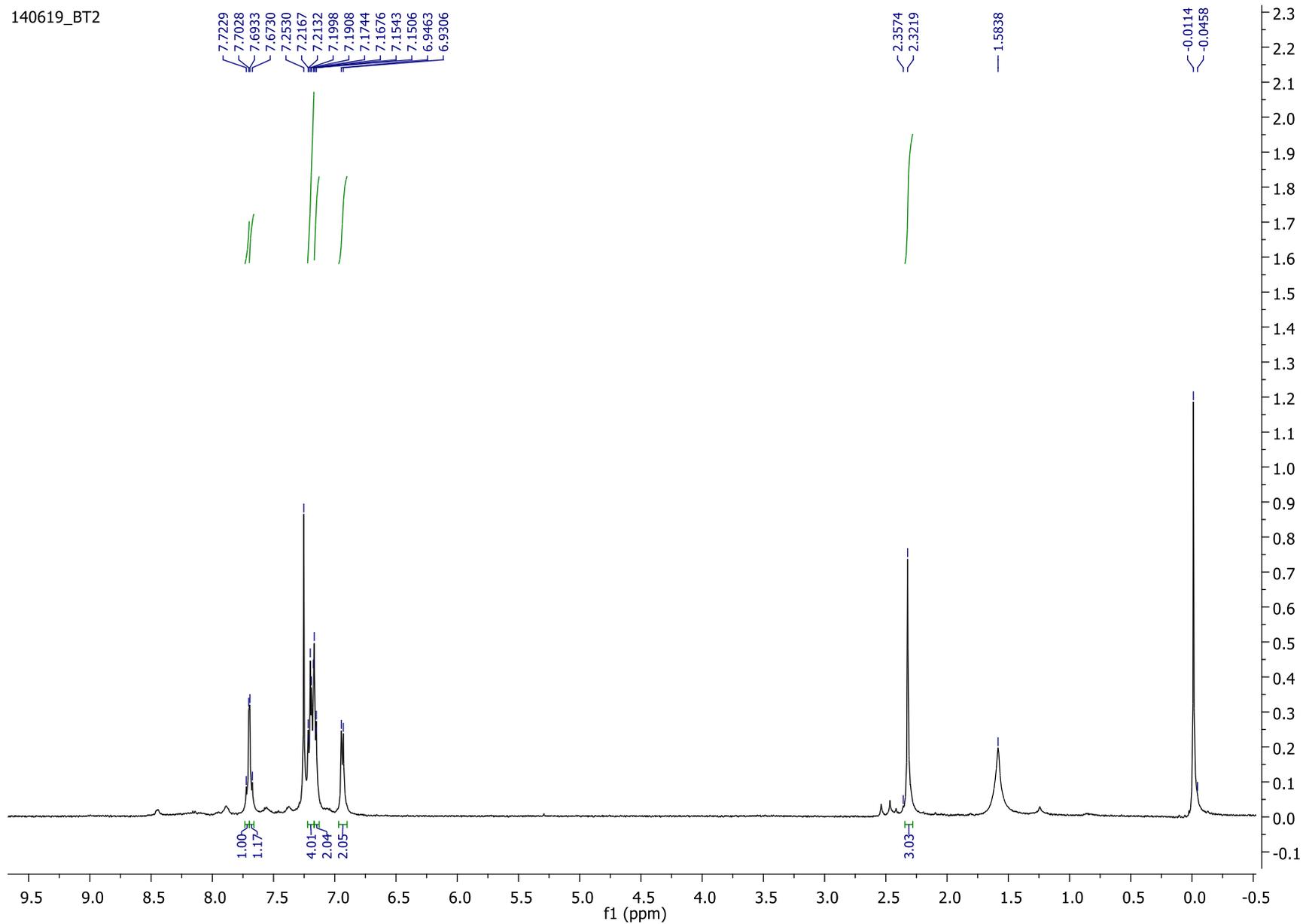


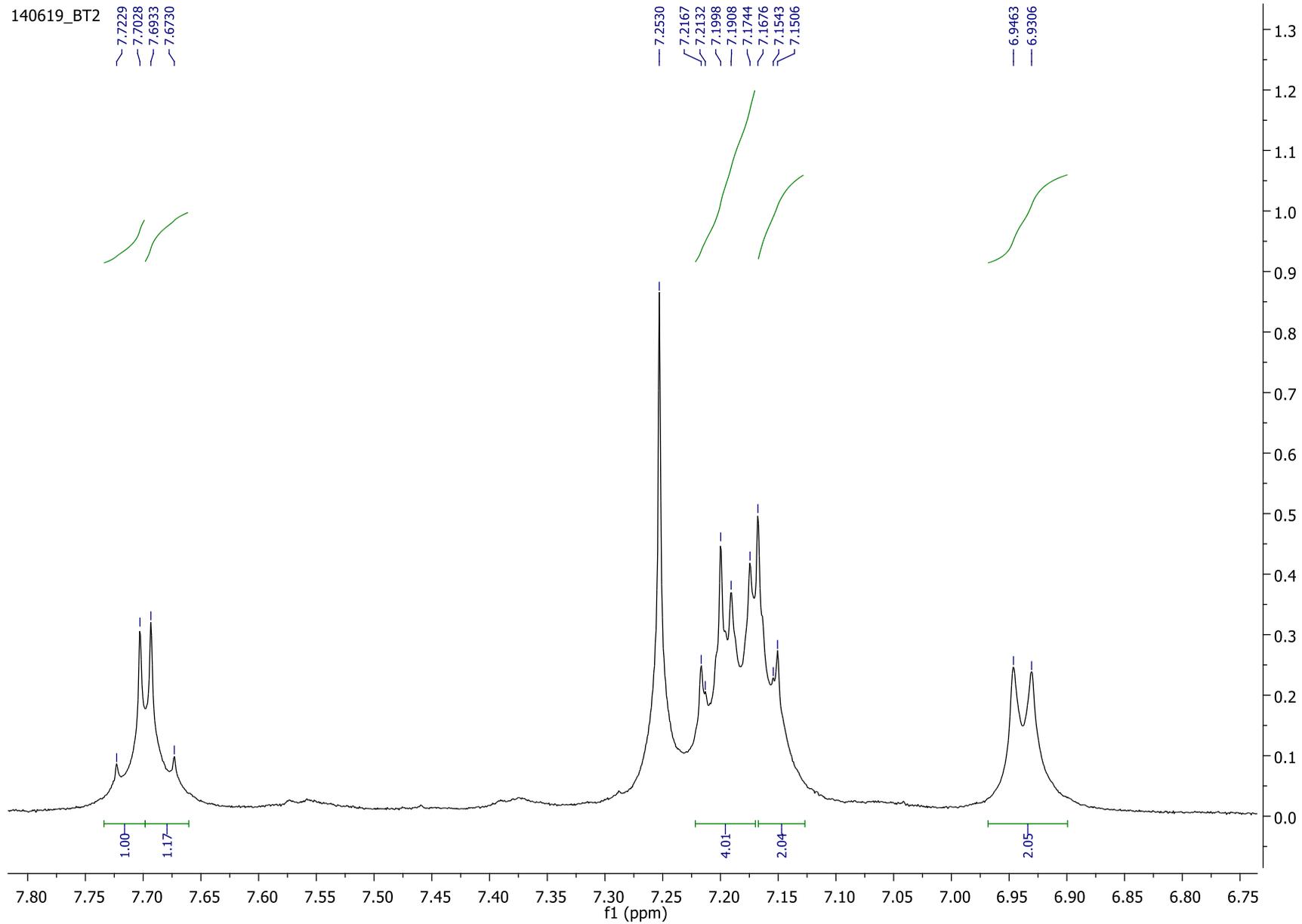
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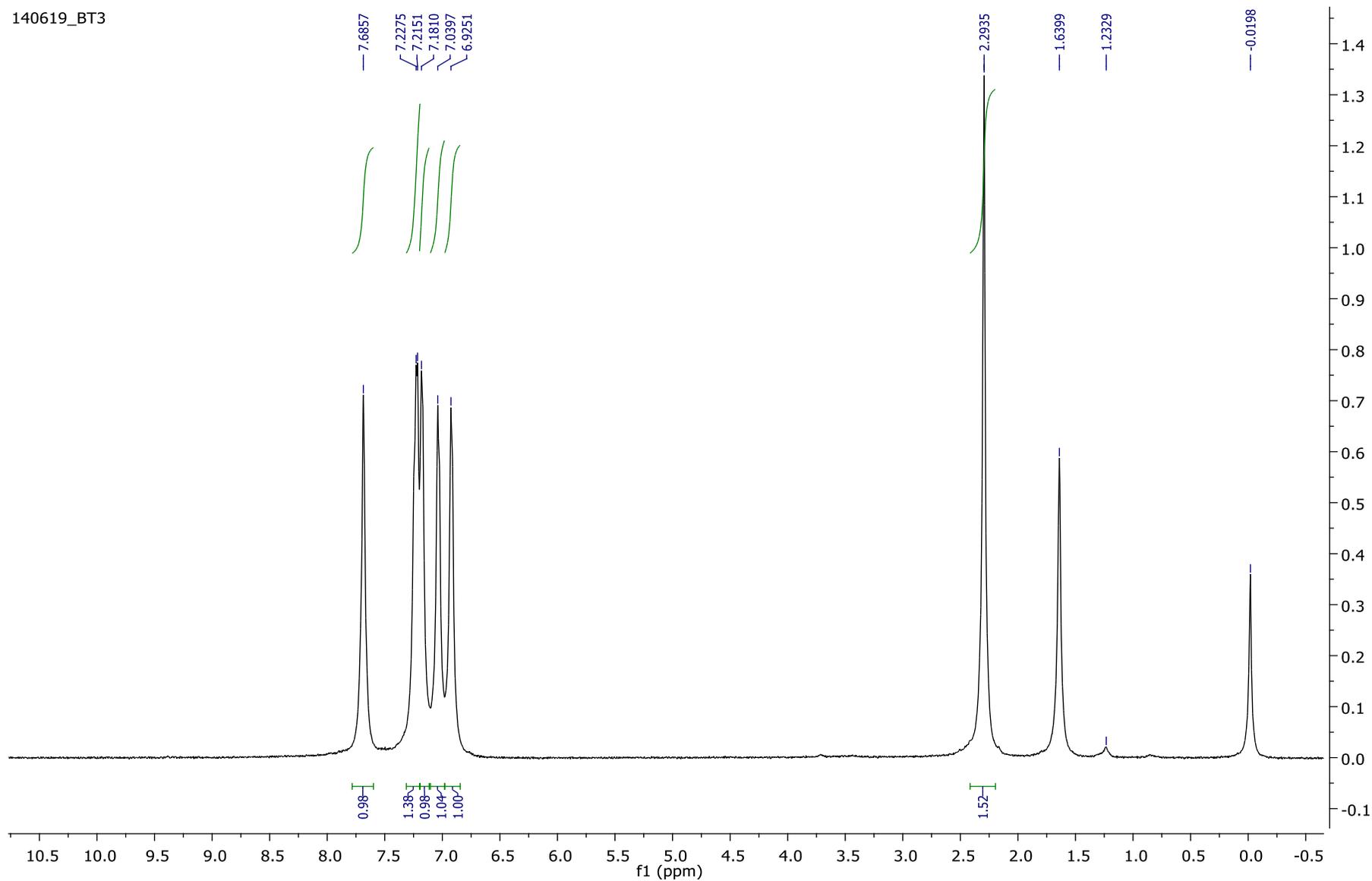


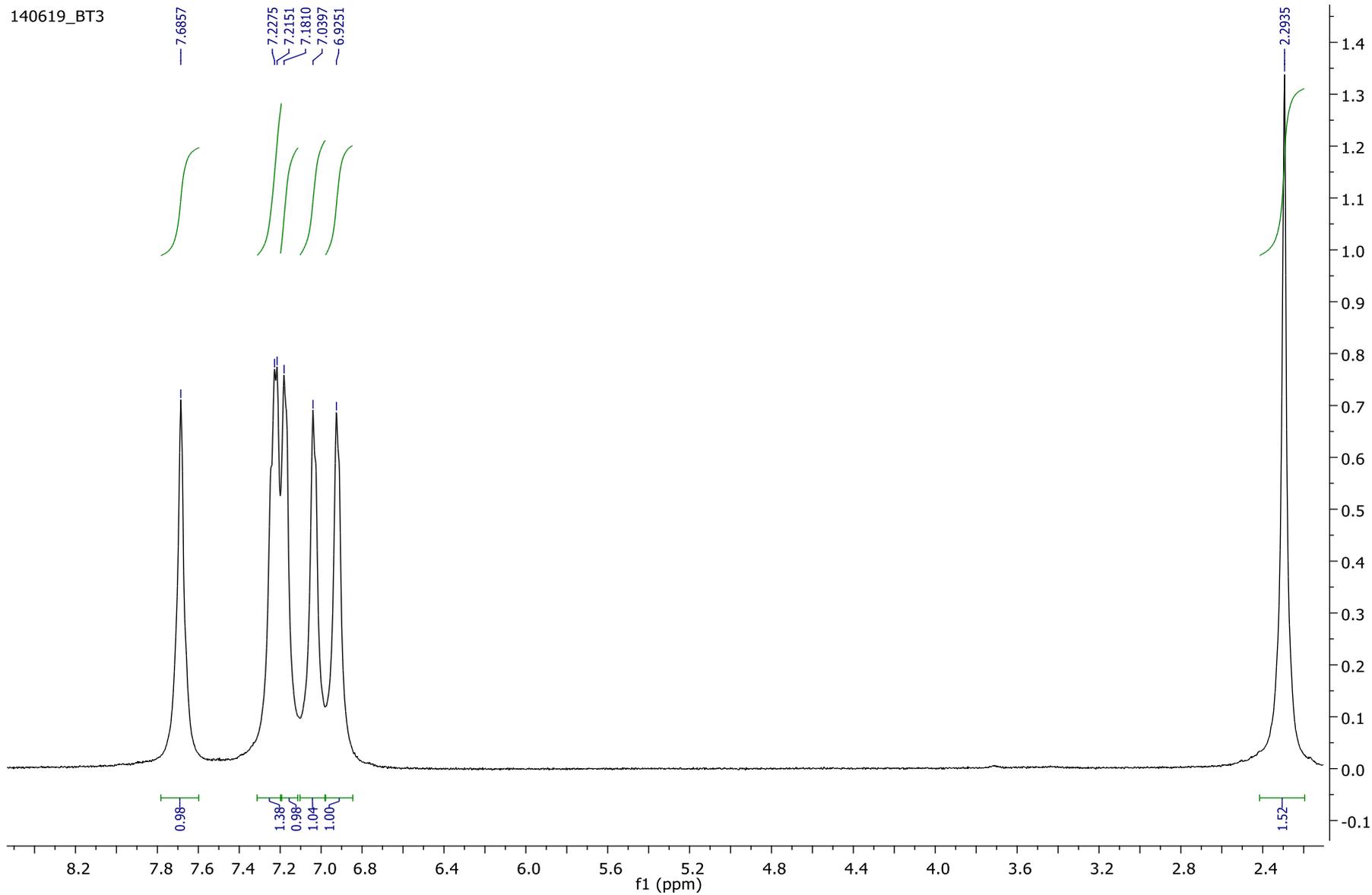
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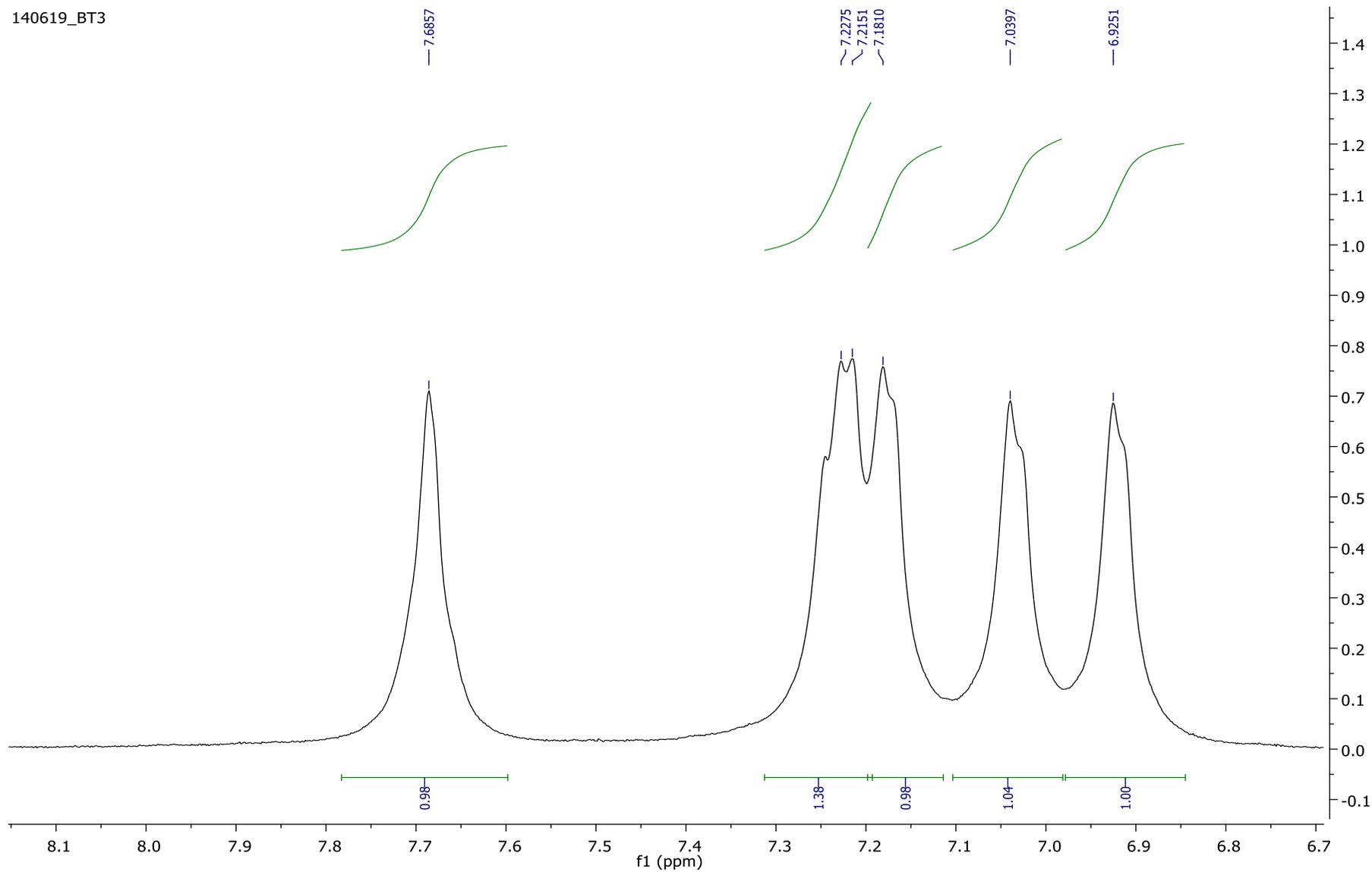


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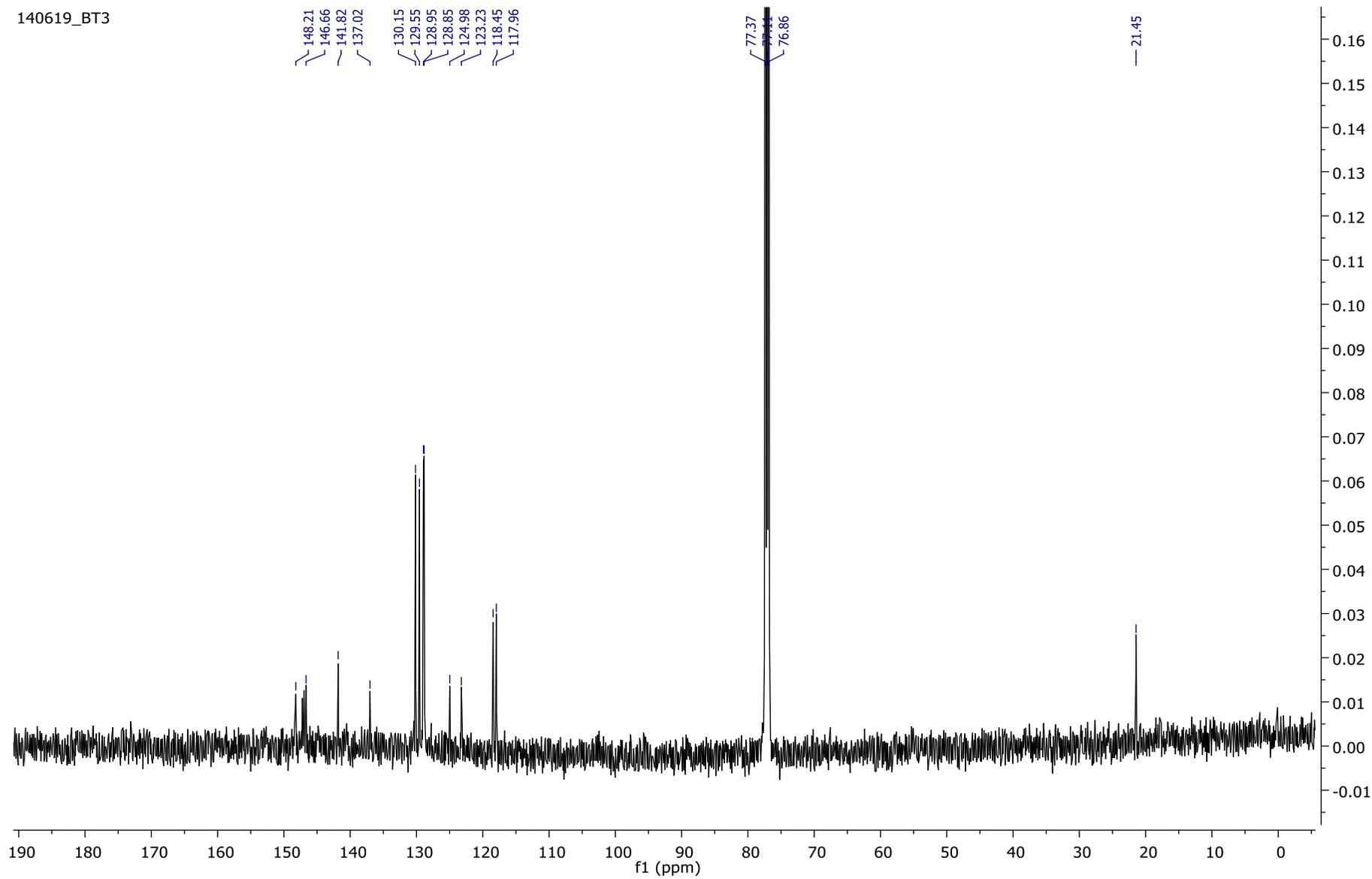


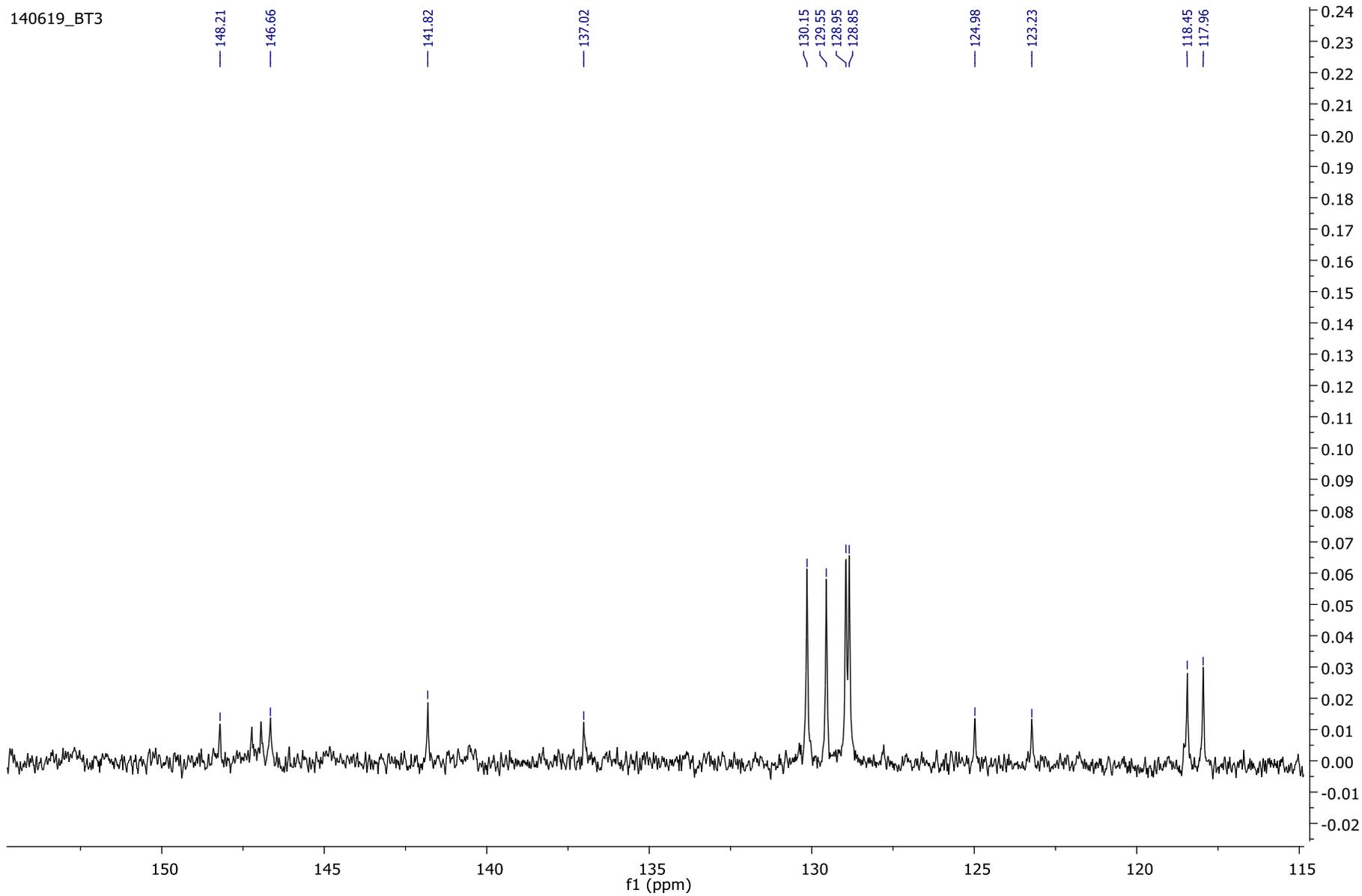


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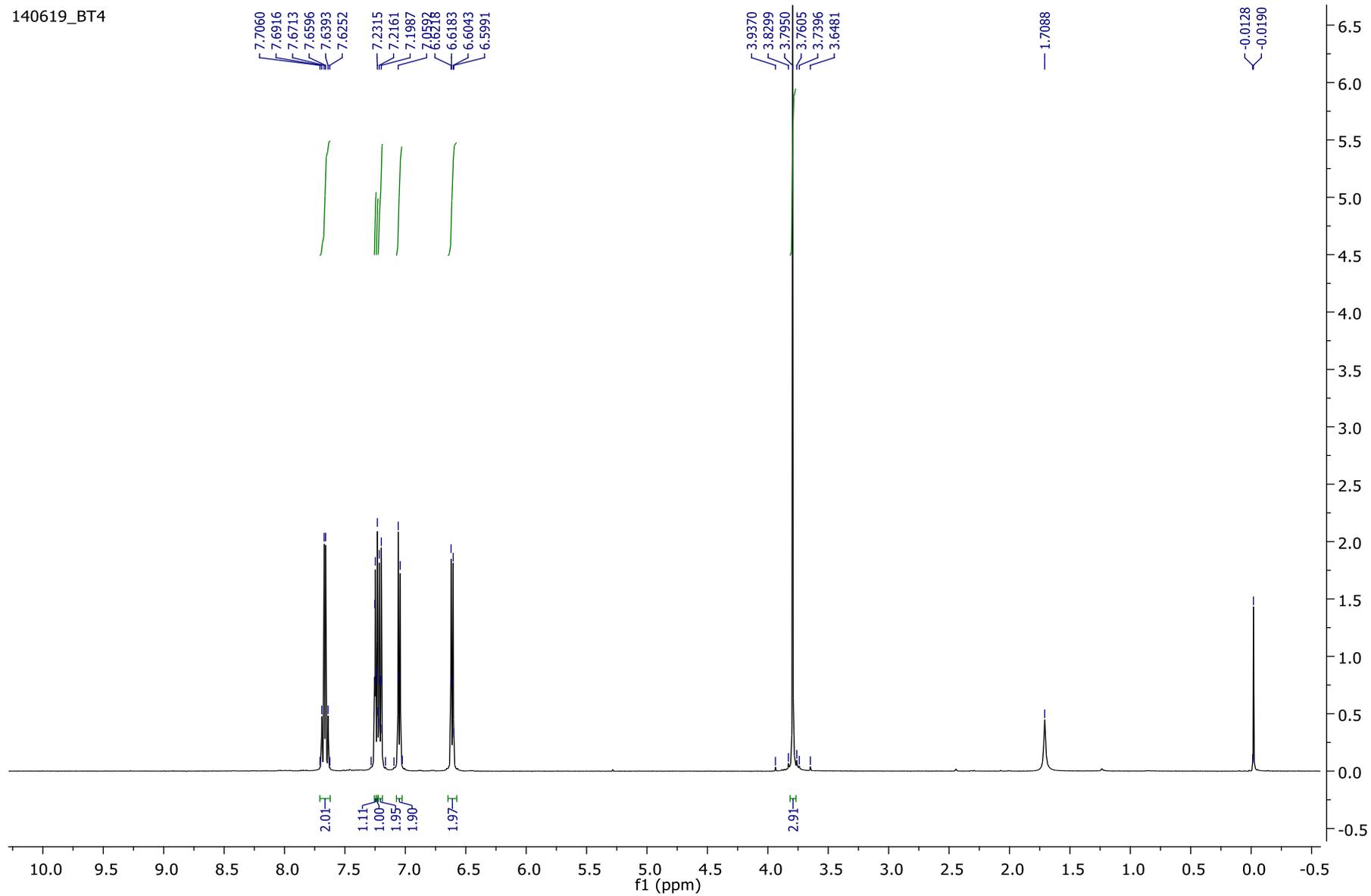


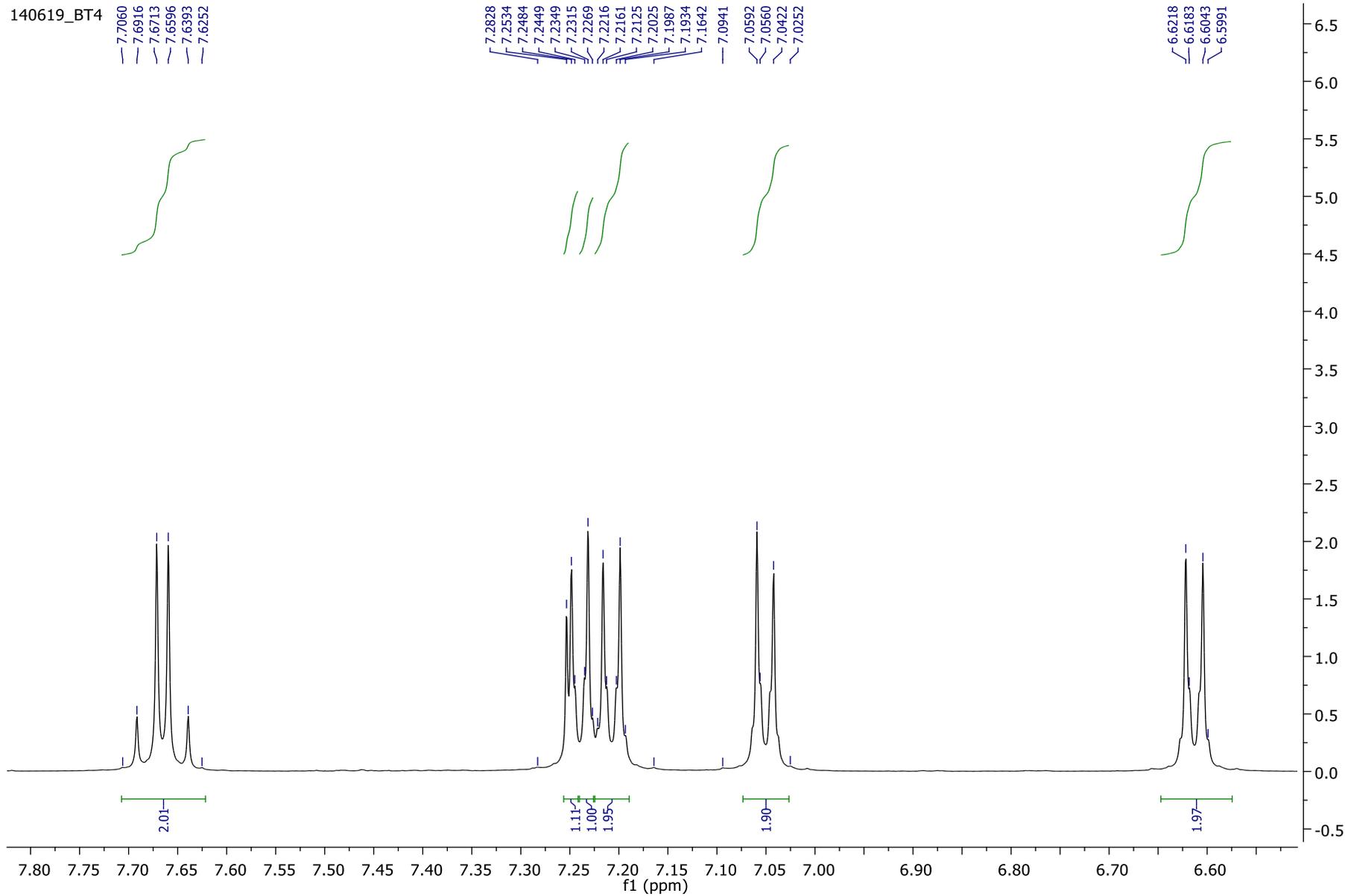
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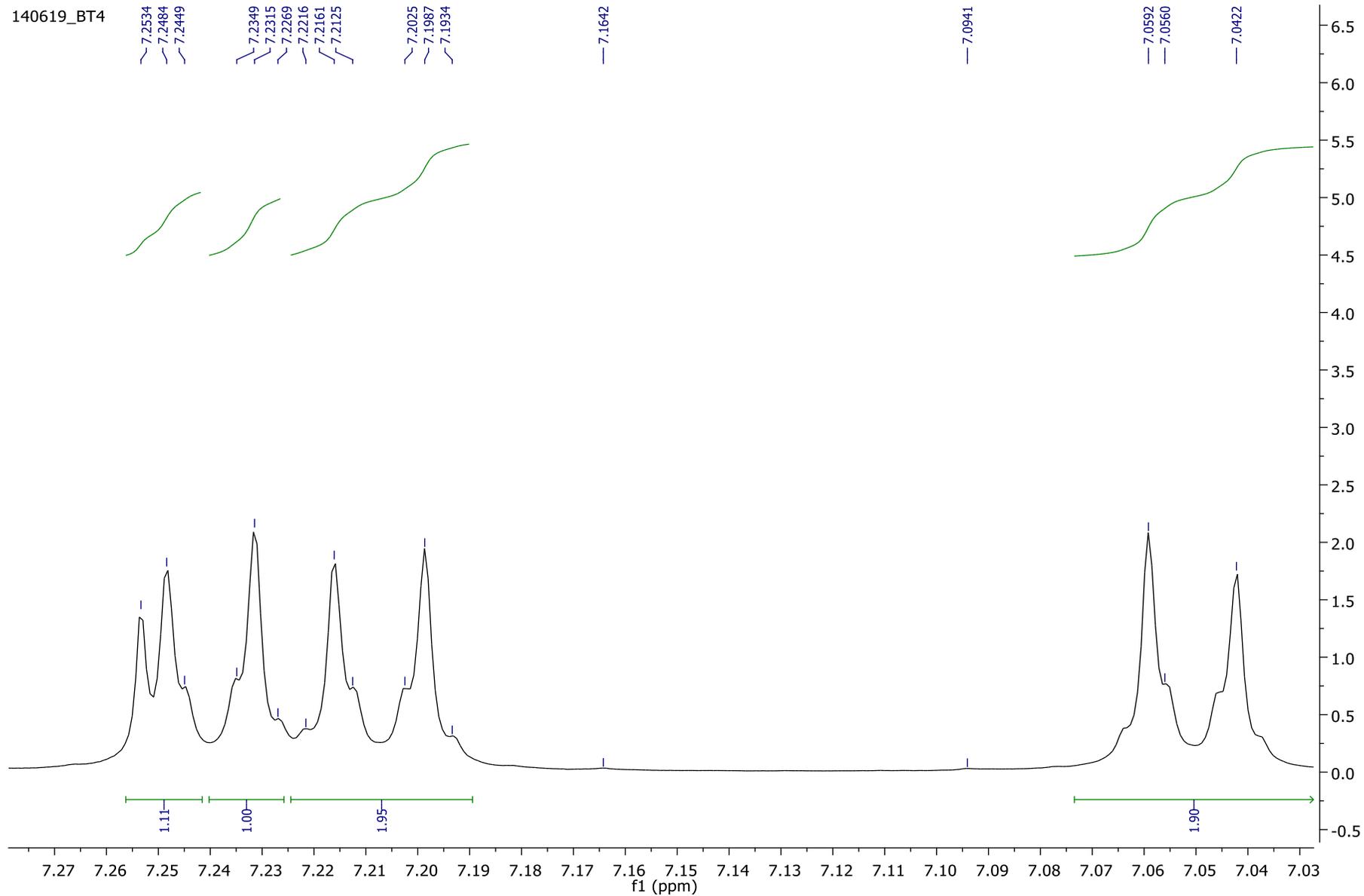


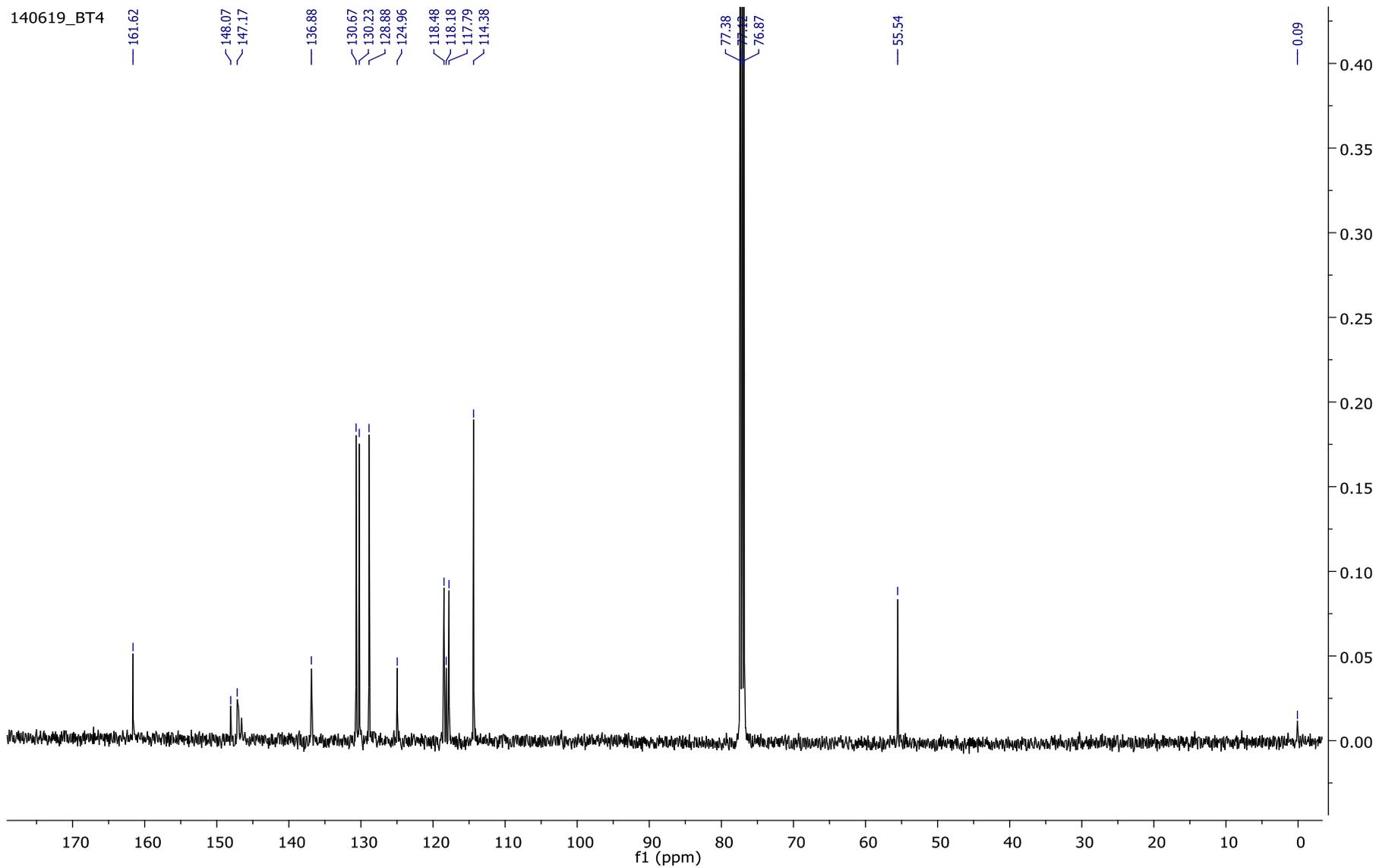


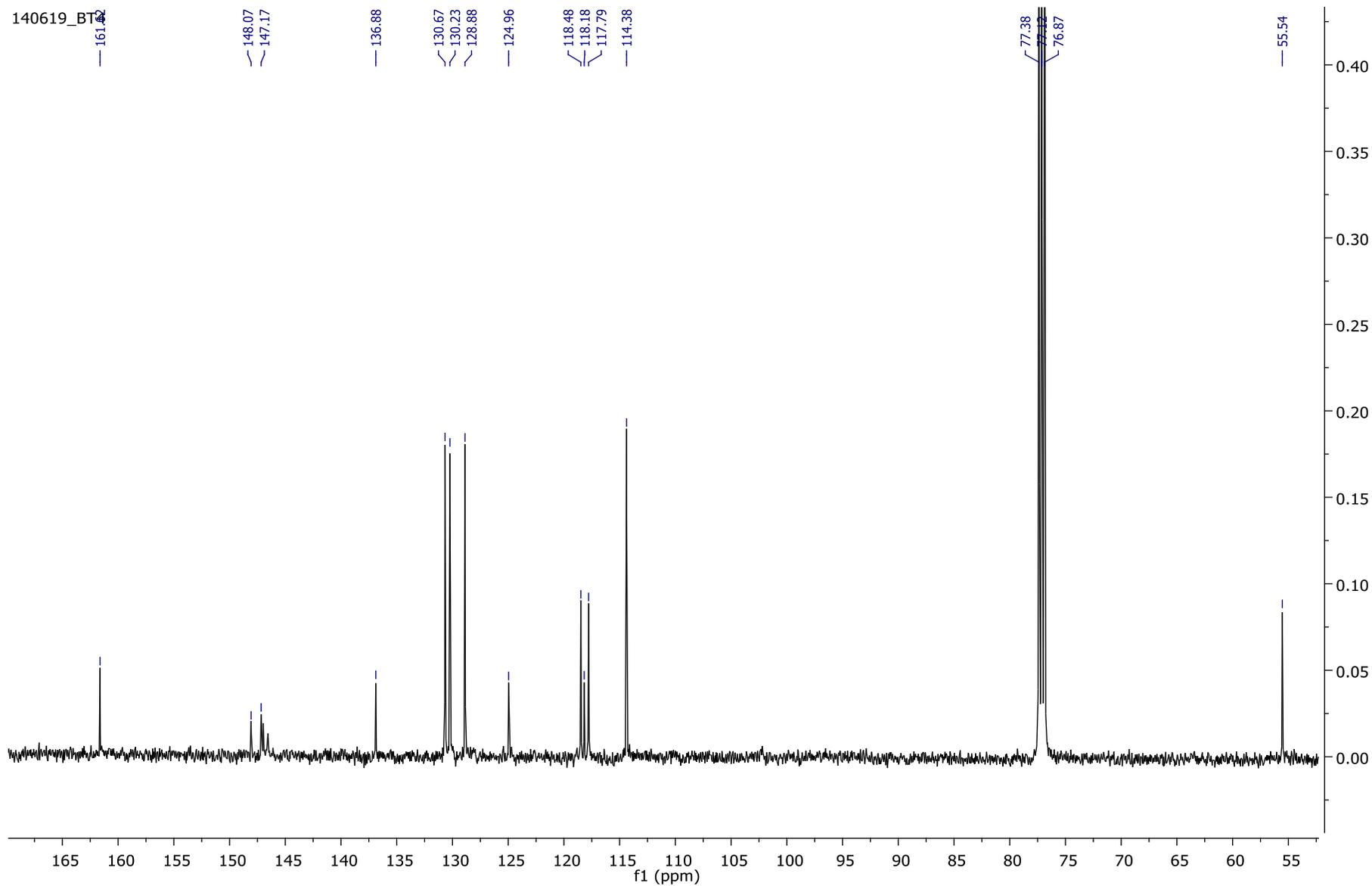
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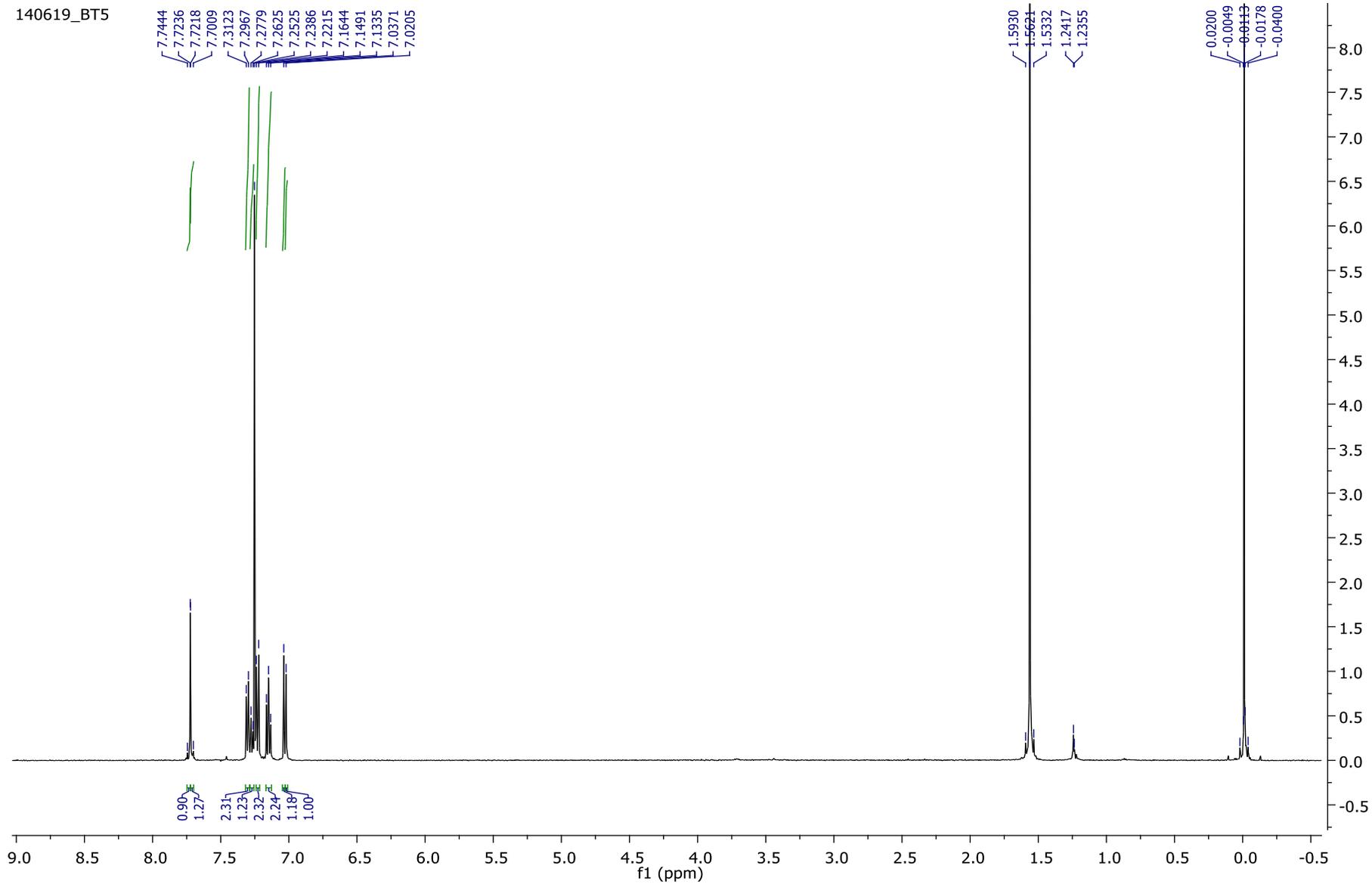


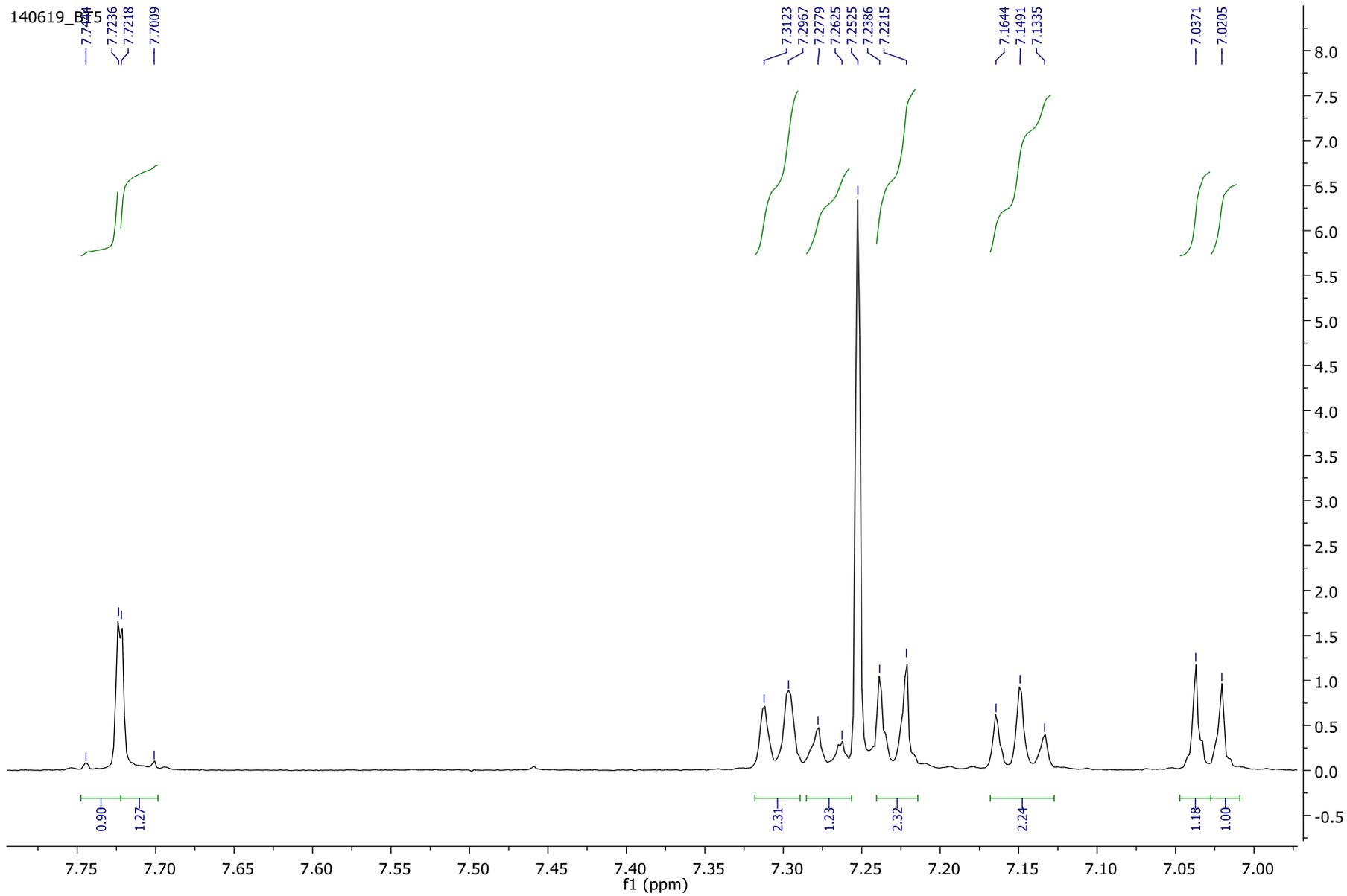


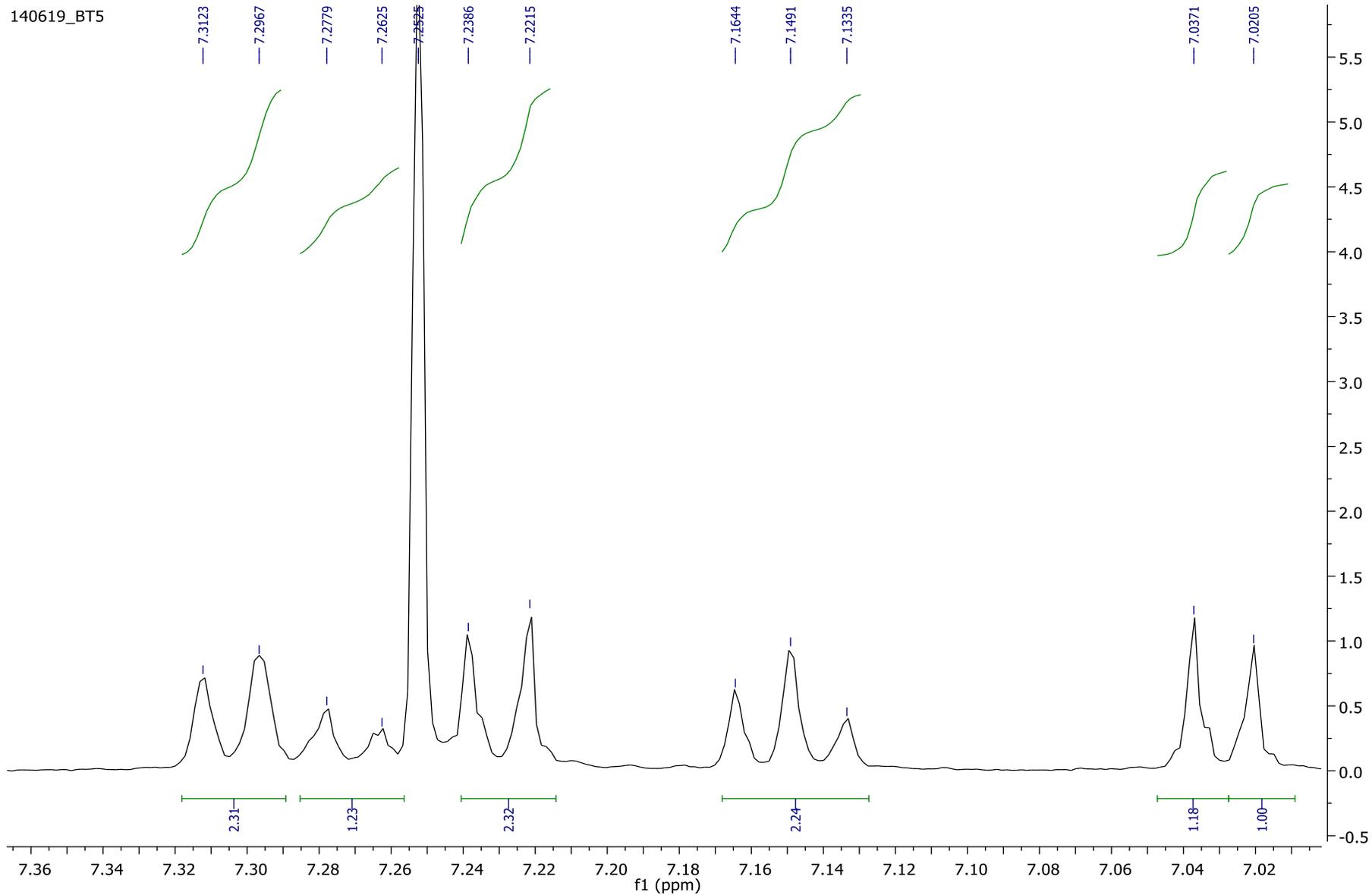




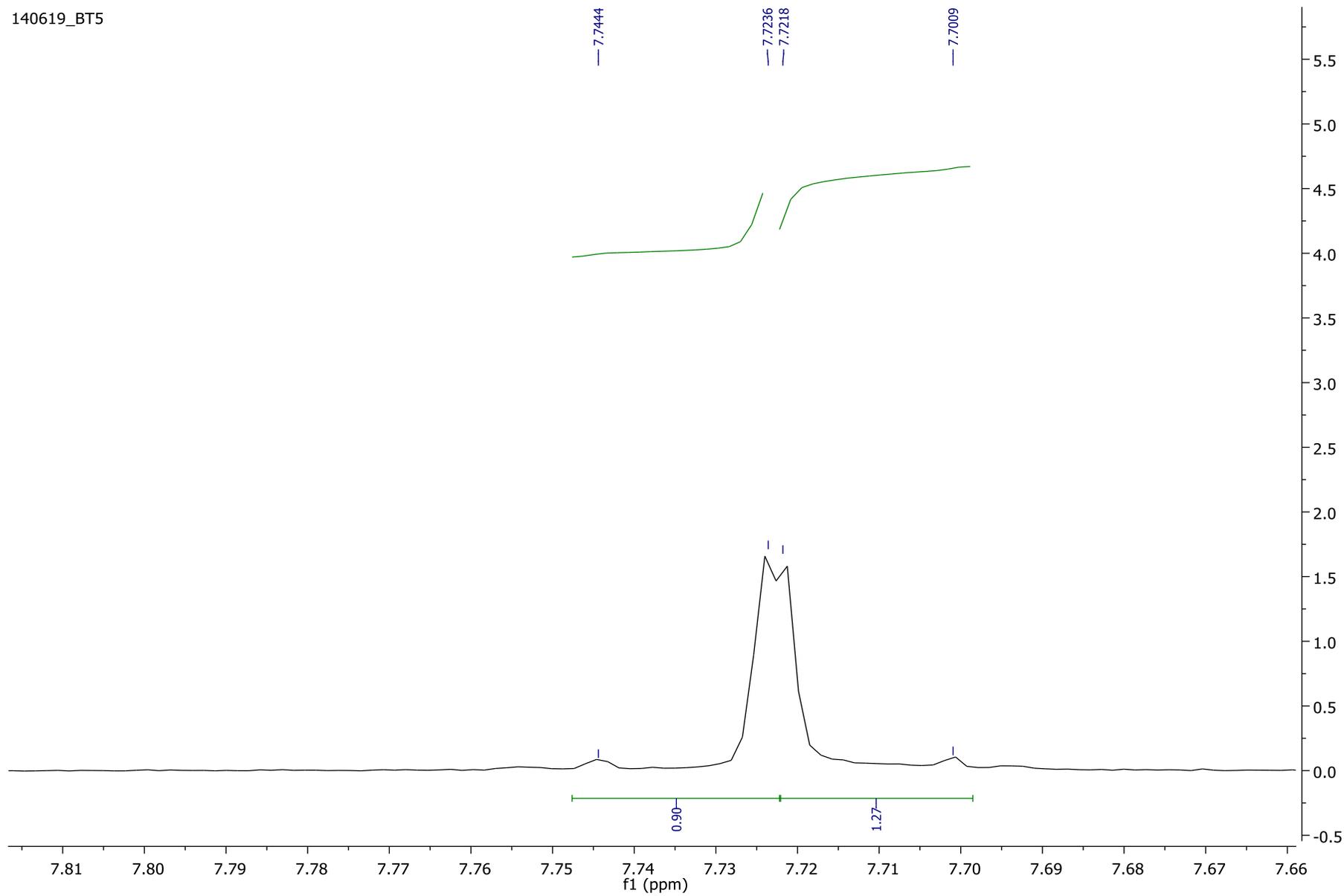


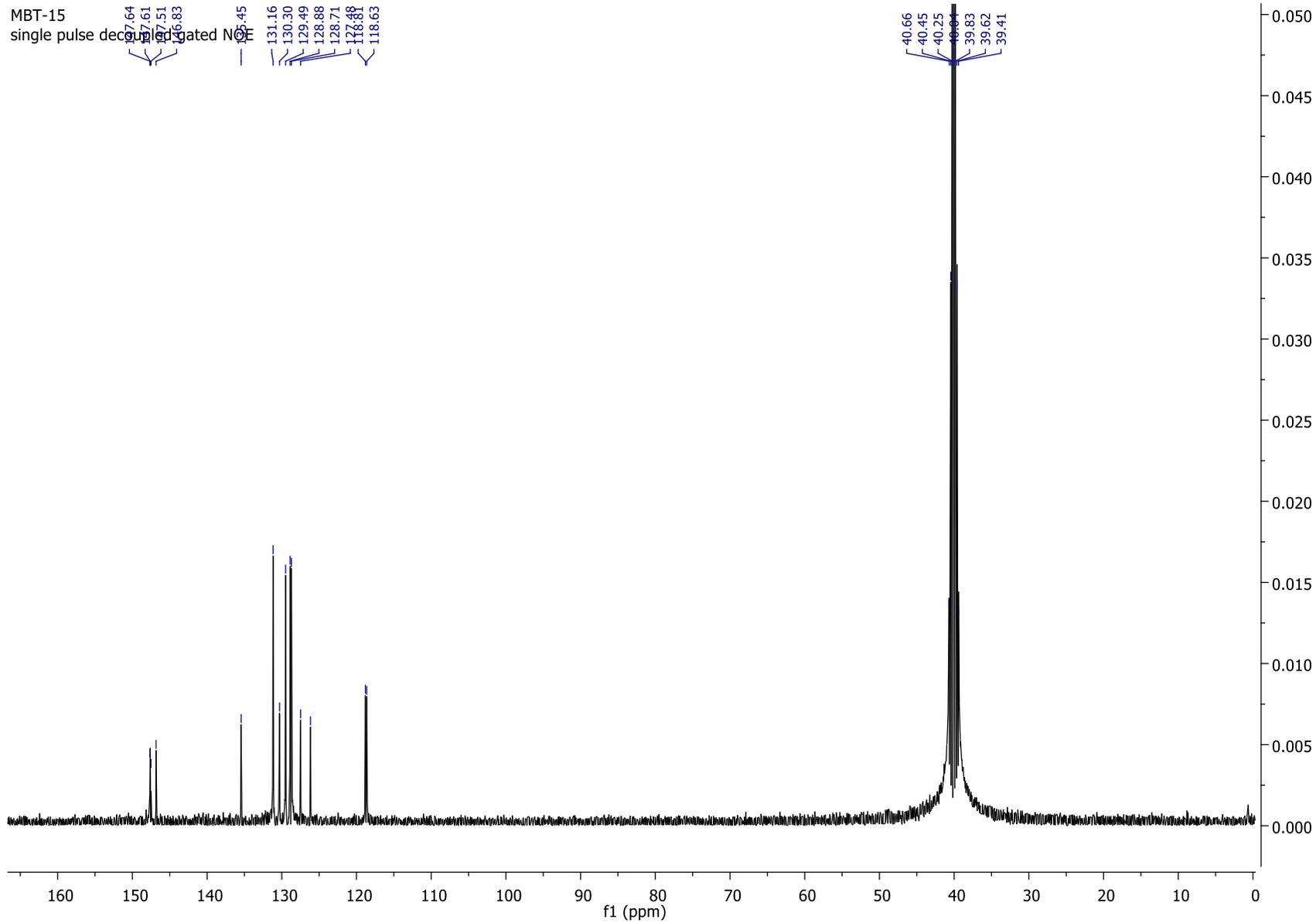




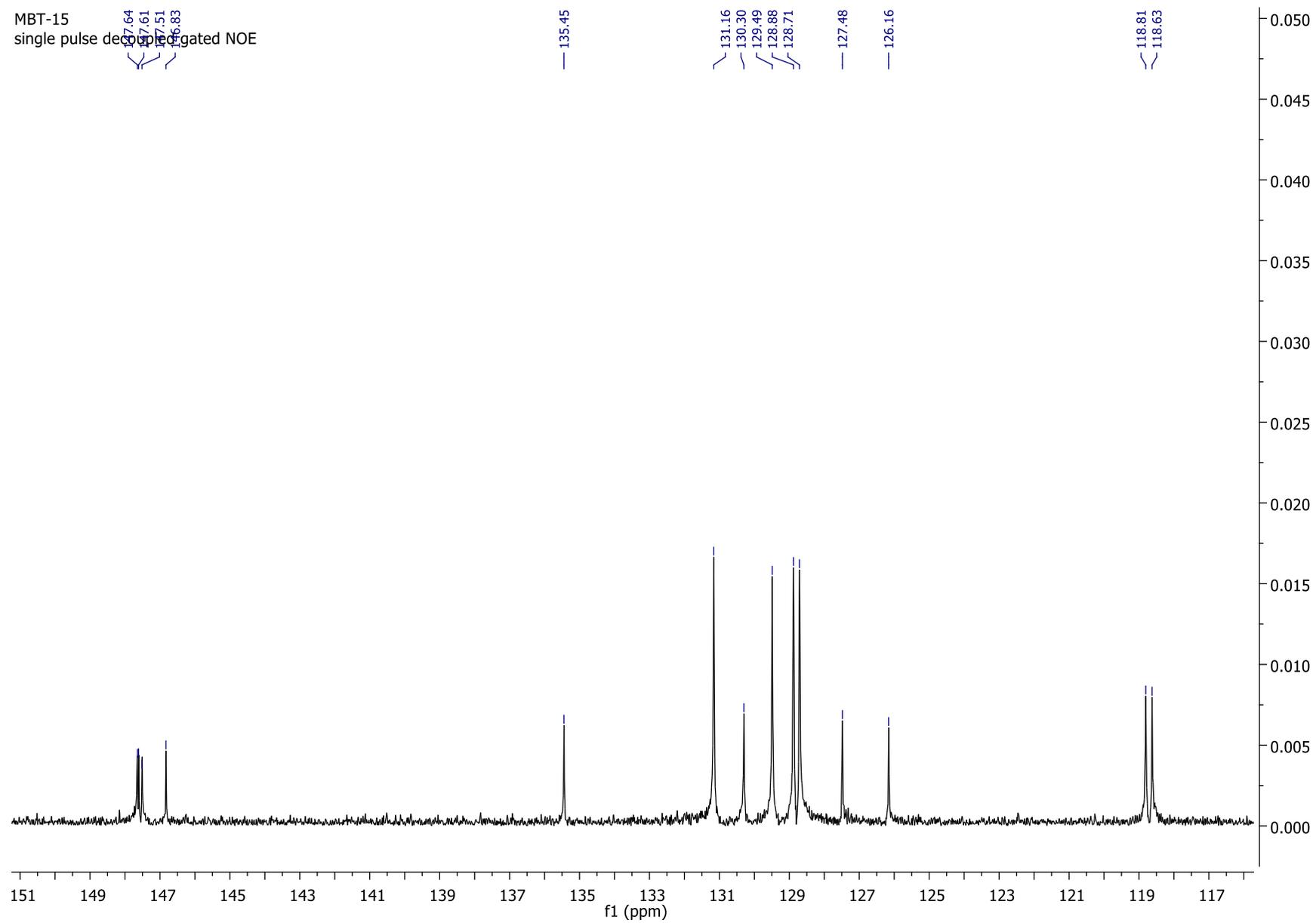


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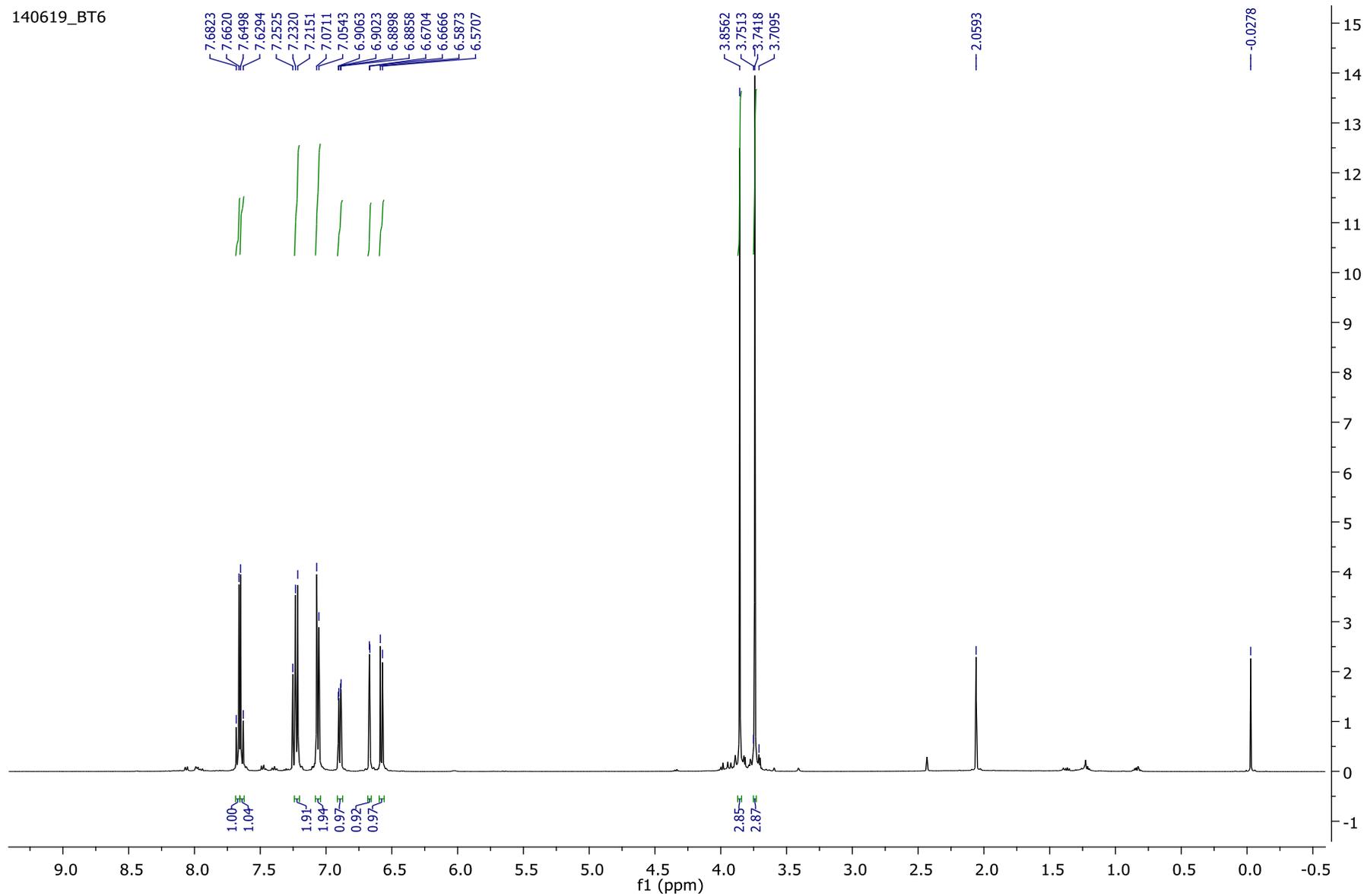


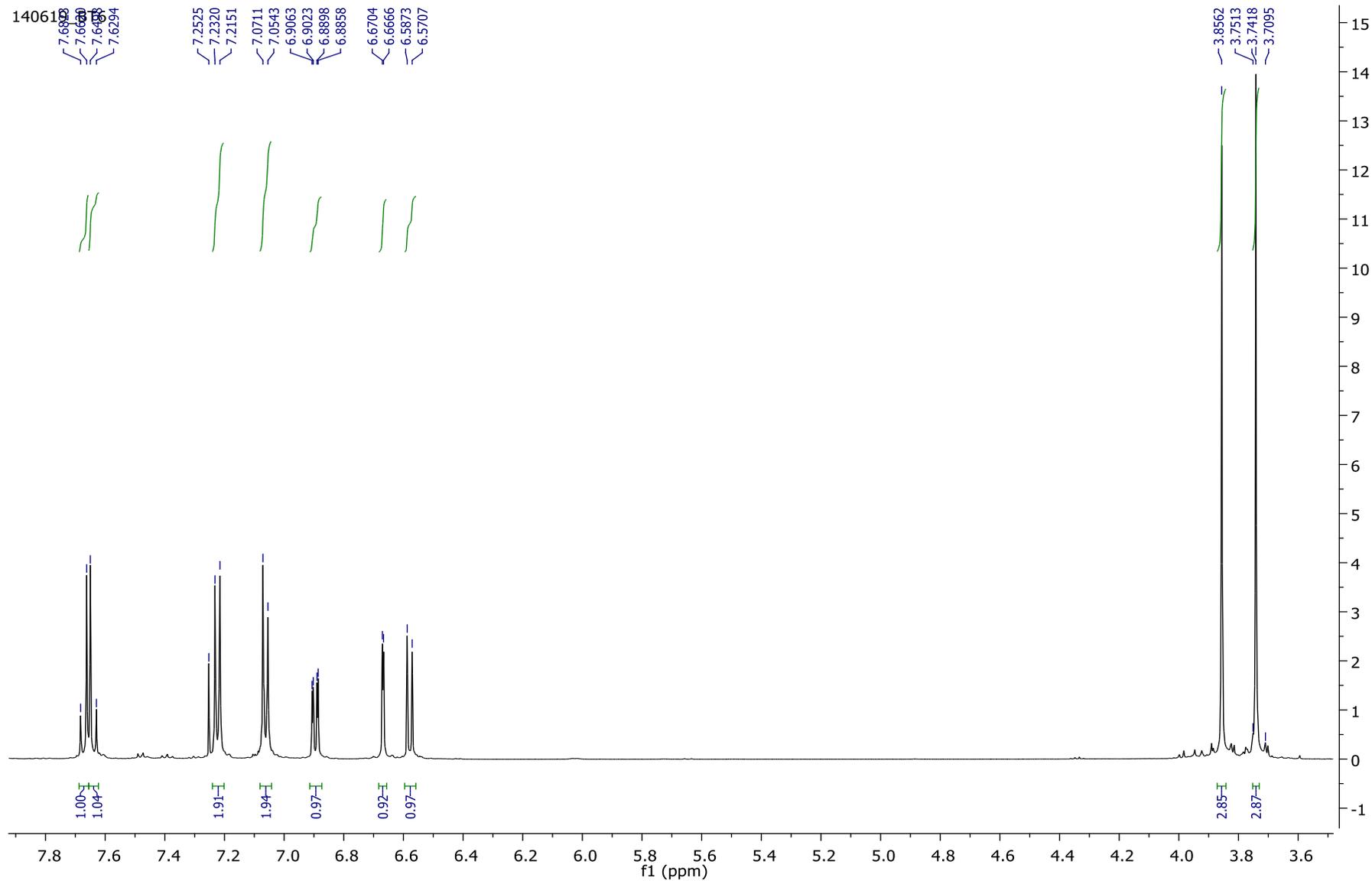


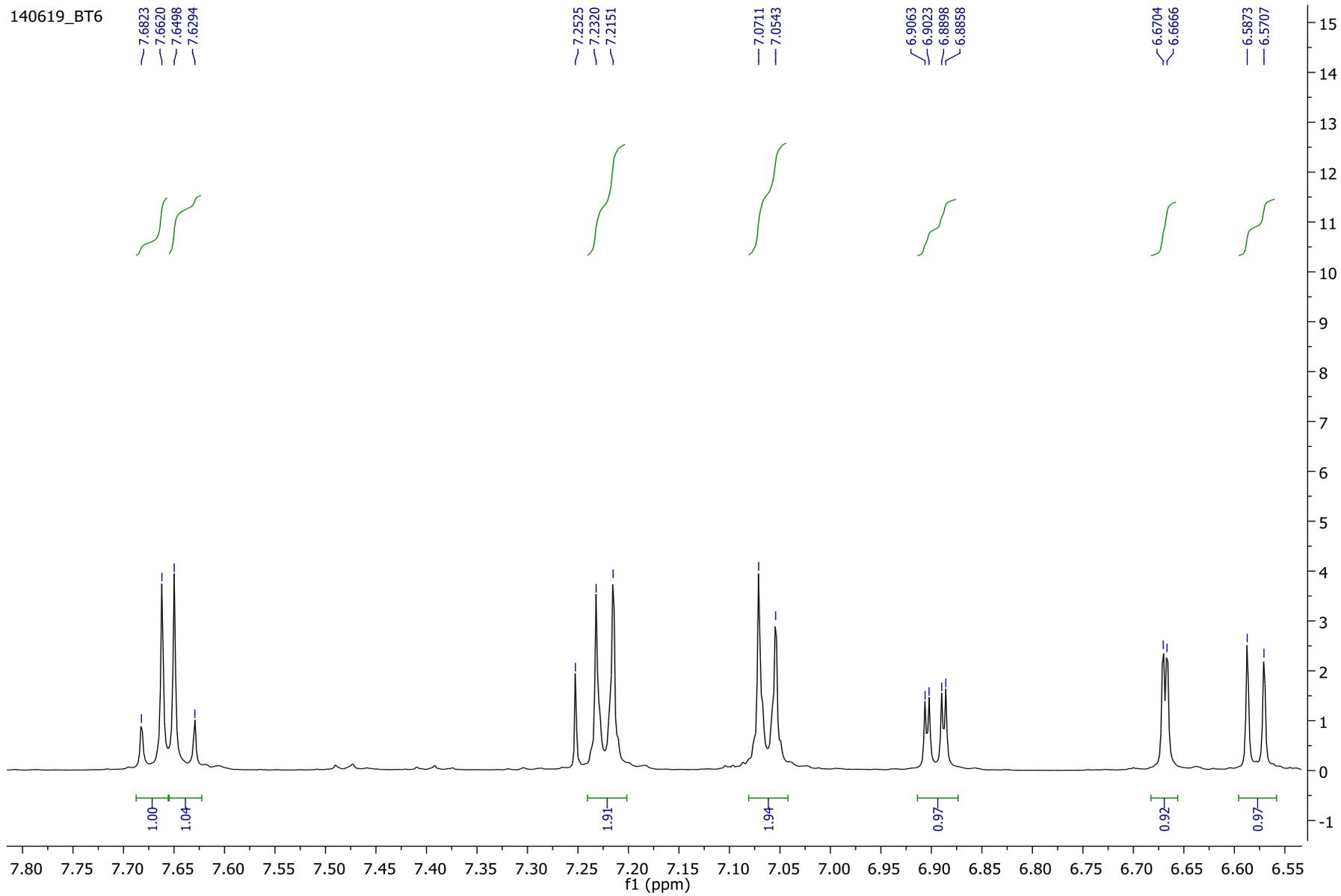
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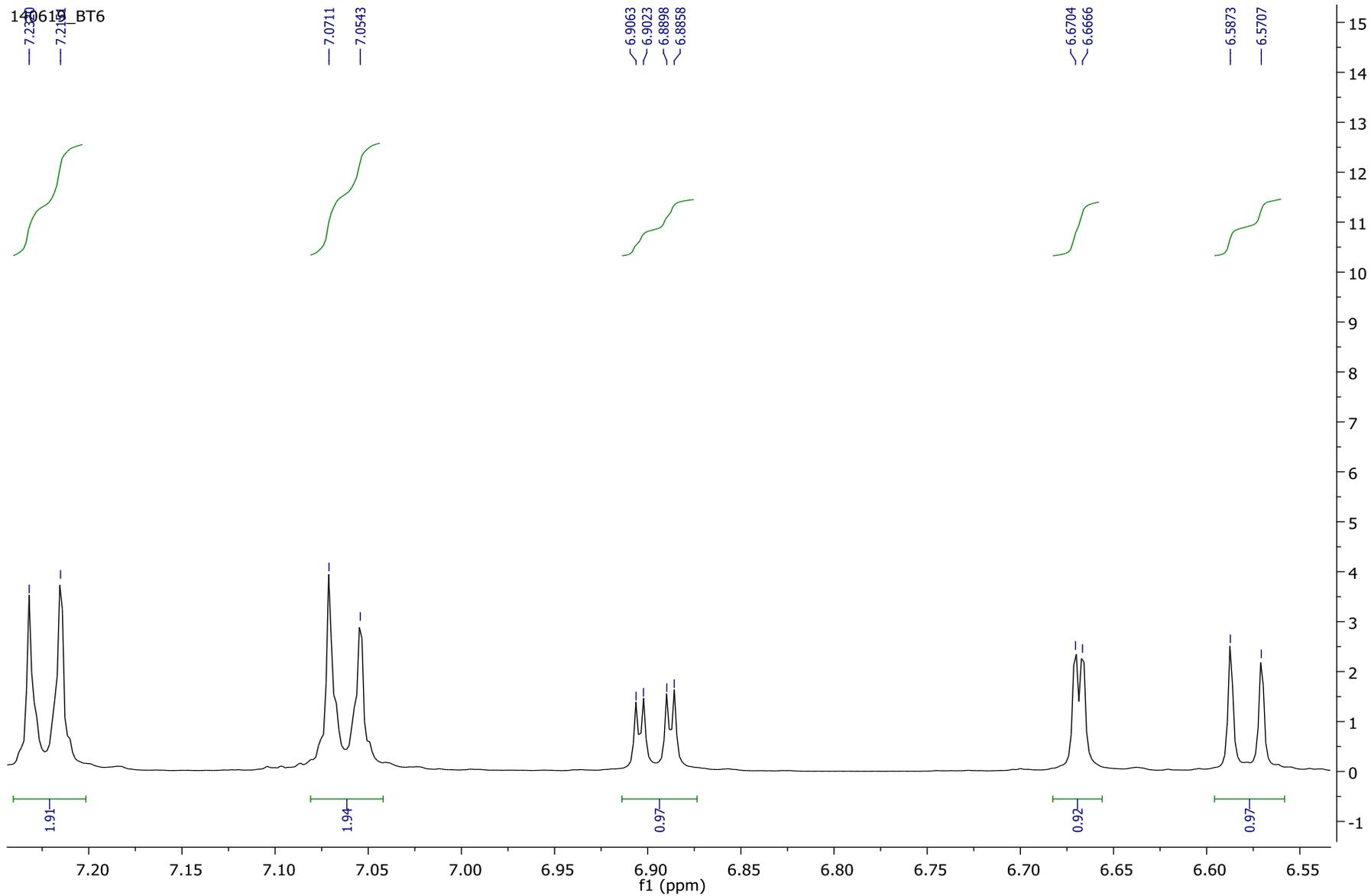


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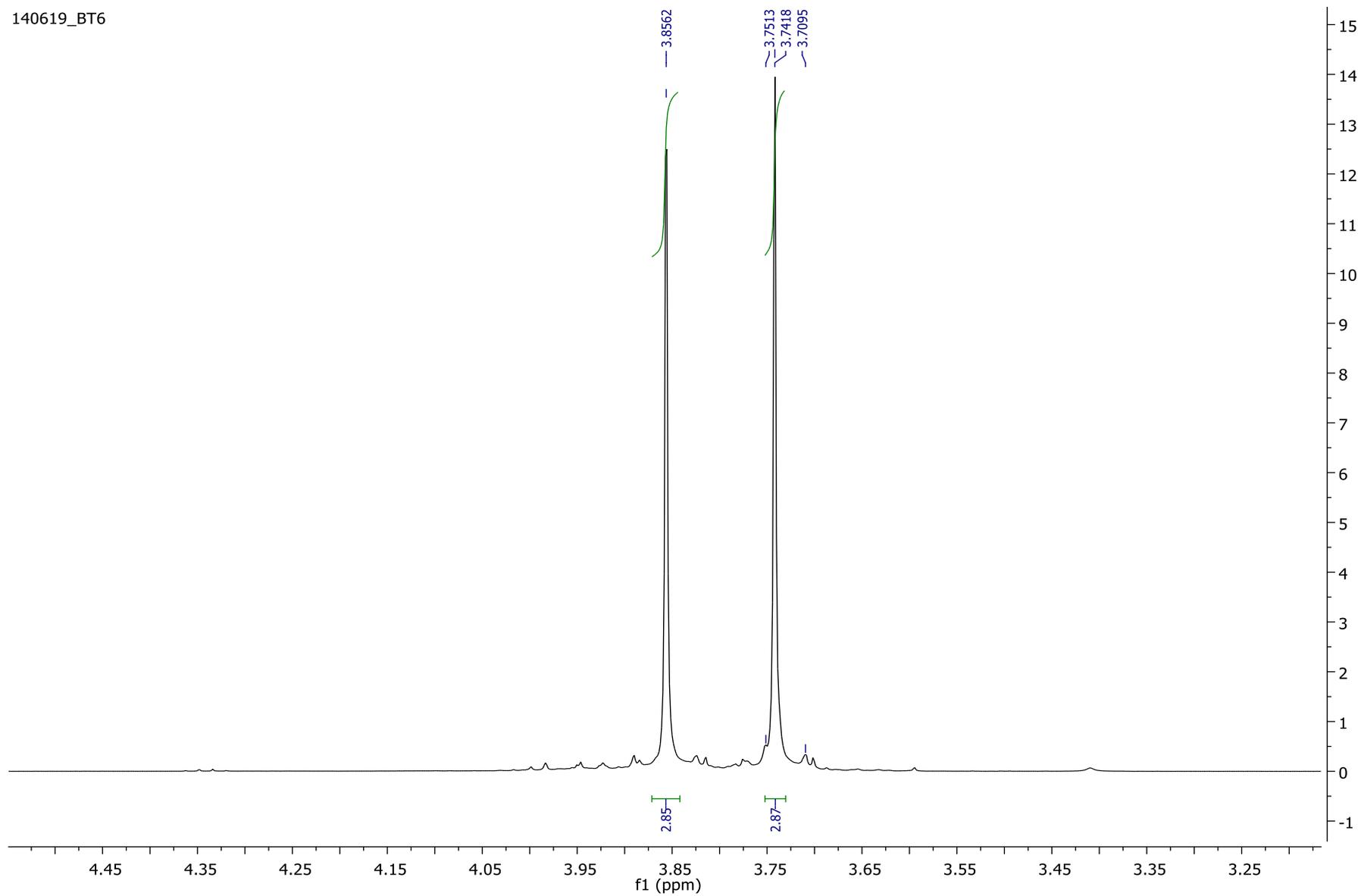




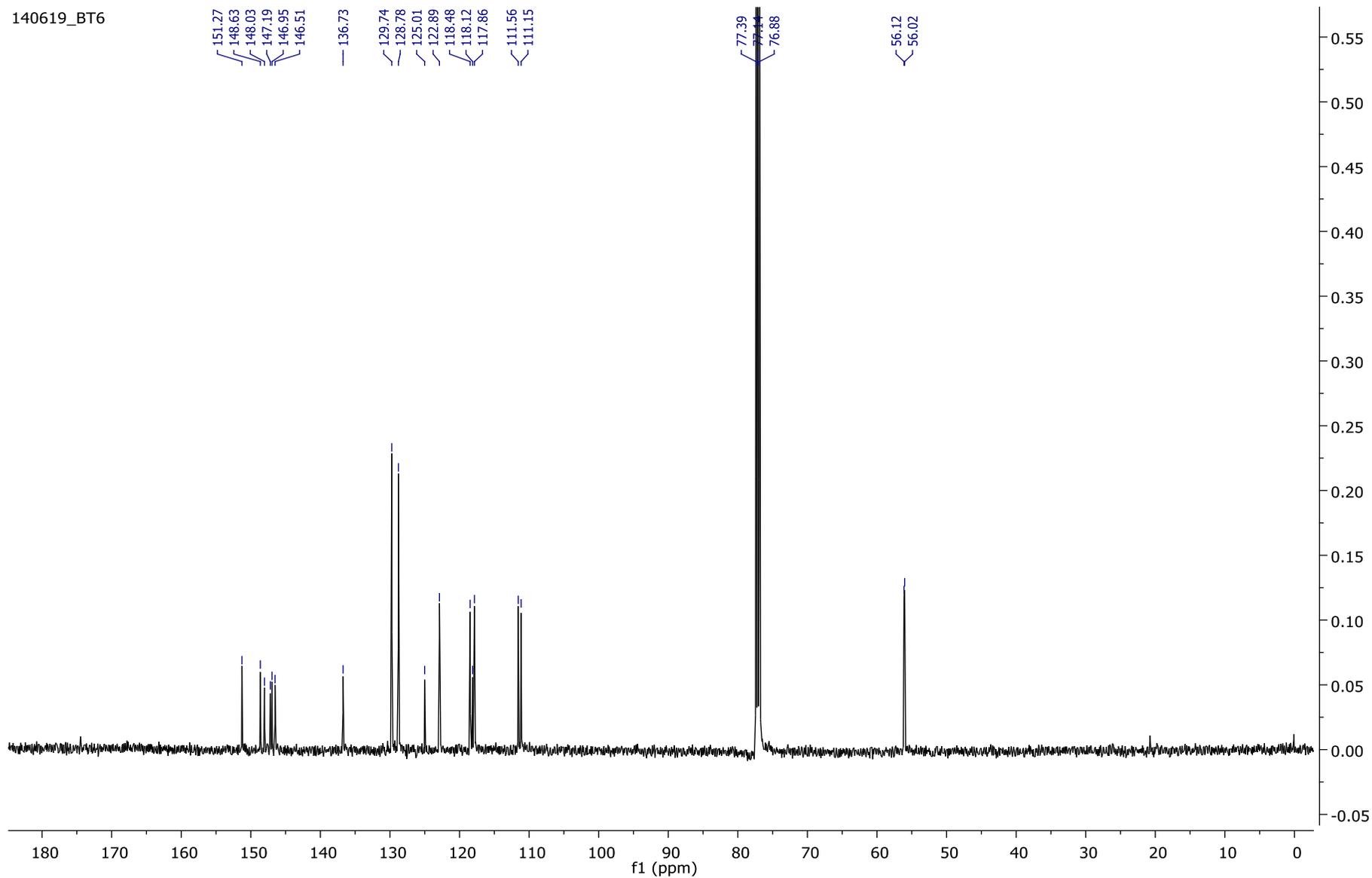


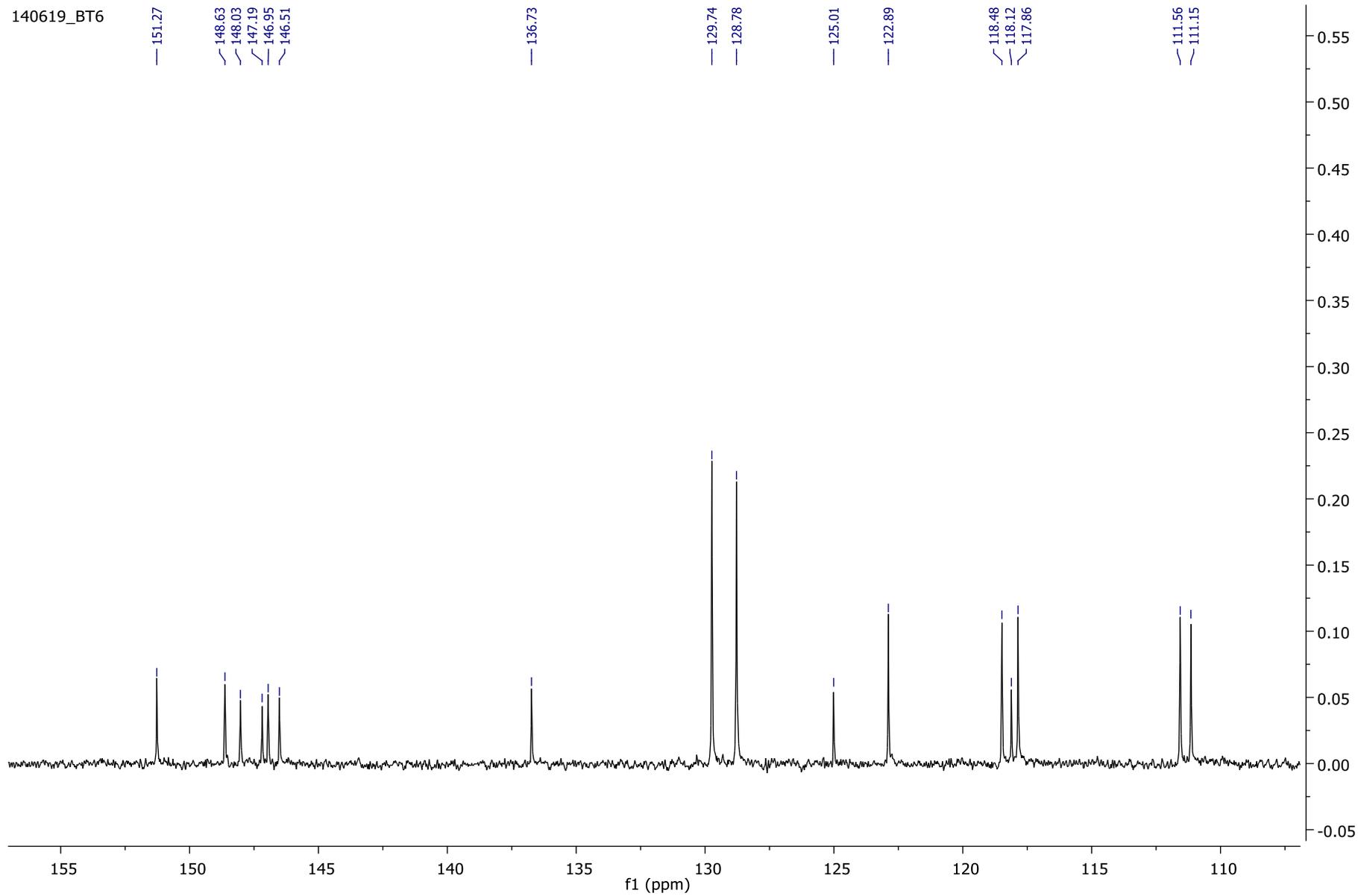


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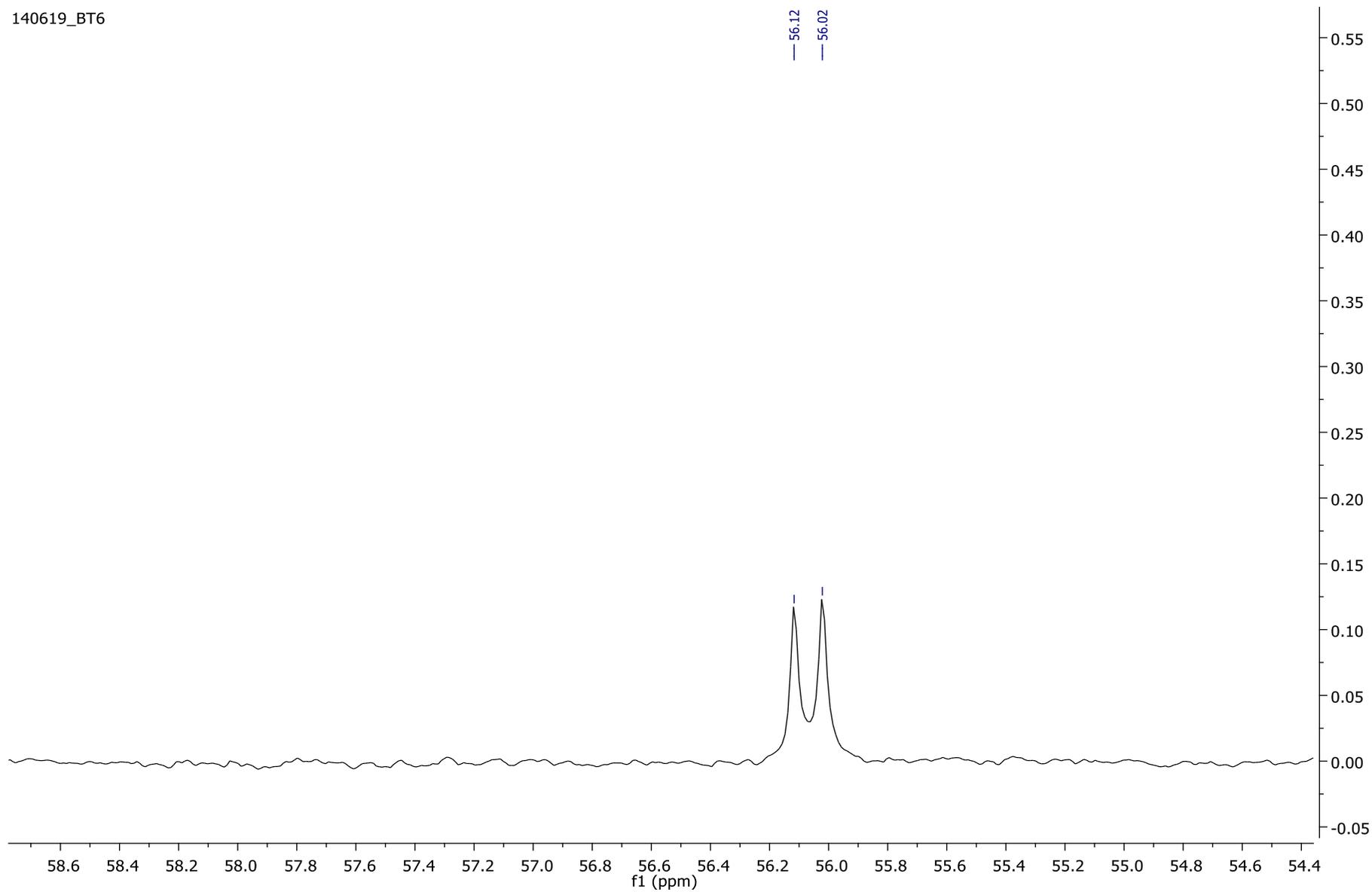


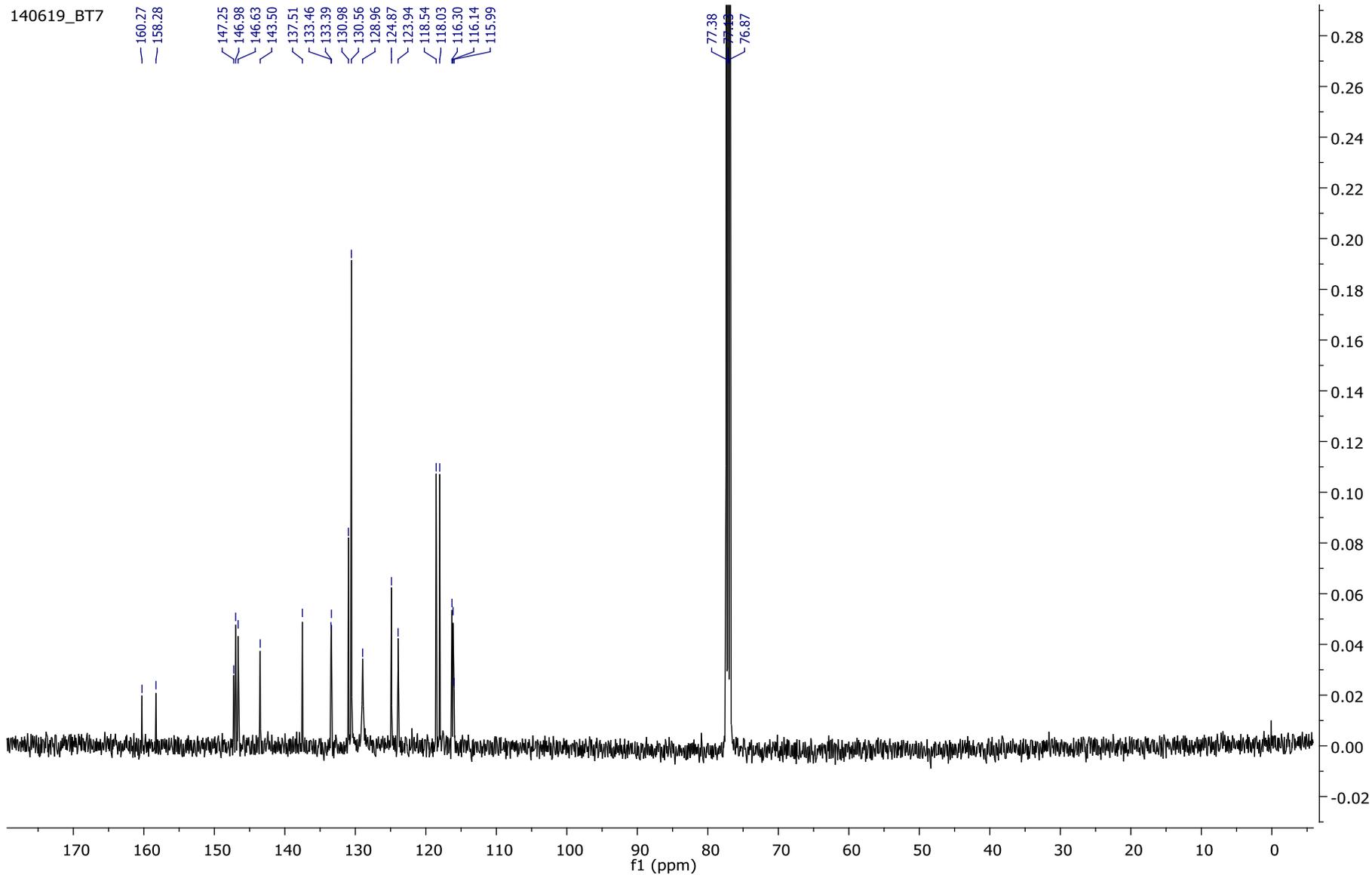
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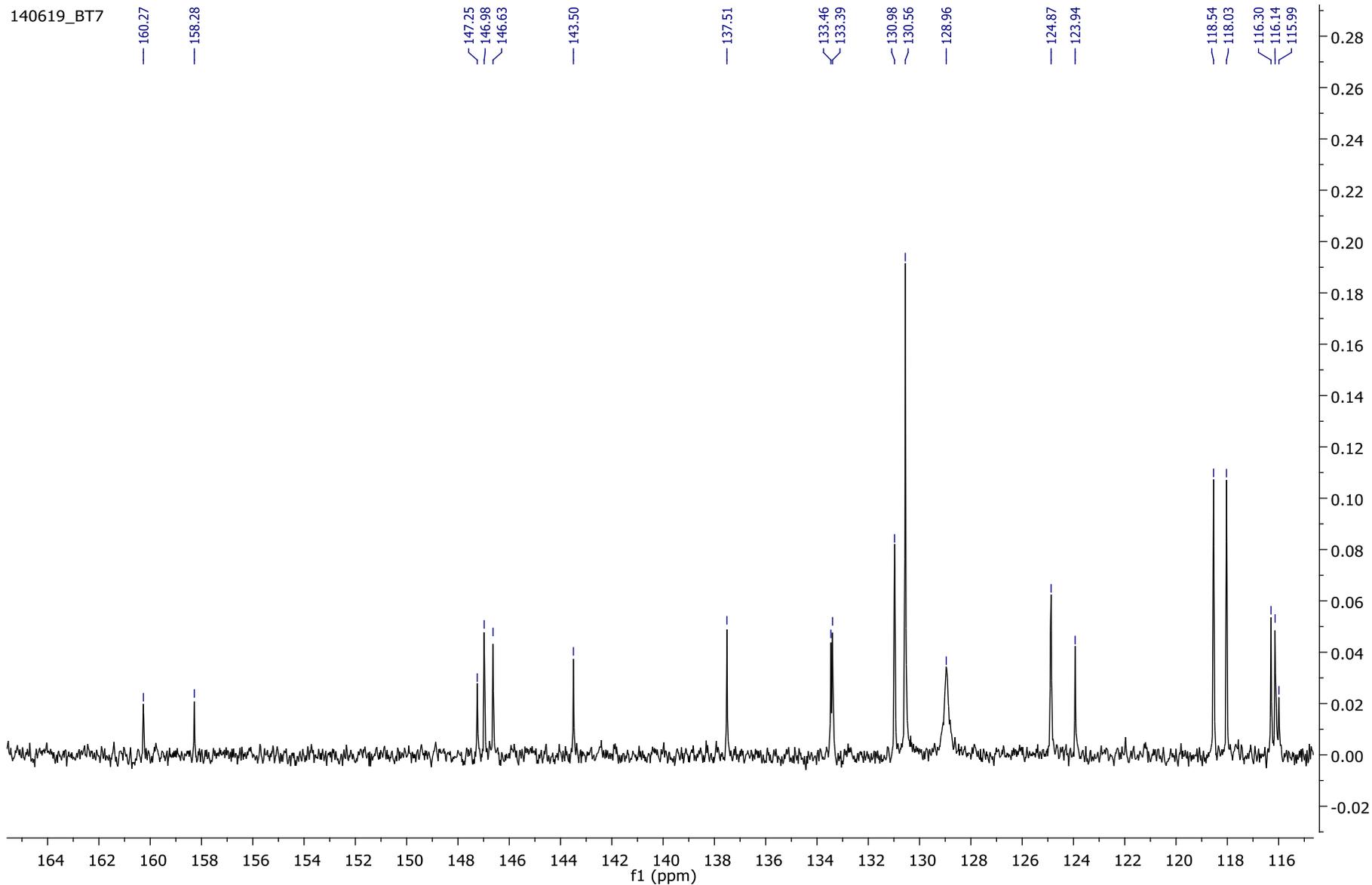


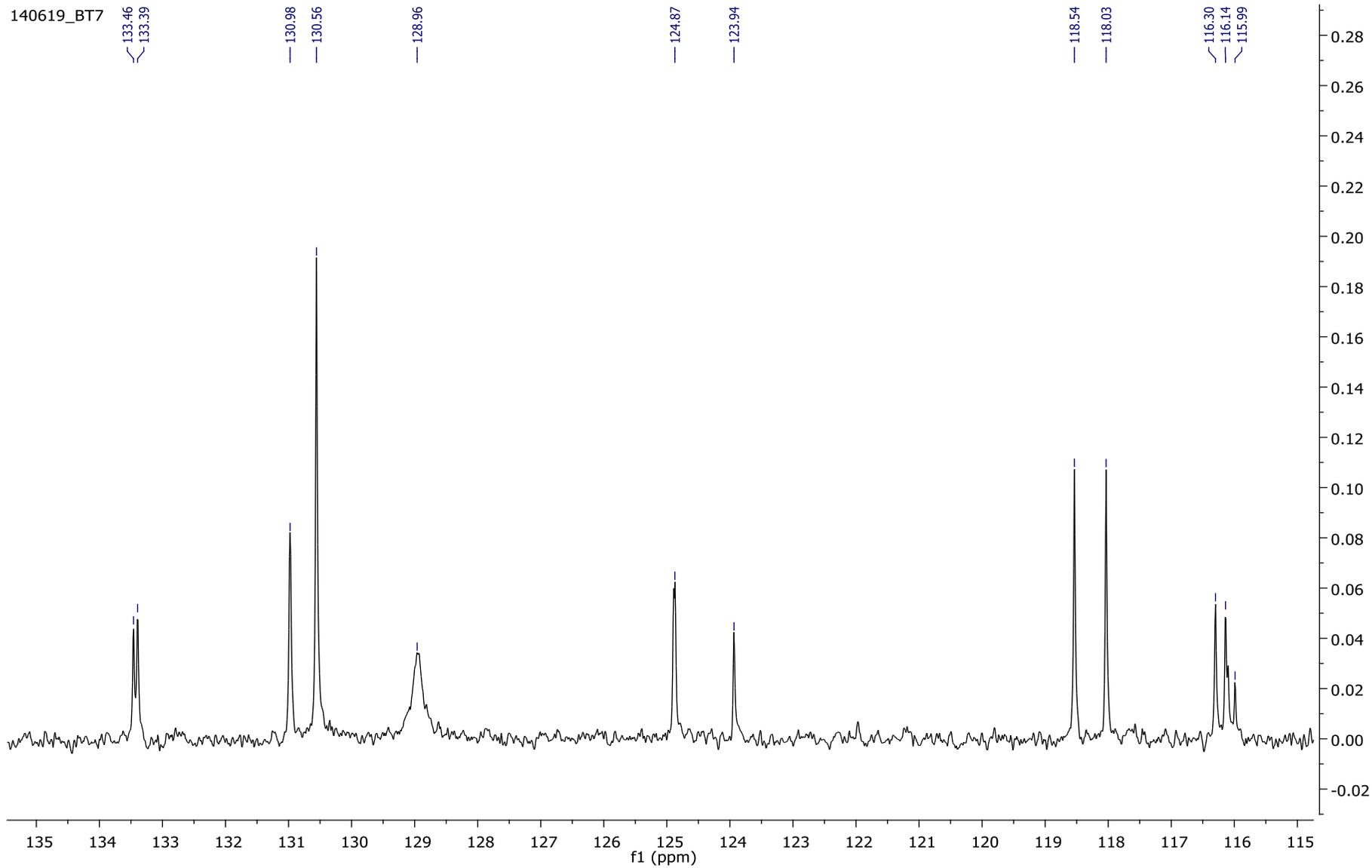


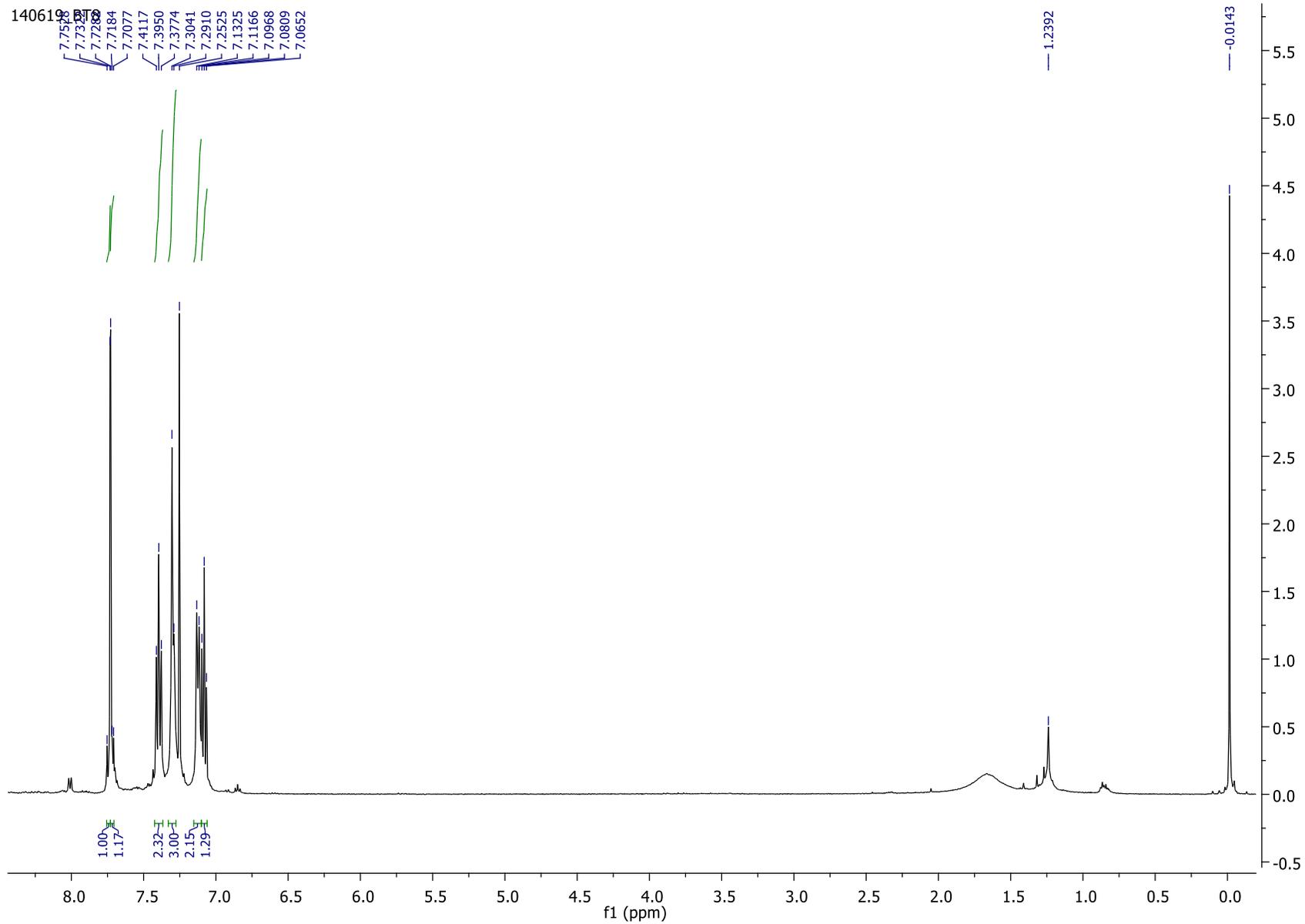
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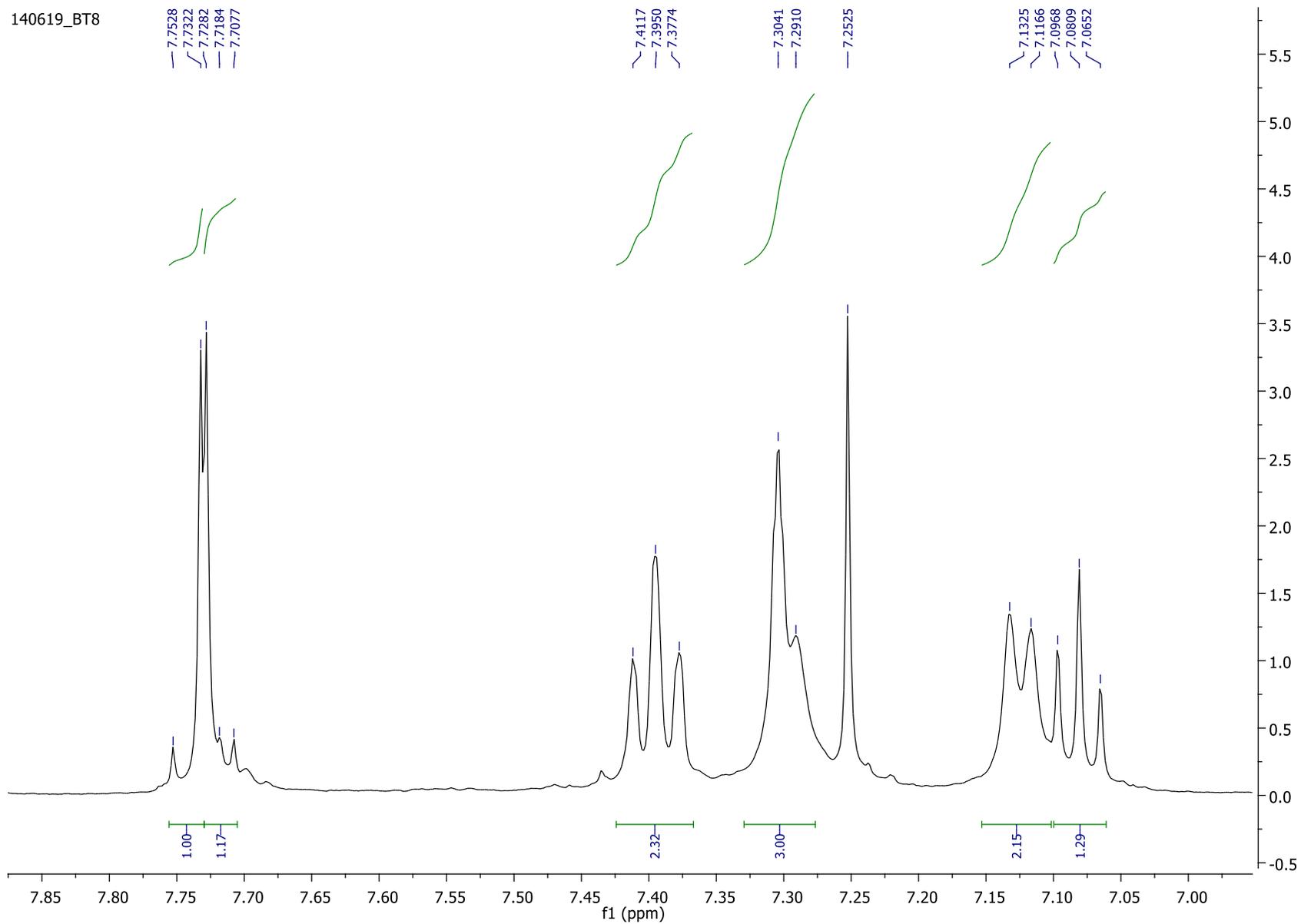


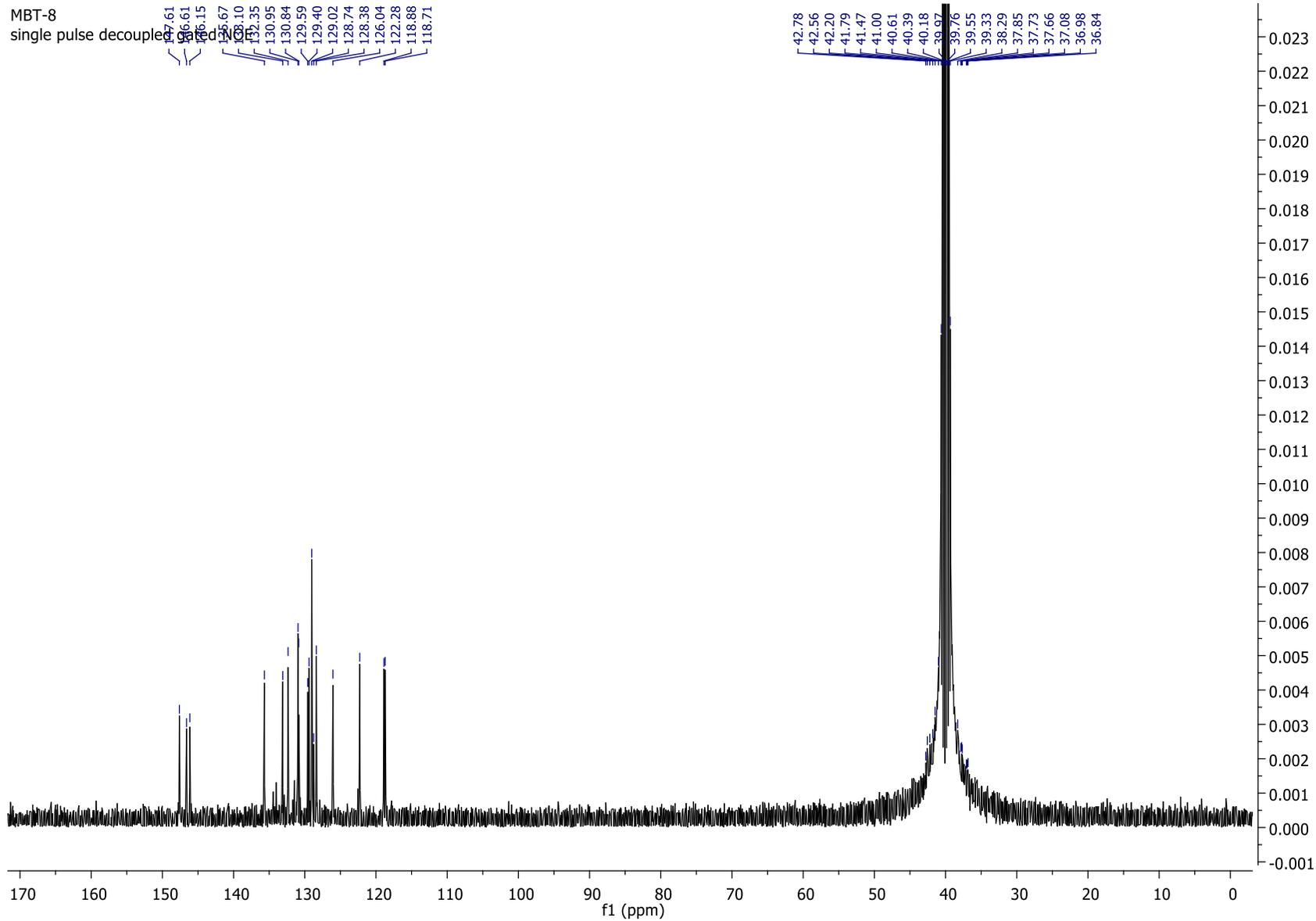


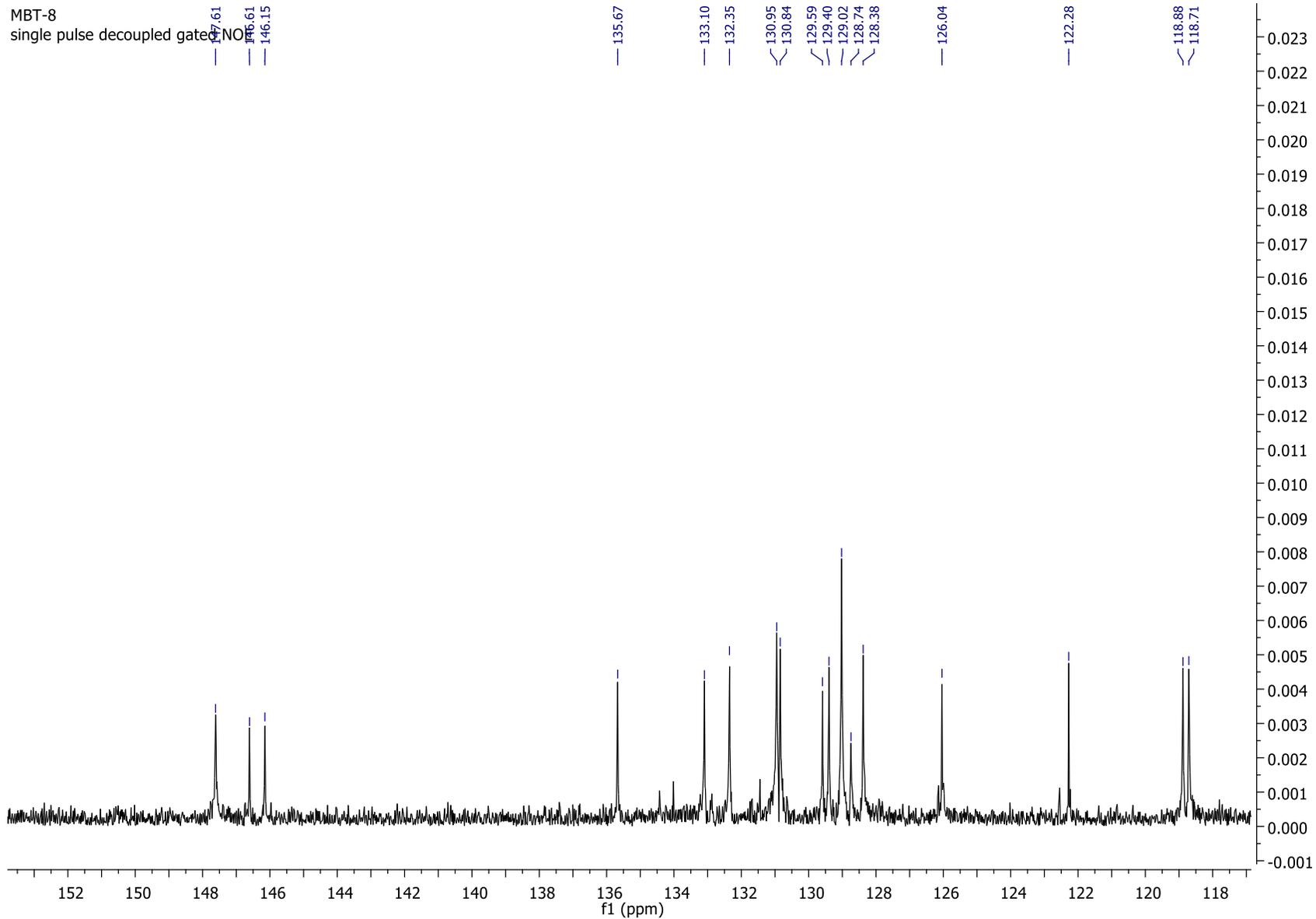


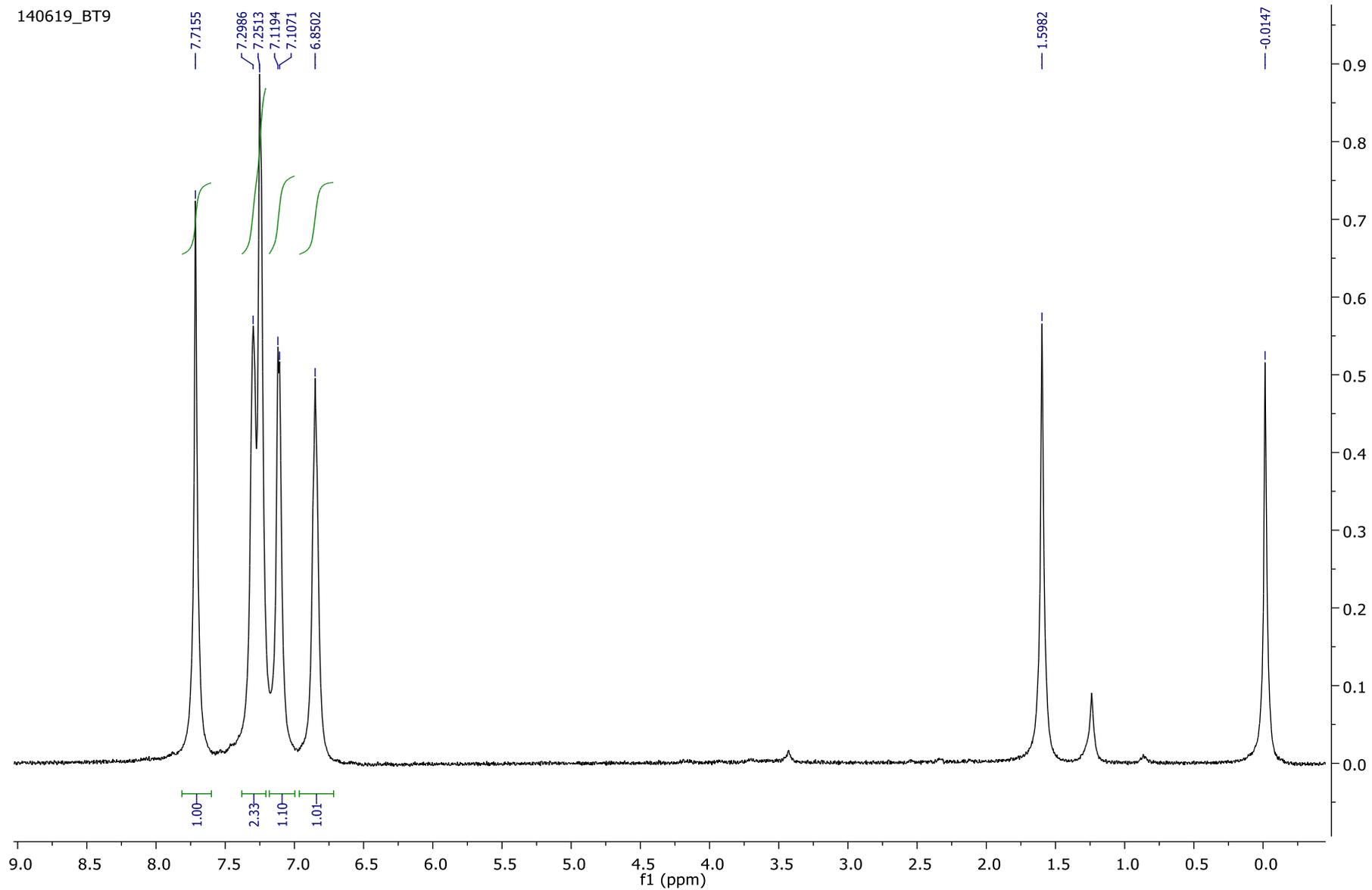


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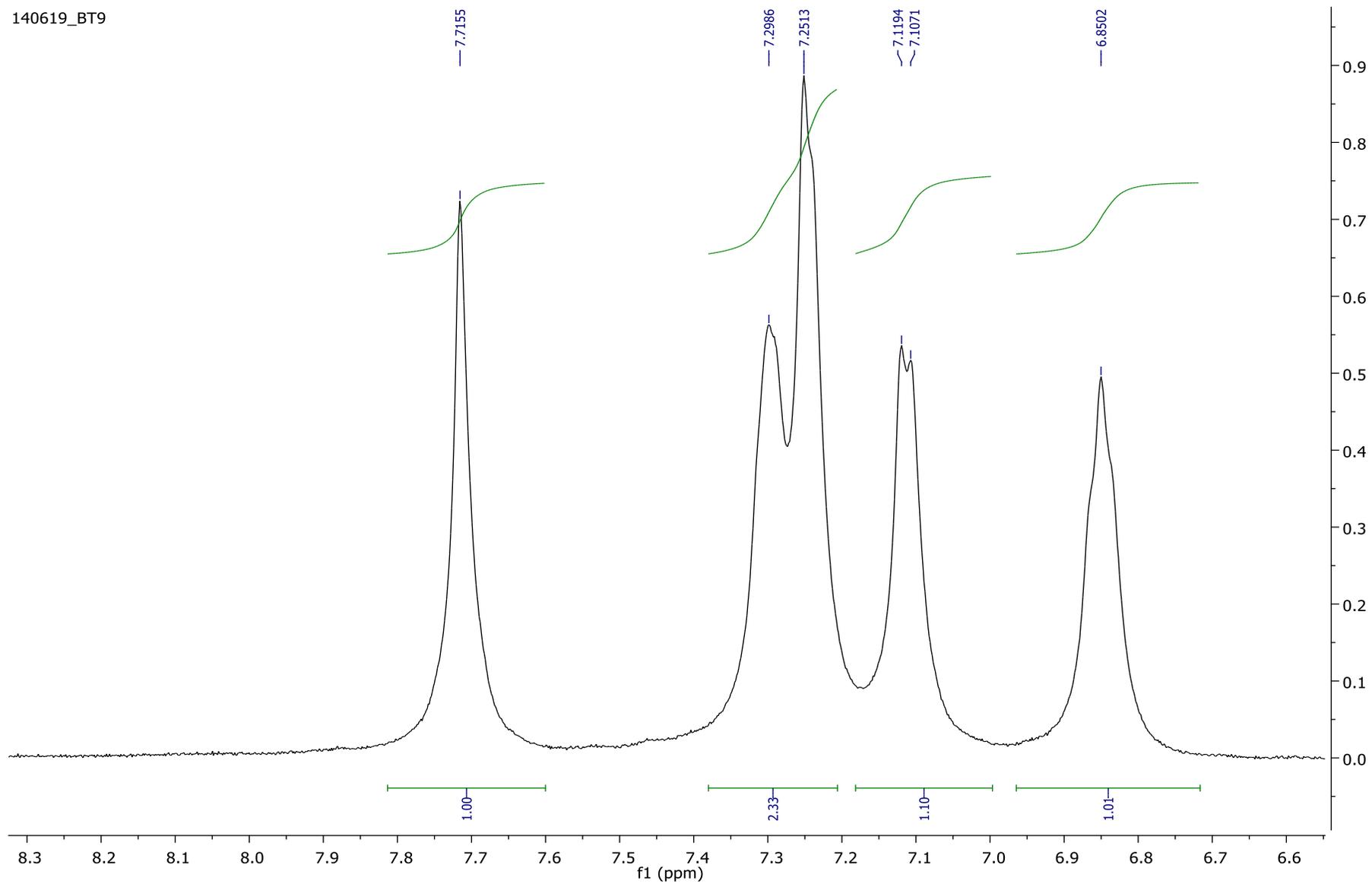


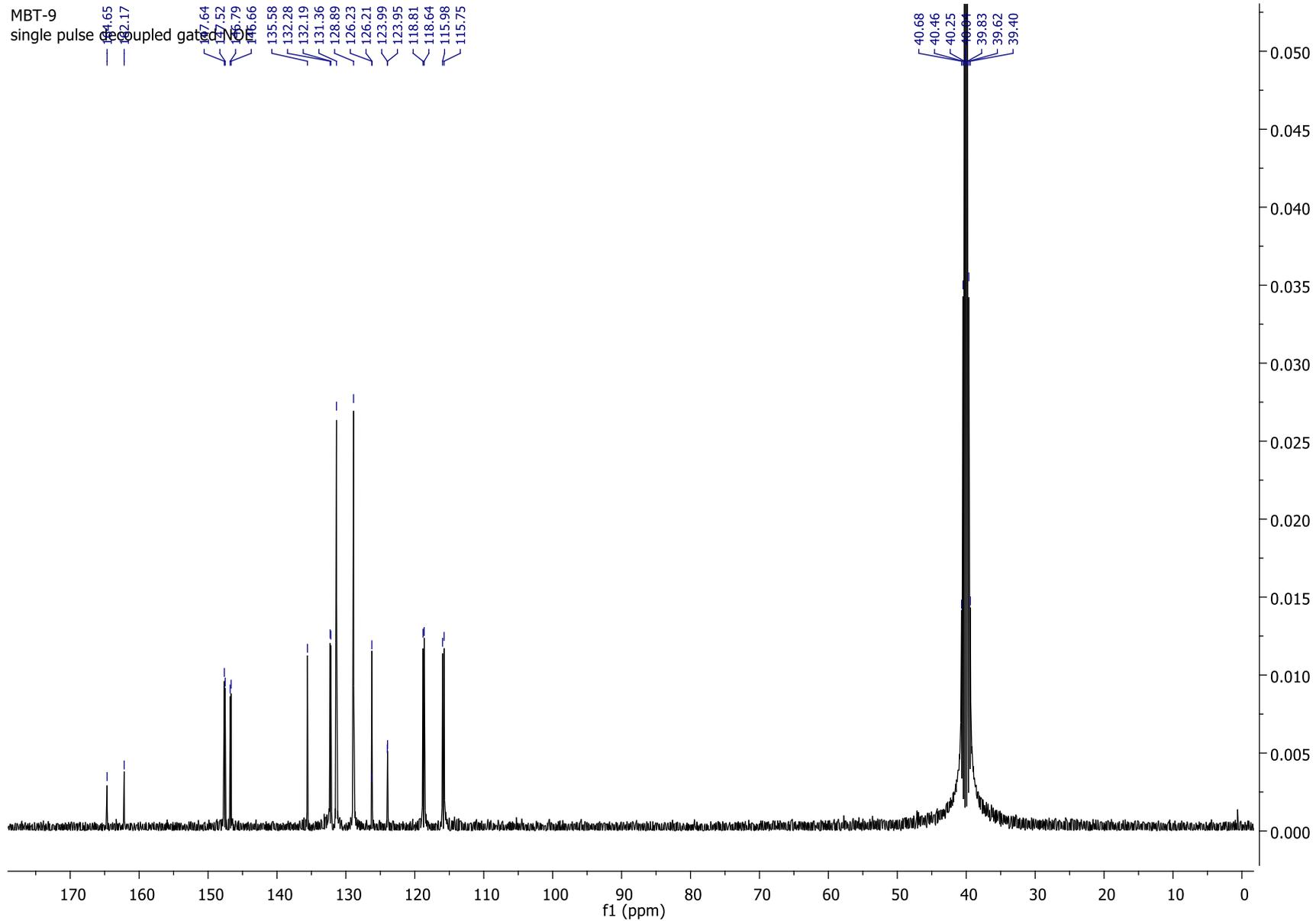


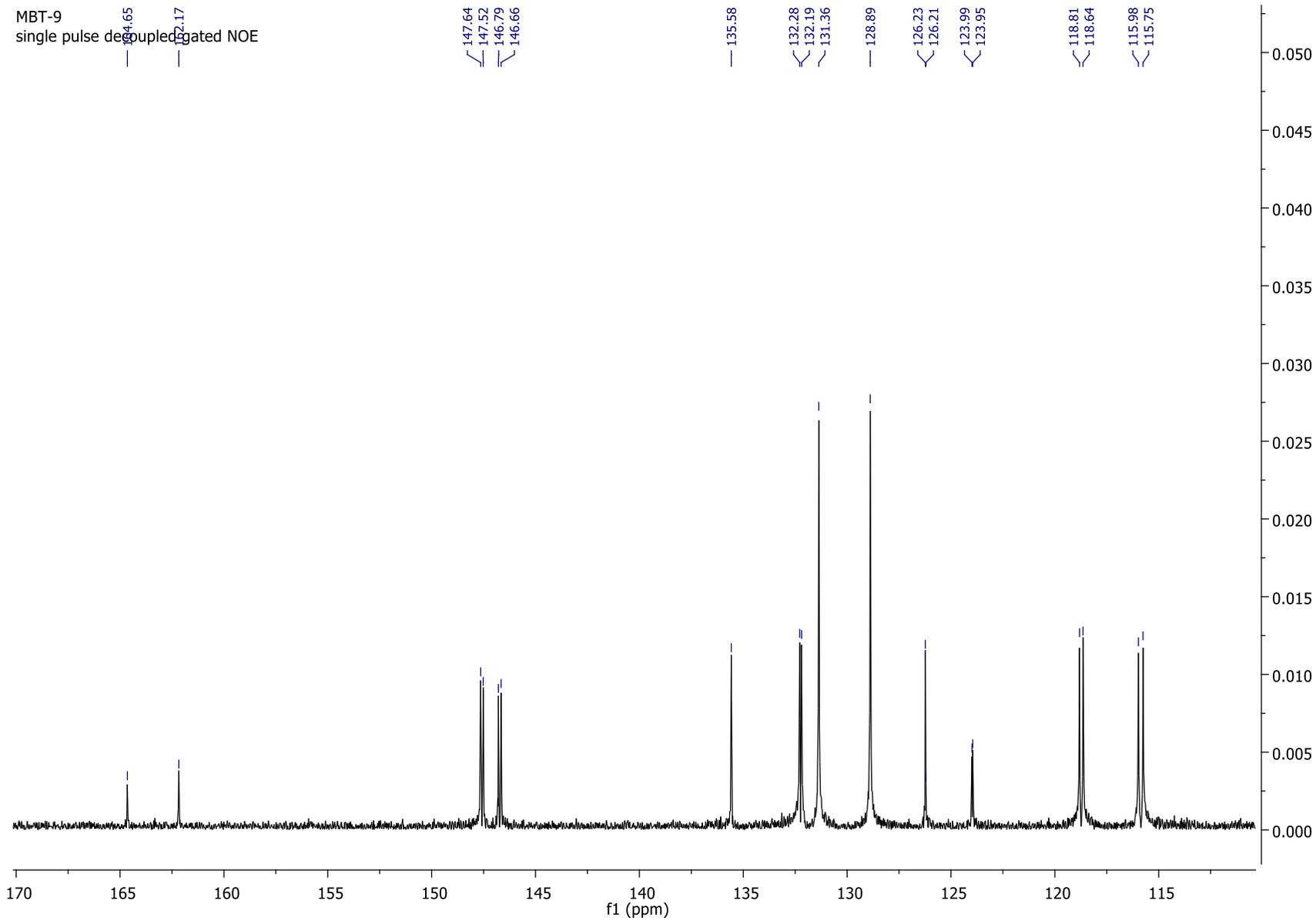


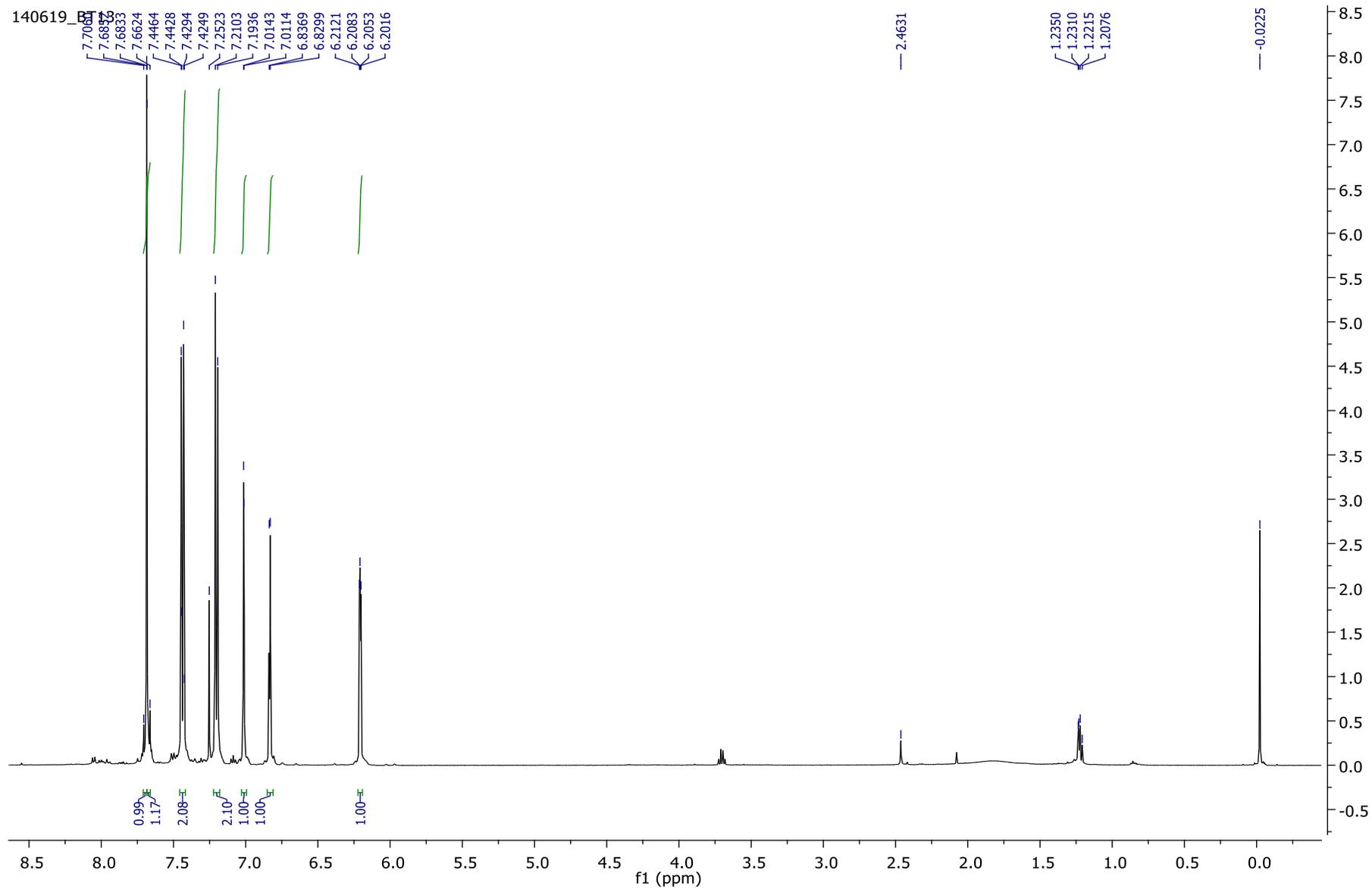


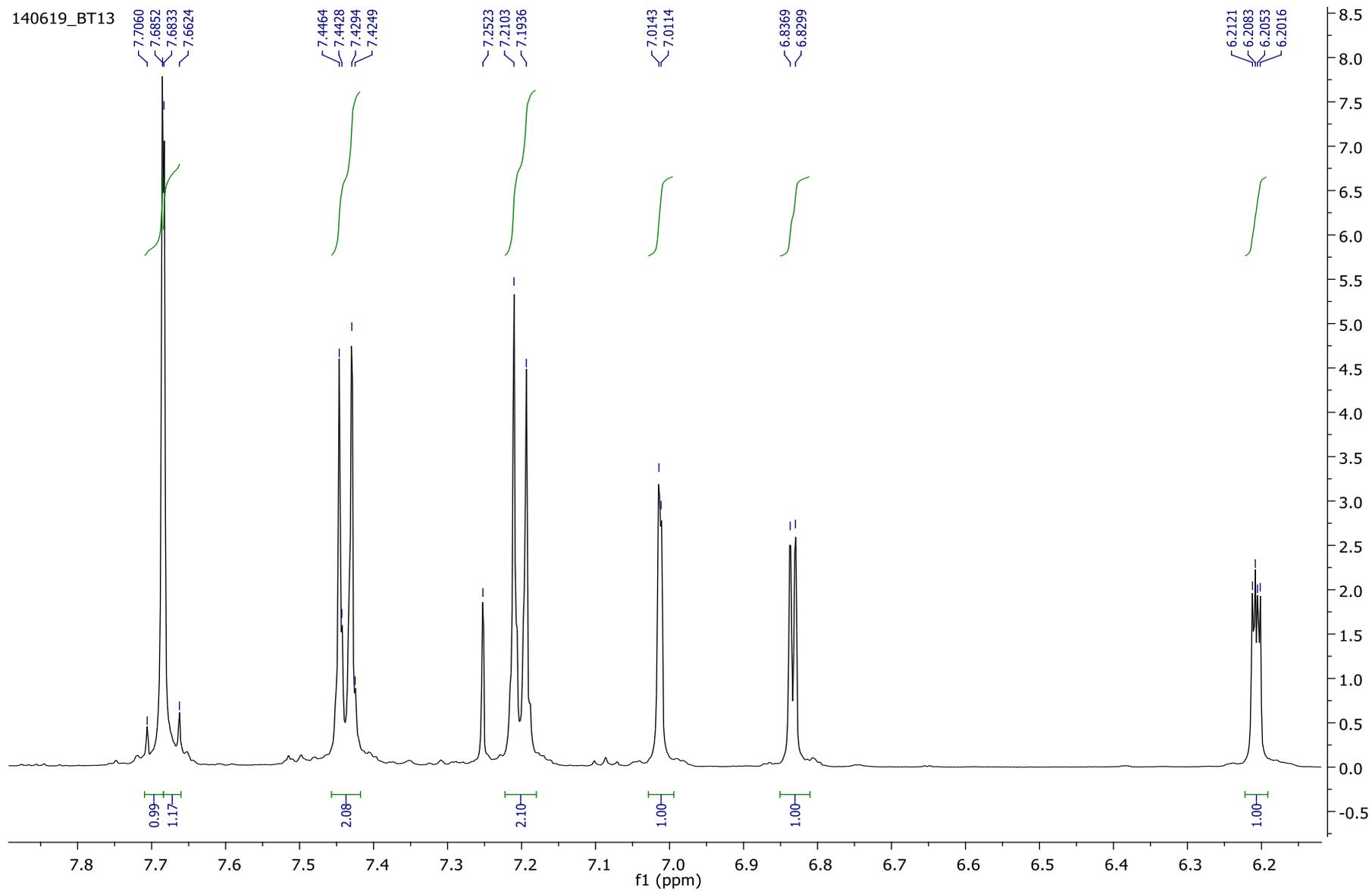
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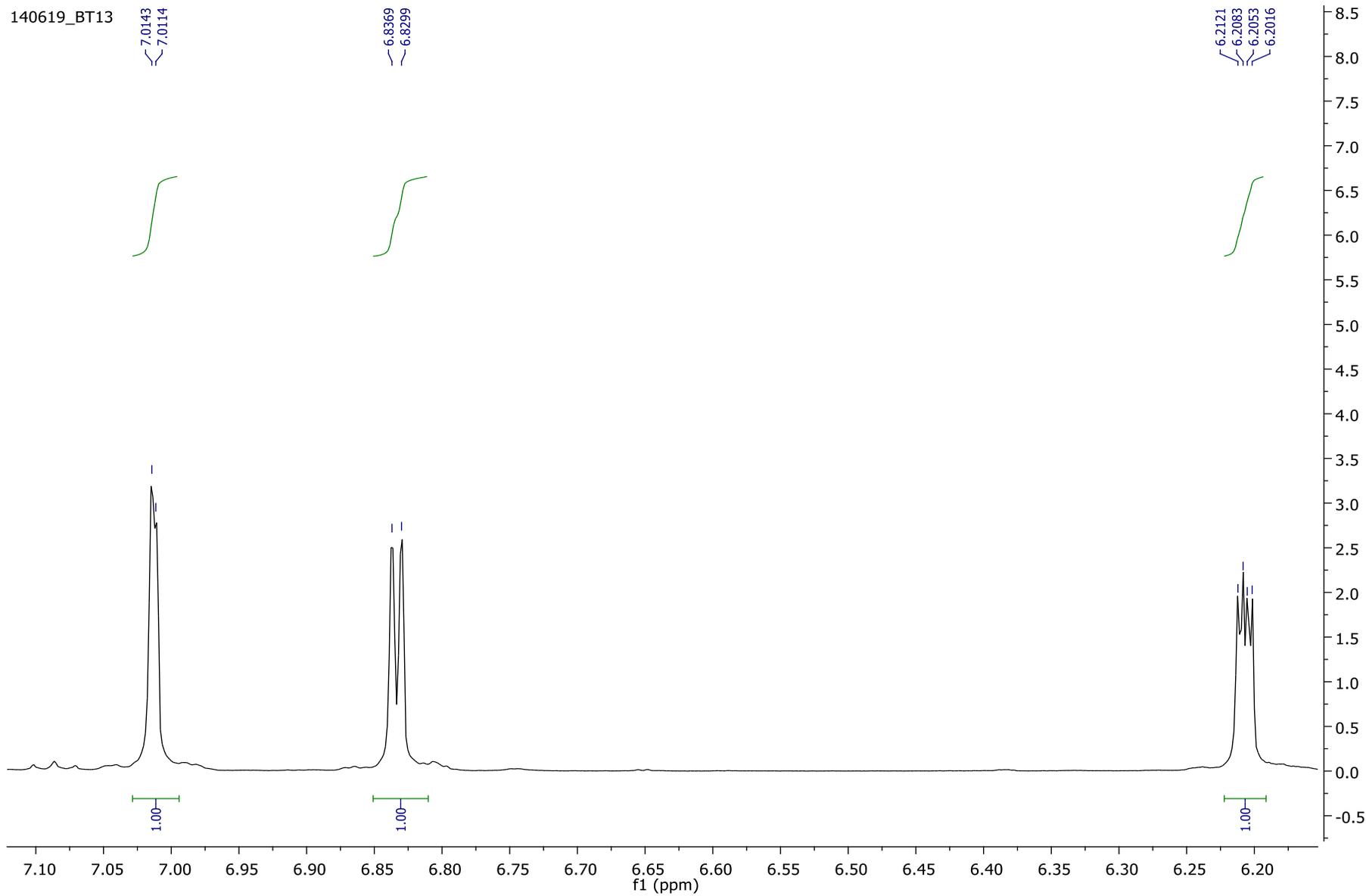


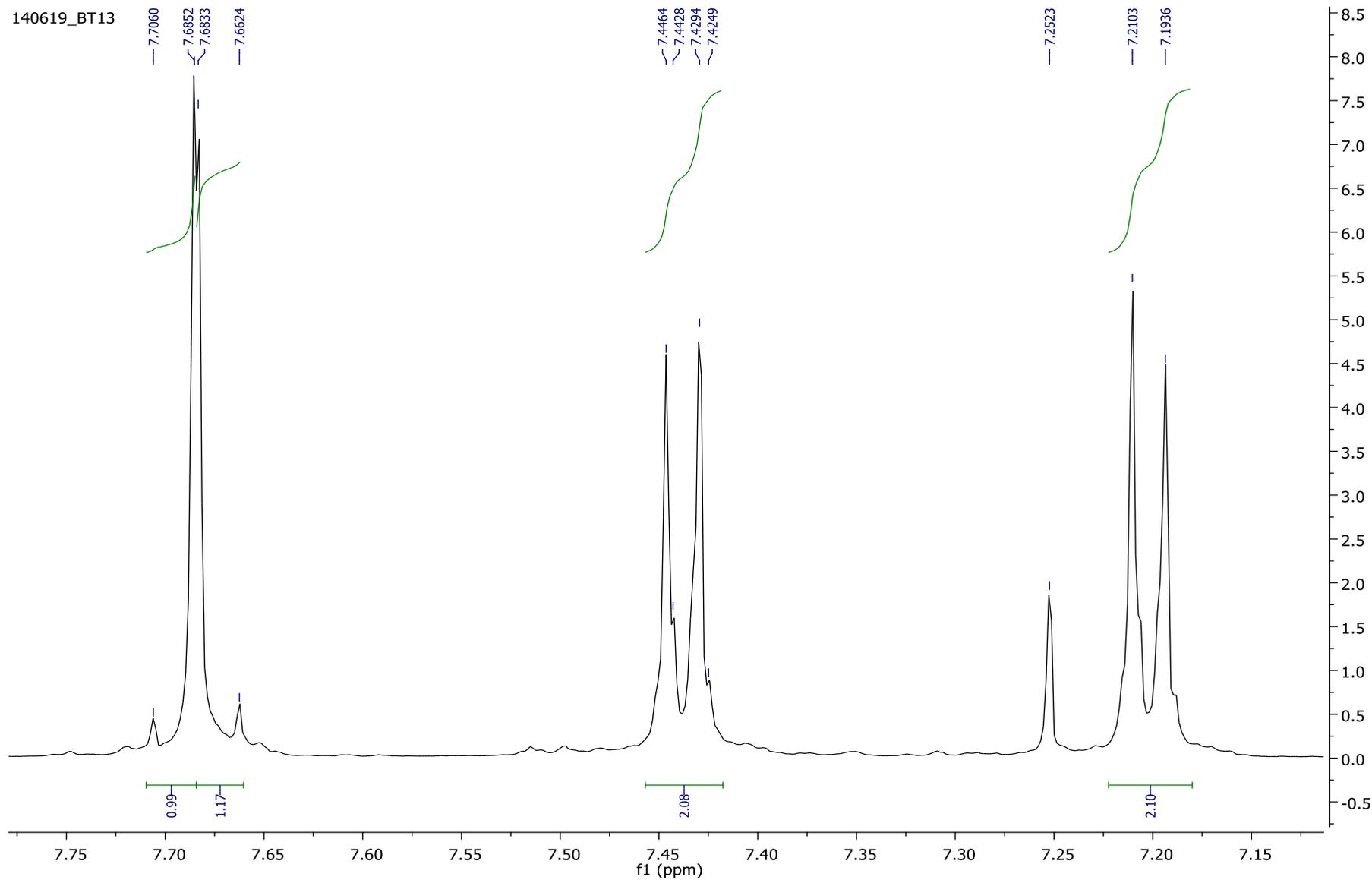


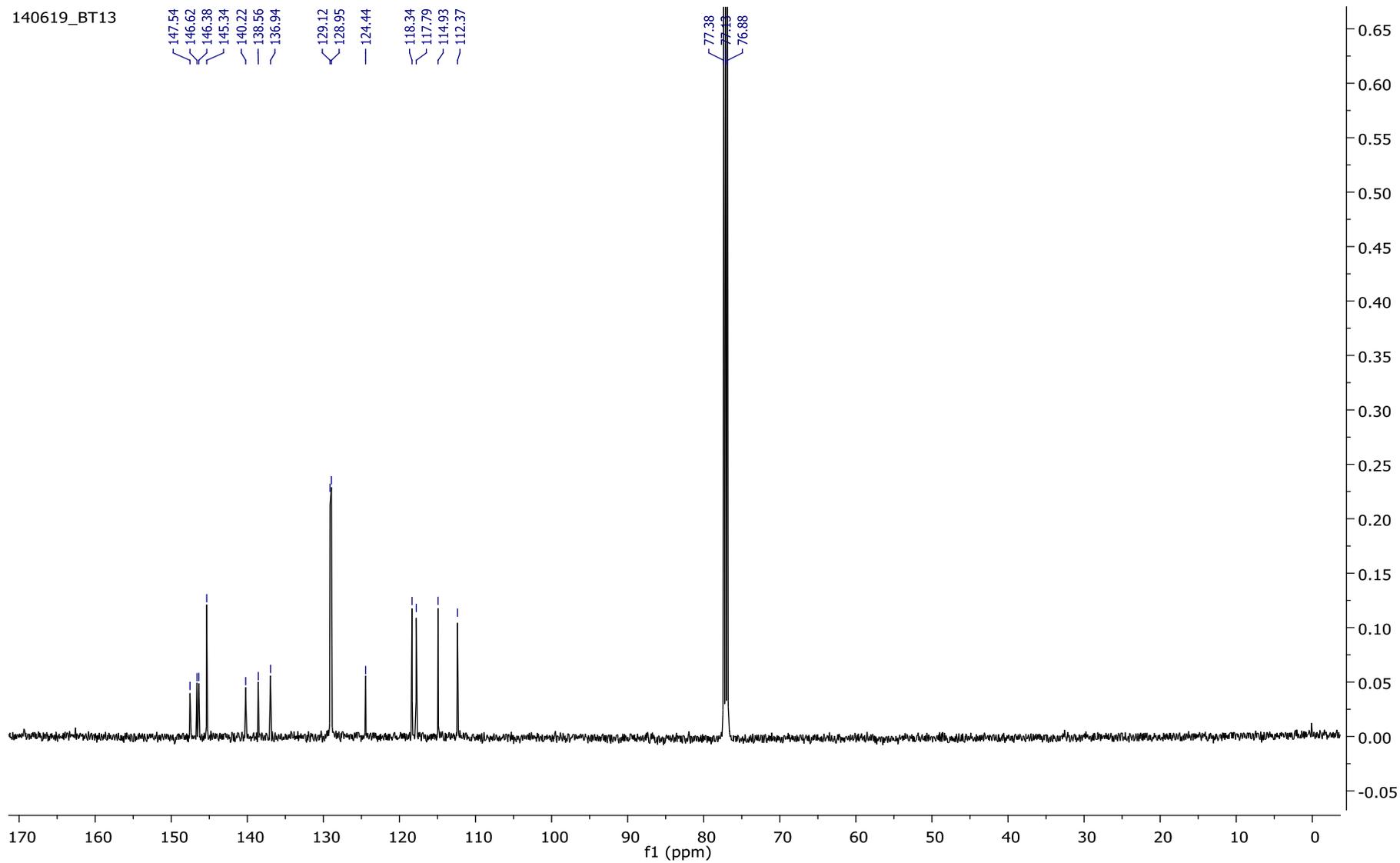


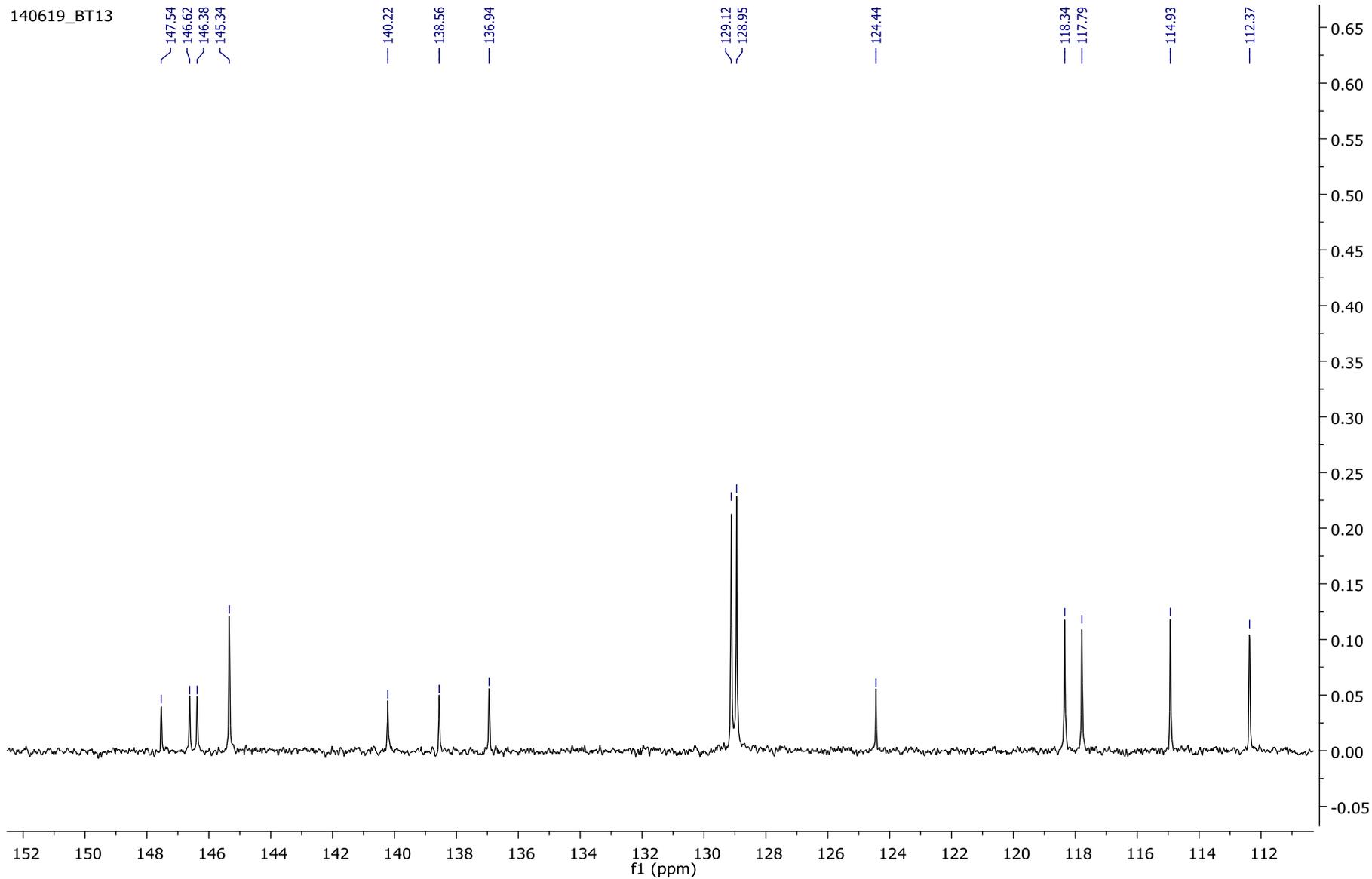


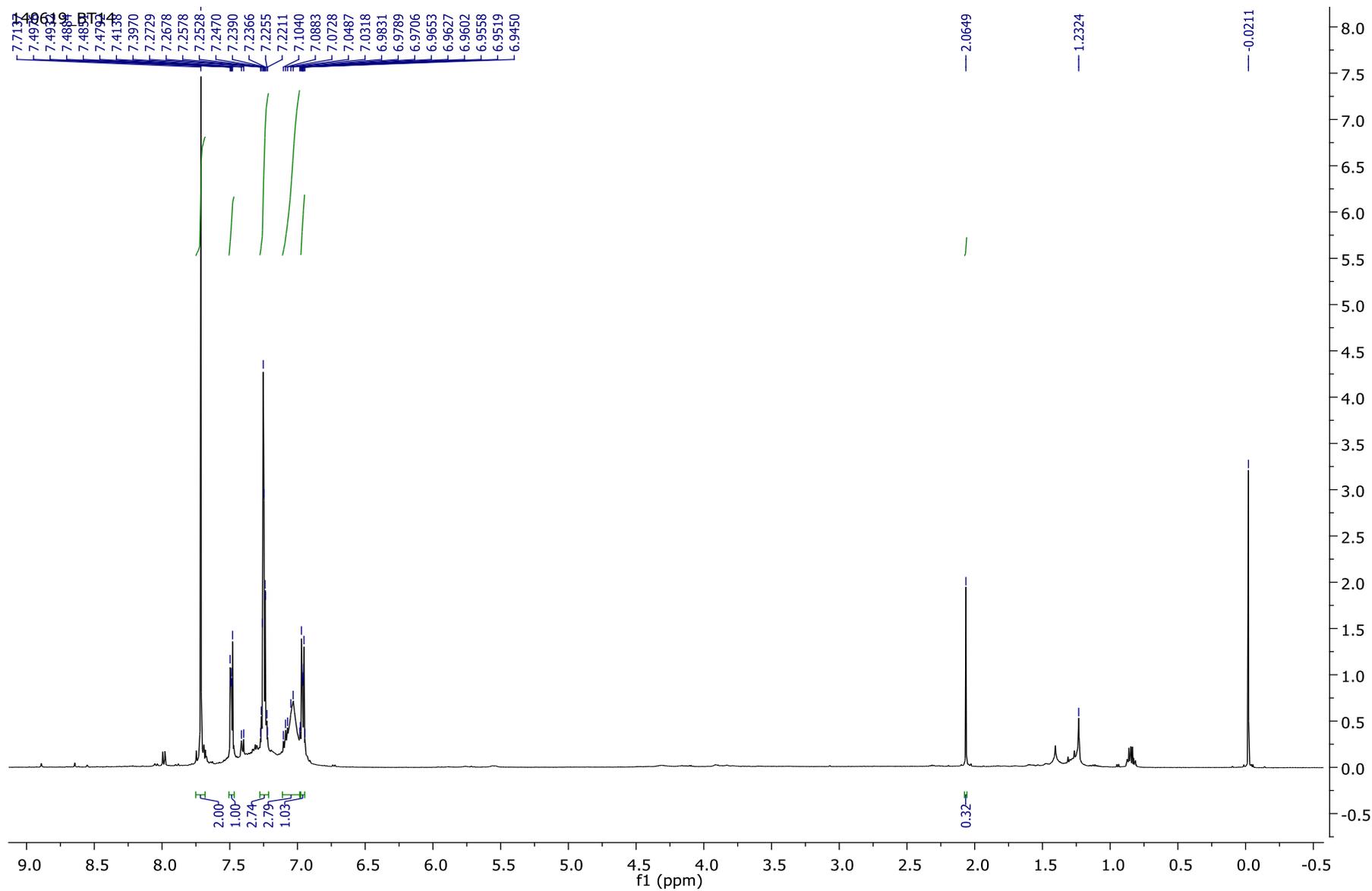




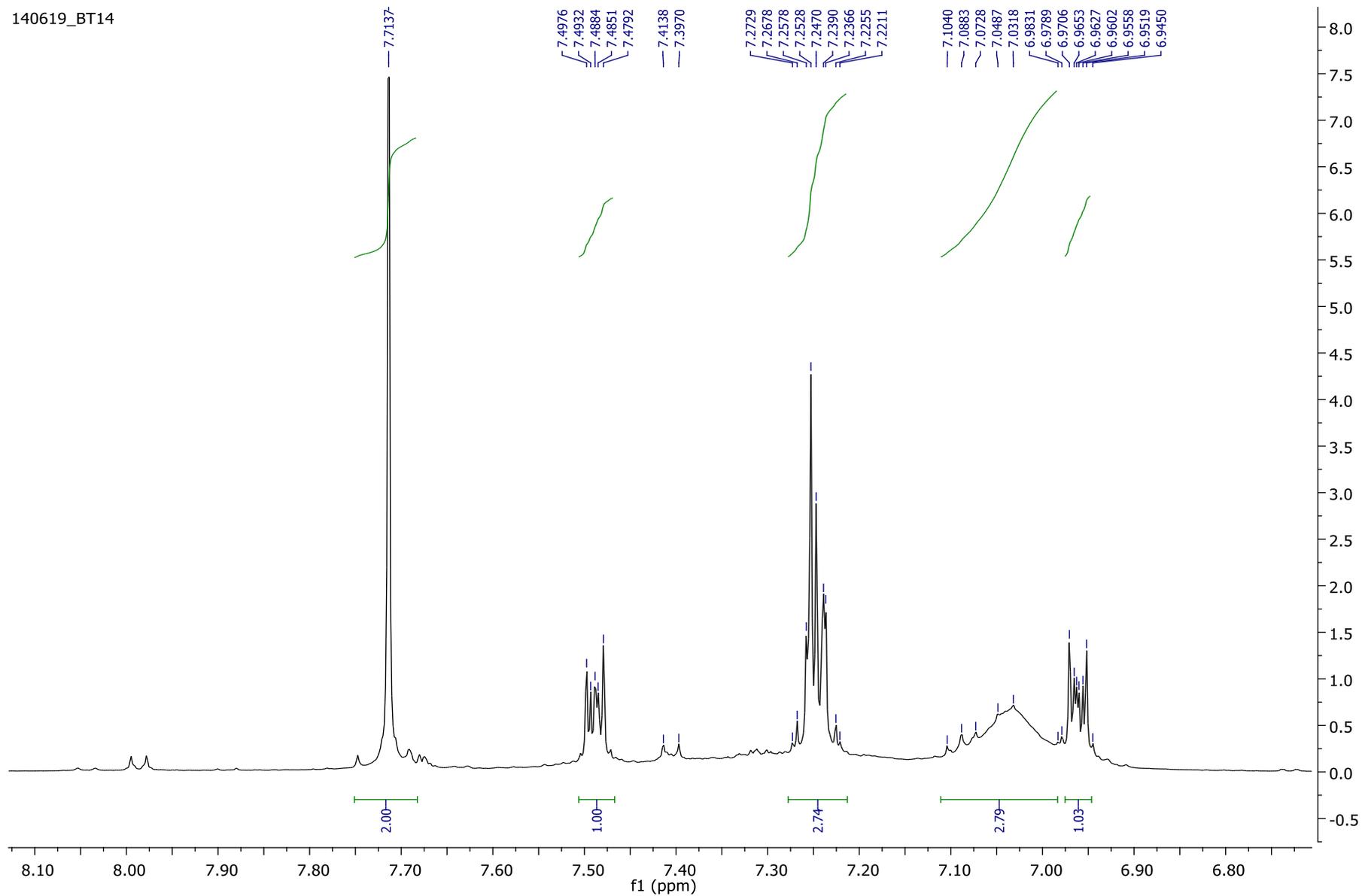


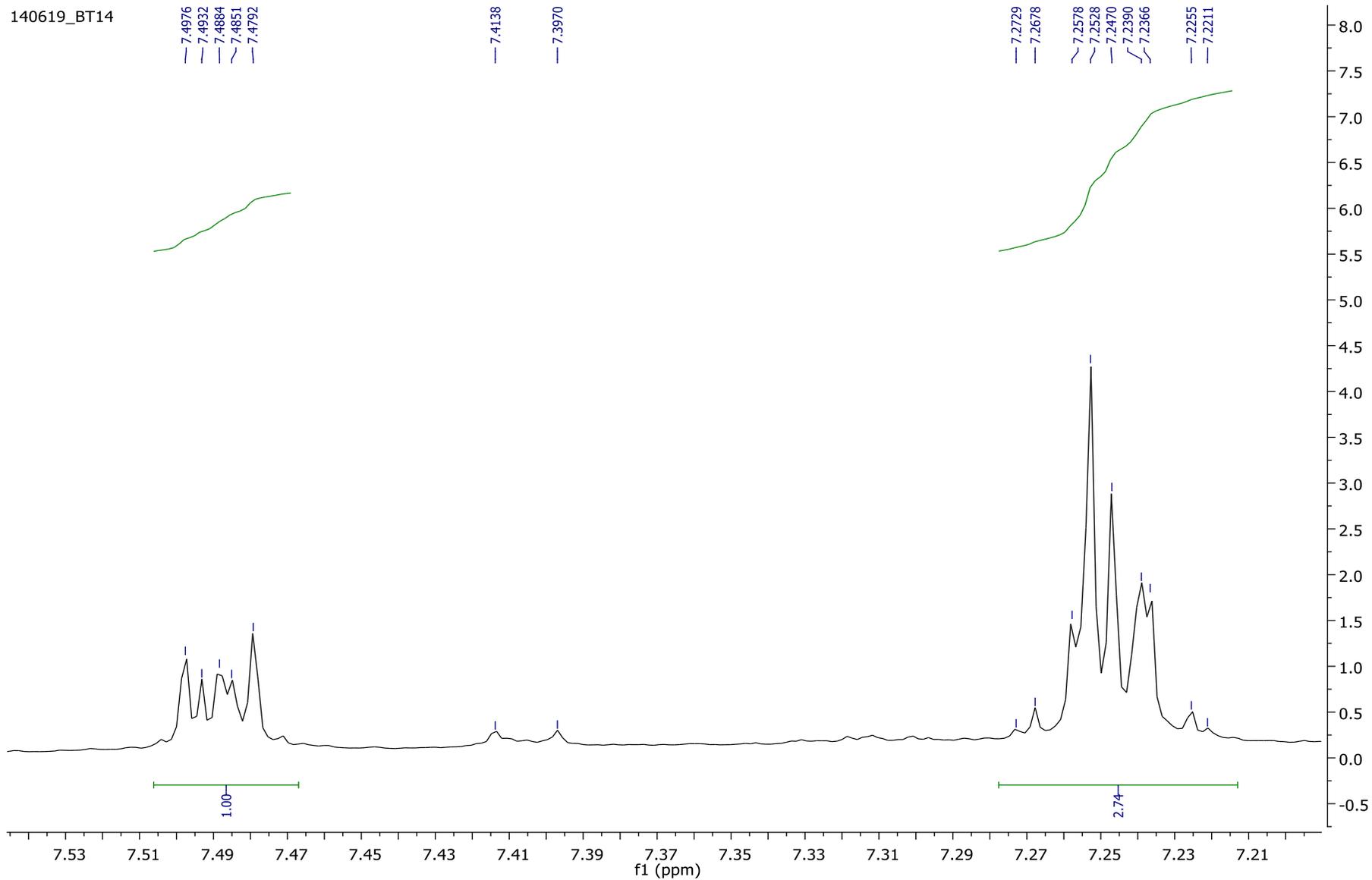






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