

Synthesis of (Z)-(arylamino)-pyrazolyl/isoxazolyl-2-propenones as Tubulin Targeting Anticancer Agents and Apoptotic Inducers

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Vishnuvardhan,^a Sowjanya Polepalli,^b Nishant Jain^b

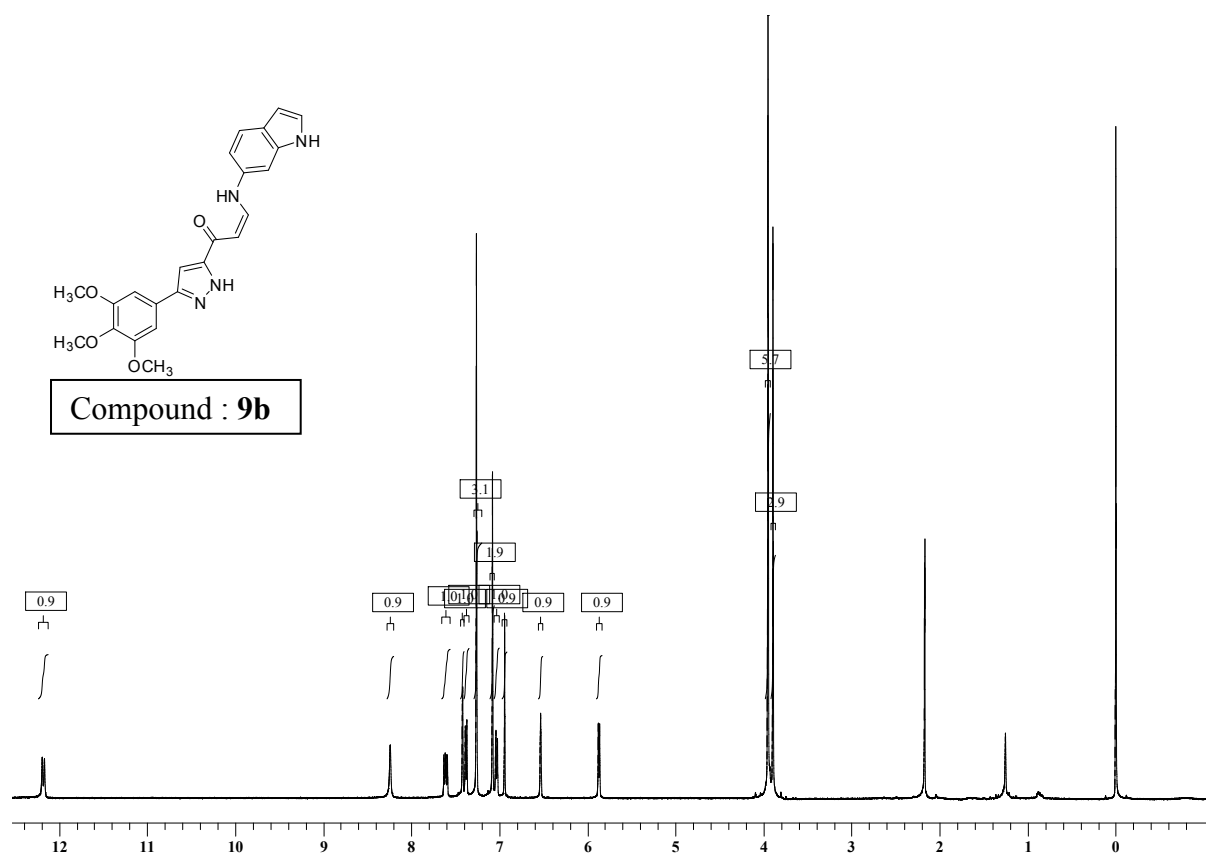
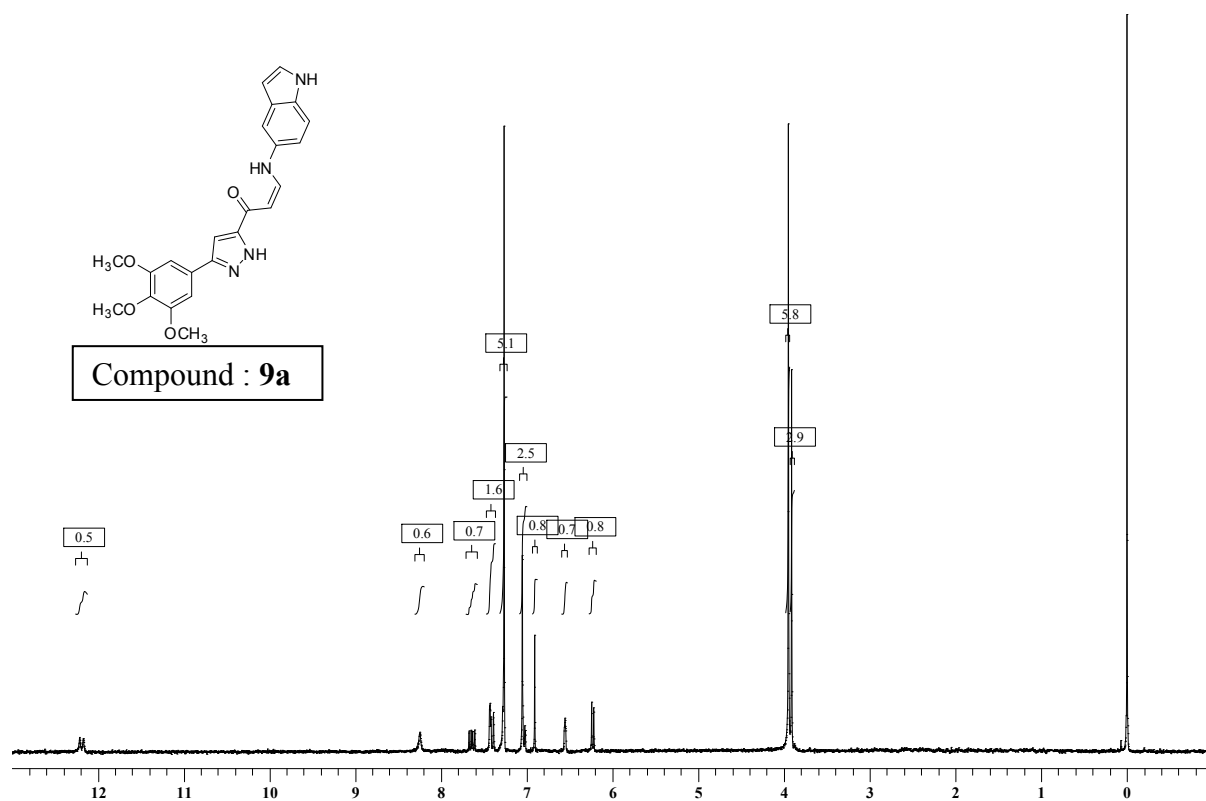
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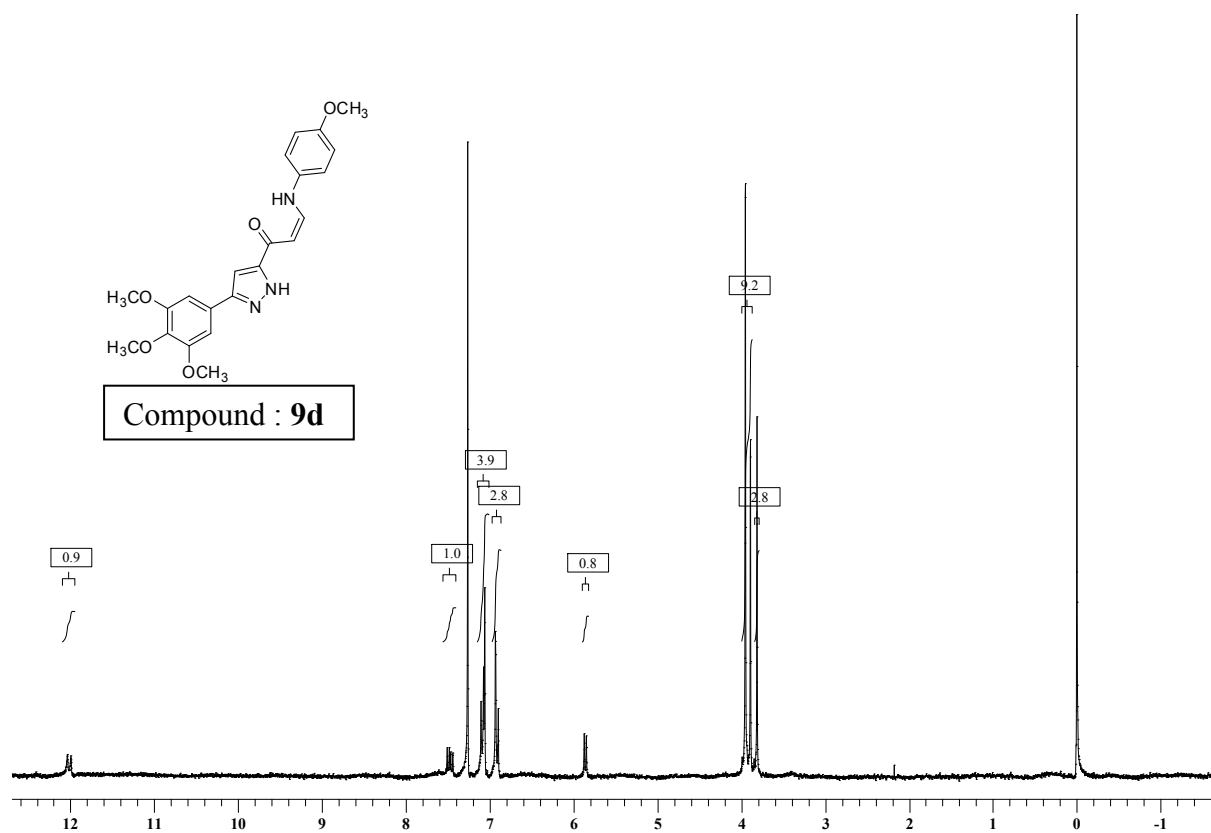
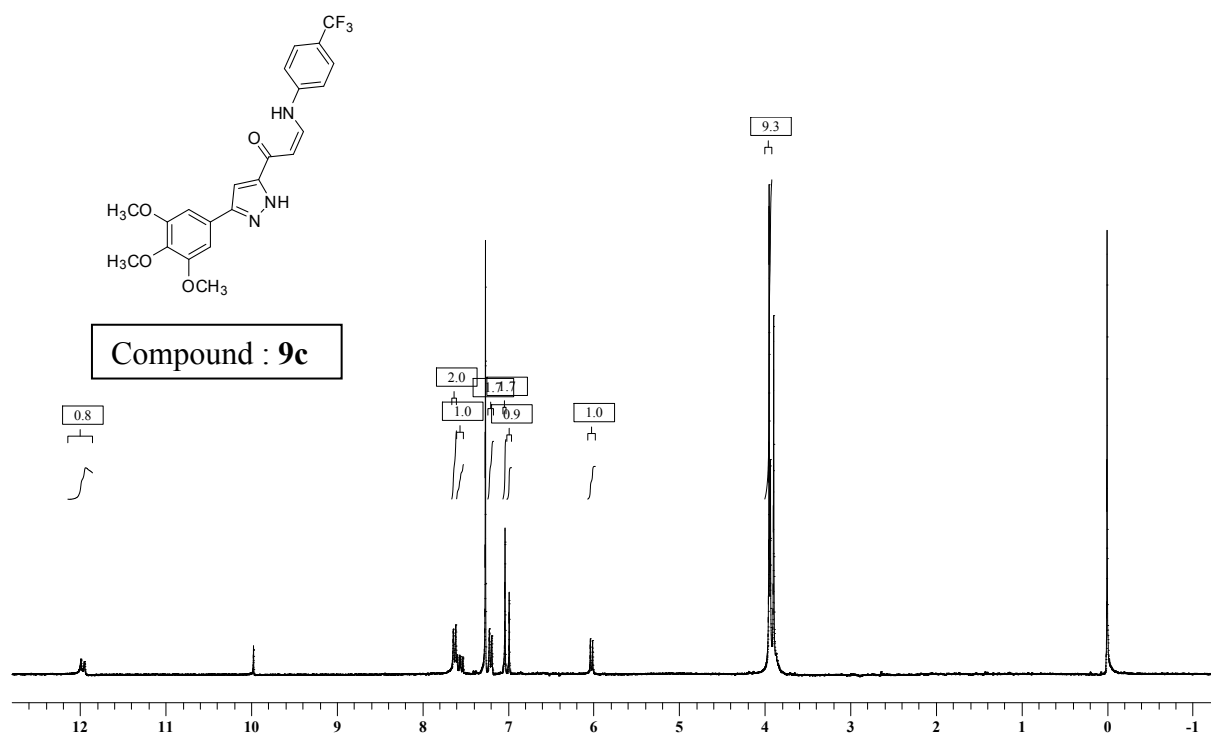
^bCentre for Chemical Biology CSIR-Indian Institute of Chemical Technology, Hyderabad, Telangana- 500 007,
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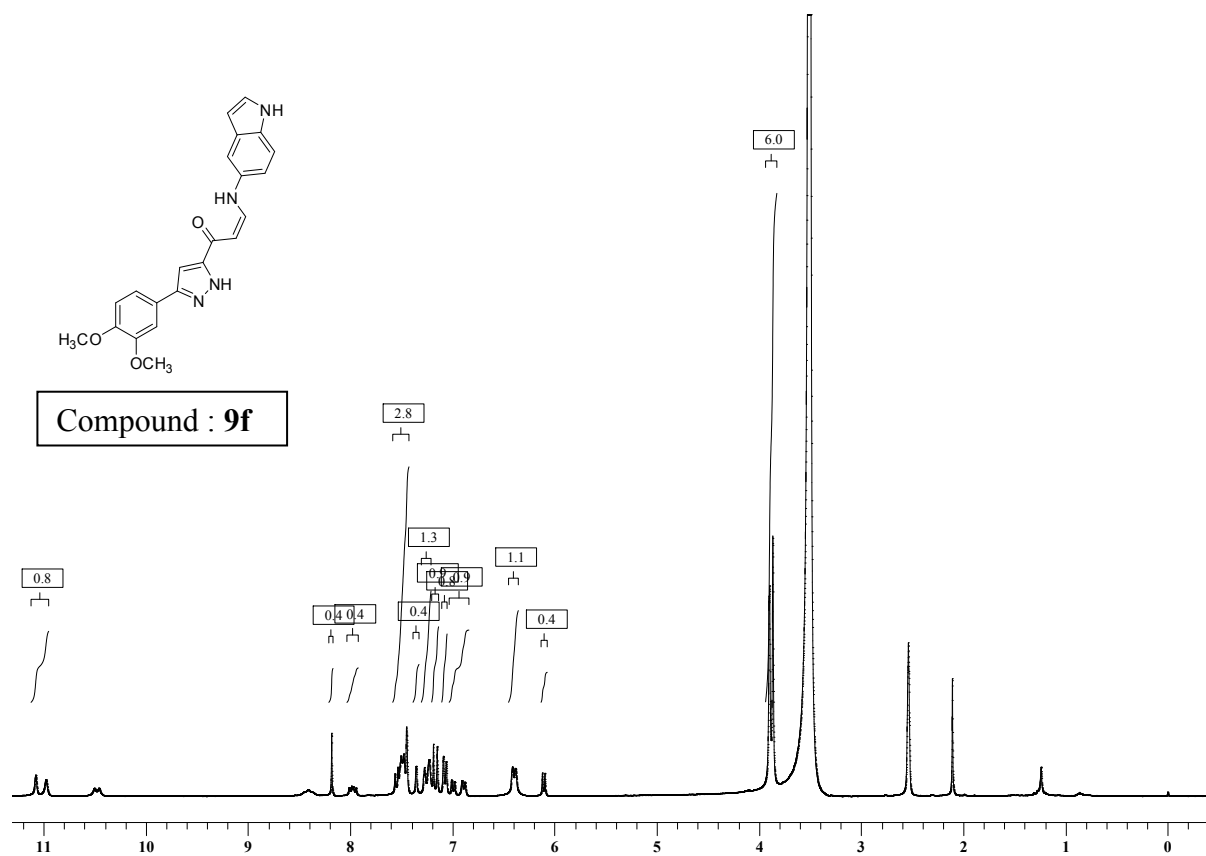
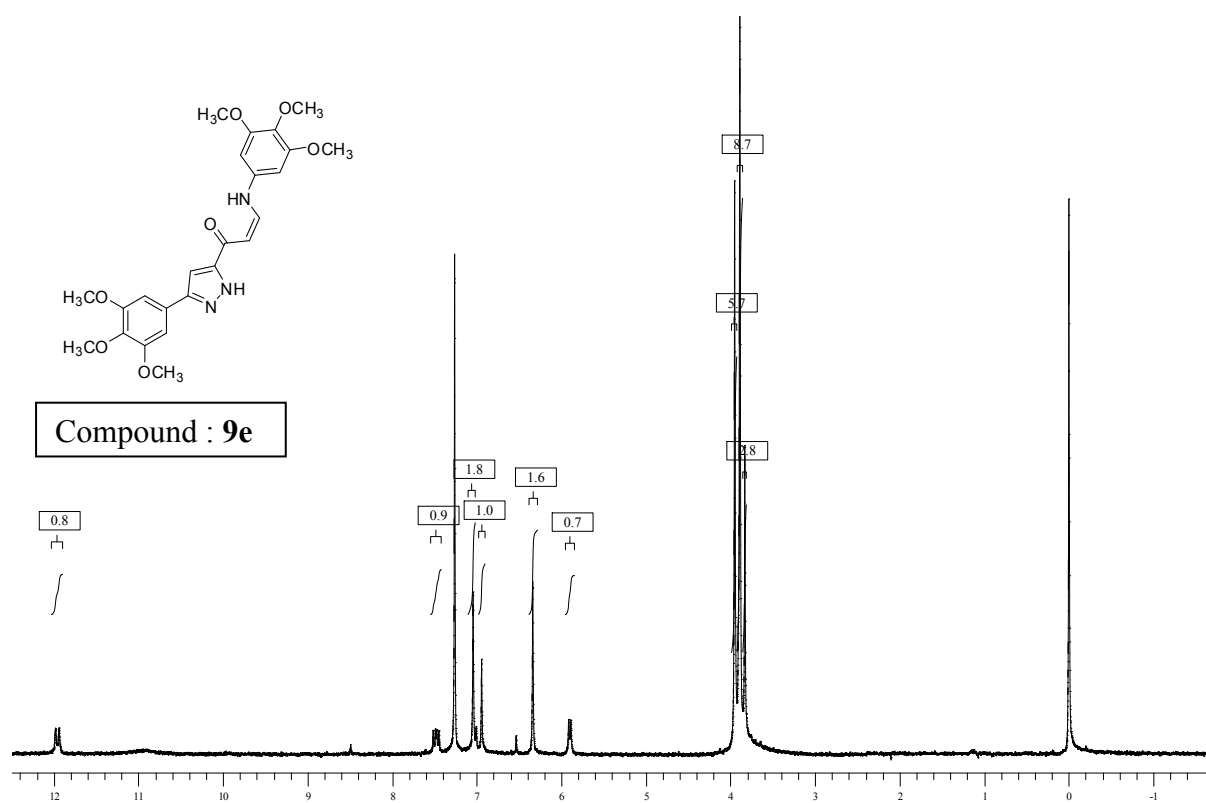
*Correspondence: ahmedkamal@iict.res.in; Phone: (+) 91-40-27193157; Fax: (+) 91-40-
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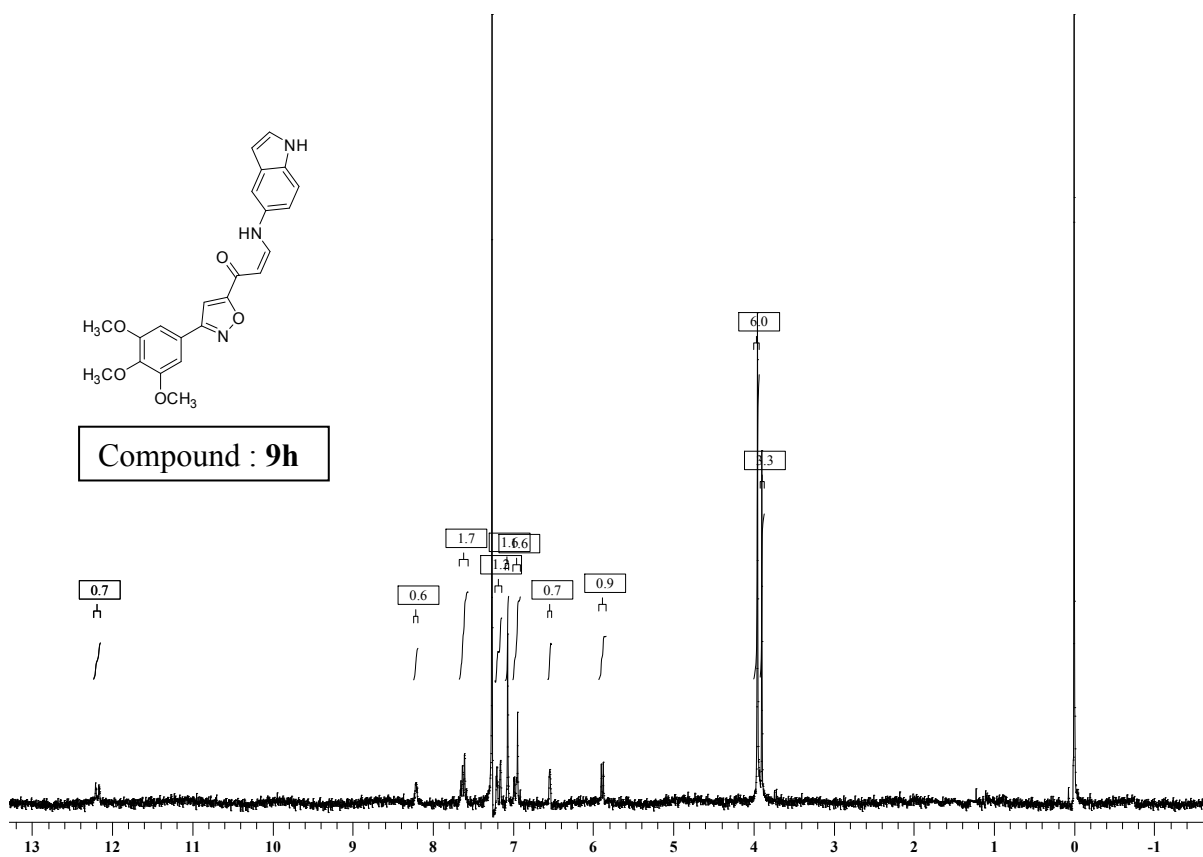
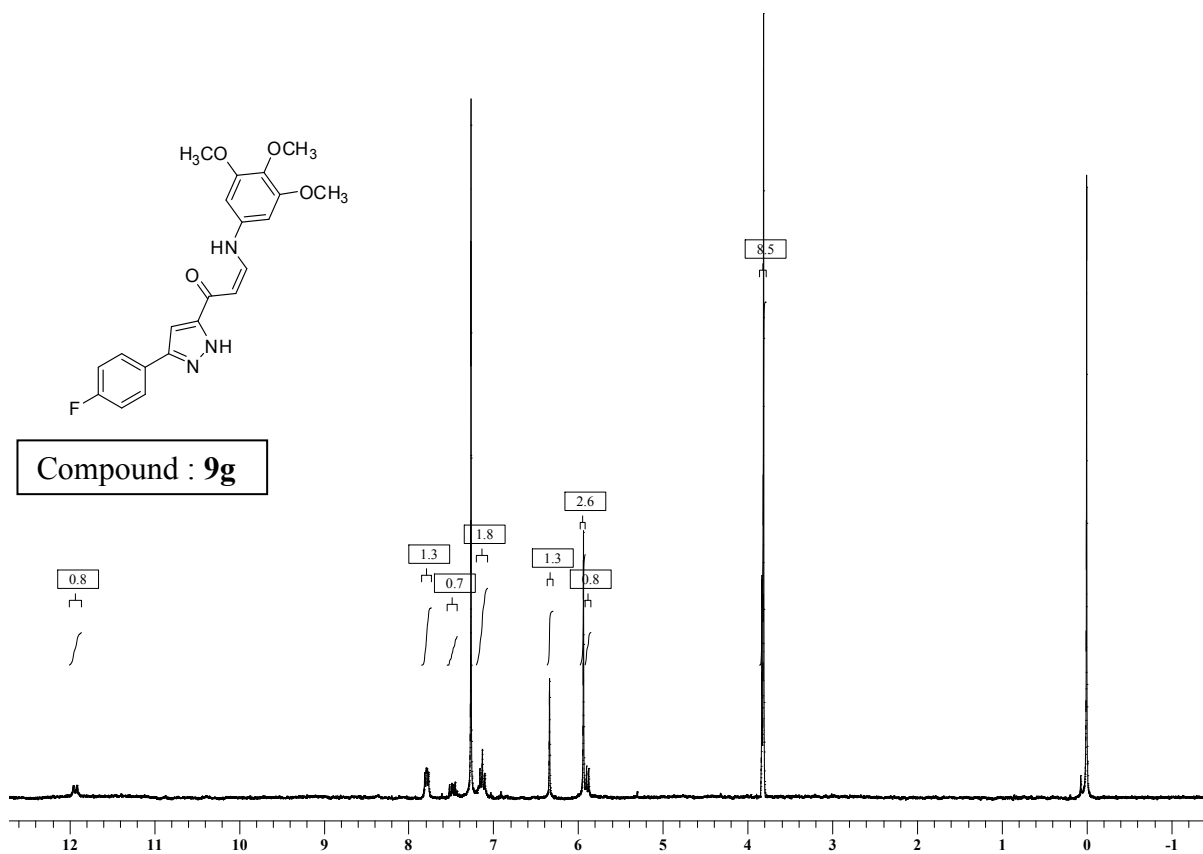
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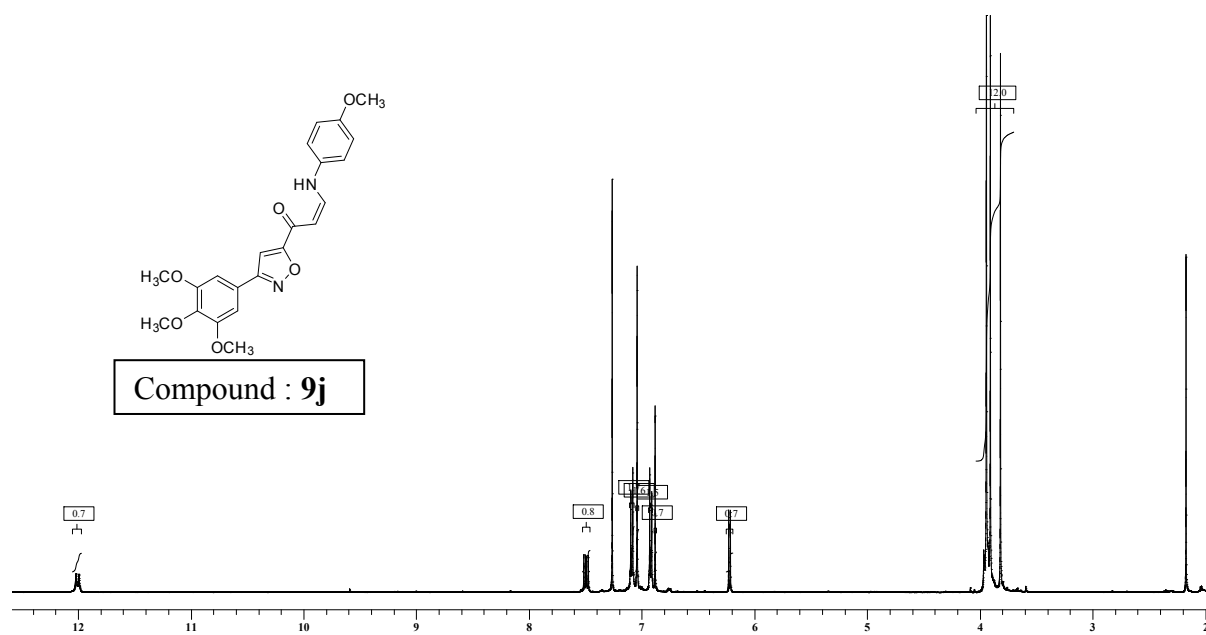
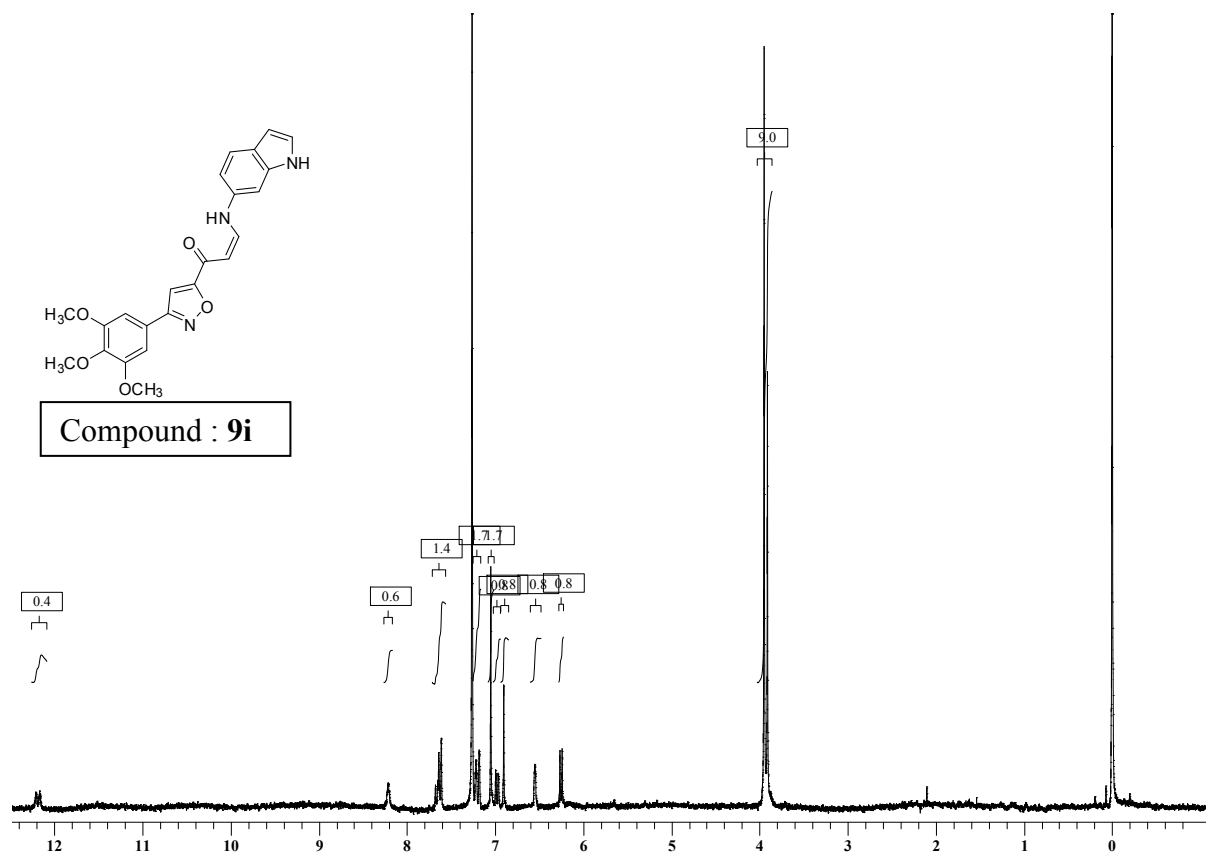
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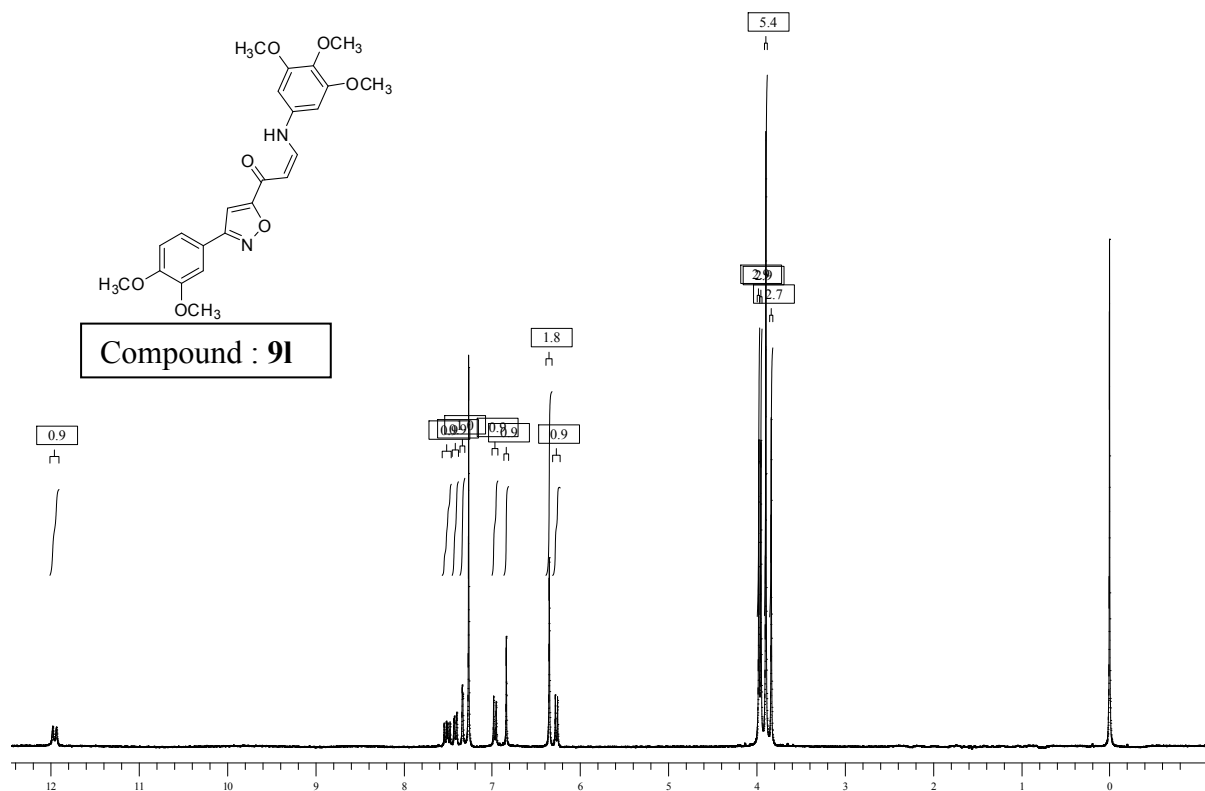
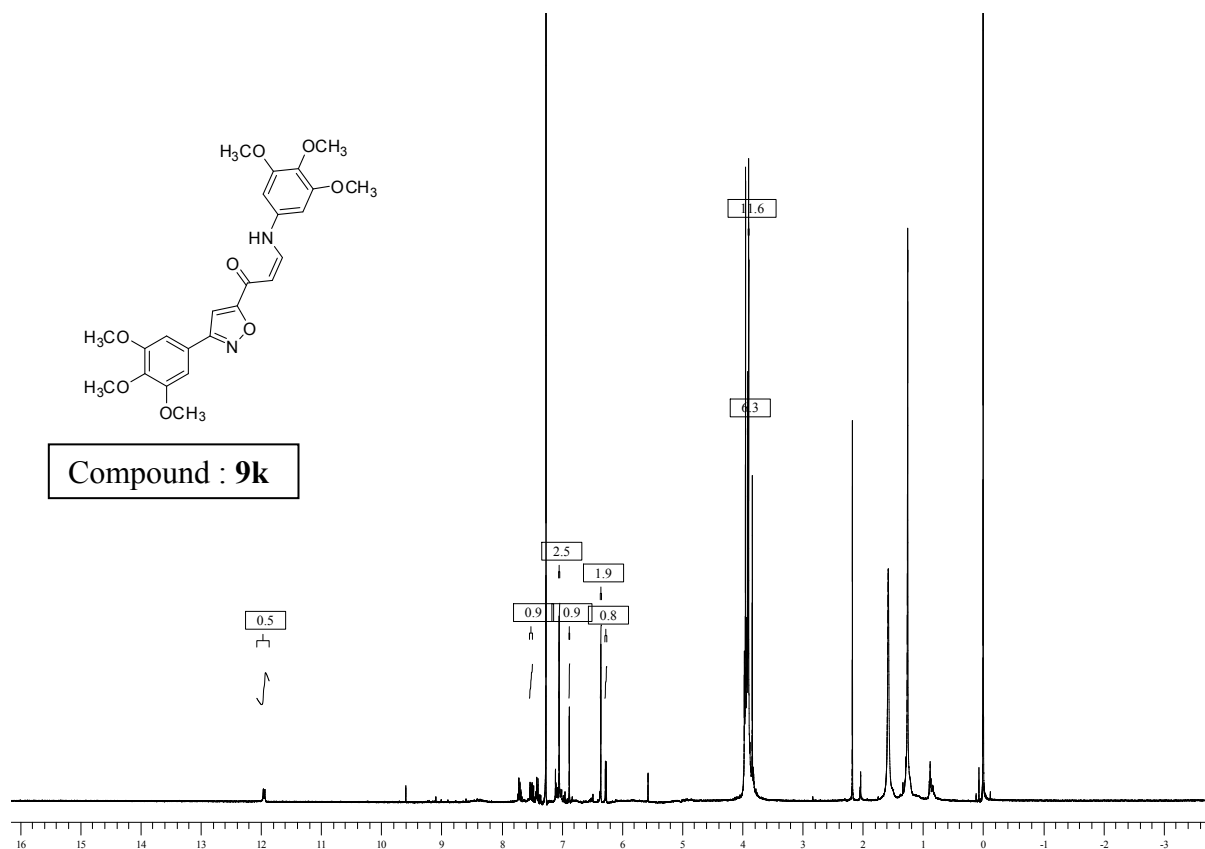


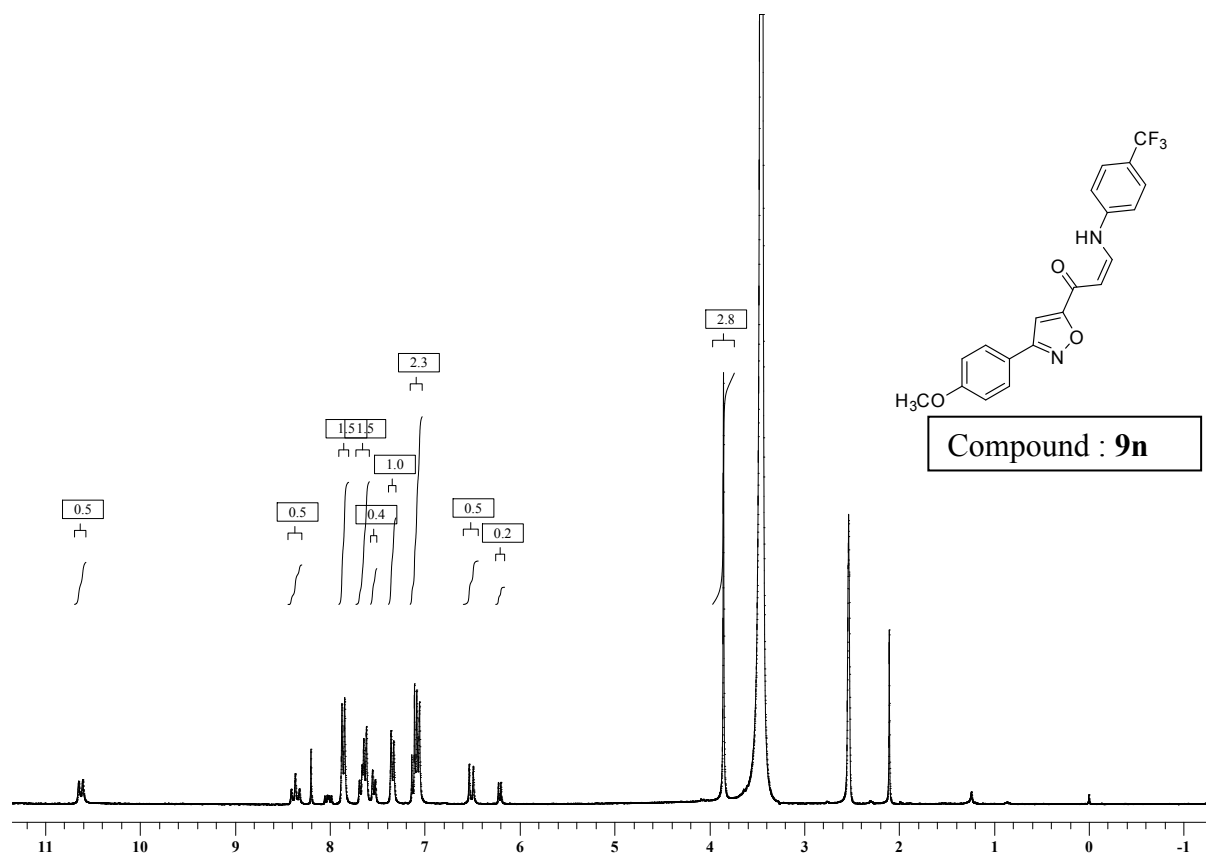
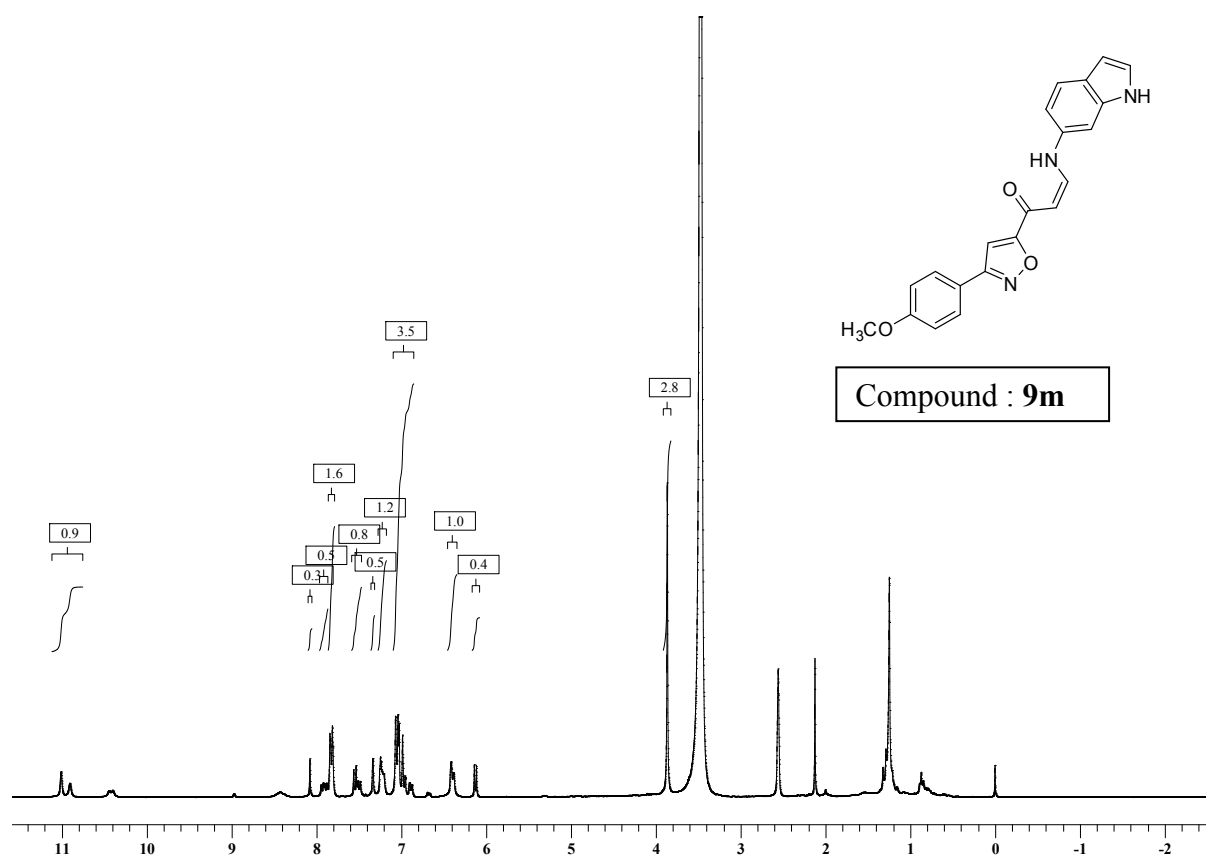


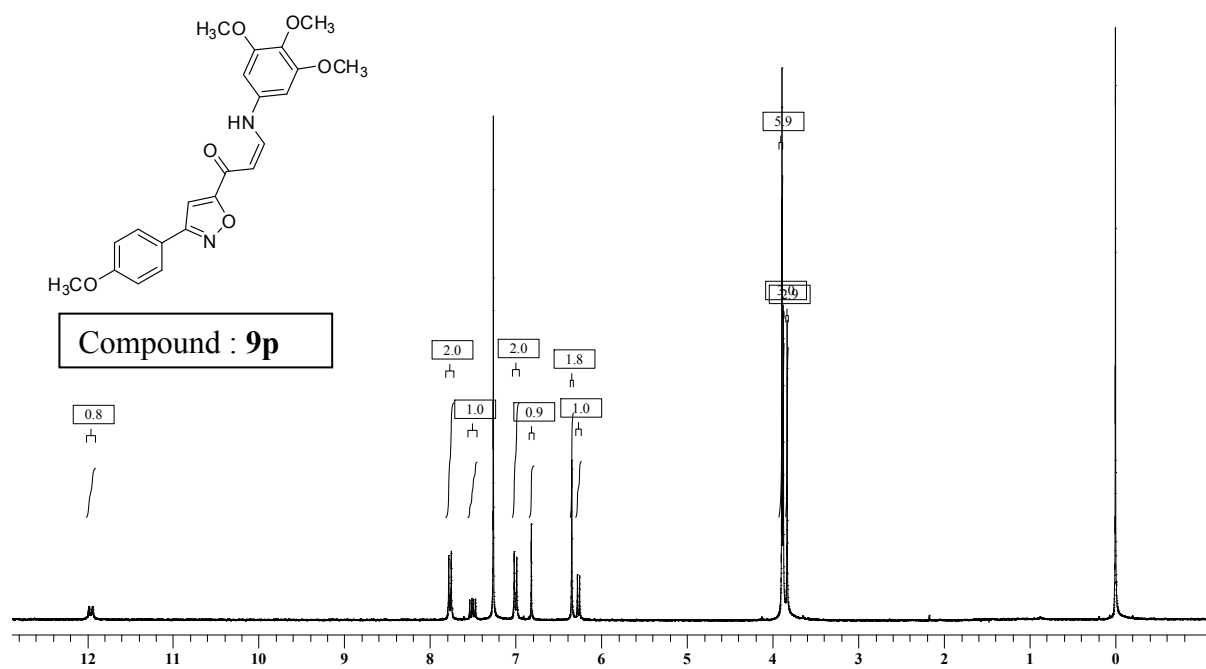
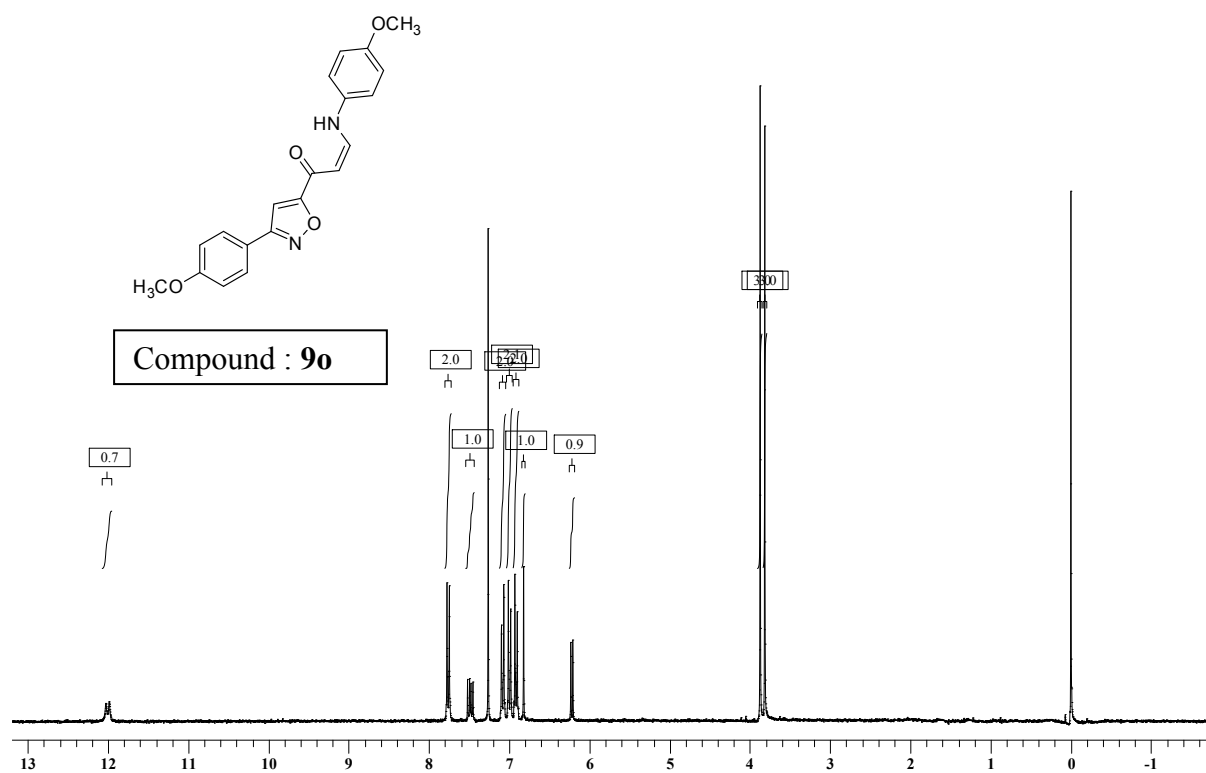


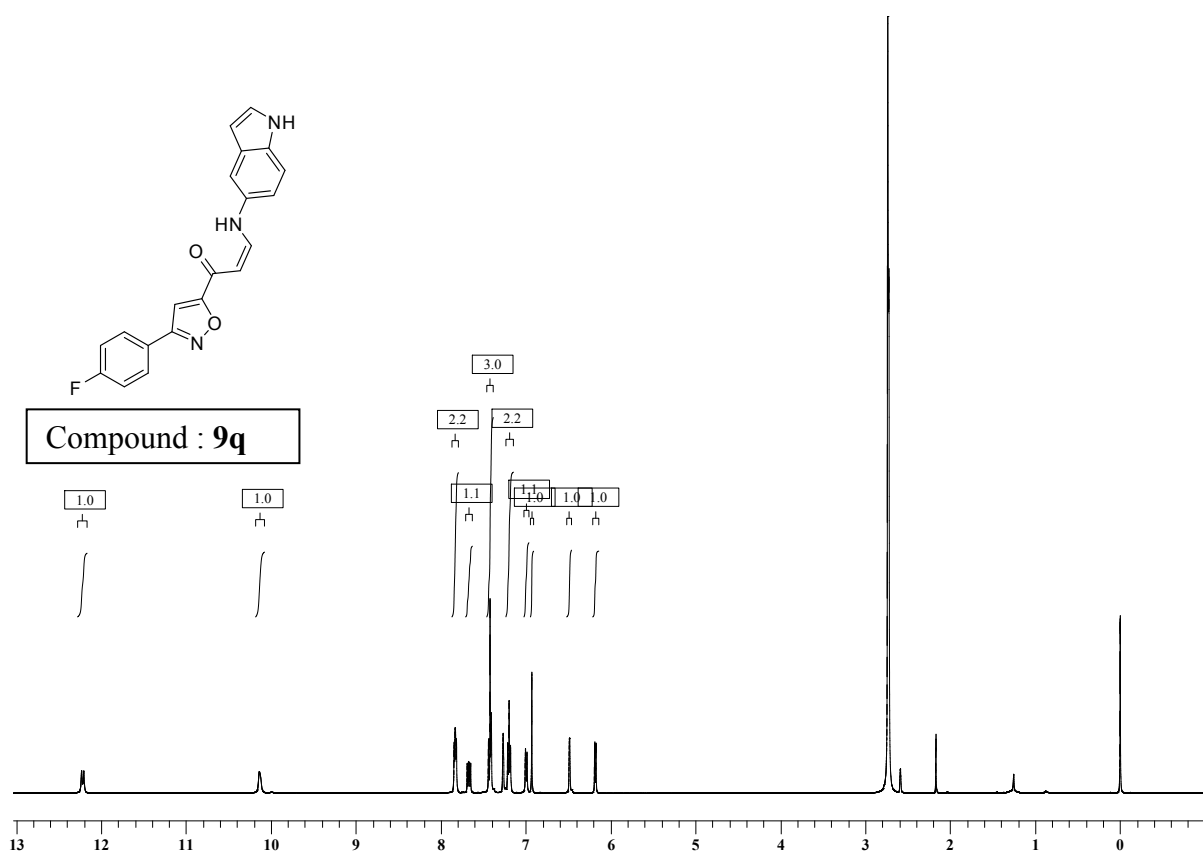




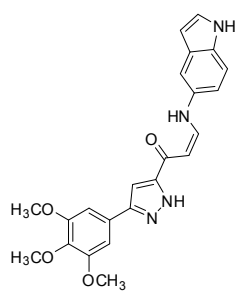




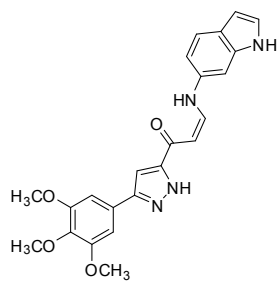
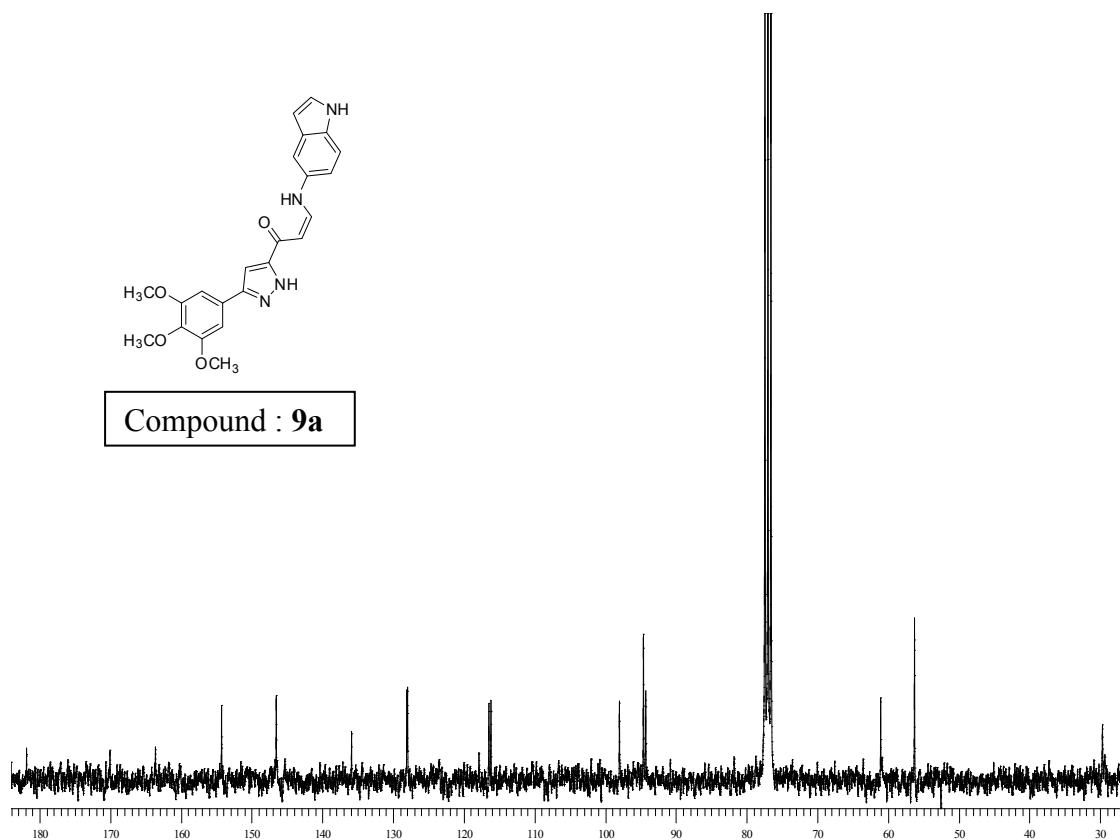




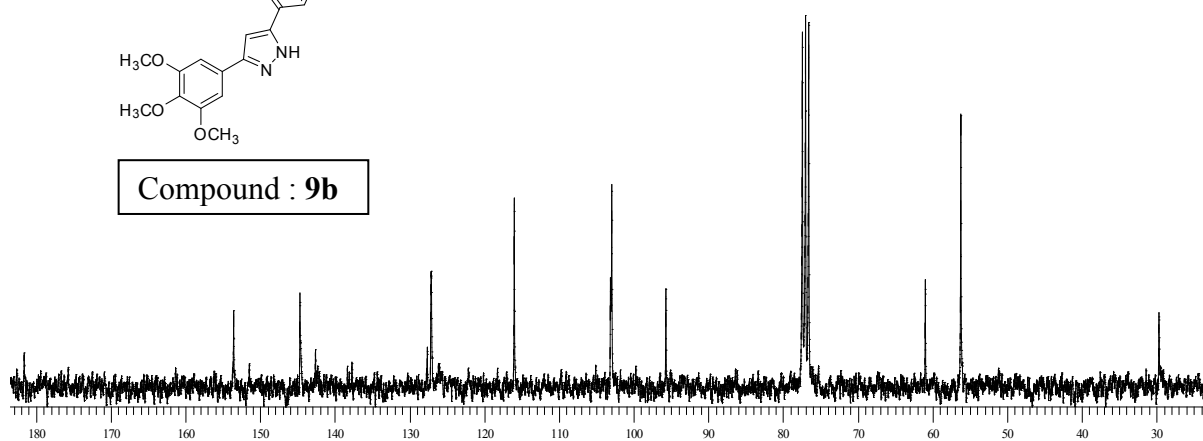
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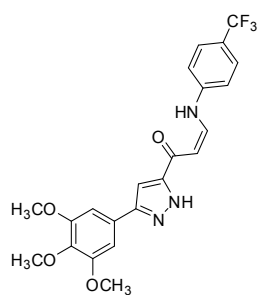


Compound : **9a**

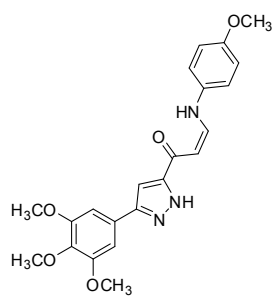
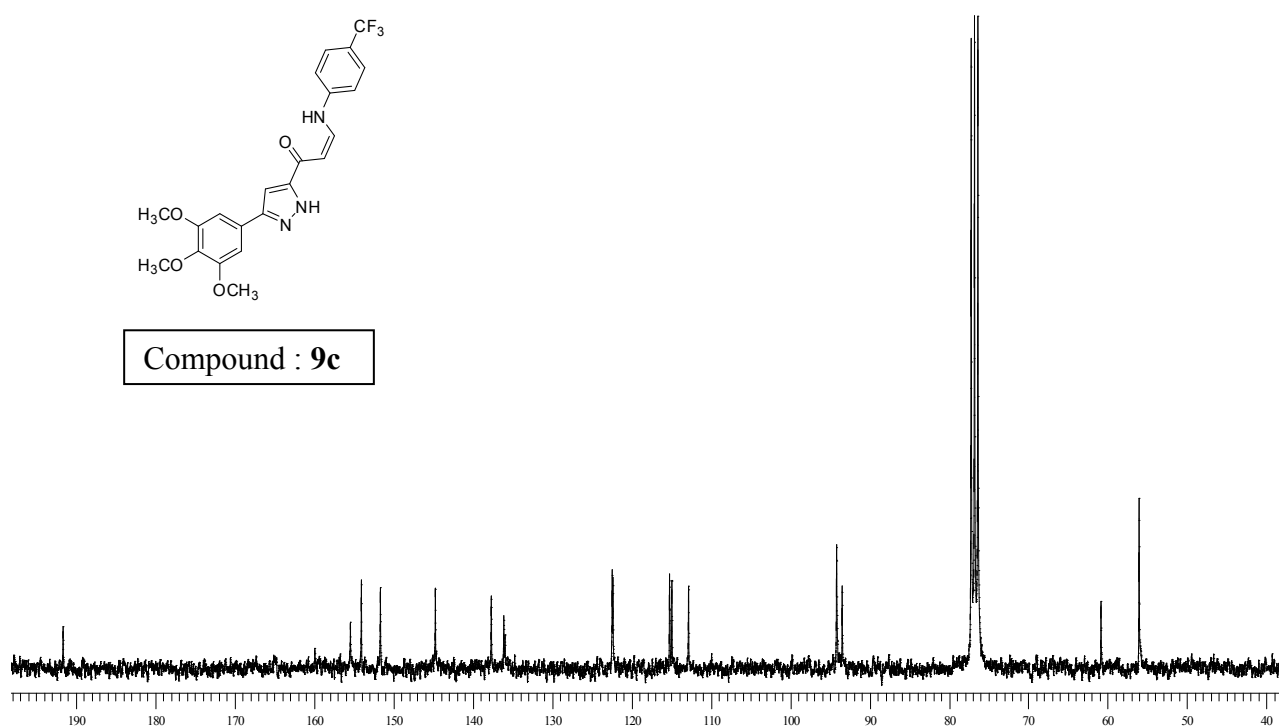


Compound : **9b**

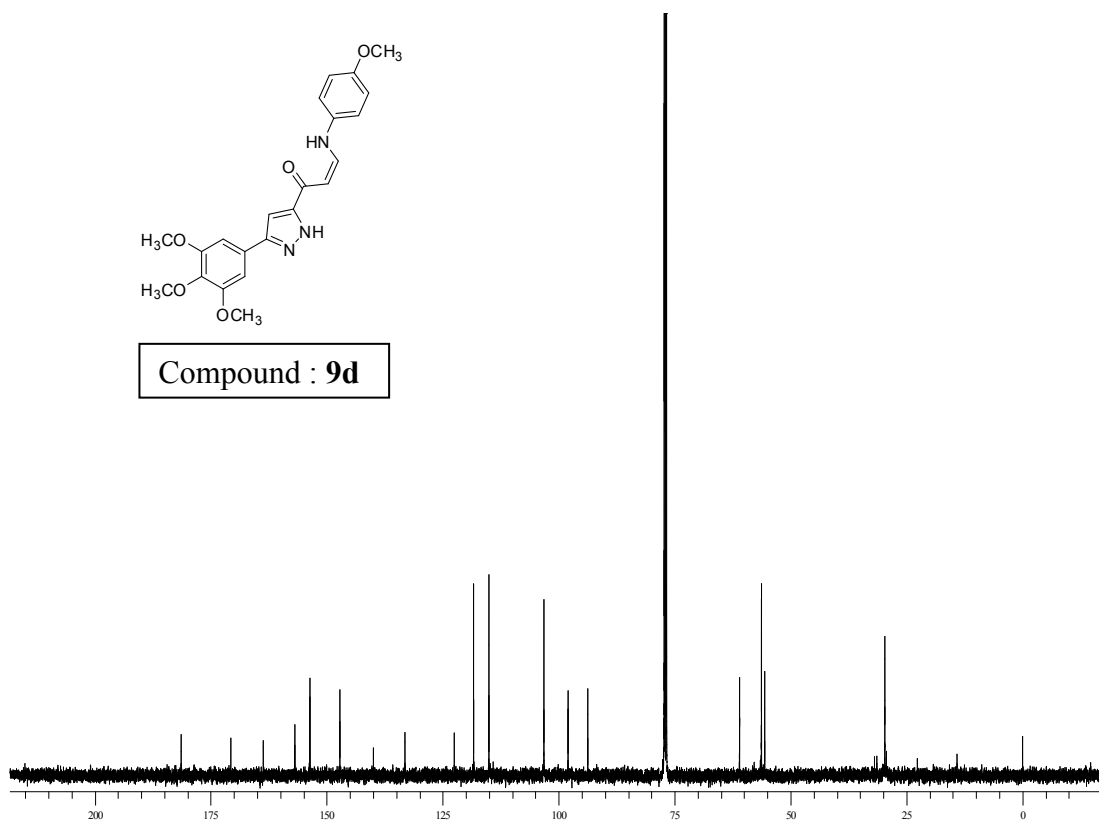


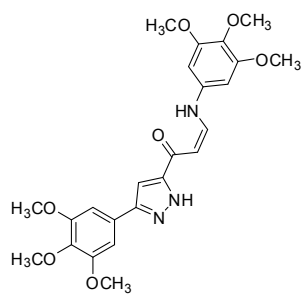


Compound : **9c**

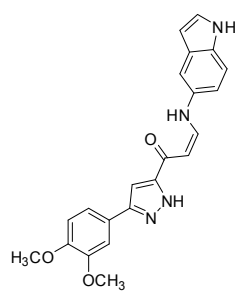
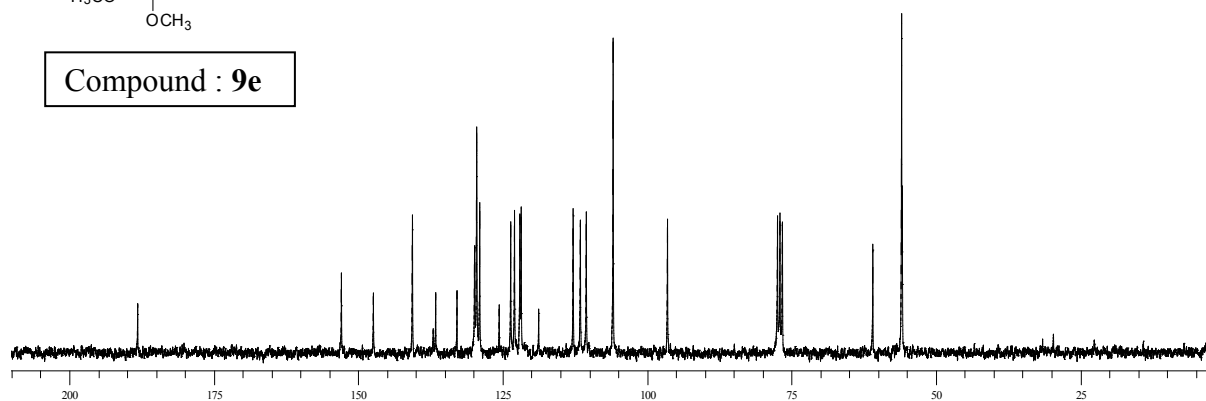


Compound : **9d**

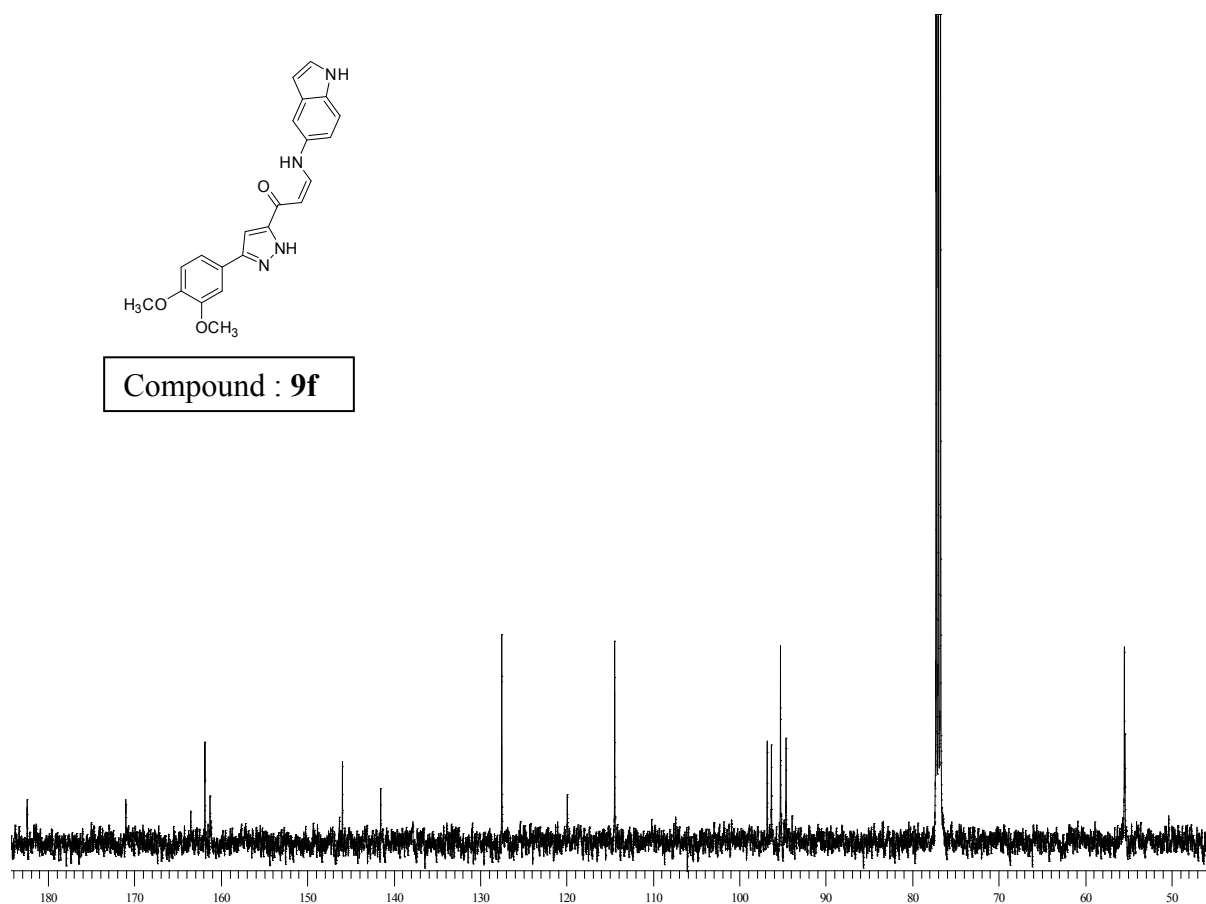


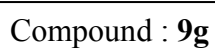


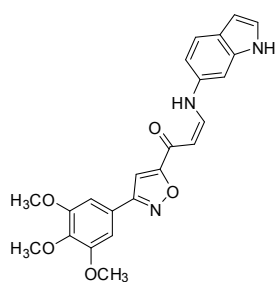
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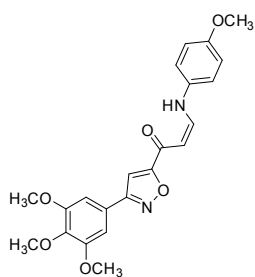
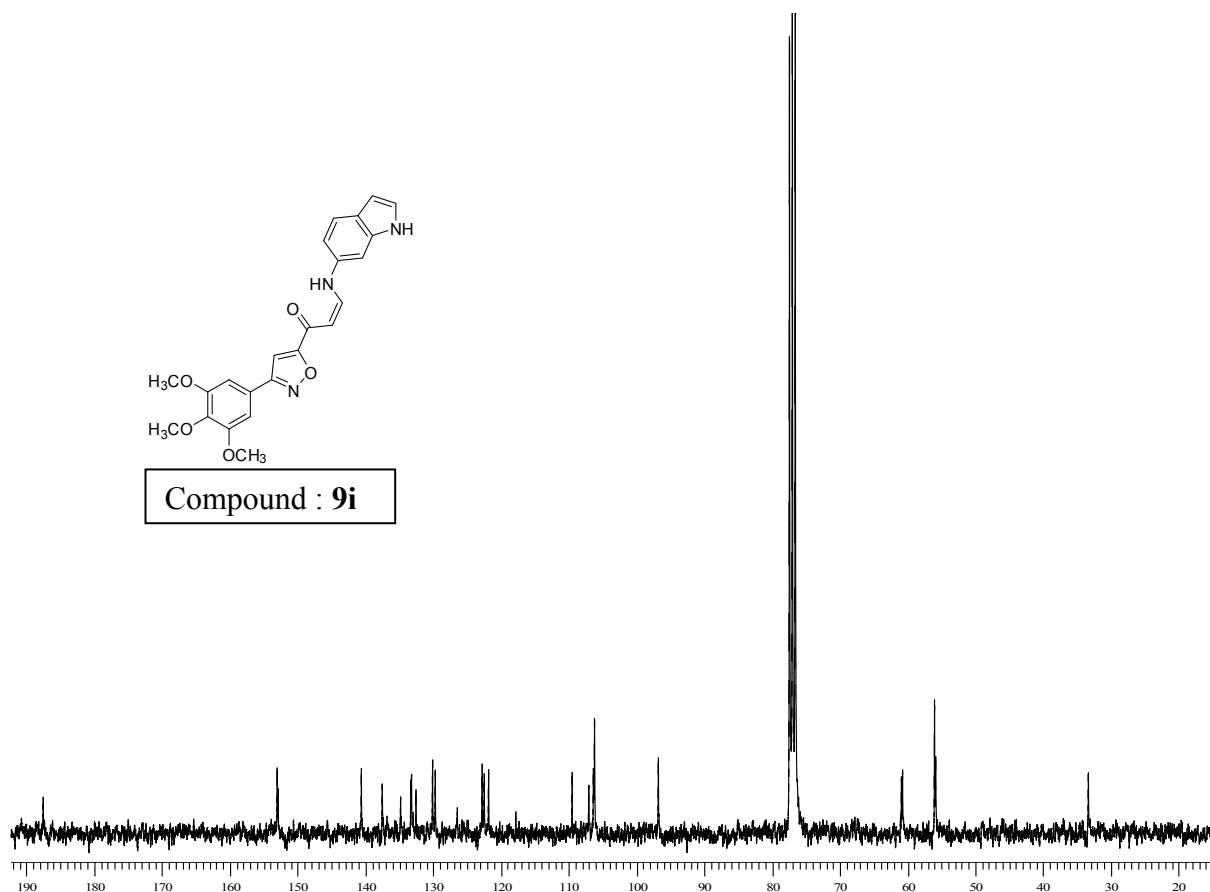
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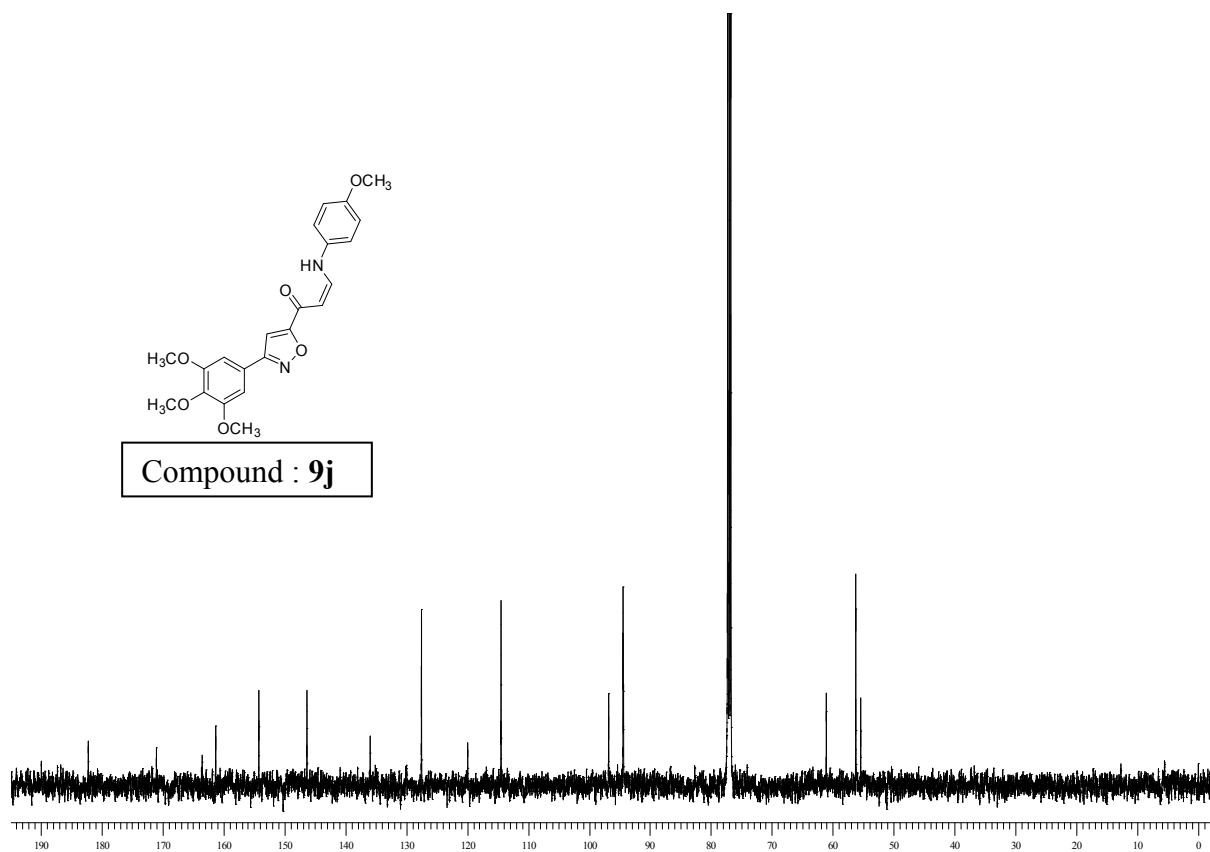


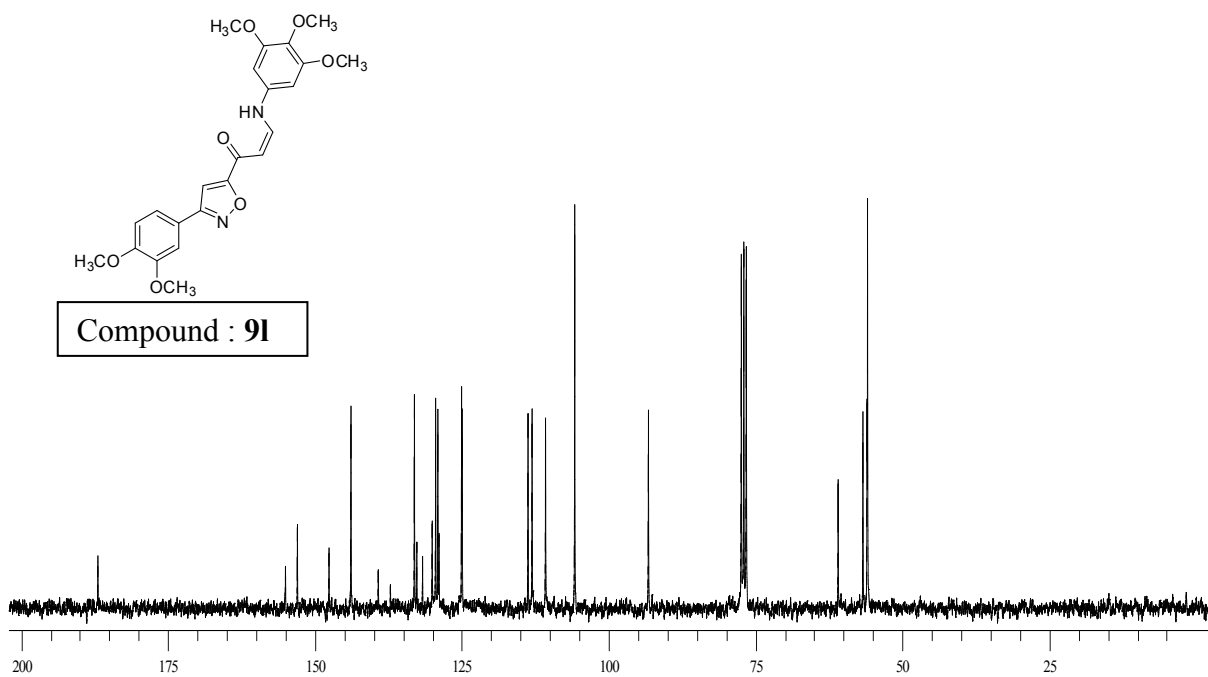
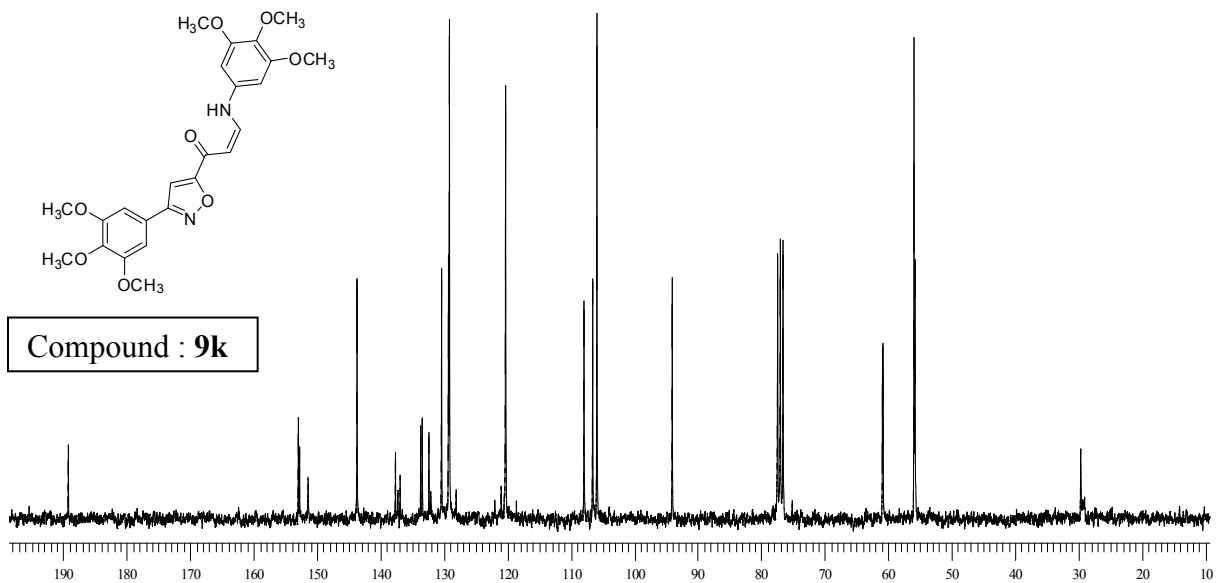
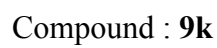


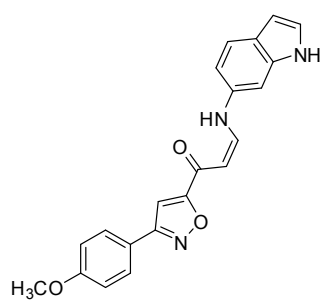
Compound : **9i**



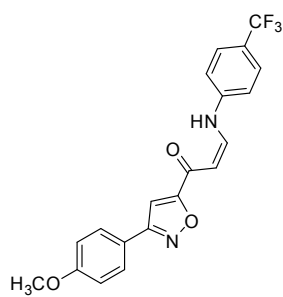
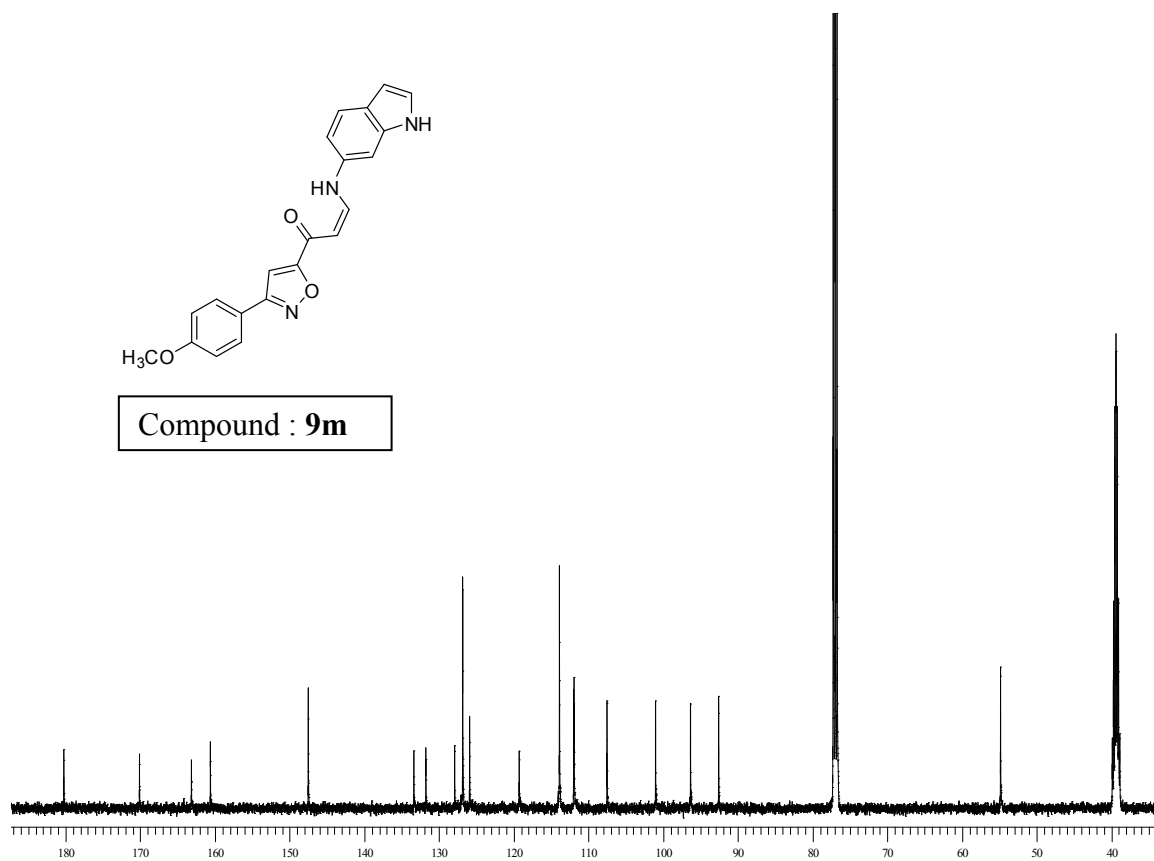
Compound : **9j**



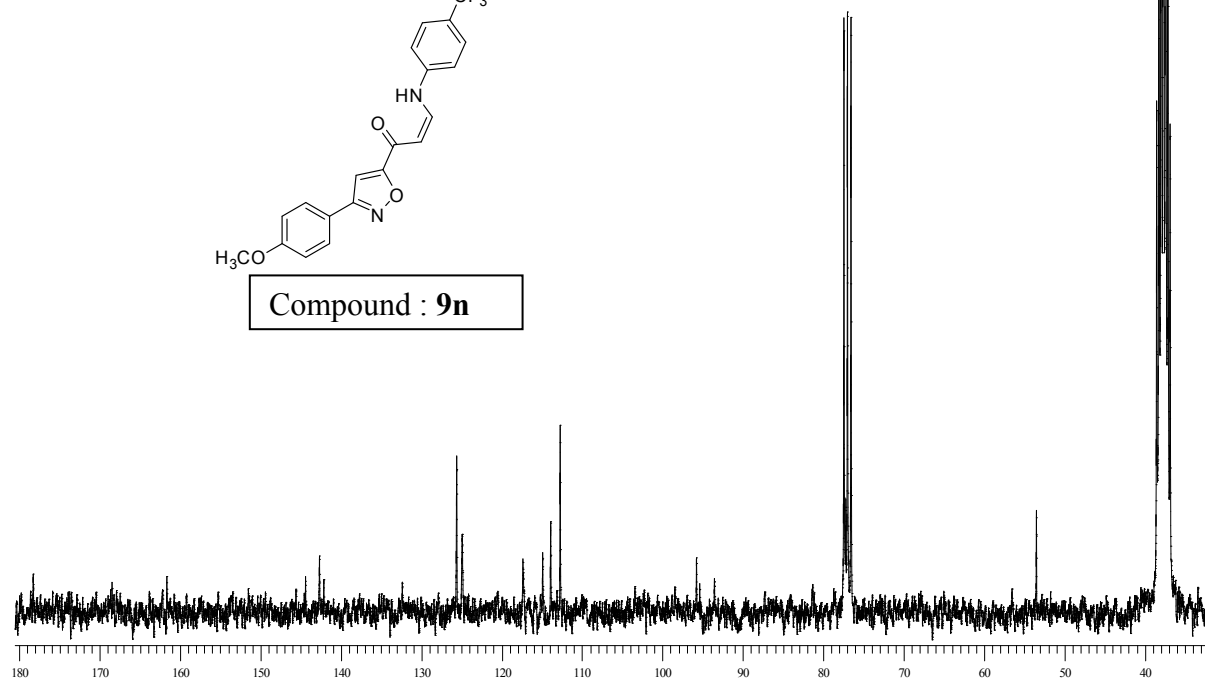


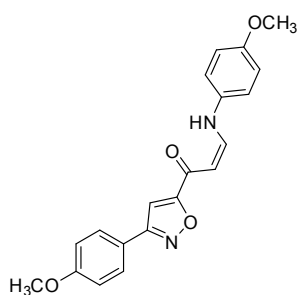


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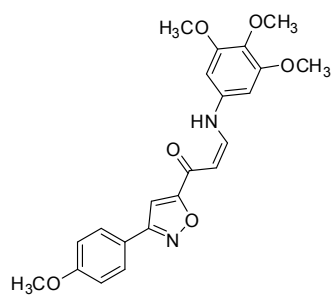
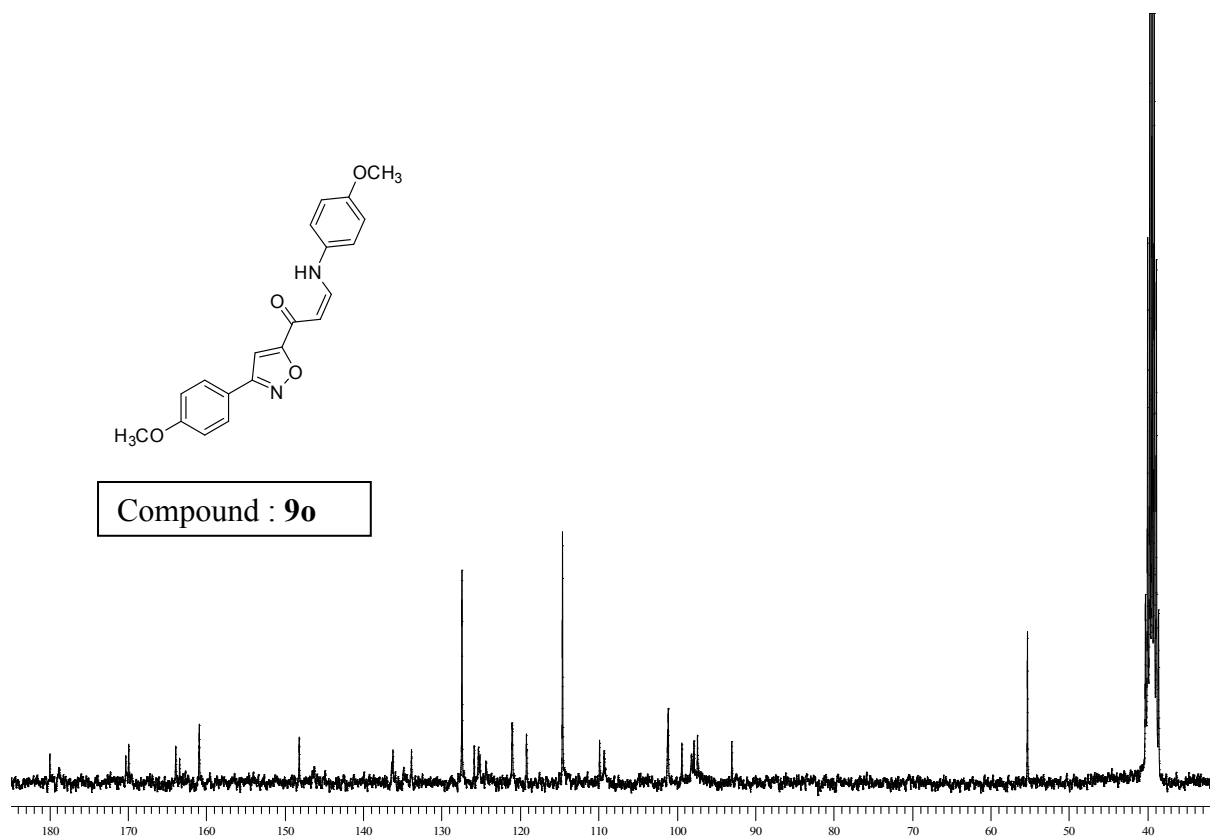


Compound : **9n**

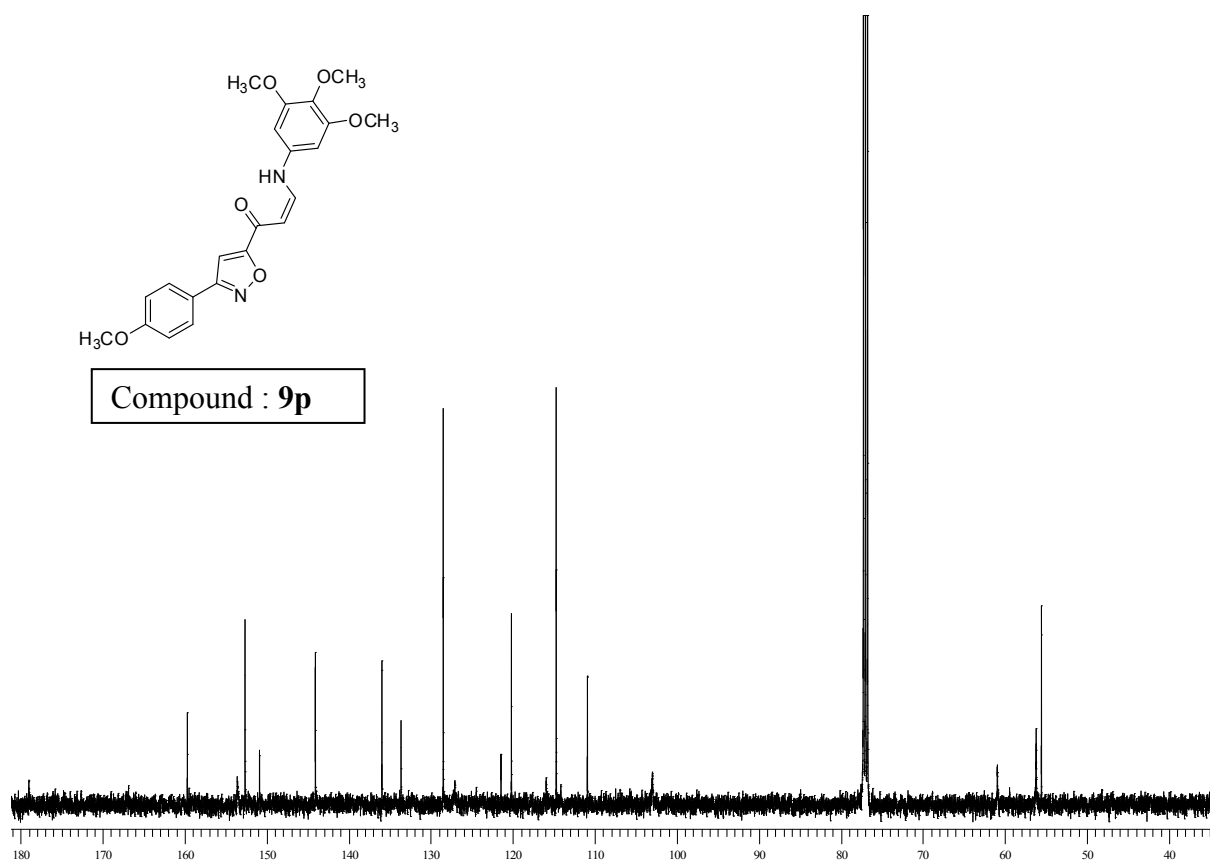


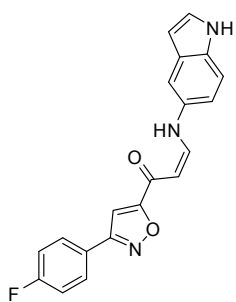


Compound : **9o**

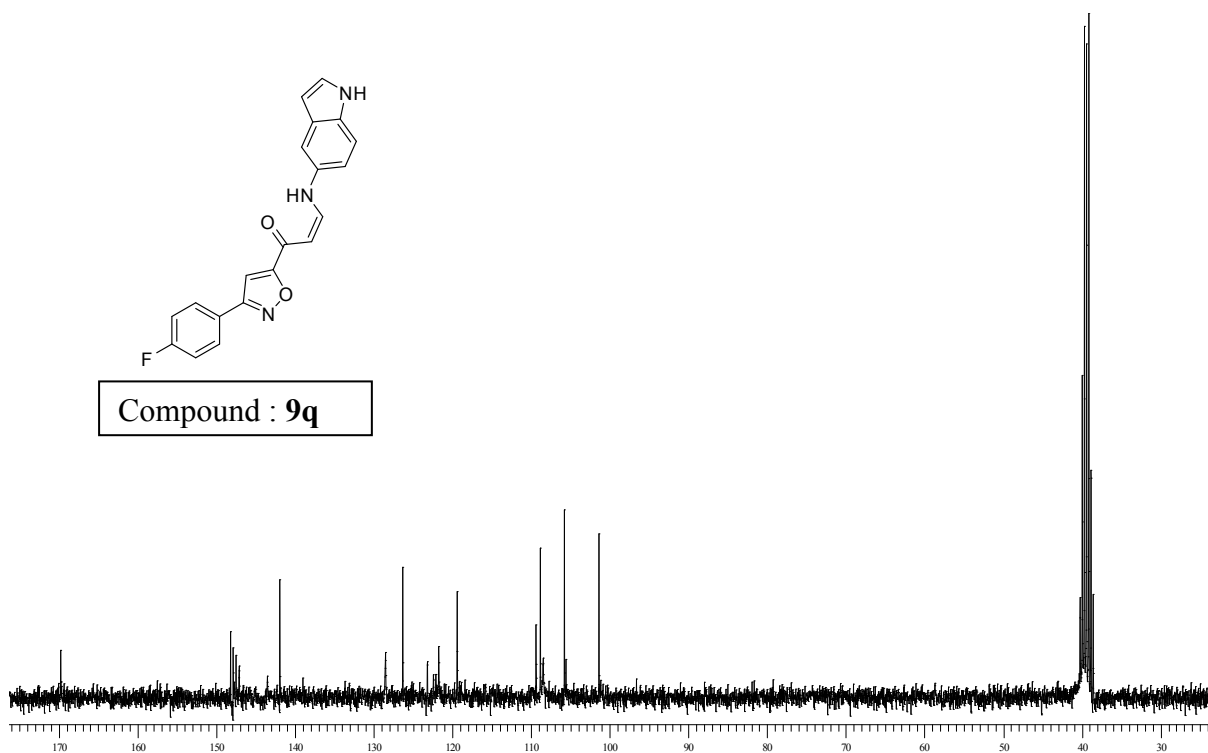


Compound : **9p**

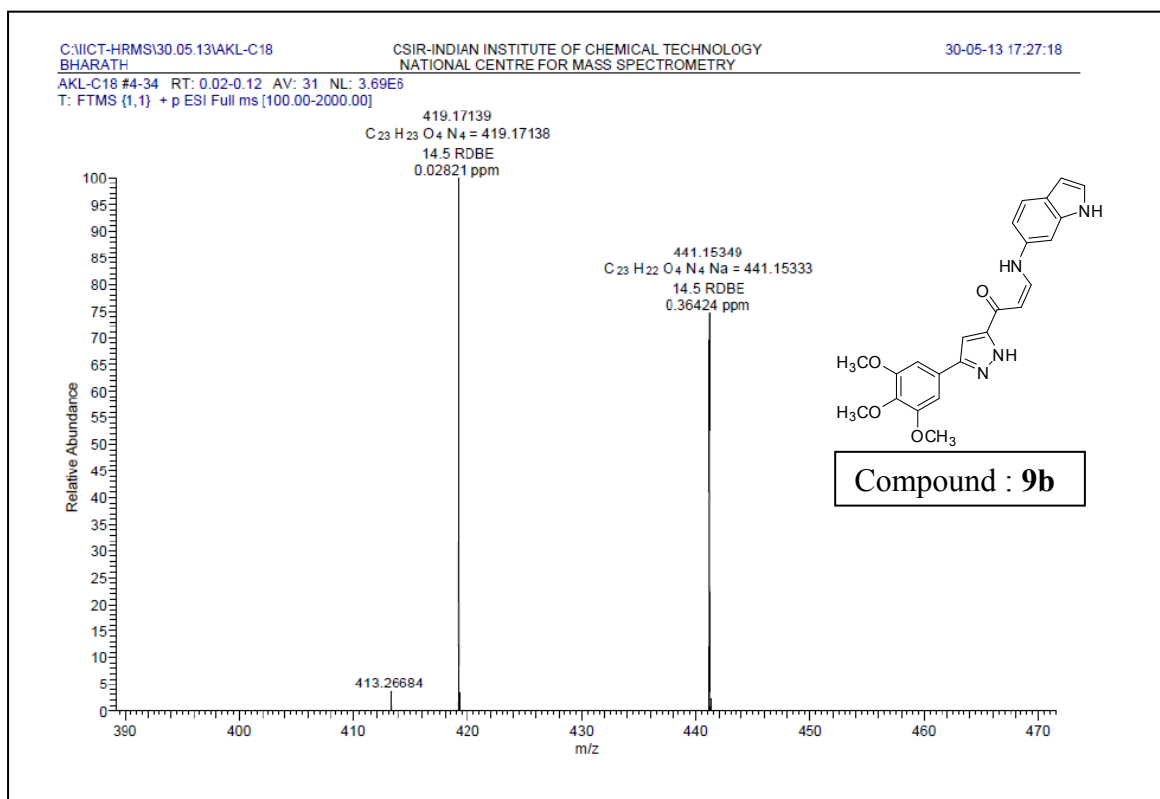
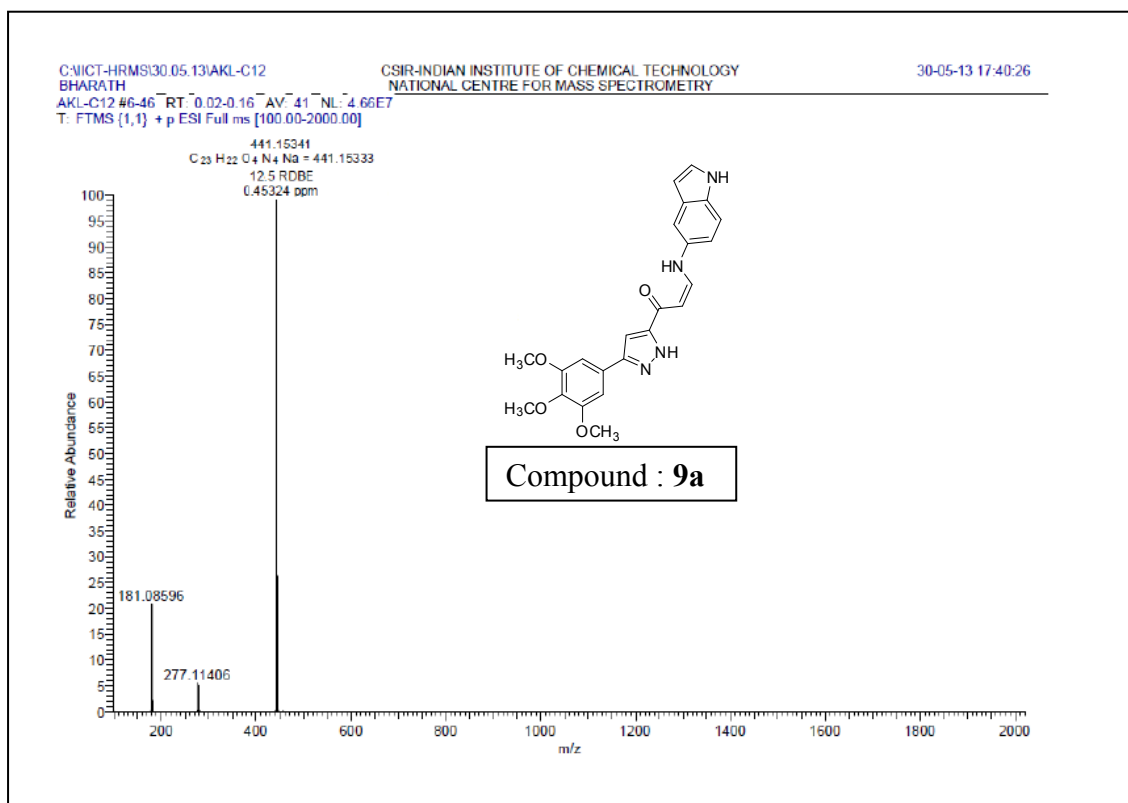




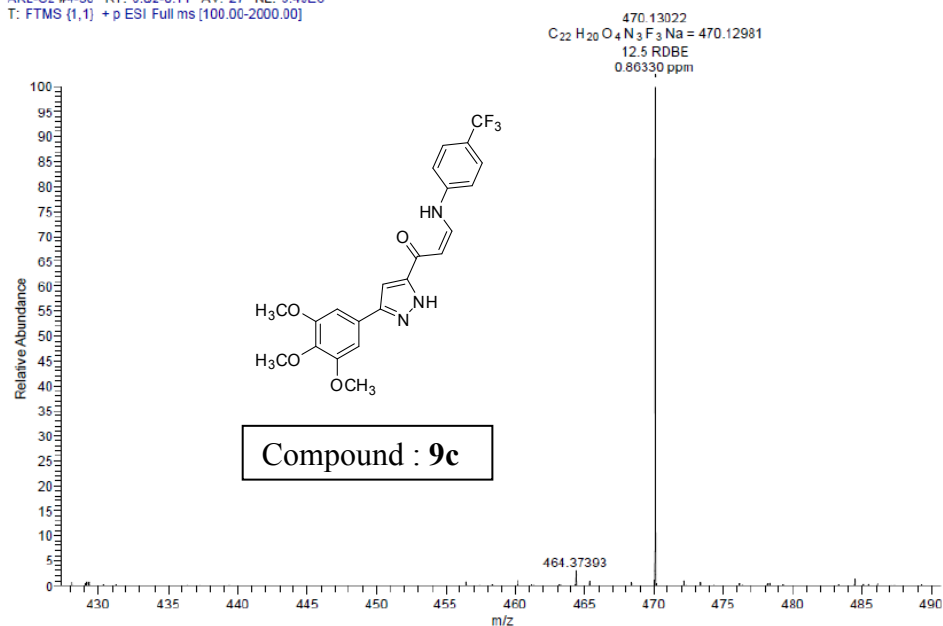
Compound : **9q**



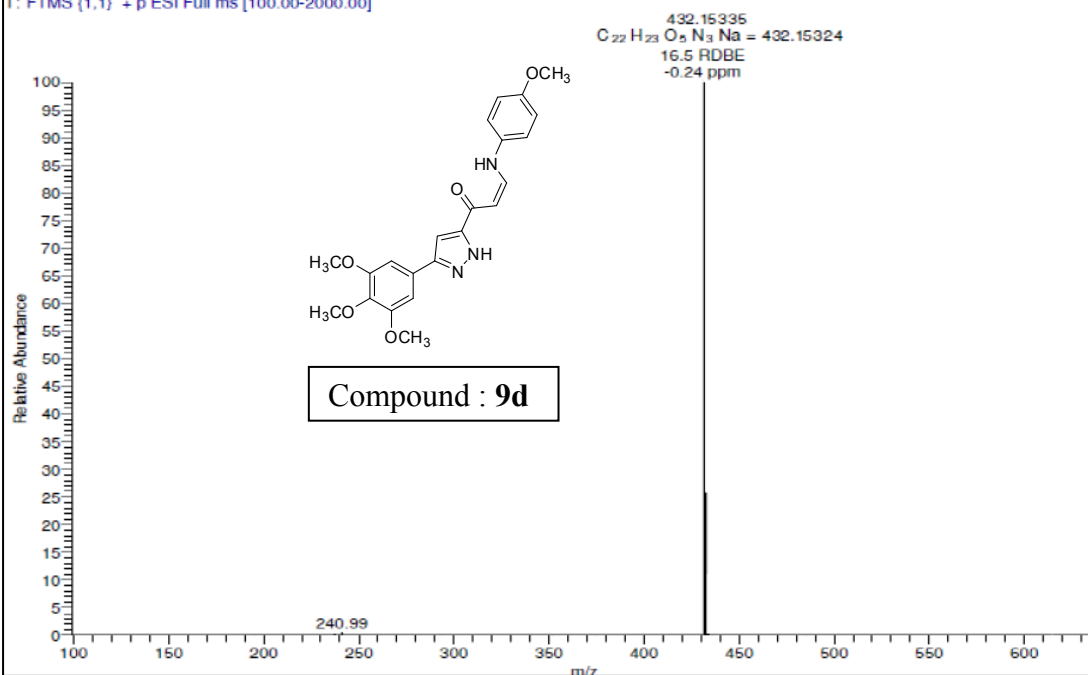
HRMS Spectra

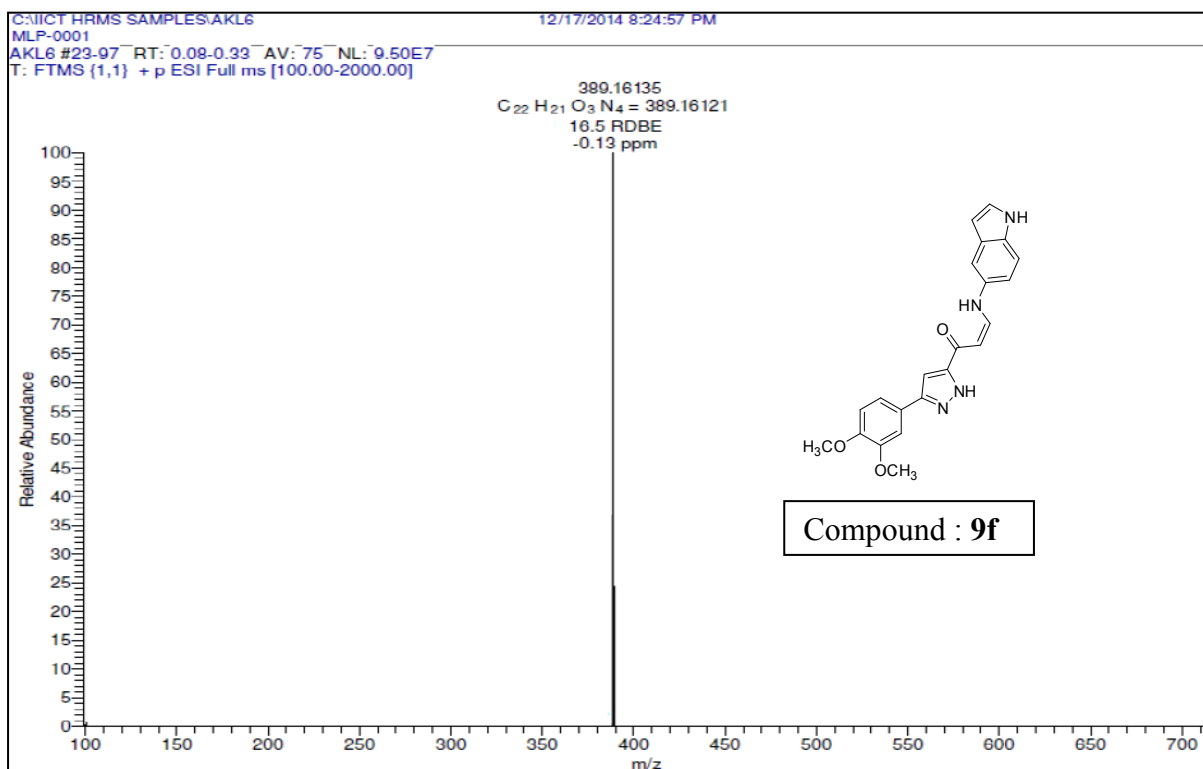
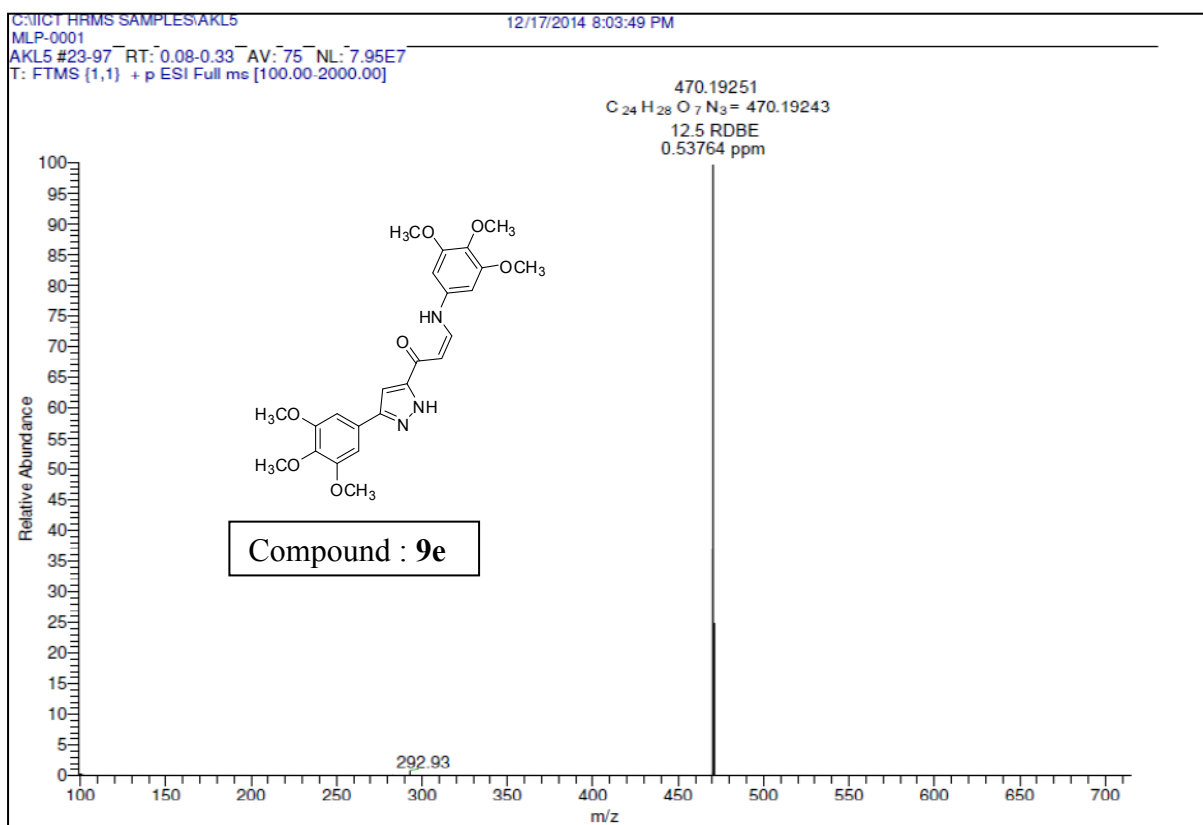


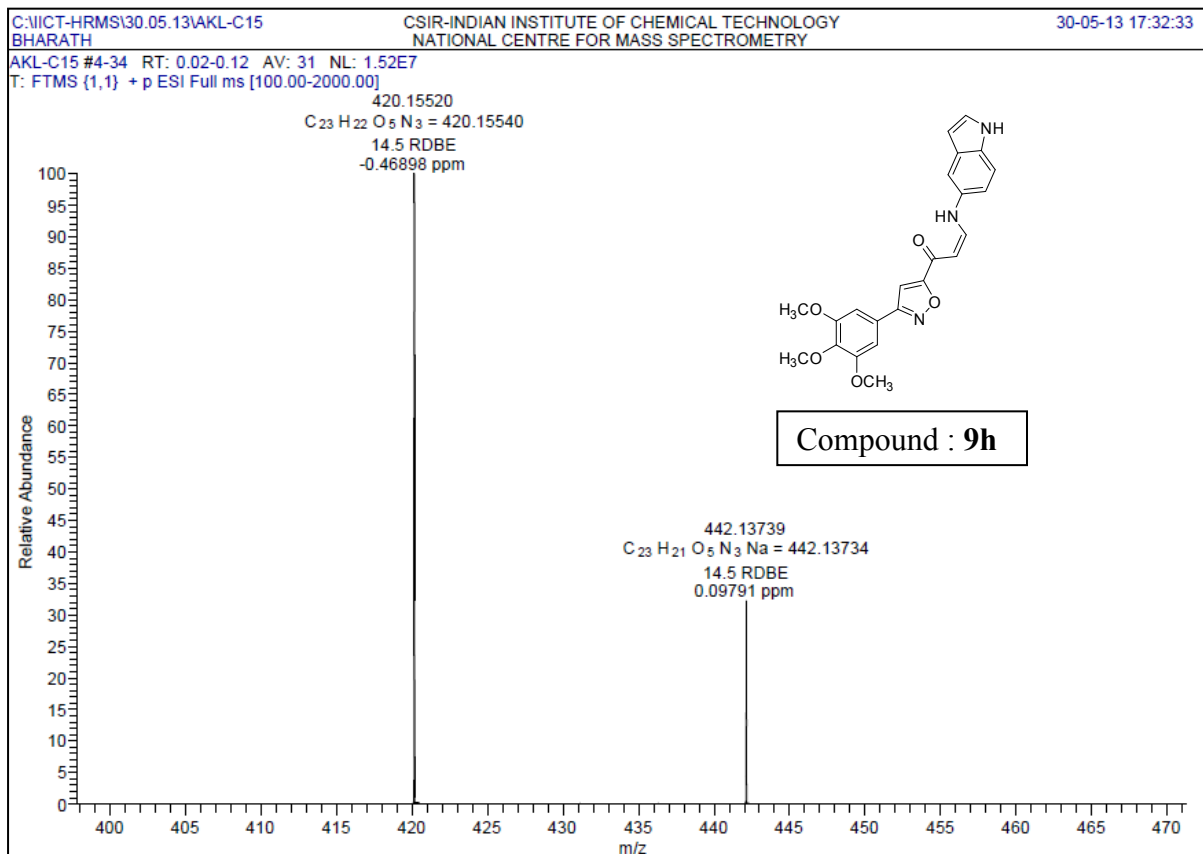
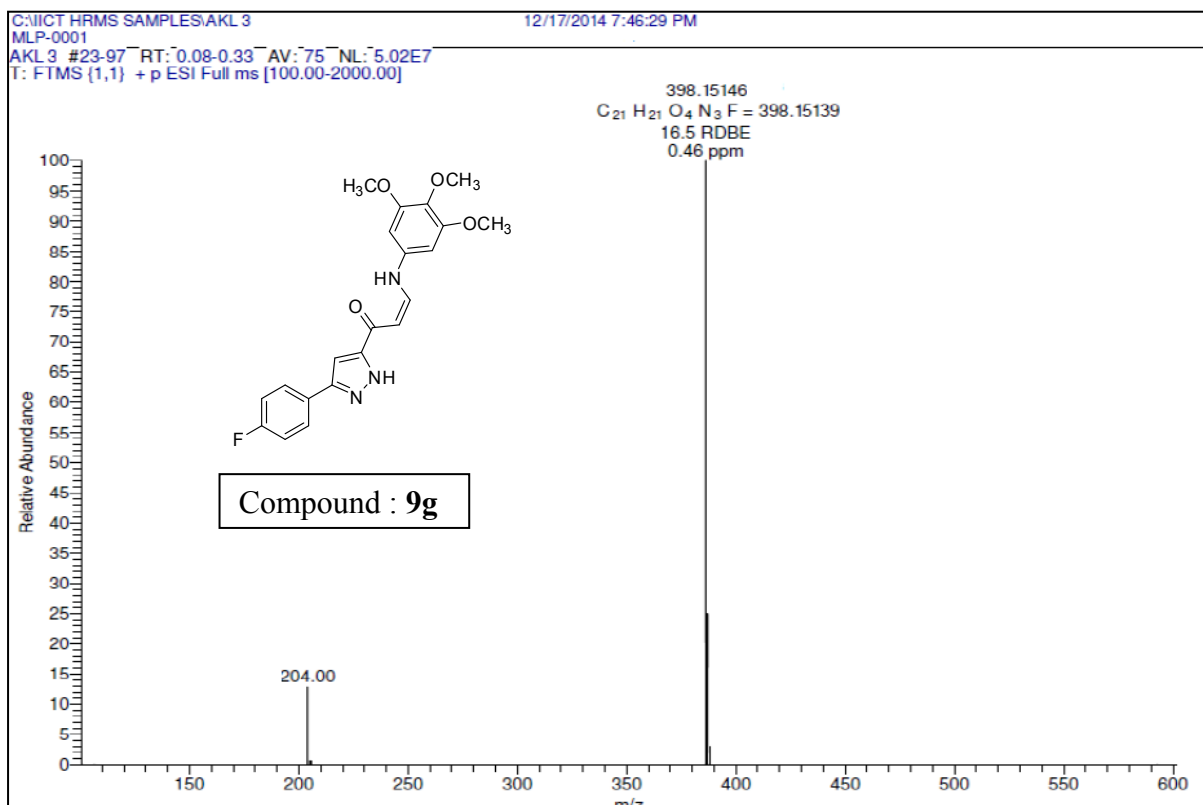
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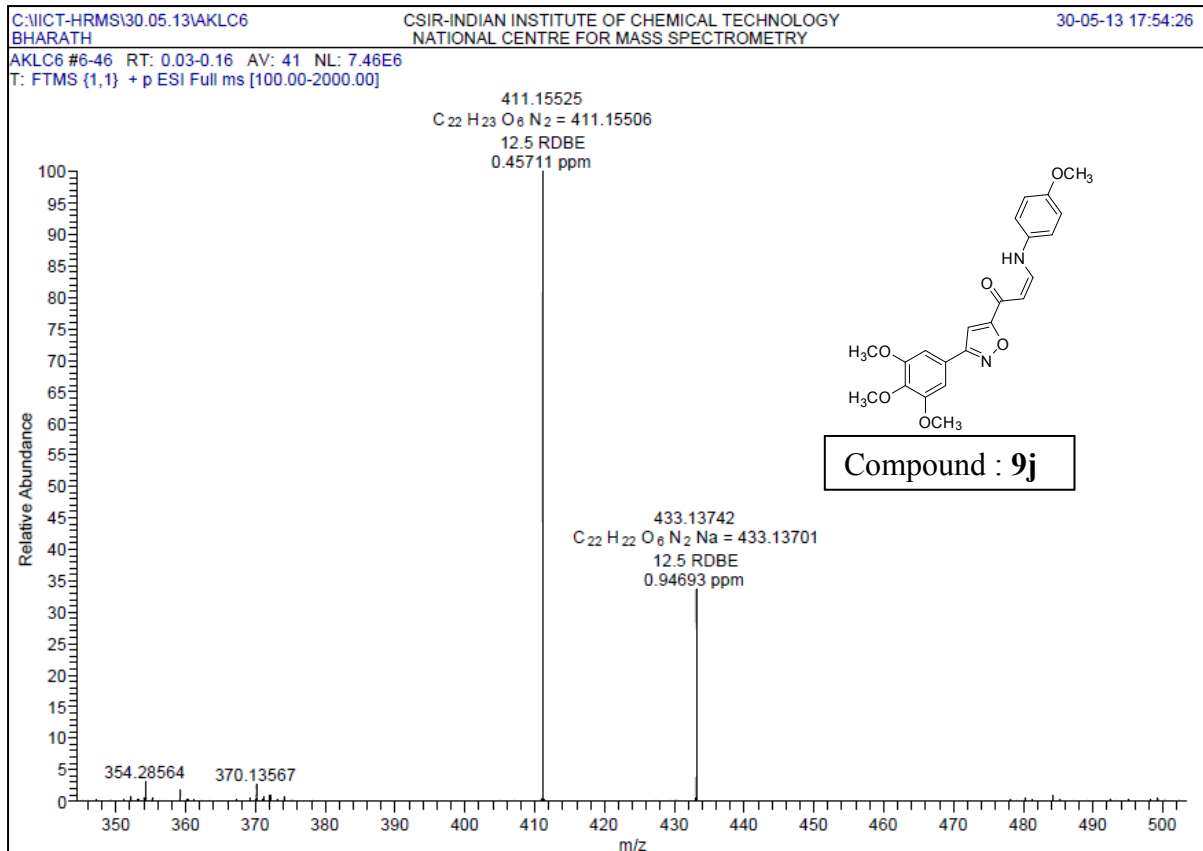
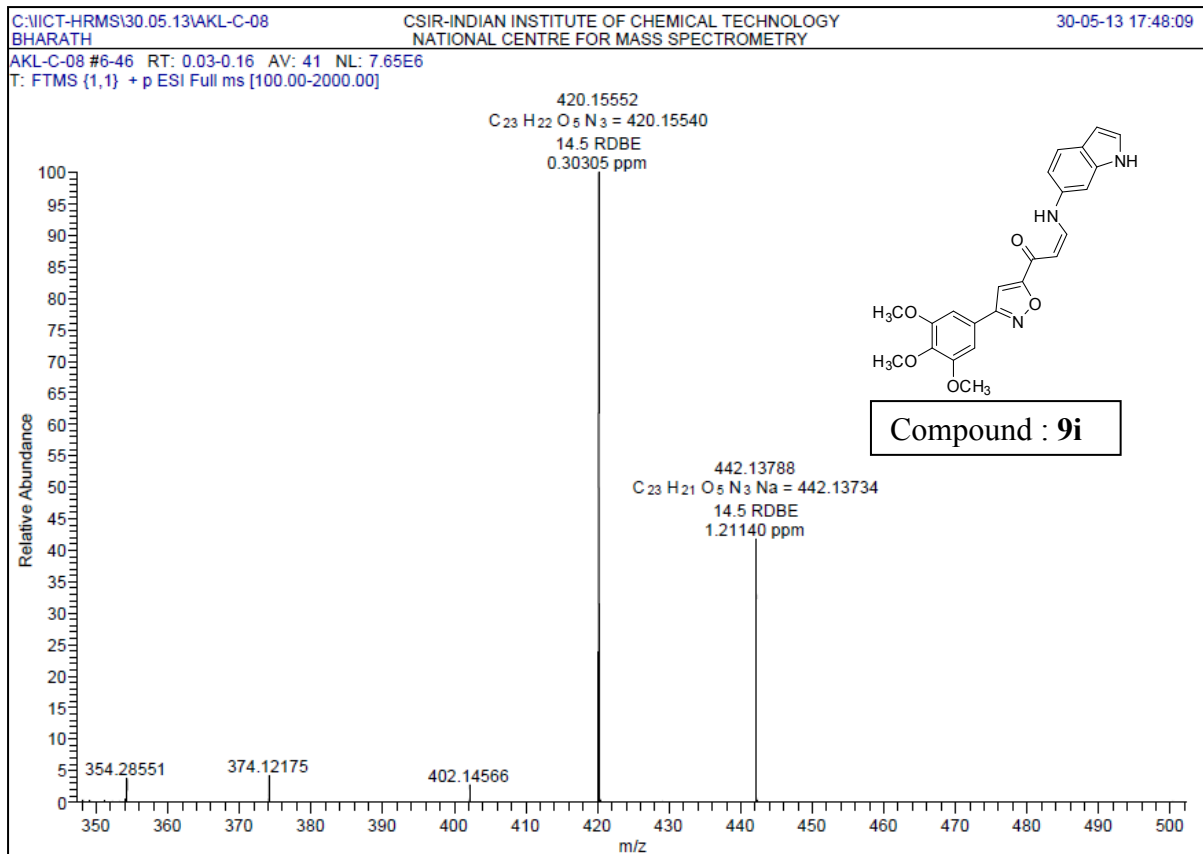


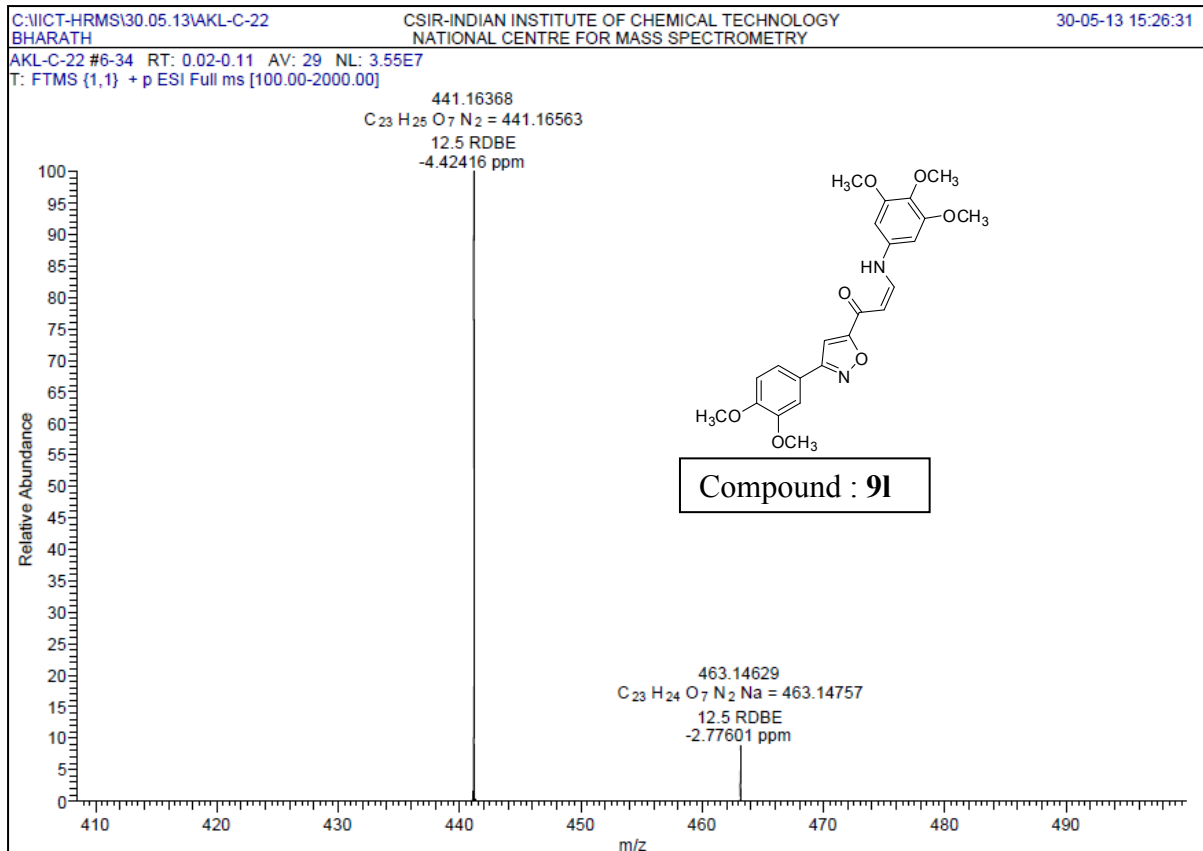
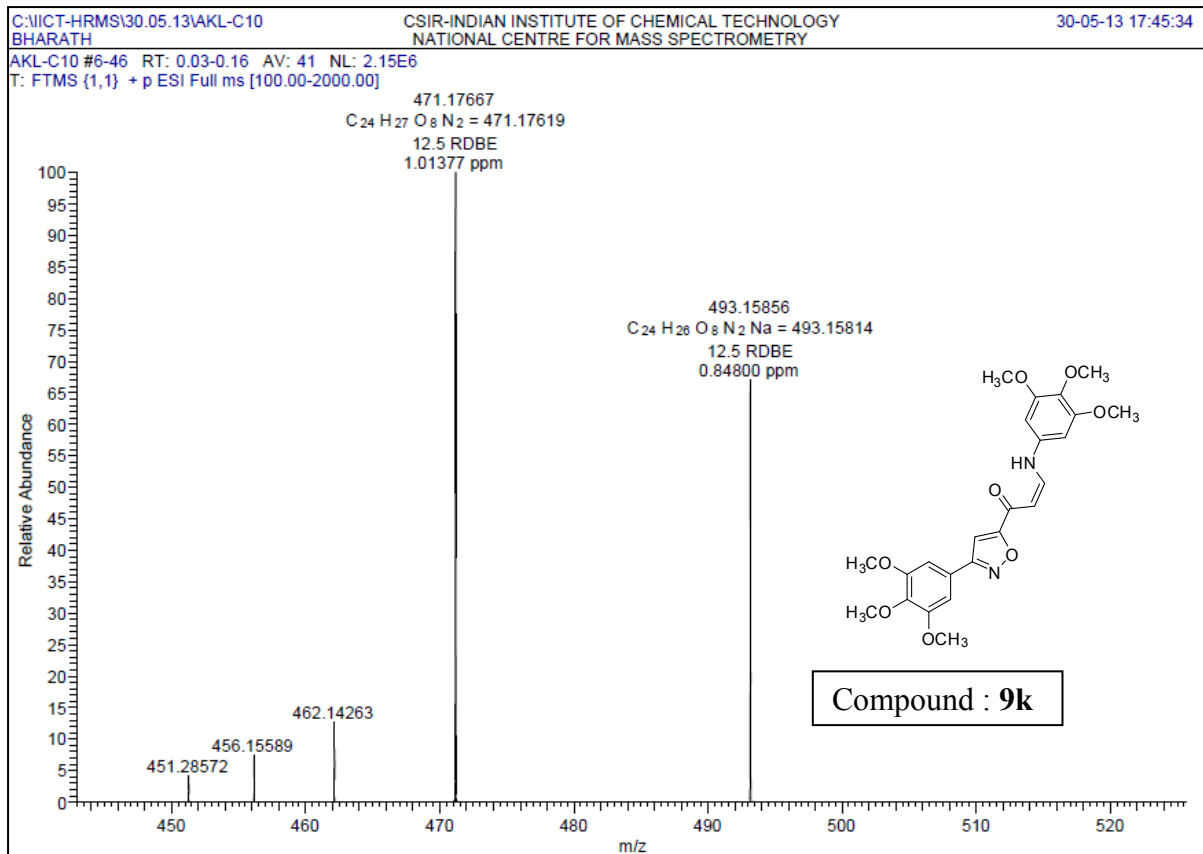
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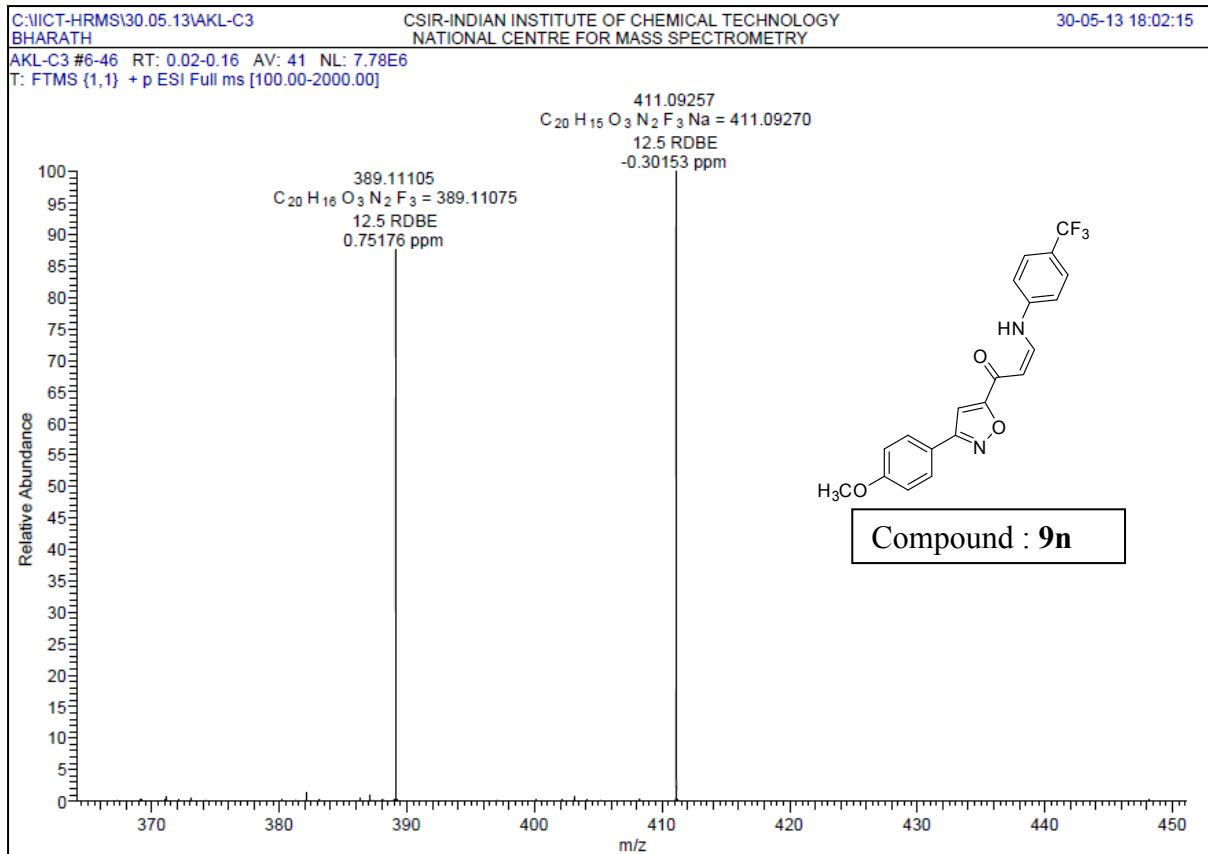
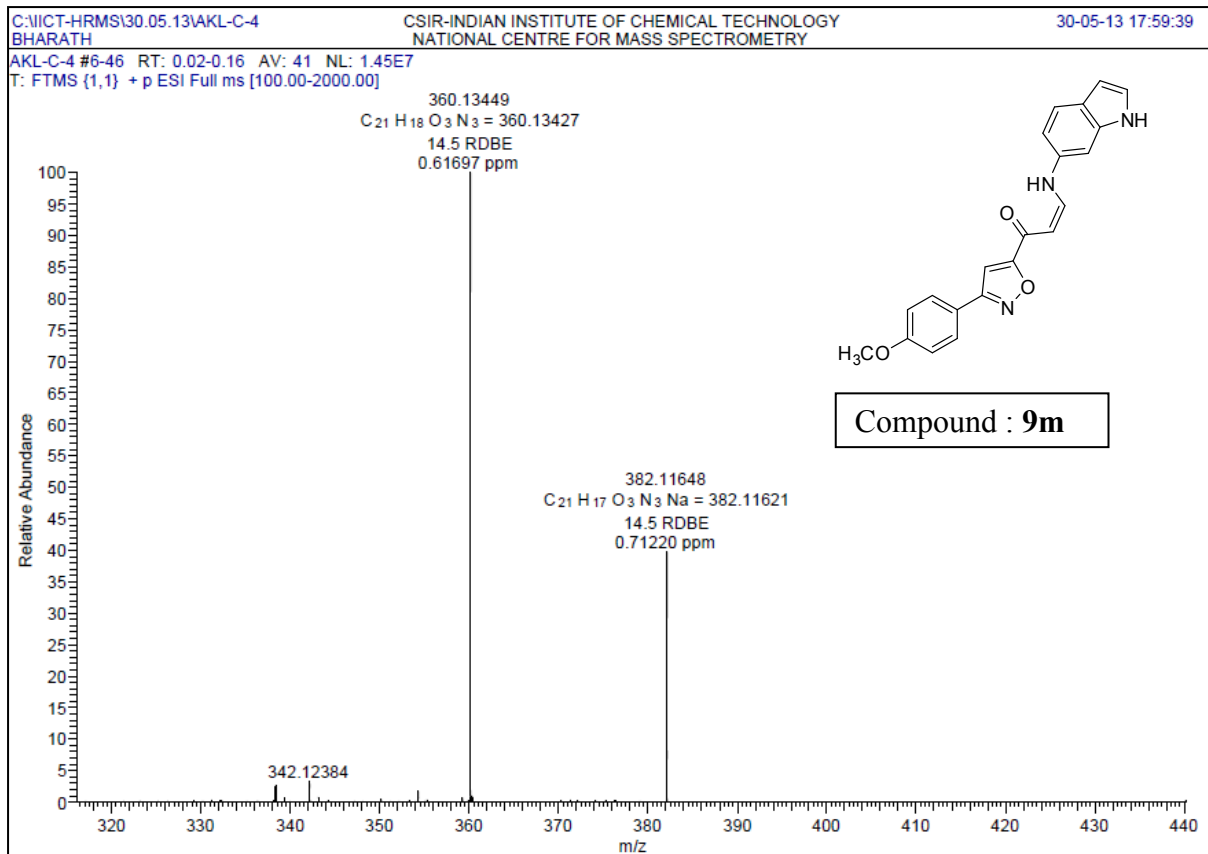


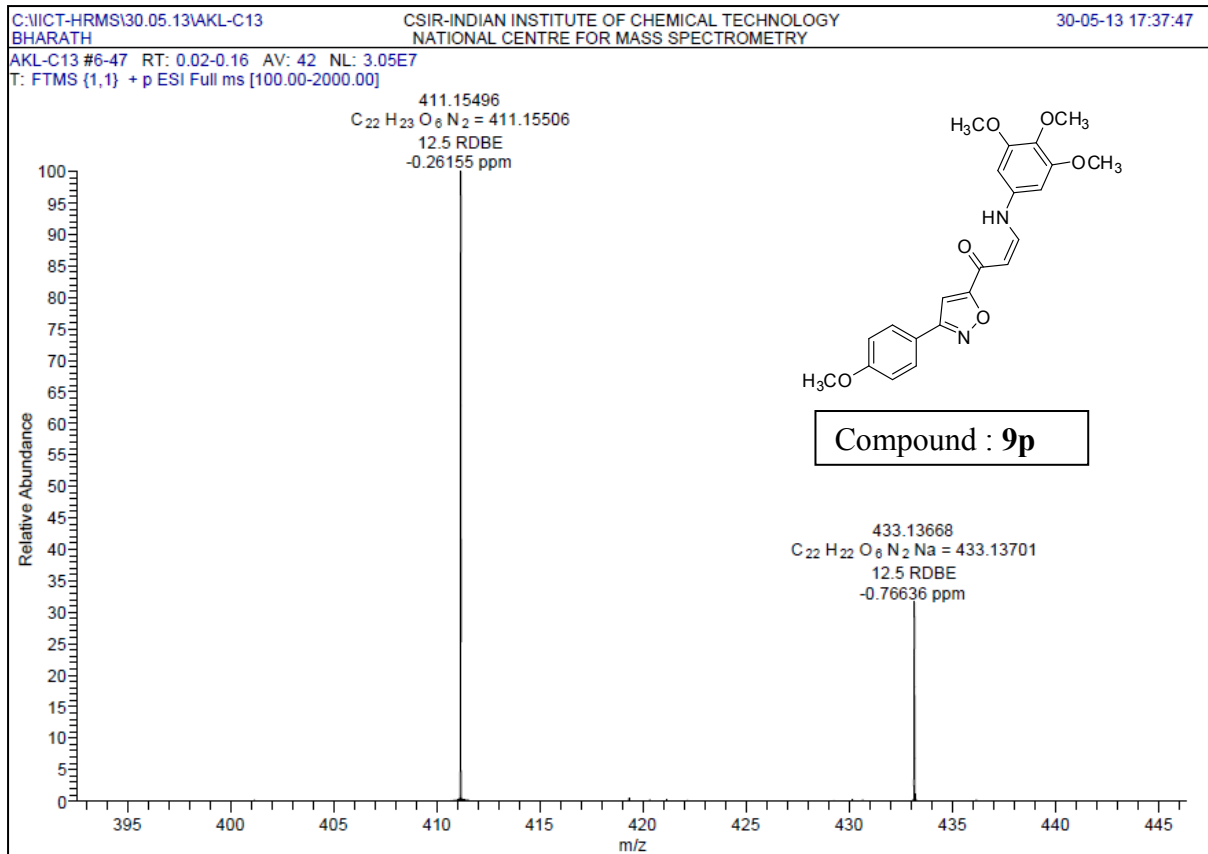
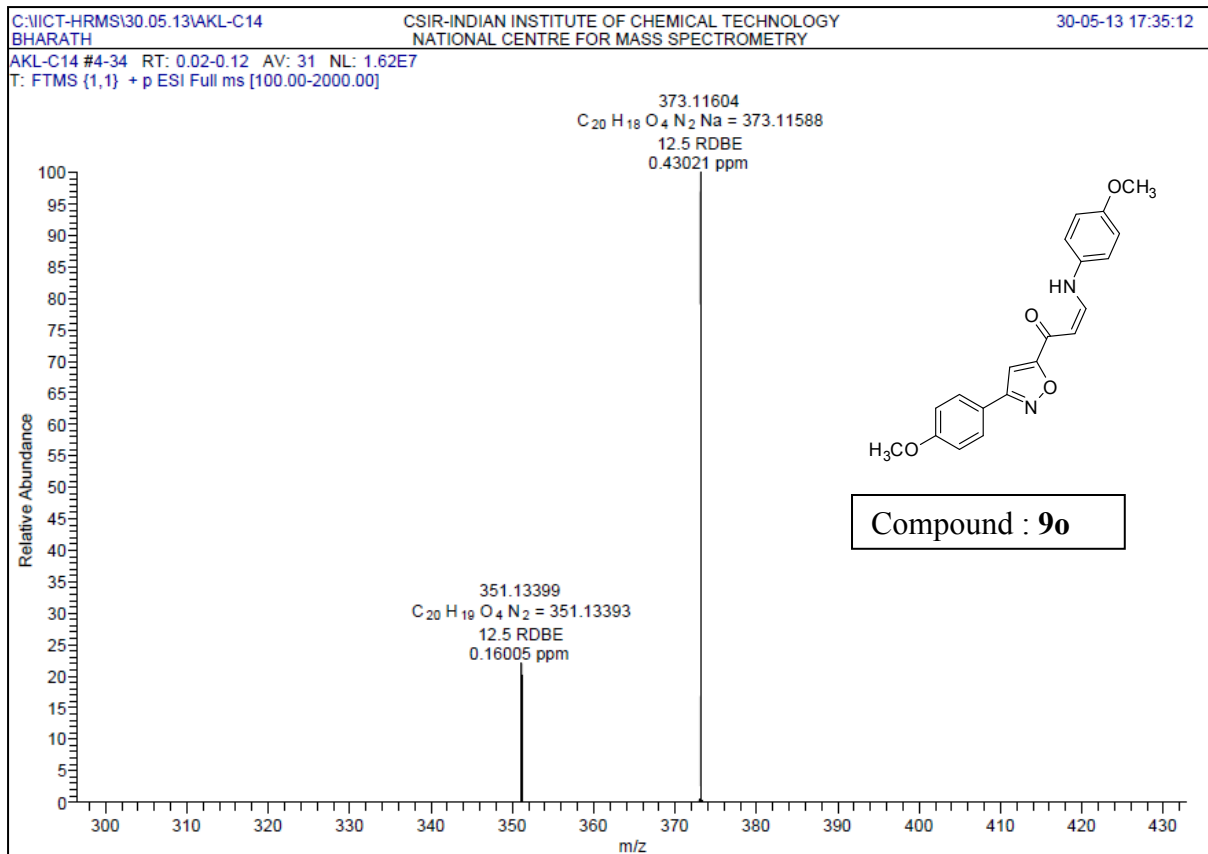




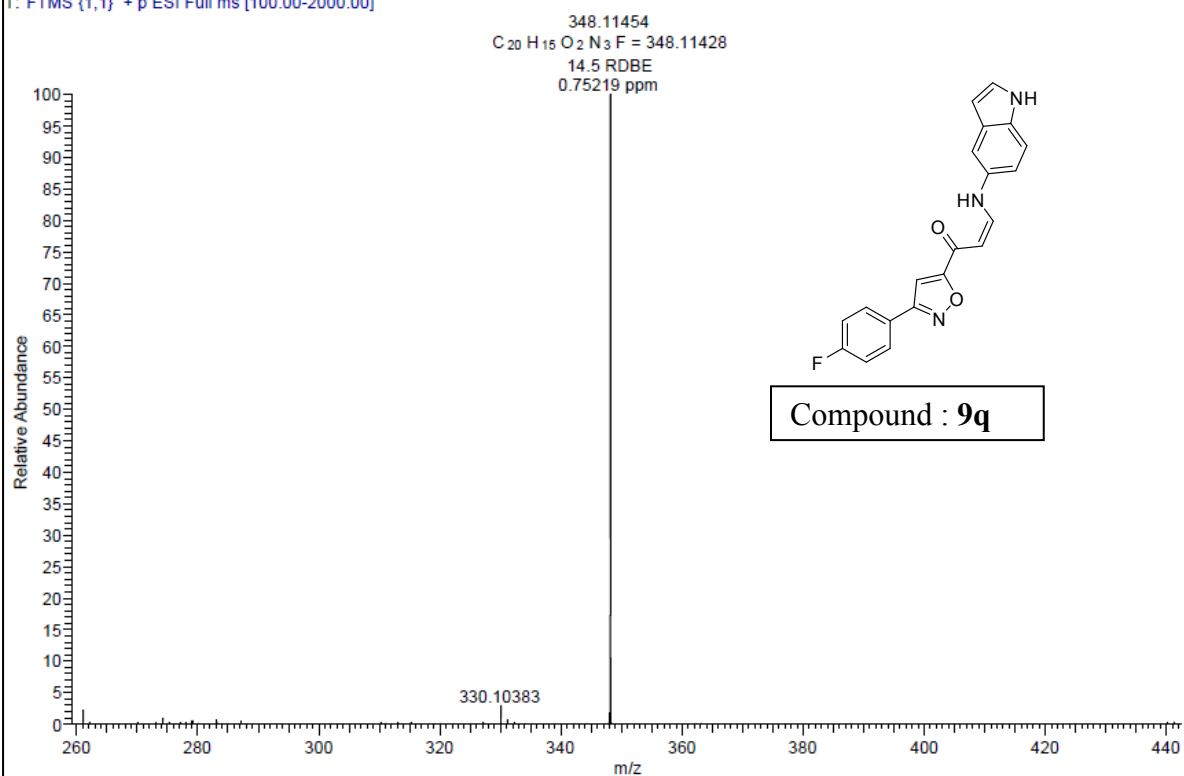








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Caspase-3 activation

There are some reports that the cell cycle arrest at G2/M phase takes place by the induction of cellular apoptosis. Hence, it was considered of interest to understand the correlation of cytotoxicity with that to apoptosis by **9a** and **9b**. Cysteine aspartase group, namely, caspases play a crucial role in the induction of apoptosis and amongst them caspase-3 happens to be one of the effector caspase. Hence, we treated A-549 cells with **9a** and **9b** examined the activation of caspase-3. The results indicate that there is nearly 2-3.5 fold induction in caspase-3 activity in cells treated with these conjugates at 2 μ M concentrations for 24 hrs. Therefore activation of caspase-3 by **9a** and **9b** indicate that they have the capacity to induce apoptosis in A-549.

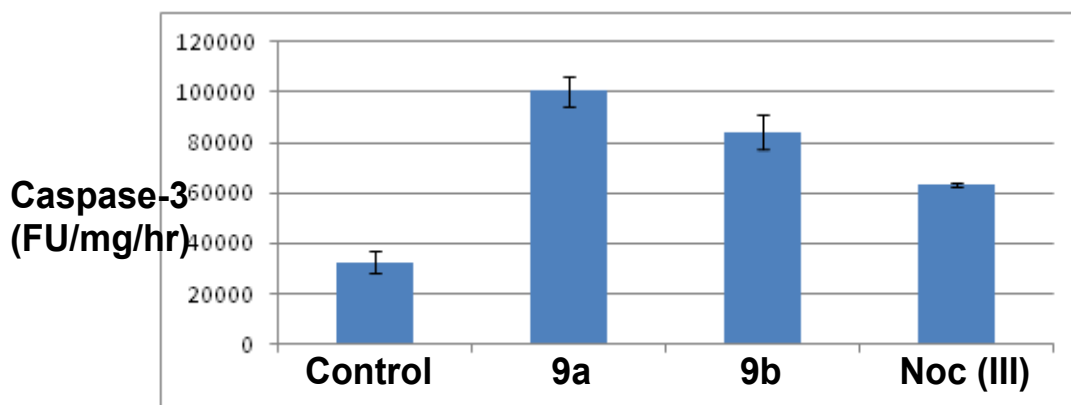


Figure: Effect of compounds 9a and 9b on caspase-3 activity: A-549 cells were treated for 24 h with 2 μ M concentrations of compounds 9a and 9b. Values indicated are the mean $\pm$ SD of two different experiments performed in triplicates.