

**SUPPORTING INFORMATION OF COMPOUNDS (5a-aa)**

**Synthesis and biological evaluation of imidazo[1,5-*a*]pyridine-benzimidazole hybrids as inhibitors of both tubulin polymerization and PI3K/Akt pathway**

Ahmed Kamal,<sup>a, b\*</sup> A.V. Subba Rao,<sup>a</sup> V. Lakshma Nayak,<sup>a</sup> N.V. Subba Reddy,<sup>a</sup>

Konderu Swapna,<sup>b</sup> G. Ramakrishna<sup>a</sup> and Mallika Alvala<sup>b</sup>

<sup>a</sup>*Medicinal Chemistry and Pharmacology, CSIR-Indian Institute of Chemical Technology, Hyderabad, 500 007, India*

<sup>b</sup>*Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), Hyderabad, 5000 037, India*

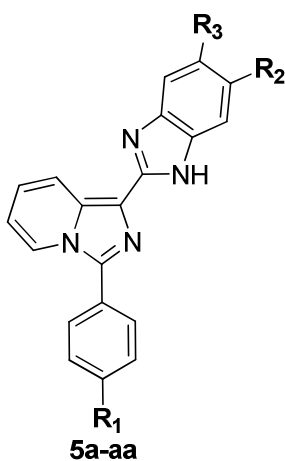
**Experimental**

**Chemistry**

**Materials and Methods.**

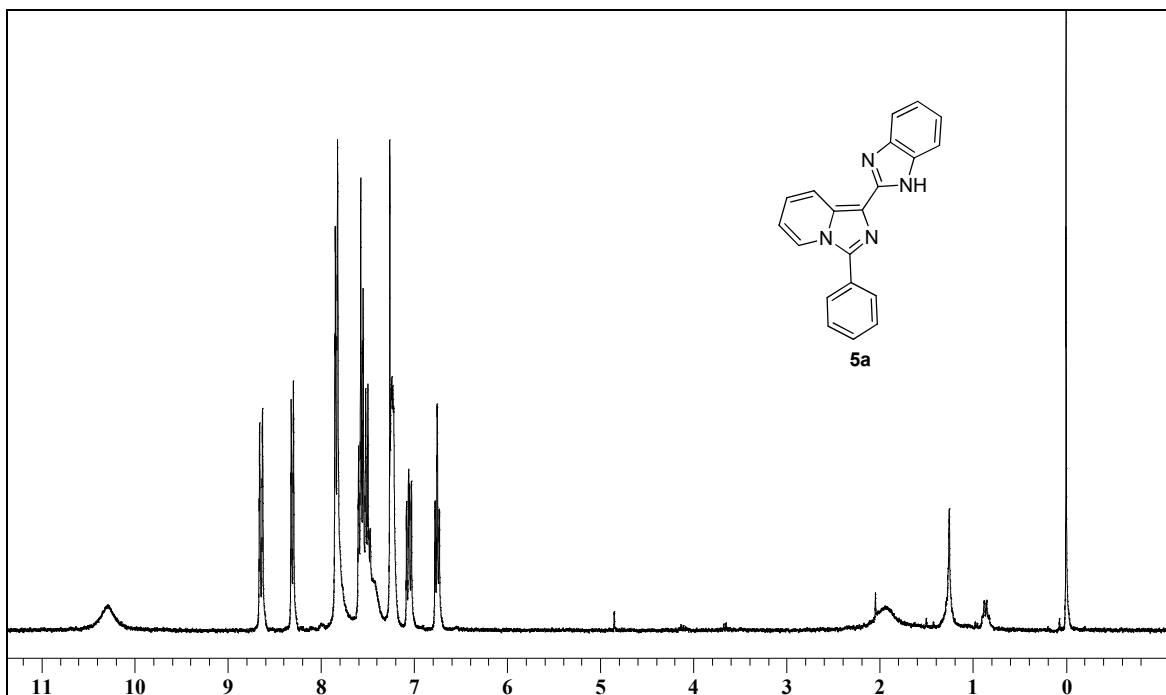
<sup>1</sup>H NMR spectra were recorded on Avance 300, Inova 400, Avance 500, and Bruker 600 MHz spectrometers using tetramethylsilane (TMS) as the internal standard. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane. Spin multiplicities are described as s (singlet), brs (broad singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), and m (multiplet). Coupling constants are reported in Hertz (Hz). Melting points were determined in a capillary tube using an Electrothermal apparatus (Model IA9200) and are uncorrected. The IR spectra were recorded by employing a Nicolet FTIR model MX-1 spectrophotometer. Analytical thin layer chromatography (TLC) was performed on MERCK precoated silica gel 60- F254 (0.5 mm) glass plates. Visualization of the spots on TLC plates was achieved either by exposure to iodine vapour or UV light or by dipping the plates into  $\beta$ -naphthol or to ethanolic anisaldehyde or to ethanolic ninhydrin solution and heating the plates to 120 °C.

Column chromatography was performed using silica gel 60-120 or 100-200 mesh. Moisture sensitive reactions were carried out using standard syringe septum techniques and under inert atmosphere of nitrogen. All solvents and reagents were purified by standard techniques. *O*-Phenylenediamines (**11a-i**) and substituted benzoyl chlorides (**7a-c**) are commercially available and used as received. All evaporation of solvents was carried out under reduced pressure on rotary evaporator below 45 °C. The names of all the compounds given in the experimental section were taken from Chem Ultra, Version 11.0.

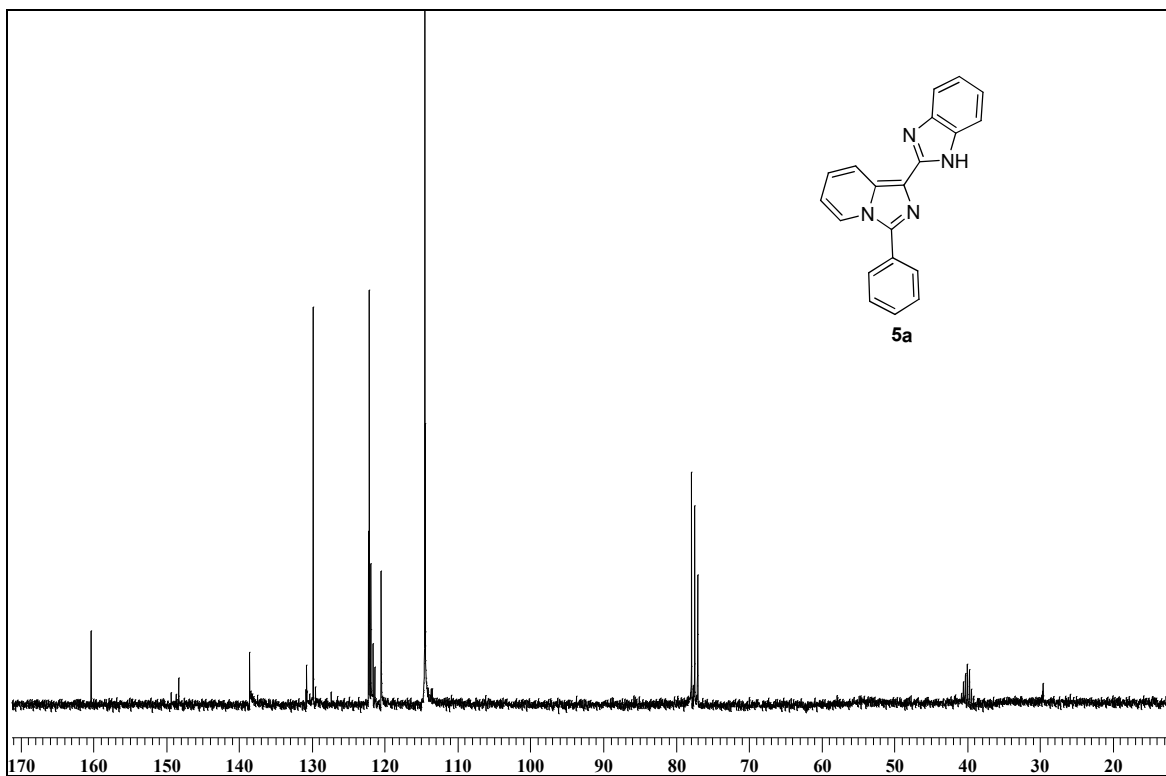


**General procedure for synthesis of compounds (5a-aa):**

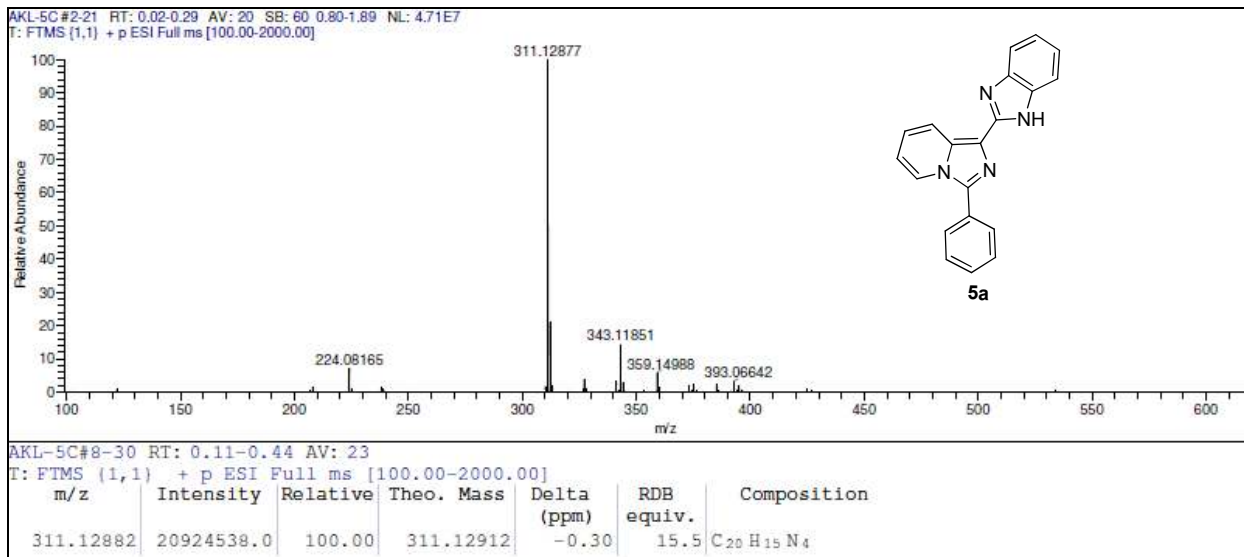
To a solution appropriate aldehyde (**10a-c**) in ethanol (10 mL), appropriate *o*-phenylenediamines (**11a-c**) (1 mmol) and sodium metabisulfite (2 mmol) dissolved in H<sub>2</sub>O (5 mL) were added sequentially and then reaction mixture was refluxed for 4 h. After completion of reaction, solvent was removed by vacuo to give crude product which was extracted with ethyl acetate. The combined organic extracts were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated to give crude products which were further purified by column chromatography by using ethylacetate and hexane as solvent system to afford pure compounds (**5a-aa**).



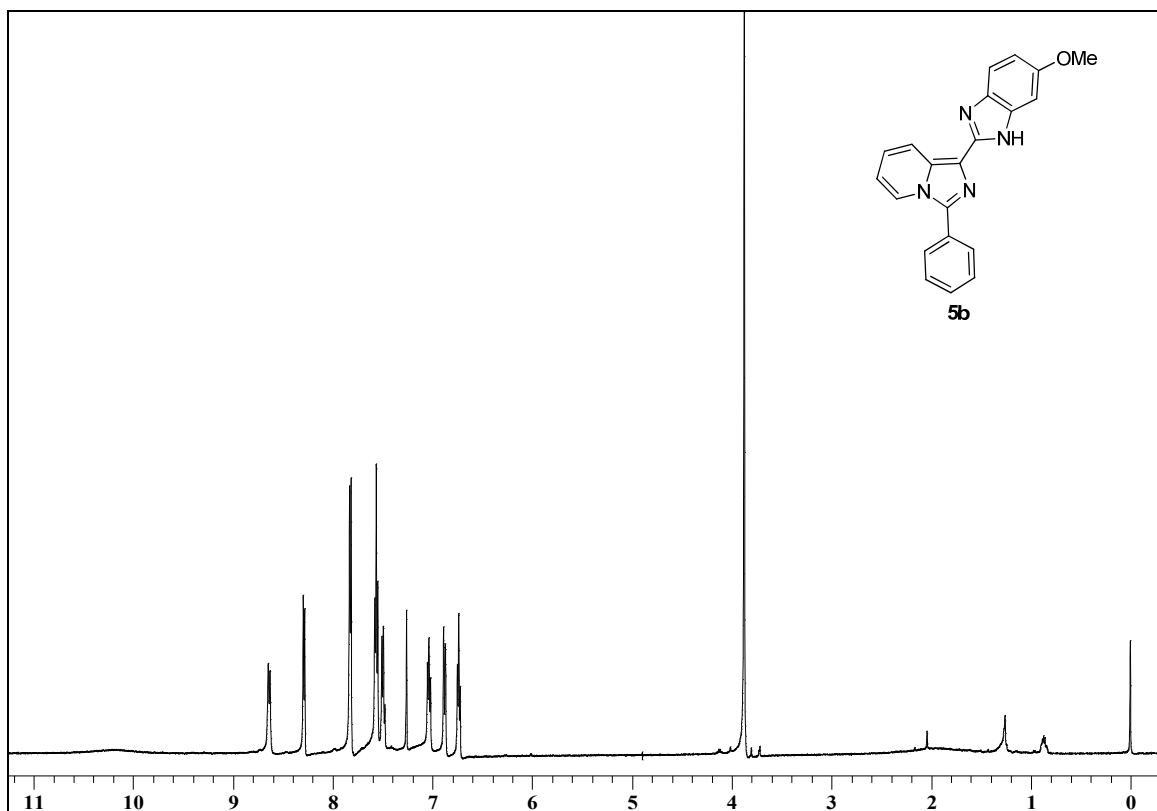
<sup>1</sup>H NMR SPECTRA OF COMPOUND 5a



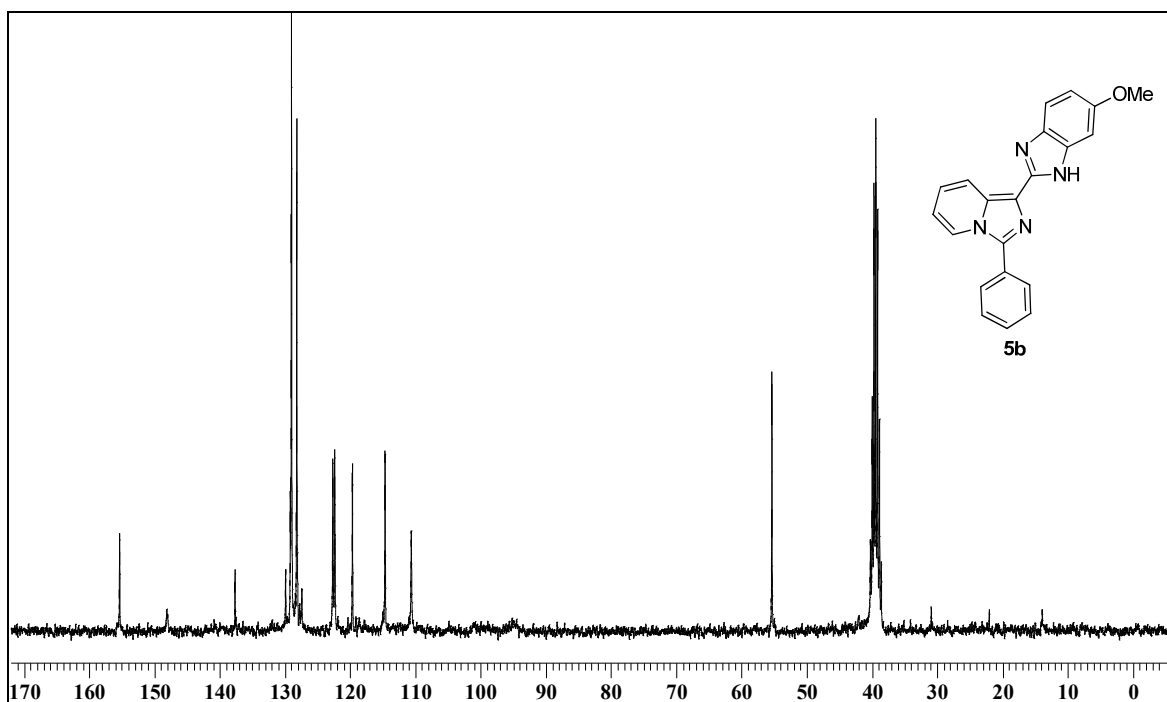
<sup>13</sup>C NMR SPECTRA OF COMPOUND 5a



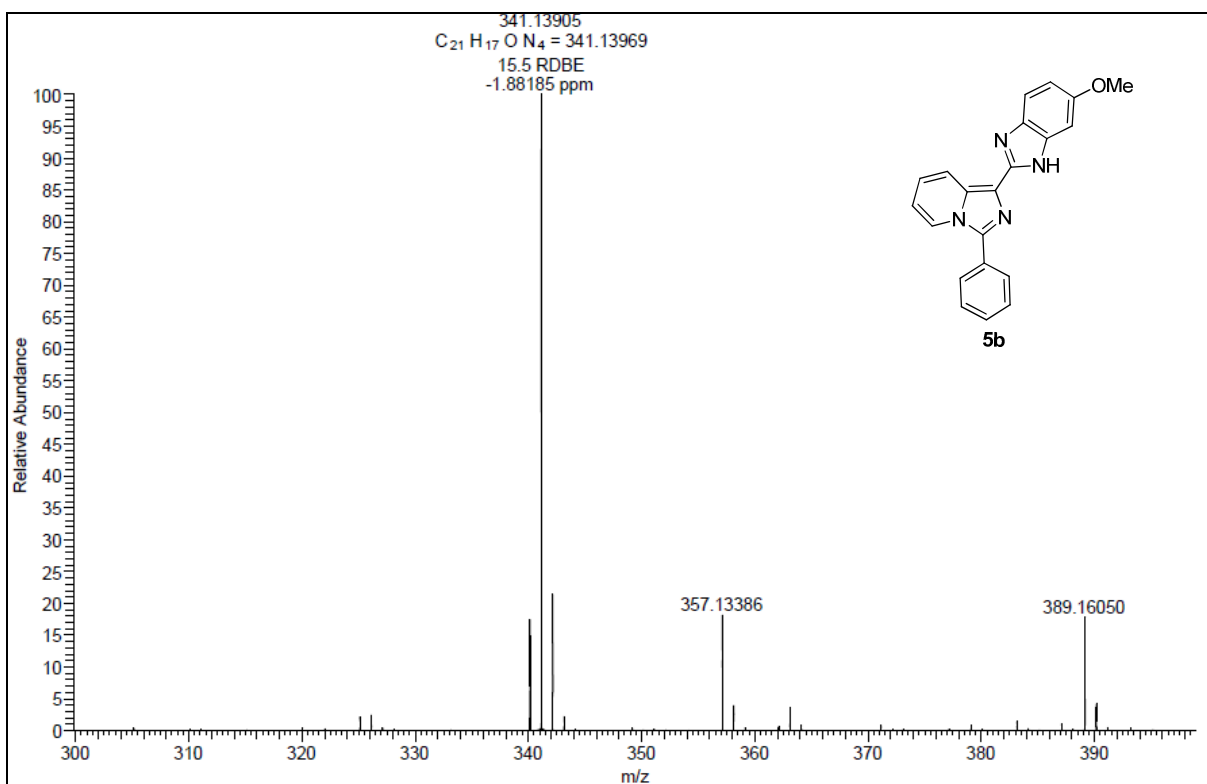
### HIGH RESOLUTION MASS SPECTRA OF COMPOUND 5a



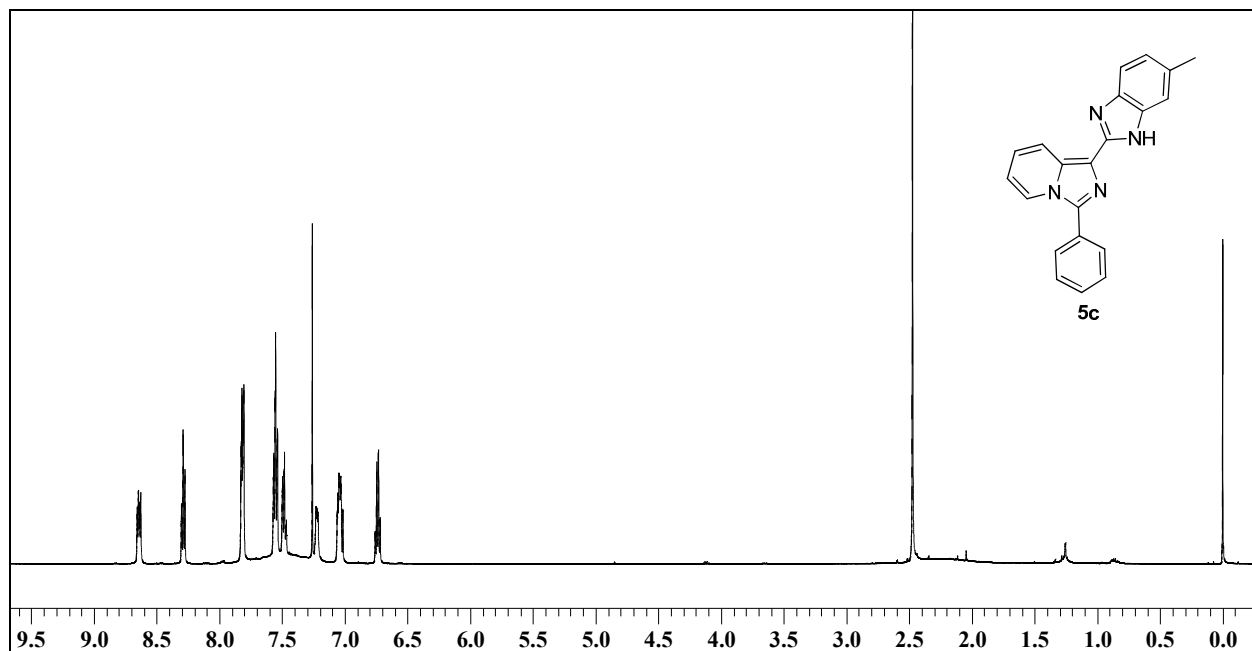
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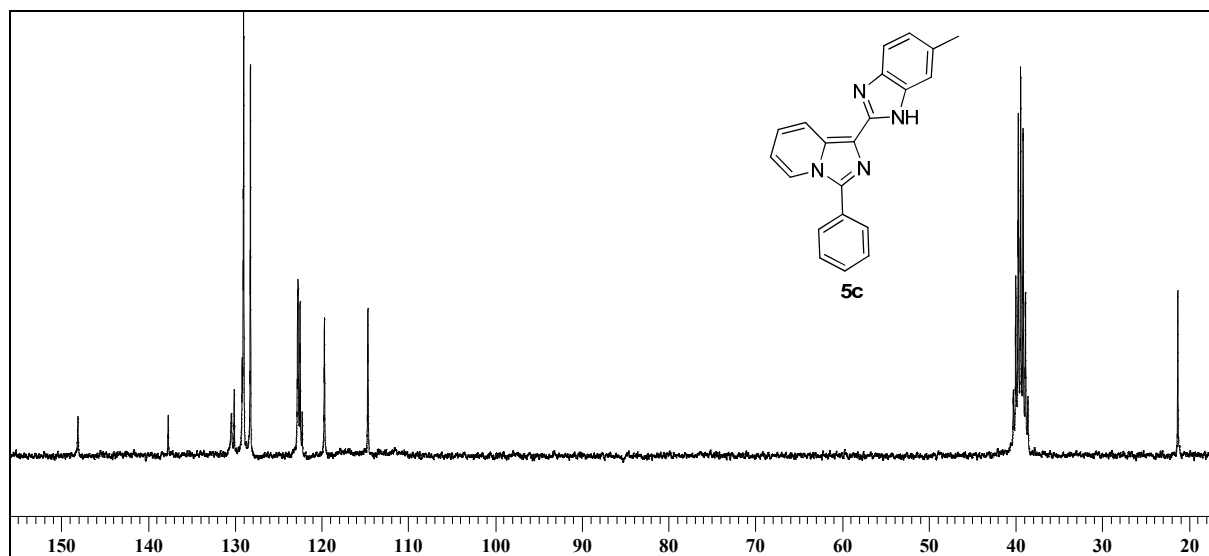
<sup>13</sup>C NMR SPECTRA OF COMPOUND 5b



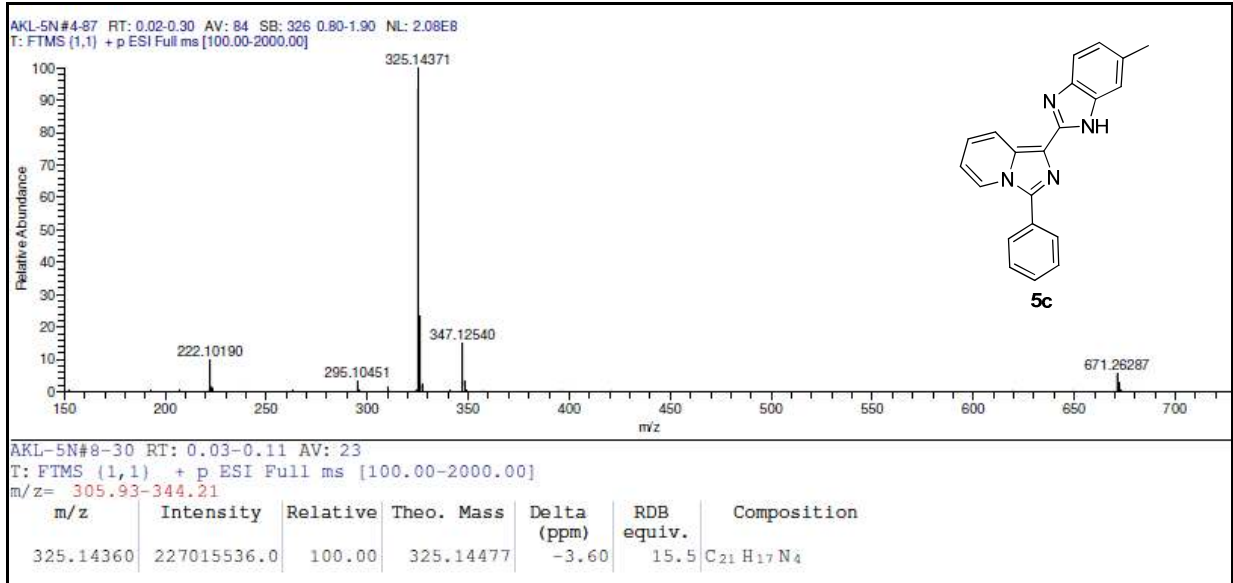
HIGH RESOLUTION MASS SPECTRA OF COMPOUND 5b



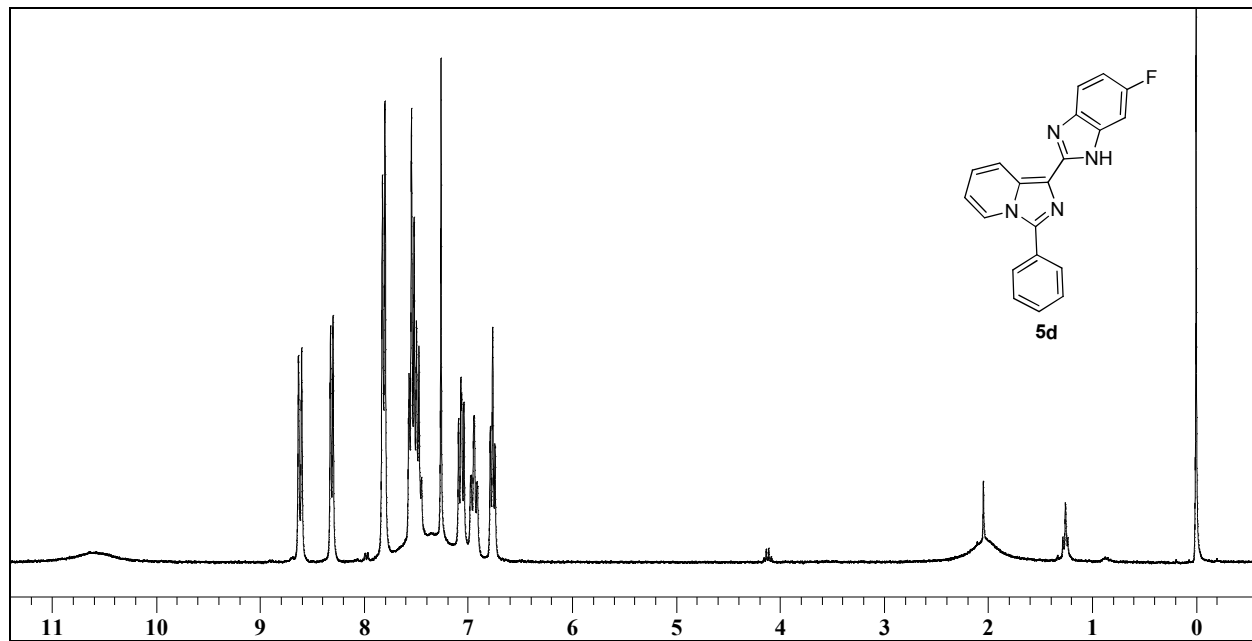
**<sup>1</sup>H NMR SPECTRA OF COMPOUND 5c**



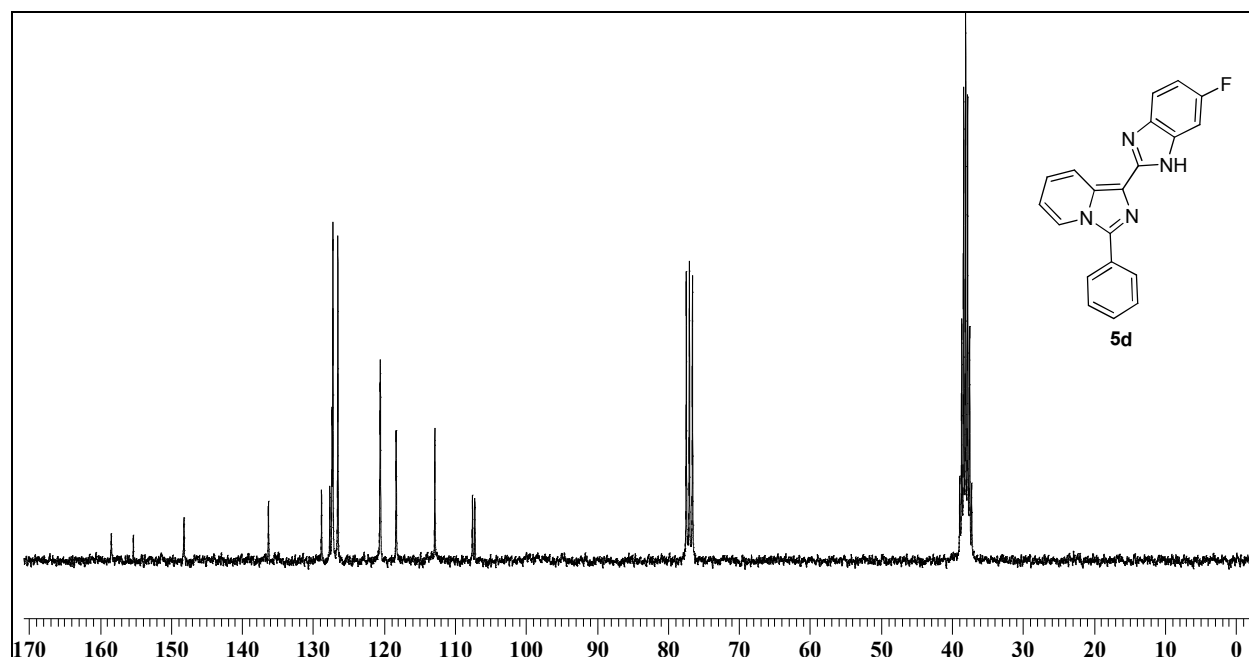
**<sup>13</sup>C NMR SPECTRA OF COMPOUND 5c**



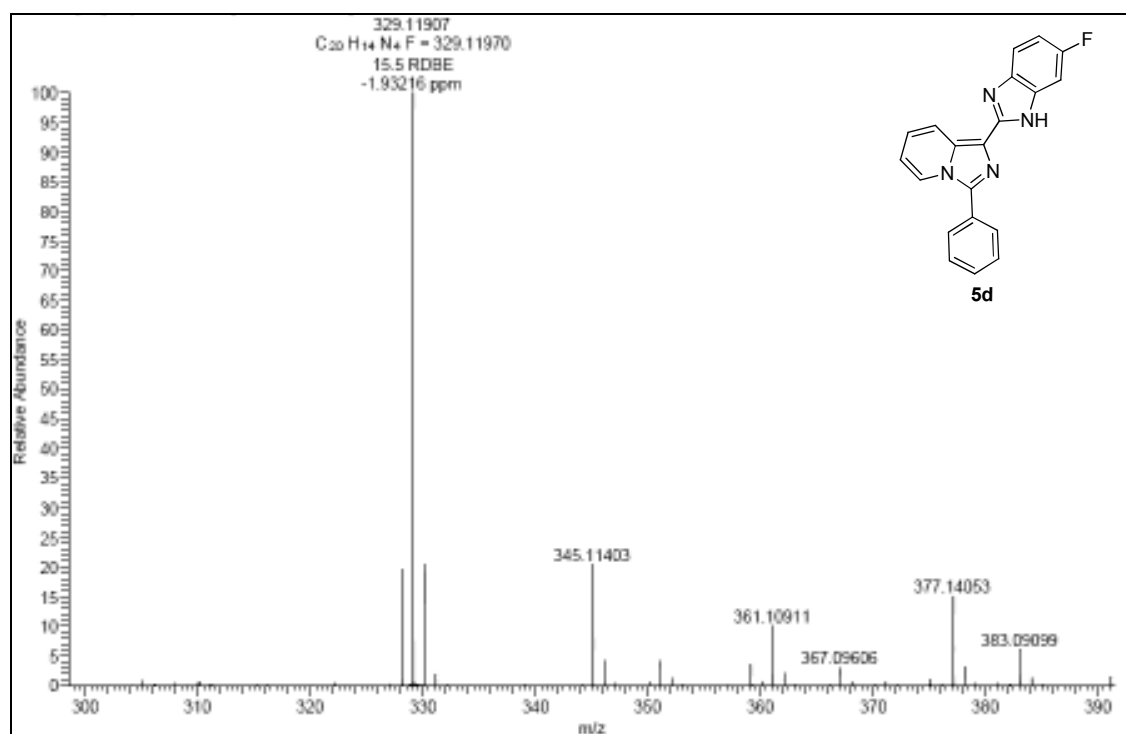
**HIGH RESOLUTION MASS SPECTRA OF COMPOUND 5c**



**<sup>1</sup>H NMR SPECTRA OF COMPOUND 5d**

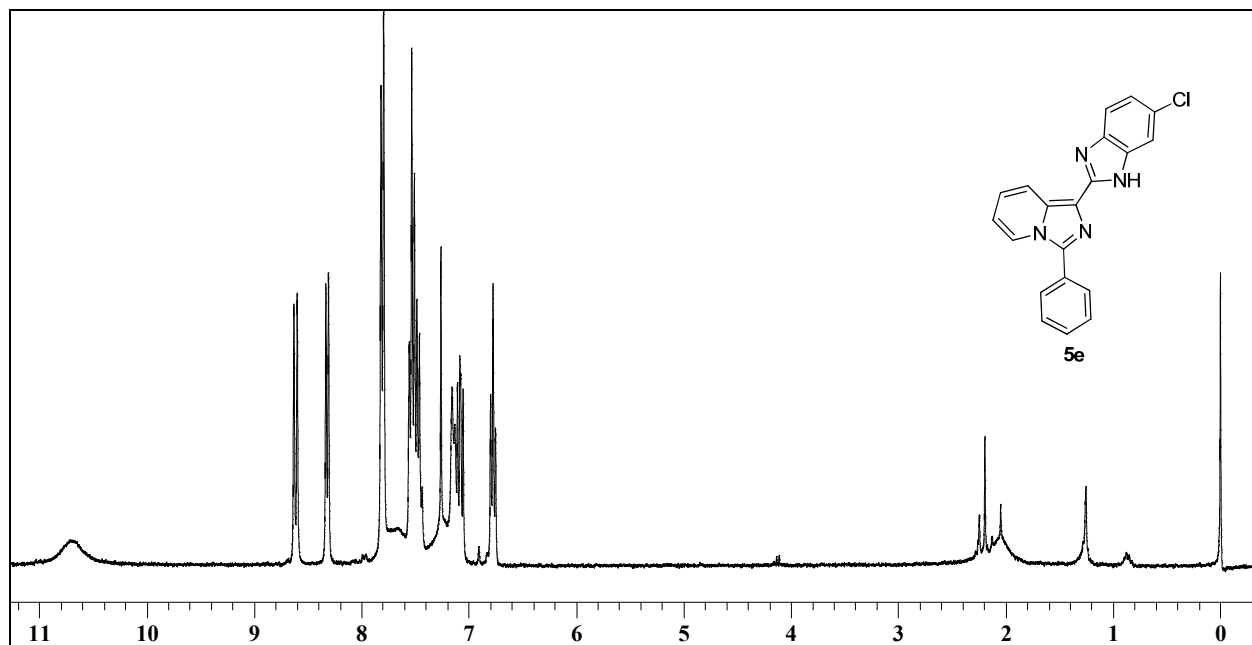


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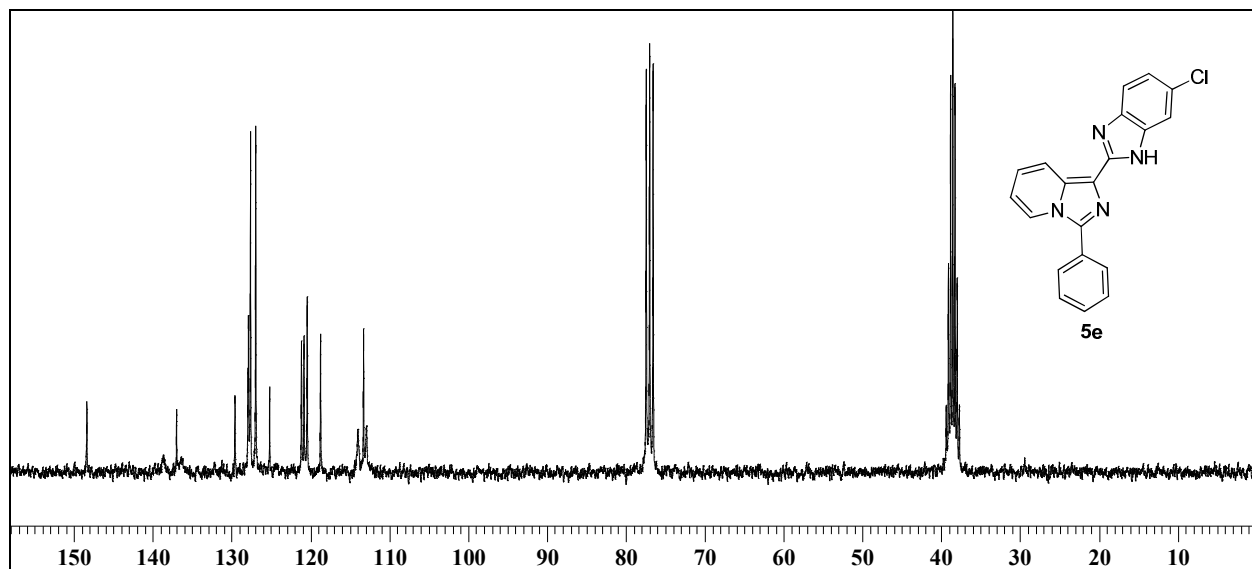


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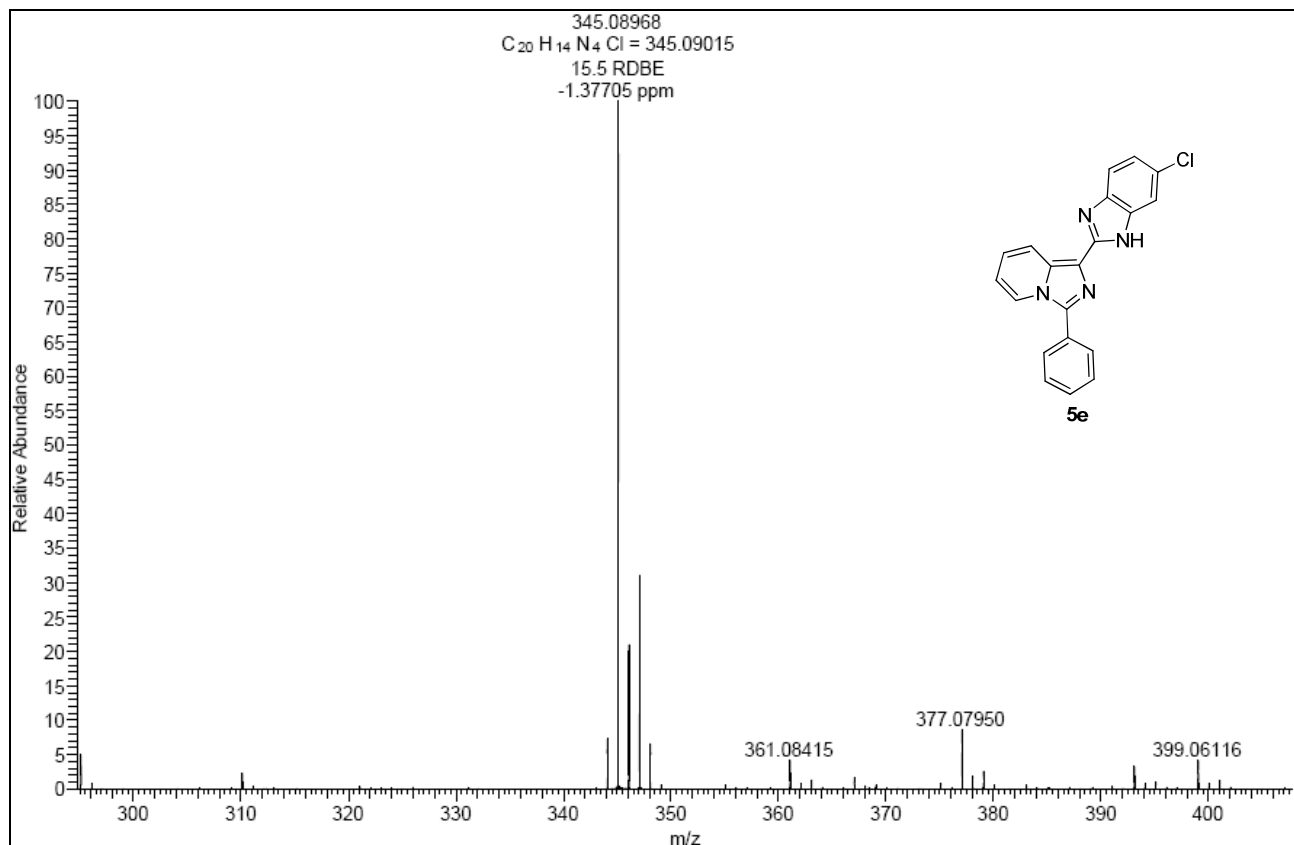




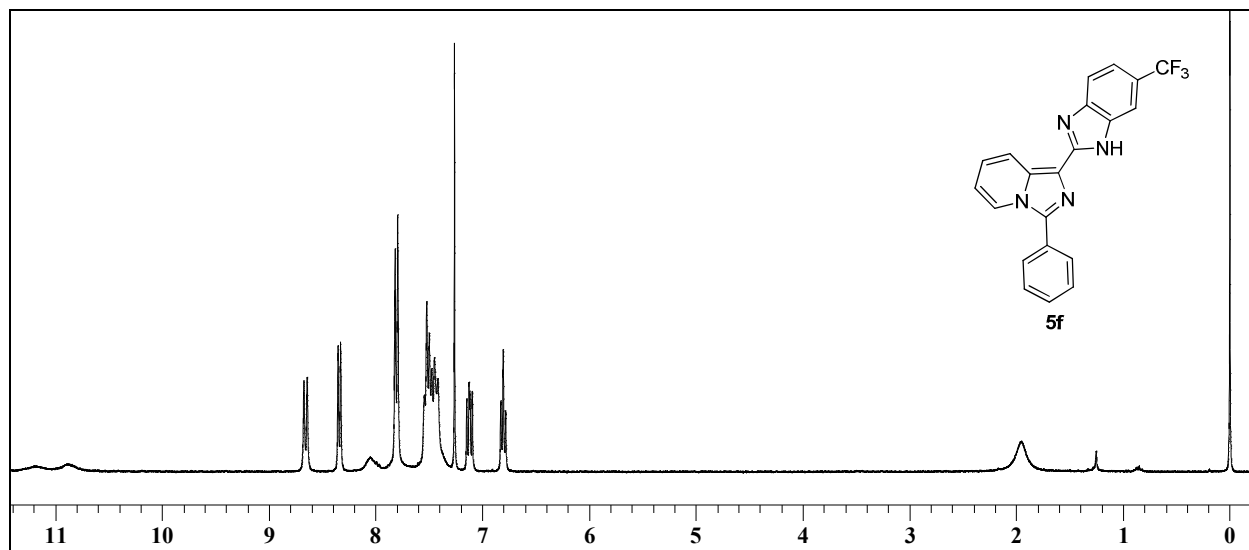
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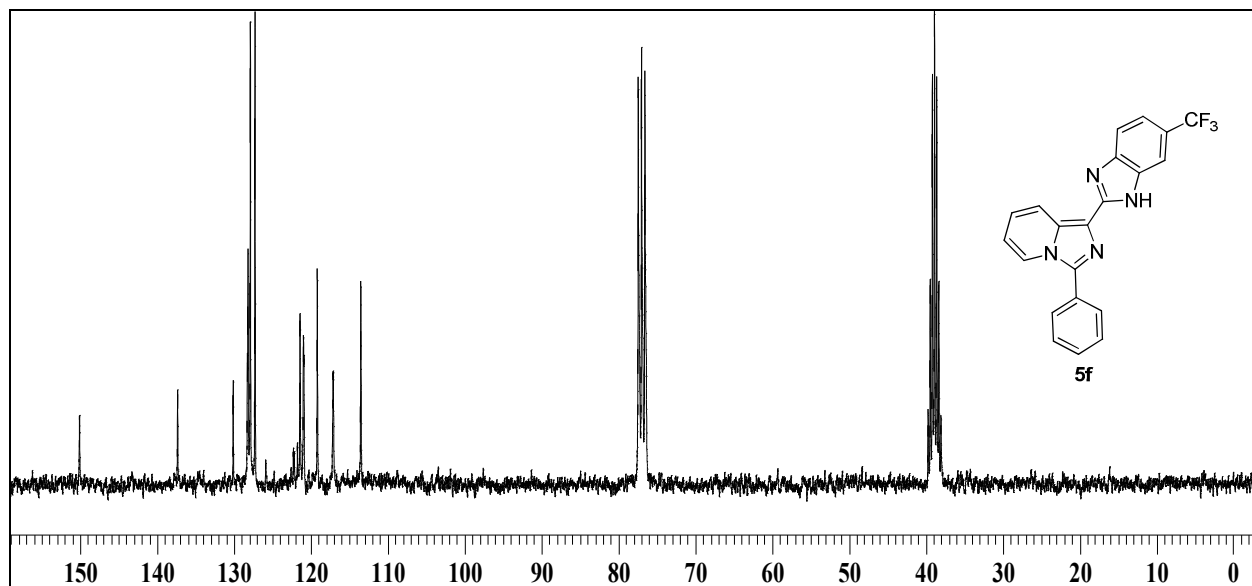
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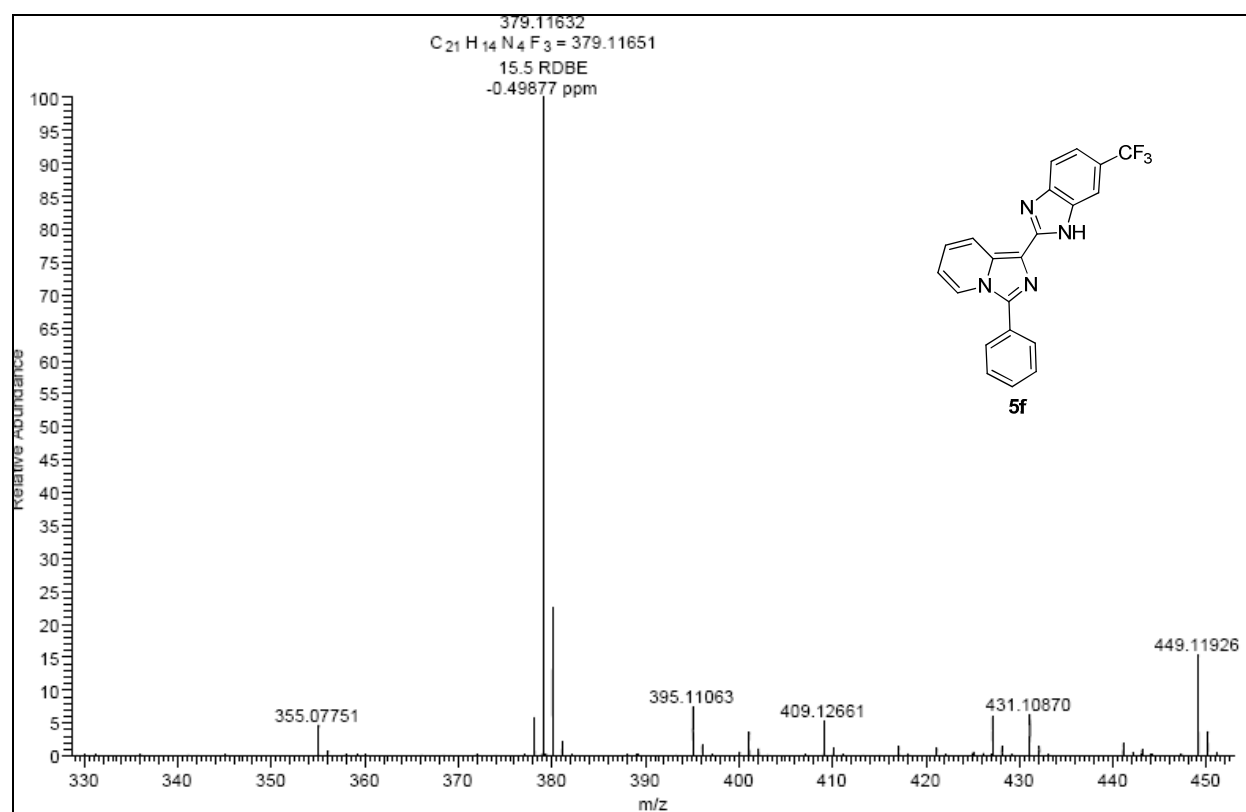
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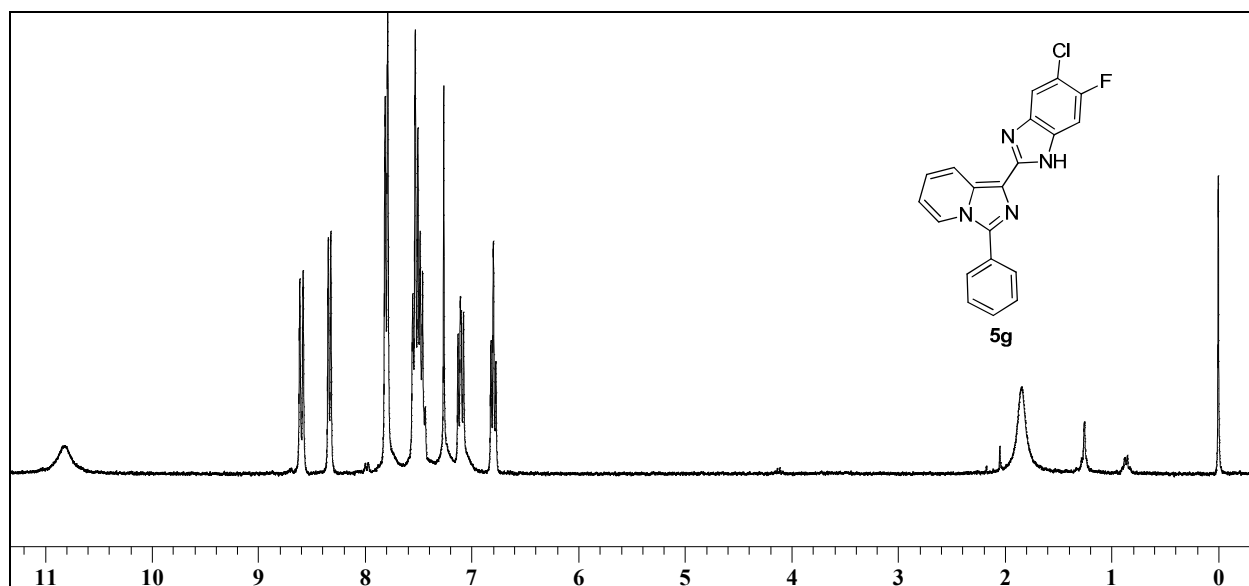
**<sup>1</sup>H NMR SPECTRA OF COMPOUND 5f**



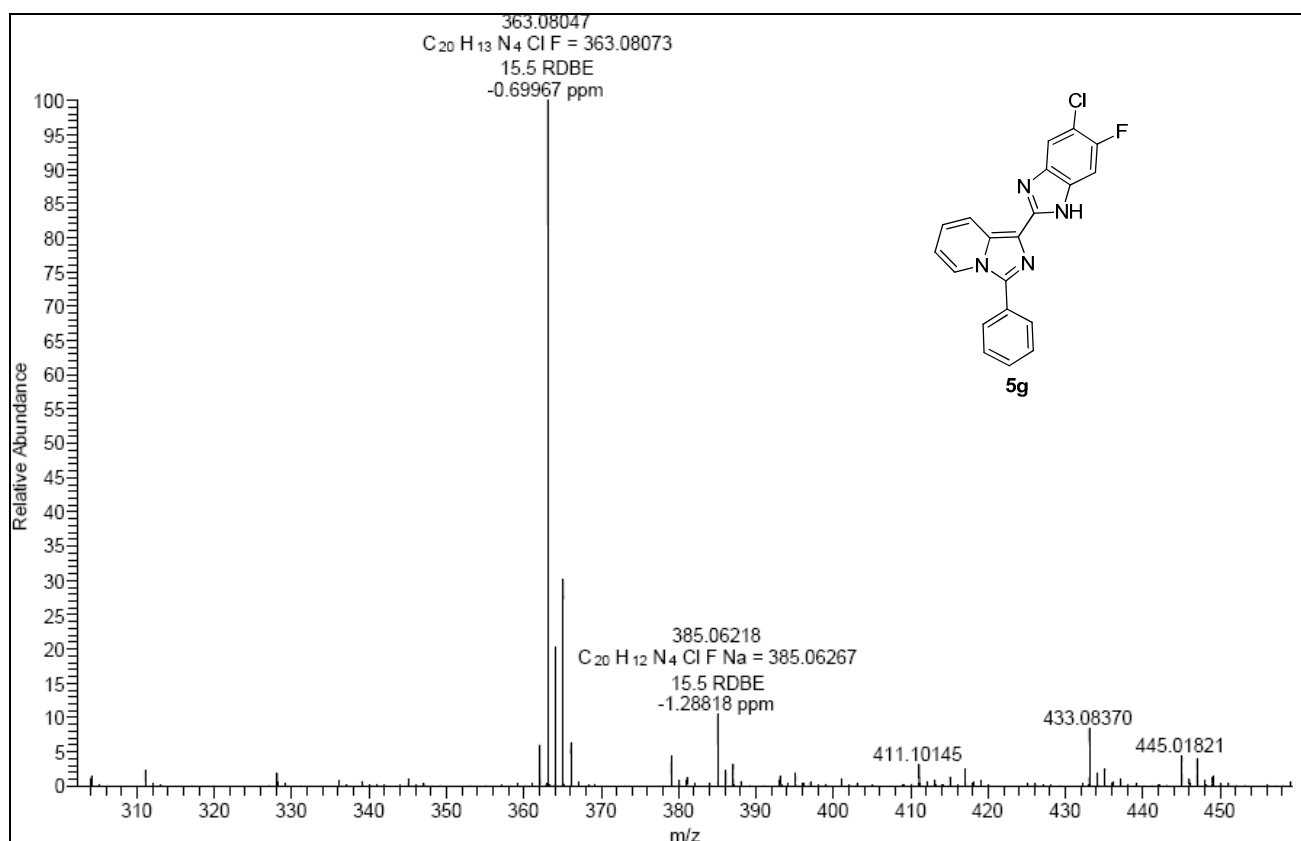
**<sup>13</sup>C NMR SPECTRA OF COMPOUND 5f**



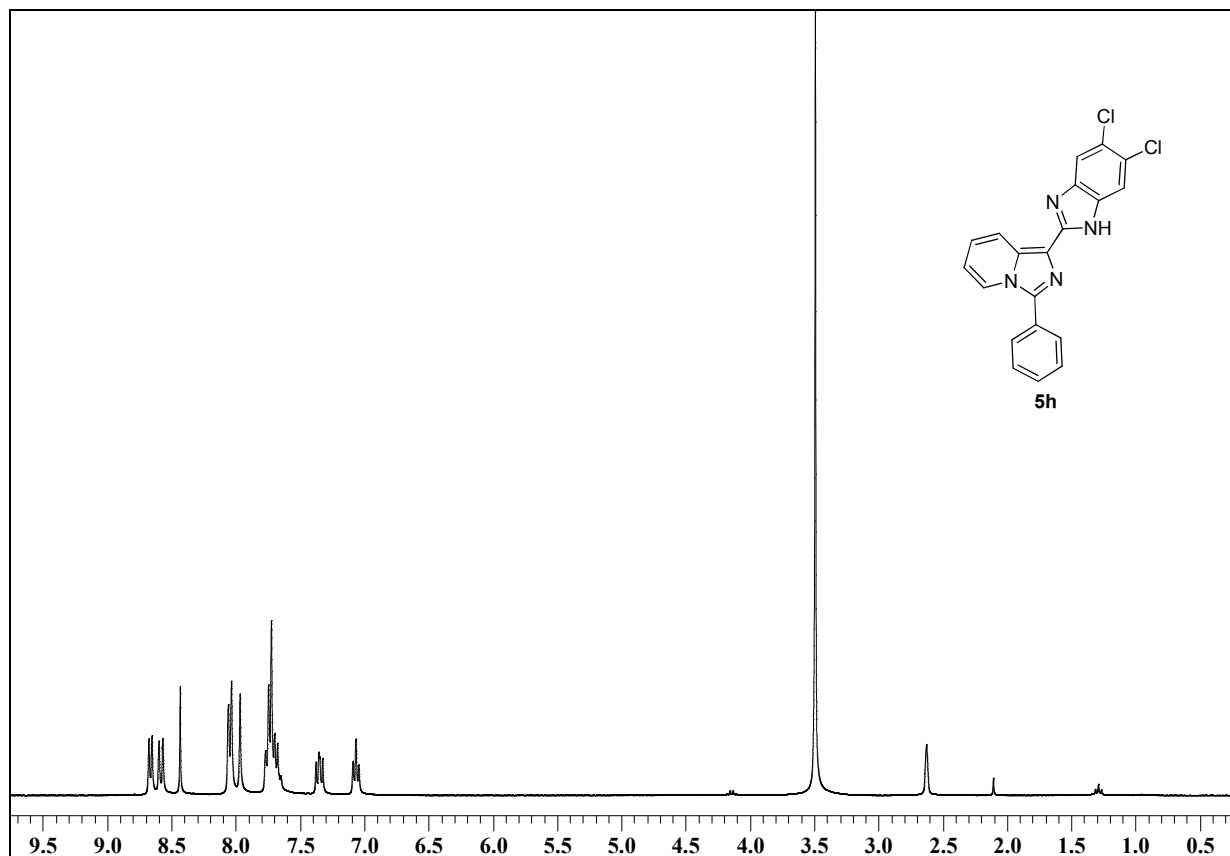
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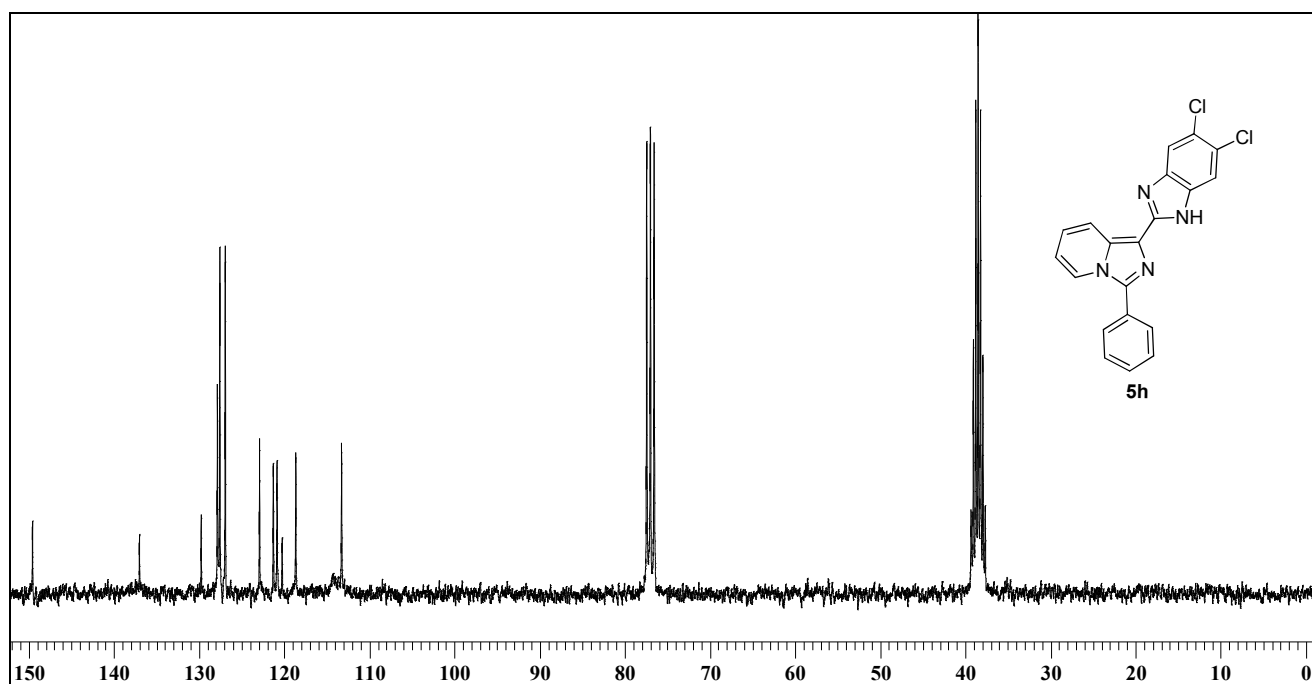
**<sup>1</sup>H NMR SPECTRA OF COMPOUND 5g**



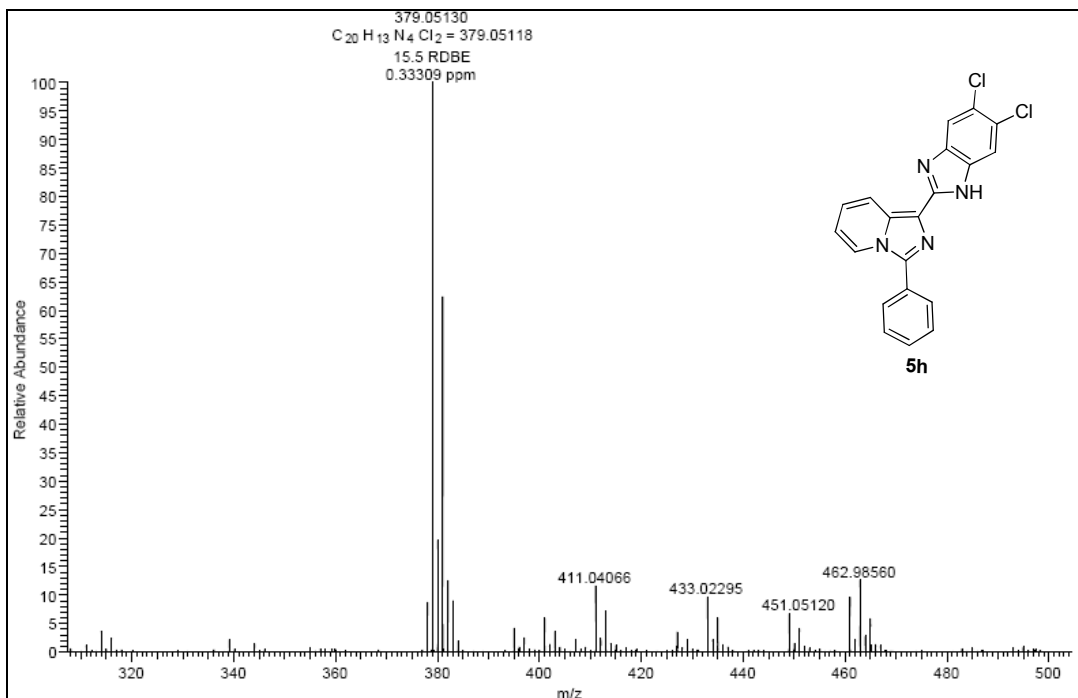
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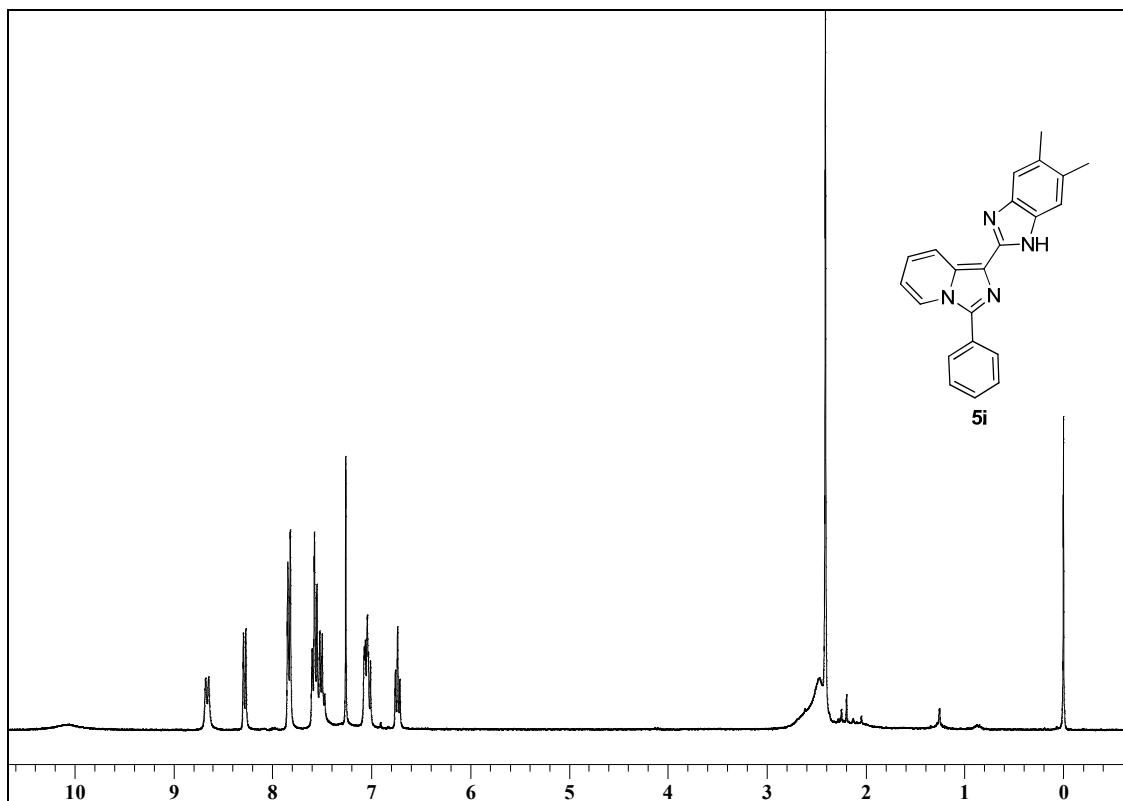
**<sup>1</sup>H NMR SPECTRA OF COMPOUND 5h**



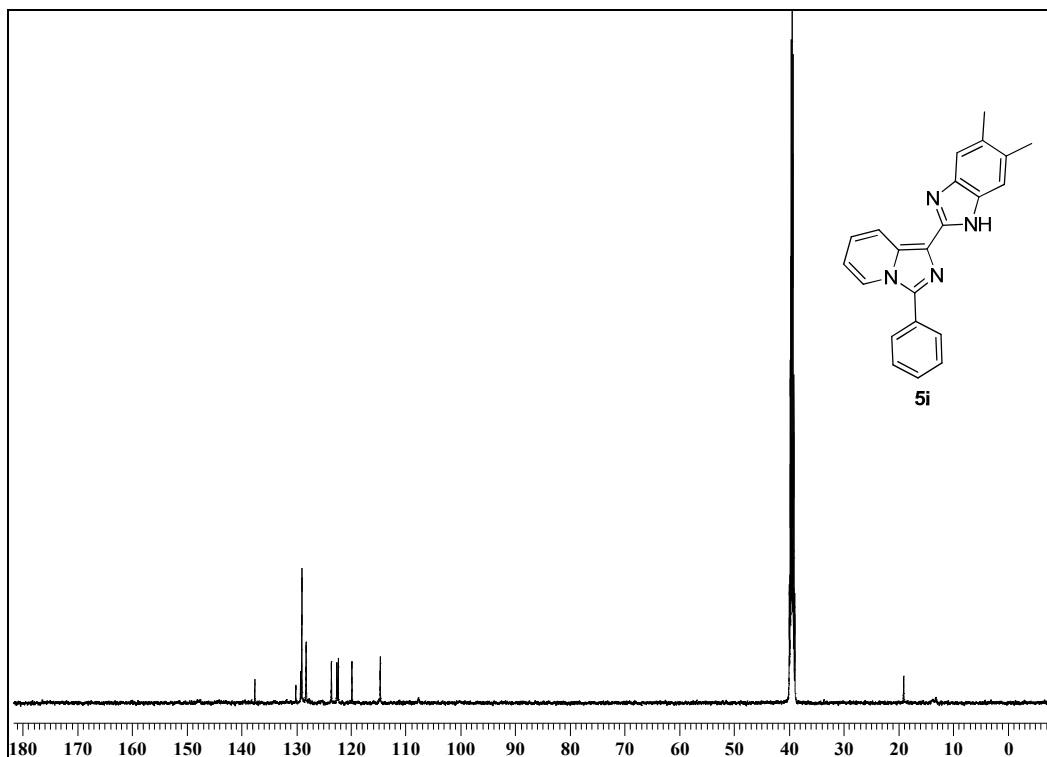
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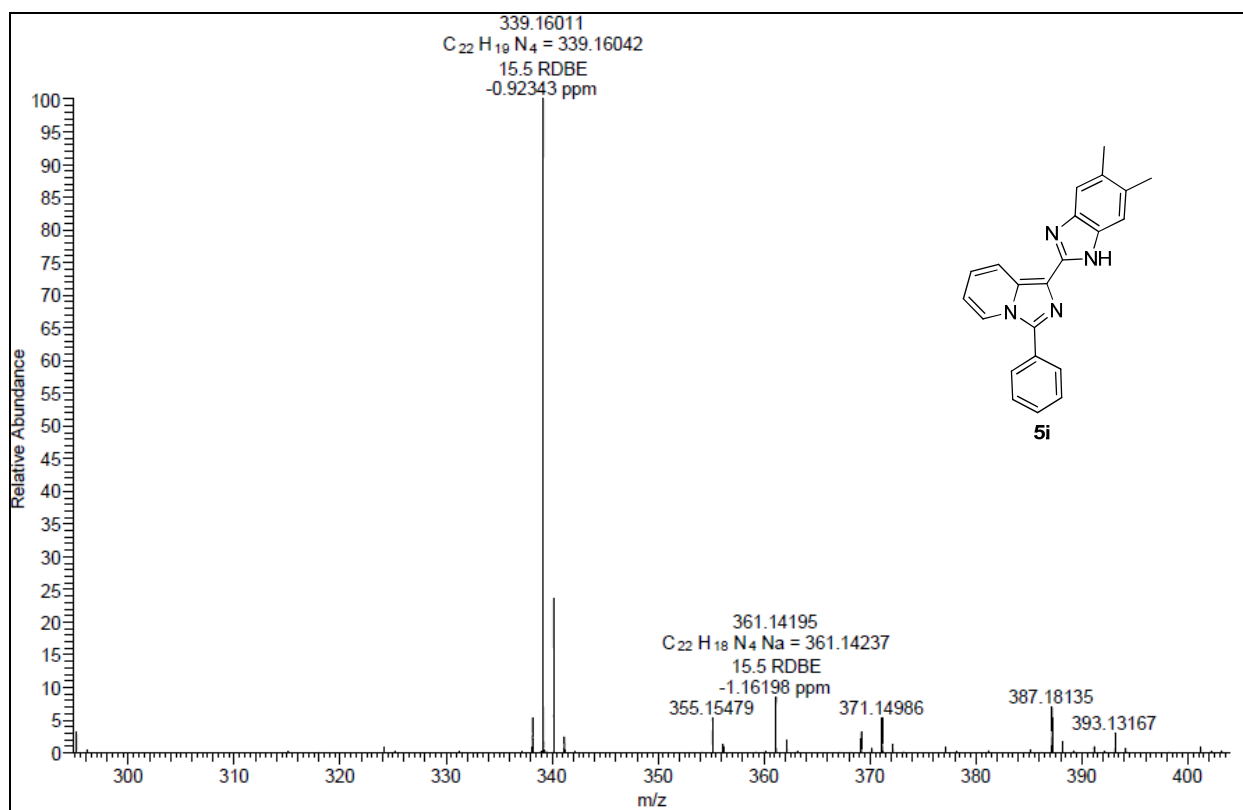
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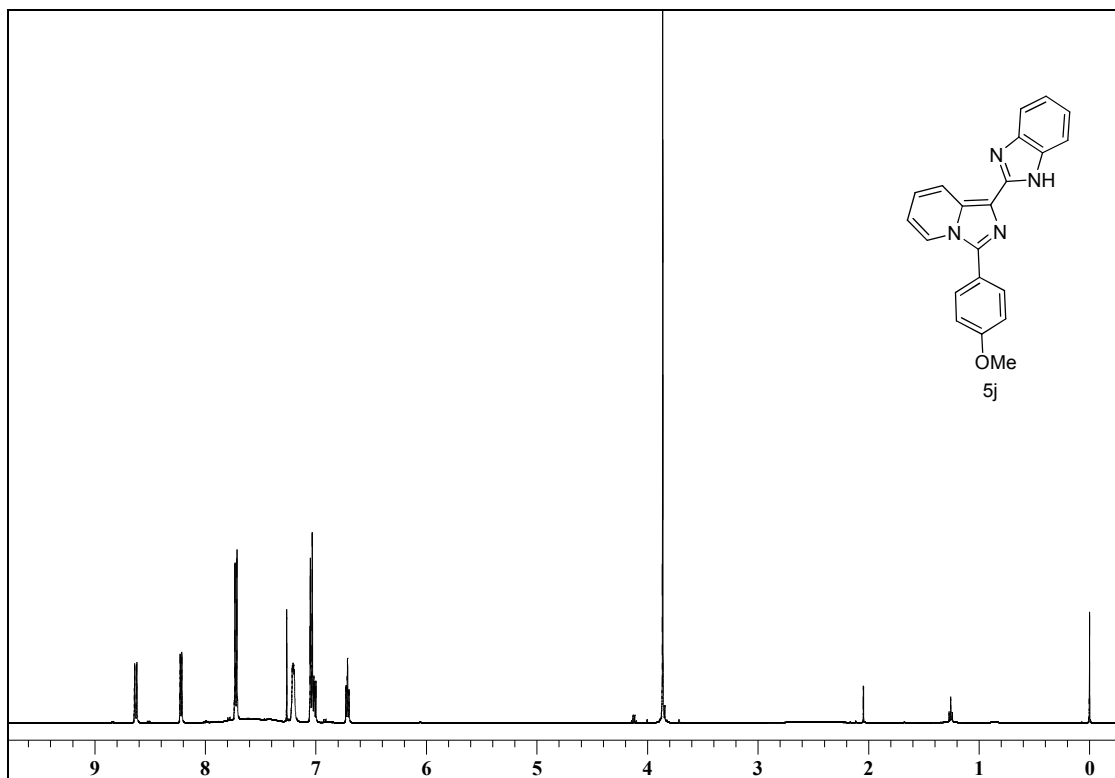
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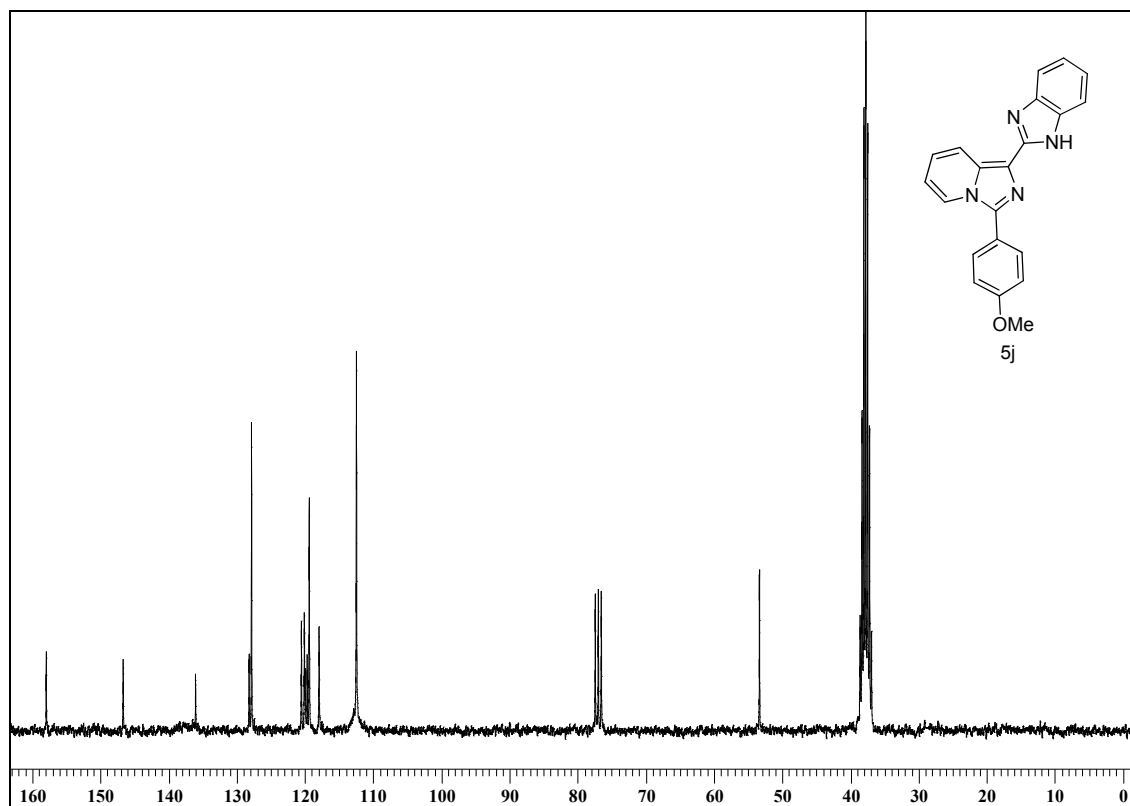
**<sup>13</sup>C NMR SPECTRA OF COMPOUND 5i**



**HIGH RESOLUTION MASS SPECTRA OF COMPOUND 5i**

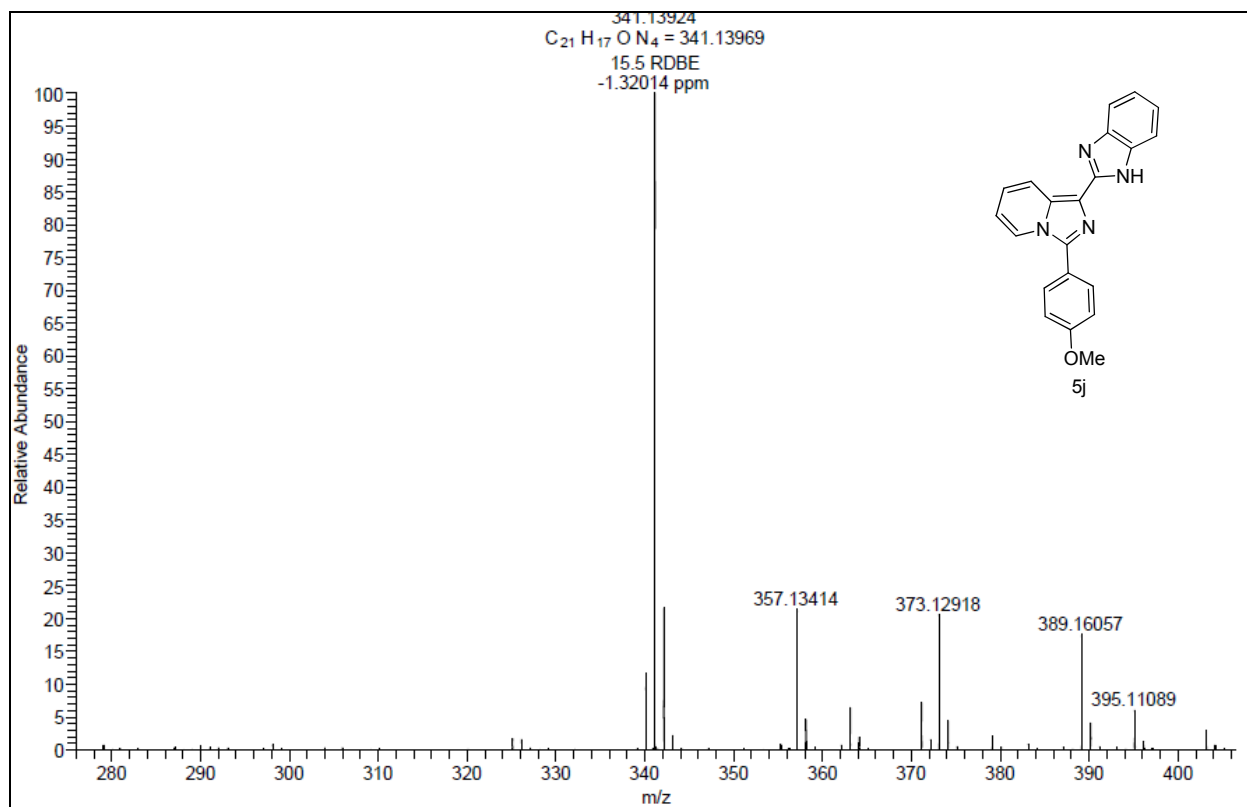


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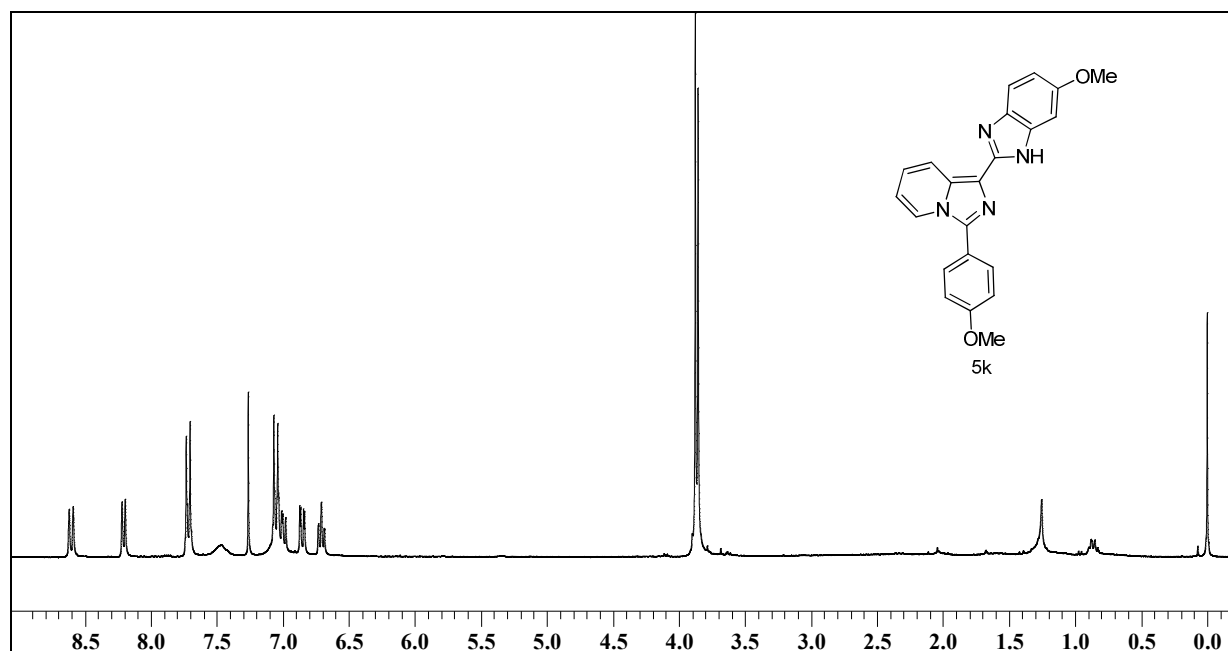


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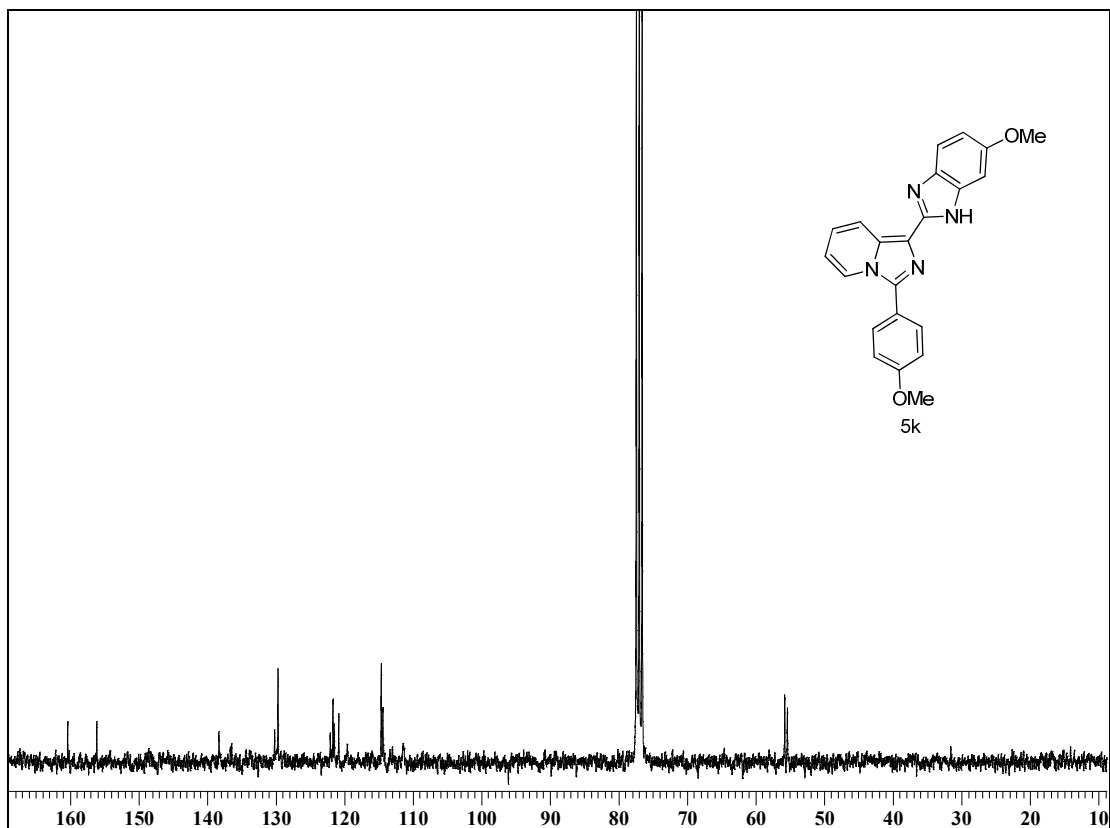




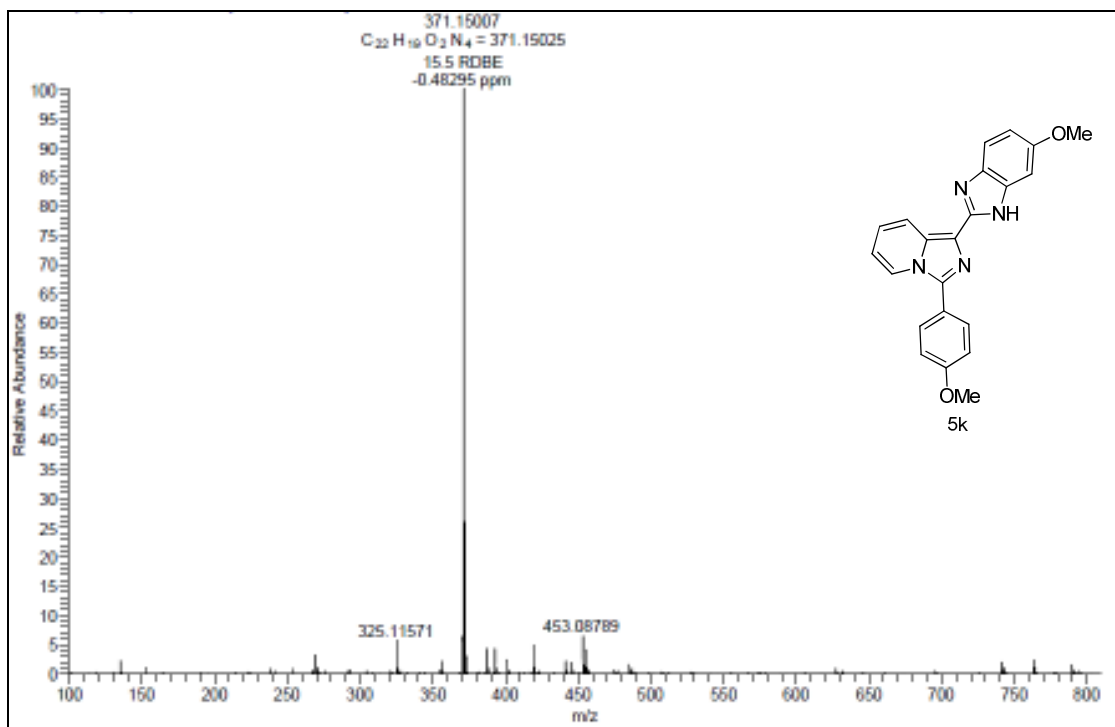
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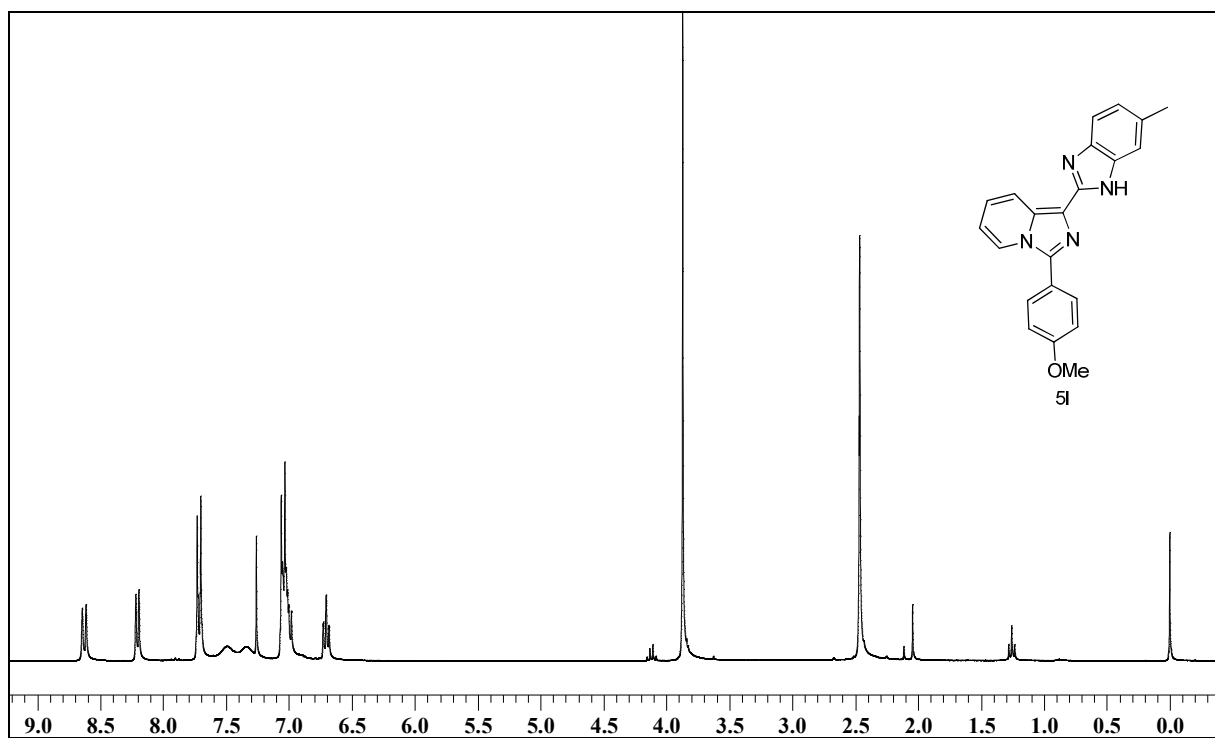
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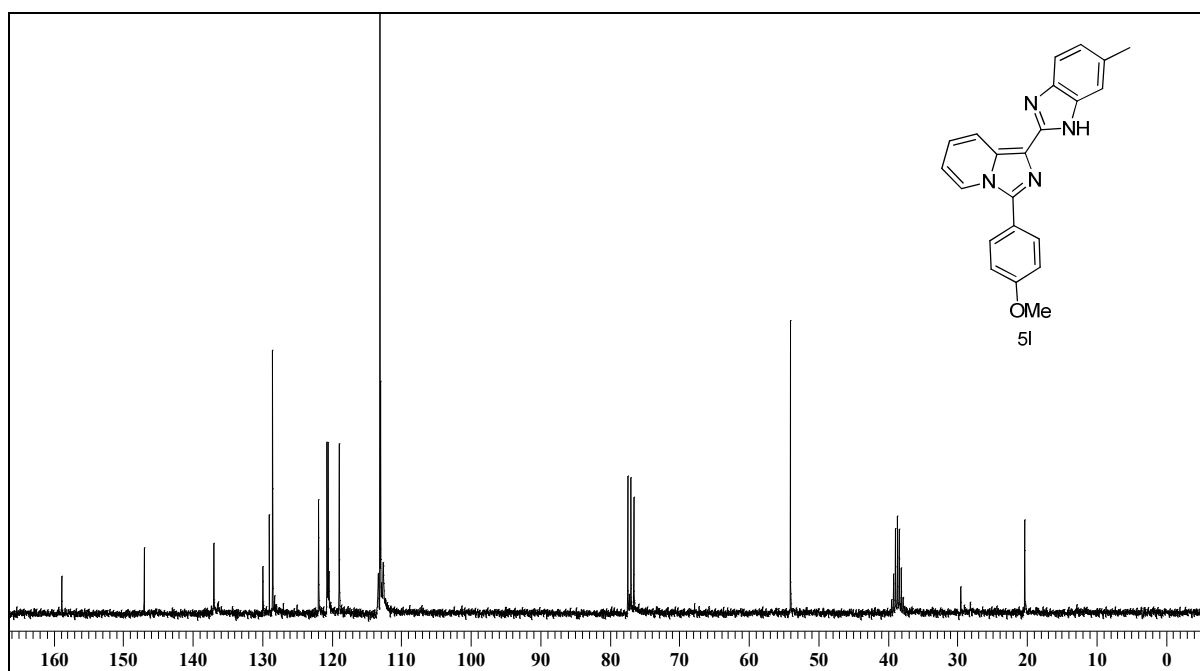
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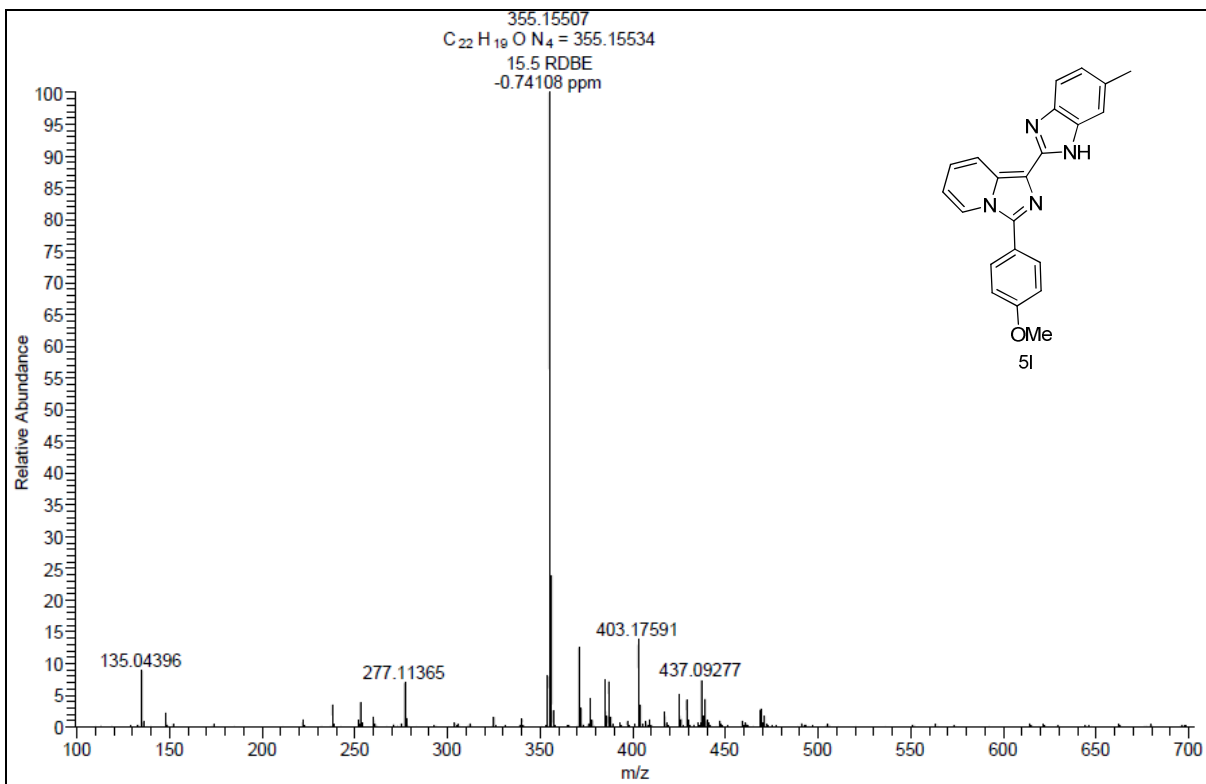
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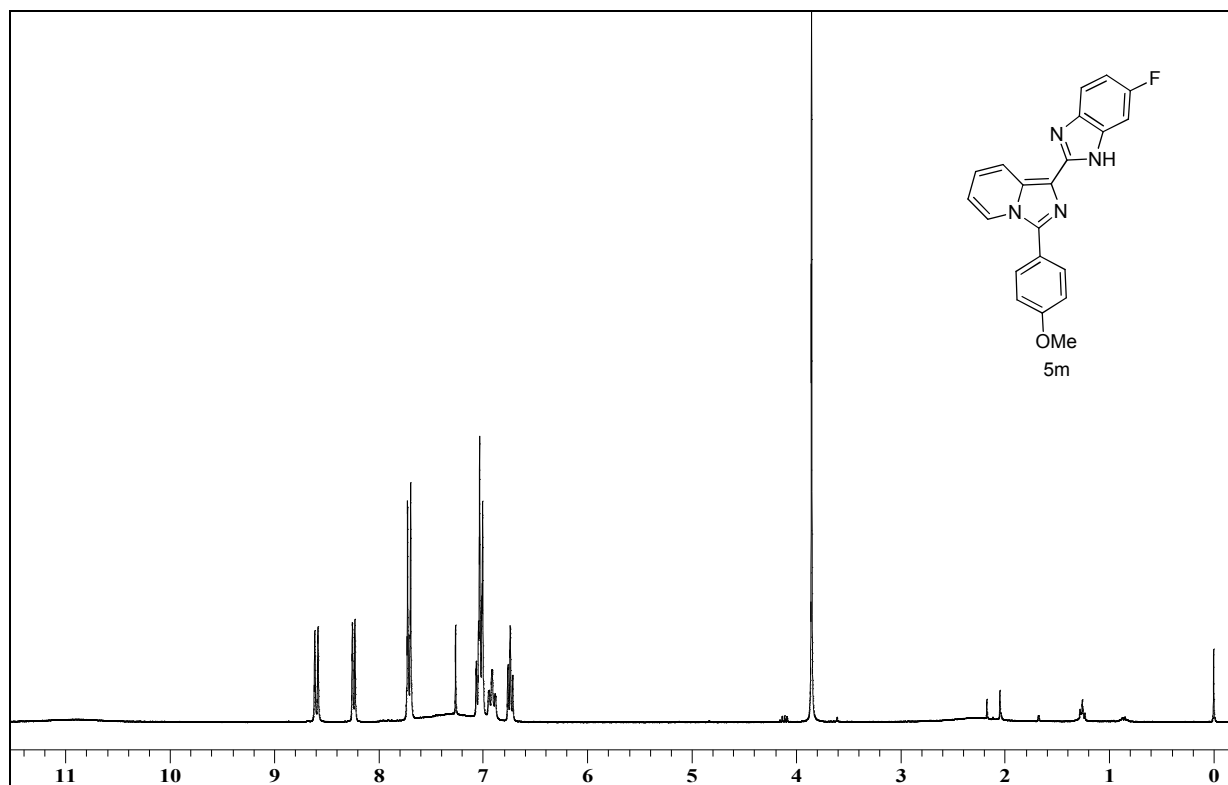
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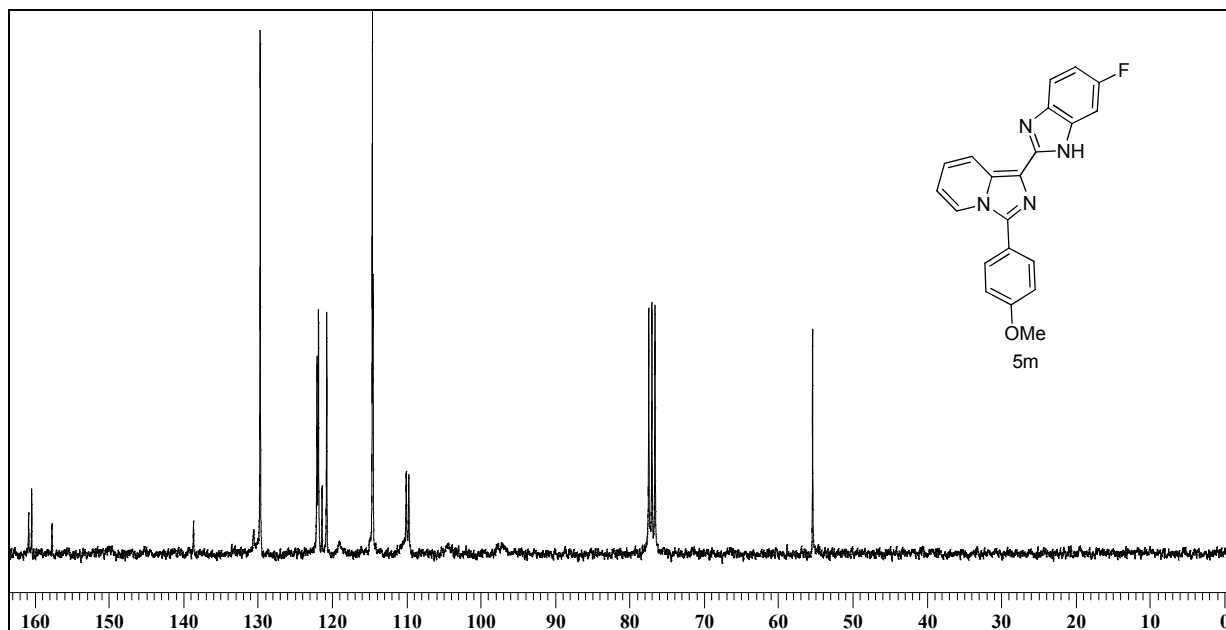
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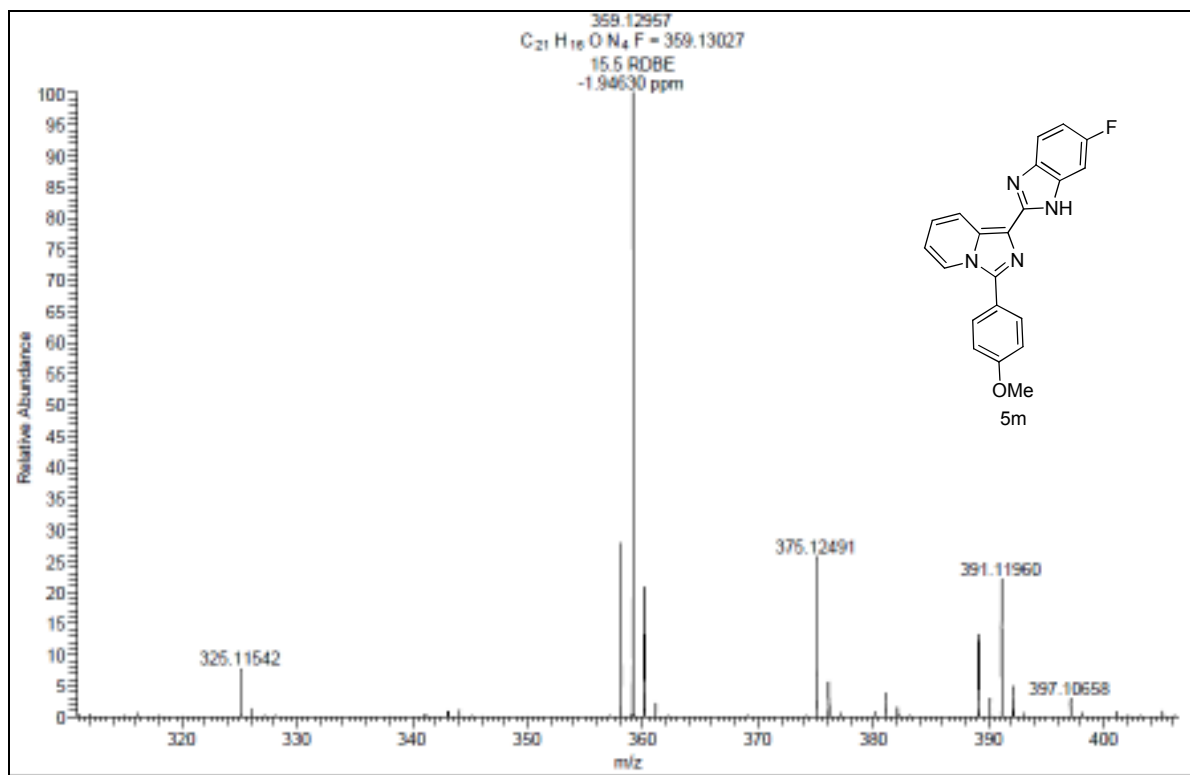
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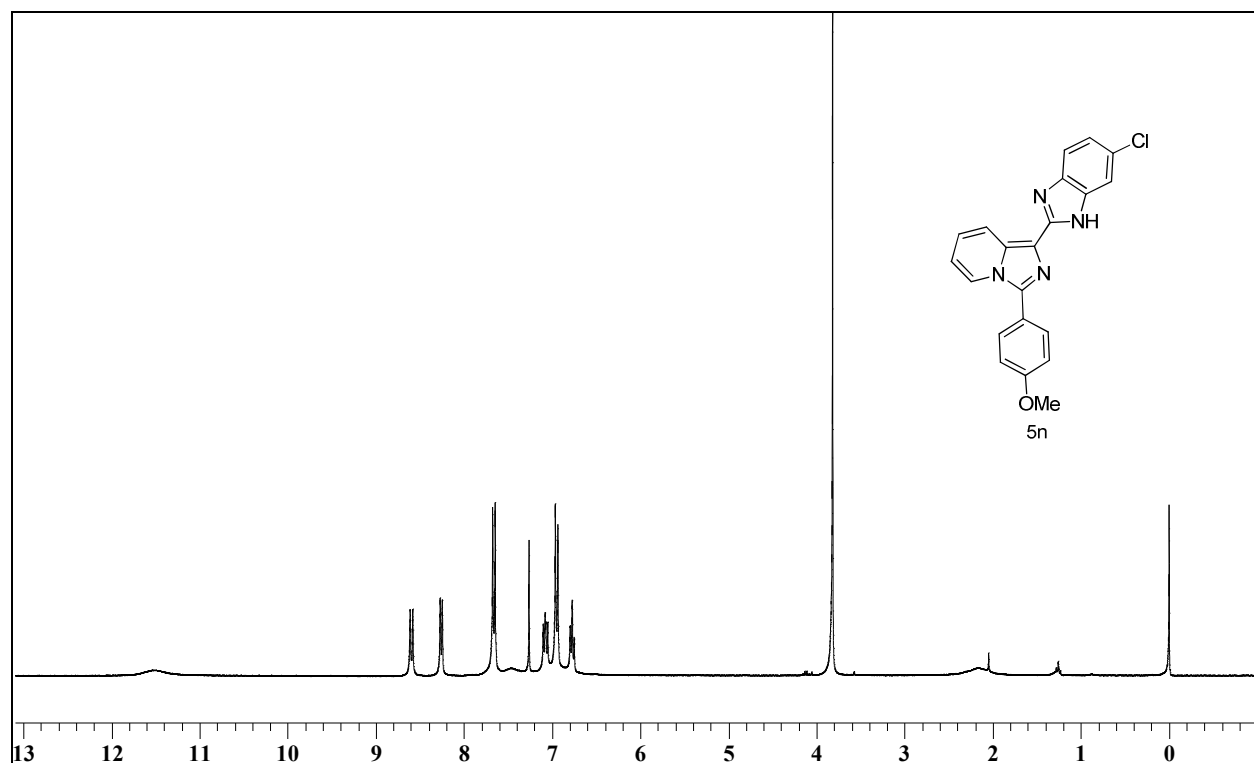
**$^1H$  NMR SPECTRA OF COMPOUND 5m**



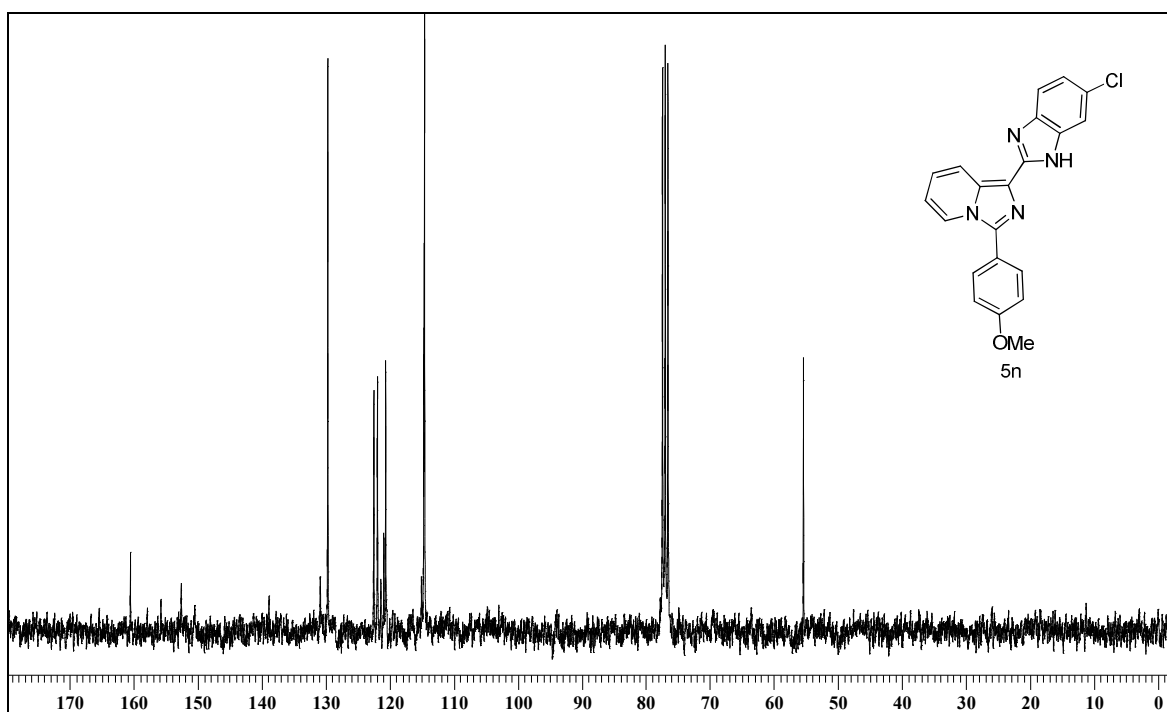
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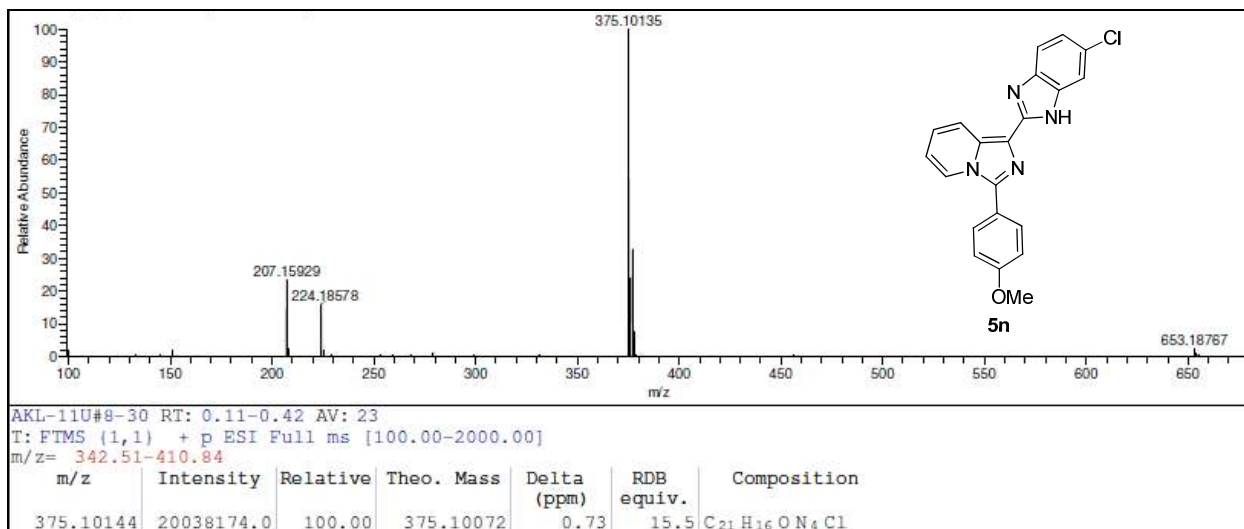
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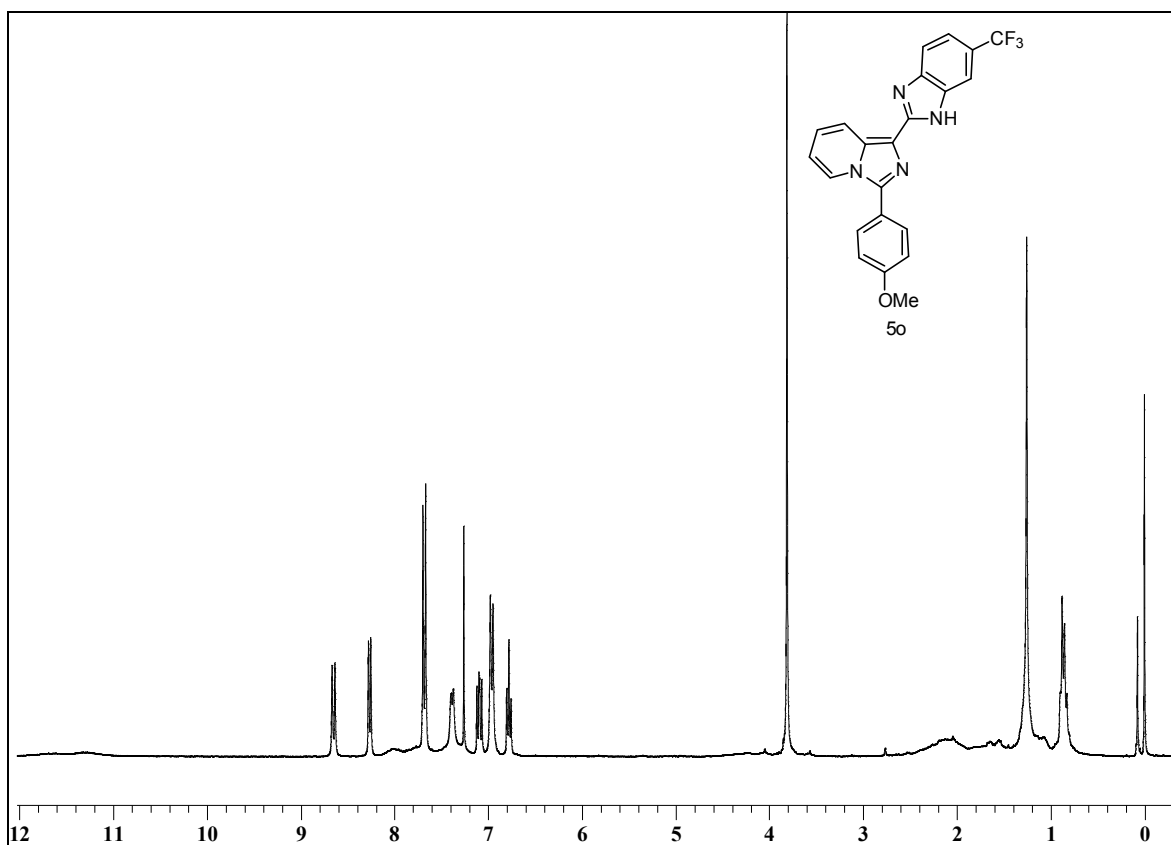
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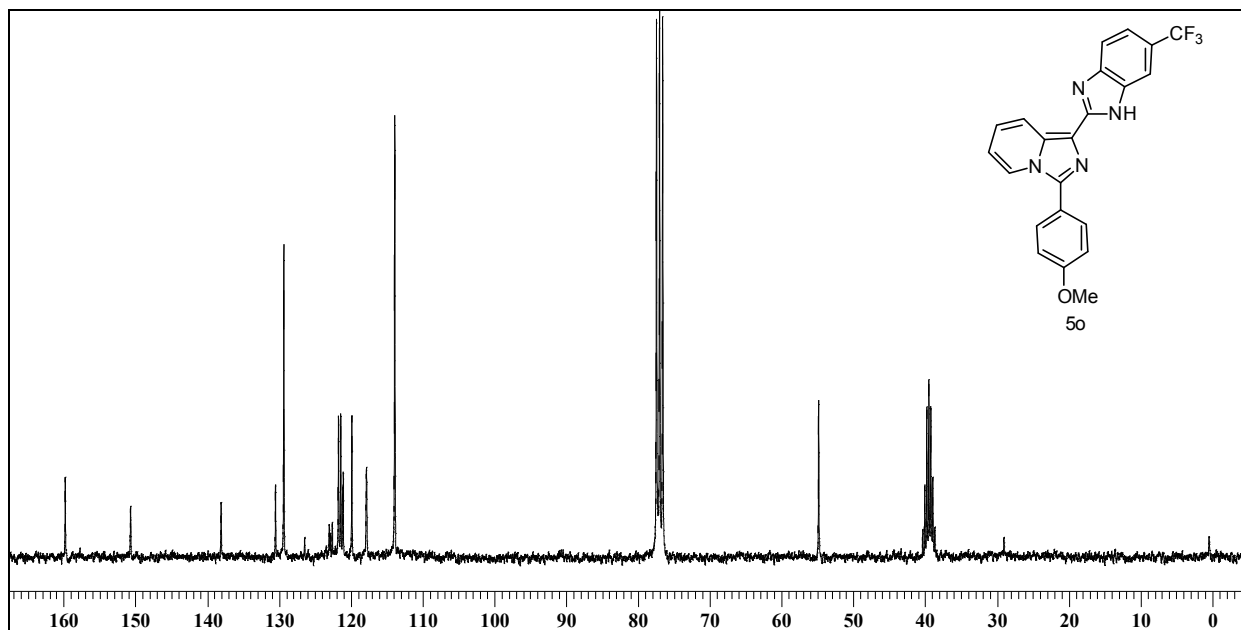
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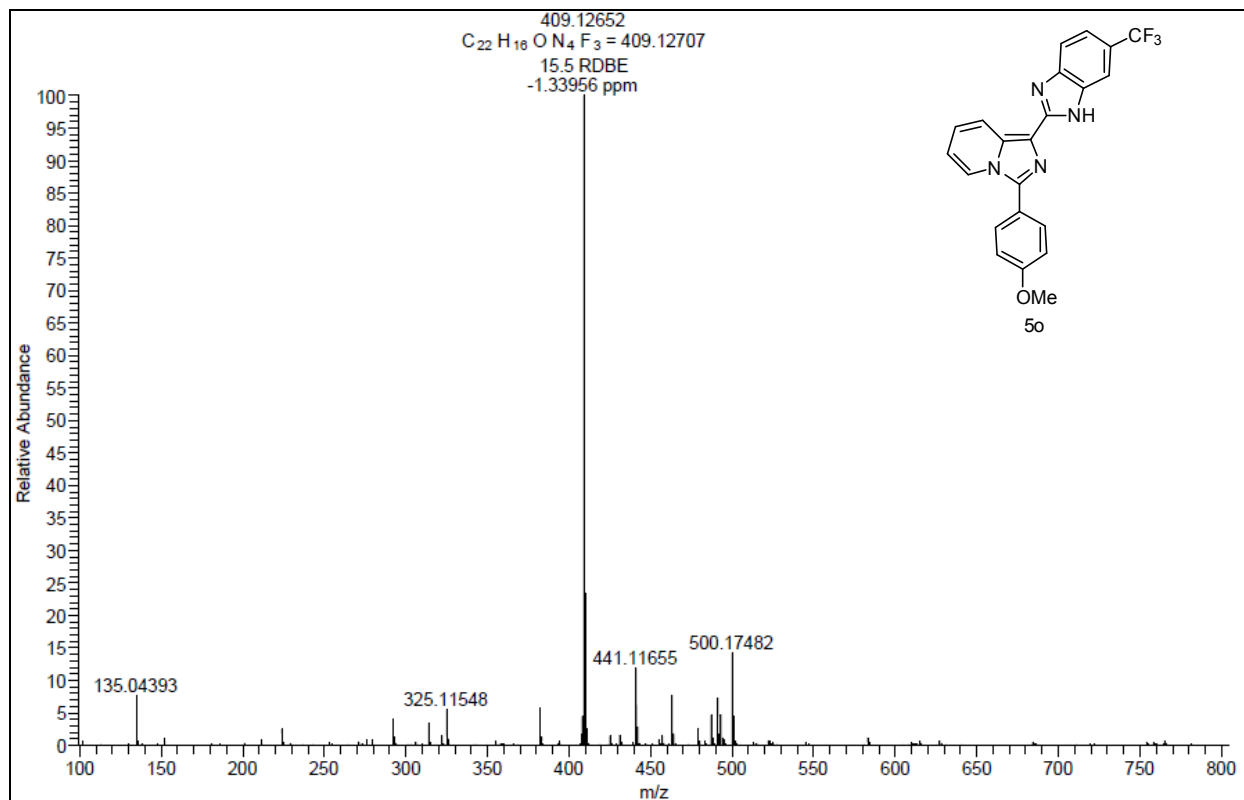
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**<sup>1</sup>H NMR SPECTRA OF COMPOUND 5o**

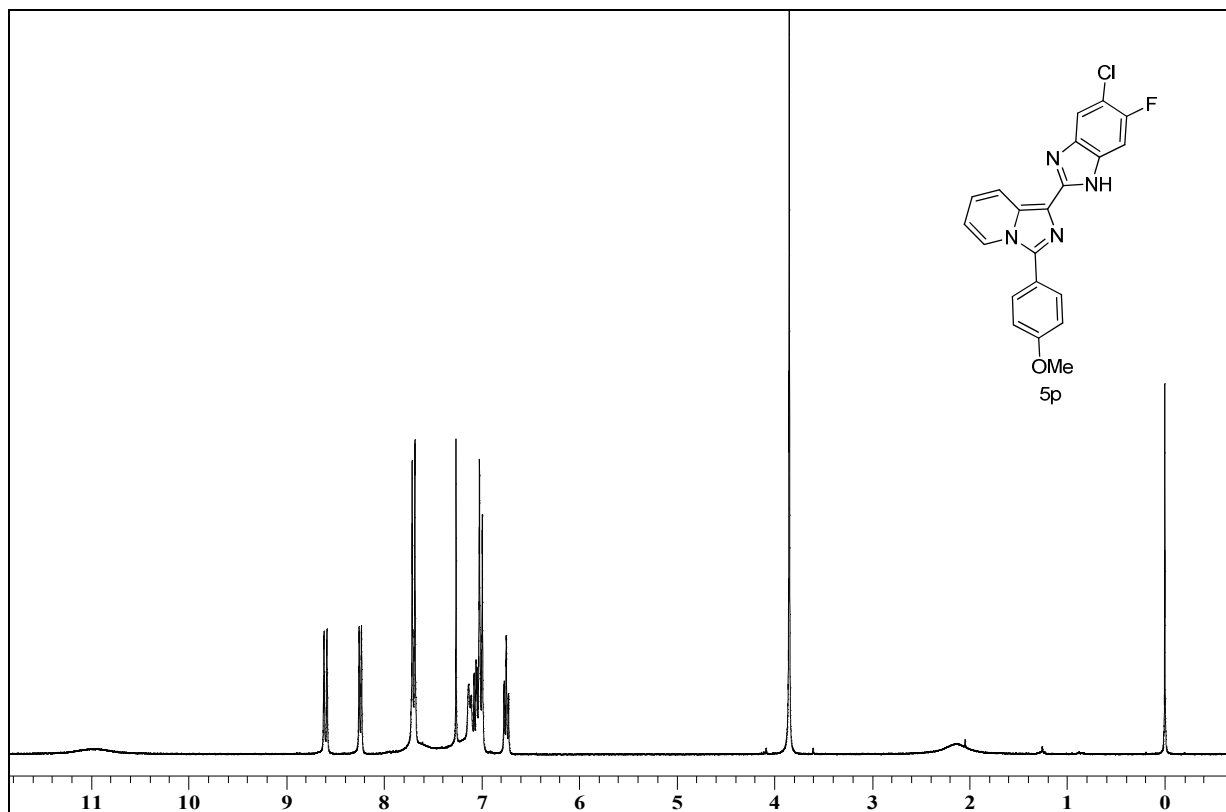


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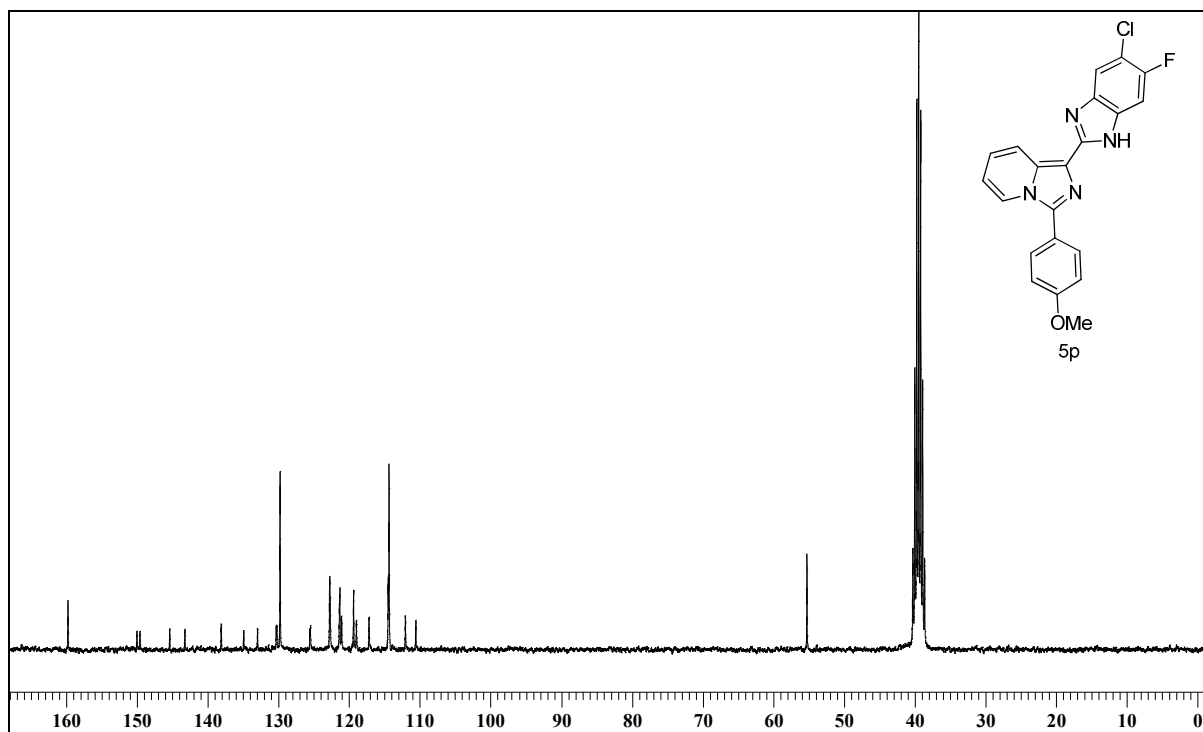


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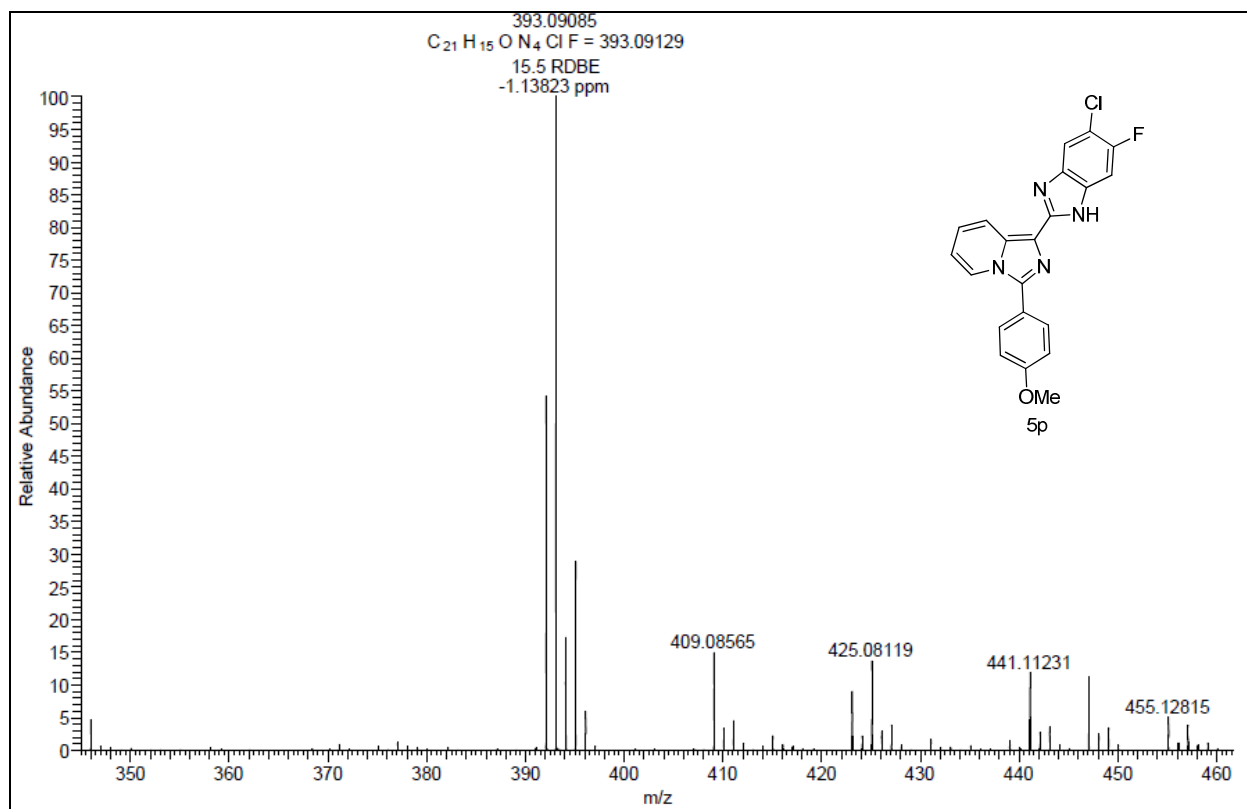




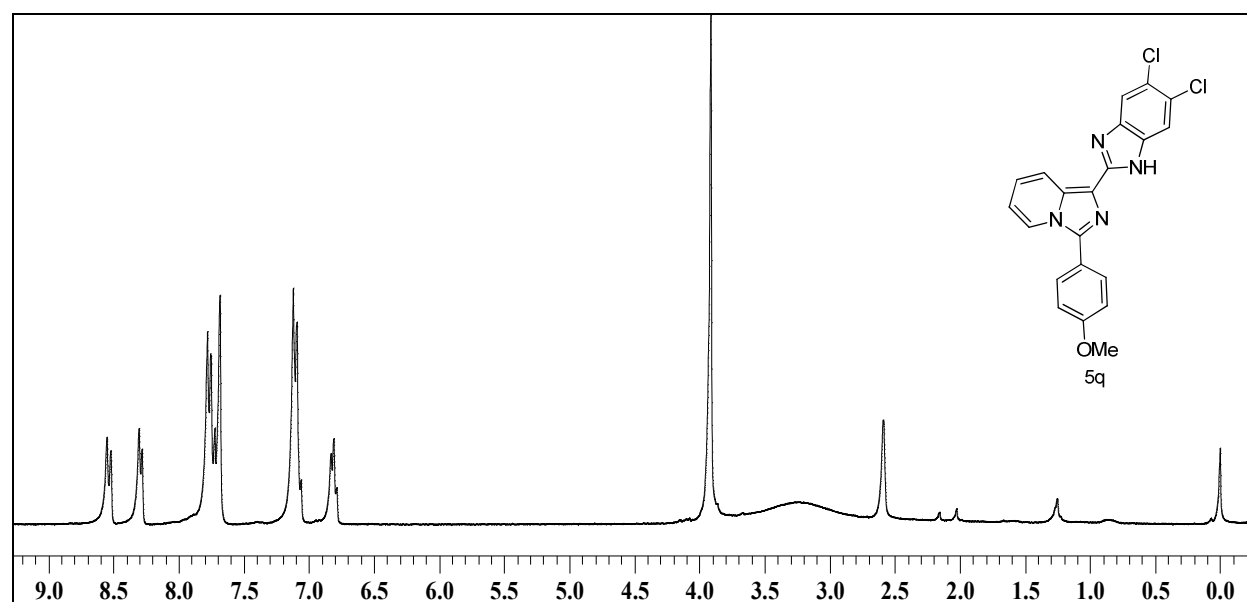
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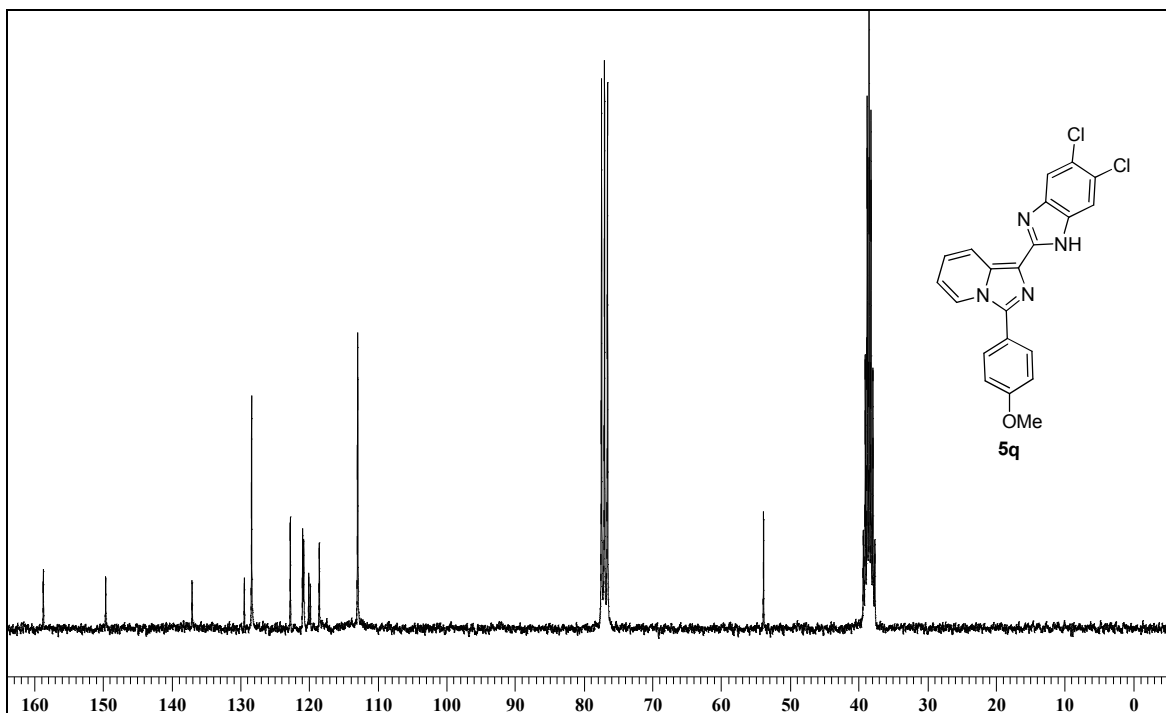
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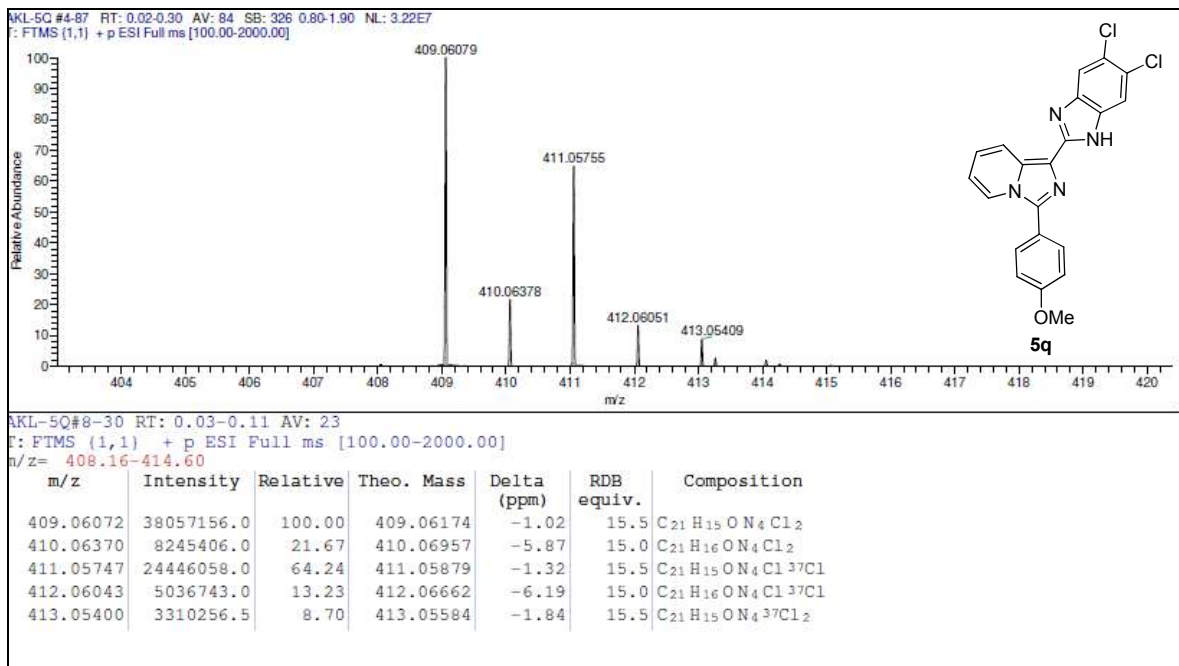
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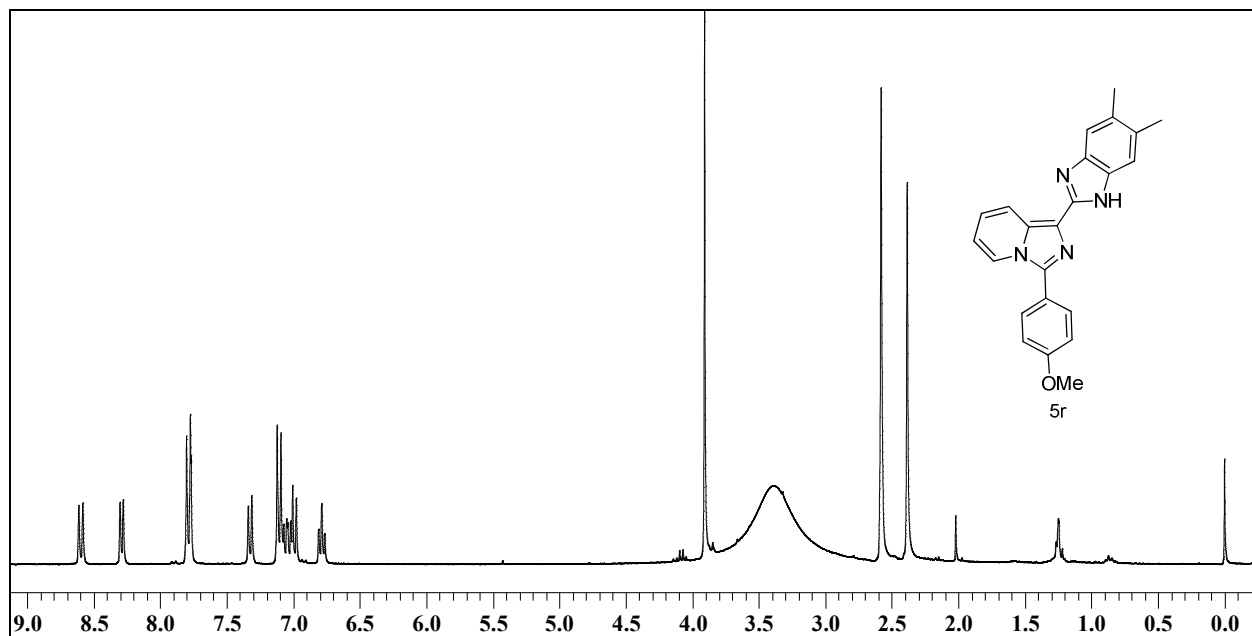
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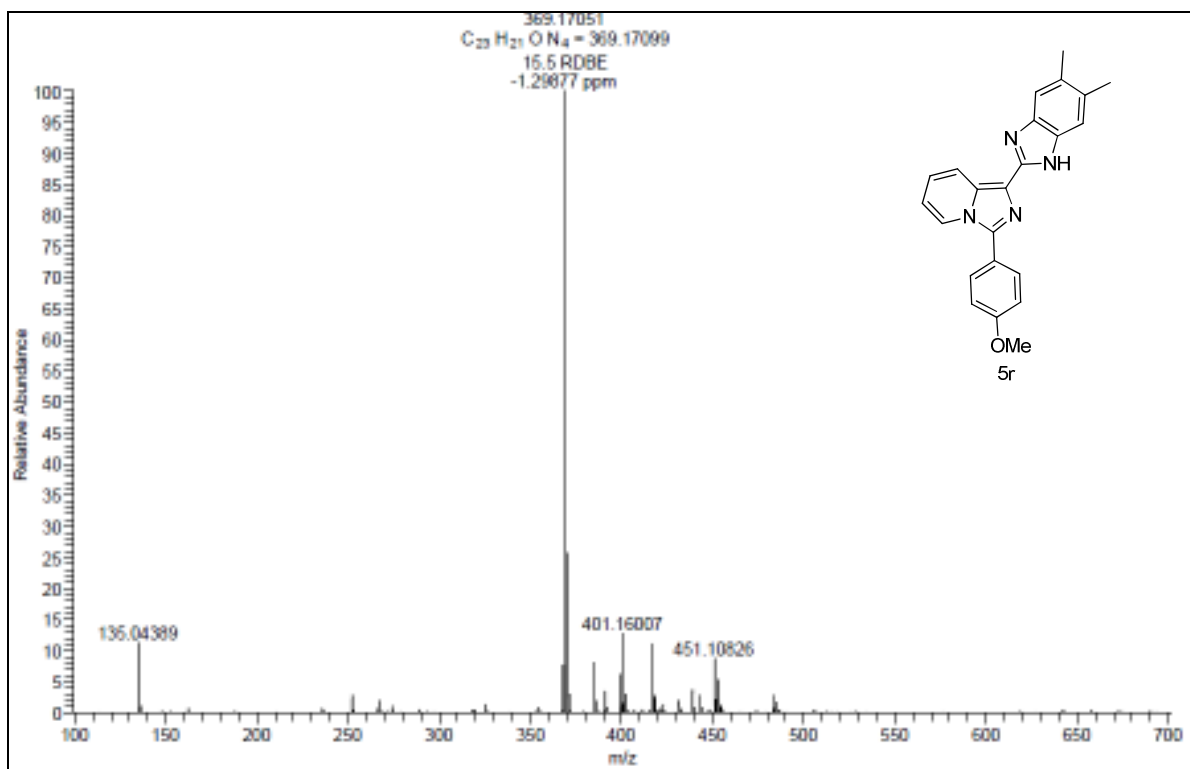
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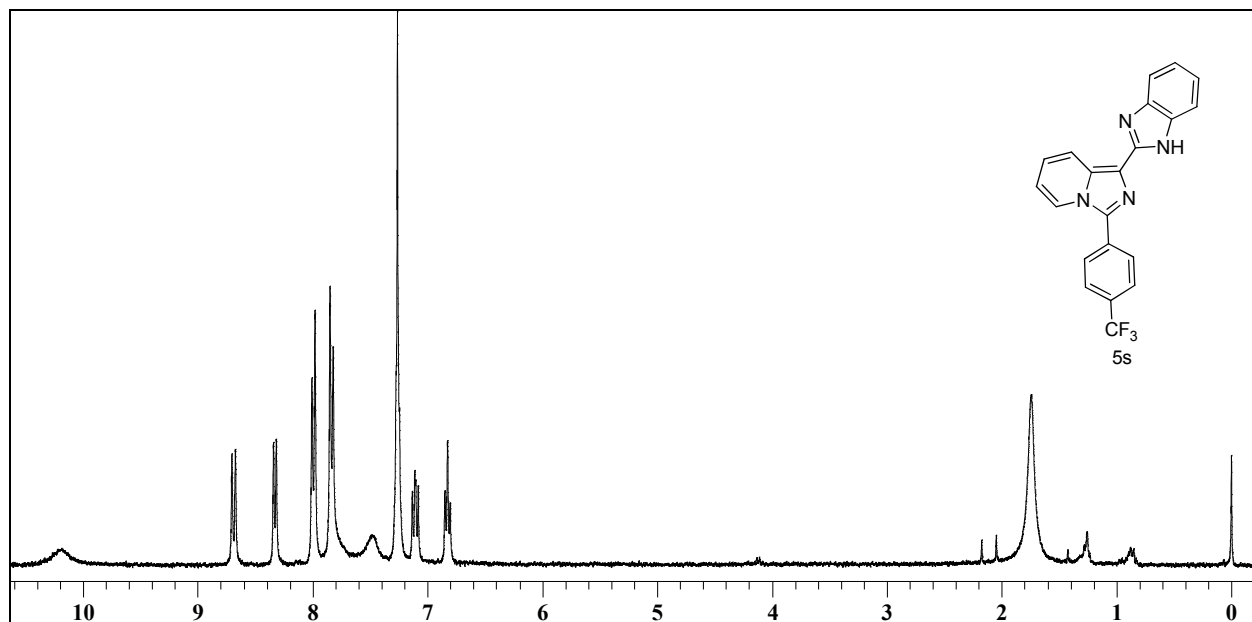
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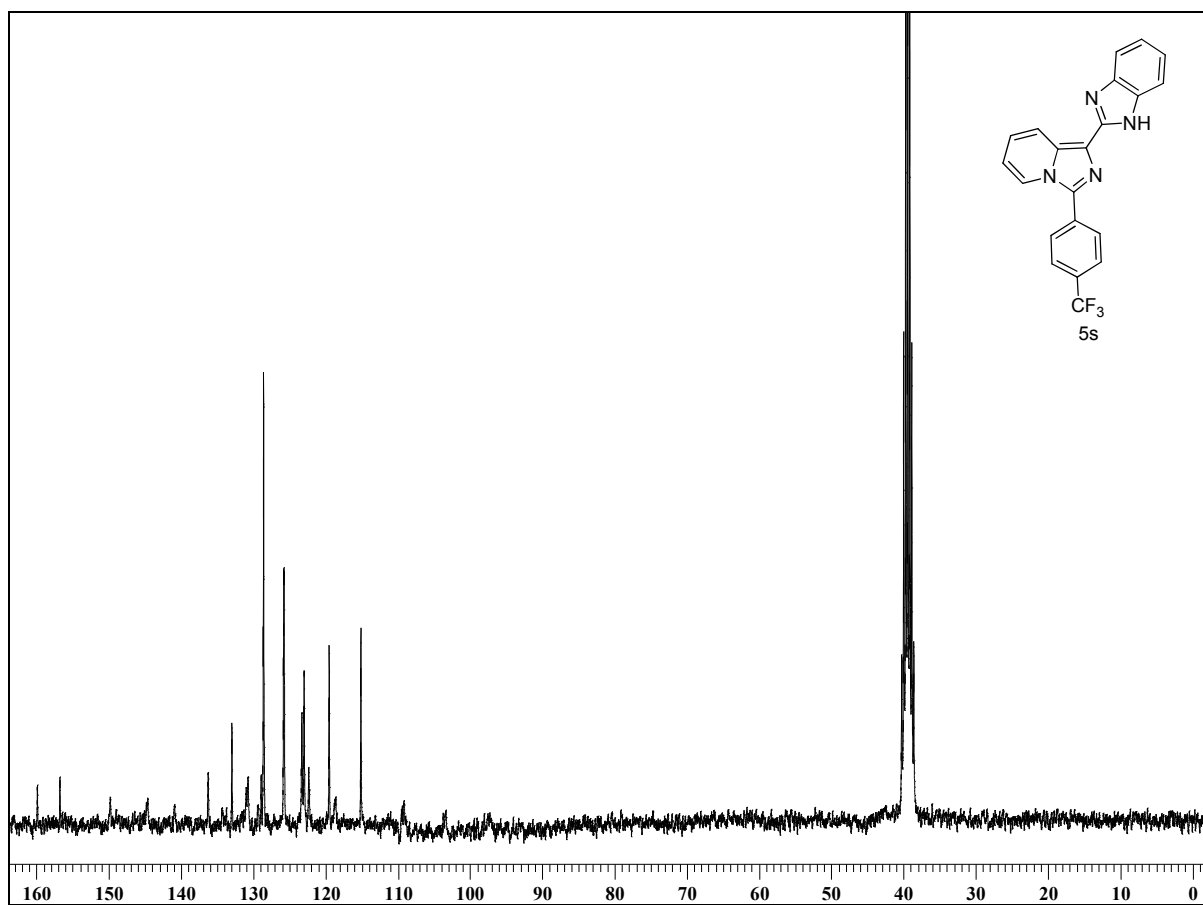
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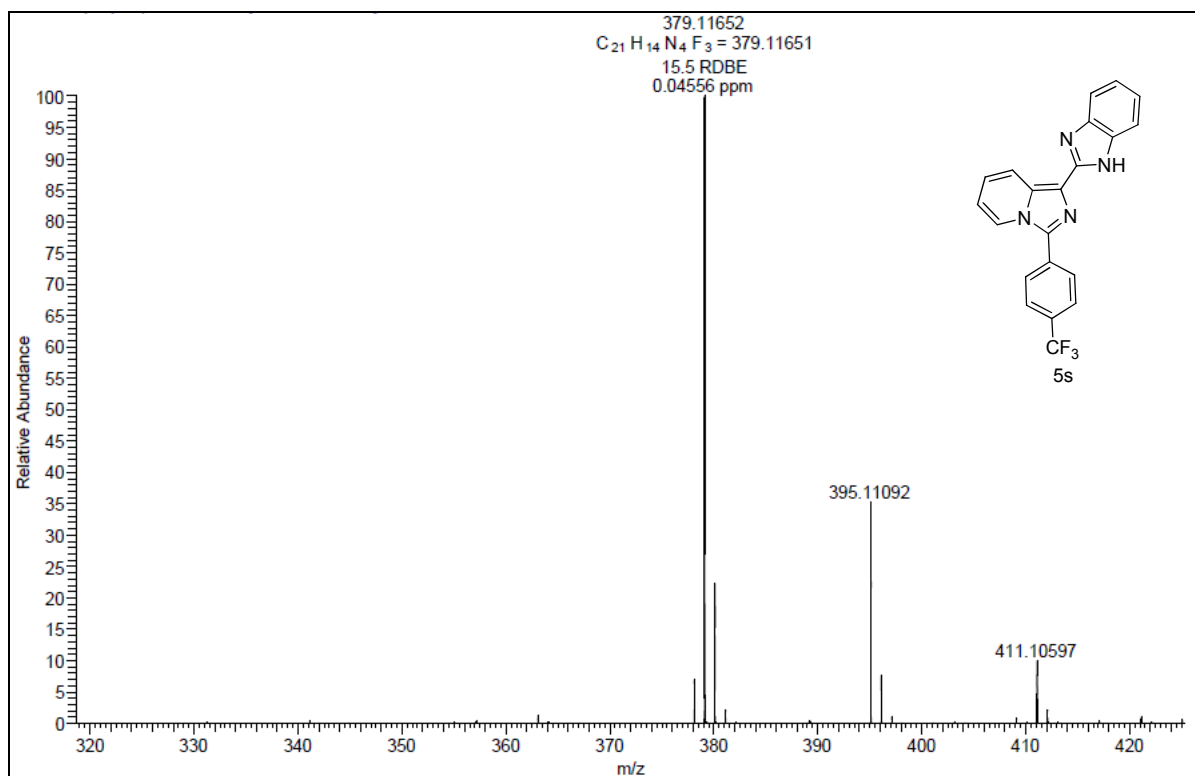
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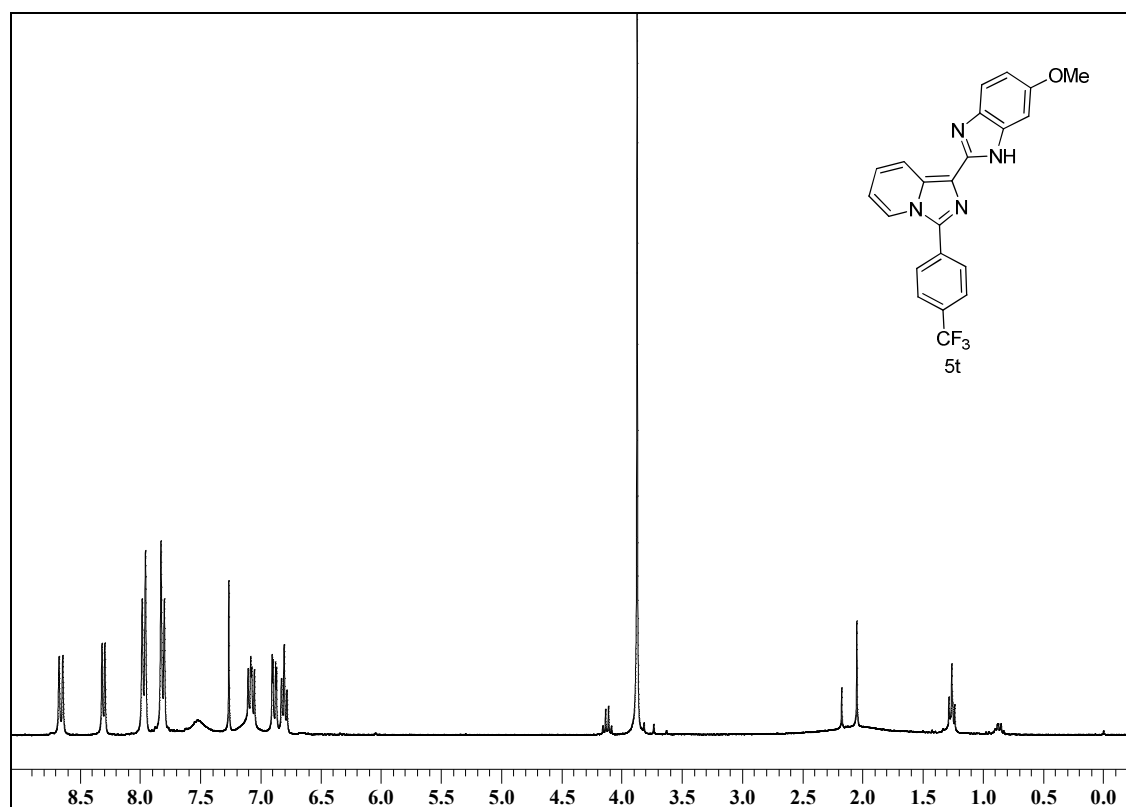
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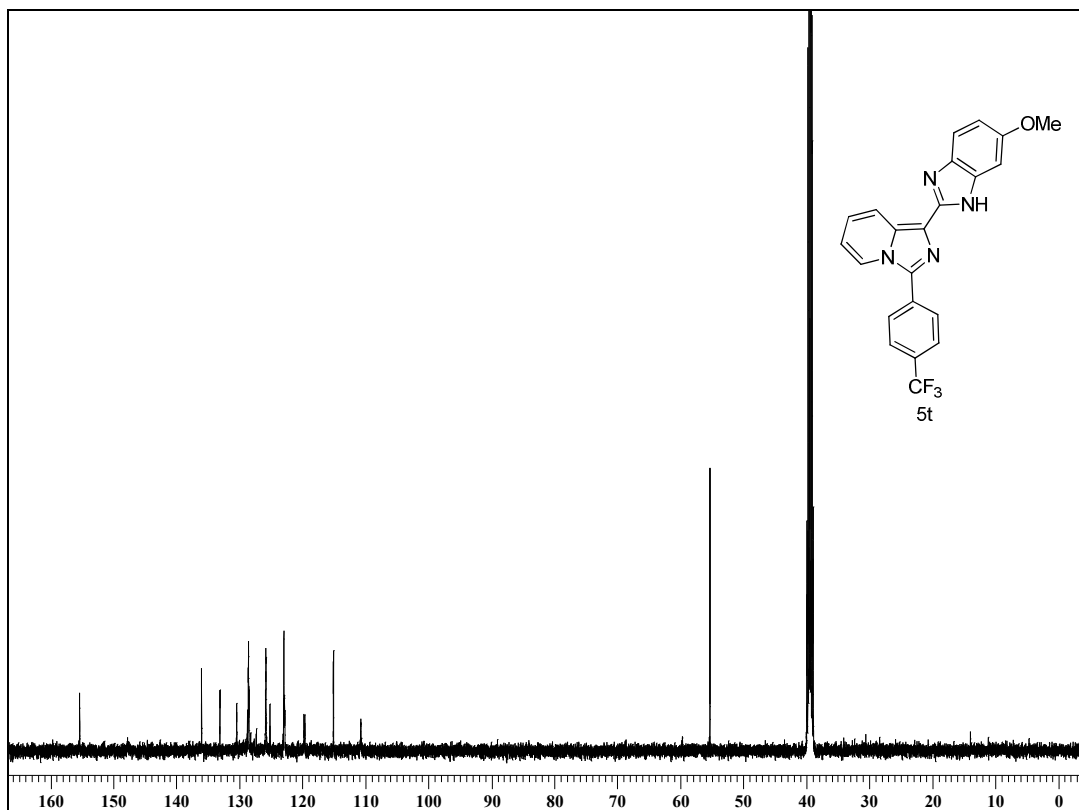
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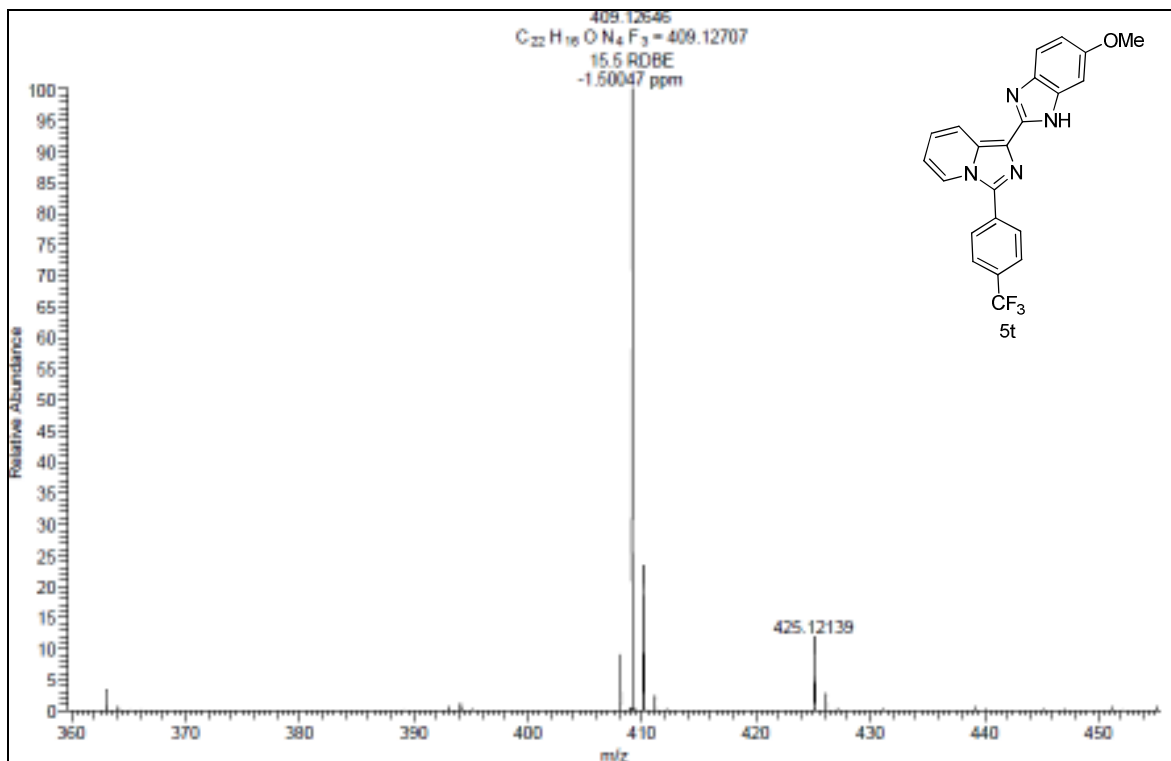
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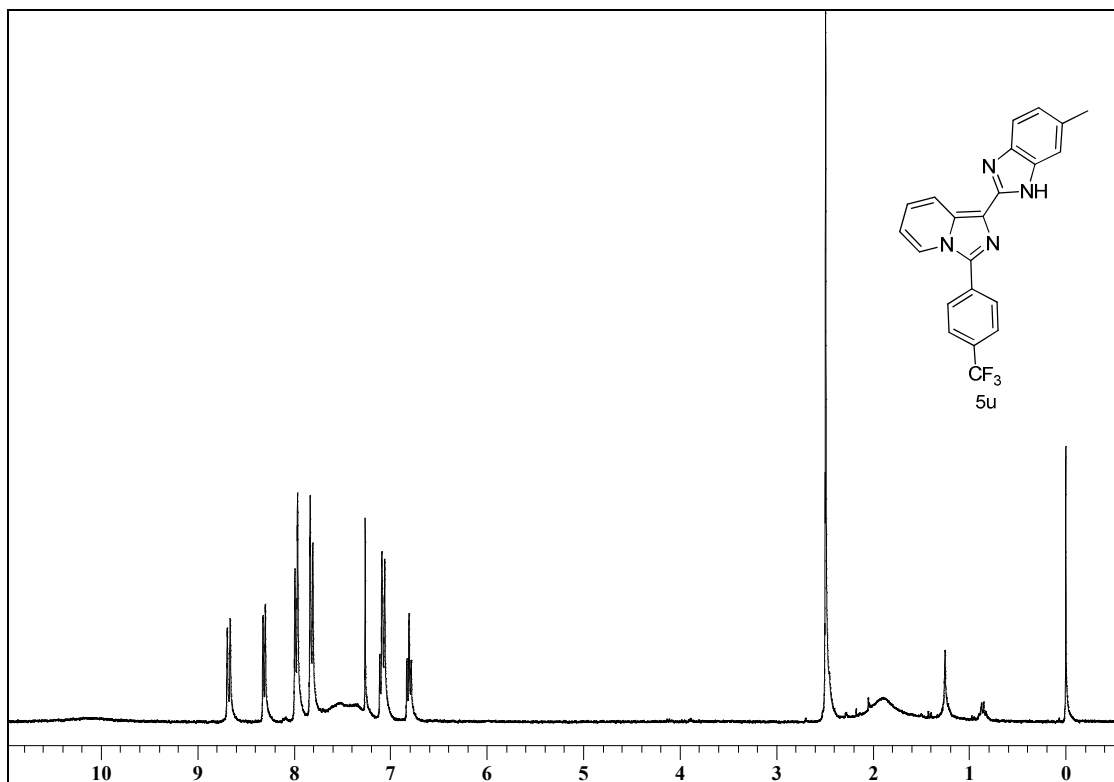
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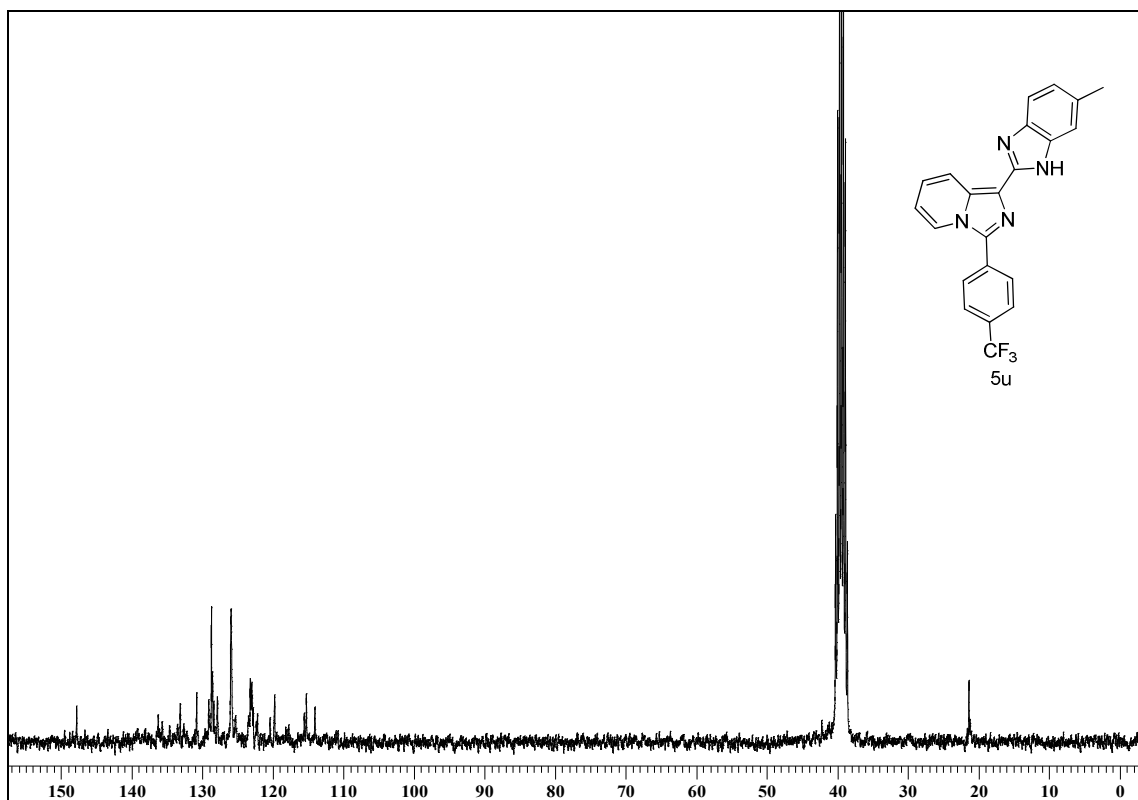
$^{13}\text{C}$  NMR SPECTRA OF COMPOUND 5t



HIGH RESOLUTION MASS SPECTRA OF COMPOUND 5t

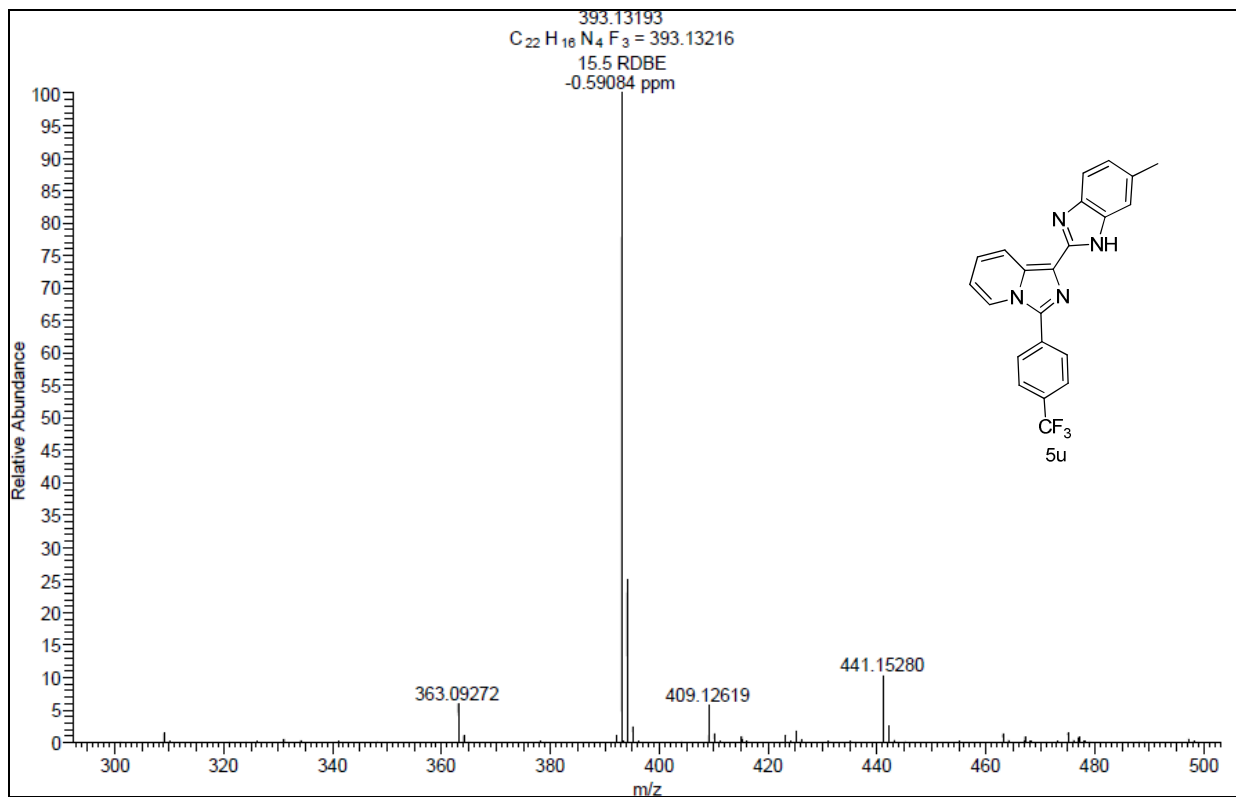


**<sup>1</sup>H NMR SPECTRA OF COMPOUND 5u**

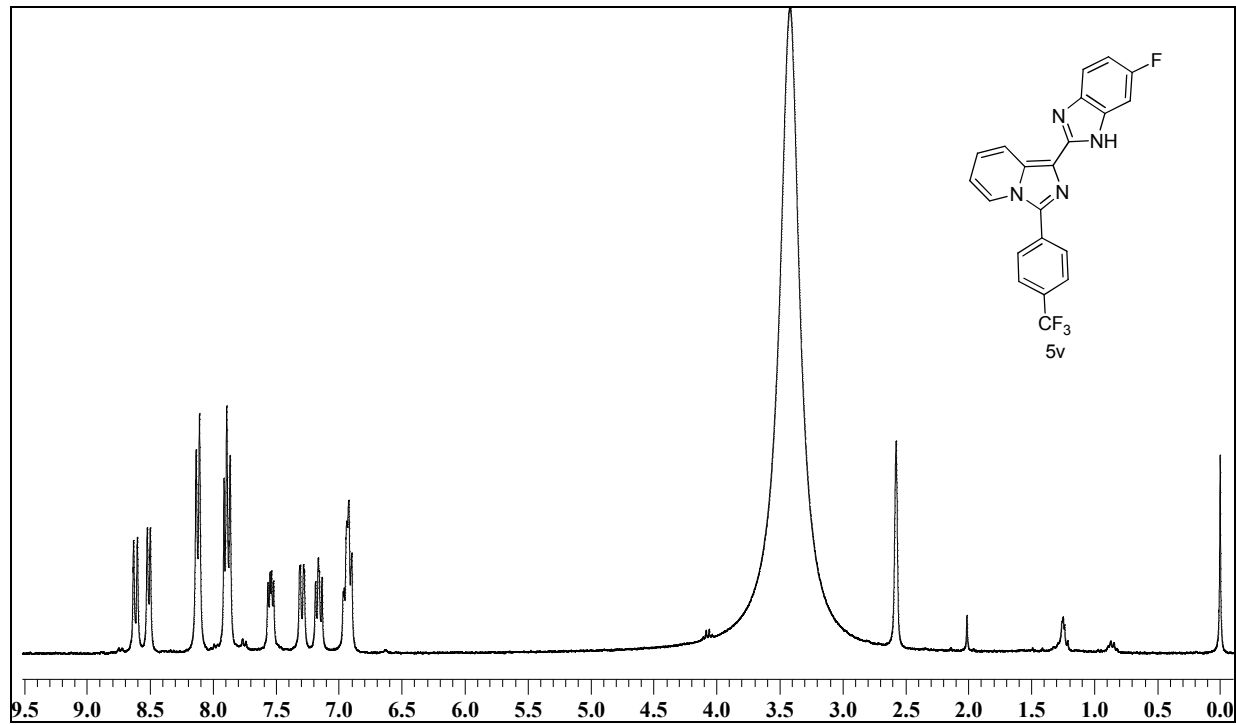


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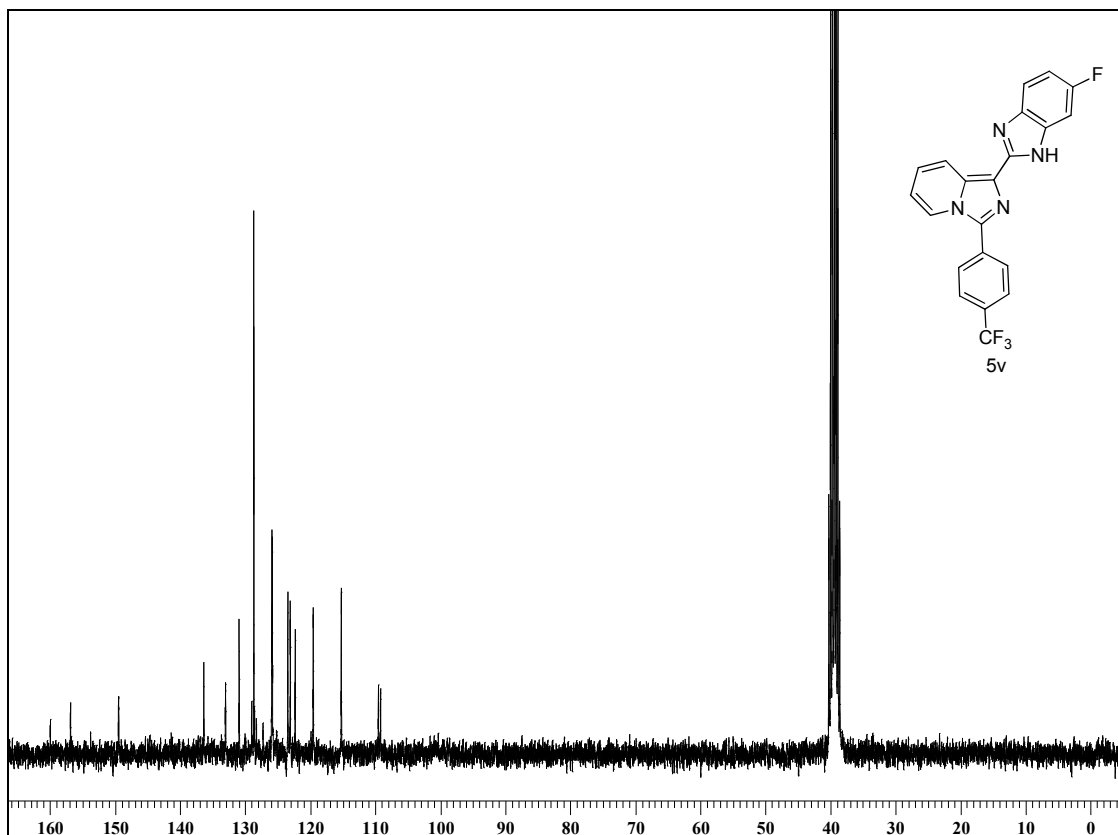




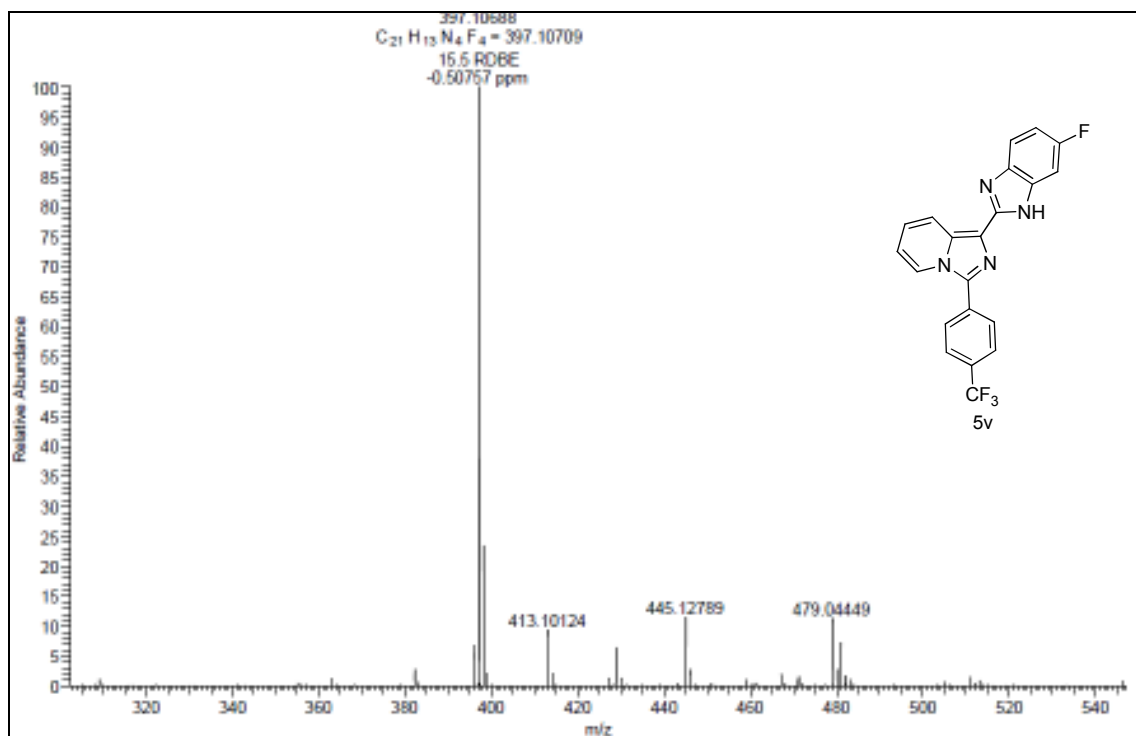
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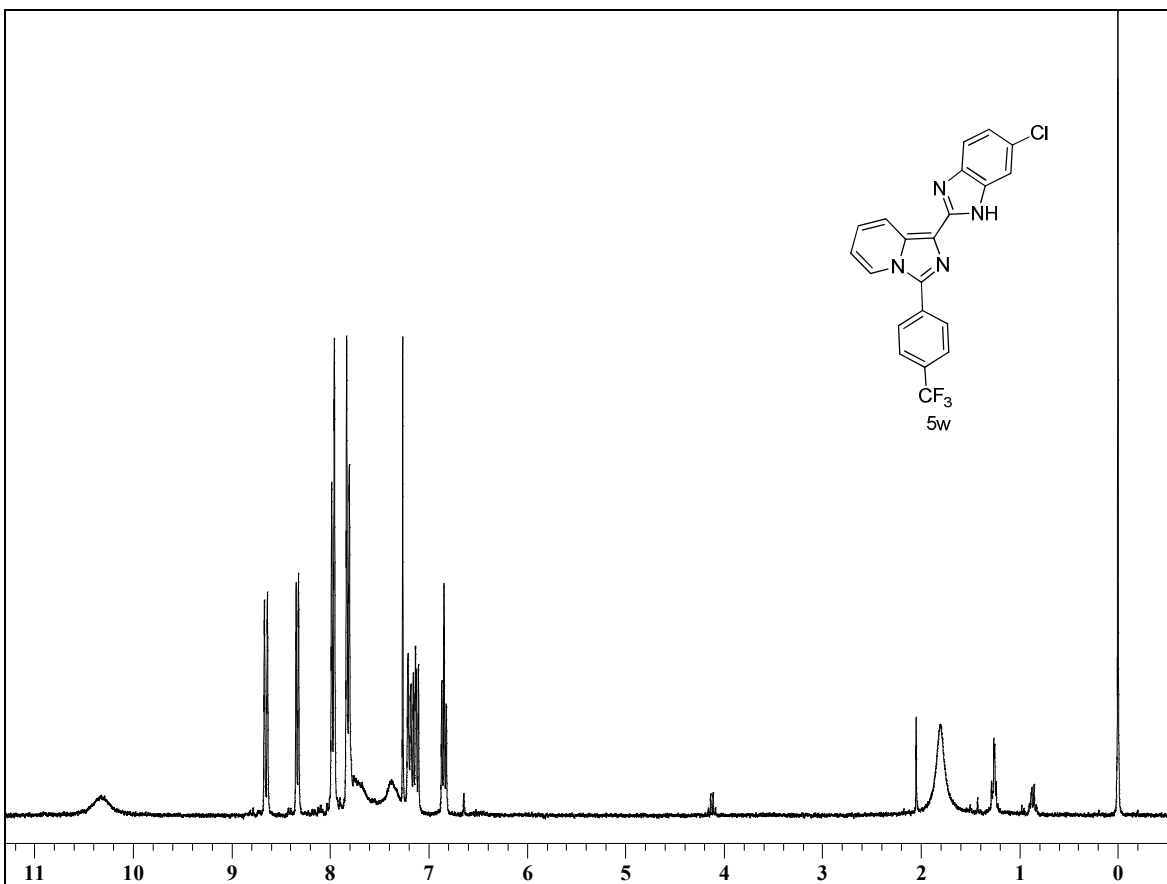
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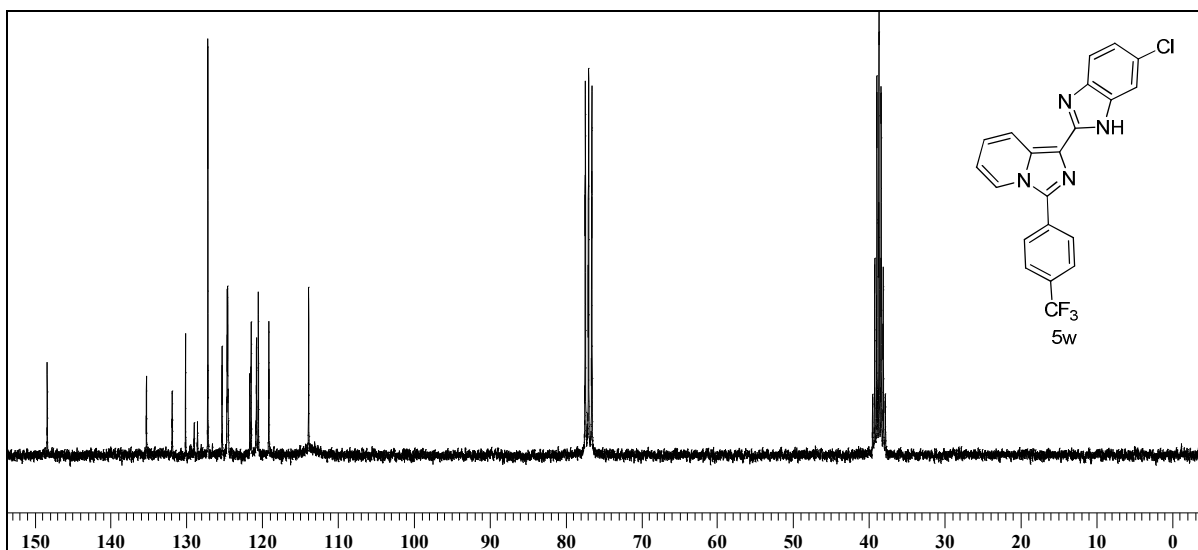
**<sup>13</sup>C NMR SPECTRA OF COMPOUND 5v**



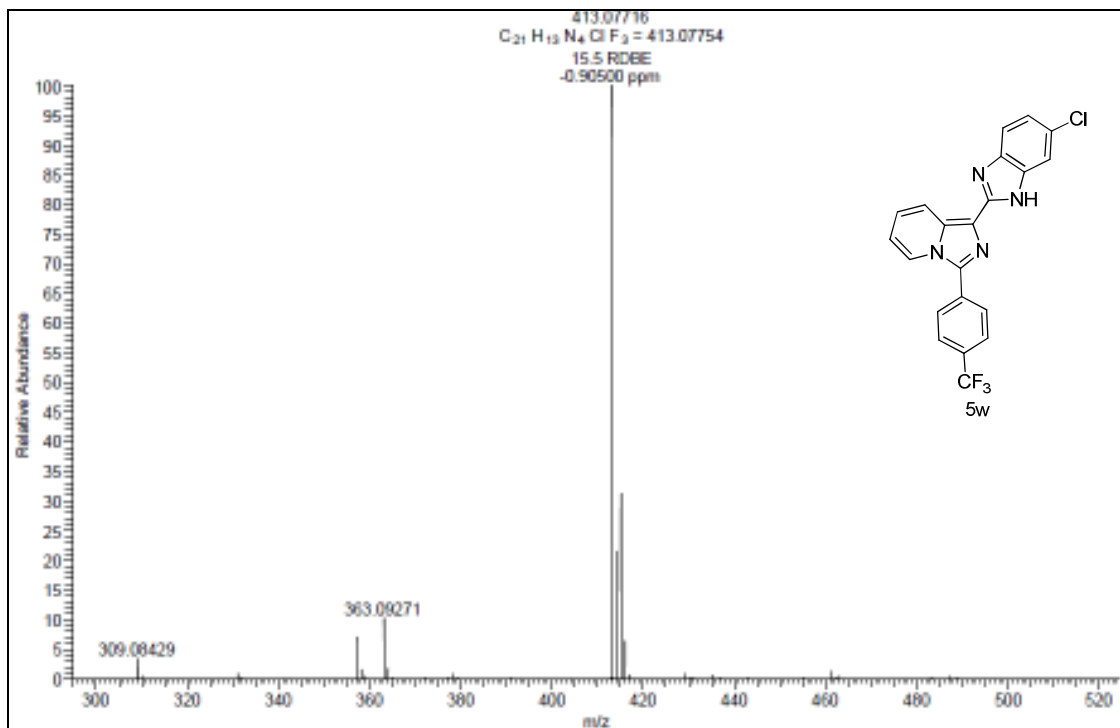
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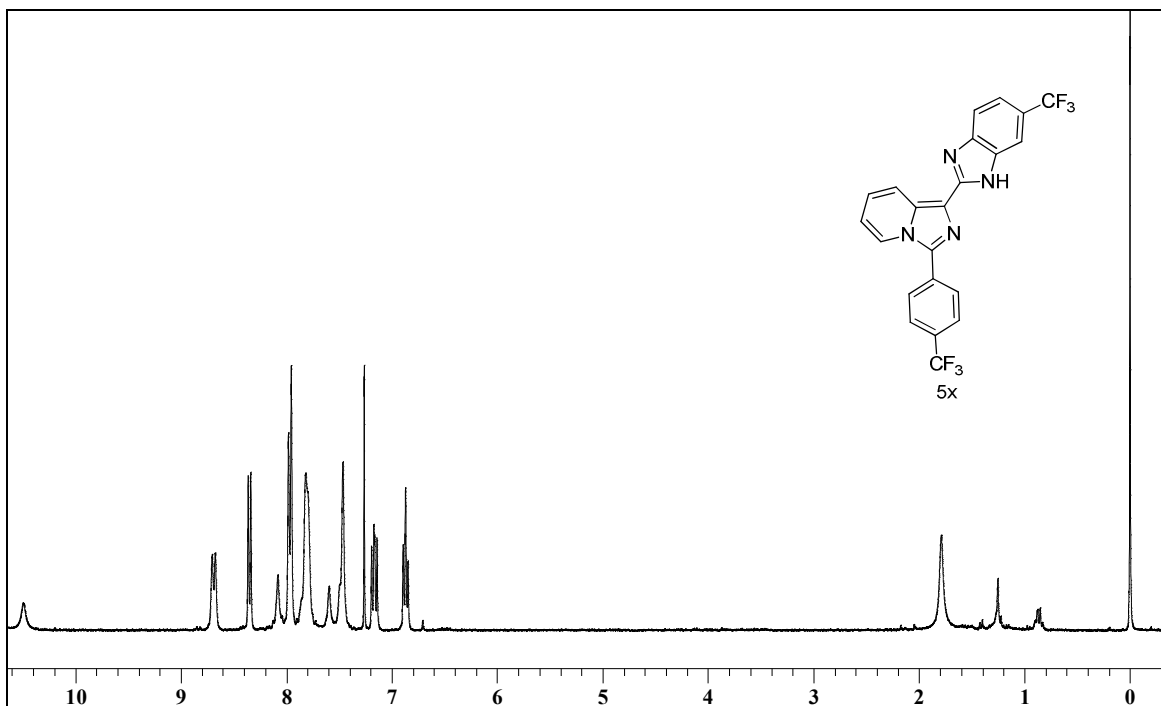
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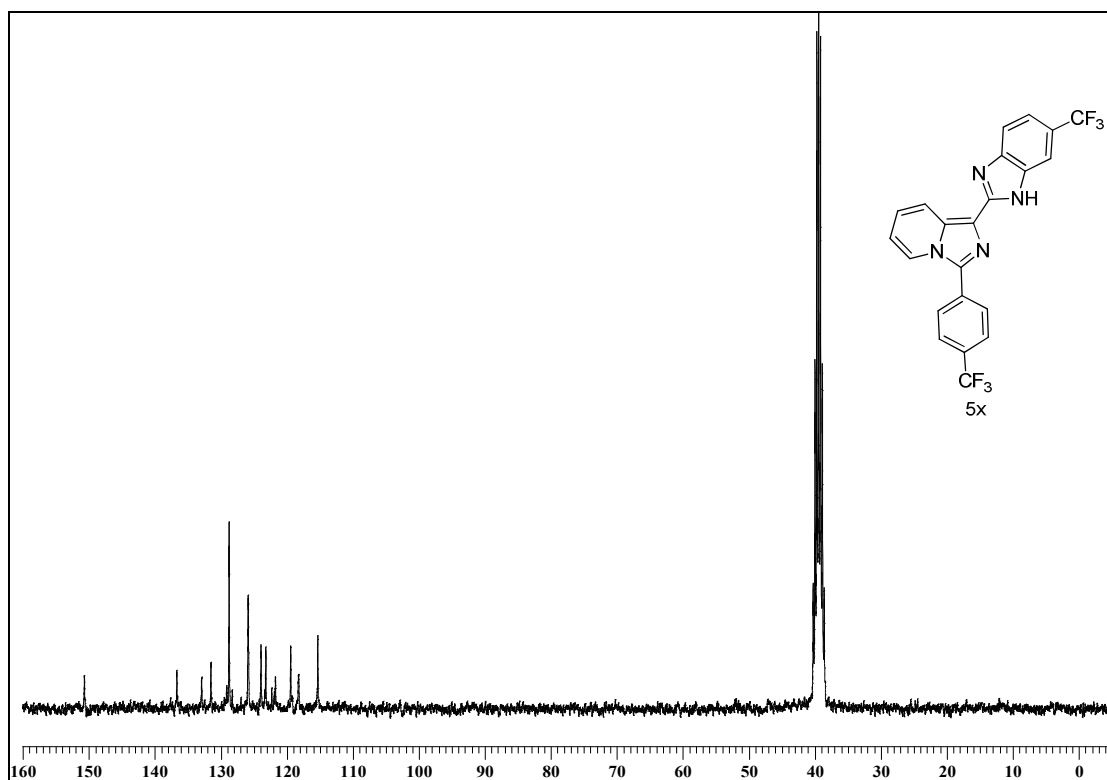
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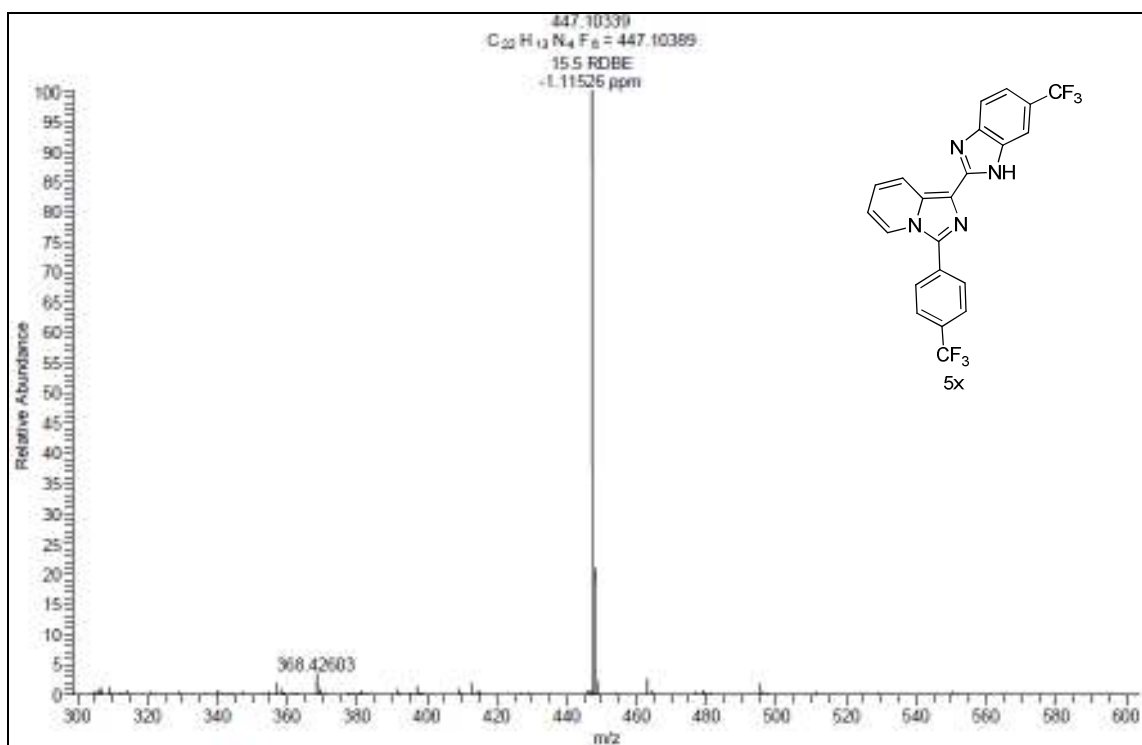
HIGH RESOLUTION MASS SPECTRA OF COMPOUND 5w



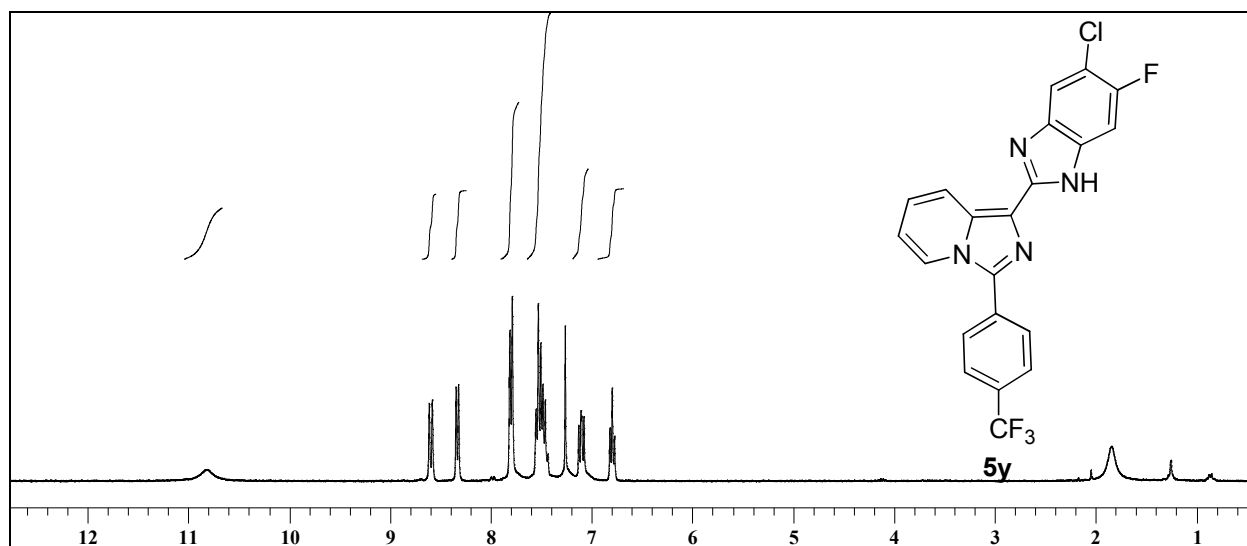
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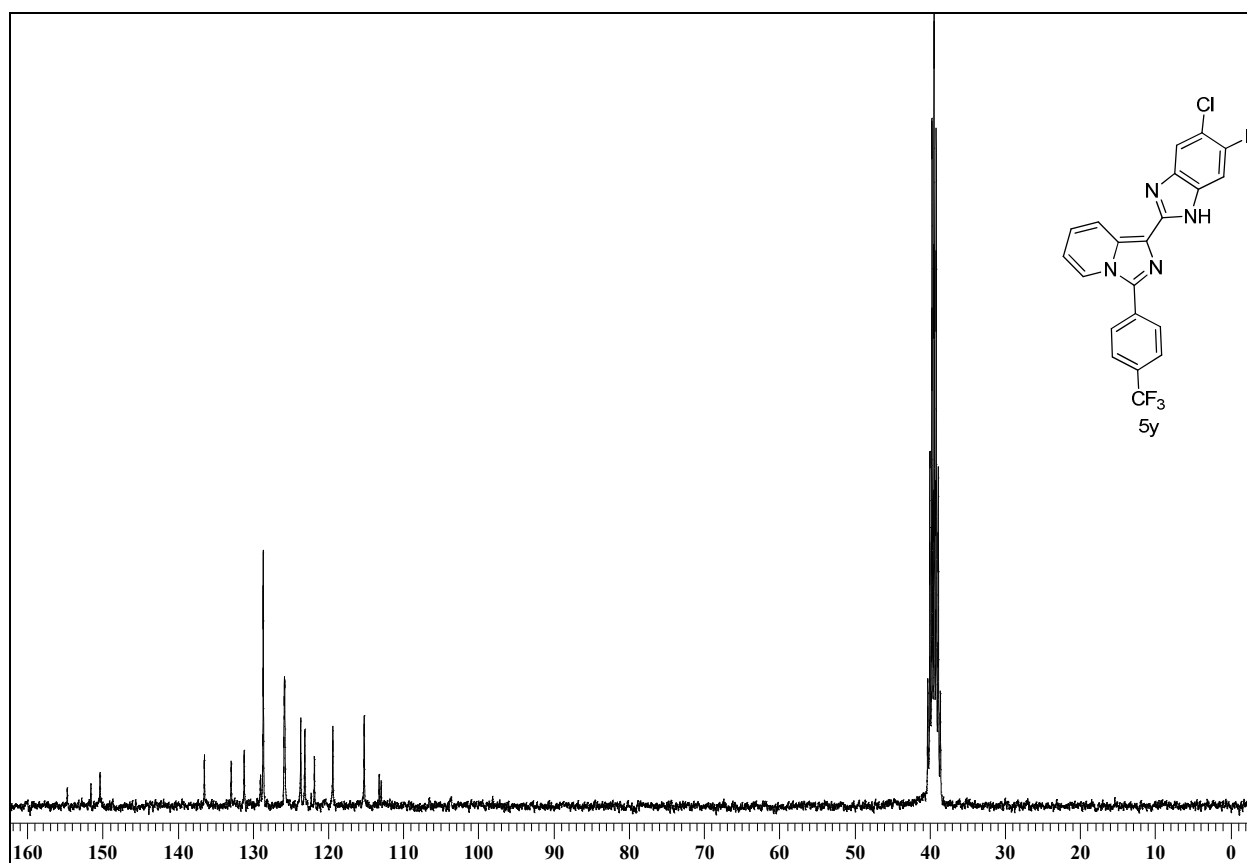
$^{13}\text{C}$  NMR SPECTRA OF COMPOUND 5x



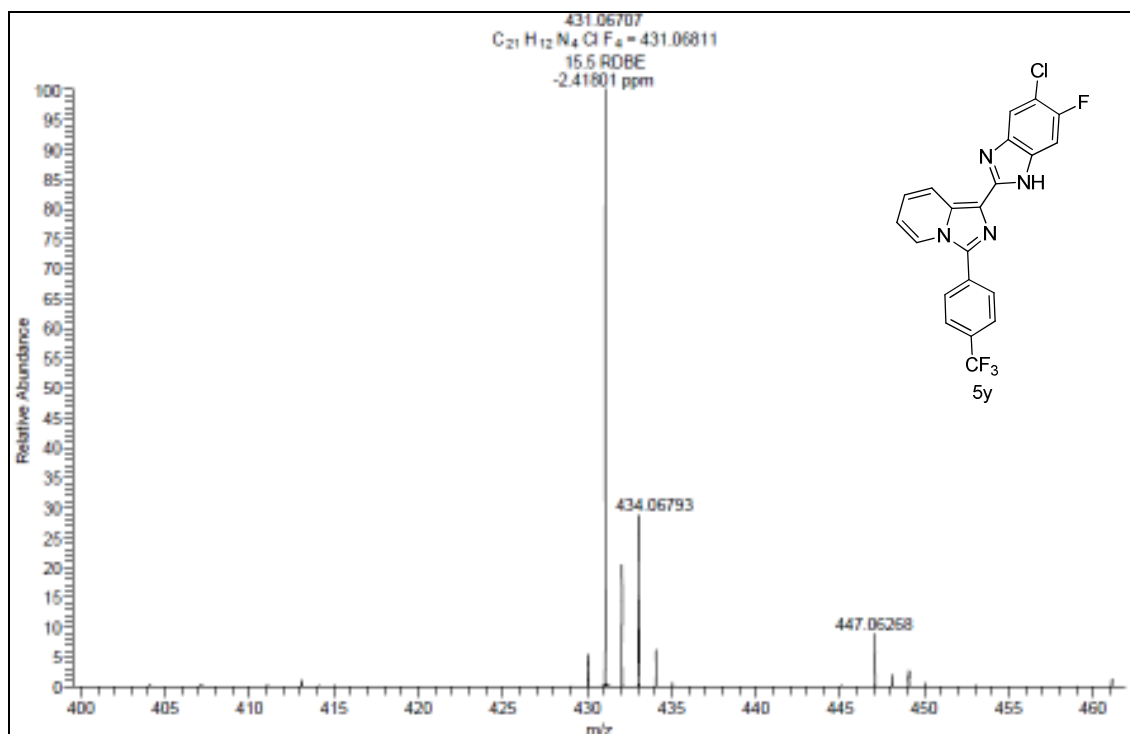
HIGH RESOLUTION MASS SPECTRA OF COMPOUND 5x



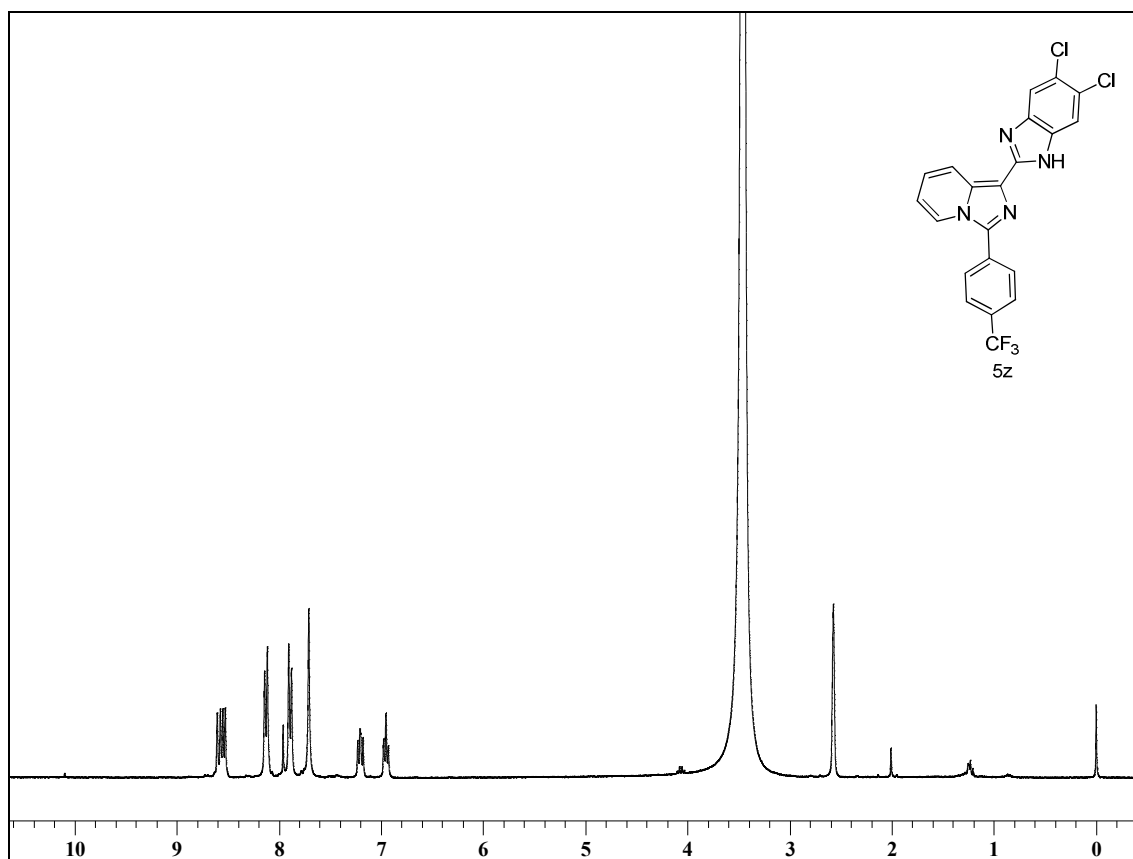
<sup>1</sup>H NMR SPECTRA OF COMPOUND 5y



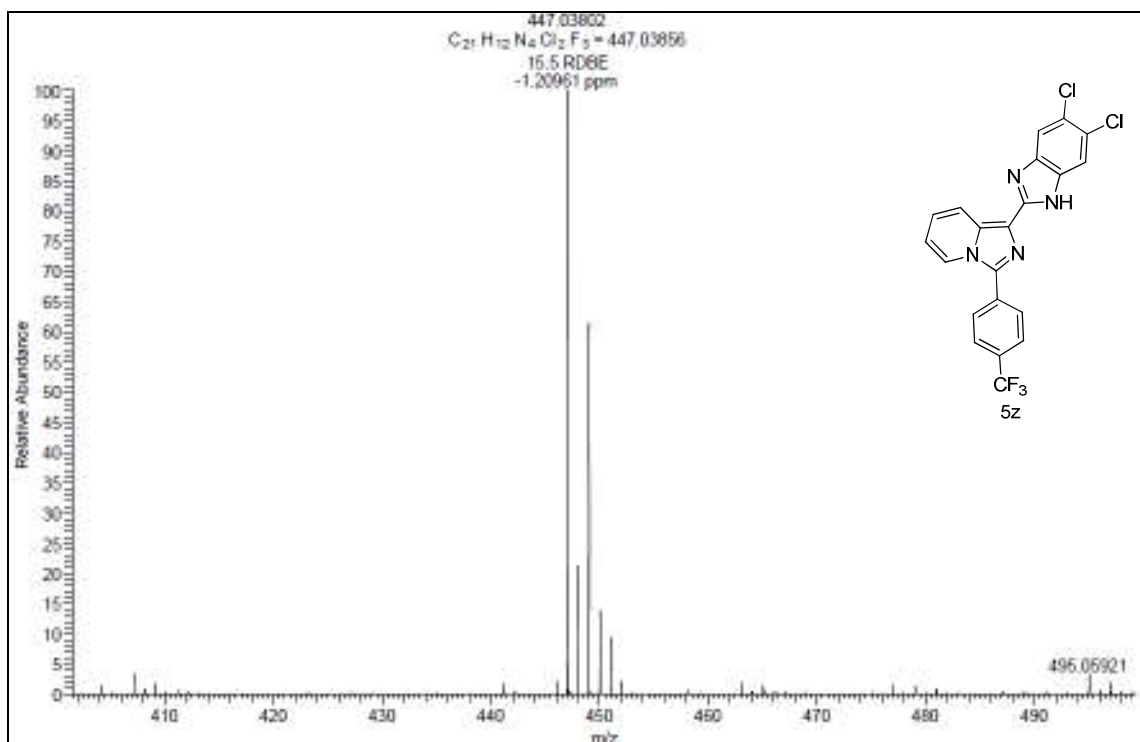
<sup>13</sup>C NMR SPECTRA OF COMPOUND 5y



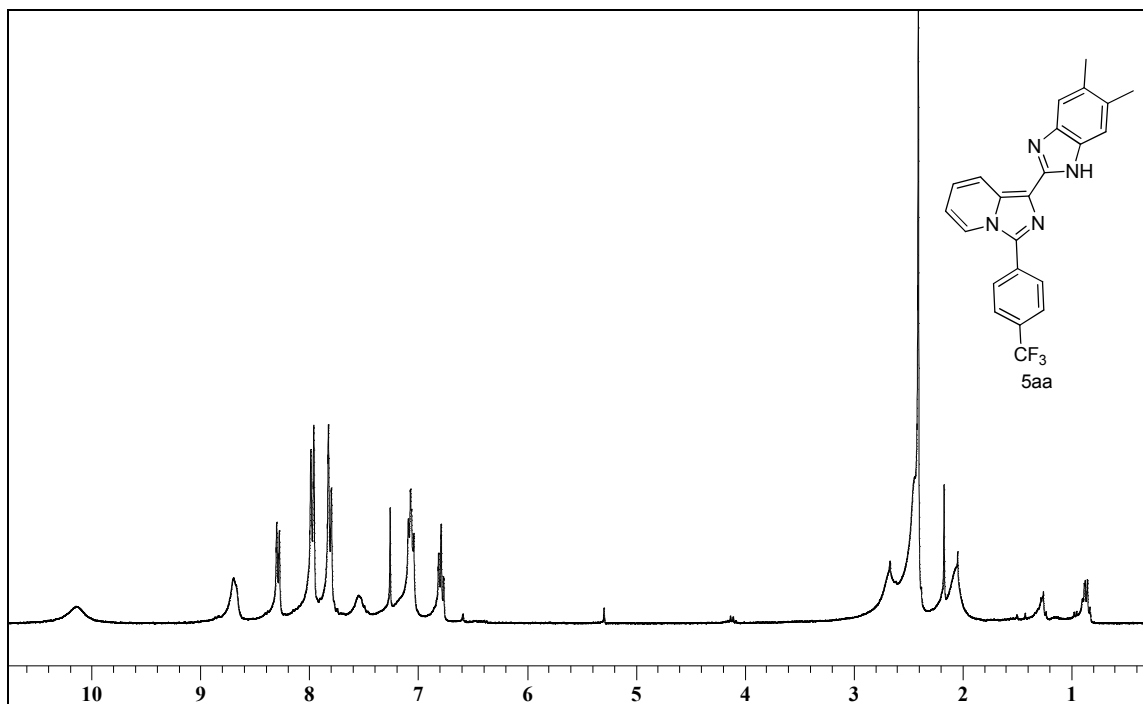
**HIGH RESOLUTION MASS SPECTRA OF COMPOUND 5y**



**<sup>1</sup>H NMR SPECTRA OF COMPOUND 5z**

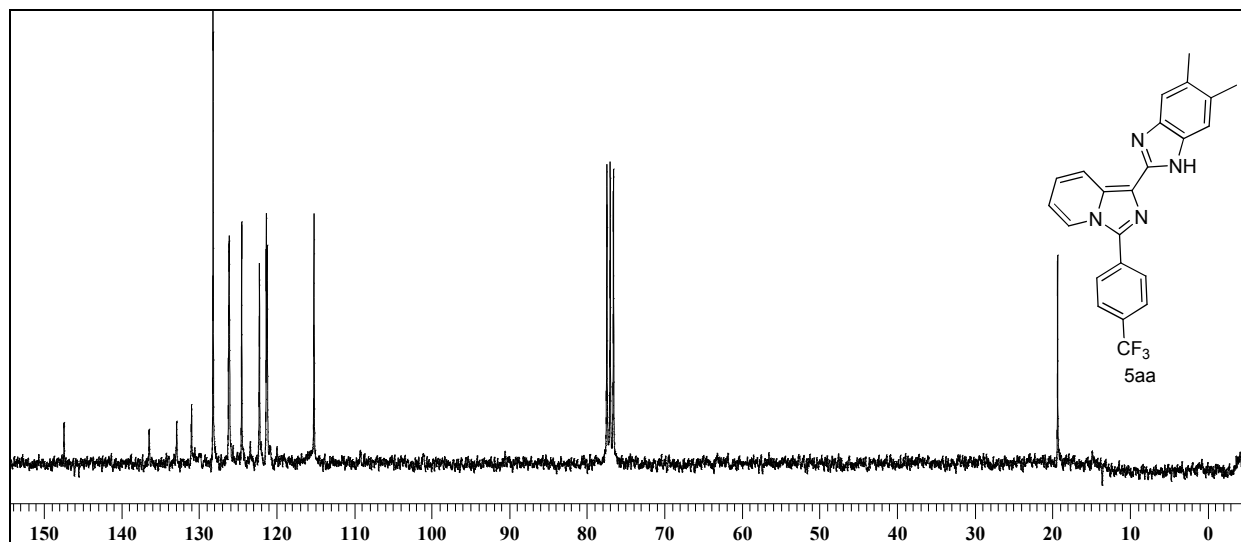


**HIGH RESOLUTION MASS SPECTRA OF COMPOUND 5z**

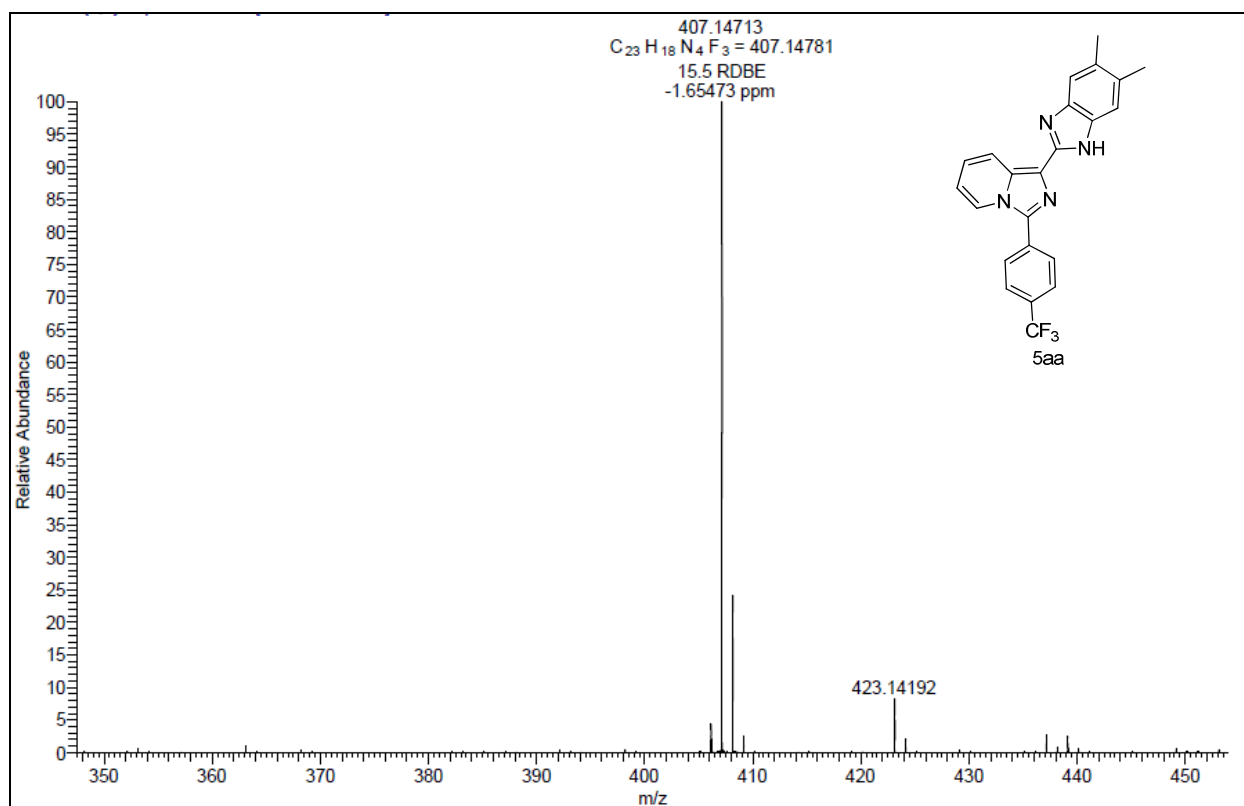


**<sup>1</sup>H NMR SPECTRA OF COMPOUND 5aa**





$^{13}\text{C}$  NMR SPECTRA OF COMPOUND 5aa



HIGH RESOLUTION MASS SPECTRA OF COMPOUND 5aa