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SUPPORTING INFORMATION

Exploration of Cytotoxic and Microtubule Disruption Potential of Novel Imidazo[1,5-a]pyridine based Chalcones

Gopathi Ramu,[a,b] Mommuleti Pradeep Kumar,[a] Gangasani Jagadeesh Kumar,[c] Syamprasad N P,[c] Bheeshma Geetanjali Kodiripaka,[a,b] V G M Naidu,[c]* and Bathini Nagendra Babu [a,b]*

[a] *Fluoro-Agrochemicals, CSIR-Indian Institute of Chemical Technology, Hyderabad 500 007, India.*

[b]*Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201 002, India.*

[c]*Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research, Guwahati, 781101, India.*

Corresponding Authors

E-mail: bathini@csiriict.in **(B. N. Babu);** vgmnaidu@niperguwahati.ac.in (Dr VGM Naidu)

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Experimental Procedure:

I. General procedure for the synthesis of substituted *N*-(2-pyridylmethyl) benzamides (3a-e): To a stirred solution of 2-pyridylmethanamine **1** (1 mmol) in dry THF was added trimethylamine (3.0 mmol) followed by substituted benzoyl chlorides (**2a-e**, 1.1 mmol) at 0 °C. The reaction mixture was stirred for 3 hours and was monitored by TLC. After the completion of the reaction, THF was removed under vacuum to get the crude products which were further purified by column chromatography using ethyl acetate and hexane as solvent system to obtain the pure compounds (**3a-e**).

II. General procedure for the synthesis of substituted phenylimidazo[1,5-*a*]pyridine (4a–e):To substituted *N*-(2-pyridylmethyl) benzamides (**3a-e**) (1 mmol), 4 mL of $POCl_3$was added and refluxed for 3 hours. This was poured into cold water and neutralized with $NaHCO_3$ solution. This water layer was extracted three times with ethyl acetate. The combined organic phases were dried over anhydrous Na_2SO_4 and evaporated under a vacuum. Thus, the residue obtained was purified by column chromatography using ethyl acetate and hexane as solvent systems to afford the pure compounds (**4a-e**).

III. General procedure for the synthesis of 3-(substituted phenyl)-imidazo[1,5-*a*]pyridine-1-carbaldehydes (5a-e) :[37]

To an ice-water cooled solution of substituted phenyl imidazo[1,5-*a*]pyridines(**4a-e**) (1 mmol) in DMF(1.4 mmol) was added dropwise $POCl_3$(1.4 mmol) with stirring, and then the reaction mixture was heated to100 °C for 2 hours. After the completion of the reaction, the reaction mixture was poured into ice water and quenched with an ammonium hydroxide solution. The aqueous solution was extracted with ethyl acetate and the resultant organic layer was dried over anhydrous sodium sulfate and evaporated under a vacuum. Thus, the residue obtained was purified by column chromatography using ethyl acetate and hexane as solvent systems to afford pure compounds (**5a-e**).

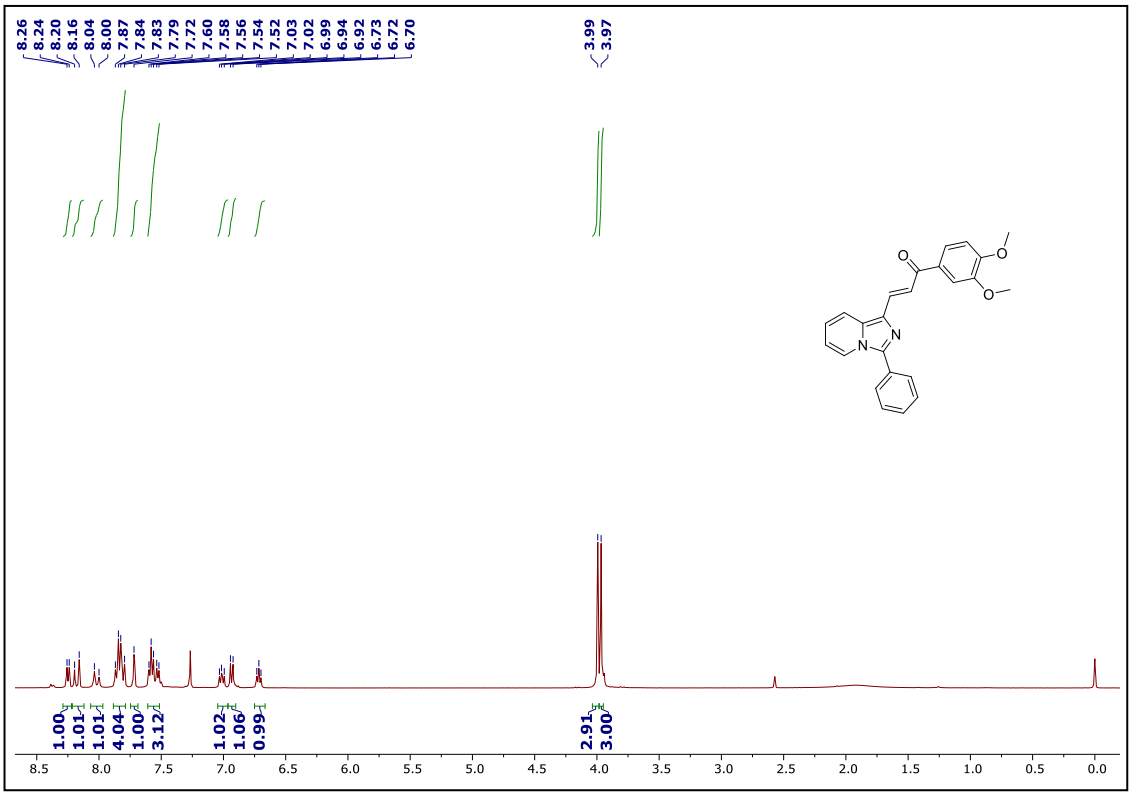


Figure S1. ^{1}H NMR spectrum of **7a** (400 MHz, $CDCl_3$).

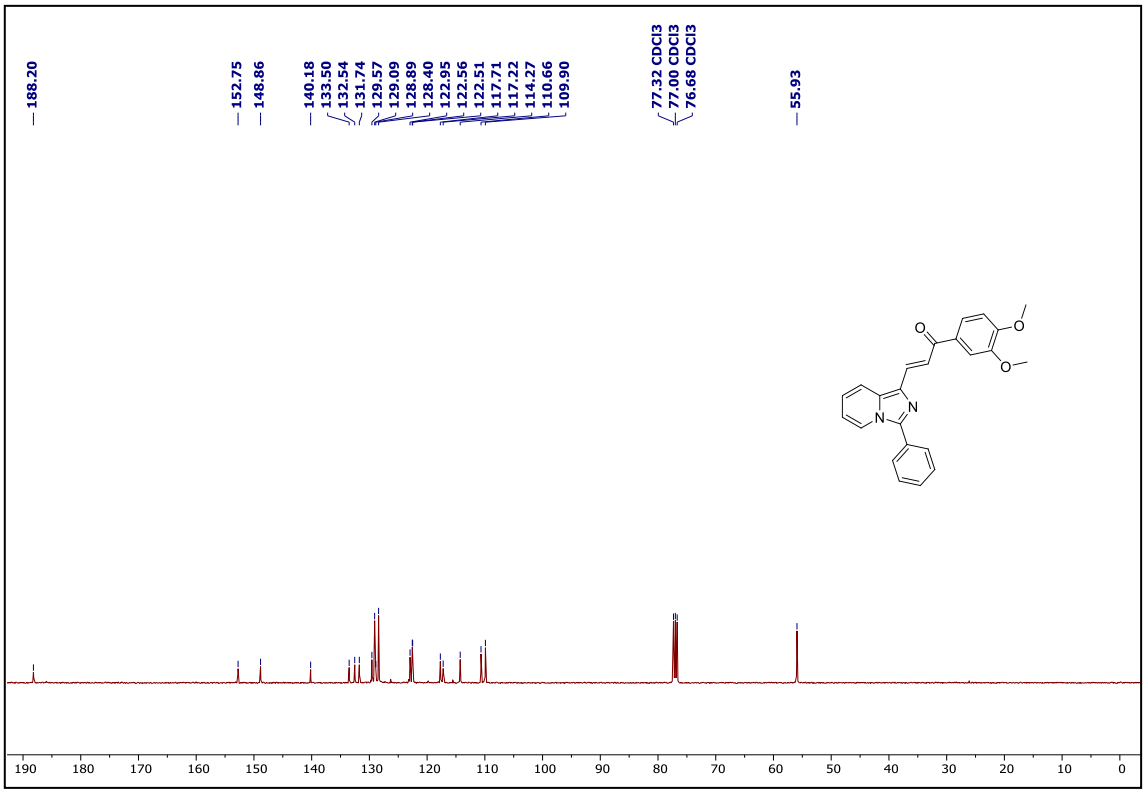


Figure S2. ^{13}C NMR spectrum of **7a** (100 MHz, $CDCl_3$).

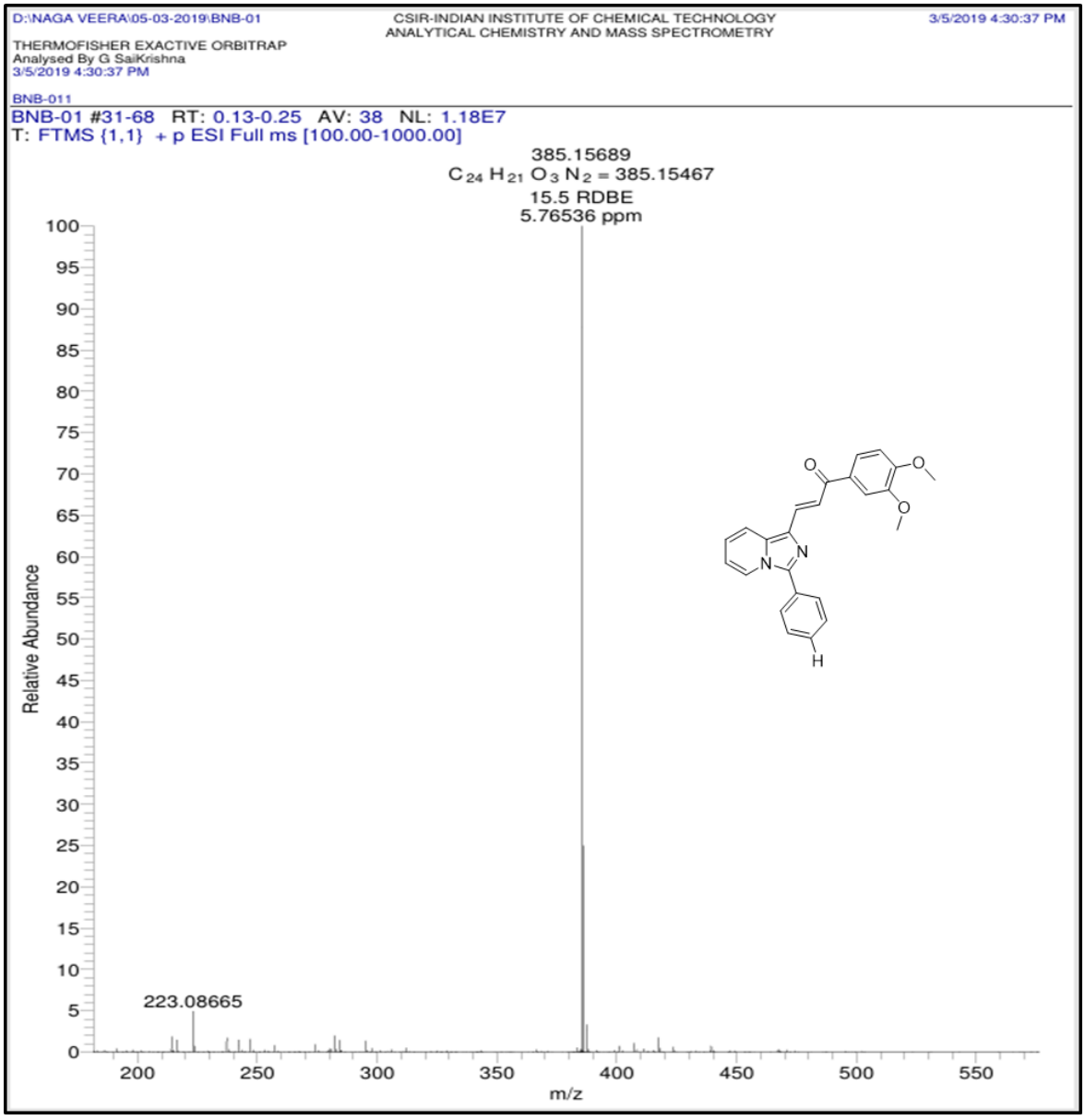


Figure S3. HRMS spectrum of **7a**

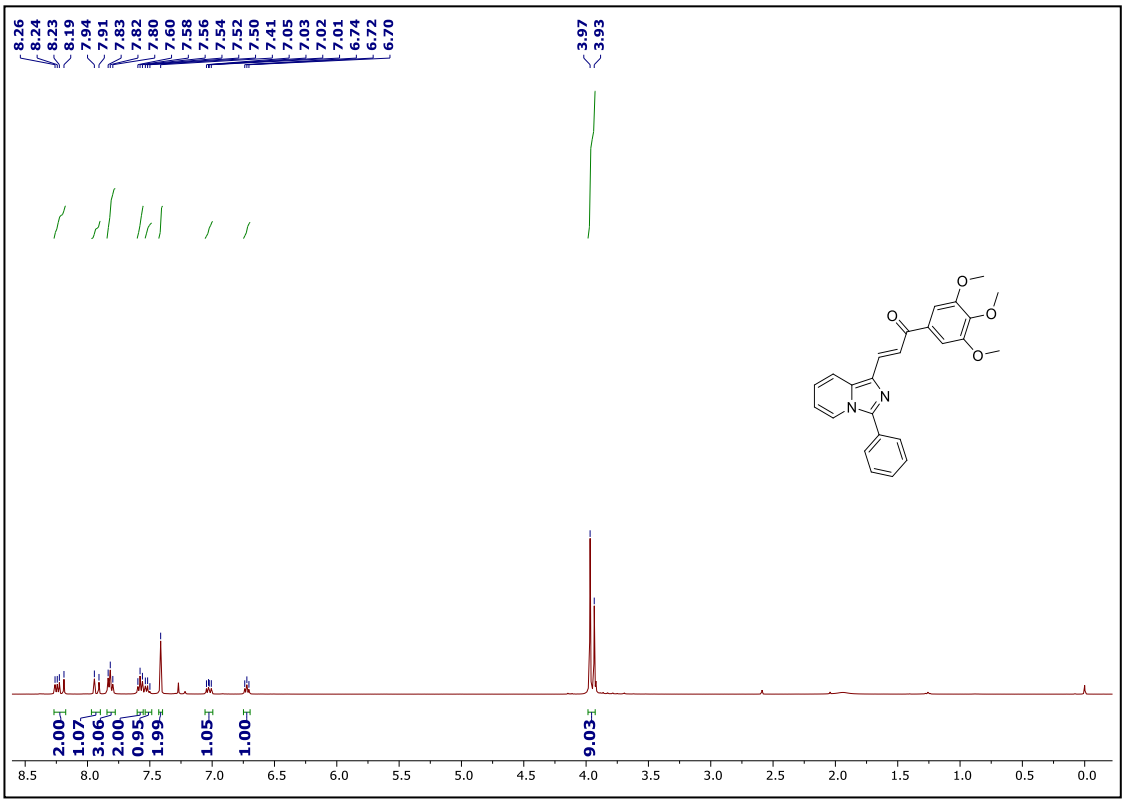


Figure S4. ^{1}H NMR spectrum of **7b** (400 MHz, $CDCl_3$).

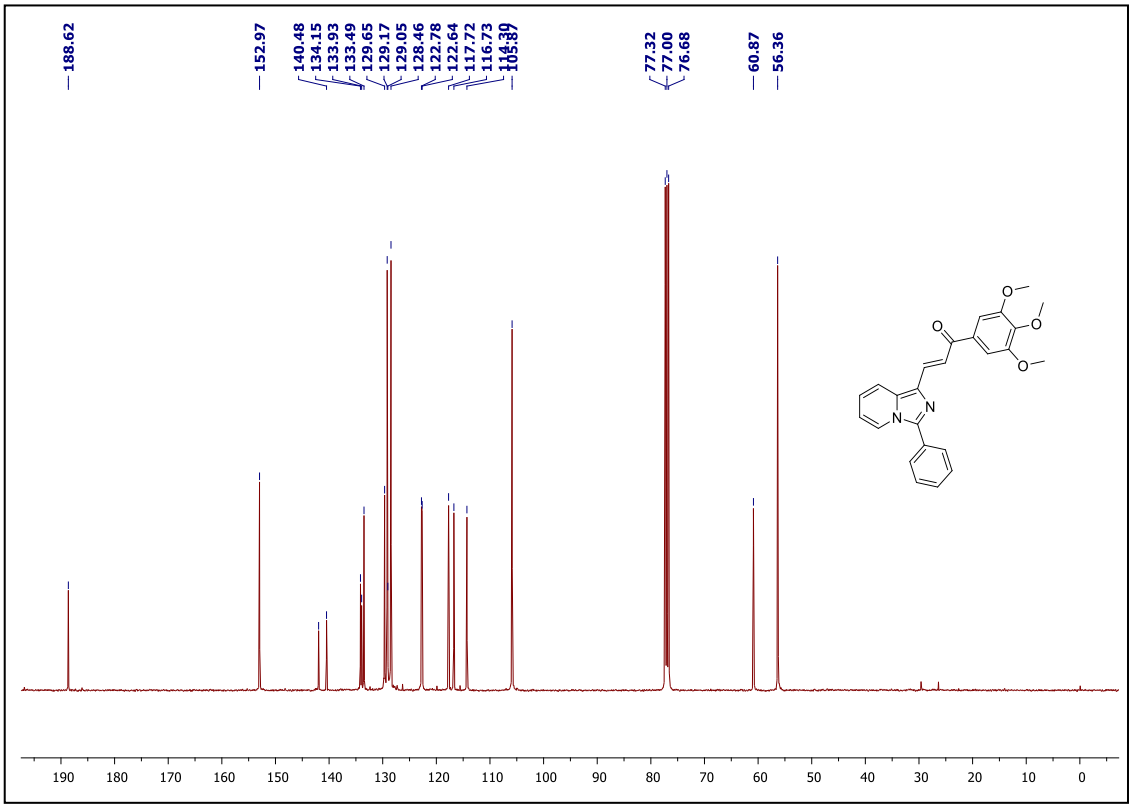


Figure S5.^{13}C NMR spectrum of **7b** (100 MHz, $CDCl_3$).

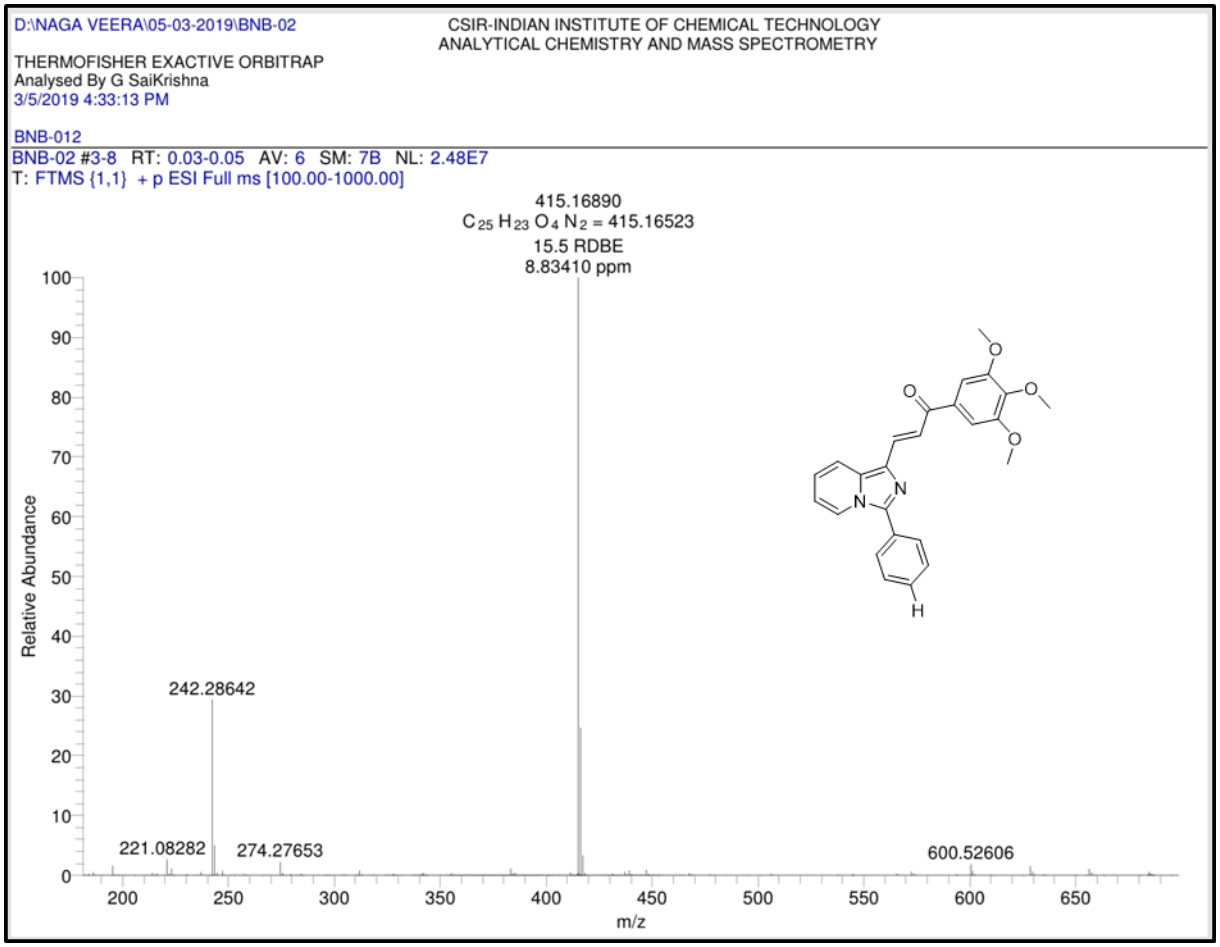


Figure S6. HRMS spectrum of **7b**

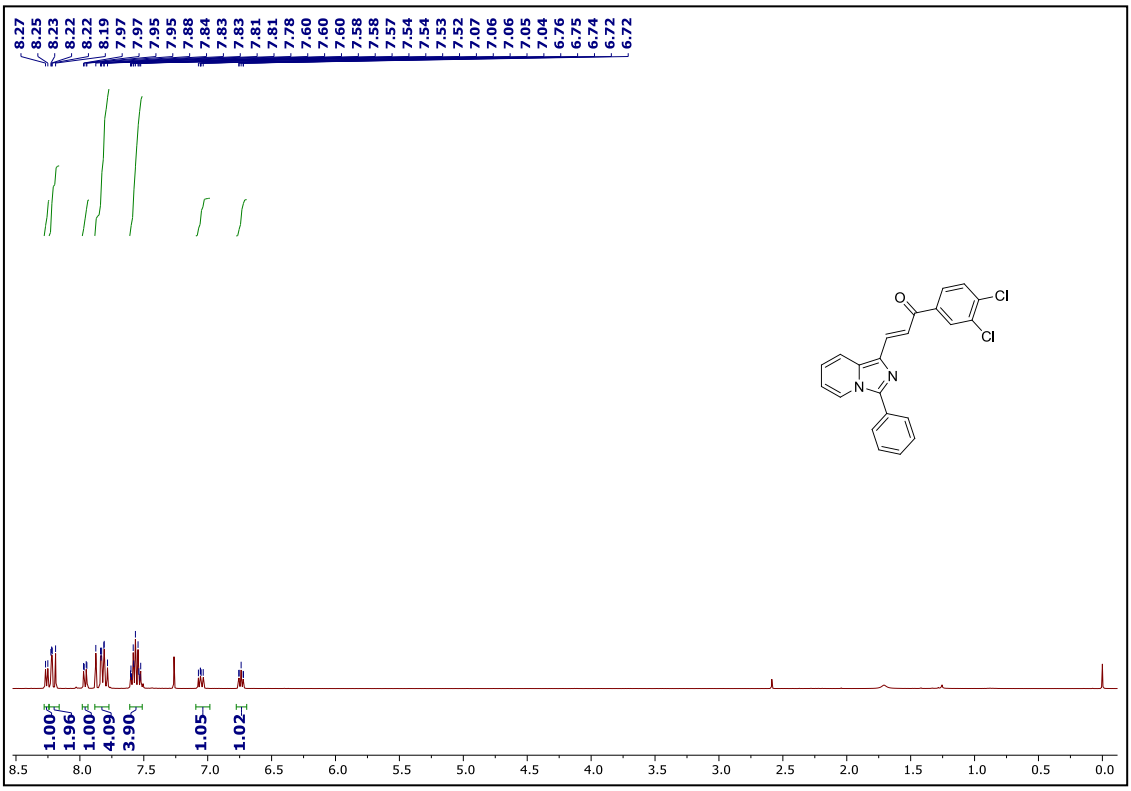


Figure S7.[1]H NMR spectrum of **7c** (400 MHz, $CDCl_3$).

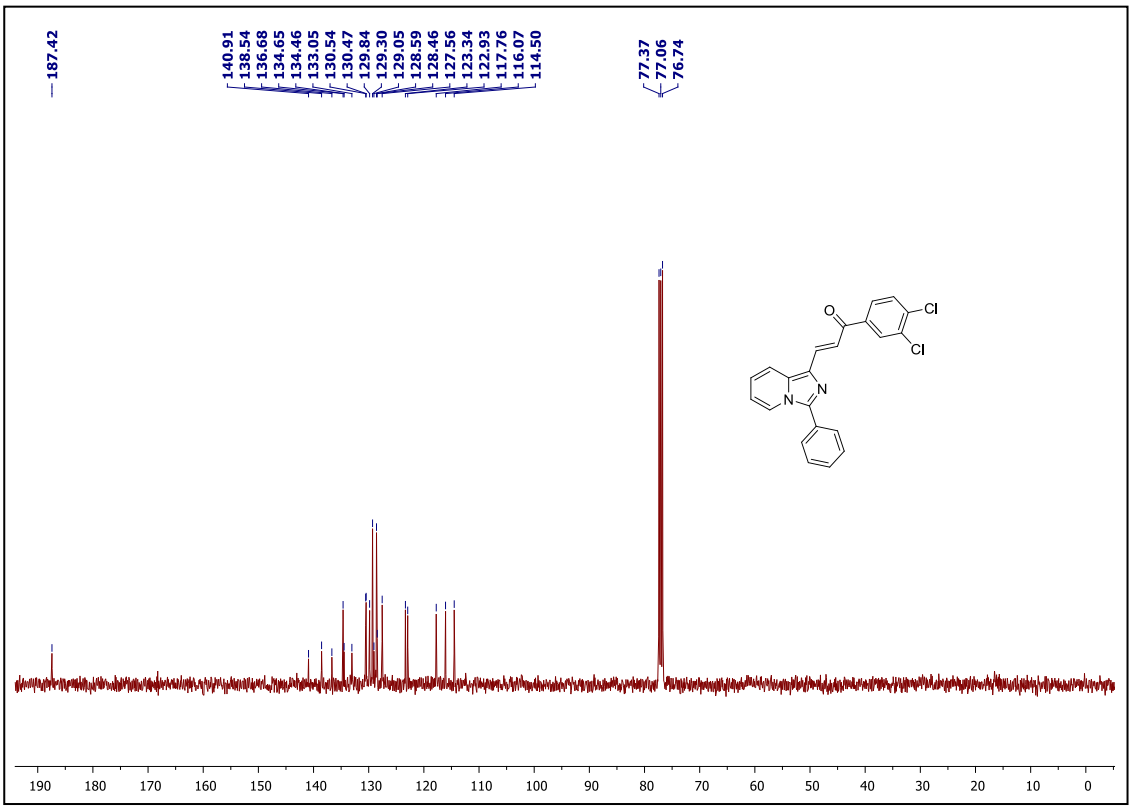
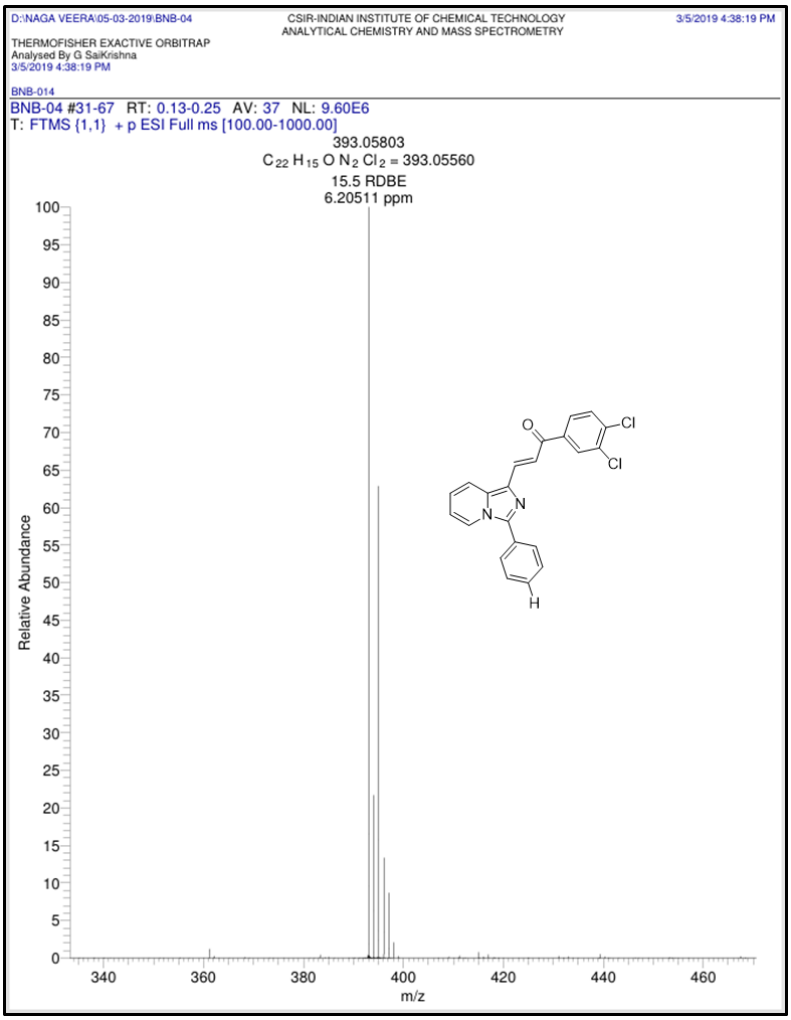


Figure S8.[13]C NMR spectrum of **7c** (100 MHz, $CDCl_3$).



FigureS9. HRMS spectrum of **7c**

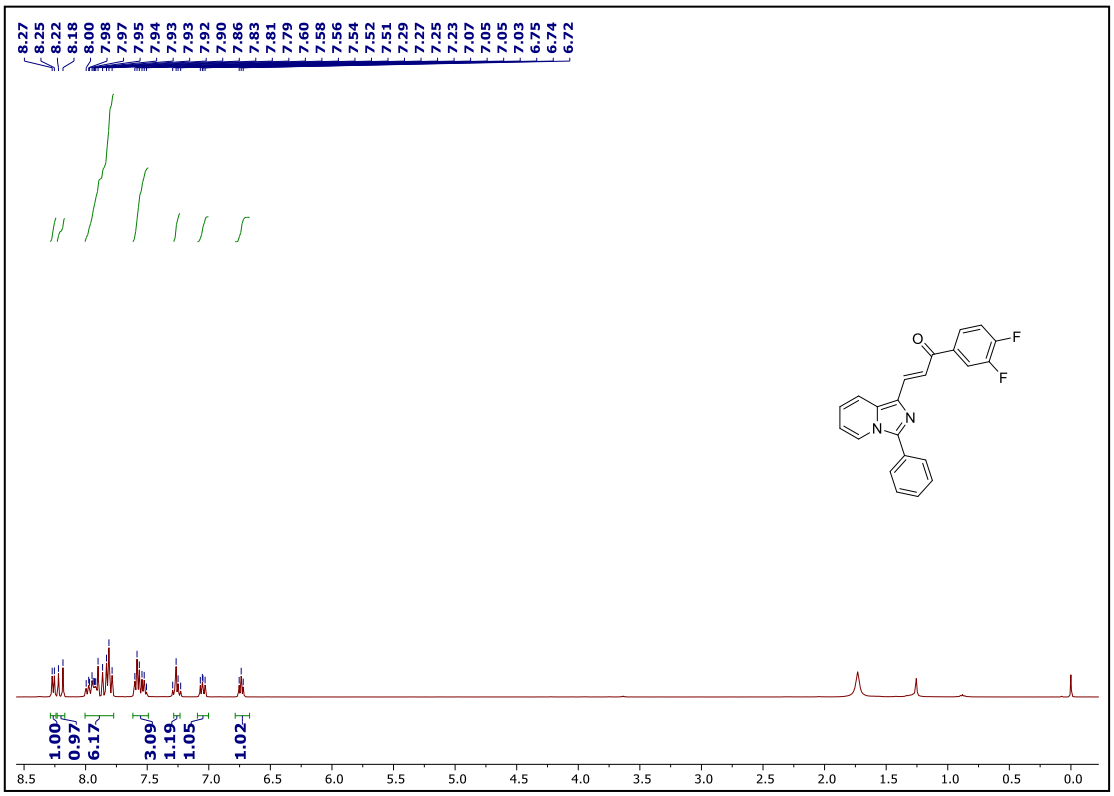


Figure S10. ^{1}H NMR spectrum of **7d** (400 MHz, $CDCl_3$).

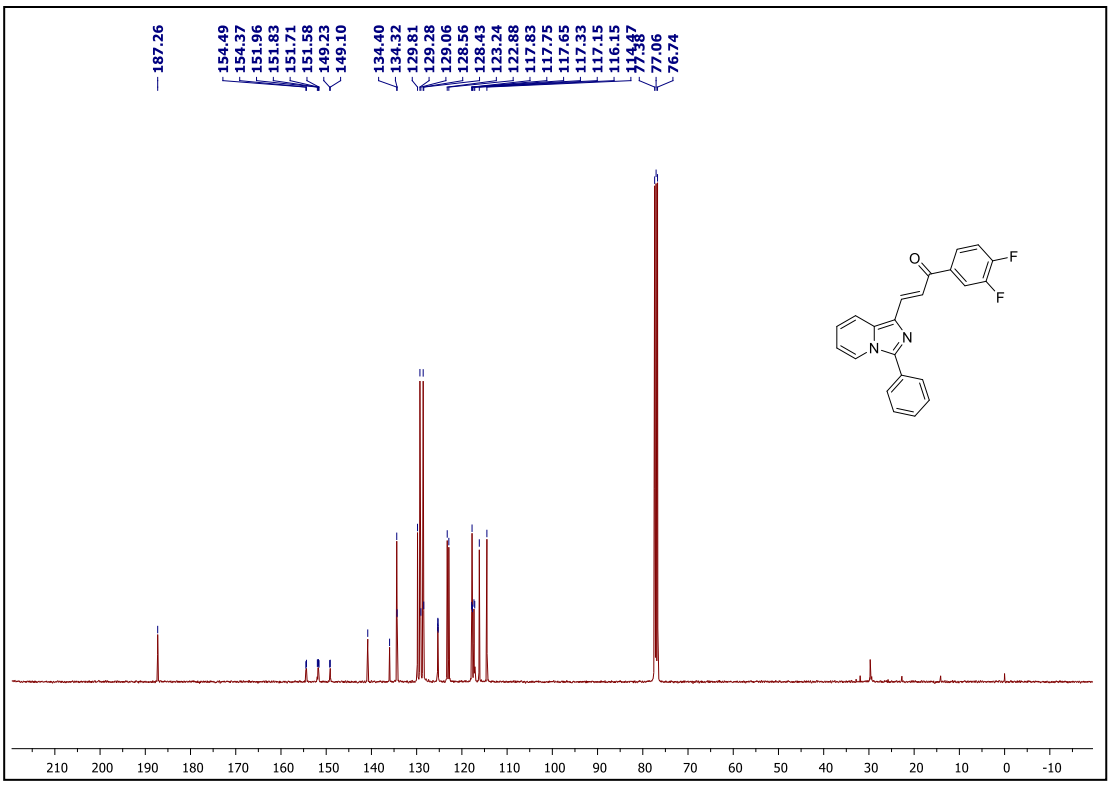


Figure S11. ^{13}C NMR spectrum of **7d** (100 MHz, $CDCl_3$).

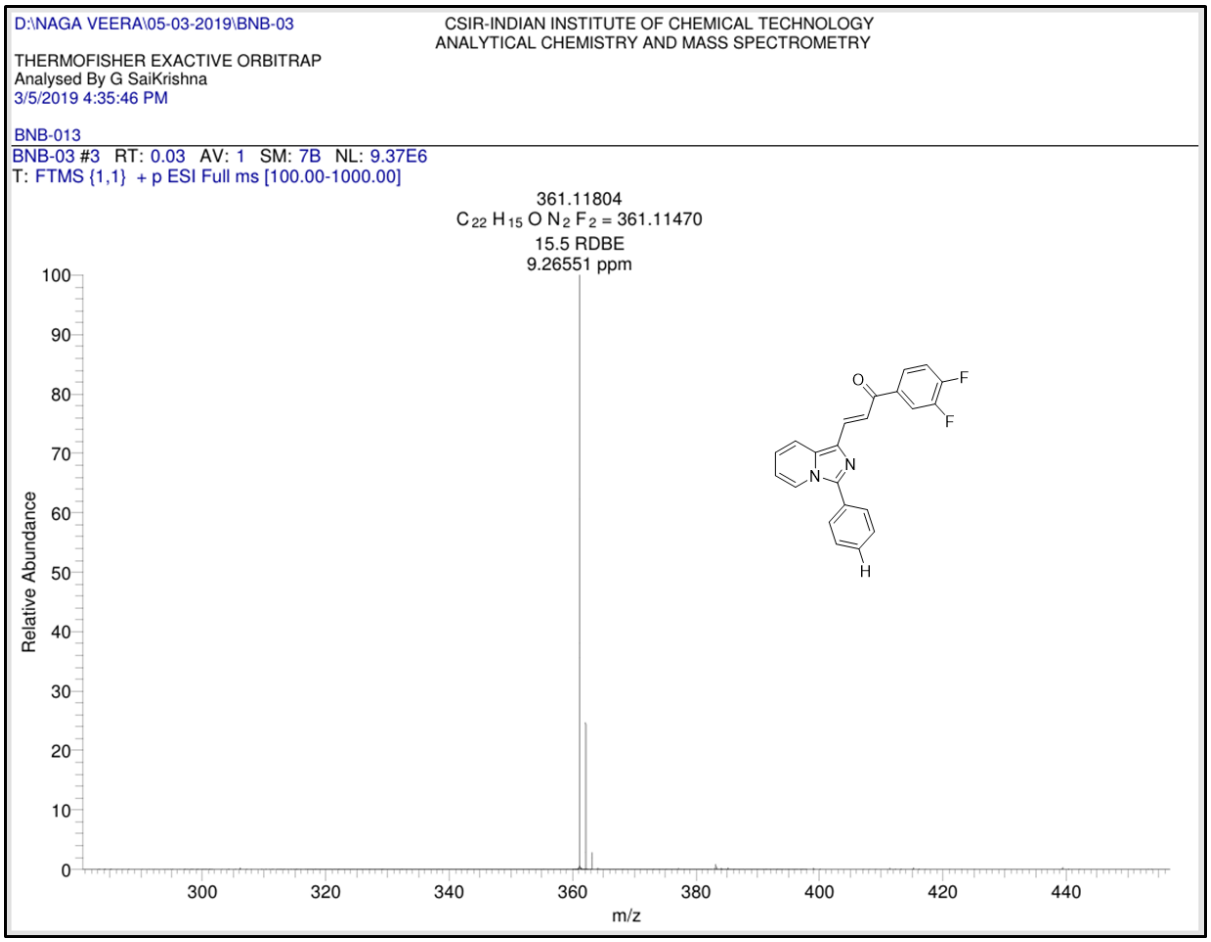


Figure S12. HRMS spectrum of **7d**

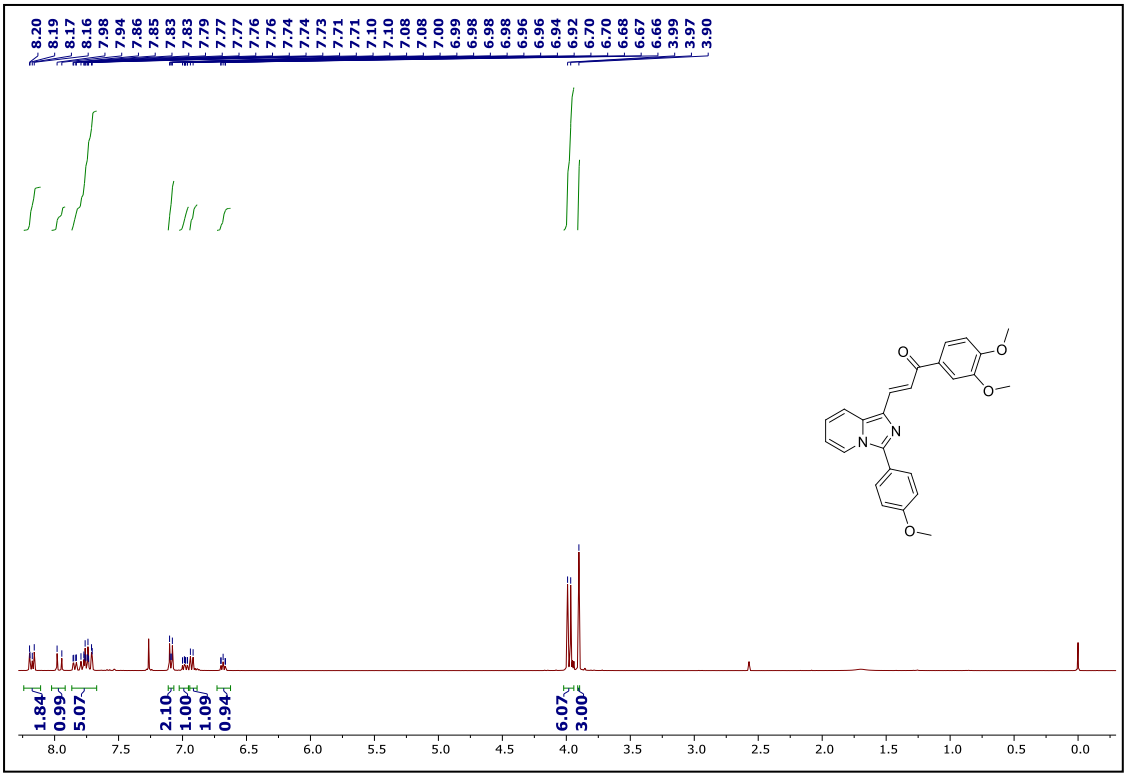


Figure S13. ^{1}H NMR spectrum of **7e** (400 MHz, $CDCl_3$).

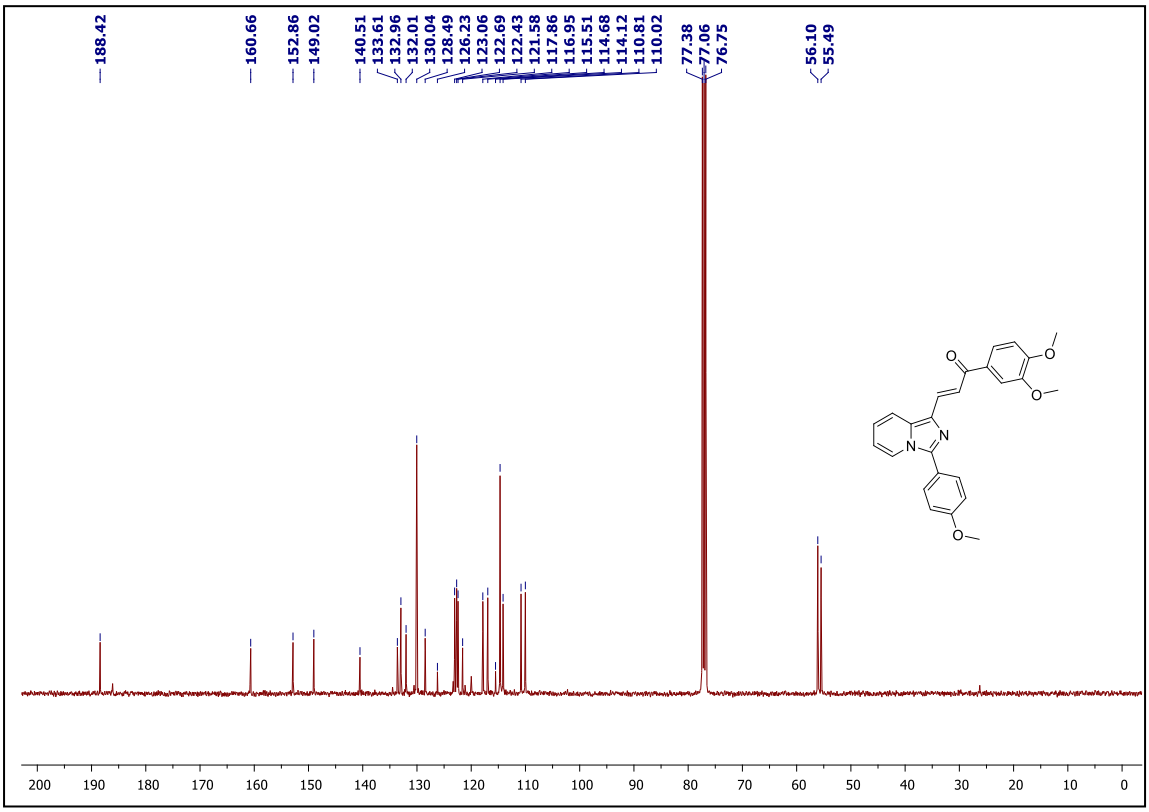


Figure S14. ^{13}C NMR spectrum of **7e** (100 MHz, $CDCl_3$).

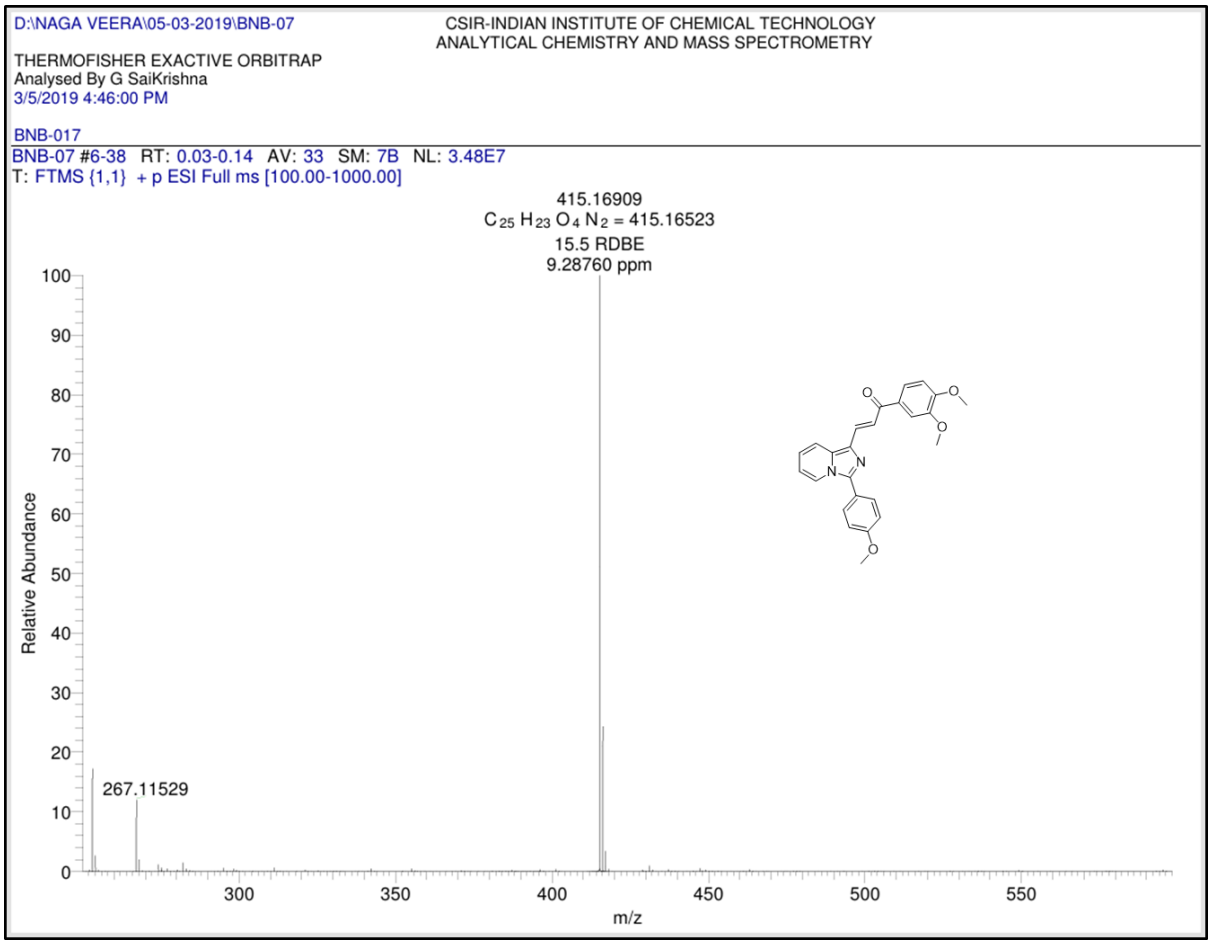


Figure S15. HRMS spectrum of **7e**

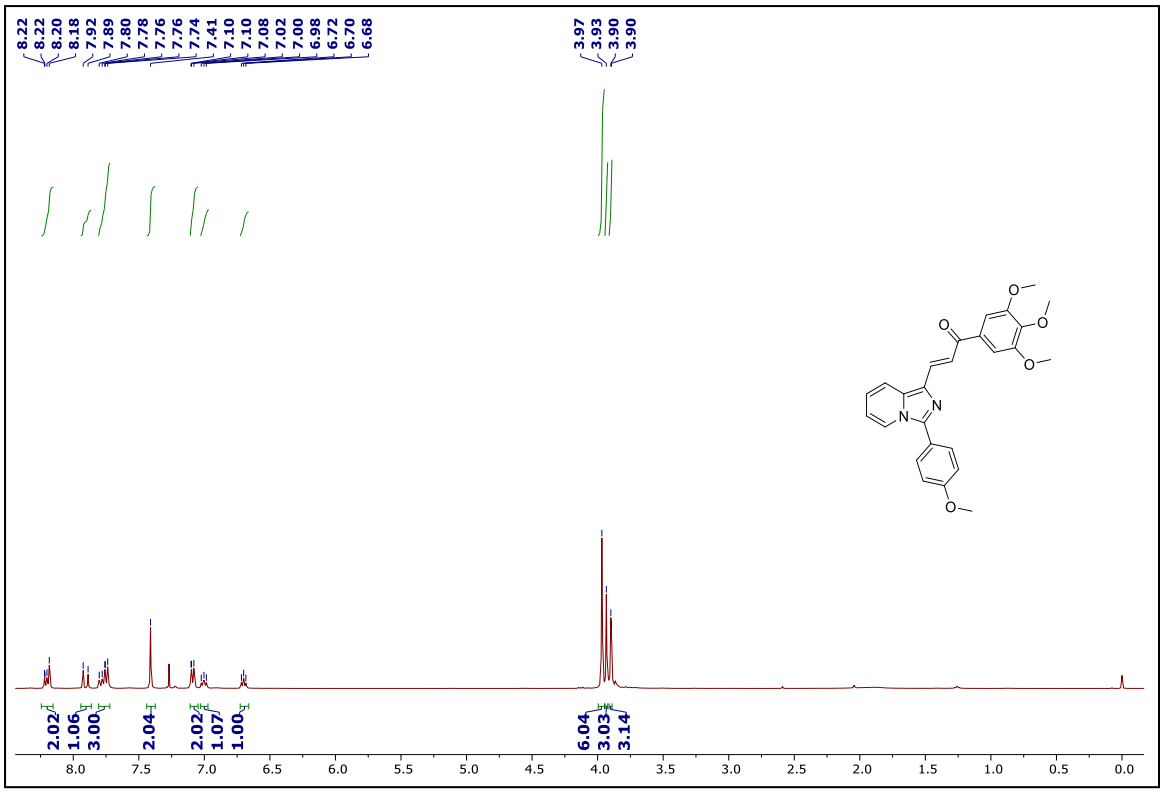


Figure S16. ^{1}H NMR spectrumof **7f**(400 MHz, $CDCl_3$).

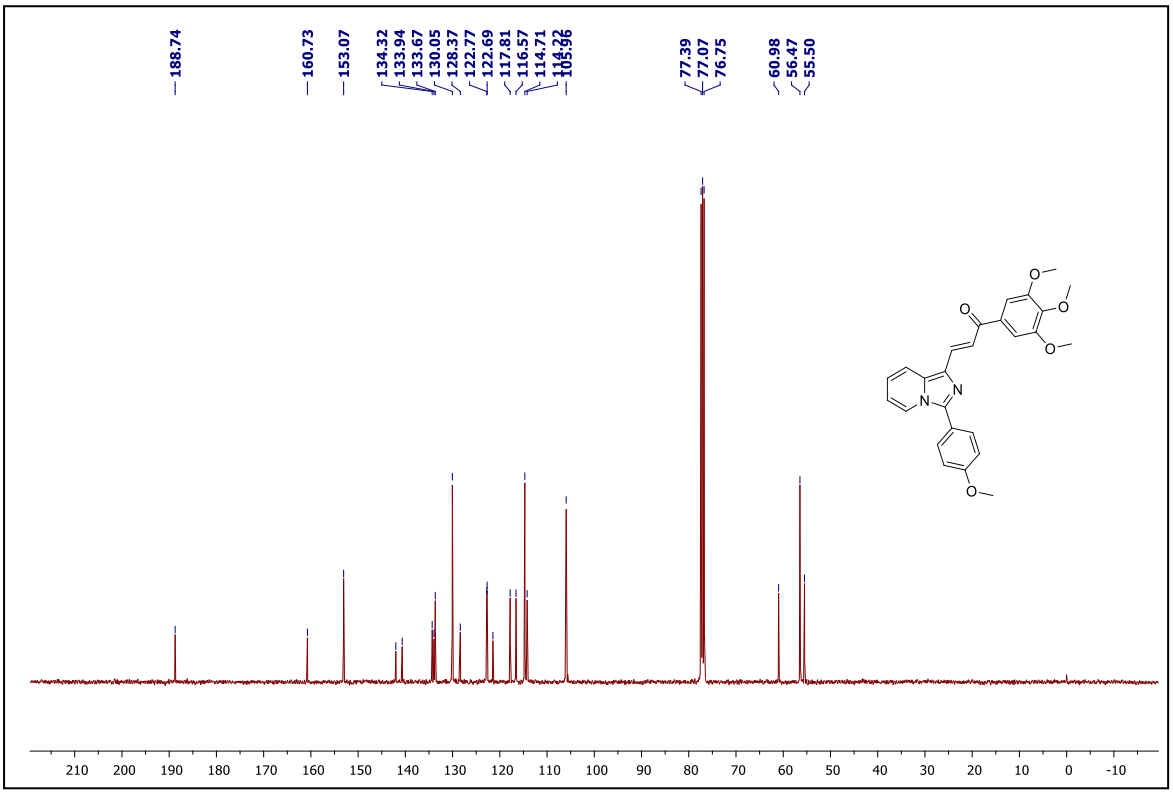


Figure S17.^{13}C NMR spectrum of **7f** (100 MHz, $CDCl_3$

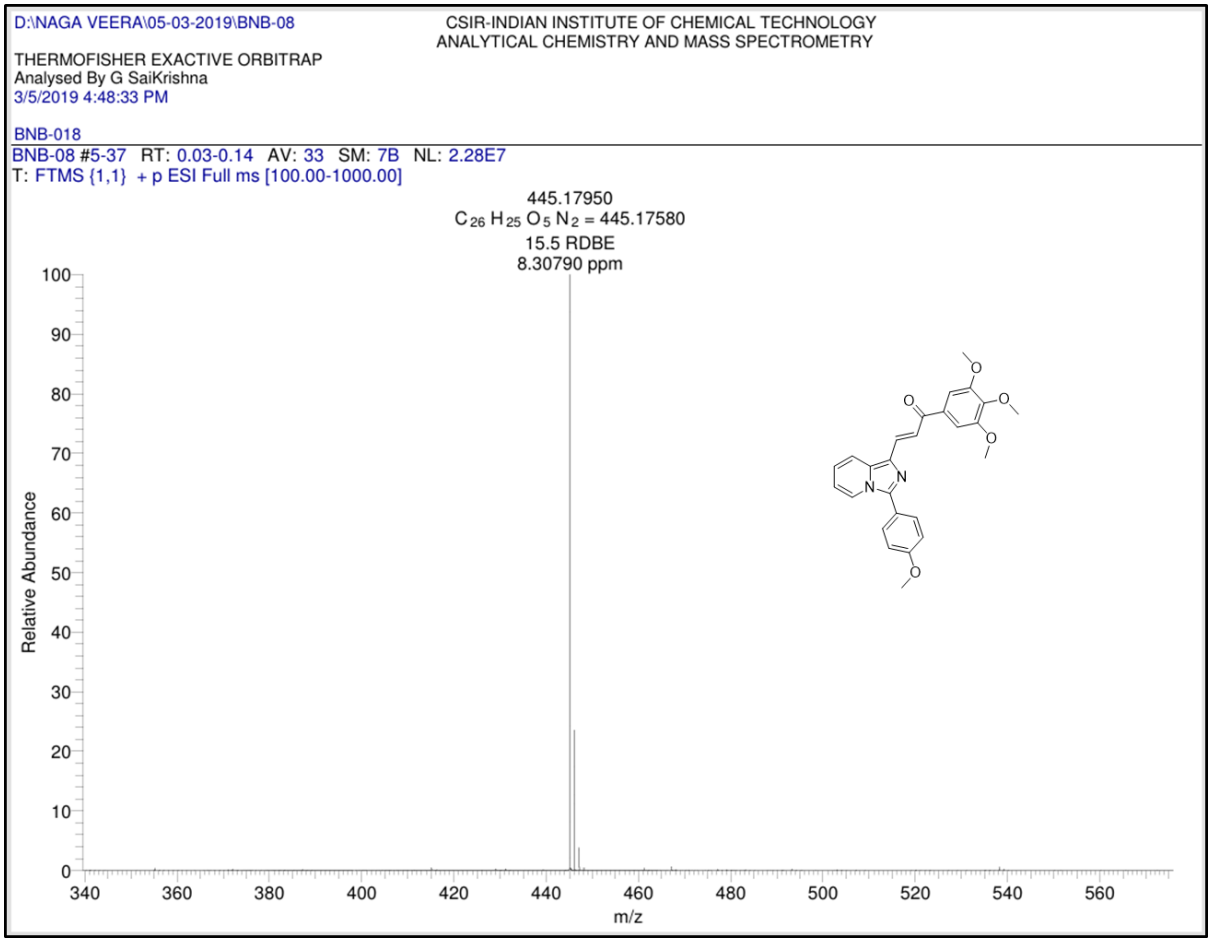


Figure S18. HRMS spectrum of **7f**

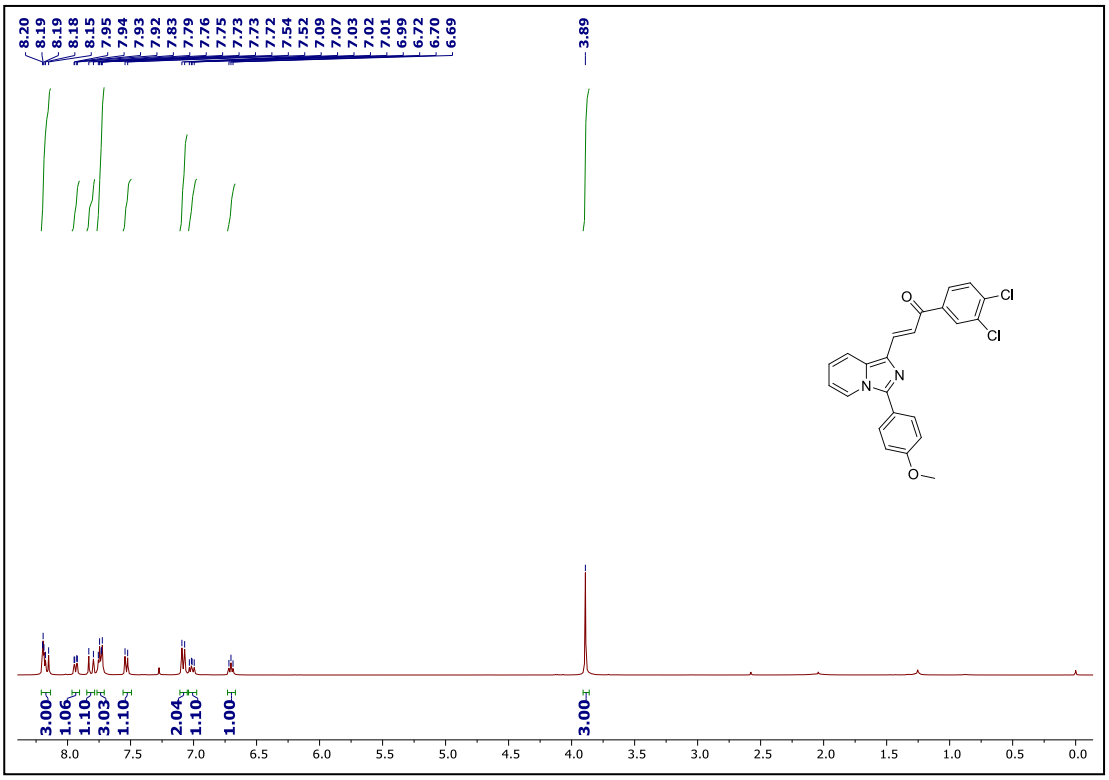


Figure S19.[1]H NMR spectrum of **7g** (500 MHz, $CDCl_3$).

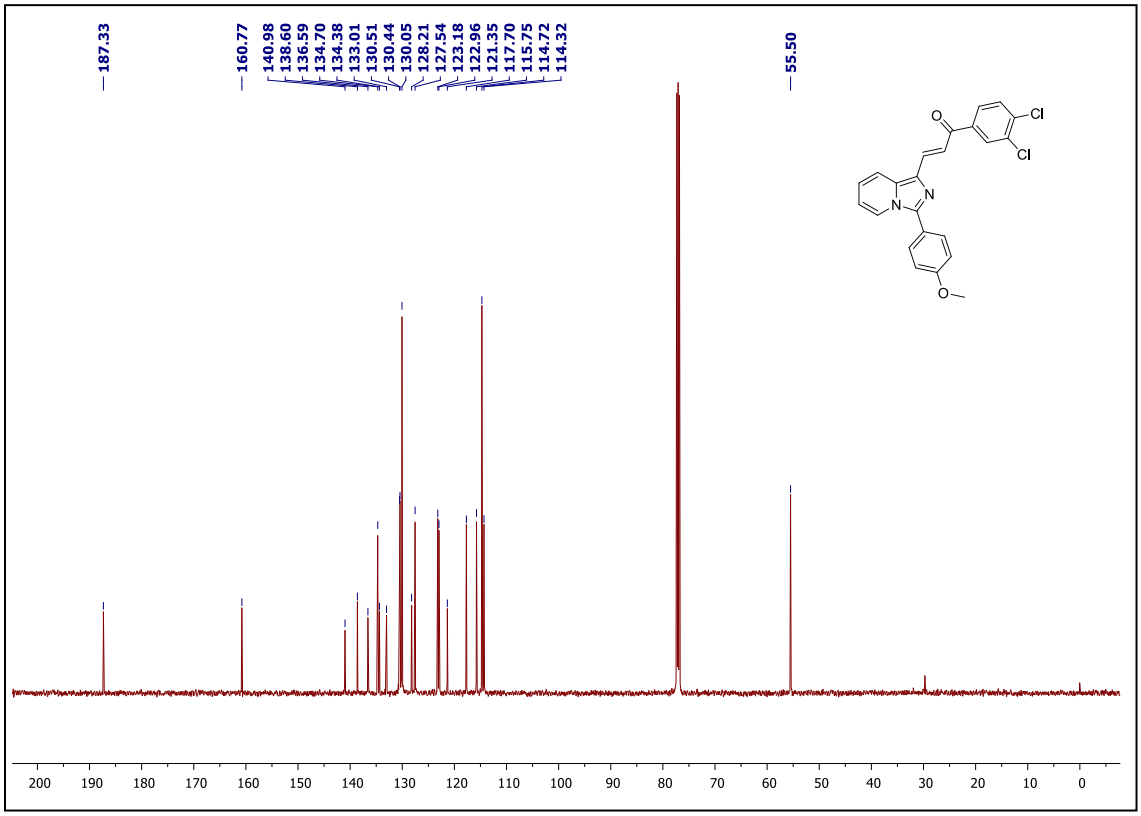
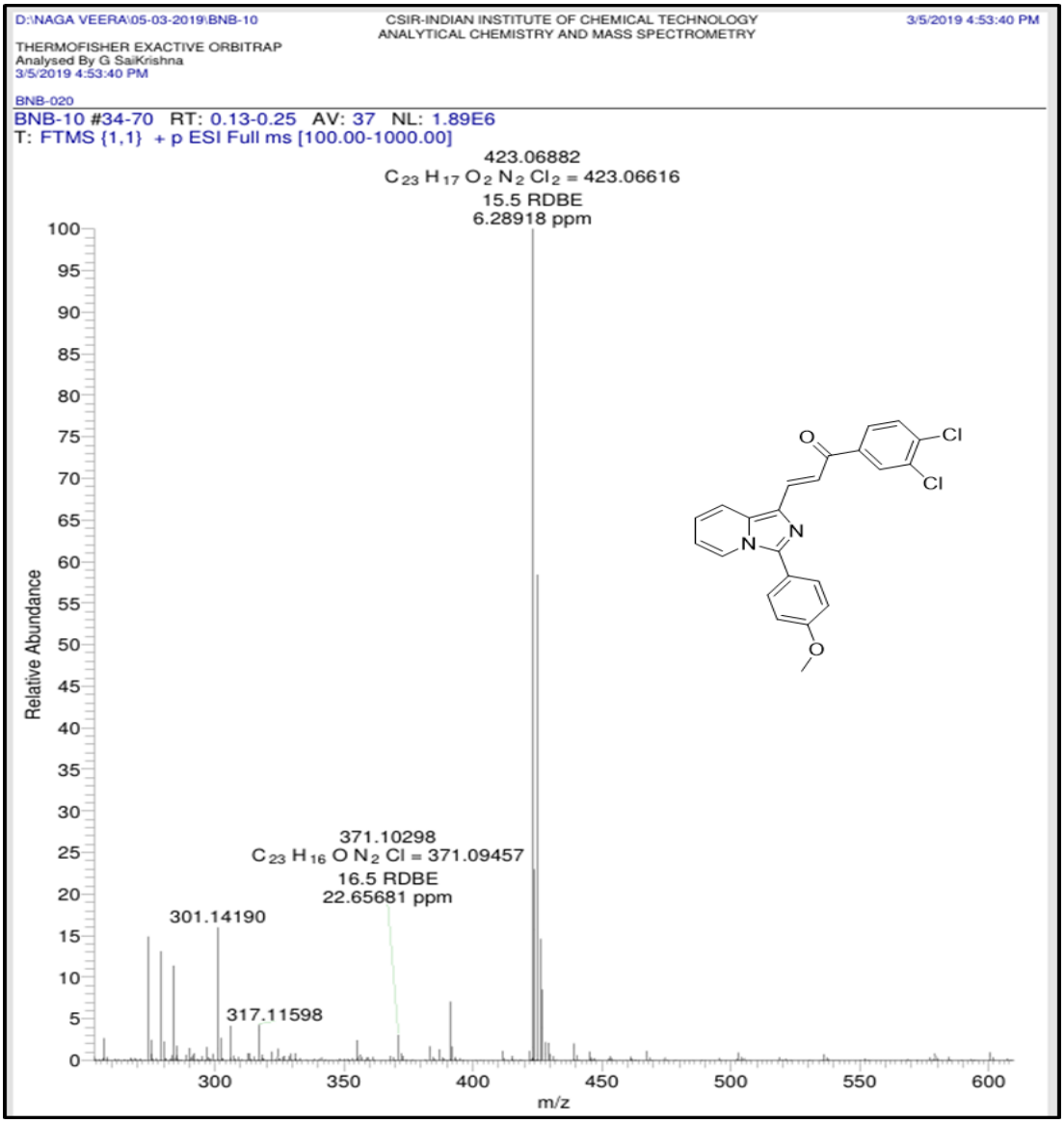


Figure S20.[13]C NMR spectrum of **7g** (100 MHz, $CDCl_3$)



FigureS21. HRMS spectrum of **7g**

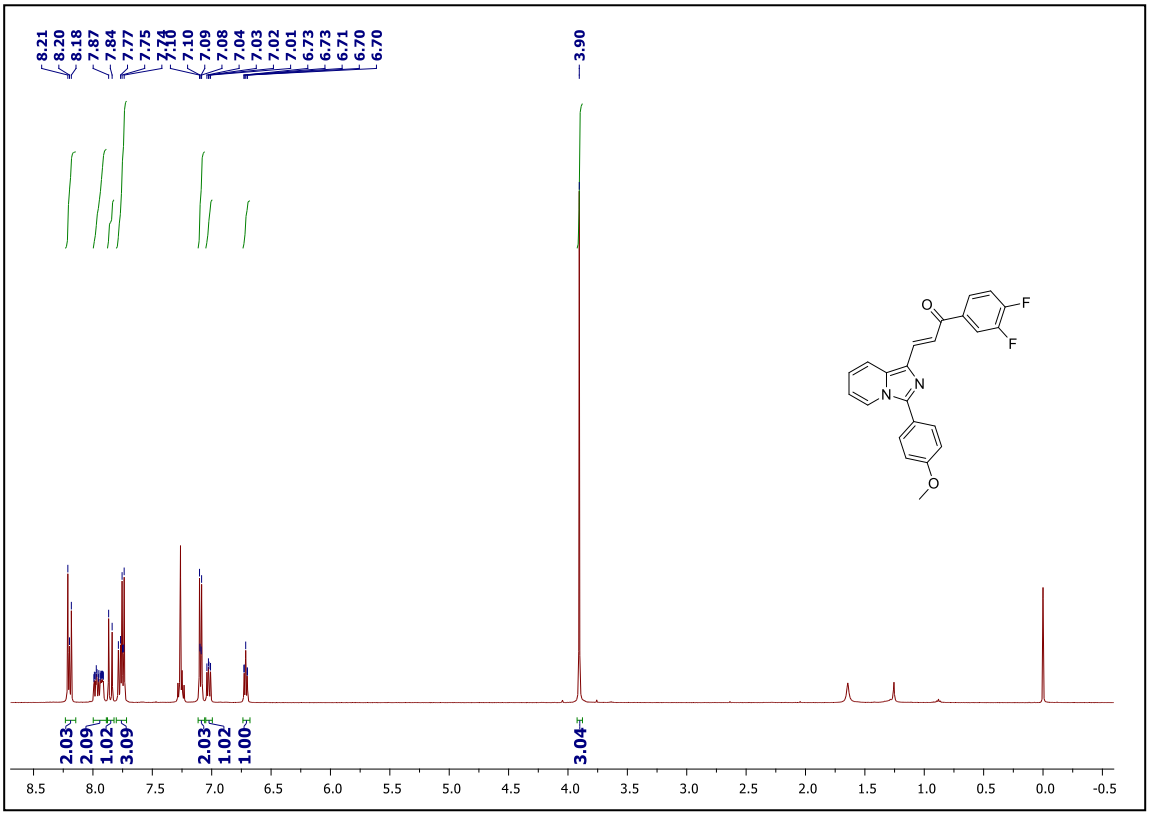


Figure S22.[1]H NMR spectrum of **7h** (400 MHz, $CDCl_3$**)**

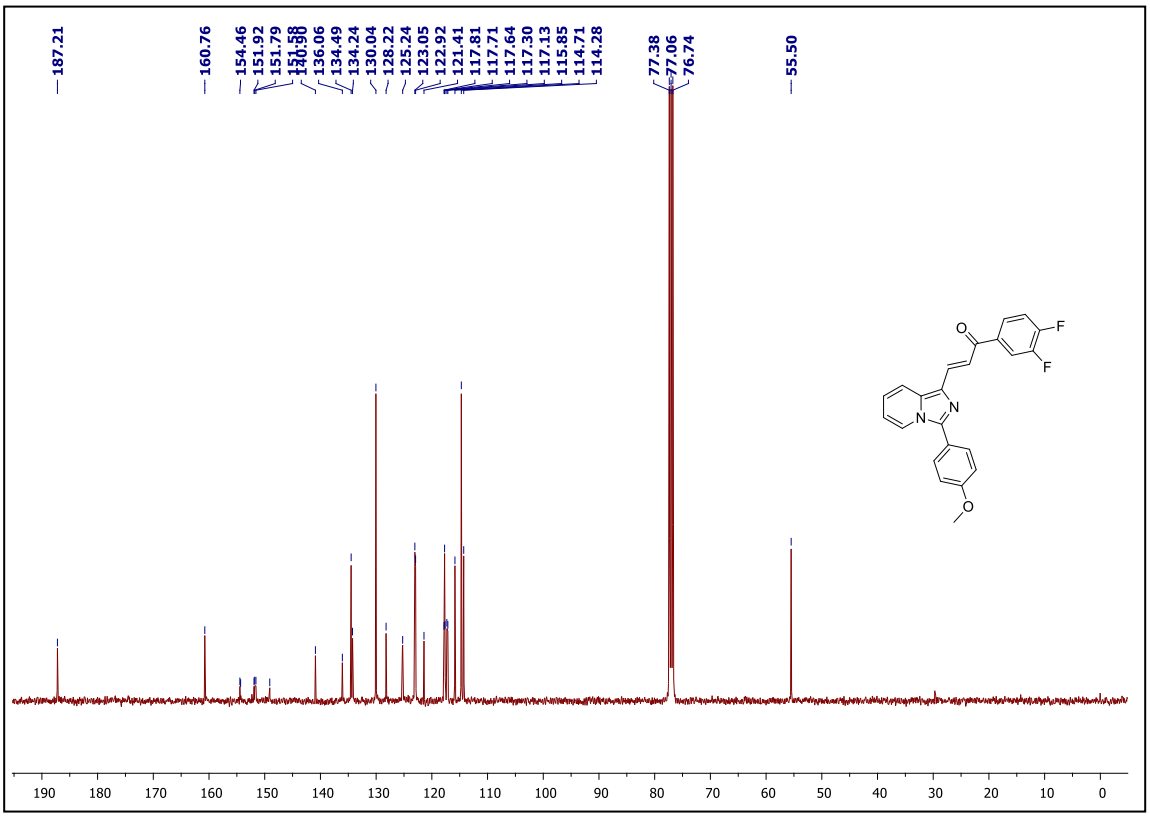


Figure S23.[13]C NMR spectrum of **7h** (100 MHz, $CDCl_3$)

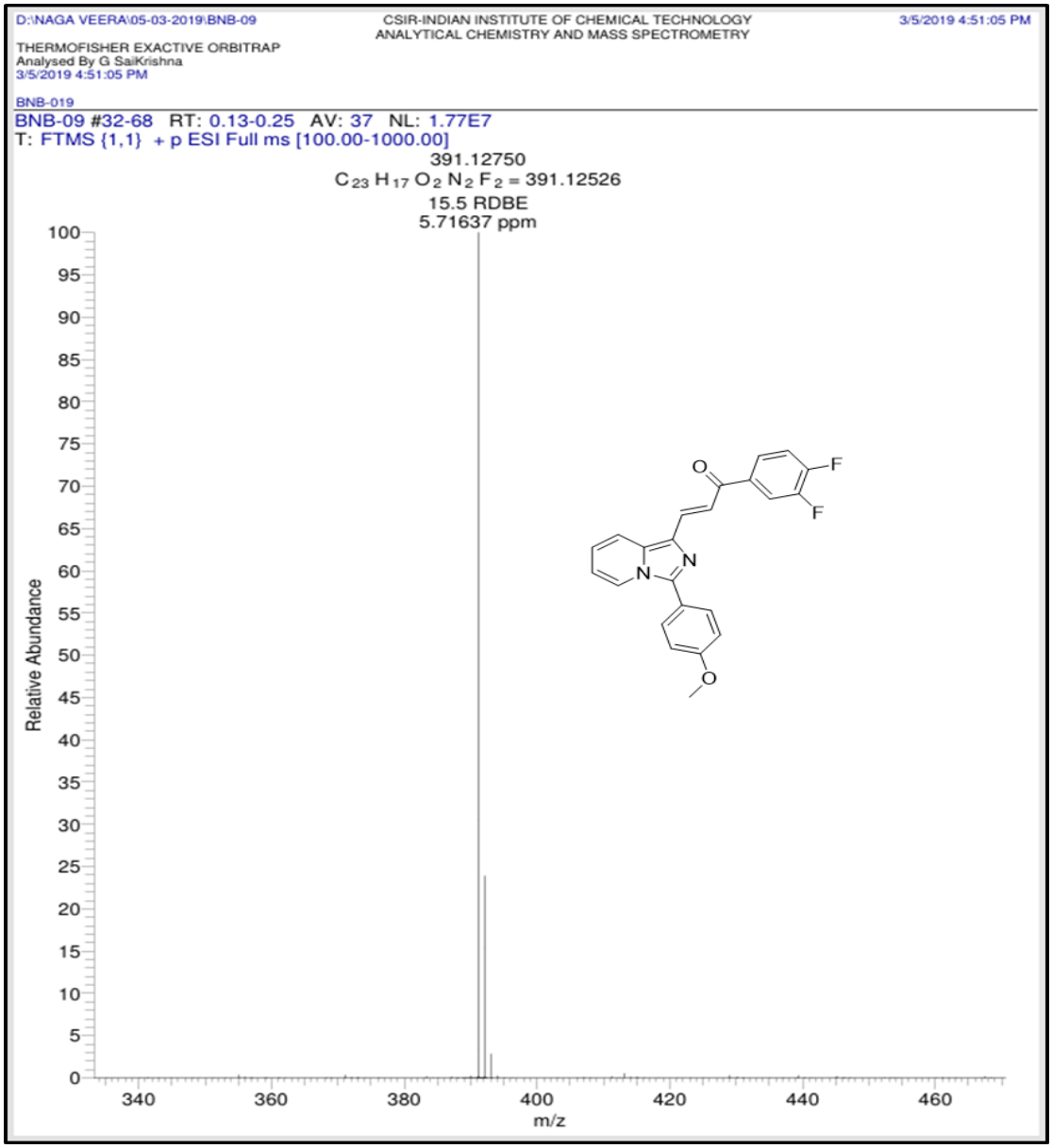


Figure S24. HRMS spectrum of **7h**

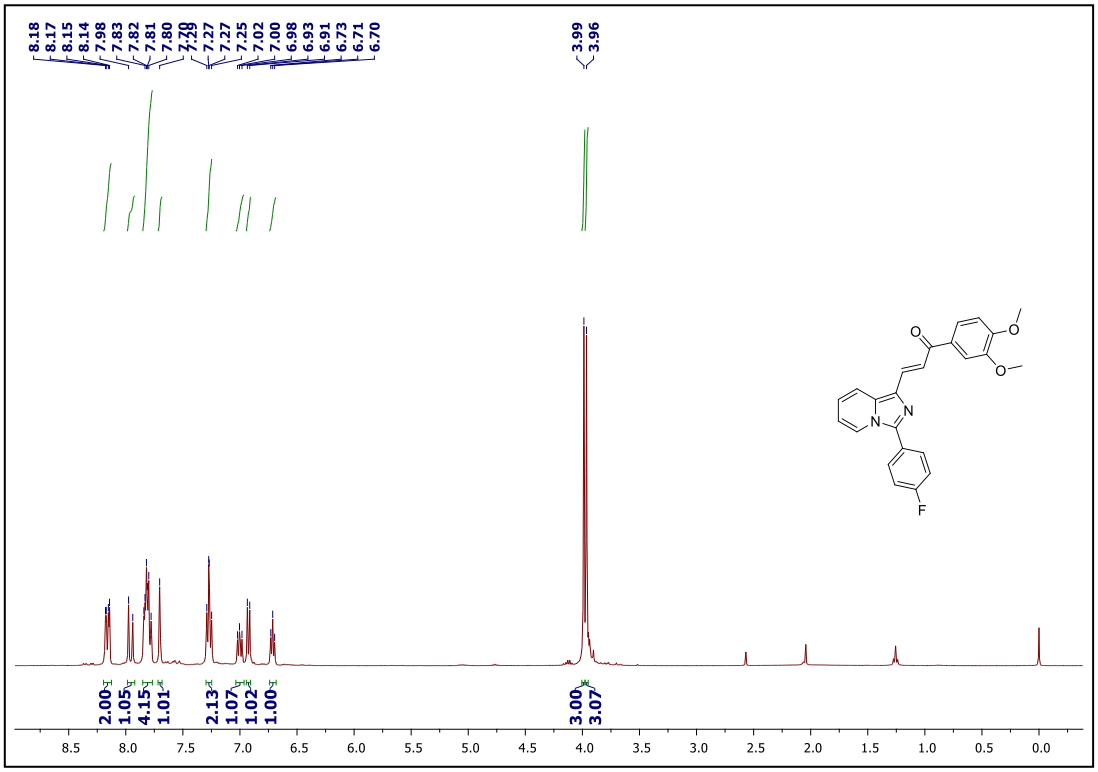


Figure S25. ^{1}H NMR spectrum of **7i** (400 MHz, $CDCl_3$).

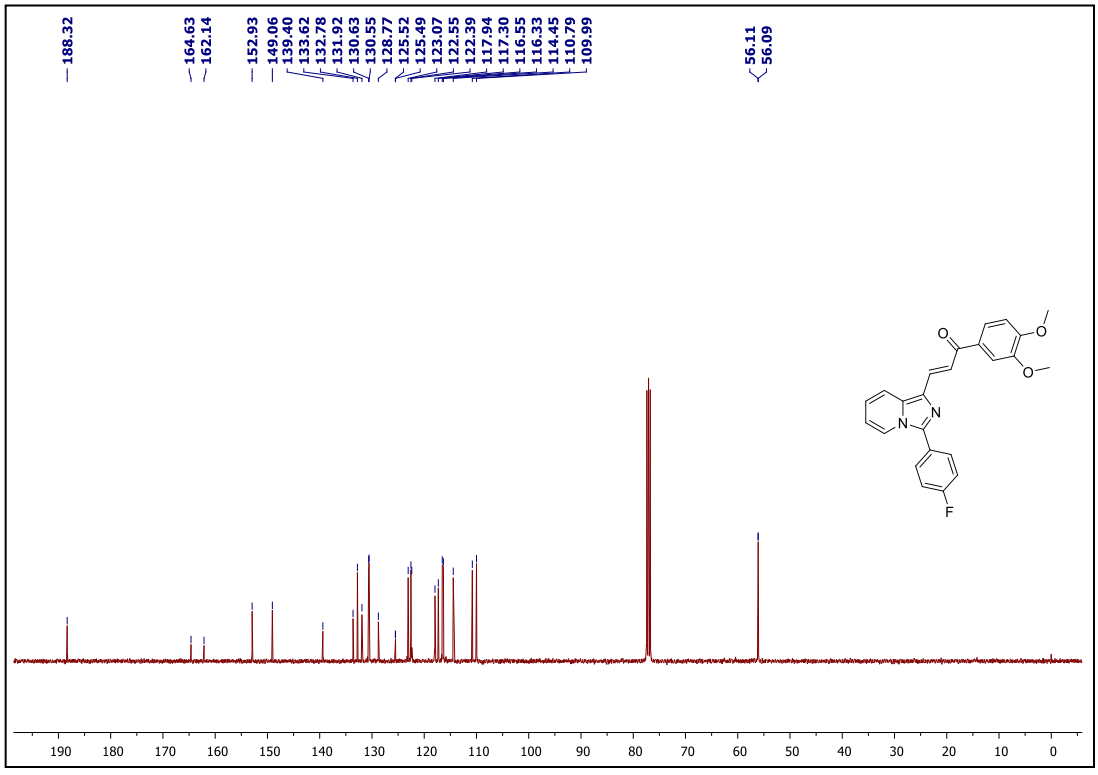


Figure S26. ^{13}C NMR spectrum of **7i** (100 MHz, $CDCl_3$).

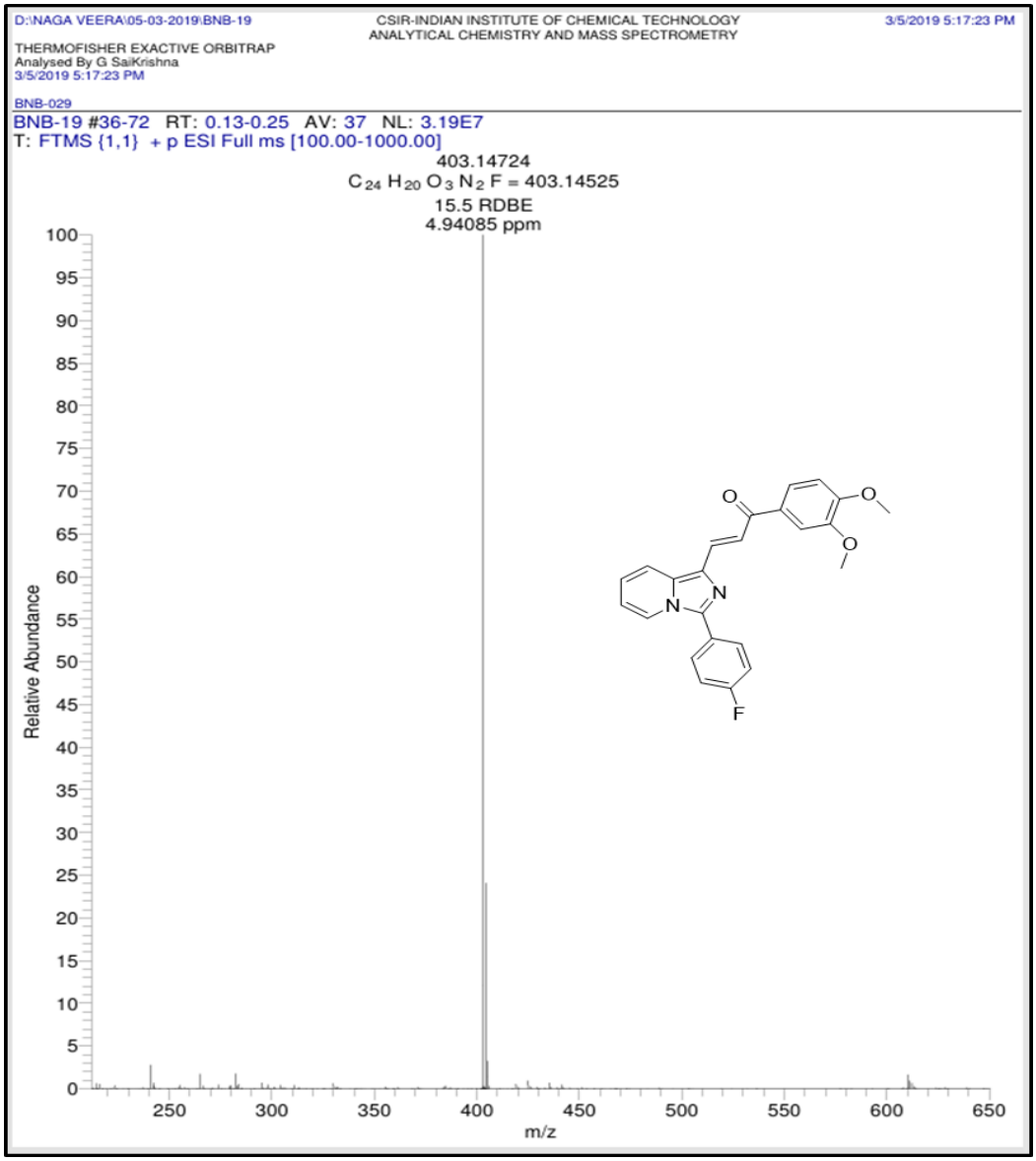


Figure S27. HRMS spectrum of **7i**

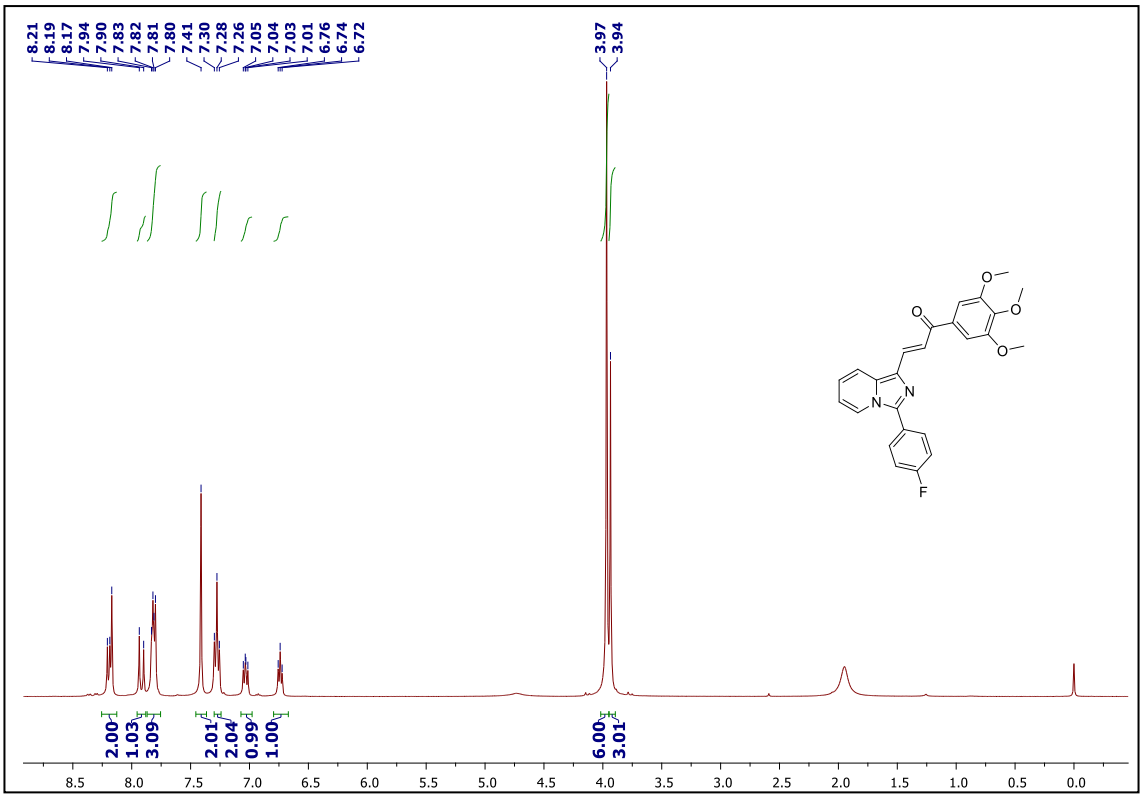


Figure S28. ^{1}H NMR spectrum of **7j** (400 MHz, $CDCl_3$).

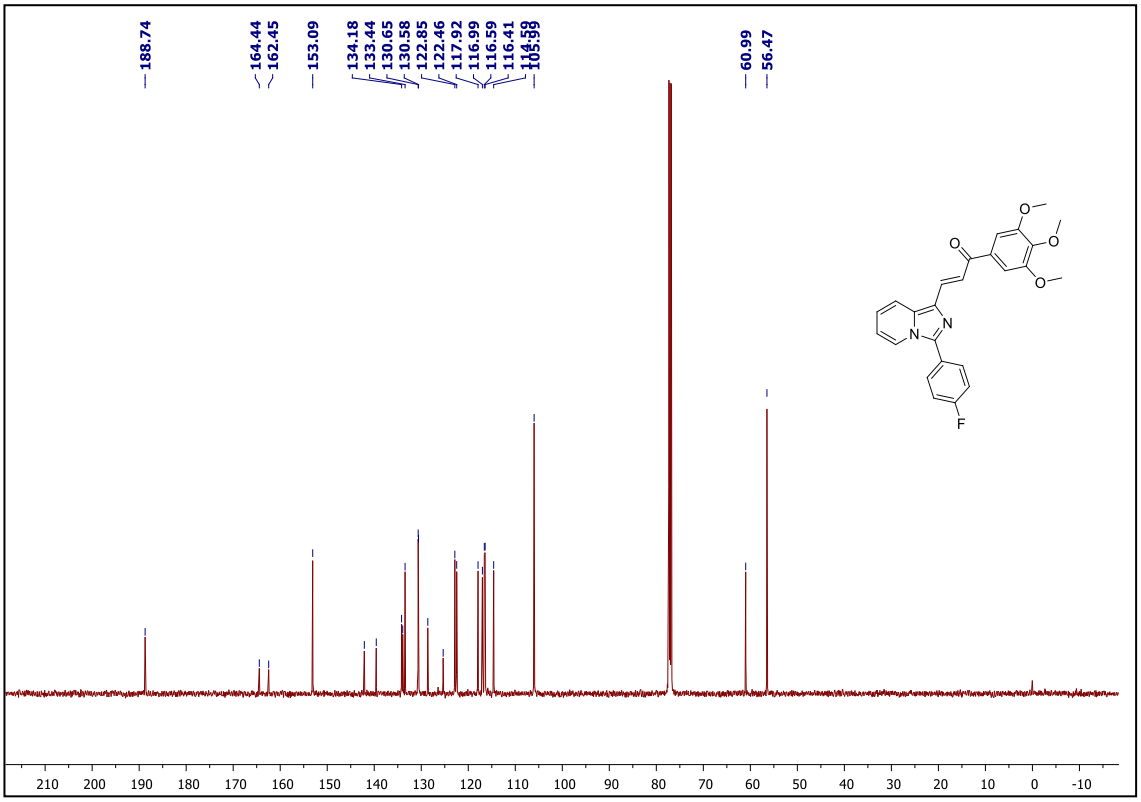


Figure S29. ^{13}C NMR spectrum of **7j** (100 MHz, $CDCl_3$).

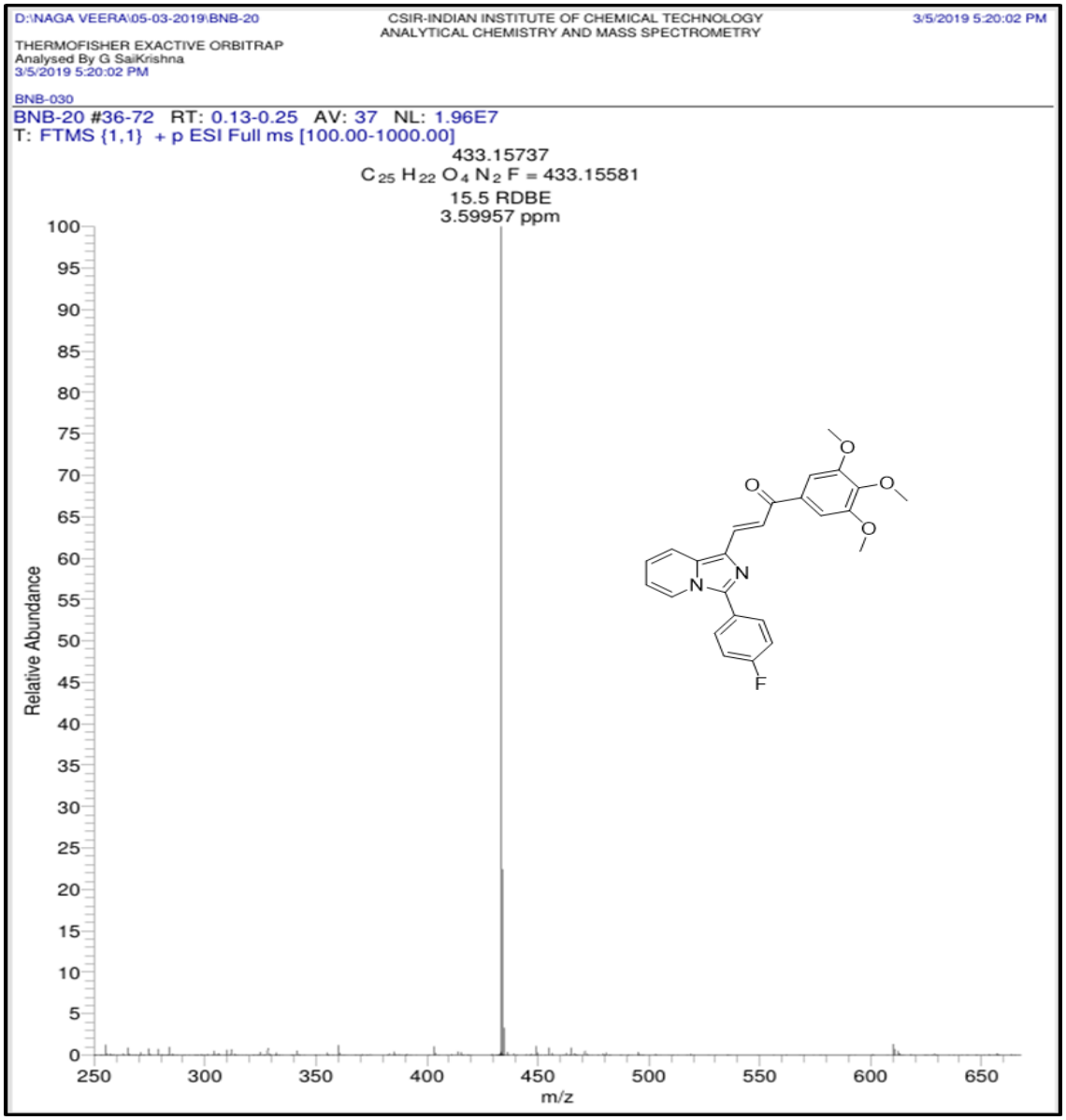


Figure S30. HRMS spectrum of **7j**

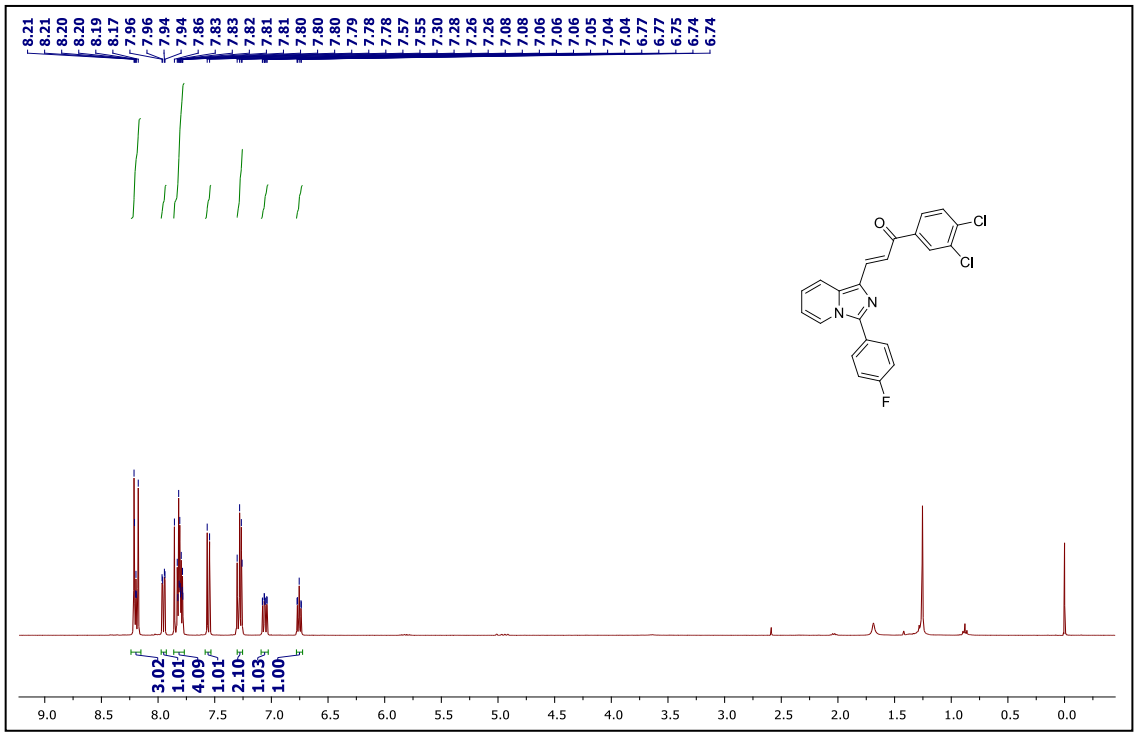


Figure S31.[1]HNMR spectrum of **7k** (400 MHz, $CDCl_3$).

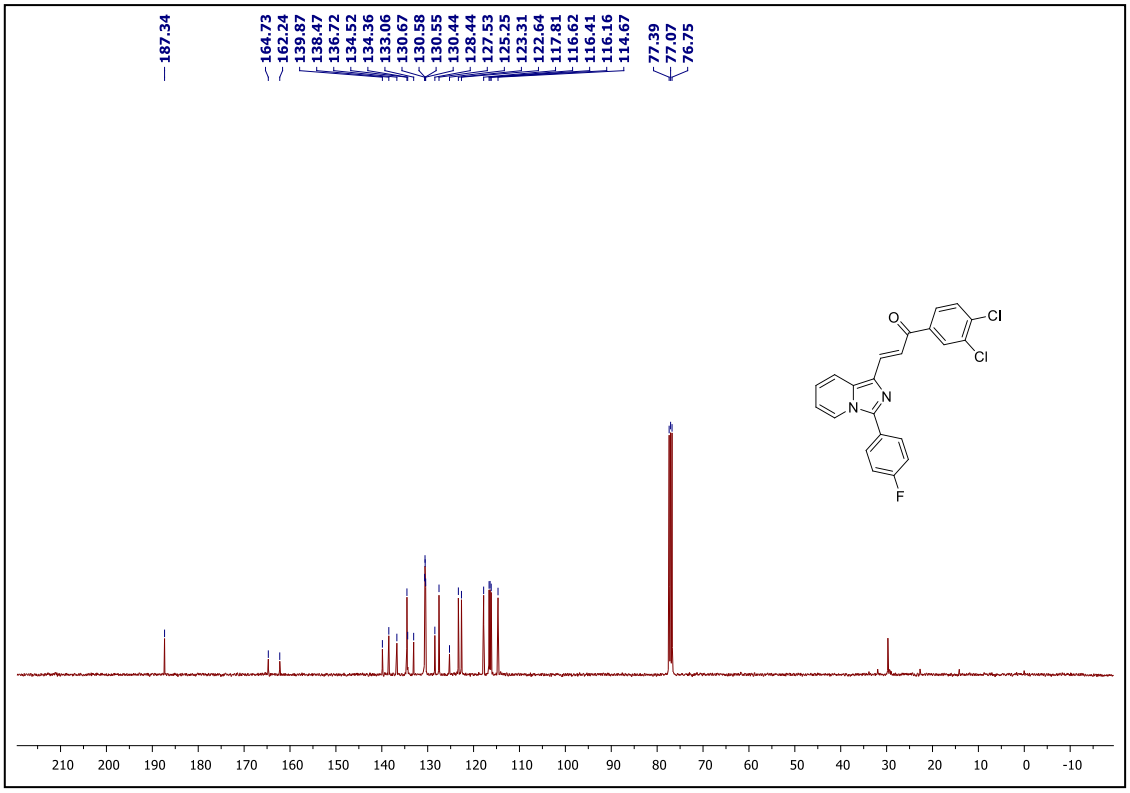


Figure S32.[13]C NMR spectrum of **7k** (100 MHz, $CDCl_3$).

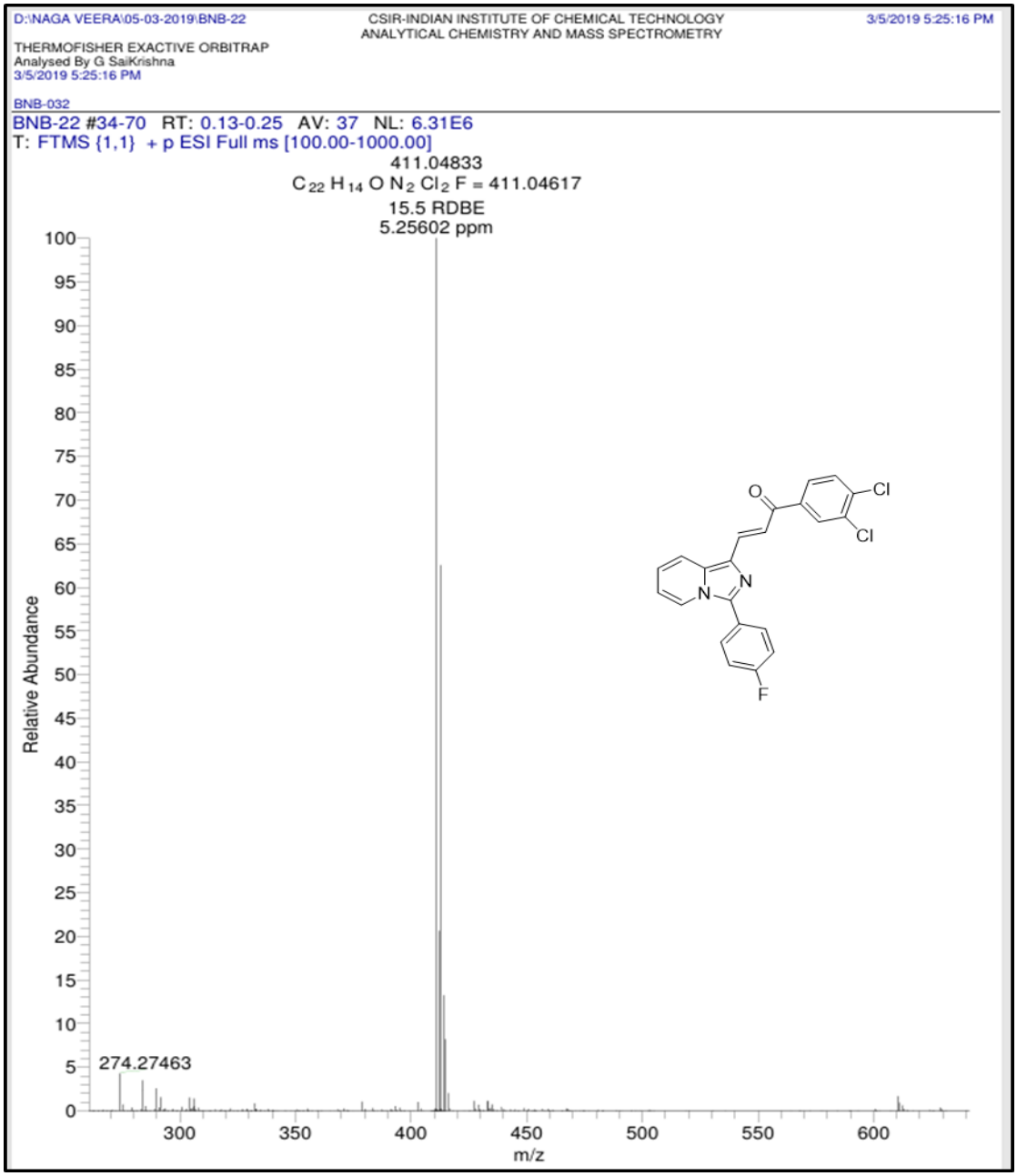


Figure S33. HRMS spectrum of **7k**

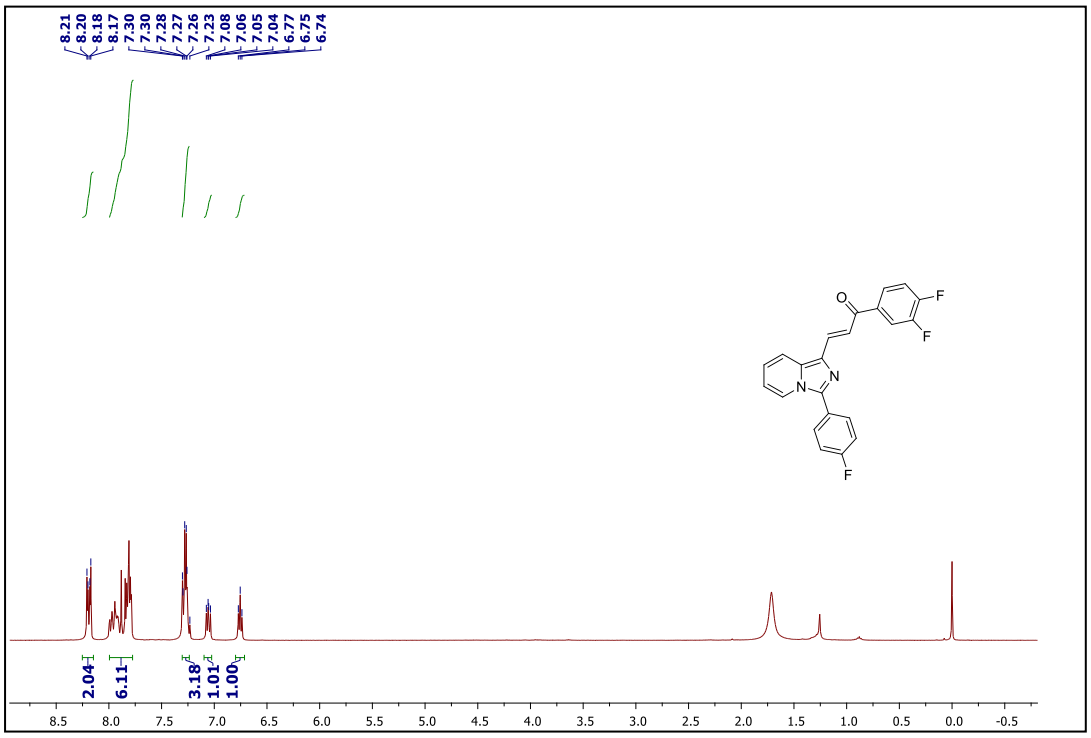


Figure S34. ^{1}H NMR spectrum of **7l** (400 MHz, $CDCl_3$).

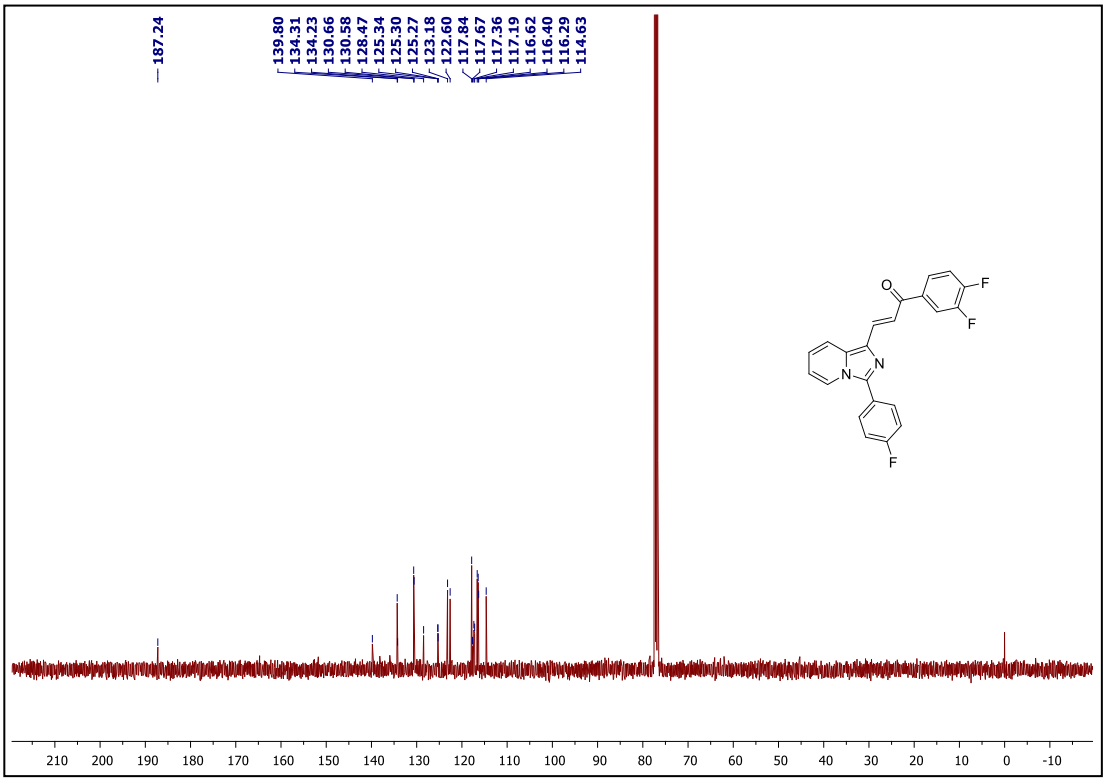


Figure S35. ^{13}C NMR spectrum of **7l** (100 MHz, $CDCl_3$).

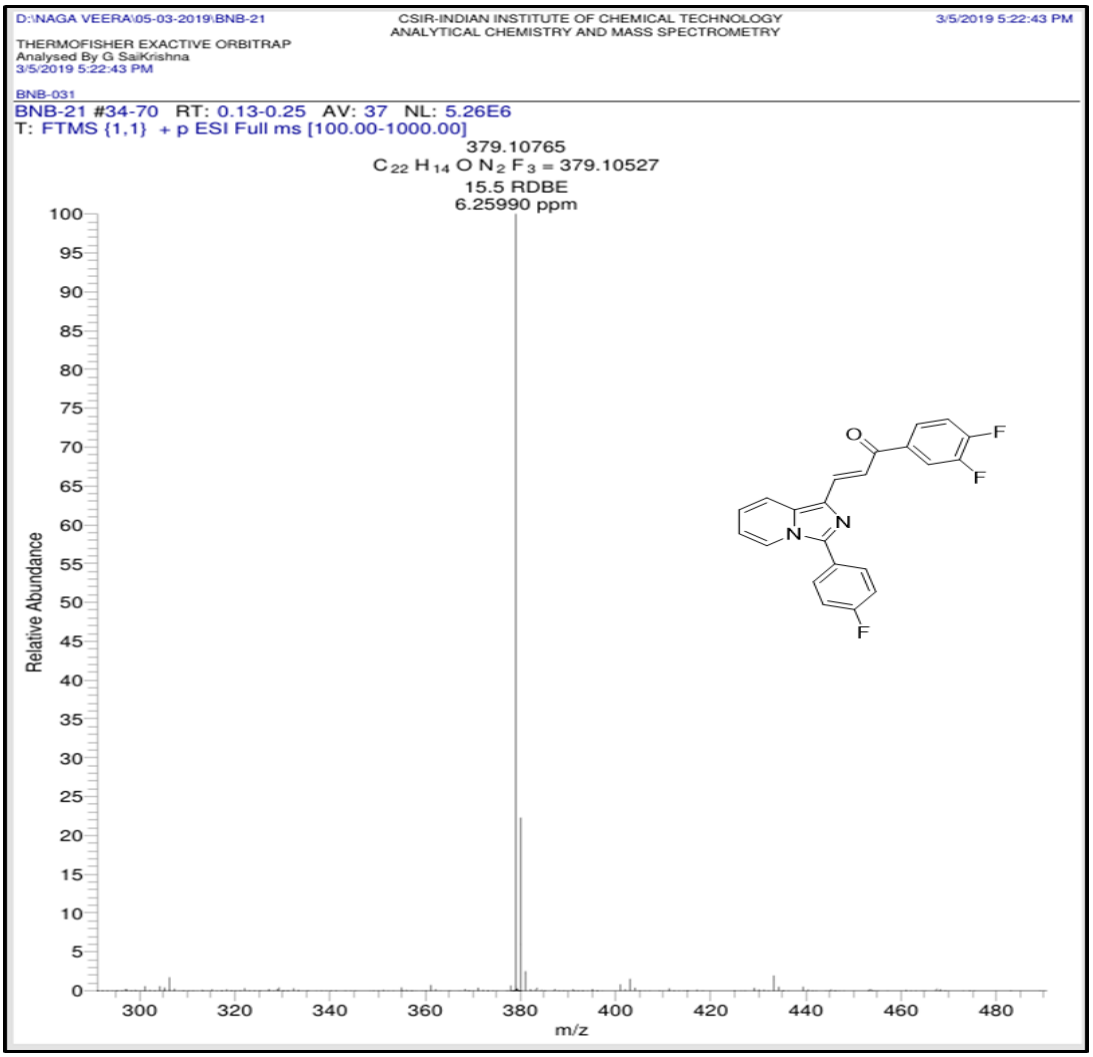


Figure S36. HRMS spectrum of **7l**

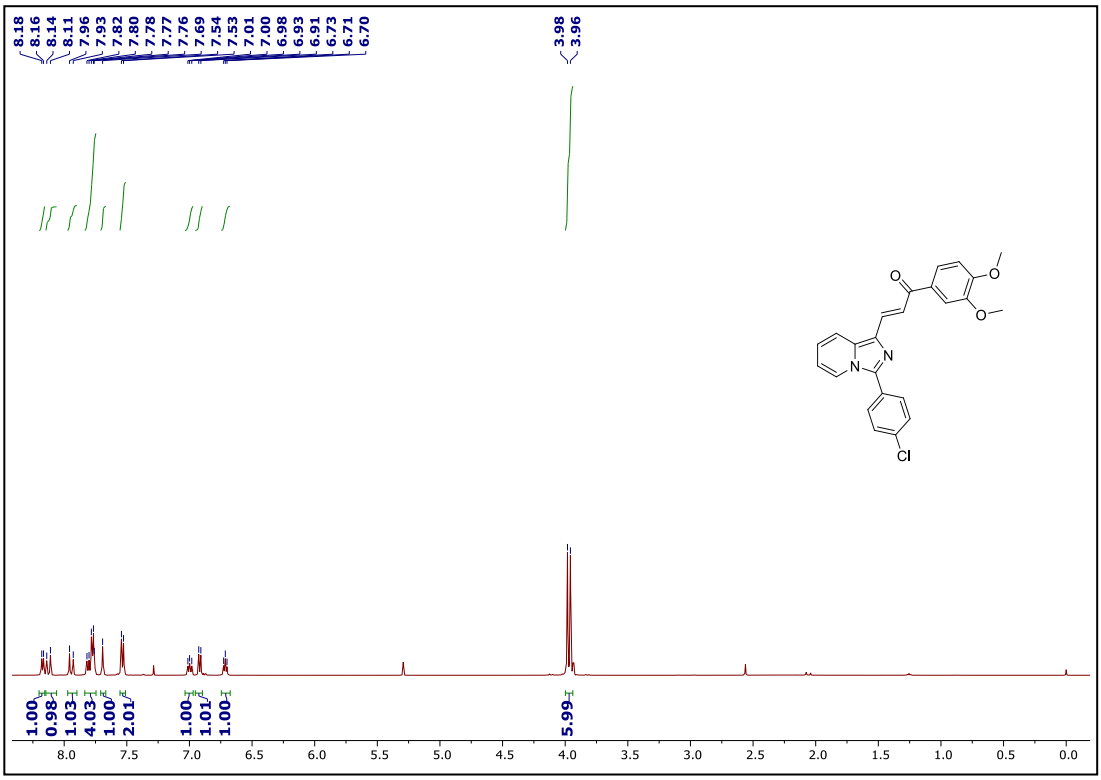


Figure S37. ^{1}H NMR spectrum of **7m** (500 MHz, $CDCl_3$).

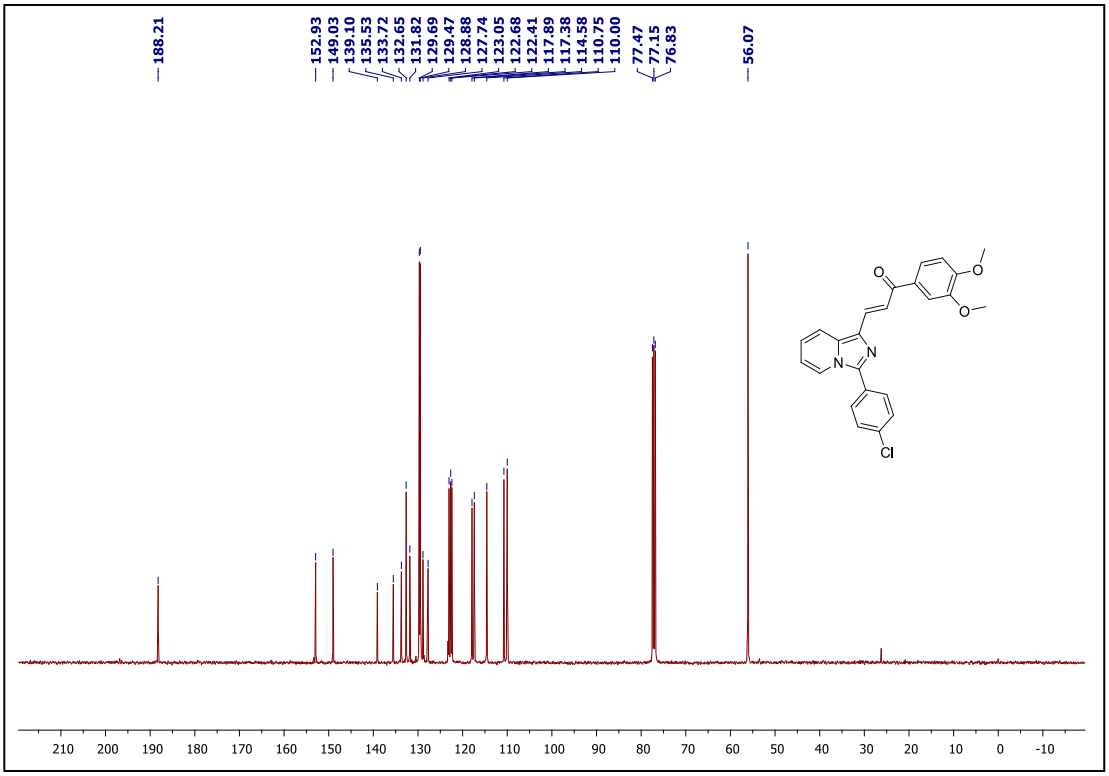


Figure S38. ^{13}C NMR spectrum of **7m** (100 MHz, $CDCl_3$).

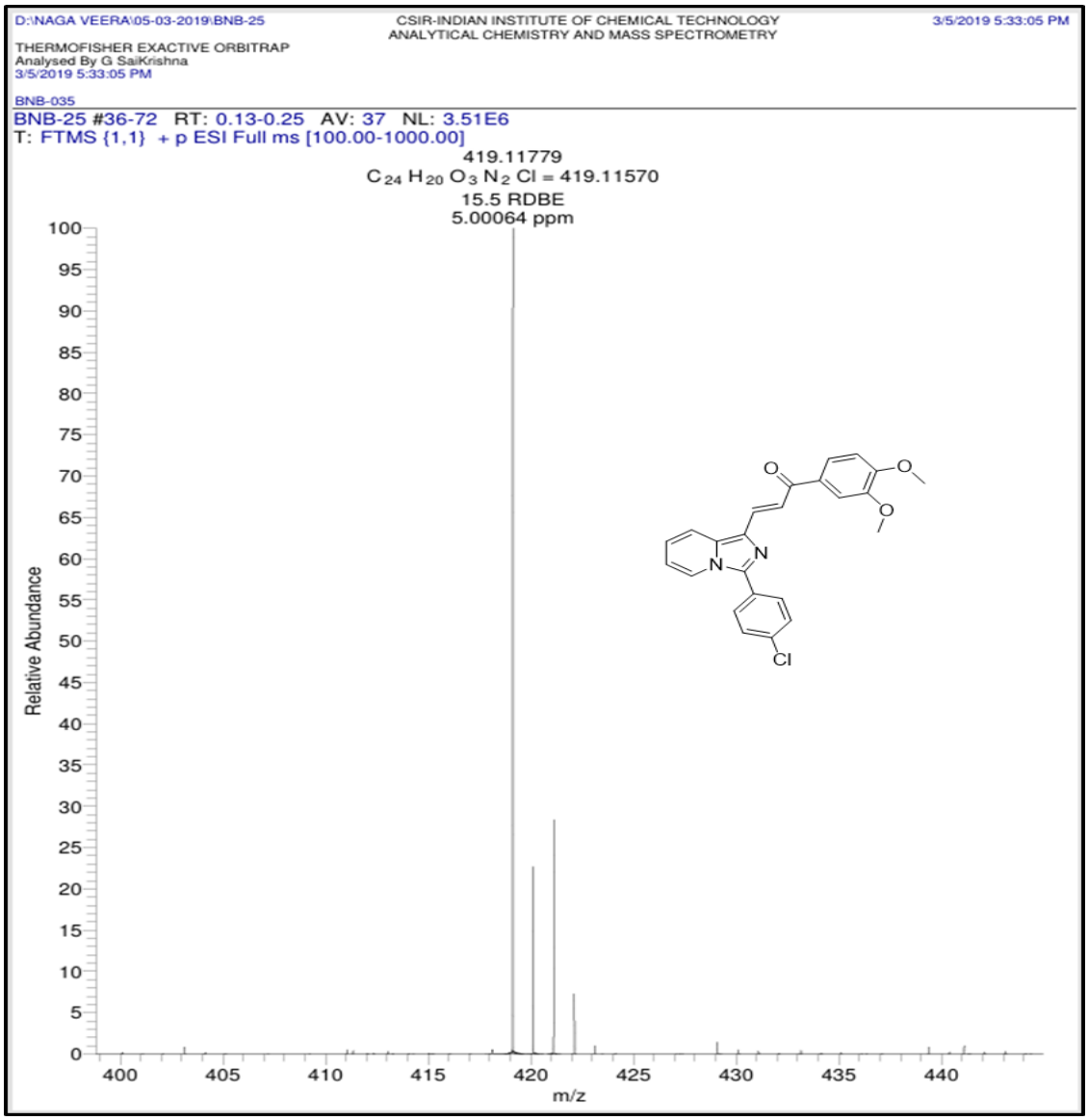


Figure S39. HRMS spectrum of **7m**

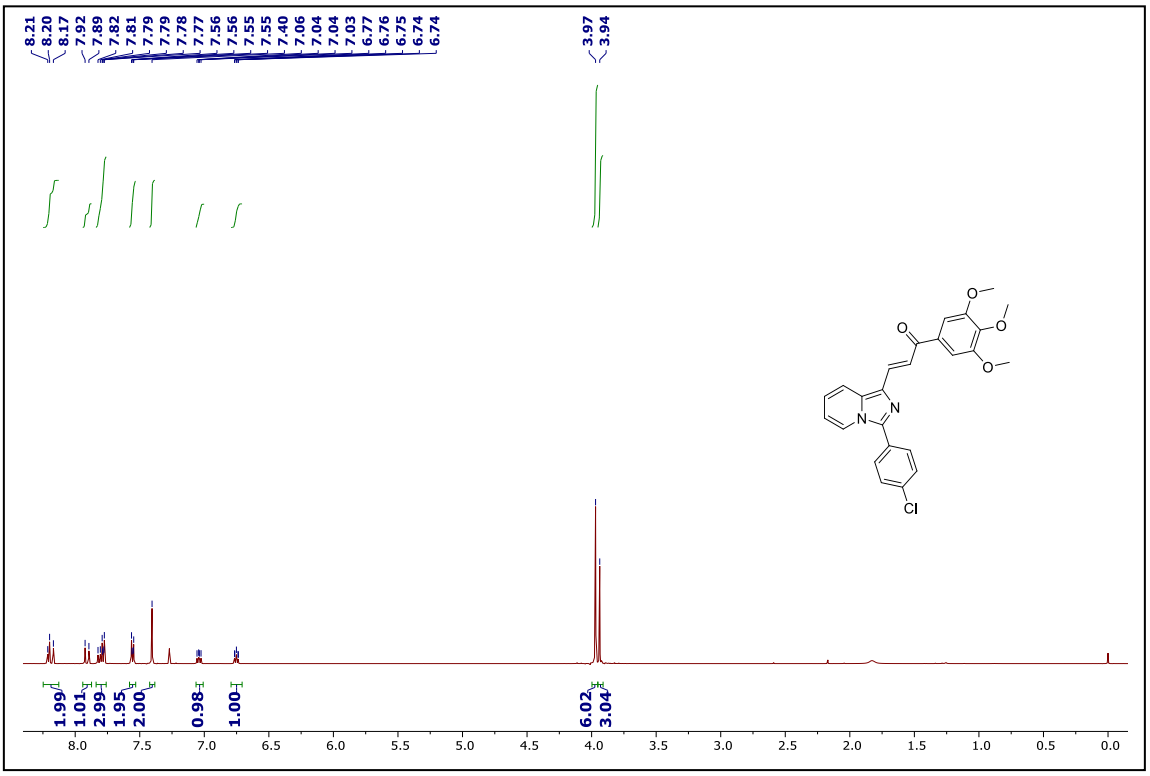


Figure S40. ^{1}H NMR spectrum of **7n** (500 MHz, $CDCl_3$).

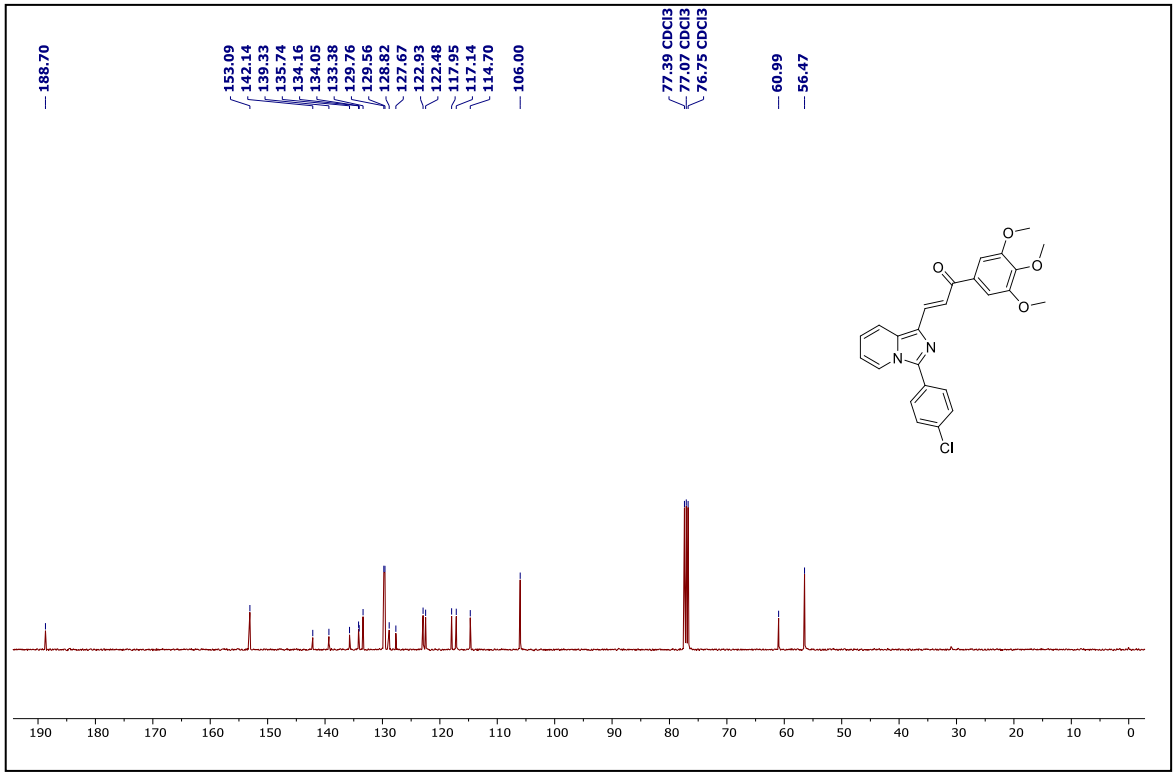


Figure S41. ^{13}C NMR spectrum of **7n** (100 MHz, $CDCl_3$).

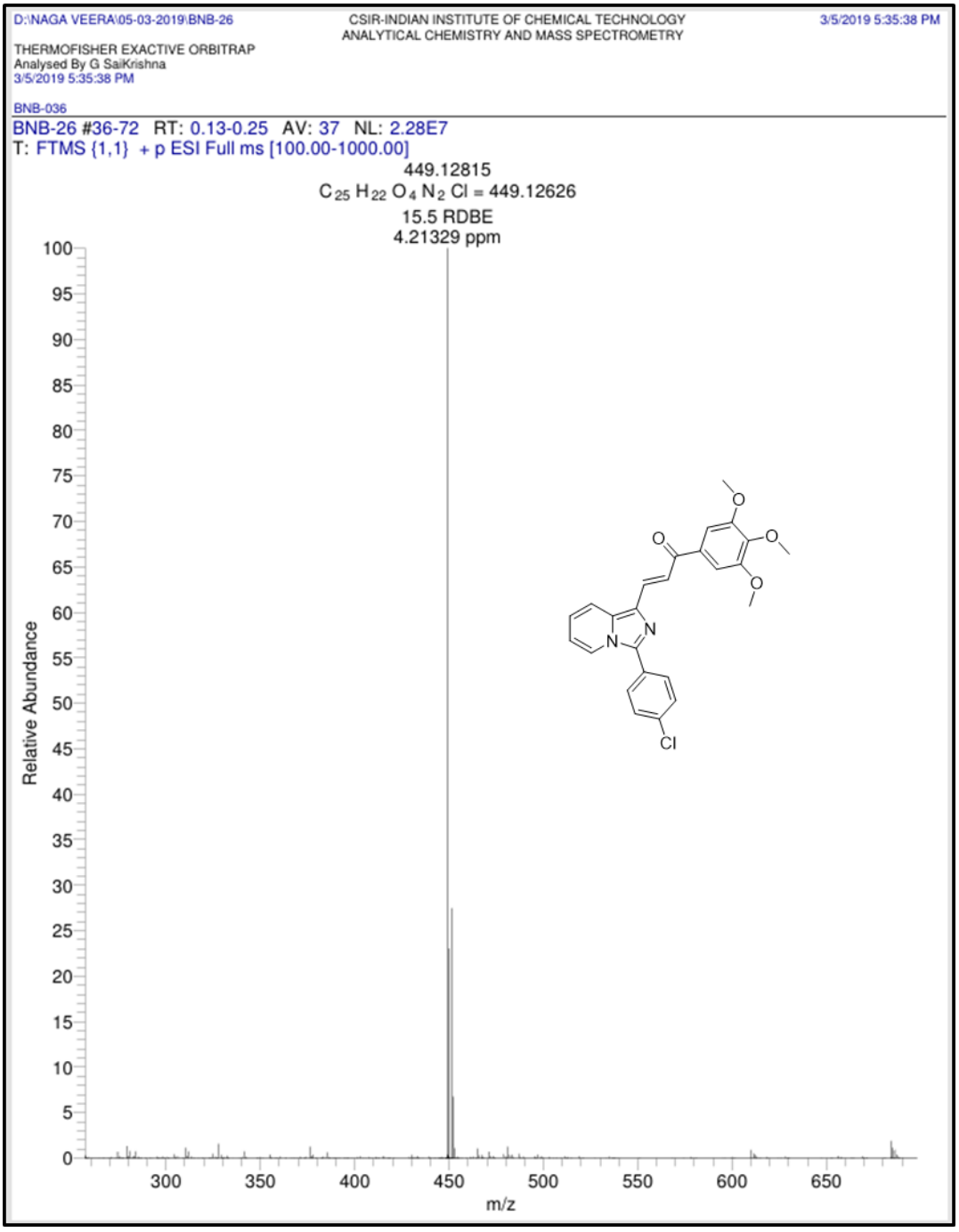


Figure S42. HRMS spectrum of **7n**

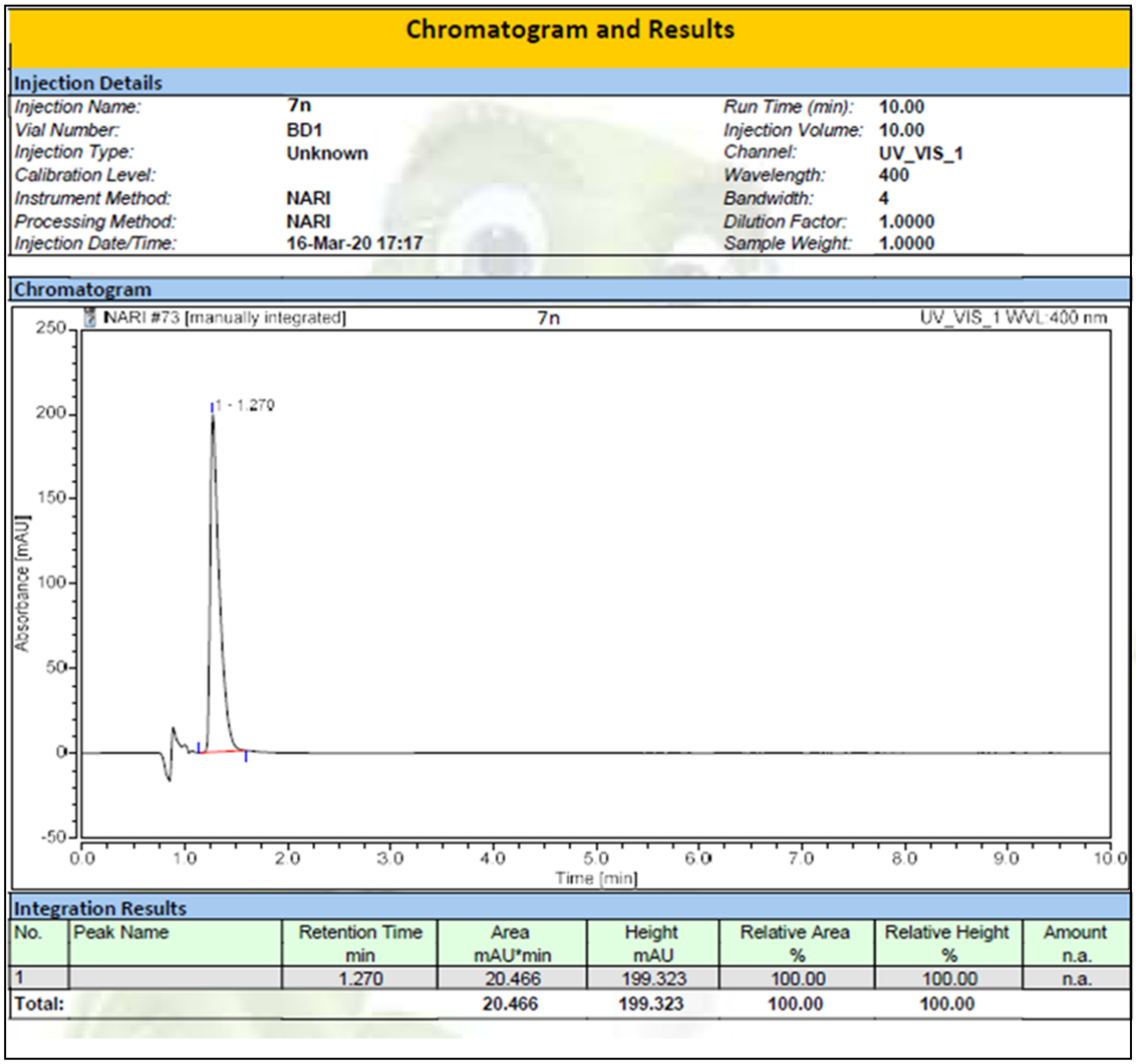


Figure S43. HPLC of **7n** (WVL: 400 nm).

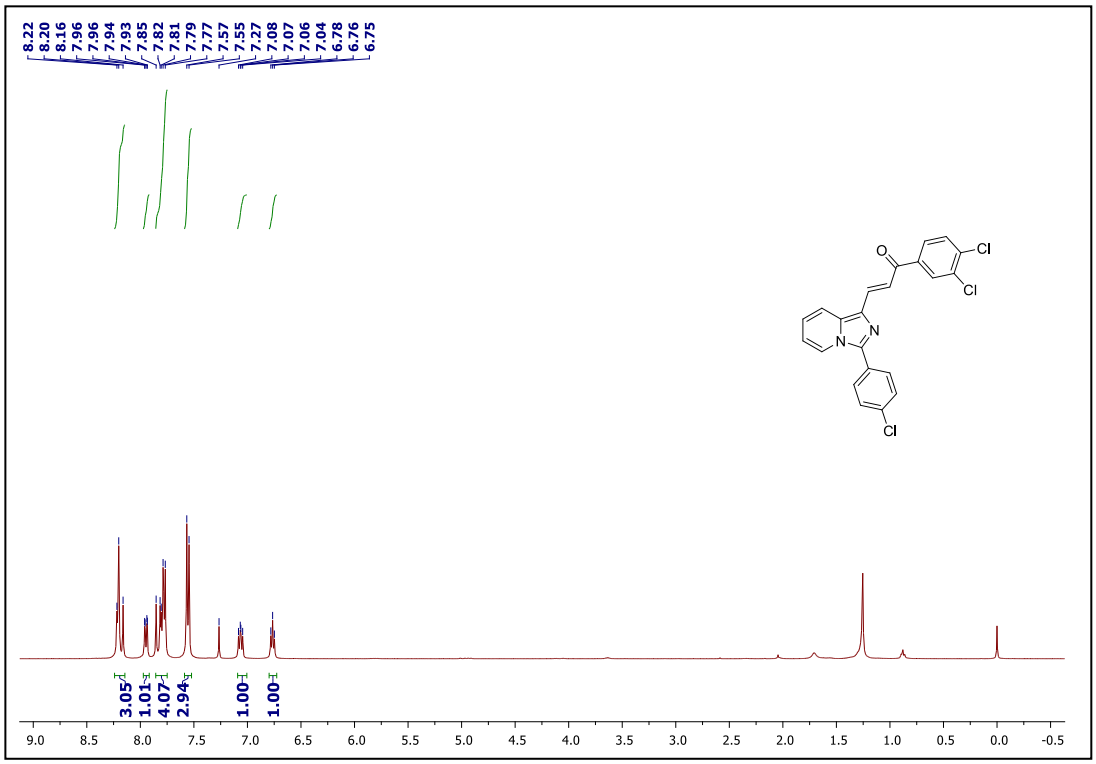


Figure S44. ^{1}H NMR spectrum of **7o** (500 MHz, $CDCl_3$).

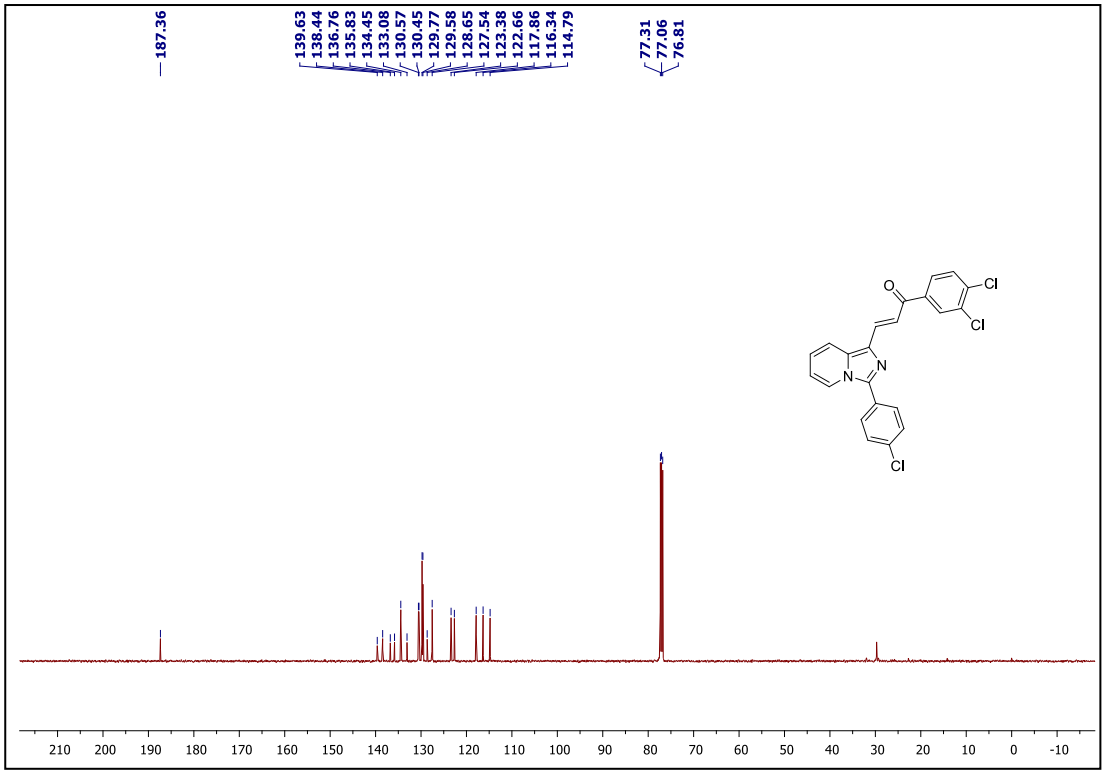


Figure S45. ^{13}C NMR spectrum of **7o** (100 MHz, $CDCl_3$).

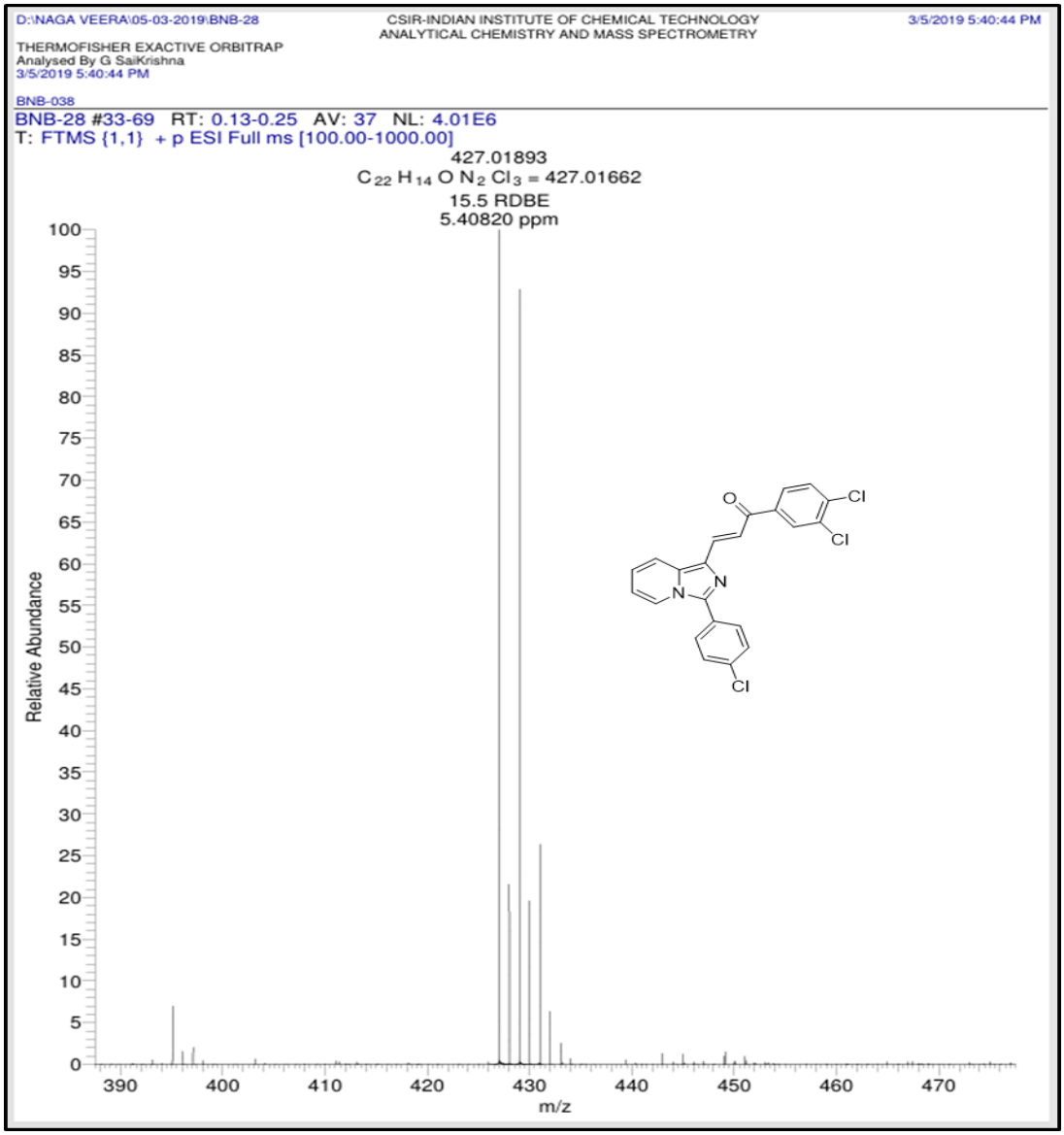


Figure S46. HRMS spectrum of **7o**

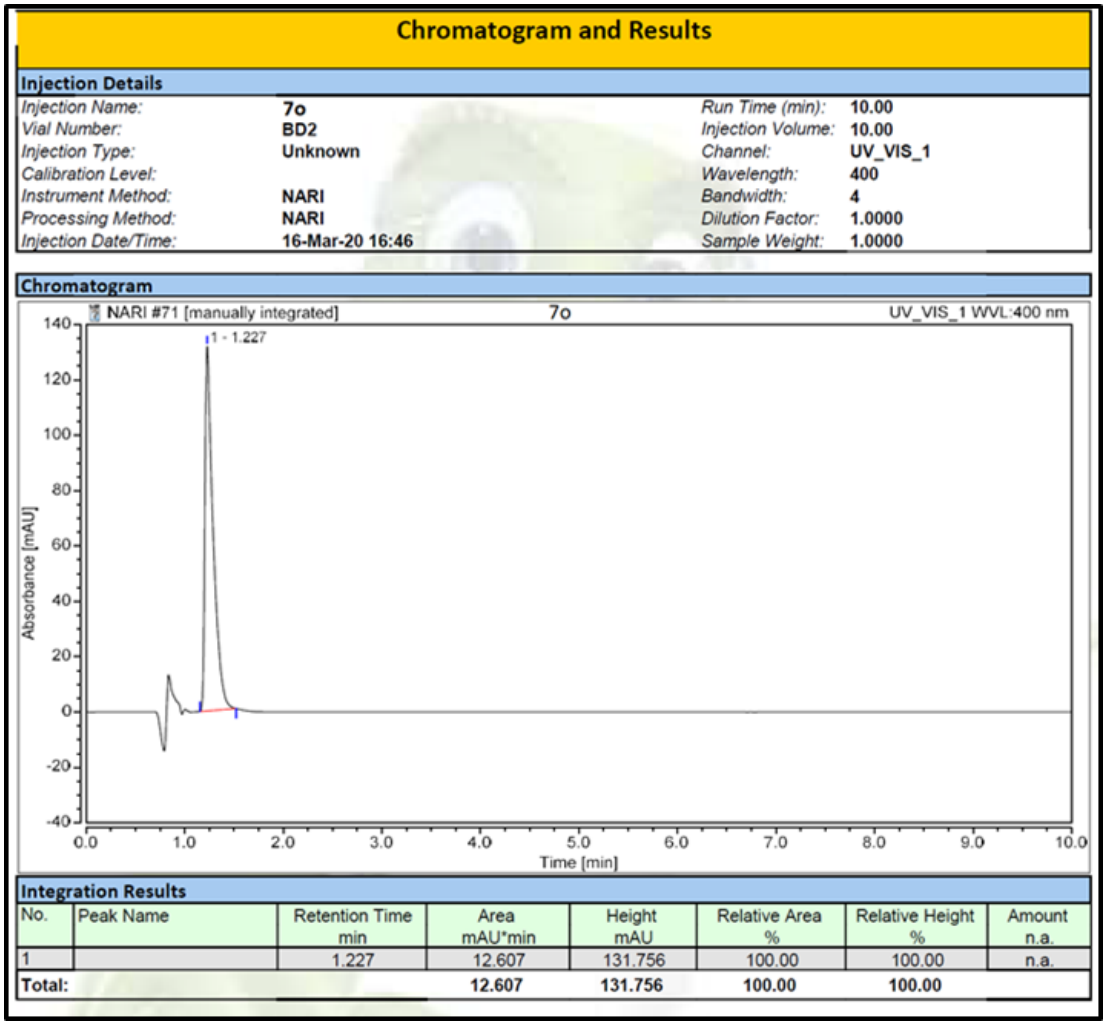


Figure S47. HPLC of **7o** (WVL: 400 nm).

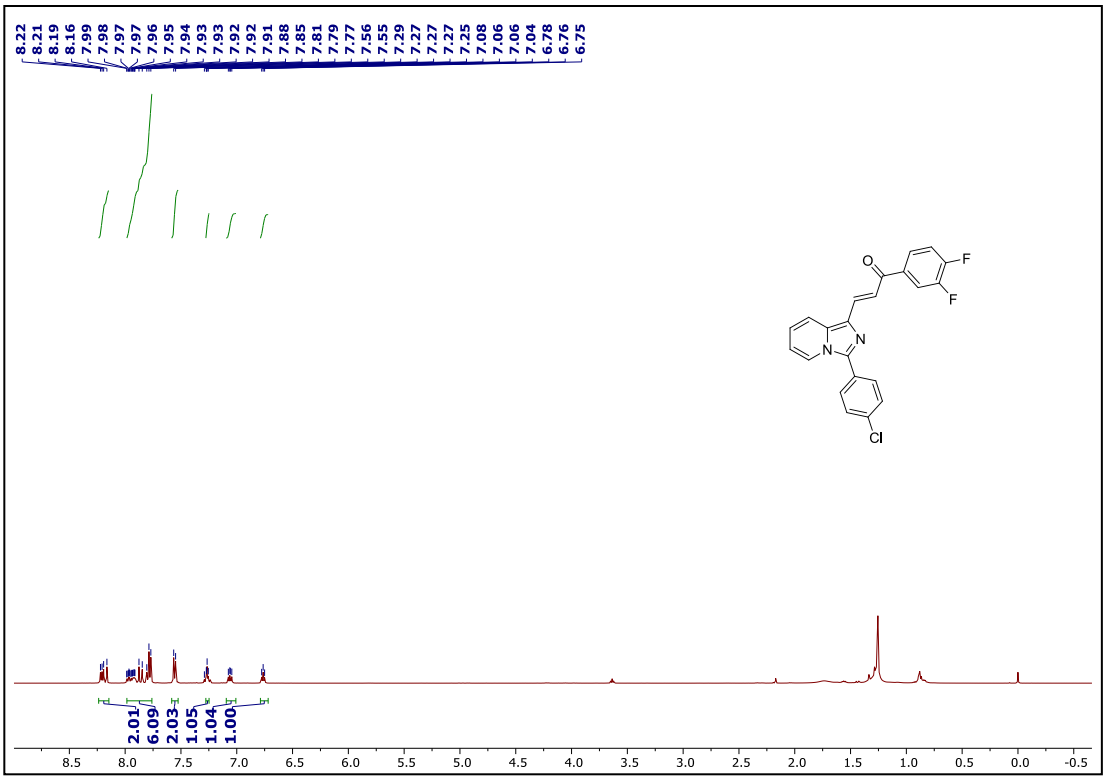


Figure S48. ^{1}H NMR spectrum of **7p** (400 MHz, $CDCl_3$).

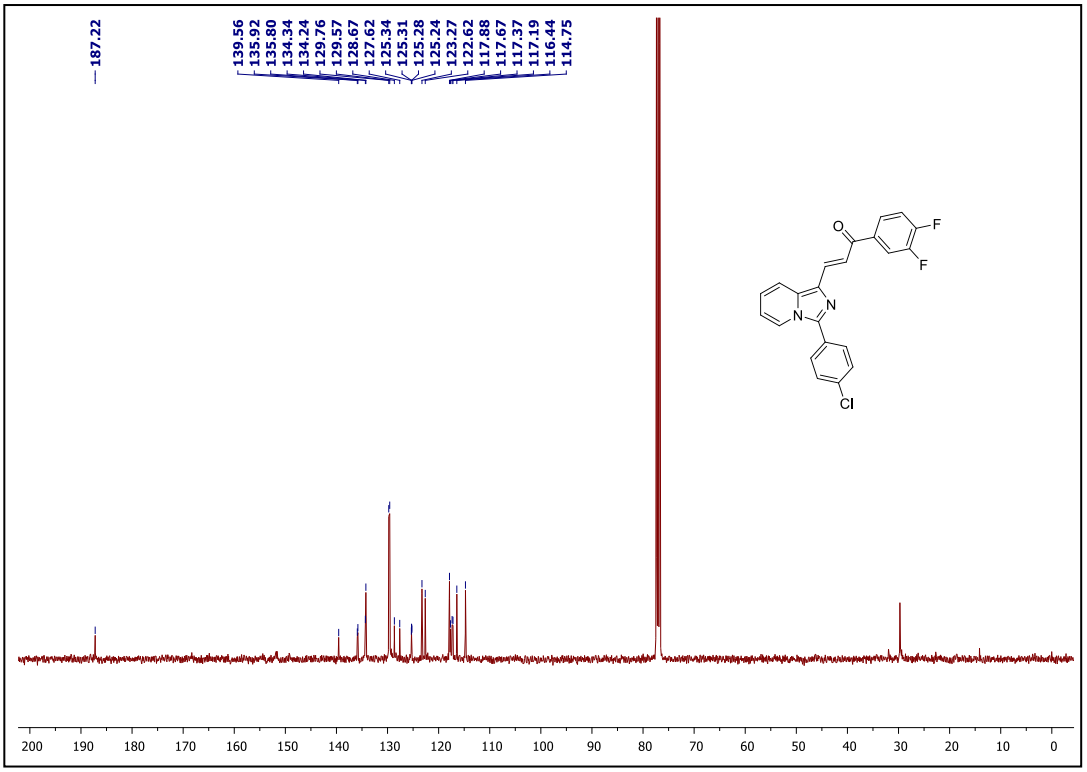


Figure S49. ^{13}C NMR spectrum of **7p** (100 MHz, $CDCl_3$).

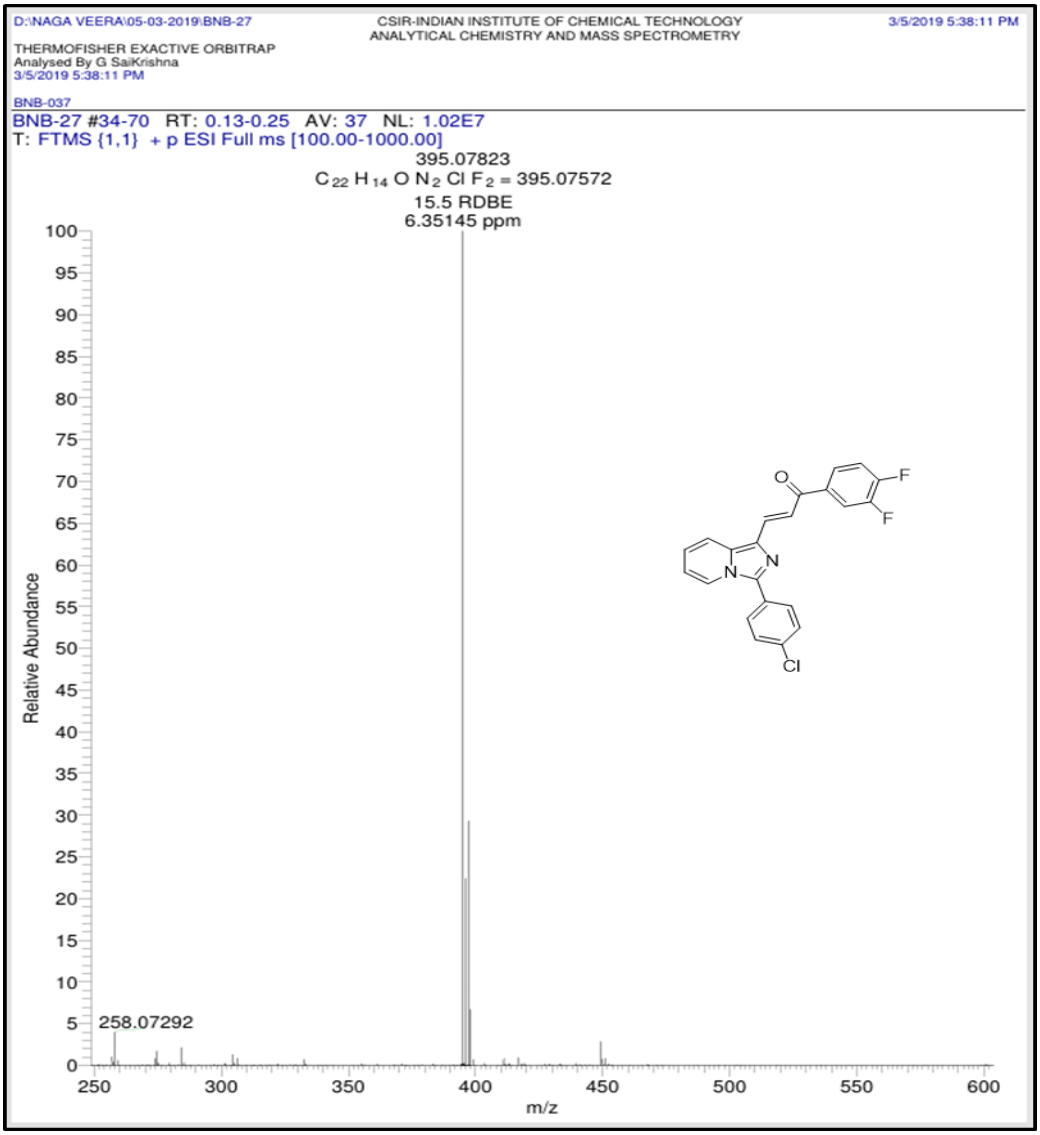


Figure S50. HRMS spectrum of **7p**

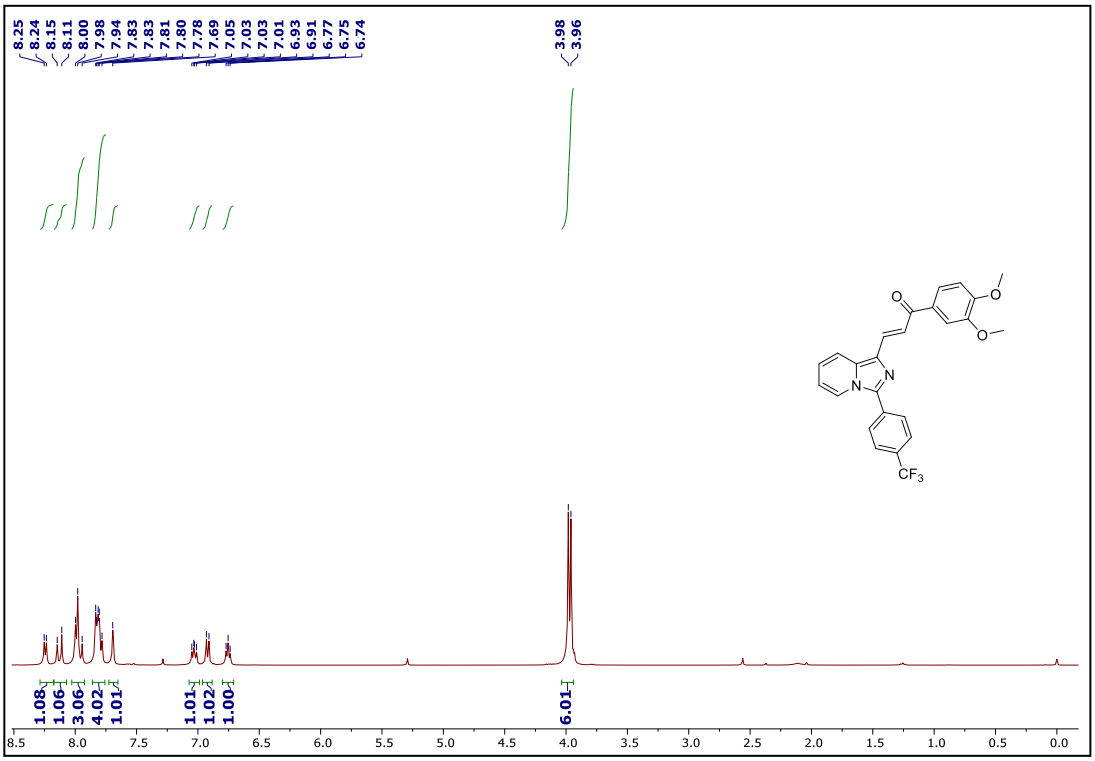


Figure S51. ^{1}H NMR spectrum of **7q** (400 MHz, $CDCl_3$).

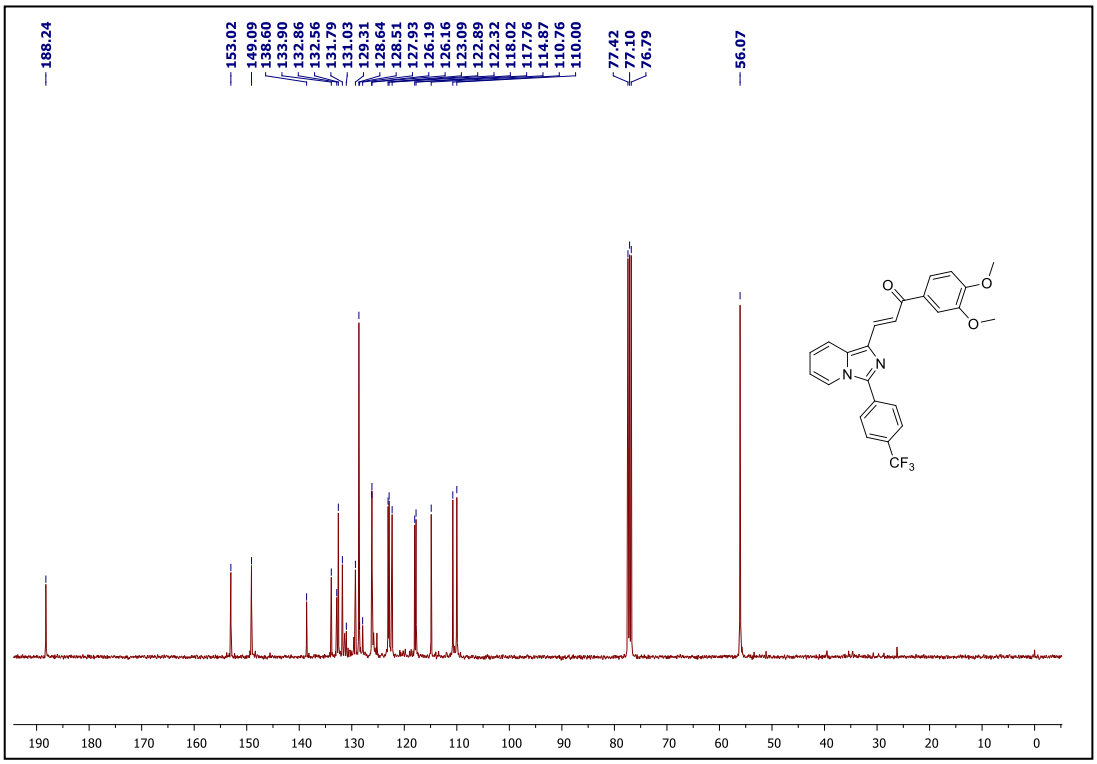


Figure S52. ^{13}C NMR spectrum of **7q** (100 MHz, $CDCl_3$).

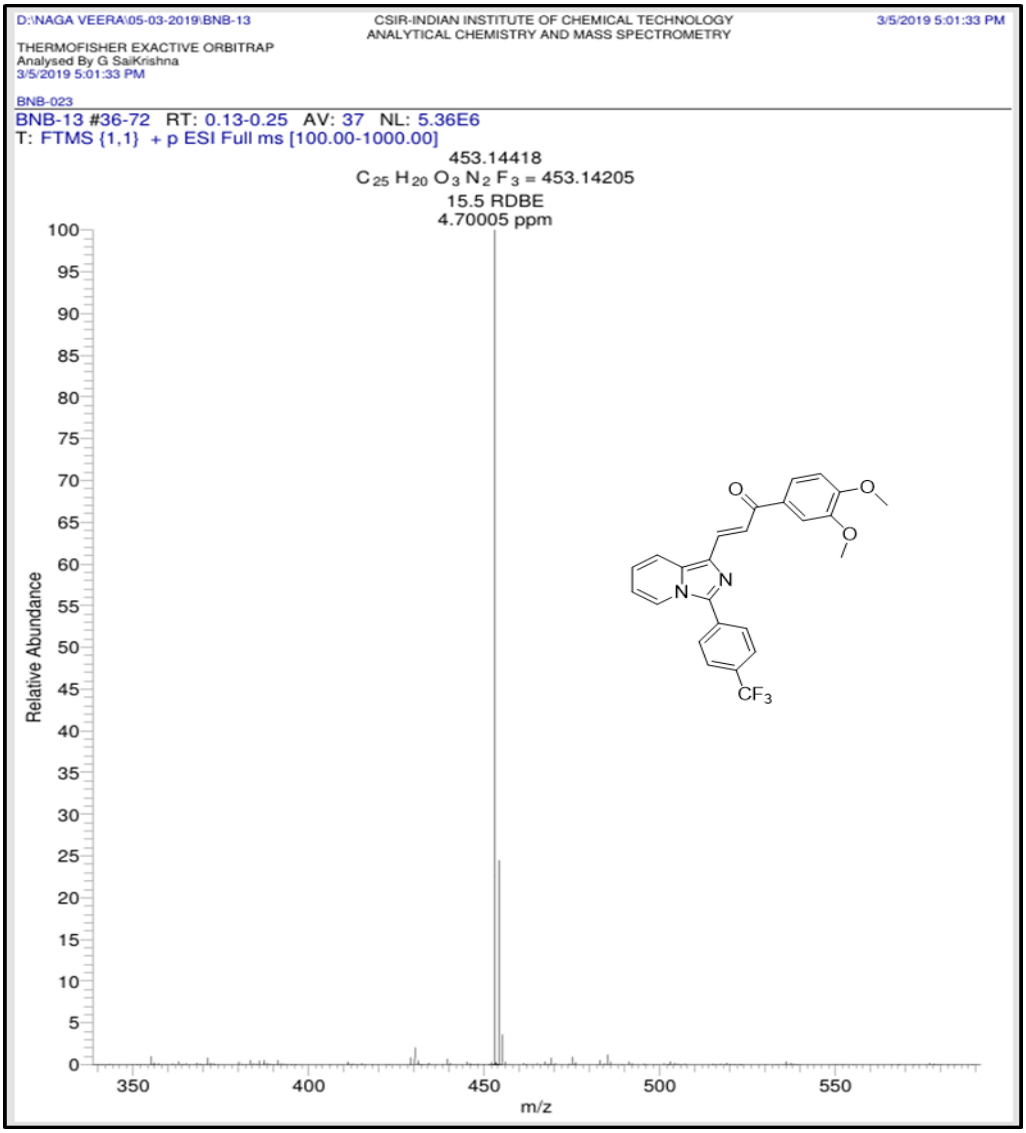


Figure S53. HRMS spectrum of **7q**

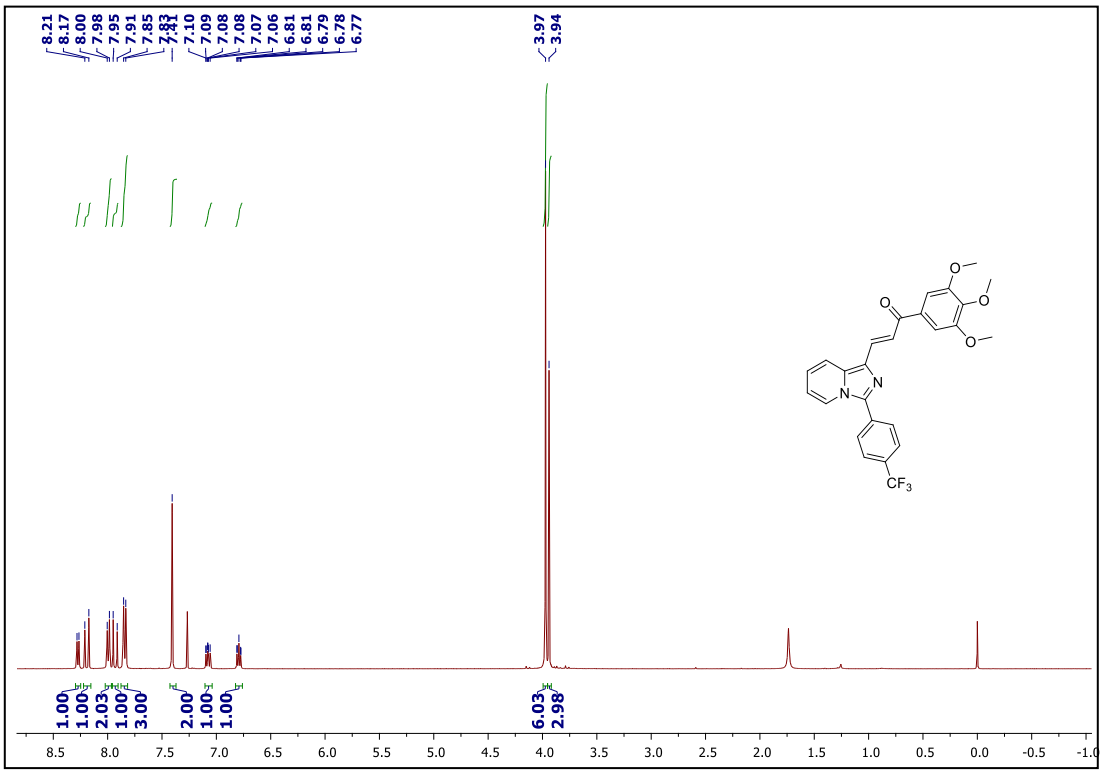


Figure S54. ^{1}H NMR spectrum of **7r** (400 MHz, $CDCl_3$).

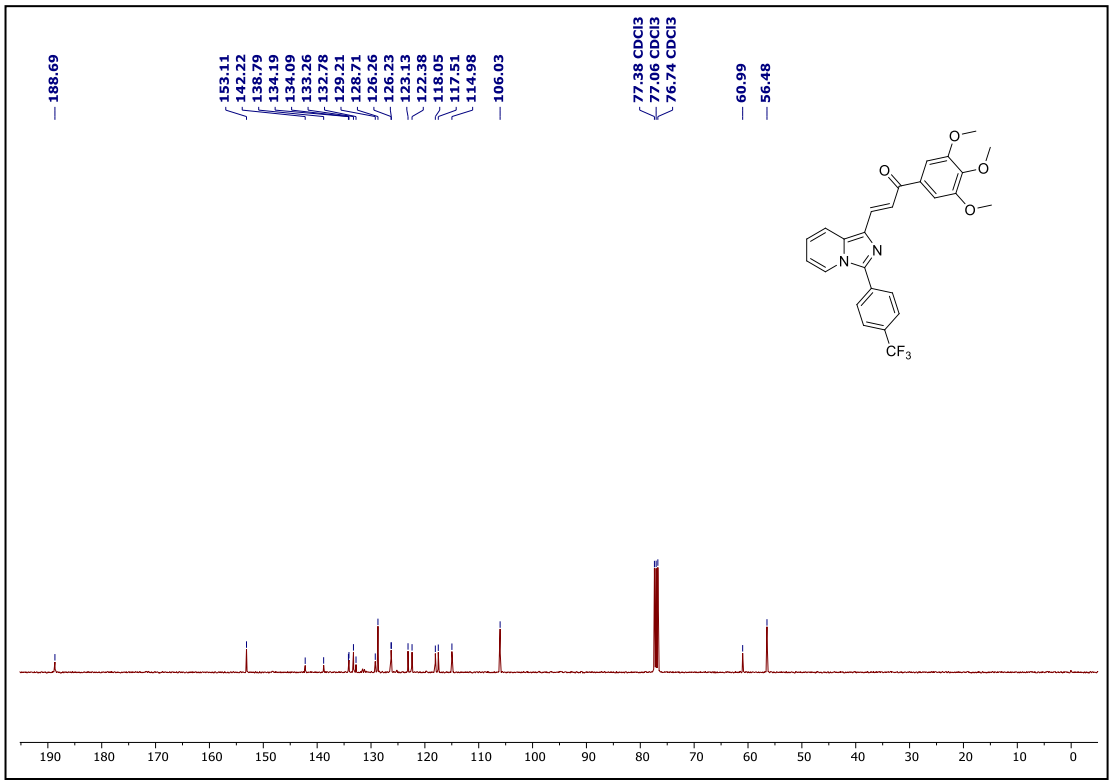


Figure S55. ^{13}C NMR spectrum of **7r** (100 MHz, $CDCl_3$).

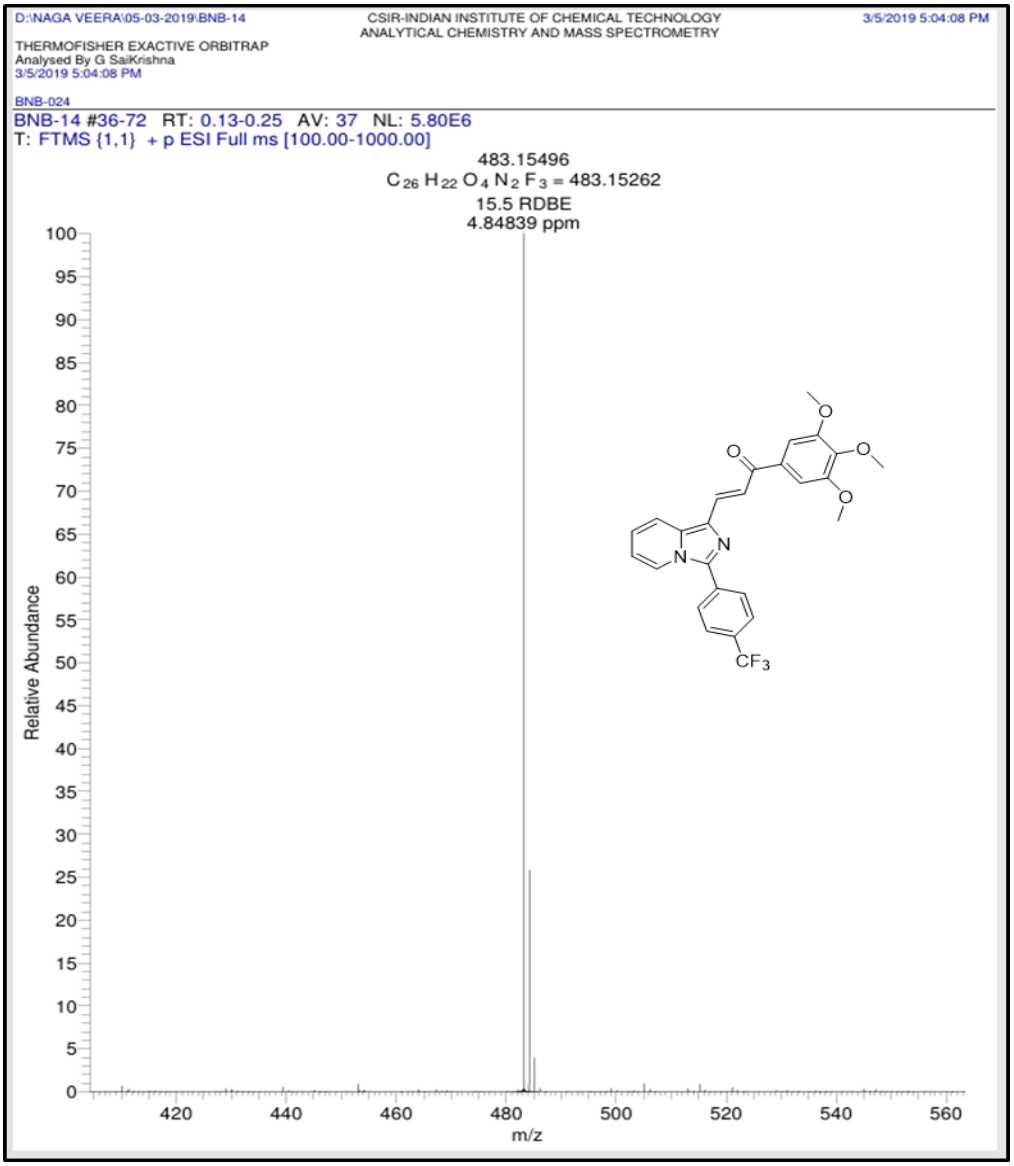


Figure S56. HRMS spectrum of **7r**

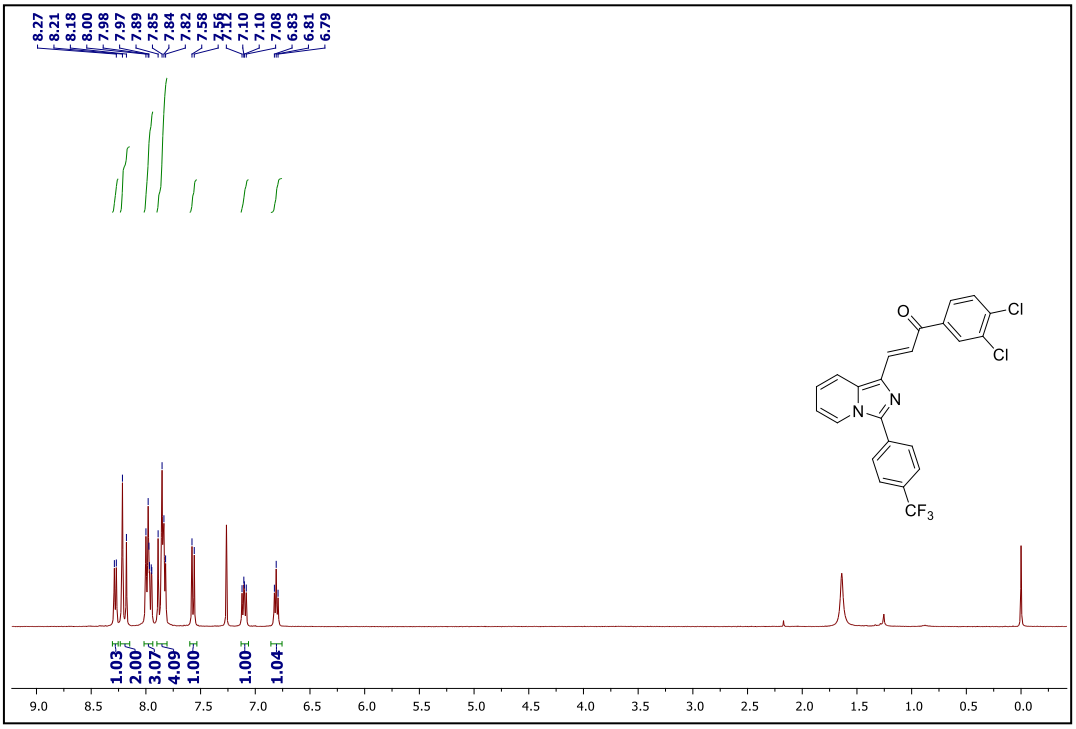


Figure S57. ^{1}H NMR spectrum of **7s** (400 MHz, $CDCl_3$).

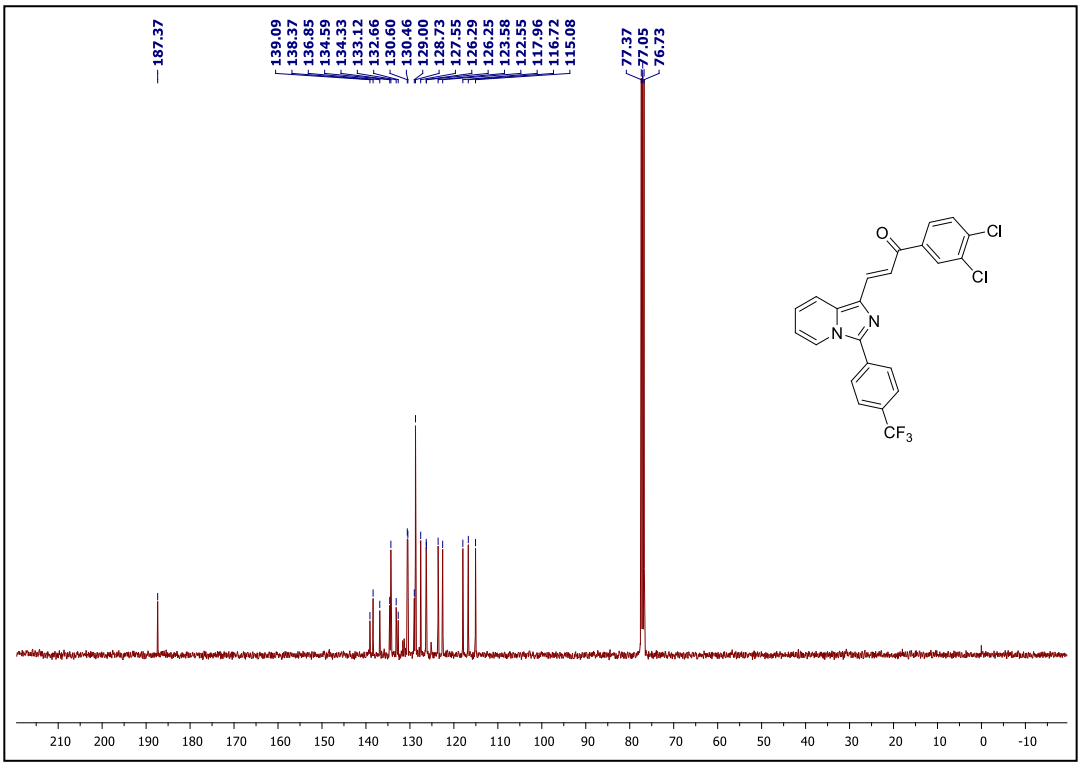


Figure S58. ^{13}C NMR spectrum of **7s** (100 MHz, $CDCl_3$).

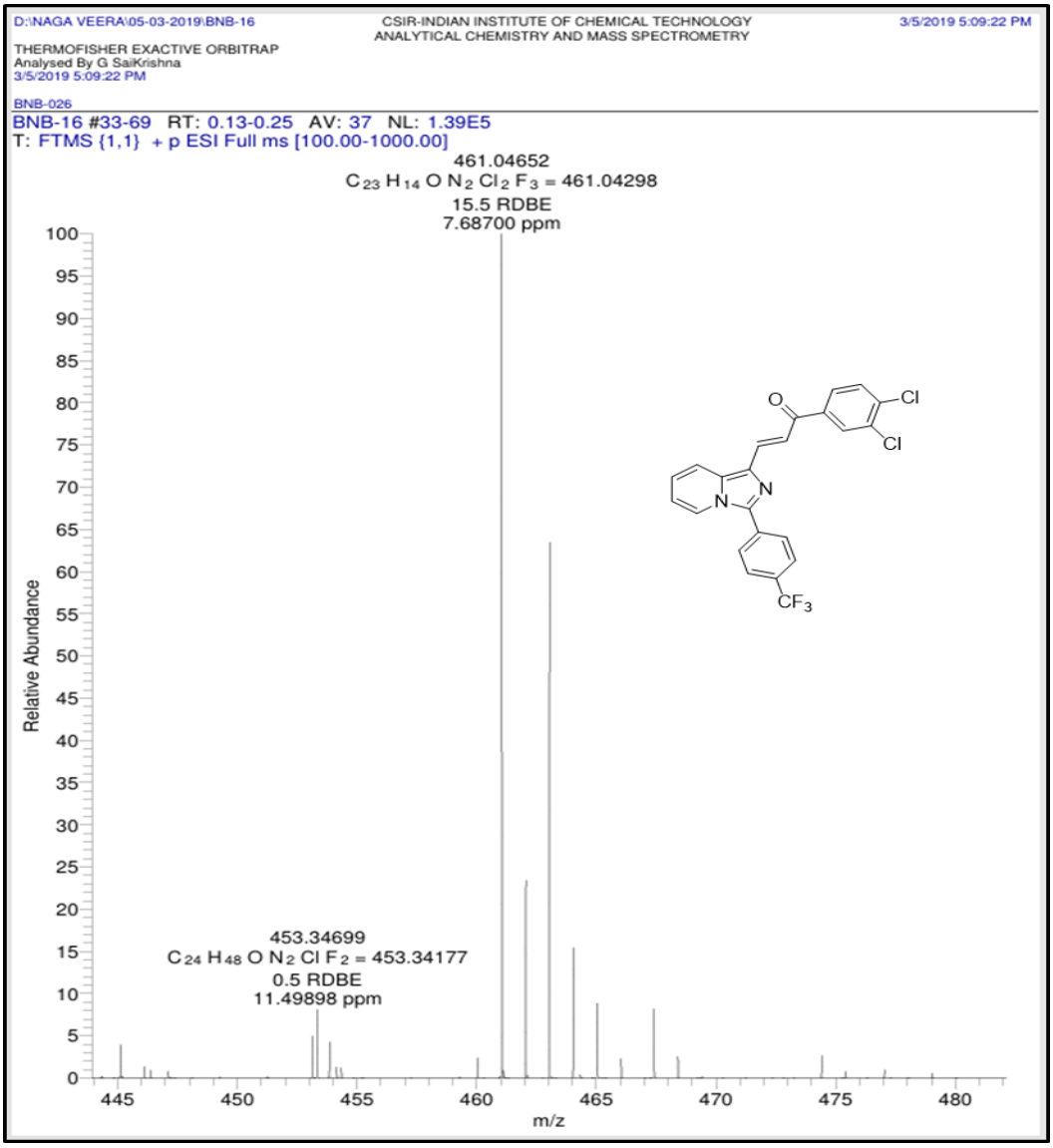


Figure S59. HRMS spectrum of **7s**

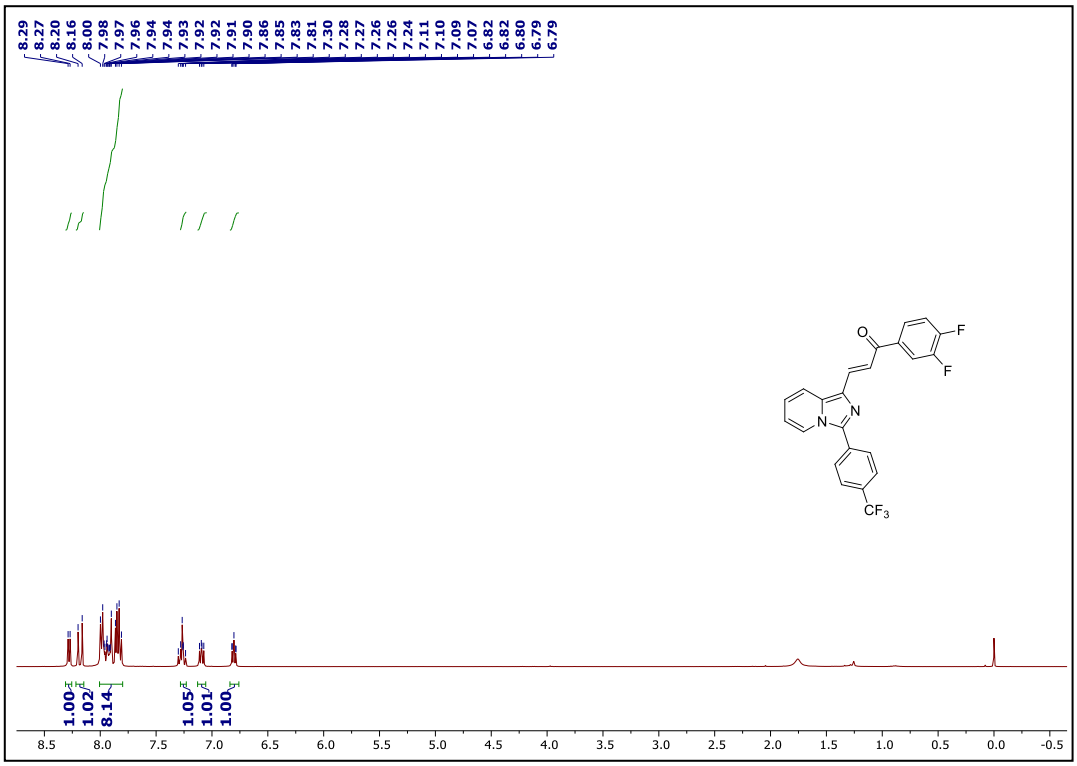


Figure S60. ^{1}H NMR spectrum of **7t** (400 MHz, $CDCl_3$).

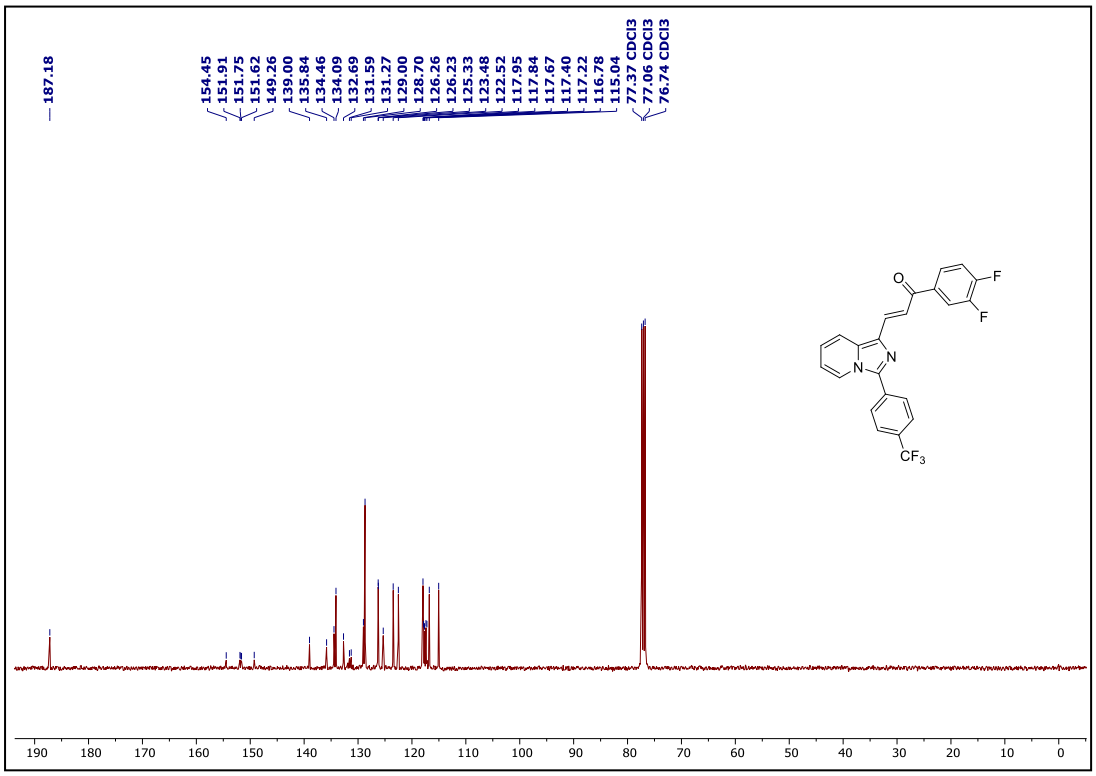


Figure S61. ^{13}C NMR spectrum of **7t** (100 MHz, $CDCl_3$).

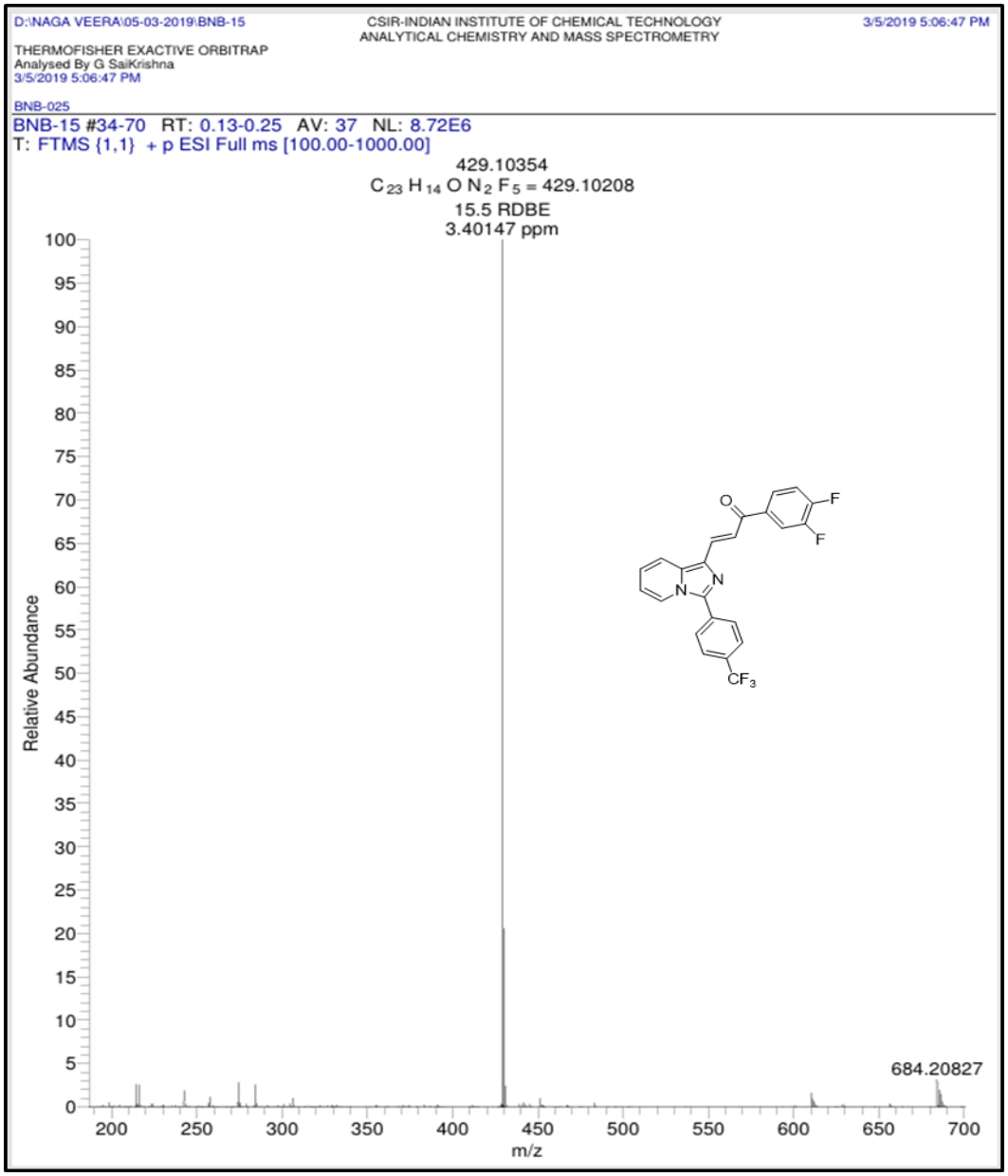


Figure 62. HRMS spectrum of **7t**