

## Synthesis of quinoline acetohydrazide-hydrazone derivatives evaluated as DNA gyrase inhibitors and potent antimicrobial agents

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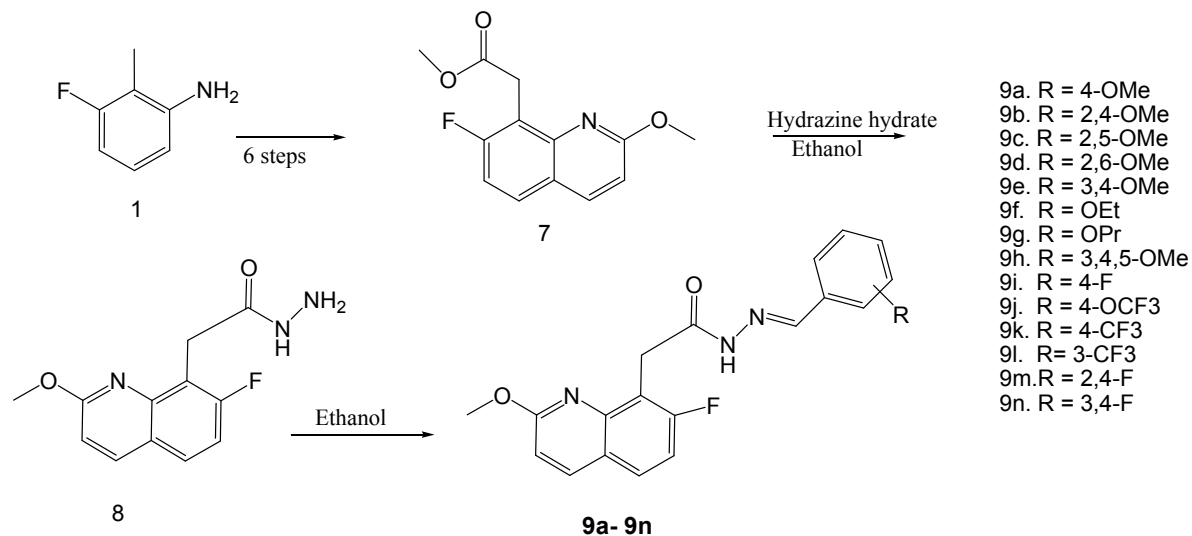
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**Scheme 1:**



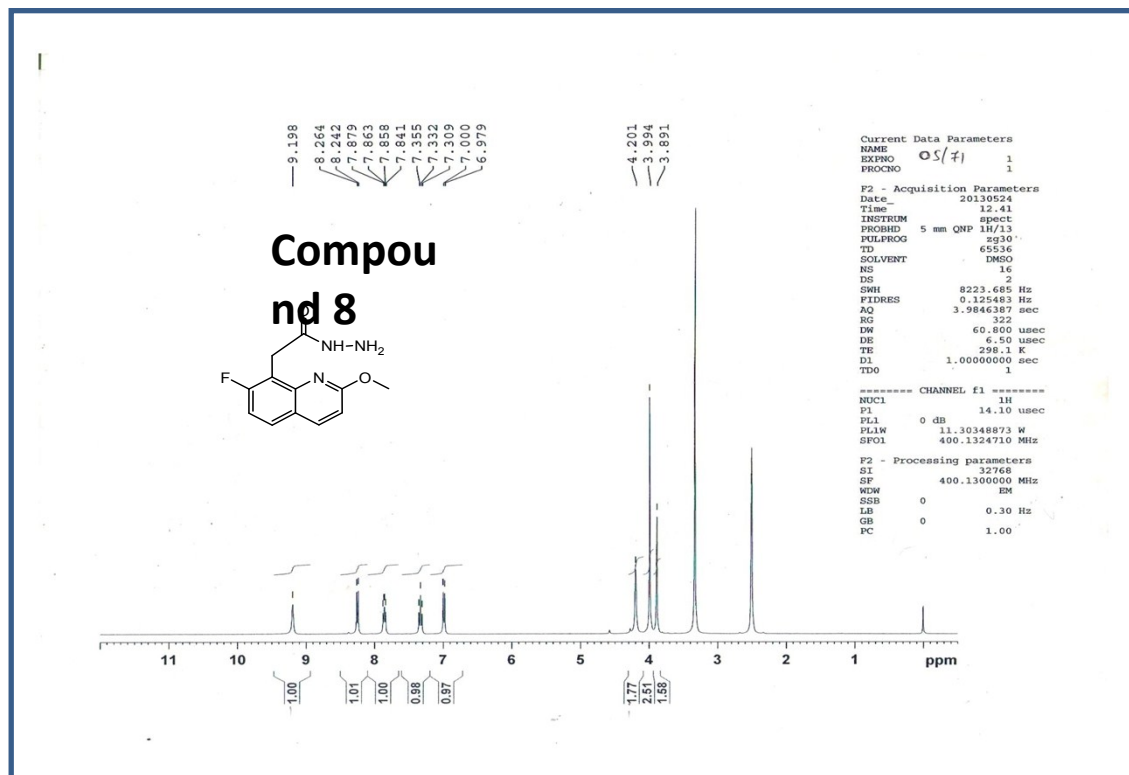
**Scheme 1:** Synthesis of novel Quinoline acetohydrazide derivatives 9a-9n

**Experimental Conditions:** a) cinnamoyl chloride, aq. NaHCO<sub>3</sub>, isopropyl acetate, room temperature, 30 min; b) AlCl<sub>3</sub>, chlorobenzene, 90 °C, 1 h; c) MeI, KtOBu, DMSO, 70 °C, 2.5 h; d) NBS, benzoyl peroxide, xylene, 70 °C, 1.5 h; e) KCN, DMF, 60 °C, 16 h; f) TMSiCl, MeOH, 70 °C, 2.5 h; g) NH<sub>2</sub>-NH<sub>2</sub>, ethanol, reflux, 20 h; h) benzaldehydes, **a-n**, ethanol, reflux, 4 h.

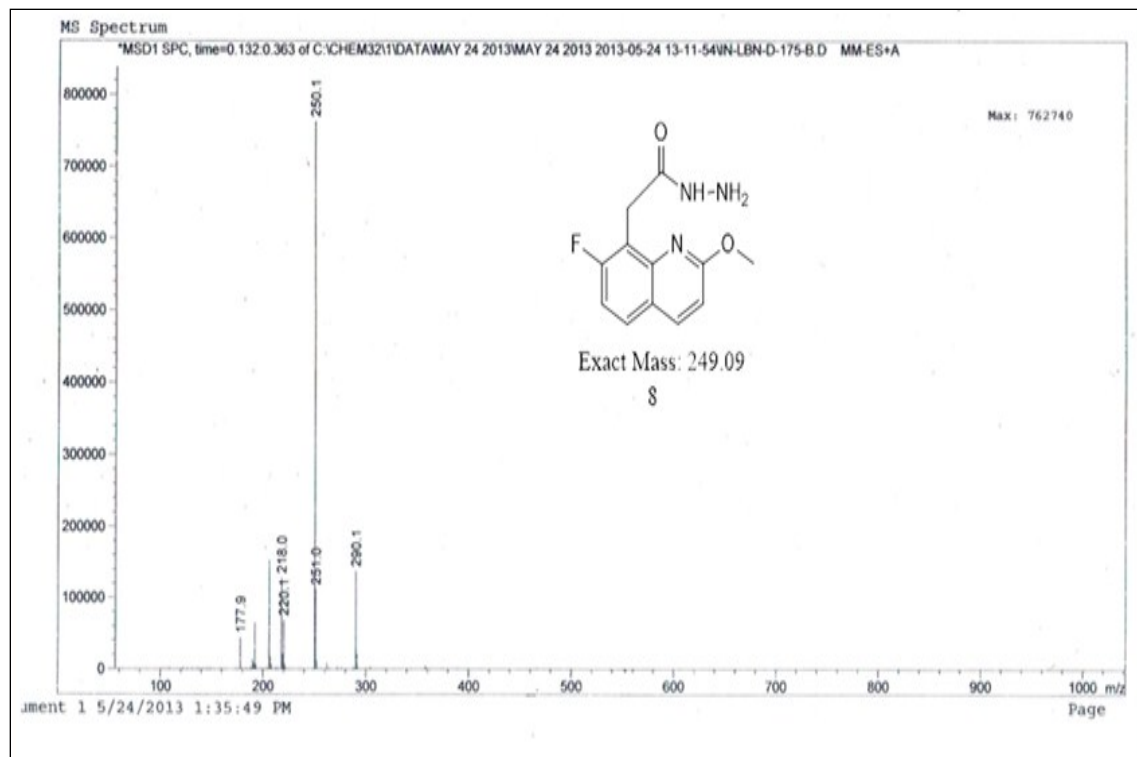
**Table 1-***In vivo* efficacy of quinoline acetohydrazide derivatives **9a-9n** for demonstrating antibacterial activity against selected pathogens

Entry	Compounds	Zone of inhibition (mM)**			
		<i>E.coli</i>	<i>P.aeruginosa</i>	<i>S.aureus</i>	<i>S.pyogenes</i>
1	9a	10	10	7	11
2	9b	9	11	8	9
3	9c	8	9	7	10
4	9d	12	12	9	11
5	9e	11	10	7	11
6	9f	12	10	7	11
7	9g	11	11	9	12
8	9h	16	17	14	16
9	9i	17	17	13	15
10	9j	16	15	13	17
11	9k	17	16	14	17
12	9l	16	17	15	17
13	9m	21	20	18	20
14	9n	20	19	18	19
15	Ampicillin	19	18	16	18
16	Control*	-	-	-	-

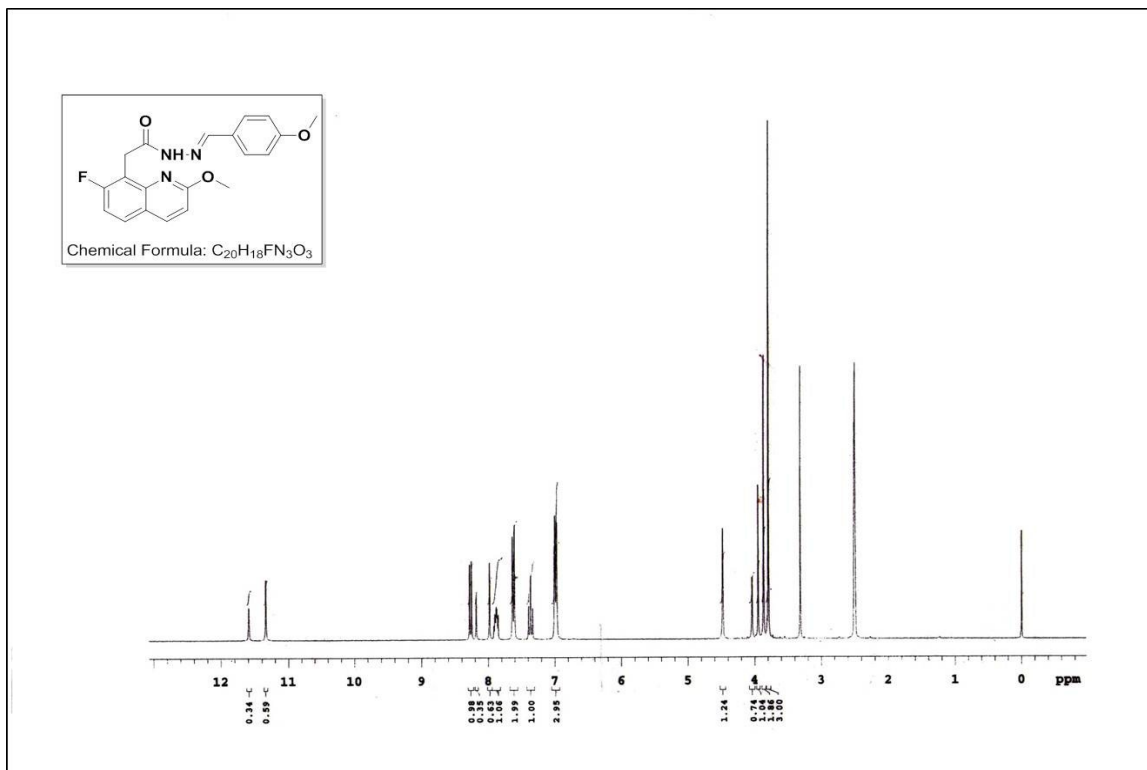
\*DMSO, \*\*Diameter of well (bore size)- 6 mm; Culture strains of bacteria were maintained on nutrient agar slant at 37±0.5 °C for 24 h; All plates were incubated at 37±0.5 °C for 24 h.



**Fig. 1:**  $^1\text{H}$  NMR spectrum of 2-(7-fluoro-2-methoxyquinolin-8-yl) acetohydrazide



**Fig. 2:** Mass spectra of Compound 8



**Fig.3:** <sup>1</sup>H NMR spectra of **9a**

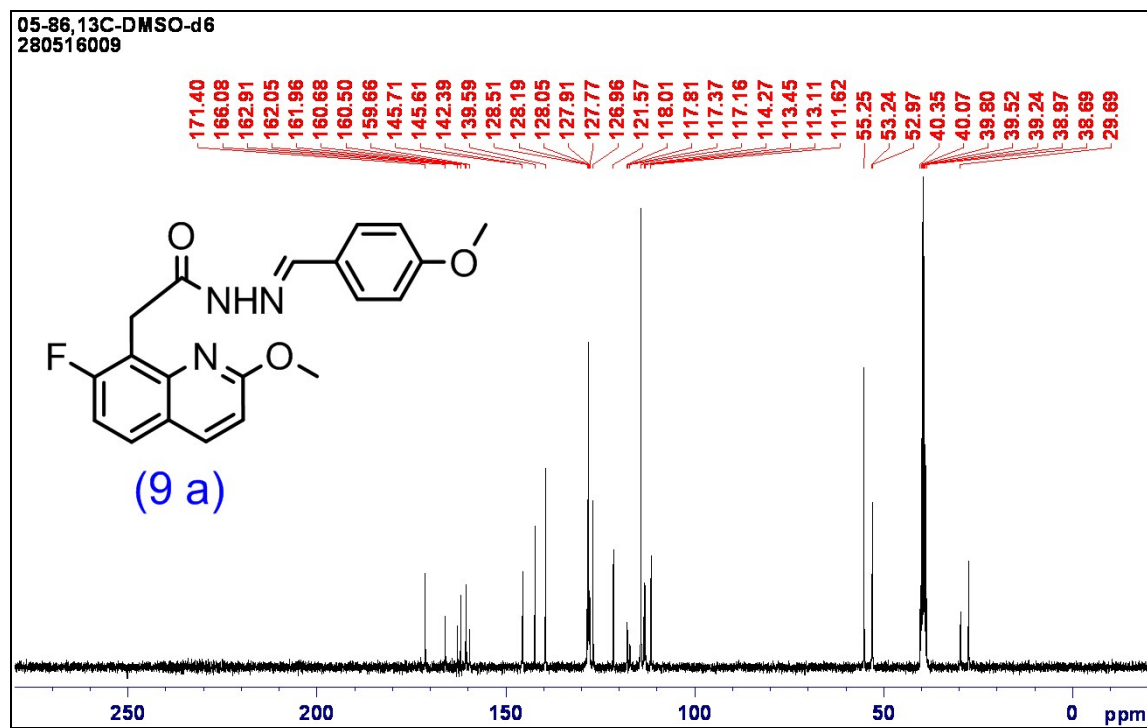
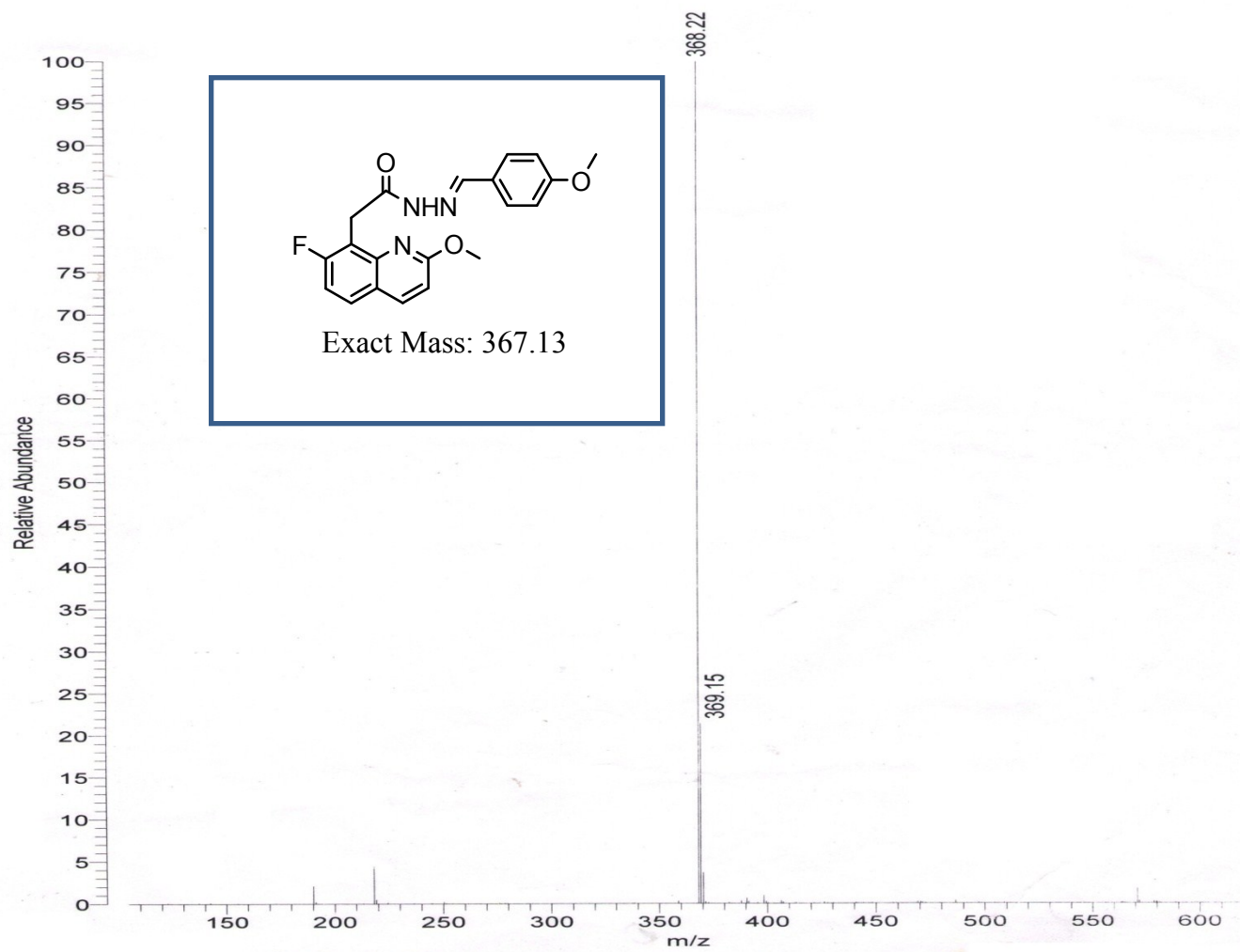
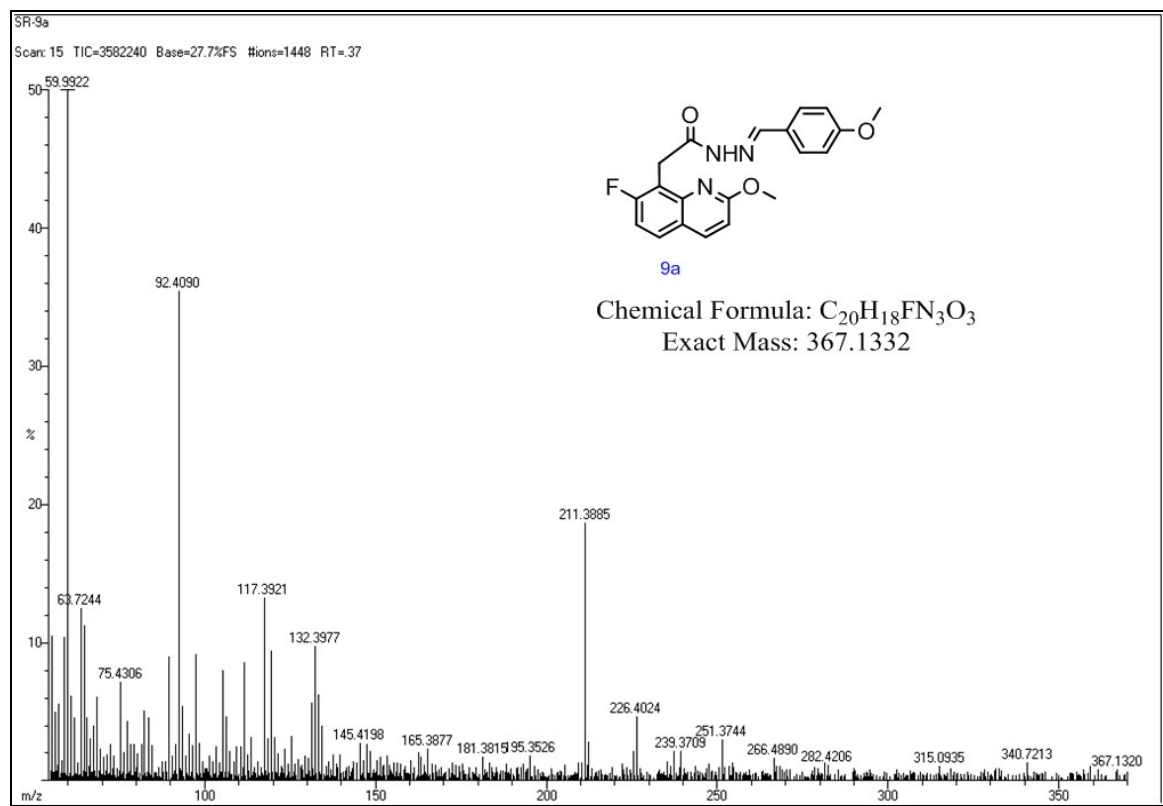


Fig.4. <sup>13</sup>C NMR spectra of 9a



**Fig. 5.** Mass spectra of **9a**





**Fig.6.** HRMS spectra of **9a**

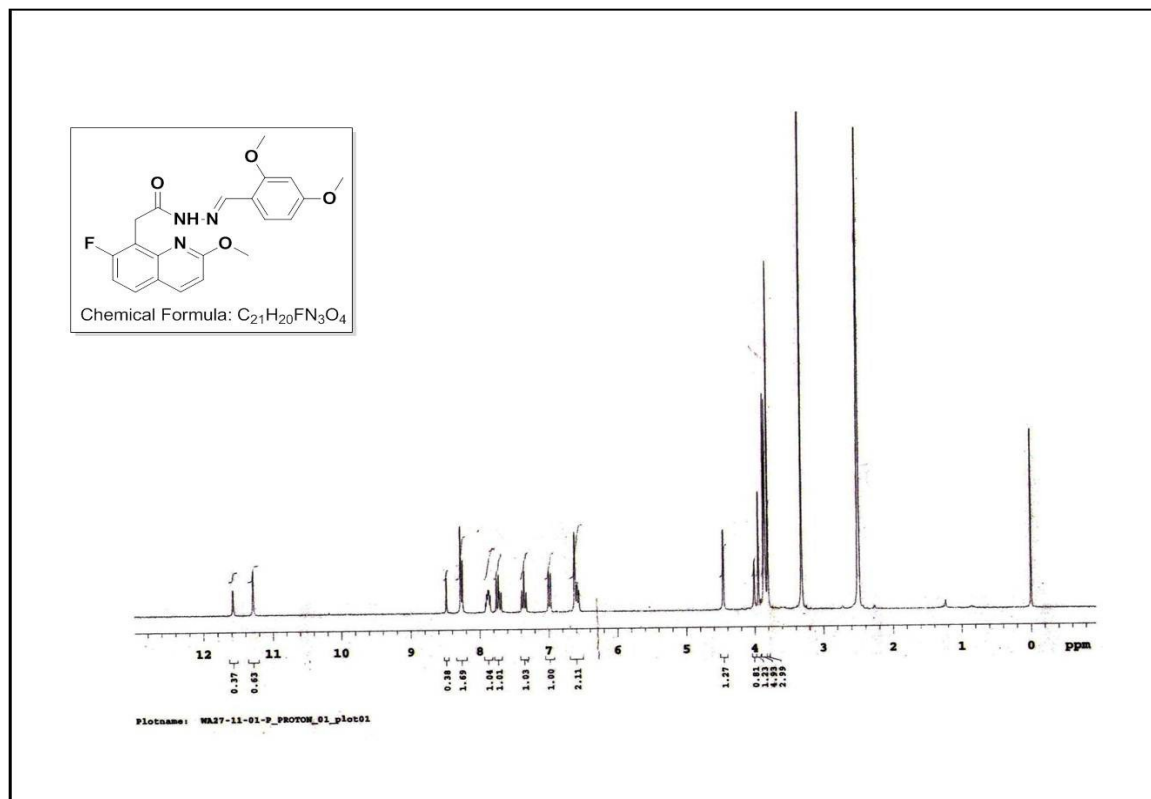
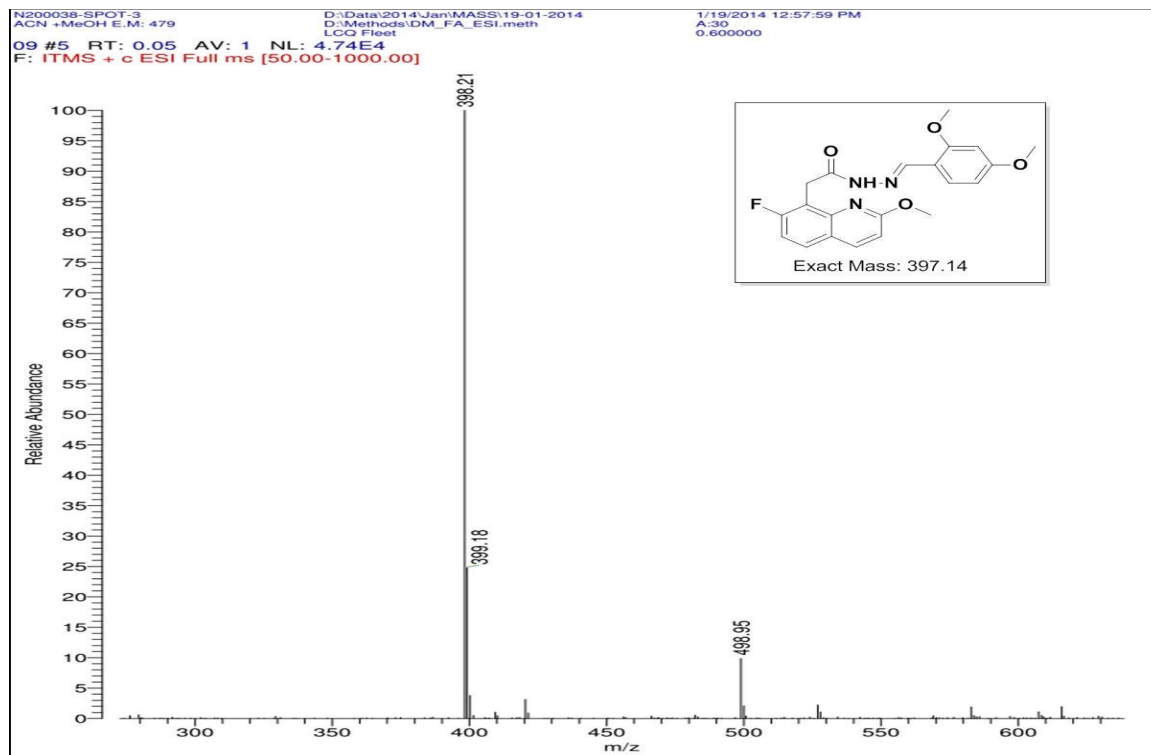


Fig. 7. <sup>1</sup>H NMR spectra of 9b



**Fig. 8.** Mass spectra of **9b**

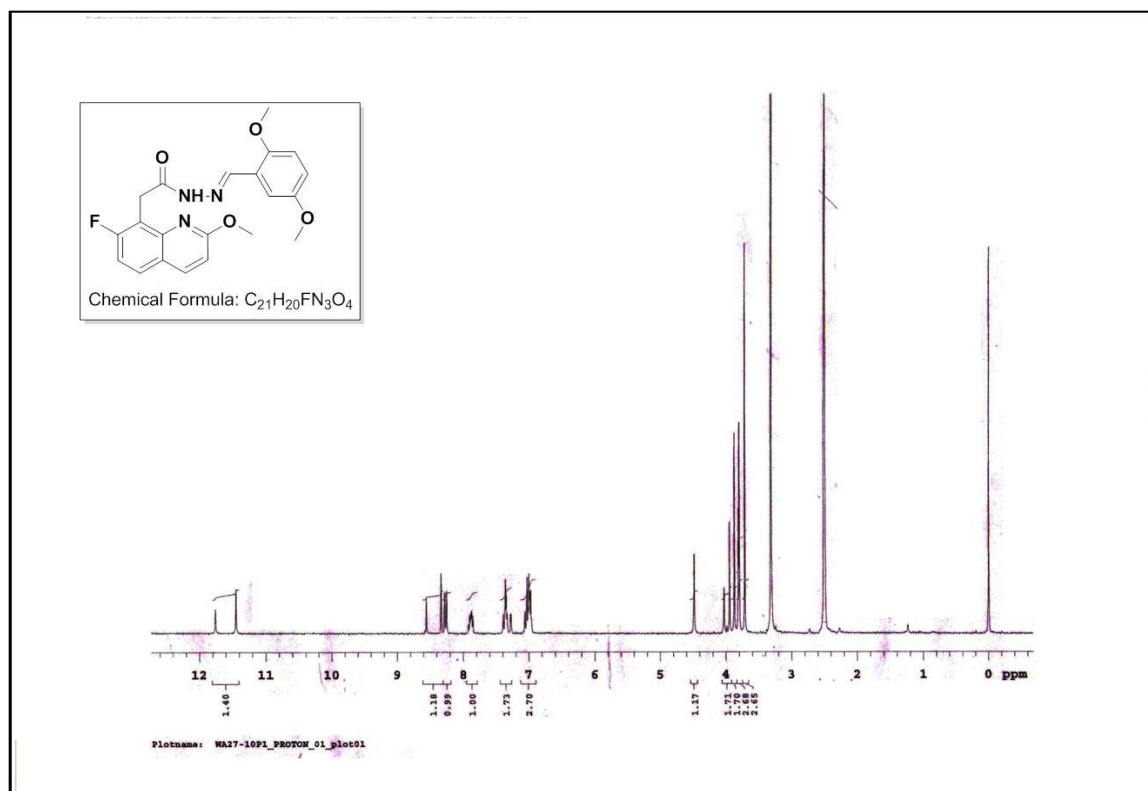


Fig. 9. <sup>1</sup>H NMR spectra of 9c

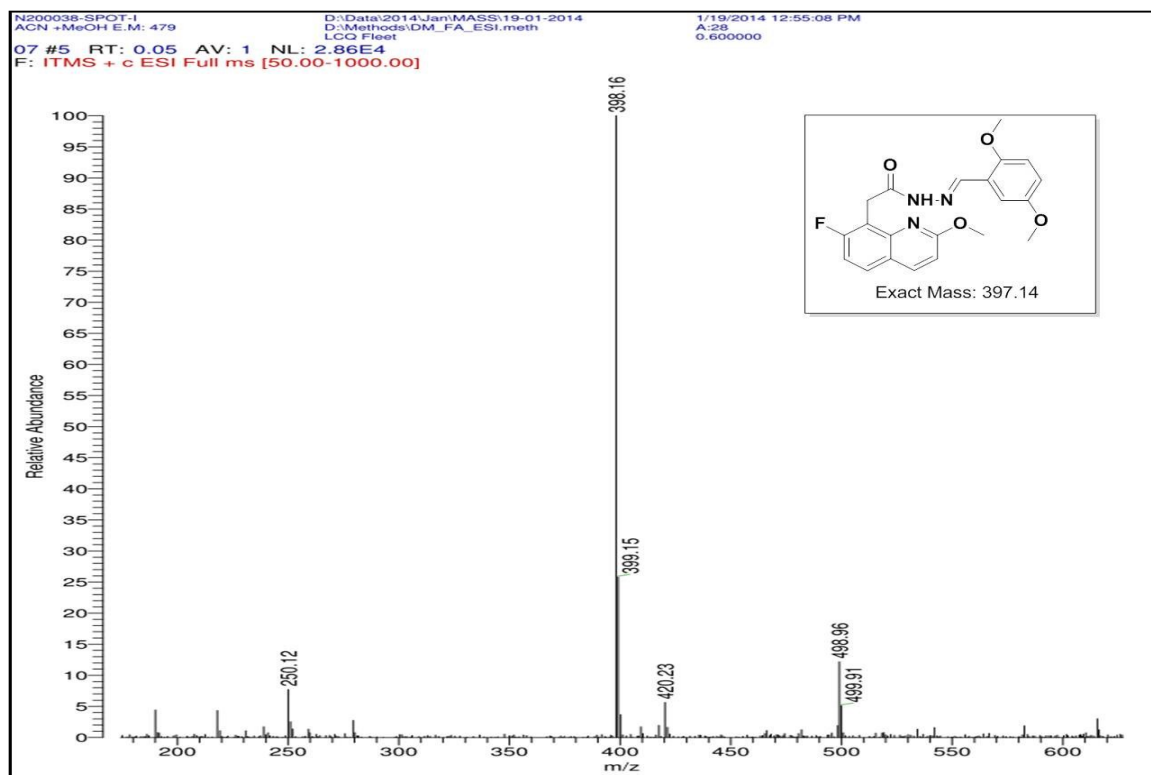


Fig. 10. Mass spectra of **9c**

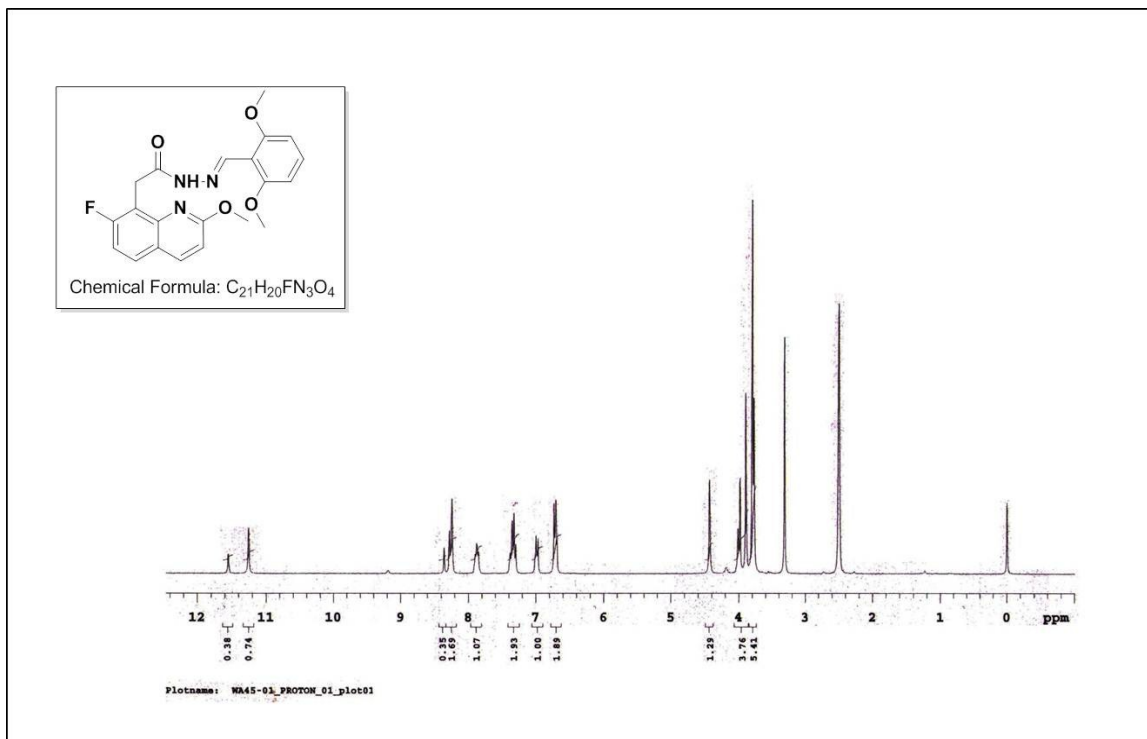


Fig. 11. <sup>1</sup>H NMR spectra of 9d

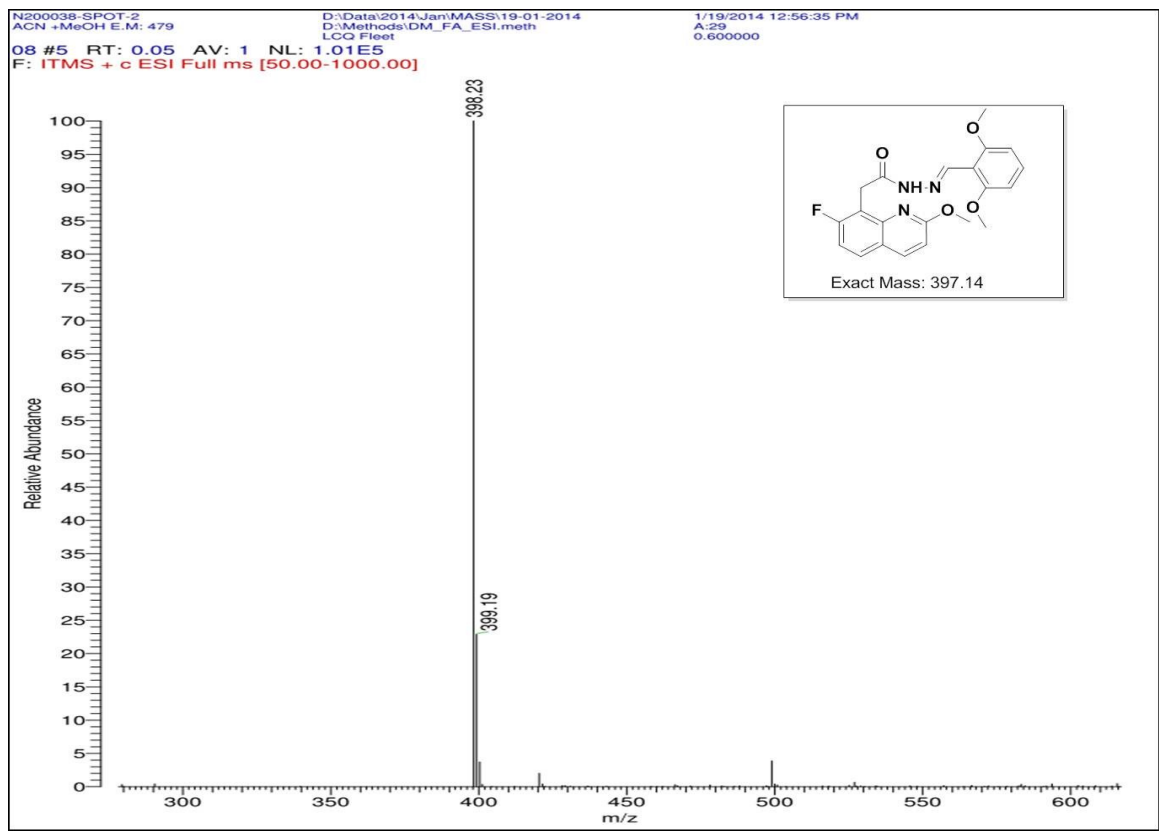


Fig. 12. Mass spectra of 9d

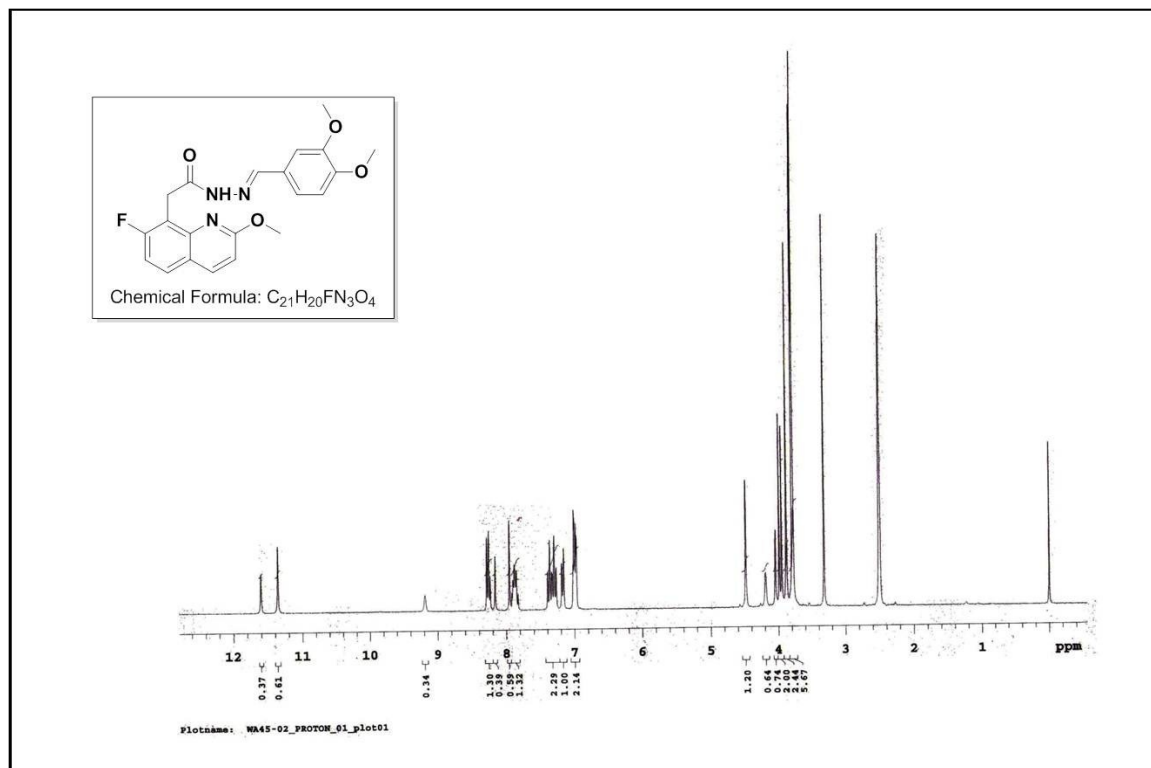
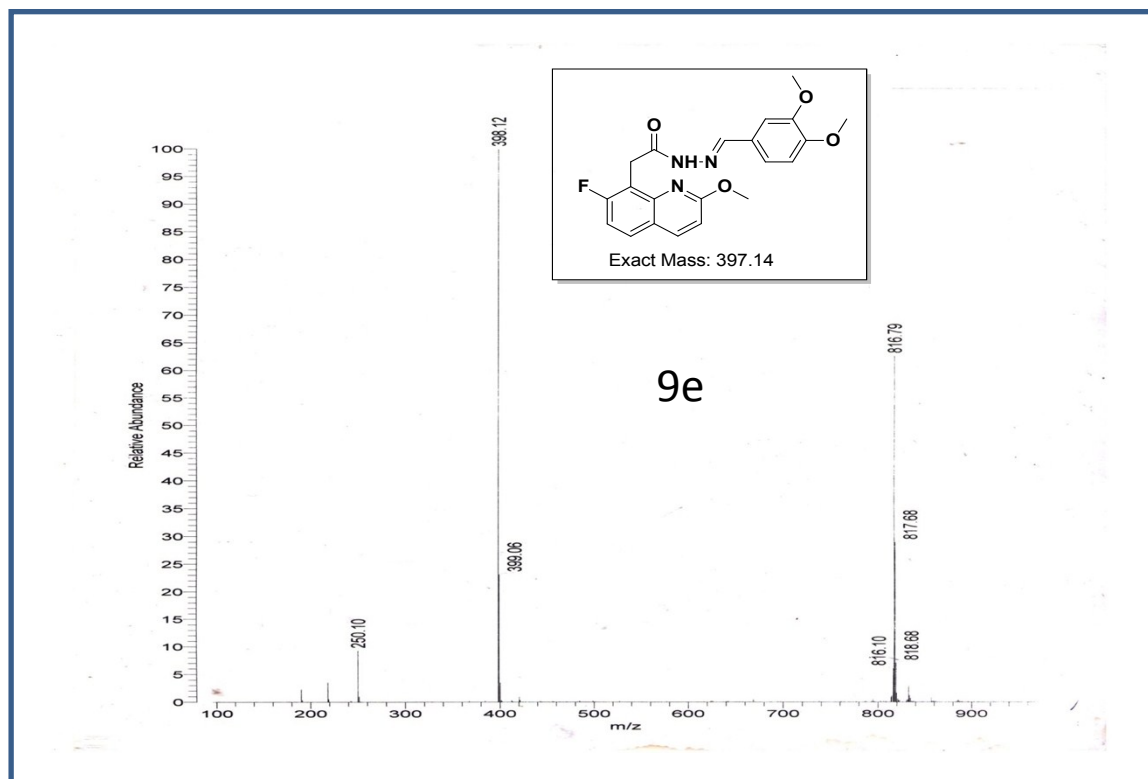


Fig. 13.  $^1H$  NMR spectra of **9e**





**Fig. 14.** Mass spectra of **9e**

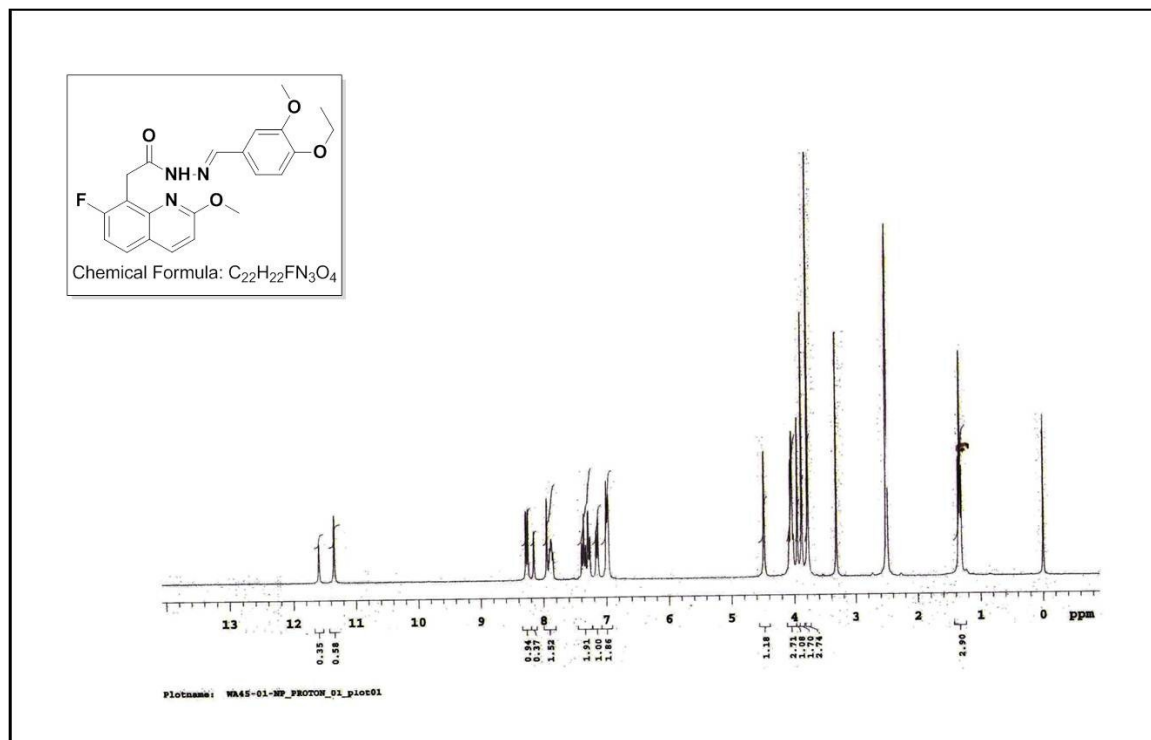


Fig. 15. <sup>1</sup>H NMR spectra of 9f

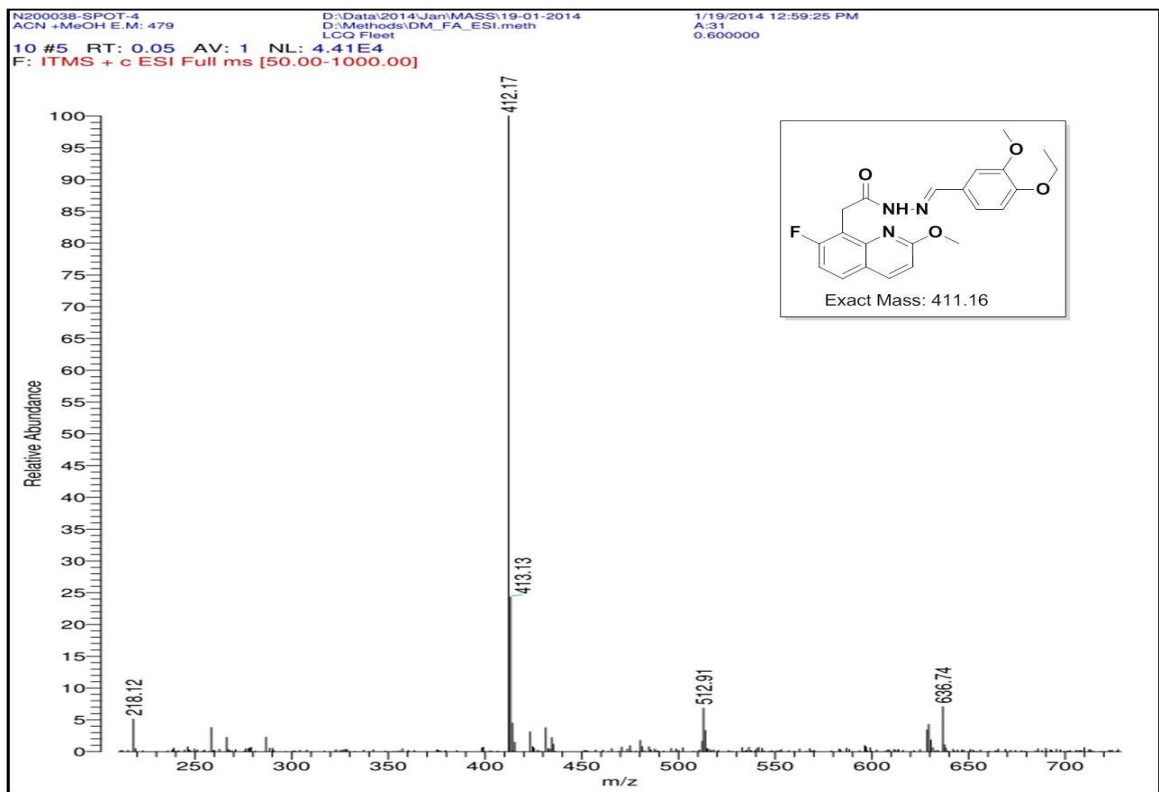
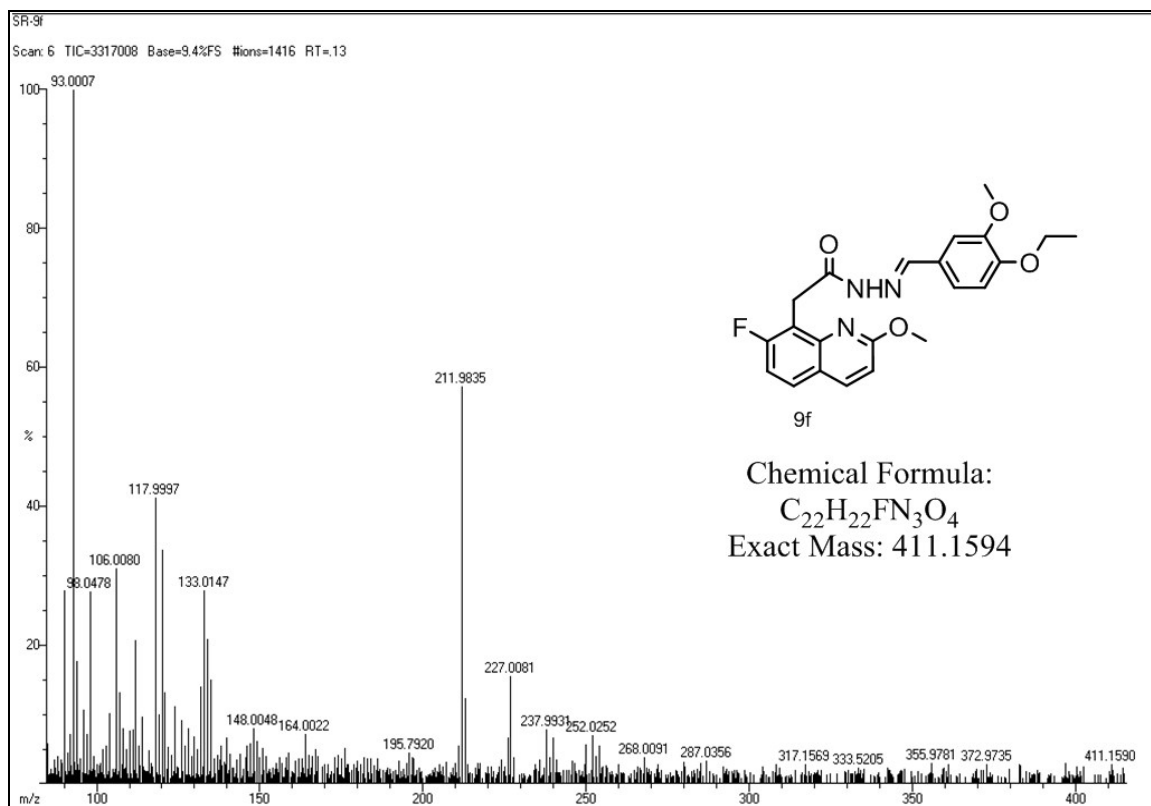


Fig. 16. Mass spectra of 9f



**Fig. 17.** HRMS spectra of **9f**

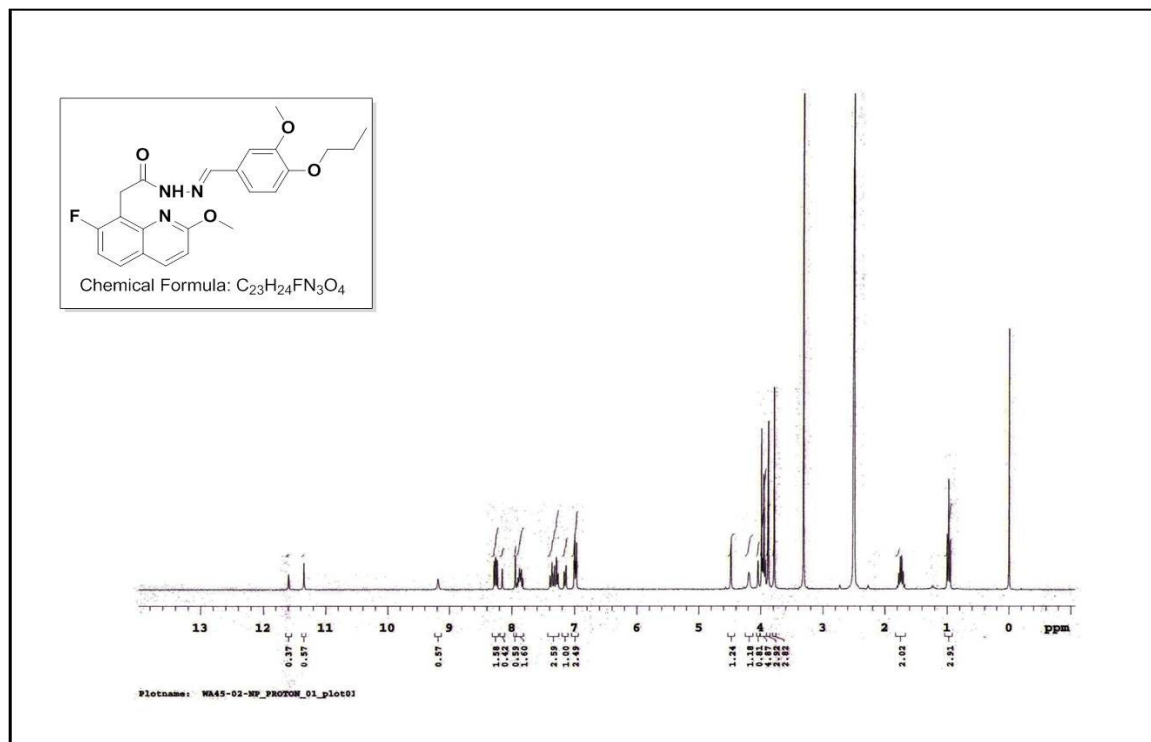


Fig. 18.  $^1H$  NMR spectra of **9g**

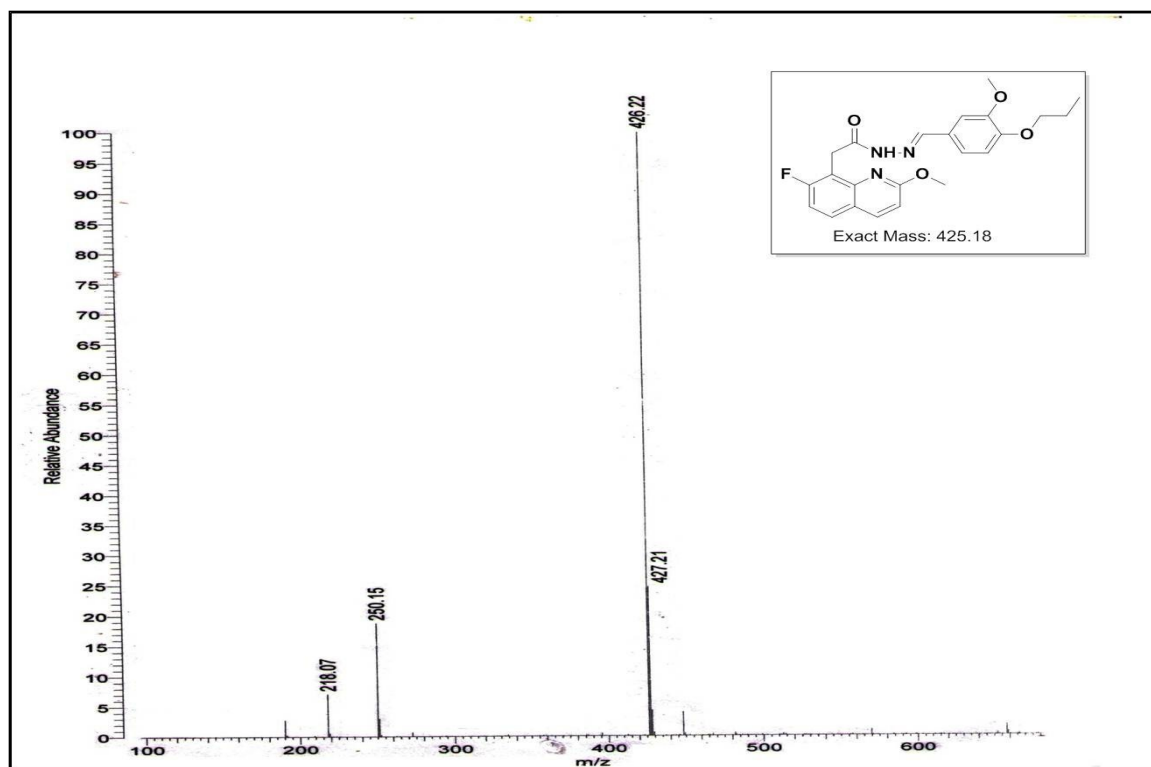
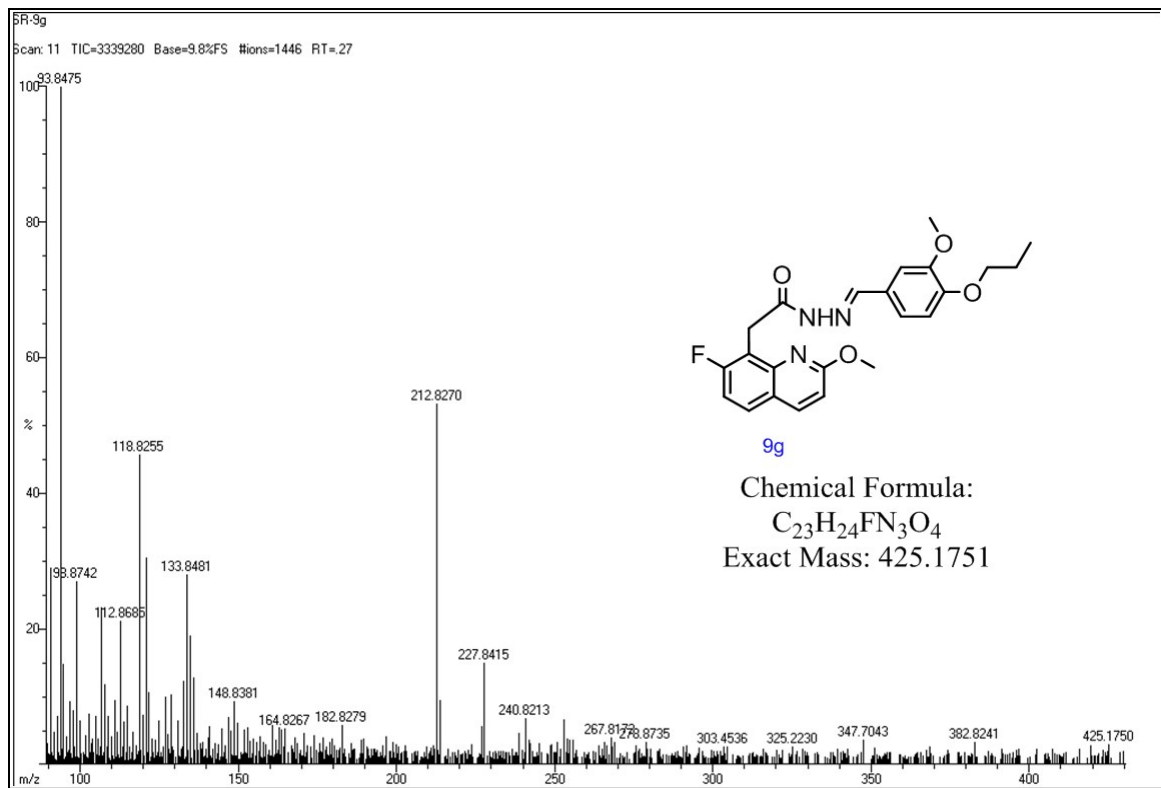


Fig. 19. Mass spectra of 9g



**Fig. 20.** HRMS spectra of **9g**

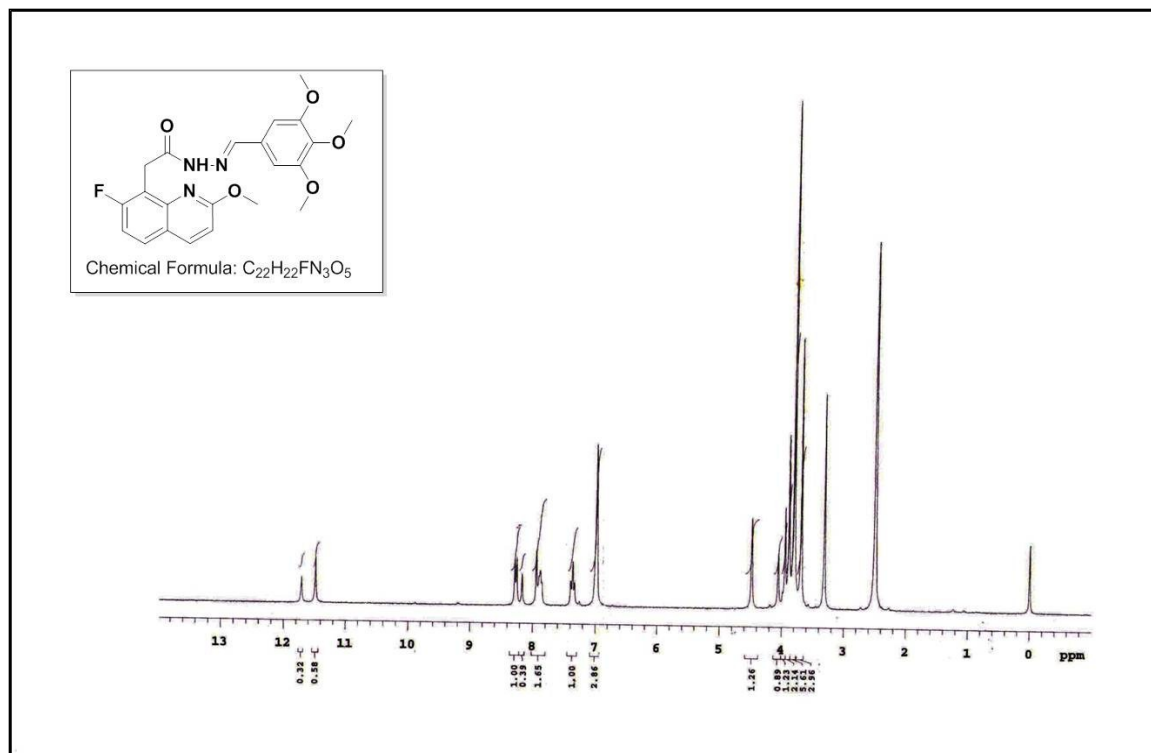


Fig. 21. <sup>1</sup>H NMR spectra of 9h



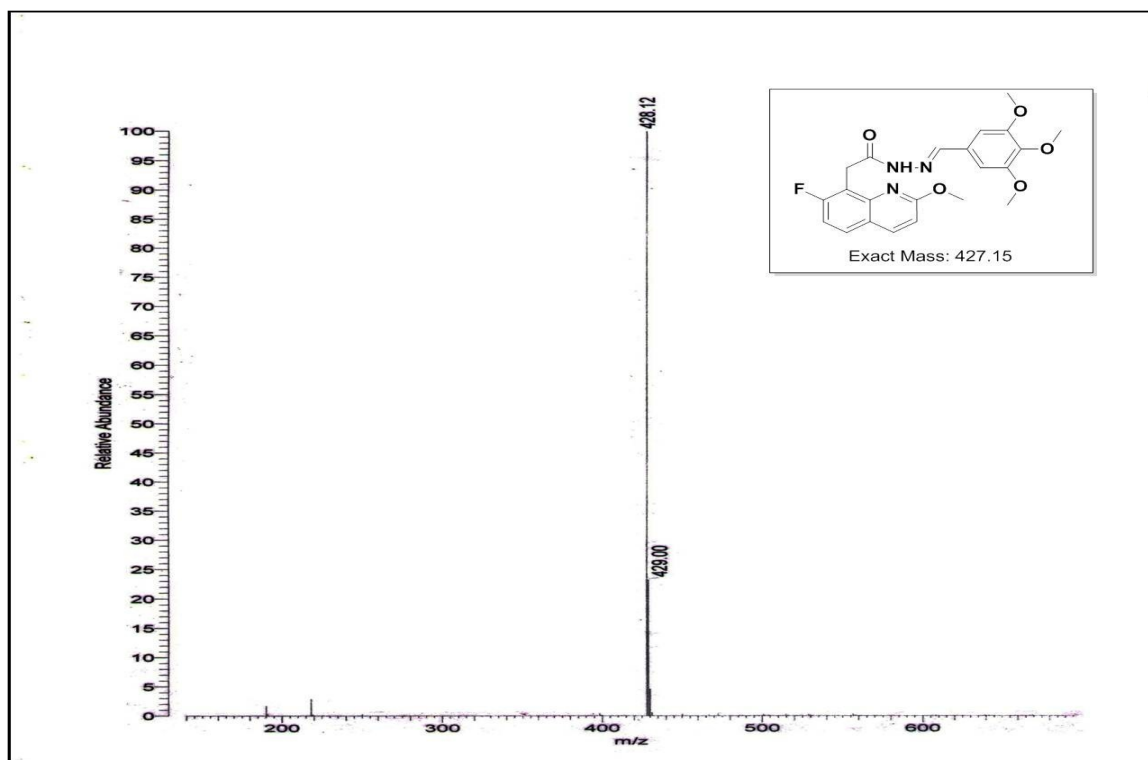
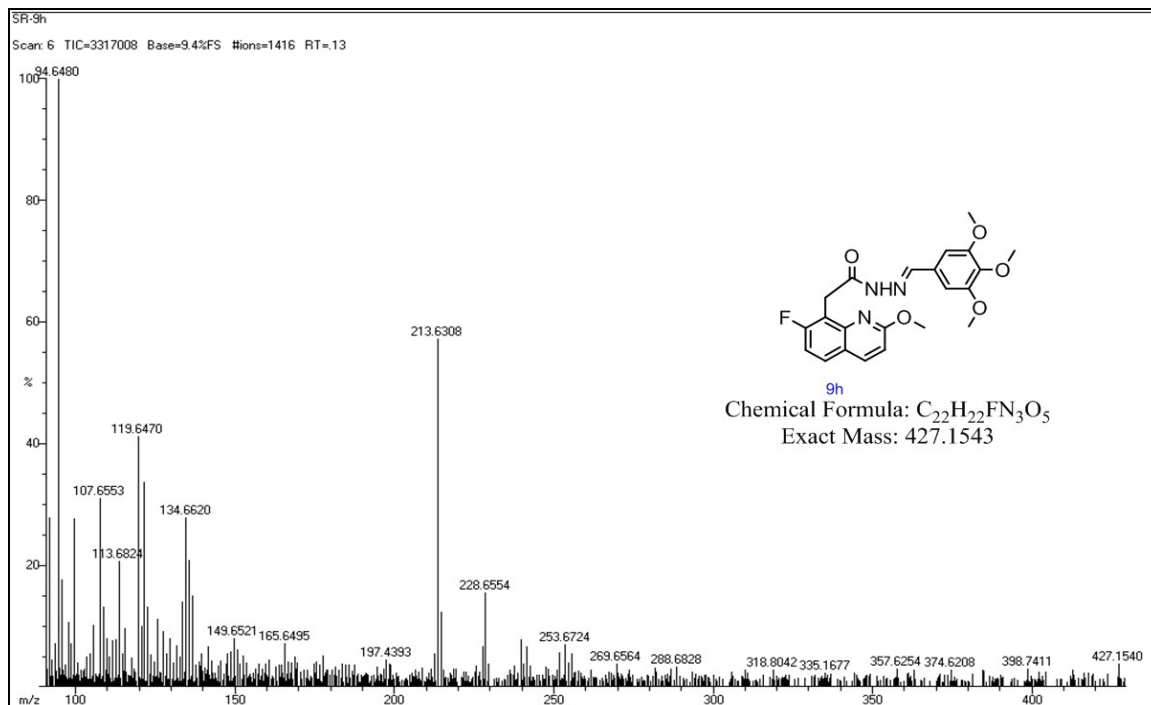


Fig. 22. Mass spectra of 9h



**Fig. 23.** HRMS spectra of **9h**

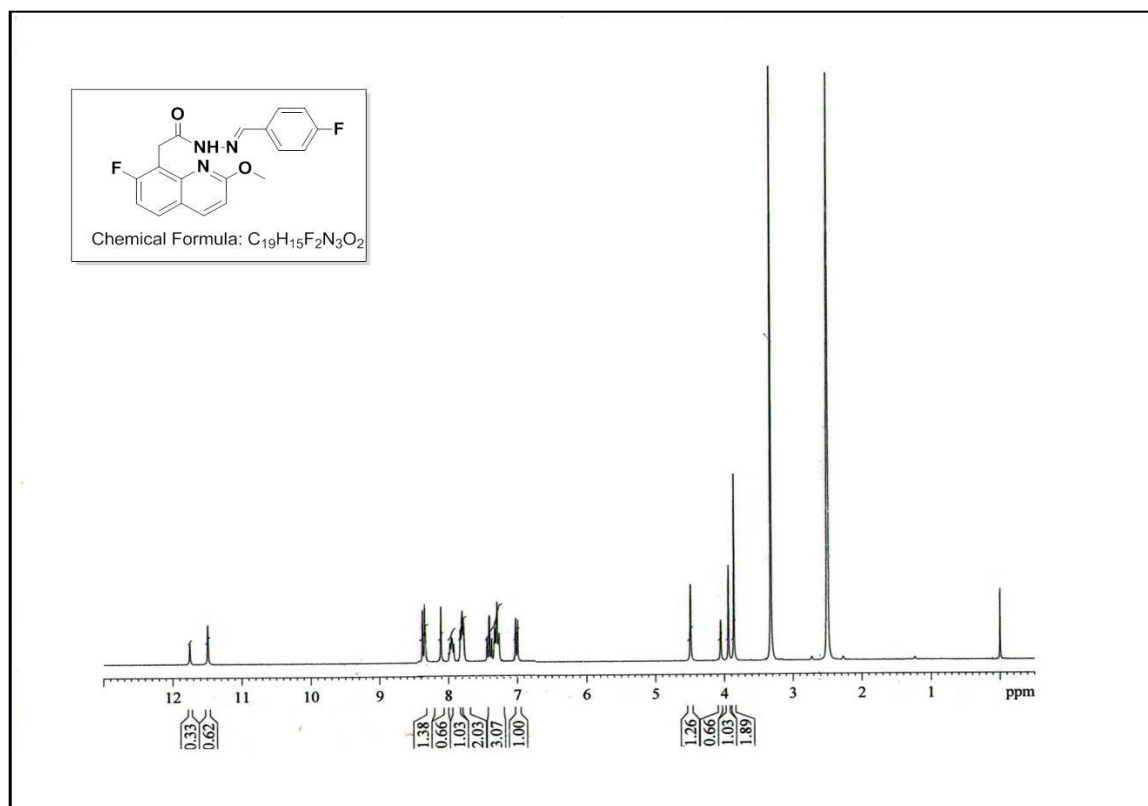


Fig. 24.  $^1H$  NMR spectra of **9i**

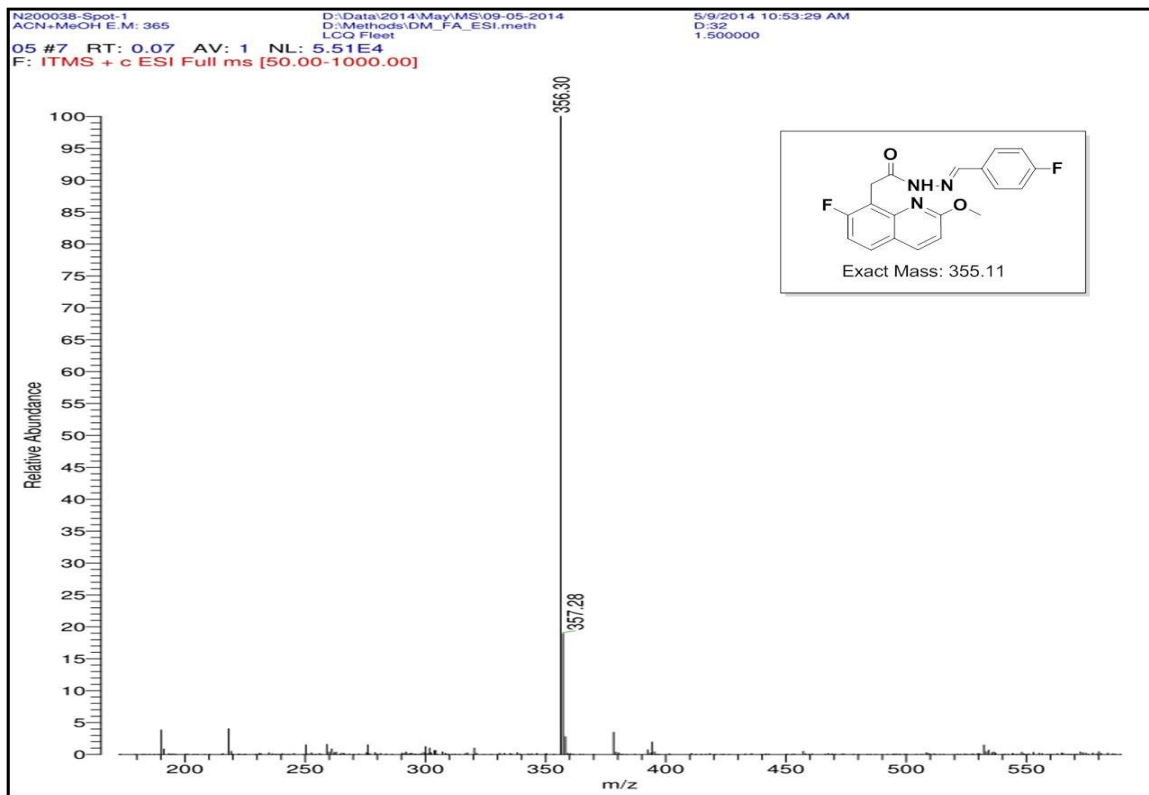


Fig. 25. Mass spectra of 9i

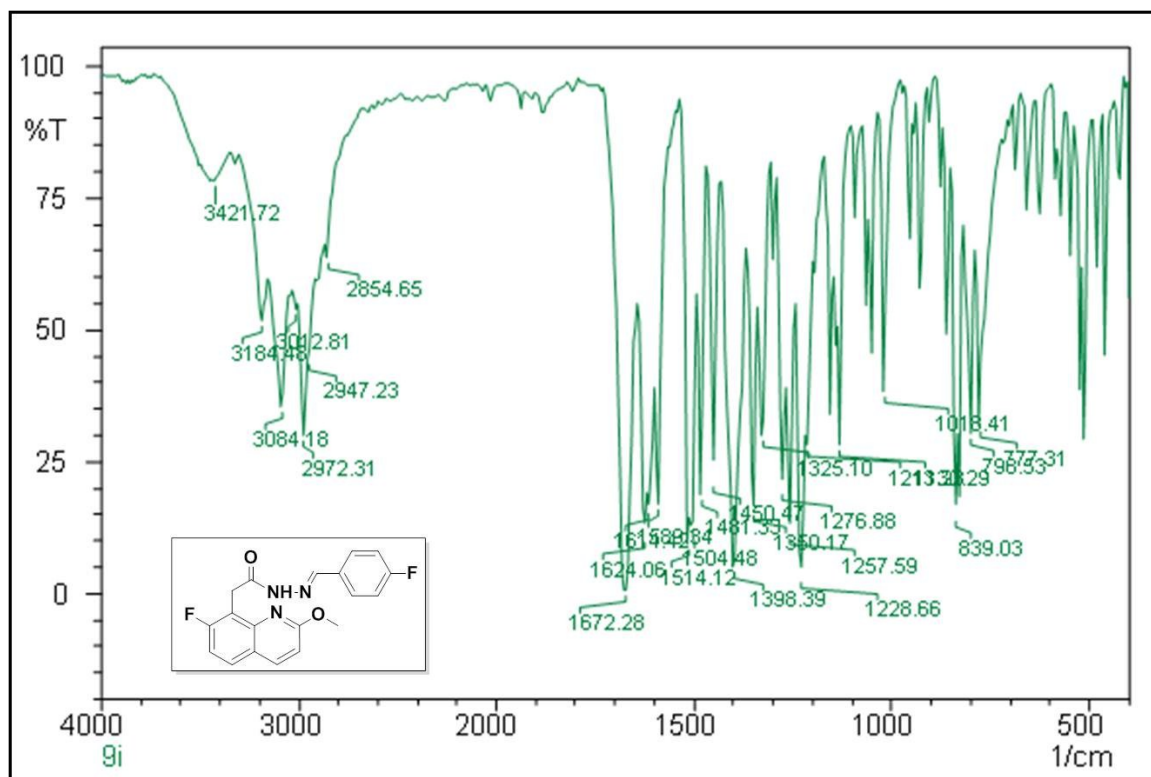


Fig. 26. IR spectra of 9i

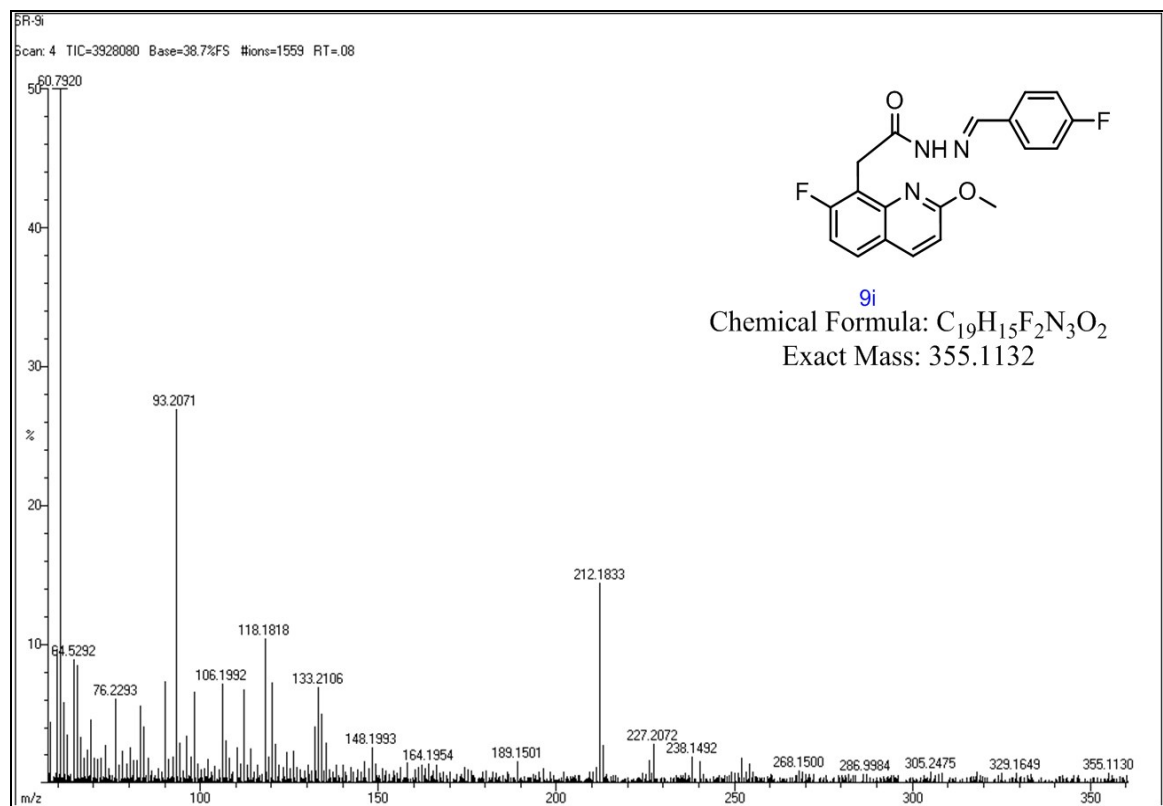
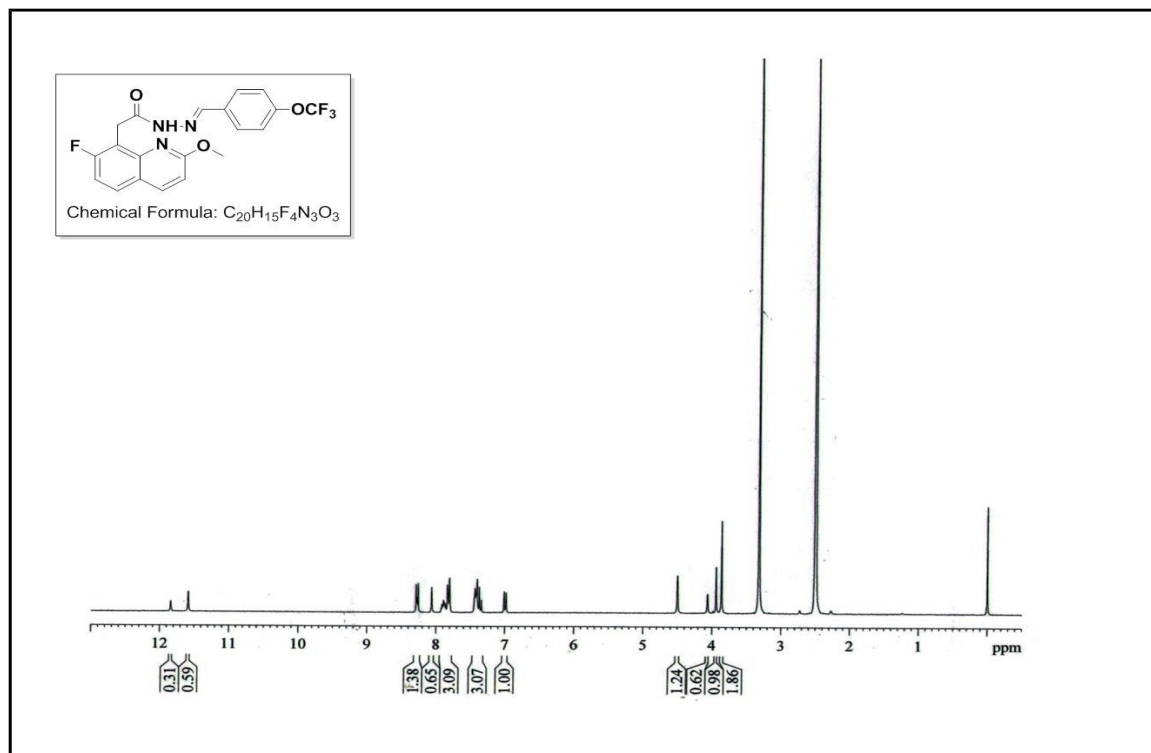


Fig. 27. HRMS spectra of **9i**



**Fig. 28.**  $^1H$  NMR spectra of **9j**

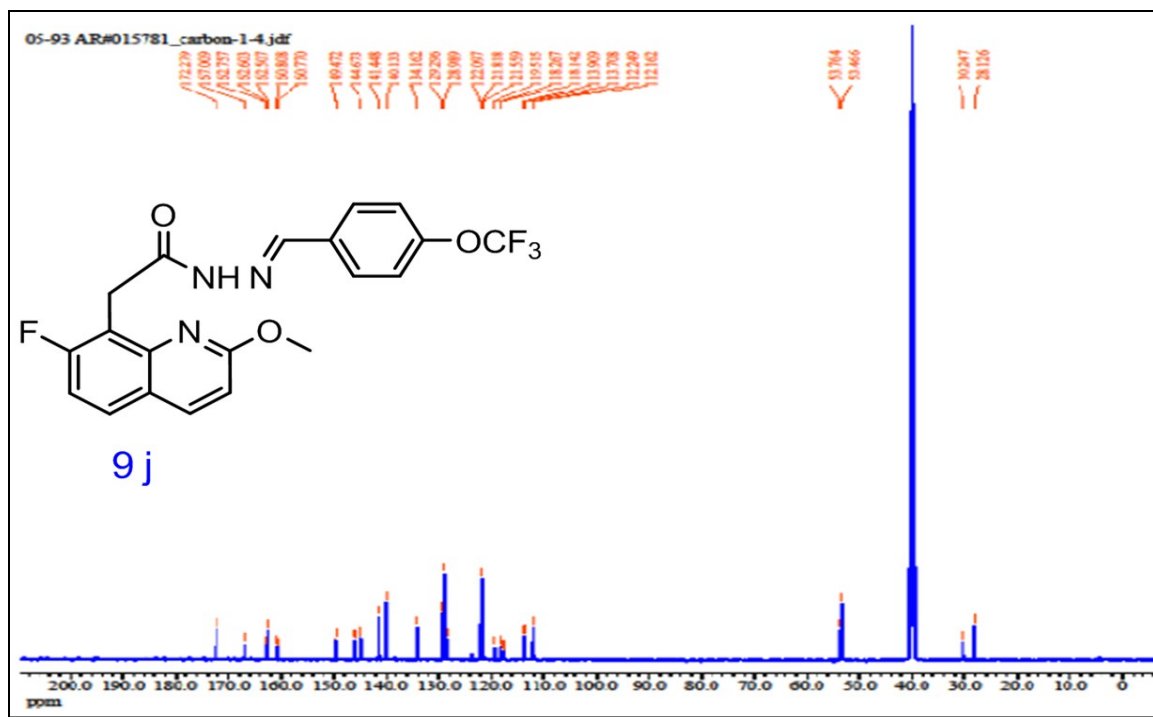


Fig. 29.  $^{13}\text{C}$  NMR spectra of 9j



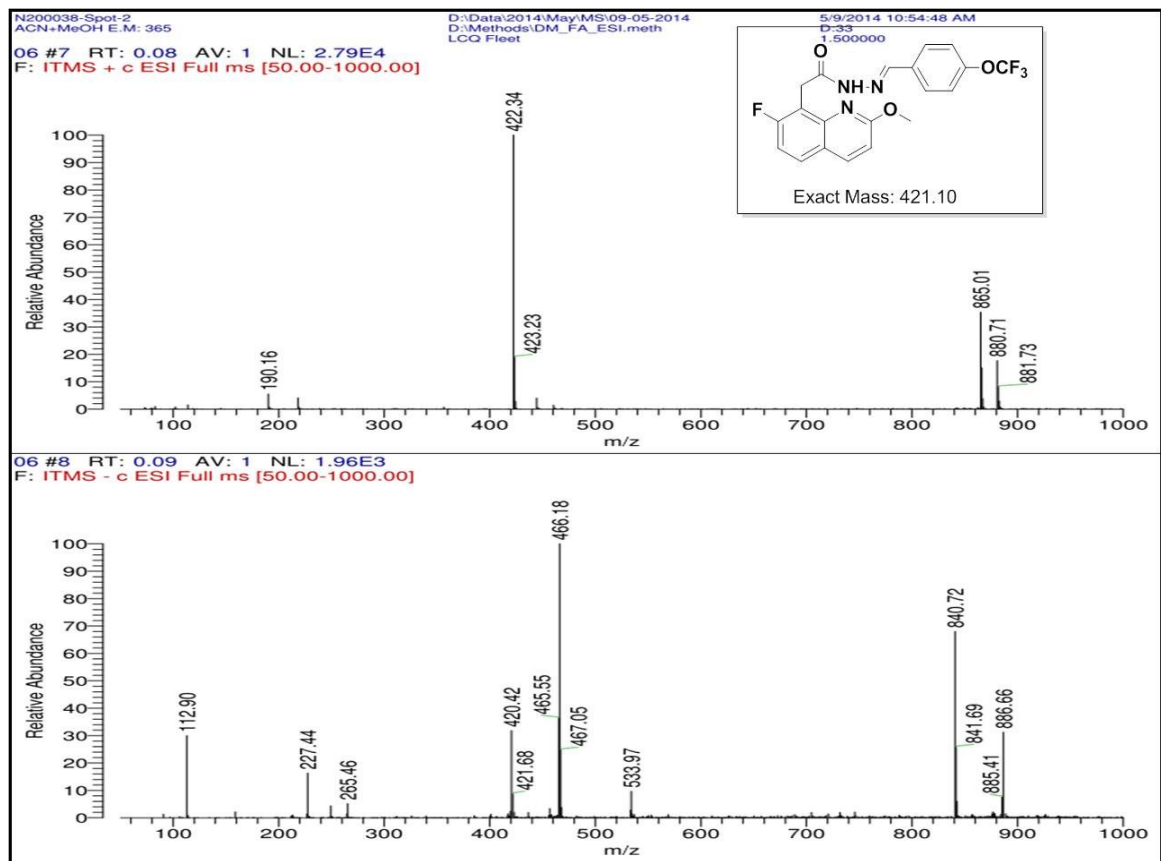
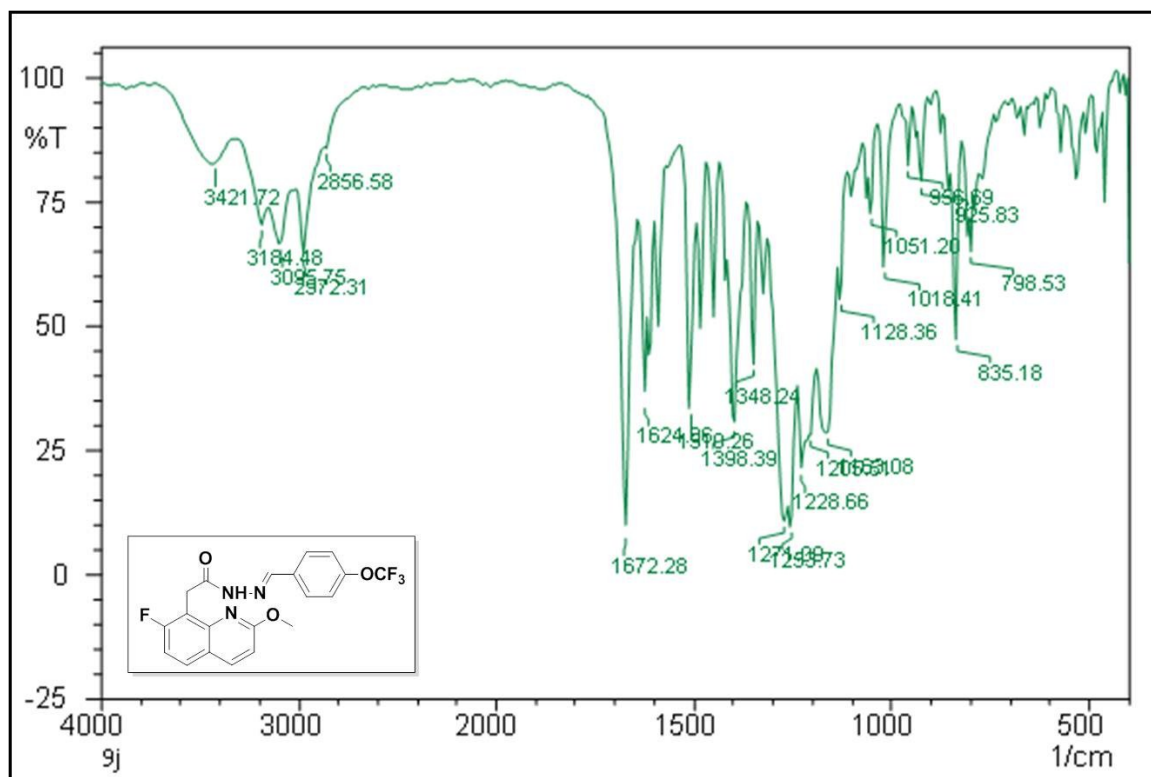
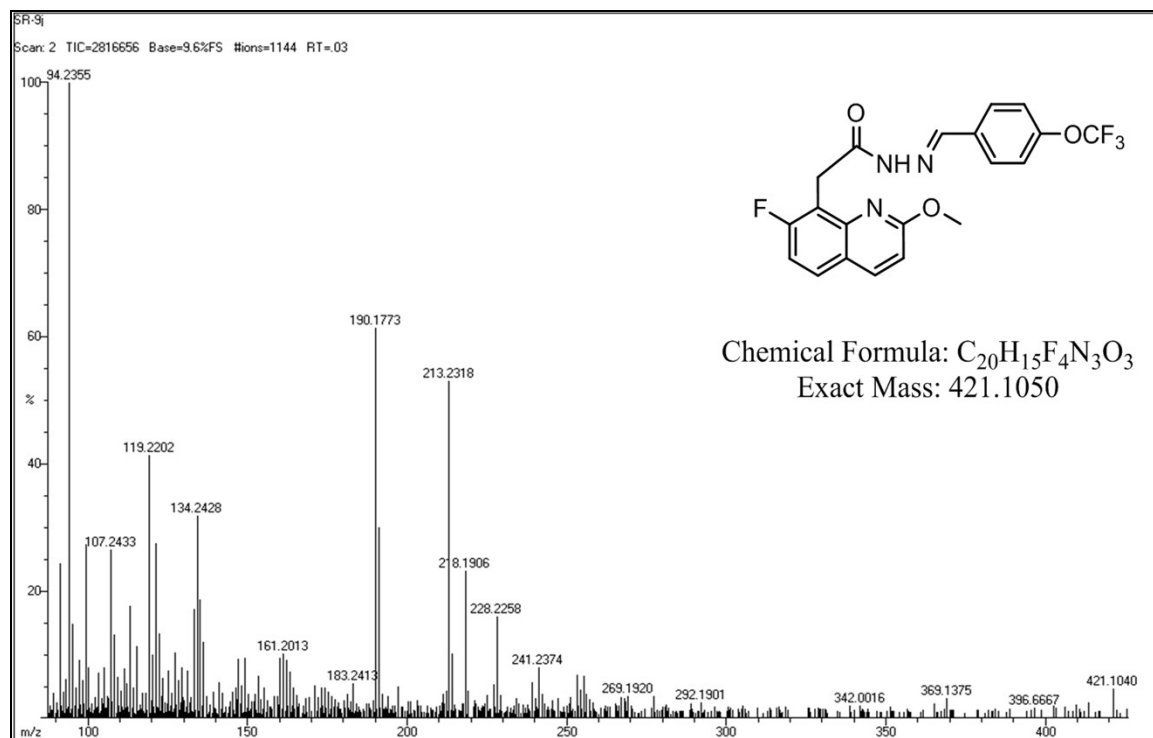


Fig. 30. Mass spectra of 9j



**Fig. 31.** IR spectra of 9j



**Fig. 32.** HRMS spectra of 9j

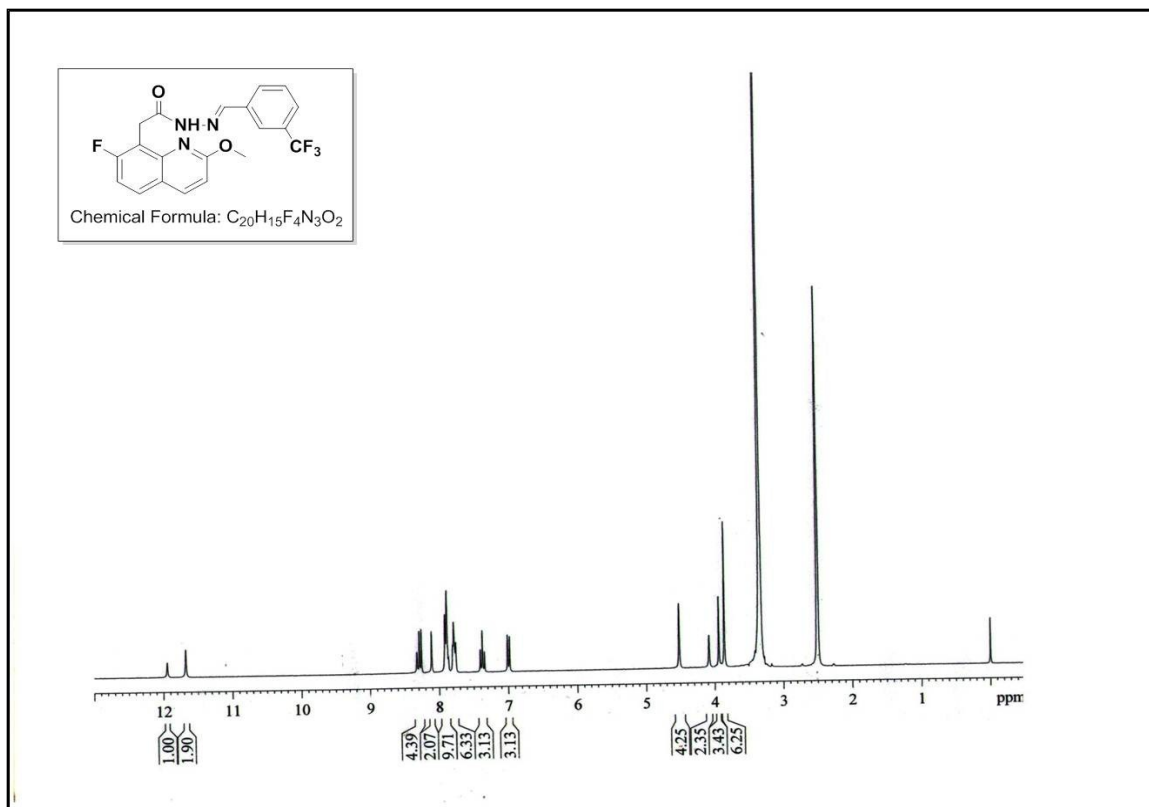


Fig. 33.  $^1H$  NMR spectra of **9k**

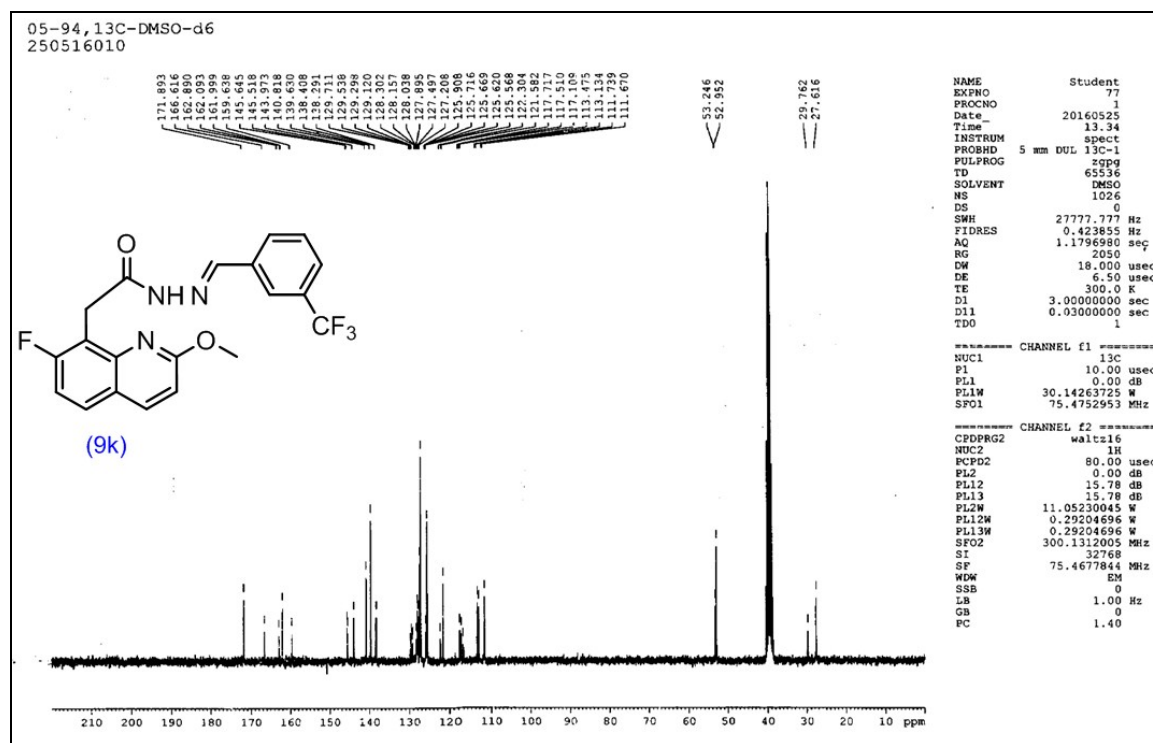


Fig. 34. <sup>13</sup>C NMR spectra of **9k**

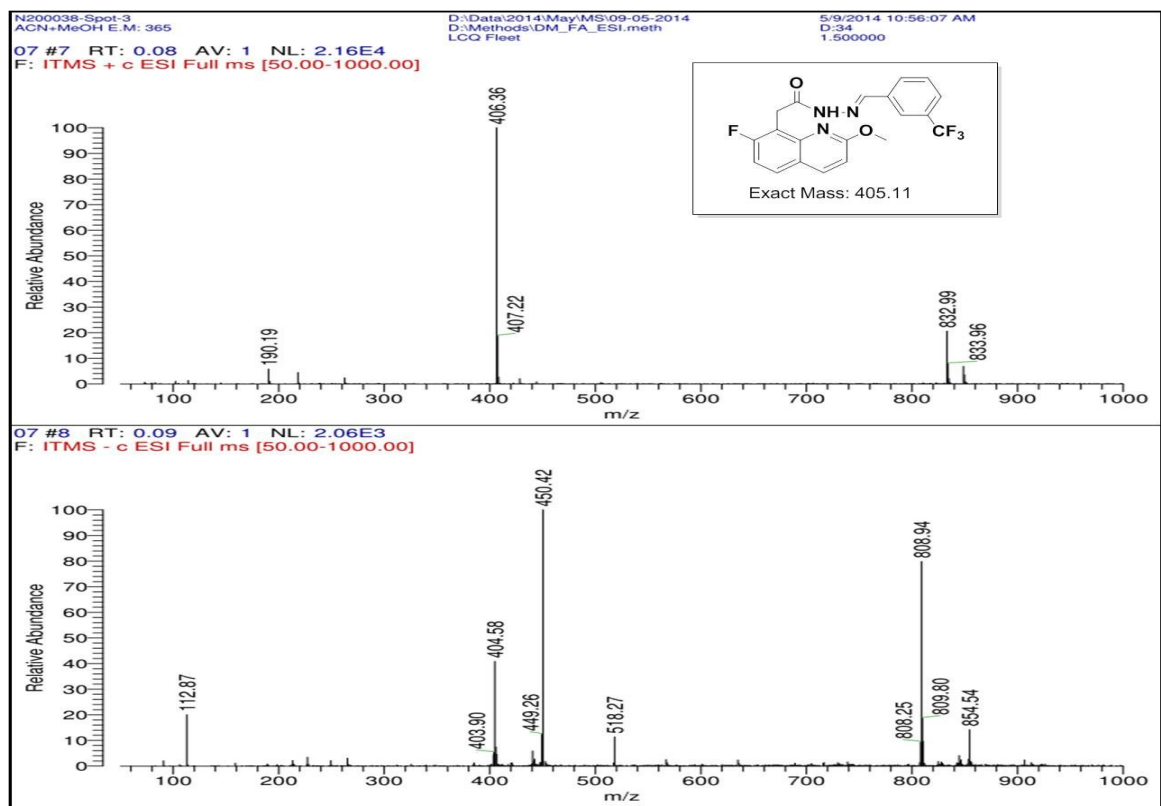


Fig. 35. Mass spectra of 9k

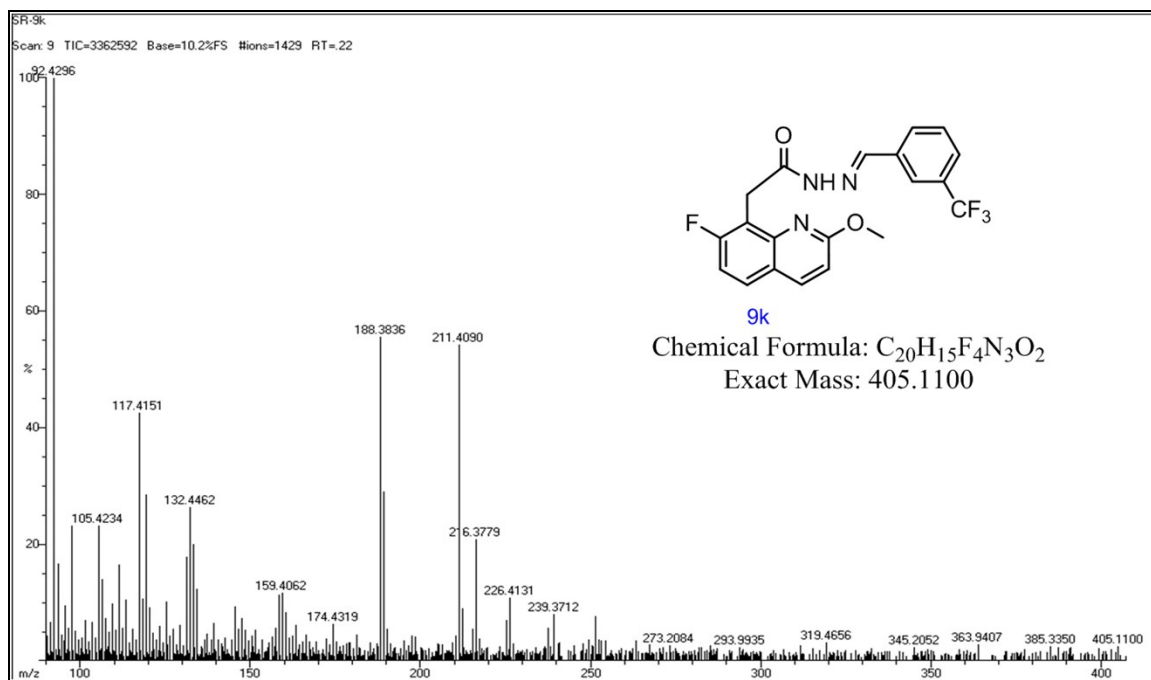


Fig. 36. HRMS spectra of **9k**

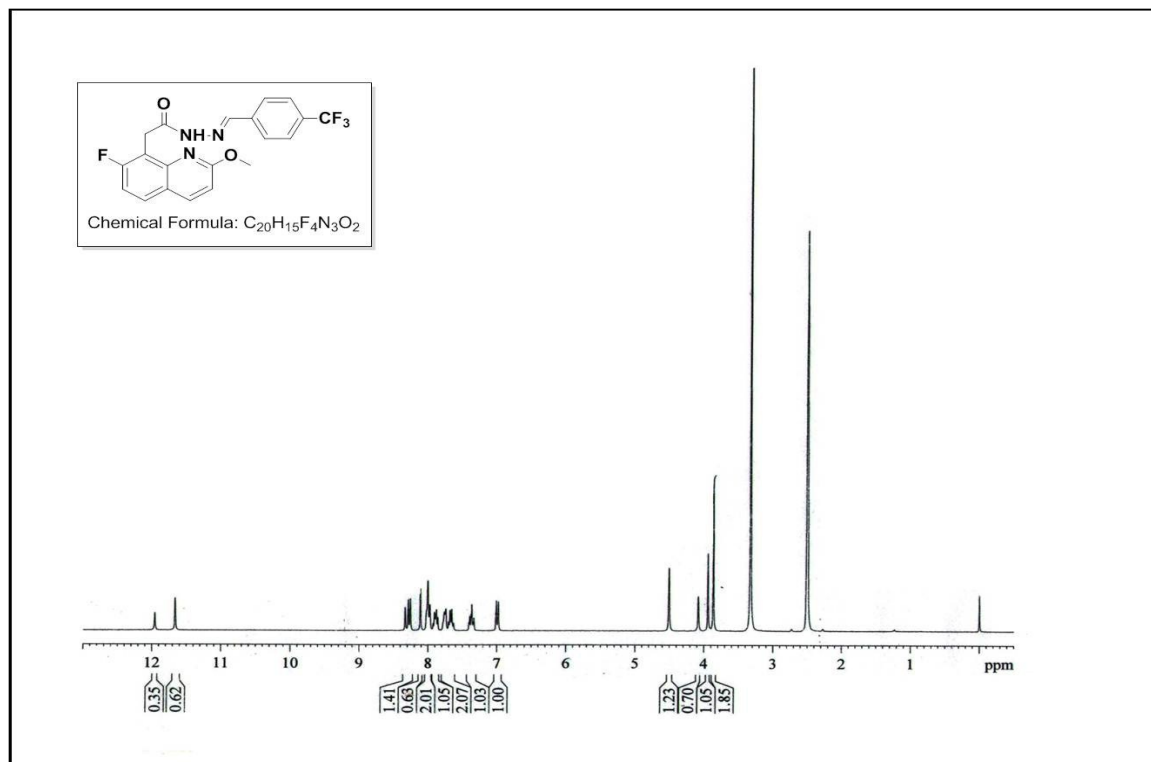


Fig. 37.  $^1H$  NMR spectra of **91**



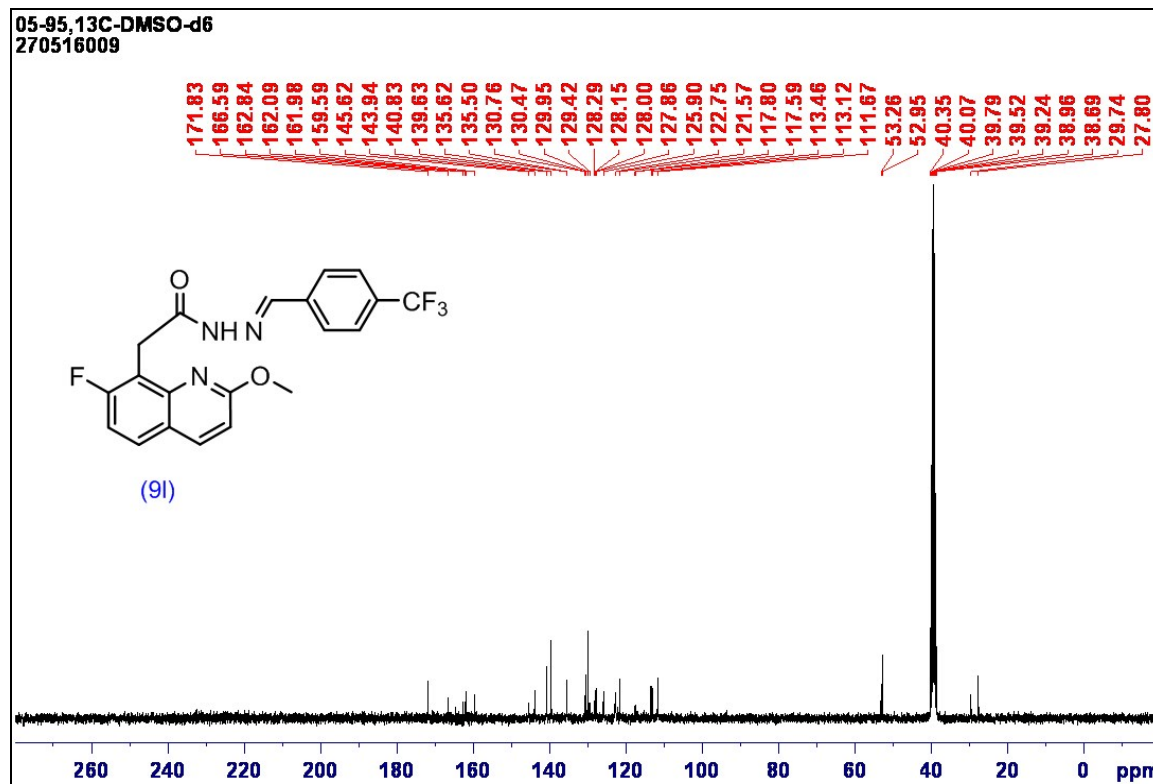


Fig. 38. <sup>13</sup>C NMR spectra of 9l

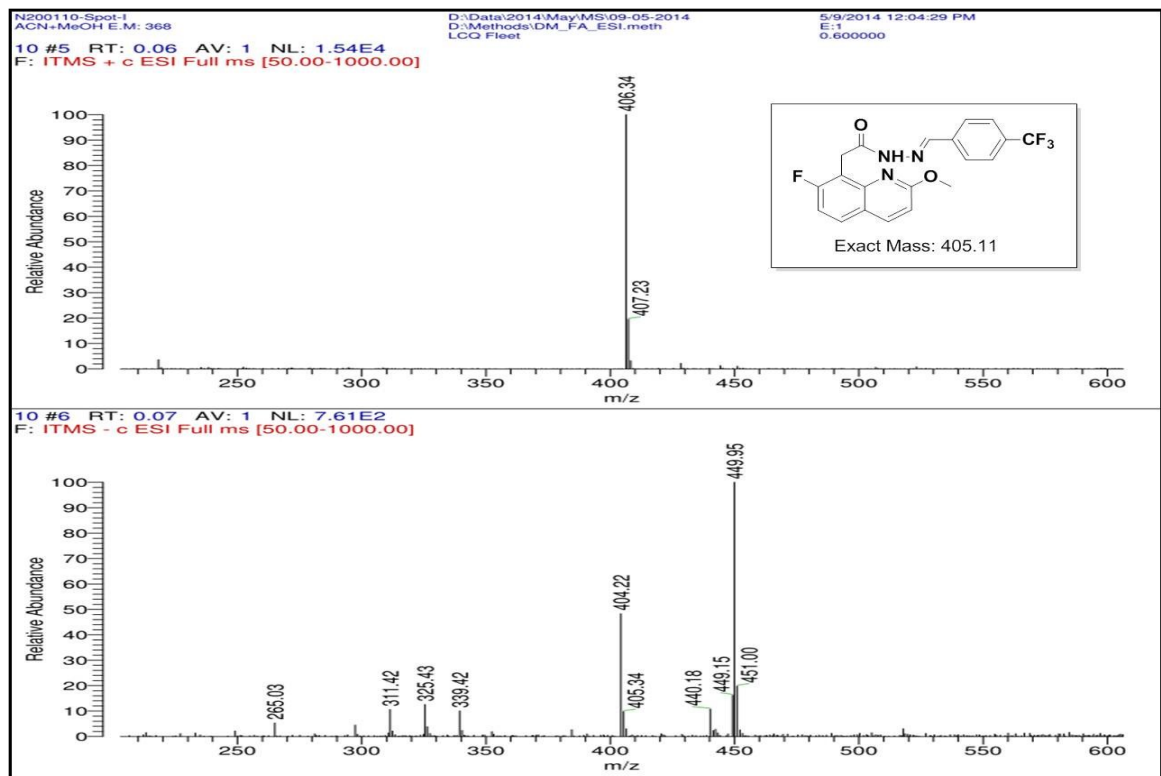
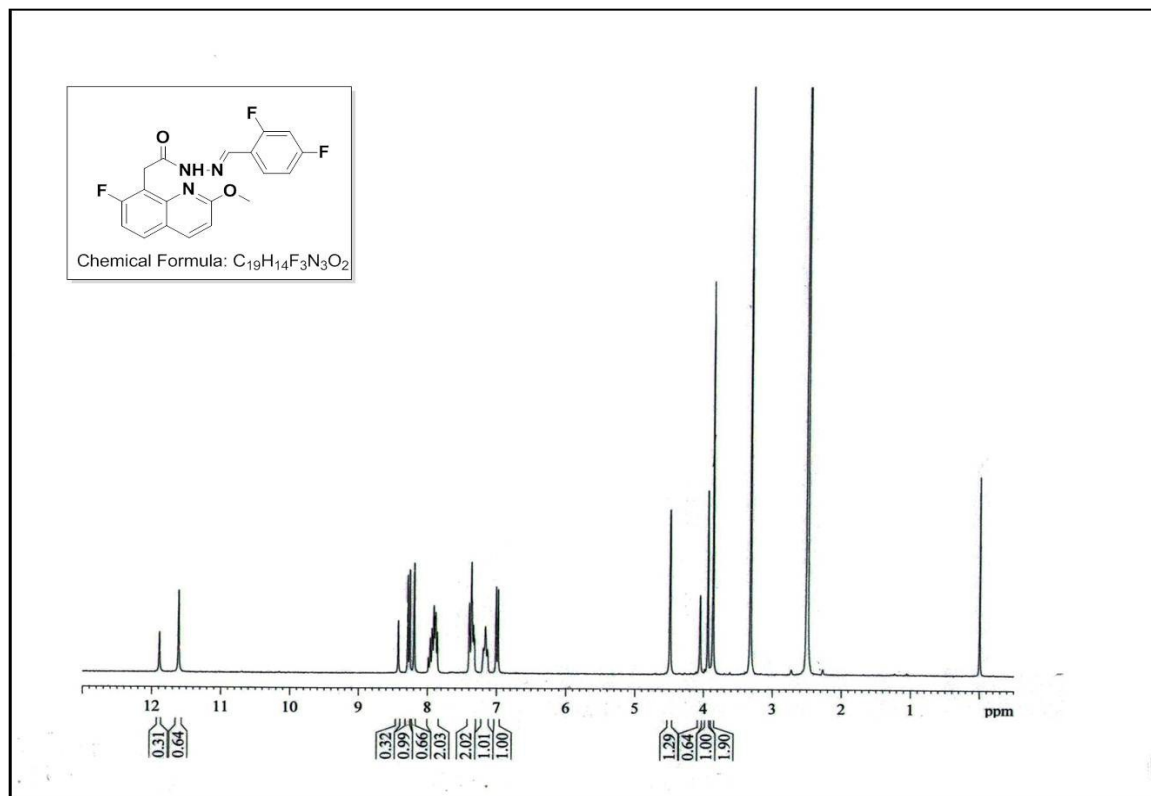


Fig. 39. Mass spectra of 91



**Fig. 40.**  $^1H$  NMR spectra of **9m**

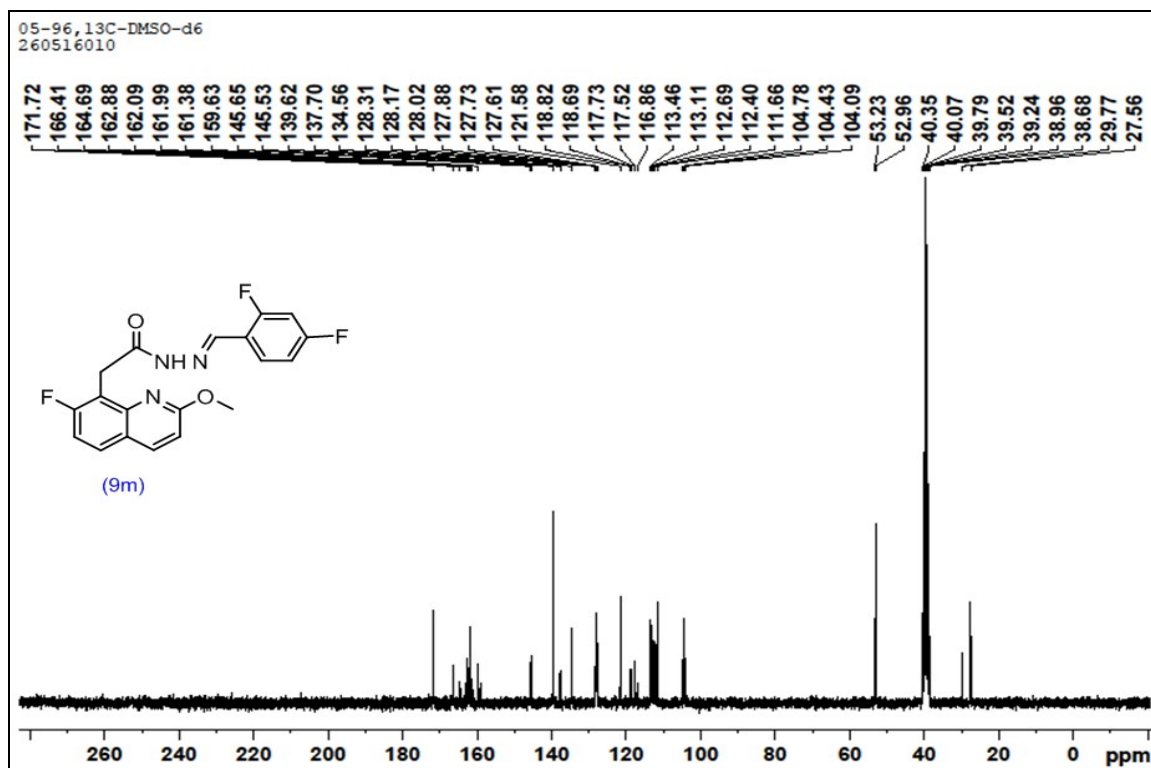


Fig.41.  $^{13}\text{C}$  NMR spectra of 9m

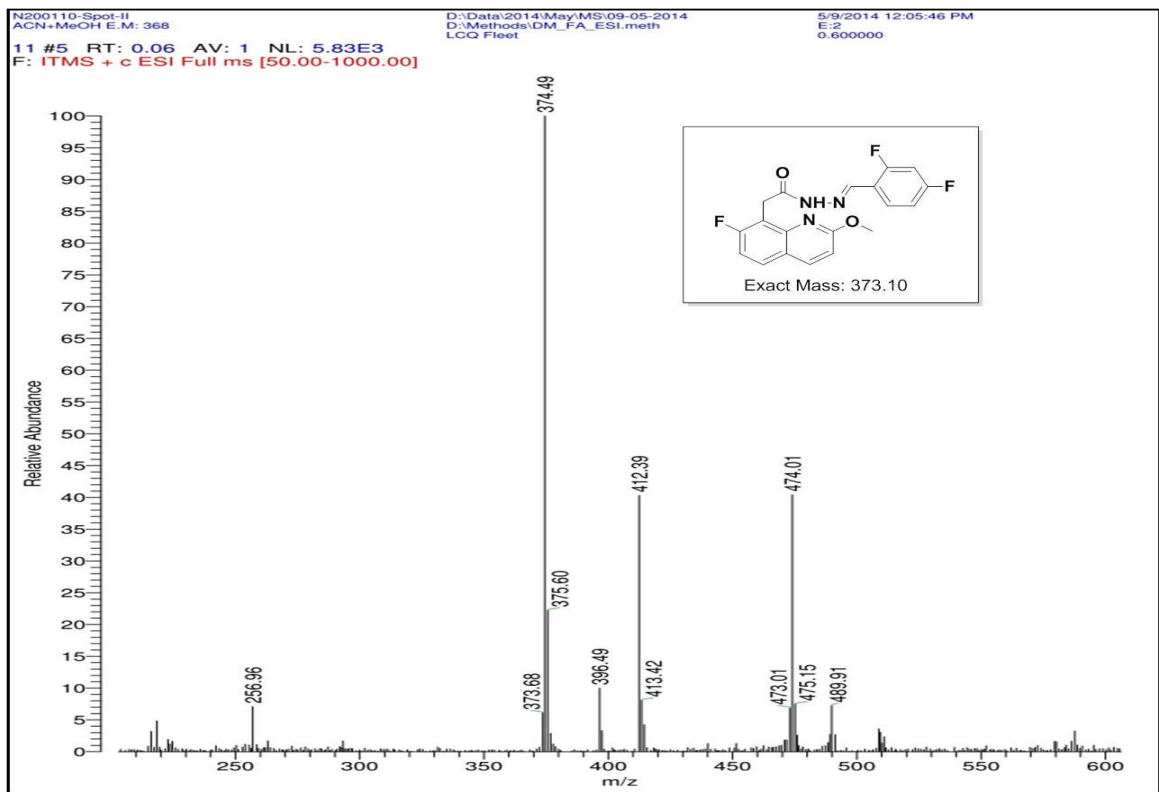


Fig. 42. Mass spectrum of 9m

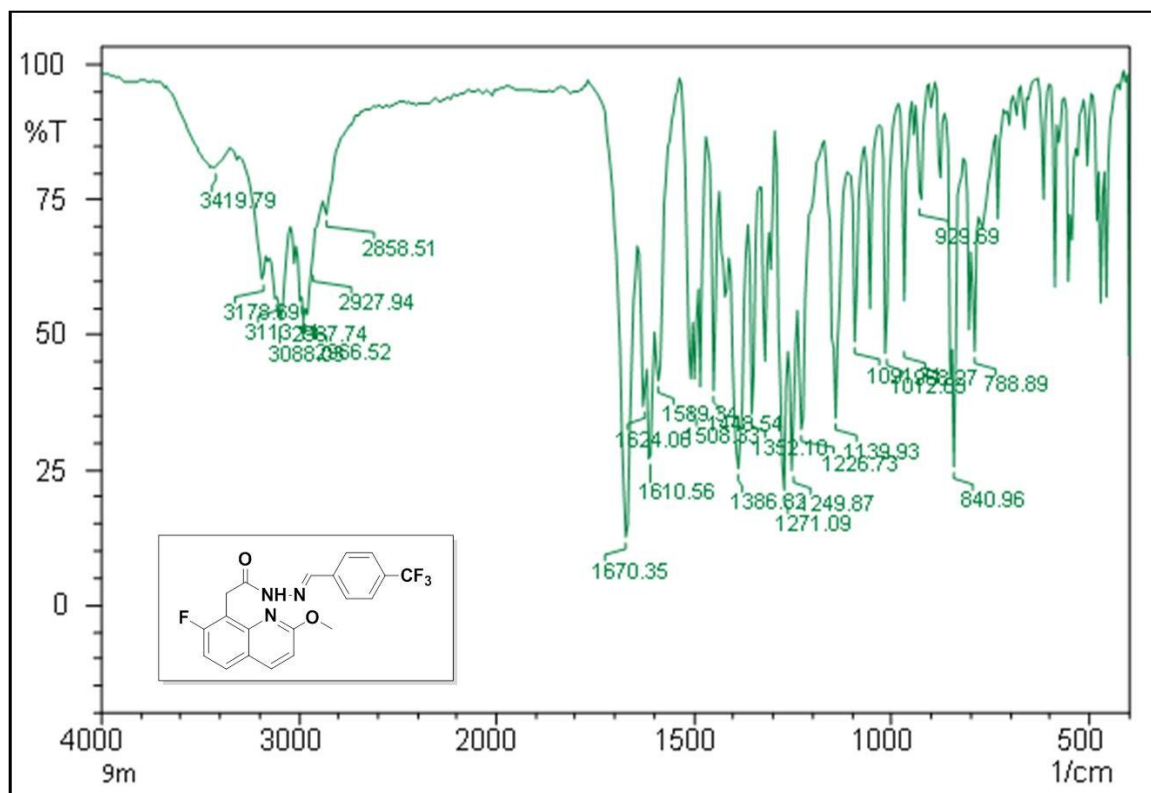


Fig. 43. IR spectra of 9m

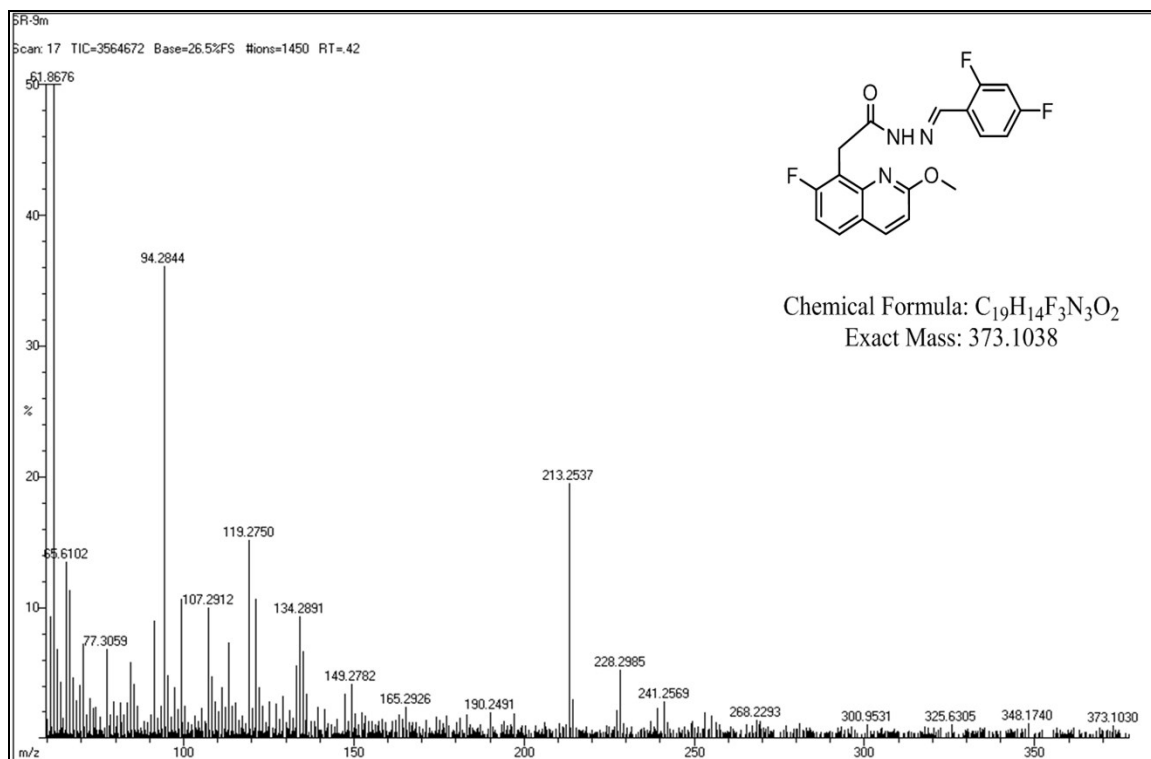


Fig.44. HRMS spectra of 9m

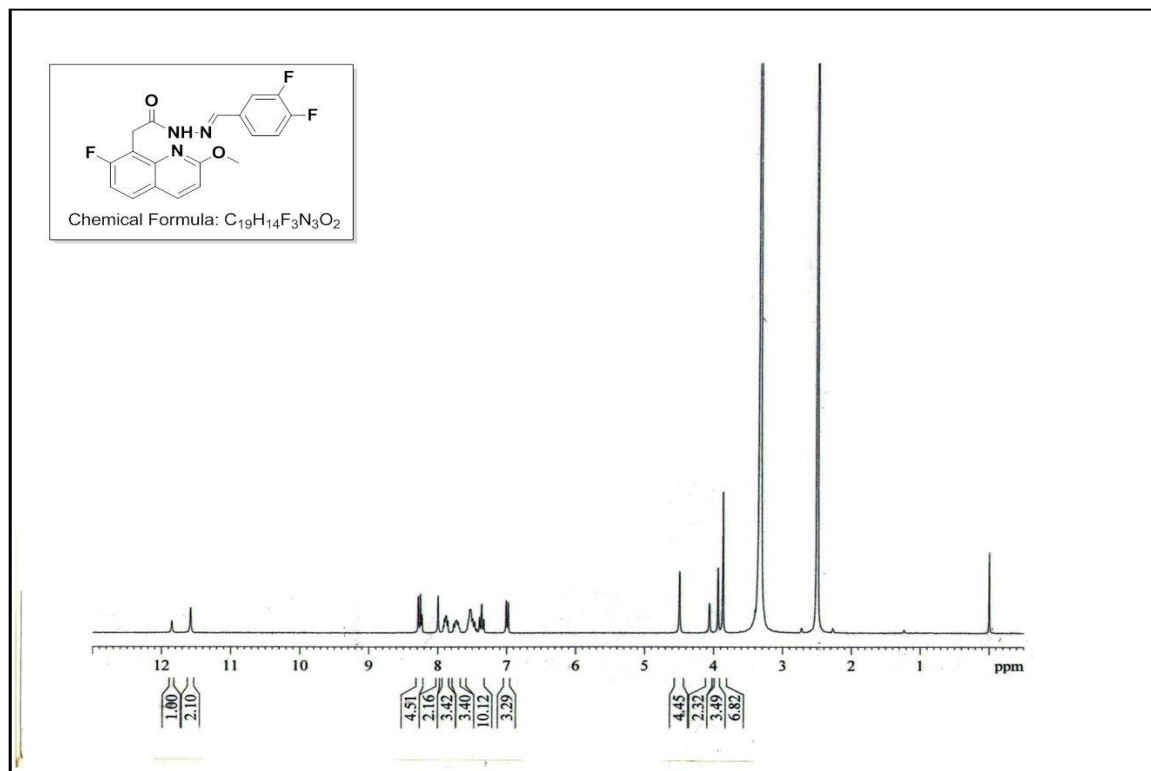


Fig. 45.  $^1H$  NMR spectra of **9n**



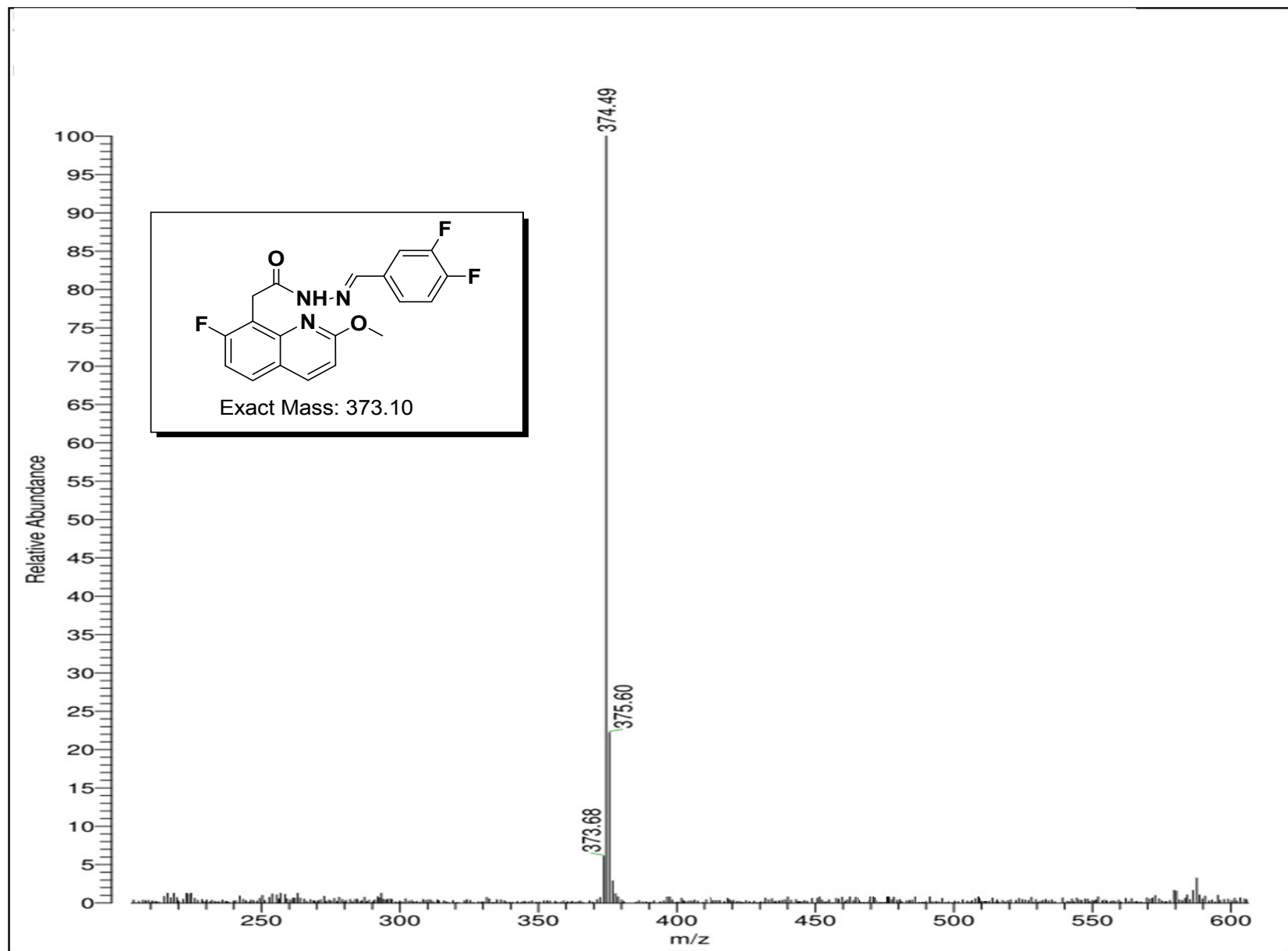
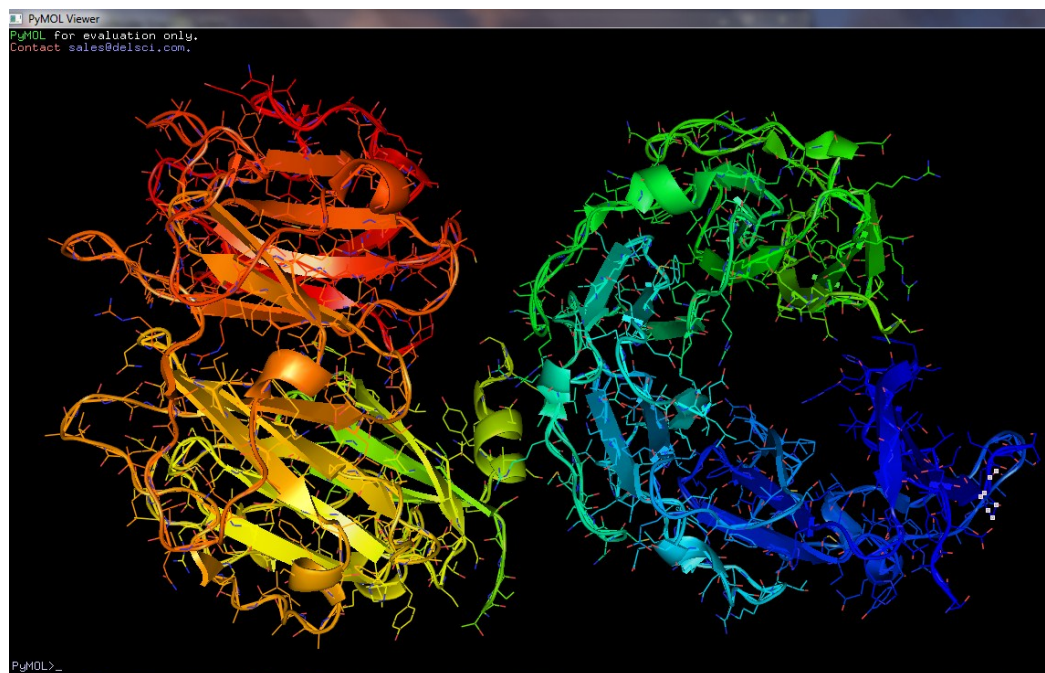
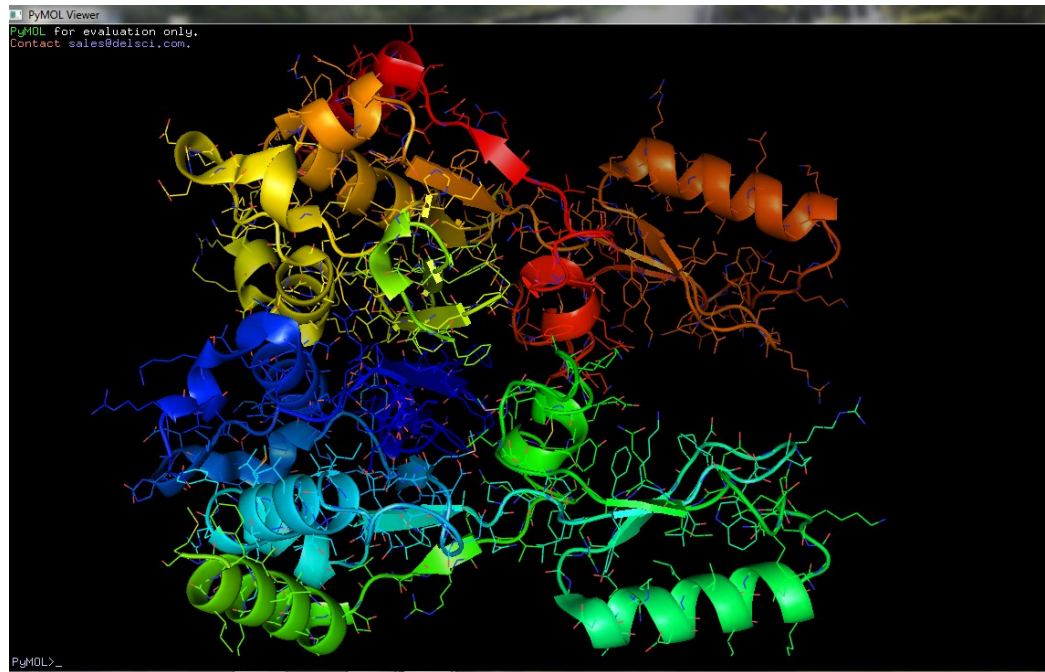


Fig. 46. Mass spectrum of **9n**



**Figure 47.** PyMOL view of DNA gyrase A (PDB ID: 1ZI0)



**Figure 48.** PyMOL view of DNA gyrase B (PDB ID: 2ZJT)

**Table 2.** *In vivo* efficacy of quinoline acetohydrazide derivatives **9a-n** for demonstrating antibacterial activity against selected pathogens

<b>Entry</b>	<b>Compounds</b>	<b>IC<sub>50</sub>(mg/mL)</b>
		<i>S.aureus</i>
1	9a	19.71
2	9b	18.24
3	9c	23.45
4	9d	19.28
5	9e	12.84
6	9f	11.47
7	9g	9.26
8	9h	6.14
9	9i	1.38
10	9j	1.98
11	9k	1.44
12	9l	1.05
13	9m	0.14
14	9n	0.19
15	Clorobiocin	0.04