Novel PPAR-γ Agonists as Potential Neuroprotective Agents Against Alzheimer's Disease: Rational Design, Synthesis, *In Silico* Evaluation, PPAR-γ Binding Assay, Transactivation and Expression Studies

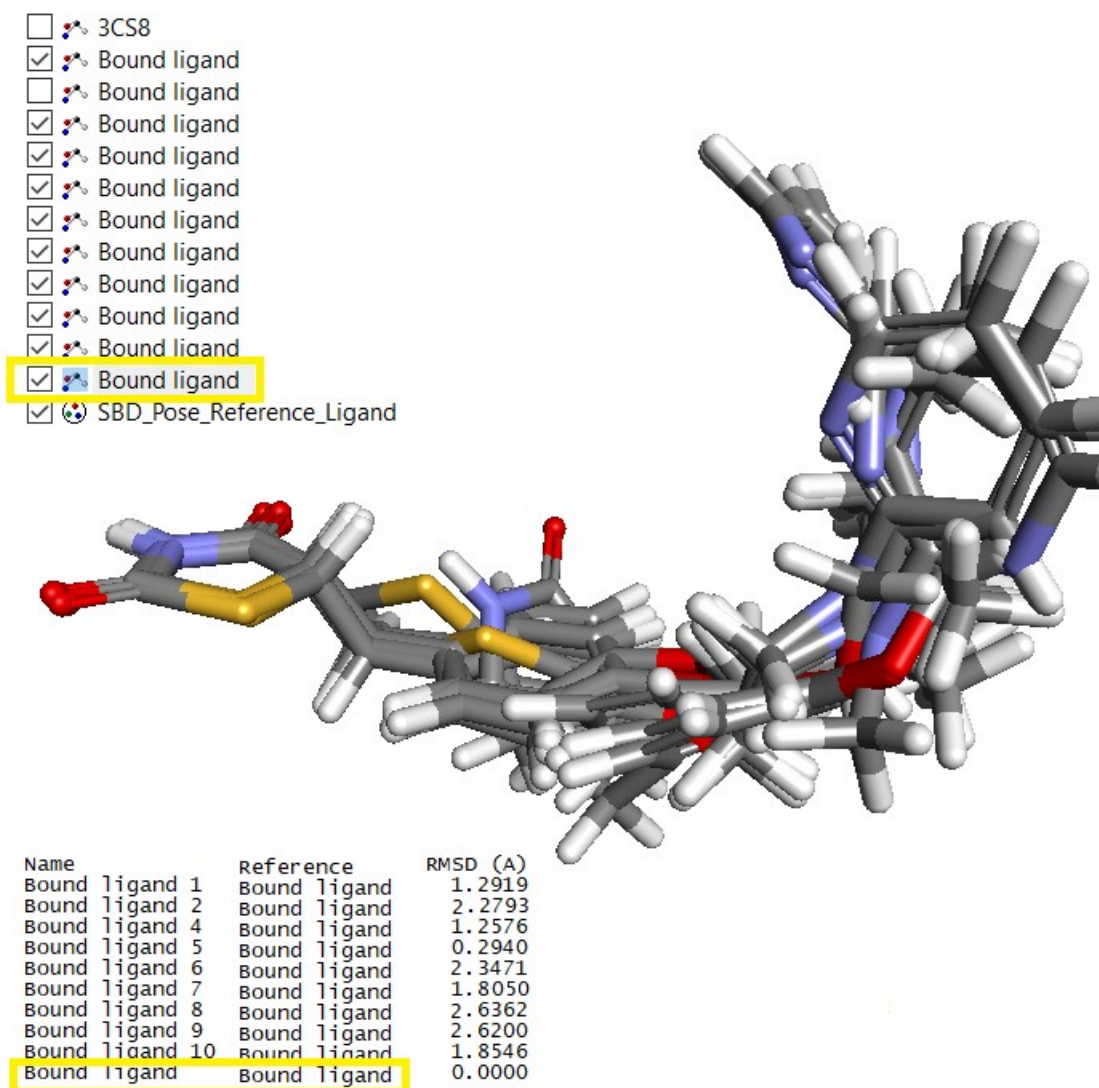Priya D[1], Umme Hani[2], Nazima Haider[3], Sirajunisa Talath[4], Dhivya Shanmugarajan[1], Prabitha P[1], Archana P[1], B. R. Prashantha Kumar[*1]

1. *Department of Pharmaceutical Chemistry, JSS College of Pharmacy, Mysuru 570 015. JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagara, Mysuru 570015, India.*

2. *Department of Pharmaceutics, College of Pharmacy, King Khalid University, Abha 62529, Saudi Arabia.*

3. *Department of Pathology, College of Medicine, King Khalid University, Abha 62529, Saudi Arabia.*

4. *Department of Pharmaceutical Chemistry, RAK College of Pharmacy, RAK Medical and Health Sciences University, Ras Al Khaimah 11172, United Arab Emirates.*

Supplementary Material

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DOCKING VALIDATION

Name	Reference	RMSD (A)
Bound ligand 1	Bound ligand	1.2919
Bound ligand 2	Bound ligand	2.2793
Bound ligand 4	Bound ligand	1.2576
Bound ligand 5	Bound ligand	0.2940
Bound ligand 6	Bound ligand	2.3471
Bound ligand 7	Bound ligand	1.8050
Bound ligand 8	Bound ligand	2.6362
Bound ligand 9	Bound ligand	2.6200
Bound ligand 10	Bound ligand	1.8546
Bound ligand	Bound ligand	0.0000

Fig. S1: Docked poses of reference ligand.

RMSD is the one the best method to validate the docking parameters. The docking RMSD validation is processed by comparing the bound ligand co-ordinates with docked poses. From the above figure and table it was observed that except few poses, other docked poses are less than 2.5 Å.
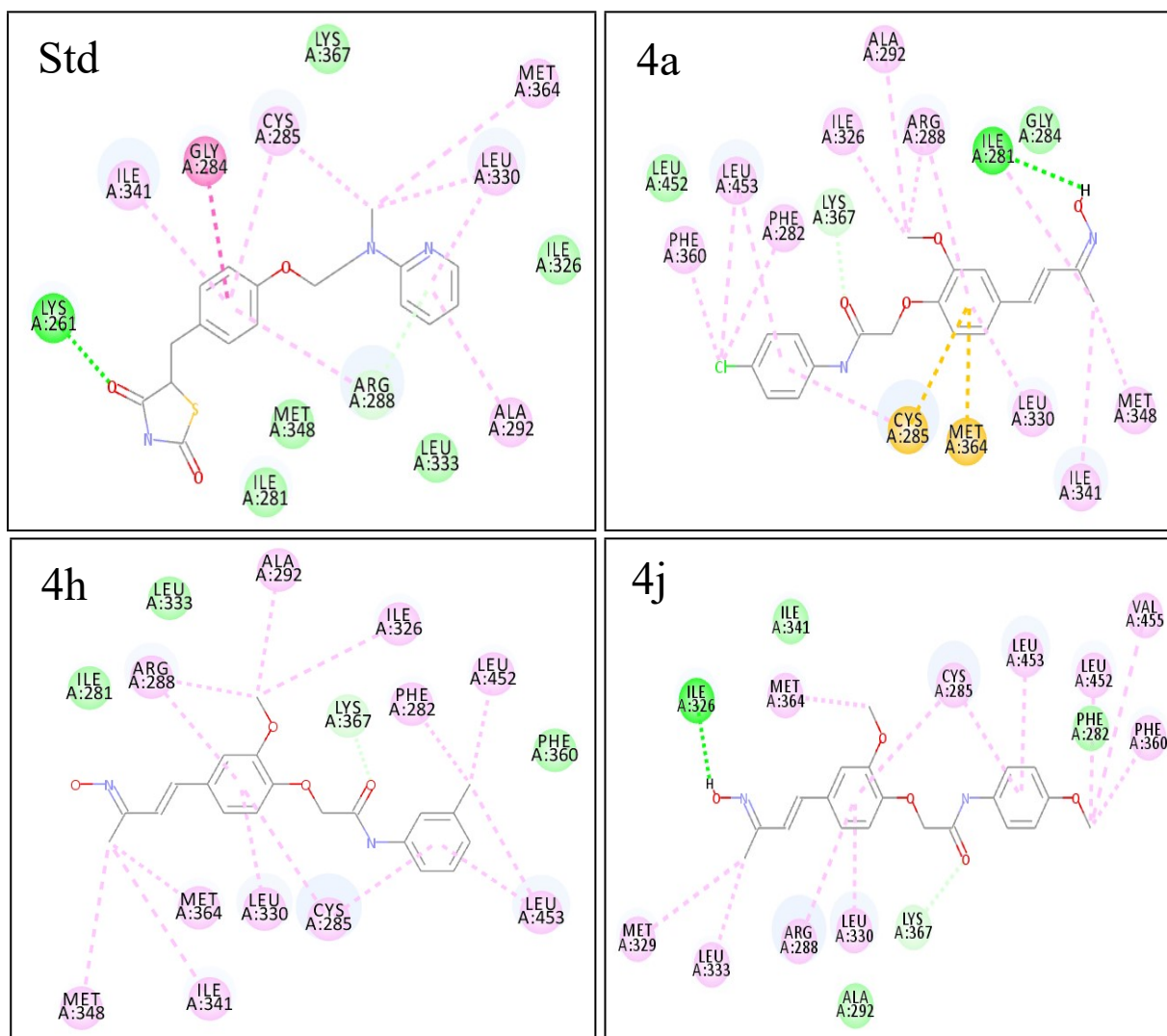
Fig. S2: 2D receptor – ligand interactions of the compounds 4a, 4h, 4j and Std (rosiglitazone) in the active binding site of PPAR-γ.

ANALYTICAL SPECTRA

Compound: 3a
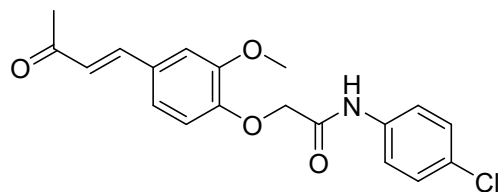
Fig. S3. Chemical structure of compound **3a**
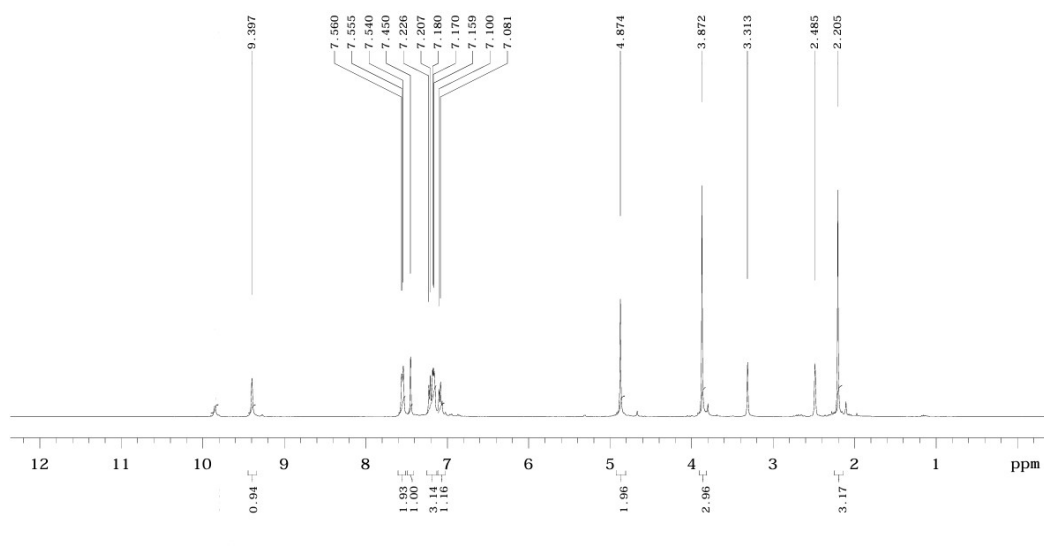
Fig. S4. ^{1}H-NMR spectrum of compound **3a**

Compound: 4a
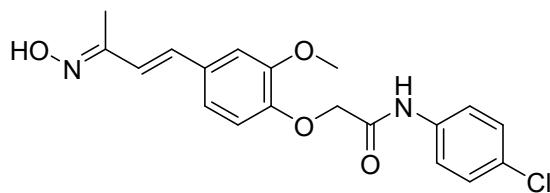
Fig. S5. Chemical structure of compound **4a**
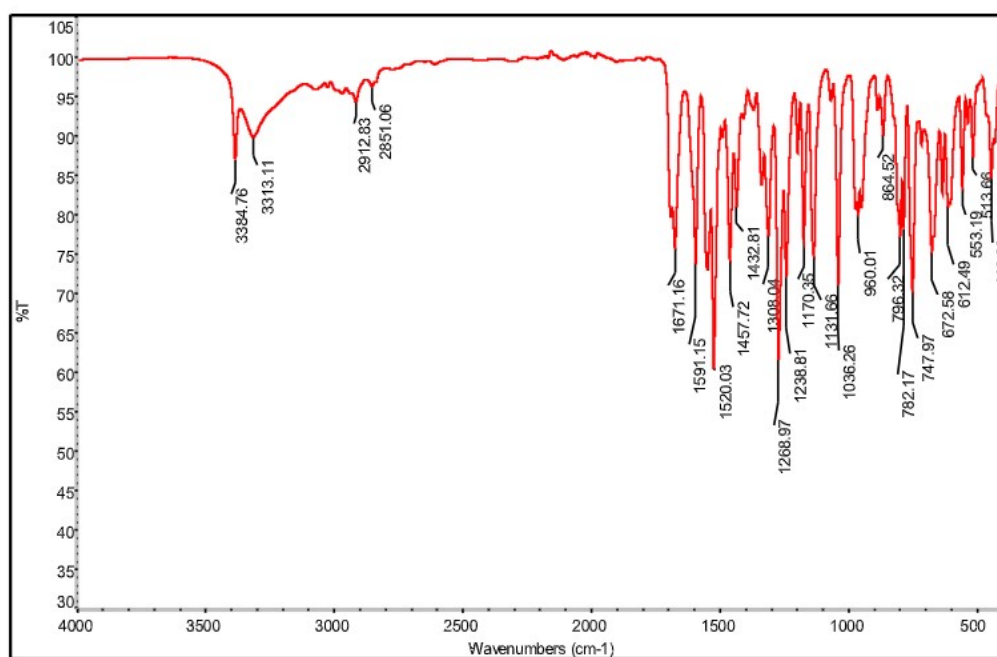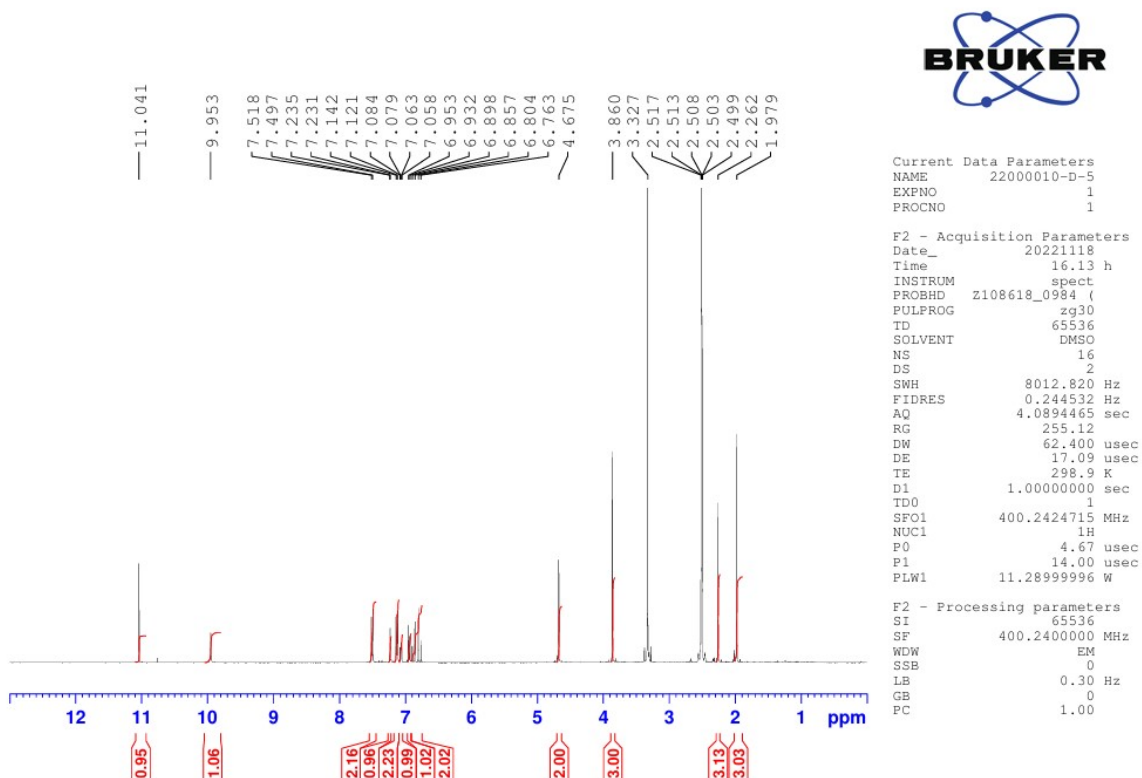

Fig. S6. IR spectrum of compound **4a.**
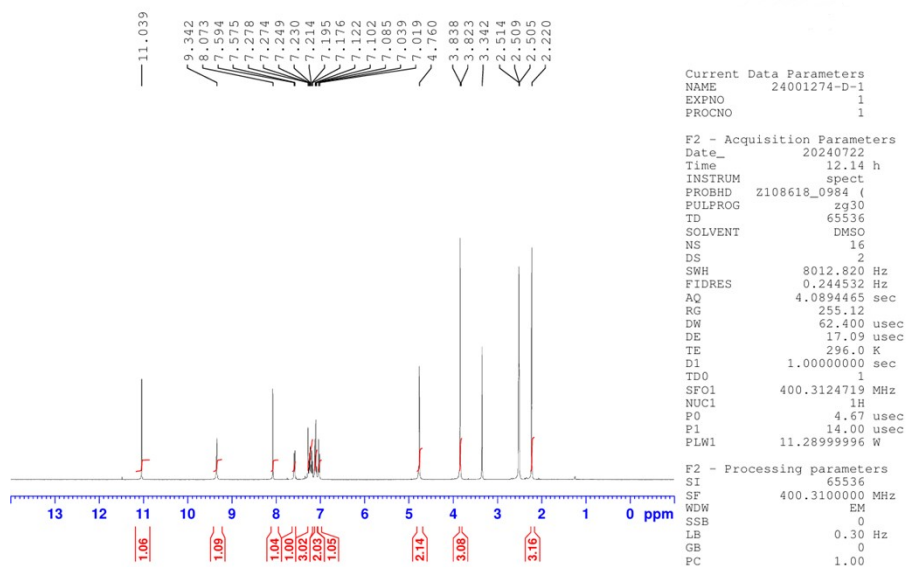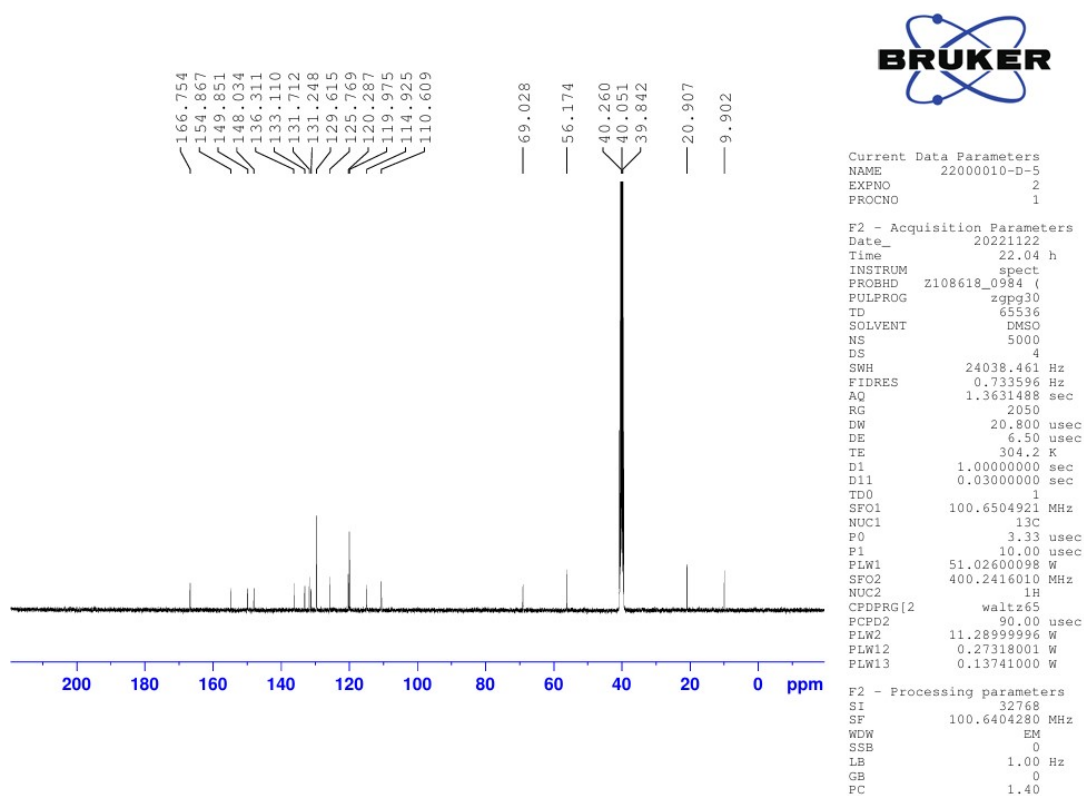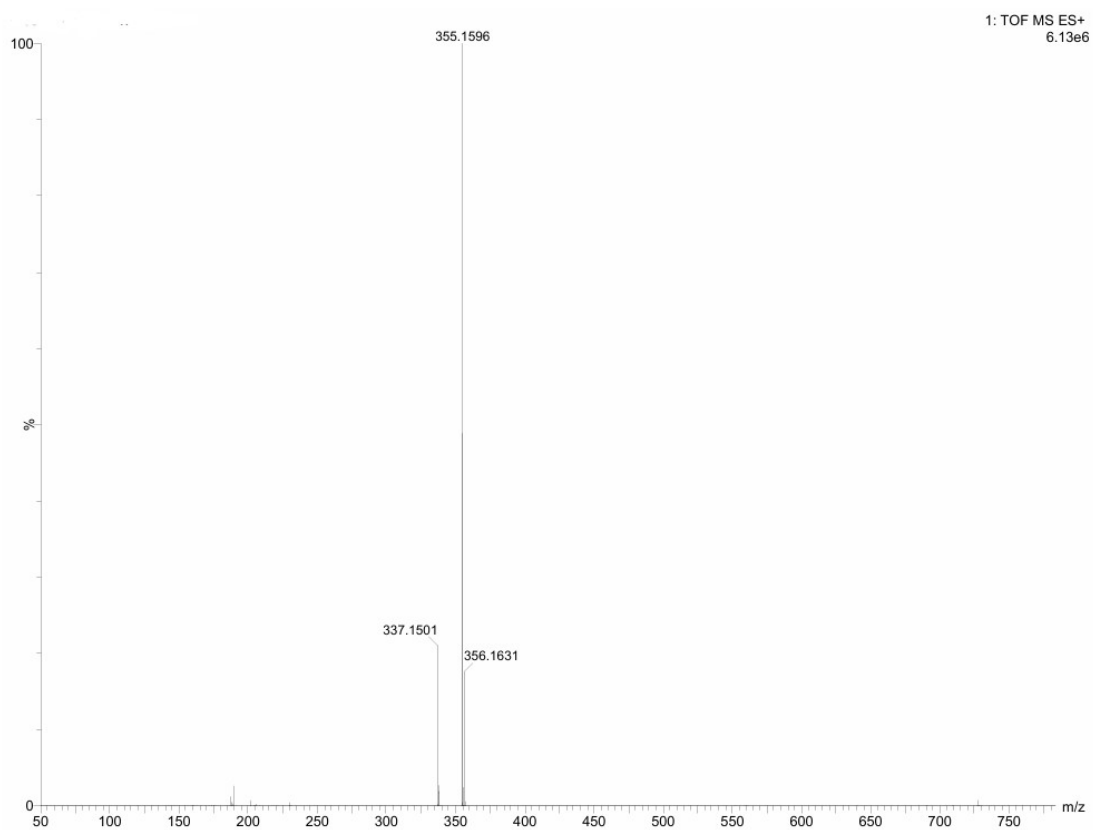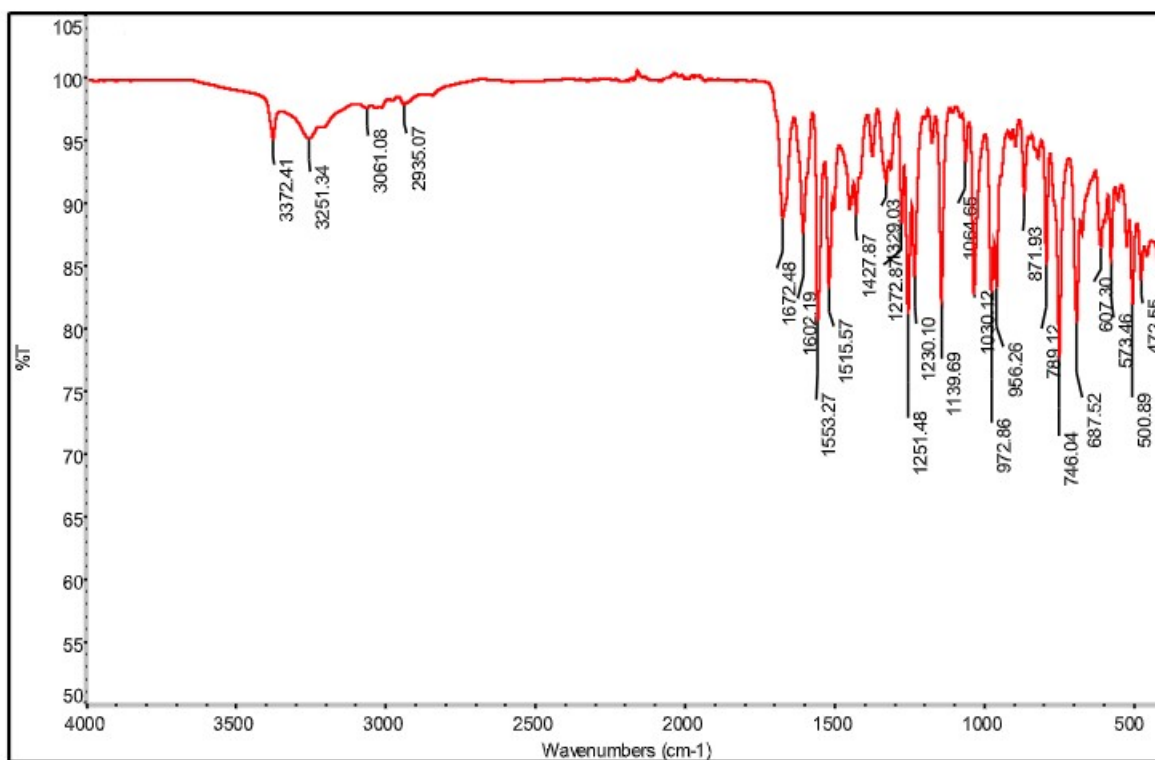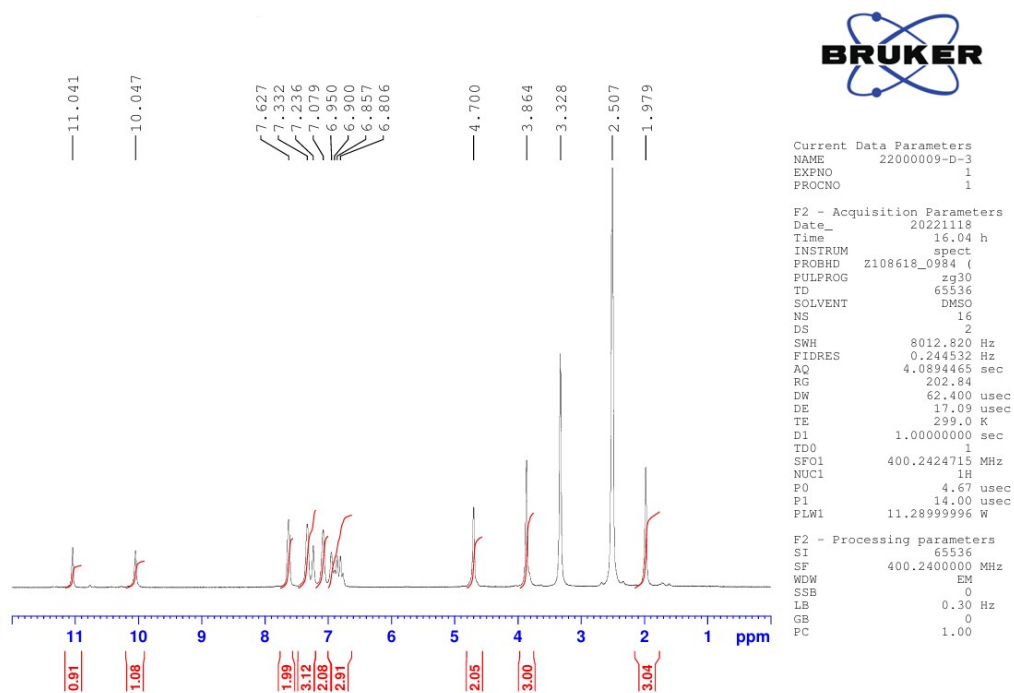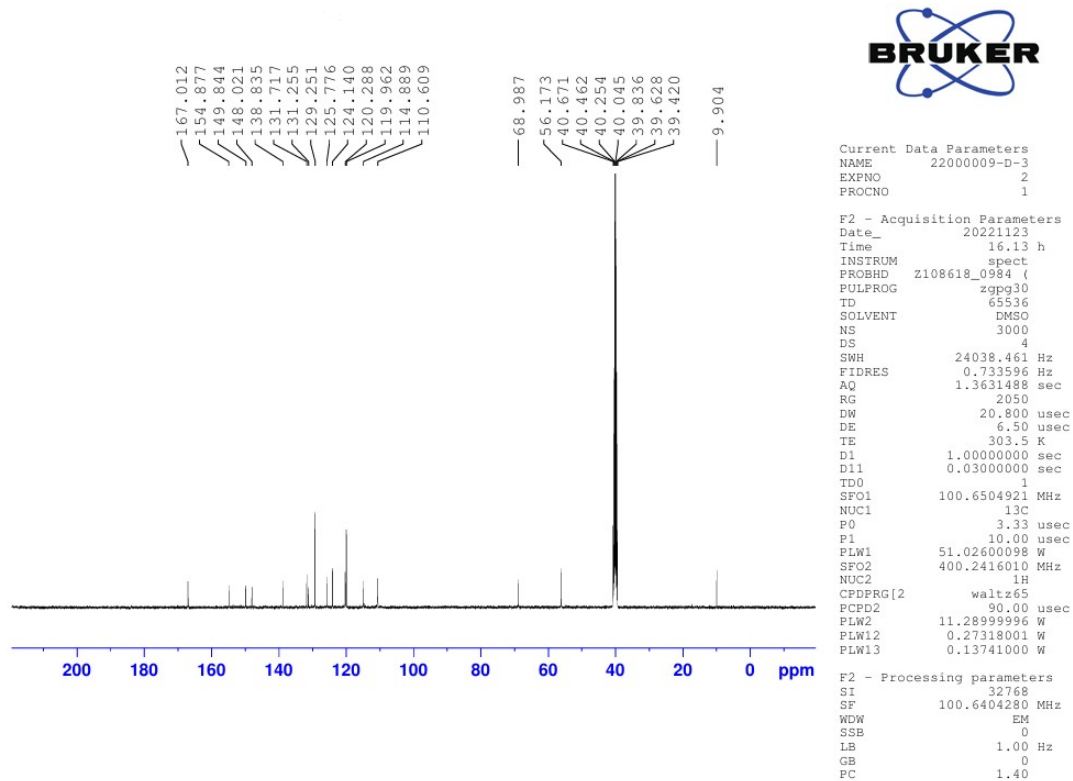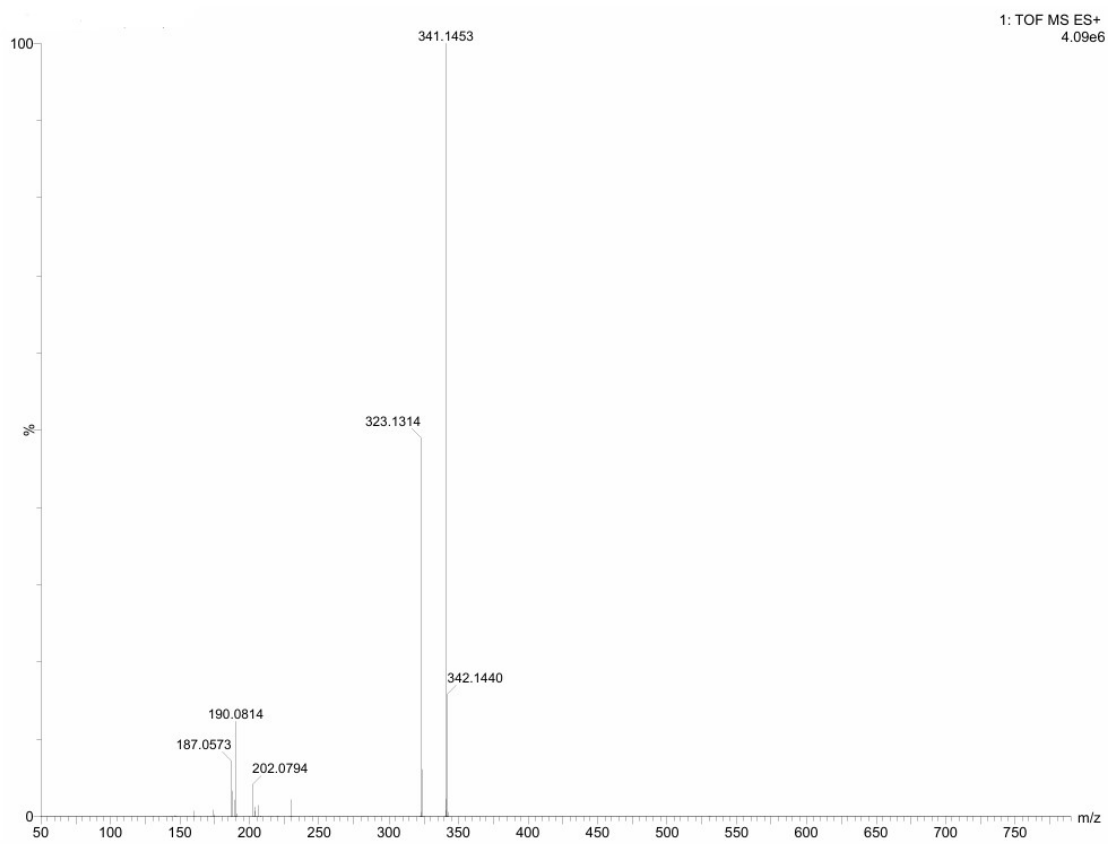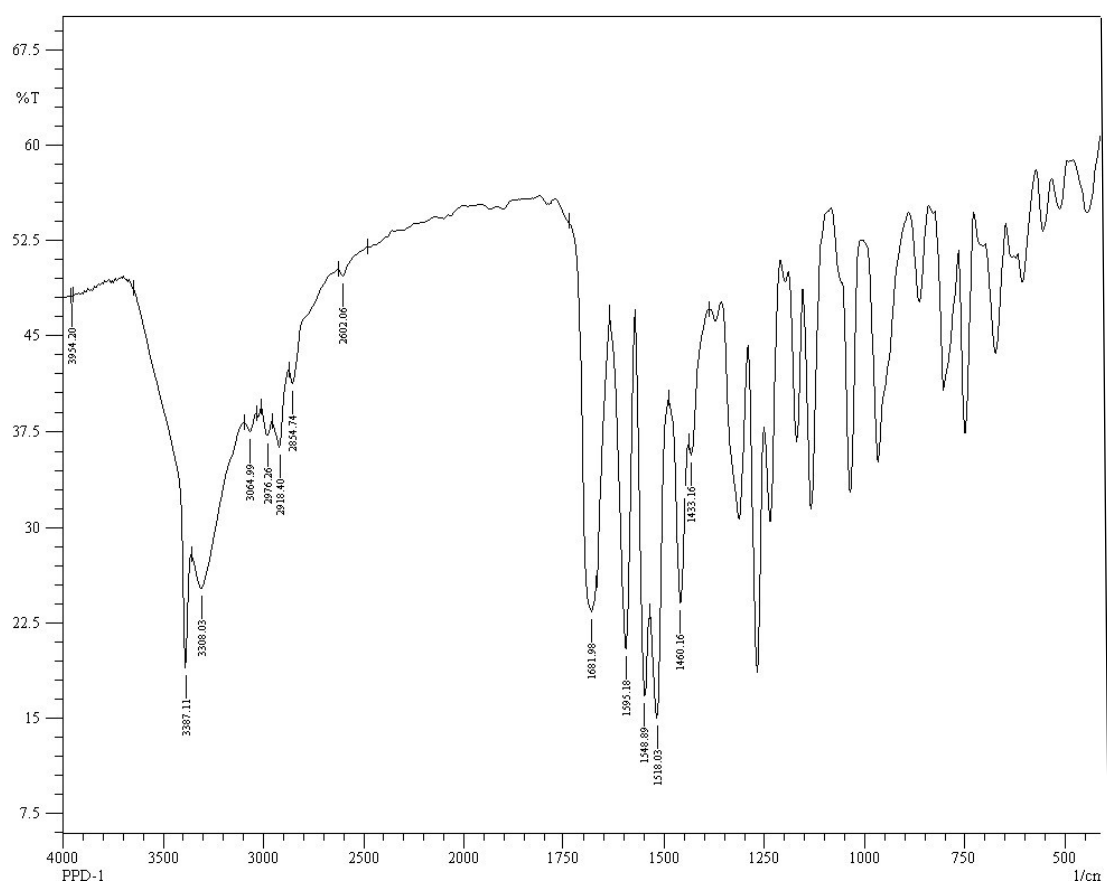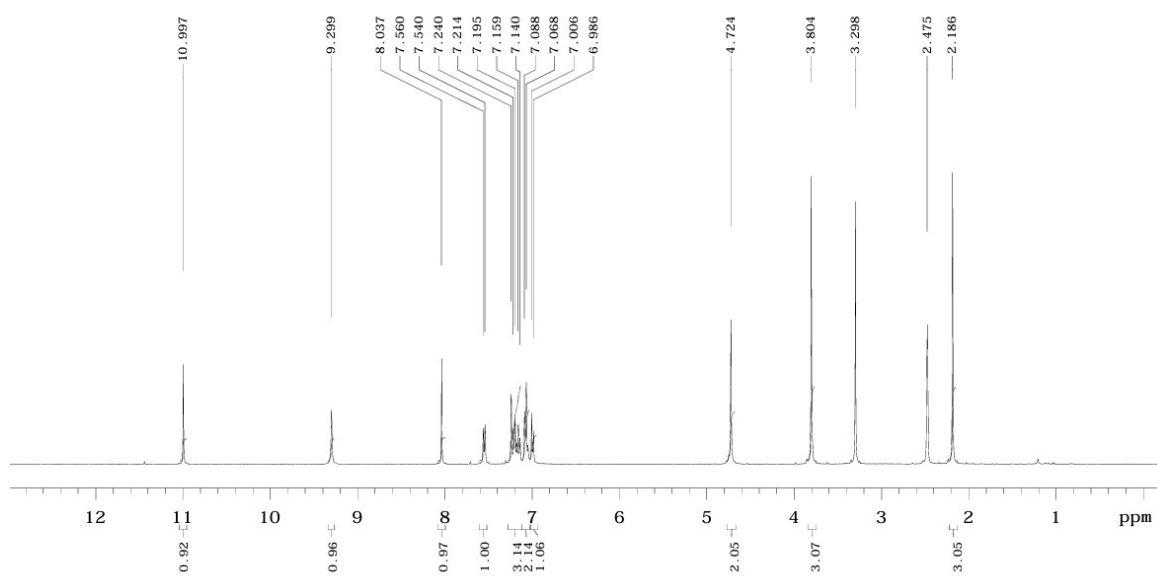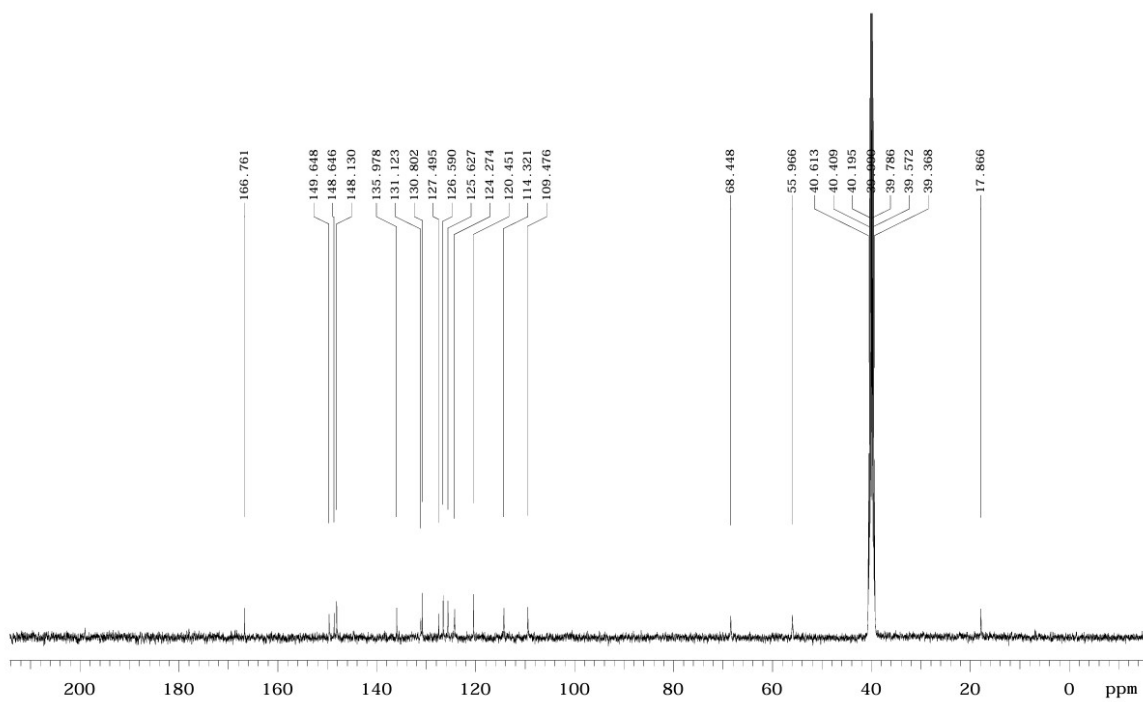

Fig. S7. ^{1}H-NMR spectrum of compound **4a.**
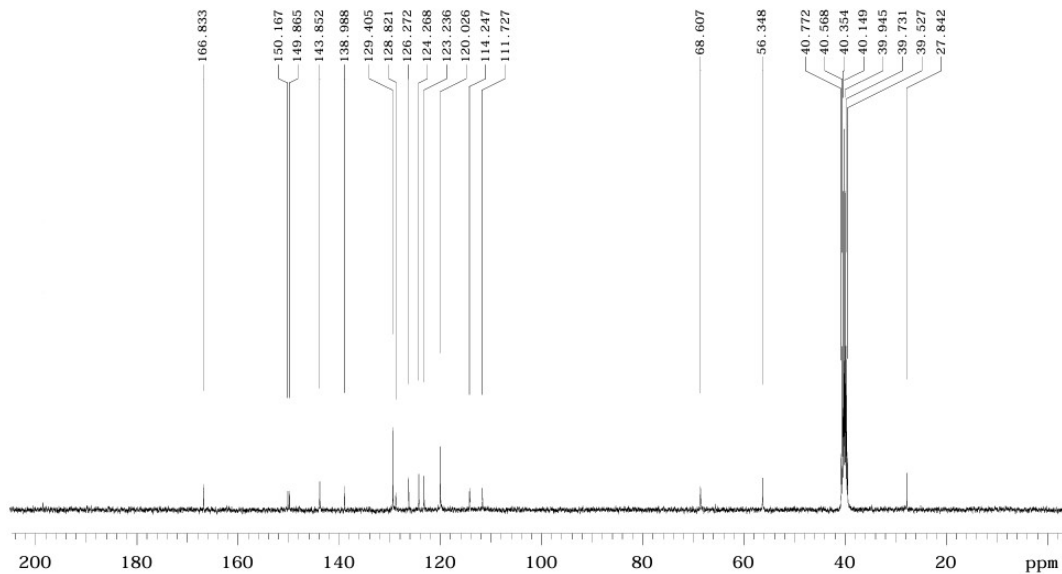
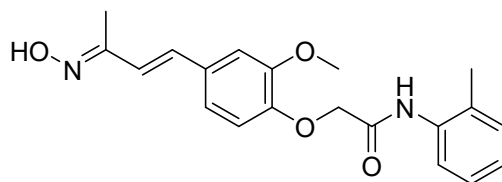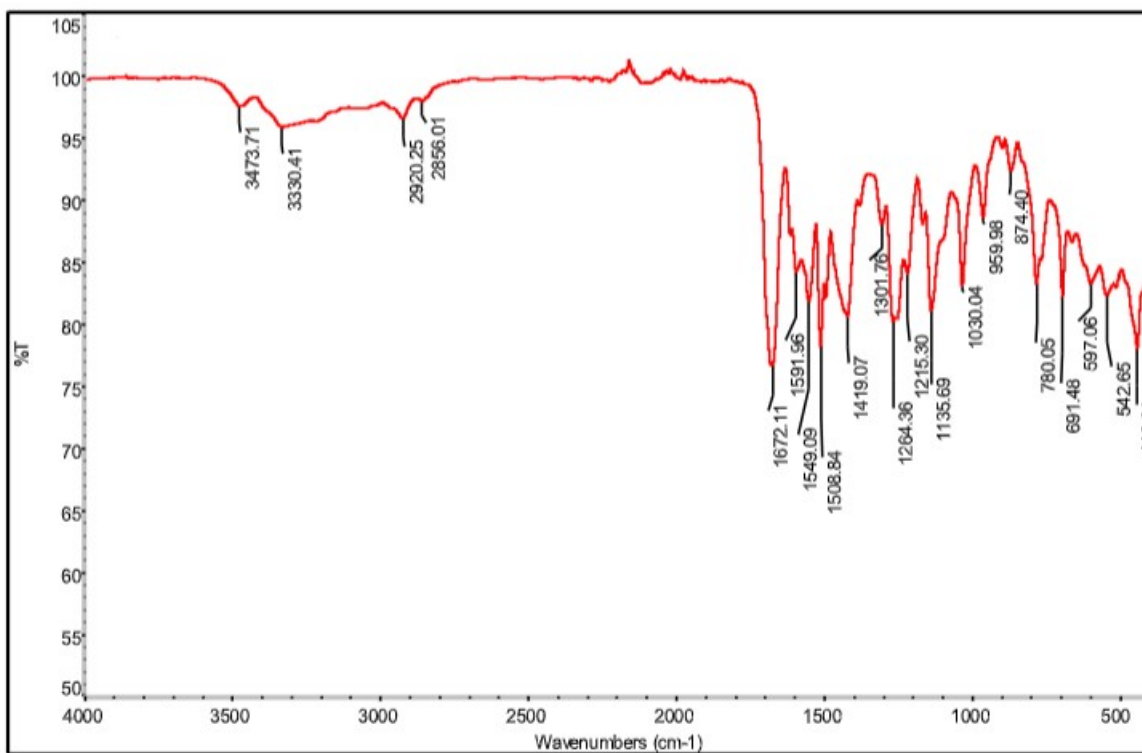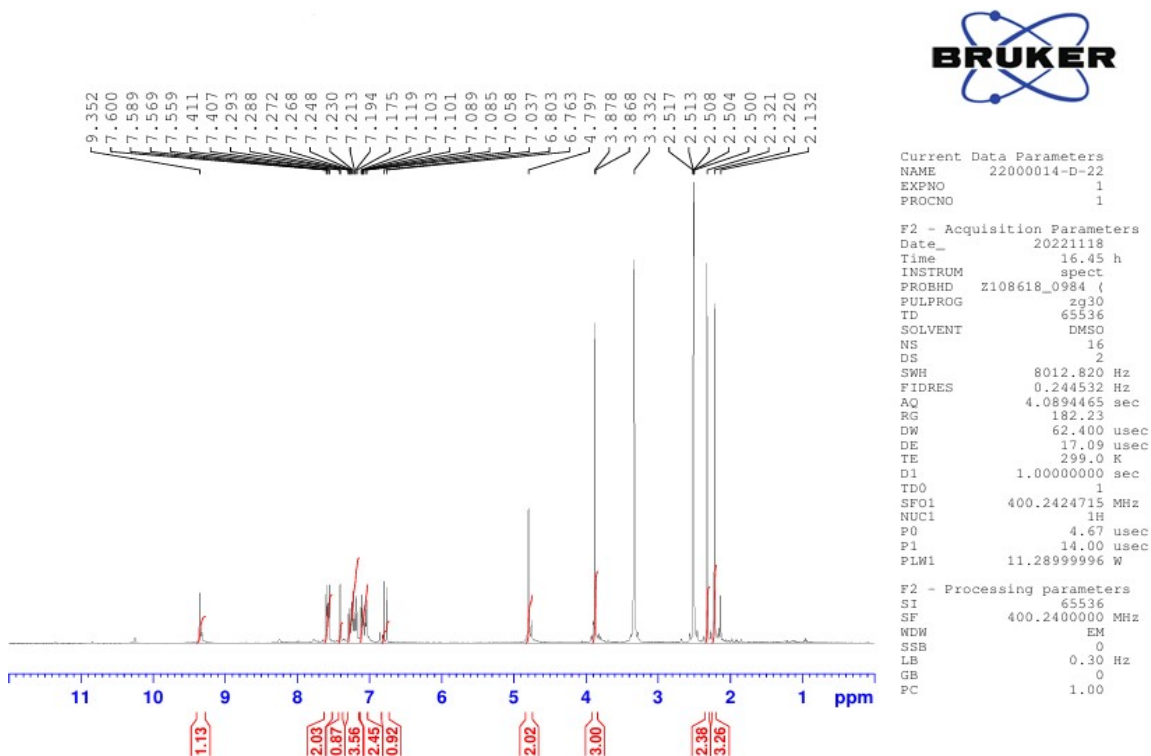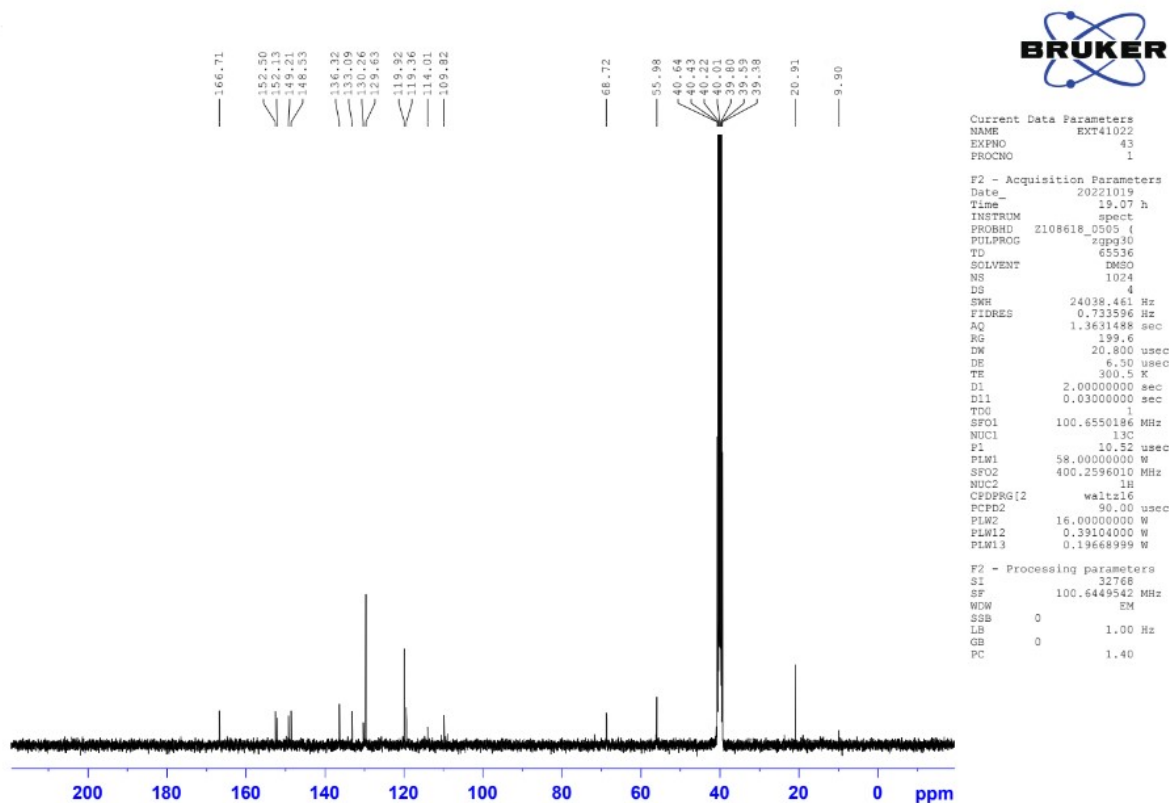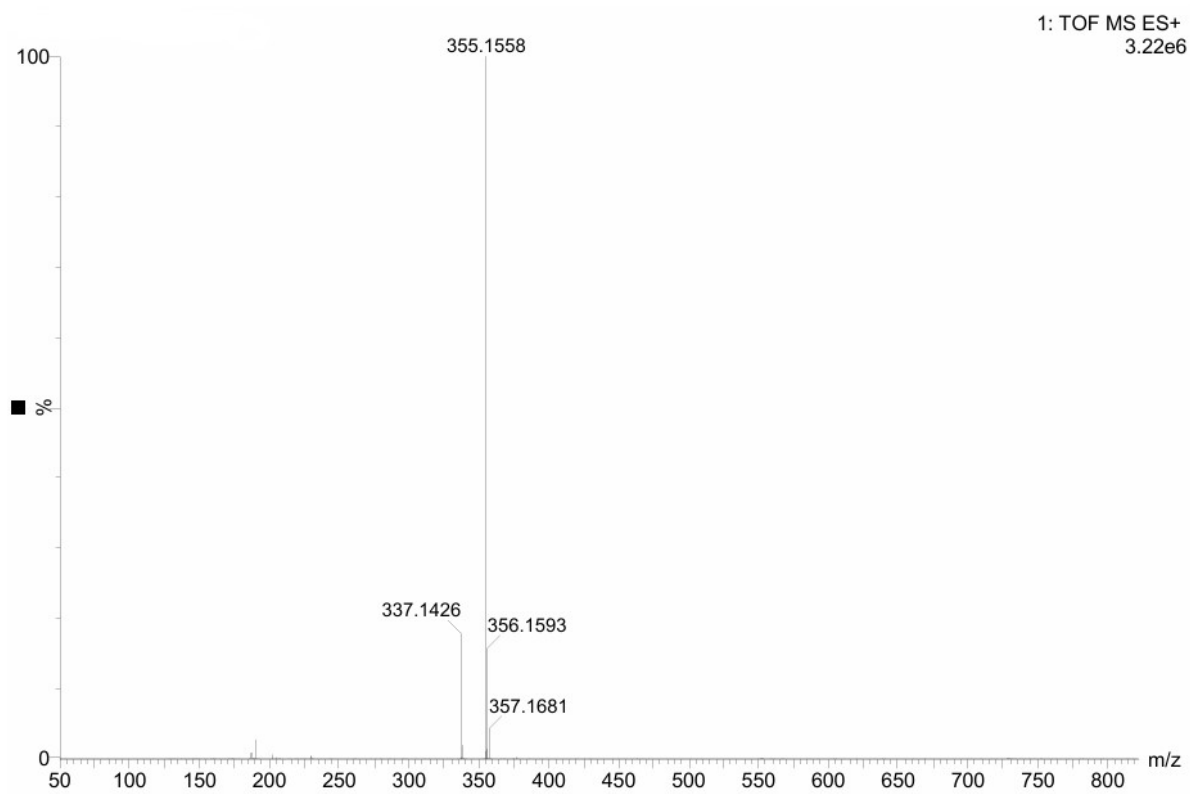**Fig. S8.** ^{13}C-NMR spectrum of compound **4a.**
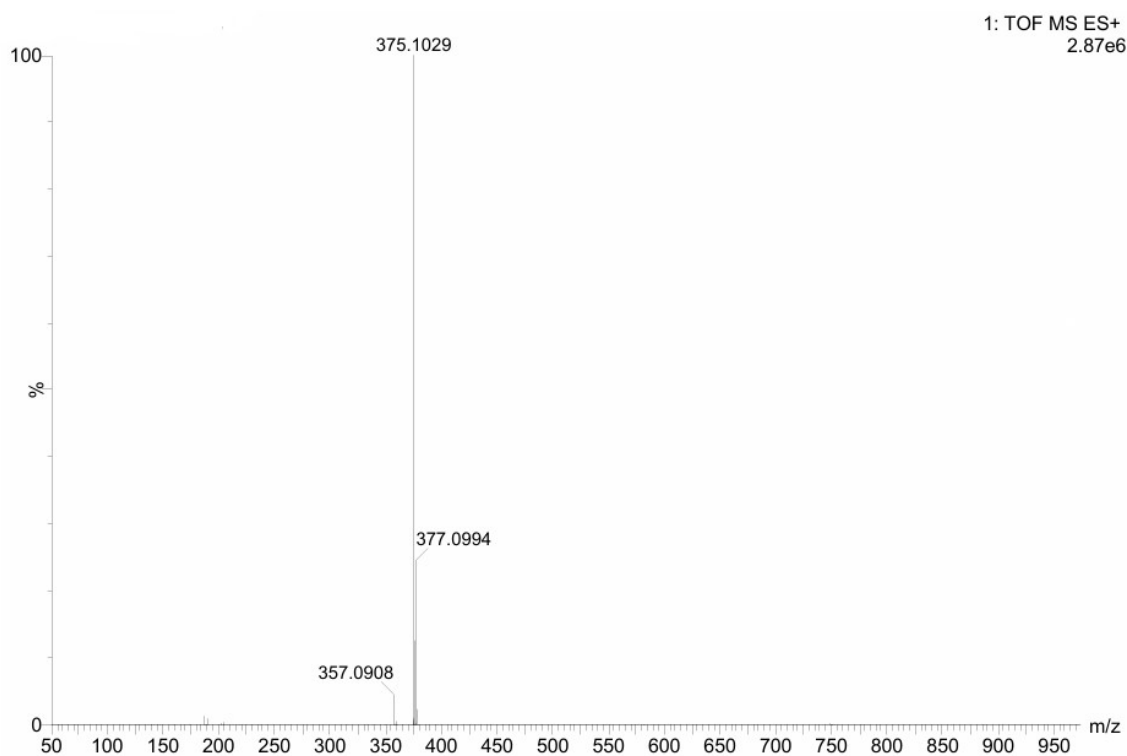
Fig. S9. Mass spectrum of compound **4a.**
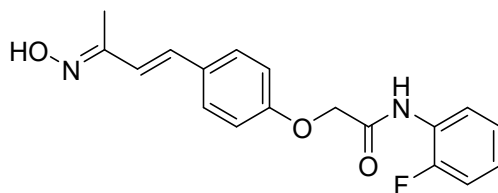
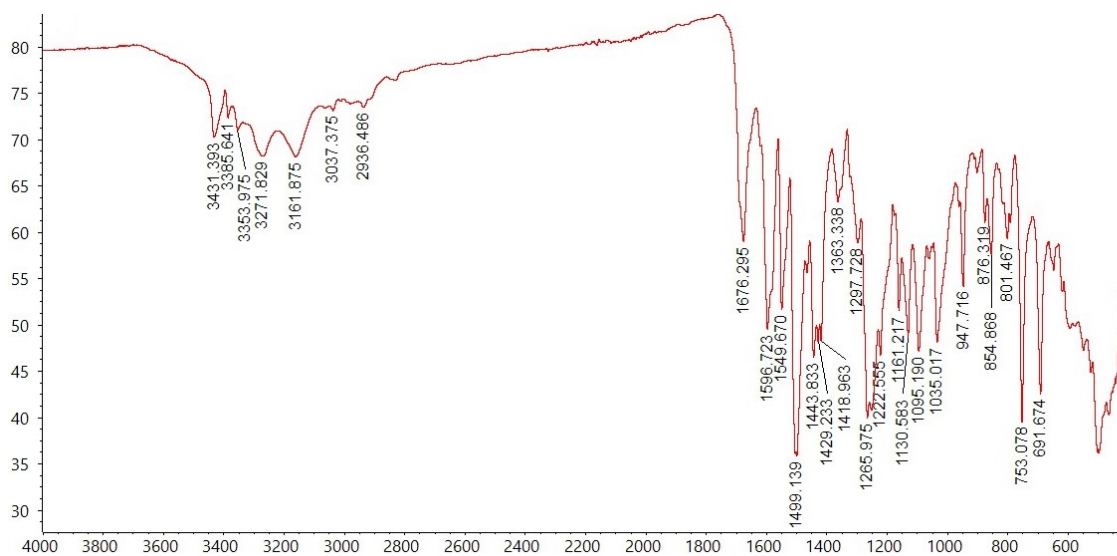## Compound:4b
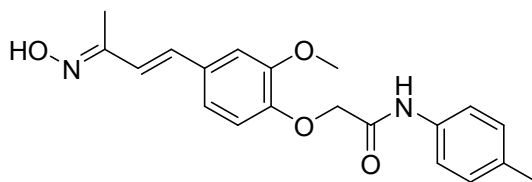
Fig. S10. Chemical structure of compound **4b.**
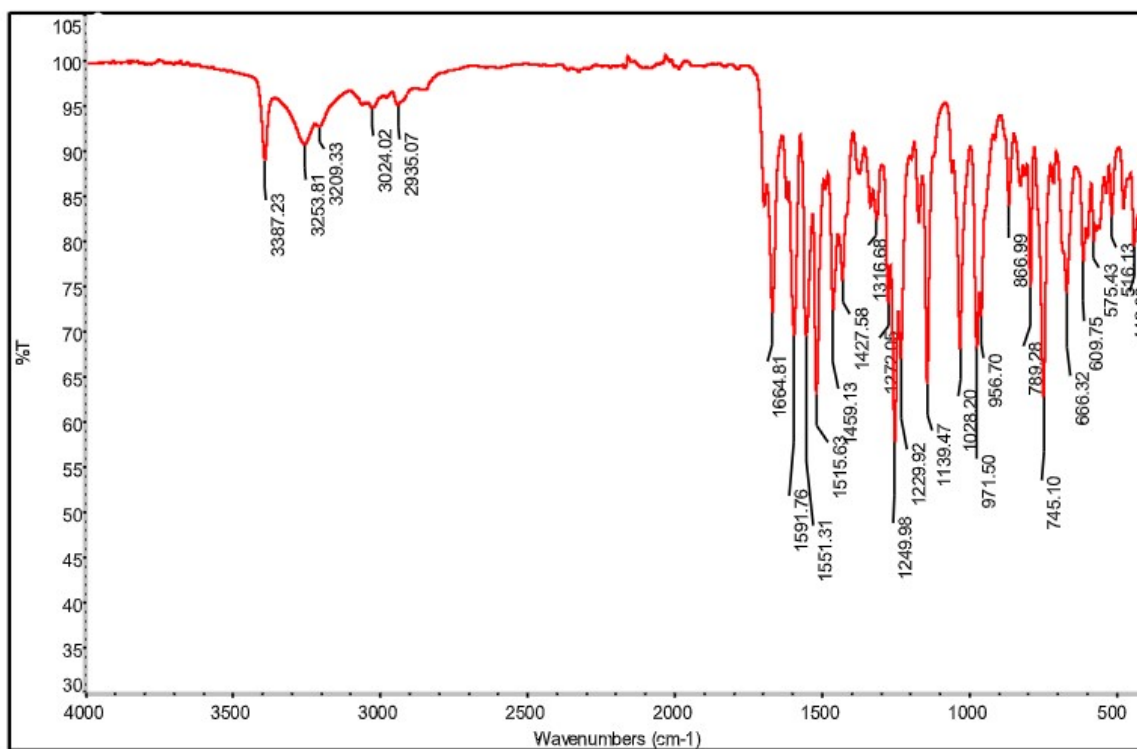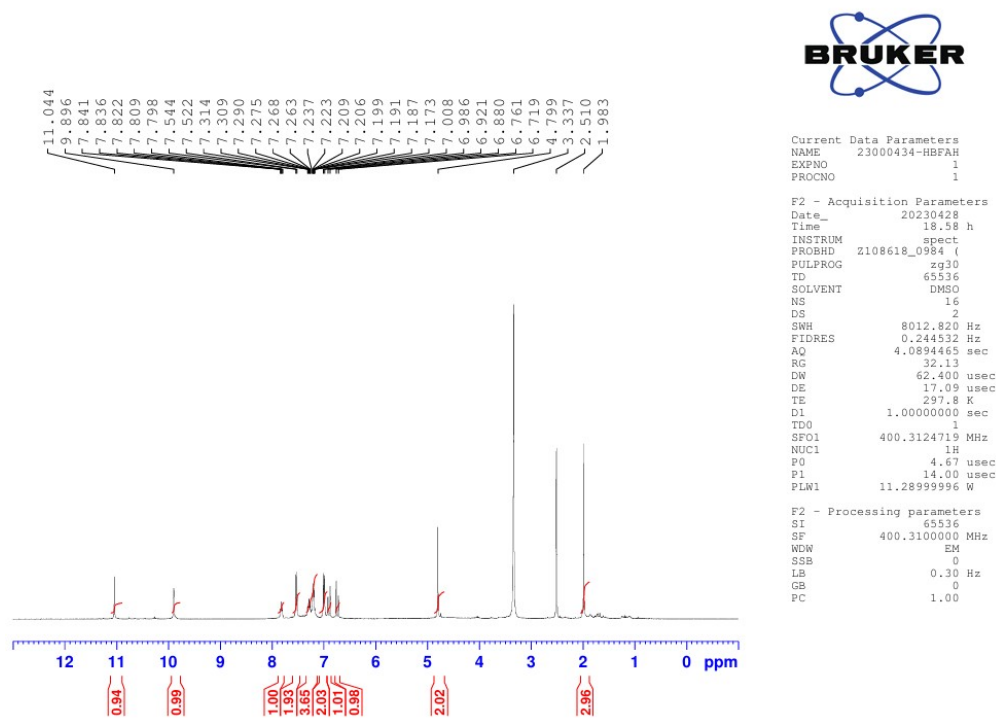

Fig. S11. IR spectrum of compound **4b.**

Fig. S12. ^{1}H-NMR spectrum of compound **4b.**

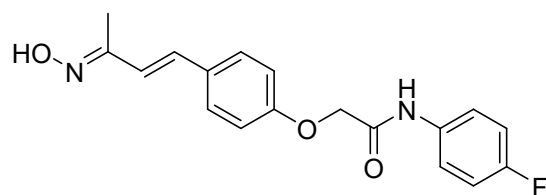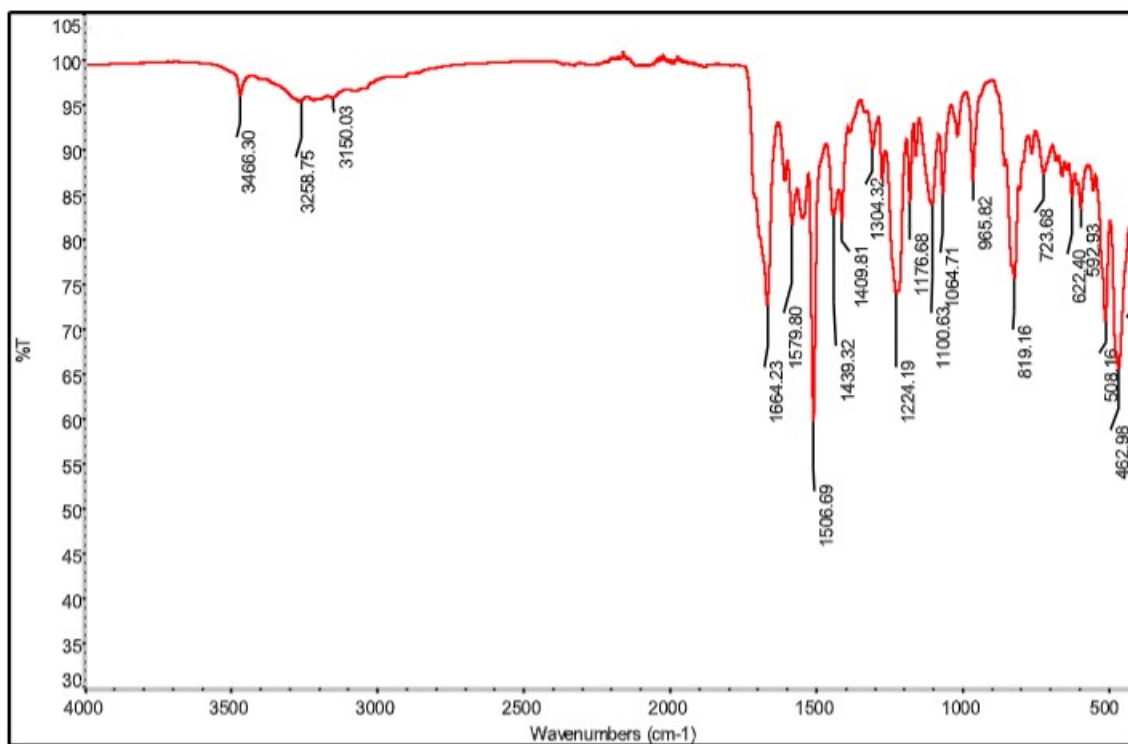**Fig. S13.** ^{13}C-NMR spectrum of compound **4b.**
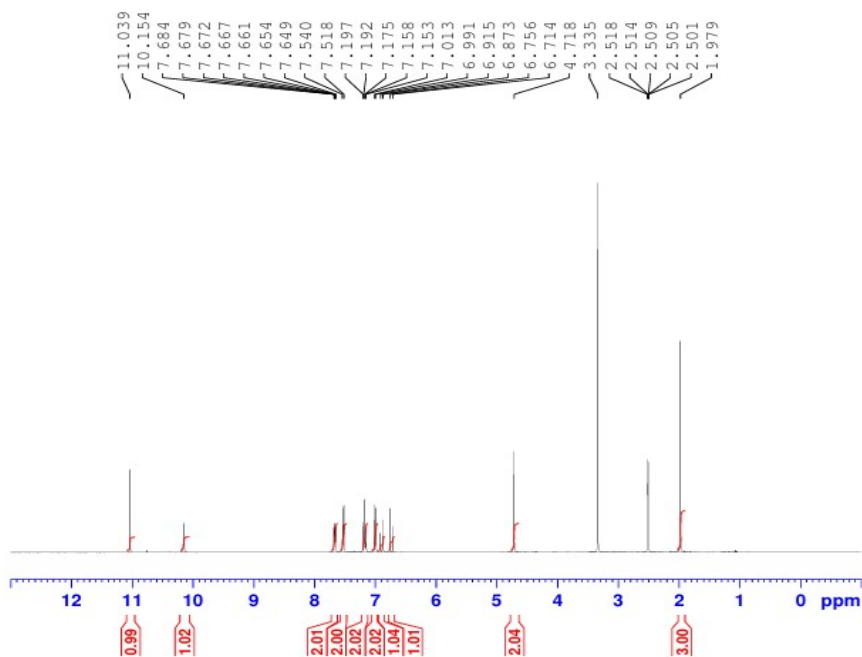
Fig. S14. Mass spectrum of compound **4b.**

Compound:4c
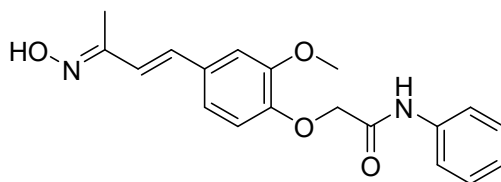
Fig. S15. Chemical structure of compound **4c.**
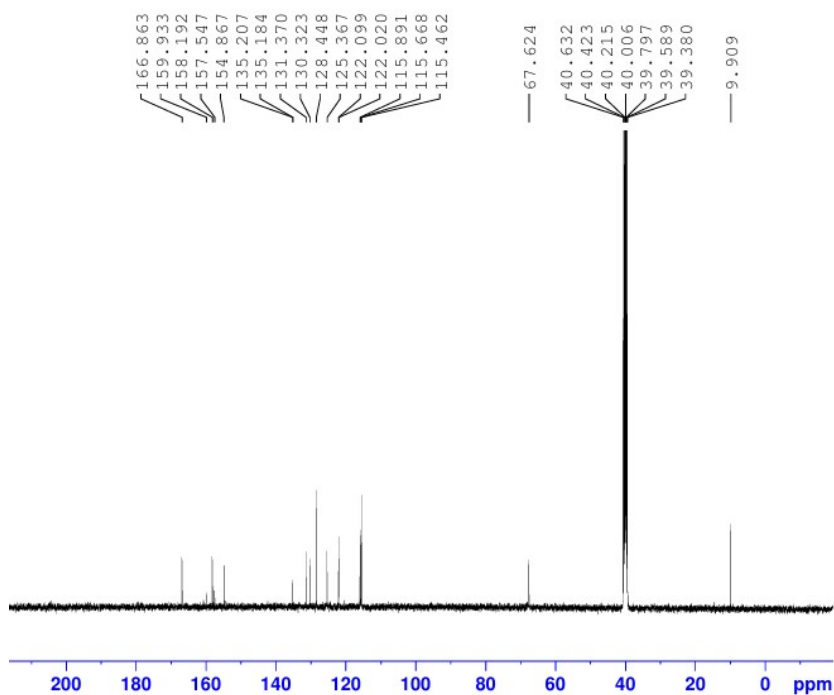

Fig. S16. IR spectrum of compound **4c.**

Fig. S17. ^{1}H-NMR spectrum of compound **4c.**

Fig. S18. ^{13}C-NMR spectrum of compound **4c.**

Fig. S19. Mass spectrum of compound **4c.**

Compound:4d
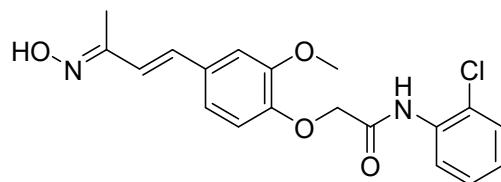
Fig. S20. Chemical structure of compound **4d.**

Fig. S21. IR spectrum of compound **4d.**

Fig. S22. ¹H-NMR spectrum of compound **4d.**

Fig. S23. ¹³C-NMR spectrum of compound **4d.**
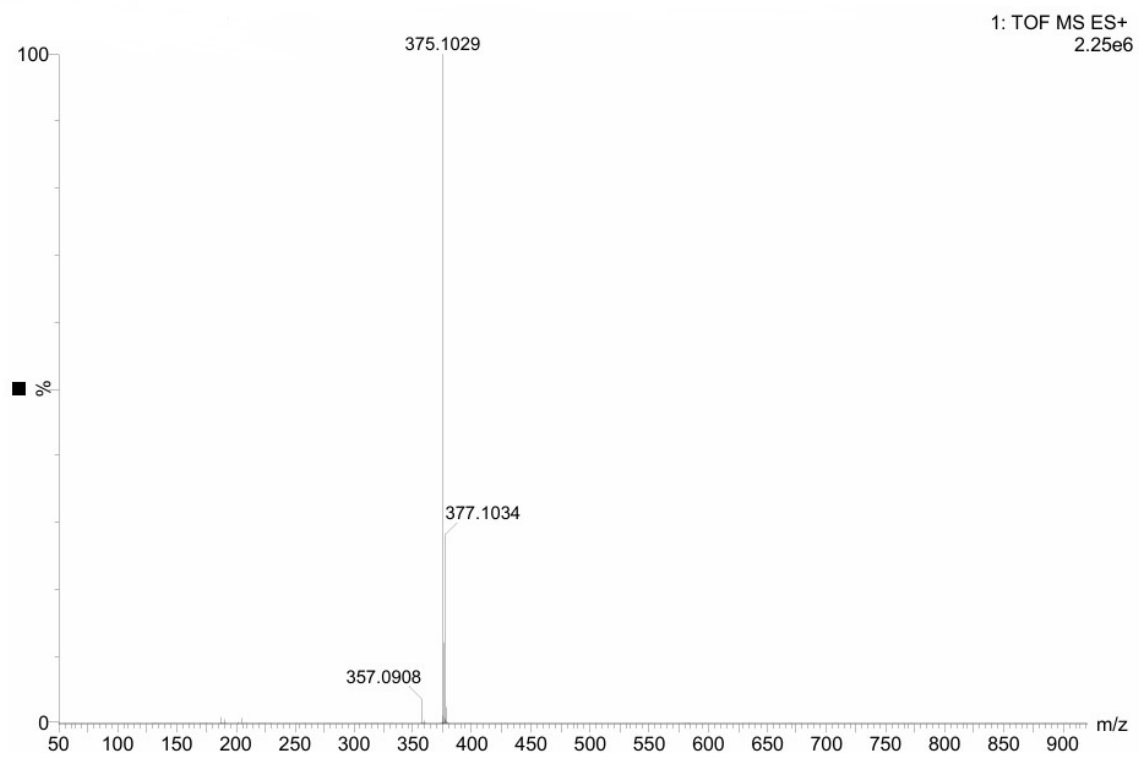
Fig. S24. Mass spectrum of compound **4d.**

<p style="text-align:center"><u>Compound:4e</u></p>

Fig. S25. Chemical structure of compound **4e.**

Fig. S26. IR spectrum of compound **4e.**

Fig. S27. ¹H-NMR spectrum of compound **4e.**

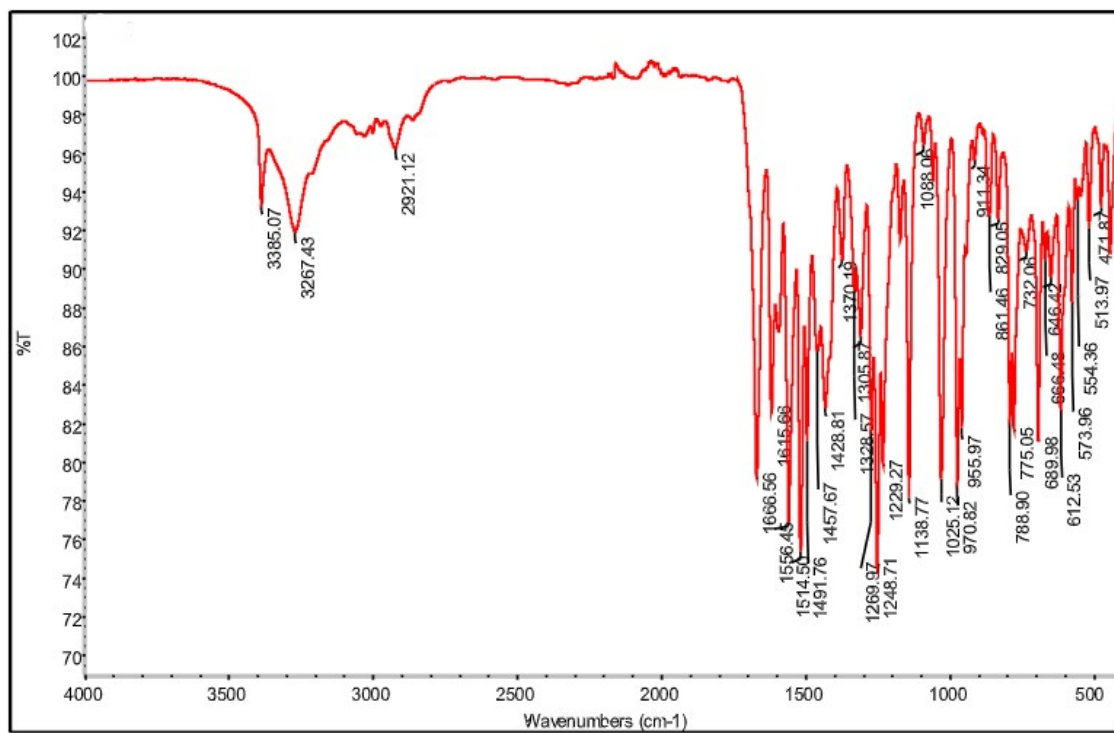
Fig. S28. ¹³C-NMR spectrum of compound **4e.**

Fig. S29. Mass spectrum of compound **4e.**

Compound:4f

Fig. S30. Chemical structure of compound **4f.**
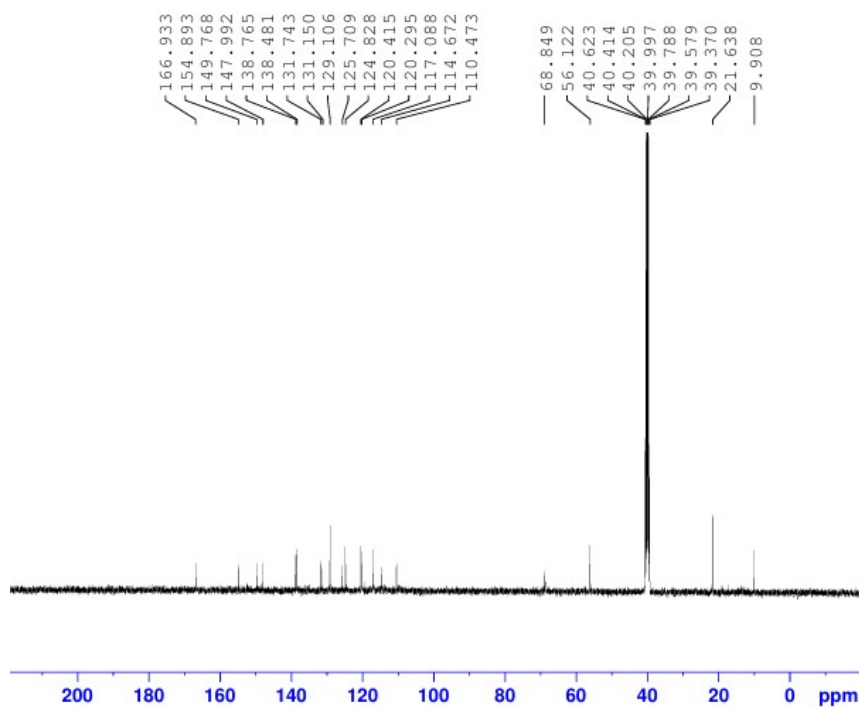

Fig. S31. IR spectrum of compound **4f.**

Fig. S32. ¹H-NMR spectrum of compound **4f.**
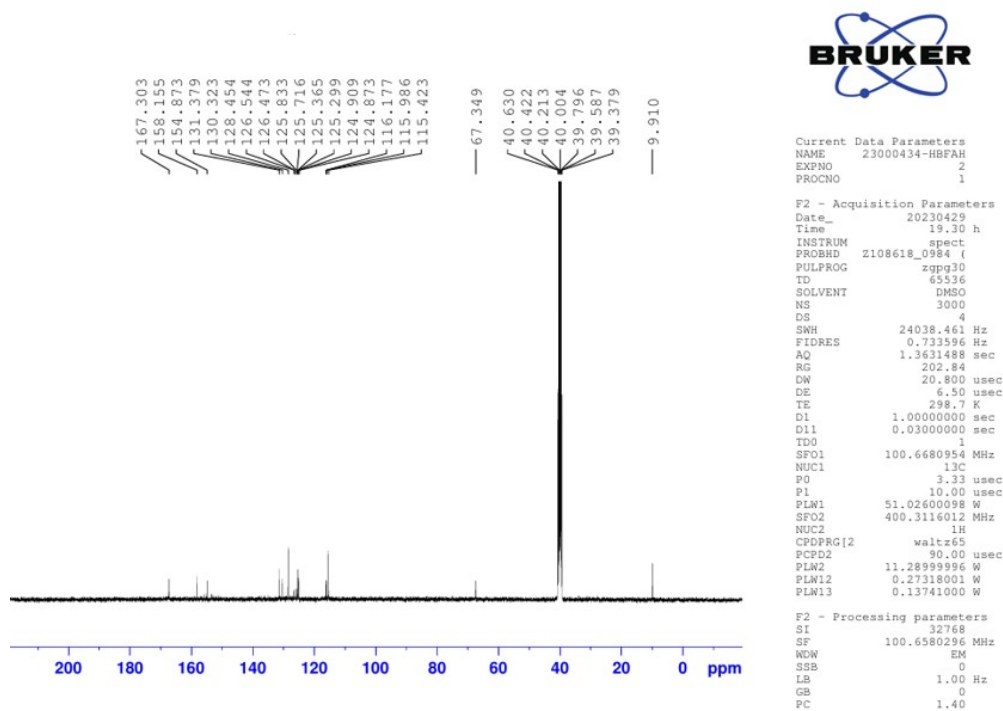
Fig. S33. ^{13}C-NMR spectrum of compound **4f.**
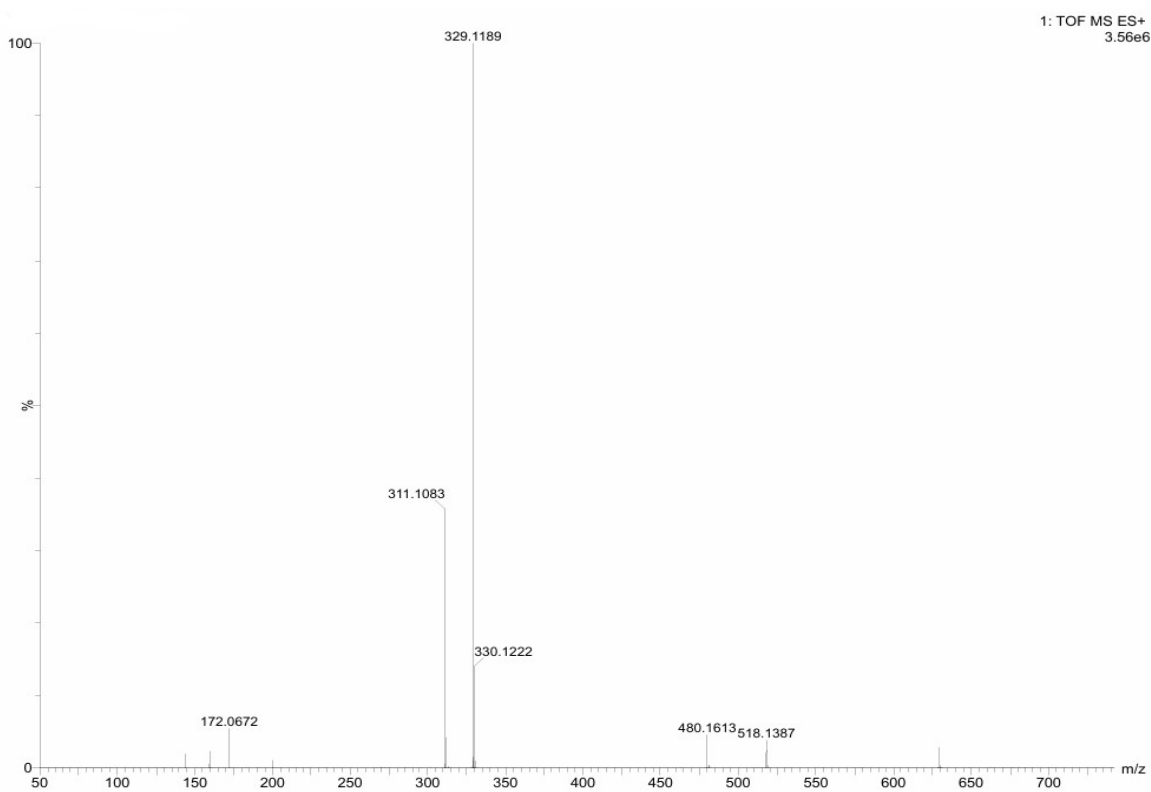
Fig. S34. Mass spectrum of compound **4f.**

Fig. S35. Chemical structure of compound **4g.**

Fig. S36. IR spectrum of compound **4g.**

Fig. S37. ^{1}H-NMR spectrum of compound **4g.**

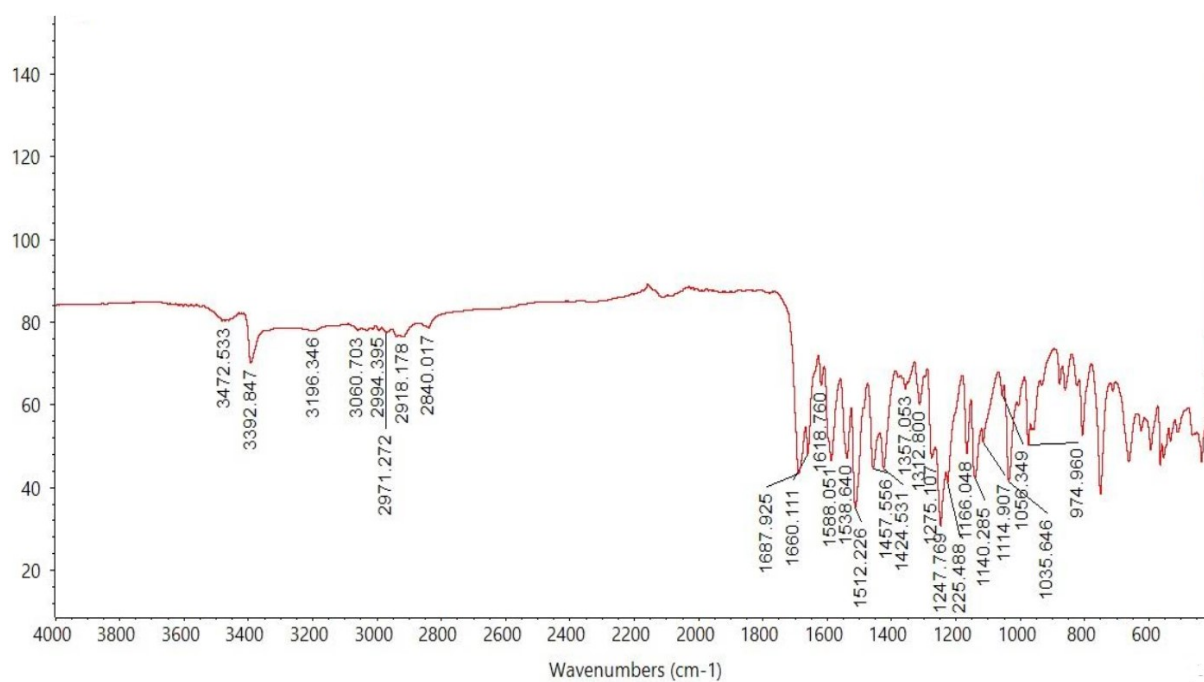**Fig. S38.** ^{13}C-NMR spectrum of compound **4g.**

Fig. S39. Mass spectrum of compound **4g.**

Compound:4h
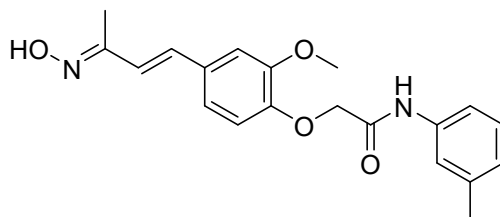
Fig. S40. Chemical structure of compound **4h.**

Fig. S41. IR spectrum of compound **4h.**

Fig. S42. ^{1}H-NMR spectrum of compound **4h.**

Fig. S43. ^{13}C-NMR spectrum of compound **4h.**

Fig. S44. Mass spectrum of compound **4h.**

Compound:4i
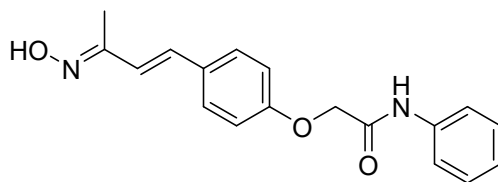
Fig. S45. Chemical structure of compound **4i.**
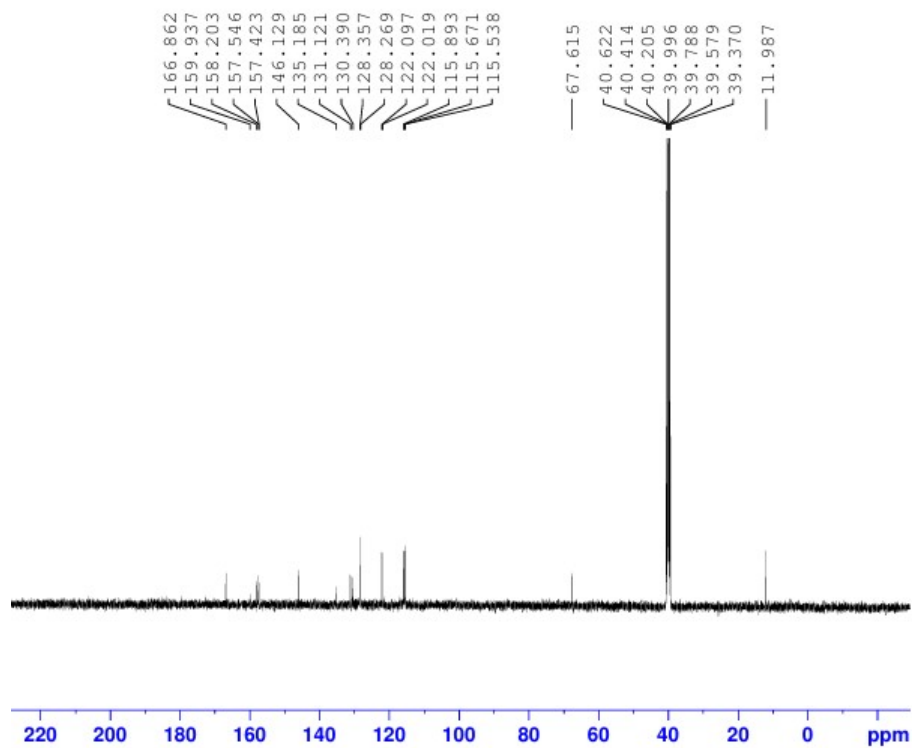

Fig. S46. IR spectrum of compound **4i.**

Fig. S47. ¹H-NMR spectrum of compound **4i.**

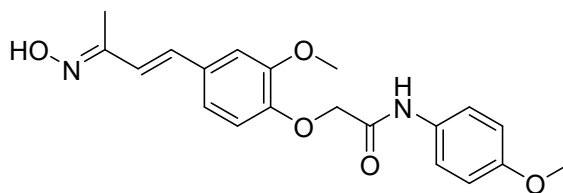**Fig. S48.** ¹³C-NMR spectrum of compound **4i.**

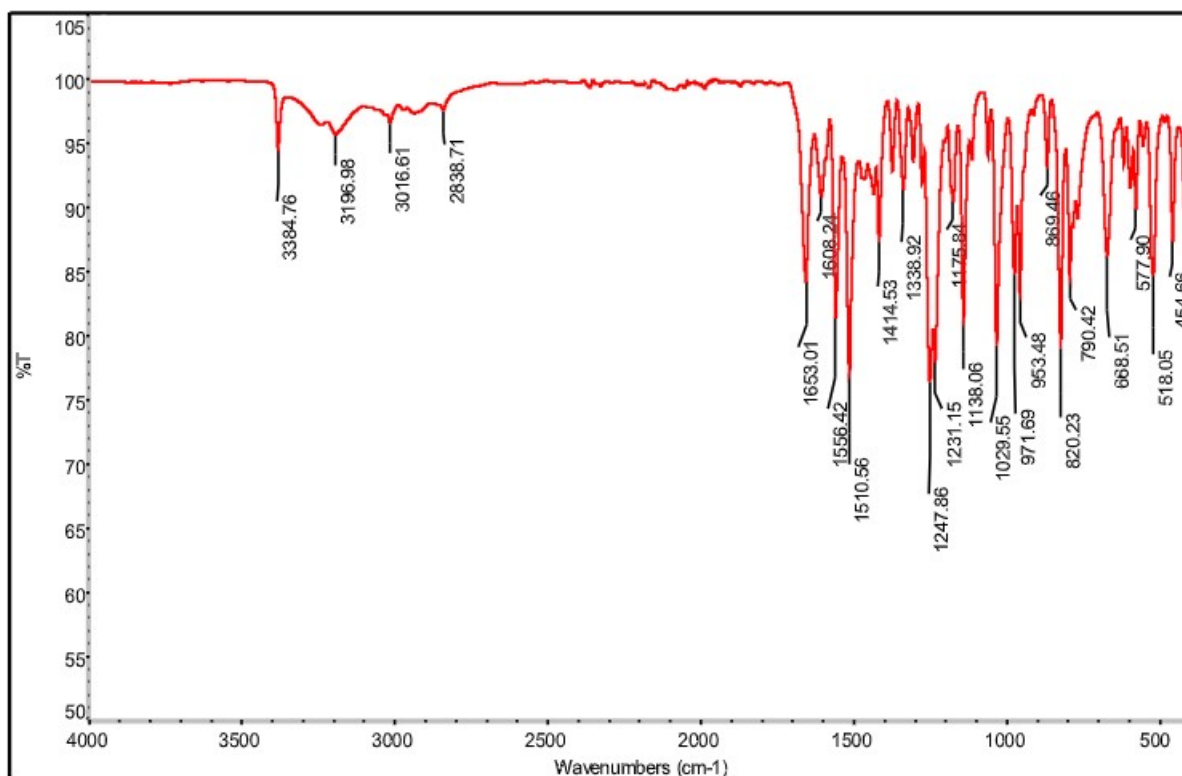**Fig. S49.** Mass spectrum of compound **4i.**

Compound:4j

Fig. S50. Chemical structure of compound **4j.**
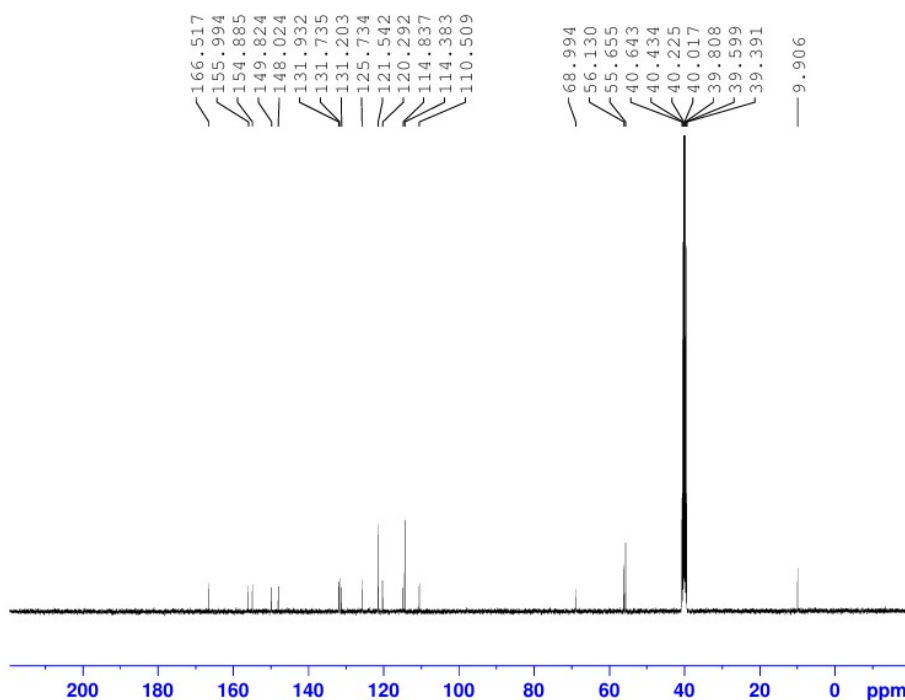

Fig. S51. IR spectrum of compound **4j.**

Fig. S52. ^{1}H-NMR spectrum of compound **4j.**

Fig. S53. ^{13}C-NMR spectrum of compound **4j.**

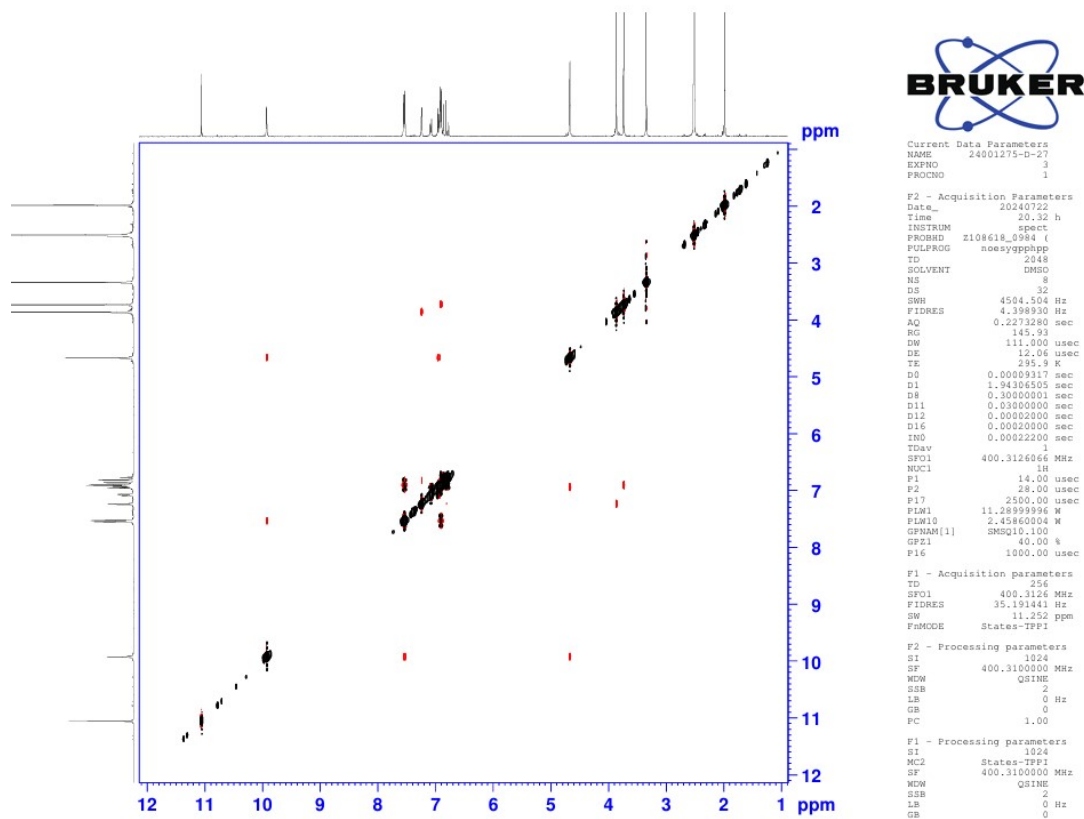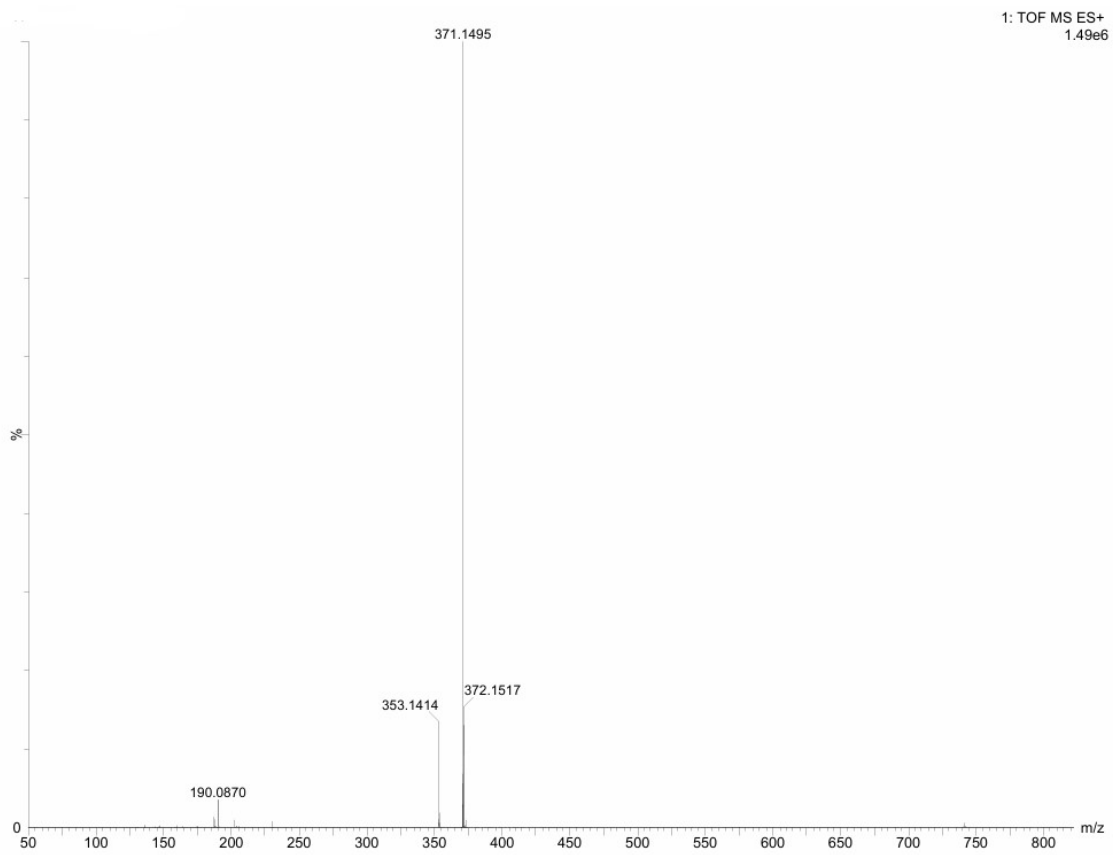**Chemical structure of compound 4j**

Fig. S54. HH-NOESY spectrum of compound **4j**.

Fig. S55. Mass spectrum of compound **4j.**
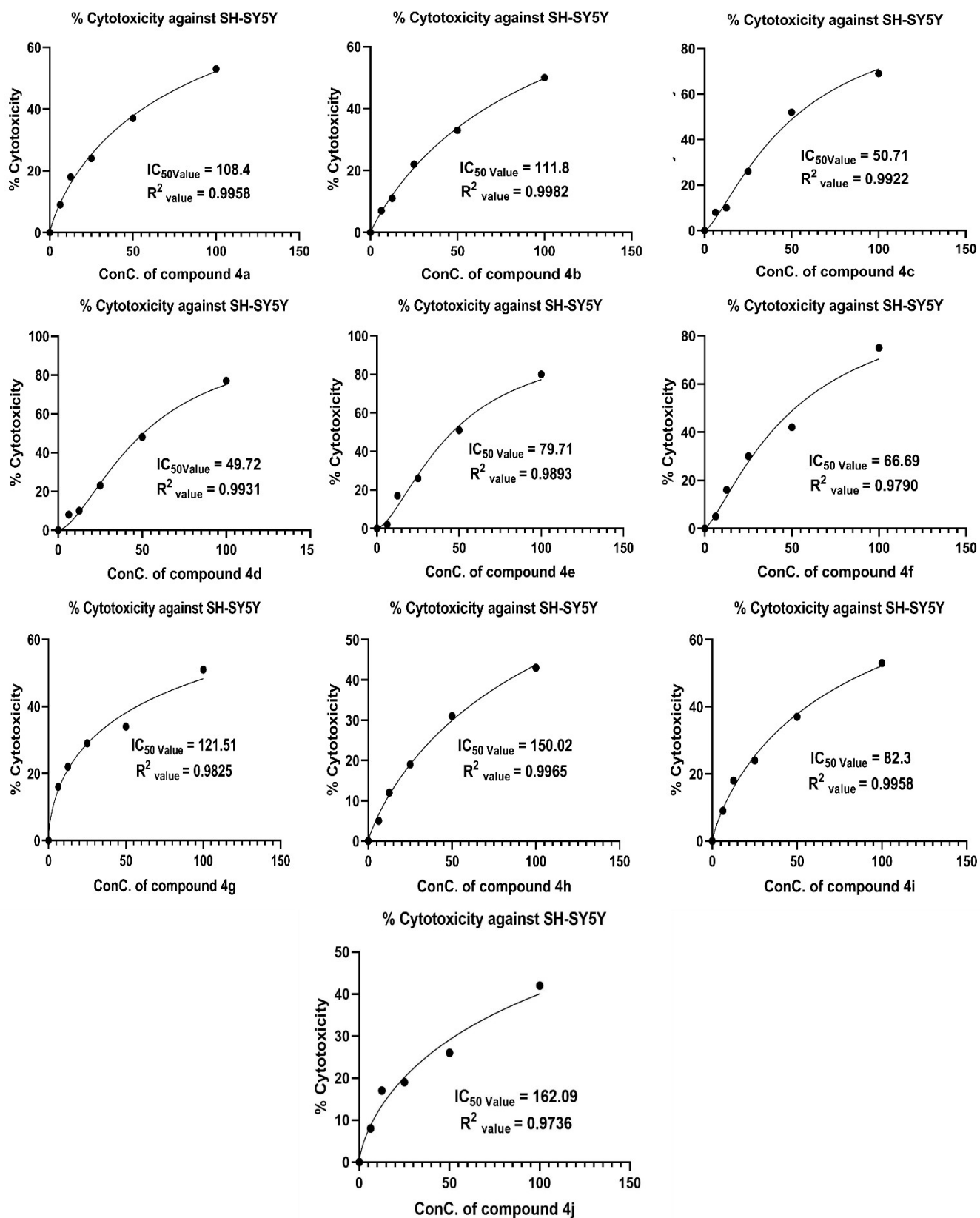
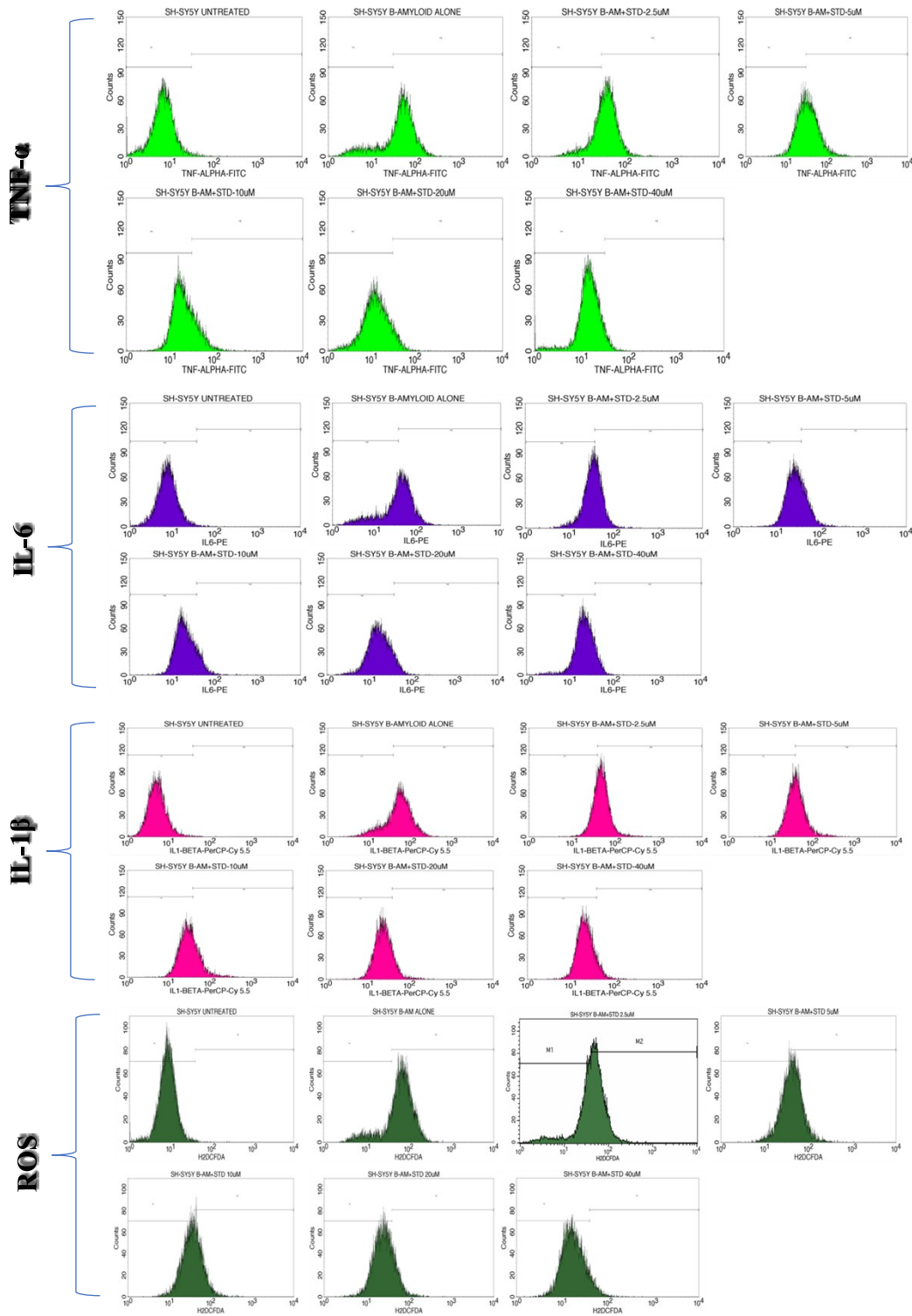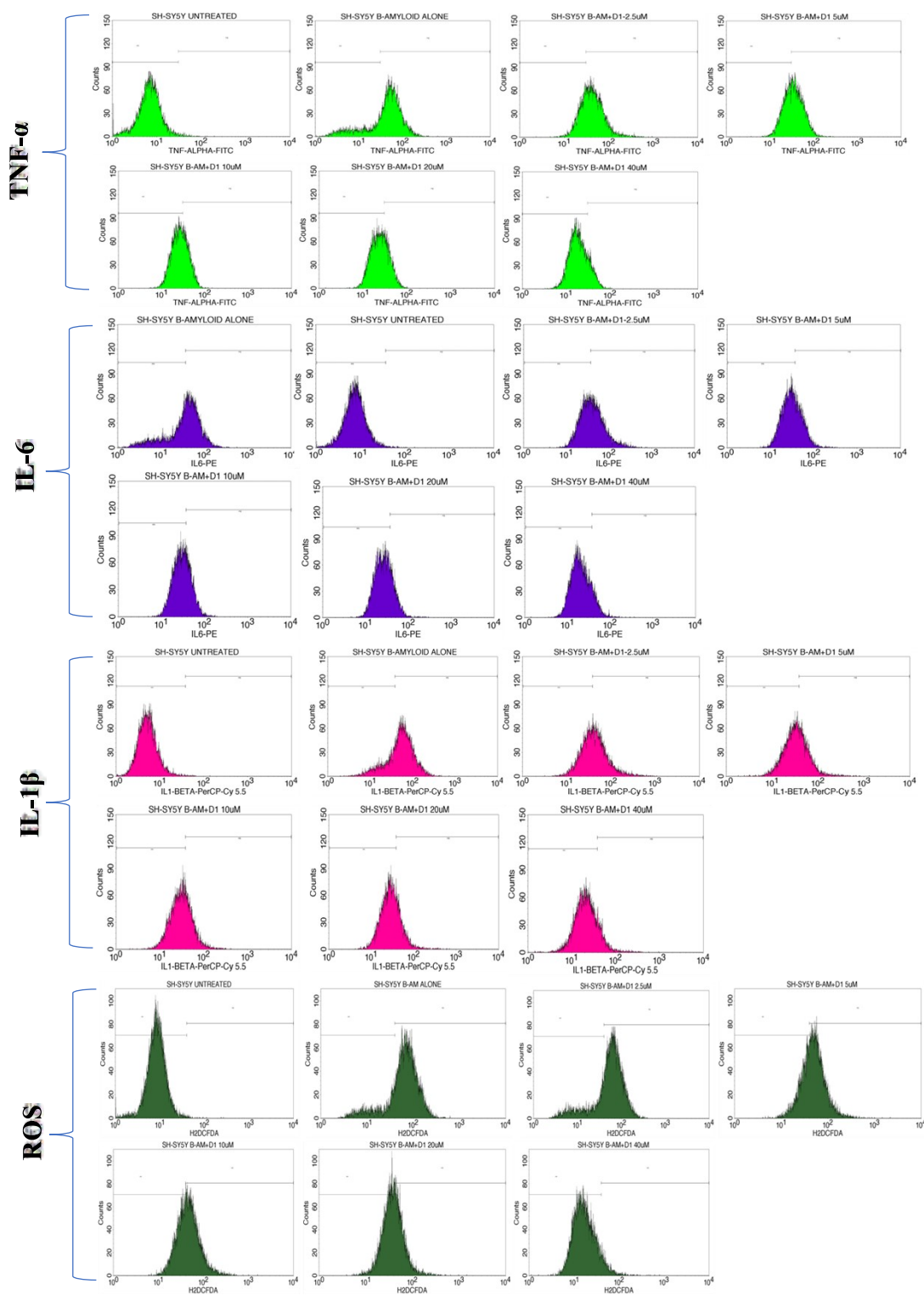# MTT Assay – IC$_{50}$ Curves

**Fig. S56.** The IC$_{50}$ curves for the MTT assay for the compounds 4(a-j).

Flow cytometry histograms

Fig. S57. Histogram showing the % cells expressed TNF-α, IL-6 and IL-1β intensity and ROS in Beta amyloid induced SHSY-5Y cell line with the treatment of standard drug.

Fig. S58. Histogram showing the % cells expressed TNF-α, IL-6 and IL-1β intensity and ROS in Beta amyloid induced SHSY-5Y cell line with the treatment of compound 4a.
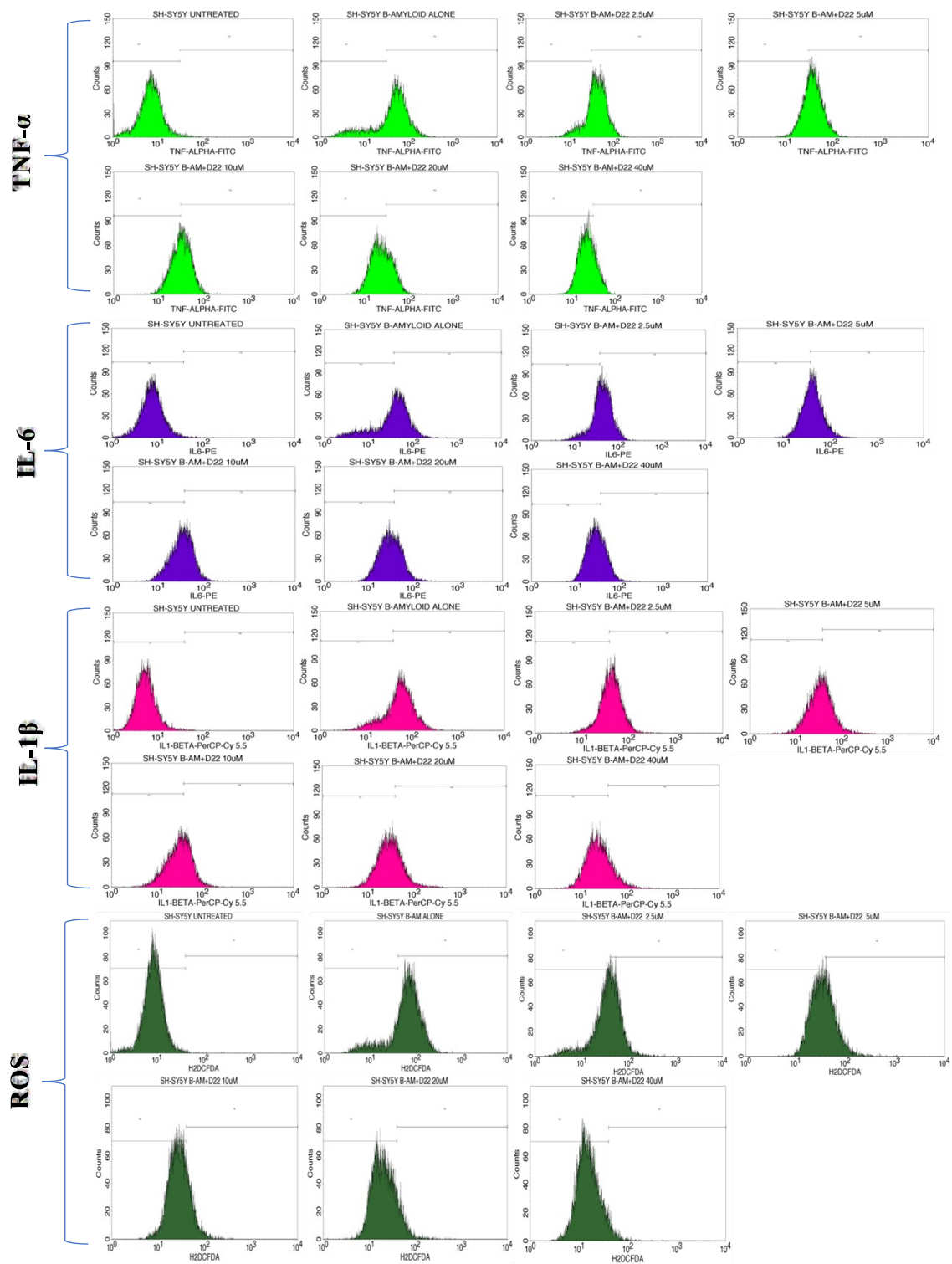
Fig. S59. Histogram showing the % cells expressed TNF-α, IL-6 and IL-1β intensity and ROS in Beta amyloid induced SHSY-5Y cell line with the treatment of compound 4h.