Microwave assisted synthesis, *in vitro* and *in silico* studies of pyrano[3,2-*c*]quinoline-3-carboxylates as dual acting anti-cancer and anti-microbial agents as potential topoisomerase II and DNA-gyrase inhibitors

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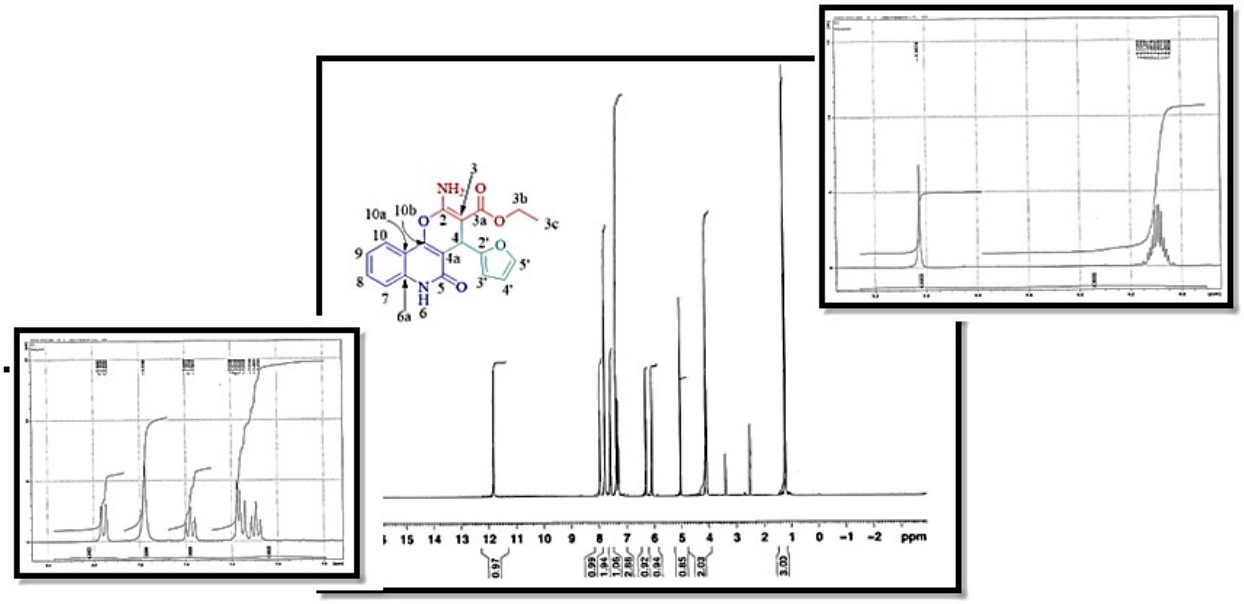
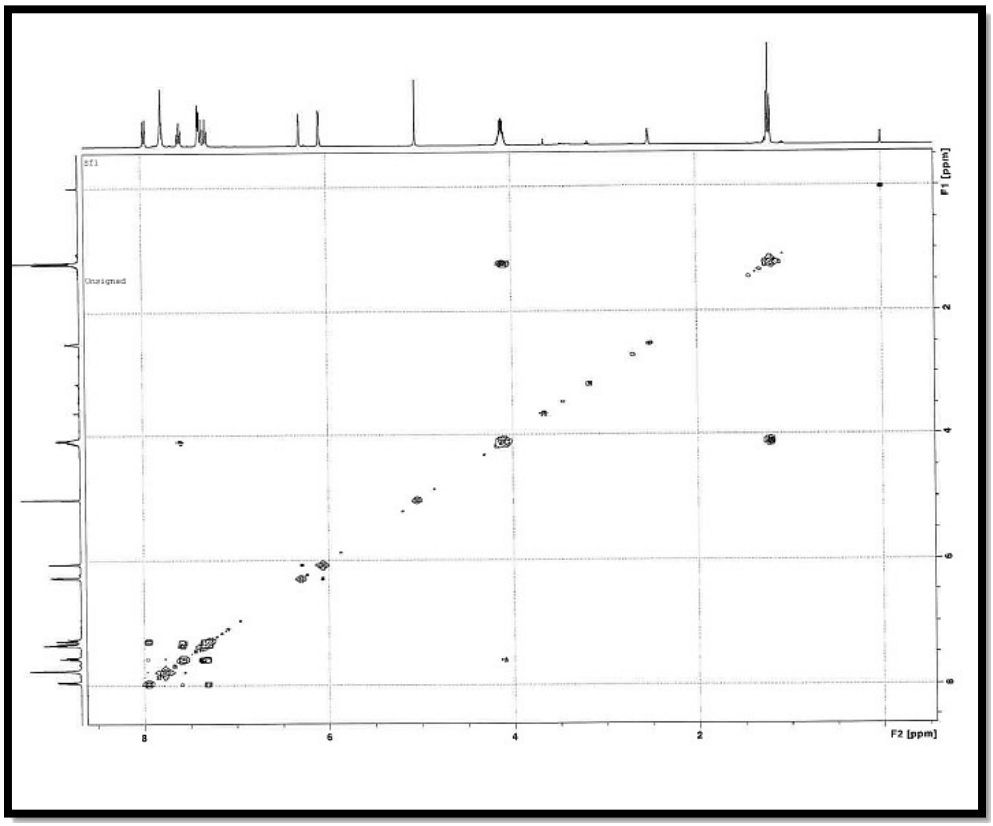
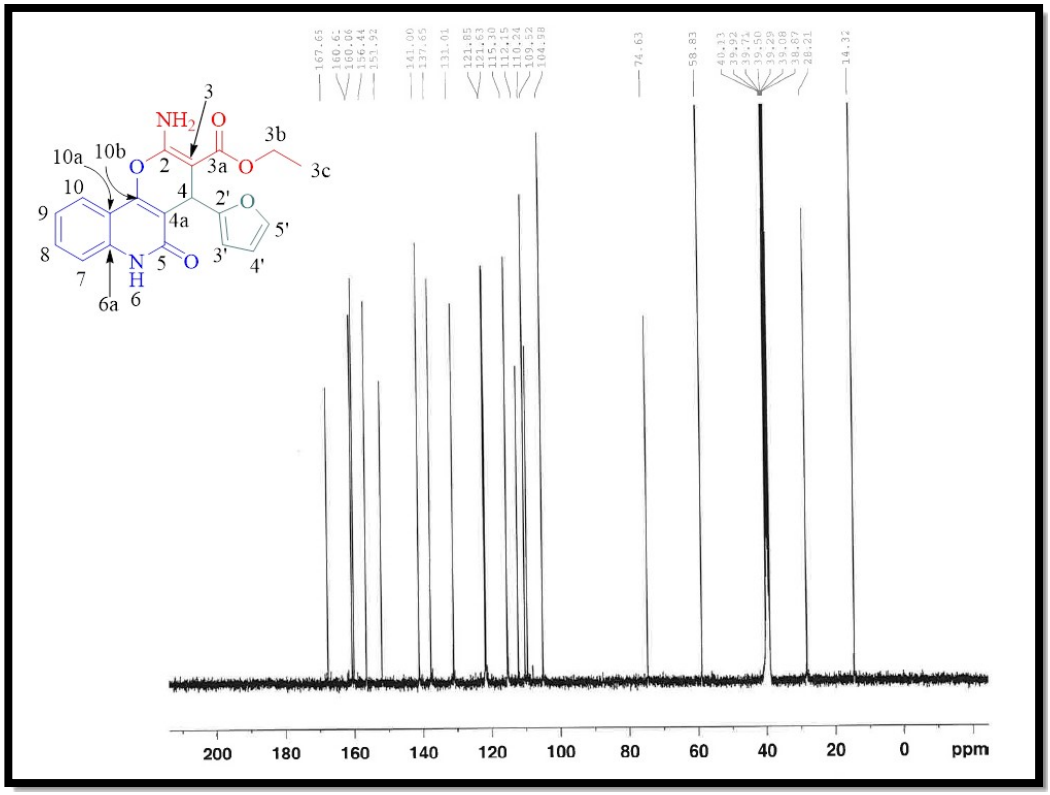


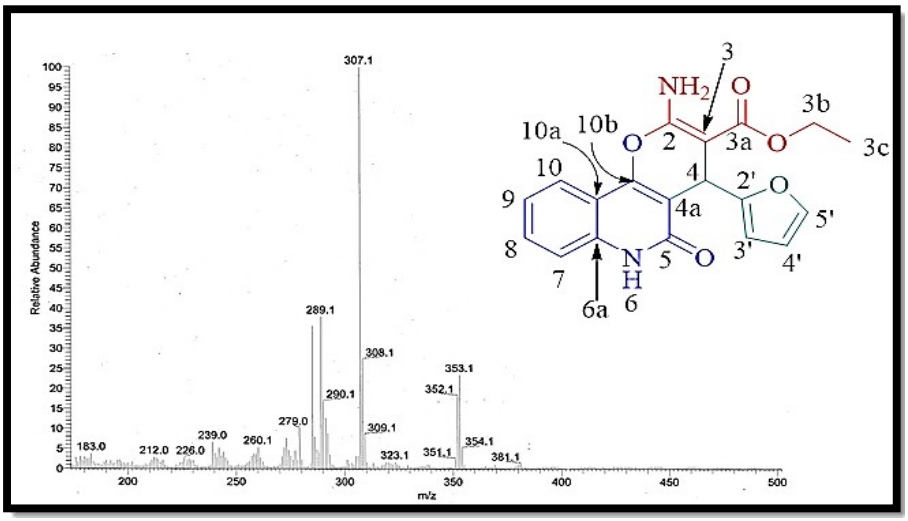
SI Figure 1. [1]H NMR spectrum of compound **3a**



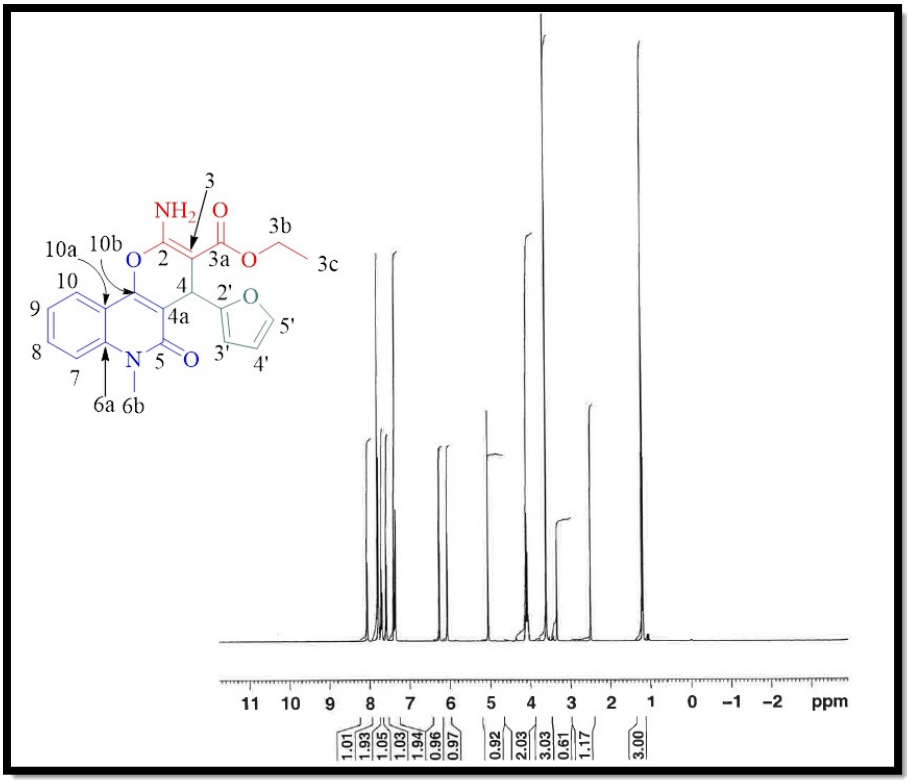
SI Figure 2. [1]H -[1]H- COSY NMR of compound **3a**



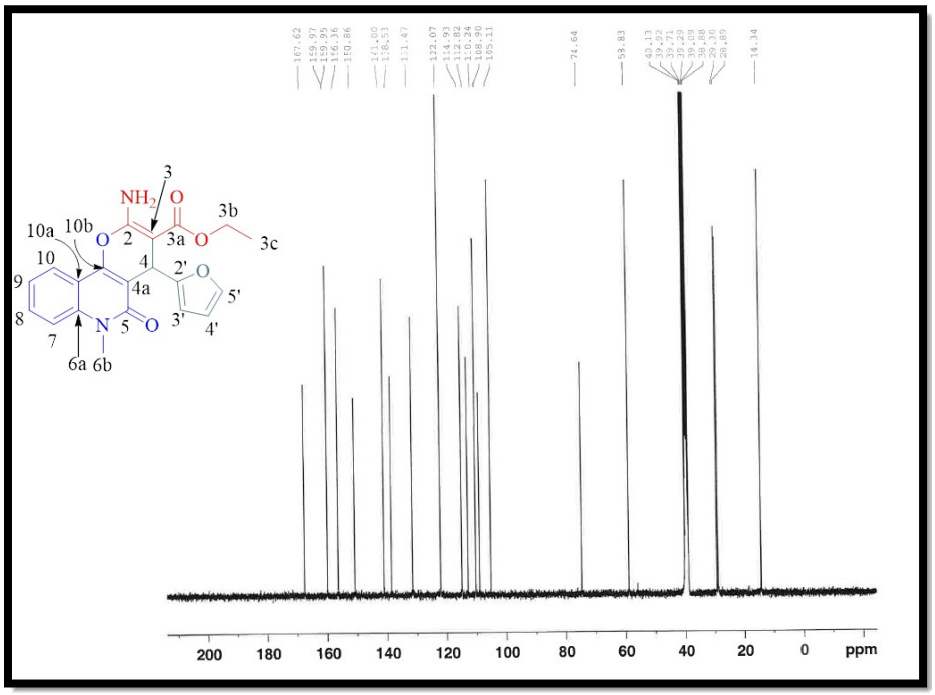
SI Figure 3. ^{13}C NMR spectrum of compound **3a**



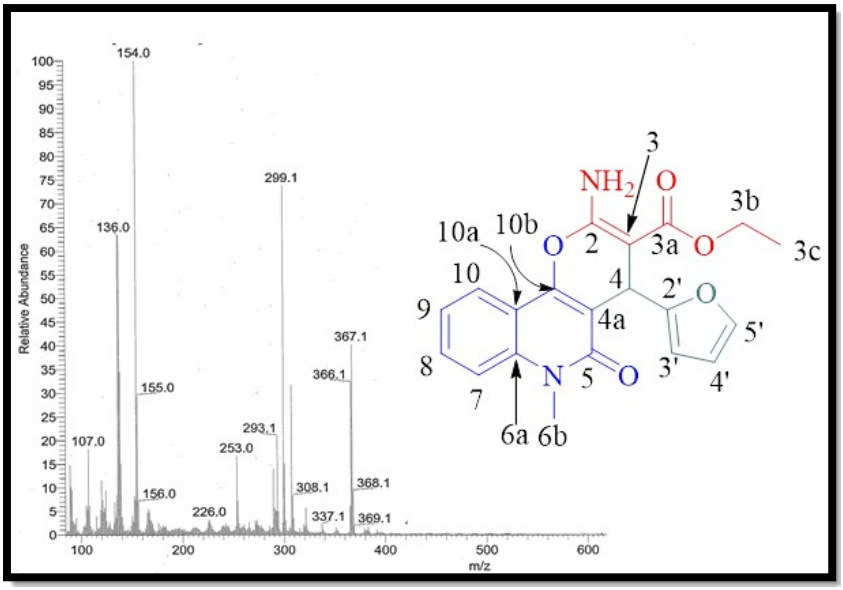
SI Figure 4. Mass spectroscopy of compound **3a**



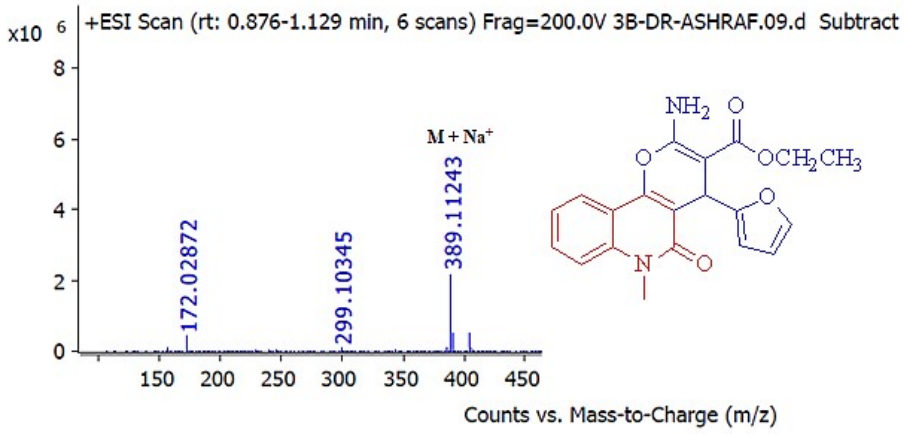
SI Figure 5. ^{1}**H** NMR spectrum of compound **3b**



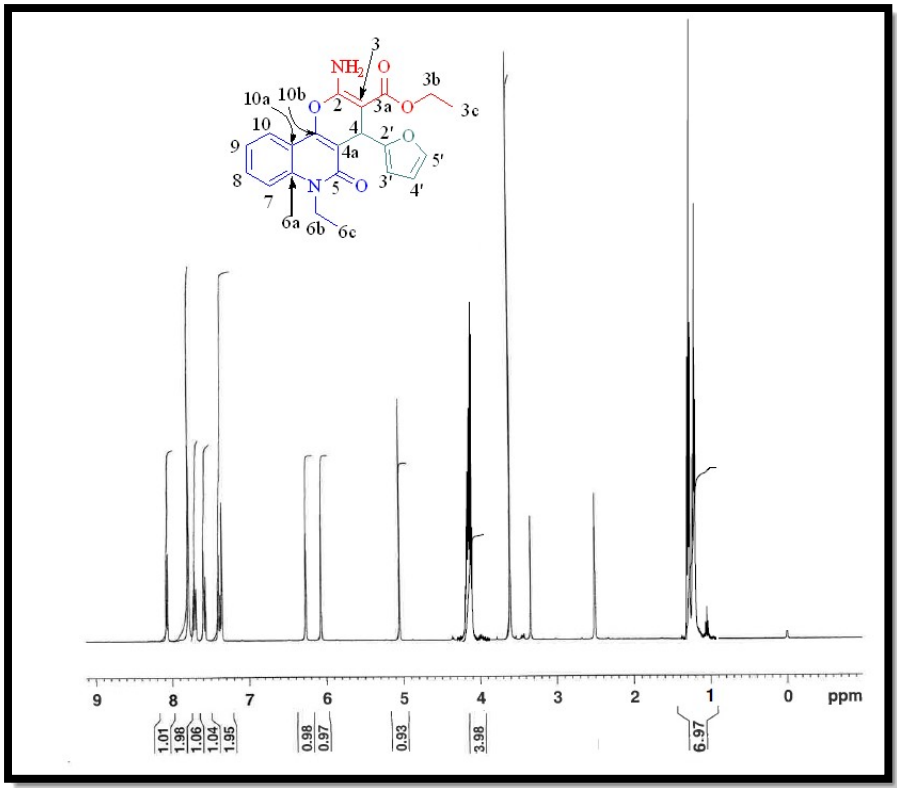
SI Figure 6. ^{13}C NMR spectrum of compound **3b**



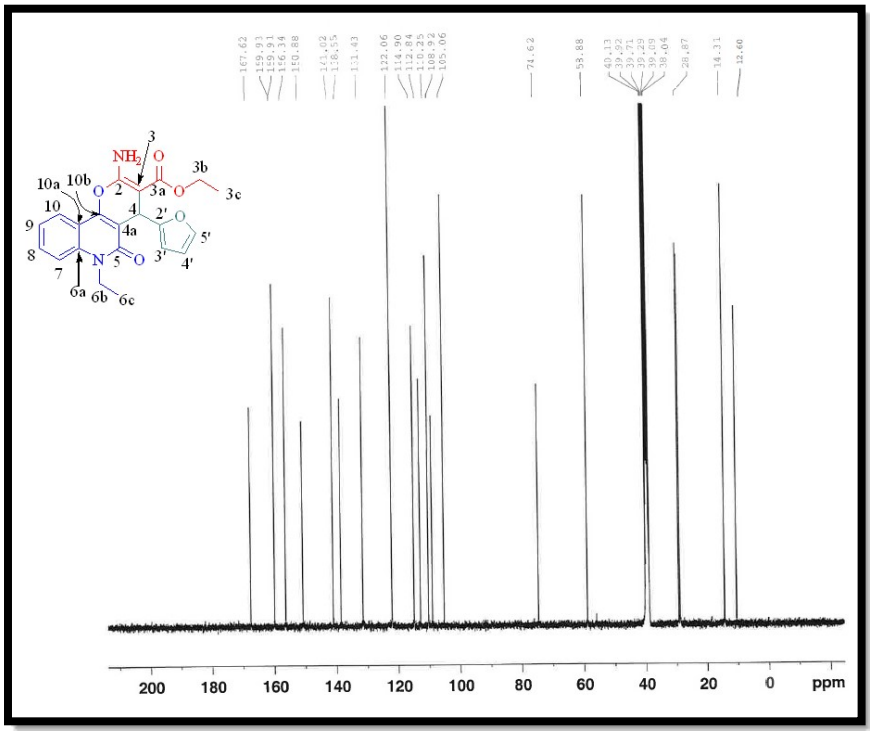
SI Figure 7. Mass spectrum of compound **3b**



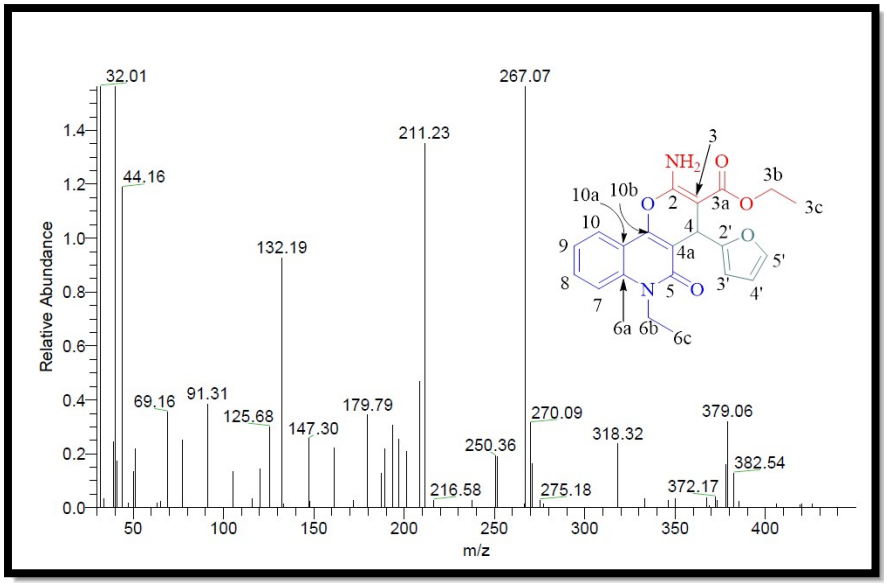
SI Figure 8. HRMS spectroscopy of compound **3b**



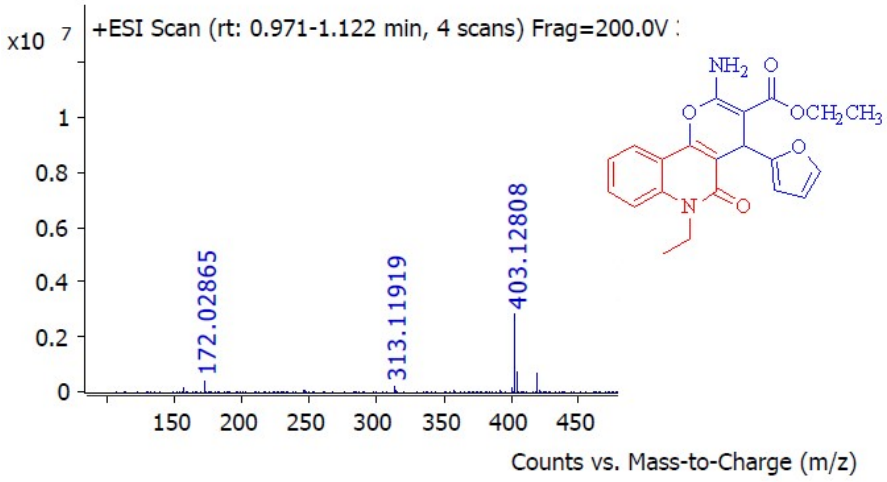
SI Figure 9. ^{1}**H** NMR spectrum of compound **3c**



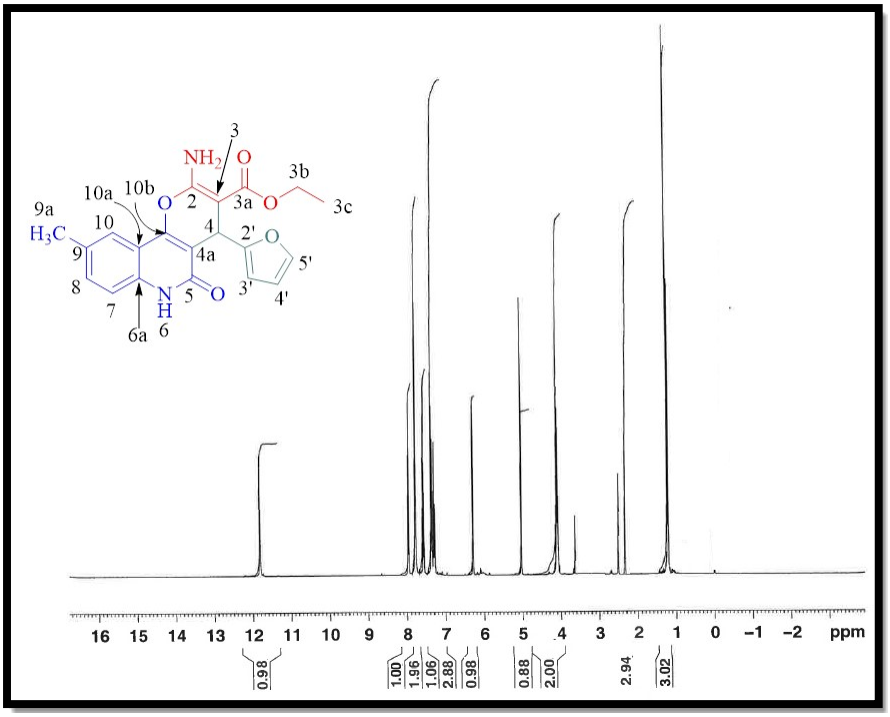
SI Figure 10. ^{13}C NMR spectrum of compound **3c**



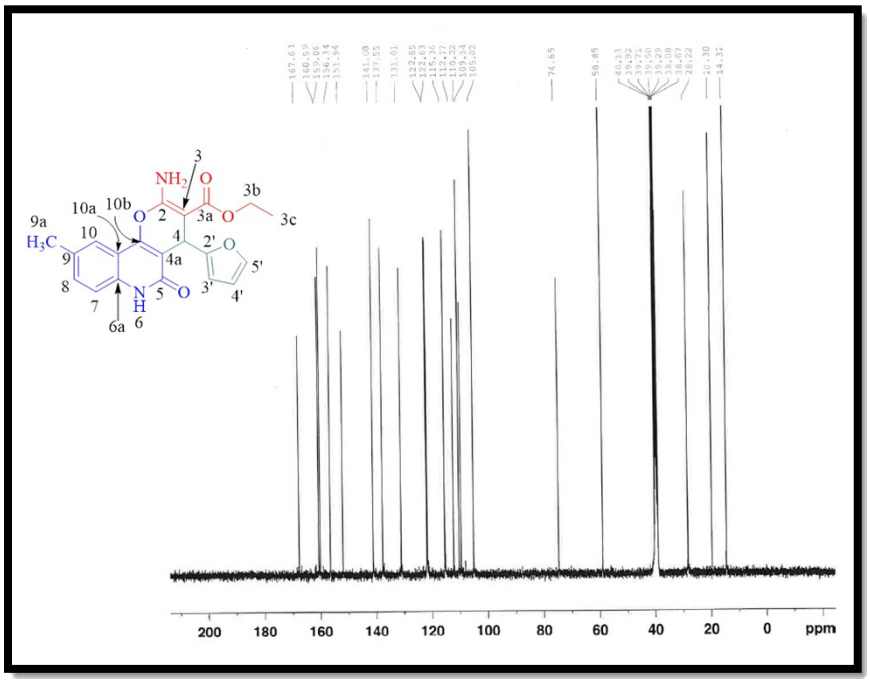
SI Figure 11. Mass spectrum of compound **3c**



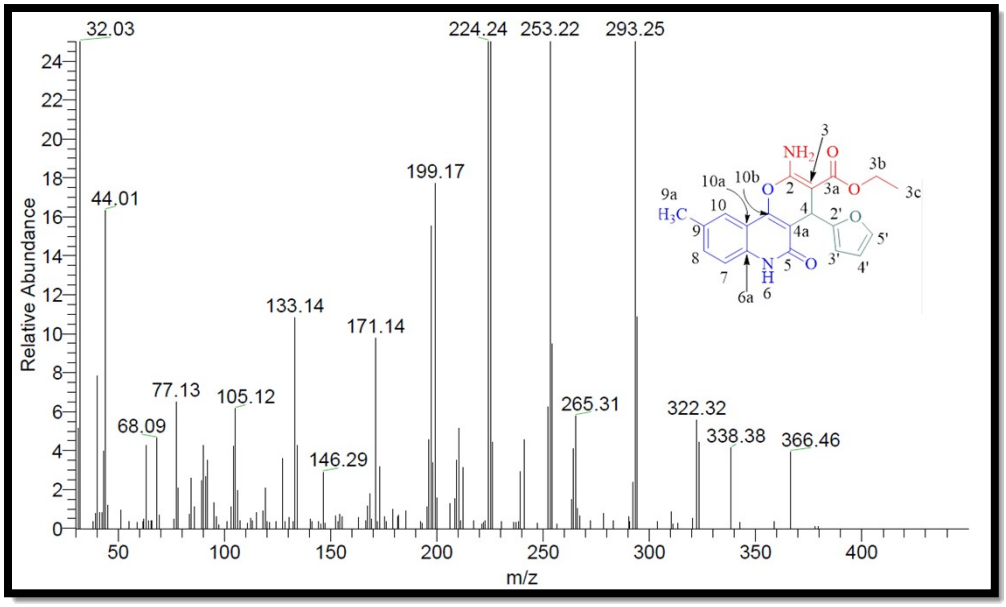
SI Figure 12. HRMS of spectroscopy of compound **3c**



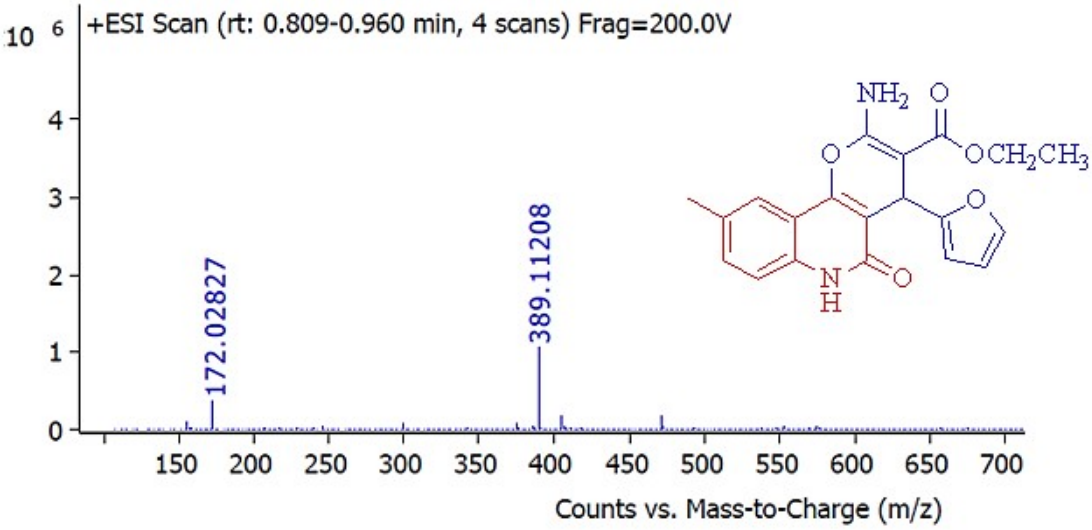
SI Figure 13. ^{1}H NMR spectrum of compound **3d**



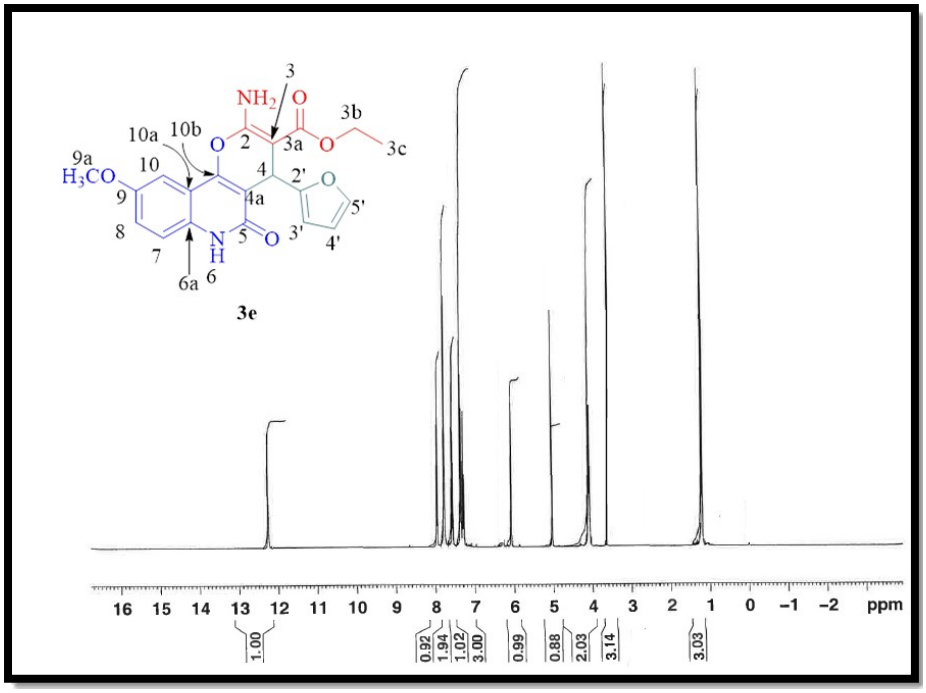
SI Figure 14. ^{13}C NMR spectrum of compound **3d**



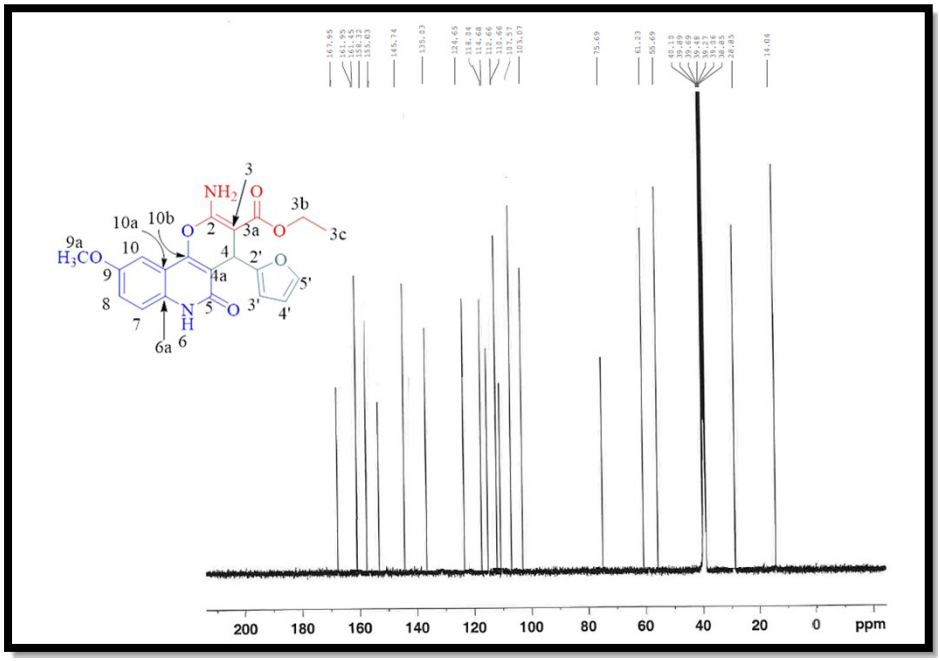
SI Figure 15. Mass spectrum of compound **3d**



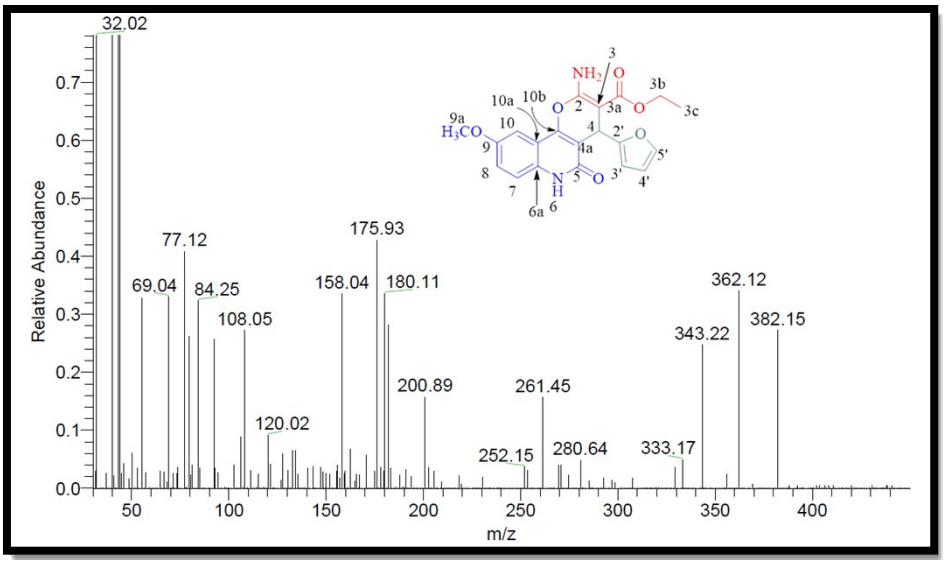
SI Figure 16. HRMS spectroscopy of compound **3d**



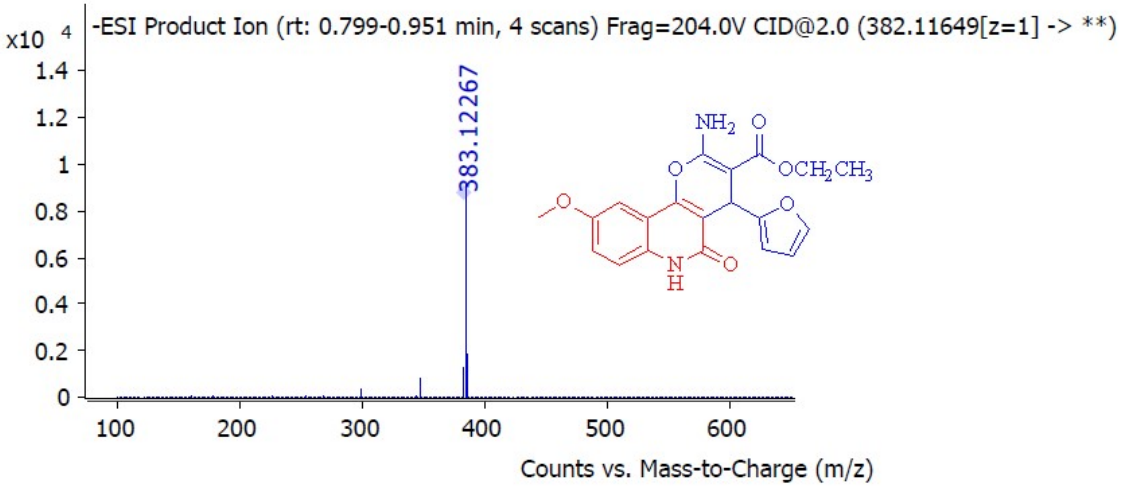
SI Figure 17. ^{1}H NMR spectrum of compound **3e**



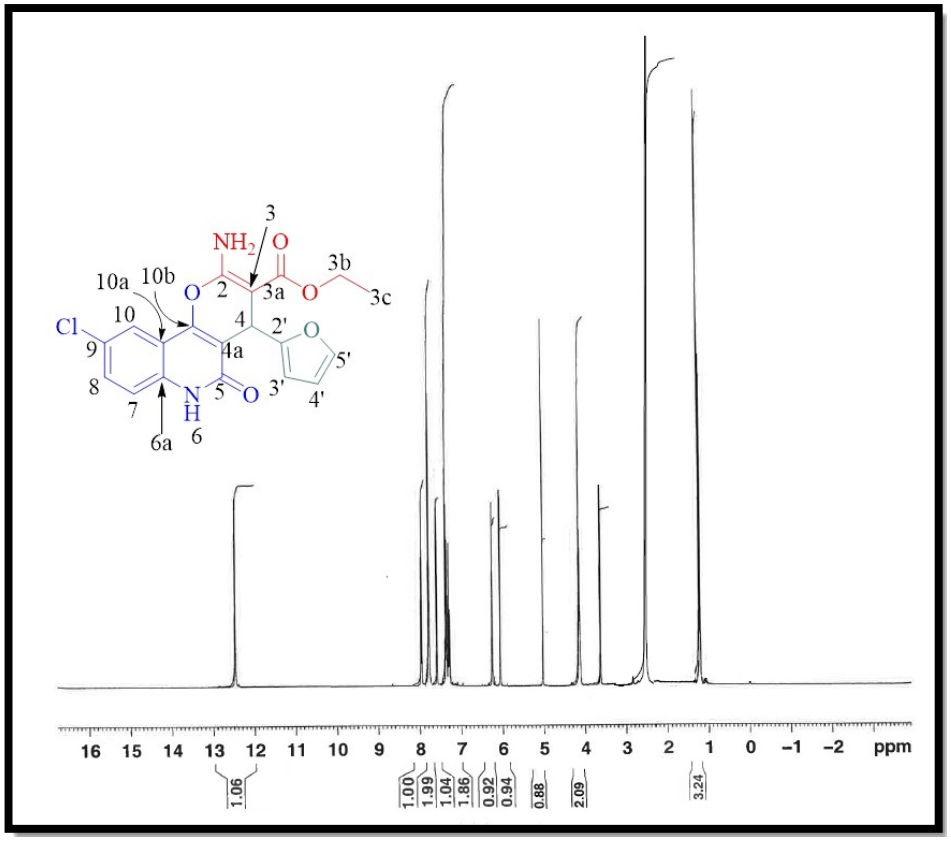
SI Figure 18. ^{13}C NMR spectrum of compound **3e**



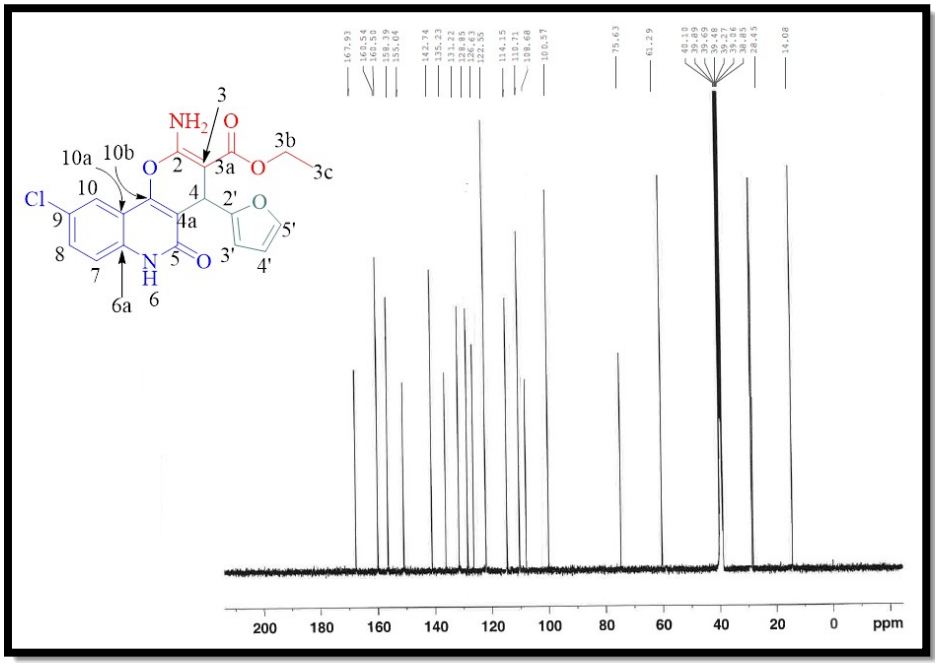
SI Figure 19. Mass spectrum of compound **3e.**



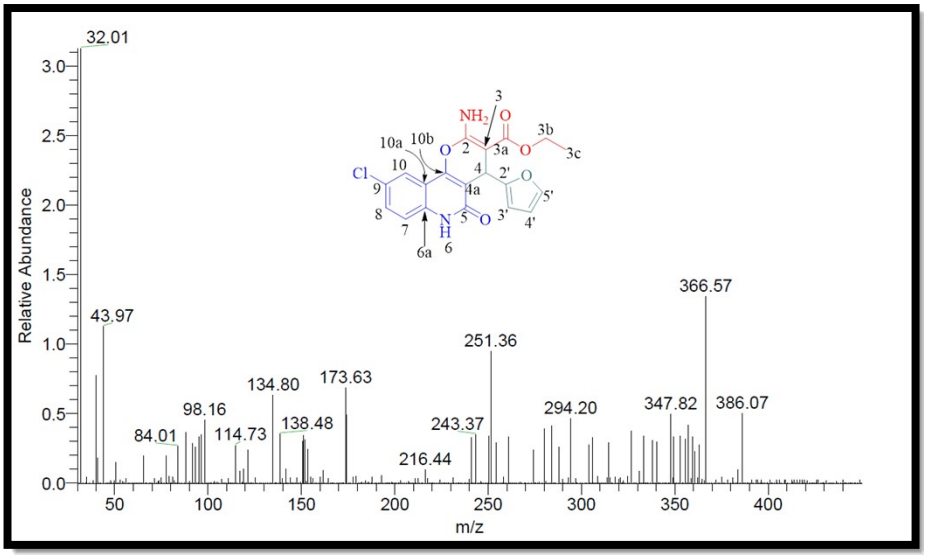
SI Figure 20. HRMS spectroscopy of compound **3e.**



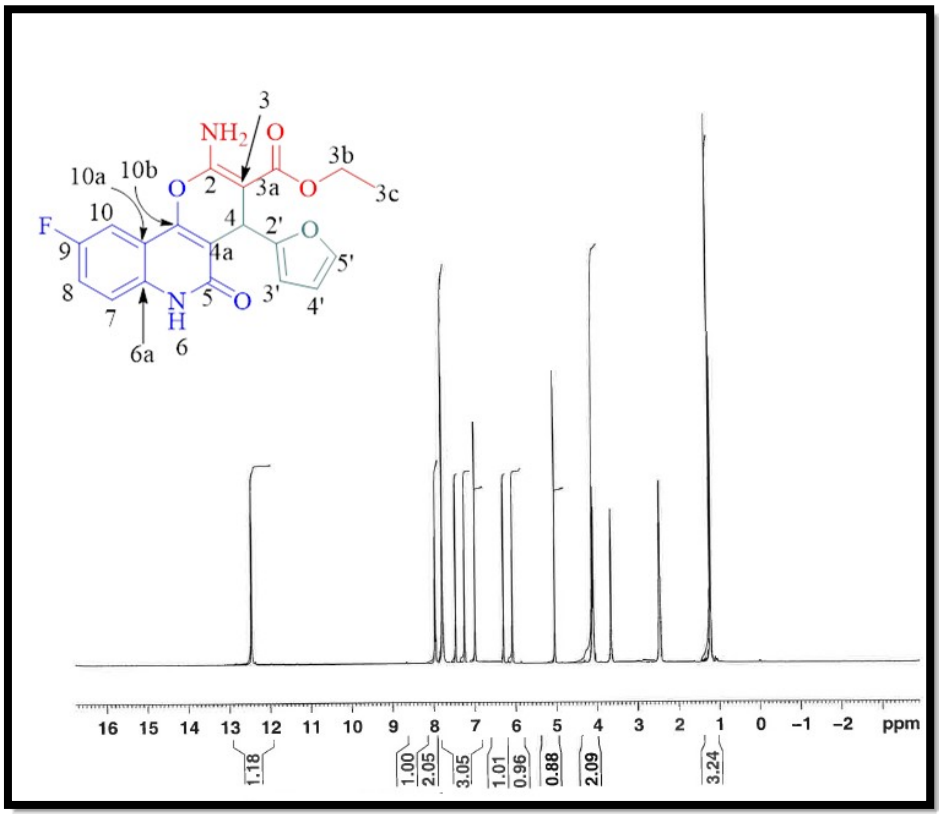
SI Figure 21. ^{1}H NMR spectrum of compound **3f**



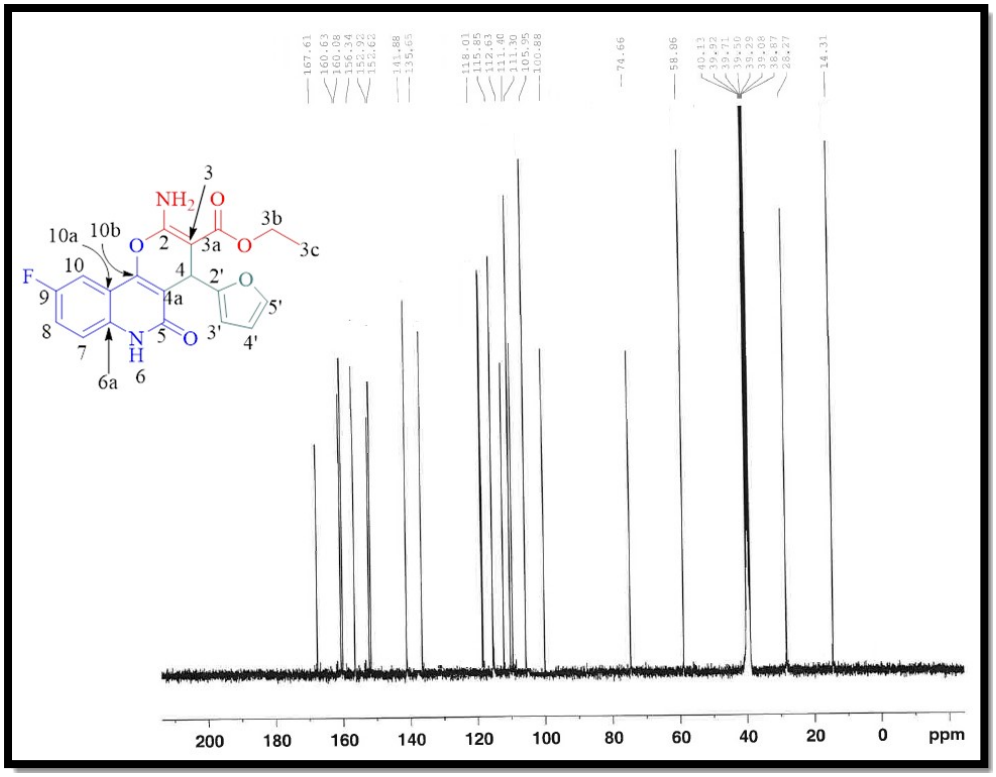
SI Figure 22. ^{13}C NMR spectrum of compound **3f**



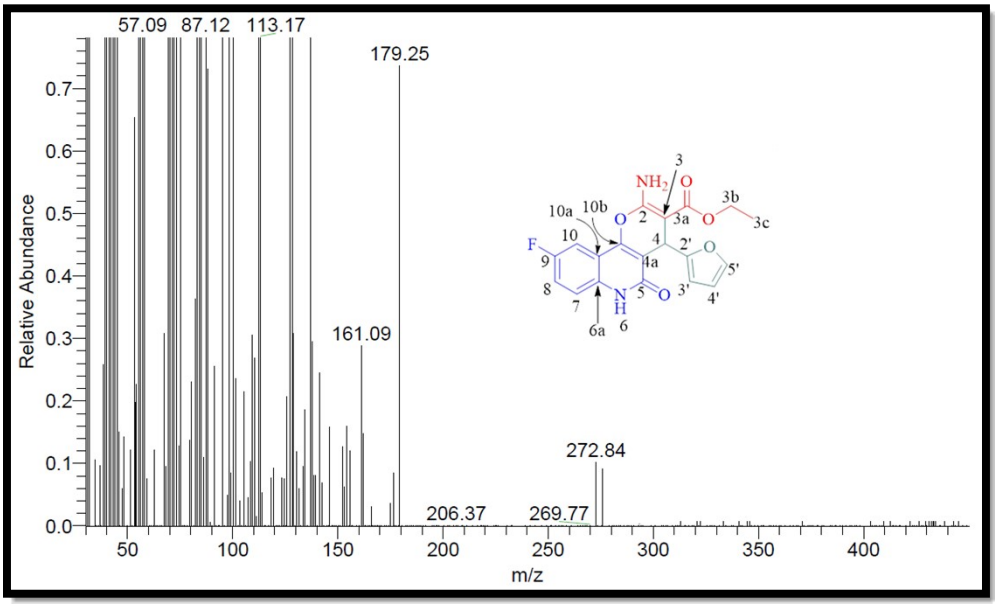
SI Figure 23. Mass spectrum of compound **3f**



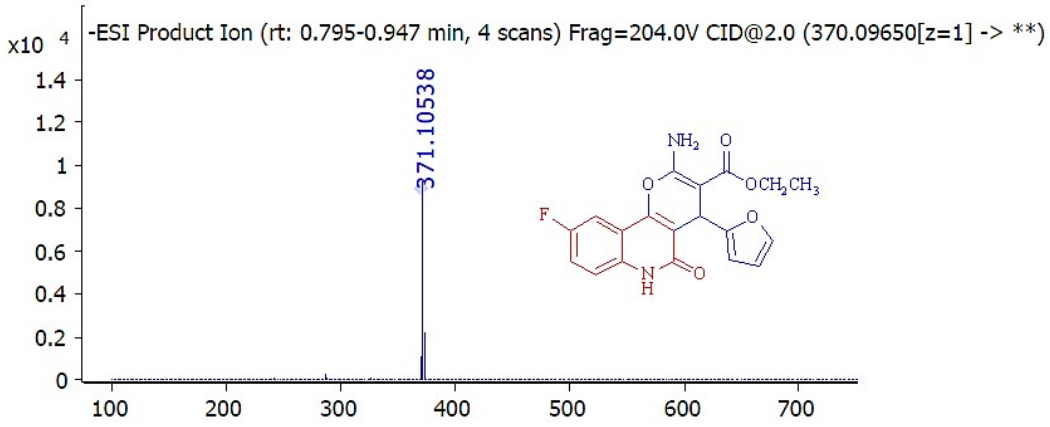
SI Figure 24. ^{1}H NMR spectrum of compound **3g**



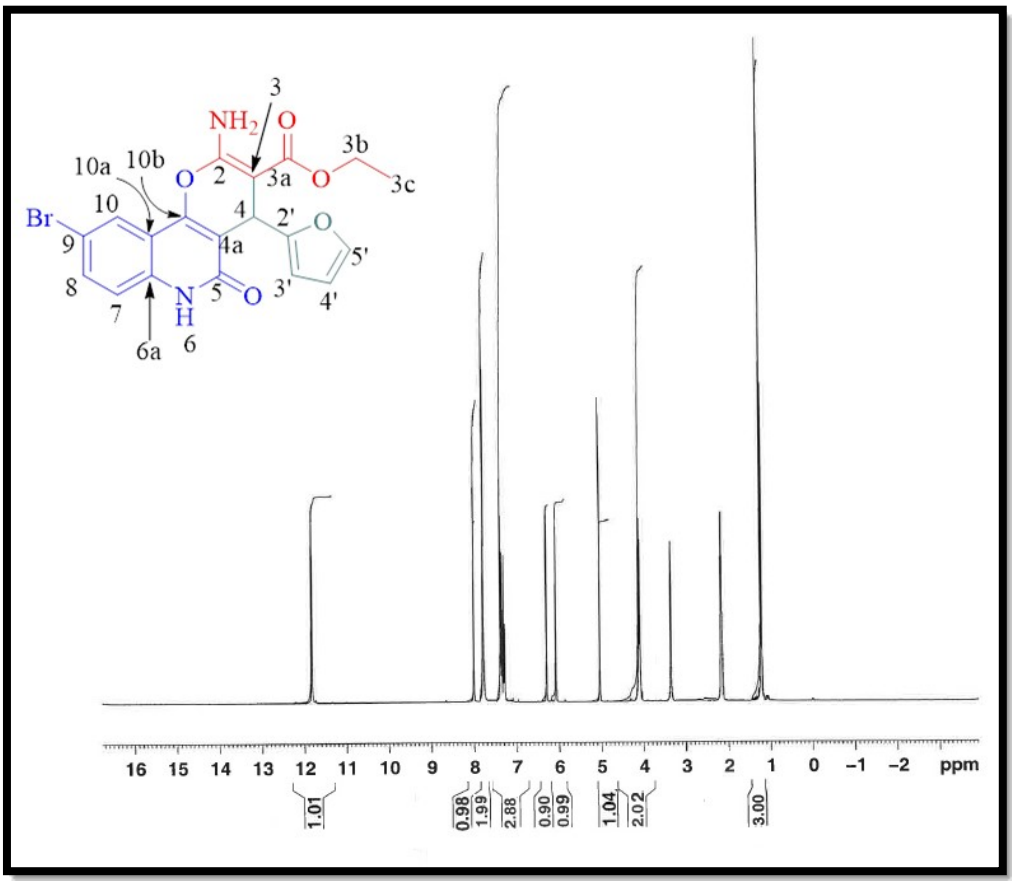
SI Figure 25. ^{13}C NMR spectrum of compound **3g**



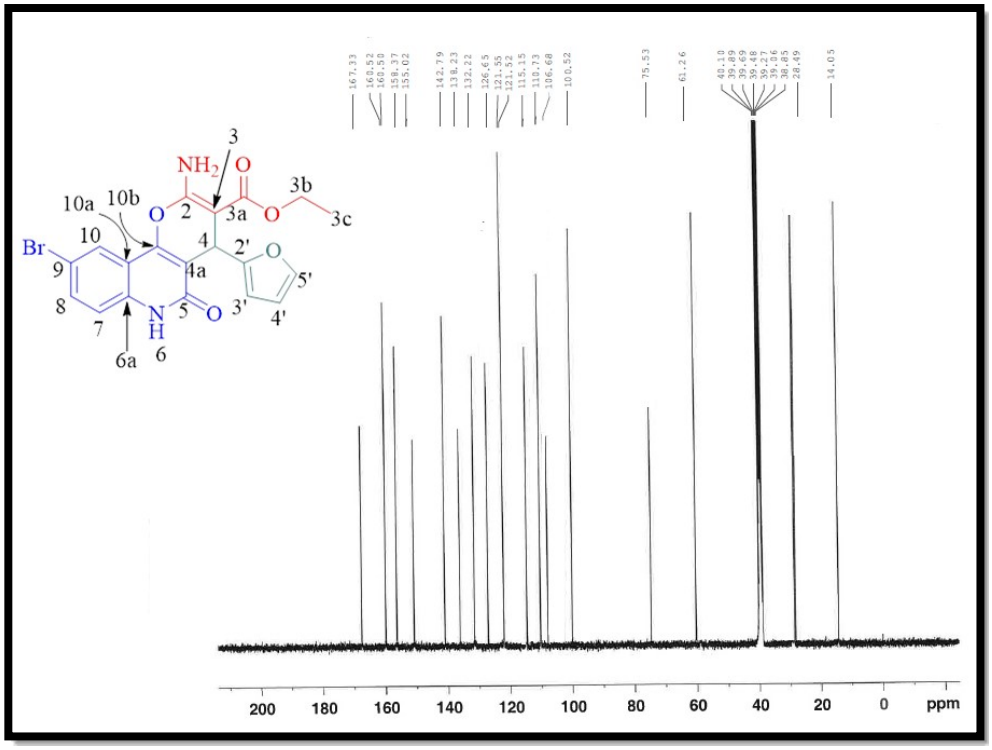
SI Figure 26. Mass spectrum of compound **3g**



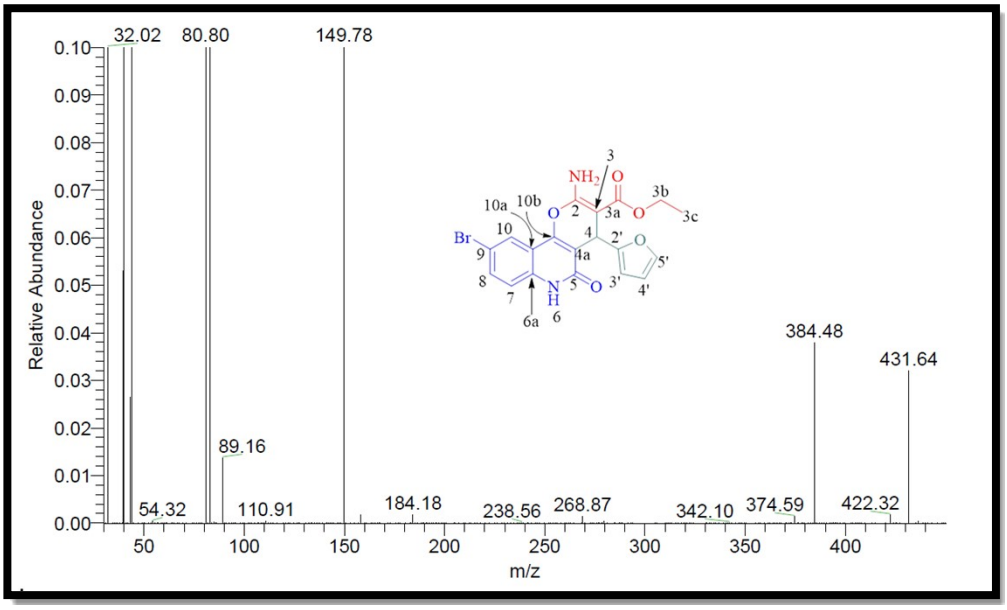
SI Figure 27. HRMS spectroscopy of compound **3g**



SI Figure 28. ^{1}H NMR spectrum of compound **3h**

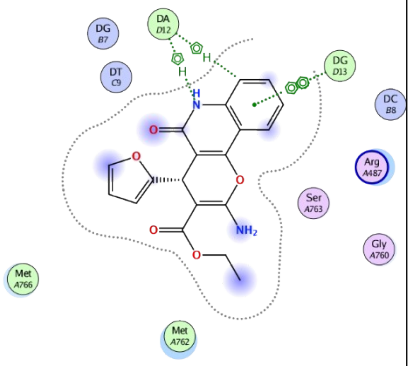
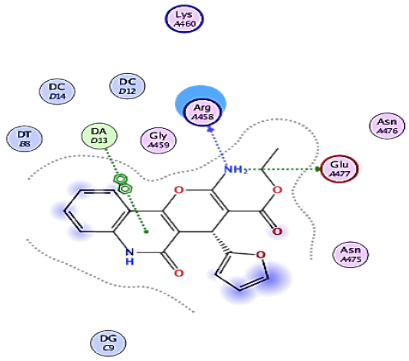
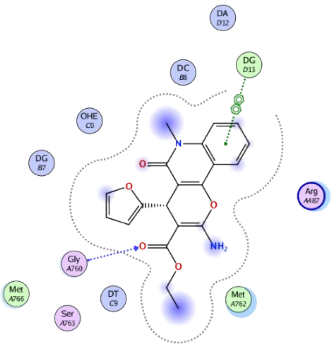
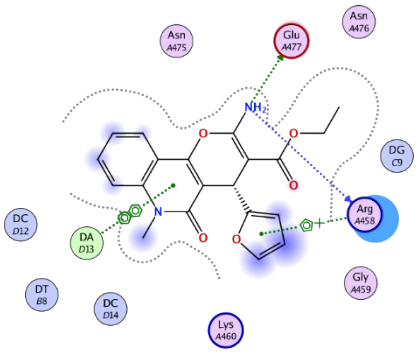
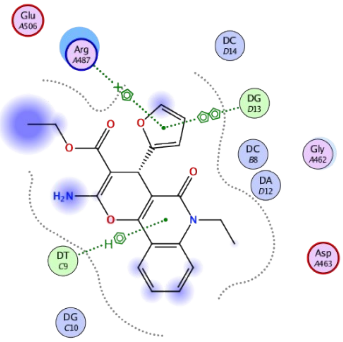
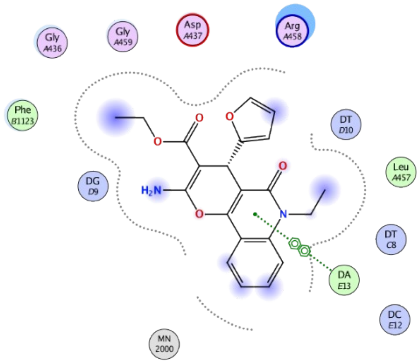


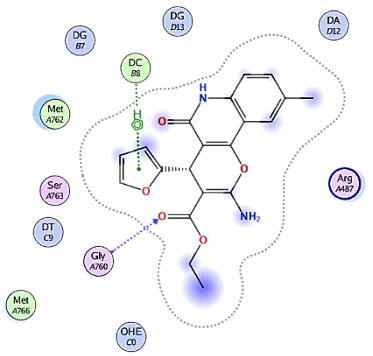
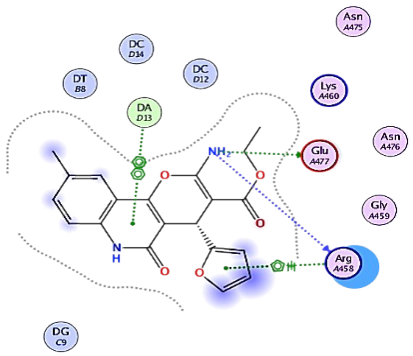
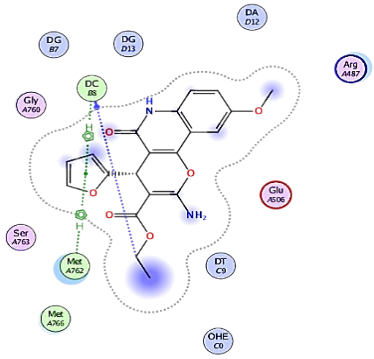
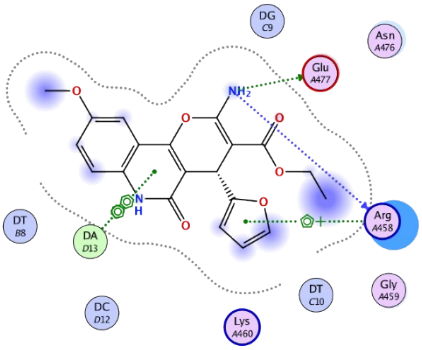
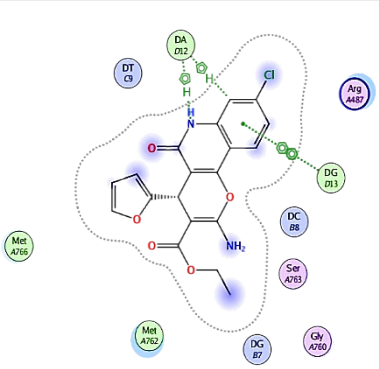
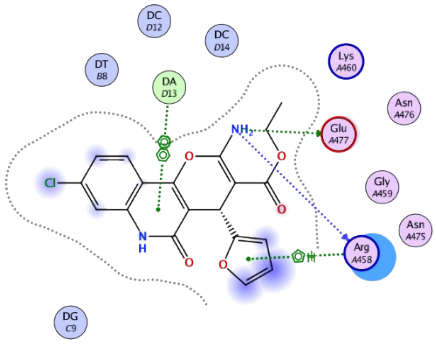
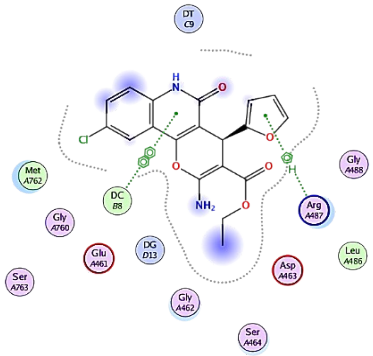
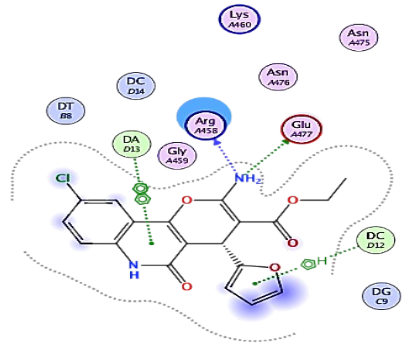
SI Figure 29. ^{13}C NMR spectrum of compound **3h**

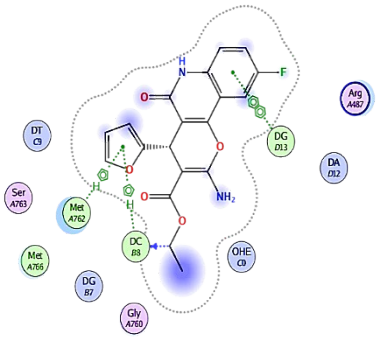
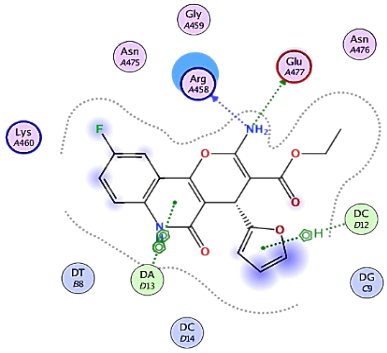
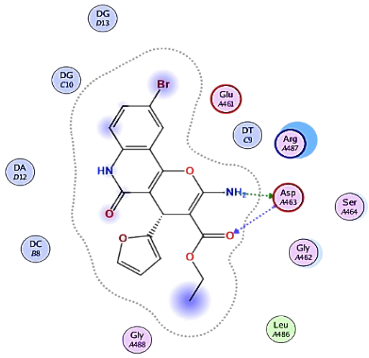
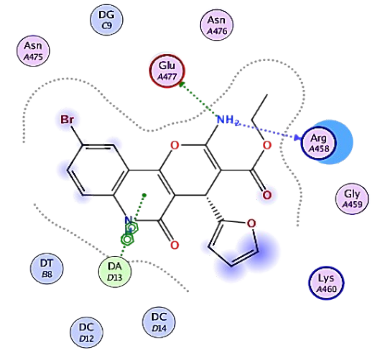
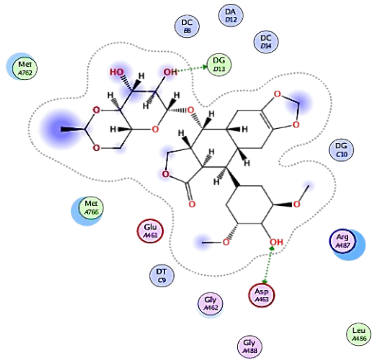
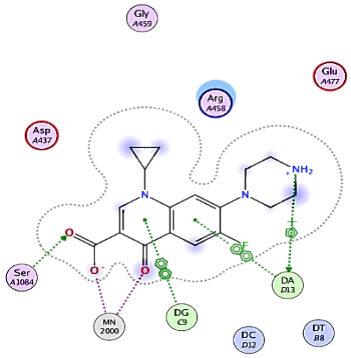


SI Figure 30. Mass spectrum of compound **3h**

Docking study

Compound	Topo II	Binding interactions with Topo II	DNA gyrase	Binding interactions with DNA Gyrase
3a	-7.63		-8.14	
3b	-7.72		-8.27	
3c	-8.01		-8.26	

3d	-7.90		-8.55	
3e	-8.19		-8.31	
3f	-7.96		-8.45	
3g	-7.55		-8.25	

3h	-7.80		-8.03	
3i	**-7.82**		**-8.63**	
Co-crystallized ligand	**-11.02 (0.35)**		**-9.92 (0.64)**	

X-Ray Crystal Structure Determinations of 3a and 3b

The single-crystal X-ray diffraction study were carried out on a Rigaku XtaLAB Synergy R diffractometer with HyPix-Arc 100 detector at 120(2) K (using Cu-K□ radiation (□ = 1.54178 Å, PhotonJet R rotating anode generator). Dual space methods (SHELXT) [G. M. Sheldrick, *Acta Crystallogr.* 2015, **A71**, 3-8] were used for structure solution and refinement was carried out using SHELXL-2014 (full-matrix least-squares on F^2) [G. M. Sheldrick, *Acta Crystallogr.* 2015, **C71**, 3-8]. Hydrogen atoms were localized by difference electron density determination and refined using a riding model (H(N) free). Semi-empirical absorption corrections were applied. In **3b** one furan-2-yl moiety was disordered (see cif-file for detaila). **3b** was refined as a 2-component twin (see cif-file for details).

3a - SB1526_HY: orange crystals, $C_{19}H_{16}N_2O_5$, M_r = 352.34, crystal size 0.10 × 0.08 × 0.04 mm, triclinic, space group *P-1* (No. 2), a = 8.2266(2) Å, b = 8.5847(3) Å, c = 12.5866(3) Å, α = 106.141(3)°, β = 103.673(2)°, γ = 100.320(2)°, V = 800.60(4) Å^3, Z = 2, ρ = 1.462 Mg/m^{-3}, μ(Cu-K$_\alpha$) = 0.90 mm^{-1}, F(000) = 368, T = 120(2) K, $2\theta_{max}$ = 158.6°, 17010 reflections, of which 3430 were independent (R_{int} = 0.024), 244 parameters, 3 restraints, R_1 = 0.039 (for 3087 I > 2σ(I)), wR_2 = 0.116 (all data), S = 1.07, largest diff. peak / hole = 0.34 / -0.26 e Å^{-3}.

3b – SB1525_HY: orange crystals, $C_{20}H_{18}N_2O_5$, M_r = 366.36, crystal size 0.14 × 0.10 × 0.03 mm, triclinic, space group *P-1* (No. 2), a = 7.9731(2) Å, b = 8.1795(2) Å, c = 28.7599(7) Å, α = 91.662(2)°, β = 90.972(2)°, γ = 115.979(2)°, V = 1684.45(8) Å^3, Z = 4, ρ = 1.445 Mg/m^{-3}, μ(Cu-K$_\alpha$) = 0.87 mm^{-1}, F(000) = 768, T = 120(2) K, $2\theta_{max}$ = 158.4°, 9888 independent reflection (R_{int} = 0.000, using a HKLF 5 file due to twin refinement), 495 parameters, 34 restraints, R_1 = 0.051 (for 8552 I > 2σ(I)), wR_2 = 0.142 (all data), S = 1.06, largest diff. peak / hole = 0.30 / -0.30 e Å^{-3}

CCDC 2312660 (**3a – SB1526_HY**) and 2312661 (**3b – SB1525_HY**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

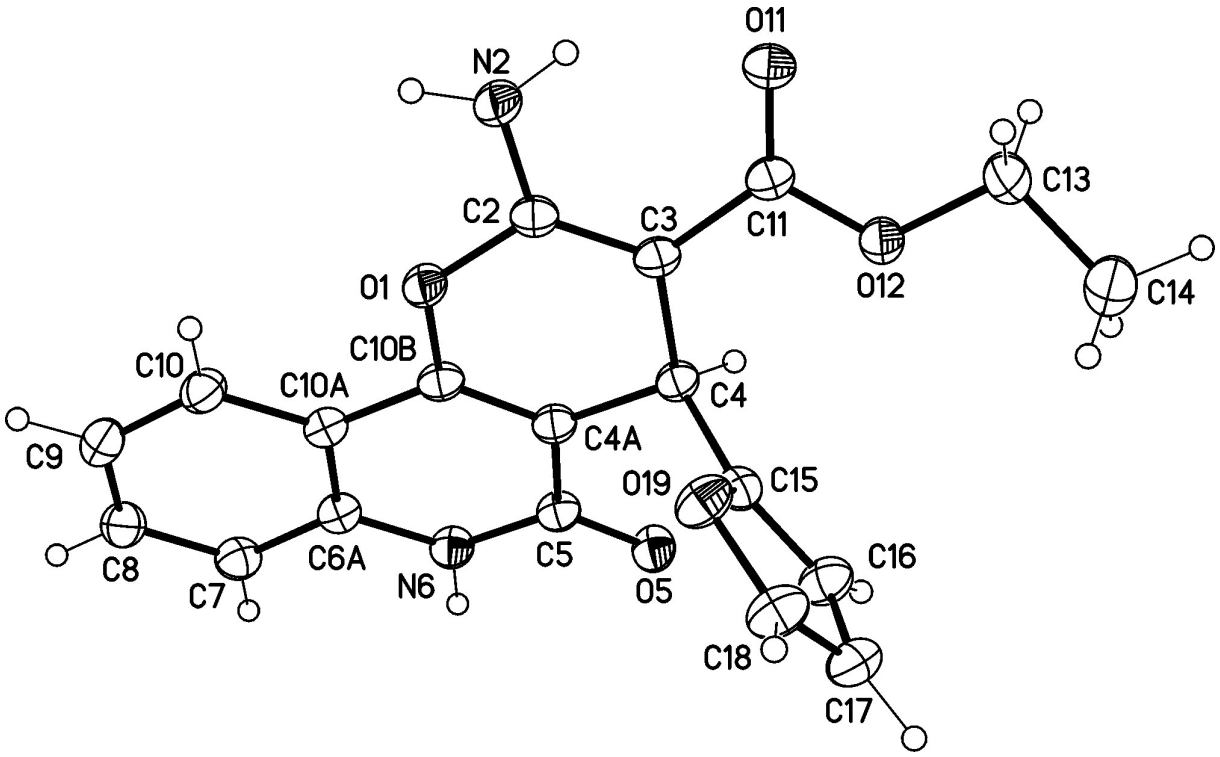


Fig. 31x. Molecular structure of **3a – SB1526_HY** (displacement parameters are drawn at 50 % probability level).

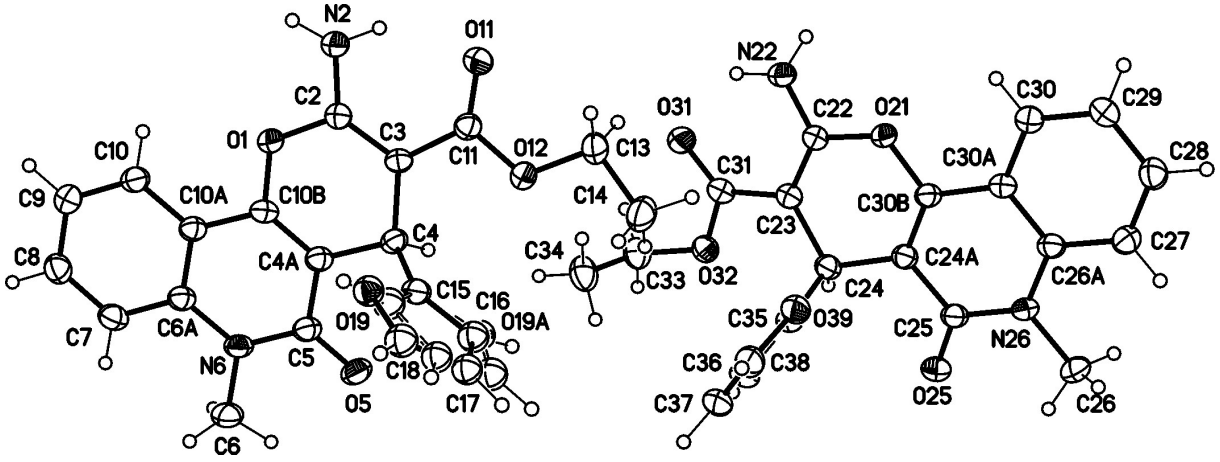


Fig. 32x. Molecular structure (asymmetric unit) of **3b – SB1525_HY** (displacement parameters are drawn at 50 % probability level).

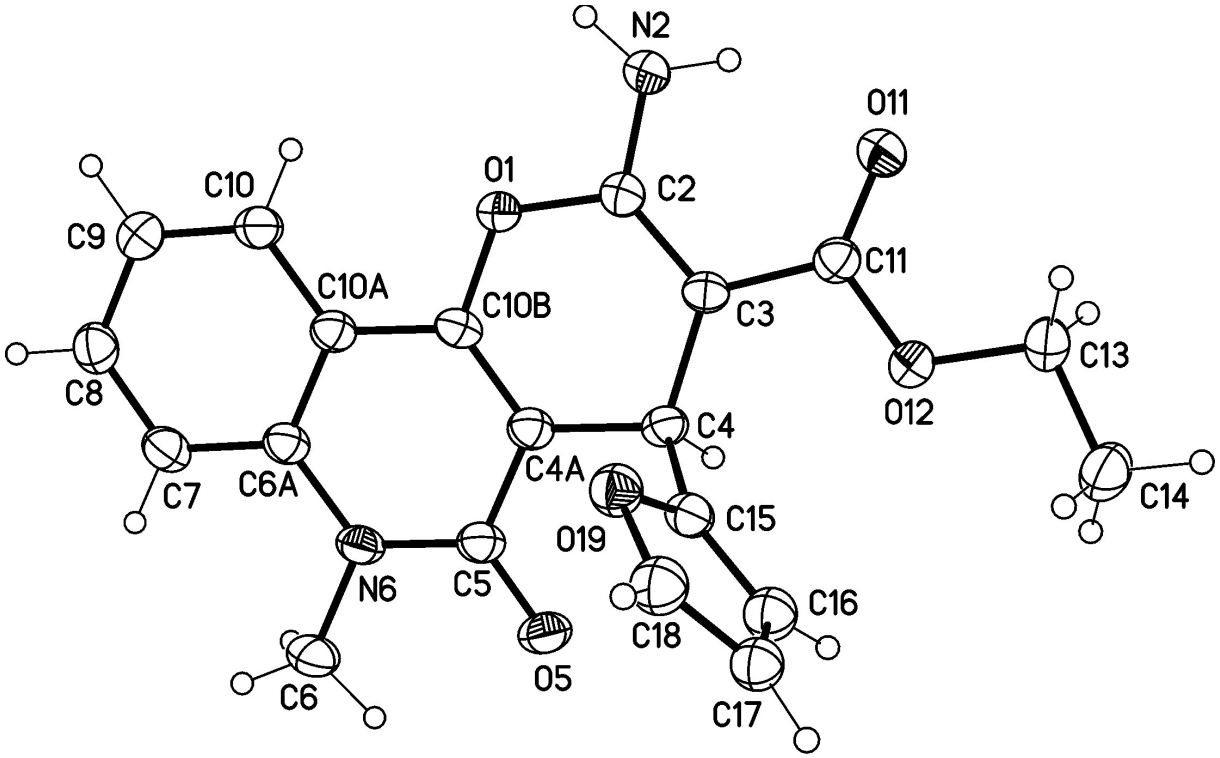


Fig. 33x. 1st crystallographic independent molecule of **3b – SB1525_HY** (displacement parameters are drawn at 50 % probability level).

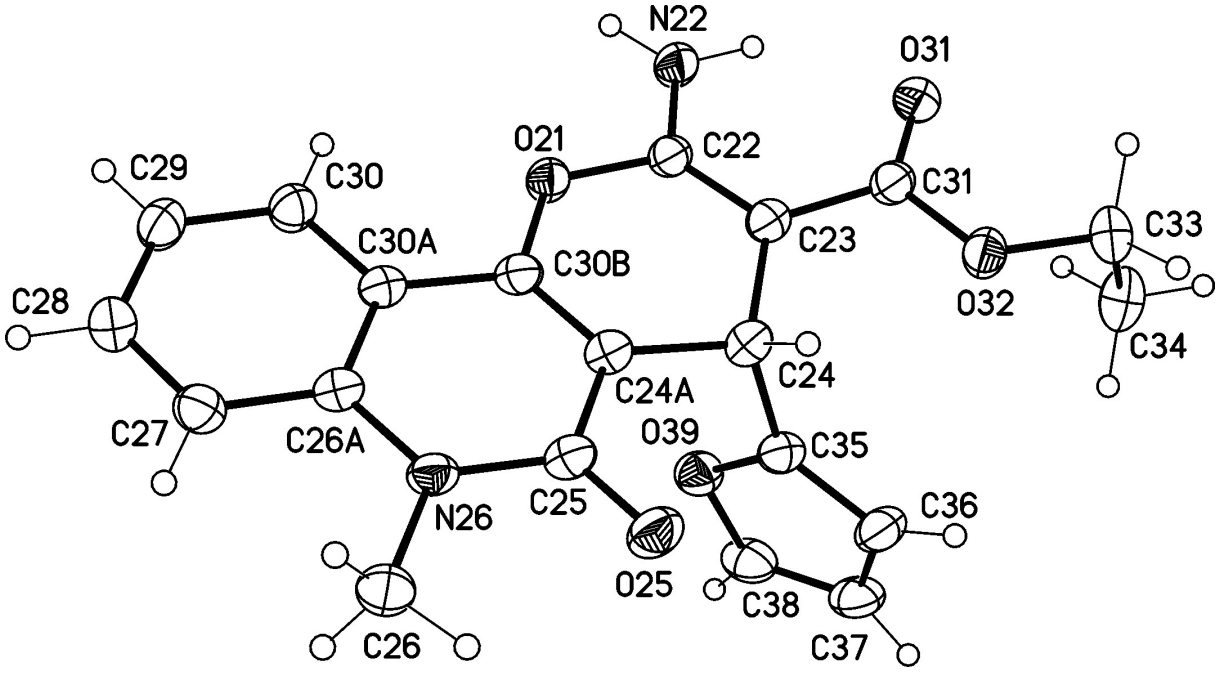


Fig. 34x. 2nd crystallographic independent molecule of **3b – SB1525_HY** (displacement parameters are drawn at 50 % probability level).