Supplementary data

Investigation of the anticancer activity of modified 4-hydroxyquinolone analogues: *in vitro* and *in silico* studies

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1. Spectra

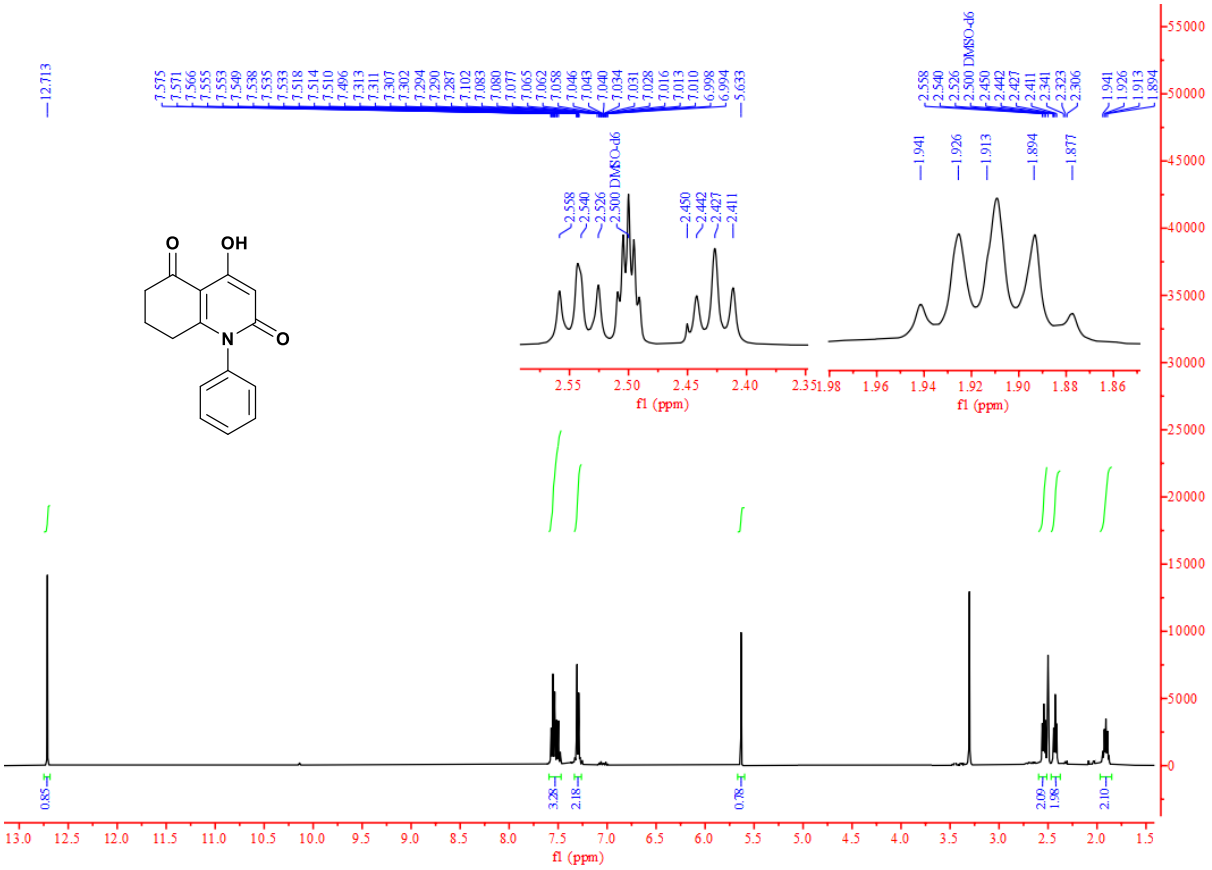


Figure S1. ^{1}H NMR spectrum of **3a** (400 MHz, DMSO-d_6).

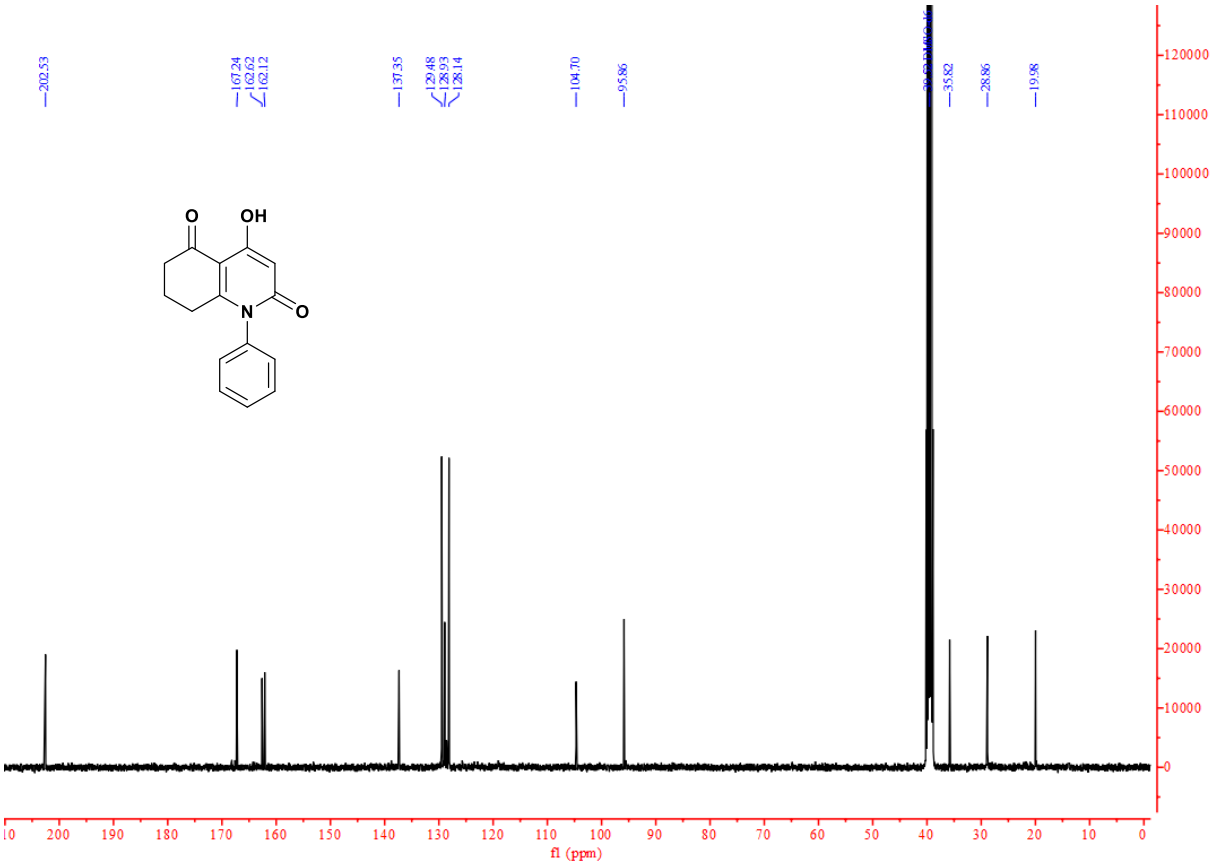


Figure S2. ^{13}C NMR spectrum of **3a** (101 MHz, DMSO-d_6).

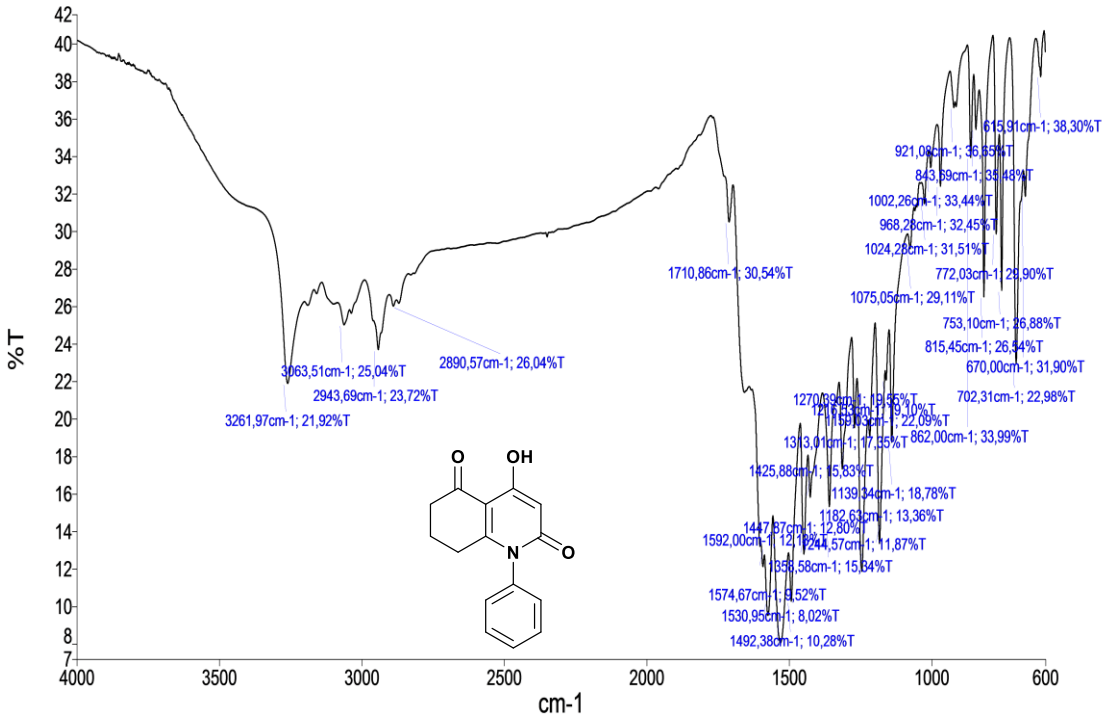


Figure S3. IR spectrum of **3a**.

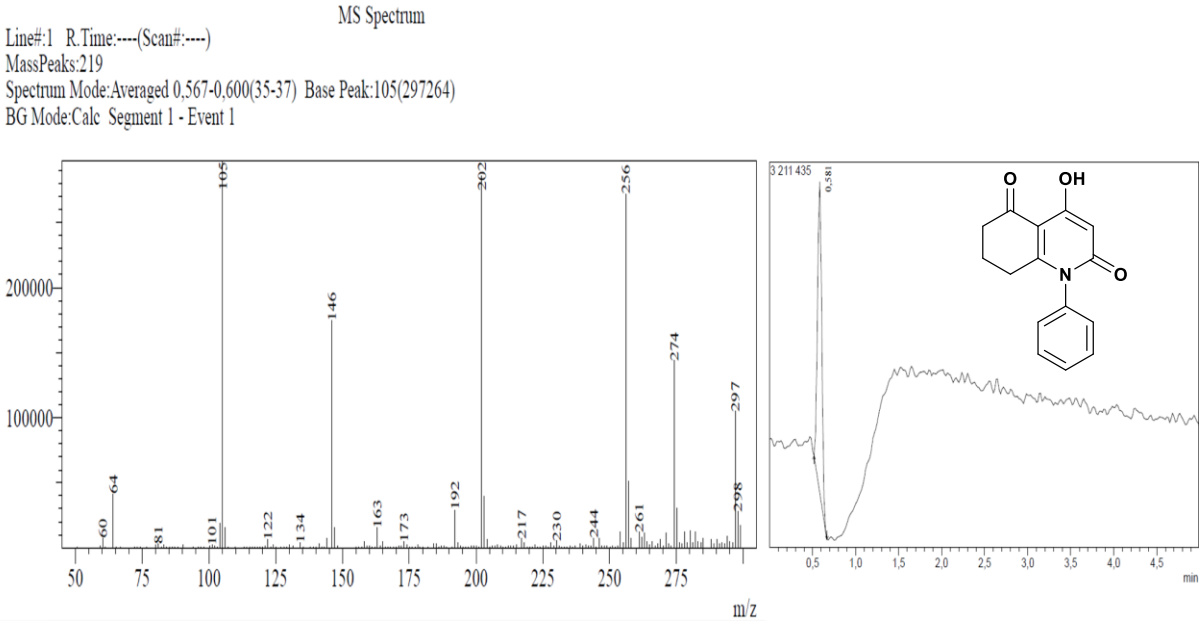


Figure S4. LC-MS spectrum of **3a**.

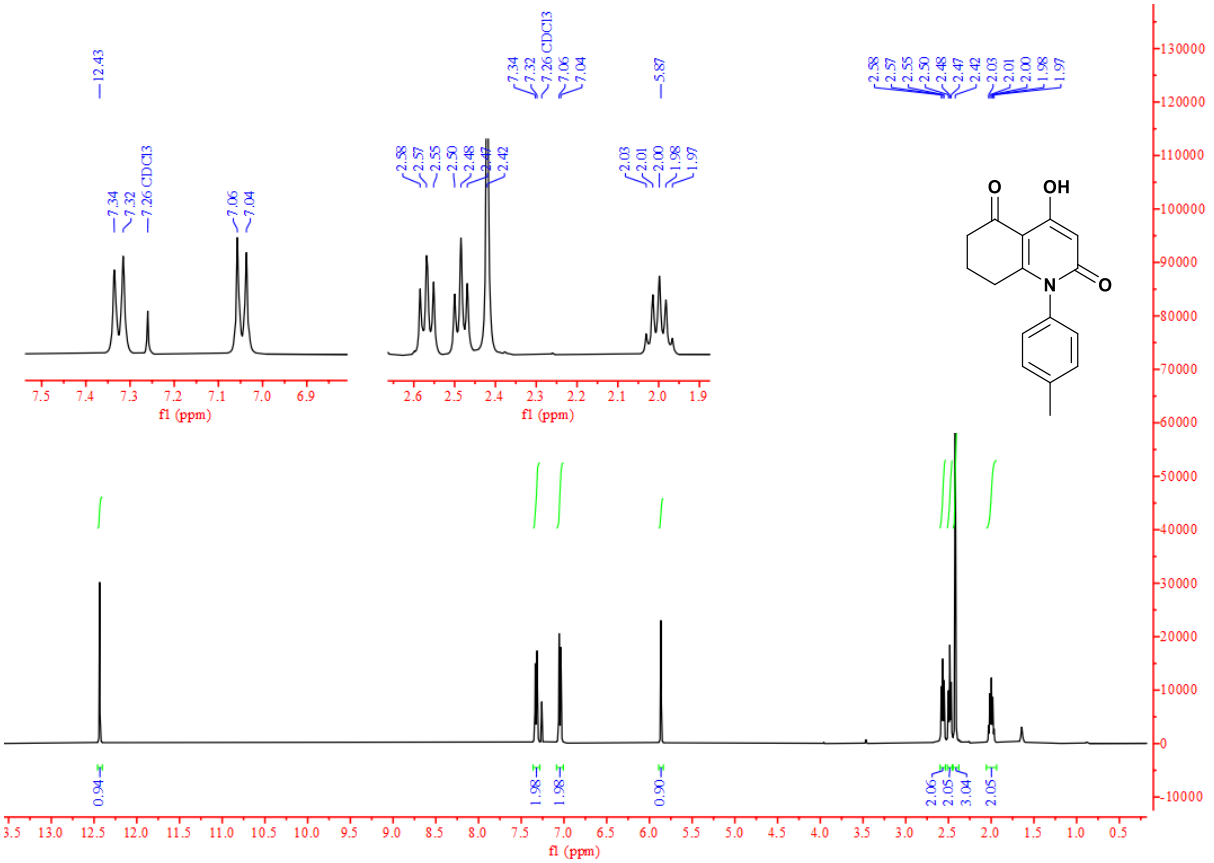


Figure S5. ^{1}H NMR spectrum of **3b** (400 MHz, $CDCl_3$).

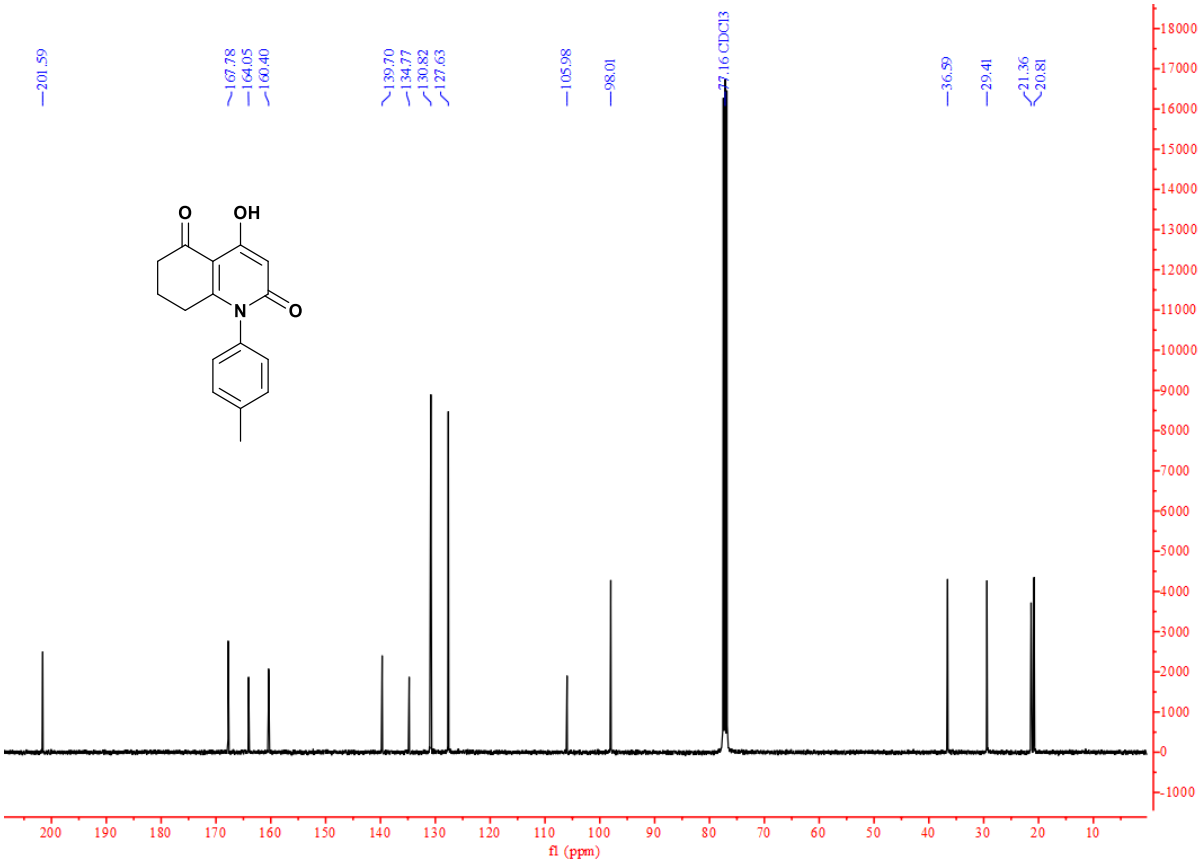


Figure S6. ^{13}C NMR spectrum of **3b** (101 MHz, $CDCl_3$).

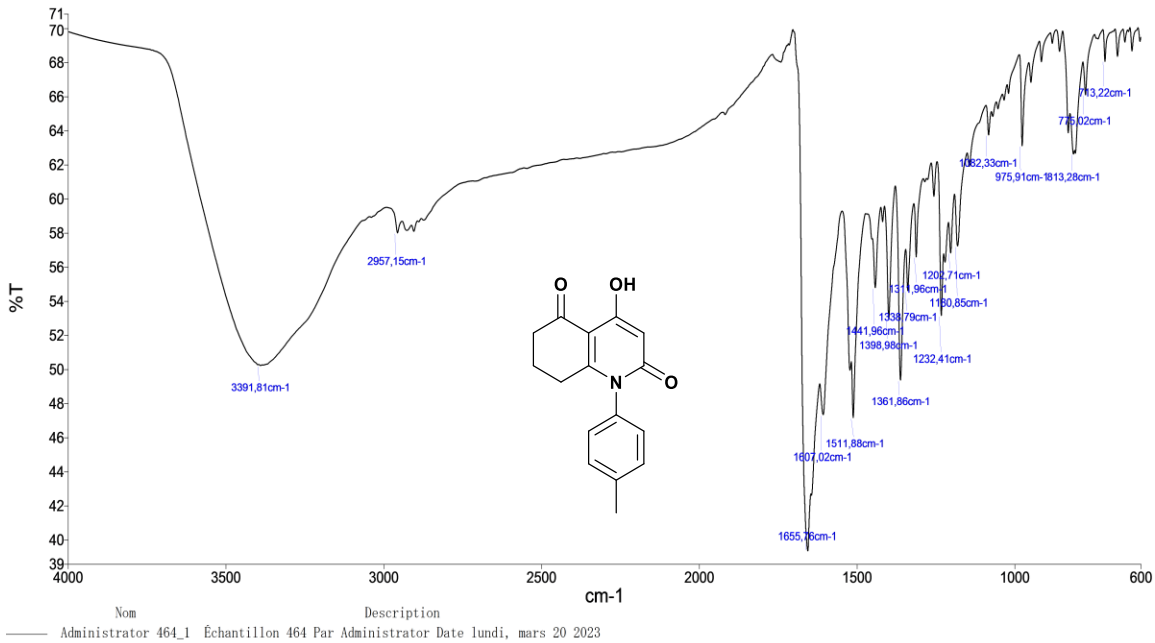


Figure S7. IR spectrum of **3b**.

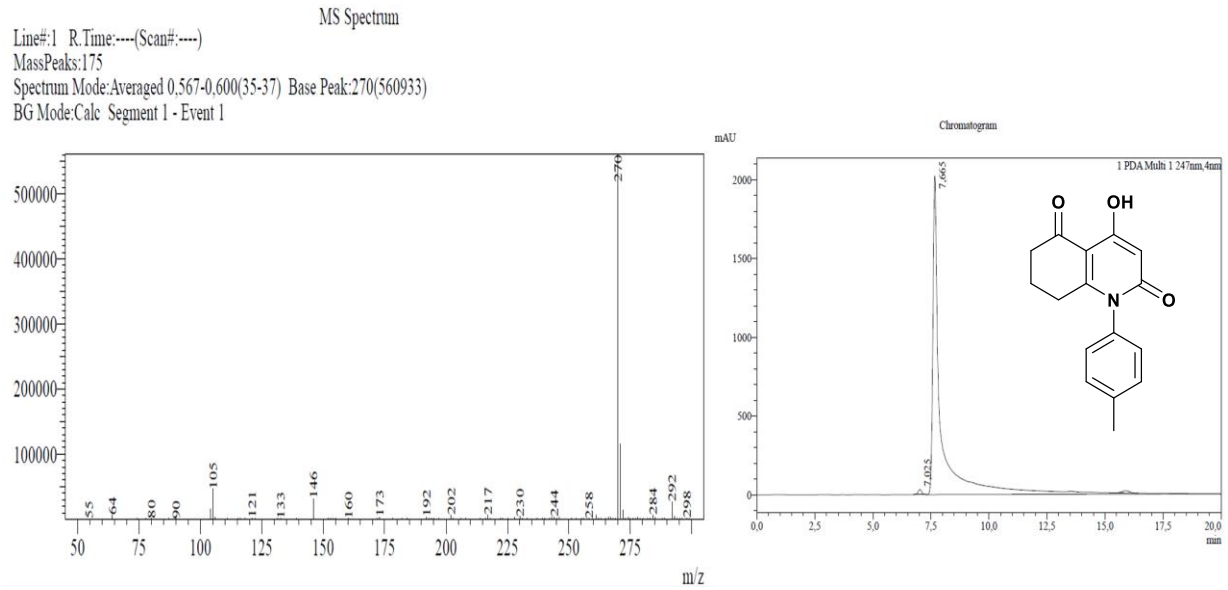


Figure S8. LC-MS spectrum of **3b**.

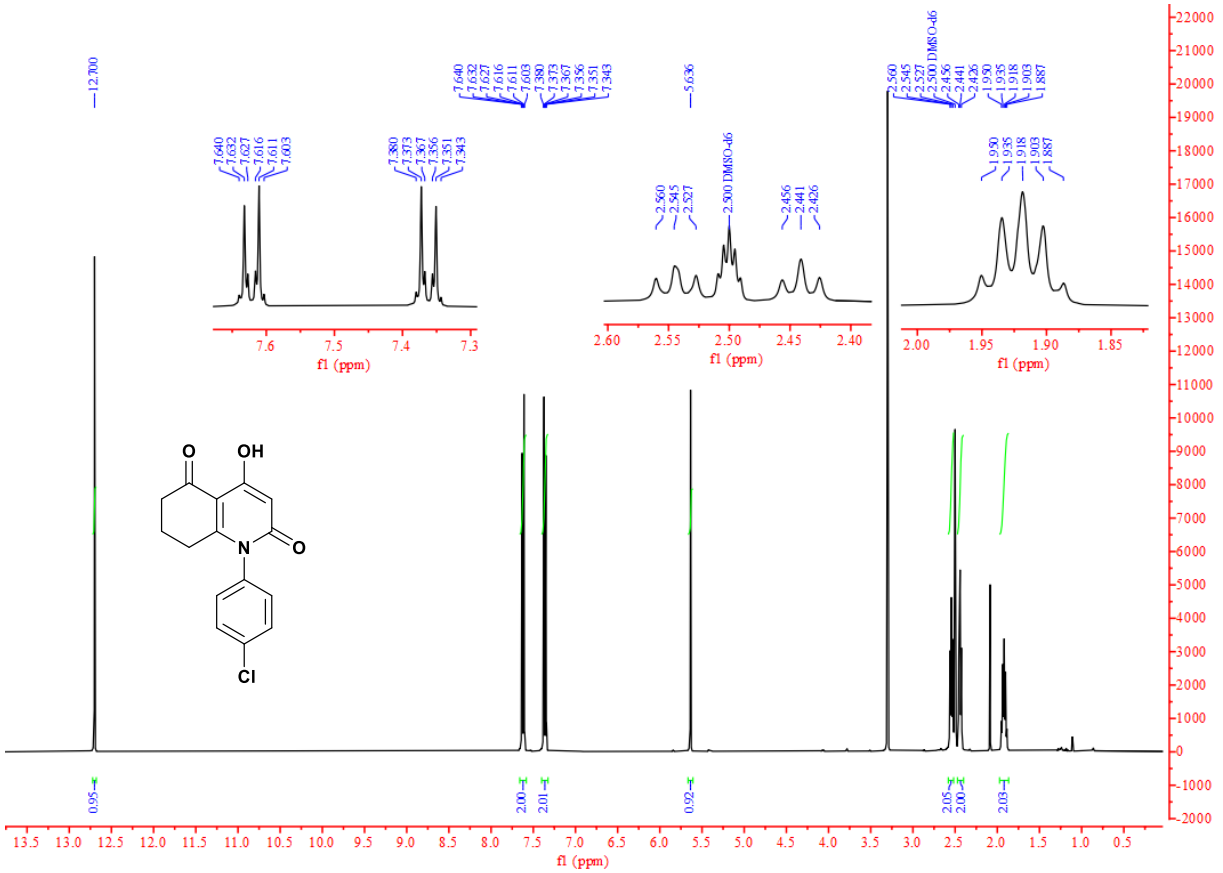


Figure S9. ^{1}H NMR spectrum of **3c** (400 MHz, DMSO-d_6).

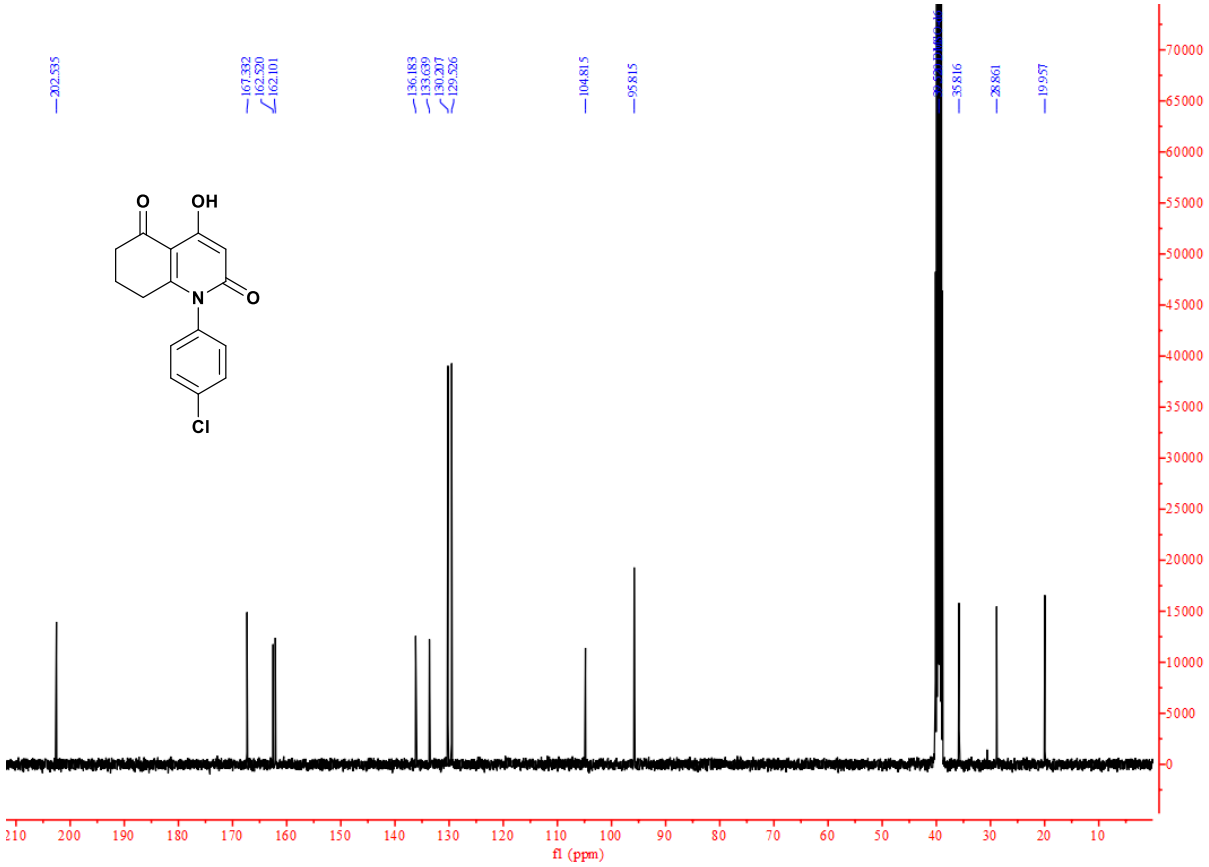


Figure S10. ^{13}C NMR spectrum of **3c** (101 MHz, DMSO-d_6).

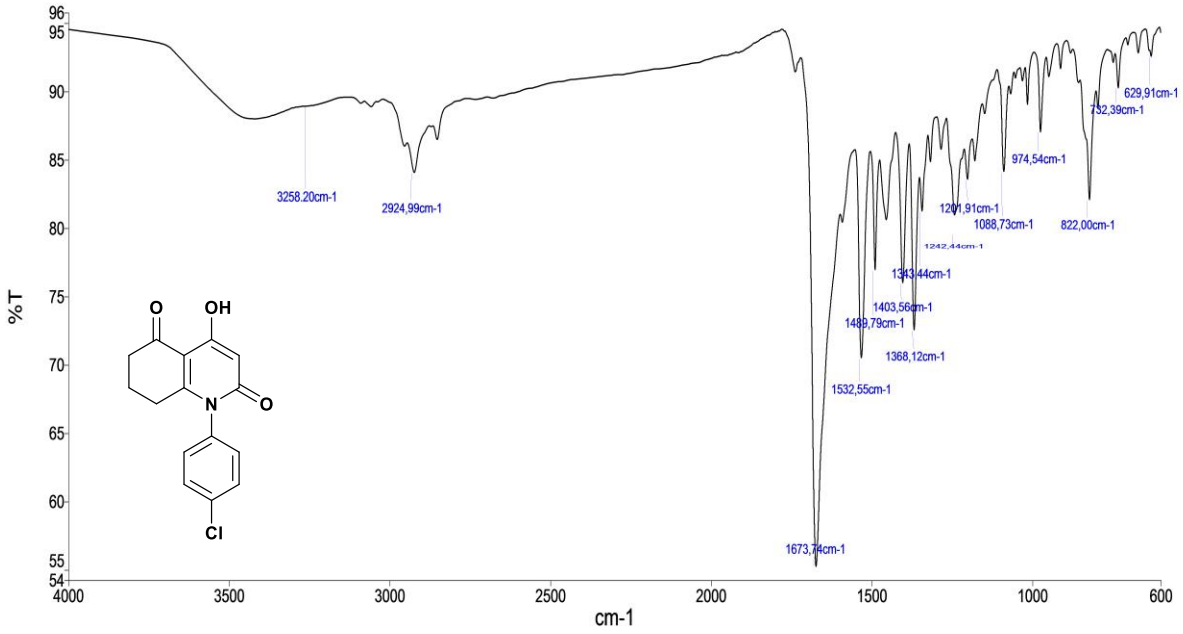


Figure S11. IR spectrum of **3c**.

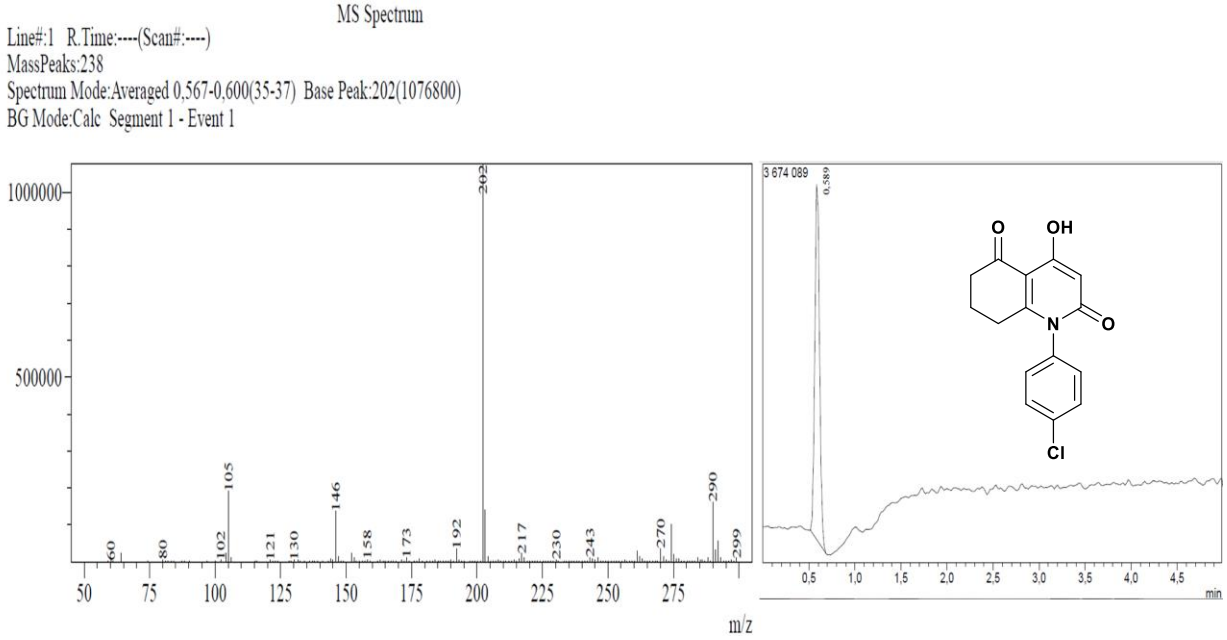


Figure S12. LC-MS spectrum of **3c**.

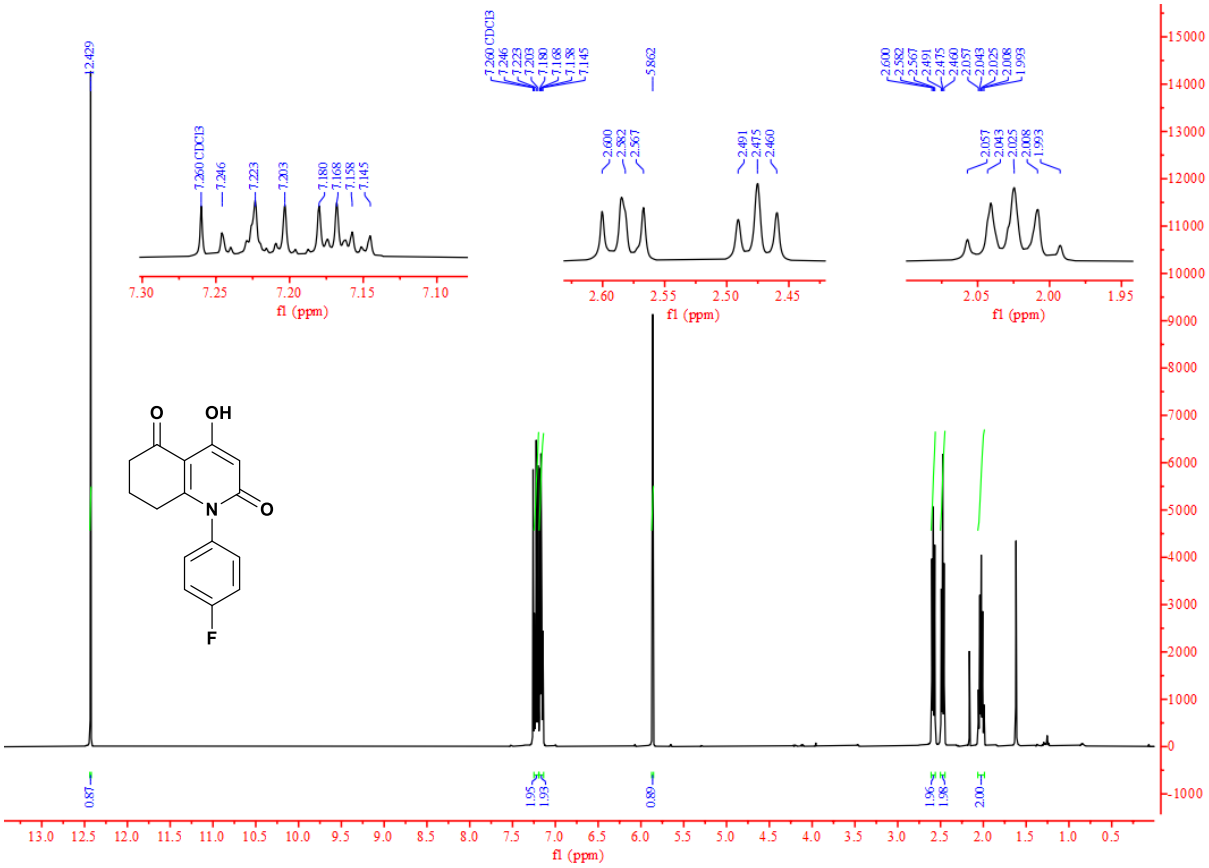


Figure S13. ^{1}H NMR spectrum of **3d** (400 MHz, $CDCl_3$).

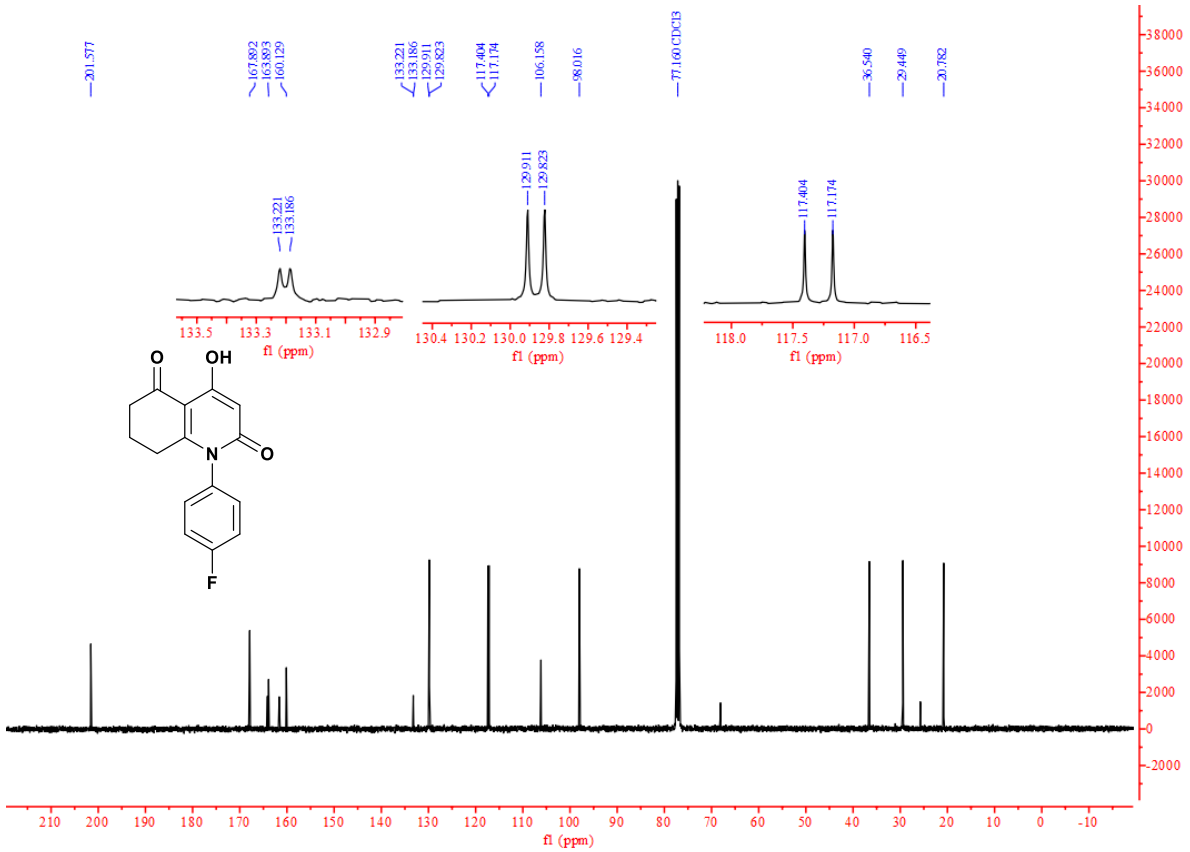


Figure S14. ^{13}C NMR spectrum of **3d** (101 MHz, $CDCl_3$).

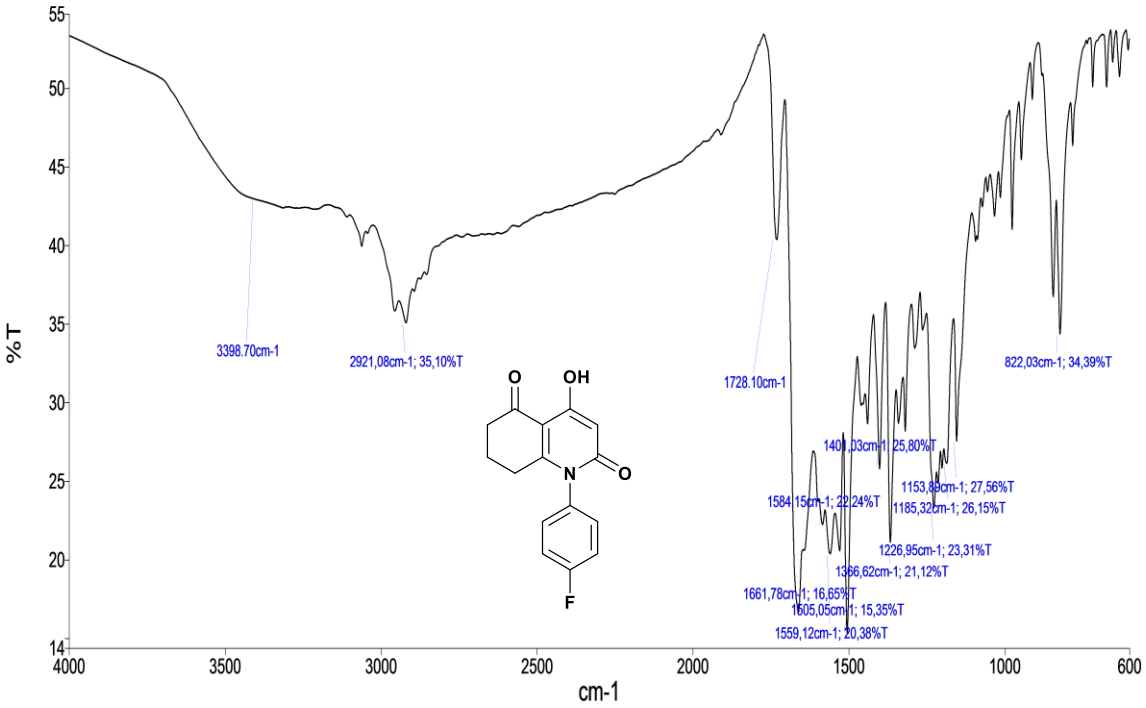


Figure S15. IR spectrum of **3d**.

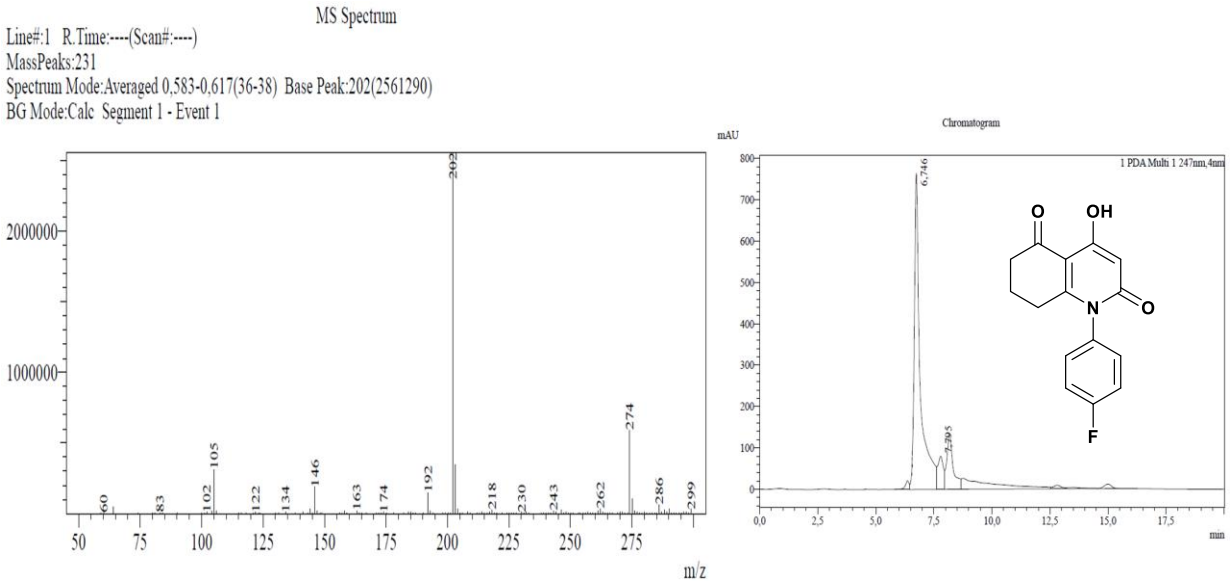


Figure S16. LC-MS spectrum of **3d**.

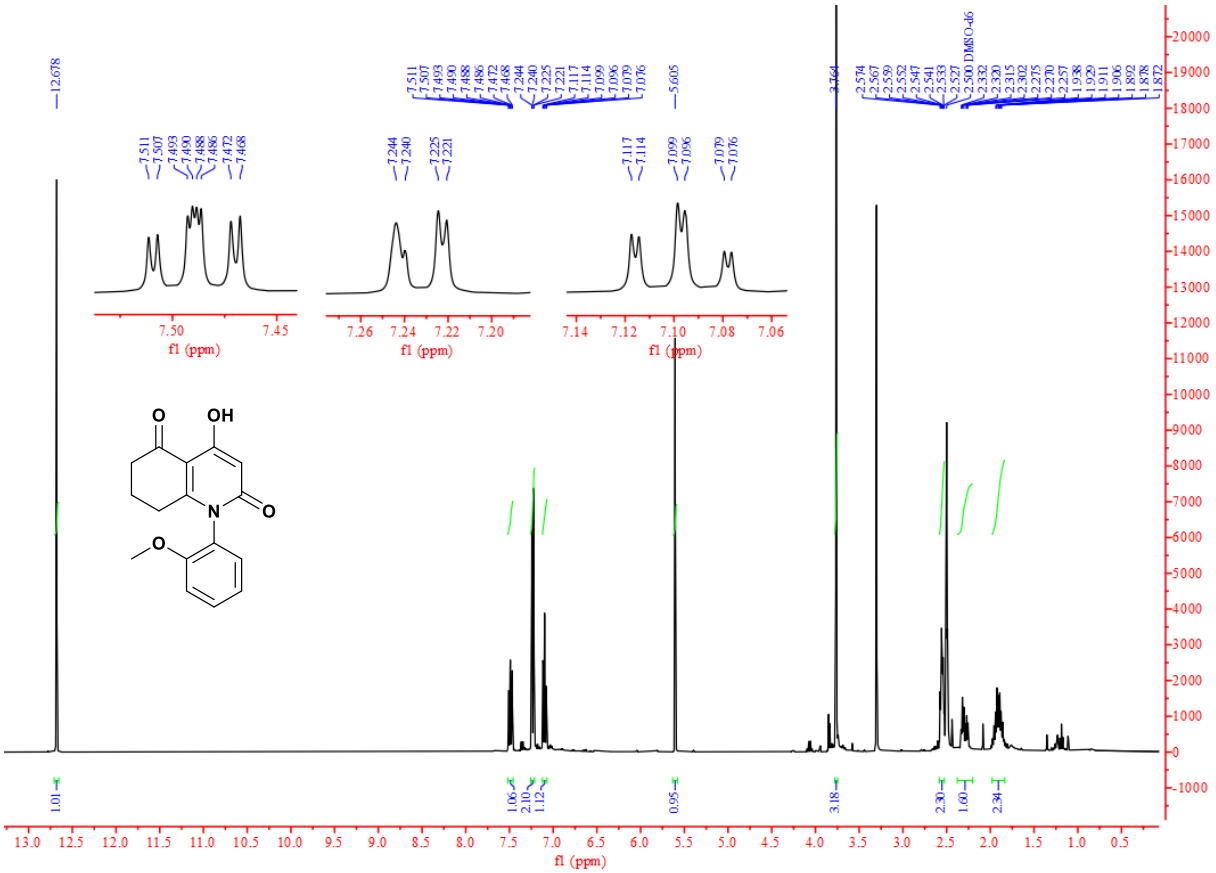


Figure S17. ^{1}H NMR spectrum of **3e** (400 MHz, DMSO-d_6).

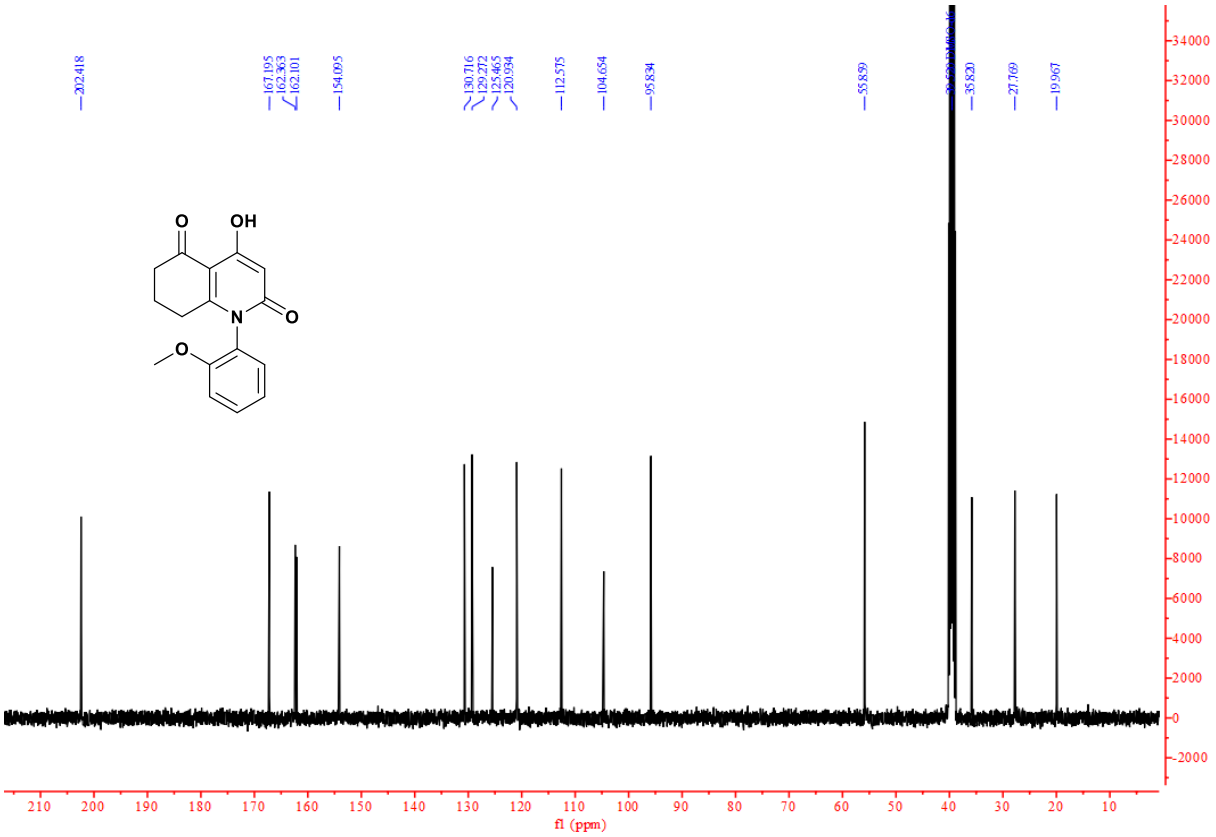


Figure S18. ^{13}C NMR spectrum of **3e** (101 MHz, DMSO-d_6).

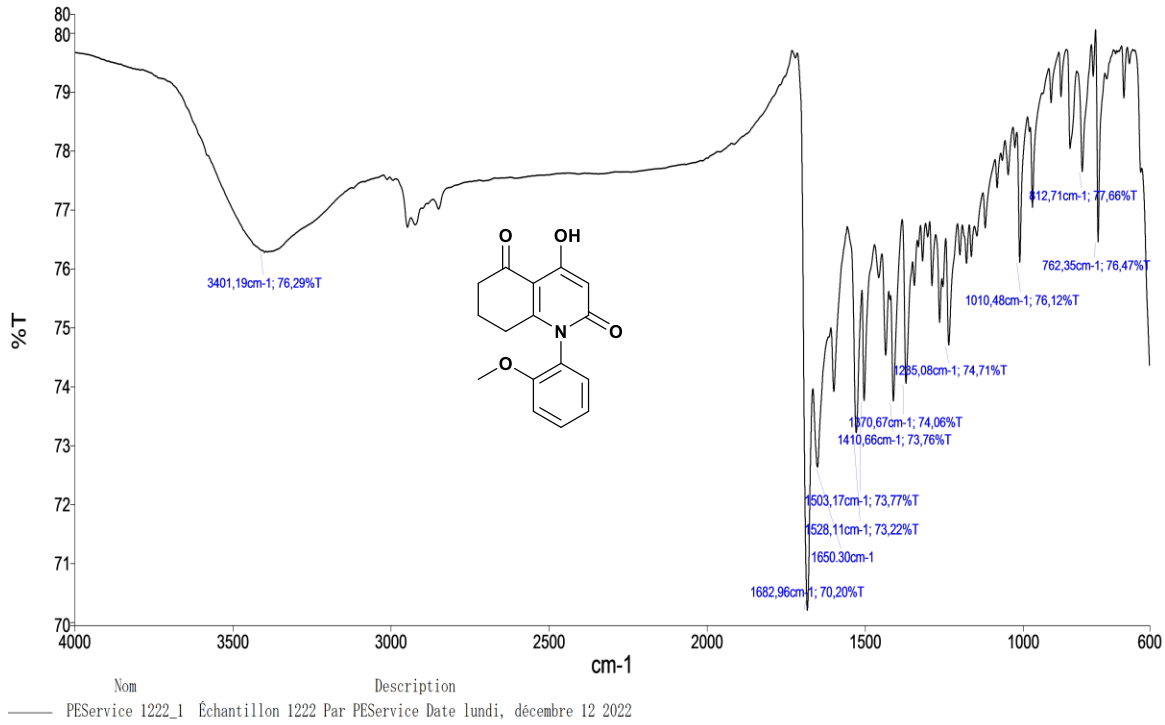


Figure S19. IR spectrum of **3e**.

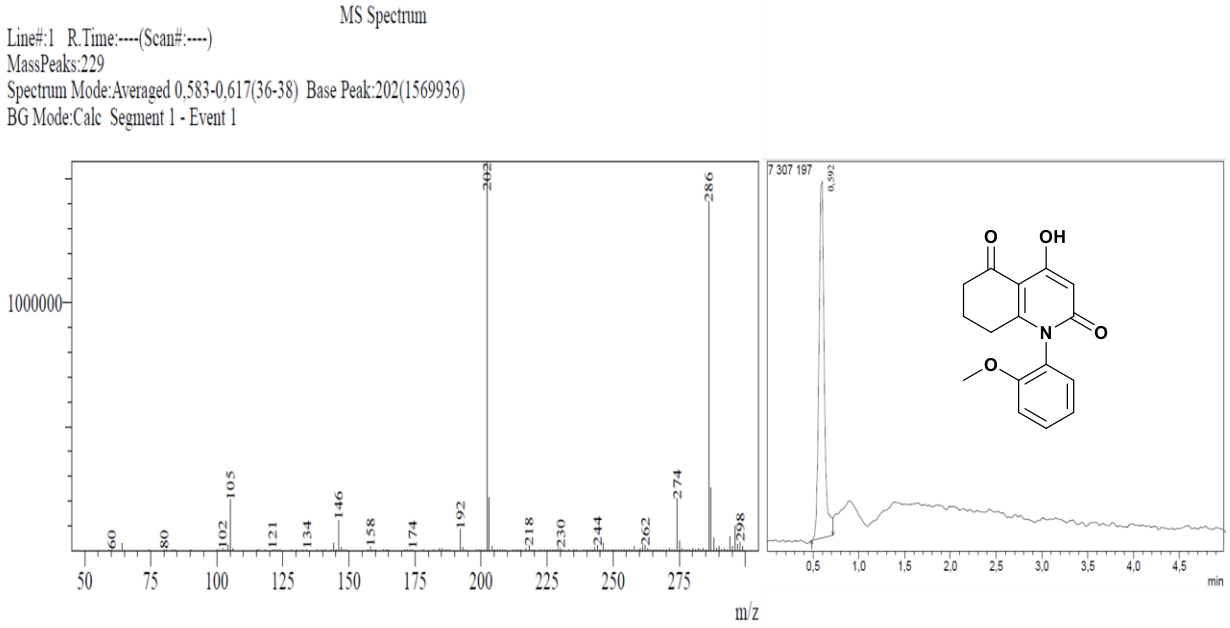


Figure S20. LC-MS spectrum of **3e**.

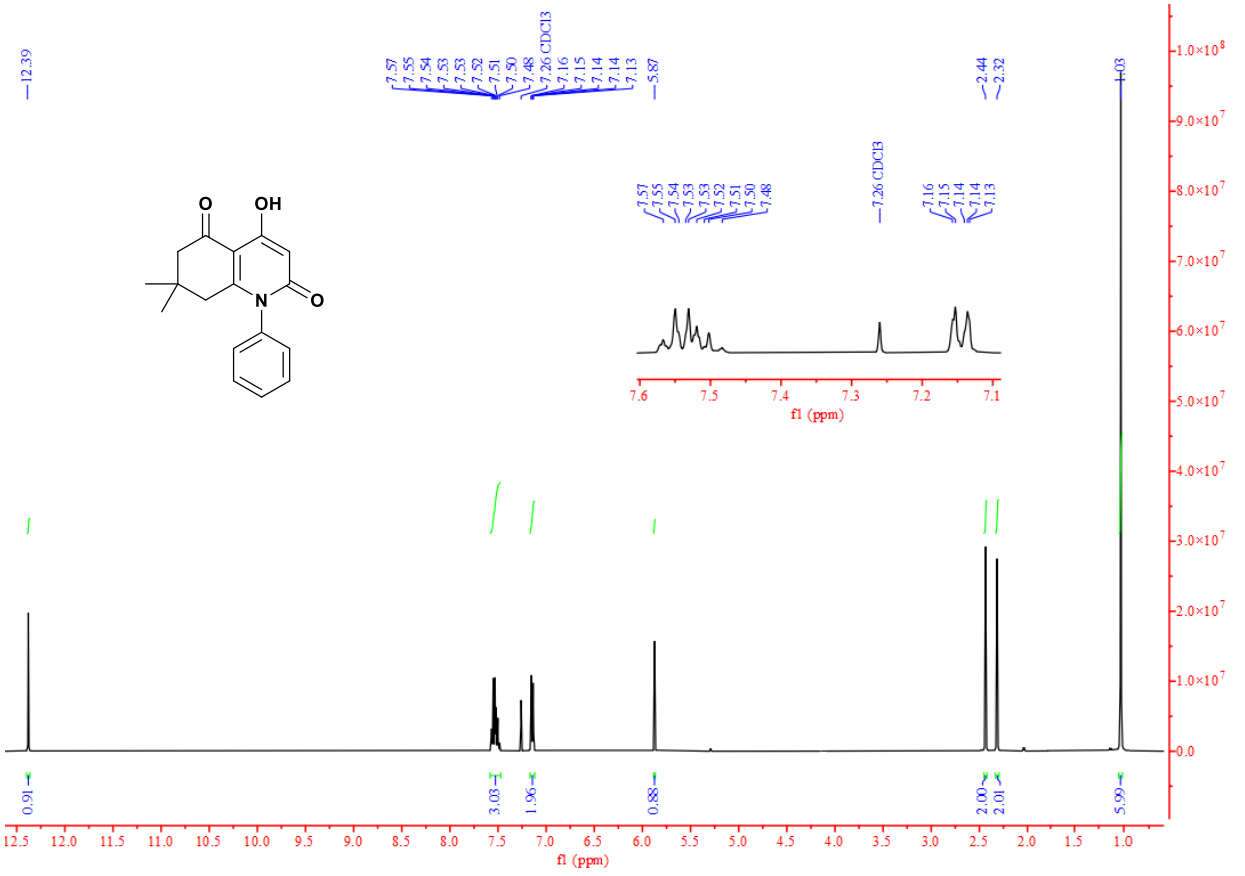


Figure S21. ^{1}H NMR spectrum of **3f** (400 MHz, $CDCl_3$).

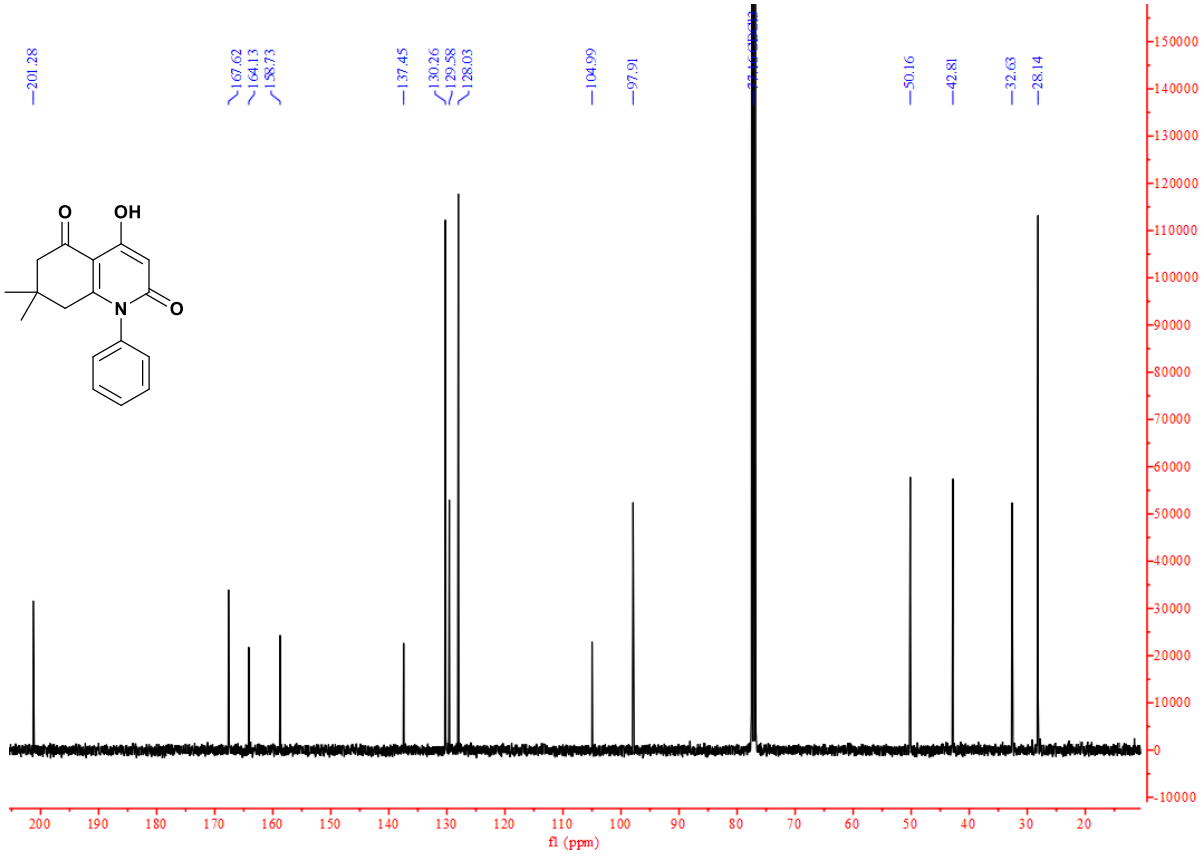


Figure S22. ^{13}C NMR spectrum of **3f** (101 MHz, $CDCl_3$).

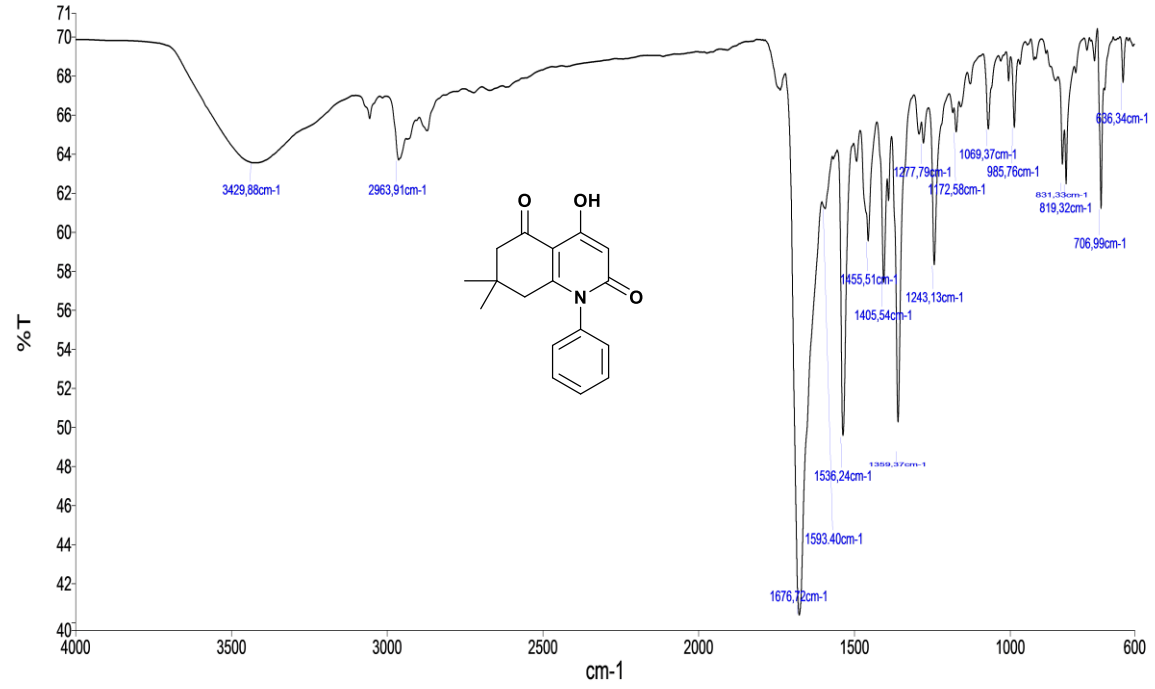


Figure S23. IR spectrum of **3f**.

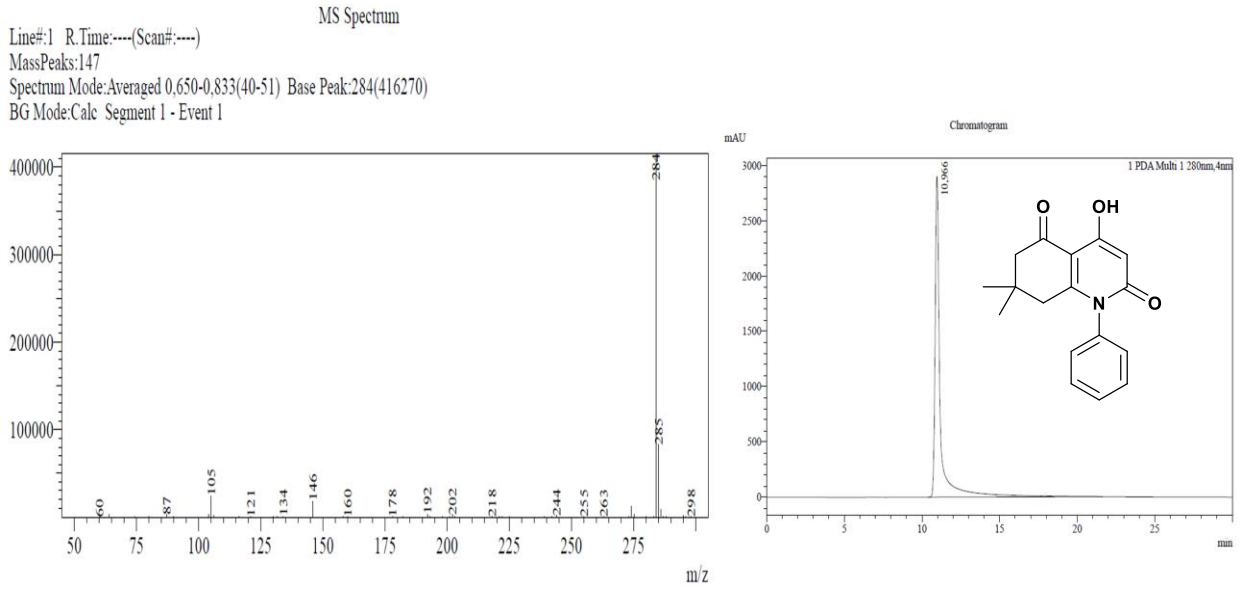


Figure S24. LC-MS spectrum of **3f**.

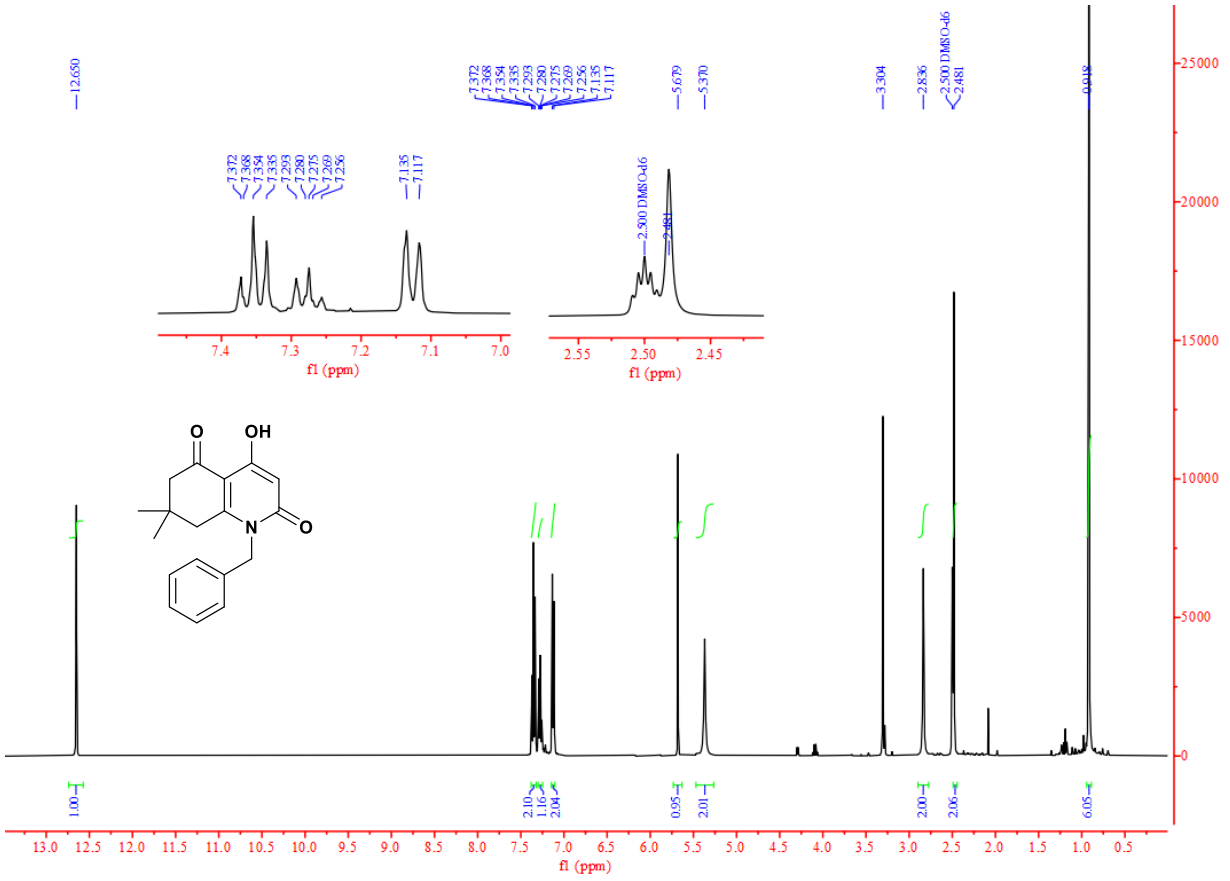


Figure S25. ^{1}H NMR spectrum of **3g** (400 MHz, DMSO-d_6).

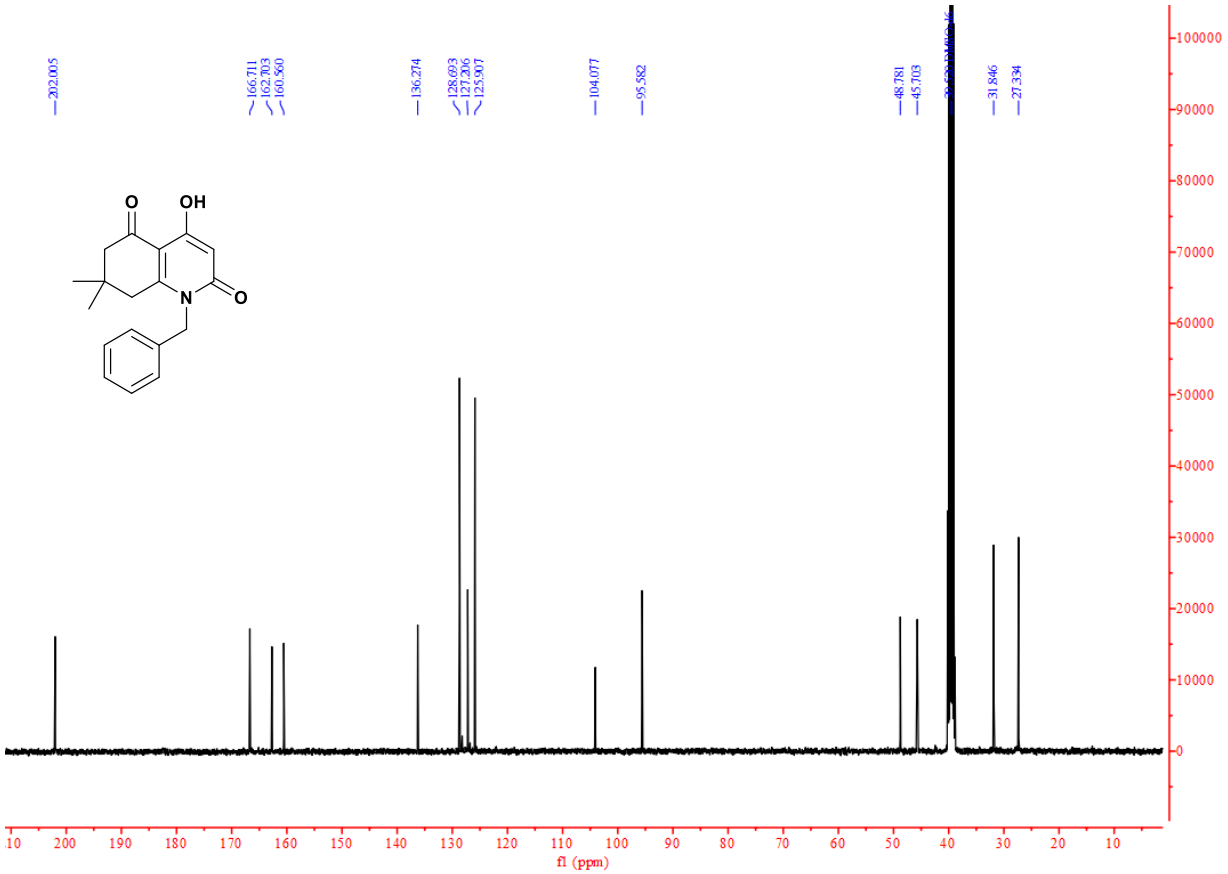


Figure S26. ^{13}C NMR spectrum of **3g** (101 MHz, DMSO-d_6).

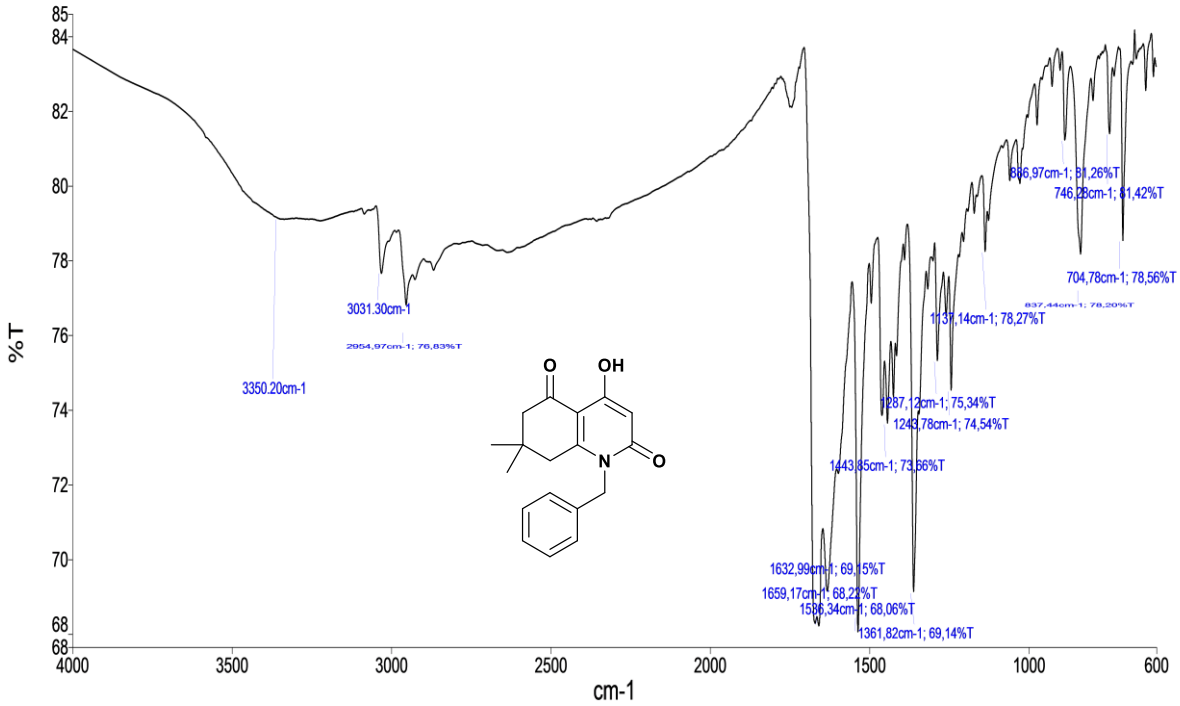


Figure S27. IR spectrum of **3g**.

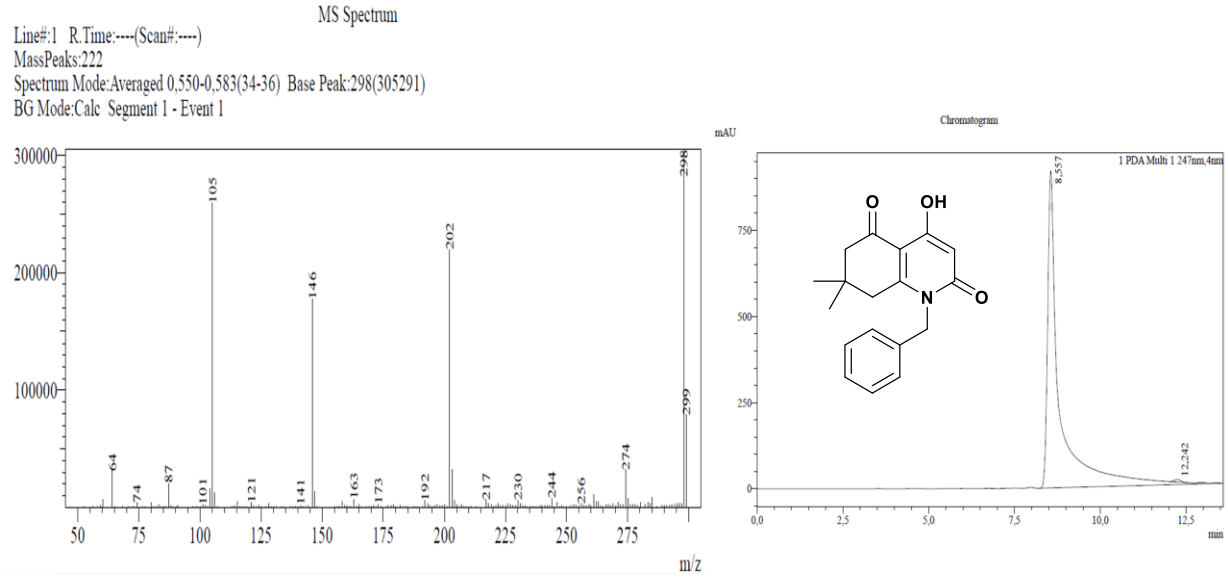


Figure S28. LC-MS spectrum of **3g**.

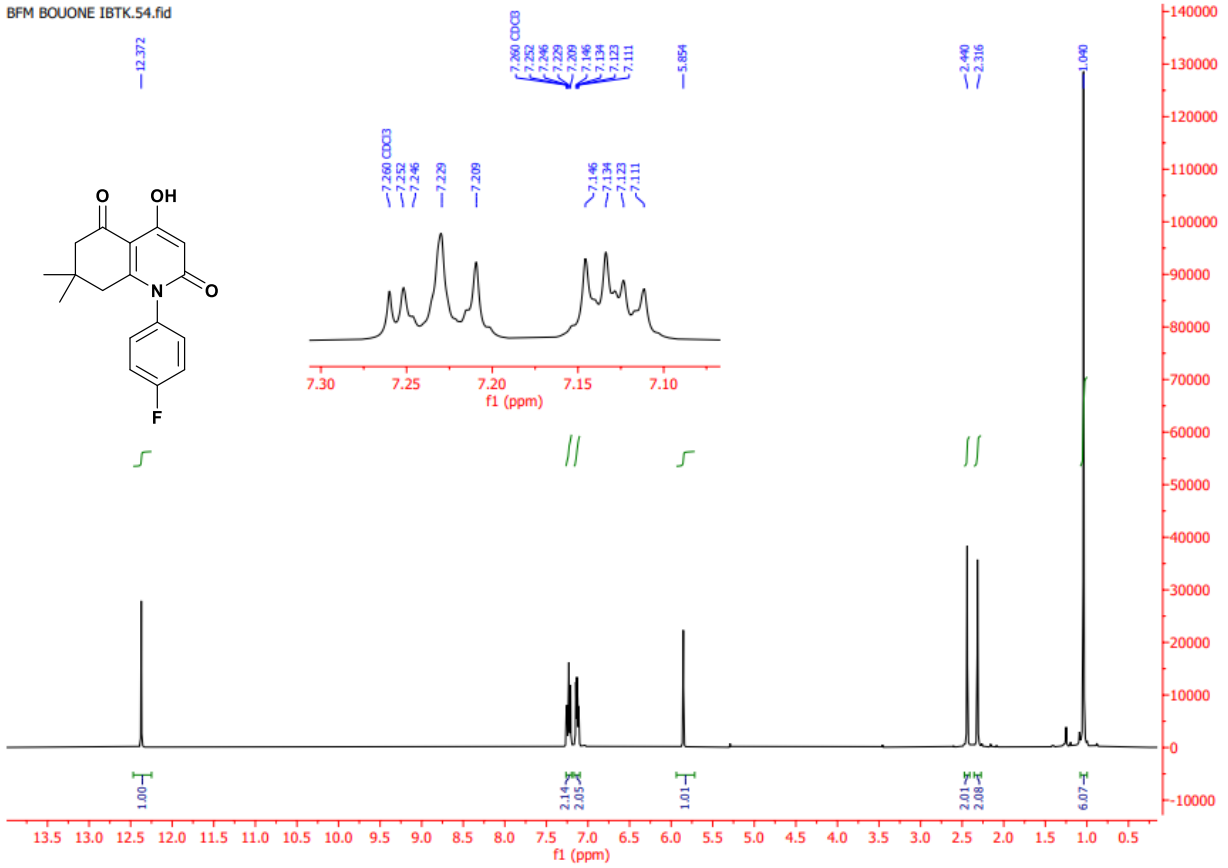


Figure S29. ^{1}H NMR spectrum of **3h** (400 MHz, $CDCl_3$).

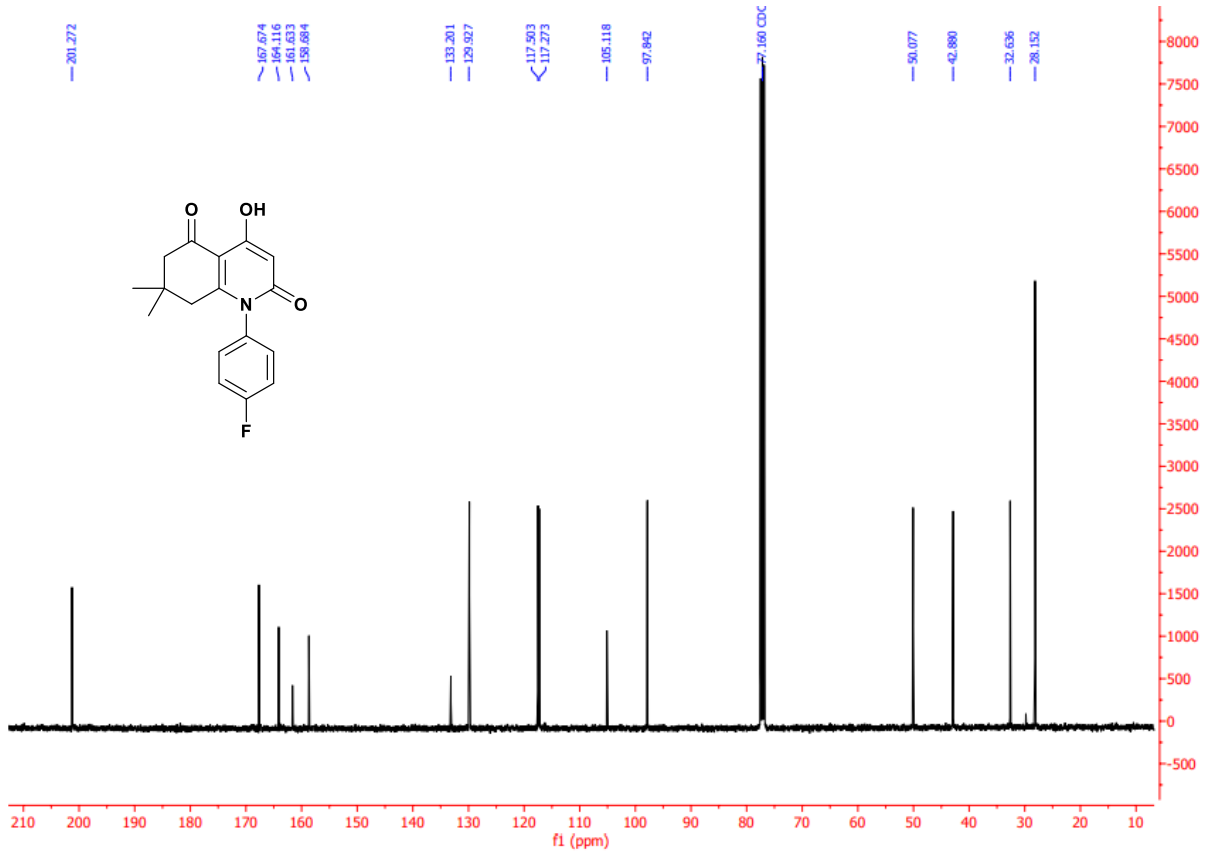


Figure S30. ^{13}C NMR spectrum of **3h** (101 MHz, $CDCl_3$).

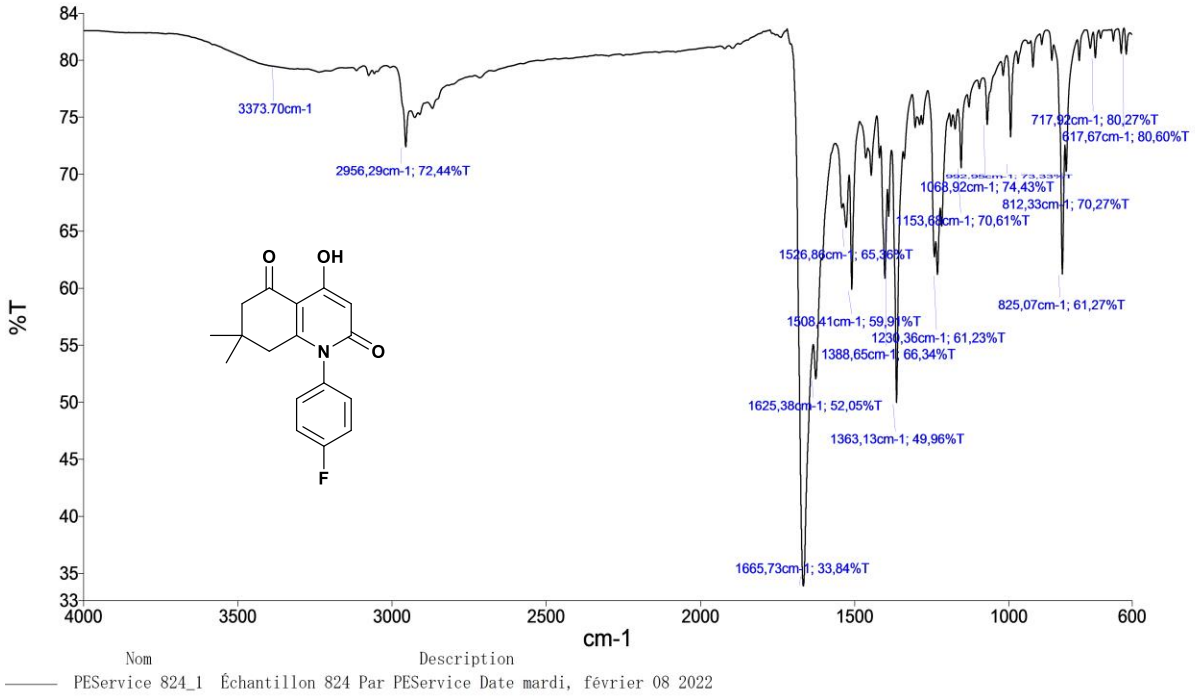


Figure S31. IR spectrum of **3h**.

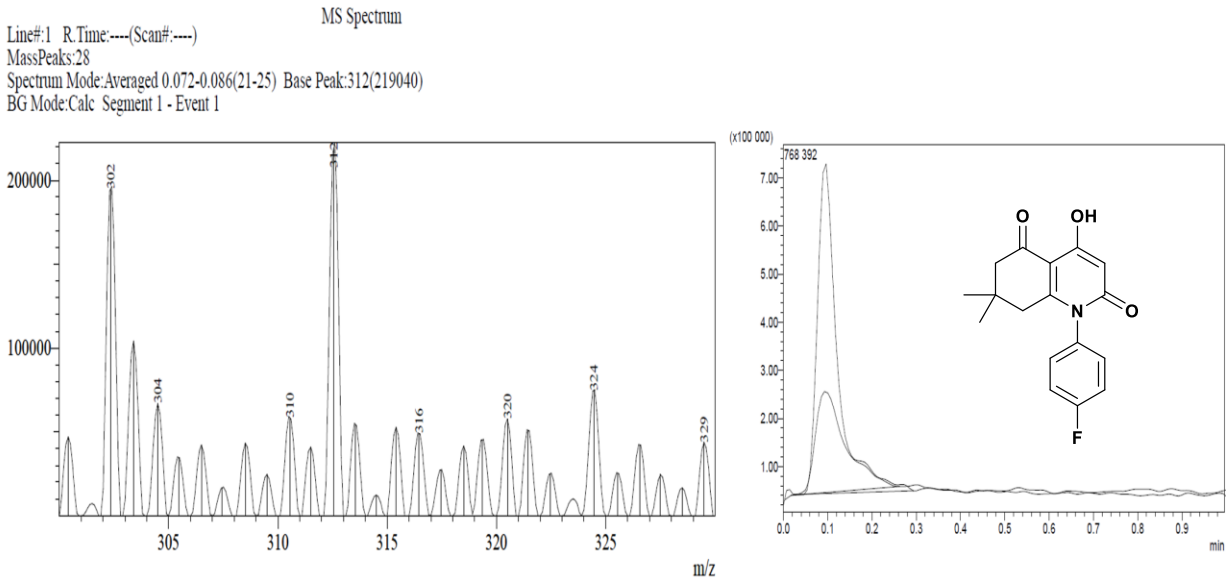


Figure S32. LC-MS spectrum of **3h**.

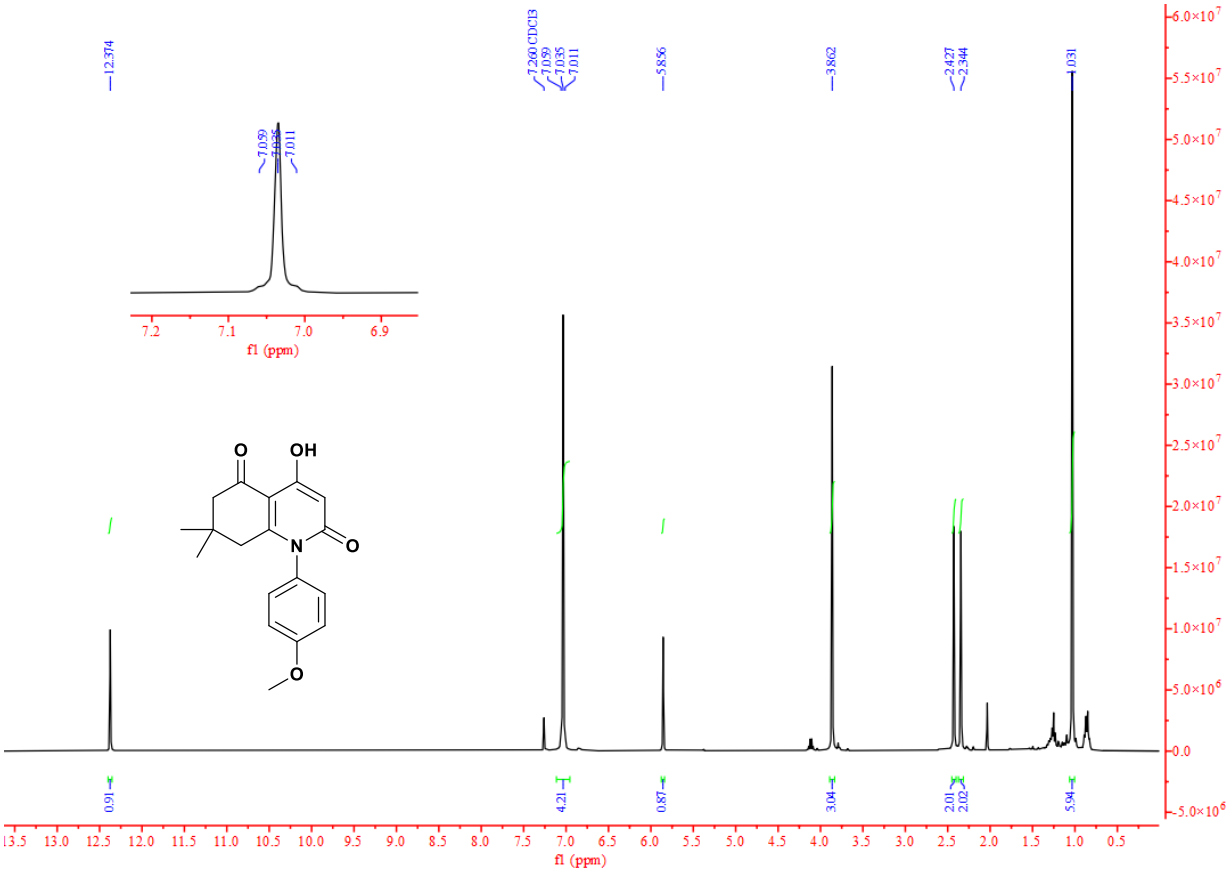


Figure S33. ^{1}H NMR spectrum of **3i** (400 MHz, $CDCl_3$).

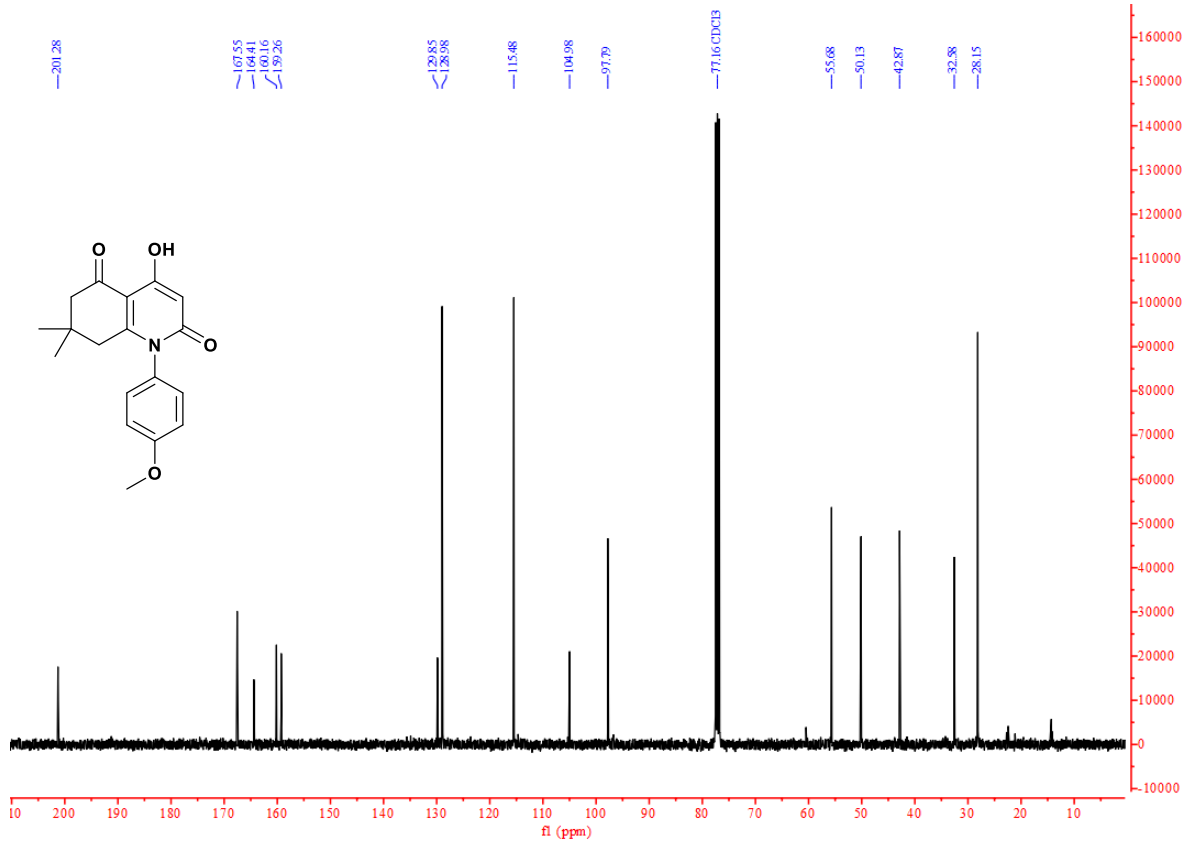


Figure S34. ^{13}C NMR spectrum of **3i** (101 MHz, $CDCl_3$).

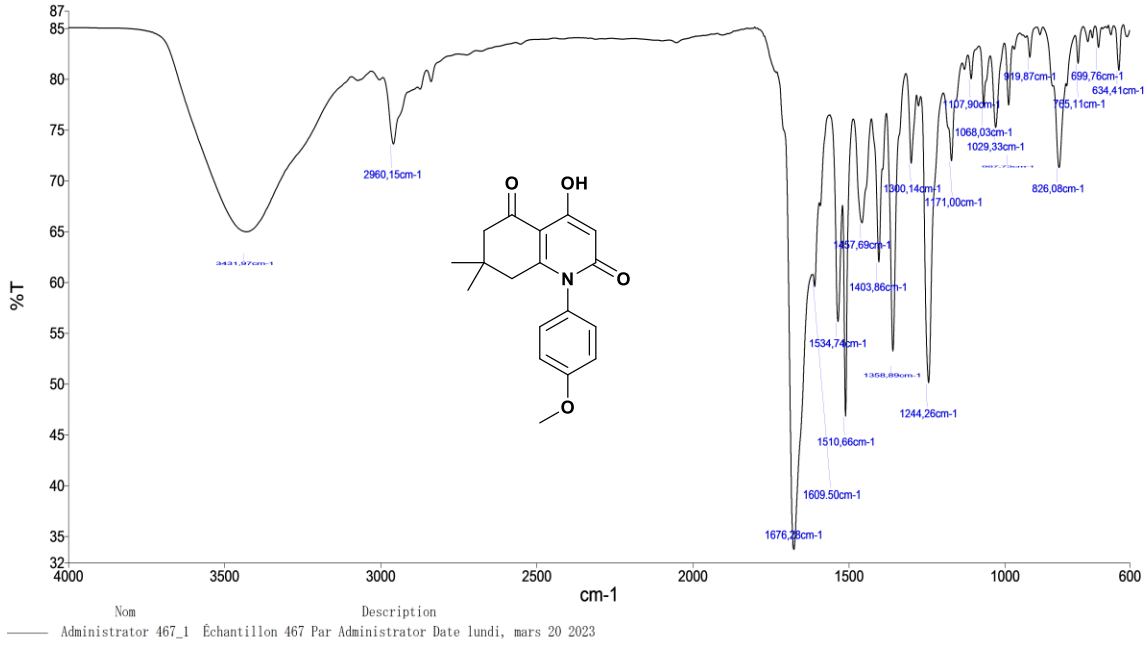


Figure S35. IR spectrum of **3i**.

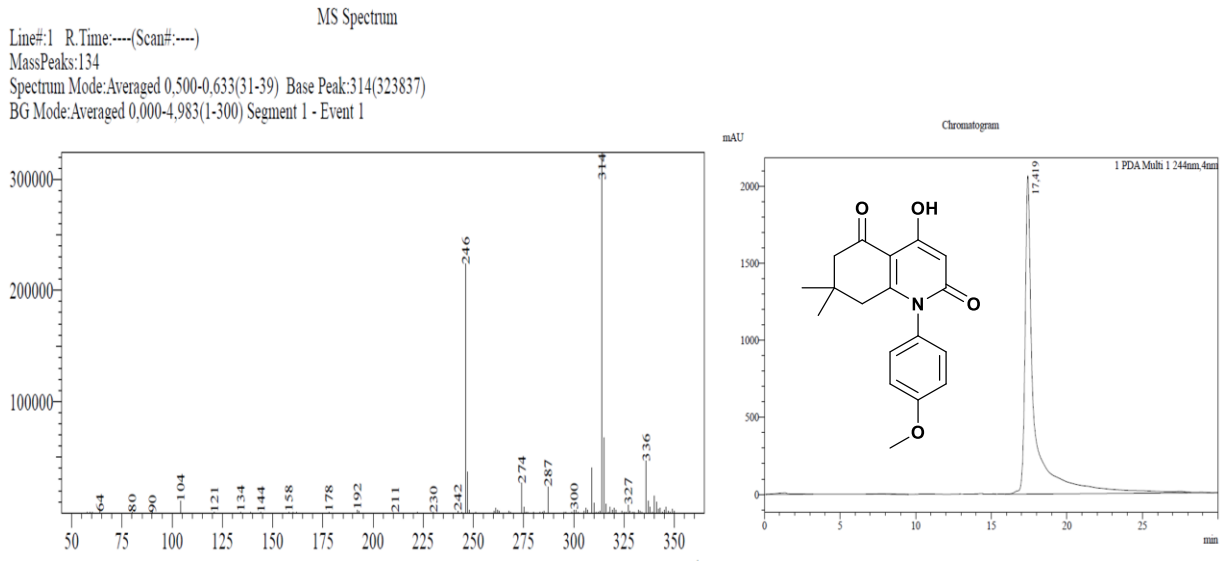


Figure S36. LC-MS spectrum of **3i**.

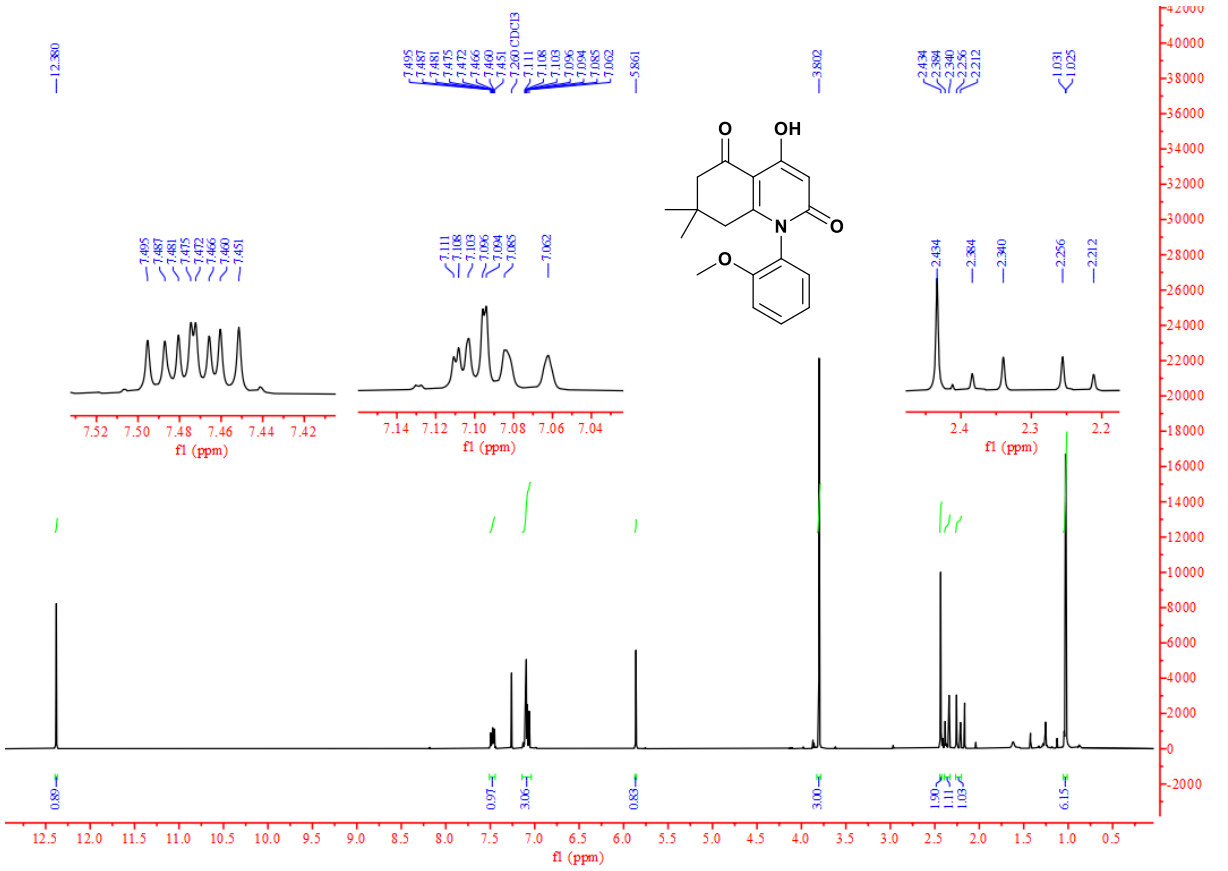


Figure S37. ^{1}H NMR spectrum of **3j** (400 MHz, $CDCl_3$).

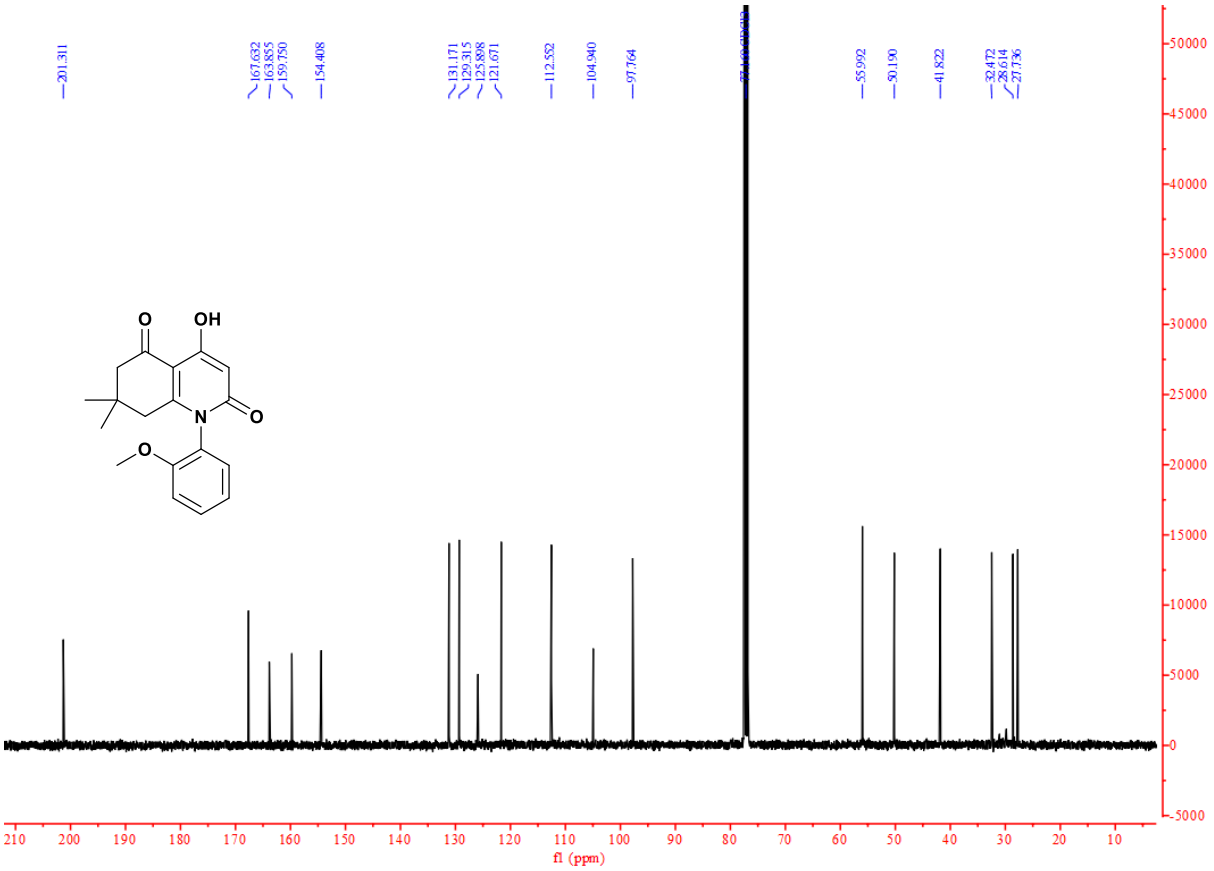


Figure S38. ^{13}C NMR spectrum of **3j** (101 MHz, $CDCl_3$).

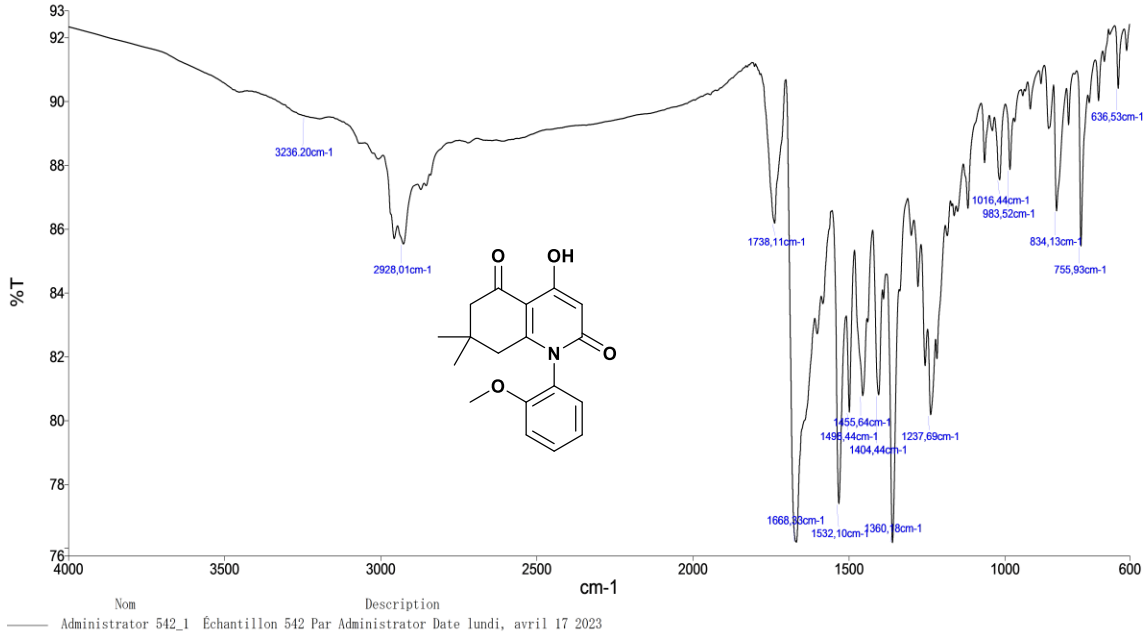


Figure S39. IR spectrum of **3j**.

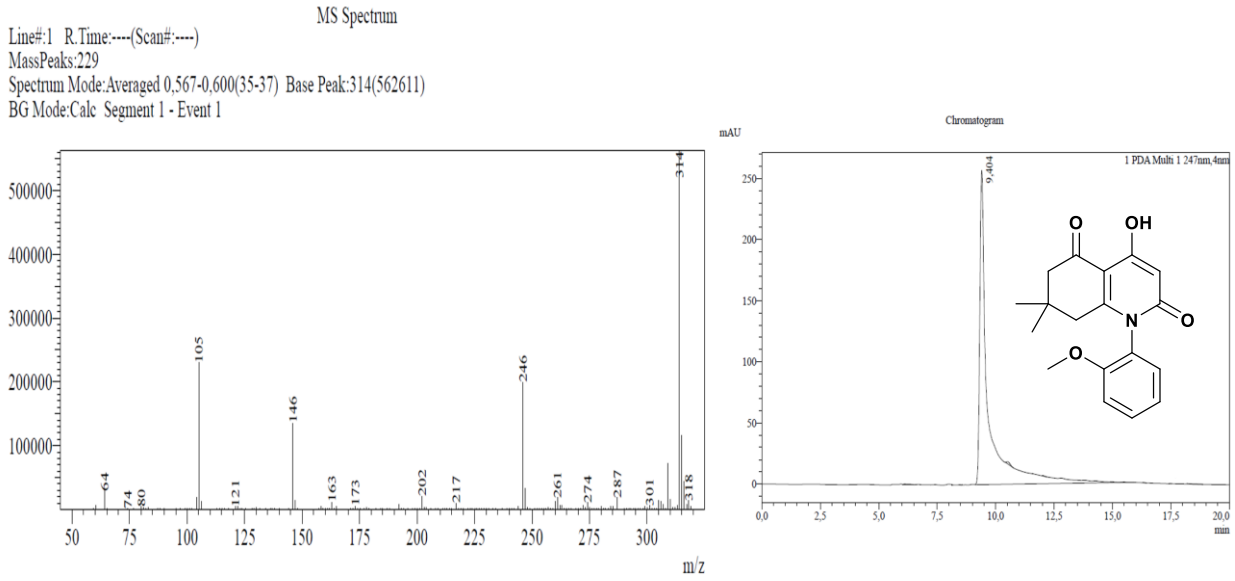


Figure S40. LC-MS spectrum of **3j**.

2. Molecular docking

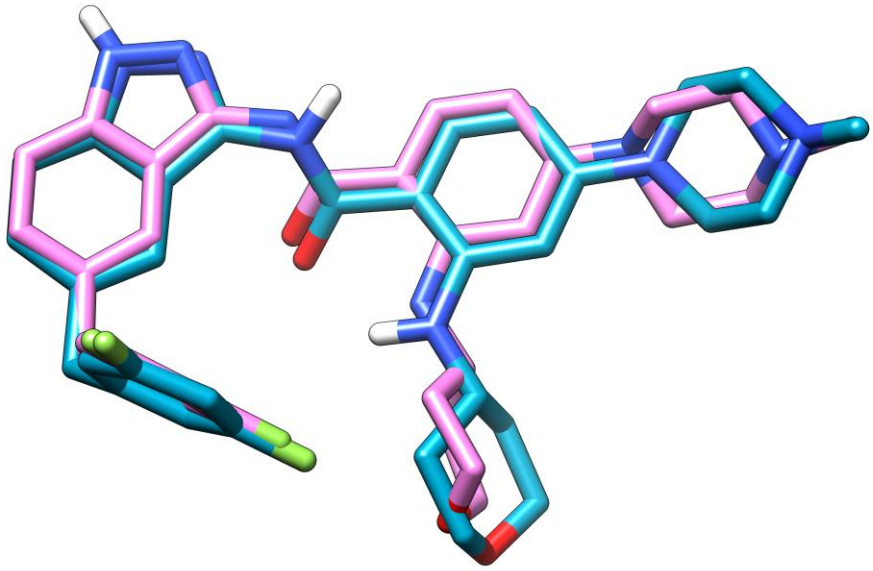


Figure S41. Superimposition of the co-crystallized and the re-docked reference ligand Entrectinib (RMSD = 0.5852 Å, PDB: 5FTO, co-crystallized: pink, re-docked: blue).

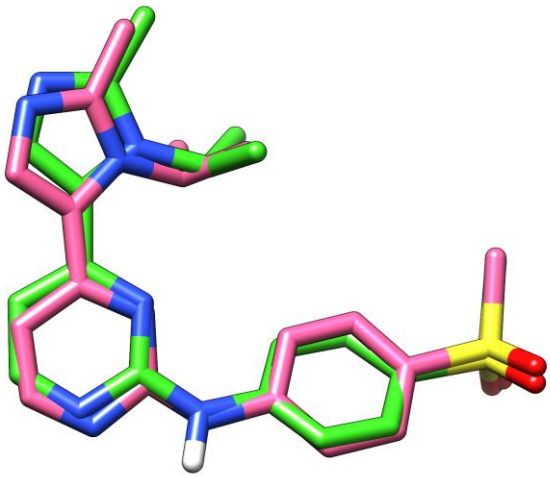
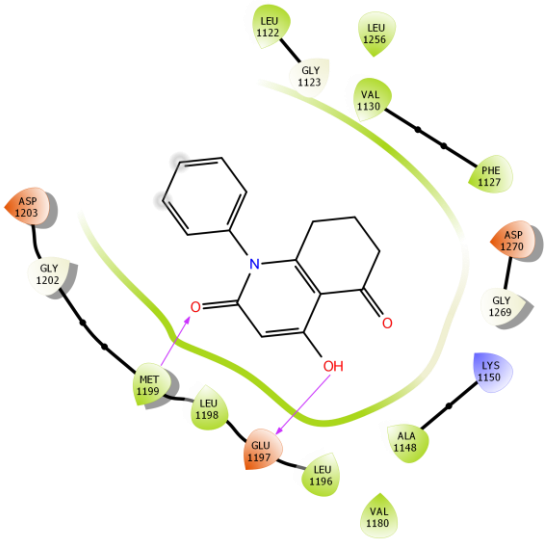
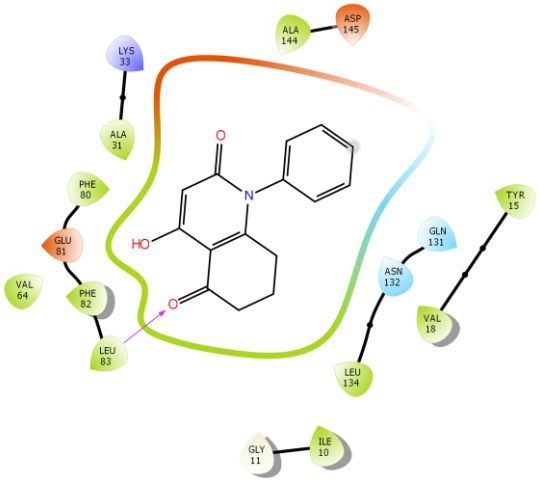
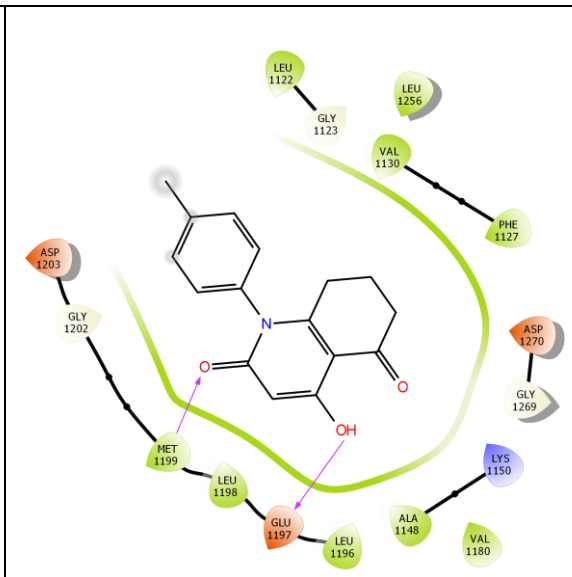
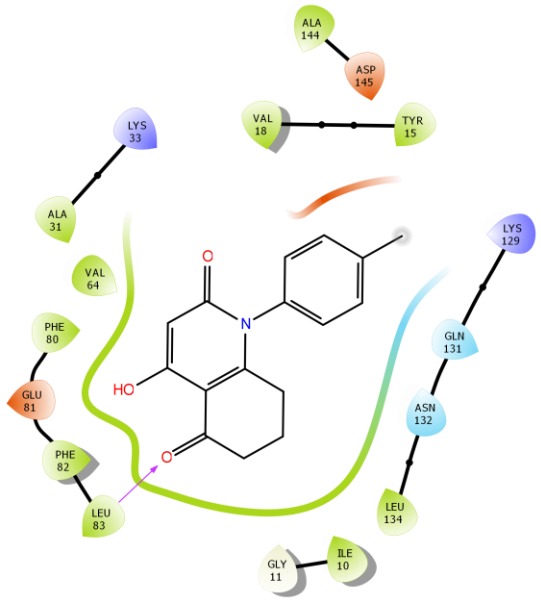
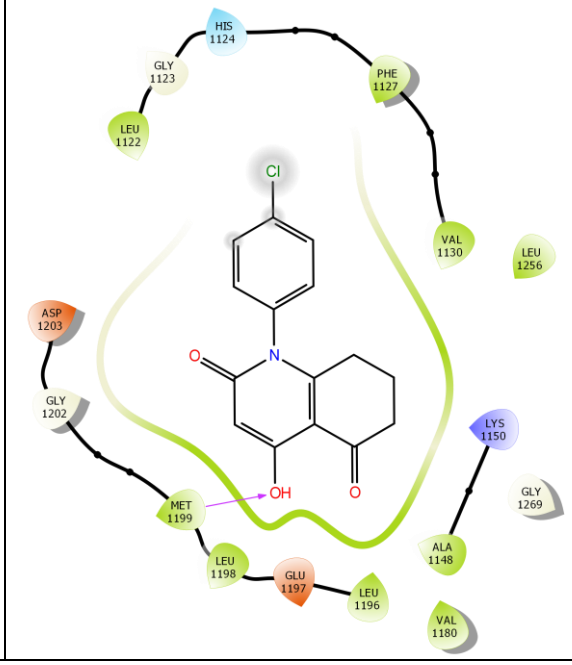
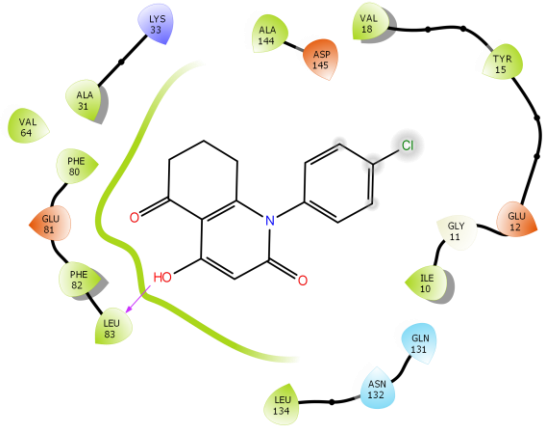
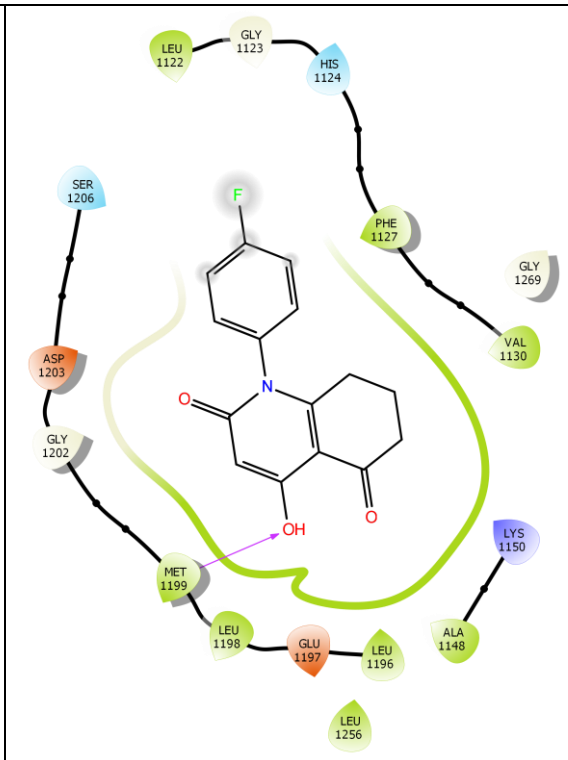
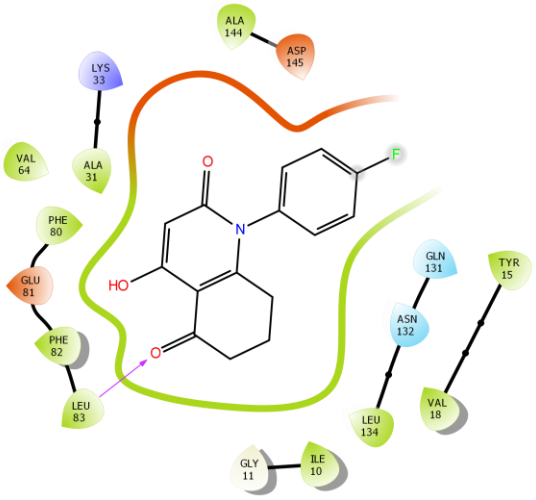
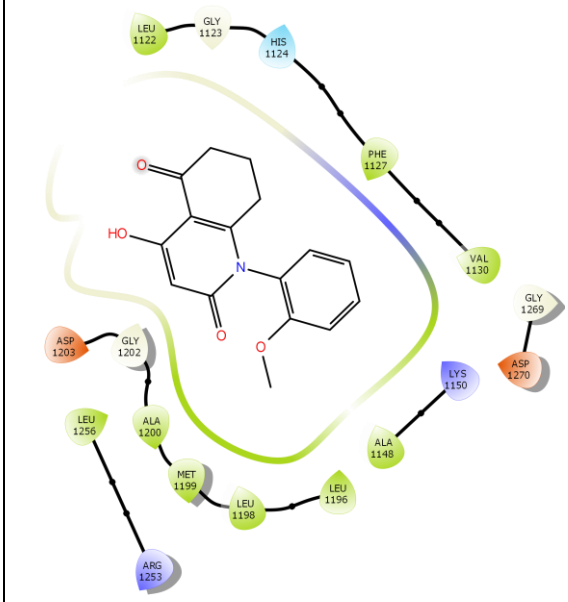
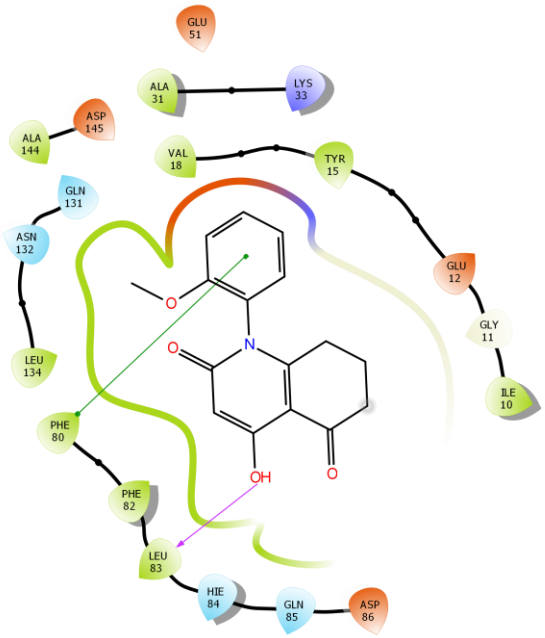


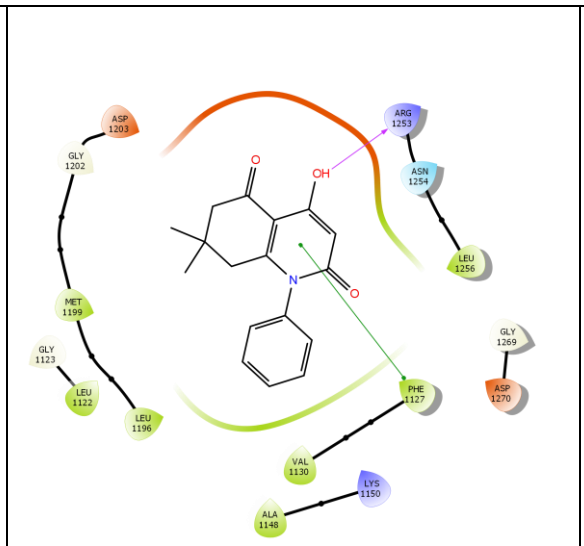
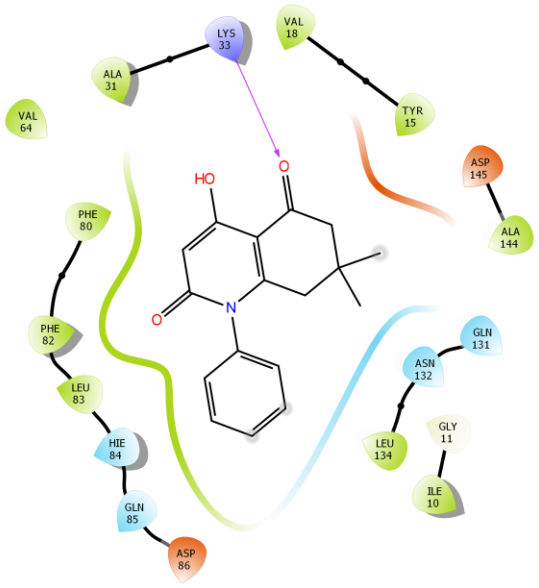
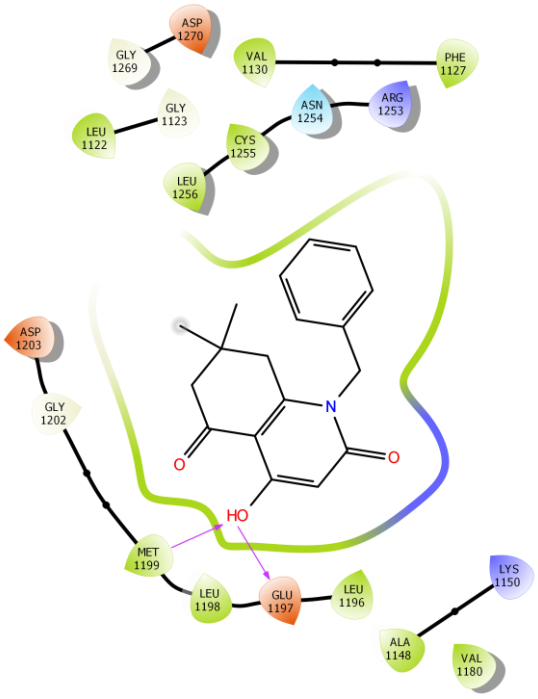
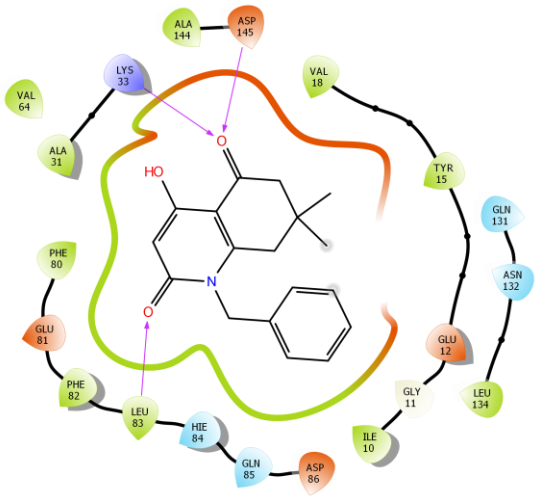
Figure S42. Superimposition of the co-crystallized and the re-docked reference ligand AZD5438 (RMSD = 0.5431 Å, PDB: 5FTO, co-crystallized: pink, re-docked: green).

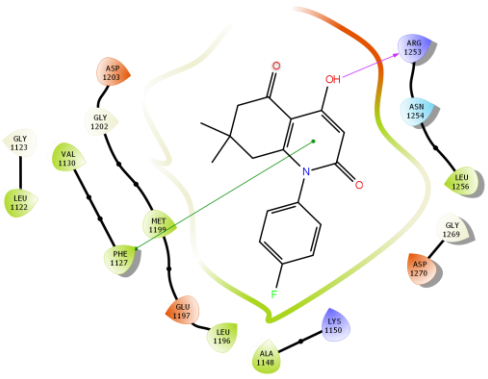
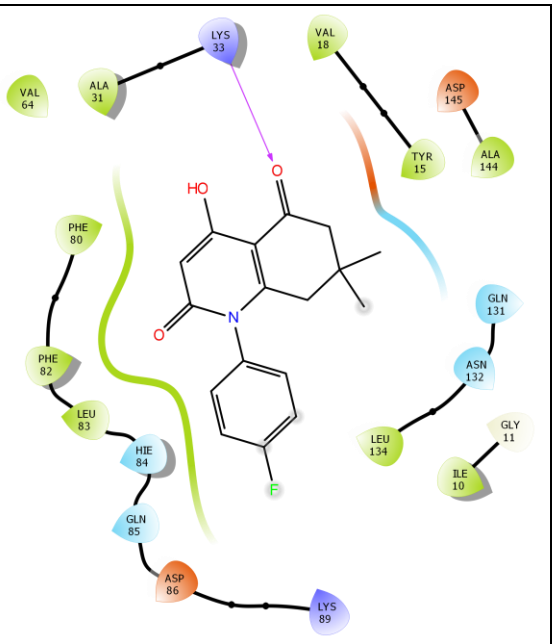
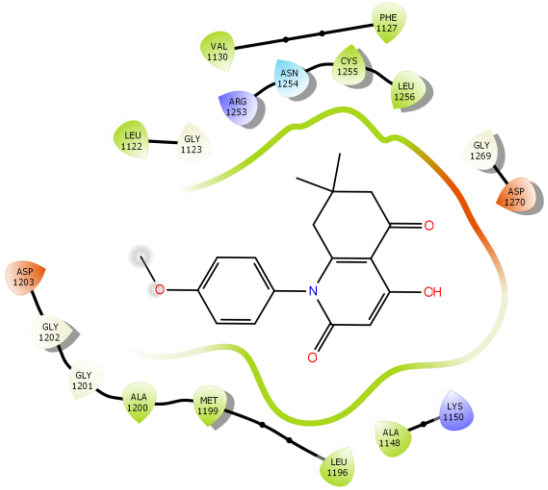
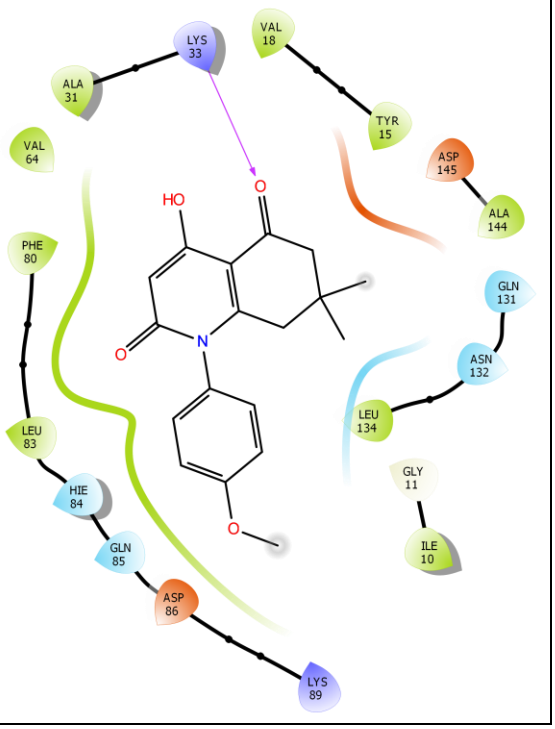
Table S1. 2D representations of docked ligands inside the cavities of ALK and CDK2.

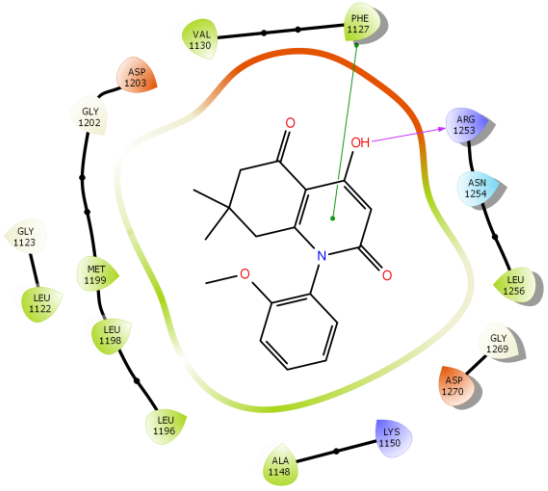
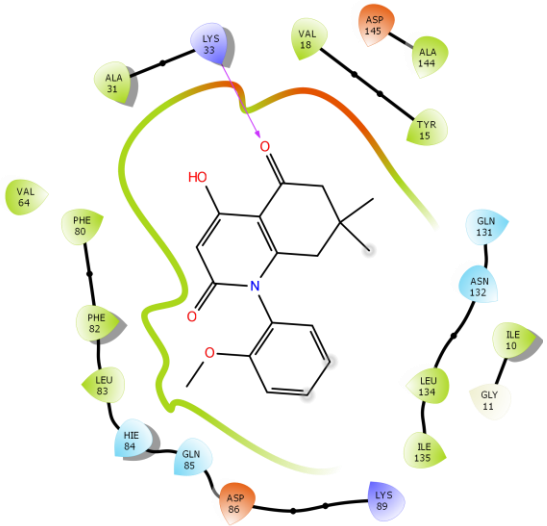
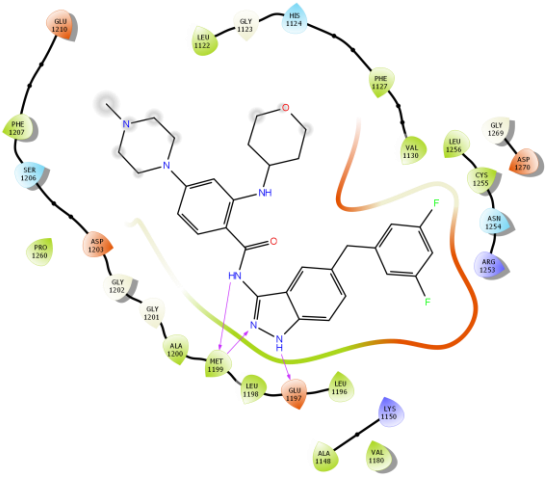
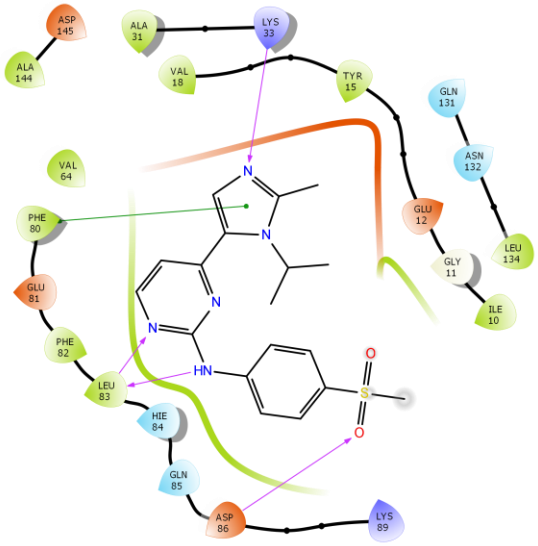
Entry	2D figures	
	5FTO	6GUE
3a		

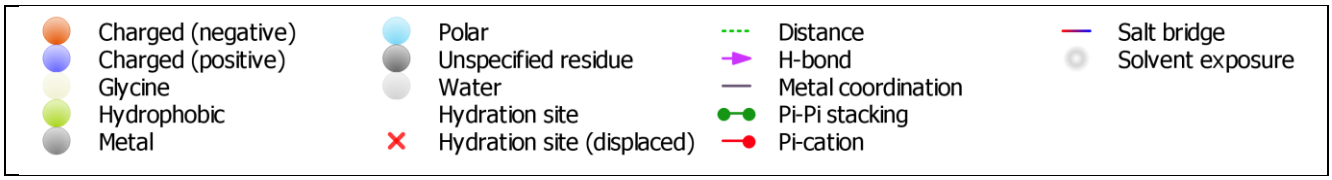
3b	 LEU 1122 GLY 1123 LEU 1256 VAL 1130 PHE 1127 ASP 1203 GLY 1202 ASP 1270 GLY 1269 LYS 1150 ALA 1148 VAL 1180 MET 1199 LEU 1198 GLU 1197 LEU 1196 N O O OH	 ALA 144 ASP 145 VAL 18 TYR 15 LYS 33 ALA 31 LYS 129 VAL 64 PHE 80 GLN 131 GLU 81 ASN 132 PHE 82 LEU 134 LEU 83 GLY 11 ILE 10 N O HO O
3c	 HIS 1124 GLY 1123 PHE 1127 LEU 1122 Cl VAL 1130 LEU 1256 ASP 1203 GLY 1202 LYS 1150 GLY 1269 ALA 1148 MET 1199 LEU 1198 GLU 1197 LEU 1196 VAL 1180 N O O OH	 LYS 33 ALA 144 ASP 145 VAL 18 TYR 15 ALA 31 VAL 64 Cl PHE 80 GLU 81 GLY 11 GLU 12 PHE 82 ILE 10 LEU 83 GLN 131 ASN 132 LEU 134 N O HO O

3d	 LEU 1122 GLY 1123 HIS 1124 PHE 1127 GLY 1269 VAL 1130 SER 1206 ASP 1203 GLY 1202 MET 1199 LEU 1198 GLU 1197 LEU 1196 LEU 1256 ALA 1148 LYS 1150 F N O OH O	 ALA 144 ASP 145 LYS 33 VAL 64 ALA 31 PHE 80 GLU 81 PHE 82 LEU 83 GLN 131 TYR 15 ASN 132 LEU 134 VAL 18 GLY 11 ILE 10 F O N HO O
3e	 LEU 1122 GLY 1123 HIS 1124 PHE 1127 VAL 1130 GLY 1269 ASP 1270 ASP 1203 GLY 1202 LEU 1256 ALA 1200 MET 1199 LEU 1198 LEU 1196 ALA 1148 LYS 1150 ARG 1253 O HO N O O	 GLU 51 ALA 31 LYS 33 ASP 145 ALA 144 VAL 18 TYR 15 GLN 131 ASN 132 GLU 12 GLY 11 LEU 134 ILE 10 PHE 80 PHE 82 LEU 83 HIE 84 GLN 85 ASP 86 O N O OH O

3f	 ASP 1203 GLY 1202 ARG 1253 ASN 1254 LEU 1256 MET 1199 GLY 1123 LEU 1122 LEU 1196 GLY 1269 ASP 1270 PHE 1127 VAL 1130 LYS 1150 ALA 1148 O OH N O	 LYS 33 VAL 18 ALA 31 TYR 15 VAL 64 ASP 145 ALA 144 PHE 80 HO O N PHE 82 GLN 131 ASN 132 LEU 83 LEU 134 GLY 11 HIE 84 ILE 10 GLN 85 ASP 86
3g	 ASP 1270 GLY 1269 VAL 1130 PHE 1127 GLY 1123 ASN 1254 ARG 1253 LEU 1122 CYS 1255 LEU 1256 ASP 1203 GLY 1202 N O O HO MET 1199 LEU 1198 GLU 1197 LEU 1196 LYS 1150 ALA 1148 VAL 1180	 ALA 144 ASP 145 LYS 33 VAL 18 VAL 64 ALA 31 TYR 15 HO O GLN 131 PHE 80 ASN 132 N O GLU 81 GLU 12 PHE 82 GLY 11 LEU 134 LEU 83 HIE 84 ILE 10 GLN 85 ASP 86

3h		
3i		

3j		
Entrectinib		--
AZD5438	--	


Charged (negative)
Charged (positive)
Glycine
Hydrophobic
Metal
Polar
Unspecified residue
Water
Hydration site
Hydration site (displaced)
Distance
H-bond
Metal coordination
Pi-Pi stacking
Pi-cation
Salt bridge
Solvent exposure