Supplementary Materials:

Synthesis, Molecular docking, Molecular Dynamics studies, and In vitro Biological evaluation of new biofunctional ketoprofen derivatives with different *N*-containing heterocycles

Stanimir Manolov, Dimitar Bojilov, Iliyan Ivanov, Gabriel Marc, Nadejda Bataklieva, Smaranda Oniga, Ovidiu Oniga, and Paraskev Nedyalkov

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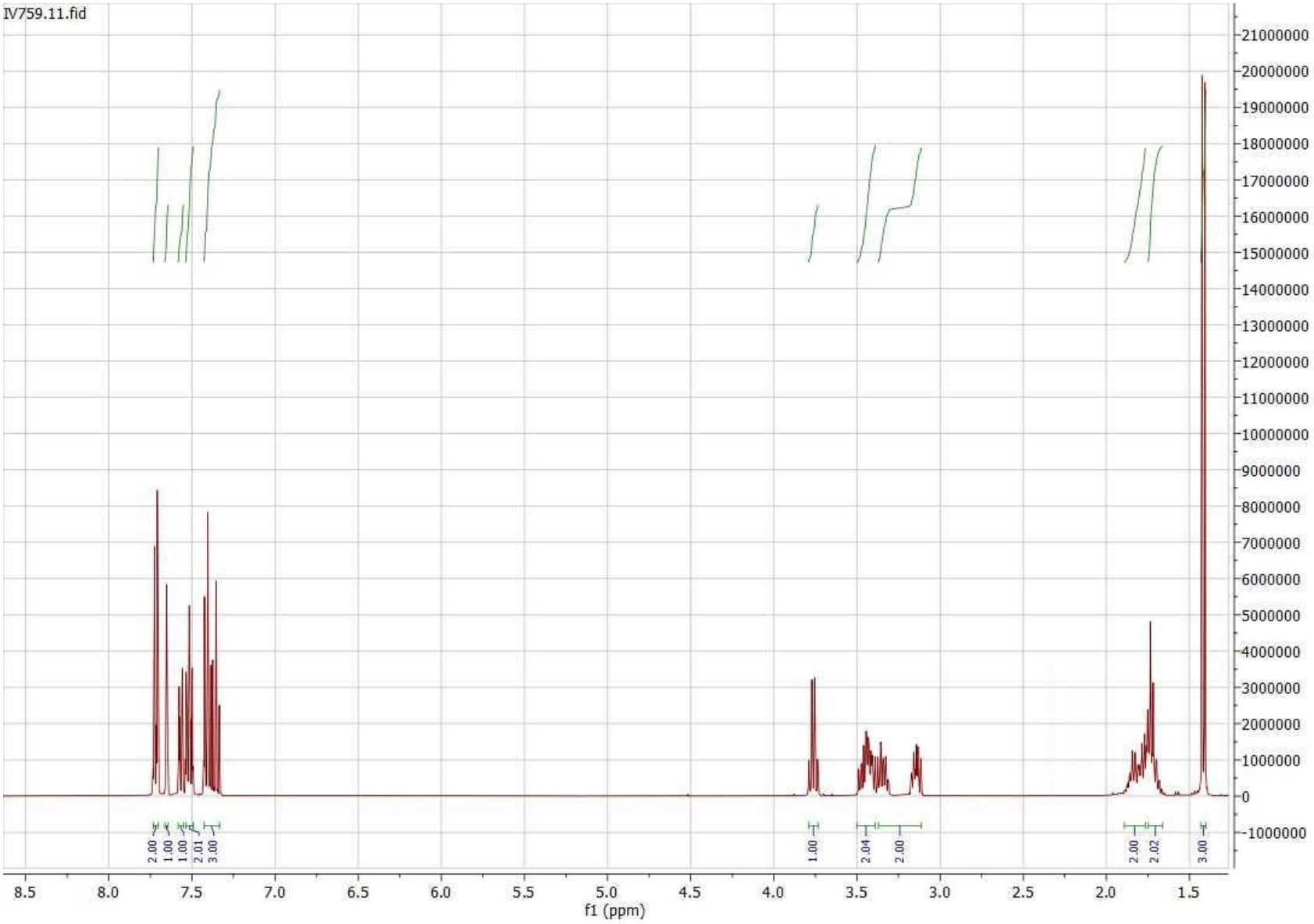


Figure S1. ^{1}H-NMR spectrum of compound **3a**.

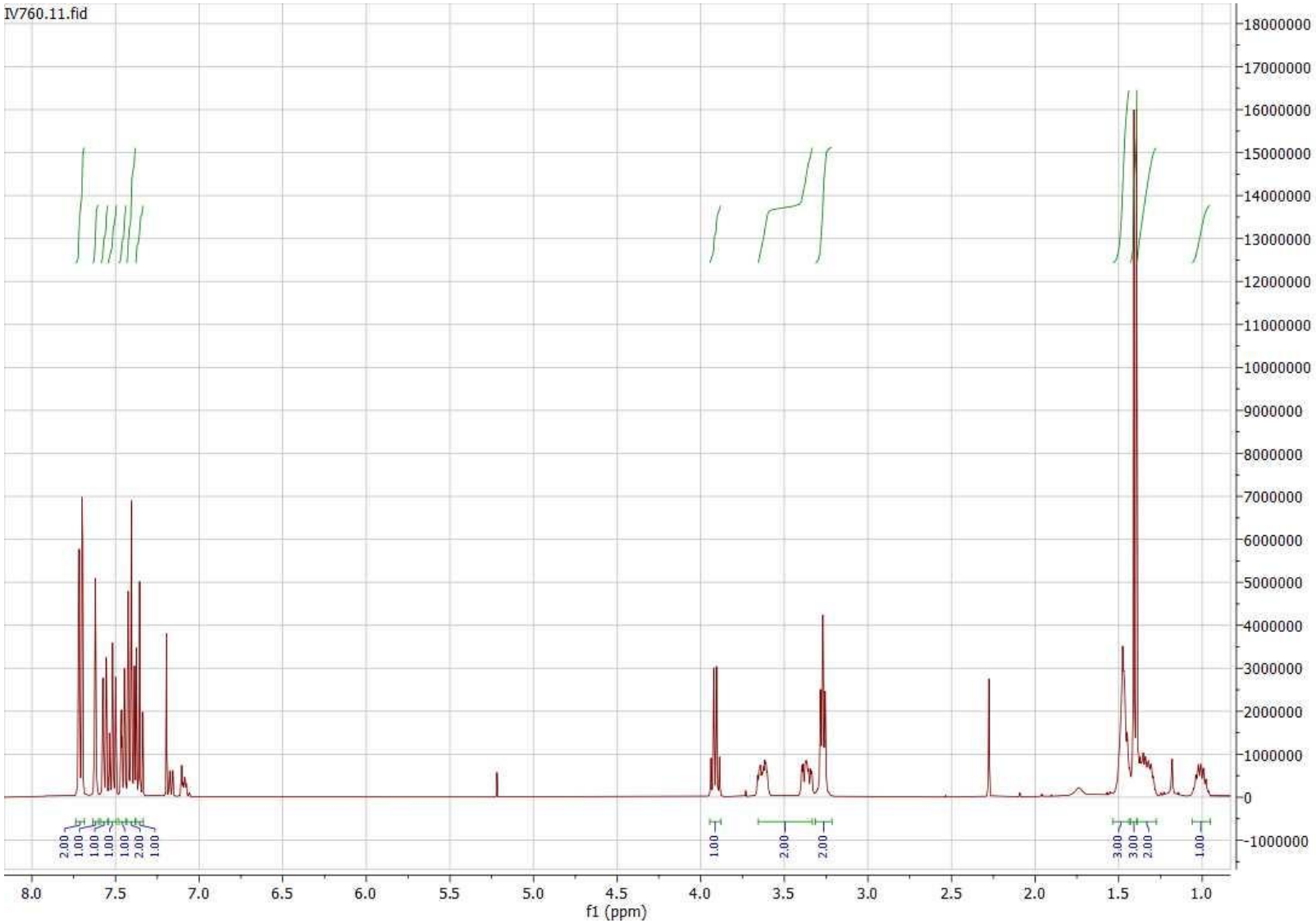


Figure S2. ^{1}H-NMR spectrum of compound **3b**.

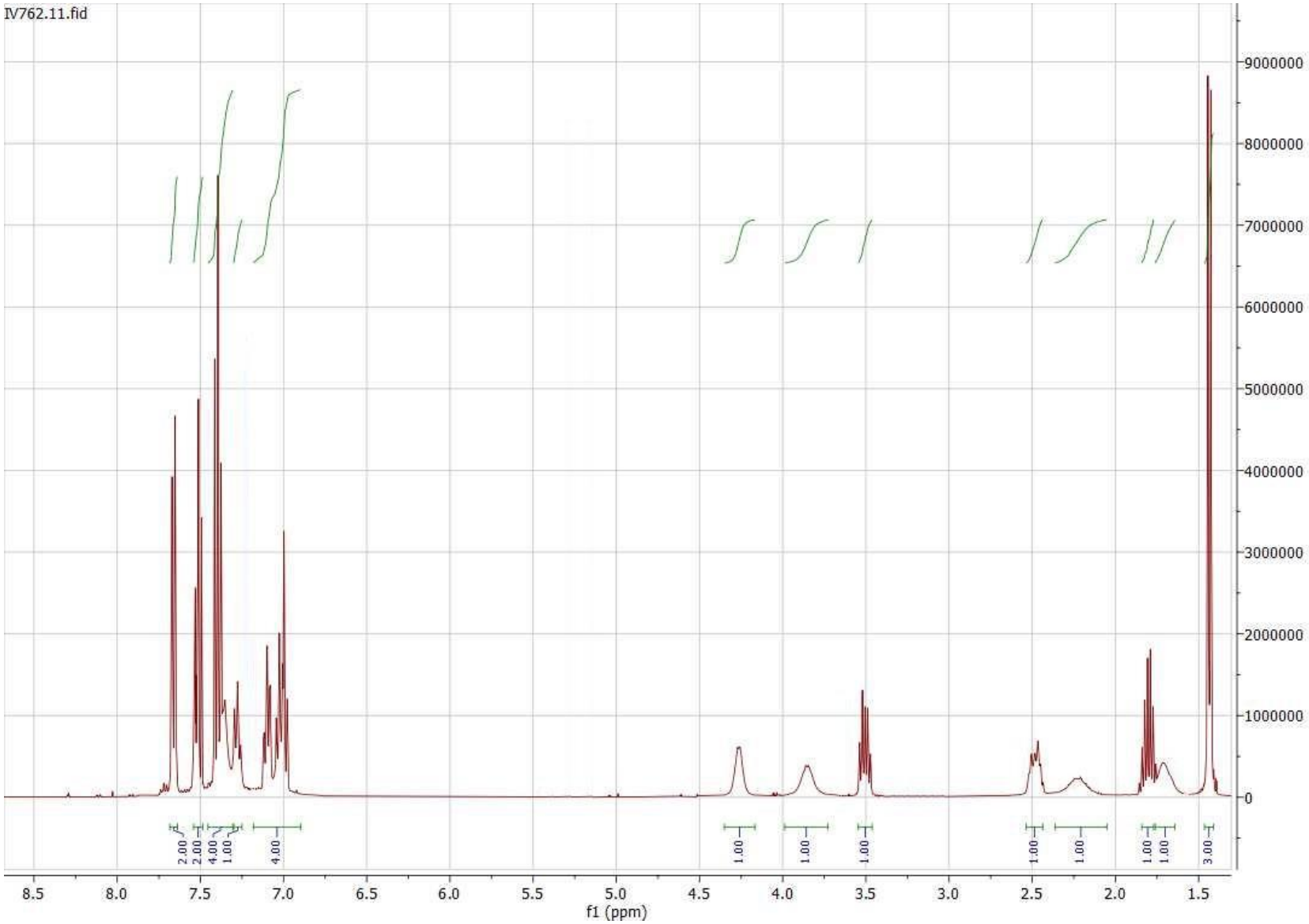


Figure S3. ^{1}H-NMR spectrum of compound **3c**.

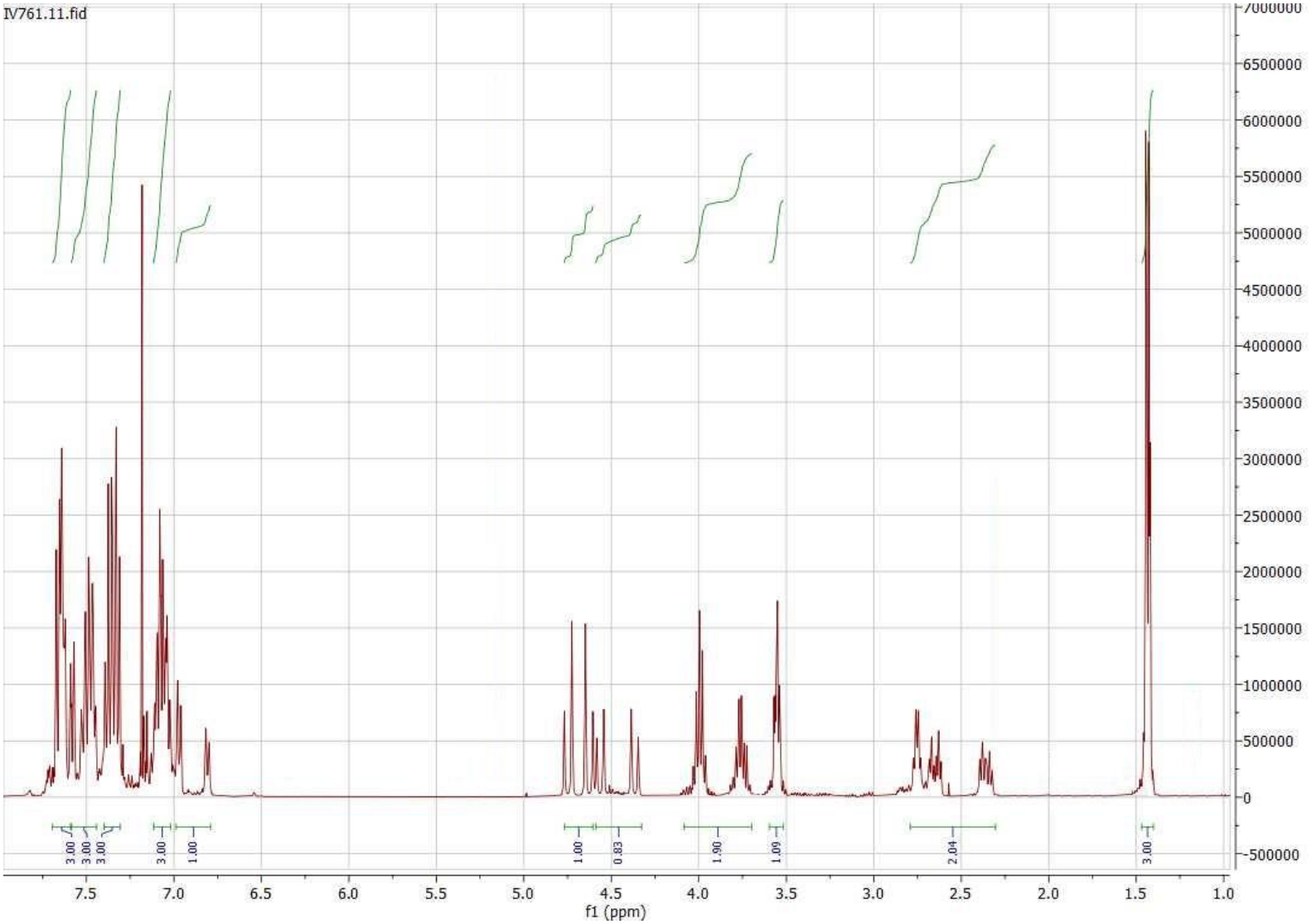


Figure S4. ^{1}H-NMR spectrum of compound **3d**.

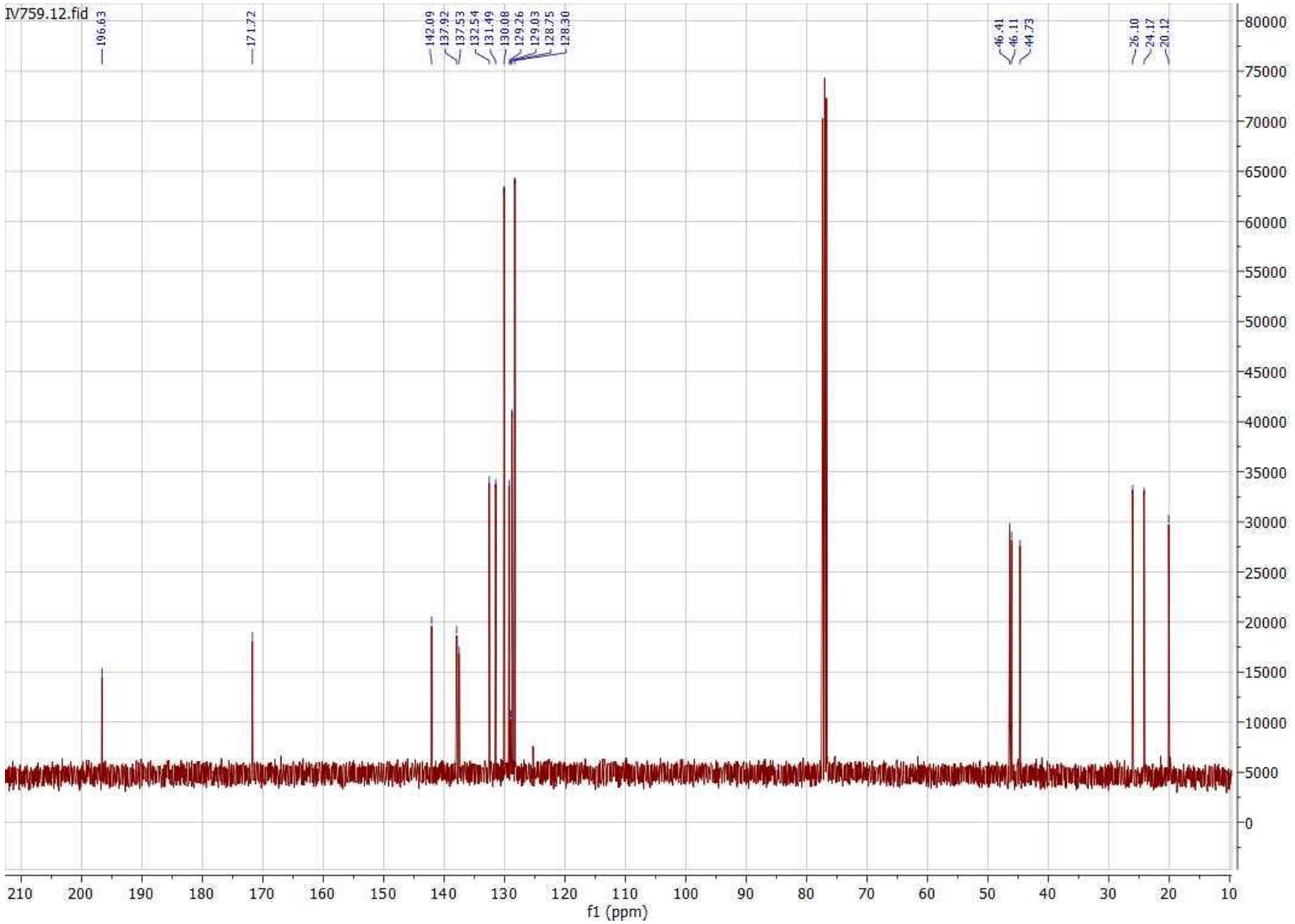


Figure S5. ^{13}C-NMR spectrum of compound **3a**.

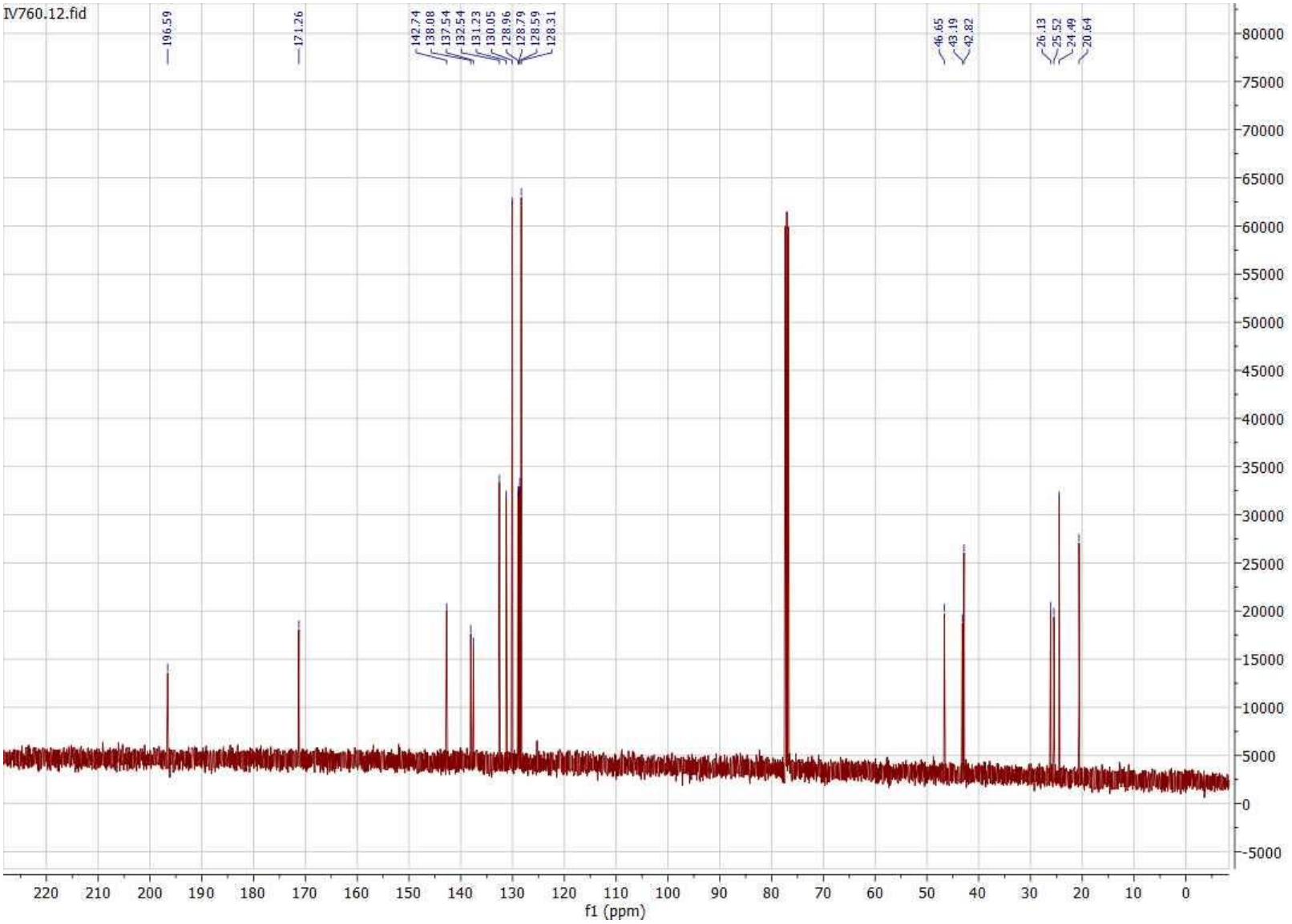


Figure S6. ^{13}C-NMR spectrum of compound **3b**.

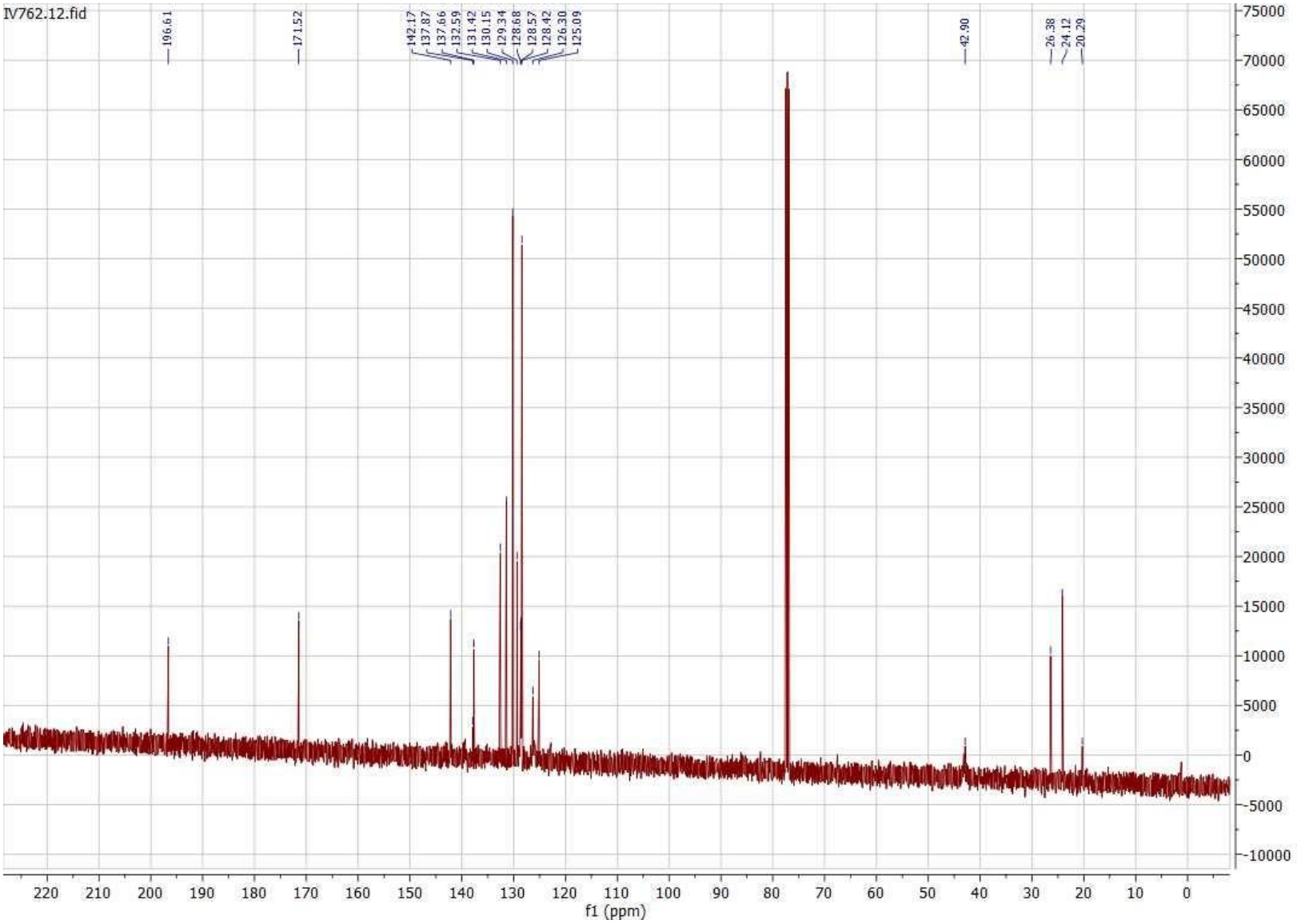


Figure S7. ^{13}C-NMR spectrum of compound **3c**.

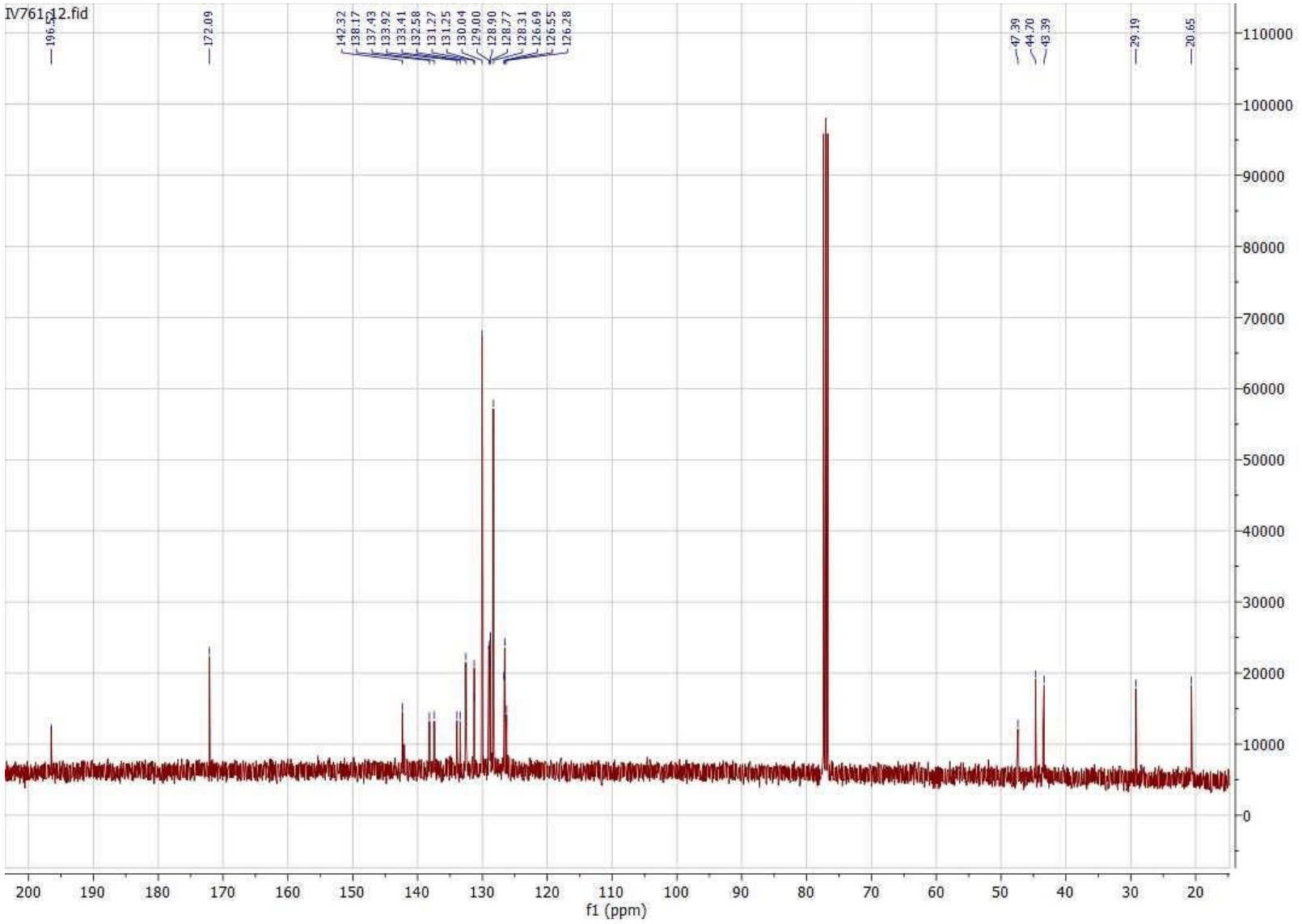


Figure S8. ^{13}C-NMR spectrum of compound **3d**.

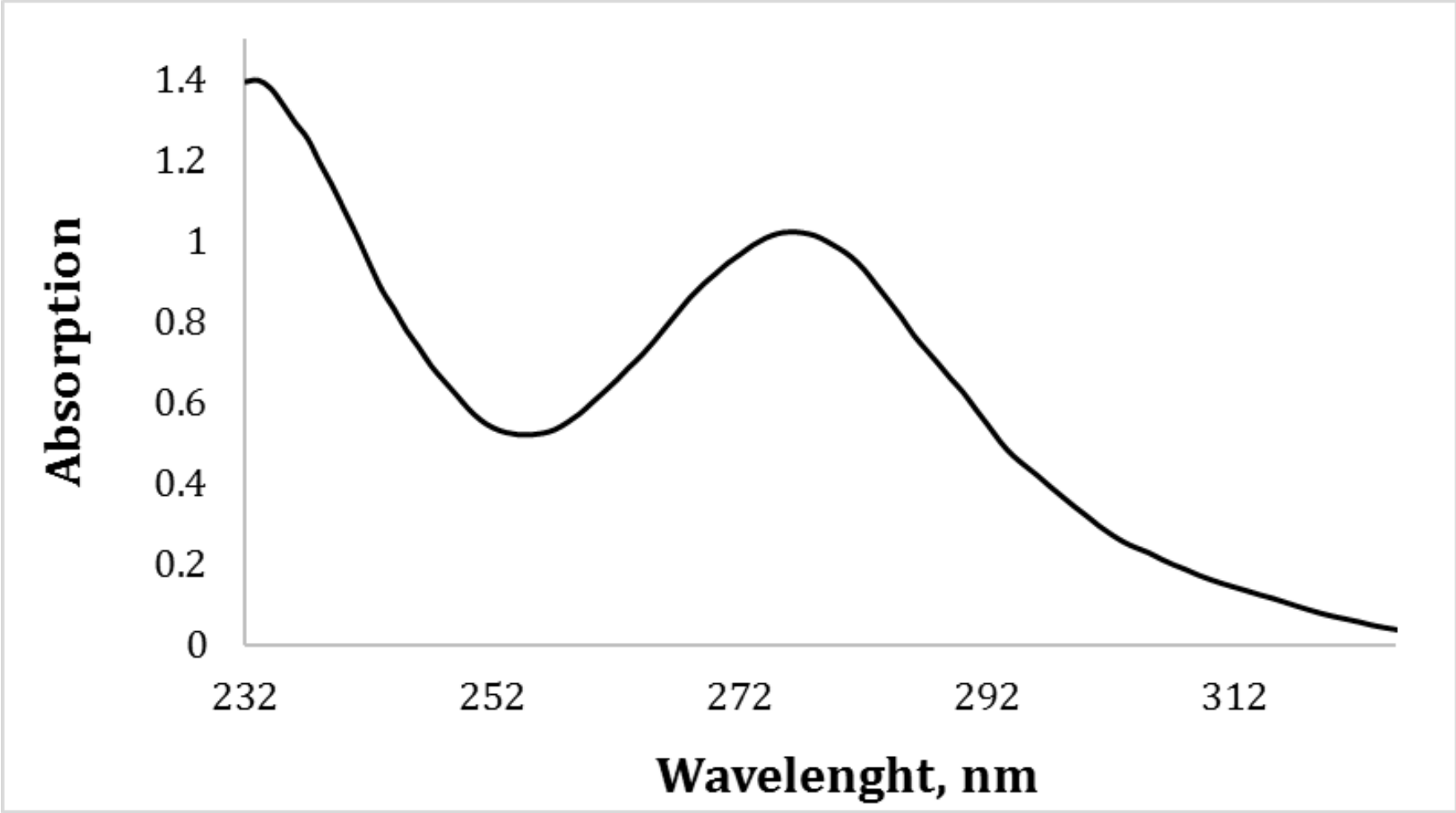
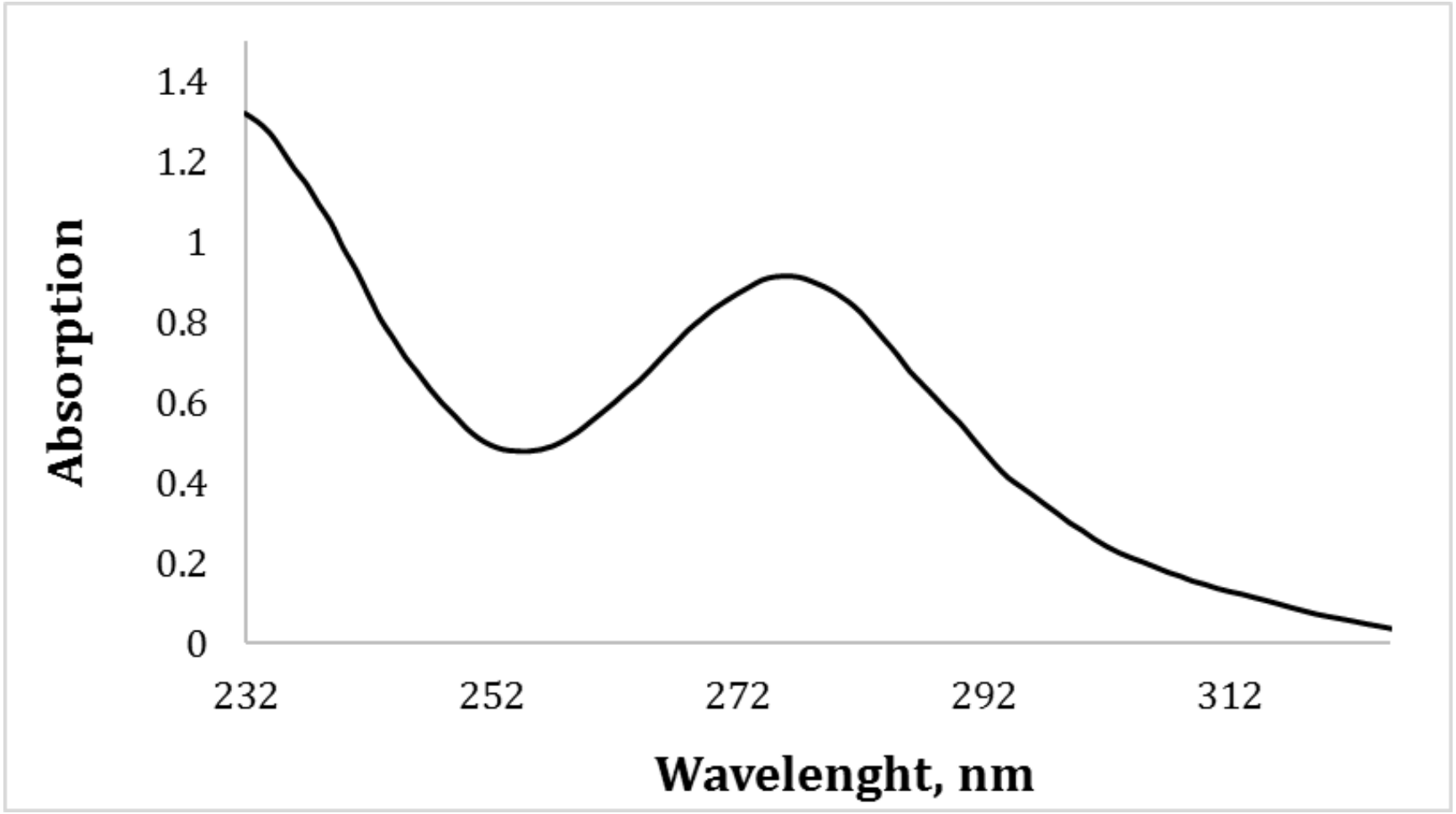


Figure S9. UV spectrum of compound **3a**.



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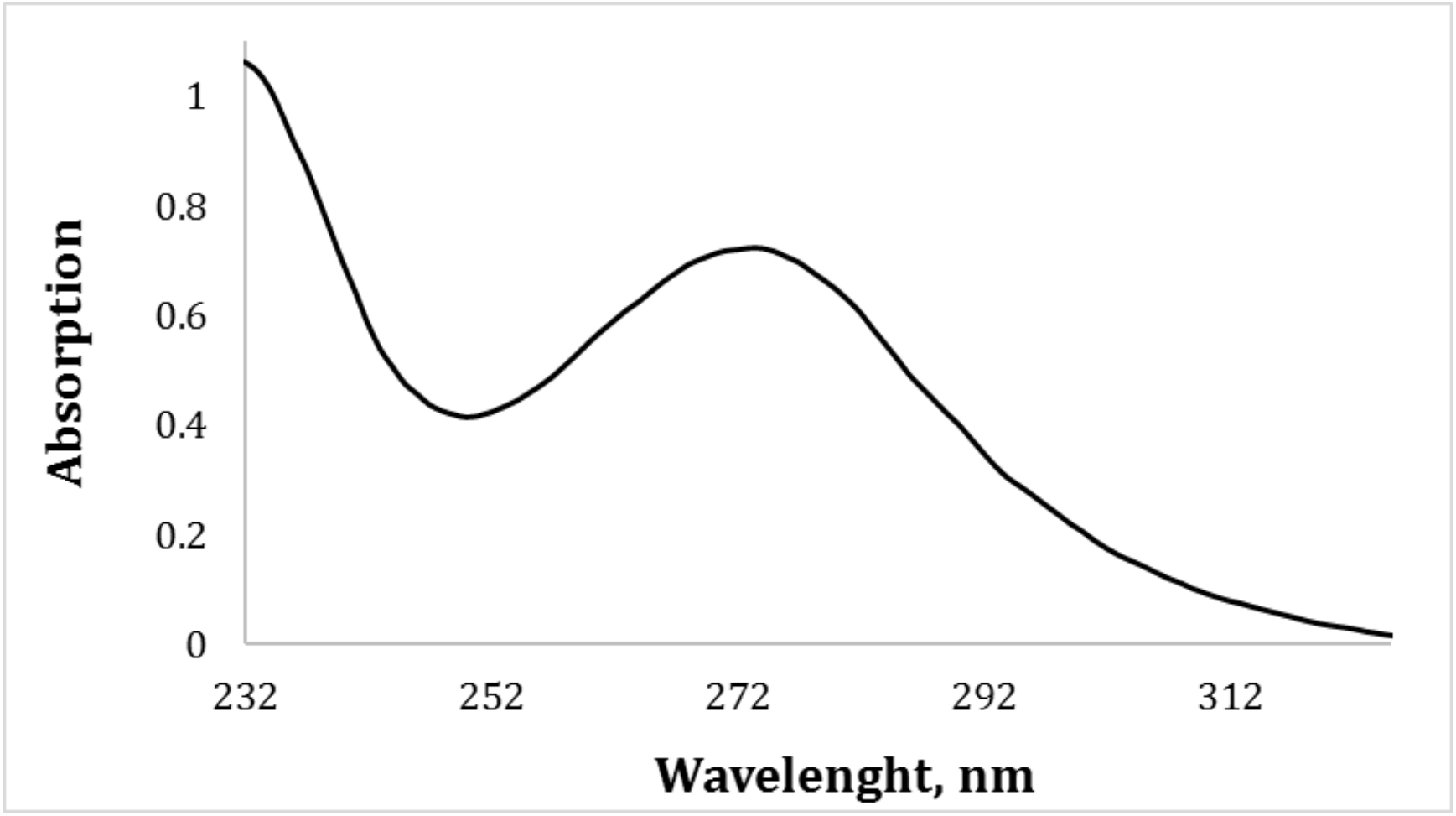


Figure S11. UV spectrum of compound **3c**.

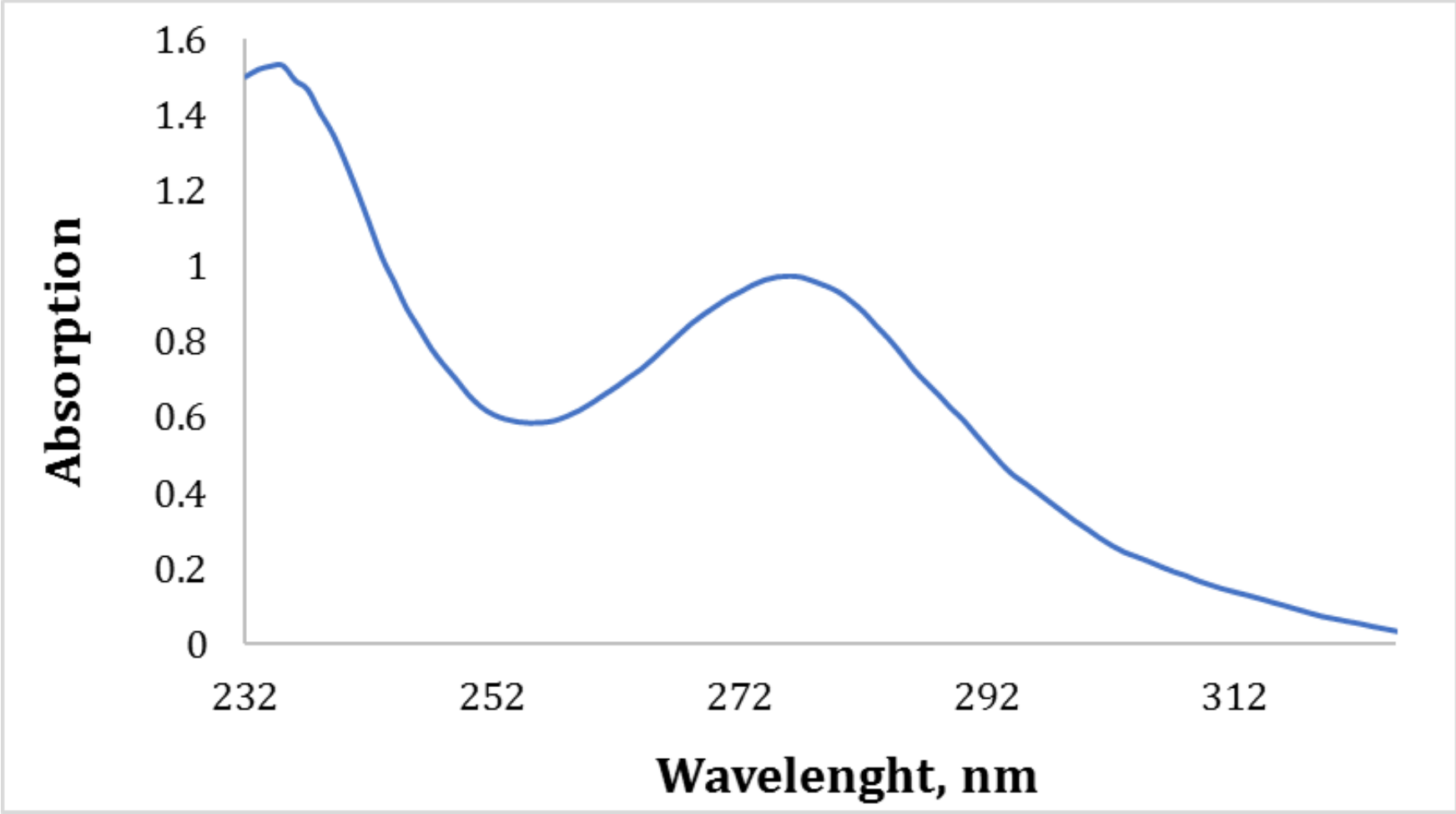


Figure S12. UV spectrum of compound **3d**.

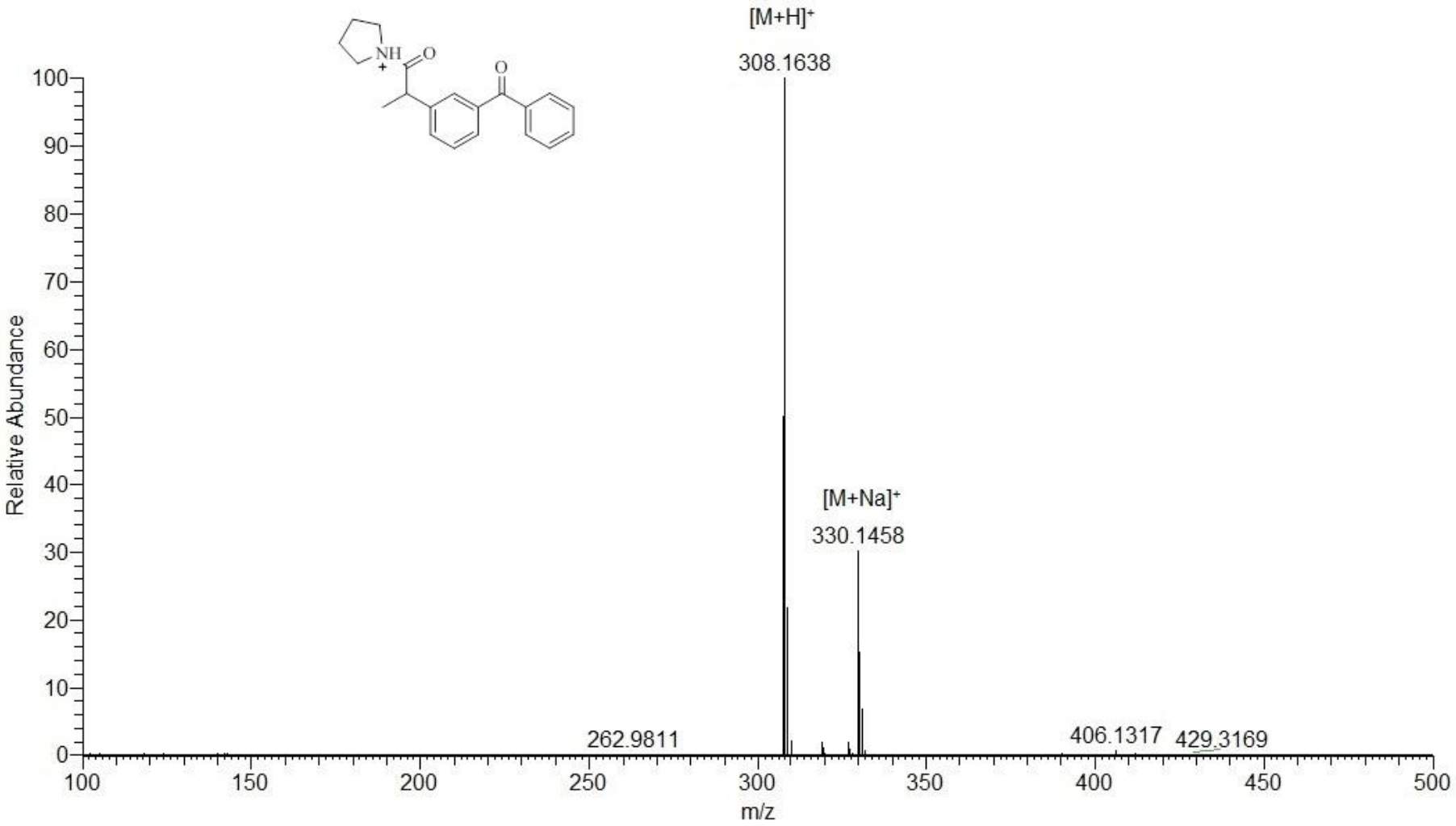


Figure S13. ESI-HRMS of compound **3a**.

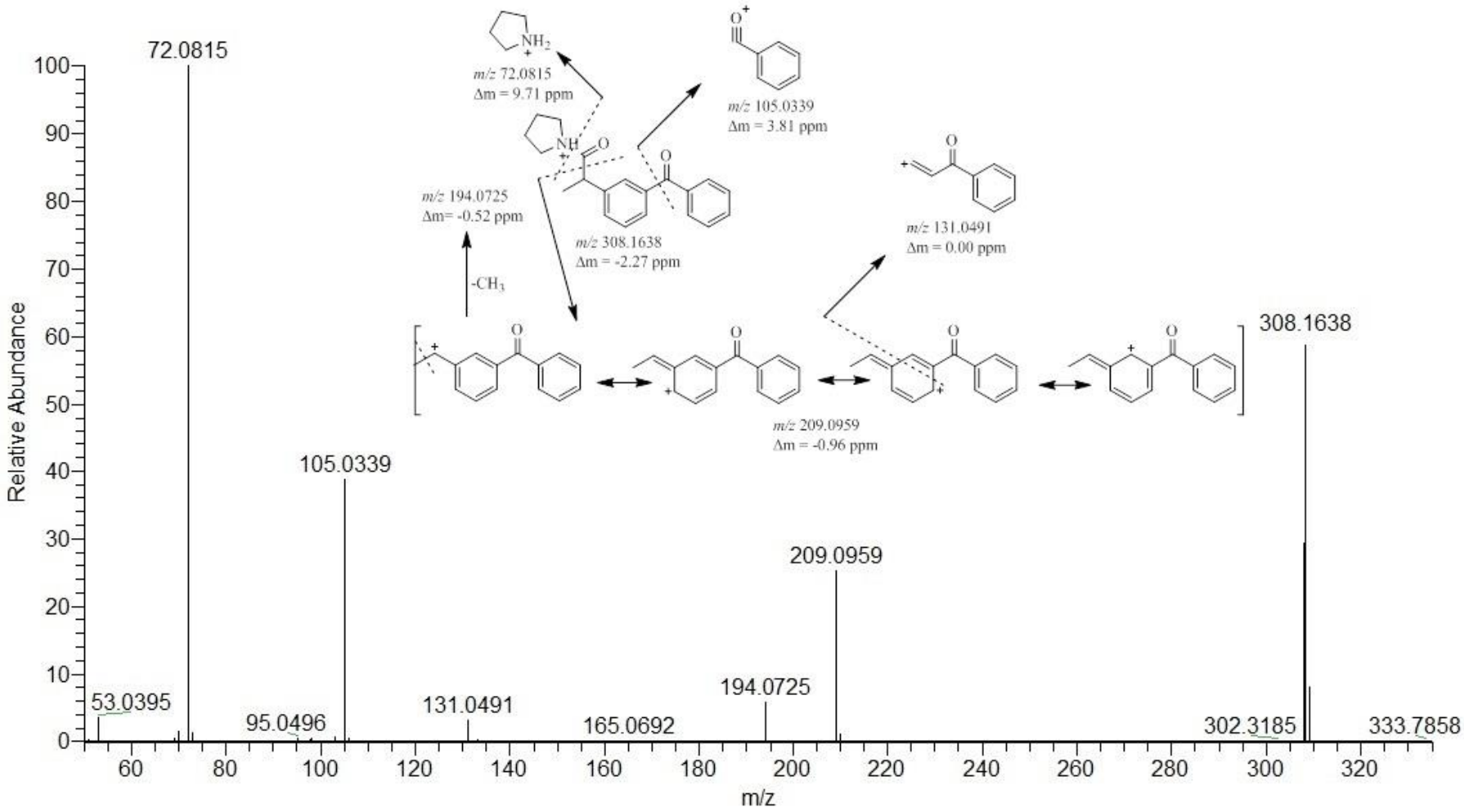


Figure S14 Mass spectrum of **4a** obtained by positive ion ESI-MS/MS. Proposed fragmentation of protonated **3a**.

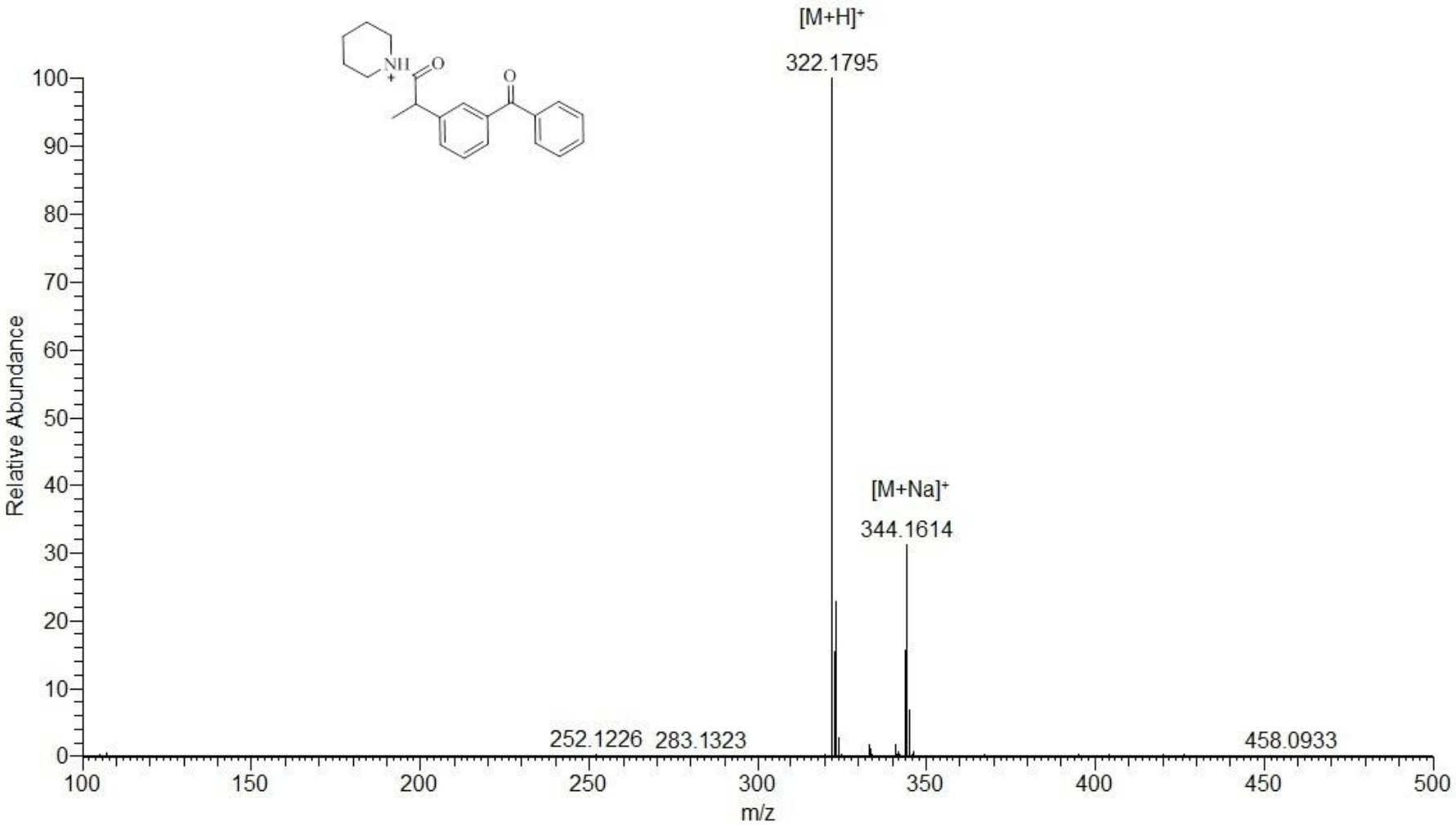


Figure S15. ESI-HRMS of compound **3b**.

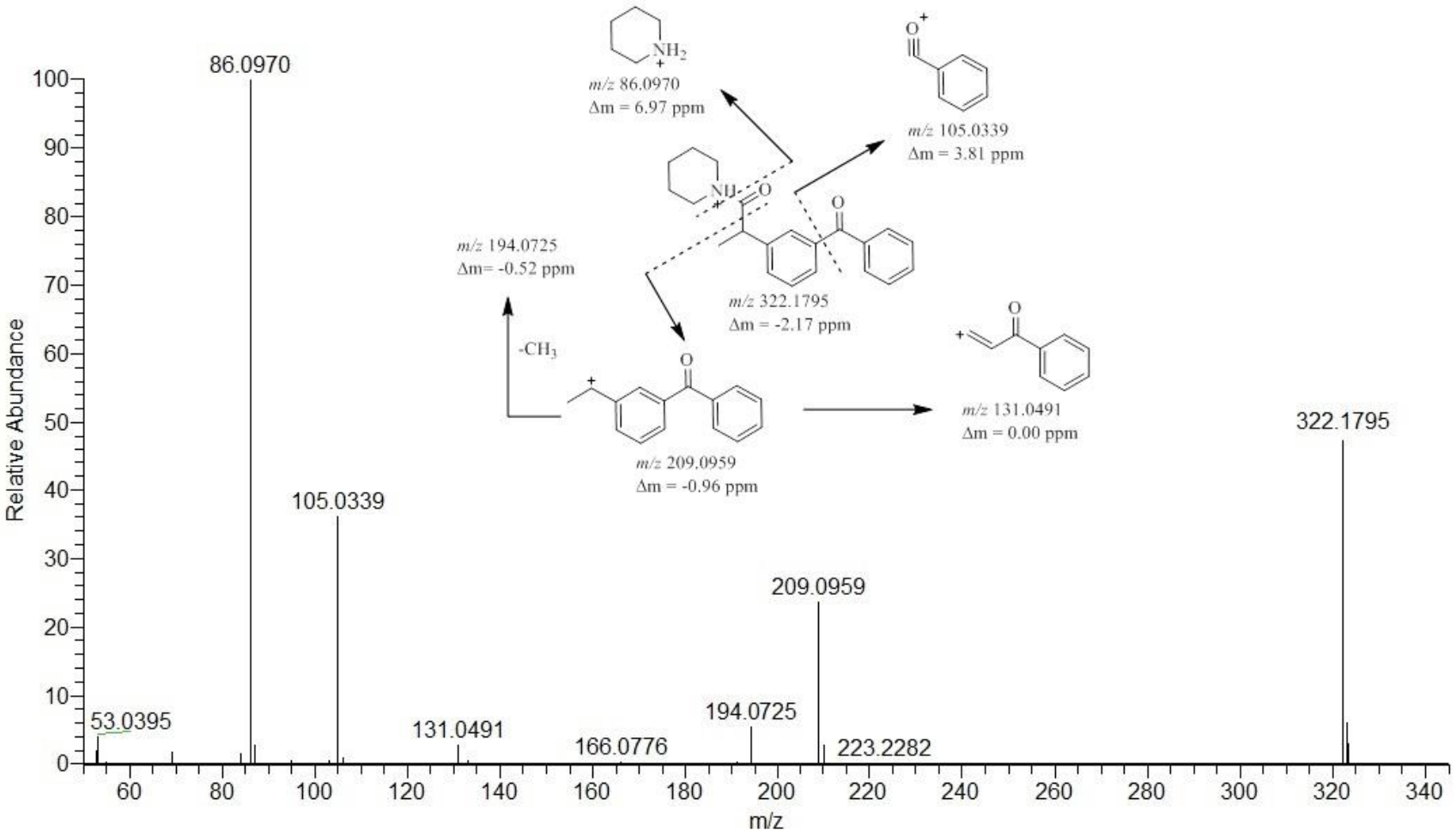


Figure S16 Mass spectrum of **4b** obtained by positive ion ESI-MS/MS. Proposed fragmentation of protonated **3b**.

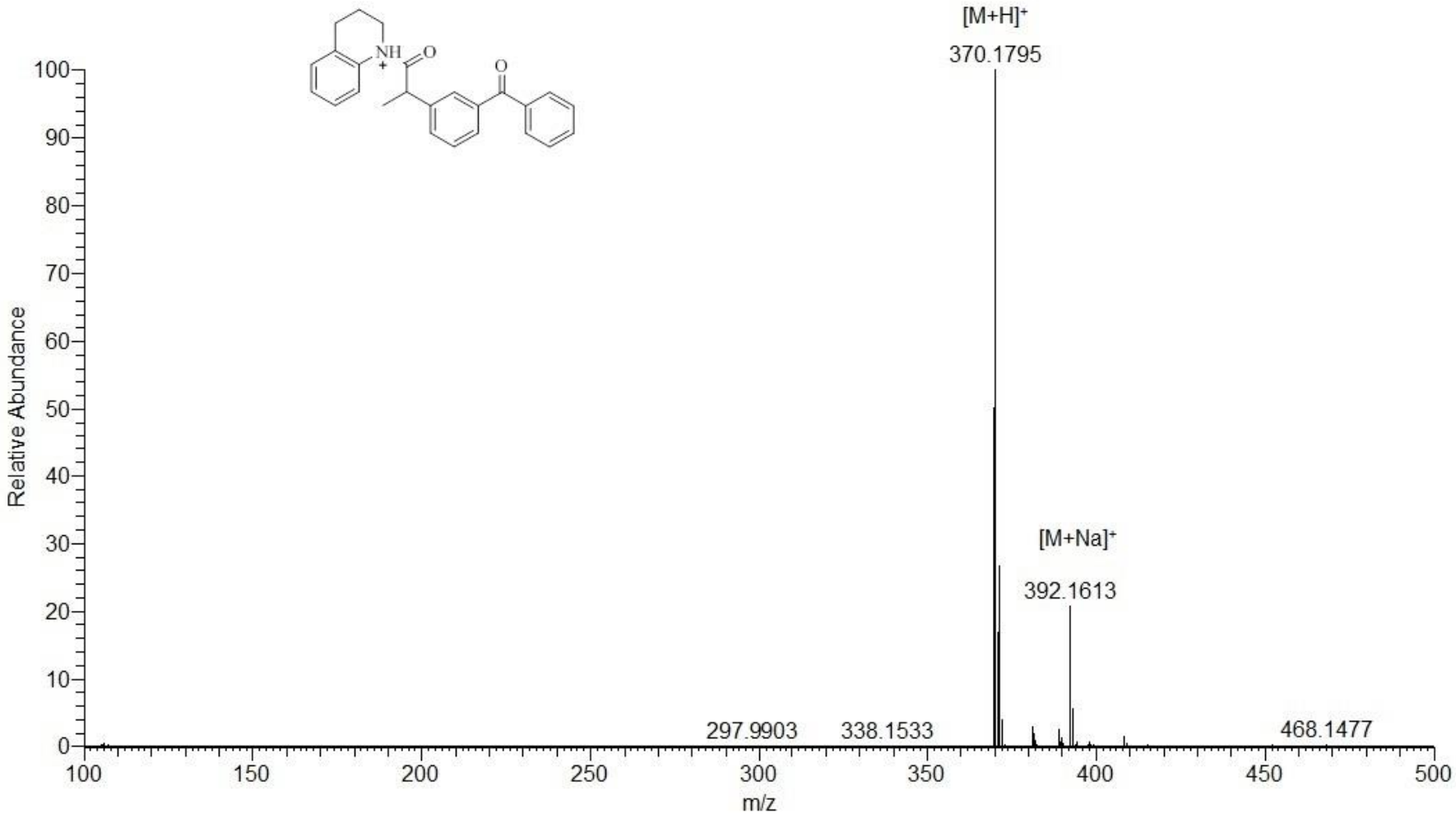


Figure S17. ESI-HRMS of compound **3c**.

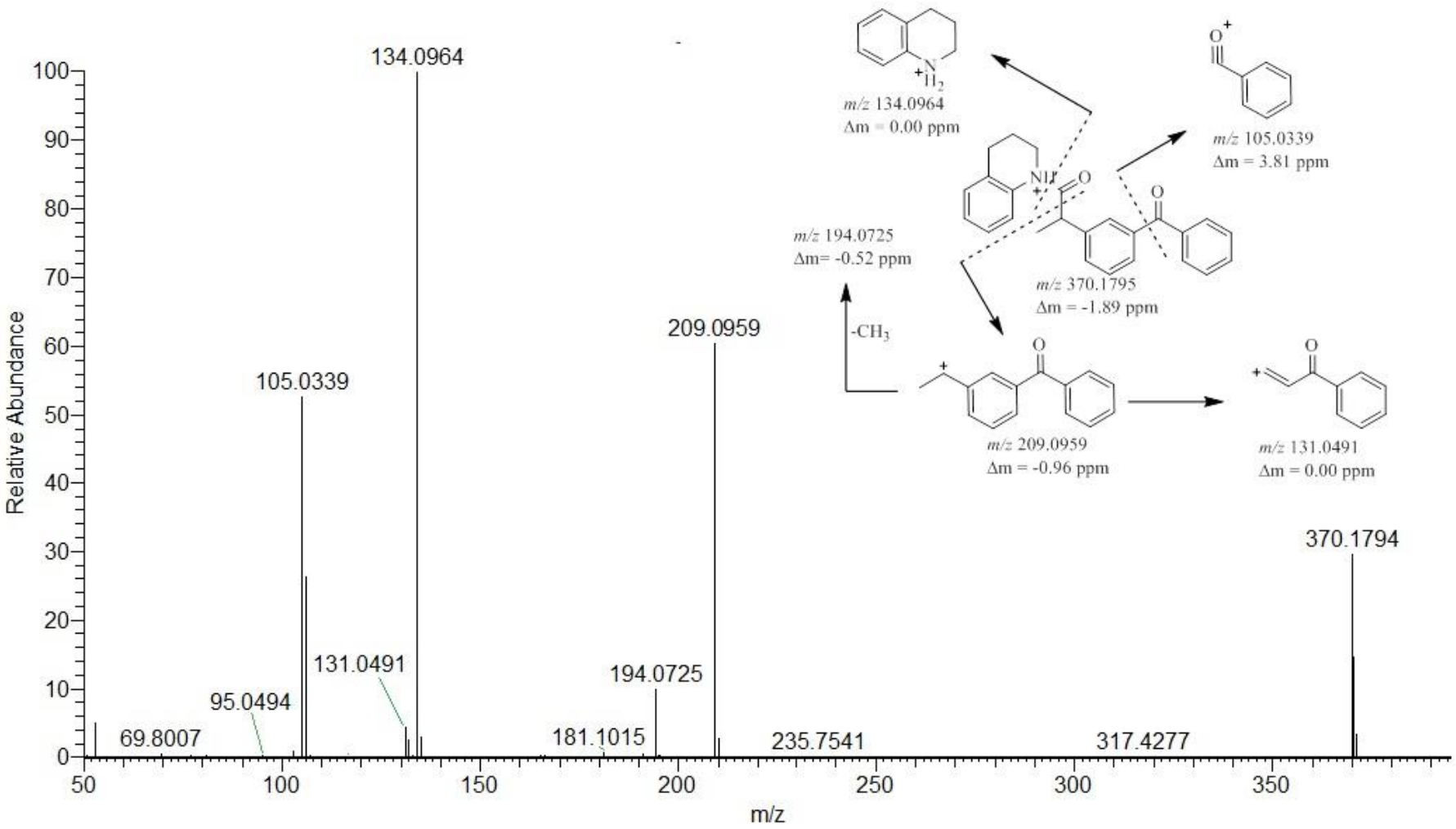


Figure S18 Mass spectrum of **4c** obtained by positive ion ESI-MS/MS. Proposed fragmentation of protonated **3c**.

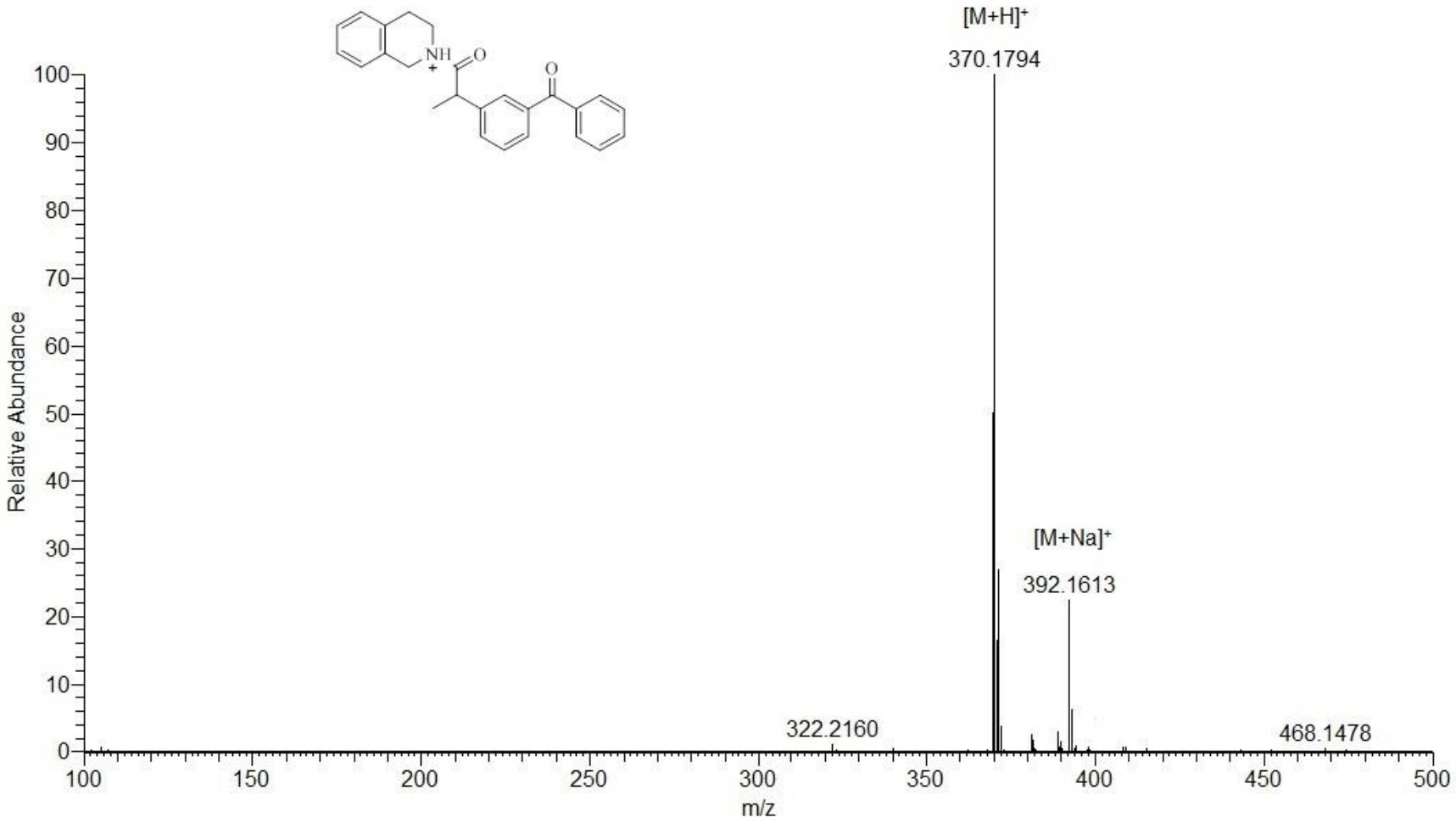


Figure S19. ESI-HRMS of compound **3d**.

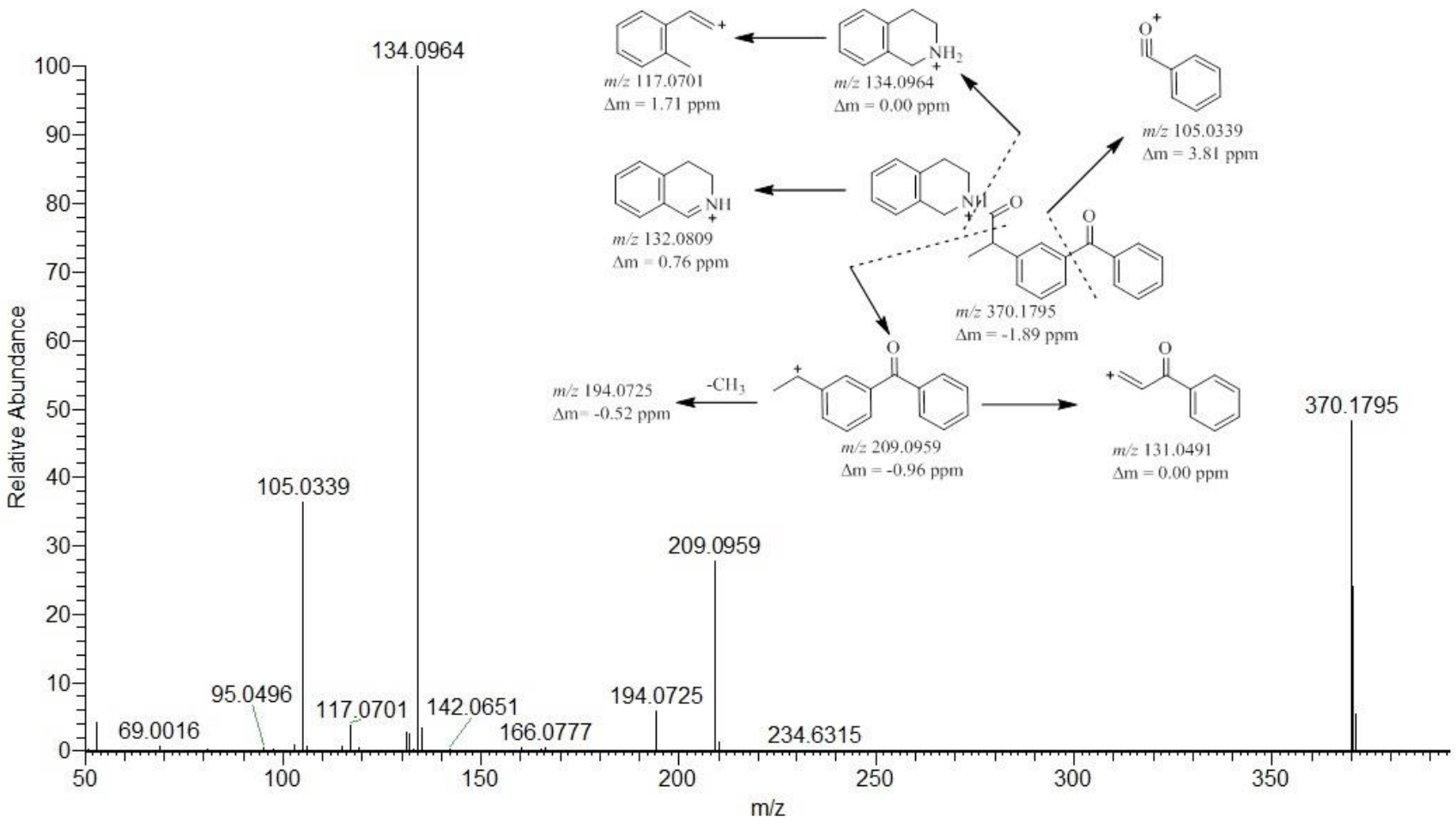
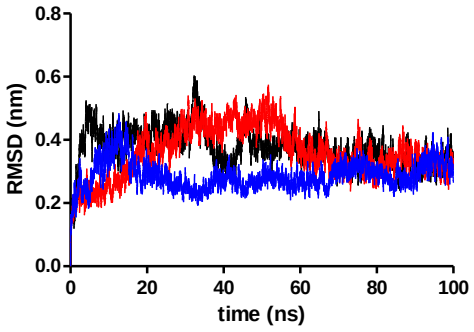
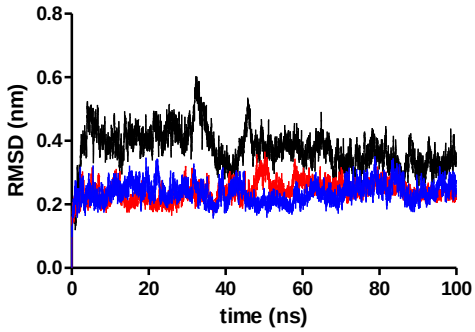
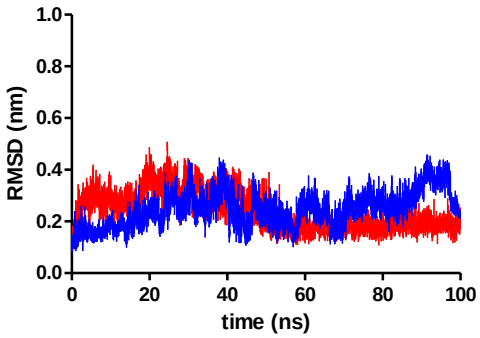
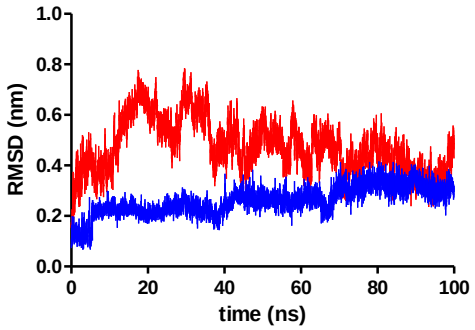
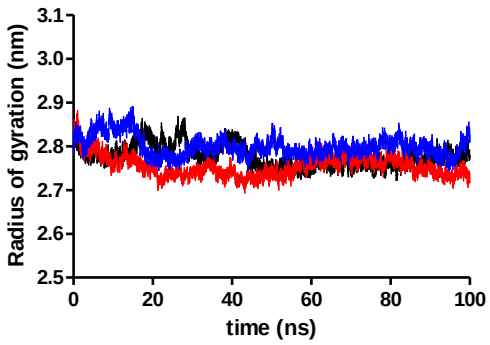
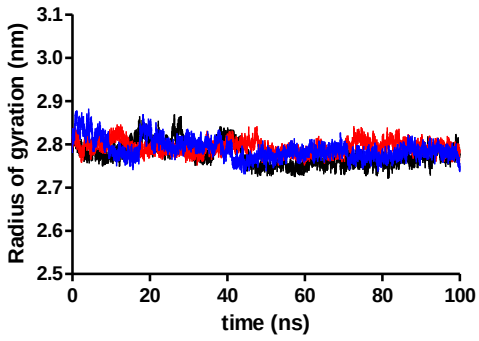
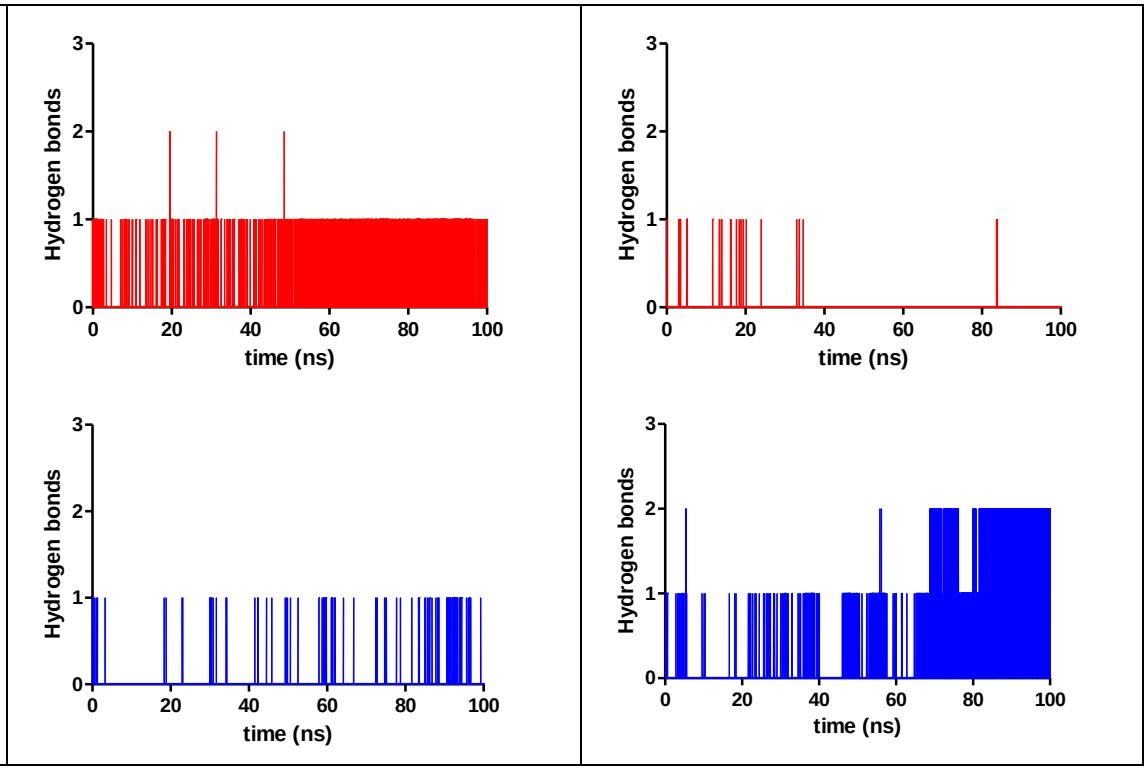


Figure S20 Mass spectrum of **4d** obtained by positive ion ESI-MS/MS. Proposed fragmentation of protonated **3d**.

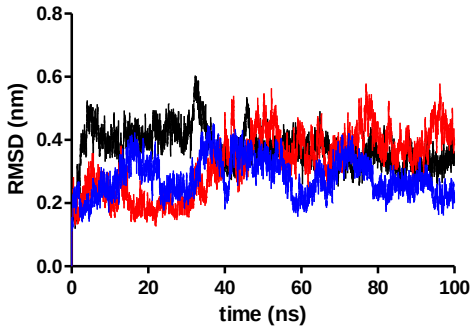
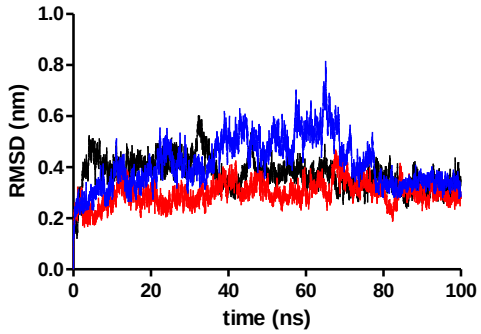
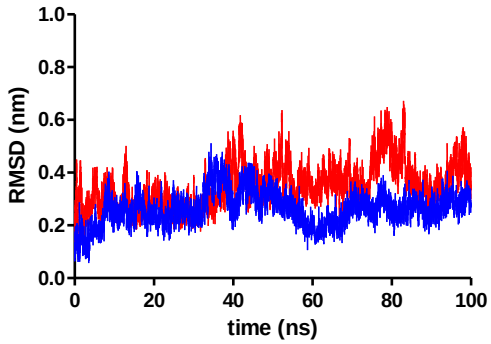
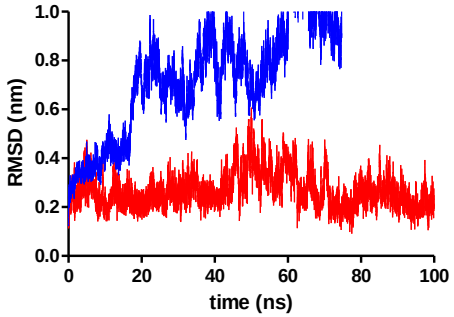
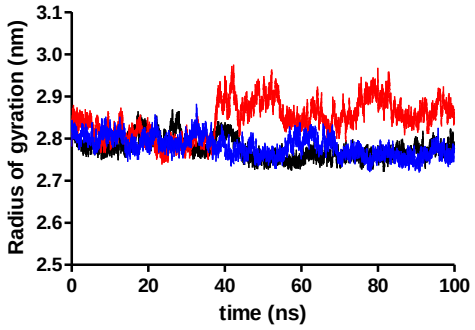
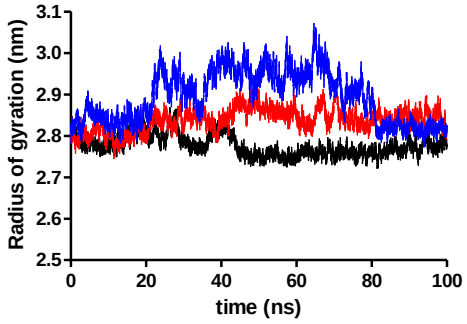
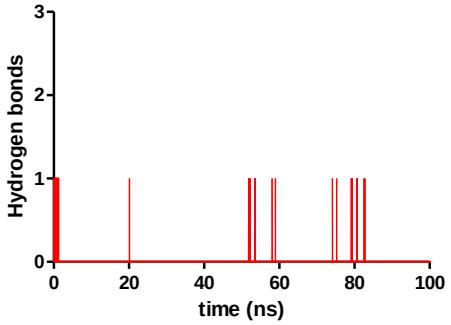
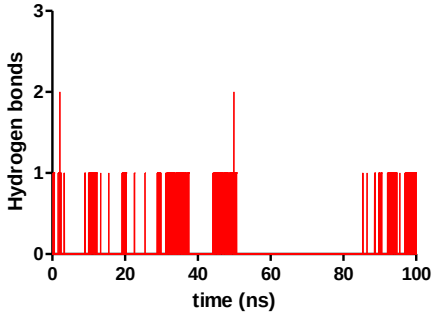
Table S1. RMSD of protein backbone, RMSD of ligands and RG of protein in the molecular dynamics study when ligands **3c** and **3d** were docked into the Sudlow 2 site.

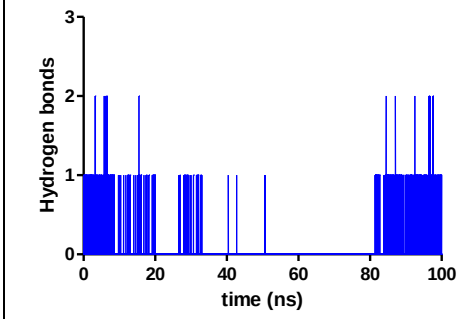
Parameter	**Compound 3c**	**Compound 3d**
RMSD protein backbone		
RMSD ligand		
RG of protein		

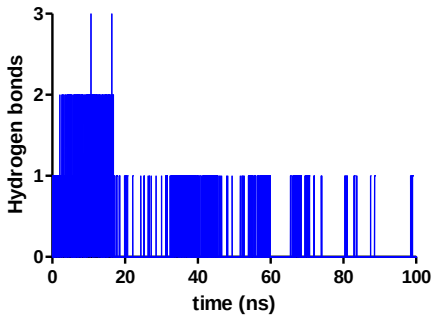
Hydrogen bonds	

black: apo; red: R enantiomer, blue: S enantiomer

Table S2. RMSD of protein backbone, RMSD of ligands and RG of protein in the molecular dynamics study when ligands **3a** and **3b** were docked into the site 3 of albumin.

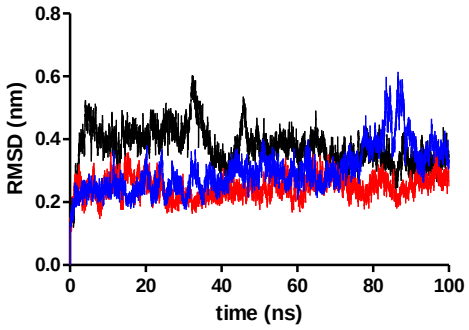
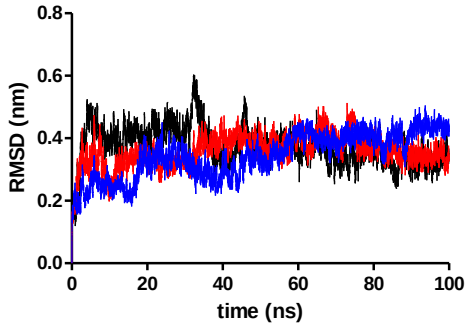
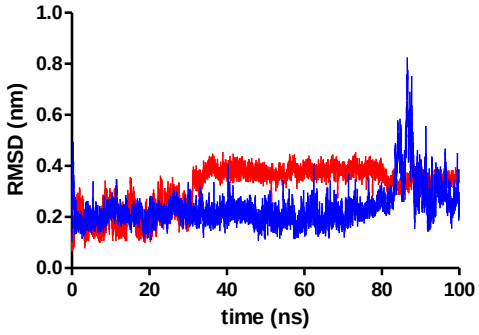
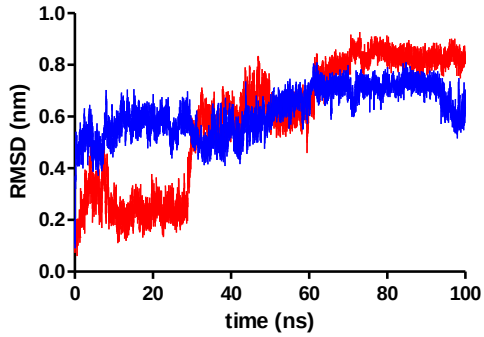
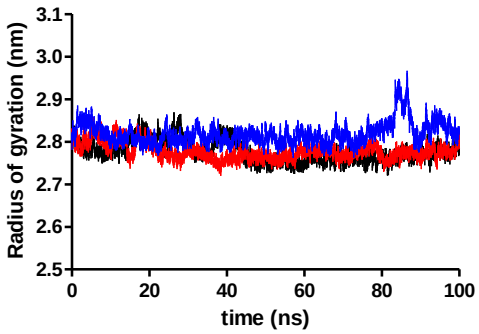
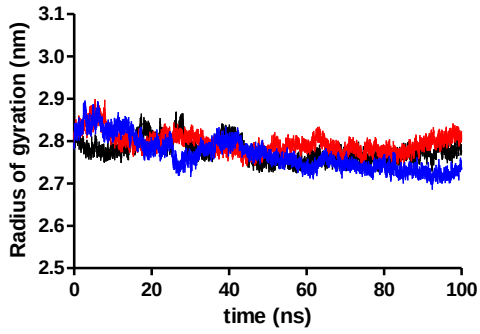
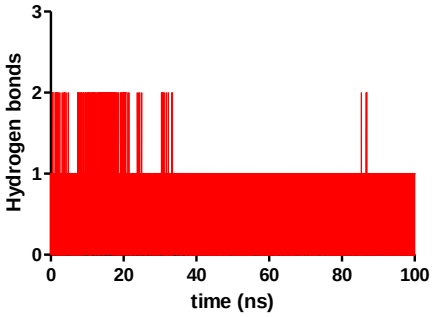
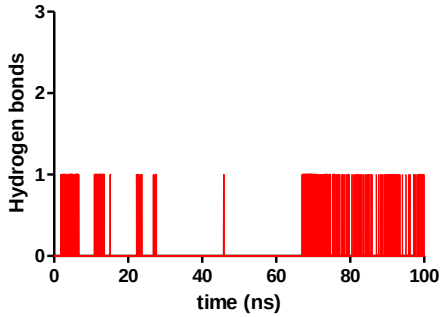
Parameter	**Compound 3a**	**Compound 3b**
RMSD protein backbone		
RMSD ligand		
RG of protein		
Hydrogen bonds		

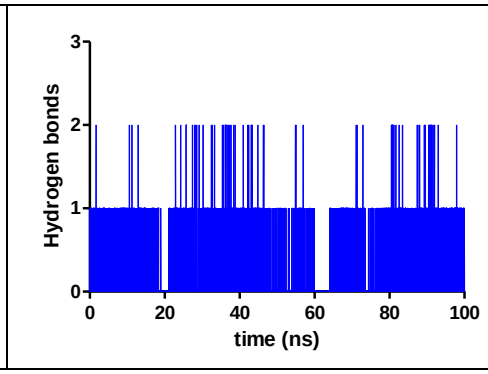


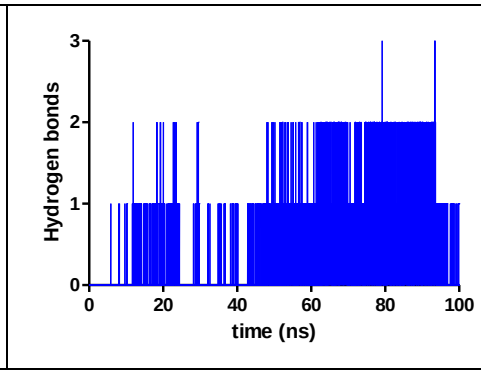


black: apo; red: R enantiomer, blue: S enantiomer

Table S3. RMSD of protein backbone, RMSD of ligands and RG of protein in the molecular dynamics study when ligands **3c** and **3d** were docked into the site 3 of albumin.

Parameter	**Compound 3c**	**Compound 3d**
RMSD protein backbone		
RMSD ligand		
RG of protein		
Hydrogen bonds		





black: apo; red: R enantiomer, blue: S enantiomer

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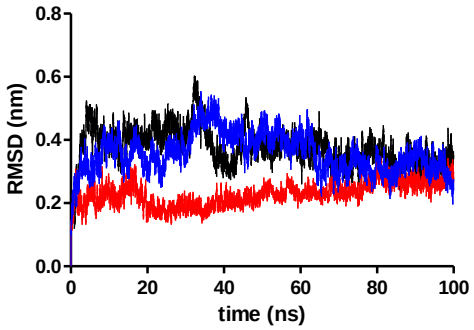
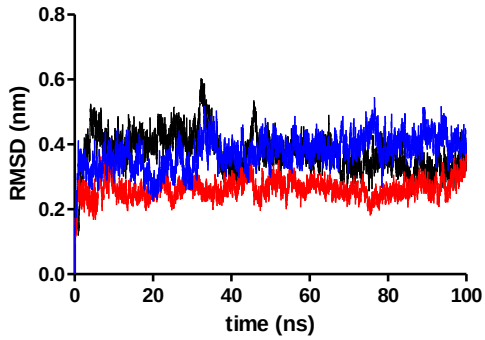
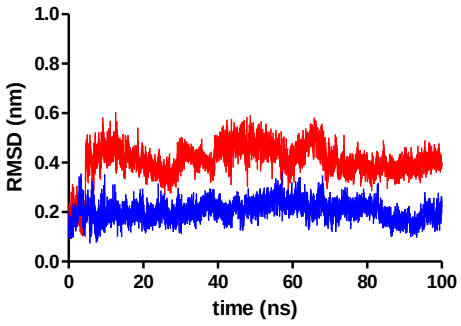
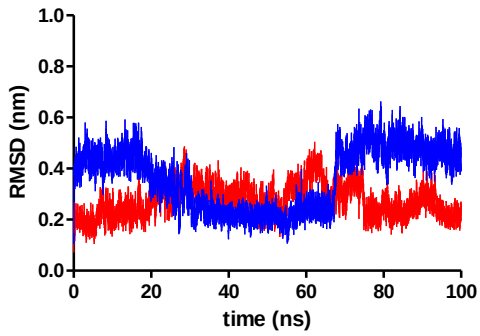
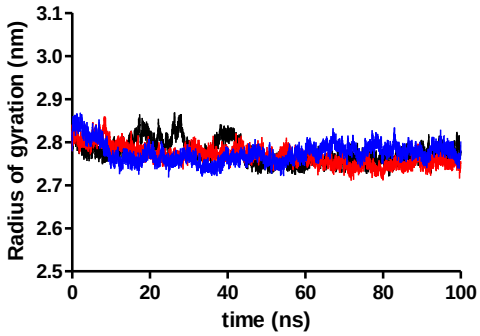
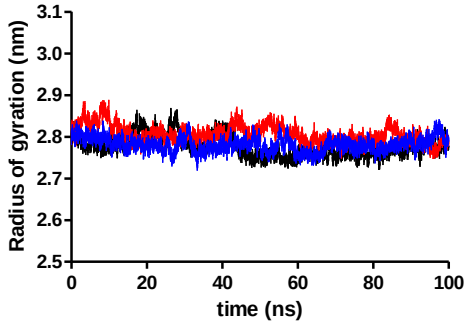
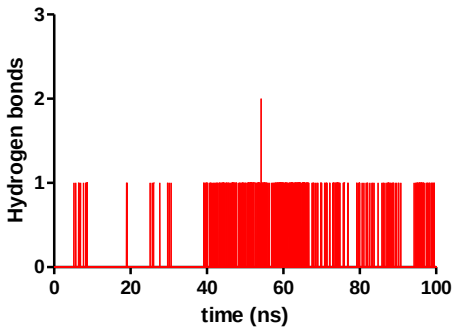
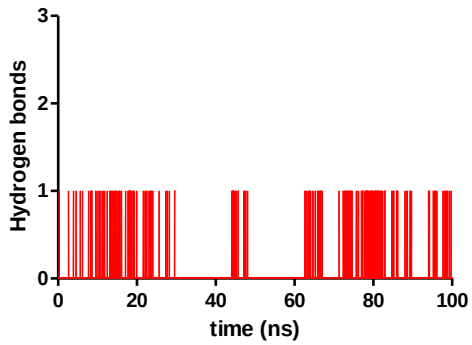
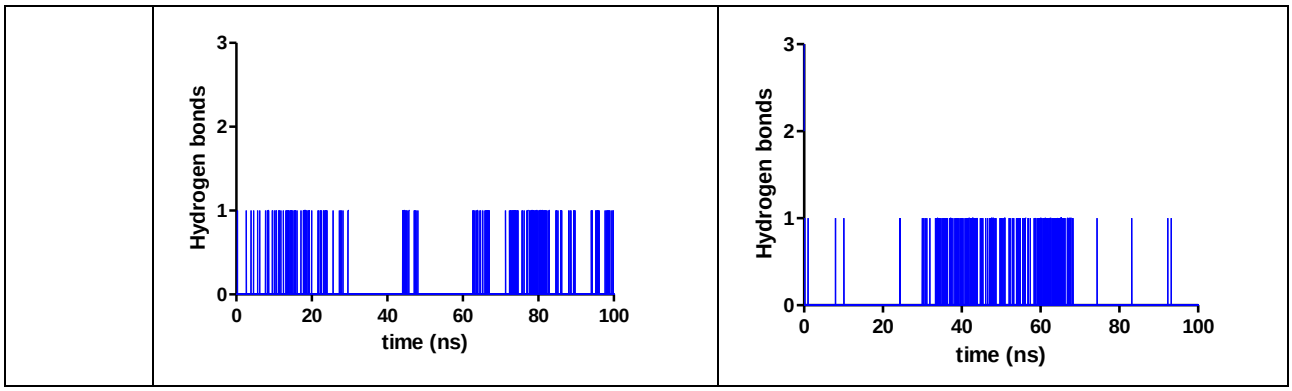
Parameter	**Compound 3c**	**Compound 3d**
RMSD protein backbone		
RMSD ligand		
RG of protein		
Hydrogen bonds		



black: apo; red: R enantiomer, blue: S enantiomer