

Supplementary Materials:

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

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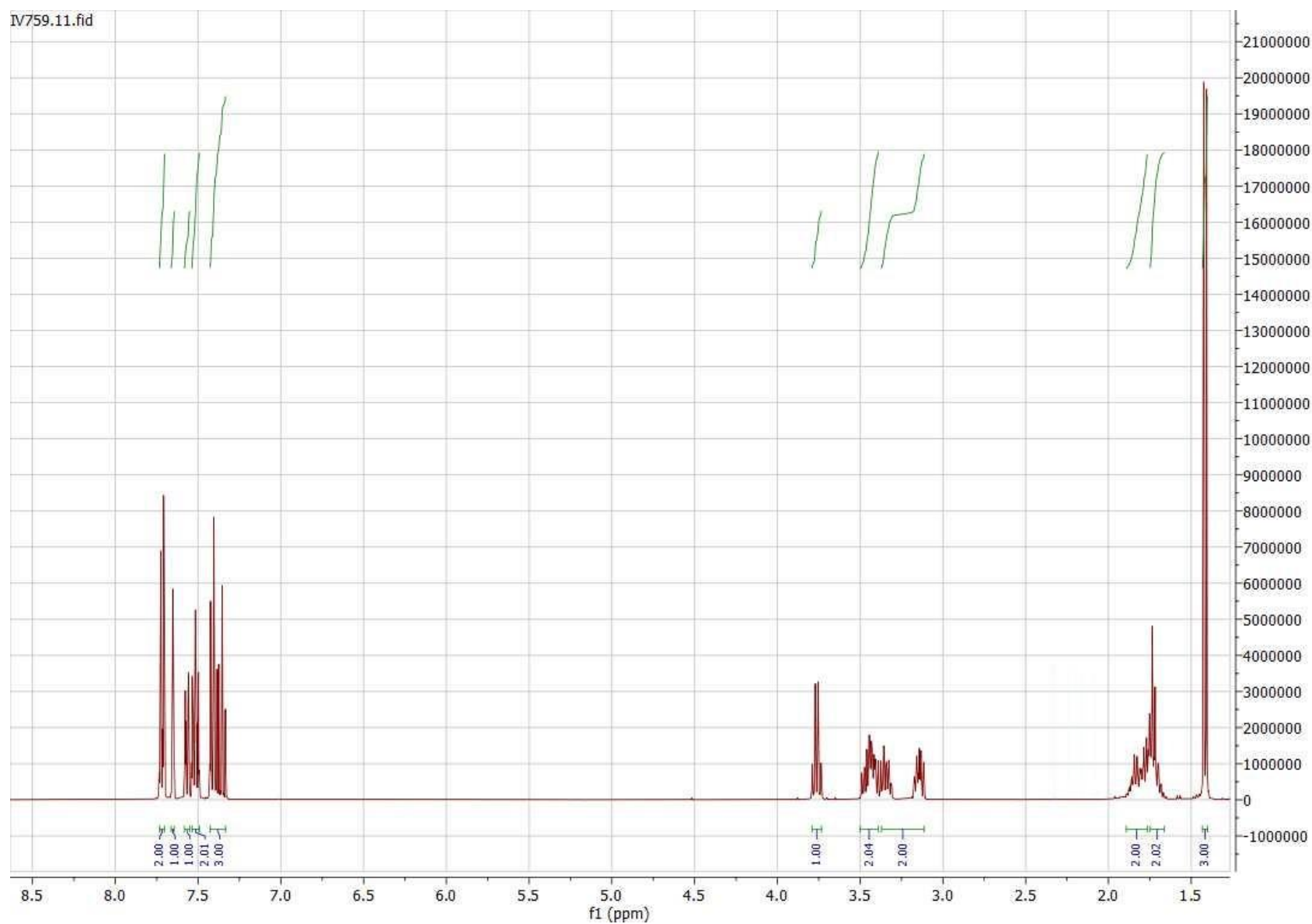


Figure S1. ^1H -NMR spectrum of compound **3a**.

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

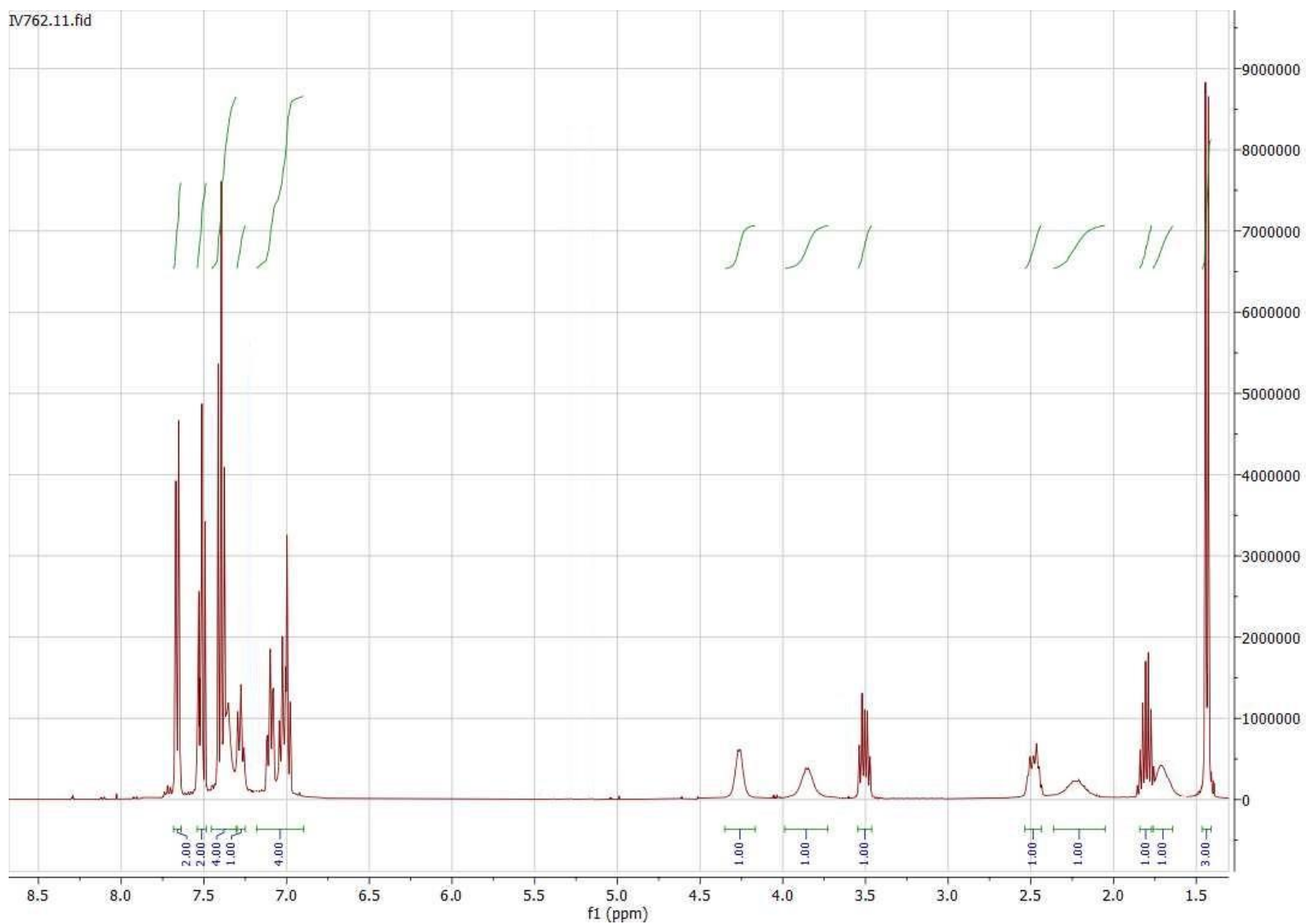


Figure S3. ^1H -NMR spectrum of compound **3c**.

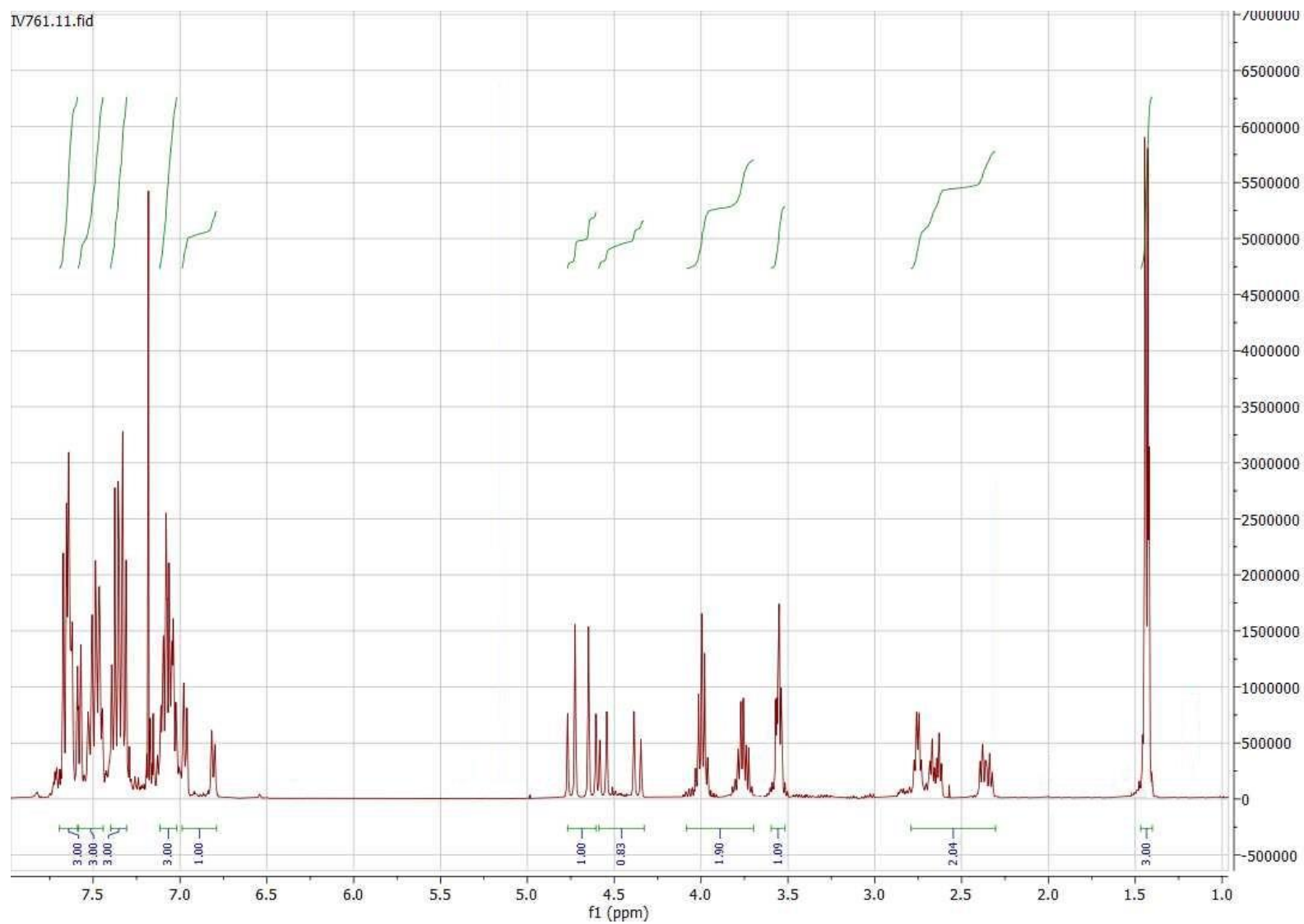


Figure S4. ^1H -NMR spectrum of compound **3d**.

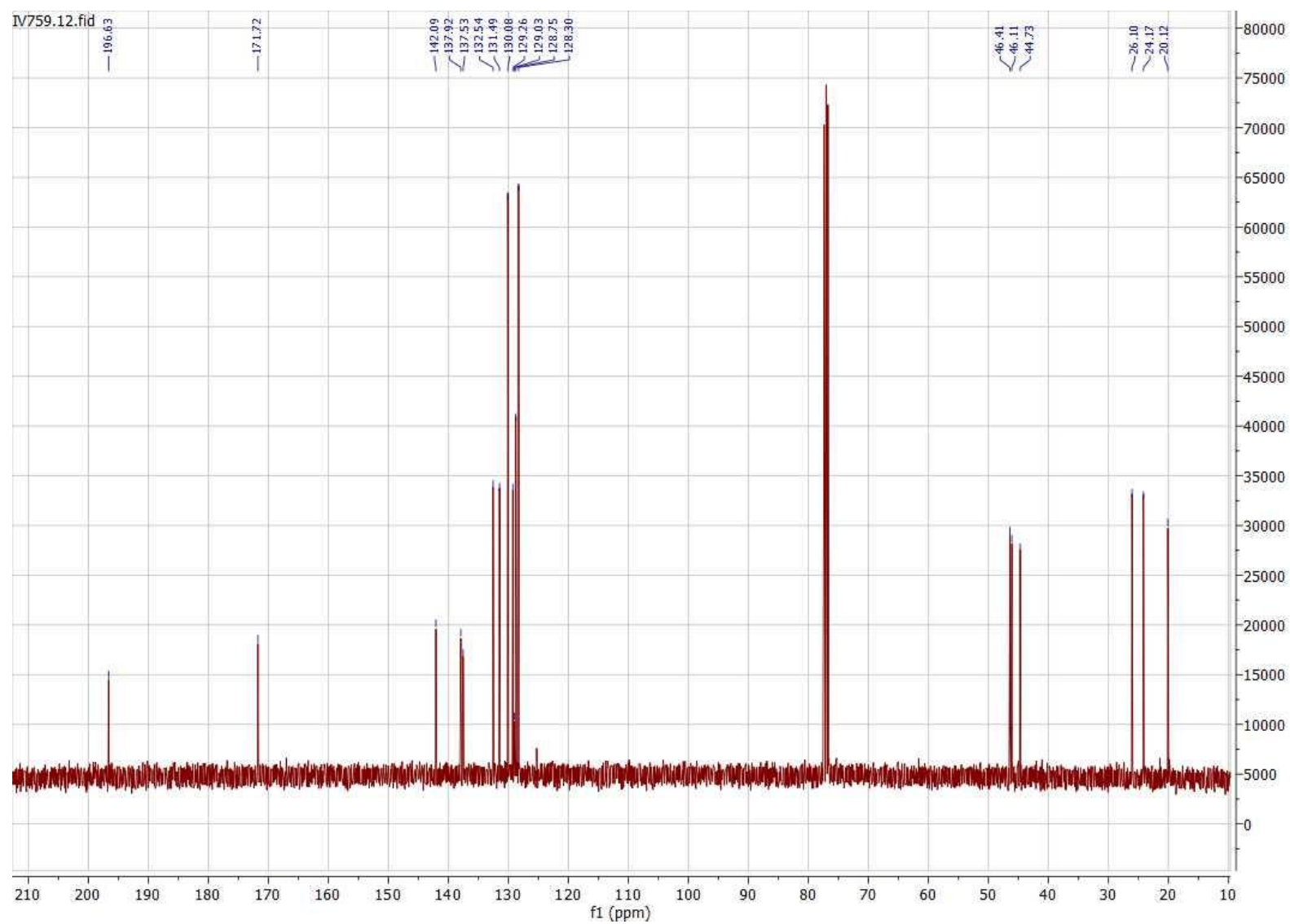


Figure S5. ^{13}C -NMR spectrum of compound 3a.

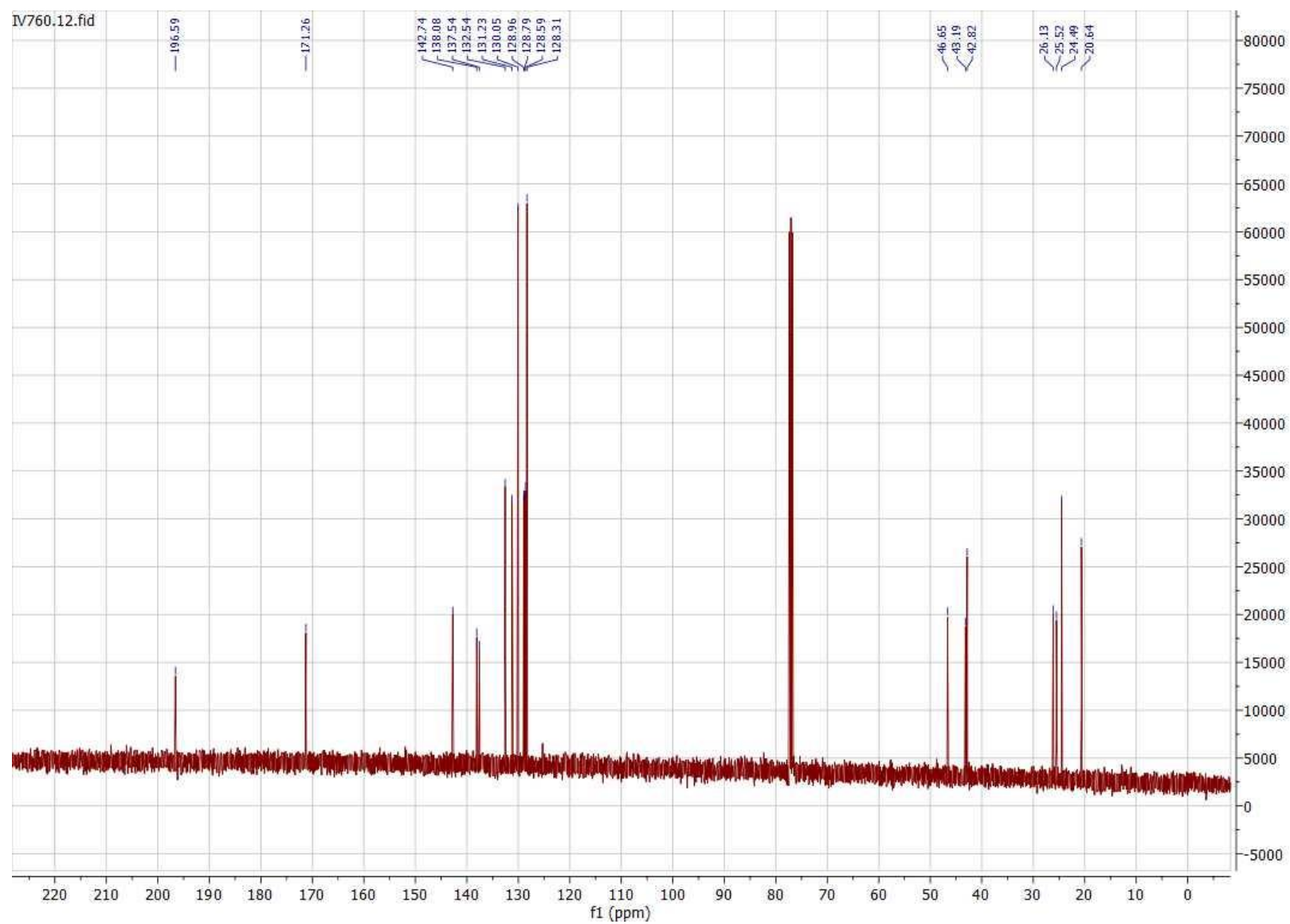


Figure S6. ^{13}C -NMR spectrum of compound 3b.

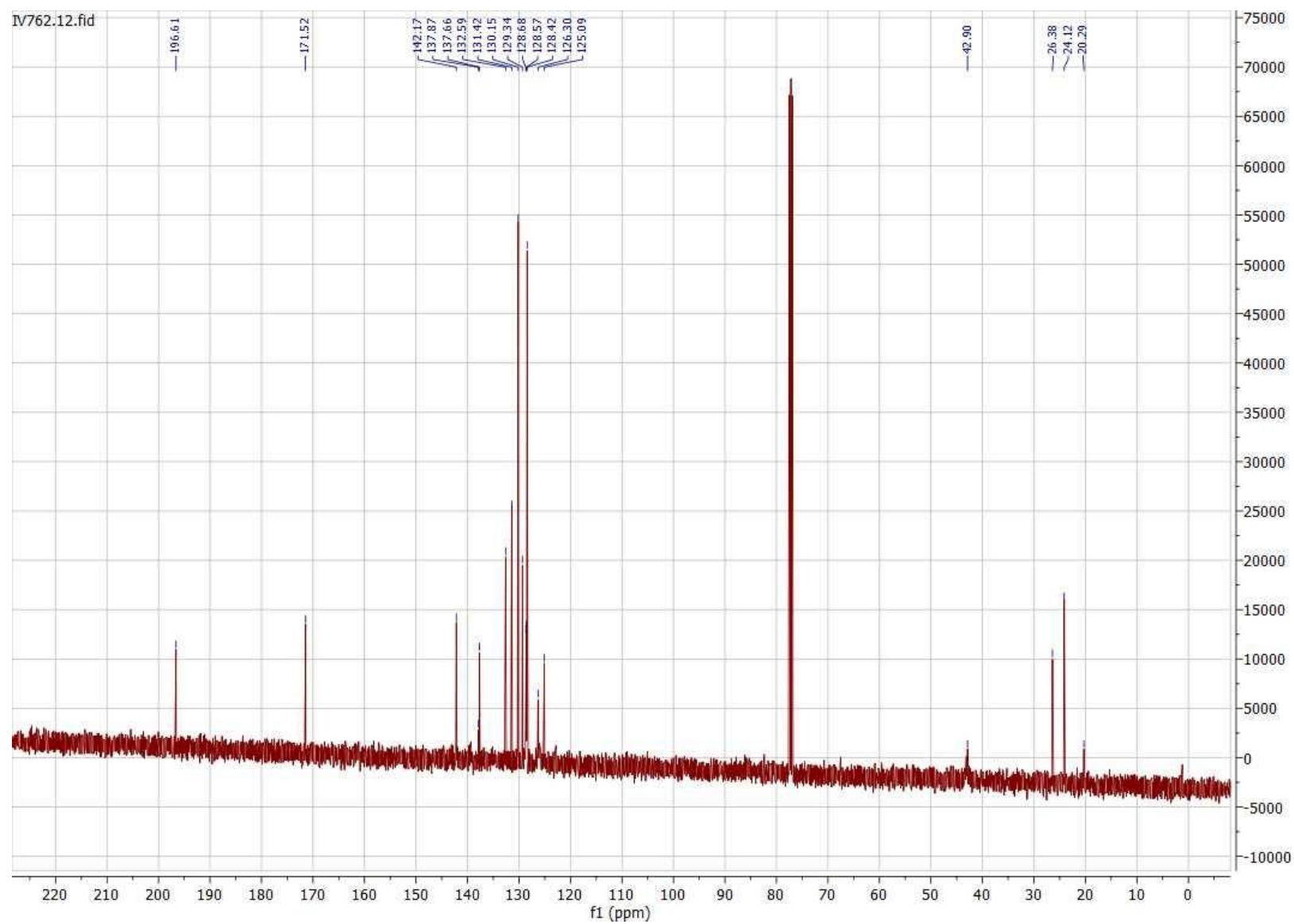


Figure S7. ^{13}C -NMR spectrum of compound **3c**.

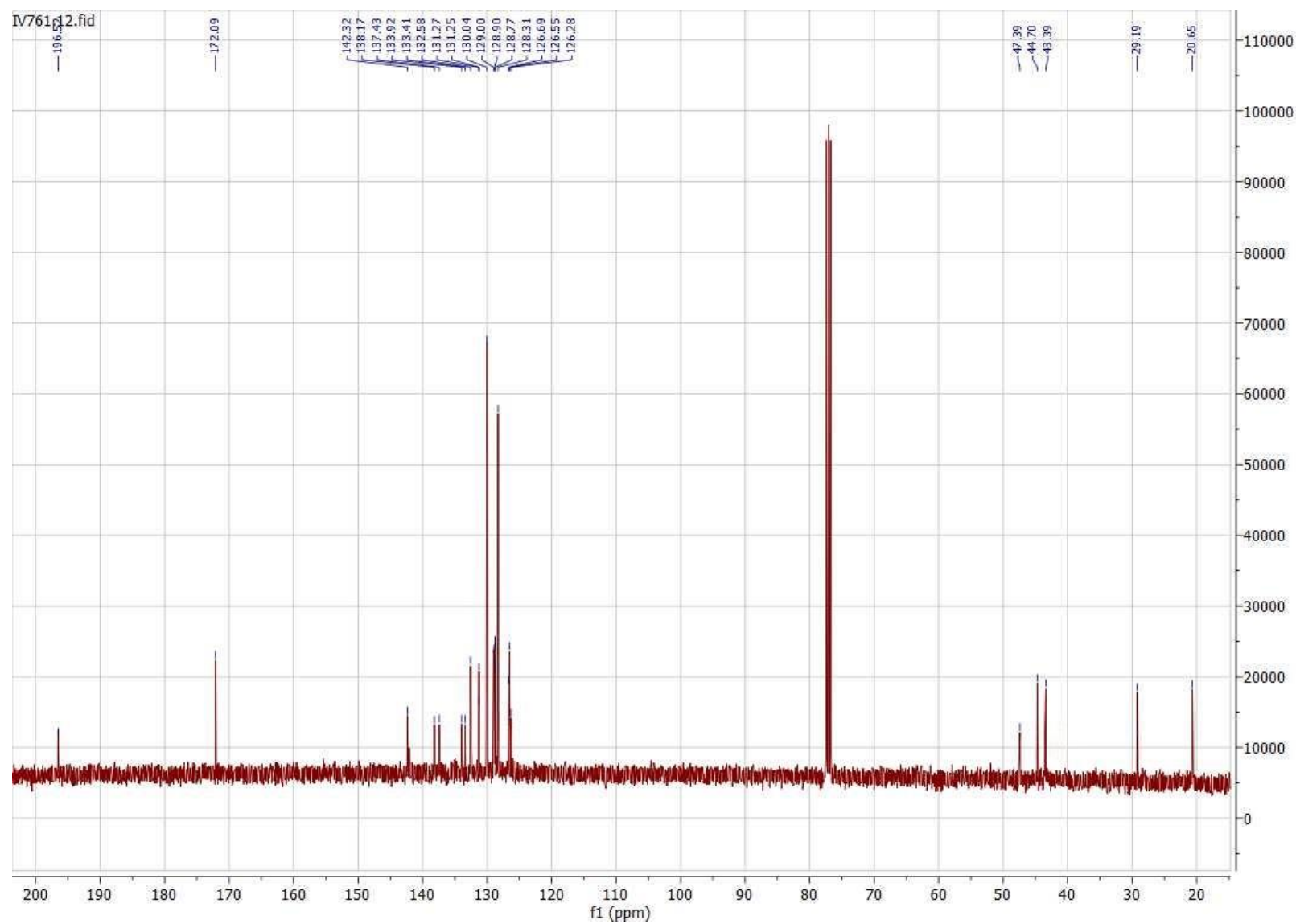


Figure S8. ¹³C-NMR spectrum of compound **3d**.

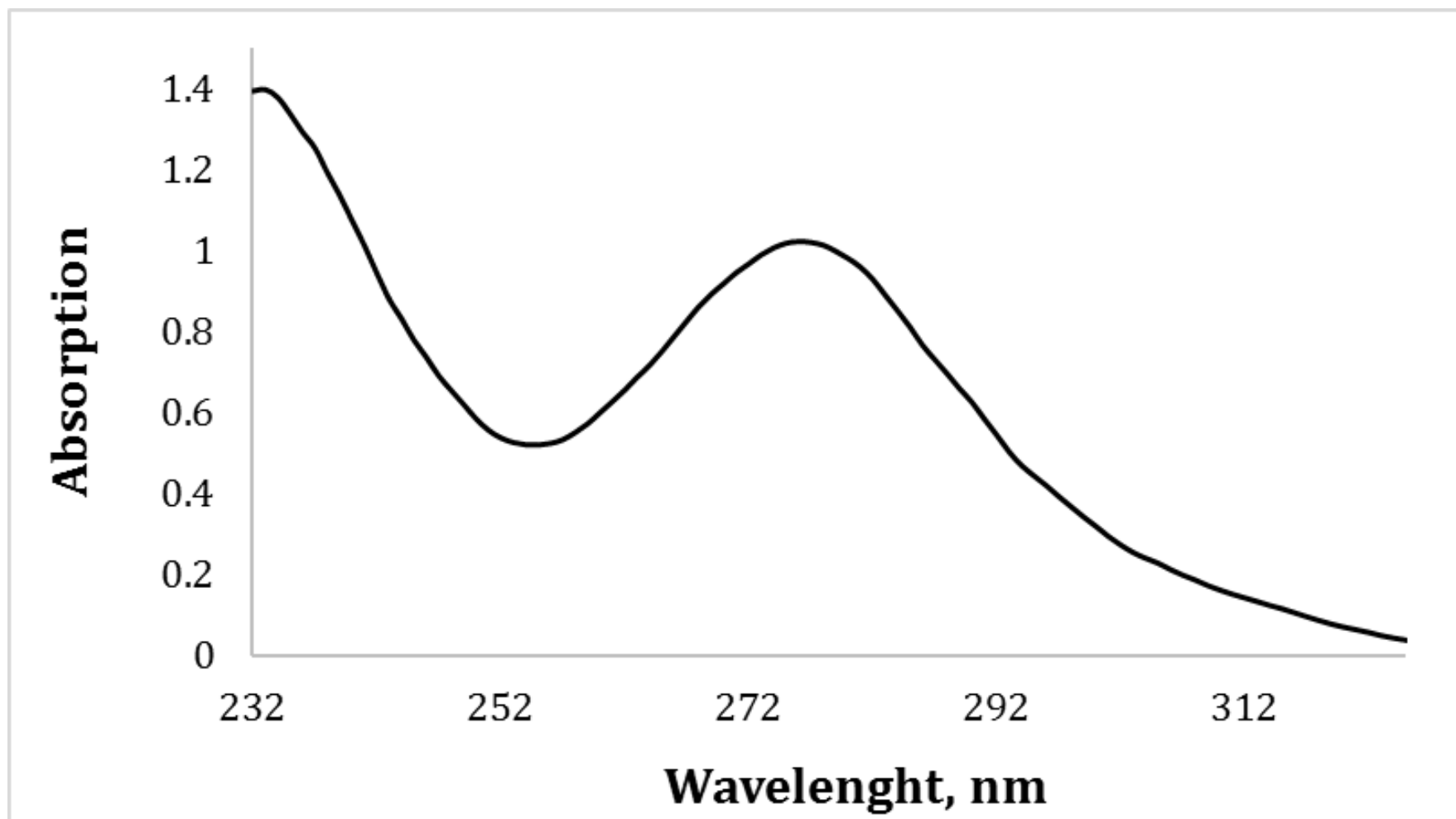


Figure S9. UV spectrum of compound 3a.

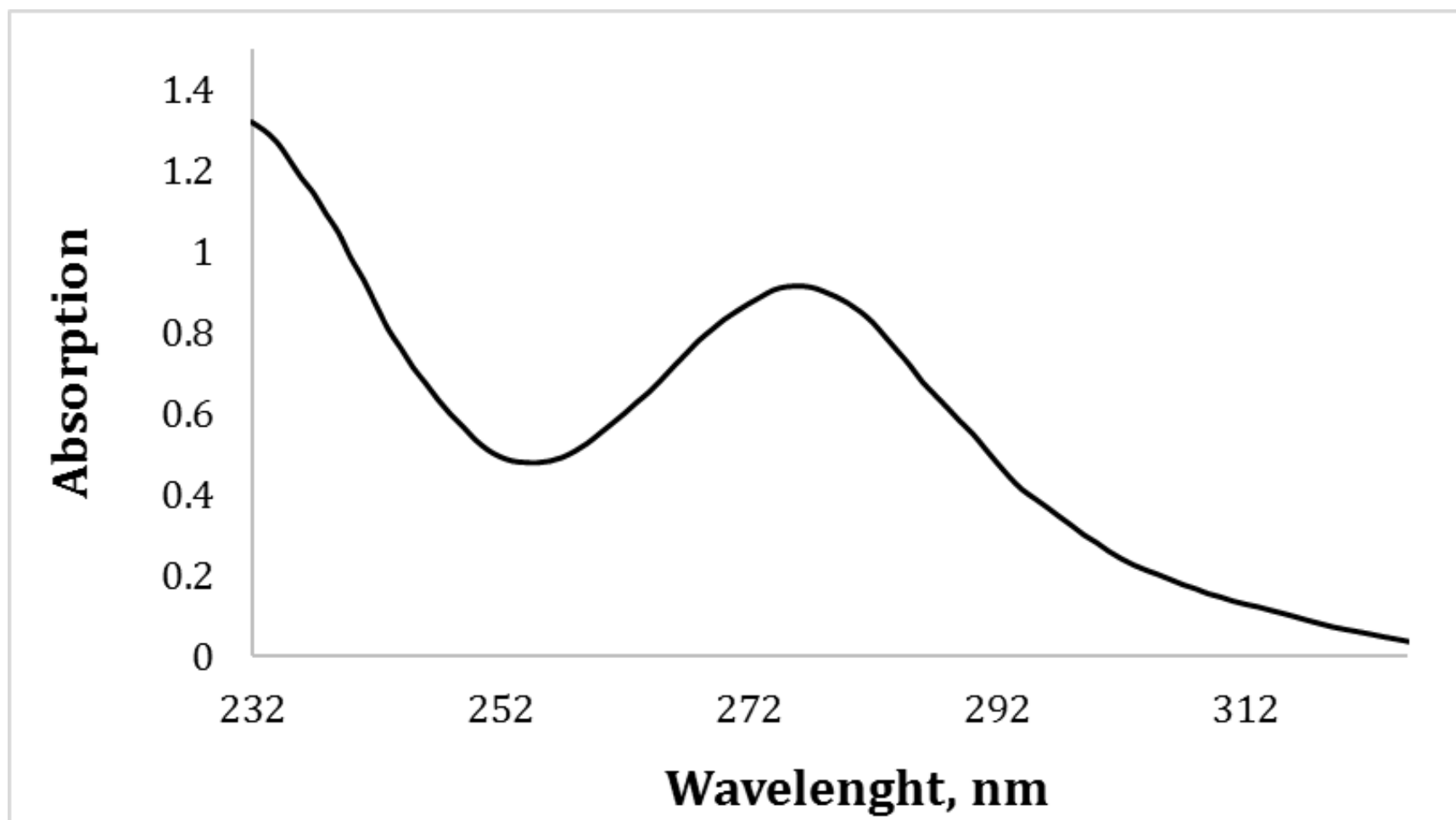


Figure S10. UV spectrum of compound **3b**.

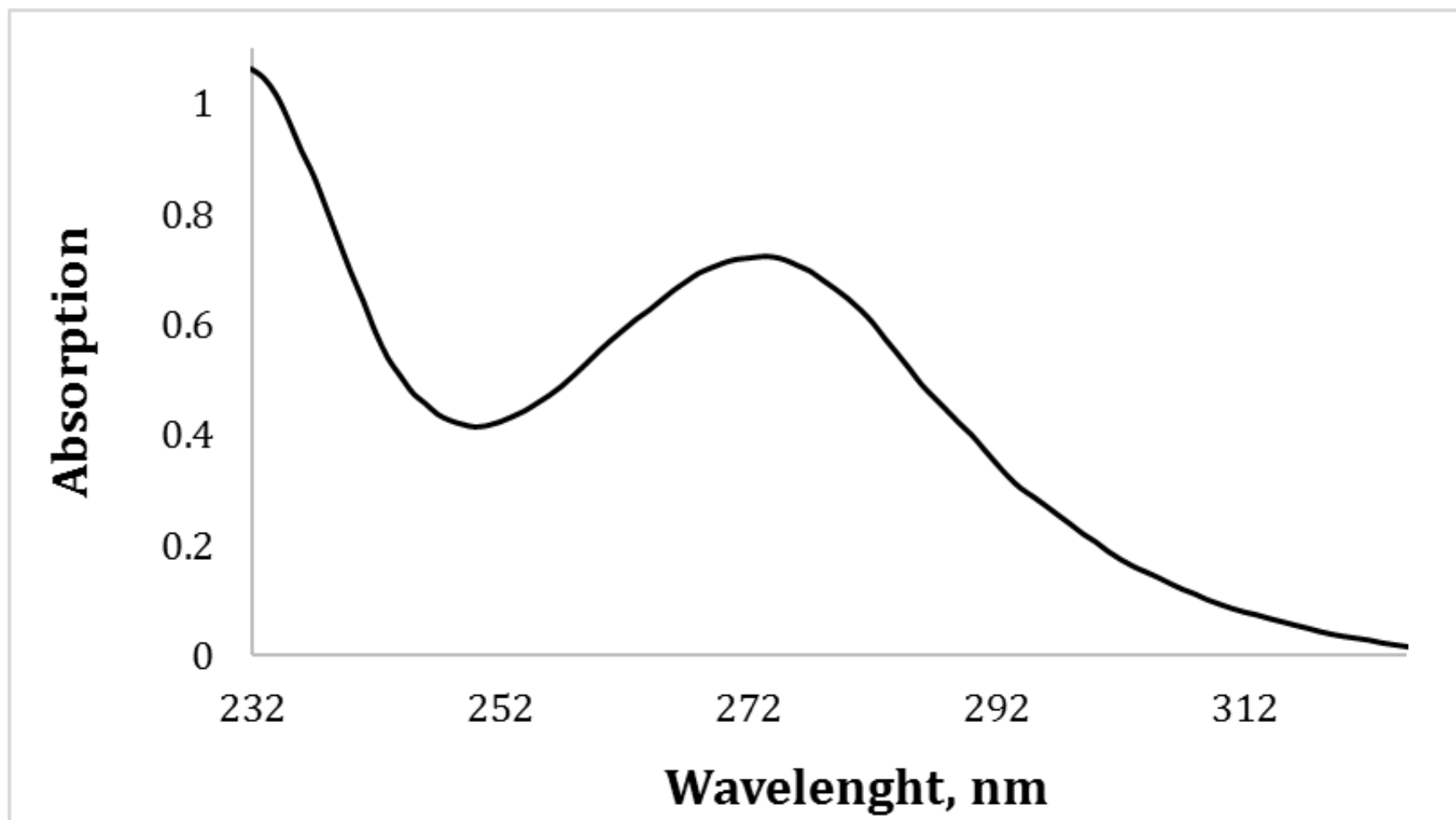


Figure S11. UV spectrum of compound **3c**.

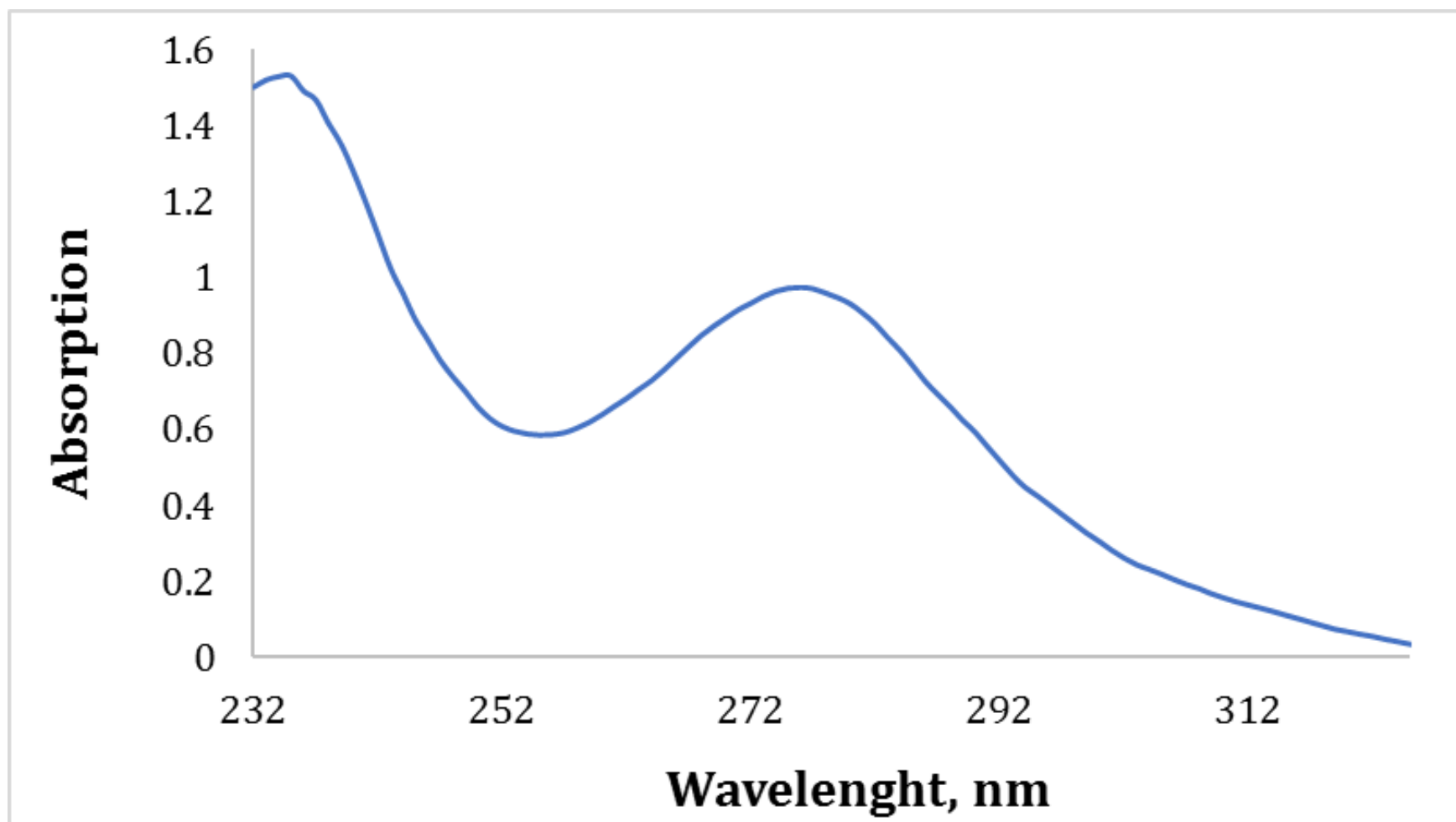


Figure S12. UV spectrum of compound **3d**.

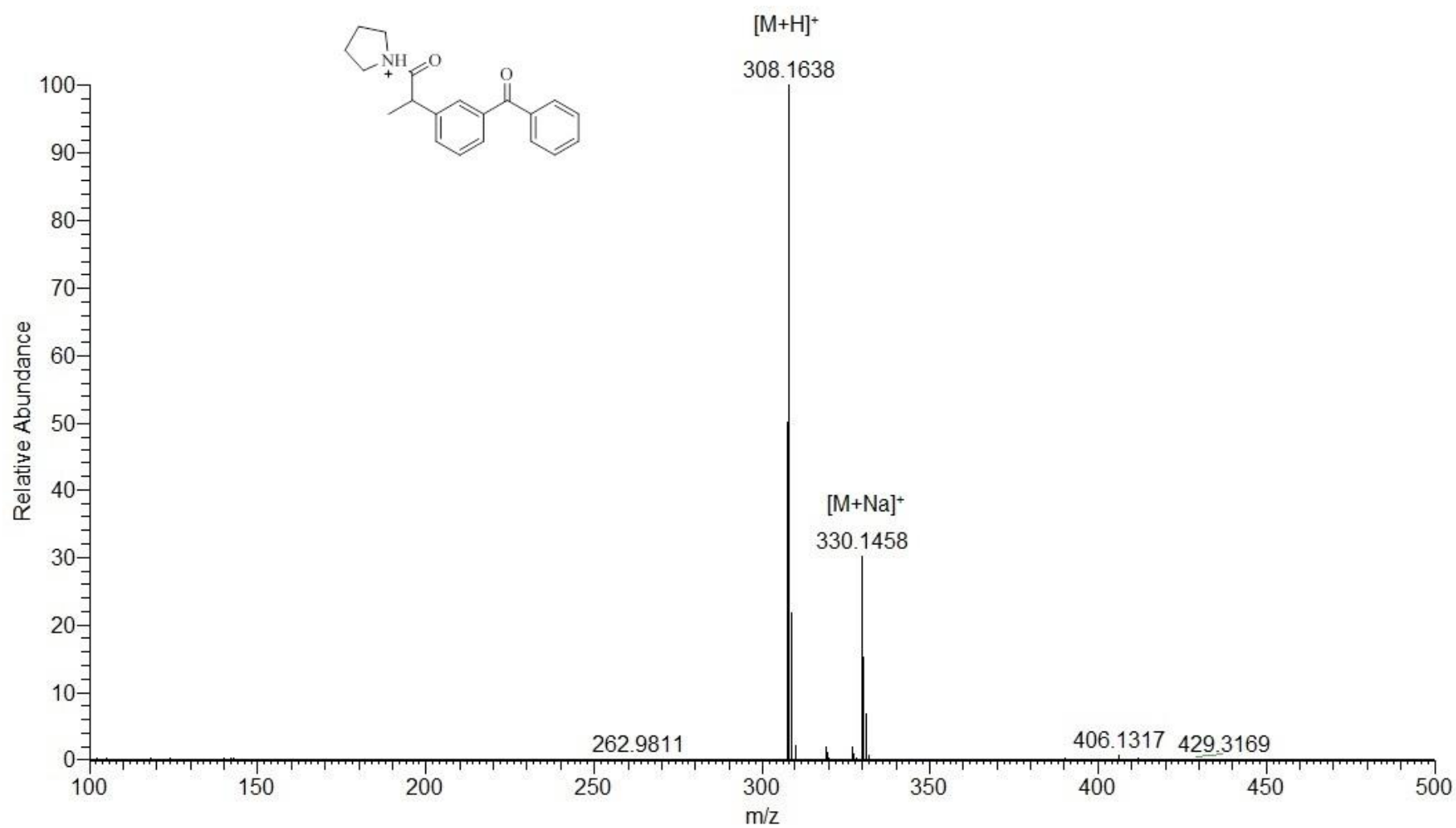


Figure S13. ESI-HRMS of compound **3a**.

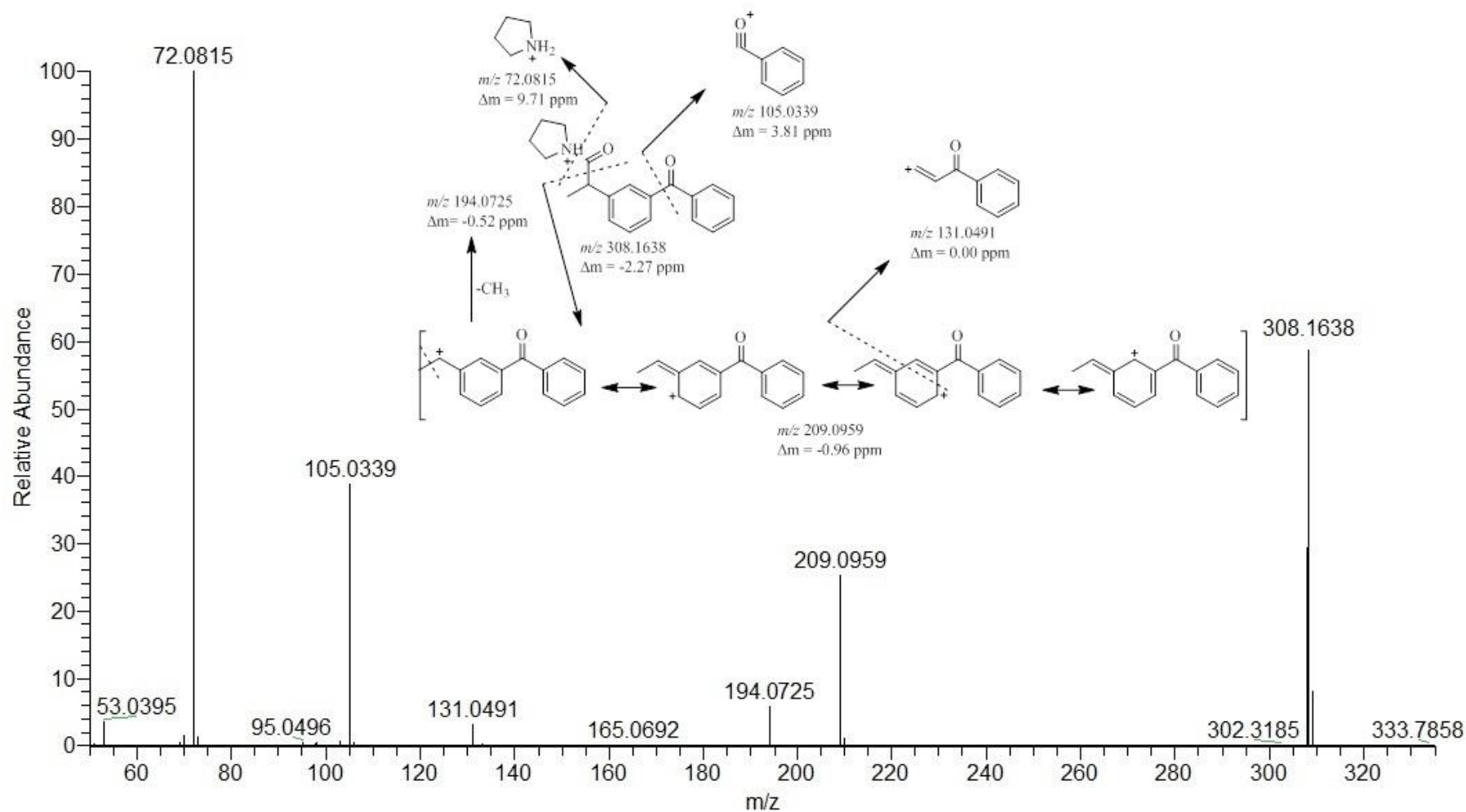


Figure S14 Mass spectrum of **4a** obtained by positive ion ESI-MS/MS. Proposed fragmentation of protonated **3a**.

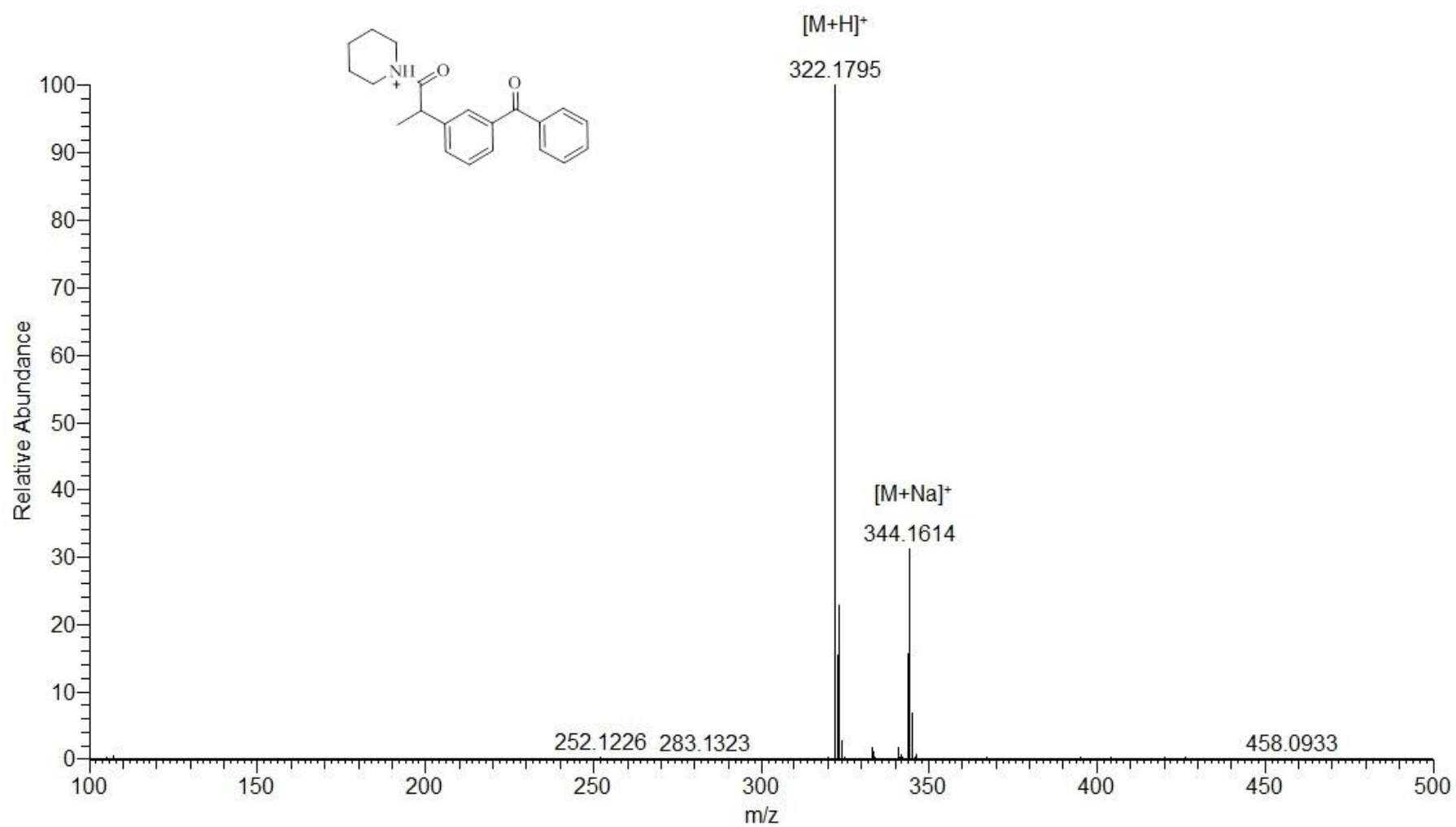


Figure S15. ESI-HRMS of compound **3b**.

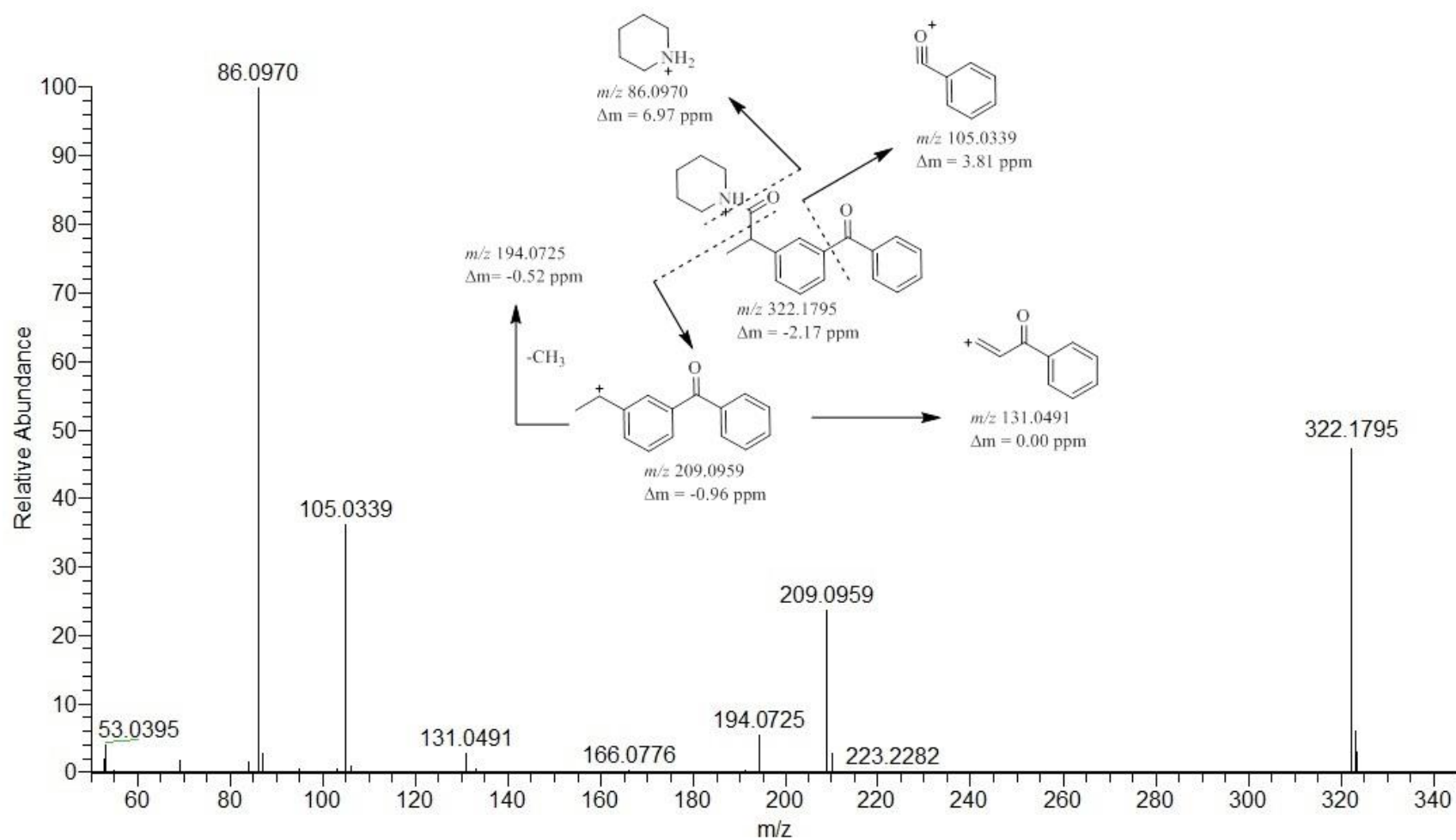


Figure S16 Mass spectrum of **4b** obtained by positive ion ESI-MS/MS. Proposed fragmentation of protonated **3b**.



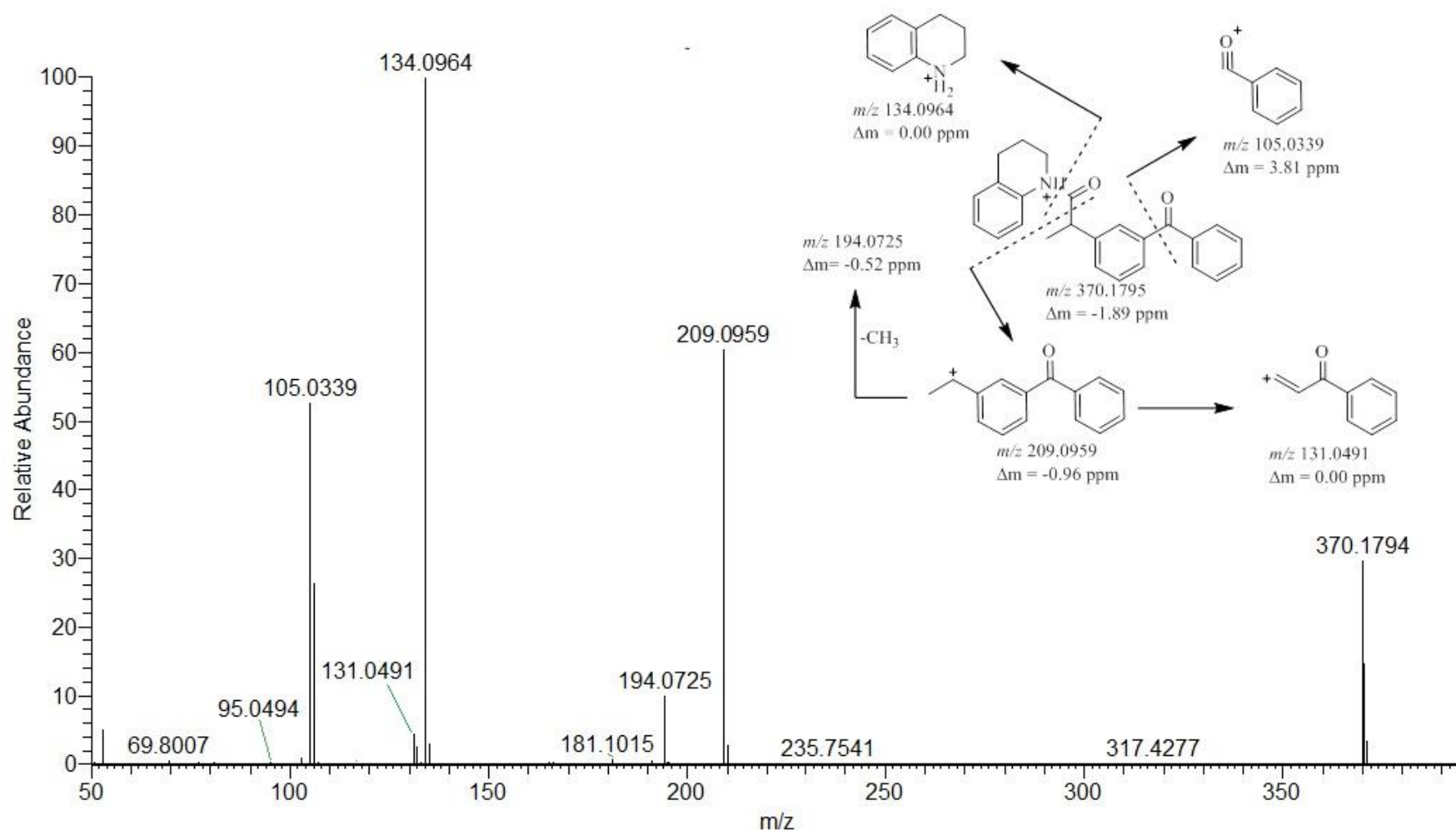


Figure S18 Mass spectrum of **4c** obtained by positive ion ESI-MS/MS. Proposed fragmentation of protonated **3c**.

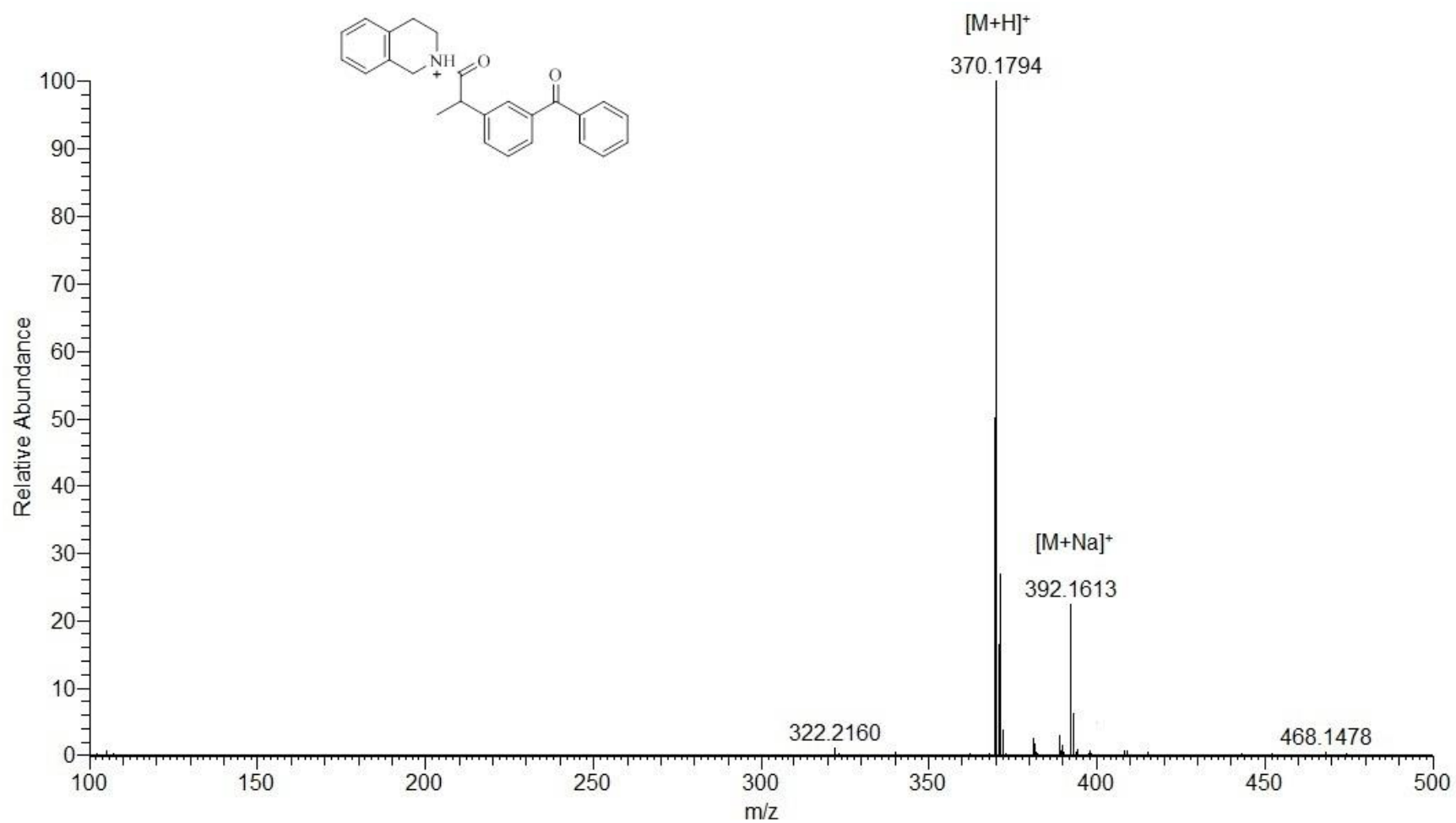


Figure S19. ESI-HRMS of compound **3d**.

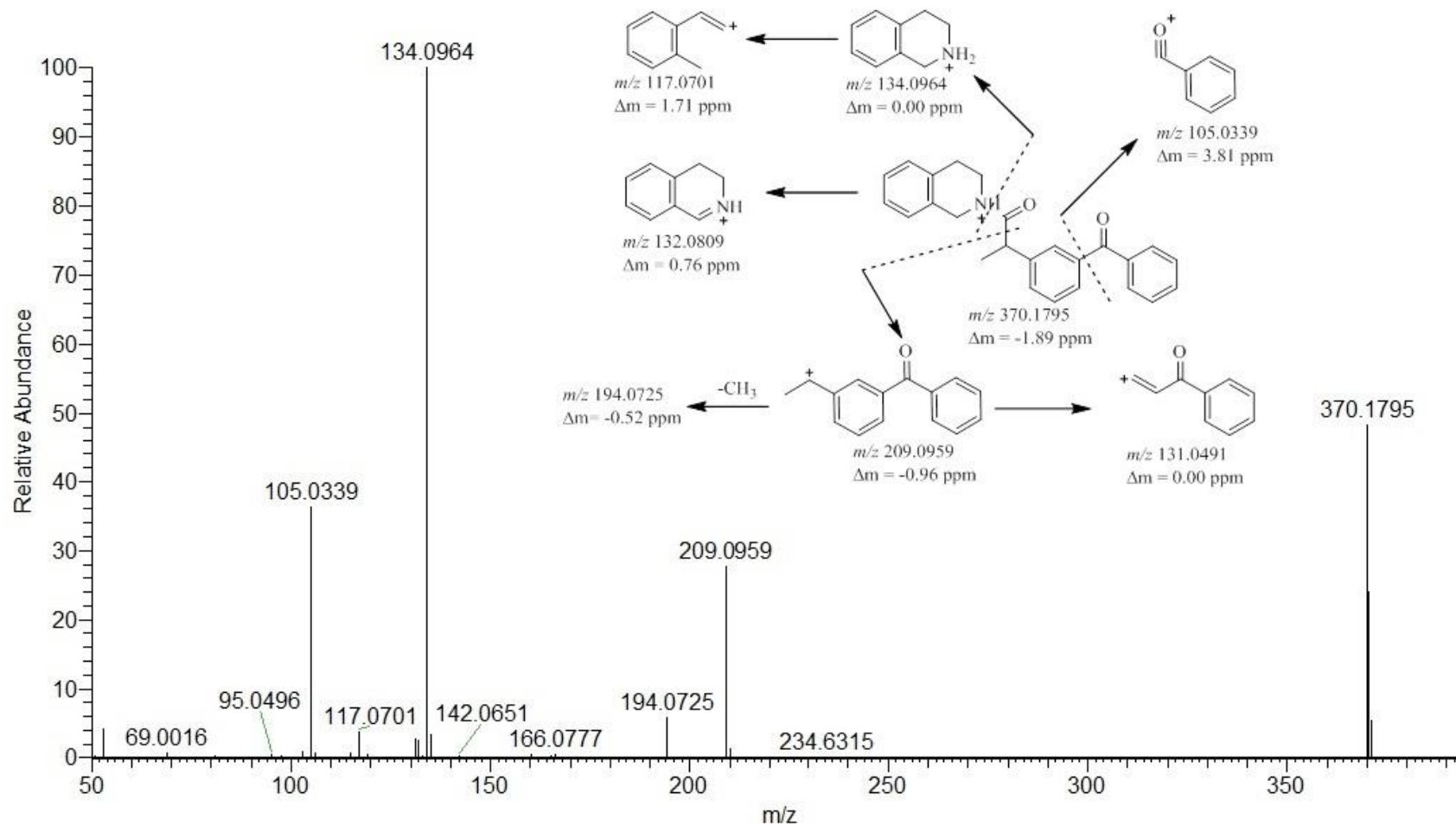
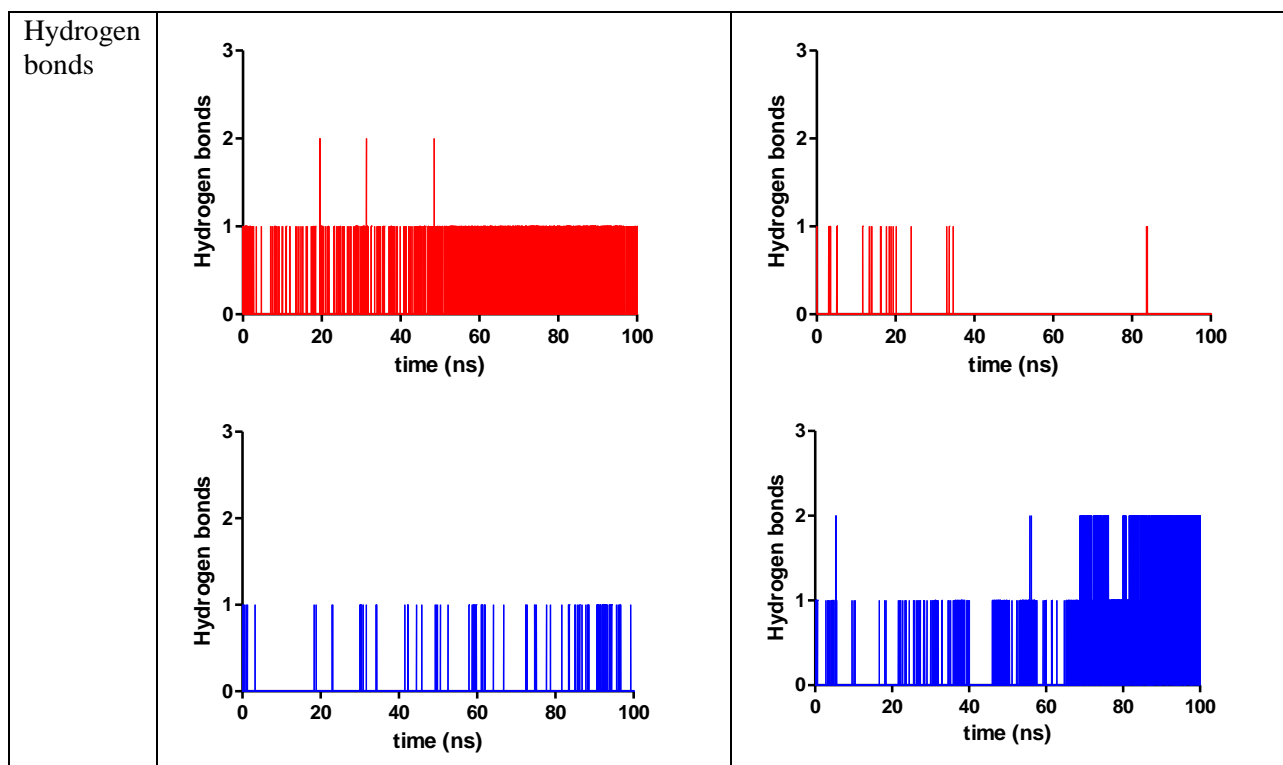


Figure S20 Mass spectrum of **4d** obtained by positive ion ESI-MS/MS. Proposed fragmentation of protonated **3d**.

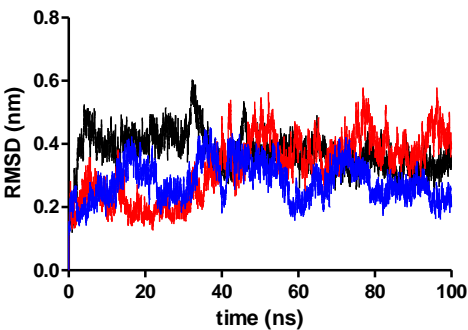
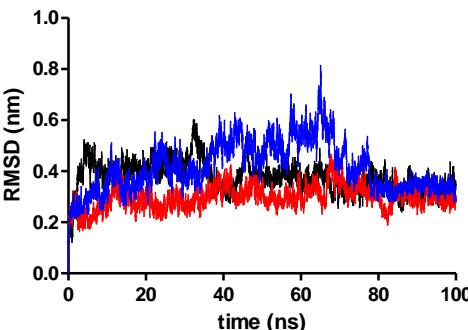
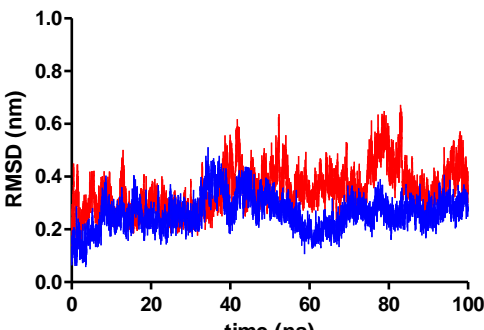
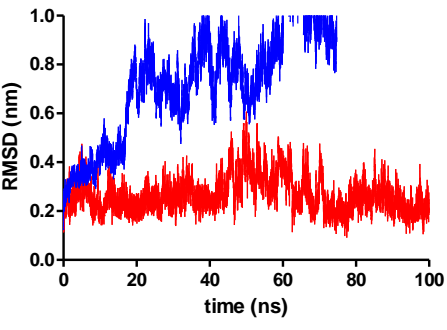
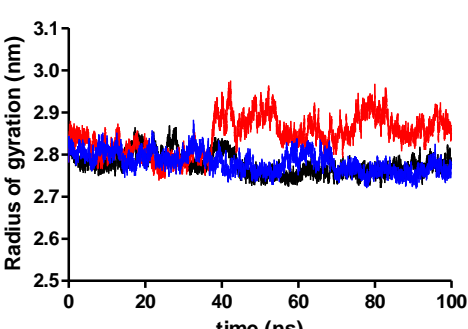
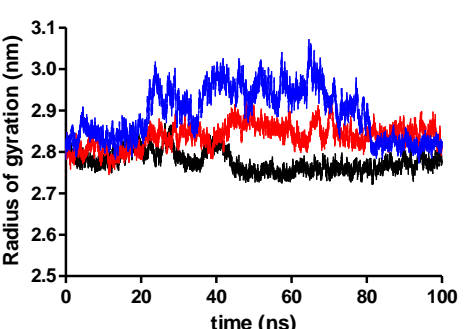
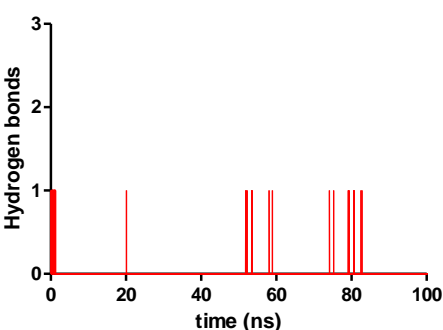
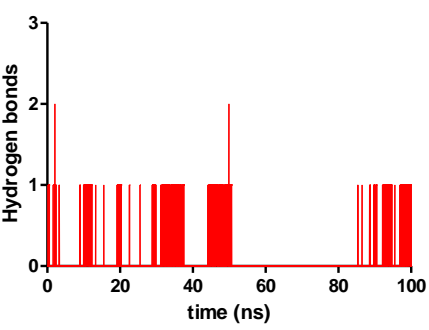
Table S1. RMSD of protein backbone, RMSD of ligands and RG of protein in the molecular dynamics study when ligands **3c** and **3d** were docked into the Sudlow 2 site.

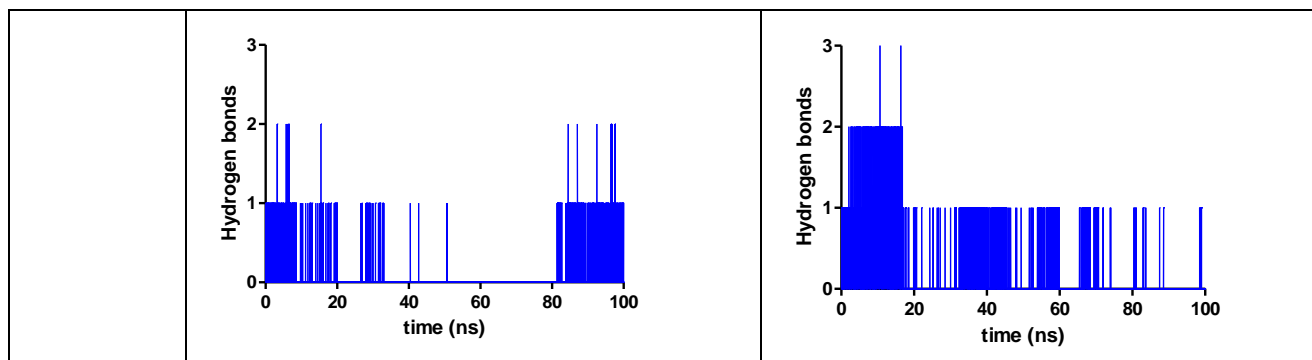
| Parameter | Compound 3c | Compound 3d |
|-----------------------|-------------|-------------|
| RMSD protein backbone | | |
| RMSD ligand | | |
| RG of protein | | |



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.

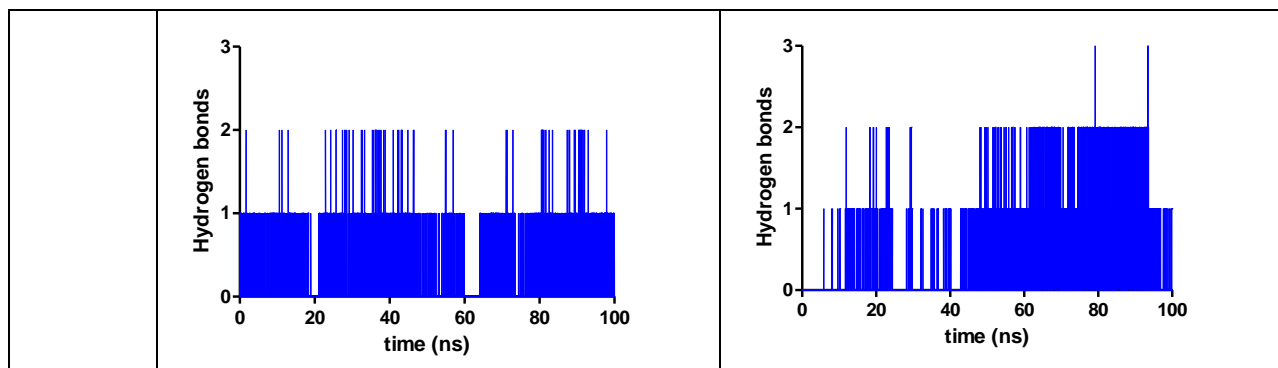
| Parameter | Compound 3a | Compound 3b |
|-----------------------------|---|--|
| RMSD protein backbone |  |  |
| RMSD ligand |  |  |
| RG of protein |  |  |
| Hydrogen bonds |  |  |



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

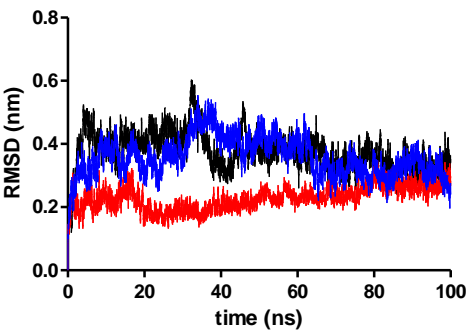
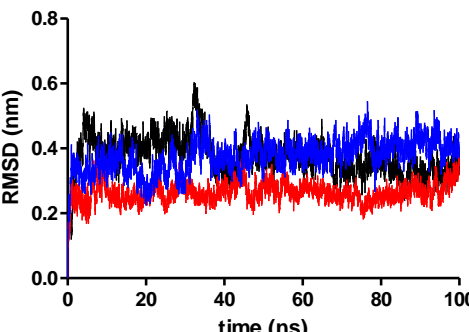
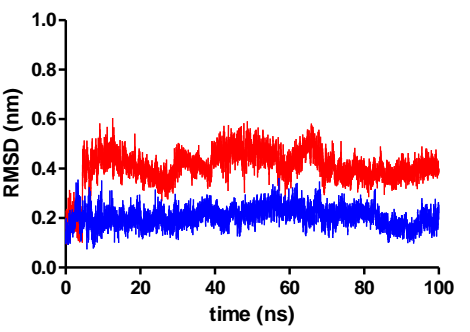
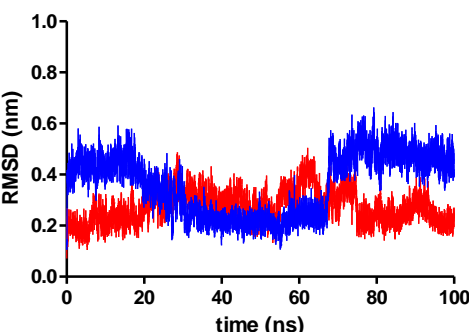
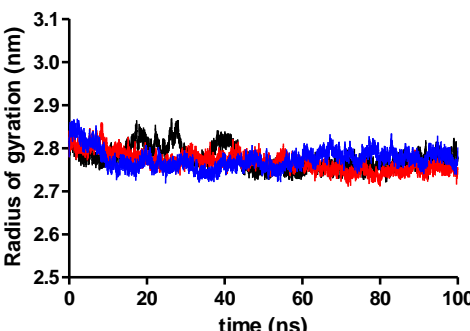
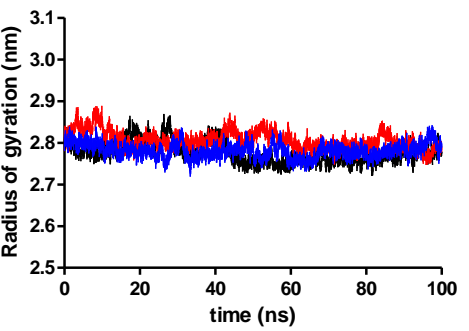
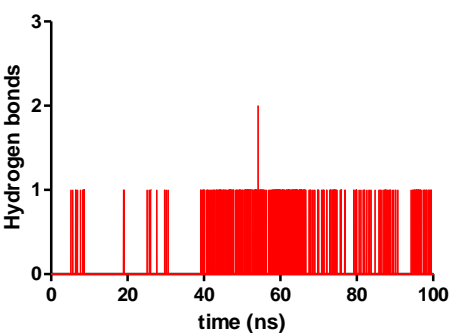
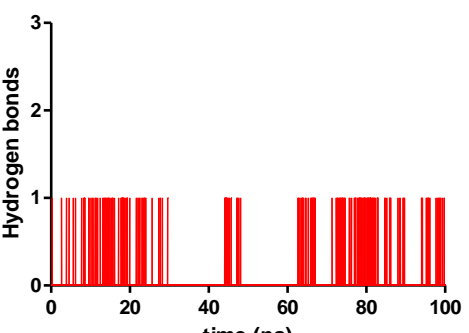
Table S3. RMSD of protein backbone, RMSD of ligands and RG of protein in the molecular dynamics study when ligands **3c** and **3d** were docked into the site 3 of albumin.

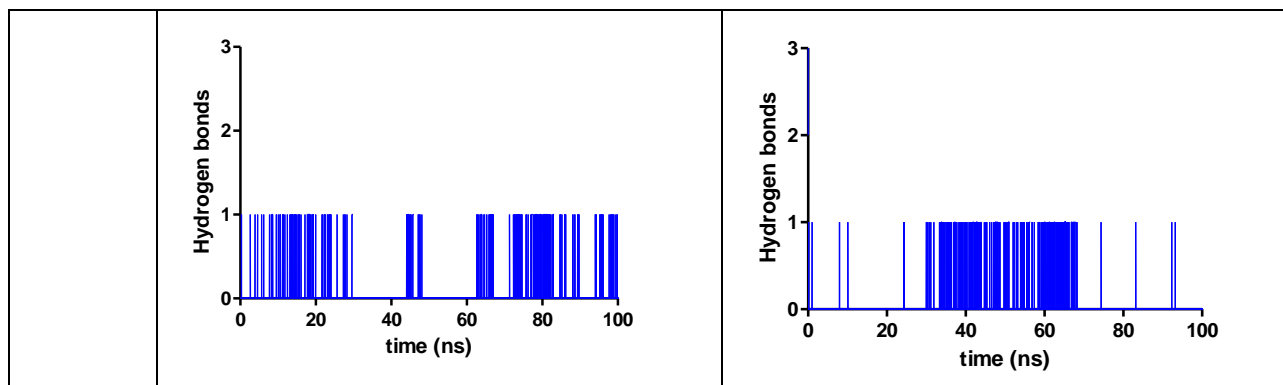
| Parameter | Compound 3c | Compound 3d |
|-----------------------|-------------|-------------|
| RMSD protein backbone | | |
| RMSD ligand | | |
| RG of protein | | |
| Hydrogen bonds | | |



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

Table S4. 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 cleft 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