Supporting Information

Design, Synthesis, and Enzyme Kinetic Evaluation of Oxadiazole Derivatives as Nucleoside Triphosphate Diphosphohydrolase (NTPDase) Inhibitors: An Integrated *In Vitro* and *In Silico* Approach

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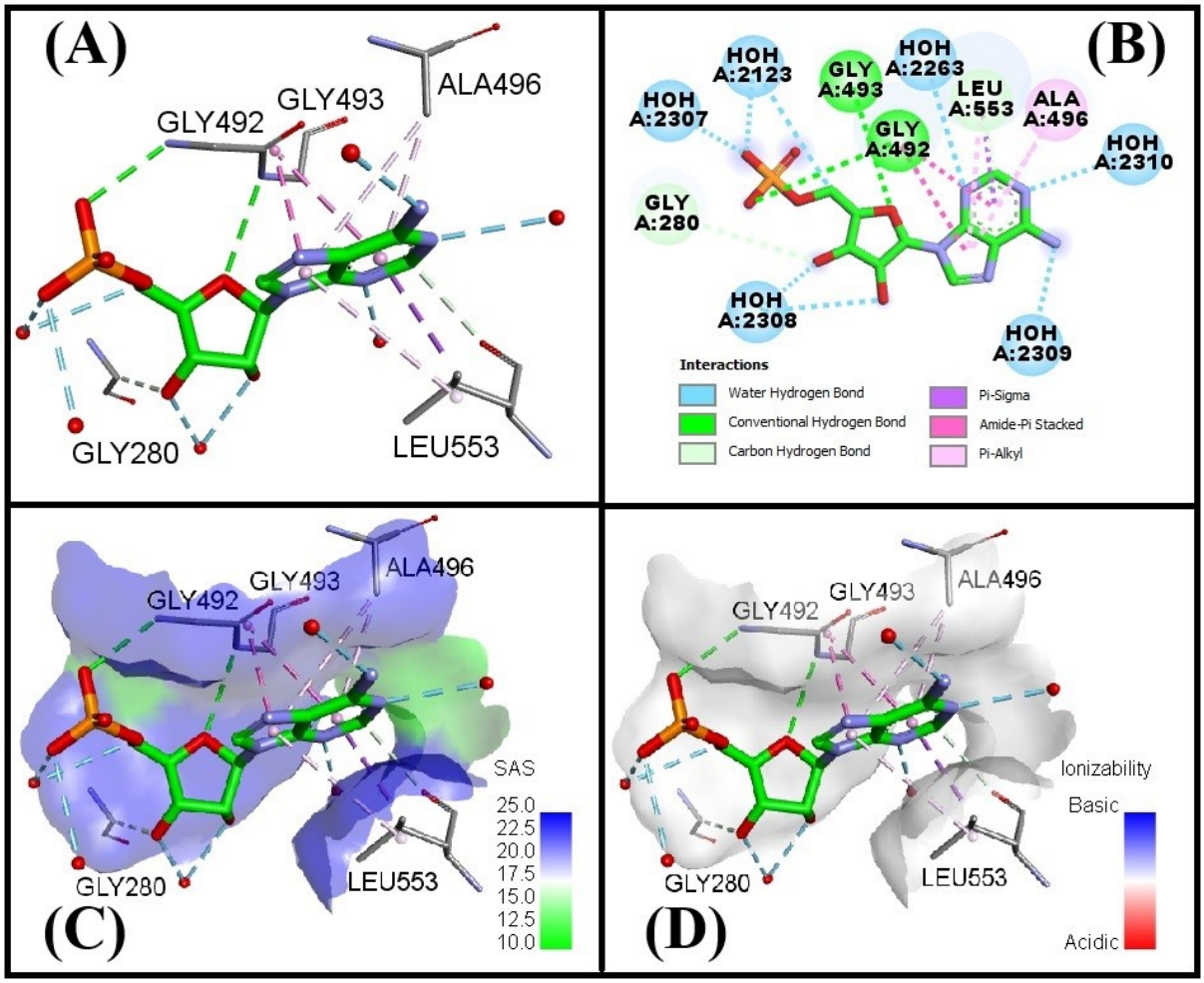


Figure S1. Binding pocket analysis for NTPDase3 containing co-crystallized ligand **Amp**700 (green); (**A**) 3D diagram for ligand's interaction, (**B**) 2D diagram for ligand interactions, (**C**) Solvent accessibility surface, (**D**) Ionizability surface.

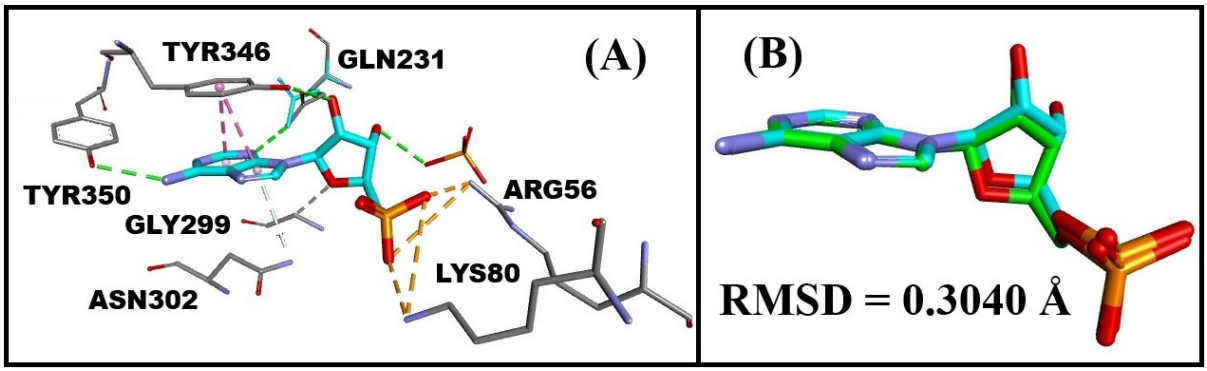


Figure S2. Docking validation for NTPDase1 (**A**) 3D diagram for redocked ligand **Amp** (cyan) (**B**) Determination of RMSD using co-crystallized (green) and redocked (cyan) **Amp** ligand.

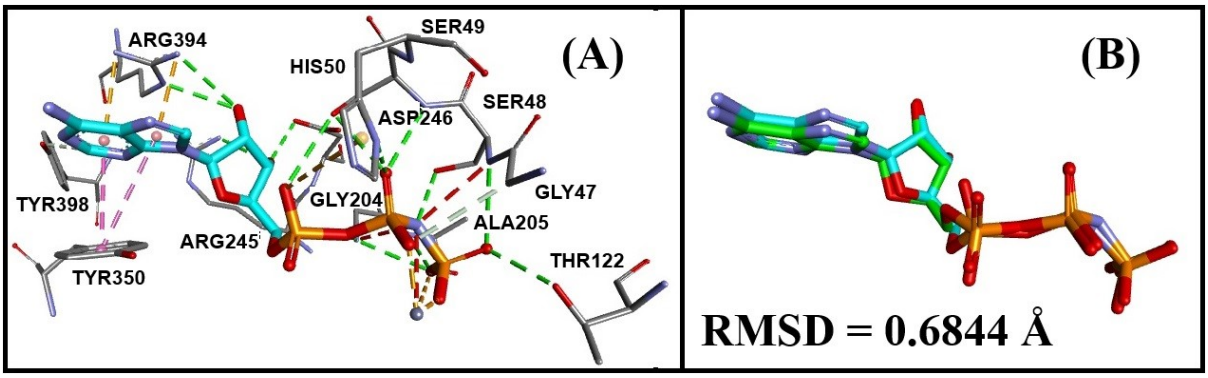


Figure S3. Docking validation for NTPDase2 (**A**) 3D diagram for redocked ligand **Anp** (cyan) (**B**) Determination of RMSD using co-crystallized (green) and redocked (cyan) **Anp** ligand.

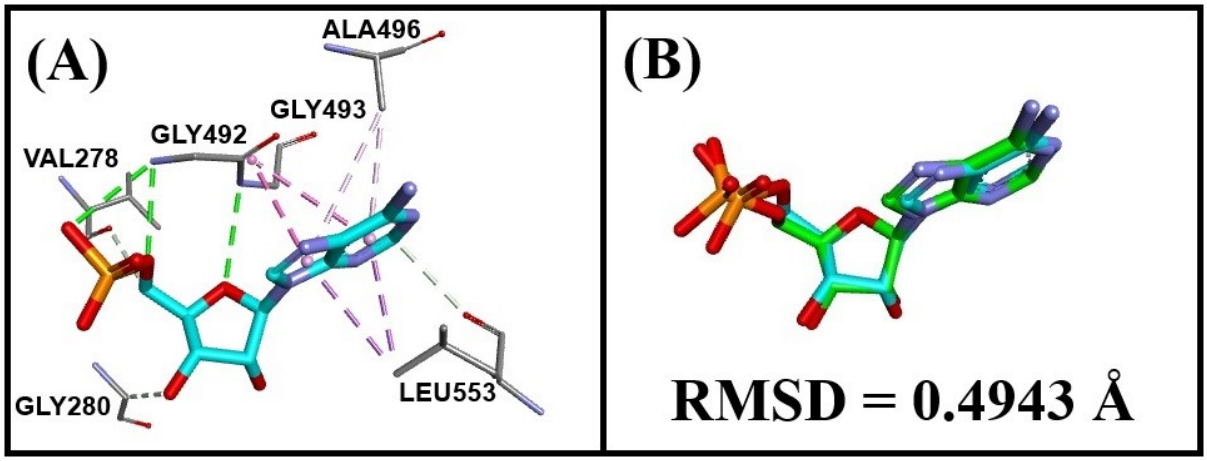


Figure S4. Docking validation for NTPDase3 (**A**) 3D diagram for redocked ligand **Amp** (cyan) (**B**) Determination of RMSD using co-crystallized (green) and redocked (cyan) **Amp** ligand.

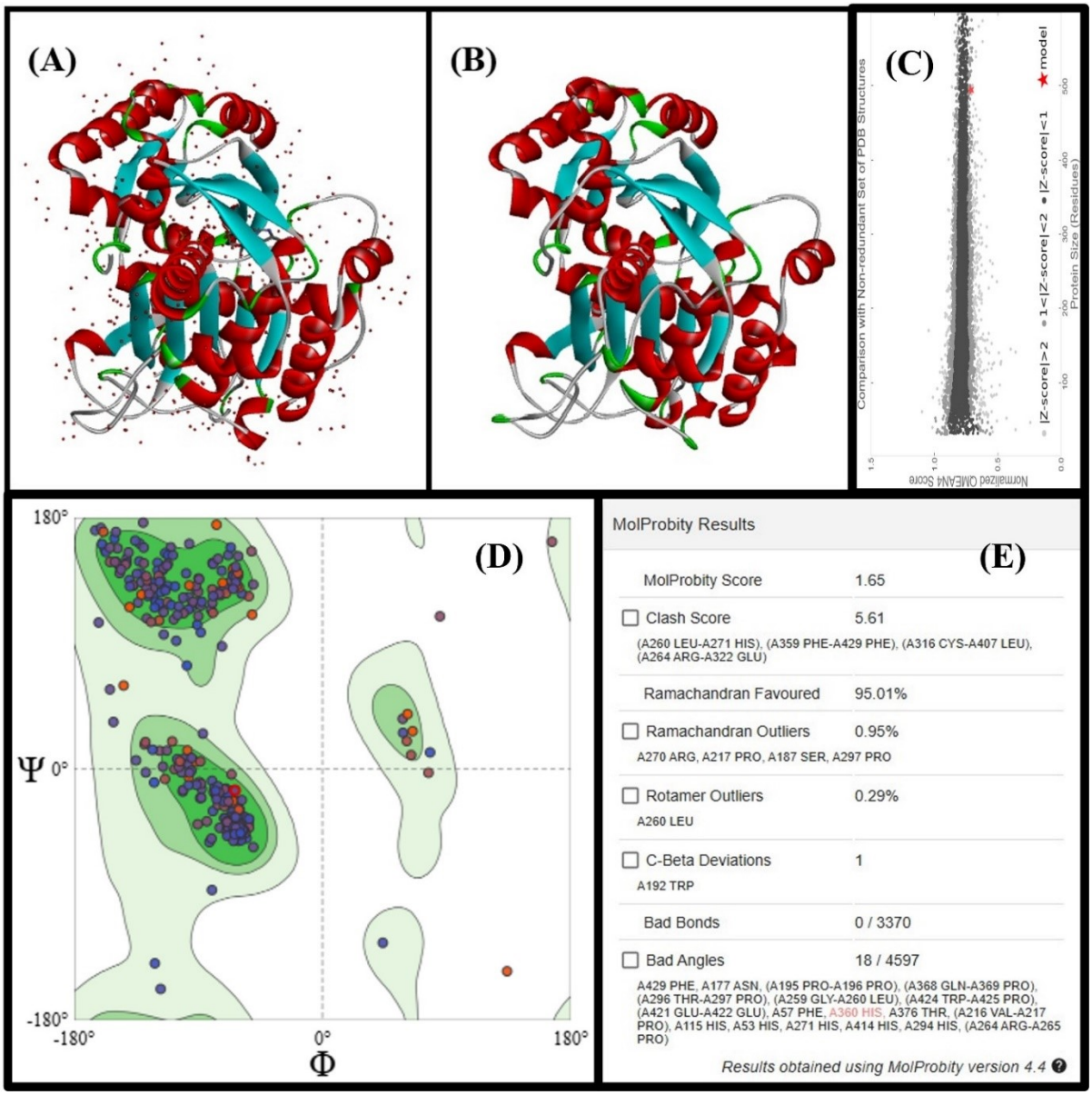


Figure S5. Homology modelling: (**A**) 3CJ9 (NTPDase2) selected for homology modelling, (**B**) NTPDase8 acquired as a homology model, (**C**) Z score, (**D**) Ramachandran plot, (**E**) MolProbity results for the reliability of the homology model.

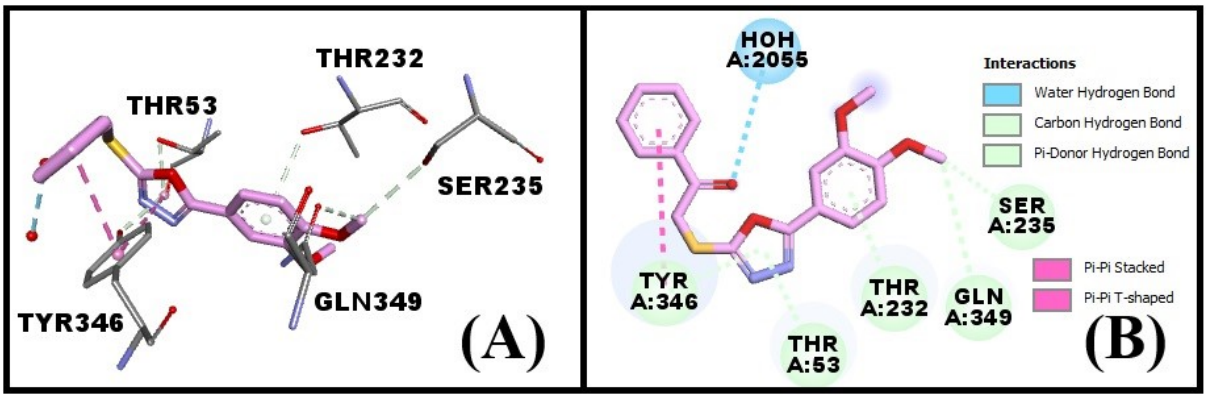


Figure S6. The ligand **7g** (pink) docked on NTPDase1 (4BRQ); (**A**) 3D interactions, (**B**) 2D interactions.

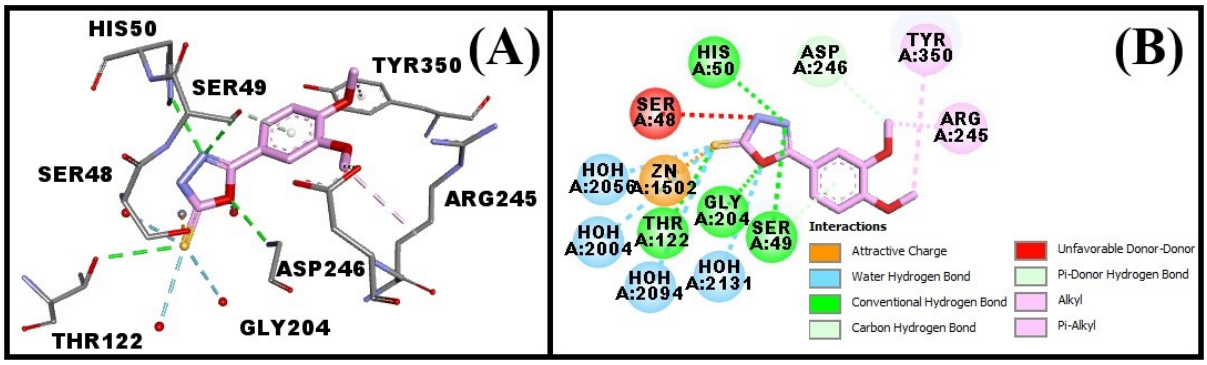


Figure S7. The ligand **4** (Thiol, pink) docked on NTPDase2 (4BR5); (**A**) 3D interaction, (**B**) 2D interaction.

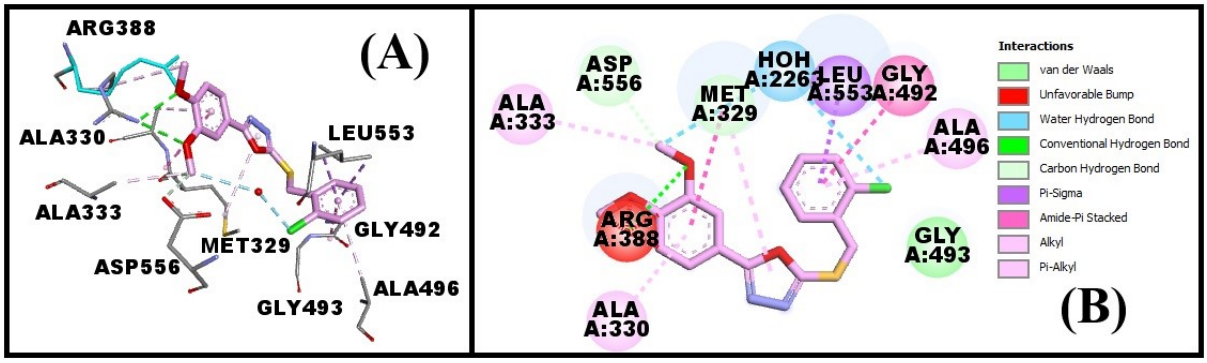


Figure S8. The ligand **7d** (pink) docked on NTPDase3 (4A59); (**A**) 3D interaction, (**B**) 2D interaction.

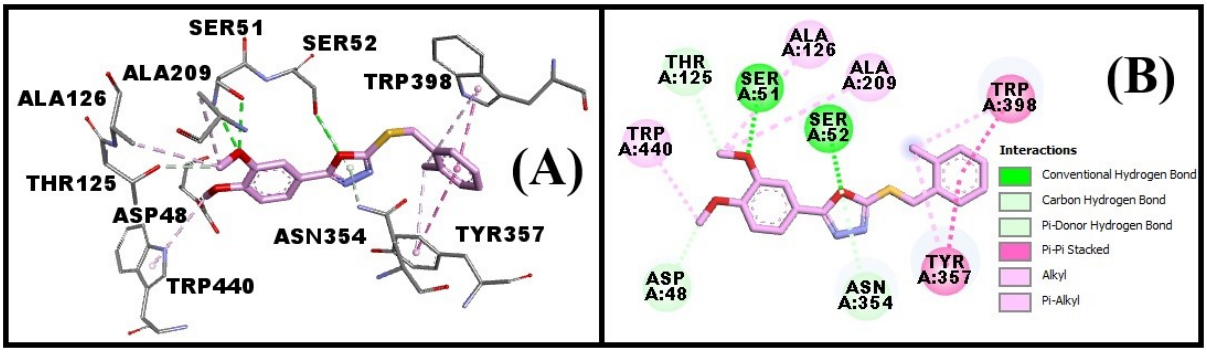


Figure S9. Ligand **7c** (pink) docked on NTPDase8; (**A**) 3D interaction, (**B**) 2D interaction. There was no redocked standard used for NTPDase 8, as it was acquired from homology modelling. The **7a-7g** series derivatives, especially **7c**, **7d,** and **7f,** could serve as promising candidates for further refinement and biological testing against NTPDase8.

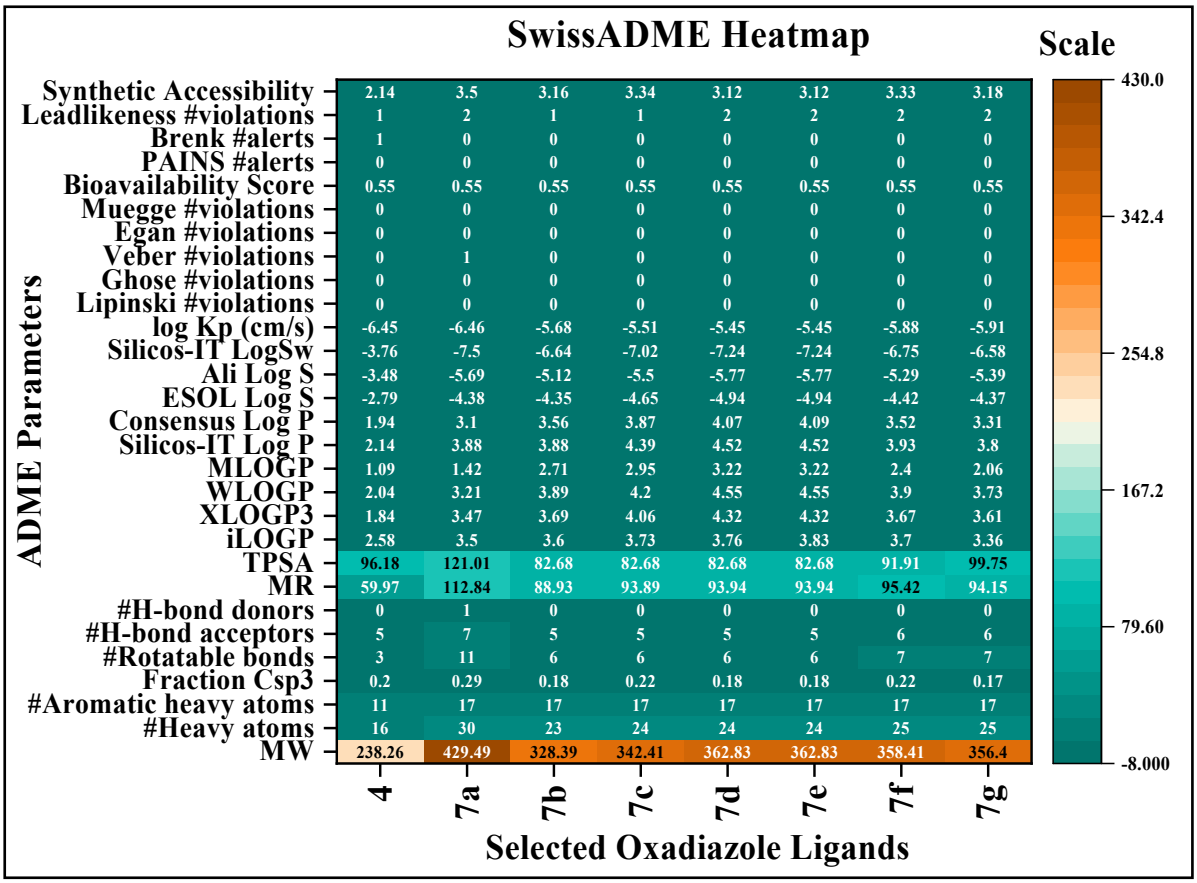


Figure S10. Heat Map for SwissADME Parameters of the Oxadiazole Compounds.

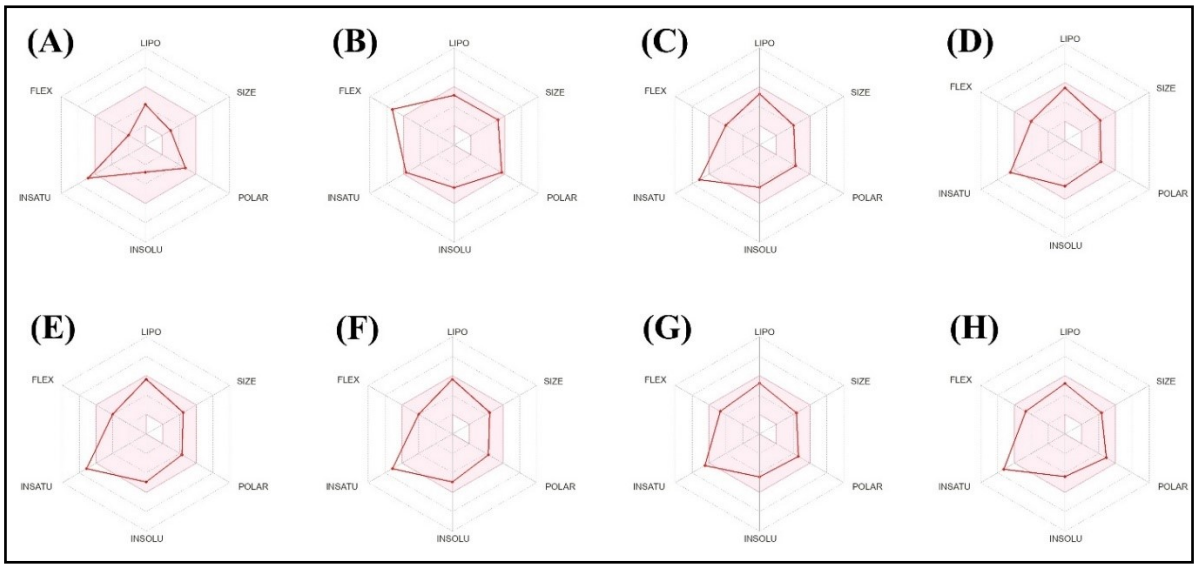
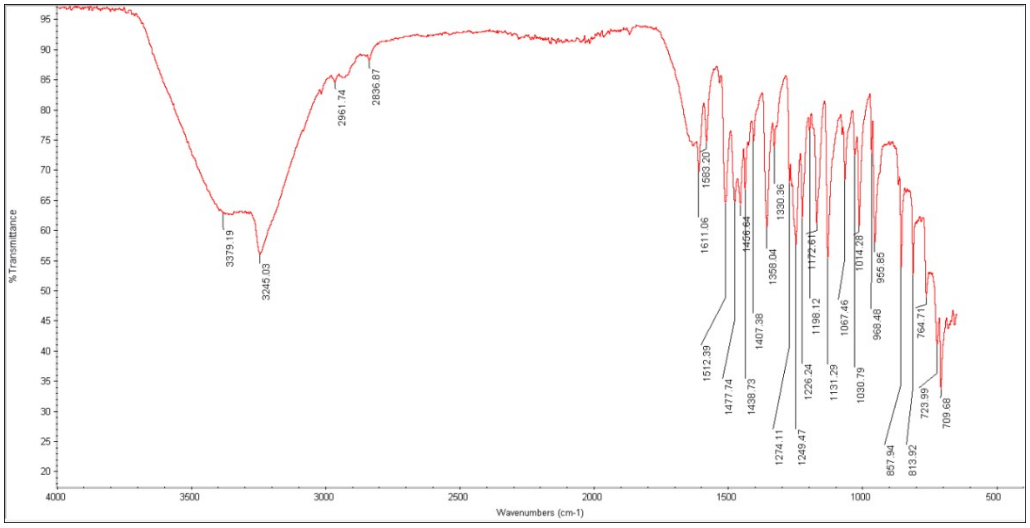
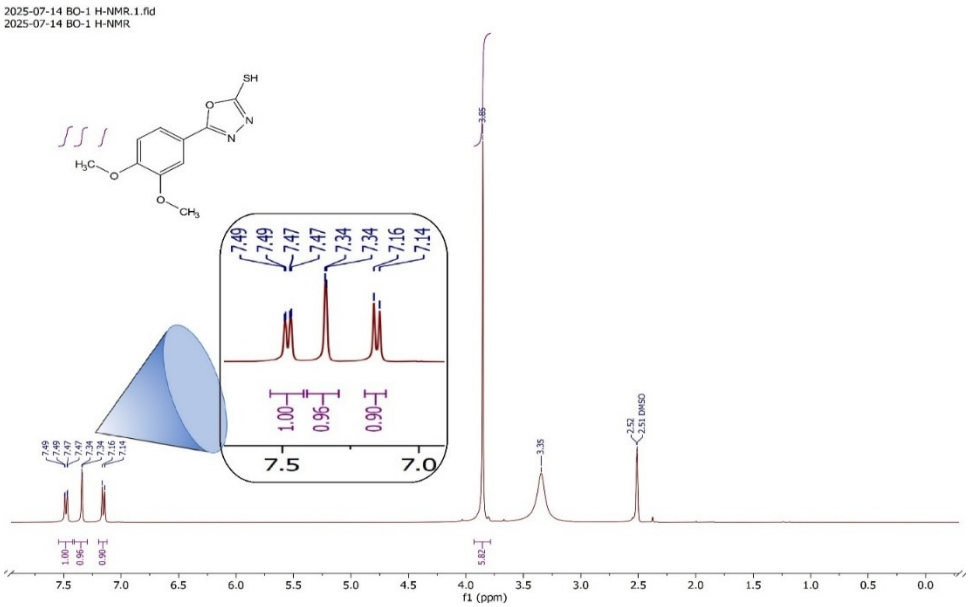


Figure S11. Spiderweb plots for the Oxadiazole Compounds; (**A**) **4,** (**B**) **7a,** (**C**) **7b,** (**D**) **7c,** (**E**) **7d,** (**F**) **7e,** (**G**) **7f,** (**H**) **7g**.





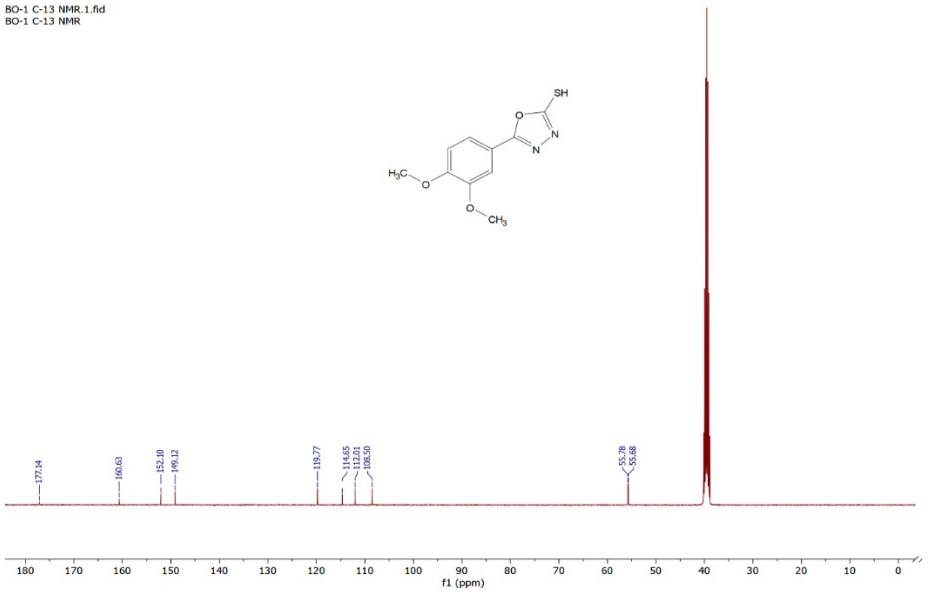
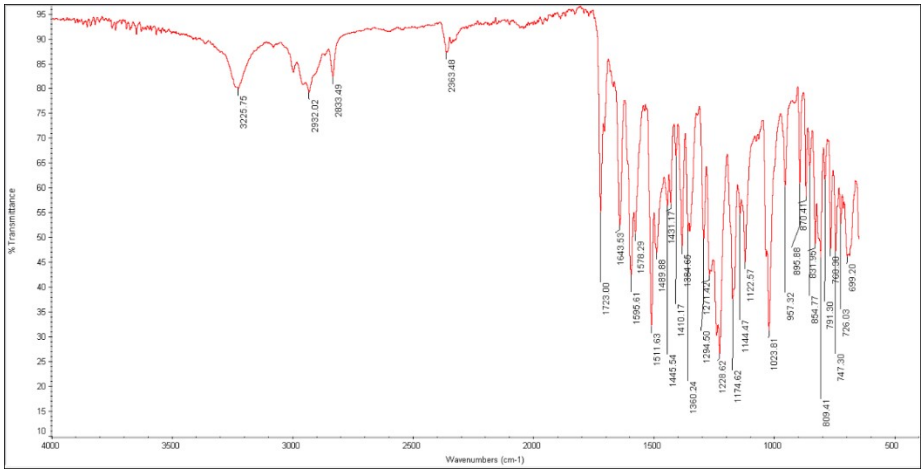
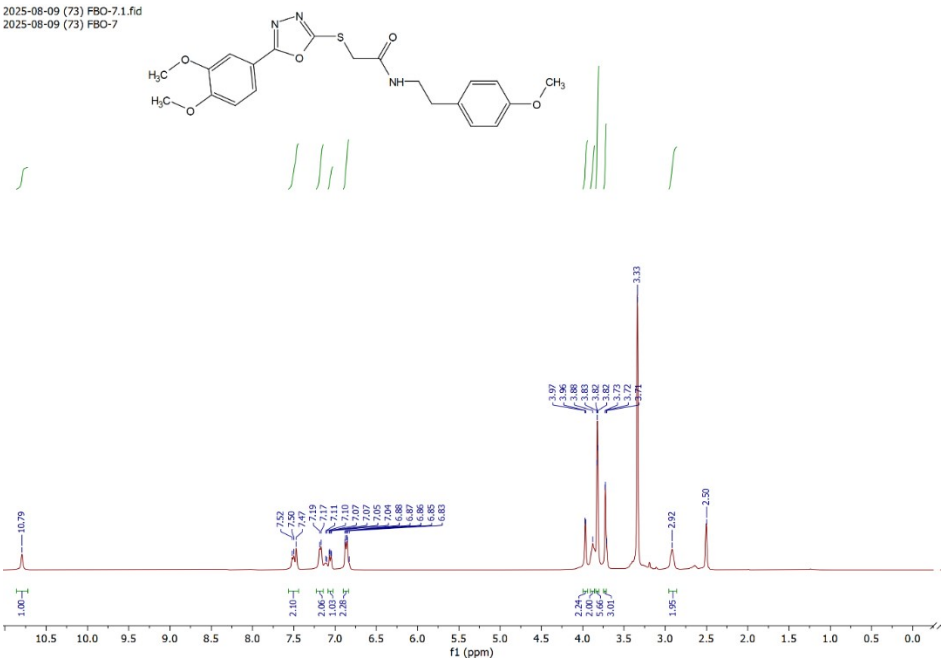


Figure S12: FT-IR, ^{1}H-, and ^{13}C-NMR spectra of compound **4**.





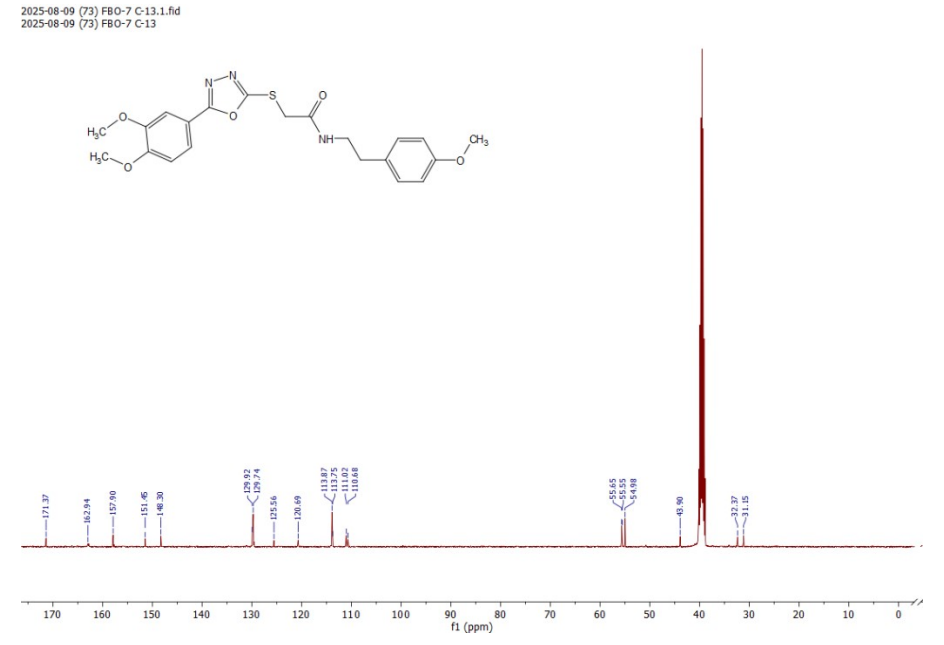


Figure S13: FT-IR, ^{1}H-, and ^{13}C-NMR spectra of compound **7a**.

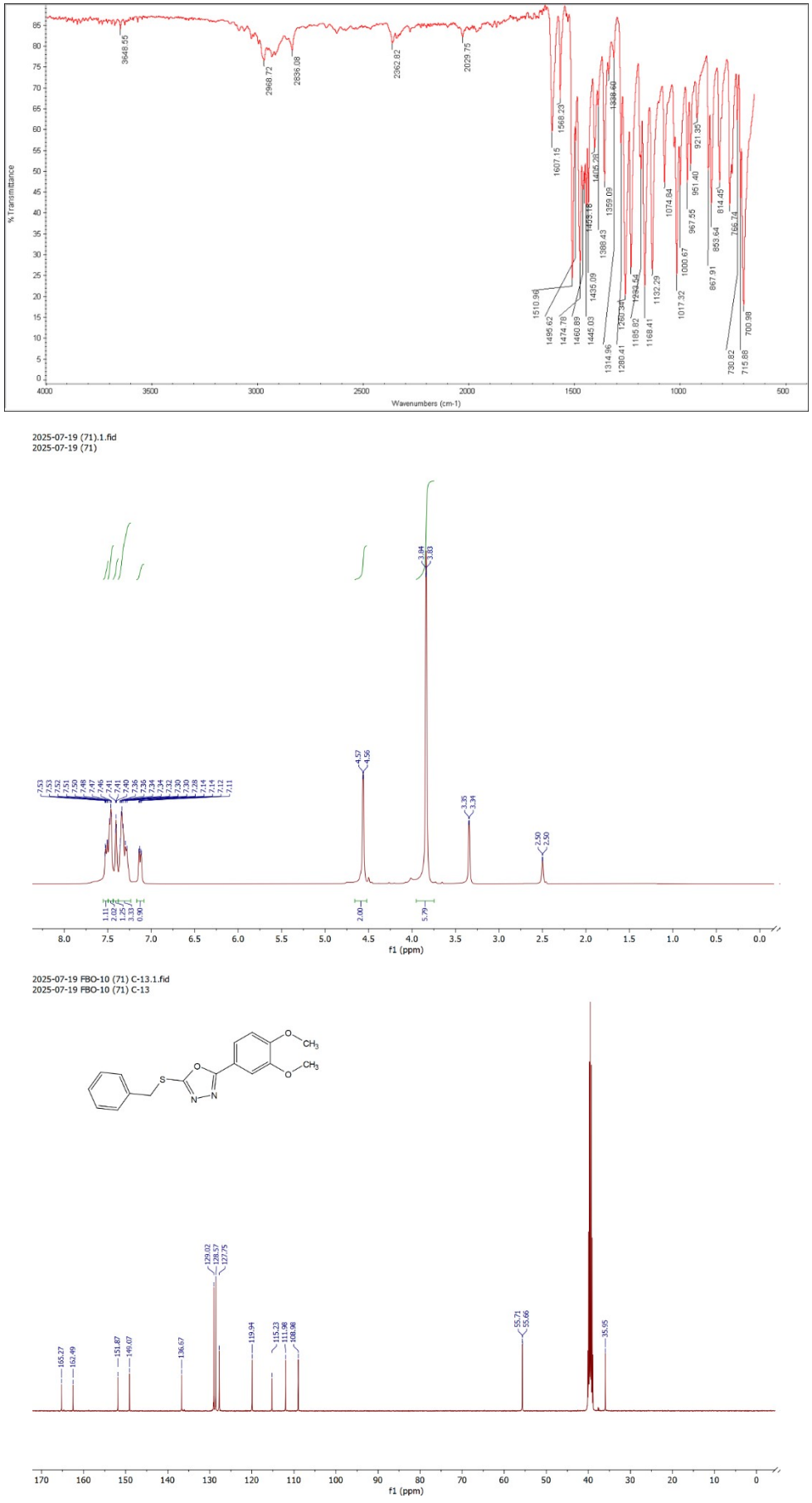
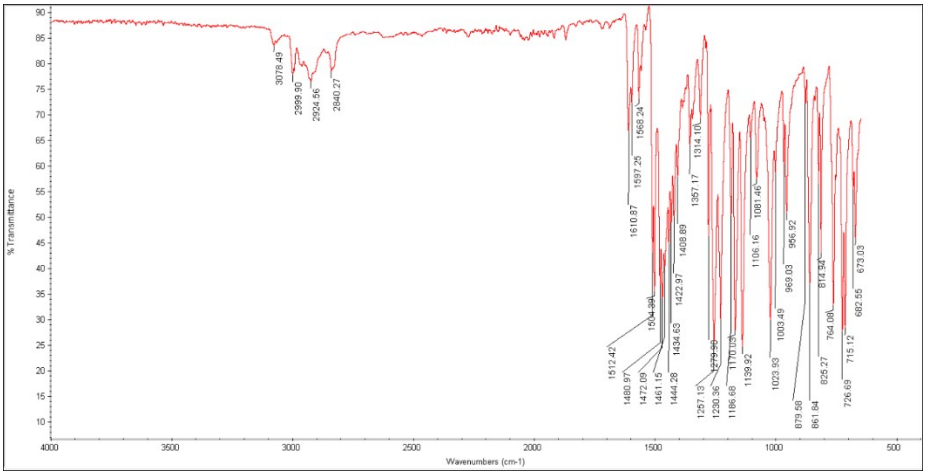
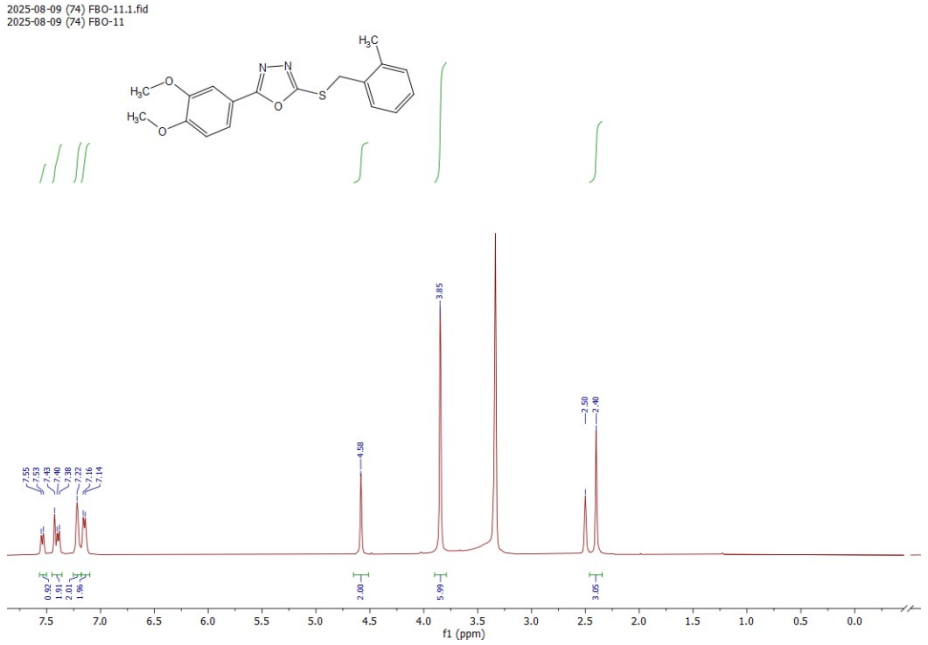


Figure S14: FT-IR, ^{1}H-, and ^{13}C-NMR spectra of compound **7b**.





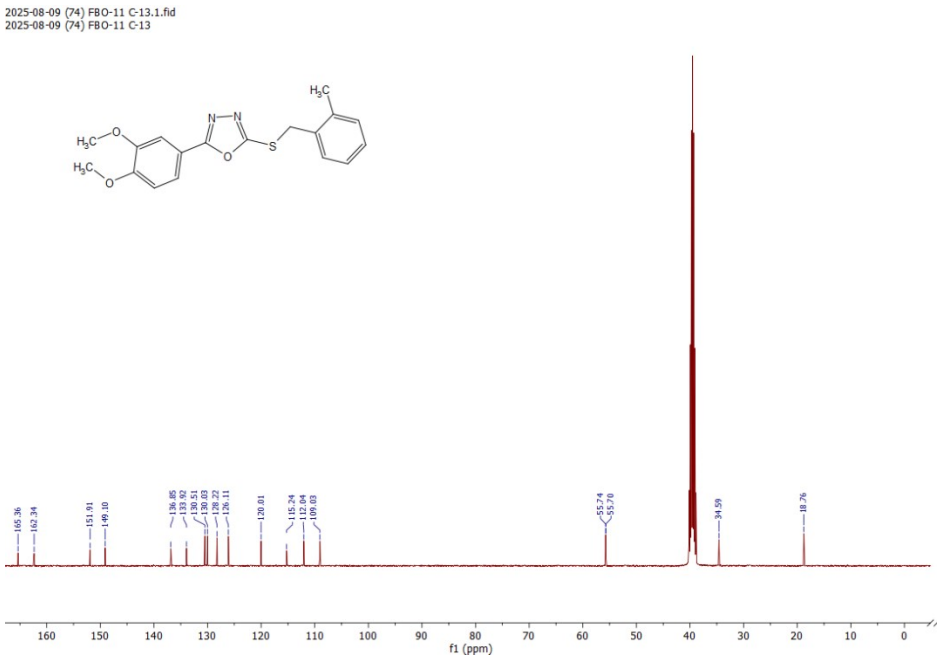
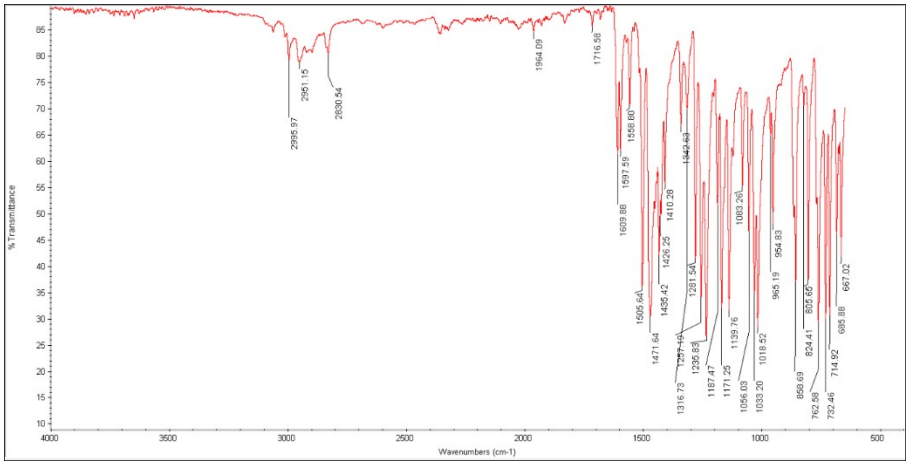
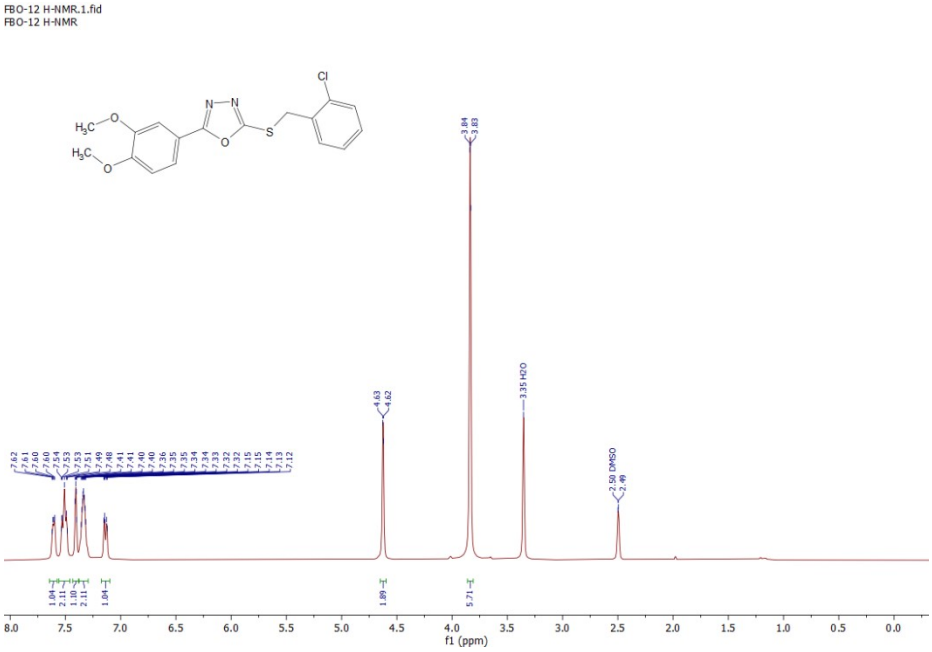


Figure S15: FT-IR, ^{1}H-, and ^{13}C-NMR spectra of compound **7c**.





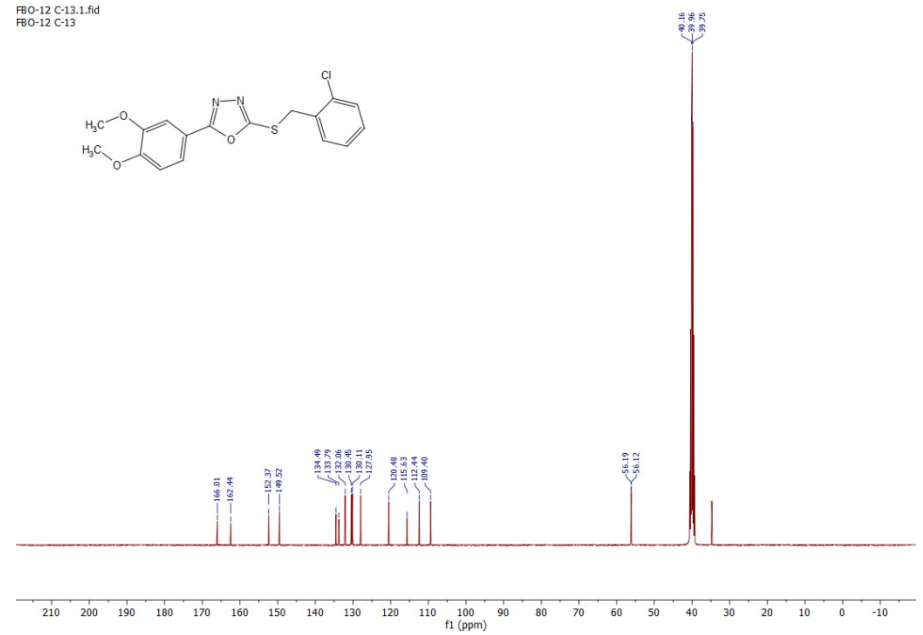


Figure S16: FT-IR, ^{1}H-, and ^{13}C-NMR spectra of compound **7d**.

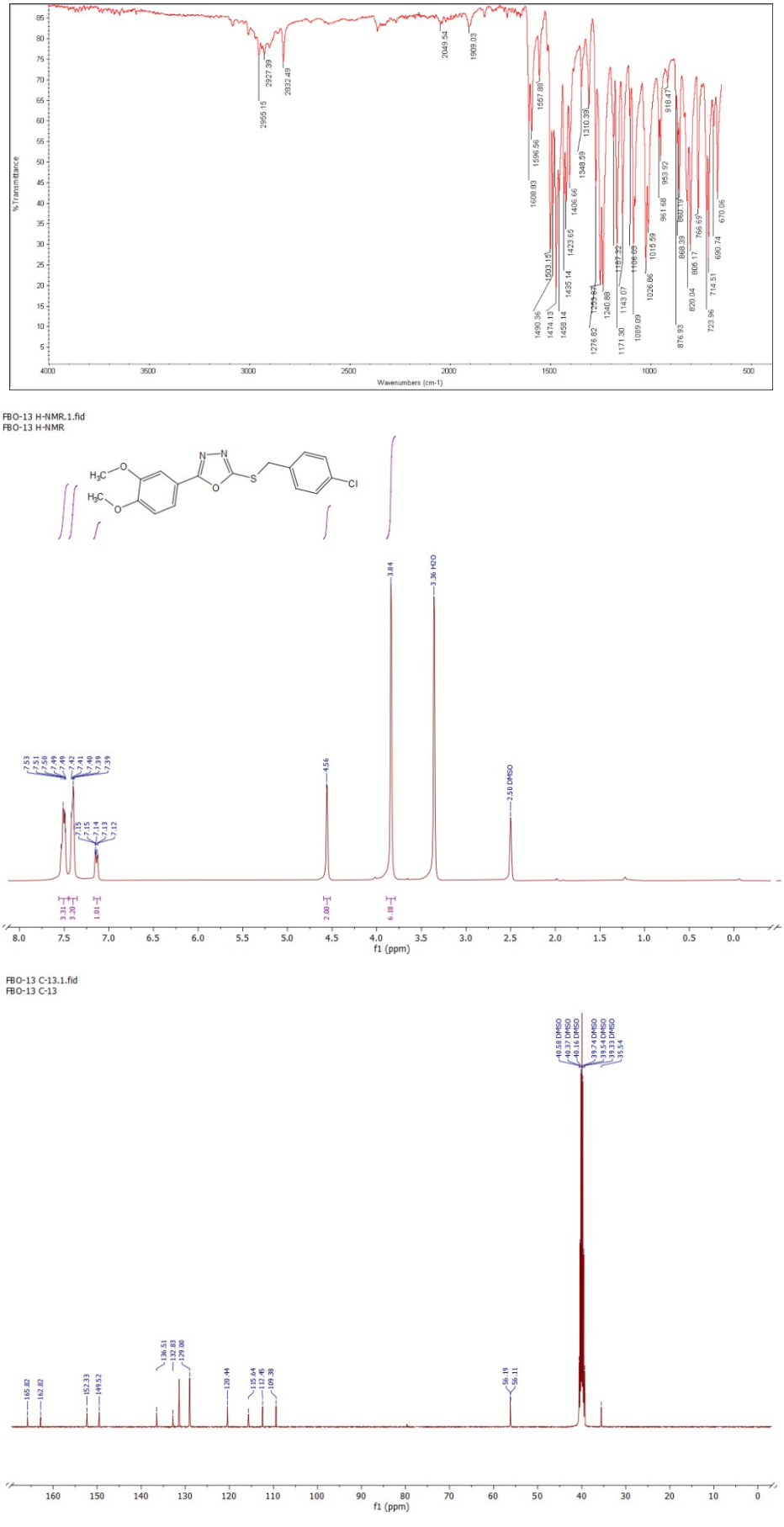
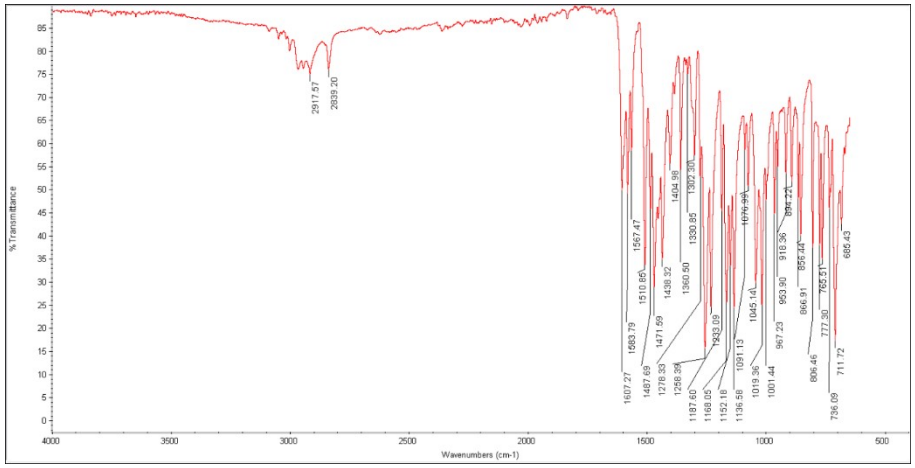
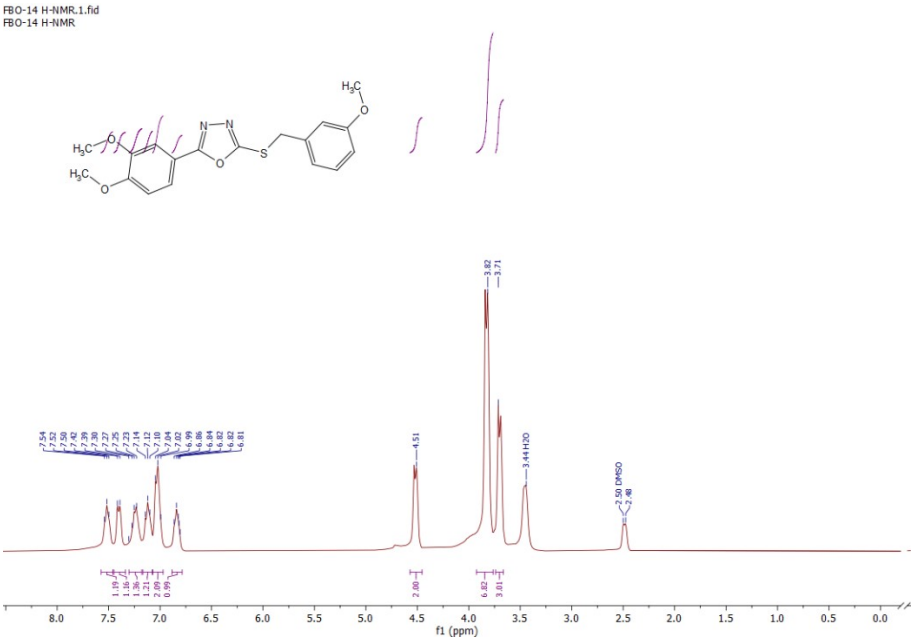


Figure S17: FT-IR, ^{1}H-, and ^{13}C-NMR spectra of compound **7e**.





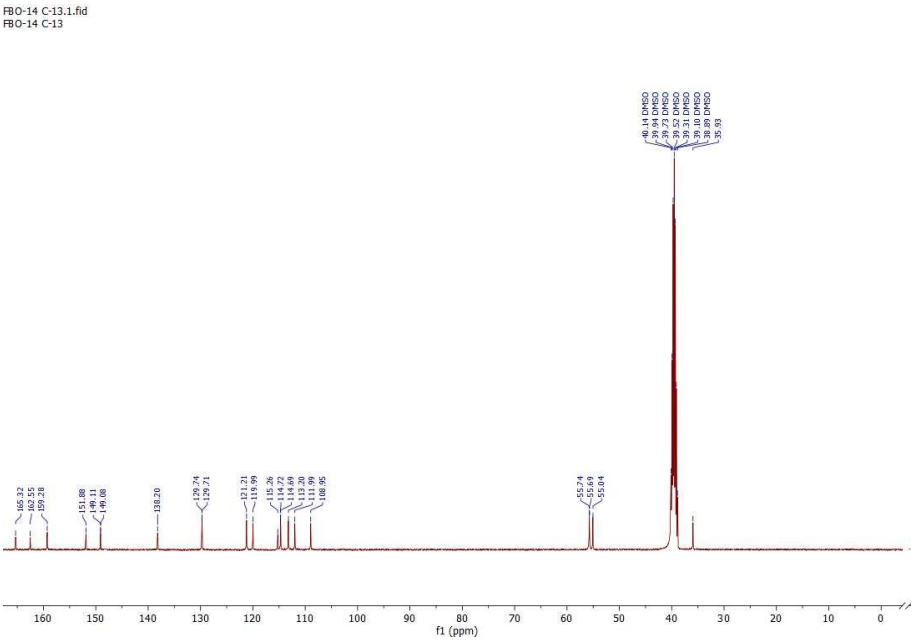
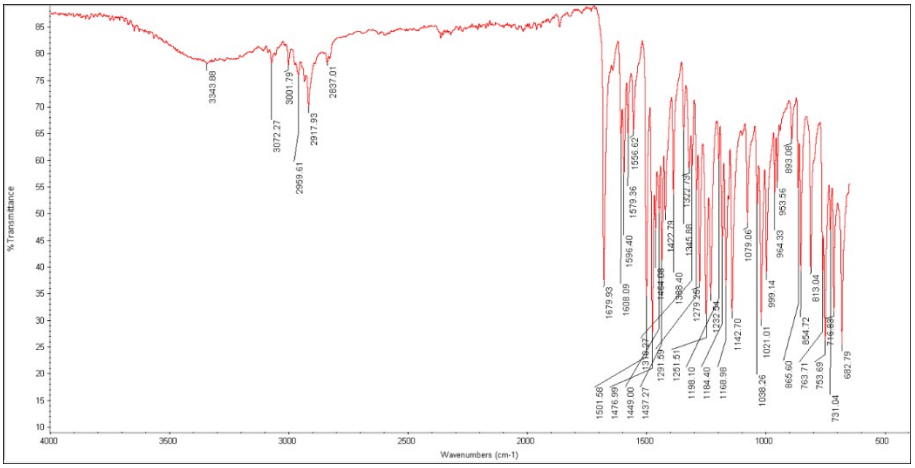
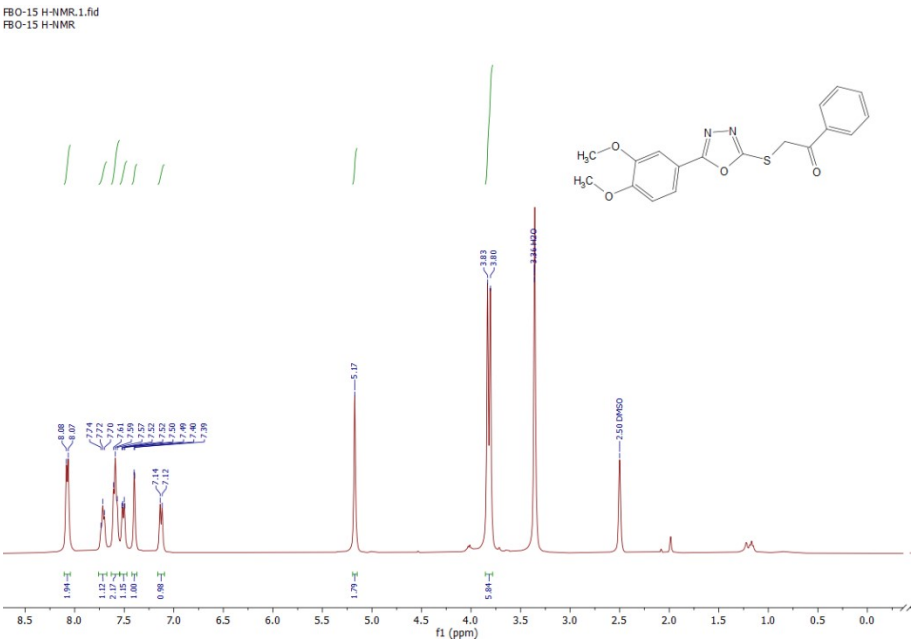


Figure S18: FT-IR, ^{1}H-, and ^{13}C-NMR spectra of compound **7f**.





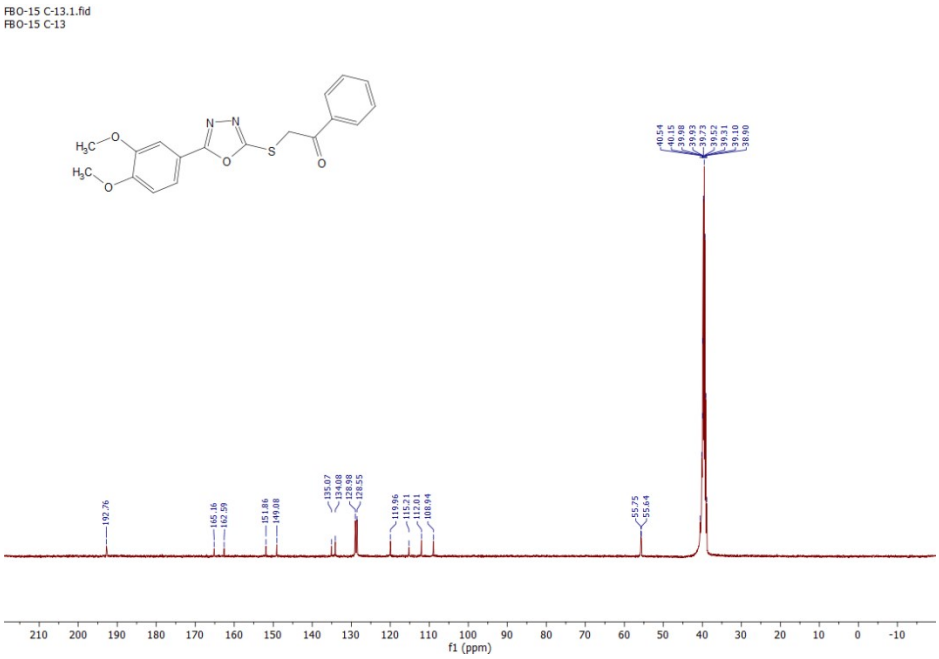


Figure S19: FT-IR, ^{1}H-, and ^{13}C-NMR spectra of compound **7g**.