

**Novel quinazolin-2,4-dione hybrid molecules as possible inhibitors against
Malaria: Synthesis and In silico molecular docking studies**

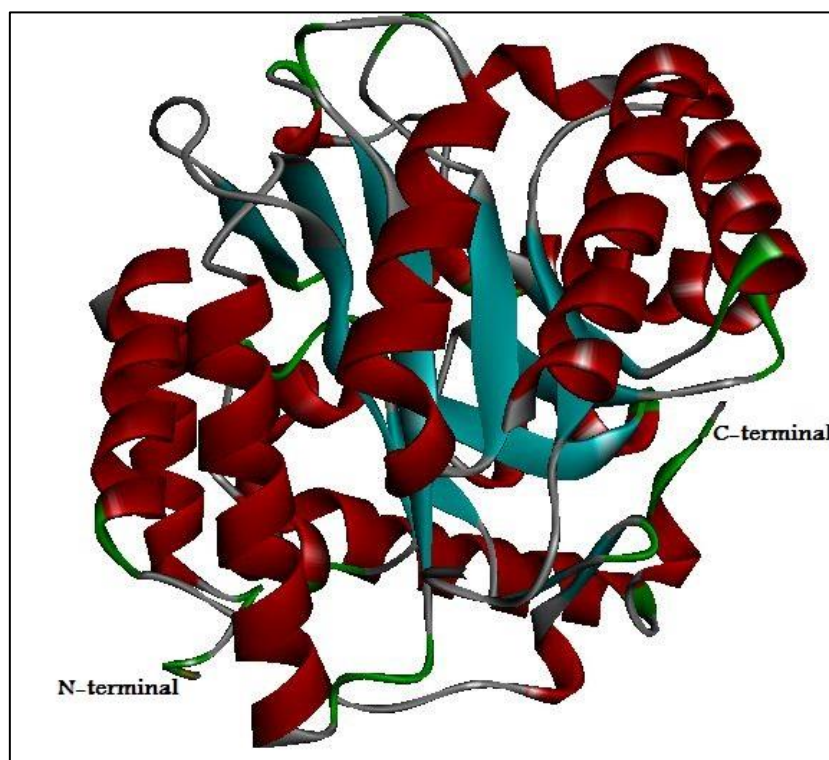
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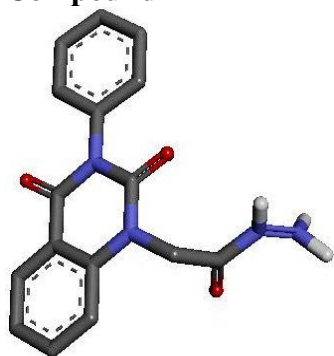
Figure S1. Three- dimensional structure of the target enzyme *pfDHODH*



The X-ray crystal structure of enzyme obtained from RCSB Protein Data Bank

Figure S2. Three- dimensional structures of the docked molecules

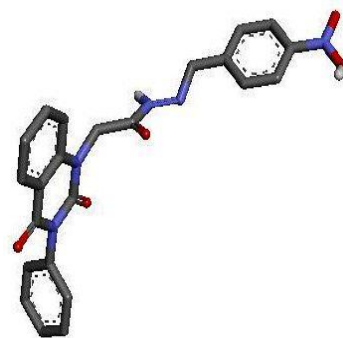
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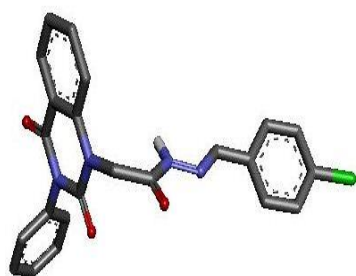
Compound 2a



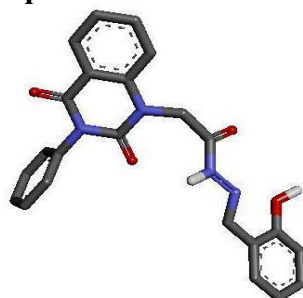
Compound 2b



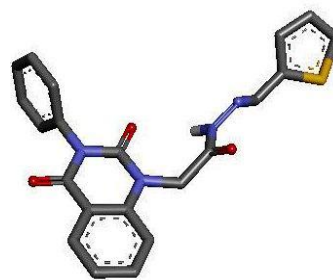
Compound 2c



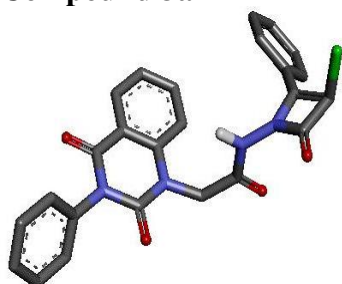
Compound 2d



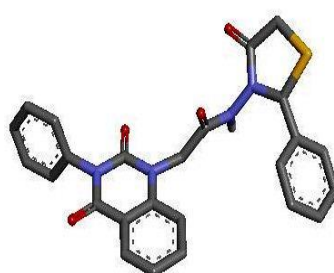
Compound 2e



Compound 3a



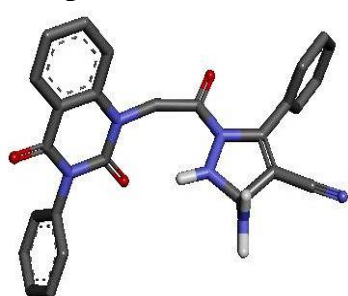
Compound 4a



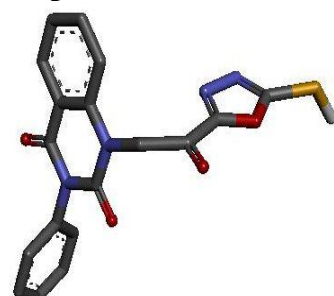
Compound 5



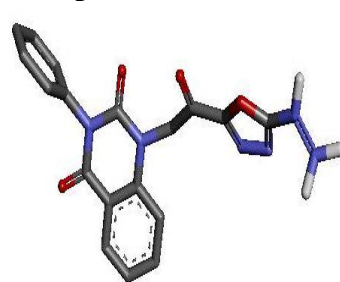
Compound 6



Compound 7



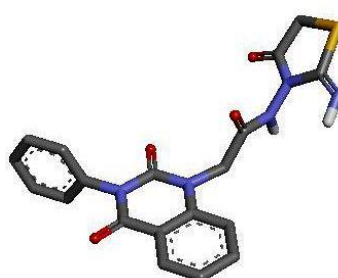
Compound 8



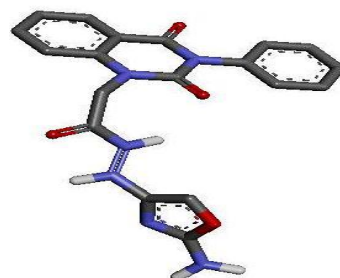
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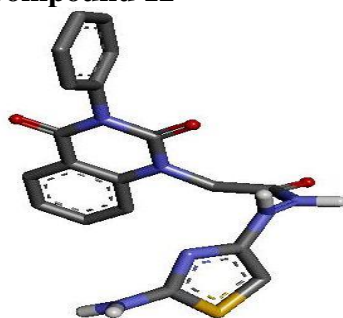
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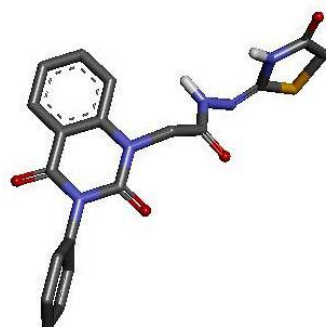
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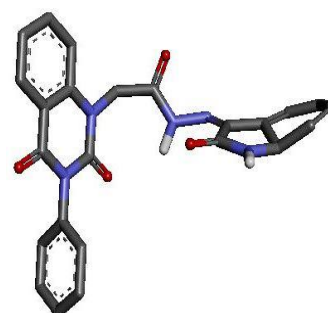
Compound 12



Compound 13



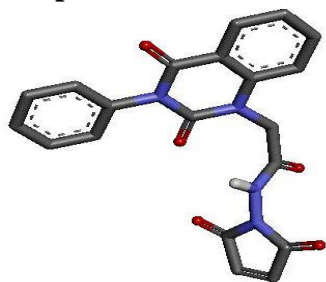
Compound 14



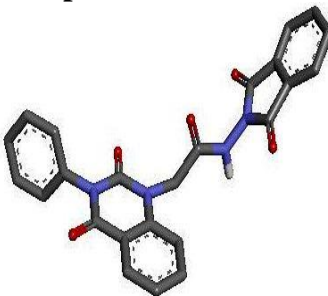
Compound 15



Compound 16a



Compound 16b



Compound 16c

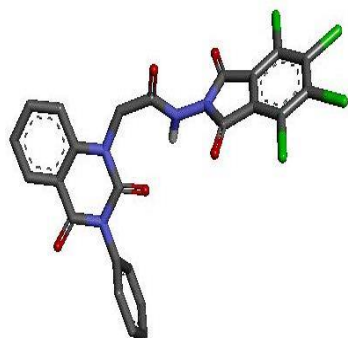
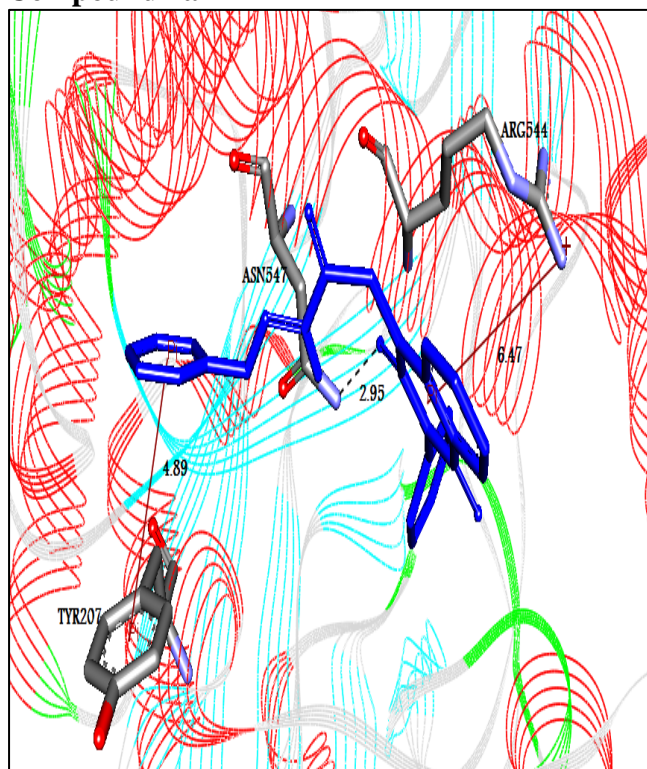
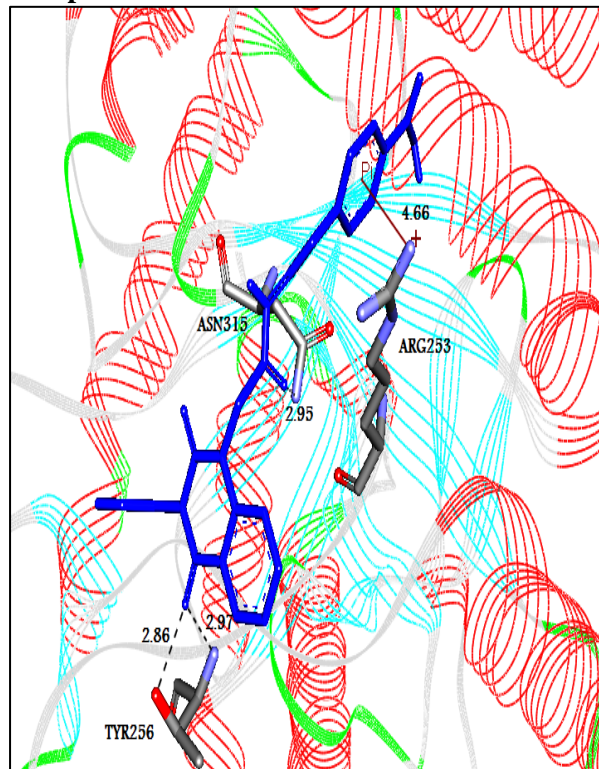


Figure S3. Molecular interactions between the rest compounds and *p*/DHODH

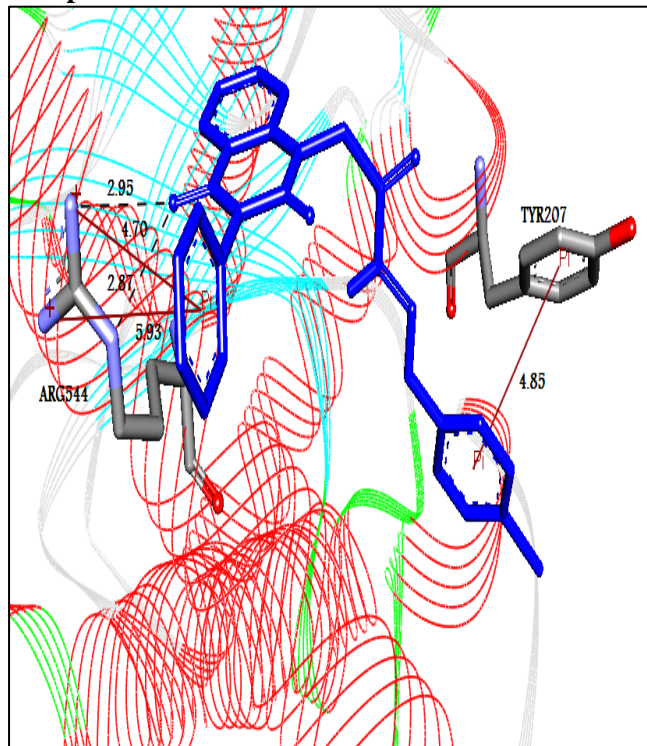
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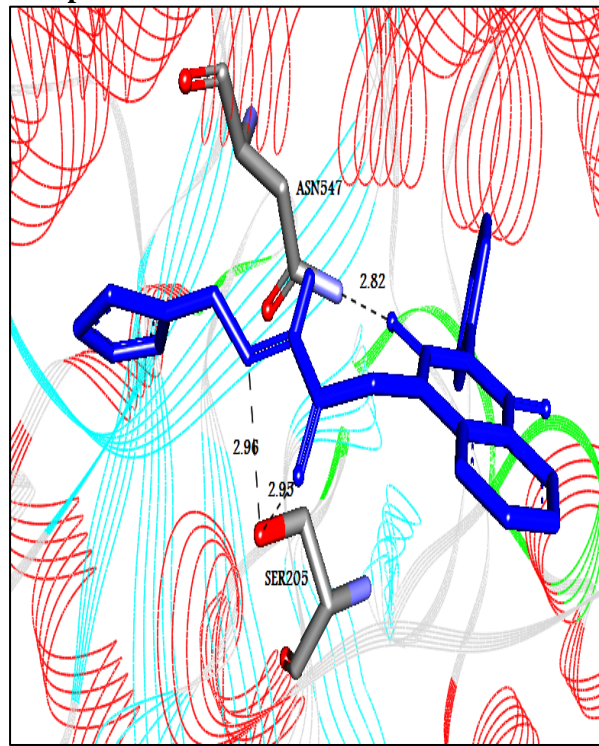
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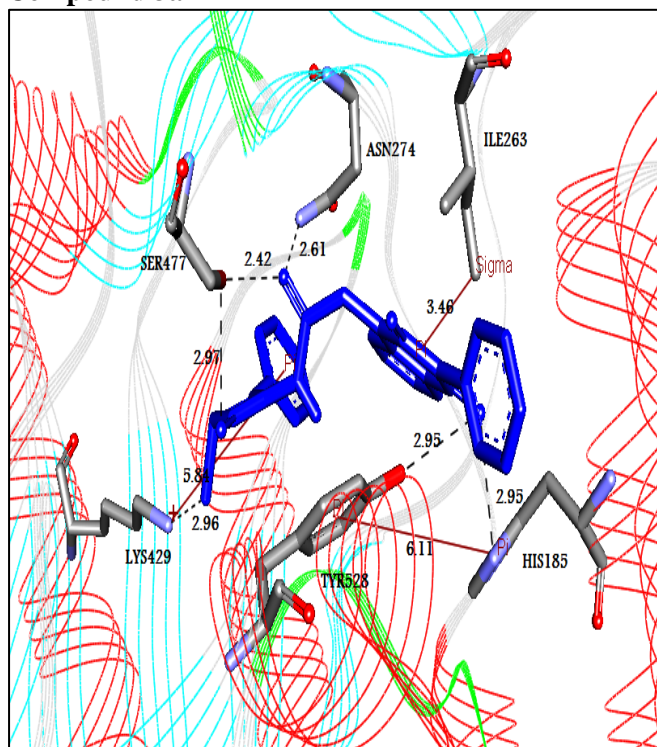
Compound 2c



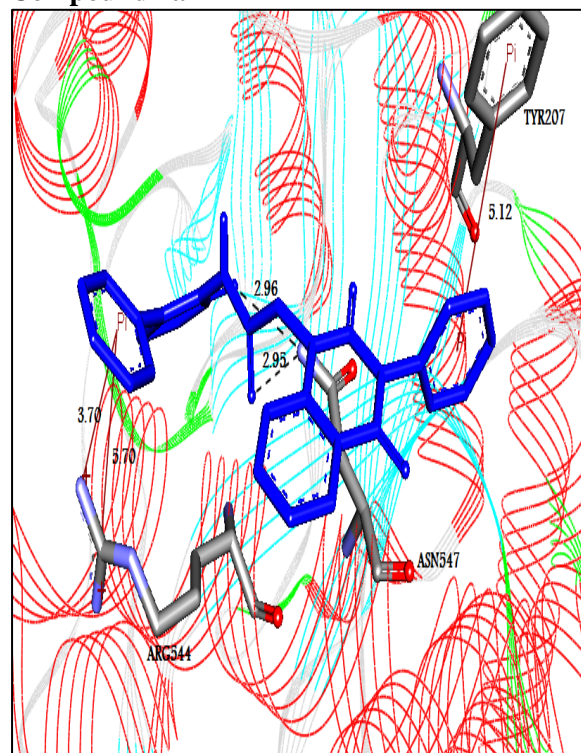
Compound 2e



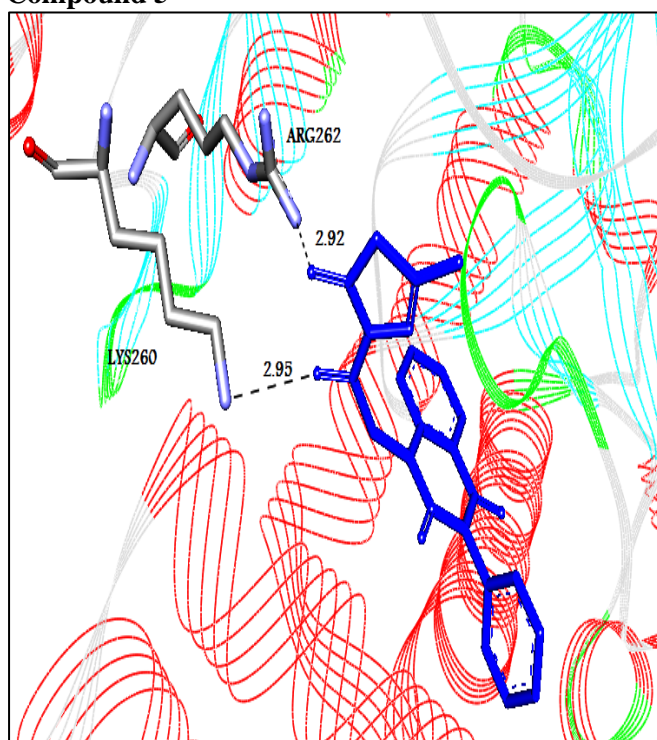
Compound 3a



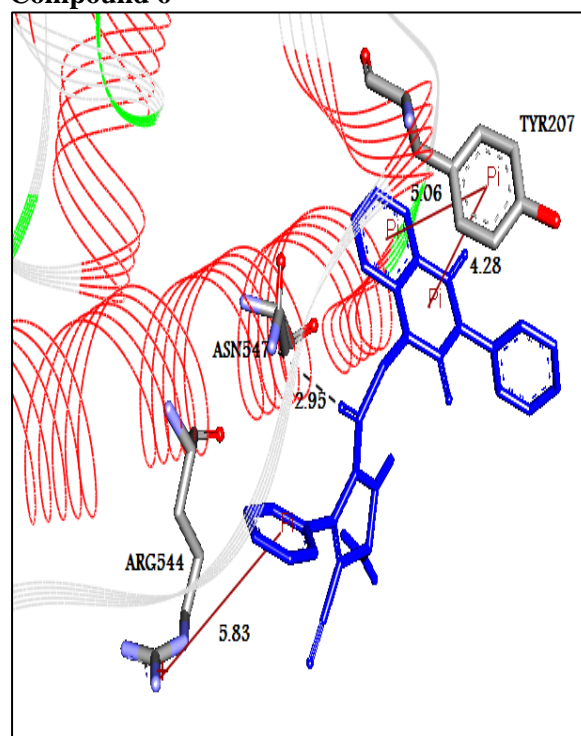
Compound 4a



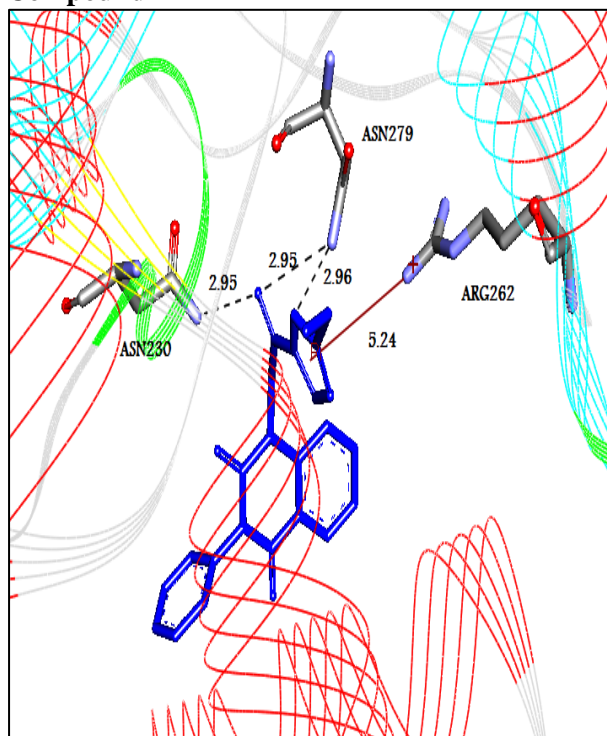
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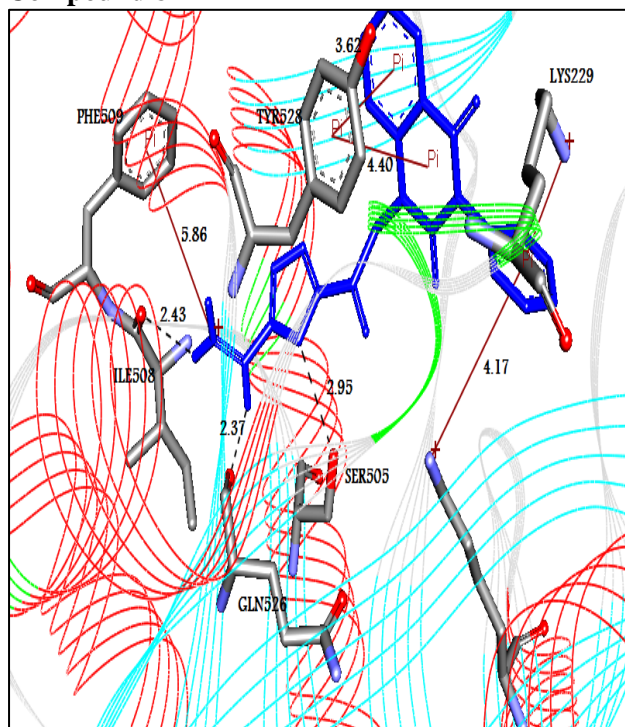
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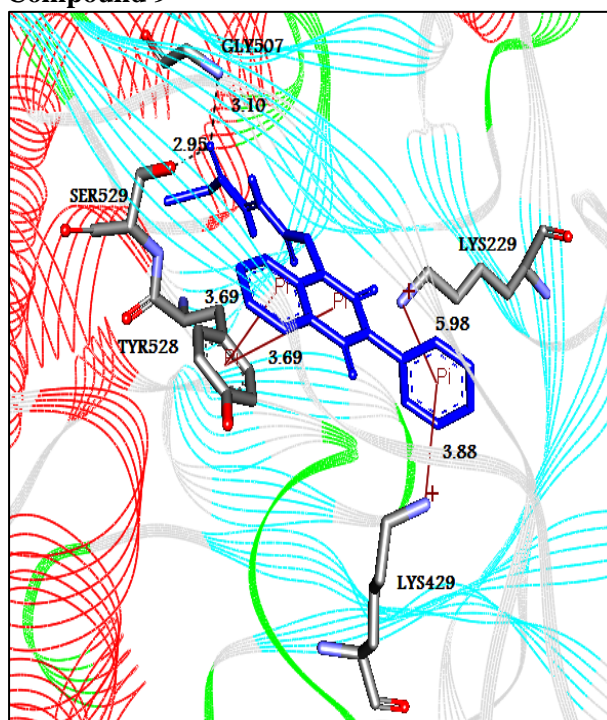
Compound 7



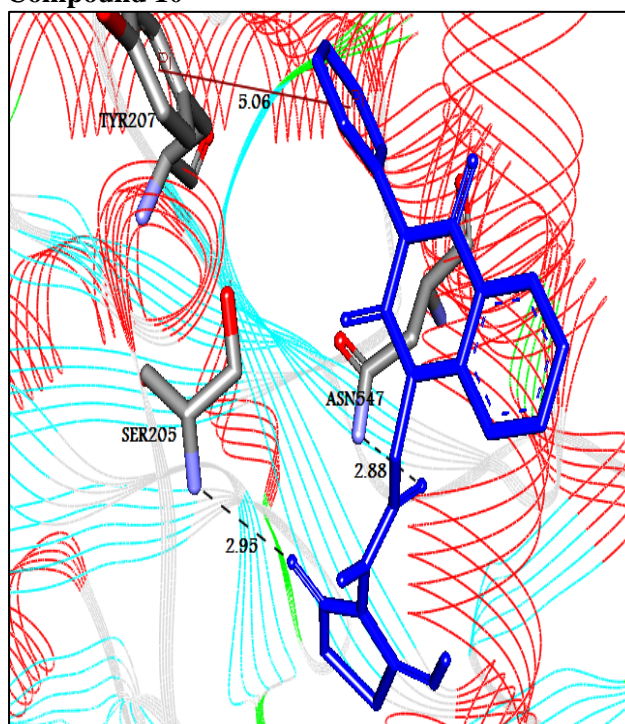
Compound 8



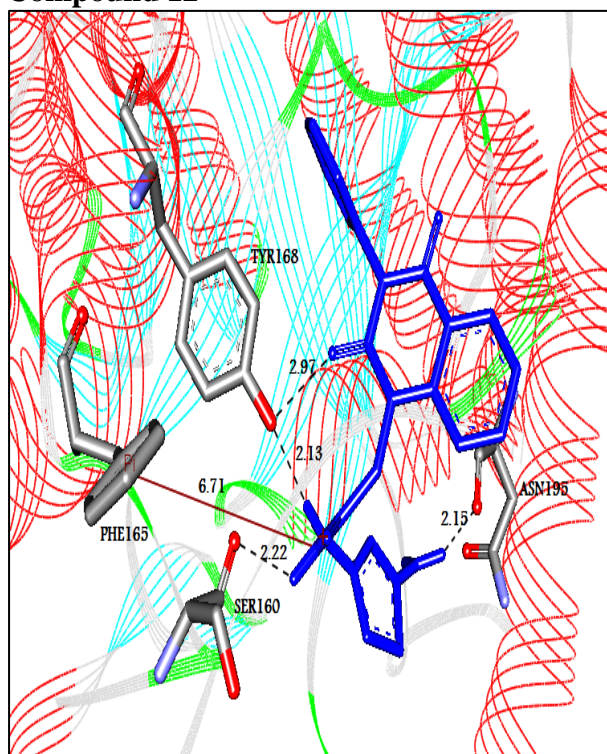
Compound 9



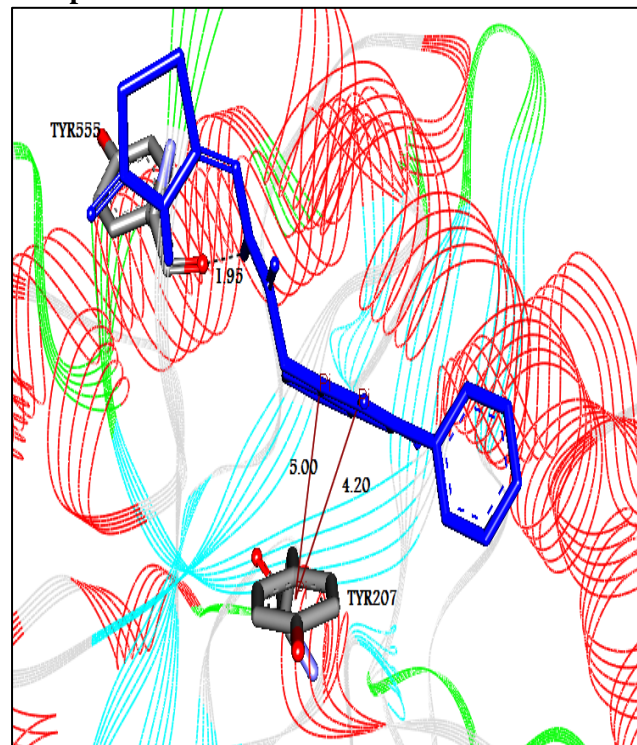
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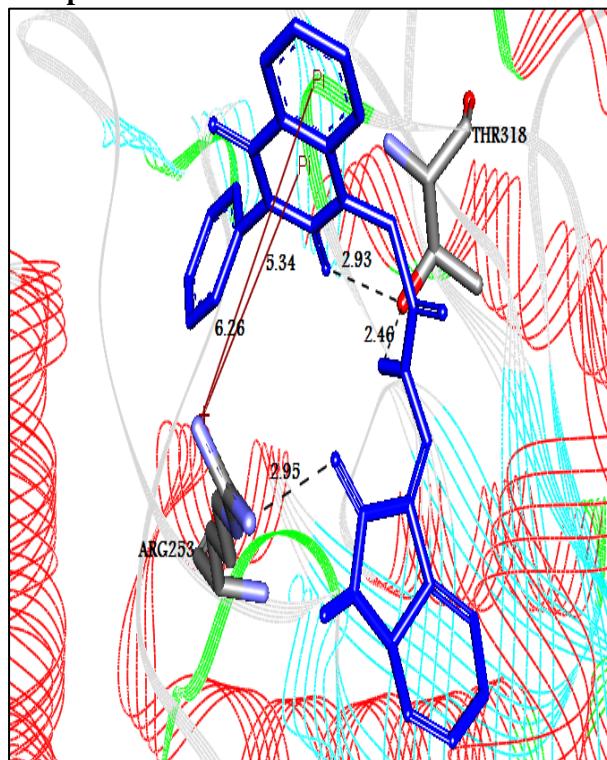
Compound 12



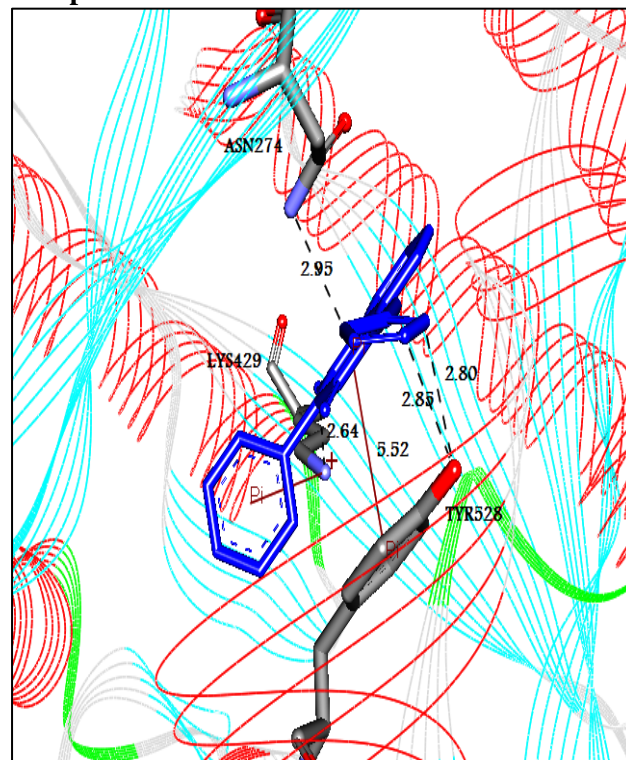
Compound 13



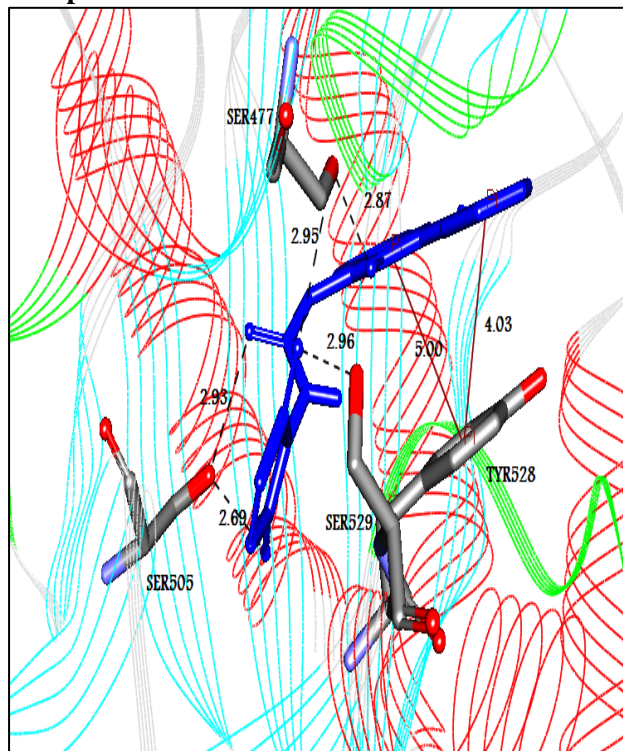
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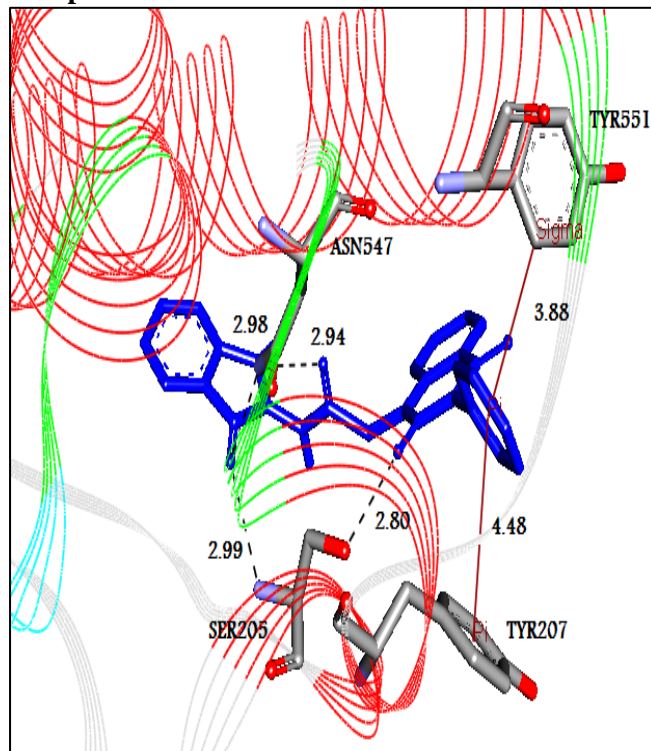
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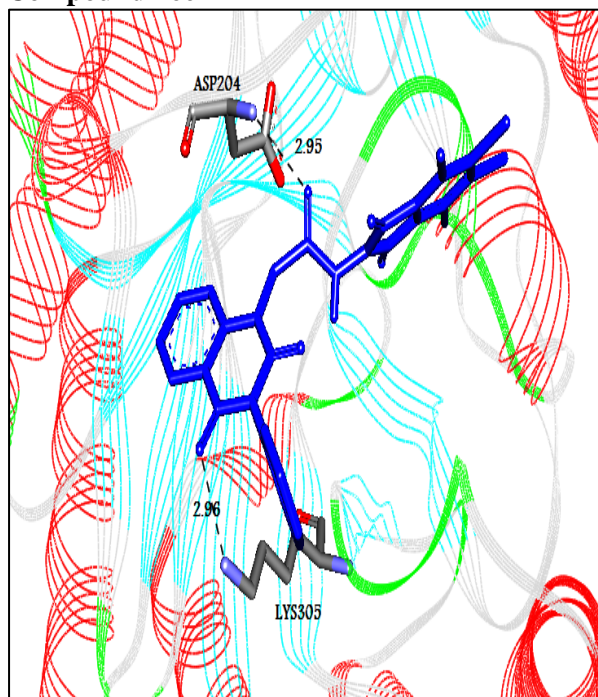
Compound 16a



Compound 16b



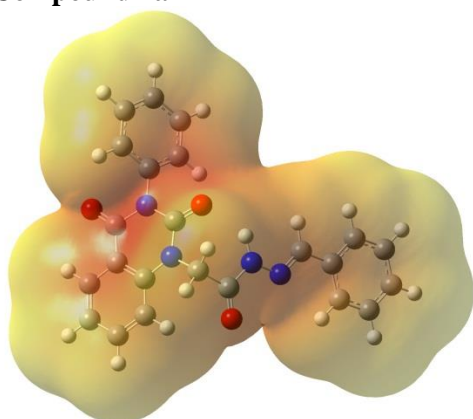
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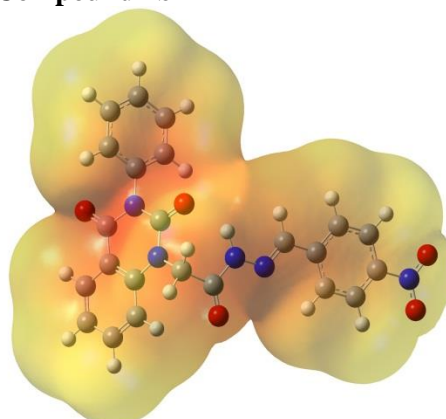
Three-dimensional of docking pose of the rest compounds in the active pocket of *pfDHODH*. Blue stick models represented the docked compounds, and gray models represented the active site region. H-bond interactions are shown in black dotted lines. π - interactions are shown in brown lines.

Figure S4. The electrostatic potential maps of the rest compounds.

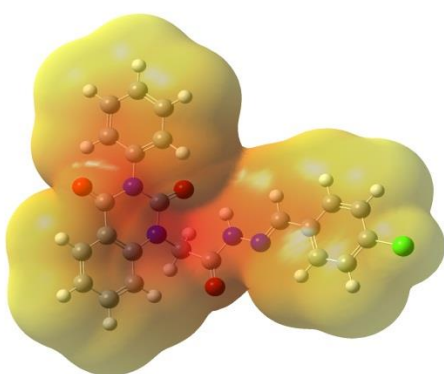
Compound 2a



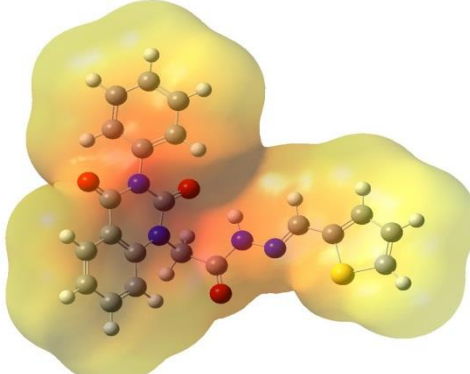
Compound 2b



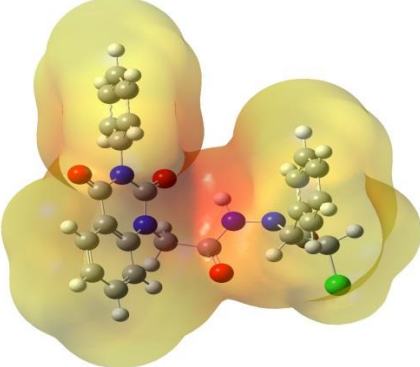
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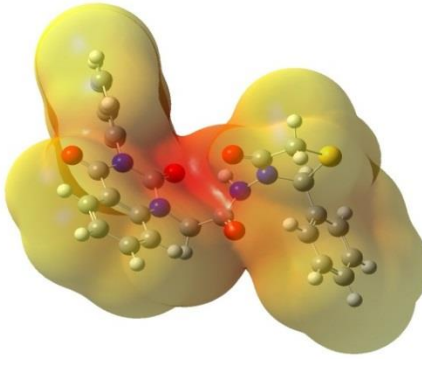
Compound 2e



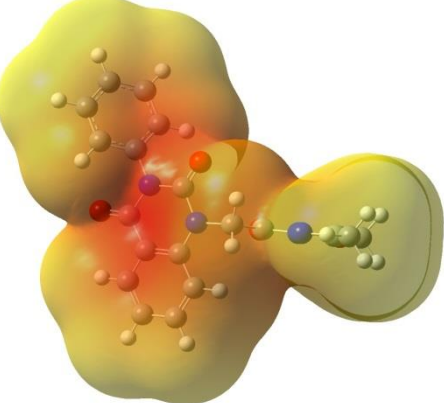
Compound 3a



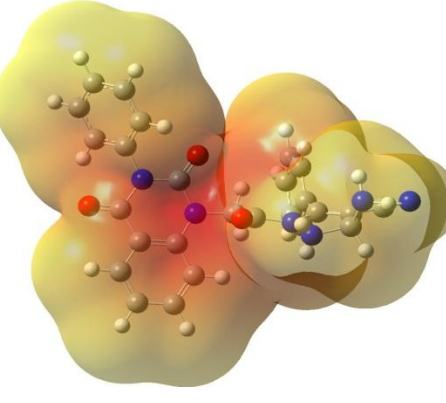
Compound 4a



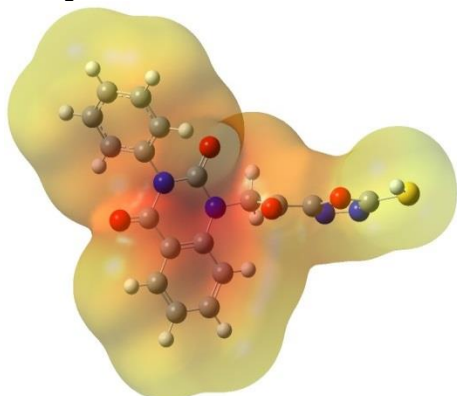
Compound 5



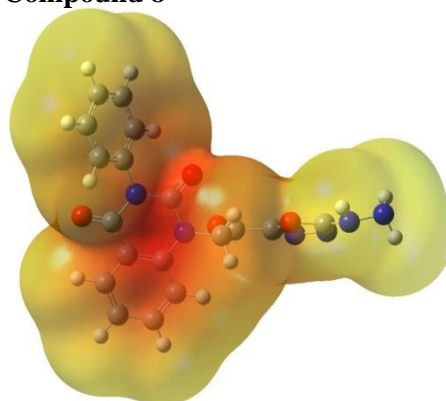
Compound 6



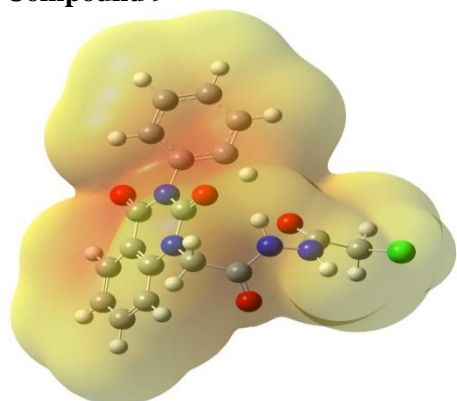
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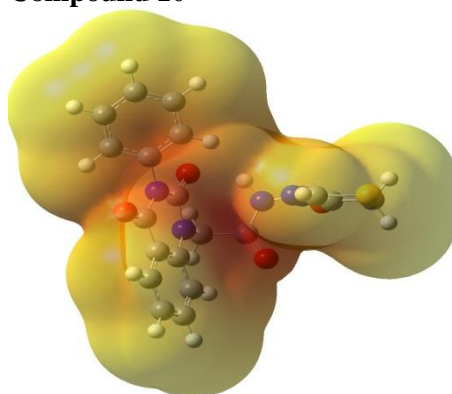
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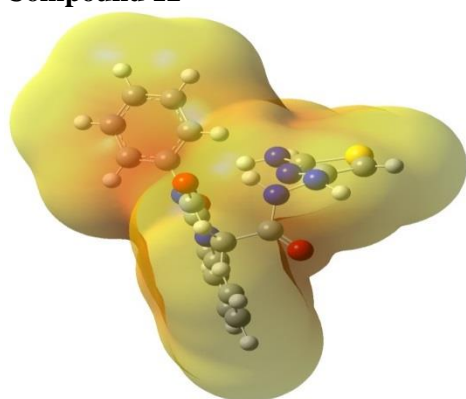
Compound 9



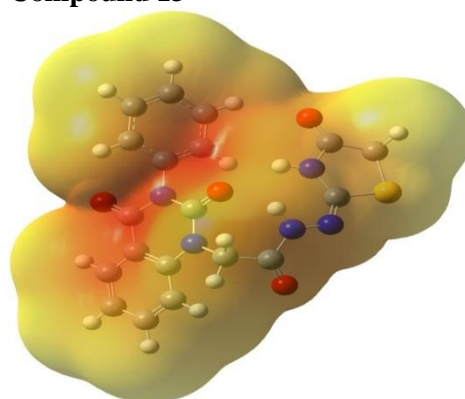
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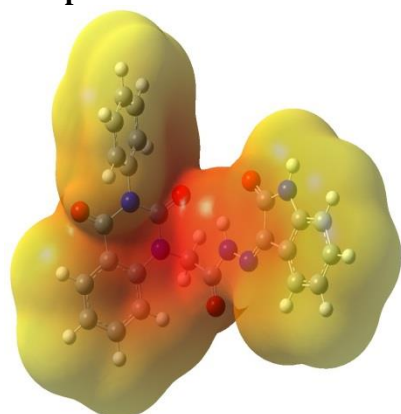
Compound 12



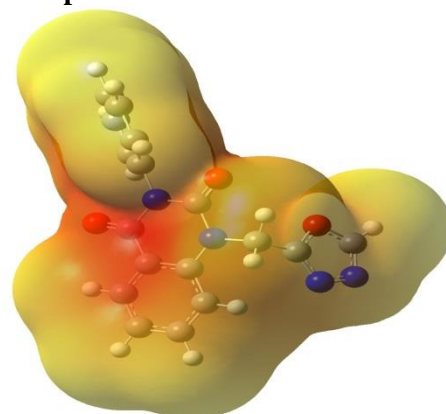
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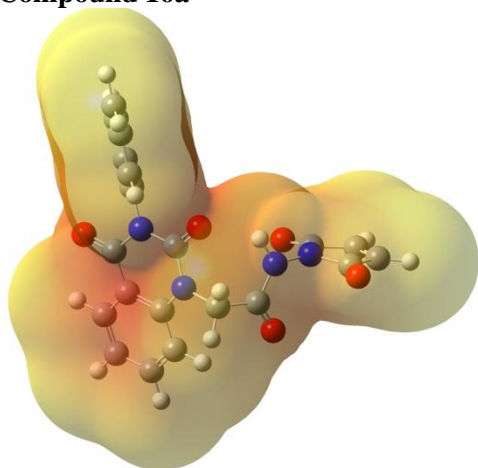
Compound 14



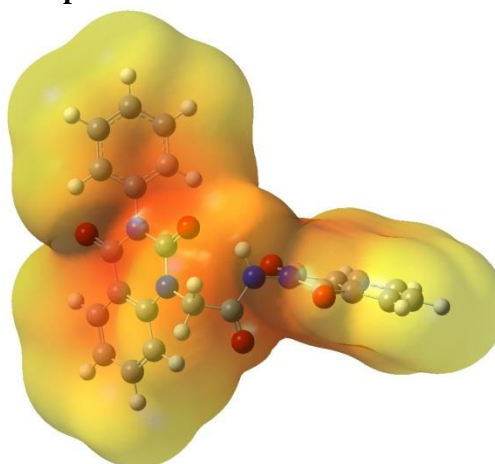
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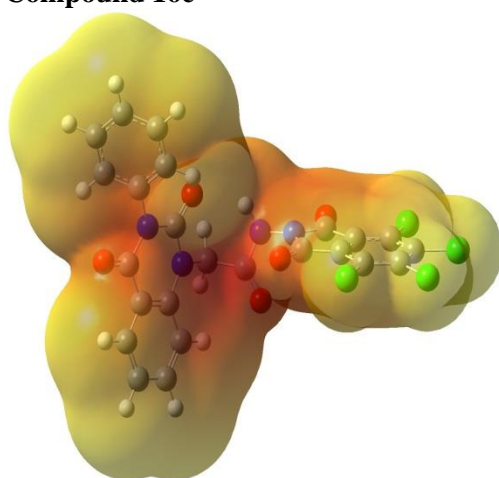
Compound 16a



Compound 16b



Compound 16c



Electrostatic potential maps around the rest compounds. The red region represents highly electron density charges (electronegative), while pale yellow represents electropositive part.

Table S1. The protonation states of the amino acid residues of *pf*DHODH.

Residue	pKa
ASP204	3.97
HIS185	4.36
TYR168	11.06
TYR207	10.10
TYR528	13.80
TYR551	10.06
TYR555	12.03
LYS229	9.26
LYS260	10.74
LYS305	10.43
LYS429	8.95
ARG253	12.51
ARG262	13.68
ARG544	13.58