Electronic Supplementary Material (ESI) for RSC Advances.

N-Aryl iminochromenes inhibit cyclooxygenase enzymes *via* π-π stacking interactions present novel class of anti-inflammatory drugs

Results

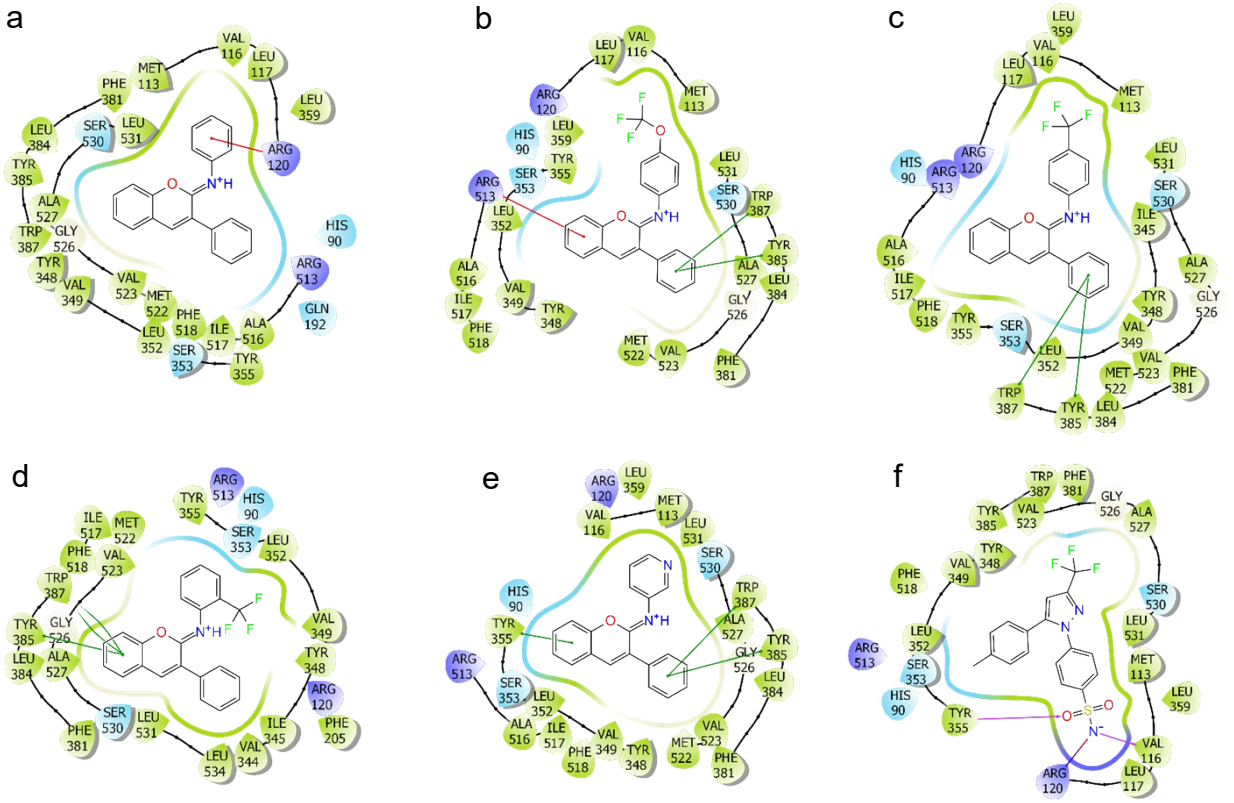
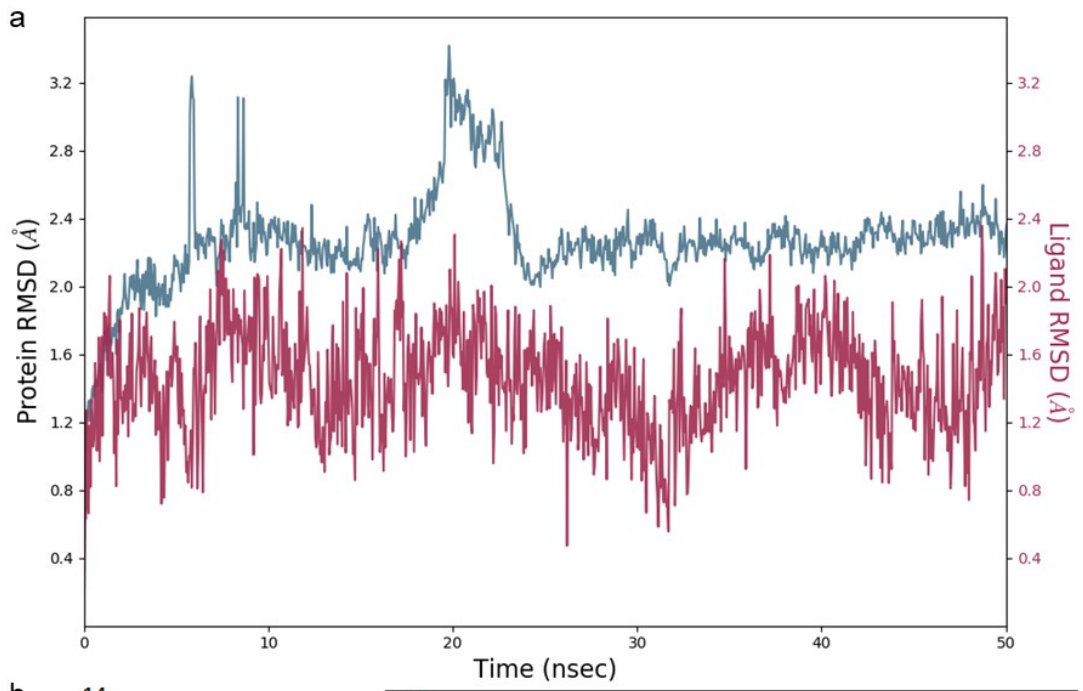
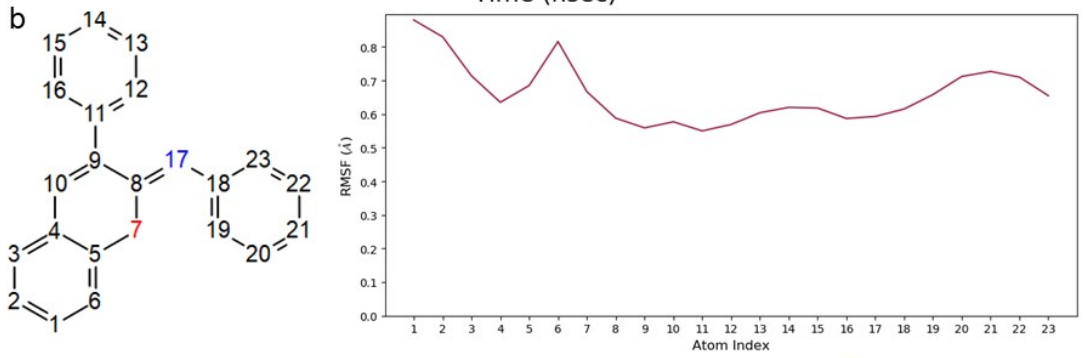
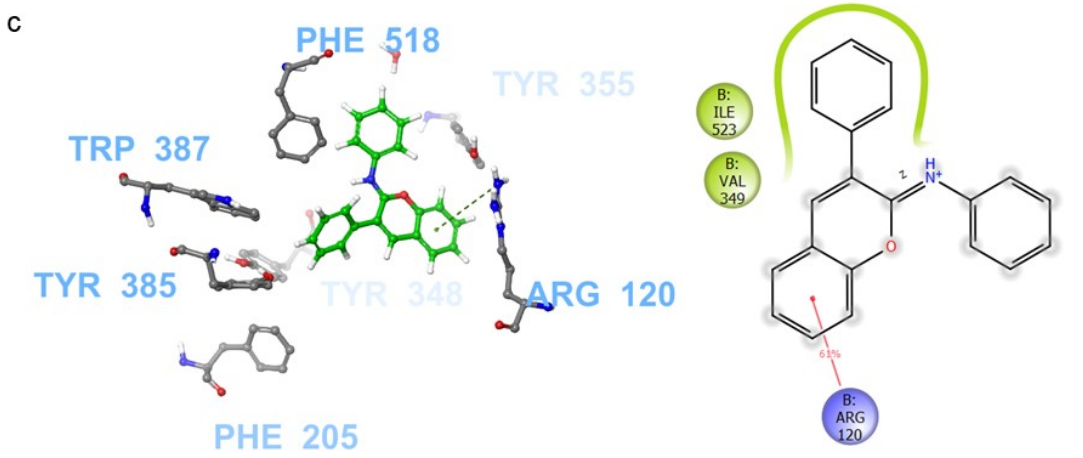


Fig. S1. The binding poses predicted in IFD Top 2 of five ligands and celecoxib with cyclooxygenase-2 protein. (a) Ligand **1**; (b) Ligand **10**; (c) Ligand **14**; (d) Ligand **15**; (e) Ligand **20**; (f) Standard drug, Celecoxib.


a
Protein RMSD (Å)
Ligand RMSD (Å)
Time (nsec)


b
RMSF (Å)
Atom Index


c
PHE 518
TYR 355
TRP 387
TYR 385
TYR 348
ARG 120
PHE 205
B: ILE 523
B: VAL 349
B: ARG 120

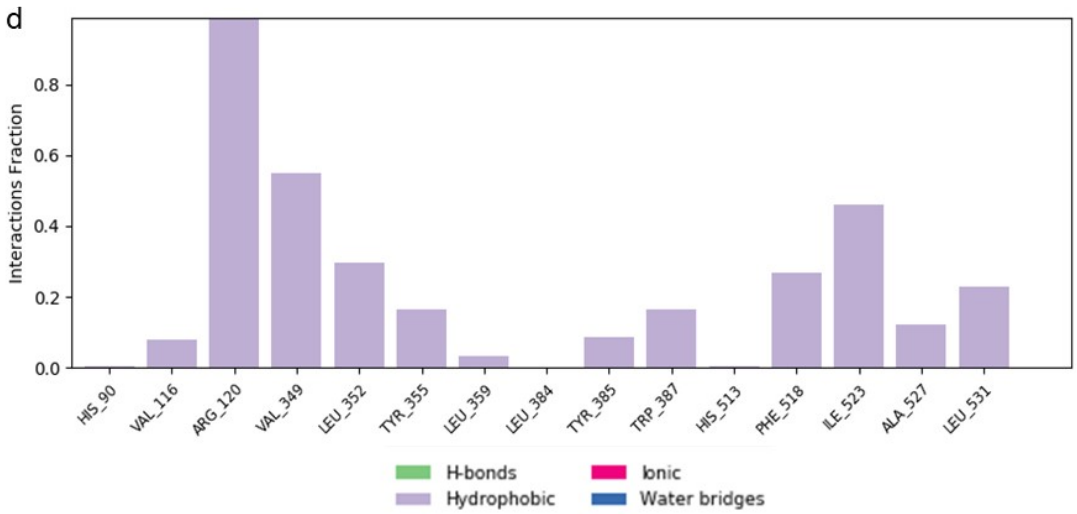
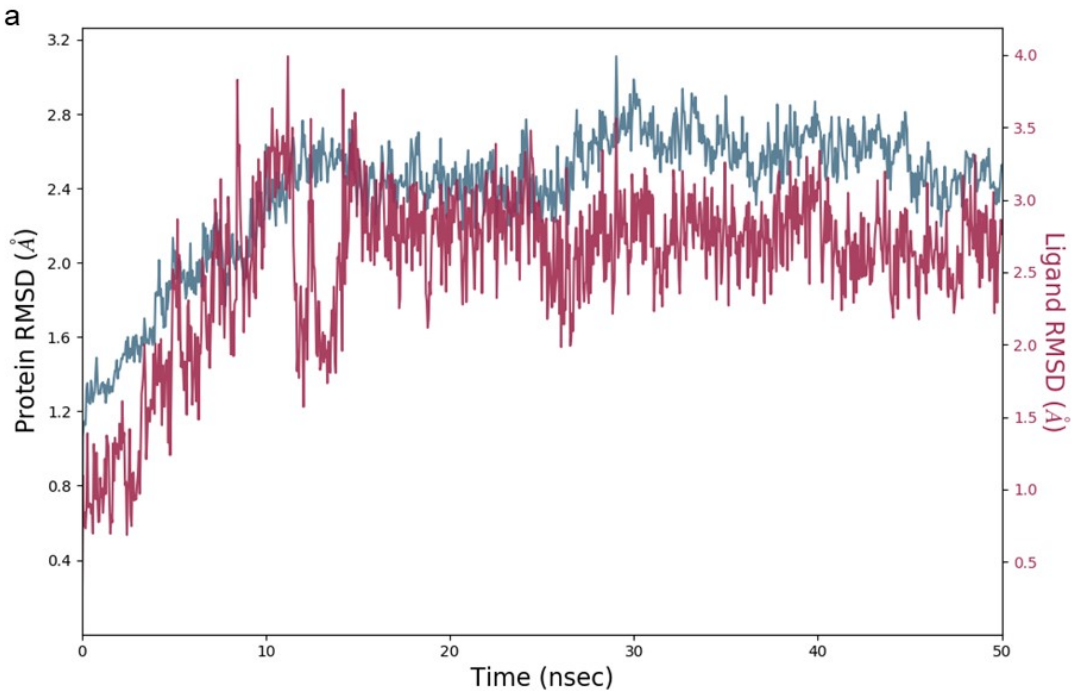


Fig. S2 Molecular dynamics simulations (MDS) of the ligand **1** – cyclooxygenase-1 protein complex. (a) Root-mean-square deviation of protein (azure) and ligand **1** (red signal). (b) Root mean squared fluctuation (RMSF) of the compound fitted on the protein (red line). The atom numbers of the ligand **1** (left) correspond to the RMSF plot X-axis (right). (c) 3D snapshots (left) from stable segments of MDS (Right). The interactions that occur more than 40.0% of the simulation time in the selected trajectory (0.00 through 50.05 nanoseconds). (d) Interaction diagram demonstrates the percentage interaction of the ligand **1** with surrounding residues.



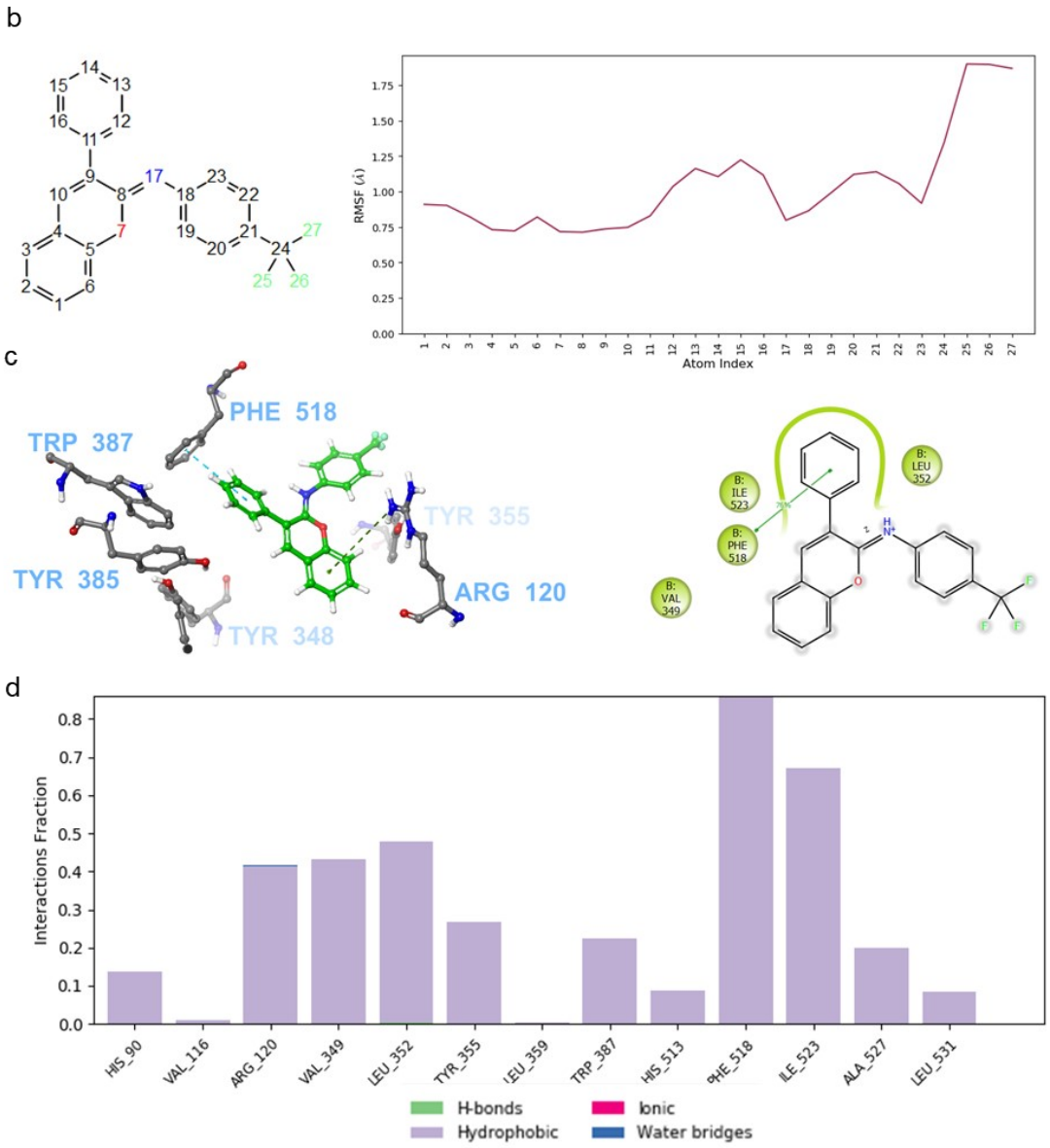
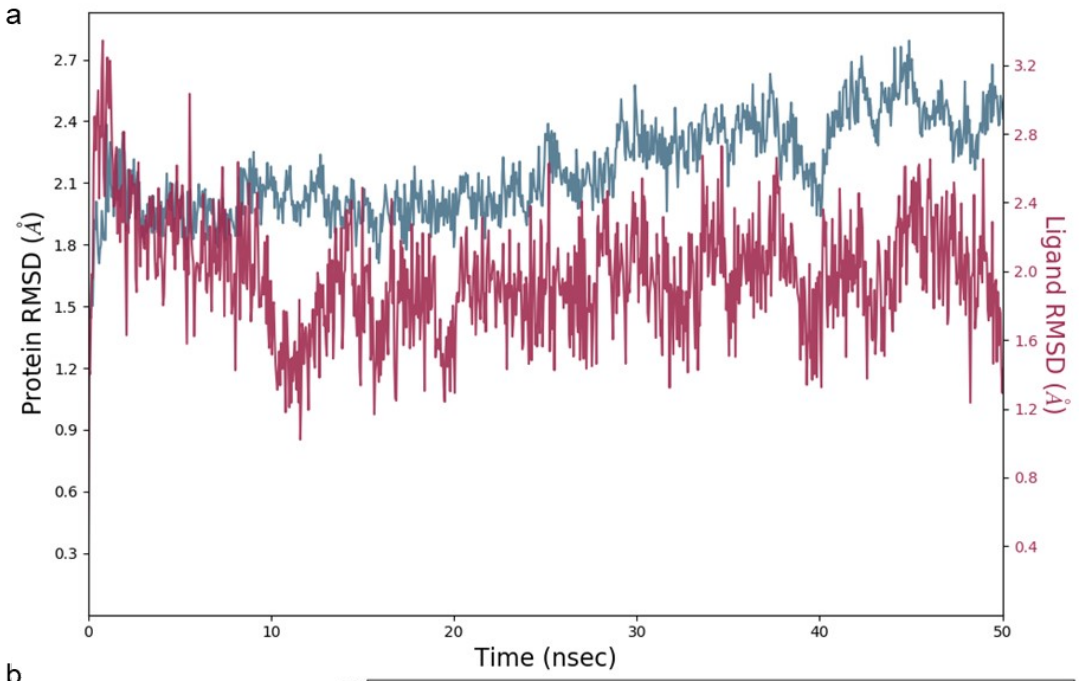
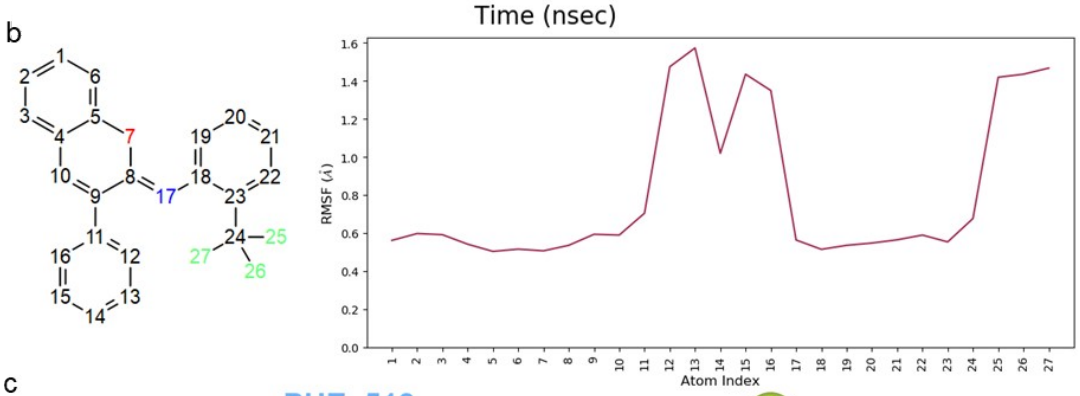
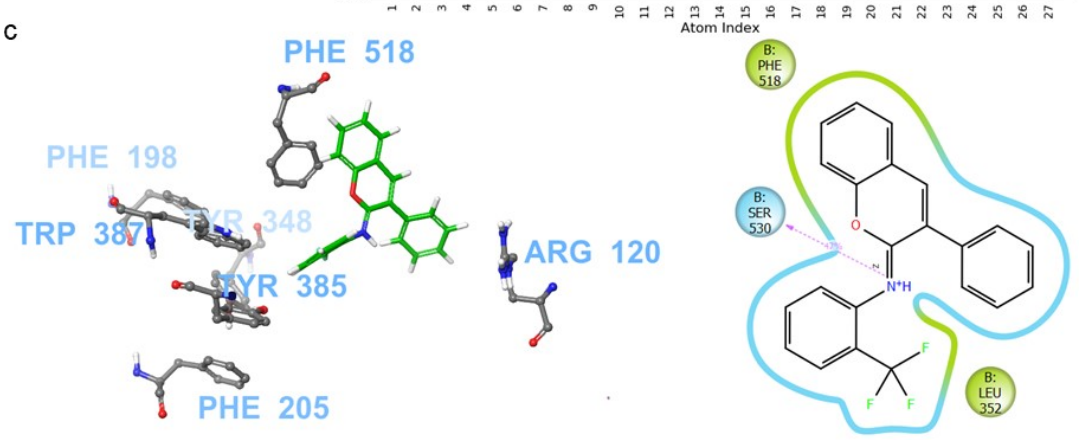


Fig. S3 Molecular dynamics simulations (MDS) of the ligand **14** – cyclooxygenase-1 protein complex. (a) Root-mean-square deviation of protein (azure) and ligand **14** (red signal). (b) Root mean squared fluctuation (RMSF) of the compound fitted on the protein (red line). The atom numbers of the ligand **14** (left) correspond to the RMSF plot X-axis (right). (c) 3D snapshots (left) from stable segments of MDS (Right). The interactions that occur more than 40.0% of the simulation time in the selected trajectory (0.00 through 50.05 nanoseconds). (d) Interaction diagram demonstrates the percentage interaction of the ligand **14** with surrounding residues.


a
Protein RMSD (Å)
Ligand RMSD (Å)
Time (nsec)


b
RMSF (Å)
Atom Index


c
PHE 518
PHE 198
TRP 387
TYR 348
TYR 385
ARG 120
PHE 205
B: PHE 518
B: SER 530
B: LEU 352
N+H

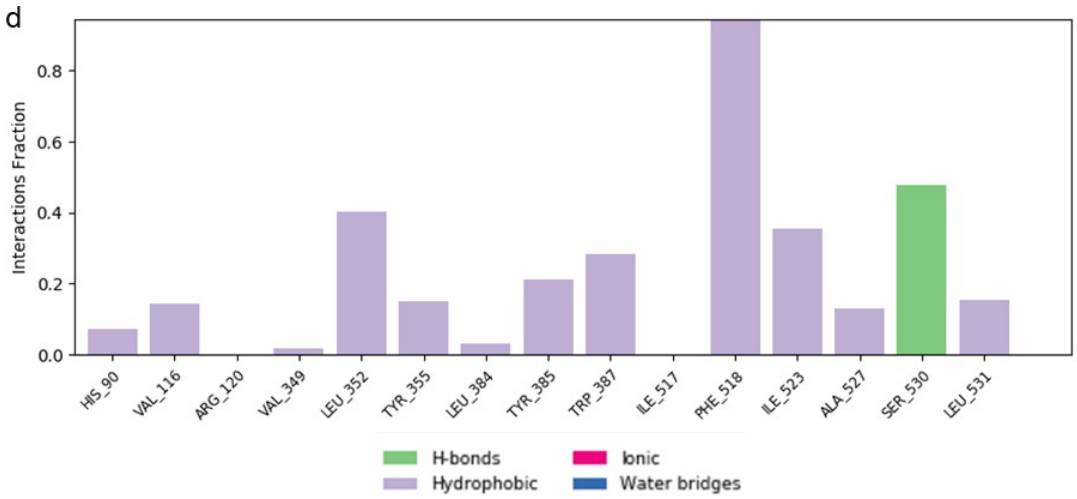
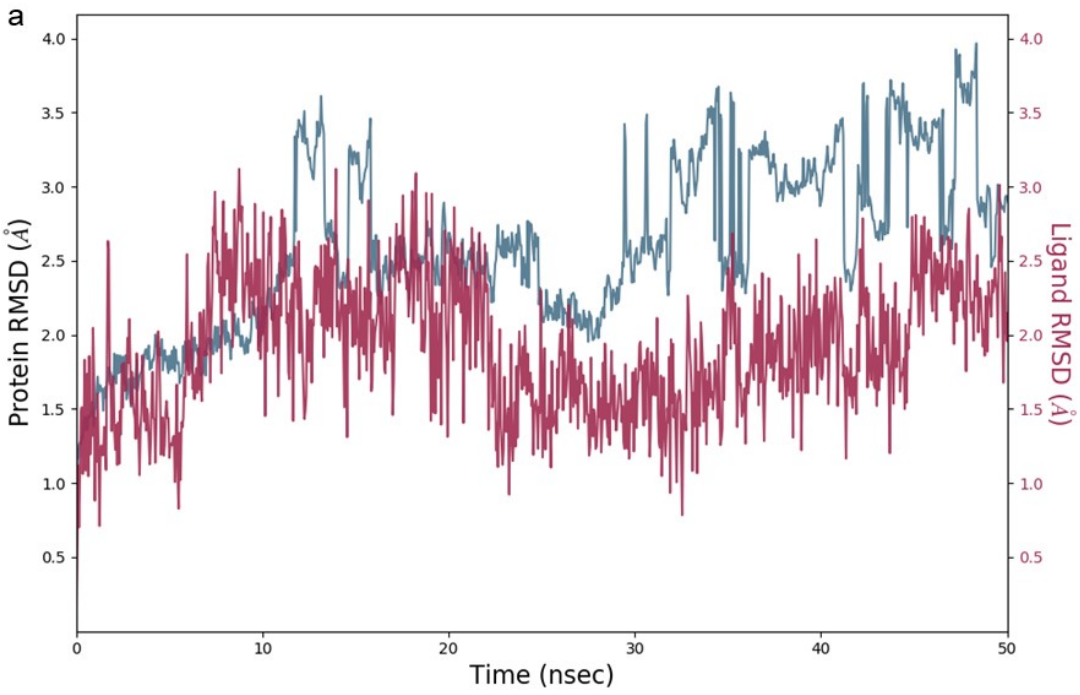


Fig. S4 Molecular dynamics simulations (MDS) of the ligand **15** – cyclooxygenase-1 protein complex. (a) Root-mean-square deviation of protein (azure) and ligand **15** (red signal). (b) Root mean squared fluctuation (RMSF) of the ligand **15** fitted on the protein (red line). The atom numbers of the compound (left) correspond to the RMSF plot X-axis (right). (c) 3D snapshots (left) from stable segments of MDS (Right). The interactions that occur more than 40.0% of the simulation time in the selected trajectory (0.00 through 50.05 nanoseconds). (d) Interaction diagram demonstrates the percentage interaction of the ligand **15** with surrounding residues.



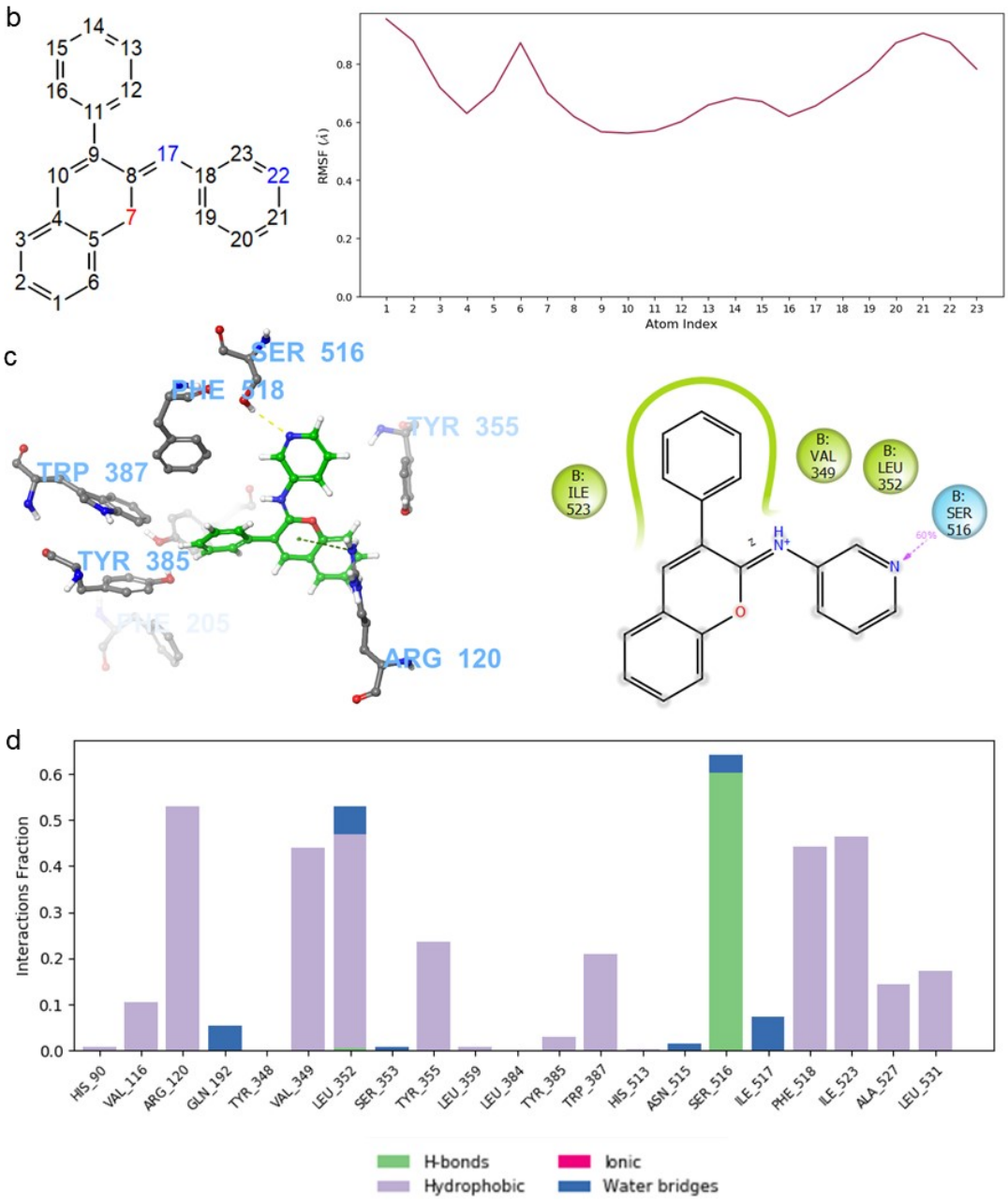


Fig. S5 Molecular dynamics simulations (MDS) of the ligand **20** – cyclooxygenase-1 protein complex. (a) Root-mean-square deviation (RMSD) of protein (azure) and ligand **20** (red signal). (b) Root mean squared fluctuation (RMSF) of the compound fitted on the protein (red line). The atom numbers of the ligand **20** (left) correspond to the RMSF plot X-axis (right). (c) 3D snapshots (left) from stable segments of MDS (Right). The interactions that occur more than 40.0% of the simulation time in the selected trajectory (0.00 through 50.05 nanoseconds). (d) Interaction diagram demonstrates the percentage interaction of the ligand **20** with surrounding residues.

Video. S1 The molecular dynamics simulations for ligand **10** – cyclooxygenase-1 protein. The trajectory showed mainly interactions of ligand **10** with Trp 387, Leu 352, Tyr 348 and Phe 518 residues.

Video. S2 The molecular dynamics simulations for ligand **1** in cyclooxygenase-1 protein. The trajectory showed mainly interactions of ligand **1** with Arg 120 residue.

Video. S3 The molecular dynamics simulations for ligand **14** in cyclooxygenase-1 protein. The trajectory showed mainly interactions of ligand **14** with Phe 518 residue.

Video. S4 The molecular dynamics simulations for ligand **15** in cyclooxygenase-1 protein. The trajectory showed mainly interactions of ligand **15** with Phe 518 residue.

Video. S5 The molecular dynamics simulations for ligand **20** in cyclooxygenase-1 protein. The trajectory showed mainly interactions of ligand **20** with Arg 120, Leu 352, Ser 516, Phe 518, and Ile 523 residues.