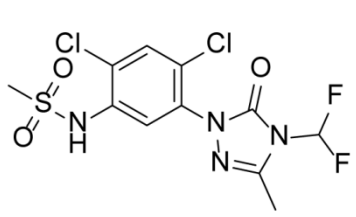
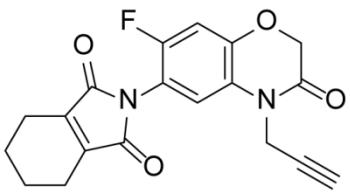
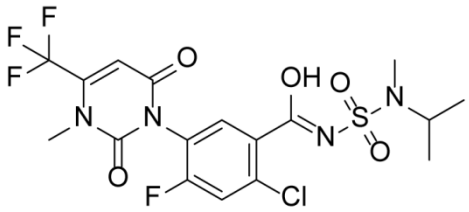


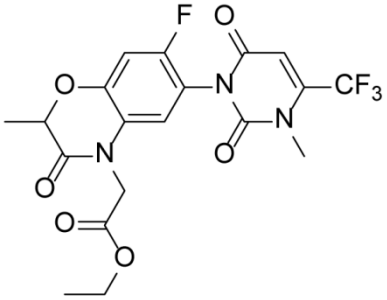
Sulfentrazone



Flumioxazin



Saflufenacil



Compound 10

Figure S1. The structure of commercialized PPO inhibitors and Compound 10

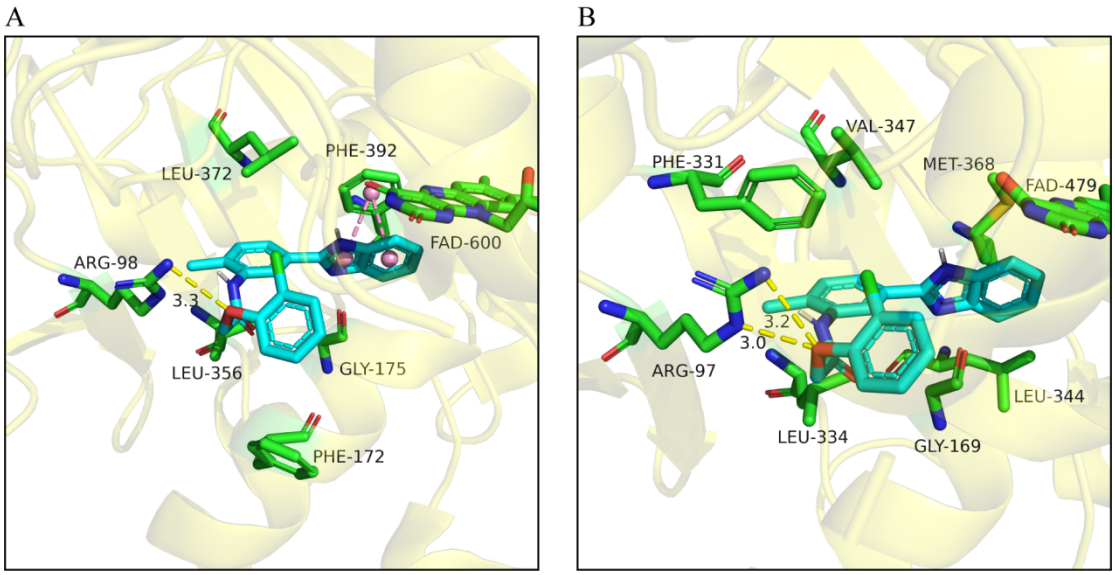


Figure S2. The binding modes of ZINC1150585 with ntPPO (A) and hPPO (C)

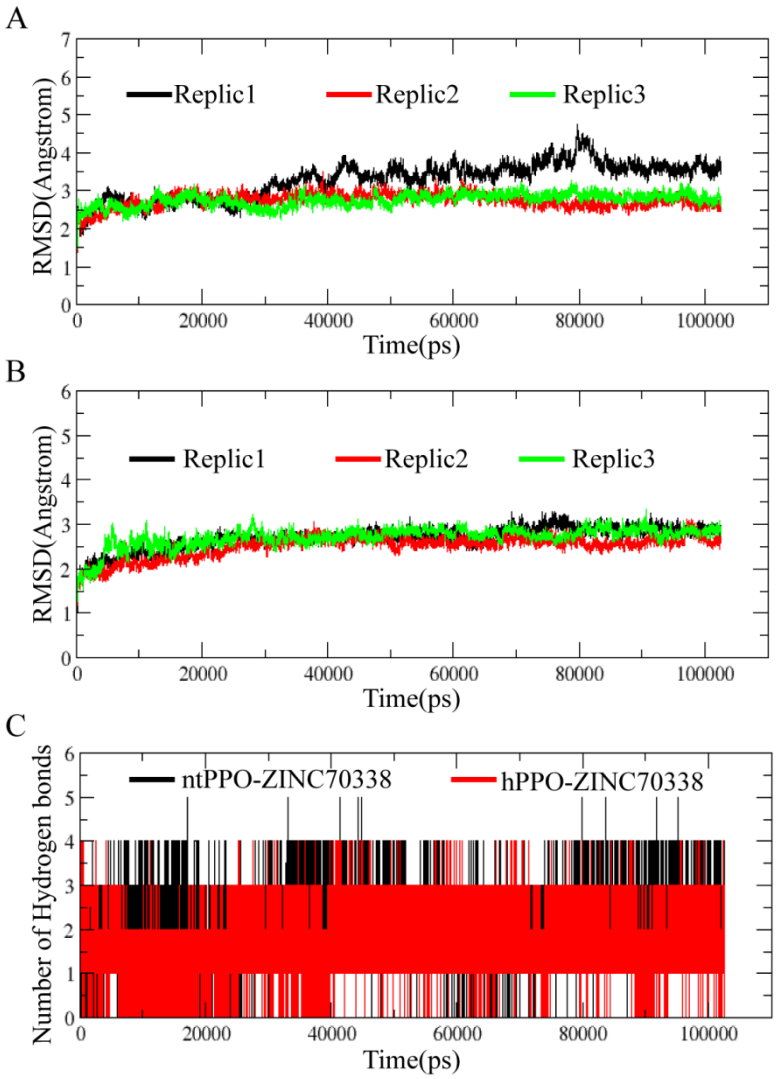


Figure S3. Root-mean-square deviations (RMSDs) of complexs of three replicas: A:ntPPO-ZINC70338; B:hPPO-ZINC70338; C: Inter molecular hydrogen bond numbers of protein-ligand complex.

Table S1. The virtual screening and molecular docking grid details (Docking Software, proteins, center points, grid size, and amino acid residues) of PPO.

Docking Software	Protein	Cavity	Center Points			Grid size (Å)			Molecular grid amino acid residues
			X	Y	Z	X	Y	Z	
Autodock Vina/ Surflex	hPPO	Active sites	-26.42	3.54	48.37	20	20	20	ARG97、GLY169、VAL170、VAL314 PHE331、LEU334、LEU344、VAL347 MET368
		Substrate conduction channel	25.93	-2.39	57.34	20	20	20	VAL146、ALA150、LEU154、VAL158 ALA159、ALA162、MET163、ASP164 LEU166、CYS167、PHE184、LEU187
	ntPPO	Active sites	-39.91	-6.2	28.68	20	20	20	ARG98、PHE172、GLY175、THR176 LEU334、PHE353、LEU356、LEU369 LEU372、PHE392
		Substrate conduction channel	44.08	3.76	42.46	20	20	20	VAL152、SER153、PHE156、PHE160 LYS162、VAL164、VAL165、LEU168 ILE169、ASP170、PRO171、PHE190

Table S2. The physical characteristics of the other 11 selected compounds

Compound	MW	HBD	HBA	ROB	HA	LogPo/w	TPSA
ZINC649024	371.47	1	2	6	28	5.426	38.33
ZINC2078708	415.87	0	4	6	30	5.735	56.26
ZINC836537	438.27	1	4	8	28	4.086	72.47
ZINC16023063	418.51	0	3	4	30	4.338	66.07
ZINC4680768	381.44	1	2	5	29	6.053	29.10
ZINC887010	415.51	1	4	7	30	5.196	89.41
ZINC2079610	409.48	1	3	8	31	5.260	55.40
ZINC6147185	398.45	2	4	8	28	3.498	83.65
ZINC10311685	336.41	0	4	5	24	4.298	80.55
ZINC686711	403.42	1	6	7	28	4.728	80.18
ZINC1069729	420.89	2	3	5	30	3.811	83.63

Table S3. The average RMSD, RMSF, RoG, SASA of ZINC70338 binding with ntPPO and hPPO of three replicas

Complexes	Repeat times	RMSD (Å)	RMSF (Å)	RoG (Å)	SASA ($Å^2$)
ntPPO-ZINC70338	1	3.28	7.17	23.53	20416.53
	2	2.74		23.77	20815.10
	3	2.75		23.63	20284.33
hPPO-ZINC70338	1	2.70	8.88	22.62	21221.31
	2	2.51		22.69	21595.34
	3	2.71		22.67	21382.71

Table S4. The average values of each energy of binding free energy (kcal/mol)

Complexes	contributions						ΔG_{bind}
	ΔE_{vdw}	ΔE_{ele}	ΔE_{GB}	ΔE_{surf}	ΔE_{MM}	ΔE_{sol}	
ntPPO-ZINC70338	-49.52	-41.74	47.12	-4.39	-91.26	42.73	-48.53
hPPO-ZINC70338	-45.84	-30.80	42.87	-4.04	-76.64	38.82	-37.82

Table S5. The residue decomposition analysis of ntPPO-ZINC70338 (kcal/mol)

Residue	Van der Waals	Polar	Non-Polar Solv	Total
ARG 98	-1.52	-2.58	-0.22	-4.32
PHE 172	-1.42	0.00	-0.18	-1.59
GLY 175	-1.96	-1.91	-0.22	-4.10
THR 176	-1.68	0.44	-0.08	-1.32
LEU 334	-0.74	-0.05	-0.04	-0.84
PHE 353	-1.17	0.31	-0.07	-0.93
VAL 355	-0.51	-0.15	0.00	-0.67
LEU 356	-1.77	0.14	-0.15	-1.78
THR 371	-0.56	0.11	-0.02	-0.47
LEU 372	-1.60	-0.52	-0.10	-2.21
PHE 392	-2.39	-0.22	-0.15	-2.76
FAD	-1.82	0.73	-0.14	-1.23

Table S6. The residue decomposition analysis of hPPO-ZINC70338 (kcal/mol)

Residue	Van der Waals	Polar	Non-Polar Solv	Total
ARG 97	-2.15	-0.80	-0.23	-3.18
LEU 166	-0.87	0.10	-0.10	-0.86
GLY 169	-1.49	-1.81	-0.16	-3.46
VAL 170	-1.80	0.51	-0.13	-1.42
VAL 314	-0.38	0.01	-0.02	-0.39
PHE 331	-1.72	0.20	-0.14	-1.66
HIS 333	-0.76	-0.13	-0.01	-0.90
LEU 334	-1.90	0.09	-0.15	-1.95
ILE 346	-0.45	-0.13	0.00	-0.58
VAL 347	-0.89	-0.48	-0.06	-1.43
MET 368	-1.35	0.15	-0.12	-1.32
FAD	-2.14	0.49	-0.17	-1.82