

HPC-C2  
 Pulse Sequence: zgpg30  
 Solvent: DMSO  
 Ambient Temperature  
 CTR11-26926 "Gcmln300"  
 Relax. delay 2.930 sec  
 Pulse pr 9 degrees  
 Acq. time 1.930 sec  
 Width 489.1 Hz  
 SS repetitions  
 DQ1 (1) 360.0722571 MHz  
 DQ 1A PULPROG30  
 Kernel enhancement 1.6 Hz  
 Cause modification C 239 sec  
 FT size 52768  
 Total time 2 min, 10 sec

Pulse Sequence: zgpg1  
Solvent: DMSO  
Acquire temperature:  
CEMINT-200BS 7mm/ni300H

Relax. delay 5.000 sec  
Pulse 46.0 degrees  
Acq. time 1.066 sec  
Width 17500.0 Hz  
256 repetitions  
9.383 MHz 175.000 degrees  
F1 125.000 MHz  
VOLTAGE-16 modulated  
DATA PROCESSING  
Line broadening 2.0 Hz  
F size 131072  
Total time 6 hr. 25 min. 17 sec

The NMR spectrum displays several distinct peaks against a noisy baseline. The x-axis represents the chemical shift in ppm, ranging from approximately 180 to 0. Key peaks are labeled with their corresponding chemical shift values.

Chemical Shift (ppm)
176.192
176.006
171.076
156.891
156.882
156.493
138.349
134.428
119.535
44.334
46.379
23.286
22.905
21.422

Figure S2. The  $^{13}\text{C}$ -NMR spectra of N-(1,3-dioxohexahydro-1*H*-isoindol-2(3*H*)-yl)-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)acetamide (Compound **2**)





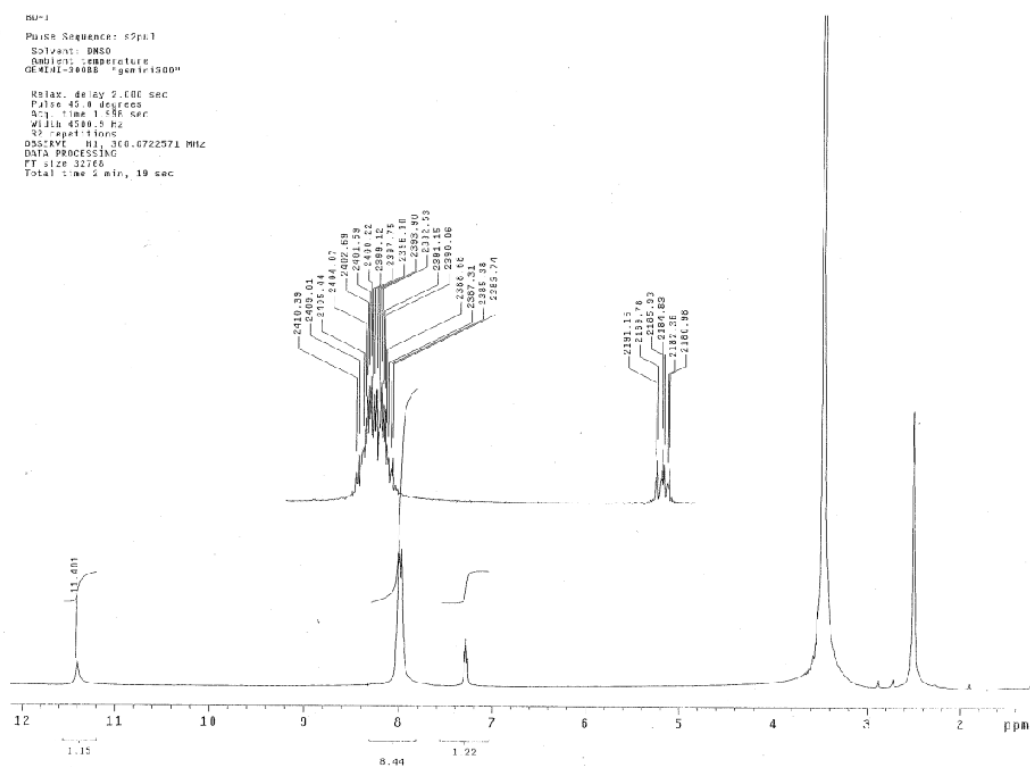


Figure S7. The  $^1\text{H}$ -NMR spectra of N-(1,3-dioxoisindol-2-yl)thiophene-2-carboxamide (Compound **1b**)

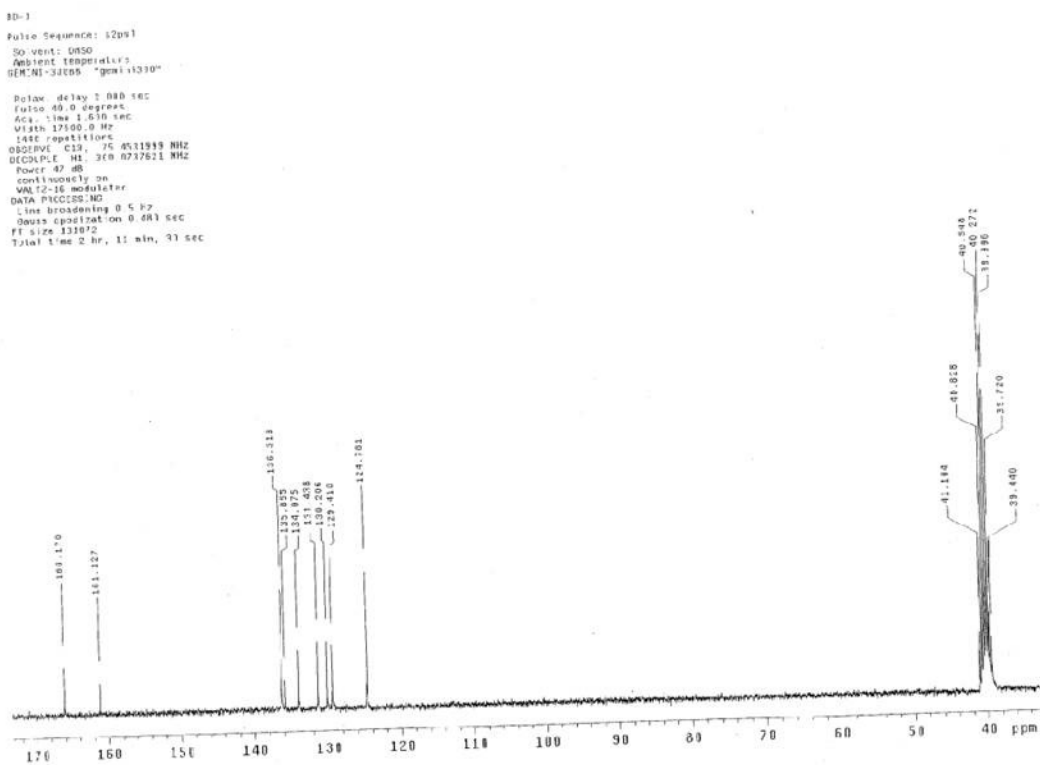


Figure S8. The  $^{13}\text{C}$ -NMR spectra of N-(1,3-dioxoisindol-2-yl)thiophene-2-carboxamide (Compound **1b**)

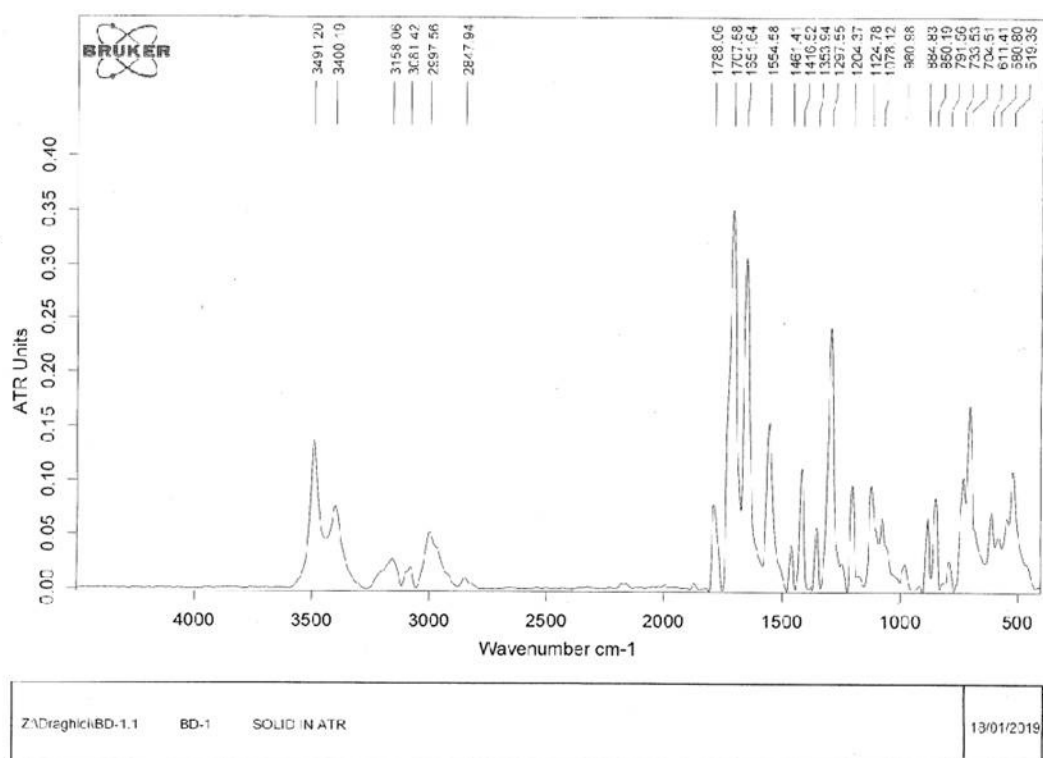


Figure S9. The FT-IR spectra of N-(1,3-dioxisoindol-2-yl)thiophene-2-carboxamide (Compound **1b**)

Here, we will discuss the 2D interactions of compounds 1a, 1b, and 2 with the three proteins we have chosen as our targets: NF-KB, COX-2, and MAO-B.

Compound 1a interacts with the AA residues ARG 57, ARG 59, HIS 67, GLY 68, and ILE 142 of NF-KB in a conventional hydrogen bond manner (Figure 1 S.M.).

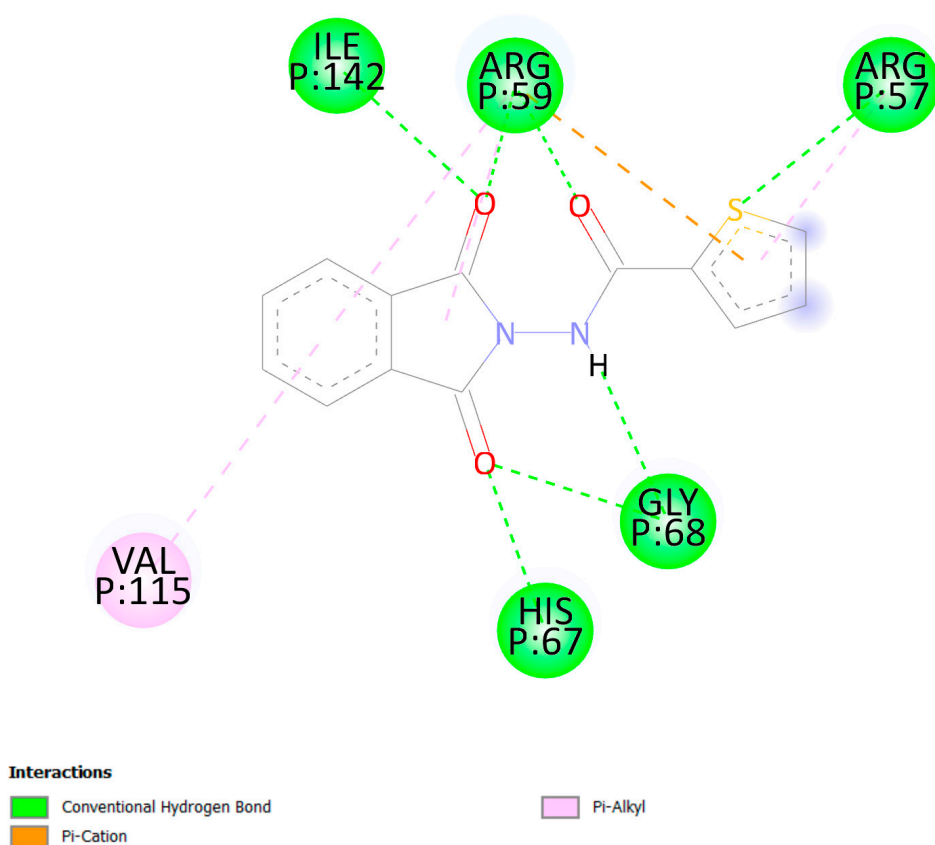
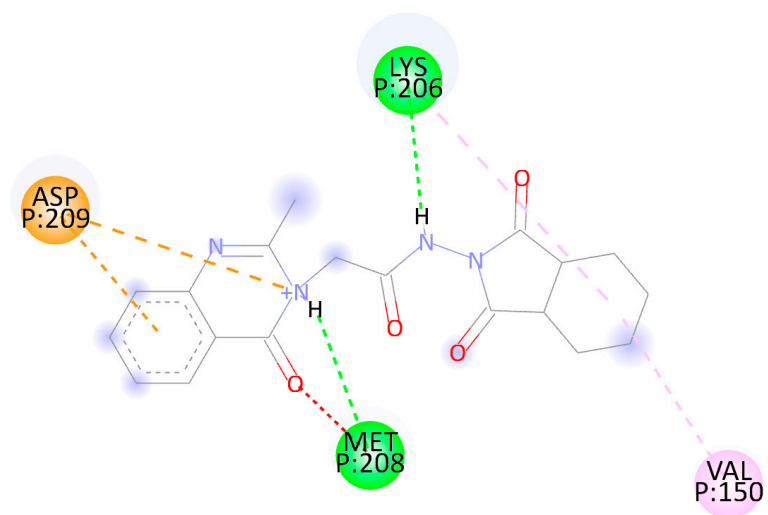


Figure S10. The 2D interaction between NF-KB and compound **1a**

Compound 1b forms conventional hydrogen bond interactions with AA residues LYS 206 and MET 208 of NF-KB (Figure 2 S.M.)



#### Interactions






	Attractive Charge		Pi-Anion
	Conventional Hydrogen Bond		Alkyl
	Unfavorable Acceptor-Acceptor		

Figure S11. The 2D interaction between NF-KB and compound **1b**

Compound 2 forms conventional hydrogen bond interactions with AA residue MET 208 of NF-KB (Figure 3 S.M.)

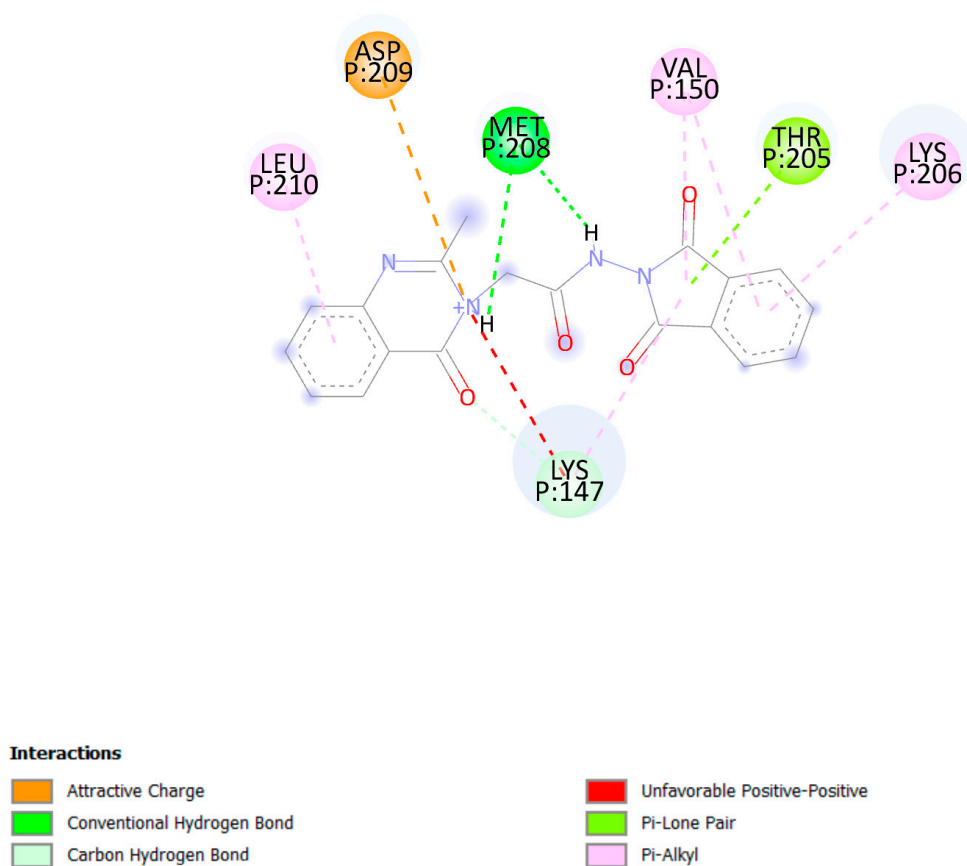


Figure S12. Interaction between NF-KB and compound **2**

Similar interactions are formed by compound 1b and compound 2 with AA residue MET 208 suggesting a similar potential interaction site.

Compound 1a forms conventional hydrogen bond interactions with AA residues ASP125, THR129, and ARG 469 of COX-2 (Figure 4 S.M.).

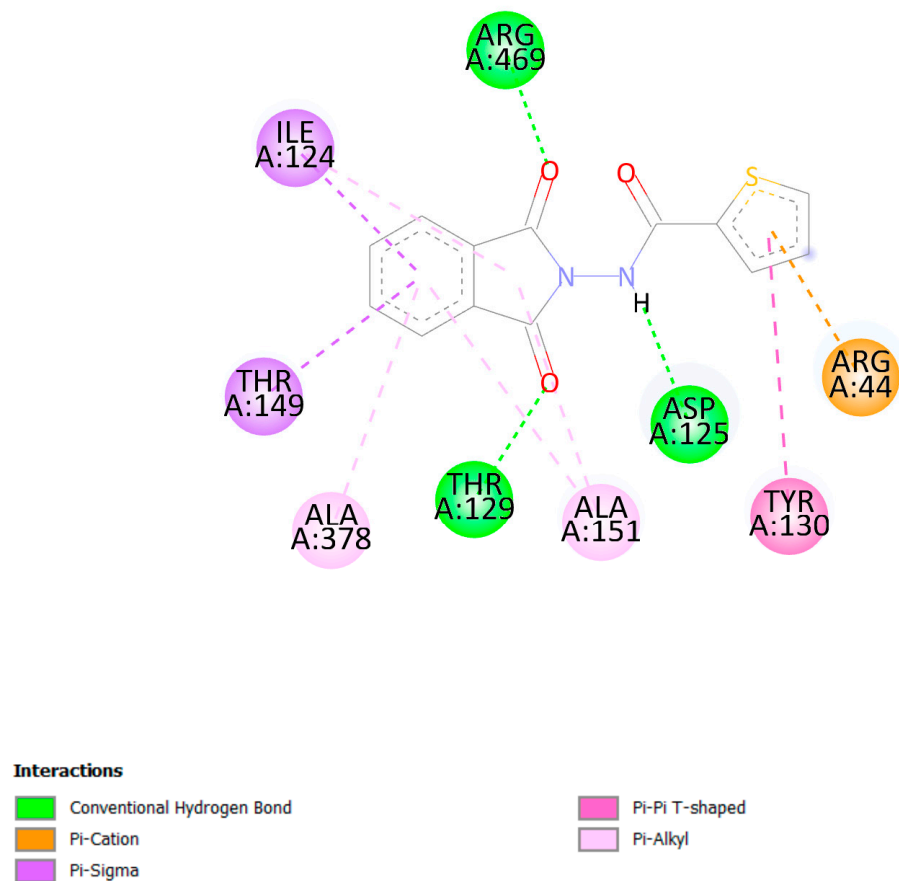


Figure S13. Interaction between COX-2 and compound **1a**

Compound **1b** forms conventional hydrogen bond interactions with AA residues HIS 39, CYS 41, CYS47, and GLN 461of COX-2 (Figure 5 S.M.).

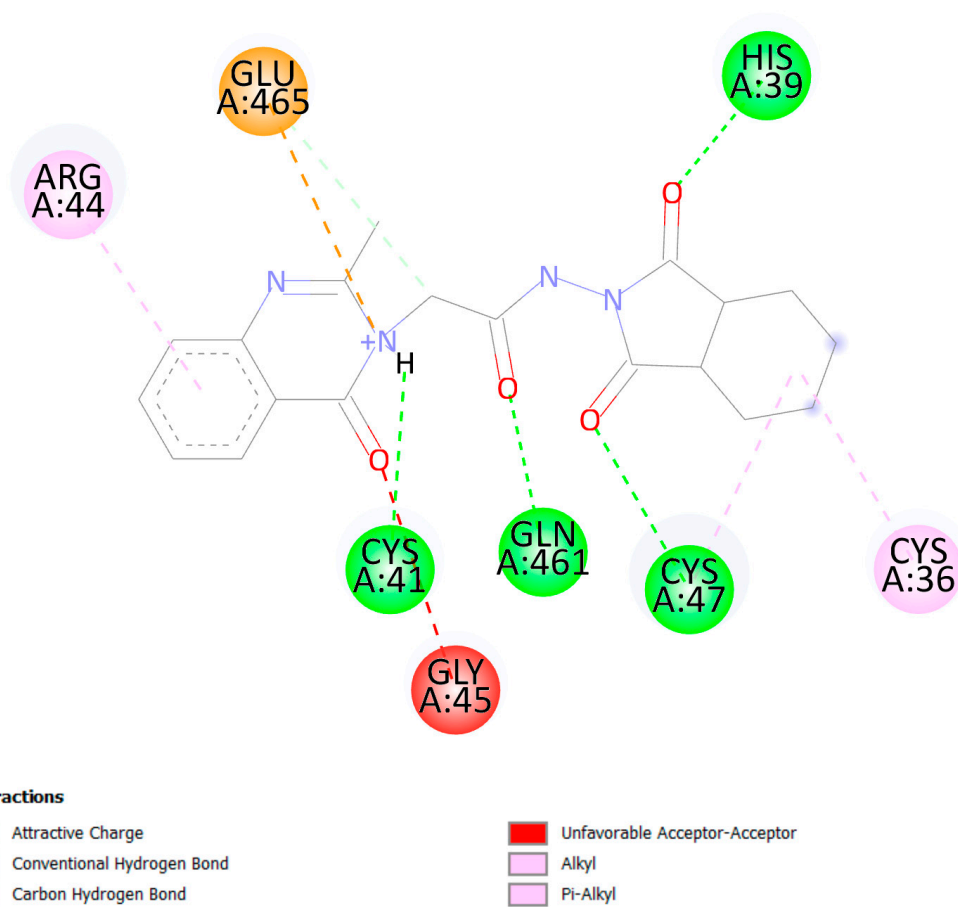


Figure S14. Interaction between COX-2 and compound **1b**

Compound 2 forms conventional hydrogen bond interactions with AA residues CYS 41, CYS 42, and LYS 468 of COX-2 (Figure 6 S.M.).

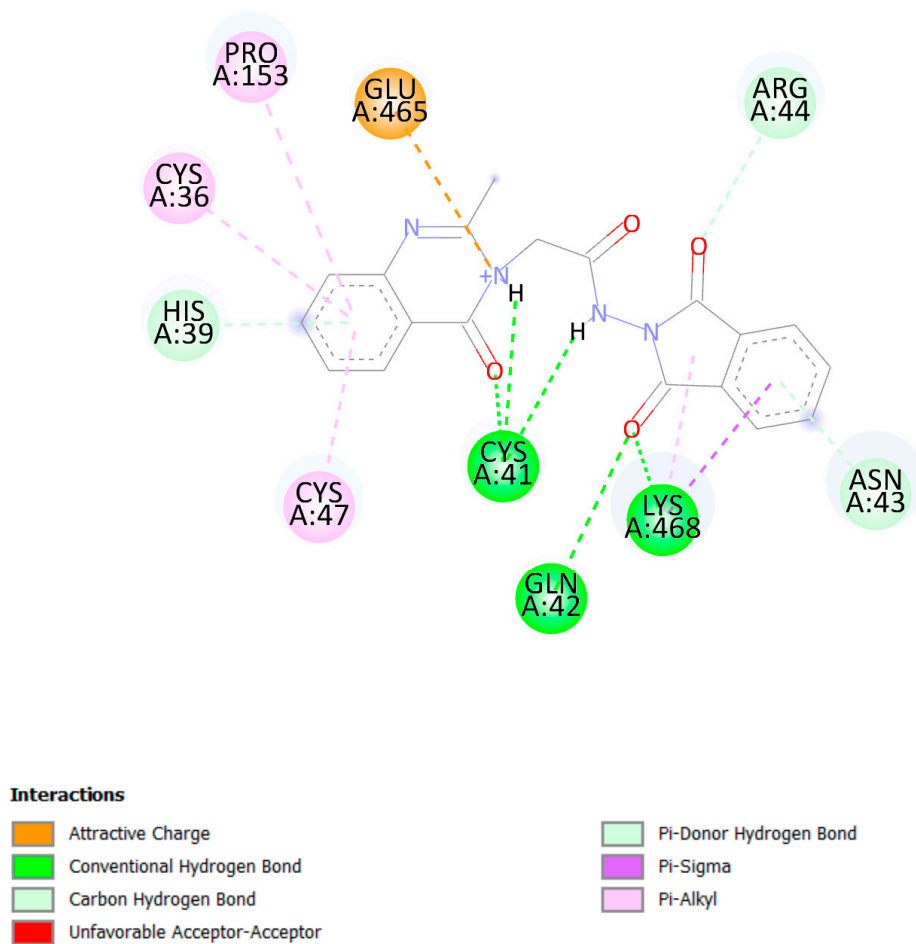
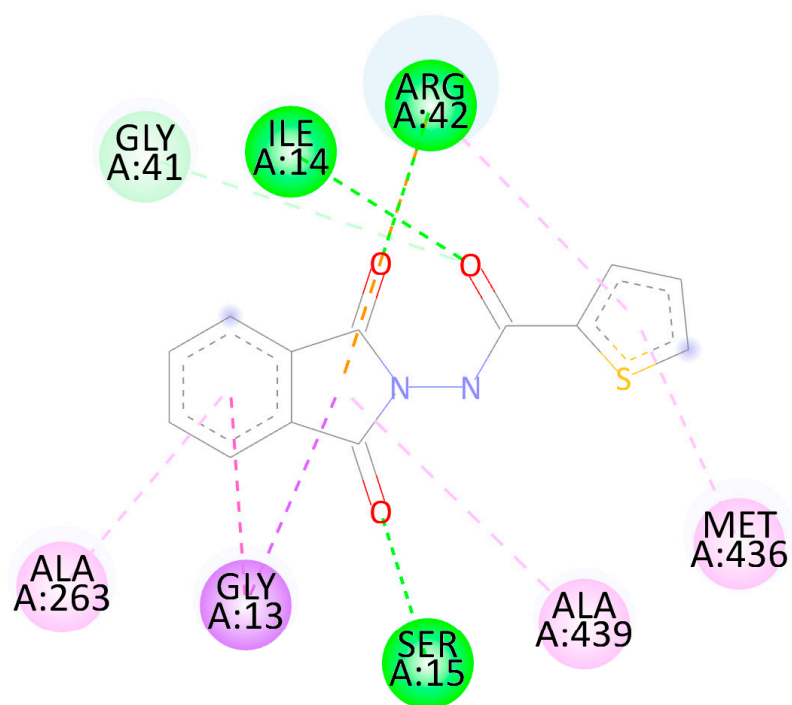


Figure S15. Interaction between COX-2 and compound 2

The similar interactions that compound 1b and 2 have with the AA residue CYS 41 suggest the potential of a similar interaction mechanism at this specific location within the molecular structure.

Compound 1a forms conventional hydrogen bond interactions with AA residues ILE14, SER 15, and ARG 42 of MAO-B (Figure 7 S.M.).



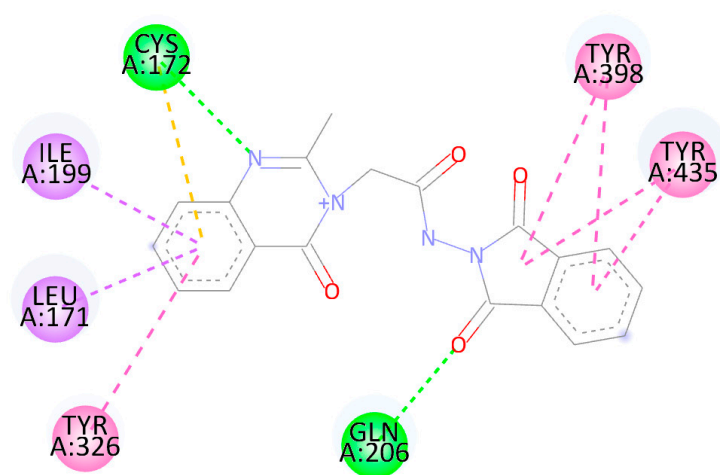
#### Interactions

- Conventional Hydrogen Bond
- Carbon Hydrogen Bond
- Pi-Cation

- Pi-Sigma
- Amide-Pi Stacked
- Pi-Alkyl

Figure S16. Interaction between MAO-B and compound **1a**

Compound 2 forms conventional hydrogen bond interactions with AA residues CYS 172, and GLN 206 of MAO-B (Figure 8 S.M.).



#### Interactions

■ Conventional Hydrogen Bond  
■ Pi-Sigma  
■ Pi-Sulfur

■ Pi-Pi Stacked  
■ Pi-Pi T-shaped

Figure S17. Interaction between MAO-B and compound 2