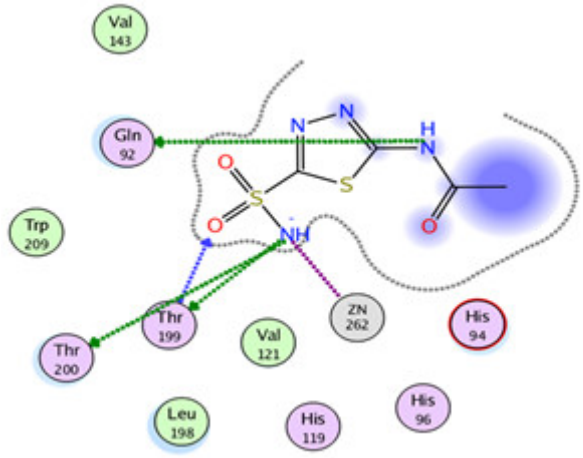
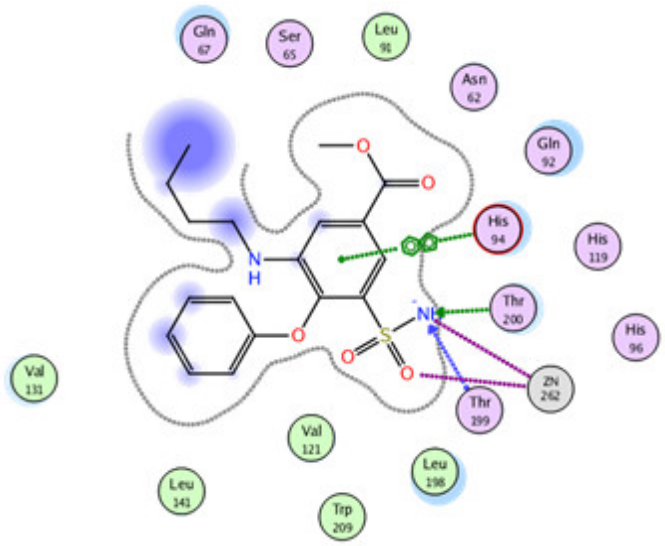
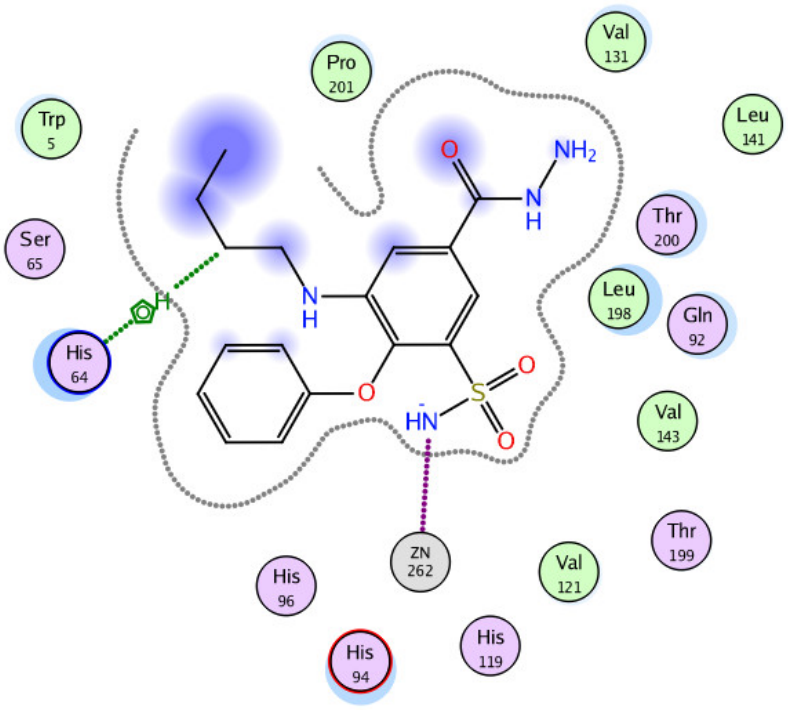
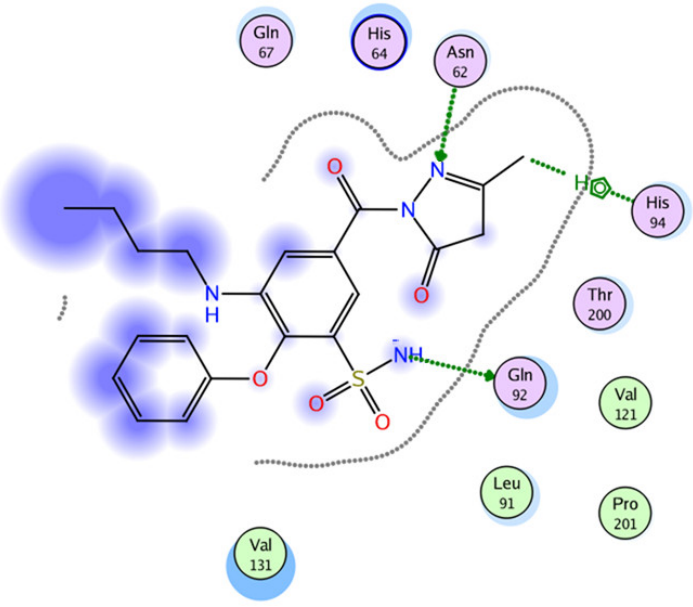
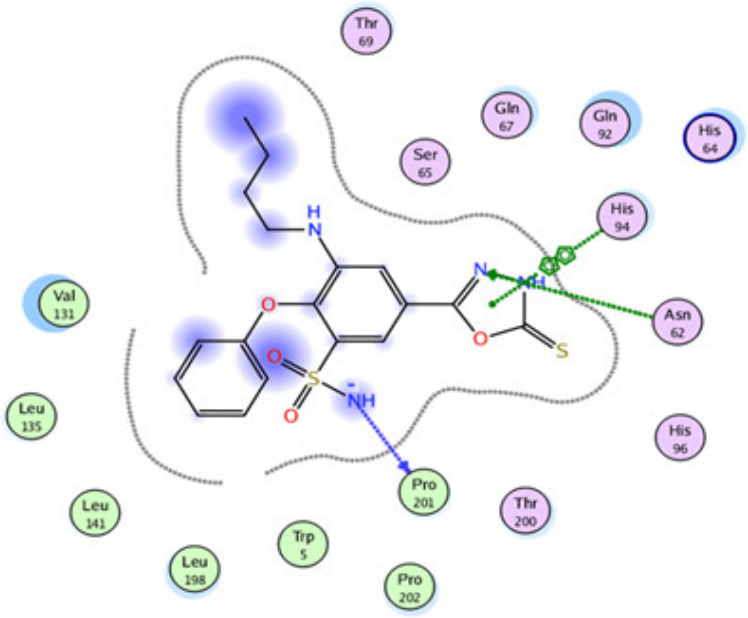
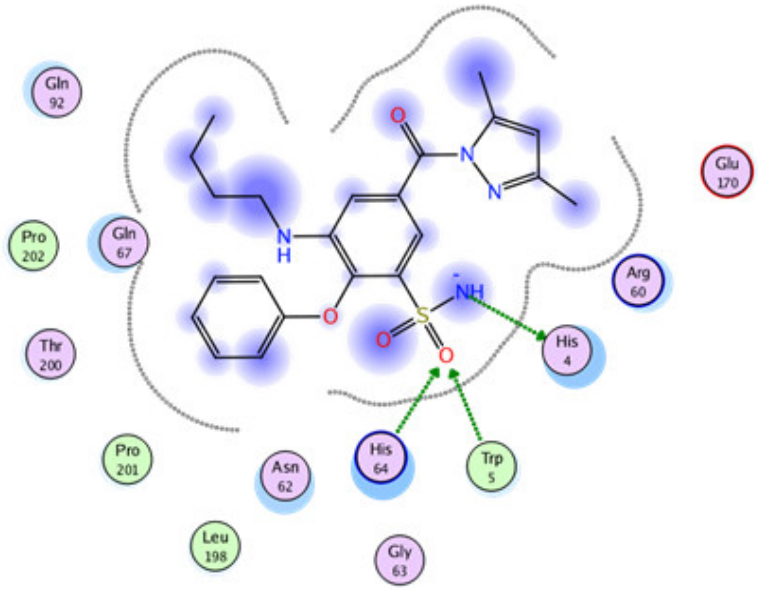
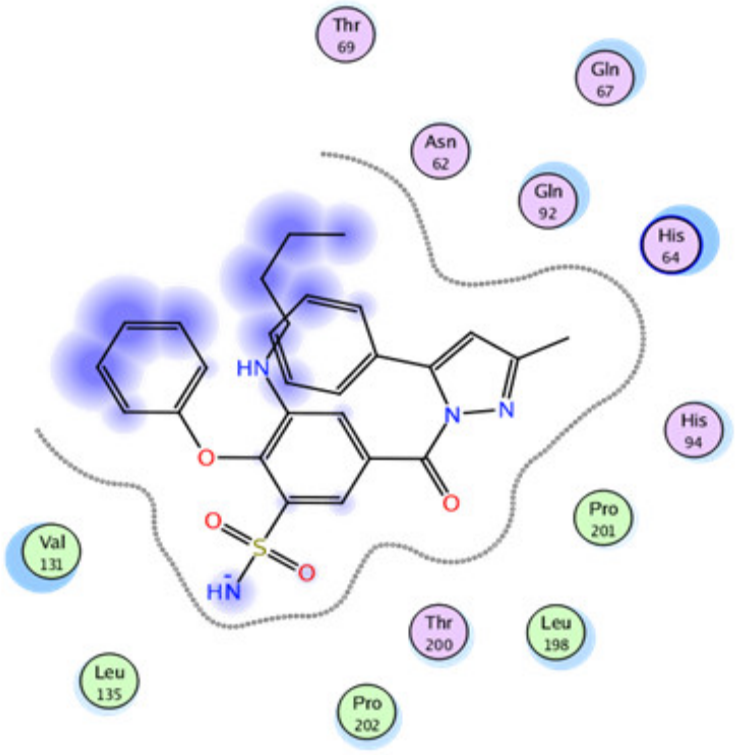
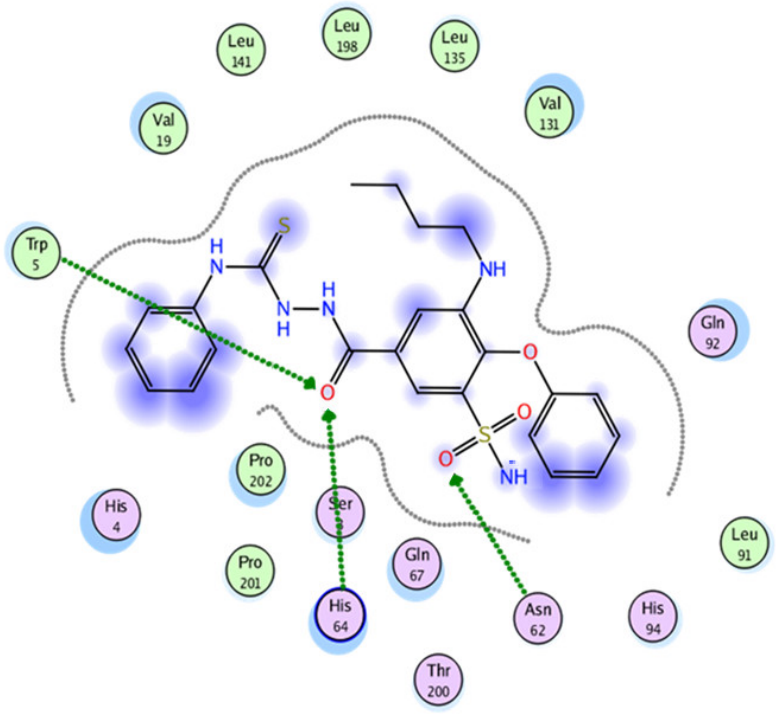
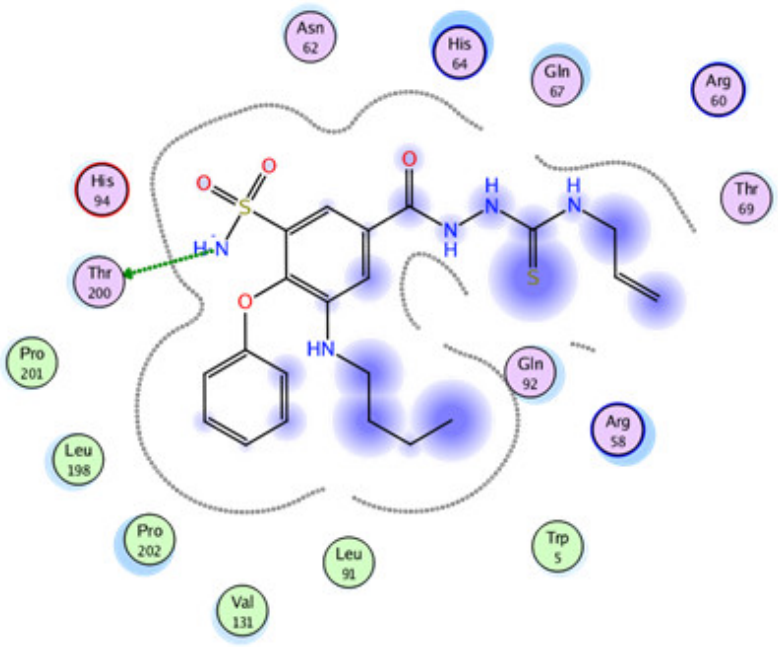
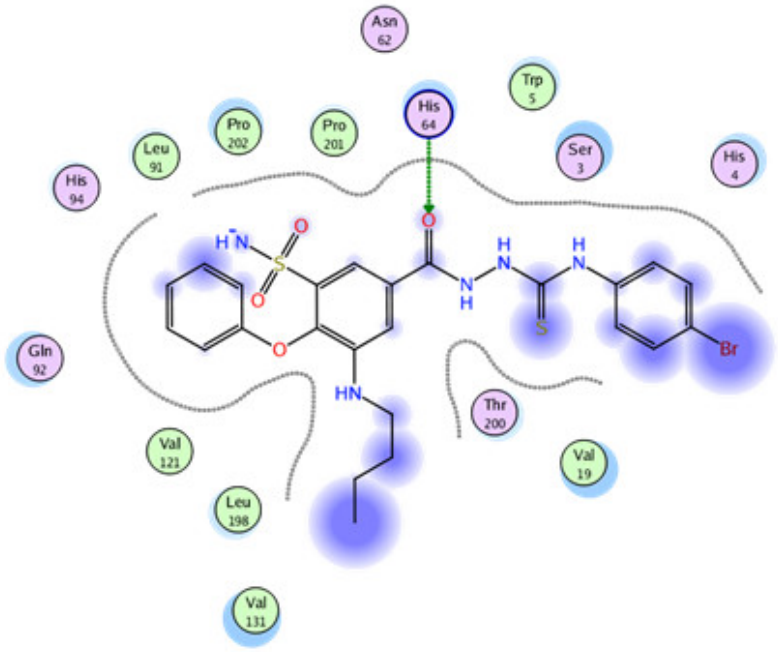
Table S1: Data of the virtula docking simulations conducted for the bumetanide compounds against the human carbonic anhydrase isozyme-type IX

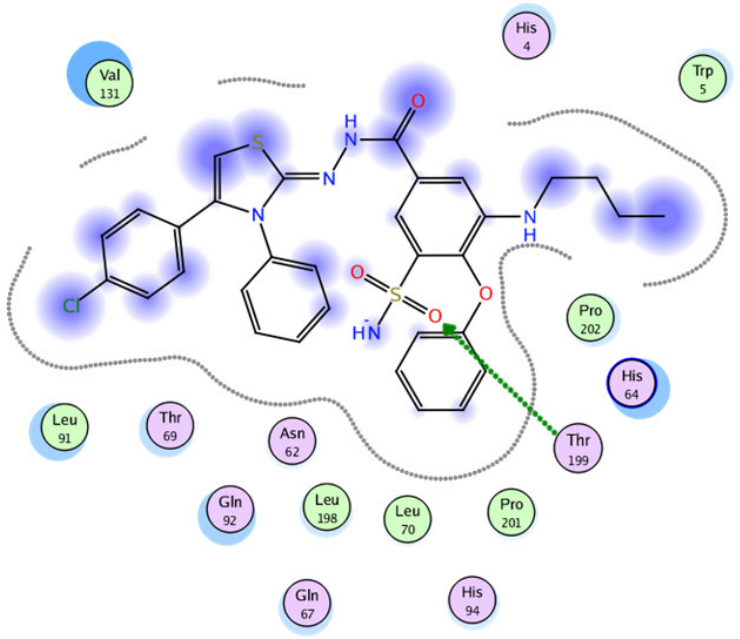
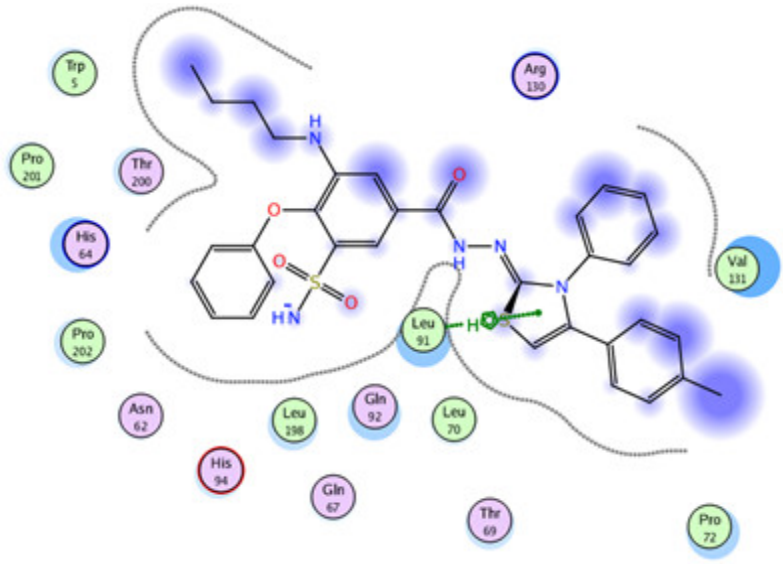
Docked Ligand	MOE (S) [a] (Kcal/moL)	RMSD [b] (Å)	Ligand-target interaction descriptions [c] [Type of Interactions; Length (Å); Angle (°); Interacting Residues]
Crystallized Ligand (Redocked)	-2.1678	2.07	 Coordination **;** 2.9 **Å ;** ZnII prosthetic group H-bonding **;** 2.4 **Å ;** 110.7° **;** Thr-200 (Side chain **–O**H) H-bonding **;** 1.9 **Å ;** 140.5° **;** Thr-199 (Side chain **–O**H) H-bonding **;** 2.0 **Å ;** 146.6° **;** Thr-199 (Side chain **–O**H) H-bonding **;** 2.5 **Å ;** 120° **;** Gln-92 (Side chain –C(**O**)NH–)
Ligand 2	-5.2332	1.99	 Coordination **;** 3.7 **Å ;** ZnII prosthetic group Coordination **;** 3.2 **Å ;** ZnII prosthetic group H-bonding **;** 2.1 **Å ;** 110.7° **;** Thr-199 (Side chain **–O**H) H-bonding **;** 2.2 **Å ;** 110.7° **;** Thr-200 (Side chain –O**H**) Arene-Arene interaction **;** 2.6 **Å ;** His-94

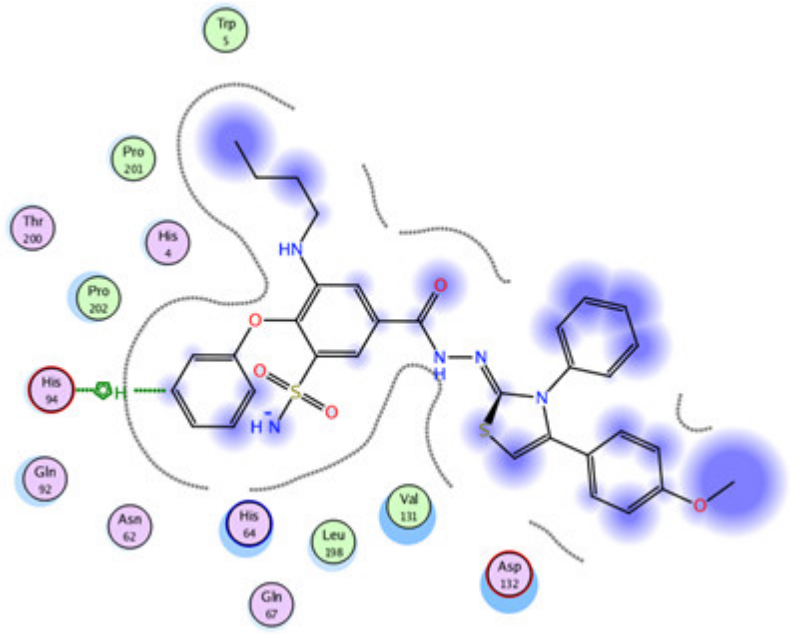
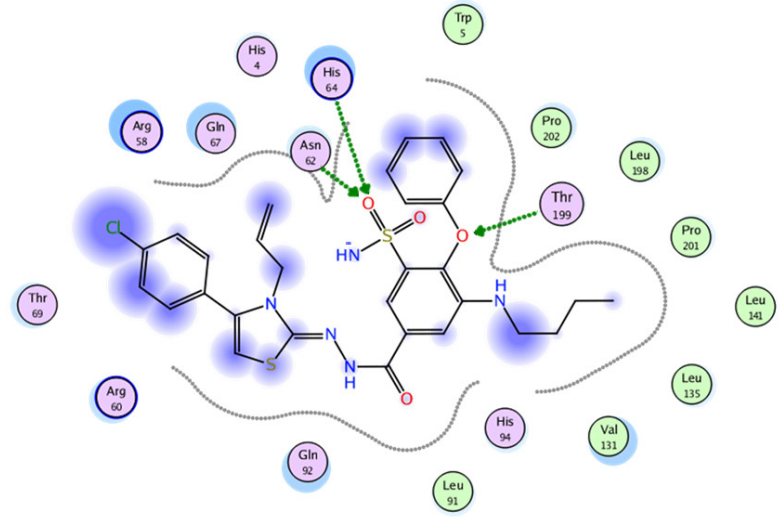
Ligand 3	-5.0587	1.80	 Coordination ; 3.0 **Å** ; ZnII prosthetic group Arene-Hydrogen interaction ; 3.7 **Å** ; His-94
Ligand 4	-4.6697	3.09	 Hydrogen bonding ; 2.5 **Å** ; 113.1° ; Asn-62 (Side chain –NH**H**) Hydrogen bonding ; 1.9 **Å** ; 160.8° ; Gln-92 (Side chain –**N**H$_2$) Arene-Hydrogen interaction ; 3.2 **Å** ; His-94

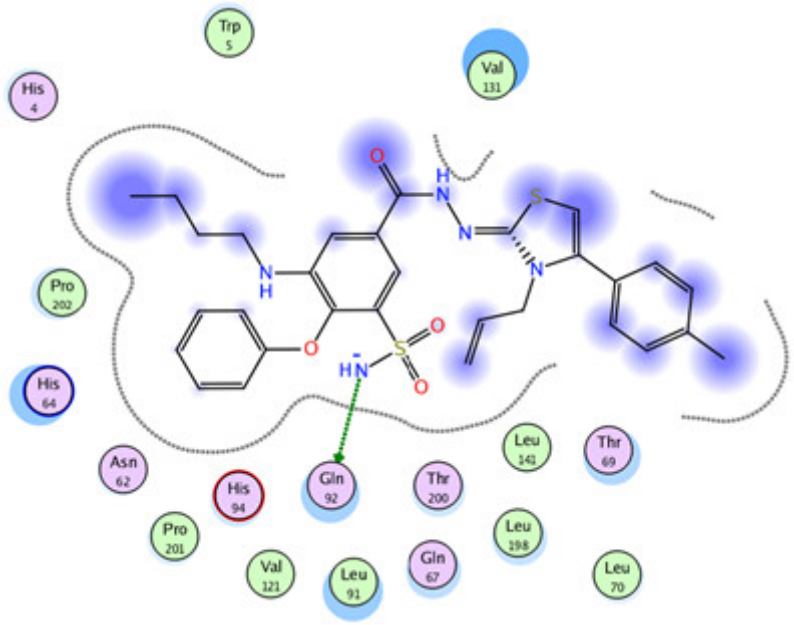
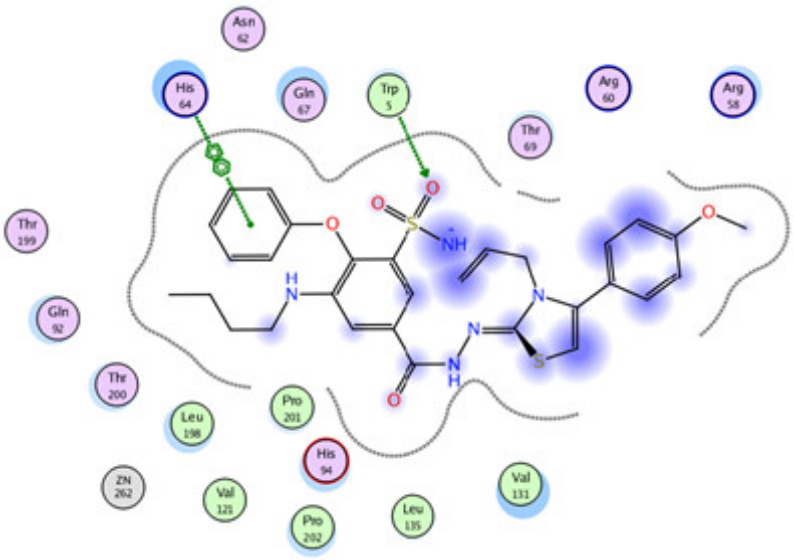
Ligand 5	-5.1975	2.36	 Hydrogen bonding ; 2.1 **Å** ; 135.2° ; Asn-62 (Side chain –NH**H**) Hydrogen bonding ; 2.3 **Å** ; 148.9° ; Pro-201 (Main chain –C(**O**)NH–) Arene-Arene interaction ; 3.2 **Å** ; His-94
Ligand 6a	-5.0228	1.64	 Hydrogen bonding ; 2.3 **Å** ; 159.8° ; His-4 (Side chain =**N**) Hydrogen bonding ; 2.2 **Å** ; 134.2° ; His-64 (Side chain –N**H**) Hydrogen bonding ; 2.4 **Å** ; 131.3° ; Trp-5 (Side chain –N**H**)

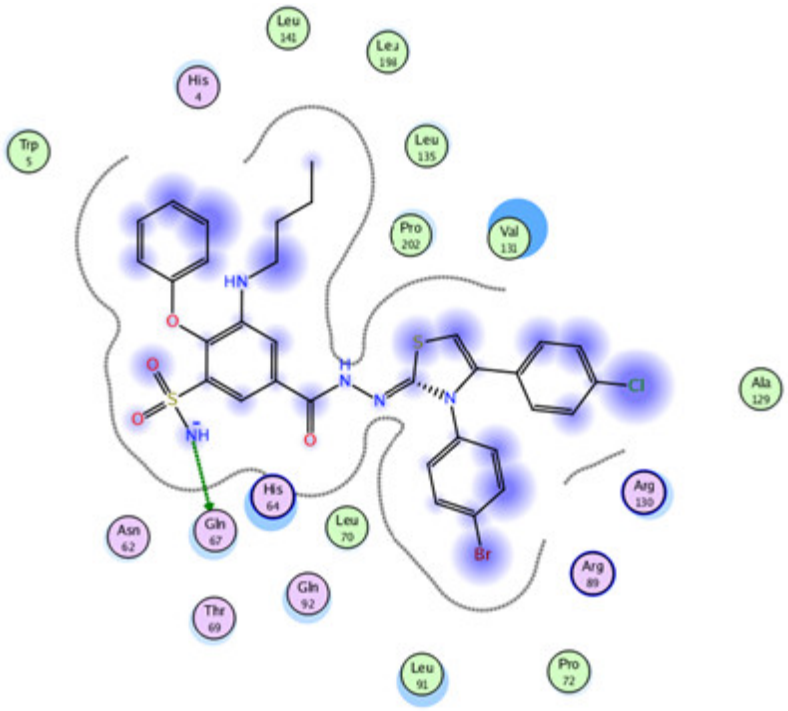
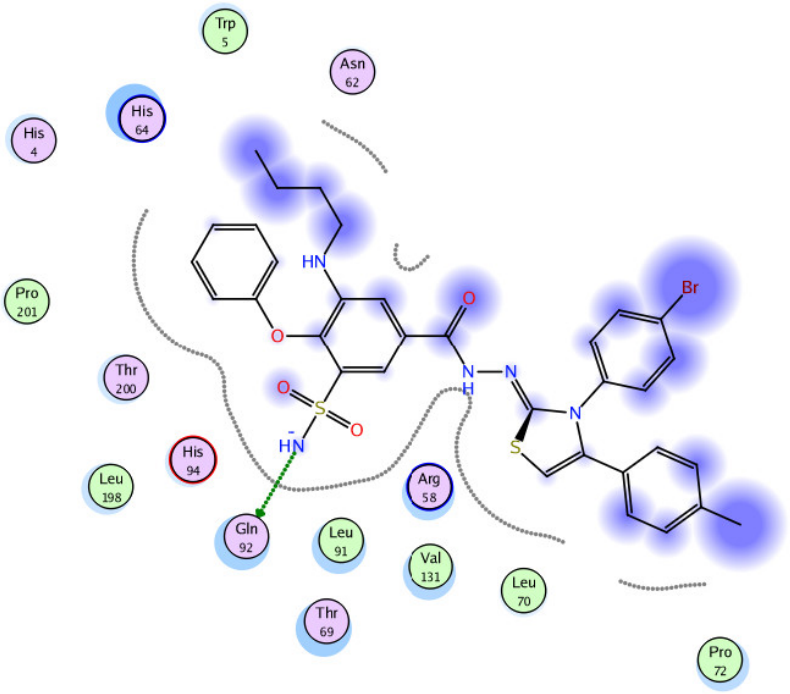
Ligand 6b	-4.8280	2.01	
Ligand 7a	-6.2632	1.56	 Hydrogen bonding ; 2.7 **Å** ; 107.1° ; Asn-62 (Side chain –NH**H**) Hydrogen bonding ; 2.4 **Å** ; 108.2° ; His-64 (Side chain –N**H**) Hydrogen bonding ; 3.2 **Å** ; 132.7° ; Trp-5 (Side chain –N**H**)

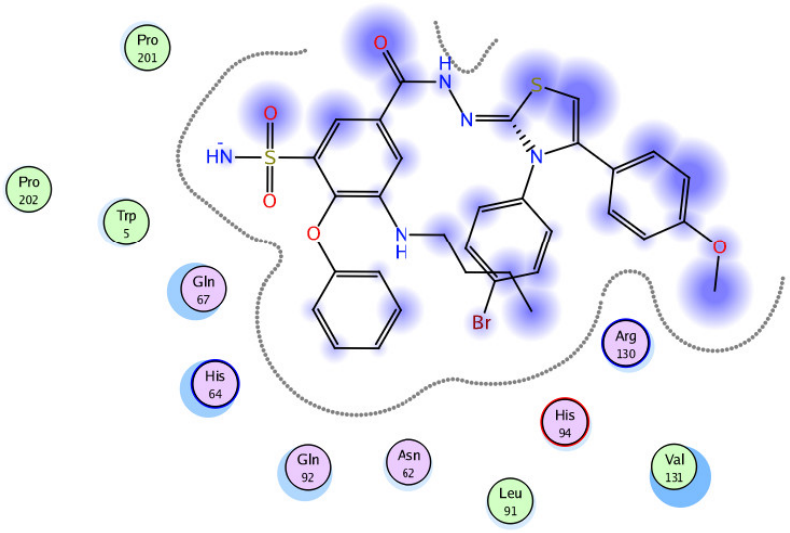
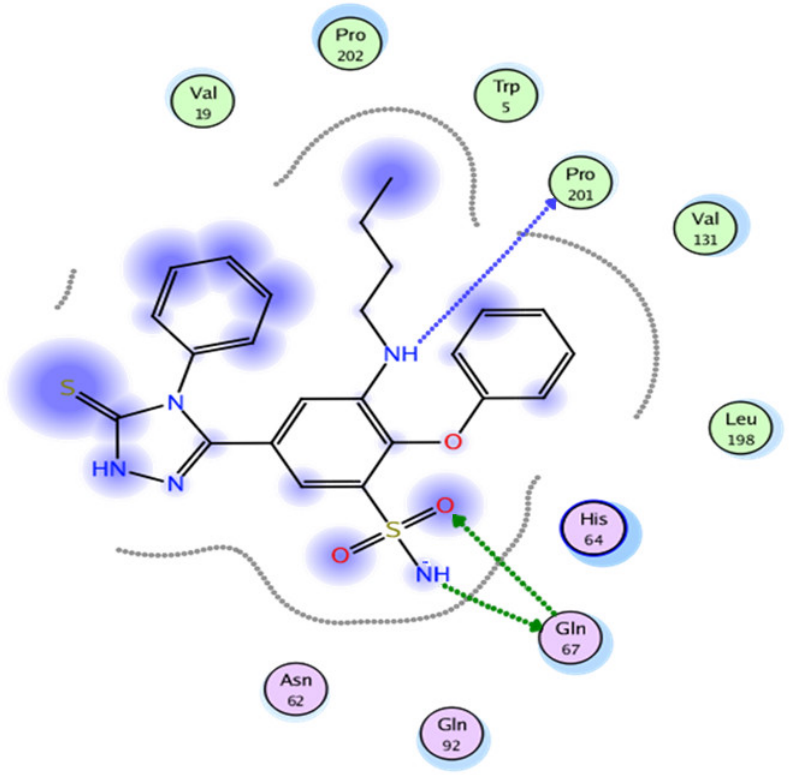
Ligand 7b	-5.2799	3.37	 Hydrogen bonding ; 2.5 **Å** ; 137.4° ; Thr-200 (Side chain –**O**H)
Ligand 7c	-5.8080	1.81	 Hydrogen bonding ; 2.3 **Å** ; 119.3° ; His-64 (Side chain –N**H**)

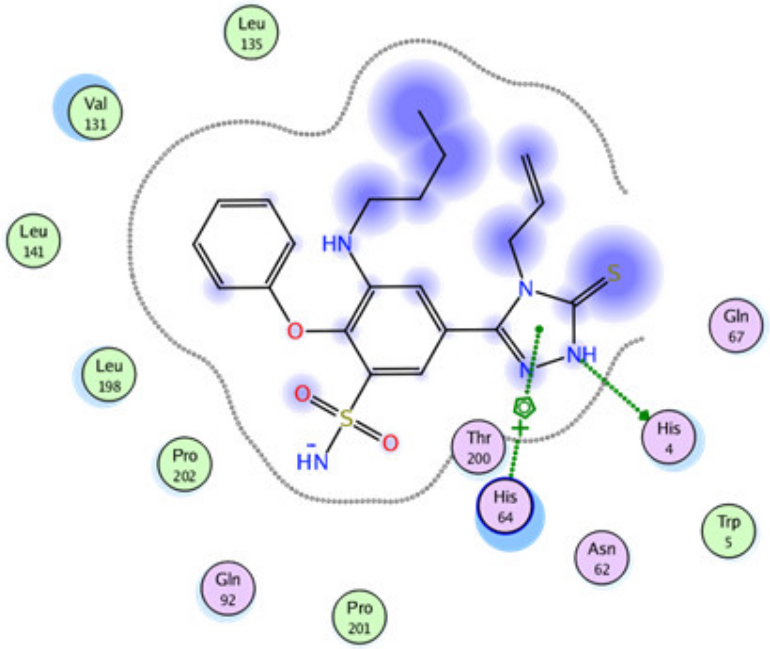
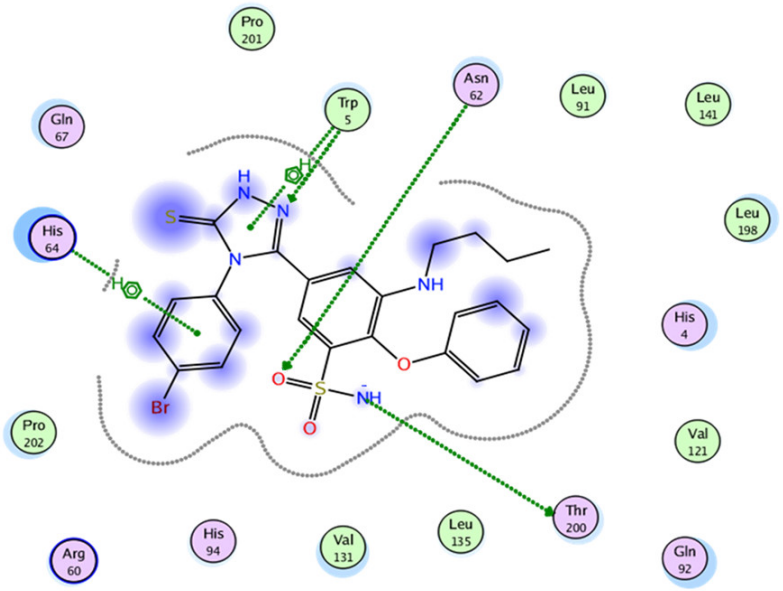
Ligand 8a	-5.4913	3.08	 Hydrogen bonding ; 2.5 **Å** ; 139.4° ; Thr-199 (Side chain –N**H**)
Ligand 8b	-6.4351	2.91	 Arene-Hydrogen interaction ; 3.2 **Å** ; Leu-91 (Side chain –CH**H**–)

Ligand 8c	-4.8966	3.16	 Arene-Hydrogen interaction ; 4.4 **Å** ; His-94
Ligand 8d	-6.2110	2.54	 Hydrogen bonding ; 2.9 **Å** ; 129.4° ; His-64 (Side chain –N**H**) Hydrogen bonding ; 3.1 **Å** ; 144.5° ; Asn-62 (Side chain –N**H**) Hydrogen bonding ; 3.2 **Å** ; 122.5° ; Thr-199 (Side chain –O**H**)

Ligand 8e	-5.7674	2.77	 Hydrogen bonding ; 2.3 **Å** ; 146.5° ; Gln-92 (Side chain –C(**O**)NH–)
Ligand 8f	-5.1837	1.70	 Hydrogen bonding ; 2.2 **Å** ; 152.6° ; Trp-5 (Side chain –N**H**) Arene-Arene interaction ; 3.7 **Å** ; His-64

Ligand 8g	-6.2308	2.50	 Hydrogen bonding ; 2.1 **Å** ; 153.0° ; Gln-67 (Side chain –C(**O**)NH–)
Ligand 8h	-5.4212	1.69	 Hydrogen bonding ; 2.1 **Å** ; 144.0° ; Gln-92 (Side chain –C(**O**)NH–)

Ligand 8i	-4.9819	1.05	
Ligand 9a	-4.3762	2.39	 Hydrogen bonding ; 2.6 **Å** ; 141.0° ; Gln-67 (Side chain –C(**O**)NH_2) Hydrogen bonding ; 2.9 **Å** ; 122.9° ; Gln-67 (Side chain –C(O)NH**H**) Hydrogen bonding ; 3.0 **Å** ; 161.0° ; Pro-201 (Main chain –C(**O**)NH–)

Ligand 9b	-6.4845	1.94	 Hydrogen bonding ; 2.1 **Å** ; 147.7° ; His-4 (Side chain =**N**–) Arene-Cation interaction ; 3.5 **Å** ; His-64 (Side chain –**N**$^{+}$H$_2$–)
Ligand 9c	-5.8355	1.63	 Hydrogen bonding ; 2.7 **Å** ; 129.6° ; Thr-200 (Side chain –**O**H) Hydrogen bonding ; 3.0 **Å** ; 106.9° ; Asn-62 (Side chain –N**H**) Hydrogen bonding ; 2.7 **Å** ; 124.**5°** ; Typ-5 (Side chain –N**H**) Arene-Hydrogen interaction ; 3.2 **Å** ; Trp-5 (Side chain –N**H**) Arene-Hydrogen interaction ; 3.0 **Å** ; His-64 (Side chain =C**H**–)

[a] MOE (***S***); Docking scores utilizing the scoring function assigned for the best-ranking poses which have been selected relying on the visual examination and after refinement through the rescoring function of the GBVI/WSA dG.

[b] RMSD; root mean square deviation of the best-ranking pose as compared to the crystal.

[c] The Legand for the predicted Ligand-enzyme residues interactions as follows: