2.1.3 Docking method of AM1 – 6 into COX-1 and COX-2

The 3D structures of COX-1 and COX-2 were downloaded from the protein data bank (PDB, ID: 3N8Z and 3NT1) and then all water molecules were removed . Partial charges were assigned to all atoms using Kollman united atom model that exists in the Autodock Tool software. Preparations of the COX-1 and COX-2 active site were completed by creating a grid box of a 50 x 50 x 50 Å size with a grid spacing of 0.375 Å using Autogrid (part of the Autodock software package). The active site was identified using the COX1 and COX2 co-crystallized ligands. After preparing the protein structures, the ligand preparation process was initiated by building their own 3D structures using the Maestro software. A minimization process was carried out on each ligand structure using OPLS force field. Subsequently, Gasteiger-Marsili model was employed to assign partial charges for all prepared ligands. Tertiary amines of all ligands were set as protonated. The ligands were separately docked into the previously prepared active site using Autodock (version 4.2). Whereas the protein structure was treated as a rigid entity, the ligand structures were treated as flexible and a conformational sampling process was carried out using Lamarckian Genetic Algorithm. The Autodock scoring function was then used to score all docked poses. The Autodock scoring function includes different terms for van der Waals, hydrogen bond, electrostatic interactions, and the ligand internal energy. Compound 5 has two tertiary amine groups in the piperazine ring where one of