MP2 and DFT analysis of the ligand selectivity of a sulfotransferase enzyme

Diana J. Bigler, and Mauricio Cafiero
Department of Chemistry, Rhodes College, 2000 North Parkway, Memphis, TN 38112

We have studied the substrate selectivity of the sulfotransferase enzyme (SULT1A3) by identifying important protein-ligand interactions in the active-site through electronic structure calculations. The sulfotransferase enzymes (SULTs) catalyze the addition of a sulfate group to a variety of small molecules, including neurotransmitters and xenobiotics. This reaction can activate or deactivate bio-active molecules or change their pharmacokinetic behavior. A variety of ligands analogous to known substrates of the SULT were chosen for study. Docking and M062X/6-31G optimization of the ligands were used to find the structures of the ligand-protein complexes assuming a static active-site. Interaction energies between the ligands and the amino-acids of the active-site were calculated using MP2 and M062X with 6-311+g*. Optimizations were also performed to allow flexibility of the amino-acid residue side-chains in the active-site and interaction energies were calculated for these complexes as well. Differences in ligand binding between *p*-nitrophenol analogues and dopamine analogues suggest a preliminary pharmacophore model.

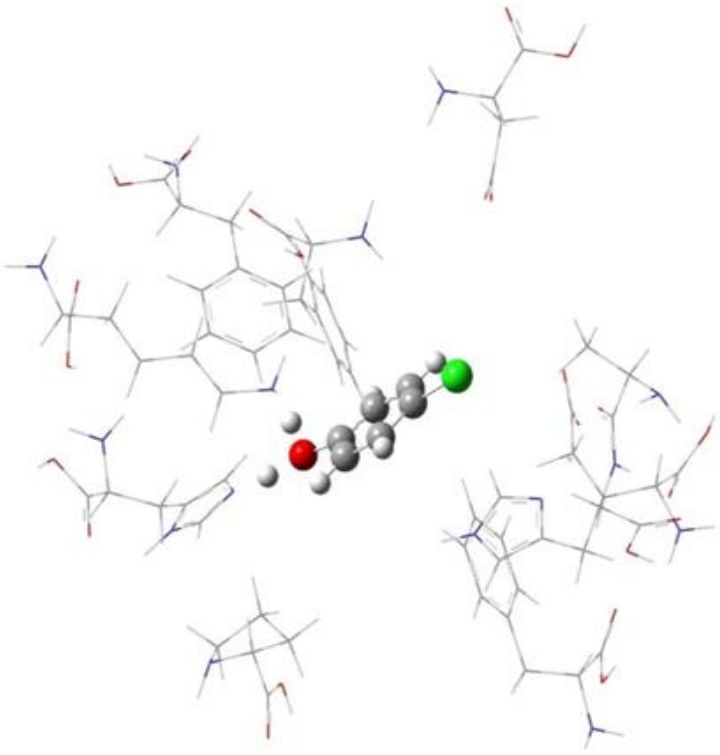

Figure 1: *p*-chlorophenol docked in the sulfotransferase active site