Ligand binding affinities for novel biomimetic models of Ni-ARD

Gabrielle Ware, Santiago Toledo, and Tricia D. Shepherd
Dept. of Chemistry, St. Edward's University, Austin TX

The metalloenzyme Nickel-acidreductone dioxygenase (Ni-ARD) found in the methionine salvage pathway (MSP) in different plants, mammals and bacteria has been shown to completely alter the outcome of the pathway. Enzyme-ligand complexes can provide insight into substrate binding, which is the scope of this work. Using density functional theory with implicit solvation, we computed the binding energies of a series of metal ligand complexes with a variety of substrates. Small molecule analogues of the active site of Ni-ARD were modeled using previously synthesized crystal structures as templates. These structures were optimized and the bond lengths, bond angles and energies were measured and analyzed. These calculations reveal the affinity for a complex to bind to a substrate at a specific position, which is determined by the metal ion at the center of the molecule. The results of this study will be used to inform both efficiency and additional target structures for future synthetic work.