# Metalloenzyme Active Site Modeling Studies Using Amide Functionalized Imidazole Tripod Ligands.

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Non heme metalloenzyme active sites contain both metal binding pockets (primary coordination sphere) that are composed of amino acid ligands (e.g. histidine), as well as non coordinating residues (second coordination sphere) that regulate important structural and chemical properties of the protein. This second coordination sphere is important to the selectivity of a large number of chemical transformations and is regulated by modulation of hydrophobic, hydrophilic interactions in the vicinity of the metal binding pocket, and donor-acceptor interactions between proximal amino acid residues and targeted substrate molecules. There is much current interest in active site models that include second coordination sphere properties, as well as biologically relevant metal binding pockets. In our studies, we have focused on the synthesis and properties of biologically relevant amide functionalized polymidazole ligands (I) that mimic histidine amino acid residues present in metalloproteins. These complexes form strong hydrogen bonds with reactive M-OH and M-OOH species. The structure and properties of several new hydrogen-bonding ligands and their metal complexes will be presented and compared to related metalloprotein systems and previous amide functionalized ligands prepared by our group.