Copper and Zinc Complexes of Pyridylmethylamide Ligands – Synthesis, Characterization and DNA Cleavage Studies

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Biomimetic hydrolysis of DNA or RNA is of increasing importance in biotechnology and medicine. Most natural nuclease enzymes that mediate such reactions utilize metal ion cofactors. Recent progress in the design of synthetic metallonucleases has included metal complexes of antibiotics, peptides, nucleic acids and other organic ligands. We have synthesized copper and zinc complexes of a family of pyridylmethylamide ligands that have been spectroscopically and structurally characterized. These are of varying nuclearity which is due to the ability of the ligand to adopt different coordination modes depending on whether the amide nitrogen is protonated (RNHCO) or deprotonated ($RN^{-}CO$). If the amide nitrogen is deprotonated, metal clusters are isolated where the ligand adopts a chelating and bridging mode. Otherwise the carbonyl oxygen coordinates to the metal center generating mononuclear or dinuclear derivatives. These complexes also share characteristics with other artificial metallonucleases indicating their potential as DNA cleavage agents. The kinetic and thermodyanamic parameters of hydrolysis studies using model phosphate esters and plasmid DNA will be presented.