(□)-Orn-Linked Cu(II)• or Ni(II)•Gly-Gly-His-Like "Tandem-Array" Metal Binding Oligopeptides

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Metallopeptides of the general form M(II)•Xaa_1-Xaa_2-His (where M is Cu or Ni) serve as models of the native amino-terminal metal binding and transport domain of the serum albumins. These peptide systems have been studied extensively and exist as well-characterized 1:1 complexes at physiological pH or above through chelation of the terminal peptide amine, two intervening deprotonated peptide amides, and the His imidazole ring. In lieu of the free terminal peptide amine required to complete the 4-coordinate metal binding site of these systems in native peptides and proteins, several years ago we demonstrated the ability to substitute an Orn residue for Xaa_1 and, with appropriate side chain protection of the □-amino side chain and □-amine functionalities of Orn, continue solid-phase peptide synthesis (Shullenberger, Eason, & Long *J. Am. Chem. Soc*. **1993**, *115*, 11038). This strategy thus allowed the placement of an Xaa-Xaa-His metal binding domain at any location within a linear, synthetic peptide chain (*i.e*., at the amino-terminal, intervening, or carboxy-terminal positions within a linear peptide). As a continuation of this investigation, we have synthesized a tandem array of Xaa-Xaa-His metal binding motifs in the peptide NH_2-Gly-Gly-His-[(□)-Orn-Gly-His]$_2$-(□)-Orn-Gly-His-$CONH_2$ or shorter versions thereof. Metal binding titrations and EI-MS indicate that these tandem array peptides maintain the ability to bind both Cu^{2+} and Ni^{2+} at each available metal binding site within a given peptide. Furthermore, UV-vis titrations suggest that each Xaa-Xaa-His site acts as an independent metal binding site for Cu^{2+} and Ni^{2+}; however, exposure of preformed Co^{2+} "dimer"peptides to ambient dioxygen suggests that metals within the linear peptide chain can act intramolecularly to bind dioxygen resulting in intramolecular □–peroxo species. The synthesis and characterization of these metal binding oligopeptides will be presented.