

CHARACTERIZATION OF HELIX FLEXIBILITY AND HYDROGEN BOND STRENGTH IN AN 8-RESIDUE PEPTIDE CONTAINING ALANINE & α -AMINOISOBUTYRIC ACID, A. E. Getschman, M. A. Cocchiola, A. P. Loh*, University of Wisconsin – La Crosse, Department of Chemistry, La Crosse, WI 54601, loh.adri@uwlax.edu

Protein function is governed by physical characteristics such as flexibility and structure. The formation of secondary and tertiary structures is accomplished through the interaction of atoms and accompanying weak forces, which ultimately control protein flexibility. One of the most important weak forces is the hydrogen bond, which is found to occur between backbone atoms in secondary structures such as helices, sheets and coils. The most common helix conformation is the α -helix, characterized by an ($i \rightarrow i + 4$) hydrogen bonding pattern. A less common helix structure, sometimes found in protein binding sites and possibly as an intermediate during α -helical formation, is the 3_{10} -helix (characterized by an ($i \rightarrow i + 3$) hydrogen bonding pattern). It has been found that peptides primarily composed of the amino acid Aib (α -aminoisobutyric acid) will readily fold into 3_{10} -helices, even in peptides as short as three residues. Aib amino acids are structurally similar to alanine except for a methyl group in place of a hydrogen at the α -carbon. The dialkylation at the α -carbon creates significant steric hindrance, which is responsible for the helical preference of Aib. We are interested in the role that steric hindrance plays in governing helical structure and flexibility. The peptide of interest in this study is an eight residue chain with alanine amino acids at positions three and six and Aib residues at the remaining positions ("AA36"). Since Aib is sterically hindered and will drive the formation of a 3_{10} -helix, the two alanine residues will create two less sterically hindered and presumably more flexible regions of the helix. In this project, the AA36 peptide is prepared using solution phase synthesis, and ^1H NMR is used to study amide proton exchange with deuterons in the solvent to characterize helical flexibility. The analysis of this data and comparison to that for similar peptides will lend insight to the role of steric hindrance and hydrogen bond strength in helix flexibility.