CONFORMATION-SPECIFIC INFRARED AND ULTRAVIOLET SPECTROSCOPY OF COLD [YAPAA+H]$^+$ AND [YGPAA+H]$^+$ IONS: A STEREOCHEMICAL "TWIST" ON THE β-HAIRPIN TURN

ANDREW F DeBLASE, CHRISTOPHER P HARRILAL, JOHN T LAWLER, NICOLE L BURKE, SCOTT A McLUCKEY, TIMOTHY S. ZWIER, *Department of Chemistry, Purdue University, West Lafayette, IN, USA*.

Incorporation of the unnatural D-proline (^{D}P) stereoisomer into a polypeptide sequence is a typical strategy to encourage formation of β-hairpin loops because natural sequences are often unstructured in solution. Using conformation-specific IR and UV spectroscopy of cold (10 K) gas-phase ions, we probe the inherent conformational preferences of the ^{D}P and ^{L}P diastereomers in the protonated peptide [YAPAA+H]$^+$, where only intramolecular interactions are possible. Consistent with the solution phase studies, one of the conformers of [YADPAA+H]$^+$ is folded into a charge-stabilized β-hairpin turn. However, a second predominant conformer family containing two sequential γ-turns is also identified, with similar energetic stability. A single conformational isomer of the ^{L}P diastereomer, [YALPAA+H]$^+$, is found and assigned to a structure that is not the anticipated "mirror image" β-turn. Instead, the ^{L}P stereo center promotes a cis alanine-proline amide bond. The assigned structures contain clues that the preference of the ^{D}P diastereomer to support a trans-amide bond and the proclivity of ^{L}P for a cis-amide bond is sterically driven and can be reversed by substituting glycine for alanine in position 2, forming [YGLPAA+H]$^+$. These results provide a basis for understanding the residue-specific and stereo-specific alterations in the potential energy surface that underlie these changing preferences, providing insights to the origin of β-hairpin formation.