CYCLIC CONSTRAINTS ON CONFORMATIONAL FLEXIBILITY IN γ-PEPTIDES: CONFORMATION-SPECIFIC IR AND UV SPECTROSCOPY

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Spectroscopic studies of flexible peptides in the gas phase can provide insight to their inherent structural preferences in the absence of solvent. Recently, there has been increased attention paid to synthetic foldamers containing non-natural residues that can be specifically engineered to robustly form particular secondary structures. These engineered peptides have potential in therapeutic drug design because they are resistant to enzymatic degradation. Specifically, the Gellman group has synthesized a γ-peptide with a six membered cyclic constraint in the γ^4-γ^3 position and an ethyl group at the γ^2 position (γ_{ACHC}). The three stereocenters have a well-defined chirality [S,S,S]. These two features constrain the relative orientation of adjacent amide groups, thereby favoring a particular "pitch" to the turn. Solution phase results indicate that constrained γ-peptides induce the formation of a 14-helix.[a] Ac-γ_{ACHC}-NHBz, its monohydrate and Ac-γ_{ACHC}-γ_{ACHC}-NHBz have been studied using ultraviolet (UV) and infrared (IR) double-resonance methods to obtain conformation-specific spectra under jet-cooled conditions in the gas phase. IR spectra in the hydride stretch (3300-3750 cm^{-1}), amide I/II and OH bend (1400-1800 cm^{-1}) were recorded and compared to predictions using density functional methods (DFT) and harmonic frequency calculations. We will compare the present results on constrained γ-peptides with corresponding results on unconstrained analogs. Data obtained for the monohydrated water cluster of Ac-γ_{ACHC}-NHBz will also be presented, including assignment of the water bend fundamental, which appears in the midst of transitions due to the amide II vibrations.

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