CONFORMATION-SPECIFIC INFRARED SPECTROSCOPY OF γ^2-PEPTIDE FOLDAMERS: Ac-γ^2-hPhe-γ^2-hAla-NHMe AND Ac-γ^2-hAla-γ^2-hPhe-NHMe

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IR/UV double-resonance spectroscopy has been used to study the intrinsic conformational preferences of naturally occurring and synthetic peptides. These studies demonstrated the power of double-resonance methods and highlighted the ability of even short peptide mimics to form a variety of intramolecular hydrogen bonded architectures. Currently, we are extending these studies to a series of model γ^2-peptides, which differ from α-peptides by virtue of having two additional, substitutable methylene units separating amide groups in the peptide backbone. Initial studies centered on the conformation-specific infrared spectra of Ac-γ^2-hPhe-NHMe, where three unique conformational isomers (two hydrogen-bonded and one intramolecular amide stacked) were observed under the isolated-molecule conditions of a jet-cooled environment. This talk will focus on on two larger γ^2-peptides, Ac-γ^2-hPhe-γ^2-hAla-NHMe and Ac-γ^2-hAla-γ^2-hPhe-NHMe. Utilizing resonant ion-dip infrared spectroscopy, the single-conformation infrared spectra of eight resolved conformers of the two molecules were recorded in the amide NH stretch region. The resulting infrared spectra of the tri-amides contain evidence for structures comprised of one, two, and three intramolecular amide-amide hydrogen bonds, the last of which is unprecedented for a tri-amide. In an effort to make firm conformational assignments, the spectroscopic data will be compared to the results of harmonic vibrational frequency calculations using traditional DFT and dispersion-corrected DFT methods, the results of which will be discussed.