CONFORMATION-SPECIFIC IR AND UV SPECTROSCOPY OF A SERIES OF SYNTHETIC FOLDAMERS: α/β^3- AND β^3- ALA DIPEPTIDES

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With the development of designed foldamers that display biological activity and aid in drug delivery processes, there is an increasing interest in exploring the inherent conformational properties of model foldamers to understand better the subtle counter-balance of forces at play β-amino acids have one additional backbone carbon atom that extends the spacing between amide groups, thereby providing flexibility in construction of β- and α/β- peptides, leading to secondary structures that either mimic or are complementary to those found in nature. Here we explore the conformational preferences of a series of β- and α/β- dipeptides under jet-cooled conditions in the gas phase. The molecules are brought into the gas phase using laser desorption. Our studies include two capped α/β - dipeptides, Ac-L-Ala-β^3-(R)-hAla-NHBn and Ac-β^3-(R)-hAla-L-Ala-NHBn as structural isomers, and one capped pure β^3-dipeptide, Ac-(R)-hAla-β^3-(S)-hAla-NHBn . By incorporating an NHBn cap, a UV chromophore is present that can be used to record resonant two-photon ionization (R2PI) spectra. Conformation-specific infrared and ultraviolet spectra are then recorded using resonant ion-dip infrared (RIDIR) and IR-UV hole burning spectroscopies, respectively. With this set of peptides, we are able to probe the effect of a chirality switch at a single chiral center on inherent local conformational preferences. Following an exhaustive computational search of the conformational potential energy surface, low-lying minima are optimized and IR spectra calculated for comparison with the experimental RIDIR spectra provide conformational assignments. Lowest-energy conformers are observed for the α/β-peptides and assigned to C7/C8 (C8/C7) hydrogen-bonded architectures, while for the pure β^3-peptide analog, only one conformer is observed experimentally and assigned to a C12 hydrogen-bonded architecture.