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

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In order to further understand the intramolecular forces governing secondary structure formation in peptides and to provide benchmarks for the computational community, conformation-specific spectroscopy techniques have been applied to several model systems provided by Dr. Sam Gellman's research group at the University of Wisconsin-Madison. In the present work, two model β/γ-peptides, Ac-β_{ACPC}-γ_{ACHC}-NHBz and Ac-γ_{ACHC}-β_{ACPC}-NHBz have been investigated using single and double resonance ultraviolet and infrared spectroscopy to elucidate their intrinsic folding propensities. The β-peptide is constrained by a five-membered ring spanning the β^3-β^2 positions (β_{ACPC}) and the γ-peptide is constrained by a six-membered ring spanning the γ^4-γ^3 positions with an additional ethyl group at γ^2 (γ_{ACHC}). Resonant two-photon ionization (R2PI) spectra from 37250 to 37750 cm^{-1} were obtained and subsequently interrogated using UV-UV hole-burning to reveal the presence of three conformations for Ac-β_{ACPC}-γ_{ACHC}-NHBz, and a single conformation for Ac-γ_{ACHC}-β_{ACPC}-NHBz. Resonant ion-dip infrared (RIDIR) spectra were obtained in the NH stretch region from 3300 to 3500 cm^{-1} and in both the amide I and II regions from 1400 to 1800 cm^{-1}. These spectra were compared to computational predictions given by DFT calculations using the M05-2X functional with a 6-31G+(d) basis set revealing two slightly varied iterations of a bifurcated C-8/13 double ring structure for Ac-β_{ACPC}-γ_{ACHC}-NHBz and one bifurcated C-9/13 double ring structure for Ac-γ_{ACHC}-β_{ACPC}-NHBz. The appearance of C-13 rings was also seen in solution phase studies.[a] This work is a complement to studies performed on pure γ-peptides and α/γ-peptides.

[a] L. Guo, A. M. Almeida, W. Zhang, A. G. Reidenbach, S. H. Choi, I.. A. Guzei, and S. H. Gellman *J. Am. Chem. Soc.* 2010, **132**, 7868-7869