CONFORMATION SPECIFIC SPECTROSCOPY OF AC-γ^4-PHE-NHME: RELATIVE ABUNDANCES IN A SUPERSONIC EXPANSION DETERMINED USING IR POPULATION TRANSFER

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Foldamers are peptides synthesized to adopt specific motifs, for instance, helices. One class of foldamers that has received particular attention are β-peptides,with two carbons between amide groups, or γ-peptides, with three. This extension of the carbon backbone provides additional conformational flexibility and more choice for the position(s) of peptidomimetic substitution. Previous gas-phase jet-cooled conformation specific spectroscopy of the γ-peptide, Ac-γ^2-Phe-NHMe, found three different conformers and provided the first spectroscopic signature of amide stacking.[1] The study also utilized infrared population transfer (IRPT) studies that determined the relative population of each conformer in the expansion, and later, the binding of a single water molecule.[2] Here, we expand the study further to include Ac-γ^4-Phe-NHMe. Repositioning of the peptidomimetic side chains from the 2- to the 4-position of γ-peptides has been shown to induce helix formation in solution. This motivates a study of the intrinsic change in conformational preferences induced by γ^2- vs. γ^4-Phe substitution. Conformation specific IR-UV double resonance spectra were recorded for the jet-cooled γ^4 conformers in the NH stretch and amide I/II regions. DFT calculations at the B3LYP level of theory (6-31+G(D), D3BJ) were compared with experiment to assign structures. Two structures were assigned as phenyl rotamers of a nine-membered ring closed by an NH...O=C hydrogen bond (C9). Tentative assignment for the third conformer is to a strained seven-membered ring closed by a hydrogen bond. Currently, IRPT is being used to determine the relative populations of the conformers in the expansion. Additionally, Ac-γ^4-Phe-NHMe•H2O will be studied to compare bare and partially solvated structures.

[1] James III, W. H.; Müller, C. W.; Buchanan, E. G.; Nix, M. G.; Guo, L.; Roskop, L.; Gordon, M. S.; Slipchenko, L. V.; Gellman, S. H.; Zwier, T. S., J. Am. Chem. Soc. 2009, 131, 14243-14245. [2] Buchanan, E. G.; James III, W. H.; Gutberlet, A.; Dean, J. C.; Guo, L.; Gellman, S. H.; Zwier, T. S., Faraday Discuss. 2011, 150, 209-226.