CONFORMATION-SPECIFIC UV and IR SPECTROSCOPY OF CONFORMATIONALLY CONSTRAINED α/γ PEPTIDE FOLDAMERS

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Synthetic foldamers composed of heterogeneous backbones offer constructs for building unique secondary structures. α/γ-peptides juxtapose the α-amino acid sub-units typical of proteins with γ-amino sub-units. Gellman and co-workers have developed efficient syntheses of α/γ-peptides that incorporate a cyclohexyl ring constraint at the γ^3-γ^4 bond to limit backbone torsional mobility, and found that they form helices held together by C=O(*i*)···H-N(*i*+3) H-bonds composing 12-membered rings both in solution and in crystalline form. [a] This talk will present a detailed study of the single-conformation double-resonance UV and IR spectroscopy of Ac-Ala-γ_{ACHC}-NH-benzyl ($\alpha\gamma$) and Ac-γ_{ACHC}-Ala-NH-benzyl ($\gamma\alpha$) capped peptides, in which γ_{ACHC} residues are constrained by a *cis* cyclohexyl ring at γ^3-γ^4 bond with an ethyl group at γ^2 position. The two $\alpha\gamma$ and $\gamma\alpha$ peptides have three amide groups that are the minimum length necessary to form a 12-membered H-bond. Conformational assignments were made using the NH stretch, C=O stretch (amide I), and NH bend (amide II) regions of the IR spectrum with the aid of DFT calculations. The double-resonance UV and IR spectroscopy uncovered the presence of 6 conformers for $\alpha\gamma$ and 4 conformers for $\gamma\alpha$. In the two peptides, three of ten structures incorporate bifurcated double rings made of 12-membered C=O(1)···H-N(3) ring, which is the first stage of the 12-helix, and 7- or 9-membered C=O(1)···H-N(2) ring via nearest-neighbor interaction. The other seven structures are constructed based on 5-, 7-, and 9-membered nearest-neighbor H-bonds. The similarities and differences between structures observed for the two two $\alpha\gamma$ and $\gamma\alpha$ peptides will be discussed.

[a] L. Guo, Y. G. Chi, A. M. Almeida, I. A. Guzei, B. K. Parker, and S. H. Gellman, J Am Chem Soc, 2009, 131, 16018-16020.