Turning peptide structures using nitrogen chirality

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The privileged role of turns in molecular recognition of peptides drives interest in mimicry of the backbone orientation and side chain pharmacophores of these important secondary structures. Previously, the stereoelectronic effects of semicarbazides have been used to induce turn geometry in azapeptides.[1] Moreover, the covalent constraint of α-amino-γ-lactam (Agl) residues, so-called Freidinger-Veber lactams, have been shown to favor beta-turns.[2, 3] More recently, *N*-amino-imidazolinone (Nai) residues have been shown to combine stereoelectronic and covalent effects to augment potential to induce turn conformation.[4] Focusing on the relevance of nitrogen chirality as a turn inducing factor in a model azapeptide, our presentation examines a minimal turn sequence to study turn formation without stereogenic carbon. Notably, diastereotopic glycine methylene proton signals have been observed to indicate pyramidal nitrogen for which the barrier for inversion was measured using variable temperature NMR spectroscopy and coalescence experiments. Efforts to crystalize and further characterize the model azapeptide conformation are under investigation.

References:

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