Conformational preferences of foldamers of γ-peptides

Prof. **Young Kee KANG**

Department of Chemistry and *BK21 Plus Research Team*, Chungbuk National University, Korea
Professeur invité LabEx CheMISyst et IBMM

Foldamers are non-natural oligomers that have well-defined three-dimensional structures akin to those of natural biopolymers. For more a decade, considerable works on the oligomers of β- or γ-amino acid residues (i.e., β- or γ-peptides) as well as their hybrids with α-amino acid residues have been carried out to obtain the helix, sheet, β-turn, and β-hairpin foldamers akin to the secondary structures of peptides and proteins. Conformationally constrained γ-aminobutyric acid (γAbu) analogues with a cycloalkane ring in the backbone have been extensively studied to obtain the conformation necessary for binding to the γAbu receptor. However, only a few works have reported the γ-peptide-containing foldamers with a cycloalkyl constraint on the C^{α}–C^{β} or C^{β}–C^{γ} bonds of the backbone due to the lack of efficient synthetic methods for chirospecific building blocks and their couplings until now. Here, I will talk about the various foldamers such as helices, turns, and hairpins of γ-peptides with cyclohexyl or cyclopentyl constraints on the C^{α}–C^{β} or C^{β}–C^{γ} bonds of the backbone designed by quantum-chemical methods. The rigidities of the torsion angle ζ about the C^{α}–C^{β} bond or the torsion angle θ about the C^{β}–C^{γ} bond seem to be crucial for the determination of the conformational preference of each foldamer. In particular, the repeated dipeptides with different chiralities could provide us the cyclic peptide nanorings with the radii of about 8−17 Å, from which the various peptide nanotubes could be generated. In addition, some dipeptides with the (*1S*, *2R*) chirality at the C^{α}–C^{β} bond produced the cyclic peptides with somewhat declined peptide bonds, which formed the peptide funnel.

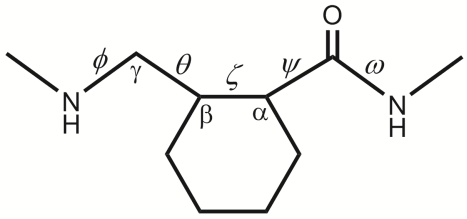

Figure. Chemical structures of 2-(aminomethyl)cyclohexanecarboxylic acid (γAmc_6) with a cyclohexyl constraint on the C^{α}–C^{β} bond and their backbone torsion angles.

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