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Design and Synthesis of non-Proteinogenic Amino Acids and Secondary Structures of Their Peptides

Masakazu TANAKA
(Graduate School of Pharmaceutical Sciences, Kyushu University)

Understanding the secondary structures of peptides and proteins, for example, α-helix, β-sheet, and reversed-turn, is important as they play a vital role in biological processes. Many peptide and organic chemists have made every endeavor to understand the mechanisms of forming secondary structures.

Replacement of the α-hydrogen atom of natural L-α-amino acids with an alkyl substituent results in α,α-disubstituted α-amino acids (dAAs). Incorporation of dAA into oligopeptides would restrict the freedom of the secondary structure of their peptides. For example, oligopeptides composed of achiral dAA; α-aminoisobutyric acid (Aib; dimethylglycine) preferentially form a 3_{10}-helical structure. We have focused our research on the secondary structures of peptides composed of chiral dAAs.

1. Secondary structure of peptides composed of chiral α-alkylated dAAs. Homo- and heteropeptides composed of chiral α-ethylated dAAs preferentially formed the fully planar C_5-conformation, whereas those of chiral α-methylated dAAs formed the 3_{10}-helical structures.

2. Secondary structure of peptides composed of chiral cyclic dAAs. α-Helical structure in proteins, almost always form a right-handed (*P*) helical-screw sense, which is believed to result from the asymmetric center at the α-position of L-α-amino acids. We designed chiral cyclic dAA; (*S*,*S*)-Ac_5c^{dOM}, which does not have a chiral center at the α-position, but does have chiral centers on the side-chain cyclopentane. Homopeptides composed of (*S*,*S*)-Ac_5c^{dOM} preferentially formed the left-handed (*M*) 3_{10}- or (*M*) α-helical structure both in solution and in the solid state. These results imply that side-chain chiral centers of L-isoleucine and L-threonine would affect the secondary structure of their oligopeptides.