

Preferential Conformations of Blocked Amino Acids in Water

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Determination of the preferential amino acid conformations and understanding the physical basis of intrinsic preferences of amino acid residues in water are crucial for solving the protein folding problem. Dipeptides of type Ac-X-NHMe, (X is an amino acid) represent an ideal system for studying the intrinsic conformational preferences of residues. They are the smallest fragments that preserve the main characteristic of the individual amino acids within the host molecules. Moreover, the effects of neighbouring residues are absent.

Conformational behaviour of 19 dipeptides has been studied using infrared and Raman spectroscopy. Previously, we showed by applying $^3J(H^\alpha, H^N)$ coupling constants [1] that the distribution of amino acid conformations depends on the type of the side chain. However, by applying these coupling constants and Karplus equation we can distinguish only between conformations with similar ψ and different ϕ angles. The difficulty occurs when we try to determine the conformations with different ψ angles (P_{II} and α_R). Namely, the largeness of coupling constant for α_R structure is comparable to those characteristic for P_{II} structure. Therefore, we apply the vibration spectroscopy. We have utilized three distinct indicator vibrations sensitive to values of ψ and ϕ angles: infrared Amide I and Amide III vibrations and skeletal Raman vibration. Applying those vibrations we had the opportunity to unambiguously determine the existence of α_R conformation [2]. Experimental results from the vibrational spectroscopy correlates with NMR coupling constants. Taking into account experimental results from the vibrational study the main conformations of amino acids remain P_{II} and β . The α_R structure represents the minor contribution to distribution of amino acid conformations in water. The distribution of these conformations strongly depends on the type of side chain. Thus the prevailing conformation of His, Thr, Cys, Ile and Val dipeptides is β (57%, 55%, 55%, 52% and 49% respectively), while dipeptides such as Ala, Trp, Lys, Arg, Met and Leu adopt predominately P_{II} conformation (62%, 54%, 53%, 53%, and 50% respectively). The part of α_R conformation varies between 1% and 10%, except for Gly dipeptide where a population of α_R conformers rises up to 51%.

The experimental results are explained by the electrostatic screening model [3, 4]. The model is based on a hypothesis that the peptide conformations are affected by electrostatic dipole-dipole interactions in the peptide backbone and by screening of these interactions with surrounded water molecules. The extent of screening effect depends on nearby side chains.

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