HAIRED TURN AND POLAR β-SHEET ASSEMBLY BY PEPTIDES CONTAINING β-AMINO ACID RESIDUES

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Hexa- to deca- peptides, designed with the inclusion of several β-amino acids in their sequences, make hairpin turns and C=O…HN hydrogen bonds between the antiparallel strands of the backbone. A centrally placed d-Pro-Gly segment in a sequence of hydrophobic residues has been shown to facilitate β-hairpin formation. The peptides containing β-residues have been designed with β-residues facing each other across the strands. The manner of hairpin formations is similar to that observed in hairpins containing only α-amino acid residues. The differences in the types of hairpins are extra pleats, when seen at the hairpin is viewed from the side, that reflect the additional length of the backbone in a β-residue. More important is the formation of polar areas in the hairpin and the extended pleated β-sheet, caused by the alignment of C=O…HN bonds in the same direction between strands, instead of alternating directions as in hairpins made with all α-residues. Crystal structures of (a) Boc-beta-Phe-β-Phe-d-Pro-Gly-beta-Phe-beta-Phe-Phe-O-Me, an all β-peptide except at the hairpin turn; (b) Boc-Leu-Val-beta-Val-d-Pro-Gly-beta-Leu-Val-Val-O-Me with mixed α- and β- residues and (c) Boc-Leu-Val-beta-Phe-Val-d-Pro-Gly-Leu-beta-Phe-Val-Val-O-Me with mixed α- and β- residues show fully hydrogen-bonded infinite β-sheets that differ from each other and differ in the extent of the polar areas, depending upon the placement of the β-residues in the sequence. Attempts to construct β-hairpins with longer strand lengths exclusively composed of β-Phe residues resulted in peptides with extremely poor solubility.

Keywords: β PEPTIDES, β HAIRPINS, POLAR β SHEETS

CRYSTAL AND MOLECULAR STRUCTURE OF THE ANTIHIVANTITUMOR COMPOUND TAUROLIDINE

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The structure of taurolidine, a broad spectrum antibiotic with anticancer potential, was determined by using single crystal X-ray diffraction techniques and solved by direct methods. The crystals are triclinic and crystallize in space group P-1, with two molecules in the asymmetric unit. The unit cell dimensions are: a = 10.892(7) Å, b = 9.178(5) Å, c = 13.916(9), α = 87.36° (2), β = 69.77° (2), γ = 70.03°(2). The structure was refined to a final R = 0.065. The molecules in the asymmetric unit have slightly different conformations, associated mainly with rotation about the central N-C bond. Molecular mechanics techniques to determine the difference in conformational energy between the two molecules were applied. A slight difference was observed in the two crystallographic conformations at room temperature. The main difference in rotation between the two conformers is also the point at which the molecule is hydrolyzed upon contact with aqueous media. This structural breakdown of the drug is necessary for the exhibition of antibacterial and probably, its antitumor activity.

Keywords: ANTIBIOTIC, ANTITUMOR, CRYSTAL STRUCTURE