β-Turns, Peptides, Peptoids and CO···CO interactions

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β-turns represent the most prevalent type of nonrepetitive secondary structure in proteins. A β-turn is a region of four consecutive residues, where the polypeptide chain reverses its direction and the distance between the α-carbon atoms of the residues *i* and *i*+3 is less than 7 Å. In 1968 Venkatachalam recognized the existence of β-turns by showing three distinct conformations characterized by specific values of the φ and ψ torsion angles and by the presence of a hydrogen bond between the peptide backbone carbonyl group of the first residue C=O(*i*) and the backbone amino group of the fourth residue N-H(*i*+3). In the next 50 years of research, several classifications of β-turns were proposed, based exclusively on the evaluation of the φ and ψ dihedral angles [1]. Recently, Newberry and Raines evidenced the importance of weak chemical interactions, such as n → π* interactions, in the formation of protein secondary structures [2].

Then, we succeeded in identifying repeated patterns of $n \rightarrow \pi^*$ interactions between carbonyl groups of successive residues in proteins and cyclic peptides. We considered 1424 X-ray protein structures in the Protein Data Bank with a resolution of 1.2 Å or better, *R*-factor of 0.2 or better and sequence identity of 50% or lower. We also performed a statistical analysis on the geometrical features of CO···CO interactions in turn mimetic compounds as cyclic peptides, cyclic depsipeptides and cyclic peptoids, considering a total of 232 compounds in the Cambridge Structural Database [3].

The obtained results show that CO···CO interactions could allow to discriminate among different turn types and explain the peculiar differences from a chemical point of view. Thus, we evidenced that φ values in the range between -40° and -90° and between 40° and 90° correspond to CO···CO distances below 3.22 Å (Figure 1).

Noteworthy, the lack of the amide proton in peptoids prevents the formation of NH···CO hydrogen bonds and makes peptoids the ideal platform for evidencing the influence of CH···OC and CO···OC interactions in stabilizing molecular conformations and solid-state assembly [4]. Thus, we were able to highlight the role of intramolecular backbone-to-backbone CO···CO interactions and CH···OC hydrogen bonds in the stabilization of enantiomorphic right- and left-handed polyproline type I helices in cyclic dodecapeptoids [5].

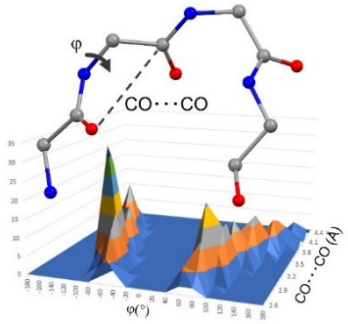

Figure 1. Shortest CO···CO distance (Å) vs φ angle (°) in cyclic peptides, depsipeptides and peptoids for left-handed turns (negative φ values) and right-handed turns (positive φ values), respectively.

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