ANALYSIS OF CONFORMATIONAL PREFERENCES OF TRIAZOLE CONTAINING CARBOPEPTOIDS

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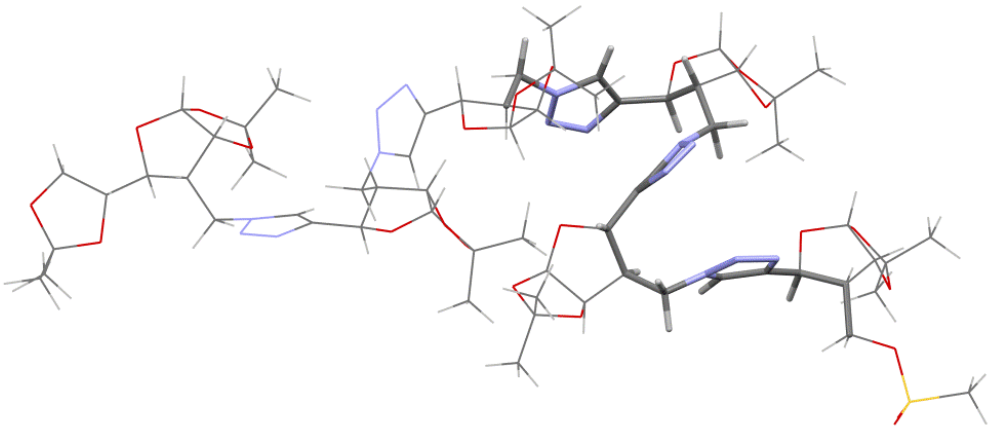
Modulation of protein-protein interaction can be achieved either by its stimulation [1] or by inhibition [2] by both small and large molecules. In the case of the latter, it is important that the conformation of the macromolecule can be defined by incorporation of specific synthetic building blocks. These building blocks can possess structural features with specific folding patterns or they can incorporate functions (amides, sulfides, alkenes [2]) that allow intramolecular stabilization of the active conformation by covalent or hydrogen bond bridging.

Many molecular scaffolds were studied as the building blocks for the foldamers, including sugar amino acids (SAAs) [3] that were used to mimic both the amide bonds of peptides and the foldamer abilities of them. Oligomeric carbopeptoids synthesized from them were shown to exhibit stable secondary structures [4].



Herein we present the synthesis and spectroscopic studies of the furanose-based amide- and triazole-linked carbopeptoides. Acetonide protected furanose rings are stereochemically defined molecular scaffolds that impose certain rigidity to the oligomeric structures made from them. Linking with an amide provides open sites for the formation of intramolecular hydrogen bonds when incorporated in the larger molecules, while triazole linkers add conformational stability and rigidity.

Molecular dynamics simulations showed that in both series of the oligosaccharides the β-turn-type structures can be formed. The presence of β-turns is strongly supported by the corresponding NMR data in the case of all triazole-linked oligosaccharides. Due to the fact that the structures of amide- and triazole-linked oligosaccharides are more flexible, the presence of β-turns in them is not unambiguously supported by their NMR data.

References

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