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Synthesis and Spectroscopic Studies of Glucose-Derived Carbopeptoids

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Oligopeptides arising from synthetic sugar amino acids exhibit interesting self-assembling structures in solution, and were intensively studied as peptidomimetics [1]. After the discovery of click synthesis of 1,2,3-triazoles [2], the latter were studied as amide bond isosteres as they exhibit similar spatial arrangement and geometry [3].

Present research focuses on the hybrid building blocks that can be used to synthesize carbapeptoids with *trans*-orientated functional groups. Structural hybrid **1** (Figure 1) contains two carbohydrate-based bicyclic rings with defined molecular scaffold, and amide functionality that can participate in intramolecular hydrogen bond formation. It also contains *C*-terminal alkyne along with masked *N*-terminal azide for differentiated copper-catalyzed azide alkyne cycloadditions.

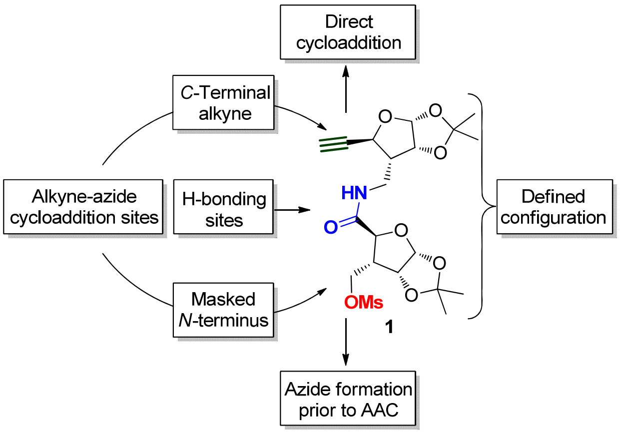

Figure 1. Dimeric structural hybrid **1**

Iterative cycloaddition reaction azidation sequence using this hybrid allows for the synthesis of oligomeric carbopeptoids of type **I** (Figure 2), which has both the amide and triazole linkers between carbohydrate cores.

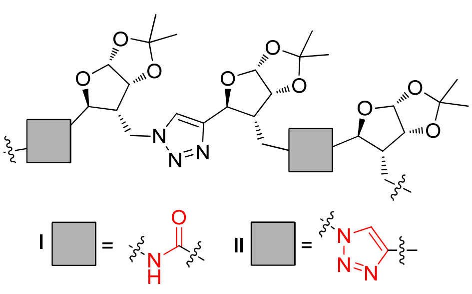

Figure 2. Main backbones of the oligomers

Substitution of the amide linker in dimeric hybrid with 1,2,3-triazole moiety brings another degree of rigidity and opens the opportunity for the synthesis of type **II** saccharopeptides with all-triazole linkages.

Oligomers of type **I** and **II**, as well as their synthetic precursors were studied by NMR and CD spectroscopies. ROESY spectra were acquired and distances between adjacent protons were determined. These results were used as the constraints in MD calculations using CHARMM force field in order to determine possible conformations of oligomers.

Circular dichroism spectroscopy was used to determine influence of the solvent on the possible conformation distribution and the chain length dependence of CD (Figure 3).

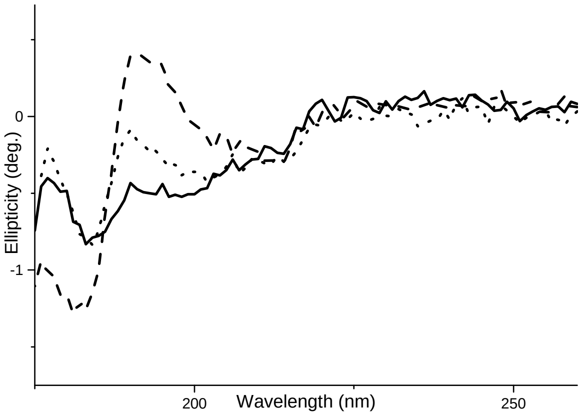

Figure 3. CD spectra of type **I** tetramer (hashed), hexamer (dotted), and octamer (solid) in trifluoroethanol

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