Abstract

Peptoids (polymers of *N*-substituted glycines) constitute a fascinating class of biomimetic oligoamides as peptides but exhibiting distinct structural and biological features. Cyclic peptoids, macrocycles derived from the cyclization of linear peptoids are attractive scaffolds for several applications. They are stable and easily accessible by the so called submonomer approach on solid-phase and subsequent cyclization in solution in high dilution conditions.[1] Within last years, cyclic peptoids have been investigated as versatile scaffolds to perform numerous functions. In particular, macrocyclic *N*-substituted glycine oligomers have shown a significant potential in catalysis,[2] as bioactive agents,[3] in material science[4] and as precursors of peraza-macrocycles.[5] Moreover, the versatility of their preparation method enables wide structural flexibility and effortless introduction of diverse aromatic spacers into the peptoid oligoamide backbone, producing the valuable class of "extended" peptoids[6,7] with excellent conformational properties[8,9] and metal chelating abilities.[10]

This PhD thesis is focused on developping new sequence-defined macrocycles based on peptoidic scaffold. Chapter 2 describes synthesis and characterization of new chiral peraza-macrocycles and their sodium complexes. The preparation of such macrocyclic ligands has been accomplished *via* backbone amides' reduction of corresponding cyclic peptoids. Chapter 3 is devoted to attempt the synthesis of cyclic thiopeptoids (possessing C=O backbone bonds replaced with C=S ones). The synthesis of two thioamide bond precursors in peptoids and on-resin thioacylation trials are described. Chapter 4 can be considered as an interface between the versatility of the copper(I)-catalyzed alkyne-azide cycloaddition chemistry and peptoid synthesis. In the first place, preparation, and characterization of a new class of macrocyclic triazole-containing "extended" peptoids are described. The next study is dedicated to expanding the concept of backbone amide reduction for these new oligoamide macrocycles (including chiral derivatives), which leads to a new class of macrocycles possessing complexation abilities. Lastly, a preparation of new polar macrocyclic peptoids *via* CuAAC-mediated conjugation between propargyl-functionalized cyclopeptoidic platforms and suitably designed azides is described.

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