Tesi di dottorato: **"Synthesis, structure and properties of cyclopeptoids and cyclopeptides"**

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Aim of the research project has been the synthesis of cyclopeptides and cyclopeptoids in order to investigate their structural properties and catalytic activities.

In particular, studies of the arrangement and the cyclopeptoids organization in the crystal structure have been realized. Moreover, the influence of some aminoacidic residues on conformational control of peptoid skeleton was evaluated. In this context, the effect of proline, an amminoacid with an important role in the formation of secondary protein structures,[1] and of a pseudo-proline residue on the cystal structure and conformational equilibria of some cyclopeptoids was evaluated. In particular, *N*-methoxyethyl cyclic peptoids containing proline and *N*-methoxyethyl hexacyclopeptoid (proline-free) in complexed and uncomplexed form (**1-3**, figure 1) were successfully synthesized and characterized by X-ray diffraction. In addition, the synthesis of a cyclohexapeptoid containing a pseudo-proline residue was obtained (**4**, figure 1).

Furthermore, two isomeric amphiphilic peptoids (**5** and **6**, figure 1) were synthesized in order to investigate the effect of amphiphilicity on the crystal frame.

All that is described in sections 2,3.

Moreover, considering the well documented complexation properties of cyclopeptoids towards alkaline metals,[2] the ability of some cyclohexapeptoids to work as phase-transfer catalysts was investigated in a benchmark S_N2 reaction. In particular, the cyclopeptoid which revealed to be the most active was the *N*-[2-(2-methoxyethoxy)ethyl] side chain cyclohexapeptoid (**7**, figure 2). Therefore, we also tested some proline-rich cyclopeptoids in asymmetric phase transfer catalysis and the most promising demonstrated to be the cyclopeptoid **8** (figure 2) alternating *N*-3,5-dimethyl benzylamine glycine and proline residues.

The catalytic studies mentioned are illustrated in section 4.

Finally, in section 5 is reported a novel synthetic strategy for the synthesis of the biologically active cyclotide kalata B1 (**9**, figure 4) based on Fmoc/t-Bu solid phase synthesis and on the use of an innovative linker.

[1] M. Mutter, G. G. Tuchscherer, C. Miller, K. H. Altmann, R. I. Carey, D. F. Wyss, A. M. Labhardt, J. E. Rivier, *J. Am. Chem. Soc.*, **1992**, *114*, 1463 –1470.

[2] N. Maulucci, I. Izzo, G. Bifulco, A. Aliberti, C. De Cola, D. Comegna, C. Gaeta, A. Napolitano, C. Pizza, C. Tedesco, D. Flot, F. De Riccardis *Chem. Commun.*, **2008**, 3927-3929; C. De Cola, S. Licen, D. Comegna, E. Cafaro, G. Bifulco, I. Izzo, P. Tecilla, F. De Riccardis *Org. Biomol. Chem.*, **2009**, *7*, 2851-2854.

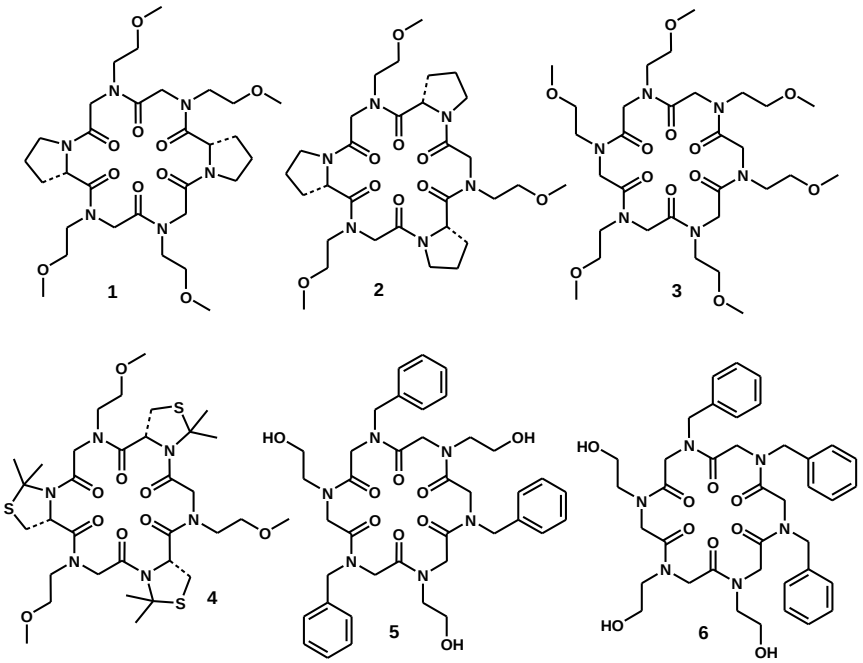

Figure 1: Cyclopeptoids synthesized for structural studies.

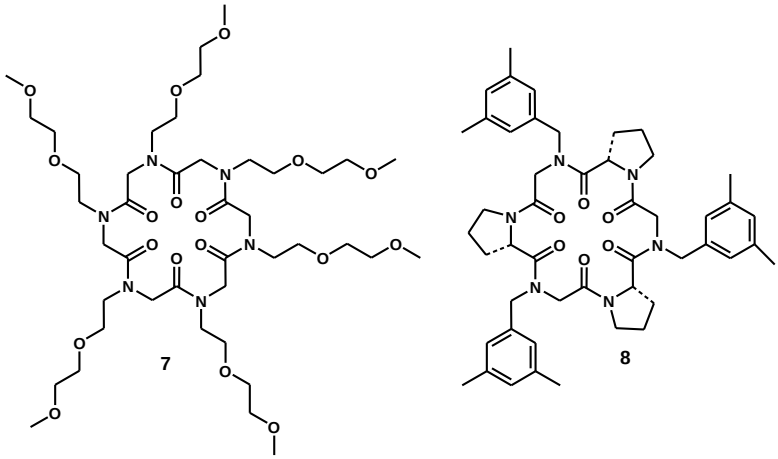

Figure 2: Cyclopeptoids resulted to be the most active in the phase-transfer catalysis studies.

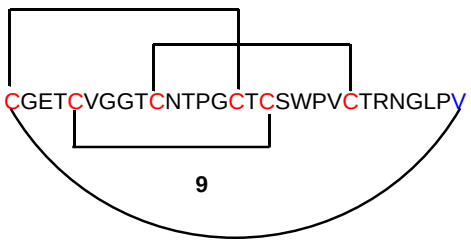

Figure 3: Cyclotide kalata B1.