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Conformational Analysis and Biological Evaluation of Ferrocene Peptidomimetics

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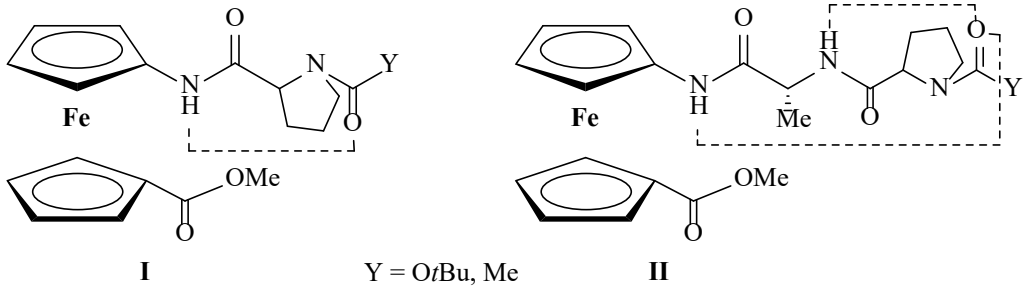
The low metabolic stability as well as poor absorption and undesired side effects caused by interaction of conformationally changeable peptides with diverse receptors represent the major obstacles to their pharmaceutical application. The development of peptidomimetics with rigidified conformation and improved biostability has proven as an efficient step towards overcoming these drawbacks. One of the strategic approaches to the peptidomimetic design is based on the utilization of small molecular scaffold capable of inducing the secondary structure upon incorporation into peptide backbone. In this respect, 1,1′-disubstituted ferrocene (Fc) scaffolds, equipped with hydrogen bonding functionalities, have been employed to nucleate turns and β-sheet-like structures.[1]

The previous results[2] obtained on peptides **I** composed of –NH–Fc–CO– scaffold and Pro confirmed the presence of γ-turn, realized through intrachain hydrogen bonding. Their biological evaluation, performed with regard to antiproliferative effect on MCF7 and He La cell line, has been demonstrated no or rather modest cytotoxic effect. In order to improve the biological activity of the ferrocene conjugates with Pro **I**, we have synthesized their higher homologues **II** with inserted Ala unit between ferrocene unit and Pro. This structural modification was found to influence the conformational pattern of the peptides **II**, but the significant impact on their biological activity with respect to cytotoxicity toward human tumor cell lines was not observed.



I **II**

Figure 1. Ferrocene bioconjugates **I** and **II**

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[2]M. Kovačević, K. Molčanov, K. Radošević, V. Gaurina Srček, S. Roca, A. Čače, L. Barišić, Molecules 19 (2014) 12852-12880.

Biography:

Lidija Barisic, Ph.D, is Professor of Organic Chemistry, Instrumental Analysis, Peptidomimetics and Bioorganometallic Chemistry at Faculty of Food Technology and Biotechnology, University of Zagreb, Croatia. Her main research interest is focused on the synthesis and biological evaluation of peptidomimetics and ferrocene-derivatized biomolecules. She has published 31 papers in peer reviewed journals and has attended 19 international conferences with presentation of own research. During doctoral education, she visited Institute of Pharmacy and Molecular Biotechnology, University of Heidelberg, Germany. She had a postdoctoral appointment at Department of Chemistry and Biochemistry, Florida Atlantic University, USA.