

CYCLE DE CONFÉRENCES DE CHIMIE

Avec le concours de : **Manufacture Française des Pneumatiques MICHELIN**
Centre de Développement Préclinique, Schering-Plough
Fédération de Chimie (FR2404)
Section Auvergne de la Société Française de Chimie
U.F.R.S.T. / Master de Chimie / Département de Chimie

Mercredi 11 Mai 2011 à 16 h

Amphi de Chimie Paul REMI - (Site des Cézeaux)

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Development of tools for fine tuning of peptide secondary structures. Structural and pharmacological applications.

The conformational freedom of peptides is often considered as a major drawback in their use as suitable therapeutic agents.^[1] Indeed, backbone and amino acids side chains flexibility is associated to low selectivity together with poor metabolic stability. However this flexibility is also responsible for the high affinities of peptides for their biological targets, allowing them to interact in the ideal conformation upon binding. The restriction of peptide conformational space is a major approach in order to improve both receptor selectivity and metabolic stability.^[2] However, reaching high binding affinities with this strategy requires a range of tools allowing fine tuning in the control of the three-dimensional space of peptide backbone while keeping all the crucial information brought by amino acids side chains, in terms of functional groups and spatial orientation. To this end, for the past few years, synthetic methodologies easy to scale up have been explored, to prepare natural amino acids surrogates such as proline chimeras,^[3] cyclopropyl^[4] and α -amino acids derivatives.^[5] These tools have known applications for pharmaceutical use,^[6] for probing bioactive conformations of peptides,^[7] and for stabilizing peptide secondary structure elements such as PPII helix^[8] or α -turns.^[1,9] In this communication, we will present their uses as tools to build i) short, fully functionalized and water-stable α -turns mimetics targeting somatostatin receptors and ii) proteinomimetics targeting IAP/Smac/DIABLO interaction. Syntheses, structural and pharmacological studies will be described.

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