INVERSE PEPTIDE SYNTHESIS VIA ACTIVATED $\alpha$-AMINOESTERS

Jean-Marc CAMPAGNE

ICGM, UMR5253, ENSCM, 8 Rue de l’Ecole Normale, 34296 Montpellier (France)
jean-marc.campagne@enscm.fr, http://am2n.enscm.fr

Peptides are attracting increasing attention on different fields such as medicinal chemistry, polymers and materials science. While these molecules are naturally built up from the $N\rightarrow C$ direction, they are chemically synthesized from the opposite direction ($C\rightarrow N$). Indeed, the traditional synthesis proceeds through the activation of the carboxylic acid moiety of a first aminoacid, by means of coupling reagents, allowing the nucleophilic attack of the amino partner of a second aminoacid with concomitant formation of the amide bond (Scheme 1, a).$^1$ Although very efficient, these coupling reagent strategies suffer from some drawbacks, notably those associated with epimerization.

So, we embarked on a program aiming to synthesize amides for application in peptide synthesis via the activation of the amine function instead of the carboxylic acid (Scheme 1, b). By doing so, we wish to avoid some inherent problems found on classic peptide synthesis (e.g. epimerization) and also to approach from the natural synthesis of peptides ($N\rightarrow C$ direction).

The use of $N,N'$-carbonyldiimidazole (CDI) for the preparation of unprecedented activated $\alpha$-aminoesters, and their transformations into several dipeptides and tripeptides will be discussed (Scheme 2).$^2$

References: