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Bioinspired Catalysis using Oligourea Helical Foldamers

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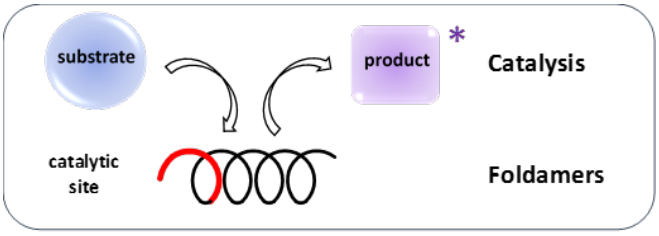
Catalysis and folding are two closely interwoven notions in Nature particularly among enzymes, and by extension can be applied to synthetic catalysts designed by chemists. Artificial monomers have been created for two decades to synthesize new oligomeric molecular architectures with a high propensity to fold, which are called foldamers.[1] In many systems, folded structure is stabilized by a strong hydrogen-bonding network, in a similar way to biopolymer structures. These folded backbones may provide significant advantages as catalyst as they could offer cooperativity in ligand binding, a greater stabilization of charged intermediates and then a minimization of entropic cost of the transition state binding.[2] They constitute a class of potential organocatalysts which deserves more investigation. Organocatalysis is an area of strong interest nowadays because of the lower toxicity of the catalysts and meta free procedures, their modularity and easiness to handle them. But generally high loading (5-20 mol%) are needed to perform chemical transformations with good yields and good stereoselectivities.[3] The synergistic effect brought by the well-defined structures of foldamers through the strong hydrogen-bonding network can be in favour of a decrease of the catalyst loading.

Oligo(thio)urea foldamers are peptides analogues, with a helical secondary structure, 2.5 residues per turn and 12- and 14-membered H-bond ring[4] and present a macrodipole which can be reinforced through activation with electro-withdrawing group at the positive pole. Binding of anions to oligourea has been studied and was shown to be site specific and not to have any impact on the helical structure thus illustrating the high potential of coordination of negatively charged species to oligourea foldamers.[5] Urea and thiourea small molecules have been widely used as H-bond donors for organocatalysis with very satisfying results.[6-8] These concepts are the basis of the development of an innovative organocatalyst with oligo(thio)urea foldamers, acting through H-bond activation. A structure-activity relationship study combining an extended substrate scope and NMR mechanistic studies was performed allowing delineation of the principles governing oligourea foldamer-based catalysis.[9]



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