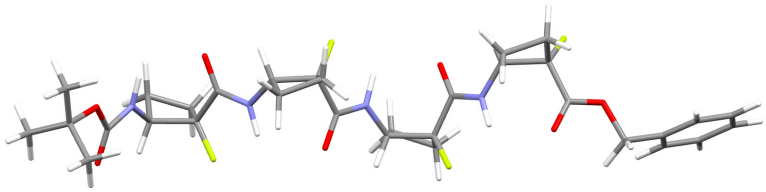
Fluorinated and oxygenated 4-membered ring β-amino acids

(Ammar Hassoun, Anh Minh Thao Nguyen, Ahmad Kassir, Thomas Boddaert and David J. Aitken)

In the field of foldamer, our research of new building blocks amenable to adopt well-defined folded and interesting shapes is made by design where the key to this fundamental concept is: minor modification at the atomic level to induce major changes at the higher levels.

We started our study from a well-established β-amino acid building block: the 2-aminocyclobutane-1-carboxylic acid (ACBC) and decided to introduce specific heteroatom modifications on the core structure to analyse potential modifications induced in the foldamer behaviour of oligomers made therefrom.

In this project our first objective was to replace the hydrogen atom in α-position by a fluorine atom of the *cis*-ACBC and decided to examine the corresponding *cis*-2-amino-1-fluorocyclobutane-1-carboxylic acid (*cis*-FACBC). With a similar steric hindrance this new building-blocks gave the electronic effects of the fluorine atom in specific backbone position in homologated amino acid on the preferred secondary structure of peptides which contain them. The conformational analysis suggested a strong conformational preference for a well-defined strand-like structure in which intra-residue hydrogen bonding is weak at best and is not consequential for adoption of the secondary structure. *(Ammar Hassoun et al. New. J. Chem. 2015, 39, 3270-3279)*



In the same concept, we actually work on the synthesis and the conformational analysis of foldamers built with the *cis*- and *trans*-3-aminooxetane-2-carboxylic acid (AOC) to study the influence of an oxygen atom in a constrained amino acid on the oligomer made therefrom. *(Anh Minh Thao Nguyen and Ahmad Kassir)*

3-membered ring β-amino acids

(James E. Taylor, Steven D. Bull, Thomas Boddaert, David J. Aitken)

Trans-2-aminocyclopropane-1-carboxylic acid (*trans*-ACPC) is the most conformationally restricted cyclic β-amino acid and is therefore an attractive target for foldamer synthesis. However, the synthesis and use of β-ACPC in oligopeptide synthesis is challenging due to its instability. Nevertheless a strategy is actually under study to thwart this problem and allow the synthesis of their oligomers. *(James E. Taylor)*