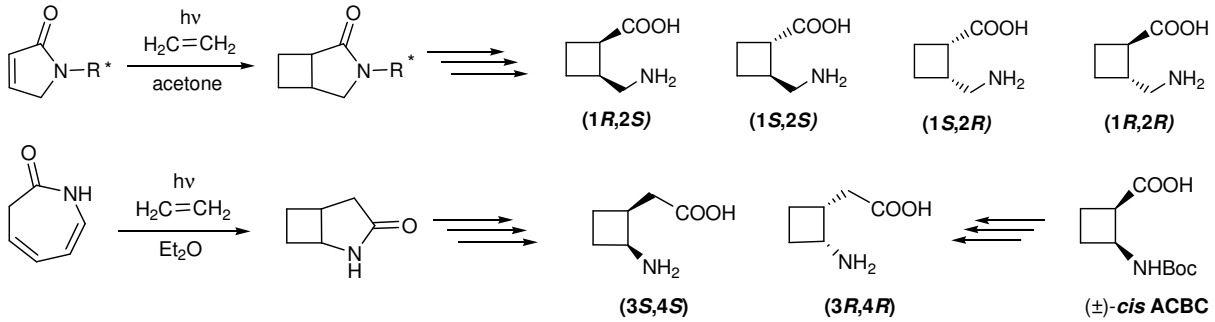
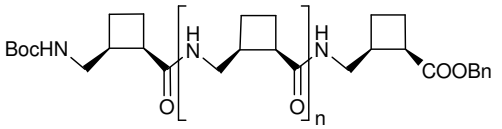
γ-Aminobutyric acid (GABA) plays a key role as a neurotransmitter in the mammalian central nervous system. A wide variety of derivatives of GABA have therefore been of interest to chemists and pharmacologists and some structural analogues are of significant therapeutic value.

Synthesis of enantiopure conformationally restricted GABA via photochemical reaction conditions.



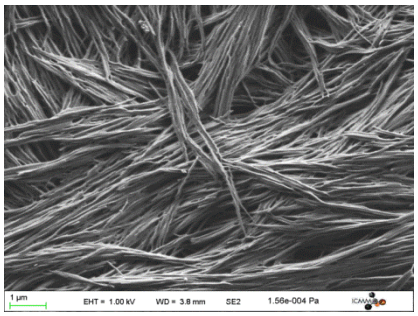
Oligopeptides containing γ-amino acids are capable of adopting well-defined secondary structures whilst being resistant to proteolytic degradation, which make them of considerable interest as peptidomimetics. Several stable helical conformers are predicted for β,γ-peptides, including the 13-helix, which is a mime of Nature's α-helix.[1] A mimetic of the α-helix is an attractive manifold for an inhibitor of protein interactions. The severe conformational restrictions imposed by the presence of a cyclobutane ring on a peptide backbone are expected to favour a limited number of secondary structures.

Preparation of homo-oligomers of cis-^{2,3}cyclobutyl-GABA :

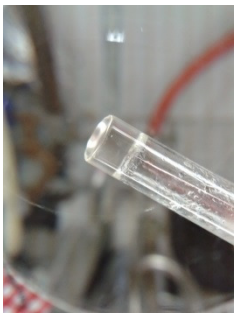


n = 0, 1, 2.

MEB image of fibrils of tetrapeptide



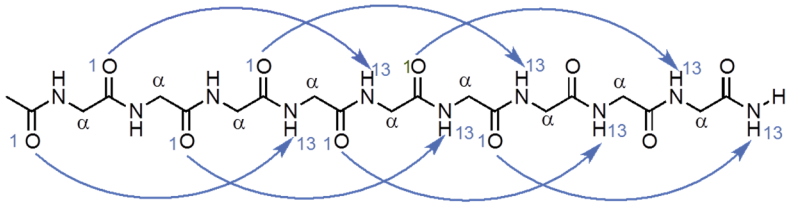
Gel of tripeptide in toluene



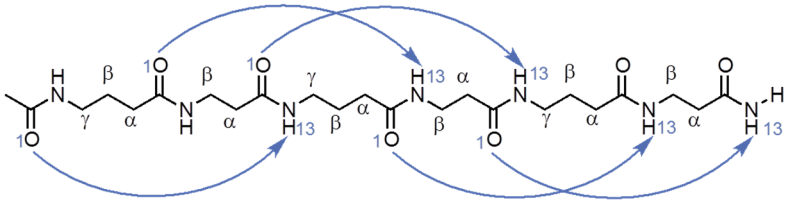
Preparation of hetero-oligomers of β,γ-peptides:

At present, we are studying the influence of the introduction of a *trans*-cyclobutane β-amino acid on β,γ-oligomer folding, with no constraint on the γ-amino acid.

- α-Helix = 13-Helix



α-AA, interactions N–H_i···C=O_{i-5}



Alternating γ-AA and β-AA, interactions N–H_i···C=O_{i-4}

Recent publications

-" Pushing the limit of the resolution for couplings measurment. " J.E. Herbert Pucheta, D. Pitoux, C. Grison, S.Robin, D. Merlet, D. Aitken, N Giraud and J. Farjon Chem.Commun, **2015**, *51*, 7939-7942.

-" Practical syntheses of both enantiomers of the conformationally restricted GABA analogue cis-(2-aminocyclobutyl)acetic acid. " Awada Hawraa, Robin Sylvie, Guillot Régis, Yazbeck Ogaritte, Naoufal Daoud, Jaber Nada , Hachem Ali , Aitken David J. *Eur. J. Org. Chem.* **2014**, 7148-7155.

-" A unified synthesis of all stereoisomers of 2-(aminomethyl)cyclobutane-1-carboxylic acid " André Virginie, Gras Marjolaine, Awada Hawraa, Guillot Régis, Robin Sylvie, Aitken David J. *Tetrahedron* **2013**, *69*, 3571-3576.

-" Rapid access to cis-cyclobutane γ-amino acids in enantiomerically pure form " André Virginie, Vidal Anne, Ollivier Jean, Robin Sylvie, Aitken David J. *Tetrahedron Lett.* **2011**, *52*, 1253-1255.