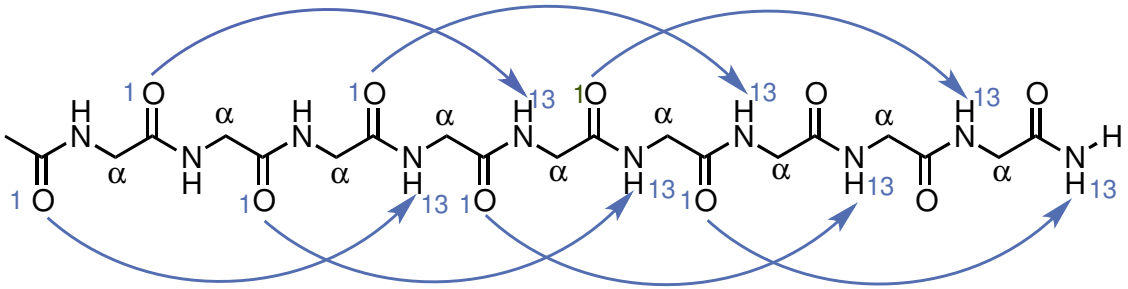
Preparation of hetero-oligomers of β,γ-peptides

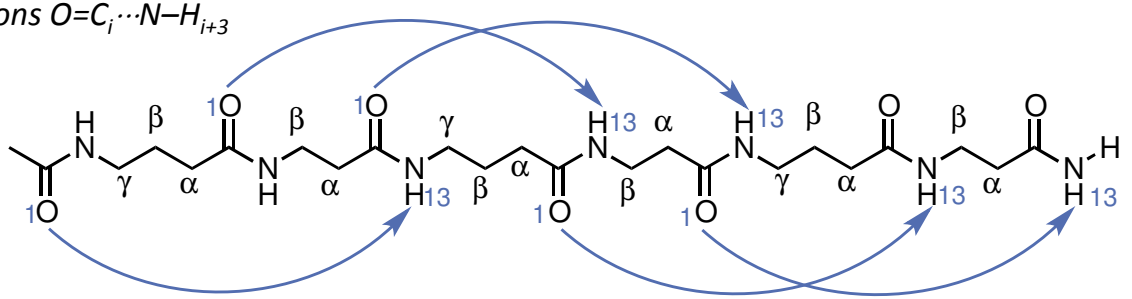
Several stable helical conformers are predicted for β,γ-peptides, including the 13-helix, which is a mime of Nature's α-helix.[1] A mimetic of the α-helix is an attractive manifold for an inhibitor of protein interactions. The severe conformational restrictions imposed by the presence of a cyclobutane ring on a peptide backbone are expected to favour a limited number of secondary structures.

α-Helix = 13-Helix

α-AA, interactions $O{=}C_i{\cdots}N{-}H_{i+4}$



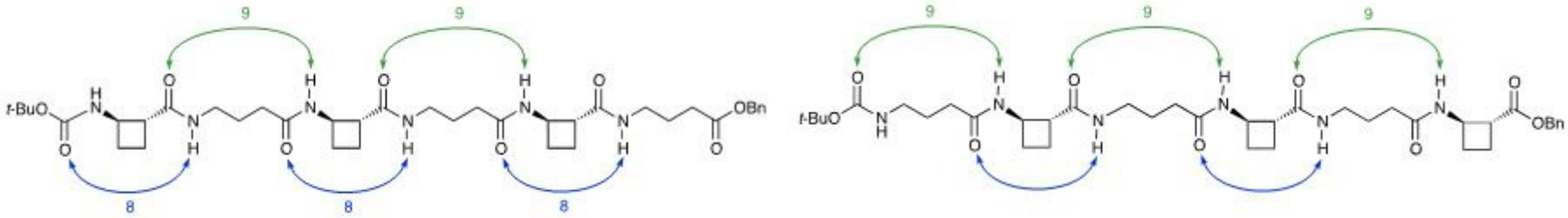
***Alternating γ-AA and β-AA**, interactions $O{=}C_i{\cdots}N{-}H_{i+3}$*



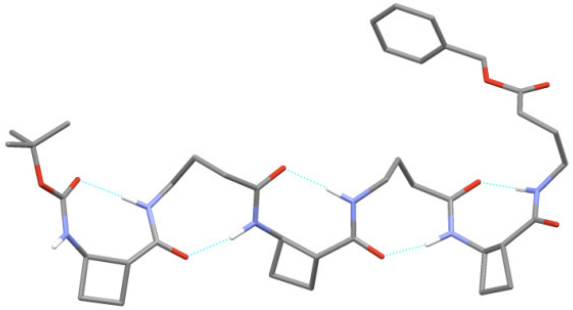
We are actually studying the influence of the introduction of a trans-cyclobutane β-amino acid on β,γ-oligomer folding, with no constraint on the γ-amino acid.

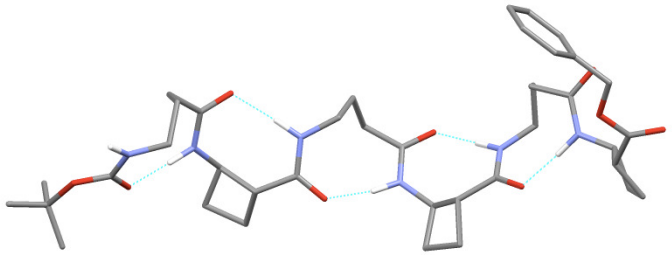
We have shown that the association of rigid trans-ACBC and flexible GABA leads to heterooligomers capable of a 9/8 ribbon structuration.

interactions $O{=}C_i\cdots N{-}H_{i+2}$ *deduced from ROESY and NOESY experiments*



Molecular modelling





- J. E. H. Pucheta, D. Pitoux, C. M. Grison, S. Robin, D. Merlet, D. J. Aitken, N. Giraud, J. Farjon, *Chemical Communications (Cambridge, United Kingdom)*, **2015**, *51*, 7939-7942
- C. M. Grison, S. Robin, D. J. Aitken *Chem. Commun.*, **2015**, *51*, 16233-16236