

Short peptides containing Norbornene amino acid (NRB): role of the NRB scaffold in self-assembly

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A number of papers report on spontaneous assembly of peptides into ordered nanostructures with a variety of morphologies and this number is still expanding.^[1] Besides the numerous advantages of using peptides as building blocks for different types of nanostructures, some limitations are well-known such as a low stability in biological medium and their unstable conformation especially when they are short or medium-sized. The insertion of unnatural amino acids in the peptide sequences is a well-known tool to overcome these problems. Both theoretical and experimental studies on this subject have been published and, in particular, the group of α,α -tetrasubstituted residues, in which the quaternary α -carbon is part of a ring has been the object of extensive investigation.^[2] Notwithstanding this interest, studies on the self-assembly of short peptides containing cyclic α,α -tetrasubstituted amino acids are very rare.^[3] The two diastereoisomeric pentapeptides AcAla-NRB-Ala-Aib-AlaNH₂ **1** and **2**, containing the two enantiomers of the non-proteinogenic α,α -tetrasubstituted norbornene amino acid (NRB), were synthesized and their conformational analysis was performed. Interestingly, despite they are made of hydrophobic amino acids, they resulted insoluble in organic solvent, but completely soluble in water. The formation of supramolecular assemblies in water was assessed by DLS. A comparison between NRB containing peptides and other peptides containing cyclic and non-cyclic α,α -tetrasubstituted residues (i.e. Aib, Ac5AA) was done in order to better understand the role played by the NRB residue in aggregation phenomena.

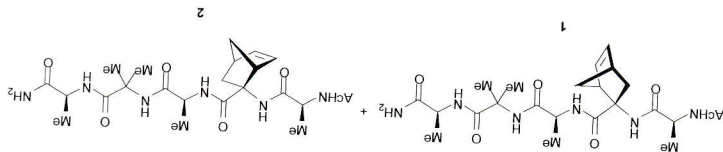


Figure 1. Pentapeptides AcAla-NRB-Ala-Aib-AlaNH₂ containing the two enantiomers of norbornene amino acid (NRB)

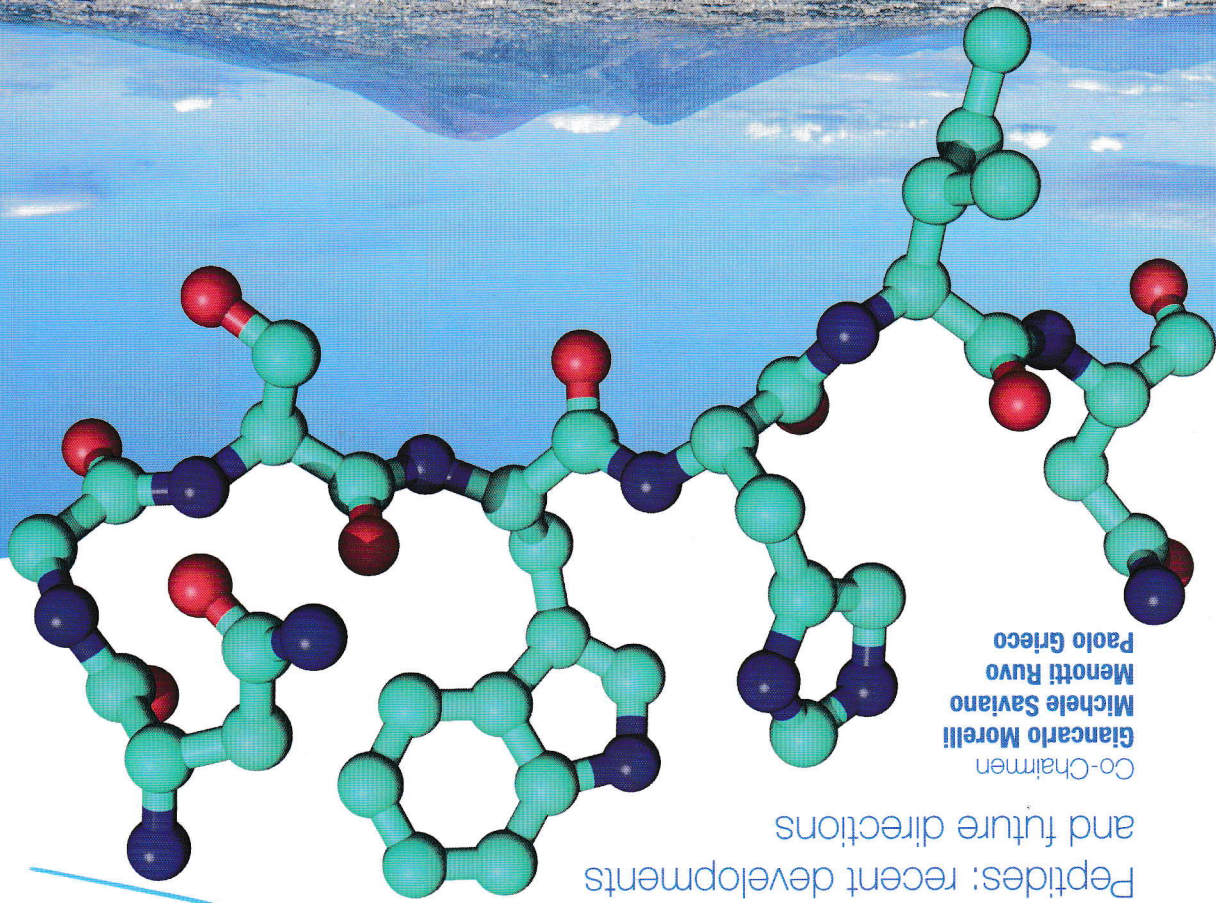
References

1. *Peptide materials From nanostructures to applications* Eds.: C. Aleman, A. Bianco, M. Venanzi, Wiley-VCH, 2013. ISBN: 978-1-119-95373-9.
2. C. Toniolo, M. Crisma, F. Formaggio, C. Peggion, *Biopolymers (Peptide Sciences)* (2001), 60, 396 and references therein; I. Maffucci, S. Pellegrino, J. Clayden, A. Conini, *J. Phys. Chem. B.* (2015), 119, 1350.
3. N. Zhou, X. Gao, Y. Lv, J. Cheng, W. Zhou, K. Liu, J. Pepl. *Sci.* (2014), 20, 868.

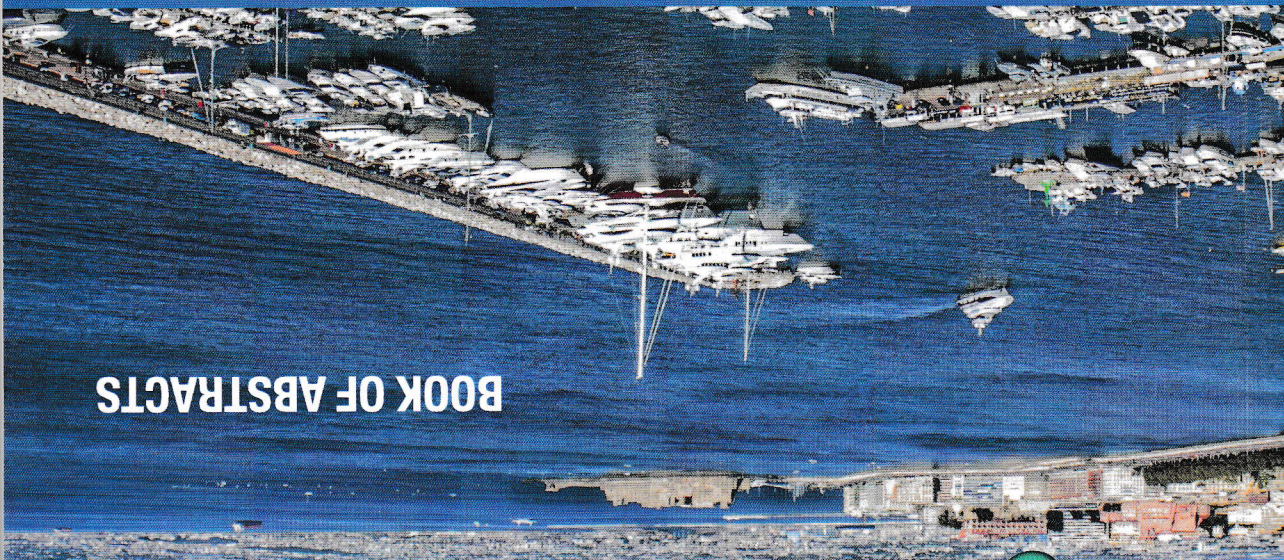
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