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Synthesis of peptidomimetics using Diaryl-β^{2,3} amino acids for the preparation of smart materials

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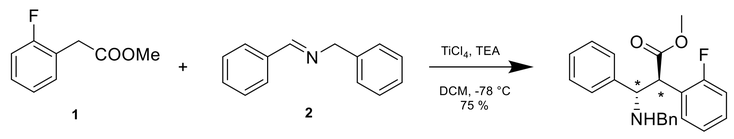
Introduction

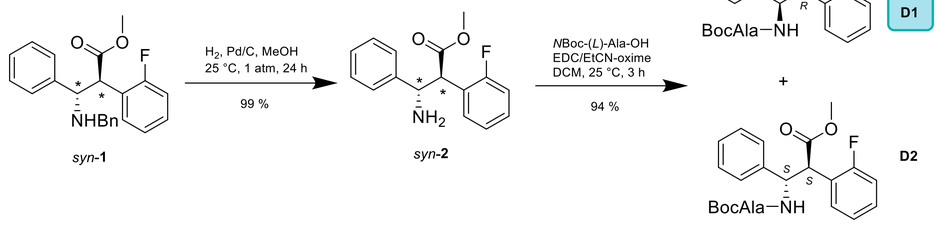
α-Amino acids are at the basis of the living world, being the building blocks of peptides and proteins. The advantages of α-peptides, *i.e.* versatility, biocompatibility and ease of preparation, make them the perfect candidates in different applications, for example biology and pharmaceutical science. However, they show some drawbacks mainly due to their protease sensitivity. To overcome this limitation, non-standard amino acids such as β-amino acids are inserted in peptide sequences to produce peptidomimetics, molecules with the same biological activity of the natural peptides but with enhanced proteolytic and conformational stability.[1] In addition, the ability of peptides or amino acids alone to self-assemble and self-organize, allows their use in wide and variable applications, from nanomedicine to electrochemistry and catalysis, as well as bioelectronic materials.[2]

Synthesis of unnatural fluorine-substituted β^{2,3}-diarylamino acid

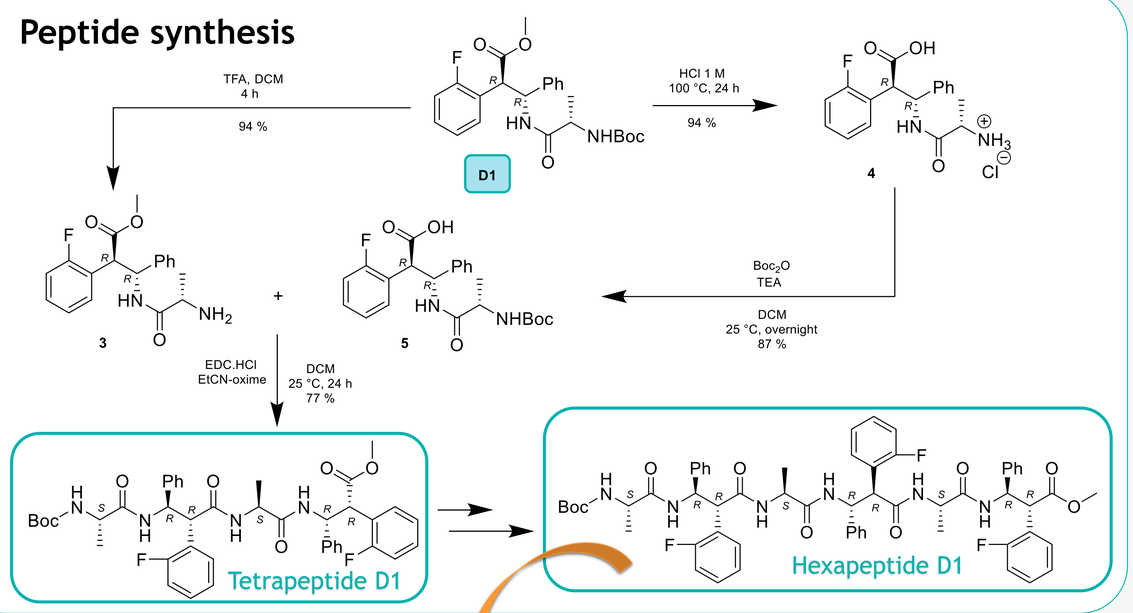
Stereoselective Mannich-like reaction[3]



L-Ala used to resolve the racemic mixture

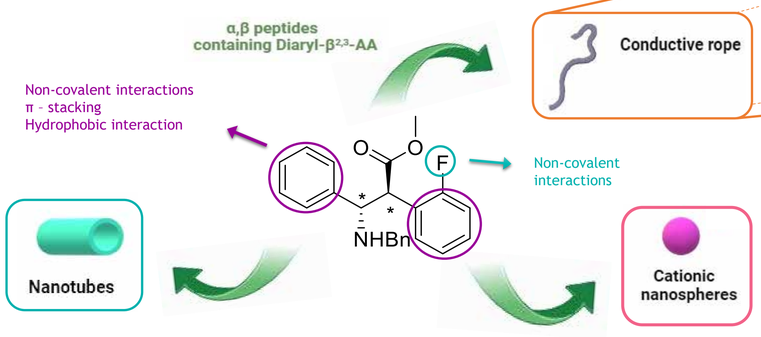


Peptide synthesis

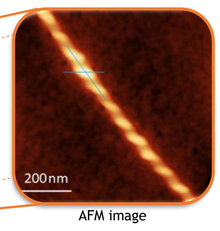


β^{2,3}-Syn Diaryl AA

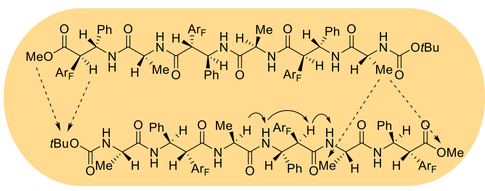
This β-amino acid triggers the formation of different bioinspired architectures, depending on the peptide sequence in which it is inserted. So far, different nanomaterials such as nanotubes,[4] supramolecular conductive ropes,[5] and cationic nanospheres,[6] were obtained and characterized.



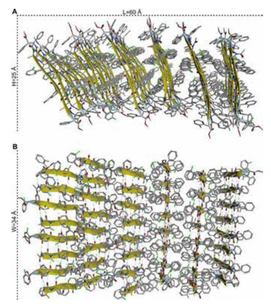
Extended conformation → self-assembles to form an antiparallel β-sheet structure



AFM image



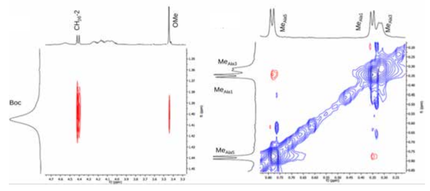
Conductive Nanorope



Nanorope structure where the aromatic groups are close to each other allowing to have electron conduction properties.[5]

D1

ROESY zoom of Boc and Me region spectrum



TOR VERGATA UNIVERSITÀ DEGLI STUDI DI ROMA

In collaboration with Prof. Gatto University of Tor Vergata

Electrochemical characterization

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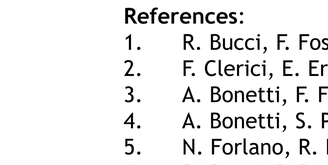
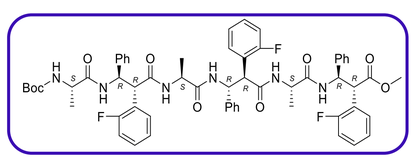
In collaboration with D.C. 13, Merve Gul
NanoReMedi programme
Polytechnic University of Catalonia



Tetrapeptide D1(TP1)



Hexapeptide D1 (HP1)

Working Electrode: Stainless Steel

- Hexapeptide showed a good electroactivity → Biosensor for biomolecule detection
- Tetrapeptide showed good capacitive behavior → Bio-supercapacitor

Cyclic Voltammetry (CV)

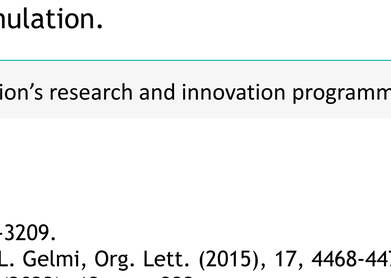
Electrochemical Impedance Spectroscopy (EIS)

Dipeptide D1

Dipeptide D2

Tetrapeptide D2 (TP2)

Modification of Working Electrode:

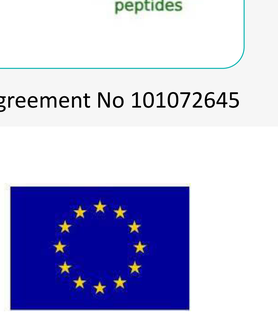


Factors influencing the electrochemical behavior:

- Spatial disposition of the amino and carboxyl groups.
- Spatial disposition of the phenyl and flourobenzene.
- Length and surface area according to dipeptides, tetrapeptides and hexapeptide.

CV

EIS - Nyquist Plot



Applications and future work

- Self-assembly studies.
- Study of the relationship between self-assembly and electrochemical activity.
- Development of electrically responsive peptides able to prevent bacterial contamination on implants.
- Controlled release of drugs and antimicrobials by electrostimulation.

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