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Digest paper

Non-standard amino acids and peptides: From self-assembly to nanomaterials

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ABSTRACT

The exploitation of peptides in the development of smart nanomaterials is gaining increasing attention in the last few years. Amino acids are indeed able to drive the self-assembly and the self-organization at the molecular level. By using non-standard amino acids, it is possible to expand the scope of the possible applications, ranging from biomaterials, biosensors to drug delivery systems. In this digest, the recent advances in this field are presented.

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Introduction

Amino acids are the building blocks of peptides and proteins. In million years of evolution, Nature has optimized their structures to absolve numerous functions in almost all the biological processes. They are indeed able to induce a high molecular complexity starting from relatively simple molecules, being at the molecular basis of the living world. Taking inspiration from Nature, scientists are now trying to develop smart peptide materials for a wide range of applications, such as biomolecular devices, biosensors, and hybrid catalysts. The modularity of amino acids and their ability at driving self-assembly and self-organization leads to a high versatility in functions. Amino acids can both function as single molecules and when inserted in peptides. Furthermore, by tailoring the functional groups on the side chains and at the N- and C-terminus it is possible to expand endlessly their molecular variability. Different kinds of materials could be thus developed, and, depending on the solvent and the environmental conditions, hydro- and organogel, nanoarchitectures, vesicles and micelles have been obtained. In the case of standard or coded amino acids, many papers, some reviews and books have recently been published.[1] In this digest,

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NON-STANDARD AMINO ACIDS:
- N- and/or C-terminus capping
- Side chains modification
- β-amino acids
- γ-amino acids

NANOMATERIALS:
- Hydro- and organo-gels
- Vesicles
- Nanotubes
- Nanorings
- Complex architectures (catenanes, collagens….)

Fig. 1. Examples of non-standard amino acids and nanomaterials developed.

we aimed to explore the advances in using non-standard amino acids for the design of nanomaterials, highlighting in particular some new developments which have been reported since 2010. A comprehensive review of all obtained peptide nanostructures is beyond the scope of this manuscript. We focused our attention on the different amino acid features, starting from simple variation at N- and C-terminus of standard amino acids to unnatural α, β and γ-amino acids. We envisaged the use of non-coded amino acids to be of particular relevance, expanding the scope of the nanoarchitectures so obtained. In particular, the use of non-coded amino acids opens the doors to more stable materials that could be, for instance, exploited in biomedical applications such as drug delivery systems (See Fig. 1).

Capped natural amino acids

A simple and widely used strategy to modify the amino acid scaffold is the introduction of substituents at N- or C-terminus.[2] The most common functionalization is the attachment of an aromatic moiety, such as pyrene[3] and ferrocene[4], through amide bond formation. In these examples, π–π interactions drive the self-assembly of the constructs yielding, in most cases, hydrogelators. Naphthalene group has been used to functionalize dendrons composed of aspartic acid (Asp) and alanine (Ala), (**Nap-G1** and **Nap-G2**, Fig. 2).[5]

Nap-G1 in cyclohexane develops a gel, formed by a fibrous network with β-sheet architecture, but in mixed solvents (chloroform/petroleum ether 1:5, v/v) exhibits a spherulitic network (Fig. 2). On the other hand, **Nap-G2** acts as an efficient organogelator in chloroform but forms crystalline microbelts in relatively high polarity solvents, such as acetone and methanol (Fig. 2). These polymorphic features are due to the bulky naphthyl group at the N terminus that drives the molecular architectures formation during the self-assembly in different solvents.

The derivatization of amino acids with arylenediimides has also been investigated. Particularly, naphthalenediimides (**NDI**s) and perylenediimides (**PDI**s) (Fig. 3) give access to a wide variety of applications ranging from biomedicine to electronics, as reviewed

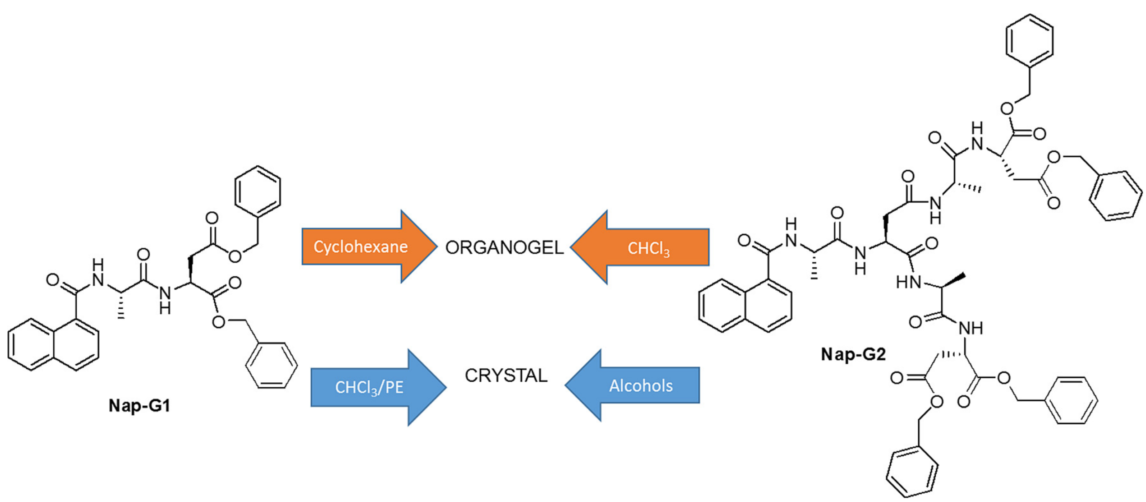
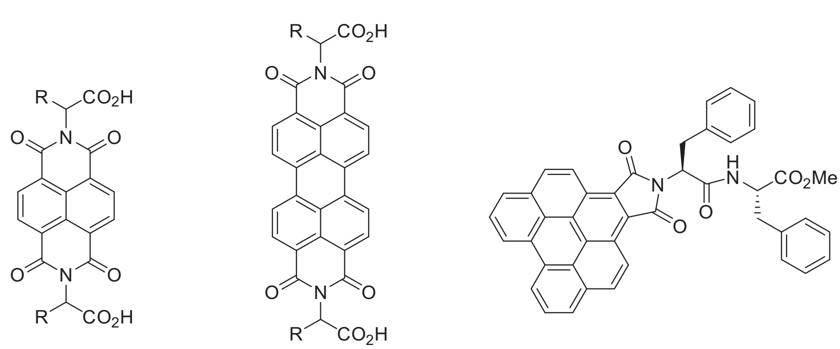


Fig. 2. Naphtalene functionalized dendrons.



NDI PDI BPI-FF

Fig. 3. *N*-Arylenediimides derivatives of single amino acids (**NDI** and **PDI**) and of Phe-Phe dipeptide (**BPI-FF**).