Abstract

Chirality and self-assembly are basic attributes of nature and closely related life activity. In materials science, chirality and self-assembly of biopolymers also inspire the development of functional materials, especially in cases of amino acids and polypeptides. Synthetic polypeptides have been studied in many fields, especially in medical applications such as nanoparticles, drug delivery system, and tissue engineering.

2,5-Diketopiperazines (DKPs), which are cyclic dipeptides, are common in nature or easily synthesized by the condensation of α-amino acids. Based on two symmetrical amide groups in a six-membered ring, DKPs have four sites able to form hydrogen bond, which result in highly molecular arrangement properties. Due to the strong hydrogen bonding and chiral structure, DKPs have been studied in medicine design, chiral catalyst, low molecular weight gelators, and annexing agent for polymers. However, though DKPs have many interesting properties, only a few DKP-based polymers were reported and the effects of DKP moiety on the corresponding properties of polymers are not clear. Otherwise, the synthesis of DKP monomer is challenging and important for the synthesis of polymers.

The aim of this work is to study chirality and self-assembly properties of DKP monomers and resulting polyamides. This work is divided into three parts: (1) syntheses and configurational studies of diketopiperazine stereoisomers; (2) syntheses and solvent-controlled self-assembly of diketopiperazine-based polyamides from aspartame; (3) syntheses and stereochemistry-property studies of diketopiperazine-based polyamides.

In chapter II, to synthesize AB-type DKP monomers, cyclo(aspartyl-4-amino-phenylalanyl) (ADKP), step-wise protection and deprotection of (L/D)-aspartic acid and (L/D)-4-nitro phenylalanine was performed. Caused by the solubility problem of precursors of trans-ADKPs, LD- and DL-ADKP were synthesized in low yield. No racemization occurred during the synthesis. Structural characterizations and studies of stereoisomers were performed by 1H NMR, ROESY, FTIR, and CD. In DMSO solution, configurations of cis- and trans-ADKP were confirmed, in which DKP ring was in planer structure, and the folded benzene ring was stabilized by Cβ-H…π interaction in cis-structures and Cα-H…π interaction in trans-structures. Self-assemble behavior of stereoisomer was studied by solvent displacement method. LL- and DD-ADKP show similar chrysanthemum-like morphology, while LD-ADKP shows rose-like morphology. The present study provides a synthesis method for stereoisomers of DKP, and structural insight of phenylalanine-aspartic acid-based DKP, which have potential for drug and catalyst design.

In chapter III, LL-type ADKP was synthesized from aspartame and subsequently utilized in the polycondensation of homo-polyamide (PA1) with high molecular weights. By using various amino acid, dicarboxylic acid, and diamine, random DKP-based copolymers were also synthesized. The self-assembly properties of ADKP and PA1 were studied via the solvent displacement method. Notably, PA1 self-assembled into particles with various morphologies in different solvent systems, such as irregular networks, ellipsoids, and vesicles. The morphological transformation was also confirmed by dropping acetone and toluene onto the PA1 particles. Furthermore, infrared spectra and Hansen solubility parameters of PA1 and different solvents revealed the particle formation mechanism, which provided more insights into the relationship between the morphology and strength of the hydrogen bonding of each solvent.

In chapter IV, Homo-polyamides and co-polyamides from ADKP stereoisomers were synthesized. Due to same chemical structure, all PAs showed similar molecular weight, thermal properties and solubility. Determined by CD spectroscopy, all PAs showed optical activity. Moreover, solvent/third molecule effect on LL-PA was investigated by adding other solvents into the LL-PA DMSO solution. When water and ethanol were added, LL-PA in DMSO became optical inactivity. It is suggested that water or ethanol disturbed hydrogen bond between DKP units in polymer chain, which played an important role in stabilizing secondary structure of polymer. Self-assembly of PAs were investigated. LL-PA, DD-PA and LLcoDD-PA self-assembled into vesicles, while LD-PA self-assembled into cubic structure in toluene and acetone. The present study provides structural insights of DKP-based polymers with stereochemistry, and reveals their optical and self-assemble properties.

As conclusions, DKP unit is an important building block for medicines, catalysts, supramolecules, and has enormous potential for development of functional materials. However, polymers carrying DKP unit in backbone have not been well explored and are lack of study. In this study, novel AB-type DKP monomers and relative polyamides with stereochemistry were successfully synthesized. Chirality and self-assembly properties of obtained monomers and polyamides were well studied. This study creates a new insight on stereochemistry and self-assembly of DKP monomers and polymers, which could lead to the development of functional materials.

Keywords: bio-based polymers, diketopiperazine, self-assembly, nanoparticles, stereochemistry