Chirality-dependent self-assembly of oligo(*N*-phenylacrylamides) prepared by controlled radical polymerization

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Abstract

Chirality-based assembly is essential for the development of functional molecular systems. Polynucleotides, for example, preserve genetic information by forming right-handed double helix, depending on chirality of their backbones. However, little has been reported about chirality-based self-assembly of acrylic polymers, although acrylic polymers have a robust C-C bond in the main chain and can be easily polymerized from inexpensive and versatile monomers. This is due to the lack of techniques for preparing optically pure acrylic polymers. In this study, we report chirality-based self-assembly of oligo(*N*-phenylacrylamides) (PAAm) that can be synthesized by radical polymerization. Optically pure oligo(*N*-phenylacrylamides) were prepared by RAFT polymerization followed with two-step column chromatography (Fig. 1).[1,2] The six stereoisomers and one racemic mixture of the tri(*N*-phenylacrylamides) were isolated. Self-assembly of the oligo(*N*-phenylacrylamides) were investigated by testing concentration dependent gelation of each isomers and combination of the isomers.

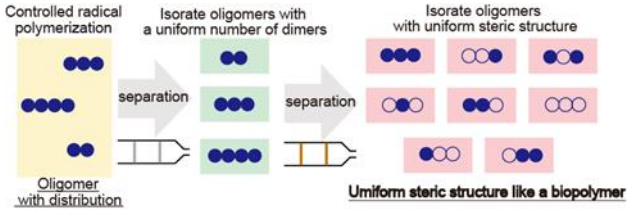

Fig. 1 Procedure for preparing oligomers with uniform

1. Introduction

Biomacromolecules recognize three-dimensional structure of target molecules and form complex to perform various functions. For example, DNA recognizes three-dimensional structure of complementary strand and forming a double helical structure in order to stably stores genetic information. We have been developing synthetic polymer materials with advanced functions like biomacromolecules by using radical polymerization. Recently, a technique for preparing the polymers of defined molecular weight and monomer sequence (homogeneous oligomers) has been reported.[1] Furthermore, the homogeneous oligomers recognize specific amino acid sequence of a target peptides.[2] However, three-dimensional structure of the homogeneous oligomers are not homogeneous, and thus little has been reported about three-dimensional structures dependent target recognition ability of the synthetic polymers. In this study, we isolated completely conformationally defined oligomers with relatively rigid side chains using *N*-phenyl acrylamide (PAAm) as a monomer, and investigated the chirality-dependent self-assembly ability of the synthetic oligomers. Specifically, PAAm oligomers with narrow molecular weight distribution were synthesized by reversible addition fragmentation chain transfer (RAFT) polymerization, and seven stereoisomers of PAAm trimer with completely defined stereostructure were isolated by a combination of reverse phase- and chiral-chromatography (Fig. 1). Self-assembly of the oligo(*N*-phenylacrylamides) were investigated by testing concentration dependent gelation of each isomers and combination of the isomers.

2. Experiment

Oligomers prepared by RAFT polymerization were first separated based on differences in degree of polymerization using reversed-phase chromatography, followed by separation based

on differences in steric structure using normal-phase chiral chromatography. Each fraction was analyzed by molecular weight, ^{1}H NMR, and CD spectra. The gelation concentration of the mixed oligomers was also measured to confirm the interaction between the oligomers of each conformation. The gels were evaluated and analyzed.

3. Results and discussion

Fig. 2 (left) shows the results of the separation of molecular wight using reversed-phase chromatography. Mass spectra analysis established that oligomer was separated by the number of hydrophobic phenyl groups. In addition, we confirmed that dimer (Frac. 2) and trimer (Frac. 3) was divided into two and three diastereomers, respectively. These three diastereomers of trimer were separated by normal-phase chiral chromatography, and seven isomers of the eight stereoisomers were successfully isolated (Fig. 2 (right)).

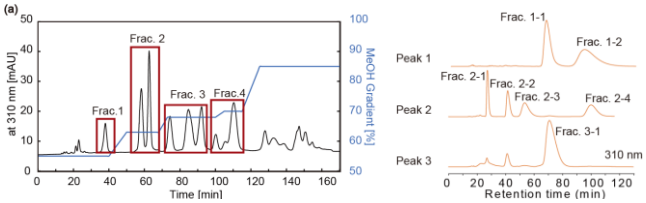

Fig. 2 Isolation of structure-defined oligomers by combination of reverse phase- (left) and chiral chromatography.

Each isomer was analyzed by ^{1}H NMR, and the stereo configuration of the main chain was assigned based on the spectral shape and coupling constant of the main chain (Fig. 3 (left)). Three pairs of the same NMR spectral shape were identified, and these were predicted to be in an enantiomeric relationship with each other. The results of the CD spectra of each fraction are shown in Fig. 3 (right). 6 peaks except Frac. 3-1 all showed the characteristic three-pattern cotton effect, but the main-chain-derived cotton effect could not be confirmed in Frac. 3-1. This was considered to indicate that Frac. 3-1 contains two oligomers with different steric structures that are in an enantiomeric relationship with each other. Gelation of Frac. 3-1 was observed at relatively low concentrations. The other trimeric oligomers showed no gelation in a comparable concentration range, indicating that only certain combinations of conformations interact strongly with each other.

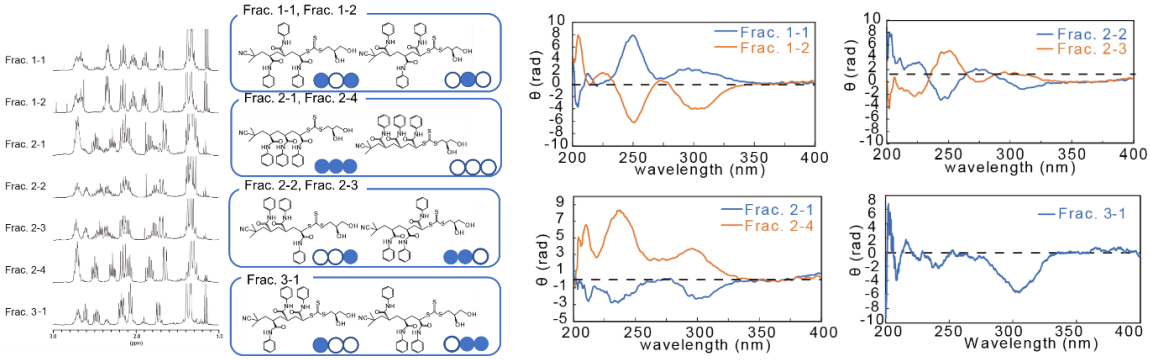

Fig. 3 ^{1}H NMR and CD spectra of isolated tri(*N*-phenylacrylamides).

4. Conclusions

Oligomers prepared by RAFT polymerization were subjected to separation of molecular wight, and the eight stereoisomers of the trimer were successfully separated into seven by the difference in the stereochemistry of the oligomer's main chain using chiral separation. We also found that specific pair of stereo-isomers recognize each other and self-assembled to form organogels.

References

1) J. Lawrence, et ak. J. Am. Chem. Soc., 2016, 138, 6306.

2) Y. Hoshino, et al. *Angew. Chem. Inter. Ed.*, 2020 59, 679.