Macromolecular helicity inversion of an optically active helical poly(phenylacetylene) by chemical modification of the side groups†‡

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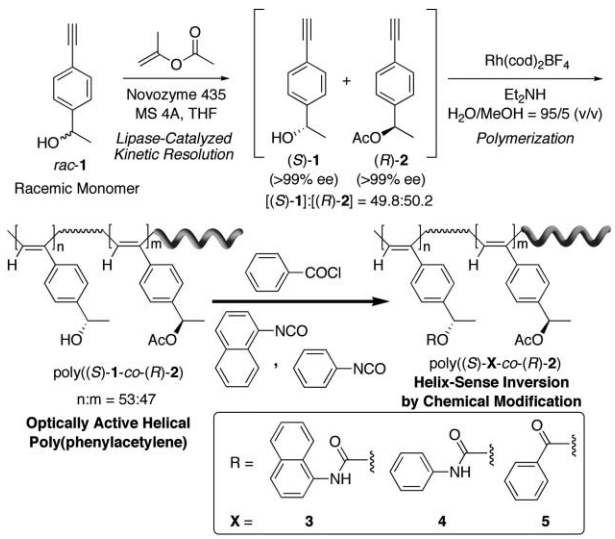
An optically active helical poly(phenylacetylene) was synthesized by the copolymerization of phenylacetylenes bearing optically active hydroxy or ester groups obtained by the kinetic resolution of a racemic phenylacetylene with lipase; the helix-sense was inverted from one helix to another by the further chemical modification of the hydroxy groups with achiral bulky isocyanates or an acid chloride.

The enzyme-catalyzed reaction is one of the most useful and powerful methods for obtaining optically active compounds because enzymes possess a high catalytic activity and excellent stereoselectivity for specific substrates, thus producing enantiomerically pure compounds.[1] For examples, lipases, one of the esterases, can be used as biocatalysts in organic media and kinetically resolve racemic alcohols, especially secondary alcohols, into optically active alcohols and esters by enantioselective transesterification with acetylating agents such as isopropenyl acetate.[2] To date, the kinetic resolution of racemic alcohols with lipases has been extensively studied and has become one of the standard techniques to obtain optically pure alcohols and esters. Recently, the chemoenzymatic kinetic resolution with lipase was also applied to the polymerization of racemic lactones to yield optically active polyesters.[3]

On the other hand, significant attention has recently been paid to developing synthetic helical polymers with a controlled helix-sense not only to mimic biological helices, such as DNA and proteins, but also for their potential applications in functional chiral materials, such as enantioselective catalysts, chirality sensors, and liquid crystals.[4] Polyacetylenes are some of the typical dynamic helical polymers composed of interconvertible right- and left-handed helical conformations separated by the rarely occurring helical reversals. Therefore, the introduction of optically active substituents into the pendant groups forces the main chain to form a predominantly one-handed helical conformation, resulting in a characteristic induced circular dichroism (ICD) in the polyene backbone regions.[5] Accordingly, the synthesis of optically active monomers and subsequent polymerization with transition metal catalysts are essential for the preparation of optically active helical polyacetylenes.[6] We now report a unique and versatile method to synthesize an optically active, helical poly(phenylacetylene) starting from an optically inactive, racemic phenylacetylene bearing a secondary alcohol pendant (*rac*-**1**) assisted by the kinetic resolution of the monomer with lipase in the presence of isopropenyl acetate as an acetylating agent, followed by the copolymerization of the resulting optically active monomers bearing an alcohol ((*S*)-**1**) and ester group ((*R*)-**2**) as the pendants (Scheme 1). In addition, the preferred helical sense of the copolymer can be further inverted by the reaction of the pendant hydroxy groups with bulky achiral isocyanates and an acid chloride.

The kinetic resolution of *rac*-**1** with lipase was performed in tetrahydrofuran (THF) in the presence of isopropenyl acetate and molecular sieves (4 Å) (MS 4A) at 40 °C (Scheme 1).[7] Novozyme 435 (Novozymes Corp.), a commercially available, macroporous acrylic resin on which lipase B from *Candida antarctica* was immobilized, was used as the enzymatic catalyst. The conversion of *rac*-**1** to (*R*)-**2**, thus producing (*S*)-**1** as the unreacted **1**, was monitored by measuring the ^{1}H NMR spectra of the mixture of **1** and (*R*)-**2**. After 5 h, approximately half of the *rac*-**1** had been converted to (*R*)-**2** (Fig. S1), and the reaction was terminated by filtration of Novozyme 435 from the reaction mixtures. The obtained enantiomeric excess (ee) values of (*S*)-**1** and (*R*)-**2** were determined by HPLC using chiral columns and were greater than 99% (Fig. S2).[8] These results indicate that the kinetic resolution of *rac*-**1** proceeded ideally.



Scheme 1

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† Electronic supplementary information (ESI) available: Synthetic details, ^{1}H NMR and chiral HPLC measurement results of kinetically resolved monomers, ^{1}H NMR spectrum of poly((*S*)-**1**-*co*-(*R*)-**2**), and CD spectra of homopolymers of (*S*)-**1**, (*R*)-**2**, and (*S*)-**3**. See DOI: 10.1039/b701281k

‡ The HTML version of this article has been enhanced with colour images.

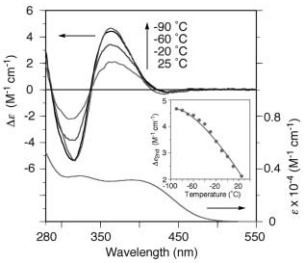

Fig. 1 CD spectra of poly((*S*)-**1**-*co*-(*R*)-**2**) in THF at various temperatures. Absorption spectrum of poly((*S*)-**1**-*co*-(*R*)-**2**) at *ca.* 25 °C is also shown. Inset shows the temperature-dependent CD intensity (2nd Cotton effect) changes of poly((*S*)-**1**-*co*-(*R*)-**2**) in THF.

Next we copolymerized (*S*)-**1** and (*R*)-**2** obtained by the kinetic resolution of *rac*-**1** without further purification and isolation with $Rh(cod)_2BF_4$ (cod: cyclooctadiene) as a catalyst in water–methanol (95 : 5, v/v) in the presence of diethylamine at 30 °C.[7] The copolymerization rapidly proceeded, and the polymer (poly((*S*)-**1**-*co*-(*R*)-**2**)) precipitated within a few minutes. After 26 h, poly((*S*)-**1**-*co*-(*R*)-**2**), soluble in DMSO, DMF, pyridine, $CHCl_3$, and THF, was obtained in an 85% yield. The molecular weight (M_n) and its distribution (M_w/M_n) estimated by size exclusion chromatography (SEC) were 8.9×10^4 and 2.0 (PEO-PEG standards), respectively. The stereoregularity of poly((*S*)-**1**-*co*-(*R*)-**2**) was investigated using ^{1}H NMR spectroscopy. The ^{1}H NMR spectrum of poly((*S*)-**1**-*co*-(*R*)-**2**) in DMSO-d_6 showed a rather sharp singlet centered at 5.72 ppm due to the main chain's protons, indicating that poly((*S*)-**1**-*co*-(*R*)-**2**) possesses a highly *cis-transoidal* stereoregular structure (Fig. S3). The composition of the (*S*)-**1** and (*R*)-**2** units in the copolymer was determined to be 53 : 47 based on its ^{1}H NMR spectrum and elemental analysis.[9]

Fig. 1 shows the CD and absorption spectra of poly((*S*)-**1**-*co*-(*R*)-**2**) in THF at various temperatures. The copolymer exhibited a split-type ICD in the long absorption region of the conjugated polymer backbone; the ICD was similar in pattern to those of the previously reported optically active poly(phenylacetylene)s,[5a,b] indicating that poly((*S*)-**1**-*co*-(*R*)-**2**) has a predominantly one-handed helical conformation, even though the starting monomer was racemic. A small chiral bias in the pendants generated by the enzyme-assisted resolution was transformed into a main chain conformational change with a large amplification, resulting in the formation of an excess of the preferred helical sense. The CD intensity of the second Cotton effect ($\Delta\varepsilon_{2nd}$) monotonically increased with the decrease in temperature (Fig. 1, inset).

Poly((*S*)-**1**-*co*-(*R*)-**2**) possesses reactive hydroxy groups at the pendants. We anticipated that the conversion of the hydroxy groups to more bulky carbamoyl or ester groups than the acetyl groups through the reaction with isocyanates or acid chlorides might enhance the helical sense excess and further invert the helical sense of the poly((*S*)-**1**-*co*-(*R*)-**2**). The polymer reactions of the hydroxy groups of poly((*S*)-**1**-*co*-(*R*)-**2**) with naphthyl and phenyl isocyanates and benzoyl chloride produced the copolymers, poly((*S*)-**3**-*co*-(*R*)-**2**), poly((*S*)-**4**-*co*-(*R*)-**2**), and poly((*S*)-**5**-*co*-(*R*)-**2**), respectively (Scheme 1).[7] The ^{1}H NMR spectra of the modified copolymers showed that the hydroxy groups were completely converted into the corresponding carbamoyl and ester groups. Fig. 2A shows the CD spectra of those modified copolymers together with that of poly((*S*)-**1**-*co*-(*R*)-**2**) for comparison in THF at −80 °C. As expected, the ICD pattern of the copolymers after modification was completely inverted, thus showing mirror image ICDs to that of poly((*S*)-**1**-*co*-(*R*)-**2**), indicating that the helix-sense of poly((*S*)-**1**-*co*-(*R*)-**2**) was opposite to those of poly((*S*)-**3**-*co*-(*R*)-**2**)–poly((*S*)-**5**-*co*-(*R*)-**2**).[10] Poly((*S*)-**3**-*co*-(*R*)-**2**) bearing the most bulky naphthylcarbamoyl groups exhibited the most intense ICD. Although the inversion of helicity has been reported for several helical polymers in response to various external achiral and chiral stimuli, such as temperature, solvent, and chiral additives,[11] to the best of our knowledge, this is the first example of helicity inversion by chemical modification using achiral compounds.[12] The ICD intensities of poly((*S*)-**3**-*co*-(*R*)-**2**)–poly((*S*)-**5**-*co*-(*R*)-**2**) also increased when temperature was lowered (Fig. 2B), due to the reduction of the population of the helical reversals between the right- and left-handed helical segments of the copolymer chains.[4,5b,13] All the copolymers prepared in this study, however, showed a rather weak ICD when compared to those of the previously prepared helical poly(phenylacetylene)s.[4e,5a,b] This means that the helical sense excesses of the copolymers may be imperfect even at low temperature. The introduction of more bulky pendant groups may further amplify the helical sense excess.

In conclusion, we succeeded in the synthesis of an optically active, helical poly(phenylacetylene) (poly((*S*)-**1**-*co*-(*R*)-**2**)) by the enzymatic enantioselective transesterification of a racemic phenylacetylene bearing a secondary alcohol moiety (*rac*-**1**) followed by

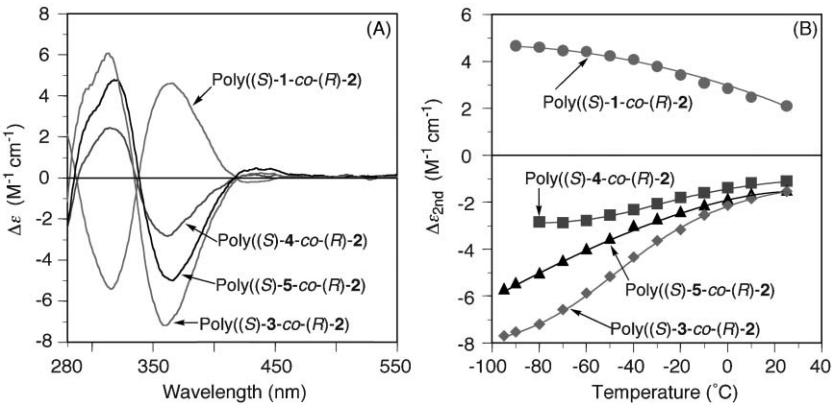

Fig. 2 (A) CD spectra of poly((*S*)-**1**-*co*-(*R*)-**2**), poly((*S*)-**3**-*co*-(*R*)-**2**), poly((*S*)-**4**-*co*-(*R*)-**2**), and poly((*S*)-**5**-*co*-(*R*)-**2**) in THF at −80 °C. (B) Temperature-dependent CD intensity (2nd Cotton effect) changes of poly((*S*)-**1**-*co*-(*R*)-**2**), poly((*S*)-**3**-*co*-(*R*)-**2**), poly((*S*)-**4**-*co*-(*R*)-**2**), and poly((*S*)-**5**-*co*-(*R*)-**2**) in THF.

the subsequent copolymerization of the obtained optically active phenylacetylenes in one-pot without further isolation and purification using a rhodium catalyst. The helix-sense of the resulting copolymer was inverted from one helix to another by further modification of the pendant hydroxy groups with achiral bulky isocyanates and an acid chloride. We believe that this concept will become a novel methodology for the construction of helical polymers with a controlled helix-sense based on *racemic* monomers. In addition, the dynamic kinetic resolution (DKR) of secondary alcohols by the enzyme-catalyzed enantioselective transesterification coupled with the racemization of secondary alcohols using various transition metal catalysts has been reported. Based on this process, enantiomerically pure esters can be quantitatively synthesized by the DKR of racemic secondary alcohols.[14] Therefore, the combination of our concept developed in this study and DKR may lead to producing optically active, helical homopolymers with a perfect helical sense excess. This work is now in progress.

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10 The CD and absorption spectra of all the copolymers in THF did not change after the samples had been allowed to stand at room temperature for 1 day.

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12 The significant difference between the CD spectrum of the sum of the homopolymers of poly((*S*)-**1**) and poly((*R*)-**2**) (**1** : **2** = 53 : 47, mol/mol) and the CD spectrum of the copolymer (poly((*S*)-**1**-*co*-(*R*)-**2**)) (**1** : **2** = 53 : 47, mol/mol) (Fig. S4A) indicates that the poly((*S*)-**1**-*co*-(*R*)-**2**)) is not composed of the blocks of poly((*S*)-**1**) and poly((*R*)-**2**). A similar great difference between the CD spectrum of poly((*S*)-**3**-*co*-(*R*)-**2**) and the sum of the CD spectra of the corresponding homopolymers, poly((*S*)-**3**) and poly((*R*)-**2**) (Fig. S4B), also supports the random monomer distributions in the poly((*S*)-**3**-*co*-(*R*)-**2**). These results clearly revealed the inversion of the helix-sense of the poly((*S*)-**1**-*co*-(*R*)-**2**) main-chain that takes place after the chemical modification of the hydroxy groups with bulky substituents.

13 The different temperature-dependent ICD intensity changes observed for the copolymers (Fig. 2B) may be determined by cooperative interactions with neighboring monomer units;[5b] the absolute $\Delta\varepsilon_{2nd}$ values tended to increase more steeply with increasing the bulkiness of the substituents introduced when temperature was lowered.

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