

Asymmetric Catalytic Polymerization: Advances and Challenges

Most naturally occurring biomacromolecules are optically active owing to their unique chiral structural units and/or helical conformations. Some of them show specific functionalities, such as supersensitive responses to external stimuli, highly selective recognition abilities, superior mechanical properties, and excellent catalytic activity under extremely mild conditions. These functionalities result from the unique chiral structural units and orderly arrangement of building blocks in the main-chain backbones of these biological macromolecules, such as enzymes, genes, and proteins. Indeed, the sequence and stereochemistry of the repeating units in a polymeric chain also have significant influence on their material performance. Therefore, construction of functional polymers with precise control of chirality and sequence, similar to those in living systems, is of great significance.

Asymmetric catalytic polymerization, in which chirality is introduced into a polymeric main-chain by repetitive, asymmetric reactions of prochiral monomers *via* enantioselective catalysis or by enantiomer-selective polymerization of only one enantiopure isomer of the *racemic* monomers *via* catalytic kinetic resolution, is expected to play an important role in achieving this challenging goal. Undoubtedly, catalyst selection is central to controlling features like the reaction rate, productivity, regioselectivity, enantioselectivity, and molar mass of the synthesized polymers. As early as 1962, Natta and coworkers studied asymmetric catalytic polymerizations using Ziegler-Natta catalysts to conduct enantioselective polymerization of *racemic* mono-substituted vinyl olefins.^[1] This process afforded a mixture of two types of polymers, one predominantly originating from the (*R*)-enantiomer and the other from the (*S*)-enantiomer, which could be successfully separated by chromatographic methods. Also, optically active polyolefins, poly(vinyl ether)s and polymethacrylates, could be prepared from *racemic* monomers using chiral catalyst systems *via* a catalytic kinetic resolution process. The enantioselective cyclopolymerization of 1,5-hexadiene was realized by Coates and Waymouth using chiral zirconium complexes with axial chirality in the presence of excess methylaluminoxane, yielding enantioenriched poly(methylene-1,3-cyclopentane) with the highest enantioface selectivity of 91%.^[2] This is the first enantioselective cyclopolymerization to produce a polymer possessing main-chain chirality. The resultant polymer was rich in *trans* units (73%), with no plane of symmetry. Various chiral ligands have been employed in conjunction with metal ions in the asymmetric polymerization process of carbon monoxide (CO) with olefins. A representative study is that by Consiglio *et al.*, who prepared polyketones with >99% head-to-tail regioselectivity and high diad stereoselectivity of up to 97.5% using chiral palladium complexes.^[3] Both 1,4-ketone and spiroketal repeating units coexisted in the backbone of the CO/ α -olefin copolymers. Unfortun-

nately, there is no method to quantitatively determine the optical purity of the stereogenic centers of these polymers, and their optical performances have only been analyzed qualitatively by specific rotation measurements or in combination with ¹³C-NMR analysis.

Although isotactic polyethers (e.g., poly(propylene oxide)) were discovered as early as the extensively used isotactic polypropylene, significant advances have been made in recent years. Most importantly, Coates *et al.* reported the development of binaphthol-linked bimetallic catalysts that allow the rapid production of highly isotactic polyethers *via* the kinetic resolution polymerization of terminal epoxides.^[4] The *[mm]* triad values of the obtained polyethers were typically higher than 95%, with a selectivity factor in the range of 50–300 for a variety of mono-substituted epoxides. The chirality of the axial binaphthol linker of the ligand is responsible for the chiral induction of the kinetic resolution polymerization. Recently, an exciting study by Chen and coworkers demonstrated that the chiral salcy-yttrium complex bearing bulky substituents at the *ortho* positions of the phenolate moiety could efficiently catalyze the kinetic resolution polymerization of *racemic* eight-membered cyclic diolide, which automatically terminated at 50% conversion to afford poly(3-hydroxybutyrate) with perfect isotacticity (*[mm]*>99%), low dispersity, and high molecular weight.^[5] In this resolution polymerization, the (*S,S*)-catalyst preferentially polymerized the (*S,S*)-cyclic diolide to yield highly isotactic (*S,S*)-polyesters, and the unreacted (*R,R*)-monomer was retained with an enantioselectivity of >99%.

Substituted epoxides bearing stereogenic centers have been extensively studied as versatile synthetic intermediates that undergo asymmetric nucleophilic ring-opening reactions to afford various chiral organic compounds. When such a powerful synthetic strategy is applied to the alternating copolymerization of substituted epoxides with nucleophiles such as CO₂, carbonyl sulfide (COS), or cyclic anhydrides, optically active copolymers with chiral diol units in the main chain are produced.^[6] For example, desymmetrization copolymerization of CO₂ and *meso*-epoxides is a valuable strategy for the synthesis of optically active polycarbonates with two contiguous chiral centers, owing to the configurational inversion at one of the two stereogenic centers of the *meso*-epoxides that are incorporated into the copolymer. In 2013, our group reported a privileged chiral catalyst system based on biphenol-linked dinuclear [salcyCo(III)DNP]₂ (DNP, 2,4-dinitrophenoxide) with multiple chiralities, which enabled the efficient and highly enantioselective copolymerization of a variety of *meso*-epoxides and CO₂ to afford isotactic polycarbonates with more than 99% carbonate units and enantioselectivities of up to 99%.^[7] The reactivities were in the range of 120–1400 h^{−1} at ambient temperature, and most of the

obtained isotactic polycarbonates were crystalline, with melting points in the range of 179–257 °C. With further modification of the steric hindrance of the phenolate *ortho*-substituents and axial linker of the ligands, as well as the metallic ions, the similar bimetallic catalyst systems with multiple chiralities were found to be very effective for the highly enantioselective copolymerization of *meso*-epoxides and COS or cyclic anhydrides, affording the corresponding poly(monothiocarbonate)s and polyesters with over 99% isotacticity and excellent enantioselectivity (up to 99%). Moreover, using multichiral dinuclear [salcyAlCl]₂ or [salcyCo(III)DNP]₂ with a binaphthol linker, exceptional levels of enantioselectivity with a kinetic resolution coefficient exceeding 300 were observed in the copolymerization of various *racemic* terminal epoxides and cyclic anhydrides, affording highly isotactic copolymers (selectivity factors > 300) with completely alternating structures and low dispersities.^[8] Moreover, the chiral-privileged dinuclear Al(III) catalyst system with multiple chiralities was demonstrated to be efficient in the enantioselective terpolymerization of *racemic* terminal epoxides, *meso*-epoxides, and anhydrides, producing optically active polyester terpolymers with more than 95% ee with either gradient or random distribution. Unexpected stereoconvergence was observed in the resolution copolymerization of *racemic cis*-internal epoxides and anhydrides, where the selectivity factor for the enantioselective formation of the polyester significantly exceeded the kinetic resolution coefficient based on the unreacted epoxide at various conversions.^[6]

It should be pointed out that in recent decades, significant progress has been made in helix-sense-selective polymerization, whose chirality usually arises not from stereogenic centers but exclusively from a single-handed helical conformation of the main chain. However, despite several decades of research, asymmetric catalytic polymerization remains a fledgling field. Two critical problems have affected the advancement of this field. The first is the difficulty in the quantitative determination of the optical purity of the stereogenic centers of chiral polymers. Only a very limited number of polymers, such as 1,3-diene polymers, polyesters, and polycarbonates, can be directly determined by chiral GC or HPLC, based on their degradation into small molecules or derivatives. The other one is the lack of highly efficient, chiral-privileged catalysts for producing polymers with accurate sequences and stereochemistry at each repeat unit.

The discovery of biaryl-linked bimetallic catalysts with multiple chiralities for highly active and enantioselective epoxide copolymerization or terpolymerization is significant. In these catalyst systems, both bimetallic synergistic effects and multichiral induction ensure high activity and enantioselectivity. In recent decades, significant progress has been made in the development of chiral-privileged ligands and asymmetric catalysis for the preparation of a variety of chiral organic compounds. Some of them are expected to be applied to the asymmetric catalytic polymerization in terms of both high activity and enantioselectivity.

Indeed, in many naturally occurring macromolecules, there exist both chiral structural units and helical conformations, wherein their synergy results in specific functionalities. Unfortunately, there are significant gaps in our

knowledge of the structures and functionalities of artificial and naturally occurring polymers. The latter has extraordinary functionalities originating from their hierarchically ordered assemblies. Therefore, the synthesis of optically active polymers possessing both stereogenic centers and helical conformations in the main chain, similar to those in some of the naturally occurring macromolecules, remains a significant challenge.

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