

Asymmetric Alternating Copolymerization of Meso-epoxides and Cyclic Anhydrides: Efficient Access to Enantiopure Polyesters

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S Supporting Information

ABSTRACT: Synthesis of stereoregular polyesters with main-chain chirality was achieved for the first time by the asymmetric copolymerization of *meso*-epoxides and cyclic anhydrides using catalyst systems based on enantiopure bimetallic complexes. The combination of the biphenol-linked dinuclear aluminum complex with *tert*-butyl groups in the phenolate *ortho*-positions and a nucleophilic co-catalyst was found to be more efficient in catalyzing this asymmetric copolymerization, affording enantiomerically enriched polyesters (up to 91% *ee*) with completely alternating structure and narrow molecular weight distribution. It was discovered that the isotactic-enriched poly(cyclopentene phthalate) is a typical semicrystalline material with a melting endothermic peak at 221 °C. This study is expected to provide a promising route to prepare various stereoregular polyesters having a wide variety of physical properties and degradability.

The alternating copolymerization of epoxides and cyclic anhydrides is of much interest as a promising method to produce aliphatic polyesters,¹ an alternative route to the step-growth condensation of diols and diesters at high temperatures (>250 °C) for most polyesters' synthesis. This process allows for polymer functionality to be easily adjusted due to the wide availability of cyclic anhydrides and epoxides. Additionally, the stereochemistry inherent to the epoxide monomer provides the possibility to synthesize stereoregular polyesters by establishing chiral centers in the main chain of the resultant polymers with control of the absolute configuration. Although a variety of metal complexes have been reported to catalyze this copolymerization,^{2–7} several of which are capable of giving highly alternating copolymers, no literature demonstrates the formation of enantiomerically enriched polyesters from achiral *meso*-epoxide monomers. In 2013, we were the first to achieve a highly regioregular ring-opening step with a concomitant >99% retention of configuration at the methine carbon center of epoxide incorporated into the polyester during a bimetallic chromium complex-catalyzed copolymerization of maleic anhydride and (*S*)-phenylglycidyl ether.⁸ More recently, Coates's group reported the synthesis of semicrystalline polyesters via enantiopure salenCo(III) complexes-mediated regioselective copolymerization of chiral propylene oxide with various anhydrides.⁹ Herein, we report the first example of asymmetric copolymerization of *meso*-epoxides with cyclic anhydrides using enantiopure bimetallic complexes, affording enantiomerically enriched polyesters with completely alternat-

ing structure and narrow molecular weight distribution. Since the ring-opening of a *meso*-epoxide proceeds with inversion at one of the two chiral centers, a successful desymmetrization ring-opening by a chiral catalyst can provide enantiopure polyester with an (*R,R*)- or (*S,S*)-*trans*-1,2-diol unit in polymer main chains (Scheme 1).

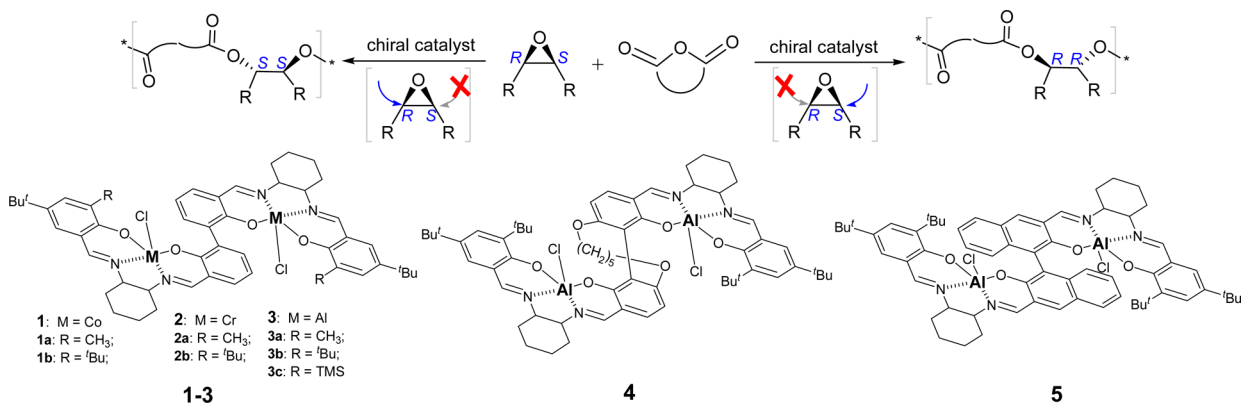
Previously, we have demonstrated that enantiopure biphenol-linked dinuclear Co(III) complexes are rare privileged chiral catalysts for the enantioselective copolymerization of carbon dioxide and various *meso*-epoxides, affording the corresponding polycarbonates with more than 99% carbonate unit and ≥98% enantioselectivity.¹⁰ Prior to this study, Coates's group developed chiral binaphthol-linked dinuclear Co(III) complexes for highly enantioselective homopolymerization of terminal epoxides through a kinetic resolution.¹¹ On the basis of this exciting result, we anticipated that these enantiopure dinuclear Co(III) complexes might serve as highly enantioselective and active catalysts for asymmetric copolymerization of *meso*-epoxides and cyclic anhydrides. We initially explored dinuclear Co(III) complexes **1a** and **1b** for the copolymerization of cyclohexene oxide (CHO) with phthalic anhydride (PA). Unfortunately, no or very low enantioselectivity was observed in the resulting polymers, though these enantiopure Co(III) complexes showed activity in catalyzing this copolymerization to afford the polyester with perfectly alternating structure (Table 1, entries 1 and 2). Similar results were also found in the corresponding chromium complexes (**2a** and **2b**) of these ligands as catalysts (entries 3 and 4). Furthermore, we delightfully discovered that the biphenol-linked dinuclear aluminum complexes **3** showed high activity and enantioselectivity in catalyzing CHO/PA copolymerization (entries 5–14). The presence of a nucleophilic co-catalyst such as PPNCl (PPN = bis(triphenylphosphine)iminium) is a prerequisite for obtaining polyester in high selectivity. With (*R,R,R,R*)-**3b** alone as catalyst (entry 8), no polyester but polyether was formed in the system, indicating the homopolymerization of epoxide predominantly overwhelming the copolymerization with cyclic anhydride.

There is a significant steric effect of the phenolate *ortho* substituents of the ligand on the catalytic activity and product enantioselectivity. Neither low (e.g., methyl group) nor highly steric hindrance (e.g., trimethylsilyl (TMS)) is beneficial for this asymmetric copolymerization (entries 5–7). The screen experiments suggested that (*R,R,R,R*)- or (*S,S,S,S*)-**3b**, with a ligand that is intermediate in steric bulk relative to those of **3a**

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Scheme 1. Asymmetric Alternating Copolymerization of Meso-epoxides and Cyclic Anhydrides

Table 1. Catalyst Screening for CHO/PA Asymmetric Copolymerization^a

entry	catalyst	time [h]	temp [°C]	conv ^b [%]	TOF ^c [h ⁻¹]	ester ^d [%]	M _n ^e [kg/mol]	PDI ^e	ee ^f [%]	specific rotation ^g [deg]
1	(<i>R,R,R,R</i>)-1a	0.5	50	60	300	>99	6.4	1.22	0	0
2	(<i>R,R,R,R</i>)-1b	0.3	50	64	539	>99	7.3	1.19	5 (<i>R,R</i>)	1 (-)
3	(<i>R,R,R,R</i>)-2a	2	50	58	73	>99	4.7	1.23	0	0
4	(<i>R,R,R,R</i>)-2b	1	50	78	196	>99	6.2	1.20	7 (<i>R,R</i>)	1 (-)
5	(<i>R,R,R,R</i>)-3a	6	50	63	26	42	5.9	8.16	11 (<i>R,R</i>)	2 (-)
6	(<i>R,R,R,R</i>)-3b	0.3	50	90	750	>99	9.8	1.14	71 (<i>R,R</i>)	14 (-)
7	(<i>R,R,R,R</i>)-3c	5.3	50	99	47	>99	3.9	1.10	21 (<i>R,R</i>)	4 (-)
8 ^h	(<i>R,R,R,R</i>)-3b	0.1	50	0	0	0 (polyether)	8.4	6.65		
9	(<i>R,R,R,R</i>)-3b	2.5	25	98	98	>99	6.6	1.11	85 (<i>R,R</i>)	18 (-)
10	(<i>R,R,R,R</i>)-3b	24	0	96	10	>99	9.5	1.09	87 (<i>R,R</i>)	18 (-)
11	(<i>R,R,R,R</i>)-3b	36	-10	99	7	>99	9.0	1.12	91(<i>R,R</i>)	27(-)
12 ⁱ	(<i>R,R,R,R</i>)-3b	1	50	98	490	>99	10.6	1.13	70 (<i>R,R</i>)	14 (-)
13 ^j	(<i>R,R,R,R</i>)-3b	24	0	96	10	>99	9.5	1.12	91 (<i>R,R</i>)	27 (-)
14 ^j	(<i>S,S,S,S</i>)-3b	24	0	97	10	>99	9.0	1.12	91 (<i>S,S</i>)	27 (+)
15	(<i>R,R,R,R</i>)-4	2.5	25	44	44	>99	8.7	1.14	90 (<i>R,R</i>)	26 (-)
16	(<i>R,R,S,R</i>)-4	48	25	58	3	>99	4.7	1.23	27(<i>R,R</i>)	4(-)
17 ^k	(<i>R,R,R,R</i>)-4	6	25	63	26	>99	9.8	1.19	83 (<i>R,R</i>)	17 (-)
	/ <i>(R,R,S,R,R)</i> -4									
18	(<i>S,S,S,S</i>)-5	18	25	99	14	>99	7.8	1.11	81 (<i>S,S</i>)	16 (+)

^aConditions: The reaction was performed in neat CHO (5.0 mL, 50 mmol) in a 20 mL autoclave, CHO/PA/catalyst/PPNCl = 1000/250/1/2, molar ratio, except for entries 8 and 12. ^bCalculated using ¹H NMR spectroscopy based on PA as the limiting reagent. ^cTurnover frequency (TOF) = mol of product (polyester)/mol of catalyst per hour. ^dSelectivity for ester over ether unit in the resulting copolymer, determined by ¹H NMR spectroscopy. ^eDetermined by using gel permeation chromatography in THF, calibrated with polystyrene. ^fMeasured by hydrolyzing the polymer and analyzing the resulting diol by chiral GC, and the (*R,R*)-diol is the major enantiomer when (*R,R,R,R*)-catalyst was used. ^gSpecific rotation of the polymers was determined in chloroform at 20 °C (*c* = 1) by using a polarimeter. The wavelength of the polarized light was 589.3 nm. ^hIn the absence of PPNCl. ⁱCHO/PA/Catalyst/PPNCl = 1000/500/1/2, molar ratio. ^jThe reaction was carried out in toluene solution CHO/toluene = 1:2 (volume ratio). ^kEquimolecular.

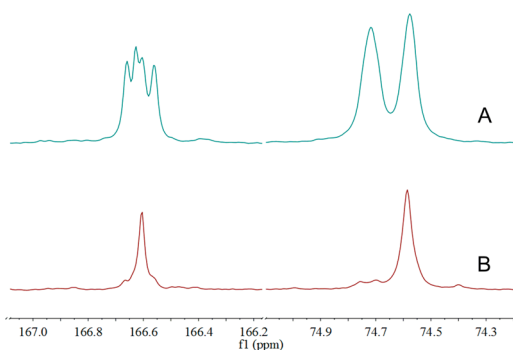
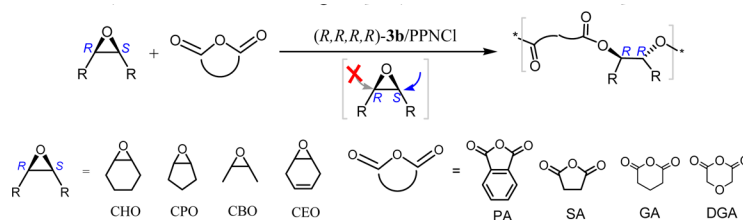


Figure 1. ¹³C NMR spectra of carbonyl (left) and methine (right) regions of CHO/PA copolymer: (A) atactic and (B) isotactic-enriched (91% ee).

and 3c, proved to be the most active and enantioselective catalyst. The highest activity is up to 750 h⁻¹ turnover frequency (TOF) at 50 °C, and the enantioselectivity of the resulting polyester is 71% ee. A decrease in reaction temperature resulted in an enhancement of the product enantioselectivity but had a negative effect on the rate. When the dinuclear aluminum complex (*R,R,R,R*)-3b was used at -10 °C, a completely alternating copolymer with an enantioselectivity of 91% ee with (*R,R*)-configuration was obtained (entry 11).

Indeed, the biphenol-linked dinuclear Al(III) complex 3b with (*R,R,R,R*)-configuration has two diastereoisomers with (*R*)- or (*S*)-biphenol stereochemistry, (*R,R,R,R,R*)- and (*R,R,S,R,R*)-conformers, though it originates from an achiral biphenol linker.¹² The X-ray crystal analysis suggests that the Al-Al distance in the (*R,R,R,R,R*)-conformer is 7.89 Å and the

Table 2. Optimized Conditions for Asymmetric Alternating Copolymerization of *Meso*-epoxides and Cyclic Anhydrides^a

entry	reactants	time [h]	temp [°C]	TOF ^b [h ⁻¹]	ester ^c [%]	M _n ^d [kg/mol]	PDI ^d	ee ^e [%]	specific rotation ^f [deg]
1	CHO/SA	36	25	2	>99	2.3	1.15	61 (R,R)	8 (-)
2	CHO/GA	36	25	3	>99	3.9	1.34	60 (R,R)	8 (-)
3	CHO/DGA	36	25	7	47	0.5	1.45	15 (R,R)	2 (-)
4	CPO/PA	32	25	4	>99	3.3	1.38	65 (R,R)	39 (-)
5 ^g	CPO/PA	50	25	2	>99	6.1	1.24	67 (R,R)	40 (-)
6	CBO/PA	30	25	4	>99	10.1	1.18	75 (R,R)	21 (+)
7 ^g	CBO/PA	13	25	10	>99	4.8	1.10	85 (R,R)	28 (+)
8	CEO/PA	48	0	2	>99	4.0	1.10	81 (R,R)	113 (-)
9 ^g	CEO/PA	48	0	3	>99	5.0	1.13	90 (R,R)	125 (-)

^aConditions: The reaction was performed in neat *meso*-epoxide (5.0 mL, 50 mmol) in a 20 mL autoclave, *meso*-epoxide/anhydride/(*R,R,R,R*)-**3b**/PPNCl = 1000/250/1/2, molar ratio, except for entries 5, 7, and 9. ^bTurnover frequency (TOF) = mol of product (polyester)/mol of catalyst per hour. ^cSelectivity for ester over ether unit in the resulting copolymer, determined by ¹H NMR spectroscopy. ^dDetermined by using gel permeation chromatography in THF, calibrated with polystyrene. ^eMeasured by hydrolyzing the polymer and analyzing the resulting diol by chiral GC, and the (*R,R*)-diol is the major enantiomer. ^fSpecific rotation of the polymers was determined in chloroform at 20 °C (*c* = 1) by using a polarimeter. The wavelength of the polarized light was 589.3 nm. ^gEpoxide/anhydride/catalyst/PPNCl = 250/250/1/2, molar ratio; epoxide/toluene = 1:2 (volume ratio).

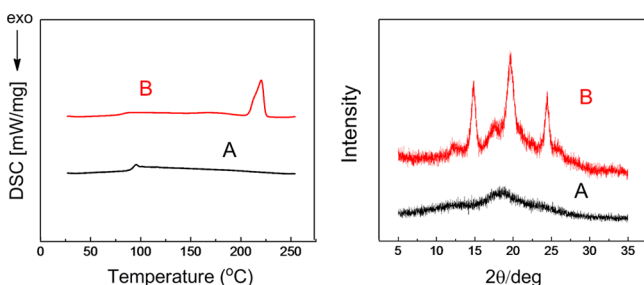


Figure 2. DSC thermograms (left) and WAXD profiles (right) of (A) atactic and (B) isotactic-enriched (65% *ee*) poly(cyclopentene phthalate)s.

endo phenol–phenol dihedral angle is 134.9°, while in the (*R,R,S,R*)-conformer the corresponding values are 7.67 Å and 114.9°. In a recent contribution regarding biphenol-linked dinuclear Co(III) complexes **1a** and **1b** with (*S,S,S,S*)-configuration-mediated CO₂/*meso*-epoxide copolymerization, density functional theory calculations suggested that, in the two diastereoisomers of the dinuclear Co(III) complexes, the matched configuration was (*S,S,S,S*) rather than (*S,S,R,S*) for giving the corresponding polycarbonate with (*S,S*)-configuration.¹² Based on this result, we tentatively assume that, in the two diastereoisomers of the dinuclear Al(III) complex (*R,R,R,R*)-**3b**, only one conformer plays a main role in catalyzing CHO/PA asymmetric copolymerization. In order to better understand the chiral induction in this asymmetric catalytic process, both (*R,R,R,R*)- and (*R,R,S,R*)-**4** dinuclear Al(III) complexes based on chiral biphenol linker were also prepared for the asymmetric copolymerization of CHO and PA (Table 1, entries 15 and 16). It was discovered that (*R,R,R,R*)-**4** in conjunction with PPNCl could catalyze this copolymerization, with a TOF of 44 h⁻¹ at ambient temperature, the resultant copolymers had an enantioselectivity of 90% *ee* with (*R,R*)-configuration (entry 15), higher than that of

the system using (*R,R,R,R*)-**3b** as catalyst (85% *ee*) at the same conditions. On the contrary, both very low activity of 3 h⁻¹ and enantioselectivity of 27% *ee* were observed in the catalyst system based on (*R,R,S,R*)-**4** (entry 16). The 1/1 mixture of (*R,R,R,R*)- and (*R,R,S,R*)-**4** provided the polyester with 83% *ee* for (*R,R*)-configuration in a TOF of 26 h⁻¹ (entry 17). This result indicates that in the two diastereoisomers of the dinuclear Al(III) catalyst (*R,R,R,R*)-**3b**, the conformer with (*R,R,R,R*)-configuration was beneficial for enantioselectivity control. For a comparison purpose, the dinuclear aluminum complex (*S,S,S,S*)-**5** based on binaphthol linker was synthesized for CHO/PA asymmetric copolymerization. The catalyst system afforded the completely alternating copolymer with an enantioselectivity of 81% *ee* with (*S,S*)-configuration, but exhibited relatively low activity of 14 h⁻¹ at ambient temperature (entry 18).

Most of the resultant polyesters show isotactic-enriched structures. Although we have not given the accurate assignment of the microstructure of CHO/PA copolymer, significant differences in carbonyl and methine regions between the atactic and isotactic polymers are easily identified by ¹³C NMR spectroscopy (Figure 1). Only single peaks at 166.60 and 74.57 ppm were detected in the isotactic polyester, while the atactic copolymer shows multiple peaks at the carbonyl region and double peaks at the methine region.

With a competent enantioselective catalyst (*R,R,R,R*)-**3b** in hand, we explored the asymmetric copolymerization of a series of *meso*-epoxides and various cyclic anhydrides for the synthesis of a variety of stereoregular polyesters (Table 2). Since CHO has relatively high reactivity in copolymerizing with cyclic anhydrides, it was chosen as a model monomer of *meso*-epoxides for testing the catalytic activity and enantioselectivity. Compared with the high activity and enantioselectivity for CHO/PA copolymerization, (*R,R,R,R*)-**3b**-mediated copolymerization of CHO with various cyclic anhydrides, including succinic anhydride (SA), glutaric anhydride (GA), and

diglycolic anhydride (DGA), exhibited low activity and enantioselectivity (Table 2, entries 1–3). The polymer resulting from CHO/DGA copolymerization has consecutive epoxide sequences up to 53% and very low enantioselectivity of 15% *ee* for (*R,R*)-configuration. With PA as a model monomer of cyclic anhydrides, the copolymerization with various *meso*-epoxides, such as cyclopentene oxide (CPO), *cis*-2,3-epoxybutane (CBO), and 1,2-epoxy-4-cyclohexene (CEO), was tested at ambient temperature or 0 °C (Table 2, entries 4–9). All resultant copolymers possess perfectly alternating structure and have moderate or high enantioselectivity (65–90% *ee*). Interestingly, the CEO/PA copolymer of 90% *ee* with (*R,R*)-configuration shows a highly specific rotation value of -125° ($c = 1$, in CHCl_3) at 20 °C (entry 9). Notably, the isotactic-enriched (65% *ee*) CPO/PA copolymer (poly(cyclopentene phthalate)) was found to be a typical semicrystalline material with a melting endothermic peak at 221 °C ($\Delta H_m = 23.63 \text{ J/g}$) (Figure 2). The crystallizability of the isotactic-enriched poly(cyclopentene phthalate) was further identified by powder X-ray diffraction (XRD). No diffraction signal was observed in the atactic copolymer, confirming its amorphous nature. On the contrary, for the isotactic-enriched poly(cyclopentene phthalate) sample, evident diffraction peaks at 14.9°, 19.7°, and 24.5° were observed, demonstrating its semicrystalline structure.

In conclusion, we have demonstrated the asymmetric copolymerization of *meso*-epoxides and cyclic anhydrides using enantiopure bimetallic complexes, affording enantiomerically enriched polyesters with completely alternating structure and narrow molecular weight distribution. The highly isotactic polyesters from *meso*-epoxides have been prepared in optically active form, for the first time. Notably, the isotactic-enriched poly(cyclopentene phthalate) was found to be a typical semicrystalline material with a melting endothermic peak at 221 °C. This study is expected to provide a promising route to prepare various stereoregular polyesters having a wide variety of physical properties and degradability. Further studies are focused on elucidating the copolymerization mechanism, increasing the efficiency, and developing highly enantioselective privileged catalysts.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b07520.

Experimental procedures, characterizations, synthetic details, equipment specifications, NMR, and statistical analysis (PDF)

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Notes

The authors declare no competing financial interest.

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