

Alternating Copolymerization of Epoxides and Cyclic Anhydrides: An Improved Route to Aliphatic Polyesters

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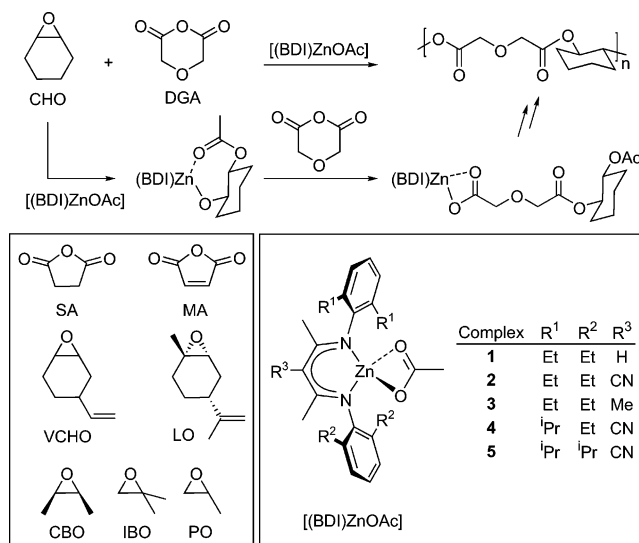
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Aliphatic polyesters constitute an important class of polymers because of their biodegradability^{1,2} and biocompatibility,^{2,3} which enable their use in drug delivery systems,² artificial tissues,³ and commodity materials.⁴ Polyesters such as poly(butylene succinate) are commonly produced through condensation polymerization; however, this method is energy intensive, requiring high temperature and removal of the alcohol or water byproduct to achieve high molecular weight (M_n) polymers.⁵ Conversely, poly(hydroxy-alkanoate)s can be synthesized through bacterial fermentation, a process which is also energy intensive.⁶ Alternatively, polyesters such as poly(lactic acid) (PLA) and poly(ϵ -caprolactone) may be prepared by the ring-opening polymerization of cyclic esters.^{1c,2,4,7} Although this technique uses mild reaction conditions and avoids the formation of small molecule byproducts, the scope of the polymer architecture is generally limited by the availability of structurally diverse monomers. A different approach, the ring-opening copolymerization of epoxides and cyclic anhydrides, has the potential to produce a wider variety of polymer backbone structures.⁸ However, catalysts reported for this reaction exhibit relatively low activities^{8a,b,e} and produce polyesters with low M_n values.^{8a–d}

We have previously reported highly active (BDI)ZnOAc (BDI = β -diiminate) catalysts for the copolymerization of epoxides and CO₂.⁹ Additionally, we have shown that (BDI)Zn-alkoxide complexes polymerize lactones and lactides by acyl bond cleavage.¹⁰ On the basis of these prior results, we anticipated that (BDI)Zn complexes might serve as active catalysts for the ring-opening copolymerization of epoxides and cyclic anhydrides (Scheme 1). Herein, we report (BDI)ZnOAc catalysts for the synthesis of new aliphatic polyesters with high M_n values and narrow molecular weight distributions (MWD = M_w/M_n) via the highly alternating copolymerization of epoxides and cyclic anhydrides under mild reaction conditions.

Initially, we focused on the copolymerization of diglycolic anhydride (DGA) and cyclohexene oxide (CHO) using **1**, a catalyst previously shown to be active for CHO/CO₂ copolymerization^{9b} (Scheme 1). Much to our dismay, we were unable to obtain poly(cyclohexene diglycolate) regardless of the reaction conditions (Table 1, entry 1). Investigation of the stoichiometric interaction of **1** with DGA using ¹H NMR spectroscopy revealed nearly complete degradation of **1** after 1 h at 25 °C. We hypothesize that DGA reacts with the BDI ligand at the carbon bearing R³, destroying the complex.¹¹ Therefore, we screened complex **2**, which has a nitrile group at R³. This complex is stable to DGA for 24 h at 50 °C and is active for the copolymerization of CHO/DGA (entry 2). The electron withdrawing nature of the nitrile group is a significant factor in preventing ligand degradation given that a sterically similar methyl substituent at R³ (**3**) also leads to an inactive catalyst (entry 3). In addition to the dramatic impact that ligand electronics has on activity, there is also a significant steric

Scheme 1. Alternating Copolymerization of Epoxides and Cyclic Anhydrides**Table 1.** Catalyst Screening for CHO/DGA Copolymerization^a

entry	complex	conversion ^b (%)	M_n^c (g/mol)	MWD ^c (M_w/M_n)
1 ^d	1	<1	ND ^e	ND ^e
2	2	14	4 000	1.4
3 ^d	3	<1	ND ^e	ND ^e
4	4	79	23 000	1.2
5	5	33	12 000	1.3

^a Conditions: 20 μ mol Zn, 4 mmol CHO, 4 mmol DGA, 1.2 mL of toluene, 50 °C, 2 h. ^b Determined by ¹H NMR spectroscopy, conversion of CHO. ^c Determined by gel permeation chromatography (GPC), in THF, calibrated by polystyrene standards. ^d Polymerization run for 24 h. ^e Not determined.

effect of the aryl substituents (entries 2, 4, 5). Complex **4**, with a ligand that is intermediate in steric bulk relative to those of **2** and **5**, proved to be the most active catalyst. We also attempted the polymerization in the absence of catalyst, which gave no conversion.

With a competent catalyst in hand, we explored the copolymerization of a series of epoxides with DGA for the synthesis of a variety of aliphatic polyesters (Table 2, entries 1–6).¹² Under optimized conditions, the CHO/DGA copolymerization afforded poly(cyclohexene diglycolate) with high M_n and narrow MWD (entry 1). Vinyl cyclohexene oxide (VCHO) reacted with DGA under the same conditions as the CHO/DGA copolymerization (entry 2). The comonomer *trans*-(*R*)-limonene oxide¹³ (LO) also copolymerized with DGA; however, higher temperature and a longer reaction time are required (entry 3). Notably, polyesters containing LO and VCHO subunits have the potential to be useful precursors to more elaborate polymers through postpolymerization modification of the pendant vinyl groups. Aliphatic epoxides,

Table 2. Optimized Conditions for Alternating Copolymerization of Epoxides and Cyclic Anhydrides Using Complex **4**^a

entry	epoxide	anhydride	Zn (mol %) ^b	toluene (mL)	<i>T</i> _{rxn} (°C)	<i>t</i> _{rxn} (h)	conversion ^c (%)	<i>M</i> _n ^d (g/mol)	MWD ^d (<i>M</i> _w / <i>M</i> _n)	<i>T</i> _g ^e (°C)
1	CHO	DGA	0.33	1.2	50	6	91	31 000	1.2	51
2	VCHO	DGA	0.33	1.2	50	6	93	55 000	1.2	54
3	LO	DGA	0.33	1.2	70	16	81	36 000	1.2	51
4 ^f	PO	DGA	0.50	0.0	30	16	89	18 000	1.3	−1.8
5 ^f	CBO	DGA	0.50	0.0	30	8	93	24 000	1.5	27
6 ^f	IBO	DGA	0.50	0.0	30	48	53	10 000	1.5	−1.3
7	CHO	SA	1.0	2.4	70	16	93	12 000	1.2	57
8	VCHO	SA	1.0	2.4	70	16	84	20 000	1.3	50
9	LO	MA	1.0	0.3	60	24	55	12 000	1.1	62

^a All reactions were carried out with 20 μmol catalyst; [epoxide] = [anhydride] unless otherwise noted. ^b With respect to anhydride. ^c Conversion of epoxide (entries 1, 3, 7, 9), conversion of anhydride (entries 2, 4–6, 8); determined by ¹H NMR spectroscopy. ^d Determined by GPC, in THF vs polystyrene standards. ^e Determined by differential scanning calorimetry (DSC). ^f [Zn]:[epoxide]:[anhydride] = 1:800:200.

including propylene oxide (PO), isobutylene oxide (IBO), and *cis*-butene oxide (CBO) are also viable monomers for copolymerization with DGA (entries 4–6); neat conditions were optimal for these reactions. Hydrolysis of the copolymer resulting from the polymerization of (*R*)-PO and DGA yielded (*R*)-propylene glycol in 78% ee, consistent with an 8:1 preference for ring-opening at the methylene carbon of (*R*)-PO. Conversely, NMR analysis of the polymer derived from IBO (entry 6) showed peaks consistent with regiorandom insertion of this epoxide.¹² We also explored other anhydrides as comonomers and found that succinic anhydride (SA) copolymerizes with CHO (entry 7) and VCHO (entry 8), although the *M*_n values of the resulting copolymers are significantly lower than the DGA-containing polymers. Maleic anhydride (MA) reacts with LO to give polyester with a moderate *M*_n (entry 9). The success of this copolymerization is surprising because we have thus far been unable to cleanly copolymerize MA with other epoxides, including CHO.

The ¹H NMR spectra of the polymers do not show consecutive anhydride or epoxide sequences, which supports the alternating structure shown in Scheme 1.¹² GPC results revealed high *M*_n values and narrow MWDs. In many cases, the GPC chromatograph exhibits a higher molecular weight shoulder. We attribute this to the presence of trace amounts of hydrolyzed anhydride, which could act as a bifunctional initiator and give an *M*_n value twice as large as expected. Glass transition temperatures of the polymers with alicyclic backbones (*T*_g, Table 2, entries 1–3, 7–9) are comparable to PLA (*T*_g = 55–60 °C).² The polyesters reported herein have decomposition temperatures approaching 290 °C, which allow easier melt processing than poly(3-hydroxybutyrate), a polymer that decomposes at a temperature close to its melting point.³

We have demonstrated the first highly active catalyst for the alternating copolymerization of a range of epoxides and cyclic anhydrides. This work resulted in the efficient synthesis of new aliphatic polyesters with high *M*_n values and narrow MWDs. Studies focused on the elucidation of the mechanism of the copolymerization, increasing the efficiency, and expanding the substrate scope to include substituted succinic anhydrides¹⁴ are currently underway.

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Supporting Information Available: Experimental procedures, NMR spectra of polymers, and X-ray data for **4** and **5**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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