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Ring-Opening Copolymerization of Maleic Anhydride with Epoxides: A Chain-Growth Approach to Unsaturated Polyesters

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Supporting Information

ABSTRACT: We report the ring-opening copolymerization of maleic anhydride with a variety of epoxides catalyzed by a chromium(III) salen complex. Quantitative isomerization of the *cis*-maleate form of all polymers affords the *trans*-fumarate analogues. Addition of chain transfer reagents yields low M_n, narrow PDI polymer samples. This method provides access to a range of new unsaturated polyesters with versatile functionality, as well as the first synthesis of high molecular weight poly(propylene fumarate).

Approximately 1.7 million metric tons of maleic anhydride (MA)[1] were produced and consumed in 2009, over 40% of which was used for the production of unsaturated polyesters (UPs).[2,3] Utilization of UPs in resins,[4] composite materials,[5] biomedical devices,[6] and drug delivery[7] applications benefits from the ability to enhance polymer properties through post-polymerization modifications of the maleate or fumarate units provided by MA. For example, easily cured UPs excel in lightweight, sustainable coatings and materials technology, namely in applications such as wind turbines and high-performance housing and marine materials.[8c] Biodegradable UPs, such as poly(propylene fumarate) (PPF),[9] can be used in orthopedic implants and tissue repair systems, as they provide easy formation of robust, noncytotoxic tissue/bone scaffolds[6] that degrade to benign metabolic products.[10]

While UPs are well-established materials, their applications are currently limited by the inability to incorporate diverse functionality into the polymer chain, difficulty achieving high molecular weight, and formation of undesired ether linkages.[4a] The common method for polyester synthesis, step-growth copolymerization (Scheme 1a), requires high energy input and long reaction times and often affords low-molecular-weight polymers with uncontrolled isomerization.[11] Other frequent problems include conjugate addition side reactions and unwanted cross-linking.[4b] The development of a versatile, mild synthetic route to functionalized, unsaturated polyesters will advance the properties and expand the applications of this important class of materials.

A mild catalytic chain-growth copolymerization (Scheme 1b) could circumvent many of the disadvantages of step-growth routes.[12] To our knowledge, no literature reports demonstrate catalytic, highly alternating copolymerization of MA with a broad range of epoxides.[13,14] Systems reported for MA/epoxide copolymerizations generally suffer from harsh conditions, low reactivity, low molecular weight, and/or ether formation (Table 1, entries 1 and 2).[14] In this Communication, we report a chromium(III) salen complex capable of copolymerizing MA with a range of epoxides under mild conditions to afford a variety of new functionalized unsaturated polyesters. We also present the first synthesis of highly alternating PPF with number-average molecular weight (M_n) above 15 kDa.

Initially, we focused on catalyzing the ring-opening copolymerization of MA with propylene oxide (PO), to produce poly(propylene maleate) (PPM). We hypothesized that *cis*−*trans* isomerization of the backbone in isolated PPM would provide access to PPF.

We previously reported a highly active (BDI)ZnOAc[15] (**3**; BDI = β-diiminate) catalyst for the copolymerization of saturated anhydrides with epoxides. However, with the unsaturated anhydride MA, the (BDI)ZnOAc system displayed low activity and significant amounts of ether linkages (Table 1, entry 3). These results were similar to earlier reports using other zinc-based catalysts for this reaction (entry 2).[14b−d]

Given the catalytic role of **3** in both CO_2/epoxide and anhydride/epoxide copolymerizations, we investigated other complexes which can catalyze CO_2/epoxide copolymerization.[16] The aluminum porphyrin complex (**4**, entry 4) exhibited low activity and produced a large percent of ether linkages, while the cobalt salen complex (**5**, entry 5) demonstrated moderate activity with no ether formation. The chromium(III) salen complex (**6**, entry 6) exhibited the highest activity and selectivity for the preparation of PPM. Using hexanes as a solvent afforded quantitative conversion (99%) and a relatively high M_n (17 kDa, entry 7). Polyester purity was confirmed by ^{1}H and ^{13}C NMR spectroscopy.

With an efficient synthesis of PPM in hand, we investigated the controlled *cis*−*trans* isomerization to form PPF.[14a] Catalytic isomerization of PPM with diethylamine[17,18] in chloroform at room temperature afforded PPF quantitatively, as shown by ^{1}H NMR spectroscopy (Figure 1). After reaction with diethylamine, the signal at 6.21 ppm of the *cis*-alkene of PPM is no longer present, and a new signal at 6.84 ppm is observed, corresponding to the *trans*-alkene of PPF. The isomerization can be performed as a one-pot procedure or with an isolated polymer sample. The molecular weight and M_w/M_n of the polymer remain consistent throughout the isomerization, and the T_g (Figure 1) of the polymer increases. To the best of our knowledge, this is the highest T_g reported to date for these polymers.

To explore the substrate scope of this copolymerization, we screened a variety of epoxides with MA (Table 2, entries 1−7).

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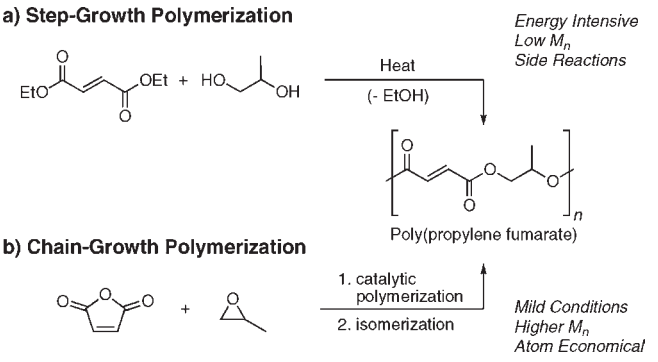
1-Butene oxide (**8**, entry 1) exhibited reactivity comparable to that of PO. The functionalized epoxides epichlorohydrin (**9**, entry 2) and allyl glycidyl ether (**10**, entry 3) were polymerized with high conversions (99 and 98% respectively) and showed no evidence of ether linkages by ^{1}H NMR spectroscopy. The resulting pendant functionalities provide an opportunity to tune the properties of these polyesters: for example, nucleophilic displacement of the alkyl halide can be envisioned for the epichlorohydrin-derived polymer. Other types of functionality can also be incorporated to alter the bulk properties of the unsaturated polyesters. Epoxide **11**, bearing a diethylene glycol (PEG) unit (entry 4), polymerized with high conversion (90%) and no detectable ether linkages. Recent efforts to incorporate PEG units into unsaturated polyesters couple maleate or fumarate units to oligo-PEG diols for applications ranging from biomedical to commodity materials.[5g,7a,20] Our method provides a simple polymerization approach to appending PEG units off of an unsaturated polyester core while maintaining the biocompatible monomers. Perfluoro alkyl chain-appended epoxide **12** (entry 5) copolymerized cleanly and in high conversion (90%) with MA. Fluorinated functionality offers distinctive properties, such as low coefficients of friction, good chemical resistance, and low surface energies, which are excellent for unsaturated polyesters used in material coatings and biomedical applications.[21] Furthermore, epoxides with greater steric bulk near the reactive epoxide base, such as acetal-protected epoxide **13** (entry 6) and phenyl glycidyl ether **14** (entry 7), polymerized to high molecular weight (22 and 31 kDa, respectively) with no evidence of ether linkages. Deprotection of THP from **13** would yield

Scheme 1. Polymerization Routes for the Synthesis of Poly(propylene fumarate): (a) Reported Step-Growth and (b) Proposed Chain-Growth



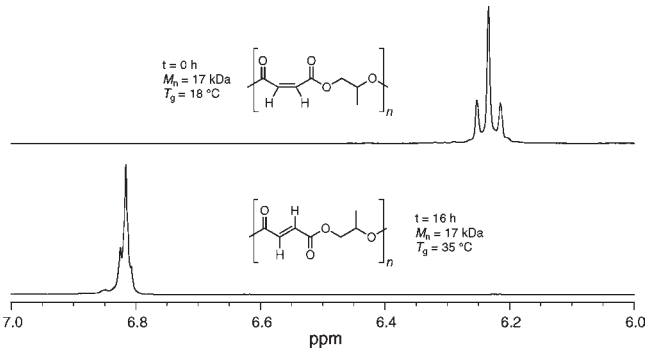
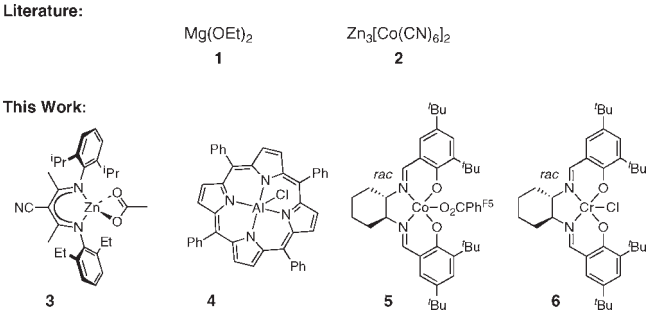


Figure 1. Alkene regions of the ^{1}H NMR spectra of PPM and PPF, demonstrating the clean *cis*−*trans* conversion by catalytic $HNEt_2$.[19]

Table 1. Recent Catalysts Applied for Copolymerization of Maleic Anhydride with Propylene Oxide from Literature (1, 2) and This Work (3−6)



entry	catalyst	temp (°C)	time (h)	conv (%)[a]	ether (%)[a]	M_n (kDa)[b]	M_w/M_n[b]	ref
1	**1**	80	48	42	5[c]	4	1.2	14a
2	**2**	100	16	97	20[c]	3	1.4	14b
3[d]	**3**	45	15	5	86	5	1.2	–
4[d]	**4**	45	15	7	50	14	1.1	–
5[d]	**5**	45	15	12	<1[e]	5	1.1	–
6[d]	**6**	45	15	47	<1[e]	6	1.3	–
7[f]	**6**	45	15	>99	<1[e]	17	1.6	–

[a] Conversion and ether linkage percents (consecutive epoxide enchainment) determined by ^{1}H NMR spectroscopy of crude reaction. [b] Determined by gel permeation chromatography (GPC) calibrated with polystyrene standards in $CHCl_3$ at 40 °C. [c] Estimated on the basis of shifts due to ether linkages in the ^{1}H NMR spectrum. [d] Reaction conditions: [MA]:[PO]:[cat] = 200:200:1, [MA] and [PO] = 4 mM in toluene. [e] No evidence of ether linkages detected in ^{1}H NMR spectrum. [f] Reaction conditions the same as *d* except hexanes are used as a solvent. The reaction mixture is homogeneous at the beginning of the reaction and solidifies upon consumption of the monomers.

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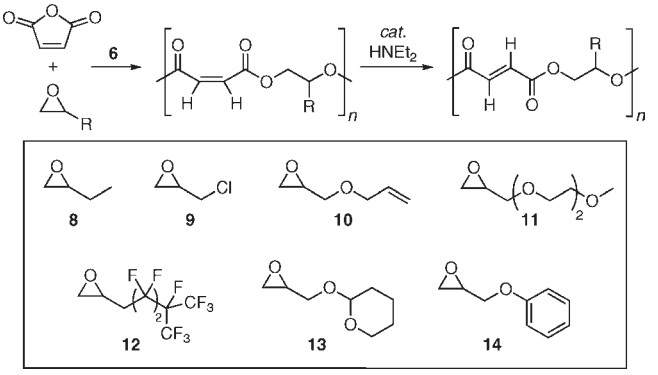
Table 2. MA Copolymers with Other Epoxides Using Catalyst 6[a]



entry	epoxide	time (h)	conv[b] (%)	ether[b] (%)	M_n (kDa)[c]	M_w/M_n[c]	T_g[d] (°C) m	T_g[d] (°C) f
1	**8**	14	90	<1	21	1.5	11	−14
2	**9**	6	99	<1	25	1.7	33	45
3	**10**	15	98	<1	25	1.3	−10	−6
4	**11**	4	99	<1[22]	33	1.1	−26	−29
5	**12**	16	90	<1	25	1.7	40	53
6	**13**	15	99	<1	21	1.4	35	36
7	**14**	12	99	<1	31	1.4	41	50

[a] Reaction conditions: [MA]:[epoxide]:[**6**] = 200:200:1, [MA] and [epoxide] = 4 mmol in 1 mL of hexanes, T_{rxn} = 45 °C. [b] Determined by ^{1}H NMR spectroscopy of crude reaction. [c] Molecular weight data were determined on GPC calibrated with polystyrene standards in $CHCl_3$ at 40 °C. M_n data collected for isomerized polymers were within ±10% of the values reported for their maleate analogues and within the error of the GPC instrument used. The M_w/M_n of the isomerized polymers changed by ±0.2. [d] Determined by DSC analysis, m = maleate and f = fumarate forms of the polymer.

unsaturated polyester appended with a glycol per repeat unit. Finally, isomerization of all *cis*-polyesters from terminal epoxides (entries 1−7) quantitatively yielded the *trans*-fumarate analogues using the route described above.

Given the industrial importance of unsaturated polyester resins, we investigated whether low molecular weight unsaturated polyesters could be produced with our system without increasing catalyst loading. By using the same reaction conditions and adding isopropanol as a chain-transfer reagent, we were able to control the relative number of polymer chains produced and thus M_n without a decrease in activity (Table 3).

As the molar ratio of isopropanol increases, the measured M_n of the polymer sample decreases while maintaining a narrow polydispersity. This process can be tuned using a variety of chain-transfer agents to achieve polymer samples of desired molecular weight and end group.

In conclusion, we report the alternating ring-opening copolymerization of MA with terminal epoxides catalyzed by a chromium(III) salen complex. This method, followed by isomerization, allowed the quantitative formation of PPF with M_n > 15 kDa under mild conditions. This system also copolymerizes epoxides containing new biocompatible and multifunctional

Table 3. M_n Changes as a Function of ^{i}PrOH Addition[a]

entry	[MA]:[^{i}PrOH]	conv[b] (%)	ether[b] (%)	M_n (kDa)[c]	M_w/M_n[c]
1	200:3	87	<1	6.4	1.2
2	200:5	94	<1	5.0	1.2
3	200:6	92	<1	4.8	1.1
4	200:7	94	<1	4.5	1.1
5	200:9	93	<1	3.9	1.1

[a] Reaction conditions: [MA]:[epoxide]:[**6**] = 200:200:1, [MA] and [epoxide] = 4 mmol in 1 mL of hexanes, T_{rxn} = 45 °C, t_{rxn} = 20 h, quenched with addition of glacial AcOH. [b] Determined by ^{1}H NMR spectroscopy of crude reaction. [c] Determined by GPC calibrated with polystyrene standards in $CHCl_3$ at 40 °C.

substituents. Additionally, chain transfer was demonstrated with this system to afford low-molecular-weight unsaturated resin precursors under mild conditions, with low catalyst loading and narrow polydispersity. Post-polymerization modification, mechanistic studies, and expansion of the substrate scope to include additional biorelevant, renewable monomers are currently in progress.

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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