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Bifunctional Catalysis Prevents Inhibition in Reversible-Deactivation Ring-Opening Copolymerizations of Epoxides and Cyclic Anhydrides

Claire A. L. Lidston, Brooks A. Abel, and Geoffrey W. Coates*

Abstract: Reversible-deactivation chain transfer is a viable strategy to increase the catalytic efficiency of ring-opening polymerizations, such as the alternating copolymerization of epoxides and cyclic anhydrides. In conjunction with the catalyst, protic chain transfer agents (CTAs) initiate polymerization and facilitate rapid proton transfer between active and dormant chains. Functional-group-tolerant Lewis acid catalysts are therefore required to successfully apply protic CTAs in reversible-deactivation ring-opening copolymerizations (RD-ROCOP), yet the predominant binary Lewis acid catalyst/nucleophilic cocatalyst systems suffer lower polymerization rates when used with protic CTAs. New mechanistic insight into the inhibition pathways reveals that the alcohol chain ends compete with epoxide binding to the Lewis acid and hydrogen-bond with anionic chain ends to impede epoxide ring opening. We report that a bifunctional aminocyclopropenium and aluminum salen complex maintains excellent activity in the presence of protic functionality, exhibiting resilience against these inhibition pathways, even at high CTA concentrations. We apply reversible-deactivation chain transfer in the bifunctional ROCOP system to demonstrate precise molecular-weight control, CTA functional group scope, and accessible polymer architectures.

Introduction

Ring-opening polymerizations are controlled alternatives to cumbersome polycondensation routes to synthesize aliphatic and semiaromatic polyesters.1−6 In contrast to step-growth methods, living ring-opening polymerizations enable tunable molecular weights and low dispersities (D ≤ 1.3). While ring-opening polymerizations of lactones or lactide have received significant attention, challenging monomer derivatization constrains accessible functionality and limits the range of resultant polymer properties.7−9 By contrast, the alternating ring-opening copolymerization (ROCOP) of epoxides and cyclic anhydrides enchains a wide variety of commercially available and readily synthesized comonomers pairs with excellent control over the molecular weight and dispersity.10,11 Living epoxide/cyclic anhydride ROCOPs are commonly catalyzed by metal salen complexes paired with nucleophilic cocatalysts; these species initiate polymerization and modulate the activity of the growing chain ends (Scheme 1a).12−27 Adjusting the catalyst/cocatalyst/comonomer stoichiometry provides control over polymer molecular weight, but this approach produces only two polymer chains per catalyst. It is highly desirable to improve catalytic efficiency by producing multiple polymer chains per catalyst. Decreasing the catalyst loading will reduce costs, minimize toxic organometallic residue, and prevent premature polymer degradation.

Chain transfer agents (CTAs) are often employed in ring-opening copolymerizations to increase the number of polymer chains per catalyst.28,29 In ROCOP, each equivalent of protic chain transfer agent produces a dormant chain in addition to the active anionic chains initially derived from the catalyst and cocatalyst. Polymer molecular weights therefore depend on the total initiator concentration and can be tailored by varying both the catalyst and CTA loadings. Rapid, reversible proton transfer between dormant and active chains relative to the rate of propagation (Scheme 2) ensures uniform chain growth, affording narrow molecular-weight distributions.28 A 2011 report from our group demonstrated that the addition of isopropyl alcohol to chromium salcy-catalyzed (salcy = N,N′-bis(salicylidene)-1,2-diaminocyclohexane) copolymerizations of epoxides and maleic anhydride decreased molecular weights and dispersities in proportion to the amount of alcohol added.13 In addition to alcohols, carboxylic acids and amines have been reported as CTAs for reversible-deactivation chain transfer in epoxide/cyclic anhydride ring-opening copolymerization (RD-ROCOP).30,31 Recent applications of RD-

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Scheme 1. (a) Binary and (b) Bifunctional Complexes Catalyze the Alternating Ring-Opening Copolymerization of Epoxides and Cyclic Anhydrides in Conjunction with Protic Chain Transfer Agents

ROROP have used multifunctional CTAs to control polyester dispersity and access both linear and star architectures.

Binary systems comprising distinct Lewis acid complexes and nucleophilic cocatalysts have dominated epoxide/cyclic anhydride copolymerization catalysis. Yet these binary systems are vulnerable to dilution effects that retard polymerization rates at low catalyst loadings. Moreover, close examination of our group’s 2018 report on RD-ROCOP reveals that the addition of CTA further diminished binary aluminum salp (salp = N,N'-bis(salicylidene)phenylenediamine) catalyst activity (turnover frequency, TOF = 75 h\(^{-1}\) with CTA versus 99 h\(^{-1}\) without CTA). Bifunctional catalysts in which the Lewis acid and cocatalyst are covalently tethered have demonstrated improved protic CTA tolerance in epoxide/cyclic anhydride copolymerizations. Although such catalysts have only sparsely been applied to epoxide/cyclic anhydride ROCOP, two terpolymerization reports suggest bifunctional catalyst compatibility with CTAs may extend to systems incorporating cyclic anhydrides. In a series of control reactions, Lee and co-workers used a quaternary ammonium-functionalized cobalt salcy complex to polymerize propylene oxide (PO) and phthalic anhydride (PA) in the presence of ethanol CTA without notable deceleration. Taken together, these reports suggest disparate rate effects of reversible-deactivation chain transfer on binary- and bifunctional-catalyzed ROCOP.

We therefore wanted to explore the differences in RD-ROCOP activity across comparable binary and bifunctional systems. We recently reported a bifunctional aluminum salp catalyst (2-Cl, Scheme 1b) that operates via an analogous mechanism to binary 1-Cl in epoxide/cyclic anhydride copolymerization. The study demonstrated that covalently tethering the Lewis acid and aminocyclopropenium cocatalyst prevents common transesterification and epimerization side reactions while maintaining high polymerization rates at low loadings. The notable differences in activities and selectivities of the binary and bifunctional systems motivated the current study aimed at understanding the effect of protic chain transfer agents on catalyst performance.

Polymerization rates slowed dramatically using binary system 1-Cl/[CyPr]Cl (where [CyPr] = tris(cyclohexylmethyl) aminocyclopropenium) and even small quantities of protic CTA (<10 equiv). Gratifyingly, 2-Cl maintained good TOFs (>70 h\(^{-1}\)), even at high CTA loadings (≤50 equiv). Taking inspiration from enzymatic kinetic analysis, we demonstrate that protic chain ends can inhibit both epoxide activation at the Lewis acid and rate-limiting epoxide ring opening. Catalyst 2-Cl minimizes these disruptions to maintain high polymerization rates in the presence of CTA, further underscoring the advantages of using a bifunctional ROCOP catalyst. Applying 2-Cl in RD-ROCOP achieves precise molecular-weight control, expanded protic CTA scope, and direct access to advanced polymer architectures.

RESULTS AND DISCUSSION

Catalyst Activity in RD-ROCOP. To elucidate the effects of protic CTA on the binary 1-Cl and bifunctional 2-Cl catalysts, we compared copolymerizations of PO and carbic anhydride (CPMA) at varied loadings of 1-adamantanecarboxylic acid (3a) (Figure 1). In the bifunctional system, polymerization rates were invariant with CTA loading up to 25 equiv of 3a relative to 1 equiv of 2-Cl. At higher CTA loadings (50 equiv of 3a), rates declined only modestly and 2-Cl maintained good activity (TOF 70 h\(^{-1}\)). By contrast, rates declined rapidly with increasing equivalents of 3a in polymerizations catalyzed by 1-Cl/[CyPr]Cl. Polymerizations performed with 1-Cl and the more common [PPN]Cl cocatalyst exhibited nearly identical behaviors, indicating that deceleration in binary RD-ROCOP systems is not unique to the [CyPr]Cl cocatalyst (Figure 1, Table S1).

Characterization of Active and Dormant Chain Ends. Active and dormant chains differ only by a protonated chain end; we therefore characterized their \(\omega\)-termini to understand how these species impact binary- and bifunctional-catalyzed RD-ROCOP. Because of the polymerization’s alternating nature, the \(\omega\)-terminus of any active (dormant) chain may be either an alkoxide (alcohol) or a carboxylate (carboxylic acid). On the basis of the different \(pK_a\) values of the possible end groups, we hypothesized that reversible-deactivation chain transfer protonates the most basic species; that is, most dormant chains would possess alcohol end groups rather than more acidic carboxylic acid end groups. We prepared salp aluminum complexes designed to model active alkoxide or carboxylate chain ends bound to the Lewis acid. We therefore wanted to explore the differences in RD-ROCOP activity across comparable binary and bifunctional systems. We recently reported a bifunctional aluminum salp catalyst (2-Cl, Scheme 1b) that operates via an analogous mechanism to binary 1-Cl in epoxide/cyclic anhydride copolymerization.

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salp aluminum isopropoxide (1-OiPr) and salp aluminum acetate (1-OAc) species were then each treated with either 2,2,2-trifluoroethanol or 4-fluorobenzoic acid to mimic the possible end groups of dormant chains. The equilibrium product distribution was monitored by 19F NMR in tetrahydrofuran solvent (Figure 2). Reacting either 1-OiPr or 1-OAc with the more acidic 4-fluorobenzoic acid produced the salp aluminum 4-fluorobenzoate complex as the major product (Figure 2a,c). Treating 1-OiPr with 2,2,2-trifluoroethanol produced a mixture of the two salp aluminum alkoxides (Figure 2d), while reacting 1-OAc with 2,2,2-trifluoroethanol afforded almost no conversion (Figure 2b).

These studies corroborate that pKₐ governs reversible-deactivation chain transfer between anionic and protic chain ends.

Previous mechanistic studies performed in the absence of CTA have identified a resting state in which two propagating carboxylates bind to the Lewis acid.6,33 MALDI-TOF analysis of PO/CPMA copolymerizations catalyzed by 2-Cl further validate this bis-carboxylate resting state in the absence of CTA: the spectrum reveals primarily carboxylic acid end groups (Figure 3a and Figure S20). For copolymerizations performed using CTA 3a and 2-Cl, the MALDI-TOF spectrum reveals mass distributions dominated by alcohol end groups (Figure 3b and Figure S19). This prevalence of alcohol chain ends in RD-ROCOP is consistent with the small-molecule 19F NMR equilibrium studies: given the two possible protic chain end resting states, the higher pKₐ alcohol predominates.

RD-ROCOP Mechanism. We investigated the kinetic behavior of RD-ROCOP to understand how alcohol chain ends interact with the binary and bifunctional catalysts. Examining the reaction profiles of PO/CPMA copolymerizations catalyzed by either 1-Cl/[CyPr]Cl or 2-Cl reveals no evidence of an induction period caused by CTA (Figures S30 and S38). We therefore conclude the rate retardation in the presence of alcohol chain ends arises from a change in mechanism or persistent inhibition throughout the polymerization.

Epoxide/cyclic anhydride ROCOP can proceed via two possible catalytic cycles sharing a common alkoxide/carboxylate intermediate; this mixed alkoxide/carboxylate complex may ring-open either epoxide or cyclic anhydride. In the absence of CTA, cyclic anhydride is ring-opened more rapidly than epoxide such that the primary propagation cycle proceeds via carboxylate/carboxylate and carboxylate/alkoxide intermediates.6 Performing a competition experiment in the presence of tert-butanol (3c) reveals that the mixed alkoxide/carboxylate species first ring-opens 1 equiv of CPMA, after which CPMA and PO are consumed at similar rates (Figure S33). Accordingly, the presence of protic species does not change the primary propagation cycle. Variable time normalization analysis was used to identify reaction orders in the comonomers and catalytic components.37,38 In RD-ROCOP using CTA 3a and either binary or bifunctional catalyst, reaction rates exhibited a zero-order dependence on cyclic anhydride, a first-order dependence on epoxide, and a first-order dependence on each catalytic unit (1-Cl and

Figure 1. Turnover frequency as a function of 3a concentration in binary (1-Cl/[CyPr]Cl) and bifunctional (2-Cl) catalyst systems. [catalyst]₀:[CPMA]₀:[PO]₀ = 1:1200:6000. For polymerizations performed using 1-Cl, [catalyst]₀:[cocatalyst]₀ = 1:1. TOF = Turnover frequency, mol anhydride consumed × mol catalyst⁻¹ × h⁻¹.

Figure 2. 19F NMR spectra of reactions of model complexes 1-OAc (a and b) and 1-OiPr (c and d) with fluorinated alcohols and carboxylic acids in THF. Referenced to fluorobenzene internal standard (−113.15 ppm, black).
[CyPr]Cl or 2-Cl) ([Figures S34–S41]). These reaction orders are consistent with pre-equilibrium epoxide binding and rate-limiting epoxide ring opening, as observed in ROCOP systems in the absence of CTA.6,33

While the primary enchainment mechanism is unchanged by the presence of alcohol chain ends, two discrepancies in kinetic behavior suggest possible inhibition pathways. In the absence of CTA, saturation kinetic behavior in epoxide was observed at high PO concentrations ([PO]0 ≥ 10 M, [CPMA]0:[PO]0 = 1:5).6,33 Intriguingly, reversible-deactivation copolymerizations using 3a and 1-Cl/[CyPr]Cl remained first-order in PO, even when performed neat ([CPMA]0:[PO]0 = 1:5, Figure S36). Second, in RD-ROCOP catalyzed by 2-Cl, exogenous [CyPr]Cl cocatalyst did not accelerate rate-limiting ring opening until the concentration of anionic chain ends exceeded that of protic chain ends ([CyPrCl]0 + 2 × [2-Cl]0 > [3a]0) (Table S9). We therefore propose two possible mechanisms by which alcohol chain ends may inhibit RD-ROCOP (Scheme 3). First, the Lewis basic alcohol ω-terminus of dormant chains may compete with epoxide to bind the Lewis acid but do not affect monomer enchainment. Conversely, best fit lines that have a common intersection on the x-axis suggest the theoretical maximum copolymerization rate depends on [Pn−OH] rather than [PO]0. Such noncompetitive inhibition is consistent with hydrogen bonding between alcohol and anionic chain ends slowing epoxide ring opening. An off-axis common intersection point suggests both competitive binding and hydrogen-bonding inhibition pathways contribute to decelerated polymerization rates.

**Lineweaver–Burk Analysis of Inhibition in RD-ROCOP.** The observed Michaelis–Menten kinetic behavior in RD-ROCOP (vide supra) permits enzymatic inhibition analysis. Lineweaver–Burk plots of inverse initial rate versus inverse PO concentration were constructed at various inhibitor concentrations ([Pn−OH] = [3a]0 after initiation) to graphically distinguish inhibition pathways (Figure 4).59 Best fit lines that have a common intersection on the y-axis indicate that the theoretical maximum polymerization rate is invariant with [Pn−OH], but higher PO concentrations are required to achieve it. In this case, alcohol chain ends compete with epoxide to bind the Lewis acid but do not affect monomer enchainment. Conversely, best fit lines that share a common intersection on the x-axis suggest the theoretical maximum copolymerization rate depends on [Pn−OH] rather than [PO]0. Such noncompetitive inhibition is consistent with
To this end, we applied 1-Cl feature of catalysis, rather than the PO/CPMA comonomers. With and without CTA copolymerizations of other epoxides and cyclic anhydrides rate effect modestly a within the catalytic unit may exclude dormant chains to and alcohol chain ends; intramolecular epoxide ring opening ends at the Lewis acid. Moreover, bifunctional complex, suppressing competitive binding of alcohol chain ends at the Lewis acid.33 We propose that covalently epimerization side reactions by keeping anionic chain ends associated with the Lewis acid.33 We further validate that the Monomer Scope. We sought to further validate that the rate effects observed using 1-Cl and 2-Cl in RD-ROCOP are a feature of catalysis, rather than the PO/CPMA comonomers. To this end, we applied 1-Cl/[CyPr]Cl or 2-Cl in copolymerizations of other epoxides and cyclic anhydrides with and without CTA 3a (Tables S5 and S6). Copolymerizations of CPMA with epoxides bearing larger substituents (tert-butyl glycidyl ether, BGE, or 1,2-epoxy-5-hexene, EHX) catalyzed by 2-Cl exhibited somewhat slower rates as compared to those incorporating PO (TOF = 22 or 52 h⁻¹ versus 86 h⁻¹, respectively). Nonetheless, the addition of 10 equiv of 3a did not affect the activity of 2-Cl (TOF = 24 h⁻¹ for BGE, 54 h⁻¹ for EHX). By contrast, the activity of 1-Cl/[CyPr]Cl was nearly halved by the addition of 10 equiv of 3a in copolymerizations of CPMA with BGE (TOF = 7 and 3.5 h⁻¹) or EHX (TOF = 13 and 7 h⁻¹). Copolymerizations of PO and PA exhibited similar behavior: the addition of 3a did not affect the activity of 2-Cl (TOF = 114 and 117 h⁻¹) but did decrease the efficacy of 1-Cl/[CyPr]Cl (TOF = 95 and 56 h⁻¹). Interestingly, the addition of 3a to copolymerizations PO and 4-chlorophthalic anhydride (Cl-PA) did not significantly affect the activity of either 2-Cl (TOF = 82 and 81 h⁻¹) or 1-Cl/[CyPr]Cl (TOF = 48 and 42 h⁻¹). These results confirm that 2-Cl maintains good activity in RD-ROCOP of a variety of epoxide and cyclic anhydride comonomers.

Molecular-Weight Control in RD-ROCOP. A key advantage of RD-ROCOP is the ability to control molecular weight at reduced catalyst loadings: Molecular weight depends on the total concentration of catalyst and CTA and may therefore be controlled independently of [2-Cl]. As expected, increasing equivalents of CTA 3a relative to those of 2-Cl resulted in decreasing molecular weight (Figure 5a, Table S2, entries 1−8). RD-ROCOP can also be used to reduce the catalyst loading required to achieve a targeted molecular weight by maintaining a constant concentration of total initiating species (2 × [2-Cl]₀ + [3a]₀), Figure 5b, Table S2, entries 9−15. Decreasing [2-Cl]₀ while proportionately increasing [3a]₀ afforded polyesters with molecular weights in the narrow range of ~18−19 kDa while maintaining low dispersities. Notably, decreasing [2-Cl]₀ in the presence of CTA had no measurable influence on catalyst activity at each loading (TOF = 86−89 h⁻¹). These results demonstrate the remarkable advantages of using bifunctional 2-Cl in RD-

Copolymerizations using 3a and 1-Cl/[CyPr]Cl exhibit mixed inhibition with best fit lines exhibiting a common intersection in the second quadrant (−,+), Figure 4a,c): Alcohol chain ends therefore both compete with epoxide to bind the Lewis acid and hydrogen-bond to anionic chains to slow ring opening. As high CTA loadings do not fully suppress reversible-deactivation ROCOP, ring opening by H-bonded chains is slow but productive. By contrast, Lineweaver−Burk analysis of 2-Cl-catalyzed RD-ROCOP reveals a common intersection nearer to the x-axis (Figure 4b,d), consistent with a predominantly noncompetitive inhibition pathway. We recently reported that 2-Cl prevents transesterification and epimerization side reactions by keeping anionic chain ends associated with the Lewis acid.33 We propose that covalently tethering the aluminum salph and aminocyclopropenium cocation and epimerization side reactions by keeping anionic chain ends associated with the Lewis acid.33 We further validate that the rate effects observed using 1-Cl and 2-Cl in RD-ROCOP are a feature of catalysis, rather than the PO/CPMA comonomers. To this end, we applied 1-Cl/[CyPr]Cl or 2-Cl in copolymerizations of other epoxides and cyclic anhydrides with and without CTA 3a (Tables S5 and S6). Copolymerizations of CPMA with epoxides bearing larger substituents (tert-butyl glycidyl ether, BGE, or 1,2-epoxy-5-hexene, EHX) catalyzed by 2-Cl exhibited somewhat slower rates as compared to those incorporating PO (TOF = 22 or 52 h⁻¹ versus 86 h⁻¹, respectively). Nonetheless, the addition of 10 equiv of 3a did not affect the activity of 2-Cl (TOF = 24 h⁻¹ for BGE, 54 h⁻¹ for EHX). By contrast, the activity of 1-Cl/[CyPr]Cl was nearly halved by the addition of 10 equiv of 3a in copolymerizations of CPMA with BGE (TOF = 7 and 3.5 h⁻¹) or EHX (TOF = 13 and 7 h⁻¹). Copolymerizations of PO and PA exhibited similar behavior: the addition of 3a did not affect the activity of 2-Cl (TOF = 114 and 117 h⁻¹) but did decrease the efficacy of 1-Cl/[CyPr]Cl (TOF = 95 and 56 h⁻¹). Interestingly, the addition of 3a to copolymerizations PO and 4-chlorophthalic anhydride (Cl-PA) did not significantly affect the activity of either 2-Cl (TOF = 82 and 81 h⁻¹) or 1-Cl/[CyPr]Cl (TOF = 48 and 42 h⁻¹). These results confirm that 2-Cl maintains good activity in RD-ROCOP of a variety of epoxide and cyclic anhydride comonomers.

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Figure 4. Lineweaver−Burk plots of inhibition by CTA 3a in the binary (a and c, left) and bifunctional (b and d, right) catalyst systems. Top plots (a and b) show full kinetic analyses where each point represents the mean of four independent measurements at each PO concentration and 3a loading (equivalents of CTA relative to the catalyst noted on plots). Bottom plots (c and d) are magnified replicates to show common intersection points (highlighted with gray circles).

ROCOR to simultaneously control polymer molecular weight and reduce catalyst loadings without loss of catalytic activity.

**CTA Functional Group Scope.** We next examined other protic functional groups as viable CTAs (3a–3m) for RD-ROCOR of PO and CPMA (Table 1). Successful chain transfer by each functional group was assessed by comparing $M_n$ values to the molecular weight calculated on complete initiation by 3 and 2-Cl ($M_{n,th}$). Excellent agreement between $M_n$ and $M_{n,th}$ was observed for polymerizations employing CTAs possessing carboxylic acid (3a), unhindered alcohol (3b and 3c), amine (3g, 3h, and 3j), and thiol (3k) functional groups. Meanwhile, sterically hindered (3c and 3d) or weakly nucleophilic (3l and 3m) functional groups performed poorly as CTAs with noticeable discrepancies in $M_n$ and $M_{n,th}$ values and increased dispersities. Polymerizations employing sterically hindered 3c gave intermediate $M_n$ values with a low-molecular-weight tail (Figure S3), consistent with partial chain transfer. Polymerizations using 3d demonstrated that increasing the steric bulk surrounding the alcohol unit fully suppressed chain transfer. Polymerizations performed using 3f or 3i gave $M_n$ values in agreement with values expected for initiation only by 2-Cl, indicating chain transfer did not occur. Despite the structural similarity of naphthylamines 3i and 3j, only polymerizations employing primary naphthylamine 3j gave $M_n$ values consistent with the $M_{n,th}$ expected for chain transfer. Attenuated polymerization rates were also observed when using CTAs N-methylbenzamide (3f, TOF = 76 h$^{-1}$) and dimethylurea (3i, TOF = 50 h$^{-1}$), which suggests that highly polar protic functional groups such as amides and ureas can inhibit ROCOR when used with bifunctional catalysts.

To further corroborate the chain transfer results summarized in Table 1, we prepared low-molecular-weight polymers using 2-Cl and 3a–3m for end group analysis by MALDI-TOF mass spectrometry (Table S3, Figures S5–S17). Polymerizations performed using CTAs 3a, 3b, 3c, 3g, 3h, 3j, and 3k afforded low-molecular-weight polymers that were subsequently analyzed by MALDI-TOF mass spectrometry. Polymers synthesized using 3c, 3d, 3f, 3i, 3l, and 3m possessed molecular weights that exceeded the detection limit of the instrument used for MALDI-TOF analysis, corroborating that these species do not promote chain transfer.

Interestingly, only water-derived chains were observed by MALDI-TOF analysis when primary amine CTAs 3h (Figure S11) or 3j (Figure S19) were combined with 2-Cl and CPMA prior to the addition of PO (Table 1, entries 9 and 12). We hypothesized that the reaction of 3h and 3j with CPMA formed the corresponding imides and 1 equiv of water, which then functioned as the CTA to give water-derived chains. To test this hypothesis, we combined 3j, CPMA, and 2-Cl in THF and heated at 60 °C for 4 h. $^1$H NMR analysis of the crude reaction mixture revealed primary formation of the imide derived from 3j and CPMA (Figure S18). These results corroborate the MALDI-TOF data that primary amines do not function directly as CTAs when added to the polymerization prior to PO. Instead, most chains are initiated by the water function directly as CTAs when added to the polymerization prior to PO, corroborating the MALDI-TOF data that primary amines do not function directly as CTAs when added to the polymerization prior to PO.

To assess whether primary amines might function as CTAs if imide formation were suppressed, we investigated the effect of the CTA order of addition. 2-Cl, CPMA, and PO were first combined, followed by the addition of 3h or 3j prior to heating at 60 °C. In contrast to the water-derived chains obtained when 3h or 3j were added before PO, MALDI-TOF analysis revealed that adding 3h or 3j as the last reagent produced polymer chains that were primarily initiated by 3h (Figure S10) or 3j (Figure S12) with a secondary distribution of chloride-initiated chains derived from 2-Cl. We reason that prior to the addition of the primary amine, 2-Cl, CPMA, and PO rapidly react to give the corresponding coordinately saturated complex 2-X$_3$ (Scheme 4a). A detailed mechanistic
study by Fieser et al. showed that initiation with the analogous 1-Cl/[PPN]Cl binary catalyst system is rapid, leading to the formation of a bis-alkoxide complex that can react further with cyclic anhydride. Given that an open coordination site is likely required for amide-acid ring closure (Scheme 4b), we hypothesize that the formation of coordinatively saturated 2-Cl prior to the amide-acid prevents Lewis acid catalyzed imide formation, allowing the amide-acid to initiate polymerization (Scheme 4c).

Advanced Polymer Architectures via RD-ROCOP. We next applied the high activity and functional group tolerance of 2-Cl in RD-ROCOP to prepare polyester-based architectures that would otherwise be inaccessible using binary catalyst systems. To demonstrate the versatility of bifunctional catalyst 2-Cl, we synthesized telechelic, multiblock, and branched polyester by RD-ROCOP using multifunctional CTAs with excess dithiothreitol (DTT). The molecular weight of the polyester following reduction (M\text{GPC} = 2.5) was approximately half that of the parent polymer (M\text{GPC} = 5.7), as evidenced by a complete shift in the GPC RI peak of the parent polymer to a higher elution volume (Figure S20b, Table S4). Cleavage of the central disulfide linkage may enable orthogonal postpolymerization modification of the hydroxyl-thiol polymer chain ends.

MacroCTAs (3p and 3q) underwent efficient chain transfer to give the corresponding ABA triblock copolymers with low dispersities (D < 1.20). Of note, chain extension of poly(ε-caprolactone) (3q) occurred without transesterification to the sterically unhindered polyester backbone. As discussed in prior work, 2-Cl is particularly adept at preventing such side reactions.

Tetrafunctional CTA 3r was successfully chain-extended to the corresponding star copolymer with poly(ethylene oxide) core and polyester outer block. Uniform polymer growth from each arm was evidenced by the near monomodal GPC trace and low dispersity (D = 1.19) of the star copolymer. 1,3,4-Benzenetricarboxylic anhydride (3s) was employed as a polymerizable CTA to produce a hyperbranched polyester with a high dispersity (D = 1.79) and broad GPC trace (Figure S4), which is likely a consequence of nonuniform branching. Furthermore, catalyst activity was reduced when using 3s (TOF = 43 h\textsuperscript{-1}) as compared to the other CTAs summarized in Table 2 (TOFs = 84–86 h\textsuperscript{-1}), which may be due in part to the high CTA loading (50 equiv). Steric hindrance impeding efficient chain transfer likely further contributes to the suppressed reaction rate and high dispersity observed using CTA 3s.

Recently, Wang and co-workers demonstrated simultaneous ROCOP and reversible addition-fragmentation chain transfer (RAFT) polymerization using a bifunctional CTA comprising carboxylic acid and thiocarbonate groups. Similarly, we employed thiocarbonate-containing bifunctional CTA 3s to synthesize a diblock copolymer using sequential RD-ROCOP and RAFT polymerization. 3s was chain-extended with PO and PA to give macroRAFT agent P1 (M\text{GPC} = 3.6 kDa, D = 1.08). P1 was then chain-extended with ethyl acrylate by RAFT polymerization to give polyester-\textit{b}-poly(ethyl acrylate) P2 (M\text{GPC} = 37.1 kDa, D = 1.25) (Figure S20a, Table S4).

**CONCLUSION**

Replacing catalyst equivalents with chain transfer agent can significantly improve catalytic efficiency in epoxide/cyclic anhydride copolymerizations while minimizing catalyst residue.

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