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Diblock Copolymers

Pre-Rate-Determining Selectivity in the Terpolymerization of Epoxides, Cyclic Anhydrides, and CO_2: A One-Step Route to Diblock Copolymers **

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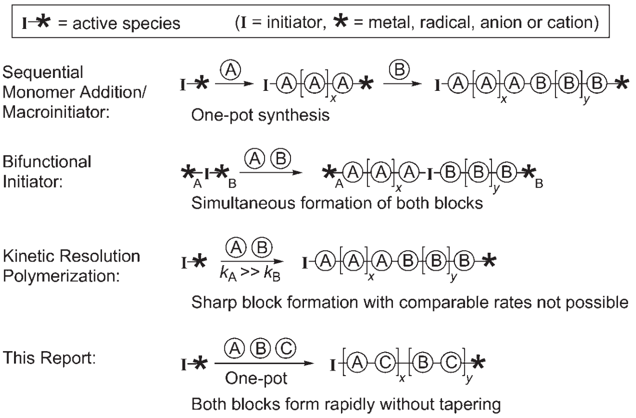
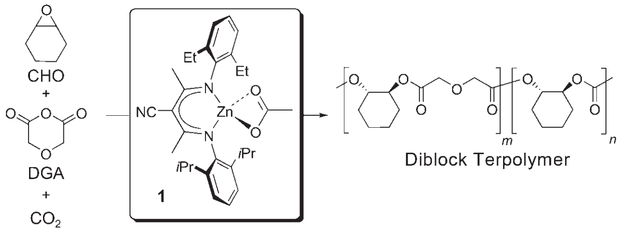
Block copolymers have found widespread use in membrane synthesis,[1] drug delivery,[2] lithography[3] and as thermoplastic elastomers.[4,5] While these types of polymers are typically synthesized by sequential monomer addition or macroinitiation,[4,6] a few specialized techniques for the synthesis of block copolymers have been developed (Scheme 1). Hillmyer has reviewed a technique termed "change of mechanism polymerization", or CHOMP. This method, a variation of macroinitiation, allows for the incorporation of two mechanistically incompatible monomers by changing the active species after the first block is formed.[7] Another specialized method for the synthesis of diblock copolymers is the use of bifunctional initiators. Hawker and co-workers described the application of a bifunctional initiator containing an alcohol and an alkoxyamine in order to simultaneously carry out the ring-opening polymerization of ε-caprolactone and the living free radical polymerization of styrene to afford poly(styrene-*block*-caprolactone).[8] A report by Sogah and co-workers demonstrated the use of a similar bifunctional initiator for the preparation of poly(styrene-*block*-2-phenyl-2-oxazoline).[9] Grubbs and co-workers designed a ruthenium olefin metathesis catalyst with an alkylidene ligand containing a pendant radical initiator. They employed this complex in the simultaneous ring-opening metathesis polymerization of 1,5-cyclooctadiene and radical polymerization of methyl methacrylate to afford poly(cyclooctadiene-*block*-methyl methacrylate).[10] Finally, kinetic resolution polymerization has been shown to produce diblock copolymers. Spassky and co-workers reported a chiral aluminum alkoxide complex which showed a preference for (*R*,*R*)-lactide over the (*S*,*S*) enantiomer by a factor of 20. When polymerizations of *rac*-lactide were allowed to proceed to full conversion, a stereoblock copolymer resulted with moderate tapering.[11] A facile and rapid synthetic route to diblock copolymers which does not require the use of macro or bifunctional initiators would represent a new strategy to complement these other important contributions. Herein, we report a method for the synthesis of poly(ester-*block*-carbonate)s through a one-step, one-pot procedure with a β-diiminate (bdi) zinc catalyst (**1**, Scheme 2).



Scheme 1. Comparison of methods for diblock copolymer synthesis.



Scheme 2. Terpolymerization of CHO, DGA and CO_2.

Polymers containing ester and carbonate linkages are useful as biodegradable implants[12] and have been shown to have adjustable degradation rates. For example, Liu and co-workers reported the copolymerization of a cyclic carbonate with *rac*-lactide to afford the corresponding random copolymer. By tuning the feed ratio of each monomer, they tailored the degradation rate, an advantage for applications in drug delivery.[13]

Recently, we reported the synthesis of aliphatic polyesters from epoxides and cyclic anhydrides[14] using (bdi)ZnOAc catalysts[15] previously developed in our group. Because the bdi catalysts are also highly active for the copolymerization of epoxides and CO_2, we introduced CO_2 to a cyclohexene oxide

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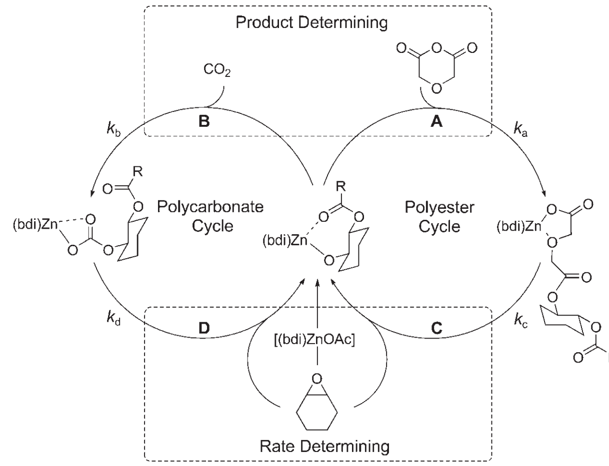
(CHO) and diglycolic anhydride (DGA) copolymerization (Scheme 2). The product was anticipated to be a random poly(ester-carbonate); however, the ^{1}H NMR spectrum was consistent with two separate homopolymers. During the polymerization, it was noted that the CO_2 pressure remained constant (6.8 atm) until the anhydride was consumed, at which point it began to decrease. When the reaction was repeated and quenched before the anhydride was completely consumed, the ^{1}H NMR spectrum revealed that about 90 % of the anhydride was incorporated into polyester, but very little polycarbonate (ca. 1 %) was present. This led us to hypothesize that a diblock terpolymer was generated in the initial reaction via the mechanism proposed in Scheme 3, in which the rate of step **A** is much higher than the rate of step **B**.



Scheme 3. Proposed mechanism for terpolymerization of CHO, DGA and CO_2 (R = alkyl or polymer).

We screened a number of (bdi)ZnOAc complexes[16] for this reaction and found that complex **1**[14] (Scheme 2) was the most active. We then examined the effect of anhydride loading. As shown in Table 1, as [DGA] increases relative to [CHO] and [CO_2], (entries 1–5) more polyester is produced, but the overall polymerization is slower due to the lower rate of polyester formation.[17] Entries 6 and 7, which were quenched before complete conversion of DGA, support a block structure as shown by the very low conversion to polycarbonate.[18] There are a few reports of terpolymerizations that incorporate CO_2. These include the terpolymerization of CO_2, propylene oxide (PO) and CL;[19] CO_2, PO and maleic anhydride;[20] and CO_2, CHO and lactide.[21] However, all of these examples require high pressures of CO_2 (>27 atm), one case resulted in concomitant polyether formation,[20] and, most significantly, all produce random terpolymers.

Table 1: Effect of DGA loading on terpolymerization.[a]

Entry	DGA [mmol]	t_{rxn} [min]	% CHO conv. to[b] PE	PC	M_n[c] [g mol^{-1}]	MWD[c] [M_w/M_n]
1	0	15	0	45	32 000	1.2
2	1.0	30	10	55	27 000	1.2
3	2.0	60	20	70	37 000	1.2
4	4.0	110	41	44	29 000	1.2
5	6.0	180	62	30	30 000	1.3
6	2.0	30	18	1.3	12 000	1.3
7	4.0	60	29	1.3	13 000	1.3

[a] Conditions: 20 μmol **1**, 10 mmol CHO, 2.0 mL toluene, 50 °C, 6.8 atm CO_2. [b] PE = polyester, PC = polycarbonate. Determined by ^{1}H NMR spectroscopy of the crude polymer. [c] Determined by gel permeation chromatography (GPC), calibrated by polystyrene standards.

To more clearly observe the synthesis of polyester and polycarbonate blocks we monitored the terpolymerization of CHO, DGA, and CO_2 by in situ IR spectroscopy.[15c,22,23] A plot of the polymer repeat unit concentration as a function of time demonstrates that polyester is formed first followed by polycarbonate in two very distinct blocks with little tapering (Figure 1). Surprisingly little polycarbonate was produced with the polyester block, even though the second block formed significantly faster than the first. We hypothesized that this remarkable two-stage catalysis must result from the interplay of two competing catalytic cycles.[23]

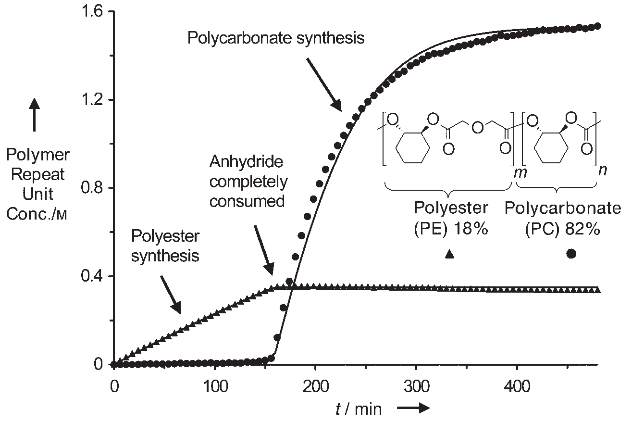


Figure 1. Plot of the experimental concentrations of polyester and polycarbonate repeat units during the terpolymerization (polyester: ▲; polycarbonate: ●) as measured by in situ IR spectroscopy ($\tilde{\nu}_{C\text{-}O}$ polycarbonate = 1328 cm^{-1} and $\tilde{\nu}_{C\text{-}O}$ polyester = 1139 cm^{-1}). 37 μmol **1**, 20 mmol CHO, 3.7 mmol DGA, 8.0 mL toluene, 6.8 atm CO_2, 50 °C. Solid lines are calculated concentrations.[16]

The proposed mechanism of terpolymerization is a combination of reported catalytic cycles[14,15c] which share a common zinc alkoxide intermediate (Scheme 3). Previous mechanistic studies for (bdi)Zn catalysts have shown that for polycarbonate synthesis, insertion of CO_2 is rapid (**B**), whereas insertion of CHO is rate limiting (**D**).[15c] Based on the typical reactivity of the monomers, insertion of anhydride (**A**) is expected to be much faster than insertion of CO_2 (**B**), and insertion of CHO is likely the rate-determining step for polyester (**C**) as well as polycarbonate (**D**) formation.

Based on these predicted activities, the observed block formation is consistent with a *product-determining step* that is *pre-rate-determining*. The polymerization initiates when (bdi)ZnOAc ring opens CHO to give a zinc alkoxide intermediate. Then, in the product-determining step (**A** vs. **B**), the zinc alkoxide reacts preferentially and irreversibly with DGA to form a zinc carboxylate and an ester bond (**A**) followed by a slower, rate-determining insertion of CHO (**C**) to produce polyester and regenerate zinc alkoxide. Production of the polyester block continues until nearly all the DGA is consumed, at which point incorporation of CO_2 becomes competitive (ca. 150 min, Figure 1). Then the zinc alkoxide can react with CO_2, form a zinc carbonate, and insert CHO to form polycarbonate (**B** and **D**). This second block is produced more rapidly than the first because, in the rate-determining step, insertion of CHO into a zinc carbonate (**D**) is more rapid than insertion into a zinc carboxylate (**C**).[24]

To verify that the proposed mechanism results in the observed selectivity and relative rates of block formation, we derived a kinetic model to predict the concentrations of polyester and polycarbonate as a function of time during the reaction. Using experimentally measured values for the rate constants k_c and k_d and estimated values for k_a and k_b, we were able to fit the simulated concentrations to the experimental data. The best fit resulted from $k_a/k_b = 130 \pm 10$.[25] As seen from Figure 1, the simulated (solid lines) and experimental data (points) were in excellent agreement throughout the reaction, particularly when the product and, consequently, the rate of polymerization change dramatically. Thus, the proposed mechanism accurately models the observed synthesis of discrete blocks with the second block produced faster than the first.

There are very few examples of diblock polymer synthesis via kinetic resolution. In the previously mentioned report by Spassky,[11] the reaction only slowly approached 100% conversion because of the inactivity of the (*S*,*S*) enantiomer. This example, which exhibits a lower rate of formation for the second block, is in stark contrast to our terpolymerization, in which the second block (polycarbonate) has a higher overall rate of formation than the first block, (polyester, Figure 1) yet displays little tapering.

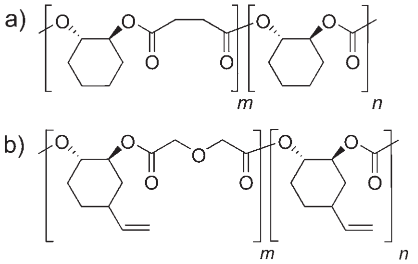
We next explored the effect of CO_2 pressure on composition and rate. As seen in Table 2, as CO_2 pressure increases to 27 atm, the reaction proceeds with little change. Above 27 atm, the overall rate decreases, and CO_2 insertion becomes more competitive with DGA insertion (entries 6 and 7). Inspection of the ^{13}C NMR spectra of reactions with varying CO_2 pressure reveals a small shoulder emerging on the polyester carbonyl resonance (169 ppm) as pressure increases from 6.8 to 54 atm (Figure S8).[16] We attribute this peak to the random incorporation of CO_2 into the polyester block, which increases as CO_2 pressure increases. Entry 8 of Table 2 shows that the reaction does not stop, but merely continues at a lower rate at 54 atm. The rate inhibition above 27 atm can be ascribed to a dilution effect resulting from the increased amount of CO_2 in the reactor.

Table 2: Effect of CO_2 pressure on terpolymerization.

Entry	CO_2 [atm]	% CHO conv. to[b] PE	PC	M_n[c] [g mol^{-1}]	MWD[c] [M_w/M_n]
1[d]	0	17	0	13000	1.3
2	3.4	18	51	17000	1.3
3	6.8	18	54	22000	1.4
4	14	20	67	31000	1.2
5	27	19	51	34000	1.2
6	41	14	6	13000	1.2
7	54	8	3	650	1.3
8[e]	54	17	55	29000	1.3

[a] Conditions: 40 μmol **1**, 20 mmol CHO, 4.0 mmol DGA, 4.0 mL toluene, 55 °C, 1 h. [b] PE = polyester, PC = polycarbonate. Conversion determined by ^{1}H NMR spectroscopy of crude polymer. [c] Determined by GPC. [d] Reaction run for 30 min. [e] Reaction run for 2 h.[16]

We have also found that succinic anhydride will react with CHO and CO_2 to form a diblock terpolymer with similar properties to the DGA containing polymer, albeit with a lower overall rate (Scheme 4a).[14] Furthermore, incorporation of vinyl cyclohexene oxide offers the opportunity for post polymerization modification (Scheme 4b).



Scheme 4. Other diblock terpolymer structures. a) CHO, succinic anhydride and CO_2; b) vinyl cyclohexene oxide, DGA and CO_2.

We have described a novel method for the block terpolymerization of epoxides, cyclic anhydrides, and CO_2 in a simple one-step, one-pot procedure under mild reaction conditions. This reaction is of significant interest because it produces diblock terpolymers with very little tapering, which is clearly evident from a plot of repeat unit concentration versus time for each polymer block (Figure 1). The precise block structure results from a highly selective product-determining step that is pre-rate-determining. Calculations of the concentrations of both polymer blocks as a function of time support the proposed mechanism shown in Scheme 3. Future efforts will be directed towards obtaining block polymers that exhibit micro-phase separation and towards the incorporation of additional monomers.

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[16] See Supporting Information.

[17] In some cases, the experimental molecular weights are much less than the theoretical molecular weights. Despite rigorous purification, we propose that trace protic impurities, likely diacid, act as chain transfer agents and are responsible for this discrepancy.

[18] The ratio of polyester to polycarbonate repeat units in the diblock polymer is identical before and after precipitation in methanol; however, the precipitation of a 1:1 ratio of polyester and polycarbonate homopolymers leads to significant enrichment in polycarbonate.

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[23] For an example of a related two-stage mechanism see: J. M. Rowley, E. B. Lobkovsky, G. W. Coates, *J. Am. Chem. Soc.* **2007**, *129*, 4948 – 4960.

[24] For further discussion of the mechanism see Supporting Information.

[25] The error bars associated with this measurement result from the uncertainty in the CO_2 concentration measurement; see Supporting Information.