Chemoselective Polymerizations from Mixtures of Epoxide, Lactone, Anhydride, and Carbon Dioxide

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ABSTRACT: Controlling polymer composition starting from mixtures of monomers is an important, but rarely achieved, target. Here a single switchable catalyst for both ring-opening polymerization (ROP) of lactones and ring-opening copolymerization (ROCOP) of epoxides, anhydrides, and CO₂ is investigated, using both experimental and theoretical methods. Different combinations of four model monomers—ε-caprolactone, cyclohexene oxide, phthalic anhydride, and carbon dioxide—are investigated using a single dizinc catalyst. The catalyst switches between the distinct polymerization cycles and shows high monomer selectivity, resulting in block sequence control and predictable compositions (esters and carbonates) in the polymer chain. The understanding gained of the orthogonal reactivity of monomers, specifically controlled by the nature of the metal-chain end group, opens the way to engineer polymer block sequences.

INTRODUCTION

Discovering selective transformations using monomer mixtures to yield polymers of homogeneous compositions, including block sequences, are highly desirable both to reduce costs and to enhance chemical complexity. Block copolymers are important in commodity applications but also allow finer control of properties thereby allowing tailoring for higher-value applications. Pioneering monomer sequence selectivity has been demonstrated in processes including controlled radical polymerizations, stepwise monomer coupling reactions, and ring-opening metathesis polymerization. Nonetheless, significant challenges remain, particularly to expand the methods to oxygenated polymers and to allow controllable enchainment from mixtures. Methods to switch polymerization reactions “on/off” or between different catalytic cycles are generally useful and will be essential to enable block selectivity and diversity. Matyjaszewski and co-workers pioneered an electrochemical “switch”, controlling the oxidation state and reactivity of Cu catalysts for atom transfer radical polymerizations. Furthermore, photoelectrochemical triggers can be used to control radical polymerizations. In the distinct area of lactone ring-opening polymerizations (ROP), it is also feasible to switch on/off the reactivity of metal alkoxide catalysts by changing the oxidation state. Using this method it was even possible to discriminate between two very similar monomers, lactide and ε-caprolactone, in ROP. Mirkin and co-workers demonstrated allostere switchable polymerization catalysts, whereby the addition of halide ions switched the catalyst conformation enabling a switch on/off ROP. Dubois, Coulombier, and co-workers developed a switch process for ROP of lactone and cyclic carbonates that is controlled by the presence/absence of carbon dioxide.

Kinetic control is of long-standing interest as a means to control polymer composition from mixtures, albeit requiring that a common polymerization method is used. For example, Coates and co-workers discovered that the ring-opening copolymerizations (ROCOP) of an epoxide, anhydride, and carbon dioxide occurred with very high selectivity to yield only block copoly(ester-carbonates). The ROCOP of epoxide/anhydride occurred first, followed by epoxide/CO₂ polymerizations. Subsequently, various other ROCOP catalysts showed the same selectivity allowing various new semi-aromatic polyesters to be prepared. Albertsson and co-workers exploited differences in polymerization rates, enhanced using thermal switches, in the ROP of ε-caprolactone and a cyclic carbonate to prepare multi-block copolymers. Stereochemical control is a special case of kinetic selectivity, an outstanding control in lactone ROP was first demonstrated by Coates and Thomas using chiral catalysts and racemic mixtures of two similar, but subtly different, lactones to yield syndiotactic polyesters.

Another strategy in block selectivity is to link together two different polymerization cycles, in the best cases these occur via “one-pot” processes using tandem catalysis and sequential monomer additions. For example, Darenbourg and Lu...
applied organocatalysts for lactide ROP which were subsequently deactivated by water addition, allowing a second metal catalyst to initiate the ROCOP of epoxide/CO₂.

Hadjichristidis and Gnanou prepared block copoly(ether-ester/carbonates) using base-catalyzed epoxide ROP, followed by addition of an organo-catalyst to deactivate the base and simultaneously initiate lactone/cyclic carbonate ROP. In 2014, our group reported the first example of a single catalyst, 1 (Supporting Information (SI), Figure S1), which was active for two distinct polymerization cycles and which could be "switched" between them by a new type of chemoselective control. The selectivity arises by controlling the chemistry of the metal—polymer chain end group, with metal alkoxides and carbonates having orthogonal reactivities toward the monomers. Using this method, mixtures of cyclohexene oxide, ε-caprolactone, and carbon dioxide were first polymerized by ROCOP (epoxide/CO₂) to produce a perfectly alternating polycarbonate block and, once the carbon dioxide was consumed/removed, the same catalyst selectively polymerized the lactone, by ROP, ultimately producing block copoly(ester-carbonates). This surprising result was rationalized by kinetic phenomena: i.e., relatively faster rate of carbon dioxide insertion into the zinc alkoxide intermediate, which is common to both catalytic cycles. To our knowledge such chemoselective control is conceptually and practically distinct from the previous switches because it operates via control of the chemistry of the chain end group and it applies just one catalyst (and pot) for two distinct polymerization cycles (Scheme 1). Exploiting the “chemoselective switch” allows epoxides to be used to switch-on catalysts, such as 1, for efficient ROP of lactones. Furthermore, it can be used to selectively prepare ABA type block copoly(ester-carbonates). Very recently, it was used to prepare multi-block copolymers, using mixtures of ε-decalactone, phthalic anhydride, and epoxides and switching between ROCOP (epoxide/anhydride) and ROP (lactone). Despite the promising results, the fundamental basis for the selectivity is not yet understood. Here, we combine experimental and theoretical studies to examine the thermodynamic factors under-pinning the selective transformations.

### RESULTS AND DISCUSSION

A detailed study comparing the products of polymerizations conducted using mixtures selected from four generic types of oxygenated precursors was undertaken (Scheme 2). The

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**Scheme 2. Four Exemplar Monomers and the Range of Polymer Products Produced Using Chemoselective Catalysis**

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**Figure 1. Poly(carbonate-block-ester) formation from mixtures of ε-caprolactone (ε-CL), cyclohexene oxide (CHO), and CO₂.**

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“See Figure S1 for dizinc catalyst structure.”

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The PCL molecular weight (MW) can be controlled over the spectroscopy (Figure S1). The spectroscopic study confirmed that zinc alkoxide; it is this alkoxide which is an active initiator for poly(caprolactone) (PCL) in less than 1 h (Table 1, runs 1–4). The "switch-on" of ROP occurred due to the reaction of 1 with the epoxy to form an alkoxide intermediate, which was characterized by in situ spectroscopy (Figure S1). The spectroscopic study confirmed that the acetate co-ligand of catalyst 1 attacks CHO, forming a zinc alkoxide; it is this alkoxide which is an active initiator for ROP (Figure 2).

The rapid polymerization of ε-CL, catalyzed by 1 in the presence of epoxide, over a range of loadings (1:monomer 1:200–800 mol/mol, results in quantitative conversion of poly(caprolactone) (PCL) in less than 1 h (Table 1, runs 1–4). The PCL molecular weight (MW) can be controlled over the range 6–45 kg·mol⁻¹ (Table 1 and Figure S2). The catalyst system is highly active, having a turnover frequency of 620 h⁻¹ (Table 1, run 4), which compares well with some of the best systems. The polymerization control is high, as assessed by an aliquot method; there is a linear relationship between MW and conversion (Figure 3) and a linear relationship between MW and ε-CL conversion remaining at 70% by ¹H NMR spectroscopy (Figure S6). The short time (~6 min) taken to completely stop polymerization likely corresponds to the rate of CO₂ dissolution. Indeed, using other related catalysts, if vacuum is applied prior to CO₂ addition, immediate cessation of polymerization occurred. Careful analysis of the polymer, using NMR spectroscopy, showed only PCL formation; there was no evidence for any CO₂ insertion into the polymer backbone (Figure S6). The zinc alkoxide intermediate, generated by reaction between 1 and CHO, immediately formed a new zinc carbonate species on exposure to just 1 bar pressure of CO₂ (as monitored by ATR-IR spectroscopy, Figure S6). Other researchers have also recently reported that CO₂ can be used to inhibit ROP of either ε-CL or cyclic carbonates, using quite different organo-catalysts. Thus, there is growing evidence that either metal or organic carbonate species are not viable initiators/catalysts for lactone ROP.

In order to shed light on the high degrees of selectivity observed experimentally, a DFT study was undertaken. It should be noted that the CHO/CO₂ ROCOP process using catalyst 1 has already been studied by DFT; therefore, the same level of theory was applied. For all calculations, the oB97XD/6-31G(d)/SCRF (pcm, solvent = dichloromethane) protocol was used. In fact, this protocol yields results in close agreement to those determined using higher basis sets (see Tables S7 and S8) and to those obtained using CCSD calculations; furthermore, the results are in excellent agreement with experimentally determined activation barriers.22 The calculations were conducted at the same temperatures as applied experimentally (ROP ε-CL, ROCOP CHO/CO₂ = 80 °C, and ROCOP PA/CHO = 100 °C). It is notable that there are very few theoretical studies of epoxide/CO₂ as yet there are none for epoxide/anhydride polymerizations. A recent finding was proposed to be caused by competitive coordination of ε-CL at the catalyst preventing copolymerization occurring by blocking epoxide binding. In order to understand the influence of CO₂ on ROP, the polymerization of ε-CL (600 equiv) was conducted, under a nitrogen gas atmosphere in the presence of CHO (2000 equiv), with the gas atmosphere exchanged to CO₂ after 36 min (Figure S5).

Analysis using in situ ATR-IR spectroscopy shows that shortly after CO₂ addition there is complete cessation of the polymerization, with the ε-CL conversion remaining at 70% by ¹H NMR spectroscopy (Figure S6). The short time (~6 min) taken to completely stop polymerization likely corresponds to the rate of CO₂ dissolution. Indeed, using other related catalysts, if vacuum is applied prior to CO₂ addition, immediate cessation of polymerization occurred. Careful analysis of the polymer, using NMR spectroscopy, showed only PCL formation; there was no evidence for any CO₂ insertion into the polymer backbone (Figure S6). The zinc alkoxide intermediate, generated by reaction between 1 and CHO, immediately formed a new zinc carbonate species on exposure to just 1 bar pressure of CO₂ (as monitored by ATR-IR spectroscopy, Figure S6). Other researchers have also recently reported that CO₂ can be used to inhibit ROP of either ε-CL or cyclic carbonates, using quite different organo-catalysts. Thus, there is growing evidence that either metal or organic carbonate species are not viable initiators/catalysts for lactone ROP.

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**Table 1. Polymerizations Using Lactone, Epoxide, and CO₂**

<table>
<thead>
<tr>
<th>run no.</th>
<th>I/CHO/ε-CL (equiv)</th>
<th>CO₂ (atm)</th>
<th>time (min)</th>
<th>ε-CL (%)</th>
<th>CHO (%)</th>
<th>ε-CL conversion (%)</th>
<th>M_n (D) (kg·mol⁻¹)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>1/800/200</td>
<td>0</td>
<td>45</td>
<td>100</td>
<td>0</td>
<td>7.4 (1.90)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1/600/400</td>
<td>0</td>
<td>40</td>
<td>100</td>
<td>0</td>
<td>22.2 (1.50)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1/400/600</td>
<td>0</td>
<td>35</td>
<td>100</td>
<td>0</td>
<td>38.0 (1.4)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1/200/800</td>
<td>0</td>
<td>45</td>
<td>58</td>
<td>0</td>
<td>44.9 (1.4)</td>
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<td>5</td>
<td>1/900/100</td>
<td>1</td>
<td>20</td>
<td>0</td>
<td>15</td>
<td>1.8 (1.08)</td>
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</tr>
<tr>
<td>6</td>
<td>1/100/900</td>
<td>0</td>
<td>17</td>
<td>100</td>
<td>0</td>
<td>38.0 (1.4)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1/400/600</td>
<td>1</td>
<td>8.5</td>
<td>0</td>
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<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*Reaction conditions: I = 1 equiv, 80 °C, monomer mixture as solvent. Conv determined by ¹H NMR spectroscopy (see SI). Determined by SEC, with polystyrene standards.

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**Figure 2.** In situ catalyst activation for the ring-opening polymerization (ROP) of ε-CL.
review contrasts the theoretical methods applied to this field of catalysis.\textsuperscript{25}

The Gibbs free energy profile (including key transition states) was calculated for all possible polymerization reactions between CHO, \(\varepsilon\)-CL, and CO\(_2\), catalyzed by 1, and the most viable of these are illustrated in Figures 4 and 5 (all the data are available in the SI, Figures S7 and S8, and Tables S3 and S4). In Figure 4 the reactions corresponding to Activation and Initiation are shown, whereby the catalyst reacts first with a molecule of epoxide to generate an alkoxide intermediate which subsequently reacts with a molecule of \(\varepsilon\)-CL. The second monomer addition cycle, illustrated in Figure 5, Propagation, whereby the metal alkoxide intermediate reacts with a second molecule of \(\varepsilon\)-CL. In order to understand the relative barriers to other possible polymerization pathways, the reactions of the alkoxide intermediates (6 and 12\textsubscript{CL}) with carbon dioxide or epoxide are also illustrated (purple and blue pathways, respectively, Figures 4 and 5).\textsuperscript{22}

Considering the Activation reaction, it was not possible to locate any transition states or intermediates for the direct attack and ring-opening of \(\varepsilon\)-CL by catalyst 1. Experiments show that 1 is not a catalyst, even when significant energy is provided in the form of heating: these results confirm the ring-opening is not thermodynamically favorable. In contrast, 1 can react with CHO (Activation) (the energies of various intermediates and transition states are shown in the SI, Table S3 and Figure S7), to form the zinc alkoxide species 6 (\(\Delta G\textsubscript{353} = -5.2\) kcal mol\(^{-1}\)), which was characterized spectroscopically. Importantly, 6 has a coordinative vacancy at one of the zinc centers, resulting from the (growing) polymer chain rotating away from the metals, and is the common intermediate from which the various monomer additions are compared. It is also thermodynamically favorable compared to the isolated starting species (1+ epoxide), due to the relatively high ring-strain of the epoxide.

Intermediate 6 can initiate \(\varepsilon\)-CL ROP by a coordination/insertion mechanism (for the entire pathway see Figure S7), leading to the formation of intermediate 12\textsubscript{CL} (Figure 4). Coordination of \(\varepsilon\)-CL forms intermediate 7\textsubscript{CL} (\(\Delta G\textsubscript{353} = -2.9\) kcal mol\(^{-1}\)) and is followed by intramolecular attack on the lactone by the zinc alkoxide, leading to the hemi-acetal intermediate 9\textsubscript{CL} (\(\Delta G\textsubscript{353} = -2.8\) kcal mol\(^{-1}\)). The attack occurs via a relatively high energy transition state 8\textsubscript{CL}-TS (\(\Delta G\textsubscript{7} = +30.7\) kcal mol\(^{-1}\)), in line with the reaction requiring temperatures above 80 °C to occur at an appreciable rate. Intermediate 9\textsubscript{CL} is able to react further, by ring-opening of the hemi-acetal, leading to the formation of a new zinc alkoxide intermediate, 11\textsubscript{CL} (\(\Delta G = +9.4\) kcal mol\(^{-1}\)). The ring-opening step occurs through a lower energy transition state 10\textsubscript{CL}-TS (\(\Delta G\textsubscript{8CL-TS} = +13.1\) kcal mol\(^{-1}\)) involving acyl bond cleavage and zinc alkoxide bond formation. A slightly more stable intermediate 12\textsubscript{CL} (\(\Delta G\textsubscript{353} = +2.5\) kcal mol\(^{-1}\)) has a coordinative vacancy and is proposed as the intermediate for further propagations (Figure 4). Other groups have studied \(\varepsilon\)-CL ROP, using DFT, and have isolated related transition states and found that the process may be exergonic.\textsuperscript{26}

The alternative pathway, which is not observed experimentally, whereby intermediate 6 reacts with a second epoxide molecule, via a coordination/insertion pathway, was also considered (Figure 4, blue pathway). Accordingly, the barrier to epoxide ring-opening is significantly higher (\(\Delta \Delta G\textsubscript{353} = +39.1\) kcal mol\(^{-1}\) between 7\textsubscript{CHO} and 8\textsubscript{CHO}-TS) compared to that for \(\varepsilon\)-CL ring-opening (\(\Delta \Delta G\textsubscript{353} = +33.6\) kcal mol\(^{-1}\) between 7\textsubscript{CL} and 8\textsubscript{CL}-TS). Nonetheless, the putative alkoxide intermediate formed by epoxide ring-opening would be stabilized (\(\Delta G\textsubscript{353} = -22.1\) kcal mol\(^{-1}\)). In addition, the relative energies for the alternative copolymerization reactions, involving CO\(_2\) and CHO, were considered (Figure 4, purple pathway). In line with the experimental findings, if CO\(_2\) is present, the most
favorable pathway is via CO$_2$ insertion, which has a significantly lower energy barrier ($\Delta\Delta G_{353} = +11.4$ kcal mol$^{-1}$) and leads to a stable zinc carbonate intermediate $12$CO$_2$ ($\Delta G_{353} = -12.7$ kcal mol$^{-1}$). There was no evidence that the zinc carbonate intermediate could subsequently insert an $\varepsilon$-CL molecule. Thus, the theoretical study is in line with the experimental observation that formation of a zinc carbonate prevents ROP.

The propagation pathway for $\varepsilon$-CL ROP leads to identification of various intermediates $12$CL$^{-}$-$17$CL (Figure 5). The overall energies for the propagating species are lower than for the initiation species, and the energy decreases as polymerization progresses. Furthermore, the highest energy barrier, between $13$ and $14^{41}$-TS ($\Delta\Delta G^\# = +25.8$ kcal mol$^{-1}$) is significantly lower than the equivalent barrier during initiation ($\Delta\Delta G_{353} = +33.6$ kcal mol$^{-1}$). This is because the barrier to $\varepsilon$-caprolactone ring-opening depends on the nature of the metal alkoxide group: the secondary cyclohexylene alkoxide has a higher barrier than the primary alkoxide group. Such a difference is in line with the experimental observations that the rate of initiation ($k_i$) (from the secondary alkoxide, cyclohexylene alkoxide) is slower than that of propagation ($k_p$) (from the primary alkoxide, caproyl alkoxide); the ratio of $k_p/k_i$ was determined to be 8.$^{16}$ It was possible to experimentally further exploit the differences in activation barriers: thus, following polymerization of 100 equiv of $\varepsilon$-CL at 80 °C for 2.0 h, subsequent addition of $\varepsilon$-CL (100 equiv), at room temperature, led to formation of PCL (25 °C, 6.0 h), as observed by NMR and SEC analysis (the $M_n$ increases from 8.8 to 18.8 kDa; see Figures S9 and S10, and Table S5).

Other monomer coordination/insertion pathways were also compared. CO$_2$ inserts via a series of lower energy intermediates/transition states ($13$CO$_2$--$16$CO$_2$), leading to the formation of a significantly more stabilized zinc carbonate intermediate $18$CO$_2$ ($\Delta G_{353} = -9.6$ kcal mol$^{-1}$). In addition to lower energy intermediates and transition states, the stabilization may, in part, explain the observed experimental selectivity whereby polymerizations conducted using mixtures of CHO, $\varepsilon$-CL, and CO$_2$ result only in the formation of polycarbonate. $18$CO$_2$ reacts further with CHO, leading to a new zinc alkoxide intermediate $21$CO$_2$ (see Figure S8). In contrast, it was not possible to locate a transition state for further reaction of $18$CO$_2$ with another lactone. These findings are consistent with the experimental observations that $\varepsilon$-CL remains unreacted during epoxide/CO$_2$ ROCOP and that addition of CO$_2$ “easily” switches to the formation of a carbonate intermediate. A further possible side reaction could be the insertion of CHO and thus sequential enchainment of epoxide (by ROP), leading to (poly)ether linkages (Figure 5, blue). However, the transition state for this transformation is likely too high to be accessible ($\Delta\Delta G^\#_{353} = +42.7$ kcal mol$^{-1}$), which may explain the lack of experimental evidence of such linkages.

**Lactone, Anhydride, and Epoxide Polymerizations.** Polymerizations from mixtures of anhydride, epoxide, and $\varepsilon$-CL were investigated (Figure 6). 1 can catalyze the ROCOP of phthalic anhydride (PA) and cyclohexene oxide (CHO). The polymerizations occur rapidly, forming perfectly alternating polyesters (>99% ester linkages) with very high selectivity (Table 2, run 1). In addition, it was already reported that 1 is a viable catalyst for $\varepsilon$-CL ROP, in the presence of epoxide. Thus, polymerizations from mixed feedstock of anhydride, epoxide, and $\varepsilon$-CL was investigated. The mixture polymerization, monitored using in situ ATR-IR spectroscopy,
Figure 6. Poly(ester-block-ester) formation from mixture of PA, CHO, and ε-CL.

Table 2. Polymerizations of ε-CL, CHO, and PA, Catalyzed by 1

<table>
<thead>
<tr>
<th>run no.</th>
<th>1/CHO/PA/ε-CL (equiv)</th>
<th>Mw (kg·mol⁻¹)</th>
<th>PCL linkages (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1/800/100/0</td>
<td>2.6 (1.42)</td>
<td>0 0</td>
</tr>
<tr>
<td>2</td>
<td>1/400/20/100</td>
<td>12.2 (1.42)</td>
<td>19 17</td>
</tr>
<tr>
<td>3</td>
<td>1/400/20/150</td>
<td>15.8 (1.43)</td>
<td>14 12</td>
</tr>
<tr>
<td>4</td>
<td>1/400/20/200</td>
<td>18.7 (1.57)</td>
<td>9 9</td>
</tr>
<tr>
<td>5</td>
<td>1/400/10/150</td>
<td>22.5 (1.46)</td>
<td>8 6</td>
</tr>
</tbody>
</table>

Reaction conditions: 1 = 1 equiv, 100 °C, monomer mixture as the solvent. All polymerizations were run to complete conversion (>99%) of PA and ε-CL.

1 Determined by SEC, using calibration with polystyrene standards. Determined by 1H NMR spectroscopy, by comparing the relative integrals of the signals assigned to PCHPE ester groups (5.16 ppm) compared with those assigned to PCL ester groups (4.07 ppm) in the copolymers.

Figure 7. Time-resolved ATR-IR spectra during the polymerization of mixtures of PA, CHO, and ε-CL. The spectra show that ROCOP of PA/CHO occurs first (producing PCHPE), followed by ROP of ε-CL to produce a copolymer (PCHPE–PCL). Insert: enlarged spectra of the time period during which ε-CL ROP occurs. Reaction conditions: 1/CHO/PA/ε-CL = 1/400/20/200, 100 °C, monomer mixture as the solvent.

No extra signals attributed to PCL or PCHPE homopolymers are observed in the DOSY spectrum. For reference, mixing isolated samples of the polymers results in two different signals attributed to the different solution properties (diffusion coefficients) in the blend (Figure S16).

It is notable that PA/CHO copolymerization occurs before ε-CL polymerization even though this latter reaction is significantly faster. The addition of phthalic anhydride during ε-CL ROP quickly stops propagation (Figure S17). The selectivity is attributed to the PA insertion into the Zn–O bond being more favorable compared to ε-CL insertion.

To better understand the thermodynamic influences, DFT calculations were performed under the same conditions (Figure 9). To our knowledge, this is the first such theoretical study of polyester formation by ROCOP. The epoxide/anhydride copolymerization is conducted at slightly higher temperatures (100 °C), so intermediates 1–6 were re-optimised (intermediate 1’–6’ at the experimental temperature, leading to only minor changes in energy (Tables S3 and S6). From the common zinc alkoxide intermediate 6’, coordination of anhydride leads to intermediate 7PA (DG = −1.6 kcal·mol⁻¹). There are in fact, two enantiomeric approaches during the ring-opening of PA by the CHO alkoxide, and so two transition states for 8PA–TS (DG = +11.7 kcal·mol⁻¹) were found. Both structures and transition states are essentially isoenergetic, with almost identical activation barriers, and as both would lead to the same product after ring-opening, i.e., intermediate 12, only one pathway was studied further. The “forward” intrinsic reaction coordinate calculation from 8PA–TS (Figures S18 and S19) showed two hidden intermediates, 9PA and 10PA, leading to intermediate 11PA (DG = −28.9 kcal·mol⁻¹). These structures involve the ring-opening of the anhydride, followed by cleavage of the cyclohexyl Zn–O bond and coordination of the carboxylate oxygen at the other zinc center. These hidden intermediates are not true stationary points on the potential energy surface, as their first derivatives never quite approach zero, but can be thought of as frustrated minima which can only be characterized in the context of the IRC pathway. Intermediate 11PA is thermodynamically favored compared to the previous intermediates (DG = −28.9 kcal·mol⁻¹).
Intermediate 12PA\textsuperscript{f} is stabilized ($\Delta G_{373} = -14.1$ kcal-mol\textsuperscript{-1}) and features a coordinative vacancy at the metal center, which is essential for forward polymerizations, for example leading to intermediate 13PA\textsuperscript{f} ($\Delta G_{373} = -14.0$ kcal-mol\textsuperscript{-1}). The latter undergoes intramolecular nucleophilic attack of the zinc carboxylate at the epoxide and proceeds via a transition state, 14PA\textsuperscript{f}-TS ($\Delta G_{373} = 10.4$ kcal-mol\textsuperscript{-1}). The overall energy barrier for CHO insertion ($13_{PA} \rightarrow 14_{PA}$-TS) is expected to be accessible ($\Delta \Delta G_{373} = +24.4$ kcal-mol\textsuperscript{-1}) and leads to the formation of intermediate 15PA\textsuperscript{f} ($\Delta G_{373} = -11.9$ kcal-mol\textsuperscript{-1}), where a new zinc alkoxide bond is formed and a cyclohexylene oxide group has been inserted. Thus, the free energy profile for CHO/PA ROCOP is expected to be driven in part by the thermodynamic stability of some of the ring-opened intermediates.

The energy profile for epoxide/anhydride polymerization is also compared to the ROP of $\varepsilon$-CL (Figure 10). Starting from the common zinc alkoxide intermediate 6\textsuperscript{f}, there is little energy difference between the coordination of the anhydride and lactone monomers. However, the energy barrier to ring-open the anhydride is significantly larger than that to open the lactone ($\Delta G_{373}^{\text{EPa}} = +15.5$ kcal-mol\textsuperscript{-1} vs $\Delta G_{373}^{\text{FCL}} = +34.4$ kcal-mol\textsuperscript{-1}). Furthermore, when comparing the energy of the intermediate after ring-opening, 11PA\textsuperscript{f} or 11CL\textsuperscript{f}, it is clear that ROCOP results in a significantly lower energy intermediate ($\Delta G_{373}^{\text{PA}} = -23.2$ kcal-mol\textsuperscript{-1} vs $\Delta G_{373}^{\text{CL}} = +15.2$ kcal-mol\textsuperscript{-1}), signaling a thermodynamic driving force favoring ROCOP.

**Epoxide, Anhydride, and Carbon Dioxide Polymerizations.** Mixtures of CHO, PA, and CO$_2$ were polymerized selectively by catalyst 1 using ROCOP, to form only copoly(ester-block-carbonates).\textsuperscript{12c} First, epoxide/anhydride copolymerization occurred, until complete consumption of PA, after which point epoxide/CO$_2$ copolymerization occurred (Figures 8 and S20).

Once again, the calculated energy profiles at 100 °C for both polymerizations were compared (Figure 11). From the common zinc alkoxide intermediate 6\textsuperscript{f}, either PA or CO$_2$ is coordinated, leading to intermediates $\sigma_{PA}$ and $\sigma_{CO2}$, respectively, which are of very similar energy. Next, insertion into the zinc alkoxide bond occurs (via transition states 8PA\textsuperscript{f}-TS and 8CO$_2$\textsuperscript{f}-TS, whose energies are less than 5 kcal-mol\textsuperscript{-1} different). As stated, experimentally PA insertion occurs before CO$_2$ insertion, furthermore CO$_2$ is not polymerized at all in the presence of PA. This could be attributed, in part, to the lower energy of intermediate 11PA\textsuperscript{f}, compared to 11CO$_2$\textsuperscript{f}. This energetic stabilization may be sufficient that CHO/PA ROCOP is essentially irreversible and therefore the dominant pathway of the two competing options.

**Comparison of Monomer Selectivity.** The dizinc catalyst shows unexpected chemoselectivity in polymerizations using different monomer mixtures yielding predictable compositions and block sequences in copolymers. The monomers are polymerized using two distinct catalytic cycles: the ring-opening copolymerizations (ROCOP) of epoxides/CO$_2$ or epoxides/anhydrides and the ring-opening polymerizations (ROP) of lactones. It is feasible for one catalyst to bridge the two distinct cycles as both involve a zinc alkoxide intermediate (Scheme 1). Experimentally the preference for addition into the zinc–alkoxide bond follows the trend PA $>$ CO$_2$ $>$ $\varepsilon$-CL, and by exploiting this finding copoly(ester-carbonates) and copoly-esters are formed (Scheme 2).

In order to understand and compare the elementary steps in the polymerization cycles, a series of DFT studies were undertaken considering two cycles of monomer additions and different permutations of the monomers. Common to all the polymerizations was the zinc alkoxide intermediate 6, generated by the reaction between the catalyst, zinc acetate, and an epoxide molecule. Figure 12 and Table 3 summarize the limiting energy barriers to the key transition states ($\Delta G^\text{TS}$) and the free energy differences ($\Delta G$) between the corresponding intermediates in the various polymerization cycles.

**Epoxide/Anhydride/CO$_2$.** Of the combinations of monomers investigated, only mixtures of epoxides/anhydrides/CO$_2$ have been explored previously. In those studies, it was observed that various different types of homogeneous catalysts gave rise to high degrees of selectivity. Generally, the anhydride/epoxide ROCOP occurred prior to the CO$_2$/epoxide reaction.\textsuperscript{10,11a-c,12a-c,29} In the field of heterogeneous catalysis, there was much less discrimination between the monomers, with studies using zinc glutarate or zinc–cobalt double metal cyanides resulting in the formation of tapered or gradient block copoly(ester-carbonates).\textsuperscript{30} The rationale for the observed selectivity was always kinetic; i.e., it was argued that the rates of insertion of anhydride vs CO$_2$ into metal alkoxide intermediates determined the order of monomer enchainment. Here, it has been demonstrated that in addition to a kinetic rationale, there are also thermodynamic driving forces which could rationalize the experimental data. In particular, the ester linkage formed after anhydride insertion is significantly more thermodynamically stable compared to the carbonate linkage formed after CO$_2$ insertion. Furthermore, the calculated barriers for the insertions of either PA or CO$_2$ are not significantly different, particularly at the relevant temperatures for such reactions, to one another. These findings suggest that the observed selectivity in the terpolymerizations may result from a thermodynamic driving force toward formation of a more stable linkage.\textsuperscript{10}

**Lactone ROP and Epoxide/Anhydride or Epoxide/CO$_2$ ROCOP.** Mixtures of epoxides, lactones, and carbon dioxide result in selective formation of block copoly(ester-carbonates), whereby the CHO/CO$_2$ ROCOP occurs prior to the $\varepsilon$-CL ROP.\textsuperscript{17} The theoretical study shows a significantly higher barrier to $\varepsilon$-CL insertion, compared to CO$_2$, starting from the same zinc alkoxide intermediate. Furthermore, the product ester linkage is less stable compared to the carbonate linkage. Thus, in addition to kinetic phenomena governing the polymerization selectivity, the thermodynamic stability of the different linkages may also influence the observed selectivity. It is also notable that the initiation of the first $\varepsilon$-CL unit has a significantly higher barrier compared to subsequent propagation; this is because the initiation reaction involves attack by a secondary alkoxide compared to propagation occurring with attack by a primary alkoxide.

Polymerizations conducted using mixtures of epoxide/anhydride/lactone result in the selective formation of block...
Figure 9. Calculated potential energy surface for ROCOP of CHO/PA that includes two hidden intermediates between $8^{PA'}$-TS and $11^{PA'}$. (Data are available at http://doi.org/10.14469/hpc/281.)

Figure 10. Polymerization pathways from mixtures of CHO, PA, and $\varepsilon$-CL. In red, the ROCOP of CHO/PA; in green, the ROP of $\varepsilon$-CL. (An interactive version of this figure is accessible online.)
The study also highlights the importance of considering both a kinetic and thermodynamic basis for future selective polymerizations. Nevertheless, it is also important to consider some other influences over catalytic selectivity. A notable observation is that the catalyst does not enchain epoxide units, and therefore ether linkages are barely detected. It could be concluded from this that sequential epoxide enchainment, by ROP, is not an experimentally accessible pathway, at least at...
temperatures up to 100 °C. However, an examination only of the thermodynamic parameters, particularly during initiation, reveals that although the barriers to epoxide insertion are higher than for other monomers, there is a significant stability associated with the putative products. In contrast, during propagation, there is a much more significant difference in the energy barriers, with the epoxide enchainment requiring >10 kcal·mol\(^{-1}\) more than the lactone enchainment.

Furthermore, the calculations do not provide kinetic models for initiation/propagation. It is difficult to directly measure the rates of monomer insertion into the zinc–alkoxide bond, particularly in the case of CO\(_2\)/anhydride as these are pre-rate-limiting reactions. A recent study of CO\(_2\) insertion into a zinc hydride complex, featuring similar amine–phenolate ligands, revealed that the measured rate in fact corresponded with the rates of CO\(_2\) dissolution/diffusion into the reaction medium (i.e., the reaction was diffusion limited).\(^{31}\) Given that the rate observed in that study was typical of other zinc complexes reported for CO\(_2\) insertion processes,\(^{32}\) it seems likely that related insertion reactions may also occur under diffusion-limited conditions. Another factor which would be expected to influence the order of monomer insertion is the concentration of the particular monomer coordinated intermediate. The coordination of the relevant monomer to the catalyst is likely an equilibrium process which would be affected by the relative concentrations of monomers.

### Table 3. Illustration and Quantification of the Key Energy Barriers in the Polymerization Processes (kcal·mol\(^{-1}\))

<table>
<thead>
<tr>
<th>Monomers (M)</th>
<th>Zn alkoxide</th>
<th>Zn carbonate</th>
<th>Zn carboxylate</th>
</tr>
</thead>
<tbody>
<tr>
<td>R = R(_1)</td>
<td>(\Delta_{TS})G = +39.1 (\Delta_{P}G) = -16.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R = R(_2)</td>
<td>(\Delta_{TS})G = +40.4 (\Delta_{P}G) = -11.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R = R(_3)</td>
<td>(\Delta_{TS})G = +11.4 (+9.8) (\Delta_{P}G) = -5.0 (-6.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R = R(_4)</td>
<td>(\Delta_{TS})G = +1.6 (\Delta_{P}G) = -19.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R = R(_5)</td>
<td>(\Delta_{TS})G = +23.5 (\Delta_{P}G) = +0.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R = R(_6)</td>
<td>(\Delta_{TS})G = +25.3 (\Delta_{P}G) = +0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R = R(_7)</td>
<td>(\Delta_{TS})G = +10.5 (\Delta_{P}G) = +8.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R = R(_8)</td>
<td>(\Delta_{TS})G = +24.4 (\Delta_{P}G) = +2.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R = R(_9)</td>
<td>(\Delta_{TS})G = +33.8 (34.4) (\Delta_{P}G) = +5.4 (+11.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R = R(_{10})</td>
<td>(\Delta_{TS})G = +25.8 (\Delta_{P}G) = +4.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R = R(_{11})</td>
<td>not observed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R = R(_{12})</td>
<td>not observed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^{a}\)\(T = 373.15\) K. \(^{b}\)\(T = 273.15\) K.\(^{22}\)
different loadings have been explored, and, in most cases, the concentration of the epoxide was significantly greater than that of any other species present. This might be expected to bias somewhat the concentration of the epoxide-coordinated intermediate and thereby enable epoxide enchainment; however, this was never observed experimentally. Finally, it might be expected that if polymerizations could be run at significantly higher temperatures the apparent barrier to epoxide enchainment could be overcome. This is not practical experimentally due to competing factors: (1) ROCOP is an equilibrium processes, where in the case of CO₂/epoxide ROCOP the polymer is the kinetic product, and thus elevated temperatures lead to back-biting and formation of the cyclic carbonate. (2) ROP is also an equilibrium process, and elevated temperatures lead to the back-reaction and increase monomer concentration/polymer degradation. Thus, the epoxide enchainment reaction does not occur using the dizinc catalysts under any of the experimentally studied conditions. This may relate to relatively higher barriers, particularly during polymerization, including Figures S1–S33 and Tables S1–S8 (PDF).

**Web-Enhanced Features**
Interactive versions of Figures 10 and 11 are accessible in the HTML version of the article.

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**Notes**

The authors declare the following competing financial interest(s): C.K.W. is a director at Econic Technologies.

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