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Exploiting controlled transesterification as a "top down" approach to tailor poly(ε-caprolactone)-poly(lactic acid) copolymer structures with bis-Zn catalysts†

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Poly(ε-caprolactone)-poly(lactic acid) (PCL-PLA) copolymers have wide-ranging applications, where the polymer properties are controlled by the chain structure (*i.e.* block or random). Yet the synthesis of well-defined higher order multiblock PCL-PLA copolymers remains challenging, as competitive transesterification processes can occur that disrupt the polymer structure. Herein, we demonstrate that controlled transesterification can be harnessed as a "top down" method of tailoring PCL-PLA copolymer structures, instigated by the addition of ε-caprolactone to a living PCL-PLA-Zn copolymer chain. The extent of transesterification can be enhanced by increasing the ε-CL stoichiometry and decreasing the chain length of the diblock PCL-PLA precursors. While transesterification decreases the average length of the PCL and PLA blocks, the polymers retained their "blocky" nature as evidenced by DSC analysis. Novel computer simulations on simplified oligomeric systems show that transesterification occurs in both the PCL and PLA blocks of the original copolymer. This methodology also successfully transesterified an isolated PCL-*block*-PLA copolymer, suggesting that this zinc-catalysed approach may be a versatile post-polymerisation method for diversifying copolymer structures.

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Introduction

Plastics are essential to everyday life and are used in a number of beneficial applications including packaging to reduce food waste,[1] insulation to reduce energy consumption,[2] and medical devices to improve quality of life.[3] Yet despite these benefits, plastic pollution has caused significant environmental damage. Chemically recyclable and biodegradable polymers, such as poly(lactic acid) (PLA) and poly(ε-caprolactone) (PCL), are attractive alternatives to conventional commodity plastics.[4–10] However, their applications are currently limited by their material properties.[11] The synthesis of copolymers is a useful method of expanding and enhancing the range of properties available, by harnessing the beneficial properties of two (or more) different monomers. For example, combining lypophilic and hydrophilic monomers generates amphiphilic copolymers with applications spanning drug delivery, polymer coatings, and the compatibilisation of polymer blends,[12–16] whilst copolymers combining biodegradable and non-degradable polymers offer a potential method of mitigating the release of micro-plastics into the environment.[17–20] PCL/PLA copolymers are of particular interest as their complementary properties enable the formation of biodegradable thermoplastic elastomers that can be used in applications such as tissue engineering.[21–23]

In addition to the choice of monomers, the copolymer properties are dictated by the composition and structure. The monomer distribution can vary from completely random to fully segmented block copolymers;[24–31] the latter can give nanoscale phase-separation between the individual blocks, which can lead to favourable thermal and mechanical properties.[32,33] Yet while the synthesis of PCL and PLA homopolymers *via* the ring opening polymerisation (ROP) of ε-caprolactone (ε-CL) or lactide (LA) is straightforward to achieve, the synthesis of PCL-*block*-PLA multiblock copolymers is challenging because transesterification can disrupt the block copolymer structure.[34–36] Transesterification is particularly prevalent when extending a PLA* chain (* denotes a living polymer chain) with ε-CL, and very few catalysts have been successful in generating well-controlled di- or tri-block copolymers from PLA*.[37,38] We previously reported that catalyst **LZn$_2$Et**/BnOH (Fig. 1) delivered excellent activity and control in the synthesis

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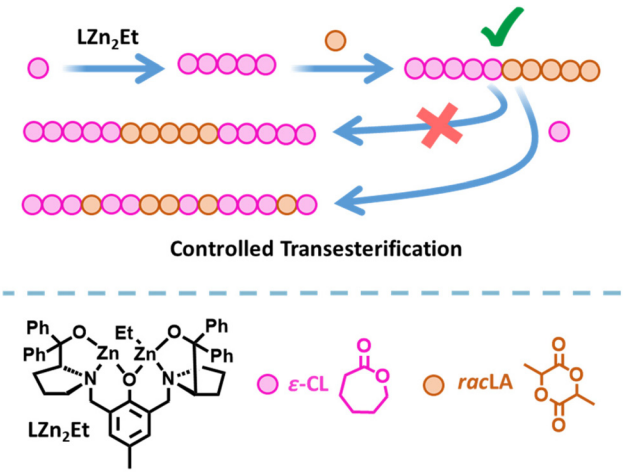


Fig. 1 Synthesis of PCL-PLA diblock copolymers *via* ROP using **LZn$_2$Et**/BnOH,[39] and the strategy investigated herein to modify the copolymer structure using controlled transesterification.

of PCL-*block*-PLA copolymers (*i.e.* when ε-CL was polymerised first and LA second), yet gave random copolymer structures when ε-CL was added to a living PLA* chain.[39]

Other methods to prepare multiblock copolymers have included the use of diethylene glycol as a bifunctional alcohol initiator to prepare PLA-PCL-PLA triblock copolymers *via* formation of a PCL homopolymer with two active chain ends; this approach was limited to the formation of triblock copolymers.[40] To achieve higher-order PCL-PLA multiblocks, relatively short hydroxy-end capped block copolymers have been reacted with a diisocyanate, to form urethane linkages between the copolymer chains.[41] However, this method is often poorly controlled and leads to broad dispersities.

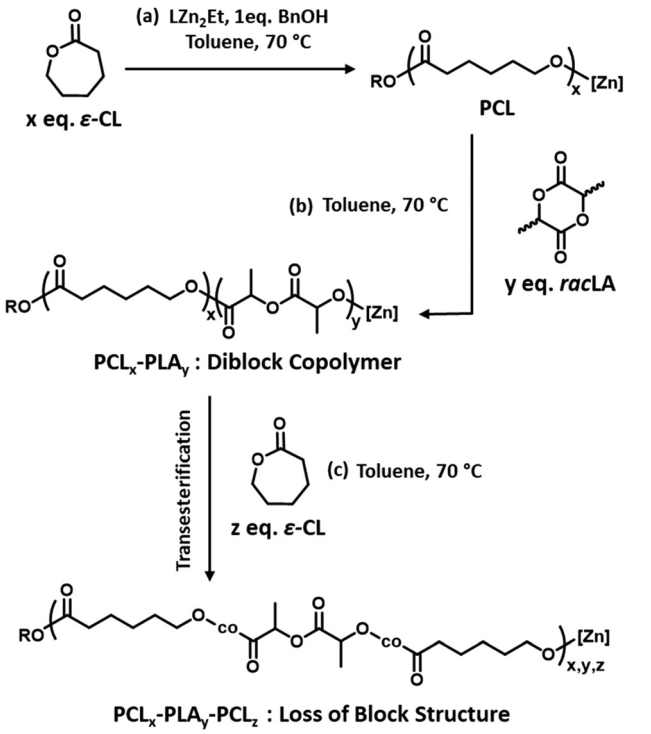
Could transesterification be a friend instead of a foe? The Platel group recently showed that transesterification can deliver tuneable copolymer structures from mixed LA/CL monomer feeds *i.e. via* a "bottom up" approach.[42] Herein, we report an alternative "top down" method that uses a controlled degree of transesterification to tailor the structure of PCL-*block*-PLA copolymers to generate higher-order multi-block structures. Transesterification is instigated and controlled by the addition of ε-CL to a PCL-*block*-PLA* chain in the presence of a bis-zinc catalyst. Through novel modelling simulations underpinned by ^{13}C NMR studies, we investigate the microstructures of the resultant PCL-PLA copolymers and show how this methodology can be utilised to modify isolated copolymers.

Results and discussion

Synthesis of PCL-PLA copolymers

In the presence of BnOH, **LZn$_2$Et** was previously established as a highly active catalyst for the preparation of well-controlled PCL$_{50}$-*block*-PLA$_{50}$ copolymers through the sequential addition of ε-CL then LA (where 50 represents the targeted degree of polymerisation, DP, of each block).[39] Here, the reaction conditions were optimised to prepare extended diblock structures (PCL$_n$-*block*-PLA$_n$, n = 100, 200 or 400), by increasing the monomer concentration and temperature (ε-CL loading of 22% w/w in toluene, 70 °C). The polymerisation of ε-CL was rapid and well-controlled (≥95% in <5 min, $Đ$ = 1.14, Fig. S2a†), and LA was subsequently added to extend PCL into a diblock copolymer (Scheme 1b). ^{1}H NMR analysis showed high conversion of *rac*-LA to PLA in under 1 h (≥80%), and SEC analysis confirmed extension of the PCL block (refer to Fig. S2† for details). Notably, this also showcases the tolerance of the **LZn$_2$Et**/BnOH catalyst system towards higher monomer loadings of n = 400.

The resultant copolymer composition, structure, and the extent of transesterification within the targeted PCL$_{100}$-*block*-PLA$_{100}$, PCL$_{200}$-*block*-PLA$_{200}$ and PCL$_{400}$-*block*-PLA$_{400}$ copolymers was investigated using ^{1}H NMR spectroscopy. For PCL$_{100}$-*block*-PLA$_{100}$, integration of the PCL and PLA resonances determined the PCL : PLA composition to be 116 : 84 (Fig. S2b†), which was comparable to the targeted value. The ^{1}H NMR spectrum also shows distinct resonances for the PCL units that are directly adjacent to PLA units compared to the other PCL units (Fig. S2b†). The relative integrations of these signals can be used to approximate the number average sequence length of each block (l_{CL} and l_{LA}) and the randomness character of the copolymer (R) (see ESI† for details).[43] An R value close to 0 suggests a well-defined block copolymer structure



Scheme 1 The one-pot synthesis of PCL-PLA copolymers *via* ROP using **LZn$_2$Et**/BnOH where step (a) forms the PCL homopolymer, step (b) forms the PCL-PLA diblock copolymer, and step (c) uses transesterification to tailor the PCL-PLA copolymer structures.

whereas an R value close to 1 suggests a random distribution of monomer units. For PCL_{100}-*block*-PLA_{100}, l_{CL} and l_{LA} were calculated to be 37 and 50, respectively, with an R value of 0.05. These values are close to the theoretical values for PCL_{100}-*block*-PLA_{100} (where R, l_{CL} and l_{LA} are calculated to be 0.02, 100 and 100, respectively) suggesting that minimal structure-disrupting transesterification occurs. Intriguingly, the relative integrations remain constant after 24 h at 70 °C (Fig. S3†), suggesting that no additional transesterification occurs without an external source, and that the structure of the living PCL_{100}-*block*-PLA_{100}* copolymer is stable under these conditions.

Factors influencing the extent of transesterification

As previous studies from our group showed that the addition of 50 eq. of ε-CL to a PLA_{50}* homopolymer gave a random copolymer structure,[39] we decided to investigate the influence of adding a lower quantity of ε-CL to a PCL_{200}-*block*-PLA_{200}* diblock copolymer, to investigate whether a lower degree of transesterification could give a copolymer with a more "blocky" structure. Therefore, 10, 20, 40, and 80 equivalents of ε-CL were added to a living PCL_{200}-*block*-PLA_{200}* diblock copolymer (prepared *in situ* using the bis-zinc catalyst) as a neat liquid, and the resultant transesterification was assessed by ^{1}H NMR spectroscopy. The high concentration of ε-CL drives the ring-opening of the third monomer, a feature that has been previously reported for other systems.[44,45] The l and R values showed a clear increase in transesterification upon increasing the ε-CL stoichiometry (Fig. 2 and Table 1). Upon addition of 10 equivalents of ε-CL to the PCL_{200}-*block*-PLA_{200}* chain, the R value remained close to 0 (0.08), indicating a relatively blocky structure. However, it is worth noting that the R value has increased compared to the diblock copolymer precursor (R = 0.02), indicating that some transesterification has occurred. Upon increasing the ε-CL equivalents to 20, 40 and 80 eq., the R value further increased to 0.18, 0.26, and 0.30, respectively (Fig. 2b), showing that the degree of transesterification and thus the blocky/random nature of the copolymer is dictated by the quantity of ε-CL added. For example, the average sequence length for each copolymer unit was relatively high when 10 eq. of ε-CL was added (l_{LA} = 33; l_{CL} = 21), but this was significantly reduced when 80 eq. of ε-CL was added (l_{LA} = 7; l_{CL} = 6). Notably, the addition of 20 eq. of ε-CL to PCL_{200}-*block*-PLA_{200} gave very similar R and l values independent of whether all 20 eq. were added at the same time (sample **2**, Fig. S5†), or as two portions of 10 eq. (sample **5**, refer to ESI† for details). In all cases, SEC analysis shows that addition of ε-CL increases the dispersity, providing additional evidence for transesterification (Table S1†).[46] In some instances, the molar mass decreased after ε-CL was added, suggesting that some intramolecular transesterification/degradation has occurred in these samples.[46] Moreover, the DOSY NMR spectra of sample **4**, where the highest reduction of molar mass is observed, shows two observable diffusion coefficients that each contain both PCL and PLA units (Fig. S6†), which may be due to intramolecular transesterification resulting in the formation of lower molar mass cyclic species (refer to ESI† for details).

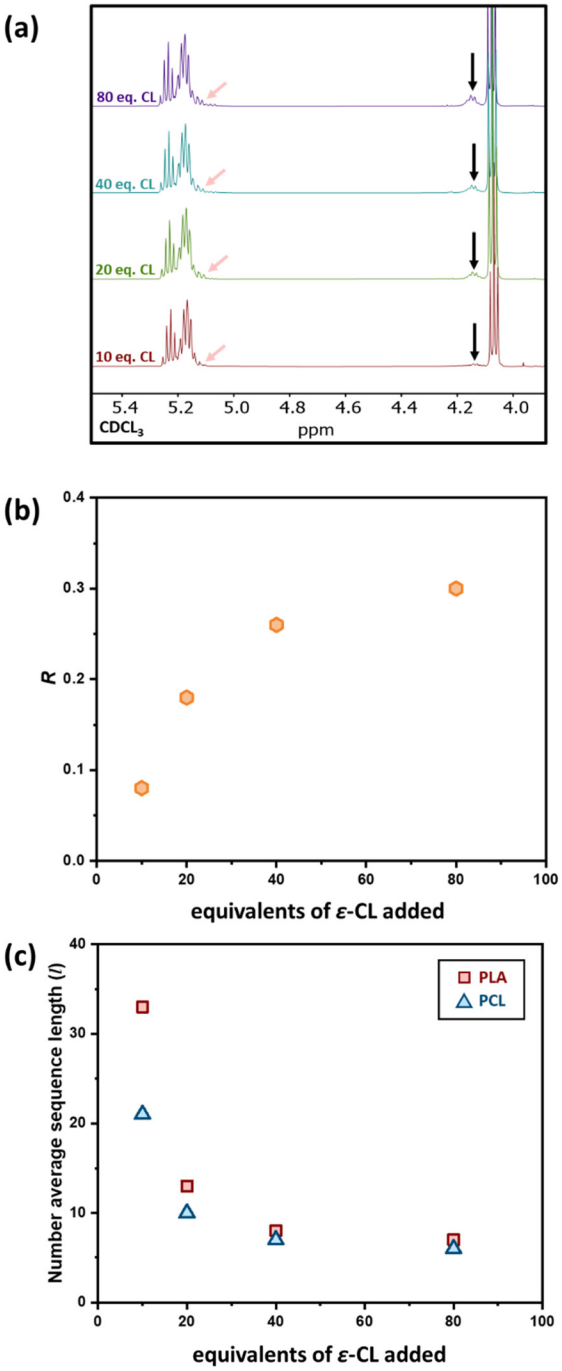


Fig. 2 (a) ^{1}H NMR spectra of PCL_{200}-*block*-PLA_{200} with various eq. of ε-CL added (indicated on the spectra), where the black arrow indicates PCL protons adjacent to a PLA unit and the pink arrow indicates PLA protons adjacent to a PCL unit. Plots of (b) the randomness value R and (c) the number average sequence length (l) calculated using ^{1}H NMR spectroscopy against the equivalents of ε-CL added.

The effect of the initial block length also influences the blockiness of the copolymer structure upon transesterification. This was investigated by adding 20 eq. of ε-CL to PCL_{100}-*block*-

Table 1 Targeted copolymer composition, and copolymer structure determined by ^{1}H NMR spectroscopy

Sample	Diblock copolymer		Transesterification Eq. of ε-CL added	Post-transesterification copolymer structure		
	Targeted PCL DP[a]	Targeted PLA DP[b]		l_{LA}[c]	l_{CL}[c]	R[c]
Control	200	200	0	100	101	0.02
1	200	200	10	33	21	0.08
2	200	200	20	13	10	0.18
3	200	200	40	8	7	0.26
4	200	200	80	7	6	0.30
5[d]	200	200	20	11	9	0.20
6	100	100	20	5	5	0.42
7	400	400	20	33	27	0.07

[a] Conversion of ε-CL was ≥93% in all cases (see Table S1† for additional details). [b] Conversion of *rac*-LA was ≥80% in all cases (see Table S1† for additional details). [c] Calculated using ^{1}H NMR spectroscopy. [d] 10 equivalents of ε-CL added initially and then another 10 equivalents were added (refer to Fig. S5†).

PLA_{100}* (sample **6**) and PCL_{400}-*block*-PLA_{400}* (sample **7**). Specifically, higher number-average sequence lengths were achieved when a longer diblock copolymer was used (Table 1 and Fig. 3a). Overall, these results show that the R and l values, *i.e.* the level of "blockiness" of the resulting copolymer, can be fine-tuned by varying the number of equivalents of ε-CL added to a living PCL-*block*-PLA-Zn chain as well as the block length of the diblock copolymer precursor. This raises the question: could Zn-mediated transesterification provide a simple method of modifying the copolymer structure from blocky to tailored random copolymers? To answer this, it is important to understand the discrepancy between the number-average sequence length and the true sequence lengths along a polymer backbone.

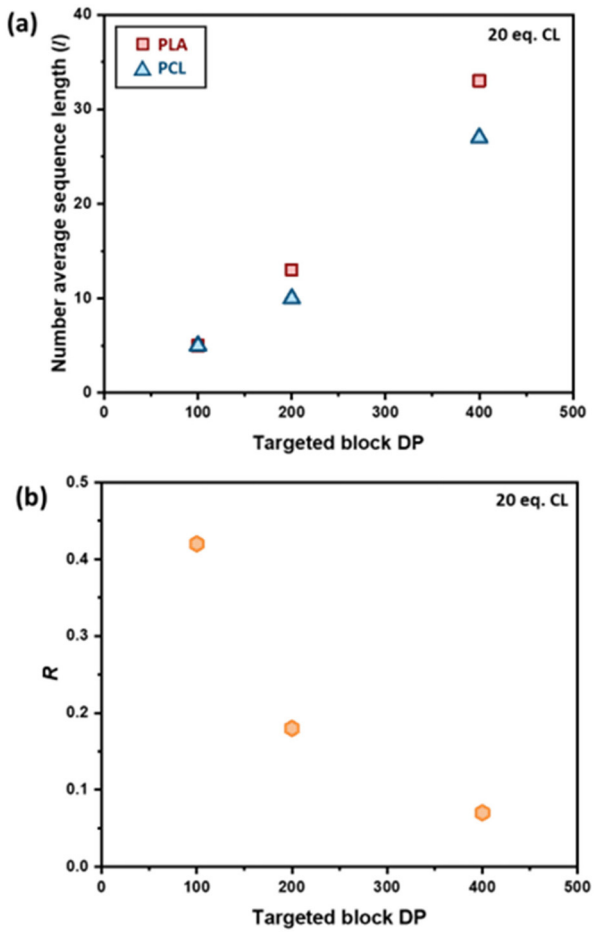


Fig. 3 Plots of (a) the number average sequence length (l) and (b) the randomness value R calculated using ^{1}H NMR spectroscopy against the targeted block DP for adding 20 equivalents of ε-CL to PCL_{100}-*block*-PLA_{100}*, PCL_{200}-*block*-PLA_{200}* and PCL_{400}-*block*-PLA_{400}*.

Further understanding the influence of transesterification on the copolymer structure

Differential scanning calorimetry (DSC) analysis indicated that copolymer samples **1–4** (Table 1) have a largely segmented structure post-transesterification, as all four polymers displayed thermal behaviours that are associated with block copolymers. Each thermogram showed two distinct glass transition temperatures (T_g) for each component of the copolymer, with no significant reduction in the crystallinity (Fig. S7a†). In contrast, DSC analysis of a fully statistical PCL_{200}-PLA_{200} copolymer showed a single broad T_g and only a small melting peak (T_m), respectively indicating a lack of block structure and crystallinity (Fig. S8† and Table S2†). These results suggest that transesterified copolymers **1–4** have a somewhat "blocky" structure despite the relatively short average sequence lengths (Table 1). No significant trend was observed between the PCL T_g or T_m and the extent of transesterification (Table S2†). This was largely expected as the thermal transitions of PCL have been reported to remain fairly constant to lower molar masses in block copolymers.[47] However, the PLA T_g decreased upon reduction of the number average sequence length (Fig. S7b†). Furthermore, the observed PLA T_g (33–45 °C) is significantly lower than the literature value reported for PLA homopolymers (*ca.* 60 °C),[48] indicating that the presence of PCL/short nature of the PLA blocks has a significant effect on the thermal transitions of the PLA blocks. These results indicate that there is enough 'blocky' structure for the individual copolymer components to phase separate and provide two distinct T_g values.

We therefore probed the polymer structures by quantitative ^{13}C NMR analysis, as the ^{13}C carbonyl resonances are very sensitive to the sequence of monomer units along the PCL-PLA chain (Fig. 4).[49,50] With copolymers **1–4**, the most intense signals observed were the CCC and LLL triads, where C and L indicate ring-opened caprolactone and lactic acid units (*i.e.* half a lactide monomer), respectively. The intensity of these resonances suggest that there are some large blocks of PCL and PLA present even after transesterification, which agrees with the observation of two distinct T_g values in the DSC thermograms. However, transesterification is evident, as baseline resonances due to the LCC, CCL, LCL, CLC, LLC and CLL triads were observed with greater intensities than expected for the triblock copolymer. Importantly, the presence of the CLC signal at 170.8 ppm confirms that transesterification has occurred, as this triad requires the disruption of LL units formed through the ring opening polymerisation of a lactide monomer. The l_{LA} and l_{CL} values were also calculated using the triad intensities from the quantitative ^{13}C NMR spectra.[35] For example, sample **3** (Table 1) was calculated to have l_{LA} and l_{CL} values of 12 and 10, respectively, which gave relatively good agreement with the values calculated from the ^{1}H NMR spectra (*vide supra*). The ^{13}C NMR spectra provided further support for increased transesterification upon increasing the quantity of ε-CL added to PCL$_{200}$-*block*-PLA$_{200}$ (Table 1 and Fig. 4). For sample **1** (10 eq. ε-CL), no signals for the CLC or LCL triads were observed, although small baseline signals for the LCC, CCL, LLC and CLL triads were present. Conversely, all the triad signals are observed for sample **4** (80 eq. ε-CL), with an increase in the CLC signal emphasizing a greater degree of transesterification.

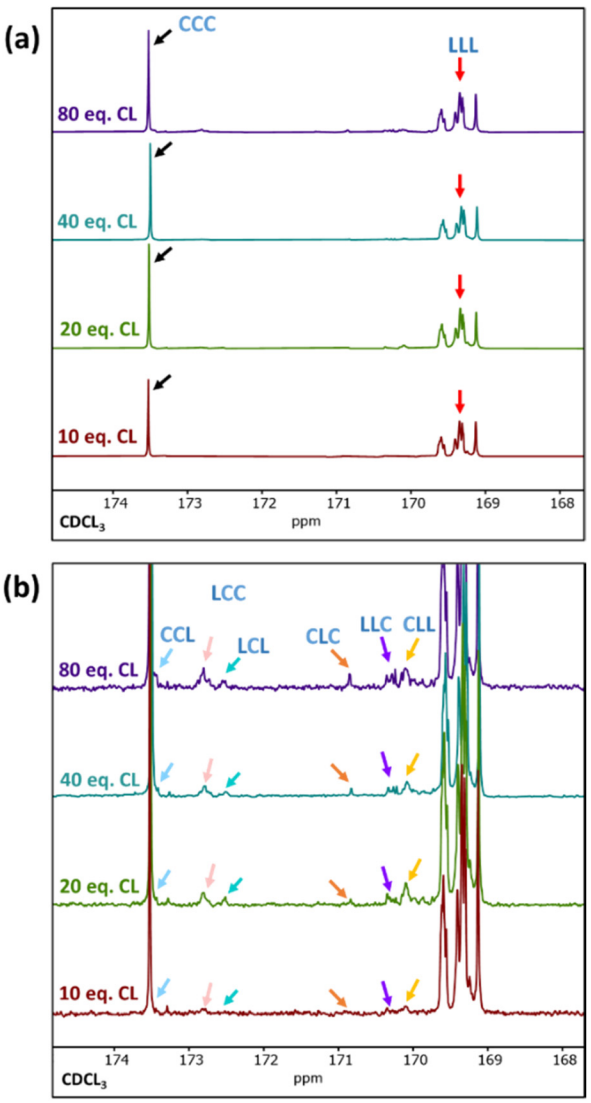


Fig. 4 (a) Expanded ^{13}C NMR spectra of PCL$_{200}$-*block*-PLA$_{200}$ with 10–80 eq. of ε-CL added and the respective peak assignments indicated on the spectra. (b) Shows the same ^{13}C NMR spectra with a magnified baseline.

Overall, the observation of the CLC and LCL resonances shows that the structure is not completely "blocky", and there are some individual caprolactone and lactic acid units along the polymer chain. It is important to note that, while useful, the ^{1}H and ^{13}C NMR spectra give information that is an average of the entire system. This means that transesterification may only occur in a fraction of the copolymers with others remaining unaffected. Therefore, polymer sample **3** was separated into different molar mass fractions using SEC, and the *R* value of each fraction was subsequently examined by ^{1}H NMR spectroscopy (Fig. S9†). To confirm that the copolymer sample had been successfully fractionated, SEC analysis was performed and showed that each fraction had a different peak molar mass (M_p, Fig. S9†). Importantly, the ^{1}H NMR spectra showed the *R* values to be relatively constant across the molar mass fractions, suggesting that the transesterified copolymer structure is fairly consistent across the copolymer sample.

In order to probe the trade-off between transesterification and ε-CL propagation, we investigated the impact of adding 20 eq. of ε-CL to PLA* homopolymer with a DP of 200 (Fig. S10†). ^{13}C NMR signals for the CCL, LCL, CLC, LLC, and CLL triads confirmed that the ε-CL units have been inserted into the copolymer chain. However, the CCC triad was absent. This suggests that no significant propagation of ε-CL occurs, although the observation of the CCL signal indicates the potential for sequential insertion of two ε-CL monomers. This indicates that transesterification occurs more rapidly than ε-CL propagation, which is further supported by the observation of the LCL triad. On the basis of these results, we tentatively propose that monomer insertion is likely to proceed *via* insertion of a single ring-opened ε-CL monomer to the PLA* chain (*i.e.* PLA-CL*), which subsequently initiates transesterification of an exogenous PLA* chain resulting in a shorter PLA* homopolymer and a longer PLA* copolymer with a single ring-opened ε-CL unit inserted into the chain (Fig. S11†). Due to the living nature of these chains, which are capped by Zn, this procedure is repeated until maximum conversion of monomeric ε-CL is reached. If the point along the polymer chain at which transesterification occurs is randomly selected, then the distribution of ε-CL units along the chain will also be random.

We were curious to understand whether transesterification of PCL-*block*-PLA* disrupted solely the PLA* block, or also the initial PCL block. Therefore, we compared the ^{1}H and ^{13}C NMR spectra produced from the reaction of PLA_{20}* oligomers with 20 eq. of ε-CL, to that of PCL_{10}-PLA_{20}* oligomers with 10 eq. of ε-CL (Fig. 5 and S12†). Oligomers were used as simpler model systems to facilitate analysis of the polymer structure, with a relatively large ε-CL : polymer ratio used to increase the extent of transesterification.

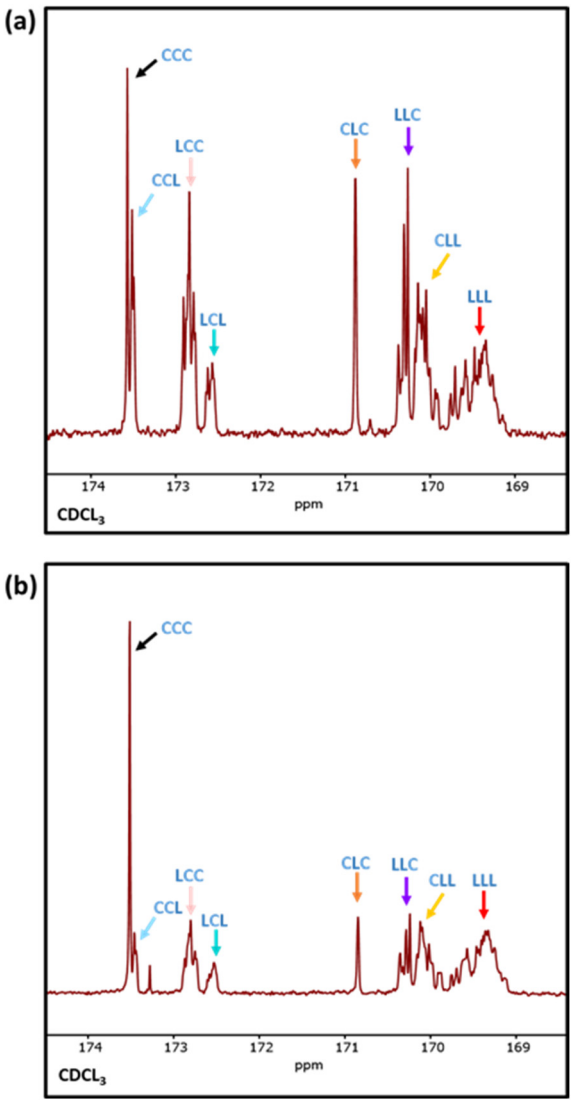


Fig. 5 Expanded ^{13}C NMR spectra of (a) PLA_{20}* with 20 eq. of ε-CL (sample **8**) and (b) PCL_{10}-*block*-PLA_{20} with 10 eq. of ε-CL (sample **9**), showing the respective peak assignments.

Firstly, 20 eq. of monomeric ε-CL was added to the PLA_{20}* homopolymer. This increased the M_n value from 6.2 kg mol^{-1} to 11.8 kg mol^{-1}, confirming incorporation of ring-opened ε-CL into the PLA_{20}* chains (sample **8**, Table 2 and Fig. S13a†). Significant transesterification occurred, as evidenced by a substantial signal at 4.13 ppm in the ^{1}H NMR spectrum (Fig. S12a†), and CLC triads in the ^{13}C NMR spectrum (Fig. 5a). The resulting copolymer was determined to have a random structure; both l_{LA} and l_{CL} were calculated to be 1 and 2, respectively (by ^{1}H NMR spectroscopy), and the R value was determined to be 1.33. Notably, this value is greater than 1, which indicates a high concentration of alternating sequences (*i.e.* CLC and LCL).[51] This value is also much greater than the R values of copolymers **1–7**, despite using a homopolymer precursor rather than a diblock copolymer, corroborating the influence of block length and ε-CL stoichiometry upon the extent of transesterification. As PLA_{20}* has a low chain length, and the stoichiometry of ε-CL : LA is 1 : 1, ring-opening and insertion of all ε-CL leads to a highly random copolymer structure. A notable difference between the addition of 20 eq. of ε-CL to PLA_{20}* or PLA_{200}* (*vide supra*) is that the CCC triad is observed in the former, but not the latter. This suggests that the ε-CL : PLA_n ratio influences the relative rates of ε-CL propagation *vs.* transesterification, with an increased quantity of ε-CL promoting propagation.

Secondly, 10 eq. of ε-CL was added to a PCL_{10}-*block*-PLA_{20} oligomer (sample **9**, Table 2) and SEC analysis confirmed uptake of ε-CL into the polymer structure (M_n increased from 6.6 kg mol^{-1} to 9.0 kg mol^{-1}, Fig. S13b†). ^{1}H and ^{13}C NMR analysis confirmed the formation of a random copolymer ($l_{LA} = l_{CL} = 2$ and $R = 1.05$, with observation of all eight triads, Fig. 5b and S12b†). Importantly, the relative intensity of both the CCC and LLL resonances was reduced after transesterification with ε-CL. The percentage of ring-opened ε-CL in CCC sequences reduced to 37% (see Fig. S14† for calculation) from 91% (theoretical value of 90%, *i.e.* 9 PCL units in CCC sequences and 1 in a CCL sequence) after transesterification, and the percentage of LA present in LLL sequences reduced to 52% (see Figure) from 96% (theoretical value of 95%, *i.e.* 19 PLA units in LLL sequences and 1 in a CLL sequence). If ε-CL was exclusively inserted into the PLA block of the PCL_{10}-PLA_{20}

Table 2 Targeted copolymer composition, and copolymer structure determined by ^{1}H NMR spectroscopy of the copolymer oligomers

	(Co)polymer			Post-transesterification copolymer structure			
Sample	Targeted PCL DP	Targeted PLA DP	Transesterification Eq. of ε-CL added	l_{LA}[a]	l_{L}[b]	l_{CL}[a]	R[c]
8	—	20	20	1	2	2	1.33
9	10	20	10	2	3	2	1.05

[a] Calculated using ^{1}H NMR spectroscopy and rounded to the nearest integer. [b] Average sequence length of lactic acid unit, L, which is half an LA unit, rounded to the nearest integer. [c] Calculated using ^{1}H NMR spectroscopy.

precursor then the minimum percentage of ε-CL in CCC sequences would be 45% (refer to Fig. S13 in the ESI† for details). Therefore, a reduction to 37% suggests that the PCL block is also disrupted during the transesterification.

DSC analysis of samples **8** and **9** confirmed the highly random post-transesterification structure suggested by the ^{13}C NMR analysis, as only one T_g was observed at −22 °C and −25 °C respectively (Fig. S15†), with no evidence of PCL crystallinity. Additionally, a PCL_{20}-*block*-PLA_{20} diblock copolymer was synthesised and used as a reference, which displayed two distinct T_g values (−57 °C and 25 °C) and PCL crystallinity.

Simulation of copolymer structure

The ratio of triads present in the ^{13}C NMR spectra is a rich source of structural information, and computer simulations offer an opportunity to convert this into insight into the polymer structure. Therefore, we simulated potential structures of oligomeric copolymers **8** and **9** using a reverse Monte Carlo procedure (Fig. 6 and S16–S18, see ESI† for more details).[52] For 5×10^4 iterations, approximately 6500 sequences with a minimum score of 14 were found for sample **8** whereas approximately 1500 lowest scoring sequences (11) were found for sample **9** (Fig. S16†). For comparison, a random sequence gives a score of 28. For sample **8** the modal mean average sequence lengths for ε-CL and lactic acid (L, which is half an LA unit as LA contains two ester groups that can undergo transesterification, and is denoted as $l_L = 2l_{LA}$) were found to be 1.8 (52% of lowest score sequences) and 2.9 (57% of lowest score sequences), respectively. Furthermore, the standard deviation of the sequence length was 0.93 for ε-CL sequences and 1.79 for L. Sample **9** showed somewhat similar model mean average sequence lengths of 2.1 for ε-CL (53% of lowest score sequences) and 4.0 for L (69% of lowest score sequences), with standard deviations of 1.66 and 2.50, respectively. Examples of the structures simulated for samples **8** and **9** are shown in Fig. S17.† In all cases, largely random copolymer structures were generated, which is concordant with the conclusions manually drawn from the experimental data.

Individual sequence lengths for each monomer in the lowest scoring sequences were extracted for samples **8** and **9**. To show the frequency with which these sequence lengths occur in the lowest scoring sequences, 2D histograms of

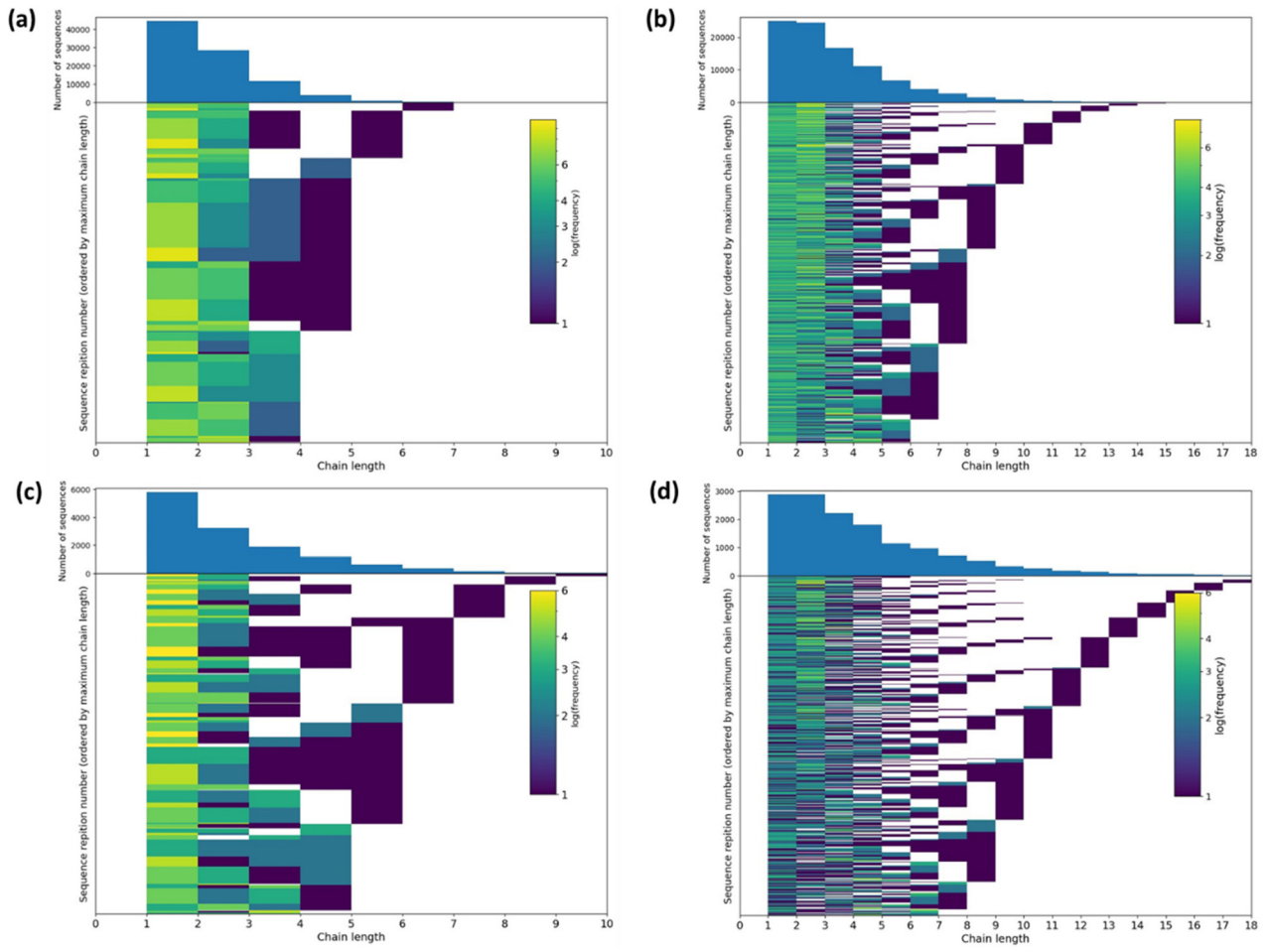


Fig. 6 2D histograms of sequence number against sequence length, with the 1D histogram above, for PLA_{20}-PCL_{20} (sample **8**), where (a) is ε-CL and (b) is L, and for PCL_{10}-PLA_{20}-PCL_{10} (sample **9**), where (c) is ε-CL and (d) is L.

sequence number against sequence length were prepared (Fig. 6). These histograms illustrate that there are a high number of low sequence lengths (1–4) present in the majority of the lowest scoring patterns, and that the frequency of sequence lengths present decreases rapidly for higher sequence lengths (>4). The histogram obtained from sample **9** shows a slightly longer tail, which may arise from the lower number of equivalents of ε-CL added compared to sample **8**, giving less transesterification. These histograms further demonstrate the randomness of the oligomeric structures produced *via* transesterification.

Examination of δ-valerolactone

In the trade-off between propagation and transesterification, the monomer propagation rate could play a key role in determining the copolymer structure. δ-Valerolactone (δ-VL) has a lower ring-strain than both *rac*-LA and ε-CL,[53] and so it was hypothesised that adding δ-VL as the third monomer would tip the balance towards transesterification instead of propagation. Therefore, 20 equivalents of δ-VL was added to PLA_{20}* and PCL_{20}* homopolymers (samples **10** and **11**, respectively, Table 3).

^{1}H NMR analysis of copolymer **10** showed a significant resonance at 4.14 ppm, indicative of δ-VL units adjacent to LA units and providing clear evidence for δ-VL initiating transesterification (Fig. 7a).[54] The ^{1}H NMR spectra of sample **11** does not provide useful information on transesterification due to overlapping resonances for PCL and PVL. However, the ^{13}C NMR spectrum clearly distinguishes between the different α-carbon environments (*i.e.* the carbon adjacent to the carbonyl), and four resonances are observed between 63.5–64.5 ppm relating to the VC, CC, VV, and CV diads (V and C represent ring-opened δ-VL and ε-CL units, respectively).[55] The presence of these diads confirms that δ-VL can be used to transesterify a PCL homopolymer. As the ring-strain of the cyclic esters decreases in the order LA > ε-CL > δ-VL,[53] this may explain why δ-VL can transesterify both PCL* and PLA* homopolymers, and why ε-CL transesterifies PLA* homopolymers, yet LA does not transesterify PCL* homopolymers.

Transesterification of an isolated diblock copolymer

Having demonstrated that transesterification can be used to modulate (co)polymer structures in the presence of a bis-Zn catalyst, we wondered whether this approach could be used as a post-polymerisation modification method for isolated PCL-*block*-PLA copolymers. Therefore, a PCL_{200}-*block*-PLA_{200} copolymer was prepared and isolated through precipitation from methanol. This α-benzoxy, ω-hydroxy-end capped copolymer was subsequently reacted with **LZn$_2$Et** to generate an active, PCL_{200}-*block*-PLA_{200}*-Zn copolymer. Subsequent addition of 40 eq. of ε-CL instigated transesterification, as confirmed by ^{1}H and ^{13}C NMR spectroscopy (Fig. S19†). Notably, the copolymer structure obtained through this post-polymerisation modification route deviated slightly from the comparable one-pot synthesis route (sample **3**, Table 1). Specifically, l_{LA}, l_{CL} and R were calculated to be 15, 13 and 0.15, respectively (*cf* 8, 7 and

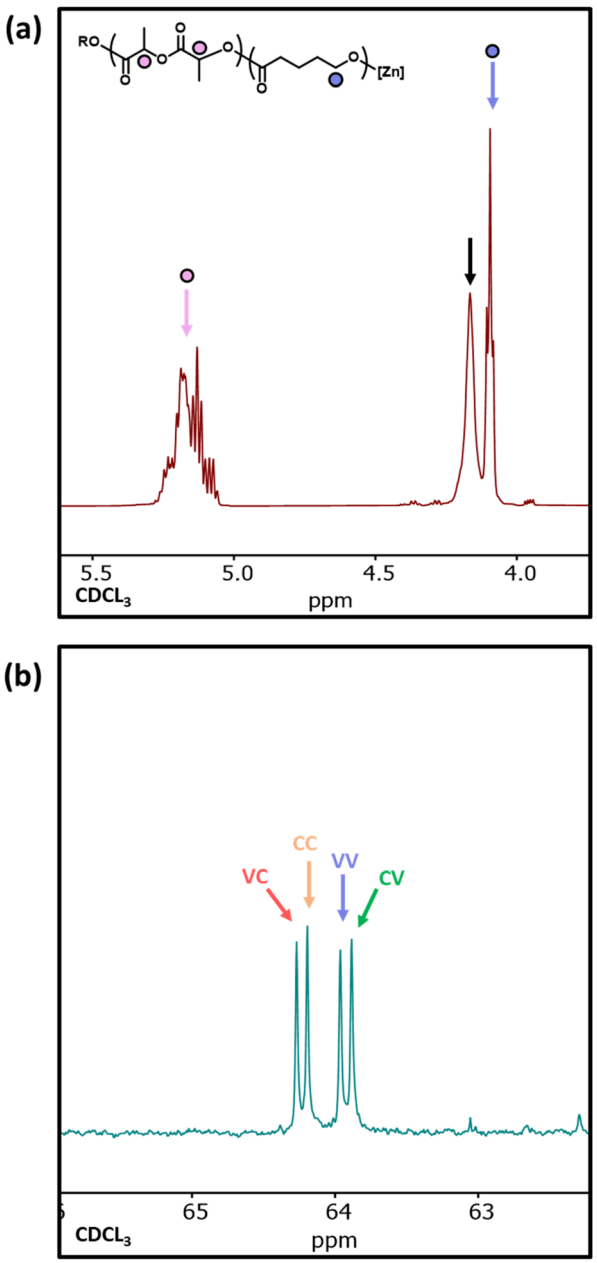


Fig. 7 (a) ^{1}H NMR spectra of PLA_{20}-PVL_{20} (sample **10**) where, the black arrow indicates PVL protons adjacent to a PLA unit. (b) Expanded ^{13}C NMR spectra of PCL_{20}-PVL_{20} (sample **11**) with the respective peak assignments indicated on the spectra where V and C represent ring-opened δ-VL and ε-CL units, respectively.

Table 3 Targeted copolymer composition of the copolymer oligomers using δ-VL as the transesterification agent

Sample	Initial polymer		Transesterification Eq. of δ-VL added
	Targeted PCL DP	Targeted PLA DP	
10	—	20	20
11	20	—	20

0.26 for sample **3**). This deviation may arise through inefficiencies in forming the activated copolymer, *i.e.*, not all copolymer chains are activated by **LZn$_2$Et**. Furthermore, no CLC or LCL triads were observed in the ^{13}C NMR spectra, which shows that the extent of transesterification is lower when using an isolated diblock copolymer precursor. Yet transesterification clearly occurs, as there is a marked decrease in the l_{LA}, l_{CL} and R values compared to the PCL$_{200}$-*block*-PLA$_{200}$ precursor. Therefore, this novel post-polymerisation modification *via* Zn-mediated transesterification has the potential to be a useful methodology to modify polymer structures.

Conclusions

Overall, these results show that transesterification can be used as a one-pot method of modulating PCL-*block*-PLA copolymer structures in the presence of a bis-zinc catalyst. Transesterification was instigated by the addition of ε-CL, and the randomness of the copolymer structure was increased by increasing the ε-CL : PCL-*block*-PLA* copolymer ratio and decreasing the PCL-*block*-PLA* block length. In contrast, using a low quantity of ε-CL and a high PCL-PLA block length delivers copolymers with a relatively "blocky" structure after transesterification, as confirmed by DSC and ^{13}C NMR analysis. The trade-off between transesterification and propagation is key, and low ε-CL concentration or the use of δ-VL as a monomer with low ring-strain both tipped the balance towards transesterification instead of propagation.

NMR studies combined with novel reverse Monte Carlo simulations of oligomeric copolymer structures showed that transesterification occurs in both the PCL and PLA blocks of the PCL-*block*-PLA* oligomer precursors to generate highly random structures with low average sequence lengths. The use of computer simulations is a potentially powerful yet currently underused tool for determining and predicting polymer structures, and provides an interesting avenue for future exploration.

The synthesis of targeted copolymer architectures often relies on an understanding of the monomer reactivity ratios and careful catalyst selection *i.e.* a "bottom up" approach.[41] Here, we show that the post-synthesis addition of ε-CL to a living PCL-*block*-PLA-Zn chain can disrupt block copolymer structures, providing a complementary "top down" route to generate a diverse range of tailored polymer structures. This approach was successfully used in the post-polymerisation modification of an isolated PCL-*block*-PLA copolymer. Overall, these results indicate that Zn-mediated transesterification can be used as a method of decreasing the average block length, while maintaining a significantly "blocky" structure.

Author contributions

T. J. N. and J. A. G. designed the project. T. J. N. performed the experiments. E. D. N. wrote the reverse Monte Carlo simulation with consultation from J. C. The manuscript was written by all authors. J. A. G. and J. C. edited the manuscript. J. A. G. acquired the funding and directed the research.

Conflicts of interest

There are no conflicts to declare.

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