**Polymers from Macrolactones: From Pheromones to Functional Materials**

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# Abstract

Recent advances in the ring-opening polymerisation (ROP) of macrolactones (MLs) have afforded access to novel, potentially degradable polymeric materials featuring long aliphatic chains. These developments extend the synthetic robustness and versatility of ROP to a greater range of interesting monomers, many of which can be derived from sustainable or renewable feedstocks, to access polymeric materials boasting a diversity of properties and potential applications. This review discusses current strategies to catalyse the ROP of MLs, comparing and contrasting them with those known for the ROP of small and medium sized lactones, and highlights recent developments in the preparation, functionalisation, and application of materials featuring poly(macrolactone)s (PMLs).

**Keywords**: ring opening polymerisation, polyesters, organo-catalysis, enzyme catalysis, biomaterials.

# Introduction

Aliphatic polyesters are widely utilised in biomedical and pharmaceutical applications since they maintain appropriate chemical, thermal and mechanical properties and are frequently both biodegradable and biocompatible (degradation products inclusive).[1-3] Furthermore, polyesters derived from sustainable resources are receiving increasing interest as environmentally-friendly materials. ROP performed on small (up to 6 atom) and medium (between 7 and 11 atom) lactones is well-understood and thermodynamically driven by a negative change in entropy during the release of angular or transannular strains, respectively. MLs (consisting of 12 or more atoms), however, possess little or no ring strain and consequently, early attempts to polymerise MLs using conventional ROP catalysts typically proceeded in the absence of control or yielded low molecular weight material.[4-7] Developments in the ROP of MLs since the 1990s have facilitated the preparation of a range of novel polymeric materials that are often challenging to access *via* other synthetic strategies.

For centuries, MLs have been applied in fragrances for their musky odour.[8, 9] Although originally obtained from animal sources, numerous MLs can be isolated or synthesised from plant oils.[10] The isolation of exaltolide (ω-pentadecalactone, PDL) by Kerschbaum in 1927[11] generated interest in MLs, which have since been developed into fragrances, pheromones, insecticides, pharmaceuticals, and phytotoxic agents, amongst other applications.[12] Today PDL is FDA-approved for use as an indirect food additive and is widely used as a fragrance in consumer products.[13] Although it is commercially sourced from fossil fuels, PDL can also be extracted from natural sources including the angelica plant root (*Angelica archangelica*) and musk deer (genus *Moschus*).[8, 9] Interestingly, PDL is a mammalian pheromone secreted by apocrine glands in the human male armpit.[14, 15] As the most commercially available ML, PDL is routinely investigated as a key macrolactone in ROP studies, and the discovery that poly(ω-pentadecalactone) (PPDL) maintains similar properties to low-density polyethylene (LDPE)[16-18] or high-density polyethylene (HDPE),[19] depending on its molecular weight, has attracted considerable interest in PMLs.

Developments in the ROP of MLs have expanded the diversity of properties and potential applications of polyester materials. Furthermore, these developments have led to exciting new processes in polymer science. Herein, recent advances in the ROP of MLs are discussed and developments in the preparation, functionalisation, and application of materials featuring PMLs are highlighted.

# Ring-opening polymerisation of MLs

Aliphatic polyesters were originally prepared *via* condensation polymerisation of hydroxyl acids or diacids and diols (Scheme 1).[20] Disadvantages of condensation polymerisation, however, include the requirement for stringent monomer purification, precise stoichiometry, and high reaction temperatures that promote undesirable side reactions. Since condensation polymerisation proceeds *via* step-growth polymerisation kinetics, the ability to both control the reaction and obtain high molecular weight material is challenging to achieve. Nonetheless, condensation polymerisation has been reported as a successful strategy to prepare PMLs that are equivalent to those prepared *via* ROP.[21-24] Additional strategies to prepare PMLs include transesterification of diesters and diols,[25] acyclic diene metathesis (ADMET) polymerisation,[26-31] acyclic triene metathesis polymerisation,[32] ring-opening metathesis polymerisation (ROMP)[33], and thiol-ene addition.[29, 31, 34]



**Scheme 1** Preparation of polyesters *via* condensation polymerisation of a) hydroxyl acids, and b) diacids and diols.

The modern preparation of aliphatic polyesters *via* the ROP of lactones (*i.e.* cyclic esters) affords excellent control over the polymerisation to produce high molecular weight material under relatively mild reaction conditions. ROP techniques are regarded as controlled/living polymerisation systems since 1) they proceed *via* chain-growth kinetics, resulting in a linear increase in the molecular weight of the polymer with increasing monomer conversion, 2) the molecular weight of the polymer can be directly controlled by the ratio of monomer to initiator in the initial reaction mixture, 3) the resulting polymer maintains a narrow, monomodal dispersity (*Ð*M), and 4) high end-group fidelity is preserved throughout the polymerisation. The ability to perform a polymerisation with living characteristics ultimately enables control over the bulk properties of a material, which is crucial for a number of applications.

Since both nucleophiles and electrophiles can initiate the ionic polymerisation of polarised monomers, the range of catalysts appropriate for ROP is vast and includes metal complexes, organic compounds, and enzymes.[35] Initiation in ROP ultimately proceeds *via* either an anionic, cationic, coordination-insertion, or activated monomer mechanism. Alkali and earth-alkaline alkoxides were amongst the first classes of catalysts demonstrated to initiate the anionic polymerisation of lactones. Specifically, the alkoxide anion undergoes nucleophilic addition to the carbonyl carbon of the cyclic ester, releasing an alkoxide end-group that propagates in the same manner (Scheme 2).



**Scheme 2** Mechanism for the anionic ring-opening polymerisation of lactones using metal-based catalysts.

A significant disadvantage of this strategy, however, is that the propagation step is typically accompanied by numerous side reactions, in particular backbiting to regenerate the monomer or yield macrocyclic oligomers. Backbiting results from the reversible nature of the polymerisation, and backbiting to form macrocycles is an example of a transesterification side reaction whereby the catalyst coordinates an alkoxide chain-end and an ester linkage within the polymer backbone, the alkoxide attacks the activated carbonyl to form a new ester linkage, and another alkoxide is eliminated in the process. Transesterification can occur intramolecularly, shortening the linear chain and generating a cyclic species, or intermolecularly, generating two linear polymers of different chain lengths. Consequences of either transesterification reaction, however, include an increase in *Ð*M and a loss of control over the system.

The ROP of small and medium sized lactones is driven by a positive release of enthalpy and a negative change in entropy during the release of angular and transannular strains, resulting in rapid rates of polymerisation at low reaction temperatures.[35] MLs exhibit minimal ring strain and therefore, since the enthalpic gain during ROP is negligible, the main driving force in the ROP of MLs is the entropic gain achieved through ring-opening to attain less hindered chain rotation.[35] Additionally, since the entropic term in the Gibbs free energy equation can be increased with temperature, the polymerisation of MLs requires higher reaction temperatures than small and medium sized lactones.

Interestingly, the Jacobsen-Stockmeyer model for reversible ring-formation[37] indicates that, in the ROP of strainless MLs, 1) cyclic polymers always form *in situ* within linear polymerisation systems as a consequence of concurrent transesterification side reactions, and 2) as a consequence of thermodynamics, a small concentration of cyclic oligomers (~2-5 repeat units) must be generated in advance of linear polymerisation.[37] Ultimately, the absence of ring strain in MLs results in similar rates of polymerisation and transesterification, and consequently, a lack of control over the ROP process such that cyclic species are formed, and lower number average molecular masses (*M*n) and higher dispersitiesare obtained relative to theoretical chain-growth polymerisation values.[37] Despite these challenges, numerous catalysts including enzymes, organometallic complexes, and organic compounds have been established in the ROP of MLs.

## Enzymatic ROP (eROP)

There is a tremendous amount of interest in utilising enzymes for chemical transformations since they perform biochemical transformations with remarkable precision and efficiency, specifically with a high degree of chemo-, regio-, and enantio-selectivity, all under mild conditions. Furthermore, enzymes are non-toxic, recyclable, and easily removed *via* gravity filtration when immobilised on a solid support.[38] Consequently, enzymes are receiving increasing interest as ‘green’ alternatives to conventional polymerisation catalysts. Beginning in the 1990s, enzymes were explored as catalysts for the ROP of MLs and the success of enzymatic ring-opening polymerisation (eROP) has resulted in the preparation of novel polymeric materials and the development of new processes in polymer synthesis.[39]

Initial eROP reactions were attempted on conventional ROP monomers including ε-caprolactone (CL),[40-42] and an initial bulk copolymerisation of CL and PDL using the lipase *Pseudomonas fluorescens* reported only trace incorporation of PDL after 10 days.[43] Thereafter, the eROP of ω-undecalactone (UDL), ω-dodecalactone (DDL), and PDL was investigated using various lipases, notably lipases derived from *Pseudomonas fluorescens* (lipase P) and *Candida cylindracea* (Lipase B) in bulk conditions and at various reaction temperatures (Figure 1). Uyama and co-workers[44-46] discovered that the rate of eROP varies depending on the origin of the lipase, increases with temperature and immobilisation on Celite®, and proceeds more rapidly for MLs than for smaller lactones. Subsequently, it was discovered that the rate of the eROP of PDL could be increased 100-fold, further increasing monomer conversion and *M*n, and improving the *Ð*M of the polymer product, by utilising immobilised, surfactant-coated lipases in organic solvents, notably toluene.[35, 46-48]



**Figure 1** Structures of commercially available macrolactones.

Bisht *et al.*[49] further investigated lipase choice in the eROP of PDL in bulk conditions at 80 °C by screening commercially available lipases over 24 hour polymerisation times. Novozyme-435, *i.e.* *Candida antartica* lipase B (CALB)[50] immobilised on an acrylic resin, notably yielded the highest conversion and has since become the enzyme of choice for the eROP of MLs.[51] Although an extensive range of enzymes have been studied for the eROP of MLs, they have all been lipases with the exception of a cutinase from *Humicola insolens*,[52] which exhibits similar kinetics to Novozyme-435.[53] Temperature was determined to be an important factor in eROP such that increasing the reaction temperature from 60 °C to 80 °C increases both the rate of polymerisation and the *M*n of the polymer product, however further increasing the reaction temperature to 110 °C decreases both the rate of polymerisation and the *M*n of the polymer product.[49] Similarly, analysis of PPDL synthesised at 70 °C and 90 °C revealed a significant reduction in the molecular weight and crystallinity of material prepared at 90 °C relative to 70 °C .[54] Therefore, it can be concluded that elevated reaction temperatures denature the native structure of the enzyme, impairing its ability to perform transesterification reactions.

Bisht *et al.*[49]additionallyinvestigated water content, which was found to affect both the rate and *M*n such that increasing the water content increases the rate of polymerisation, however decreases the *M*n of the polymer product. This result is consistent with the conclusion of Matsumoto *et al.*[55]that water is the initiating species. The rate of eROP reactions can be increased by using nucleophilic initiating species such as an alcohol, an amine, or a thiol and it has been demonstrated that alcohols are more efficient initiators in eROP reactions than thiols since thiols exhibit higher binding affinities to lipases.[56] However, the presence of some water is critical for the enzyme to adopt the correct structure *via* non-covalent bonding, and consequently too little water greatly reduces enzymatic activity.[35] Interestingly, the eROP of PDL affords relatively high weight average molecular weight (*M*w) polyesters (*M*w = 36,300 g mol-1; *Ð*M = 1.44) even where the polymerisation is carried out in the presence of water and in the absence of inert conditions.[57] Performing eROP under inert conditions, however, is desirable to attain precise *M*n and end-group control.

Lipases hydrolyse fatty acid esters *in vivo* and eROP is understood to proceed *via* an activated monomer mechanism.[49, 58, 59] The hydrophobic catalytic site consists of a serine, histidine, and aspartate residue and it is proposed that a lactone substrate undergoes nucleophilic addition by the serine alcohol to generate an intermediate that cleaves the monomer acyl bond and releases an alkoxy anion to generate the enzyme-activated monomer (EAM) species.[35, 60] The resulting EAM subsequently undergoes nucleophilic addition of the initiating or propagating alcohol species to generate a new intermediate, the final product of which is released *via* cleavage of the acyl bond to regenerate the enzyme (Scheme 3). Therefore, in eROP, the substrate initially coordinates to the catalyst, unlike with non-enzymatic catalysts, which usually coordinate the initiating species in the first instance.[60] Since the enzyme does not discriminate between ester groups, transesterification side reactions occur, resulting in chain scission and the production of cyclic and linear polymer products, ultimately increasing the *Ð*M,and decreasing the *M*n and end-group fidelity of the polymer product.[18] Furthermore, enzymes such as lipases and proteases only catalyse polymerisations at high monomer concentrations, where the equilibrium favours polymerisation.[61, 62] Therefore, eROP cannot be considered a living polymerisation process even though reasonable *M*n values and end-group control can be achieved using this technique.

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**Scheme 3** Proposed enzyme-activated monomer mechanism for the enzymatic ring-opening polymerisation of lactones. Scheme adapted from Dubois *et al.*[35]

Kinetic investigations into the eROP of various sized lactones determined that eROP proceeds more rapidly for larger rather than smaller lactones since formation of the EAM is promoted by increasing the hydrophobicity of the monomer following the hydrophobic nature of the enzyme active site.[63-67] To date, the eROP of numerous large MLs including nonadecalactone (NDL) and tricosalactone (TCL) has been reported.[68] Furthermore, studies into the enantioselective eROP of substituted lactones report varied selectivities and rates.[67] However, these differences can be attributed to the lactone ester conformation, which can exist in either the higher-energy *cisoid* or lower-energy *transoid* conformation, where the latter exhibits dramatically increased rates of eROP (Figure 2).[35, 67] Critically, seven-membered rings and smaller can only exist in the *cisoid* conformation whereas 10-membered rings and larger exist exclusively in the *transoid* conformation.[35] Although the eROP of monomers that can adopt both ester conformations is non-selective, polymerisations are *S*-selective with exclusively *cisoid* monomers and *R*-selective with exclusively *transoid* monomers in order to afford an *R*-secondary alcohol as a nucleophile, which propagates considerably more rapidly than the *S*-stereoisomer.[35, 63] Since lipases have a strong preference for *R*-secondary alcohols in the deacylation step, they can be utilised to prepare stereoregular polyesters *via* kinetic resolution polymerisation.[35] Interestingly, the rate of eROP decreases for substituted MLs where a methyl group is present in the α-position.[69]



**Figure 2** *Cisoid* and *transoid* conformations of ester bonds where bold bonds signify conformationally locked bonds.

The rate of eROP can be further increased by performing the polymerisation in a miniemulsion, which is reported as a useful method for preparing PML nanoparticles.[70-73] Furthermore, high *M*w PPDL (163,000 g mol-1) was obtained in as little as 15 minutes with high monomer conversion (>99%) *via* eROP by reactive extrusion in bulk and at high reaction temperatures (90 °C – 130 °C) .[74] Aliphatic polyesters including PPDL can additionally be prepared *via* continuous-flow eROP using a packed-bed reactor.[75] This method reduces the amount of solvent required to separate the enzyme from the polymer product, and therefore greatly reduces the amount of solvent consumed during polymer purification. Similarly, a variable-volume view reactor was utilised to evaluate less toxic, lower boiling point solvents for eROP,[76, 77] and supercritical carbon dioxide (scCO2) has additionally been reported as a solvent for the eROP of MLs.[78-80]

### Copolymerisation of MLs *via* eROP

The majority of copolyesters prepared *via* eROP are statistical, the sequence composition for which can be evaluated by quantitative 13C NMR spectroscopic analysis, following the indiscriminate transesterase activity of lipases.[81] For example, Kumar *et al*.[58]investigated the copolymerisation of CL and PDL using Novozyme-435, optimizing the reaction temperature (70 °C) and volume of toluene (1:1 wt./vol.), and obtained a statistical copolymer (*M*n = 22,300 g mol‑1, *Ð*M = 1.97) after 6 h despite the fact that PDL is 13 times more reactive than CL using this enzyme (Scheme 4). This study ultimately highlighted the ability of lipases to not only polymerise lactones but to also perform intermolecular transesterification reactions by combining poly(CL) (PCL) (*M*n = 44,000 g mol-1, *Ð*M = 1.65), PPDL (*M*n = 40,000 g mol-1, *Ð*M = 1.71), and Novozyme-435 to yield multiblock copolymers (*M*n = 18,200 g mol-1, *Ð*M = 1.92) within the first hour and statistical copolymers (*M*n = 31,200 g mol-1, *Ð*M = 1.87) after 30 h.[82]



**Scheme 4** Copolymerisation of CL and PDL.

## ROP of MLs using metal-based catalysts

Duda *et al.*[66] evaluated the polymerisation kinetics of various sized lactones in bulk using a zinc 2-ethylhexanoate/butanol catalyst-initiator system at 100 °C and compared the values obtained to those reported by Namekawa *et al.*[64] using *Pseudomonas fluorescens*/octanol in isopropyl ether at 60 °C. A reverse trend was revealed such that the relative orders of polymerisation were determined to be 2500 : 330 : 21 : 0.9 : 1.0 : 0.9 : 1.0 for 6-, 7-, 9-, 12-, 13-, 16-, and 17-membered lactones, respectively using zinc 2-ethylhexanoate, compared to 0.1 : 0.13 : 0.19 : 0.74 : 1.0 for 7-, 12-, 13‑, 16- and 17-membered lactones using *Pseudomonas fluorescens*. These results corroborate thermodynamic calculations which indicate that the ROP of small and medium sized lactones is driven by a positive release of enthalpy and a negative change in entropy during the release of angular and transannular strains, which decreases with increasing ring size, and that the rate of eROP is promoted by monomer hydrophobicity, which increases with ring size. Therefore, it is not surprising that early attempts to polymerise MLs using conventional, non-enzymatic catalysts were inefficient, yielding relatively low molecular weight material and/or exhibiting poor control over the polymerisation.[4-7, 66, 83-86] For example, the anionic polymerisation of UDL and DDL initiated from lithium, sodium, or potassium methoxide in bulk and in tetrahydrofuran at temperatures ranging between 90 °C and 150 °C yielded low molecular weight material (*M*n ≤ 11,000 g mol-1).[6] Although the anionic polymerization of PDL initiated from potassium alkoxides in tetrahydrofuran at 35 ⁰C yielded relatively high molecular weight material (*M*n ≤ 92,000 g mol-1), no correlation was observed between the monomer-to-initiator ratio and the *M*n of the polyesters obtained.[7] Controlled ROP of PDL was achieved using yttrium isopropoxide in bulk and in toluene between 60 ⁰C and 100 ⁰C, proceeding to high monomer conversions within as little as 5 minutes, however only relatively low molecular weight material was obtained (*M*n ≤ 32,000 g mol-1).[83] Similarly, the ROP of PDL using both tetrahydroborate complexes of rare earth metals lanthanum, neodymium, and ytterbium[86] at temperatures up to 60 ⁰C, and using aluminium triflate[85] as a catalyst and glycerol as an initiator in bulk at 110 °C yielded relatively low molecular weight material (*M*n ≤ 39,000 g mol-1 and *M*n ≤ 12,400 g mol-1, respectively). Developments in the ROP of MLs using metal-based catalysts nevertheless were pursued in order to overcome limitations of eROP, namely to 1) control the microstructure of the resulting polymer, and 2) polymerise MLs to high monomer conversion in bulk and in melt in order to obtain high molecular weight material.

Catalysts based on Li,[6] Na,[6, 87] K,[6, 7] Mg,[88-92] Ca,[93, 94] Al,[10, 37, 85, 87, 93, 95-102] Sn,[84, 87, 103-118] Bi,[119-124] Zn,[4, 5, 66, 93, 94, 125] Y,[83, 126, 127] La,[86] Nd,[86] and Yb[86] metal centres have been reported to polymerise MLs with varied efficacy (Figure 3). Many of these catalysts proceed *via* a coordination-insertion mechanism whereby coordination of the monomer carbonyl oxygen to the metal alkoxide complex activates the monomer and promotes the nucleophilic addition of the alkoxide to the monomer carbonyl carbon. Acyl bond cleavage ring-opens the monomer and generates a metal alkoxide, from which the polymerisation propagates (Scheme 5).[20] Despite following chain-growth kinetics, the *Ð*M of polymers obtained *via* ROP using metal-based catalysts is typically similar to that obtained *via* eROP due to transesterification side reactions and the formation of cyclic oligomers.



**Figure 3** Highly active metal-based catalysts reported in the ROP of MLs.

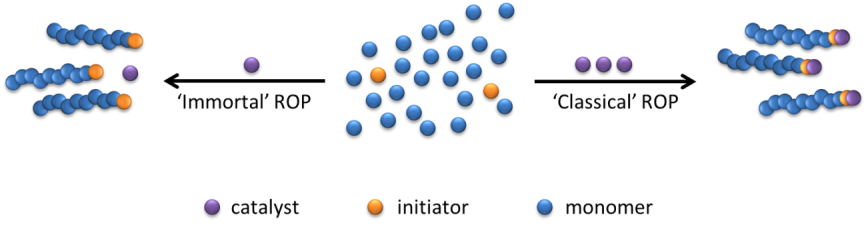


**Scheme 5** Coordination/insertion mechanism for the ring-opening polymerisation of lactones using metal-based catalysts.

Several catalysts including tridentate zinc and calcium Schiff base complexes[93, 94, 125] and aluminium-salen complexes[10, 37, 95-101] have been discovered to catalyse the controlled ROP of PDL to both high monomer conversions and high molecular weights (*i.e.* *M*n ≥ 150,000 g mol-1).[95] Kinetic investigations into the ROP of PDL, ambrettolide (Amb), butylene adipate (BA), *l*-lactide (*l*-LA), CL, ε-decalactone (DL), and *β*-butyrolactone (*β*BL) were undertaken using various aluminium-salen complexes.[96] It was determined that 1) there is a first order reaction for both the catalyst and the monomer, following the monometallic mechanism, 2) increasing the size of the catalyst diamine bridge dramatically increases the rate of ROP of small lactones, and 3) increasing the steric bulk of the catalyst decreases the rate of polymerisation for all lactones.[96] The effect of α-substitution on the ROP of lactones was furthermore investigated using aluminium-salen catalysts and it was determined that α-substitution significantly reduces the reactivity of monomers in the *transoid* and not the *cisoid* conformation, therefore greatly reducing the rate of polymerisation of MLs and not small or medium sized lactones.[100] Interestingly, Pepels *et al.*[100] determined that the choice of initiator not only influences the rate of initiation but also the rate of ROP using aluminium-salen catalysts such that a secondary alcohol reduces the rate of propagation and a primary alcohol increases the rate of polymerisation, although *via* chain-end transesterification and not ROP. Ultimately, aluminium-salen catalysts have been shown to be efficient catalysts for the ROP of lactones of various sizes, including lactones as large as NDL and TCL.[10]

### ‘Immortal’ ROP (iROP)

‘Classical’ ROP techniques require interaction between the catalyst and the initiator to form a complex, such as a metal-alkoxide, to initiate polymerisation, one chain at a time.[128] Consequently, the resulting polymers are defined not only from the molar ratio of monomer-to-initiator but also the molar ratio of initiator-to-catalyst, and therefore the monomer-to-initiator-to-catalyst ratio. Since ‘classical’ ROP techniques typically require an equimolar quantity of catalyst and initiator to generate the catalyst/initiator complex, Inoue and co-workers[129, 130]coined the term ‘immortal’ ROP (iROP) to describe ROP reactions where the quantity of catalyst does not affect the *M*n of the polymer product, and a lower than equimolar quantity of catalyst with respect to initiator can be used. Hence, in iROP, one catalytic unit can polymerise multiple chains concurrently, and the *M*n of the resultant polymers is defined solely by the monomer-to-initiator ratio (Figure 4).[128] Recently, several catalysts exhibiting ‘immortal’ characteristics have been reported in the efficient ROP of MLs including bis(phenoxy)magnesium,[88-92] which proceeds with good end-group fidelity in the absence of inert conditions, and a zinc Schiff base complex,[93] which proceeds in the absence of any significant transesterification side reactions.



**Figure 4** Comparison of ‘immortal’ and ‘classical’ ROP.

### Copolymerisation of MLs using metal-based catalysts

Random copolyesters of PDL and CL are readily prepared in one pot *via* ROP using zinc, calcium, and aluminium tridentate Schiff base complexes,[93, 94, 125] bis(phenoxy)magnesium,[89] and aluminium-salen catalysts.[96, 98] Unlike in eROP, where PDL is polymerised in advance of CL due to the hydrophobicity of the enzyme active site, it is thermodynamically favourable for CL to polymerise in advance of PDL using most metal-based catalysts, after which intra- and intermolecular transesterification randomises the polymer sequence. Random copolyesters of PDL have additionally been reported with δ-valerolactone (δVL), η-caprolactone (ηCL), and DDL using bis(phenoxy)magnesium as a catalyst.[89] Similarly, random copolyesters of the Amb isomer ω-6-hexadecenlactone (6HDL) and CL have been prepared in one pot using a dimethyl(salicylaldiminato) aluminium complex.[102]

Block copolymers of PDL and CL or *L*-LA, however, have been prepared *via* sequential feed reactions using zinc and calcium tridentate Schiff base complexes,[93, 94, 125] and aluminium-salen complexes.[96, 99] Similarly, block copolymers of 6HDL and CL or *rac*-lactide (*rac*-LA) have been prepared using a dimethyl(salicylaldiminato) aluminium complex and this strategy was extended to prepare poly(6HDL-*co*-CL)-*b*-poly(*rac*-LA).[102] Interestingly, PPDL-*b*-PCL prepared using zinc and calcium tridentate Schiff base complexes[94, 125] did not randomise with further reaction time, indicating the absence of transesterification side reactions, however did randomise with other catalysts including aluminium-salen complexes[96] and an aluminium tridentate Schiff base complex.[93] Therefore, good control over both *M*n and sequence composition can be achieved using calcium and aluminium tridentate Schiff base complexes.[93, 94]

Interestingly, Jasinska-Walc *et al.*[94, 125] discovered that the one-pot copolymerisation of PDL and *ε*-decalactone (εDL) using zinc and calcium tridentate Schiff base complexes yielded block copolymers that do not randomise with further reaction time, unlike copolymers of εDL and CL (Scheme 6). The one-pot copolymerisation of PDL and other *ε*-substituted lactones including menthide (MI), ζ-heptalactone (ζHL), and dihydrocarvide (DHC) has additionally been reported using bis(phenoxy)magnesium as a catalyst, which similarly yielded block-like copolymers with a short graduation between blocks.[90] Investigating the copolymerisation of MI with a range of nonsubstituted lactones, specifically 6-, 7-, 8-, and 9-membered rings, Wilson *et al.*[91] determined that sequence composition depends on the relative rates of monomer polymerisation such that copolymerisation of *ε*-substituted lactones with a 7-membered lactone or smaller resulted in random sequencing, whereas copolymerisation with an 8-membered lactone or larger resulted in block copolymers. Therefore, in the copolymerisation of *ε*-substituted lactones, the smaller lactone polymerises first, after which transesterification occurs as MI is incorporated. Where the comonomer is an 8-membered lactone or larger, transesterification between resulting blocks is severely retarded since α-substitution prevents transesterification *via* steric hindrance, and insertion of a ML into a branched alkoxide is thermodynamically unfavourable.[91, 94] Transesterification within the ML block, however, still occurs as evidenced with by an increase in *Ð*M with increasing reaction times.[91, 125] Random copolymers of PDL and εDL[119] or δ-hexalactone (δHL),[120] in addition to the macro(di)lactone ethylene brassylate (EB) and δHL[121], δVL,[123] or *D*,*L*-LA,[124] however have been reported using triphenyl bismuth as a catalyst. Interestingly, differences in the rate of ROP and transesterification of MI, CL, and PDL were exploited to prepare random terpolymers where all reagents were added at the start of the reaction, and triblock copolymers where CL was polymerised sequentially.[91]



**Scheme 6** Copolymerisation of PDL with *ε*DL.

## ROP of MLs using organo-catalysts

Although several metal-based catalysts efficiently polymerise MLs with living characteristics, the requirement for metal-free processes in biomedical and microelectronic applications, where metals are incompatible even in trace amounts, has driven the development of organic catalysts (Figure 5). An added advantage of most organo-catalysts over metal-based catalysts is that anhydrous conditions are only required to control the molecular weight and end-group fidelity of the polymer product since water is a competitive initiator.[131] The majority of organo-catalysts mediate ROP *via* an activated monomer mechanisms. For example, the pyridine-based organo-catalyst 4-(dimethylamino)pyridine (DMAP) undergoes nucleophilic addition to the carbonyl carbon of the monomer to form a zwitterion intermediate, which undergoes ring-opening of the monomer acyl bond. The resulting alkoxide deprotonates the initiator or propagating alcohol species to generate another anion that undergoes nucleophilic addition to the monomer carbonyl carbon to regenerate the catalyst and yield the hydroxyl-terminated propagating species (Scheme 7).[132]

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**Scheme 7** Mechanism for the ring-opening polymerisation of cyclic esters mediated by DMAP. Scheme adapted from Nederberg *et al*.[132]

Highly active organic ‘superbases’ have demonstrated tremendous versatility in the range of monomers they are capable of polymerising. For example, 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) catalyses the ROP of lactones *via* dual activation of the monomer and initiating species (Scheme 8).[133] Since intramolecular transesterification side reactions result as a consequence of the catalytic mechanism, increased dispersities and lower than theoretical *M*n values are obtained, however can be reduced by deactivating the catalyst at ≤85% monomer conversion, in addition to altering the polymerisation temperature and solvent. The ROP of PDL has been reported in bulk and in toluene at 100 °C using TBD as a catalyst and benzyl alcohol as an initiator (*M*n ≤ 108,000 g mol−1; *Ð*M = 1.10-1.90).[134, 135] Similarly, the bulk ROP of EB has been reported using TBD at 80 °C.[136]

**Scheme 8** Mechanism for the ring-opening polymerisation of lactones mediated by TBD. Scheme adapted from Kamber *et al*.[133]

Phosphazene ‘superbases’ have also been reported to catalyse the ROP of PDL. The rapid rate of polymerisation observed in the ROP of PDL using *t*-BuP4 and *t*-OctP4 as catalysts and 3-phenyl-1-propanol as an initiator was decreased by using *t*-BuP2 instead, affording increased control over the polymerisation (*M*n ≤ 37,500 g mol−1; *Ð*M typically ≤ 2.00).[137] Interestingly, high conversions were achieved both in bulk at 80 °C and in dilute concentrations at ambient temperature. Furthermore, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was reported to efficiently polymerised PDL in bulk at 100 °C using benzyl alcohol as an initiator,[134] and 1,2,3-tricyclohexylguanidine (TCHG) and 1,2,3-triisopropylguanidine (TIPG) have been reported to polymerise EB with varied efficacy in bulk at 80 °C using benzyl alcohol as an initiator (*M*n ≈ 7,000 g mol−1; *Ð*M = 1.50).[136]

Although the *N*-heterocyclic olefin (NHO) 2-isopropylidene-1,3,4,5-tetramethylimidazoline has been reported in the ROP of PDL (*M*n = 6,300 g mol−1; *Ð*M = 2.36),[138] the majority of organic bases (p*K*a < 25) have been unable to efficiently polymerise MLs in the absence of a Lewis acid. Dual catalyst systems, in which a Lewis acid enhances the catalytic activity of a nucleophile, have been investigated using DBU, DMAP, and *N*-heterocyclic carbenes (NHCs) alongside a range of Lewis acid metal salts in the ROP of PDL and, remarkably, it was determined that cocatalyst reactivity is dictated by the Lewis acid.[139] Similarly, NHO/Lewis acid cocatalyst systems rapidly polymerised PDL to high monomer conversions, with moderate control and reduced transesterification side reactions, where a mildly activating Lewis acid was utilised (*M*n ≤ 40,800 g mol−1; *Ð*M = 1.45-1.79).[140] Furthermore, the DBU/Zn(C6F5)2 cocatalyst system has recently been reported to prepare PPDL (*M*w ≤ 65,500 g mol−1; *Ð*M = 1.70-1.90) with minimal transesterification side reactions by performing the polymerisation in the absence of an initiator and terminating with a bulky secondary alcohol such as diphenyl methanol.[141] Interestingly, in the absence of a terminating species, high *M*w cyclic PPDL can be obtained (*M*w > 100,000 g mol−1; *Ð*M = 1.60-1.90).[141]

Finally, organic acids have been investigated in the ROP of MLs. For example, dodecylbenzenesulfonic acid (DBSA), diphenyl phosphate (DPP), and trifluoromethanesulfonic acid (TfOH) have been utilised to catalyse the ROP of PDL, Gl, and Amb in bulk using benzyl alcohol as a initiator (*M*n ≤ 21,000 g mol−1; *Ð*M = 1.65-2.94).[142] The rate of polymerisation was dependent on the p*K*a of the acid (TfOH > DBSA > DPP) and the broad dispersities obtained indicate the occurrence of transesterification side reactions. Where the reaction was performed in an aqueous miniemulsion, the polymerisation proceeded *via* a condensation mechanism and yielded oligo(ester)s (*M*n ≤ 1,660 g mol−1).[142, 143] EB has additionally been polymerised with varied efficiency using *p*-toluene sulfonic acid (PTSA) (*M*n = 2,000 g mol−1; *Ð*M = 2.70), DBSA (*M*n = 5,900 g mol−1; *Ð*M = 1.90), and DPP (*M*n = 7,100 g mol−1; *Ð*M = 1.90).[136]



**Figure 5** Selected organic cocatalysts for the ROP of MLs.

### Copolymerisation of MLs using organo-catalysts

One-pot and sequential copolymerisation of PDL and CL using TBD yielded random PPDL-*co*-PCL copolyesters following the transesterase activity of the catalyst.[135] Interestingly, the transesterase activity of TBD was utilised to randomise PPDL-*b*-poly(DL) and PPDL-*b*-PCL block copolyesters prepared using zinc and calcium tridentate Schiff base complexes that did not randomise with additional reaction time.[93, 94, 125] Sequential copolymerisation of PDL followed by *l*-LA using TBD or DBU as catalysts, however yielded block copolyesters since the rate of ROP of *l*-LA greatly exceeded that of transesterification at ambient temperature.[134] TBD has additionally been utilised to copolymerise PDL and UDL or β,δ-trimethyl-ε-caprolactone isomers in one pot and sequentially to yield both random and block-like copolyesters by varying the PDL content such that decreasing the ratio of PDL increased the random character of the copolyester.[144]

Random copolyesters of MLs DDL, PDL, or HDL and δVL or CL have additionally been prepared both in one pot and *via* sequential polymerisation as a consequence of transesterification side reactions using *t*-BuP4 as a catalyst and benzyl alcohol as an initiator.[145] Employing a catalyst-switch method, however, enabled the preparation of block copolymers in one pot whereby the ML was polymerised to high conversion using *t*-BuP4, after which the catalyst was neutralised with DPP and the small lactone polymerised from the PML macroinitiator using *t*-BuP2.[145] Statistical copolymerisation of PDL and γ-butyrolactone, δVL, or CL have additionally been reported using a NHO/Lewis acid dual catalyst systems.[140] Interestingly, Wang *et al*.[141] report that relatively high *M*w cyclic or linear block copolymers of PPDL can be prepared *via* sequential polymerisation of PDL with CL or lactide using the DBU/Zn(C6F5)2 dual catalyst system in the absence or presence of a terminating species, respectively.

# Functionalisation of poly(macrolactone)s

Introduction of functional groups beyond the polyester backbone enables the ability to not only tune polyester properties but also design polymer architecture and function. Furthermore, the introduction of specific functionality such as bioconjugation, biodegradation, or surface wettability enables the design of materials to perform particular functions as medical devices, tissue scaffolds, and drug delivery systems, for example.[146-152] Methods to introduce functionality into polyesters prepared *via* ROP include, however are not limited to using functional monomers or initiators, many of which are available for post-polymerisation modification.[20] Combining polymer functionalisation with the ability to tune sequence control, stereochemistry, and polymer architecture in some instances *via* catalyst and monomer choice affords access to a multitude of potential polymeric materials featuring PMLs (Figure 6).



**Figure 6** Copolymerisation of MLs using a) non-substituted lactones, b) substituted lactones, c) monomers featuring functionalities that may be modified post-polymerisation, and d) macroinitiators.

## Functional initiation and termination

End-group functionality can be introduced onto PML chain-ends through choice of initiator and/or end-capping compound, enabling the preparation of functional polymers and higher polymer architectures. For example, the eROP of DDL initiated from 5-hexen-1-ol, 5-hexyn-1-ol, and 2-hydroxyethyl methacrylate (HEMA) generated alkenyl, alkynyl, and methacryl ω-functional poly(DDL), respectively.[65, 153] Similarly, alkenyl functional PPDL has been prepared by initiating the ROP of PDL from buten-1-ol.[154] PPDL macromonomers obtained from the eROP of PDL initiated from HEMA or ω-hydroxyl-ω’-methacrylate-poly(ethylene glycol) (PEGMA) (*M*n = 360 g mol-1) were further grafted *via* free radical polymerisation to prepare PPDL brush copolymers (Scheme 9).[155] Use of initiators featuring cleavable ester bonds in eROP, however can yield polymers with mixed compositions and end-groups. For example, the eROP of PDL initiated from 2-hydroxyl acrylate (HEA) or HEMA has been reported to yield a mixture of polymers with 0, 1, or 2 acrylate or methacrylate end-groups, respectively, following the indiscriminate transesterase activity of lipases.[156, 157] Evidence for the incorporation of the 1,2-ethanediol moiety of HEA or HEMA within the polyester indicates that lipases catalyse two major transesterification side reactions, namely polyester transfer and acrylate/methacrylate transfer, although transacylation can be minimized by reducing reaction times.[156, 157] Oligoesters prepared *via* the eROP of PDL have additionally been end-capped with 10-undecen-1-ol and linoleic acid to introduce alkene and diene functionality, respectively.[70] Interestingly, the transesterase activity of lipases has been exploited to prepare methacryl and ω-alkenyl macromonomers by performing the eROP of DDL in the presence of vinyl methacrylate and vinyl 10-undecanoate, respectively.[63, 65, 158, 159] Furthermore, end-group functionalisation of PMLs has been reported to reduce cyclic oligomer formation.[160]



**Scheme 9** Preparation of PPDL brush copolymers *via* the eROP of PDL using HEMA as an initiator and radical polymerisation of the resultant macromonomer. Scheme adapted from Kalra *et al*.[155]

Telechelic PMLs have been prepared using several combinations of initiators and end-capping compounds. For example, the eROP of PDL initiated from HEMA and end-capped with vinyl methacrylate yielded α,ω-dimethacrylated PPDL.[156] Similarly, α,ω-difunctional PPDL featuring thiol-thiol or thiol-acrylate end-groups was prepared by initiating the eROP of PDL from 6-mercapto-1-hexanol and end-capping with either γ-thiobutyrolactone, 11-mercapto-1-undecanoic acid, or vinyl acrylate (Scheme 10).[161-163] The resultant α,ω-dithiol macromonomer was crosslinked with tetrafunctional norbornene, a trifunctional allyl ether maleate species, or trimethylolpropane tri(3-mercaptopropionate) (TRIS) *via* radical thiol-ene addition using a photoinitiator to generate semicrystalline or amorphous crosslinked films, depending on the crosslinker used.[163] The simultaneous ROP and transacylation activity of lipases has additionally been applied to prepare telechelic PMLs using divinyl esters. For example, α,ω-dicarboxylic acid functional poly(DDL) has been prepared by performing the eROP of DDL in the presence of divinyl sebacate.[63, 65, 159] Similarly, α,ω-diacryl and α,ω-dimethacryl PPDL macromonomers were prepared by performing the eROP of PDL in the presence of ethylene glycol diacrylate and ethylene glycol dimethacrylate, respectively.[162] Furthermore, α,ω-dihydroxy PPDL has been obtained using tetrahydroborate complexes of rare earth metals as ROP catalysts,[86] in addition to dialkyltin oxide/diol catalyst/initiator systems.[106, 109, 111, 114, 115, 117, 118]



**Scheme 10** Preparation of an α,ω-dithiol functional polyester *via* the eROP of PDL initiated from 6-mercapto-1-hexanol and terminated with γ-thiobutyrolactone. Scheme adapted from Takwa *et al*.[161]

Functional initiation can also be employed as a strategy to prepare block copolymers and higher architectures of PMLs. For example, the eROP of MLs was initiated from a monohydroxyl-terminated polymer to prepare poly(butadiene)-*b*-PPDL,[164] methoxyPEG-*b*-PPDL,[137] methoxyPEG-*b*-poly(EB),[165] methoxyPEG-*b*-poly(DL)-*b*-PPDL,[166, 167] and HDPE-*b*-PPDL.[101] Graft copolymers of poly(ethylene) (PE) and PPDL were similarly prepared by initiating the ROP of PDL from randomly hydroxylated HDPE or LDPE, or *via* transesterification of PPDL with randomly hydroxylated HDPE or LDPE.[101] Conversely, using monohydroxyl-terminated PPDL as a macroinitiator for the ROP of *l*-LA using TBD, DBU, and aluminium-salen catalysts yielded PPDL-*b*-poly(*l*-LA) diblock copolyesters following the rapid rate of ROP relative to transesterification, although intrablock transesterification still occurred as evidenced by increased dispersities.[99, 134] Similarly, monohydroxyl-terminated PMLs PPDL, poly(DDL), and poly(HDL) were utilised as macroinitiators to prepare diblock copolymers with δVL or CL using *t*-BuP2 as a catalyst.[145] Furthermore, exploiting the fact that ε-substituted lactones polymerise in advance of and do not transesterify with MLs, PPDL-*b*-poly(MI)-*b*-PPDL triblock copolymers were prepared in one pot using 1,4-benzenedimethanol as an initiator and bis(phenoxy)magnesium as a catalyst.[91]

Block copolymers and higher architectures featuring PMLs can additionally be prepared by combining functional initiation with other polymerisation techniques. For example, PPDL-*b*-HDPE has been prepared *via* cross metathesisof alkenyl end-functional homopolymers.[154] Furthermore, use of a bifunctional initiator has been reported as a strategy to prepare acrylic and styrenic diblock copolymers of PPDL *via* a combination of eROP and reversible addition-fragmentation chain-transfer (RAFT) polymerisation techniques (Scheme 11).[168]ROP and RAFT polymerisation techniques have additionally been utilised to prepare 4-armed star copolymers by initiating the ROP of EB from pentaerythritol, condensing the chain-transfer agent (CTA) *S*-1-dodecyl-*S*’-(α,α’-dimethyl-α’’-acetic acid)trithiocarbonate onto the resulting hydroxyl-functional chain ends, and polymerising PEGMA from the macro-CTA *via* the RAFT process.[169] Finally, cationic polymerisation of α,ω-dihydroxyl functional PPDL with the diepoxide 3,4-epoxycyclohexyl-30,4’-epoxycyclohexane carboxylate yielded switchable shape memory polymers.[170]



**Scheme 11** Synthesis of acrylic and styrenic diblock copolymers of PPDL *via* a combination of eROP and RAFT polymerisation techniques.[168]

Condensation between hydroxyl-functional PMLs and diisocynates has been utilised as a strategy to prepare a range of polyesterurethane materials. For example, condensation between α,ω-dihydroxyl-PPDL and α,ω-dihydroxyl-PCL using a diisocyanate yielded multiblock copolyesterurethanes.[106, 109, 111, 114, 115, 117, 118] This strategy was extended to prepare copolyesterurethane crosslinked networks from hydroxyl-functional three-armed PPDL and four-armed PCL stars.[104, 105, 107] Where α,ω-dihydroxyl-PPDL and α,ω-dihydroxyl-PCL were condensed with a diisocyanate and *N*,*N*-bis(2-hydroxyethyl) cinnamide, crosslinked copolyesterurethanes could be obtained *via* reversible photoinitiated [2+2] cycloaddition reactions.[171] Furthermore, PPDL surface functionalised magnetic nanoparticles, prepared *via* the ROP of PDL initiated from glycolic acid functionalised nanoparticles,[110] were subsequently polymerised with CL to prepare bilayer coated magnetic nanoparticles[116] or condensed with hydroxyl-functional three-armed PPDL stars using 1,6-hexane diisocyanate to form hybrid nanocomposite materials.[112, 113] Finally, condensation between mono-hydroxyl functional PPDL and 2-isocyanatoethyl methacrylate was utilised to prepare methacrylate-functional PPDL, which was radically copolymerised with *N*-vinyl-2-pyrrolidone and oligo(ethylene glycol)dimethacrylate using 2,2-azobis(2-methylpropionitrile) (AIBN) to prepare hydrogel networks.[108]

## Functional monomers

Main-chain and pendant functionality is readily introduced into polyesters *via* the polymerisation of lactones with added functionality.[172] For example, numerous homopolymers prepared from functional MLs including Amb,[37, 96, 173-175] the corresponding epoxide of Amb (AmbE),[173] Gl,[174, 175] 6HDL,[102] BA,[96] 2-oxo-12-crown-4-ether (OC),[176] and crown-ether-like macrocyclic dilactones 15,15-dimethyl-1,4,7,10,13-pentaoxacyclohexadecane-14,16-dione[177] and 5,8,11,14,17-pentaoxaspiro[2,15]octadecane-4,18-dione[177] have been reported. Furthermore, macrocycles containing up to 84 atoms and featuring significant in-chain functional moieties including steroid residues have been successfully polymerised *via* eROP.[178] Copolymerisation of PDL with *p*-dioxanone (*p*DO),[179, 180] γ-methacryloyl-ε-caprolactone (McrCL),[173] γ-benzoyl-ε-caprolactone (BnzCL),[173] β,δ-trimethyl-ε-caprolactone isomers,[144] 1-oxa-8-aza-cyclotetradecan-9,14-dione (cEA),[173] DL,[90, 94, 119, 125] MI,[90, 91] ζHL,[90] δHL,[119] DHC,[90] OC,[176, 181] Amb,[97, 173] AmbE,[173] and cyclic butylene terephthalate oligomers[182] has additionally yielded copolymers with main-chain or pendant group functionalities, many of which are accessible for post-polymerisation modification (Figure 7, Table 1). Interestingly, the eROP of cEA proceeds exclusively *via* the lactone and not the cyclic amide, and not all γ-substituted ε-lactones can copolymerise with MLs since many, including γ-acetyloxy-ε-caprolactone and γ-acryloyloxy-ε-caprolactone, rearrange to form γ-butyrolactones, which cannot copolymerise.[173]

Additional functional copolyesters that have been reported include poly(Gl)-*co*-PCL,[79] poly(6HDL)-*co*-PCL,[102] poly(6HDL)-*co*-poly(*rac*-LA),[102] and poly(EB)-*co*-poly(δHL),[121] for example. Interestingly, a novel series of poly(hydroxyalkanoate)s was reported *via* the copolymerisation of (*R*)-βBL with several MLs including PDL, HDL, ethylene dodecanedioate, ethylene tridecanedioate, and 11-oxa-16-hexadecanolide using 1-ethoxy-3-chlorotetrabutyldistannoxane as a catalyst.[103] Furthermore, α,ω-dihydroxyl functional poly(OC)-*co*-PCL random copolymers, prepared by initiating the ring-opening copolymerisation from 1,6-hexanediol, were condensed with diisocyanatobutane using dibutyltin dilaurate as a catalyst and chain extended with 1,4-diaminobutane to yield poly(urethane urea)s.[183] Finally, copolymerisation of MLs alongside other monomer classes suitable for ROP has been demonstrated. For example, PDL has been copolymerised with TMC *via* eROP and using sodium ethoxide to yield statistical copolymers, and other metal-based catalysts to yield block copolymers with limited incorporation of PDL.[87, 184]



**Figure 7** Examples of substituted lactones copolymerised with MLs.

**Table 1**PML homopolymer and copolymer properties.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Macrolactone** | **Comonomer*a*** | **Catalyst*b*** | **Sequencing*c*** | ***T*m (°C)*d*** | ***T*c(°C)*d*** |
| PDL | -[33] | E/I/O | - | 95.7 | 81.2 |
|  | γBL[140] | I | Random*e* | 85 | 70 |
|  | δVL[89] | I | Random | 74.1 | 58.9 |
|  | *p*DO[106] | E | Random | 57 | 42 |
|  | δHL[120] | I | Random | 63.2 | - |
|  | δUDL[144] | O | Block/Random | 61/67 | - |
|  | εCL[89] | E/I/O | Random | 74.9 | 58.2 |
|  | BnzCL[173] | E | Random*e* | 80.1 | - |
|  | DHC[90] | I | Block | - | - |
|  | εDL[119] | I | Block | 84.0 | 56.3 |
|  | εHL[90] | I | Block | - | - |
|  | McrCL[173] | E | Random *f* | 82.9 | - |
|  | MI[90] | I | Block | - | - |
|  | ηCL[89] | I | Random | 77.7 | 60.2 |
|  | cEA[173] | E | Random | 80.3 | - |
|  | Amb[173] | E | Random | 72.5 | - |
|  | AmbE[173] | E | Random | 72.5 | - |
| Gl | -[174] | E/O | - | 46.2 | 29.8 |
|  | εCL[194] | E | Random | 39*g* | 20 |
|  | DXO[31] | E | Random | 26.6 | 5.6 |
|  | 4MeCL[31] | E | Random | 36.5 | 18.3 |
| HDL | -[174] | E | - | 96.2 | 76.6 |
| Amb | -[174] | E/I/O | - | 54.9 | 37.7 |
|  | cCO[33] | I | Random | 105.0 | 89.8 |
|  | DXO[31] | E | Random | - | - |
| 6HDL | -[102] | I | - | 72.9 | - |
|  | εCL[102] | I | Random | 44.1 | - |
| NDL | -[10] | E/I | - | 103 | 84 |
| TCL | -[10] | E/I | - | 104 | 88 |

*a* Reference for DSC values only. *b* Where E = enzyme, I = inorganic catalyst and O = organic catalyst. *c* Determined by quantitative 13C NMR spectroscopy. *d* Determined by DSC for a 50 : 50 molar ratio of comonomers unless otherwise stated. *e* Maximum ratio of incorporated PDL : comonomer achieved is 78 : 22. *f* Maximum ratio of incorporated PDL : comonomer achieved is 85 : 15. *g* Double *T*m as a consequence of low cocrystallinity.

Alkenes are versatile sites for pre- and post-polymerisation modification. For example, Baeyer-Villiger oxidation has been utilised to epoxidise Amb, which was subsequently homopolymerised,[173, 185] and poly(6HDL), which was subsequently crosslinked *via* ring-opening the resultant epoxides using NaCNBH3.[102] Furthermore, the eROP of α-(alkyoxymethyl)acrylate 2-methylene-4-oxa-12-dodecanolide and copolymerisation with DDL yielded polyesters with *exo*-methylene groups along the main chain.[186] Additional MLs featuring α-methylene groups, including a selection containing aromatic, ether, and amine groups, have been polymerised *via* eROP and subsequently crosslinked *via* radical polymerisation to yield polymeric gels.[187] Interestingly, radical and anionic polymerisation *via* the α-methylene group of these MLs has been reported to generate polymers with macrocyclic moieties along the main chain.[187-189] Poly(Gl) (PGl) and poly(Amb) homopolymers[174] and random copolymers[175] with CL, 4-methyl caprolactone (4MeCL), and 1,5-dioxepan-2-one (DXO) have additionally been thermally crosslinked using dicumyl peroxide to yield amorphous networks (Figure 10). Similarly, PPDL-*co*-poly(Amb) latexes were crosslinked using benzoyl peroxide to prepare polyester films.[142] Furthermore, ring-opening metathesis copolymerization of Amb and *cis*-cyclooctene, followed by hydrogenation, was utilised as a strategy to prepare aliphatic long chain polyesters.[33]



**Figure 10** Copolymers from unsaturated MLs GI and Amb, and their thermal cross-linking with dicumyl peroxide (poly(Gl-*co*-4MeCl) (75:25); films before (left) and after (right) thermal cross-linking). Scheme adapted from van der Meulen *et al.*[175]

Thiol-ene addition to monomer and polymer alkenes has additionally been investigated. For example, thiol-ene addition of 6-mercapto-1-hexanol, butyl-3-mercapto propionate, and *N*-acetylcysteamine to Gl and PGl has been reported using AIBN (Figure 9).[190, 191] Similarly, thiol-ene addition of 6-mercapto-1-hexanol to poly(6HDL) has been reported using AIBN,[102] and thiol-ene addition of mercaptoethanol, benzyl mercaptan, and dodecanethiol to block-like PPDL-*co*-poly(DHC) has been reported using a photoinitiator.[90] Additionally, PGl[191-193] and PGl-*co*-PCL[194] were crosslinked *via* the thiol-ene addition of ethylene glycol bis(3-mercaptopropionate),[191-193] 1,5-pentanedithiol,[193] or trimethylolpropane tris(3-mercaptopropionate)[194] using a photoinitiator. PGl crosslinked films were further reacted with 6-mercapto-1-hexanol using a photoinitiator, and the resulting hydroxyl groups reacted with α-bromoisobutyryl bromide to form ATRP macroinitiators from which *tert*-butyl acrylate was grafted, deprotected, and conjugated to biological molecules.[192] Additionally, thiol-ene addition of 1-pentanethiol and 6-mercapto-1-hexanol to Amb using AIBN, and subsequent copolymerisation with PDL yielded substituted linear and branched copolymers, respectively.[97] Finally, α,ω-dimethacryloyl terminated PPDL-*co*-PCL and PCL, prepared *via* post-polymerisation modification of the dihydroxylated polymers with methacryloyl chloride, were reacted with pentaerythritol tetrakis(3-mercaptopropionate) using a photoinitiator to yield a reversible shape memory crosslinked polymer network.[195]



**Figure 9** Synthetic routes to functional crosslinked films from MLs using thiol–ene chemistry. Scheme adapted from Ates *et al.*[191]

## Simultaneous ROP and condensation polymerisation

An additional method of introducing functionality into PMLs is to perform simultaneous eROP of MLs and condensation polymerisation[59, 196] of diols with diesters in one pot to generate statistical copolyesters. For example, aliphatic copolyesters have been prepared *via* simultaneous eROP of MLs UDL, DDL, or PDL and condensation of divinyl esters of adipic or sebacic acid and α,ω-glycols.[63, 197-208] This strategy has been extended to prepare PEG-*co*-polyesters and methoxyPEG-*co*-polyesters through copolymerising PEG or monomethoxyPEG with PDL, divinyl adipate, and glycerol.[209, 210] Similarly, the copolymerisation of PDL, diethyl succinate, and 1,4-butanediol has been reported.[211-213] The latter reaction was performed in the following two stages: 1) oligomerisation under low vacuum to prevent monomer evaporation, followed by 2) polymerisation under high vacuum to drive the equilibrium of transesterification to high conversion (Scheme 12).[211]

Simultaneous eROP and condensation polymerisation has also been reported in the preparation of 1) copolyesters from PDL and ethyl glycolate,[214] 2) poly(amine-*co*-ester)s[215, 216] from DDL, PDL, or HDL, diethyl sebacate, and *N*-methyldiethanolamine, 3) poly(PDL-*co*-butylene-*co*-3,3’-dithiodipropionate) copolyesters[217] from PDL, 1,4-butanediol, and dimethyl 3,3-dithiodipropionate, 4) poly(carbonate-*co*-ester)s[218, 219] from PDL, diethyl carbonate, and 1,4-butanediol, 5) poly(PDL-*co*-β-amino ester)s[220] from PDL and ethyl 3-(4-(hydroxymethyl)piperidin-1-yl)propanoate (EHMPP), and 6) poly(amide)s[221] *via* simultaneous ring-opening and aminolysis-condensation polymerisation between EB and various diamines using TBD as a catalyst at 100 °C. Furthermore, this strategy has been extended to prepare PEGylated poly(amine-*co*-ester)s,[217, 222, 223] poly(PDL-*co*-butylene-*co*-3,3’-dithiodipropionate) copolyesters,[224] and poly(PDL-*co*-β-amino ester)s[225] by copolymerising the respective monomers with PEG or monomethoxyPEG. Finally, telechelic PMLs have been obtained *via* simultaneous eROP and condensation polymerisation by performing the eROP of PDL in the presence of divinyl adipate and glycidol to yield α,ω-diepoxy functional PPDL.[226] Cationic photopolymerisation of α,ω-diepoxy macromonomers and crosslinking using cycloaliphatic diepoxide formed durable crystalline films.[226]



**Scheme 12** Two-stage process for the copolymerisation of PDL, diethyl succinate, and 1,4‑butanediol. Scheme adapted from Jiang.[211]

# Functional materials from PMLs

The long aliphatic backbone in PMLs gives rise to thermal and mechanical properties comparable to PE,[16-19] attracting interest in PMLs for numerous applications. Since properties of PMLs, including hydrophobicity and degradability, can be tuned through copolymerisation, functionalisation, and post-polymerisation modification, for example, the range of potential applications for materials derived from PMLs is extensive. Importantly, the discovery that PPDL is biocompatible and nontoxic to cell activity[174] has enhanced interest in PMLs for biomedical applications, which is a significant area of research for polyesters derived from small and medium sized lactones,[227-229] and ultimately expands the scope of materials that can that can be prepared *via* ROP.

## PMLs as polyethylene-like materials

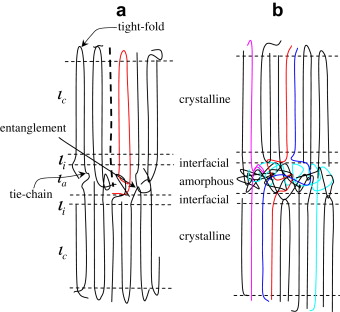
PPDL is highly crystalline[230] and its thermal[5, 16, 17, 83, 231] and mechanical properties[18, 19, 232] are comparable to those for LDPE[16-18] or HDPE,[19] depending on its molecular weight. For example, the melting temperature (*T*m) and glass transition temperature (*T*g) of PPDL (*M*n = 64,500 g mol−1; *Ð*M = 2.00; *T*m = 97 °C; *T*g = -27 °C)[18] are comparable to values reported for PE (*T*m = 136 °C; *T*g = -120 °C) (Figure 10). Molecular weight profoundly affects the properties of PPDL, particularly *via* chain-end effects, which reduce the crystallinity and *T*m of lower molecular weight material.[16, 17, 231] Since crystallinity influences the Young’s modulus and stress at break, the mechanical strength of PPDL can be increased by using high molecular weight material, which reduces the number of plasticising chain ends, and applying processing procedures that maximise lateral chain interactions.[19, 232]



**Figure 10** Plot of *M*n versus monomer conversion for the bulk polymerisation of PDL using an aluminium-salen catalyst (X = Et) and benzyl alcohol as initiator ([M]/[I] = 100). *M*n values were obtained from HT-SEC chromatography in trichlorobenzene. Adapted with permission from van der Meulen *et al.*, *Macromolecules*, 2011, 44 (11), 4301-4305. Copyright 2018 American Chemical Society*.*[95]

Samples prepared by press-moulding high *M*w PPDL (189,000 g mol-1) revealed a Young’s modulus of 450 MPa, up to 650% elongation at break, and tensile strengths of up to 60.8 MPa since, at high molecular weights, the strength of the entanglement network is enhanced and results in strain-hardening prior to break (Figure 11).[19, 233] Furthermore, analysis of high *M*w PPDL (143,000 g mol-1) melt processed into fibres that were elongated 9-10 times their original length through various processing conditions yielded tensile strengths of up to 740 MPa for fibres with the highest degree of crystal orientation, and elongations at break exceeding 1200%.[232] Interestingly, the increased crystallinity observed in poly(NDL) (*M*n = 80,000 g mol-1) and poly(TCL) (*M*n = 120,000 g mol-1) reduced the elongation at break of these materials (270% and 210%, respectively) relative to PPDL of similar molecular weights despite having recorded higher Young’s moduli (647 MPa and 612 MPa, respectively).[68] Ultimately, the mechanical performance of these PMLs is approaching values for HDPE (Young’s modulus = 900 MPa; elongation at break ≈ 900%).[234]

Interestingly, the tensile performance of melt-drawn PPDL fibres reinforced *in situ* with a vanillic acid-based thermotropic liquid crystalline polyester (LCP) was enhanced with increasing LCP orientation and concentration (up to 30 wt.%) *via* interfacial crystallisation, which delocalises stress between the PPDL/LCP interface (Figure 13).[235] Furthermore, PPDL and random PPDL-*co*-PCL copolyesters were demonstrated to be effective nucleating agents for commercial PCL, increasing the number of spherulites, accelerating the nonisothermal rate of crystallisation, increasing the *T*c, and enhancing the tensile strength of the material by 12.4% while maintaining the same elongation at break.[236] Blending PPDL (up to 30 wt.%) into poly(*L*-LA) (PLLA) films increased the Young`s moduli of these materials from 670 MPa to 1010 MPa,[57] and PPDL-*b*-PLLA copolymers were shown to be efficient compatilising agents in blending PLLA with high carbon content polymers such as poly(ω-hydroxytetradecanoate), HDPE, and LDPE.[99, 134] Similarly, PPDL-*b*-HDPE diblock copolymers were demonstrated to compatilise HDPE/PPDL polymer blends.[154] Finally, Pepels *et al*.[97] demonstrated that it is possible to prepare short- and long-chain branched LDPE-like polyesters *via* the ROP of Amb modified *via* radial thiol-ene addition in the presence and absence of PDL.



**Figure 11** Possible mechanism responsible for the brittle-to-ductile transition in: (a) lower molecular mass PPDL and (b) higher molecular mass PPDL. Reprinted from *Polymer*, 51 (5), Cai *et al.*, Effects of molecular weght on poly(ω-pentadecalactone) mechanical and thermal properties, 1088-1099, Copyright 2018, with permission from Elsevier. [19]



**Figure 13** Morphology as observed with SEM after blending and extrusion of (A) PPDL, (B) PPDL : LCP 80 : 20 blend, (C) PPDL after melt drawing, and (D) PPDL : LCP 80 : 20 after melt-drawing (draw-ratio of 400). Adapted with permission from Wilsens *et al.*, *Macromolecules*, 2016, 49, 2228-37. Copyright 2018 American Chemical Society. [235]

Although the recurring ester linkage in PMLs are sites for hydrolytic degradation,[237] hydrophobicity and a high degree of crystallinity limit the accessibility of ester linkages in PPDL. Consequently, PPDL is stable to hydrolytic and enzymatic (*Pseudonomas cepacia*) degradation in phosphate buffer solution (PBS) at 37 °C.[174] Biodegradation of PPDL in compost at 60 °C, however, has been reported, although only 18 wt.% degradation was observed after 280 days.[86] Numerous factors influence polymer degradation including environment, crystallinity, molecular weight, surface chemistry, mechanical properties, and morphology,[238] however since the molar ratio of ester bonds in the polymer backbone directly affect polymer degradation, copolymerisation of PMLs with other monomers including smaller lactones can potentially increase the degradability of these materials.

## Tuning the thermal, mechanical, and degradation properties of PML-based materials

The crystallinity, thermal and mechanical properties, hydrophobicity, and degradability of PMLs can be tailored through copolymerisation. Although the crystal structure and lamellar thickness of PMLs and copolyesters of MLs are only moderately affected by the inclusion of ester groups, since ester groups reduce the stability of the crystal lattice, the melting temperature (*T*m) of these materials varies according to the ratio of methylene-to-ester units.[33, 98] For example, as the ratio of methylene-to-ester units is increased, the *T*m of a PML can approximate that of HDPE (*T*m ≈ 130 °C).[33] Conversely, random or statistical copolyesters of MLs, which are highly crystalline over the entire composition range due to cocrystallisation in a common lattice *via* comonomer isomorphic substitution, maintain reduced *T*m values relative to those of the PML homopolymers. Interestingly, in the copolymerisation of PDL and CL, varying the molar ratio of PDL to CL revealed a linear relationship between the comonomer molar ratio and the *T*m/*T*c such that as the ratio of one lactone increases, the copolyester *T*m and *T*c shift linearly towards values for the corresponding homopolymer.[89, 135, 239] This trend has also be observed in the copolymerisation of PDL with other non-substituted lactones including δVL, ηCL, and DDL.[89] Furthermore, this trend has also been reported in the copolymerisation of several functional MLs with smaller lactones, although the *T*m values for PGl (*T*m = 46 °C), poly(Amb) (*T*m = 55 °C), and poly(AmbE) (*T*m = 73 °C) are significantly lower than that for PPDL.[173, 175] Interestingly, the *T*m of poly(cEA) (140 °C) greatly exceeds that of PPDL.[173] Additional monomers that have been determined to cocrystallise with PPDL include *p*DO,[179, 180] TMC,[87, 184] and ethyl glycolate,[214] for example.

Several monomers including DL,[94, 119, 125] δHL,[120] UDL,[144] OC,[176, 181] and EHMPP[220] do not cocrystallise with PDL despite their semicrystalline properties (Scheme 13). Similarly, poly(EB-*co*-δHL)[121] copolyesters do not cocrystallise. Varying the monomer feed ratio of these copolymers alters the crystallinity of the resulting material to a minimum *T*m observed near equimolar incorporation. Interestingly, many of these copolymers rapidly crystallise from melt, which prevents physical aging during their application, and are easier to process as a consequence of their low *T*g values.[119-121]



**Scheme 13** Copolymerisation of PDL with EHMPP.

Copolymerisation of MLs with other monomers also affects the mechanical properties of the resultant materials. For example, PPDL-*co*-PCL copolyesters maintain significantly reduced yield stress values relative to PPDL due to the increased mobility of the crystalline phase following irregular stacking of the ester groups in the crystal lamellae.[98] Copolymerisation of MLs with other monomers, however is utilised to tune the mechanical properties of these materials for specific applications.[103, 119-121, 124]

Finally, copolymerisation of MLs with smaller lactones enhances the degradability of the resultant copolyesters relative to PML homopolymers. For example, degradation of random copolyesters with varied molar ratios of PDL, δVL, CL, and ηCL (42:58 PPDL-*co*-poly(δVL); 41:59 PPDL-*co*-PCL; 25:75 PPDL-*co*-poly(ηCL)) and identical *T*m and *T*c values (*T*m = 70 °C; *T*c = 54 °C) were monitored in 5 M NaOH(aq) solution at 37 °C.[89] Interestingly, it was determined that the rate of degradation is independent of thermal properties, however increases with increasing ester-to-methylene unit ratios (PPDL-*co*-poly(δVL) = 50 days; PPDL-*co*-PCL = 65 days; PPDL-*co*-poly(ηCL) = 10 wt.% mass loss after 120 days).[89] However, PPDL-*co*-poly(DL) copolyesters, where the molar content of PDL was varied from 30-78%,[119] and PPDL-*co*-poly(δHL) copolyesters, where the molar content of PDL was varied from 39-82%,[120] were determined to be stable to hydrolytic degradation in PBS at 37 °C for 182 days.

## Biomaterials derived from PMLs

### Biocompatible scaffolds and implants

Although PPDL, poly(HDL), PGl, and poly(Amb) homopolymers are neither enzymatically nor hydrolytically degradable, an MTT assay for metabolic cell activity in a 3T3 mouse fibroblast cell line indicated that these polymers are not cytotoxic.[174] Numerous PML-based materials have additionally been determined to be biocompatible. For example, subcutaneous implantation of copolymer films in mice determined PPDL-*co*-poly(DO) copolymers to be biocompatible,[180] and metabolic activity and cell morphology studies determined that poly(EB-*co*-δHL) is compatible with human dermal fibroblasts.[121] The requirement for biodegradability in a biocompatible material is application dependent. For example, biodegradation is an essential feature of *in vivo* tissue scaffolds and drug delivery devices, however is not desirable for biomedical implants.

Several PML-based materials have been investigated for biomedical scaffold and implant applications. For example, PPDL,[160] electrospun PPDL fibrous scaffolds,[240] and PPDL-*co*-PCL[80] copolyesters were prepared as potential porous scaffolds for tissue regeneration applications. Furthermore, poly(EB-*co*-δHL) has been investigated as a potential material for degradable scaffolds, however rates of hydrolytic degradation at 37 °C in PBS (*t*½ = 169-248 days) were determined to be too long for this application.[121] Interestingly, simultaneous *in situ* photoinitiated thiol-ene crosslinking and electrospinning of Gl yielded biocompatible and swellable crosslinked amorphous PGl microfibers.[193] Hydrolytic degradation of these microfibers (up to 34 wt.% after 90 days in PBS at 37 °C), in addition to loading and subsequent release of rhodamine-B, demonstrates their potential for drug loading applications.[193] Furthermore, electrospun PLLA fibres compatilised with PPDL-*co*-PLLA were determined to enhance neurite outgrowth of chick dorsal root ganglia *in vitro* relative to PLLA fibres, potentially due to differences in fibre diameter and surface nanotopology.[241] Finally, PPDL-based shape memory materials[104-117, 171] have been developed with potential applications as stimuli-responsive implant devices or nanocomposite materials for regenerative therapies. For example, electrospun PPDL-*co*-PCL polyesterurethane non-woven fabrics consisting of PPDL hard segments and PCL switching segments were demonstrated to be shape memory materials with potential applications as responsive textiles or devices.[111]

### Biofunctional crosslinked films

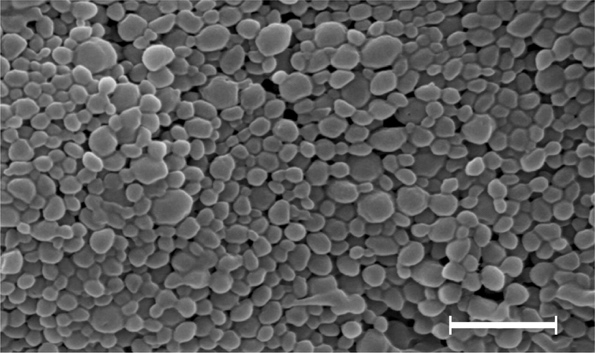
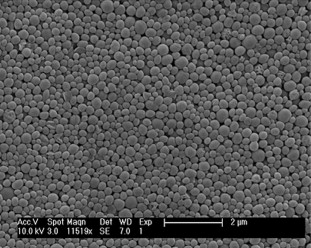
Functional PML-based polymers have been utilised to prepare a range of crystalline, semicrystalline, and amorphous crosslinked films.[142, 163, 174, 175, 187, 191, 192, 194, 226] Although crosslinked PGl and poly(Amb) films do not undergo degradation using *Pseudomonas cepacia* in PBS at 37 °C due to the high crystallinity and hydrophobicity of these materials,[174, 191] a 20 wt.% degradation of PGl crosslinked with ethylene glycol bis(3-mercaptopropionate) was reported after 50 days under the same conditions.[191] Since polyester degradation predominantly takes place in amorphous regions and progresses into crystalline regions at a reduced rate,[242] integration of hydrophilic comonomers such as DXO was determined to enhance enzymatic degradation by up to 90 wt.% after 100 days.[175] Biofunctional films derived from PMLs have been reported, including conjugation of green fluorescent protein and chitobiase onto poly(acrylic acid)-functionalised crosslinked PGl films.[192]

### Biodegradable particles

Biodegradable polyesters are routinely investigated as nano-carriers for controlled drug delivery and the incorporation of MLs increases the hydrophobicity of these systems, which influences drug loading and degradation behaviour, for example, and can be tuned by varying the size and molar ratio of the ML. PEG-stabilised PPDL and polyHDL nanoparticles were amongst the first PML-based nanoparticles prepared *via* eROP in miniemulsions between 45 °C and 90 °C,[70, 71] and PPDL and PGl nanoparticles have since been prepared between 45 °C and 60 °C.[73] The ability to polymerise at lower temperatures reduces thermal stress on any potential drug load, however reaction temperature was determined to affect particle morphology such that non-spherical aggregates were produced at lower temperatures as a consequence of crystallisation, and at higher temperatures, lemon shaped particles were obtained instead of spheres following post-polymerisation cooling and crystalisation.[70, 73] PPDL-*co*-poly(DO) nanoparticles prepared using a modified oil-in-water single emulsion technique were reported to degrade hydrolytically over 60-70 days under physiological conditions.[180] Doxorubicin loaded PPDL-*co*-poly(DO) nanoparticles exhibited continuous controlled release over 20-60 days *in vitro* and siLUC encapsulated nanoparticles inhibited luciferase gene expression in LUC-RKO cells.[180] Additionally, amphiphilic methoxyPEG-*b*-poly(DL)-*b*-PPDL terpolymers self-assembled into micelles have been reported to incorporate Nile Red[166] and curcumin[167] *via* a nanoprecipitation method. Similarly, methoxyPEG-*b*-poly(EB) diblock copolymers assembled into multimorphological aggregates[165] and 4-armed poly(EB)-*b*-poly(PEGMA) copolymers assembled into micelles[169] were reported to encapsulate and release doxorubicin *in vitro*.

Numerous microspheres prepared *via* simultaneous eROP and condensation polymerisation have been investigated for encapsulation and drug delivery applications. For example, PPDL-*co*-poly(glycolate) nanoparticles have been prepared using an oil-in-water single emulsion system with average particle sizes ranging from 174 nm to 190 nm, and poly(PDL-*co*-butylene-*co*-succinate) nanoparticles[212, 213] prepared *via* a similar method were reported to deliver camptothecin to tumour cells *in vivo* following intravenous administration (Figure 14).[213] The encapsulation and controlled release of ibuprofen from copolyester nanospheres prepared from the copolymerisation of PDL, divinyl adipate, and propane-1,3-diol or glycerol have also been evaluated.[198] Interestingly, the efficacy of doxorubicin-loaded PEGylated poly(PDL-*co*-butylene-*co*-3,3’-dithiodipropionate) copolyester micelles was determined to be enhanced against HepG2 cancer cells by intracellular glutathione following internalisation of the micelles by the cells *in vitro*.[217]

PDL-*co*-(glycerol adipate), PEG-*co*-(PDL-*co*-glycerol adipate), and methoxyPEG-*co*-(PDL-*co*-glycerol adipate) copolyester nanoparticles have similarly been investigated for numerous drug delivery applications.[199-205, 207-210] For example, bovine serum albumin adsorbed PDL-*co*-(glycerol adipate) copolyester nanoparticles with *L*-leucine micro-carriers were investigated for vaccine delivery applications *via* dry powder inhalation.[206] Furthermore, α-chymotrypsin and DNase I loaded PEG-*co*-(glycerol adipate-*co*-PDL) microparticles prepared *via* spray drying from double emulsion were investigated as a potential dry powder inhalation treatment for local pulmonary diseases.[209] Additionally, poly(amine-*co*-ester) nanoparticles prepared from DDL, PDL, or HDL, diethyl sebacate, and *N*-methyldiethanolamine were investigated as non-viral carriers for gene transfection and copolymers containing PDL were determined to be effective for luciferase gene transfection of HEK293 cells *in vitro*[215] and targeted gene delivery to tumour cells *in vivo*.[216] Finally, PEGylated poly(amine-*co*-ester),[222, 223] poly(lactone-*co*-β-amino ester),[225] and poly(amine-*co*-disulfide ester)[224] block copolymer micelles featuring PDL have been determined to be promising new pH and/or redox responsive vectors for drug and gene delivery applications.



**Figure 14** SEM micrograph of poly(PDL-*co*-butylene-*co*-succinate) copolymer (20 mol% PDL) nanoparticles (187 ± 37 nm; Scale bar: 1 µm; right)[212] and of poly(PDL-*co*-GA) copolymer (21 mol% GA) nanoparticles (181 ± 45 nm; Scale bar: 2 µm; left).[214] Left image reprinted from *European Polymer Journal*, 47, Mazzochetti *et al.*, Copolymers of ethyl glycolate and ω–pentadecalactone: Enzymatic synthesis and solid-state characterization, 942-948, Copyright 2018, with permission from Elsevier. Right image reprinted with permission from Mazzochetti *et al.*, *Macromolecules*, 2009, 42, 7811-7819. Copyright 2018 American Chemical Society.

# Conclusions

Advances in the ROP of MLs have afforded access to novel polymeric materials featuring aliphatic polyester moieties. The range of catalysts investigated to date for the ROP of MLs enable the ability to tune sequence control, stereochemistry, and polymer architecture in some instances *via* catalyst and monomer choice. Furthermore, polymer functionalisation *via* functional initiation, termination, copolymerisation, and post-polymerisation modification enables the ability to not only tune polymer properties but also design polymer architecture and function. Ultimately, a diversity of polymeric materials featuring PMLs have been prepared to date and hold promise as functional materials for biomedical applications and beyond.

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# References

[1] Albertsson AC, Varma IK. Recent developments in ring opening polymerization of lactones for biomedical applications. Biomacromolecules. 2003;4:1466-86.

[2] Place ES, George JH, Williams CK, Stevens MM. Synthetic polymer scaffolds for tissue engineering. Chemical Society Reviews. 2009;38:1139-51.

[3] Uhrich KE, Cannizzaro SM, Langer RS, Shakesheff KM. Polymeric Systems for Controlled Drug Release. Chemical Reviews (Washington, DC, United States). 1999;99:3181-98.

[4] Yevstropov AA, Lebedev BV, Kiparisova YG. Thermodynamics Of Pentadecalactone, Of The Process Of Its Polymerization And Of Formed Polypentadecalactone In The 0-K-400-K Region. Vysokomolekulyarnye Soedineniya Seriya A. 1983;25:1679-85.

[5] Lebedev B, Yevstropov A. Thermodynamic Properties Of Polylactones. Makromolekulare Chemie-Macromolecular Chemistry and Physics. 1984;185:1235-53.

[6] Nomura R, Ueno A, Endo T. Anionic Ring-Opening Polymerization Of Macrocyclic Esters. Macromolecules. 1994;27:620-1.

[7] Jedlinski Z, Juzwa M, Adamus G, Kowalczuk M, Montaudo M. Anionic polymerization of pentadecanolide. A new route to a potentially biodegradable aliphatic polyester. Macromolecular Chemistry and Physics. 1996;197:2923-9.

[8] Williams AS. The synthesis of macrocyclic musks. Synthesis-Stuttgart. 1999:1707-23.

[9] Kraft P, Bajgrowicz JA, Denis C, Frater G. Odds and Trends: Recent Developments in the Chemistry of Odorants. Angew Chem Int Ed Engl. 2000;39:2980-3010.

[10] Witt T, Mecking S. Large-ring lactones from plant oils. Green Chemistry. 2013;15:2361-4.

[11] Kerschbaum M. Large lactone rings - The carriers of the musky vegetable aroma. Berichte Der Deutschen Chemischen Gesellschaft. 1927;60:902-9.

[12] Parenty A, Moreau X, Niel G, Campagne JM. Update 1 of: Macrolactonizations in the Total Synthesis of Natural Products. Chemical Reviews (Washington, DC, United States). 2013;113:PR1-PR40.

[13] McGinty D, Letizia CS, Api AM. Fragrance material review on omega-pentadecalactone. Food and Chemical Toxicology. 2011;49:S193-S201.

[14] Grammer K. 5-α-androst-16en-3α-on: A male pheromone? A brief report. Ethology and Sociobiology. 1993;14:201-7.

[15] Amoore JE, Pelosi P, Forrester LJ. Specific Anosmias To 5-Alpha-Androst-16-En-3-One And Omega-Pentadecalactone - Urinous And Musky Primary Odors. Chem Sens Flav. 1977;2:401-25.

[16] Skoglund P, Fransson Å. Thermophysical properties of polypentadecanolactone. Polymer. 1998;39:1899-906.

[17] Skoglund P, Fransson Å. Crystallization kinetics of polytridecanolactone and polypentadecanolactone. Polymer. 1998;39:3143-6.

[18] Focarete ML, Scandola M, Kumar A, Gross RA. Physical characterization of poly(omega-pentadecalactone) synthesized by lipase-catalyzed ring-opening polymerization. Journal of Polymer Science Part B-Polymer Physics. 2001;39:1721-9.

[19] Cai J, Liu C, Cai M, Zhu J, Zuo F, Hsiao BS, et al. Effects of molecular weight on poly(ω-pentadecalactone) mechanical and thermal properties. Polymer. 2010;51:1088-99.

[20] Williams CK. Synthesis of functionalized biodegradable polyesters. Chemical Society Reviews. 2007;36:1573-80.

[21] Quinzler D, Mecking S. Linear Semicrystalline Polyesters from Fatty Acids by Complete Feedstock Molecule Utilization. Angewandte Chemie-International Edition. 2010;49:4306-8.

[22] Liu C, Liu F, Cai JL, Xie WC, Long TE, Turner SR, et al. Polymers from Fatty Acids: Poly(omega-hydroxyl tetradecanoic acid) Synthesis and Physico-Mechanical Studies. Biomacromolecules. 2011;12:3291-8.

[23] Stempfle F, Quinzler D, Heckler I, Mecking S. Long-Chain Linear C-19 and C-23 Monomers and Polycondensates from Unsaturated Fatty Acid Esters. Macromolecules. 2011;44:4159-66.

[24] Vilela C, Silvestre AJD, Meier MAR. Plant Oil-Based Long-Chain C-26 Monomers and Their Polymers. Macromolecular Chemistry and Physics. 2012;213:2220-7.

[25] Mutlu H, Hofsass R, Montenegro RE, Meier MAR. Self-metathesis of fatty acid methyl esters: full conversion by choosing the appropriate plant oil. RSC Advances. 2013;3:4927-34.

[26] Rybak A, Meier MAR. Acyclic Diene Metathesis with a Monomer from Renewable Resources: Control of Molecular Weight and One-Step Preparation of Block Copolymers. Chemsuschem. 2008;1:542-7.

[27] Fokou PA, Meier MAR. Studying and Suppressing Olefin Isomerization Side Reactions During ADMET Polymerizations. Macromolecular Rapid Communications. 2010;31:368-73.

[28] Trzaskowski J, Quinzler D, Bahrle C, Mecking S. Aliphatic Long-Chain C-20 Polyesters from Olefin Metathesis. Macromolecular Rapid Communications. 2011;32:1352-6.

[29] Turunc O, de Espinosa LM, Meier MAR. Renewable Polyethylene Mimics Derived from Castor Oil. Macromolecular Rapid Communications. 2011;32:1357-61.

[30] Kreye O, Toth T, Meier MAR. Introducing Multicomponent Reactions to Polymer Science: Passerini Reactions of Renewable Monomers. Journal of the American Chemical Society. 2011;133:1790-2.

[31] de Espinosa LM, Meier MAR. Plant oils: The perfect renewable resource for polymer science?! European Polymer Journal. 2011;47:837-52.

[32] Akintayo CO, Mutlu H, Kempf M, Wilhelm M, Meier MAR. Acyclic Triene Metathesis Polymerization of Plukenetia Conophora Oil: Branched Polymers by Direct Polymerization of Renewable Resources. Macromolecular Chemistry and Physics. 2012;213:87-96.

[33] Pepels MPF, Hansen MR, Goossens H, Duchateau R. From Polyethylene to Polyester: Influence of Ester Groups on the Physical Properties. Macromolecules. 2013;46:7668-77.

[34] Turunc O, Meier MAR. Thiol-ene vs. ADMET: a complementary approach to fatty acid-based biodegradable polymers. Green Chemistry. 2011;13:314-20.

[35] Dubois P, Coulembier O, Raquez J-M. Handbook of Ring-Opening Polymerization: WILEY-VCH Verlag; 2009.

[36] Dove AP. Controlled ring-opening polymerisation of cyclic esters: polymer blocks in self-assembled nanostructures. Chemical Communications. 2008;122:6446-70.

[37] Pepels MPF, Souljé P, Peters R, Duchateau R. Theoretical and Experimental Approach to Accurately Predict the Complex Molecular Weight Distribution in the Polymerization of Strainless Cyclic Esters. Macromolecules. 2014;47:5542-50.

[38] Kobayashi S, Uyama H, Kimura S. Enzymatic polymerization. Chemical Reviews (Washington, DC, United States). 2001;101:3793-818.

[39] Champagne E, Strandman S, Zhu X-X. Recent Developments and Optimization of Lipase-Catalyzed Lactone Formation and Ring-Opening Polymerization. Macromolecular Rapid Communications. 2016;37:1986-2004.

[40] Uyama H, Kobayashi S. Enzymatic Ring-Opening Polymerization of Lactones Catalyzed by Lipase. Chem Lett. 1993:1149-50.

[41] Knani D, Gutman AL, Kohn DH. Enzymatic polyesterification in organic media. Enzyme-catalyzed synthesis of linear polyesters. I. Condensation polymerization of linear hydroxyesters. II. Ring-opening polymerization of ϵ-caprolactone. Journal of Polymer Science Part A: Polymer Chemistry. 1993;31:1221-32.

[42] MacDonald RT, Pulapura SK, Svirkin YY, Gross RA, Kaplan DL, Akkara J, et al. Enzyme-Catalyzed .epsilon.-Caprolactone Ring-Opening Polymerization. Macromolecules. 1995;28:73-8.

[43] Uyama H, Takeya K, Kobayashi S. Synthesis of Polyesters by Enzymatic Ring-Opening Copolymerization Using Lipase Catalyst. P Jpn Acad B-Phys. 1993;69:203-7.

[44] Uyama H, Takeya K, Hoshi N, Kobayashi S. Lipase-Catalyzed Ring-Opening Polymerization Of 12-Dodecanolide. Macromolecules. 1995;28:7046-50.

[45] Uyama H, Takeya K, Kobayashi S. Enzymatic Ring-Opening Polymerization of Lactones to Polyesters by Lipase Catalyst - Unusually High Reactivity of Macrolides. B Chem Soc Jpn. 1995;68:56-61.

[46] Uyama H, Kikuchi H, Takeya K, Kobayashi S. Lipase-catalyzed ring-opening polymerization and copolymerization of 15-pentadecanolide. Acta Polymerica. 1996;47:357-60.

[47] Noda S, Kamiya N, Goto M, Nakashio F. Enzymatic polymerization catalyzed by surfactant-coated lipases in organic media. Biotechnology Letters. 1997;19:307-9.

[48] Uyama H, Kuwabara M, Tsujimoto T, Kobayashi S. High-Performance Immobilized Lipase Catalyst for Polyester Synthesis. Polymer Journal. 2002;34:970.

[49] Bisht KS, Henderson LA, Gross RA, Kaplan DL, Swift G. Enzyme-Catalyzed Ring-Opening Polymerization of ω-Pentadecalactone. Macromolecules. 1997;30:2705-11.

[50] Kundys A, Białecka-Florjańczyk E, Fabiszewska A, Małajowicz J. Candida antarctica Lipase B as Catalyst for Cyclic Esters Synthesis, Their Polymerization and Degradation of Aliphatic Polyesters. Journal of Polymers and the Environment. 2018;26:396-407.

[51] Polloni AE, Chiaradia V, Figura EM, De Paoli JP, de Oliveira D, de Oliveira JV, et al. Polyesters from Macrolactones Using Commercial Lipase NS 88011 and Novozym 435 as Biocatalysts. Applied Biochemistry and Biotechnology. 2018;184:659-72.

[52] Hunsen M, Azim A, Mang H, Wallner SR, Ronkvist A, Xie W, et al. A Cutinase with Polyester Synthesis Activity. Macromolecules. 2007;40:148-50.

[53] Hunsen M, Abul A, Xie W, Gross R. Humicola insolens Cutinase-Catalyzed Lactone Ring-Opening Polymerizations: Kinetic and Mechanistic Studies. Biomacromolecules. 2008;9:518-22.

[54] Herrera-Kao W, Cervantes-Uc JM, Lara-Ceniceros T, Aguilar-Vega M. Effect of reaction temperature on the physicochemical properties of poly(pentadecanolide) obtained by enzyme-catalyzed ring-opening polymerization. Polymer Bulletin. 2015;72:441-52.

[55] Matsumoto M, Odachi D, Kondo K. Kinetics of ring-opening polymerization of lactones by lipase. Biochemical Engineering Journal. 1999;4:73-6.

[56] Hedfors C, Hult K, Martinelle M. Lipase chemoselectivity towards alcohol and thiol acyl acceptors in a transacylation reaction. Journal of Molecular Catalysis B: Enzymatic. 2010;66:120-3.

[57] Nakane K, Tamaki C, Hata Y, Ogihara T, Ogata N. Blends of poly(L-lactic acid) with poly(ω-pentadecalactone) synthesized by enzyme-catalyzed polymerization. Journal of Applied Polymer Science. 2008;108:2139-43.

[58] Kumar A, Kalra B, Dekhterman A, Gross RA. Efficient ring-opening polymerization and copolymerization of epsilon-caprolactone and omega-pentadecalactone catalyzed by Candida antartica lipase B. Macromolecules. 2000;33:6303-9.

[59] Varma IK, Albertsson A-C, Rajkhowa R, Srivastava RK. Enzyme catalyzed synthesis of polyesters. Prog Polym Sci. 2005;30:949-81.

[60] Mei Y, Kumar A, Gross R. Kinetics and Mechanism of Candida antarctica Lipase B Catalyzed Solution Polymerization of ε-Caprolactone. Macromolecules. 2003;36:5530-6.

[61] Albertsson A-C, Srivastava RK. Recent developments in enzyme-catalyzed ring-opening polymerization. Advanced Drug Delivery Reviews. 2008;60:1077-93.

[62] Kobayashi S. Lipase-catalyzed polyester synthesis – A green polymer chemistry. Proceedings of the Japan Academy Series B, Physical and Biological Sciences. 2010;86:338-65.

[63] Kobayashi S, Uyama H, Namekawa S. In vitro biosynthesis of polyesters with isolated enzymes in aqueous systems and organic solvents. Polym Degrad Stabil. 1998;59:195-201.

[64] Namekawa S, Uyama H, Kobayashi S. Lipase-catalyzed ring-opening polymerization of 16-hexadecanolide. P Jpn Acad B-Phys. 1998;74:65-8.

[65] Namekawa S, Suda S, Uyama H, Kobayashi S. Lipase-catalyzed ring-opening polymerization of lactones to polyesters and its mechanistic aspects. International Journal of Biological Macromolecules. 1999;25:145-51.

[66] Duda A, Kowalski A, Penczek S, Uyama H, Kobayashi S. Kinetics of the ring-opening polymerization of 6-, 7-, 9-, 12-, 13-, 16-, and 17-membered lactones. Comparison of chemical and enzymatic polymerizations. Macromolecules. 2002;35:4266-70.

[67] van der Mee L, Helmich F, de Bruijn R, Vekemans JAJM, Palmans ARA, Meijer EW. Investigation of Lipase-Catalyzed Ring-Opening Polymerizations of Lactones with Various Ring Sizes:  Kinetic Evaluation. Macromolecules. 2006;39:5021-7.

[68] Witt T, Häußler M, Mecking S. No Strain, No Gain? Enzymatic Ring‐Opening Polymerization of Strainless Aliphatic Macrolactones. Macromolecular Rapid Communications. 2017;38:1600638.

[69] Kikuchi H, Uyama H, Kobayashi S. Lipase-catalyzed ring-opening polymerization of substituted lactones. Polym J. 2002;34:835-40.

[70] Taden A, Antonietti M, Landfester K. Enzymatic Polymerization towards Biodegradable Polyester Nanoparticles. Macromolecular Rapid Communications. 2003;24:512-6.

[71] Målberg S, Finne-Wistrand A, Albertsson A-C. The environmental influence in enzymatic polymerization of aliphatic polyesters in bulk and aqueous mini-emulsion. Polymer. 2010;51:5318-22.

[72] Panlawan P, Luangthongkam P, Wiemann LO, Sieber V, Marie E, Durand A, et al. Lipase-catalyzed interfacial polymerization of omega-pentadecalactone in aqueous biphasic medium: A mechanistic study. Journal of Molecular Catalysis B-Enzymatic. 2013;88:69-76.

[73] Chiaradia V, Polloni AE, de Oliveira D, de Oliveira JV, Araujo PHH, Sayer C. Polyester nanoparticles from macrolactones via miniemulsion enzymatic ring-opening polymerization. Colloid and Polymer Science. 2018;296:861-9.

[74] Spinella S, Ganesh M, Lo Re G, Zhang S, Raquez JM, Dubois P, et al. Enzymatic reactive extrusion: moving towards continuous enzyme-catalysed polyester polymerisation and processing. Green Chemistry. 2015;17:4146-50.

[75] Wosnick JH, Faucher S, Pereira L. Enzymatic ring-opening polymerization in a continuous-flow system. Abstracts of Papers of the American Chemical Society. 2010;240.

[76] Polloni AE, Rebelatto EA, Veneral JG, de Oliveira D, Oliveira JV, Araújo PHH, et al. Enzymatic ring opening polymerization of ω-Pentadecalactone in different solvents in a variable-volume view reactor. Journal of Polymer Science Part A: Polymer Chemistry. 2017;55:1219-27.

[77] Rebelatto EA, Polloni AE, Andrade KS, Bender JP, Corazza ML, Lanza M, et al. High-pressure phase equilibrium data for systems containing carbon dioxide, ω-pentadecalactone, chloroform and water. Journal of Chemical Thermodynamics. 2018;122:125-32.

[78] Polloni AE, Veneral JG, Rebelatto EA, de Oliveira D, Oliveira JV, Araújo PHH, et al. Enzymatic ring opening polymerization of ω-pentadecalactone using supercritical carbon dioxide. Journal of Supercritical Fluids. 2017;119:221-8.

[79] Guindani C, Dozoretz P, Veneral JG, da Silva DM, Araújo PHH, Ferreira SRS, et al. Enzymatic ring opening copolymerization of globalide and ε-caprolactone under supercritical conditions. Journal of Supercritical Fluids. 2017;128:404-11.

[80] Gualandi C, White LJ, Chen L, Gross RA, Shakesheff KM, Howdle SM, et al. Scaffold for tissue engineering fabricated by non-isothermal supercritical carbon dioxide foaming of a highly crystalline polyester. Acta Biomaterialia. 2010;6:130-6.

[81] Hunley MT, Sari N, Beers KL. Microstructure Analysis and Model Discrimination of Enzyme-Catalyzed Copolyesters. ACS Macro Lett. 2013;2:375-9.

[82] Kumar A, Gross RA. Candida antarctica Lipase B-Catalyzed Transesterification:  New Synthetic Routes to Copolyesters. J Am Chem Soc. 2000;122:11767-70.

[83] Zhong Z, Dijkstra PJ, Feijen J. Controlled ring-opening polymerization of ω-pentadecalactone with yttrium isopropoxide as an initiator. Macromolecular Chemistry and Physics. 2000;201:1329-33.

[84] Slivniak R, Domb AJ. Macrolactones and Polyesters from Ricinoleic Acid. Biomacromolecules. 2005;6:1679-88.

[85] Wang Y, Kunioka M. Ring-Opening Polymerization of Cyclic Monomers with Aluminum Triflate. Macromol Symp. 2005;224:193-206.

[86] Nakayama Y, Watanabe N, Kusaba K, Sasaki K, Cai Z, Shiono T, et al. High activity of rare earth tetrahydroborates for ring-opening polymerization of ω-pentadecalactone. J Appl Polym Sci. 2011;121:2098-103.

[87] Kumar A, Garg K, Gross RA. Copolymerizations of ω-Pentadecalactone and Trimethylene Carbonate by Chemical and Lipase Catalysis. Macromolecules. 2001;34:3527-33.

[88] Wilson JA, Hopkins SA, Wright PM, Dove AP. 'Immortal' ring-opening polymerization of [small omega]-pentadecalactone by Mg(BHT)2(THF)2. Polym Chem. 2014;5:2691-4.

[89] Wilson JA, Hopkins SA, Wright PM, Dove AP. Synthesis of ω-Pentadecalactone Copolymers with Independently Tunable Thermal and Degradation Behavior. Macromolecules. 2015;48:950-8.

[90] Wilson JA, Hopkins SA, Wright PM, Dove AP. Synthesis and Postpolymerization Modification of One-Pot ω-Pentadecalactone Block-like Copolymers. Biomacromolecules. 2015;16:3191-200.

[91] Wilson JA, Hopkins SA, Wright PM, Dove AP. Dependence of Copolymer Sequencing Based on Lactone Ring Size and ε-Substitution. ACS Macro Lett. 2016;5:346-50.

[92] Nifant'ev IE, Shlyakhtin AV, Tavtorkin AN, Ivchenko PV, Borisov RS, Churakov AV. Monomeric and dimeric magnesium mono-BHT complexes as effective ROP catalysts. Catalysis Communications. 2016;87:106-11.

[93] Bouyahyi M, Duchateau R. Metal-Based Catalysts for Controlled Ring-Opening Polymerization of Macrolactones: High Molecular Weight and Well-Defined Copolymer Architectures. Macromolecules. 2014;47:517-24.

[94] Jasinska-Walc L, Bouyahyi M, Rozanski A, Graf R, Hansen MR, Duchateau R. Synthetic Principles Determining Local Organization of Copolyesters Prepared from Lactones and Macrolactones. Macromolecules. 2015;48:502-10.

[95] van der Meulen I, Gubbels E, Huijser S, Sablong R, Koning CE, Heise A, et al. Catalytic Ring-Opening Polymerization of Renewable Macrolactones to High Molecular Weight Polyethylene-like Polymers. Macromolecules. 2011;44:4301-5.

[96] Pepels MPF, Bouyahyi M, Heise A, Duchateau R. Kinetic Investigation on the Catalytic Ring-Opening (Co)Polymerization of (Macro)Lactones Using Aluminum Salen Catalysts. Macromolecules. 2013;46:4324-34.

[97] Pepels MPF, Koeken RAC, van der Linden SJJ, Heise A, Duchateau R. Mimicking (Linear) Low-Density Polyethylenes Using Modified Polymacrolactones. Macromolecules. 2015;48:4779-92.

[98] Pepels MPF, Govaert LE, Duchateau R. Influence of the Main-Chain Configuration on the Mechanical Properties of Linear Aliphatic Polyesters. Macromolecules. 2015;48:5845-54.

[99] Pepels MPF, Hofman WP, Kleijnen R, Spoelstra AB, Koning CE, Goossens H, et al. Block Copolymers of "PE-Like" Poly(pentadecalactone) and Poly(L-lactide): Synthesis, Properties, and Compatibilization of Polyethylene/Poly(L-lactide) Blends. Macromolecules. 2015;48:6909-21.

[100] Pepels MPF, Hermsen I, Noordzij GJ, Duchateau R. Molecular Structure–Catalytic Activity Relationship in the Ring-Opening Polymerization of (Macro)lactones. Macromolecules. 2016;49:796-806.

[101] Rutkowski S, Zych A, Przybysz M, Bouyahyi M, Sowinski P, Koevoets R, et al. Toward Polyethylene-Polyester Block and Graft Copolymers with Tunable Polarity. Macromolecules. 2017;50:107-22.

[102] Fuoco T, Meduri A, Lamberti M, Venditto V, Pellecchia C, Pappalardo D. Ring-opening polymerization of [small omega]-6-hexadecenlactone by a salicylaldiminato aluminum complex: a route to semicrystalline and functional poly(ester)s. Polymer Chemistry. 2015;6:1727-40.

[103] Hori Y, Hongo H, Hagiwara T. Ring-opening copolymerization of (R)-beta-butyrolactone with macrolide: A new series of poly(hydroxyalkanoate)s. Macromolecules. 1999;32:3537-9.

[104] Zotzmann J, Behl M, Feng Y, Lendlein A. Copolymer Networks Based on Poly(ω-pentadecalactone) and Poly(ϵ-caprolactone)Segments as a Versatile Triple-Shape Polymer System. Adv Funct Mater. 2010;20:3583-94.

[105] Zotzmann J, Behl M, Hofmann D, Lendlein A. Reversible Triple-Shape Effect of Polymer Networks Containing Polypentadecalactone- and Poly(epsilon-caprolactone)-Segments. Advanced Materials. 2010;22:3424-9.

[106] Zotzmann J, Ziegler H-J, Behl M, Zierke M, Radke W, Lendlein A. Upscaling the synthesis of biodegradable multiblock copolymers capable of a shape-memory effect. Journal of Materials Science: Materials in Medicine. 2011;22:2147.

[107] Behl M, Zotzmann J, Lendlein A. One-way and reversible dual-shape effect of polymer networks based on polypentadecalactone segments. Journal of Artificial Organs. 2011;34:231-7.

[108] Balk M, Behl M, Nöchel U, Lendlein A. Shape-Memory Hydrogels with Switching Segments Based on Oligo(ω-pentadecalactone). Macromolecular Materials and Engineering. 2012;297:1184-92.

[109] Kratz K, Voigt U, Lendlein A. Temperature-Memory Effect of Copolyesterurethanes and their Application Potential in Minimally Invasive Medical Technologies. Advanced Functional Materials. 2012;22:3057-65.

[110] Razzaq MY, Behl M, Frank U, Koetz J, Szczerba W, Lendlein A. Oligo(ω-pentadecalactone) decorated magnetic nanoparticles. Journal of Materials Chemistry. 2012;22:9237.

[111] Matsumoto H, Ishiguro T, Konosu Y, Minagawa M, Tanioka A, Richau K, et al. Shape-memory properties of electrospun non-woven fabrics prepared from degradable polyesterurethanes containing poly(ω-pentadecalactone) hard segments. European Polymer Journal. 2012;48:1866-74.

[112] Razzaq MY, Behl M, Kratz K, Lendlein A. Multifunctional Hybrid Nanocomposites with Magnetically Controlled Reversible Shape–Memory Effect. Advanced Materials (Weinheim, Germany). 2013;25:5730-3.

[113] Razzaq MY, Behl M, Nochel U, Lendlein A. Magnetically controlled shape-memory effects of hybrid nanocomposites from oligo(omega-pentadecalactone) and covalently integrated magnetite nanoparticles. Polymer. 2014;55:5953-60.

[114] Schone AC, Schulz B, Richau K, Kratz K, Lendlein A. Characterization of Langmuir Films Prepared from Copolyesterurethanes Based on Oligo(omega-pentadecalactone) and Oligo(epsilon-caprolactone) Segments. Macromolecular Chemistry and Physics. 2014;215:2437-45.

[115] Wischke C, Lendlein A. Method for Preparation, Programming, and Characterization of Miniaturized Particulate Shape-Memory Polymer Matrices. Langmuir. 2014;30:2820-7.

[116] Wang L, Baudis S, Kratz K, Lendlein A. Characterization of bi-layered magnetic nanoparticles synthesized via two-step surface-initiated ring-opening polymerization. Pure and Applied Chemistry. 2015;87:1085-97.

[117] Fang L, Yan W, Nochel U, Kratz K, Lendlein A. Programming structural functions in phase-segregated polymers by implementing a defined thermomechanical history. Polymer. 2016;102:54-62.

[118] Schone AC, Kratz K, Schulz B, Lendlein A. The relevance of hydrophobic segments in multiblock copolyesterurethanes for their enzymatic degradation at the air-water interface. Polymer. 2016;102:92-8.

[119] Fernández J, Etxeberria A, Varga AL, Sarasua J-R. Synthesis and characterization of ω-pentadecalactone-co-ε-decalactone copolymers: Evaluation of thermal, mechanical and biodegradation properties. Polymer. 2015;81:12-22.

[120] Fernandez J, Etxeberria A, Sarasua J-R. Synthesis and properties of [small omega]-pentadecalactone-co-[small delta]-hexalactone copolymers: a biodegradable thermoplastic elastomer as an alternative to poly(?-caprolactone). RSC Advances. 2016;6:3137-49.

[121] Fernandez J, Larranaga A, Etxeberria A, Sarasua J-R. Ethylene brassylate-co-[small delta]-hexalactone biobased polymers for application in the medical field: synthesis, characterization and cell culture studies. RSC Advances. 2016;6:22121-36.

[122] Fernandez J, Amestoy H, Sardon H, Aguirre M, Varga AL, Sarasua JR. Effect of molecular weight on the physical properties of poly(ethylene brassylate) homopolymers. Journal of the Mechanical Behavior of Biomedical Materials. 2016;64:209-19.

[123] Jin CH, Wei ZY, Yu Y, Sui ML, Leng XF, Li Y. Copolymerization of ethylene brassylate with delta-valerolactone towards isodimorphic random copolyesters with continuously tunable mechanical properties. European Polymer Journal. 2018;102:90-100.

[124] Fernandez J, Montero M, Etxeberria A, Sarasua JR. Ethylene brassylate: Searching for new comonomers that enhance the ductility and biodegradability of polylactides. Polym Degrad Stabil. 2017;137:23-34.

[125] Jasinska-Walc L, Hansen MR, Dudenko DV, Rozanski A, Bouyahyi M, Wagner M, et al. Topological Behaviour Mimicking Ethylene - Hexene Copolymers Using Branched Lactones and Macrolactones. Polym Chem. 2014;5:3306-10.

[126] Chang Q, Li L, Yang DL, Zhang MY, Minh-Tan TT, Hu W, et al. Synthesis and Characterization of Poly(omega-pentadecalactone) for Its Industrial-scale Production. Chemical Research in Chinese Universities. 2015;31:640-4.

[127] Myers D, Witt T, Cyriac A, Bown M, Mecking S, Williams CK. Ring opening polymerization of macrolactones: high conversions and activities using an yttrium catalyst. Polymer Chemistry. 2017;8:5780-5.

[128] Guillaume SM, Carpentier J-F. Recent advances in metallo/organo-catalyzed immortal ring-opening polymerization of cyclic carbonates. Catal Sci Tech. 2012;2:898-906.

[129] Asano S, Aida T, Inoue S. 'Immortal' polymerization. Polymerization of epoxide catalysed by an aluminium porphyrin-alcohol system. J Chem Soc, Chem Commun. 1985:1148-9.

[130] Endo M, Aida T, Inoue S. Immortal polymerization of .epsilon.-caprolactone initiated by aluminum porphyrin in the presence of alcohol. Macromolecules. 1987;20:2982-8.

[131] Dove AP. Organic Catalysis for Ring-Opening Polymerization. ACS Macro Letters. 2012;1:1409-12.

[132] Nederberg F, Connor EF, Moller M, Glauser T, Hedrick JL. New paradigms for organic catalysts: The first organocatalytic living polymerization. Angewandte Chemie-International Edition. 2001;40:2712-5.

[133] Kamber NE, Jeong W, Waymouth RM, Pratt RC, Lohmeijer BGG, Hedrick JL. Organocatalytic ring-opening polymerization. Chem Rev. 2007;107:5813-5840.

[134] Todd R, Tempelaar S, Lo Re G, Spinella S, McCallum SA, Gross RA, et al. Poly(ω-pentadecalactone)-b-poly(l-lactide) Block Copolymers via Organic-Catalyzed Ring Opening Polymerization and Potential Applications. ACS Macro Lett. 2015;4:408-11.

[135] Bouyahyi M, Pepels MPF, Heise A, Duchateau R. ω-Pentandecalactone Polymerization and ω-Pentadecalactone/ε-Caprolactone Copolymerization Reactions Using Organic Catalysts. Macromolecules. 2012;45:3356-66.

[136] Pascual A, Sardon H, Veloso A, Ruiperez F, Mecerreyes D. Organocatalyzed Synthesis of Aliphatic Polyesters from Ethylene Brassy late: A Cheap and Renewable Macrolactone. ACS Macro Lett. 2014;3:849-53.

[137] Ladelta V, Bilalis P, Gnanou Y, Hadjichristidis N. Ring-opening polymerization of [small omega]-pentadecalactone catalyzed by phosphazene superbases. Polymer Chemistry. 2017;8:511-5.

[138] Naumann S, Thomas AW, Dove AP. Highly Polarized Alkenes as Organocatalysts for the Polymerization of Lactones and Trimethylene Carbonate. ACS Macro Letters. 2016;5:134-8.

[139] Naumann S, Scholten PBV, Wilson JA, Dove AP. Dual Catalysis for Selective Ring-Opening Polymerization of Lactones: Evolution toward Simplicity. Journal of the American Chemical Society. 2015;137:14439-45.

[140] Walther P, Naumann S. N-Heterocyclic Olefin-Based (Co)polymerization of a Challenging Monomer: Homopolymerization of ω-Pentadecalactone and Its Copolymers with γ-Butyrolactone, δ-Valerolactone, and ε-Caprolactone. Macromolecules. 2017;50:8406-16.

[141] Wang B, Pan L, Ma Z, Li Y. Ring-Opening Polymerization with Lewis Pairs and Subsequent Nucleophilic Substitution: A Promising Strategy to Well-Defined Polyethylene-like Polyesters without Transesterification. Macromolecules. 2018;51:836-45.

[142] Pascual A, Leiza JR, Mecerreyes D. Acid catalyzed polymerization of macrolactones in bulk and aqueous miniemulsion: Ring opening vs. condensation. European Polymer Journal. 2013;49:1601-9.

[143] Barrère M, Landfester K. Polyester synthesis in aqueous miniemulsion. Polymer. 2003;44:2833-41.

[144] Delgove MAF, Luchies J, Wauters I, Deroover GGP, De Wildeman SMA, Bernaerts KV. Increasing the solubility range of polyesters by tuning their microstructure with comonomers. Polymer Chemistry. 2017;8:4696-706.

[145] Ladelta V, Kim JD, Bilalis P, Gnanou Y, Hadjichristidis N. Block Copolymers of Macrolactones/Small Lactones by a “Catalyst-Switch” Organocatalytic Strategy. Thermal Properties and Phase Behavior. Macromolecules. 2018;51:2428-36.

[146] Ravichandran R, Sundarrajan S, Venugopal JR, Mukherjee S, Ramakrishna S. Advances in Polymeric Systems for Tissue Engineering and Biomedical Applications. Macromolecular Bioscience. 2012;12:286-311.

[147] Sokolsky-Papkov M, Agashi K, Olaye A, Shakesheff K, Domb AJ. Polymer carriers for drug delivery in tissue engineering. Advanced Drug Delivery Reviews. 2007;59:187-206.

[148] Saralidze K, Koole LH, Knetsch MLW. Polymeric Microspheres for Medical Applications. Materials. 2010;3:3537-64.

[149] Plikk P, Målberg S, Albertsson A-C. Design of Resorbable Porous Tubular Copolyester Scaffolds for Use in Nerve Regeneration. Biomacromolecules. 2009;10:1259-64.

[150] Jain R, Shah NH, Malick AW, Rhodes CT. Controlled Drug Delivery by Biodegradable Poly(Ester) Devices: Different Preparative Approaches. Drug Development and Industrial Pharmacy. 1998;24:703-27.

[151] Jiao Y-P, Cui F-Z. Surface modification of polyester biomaterials for tissue engineering. Biomedical Materials. 2007;2:R24.

[152] Goddard JM, Hotchkiss JH. Polymer surface modification for the attachment of bioactive compounds. Progress in Polymer Science. 2007;32:698-725.

[153] Uyama H, Suda S, Kobayashi S. Enzymatic synthesis of terminal-functionalized polyesters by initiator method. Acta Polymerica. 1998;49:700-3.

[154] Descour C, Macko T, Schreur-Piet I, Pepels MPF, Duchateau R. In situ compatibilisation of alkenyl-terminated polymer blends using cross metathesis. RSC Advances. 2015;5:9658-66.

[155] Kalra B, Kumar A, Gross RA, Baiardo M, Scandola M. Chemoenzymatic Synthesis of New Brush Copolymers Comprising Poly(ω-pentadecalactone) with Unusual Thermal and Crystalline Properties. Macromolecules. 2004;37:1243-50.

[156] Takwa M, Xiao Y, Simpson N, Malmstrom E, Hult K, Koning CE, et al. Lipase catalyzed HEMA initiated ring-opening polymerization: In situ formation of mixed polyester methacrylates by transesterification. Biomacromolecules. 2008;9:704-10.

[157] Xiao Y, Takwa M, Hult K, Koning CE, Heise A, Martinelle M. Systematic Comparison of HEA and HEMA as Initiators in Enzymatic Ring-Opening Polymerizations. Macromol Biosci. 2009;9:713-20.

[158] Uyama H, Kikuchi H, Kobayashi S. One-Shot Synthesis Of Polyester Macromonomer By Enzymatic Ring-Opening Polymerization Of Lactone In The Presence Of Vinyl Ester. Chem Lett. 1995:1047-8.

[159] Uyama H, Kikuchi H, Kobayashi S. Single-step acylation of polyester terminals by enzymatic ring-opening polymerization of 12-dodecanolide in the presence of acyclic vinyl esters. B Chem Soc Jpn. 1997;70:1691-5.

[160] Korzhikov VA, Gusevskaya KV, Litvinchuk EN, Vlakh EG, Tennikova TB. Enzyme-Mediated Ring-Opening Polymerization of Pentadecalactone to Obtain Biodegradable Polymer for Fabrication of Scaffolds for Bone Tissue Engineering. Int J Polym Sci. 2013;2013:10.

[161] Takwa M, Simpson N, Malmström E, Hult K, Martinelle M. One-Pot Difunctionalization of Poly(ω-pentadecalactone) with Thiol-Thiol or Thiol-Acrylate Groups, Catalyzed by Candida antarctica Lipase B. Macromol Rapid Commun. 2006;27:1932-6.

[162] Takwa M, Hult K, Martinelle M. Single-step, solvent-free enzymatic route to alpha,omega-functionalized polypentadecalactone macromonomers. Macromolecules. 2008;41:5230-6.

[163] Simpson N, Takwa M, Hult K, Johansson M, Martinelle M, Malmström E. Thiol-Functionalized Poly(ω-pentadecalactone) Telechelics for Semicrystalline Polymer Networks. Macromolecules. 2008;41:3613-9.

[164] Kumar A, Gross RA, Wang Y, Hillmyer MA. Recognition by Lipases of ω-Hydroxyl Macroinitiators for Diblock Copolymer Synthesis. Macromolecules. 2002;35:7606-11.

[165] Chen JC, Li JZ, Liu JH, Xu LQ. Amphiphilic poly(ethylene glycol)-b-poly(ethylene brassylate) copolymers: One-pot synthesis, self-assembly, and controlled drug release. Chinese Chemical Letters. 2015;26:1319-21.

[166] Bansal KK, Kakde D, Purdie L, Irvine DJ, Howdle SM, Mantovani G, et al. New biomaterials from renewable resources - amphiphilic block copolymers from delta-decalactone. Polymer Chemistry. 2015;6:7196-210.

[167] Bansal KK, Gupta J, Rosling A, Rosenholm JM. Renewable poly(delta-decalactone) based block copolymer micelles as drug delivery vehicle: in vitro and in vivo evaluation. Saudi Pharmaceutical Journal. 2018;26:358-68.

[168] Pflughaupt RL, Hopkins SA, Wright PM, Dove AP. Synthesis of poly(ω-pentadecalactone)-b-poly(acrylate) diblock copolymers via a combination of enzymatic ring-opening and RAFT polymerization techniques. Journal of Polymer Science Part A: Polymer Chemistry. 2016;54:3326-35.

[169] Chen JC, Li JZ, Liu JH, Weng B, Xu LQ. Synthesis and self-assembly of four-armed star copolymer based on poly(ethylene brassylate) hydrophobic block as potential drug carries. Journal of Nanoparticle Research. 2016;18.

[170] Arnebold A, Hartwig A. Fast switchable, epoxy based shape-memory polymers with high strength and toughness. Polymer. 2016;83:40-9.

[171] Pilate F, Stoclet G, Mincheva R, Dubois P, Raquez JM. Poly(epsilon-caprolactone) and Poly(omega-pentadecalactone)-Based Networks with Two-Way Shape-Memory Effect through 2+2 Cycloaddition Reactions. Macromolecular Chemistry and Physics. 2018;219.

[172] Jérôme C, Lecomte P. Recent advances in the synthesis of aliphatic polyesters by ring-opening polymerization. Advanced Drug Delivery Reviews. 2008;60:1056-76.

[173] Vaida C, Keul H, Moeller M. Tailor-made polyesters based on pentadecalactone via enzymatic catalysis. Green Chem. 2011;13:889-99.

[174] van der Meulen I, de Geus M, Antheunis H, Deumens R, Joosten EAJ, Koning CE, et al. Polymers from Functional Macrolactones as Potential Biomaterials: Enzymatic Ring Opening Polymerization, Biodegradation, and Biocompatibility. Biomacromolecules. 2008;9:3404-10.

[175] van der Meulen I, Li Y, Deumens R, Joosten EAJ, Koning CE, Heise A. Copolymers from Unsaturated Macrolactones: Toward the Design of Cross-Linked Biodegradable Polyesters. Biomacromolecules. 2011;12:837-43.

[176] Van Der Mee L, Antens J, Van De Kruijs B, Palmans ARA, Meijer EW. Oxo-crown-ethers as comonomers for tuning polyester properties. J Polym Sci, Part A: Polym Chem. 2006;44:2166-76.

[177] Illy N, Taylan E, Brissault B, Wojno J, Boileau S, Barbier V, et al. Synthesis and anionic ring-opening polymerization of crown-ether-like macrocyclic dilactones: An alternative route to peg-containing polyesters PEG-containing polyesters and related networks. European Polymer Journal. 2013;49:4087-97.

[178] Manzini B, Hodge P, Ben-Haida A. Entropically-driven ring-opening polymerization of macrocyclic esters with up to 84-membered rings catalysed by polymer-supported Candida antarctica lipase B. Polymer Chemistry. 2010;1:339-46.

[179] Jiang Z, Azim H, Gross RA, Focarete ML, Scandola M. Lipase-Catalyzed Copolymerization of ω-Pentadecalactone with p-Dioxanone and Characterization of Copolymer Thermal and Crystalline Properties. Biomacromolecules. 2007;8:2262-9.

[180] Liu J, Jiang Z, Zhang S, Liu C, Gross RA, Kyriakides TR, et al. Biodegradation, biocompatibility, and drug delivery in poly(ω-pentadecalactone-co-p-dioxanone) copolyesters. Biomaterials. 2011;32:6646-54.

[181] Magusin PCMM, Mezari B, van der Mee L, Palmans ARA, Meijer EW. Novel Biodegradable Poly(pentadecalactone-co-oxo-crown ether) Studied with Solid-State 1H and 13C NMR. Macromol Symp. 2005;230:126-32.

[182] Pepels MPF, van der Sanden F, Gubbels E, Duchateau R. Catalytic Ring-Opening (Co)polymerization of Semiaromatic and Aliphatic (Macro)lactones. Macromolecules. 2016;49:4441-51.

[183] Wisse E, Renken RAE, Roosma JR, Palmans ARA, Meijer EW. Poly(caprolactone-co-oxo-crown ether)-based poly(urethane)urea for soft tissue engineering applications. Biomacromolecules. 2007;8:2739-45.

[184] Focarete ML, Gazzano M, Scandola M, Kumar A, Gross RA. Copolymers of ω-Pentadecalactone and Trimethylene Carbonate from Lipase Catalysis:  Influence of Microstructure on Solid-State Properties. Macromolecules. 2002;35:8066-71.

[185] Veld MAJ, Palmans ARA, Meijer EW. Selective polymerization of functional monomers with novozym 435. Journal of Polymer Science Part a-Polymer Chemistry. 2007;45:5968-78.

[186] Uyama H, Kobayashi S, Morita M, Habaue S, Okamoto Y. Chemoselective ring-opening polymerization of a lactone having exo-methylene group with lipase catalysis. Macromolecules. 2001;34:6554-6.

[187] Habaue S, Asai M, Morita M, Okamoto Y, Uyama H, Kobayashi S. Chemospecific ring-opening polymerization of α-methylenemacrolides. Polymer. 2003;44:5195-200.

[188] Habaue S, Morita M, Okamoto Y. Stereospecific anionic polymerization of alpha-(alkoxymethyl)acrylate derivatives affording novel vinyl polymers with macrocyclic side chains. Polymer. 2002;43:3469-74.

[189] Habaue S, Morita M, Okamoto Y. Anionic polymerization of macrocyclic alpha-(alkoxymethyl)acrylates leading to novel vinyl polymer with crown ether type side chain. Macromolecules. 2002;35:2432-4.

[190] Ates Z, Thornton PD, Heise A. Side-chain functionalisation of unsaturated polyesters from ring-opening polymerisation of macrolactones by thiol-ene click chemistry. Polym Chem. 2011;2:309-12.

[191] Ates Z, Heise A. Functional films from unsaturated poly(macrolactones) by thiol-ene cross-linking and functionalisation. Polymer Chemistry. 2014;5:2936-41.

[192] Ates Z, Audouin F, Harrington A, O'Connor B, Heise A. Functional Brush-Decorated Poly(globalide) Films by ARGET-ATRP for Bioconjugation. Macromolecular Bioscience. 2014;14:1600-8.

[193] de Oliveira FCS, Olvera D, Sawkins MJ, Cryan S-A, Kimmins SD, da Silva TE, et al. Direct UV-Triggered Thiol–ene Cross-Linking of Electrospun Polyester Fibers from Unsaturated Poly(macrolactone)s and Their Drug Loading by Solvent Swelling. Biomacromolecules. 2017;18:4292-8.

[194] Claudino M, van der Meulen I, Trey S, Jonsson M, Heise A, Johansson M. Photoinduced thiol-ene crosslinking of globalide/ε-caprolactone copolymers: Curing performance and resulting thermoset properties. J Polym Sci, Part A: Polym Chem. 2012;50:16-24.

[195] Wang KJ, Jia YG, Zhu XX. Two-Way Reversible Shape Memory Polymers Made of Cross-Linked Cocrystallizable Random Copolymers with Tunable Actuation Temperatures. Macromolecules. 2017;50:8570-9.

[196] Yu Y, Wu D, Liu CB, Zhao ZH, Yang Y, Li QS. Lipase/esterase-catalyzed synthesis of aliphatic polyesters via polycondensation: A review. Process Biochemistry. 2012;47:1027-36.

[197] Namekawa S, Uyama H, Kobayashi S. Enzymatic Synthesis of Polyesters from Lactones, Dicarboxylic Acid Divinyl Esters, and Glycols through Combination of Ring-Opening Polymerization and Polycondensation. Biomacromolecules. 2000;1:335-8.

[198] Thompson CJ, Hansford D, Higgins S, Rostron C, Hutcheon GA, Munday DL. Evaluation of ibuprofen-loaded microspheres prepared from novel copolyesters. International Journal of Pharmaceutics. 2007;329:53-61.

[199] Gaskell EE, Hobbs G, Rostron C, Hutcheon GA. Encapsulation and release of alpha-chymotrypsin from poly(glycerol adipate-co-omega-pentadecalactone) microparticles. Journal of Microencapsulation. 2008;25:187-95.

[200] Thompson CJ, Hansford D, Munday DL, Higgins S, Rostron C, Hutcheon GA. Synthesis and evaluation of novel polyester-ibuprofen conjugates for modified drug release. Drug Development and Industrial Pharmacy. 2008;34:877-84.

[201] Thompson CJ, Hansford D, Higgins S, Rostron C, Hutcheon GA, Munday DL. Preparation and evaluation of microspheres prepared from novel polyester-ibuprofen conjugates blended with non-conjugated ibuprofen. Journal of Microencapsulation. 2009;26:676-83.

[202] Tawfeek H, Khidr S, Samy E, Ahmed S, Murphy M, Mohammed A, et al. Poly(Glycerol Adipate-co-omega-Pentadecalactone) Spray-Dried Microparticles as Sustained Release Carriers for Pulmonary Delivery. Pharmaceutical Research. 2011;28:2086-97.

[203] Jan SU, Khan GM, Hussain I, Gaskell EE, Hutcheon GH. Synthesis, conjugation and evaluation of some novel polymers and their micro particles for sustained release drug formulations. Pakistan Journal of Pharmaceutical Sciences. 2013;26:741-6.

[204] Tawfeek HM, Khidr SH, Samy EM, Ahmed SM, Gaskell EE, Hutcheon GA. Evaluation of biodegradable polyester-co-lactone microparticles for protein delivery. Drug Development and Industrial Pharmacy. 2014;40:1213-22.

[205] Alfagih I, Kunda N, Alanazi F, Dennison SR, Somavarapu S, Hutcheon GA, et al. Pulmonary Delivery of Proteins Using Nanocomposite Microcarriers. J Pharm Sci. 2015;104:4386-98.

[206] Kunda NK, Alfagih IM, Dennison SR, Tawfeek HM, Somavarapu S, Hutcheon GA, et al. Bovine Serum Albumin Adsorbed PGA-co-PDL Nanocarriers for Vaccine Delivery via Dry Powder Inhalation. Pharmaceutical Research. 2015;32:1341-53.

[207] Tawfeek HM, Abdellatif AAH, Dennison TJ, Mohammed AR, Sadiq Y, Saleem IY. Colonic delivery of indometacin loaded PGA-co-PDL microparticles coated with Eudragit L100-55 from fast disintegrating tablets. International Journal of Pharmaceutics. 2017;531:80-9.

[208] Rodrigues TC, Oliveira MLS, Soares-Schanoski A, Chavez-Rico SL, Figueiredo DB, Goncalves VM, et al. Mucosal immunization with PspA (Pneumococcal surface protein A)-adsorbed nanoparticles targeting the lungs for protection against pneumococcal infection. Plos One. 2018;13:e0191692.

[209] Tawfeek HM, Evans AR, Iftikhar A, Mohammed AR, Shabir A, Somavarapu S, et al. Dry powder inhalation of macromolecules using novel PEG-co-polyester microparticle carriers. International Journal of Pharmaceutics. 2013;441:611-9.

[210] Tawfeek HM. Evaluation of PEG and mPEG-co-(PGA-co-PDL) microparticles loaded with sodium diclofenac. Saudi Pharmaceutical Journal. 2013;21:387-97.

[211] Jiang Z. Lipase-Catalyzed Synthesis of Aliphatic Polyesters via Copolymerization of Lactone, Dialkyl Diester, and Diol. Biomacromolecules. 2008;9:3246-51.

[212] Mazzocchetti L, Scandola M, Jiang Z. Enzymatic Synthesis and Structural and Thermal Properties of Poly(ω-pentadecalactone-co-butylene-co-succinate). Macromolecules. 2009;42:7811-9.

[213] Liu J, Jiang Z, Zhang S, Saltzman WM. Poly(ω-pentadecalactone-co-butylene-co-succinate) nanoparticles as biodegradable carriers for camptothecin delivery. Biomaterials. 2009;30:5707-19.

[214] Mazzocchetti L, Scandola M, Jiang Z. Copolymers of ethyl glycolate and ω–pentadecalactone: Enzymatic synthesis and solid-state characterization. European Polymer Journal. 2011;47:942-8.

[215] Voevodina I, Scandola M, Zhang J, Jiang Z. Exploring the solid state properties of enzymatic poly(amine-co-ester) terpolymers to expand their applications in gene transfection. RSC Adv. 2014;4:8953-61.

[216] Zhou J, Liu J, Cheng CJ, Patel TR, Weller CE, Piepmeier JM, et al. Biodegradable poly(amine-co-ester) terpolymers for targeted gene delivery. Nature Materials. 2011;11:82.

[217] Liu B, Zhang XF, Chen Y, Yao ZC, Yang Z, Gao D, et al. Enzymatic synthesis of poly(omega-pentadecalactone-co-butylene-co-3,3 '-dithiodipropionate) copolyesters and self-assembly of the PEGylated copolymer micelles as redox-responsive nanocarriers for doxorubicin delivery. Polymer Chemistry. 2015;6:1997-2010.

[218] Jiang Z. Lipase-Catalyzed Copolymerization of Dialkyl Carbonate with 1,4-Butanediol and ω-Pentadecalactone: Synthesis of Poly(ω-pentadecalactone-co-butylene-co-carbonate). Biomacromolecules. 2011;12:1912-9.

[219] Mazzocchetti L, Scandola M, Jiang Z. Random copolymerization with a large lactone enhances aliphatic polycarbonate crystallinity. Eur Polym J. 2012;48:1883-91.

[220] Martino L, Scandola M, Jiang Z. Enzymatic synthesis, thermal and crystalline properties of a poly(β–amino ester) and poly(lactone-co-β–amino ester) copolymers. Polymer. 2012;53:1839-48.

[221] Hua G, Odelius K. Exploiting Ring-Opening Aminolysis-Condensation as a Polymerization Pathway to Structurally Diverse Biobased Polyamides. Biomacromolecules. 2018;19:1573-81.

[222] Zhang XF, Liu B, Yang Z, Zhang C, Li H, Luo X, et al. Micelles of enzymatically synthesized PEG-poly(amine-co-ester) block copolymers as pH-responsive nanocarriers for docetaxel delivery. Colloids and Surfaces B-Biointerfaces. 2014;115:349-58.

[223] Zhang XF, Tang WX, Yang Z, Luo XG, Luo HY, Gao D, et al. PEGylated poly(amine-co-ester) micelles as biodegradable non-viral gene vectors with enhanced stability, reduced toxicity and higher in vivo transfection efficacy. Journal of Materials Chemistry B. 2014;2:4034-44.

[224] Chen Y, Su MF, Li YQ, Gao JB, Zhang C, Cao Z, et al. Enzymatic PEG-Poly(amine-co-disulfide ester) Nanoparticles as pH-and Redox-Responsive Drug Nanocarriers for Efficient Antitumor Treatment. Acs Applied Materials & Interfaces. 2017;9:30519-35.

[225] Chen Y, Li YQ, Gao JB, Cao Z, Jiang Q, Liu J, et al. Enzymatic PEGylated Poly(lactone-co-beta-amino ester) Nanoparticles as Biodegradable, Biocompatible and Stable Vectors for Gene Delivery. Acs Applied Materials & Interfaces. 2016;8:490-501.

[226] Eriksson M, Fogelstrom L, Hult K, Malmstrom E, Johansson M, Trey S, et al. Enzymatic One-Pot Route to Telechelic Polypentadecalactone Epoxide: Synthesis, UV Curing, and Characterization. Biomacromolecules. 2009;10:3108-13.

[227] Seyednejad H, Ghassemi AH, van Nostrum CF, Vermonden T, Hennink WE. Functional aliphatic polyesters for biomedical and pharmaceutical applications. Journal of Controlled Release. 2011;152:168-76.

[228] Amass W, Amass A, Tighe B. A review of biodegradable polymers: uses, current developments in the synthesis and characterization of biodegradable polyesters, blends of biodegradable polymers and recent advances in biodegradation studies. Polymer International. 1998;47:89-144.

[229] Vert M. Aliphatic Polyesters:  Great Degradable Polymers That Cannot Do Everything. Biomacromolecules. 2005;6:538-46.

[230] Gazzano M, Malta V, Focarete ML, Scandola M, Gross RA. Crystal structure of poly(ω-pentadecalactone). Journal of Polymer Science Part B: Polymer Physics. 2003;41:1009-13.

[231] Cai J, Hsiao BS, Gross RA. Polypentadecalactone prepared by lipase catalysis: crystallization kinetics and morphology. Polymer International. 2009;58:944-53.

[232] de Geus M, van der Meulen I, Goderis B, van Hecke K, Dorschu M, van der Werff H, et al. Performance polymers from renewable monomers: high molecular weight poly(pentadecalactone) for fiber applications. Polym Chem. 2010;1:525-33.

[233] Cai JL, Hsiao BS, Gross RA. Real-Time Structure Changes during Uniaxial Stretching of Poly (omega-pentadecalactone) by in Situ Synchrotron WAXD/SAXS Techniques. Macromolecules. 2011;44:3874-83.

[234] Jeremic D. Ullmann’s Encyclopedia of Industrial Chemistry. Weinheim, Germany: Wiley-VCH; 2014.

[235] Wilsens CHRM, Pepels MPF, Spoelstra AB, Portale G, Auhl D, Deshmukh YS, et al. Improving Stiffness, Strength, and Toughness of Poly(ω-pentadecalactone) Fibers through in Situ Reinforcement with a Vanillic Acid-Based Thermotropic Liquid Crystalline Polyester. Macromolecules. 2016;49:2228-37.

[236] Ye HM, Yao SF. Supernucleating Role of Poly(omega-pentadecalactone) during the Crystallization of Poly(epsilon-caprolactone) Composites. Industrial & Engineering Chemistry Research. 2017;56:13725-33.

[237] Ulery BD, Nair LS, Laurencin CT. Biomedical applications of biodegradable polymers. Journal of Polymer Science Part B: Polymer Physics. 2011;49:832-64.

[238] Azevedo HS, Reis RL. Understanding the Enzymatic Degradation of Biodegradable Polymers and Strategies to Control Their Degradation Rate. In: Reis RL, Roman JS, editors. Biodegradable Systems in Tissue Engineering and Regenerative Medicine. USA: CRC Press; 2005.

[239] Ceccorulli G, Scandola M, Kumar A, Kalra B, Gross RA. Cocrystallization of random copolymers of omega-pentadecalactone and epsilon-caprolactone synthesized by lipase catalysis. Biomacromolecules. 2005;6:902-7.

[240] Focarete ML, Gualandi C, Scandola M, Govoni M, Giordano E, Foroni L, et al. Electrospun Scaffolds of a Polyhydroxyalkanoate Consisting of omega-Hydroxylpentadecanoate Repeat Units: Fabrication and In Vitro Biocompatibility Studies. Journal of Biomaterials Science-Polymer Edition. 2010;21:1283-96.

[241] Ziemba AM, Lane KP, Segundo IMS, D'Amato AR, Mason AK, Sexton RJ, et al. Poly-L-lactic acid-co-poly(pentadecalactone) Electrospun Fibers Result in Greater Neurite Outgrowth of Chick Dorsal Root Ganglia in Vitro Compared to Poly-L-lactic Acid Fibers. Acs Biomaterials Science & Engineering. 2018;4:1491-7.

[242] Albertsson A-C, Varma IK. Aliphatic Polyesters: Synthesis, Properties and Applications. Degradable Aliphatic Polyesters. Berlin, Heidelberg: Springer Berlin Heidelberg; 2002. p. 1-40.