



# ANIONIC, CATIONIC AND CO-ORDINATION INSERTION RING OPENING POLYMERIZATION MECHANISMS OF POLYLACTIDE USING VARIOUS INITIATORS

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**Abstract:** Biodegradable polymers degrade completely when exposed to microorganisms, aerobic and anaerobic processes. Poly (lactic acid), PLA is one of the most promising biodegradable polymers (biopolymers). PLA has excellent mechanical, thermal and barrier properties. PLA can be synthesized by two major routes, first route involves removal of water by the use of solvent under high vacuum and high temperature (condensation polymerization) to yield low molecular weight of polylactide and the other route, water is removed under mild conditions to give an intermediate dimer (the lactide), which on ring-opening polymerization gives high molecular weight PLA. Three major polymerization mechanisms: cationic, anionic, and coordination-insertion have been discussed in this paper by using various initiators.

**Index Terms - Poly (lactic acid), synthesis, polycondensation, ring-opening polymerization, reaction mechanism.**

## I. INTRODUCTION

Poly (lactic acid), PLA is the first commodity bio based polymer which can be synthesised from the renewable resources. PLA is a clear, colourless thermoplastic when quenched from the melt and is similar in many respects to polystyrene. The hardness, stiffness, impact strength and elasticity of PLA, important for applications such as beverage flasks, are similar to those for (polyethylene terephthalate) PET. PLA slowly degrades by hydrolysis in even a slightly moist environment over a period of several months to a year to environmentally friendly products, which, in turn, biodegrade to carbon dioxide, methane and water. The degradation may occur via different pathway, such as catalysis of aerobic or anaerobic microorganisms, biologically active processes (e.g., enzyme reactions), and hydrolytic cleavage [1]. Polylactide is used in various medical applications including as carriers for controlled release drug delivery systems, and in biodegradable pins, screws, and cell scaffolds in tissue engineering. Large number of initiators is used for the synthesis of PLA. Stannous octoate  $\text{Sn}(\text{Oct})_2$  has been widely used as the initiator [2-5].  $\text{Sn}(\text{Oct})_2$  is very efficient, its cytotoxicity, however, has recently caused deep concern about biosafety of the materials synthesized from it and used for man-purpose [6-9]. A number of iron compounds have been found in living organisms and in nature. They are regarded as less harmful than most other metal compounds. Attempts have been made to use ferric oxide [10-11], ferric chloride [11-12], iron porphyrins [13], iron lactate [14] and monocarboxylic iron derivatives [15] as initiators for the polymerization of lactones. The ring-opening polymerization requires the use of heavy metals- based catalysts, such as oxides of Zn and Sn, chlorides of zinc and tin, or stannous octoate, which commonly contaminate the obtained polymer. This contamination of PLA could limit some specific applications on food packaging engineering and medical system. In addition, high-purity monomers for PLA ring opening polymerization are needed, and severe conditions of temperature and vacuum must be used. Based on the above disadvantages of the ring opening polymerization methods, some researchers have focused on choosing nontoxic catalysts, using some special treatment, or exploring other polymerization ways [16].

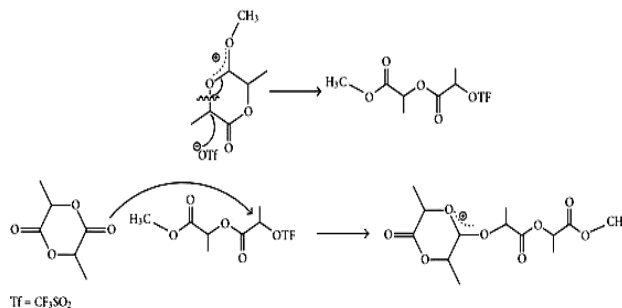
Stannous octoate, dibutyltindimethoxide and zinc stearate with co initiator triphenylphosphine were used for the ring opening polymerization [17]. A review article is showing various mechanism of ring opening polymerization of polylactide using various initiators like Stannous octoate, zinc etc [18,19]. A detailed account of the relevant mechanism and kinetics is provided to better understand the role of each external field in polymerization [20]. The ring-opening transesterification polymerization (ROTEP) of rac-lactide (rac-LA) using LXZn catalysts (LX = ligand having phenolate, amine, and pyridine donors with variable para substituents X on the bound phenolate donor; X =  $\text{NO}_2$ , Br, t-Bu, OMe) was evaluated through kinetics experiments and density functional theory, with the aim of determining how electronic modulation of the ligand framework influences polymerization rate, selectivity, and control [21]. Three major polymerization mechanisms, cationic, anionic, and coordination-insertion were used for the synthesis of PLA and each is described in detail.

## II. POLYMERIZATION MECHANISM

### 2.1 Cationic Ring-Opening Polymerization

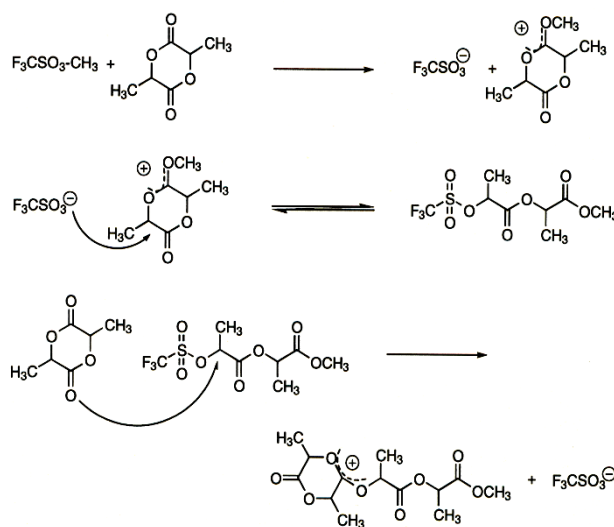
The cationic ring-opening polymerization involves the formation of a positively charged species which are subsequently attacked by a monomer. The attack results in ring opening of the positively charged species through the  $S_N2$  type process. The cationic ring-opening polymerization reaction of lactones has been achieved using alkylating agents, acylating agents, Lewis acids and protic acids.

Methyl triflate (MeOTf) was found to be a useful initiator for the cationic ring-opening polymerization reaction of L-lactide. The reactions were performed in nitrobenzene for 48 hr and at optimized 50 °C. The methyl ester end groups were formed when methyl triflate was used as the initiator and it was suggested that the polymerization proceeds by cleavage of the alkyl-oxygen bond rather than the acyl-oxygen bond. According to their proposal, reaction propagates through the activation of the monomer by methylation with methyl triflate followed by  $S_N2$  attack of the triflate anion on the positively charged lactide ring with the inversion of stereochemistry. Propagation was proposed to proceed by nucleophilic attack by lactide on the activated cationic chain end with inversion, leading to net retention of the configuration [18]. The polymerization proceeded by the cleavage of the alkyl-oxygen bond rather than the acyl-oxygen bond (Fig. 1).



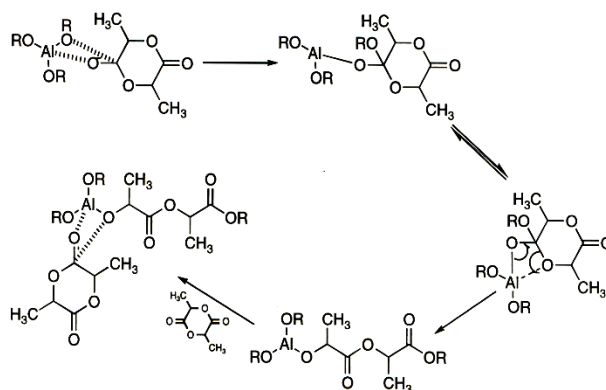
**Figure 1** Proposed pathway for cationic ring-opening polymerization of lactone

Trifluoromethane sulfonic acid (triflic acid) and methyl trifluoromethanes sulfonic acid (methyl triflate) are the only cationic initiators to polymerize lactide [22-24]. The polymerization proceeds via triflate ester end-groups instead of free carbenium ions, which yields, at low temperatures (<100 °C), an optically active polymer without racemization. The chain growth proceeds by cleavage of the alkyl oxygen bond. The propagation mechanism begins with the positively charged lactide ring being cleaved at the alkyl-oxygen bond by an  $S_N2$  attack by the triflate anion. The triflate end-group reacts with a second molecule of lactide again in an  $S_N2$  fashion to yield a positively charged lactide. Then the triflate anion again opens the charged lactide, and polymerization proceeds [18]. The cationic polymerization mechanism with methyl trifluoromethanes sulfonic acid (methyl triflate) initiator is shown in Figure 2.



**Figure 2** Cationic ring-opening polymerization mechanism of PLA using methyl triflate

The ring-opening polymerization of lactides in toluene at 70 °C with an effective initiator aluminium isopropoxide was studied which generally proceeds through a coordination-insertion mechanism. It involves the insertion of the lactide into the initiator bond with acyl-oxygen cleavage [18] is shown in Figure 3.

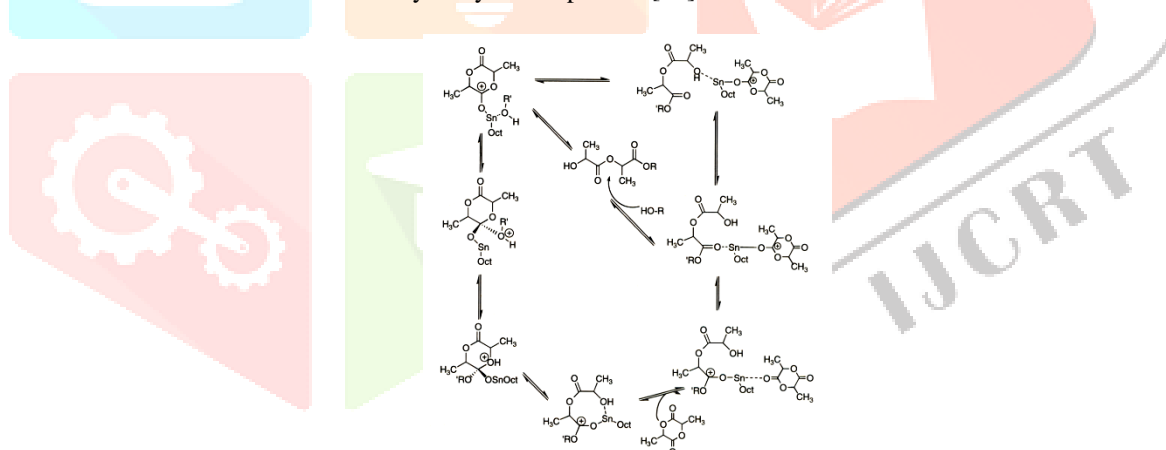


**Figure 3** Polymerization mechanism of PLA using Aluminum Isopropoxide

Nijenhuis *et al.* (1992) studied the kinetics and mechanism of L- lactide bulk polymerization using stannous octoate and zinc bis (2,2-dimethyl-3,5-heptanedionate-O,O'). Up to 80% conversion, the rate of polymerization using tin compound was higher than that with zinc-containing catalyst, while at conversions beyond 80%, the latter catalyst gave the higher rate of polymerization. Crystallization of the newly formed polymer has an accelerating effect on the polymerization. The differences in the rate of polymerizations at high conversion for the two catalysts have been suggested to be caused by a difference in crystallinity of the newly formed polymer. It is further suggested that contaminants in the catalyst (such as tin-oxo or tin-hydroxyl contaminants) and the monomer are the true initiators. Initiation as well as polymerization proceeds through a Lewis acid catalyzed transesterification reaction between an activated lactone and a hydroxyl group [26].

Zhang *et al.* (1994) studied the effect of hydroxyl and carboxylic acid on the polymerization of lactide in the presence of stannous octoate as a catalyst. Stannous octoate and alcohol react to form stannous alkoxide as a reaction product. This polymerization was initiated by coordination insertion of lactide. Hydroxyl substances affect the polymerization through reactions lead to initiator formation, chain transfer, and transesterification. Carboxylic acids affect the polymerization by deactivation reaction [27].

Various authors have described mechanisms for the tin octoate catalyzed polymerization of lactide but only a few have incorporated the effect the impurities on the polymerization. Figure 4 is a hypothetical reaction mechanism put forth by (Du *et al.*, 1995) which includes the effect of different hydroxylic compounds [29].



**Figure 4** Polymerization mechanism of lactide in presence of stannous octoate

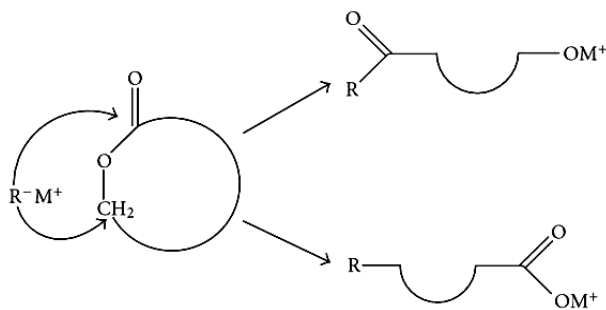
Schwach *et al.* (1997) reexamined the ring-opening polymerization of PLA in the presence of stannous octoate under conditions allowing for the end-group characterization of growing chains by high-resolution <sup>1</sup>H-NMR. For low values of monomer to initiator ratios, the DL- lactide ring was opened to yield lactyl octoate-terminated short chains [29].

Stannous (II) trifluoromethane sulfonate and scandium(III) trifluoromethane sulfonate have also been studied as catalysts for PLA synthesis. It was found that polymers of predictable molecular weights and narrow polydispersities could be obtained. The addition of base either as a solvent or as an additive significantly enhanced the polymerization rate with minimal loss to the polymerization control [30].

Atthoff and co-workers reported bulk ring-opening polymerization of lactide at 130 °C using 5 mol% diphenylammonium triflate (DPAT) as an acid-proton initiator in ethanol as initiator. Under these conditions, they were able to get PLA with molecular weight up to 12000 g/mol with dispersity 1.24 to 1.51 in 4 days. They also suggested that such a high dispersity is due to transesterification with prolonged reaction time [31].

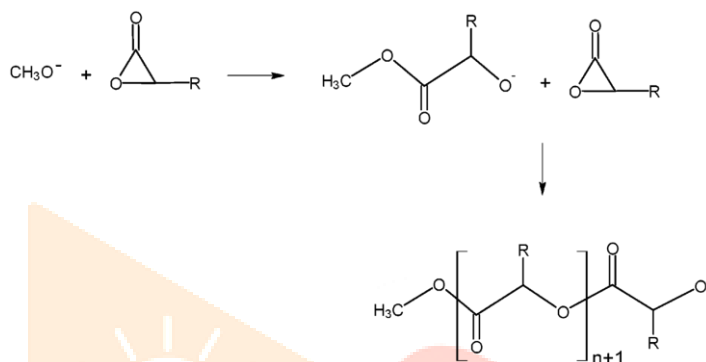
## 2.2 Anionic Ring-Opening Polymerization

The effective initiators for anionic polymerization of lactones are alkali metals, alkali metal oxides, alkali metal naphthalenide complexes with crown ethers, etc. The reaction is initiated by nucleophilic attack of negatively charged initiator on the carbon of the carbonyl group or on the alkyl-oxygen, resulting in formation of linear polyester [32]. The polymerization of β- lactones proceeds through alkyl-oxygen or acyl-oxygen cleavage giving both carboxylate and alkoxide end groups (Fig. 5).



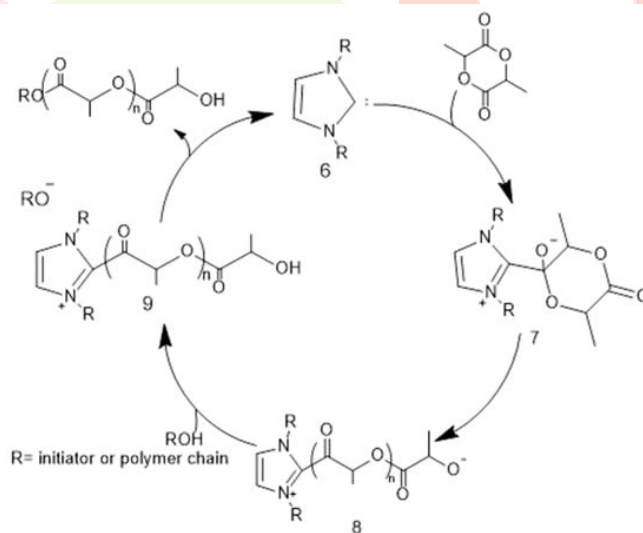
**Figure 5** Initiation of ring-opening polymerization of lactones

In larger lactones, such as caprolactone or lactide, the reaction proceeds by the acyl-oxygen scission only thereby leading to the formation of an alkoxide ion as the propagating species (Figure 6).



**Figure 6** Anionic polymerization of lactone showing acyl oxygen

A third mechanism for acquiring high molecular weight PLA is through nucleophilic activation of the polymer chain end. Nucleophilic activation is one the most efficient way to homopolymerize DL-LA and was consequently used for synthesizing the first PDLLA block with terminal OH groups. Nucleophilic catalysts, such as N-heterocyclic carbenes [33] (NHCs, e.g.,6, Figure 7)



**Figure 7** Ring-opening polymerization of lactide by a mechanism involving nucleophilic activation of the polymer chain end in the presence of an N-heterocyclic carbene catalyst

The anionic polymerization of lactide has gained little interest until today. Kricheldorf et al., was the first who reported that various strong bases (including  $\text{LiAlH}_4$ ) initiate the anionic polymerization of L-lactide in toluene solution [34] (Figure 8). Kricheldorf et al. found that initiators of higher nucleophilicity are required for initiating the lactide [35]. Weaker bases, such as potassium benzoate, potassium phenoxide, or zinc stearate, do not act as initiators at low temperatures, rather than high temperatures ( $120\text{ }^\circ\text{C}$ ) [36]. They found out that only tert-BuOK and BuLi are effective initiators, but molecular weight was low and fast racemization occurred.

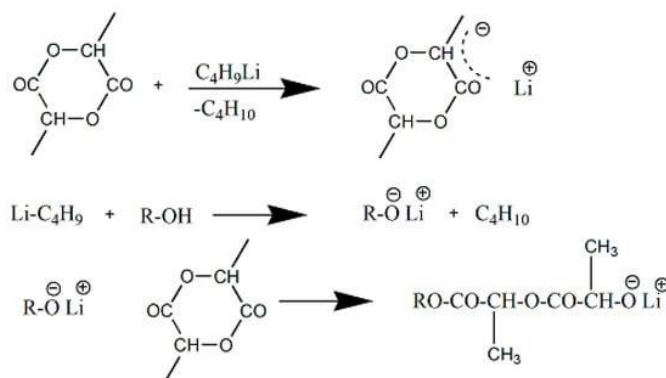


Figure 8 Anionic ROP of LA for PLA

Anionic ring-opening polymerization of cyclic ester monomers takes place by the nucleophilic attack of a negatively charged initiator on the carbonyl carbon or on the carbon atom adjacent to the acyl-oxygen, resolving in linear polyester (Figure 9). The propagating species are negatively charged and counter-balanced with a positive ion [38].

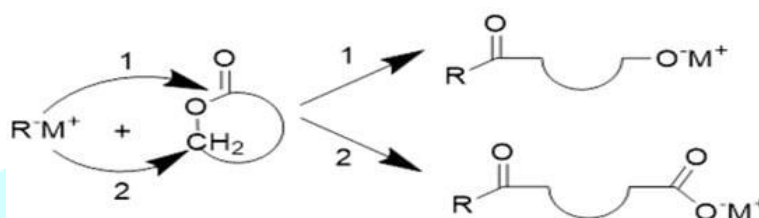


Figure 9 Ring-opening of monomer by (1) acyl- oxygen bond cleavage and (2) alkyl-oxygen bond cleavage

#### Proposed Anionic Ring-Opening Polymerization Mechanism of Stannous Octoate

The sequence of ring-opening polymerization mechanism for PLA using stannous octoate is shown in Fig. 10 and Fig. 11. The Stannous octoate opens the ring at O=CH-O- position of the monomer molecule giving rise to product  $P_j$  and the sequence continues further as shown ultimately giving a polymer  $M_j$  and stannous octoate back [17].

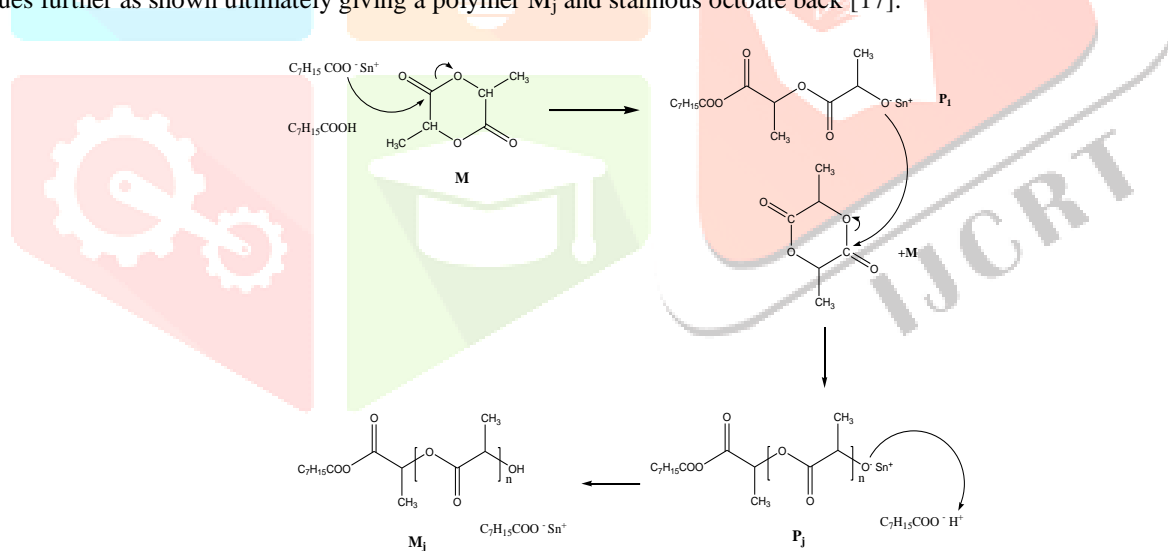
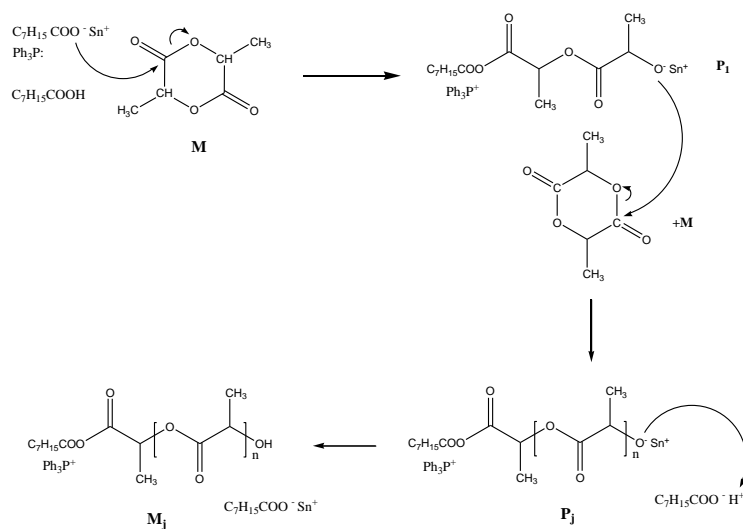


Figure 10 Proposed anionic ring-opening polymerization mechanism of stannous octoate

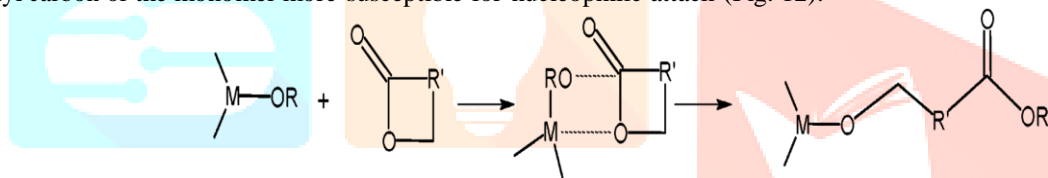




**Figure 11** Proposed anionic ring-opening polymerization mechanism of stannous octoate/ triphenylphosphine

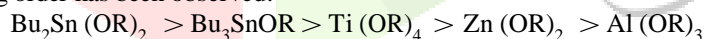
### 2.3 Co-ordination Insertion Ring-Opening Polymerization

Coordination insertion polymerization has been extensively used for the preparation of aliphatic polyesters with well defined structure and architecture. The most widely used initiators are various aluminum and tin alkoxides and carboxylates. The covalent metal alkoxides or carboxylates with vacant “d” orbital react as coordination initiators and not as anionic initiators in these polymerizations. These initiators are capable of producing stereoregular polymers of narrow MWD and controlled molecular mass, with well defined end groups. The carboxylates are weaker nucleophiles in comparison to alkoxides. The polymerization proceeds via acyl oxygen cleavage of the lactone with insertion of the monomer into the metal-oxygen bond of initiator [27-29, 39-41]. The coordination of the exo-cyclic oxygen to the metal results in the polarization and makes the carbonyl carbon of the monomer more susceptible for nucleophilic attack (Fig. 12).



**Figure 12** Coordination insertion mechanism of lactone polymerization

The formation of octanoic acid when tin (II) 2-ethylhexanoate was heated above 100 °C. The acid, thus liberated, may bring about the esterification of alcohol (active hydrogen co-initiator) leading to the formation of water, which may react with Sn(Oct)<sub>2</sub> to form stannoxanes and tin hydroxides. Under such conditions, it would be difficult to control the molecular mass and side reactions because the presence of water or other hydroxyl compounds is likely to initiate polymerization. The relative reactivity of different metal alkoxide initiators for transesterification reaction depends on the metal and is lowest for aluminum alkoxides [6]. The following order has been observed:



Stannous octoate has been the most widely used initiator because of high reaction rates, the solubility in the monomer melt and the ability to produce high molecular weight polylactide [42-44]. The addition of an equimolar amount of Lewis base, particularly triphenylphosphine into 2-ethylhexanoic acid, significantly enhances the lactide polymerization rate in bulk. Triphenylphosphine has two beneficial effects: it increases the polymerization rate and delays the occurrence of the undesirable back biting reactions at monomer/initiator ratios greater or equal to 5000 [45].

The ring-opening polymerization of lactide cyclic monomers in the bulk in the presence of tin (II) 2-ethylhexanoate was reexamined under appropriate conditions for the end-group characterization of growing chains by high-resolution <sup>1</sup>H NMR. The formation of a side product, hydroxytin (II) lactate, was found which appeared to initiate lactide polymerization and to yield a high molecular weight PLA50 polymer. However, the polymerization with stannous octoate was faster than with hydroxytin (II) lactate [46].

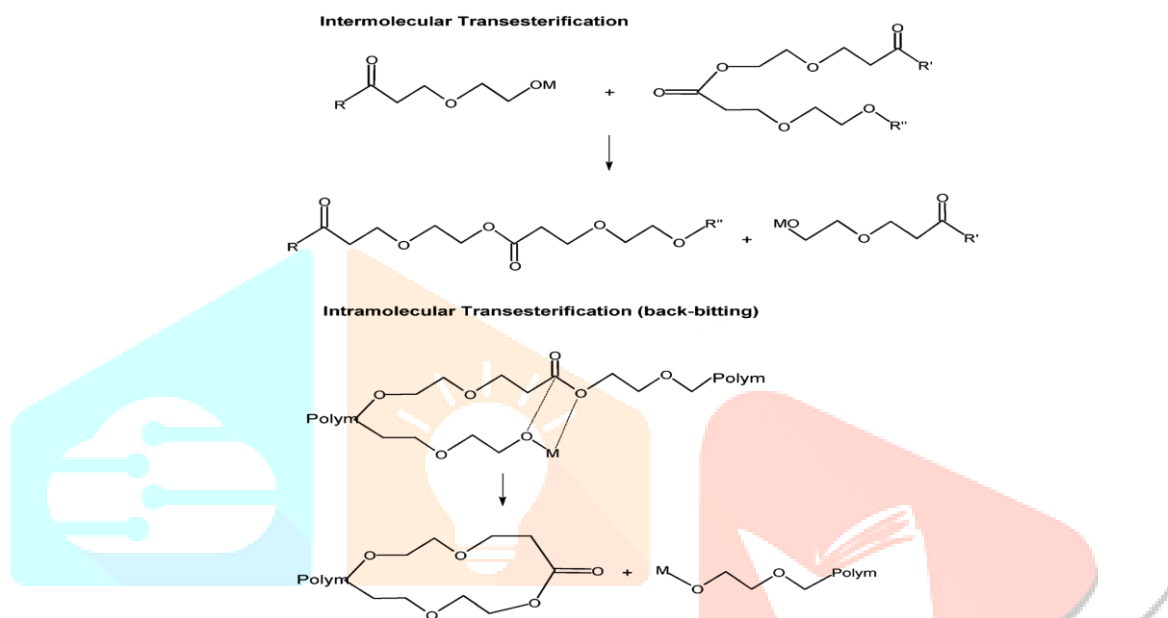
The polymerization was moisture sensitive and that only a fraction of zinc used was active. Small quantities of a side-product was detected and identified as zinc lactate. This compound appeared to be an efficient initiator of the ring-opening polymerization in the bulk. Initiation by zinc lactate yielded high molecular weight polymers with a high degree of conversion and high polymerization rates [9].

The co-ordination insertion mechanism of the ring-opening polymerization of the cyclic esters was studied [47]. Originally it was assumed that stannous octoate was the initiator but this was later disproved by the fact that the polymer molecular weight did not depend upon the monomer: stannous octoate molar ratio. Instead it was concluded that hydroxyl containing impurities (e.g. hydroxyl acids) in the system, including any trace amounts of moisture, were the true initiating species with the stannous octoate acting as a initiator to activate the carbonyl of the monomer towards nucleophilic attack by OH group. This was then followed by acyl-oxygen bond cleavage and ring opening of the monomer. It is now believed that rather than effecting simple complexation with the stannous octoate, the alcohol (ROH) actually reacts with it to form a tin alkoxides, Sn(OR)<sub>2</sub>, and that it is this Sn(OR)<sub>2</sub> which is the true initiating specie. Thus, the stannous octoate is more correctly termed as initiator and the ROH as the co-initiator. Copolymers with various compositions were synthesized by bulk ring-opening polymerization of glycolide and ε-caprolactone, using stannous (II) octoate or zirconium (IV) acetylacetonate as initiator. Reaction time and temperature were varied to induce

different chain microstructures. Stannous (II) octoate leads to less transesterification than zirconium (IV) acetylacetonate, and lower temperatures lead to less transesterification than higher ones [48].

Aluminum-alkoxide initiated polymerization of lactones proceeds according to a coordination-insertion mechanism. Aluminum isopropoxide coordinates to the exocyclic carbonyl oxygen, and the acyl-oxygen cleavage yields an isopropyl ester end-group. Termination of growing chain with dilute HCl leads to the formation of a hydroxy end-group. A narrow molecular mass distribution and an increase in DP with an increase in  $[M]/[I]$  ratio confirmed the living character of the polymerization [49].

Ferric alkoxides were used as initiators for bulk ring-opening polymerization of lactides. The molecular weight decreased and the molecular weight distribution broadened as the polymerization temperature increased. Intermolecular transesterification took place during polymerization of D, L- lactide as evidenced by the results of MALDITOF MS analysis, and the quantitative evaluation for each initiation system was made by  $^{13}\text{C}$  NMR analysis.  $^1\text{H}$  NMR, and MALDI-TOF MS analyses indicated that the polymerization of lactides proceeded via a coordination-insertion mechanism involving cleavage of the acyl-oxygen bond of the lactides [50]. ROP of lactones with these Organometallic initiators at high temperatures or long reaction time leads to both inter- as well as intra-molecular transesterification reactions. Both types of transesterification reactions lead to an increase in dispersity of the polyesters (Fig. 13).

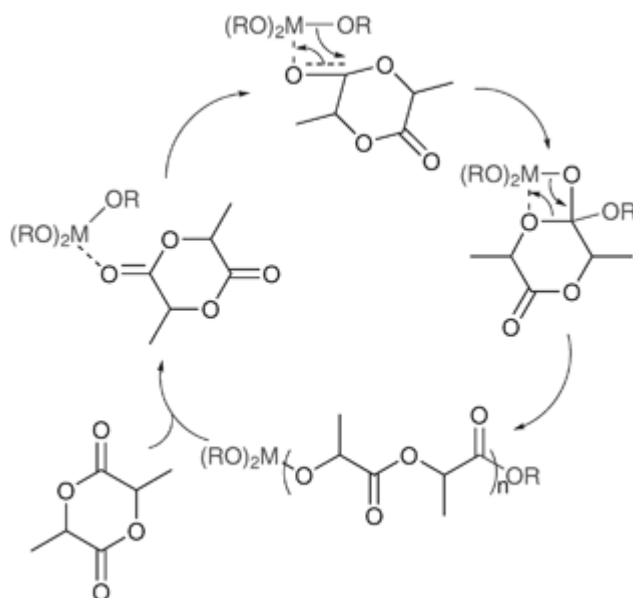


**Figure 13** Inter- and intra-molecular transesterification reactions

The reaction parameters which influence transesterification reactions are temperature, reaction time, the type and concentration of initiator and the nature of the lactone or lactides [25]. Higher flexibility of the polyester backbone leads to an increase in the extent of side reactions (transesterification).

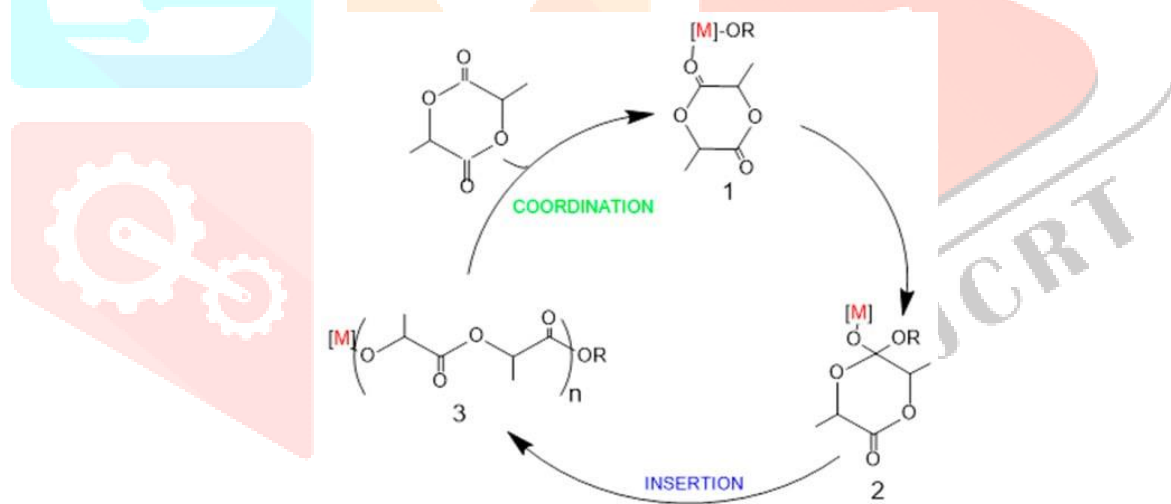
$\text{Bu}_3\text{SnOMe}$  and  $\text{Bu}_2\text{Sn}(\text{OMe})_2$  are effective transesterification catalysts and cause 'back-biting' degradation even at  $90^\circ\text{C}$ . In all series of polymerizations initiated with tin methoxides two tendencies are detectable: increasing randomization of the stereosequence with increasing reaction time and with higher reaction temperatures. In contrast,  $\text{Sn}(\text{II})$  octoate does not cause transesterification at  $\leq 120^\circ\text{C}$  and even at  $180^\circ\text{C}$  randomization of the stereosequences is slow [56]. Initiators with higher nucleophilicity are required to initiate lactide and weaker bases such as zinc stearate, potassium phenoxide, and potassium benzoate initiate only at higher temperatures ( $120^\circ\text{C}$ ). Initiations at high temperature are in bulk but accompanied by racemization and other side reaction which are obstacle to propagation [10,13,34,51].

Poly (L- lactide), PLLA with ultra-high weight average molecular mass and narrow polydispersity index was synthesized by ring-opening polymerization. A synthetic purification method involving a water bath and two time recrystallization could improve the purity of L- lactide to 100%. The yield of L- lactide reached 40.6% and increased 12.1% compared with the recrystallization method. Poly (L-lactide) with a weight average molecular mass of about  $102.4 \times 10^4$  and a polydispersity index of 1.16 was obtained when polymerization was conducted with molar ratio of monomer to initiator  $[M_0]/[I_0]$  of 12000 for 24 h at  $140^\circ\text{C}$  [52]. Among the various ROP processes, including anionic, cationic, organocatalytic and coordination-insertion, the latter has gained increasing attention [44]. It is now commonly accepted that the most efficient method for the production of well-controlled polyesters in terms of molecular weight, composition and microstructure is the ROP with metal-coordination initiators. Therefore, a large number of investigations have been directed towards synthesizing efficient metal-based initiators and studying their reactivities. The first generation of active initiators was mainly constituted by simple homoleptic metal complexes, [35]. principally the industrially relevant tin(II) bis(2-ethylhexanoate), zinc(II) lactate and aluminium(III) isopropoxide ( $\text{Al}(\text{OiPr})_3$ ) [54-55]. These metal-based initiating systems were widely used for the controlled ring-opening polymerization of cyclic esters and brought important contributions for the mechanism understanding. Dittrich and Schulz were the first to define a three-step coordination-insertion mechanism for the ROP of cyclic esters [24]. Then, Researchers have beautifully demonstrated that such a mechanism was involved in the  $\text{Al}(\text{OiPr})_3$ -initiated polymerization of different lactones [35,53]. The coordination-insertion mechanism of lactide polymerization proceeds via coordination of the monomer to the metal center, followed by insertion into the metal-alkoxide species through the acyl-oxygen bond with retention of configuration (Figure 14) [35]. This results in a new metal-alkoxide species capable of further insertion.



**Figure 14** Coordination–insertion mechanism of lactide polymerization using metal-alkoxide catalysts

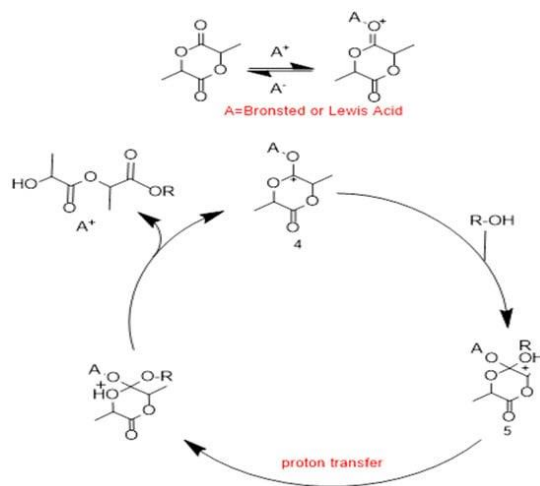
In this mechanism, the electrophilic activation of the lactide for attack by the nucleophilic alkoxide group on the metal is caused by coordination of lactide by a Lewis acidic metal, frequently a metal alkoxide (Figure 15). This results in formation of an intermediate that is similar to the tetrahedral intermediate commonly observed in organic chemistry during the interconversion of carboxylic acid derivatives (Figure 16). Then this intermediate collapses and gives a reformed alkoxide that incorporates a unit of lactide, thus aiding the continuation of ROP. Propagation occurs by subsequent lactide coordination and alkoxide insertion until the metal–alkoxide bond is cleaved by termination reactions. Consequently, PLA with an ester end group derived from the initiator is obtained.



**Figure 15** Coordination–insertion mechanism for ROP of lactide

Aside from the coordination–insertion mechanism, another frequent route proposed for lactide polymerization reactions is the activated monomer mechanism (AM) (Figure 16) [57-60]





**Figure 16** Activated monomer mechanism for ROP of lactide

## CONCLUSION

In this paper, three major ring opening polymerization processes, including anionic, cationic and coordination–insertion mechanisms were discussed by various researchers but later was the most efficient method for the production of well-controlled polyesters in terms of molecular weight, composition and microstructure is the ROP with metal-coordination initiators. Author had synthesized polylactide by using stannous octoate as initiator along with triphenylphosphine as co-initiator and their ring opening polymerization mechanisms were proposed and discussed. It has been observed that molecular weight of polylactide has increased from thousands to several ten thousands  $\text{g mol}^{-1}$ , when triphenylphosphine was used as co-initiator. Several new co-initiators will be needed for the production of greater molecular mass of polylactide at laboratory scale.

## REFERENCES

- Satyanarayana and Chatterji PR (1993) Biodegradable polymers: challenges and strategies. *Journal of Macromolecular Science*, C33, **3**, 349–368.
- Zell MT, Padden BE, Paterick AJ, Thakur KAM, Kean RT, Hillmyer MA and Munson EJ (2002) Unambiguous determination of the  $^{13}\text{C}$  and  $^1\text{H}$  NMR stereosequence assignments of polylactide using high-resolution solution NMR spectroscopy. *Macromolecule*, **35**, 7700.
- Penczek S, Duda A, Kowalski A, Libiszowski J, Majerska K and Biela T (2000) On the mechanism of polymerization of cyclic esters induced by tin(II) octoate. *Macromol Symp*, **157**, 6.
- Kricheldorf HR, Saunders IK and Striker A (2000) Poly lactones 48. SnOct<sub>2</sub>-Initiated polymerizations of lactide: a mechanistic study, *Macromolecules*, **33**, 702.
- Albertsson AC, Edlund U and Stridsberg K (2000) Controlled ring-opening polymerization of lactones and lactides, *Macromol Symp*, **157**, 39.
- Kricheldorf HR, Saunders IK and Damrau DO (2000) Resorbable initiators for polymerizations of lactones, *Macromol Symp*, **159**, 247.
- Kricheldorf HR, Saunders IK and Damrau DO (1999) Precision enzymatic polymerization to polyesters with lipase catalysts, *Macromol Symp.*, **144**, 237.
- Saunders IK and Kricheldorf HR (1998) Poly lactones, 39. Zn lactate catalyzed copolymerization of l-lactide with glycolide or ε-caprolactone, *Macromol Chem Phys.*, **199**, 1081.
- Schwarch G, Coudane J, Engel R and Vert M (1998) Ring opening polymerization of d,l-lactide in the presence of zinc metal and zinc lactate, *Polym Int*, **46**, 177.
- Kricheldorf HR and Serra A (1995) A. *Polym. Bull. (Berlin)*, **14**, 497-502.
- Sodergard A and Stolt M (1998) M. *Macromol. Symp.* **130**, 393- 402.
- Arvanitoyannis I, A. Nakayama, E. Psomidou, N. Kawasaki and N. Yamamoto, *Polymer.*, **37**, 651-660 (1996).
- H. R.. Kricheldorf and C. Boettcher, *Makromol. Chem.*, **194**, 463-473 (1993).
- H.R. Kricheldorf and D.O. Damrau, *Macromol. Chem. Phys.*, **198**, 1767-1774 (1997).
- M. Stolt and A. Sodergard, *Macromolecules*, **32**, 6412-6417 (1999).
- V.L. Lassalle and M. L. Ferreira, *Chem. Technol. Biotechnol.*, **83**, 1493 (2008).
- Paramjit kaur thesis
- H.R. Kricheldorf and R., Dunsing, Poly lactones, 8. Mechanism of the cationic polymerization of L, L-dilactide. *The Macromolecular Chemistry*, **187**, 1611–1625 (1986).
- E. Balla, V. Daniilidis, G. Karlioti, T. Kalamas, M. Stefanidou, N. D. Bikiaris, A. Vlachopoulos, I. Koumentakou and I.N. Bikiaris, Poly(lactic Acid): A Versatile Biobased Polymer for the Future with Multifunctional Properties—From Monomer Synthesis, Polymerization Techniques and Molecular Weight Increase to PLA Applications, *Polymers*, **13**(11), 1822 (2021). <https://doi.org/10.3390/polym13111822>.
- Y.N. Zhou, J.J. Li, Y.Y. Wu and Z.H. Luo, Role of External Field in Polymerization: Mechanism and Kinetics, (2020). <https://dx.doi.org/10.1021/acs.chemrev.9b00744>.

21. D.E. Stasiw, A. M. Luke, T. Rosen, A.B. League, M. Mandal, B.D. Neisen, C.J. Cramer, M. Kol. and W.B. Tolman, Mechanism of the Polymerization of rac-Lactide by Fast Zinc Alkoxide Catalysts, *Inorg. Chem.* **56**, 22, 14366–14372 (2017).
22. H.R. KRICHELDORF AND I. KREISER, POLYLACTONES, 11. CATIONIC COPOLYMERIZATION OF GLYCOLIDE WITH L, L-DILACTIDE, *THE MACROMOLECULAR CHEMISTRY*, **188**, 1861–1873 (1987).
23. H.R. Kricheldorf and M. Sumbel, Poly lactones—18. Polymerization of L, L-lactide with Sn(II) and Sn(IV) halogenides, *European Polymer Journal*, **25**(6), 585–591 (1989).
24. V.W. Dittrich and R.C. Schulz, Kinetics and mechanism of ring-opening polymerization of L (-)-lactide, *The Macromolecular Chemistry*, **15**, 109–126 (1971).
25. P. Dubois, R. Jerome, C. Jacobs and P. Teyssie, **Macromolecular engineering of polylactones and poly lactides. Mechanism and Kinetics of lactide homopolymerization by Aluminium isopropoxide**, *Macromolecules*, **24**, 2266–2270 (1991).
26. A.J. Nijenhuis, D.W. Grijpma and A.J. Pennings, Lewis acid catalyzed polymerization of L- lactide. Kinetics and Mechanism of bulk polymerization, *Macromolecules*, **25**, 6419–6424 (1992).
27. X. Zhang, X., D.A. Macdonald, M. Goosen and K. Maculey, Mechanism of lactide polymerization in the presence of stannous octoate: The effect of Hydroxy and Carboxylic acid substances, *Journal of Polymer Science Part A: Polymer Chemistry*, **32**, 2965–2970 (1994).
28. Y.J. DU, A.J., NIJENHUIS, C. BASTIAANSEN AND P.J. LEMSTRA, NEW APPROACHES TO RING OPENING POLYMERIZATION-EVIDENCES OF STEP TRANSFER POLYMERIZATION. *J.MACROMOL. SCI. PURE APPL. CHEM.*, **A32**, 1061–1069 (1995).
29. G. Schwach, J. Coudane, R. Engel and M. Vert, More about the polymerization of lactides in the presence of stannous octoate. *J. Polym. Sci., Polym.Chem.*, **35**, 3431–3440 (1997).
30. M. Moller, F. Nederberg, L.S. Lim, R. Kange, C.J. Hawker, J.L. Hedrick, Y. Gu, R. Shah and N.L. Abbott, Stannous(II) trifluoromethane sulfonate: a versatile catalyst for the controlled ring-opening polymerization of lactides: Formation of stereoregular surfaces from polylactide “brushes”. *Journal of Polymer Science, Part A: Polymer Chemistry*, **39**, 3529–3538 (2001).
31. B. Athhoff, J. Hilborn and T. Bowden, Polymeric Materials Science and Engineering (PMSE) Preprints, **88**, 369 (2003).
32. A.C. ALBERTSSON AND I.K. VARMA, RECENT DEVELOPMENTS IN RING-OPENING POLYMERIZATION OF LACTONES FOR BIOMEDICAL APPLICATIONS. *BIOMACROMOLECULES*, **4**(6), 1466–1486 (2003).
33. J.A. Byers, A.B. Biernesser, K.R. Delle Chiaie, A. Kaur and J.A. Kehl, Catalytic systems for the production of poly(lactic acid). *Adv.Polym. Sci.*, **279**, 67–118 (2018).
34. V. J. Kleine and H.H. Kleine, Proceed over high molecular weight, in particular optically active polyester of lactic acid, a contribution to the connections of macromolecular stereochemistry. *The Macromolecular Chemistry*, **30**(1), 23–38 (1959).
35. M. Berl, H.R. Kricheldorf and N. Scharnagl, Polymerisation Mechanism of Metal Alkoxide Initiated Polymerisations of Lactide and Various Lactones, *Macromolecules*, **21**, 286 (1988).
36. L.S. Zaremba and W.H. Smolenski, Optimal portfolio choice under a liability constraint. *Ann. Oper. Res.*, **97**, 131–141 (2000).
37. H.R. Kricheldorf and C. Boettcher, Poly lactones 26. Lithium alkoxide-initiated polymerizations of L-lactide. In *Die Makromolekulare Chemie*; Wiley: Hoboken, NJ, USA, **1669**, 1665–1669 (1993).
38. K.M. Stridsberg, M. Ryner and A.C. Albertsson, Controlled ring-opening polymerization: Polymers with designed macromolecular architecture. In *Degradable Aliphatic Polyesters*; Springer: Berlin/Heidelberg, Germany,; ISBN 9171705228 (2002).
39. A. Kowalski, A. Duda and S. Penczek, Kinetics and mechanism of cyclic esters polymerization initiated with tin (II) octoate. 1. Polymerization of  $\epsilon$ -caprolactone. *Macromol. Rapid Commun.*, **19**, 567–572 (1998).
40. H.R. Kricheldorf, I. Kreiser-Saunders and C. Boettcher, Poly lactones: 31. Sn(II)octoate-initiated polymerization of L-lactide: a mechanistic study. *Polymer*, **36**, 1253–1259 (1995).
41. P.J.A. IN’T VELD, E.M. VELNER, P. VANDEWITTE, J. HAMHUIS, P.J. DIJKSTRA AND J. FEIJEN, MELT BLOCK COPOLYMERIZATION OF  $\epsilon$ -CAPROLACTONE AND L- LACTIDE. *J. POLYM. SCI, POLYM. CHEM.*, **35** (2), 219–226 (1997).
42. G. Swift, *Acc. Chem. Res.*, **26**, 105 (1993).
43. G. Schwach, J. Coudane, R. Engel and M. Vert, Stannous-octoate versus zinc-initiated polymerization of racemic lactide-effect of configurational structure. *Polymer Bulletin (Berlin)*, **32** (5-6), 617–623(1994).
44. O.D. CABARET, B.M. VACA AND D. BOURISSOU, CONTROLLED RING-OPENING POLYMERIZATION OF LACTIDE AND GLYCOLIDE. *CHEM. REV.*, **104**(12), 6147–6176 (2004).
45. O. Degee, P. Dubois, S. Jacobsen, S.G. Fritz and R. Jerome, Beneficial effect of triphenylphosphine on the bulk polymerization of L, L- lactide promoted by 2-ethylhexanoic acid tin(II) salt. *J. Polym. Sci. Part A: Polym. Chem.*, **37**, 2413–2420 (1999).
46. R. Engel, G. Schwach, J. Coudane and M. Vert, **More about the polymerization of lactides in the presence of stannous octoate**, *Journal of Polymer Science Part A: Polymer Chemistry*, **35** (16), 3431–3440 (1997).
47. A. Kleawkla, W. Suksomran, M. Srisa-ared, Y. Baimark, R. Molloy, J. Siritayananon, W. Punyodom, K. Nalampang and M. Sriyai, Controlled ring-opening polymerization of cyclic eaters, B03 (2005).
48. J. Kasperczyk and M. Bero, Stereoselective polymerization of racemic DL- lactide in the presence of butyl lithium and butyl magnesium, Structural investigations of the polymers. *Polymer*, **41**, 391–395 (2000).
49. A. Lofgren, A.C. Albertsson, A.C. Dubois, R. Jerome and P. Teyessie, Synthesis and Characterization of Biodegradable Homopolymers and Block Copolymers Based on 1,5-Dioxepan-2-one. *Macromolecules*, **27** (20), 5556–5562 (1994).
50. X. Wang, K. Liao, D. Quan and Q. Wu, Bulk Ring-Opening Polymerization of Lactides Initiated by Ferric Alkoxides. *Macromolecules*, **38**, 4611–4617 (2005).
51. H.R. Kricheldorf and I.K. Saunders, Poly lactones 19. Anionic polymerization of L-lactide in solution. *The Macromolecular Chemistry*, **191**(5), 1057–1066 (1990).

52. Z.H. Zhou, X.P. Liu and L.H. Liu, 2008. Synthesis of ultra-high weight average molecular mass of poly (l-lactide). *International Journal of Polymeric Materials*, **57**,532–542 (2008).
53. P. Dubois, R. Jerome and P. Teyssie, *Makromol. Chem., Macromol. Symp.*, 42/43, 103 (1991).
54. C. Wang, H. Li and X. Zhao, *Biomaterials*, **25**, 5797 (2004).
55. R.E. Drumright, P.R. Gruber and E. Henton, *Adv. Mater.*, **12**, 1841 (2000).
56. H.R. Kricheldorf, C. Boettcher, and K.U. Tonnes, *Polylactones: 23. Polymerization of racemic and meso-D,L-lactide with various organotin catalysts-stereochemical aspects. *Polymer*. **33**(13), 2817-2824 (1992).*
57. K. Masutani and Kimura. *PLA Synthesis and Polymerization*; Royal Society of Chemistry: London, UK, ISBN 9781782624806 (2014).
58. M. Basko and P. Kubisa, Cationic polymerization of L,L-lactide. *J. Polym. Sci. Part A Polym. Chem.***48**, 2650–2658 (2010).
59. S. Matsumura, A.R. Hlil, C. Lepiller, J. Gaudet, D. Guay, Z. Shi, S. Holdcroft, and Hay, A.S. Stability and utility of pyridyl disulfide functionality in RAFT and conventional radical polymerizations. *J. Polym. Sci. Part A Polym. Chem.* **46**, 7207–7224 (2008).
60. E. Balla, V. Daniilidis, G. Karlioti, T. Kalamas, M. Stefanidou, N. D. Bikiaris, A. Vlachopoulos, I. Koumentakou and N. Bikiaris, Poly(lactic Acid): A Versatile Biobased Polymer for the Future with Multifunctional Properties—From Monomer Synthesis, Polymerization Techniques and Molecular Weight Increase to PLA Applications, *Polymers*,**13**(11) 1822, (2021) .; <https://doi.org/10.3390/polym13111822>

