CHAPTER II

THEORY AND LITERATURE REVIEW

There are several reasons for studying the polymerization of cyclic esters. First, exploit the potential of synthetic polymer chemistry to prepare a variety of polymers with control of the major variables affecting polymer properties. Experimental conditions have to be optimized in order to find the best polymerization system for a desired technological or industrial process. Factors such as economy, toxicology, and technical apparatus development are important. A second reason for studying ROP is to enable various advanced macromolecules, including homopolymers with well-defined structures or end group, to be prepared, as well as copolymers with different architectures, e.g., block, graft, or star copolymer [10]. The physical, mechanical, and degradation properties of these various macromolecules are studied to determine the structure-to-property relationship [11-12]. The third reason for studying these kinds of systems is that they are valuable models for the examination of the kinetics and mechanism of elementary reactions in polymerization.

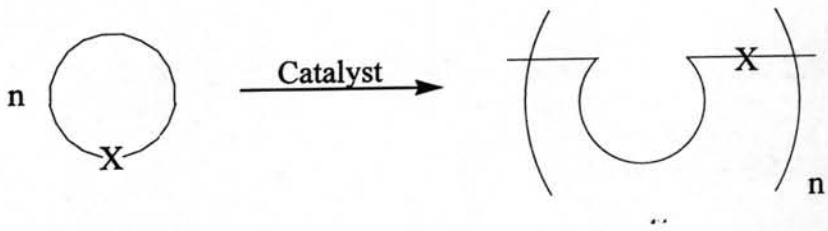
Polylactones and polylactides can be prepared by two different approaches, by the polycondensation of hydroxycarboxylic acids or by the ring-opening polymerization (ROP) of cyclic esters [1, 5, 10, 13]. The polycondensation technique is less expensive than ROP, but it is difficult to obtain high molecular weight polymers, to achieve specific end groups, and to prepare well-defined copolyesters. The ROP of lactones and lactides has been thoroughly investigated during the last 40 years, due to its versatility in producing a variety of biomedical polymers in a controlled manner.

2.1 Ring-opening polymerization [13]

There are three polymerization mechanisms: step, chain, and ring-opening polymerization (ROP) [14-16]. While small molecules of by-products are formed in

step polymerization, chain polymerization involves exothermic conversion of multiple bonds to single bonds. These disadvantages are not likely to occur in ROP mechanism; therefore, ROP is considered to be the most favorable polymerization mechanism [6, 8].

High molecular weight polylactones and polylactide are produced by the ROP of the corresponding cyclic monomers. Polyester is formed when cyclic esters are reacted with a catalyst or initiator. Scheme 2.1 represents the reaction pathway for the ROP of a cyclic ester [13].



Scheme 2.1 Ring-opening polymerization (ROP) of a cyclic ester: x is heteroatom such as oxygen

On the other hand, ROP has some characteristics which are similar to some of step and chain polymerization. In term of the relationship between polymer molecular weight and conversion, ROP mostly behaves as step polymerization in that the polymer molecular weight increases relatively slowly with conversion while high molecular weight polymer is formed throughout the course of a polymerization. This is because the rate constants for ROP of cyclic monomers is much closer to those for the reactions of step polymerization than for chain polymerization.

Ring-opening polymerization (ROP) constitutes one of the most important fields of polymer chemistry. Along with step and chain mechanisms for the formation of polymers, ring-opening reaction provides an important methodology for polymer formation. Moreover, it is possible for ROP to use the living mechanism [10]. To achieve this, the rate of polymerization in three steps has been optimized, the initiation step is faster than the propagation step and propagation step is faster than termination step. As a result, each molecule of initiator would become associated with

a growing chain of polymer and those chains would continue to grow until all monomer is depleted.

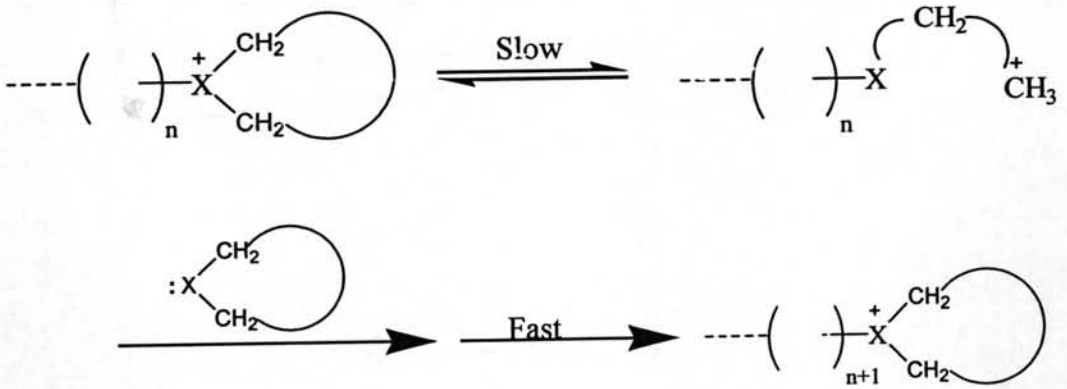
The ROP reaction can be performed either as a bulk polymerization, or in solution, emulsion, or dispersion. A catalyst or initiator is necessary to start the polymerization. Under rather mild conditions, high molecular weight aliphatic polyesters of low polydispersity can be prepared in short periods of time. Problems associated with condensation polymerization, such as the need for exact stoichiometry, high reaction temperatures, and the removal of low molecular weight by-products (e.g. water) are excluded in ROP.

Depending on the initiator, the polymerization proceeds according to three different major reaction mechanisms, *viz*, cationic, anionic or coordination-insertion mechanisms. In addition, radical, zwitterionic, or active hydrogen initiation is possible, although such techniques are not used to any great extent. The focus in this field is on the "coordination-insertion mechanism" and the other methods are described in this thesis [10, 13].

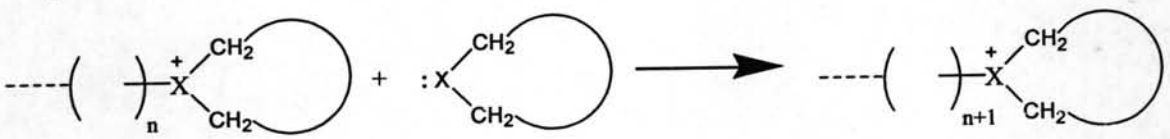
2.1.1 Cationic ring-opening polymerization (CROP)

Polyester is formed from cyclic ester when reacting with cationic catalysts. The propagation step can described as a nucleophilic reaction, in which the positively charged active species is the electrophile and the monomer is the nucleophile. The interaction can be classified as the S_N1 type or as the S_N2 type process. These two typical examples are shown in Scheme 2.2

S_N1 :



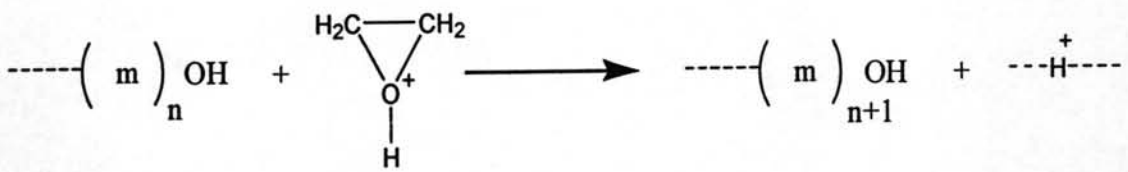
S_N2 :



Scheme 2.2 S_N1 and S_N2 mechanism in propagation step of CROP or active chain end mechanism (ACE) (counter ion is omitted; X is a heteroatom).

The S_N1 mechanism is favorable if the structure of the monomer is stable carbenium ion or weak nucleophile; for instance, cyclic acetals or cyclic orthoesters [10, 13].

In the polymerization mechanisms described above, ions are located at the end of macromolecules, thus, the process is called "active chain end polymerization" (ACE). More recently a new mechanism of propagation has been postulated, so called "activated monomer polymerization" (AM). In this polymerization, the growing end of the molecule is (*e.g.*, for cyclic esters) an –OH group. The positive charge is located on the monomer molecules (Scheme 2.3).



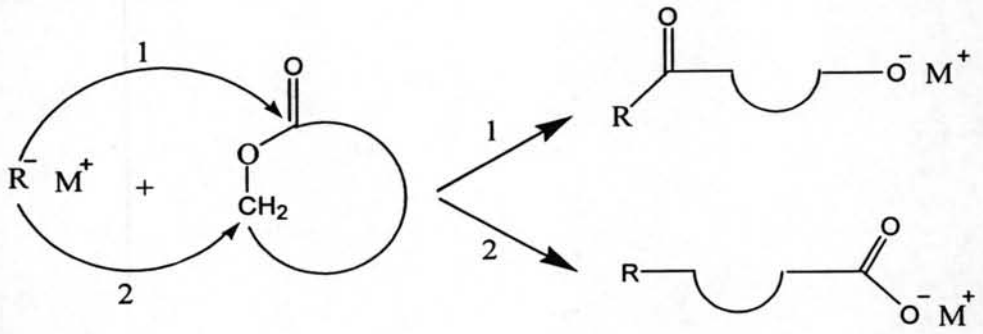
Scheme 2.3 The activated monomer mechanism (AM) in propagation step of CROP.

In CROP, proceeding by the ACE mechanism, the bond breaking in the active end (onium ion) has been shown to be the decisive factor, determining the rate constant of propagation for a given monomer. It is well known that carbonium bonds provide better leaving groups compared with the corresponding carbon hetero atom bonds (*e.g.*, ammonium *vs.* amine, oxonium *vs.* ether).

However, cationic polymerization is difficult to control. Only low-molecular weight polymers are formed. When the bulk and solution polymerization of 1,5-dioxepan-2-one (DXO) with cationic initiators were studied, the highest molecular weight achieved was approximately only 10,000.

2.1.2 Anionic ring-opening polymerization (AROP)

Anionic ring-opening polymerization of cyclic ester monomers takes place by the nucleophillic attack of a negatively charged initiator on the carbonyl carbon or on the carbon atom adjacent to the acyl oxygen, resulting in linear polyester (Scheme 2.4) [10, 13].



Scheme 2.4 The reaction pathway for the ROP of a cyclic ester by anionic initiation. Ring opening of monomer by 1) acyl-oxygen bond cleavage and 2) alkyl-oxygen bond cleavage.

Each propagation step involves a nucleophillic attack of the anionic active center, located at the end of the growing macromolecule, on the heterocyclic monomer. This attack results in a polymer chain extension with regeneration of the active center at the terminal position. The propagating species is negatively charged and is counter-balanced with a positive ion. Depending on the nature of the ionic

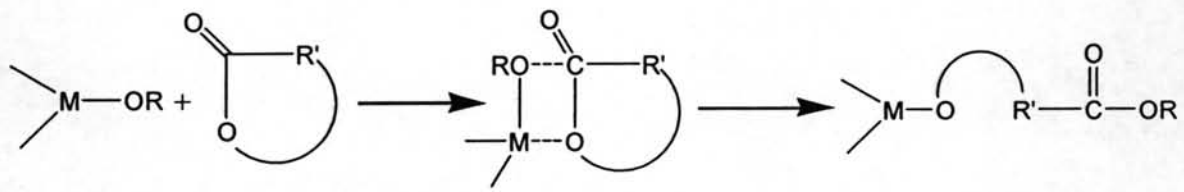
propagating chain end and the solvent, the reacting complex varies from complete ionic to almost covalent.

One of the best controlled methods leading to high molecular weight polymers is anionic polymerization carried out in a polar solvent. However, a problem associated with the anionic ROP is the extensive back-biting, and in some cases only polyesters of low molecular weight are achieved.

In spite of the substantial progress made within the last two decades anionic ring-opening polymerization cannot be considered as a closed field. Although the number of cyclic monomers known to polymerize anionically is rather limited, the anionic ring-opening polymerization often creates unique possibilities of the controlled synthesis of macromolecules with various regularly repeated carbon and hetero atoms.

2.1.3 Coordination-insertion ring-opening polymerization (CIROP)

The pseudo-anionic ROP is often referred to coordination-insertion ROP, since the propagation is thought to proceed by coordination of the monomer to the active species, followed by insertion of the monomer into the metal-oxygen bond by rearrangement of the electrons [10].



Scheme 2.5 The proposed reaction pathway for the ROP of a cyclic ester by the coordination-insertion mechanism.

Scheme 2.5 shows a schematic presentation of the coordination-insertion mechanism. The growing chain remains attached to the metal through an alkoxide bond during the propagation. The reaction is terminated by hydrolysis forming a

hydroxyl end group. With functional alkoxy-substituted initiators, macromers with end groups active in post-polymerization reactions are produced.

The coordination-insertion type of polymerization has been thoroughly investigated since it possibly yields well-defined polyesters through living polymerization. When two monomers of similar reactivity are used, block copolymers can be formed by sequential addition to the living system.

2.2 Initiators

The synthesis of novel initiators and the ROP of existing or new monomers and macromers substituted with functional groups provide a very interesting and promising strategy for producing structurally advanced macromolecules [14-17].

A large variety of organometallic compounds, *e.g.*, metal alkoxides and metal carboxylates, has been studied as initiators or catalysts in order to achieve effective polymer synthesis. Many reactions catalyzed by metal complexes are highly specific and, by careful selection of metal and ligands, reactions can be generated to form a desired polymer structure. The covalent metal alkoxides with free *p* or *d* orbitals react as coordination initiators and not as anionic or cationic initiators.

2.2.1 Stannous 2-ethylhexanoate ($Sn(Oct)_2$)

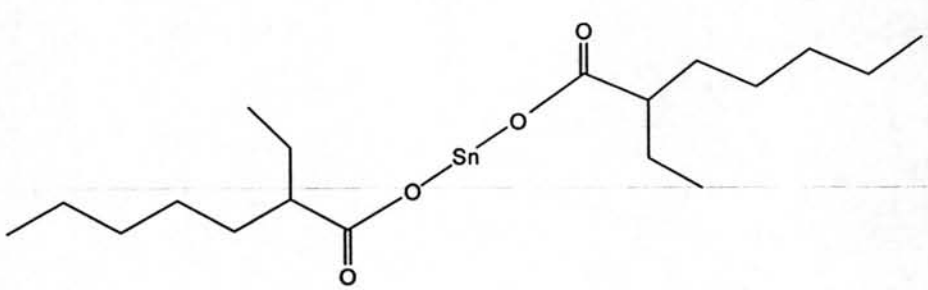
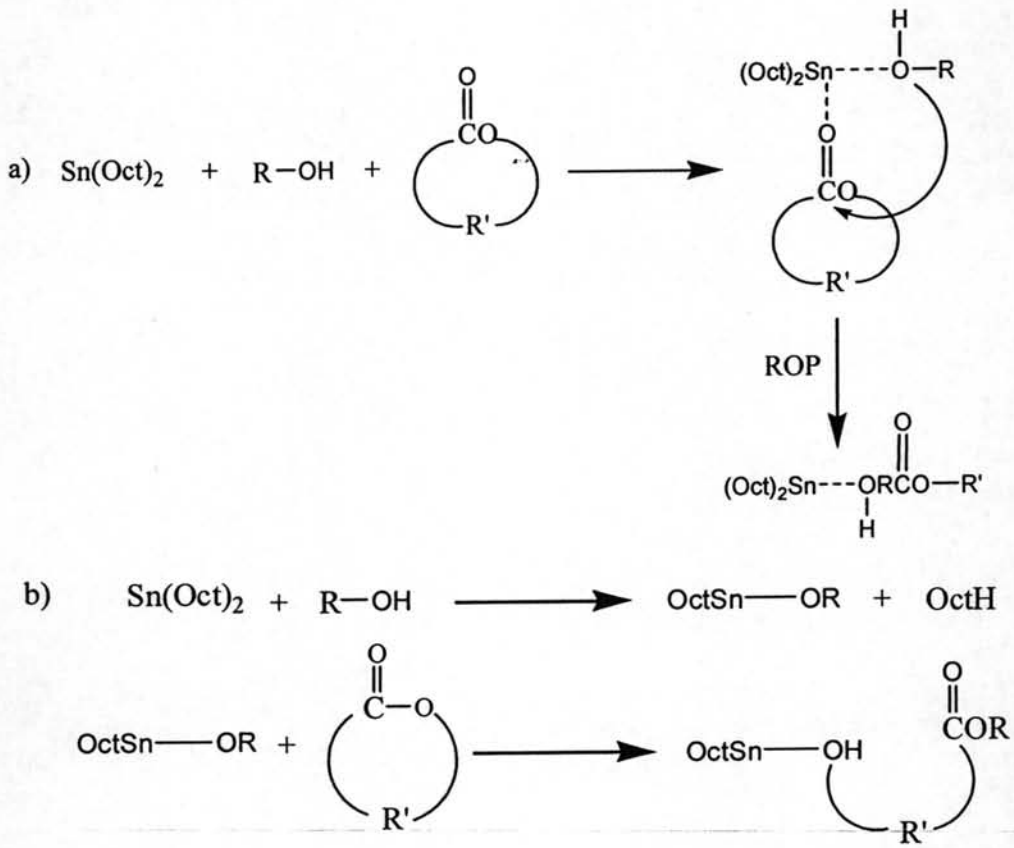


Figure 2.2 The structure of stannous 2-ethylhexanoate

Stannous 2-ethylhexanoate or tin (II) 2-ethylhexanoate, commonly refered to stannous octoate ($Sn(Oct)_2$), is a frequently used catalyst in the ROP of lactones and

lactides. $Sn(Oct)_2$ has been approved as a food additive by the American Food and Drug Administration (FDA) [6, 10]. The mechanism of polymerization has been widely discussed. Despite several proposals over a long period of time, until now the ROP mechanism has not been elucidated. The $Sn(Oct)_2$ is not thought to be the actual initiator since the molecular weight does not depend on the monomer to $Sn(Oct)_2$ molar ratio. The most promising mechanism is a coordination-insertion mechanism where a hydroxyl functional group is thought to coordinate to $Sn(Oct)_2$, forming the initiating tin alkoxide complex [5-7].

Coordination-insertion mechanism can be proposed into two slightly different reaction pathways [10].



Scheme 2.6 The main ROP mechanism proposals with $Sn(Oct)_2$ as catalyst, a) complexation of a monomer and alcohol prior to ROP and b) formation of a tin-alkoxide before ROP of cyclic ester.

Scheme 2.6 shows two different mechanisms. In the first mechanism, the co-initiating alcohol functionality and the monomer are both coordinated to the $Sn(Oct)_2$

complex during propagation. Secondly, $Sn(Oct)_2$ complex is converted into a tin alkoxide before complexing and ring-opening of the monomer. Direct observation of this tin alkoxide complex has been reported by using MALDI-TOF spectrometry for both lactide and cyclic ester polymerization.

The $Sn(Oct)_2$ catalyst is a strong transesterification agent, and the resulting co-polymers normally have a randomized microstructure. The increasing of reaction temperature or reaction time will also increase the amount of transesterification reactions.

The ROP of lactide with $Sn(Oct)_2$ is fairly slow and it is desirable for economic and commercial reasons to increase the rate of polymerization. The addition of an equimolar amount of triphenylphosphine was increased the rate, and as an additional advantage, this compound delays the occurrence of the undesirable back-biting reactions.

2.2.2 Creatine hydrate [1]

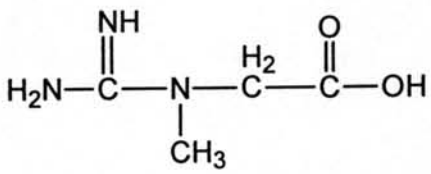


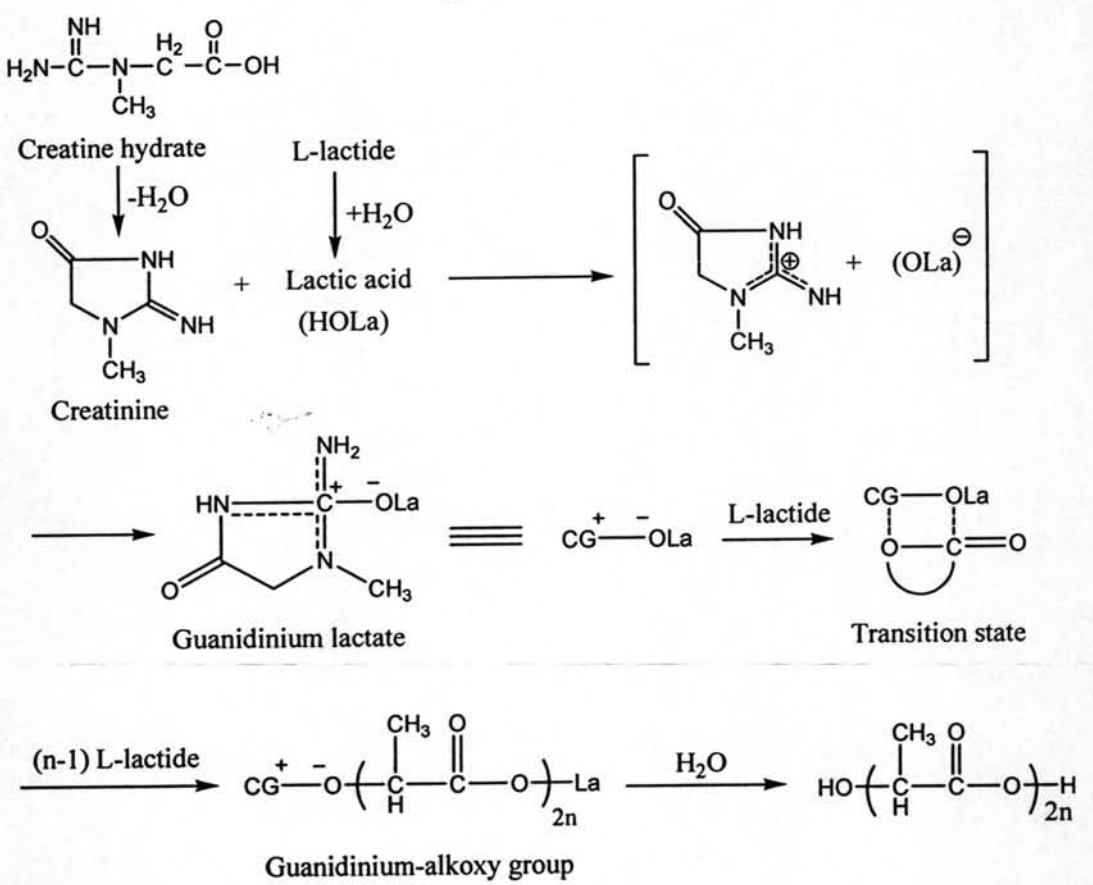
Figure 2.3 The structure of creatine hydrate.

Polylactide are obtained from the corresponding monomers by ring-opening polymerization. Stannous 2-ethylhexanoate ($Sn(Oct)_2$) has been widely used as the initiator. $Sn(Oct)_2$ is very efficient, its cytotoxicity, however, has recently caused deep concern about biosafety of the materials synthesized from it and used for biomedical. Seeking for tin-free catalysts of highly biosafety is hence a new challenge in this field.

Guanidine is a natural organic base existing in human body. Creatine hydrate and arginine, for example, are guanidine derivatives participating in arginine metabolism process. Some guanidine derivatives are the key components of some

pharmaceuticals (such as anti-cancers and anti-AIDS). The utilization of guanidine as catalysts for synthesizing non-toxic organic compounds is a new and instructive trend in the field of organic synthesis. Recently, it is found that creatine hydrate, a non toxic metabolite in the human body, shows rather satisfactory catalytic properties for polymerization of lactides as well.

The polymerization mechanism is possible of free radical, or ionic polymerizations. TEMPO (2, 2, 6, 6-tetramethyl-1-piperidinyloxy, a free radical capturer), NaOH/MeOH-toluene (cation terminator), BuOH/toluene (anion terminator) of equimolar amount as the creatine hydrate dosage were added to the started polymerization system, respectively. Polymerizations in all the three systems were not terminated, but continued. This verified our conjectures that the polymerization follows neither the radical nor the ionic mechanism.



Scheme 2.7 A mechanism of ring-opening polymerization of L-lactide initiated by creatine hydrate.

The polymerization of L-lactide initiated by creatine hydrate follows the coordination-insertion mechanism. The initiation species is deduced to be a guanidinum lactate formed by the reaction of creatinine with the trace amount of lactic acid which is generated from the hydrolysis of L-lactide. The existence of lactic acid in the original reaction system is unavoidable. To verify the conjecture, in a separate experiment lactic acid (in equimolar amount as creatine dosage) was added to the original system, the polymerization was found to be accelerated.

Propagation proceeds in the following way: coordination of L-lactide with the guanidinum lactate forms a four-membered transition state, formation of the latter is followed by the cleavage of acyl-oxygen bond in the coordinated L-lactide molecule and the simultaneous insertion of the cloven L-lactide residue into the guanidyl-oxygen bond in the guanidinium lactate. The propagation species thus formed bears guanidinium-alkoxy group CG-O-CH(Me) as its active end.

2.3 Chain extender [10, 18-20]

Polyester synthesis via diacid/dialcohol thermal polycondensation is the traditional and most economic procedure for polyester synthesis. Unfortunately, it encounters problem due to the difficulty in obtaining high molecular weight material, due to a slow equilibrium and to hydrolysis in the presence of water obtained as side product. A useful way to overcome the problems of incomplete polymerization and short chain length is by the chain-extender technology, usually carried out in the presence of coupling agents reacting with the reactive functions located at prepolymer chain ends. It is well known, in fact, that an increase in the molecular weight of a polymeric material means an improvement in the physical performance of the polymers.

Typical chain extenders for polylactide, which contain –OH and –COOH groups, are diisocyanates, diepoxides, bisoxazolines, dianhydrides, and bisketeneacetals.

2.3.1 1,6-Hexamethylene diisocyanate (HMDI)

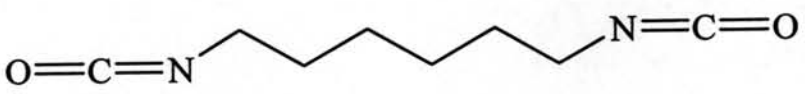
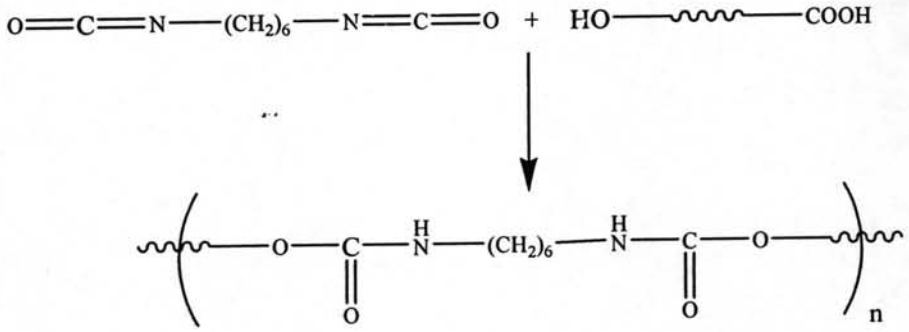


Figure 2.4 The structure of 1,6-hexamethylene diisocyanate.

The 1,6-hexamethylene diisocyanate is a chain extender which contains molecular weight 168.2. This chain extender is commonly used in PLA synthesis. Because of diisocyanate group at the end can be reacted with –OH and –COOH groups of PLA.



Scheme 2.8 A reaction of 1,6-hexamethylene diisocyanate to produce high molecular weight PLLA.

These chain extension reactions are economically advantageous because they could be carried out in melt, with only low concentrations of chain extending agents, and because separate purification steps are not required. Improved mechanical properties and the flexibility to manufacture copolymers with different functional groups are other benefits of the use of 1,6-hexamethylene diisocyanate as chain extending agents.

2.3.2 Tolylene 2,4-diisocyanate terminated poly 1,4-butanediol prepolymer

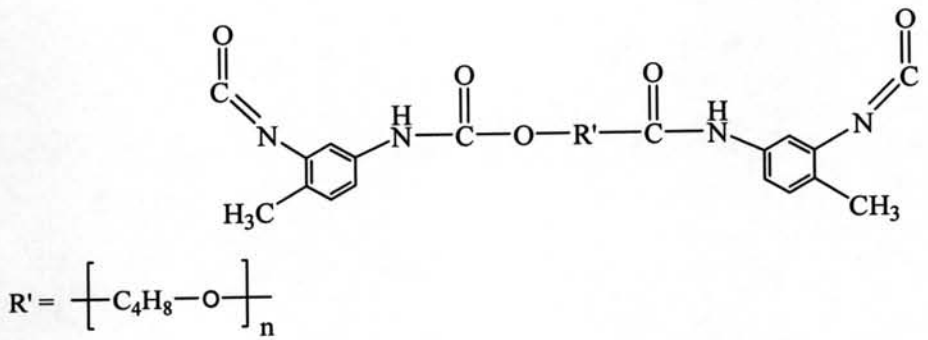
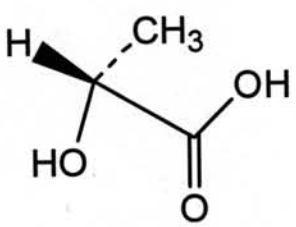


Figure 2.5 The structure of tolylene 2,4-diisocyanate terminated poly 1,4-butanediol prepolymer.

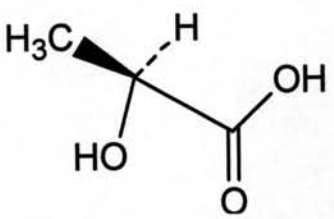
In Figure 2.5, the molecular weight of tolylene 2,4-diisocyanate terminated poly 1,4-butanediol prepolymer is 900. This chain extender is common used in polyurethane synthesis. Because the structure of tolylene 2,4-diisocyanate terminated poly 1,4-butanediol prepolymer contains diisocyanate group which can be reacted with –OH and –COOH of PLA. Tolylene 2,4-diisocyanate terminated poly 1,4-butanediol prepolymer could be used as novel chain extender for PLA synthesis.

2.4 Lactic acid

Lactic acid can be produced by chemical synthesis or fermentation. Commercially, chemical synthesis of lactic acid is produced by the hydrolysis of lactonitrile. Lactonitrile is obtained by hydrogen cyanide reacted with acetaldehyde in the presence of an alkali. The chemical synthesis produces a racemic mixture of lactic acid [21-23].



D-lactic acid



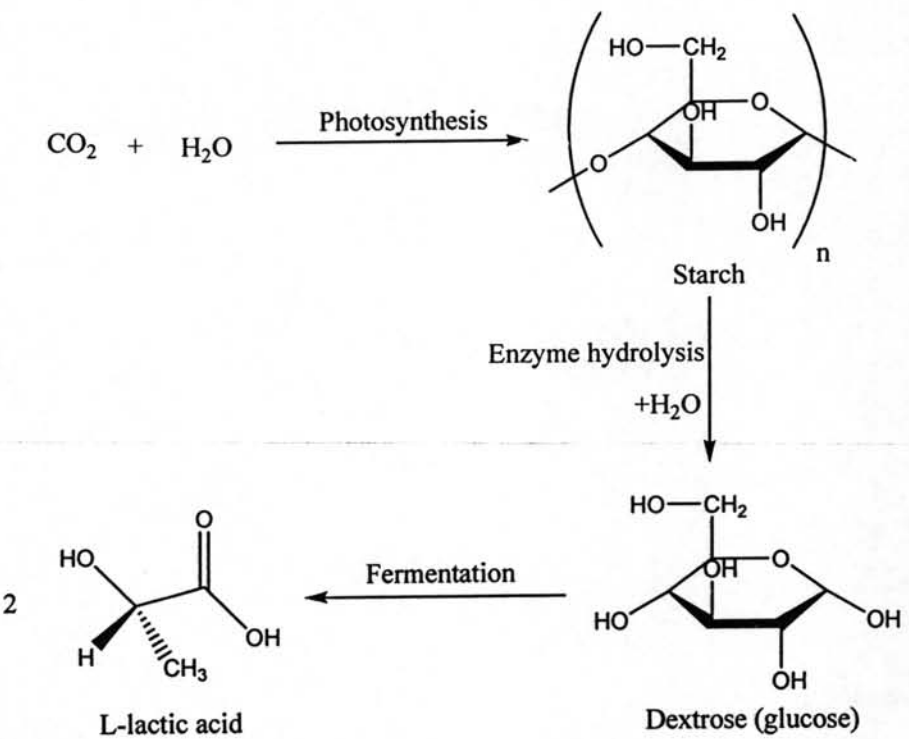
L-lactic acid

Figure 2.6 Stereoisomer of lactic acid.

Lactic acid can be also produced by bacterial and fungal fermentation. Lactic acid bacteria, *Lactobacilli,* have been extensively used in lactic acid fermentation because they can synthesize the optical isomers of lactic acid at a high production rate. The filamentous fungus, *Rhizopus* is an obligate aerobe that is often used for industrial production of optically pure L-lactic acid. The advantages of using *Rhizopus* species as an alternative to lactic acid bacteria include use of inexpensive raw materials and production of optically pure L-lactic acid. Since pure stereoisomer of lactic acid is strictly required for biodegradable polylactic acid production, production of lactic acid by fungal fermentation eases the purification process by omitting the separation of stereoisomer compared to lactic acid obtained from bacterial fermentation [10].

2.4.1 Direct fermentation of starch to L-lactic acid

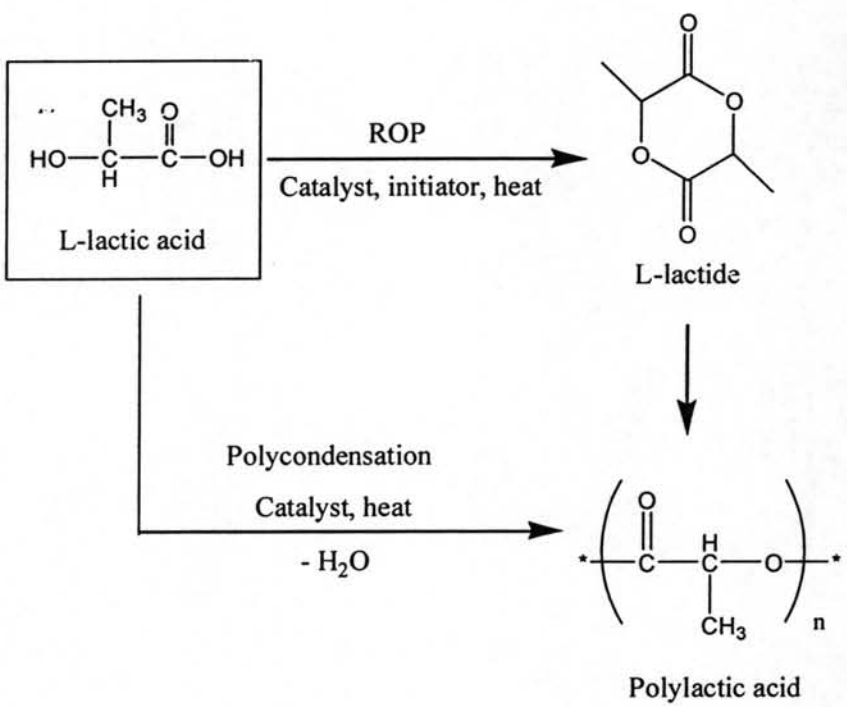
Lactic acid can be used in food technology as preservative or flavoring agent, and the precursor of polylactic acid, a polymer used as biodegradable plastic. L-lactic acid can be produced from starch by bacterial or fungal fermentation [7, 23].



Scheme 2.9 Fermentation of starch to produce L-lactic acid.

Lactic acid can be separated and substantially purified from fermentation broth by various separation techniques such as reactive extraction, membrane separation, ion exchange, electrodialysis, chemical reaction distillation, and reverse osmosis. Depending on the nature of fermentation broth and the use of lactic acid, particular technique provides different advantages and disadvantages. The disadvantages of reactive extraction are use of toxic solvent and contaminated recovery products. The membrane separation has a major problem in fouling of particles from fermentation broth. The chemical reaction distillation is a time consuming process and uses high energy consumption for separation.

2.4.2 Chemical uses of lactic acid

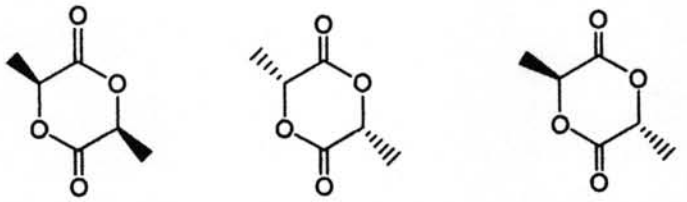


Scheme 2.10 Polycondensation of L-lactic acid and ring-opening polymerization of L-lactic acid.

There are two optical isomers of lactic acid, D-and L-type, of whose molecule has hydroxyl and carboxyl groups. The chemicals were used to synthesize unique functional organic compounds.

2.5 Lactide [10]

A cyclic dimer of lactide produced from the dehydration of lactic acid. When dilactide is prepared from racemic lactic acid, the three isomers that result are D-lactide, L-lactide and *meso-* lactide.

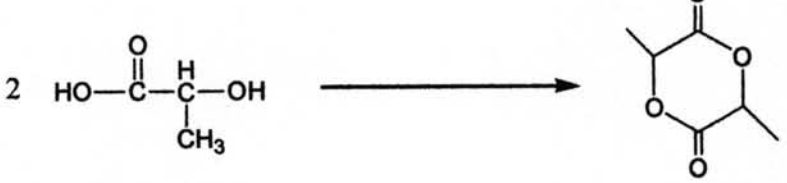


L-lactide D-lactide meso-lactide

Figure 2.7 The structure of lactide in different stereoisomer.

The meso isomer can be removed, but D and L-lactide are enantiomers that comprise the racemic form, *rac* -lactide. When *rac*-lactide is polymerized with simple catalysts, an amorphous polymer results from an essentially random incorporation of D and L- lactide units in the growing chain.

Since the properties of the racemic polymer are not suitable for most practical applications, commercial processes presently utilize L-lactide produced from L-lactic acid.



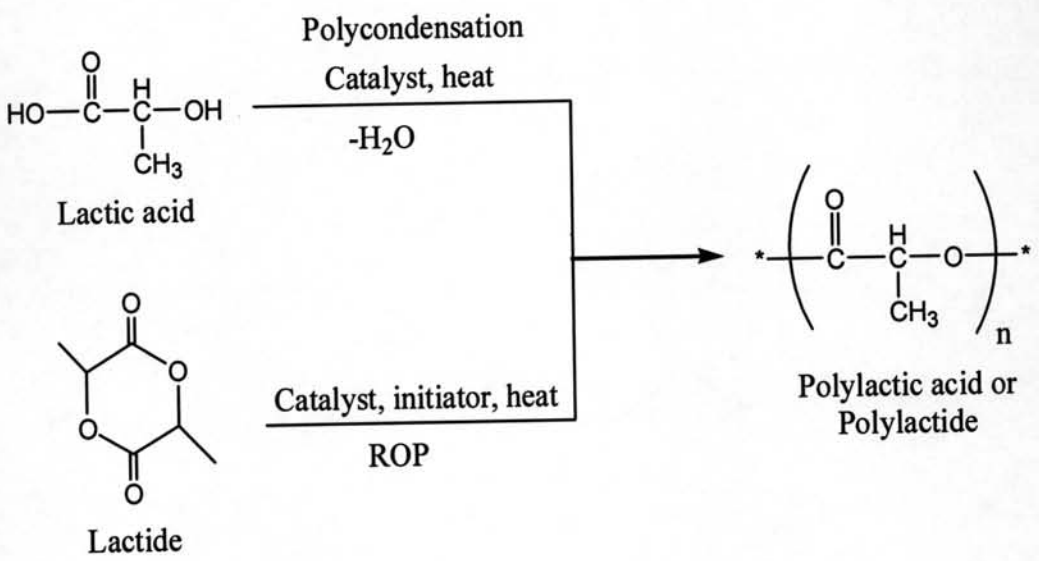
Lactic acid Lactide

Scheme 2.11 Production of L-lactide by dehydration 2 molar of lactic acid.

2.6 Polylactide

2.6.1 Properties and applications of polylactide

Polylactide or poly(lactic acid) (PLA) is the aliphatic polyester, containing lactide (LA) repeating units. PLA can be synthesized by two methods: polymerization of lactic acid and ring-opening polymerization (ROP) of lactides, which are schematically illustrated in Scheme 2.11.

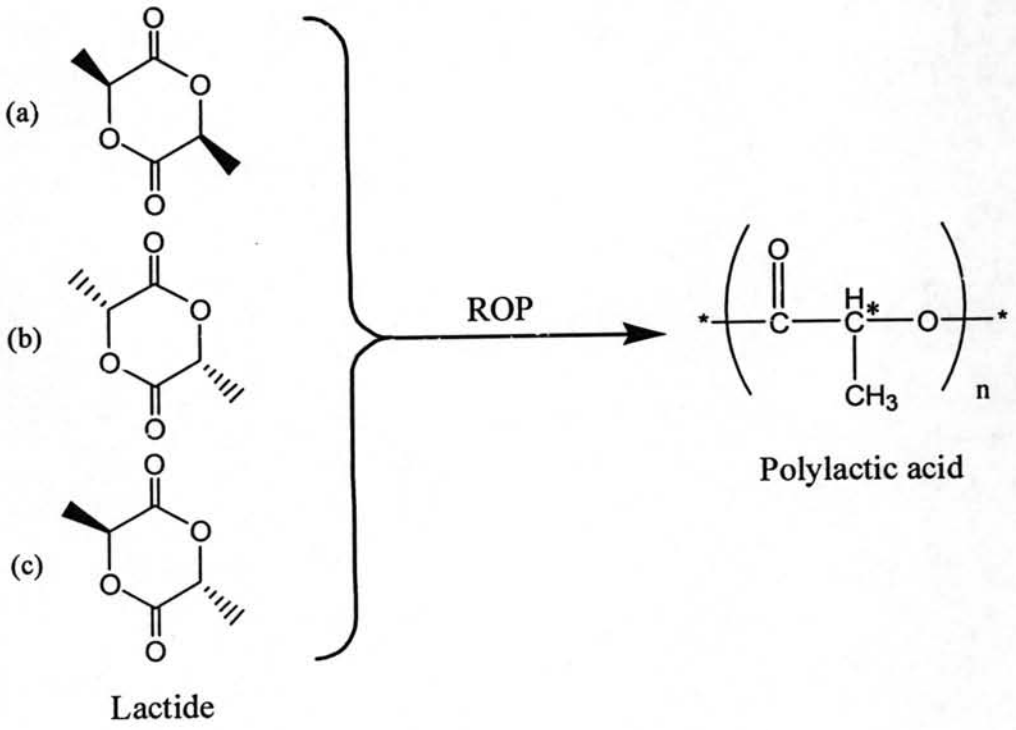


Scheme 2.12 Production of polylactide by polycondensation and ring-opening polymerization.

The most efficient way of preparing polylactides is ROP, by coordination initiators such as aluminum alkoxide or stannous alkoxide. This method usually allows a controlled synthesis leading to a narrow molecular weight distribution (MWD). Polymerization of PLA is highly sensitive to heat, especially temperatures higher than 190 °C [10]. Heating these materials above this temperature results in a noticeable decrease of molecular weights.

Polymerization of the different streoforms results in materials with different properties (Scheme 2.12). The polymers derived from the pure L-LA or D-LA monomer are semi-crystalline, relatively hard materials with melting temperatures

around 184 °C, and the glass transition temperatures of about 55 °C. The pure enantiomeric PLLA is naturally occurring. Polymerization of the rac-(D,L)-lactide and meso-lactide results in amorphous materials with a glass transition similar to that of the semicrystalline counterparts.

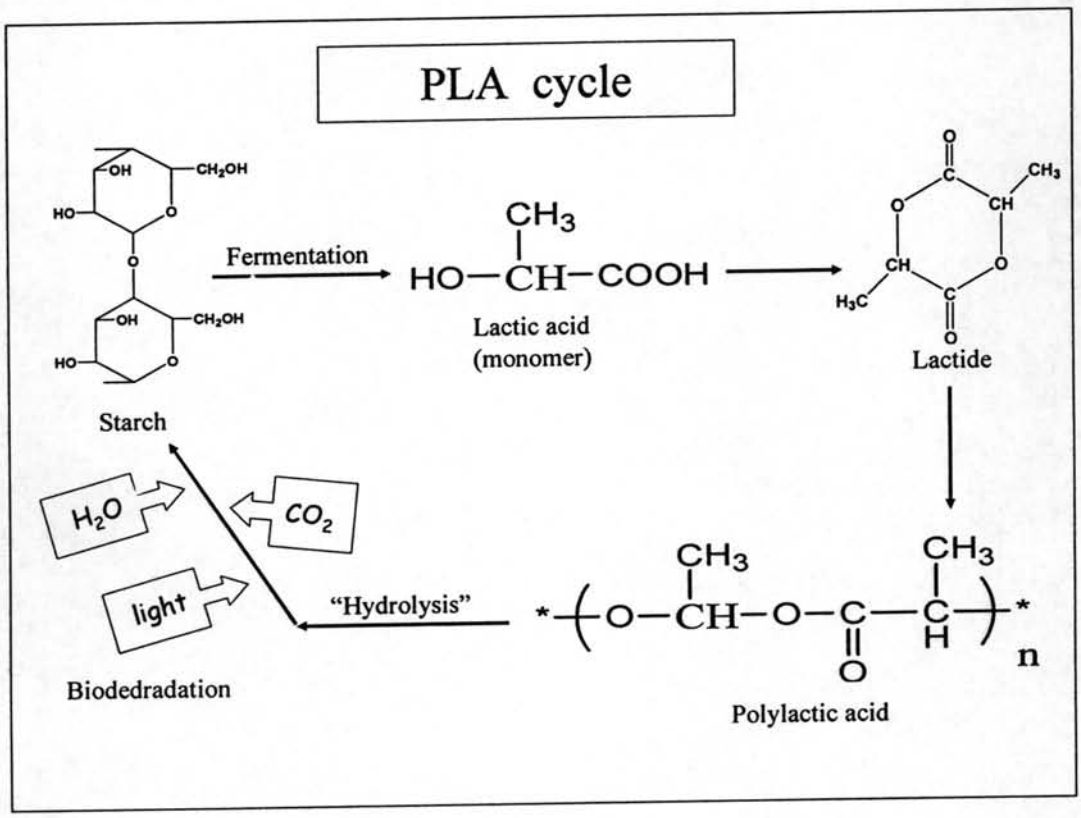


Scheme 2.13 Structures of the different stereoisomer of the lactide monomer and the resulting repeating unit, the chiral center marked with *, (a) L,L-lactide, (b) D,D-lactide, and (c) D,L-lactide.

Early reports of the biomedical use of PLA are dated back to the 1960s. Since then PLA had gained wide spread application in the medical field, for use in sutures, drug delivery devices, prosthetics, scaffolds, vascular grafts, and bone screws, pins and plates for temporary internal fracture fixation. Good mechanical properties and the fact that it degrades into non-toxic products explain the popularity of PLA. A good number of studies agree that PLA is completely resorbable, triggering no or very mild and transient adverse tissue responses.

2.6.2 Degradation of polylactide

In addition, PLA has been approved by The American Food and Drug Administration (FDA) for medical use and is commercially available in various of grades. Hydrolytic degradation of PLLA eventually generates lactic acid monomer, which is metabolized via the tricarboxylic acid cycle and subsequently eliminated as CO_2 via the respiratory system.

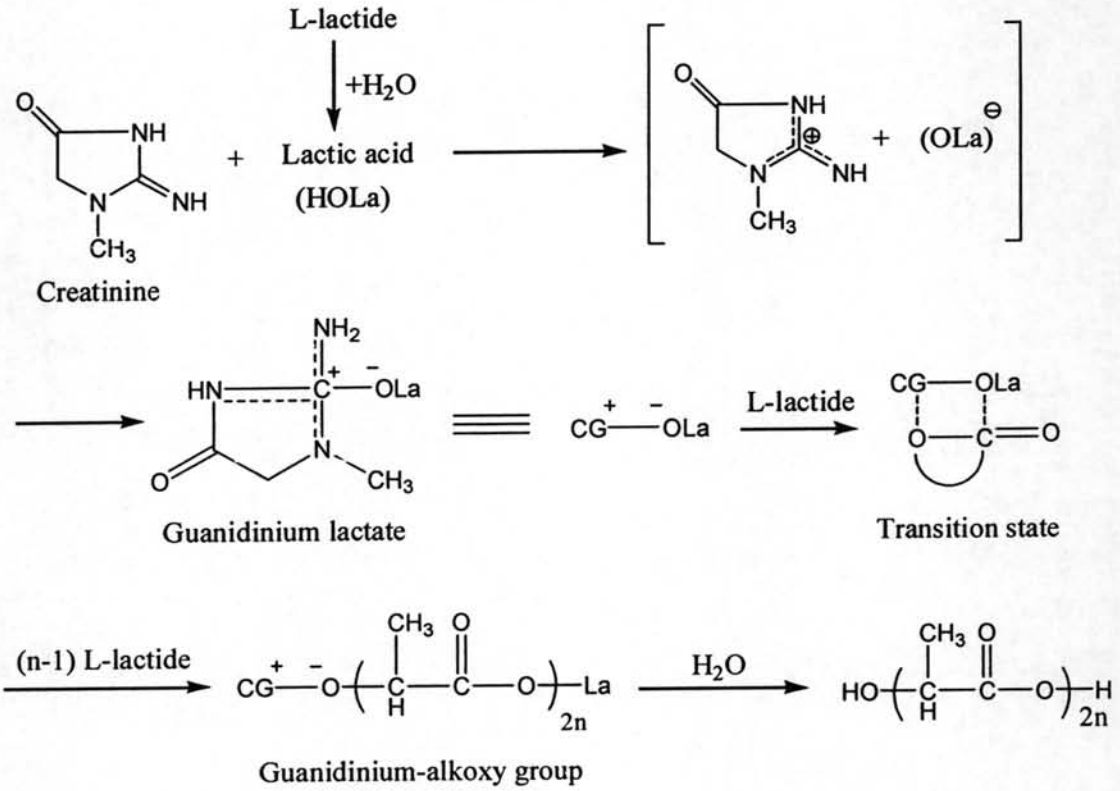


Scheme 2.14 The cycle of PLA in environmental.

The interested commercial PLA is continuously growing. This is governed by the recent advances in processing and engineering of the product properties, but most of all by the recent development in manufacturing the monomer from renewable resources. Up until the mid 1990s, PLA was produced from a petrochemical feed stock and the high product price limited its potential uses. Now, the monomer can be economically obtained by bacterial fermentation of D-glucose from corn and the lowered market price of PLA opens up a range of new applications, including packaging and other disposable items [24-30].

2.7 The relevant research

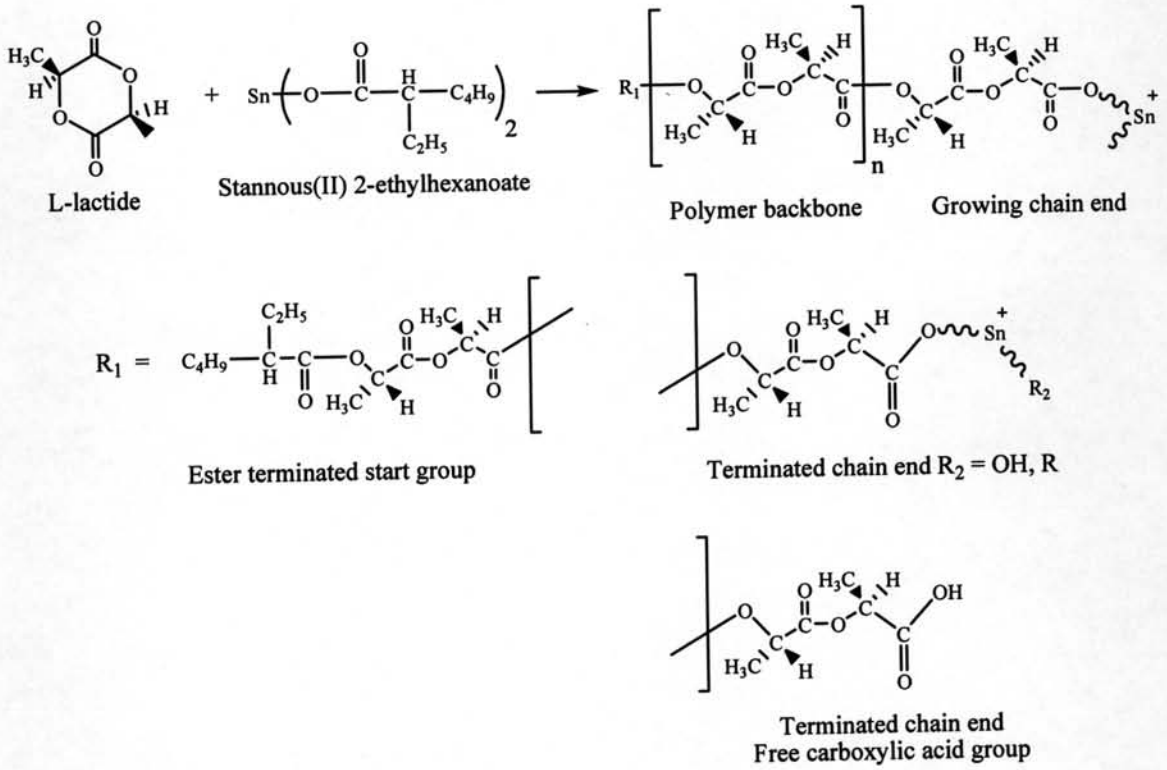
In 2004, Wang, C. H. et. al. [1] reported the ring-opening of L-lactide can be initiated by creatinine. Due to creatinine, a non-toxic metabolite in the human body, is metal-free catalyst and high biosafety which suitable for the cancer materials of controlled drug release devices.



Scheme 2.15 A mechanism of ring-opening polymerization of L-lactide initiated by creatinine.

This research was investigated the effect of reaction temperature and reaction time of PLLA synthesis. Suitable condition for high yield polymerization and pretty narrow molecular weight distribution of PLLA was 160°C, 96 hours.

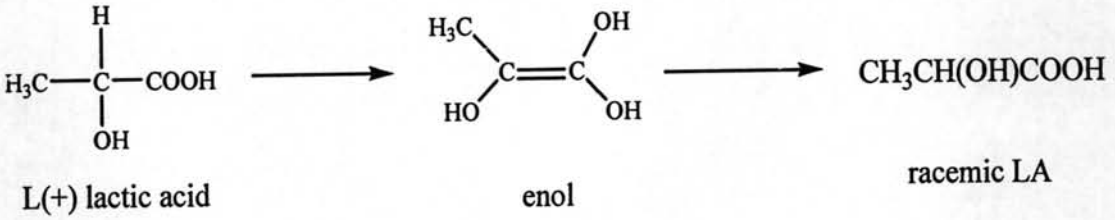
In 1997, Bendix, D. et. al. [2] reported the Chemical synthesis of polylactide and its copolymers for medical applications. Polylactide and its copolymers are produced by ring-opening polymerization of cyclic monomers.



Scheme 2.16 Tentative reaction scheme for the ring opening polymerization (ROP) of L-lactide, using stannous octoate as catalyst.

The polymerization is an equilibrium reaction. The reaction in Scheme 2.16 is depending on the reaction conditions, residual L-lactide can be found in amounts of up to 15%. Additionally, for chemicals used in medical applications generally a high purity is required, and monomers can be considered as an impurity.

In 2003, Dutkiewiez, S. et. al. [5] reported the synthesize process of poly(L(+) lactic acid) by using polycondensation method in solution.



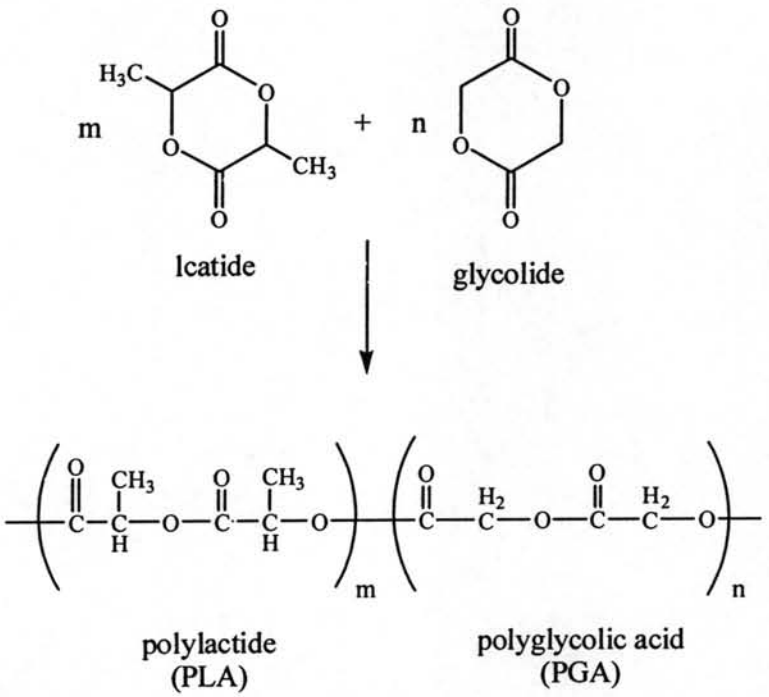
Scheme 2.17 Synthesis of poly(L(+) lactic acid) by polycondensation method in solution.

In this research, the solution polymerization was used diphenyl ether as the solvent. The reaction temperature should not be higher than 140°C because the racemisation of PLA was obtained at the high temperature. The poly(L(+) lactic acids) was shown fibre-forming properties in diphenyl ether.

In 1995, Kricheldorf, H. R. et. al. [6] reported the polymerization of L-lactide which initiated by Sn(II) 2-ethylhexanoate and study about mechanistic. $Sn(Oct)_2$ is a highly efficient catalyst, 99% optically pure poly(L-lactide) and permitted food additive in numerous countries. Kricheldorf was presented in two series of polymerizations, with benzyl alcohol as coinitiator and without benzyl alcohol, all polymerizations were conducted in bulk at 120 °C for 24 hours. The polymerization mechanism proposed in this work is neither a cationic, anionic nor pseudoanionic mechanism, and is probably best called a complexation mechanism or second-order insertion mechanism.

In 1999, Kiremitci-Gumusderelioglu, M. et. al. [17] studied the process of synthesis and degradation of poly(dl-lactide) and poly(dl-lactide-co-glycolide). Homopolymerization of dl-lactide was preformed by ring-opening polymerization in the presence of catalyst, stannous octoate, and a chain control agent, lauryl alcohol. The polymerization reaction was carried out in different conditions by changing the reaction temperature, reaction time, catalyst concentration and chain control agent in

order to determine the optimum polymerization conditions. The polymerization yield is not affected by the variation of temperature between 165-200°C. By increasing temperature above the optimal level, the yield of polymerization decreases because the formation of residual monomer increases.



Scheme 2.18 Chemical structure of dimers, polymers, and copolymerization reaction.

Copolymer of lactide and glycolide monomers were synthesized to contain lactide-to-glycolide ratios of 90:10 and 70:30. They are random copolymers obtained by a ring-opening polymerization of cyclic dimmers, lactide and glycolide, as illustrated.