# CHAPTER 1

# Introduction

## 1.1 Biodegradable Polymers

Biodegradable polymers, especially aliphatic polyesters, have been investigated worldwide as biomaterials for medical, pharmaceutical and industrial applications due to their biocompatibility and biodegradability. The term "biodegradable" refers to degradation induced by the vital activity of an organism, not simply the degradation of a material in a physiological environment. However, the term "biodegradable polymer" is now widely used to convey the meaning of a polymer that degrades in the human body. The generally accepted definition of "polymer biodegradation" is; hydrolytic, enzymatic or bacteriological degradation processes occurring in a polymer which do not necessarily proceed to a stage where the physical form of the polymer is altered. Consequently, the design of biodegradable polymers with tailored properties has become one of the most challenging problems for polymer scientists. A basic prerequisite for medical applications is the absolute biocompatibility of the polymers and their degradation products [1-4].

Polyesters are one of the most important biodegradable plastics being used in industry, due to their potentially hydrolysable ester bonds. Morphology is an important factor in determining the *in vitro* performance. In general, polymers derived from nature are more biodegradable than synthetic polymers; especially those polymers containing ester functionality, which are called polyesters. Their degradable products can be quickly metabolised by microorganisms. The presence of ester linkages in the polyester backbones allows gradual hydrolytic degradation of polyesters. The initial degradation products are low-molecular weight polyesters, which are endogenous compounds and as such are non-toxic. When the cleavage of the ester linkages continues by water hydrolysis, the final products are carbon dioxide and water. In recent years, aliphatic polyesters are being used in several fields ranging from agricultural implements to biomedical application such as sutures, tissue-supporting scaffolds, drug delivery devices, biodegradable plastics and packaging materials that are produced from plants instead of petroleum [5].

Aliphatic polyesters such as polylactide (PLLA), poly(ε-caprolactone) (PCL) and polyglycolide (PG) are widely used in medical applications because of these polymers can be degraded within the human body *via* a simple hydrolysis and the by-products are either metabolizable or excretable from the human body without any adverse toxicological effects. The US Food and Drug Administration has already approved them for use in biological systems. In the theory, ester group will be hydrolysable, degradable and absorbable while methylene group and ether bond in the polymer structure will increase the main chain flexible [6, 7]. Therefore, their copolymers are found more use in a broad variety of medical applications due to their complimentary properties. That is the properties of copolyesters (such as hydrophilicity, rate of biodegradation, etc.) can also be tailored by introducing functional groups along the polymer chains. Such functional polyesters have been reported in the literature [8, 9].

## 1.2 Physical and Biodegradable Properties of Aliphatic Polyesters for Use in Biomedical Applications

The physical properties of aliphatic polyesters depend on several factors such as the composition of repeat units, flexibility of the chain, presence of polar groups, molecular mass, degree of branching, crystallinity, orientation, etc. Short-chain branches reduce the degree of crystallinity of polymers while long chain branches lower the melt viscosity and impact elongational viscosity with tension-stiffening behavior. The properties of these materials can further be tailored by blending, and copolymerisation [10-12] or by a change in the macromolecular architecture (i.e., hyper-branched polymers, star-shaped or dendrimers, etc.) [13].

The development of new biodegradable polyesters is an attractive area of research aimed at producing polymers that can be used in biomedical and pharmaceutical applications such as absorbable sutures, nerve guides, bone fixation rods, screws and clips. In addition to biocompatibility, the other properties of these polymers that make them uniquely suitable for these and other applications: biodegradability, high strength, permeability, controlled hydrophilicity and non toxicity. Other potential medical uses include bone plates and other orthopedic applications, ear vent tubes, nerve growth tubes and wound dressing. These applications are divided into three major functional areas: surgical sutures, tissue repair and regeneration and drug delivery. The main goal of this research is to synthesise copolyesters (copolymers of L-lactide and ε-caprolactone) for fabrication of monofilament absorbable surgical sutures.

### 1.3 Absorbable Surgical Sutures

The absorbable surgical suture acts as a temporary scaffold while the process of wound healing is taking place following surgery. The suture is used to hold tissues together until sufficient collagen synthesis has taken place to hold the wound together unassisted [14].

Absorbable suture can be fabricated as multifilaments or monofilaments that are shown in Figure 1.1. Whereas multifilament sutures are made up of tiny fibres braided or twisted together, monofilament sutures are single-stranded fibres which have no braiding or twisting. Both have their advantages and disadvantages. Multifilament sutures are soft, flexible and easy to handle, but there are interstices formed by the relatively loose braid of the fibres which permit serum and blood to penetrate the suture and from a perfect refuge for bacteria. Therefore, multifilament sutures should not be used in a wound which is likely to become infected. Moreover, their outer surface is rough which can make it difficult to pull the suture through delicate tissue without tearing the tissue in the process. Monofilament sutures have less affinity for bacteria and a smoother surface which are major advantages in exhibiting less tissue drag. On the other hand, they are quite stiff and difficult to handle and tie, which are disadvantages [15].

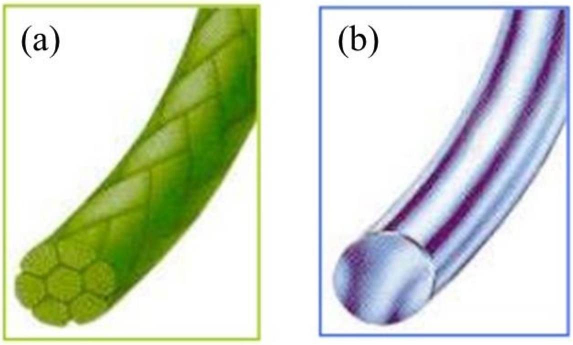
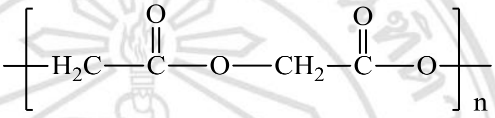
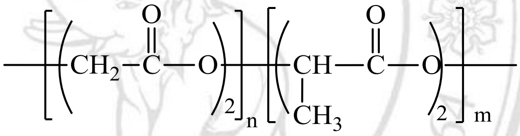
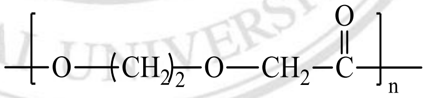
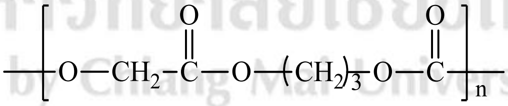
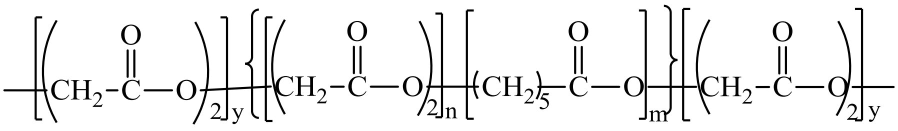


Figure 1.1 Physical forms of (a) braided multifilament and (b) monofilament sutures.

## 1.4 Historical Development of Synthetic Absorbable Sutures

Synthetic biodegradable polyesters have the advantage over natural materials in that they can be tailored to give a wider range of properties. They have been widely used for many biomedical purposes. In this research, attention is focused on absorbable suture applications, the historical development of which is now described in more details and the chemical structures of some commercial synthetic absorbable suture are listed in Table 1.1.

Table 1.1 The chemical structures of some commercial synthetic absorbable sutures.

| **Trade Name** | **Chemical Structure** |
|---|---|
| DEXON |  $\left[-H_2C-\overset{O}{\overset{\Vert}{C}}-O-CH_2-\overset{O}{\overset{\Vert}{C}}-O-\right]_n$<br>poly(glycolide) |
| VICRYL |  $\left[\left(CH_2-\overset{O}{\overset{\Vert}{C}}-O\right)_2\right]_n\left[\left(\underset{CH_3}{\underset{\vert}{CH}}-\overset{O}{\overset{\Vert}{C}}-O\right)_2\right]_m$<br>poly(glycolide-co-L-lactide)<br>n : m = 90 : 10 mol % |
| PDS II |  $\left[O-(CH_2)_2-O-CH_2-\overset{O}{\overset{\Vert}{C}}\right]_n$<br>poly(p-dioxanone) |
| MAXON |  $\left[O-CH_2-\overset{O}{\overset{\Vert}{C}}-O-(CH_2)_3-O-\overset{O}{\overset{\Vert}{C}}\right]_n$<br>poly(glycolide-co-trimethylene carbonate) |
| MONOCRYL |  $\left[\left(CH_2-\overset{O}{\overset{\Vert}{C}}-O\right)_2\right]_y\left\{\left[\left(CH_2-\overset{O}{\overset{\Vert}{C}}-O\right)_2\right]_n\left[(CH_2)_5-\overset{O}{\overset{\Vert}{C}}-O\right]_m\right\}\left[\left(CH_2-\overset{O}{\overset{\Vert}{C}}-O\right)_2\right]_y$<br>poly[glycolide-b-(glycolide-co-ε-caprolactone)-b-glycolide] |

The first synthetic absorbable suture was made of poly(glycolide) by Davis & Geck (USA) and was initially marketed in 1970 under the trade name of DEXON. DEXON is a braided multifilament suture. A similar synthetic absorbable suture to DEXON was developed by Ethicon, Inc. (USA), in 1974 from a 90:10 copolymer of glycolide and L-lactide under the trade name of VICRYL. It was also a braided multifilament suture with properties similar to those of DEXON. However, there are some concerns with braided sutures that relate to tissue drag and the trauma that may cause, as well as the possible potentiation of infection through the interstices of the braid structure.

To eliminate some of the concerns about braided sutures, the absorbable monofilament sutures, PDS II (a homopolymer of p-dioxanone; Ethicon, Inc.) and MAXON (a copolymer of trimethylene carbonate and glycolide; Davis & Geck) were introduced in the 1980s. Subsequently, MONOCRYL appeared on the market as a more pliable monofilament. This suture is made from a segmented triblock copolymer of ε-caprolactone (CL) and glycolide (G). The triblocks are comprised of a soft center-block of a random copolymer of P(G -co- CL) with a 55 : 45 mole % composition and two hard end-blocks of poly(glycolide) to add up to an overall composition of 25 : 75 mole %. The soft center-block provides good handling characteristics while hard end-blocks of poly(glycolide) provide high strength [16-18]. The molecular formula of MONOCRYL is also shown in table 1.1. While MONOCRYL has been shown to have superior handling properties, its breaking strength decreases faster than both PDS II and MAXON [18]. The challenge lies in tailoring the polymer microstructure to give the correct balance of handling and healing characteristics to meet the requirements of the application.

## 1.5 Polyester Synthesis

The traditional way of synthesising polyesters has been by polycondensation using diols and diacid (or an acid derivative), or from a hydroxyl acid. This method suffers, however, from some major shortcomings. These are the need for (a) high temperature, (b) long reaction times, (c) removal of reaction by-products, and (d) a precise stoichiometric balance between reactive acid and hydroxyl groups. Very high conversion is desirable to get polymer chains of sufficiently high molecular masses to provide useful mechanical properties in the final product. In spite of all precautions, a high degree of polymerisation is very difficult to achieve by this method because of side-reactions and the volatilization of monomers, which leads to a stoichiometric imbalance of reactants.

The ring-opening polymerisation (ROP) of lactones, cyclic diesters (lactides and glycoides), and cyclic ketene acetals is an alternative method, which has been successfully employed to yield high molecular mass polymers under relatively mild conditions. This polyaddition reaction can be carried out with no or very limited side-reactions, and this makes it possible to control properties like molecular weight and molecular weight distribution.

The increasing demands of a large number of biomedical applications have resulted in an increasing interest in producing macromolecules through controlled polymerisation.

### 1.5.1 Mechanisms of ROP of Cyclic Esters

Carothers and colleagues were the first to explore the ROP of lactones. Many research laboratories have now been involved in this research area. The ROP of lactones is the method of choice for the production of biocompatible and biodegradable polyesters. Lactones are ambidentate and the polymerisation may proceed by either alkyl-oxygen or acyl-oxygen scission.

Polylactones and polylactides of high molecular weight are exclusively produced by the ROP of the corresponding cyclic monomers. A polyester is formed when cyclic esters are reacted with a catalyst or initiator. Figure 1.2 presents the reaction pathway for the ROP of a cyclic ester.

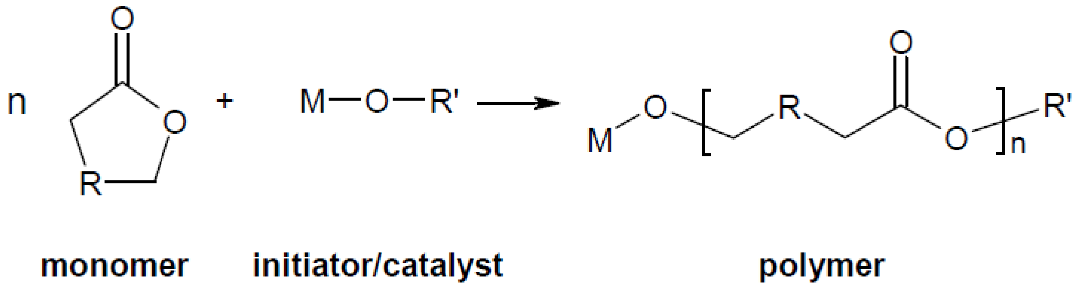


Figure 1.2 Schematic representation of the ring-opening polymerisation of a cyclic ester (R = $(CH_2)_{0-3}$ and/or (CHR'')).

Each macromolecule formed will generally contain one chain end terminated with a functional group originating from the termination reaction and one terminus end-capped with a functional group originating from the initiator. By altering the catalyst or initiator and the termination reaction, the nature of the functional groups can be varied to fit the application of the polymer. The types of initiator and end-group play an important role in both the thermal stability and hydrolytic stability of the resulting polyester [19-21].

The ring-opening reaction can be performed either as a bulk polymerisation, or in solution, emulsion or dispersion [22, 23]. A catalyst or initiator is necessary to start the polymerisation. Under rather mild conditions, high-molecular weight aliphatic polyesters of low polydispersity can be prepared in short periods of time. Problems associated with condensation polymerisation, 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 [24]. The ROP of cyclic esters can be carried out using several methods such as anionic, cationic and coordination-insertion (pseudo-anionic) polymerisation [25].

### 1.5.1.1 Cationic Ring-opening Polymerisation

Cationic initiators for the ring-opening polymerisation of lactones can be divided into four groups: (a) protonic acids (HCl, RCOOH, $RSO_3H$, etc.), (b) Lewis acids ($AlCl_3$, $BF_3$, $FeCl_3$, $ZnCl_2$, etc.), (c) alkylating agents (stabilized carbocations, e.g. $Et_3O^{(+)}$ $BF_4^{(-)}$, $CF_3SO_3CH_3$), and (d) acylating agents $(CH_3CO)^{(+)(-)}OCl_4$.

Among the cyclic esters, 4-, 6- and 7-membered rings form polyesters when reacted with cationic catalysts [25]. The cationic ring-opening polymerisation involves the formation of a positively charged species which is subsequently attacked by a monomer (Figure 1.3). The attack results in a ring-opening of the positively charged species through an $S_N2$-type process.

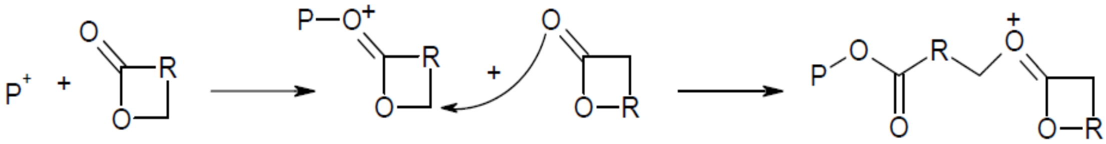


Figure 1.3 The reaction pathway for the ring-opening polymerisation of a cyclic ester by cationic initiation.

The cationic polymerisation is difficult to control and often only low molecular weight polymers are formed [26].

### 1.5.1.2 Anionic Ring-opening Polymerisation

Anionic ring-opening polymerisation of cyclic ester monomers takes place by the nucleophilic attack of an negatively charged initiator on the carbonyl carbon or on the carbon atom adjacent to the acyl-oxygen, resulting in a linear polyester (Figure 1.4) [27, 28]. The propagating species is negatively charged and counter-balanced with a positive ion. Depending on the nature of the ionic propagating chain end and the solvent, the reacting complex varies from completely ionic to almost covalent.

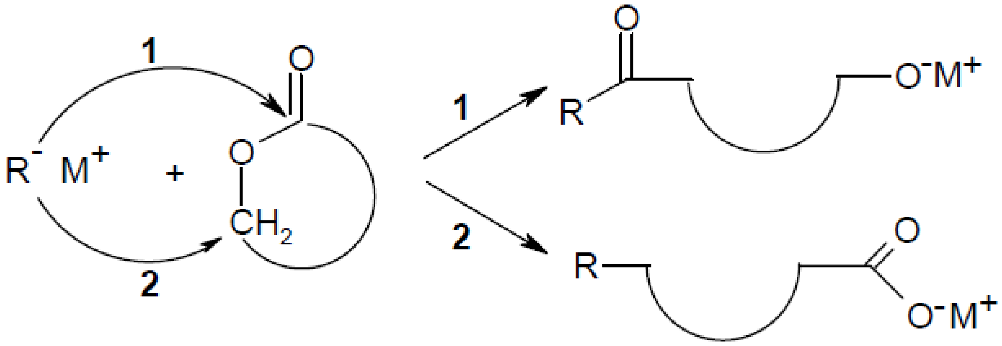


Figure 1.4 The reaction pathway for the ring-opening polymerisation of a cyclic ester by anionic initiation. Ring-opening of monomer by 1) acyl-oxygen bond cleavage and 2) alkyl-oxygen bond cleavage.

Larger lactones, such as ε-caprolactone or lactide, react only by an attack of the anion on the carbonyl carbon atom with acyl-oxygen scission and the formation of an alkoxide as the growing species [29, 30]. A problem associated with the anionic ROP is the extensive back-biting, and in some cases only polyesters of low molecular weight are achieved [31].

### 1.5.1.3 Coordination-Insertion Ring-opening Polymerisation

The pseudo-anionic ring-opening polymerisation is often referred to as “coordination-insertion” ROP, since the propagation is thought to proceed by coordination of the monomer to the active species and then insertion of the monomer into the metal-oxygen bond by rearrangement of the electrons [32, 33]. Figure 1.5

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 polymerisation reactions are produced.

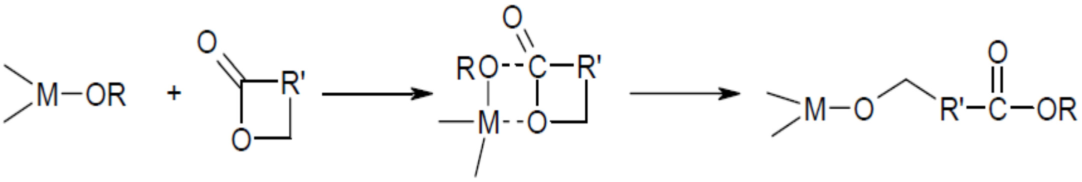


Figure 1.5 The proposed reaction pathway for the ring-opening polymerisation of a cyclic ester by the coordination-insertion mechanism.

The coordination-insertion type of polymerisation has been thoroughly investigated since it may yield well-defined polyesters through living polymerisation [33]. When two monomers of similar reactivity are used, block copolymers can be formed by sequential addition to the “living” system [34].

### 1.5.2 Organometallic Compounds as Initiators for the ROP of Lactones and Lactides

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 to produce structurally advanced macromolecules. A large variety of organometallic compounds, *i.e.* metal alkoxides and metal carboxylates, have been studied 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.

### Transesterification reactions

It is well known from the ring-opening polymerisation of lactones and lactides that the catalyst or initiator causes transesterification reactions at elevated temperatures, or at long reaction times [35, 36] (Figure 1.6). Intermolecular transesterification reactions modify the sequences of copolylactones and prevent the formation of block copolymers. Intramolecular transesterification reactions, *i.e.* back-biting, cause degradation of the polymer chain and the formation of cyclic oligomers [37]. Both types of transesterification reactions broaden the molecular weight distribution.

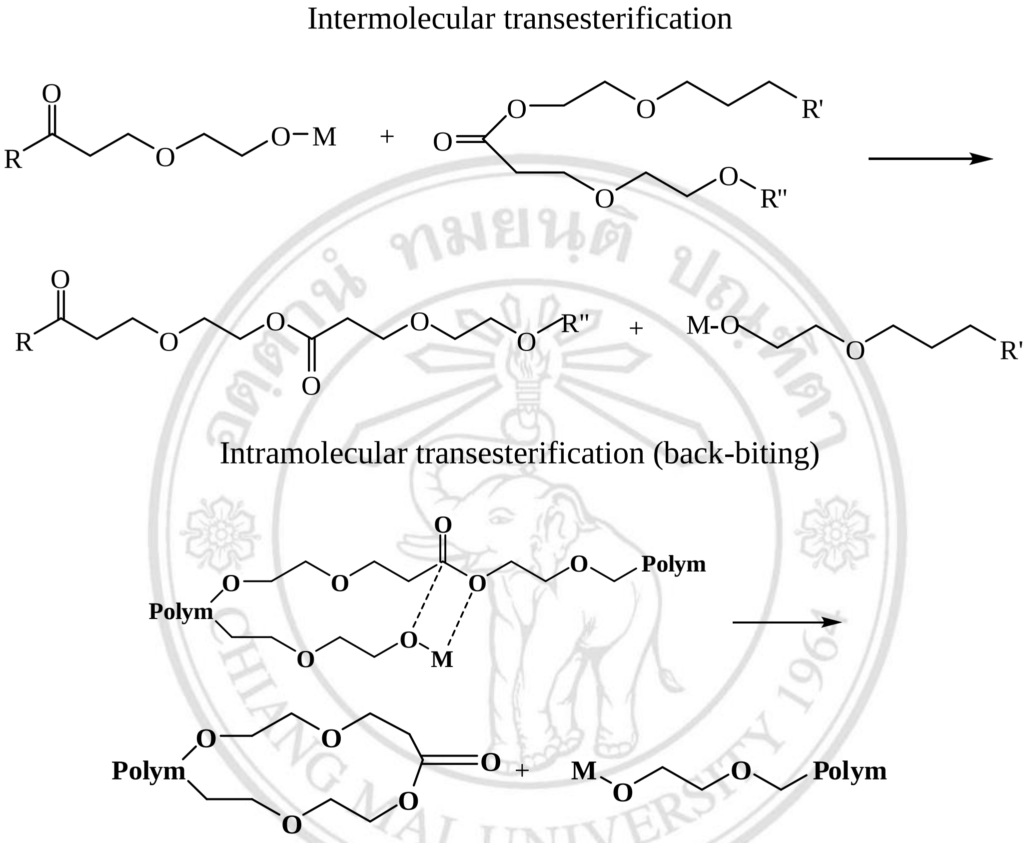
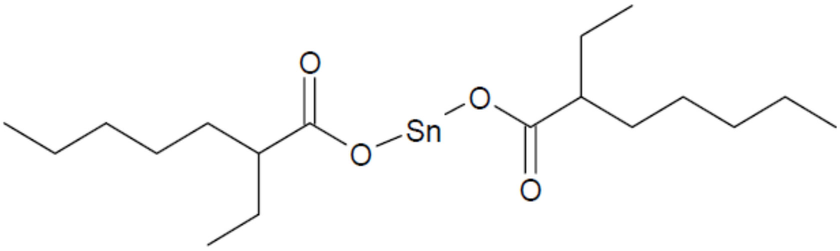


Figure 1.6 Reaction scheme for intermolecular and intramolecular transesterification reactions.

A number of architectures may be produced as a result of the great versatility of the ROP of cyclic ester. Different strategies have been applied for the design of new polymeric materials. A careful selection of the appropriate initiator or catalyst for ROP of a specific system is crucial.

### 1.5.2.1 Tin(II) 2-ethylhexanoate

Tin(II) 2-ethylhexanoate, commonly referred to as stannous octoate [$Sn(Oct)_2$], is a frequently used catalyst in the ROP of lactones and lactides [38]. It has been approved as a food additive by the Food and Drug Administration (FDA). $Sn(Oct)_2$ in the industry and exists in the form shown below.



Tin(II) 2-ethylhexanoate [$Sn(Oct)_2$]

$Sn(Oct)_2$ is not thought to be the actual initiator since the molecular weight does not depend on the monomer-to-$Sn(Oct)_2$ molar ratio. $Sn(Oct)_2$ is also a strong transesterification agent, and resulting copolymers normally having a randomized microstructure. An increase in reaction temperature or reaction time increases the amount of transesterification reactions.

The most promising mechanism is a coordination insertion mechanism. Investigations of the coordination-insertion mechanism have resulted in two slightly different reaction pathways. Kricheldorf and coworkers have proposed a mechanism [39, 40] where the coinitiating alcohol functionality and the monomer are both coordinated to the $Sn(Oct)_2$-complex during propagation. Penczek and coworkers have presented a mechanism [41] where the $Sn(Oct)_2$ is converted into a tin-alkoxide before complexing and ring-opening of the monomer. Figure 1.7 shows the two different proposals.

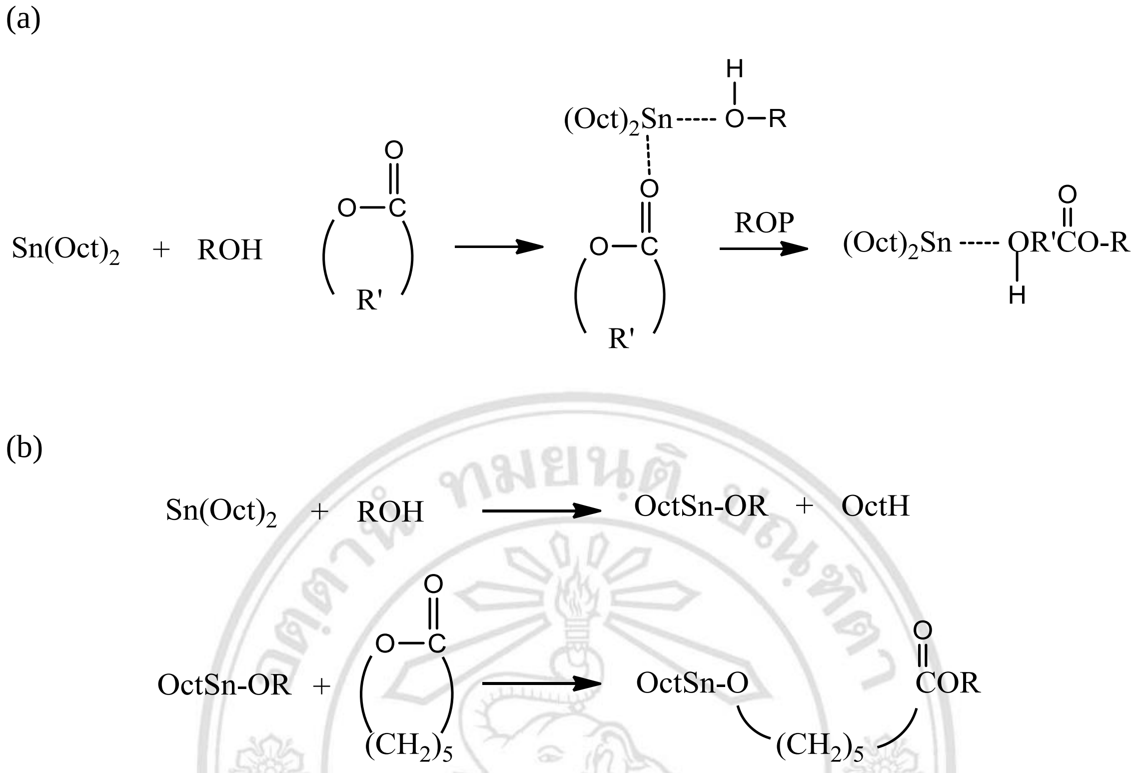


Figure 1.7 The main ring-opening polymerisation mechanism proposals with Tin(II) 2-ethylhexanoate as catalyst,
a) complexation of a monomer and alcohol prior to ROP
b) formation of a tin-alkoxide before ROP of ε-caprolactone.

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 polymerisation. The $Sn(Oct)_2$ catalyst is generally active at elevated temperature, leading to some intermolecular and intramolecular transesterification reaction [42]. $Sn(Oct)_2$ is rather easy to use, but it is also a strong transesterification catalyst and it should not therefore be recommended for the synthesis of advanced molecular structures.

From the mechanisms described above, the actual initiators for the ROP of cyclic esters in bulk are tin alkoxides, which are generated *in situ* via the reaction between $Sn(Oct)_2$ and ROH. If tin alkoxides are used directly prior to the synthesis, ROP of macromolecule with advanced architecture can be controlled.

### 1.5.2.2 Tin(II) Alkoxides

Mono-tin-alkoxides, tin-dialkoxides and cyclic tin-alkoxides have been utilized as initiators in the ring-opening polymerisation of cyclic esters. The polymerisation of lactones with tin-alkoxides is thought to follow the coordination-insertion mechanism and proceeds by acyl-oxygen cleavage with retention of configuration [40, 43, 44]. The main purpose of this research is to synthesise some novel tin(II) alkoxides for use as initiators in the ring-opening polymerisation (ROP) of cyclic esters. The methods for the synthesis of tin(II) alkoxide initiators are described in section 1.9.

## 1.6 Kinetics of Ring-opening Polymerisation

The kinetics of polymerisation have been investigated in order to study the mechanism of controlled ring-opening polymerisation (ROP). The results of the kinetic experiments could be utilized to understand the action of the initiator in more detail. The kinetics of the L-LA polymerisation were studied in chloroform at 60 °C [45] and the rate equation could be described as:

$$-d[M]/dt = k_{app}[M] \qquad (1.1)$$

where [M] is the lactide concentration at a given reaction time t and $k_{app}$ is the apparent rate constant.

Normally, the ROP reaction initiated by metal alkoxide is pseudo first order with respect to monomer concentration. Therefore, the apparent rate constant of polymerisation can be expressed by eq. (1.2).

$$-\ln(1-p) = k_{app}(t) \qquad (1.2)$$

where p is degree of conversion.

ROP reactions initiated with a metal alkoxide initiator are generally characterised by equilibrium between the free and the aggregated metal alkoxide [46].

$$(P^*_n)_m \overset{k_{da}}{\rightleftharpoons} mP^*_n \qquad (1.3)$$

$$P^*_n + M \xrightarrow{k_p} P^*_{n+1} \qquad (1.4)$$

where $P^*_n$, $(P^*_n)$ and M are the non-aggregated active centers, aggregated active centers and monomer, respectively, $k_{da}$ is the aggregation equilibrium constant, $k_p$ is the propagation rate constant, and m is the degree of aggregation. Aggregation causes a temporary termination of the growing species, since the chains propagate only if they are non-aggregated. The kinetics of polymerisation can be influenced by the difference in reactivities between the aggregated compounds.

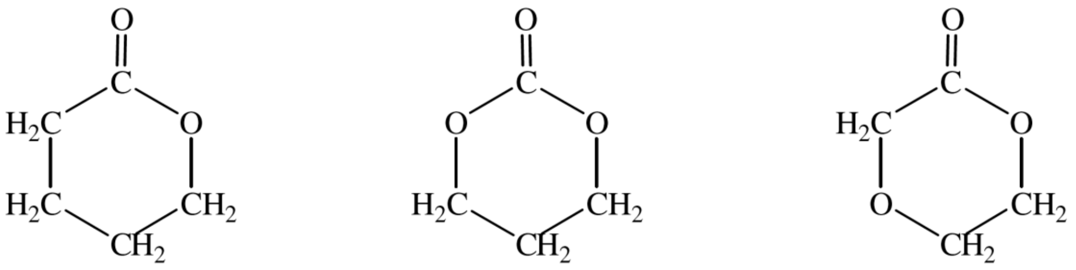
The rate of a chemical reaction can be followed by observing any property of a system which changes proportionately with the concentration of the reaction species. In order to determine the rate of polymerisation, it is necessary to measure the monomer concentration as a function of reaction for process development and the prediction of optimum rate of reactions. In this work, kinetic investigation of ROP can be studied by dilatomertry.

## 1.7 Factors Governing Ring-opening Polymerisability

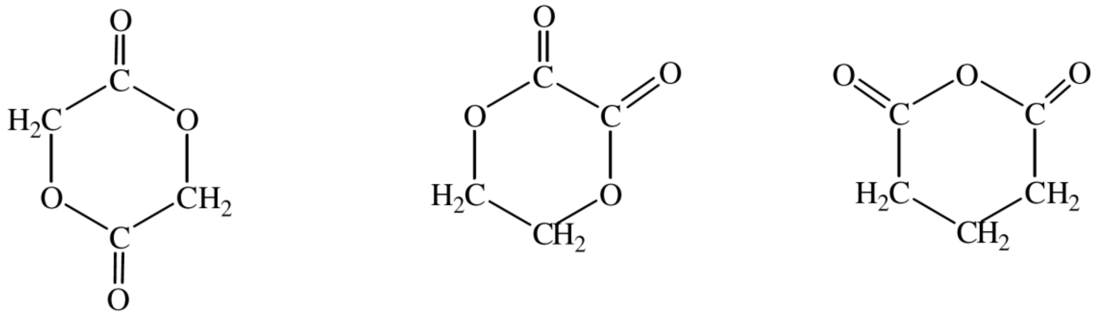
The important factors that influence cyclic ester monomer polymerisability are the chemical structure within the ring, the ring strain, the nature of any substituents external to the ring and the nature of the reaction conditions employed. Apart from these factors, steric hindrance of initiator can also be important for the polymerisability [47].

### 1.7.1 Chemical Structure within the Ring

The different internal chemical structures result in different polymerisabilities. Some examples of unsubstituted cyclic esters which have the same ring size but different ester group configurations are compared in Figure 1.8. As would be expected, their physical properties vary and the conditions used in their polymerisations also tend to vary accordingly.



δ–valerolactone trimethylene carbonate p-dioxanone



glycolide ethylene oxalate glutaric anhydride

Figure 1.8 The variations of cyclic ester monomer structure.

### 1.7.2 Ring Strain

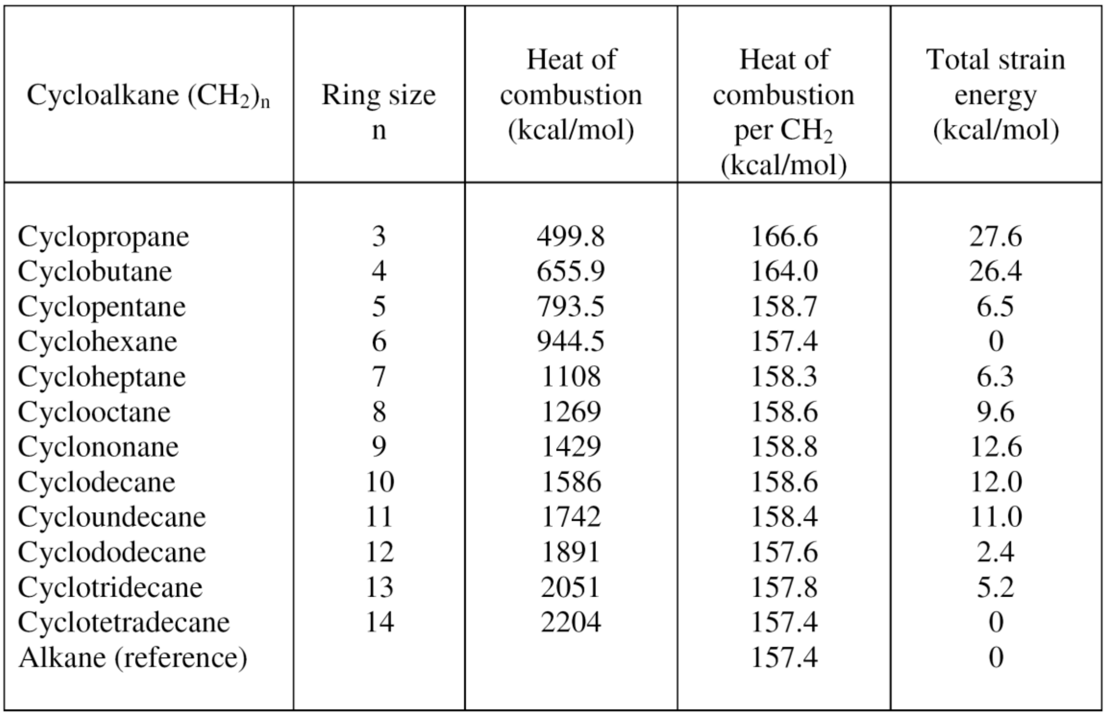
Ring strain is a thermodynamic property caused by either forcing the bonds between ring atoms into angular distortion or by the steric interaction of substituents on the ring atoms. It is the release of ring strain by polymerisation that provides the principle driving force for the polymerisation of cyclic monomers.

The theory about ring strain was originally proposed in 1885 by Adolf von Baeyer, and later has been recognized as “Baeyer ring strain theory”. The principle of this theory is quite simple which stated that, if carbon prefers to have tetrahedral geometry with bond angles of $109^{o}$, ring sizes other than five and six may be too strained to exist.

The ring strain in a compound can be quantitatively measured in term of ring strain energy, which is the difference between the total amount of energy in the compound and the amount of energy in a hypothetical strain-free reference compound. The simplest way to determine strain energies is to measure heats of combustion (amount of heat energy released when the compound burns completely with oxygen) of the cycloalkanes. Example data for the heats of combustion of cycloalkanes are summarized in Table 1.2 This data show clearly that Baeyer's theory is not fully correct. Cyclopropane and cyclobutane are indeed quite strained, just as predicted, but cyclopentane is more strained than predicted, and cyclohexane is strain-free. For rings of larger size, there is no regular increase in strain, and rings having more than 14 carbons are again strain-free.

The failure of Baeyer's theory can be expected from one very simple reason. It assumed that all rings are flat but, in reality, most cycloalkanes are not flat. Thus, the flexibilities of the rings are not taken into account. Several factors are used to describe the shape and total strain energy of rings, such as angle strain, torsional strain and steric strain.

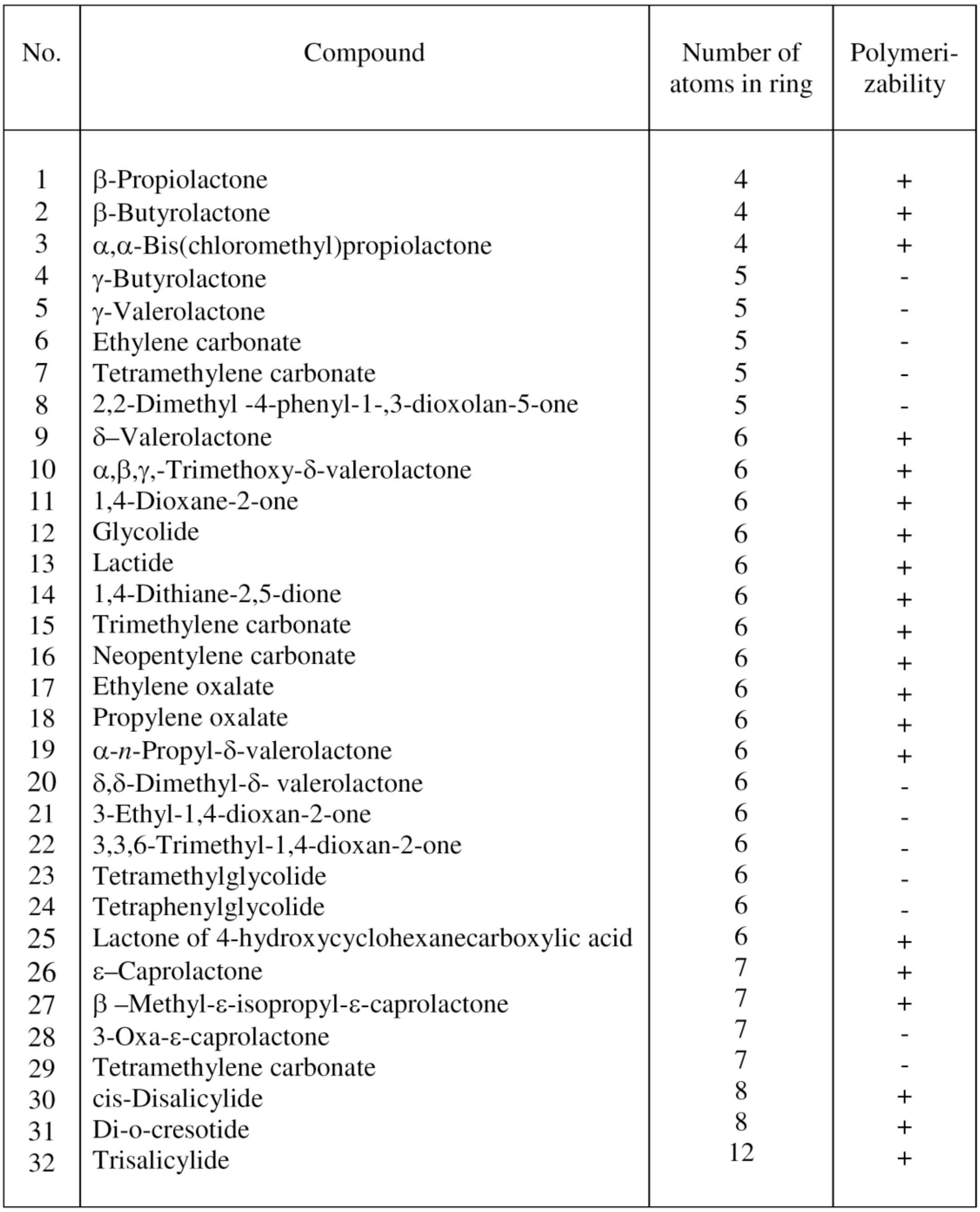
Table 1.2 Heats of combustion of cycloalkanes [48].



| Cycloalkane $(CH_2)_n$ | Ring size n | Heat of combustion (kcal/mol) | Heat of combustion per $CH_2$ (kcal/mol) | Total strain energy (kcal/mol) |
|---|---|---|---|---|
| Cyclopropane | 3 | 499.8 | 166.6 | 27.6 |
| Cyclobutane | 4 | 655.9 | 164.0 | 26.4 |
| Cyclopentane | 5 | 793.5 | 158.7 | 6.5 |
| Cyclohexane | 6 | 944.5 | 157.4 | 0 |
| Cycloheptane | 7 | 1108 | 158.3 | 6.3 |
| Cyclooctane | 8 | 1269 | 158.6 | 9.6 |
| Cyclononane | 9 | 1429 | 158.8 | 12.6 |
| Cyclodecane | 10 | 1586 | 158.6 | 12.0 |
| Cycloundecane | 11 | 1742 | 158.4 | 11.0 |
| Cyclododecane | 12 | 1891 | 157.6 | 2.4 |
| Cyclotridecane | 13 | 2051 | 157.8 | 5.2 |
| Cyclotetradecane | 14 | 2204 | 157.4 | 0 |
| Alkane (reference) |  |  | 157.4 | 0 |

Important evidence for the ring strain and polymerisability of cyclic esters has been shown by Hall and Schneider [49]. They report a set of data concerning lactone polymerisability, as summarized in Table 1.3, and have suggested a common observation for the polymerisability of carbonyl cyclic monomers.

Table 1.3 Polymerisability of cyclic ester compounds [49].



| No. | Compound | Number of atoms in ring | Polymeri-zability |
|---|---|---|---|
| 1 | β-Propiolactone | 4 | + |
| 2 | β-Butyrolactone | 4 | + |
| 3 | α,α-Bis(chloromethyl)propiolactone | 4 | + |
| 4 | γ-Butyrolactone | 5 | - |
| 5 | γ-Valerolactone | 5 | - |
| 6 | Ethylene carbonate | 5 | - |
| 7 | Tetramethylene carbonate | 5 | - |
| 8 | 2,2-Dimethyl -4-phenyl-1-,3-dioxolan-5-one | 5 | - |
| 9 | δ–Valerolactone | 6 | + |
| 10 | α,β,γ,-Trimethoxy-δ-valerolactone | 6 | + |
| 11 | 1,4-Dioxane-2-one | 6 | + |
| 12 | Glycolide | 6 | + |
| 13 | Lactide | 6 | + |
| 14 | 1,4-Dithiane-2,5-dione | 6 | + |
| 15 | Trimethylene carbonate | 6 | + |
| 16 | Neopentylene carbonate | 6 | + |
| 17 | Ethylene oxalate | 6 | + |
| 18 | Propylene oxalate | 6 | + |
| 19 | α-*n*-Propyl-δ-valerolactone | 6 | + |
| 20 | δ,δ-Dimethyl-δ- valerolactone | 6 | - |
| 21 | 3-Ethyl-1,4-dioxan-2-one | 6 | - |
| 22 | 3,3,6-Trimethyl-1,4-dioxan-2-one | 6 | - |
| 23 | Tetramethylglycolide | 6 | - |
| 24 | Tetraphenylglycolide | 6 | - |
| 25 | Lactone of 4-hydroxycyclohexanecarboxylic acid | 6 | + |
| 26 | ε–Caprolactone | 7 | + |
| 27 | β –Methyl-ε-isopropyl-ε-caprolactone | 7 | + |
| 28 | 3-Oxa-ε-caprolactone | 7 | - |
| 29 | Tetramethylene carbonate | 7 | - |
| 30 | cis-Disalicylide | 8 | + |
| 31 | Di-o-cresotide | 8 | + |
| 32 | Trisalicylide | 12 | + |

According to these data, five-membered ring lactones as well as some substituted six-membered δ-valerolactones do not homopolymerise. The general qualitative observations on the polymerisability of carbonyl cyclic monomers proposed by Hall and Schneider were:

1) The polymerisability of five-and six-membered carbonyl cyclic monomers depends on the class of compound.

2) Four-, seven-, and eight-membered rings polymerise in all cases.

3) Alkyl or acyl substituents on a ring always decrease polymerisability.

It is significant that, of the simple unsubstituted lactones, only the five-membered ring $\gamma$-butyrolactone is apparently not polymerisable under conditions where the four-, six-, and seven-membered rings readily polymerise.

### 1.7.3 Nature of Substituents External to the Ring

In equilibrium between a cyclic monomer and a linear polymer, steric interference between the side groups or between side groups and main chain atoms will change the equilibrium to favor the low molecular weight cyclic monomer. Steric repulsion of the b and c types illustrated in Figure 1.9 are more serious in an open chain polymer than in a cyclic monomer. Since steric repulsions must raise the internal energy, interactions of this type will raise the enthalpy of the polymer relative to the cyclic monomer, and so $\Delta H^{\circ}{}_{p}$ will be made less negative and possibly even approach zero. On the other hand, steric hindrance between two side groups on the same carbon atom should cause the external bond angle between those groups to widen. This, in turn, should bring about a narrowing of the opposite skeletal bond angle owing to a hybridsation change. Clearly, narrowing of the skeletal angle will favour the formation of small rings rather than larger rings. It will also force the various components of the polymer closer together. If appreciable intermolecular crowding is present, a small change in the skeletal angle will have a relatively large effect on the enthalpy of the polymer, but less effect on the cyclic monomer. This general effect is often referred to as the “gem-dimethyl effect” [50].

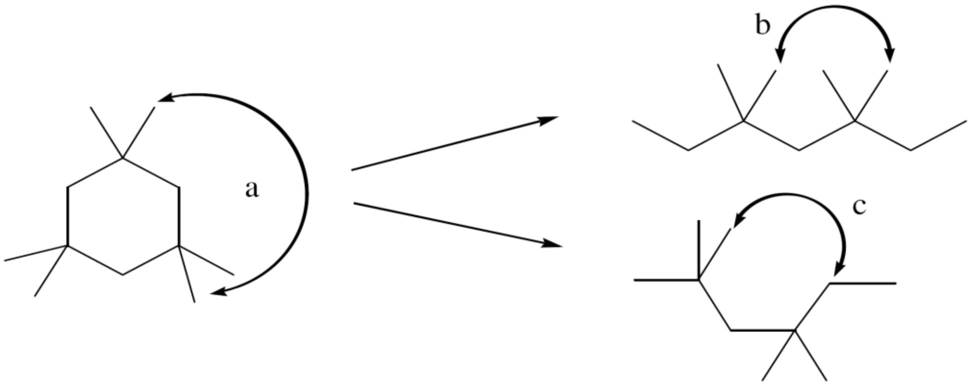


Figure 1.9 Changes in side-group repulsions on the ROP.

### 1.7.4 Nature of the Reaction Conditions Employed

The reaction variables which need to be carefully controlled in the ROP of cyclic esters are:

1) Pressure has some influence on the reaction rate. For example, $\gamma$-butyrolactone cannot polymerise at normal pressure but polymerisation can be achieved at 20,000 atm and 160 $^{o}$C to yield stable polymer of modest molecular weight ($\overline{M}_n$ = 1,000 – 3,000). Similar results can be obtained with $\delta$-valerolactam although here polymerisation is also possible at 1 atm 60 $^{o}$C. It is possible that, in this latter case, crystallization of the polymer makes a crucial negative contribution to $\Delta G_p$.

2) Temperature has a great influence on the reaction rate and on the nature of the products formed. The profile of monomer conversion with time at different temperatures shows that an increase in temperature usually results in an expected acceleration of polymerisation and in an increase in $\overline{M}_n$. However, there are exceptions to these trends.

3) Time obviously influences the reaction rate, % conversion, and molecular weight of the polymer formed.

4) High purity of the reagents is a basic prerequisite to achieve a high degree of polymerisation. The reagent should not contain any impurities that initiate additional chains or hinder the build up of chains by forming non-reactive end-groups.

5) Method of mixing the monomer and the initiator; there are two methods for doing this. In the first method, the monomer and the initiator are mixed together at

room temperature before heating to the polymerisation temperature. This contrasts with the second approach in which the monomer is pre-heated by itself up to the polymerisation temperature and the initiator then injected rapidly with efficient stirring. It is often found in practice that these different methods lead to differences in % conversion and molecular weight distribution. It may also have an effect on the monomer sequence distribution in random copolymers. In copolymerisation, sequential monomer addition is another procedural variation.

## 1.8 Previous Work Relevant to This Study

Zhang *et al.* [51] postulated that the reaction of $Sn(Oct)_2$ with an alcohol, ROH, yields a tin monoalkoxide (OctSnOR) and/or dialkoxide (ROSnOR) that initiates the polymerisation of lactide and lactones via the coordination-insertion mechanism. They also believed that $Sn(Oct)_2$, and most probably any other covalent metal carboxylate, also has to be able to initiate polymerisation by itself via monomer insertion into the metal-oxygen bond, as with metal alkoxide initiators. Kricheldorf *et al.* [39] proposed a mechanism where the initiating alcohol functionality and the monomer are both coordinated to the $Sn(Oct)_2$ during propagation.

Yuan *et al.* [52] and Köhn *et al.* [53] studied the effects of the monomer to initiator ([M] : [I]) molar ratio, reaction temperature and reaction time on the properties of poly(DL-lactide). The results showed that the yield and molecular weight of the polymer increased with the reaction temperature and time during the initial stage, then reached maximum values, before rapid decreases at long reaction times and higher temperatures due to transesterification. Furthermore, the yield of polymer increased with decreasing in the [M] : [I] ratio, while the molecular weight increased with increasing [M] : [I]. Kricheldorf *et al.* [54] studied the $Bu_4Sn$-initiated polymerisation of ε-caprolactone at 100°C accelerated by the addition of benzyl alcohol. It was found that $Bu_4Sn$ was sensitive to oxidation by oxygen (air), a process which yielded mainly $Bu_2SnO$ and only a trace of $Bu_3SnOBu$. It was concluded that the $Bu_2SnO$ dissolved in the $Bu_4Sn$ as the main initiator while the added benyzl alcohol acted as co-initiator yielding benzyl ester chain ends.

Dong *et al.* [55, 56] synthesised poly(D,L-lactic acid–alt-glycolic acid) and poly(ε-caprolactone)-b-poly(D,L-lactic acid–alt-glycolic acid) using multifunctional alcohols such as 1,1,1- tris(hydroxymethyl)propane (TMP) (3-OH) and pentaerythritol (PTOL) (4-OH) in combination with $Sn(Oct)_2$ in bulk at 110°C. $^1$H-NMR spectra of the resulting polymers showed that TMP or PTOL with $Sn(Oct)_2$ produced two types of three-arm or four-arm star-shaped polymers. Studies of the effect of the monomer to alcohol ratio on the molecular weight indicated that the molecular weight of polymer was proportional to the molar ratio of monomer to alcohol.

Fu *et al.* [57] studied the structure and properties of bioabsorbable poly(glycolide-co-lactide) (PGA-co-PLA) fibres. During in vitro degradation, crystallinity was found to increase with time while the heat shrinkage near $T_g$ and in the supercooling region was greatly reduced. These results supported the process of cleavage-induced crystallization. Deng *et al.* [58] studied the in vitro degradation behavior of a poly(glycolide-co-L-lactide) monofilament at pH 7.4 over the temperature range of 27.5–47.5 $^{o}$C. Results showed that the polymer monofilament gradually lost its tensile strength and molecular weight with time. Higher temperatures accelerated the degradation process significantly. Analysis indicated that there were well-defined relationships between molecular weight and tensile strength which could be illustrated mathematically.

Liu *et al.* [59] studied the synthesis and characterisation of biodegradable aliphatic polyesters via the ROP of the corresponding lactones initiated with dibutylmagnesium, both in bulk and in solution. Their results indicated that dibutylmagnesium is an effective initiator for the ROP of lactones.

Chisholm [60] studied the ROP of lactide using coordination metal catalysts and summarized the reactions involved including competing reactions. Particular attention was given to the stereoselective polymerisation of rac-LA to give heterotactic PLA and meso-LA to give syndiotactic PLA by aluminum Schiff-based catalysts and to the development of highly active group 2 metal single-site catalysts. Melt or solvent-free polymerisation was also described along with the reactions that led exclusively to cyclic polylactides.

Fernandez *et al.* [61] studied the effects of chain microstructure on the mechanical behaviour of poly(L-lactide-co-ε-caprolactone) biomedical thermoplastic-elastomers. The randomness character (R) and the number-average sequence lengths in copolymers of approximately 70% L-lactide molar content were determined by $^1$H and $^{13}$C-NMR analysis. The results demonstrated that a higher randomness character (R → 1) limited the crystallizability of LA-unit sequences and lowered the melting temperature of the copolymers. The effect of different monomer sequence distributions on crystallization and phase behavior was also studied by DSC for different storage times at room temperature.

This project draws heavily on the knowledge and experience which has been built up within the **Biomedical Polymers Technology Unit** during the past 20 years in both polymer synthesis and fibre processing as follows.

Punyodom *et al.* [62] studied the influence of polymerisation conditions such as reaction temperature, reaction time and concentration of initiator on the properties of poly(L-lactide-co-ε-caprolactone-co-glycolide) 45: 45: 10 mole % for use as an absorbable nerve guide using $Sn(Oct)_2$ and 1-hexanol as the initiating system via bulk ROP. It was found that increasing temperature gave a higher yield of polymer but that above 140°C and at longer reaction times transesterification reactions decreased the molecular weight of the polymer. Furthermore, the concentration of 1-hexanol could control the molecular weight of the final polymer.

Saiyasombat *et al.* [63] studied ring strain and polymerisability of cyclic esters. From the results, they found that ring strain is one of the most important factors affecting the polymerisability of γ-butyrolactone, δ-valerolactone and ε-caprolactone. The ring strain increased with increasing ring size for the three lactones studied which increased the thermodynamic scope for these monomers to polymerise. For the glycolide series, ring strain and polymerisability decreased with increasing substitution on the α-carbon.

Srisa-ard *et al.* [64] studied synthesis and characterisation of a random terpolymer of L-lactide (LL), ε-caprolactone (CL) and glycolide (G). Terpolymer was synthesised in bulk at 130°C using stannous octoate. The terpolymer obtained had quite high molecular weight; $\overline{M}_n = 1.01 \times 10^5$ g mol$^{-1}$ and $\overline{M}_w/\overline{M}_n = 2.17$. Composition of terpolymer (LL:CL:G = 74:15:11 mol %) with a chain microstructure consistent with random monomer sequencing.

Baimark *et al.* [65, 66] studied synthesis, characterisation and melt spinning of a block copolymer of L-Lactide and ε-caprolactone using macroinitiator for potential use as an absorbable monofilament surgical suture. From the results, all of the triblock copolymers synthesised had molecular weights higher than their respective prepolymers. $^{13}$C-NMR analysis confirmed that the prepolymers contained at least some random character and that the triblock copolymers consisted of additional terminal PLL end (A) blocks. From their DSC curves, the triblock copolymers were seen to be semi-crystalline in morphology. Their glass transition, solid-state crystallization, and melting temperature ranges, together with their heats of melting, all increased as the PLL end (A) block length increased. The block copolymer was then processed into a monofilament fibre. Fibre's tensile properties were developed, as indicated by the changes in its stress-strain curve. The final drawn and annealed fibre had a tensile strength of >400 MPa approaching that of a commercial PDS II suture of similar size.

Suksomran [67] studied kinetics of the ring-opening polymerisation of cyclic ester (lactone); (γ-butyrolactone (γ-BL), δ-valerolactone (δ-VL) and ε-caprolactone (ε-CL)). Polymers were synthesised in bulk at 90, 120 and 140°C using either stannous octoate ($Sn(Oct)_2$) or stannous acetate ($Sn(Acet)_2$) as initiator in combination with 1-hexanol or 1,6-hexanediol as coinitiator. The kinetics were studied by means of dilatometry and gravimetry. All polymerisations were found to show good adherence to first order kinetics relative to monomer conversion.

Channuan *et al.* [68-71] studied crystal structure of segmented triblock (LL:CL:G = 70:25:5 mol %) using X-ray diffraction (XRD). They found that the crystal structure in the fibre after hot-drawing and annealing was predominantly of poly(L-lactide) and that it was this part of the matrix which was responsible for the fibre’s tensile strength. Moreover, they found that there were some variations in the development of a two-phase structure which reflected the differences in the chain architectures. In addition, they studied physical structure and properties in monofilaments of a block terpolymer for potential use as absorbable surgical sutures. The block terpolymer, P[(LLco-G)-b-

(LL-co-CL)-b-(LL-co-G)], with LL:CL:G = 71:25:4 mol % using $Sn(Oct)_2$ and DEG as the initiator had $\overline{M}_n$ of 27,000. As-spun fibres of the terpolymers were produced by melt spinning and subsequent hot drawing was employed to enhance their mechanical properties. WAXS and SAXS results coupled with DSC of the drawn fibre demonstrated that hot drawing leaded to an orientated amorphous matrix containing small highly aligned crystals. There was a steady increase in the fraction of oriented crystalline material with increasing hot draw temperature, although the level of crystallinity was ultimately limited by the statistical nature of the terpolymer. The material showed highly promising potential properties for use as a monofilament suture.

Chaichompoo [72] studied effects of the glycolide content in poly(L-lactide-co-ε-caprolactone-co-glycolide) on the polymer products**.** Poly(L-lactide-co-ε-caprolactone-co-glycolide) 60:20:20 and 45:20:35 mol % were synthesised via bulk polymerisation at 130°C for 48 hrs using 0.02 mol % stannous octoate as the initiator. Comparing the effects of the glycolide content on in P(LL-co-CL-co-G) the polymer products by using LL:CL:G ratios of 80:20:0, 70:25:35, 75:15:10, 60:20:20, 33:33:33, 45:20:3, and 10:20:70 mol % revealed that the main factor in the synthesis to obtain high molecular weight was to use a low initiator concentration of $Sn(Oct)_2 \leq 0.02$ mol %. The sequencing and timing of monomer addition had significant effects on the monomer composition ratios in the resultant polymers.

Kleawkla *et al.* [43, 73, 74] studied ring-opening polymerisation of two cyclic ester monomers (L-lactide (LL) and ε-caprolactone (CL)) using a series of six tin(II) dialkoxides, $Sn(OR)_2$ (R = $CH_3$, $C_2H_5$, $C_3H_7$, $C_4H_9$, $C_6H_{13}$ and $C_8H_{17}$), as initiators at 90 and 140 °C. In CL polymerisation at the lower temperature of 90 °C, and using an initiator concentration [$Sn(OR)_2$] of 0.1 mol % polymerisation did not occur. Therefore, temperature at 140 °C was employed for bulk polymerisation and kinetics of CL using tin(II) alkoxide initiators, namely: tin(II) hexoxide, $Sn(OC_6H_{13})_2$ and tin(II) octoxide, $Sn(OC_8H_{17})_2$, at 140 °C. It was found that tin(II) hexoxide took time to dissolve in the monomer due to its molecular aggregation, leading to a prolonged induction period. Despite this, first-order kinetics, a high conversion (>90%) and a polycaprolactone (PCL) molecular weight sufficiently high for melt processing were obtained.

Nalampang *et al.* [75] studied synthesis and characterisation of poly(L-lactide-co-ε-caprolactone) copolymers. The copolymers were synthesised by bulk ring-opening polymerisation using stannous octoate ($Sn(Oct)_2$) and 1-hexanol as the initiating system. For the sequential two-step polymerisation, a poly(ε-caprolactone) prepolymer was polymerised first to a percent conversion of approximately 70% and L-lactide then added in order to produce a copolymer with a chain microstructure different from that obtained from the corresponding one-step reaction. The copolymers all showed at least some blocky chain structure as a result of the significant difference in monomer reactivity. Thermal properties including stability depended on both composition and chain microstructure.

Tariyawong [76] studied effects of hot-drawing rates on mechanical properties of fibre of poly(L-lactide-co-ε- caprolactone) with a composition of 75:25 mol %. It was found that drawing enhanced the fibre's strength while annealing increased its flexibility. Further more, by hot-drawing twice alternated with annealing, the fibre with high strength and good precision was obtained. Different mechanical properties were due to the differences in molecular orientation.

Siripitayananon *et al.* [77] studied effects of hot-drawing and annealing on the morphology and mechanical properties of monofilament fibres of random co/terpolymers with different compositions of LL, CL and G. Their fibre's tensile testings showed that the fibre's strength was strongly dependent on the draw ratio. A high draw ratio was obtained by multiple off-line hot-drawings with intermediate annealing. The first hot-drawing step dramatically enhanced the mechanical properties relative to those of the weak, highly extensible as-spun fibre. Subsequent annealing at a suitable temperature and for an appropriate length of time increased fibre flexibility as a result of molecular relaxation. Additional hot-drawing steps, again under precise temperature-time conditions, increased the total draw ratio and further enhanced the fibre's mechanical strength.

Chooprayoon *et al.* [78, 79] studied processing, mechanical and *in vitro* hydrolytic degradation of a poly(L-lactide-co-ε-caprolactone) monofilament fibre for use as an absorbable surgical suture. Poly(L-lactide-co-ε-caprolactone), composition ratios of LL:CL= 75:25, 80:20 mol %, was synthesised in bulk at 120 °C for 48 hrs using stannous acetate with hexanol, stannous octoate with hexanol, and stannous octoate alone as the initiating systems. The copolymers obtained were melt spun to produce an as-spun monofilament fibre. Alternate off-line hot-drawing and annealing was carried out in order to develop the fibre's oriented semi-crystalline morphology. *In vitro* hydrolytic degradation studied in a phosphate buffer saline (PBS) solution of pH 7.4 at 37.0 ± 0.1 °C indicated that, after 6 weeks immersion in the buffer, the fibre's tensile strength decreased by approximately 50% whereas a commercial 'PDS' suture of similar size lost its strength completely after only 4 weeks.

Dumklang *et al.* [80] studied the tin(II) butoxides for use as initiators in the ring-opening polymerisation of CL at 120 °C. Three tin(II) butoxides, namely: tin(II) n-butoxide, $Sn(n\text{-}OBu)_2$; tin(II) i-butoxide, $Sn(i\text{-}OBu)_2$; and tin(II) t-butoxide, $Sn(t\text{-}OBu)_2$, were synthesised via two different methods. From the results, the liquid $Sn(n\text{-}OBu)_2$ initiator had the advantage for being much more soluble than the solid $Sn(n\text{-}OBu)_2$ due to its lower degree of molecular aggregation. They also found that increasing the bulkiness of the OBu group resulted in solid products with decreased solubility and initiating efficiency for $Sn(i\text{-}OBu)_2$.

Pomanan [81] studied synthesis and characterisation of tin(II) alkoxides($Sn(OR)_2$) for use as initiators in the ring-opening polymerisation of PLC. Polymerisation was carried out at 120 $^{o}$C for 72 hrs using both the solid and liquid tin(II) alkoxide initiators. Kinetics of CL polymerisation were studied via dilatometry at temperatures of 110-140 °C with initiator concentrations of 0.05-0.40 mol %. It was found that the expected adherence to first-order kinetic with respect to monomer was only partially obeyed due to a combination of factors, the main one being the molecular aggregation of the initiator and its effect on the initiator’s solubility in the CL.

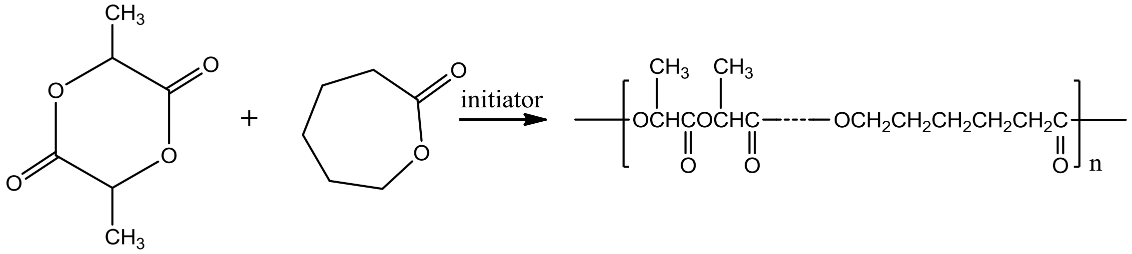
Kalaithong [82] studied synthesis, characterisation and melt spinning of random copolymers. Copolymers with monomer ratios of G:LL:CL = 60:20:20, 55:25:20, 57:23:20 and 57:28:15 mol % were prepared using either $Sn(Oct)_2$ alone or $Sn(Oct)_2$/diethylene glycol (DEG) in combination as the initiating system under various time and temperature conditions. It was found that including DEG tended to give rise to air bubbles in the system, $Sn(Oct)_2$ alone was therefore the preferred initiator. Refinements to the synthesis procedure was done by applying a vacuum to the system after the monomers had melted and mixed at 120 $^{o}$C before increasing the temperature to 150 $^{o}$C for 24 hrs. In conclusion, the monomer ratio of G:LL:CL = 57:28:15 mol % gave the copolymer with the highest molecular weight. The copolymer could be melt spun into monofilament fibres of uniform diameter and smooth surface appearance but with very limited hot-drawability. Nevertheless, the tensile strength of the as-spun fibre could be improved slightly by fixed annealing at 60 $^{o}$C for 3 hrs.

Chaisangkham [83] studied synthesis, characterisation, processing and testing of speciality copolyesters for use as fast-absorbable monofilament sutures. A statistical copolymer of glycolide (G), L-lactide (LL), ε-caprolactone (CL) and DL-lactide (DLL) was synthesised by bulk ring-opening polymerisation. Of the various comonomer ratios and initiators studied, the most suitable for processing the copolymer product by melt spinning into a monofilament fibre was G:LL:CL:DLL = 20:65:10:5 mol % using stannous octoate as the initiator. The final drawn and annealed fibre had a tensile strength of approximately 200 MPa.

All the researches studied above have not only given knowledge and experience but also indicated the problems in the mechanical properties improvement of the fibre for use as absorbable surgical suture. The fibre morphology modification has been well established by off-line hot drawing alternated with annealing. The remain factors for suitable suture properties involve refinement of the fibre processing conditions for each polymer material. However, the polymer materials to be used need to have high molecular weight enough for fibre spinning and subsequently mechanical properties improvement. One of the main objectives of this research is therefore to synthesise some novel initiators for use in the ROP of cyclic esters to give high molecular weight polyesters with well-defined microstructures.

## 1.9 Aims of This Study

The main purpose of this research is to study the synthesis of some novel tin(II) alkoxides for use as initiators in the ring-opening polymerisation (ROP) of cyclic esters. The polyesters of particular interest are random copolymers of L-lactide and ε-caprolactone with 75:25 mol % for use as absorbable surgical suture, as shown below.



L-lactide (LL) + ε-caprolactone (CL) → poly(L-lactide-*co*-ε-caprolactone) (PLC)

There are two methods for the synthesis of tin(II) alkoxide initiators. The first method, tin(II) alkoxides are synthesised via the reaction between anhydrous stannous chloride and corresponding alcohols with triethylamine added to combine with the hydrogen chloride also formed, as shown in the equation below:

$$SnCl_2 + 2HOROH + 2(C_2H_5)_3N \rightarrow Sn(OROH)_2 + 2(C_2H_5)_3N.HCl$$

where, HOROH used are polyethylene glycol 300 (PEG300), polypropylene glycol 400 (PPG400), polypropylene glycol 1200 (PPG1200), diethylene glycol (DEG).

In the second method, tin(II) alkoxides are synthesised via the reaction between tin(II) 2-ethylhexanoate and corresponding alcohols, as shown in the equation below:

$$2Sn(Oct)_2 + HO\text{-}R\text{-}OH \rightarrow (Oct)Sn\text{-}O\text{-}R\text{-}O\text{-}Sn(Oct) + 2OctH$$

where, ROH used are diethylene glycol (DEG) and ethylene glycol (EG).

The tin(II) alkoxide initiators synthesised will be characterised by various analytical techniques; FT-IR, LC-MS, NMR, DSC and TGA.

Kinetics of polymerisation of ε-caprolactone, using $Sn(Oct)_2$, $Sn(OR)_2/ROH$ and novel $Sn(OR)_2$ initiating systems, will be studied by means of dilatometry using a purpose-built apparatus. The kinetic results will be interpreted in the light of the latest coordination-insertion mechanism. Clearer understanding of how more controlled ring-opening polymerisations can then be achieved.

To compare efficiency of the initiators for ring-opening-polymerisation of polyesters, ε-caprolactone monomer is used for bulk ring-opening polymerisation. The PCL homopolymer obtained will be characterised by a combination of analytical techniques such as FT-IR, NMR, DSC, TGA and dilute-solution viscometry. These findings would have important implications for the controlled synthesis of high $\overline{M}_w$ aliphatic biodegradable polyesters.

Copolymers of L-lactide and ε-caproactone with a composition ratio of 75:25 mol % will then be synthesised using high efficient $Sn(OR)_2$ initiating systems to achieve high $\overline{M}_w$ and well defined microstructures. Characterisation of the copolymers synthesised will be carried out by FT-IR, NMR, DSC, TGA, GPC and dilute-solution viscometry.

The synthesised copolymers will subsequently be fabricated into monofilament fibre by a small-scale melt spinning apparatus. Fibre mechanical properties are then to be improved via hot-drawing and annealing under appropriate conditions. Fibre obtained at various conditions through the whole process will be characterised by DSC and tested by Universal Mechanical Testing Machine for evaluating its properties suitable for use as absorbable surgical sutures.