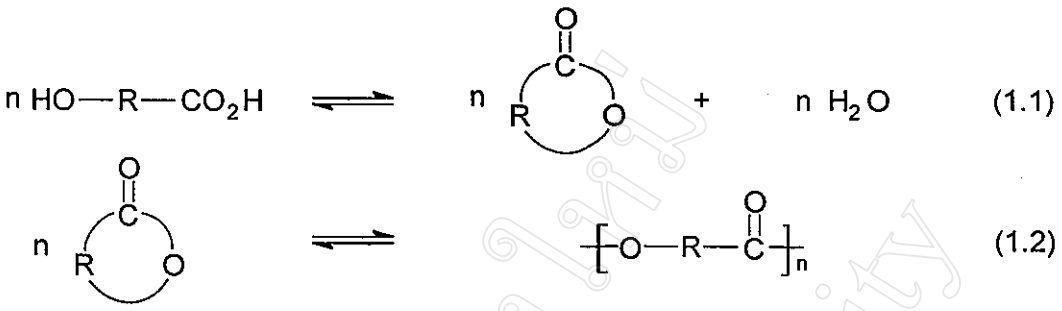
CHAPTER 1

RING-OPENING POLYMERISATION OF CYCLIC ESTERS

1.1 Introduction [1, 2]

Polyesters are usually synthesized by a step-growth polycondensation mechanism from a mixture of a diol and a diacid (or a diacid derivative), or from a hydroxy acid when available. Ring-opening polymerisation of lactones and related compounds is an alternative method for the synthesis of aliphatic polyesters. The drawbacks of polycondensation are well known: high temperatures and long reaction times are required to produce high molecular weight chains. Even though conversion of the hydroxyl and acid groups is close to completion, any departure from the reaction stoichiometry has a detrimental effect on the chain length. In contrast, ring-opening polymerisation is usually free of these limitations. Under rather mild conditions, high molecular weight aliphatic polyesters can be prepared in short periods of time as a result of complete monomer conversion. Provided that propagation is free from transfer and termination reactions, molecular weight is predictable from the monomer-to-initiator molar ratio. Chains can be end-capped with a functional group (ω- and α, ω- telechelics) and block copolymerisation is relatively straightforward.

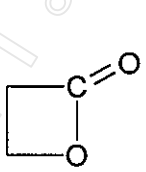
The term ***lactone*** implies a cyclic ester which can be considered as being derived from a hydroxy acid, as shown in reaction 1.1. The ring-opening polymerisation of such compounds then leads to a polyester, as shown in reaction 1.2.



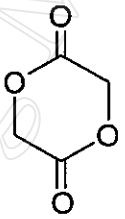
(1.1)

(1.2)

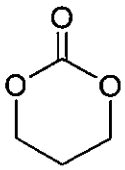
For simple lactones, where R is $(CH_2)_n$, the first member of the series which can be readily prepared is the 4-membered ring, n=2, β-propiolactone, **1**. Diester lactones are also well known, the simplest being glycolide, **2**, the dimer of glycolic acid. Many other cyclic ester monomers with reactivities related to those of the lactones give analogous polyesters on polymerisation [3]. Among these are cyclic carbonates, **3**, dioxanones, **4**, cyclic oxalates, **5**, cyclic anhydrides, **6**, and thio-derivatives, **7**, **8**. Macrolides, **9**, are also lactones. They are natural products composed of large lactone rings but are of interest primarily for clinical applications, not as monomers; reviews concerning them are available in the literature [4, 5].



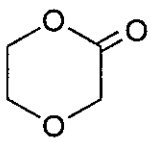
β-propiolactone
(2-oxetanone)
1



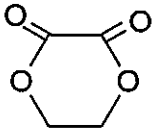
glycolide
(1,4-dioxane-2,5-dione)
2



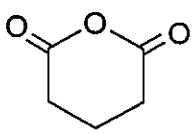
trimethylene carbonate
(1,3-dioxane-2-one)
3



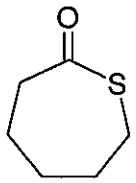
p-dioxanone
(1,4-dioxane-2-one)
4



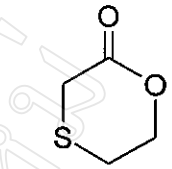
ethylene oxalate
(1,4-dioxane-2,3-dione)
5



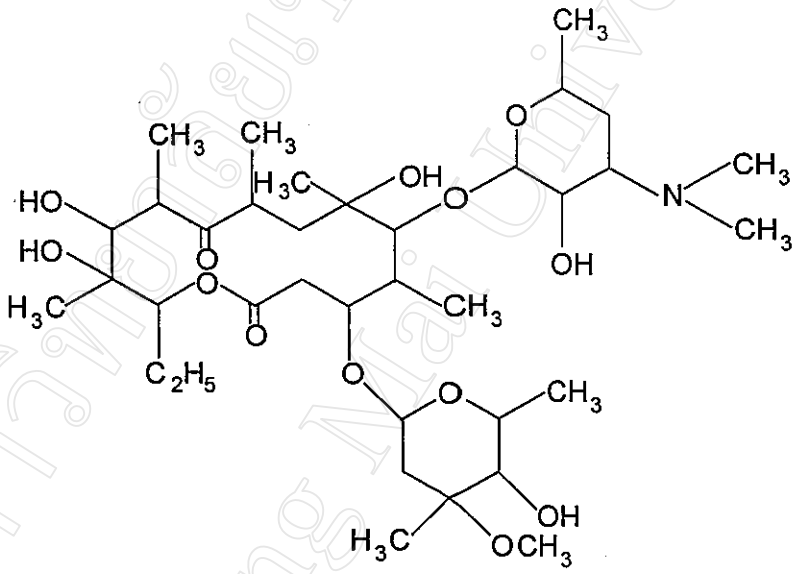
glutaric anhydride
(dihydro-2H-pyran-2,6(3H)dione)
6



ε-thiolactone
(thioxepane-2-one)
7



common name unknown
(1,4-thioxane-2-one)
8



erythromycin A
9

This introductory chapter is primarily concerned with the synthesis and polymerisation of simple lactones, and their alkyl-substituted derivatives, with particular emphasis on factors affecting their polymerisability and their possible ring-opening mechanisms. The cyclic ester monomers mentioned previously are included in many instances to provide insight into this class of compound, but are not reviewed in detail.

A brief mention of nomenclature is worthwhile because the nomenclature of lactones and their polyesters, unfortunately, has not been systematic over the years. More often than not, lactones are referred to by common or trivial names, as are their polymers. For example, compound **1** previously is usually termed β-propiolactone and its polymer, poly-β-propiolactone. This same compound can also be named by IUPAC rules as 2-oxetanone and its polymer, correspondingly, as poly-2-oxetanone. Thus, lactone literature can be difficult to trace, and the *Index Guide Supplements of Chemical Abstracts* need to be consulted for searching the literature.

The polymerisation of lactones and related compounds has been known for many years. δ-valerolactone was polymerised by Fichter and Beisswenger in 1903 [6] and, prior to that, in 1893, Bischoff and Walden [7,8] polymerised glycolide. Carothers made the first systematic investigation of lactones and other cyclic esters [9], while Hall and co-workers made an extensive review of this field in a series of articles published in 1958 [10-13]. Since that time, many other laboratories have entered this field and, as a result, the lactone literature has greatly multiplied. Two major reviews of lactone polymerisation appeared in 1969 [3,14], since when many references to lactone polymerisation have appeared in the patent literature, mostly concerning ε-caprolactone and its polymers, copolymers and polymerisation catalysts. This is because ε-caprolactone is one of the few lactones to have attracted commercial interest over these past 30 years.

Lactones have been polymerised by a variety of initiators [15] including anionic, cationic and organometallic compounds. Among these are: alkali and alkaline earth metal hydrides, alkoxides and alkyls; carboxylic acids; carboxylate salts; alcohols; glycols; primary, secondary and tertiary amines; alkanolamines; alkyl aluminium or zinc compounds; trityl salts; betaines; Friedel-Crafts compounds; titanates; silicates; and phosphates; to name but a few. The reaction conditions used vary greatly with the monomer and initiator system employed. Polymerisation reactions have been carried out in bulk, in the solid state and in solution over a wide range of temperatures.

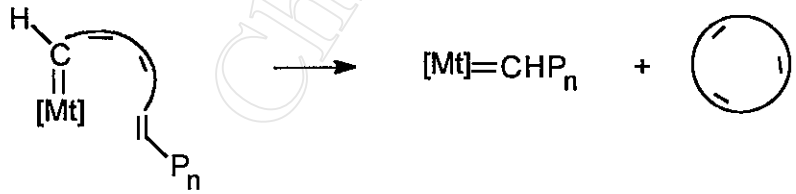
1.2 Ring-Chain Equilibria [2]

No chemical reaction can proceed to a substantial extent at a given temperature and pressure unless two conditions are fulfilled: (1) the equilibrium between reactants and products must favour the products and (2) there must be a mechanism which allows the reaction to occur. A reaction involving only small molecules, such as the synthesis of ammonia from nitrogen and hydrogen, can proceed to some extent even when the thermodynamic change is somewhat unfavourable, that is when the equilibrium position lies on the side of the reactants; but for the formation of high polymer by the ring-opening of a cyclic monomer, many hundreds of molecules must come together to form one large molecule. An unfavourable equilibrium position for the propagation reaction is then multiplied many times which means that, if the free energy change for the propagation reaction is only slightly positive, the formation of high polymer will be scarcely detectable. For this reason, ring-opening polymerisation, and indeed addition polymerisation in general, exhibits discontinuities of a kind more usually associated with physical aggregation processes. Thus, for a given solvent and monomer concentration [M], there exists a sharp temperature, defined as the ***ceiling temperature,*** T_c, above which the formation of long-chain polymer does not occur. Experimentally, such temperatures can be almost as well-defined as melting points. A physical analogy is the condensation of a vapour, which occurs only when the temperature falls below the dew point appropriate to the particular concentration of vapour. Conversely, at a given temperature, the aggregation process, whether polymerisation of monomer or condensation of vapour, occurs only if the concentration of the unaggregated form exceeds a critical value: the equilibrium monomer concentration $[M]_e$ in the case of polymerisation; the saturation vapour pressure in the case of condensation of vapour. Thus, any ring-opening polymerisation to form long-chain polymer only occurs (a) if $[M] > [M]_e$ at a given temperature, or (b) if $T < T_c$ at a given monomer concentration.

1.2.1 Previous Experimental Observations

An example of the monomer concentration effect in a ring-chain equilibrium reaction is provided by tetraoxane, the cyclic tetramer of formaldehyde. When tetraoxane is cationically polymerised in solution in 1,2-dichloroethane at 50°C, the concentration of tetraoxane falls to an equilibrium value of less than 0.008M but, at the same time, an equilibrium concentration of 0.2M trioxane, the cyclic trimer, is built up [16]. At concentrations of tetraoxane below 0.008M, no linear polymer is formed but trioxane is rapidly produced [17]. Such behaviour is typical of a whole range of cyclic compounds.

Other examples include cyclopentene [18], cyclooctene [19], cyclodecene [19], and norbornene [20] where series of cyclic oligomers with up to 14 repeat units have been identified by GLC and GPC in the products of metathesis polymerisation. For cycloocta-1,5-diene, the cyclic oligomers form a continuous series $(C_4H_6)_n$, as though the parent molecule was cyclobutene [21]. This is clear evidence that the cyclic species are formed by an intramolecular reaction of a linear intermediate, thought to be a metallacarbene. The yield of cyclic oligomers relative to linear polymer is always greatest when the monomer concentration is kept low, as is to be expected when a first-order intramolecular reaction, equation 1.3, is in competition with a second-order propagation reaction, equation 1.4.



(1.3)

$$[Mt]{=}CHP_{n+3} + M \longrightarrow [Mt]{=}CHP_{n+4} \qquad (1.4)$$

Cyclic oligomeric species have likewise been identified in the products of the ring-opening polymerisation of cyclic ethers. Under certain conditions, macrocyclic ethers are the predominant products of polymerisation of ethylene oxide [22] and

may account for as much as 35% by weight of the polymerisation products of oxetane [23, 24]. Cyclic oligomers of tetrahydrofuran are formed in comparatively small amounts (3%) under normal conditions and escaped detection until comparatively recently [25, 26]. Using CF_3SO_3H as the catalyst, the ring series $[O(CH_2)_4]_n$, n = 2-9, has been detected by GLC/MS (using chemical ionisation), the tetramer 20-crown-4 being the most abundant cyclic species. Similarly, the ring series, $[OCH_2CH_2C_6H_{10}]_n$, n= 2-5, has been found in the polymerisation of trans-7-oxabicyclo[4,3,0]-nonane [27].

Cyclic polyethers also yield cyclic oligomers in the products of polymerisation. For example, the polymerisations of the ring monomers $[OCH_2(OCH_2CH_2)_z]$, z = 3, 4, 5, and also 1,3,6,11-tetraoxacyclotridecane and 1,3-dioxacycloundecane, have been initiated by CF_3SO_3H in solution in dichloromethane and a series of cyclic oligomers observed [28, 29]. For z = 3, cyclic species up to $[OCH_2(OCH_2CH_2)_3]_{20}$, containing 220 ring atoms, have been identified and quantitatively determined by high resolution GPC. The data so obtained provided the first and still one of the best tests of the so-called Jacobson-Stockmayer theory of ring-chain equilibria [30].

Finally it should be noted that ring-chain equilibria can also be found in inorganic systems such as $[PNCl_2]_{3-7}$ [31], S_{2-10} [32] and $[RPO_3]_{3-8}$ [32]. It has also been found that cyclic oligomers can sometimes be generated from polymers formed originally by linear condensation reactions, for example from poly(ethylene terephthalate) [33] and poly(decamethylene adipate) [34].

1.2.2 The Jacobson-Stockmayer Theory

The basic postulates of the Jacobson-Stockmayer theory are : (1) that the distribution of ring sizes is determined only by entropy considerations, i.e., all rings are strainless; (2) that the end-to-end distances of linear chains obey Gaussian

statistics; the random flight model is assumed and no allowance is made for the excluded volume effect; (3) that the probability of ring formation is governed by the frequency with which the ends of a given chain coincide; (4) that the probability of bond formation is independent of whether the ends form part of the same chain or are ends of separate chains.

The theory predicts that: (a) no linear polymer should be formed below a critical concentration of starting monomer, expressed as moles of repeat units per litre; (b) the concentration of rings, c-M_x, in equilibrium with linear polymer, M_y, should be independent of dilution (in fact, it has been seen that the polymer concentration can affect $[M]_e$ because of polymer-monomer interactions); (c) the equilibrium constant, K_x, for the equilibrium $M_y \rightleftharpoons M_{y-x} + c\text{-}M_x$ should be proportional to $x^{-2.5}$ and independent of temperature (since it has been tacitly assumed that this equilibrium is thermoneutral). In contrast to the thermodynamic distribution of linear polymers, this means that the weight distribution of macrocyclic constituents at equilibrium is predicted to be a monotonically decreasing function of ring size.

All these predictions are in reasonable agreement with experiment for all the systems that have been mentioned, provided x is sufficiently large. For the polydimethylsiloxane system, K_x is nearly a linear function of $x^{-2.5}$ for x greater than 15. Deviations at lower values of x may be attributed to the failure of postulate (1) for smaller rings. K_x and, hence, $[c\text{-}M_x]_e$, are also dependent on the nature of the medium for small values of x.

The postulate of a random-flight model is, of course, a very rough approximation; bond angles have well-defined values and there is restricted rotation about the bonds arising from both short-range and long-range interactions. This explains why the theoretical proportionality constant between K_x and $x^{-2.5}$ differs markedly from that observed. Jacobson and Stockmayer expressed this deviation in terms of an effective length of chain link, some three times greater than actual bond lengths. Later, Flory and Semlyen [35] revised the theory, replacing the

random-flight model with the rotational-isomeric-states model. This enables the proportionality constant to be expressed in terms of the parameters describing the proportion of conformers about each main-chain bond. These parameters may be obtained from a study of the solution properties of linear polydimethylsiloxane. The predicted absolute values of K_x are then in good agreement with experiment for large values of x. The weak minimum in the experimental curve at lower values of x appears to be genuine and is found for other polysiloxanes [36]. It is to be noted that the experimental and calculated curves agree at one particular small value of x corresponding to the value expected for an approximately strainless ring.

1.3 Thermodynamic Approach [37]

The Gibbs free energy, G, of a system at temperature T is defined as

$$G = H - TS \qquad (1.5)$$

where H is the enthalpy and S is the entropy of the system. The free energy change for any polymerisation, ΔG_p, will therefore be

$$\Delta G_p = G_{polymer} - G_{monomer}$$

$$= H_{polymer} - H_{monomer} - T(S_{polymer} - S_{monomer})$$

$$= \Delta H_p - T\Delta S_p \qquad (1.6)$$

When the polymer has a lower free energy than the initial monomer, a polymerisation can occur spontaneously, and the sign of ΔG_p is negative. Conversely, a positive sign for ΔG_p signifies that the polymerisation is not spontaneous. When the system is in equilibrium at a certain critical temperature, there is no tendency for polymerisation and, hence, $\Delta G_p = 0$. This temperature is the previously mentioned ***ceiling temperature, T_c***. These three possible conditions for the free energy change of a polymerisation may be summarized as follows :

monomer $\rightarrow$ polymer $\quad \Delta G_p = -$ (spontaneous)

monomer $\leftarrow$ polymer $\quad \Delta G_p = +$ (non-spontaneous)

monomer $\rightleftharpoons$ polymer $\quad \Delta G_p = 0$ (equilibrium)

At the ceiling temperature, T_c , ΔG_p is zero, so that

$$T_c = \Delta H_p/\Delta S_p \qquad (1.7)$$

where ΔH_p and ΔS_p are the enthalpy and entropy changes per monomer unit. When the polymer chains are long, these quantities are identical with the heat and entropy changes of polymerisation. If the standard state refers to unit concentration and the monomer behaves ideally, $\Delta S_p = \Delta S^0 + R\ln[M]$; thus

$$T_c = \frac{\Delta H_p}{\Delta S^0 + R\ln[M]} \qquad (1.8)$$

where ΔS^0 is the entropy change accompanying polymerisation in the standard state when the concentration of monomer [M] is unity. Therefore, where ΔS^0 is negative, as it usually is, T_c can be raised by increasing the concentration of monomer when solvent is present. Equation 1.8 emphasizes that T_c is characteristic of the monomer-polymer equilibrium only and is quite independent of the monomer or the nature of the active centres in the system; for a given value of

[M], the ceiling temperature should, therefore, be the same whether the active centres are radicals or ions.

Many polymers are stable even above the ceiling temperature because of the difficulty of initiating degradative centres on the polymer molecule, the terminated polymer being in a state of metastable equilibrium. Therefore, the polymer cannot depolymerise spontaneously but can do so under appropriate conditions. Catalyst residues that are not removed during the purification of a polymer may also cause depolymerisation reactions.

There are therefore four important thermodynamic possibilities for polymerisation :

(a) When ΔH_p and ΔS_p are both negative, as is usually the case, ΔG_p becomes positive above the ceiling temperature of the system. Thus, high polymer cannot be formed above the ceiling temperature.

(b) Conversely, although less commonly, if the polymerisation is endothermic ($\Delta H_p > 0$) and ΔS_p is greater than zero, no polymer can exist below a certain ***floor temperature***, above which ΔG_p becomes negative. This phenomenon of a ***floor temperature*** is exhibited by the polymerisation of rhombic sulphur (S_8) rings to give linear polymeric sulphur $-[S_8]-$.

(c) When ΔH_p is positive and ΔS_p negative, ΔG_p is always positive; therefore, polymer cannot exist at any temperature.

(d) When ΔH_p is negative and ΔS_p positive, ΔG_p is always negative; therefore, polymer can exist at any temperature.

In order to illustrate the operation of thermodynamic restrictions on ring-opening polymerisation, in combination with the mechanistic possibilities, let us consider the polymerisabilities of cycloalkanes and cycloalkenes (Table 1.1). Values of ΔG_p for the polymerisation of cycloalkanes can be estimated from thermodynamic data and are plotted against ring size in Fig. 1.1. It can be seen that all values are negative except that for the polymerisation of cyclohexane. However, there is in fact no catalyst known which is capable of bringing about the polymerisation of any of the simple cycloalkanes by a chain reaction. ΔG_p values for the ring-opening polymerisation of cycloalkenes are likely to be very similar to those for the cycloalkanes. That the signs are the same is shown by the fact that all except cyclohexene will undergo ring-opening polymerisation in the presence of metathesis catalysts such as $WCl_6/EtAlCl_2$. The polymerisations of cyclobutene and cyclooctene proceed essentially to completion (ΔG_p large negative) but that of cyclopentene stops short at a measurable equilibrium concentration (small negative ΔG_p)

When cyclic compounds are polymerised by ring-opening, it is frequently found that, in addition to linear high polymer, there is formed a series of cyclic oligomers having the same chemical composition as the monomer. If isolated, the individual cyclic oligomers will themselves undergo polymerisation, if their concentration exceeds the appropriate critical value, to yield the same linear high polymer and series of cyclic oligomers as before.

Thus, the standard free energy change associated with any ring-opening polymerisation is made up of an enthalpy term and an entropy term $\left(\Delta G_p^o = \Delta H_p^o - T\Delta S_p^o\right)$. The values of these two terms, and hence the magnitude and sign of ΔG^o, are determined by a number of chemical and physical factors, as will now be described in the following section 1.4. The actual mechanisms of polymerisation will be described in the final section 1.5 of this introductory chapter.

Table 1.1 : Polymerisability of some cyclic hydrocarbons [2].

Cyclic Compound	ΔG_p^a	Mechanism Available	Polymerises
Cyclobutane	large negative	no	no
Cyclopentane	small negative	no	no
Cyclohexane	small positive	no	no
Cycloheptane	small negative	no	no
Cyclobutene	large negative	yes	yes[b]
Cyclopentene	small negative	yes	yes[c]
Cyclohexene	small positive	yes	no
Cycloheptene	small negative	yes	yes[c]

[a] Free energy of polymerisation of liquid monomer to condensed amorphous polymer

[b] To high conversion

[c] To limited conversion

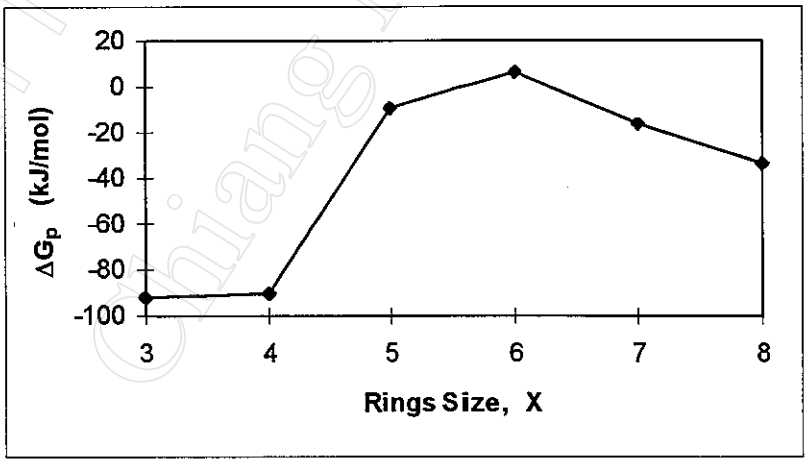


Fig. 1.1 : Free energy of polymerisation of unsubstituted cycloalkanes as a function of the number of atoms in the ring, X, [38, 39].

1.4 Factors Affecting Ring Polymerisability

The polymerisability of cyclic monomers is influenced by various physical and chemical factors, the most important of which are:

(1) the internal chemical structure within the ring

(2) the ring strain

(3) the nature of any substituents external to the ring

(4) the type of initiator/catalyst used

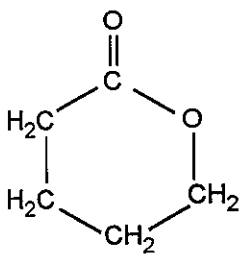
(5) the precise nature of the reaction conditions employed

Each of these factors will now be briefly described.

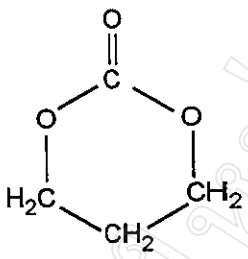
1.4.1 Internal Chemical Structure within the Ring

The relationship between the internal chemical structure within the ring and the polymerisability of the monomer has apparently not yet been clearly defined in the literature for cyclic esters. However, it is generally assumed that different internal chemical structures result in different polymerisabilities.

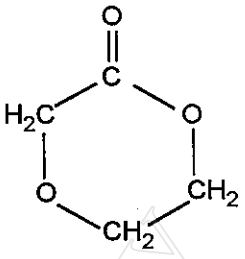
Some examples of unsubstituted cyclic esters which have the same ring size but different ester group configurations are compared on the following page. As would be expected, their physical properties vary; hence, the conditions used in their polymerisations also tend to vary accordingly. This complicates comparisons of their polymerisabilities and may be one of the reasons why no definitive study has yet been reported.



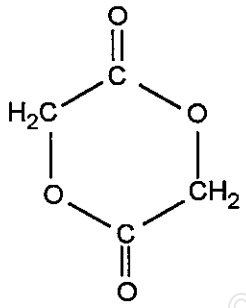
δ-valerolactone



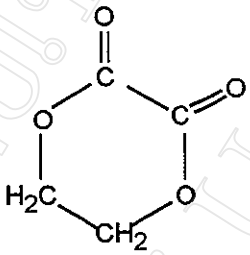
trimethylene carbonate



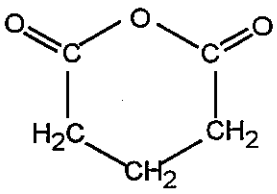
p-dioxanone



glycolide



ethylene oxalate



glutaric anhydride

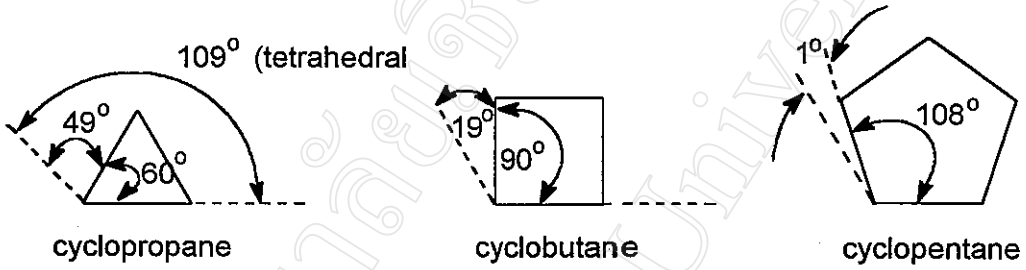
As these structures show, the ester group can vary both in number (1 = lactone, 2 = lactide) and type (simple ester, carbonate, ether ester, oxalate, anhydride) within the ring. These structural variations obviously affect the chemical environment of the ester group and therefore its reactivity towards poymerisation.

1.4.2 Ring Strain

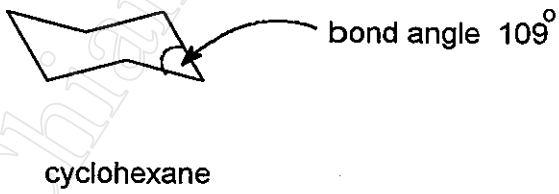
1.4.2.1 The Baeyer Ring Strain Theory [40]

In 1885, Adolf van Baeyer, a German chemist, theorized that cyclic compounds form planar rings. Baeyer based his hypothesis on the simple geometric notion that an equilateral triangle (cyclopropane skeleton) must have bond angles of 60°, a square (cyclobutane skeleton) must have bond angles of 90°, a regular pentagon (cyclopentane skeleton) must have bond angles of 108°, and so on. According to this analysis, cyclopropane, with a bond-angle compression of 109°-60° = 49°, has a large amount of ***angle strain*** and would therefore be highly

reactive. Cyclobutane (109^{o}- 90^{o} = 19^{o} angle strain) would also be reactive but less so, while cyclopentane (109^{o}-108^{o} = 1^{o} angle strain) would be nearly strain-free. Cyclohexane (109^{o}-120^{o} = -11^{o} angle strain) would be somewhat strained, but cycloheptane (109^{o}-128^{o} = -19^{o} angle strain) and higher cycloalkanes would have bond angles that are forced to be too large. Carrying this line of reasoning further, Baeyer suggested that very large rings should be impossibly strained and incapable of existence.



Of course, Baeyer's theory, as we now know, was not entirely correct. Cyclohexane and larger-sized rings are not more reactive than cyclopentane. Moreover, cyclohexane is not a planar ring with bond angles of 120^{o}, but rather a puckered ring with bond angles close to 109^{o}, the normal sp^3 tetrahedral bond angle.



1.4.2.2 Ring Strain Energy

The amount of strain in a cycloalkane ring can be measured by measuring the total amount of energy in a compound and then subtracting the amount of energy in a hypothetical strain-free reference compound. The difference between the two values should represent the amount of extra energy due to the ring strain possessed by the molecule in question.

The simplest way to do this is to measure the ***heat of combustion*** of the cycloalkane. The heat of combustion of a compound is the amount of heat (energy) released when the compound burns completely with oxygen :

$$-CH_2- + \frac{3}{2}O_2 \rightarrow CO_2 + H_2O + \text{heat}$$

The more energy (strain) the sample contains, the more energy (heat) is released on combustion. This relationship between strain and heat of combustion is shown schematically in Fig. 1.2. If we compare the heat of combustion of two isomeric substances, more energy is released during combustion of the more strained substance because that compound has a higher energy level to begin with. It should be noted that heats of combustion are a measure of the enthalpy change (ΔH^o) that occurs during oxidation, rather than of the total free energy change (ΔG^o). Thus, only ΔH^o is shown in Fig. 1.2.

Since the heat of combustion of a hydrocarbon depends on its molecular weight, it is more useful to look at heats of combustion per CH_2 unit. In this way, the size of the hydrocarbon is not a factor and we can therefore compare cycloalkane rings of different sizes to a standard, strain-free, acyclic alkane. Table 1.2 shows the results of this comparison. Total strain energies are calculated by taking the difference between the sample heat of combustion per CH_2 unit and the reference heat of combustion per CH_2 unit and then multiplying by the number of carbons, n, in the sample ring.

The data in Table 1.2 and the graph in Fig. 1.3 show clearly that Baeyer's ring strain theory is not fully correct. Cyclopropane and cyclobutane are indeed quite strained, just as predicted. Cyclopentane, however, is more strained than predicted, and cyclohexane is perfectly strain-free. Moreover, for rings of larger sizes, there is no regular increase in strain, and rings having more than 14 members are again strain-free.

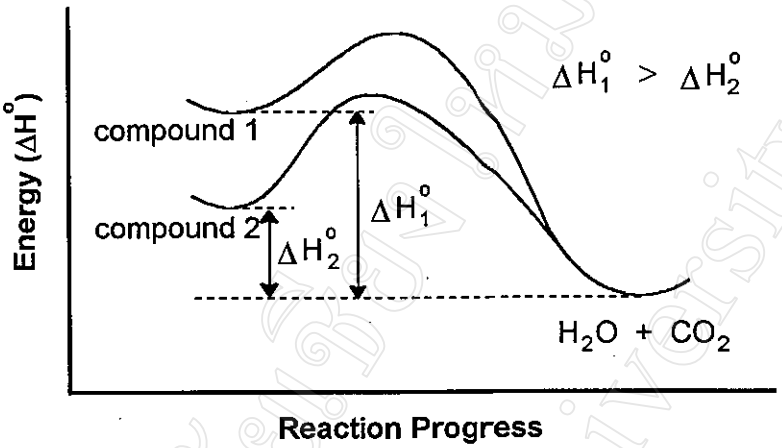


Fig. 1.2 : Comparison of the heats of combustion of two substances [40].

Compound 1 is more strained and is therefore higher in energy than compound 2. The vertical axis represents the standard enthalpy change (ΔH^o) during combustion.

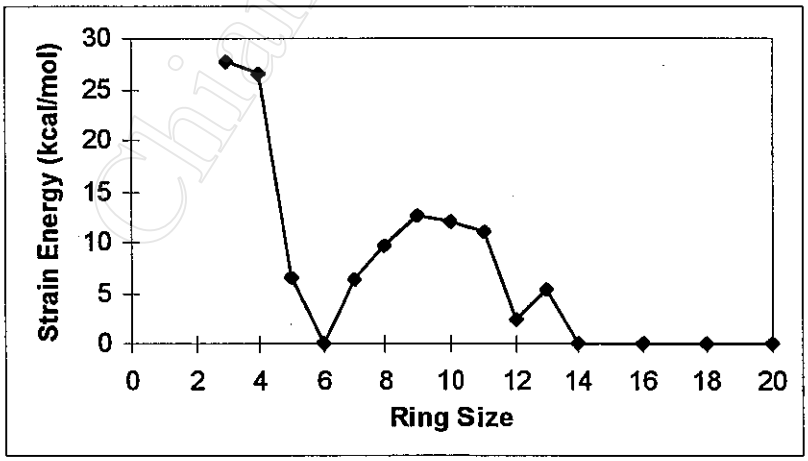


Fig. 1.3 : Cycloalkane strain energy as a function of ring size [40].

Table 1.2 : Heats of combustion of cycloalkanes [40].

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

Baeyer's theory falls down because he assumed that all rings were flat. In fact, most cycloalkanes are not flat; they adopt puckered three-dimensional conformations which allow bond angles to be nearly tetrahedral. Nevertheless, the concept of angle strain is a valuable one that goes far towards explaining the reactivities of planar three- and four-membered rings.

There are several other factors in addition to angle strain that are important in determining the shape and total strain energy of rings. One of these is ***eclipsing strain*** (also called ***torsional strain***). It is known that acyclic alkanes are most stable in the staggered conformation and least stable in the eclipsed conformation. A similar conclusion holds for cycloalkanes - eclipsing strain is present in a cycloalkane unless all the bonds have a staggered arrangement. For example, cyclopropane must have considerable eclipsing strain (in addition to angle strain), since C-H bonds on neighbouring carbon atoms are eclipsed (Fig. 1.4). Larger cycloalkanes attempt to minimize this strain by adopting puckered, non-planar conformations.

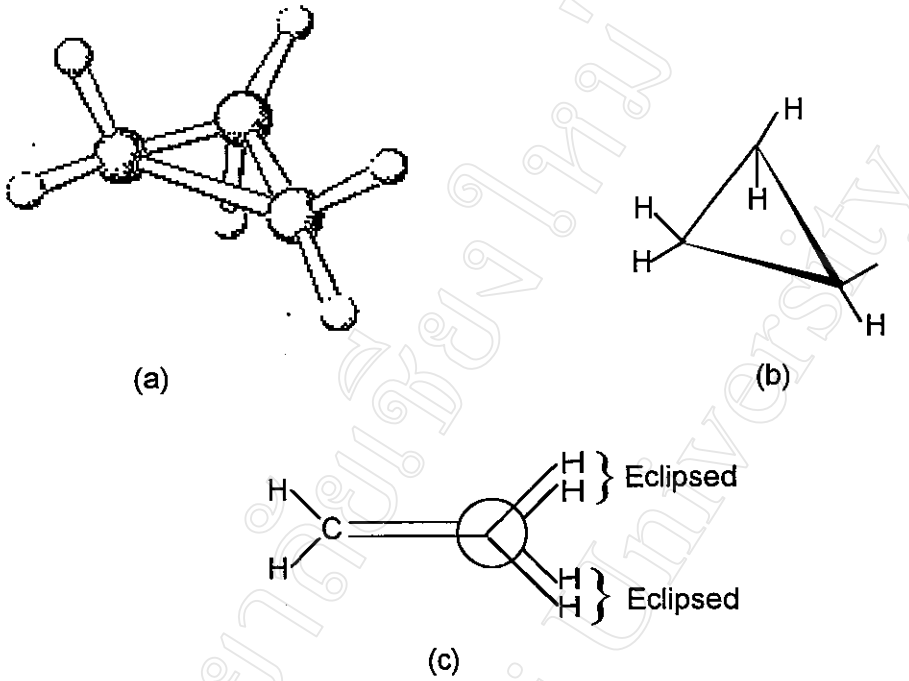


Fig. 1.4 : Conformation of cyclopropane [40].

(Structure (c) is a Newman projection along the C-C bond.)

Steric strain (or ***transannular strain***) is a third factor that contributes to the overall strain energy of a molecule. Two non-bonded groups repel each other if they approach too closely and attempt to occupy the same point in space. Such non-bonded steric interactions are particularly important in determining the minimum-energy conformation of medium-ring (C_7-C_{11}) cycloalkanes.

In summary, the Baeyer theory is insufficient to explain the observed strain energies and geometries of cycloalkanes. Cycloalkanes adopt their minimum-energy conformation for a combination of reasons:

1. Angle strain, the strain due to expansion or compression of bond angles

2. Eclipsing strain (torsional strain), the strain due to the eclipsing of neighbouring bonds

3. Steric strain (transannular strain), the strain due to repulsive interactions of atoms approaching too closely

Rings can therefore be classified according to their ring size and degree of ring strain as follows:

Ring Classification	Ring Size	Amount and Type of Ring Strain
Small rings	3,4	Very large strain, mostly bond angle
Regular rings	5-7	Moderate or no strain, mostly torsional
Medium-size rings	8-11	Large strain, mostly transannular, van der Waals, and bond angle
Large rings	≥12	Little or no strain, mostly torsional

1.4.2.3. Ring Strain and Polymerisability of Cyclic Esters [3]

In their pioneering studies on lactone polymerisation, Carothers et al [41] postulated a relation between cyclic ester hydrolysis rates and a tendency for polymerisation. In one of a series of papers directed towards the polymerisation of cyclic monomers, Hall et al [12] examined this proposal in greater depth and showed that it was not generally valid. For example, β-propiolactone polymerises readily, whereas γ-butyrolactone does not; yet both lactones hydrolyze at comparable rates. Hall reasoned that the polymerisability of a cyclic compound is an indication of the strain in the ring. However, since the hydrolysis rate is not determined by ring strain, it follows that the ring is not broken in the rate-determining step of hydrolysis.

The assumption by Hall et al [12] that polymerisability is a function of ring strain has since been reviewed [42] in some detail. In particular, since γ-butyrolactone is not polymerisable, this lactone would be regarded in Hall's concept as strain-free. However, examination of its IR spectrum reveals that the frequency of the absorption maximum for the carbonyl group is about 40 cm^{-1} higher than acyclic systems. Thus, the spectrum is consistent with the presence of at least some ring strain in γ-butyrolactone, which is inconsistent with Hall's assumption [43]. In a detailed study of the IR spectra of many cyclic compounds, Hall et al [13] confirmed their IR absorptions; however, they regarded the higher absorption frequency not as a manifestation of ring strain but rather on the basis of bond

hybridization. As the ring in a particular lactone series is contracted, the ring bonds to the carbonyl carbon atom become more '*p*' in character which in turn, confers more '*s*' character to the C=O bond. As a result, an increased absorption frequency for the carbonyl group should be observed.

Gol'dfarb and Belen'kii [42] took issue with Hall's assumption that the polymerisability of a cyclic derivative is an indication of ring strain. They maintained that "no direct relation exists between the strain in a ring and its tendency to polymerise". Furthermore, it was their contention that no grounds existed for a relation between the ring stability and ring strain.

While, strictly speaking, this view is correct and no all-encompassing statement quantitatively relating ring strain and polymerisability is possible, some general and useful trends are evident. The influence of ring size and substitution on lactone systems has been reviewed by Hall and Schneider [10]. From their findings, the polymerisabilities of a wide of cyclic esters is compared in Table 1.3.

Table 1.3 : Polymerisability of cyclic ester compounds [10].

No.	Cyclic Ester Compound	Ring Size	Polymerisability
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	2,2-Dimethyl-4-phenyl-1,3-dioxolan-5-one	5	-
8	Lactone of trans-2-hydroxycyclohexaneacetic acid	5	-
9	δ-Valerolactone	6	+
10	α,β,γ-Trimethoxy-δ-valerolactone	6	+
11	1,4-Dioxane-2-one	6	+
12	Glycolide	6	+

Table 1.3 (continued)

No.	Cyclic Ester Compound	Ring Size	Polymerisability
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	+

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 nearly always polymerise.

3. Alkyl or aryl substituents on a ring always decrease polymerisability.

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

1.4.3 Ring Substitution [3, 37]

In an 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 Fig. 1.5, 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 ΔH_p will be made less negative, and possibly even approach zero.

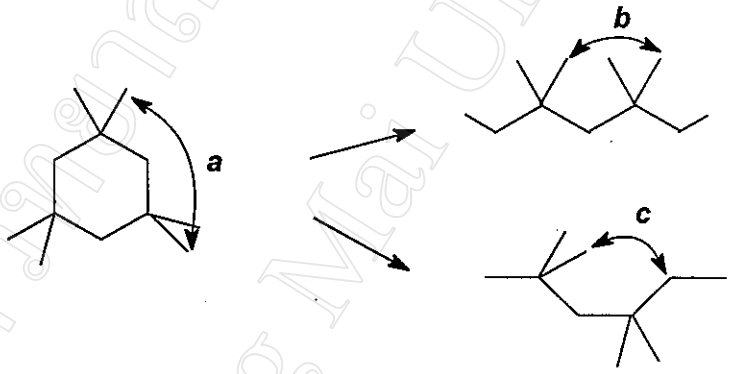


Fig. 1.5 : Changes in side-group repulsions on ring-opening polymerisation.

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 hybridization 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"** in the literature.

The gem-dimethyl effect can be quantitatively interpreted in terms of the thermodynamics of the conformation involved. The calculation of ΔH for the ring-closure reaction will be considered first. The effect of substituents on the enthalpy of ring closure is interpreted in terms of the change in the number of gauche interactions in going from the reactant to the product. The substitution decreases the change in gauche interactions on ring closure. The enthalpy of the ring-closure reaction is reduced for the substituted case and ring closure is thus favoured by substitution. Conversly, this is reflected in the lower heat of polymerisation ΔH_p for the substituted cyclic monomer.

To estimate the overall effect of substituents on the ring-closure reaction, the entropy change on cyclization must also be taken into account. A substituent will not alter the entropy of the cyclic compound relative to the unsubstituted cyclic compound very much. The substituent, however, has a much greater effect on the entropy of the open-chain compound. The substituent restricts rotation of the carbon chain due mainly to the increased height of the barriers to internal rotations, and thus decreases the entropy of the open-chain compound. Therefore, the net effect of a substituent is to make the entropy of ring closure more positive. Bulky substituents which greatly restrict rotation in the open-chain compound will facilitate ring closure through the entropy effect.

Thus, it can be seen qualitatively that both the entropy and enthalpy effects of a substituent make the free energy of the ring-opening reaction more positive relative to the unsubstituted case. The larger the dimensions of the side group, the more the equilibrium shifts to the cyclic monomer. Hence, as ΔH_p for polymerisation changes from negative towards zero, the ceiling temperature will be lowered until depolymerisation will occur at any temperature.

Experimental observations bear out these theoretical considerations. Ring substitution of lactones tends to stabilize the ring relative to the polymer. Some patents [44-52] in this area have stressed that the total number of organic substituents attached to the carbon atom contained in the cyclic ester ring should not exceed four, and preferably should not exceed three. This observation is

undoubtedly a consequence of the thermodynamic stability of the ring. It is also probable that the location and size of ring substituents will have a pronounced influence on polymerisation rate. In one particular study, Hostettler et al [53] examined the effect of ring substitution on ε-caprolactone polymerisation initiated by diethylene glycol both in the presence and absence of tetrabutyl titanate as catalyst. The polymerisation rate as well as the tendency to polymerise was adversely affected by substitution.

1.4.4 Type of Initiator/Catalyst Used

Initially, the ring-opening polymerisation of cyclic ester monomers was usually initiated with anionic and cationic species. However, the polymerisation proved difficult to control due to side intra- and intermolecular transesterification reactions, with formation of a mixture of linear and cyclic molecules [54, 55]. Later, various organometallic compounds were shown to be very effective in the synthesis of high molecular weight poly(ε-caprolactone) [44], in which the chain reaction proceeds through active covalent bonds [56]. Special attention has been paid to stannous octoate because of its acceptance as a food additive by the Food and Drug Administration (FDA) in the USA [57]. Even so, stannous octoate and most metal derivatives, e.g., metal halides, oxides, and carboxylates, are sometimes combined with a hydroxy-containing compound, such as an alcohol, which then becomes the actual initiator [58, 59]. Thus, polymerisation is very sensitive to protic impurities and, accordingly, poorly reproducible.

To illustrate this dependence on the type of initiator/catalyst used, Dahlmann and co-workers [60] reported the ring-opening polymerisation of D,L-lactide at 130 ^{o}C in the presence of different organometallic compounds. Table 1.4 summarizes the results which they obtained.

It should also be mentioned here that, in the context of cyclic ester polymerisation, the terms **"initiator"** and **"catalyst"** tend to be used almost interchangeably in the literature, especially where the later generation of organotin

compounds is concerned. This rather confusing situation may have arisen, initially, out of the uncertainty in the exact nature of their initiating/catalysing role in the polymerisation mechanism. In the subsequent chapters of this thesis, clear distinctions will be made between these two terms.

Table 1.4 : Bulk polymerisation of D,L-lactide with different initiators/catalysts at 130°C [60].

Initiator/Catalyst	I/M x 10^4 (mol/mol)	Time (hrs.)	Conversion (%)	$\overline{M}_n$ x 10^3
$Ti(OC_4H_9)_4$	1	25	-	-
$TiO(C_5H_7O_2)_2$	1	25	-	-
$Zr(C_5H_7O_2)_4$	1	25	-	-
$(C_8H_{17})_2SnO$	1	50	Gel phase	
$(C_8H_{17})_2SnO$	3	25	No precipitate	
$(C_4H_9)_2Sn(laurate)_2$	1	25	32.1	7.7
$(C_4H_9)_2Sn(laurate)_2$	3	25	37.8	4.7
$(C_4H_9)_2Sn(laurate)_2/C_{12}H_{25}OH$	3/6	50	61.1	8.3
$(C_4H_9)_2Sn(laurate)_2/C_{11}H_{23}COOH$	3/6	50	59.0	7.9
$Sn(OOC\text{-}C_7H_{15})_2$	1	24	44.3	14.8
$Sn(OOC\text{-}C_7H_{15})_2$	3	25	96.0	63.8

Note : I/M = initiator/monomer mole ratio

1.4.5 Nature of the Reaction Conditions Employed

Amongst the reaction variables which need to be carefully controlled in the ring-opening polymerisation of cyclic esters are:

(a) **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.

(b) Pressure has some influence on the reaction rate. For example, γ-butyrolactone cannot polymerise at normal pressure but polymerisation can be achieved at 20000 atm and 160°C to yield stable polymer of modest molecular weight ($\bar{M}_n$ = 1000-3000) [61]. Similar results can be obtained with δ-valerolactam although here polymerisation is also possible at 1 atm 60°C [62]. It is possible that, in this latter case, crystallisation of the polymer makes a crucial negative contribution to ΔG_p.

(c) Time obviously influences the reaction rate, % conversion, and molecular weight of the polymer formed, as in any addition-type polymerisation mechanism.

(d) 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.

(e) 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.

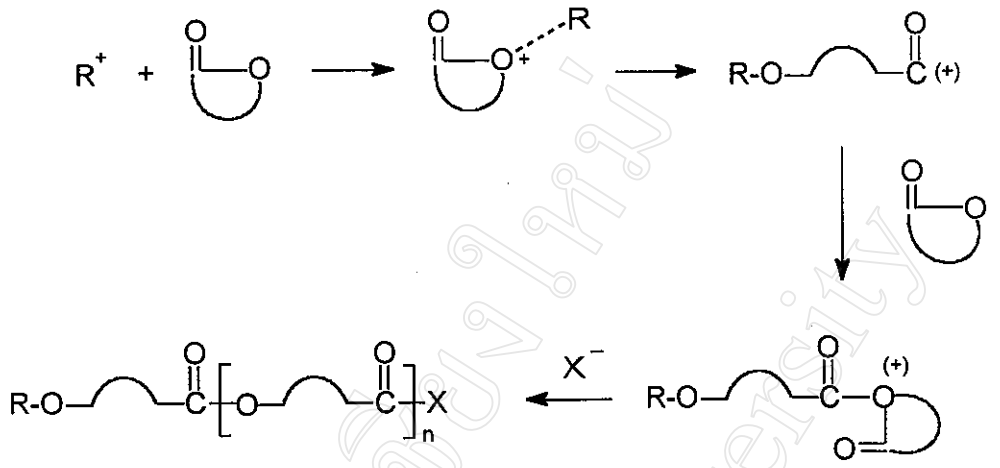
1.5 Polymerisation Mechanisms

Ring-opening polymerisation can be more or less efficiently initiated by all the major known mechanisms, i.e., cationic, anionic, coordination, free radical and those involving active hydrogen species. Each of these mechanisms is now briefly described.

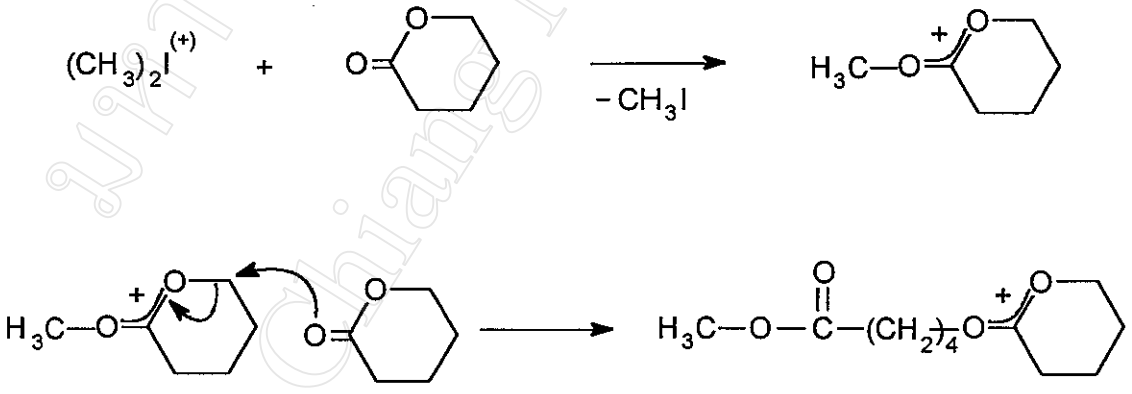
1.5.1 Cationic Mechanism [1]

The main cationic initiators used in the ring-opening polymerisation of lactones can be divided into four subgroups: (a) protonic acids (HCl, RCO_2H, RSO_3H, etc.), (b) Lewis acids ($AlCl_3$, BF_3, $FeCl_2$, $ZnCl_2$, etc.), (c) alkylating agents (stabilized carbocations, e.g., $CF_3SO_3CH_3$, $Et_3O^{(+)}BF_4^{(-)}$), and (d) acylating agents (e.g., $CH_3CO^{(+)(-)}OCl_4$) [63, 64]. In addition to these traditional acids and electrophiles, precursors of carbocations have also been considered, e.g., ammonium or phosphonium salts stabilized by complex counterions which are transformed into the active species by thermal or photochemical processes [65]. It is also worth including here diaryliodonium salts $[(Ar)_2I^{(+)(-)}AsF_6]$ which release an active cationic species upon reaction with a reducing agent [66, 67].

The cationic polymerisation mechanism proposed by Cherdron et al [68], which has long been generally accepted, consists of an electrophilic attack on the endocyclic oxygen of the lactone and the subsequent rupture of the acyl-oxygen bond with formation of an acyl carbonium ion prone to propagate.



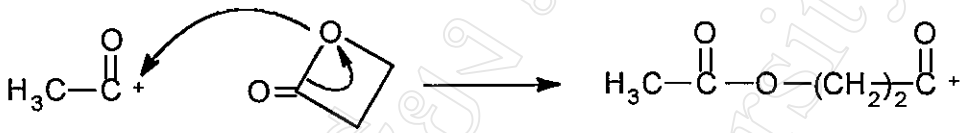
In apparent contrast, however, Penczek et al analyzed the chain ends of poly(δ-valerolactone) initiated with $(CH_3)_2I^{(+)(-)}SbF_6$ and confirmed the presence of a methyl ester function by IR and NMR. This end-group is the signature of the methylation of the exocyclic oxygen in δ-valerolactone and the subsequent rupture of the alkyl-oxygen bond [69, 70].



10

Penczek et al proposed that polymerisation via this alternative mechanism proceeds through an intermediate cyclic dialkoxycarbocationic species **10**. While initiation with alkylating agents such as $(CH_3)_2I^{(+)(-)}SbF_6$ proceeds in this way, initiation with acylating compounds leads to the formation of two different

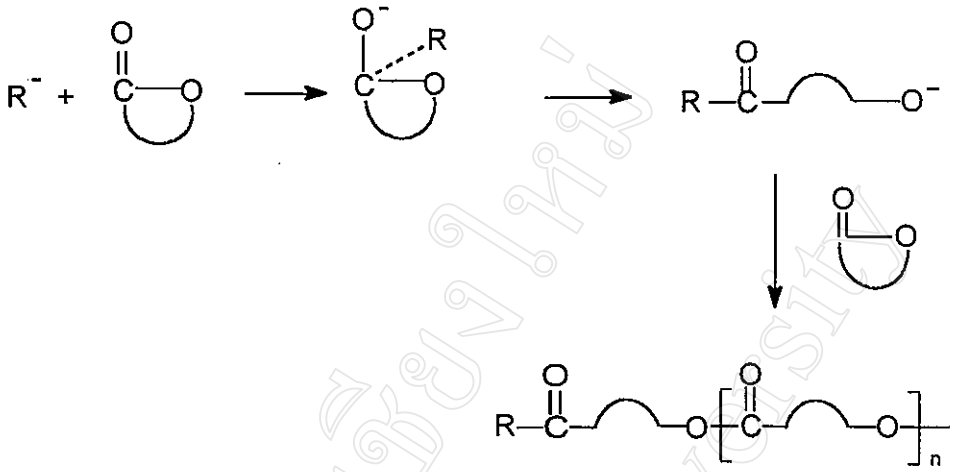
active species. In addition to the cyclic dialkoxycarbocation, an acylcarbocation, **11**, is also formed when the polymerisation of β-propiolactone is initiated with $CH_3CO^{(+)(-)}SbF_6$ [71]. The acylcarbocation species, **11**, results from the previously described acyl-oxygen bond cleavage of the lactone, leading to an ester end-group.



11

1.5.2 Anionic Mechanism [2]

The anionic polymerisation of the large-ring lactones has not been studied in detail. The literature on this subject is further complicated by having the term ***anionic*** polymerisation applied to the reactions of many organometallic compounds which are now known to function by a coordination and insertion-type mechanism instead [72], for example, in the case of aluminium alkyls. Truly anionic initiators such as metal alkoxides and carboxylate salts are known but their use has been applied more to the polymerisation of β-lactones. For many anionic initiators for large-ring lactones, it is still unclear as to exactly how they function. However, there is one generally accepted mechanism for the anionic polymerisation of large-ring lactones which involves acyl-oxygen cleavage and propagation by alkoxide ion, as originally suggested by Cherdron et al [68].

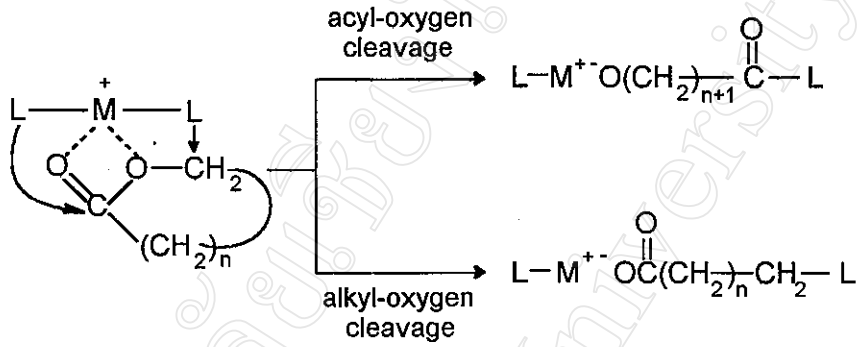


The absence of a termination reaction would lead to the formation of living polymers [73], and this has indeed been observed for both ε-caprolactone [3] and δ-valerolactone [74]. However, living polymers have been studied in great detail only for the β-lactones [6, 75]. It is also known that, in such reactions, both the solvent and the counterion have major effects on the rate of polymerisation.

1.5.3 Coordination Mechanism

Most notable among this class of initiator are the aluminium alkyls: Et_3Al, Et_2AlCl, $EtAlCl_2$, as well as organozinc compounds such as $EtZnOCH_3$ and organotin compounds such as $Sn(C_7H_{15}COO)_2$. Often, with these initiator systems, the nature of the actual initiating species is unclear because of the insolubility of most of these compounds in common organic solvents. Also, it is often found that addition of other compounds, notably alcohols and water, increase the rate of polymerisation as well as the molecular weight of the polymer formed. Such compounds most likely modify the active site of the initiating species, as is believed to be the case for the reaction of water with Et_3Al.

The mechanism of polymerisation for such initiators is now believed to involve coordination of the lactone to the metal atom (M) followed by ring opening and insertion of the monomer unit into the metal-ligand (L) bond [76].

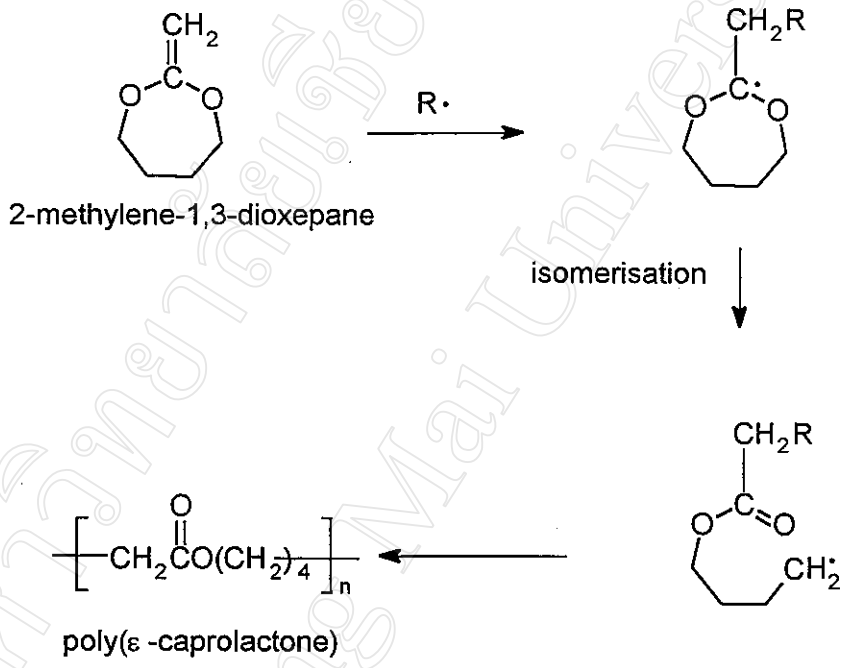


The question of whether acyl-oxygen or alkyl-oxygen cleavage occurs remains unanswered in many such reactions, but in either case a coordinated anionic species is proposed. Until recently, the most studied lactone for this type of initiation was β-propiolactone for which Brode and Koleske [77] reported that both types of cleavage are possible, the more favoured type depending on the initiator system.

1.5.4 Free Radical Mechanism

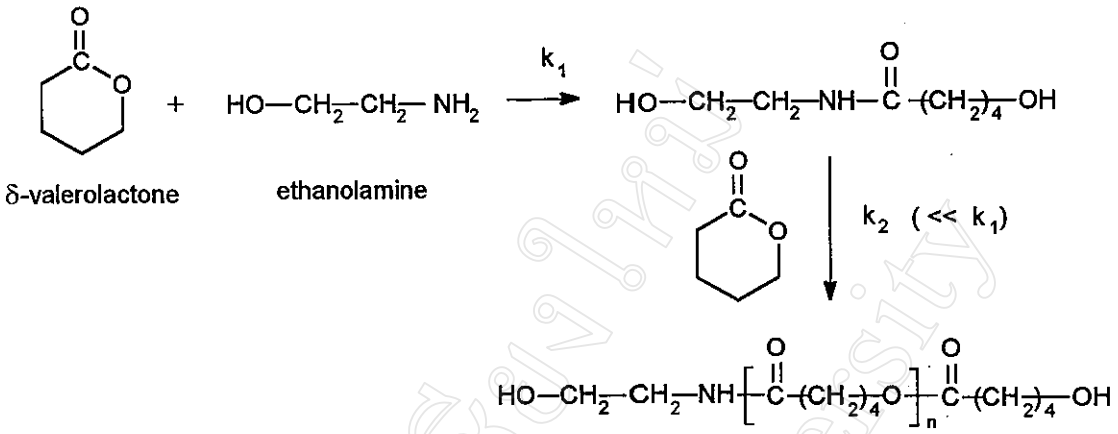
Free radicals are usually relatively ineffective in the polymerisation of lactones. Molecular weights are often low and monomer conversion limited [78]. The ring-opening polymerisation of 2-methylene-1,3-dioxepane, as shown below, represents the single example of a free radical polymerisation route to poly(ε-caprolactone) [79]. Initiation with azo-bis-isobutyronitrile (AIBN) at 50°C afforded poly(ε-caprolactone) with a $\overline{M}_v$ of 42,000 in 59% yield. Although this monomer is, in fact, not a cyclic ester, this route does have the novel advantage

that it may be used to obtain otherwise inaccessible copolymers. For example, copolymerisation with vinyl monomers has afforded copolymers of ε-caprolactone with styrene, 4-vinylanisole, methyl methacrylate, and vinyl acetate. However, apart from this, very little interest has been shown in the free radical polymerisation route to polyesters.



1.5.5 Active Hydrogen Transfer Mechanism

When initiated by an active hydrogen compound, e.g., amines or alcohols, in the absence of a catalyst, ring-opening polymerisation of lactones is a relatively slow process which produces polyesters of a usually low molecular weight. One example is the polymerisation of δ-valerolactone by ethanolamine (or ethylene glycol) at temperatures exceeding 160°C [77, 80].

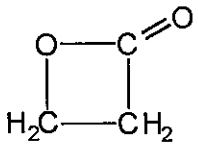


As with the free radical mechanism previously, relatively little interest has been shown in this active hydrogen transfer route due to its low efficiency compared with the ionic and coordination pathways.

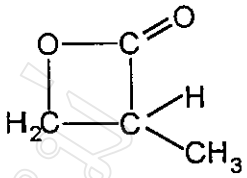
1.6 Aims of This Study

Briefly, the main aims of this research project, as seen at its outset, are: (i) to relate ring structure to cyclic ester ring polymerisability in bulk, and (ii) to study the effects of reaction variables such as initiator type, time and temperature on the reaction profile and the properties of the polymer formed. These aims are to be achieved by bringing together a combination of analytical techniques, both old and new, in an attempt to study this subject in more depth and, perhaps, from one or two different angles than have previously been reported in the literature.

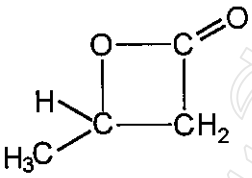
The range of cyclic ester compounds which are of particular interest in this work are as follows :



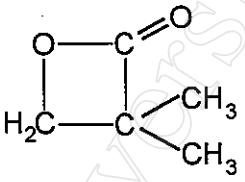
β-propiolactone



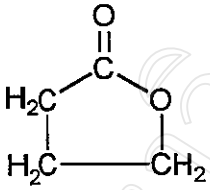
α-methyl-β-propiolactone



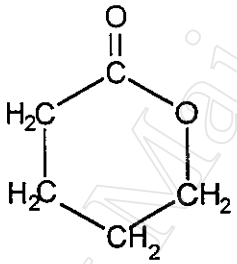
β-butyrolactone



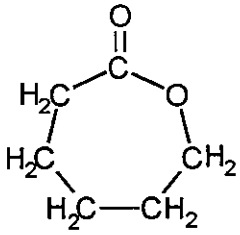
pivalolactone



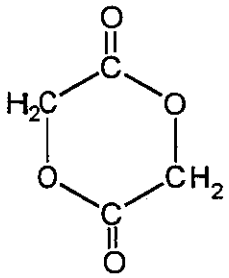
γ-butyrolactone



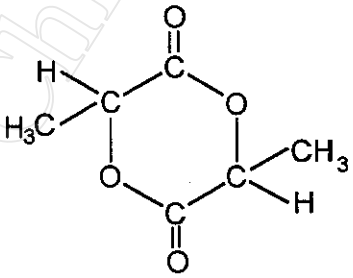
δ-valerolactone



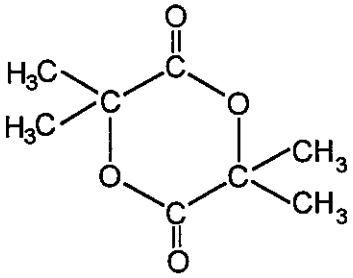
ε-caprolactone



glycolide



L-lactide



tetramethyl glycolide

It is hoped that the results obtained from this study will contribute towards developing a better understanding of the ways in which polymer properties (structure, molecular weight, morphology) can be tailored to meet the specific requirements of specialist applications. In the case of the range of aliphatic polyesters studied here, all of which are biodegradable to some extent, their main specialist applications are in the biomedical field, such as absorbable sutures, bone fixation devices and controlled-release drug delivery systems.