CHAPTER 6

DISCUSSION AND CONCLUSIONS

In the preceding Chapters 3-5, the results presented have already been discussed separately and the main conclusions drawn. This final Chapter 6 will now attempt to bring these separate conclusions together to give a more coherent description of cyclic ester polymerisability in relation to the original aims of this study as stated at the outset of this thesis (pages 35-37). A particular effort will also be made to highlight the areas in which it is felt that this study has contributed to the current state of knowledge in this specialist field.

The main factors affecting the ring-opening polymerisability of cyclic esters, encompassing reaction control and polymer properties, which this work has focussed its attention on, can be summarized as follows:

(1) ring size
(2) ring substitution
(3) ester functionality
(4) the type of initiator/catalyst used
(5) the reaction conditions employed

As they did in the previous Chapter 5, these factors provide convenient sub-headings for the final discussion and conclusions which now follow.

6.1 Effect of Ring Size

The effect of ring size on the polymerisability of unsubstituted cyclic esters is mainly associated with the degree of ring strain induced by cyclization. It is the relief of this ring strain on ring opening which provides the main driving force for

polymerisation to take place. This, in turn, is inextricably linked to the underlying reaction thermodynamics through the equation:

$$\Delta G_p = \Delta H_p - T\Delta S_p$$

For any cyclic ester to be polymerisable to high molecular weight, the ΔG_p term must be negative, i.e. $\Delta H_p < T\Delta S_p$ under the reaction conditions used. Usually, this condition is satisfied in most instances with the ΔH_p term being the more influential. The ΔH_p and ΔS_p terms lend themselves to the following interpretations:

(1) For ΔH_p, even though ring opening involves the breaking of a chemical bond, which requires an input of energy, this is invariably outweighed by the relief of ring strain, resulting in an energetically favourable (i.e., negative) ΔH_p. This has been confirmed by experiment [134-135].

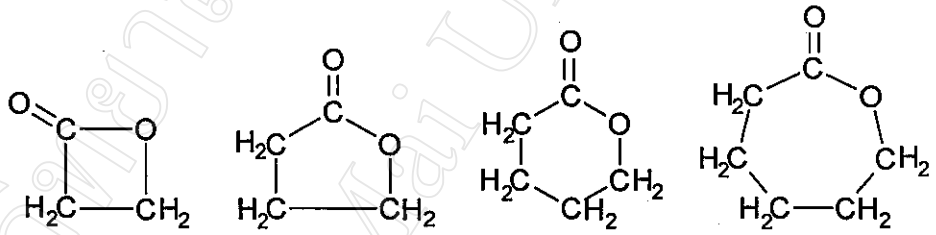
(2) For ΔS_p, there are also 2 opposing contributions to consider. First, the linear polymer chain can assume a greater number of conformations than the monomer ring, which would lead to a gain in entropy. However, this is outweighed by the loss of translational entropy brought about by the large reduction in the number of molecules present. Hence, ΔS_p is generally unfavourably negative, as also confirmed by experiment [134-135].

(3) The relative values of ΔH_p and ΔS_p depend on a range of factors and determine the sign and magnitude of ΔG_p and, hence, the balance of the ring-chain equilibrium. For cyclic esters, experimental evidence suggests that ΔH_p is the dominant term leading to a favourably negative ΔG_p.

(4) Since both ΔH_p and ΔS_p are negative, as the reaction temperature increases, the system will approach a ***ceiling temperature, T_c,*** above which ΔG_p becomes positive and polymerisation can no longer occur. This too has been borne out by experiment.

(5) Since ΔH_p is the dominant influence on ΔG_p, and the relief of ring strain is a major contributor to ΔH_p, it follows that ring strain and, hence, ring size is of central importance to thermodynamic polymerisability.

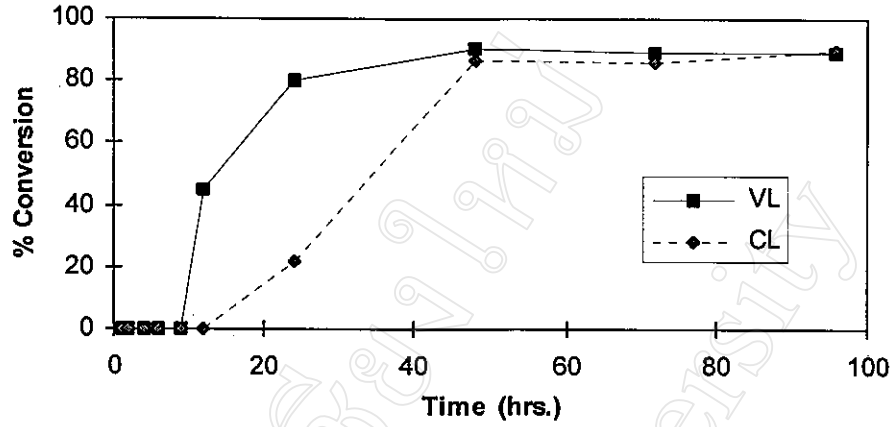
In general, the results obtained in this work have supported these interpretations. Small, highly strained rings, such as the 4-membered ring β-propiolactone, are so reactive that they can polymerise spontaneously at room temperature even without the addition of an initiator/catalyst. In complete contrast, the 5-membered ring γ-butyrolactone, with its minimal ring strain, requires extreme conditions (high temperature and pressure) to polymerise to even a moderate molecular weight.



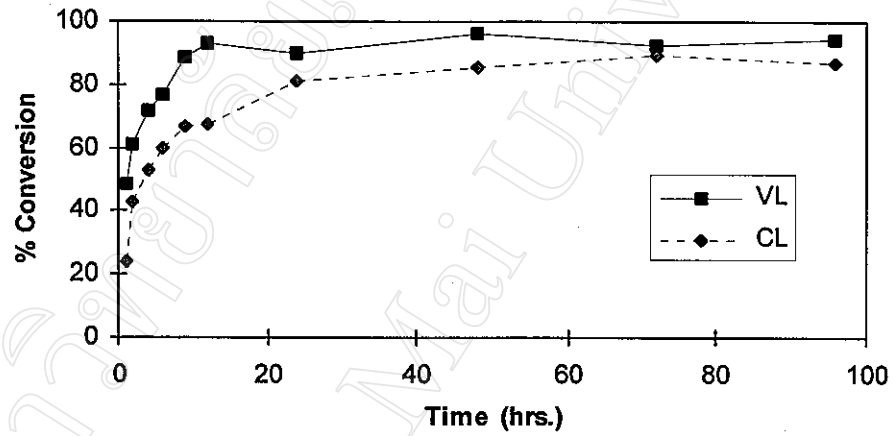
β-propiolactone **γ-butyrolactone** **δ-valerolactone** **ε-caprolactone**

Ring Size : *4* *5* *6* *7*

While this 4- and 5-membered ring comparison is undoubtedly a ring strain effect, other ring size comparisons are less straightforward. For example, from its internal bond angles, the 6-membered ring δ-valerolactone should have less ring strain than the 7-membered ring ε-caprolactone, yet this work has shown it to be consistently more polymerisable. This is illustrated in Fig. 6.1 on the following page. It is also simply illustrated by the fact that δ-valerolactone monomer needs to be stored in a refrigerator (4°C) to prevent self-polymerisation whereas ε-caprolactone can be stored indefinitely at room temperature.



(a)



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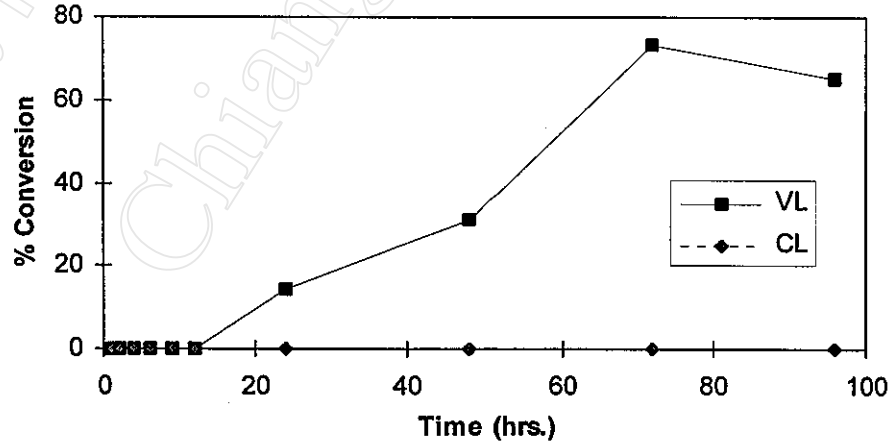
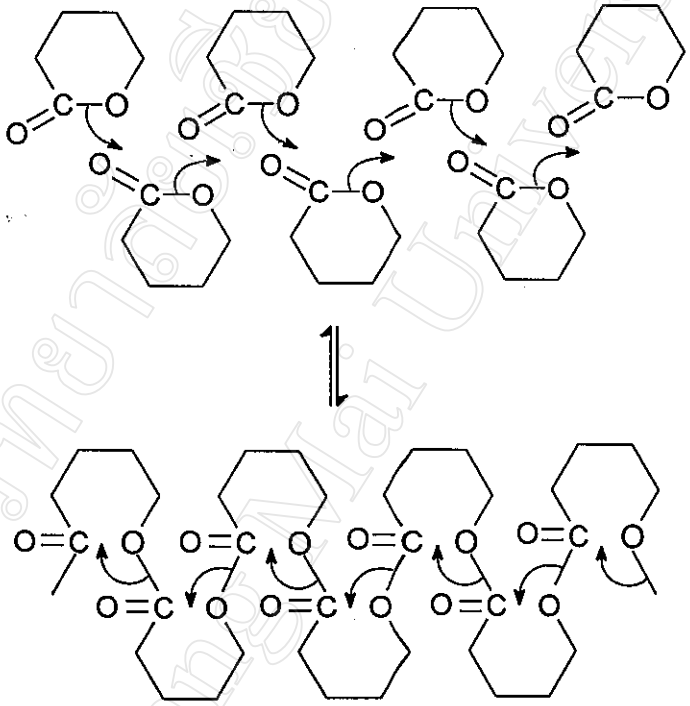


(c)

Fig. 6.1 : Comparison of the δ-valerolactone (VL) and ε-caprolactone (CL) conversion-time profiles at 100°C using (a) $Sn(Oct)_2$, (b)$BF_3{\cdot}Et_2O$ and (c) Li(*t*-OBu) as initiators.

What this anomaly indicates is that, important though ring strain is, it is not necessarily always the dominant factor with respect to ring size. Other factors may come into play such as the spatial configurations of the monomer molecules in the liquid lattice and the monomer repeat units in the polymer chain. This was mentioned previously on pages 265-266 for the specific case of δ-valerolactone (shown below) with reference to Stannett and Szwarc's earlier suggestion [139].



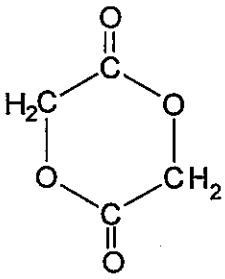
Could it be that there is something peculiar to the stereochemistry and spatial arrangement of unsubstituted 6-membered ring cyclic esters that enables the above interconversion to take place with relatively little movement of the molecules? Could this explain δ-valerolactone's unexpectedly easy polymerisability for such a relatively unstrained ring? Answers to these questions have not been found in the literature, possibly because δ-valerolactone, as with other lactones, has tended to be looked at in isolation rather than as part of a series. While this work has not been able to confirm the above mechanism, what it has done is to highlight its possibility within the wider context of cyclic ester polymerisability as a whole. The above mechanism thus provides a focal point for ideas to come together, ideas which have not hitherto been interrelated in the literature. For example, for δ-valerolactone, it links the idea of spatial configuration of molecules and repeat units with the experimental

observations made in this work of its surprising ease of polymerisation and depolymerisation. Interestingly, this phenomenon is true not only for δ-valerolactone but also for its 6-membered ring diester analogue, glycolide. When viewed as part of a series, δ-valerolactone stands out as being unusual in its high reactivity and poly(δ-valerolactone) in its low thermal stability, while glycolide has an exceptionally low ΔS_p. Simple ring strain arguments cannot account for these experimental observations, compelling us to search for new explanations. The apparent contrariety in 6-membered ring cyclic esters of relatively low ring strain with relatively easy polymerisability is one of the more significant findings to have emerged from this work.

A final comment on the effect of ring size comes from the molecular modelling work. The results presented in the previous Chapter 5 showed that molecular modelling, on the whole, is well suited to predicting the effect of ring size in unsubstituted lactones (**SERIES I**, Table 5.2, page 259) where ring strain is the dominant factor. However, when other forces become involved, such as those described above for δ-valerolactone, the modelling approach tends to break down. As with all simulation methods, it is important to understand not only its benefits but also its limitations. Molecular modelling is a valuable tool, especially when used in conjunction with advanced analytical techniques, but its true value depends on the levels of sophistication of the model and the processes of computation involved.

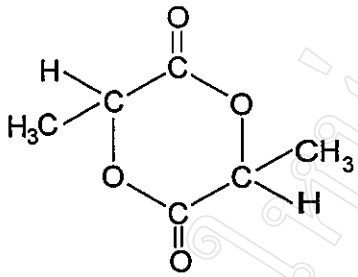
6.2 Effect of Ring Substitution

Without exception, ring substitution decreases polymerisability, whatever the nature of the substituent may be. Increasing the ***degree*** of substitution on the same ring carbon atom further decreases polymerisability. There has never been any dispute about the effect of ring substitution in the literature and the results of this work are in agreement with previous findings. This effect is clearly illustrated by the glycolide series:



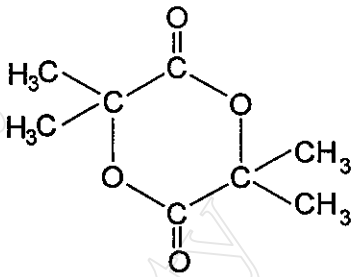
glycolide

unsubstituted



L-lactide

α,α'-disubstituted

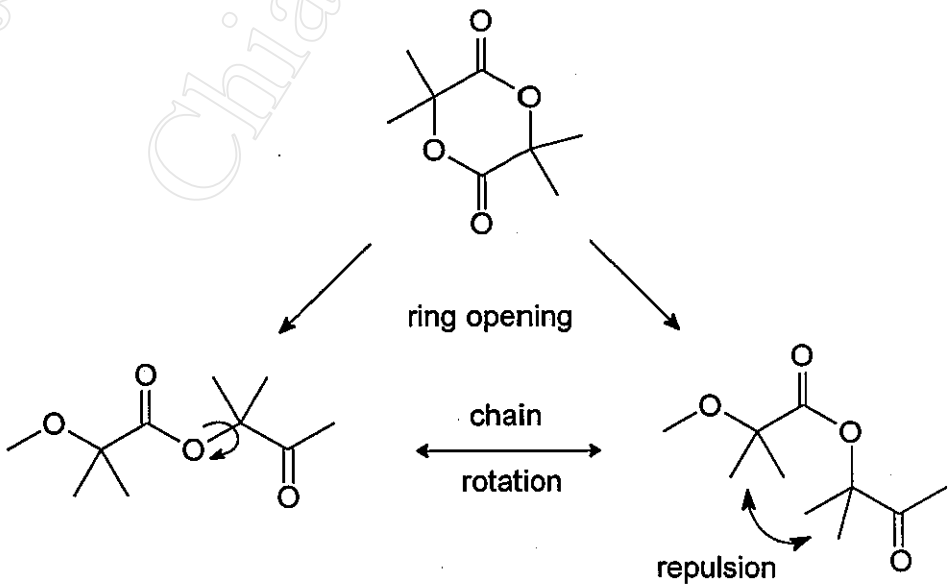


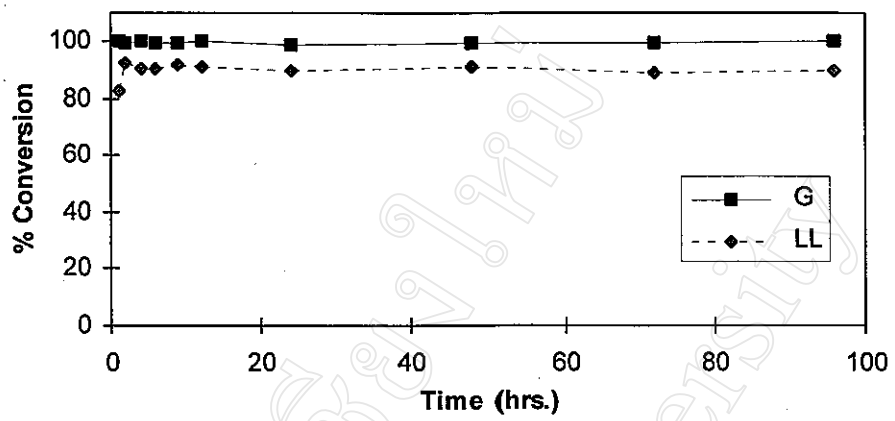
tetramethyl glycolide

α,α,α',α'-tetrasubstituted

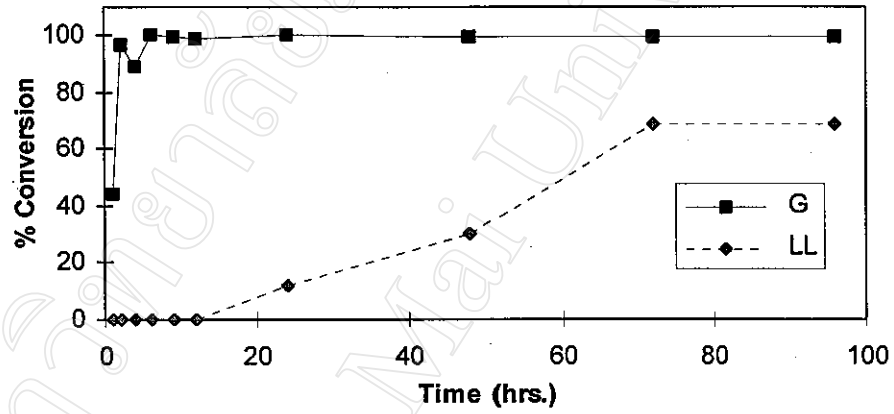
In the case of this glycolide series, the effect of substitution is particularly marked. Whereas the unsubstituted glycolide is spontaneously polymerisable on melting, L-lactide polymerisability is much lower and depends very much on the nature of the initiator (see Fig. 6.2), while tetramethyl glycolide is found not to polymerise at all.

This substitution effect is generally interpreted in terms of an increase in the steric repulsions between the substituent groups in the polymer chain relative to the monomer ring. This can be represented for tetramethyl glycolide as shown below:





(a)



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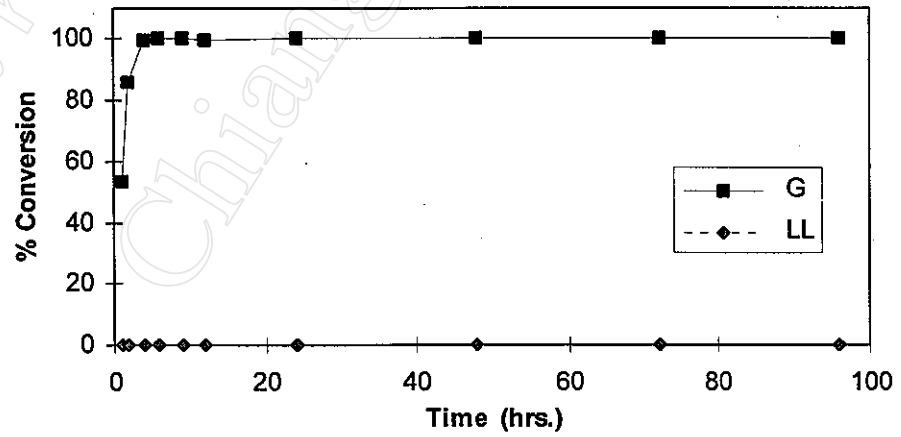


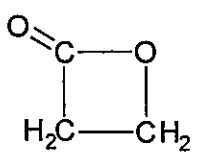
(c)

Fig. 6.2 : Comparison of the glycolide (G) and L-lactide (LL) conversion-time profiles at 150°C using (a) $Sn(Oct)_2$, (b)$BF_3{\cdot}Et_2O$ and (c) Li(*t*-OBu) as initiators.

Whereas the substituents are kept well apart in fixed positions in the ring, chain flexibility in the polymer allows for a greater probability of closer proximity leading to steric repulsions. These repulsions increase the internal energy of the chain, thereby increasing its enthalpy relative to the ring. The consequence of this is that ΔH_p becomes less negative and, therefore, the monomer less polymerisable. This interpretation is supported by the results of this work for the glycolide series (**SERIES IV**, in Table 5.2, page 260).

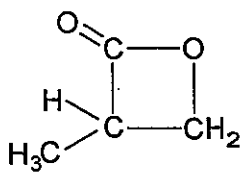
However, although the steric effect of a substituent on the ring-chain equilibrium is well documented in the literature, its steric effect on the actual polymerisation mechanism is, strangely, hardly mentioned. Clearly, ring substitution must increase the steric hindrance to the approach of the initiating species to the atom in the ring at which bond scission occurs. Likewise, the propagation step will be similarly affected. This will also decrease polymerisability, but for kinetic rather than thermodynamic reasons. Obviously, these two different steric effects are extremely difficult, if not impossible, to separate in practice, but it is still somewhat surprising that the literature has tended to emphasize the importance of one at the apparent neglect of the other. As the results in this thesis have shown, both thermodynamic and kinetic evidence is interpretable in terms of the factors affecting polymerisability. The fact that both types of evidence lead to the same conclusions lends weight to this discussion.

In addition to the ***degree*** of substitution, the ***position*** of substitution is also an important factor to consider. This positional effect has been seen most clearly in the 4-membered ring β-propiolactone series:



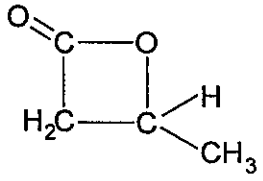
β-propiolactone

unsubstituted



α-methyl-β-propiolactone

α-monosubstituted



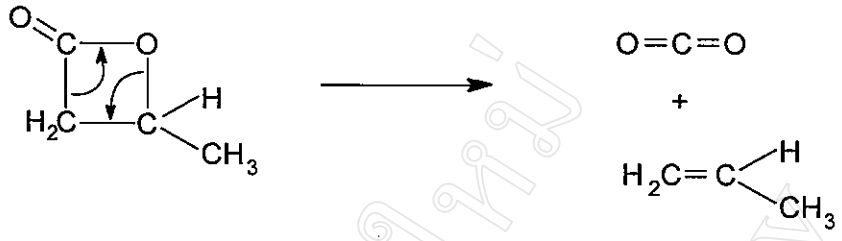
β- methyl-β-propiolactone

β-monosubstituted

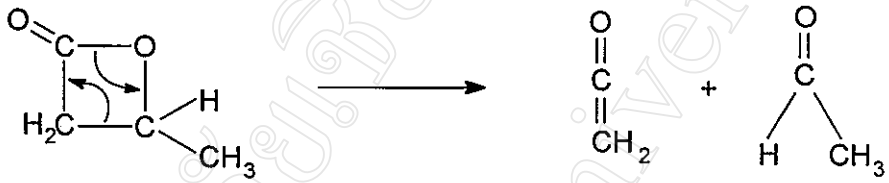
In the above series, methyl substitution, wherever it is positioned, decreases polymerisability relative to the unsubstituted ring. However, it decreases it much more in the β- than in the α-position, so much so that, whereas α-methyl-β-propiolactone is still readily polymerisable under normal conditions, β-methyl-β-propiolactone (β-butyrolactone) is extremely difficult to polymerise to even relatively low molecular weight ($\overline{M}_n < 10^4$). Indeed, even ***di***methyl substitution at the α-carbon (as in pivalolactone) decreases polymerisability much less than monomethyl substitution at the β-carbon.

Why then should β-substitution in a 4-membered ring be so much more deactivating than α-substitution? This question was posed in the previous Chapter 5 (on page 264). Strangely, no answer to this has been found in the literature and, it must be said, no obvious explanation has emerged from this work either. This situation is perhaps even more surprising when one considers that the would-be polymer of β-butyrolactone can, in fact, be easily prepared to high molecular weight ($\overline{M}_n > 10^5$) by another route, namely, bacterial fermentation. Known by its more common name of ***poly(β-hydroxybutyrate) (PHB)***, the polymer has risen to prominence in recent years as the Imperial Chemical Industries' environmentally biodegradable plastic of the future (ICI trade name : Biopol®). And yet, despite the inherent stability of the polymer ($T_m \approx 180^oC$; melt processable) and its relative abundance in the environment, its cyclic ester monomer, β-butyrolactone, is barely polymerisable.

The unusual case of PHB re-emphasizes an important point: polymer stability is not necessarily an indicator of monomer polymerisability. For some reason(s), β-butyrolactone, despite its highly strained ring, does not like to polymerise. Since polymer instability or a low ceiling temperature are clearly not the reasons for this, we must look more closely at the monomer itself. Even though neither the polymer literature nor the results of this work can offer a direct explanation, there are clues to be gained from other non-polymerisation studies. For example, it has been reported separately that, when heated, β-butyrolactone can undergo alkyl-oxygen scission to form propylene and carbon dioxide [139] as in:



or undergo acyl-oxygen scission to form acetaldehyde and ketene [140] as in:



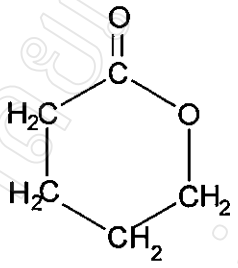
This raises the possibility that, in the case of β-butyrolactone, decomposition is favoured over polymerisation, a possibility rarely mentioned in the context of the ring opening of cyclic esters. Usually, it is taken for granted that it is a ring-chain equilibrium but unusual cases such as β-butyrolactone require unusual explanations.

Could it be then that ***thermal decomposition*** is the reason why β-butyrolactone is so difficult to polymerise? If so, is this peculiar to 4-membered rings or could rings of larger sizes be similarly affected? Also, why should β-methylation favour decomposition but α-methylation still favour polymerisation? Clearly, the thermodynamic stability of the products formed has much to do with it but it is strange that the difficult polymerisability of β-butyrolactone has not been explained more fully. Once again, this is probably because it has tended to be looked at in isolation. It is only when viewed as part of a series alongside its α-substituted analogue, as in this work, that its exceptional behavior can be fully appreciated.

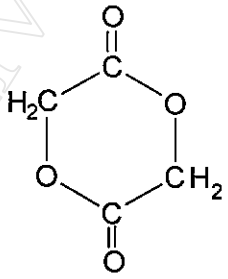
In conclusion, the ***positional*** effect of ring substitution on polymerisability has not received the attention that it deserves. This work has highlighted its importance and offered some thoughts on a particular 4-membered ring series which shows a range of polymerisability from one extreme to the other. It would be interesting to see how other larger ring series, for example, substituted 7-membered ring ε-caprolactones, compare with this.

6.3 Effect of Ester Functionality

Logically, increasing the ester functionality in a ring of fixed size should increase polymerisability, simply by increasing the number of active sites at which ring opening can occur. In this work, this functionality effect has been illustrated by comparisons between the 6-membered ring cyclic monoester, δ-valerolactone, and its diester analogue, glycolide.



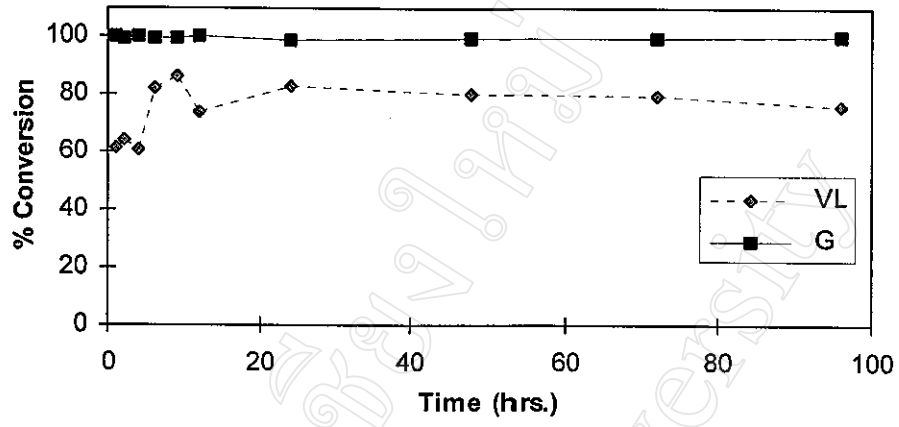
δ-valerolactone



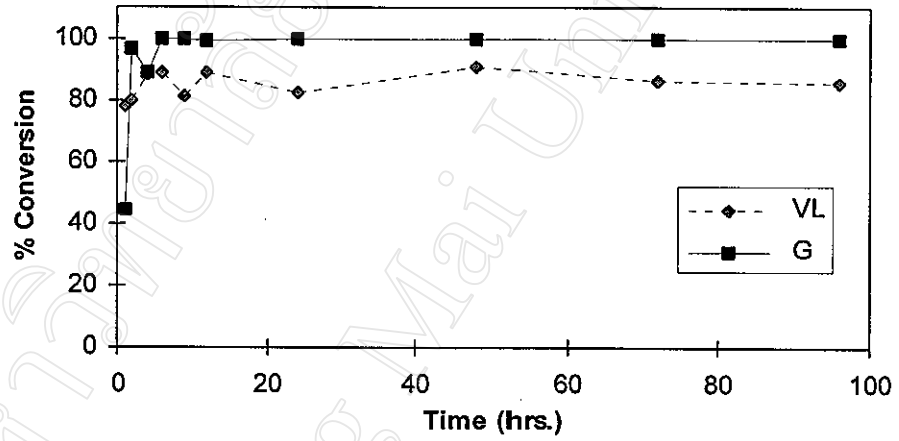
glycolide

Ester Functionality	:	*1*	*2*

In general, experimental results have supported this conclusion that polymerisability increases with functionality. For example, the thermodynamic parameters for δ-valerolactone and glycolide [134] (**SERIES V**, Table 5.2, page 260) support this view, as does the kinetic data in Fig. 6.3 on the following page. Furthermore, as mentioned earlier, glycolide is well known to be so reactive that, as soon as it melts and its molecules attain translational freedom from within the confines of the crystal lattice, it polymerises spontaneously, even without the addition of an initiator.



(a)



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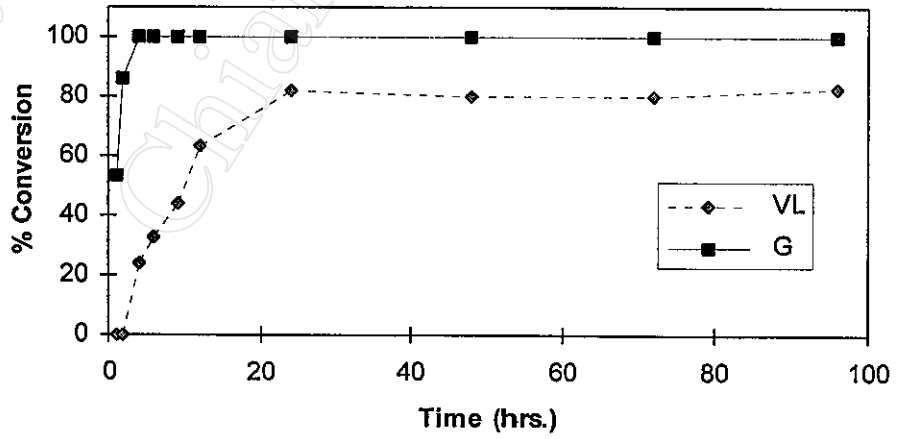


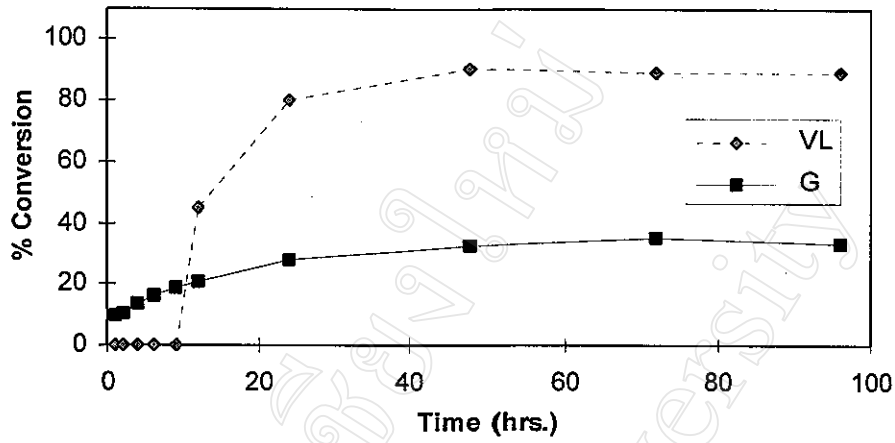
(c)

Fig. 6.3 : Comparison of the δ-valerolactone (VL) and glycolide (G) conversion-time profiles at 150°C using (a) $Sn(Oct)_2$, (b)$BF_3{\cdot}Et_2O$ and (c) Li(*t*-OBu) as initiators.

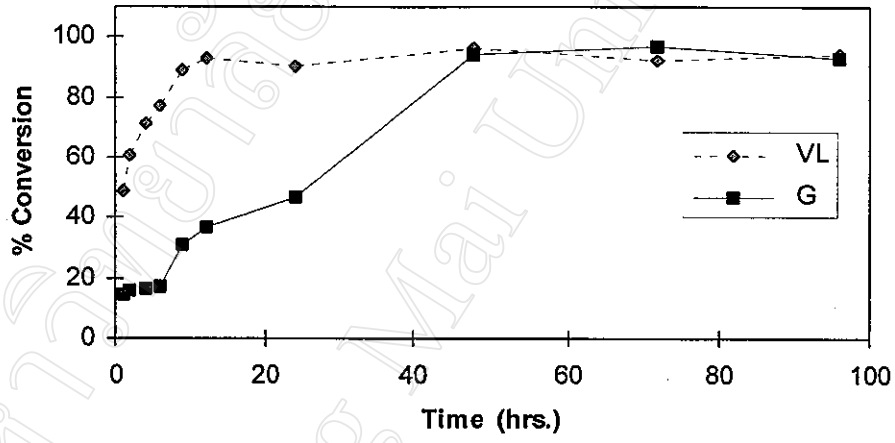
However, this δ-valerolactone-glycolide comparison also highlights an important point which has not previously been mentioned. In the case of the kinetic data obtained in this work, such as the % conversion - time profiles in Fig. 6.3, ***polymerisability*** has been compared under the same reaction conditions, i.e., using the same initiator at the same temperature. However, this fails to take account of other relevant factors such as (1) the different solubilities of the initiator in each monomer, (2) the ***ceiling temperature***, T_c, of each polymerisation and (3) any changes which may occur in the physical states of the polymerising systems.

Some of these factors are relevant to this δ-valerolactone-glycolide comparison. For example, in Fig. 6.3, the reaction profiles are compared at 150°C. From the earlier results in Chapter 3, this temperature is seen to be rather too high for δ-valerolactone since it is approaching its T_c (≈ 190°C). In contrast, 150°C is considered to be rather too low for glycolide since the polymerisate solidifies after a certain level of molecular weight has been attained, thus slowing down the reaction in the solid state. The significance of these influences is emphasized in Fig. 6.4 in which the reaction profiles are compared at a lower temperature of 100°C. This temperature is more suitable for δ-valerolactone (further removed from T_c) but is much less suitable for glycolide since solidification occurs even faster (within minutes). Consequently, the order of polymerisabilty appears to be reversed with δ-valerolactone now faster than glycolide.

This highlights the main problem of kinetic data in comparing the polymerisability of different monomers, namely the impossibility of finding a set of reaction conditions which are equally suitable for each monomer. Assuming that the reactions are to be carried out in bulk in the liquid/melt state, each monomer-polymer combination has its own unique set of temperature parameters (monomer T_m, polymer T_g and T_m, monomer-polymer T_c) which determine what the optimum polymerisation temperature should be. Polymerisability comparisons at the same temperature overlook this point which is why kinetic data, essential though it is, is inconclusive on its own. This is why this work has sought to bring together a collection of different types of data - kinetic, thermodynamic, spectroscopic and molecular modelling - upon which to base its conclusions.



(a)



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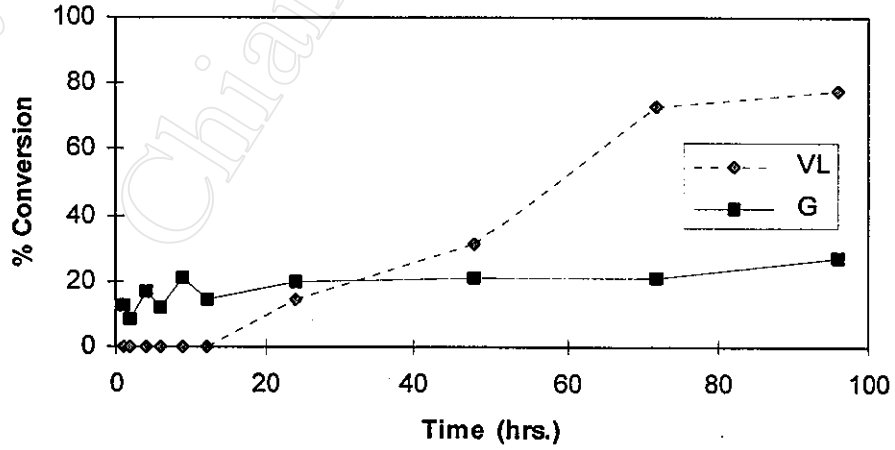


(c)

Fig. 6.4 : Comparison of the δ-valerolactone (VL) and glycolide (G) conversion-time profiles at 100°C using (a) $Sn(Oct)_2$, (b)$BF_3{\cdot}Et_2O$ and (c) Li(*t*-OBu) as initiators.

6.4 Effect of the Type of Initiator/Catalyst Used

It is well known that cyclic esters can be successfully polymerised by a wide range of ionic initiators/catalysts which can be divided into 3 main types:

(1) anionic initiators
(2) cationic initiators
(3) coordination initiators/catalysts

In this work, one common example of each type was chosen for study and their performances compared at the 0.1 mole % level under identical reaction conditions. From the results obtained, the effect of the type of initiator/catalyst on cyclic ester polymerisability has been observed. It should be reiterated here that this part of the work has not been intended as a detailed study of the actual reaction mechanisms involved since these are already well documented in the literature. It has merely been a comparative study of the initiator effectiveness as measured in terms of the increases in % conversion and molecular weight with time.

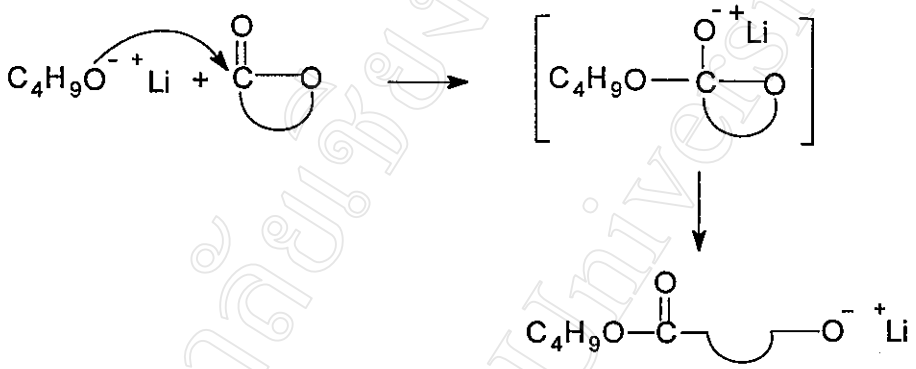
6.4.1 Anionic Initiation

The generally accepted mechanism of the anionic ring-opening polymerisation of cyclic esters is summarized in Scheme 6.1. In the case of the strongly basic **lithium *t*-butoxide**, **Li(*t*-OBu)**, initiator used here, ring-opening proceeds via nucleophilic attack of the *t*-butoxide anion at the carbonyl carbon atom in the ring. This is then followed by acyl-oxygen bond scission resulting in the formation of a new alkoxide anion as the propagating species, as originally proposed by Cherdron et al [68]. The apparent absence of a termination reaction would, in theory, lead to the formation of 'living polymers' and, indeed, this has been observed for both ε-caprolactone [3] and δ-valerolactone [73]. However, the broader-than-expected molecular weight distributions usually obtained in practice are evidence of the existence of termination reactions, assumed to be by chain transfer. Thus, the mechanism in Scheme 6.1 is nowadays generally accepted [73], the only qualification being that the overall reaction is actually a ring-chain equilibrium in which cyclic oligomers can also be formed via back-biting processes.

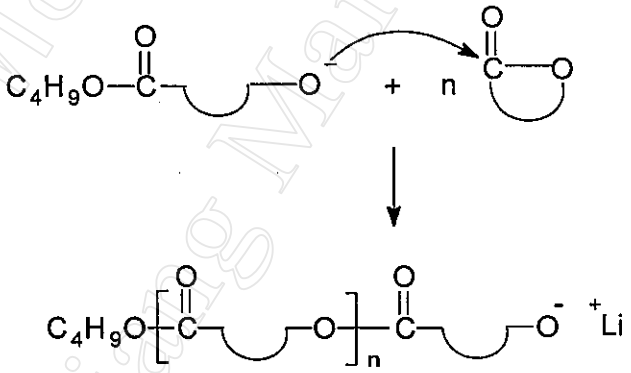
SCHEME 6.1

Reaction mechanism for the lithium *t*-butoxide-initiated anionic ring-opening polymerisation of cyclic esters.

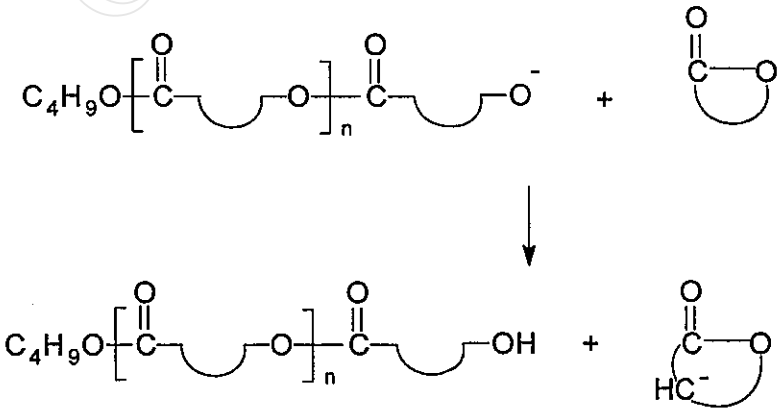
INITIATION



PROPAGATION



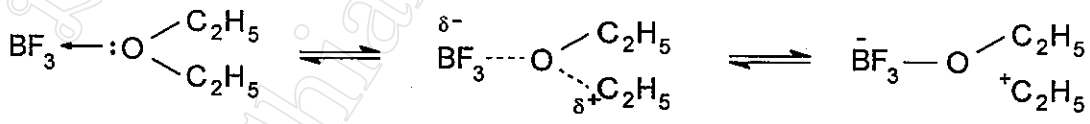
TERMINATION (e.g., by chain transfer to monomer)



In this work, Li(*t*-OBu) was chosen simply because it is one of the more commonly referred to, truly anionic alkali metal alkoxide initiators for cyclic ester polymerisation. It is also strongly basic which enables it to polymerise a wide range of cyclic ester monomers such as has been studied here. Apart from alkali metal alkoxides, other less basic anionic initiators which have been frequently reported in the literature include metal carboxylates and tertiary amines.

6.4.2 Cationic Initiation

In this work, the cationic initiator used was **boron trifluoride diethyl etherate, $BF_3{\cdot}Et_2O$,** a complex between boron trifluoride and diethyl ether (brown fuming liquid; b.p. 126°C). In $BF_3{\cdot}Et_2O$-initiated polymerisations, the active cationic species is assumed to be, although it has not been proved conclusively, an ethyl carbonium ion, $C_2H_5^+$.



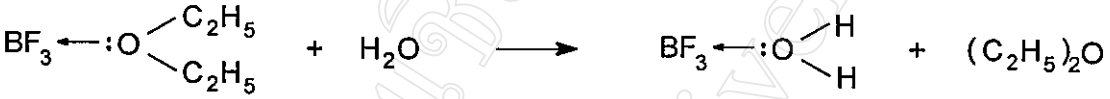
boron trifluoride diethyl etherate complex

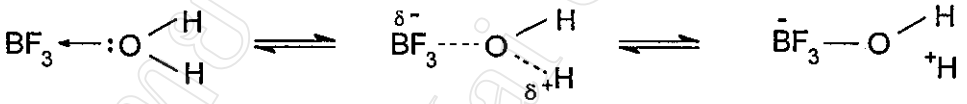
partial ionization

charge separation

The $BF_3{\cdot}Et_2O$ complex is formed as a result of the Lewis acidity of the BF_3 and the availability of the lone pair of electrons on the ether oxygen.

However, protons are usually also assumed to be involved arising from the immediate hydrolysis of $BF_3{\cdot}Et_2O$ in contact with trace amounts of moisture present in the system.



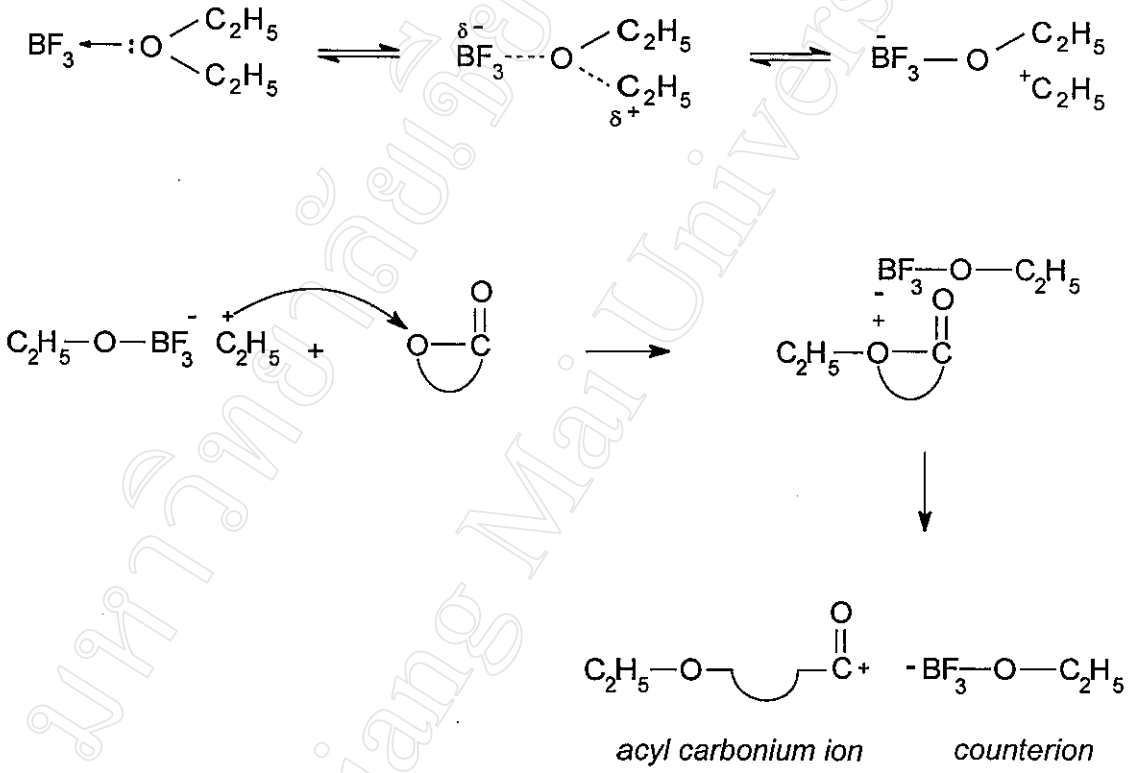


Until recently, the cationic ring-opening polymerisation mechanism proposed by Cherdron et al [68] has long been accepted as the main mechanism. As shown in Scheme 6.2 on the following page, Cherdron's mechanism proceeds via electrophilic attack of the initiating $C_2H_5^+$ cation on the endocyclic ring oxygen atom with subsequent acyl-oxygen cleavage and propagation through the resulting acyl carbonium ion. As with anionic polymerisation previously, termination is believed to occur via chain transfer reactions although, in the case of $BF_3{\cdot}Et_2O$, combination with the $[BF_3OC_2H_5]^-$ counterion is a likely alternative.

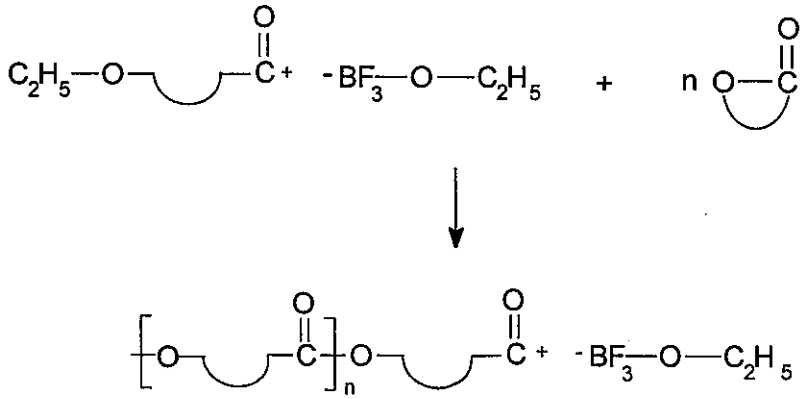
SCHEME 6.2

Reaction mechanism for the boron trifluoride diethyl etherate-initiated cationic polymerisation of cyclic esters via attack on the endocyclic ring oxygen atom.

INITIATION

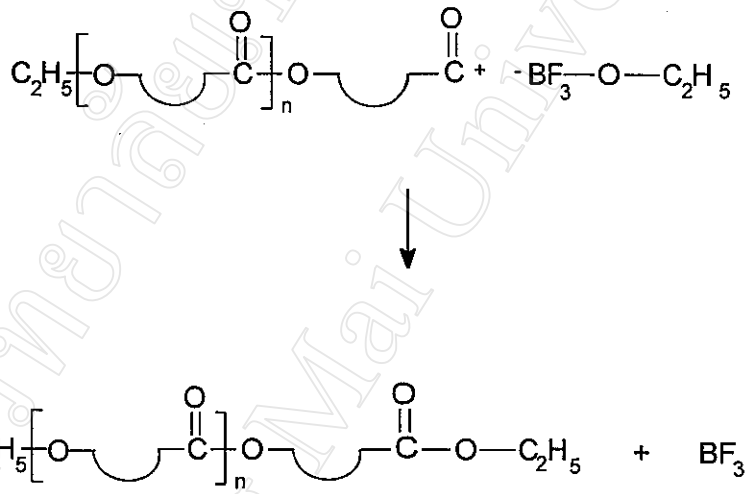


PROPAGATION



TERMINATION

In addition to the usual chain transfer reactions, termination probably also occurs via combination with the counterion in the system in the case of this Lewis acid type of cationic initiator.



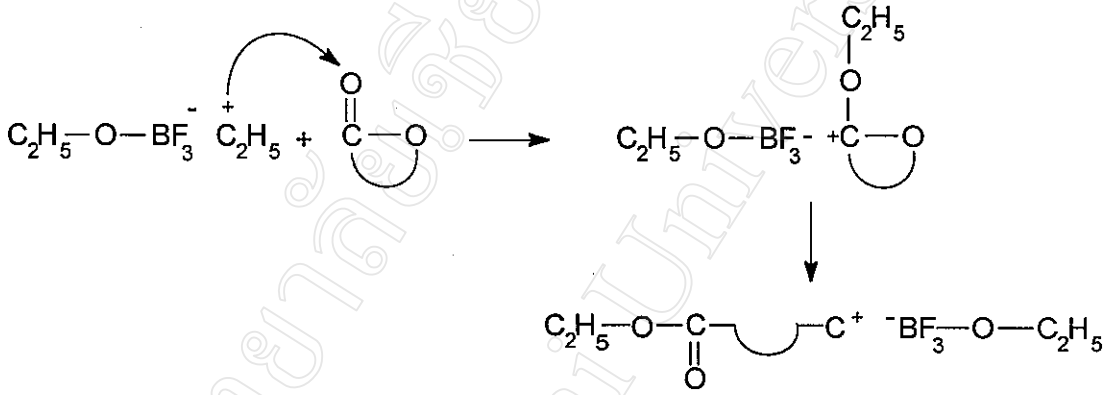
More recently, however, Cherdron's mechanism has been called into question, notably by Penczek et al [69, 70] and Kricheldrof et al [141]. These workers favour the mechanism shown in the following Scheme 6.3 whereby the initiating cation attacks not the endocyclic ring oxygen atom but the ***exocyclic carbonyl oxygen*** atom. This is then followed by ***alkyl-oxygen*** rather than acyl-oxygen bond scission.

Of these two mechanisms, the more recent one (Scheme 6.3) has gained increasing mention in recent publications but the earlier one (Scheme 6.2) is still the more widely quoted. Clearly, the controversy has not yet been totally resolved and may, in any case, be dependent on the exact nature of the particular monomer and initiator involved.

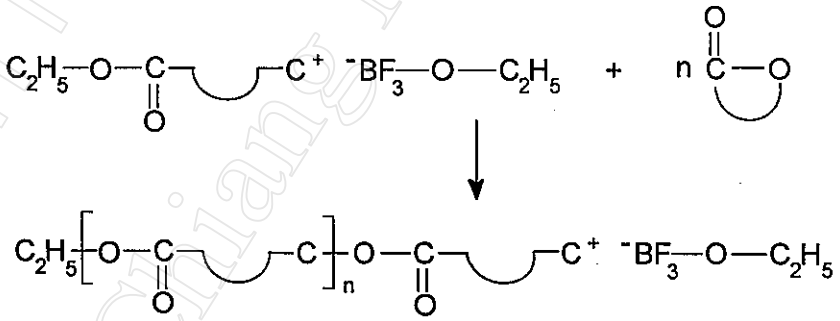
SCHEME 6.3

Reaction mechanism for the boron trifluoride diethyl etherate-initiated cationic polymerisation of cyclic esters via attack on the exocyclic carbonyl oxygen atom.

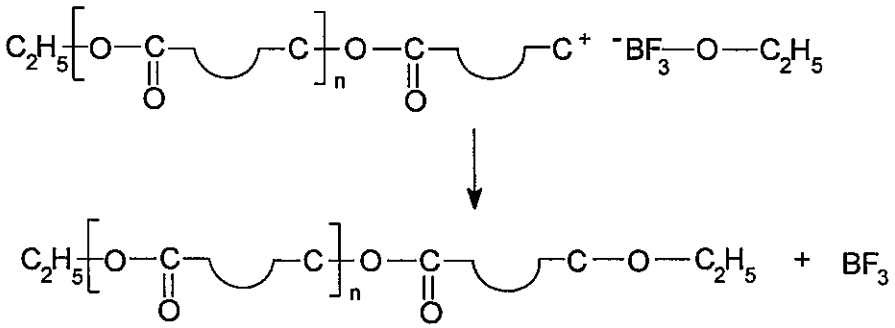
INITIATION



PROPAGATION



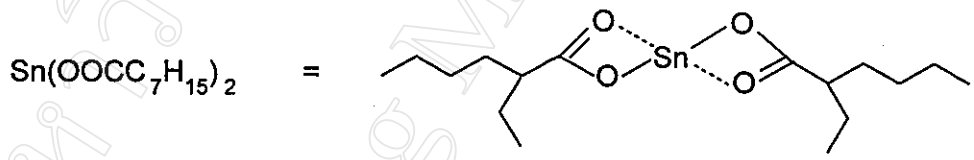
TERMINATION (for example, via counterion combinaton as in Scheme 6.2)



6.4.3 Coordination Initiation

The third type of initiator employed in this study was a so-called ***coordination*** initiator, also often referred to in the literature as a ***monomer insertion*** or ***complexation*** intiator. To complicate further this already rather confusing array of names, the ***initiator*** is sometimes referred to, rightly or wrongly, as a ***catalyst***, the distinction between which will be made clear later in this section.

The particular coordination initiator chosen in this work was **stannous octoate, $Sn(Oct)_2$,** on the grounds that it has become the most commonly used coordination-type initiator in cyclic ester polymerisation. Although it is nearly always referred to as simply **"stannous octoate",** strictly speaking, it is actually the iso-octoate isomer of the chemical structure shown below, systematic name: **tin(II) bis(2-ethyl hexanoate)**.



stannous octoate

$Sn(Oct)_2$

tin(II) bis(2-ethyl hexanoate)

$Sn(Oct)_2$

The apparent popularity of $Sn(Oct)_2$ as a coordination-type initiator/catalyst in cyclic ester polymerisations is based on a range of advantages, the main ones being that it is (1) highly efficient, even at the 0.01 mole % level, (2) as it contains ester groups itself, it is more easily miscible with cyclic ester monomers, (3) easy to handle with no special storage precautions, (4) relatively inexpensive, and (5) importantly for biomedical polyesters, has an extremely low toxicity compared with other heavy metal salts to the extent that it is now a permitted food additive. On the other hand, $Sn(Oct)_2$ does also have one or two disadvantages, namely that (1) commercial $Sn(Oct)_2$, typically 95% pure, commonly contains octanoic acid as an impurity which

is difficult to remove, and (2) it is hygroscopic in contact with air and can easily hydrolyse to a hydroxy derivative and more octanoic acid [142]:

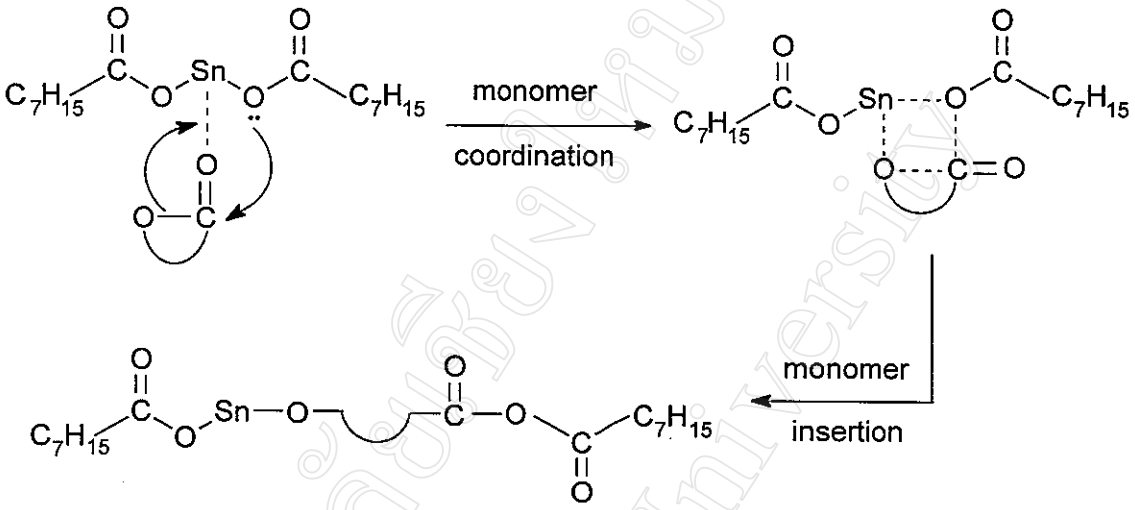
$$C_7H_{15}COO\text{-}Sn\text{-}OOCC_7H_{15} + H_2O \rightleftharpoons C_7H_{15}COO\text{-}Sn\text{-}OH + C_7H_{15}COOH$$

This hydroxy derivative may, in turn, conceivably react further with $Sn(Oct)_2$ to yield a further derivative as:

$$C_7H_{15}COO-Sn-OH + C_7H_{15}COO-Sn-OOCC_7H_{15} \rightleftharpoons C_7H_{15}COO-Sn-O-Sn-OOCC_7H_{15} + C_7H_{15}COOH$$

These various derivatives of $Sn(Oct)_2$ and, indeed, even the octanoic acid by-product are probably also active initiating species to greater or lesser extents than the $Sn(Oct)_2$ itself.

Consequently, the actual mechanism by which $Sn(Oct)_2$ acts as a coordination initiator has been the subject of much debate in the polymer literature. As the word ***coordination*** suggests, the initiation step involves coordination of the cyclic ester monomer to the Sn atom followed by ring-opening and monomer insertion into the Sn-O bond.



Where the controversy still exists is in the mechanism by which the monomer is inserted. While it is generally accepted that ring opening takes place at the acyl-oxygen bond (as in the previous anionic and cationic mechanisms), the exact natures of both the initiating and coordinated species remain uncertain. In the growing amount of literature on this subject, two main mechanisms of monomer insertion have emerged. These are generally referred to as:

(1) the non-ionic insertion mechanism
(2) the Lewis acid alcoholysis mechanism

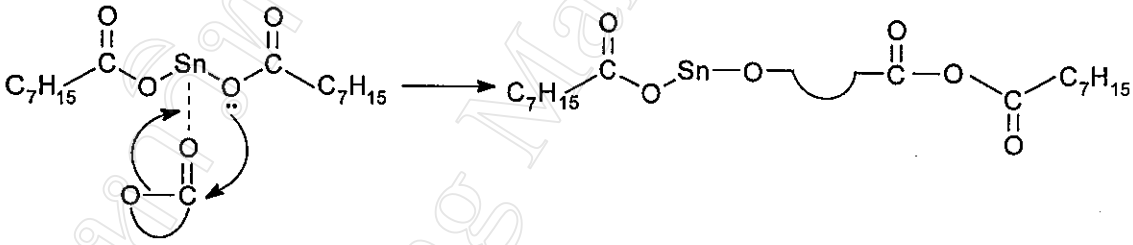
In the **non-ionic insertion** mechanism [143], as its name suggests, there is no ion formation or charge separation during the monomer coordination and insertion steps although dipole-dipole interactions are clearly involved. The proposed mechanism is summarized in Scheme 6.4. Since it is non-ionic in nature and there does not appear to be any obvious termination step, it should show, in theory, 'living' character. However, in practice, judging from the molecular weight distributions obtained, termination reactions must occur. The most popular theory seems to be that termination occurs via intramolecular transesterification by a back-biting mechanism, especially since $Sn(Oct)_2$ is also well known to be an effective transesterification catalyst. If this mechanism is indeed correct, then, as shown in

Scheme 6.4 (TERMINATION mechanism (a)), cyclic oligomers would be formed which, depending on their size and stability, may be able to undergo ring-opening again to a linear chain. Apart from transesterification, termination may also occur via hydrolysis by trace amounts of moisture present in the system (TERMINATION mechanism (b)), possibly catalysed by the octanoic acid impurity in the $Sn(Oct)_2$ initiator.

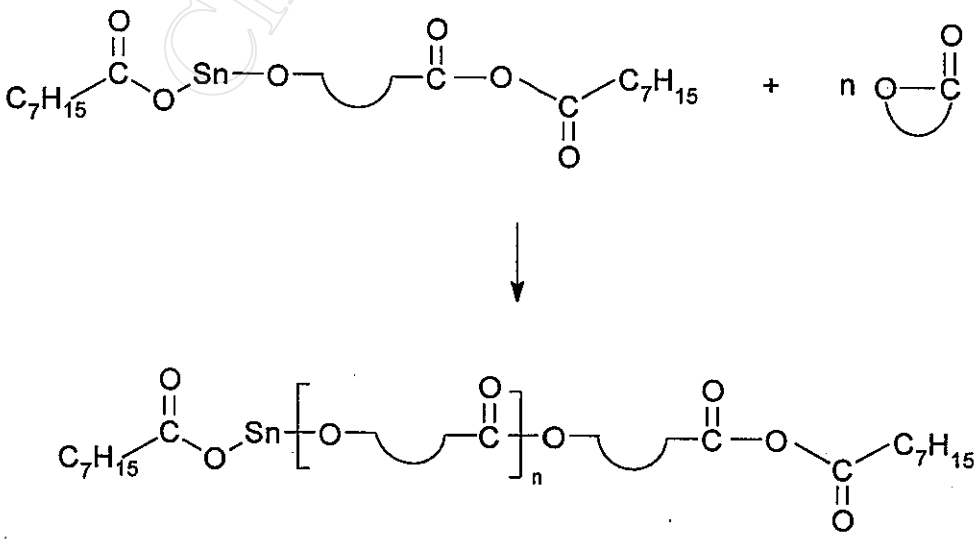
SCHEME 6.4

Reaction mechanism for the stannous octoate-initiated coordination polymerisation of cyclic esters via the non-ionic insertion mechanism.

INITIATION

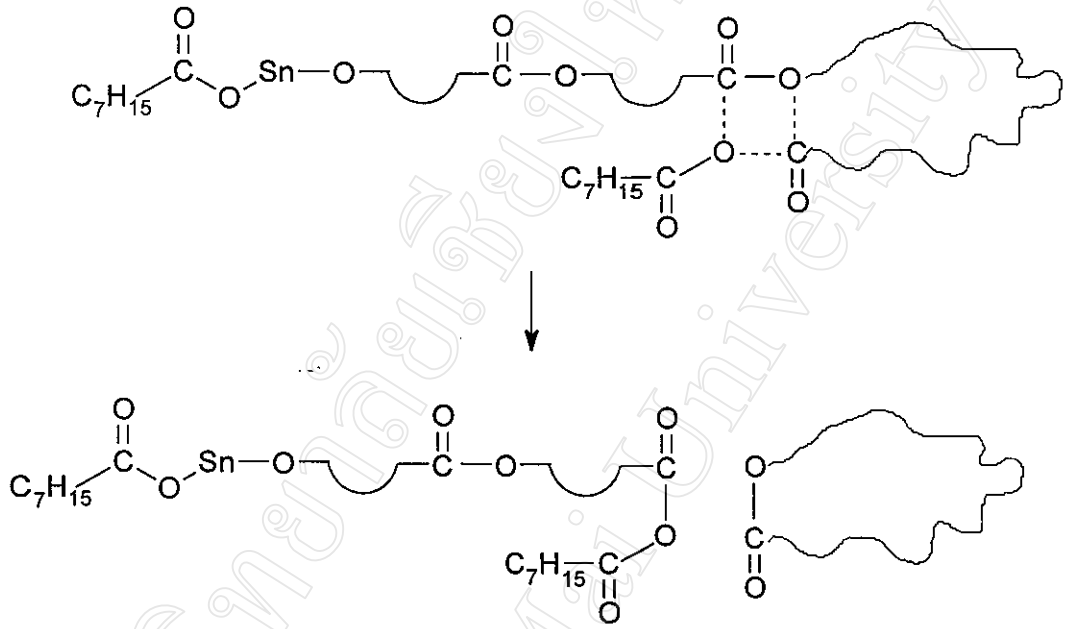


PROPAGATION



TERMINATION

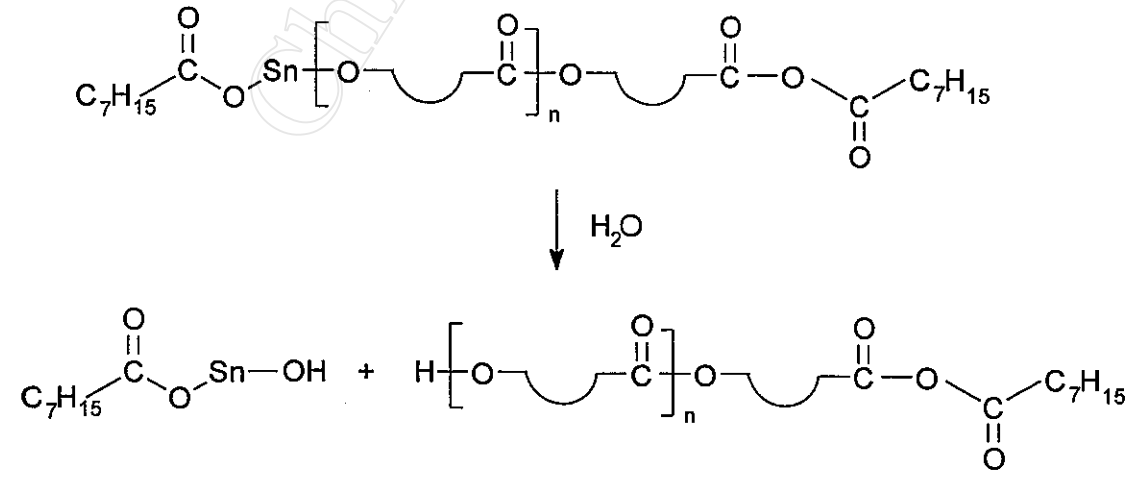
(a) Transesterification via back-biting



still contains the active Sn-O site
(can propagate further)

cyclic oligomer
(may re-polymerise)

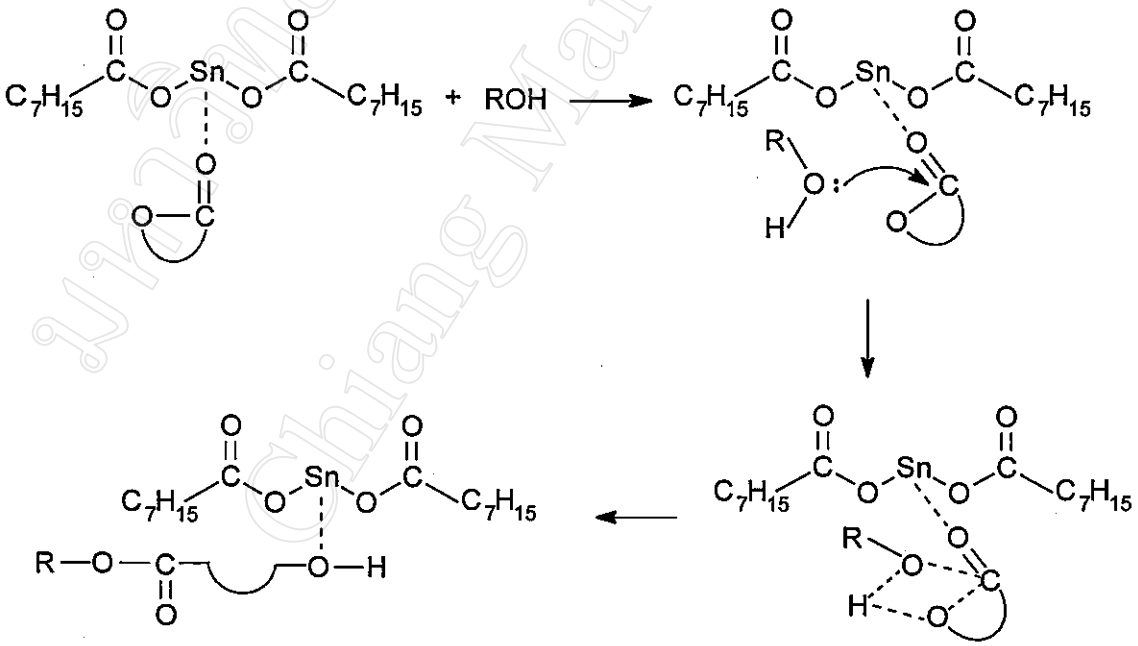
(b) Hydrolysis



still an active Sn derivative
(can initiate a new chain)

terminated polymer molecule
(no active Sn-O site)

In contrast to this non-ionic insertion mechanism, in the **Lewis acid alcoholysis** mechanism [145], the $Sn(Oct)_2$ is ***not*** incorporated into the polymer chain. First proposed by Nijenhuis et al [58], this mechanism (Scheme 6.5) is based on the presence of OH-containing compounds (including water) in the system, either as contaminants in the $Sn(Oct)_2$ and/or the monomer or, as in more usually the case, deliberately added. These hydroxyl compounds, R-OH, are believed to be the ***true initiating species*** with the $Sn(Oct)_2$ reverting to the role of a ***catalyst***. As shown below, the coordination mechanism begins with the R-OH hydroxyl compound reacting with the initial $Sn(Oct)_2$ - monomer complex via a nucleophilic attack at the carbonyl carbon in the monomer.



This mechanism is essentially a ***Lewis acid-catalysed ester alcoholysis*** reaction, hence the terminology. The complete reaction mechanism is shown in Scheme 6.5. One of the advantages of this mechanism is that it produces

telechelic polyesters with functional OH end-groups. Depending on the functionality of the alcohol initiator used, polymers with the same number of OH end-groups can be produced. This is currently being exploited in the design and synthesis of novel **block copolyesters** with specially tailored structures for use in biomedical applications.

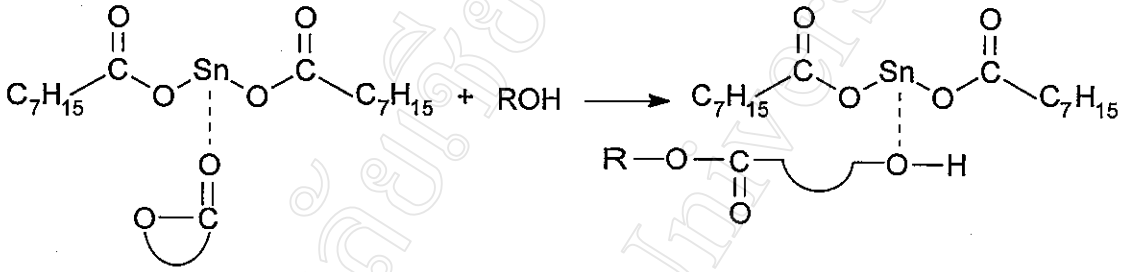
This comparison of these two mechanisms of monomer insertion serves to demonstrate how the confusion between $Sn(Oct)_2$ as an ***initiator*** and as a ***catalyst*** arises. When used on its own, as in this work, $Sn(Oct)_2$ functions primarily as an ***initiator*** via the non-ionic insertion mechanism and is incorporated into the polymer chain. However, when used in conjunction with a hydroxyl compound, it functions primarily as a ***catalyst*** via the Lewis acid alcoholysis mechanism and is not incorporated. Therefore, in this work, it has been referred to as an ***initiator*** throughout. Unfortunately, in the literature, this distinction is not always made clear and the two words, ***initiator*** and ***catalyst***, are sometimes used almost interchangeably. Hopefully, this comparison clarifies the difference between these two roles.

Thus, the true nature of the initiating species when using organometallic compounds such as $Sn(Oct)_2$ is questionable, especially when one takes into account the fact that trace amounts of water, which are invariably present in the system, can hydrolyse $Sn(Oct)_2$ to derivatives which may themselves be active. Then there is the inevitable octanoic acid impurity which may also act as an initiator and/or catalyst. Clearly, the situation in practice is a complicated one and has already attracted widespread attention in the polymer literature. Although this present work cannot add anything to the foregoing discussion, it is important to at least be aware of the mechanisms involved if meaningful comparisons of initiator efficiency are to be made. These comparisons are now summarized in the following section.

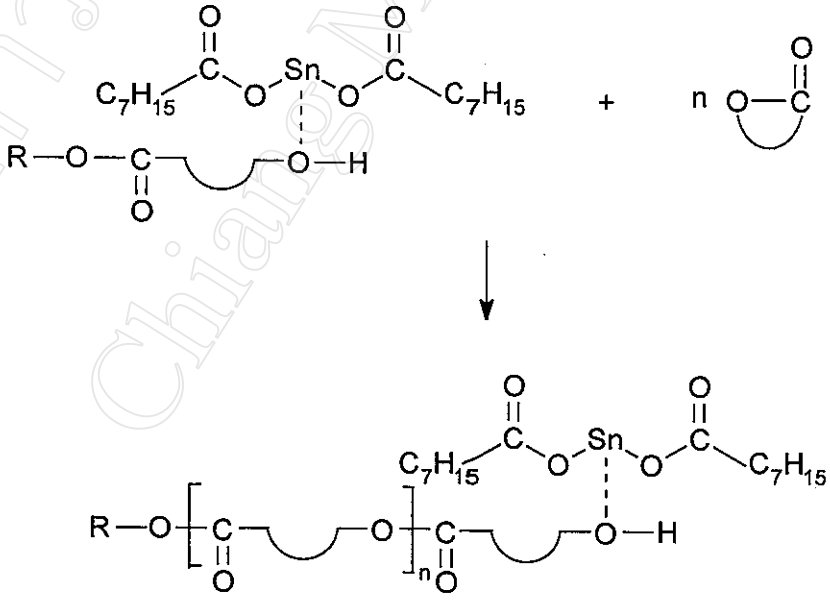
SCHEME 6.5

Reaction mechanism for the stannous octoate-catalysed coordination polymerisation of cyclic esters via the Lewis acid alcoholysis mechanism.

INITIATION

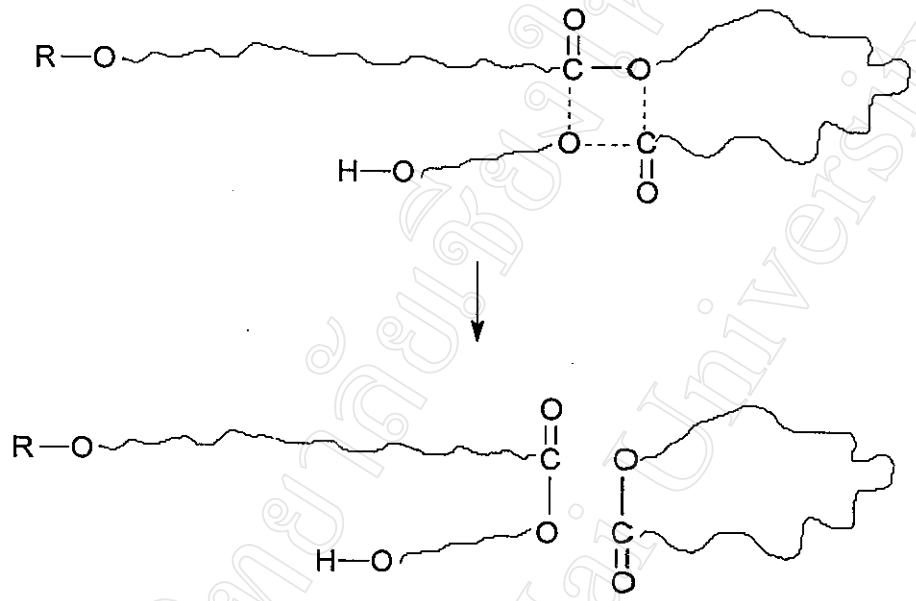


PROPAGATION

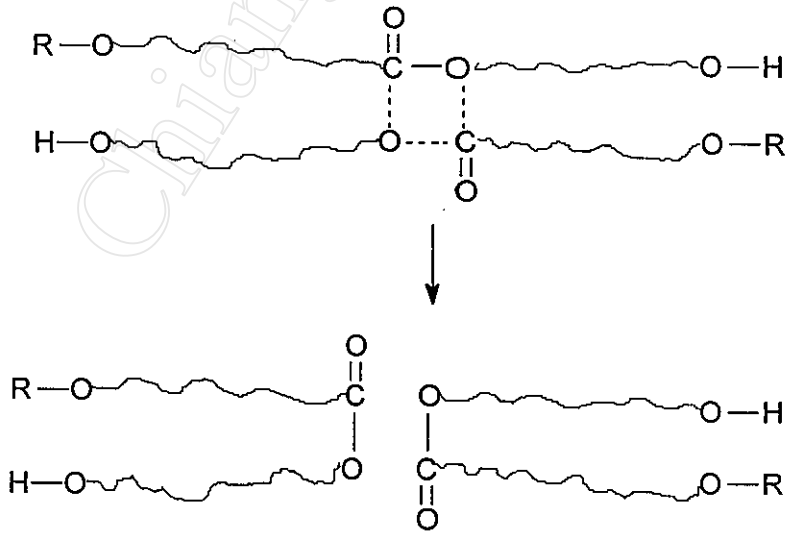


TERMINATION

(a) Intramolecular transesterification via back-biting



(b) Intermolecular transesterification



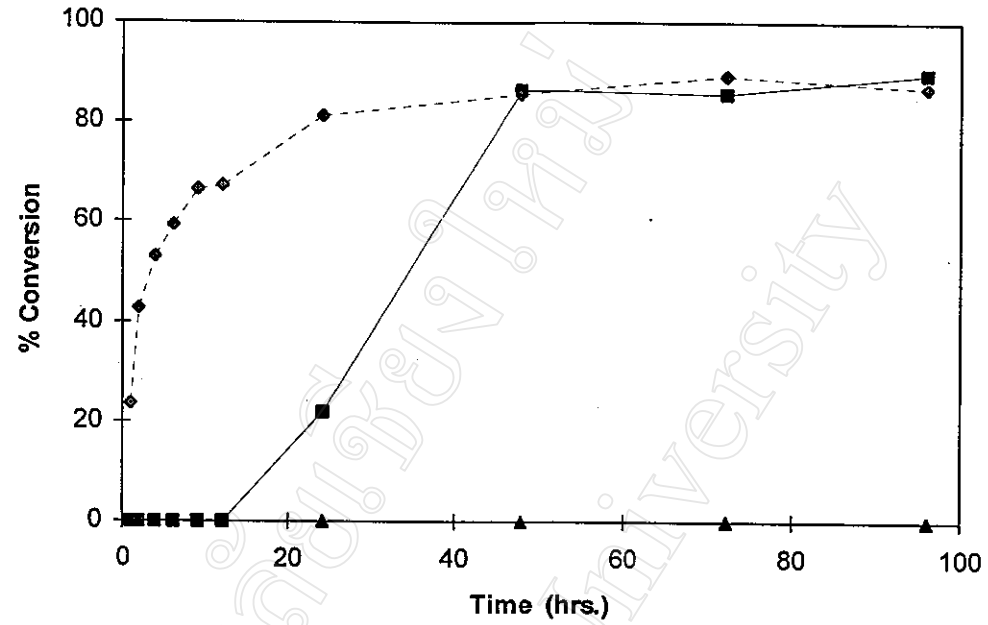
6.4.4 Comparison of Initiator Efficiency

Just as the chemical structure of the monomer is fundamental to its polymerisability, so is the chemical nature of the initiator. In this work, 3 different types of initiator were chosen with the aim of comparing their efficiencies in polymerising a given monomer under a given set of reaction conditions. For the purposes of this study, initiator efficiency is compared in terms of the increases in % conversion and polymer molecular weight ($\bar{M}_n$) with time.

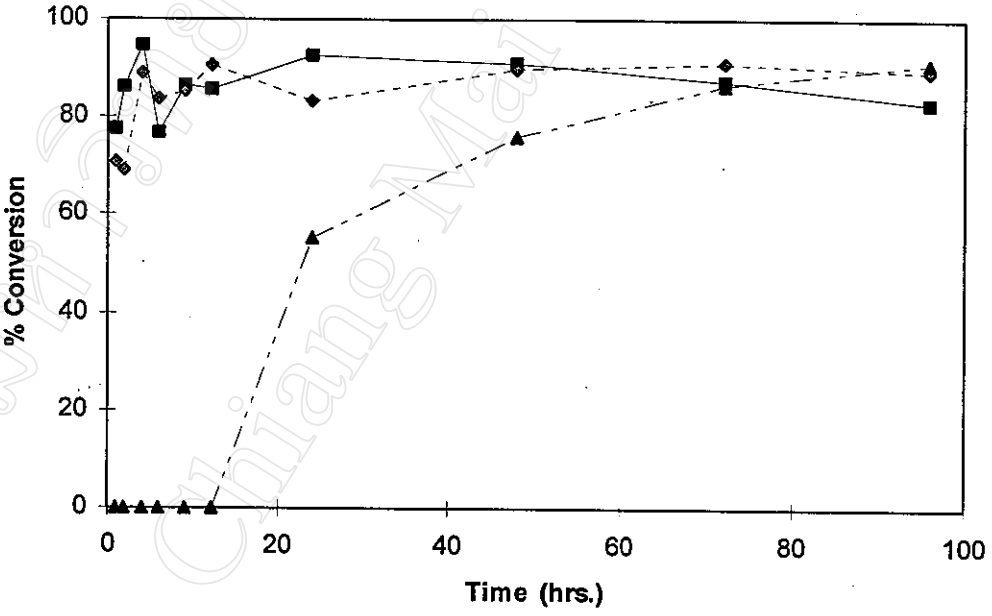
In the majority of cases, although not all, initiator efficiency, when compared on a rate (% conversion) basis, appeared to be in the order:

Initiator	:	Li(*t*-OBu)	<	$Sn(Oct)_2$	<	$BF_3{\cdot}Et_2O$
Type	:	*anionic*		*coordination*		*cationic*

This is exemplified by the results in Fig. 6.5 for ε-caprolactone at two different temperatures: 100°C and 150°C. The corresponding polymer $\bar{M}_n$-time profiles in Fig. 6.6 are less indicative, possibly because of the transesterification reactions which occur in all of the systems and which cause the $\bar{M}_n$ to tend towards a pseudo-equilibrium value at long reaction times.

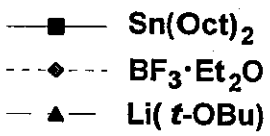


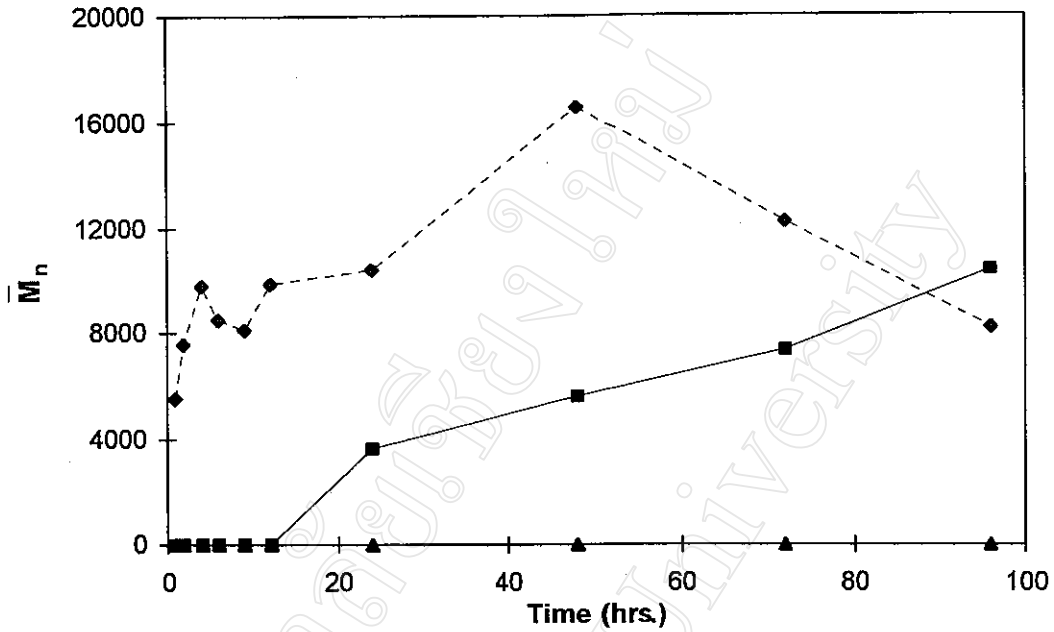
(a)



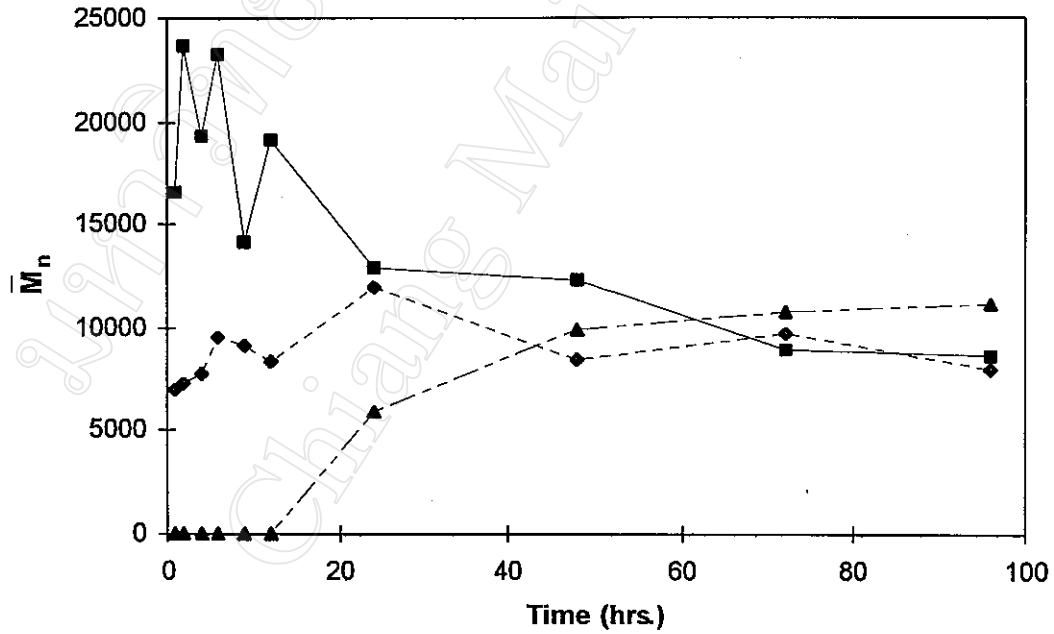
(b)

Fig. 6.5 : Comparison of the ε-caprolactone conversion-time profiles using different initiators at (a) 100°C and (b) 150°C.



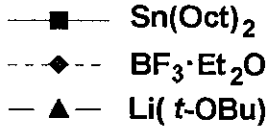


(a)



(b)

Fig. 6.6 : Comparison of the PCL number-average molecular weight $\bar{M}_n$-time profiles using different initiators at (a) 100°C and (b) 150°C.



Strictly speaking, of course, these initiator comparisons are specific to the particular monomer and reaction conditions employed. Generalizations beyond this are difficult to make. For example, even though Li(*t*-OBu) has been found here to be a much less effective initiator than $BF_3{\cdot}Et_2O$, it is possible that a different anionic initiator to Li(*t*-OBu) could be as effective if not more so than a different cationic initiator to $BF_3{\cdot}Et_2O$. Different initiators of the same mechanistic type have different solubilities in the monomer and different temperature and concentration ranges over which they are effective.

However, for the purposes of this discussion, if it is considered that the weight of evidence in Chapter 3 as a whole is sufficient to conclude that the order of initiator efficiency is:

Li(*t*-OBu)	<	$Sn(Oct)_2$	<	$BF_3{\cdot}Et_2O$
anionic		*coordination*		*cationic*

it then prompts the question as to why cyclic esters should be more reactive towards cationic than anionic initiation.

In order to answer this question, we must refer back to the reaction mechanisms previously described earlier in this section 6.4. In the case of the ***anionic*** mechanism in Scheme 6.1 (page 286), ring opening proceeds via nucleophilic attack of the $C_4H_9O^-$ anion at the carbonyl carbon atom in the ring. Because this carbon atom is shielded to some extent by the carbonyl oxygen, there will inevitably be some steric hindrance to the approach of the initiating anion to the point of attack. In contrast to this, the point of attack in the ***cationic*** mechanism is wide open. Whether it is the ring oxygen atom, as in Scheme 6.2 (page 289), or the carbonyl oxygen atom, as in Scheme 6.3 (page 291), the electrophilic attack of the $C_2H_5^+$ cation is relatively unhindered. This offer a possible explanation as to why cyclic esters appear to polymerise more readily with cationic than anionic initiators.

Compared with the Li(*t*-OBu) and $BF_3{\cdot}Et_2O$ initiators, the intermediate efficiency of the $Sn(Oct)_2$ initiator gives some indication of the driving force within the ***coordination*** mechanism. According to the non-ionic insertion mechanism in Scheme 6.4 (page 295), the Sn atom of the initiator interacts with the carbonyl oxygen atom of the monomer at the same time as the oxygen atom adjacent to the Sn attacks the carbonyl carbon. These interactions obviously have something in common with both the cationic and anionic mechanisms respectively but do not involve actual ion formation. Furthermore, the coordination mechanism should have at least some 'living' character. On top of this, there is the sensitivity of the $Sn(Oct)_2$ to moisture and OH-containing impurities which can complicate the mechanism considerably.

Thus, these comparisons of initiator efficiency are, at best, subjective. The choice of initiator in cyclic ester polymerisation is undoubtedly of fundamental importance but is inextricably linked to the choice of monomer and reaction conditions. This is a separate study in itself and one which would be a natural extension of this work.

6.5 Effect of the Reaction Conditions Employed

For any given monomer-initiator combination, the reaction conditions employed need to be chosen carefully if the kinetics of polymerisation, the % conversion, and the molecular weight of the polymer formed are to be optimized. Because of the large number of reaction variables involved, only the ones of most obvious importance, i.e. ***temperature*** and ***time***, were varied here. Apart from these two variables, all other reaction conditions were kept constant as follows:

(1) Reagent Purity

Each of the 6 monomers whose polymerisabilities were compared in Chapter 3 (as listed on page 116) were rigorously purified before use, either by vacuum distillation (liquids) or recrystallisation (solids). The 3 initiators chosen were used as supplied.

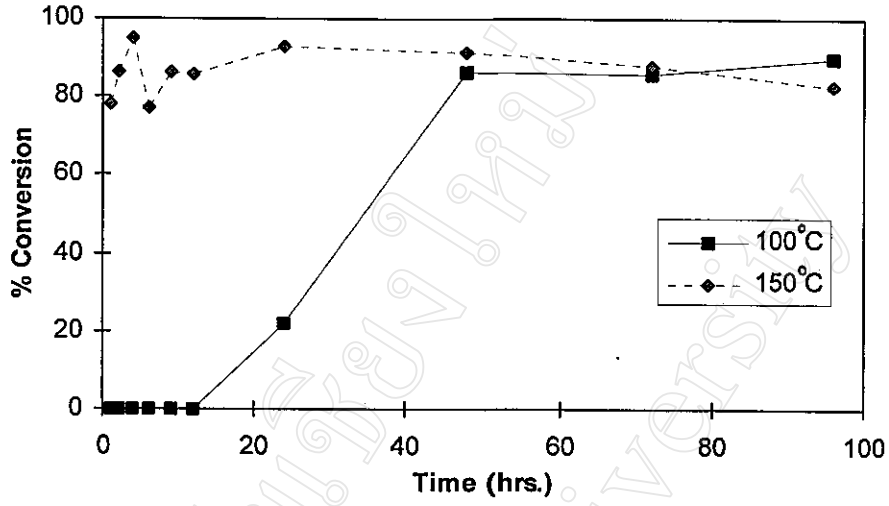
(2) Practical Method

The practical method of polymerisation employed was ***bulk polymerisation*** (pure monomer + initiator only), thus eliminating from consideration any complicating solvent/medium effects. The monomer and initiator (0.1 mole %) were mixed together at room temperature in a controlled atmosphere glove box before being heated to the chosen reaction temperature.

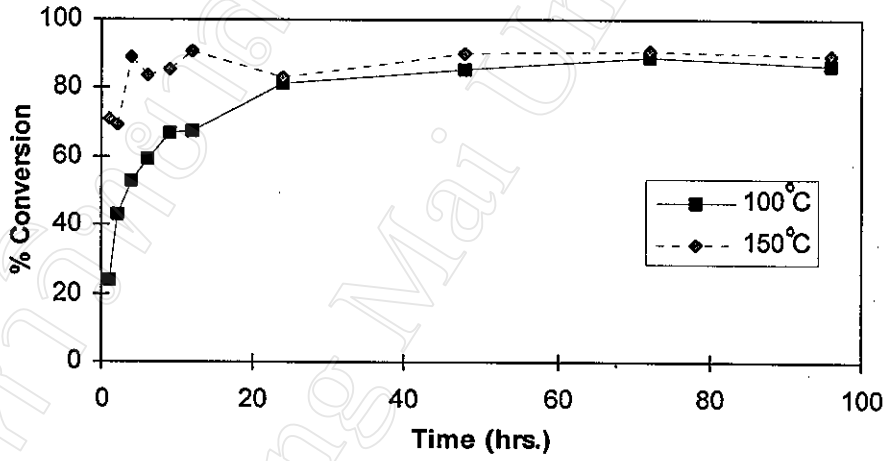
(3) Atmosphere / Pressure

All polymerisations were carried out under an inert atmosphere of dry, oxygen-free nitrogen in a sealed container. The initial pressure inside the container (after mixing the monomer and initiator at room temperature) was atmospheric pressure but this would have increased at the reaction temperature by an amount depending on the monomer volatility.

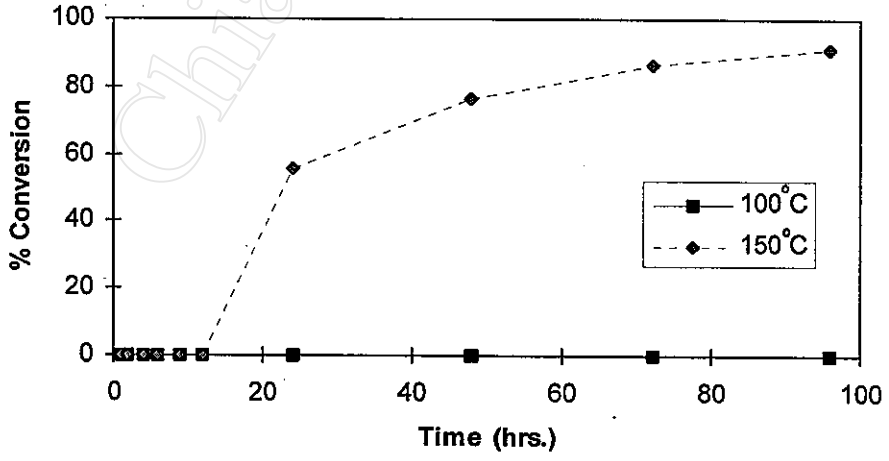
Reviewing the results in Chapter 3, in general, the effect of increasing the ***temperature*** is to increase the rate of polymerisation, as would be expected. This is illustrated in Fig. 6.7 for the case of ε-caprolactone at the two temperatures of 100°C and 150°C. The conversion-time profiles vary quite markedly with both temperature and initiator. The corresponding polymer (PCL) $\overline{M}_n$-time profiles in Fig. 6.8 also suggest a faster molecular weight build-up at the higher temperature but this effect then seems to become shrouded as time increases by what is believed to be the effects of transesterification. This tends to limit the molecular weight attainable to a pseudo-equilibrium value and is the most likely explanation as to why the final molecular weights obtained ($\overline{M}_n$ < 20,000) were generally lower than expected for a monomer : initiator mole ratio of 1000 : 1.



(a)

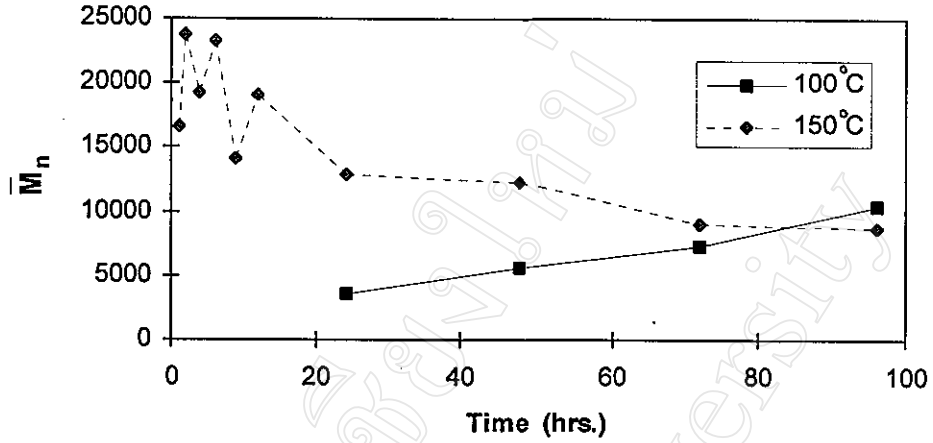


(b)

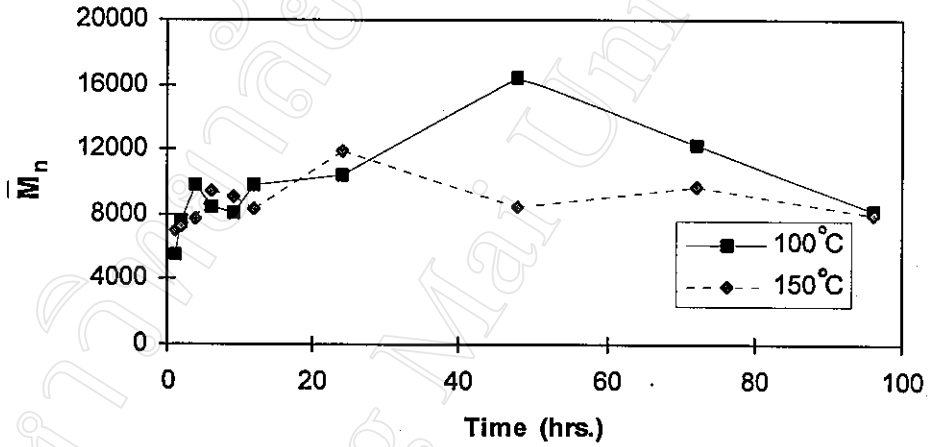


(c)

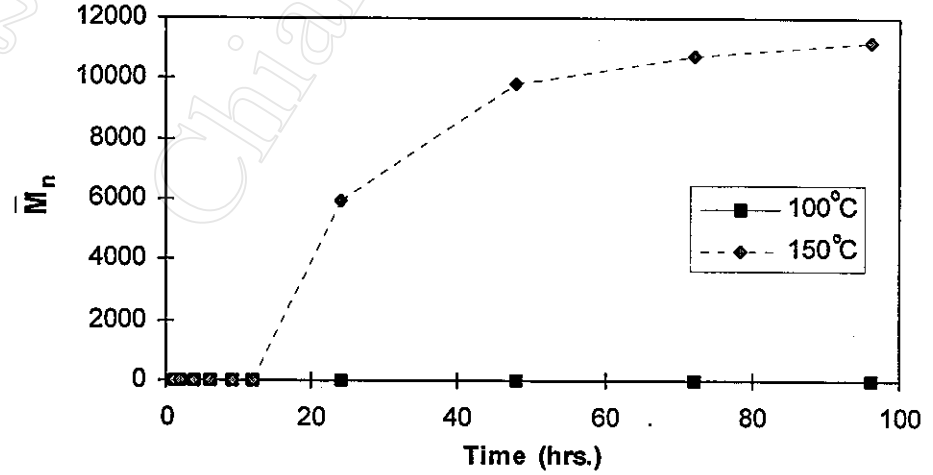
Fig. 6.7 : Effect of temperature on the ε-caprolactone conversion-time profiles using (a) $Sn(Oct)_2$, (b) $BF_3{\cdot}Et_2O$ and (c) Li(*t*-OBu) as initiators.



(a)



(b)



(c)

Fig. 6.8 : Effect of temperature on the PCL number-average molecular weight $\bar{M}_n$-time profiles using (a) $Sn(Oct)_2$, (b) $BF_3{\cdot}Et_2O$ and (c) Li(*t*-OBu) as initiators.

While these temperature/time effects are not new findings by any means, they do highlight the fact that each monomer-initiator combination has its own unique set of temperature parameters which determine what the optimum polymerisation temperature (or temperature profile) should be. These parameters include:

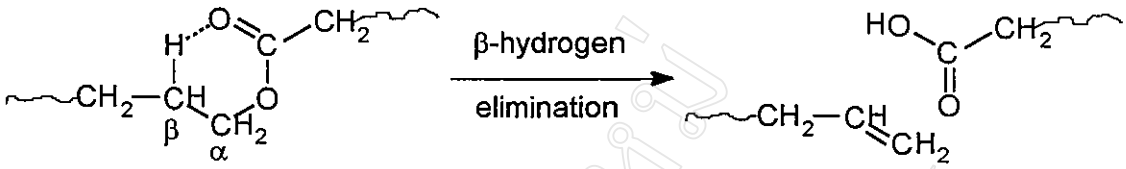
(1) **monomer T_m** - in the case that the monomer is a solid at room temperature (e.g., glycolide, L-lactide), its T_m obviously determines the lower temperature limit for bulk polymerisation in the melt

(2) **polymer T_m** - if the polymer's T_m is higher than the polymerisation temperature, the polymerisate will solidify after a certain molecular weight level has been attained whereupon the reaction rate will decrease considerably (this effect was observed in the glycolide and L-lactide polymerisations)

(3) **polymer T_g** - in the event that the polymerisate does solidify during the course of the reaction, the polymerisation temperature should be well above the polymer's T_g so that the highest possible % conversion can still be achieved

(4) **monomer-polymer T_c** - as the polymerisation temperature approaches the *ceiling temperature*, T_c, the likelihood of depolymerisation back to the cyclic monomer via intramolecular transesterification increases (this effect was observed in the δ-valerolactone polymerisations at 150°C)

(5) **polymer T_d** - depolymerisation at the T_c may be preceded by the onset of other polymer thermal degradation mechanisms at T_d such as intermolecular transesterification (influential at the higher temperature of 150°C) and β-H elimination (a higher temperature mechanism, probably not so important in this work) leading to random chain scission, as shown on the following page



(6) initiator efficiency range - each type of initiator will have its own temperature range over which it is most effective with a given monomer, as previously discussed

Therefore, what this work has highlighted with regard to the choice of reaction conditions is that the polymerisation temperature needs to be carefully chosen according to the preceding considerations. Better still, a temperature ***profile*** should be devised which can optimise conversion and molecular weight while keeping degradation to a minimum. Depending on the particular monomer, this may involve extended reaction times if the reaction needs to be concluded in the solid state. This is especially relevant to high melting point polyesters, such as PGA ($T_m \approx 220^oC$) and PLLA ($T_m \approx 170^oC$), which are known to be thermally unstable if maintained in the melt state even for short periods. However, it should be re-emphasized that the choice of temperature is inextricably linked to the choice of initiator, while the extent to which moisture can be excluded from the system is also vitally important.

Thus, the main conclusion is that, although the ring-opening polymerisation of cyclic esters is a relatively facile reaction, the attainment of both high conversion ($\rightarrow$ 100%) and high polymer molecular weight ($\overline{M}_n > 50,000$) requires knowledge and understanding of the underlying factors which control the reaction combined with practical expertise. While it has not been within the scope of this thesis to optimise the reaction conditions, a methodology of how this can be achieved has emerged which will be of benefit to future work.

6.6 Closing Remarks

In conclusion of this thesis, these closing remarks reflect briefly on the extent to which the main aims of this research project have been met. The main aims have been:

(1) to relate cyclic ester ring structure to polymerisability
(2) to study the effects of reaction variables on the reaction profile, in particular, the type of initiator used and the reaction temperature employed

As mentioned at the end of Chapter 1, a detailed understanding of the factors affecting the ring-opening polymerisation of cyclic esters is essential for tailoring polymer properties to meet specific requirements in specialist applications. Central to this understanding are the interrelationships between chemical structure, ring strain, and thermodynamic polymerisability. Although many questions still remain unanswered, this work has succeeded in revealing most of the essential features of these interrelationships, as described earlier in this chapter. Those that remain unresolved have opened up some fascinating areas for further study.

One of the key aspects of this work and, in retrospect, one of its main accomplishments, has been to bring together a combination of analytical techniques, some old some new, in order to study this subject in greater depth and from different perspectives than have previously been reported in the literature. Cyclic ester polymerisability has been studied for the best part of a century, since the pioneering work of Carothers [9], and is still being widely studied. However, what has made this present study different from previous work is that it has drawn its conclusions from a unique combination of kinetic, thermodynamic, spectroscopic and molecular modelling data. While each type of data is interpretable to varying extents in terms of the various factors affecting polymerisability, the strength of the arguments put forward in this thesis is derived from their combination. By combining different types of data to look across structurally-related series of different monomers, a deeper understanding has been gained which, it is believed, represents a new approach to this area of study.

However, as often happens in an in-depth study such as this (indeed, one might say, *should* happen), the results obtained raise almost as many questions as they answer. Such has been the fate of this research project. For example, there have been the peculiarities surrounding 6-membered ring polymerisability. Does the 6-membered ring size have a special status in cyclic esters? If so, why? Also, there has been the positional effect in 4-membered ring substitution, a most striking effect, yet still unexplained. Then, in a wider context, where precisely does the polymerisation mechanism (and hence the choice of initiator and reaction conditions) fit into the overall scheme of factors affecting polymerisability? Can mechanistic effects override structural effects via a shift in the balance between kinetic and thermodynamic contributions?

Therefore, despite the long history of work in the field of the ring-opening polymerisation of cyclic esters, there are still certain aspects of the ring-chain interconversion which remain unclear. Hopefully, the combination of methods employed here, plus any others that may be added in the future, may be able to provide answers to the questions that remain. Certainly, they provide a sound platform from which a programme of further work can be undertaken. This project is therefore seen not as the end but as the beginning of an ongoing study.

Finally, some of the results in this thesis have already been presented as posters in conferences and been published in the international journal ***Polymer*** [144] (see **APPENDIX** on pages 333 ff.). This dissemination is essential if this work is to be the beginning of a research programme which will eventually become recognised within the international polymer community. More publications are being planned.

SUGGESTIONS FOR FURTHER WORK

In continuation of the work described in this thesis, the following suggestions for further work are made:

1. 6-Membered Ring Polymerisability

The results of this work have shown that the effect of ring size on polymerisability is mainly associated with the degree of ring strain induced by cyclization. However, a notable anomaly has been the apparently easier polymerisability of the 6-membered ring δ-valerolactone than the 7-membered ring ε-caprolactone despite its lower ring strain. Furthermore, glycolide, the 6-membered ring diester analogue of δ-valerolactone, is also highly polymerisable with a remarkably low value (as reported) of ΔS_p. These findings have led to the suspicion that the 6-membered ring could have a special status in cyclic ester polymerisability, possibly for the stereochemical reasons mentioned earlier on page 274. Certainly, it is rather strange that such a relatively unstrained ring should exhibit such an unexpectedly high reactivity when compared alongside adjacent members in the series. It is an interesting anomaly which warrants further study.

2. Effect of Position of Ring Substitution

The positional influence of ring substitution has been highlighted in this study by the series of 4-membered ring β-propiolactones. Since the 4-membered ring is highly strained, it is highly polymerisable, a fact borne out by the spontaneous self-polymerisation of β-propiolactone on storage at room temperature. As would be expected, α-methyl substitution decreases polymerisability but, even so, α,α-dimethyl-β-propiolactone (pivalolactone) is still readily polymerisable. This contrasts markedly with β-substitution where even ***mono***substitution at the β-carbon, as in β-butyrolactone, suppresses polymerisability almost completely. Surprisingly, this positional effect of ring substitution has not attracted much attention in the literature,

interest mainly focussing on the ***degree*** of substitution. Consequently, the positional effect is one that remains unexplained and one which warrants further study.

3. Heat of Polymerisation, ΔH_p

In this work, values for the heat of polymerisation, ΔH_p, were either taken from the literature or calculated via molecular modelling. However, it may be possible to determine ΔH_p experimentally using differential scanning calorimetry (DSC). Modern DSC instruments, together with their advanced software programs for data analysis, are capable of studying the kinetics and determining the related thermodynamic parameters of chemical reactions (e.g., epoxy curing) carried out *in situ* in the sample pan. Whether or not this could be applied to cyclic ester polymerisation remains to be seen but it would certainly be a worthwhile investigation. One of the main problems would be to achieve complete monomer conversion ($\rightarrow$ 100%) within the timescale of the DSC run.

4. Kinetic Studies

In Chapter 4, some aspects of the kinetics of cyclic ester polymerisation were examined. However, as mentioned earlier, this was not intended as a detailed study for mechanistic purposes. Rather, it was hoped that it could contribute to the overall discussion on the effect of ring size and reaction temperature as well as provide some useful pointers for a more dedicated kinetic/mechanistic study in the future.

Thus, as far as these limited objectives went, this part of the work has achieved what it set out to achieve. One of the most interesting pointers it has provided for further work concerns the true ***order of reaction***. While the dilatometry results in Chapter 4 seemed to adhere more closely to zero-order than first-order kinetics, there was a suspicion, especially when taking the gravimetric, viscometric and molecular weight (GPC) data into consideration too, that the experimental observations were at least partly an artefact of the dilatometric method used. For

example, to convert contraction, Δh, to conversion, $\Delta[M]$, a constant factor is used which is derived from the density of ***high polymer***. At long reaction times, this may be acceptable but it is an oversimplification during the initial (oligomeric) stages when density is still increasing with degree of polymerisation (page 249). In addition to this, there is also the observed increases in rate, r_p, from the beginning of the polymerisation up to a maximum value in the range of 50-60% conversion, evidence of ***autoacceleration***. Therefore, taking all of these factors into consideration, it is quite possible that the apparent adherence to zero-order kinetics is simply fortuitous and that the polymerisation is, in fact, a ***first-order stepwise growth*** reaction. A more detailed kinetic study than that carried out here would clarify this and, at the same time, link up with the reaction mechanisms described earlier in section 6.4.3 (for stannous octoate) on pages 292-300.

5. Telechelic Polymers

Finally, as described briefly on pages 297-8, the combination of stannous octoate (as the catalyst) with an OH-containing compound (as the initiator) leads to the production of **telechelic** polymers with functional OH end-groups. This, in turn, opens up interesting possibilities for ***chain extension*** using diisocyanates and ***block copolymerisation*** via the sequential addition of a second monomer. According to the literature, these possibilities are already being exploited in the design and synthesis of polymers of controlled high molecular weight and tailored block copolyesters for biomedical applications respectively. This work provides a useful basis for venturing into these more applied areas of research.