CHAPTER 5

RING STRUCTURE AND POLYMERISABILITY

5.1 Introduction

When considering the relationship between ring structure and polymerisability in cyclic esters, the main factors to consider are ring size, ring strain, the nature and extent of ring substitution, and ester functionality within the ring. Of these factors, ring strain is particularly important. The major contributions to ring strain are bond angle distortion (angular strain), bond stretching or compression, repulsion between eclipsed hydrogen atoms (conformational strain, bond torsion) and non-bonding interactions between substituents attached to different parts of the ring (transannular strain) [40,128].

Strain energy calculations via molecular modelling can furnish valuable information about the relative ring strain in organic compounds, even when the absolute magnitudes obtained are uncertain because of assumptions made in the method and process of computation. Conventional strain energies are apparent in alicyclic compounds when the observed standard molar enthalpies of formation in the gaseous state are compared with values for strain-free structures calculated using modern bond energy schemes [129]. Such strain energies have been reported for cycloalkanes, cyclic ethers, cyclic thioethers and cyclic imines, and, for all of these compounds, minimum strain energies are observed for the 6-membered rings [130]. For simple lactones, the standard molar enthalpies of combustion which have been reported in the literature [131] are for the two 5-membered rings: γ-butyrolactone and γ-valerolactone, and one 6-membered ring: δ-valerolactone. However, if the necessary group equivalents or the heat of formation of the compound of interest are unknown, another approach is required. The ring strains in the cyclic esters studied here can be compared in terms of their internal energies as calculated from molecular modelling and also in terms of the frequencies of their respective C=O, O-C(=O) and O-CH_2 ring stretching bands from Fourier transform infrared spectroscopy (FT-IR), Fourier transform Raman spectroscopy (FT-Raman) and, again, molecular modelling.

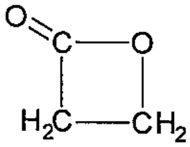
The polymerisability of a cyclic monomer is generally expressed by the extent to which the free energy of the polymerising system changes as it converts into polymer [132]. Molecular modelling was used in this work to calculate the difference in internal energy between the polymer and the monomer in each case and thus obtain an estimate of polymerisability. This modelling was performed using the *Discover* software package [98] running on a SGI Indigo R4000 Workstation, using the *Insight* interface to construct the models. The minimized energy of both the monomer (M) and the 4- and 5-mers of the polymer (P_4 and P_5) were obtained. The internal energy of a single polymer unit was estimated as the difference in energy between the 5- and 4-mers and so the change in internal energy upon polymerisation (ΔH_p) could be calculated from:

$$\Delta H_p \quad = \quad (P_5 - P_4) - M$$

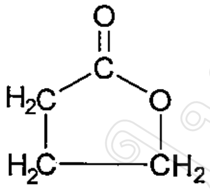
The normal modes of vibration, together with their infrared frequencies, were calculated with *Discover* [98] using a method which involves the diagonalisation of the second derivative of the energy function (the Hessian) at the calculated minimum energy conformation.

Altogether a total of 10 cyclic esters were included in this part of the work. From within these 10 compounds, the following 5 series can be identified. By comparing the results obtained for the members of each series, the various effects of ring size, substitution, and functionality can be deduced, without reference to any particular set of reaction conditions.

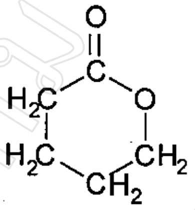
SERIES I : **Effect of Ring Size**



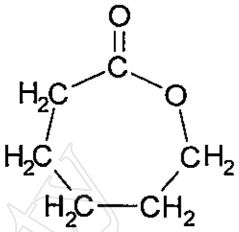
β-propiolactone



γ-butyrolactone



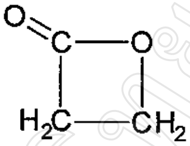
δ-valerolactone



ε-caprolactone

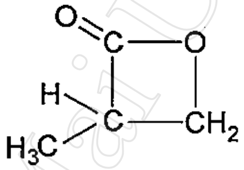
Ring Size : *4* *5* *6* *7*

SERIES II : **Effect of Degree of α-Substitution (4-Membered Ring)**



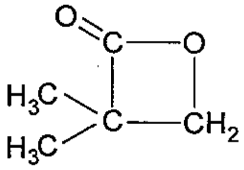
β-propiolactone

unsubstituted



α-methyl-β-propiolactone

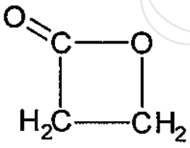
α-monosubstituted



pivalolactone

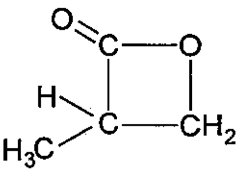
α,α-disubstituted

SERIES III : **Effect of Position of Substitution (4-Membered Ring)**



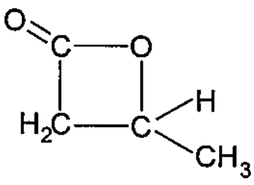
β-propiolactone

unsubstituted



α-methyl-β-propiolactone

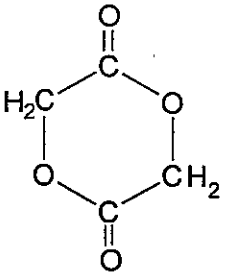
α-monosubstituted



β-butyrolactone

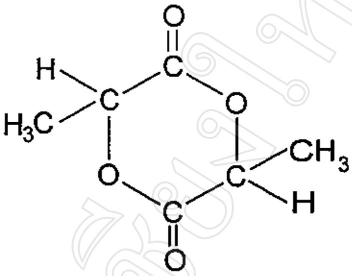
β-monosubstituted

SERIES IV : Effect of Degree of α-Substitution (6-Membered Ring)



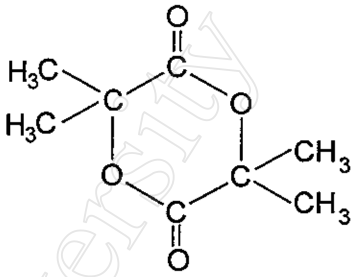
glycolide

unsubstituted



L-lactide

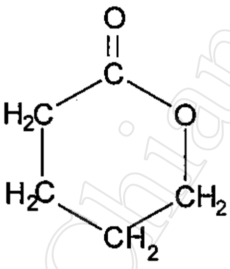
α,α'-disubstituted



tetramethyl glycolide

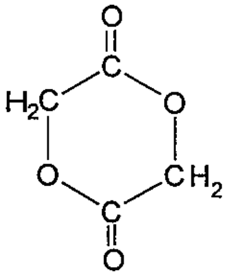
α,α,α',α'-tetrasubstituted

SERIES V : Effect of Ester Functionality



δ-valerolactone

monofunctional



glycolide

difunctional

5.2 Experimental Results

The calculated bond angles and bond lengths for the unsubstituted lactones in **SERIES I** (ring sizes 5-7), as obtained from molecular modelling, are shown in Table 5.1. It can be seen clearly that, as the ring size increases from 5 to 7, the deviations from the forcefield equilibrium values (which would be close to those found in a non-cyclic molecule) also increase. This correlates with the reported increases in strain energy [131] given in Table 5.2.

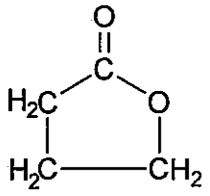
When the molecular modelling calculations of ΔH_p from this work are compared with experimental values from previous work [134], as shown in Fig. 5.1, good agreement is evident for ring sizes 5-7. For ring size 4, the large difference suggests that small highly strained rings embrace a complexity of forces which extend beyond the simulation method. On the other hand, as the ring size increases above 7, the magnitude of ΔH_p appears to approach a constant value. This is to be expected from a thermodynamic standpoint since, for larger rings (ring size > 8), the ring-chain interconversion becomes less of an equilibrium due to the unlikelihood of recyclization once the ring has been opened.

Table 5.1 : Comparison of the bond angles and bond lengths in unsubstituted lactones of different ring sizes, as calculated from molecular modelling.

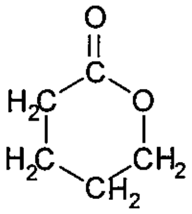
Cyclic Ester	Ring	Bond Angle (°)			Bond Length (Å)		
SERIES I	Size	C-O-(C=O)	O-(C=O)-C	C-C-C*	O-C	O-(C=O)	C-C**
γ-butyrolactone	5	109.0	110.3	102.1	1.44	1.38	1.53
δ-valerolactone	6	121.0	114.9	113.9	1.46	1.40	1.55
ε-caprolactone	7	125.5	117.6	114.4	1.46	1.40	1.54
Forcefield equilibrium value		109.5	110.0	110.5	1.425	1.370	1.526

* average of all the CH_2-CH_2-CH_2 bond angles in the ring

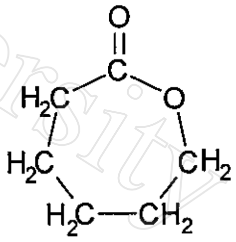
** average of all the CH_2-CH_2 bonds in the ring



γ-butyrolactone



δ-valerolactone



ε-caprolactone

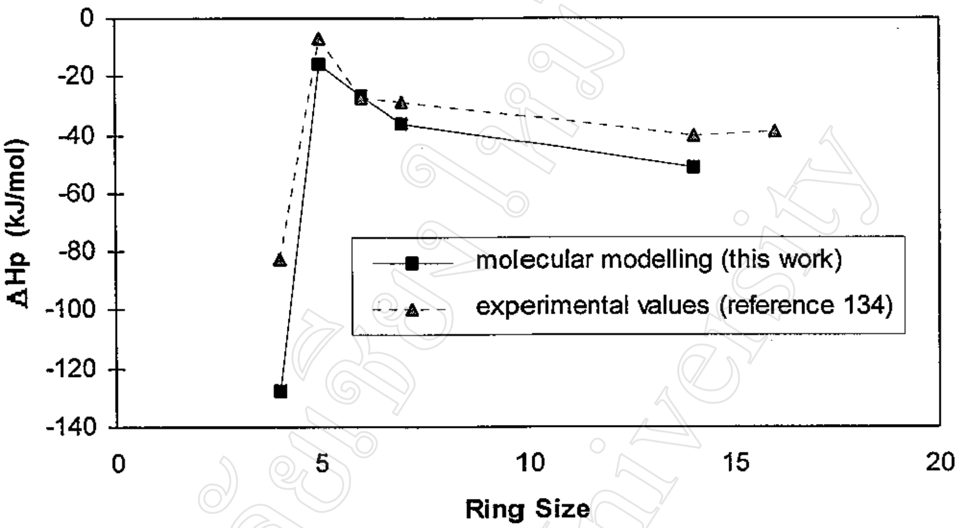


Fig. 5.1 : Comparison of the ΔH_p values calculated in this work by molecular modelling with reported experimental values for a series of lactones of different ring sizes.

In addition to the strain energies in Table 5.2, reported values of ΔH_p, ΔS_p and ΔG_p during the ring opening of some of the cyclic esters studied here are also listed for **SERIES I-V** [134-135]. It can be seen that ΔS_p remains essentially constant over the series of lactones studied (**SERIES I**). This is as would be expected since the dominant factor influencing ΔS_p is the loss of translational entropy brought about by the large reduction in the number of molecules present, a factor which is relatively constant from system to system. Therefore, the variations in ΔH_p can be used to indicate the relative thermodynamic polymerisability in place of ΔG_p. Even though the thermodynamic parameters given in Table 5.2 are not standard state values, their trends still allow for valid conclusions to be drawn since the various systems studied are closely comparable in physical terms.

Table 5.2 also allows the ΔH_p values from the literature to be compared with those calculated in this work via molecular modelling. Given the various dependencies involved in the modelling approach, notably on the accuracy of the forcefield used, the agreement is generally good and the trends consistent.

The thermodynamic data in Table 5.2 is complemented by the spectroscopic data in Table 5.3. Table 5.3 compares the frequencies of the C=O, O-C(=O) and O-CH_2 stretching vibrations for the cyclic esters studied, as obtained by the three different methods employed. The frequencies show similar trends in all cases but slightly different values depending on the method. In the case of the spectroscopic results, any uncertainties can be attributed to instrumental limitations, calibration methods, or to difficulties in accurately measuring the centre of the band. This uncertainty is estimated to be ± 2 cm^{-1}. The FT-IR and FT-Raman spectra were shown previously in Chapter 2 as evidence of spectral quality.

The absorption frequencies of the carbonyl (C=O) group in a wide range of cyclic esters have long been reported [13]. However, these reported values tend not to correlate well with ring strain, presumably because the C=O bond is not an integral part of the ring. In contrast, the O-C(=O) and O-CH_2 vibrations are for bonds actually within the ring and so may be expected to be more directly affected by the ring strain. More ring strain leads to a more rigid structure and hence the vibrational frequencies increase.

Once again, the molecular modelling calculations in Table 5.3 are highly dependent on the forcefield used and, in calculations of the type carried out here, the functional form employed produces some large differences in the absolute values of the calculated frequencies. However, general trends within the molecular modelling data are mostly in agreement with the spectroscopic data. The main shortcoming in the modelling approach appears to be that, in the forcefield used, not all the ring bonding interactions involved can be accounted for.

Table 5.2 : Comparison of the strain energies and reported thermodynamic polymerisation parameters, including ΔH_p values calculated from molecular modelling, for the range of cyclic esters studied.

SERIES	Cyclic Ester	Ring Size	Degree/Position of Substitution	Strain Energy (kJ/mol)	ΔH_p (calc)* (kJ/mol)	ΔH_p (ref 134) (kJ/mol)	ΔS_p (ref 134) (J/mol·K)	ΔG_p (ref 134) (kJ/mol)
I	β-propiolactone	4	-		-127.7	-82.3	-74.0	-60.2
	γ-butyrolactone	5	-	32.2 (ref 131)	-15.4	-6.8	-65.0	+12.6
	δ-valerolactone	6	-	39.7 (ref 131)	-26.8	-27.4	-65.0	-8.0
	ε-caprolactone	7	-		-35.9	-28.8	-57.0	-12.8
II	β-propiolactone	4	-		-127.7	-82.3	-74.0	-60.2
	α-methyl-β-propiolactone	4	α		-126.6			
	pivalolactone	4	α, α		-125.0	-84.0		
III	β-propiolactone	4	-		-127.7	-82.3	-74.0	-60.2
	α-methyl-β-propiolactone	4	α		-126.6			
	β-butyrolactone	4	β		-137.4			

* calculated from molecular modelling

Table 5.2 : continued

SERIES	Cyclic Ester	Ring Size	Degree/Position of Substitution	Strain Energy (kJ/mol)	ΔH_p (calc)* (kJ/mol)	ΔH_p (ref 134) (kJ/mol)	ΔS_p (ref 134) (J/mol·K)	ΔG_p (ref 134) (kJ/mol)
IV	glycolide	6	-	31.0 (ref 133)	-23.0	-34.0	-0.3	-32.1
	L-lactide	6	α, α'		-20.9	-22.9 (ref 135)	-41.1 (ref 135)	
	tetramethyl glycolide	6	α, α, α', α'		-13.5			
V	δ-valerolactone	6	-	39.7 (ref 131)	-26.8	-27.4	-65.0	-8.0
	glycolide	6	-	31.0 (ref 133)	-23.0	-34.0	-0.3	-32.1

* calculated from molecular modelling

Table 5.3 : Comparison of the bond vibrational frequencies from FT-IR, FT-Raman and molecular modelling for the range of cyclic esters studied.

SERIES	Cyclic Ester	Ring Size	C=O (cm^{-1})			O-(C=O) (cm^{-1})			O-CH$_2$ (cm^{-1})		
			FT-IR	FT-Raman	Molecular Modelling	FT-IR	FT-Raman	Molecular Modelling	FT-IR	FT-Raman	Molecular Modelling
I	β-propiolactone	4	1830	1822	1874	1310	1315	1309	1105	1103	1071
	γ-butyrolactone	5	1762	1764	1714	1241	1245	1231	1038	1038	1038
	δ-valerolactone	6	1734	1731	1716	1279	1280	1262	1056	1055	1033
	ε-caprolactone	7	1730	1728	1714	1292	1286	1276	1089	1091	1065
II	β-propiolactone	4	1830	1822	1874	1310	1315	1309	1105	1103	1071
	α-methyl-β-propiolactone	4	1823	1817	1867	1339	1339	1308	1111	1109	1091
	pivalolactone	4	1823	1823	1861	1367	1368	1370	1189	1191	1155
III	β-propiolactone	4	1830	1822	1874	1310	1315	1309	1105	1103	1071
	α-methyl-β-propiolactone	4	1823	1817	1867	1339	1339	1308	1111	1109	1091
	β-butyrolactone	4	1823	1822	1873	1353	1345	1325	1126	1132	1113

Table 5.3 : continued

SERIES	Cyclic Ester	Ring Size	C=O (cm^{-1})			O-(C=O) (cm^{-1})			O-CH_2 (cm^{-1})		
			FT-IR	FT-Raman	Molecular Modelling	FT-IR	FT-Raman	Molecular Modelling	FT-IR	FT-Raman	Molecular Modelling
IV	glycolide	6	1760	1758	1742	1281	1280	1279	1043	1043	1023
	L-lactide	6	1758	1779,1758	1752	1305	1303	1284	1090	1097	1066
	tetramethyl glycolide	6	1746	1746	1736	1310	1327	1308	1125	1122	1101
V	δ-valerolactone	6	1734	1731	1716	1279	1280	1262	1056	1055	1033
	glycolide	6	1760	1758	1742	1281	1280	1279	1043	1043	1023

5.3 Main Conclusions

From the experimental results described in the previous section 5.2, the main conclusions that can be drawn are as follows:

1. Effect of Ring Size

For the unsubstituted lactone **SERIES I**, as the ring size increases from 4 to 7, the ring strain and thermodynamic polymerisability vary as:

β-propiolactone >> γ-butyrolactone << δ-valerolactone < ε-caprolactone

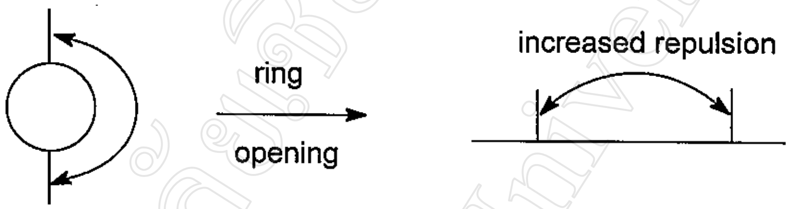
Ring Size : 4 5 6 7

The observed trends in bond angle (Table 5.1), strain energy and ΔH_p (Table 5.2) and the O-(C=O) and O-CH_2 bond stretching frequencies (Table 5.3) all combine to support this view. Thus, the 5-membered ring γ-butyrolactone shows the minimum ring strain, consistent with its observed non-polymerisability under normal conditions.

2. Effect of Degree of Substitution

In general, when the ring size is kept constant, increasing the degree of substitution (in this case, methylation) decreases polymerisability. This is borne out by the results in this work, both by the propiolactone **SERIES II** and, more clearly, by the glycolide **SERIES IV** in Table 5.2. In **SERIES IV**, whereas the unsubstituted glycolide is highly polymerisable, the disubstituted L-lactide is much less so, while the tetrasubstituted tetramethyl glycolide is found not to polymerise at all.

This substitution effect is interpreted in steric rather than ring strain terms. Indeed, from the spectroscopy results in Table 5.3 for **SERIES II** and **IV**, ring substitution, if anything, appears to increase ring strain. Increasing the degree of substitution decreases polymerisability as a result of increased intramolecular steric repulsions in the chain relative to the ring, as represented below. Such repulsions between substituents are generally more pronounced in linear rather than cyclic molecules. This is because, in cyclic molecules, the substituents are kept well apart in fixed positions relative to each other but, in a linear chain, chain flexibility allows a greater probability of closer proximity. This leads to a decrease in ΔH_p, as observed experimentally and predicted by molecular modelling.



In addition to this increase in intramolecular steric repulsion, another steric effect will surely arise from the actual reaction mechanism itself. Increased substitution will increase steric hindrance in both the initiation and propagation steps. This will increase the activation energies of these steps by increasing the energies of the respective transition states. This will be discussed in more detail in the following Chapter 6.

3 Effect of Position of Substitution

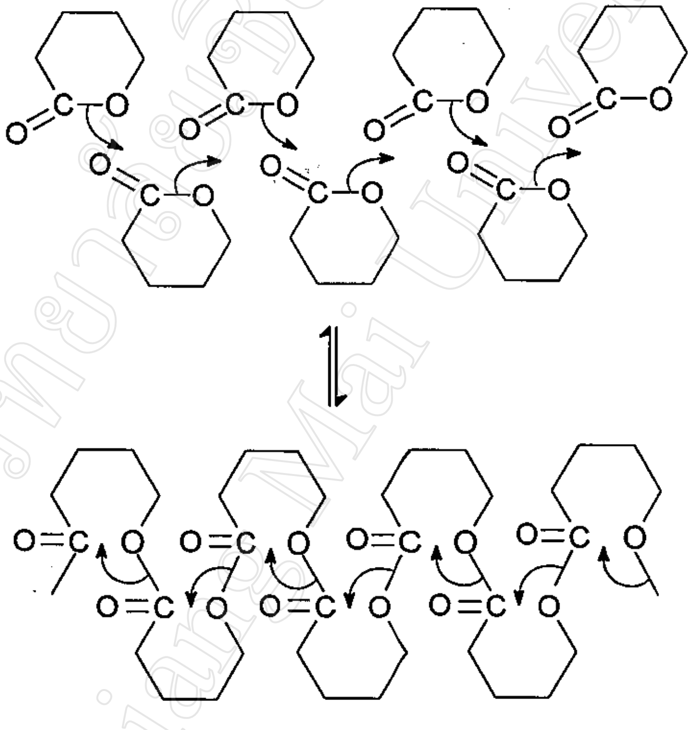
Cyclic ester polymerisability is affected not only by the degree but also by the ***position*** of substitution. This effect is illustrated by the 4-membered ring propiolactone **SERIES III**. As reported in the literature, α-methyl-β-propiolactone is polymerisable under normal conditions [136] whereas β-methyl-β-propiolactone (β-butyrolactone) is not. Moreover, even α,α-dimethyl-β-propiolactone (pivalolactone) is easily polymerisable [137]. ***Why then is β-substitution so much more deactivating than α-substitution, and is this a general rule irrespective of ring size?*** Surprisingly, answers to these questions have not been found in the literature, almost as if the positional dependence of the substitution effect has been overlooked (!). Unfortunately, the results from this work for **SERIES III** in Tables 5.2

and 5.3 shed little light on this matter. Instead, one is left to assume that β-substitution in the 4-membered ring, diagonally opposite to the C=O group, somehow stabilises the ring much more effectively than α-substitution adjacent to the C=O group. Obviously, the answer lies in the thermodynamics of the ring-chain equilibrium but whether it is ΔH_p or ΔS_p which is the dominant term remains unresolved. This is a subject for further study which the author of this thesis intends to examine in more detail in the future continuation of this work.

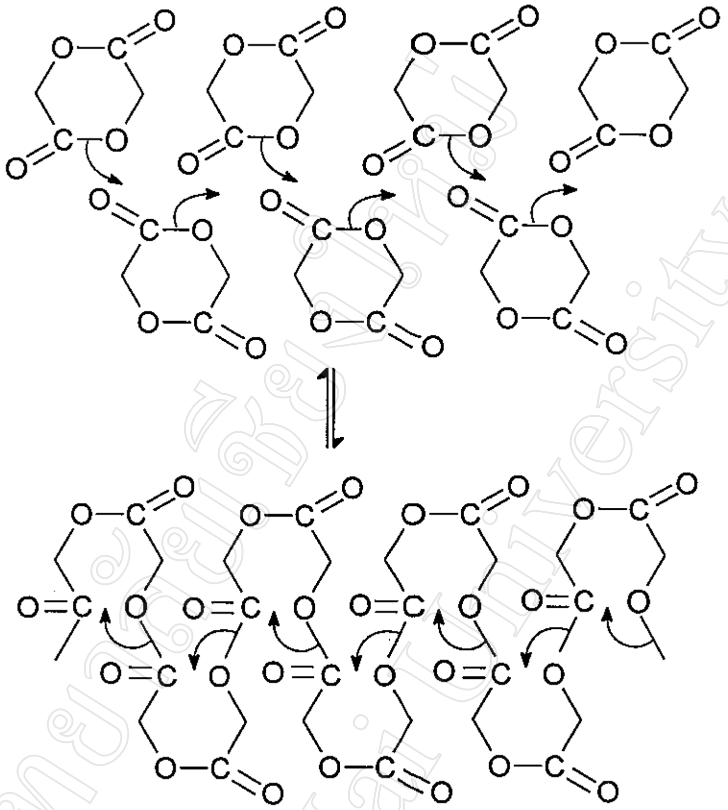
4. Effect of Ester Functionality

Comparison of the two 6-membered rings in **SERIES V** allows the effect of ester functionality to be observed. As would be expected on theoretical grounds, polymerisability increases with functionality. Thus, the difunctional glycolide is more reactive than the monofunctional δ-valerolactone. From the **SERIES V** data in Tables 5.2 and 5.3, this difference is due mainly to the extraordinarily low value of ΔS_p (= 0.3 J/mol·K) [134] for glycolide, quite exceptional when compared with the ΔS_p values for all the other cyclic esters. This is a remarkable experimental observation which, again, is surprisingly unexplained in the literature. What it implies is that there is a much lower, indeed almost negligible, loss of translational entropy during glycolide polymerisation, unique amongst the cyclic esters studied. ***What could be the reason for this?***

An experimental observation made during the course of this work may provide a clue. This is that glycolide appears to polymerise spontaneously on melting, as observed from its DSC analysis (section 2.2.2.2). When a sample of glycolide is heated just enough to make it melt, as observed from its DSC melting endotherm, then cooled and its thermogram re-run, the glycolide melting peak ($T_m \approx$ 80-84°C) completely disappears and is replaced instead by the polymer melting peak ($T_m > 200^\circ$C). This spontaneous thermal polymerisation on melting could, in turn, be linked to a suggestion made by Stannett and Szwarc [138] as long ago as 1953 in connection with the reversible polymerisation of 6-membered ring lactones. They suggested that the spatial configurations of the monomer molecules in the liquid lattice and the resultant monomer repeat units in the polymer chain are very similar, such that polymerisation (and, conversely, depolymerisation) can occur with little or no movement of the carbon centres. This is represented below for δ-valerolactone.



While there is no particular evidence from this work to support this mechanism for δ-valerolactone, it does provide an interesting means of explaining the glycolide data. If the above mechanism were to be true for glycolide, as shown on the following page, and its ester difunctionality would certainly enhance the intermolecular dipole-dipole interactions, it could explain the very low value of ΔS_p.



Significantly, the same spontaneous thermal polymerisation on melting is not observed with L-lactide and its ΔS_p (= -41.1 J/mol.k) [135] is correspondingly higher. Confirming whether or not this mechanism is indeed the reason for glycolide's exceptional ΔS_p value is another interesting subject for further work.

5. Thermodynamic Parameters

When comparing the reported experimental values of ΔH_p, ΔS_p and ΔG_p in Table 5.2, it appears that it is the differences in ΔH_p rather than ΔS_p which make the major contribution to the differences in ΔG_p. The sole exception to this is glycolide with its extraordinarily low ΔS_p, as just mentioned. However, apart from glycolide, ΔS_p is reasonably constant, such that ΔH_p can be used to indicate the relative thermodynamic polymerisability in place of ΔG_p.

The trends in these reported ΔH_p values correlate well with the relative monomer polymerisabilities observed in practice under comparable conditions. While this lends support to considering ΔH_p as a polymerisability indicator, it should be remembered that ΔH_p is itself a manifestation of a number of interrelated physical and chemical effects. Of these, ring strain is particularly influential.

6. FT-IR/FT-Raman Spectroscopy

In line with earlier comments, the C=O bond is not a reliable indicator of ring strain. From the results in Table 5.3, the vibrational frequency of the C=O bond shows little correlation with experimentally observed polymerisability, presumably because the C=O bond is not contained within the ring and, therefore, does not experience the ring strain. The simplest test for this correlation is whether or not the bond frequency for γ-butyrolactone is the lowest in **SERIES I** which, for the C=O bond in Table 5.3, it is not.

In contrast, other bonds which are actually a part of the ring, such as O-(C=O) and O-CH_2, can pass this test. Based on the criterion that ring strain stiffens the ring and therefore increases bond vibrational frequency, both the O-(C=O) and O-CH_2 bond frequencies for **SERIES I** correlate well with ring strain and polymerisability. However, they fail to correlate with the various substitution effects in **SERIES II-IV** or the functionality effect in **SERIES V** where the differences in polymerisability are less associated with ring strain.

Thus, from the results in this work, it must be concluded that the application of vibrational spectroscopy to the study of cyclic ester polymerisability is somewhat limited to the effect of ring size in simple unsubstituted lactones. In other words, it is more sensitive to the presence of strain inside the ring than, for example, steric repulsions between substituents outside it.

7. Molecular Modelling

On the whole, the molecular modelling calculations have shown good agreement with experimental measurements, both from this work and previous work. However, as with any simulation method, the agreement is only as good as the level of sophistication of the model and the process of computation allow and the method is not intended as a substitute for experiment.

From the results in Tables 5.1-5.3, it can be concluded that, where information about the relative ring strain in a series is required, the molecular modelling approach, like FT-IR/FT-Raman previously, is best suited to simple unsubstituted lactones of low to medium ring strain (i.e., ring size ≥ 5). Highly strained rings or ring substitutents introduce forces or interactions which are not included in the forcefield used in the molecular modelling. Hence, significant deviations from the experimental values can occur. Nevertheless, the molecular modelling approach is a very useful one provided that its limitations are understood and its results cross-checked with experimental data wherever possible.