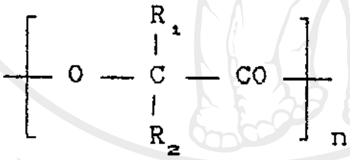
CHAPTER 1

INTRODUCTION

1.1 Poly-∝-Esters [1-13]

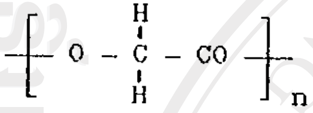
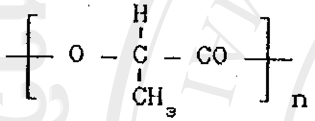
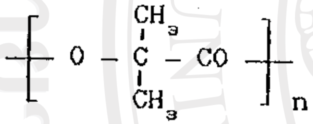
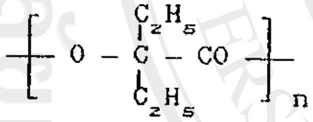
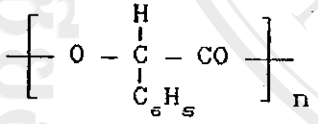
Poly-∝-esters are the simplest type of polyester. They can generally be defined as polyesters containing recurring -CO-O- groups in the main chain with only one main-chain carbon atom, the ∝-carbon, separating the successive ester repeat units. This gives a general structure which can be represented as shown below.



$$\left[-O-\overset{R_1}{\underset{R_2}{C}}-CO- \right]_n$$

Commercially, one or two members of the poly-∝-ester series have already been successfully exploited as surgical suture materials due to their combination of advantages as a synthetic polymer (e.g., high and predictable strength) with their ultimate disappearance from the body through hydrolytic degradation. Poly(glycolic acid), PGA : $R_1 = R_2 = H$; suture trade name "Dexon", is a current example while, more recently, poly(lactic acid), PLA : $R_1 = H$, $R_2 = CH_3$, has also exhibited a particular suitability in biomedical applications.

Table 1.1 : Structure and nomenclature of some poly α -esters.

α -SUBSTITUENTS		POLYMER STRUCTURE	GENERAL NAME	ABBREVIATION	SYNONYMS
R_1	R_2				
H	H	 $\left[O - \overset{H}{\underset{H}{C}} - CO \right]_n$	Poly(glycolic acid)	PGA	Polyglycolide (PG)
H	CH_3	 $\left[O - \overset{H}{\underset{CH_3}{C}} - CO \right]_n$	Poly(lactic acid)	PLA	Polylactide (PL)
CH_3	CH_3	 $\left[O - \overset{CH_3}{\underset{CH_3}{C}} - CO \right]_n$	Poly(acetonic acid)	PAA	Poly(isopropylidene carboxylate) (PIPC)
C_2H_5	C_2H_5	 $\left[O - \overset{C_2H_5}{\underset{C_2H_5}{C}} - CO \right]_n$	Poly(α-hydroxy-α-ethylbutyric acid)	PHEBA	Poly(3-pentylidene carboxylate) (P3PC)
H	C_6H_5	 $\left[O - \overset{H}{\underset{C_6H_5}{C}} - CO \right]_n$	Poly(mandelic acid)	PMA	Polymandelide (PM)

Most polyesters can be obtained by the direct esterification at high temperature of dicarboxylic acids with diols.

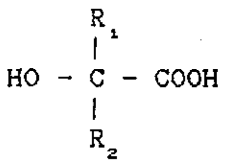
$$n\ \mathrm{HOOCRCOOH} + n\ \mathrm{HOR'OH} \rightleftharpoons \mathrm{HO}\!\leftarrow\!\mathrm{OCRCOOR'O}\!\rightarrow_{n}\!\mathrm{H} + (2n-1)\ \mathrm{H_2O}$$

Alternatively, hydroxy acids may polycondense with themselves yielding similar polyesters.

$$n\ \mathrm{HORCOOH} \rightleftharpoons \mathrm{H}\!\leftarrow\!\mathrm{ORCO}\!\rightarrow_{n}\!\mathrm{OH} + (n-1)\ \mathrm{H_2O}$$

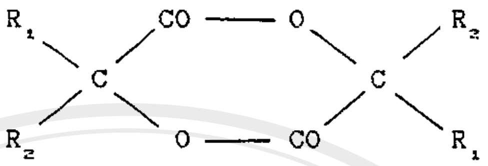
While the latter reaction has been used to prepare polyesters from hydroxy acids, it has often proved unsuitable for this purpose. For example, apart from glycolic acid and lactic acid, ∝-hydroxy acids can rarely be used for direct esterification because of the competing dehydration reaction leading to unsaturated carboxylic acids [2].

Previous work [1,3] has shown that the synthesis of poly-α-esters by direct polymerisation of ∝-hydroxy acids, via intermolecular polycondensation, yields at most only very low molecular weight oligomers. The explanation for this is the greater tendency to form 6-membered ring cylic diester intermediates (i.e., glycolides).



$$\mathrm{HO-\overset{R_1}{\underset{R_2}{C}}-COOH}$$

α -hydroxy acid



glycolide

The glycolide is formed from the thermal decomposition of the low molecular weight oligomers. Bimolecular condensation directly from the α-hydroxy acid to the glycolide is energetically unfavoured.

Consequently, it was recognised very early on, notably by Carothers [1], that the most likely route to high molecular weight poly-α-esters was via the ring-opening polymerisation of the intermediate glycolide. Indeed, Carothers's classical studies are still often referred to in this field of research. The sequence of reactions leading to the formation of high molecular weight poly-α-esters from α-hydroxy acids is summarized later in Scheme 1.1 on page 7.

1.2 Ring-Opening Polymerisation [4-6,15-19]

Ring-opening, addition (or chain) and condensation (or stepwise) polymerisations are the three major classes of polymerisation reaction. Of these three types, ring-opening is peculiar in that it possesses some features of each of the other two types. For example, it resembles addition polymerisation in that it proceeds by the addition of monomer, but never of larger units, to growing chain molecules, while, as in condensation polymerisation, the products are usually heterochain polymers such as polyesters and polyamides.

In the specific case of poly α-esters, the most likely routes via ring-opening polymerisation to high molecular weight polymers are the two methods described below.

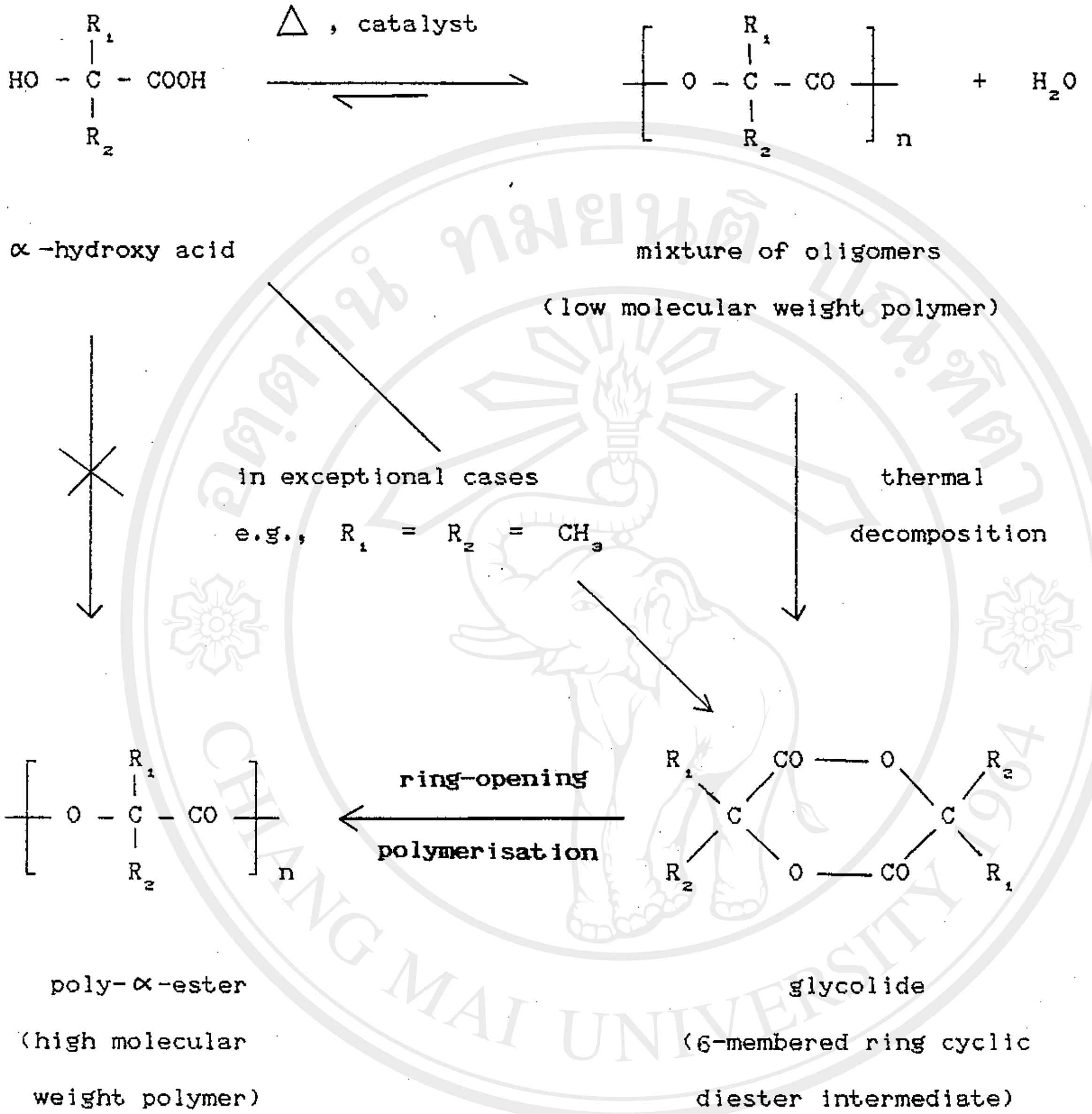
1.2.1 Ring-Opening Polymerisation of Glycolide Intermediates

This first method involves the polymerisation of a heterocyclic monomer in which no small molecule is split off during the polymerisation reaction. Briefly, this method first involves conversion of the α-hydroxy acid into the corresponding glycolide. The glycolide is then isolated and subsequently bulk polymerised in the melt at elevated temperature in the presence of a suitable initiator to form a linear, high molecular weight poly-α-ester, as shown in Scheme 1.1.

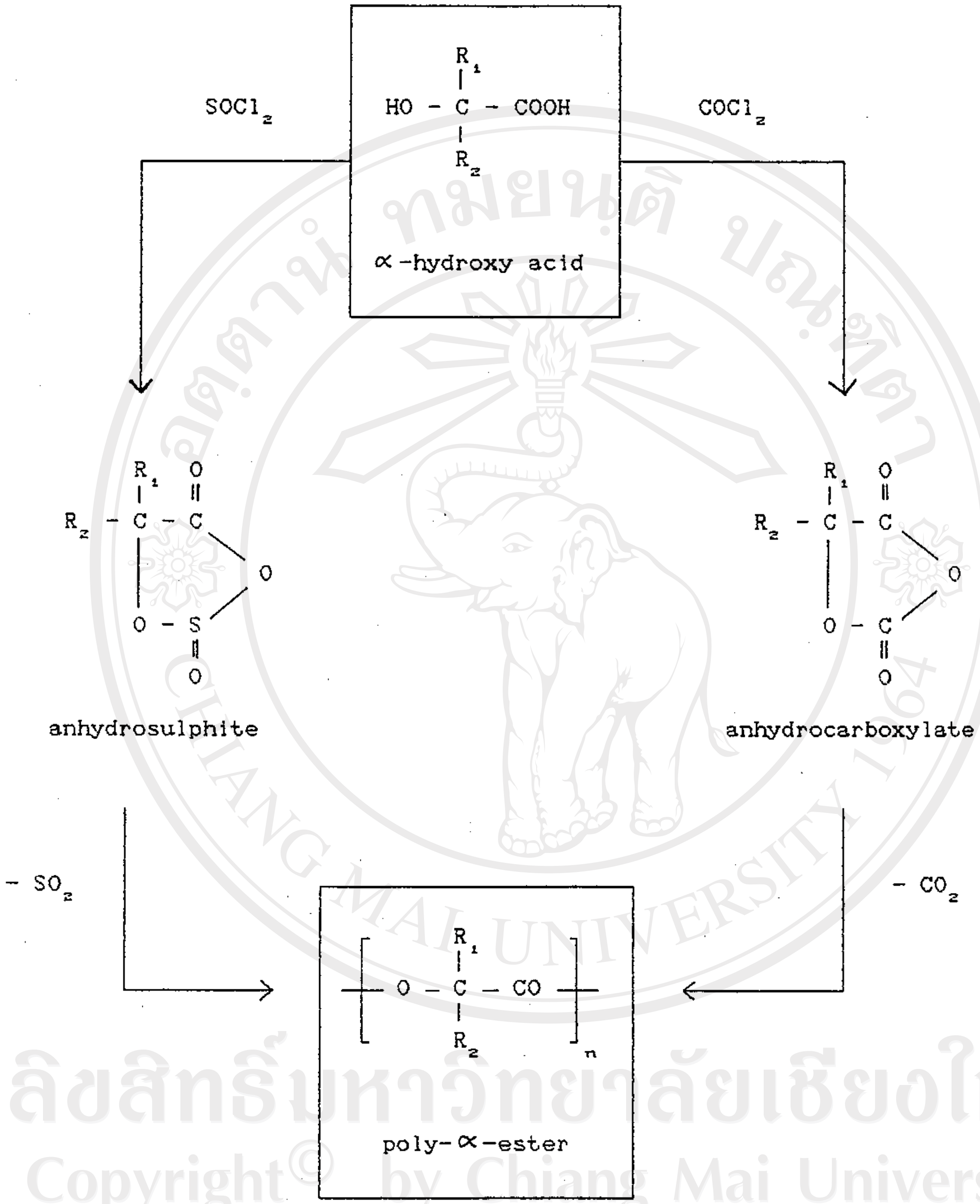
The glycolide intermediate can either be prepared via vacuum distillation of the α-hydroxy acid, based on the original method described by Carothers [1] or, in exceptional cases, via the acid-catalysed bimolecular ring closure of the α-hydroxy acid in solution, according to the procedure outlined by Deibig and co-workers [5] for the preparation of tetramethylglycolide ($R_1 = R_2 = CH_3$).

1.2.2 Ring-Opening Polymerisation of Anhydrosulphite or Anhydrocarboxylate Heterocycles

In this method, a small molecule (e.g., SO_2, CO_2) is eliminated from the cyclic monomer during the polymerisation reaction. Briefly, this method of preparation involves opening of the anhydrosulphite or anhydrocarboxylate ring either by the action of heat alone or in the presence of an initiator at elevated temperature. The poly-α-ester is then formed as shown in Scheme 1.2.



Scheme 1.1 : **Poly-α-ester synthesis via the ring-opening polymerisation of glycolide intermediates.**



Scheme 1.2 : Poly-α-ester synthesis via the ring-opening polymerisation of anhydrosulphite or anhydrocarboxylate intermediates.

1.3 Scope and Objectives of This Work

The main objective of this research project is to determine the reaction conditions under which the simplest member of the poly-α-ester series, poly(glycolic acid), may be synthesized to high molecular weight via the self-esterification of its parent α-hydroxy acid, glycolic acid. This will involve a detailed study of the kinetics and mechanisms of the various reactions involved.

The scope of this research project may be summarized as follows :

(a) to design and construct a polycondensation apparatus suitable for high temperature and reduced pressure operation ;

(b) to find a suitable method for studying the kinetics of glycolic acid polycondensation and for enabling the interpretation of the mechanisms of the reactions ;

(c) to prepare glycolide and then to polymerise it to high molecular weight poly(glycolic acid) using different polymerisation initiators ;

(d) to characterise the polymer products obtained and to discuss the mechanism of the polymerisation reactions.