THE USE OF HETEROCYCLIC MONOMERS IN THE PREPARATION AND MODIFICATION OF POLYMERS

by

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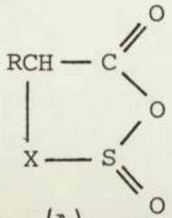
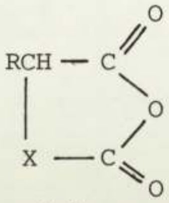
SYNOPSIS

A series of cyclic monomers of the general form (A) or (B) have been prepared from two distinct types of substituted carboxylic acid by treating the acid or its metal salt with thionyl chloride or phosgene respectively under anhydrous conditions,



(A)



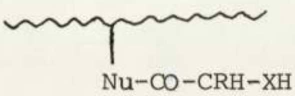
(B)

In the first, the α-thio acids ($R\text{-}\underset{XH}{CH}\text{-}COOH$), X is a sulphur atom and R is H, CH_3 or CH_2COOH (thioglycollic, thiolactic and thiomalic acids respectively). In the second, members of the α-hydroxy acid family, X is an oxygen atom and R is COOH, CH_2COOH, CH_2OH or $\underset{OH}{(CH)}_3CH_2OH$ (tartronic, malic, glyceric or gluconic acids respectively). These monomers are known as anhydrosulphites (A) and anhydrocarboxylates (B) of the parent acid and can be decomposed by nucleophiles with the evolution of sulphur dioxide or carbon dioxide.

The kinetics of ring-opening reactions were studied with a view to establishing or confirming the mechanism and to using the monomers to form novel heterochain polymers or to graft onto existing polymers containing nucleophilic sites.

Homo-polymerization proved to be largely unsuccessful due, in some cases, to difficulties in purification of the monomers and in others to competing reactions involving the substituent functional group. Ring-opening of the cyclic monomers with vinyl monomers containing a substituent nucelophilic group (NuH) indicated however that the monomers had potential value in grafting onto vinyl polymers containing such groups but that the reactivity of the nucleophilic site was greatly dependent on its molecular environment.

Grafting onto polymers of this type was carried out in two ways: firstly onto the polymer in solution and secondly onto the surface of a preformed polymer film. In both cases the grafting reaction which resulted in the introduction of hydrophilic groups from the cyclic monomer in the form



$$\text{Nu-CO-CRH-XH}$$

had a significant effect on the physical, and particularly the surface properties of the polymer which were measured using conventional surface energetic techniques. The formation, in this way, of polymers having specific arrangements of functional groups at the surface has potential value in the design of polymers for specific biomedical applications.

ACKNOWLEDGMENTS

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CONTENTS

CHAPTER I

INTRODUCTION

1.1 Ring Opening Polymerization

The polymerization of cyclic compounds possesses some of the features of both addition and condensation polymerizations. It is usually concerned with heterocyclic compounds and although cyclic olefins have been polymerized by an olefin metathesis reaction(1) this does not have the general features of ring-opening polymerization as it will be discussed in this thesis.

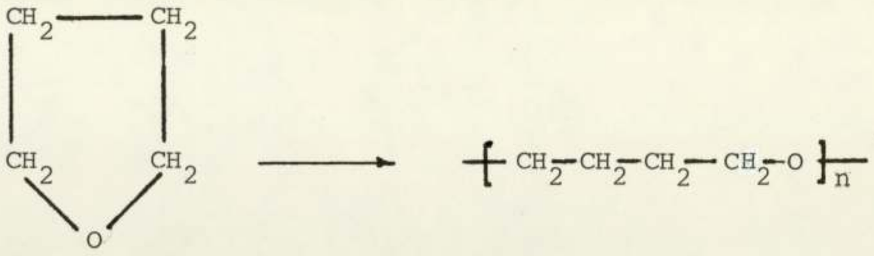
The ring-opening polymerization of heterocyclic monomers falls into two categories. In the first all the constituent elements of the monomer are incorporated in the polymer, as in addition polymerization. In the second a small part of the ring is lost, as in condensation polymerization. The polymers formed in both categories resemble condensation polymers in as much as the hetero-atom or group in the ring produces the hetero-chain structure that is characteristic of condensation polymers. On the other hand like addition polymerization ring-opening polymerization always proceeds by the addition of monomer units one at a time to the growing polymer chain. Some examples of ring-opening polymerization reactions are given in Fig. (1.1).

The polymerizability of cyclic monomers of the first category described above has been well studied and found to be influenced by several factors:-

(1) The size of the ring and other factors which affect ring strain.

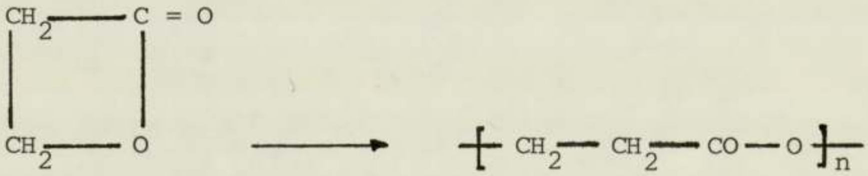
(2) The size, polarity and reactivity of the hetero-atom in the ring.

CYCLIC ETHERS

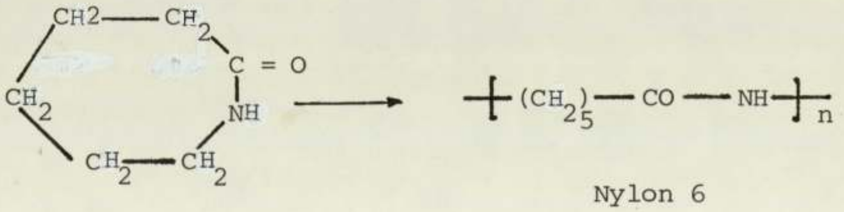


Tetrahydrofuran

LACTONES



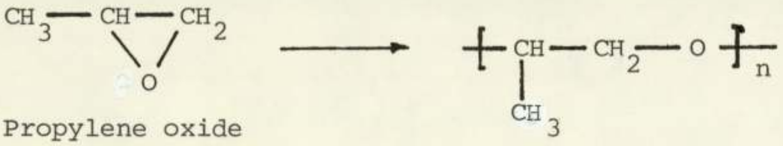
LACTAMS



Nylon 6

Caprolactam

EPOXIDES



Propylene oxide

Fig. 1.1

(3) The number and nature of any substituents on the ring.

(4) The initiator or catalyst system used.

Ring strain is one of the most important features affecting polymerizability. It is caused by distortion of the natural bond angles and is dependent on both the number of atoms in the ring and the size and nature of hetero-atoms in the ring. Thus in the series of cyclic ethers the 6-membered ring, tetrahydropyran, has no ring strain and it is not polymerizable.(2) Both smaller and largerrings have ring strain and are polymerizable. When a ring contains a carbonyl group the nature of the hetero-atom becomes important. For example in the case of lactones the five-membered ring does not polymerize whereas the six-membered ring does(3) but conversely in the case of lactams it is the six-membered ring that does not polymerize whilst the five-membered ring may be polymerized quite successfully.(4)

The effect of substituents on the polymerizability of a cyclic monomer can be demonstrated by the series of glycollide derivatives, the six-membered cyclic dimer esters derived from α-hydroxy acids (Fig. 1.2).

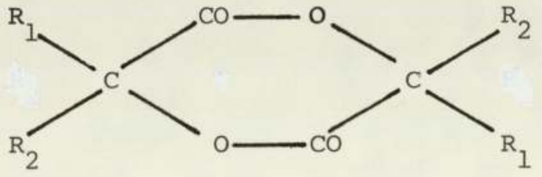


Fig. (1.2)

In the case of glycollide ($R_1 = R_2 = H$) the ring is easily polymerized, whilst with lactide ($R_1 = H$, $R_2 = CH_3$) polymerization is more difficult but still possible but when $R_1 = R_2 = CH_3$ in 1, 1, 4, 4-tetra-methylglycollide no polymerization occurs at all.(3)

In general terms the polymerizability of a cyclic compound is determined by the thermodynamic change involved in the transition from the ring to the straight chain conformation so that if the free energy change in going from the ring to the chain is positive then it will be thermodynamically impossible to polymerize that ring.(5) Unfortunately a negative free energy change for polymerization does not necessarily mean that polymerization will occur. For example the polymerization of all the cyclic alkanes, except for a few alkyl substituted cyclopropanes(2) no known polymerization method exists.

For simple heterocyclic compounds mechanisms of polymerization do exist for all monomers where it is thermodynamically possible. It has been demonstrated that in the case of cyclic ethers, lactones, lactams etc. a maximum free-energy of polymerization occurs at the size of ring that is not polymerizable.

The extent of polymerization is affected by the reaction temperature. In general as this increases the equilibrium which exists between the ring and chain conformation becomes more directed towards the ring form. A ceiling temperature exists for a particular monomer concentration above which the formation of long chain polymers is impossible.(6)

The polymerization of cyclic monomers where part of the monomer is lost has been less well-studied than that where the composition of the monomer remains intact. This type of polymerization is often referred to as 'Extrusion Polymerization'(7). It has an advantage in that there is no ring chain equilibrium between the polymer and the monomer and consequently there is no tendency towards depolymerization.

The first area to achieve prominence was the polymerization of N-carboxy-α-amino acid anhydrides (in future referred to as NCAs) Fig. (1.3)

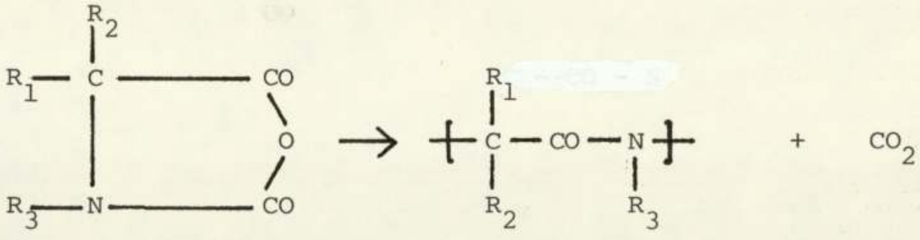


Fig. (1.3)

NCAs were first prepared by Leuchs$^{(8)}$ in 1906. They are formed from α-amino-acids and readily polymerize to form poly-α-amino acids and polypeptides these being of fundamental scientific importance in the field of model protein studies.$^{(9)}$ $^{(10)}$

The NCAs are, however, only part of a larger group of monomers having the general structure shown in Fig. (1.4)

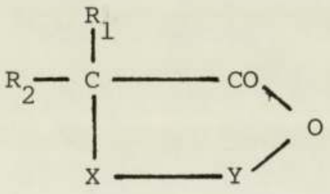


Fig. (1.4)

X, Y, R_1 and R_2 can be varied amongst the elements found in a limited area of the periodic table (Fig. (1.5).

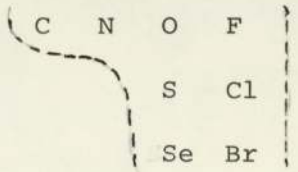


Fig. (1.5)

For example X could be O, S, NR

Y could be SO, CO, CS, SeO, etc.

R, and R_2 could be H, Alkyl, Aryl and their halogen substituted counterparts.

Apart from the NCAs the group of monomers has not been well-studied until recently when two classes within the general series have been examined. These are the anhydrosulphites (X = O, Y = SO) correctly known as 1, 3, 2 dioxathiolan-4-one-2oxides (Fig. (1.6a)) and the anhydro-carboxylates (X = O, Y = CO), correctly known as 1,3 dioxolan - 2,4 diones (Fig. 1.6b).

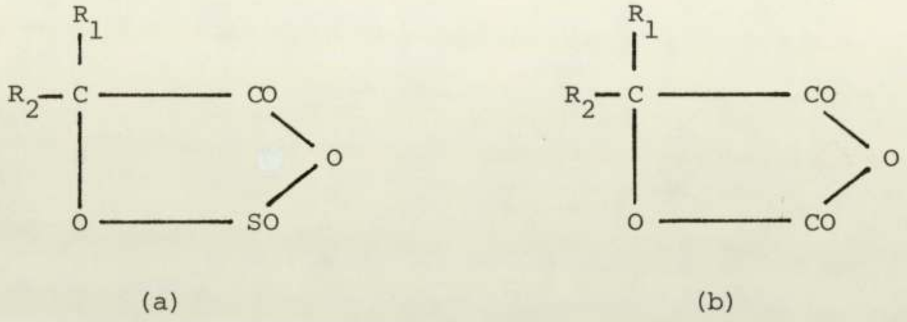


Fig. (1.6)

The synthesis of anhydrosulphites from the α-hydroxy acids lactic acid (R_1 = H, R_2 = CH_3) and hydroxy-isobutyric acid (R_1 = R_2 = CH_3) was first reported by Blaise and Montagne in 1922.(11) The first reported synthesis of the anhydrocarboxylates of α-hydroxy acids was that by W.H. Davies(12) much later in 1951.

Recent work has involved the study of both anhydrosulphites and anhydrocarboxylates with variations in R_1 and R_2 substitutents as hydrogen(13)(14) and simple alkyl(15)(16)(17) and in a very limited number of cases as larger alkyl,(18)(19) cycloalkyl(20)(21)(22) aryl,(23)(24)(25) halogen substituted alkyl(26)(27) and aryl.(28)(29)(30)

There have been three mechanisms postulated for the polymerization of this class of cyclic compounds, by which they are all potentially polymerizable although the preference of a particular monomer for one of the mechanisms is determined by its structure.

The three mechanisms will be referred to as:

(1) Thermal

(2) Protic nucleophilic

(3) Aprotic basic

(Fig. 1.7)

The first mechanism requires a thermally unstable molecule and is typified by the thermal decomposition of disubstituted α-hydroxy acid anhydrosulphite monomers$^{(15)}$ to form the highly reactive α-lactone intermediate. Polymerization of the α-lactone is initiated by an advantitious trace of moisture or another nucleophile and is propagated by the hydroxyl group produced by the decomposition of the α-lactone.

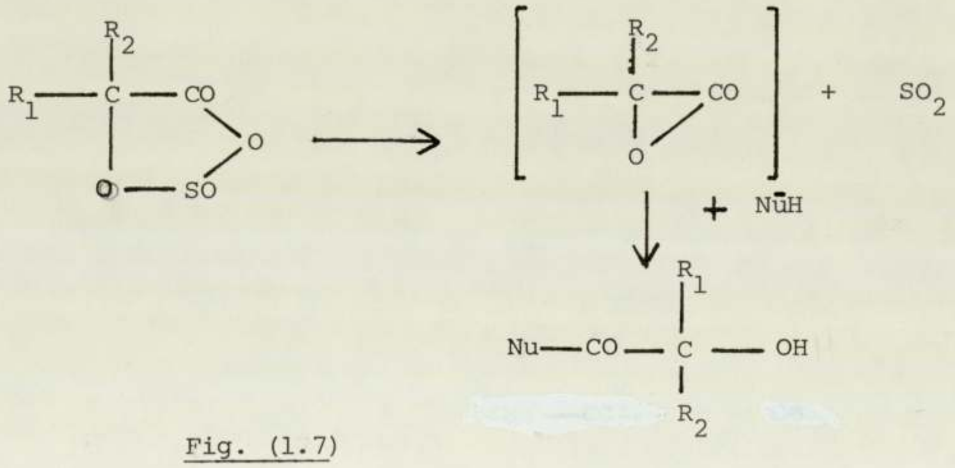


Fig. (1.7)

The anhydrosulphites are most likely to polymerize thermally because the extra ring strain imposed by the large sulphur atom in the ring renders it more thermally unstable and hence more likely to decompose to the α-lactone.

The second mechanism requires a protic nucleophile initiator, typically an amine or an alcohol and polymerization occurs via a bimolecular chain growth reaction (Fig. (1.8)) This mechanism is most frequently encountered in the amine initiated polymerization of NCAs. The stereo-chemistry of this reaction has been studied in detail.(31)

Anhydrosulphites of α-hydroxy acids also undergo an analogous polymerization mechanism but this is limited by the reduced thermal stability of the ring and the lower nucleophilicity of the hydroxyl group in the propagating species compared with the amine group generated by NCAs.

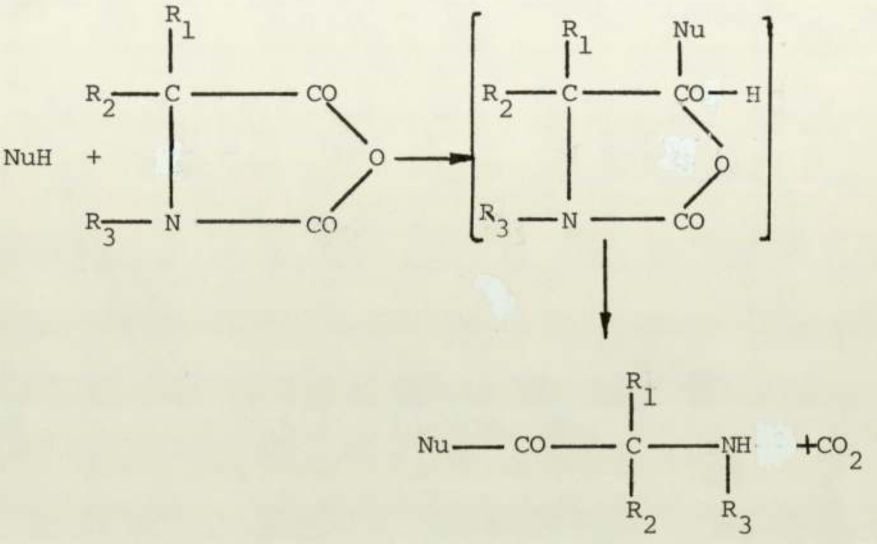


Fig. (1.8)

The effect of the substituent groups R_1 and R_2 is significant in this reaction both in the activation of the carbonyl group towards nucleophilic attack and in steric hinderance to the attack of the nucleophile. Hence the disubstituted ring is very reluctant to undergo nucleophilic polymerization.

Virtually all NCAs, anhydrosulphites and anhydrocarboxylates of α-hydroxy acids polymerize by the nucleophilic mechanism when R_1 and/or R_2 is hydrogen.

The third mechanism, less often encountered than the previous two, is polymerization in the presence of an aprotic base. It can be suitably illustrated by the polymerization of anhydrocarboxylates of hydroxyacids in the presence of pyridine(32) Fig. (1.9) The anhydrocarboxylate is more thermally stable than the anhydrosulphite and shows little tendency to polymerize by a thermal route. It is thought that the presence of pyridine facilitates the decomposition of the anhydrocarboxylate to the α-lactone by means of a charge-transfer complex.

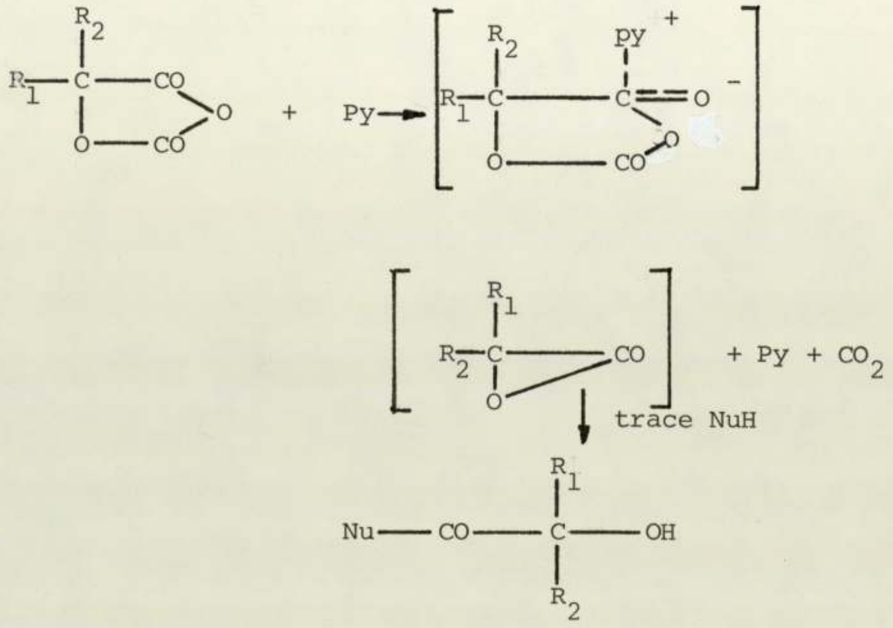


Fig. (1.9)

Again, as in thermal polymerization, the reaction is initiated by the attack of an advantitious trace nucleophile on the α-lactone and propagation occurs through the hydroxyl group generated. The proposed mechanism is supported by the fact that the reaction shows first order kinetics in both monomer and base and the fact that the molecular weight of the polymer is independent of the pyridine concentration.

NCAs also undergo base initiated polymerization. For this Bamford and Block(33) suggested a mechanism involving the abstraction of a proton from the nitrogen in the ring with the subsequent attack of the activated NCA on the C_5 carbonyl of a nonactivated NCA.

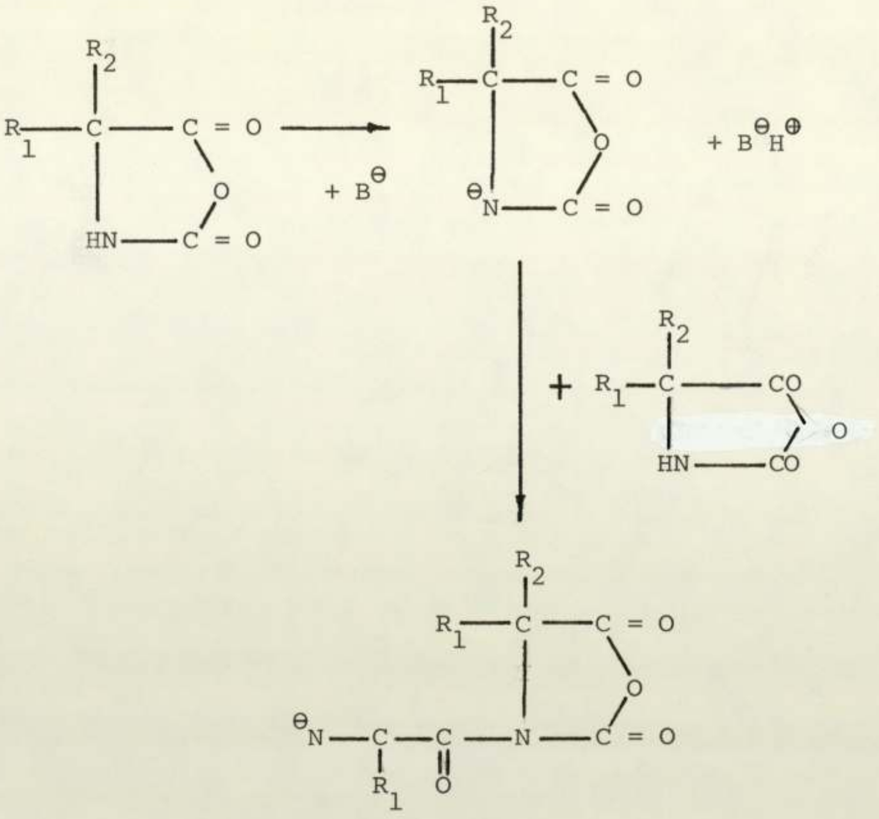


Fig. (1.10)

It has also been reported(34) that anhydrosulphites and anhydrocarboxylates of α-hydroxy acids can be polymerized using various organometallic catalyst systems for example sodium Methoxide and Lithium butyl although the mechanism of these reactions is not straightforward.

1.2 Poly-α-Esters

The polymers formed from the polymerization of α-hydroxy acid anhydrosulphites and anhydrocarboxylates are termed poly-α-esters. These have not been well studied until recently because of the difficulty of synthesis although they are potentially the most useful of all the aliphatic polyesters.

In general, aliphatic polyesters (35) do not lend themselves to the same useful applications as their aromatic counterparts typified by polyethylene terephthalate (Fig. 1.11), which is useful in the

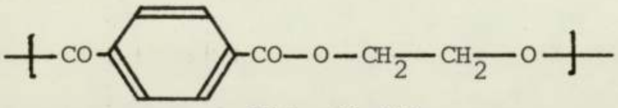
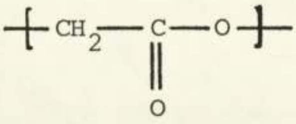


Fig. (1.11)

production of fibres and films, since they are usually soft, having low melting points and a poor resistance to hydrolysis. Poly-α-esters, however, have higher melting points (above 200°C) and the short repeat unit together with shielding of the ester group by side group substituents hinders chain scission reactions in all except polyglycollide and polylactide. Poly-α-esters have been described as being potentially useful in many fields including: films, fibres and surgical inserts but their use has been limited by the scarcity of preparitive techniques. Self-condensation techniques require high temperatures and consequently are accompanied by degradation. It seems, therefore, that the polymerization of anhydrosulphites and anhydrocarboxylates of α-hydroxy acids provides a convenient route to high molecular weight poly-α-esters.

At present the only poly-α-ester in commercial use is polyglycollide, Fig. (1.12), which is used for soluble surgical



$$\left[CH_2 - \underset{\displaystyle \overset{\Vert}{O}}{C} - O \right]$$

Fig. (1.12)

sutures under the trade name of 'Dexon'(36).

1.2 The Design of Polymers for Biomedical Applications

There is at present a great deal of interest in the development of novel polymers with specific properties which lend themselves to use in specialist applications especially in biomedical and related fields. Existing polymers have already been used in a wide variety of biomedical applications including many replacement prostheses, soft-tissue substitutes, liver and kidney support systems, contact lenses, dentures, sutures(37) etc.

For usefulness in biomedical applications a polymer must comply with the strict requirements of the conditions of use. Biocompatibility is of fundamental importance in the body's acceptance of a foreign implant.(38) Many of the polymers currently being used are not sufficiently biocompatible and tend to lead to problems from adverse reactions with body tissues such as calcification and fibrous ingrowth. Consequently there is a continual search for new polymers with increased biocompatibility. Also when a polymer is required to come into contact with blood, as for example in vascular grafts and haemodialysis membranes it is especially important that it should be blood-compatible in order to avoid serious problems with thrombus formation and many other troubles.

A group of polymeric materials which have been used in a wide variety and increasing number of biomedical applications are the 'Hydrogel Polymers'. This term covers a wide range of polymers all of which exist in the form of a gel which is extensively swollen by water.(39) Hydrogels often exhibit good biocompatibility since they are similar to the body's own highly hydrated state. The largest and most important group of hydrogel polymers are those prepared by the polymerization of combinations of hydrophilic and hydrophobic vinyl monomers. The hydrophilic monomers contain functional groups and are essential in the make up of a water swollen gel. Some examples of hydrophilic monomers are shown in fig. (1.13). Hydrophobic monomers such as styrene and methyl methacrylate may be incorporated in order to reduce the amount of swelling by water and enhance the mechanical strength of the gel which is inherently weak when in a highly hydrated state. This can also be achieved by introducing a small amount of a cross-linking agent into the material.

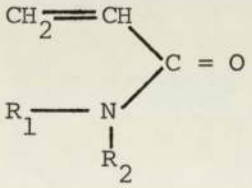
Some Hydrophilic Vinyl Monomers

(1) Hydroxy Acrylate/Methacrylate esters

Hydroxy Ethyl Methacrylate

2 Hydroxypropyl Acrylate

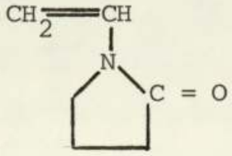
(2) Acrylamide and derivatives



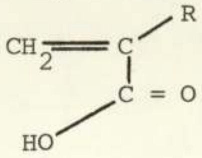
$R_1 = R_2 = H$

$R_1/R_2 = H, CH_3\ C_2H_5\ \ CH_2OH$

(3) N-Vinyl-Pyrrolidone



(4) Acrylic Acids



$R = H$:-Acrylic Acid

$R = CH_3$:-Methacryclic Acid

Fig. (1.13)

Apart from biocompatibility hydrogels also exhibit the property of good permeability to gases, water and small ions. The composition of hydrogel polymers can be varied almost infinately in the search for the optimum properties required for each specific application.

In the biomedical field hydrogels have many potential uses(40) including: soft contactlenses, artificial corneas, soft-tissue replacement and as coatings for other prosthetic materials to improve their biocompatibility(41). The permeability ofhydrogels suggests their potential as haemodialysis membranes(42)(43) in liver or kidney support systems and their adsorption and desorption properties render them useful for drug encapsulation to provide a controlled release of a therapeutic drug(44)(45) in a localized area within the body as for example in the treatment of cancerous tumours.(46) The external use of hydrogel polymers is limited by the necessity of continual contact with body fluid to maintain their hydrated state. Of course the range of use of hydrogels is not limited to biomedical applications, for example in the form of semi-permeable membranes their possible use in desalination (47)(48) and related fieldscould be very important.

At the present time hydrophilic polymers have only been prepared with a carbon-chain backbone structure but it is felt that the incorporation of hetero-atoms into the backbone of the polymer could lead to an interesting range of novel polymers. It seems likely that the introduction of hydrophilic functional groups as substituents to polyesters would result in a range of polymers of this type.

There have been no reported attempts to synthesize anhydrosulphite or anhydrocarboxylate monomers from α-hydroxy acids with substituent functional groups in the R_1 and R_2 positions although NCA's have been prepared from α-amino acids with functional groups. It was found necessary in many cases to chemically mask the functional group to avoid its interference with the desired reaction between the amino-acid and phosgene. This is often a complicated and difficult process especially when the removal of the masking group is required at some later stage. An example is glutamic acid (fig. 1.14) where it is

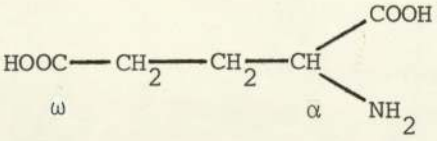


Fig. (1.14)

necessary to protect the ω-carboxylic acid group. Esterification presents difficulties due to the tendency for the formation of a diester. Selective esterification using methanol or ethanol in the presence of a hydrogen chloride catalyst and selective hydrolysis of the diester have been used with some success.(49) Unfortunately the removal of the ester group presents difficulties since most ester linkages are more stable than the peptide linkages in poly-amino acids and simple hydrolysis reactions tend to result in scission of the polymer chain. Unprotected polyglutamic acid is not easily prepared although a certain amount of success has been obtained by cleavage of the ω-benzyl-ester after polymerization using hydrogen bromide in various solvents although complete removal of the benzyl group without affecting the polymer is difficult.(50)(51) It can be seen that the more labile the protecting group, the more difficult it is to attach it selectively in the first place.

From a preliminary study carried out in this department it appears to be possible to synthesize anhydrosulphites from certain α-hydroxy-acids containing functional groups; for example, Malic acid (fig. 1.15)

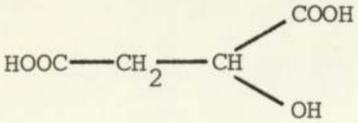


Fig. (1.15)

without protection of the substituent functional group albeit in an impure state.

From the point of view of this thesis the work described is mainly concerned with cyclic ester derivatives of α-hydroxy acids with substituents containing functional hydroxyl and carboxylic acid groups in the side chain and will be divided into three areas of examination:-

1) Synthesis and Characterization of monomers
2) Polymerization and Copolymerization
3) Grafting

The study of areas (1) and (2) will be carried out along the lines of previous investigations into the preparation of polymerization of anhydrosulphites and anhydrocarboxylates of α-hydroxy acids although it is expected that the presence of substituent functional groups may lead to some unforeseen complications.

Although the polyesters from these hydroxy acids will be interesting in their own right the monomers also seem to be potentially useful in area (3): the modification of existing polymers by means of grafting reactions. This can be achieved where there is a pendant nucleophilic site, preferably a hydroxyl or an amine group, available on the polymer.

Several of the monomers used in the preparation of hydrogels possess suitable sites for grafting.

The introduction of further functional groups into hydrogel polymers would have the effect of enhancing desirable properties such as permeability, permselectivity and adsorption. They can also have a chelating effect to enable the polymers to bind specifically certain ions and other functional molecules such as proteins.

Grafting can be achieved in two ways. Firstly the hydroxy acid can be attached to the appropriate vinyl monomer or polymer in solution so that the bulk of the polymer is modified uniformly or, secondly, modification can be allowed to take place at the polymer surface only by reaction with the hydroxy-acid derivative in a medium which is not a solvent for the polymer. In this case it is possible to alter the surface properties of the polymer whilst having little effect on the bulk properties of the polymer.

1.3 Sulphur Containing Acids

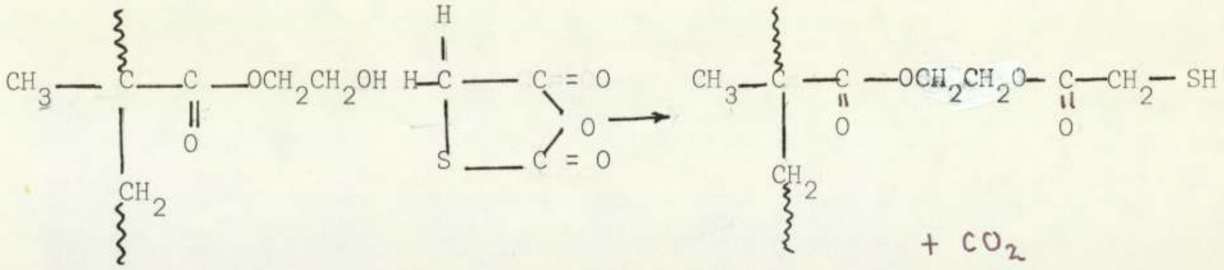
The work described in this thesis includes a study of cyclic monomers from sulphur containing carboxylic acids Mainly in view of the potential use of the SH, thiol group, in the modification of polymers by grafting.

Some limited work has been carried out on the preparation of poly-α-thioesters from the anhydrocarboxylates of thioglycollic, thiolactic and thioisobutyric acids.(52)(53)(54)(55) Kinetic studies were carried out by Ali (55) on the reactions between thio anhydrocarboxylates and various initiators- pyridine, alcohols and amines and he found that in general the reaction mechanisms were analogous to the attack of those initiators on the anhydrocarboxylates of the corresponding hydroxy acids. The presence of sulphur renders the ring more reactive than the corresponding oxygen containing ring and the thiol group generated is more nucleophillic in the propagation step than the hydroxyl group. Although Ali synthesized some of the anhydrosulphites of thioglycollic and thiolactic acids no detailed kinetic work was carried out and so the effect of the presence of two sulphur atoms in the ring has not been demonstrated. For this purpose it is proposed to take the anhydrosulphites of thio acids and present a study in two areas.

(1) Polymerization

(2) Grafting

Concerning area (2) preliminary work carried out in this department has shown that it is possible to react the anhydrocarboxylate of thioglycollic acid with a nucleophillic hydroxyl group pendant to the backbone of a polymer in order to introduce a thiol group. (Fig. 1.15)



The presence of a thiol group pendant to the backbone chain of polymer is desirable for the starting point in the preparation of model cell surfaces.

1.4 Cell Surface Model

It has been shown that if cells of different types are randomly mixed they will move about, recognise each other and group together selectively. This intercellular recognition and adhesion is the basis of all living multicellular organisms and the identification of the mechanism of these processes is of fundamental importance in the understanding of cell behaviour in important biological events such as morphogenesis and the differentiation of tissues.(56) Recent workers have attributed cell recognition and adhesion behaviour to be in some way associated with the presence of glycoproteins on the surface membrane of the cell. Their presence has been demonstrated by several methods including electrophoresis of intact cells, immunological studies and electron microscopical evidence.

Glycoproteins may be broadly defined as those proteins which contain carbohydrates attached to the polypeptide backbone by means of covalent bonds. The carbohydrate portion consists of a characteristic group of sugars; D-gallactose, D-mannose, L-Fructoses, D-gallactosamine, D-Glucosamine and Sialic acids etc.

It is hoped that were it possible to produce model glycoproteins with similar carbohydrate parts these could be used to mimic the behaviour of cells in aggregation processes leading to further understanding of the way cells behave. It is believed that the carbohydrate parts of glycoproteins are recognised by certain 'receptors' also present on cell surfaces although the chemical nature of these receptors is not known.(57) It has already been shown that cells can be made to selectively adhere to the surface of gel beads which have been modified with carbohydrates.(58)

Carbohydrates can be successfully attached to thiol functions by using either the aceto-bromo derivation or the Acetate Lewis acid as used in the preparation of thio-sugars.(59)(60)

CHAPTER 2

Experimental Techniques

2.1 Purification of Solvents and Reagents

The most important requirement for the purification of solvents and reagents used in the preparation and reactions of anhydrosulphites was the complete removal of water. The techniques described are generally modifications of techniques described in practical organic chemistry textbooks.(61)(62)

Diethyl Ether

Anhydrous Ether (maximum water content 0.02%) supplied by Fisons Ltd. was used in the preparation of anhydrosulphites. After the bottle had been opened, fresh sodium wire was added prior to use to remove any trace of moisture.

Nitrobenzene

A.R. grade nitrobenzene was allowed to stand over phosphorus pentoxide for 2 - 3 days followed by refluxing with phosphorus pentoxide for about 6 hours. It was then distilled under reduced pressure, the middle fraction distilling over at about 70 - 72°C at 1.5 mm Hg pressure was collected and stored over molecular seive.

Anisole (Methyl, Phenyl Ether)

A.R. grade anisole was allowed to stand over anhydrous calcium chloride for 24 hours followed by fractional distillation at reduced pressure onto anhydrous barium oxide. It was redistilled immediately prior to use.

Tetrahydrofuran (THF)

The solvent was allowed to stand over anhydrous calcium sulphite for several days followed by distillation at atmospheric pressure. The distillate was refluxed over sodium wire for 4 hours, distilling at atmospheric pressure onto fresh sodium wire. A trace of naphthalene was added to the system, the green colour produced by the naphthenate ion indicated that the system was completely dry.

Dioxan

A.R. Dioxan was allowed to stand over anhydrous calcium sulphate for 2 - 3 days followed by distillation at atmospheric pressuse collecting the middle fraction boiling at 101°C. The distillate was refluxed over sodium wire for 4 hours, redistilled at atmospheric pressure and collected on fresh sodium wire.

Dimethyl Sulphoxide (DMSO)

DMSO has a high equilibrium water content (10% at 20°C) so it was shaken several times with anhydrous calcium sulphate and allowed to stand overnight. It was distilled under reduced pressure and the distillate refluxed with anhydrous barium oxide for 8 hours, redistilled and stored over fresh barium oxide.

Toluene

Toluene was allowed to stand overnight over anhydrous calcium chloride. It was then distilled, refluxed over sodium wire for 8 hours and redistilled at atmospheric pressure onto fresh sodium wire, collecting the middle fraction boiling at 110.6°C.

Alcohol Initiators

A.R. grades of benzyl alcohol, isopropanol, ethyl digol, ethyl lactate etc. were all dried by standing over anhydrous calcium sulphate for 2 - 3 days and distillation at atmospheric pressure (except for benzyl alcohol where reduced pressure is used) collecting the middle fraction over fresh anhydrous calcium sulphate.

Pyridine

A.R. grade anhydrous pyridine supplied by B.D.H. Chemicals Ltd. was refluxed with A.R. potassium hydroxide for 8 hours and distilled at atmospheric pressure, collecting the middle fraction over fresh potassium hydroxide.

Solid Chemicals

Solid acids; malic acid; thiomalic acid and tartronic acid: and initiators such as benzyl mercaptan, acrylamide, acetamide, N-hydroxymethyl acrylamide etc. were all dried by standing under vacuum in a dessicator over phosphorus pentoxide for several days prior to use, changing the phosphorus pentoxide daily if it appeared moist.

Thio acids

A.R. Thioglycollic acid (mercaptosuccinic acid) and Thiolactic acid (mercaptopropionic acid)were used as supplied by Koch-Light Laboratories Ltd.

Thionyl Chloride

A.R. grade thionyl chloride as supplied by B.D.H. Chemicals Ltd. was used without further purification in the synthesis of anhydrosulphites.

Vinyl Monomers (for preparation of hydrogel polymers.)

Liquid Monomers

Styrene(St),Methyl methacrylate (MMA),methacrylic acid (MA),hydroxy propyl acrylate (HPA), hydroxyethyl methacrylate (HEMA) etc. were purified by distillation under reduced pressure using a heated column so that distillation took place rapidly.

Solid Monomers

Acrylamide, Nhydroxymethyl acrylamide etc. were used as supplied by the manufacturer.

2.2 Instrumental and Analytical Techniques

Infra-Red Spectra

IR spectra were recorded using Perkin-Elmer Infra-red spectrophotometer models 457 and 237. Samples were prepared as KBr discs in the case of solids and as thinfilms between NaCl discs in the case of liquids or solutions using air as a reference.

Mass Spectra

Mass spectra were recorded using an AFI MS9 mass spectrophotometer.

Thermogravimetric Analysis (TGA)

Analyses were carried out on a Dupont Thermogravimetric Analyser 950 in an atmosphere of nitrogen at a constant heating rate.

C.H.N. Analysis

C.H.N. Analyses were carried out by the departmental analytical service using a Hewlett Packard 185 Fand M Analyser.

Chloride Ion Determination

The amount of trace chloride ion in a sample of anhydrosulphite was determined by potentiometric titraction in an adaptation of the method first described by Ingram.(63)

Approximately 0.1g of the material was weighed out accurately and 40 ml of a 3:1 (v:v) mixture of distilled water and acetone plus a few drops of IN Nitric Acid was added. The mixture was heated to 60°C for three minutes and cooled. The chloride ion was titrated potentiometrically with 0.0IN Silver Nitrate solution using a silver/silver: silvernitrate electrode system in conjunction with an EIL Model 23A pH meter. Calibration was first carried out using standard sodium chloride solutions.

This technique enabled the quantity of ionizable chlorine containing impurity in a sample of anhydrosulphite to be determined.

Copper Determination

The copper content of copper salts of unknown composition was determined gravimetrically by the ethylene diamine Method of Vogel(61) A solution of the copper salt was treated with aqueous ethylene diamine and potassium mercuri iodide (K_2HgI_4) resulting in the precipitation of a lilac-coloured complex $Cu\,en_2\,HgI_4$

Silver Determination

The silver content of silver salts was determined gravimetrically as silver chloride by the method described by Vogel.(61)

Gravimetric Chloride Determination

The amount of Chloride ion in copper salts was determined quantitatively as silver chloride by the method described in Vogel.(61)

2.3 Practical Techniques

Azeotropic Distillation

This technique was used for removing final traces of water from the copper salts of α-hydroxy acids when it is too strongly bound to be removed by vacuum drying alone. The apparatus shown in Fig. 2.1 was used. The solvent, a mixture of 4 parts benzene with 1 part n-propanol, and the copper salt were placed in the flask, A, care being taken that there was sufficient solvent to fill the Dean and Starke apparatus, B, allowing the continuous extraction of the azeotropic mixture formed between the solvents and water at the distillation temperature. On cooling in the condenser, C, the water separated out as droplets in the Dean and Starke apparatus at the point, D, where it could be tapped off. Distillation was continued until no further droplets of water appeared. The copper salt was filtered and dried in a vacuum oven.

Dry Box

Because of the sensitivity of anhydrosulphites towards atmospheric moisture it was often necessary to carry out manipulations in an atmosphere free from moisture. This was achieved using a Gallenkamp Model MA 950 glove box. Moisture was removed from the air within the glove box by means of a circulating pump in conjunction with a cold trap consisting of glass spirals immersed in a solid carbon dioxide/acetone mixture contained in a dewar. In this way the moisture content was maintained below 20 ppm.

Kinetic Measurements

The decomposition of anhydrosulphites is accompanied by the evolution of the gas, sulphur dioxide, and so a convenient way to follow the decomposition is by monitoring the increase in pressure of evolved gas as a function of time at constant temperature and volume. The apparatus used (Fig. 2.2) was a modification of the apparatus first used by

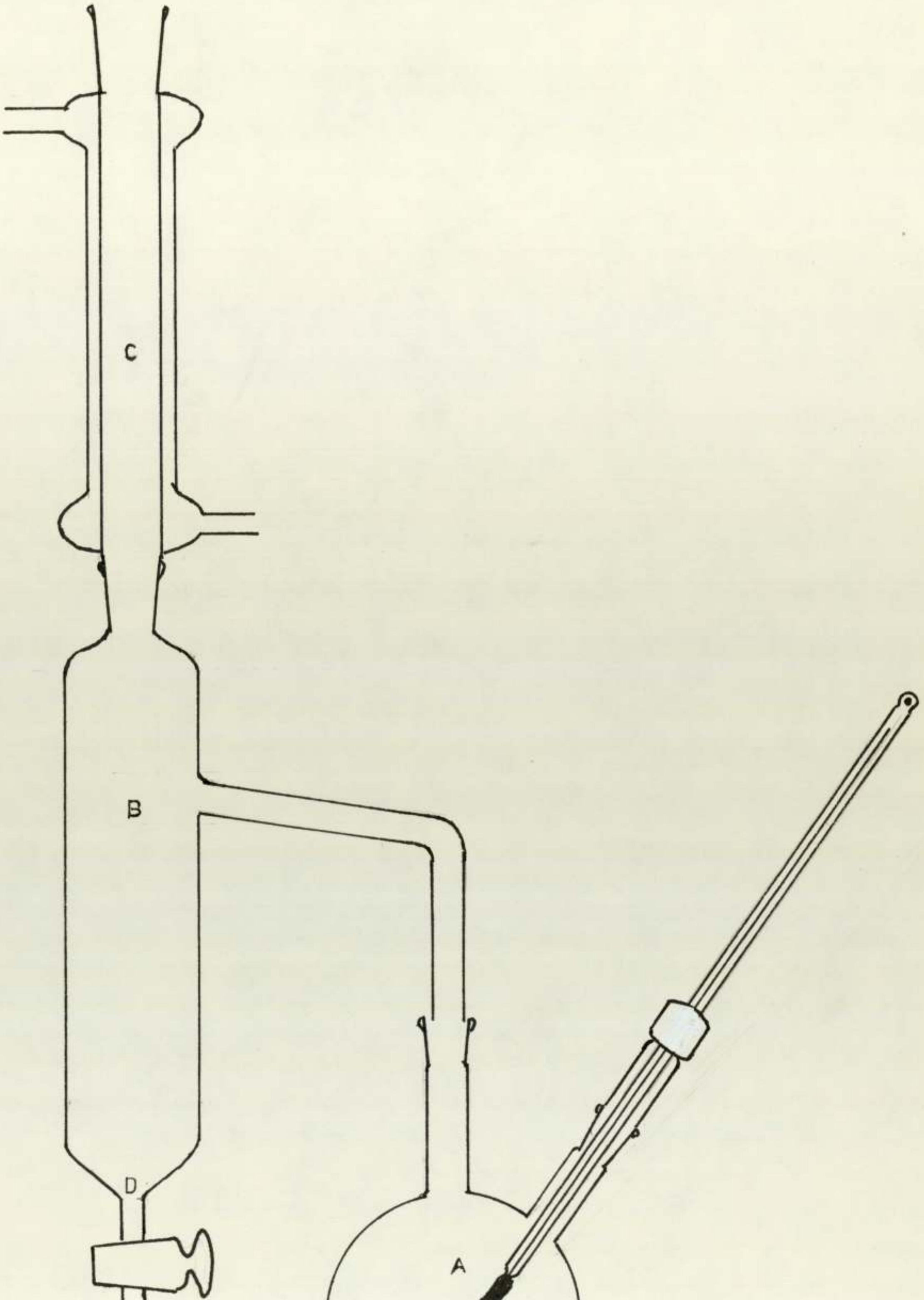


Fig. 2.1 Azeotropic Distillation Apparatus

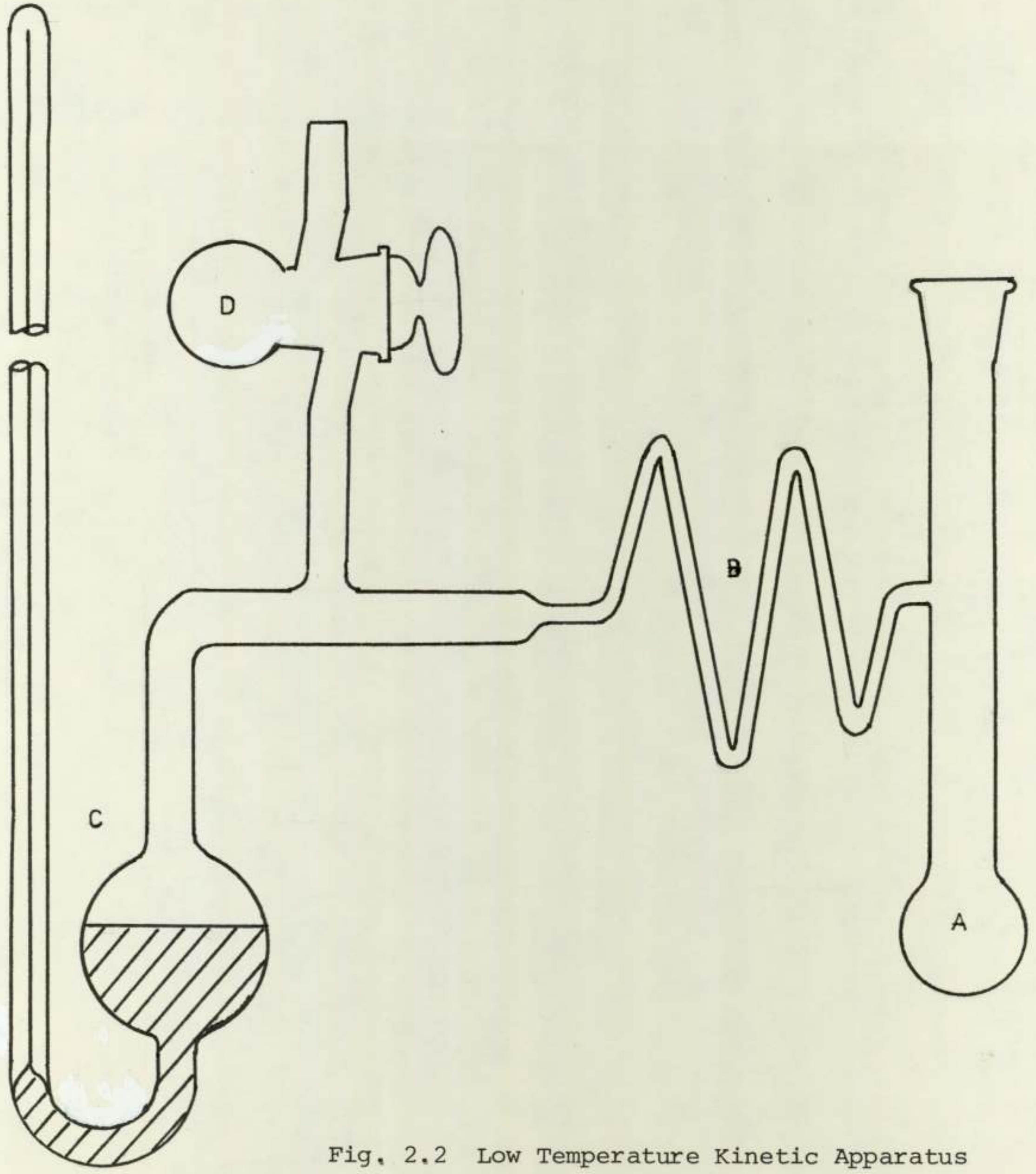


Fig. 2.2 Low Temperature Kinetic Apparatus

Waley and Watson(64) and later modified by Ballard and Bamford(32) for use in low temperature kinetic studies (below 45°C). It consists of a reaction chamber (A) where decomposition takes place which is connected via a glass spiral (B) to the manometer section (C) which is filled with mercury. The apparatus has no joints and can be evacuated by means of a safety tap (D). The apparatus was kept at constant temperature for the duration of the reaction by clamping it in a thermostatically controlled water bath.

Immediately before each reaction the apparatus was thoroughly dried and mercury was introduced into the manometer section. The required amount of monomer solution, measured by syringe, was introduced into the reaction chamber which was then closed with a 'Suba-Seal'. The apparatus was evacuated, so that the mercury level in the capillary was equal to that in the resevoir, and clamped in position in the water bath. The initiator was introduced, as quickly as possible, by injection through the Suba-Seal of the required amount from a syringe. The pressure of evolved sulphur dioxide was measured at convenient time intervals by following the rise of the mercury column in the capillary using a cathetometer. Before each reading the apparatus was agitated with a 'Pifco' vibrator to equilibrate the gas and liquid phases; vibrations were transmitted to the reaction chamber through the glass spiral. The reaction was allowed to proceed until no further increase in the height of the mercury column was observed.

In calculating the rate of monomer decomposition it was assumed that the behaviour of sulphur dioxide at constant volume and temperature was that of an ideal gas, allowing a simple relationship to be derived between the pressure of evolved gas and the monomer concentration at any time.

1 mole anhydrosulphite decomposes with the evolution of 1 mole of sulphur dioxide, so if:

$[M]_o$ is the initial monomer concentration

$[M]$ is the monomer concentration at any time

$[G]$ is the concentration of evolved gas at that time

at any time

$$[G] = [M]_o - [M] \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2.1)$$

and at the end of the reaction when all the monomer has decomposed

$$[G]_\infty = [M]_o \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2.2)$$

For an ideal gas at constant temperature and volume the pressure, p, of the gas is directly proportional to the number of moles of gas, hence

since $p_\infty \propto [G]_\infty$

from equation (2.2)

$$[M]_o = [G]_\infty = \pi p_\infty \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots (2.3)$$

where π is the proportionality constant, and from equation (2.1)

$$[M]_o - [M] = \pi p \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2.4)$$

By combining equations (2.3) and (2.4) we obtain the expression

$$\frac{[M]_o - [M]}{[M]_o} = \frac{p}{p_\infty}$$

or by rearrangement

$$\frac{[M]}{[M]_o} = \frac{p_\infty - p}{p_\infty} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2.5)$$

In terms of the measured height (h) of the mercury column in the manometer since $h \propto p$

$$\frac{[M]}{[M]_o} = \frac{h_\infty - h}{h_\infty - h_o} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2.6)$$

The kinetic profile of the reaction can be illustrated by plotting a graph of h against time t.

In an ideal reaction typified by the reaction profile of Fig. 2.3 the reaction follows the Wilhelmy form of first order kinetic rate equation.

$$[M] = [M]_o e^{-kt} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2.7)$$

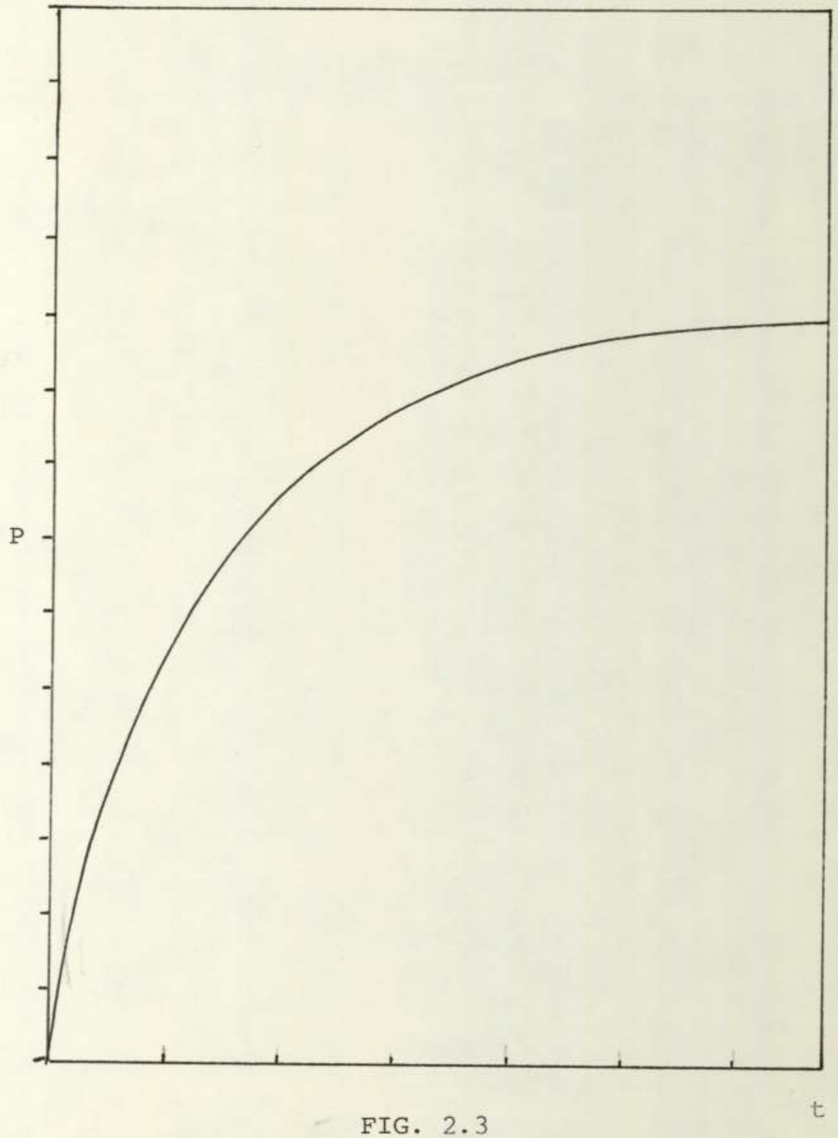


FIG. 2.3

Kinetic plot of an ideal firstorder reaction

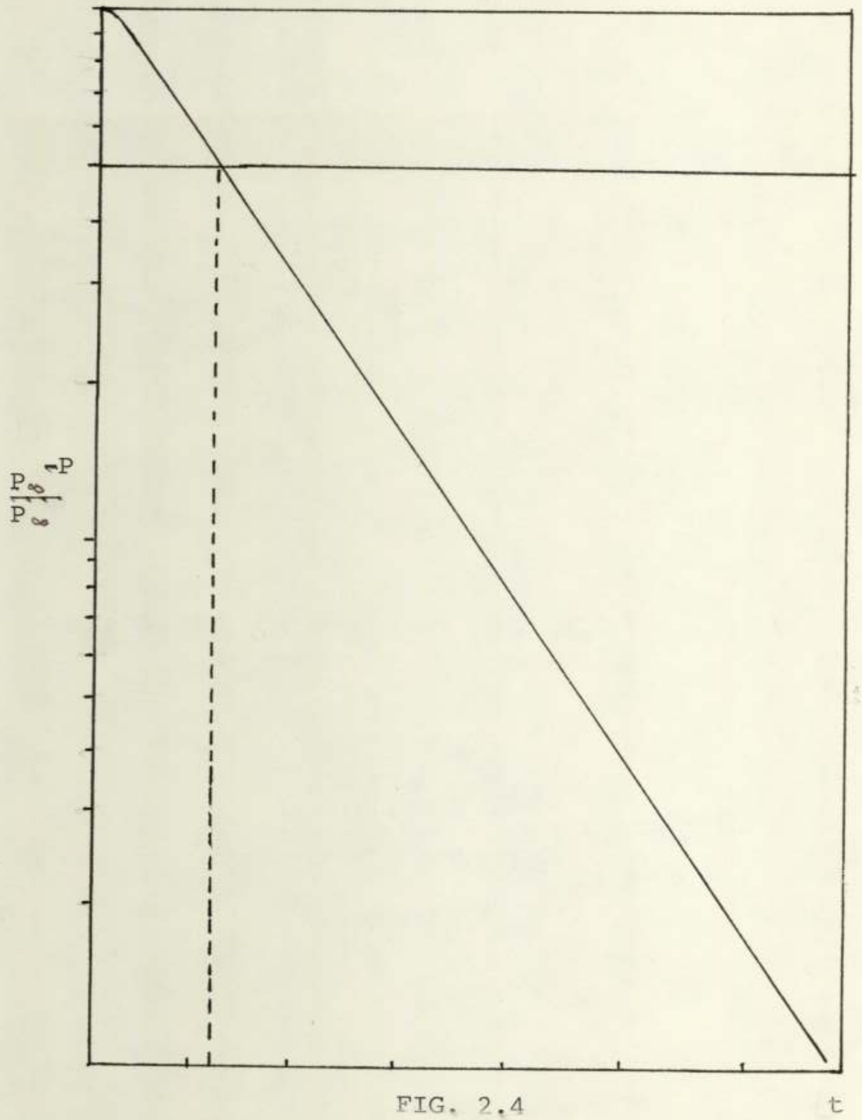


FIG. 2.4

Semi lorgarithmic plot of Fig. 2.3

where k is the rate constant for the reaction:

$$I + M \xrightarrow{k} IM$$

Since $$\log_e \frac{[M]}{[M]_0} = -kt \ldots\ldots\ldots\ldots\ldots\ldots\ldots (2.8)$$

a semi-logarithmic plot of $\log \frac{P_\infty - P}{P_\infty}$ against time should yield a straight line typified in Fig. 2.4.

It is often convenient to use the half-life technique to obtain a value for the first order rate constant k since this can readily be obtained from Fig. 2.4 as the time when $\frac{P_\infty - P}{P_\infty} = 0.5$. k is calculated from the expression

$$k = \frac{0.693}{t_{\frac{1}{2}}} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2.9)$$

where $t_{\frac{1}{2}}$ is the half-life in seconds.

For a reaction which is first order in both monomer and initiator the rate of reaction, i.e. the rate of disappearance of monomer is proportional to both the monomer and initiator concentrations.

$$\frac{d[M]}{dt} = -k[M][I] \ldots\ldots\ldots\ldots\ldots\ldots\ldots (2.10)$$

In order to compare reactions of different initiator concentrations a first order rate constant k' is used where $k' = k[OH]$ and so equation 2.10 becomes

$$\frac{d[M]}{dt} = -k'[M] \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2.11)$$

Deviation from linearity in a semi-log plot of the form of Fig. 2.4 can occur for a variety of reasons, some due to procedural difficulties and others which reflect genuine mechanistic features of the reaction.

The former difficulties include inadequate thermostatting of the bath or a slow leak occuring in the kinetic apparatus. Also any inaccuracy in the measurement or estimation of the value of P_∞ (which is always taken after an overnight period following the apparent stopping of the reaction) will lead to non-linear semi-log plots. The most common cause of this is the non-equilibrium partitioning of the evolved gas between the liquid or gas phases or inaccuracy in the preliminary estimation of the total pressure rise so that h^∞ occurs too near to the top of the capillary where the relationship $h_\infty \propto p_\infty$ does not hold strictly true. All these difficulties can be fairly easily accounted for or corrected.

Genuine non-linearity of mechanistic origin can occur if the concentration of nucleophilic initiating species changes substantially in the course of the reaction. For example, if in the reaction

$I + M \rightarrow IM$

the product IM does not react with further monomer in the same way as I or if it does react but at a substantially slower rate then the effective concentration of I is decreased which shows up in the semi-log plot. In such a case this can be corrected by using a large excess of initiator.

In the case of hydroxyl substituted monomers, the monomer itself may act as a nucleophile, initiating the decomposition of another monomer molecule, where again non-linearity of the semi-log plot would be expected.

Where first order rate constants are quoted in this thesis they are obtained as described above and any significant deviations in kinetic profile are discussed as they arise in the appropriate sections.

The determination of k' values for a particular monomer/initiator system at a series of temperatures enables a series of thermodynamic parameters to be determined which are invaluable in elucidating the reaction mechanisms occuring in that particular system.

By plotting Log k' against 1/T where T is the temperature in $^\circ$K the activation energy, E, for the reaction can be calculated from the expression

$$E = -\frac{d \text{ Log } k'}{dt} \times 2.303R \text{ K Cal Mole}^{-1} \quad \ldots\ldots\ldots\ldots (2.12)$$

where R is the gas constant = 1.98 Cal deg^{-1} mole^{-1}

Knowing the value of E it is possible to calculate the pre-exponential frequency factor, A, in the Arrhenius equation

$k' = A_e{}^{-E/RT}$ (A is in sec^{-1}) ....(2.13)

This value can be used to calculate the entropy of activation $\Delta S^{\ddagger}$ from the expression

$\Delta S^{\ddagger} = 4.57 \text{ Log } A - 60.53$ ....(2.14) taking the value for A at 25°C ($\Delta S^{\ddagger}$ is in cal deg^{-1} $mole^{-1}$)

Preparation of Hydrogel polymers by solution polymerization

Solution polymerizations were carried out in the apparatus shown in Fig. 2.5. A split resin flask, supported in a water bath at the required temperature was fitted with a condenser, thermometer, stirrer and a nitrogen bleed since oxygen must be excluded from the system to avoid premature termination by interaction between the free radicals present and oxygen molecules.

The monomers in solution were introduced into the flask and nitrogen bubbled through for about 30 mins. stirring constantly. The initiator, usually AZBN, was introduced and the reaction allowed to proceed to completion. The polymer formed was recovered by first reducing the volume of solution with a rotory evaporator and then precipitation into a tenfold excess of a non-solvent, methanol or ether.

The precipitated polymer was filtered, washed and dried in a vacuum oven.

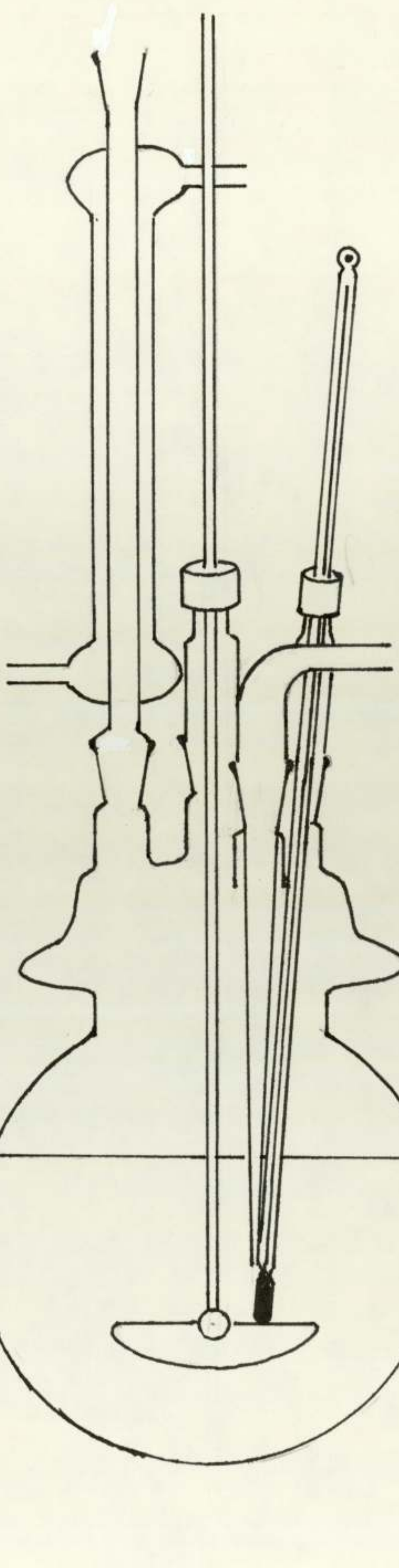


Fig. 2.5 SOLUTION POLYMERIZATION APPARATUS

Preparation of Polymer Films

Hydrogel polymer films were prepared in the cell shown in Fig. 2.6. This consisted of two glass plates which were covered with 'Mylar' (poly (ethyleneterephthalate)) film which decreased the possibility of adhesion of the polymer film to the glass plate. The covered glass plates were separated by a polyethylene gasket about 0.5mm thick and the cell was clamped together using spring clips. Purified monomers were mixed in the required composition. When there was a high proportion of the solid monomer, acrylamide or N-hydroxymethyl acrylamide it proved necessary to add a small amount of water (less than 10%) to obtain a uniform solution. The solution was filtered and degassed and about 0.05 - 0.1% AZBN added as an initiator. The solution was injected through a G25 syringe needle into the cell which was then placed in an oven at $60^{o}C$ for 3 - 4 days to allow polymerization to take place. After this the temperature of the oven was raised to $80^{o}C$ and the films allowed to post-cure for about 3 hours. The glass plates were removed from the cell and the Mylar sheets removed as carefully as possible although it was sometimes necessary to remove the film from the Mylar sheet by soaking in water. The films were allowed to hydrate for at least two weeks, changing the distilled water frequently to ensure complete removal of water soluble monomer residues from the film.

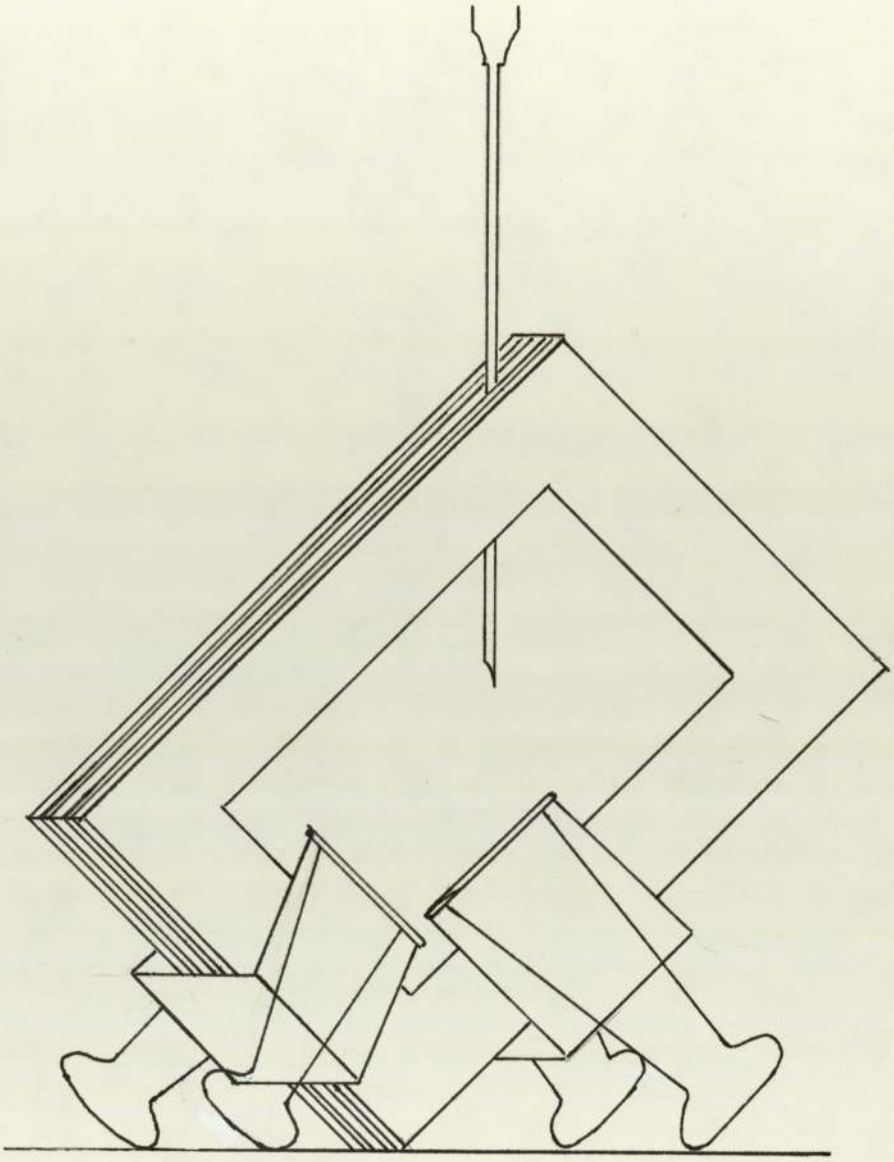


Fig. 2.6
FILM POLYMERIZATION CELL

2.4 Techniques used in the Characterization of Hydrogel Polymers and their Surfaces

Density

The density of hydrogels was measured using a density gradient column made up from mixtures of chloroform (density 1.48) and p xylene (density 0.86) so that it had a linear density gradient between 1.48 and 0.86. The density profile was calibrated with small glass floats of accurately known density and the density of the polymer measured by dropping a small chip of polymer into the column and calculating its density from its position.

Water Content

The equilibrium water content of a hydrated hydrogel polymer was determined on small samples of polymer which had been allowed to hydrate for at least two weeks. The samples were removed from the water and surface water removed with a tissue. These were then weighed in a stoppered weighing bottle. The samples were dried to constant weight in a vacuum oven at 60°C.

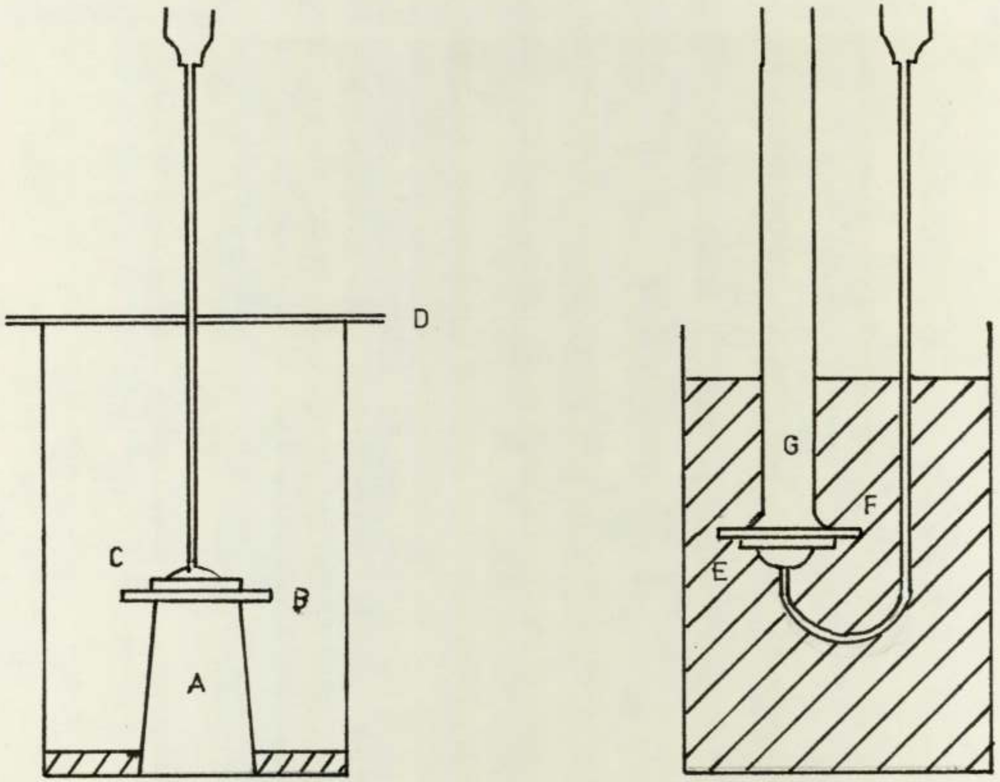
$$\text{Equilibrium Water Content} = \frac{\text{weight of hydrated sample} - \text{weight of dehydrated sample}}{\text{weight of hydrated sample}} \times 100\%$$

Contact Angle Measurement

The measurement of the contact angle formed by a drop of liquid on the surface of a polymer was a useful technique for comparison of the surface properties of hydrogel films which have been treated with anhydrosulphites. The measurement of contact angles was carried out by two different methods.

a) The Sessile Drop Method

The cell used is shown in Fig. 2.7 a. A square glass cell contained a support A which carried a glass cover slip B to which the polymer



(a) (b)

Fig. 2.7 CONTACT ANGLE CELL

sample C , usually in the dehydrated state was attached. A small amount of the drop-forming liquid was present in the cell so that the atmosphere around the polymer sample was saturated with its vapour. A cover D was placed on the cell. A small drop of liquid was placed on the surface of the polymer from a syringe needle, introduced through a hole in the cover. The syringe needle whose point had been removed, was held in place by a 'Prior' micromanipulator and connected to an 'Agla' microsyringe containing the sessile drop-forming liquid.

The cell was placed in the light path of Rank Aldis Tutor 2 slide projector so that the image of the drop was thrown onto a back projection screen to facilitate measurement of the contact angle. The contact angle was determined by drawing the tangent to drop at the surface of the sample and measuring the included angle with a protractor.

b) Hamiltons Method(65)

The cell used is shown in Fig. 2.7 b. The polymer sample E (hydrated) was glued to a glass cover slip F which was held suspended in water by a suction bulb contained in a tube G . The water which filled the cell had been previously saturated with n-octane. Drops of n-octane, which is less dense than water, were delivered to the polymer surface with a bent syringe needle. Control of the volume of the drop and measurement of the contact angle was achieved in the same way as for the sessile drop method.

Calculation of Surface Tension

The contact angle formed between a drop of liquid and a solid surface is the result of the resolution of the [illegible] forces acting at three interfaces: (Fig. 2.8):

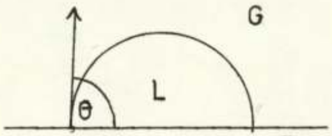


Fig. 2.8

solid/liquid, liquid/Gas, Solid/Gas. The surface tension, γ , of a Liquid or Solid can be defined as the force acting at the interface between the solid or liquid and the surrounding gas, and is normally measured as an energy per unit area.

For non-polar liquids the surface tension of the liquid has been directly correlated with the bulk cohesive energy which is a property of the dispersive forces of attraction between the molecules of the liquid. However, it was found that this relationship did not hold for polar liquids where there appeared to be some orientation of the molecules at the surface or interface in order to minimize the interfacial energy. There are also dispersive forces acting at the interface so the surface tension of a polar liquid or solid must be made up of two components, a polar component γ^p and a dispersive component γ^d: Thus:

$$\gamma_s = \gamma_s^d + \gamma_s^p \quad \text{and} \quad \gamma_l = \gamma_l^d + \gamma_l^p$$

It has been found that for non-polar liquids the contact angle, θ of the liquid on a particular solid is proportional to the surface tension of the liquid. By plotting $\cos\theta$ against n and extrapolating to $\cos\theta = 1$ ($\theta = 0$) a value for the 'critical surface tension' of the solid can be found. A liquid of this surface tension will completely wet the solid.

It must be remembered that both polar and dispersive forces are acting on the surface of the polymer. These can be determined separately by measuring the contact angle formed by two different liquids with different components of surface tension.

In the Sessile Drop technique two drop-forming liquids were used, water and methylene iodide (CH_2I_2). Their polar and dispersive component of surface tension have been measured as:

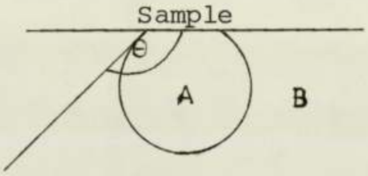
Water	$\gamma = 72.8$	$\gamma^d = 21.8$	$\gamma^p = 51.0$
Methyleneiodide	$\gamma = 50.8$,	$\gamma^d = 59.5$,	$\gamma^p = 1.3$

By measuring the contact angles formed by both on a polymer and substituting in the equation proposed by Owens and Went(66) (equ. 2.15), the two simultaneous equations

$$\cos\theta + 1 = \frac{2}{\gamma_{lg}} \left(\gamma_l^d \; \gamma_s^d \right)^{\frac{1}{2}} + \left(\gamma^p_l \; \gamma_s^p \right)^{\frac{1}{2}} \qquad \ldots.(2.15)$$

produced enable the evaluation of $\gamma^d{}_s$ and $\gamma^p{}_s$ for the polymer. The surface tension of Methylene iodide is practically entirely dispersive and its contact angle can be correlated with the dispersive component of the surface tension of the polymer.

In the Hamilton technique of contact angle measurement used for hydrated polymer samples, the contact angle is a result of the resolution of the interfacial energies of the solid/ liquid A, solid/ liquid B and liquid A/liquid B interfaces.



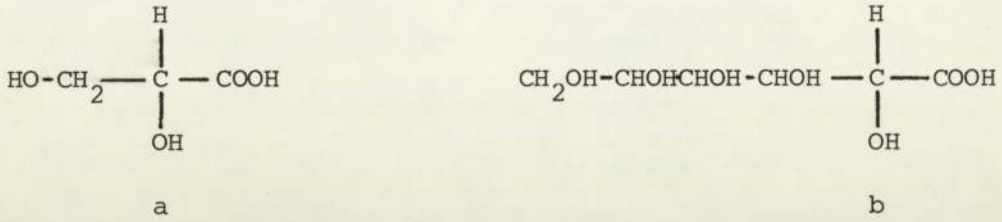
In the octane water system, octane and water have been found to have the same dispersive component of their surface free energies so a measurement of the contact angle of octane in water will directly give the polar component of the surface of the sample from the equation

$$\cos\theta \;\; \gamma_{ow} = \gamma_{w} - \gamma_{o} - 2\sqrt{\gamma^p{}_w \gamma^p{}_s}$$

CHAPTER 3

The Preparation and Reactions of Anhydrosulphites of α-Hydroxy acids with Hydroxyl-containing Substituents

Two α-hydroxy acids were chosen for this study namely glyceric acid (Fig. 3.1A) and gluconic acid (Fig. 3.1B).



$$HO\text{-}CH_2\text{—}\overset{\displaystyle H}{\underset{\displaystyle OH}{C}}\text{—}COOH \qquad CH_2OH\text{-}CHOHCHOH\text{-}CHOH\text{—}\overset{\displaystyle H}{\underset{\displaystyle OH}{C}}\text{—}COOH$$

a b

Fig. 3.1

Glyceric acid has a simpler structure and can be thought of as a derivative of lactic acid $\left(R_1=H, R_2=CH_3\right)$ where a hydroxyl group has been substituted for a hydrogen on the R_2 methyl group. Gluconic acid, which is derived from glucose is more complex but nevertheless interesting in the fact that four substituent hydroxyl groups would be expected to be extremely hydrophilic.

3·1 Preparation of Glyceric Acid Anhydrosulphite

Glyceric acid was obtained from Cambrian Chemicals Ltd. in the form of a 65% solution in water. This solution was pale yellow in colour and very viscous; it darkened on heating suggesting that the acid was not very stable thermally. It was thought that the preparation of a copper salt would provide a suitable starting point for anhydrosulphite synthesis.

Attempted preparation of Cupric Glycerate

16.32g glyceric acid solution, (calculated as containing 0.1 moles acid) was treated with 0.1 mole of ammonia solution. Heat was not used because of the instability of the acid. 0.05 moles cupric chloride dissolved in a minimum amount of hot water was added. On standing a small amount of fine green precipitate appeared which was filtered off and was washed with methanol and ether. An infra-red spectrum of the dried copper salt showed a broad carbonyl absorption occuring between 1585 and 1610 cm^{-1} which was assigned to the carboxylate anion.

Because of the low yield it was suspected that the structure of the copper salt formed was not similar to that of copper salts formed from other α-hydroxy acids. The coppersalt was quantitatively analysed for copper and chloride by the gravimetric techniques described earlier and was found to contain 47% by weight of copper whereas the desired structure shown in Fig. 3.2 has a calculated copper content of only 23.2% by weight.

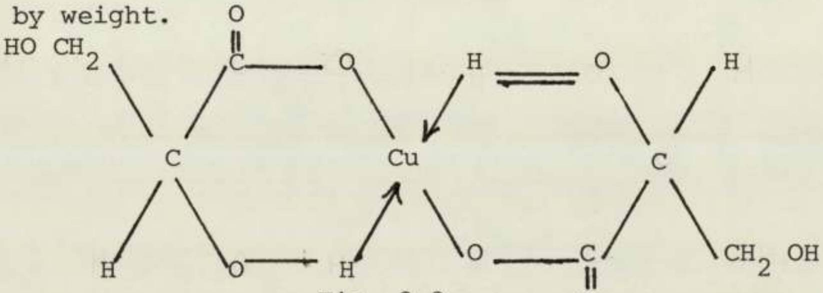


Fig. 3.2

The analysis also showed that there was 8% by weight of chlorine in the sample. Thus assuming that the remainder of the salt was the glycerate anion $CH_2OH\ CHOHCOO^-$ the following composition was calculated:

	Weight %	Molar Weight	Molar ratio
Copper	47	63.55	1
Chloride	8	35.45	0.32
Glycerate	45	105.07	0.60

This showed that the copper salt was either a non-stoichiometric compound or a mixture of salts.

The yield of copper salt was very low; calculation showed that the copper from only 17% of the initial amount of cupric chloride was used in the formation of the precipitate. An attempt was made to precipitate more copper salt from the filtrate, but precipitation into first methanol and then ether failed to produce a product other than cupric chloride.

Because of the failure to obtain a suitable copper salt from glyceric acid an attempt was made to prepare a silver salt since the silver salts of various α-hydroxy acids have proved to be successful in the preparation of anhydrosulphites.

Attempted Preparation of Silver Glycerate

The solution of 0.1 moles of gylceric acid was treated with a molar equivalent of ammonia solution followed by the addition of 0.1 moles silver nitrate dissolved in a minimum of hot water. The mixture immediately turned brown but no precipitate appeared. By dropping this solution into a tenfold excess of methanol a brown precipitate was obtained which was filtered off, washed and dried. The quantity of precipitate yielded was about 45% of the theoretical yield for complete conversion.

An infra-red spectrum of the dried silver salt showed a wide band centering at 1600 cm^{-1} indicating the presence of a carboxylate anion. Gravimetric analysis for silver indicated that there was an approximately 1:1 ratio of silver to glycerate ion. It was thus considered that this silver salt would be suitable for anhydrosulphite preparation.

Reaction between silver Glycerate and Thionyl Chloride

0.02 mole silver glycerate was taken and slurried in 25 mls of anhydrous ether. 0.03 moles of thionyl chloride dissolved in a little ether was added dropwise. The reaction mixture being kept cold in a bath containing solid carbon dioxide. After about 24 hours the silver salt turned a whitish colour indicating conversion to silver chloride. The mixture was centrifuged and the ether and excess thionyl chloride stripped off under vacuum. The residual light yellow oil was stored under vacuum at a temperature of -40°C.

3·2 Characterization

The product from the reaction between thionyl chloride and silver glycerate reacted vigorously with alcohols and amines at room temperature with the evolution of sulphur dioxide.

The Infra-red spectrum was not very clear, this was probably due to the fact that being highly reactive the anhydrosulphite was decomposing in the moist atmosphere on the sodium chloride plates of the spectrophotometer. (The spectrum is shown in Fig. 3.3). The strong carbonyl peak at about 1740 cm^{-1} is typical of an ester group. There was also a reasonably strong 'shoulder' at 1795 cm^{-1} which is typical of the carbonyl absorbtion of anhydrosulphites of α-hydroxy acids. Another shoulder appearing at 1700 cm^{-1} was attributed to the acid formed by the action of moisture on the anhydrosulphite.

The presence of the ester group was presumably due to a reaction between the substituent hydroxyl group and the anhydrosulphite ring as shown in Fig. 3.4.

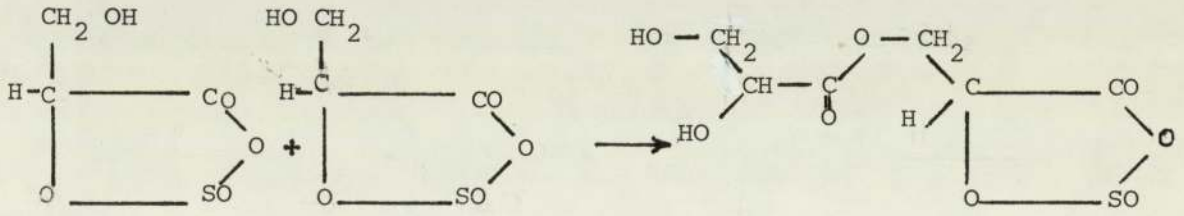


Fig. 3.4

The infra-red spectrum also showed a strong hydroxyl absorption and there was a peak at 1200 cm^{-1} which could be attributed to the $>S = O$ group in the anhydrosulphite ring.

A trace chloride ion determination showed no measureable amount of chlorine and it was assumed that the short reaction time and low temperature of the preparation reaction was responsible for a minimal amount of acid chloride impurity.

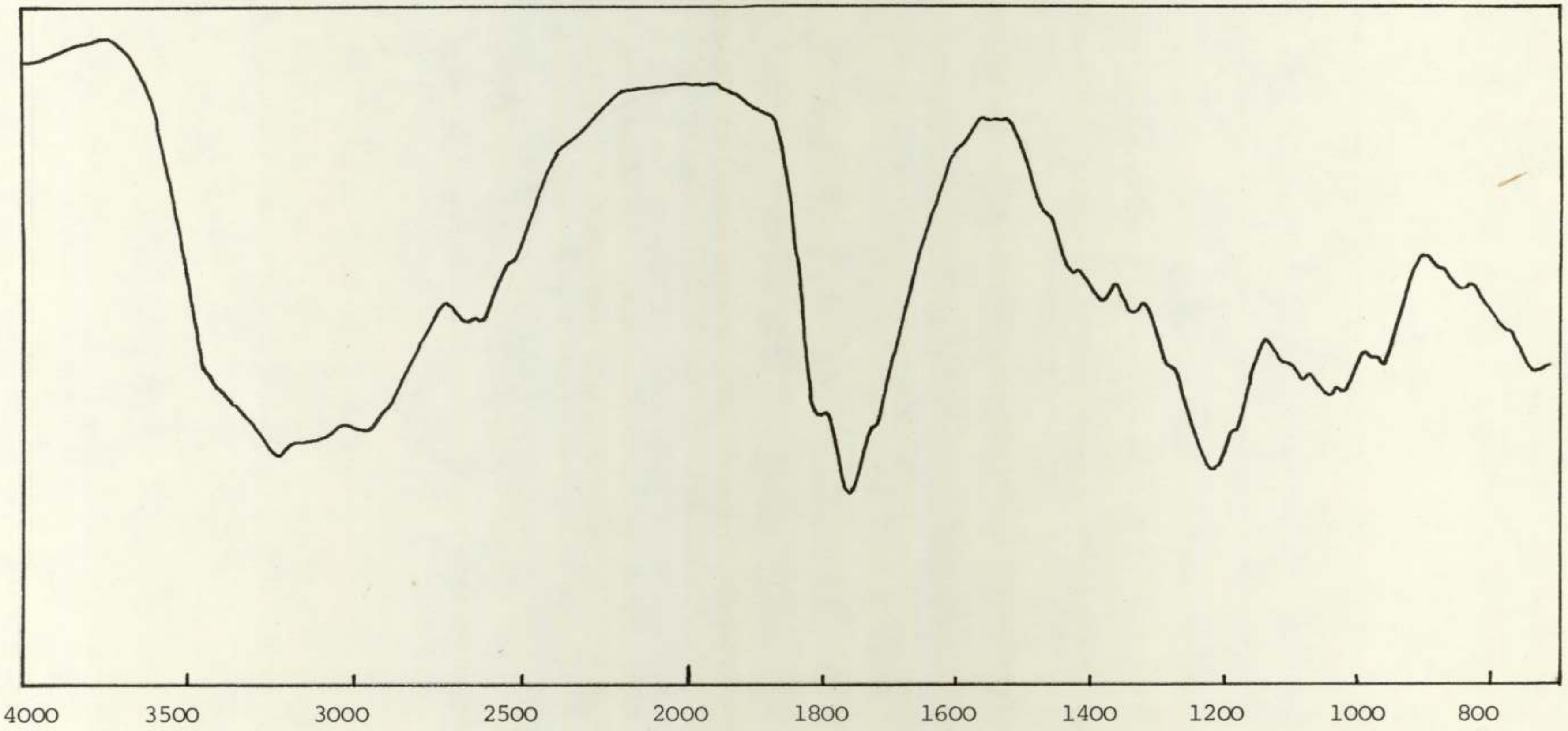


Fig. 3.3

Infra-red spectrum of Glyceric acid anhydrosulphite

3.3 Decomposition Reactions of Glyceric acid, Anhydrosulphite

The high reactivity of glyceric acid anhydrosulphite which seems to include a self decomposition reaction, precludes the possibility of purification techniques involving distillation. Since a chloride ion determination showed negligeable chlorine, in the absence of moisture, it was assumed that the major impurity present was the ester formed by the attack of the substituent hydroxyl group on the anhydrosulphite ring. From an Infra-red spectrum taken on a sample immediately on removal from cold storage it was estimated that about half the total carbonyl groups were esterified enabling suitable volumes to be taken for kinetic runs. The first kinetic study was an investigation into the rate of self decomposition of the anhydrosulphite in the absence of any initiator. A solution of glyceric acid anhydrosulphite in nitrobenzene was made up and the required quantity injected into an evacuated kinetic apparatus which was immediately transferred to a waterbath at the required temperature. The monomer decomposed fairly rapidly even at 25°C. The semi-log plot of $\frac{[M]}{[Mo]}$ against time for a typical run is shown in Fig. 3.5. The log plot is not a straight line but shows that the rate of reaction is slowing down, compared with the expected rate for first order behaviour, as the reaction proceeds.

The effect of temperature on the rate of decomposition was demonstrated by comparison of the first order rate constants for the initial rate of reaction k_o which were calculated from the slope of log $\frac{[M]}{[Mo]}$ against t at t = 0.

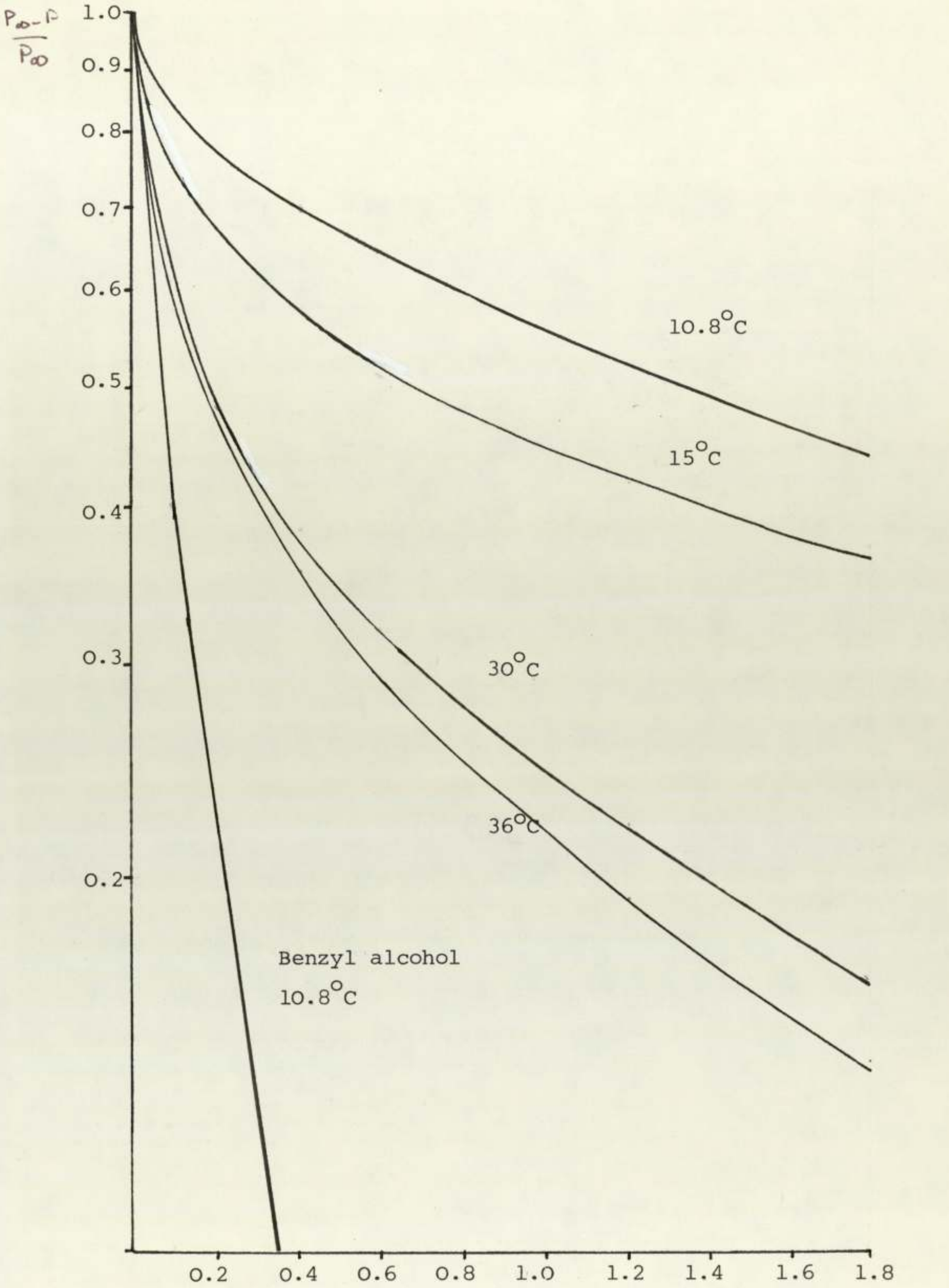


Fig. 3.5

Uninitiated decomposition of Glyceric acid anhydrosulphite

$T^{o}C$	$\frac{1}{T}{}^{o}K \times 10^{-3}$	$t_{\frac{1}{2}}$ (tan)	K_o
10.8	3.521	11820	5.86×10^{-5}
15.3	3.469	8100	8.55×10^{-5}
25.0	3.356	3120	2.22×10^{-4}
30.0	3.300	2520	2.75×10^{-4}
36.0	3.232	1620	4.28×10^{-4}

A plot of log K_o against 1/T gave a straight line which enabled the activation Engergy E for the reaction to be calculated as 15.6 K cal/mole. (Fig. 3.9)

3.4 The Use of Benzyl alcohol as a Model Nucleophile

The interaction between the ring of Fig. 3.6

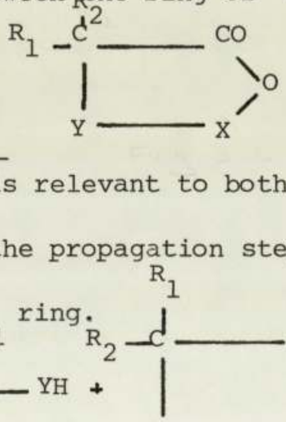
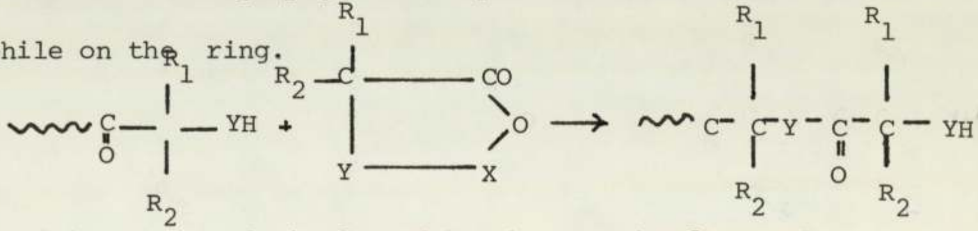


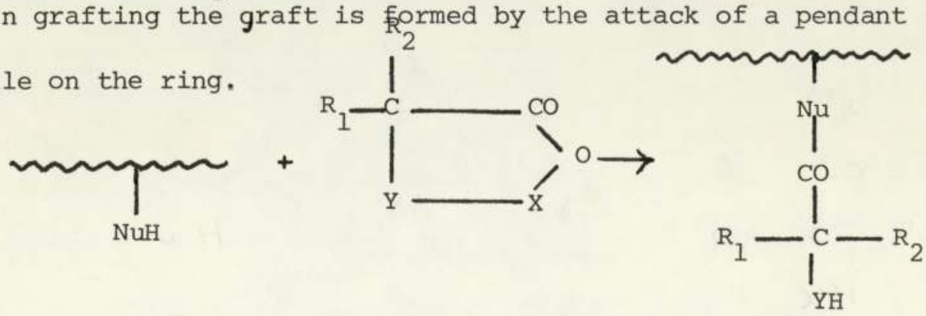
Fig. 3.6

and a weak nucleophile is relevant to both polymerization and grafting.

In polymerization the propagation step of the reaction is the attack of a nucleophile on the ring.



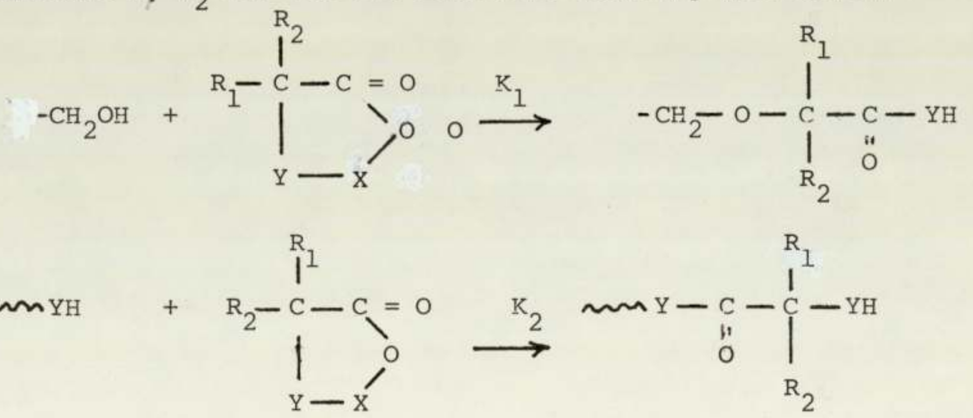
Whereas in grafting the graft is formed by the attack of a pendant nucleophile on the ring.



In order to study these reactions from a kinetic and mechanistic point of view it is convenient to choose a model weak nucleophile, usually an amine or an alcohol. From past experience amines are generally much too reactive to be followed conveniently. Alcohols have a more reasonable reactivity and benzyl alcohol is particularly suitable having a low volatility essential in low pressure systems used in kinetic studies by gas evolution methods. It can therefore be used as a solvent as well as a reagent.

Another important factor in the choice of benzyl alochol as a model nucleophile is that previous workers have built up a considerable bank of data and results concerning the reaction between benzyl alcohol and rings which is useful in making comparisons between various ring systems.

A wide variety of information can be obtained from kinetic studies involving model nucleophiles. Firstly by using an excess of benzyl alcohol the kinetic plot of log $\frac{P\infty-P}{P\infty}$ against time would be expected to be linear allowing k, the first order rate constant for the reaction to be calculated. Secondly by using an equimolar or smaller ratio of benzyl alcohol to ring the relationship between the rate constants k, k_2 for the two reactions occuring (see below)

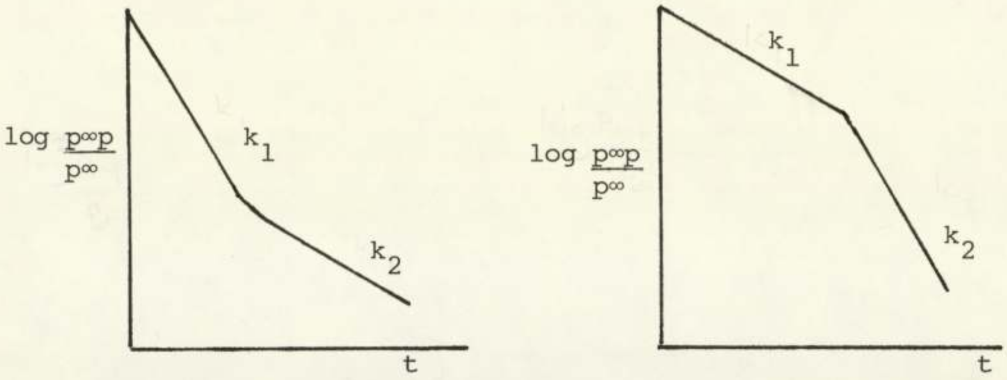


(1)

(2)

can be determined.

If k_2 were considerably less than k_1 the slope of log $\frac{P\infty-P}{P\infty}$ against time would decrease with time (fig. 3.7a) as the benzyl alcohol is used up, whereas if k_2 were greater than k_1 the opposite effect would be observed (fig. 3.7b)



a,

b

Fig. 3.7

Other information that can be obtained from the benzyl alcohol reaction includes the effect of varying the solvent using a cosolvent of low volatility which is miscible with benzyl alcohol, and the effect of temperature on the rate of reaction which enables the thermodynamic properties. Activation energy (E) Frequency factor (A) and Entropy of activation ($\Delta S^{\ddagger}$) to be evaluated.

This knowledge assists in characterizing the nature and efficiency of the ring opening reaction. In the case of hydroxyl substituted anhydrosulphite self-decomposition by the substituent hydroxyl groups also needs to be taken into consideration and compared with ring opening brought about by an excess of the model nucleophile.

3·5 Benzyl Alcohol Initiated decomposition of Glyceric acid anhydrosulphite

The same solution of glyceric acid anhydrosulphite as used in the previous investigation into its uninitiated decomposition was used for an investigation into benzyl alcohol initiated decomposition. A solution of benzyl alcohol in nitrobenzene was made up and a quantity containing an estimated twofold excess benzyl alcohol was injected into the kinetic apparatus. At the temperatures studied glyceric acid anhydrosulphite decomposed more rapidly in the presence of benzyl alcohol. The plot of log $\frac{[M]}{[M]_0}$ against time was linear, the reaction showing first order behaviour. (Fig. 3.10)

T^oC	$\frac{1}{T^oK}$	$t_{\frac{1}{2}}$	K
10.8	3.528	3550	1.96×10^{-4}
17.8	3.440	810	8.56×10^{-4}
25	3.358	510	1.36×10^{-3}
30	3.300	240	2.89×10^{-3}

$E = 21.6$ Kcal mole^{-1}

The activation energy for the reaction was of the same order as that for the self initiated decomposition of the anhydrosulphite suggesting that a similar reaction mechanism was occuring. A more detailed discussion of reaction kinetics and mechanisms will be found in chapter 5.

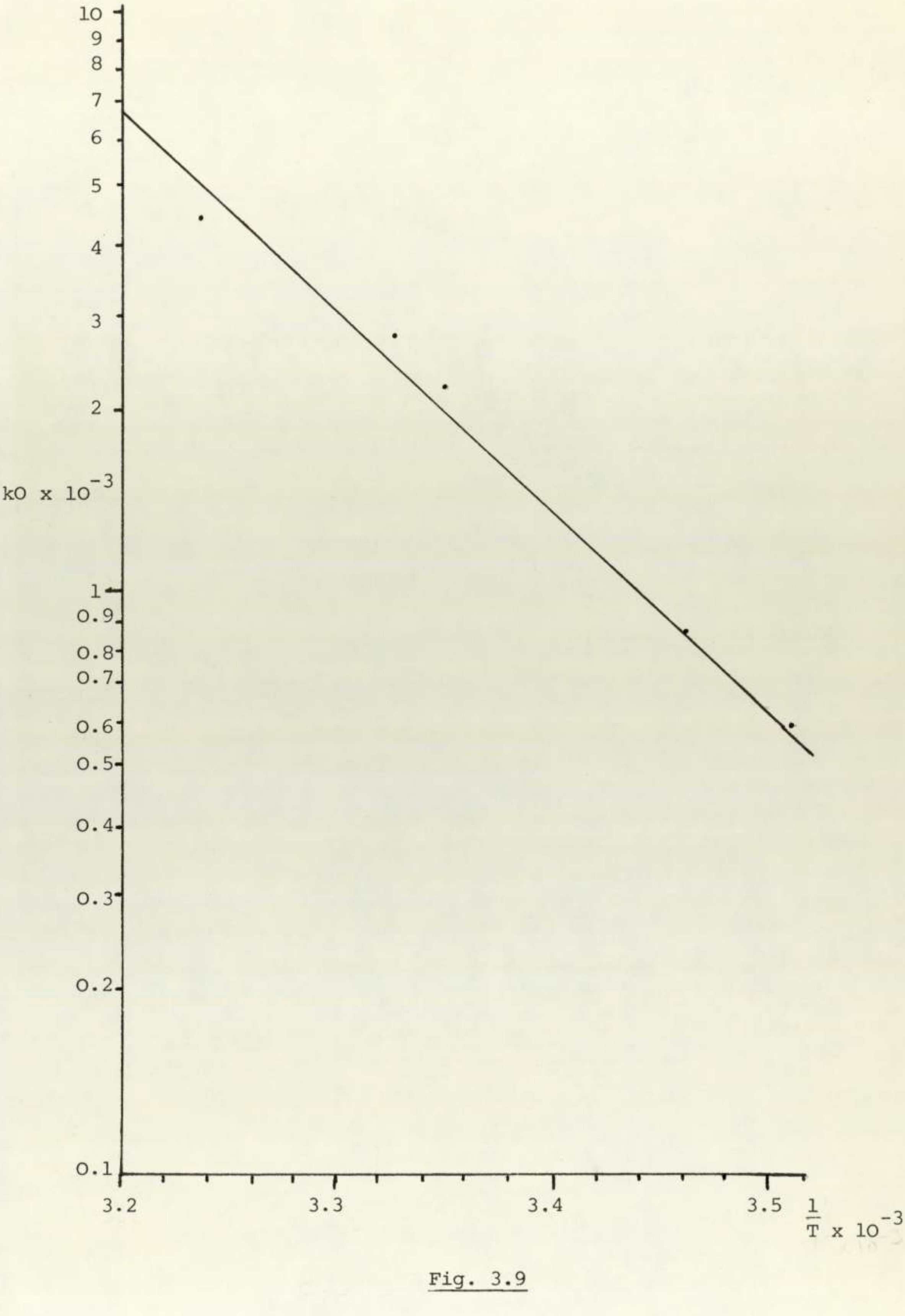


Fig. 3.9

Uninitiated decomposition of Glyceric acid anhydrosulphite in nitrobenzene.

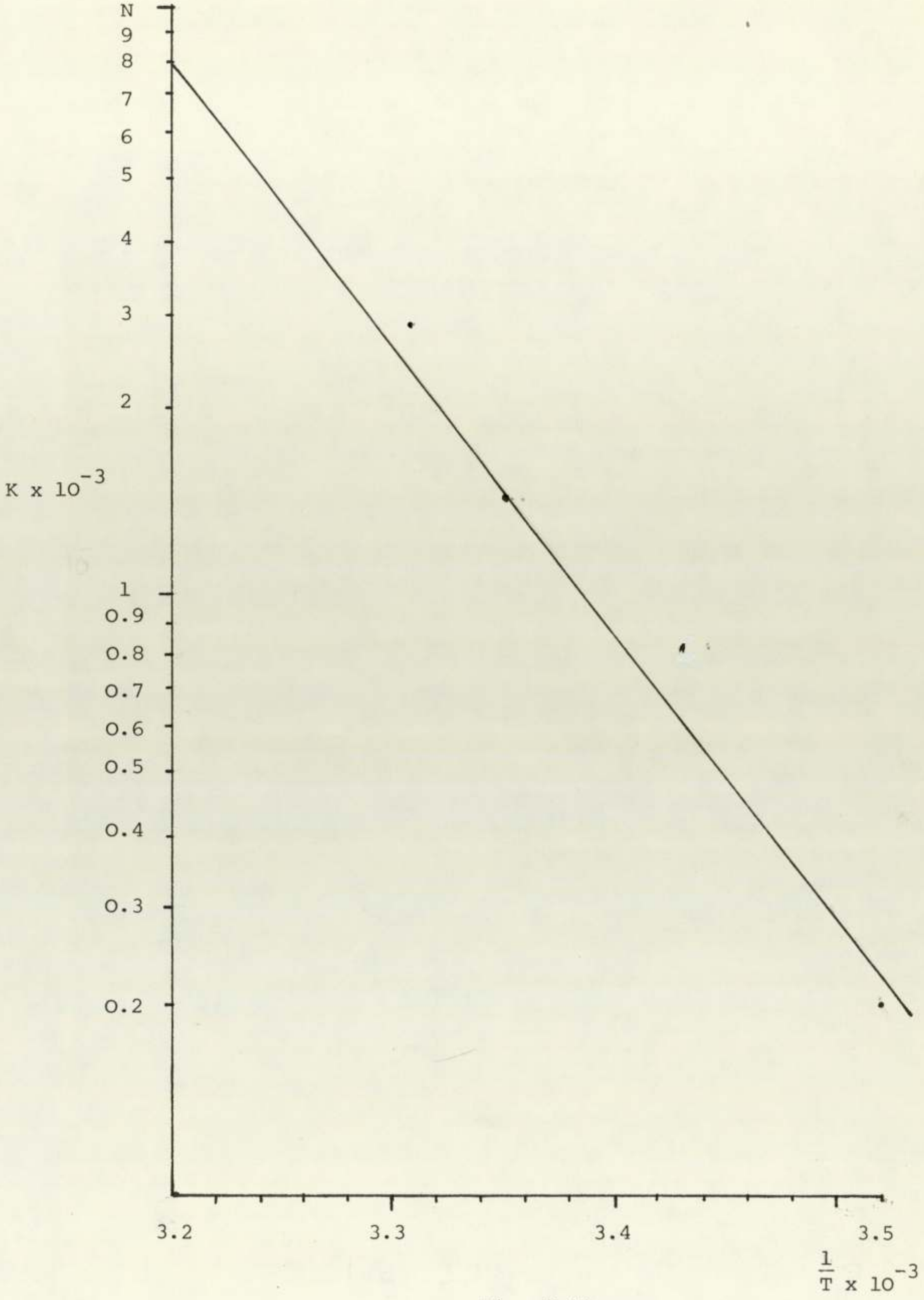


Fig. 3.10

Benzyl alcohol initiated decomposition of Glyceric acid anhydrosulphite in nitrobenzene.

3·6 Reaction Products from Decomposition Reactions

The infra-red spectra of the reaction products of both the uninitiated and benzyl alcohol initiated decomposition reactions, described in the previous section, showed a strong carbonyl absorption at 174o cm^{-1} indicating the formation of an ester. The carbonyl absorption appearing at 1795 cm^{-1} in the spectrum of the anhydrosulphite had completely disappeared.

There was no evidence of the formation of any high molecular weight polymeric product even from the uninitiated decomposition of glyceric acid anhydrosulphite. This was probably the result of premature termination brought about by the glyceric acid impurity present.

3·7 Preparation of the Anhydrosulphite of Gluconic Acid

Gluconic acid was available commerically as its cyclic ester gluconolactone (fig. 3.11).

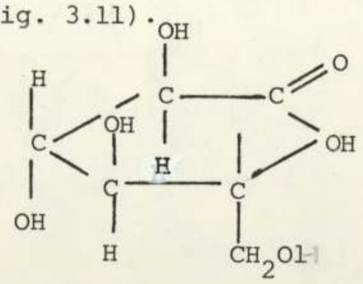


Fig. 3.11

It was decided to use this compound to prepare a copper salt for anhydrosulphite preparation since it would not be easy to prepare the acid in a pure anhydrous state by hydrolysis of the lactone.

Preparation of Cupric Gluconate

0.5 moles gluconolactone was dissolved in a minimum quanity of hot water. The solution was treated with a slight molar excess of 0.880 ammonia solution and boiled for several minutes in order to break the lactone ring and form ammonium gluconate. The excess ammonia was boiled off and the solution concentrated as much as possible. 0.25 moles cupric chloride dissolved in a minimum amount of hot water was added with continuous stirring. The mixture was allowed to cool but no precipitate appeared so it seemed that as with glyceric acid the copper salt was extremely soluble in water. Fortunately, unlike cupric glycerate precipitation could be achieved by dropping the solution into a tenfold excess of methanol which was being stirred vigorously. The fine, pale blue precipitate was found to be thermally unstable, charring when heated above 100°C, and also very hygroscopic, absorbing enough water to dissolve itself in when left exposed to a damp atmosphere for a few hours.

The extreme hydrophilicity of the copper salt presented a difficulty in the complete removal of water which was strongly bound to the hydroxyl substituents of the gluconate ion necessary to obtain the anhydrous state required in anhydrosulphite preparation. The drying procedure was divided into two stages. Firstly the precipitate was washed with methanol and ether which was removed in a vacuum oven at 70°C. Secondly an azeotropic distillation as described in Chapter 2 was carried out using a 4:1 benzene: n-propanol mixture followed by removal of residual solvents in a vacuum oven.

The copper salt was characterized by infra-red and copper anlaysis. The infra-red spectrum showed a strong carbonyl absorption centred at 1600 cm^{-1} which indicated the presence of the carboxylate anion (the carbonyl absorption for gluconolactone occurs at 1720 cm^{-1}). Gravimetric analysis for copper indicated that the copper: gluconate ratio was 1:2. This suggested that the copper salt had the structure shown in Fig. 3.12 which is suitable for anhydrosulphite preparation.

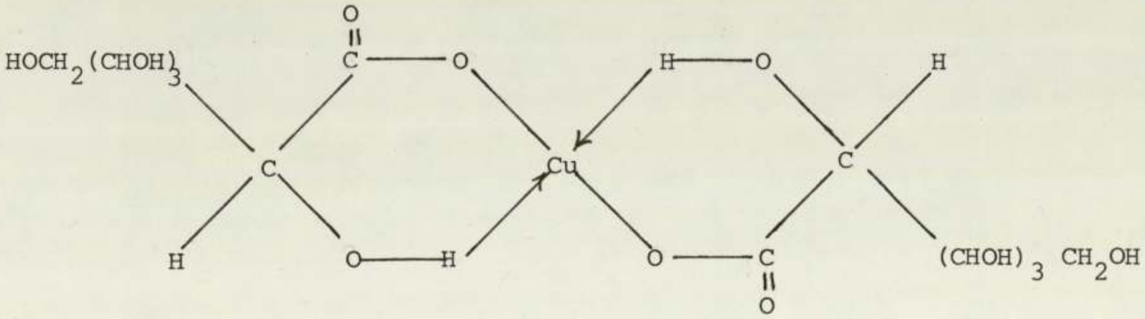


Fig. 3.12

The action of thionyl Chloride on Cupric Gluconate

0.1 mole (51 g) cupric gluconate was slurried in 100 ml anhydrous ether in a 5oo ml conical flask fitted with a condenser and dropping funnel. The mixture was stirred in a bath containing solid carbon dioxide. 0.25 moles thionyl chloride were added dropwise over a period of an hour. The reaction was allowed to warm up to room temperature and the reaction continued for 2 - 3 days during which time the copper salt gradually turned the brownish yellow colour characteristic of anhydrous cupric chloride. The ether solution was filtered off and quickly evaporated to remove the ether and excess thionyl chloride. A yellow oily solution remained. Further evacuation under high vacuum yielded a yellowish white solid.

Characterization

The product from the above reaction was characterized by infra-red spectroscopy. The spectrum obtained is shown in Fig. 3.13. There was a double carbonyl absorption at 1800 cm^{-1} and 1760 cm^{-1} and since a potentiometric titration for chloride ion indicated that there was less than 1% chlorine containing impurity, the peak at 1800 cm^{-1} was attributed to the carbonyl group in the anhydrosulphite ring. By comparison with the spectrum for glyceric acid anhydrosulphite the peak at 1760 cm^{-1} was attributed to an ester formed by reaction between the substituent hydroxyl group and another anhydrosulphite ring. Because the two peaks were of similar intensity it was estimated that roughly half the available carbonyl groups were present as the anhydrosulphite.

As expected the infra-red spectra of glyceric acid anhydrosulphite and gluconic acid anhydrosulphite strongly resembled each other; the same functional groups being present in both compounds.

3.8 Decomposition Reactions of Gluconic Acid Anhydrosulphite

It was expected that the decomposition reactions undergone by gluconic acid anhydrosulphite would be similar to those undergone by glyceric acid anhydrosulphite.

A solution of the anhydrosulphite in nitrobenzene was made up. By the estimation that approximately half the anhydrosulphite had been converted to the ester suitable quantities were taken for kinetic measurements.

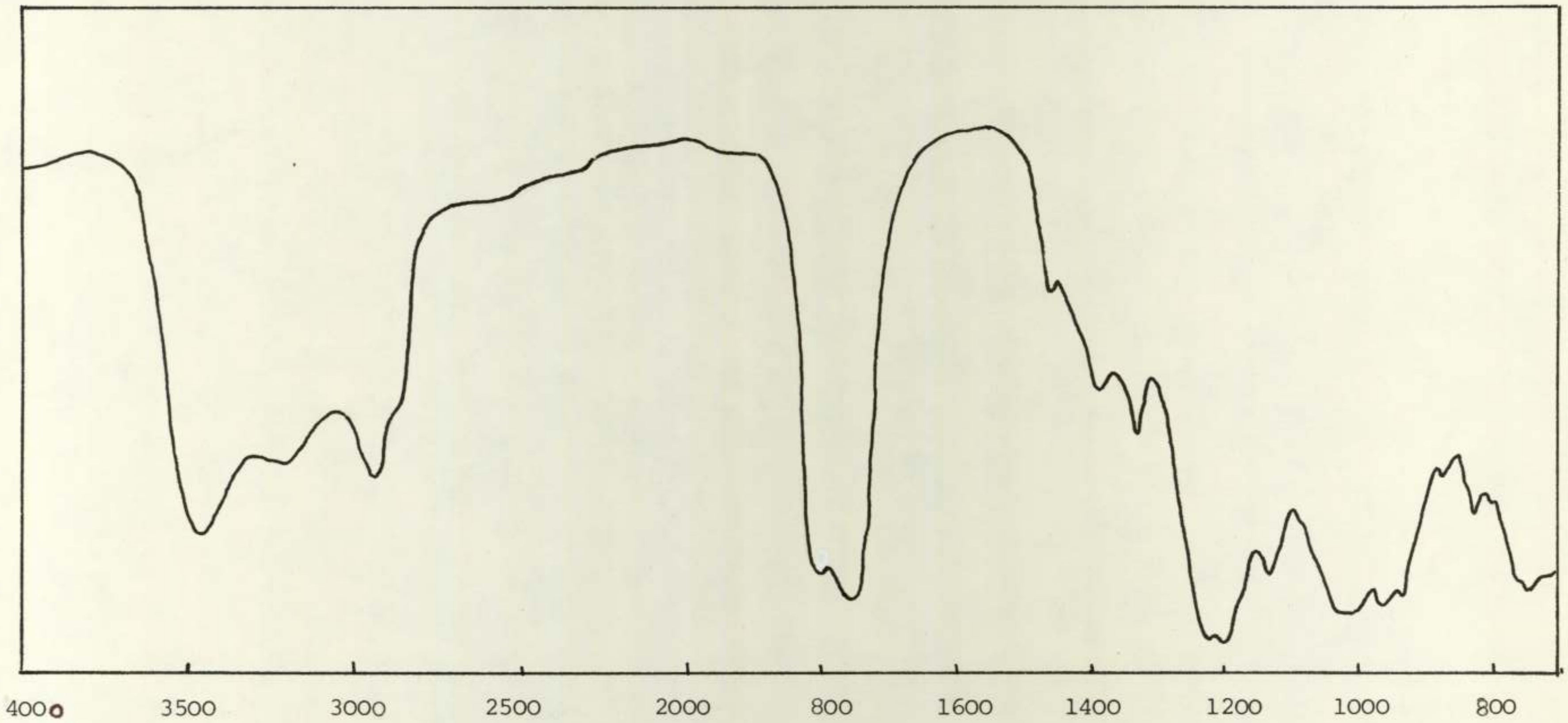


Fig. 3.13

Infra-red spectrum of Gluconic acid anhydrosulphite

An experiment was performed to compare the rate of self-initiated decomposition with the rate of decomposition in the presence of excess benzyl alcohol. The semi-log plots obtained from these reactions are shown in Fig. 3.14. For the reactions carried out at 30.1°C.K, the first order rate constant was 3.47×10^{-3} K cal mole^{-1} for decomposition in the presence of excess benzyl alcohol compared with 2.82×10^{-4} K cal mole^{-1} for self-initiated decomposition. Both these values were similar to the decomposition of glyceric acid anhydrosulphite under the same conditions where values for k were 2.89×10^{-3} K cal mole^{-1} for benzyl alcohol initiation and 2.75×10^{-4} K cal mole^{-1} for self-initiation.

Kinetic runs with excess benzyl alcohol were carried out at a series of temperatures in order to establish the activation energy for the reaction. (Fig. 3.15)

T	$\frac{1}{T} \times 10^{-3}$	t ½	$K \times 10^{-3}$
20	3.412	375	1.848
30.1	3.299	200	3.165
40	3.195	122	5.680

$$E = 11.5 \text{ K cal mol}^{-1}$$

The value of E obtained was 11.5 K cal mole^{-1} which was rather lower than that obtained for the corresponding reaction involving the benzyl alcohol initiated decomposition of glyceric acid anhydrosulphite.

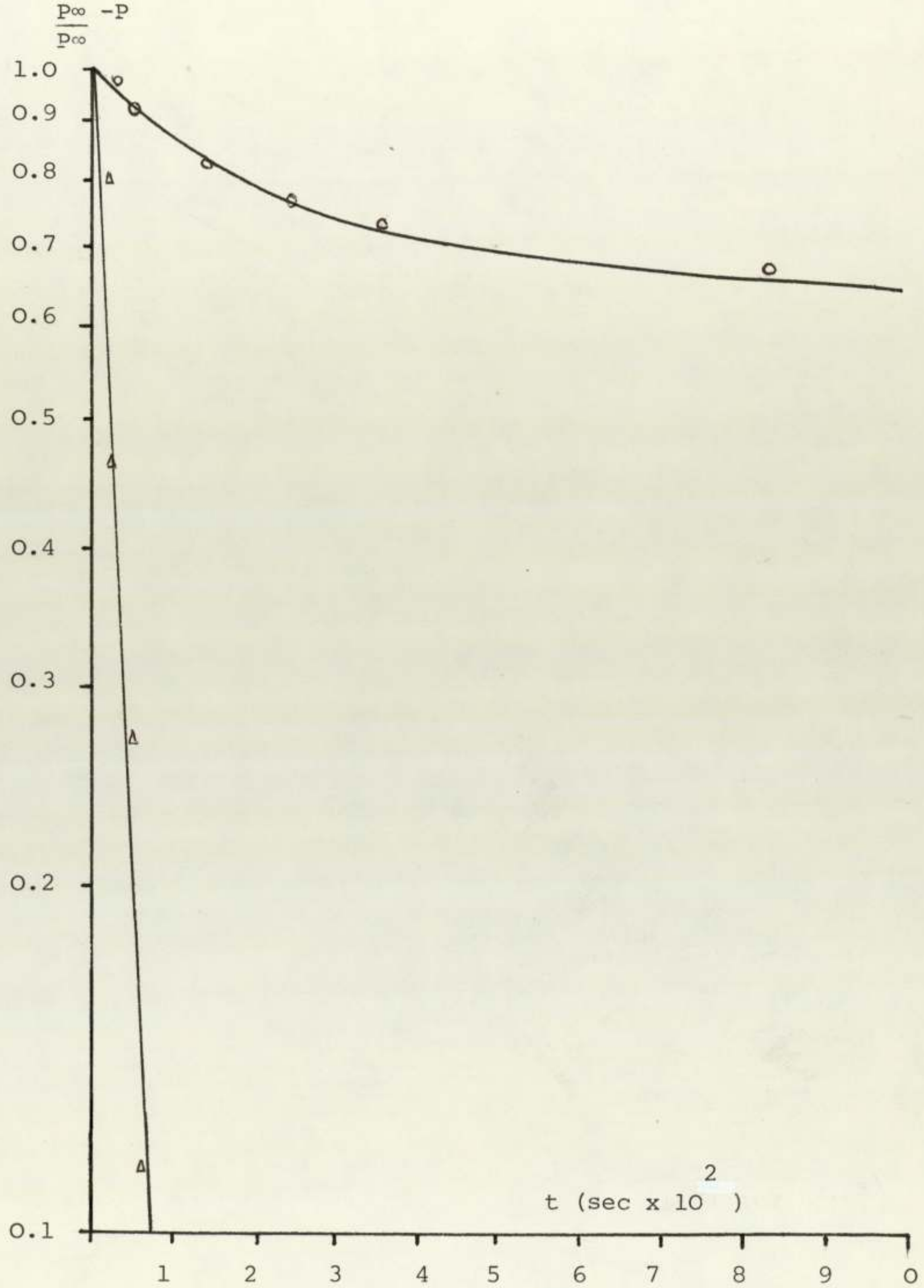
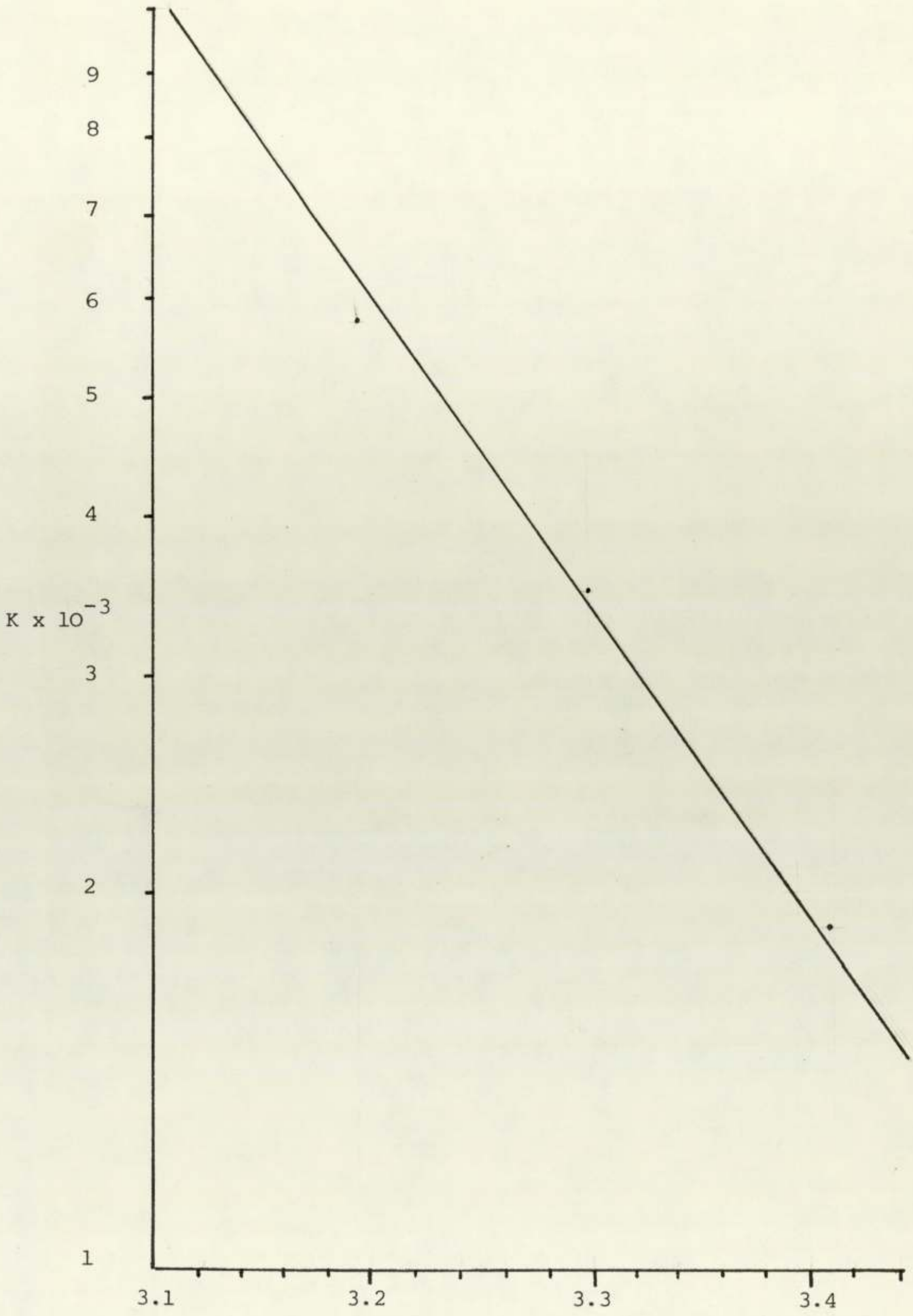


Fig. 3.14 Decomposition of gluconic anhydrosulphite in nitrobenzene at 30°C

O uninitiated
Δ benzyl alcohol initiated



<u>Fig. 3.15</u>

Benzyl alcohol initiated decomposition of gluconic acid anhydrosulphite in nitrobenzene

CHAPTER 4

The Synthesis and reactions of Anhydrosulphites containing substituent carboxylic acid groups

4.1 The Preparation and Reactions of Malic Acid Anhydrosulphite

Malic acid (Fig. 4.1) was obtained in the d,l form from BDH Chemicals Ltd.

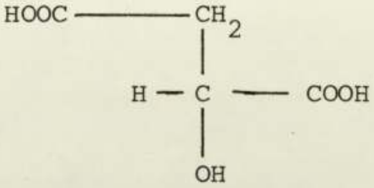


Fig. 4.1 Malic acid

It has been reported that a copper salt suitable for anhydrosulphite preparation can be prepared from malic acid.(67)

Preparation of Cupric Malate

One mole malic acid dissolved in a minimum amount of hot water was treated with one mole ammonia solution in order to neutralize one carboxylic acid group per molecule of acid. This solution was heated to boiling point, a hot solution of 0.5 moles cupric chloride was mixed in and the mixture was boiled for a few minutes. On cooling a pale blue precipitate separated out from the solution. This was filtered off washed and dried in a vacuum oven at 120°C. Thermogravimetric analysis was used to check for the complete removal of water of crystallization from the copper salt.

Gravimetric analysis for copper showed that the copper salt contained 19.5% copper which indicated that the ratio of copper to malic acid was 1:2. An infrared spectrum obtained from the copper salt

contained 19.5% copper which indicated that the ratio of copper to

in the form of a KBr disc showed two absorptions in the carbonyl region at 1600 cm^{-1} and 1710 cm^{-1}. The 1600 cm^{-1} absorption was attributed to the carboxylate anion and the 1710 cm^{-1} to a free carboxylic acid group. It was thus deduced that this copper salt had a structure equivalent to that proposed for the cupric salts of other α-hydroxy acids (Fig. 4.2)

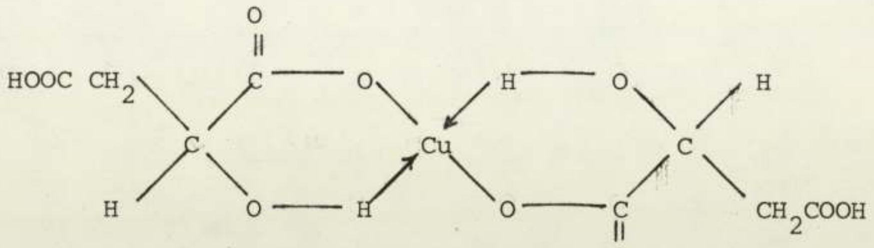


Fig. 4.2: Cupric Malate

Reaction of Thionyl Chloride and Cupric Malate

0.5 moles cupric malate was slurried in 250 mls anhydrous ether and 1.1 moles thionyl chloride added dropwise over a period of 2 - 3 hours maintaining the temperature below 0°C. On completion of the addition of thionyl chloride the mixture was allowed to warm up to room temperature and the reaction continued for four days by which time the copper salt had become brownish yellow, the colour characteristic of anhydrous cupric chloride. The mixture was filtered and the cupric chloride washed with anhydrous ether. The ether and unreacted thionyl chloride was stripped from the filtrate under vacuum, a dark yellow oily liquid remained behind.

4.2 Characterization

The carbonyl region of the infra-red spectrum of the reaction product is shown in Fig. 4.3. There were at least four distinct absorptions which suggested that the product was a mixture of compounds. The principal carbonyl absorptions appeared at 1720 cm^{-1} 1785 cm^{-1}, 1795 cm^{-1} and 1870 cm^{-1}. The first of these (1720^{-1}) was assigned to a free carboxylic acid group which would be present

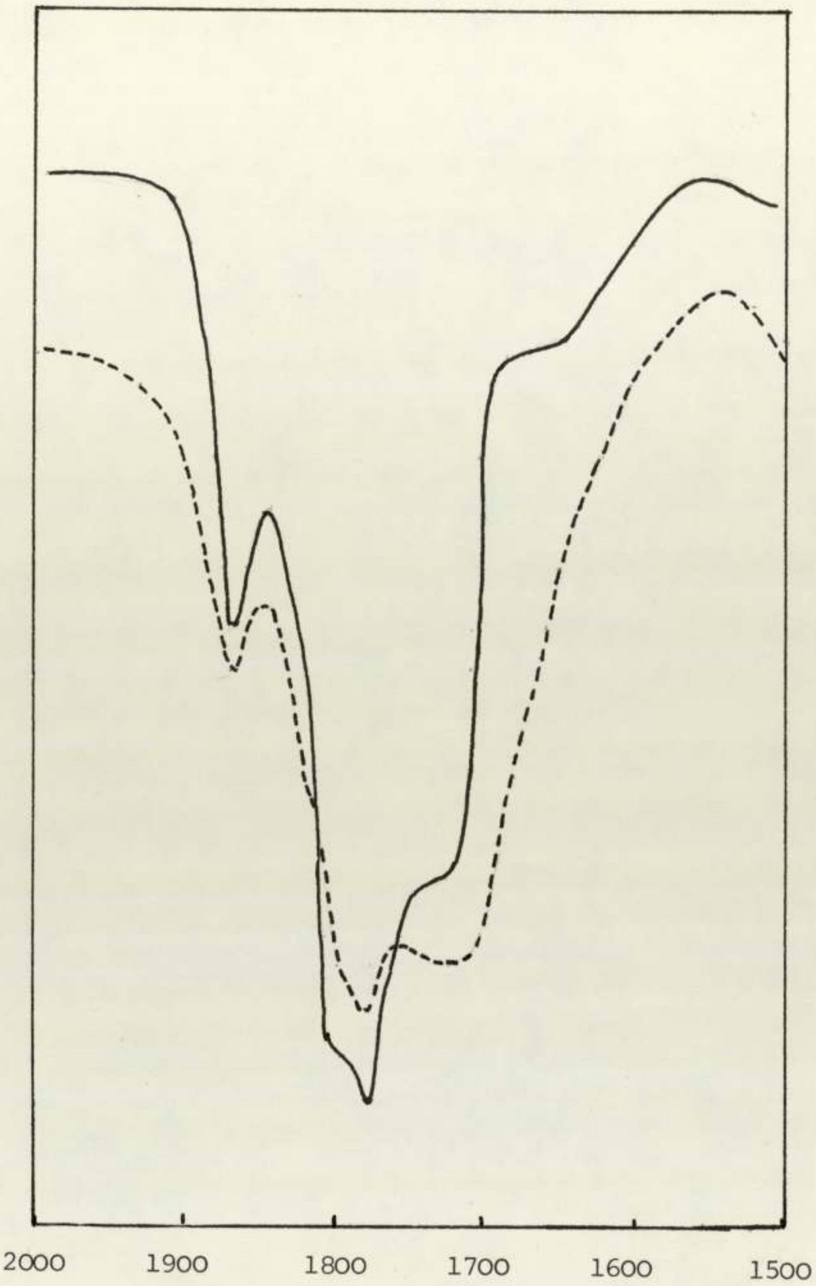


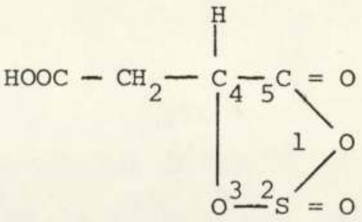
Fig. 4.3

Infra-red spectrum of carbonyl region

—— Cupric malate + Thionyl Chloride

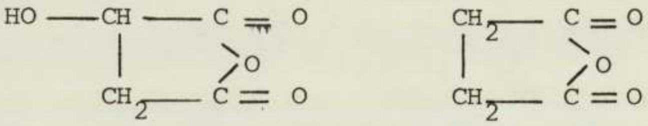
- - - - Cupric malate + phosgene

in the anhydrosulphite. The peak at 1795 cm^{-1} is typical of



the C_5 carbonyl in an anhydrosulphite. The presence of some anhydrosulphite was further confirmed by the presence of a peak at 1230 cm^{-1} which can be assigned to the S = O group in the anhydrosulphite ring.

The peak at 1870 cm^{-1} appeared to be too high for an acid chloride impurity. One relevant class of compounds which exhibits a carbonyl absorption in the 1850 cm^{-1} - 1880 cm^{-1} region is the cyclic anhydrides of dicarboxylic acids such as Malic anhydride (Fig. 4.4 a).


(a) Fig. 4.4 (b)

A similar 5-membered cyclic anhydride, succinic anhydride (Fig. 4.4 b) produced an infrared spectrum with carbonyl absorptions at 1785 cm^{-1} and 1860 cm^{-1}. Allowing for a slight shift caused by the substituent hydroxyl group the carbonyl absorptions at 1785 cm^{-1} and 1870 cm^{-1} observed in the spectrum of the reaction product (Fig. 4.3) were attributed to malic anhydride.

Because it is a stable five membered ring the formation of malic anhydride as the result of an interaction between the acyl chlorosulphite group and the free carboxylic acid group of the intermediate compound, (X) in Fig. 4.5 is feasible. The competing reactions for the formation of the anhydrosulphite and anhydride from the action by thionyl chloride on cupric malate are shown in Fig. 4.5. The feasibility of anhydride formation is further supported by the fact that thionyl chloride is widely used as a reagent in the preparation of carboxylic acid anhydrides(68) although generally more vigorous reaction conditions are employed.

The malic anhydrosulphite mixture reacted vigorously with benzyl alcohol and benzylamine with the evolution of sulphur dioxide although the volume of sulphur dioxide evolved by reaction with excess benzyl alcohol in a kinetic apparatus indicated that the mixture contained about 50% malic anhydrosulphite.

Purification

Being in the form of a high boiling point oil malic anhydrosulphite was not suitable for purification by vacuum distillation or sublimation techniques. A chloride ion titration showed that there was negligible chlorine containing impurity. Unfortunately no acceptable method for separation of the anhydrosulphite and the anhydride could be found.

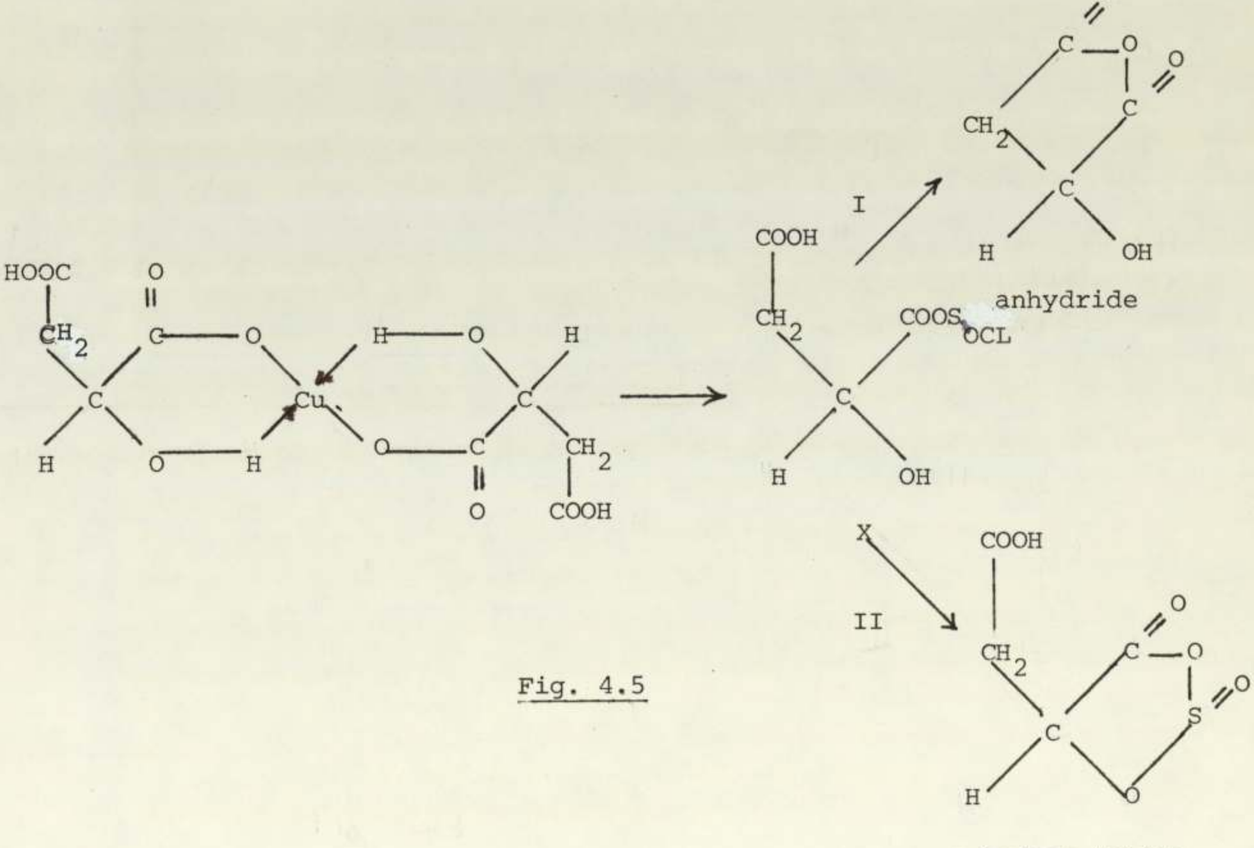


Fig. 4.5

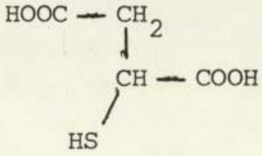
Proposed mechanism for the reaction between cupric malate and thionyl chloride

4.3 Reaction of Cupric Malate and Phosgene

Because of the unusual reactions occurring between cupric malate and thionyl chloride in the attempted synthesis of malic anhydrosulphite an attempt was made to prepare malic anhydrocarboxylate by the action of phosgene on cupric malate.

0.5 moles cupric malate was reacted with 2.1 moles phosgene (Co Cl_2) dissolved in a little ether under the same conditions as those previously described for the preparation of malic anhydrosulphite. The product from this reaction was also a dark yellow oily liquid similar in appearance to the thionyl chloride reaction product The infra-red spectrum of the product showed a pair of carbonyl absorption bands at 1785 cm^{-1} and 1870 cm^{-1} corresponding almost exactly to those observed in the spectrum of the thionyl chloride reaction project. Although carbonyl peaks for the anhydrocarboxylate might be expected to appear around these frequencies the reaction product showed no other characteristics of anhydrocarboxylates no carbon dioxide was evolved on treatment with alcohols or amines. It was, therefore, possible to assume that the anhydride had again been formed in this case to the exclusion of the anhydrcarboxylate.

At this point it seemed a logical extension of the work to include attempts at the preparation of an anhydrosulphite and an anhydrocarboxylate from the thiomalic acid since the work described in this thesis also includes the preparation of anhydrosulphites from the α-thiocarboxylic acids; thioglycollic and thiolactic acid.



An attempt was made to prepare a copper salt of thiomalic acid by the method described previously for the preparation of cupric malate.

A pale buff coloured solid was obtained, similar in appearance to copper salts of thioglycollic and thiolactic acids prepared by Ali (55) which proved ineffective in the preparation of anhydrosulphites or anhydrocarboxylates. It was therefore decided to attempt the preparations by the direct action of thionyl chloride/phosgene on thiomalic acid.

4.4 Reaction of Thiomalic acid and Thionyl Chloride

0.1 mole anhydrous thio-malic acid was slurried in ether and treated with 0.12 moles thionyl chloride under the conditions described for the preparation of malic anhydrosulphite. After about two days reaction at room temperature the acid, which is a solid insoluble in ether had dissolved. However by the fourth day a thick white precipitate had appeared, this was filtered off keeping both the precipitate and the filtrate for investigation.

The white powder had a melting point of about 19°C (thio malic acid has a melting point of 151°C) and darkened to a brown colour on further heating. The infra-red spectrum of this product showed a pair of carbonyl peaks at 1790 cm^{-1} and 1965 cm^{-1} (see Fig. 4 6).

Evaporation of the ether solution eventually yielded a yellowish-white solid having a similar infra-red spectrum to that of the white solid although it also contained a carbonyl peak at 1720 cm^{-1} corresponding to the free carboxylic acid absorption observed in the spectrum of thiomalic acid.

The absorption at 1790 cm^{-1} and 1865 cm^{-1} were again assumed to be derived from the acid anhydride. There appeared to be less evidence of anhydrosulphite formation than that occuring for malic acid. This was borne out by treatment of a known weight of the product with excess benzyl alcohol in a kinetic apparatus in which the yield of sulphur dioxide was only 10% of that calculated for a pure sample of anhydrosulphite of that weight. It is likely, therefore, that in the infra-red spectrum the peaks associated with the anhydrosulphite were completely masked by those associated with the anhydride present in a large excess.

4.5 Reaction of Thiomalic acid and Phosgene

0.1 mole thiomalic acid was treated with 0.15 mole phosgene dissolved in ether under similar conditions to the thionyl chloride reaction. The reaction was allowed to continue for 6 days at room temperature during which time the insoluble acid completely disappeared.

When the solution was evacuated to remove the ether and excess phosgene a white precipitate appeared almost immediately. An infra-red spectrum produced a pair of carbonyl peaks at 1795 cm^{-1} and 1865 cm^{-1} and since the product did not evolve carbon dioxide on treatment with alcohols and amines it was assumed that the acid anhydride had again been found.

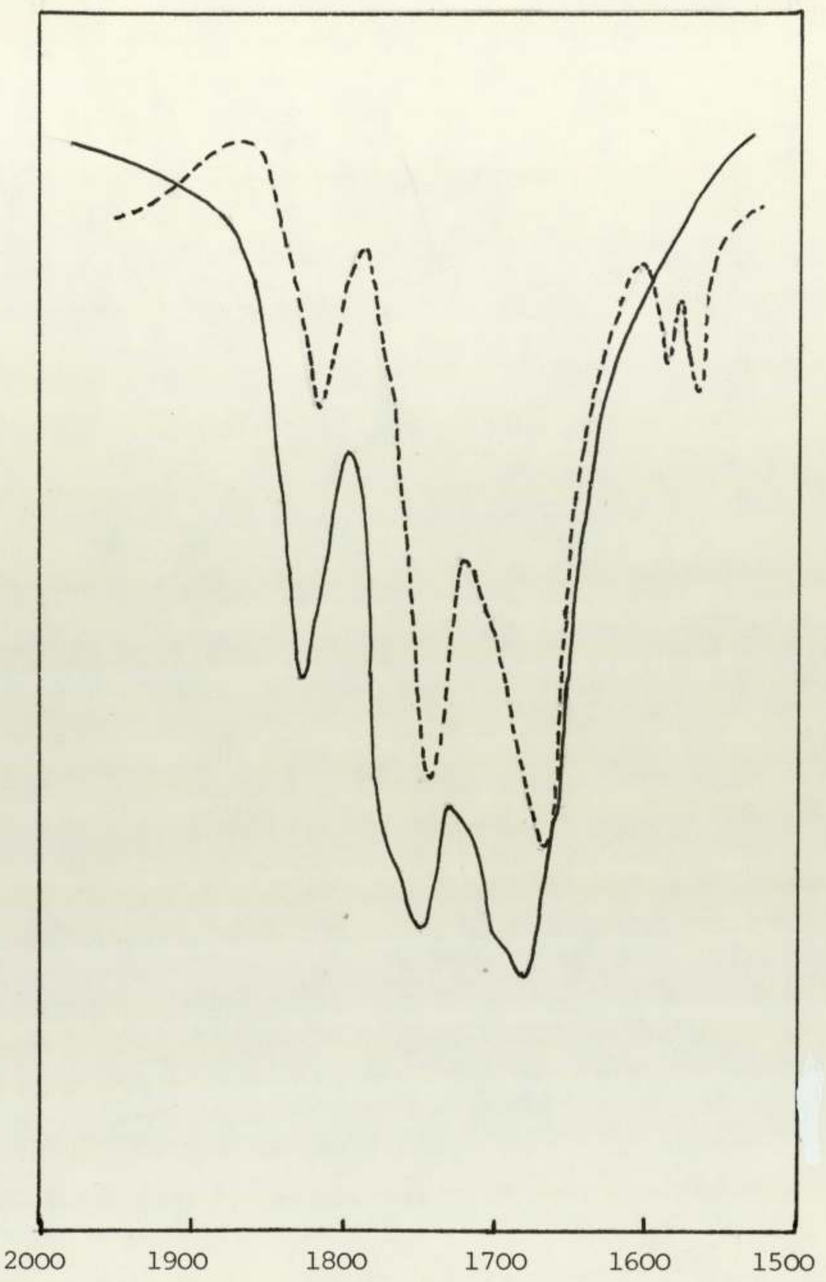


Fig. 4.6

Infra-red spectrum of carbonyl region

—— Thiomalic acid + Thionyl Chloride

- - - - Thiomalic acid + phosgene

4·6 The Preparation of Tartronic Acid Anhydrosulphite

Tartonic acid (Fig. 4.7) is the simplest member of the series of hydroxyl substituted dicarboxylic acids.

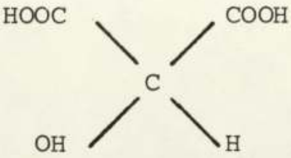


Fig. 4.7

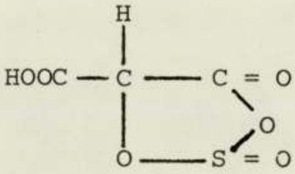
An attempt was made to prepare a copper salt from tartronic acid using the method which proved successful in the preparation of cupric malate described earlier in this chapter using a 2:1 molar ratio of tartonic acid to cupric chloride.

The resulting pale blue powder was analysed by infra-red spectroscopy and gravimetric analysis for copper. The infra-red spectrum showed a single broad carbonyl absorption centering at 1600 cm^{-1}, typical of the carboxylate anion and the copper analysis showed the ratio of copper to tartronic acid to be 1:1. Addition of a further amount of curpic chloride to the filtrate resulted in the formation of more of a similar copper salt. Since the two carboxylic acid groups of tartronic acid are equivalent it seems to be impossible to specifically bond only one of these to a metal ion. Since a copper salt of this structure would not be suitable for anhydrosulphite preparation it was decided to attempt to synthesize the anhydrosulphite directly from the acid.

Tartronic acid is a solid at room temperature but in unstable to heat. Trace moisture was removed by standing the material over phosphorus pentoxide in a vacuum dessicator for several days. 0.2 moles of the acid was slurried in 100 mls. anhydrous ether and 0.3 moles of thionyl chloride was added dropwise to the mixture over about one hour, keeping the temperature below 0°C. The reaction mixture was allowed to warm up to room temperature and stirred for a further four days. During this time the solid acid disappeared completely and the solution turned a pale yellow colour which was taken as an indication that reaction has taken place. The excess thionyl chloride and ether were stripped off under vacuum to leave a pale yellow viscous liquid.

Characterization

The infra-red spectrum of the reaction product is shown in Fig. 4.8. There are two strong absorptions in the carbonyl region at 1740 cm^{-1} and 1825 cm^{-1}. The peak at 1740 cm^{-1} was attributed to the



substituent carboxylic acid group since its position was similar to that of the carbonyl absorption shown by the infra-red spectrum of tartronic acid (Fig. 4.9). The peak at 1825 cm^{-1} was attributed to the ring carbonyl group of the anhydrosulphite. The spectrum also has a peak at 1250 cm^{-1} which was attributed to the $>S = O$ group of the anhydrosulphite. Again a potentiometric titration with silver nitrate solution gave a chloride ion content of $<1\%$ indicating that there was negligeable acid chloride impurity.

The reaction product reacted with water to yield the pure acid the quantity of sulphur dioxide evolved was indicative of the high purity of the anhydrosulphite.

4.7 Decomposition Reaction of Tartronic Acid Anhydrosulphite

A preliminary experiment with pure benzyl alcohol showed that the rate of decomposition of tartronic acid anhydrosulphite in pure benzyl alcohol was slow enough to be measured conveniently at temperatures above 20°C. The kinetic profiles were similar to those obtained [illegible] acid anhydrosulphite.

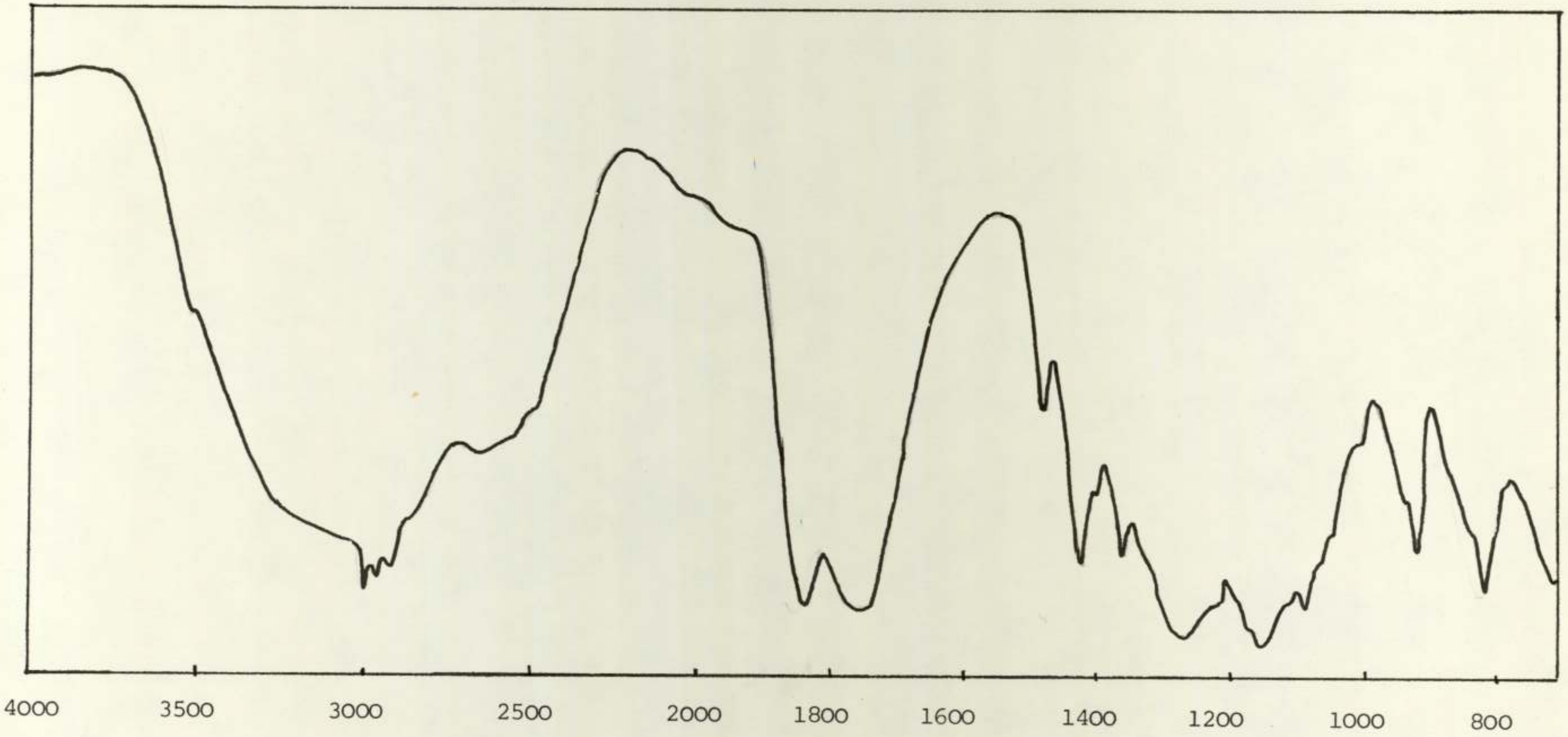


Fig. 4.6

Infra-red spectrum of tartronic acid anhydrosulphite

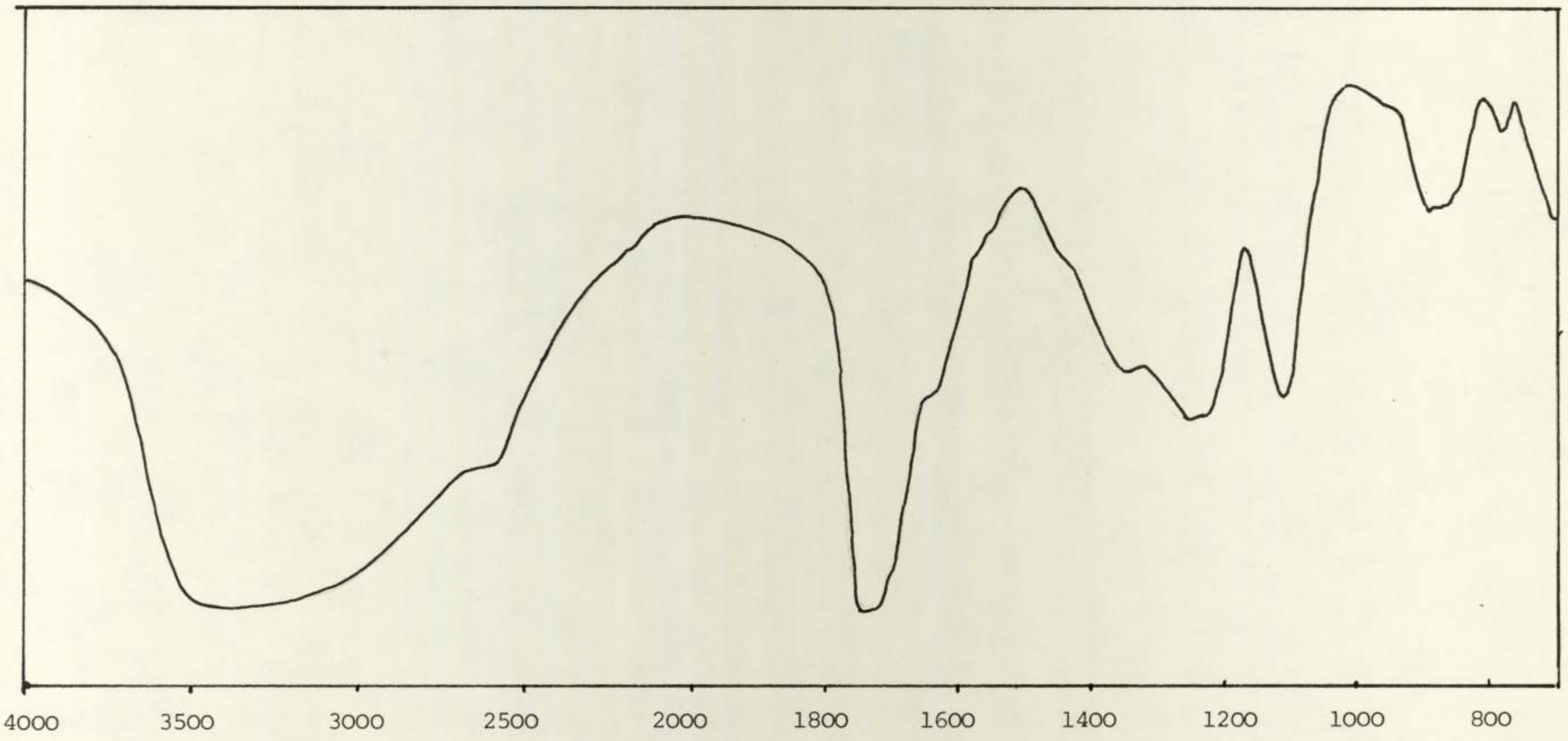


Fig. 4.9

Infra-red spectrum of tartronic acid

thereby enabling kinetic parameters to be determined.

The kinetic profiles obtained were similar to those obtained for the decomposition of glyceric acid anhydrosulphite in the presence of excess benzyl alcohol, with the important difference that tartronic acid anhydrosulphite showed no measureable tendency to undergo self decomposition. Thus a first order dependence on both the monomer and the initiating nucleophile (in this case benzyl alcohol) was obtained. The techniques of kinetic measurements and calculations used for the benzyl alcohol initiated decomposition of tartronic acid anhdrosulphite were thus similar to those described for glyceric and gluconic acid anhydrosulphite in the previous chapter.

Decomposition of Tartronic Acid Anhydrosulphite in Benzyl Alcohol

In each of the four kinetic runs carried out at temperatures between 20 and 40°C about 0.2 mls anhydrosulphite was measured into a low temperature kinetic apparatus and 5 mls of anhydrous benzyl alcohol injected in after evacuation. Both first and second order rate constants (k an k') were obtained at each temperature (table 4.1) which allowed the activation energy (El) to be calculated. The frequency factor (A) and the entropy of activation ($\Delta S^{\ddagger}$) were calculated for the reaction of 30°C.

Decomposition of Tartronic Acid Anhydrosulphite by Benzyl Alcohol in Anisole

The study of the decomposition of tartronic acid anhydrosulphite by benzyl alcohol in the presence of a co-solvent was carried out in order to be able to make comparisons with the benzyl alcohol initiated decomposition of other anhydrosulphites.

T°C	$\frac{1}{T}$ °K x 10^{-3}	$t_{\frac{1}{2}}$	K x 10^{-4}	K' x 10^{-5}
21	3.401	4380	1.58	1.97
30	3.300	1980	3.50	4.38
35	3.246	1095	6.33	7.91
40.05	3.190	480	15.4	19.3

$$E = 18.8 \text{ K cal mole}^{-1}$$

$$\text{At } 30^{\circ}\text{C} \quad A = 4.95 \times 10^{6}$$

$$\Delta S^{\ddagger} = -29.94$$

Table 4.1

Decomposition of Tartronic acid anhydrosulphite in benzyl alcohol

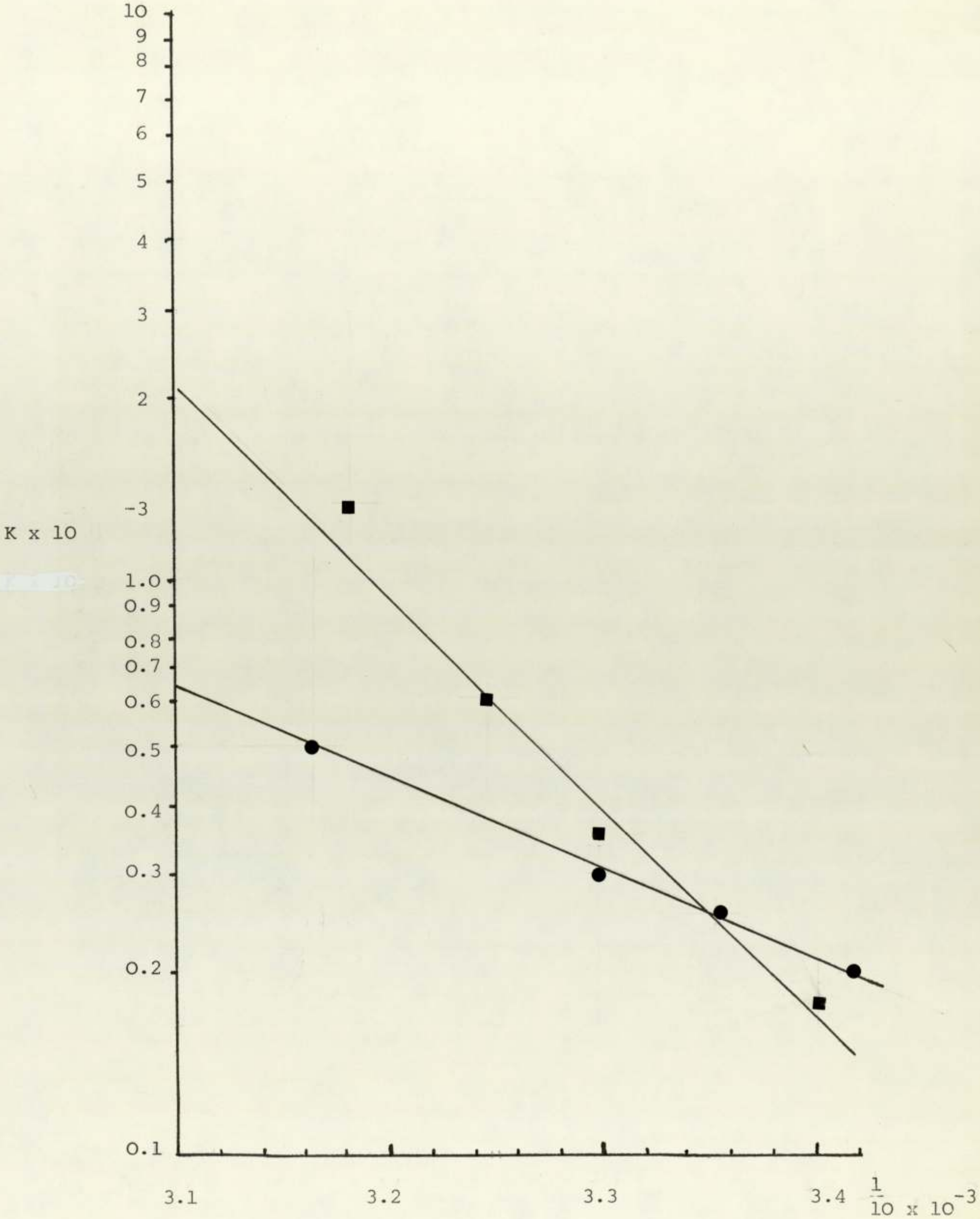


Fig. 4.10

Decomposition of Tartronic Acid Anhydrosulphite

■ in benzyl alcohol

● in anisole

T^oC	$\frac{1}{T}$ $^oK \times 10^{-3}$	$t_{\frac{1}{2}}$	$K \times 10^{-3}$	$K \times 10^{-3}$
20	3.413	348	1.99	3.98
30	3.356	275	2.52	5.04
35	3.300	235	2.95	5.90
40	3.185	140	4.95	9.90

$E = 8.7$ K cal $mole^{-1}$

At 30^oC $A = 1.17 \times 10^{-4}$

$\Delta S^{\ddagger} = - 41.94$

Table 4.2

Decomposition of Tartronic acid anhydrosulphite by benzyl alcohol in Anisole

It would have been preferable to use nitrobenzene as the cosolvent since this was used for the benzyl alcohol initiated decomposition of glyceric and gluconic acid anhydrosulphites but the reaction product formed a gel with nitrobenzene which interfered with the homogeneity of the reaction mixture. The gel was not formed when anisole was used as a solvent and it was thus chosen as a suitable medium for the reaction. Reations were carried out as described before substituting a one molar solution of benzyl alcohol in anisole for the pure benzyl alcohol. The results are summarized in Table 4.2 and Fig. 4.10.

A surprising feature of this reaction was that the decomposition of tartronic acid anhydrosulphite by benzyl alcohol proceeds considerably faster in the presence of anisole and the thermodynamic parameters were quite different. A further, more detailed discussion of these results will be found in the next chapter.

Reaction Products

The infra-red spectrum of the product from the benzyl alcohol

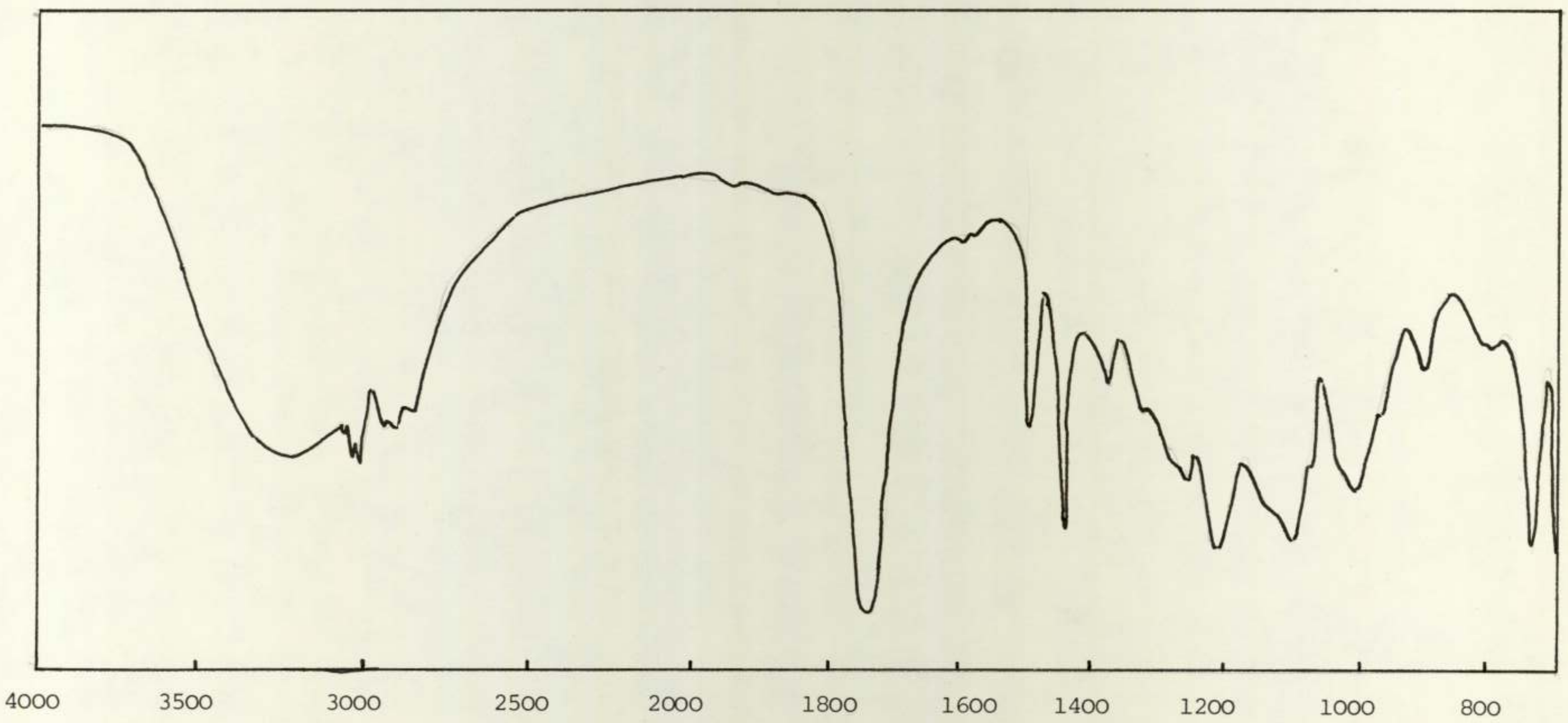


Fig. 4.11

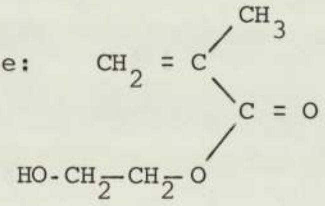
Reaction product tartronic acid anhydrosulphite + benzyl alcohol initiated decomposition of tartronic acid anhydrosulphite is shown in Fig. 4.11.

4.8 An Investigation into the Possibility of Using Tartronic Acid Anhydrosulphite in Grafting Reactions

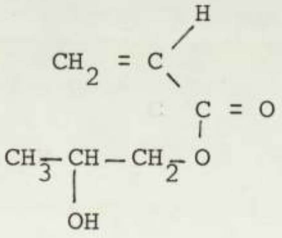
The preceding results show that tartronic acid anhydrosulphite reacts readily with the nucleophilic hydroxyl of benzyl alcohol and that anisole is a suitable solvent for this reaction. For grafting to take place there must be similar nucleophilic sites available pendant to the backbone of the polymer. Several vinyl monomers used in the preparation of hydrogel polymers contain an apparently suitable hydroxyl group, of these, three were chosen for this investigation:

2 Hydroxy ethyl Methacrylate:

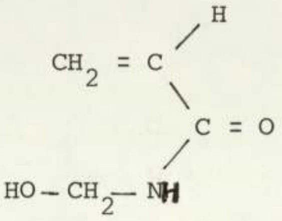
(HEMA)

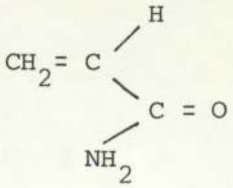


2 Hydroxy propyl acrylate:



N-methylol acrylamide





The possible use of acrylamide:

was also investigated in order to see if the $-NH_2$ group was nucleophilic enough to bring about the ring-opening of anhydrosulphites by direct attack at the carbonyl group. Solutions of 1 mole/l of each monomer were made up in anisole so that the same ratio $\frac{[OH]}{[M]}$ was used in each reaction. Fig. 4.11 shows for comparison the kinetic profiles of these reactions in the form of pressure of evolved sulphur dioxide against time for the decomposition of tartronic acid anhydrosulphite using benzyl alcohol, HEMA, HPA, NMAc and Acrylamide as initiators. From the graph it can be seen that benzyl alcohol produces the fastest rate of decomposition although the N-methylol acrylamide reaction is only marginally slower. Perhaps surprizingly HEMA and HPA react very slowly: an infra-red spectrum taken after 24 hours indicated that there was still some unreacted anhydrosulphite in the mixture. On this basis it was surprising that acrylamide decomposed the anhydrosulphite at a reasonable rate since it is known that carboxylic acids do not decompose anhydrosulphites, it must therefore be assumed that the NH_2 group was sufficiently nucleophilic to over come the deactivating effect of the carboxyl group.

These results indicate that the monomer N-methylol acrylamide will be most useful for grafting and it is likely that its hydroxyl group will be able to provide an active site for anhydrosulphite polymerization where it is incorporated in a hydrogel-forming polymer.

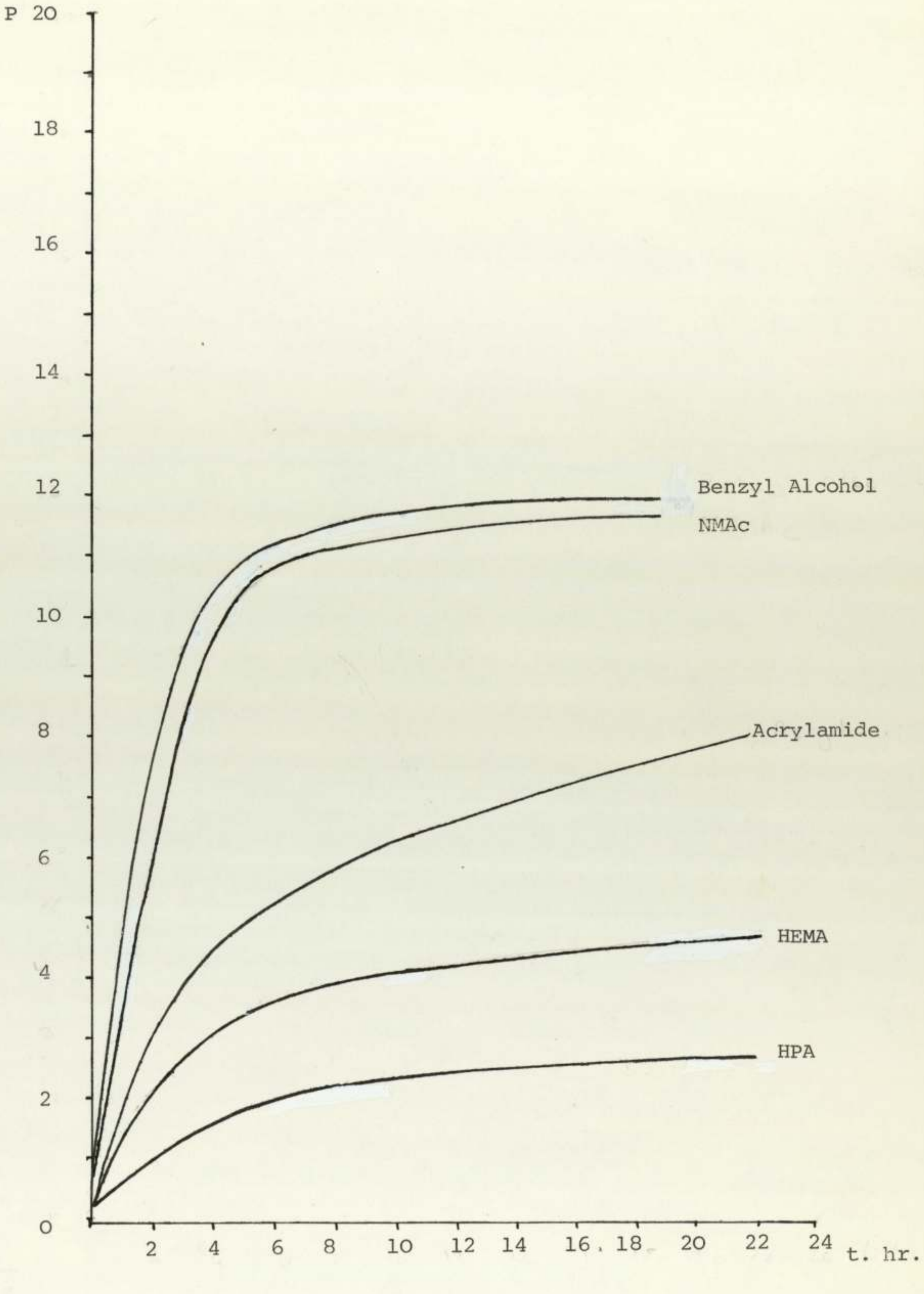


Fig. 4.11

Decomposition of tartronic acid anhydrosulphite by Vinyl Monomers

CHAPTER 5

Discussion of Hydroxyl and Carboxylic acid substituted Anhydrosulphites

5.1 Anhydrosulphite preparation

The preparation of anhydrosulphites from α-hydroxy acids with functional hydroxyl and carboxylic acid substituents presented several problems not previously encountered with in the preparation of anhydrosulphites from simple aliphatic and aromatic substituted α-hydroxy acids studied by previous workers.

Both the acids with hydroxyl-containing substituents; glyceric acid and gluconic acid formed unstable metal salts which were difficult to dry but it was necessary to use these because it was not possible to obtain the acids themselves in the anhydrous state. The reaction with thionyl chloride required a short reaction time and low temperature in order to minimize the competing self-decomposition reaction brought about by the presence of nucleophilic hydroxyl groups on the substituent, R, of the anhydrosulphite. Fortunately there was little tendency to the formation chlorine containing impurities. Because of this inherent tendency towards self-decomposition it was not possible to purify the anhydrosulphites by the usual distillation techniques as those conditions would promote the complete decomposition of the anhydrosulphites but it was possible, by storing the anhydrosulphite at a very low temperature (below -40°C), to inhibit the decomposition sufficiently to enable kinetic studies to be made.

Tartronic acid also presented problems in the preparation of a suitable metal salt. It was found to be impossible to prepare a copper salt in which only one of the two equivalent carboxylic acid groups is bonded ionically. The composition of Copper (II) compounds of tartronic acid have been studied by Popovich and others who found that copper forms complex anions with tartronic acid in the presence of ammonia and other alkalis and that only the compound $CuCHOH(COO-)_2 \cdot 3H_2O$ can be separated out from solution.(69)(70) Fortunately tartronic acid is a solid which can be dried easily and it was found that the anhydrosulphite could be successfully prepared by the direct action of thionyl chloride on the acid. Analysis showed that the anhydrosulphite prepared by this technique was reasonably pure, having a small amount of chlorine-containing impurity which could be effectively removed by treatment with baked silver oxide. The high boiling point of the anhydrosulphite precluded the use of vacuum distillation as a means of purification since even at low pressure the required distillation temperatures led to the complete decomposition of the anhydrosulphite. Tartronic acid anhydrosulphite was the only anhydrosulphite with a substituent functional group, of those attempted in this study, that could be obtained in a sufficiently pure state to enable detailed kinetic studies to be carried out from comparison with previous studies involving non-functional anhydrosulphites. Malic acid, although structurally similar to tartronic acid was interesting in the fact that whilst a suitable copper salt could be readily prepared, the preparation of the anhydrosulphite was impaired by the tendency towards the formation of malic anhydride during the thionyl chloride reaction. It is likely that this problem will only arise in the case of malic acid because the anhydride formed from it is a five-membered ring which is particularly favourable on account of its thermodynamic stability, whereas an anhydride formed from tartronic acid would be a four-membered ring which is thermodynamically unstable compared with the five-membered anhydrosulphite ring. The same problem was incurred in attempting to prepare the anhydrocarboxylate of malic acid by the phosgene reaction and also the anhydrocarboxylate and anhydrosulphite of the sulphur-containing analogue: thiomalic acid. Unfortunately no viable method for separating the anhydrosulphite from the anhydride could be found since, like tartronic acid anhydrosulphite, its high boiling point and reactivity preclude the use of distillation techniques.

Although the anhydrosulphites of glyceric, gluconic and malic acids were insufficiently pure to allow polymerization they nevertheless have a potential use in grafting reactions where substituent nucleophiles can react specifically with the anhydrosulphites allowing undesirable impurities to be removed by subsequent washing.

5.2 Decomposition Reactions of Hydroxyl-substituted Anhydrosulphites

The semi-logarithmic plots of $\frac{[M]}{[M]_o}$ against t obtained for the uninitiated decomposition of both glyceric and gluconic acid anhydrosulphites in nitrobenzene (Figs. 3.5 and 3.14) were non-linear indicating that the reaction was not following first order behaviour. The shape of the curve was consistent with a decrease in the rate of reaction as time proceeded. The activation energy of 15.6 K cal mole^{-1} obtained for glyceric acid anhydrosulphite from the apparent first order rate constant measured during the initial stages of the reactions was consistent with a reaction mechanism involving the bimolecular interaction between a nucleophilic species and a molecule of anhydrosulphite as introduced in Fig. 1.8 and specifically illustrated in Fig. 5.1. If we presume that attack occurs as shown it can be seen that although the overall concentration of hydroxyl groups present in the reaction system remains unchanged their molecular environment, which affects the nucleophilicity is changed. Before reaction the

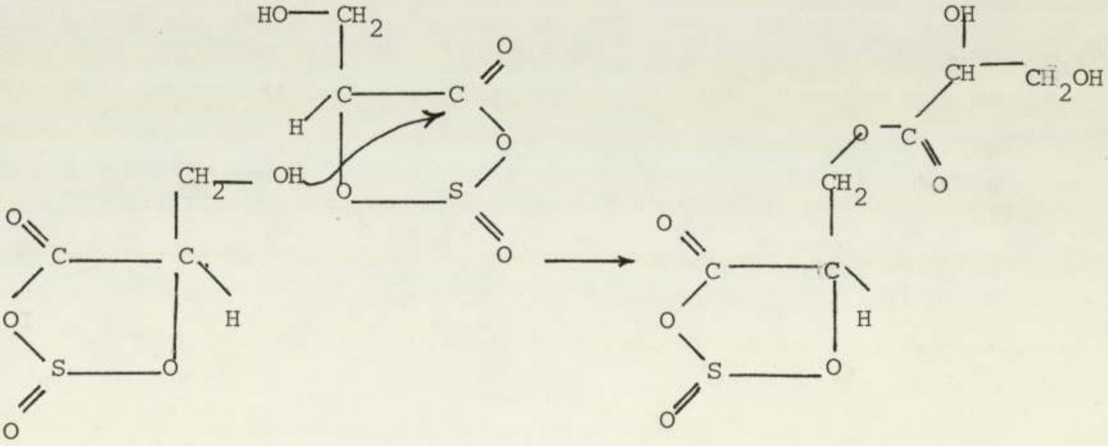


Fig. 5.1

the hydroxyl groups of the two anhydrosulphite molecules are both in the same primary position whereas in the reaction product one hydroxyl group remains in the primary position whilst the hydroxyl group produced from the decomposed anhydrosulphite is in a secondary position adjacent to a carbonyl group. It is likely that the secondary hydroxyl group will be appreciably less reactive than primary hydroxyl group since the adjacent groups both reduce its nucleophilicity and sterically interfere with its interaction with another anhydrosulphite molecule. Here there is a similarity to the benzyl alcohol initiated polymerization of anhydrosulphites (Fig. 3.7 a and b), where the rate of initiation (K_1) and rate of propagation (K_2) are often different due to the differing nucleophilicities of the attacking species in the initiation and propagation steps. When K_2 is less than K_1 a similar curve to the semi-log plot of $\frac{[M]}{[M]_o}$ against time for the uninitiated decomposition of glyceric and gluconic acid anhydrosulphites is observed. Also studies of the rate of decomposition of anhydrosulphites by different initiating species (e.g. the vinyl monomers HPA and NMAc described in Chapter 4) demonstrate that the rate of decomposition is affected by the nature of R_2CHOH.

If, in the extreme case, we assume that the rate of decomposition of the anhydrosulphite by the terminal primary hydroxyl group is very much greater than the rate of decomposition by the secondary hydroxyl group we might expect that the apparent first order rate constant, measured from the slope of a tangent to the curve of log $\frac{[M]}{[M]_o}$ against t, at 50% conversion ($\frac{[M]}{[M]_o} = 0.5$) would be at the most only half the value of the initial apparent first order rate constant. Table 5.1 shows that experimental values fit in well with this hypothesis.

T ^{o}C	K_i K Cal Mol^{-1}	K(0.5) K Cal Mol^{-1}
10.8	4.28×10^{-4}	2.05×10^{-4}
36	5.86×10^{-5}	2.85×10^{-5}

Table 5.1

This point is further reinforced by the fact that the decomposition of both glyceric and gluconic acid anhyrosulphites in the presence of excess benzyl alcohol (Figs. 3.5 and 3.14) showed kinetic behaviour which was approaching first order kinetics. Thus in the presence of an excess of primary hydroxyl groups first order behaviour is observed because the concentration of the active nucleophile does not greatly diminish during the reaction whereas in uninitiated decomposition the concentration of primary hydroxyls decreases as shown by the reaction sequence of Fig. 5.2.

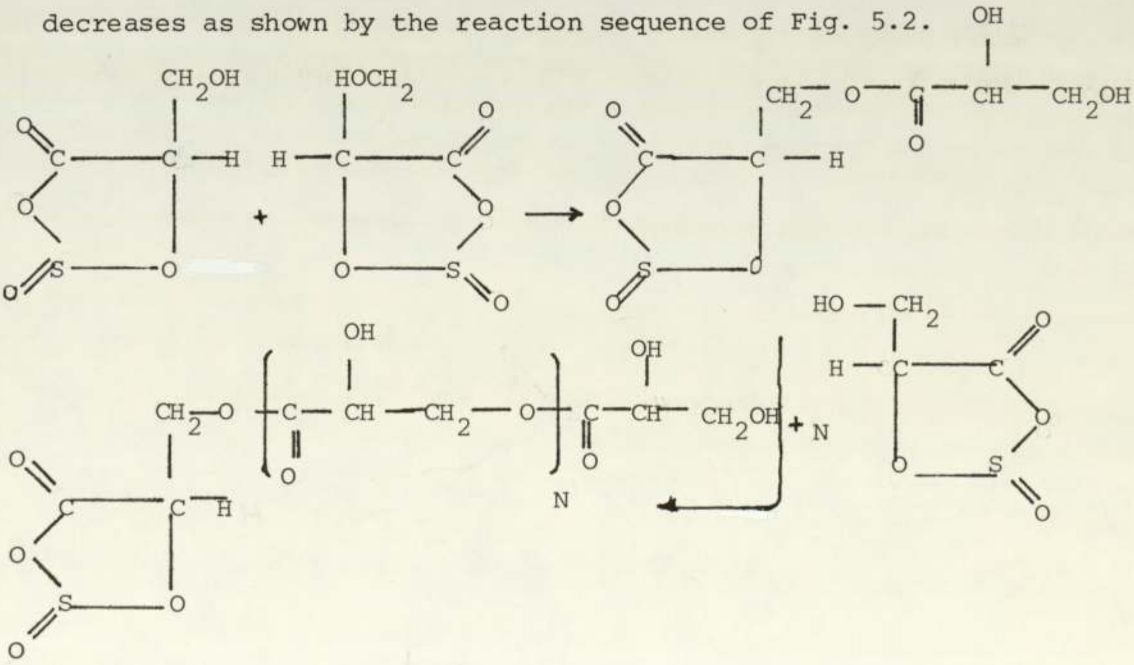
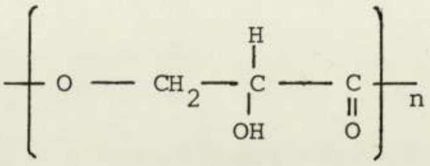


Fig. 5.2

The activation energy obtained for the benzyl alcohol initiated decomposition of glyceric and anhydrosulphite at 21.6 K cal/mole (page 56) was similar to that of the self initiated decomposition indicating that the rate-determining reaction was a bimolecular reaction. Because of the high reactivity of the terminal primary hydroxyl group compared with the secondary hydroxyl group it would be expected that any polymerization occuring would lead not to the formation of a poly-α-ester but a hydroxyl-substituted poly-ester with the repeat unit shown below.



$$\left[-O-CH_2-\overset{\overset{H}{|}}{\underset{\underset{OH}{|}}{C}}-\underset{\underset{O}{\|}}{C}- \right]_n$$

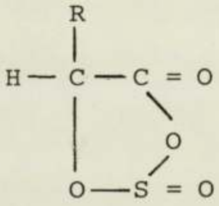
There is also the possibility of a small amount of branching through polymerization at the substituent hydroxyl groups. Unfortunately because the anhydrosulphite could not be purified effectively no high molecular weight polymer was obtained for any detailed analysis.

Similarly in the case of gluconic acid anhydrosulphite, where there are five hydroxyl groups on the substituent of the anhydrosulphite, there are five possible reaction sites within each monomer unit which makes the formation of a substituted poly-α-ester extremely unlikely. Again the curved semi-log plot of $\frac{[M]}{[M]_0}$ against time indicates that the terminal primary hydroxyl group is more reactive than the secondary hydroxyl groups.

5.3 A Comparison of the Decomposition Characteristics of Tartronic Acid Anhydrosulphite with those of other Anhydrosulphites.

Tartronic acid anhydrosulphite was the only anhydrosulphite of those attempted in Chapters 3 and 4 which could be obtained in a relatively pure state. The kinetics of its decomposition in excess benzyl alcohol showed good first order behaviour making it possible to compare the kinetic data obtained with that of other anhydrosulphites obtained by previous workers in the field.

If we limit the study to monosubstituted anhydrosulphites of the general formula:



three anhydrosulphites:- glycollic (R = H), lactic (R = CH_3) and mandelic (R = C_6H_5) have been well studied and are thus suitable for a comparative study. Table 5.2 shows the second order rate constants (K), activation energies (E), frequency factors (A) and entropy of activation ($\Delta S^{\ddagger}$) for the decomposition of these anhydrosulphites in neat benzyl alcohol.

$T^{o}C$	$\frac{1}{T^{o}}$ K x 10^{-3}	K			
		Glycollic	Lactic	Mandelic	Tartronic
21	3.401				1.9×10^{-5}
30	3.300				4.4×10^{-5}
35	3.246				7.9×10^{-5}
40	3.195	1.0×10^{-5}		4.4×10^{-5}	1.75×10^{-4}
45	3.145		1.0×10^{-5}		
60	3.003	5.3×10^{-5}		1.8×10^{-4}	
65	2.959		2.5×10^{-5}		
75	2.874			6.5×10^{-4}	
80	2.832	3.0×10^{-4}			
90	2.755	3.7×10^{-4}	8.5×10^{-5}	1.1×10^{-3}	
E (K cal $mole^{-1}$)		15.2	12.4	14.2	18.8
A (l $mole^{-1}$ sec^{-1})		5.0×10^{5}	2.7×10^{3}	4.1×10^{5}	4.95×10^{6}
$S^{\ddagger}$					29.94

Table 5.2

Fig. 5.3 illustrates the semi-log of K against $\frac{1}{T}$ for the four anhydrosulphites, plotted on the same set of axes. From this it was possible to make comparisons between the rates of decomposition in benzyl alcohol of the four anhydrosulphites at a particular temperature, with a view to determining the effect of the substituent, group R on these rates. The values of the activation energies obtained for the anhydrosulphites indicate that the rate determining step in the reaction is the bimolecular attack of the nucleophilic hydroxyl group on the C_4 carbonyl of the anhydrosulphite. Studies involving the addition of anhydrous carboxylic acids to anhydrosulphites show that the

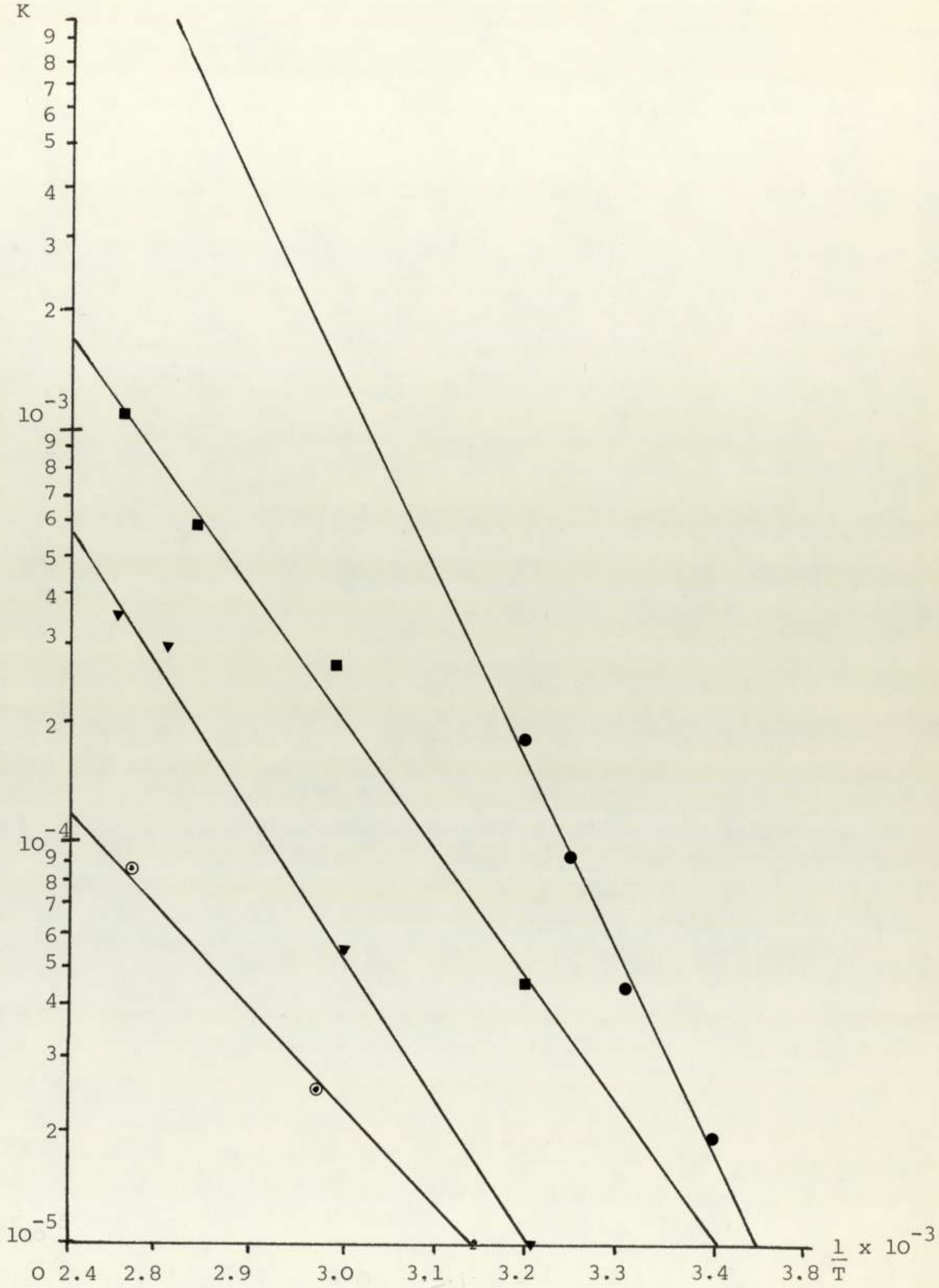


Fig. 5.3

▼ glycollic	■ mandelic
⊙ lactic	● tartronic

carboxylic acid group does not decompose the anhydrosulphite. Thus the substituent R of tartronic acid anhydrosulphite does not compete with benzyl alcohol in the reaction.

To determine the relative steric and electronic effects of the C_5 substituent on the rate of decomposition we must first consider the configuration of the ring and the direction of the attack of the hydroxyl group. The anhydrosulphite ring is essentially planar although slightly puckered, with the oxygen atoms of the $>C = O$ and $>S = O$ groups lying in the plane of the ring and the C_5 substituents lying either side of the same plane. By analogy with the nucleophilic decomposition of N-carboxy α-amino acid anhydrides it is assumed that the attacking hydroxyl approaches from behind, in line with the C-O bond of the C_4 carbonyl group as pictured in Fig. 5.4. Consequently the presence of two bulky C_5 substituents would considerably hinder this attack.

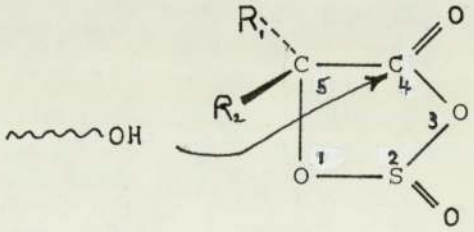


Fig. 5.4

In the case of anhydrosulphites where there is only one C_5 substituent it is likely that attack occurs predominantly from the unsubstituted side in which case the size of that substituent will have little effect on the ease of attack. It is expected, that in the case of glycollic anhydrosulphite ($R_1 = R_2 = H$), where there are no bulky C_5 substituents, consideration of the steric effects alone would indicate that the reactivity of the ring would be increased by a factor of two.

Table 5.3 compares the rate constants (K) for the decomposition of glycollic, lactic, mandelic and tartronic anhydrosulphites in benzyl alcohol at different temperatures taken from the plots of Fig. 5.3. At temperatures greater than 20°C the reactivity of the anhydrosulphites increases in the order:

Lactic $<$ glycollic $<$ mandelic $<$ tartronic

It was attempted to correlate these results with the relative electron-withdrawing effect of the C_5 substituent on the reactivity of the C_4 carbonyl. The electron-withdrawing effect of a particular group can be expressed numerically in terms of its 'Taft' polar substituent coefficient (σ^*). σ^* for a group R is defined by the equation:

$$\sigma^* = (1/2.48)\ (\log\ (\frac{k}{k_o})_B - \log\ (\frac{k}{k_o})_A) \quad (71)(72)$$

where k is the rate constant for the hydrolysis of an ester $RCOOR'$, k_o being the rate constant for $R = CH_3$, A referring to the rate of acid-catalysed hydrolysis and B referring to base-catalysed hydrolysis.

Table 5.4 gives the Taft constants for R = H, CH_3 C_6H_5 and -COOH together with those for the groups CH_2R which may be more relevant to the electronic effect of the substituent R on the reactivity of the C_4 carbonyl in the anhydrosulphite.

Figs. 5.5 and 5.6 illustrate the plots of k against σ^* for the four anhyrosulphites at the temperatures of table 5.3, Fig. 5.5 takes the value of σ^* for R alone whilst Fig. 5.6 takes the value of σ^* for CH_2R. The rate constant for

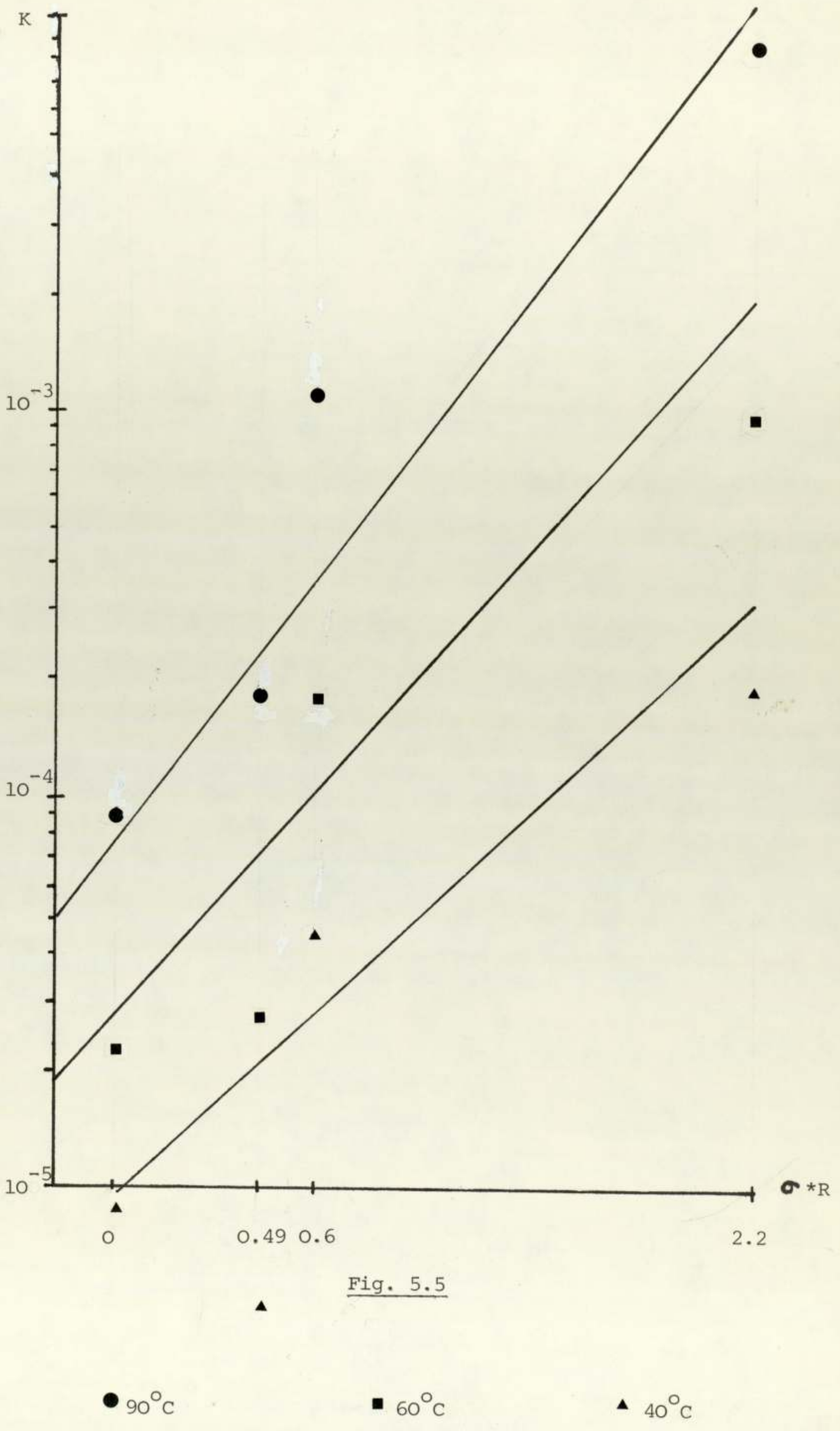


Fig. 5.5

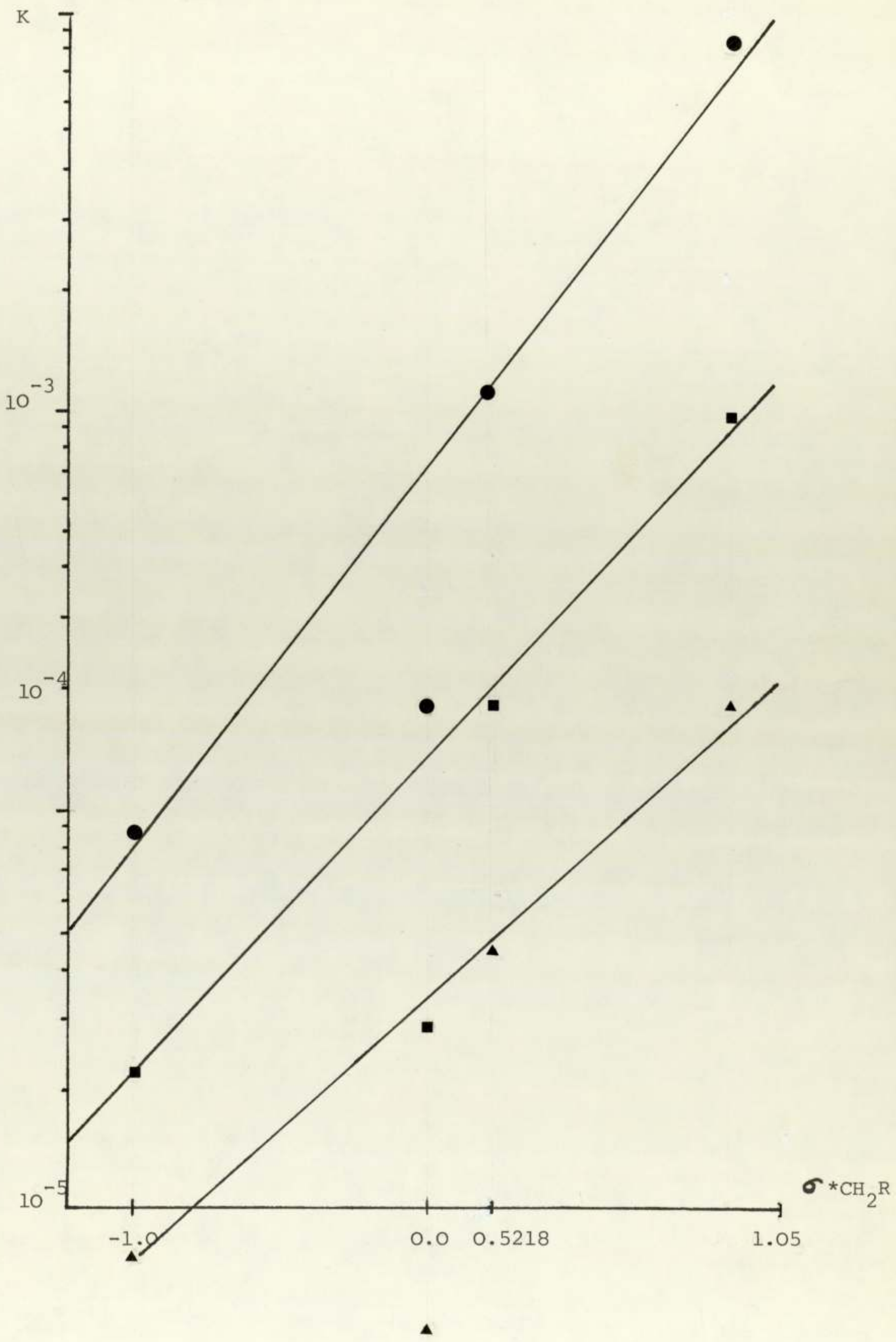


Fig. 5.6

glycollic anhydrosulphite is halved in order to take account

Temp	k			
	glycollic	lactic	mandelic	tartronic
$40^{\circ}C$	1.0×10^{-5}	7.5×10^{-6}	4.4×10^{-5}	1.75×10^{-4}
$60^{\circ}C$	5.6×10^{-5}	2.2×10^{-5}	1.8×10^{-4}	9.4×10^{-4}
$90^{\circ}C$	3.7×10^{-4}	8.5×10^{-5}	1.1×10^{-3}	8.1×10^{-3}

Table 5.3

Comparison of rate constants of glycollic, lactic, mandelic and tartronic anhydrosulphites at various temperatures

	glycollic	lactic	mandelic	tartronic
R	H	CH_3	C_6H_5	COOH
σ^*R	0.490	0.000	0.600	2.20
σ^*CH_2R	0.000	-1.000	0.216	1.05

Table 5.4

Taft polar substituent constants

of the steric effect of the absence of any bulky substituent group allowing attack to take place equally from both sides of the ring. From both figures it can be seen that, at any particular temperature the rate constants of lactic, mandelic and tartronic acid anhydrosulphites when plotted against the taft constant, σ^*, for the substituent group lie roughly on a straight line, although a better straight line is obtained by taking the values of σ^* for the group $-CH_2R$. On the other hand using the values of σ^* for the group -R alone the rate constant for glycollic acid anhydrosulphite falls near to the best line through the other three points especially at the higher temperature. It must, therefore, be assumed that glycollic anhydrosulphite is behaving oddly or that the Taft constant is not truly representative of the polar effect of the two hydrogen substituents on the activity of the C_4 carbonyl group.

5.4 Decomposition of Tartronic Acid Anhydrosulphite by Benzyl Alcohol in Anisole

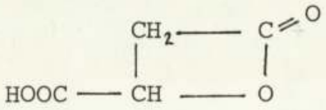
It was observed that, contrary to initial expectations, the benzyl alcohol initiated decomposition of tartronic acid anhydrosulphite in anisole proceeded considerably faster than the same reaction in neat benzyl alcohol (when allowance was made for the difference in hydroxyl concentration) as demonstrated by comparing the first order rate constants, K^1, in tables 4.1 and 4.2. Another seemingly anomalous feature was the difference in the activation energies associated with each reaction which was considerably lower (8.5 K cal mole^{-1} compared with 18.8 K cal mole^{-1}) for the reaction in anisole. This suggests that different mechanisms are operating.

It is well known that the solvent is one of the most important factors which influence the rate of a chemical reaction. There are basically two properties of solvents which can affect the rate of a reaction. Firstly, the polarity of the solvent as measured by its Dielectric constant (E), is important when the reaction proceeds through an activated intermediate complex where solvation affects the stability of that intermediate. Secondly, the ability of the solvent to donate an electron pair to a suitable electron acceptor which is referred to as its 'Donicity' (DN) is also important in determining the rate of a particular reaction. Values for the Donicity and dielectric constants of Anisole and Benzyl alcohol are given below:

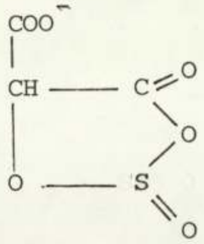
	E	DN
Benzyl Alcohol	13.6	*
Anisole	9	26

* - not directly measureable but quoted by Smith(73) as 58.3. It has been shown by previous workers that the dielectric constants of different solvents cannot always be directly related to the rate of decomposition of cyclic monomers of this type even though it is usually possible to relate the dielectric constants of mixtures of two solvents of varying composition, in any case the dielectric constants of benzyl alcohol and anisole are so close as to have little effect on the rate of decomposition. The values for the Donicities of the two solvents suggest that the reaction should proceed faster in benzyl alcohol unless the reactive intermediate was in some way stabilized by the donation of electrons by the solvent.

The most probable explanation of the otherwise puzzling behaviour encountered here lies in the effect of the solvent on the substituent functional group. The fact that nitrobenzene (E = 34.8 DN = 4.4) gave a gel with the tartronic acid anhydrosulphite reaction product and was thus unusable as a solvent for the reaction coupled with the fact that similar behaviour is observed with the substituted pivalolactone



which polymerizes much more rapidly in tetrahydrofuran (DN = 20.0) than in dimethyl sulphoxide (DN = 29.8)(74) suggests that partial ionization of the substituent carboxyl group is in some way reponsible. The formation of such ionized species as:



would readily explain both the low activity of the C_4 carbonyl to nucleophilic attack and the formation of gels.

Although it could be interesting to study this phenomenon in more detail the paucity of solvent combinations that provide homogeneous reaction mixtures makes this difficult.

CHAPTER 6

A Study of Grafting anhydrosulphites onto Hydrogel Polymers

6.1 Introduction

The studies carried out on the reactions between various hydrophilic monomers containing nucleophilic sites and anhydrosulphites, described in the chapters 3 and 4 demonstrated that it was possible to graft anhydrosulphites onto certain vinyl monomers having reactive nucleophilic sites. Some monomers containing hydroxyl groups such as 2-hydroxy ethyl Methacrylate (HEMA) were unreactive towards anhydrosulphite decomposition and the studies indicated that of the suitable monomers most commonly used in the preparation of hydrogel-forming polymers N-methylol acrylamide (Fig. 6.1) was most reactive towards anhydrosulphites. The general reaction of the grafting of one molecule of anhydrosulphite onto an N-methylol acrylamide unit in a polymer chain is given in Fig. 6.2. It was proposed to carry out a more detailed study of the physical and chemical changes brought about by grafting anhydrosulphites onto hydrogel

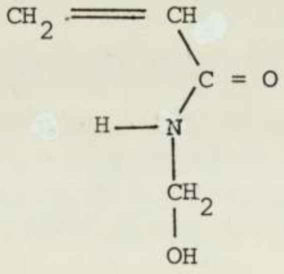


Fig. 6.1

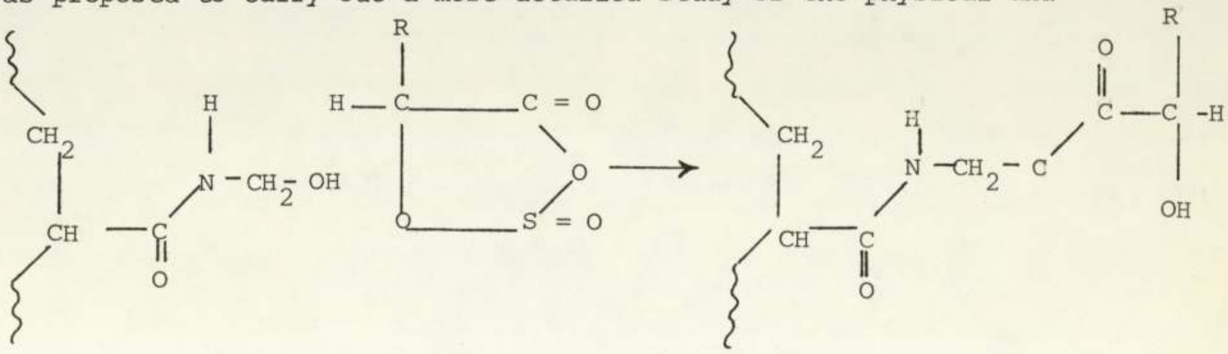


Fig. 6.2

polymers, paying special attention to the effect on surface properties of polymers as a result of the treatment of prepared polymer films with anhydrosulphites.

By using the monomers described in previous chapters substituent groups (R) containing hydroxyl or carboxylic acid groups can be introduced. Attaching these functional groups by means of this grafting reaction has the effect of increasing the molecular displacement of the functional group from the backbone chain of the polymer compared with the situation encountered with inconventional functional vinyl monomers such as methacrylic acid or hydroxy-ethyl methacrylate (although in the case of hydroxyl substituted monomers a larger displacement is available in the monomer 4 hydroxy butyl acrylate (Fig. 6.3)).

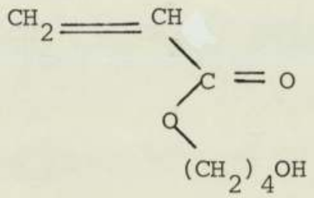


Fig. 6.3

In addition the combination of the functional group R with the terminal ω-hydroxyl group (see Fig. 6.2) offers the possibility of chelation. The effect of increasing the displacement of the functional group from the polymer backbone on the physical properties of the polymer in which it is incorporated is well known and can be demonstrated by the series of hydroxy alkyl acrylates/methacrylates. As the size of the alkyl group increases the glass transition temperature (Tg) of the dehydrated polymer decreases as does the water content of the hydrated gel. The effect of spacer units on functional group activity is also well recognised as for example in affinity chromatography

Acrylic and methacrylic acids are the only vinyl monomers containing carboxylic acid functional groups used in the preparation of hydrogels. In both monomers the carboxylic acid group appears directly adjacent to the vinyl portion of the molecule. It would be desirable for some purposes to have a carboxylic acid group more remote from the backbone of the polymer. It seems that this can be achieved by grafting a carboxylic acid substituted anhydrosulphite onto a suitable nucleophilic site on the polymer. Such an arrangement is potentially useful for introducing specific ion-binding sites into the polymer.

It was decided to limit this study to the grafting of tartronic acid anhydrosulphite because it has been shown to react readily with N-methylol acrylamide in preference to other hydroxyl containing hydrogel-forming monomers and of the four anhydrosulphites studied so far it was most easily prepared in a substantially pure form.

Grafting of the anhydrouslphite onto prepared hydrogel polymers was attempted in two ways:-

1) A homogeneous reaction in which the prepared polymer is reacted with the anhydrosulphite in solution.
2) A heterogeneous reaction between the prepared polymer in the form of a dehydrated film and a solution of the anhydrosulphite in a non-solvent for the polymer.

The second reaction was used when attempting to study the change in surface properties of the polymer brought about by grafting.

6.2 Preparation of Bulk polymers

Copolymers of N-methylol acrylamide (NMAc) and methyl methacrylate (MMA) were prepared by solution polymerization (described in section 2.3) according to the following formulations:-

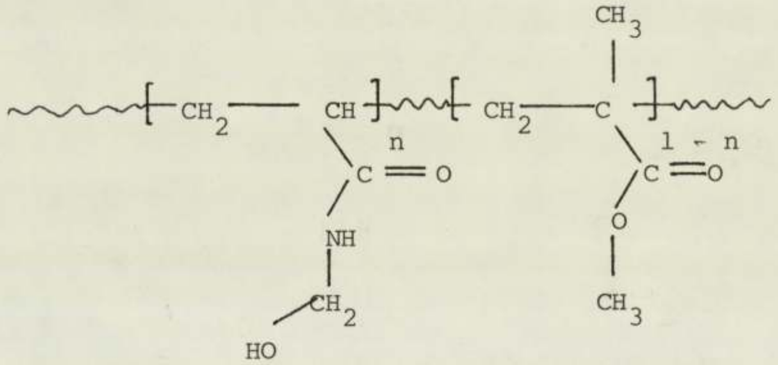
S_1:- 20% NMAc, 80% MMA

S_2:- 50% NMAc, 50% MMA

THF was used as a solvent and the polymerization was initiated with 0.2% AZBN. The reaction was carried out at 65°C for a period of six hours after which the polymer solution was evaporated and precipitated into a tenfold excess of ether. The polymer formed was washed with a further amount of ether and dried in a vacuum oven at 60°C. The polymer was ground to a fine powder with a pestle and mortar.

The polymers were characterized by infra-red spectroscopy and elemental CHN analytical techniques. A typical infra-red spectrum from a KBr disc is shown in Fig. 6.4. The values obtained from CHN analysis for the percentage of nitrogen in the polymer enabled the amount of N-methylol acrylamide in the copolymer to be calculated by the following procedure.

In the copolymer of the general formula :



If n = the fraction of N methylol acrylamide in the copolymer and

N = the percentage Nitrogen in the copolymer (from CHN analysis)

$$N = \frac{n \times 14}{101n + 100\ (1-n)} \times 100 \quad \%$$

by rearrangement

$$n = \frac{100N}{14{,}00 + 100N - 101N}$$

This calculation showed that the actual composition of the polymers prepared were:

S_1: 57% NMAc, 43% MMA

S_2: 65% NMAc, 35% MMA

The composition of both copolymers differed from the initial formulation. In fact rather less than the initial percentage of methyl methacrylate had been incorporated in the copolymer. This was nevertheless fortuitous since although it is desirable to have a high proportion of N-methylol acrylamide in the polymer in order to have a high number of grafting sites the amount of NMAc which can be incorporated in the initial formulation is limited by its poor solubility in the solvents used in solution polymerization, and other co-monomers.

6.3 Homogeneous Grafting of Tartronic acid anhydrosulphite onto bulk Polymers in solution

Before attempting the grafting reaction it was necessary to ensure complete removal of water from the polymers. After the preliminary drying in a vacuum oven the polymer powders were allowed to stand over phosphorus pentoxide in a vacuum dessiccator for several days. The use of more heat was avoided as this might initiate undesirable cross-linking reactions in the polymer which would render it insoluble. Anisole was chosen as a suitable solvent for the grafting reaction since the NMethylol acrylamide/methyl methacrylate copolymers were found to be fairly soluble in it when hot. About 1 g of each polymer was taken, mixed with a little anhydrous anisole and warmed in a water bath at 45°C until the polymer had dissolved. A molar excess (about 1 ml) of tartronic acid anhydrosulphite was added and the reaction vessel, a 25 ml 'quickfit' conical flask, sealed with a suba-seal through which the evolved sulphur dioxide was allowed to escape by means of a syringe needle inserted at regular intervals.

After the reaction had proceeded for about 24 hours (the solution now had reddish-brown colour) the polymer was recovered by precipitation into an excess of ether. The precipitated polymer was washed with ether, dried, then washed with water, to remove any trace of tartronic acid or anhydrosulphite which was not chemically attached to the polymer, and dried in a vacuum oven.

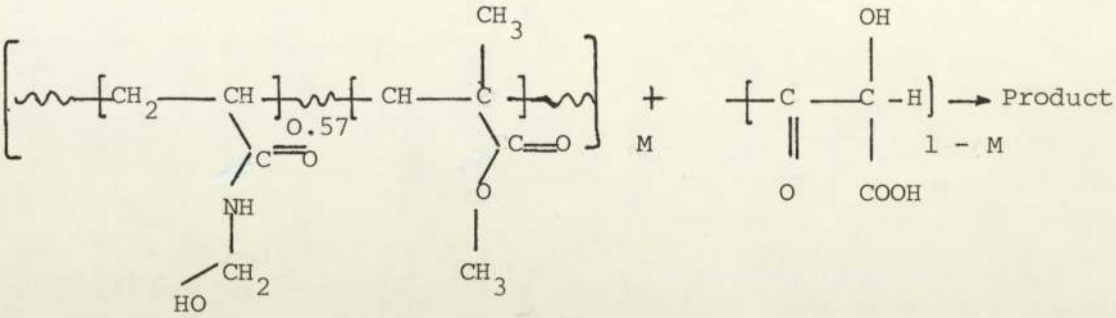
Characterization of Grafted polymers

Samples of the grafted polymers were characterized by infra-red spectroscopy and CHN analysis. The infra-red spectrum of a grafted polymer is shown in Fig. 6.5. There is a distinct absorption at 1730 cm^{-1} due to the carboxylic acid group of tartronic acid grafted onto the polymer. Another carbonyl absorption appearing at 1740 cm^{-1} can be attributed to the ester group where the tartronic acid is grafted onto the polymer. These both appear on the spectrum of the reaction product from benzyl alcohol initiated decomposition of tartronic acid anhydrosulphite and can be distinguished from the carbonyl absorptions in the ungrafted polymer at 1735 cm^{-1} due to the methyl methacrylate ester and at 1670 cm^{-1} due to the amide group in N methylol acrylamide. The absorption at 3300-3400 cm^{-1} observed more strongly in the grafted polymer was attributed to the hydroxyl group of the tartronic acid grafts. The strength of the infra-red absorptions due to the grafted tartronic acid demonstrated that quite a high proportion of tartronic acid anhydrosulphite had been grafted onto the polymer.

The CHN analysis of the grafted polymer showed a reduced nitrogen content compared with the polymer before grafting. For example, the polymer S_1 (57% NMAc, 43% MMA) had a nitrogen content of 7.94% before grafting which was reduced to 2.91% after grafting. These figures made it possible to calculate the amount of tartronic acid anhydrosulphite which had reacted with the polymer.

The average unit molecular weight of the copolymer S_1 is 100.57 and the molecular weight of the tartronic acid anhydrosulphite residue is 103.

We assume the reaction :



where M = the fraction of the original copolymer present in the grafted polymer

∴ M - 1 = the fraction of tartronic acid.

M can be calculated from the nitrogen contents before and after grafting using the following expression:

$$\%N \text{ (after grafting)} = \%N \text{ (before grafting)} \times \frac{M}{100.57M + 103\ (1 - M)} \times 100$$

$$\text{i.e. } 2.91 = \frac{7.98M \times 100}{100.57M + 103\ (1 - M)}$$

For this particular case 1 -M (the fraction of tartronic acid residue in the grafted polymer) was calculated to be 0.70. The ratio of tartronic acid to polymer is 1.7 to 1 and that of tartronic acid to N methylol acrylamide units is approximately 3 to 1. Since the N methylol acrylamide provides the initiating species for the anhydrosulphite decomposition it appears that grafts of more than one unit have been formed. It is unlikely that any long chain polyester units have been formed, since the decomposition of the anhydrosulphite by N methylol acrylamide is favoured above chain propagation reactions, so it is proposed that the grafted product is a copolymer of methyl methacrylate and grafted N methylol acrylamide units (Fig. 6.6) where x is a small number probably between 0 and 5 or 6.

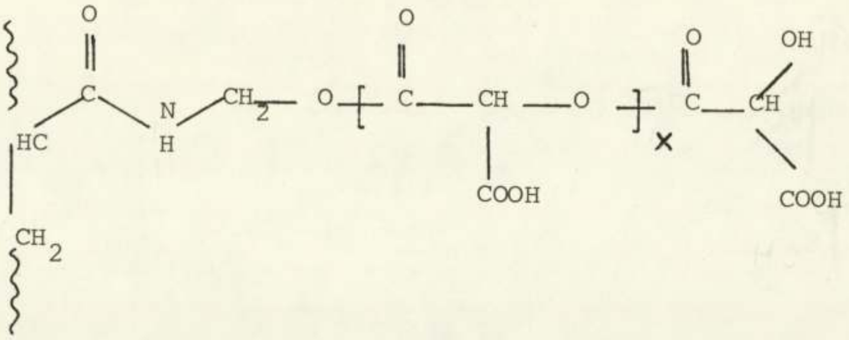


Fig. 6.6

It is evident that in order to limit the grafting to a single tartronic acid residue to each available nucleophile it is necessary to limit the quantity of anhydrosulphite used to a roughly 1:1 molar ratio to N methylol acrylamide.

Physical characteristics of polymers

In order to measure the physical properties of the prepared polymers (e.g. density, water content of hydrogel, surface properties etc.) to enable comparisons between grafted and ungrafted polymers to be made, it was necessary to mould the polymer powders. The most convenient way of doing this was to mould the powder by pressing between 'melinex' sheets inside a gasket also cut from melinex. It was found, in practice that an adequate film could be produced by pressing the polymers for 2 minutes at 120°C, lower temperatures failed to fuse the grafted polymer completely. The films from both the grafted and the ungrafted polymers were transparent but the grafted polymer had an orange colour whilst the ungrafted polymer was colourless. The pressed polymer samples were used to make comparative measurements of density, water content and contact angles. The results of which are summarized in Table 6.1

Density

For both polymers the presence of grafted tartronic acid reduced the density of the dehydrated polymer. A simple explanation for this

Polymer	Composition		Density	Water Content	Contact Angle	
	Initial	**Final**			Water	Me I_2
S_1	20 NMAc 80 MMA	57NMAc 43 MMA	1.265	35%	76	21
S_1G	S_1 + Tar AAS		1.200	20% $\pm$ 5	58	23
S_2	50 NMAc 50 MMA	65NMAc 35MMA	1.240		71	26
S_2G	S_2 + Tar AAS		1.190		58	25

<u>Table 6.1</u>

Physical properties of polymer films grafted in solution.

would be that the presence of more bulky substituents was inhibiting the close-packing of the polymer chains.

Water Content

Water contents were measured on several samples from each polymer. There was a wide variation in the values obtained. It was assumed that the pressed samples were not uniform and that the conditions of pressing also affected the water content. The values obtained for the water contents were around 35% for the ungrafted polymer and 20% for the grafted polymer. It appeared that the water content of the grafted polymer was slightly lower than the ungrafted polymer but we must not attach too much importance to this although it is generally observed that hydrogel polymers containing carboxylic acid substituted monomers tend to take up less water than polymers containing similar hydroxyl substituted monomers.

Contact Angles

The contact angles formed by water and methylene iodide on the surface of the dehydrated polymer films were measured. The water contact angle is governed by both the polar and dispersive components of the surface free energy of the polymer whilst the methylene iodide contact angle is governed by the dispersive component only. The results are summarized in Table 6.1. The methylene iodide contact angles were similar for both polymers S_1 and S_2, before and after grafting, but there was a significant decrease in the water contact angle for both polymers S_1 and S_2 brought about by grafting. The values for the polar and dispersive components of surface free energy calculated from the Owens and Wendt equation showed that for the grafted polymers there was a significant increase in the polar component of surface free energy, which is the main factor governing the water contact angle, whilst the dispersive component of the surface free energy was little affected by grafting.

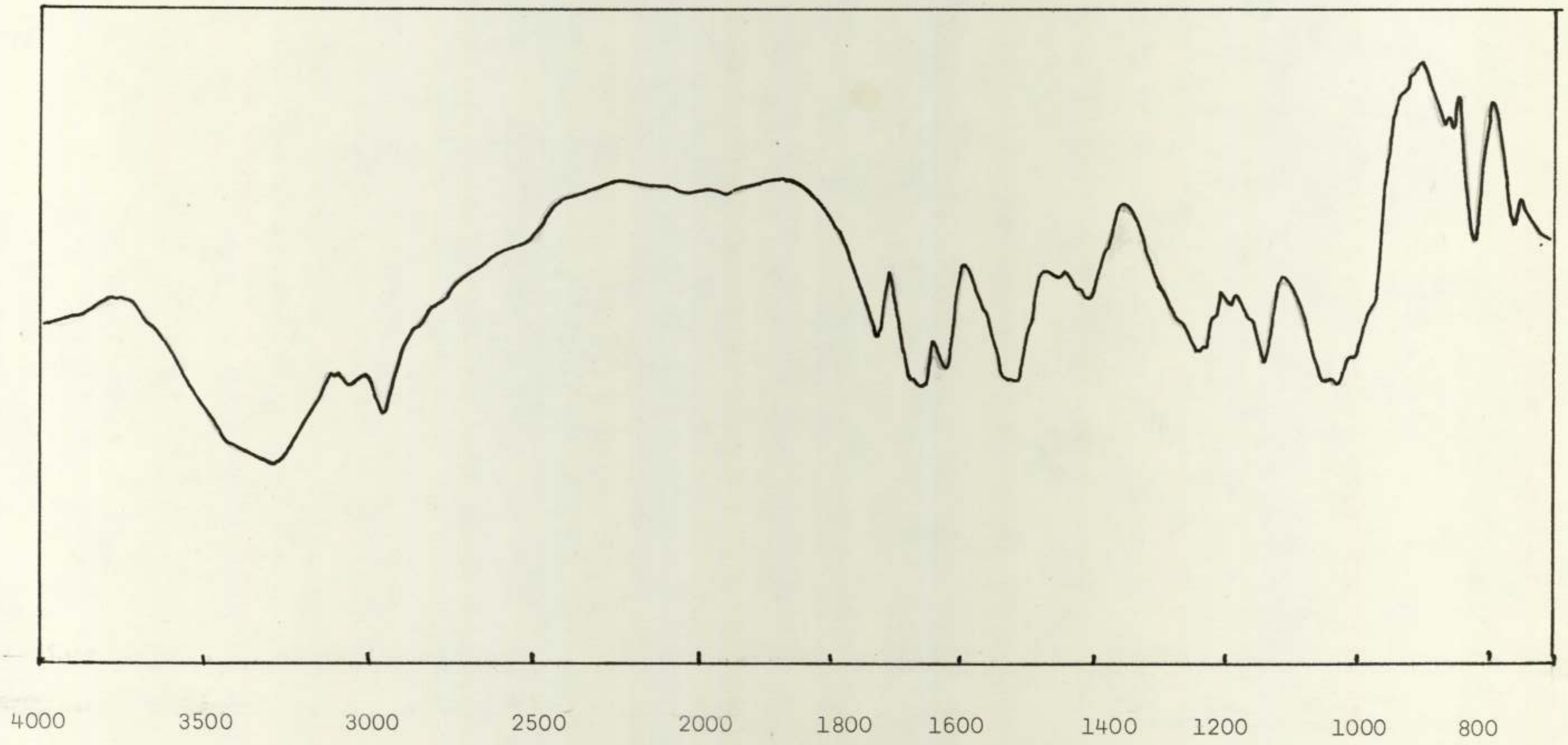


Fig. 6.4:Infra-red spectrum of Polymer S1 (80 MMA 20 NMAc)

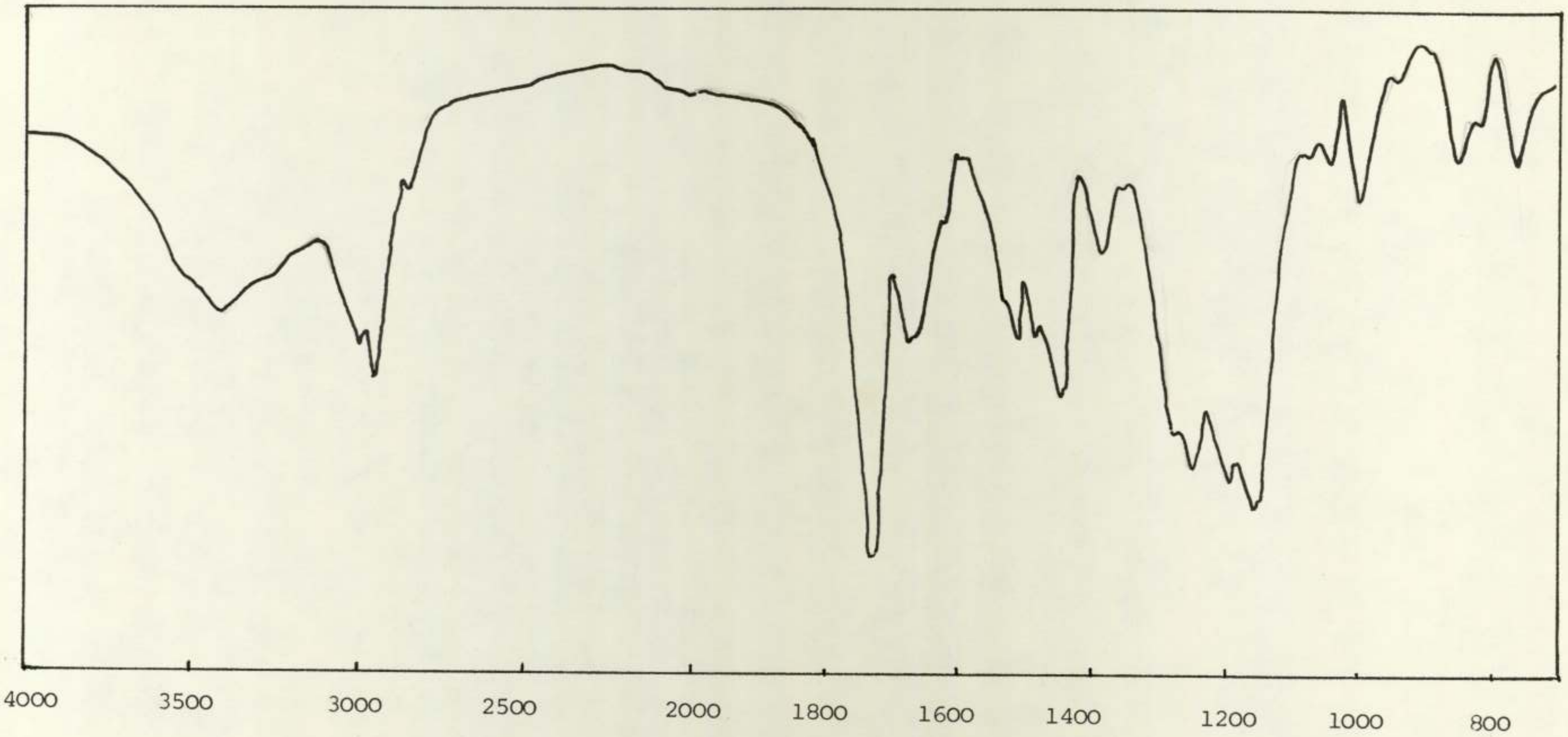


Fig. 6.5: Infra-red spectrum of grafted polymer

Preparation of Hydrogel Polymer Films

Polymer films were prepared by bulk polymerization using the cell as described in the experimental techniques section 2.3. A range of films were prepared from combinations of the monomers· N methylol acrylamide (NMAc), methyl methacrylate (MMA) methacrylic acid (MA) hydroxy propyl acrylate (HPA) according to the formulations shown in Table 6.2. Variations of the formulations were limited by the poor solubility of N methylol acrylamide (which is a solid) in both methyl methacrylate and hydroxy propyl acrylate although it was possible to increase the amount which could be incorporated by the addition of a small amount of water (up to 10% of the total weight of monomer). N methylol acrylamide was more readily soluble in methacrylic acid and up to 60% NMAc could be dissolved in this monomer in the presence of 10% water. Apart from this case the copolymer formulations included less than 50% by weight of N methylol acrylamide. It was found by experience that hydrogels containing a high proportion of hydroxy propyl acrylate were extensively swollen by water leading to inherent weakness of the hydrated film. This could be alleviated by the incorporation of a small quantity of ethylene glycol dimethyacrylate (EDMA) (Fig. 6.7) into the monomer mixtures which had the effect of introducing cross-linking into the polymer. The presence of cross-links tends to decrease the water uptake of those copolymers that contain a high proportion of very hydrophilic monomers and thus to strengthen the hydrated gel.

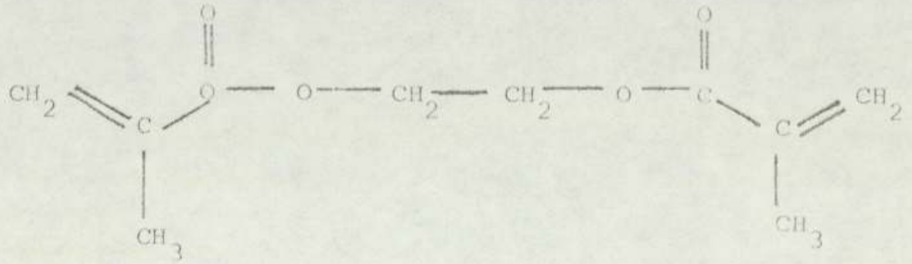


Fig. 6.7 EDMA

0.1% AZBN was used to initiate polymerization which was allowed to proceed for between three and five days in an oven at 60°C. The prepared polymer films were hydrated and left to stand in water for several days, changing the water frequently, to ensure the complete removal of residual monomer. The films were then dehydrated by removing the water under vacuum at 60°C. Complete removal of water was necessary before grafting could be attempted.

Grafting of Tartronic acid anhydrosulphite onto polymer films

The reaction was carried out by cutting small pieces from the dehydrated polymer films and suspending them in a solution of tartronic acid anhydrosulphite in anisole (about 0.5 g anhydrosulphite in 10 mls anisole). The reaction vessel used was the same as that used for the homogeneous grafting described earlier in this chapter.

Although bulk polymers S_1 and S_2 could be dissolved in anisole tests showed that none of the prepared polymer films dissolved in anisole or were even noticeably swollen by it and since it is believed that the grafting reaction takes place readily in anisole, this was chosen as the solvent for the reaction. A blank reaction between the films and anisole was performed to see if prolonged immersion in anisole had any effect on the polymer, results concluding that there were no effects that might interfere with the results obtained in comparing grafted and ungrafted polymers.

As with the homogeneous grafting reaction the reaction vessels were immersed in a water bath at 45°C for 24 hours after which the polymer films were removed from the anhydrosulphite solution and washed several times with ether before drying in a vacuum oven at 60°C.

The films were allowed to hydrate for several days to wash away any traces of tartronic acid not chemically bound.

It was observed that the surface of some of the grafted polymers became broken up on hydration. Close examination of these using an

CODE	percentage (by weight)				
	NMAc	MMA	HPA	MAA	EDMA
SF$_1$	25	50		25	
SF$_2$	10	85		5	
SF$_3$	20	40	40		
SF$_4$	33		67		
SF$_5$	40		60		
SF$_6$	20		80		
SF$_7$	33		33	33	1%
SF$_8$	40		40	20	1%
SF$_9$	20		80		1%
SF$_{10}$	40		60		1%
SF$_{11}$	50		25	25	2%
SF$_{12}$	60			40	2%

Table 6.2

Composition of polymer films

optical microscope showed that the surface of the polymer appeared to be more brittle than the gel beneath and had resisted swelling to the same extent as the bulk of the gel which caused the surface to crack and come adrift in places. This appears similar to the 'Aligatoring' effect sometimes observed on surface coatings.

The worst affected polymer films were: SF_4 (67 HPA, 33 NMAc), SF_5 (60 HPA, 40 NMAc), SF_6 (80 HPA, 20 NMAc) and SF_9 (80 HPA, 20 NMAc, 1% EDMA), all polymers that contain a high proportion of hydroxy propyl acrylate. The addition of EDMA as a cross-linking agent reduced this 'aligatoring' effect which did not occur in polymer SF_{10} (60 MPA, 40NMAc, 1% EDMA) but occurred to some extent in all other cases.

6.5 Effect of Grafting on the Properties of Polymer Films

Water Contents:

The water contents of both the ungrafted and grafted polymer films were measured and the results summarized in table 6.3. The water contents of the polymer films were not greatly affected by grafting although a slight reduction (about 2%) was observed in each case. It was also observed that the polymer films which were affected by 'alligatoring' were those polymers which had a water content before grafting in excess of 40% and that the tendency to aligatoring could be reduced by introducing cross-linking into a particular polymer formulation in order to reduce its water content.

Contact Angles:

The surface free energy of the dehydrated polymer films was determined using the 'Sessile Drop' technique of contact angle measurement with water and methylene iodide as the drop-forming liquids and the polar and dispersive components of the surface free energy were

Film No.	Composition	Water Content (%)	
			Grafted
SF$_1$	25 NMAc 50 MMA 25 MAA	19	
SF$_2$	10 NMAc 85 MMA 5 MAA	4	
SF$_3$	20 NMAc 40 MMA 40 HPA	32	
SF$_4$	33 NMAc 67 HPA	40	*
SF$_5$	40 NMAc 80 HPA	46	*
SF$_6$	20 NMAc 80 HPA	53	*
SF$_7$	33 NMAc± 33 HPA 33 MAA	26	24
SF$_8$	40 NMAc± 40 HPA 20 MAA	27	26
SF$_9$	20 NMAc 80 HPA	43	*
SF$_{10}$	40 NMAc± 60 HPA	27	25
SF$_{11}$	50 NMAc± 25 HPA 25 MAA	24	22
SF$_{12}$	60 NMAc± 40 MAA	32	29

Table 6.3

Water contents of polymer films before and after grafting

*Alligatoring occurred

±Crosslinked with EDMA

calculated from the Owens and Wendt equation as described in Chapter 2. The polar component of the surface free energy of the hydrated polymer film was determined by the 'Hamilton' technique of contact angle measurement also described in Chapter 2. The results obtained, comparing the grafted and ungrafted samples are summarized in Table 6.4.

It was observed that for all the films studied, (except for those badly affected by alligatoring (see previous pages) where contact angle measurement was impossible) that the water contact angle on the dehydrated film was reduced by grafting whilst the methylene iodide contact angle remained the same. This pointed to an increase in the polar component of the surface tension which was borne out by the calculated values of γ^{p}_{s} and γ^{d}_{s} which showed an increase in the total surface tension and the polar component whilst there was little change in the dispersive component.

Similarly the Hamilton contact angle was increased by grafting for all the polymer films studied which indicated that the polar component of the surface free energy of the hydrated polymer films was also increased by grafting.

TABLE 6.4: CONTACT ANGLES AND SURFACE TENSION VALUES FOR UNGRAFTED AND GRAFTED POLYMER FILMS

No.	COMPOSITION	UNGRAFTED POLYMER						GRAFTED POLYMER					
		DEHYDRATED				HYDRATED		DEHYDRATED				HYDRATED	
		θ_{H_2O}	θ_{MeI_2}	γ_s^p	γ_s^d	$\theta_{Oct.}$	γ_s^p	θ_{H_2O}	θ_{MeI_2}	γ_s^p	γ_s^d	$\theta_{Oct.}$	γ_s^p
Sf_1	25 NMAc 50 MMA 25 MMA	78	32	4,03	40.25	109	21,8	69	33	8.36	38.06	132	34.0
Sf_2	10 NMAc 85 MMA 5 MAA	70	29	7.30	40.05	115	25,0	67	30	9,02	39.06	145	40.2
Sf_3	20 NMAc 40 MMA 40 HPA	75	26	4.68	42.30	99	16.8	71	25	6,38	41.90	133	34.5
Sf_4	33 NMAc 67 HPA	86	37	2,10	39.20	109	21,8	*	*			*	
Sf_5	40 NMAc 60 HPA	82	24	2.08	44.54	119	27,0	*	*			*	
Sf_6	20 NMAc 80 HPA	*	*					*	*			*	

* POLYMER SURFACES TOO POOR FOR CONTACT ANGLE MEASUREMENT

No.	COMPOSITION	UNGRAFTED POLYMER						GRAFTED POLYMER					
		DEHYDRATED				HYDRATED		DEHYDRATED				HYDRATED	
		θ_{H2O}	θ_{MeI_2}	γ_s^p	γ_s^d	$\theta_{Oct.}$	γ_s^p	θ_{H2O}	θ_{MeI_2}	γ_s^p	γ_s^d	$\theta_{Oct.}$	γ_s^p
Sf_7	33 NMAc 33 HPA 33 MAA	83	35	2.54	39.80	104	19.26	74	37	6.37	37.61	116	25.6
Sf_8	40 NMAc 40 HPA 20 MAA	86	34	1.62	40.92	112	23.04	68	35	9.20	37.35	123	29.3
Sf_9	20 NMAc 80 HPA	84	29	1.81	42.02	102	18.02	*	*			112	23.4
Sf_{10}	40 NMAc 60 HPA	*	*					*	*				
Sf_{11}	50 NMAc 25 HPA 25 MAA	69	32	7.76	38.73	112	23.04	61	34	12.9	36.30	124	28.9
Sf_{12}	60 NMAc 40 MMA	74	29	5.40	40.84	103	18.08	71	30	6.92	39.81	123	29.3

6.6 DISCUSSION OF RESULTS

Ease and Effectiveness of the Techniques used

From a superficial comparison of the results obtained for the two different techniques used for the treatment of prepared polymers with anhydrosulphites it seems that the grafting reaction is more suited to modifying the surface of a preformed polymer than the modification of the bulk polymer in solution. The first problem encountered within homogeneous grafting is to find a suitable solvent for the reaction since there is only a limited number of solvents in which the anhydrosulphite decomposition reaction takes place readily. The solvent must be: non-nucleophilic, fairly polar, have a high boiling point and be easily dried. Since most copolymers containing N-methylol acrylamide are not readily soluble in non-nucleophilic solvents the range of polymer compositions which are capable of undergoing the grafting reaction in solution is further limited.

Although tartronic acid anhydrosulphite was successfully grafted onto methyl methacrylate/N-methylol acrylamide copolymers in solution the resulting grafted polymers presented difficulties in moulding not observed in the original polymers. They were not so easily pressed requiring a higher moulding temperature to bring about fusion. The pressed films obtained, which were slightly discoloured, were found to be inhomogenous and it was thought that this was due to adverse reactions such as cross-linking brought about by the severity of the moulding conditions. The pressed polymer films could not be dissolved in the solvent used for the grafting reaction which was another indication that cross-linking had taken place.

Fortunately solution grafting is of less practical importance (since it has been shown to be possible to obtain the same effect by reacting the vinyl monomer with the anhydrosulphite before polymerization to produce a similar effect). It is however important in relating the reaction of the anhydrosulphite with the reactions of the anhydrosulphite with the same nucleophilic functional group (in this case the hydroxyl group) under the differing conditions listed below.

(1) The reaction of an anhydrosulphite with a small molecule containing the nucleophilic functional group such as benzyl alcohol as it is used as a model nucleophile in kinetic studies.

(2) The reaction of an anhydrosulphite with a vinyl monomer containing the nucleophilic functional group such as N-methylol acrylamide and hydroxy ethyl methacrylate. Here other groups within the monomer become important in determining the reactivity of the functional group.

(3) The reaction of an anhydrosulphite with a polymer in solution.

(4) The reaction of an anhydrosulphite with the nucleophilic functional groups on the surface of a polymer not in solution.

The most important result obtained from the solution grafting reaction was the extent to which anhydrosulphite reacted with the polymer which showed that the reaction took place readily under the conditions used. The chemical changes taking place in the polymer were readily assessed using infra-red spectroscopy and CHN analytical techniques whilst the physical changes were less easily assessed because of the necessity of using extreme conditions when moulding the polymer tended to induce adverse reactions which effect the physical properties of the polymer.

Evaluation of Grafted Polymers

The effect of grafting on physical properties of polymers in particular those relating to their surfaces, was more readily demonstrated in the cases where the anhydrosulphite was grafted directly onto the surface of a pre-formed polymer film. Because only the surface of the polymer film is involved in a chemical reaction, the grafted film does not have a homogeneous chemical structure and the techniques of chemical characterization (Infra-red spectroscopy and CHN analysis) used for solution grafted polymers could not be applied to surface grafted polymers. An infra-red spectrum of the dehydrated film showed little chemical change obviously due to the bulk of the polymer being unchanged chemically. It seemed that ATR infra-red spectroscopy would have been a useful technique but since it can only be used to study dehydrated films the fact that these were brittle and not very flat meant that it was impossible to obtain sufficient contact between the film and the cell to give an adequate clear spectrum.

Those physical properties of the polymer films which relate to the bulk of the film such as density and water content proved, as expected, to be very little changed by grafting although the fact that there was a slight reduction in water content observed in every case studied seems to indicate that the surface of the film may be taking up less water than the bulk of the film. This seems to agree with the general observation that hydrogels containing carboxylic acid substituted monomers such as acrylic or methacrylic acid tend to take up less water than hydrogels of similar composition containing hydroxyl substituted monomers such as hydroxyethyl methacrylate. A likely explanation of this is the relatively strong attraction between carboxylic acid groups, in the form of hydrogen bonding tending to hold the polymer molecules together. This also ties in with the observation of 'alligatoring' when polymer films with a high water uptake were grafted, which can be explained as cracking of the surface layer of the film due to the extra expansion of the bulk of the polymer film as it absorbs more water than the grafted surface layer. Optical microscopy here proved to be a useful technique to study the behaviour of the polymer surface after grafting.

The most significant effects of grafting onto the surface of polymer films are those on the physical properties of the surface, especially the surface free energy. Changes in this are conveniently measured by the contact angle technique using water and methylene iodide. In the case of solution grafted polymers the contact angle results (table 6.1) show clearly that the surface properties of the polymers (particularly the polar component as reflected in the dramatic reduction of the water contact angle) are markedly changed. This is most easily appreciated in terms of the change in Critical Surface Tension of the polymers, the critical Surface Tension being the surface tension of a liquid which will, in theory, just wet the polymer (see experimental section 2.4). As the water contact angle has been reduced by the grafting process it will be apparent that the critical surface tension of the polymer has been raised, i.e. it has become more wettable. It is apparent that the hydrophilic, carboxylic acid group is responsible for this. By the same token it is the presence of these groups in the polymer matrix that has led to a reduction in the bulk water content. This apparent paradox reflects a now well-established phenomenon in that although carboxylic acid groups are extremely hydrophilic their strong tendency to form hydrogen-bonds with acrylamide substituted acrylamides and other carboxy groups, leads to the partial exclusion of water from the network.

Turning to the surface grafted polymers it was unfortunately only possible to make contact angle measurements on the surfaces of those polymer films which were not affected by 'alligatoring' but in every other case there was an overall increase in the total surface free energy of the dehydrated films. This follows from the more sophisticated (compared with the critical surface tension approach) analysis of surface properties using water and methylene iodide contact angle data and the techniques of Owens and Wendt (section 2.4).

The first point of interest in the data summarized in table 6.4 is that the measured dispersive component of the surface free energy γ_s^d is in the case of all the ungrafted, dehydrated polymers in the region of 40 dyne cm^{-1} and that in each case the grafting process reduces this by 1 - 2 dyne cm^{-1}. The most dramatic changes however are those that occur in the values of the polar component of surface free energy, $\gamma_s p$. In this case it is possible to compare changes in both hydrated and dehydrated specimens. The nature of the polar component is reflected in the difference between hydrated and dehydrated surfaces. The values of γs^p in the former case are quite low ranging from around 2 - 7 dyne cm^{-1} and on hydration rise typically to between 20 - 35 dyne cm^{-1}. In the case of both the hydrated and dehydrated surfaces, however, the grafting process leads to a considerable increase in the determined values of $\gamma_s p$. Taking the values for the hydrated polymers first the increase observed is in the range 6 - 17 dyne cm^{-1}. It is, at first sight, surprising that the greatest increases are achieved for polymers Sf_1, Sf_2 and Sf_3 which are the only polymers containing methyl methacrylate (50, 85 and 40% respectively). It appears, however, that the large increase in these three cases (12.2, 15.2 and 17.7 dyne cm^{-1} respectively) is due to the fact that methyl methacrylate does not reduce the affinity of the grafted groups for water by hydrogen bonding. (Surface-bonded water is, of course, one of the factors that govern the value of $\gamma_s p$). This argument is reinforced by the fact that polymers Sf_1, Sf_2 and Sf_3 contain decreasing amounts of methacrylic acid (25%, 5% and zero respectively) which is capable of hydrogen-bonding with the grafted carboxylic acid group.

With the remainder of the hydrated polymers the change in Hamilton contact angle and thus $\gamma_s p$ is appreciably less (i.e. from 21 ± 3 dyne cm^{-1} to 26.5 ± 3 dyne cm^{-1}) although there is possibly a disernable trend relating final values of $\gamma_s p$ of the hydrated polymer to the percentage N-methylol acrylamide in the original composition. Thus, 20, 33, 40 and 50% NMAc samples produce $\gamma_s p$ for the hydrated samples of 23.4, 25.5, 29.3 and 29.8 dyne cm^{-1} respectively. The only remaining polymer Sf_{12} contains rather more N methylol acrylamide (60%) but since the only other component in the strongly hydrogen-bonding methacrylic acid it is perhaps not surprizing that its $\gamma_s p$ hydrated value is no higher (29.3).

Although detailed interpretation of the results obtained is, in some cases, complicated by the interplay of the various factors referred to in the preceding discussion the object of the work, which was to demonstrate the possibility of grafting at nucleophilic sites with cyclic derivatives of αfunctional acids, has undoubtedly been established.

CHAPTER 7

The Synthesis and Reactions of the Anhydrosulphites of α-Thio Carboxylic acids

This chapter is concerned with the preparation and reactions of the anhydrosulphites of the two simplest αthio-carboxylic acids: thioglycollic acid (Fig. 7.1a) and thiolactic acid (Fig. 7.1b).

$H-\overset{H}{\underset{SH}{C}}-COOH$ $H-\overset{CH_3}{\underset{SH}{C}}-COOH$

(a) Fig. (7.1) (b)

7.1 Anhydrosulphite Synthesis

Ali$^{(55)}$ has attempted to prepare the anhydrocarboxylates of thioglycollic and thiolactic acids by the action of phosgene on the copper and silver salts of the thioacids. This method proved unsuccessful as it seemed that the formation of the volatile acid chloride was preferred to ring closure to the anhydrocarboxylate. Similarly an attempt to prepare the anhydrosulphites of these acids by the action of thionyl chloride on their copper salts also proved unsuccessful. It was found to be possible to prepare both anhydrocarboxylates and anhydrosulphites by the action of phosgene and thionyl chloride respectively on the thio acids. For the present study the following technique of anhydrosulphite preparation was used.

0.5 moles of the thio acid (both thioglycollic and thiolactic acids are liquid at room temperature) was dissolved in 250 mls anhydrous diethyl ether in a 500 ml 'Quickfit' conical flask which was also fitted with a condenser and calcium chloride tube, to exclude moisture from the system. The mixture was stirred continuously, maintaining the temperature below $0^{o}C$ in an ice/salt bath. 0.75 moles pure thionyl chloride dissolved in a little anhydrous ether was added dropwise from a separating funnel over a period of about 1 hour. After about 6 hours the reaction mixture was allowed to warm up to room temperature and to continue reacting for a further two days by which time the solution had changed colour from a clear solution to reddish brown (thioglycollic) or yellow (thiolactic)

The ether and excess thionyl chloride were stripped off under vacuum leaving behind a viscous liquid which was a mixture of anhydrosulphite and some chlorine containing impurities.

7.2 Purification

The crude anhydrosulphites were treated with baked silver oxide to remove chlorine containing impurities. They were then distilled under reduced pressure although it was difficult to maintain a very low pressure due to the constant evolution of sulphur dioxide from the decomposition of the anhydrosulphites at the distillation temperature.

The distillation conditions were:

Thioglycollic anhydrosulphite: 80°C (1 cm Hg)

Thiloactic anhydrosulphite : 110 - 120°C (2-3 cm Hg)

The yield after distillation was quite low because of extensive decomposition of the anhydrosulphites at the high temperature required. Thiolactic anhydrosulphite appeared to be much more stable than thioglycollic anhydrosulphite despite the higher distillation temperature required. A yield of about 50% could be obtained compared with less than 20% for thioglycollic anhydrosulphite. The distilled product from each reaction was a pale yellow viscous liquid.

The anhydrosulphites were stored in sealed containers at a temperature below -20°C because of their reactivity.

7.3 Characterization

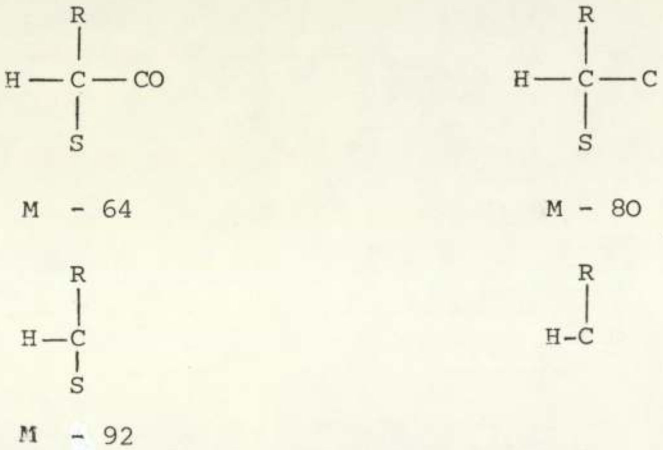
The anhydrosulphites were characterized by the combination of techniques previously used with similar compounds.(20)(29) The results are summarized for comparative purposes in Table 7.1.

Infrared Spectra

The anhydrosulphites are most easily identified from their infrared spectra which were obtained from a thin film between sodium chloride discs. The most useful characteristic absorption occurs in the carbonyl region. The carbonyl stretching frequency of α-thio carboxylic acids occurs at about 1705 cm^{-1} but in the strained ring system of the anhydrosulphite the absorption occurs at a much higher frequency $\sim$1800 cm^{-1}. This frequency is slightly lower than that encountered within the anhydrosulphites of the corresponding α-hydroxy-acids which occurs at about 1810cm^{-1}. The thioanhydrosulphites also exhibit a characteristic absorption at 1170cm^{-1} which is assigned to the S = O stretching frequency again this is somewhat lower than the frequency observed for the corresponding α-hydroxy acid anhydrosulphites which occurs at about 1215cm^{-1}.

Mass Spectra

The mass spectra obtained from thioglycollic and thiolactic anhydrosulphites do not show a top mass peak corresponding to the molecular weight of the undecomposed ring indicating that the thioanhydrosulphites are less stable thanthe α-hydroxy acid anydrosulphites both of which do exhibit the expected top mass peak. The rest of the spectrum was complex and although the expected fragmentation peaks (Fig.7.2) were present there were many others as well.



$\mathrm{H{-}\overset{R}{\underset{S}{C}}{-}CO}$ M - 64

$\mathrm{H{-}\overset{R}{\underset{S}{C}}{-}C}$ M - 80

$\mathrm{H{-}\overset{R}{\underset{S}{C}}}$ M - 92

$\mathrm{H{-}\overset{R}{C}}$

Fig. (7.2)

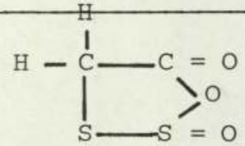
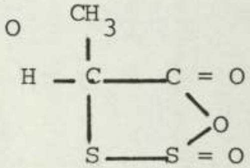
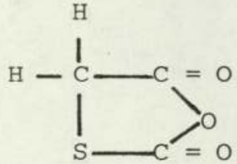
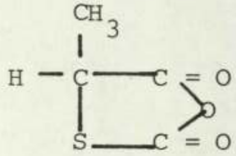
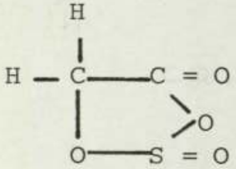
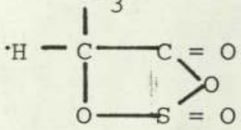
MONOMER		M.P or B.P	Infrared Spectra		Mass spectra Principal Peaks
			$V_C = O (cm^{-1})$	$V_S = O (cm^{-1})$	
TGAS		bp 80 (10 mm)	1800 (s)	1170 (m-w)	M - 64 M - 80
TLAS		bp 120 (20 mm)	1800 (s)	1170 (m-w)	M - 92 M - 124
TGAC		mp 67 - 68	1770 (s) 1845 (m)	-	M M - 44 M - 60
TLAC		mp 44 - 46	1770 (s) 1845 (m)	-	M - 72 M - 76 M - 104
GAAS		bp 68 - 70 (10 mm)	1825	1245	M M - 64 M - 80
LAAS		bp 70 (12 mm)	1815	1235	M - 92 M - 108

TABLE 7.1 A summary of the spectral characteristics of Thio acid anhydrosulphites and anhydrocarboxylates and αhydroxy acid anhydrosulphites.

It was concluded from this that mass-spectrometry alone is not very specific in the characterization of thio-anhydrosulphites.

Other Methods of Characterization

The purity of the anhydrosulphites was also assessed by chloride ion determination and hydrolysis.

After treatment with silver oxide potentiometric titration with silver nitrated showed the amount of residual chlorine-containing impurity to be negligeable.

A known amount of the anhydrosulphite was taken and hydrolysed in a kinetic apparatus. The total amount of sulphur dioxide evolved was measured as a pressure rise which was compared with the theoretical pressure rise calculated for the pure anhydrosulphite, where 1 mole anhydrosulphite yields 1 mole of sulphur dioxide, knowing the volume of the apparatus and the temperature. This technique showed the freshly distilled anhydrosulphite to be about 98% pure. The hydrolysis product, the parent acid could also be measured quantitatively to indicate the purity of the anhydrosulphite.

7.4 Decomposition Reactions of Thioglycollic and Thiolactic Anhydrosulphites

A preliminary study showed that thioglycollic and thiolactic anhydrosulphites reacted readily with benzyl alcohol evolving sulphur dioxide so it was decided that a kinetic study of the benzyl alcohol reaction would prove useful in determining the mechanism of nucleophilic decomposition and comparing it with the benzyl alcohol initiated decomposition of other ring systems.

Benzyl Alcohol Initiated Decomposition

It was found that, even at low temperatures, the decomposition of thioglycollic anhydrosulphite proceeded too rapidly for the kinetics of the reaction to be followed conveniently. It was, therefore, necessary to dilute the benzyl alcohol with a non-nucleophilic co-solvent to reduce the alcohol concentration. Nitrobenzene proved to be a suitable co-solvent. Gas evolution was followed using the low-temperature apparatus as described in Chapter 2.

The first problem was to establish the reaction mechanism and the order of reaction in both monomer and initiator.

A stock solution was made up for each anhydrosulphite in dry nitrobenzene having a concentration of 1 mole/l. A reaction carried out with an excess of benzyl alcohol gave the kinetic profile as in the plot of the amount of monomer decomposed against time shown in Fig. 7.3 $\frac{[M]}{[M_o]}$ was plotted against time on semi-log graph paper and gave a straight line which indicated that the reaction was apparently first order in monomer. From this it was possible to calculate k, the apparent first order rate constant for the reaction.

Having established that the reaction was first-order in monomer the concentration of benzyl alcohol was varied relative to that of the monomer to enable the determination of the order of the reaction in initiator. The results, summarized in Table 7.2, Fig. 7.4 and Fig. 7.5 were obtained using thioglycollic anhydrosulphite.

$\frac{[OH]}{[M]}$	$t_{\frac{1}{2}}$	k
0.53	4320	1.60×10^{-4}
0.63	3420	2.03×10^{-4}
1.00	2340	2.96×10^{-4}

Table 7.2: Effect of OH concentrated on rate of reaction between benzyl alcohol and thioglycollic anhydrosulphite in nitrobenzene at 26°C.

It was observed (Fig. 7.5) that as $\frac{[OH]}{[M]}$ decreased the semi-log plot of $\frac{[M]}{[M_o]}$ against time deviated further from linearity and the initial first order rate constant k^{o}, calculated from the slope of the semi-log

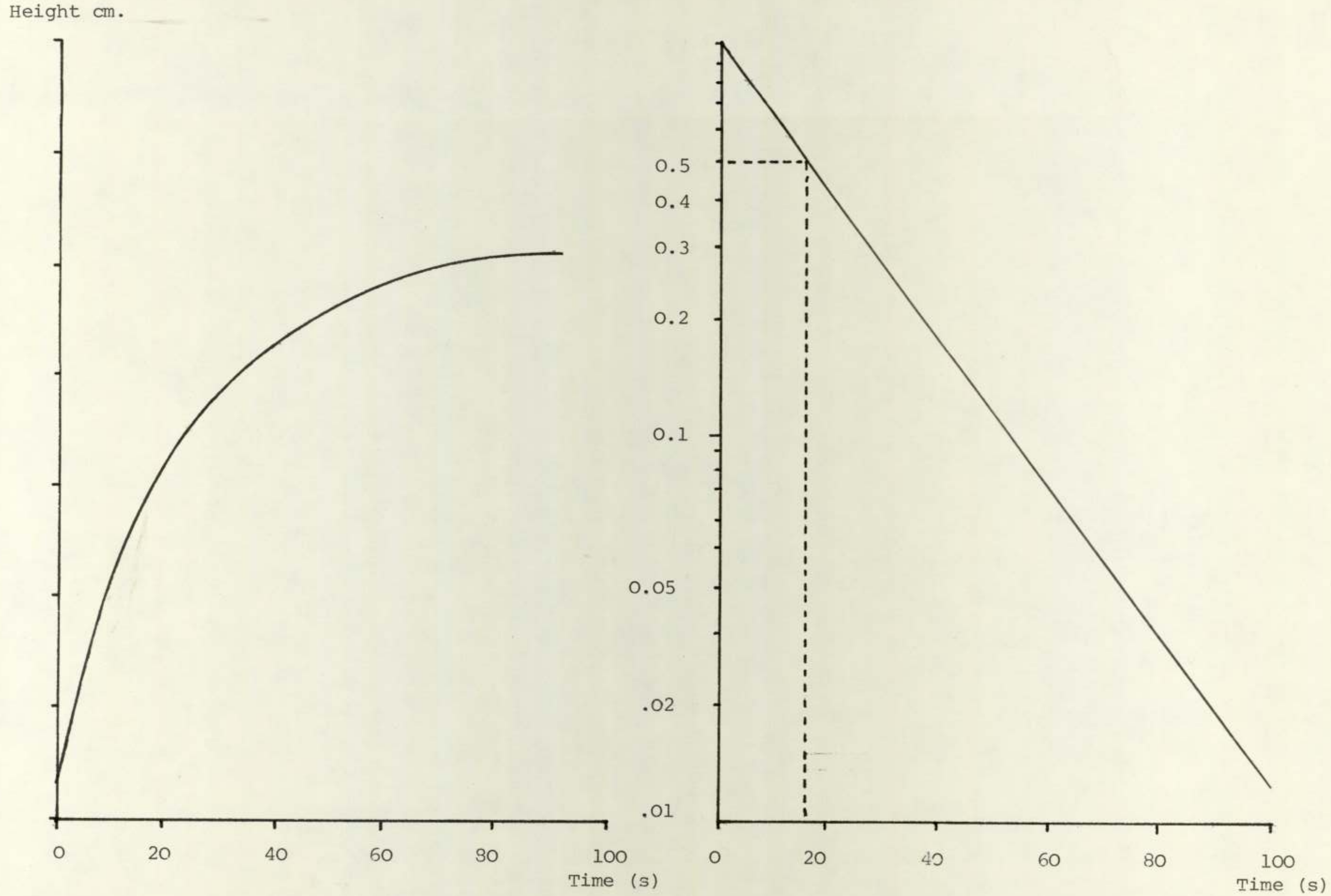


Fig. 7.3 Typical kinetic plots for benzyl alcohol initiated decomposition of TGAS

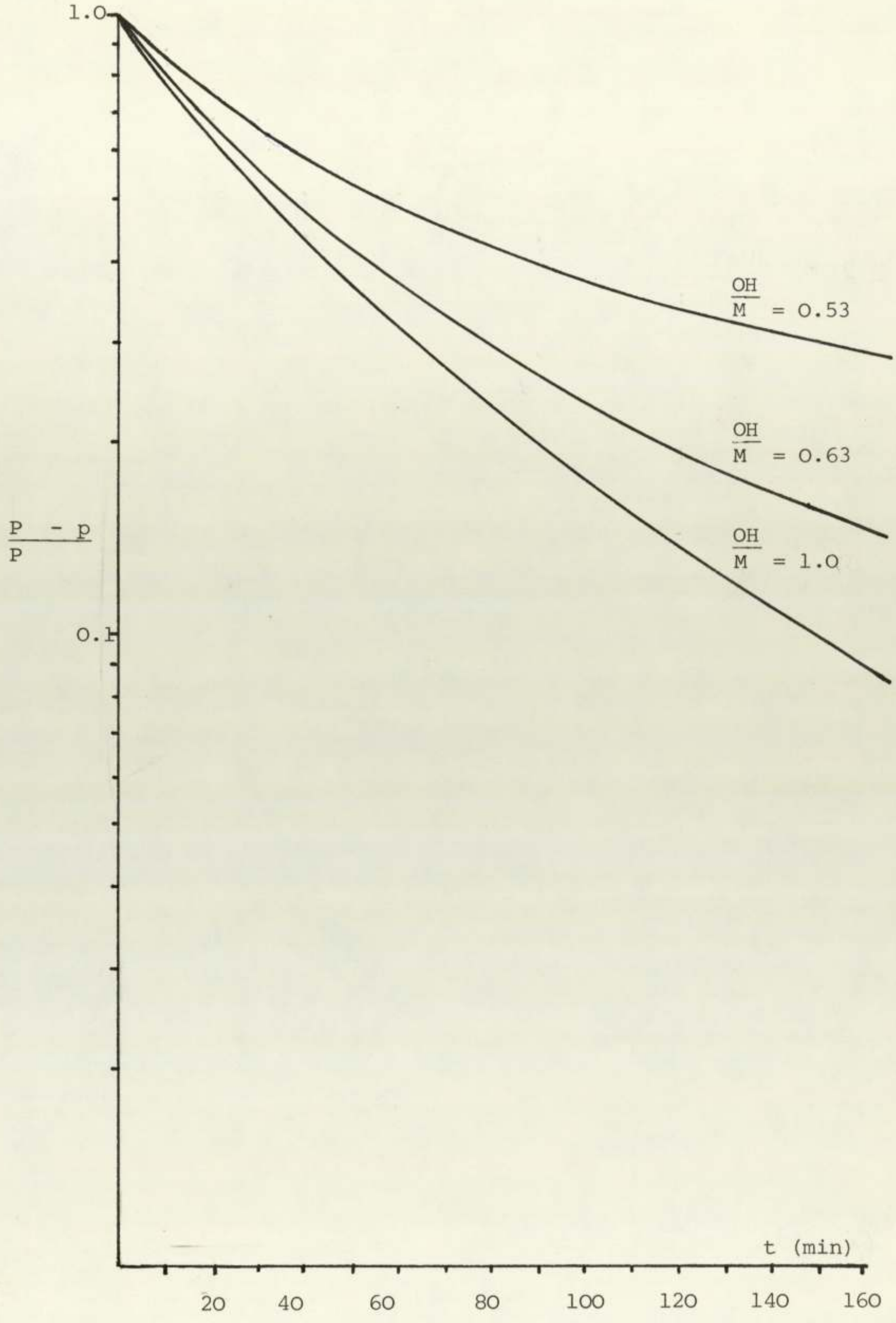


Fig. 7.4

Benzyl alcohol initiated decomposition of TGAS in nitrobenzene

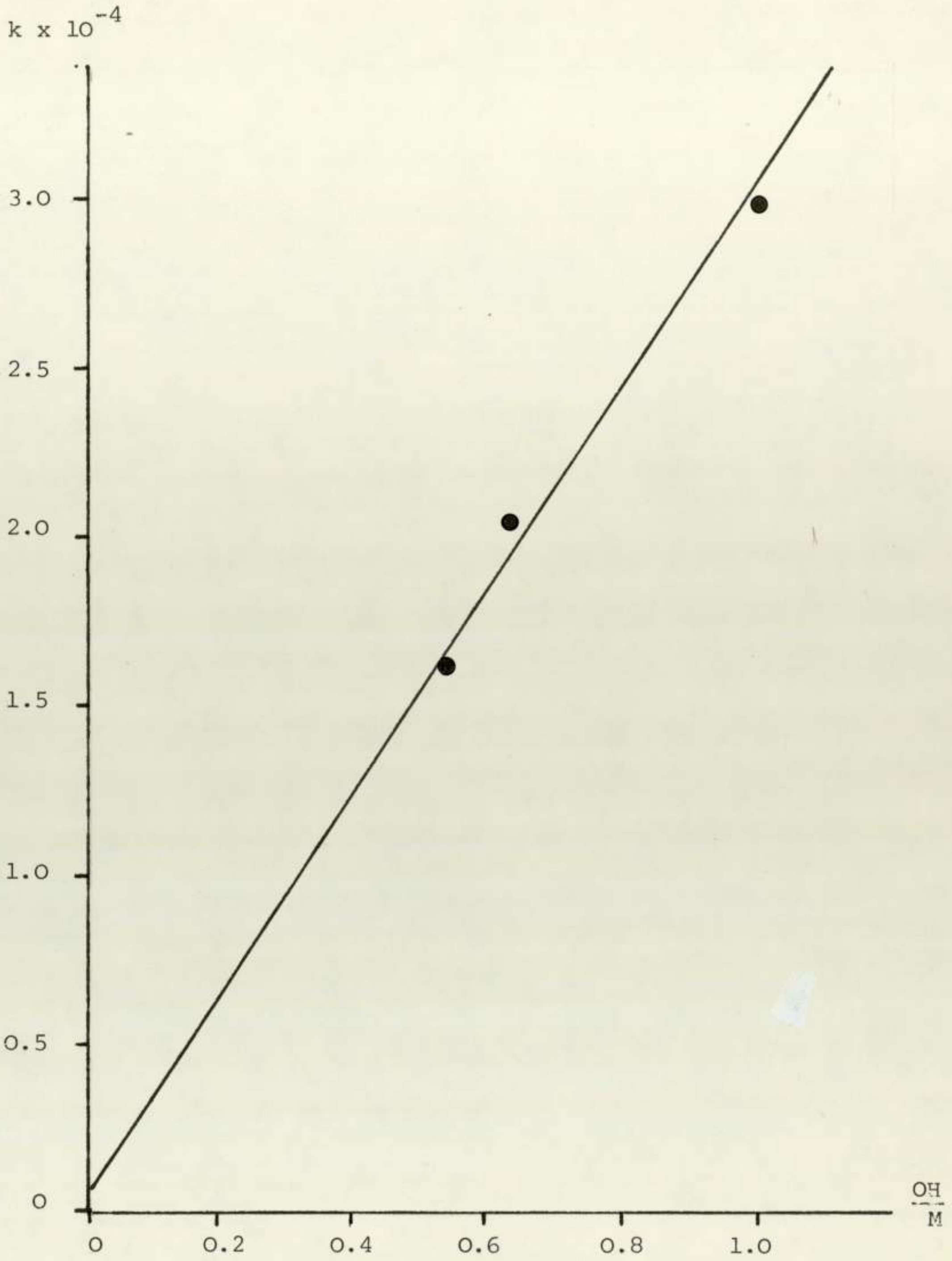


Fig. 7.5

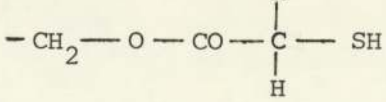
The effect of Monomer concentration on the rate of benzyl alcohol initiated decomposition of Thioglycollic Anhydrosulphite.

plot of $\frac{[M]}{[M_o]}$ during the early stages of the reaction, also decreased. A plot of k^o against $\frac{[OH]}{[M]}$ gave a straight line passing through the origin indicating that the reaction was first order in initiator concentration.

Fig. 7.5 shows the semi-log plot of $\frac{[M]}{[M_o]}$ against time at $\frac{[OH]}{[M]} = 0$ to be nearly a straight line whereas it would be expected that towards the end of the reaction the rate of decomposition would decrease as the initiator was used up and the plot would curve away from linearity. This suggested that in fact the benzyl alcohol was in excess over the anhydrosulphite and is thus not all used up at the end of the reaction. It is likely that the monomer concentration was actually less than the calculated 1 mole/l since it is inevitable, with such a highly reactive species that a certain amount of decomposition will occur during the preparation of solutions proceeding a kinetic run. It is therefore important to ensure that comparisons of rate constants are only carried out using kinetic data obtained from a single batch of monomer solution since exact duplication of monomer concentration in another batch of monomer would be impossible.

Another observation resulting from the previous experiment was the fact that for $\frac{[OH]}{[M]}$ less than 1 as the initiator concentration decreased the pressure of evolved sulphur dioxide decreased although the reaction could be restarted by a further injection of benzyl alcohol. From this it appeared that the reaction product was not involved in any further decomposition reaction with monomer.

Since the reaction product is the benzyl ester of thioglycollic acid (Fig. 7.6) it seems that the anhydrosulphite is not susceptible to attack by the SH group.



$$-CH_2-O-CO-CH_2-SH$$

Fig. 7.6

To check this theory a direct comparison of the rate of attack of OH and SH on thio-anhydrosulphites was made by carrying out reactions under the same conditions with benzyl alcohol and its sulphur-containing analogue benzyl mercaptan ($C_6H_5CH_2SH$).

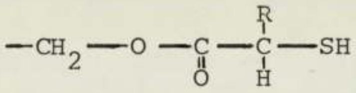
The results shown in table 7.3 demonstrate the reaction with benzyl mercaptan proceeds very slowly, the half life being some ten times longer than that of the reaction with benzyl alcohol:

Initiator / Monomer	Benzyl Alcohol		Benzyl Mercaptan	
	t½	k	t½	k
TGAS	21 min	5.5×10^{-4}	3hr 45min	5.0×10^{-5}
TLAS	99 min	1.2×10^{-4}	4hr 30min	4.6×10^{-5}

Table 7.3

Comparison of benzyl alcohol and benzyl mercaptan initiated decomposition of Thioglycollic and Thiolactic anhydrosulphites.

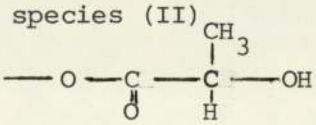
Here we have to consider whether benzyl mercaptan is a valid model for the reaction product (I) between the anhydrosulphite and alcohol.



$$-CH_2-O-\underset{\underset{O}{\|}}{C}-\overset{\overset{R}{|}}{\underset{\underset{H}{|}}{C}}-SH$$

(I)

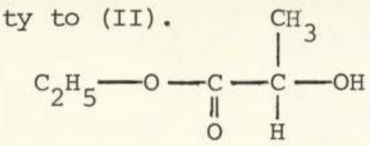
A comparison can be made with hydroxy acid anhydrosulphites. It has been calculated in the case of lactic acid (R_1 = HR_2 = CH_3) that the hydroxyl group of benzyl alcohol is nearly five times as reactive in the decomposition of the anhydrosulphite as the hydroxyl group of the propagating species (II)



$$-O-\underset{\underset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{\underset{\underset{H}{|}}{C}}-OH$$

(II)

On the other hand the hydroxyl group in ethyl lactate (III) has a similar reactivity to (II).



$$C_2H_5-O-\underset{\underset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{\underset{\underset{H}{|}}{C}}-OH$$

(III)

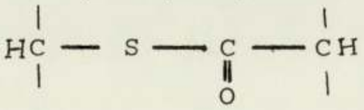
It seems that the reactivity of the hydroxyl group in the decomposition reaction is decreased by the electron-withdrawing effect of the ester group. This can be seen by comparing their Taft polar substituent constants σ^*: For $C_6H_5CH_2$- $\sigma^* = 0.215$ whereas for HO - CO - CH_2 $\sigma^* = 1.05$

Thus it can be postulated that the thiol group in species (I) will be similarly less reactive in the decomposition reaction than benzyl mercaptan. Bearing in mind the relative reactivities of benzyl mercaptan and benzyl alochol towards the thio anhydrosulphite, it is possible that the rate of the propagation step (i.e. the attack of species (I) on the ring) could be over fifty times slower than the initiation step (the attack of benzyl alcohol on the ring).

7.5 Analysis of Reaction Products

The products from the reactions described above were analysed by infrared spectroscopy, the absorption in the carbonyl region proved again to be particularly useful for characterization purposes.

The product from the benzyl alcohol reaction showed a carbonyl stretching frequency of $1730 cm^{-1}$ which is typical of a hydroxy ester group. In comparison the product from the benzyl mercaptan reaction showed a carbonyl stretching frequency at $1675 cm^{-1}$ which is typical of the thioester group:



$$\overset{|}{\underset{|}{HC}} - S - \underset{\|}{\overset{}{C}}\!\!\!\!\underset{O}{} - \overset{|}{\underset{|}{CH}}$$

A similar absorption has been observed by Ali in the Infrared spectra of polythioglycollic acid and polythiolactic acid which were prepared from their respective anhydrocarboxylates.

There was no evidence of any absorption at this frequency for the benzyl alcohol reaction product even when a low $\frac{[OH]}{[M]}$ ratio was used. This confirmed the proposal that the benzyl ester formed does not undergo further reaction with the monomer.

The Effect of Temperature on the Benzyl Alcohol initiated Decomposition of Thioglycollic and Thiolactic Anhydrosulphites

These reactions were carried out in nitrobenzene using an excess of benzyl alcohol such that the ratio $\frac{[OH]}{[M]}$ was approximately 1.6. This ratio provided a good straight line for the semi log plot of $\frac{p\infty-p}{p\infty}$ against t in the region studied. Reactions were carried out in the low temperature gas evolution apparatus at a range of temperature between 25°C and 45°C. The same stock solution of anhydrosulphite was used for all the measurement. The results are summarised in Table 7.4.

	T°C	$\frac{1}{T}$ °K	t½	k x 10^{-4}	E	A	ΔS‡
TGAS	26	3.344	55	2.10	13.5	1.58x10^{6}	-32.2
	31.5	3.284	38	3.04			
	40	3.195	21	5.50			
	42.8	3.170	17	6.79			
TLAS	28	3.322	160	0.65	13.9	7.07x10^{5}	-33.8
	40	3.195	90	1.29			
	45	3.145	41	2.75			

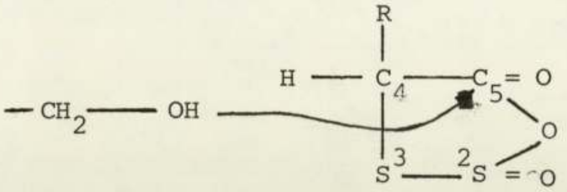
Table 7.4

Kinetic data for the benzyl alcohol initiated decomposition of T G AS and TLAS.

A plot of Log k against $\frac{1}{T}$ for a series of temperatures gave a straight line which allowed the activation engergy (E) to be calculated and from this the frequency factor (A) and the entropy of activation (ΔS‡) at 40°C were obtained. The Activation energies of thioglycollic and thiolactic anhydrosulphites were similar suggesting that the reaction was proceeding by the same mechanism in both cases. The values for E, A and $\Delta S^\ddagger$ were consistent with thosefor the nucleophilic attack of an alcohol on an anhydrosulphite.

At similar temperatures thioglycollic anhydrosulphite reacted considerably faster than thiolactic anhydrosulphite.

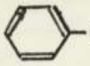
This is typical of a bimolecular reaction :



where a bulky substituent on the C_4 carbon interferes sterically with the attack of the hydroxyl group on the C_5 carbonyl since it has been shown that attack occurs from behind. There is also a certain amount of electronic deactivation of the carbonyl.

It would have been useful to measure the rate of decomposition of the thio-anhydrosulphites in pure benzyl alcohol but the concentration of the alcohol would be so great that the half-life for the thioglycollic anhydrosulphite react would be of the order of one or two minutes at 30 - 40°C which would be impossible to measure accurately.

Reactions with other Nucleophiles

Another model nucleophile useful in studying the decomposition of anhydrosulphites is benzylamine -CH_2— NH_2.

A trial run at 25°C with the solution of thioglycollic anhydrosulphite in nitrobenzene resulted in a very vigorous reaction with the gas evolution being complete in less than one minute. So it was not possible to carry out an accurate kinetic determination.

Variation of Solvent

It would be interesting to study the kinetics of the benzyl alcohol initiated decomposition of thio-anhydrosulphites in a variety of solvents with differing dielectric properties. Apart from nitrobenzene which has been taken as a standard solvent, anisole (methyl, phenyl ether) and dimethyl sulphoxide are two useful high boiling point solvents. The use of dimethyl sulphoxide was ruled out because, in attempting to make up a solution of the anhydrosulphite in it, itwas found that DMSO reacted adversely, deomposing the anhydrosulphite instantaneously.

The reaction in anisole was straightforward, proceeding at a rate similar to that of the reaction in nitrobenzene although the dielectric constants, E, of the solvents are quite different. In nitrobenzene (E = 31) the rate constant at 40°C for the benzyl alcohol initiated decomposition of thioglycollic anhydrosulphite was 1.2 x 10^{-4} K cal mole^{-1} compared with 1.6 x 10^{-4} K cal mole^{-1} for the same reaction in anisole (E = 9), suggesting that the dielectric constant of the solvent had little effect on the rate of reaction. It has been shown in previous work(73) on the nucleophilic decomposition of hydroxy acid anhydrocarboxylates that that there is no direct relationship between dielectric constant and the rate of a particular reaction if the solvents are different and in fact it has proved impossible to relate a single solvent property to the reaction rate in a satisfactory general relationship although some degree of success has been found in a limited area in correlating the 'donicity' of a solvent system to the rate of reaction in that system. The 'donicity' of a solvent is quantitatively related to the electron-donating or electron-accepting power of a solvent or mixture of solvents acting as a reaction medium.

Smith showed a direct relationship between the calculated 'donicity' and Log k for the benzyl alcohol initiated decomposition of mandelic acid anhydrocarboxylate in nitrobenzene, anisole dimethyl sulphoxide and various two-component mixtures of these solvents.

The results obtained using nitrobenzene and anisole as solvents for the benzyl alcohol initiated decomposition of thiolactic and thioglycollic anhydrosulphites fitted in well with this scheme and it was unfortunate that this could not be applied to dimethyl sulphoxide as well.

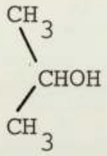
7.6 Grafting of Thioanhydrosulphites

The preceding study of the decomposition of thioanhydrosulphites (Chapter 7) indicated that they were not suitable for use as a means of preparing poly-α-thioesters which can be synthesised more successfully by the polymerization of the corresponding thioanhydrocarboxylates. Because they react readily with nucleophilic hydroxyl groups, forming esters, it seems that thioanhydrosulphites could be potentially useful in grafting reactions involving prepared polymers containing a suitable nucleophilic site in the same way that has been demonstrated with tartronic acid anhydrosulphite. Since the generated thiol group has been shown to be resistant to taking part in further propagation reactions the grafting of one monomer unit only will be most favoured. This investigation used again the three hydroxyl-containing vinyl monomers, hydroxy ethyl methacrylate, hydroxy propyl acrylate and N-methylol acrylamide which were used in the previous study involving tartronic acid anhydrosulphite. Kinetic profiles of pressure against time for the decomposition of thiolactic anhydrosulphite by the three hydroxyl containing monomers and benzyl alcohol are illustrated in Fig. 7.7. Again the reaction with HEMA and HPA proceeded very slowly with only 10% of the monomer being decomposed in 24 hours whereas the benzyl alcohol initiated reaction was complete in less than 12 hours. The reaction with N. Methylol acrylamide, as before, proceeded at a reasonably fast rate although slower than the reaction with benzyl alcohol.

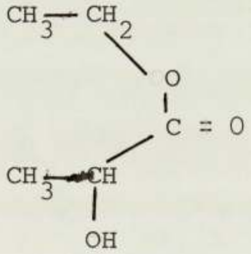
In order to obtain further information about the effect of the chemical structure of a nucleophilic species on the rate of decomposition of anhydrosulphites a series of reactions was carried out using aliphatic alcohols where the hydroxyl group appeared in different molecular environments. These were:

Ethyl oxitol $CH_3-CH_2-O-CH_2-CH_2-OH$

Isopropanol



Ethyl lactate



Ethyl oxitol a primary alcohol and isopropanol, a secondary alcohol, both reacted normally with thiolactic anhydrosulphite, the rate of decomposition being similar to that of the reaction with benzyl alcohol. On the other hand ethyl lactate, whose hydroxyl group is in a secondary position adjacent to an ester group reacted very slowly like HEMA and HPA. This confirmed that the presence of an ester group in the proximity of the hydroxyl group in the molecule reduces the nucleophilicity of the hydroxyl group sufficiently to interfere with the decomposition of anhydrosulphites. It can be inferred that the N-substituted amide group in N-methylol acrylamide has little deactivating effect and, of the available hydroxyl containing vinyl monomers N-methylol acrylamide is most suitable for the successful grafting of thio anhydrosulphites.

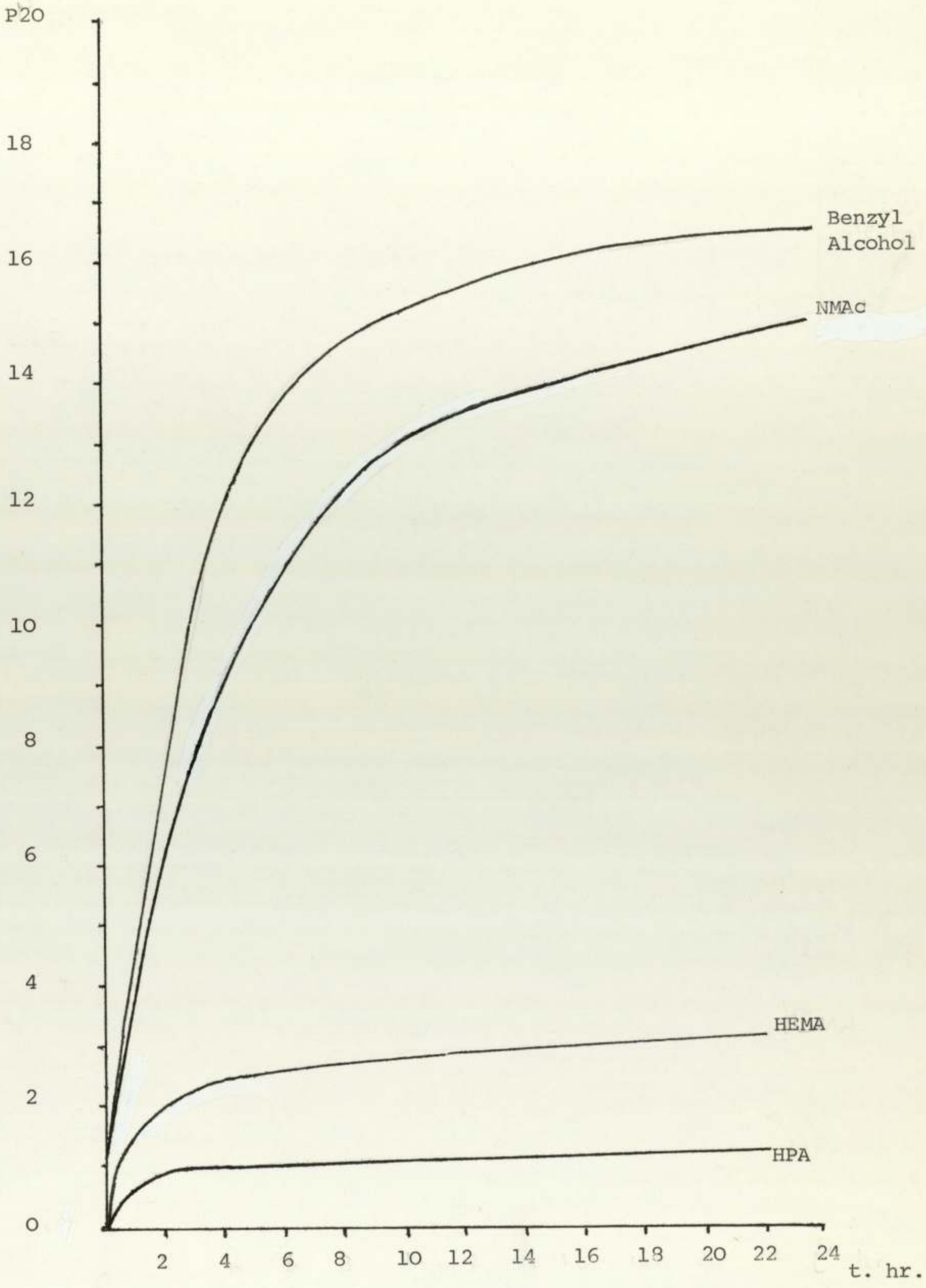


Fig. 7.7

Decomposition of Thiolactic Anhydrosulphite by Vinyl Monomers

CHAPTER 8

CONCLUSIONS AND SUGGESTIONS FOR FURTHER WORK

The work described in this thesis demonstrates that cyclic ester monomers can be successfully prepared from α-hydroxy and α-thio carboxylic acids with substituent functional groups once the appropriate reaction conditions have been determined. Of course it can only be expected that the presence of such additional functional groups will interfere with the desired reaction and produce more problems with purity than have been met with in the preparation of cyclic ester monomers from alkyl and aryl substituted α-hydroxy acids.

The blocking or protection of the extra functional groups was avoided because blocking reactions of the type required involve several additional steps in the synthesis. In addition the subsequent removal of the protecting group requires conditions likely to break the relatively weak ester linkages involved in the cyclic monomers and indeed in the products of their ring-opening reactions. One major problem in the synthesis of these compounds is the fact that strictly anhydrous conditions are required and because carboxylic acids containing more than one hydroxyl group are very hydrophilic, the anhydrous acids cannot be made and even the metal salts of these acids have a great affinity for water with consequent difficulties in drying. It appears that when the hydroxy-acid has two carboxylic acid groups there are two competing cyclization reactions involving the acyl chlorosulphinate intermediate of the thionyl chloride reaction to give either the anhydrosulphite or the anhydride. The favoured cyclization reaction seems to depend on the ring size of the product and thus in the case of malic acid $HOOCCH_2$ CHOH COOH and thiomalic acid where both the anhydrosulphite and the anhydride are five-membered rings (the most stable configuration) is the formation of the anhydride of significance.

The preparation of pure malic and anhydrosulphite would require protection of the second carboxylic acid group. In the preparation of gluconic acid anhydrosulphite, which has five hydroxyl groups, there are there are theoretically five possible sites for cyclization, but the infra-red spectrum of the reaction product is typical of only the five-membered ring. Again it is the configuration of the intermediate stage that determines the favourability of cyclization between the carboxylic acid group and a particular hydroxyl group.

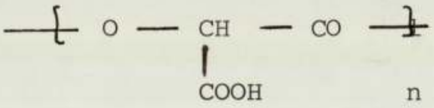
In the preparation of anhydrosulphites from the α-thio carboxylic acids thioglycollic and thiolactic acids there were, of course, no problems from additional functional groups but in these cases the metal salts behaved oddly and therefore the acids themselves were used in the preparation. The effect of the presence of two large sulphur atoms in the ring on decomposition reactions has not previously been studied. The reactions of thioanhydrosulphites with nucleophiles were found to be quite different from those of the thio-anhydrocarboxylates prepared and studied by Ali. Although the anhydrosulphites were readily decomposed by hydroxyl groups they reacted only very slowly with the SH group thus restricting polymerization by generated -SH propagation.

The kinetic studies carried out using the model nucleophile benzyl alcohol helped to establish the mechanism of the ring-opening reaction, which was found to be a bimolecular nucleophilic mechanism for all the anhydrosulphites. There was a considerable amount of self-decomposition associated with the hydroxyl substituted anhydrosulphites of glyceric and gluconic acid which will always compete with other nucleophiles and complicate the possible polymerization processes. Unusual solvent effects were observed in the ring-opening of carboxylic acid substituted anhydrosulphites which were thought to be associated with ionization of the substituent carboxylic acid group which has been observed in the polymerization of carboxylic acid substituted lactones. The kinetics of the decomposition of these anhydrosulphites in pure benzyl alcohol were similar to those observed for other mono-substituted anhydrosulphites such as those of lactic and mandelic acids. The Taft electronic substituent constants were successfully used to predict the reactivity of tartronic acid anhydrosulphite towards nucleophilic attack.

Anhydrosulphites have been successfully ring-opened with vinyl monomers containing nucleophilic groups. These reactions were performed to investigate likely sites for grafting onto hydrogel polymers. Some of these monomers which had, at first sight, apparently suitable nucleophilic sites (such as hydroxy ethyl methacrylate and hydroxy propyl acrylate) were very slow to react with anhydrosulphites. This was found to be due to the chemical structure of the molecules where the proximity of an ester group and/or the secondary position of the hydroxyl group tend to reduce its nucleophilicity N-methylol acrylamide which has a primary hydroxyl group on the carbon atom adjacent to an amide group was found to be more reactive and therefore most suitable for grafting. This study was also useful in predicting the behaviour of those monomers in cross-linking reactions of hydrogels. It was originally thought that, under high temperature moulding conditions cross-linking would take place by esterification between HEMA or HPA and acrylic or methacrylic acids in copolymers containing both. This did not happen readily in practise but it has since been found that acidic monomers can be successfully cross-linked with NMAc under acceptable moulding conditions.

Following on from this work tartronic acid anhydrosulphite was successfully grafted onto hydrogel polymers containing N-methylol acrylamide, either onto the bulk polymer in solution or onto the surface of a preformed polymer film. Grafting was shown to have a marked effect on the physical properties of the hydrogel, most significantly on the surface-free energy as measured by the contact angle. This work has proved that grafting is an extremely useful way of introducing further functional groups onto hydrogel polymers and further study should allow fine control of grafting to make polymers with desired properties. In the case of grafting of thiol groups onto hydrogel polymers some preliminary use has been made of this in attaching carbohydrate groups onto the polymers in the search for a synthetic cell-surface model.

The work of this thesis shows that of all the functional-substituted anhydrosulphites studied that of tartronic acid was synthesized most purely. It is possible that, if the right conditions were found, it would be possible to polymerize this anhydrosulphite and so it might be useful to look at other catalysts for polymerization. The polymer which would be formed from tartronic acid would be expected to have the properties required for application as a drug carrier since it has both an attachment site and will be biodegradable.



$$-\!\!\left[\,O - \underset{\displaystyle COOH}{\underset{|}{CH}} - CO\,\right]_n\!\!-$$

It would be interesting to investigate the possibility of polymerizing tartronic acid anhydrosulphite using catalysts other than the nucleophiles used here, such as bases or organo-metallic complexes.

Several other areas requiring further investigation have arisen during the course of this work, a few of which are listed below:

1) It would be interesting to attempt to prepare more ambitious cyclic-monomers from, for example, craboxylic acid derivatives of carbohydrates such as galacturonic and glucuronic acids, and also from other hydroxy acids in the series $HOOC\,(CH_2)_n CHOH\,COOH$

2) Further investigation of the solvent effects in the decomposition of carboxylic acid substituted anhydrosulphites is required to confirmation ionization theory.

3) The whole area of grafting onto hydrogel polymers is open to

further investigations now that it has been shown that grafting can be achieved readily and has a significant effect on the physical properties of the polymer.

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