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Abstract: In this chapter we will look at the nature, preparation and properties of degradable polymers. We will discuss both natural and synthetic polymers and look at how they are either isolated or prepared and also at how they degrade via both biotic and abiotic pathways.

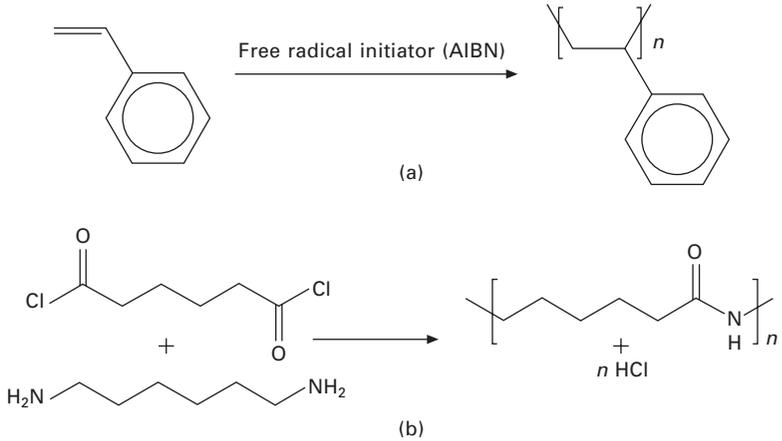
Key words: biotic, abiotic, degradation mechanism, natural polymers, synthetic polymers.

2.1 Introduction

2.1.1 Polymers

Polymers or so-called macromolecules are large molecular structures containing one or more units which are repeated within the molecule. The term 'polymer' has its origin in Greek and derived from the term 'poly' meaning many and 'mer' meaning unit. Polymers as molecules have pervaded life much longer than the synthetic materials we often associate with the word and biology has made prolific use of their diverse and unique properties. Their emergence as synthetic materials dates back to 1907 when Dr. Leo Baekeland prepared Bakelite from formaldehyde and phenol, perhaps the first fully synthetic polymer. Later the emergence of polyesters and polyethylene revolutionised life as a range of new, hardy, mouldable polymers allowed a rapid explosion in art, communication and fashion. The ability to form complex shapes while retaining their properties with little degradation made them excellent materials for the new industrial age. The term 'plastic' has become ubiquitous with the term 'polymer' although 'plastic' refers to the mechanical properties of some polymers, especially in the bulk form. However, the term polymer is far more encompassing when considering molecular materials in general.

Polymers are usually prepared by a reaction between identical or similar molecules in order to produce a theoretically infinite chain (Fig. 2.1). In reality the reactions usually result in a range of long chains as the reactions themselves are hindered by molecular motions and side reactions. There are several excellent books on polymer chemistry and reactions and we will not discuss this in detail here.



2.1 (a) Formation of polystyrene by free radical polymerisation. (b) Formation of Nylon 6,6 by condensation polymerisation. n denotes that the chains are long but polymerisation results in a range of chain lengths and molecular weight cannot be defined as a single number but is usually represented as a weight and number average molecular weight.

2.1.2 Degradable polymers

The preparation and properties of degradable polymers in general is a massive field which encompasses biomaterials, drug delivery, sustainable development and environmental impact. As a result there are a vast range of polymers, polymer blends and composite materials which could be included under this title. In order to keep this chapter to a sensible length and make it as applicable as possible to the general theme of the book we will take time to look at the main degradable polymers. The concept of a degradable material is, however, a diverse one and the definition may depend on the perspective of the application and of one's understanding of degradation. Two types of degradation often discussed in the literature are biotic and abiotic degradation. Biotic degradation relies specifically on the action of enzymes and organisms such as bacteria to break down the material. The processes can be complex and depend on a complex mix of extracellular processes, the diversity of the microbe community and, of course, the health of the microbial community. Abiotic degradation relies on processes which are not related to enzymic or bacterial processes. These may rely on a range of processes including photolysis or thermal ageing but is generally centred on hydrolysis reactions. In addition to this, the concept of degradation may be purely related to the loss of a specific property of a polymer without any resulting mass change, a mass loss of a polymer as it degrades into smaller fragments of polymer chain, or complete degradation to water and carbon

dioxide or methane. Loss of mechanical properties may be associated with photo or thermal ageing of a material, whereas break up of the polymer chains is a chemical breakdown of the polymer molecules themselves. Degradation of a polymer into carbon dioxide/methane and water is usually associated with biotic degradation, the by-products being formed as a result of the respiration process as small fragments of the polymer chain act as a hydrocarbon source for the organism.

There is also an issue over the use of the word 'degradable'. Essentially all polymers are degradable, as few will survive high temperature treatments and so on. However, usually the term is reserved for ambient conditions. Even restricting the parameters to standard temperature and pressure, this still leaves the question of the environment in which the material is left and the time over which the measurement is conducted. The latter is of particular interest as this will be strongly dictated by the application to which the polymer is to be put and allows us to put limits on what is meant by degradable. This is important as it has been shown that low density polyethylene (LDPE) shows significant degradation in soil, but the process takes 32 years (Otake *et al.*, 1995). In a similar manner the degradation of a polymer for drug delivery should be over within hours and occur at the required site of delivery, whereas a degradable tissue scaffold may need to last months before it completely degrades. Therefore a degradable polymer can be said to be degradable if it is completely broken down within the lifetime of the device or article into which it has been fashioned.

In this chapter we will particularly look at the degradation of two polymer types. Firstly those that are considered to be natural polymers and therefore derived from a biological source, though in most cases are altered later. Secondly we will consider synthetic polymers. In each case we will look at preparation methods for the polymers, their molecular structure, applications and their degradation. We do not have space to consider all possible materials here and therefore will focus on the most common examples of homopolymer systems (i.e. those which consist of one polymer type). In many cases copolymers and polymer blends have also been prepared with a range of degradation properties, but these will not be discussed in detail here.

2.2 Natural polymers

Biology has been making polymers for as long as life has existed. They form the basis of genetic encoding, cell structures and extracellular matrices. Their biodegradability is evident in the cycle of life. Of these polymers the two main classes in use today are proteins and polysaccharides. Silk and cotton are excellent examples of biodegradable natural polymers in everyday use. Silk is a protein-based material whereas cotton is a polysaccharide-based

material. Both have been used by humans for millennia to great effect. Particular interest in these materials arises from their relative stability to abiotic hydrolysis compared to relatively rapid biotic degradation. This degradation process is important for a plant where life generally involves water-based chemistry.

2.2.1 Sources and structure of natural polymers

Natural polymers are generally extracted from organisms. These are often plants or bacteria. The challenge of many of these is to obtain a commercially significant amount of material from the organism to make its breeding worthwhile. This has often given rise to an interest in bacterial synthesis where the organism may be grown in a broth under easily controlled conditions. The second challenge is purification of the material from the other components of the system. Clearly this final issue is of particular concern if a natural polymer is to be used as a biomaterial. Both the isolation and purification of these polymers varies greatly and will not be discussed in detail here.

Proteins

All proteins may be classed as biodegradable. Life relies on the ability to break down and reuse the amino acids in proteins in order to construct cells, enzymes and many other building blocks of complex organisms. Their structures are complex, not just in their chemical make up but also in their exact structure. The folding and coiling of proteins into specific geometries affects their properties and their function. The thermal disruption of these complex structures usually spells the end of life at elevated temperatures for most organisms. The degradation of proteins is left to specific enzymes and simple chemical degradation is generally slow without enzymic intervention. With this in mind we will look briefly at the chemistry and properties of silk as an example protein but would refer the reader to more in depth discussions on the more common protein-based materials such as collagen (Friess, 1998) and fibrin (Gaffney, 2001).

Silk is a protein, based to a large extent on the fragment Gly-Ala-Gly-Ala-Gly-[Ser-Gly-(Ala-Gly)_n]₈-Ser-Gly-Ala-Ala-Gly-Try (Lucas *et al.*, 1962). The material has a high tensile strength and excellent mechanical properties which make it especially interesting. The high performance of silk is thought to be a result of the folding of the proteins into large numbers of ordered sheets.

Silk itself is obtained from the cocoons of the mulberry silkworm (*Bombyx mori*) and is generally obtained by unravelling the fibres which enwrap the cocoon. The larvae themselves are now farmed. The ease of obtaining silk with little processing explains its prevalence since ancient times.

Polysaccharides

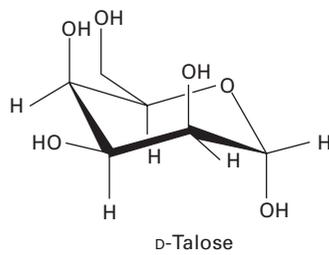
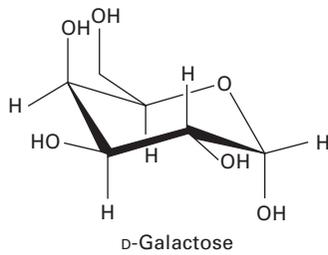
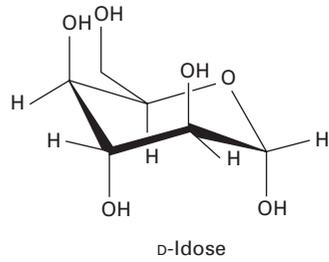
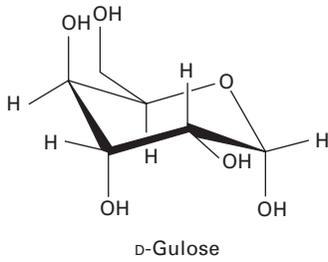
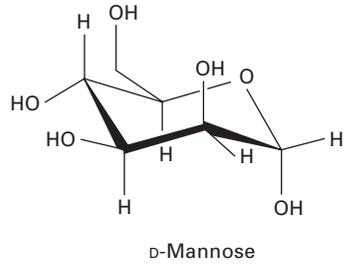
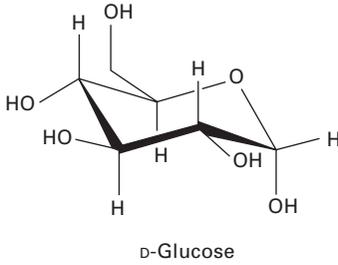
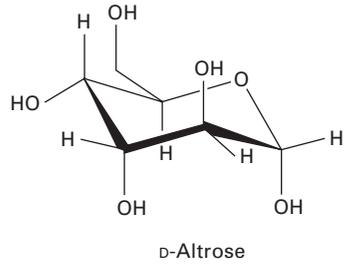
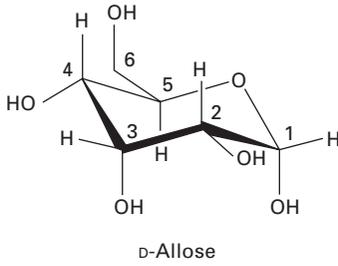
Polysaccharides form a massive class of natural polymers, often modified for use. They form some of the first polymeric materials used by humans in manufacturing, together with nitrocellulose which was once used to make film and gun cotton. The polysaccharide class of natural polymers is based on polymers with repeat units based on sugars. Figure 2.2 shows the ring structures of the hexose range of sugars which form the basic structure of many polysaccharides. The sugar repeat units on the backbone of polysaccharides have many chiral centres (five in the case of the hexoses shown). These centres determine the exact saccharide. For example all the saccharides in Fig. 2.2 have the same nominal formula, $C_6H_{12}O_6$, however each one is distinctly different owing to their chiral nature. In a polysaccharide the saccharide repeat units are connected via the oxygen on carbon 1 which forms a glycosidic bond to carbon 4 on another molecule with the subsequent elimination of water. An example of this is given in Fig. 2.3 where the structure of sucrose is shown.

There are a large number of polysaccharides being employed as degradable polymers. The most common of these is probably cellulose (Fig. 2.4) which is the most common component of cotton. Cellulose itself is usually derived from plant matter and is often modified to provide improved properties such as solubility for processing and so on. Alteration of the polymer usually involves modification of the OH groups on the backbone of the polymer using an acid anhydride. This results in various degrees of substitution to give ester functionalised celluloses (Edgar *et al.*, 2001). Similar modifications have also been attempted with other polysaccharides (Campoccia *et al.*, 1998).

Other polysaccharides which form part of this group of degradable polymers are starch, larch gum, alginic acid, agar, carrageenan, chitin, hyaluronic acid, dextran, gellan gum and pullulan. The structures of many of these polysaccharides are complex and a full discussion is given in the literature (Mano *et al.*, 2007). Of these, starch, cellulose and larch gum are plant derived (although cellulose may also be obtained from microbial sources), alginic acid, agar and carrageenan are obtained from algae, chitin and hyaluronic acid are obtained from animal sources or microbial sources and the others are obtained from microbes.

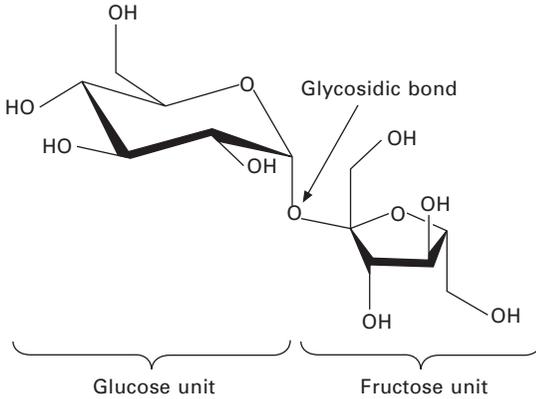
Polyesters

The structure and degradation of the naturally produced polyesters polyhydroxy butyrate (PHB) and polyhydroxyvalerate (PHV) are discussed in the next section on synthetic degradable polymers as these materials have much in common with their synthetic counterparts. These polymers were first

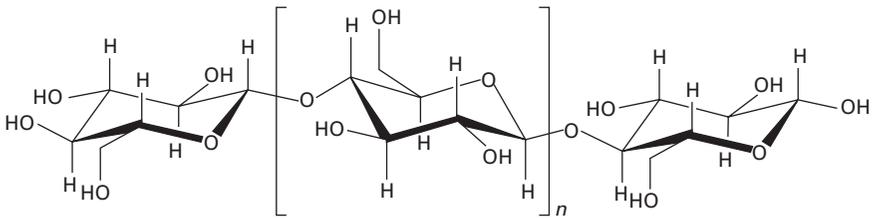


2.2 Basic hexose sugar rings. The common numbering of carbon atoms is shown in the first example (D-allose).

prepared by feeding *Alcaligenes eutrophus* with propionic or valeric acid along with glucose (Holmes *et al.*, 1985). Since then there have been several other species found which either produce these polymers naturally when



2.3 Structure of sucrose showing the glycosidic bond.



2.4 Structure of cellulose.

exposed to the correct substrate or may be genetically modified to do so (Suriyamongkol *et al.*, 2007).

2.2.2 Uses of natural polymers

The use of natural polymers in the modern world is prevalent. We have a society which mixes natural and synthetic materials in a plethora of devices and artefacts. Apart from our personal biosynthesis of polymers, we commonly use cotton, silk, wood and wool in many everyday articles. Rather than discuss here these many and often interesting and diverse applications we will restrict examples to situations where biodegradability is of foremost importance.

Uses of proteins

Proteins such as silk have been used for some time as a suture material (Postlethwait *et al.*, 1962). They are often highly resistant to hydrolysis owing to the stability of the amide bond but may be degraded by common proteases. Collagen has found numerous uses as a biomaterial in a wide

range of applications and is of particular interest as a drug delivery carrier (Friess, 1998) and in materials for reconstructive surgery of soft tissue (Sajjadian *et al.*, 2010).

Uses of polysaccharides

Whilst there is a large body of continuing work on blending polysaccharides with other polymers to enhance or control degradability, there is still great interest in using these materials, in a modified form, as hydrogels (Campoccia *et al.*, 1998; Schmidt *et al.*, 2008). These hydrogels are biocompatible and generally have excellent absorption/release properties which make them interesting materials as drug carriers.

2.2.3 Degradation of natural polymers

As we have already mentioned, the degradation of biologically derived polymers usually proceeds via an enzyme-catalysed pathway. This allows the polymer to remain stable and function for long periods of time until final degradation is required.

Degradation of proteins

Hydrolytic degradation of proteins is unfavourable owing to the resonance of the lone pair on the nitrogen in the amide bond which results in increased stability to hydrolysis. However, proteases are able to catalyse the process efficiently and thereby allow the degradation of organic matter as well as digestion of foodstuffs and removal of dead tissue by biota. Degradation initially produces amino acids and then these will also be degraded to carbon dioxide/methane and water depending on the nature of the protein, the organism acting on it and the culture's environment.

Degradation of polysaccharides

In a similar manner to proteins, the degradation of the glycosidic bond in polysaccharides is resistant to hydrolysis under normal conditions. Digestion of polysaccharides is again an enzyme-catalysed process and usually results in the organism completely digesting the sugars in order to provide energy.

2.3 Synthetic degradable polymers

Degradable synthetic polymers, unlike natural polymers, may be readily mass produced on a multi-tonne scale and have properties similar to non-degradable polymers. There are a wide range of degradable polymers and

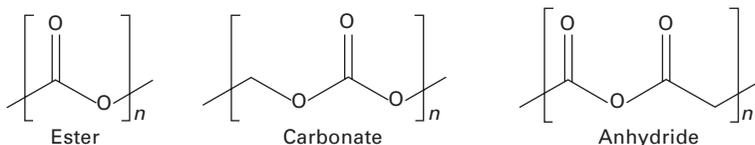
more are being discovered each day, however they may be divided into several classes, each with specific properties. Key to the properties of a degradable polymer is the ability to manufacture it and its components without significant degradation, as well as it having a suitable lifetime for the final material to fulfil its role. The challenge of balancing these factors drives continued research into this area. In addition to this there are a wide range of applications of degradable polymers and this often will dictate the types of polymer used. For example a degradable polymer for human implant as a slow release mechanism must not degrade into toxic or irritating components which may cause an inflammatory response.

2.3.1 Preparation of synthetic degradable polymers

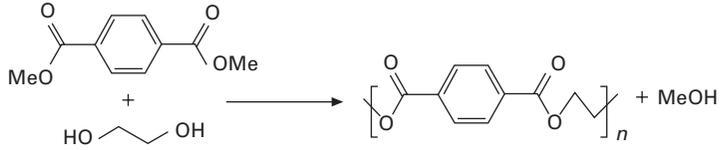
There are three main classes of degradable synthetic polymer which we will consider here: polyesters, polycarbonates and polyanhydrides (Fig. 2.5). In addition to these are a range of polymers which include other degradable groups including amino acids and phosphates. These are reviewed in detail in the primary literature and will not be discussed in detail here (Kamath and Park, 1993; Falco *et al.*, 2008).

Polyesters

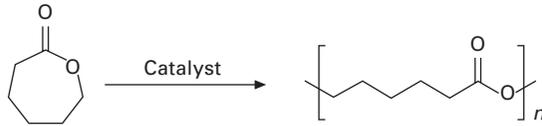
Polyesters contain the ester linkage between monomer units. This type of bond is usually, but not exclusively, formed via either a transesterification reaction or a ring opening reaction (Fig. 2.6). There are five main polyesters which are considered to be biodegradable: polyglycolic acid (PGA), polylactic acid (PLA), poly- ϵ -caprolactone (PCL), polyhydroxybutyrate (PHB) and polyhydroxyvalerate (PHV). We have already discussed the preparation of the latter two (PHB and PHV) as both of these are biologically derived. PGA, PLA and PCL are all readily prepared via ring-opening polymerisations (Deasy *et al.*, 1989; Gilding and Reed, 1979; Labet and Thielemans, 2009). Typically the polymers are prepared in the molten monomer using a catalyst to promote the ring opening process (Fig. 2.7). A traditional catalyst for this is tin octanoate. Owing to the hazards of the use of tin and its associated toxicity, there have been several other catalysts developed over recent years. Of particular interest in this respect is the development of catalysts to control



2.5 Common functional groups in degradable polymers.

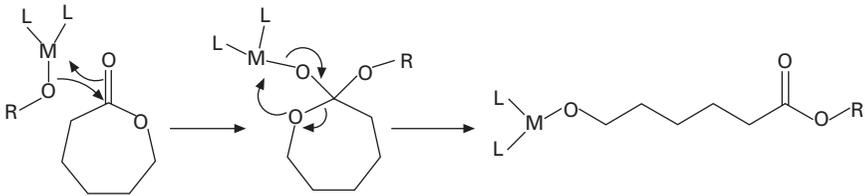


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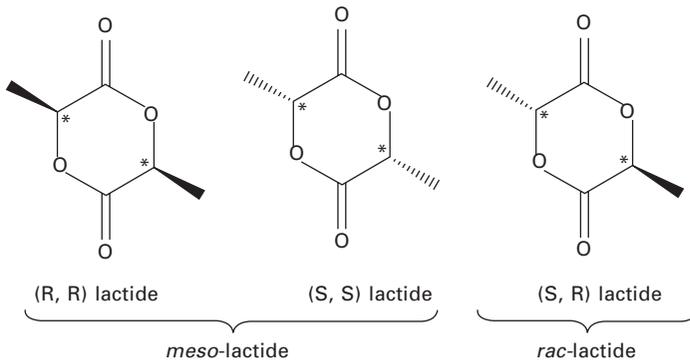


(b)

2.6 (a) Preparation of polyethylene terephthalate (non-degradable) by transesterification. (b) Preparation of polycaprolactone (PCL) via ring opening polymerisation.



2.7 Ring opening polymerisation of caprolactone where R is any alkyl group or polymer chain and L is a ligand from the metal centre.



2.8 Lactide monomers with stereo centres marked (*)

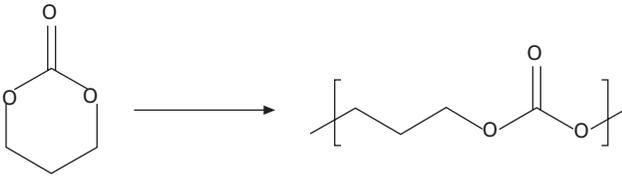
the chiral centres in PLA (Thomas, 2010). The lactide monomer has two stereo centres (Fig. 2.8) which may be either *SS*, *RR* or *SR*. The former are termed the *meso*-form and the latter the *racemic* form. Polymerisation of these monomers and their mixtures can result in a range of structural differences in the final polymer. This affects the packing of the polymer chains and hence the final properties of the polymer.

Polycarbonates

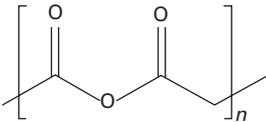
Polycarbonates are a similar class of polymer to polyesters and may be prepared by a similar ring opening polymerisation to that for the polyesters above (Fig. 2.9) (Rokicki, 2000). Examples of polycarbonate-based degradable polymers are restricted in the main to poly(trimethylene) carbonate.

Polyanhydrides

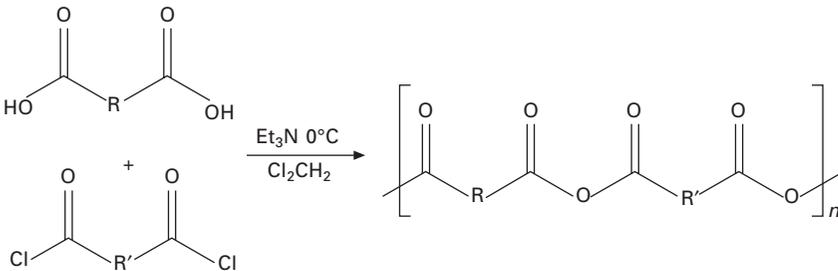
The polyanhydrides are perhaps some of the least hydrolytically stable degradable polymers. There are many examples which all contain the anhydride group (Fig. 2.10) as part of the repeat unit. Poly(1,3-bis-*p*-carboxypheloxypropane anhydride) is probably one of the best examples of a degradable polyanhydride currently in use (Kumara *et al.*, 2002). They are generally prepared by condensation reactions (Fig. 2.11).



2.9 Synthesis of polytrimethylene carbonate via ring opening polymerisation (ROP).



2.10 An example of a polyanhydride showing the anhydride group.



2.11 General method for the preparation of polyanhydrides by condensation polymerisation of a dicarboxylic acid with a diacid chloride.

2.3.2 Uses of synthetic polymers

The use of synthetic degradable polymers is generally limited owing to their ability to degrade in aqueous media. Slow degrading polyesters have been used in a range of applications including packaging (Sinclair, 1996), bone replacement materials (Nelson *et al.*, 1977), adhesives and films and coatings as well as implantable soft tissue scaffolds (Chena and Wua, 2005). The application of these polymers depends on their stiffness (modulus) and strength as well as their ability to degrade. These factors are influenced in a large part by the degree of crystallinity in the polymer, the orientation of the crystallites to the line of applied force and the temperature at which the polymer undergoes a transition from the glassy to the plastic state (the glass transition temperature or T_g).

The specific use of these types of polymer as biomaterials generally focuses on polyesters and polycarbonates. These materials can offer mechanical support for the growth of new tissue for long enough periods of time for the generation of new tissue. From a practical perspective, the properties of biomaterials such as these often need to be modified further to improve biocompatibility, elicit the correct mechanical properties and modify the degradation profile of the materials. This is achieved by a range of approaches including inclusion of bioactive molecules in the polymer (Niu *et al.*, 2009) or modification of the polymer surface (Kiss *et al.*, 2010) in order to promote tissue growth or improve biocompatibility, blending of two or more polymers or preparation of copolymers to improve the mechanical properties and modify the degradation profile (Wang *et al.*, 2010). The rest of this book will deal with specific applications of many of these polymers.

2.3.3 Degradation of synthetic polymers

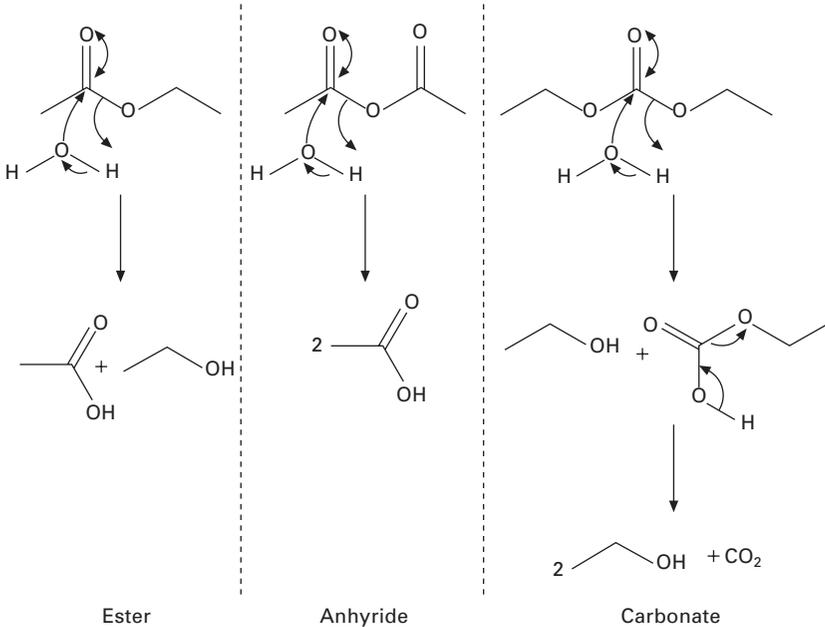
A major difference between synthetic and natural biodegradable polymers is the ability of synthetic polymers to degrade via hydrolysis rather than solely via a biotic mechanism. Clearly life could not exist if the polysaccharides, which are commonly used by biota, degraded solely on contact with water. This however does not preclude the action of biota on synthetic polymers. As we have already seen, naturally derived polymers such as PBH are polyesters which have specific roles in energy storage in some bacteria. This therefore implies that biota have developed the enzymes necessary to degrade these polymers in order to release the small molecules which are then metabolised by the organism to provide energy. We will therefore consider both processes of degradation here.

Abiotic degradation

As already mentioned the abiotic degradation of biodegradable polymers relies, for the most part, on hydrolysis of groups in the polymer chain. Degradation of these groups results in the formation of small molecules which may then be absorbed by cells and degraded further into water and carbon dioxide through normal metabolic pathways or excreted from the organism.

Hydrolytic degradation of ester (Hakkarainen, 2002), anhydride (Gopferich and Tessmar, 2002) or carbonate (Zhu *et al.*, 1991) groups is promoted by the polarity of the carbonyl bond (Fig. 2.12). The δ^+ polarity at the carbon of the carbonyl bond allows attack at the carbonyl by the oxygen on a water molecule which has a complimentary δ^- polarity. The result of the reaction is either a carboxylic acid and an alcohol, in the case of an ester, or two carboxylic acids in the case of an anhydride. The degradation of the carbonates is more complex as the hydrolysis results in the formation of an alkyl hydrogencarbonate which is not stable and readily decomposes further to an alcohol and carbon dioxide.

The degradation of the polymers proceeded generally via random chain scission. This means that the hydrolysis may occur, in principle, at any point along the chain. This in turn means that the degradation of polymers by this method results in a general broadening and decreasing of the



2.12 Hydrolytic degradation of ester, anhydride and carbonate linkages.

average molecular weight of the polymer. The process of degradation may be accelerated by changes in pH. Both an increase in pH or a decrease in pH results in catalytic acceleration of the hydrolysis process, particularly in the case of polyesters. The formation of an acid as the by-product of the degradation can result in auto acceleration of the degradation process where the acid produced during degradation becomes trapped in the polymer and further accelerates the degradation.

Often degradation of polymers is observed by looking at the mass loss of the polymer and it is worth pointing out that, although a polymer may lose mass during degradation, it does not necessarily follow that the associated mass loss is the result of direct conversion of polymer to monomer/smallest units. It is well known that degradation of polymers via hydrolysis can result in the elimination of many small molecules based on the polymer backbone (Vidil *et al.*, 1995). These may take the form of more complex molecules other than linear short chains of the polymer, for example cyclic oligomers (short polymer chains) are often observed. With time these too will degrade to the monomer and be either excreted or metabolised.

The rate of hydrolysis depends on two important factors, the sensitivity of the group to be hydrolysed and the ease with which water can penetrate the polymer. With regard to the sensitivity of the group to hydrolysis, anhydrides hydrolyse far more rapidly than esters or carbonates and it is for this reason they are often used as carriers of drugs for release over less than one week (Gopferich and Tessmar, 2002). However there is a considerable range in the degradation of even one class of polymers. Consider the two polyesters, polylactic acid (PLA) and polyethylene terephthalate (PET). The degradation of PLA may be counted in months in water (Lunt, 1998) and that of PET in tens of years (Kint and Munoz-Guerra, 1999).

Three factors play an important role in controlling the permeability of water in the polymers, the hydrophobicity of the polymer, crystallinity and polymer chain mobility. The rate of degradation of the polymer will be restricted initially to its surface as polyesters are generally insoluble in water. The magnitude of the interaction of water with the surface of the polymer will be dictated by the structure of the polymer backbone. A polyester containing a greater proportion of hydrophobic groups will be more hydrophobic than a similar polyester containing a greater proportion of hydrophilic groups. This effect can be seen in polylactic acid which has a water–polymer contact angle (Kiss and Vargha-Butler, 1999) of about 55°, whereas PET has a water–polymer contact angle (Merrill and Pocius, 1991) of 77° (this means that PET is more hydrophobic). It should also be noted that the initial contact angle at a water–polymer interface is likely to change with time as the polymer degrades. In addition to the effect of hydrophobicity, polymer crystallites also have a role to play. Many polymers form semi-ordered crystalline regions. This will offer little free volume for

water ingress and, therefore, degradation and will also impede diffusion of water through the structure as a whole, dependent on the size, shape and orientation of the crystallites within the polymer structure. A final restriction to water ingress is the free volume within the amorphous regions of the polymer. The free volume in a polymer changes markedly as the material moves from a plastic to a glassy state. In the glassy state the polymer chains are fairly immobile and there is little free volume. In the plastic state the polymer chains are more mobile and there is sufficient free volume to allow ingress of small molecules such as water. The point at which this change occurs is called the glass transition temperature.

The general approach we have taken here is greatly simplified but provides a good overview of the area and factors affecting abiotic degradation. We would refer the reader to the referenced articles for more detailed discussions of the chemistry involved.

Biotic degradation

Degradation of polymers by biota is particularly important for polymers with slow degradation rates. The action of bacteria, fungi and other biota on degradable polyesters can be marked. Many enzymes have the ability to accelerate the degradation process and in the case of biologically derived PHB, it is the main route of degradation in the environment. The by-products of degradation can depend strongly on the polymer concerned. For example, the enzymatic degradation of PLA generally results in the formation of lactic acid, however the degradation of PCL results in the formation of a range of components such as succinic acid, butyric acid, valeric acid and hexanoic acid.

There are fewer reports of enzymatic degradation of polycarbonates although it has been shown that lipases are able to degrade polytrimethylene carbonate into its cyclic monomer as well as linear and cyclic oligomers and 1,3-propanediol (Matsumura *et al.*, 2001).

2.4 Conclusions

The area of biodegradable polymers is very broad and includes a massive range of materials, both as simple polymers and as blends or composites. In this chapter we have tried to capture the bulk of this work and highlight key points in understanding polymer degradation. Other polymer types which may be of interest to the reader but have fallen outside of the scope of this chapter are reviewed in the literature including; polyperoxides (Sato and Matsumoto, 2009), polyethylenimines (Jiang *et al.*, 2008) and polycyclic acetals (Falco *et al.*, 2008).

2.5 References

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