

Chapter 8

Naturally Occurring Polymers

8.1 Naturally Occurring Polymers

There are many naturally occurring polymeric materials. Many are quite complex. It is possible, however, to apply an arbitrary classification and to divide them into six main categories. These are:

1. Polysaccharides. This category includes starch, cellulose, chitin, pectin, alginic acid, natural gums, and others.
2. Proteins or naturally occurring polyamides found in animal and vegetable sources.
3. Polyisoprenes or natural rubbers and similar materials that are isolated from saps of plants.
4. Polynucleotides include all the deoxyribonucleic acid (DNAs) and all the ribonucleic acids (RNAs) found in all living organisms.
5. Lignin or polymeric materials of coniferyl alcohol and related substances.
6. Naturally occurring miscellaneous polymers, like, for instance, shellac, a resin secreted by the Lac insect. This is a complex cross-linked polyester of 9,10,16-trihydroxy-exadecanoic acid (aleuritic acid). The structure also includes some unsaturated long-chain aliphatic acids together with other compounds [1].

8.2 Polysaccharides

Fischer [2] carried out some of the original investigations of the monomeric species of many polysaccharides during the last century. He was able to demonstrate the configurational relationships within some monosaccharides.

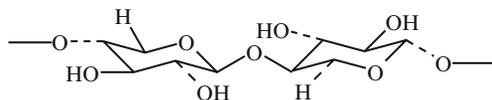
The monomers in these naturally occurring polymers are five- or six-carbon sugars. There is considerable variety among the polysaccharides and the polymers generally tend to be polydisperse, depending upon the source.

8.2.1 Hemicelluloses

Hydrolyses of hemicelluloses yield mixtures of glucose, glucuronic acid, xylose, arabinose, galactose, galacturonic acid, mannose, and rhamnose. Some common polymers of pentoses, also known as pentosans, are xylan, galactan, araban, and others. Pentosans are found in large amounts (20–40%)

in cereal straws and in brans. Large-scale industrial preparations of furfural, for instance, are based on these materials.

Xylan, one of the better-known hemicelluloses, is a component of plant cell membranes. This pentosan occurs in association with cellulose. The structure of xylan was shown to be 1,4-polyxylose [3]:



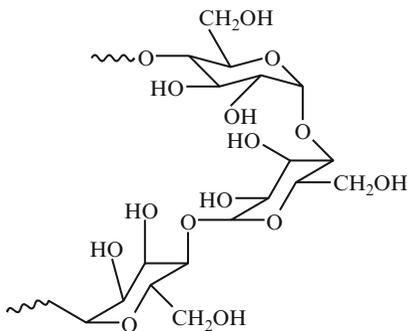
Another hemicellulose, **Galactan**, is a minor component of some coniferous and deciduous woods. Larch wood was shown to contain about 8% of this polymer [4].

Araban, or polyarabinose is found in plant saps. All **pectins** also belong to the family of hemicelluloses. These are gelatinizing substances that are found in many plants, particularly in fruit juices. Crude pectins contain pentosans, galactosans, and similar materials. Purified pectins yield on hydrolysis galacturonic acid and methanol. These high molecular weight polymers are believed to consist to a good extent of poly (galacturonic acid), partially esterified with methyl alcohol. In addition, the polymers contain galactose and arabinose molecules. The polymer is probably linear [5–10] with a 1,4-glycosidic linkage between monomers. The relative amount of various components depends upon the source of the pectin. Citrus pectin, for instance, is rich in galacturonic acid but poor in galactose and arabinose.

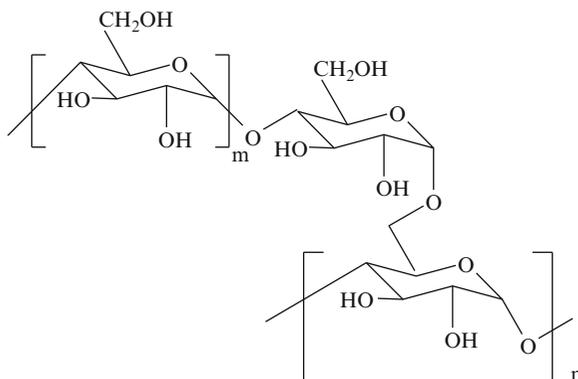
Plant gums and mucilages are high molecular weight polysaccharides composed of hexoses and pentoses. They also contain some uronic acid units. Among the gums there is gum arabic, gum tragacanth, and many others.

8.2.2 Starch

This is the most widely distributed substance in the vegetable kingdom and is the chief reserve carbohydrate of plants. Starch consists of single repeat units of D-glucose linked together through 1 and 4 carbons by α -linkages (*cis*) [10]. There are two types of starch molecules, **amylose** and **amylopectin**. The first one is mainly a linear polymer. Its molecular weight can range from 30,000 to 1,000,000, though it is mostly 200,000–300,000. Amylose is often pictured in a spiral form due to the conformation of the α -glucoside bonds:



Amylopectin, on the other hand, is branched through carbon 6:



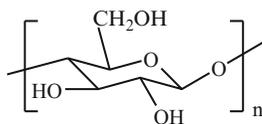
The ratios of amylopectin to amylose in many natural starches are about 3:1. The main commercial source of starch in this country is corn. Lesser amounts of industrial starch are obtained from potatoes, wheat, and tapioca (not necessarily in that order). The extraction of starch from plant material is done by grinding the plant tissues in water. The slurry is then filtered to obtain a suspension of starch granules. These granules are then collected with the aid of a centrifuge and dried.

When a water suspension of starch granules is heated to 60–80°C, the granules swell and rupture. This results in formation a viscous colloidal dispersion containing some dissolved starch molecules. Cooling this dispersion results in formation of a gel, due to aggregation of the amylose molecules. It is essentially a crystallization phenomenon, known as *retrogradation*. By comparison, amylopectin molecules cannot associate so readily due to branching and will not gel under these conditions.

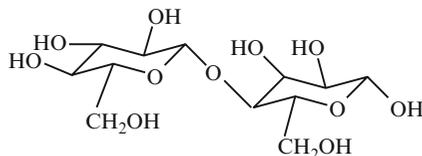
Starches are modified chemically in various ways. Some acetate and phosphate esters are produced commercially, as well as hydroxyalkyl and tertiary aminoalkyl ethers. Both unmodified and modified starches are used principally in papermaking, paper coating, paper adhesives, textile sizes, and as food thickeners. There are many reports in the literature on graft copolymers of starch. The work is often done in search of biodegradable materials for packaging and agricultural mulches. Most chemical modifications of starch parallel those of cellulose.

8.2.3 Cellulose

This polysaccharide is found widely in nature. It is a major constituent of plant tissues (50–70%, depending upon the wood), fibers, and leaf stalks. Chemically cellulose is 1,4-β-poly-anhydroglucose [12] (*trans*):



where n represents several thousand units. Hydrolysis of cellulose yields 95–96% D-glucose. This establishes its structure. Acetolysis of cellulose, however, yields cellobiose, a disaccharide, 4-O- β -D-glucopyranosyl-D-glucopyranose:



The structure of cellulose is, therefore, officially based on cellobiose units. Careful molecular weight measurements by many [12] established that the DP of cellulose ranges from 2,000 to 6,700, depending upon the source. The polymer is highly crystalline and is characterized by a very high degree of intermolecular and intramolecular hydrogen bonding. This prevents it from being thermo-plastic as it decomposes upon heating without melting.

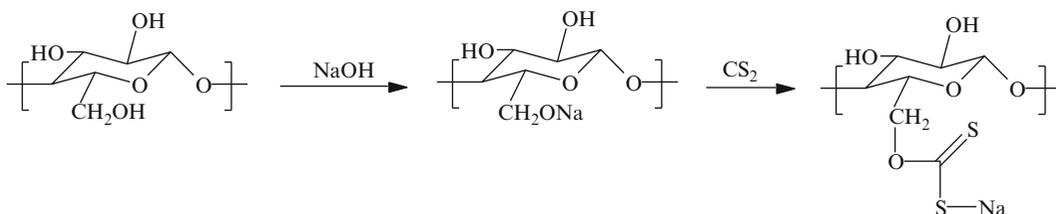
8.2.3.1 Regenerated Cellulose

Cellulose is used in many forms. Often it is modified chemically to render it soluble in organic solvents. In other modifications, it is treated in a manner that allows forming it into desired shapes, like films or fibers, followed by restoration of its chemically insoluble form. The material is then called regenerated cellulose.

Several processes evolved for preparation of regenerated cellulose. One, developed as far back as 1884, converts it first to a nitrate ester. The nitrated material is dissolved in a mixture of ethyl alcohol and diethyl ether and extruded into fibers. The fibers are then denitrated by treatment with ammonium hydrogen sulfide at about 40°C. The product is called *Chardonnet silk*. It appears that this process is no longer practiced anywhere.

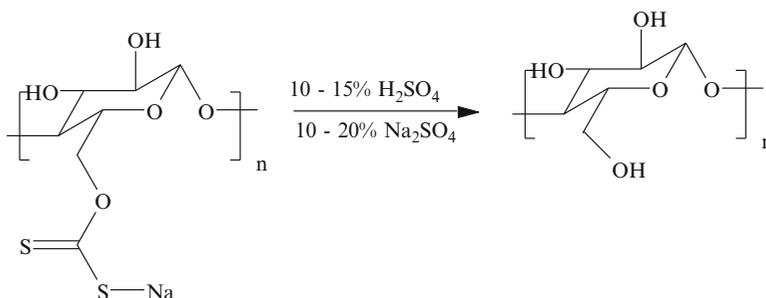
In another process cellulose is dissolved in ammoniacal cupric hydroxide ($\text{Cu}(\text{NH}_3)_4(\text{OH})_2$). The solution is then spun as a fiber into a dilute sulfuric acid solution to regenerate the cellulose. The product is called *Cuprammonium rayon*. The material may still be manufactured on a limited scale.

The third, probably major commercial process used today, forms a material that is known as *Viscose rayon*. The regenerated cellulose is prepared and sold as a fiber as well as a film, known as *cellophane*. The viscose, or more properly referred to as the *xanthate* process, consists of forming cellulose xanthate by reacting alkali cellulose with carbon disulfide:



In a typical procedure, cellulose is steeped in an approximately 20% aqueous sodium hydroxide solution at room temperature for anywhere from 20 min to a whole hour. It is believed that this treatment results in formation of sodium alcoholate at every hydroxymethyl group. The resultant material is pressed out to remove excess liquid, shredded, and aged for 2–3 days. The aging is known to cause some molecular weight reduction. After aging, the alkali cellulose is treated with carbon disulfide for 2–4 h to form cellulose xanthate. The amount of xanthate groups in the product average out to one per every two glucose units. The material is dissolved in a dilute sodium hydroxide solution

and again aged for 2–5 days. During the aging period, some xanthate groups decompose. The solution is then spun into dilute sulfuric acid to regenerate the cellulose and form fibers:



The rayon fibers are washed, bleached, and submitted to other various treatments, like dyeing, etc., depending upon intended use.

When cellulose xanthate is extruded through narrow slits into acid baths, cellophane films form. These films are usually plasticized by washing in baths containing some glycerin.

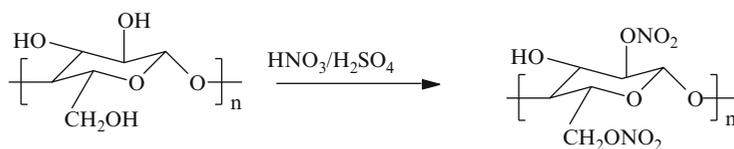
8.2.3.2 Derivatives of Cellulose

Many *derivatives of cellulose* have been synthesized over the years [12–14]. These include esters of both organic and inorganic acids, ethers, and various graft copolymers. Only some of them, however, achieved commercial importance.

One of the earliest commercial esters of cellulose was **cellulose nitrate**. It was originally prepared as an explosive (**gun cotton**) in the middle of the nineteenth century, and later as a medical aid (**collodion**, for covering wounds). Later films from cellulose nitrate were used in photography, called **celluloid**. Nitrocellulose was also probably the first successful commercial plastic, used to form many articles. Today it is generally displaced by other materials. Cellulose nitrate, however, is still being used in some surface finishes, though here too it is gradually being displaced.

Cellulose is nitrated by mixtures of nitric and sulfuric acids. The type of acid mixture used depends on the intended products. For the preparation of plastic grade materials, 25% of nitric acid is combined with 55% of sulfuric acid and 20% water. The dried cellulose is soaked for 20–60 min at 30–40°C. There is little change in appearance as the structure of the cellulose is maintained. The bulk of the acid is then removed, usually by spinning in a centrifuge and the remaining acid washed out with copious amounts of water. The product is often bleached with sodium hypochlorite and washed.

The degree of nitration is controlled by reaction conditions and particularly by the amount of water in the nitrating bath. Products with 1.9–2.0 nitrate groups per each glucose unit are used in plastics and lacquers. Some materials, however, with a nitrate content as high as 2.0–2.4 groups per each glucose have been used in some lacquers. The higher nitrate content of 2.4–2.8 groups per each glucose is in materials intended for use as explosives. The esterification reaction can be illustrated as follows:



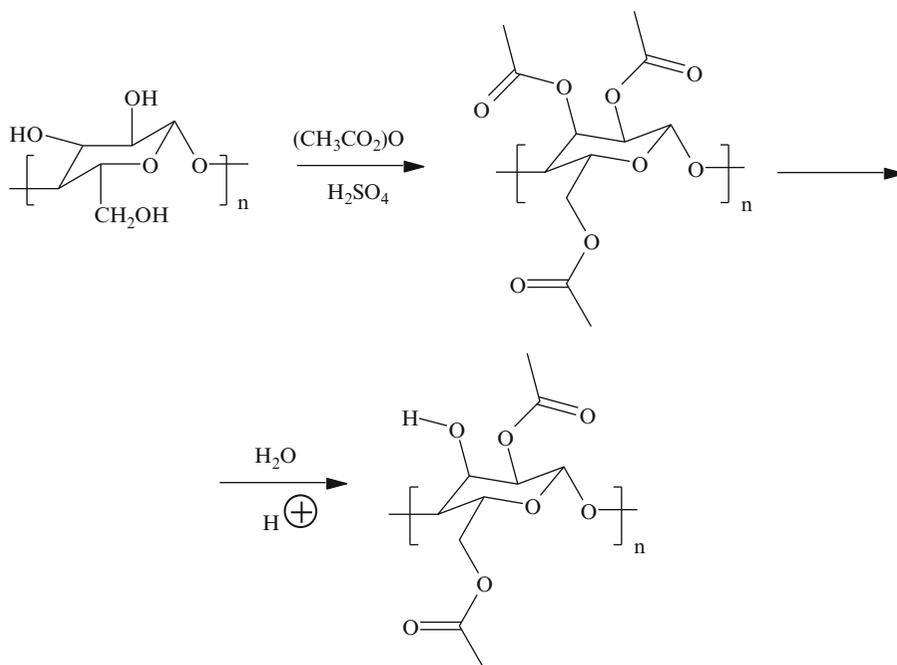
The molecular weight of cellulose nitrates used in plastics and lacquers is usually reduced. This is done by heating the slurry of the polymer in water at about 130–160°C for up to 30 min under pressure.

Cellulose acetate was also prepared originally in the nineteenth century. Commercial development, however, started early in twentieth century. In the 1920s acetate rayon and acetate fibers were developed and cellulose acetate became an important molding material. At about the same time cellulose lacquers were also developed. Today, however, many of these materials have been replaced by other polymers.

The acetylation reaction of cellulose is often prepared by forming a solution in a mixture of acetic anhydride and sulfuric acid. This results in formation of a triacetate. When a lower degree of esterification is desired, the triacetate is partially hydrolyzed. A two-step procedure is needed because it is not possible to control the degree of esterification in the reaction with acetic anhydride and sulfuric acid. In a typical process, dry cellulose is pretreated with 300 parts acetic anhydride, 1 part sulfuric acid, and 400 parts methylene chloride. The reaction mixture is agitated while the temperature is maintained at 25–35°C for 5–8 h. By the end of that period, all the cellulose is dissolved and the cellulose triacetate has formed in the solution.

Partial hydrolysis is accomplished by adding to the methylene chloride solution aqueous acetic acid (50%). The solution is then allowed to stand to reach the desired degree of hydrolysis. This usually takes about 72 h at room temperature. Sulfuric acid, still present from acetylation, is then neutralized by addition of sodium acetate and most of the methylene chloride is distilled off. The partially hydrolyzed cellulose acetate is then precipitated by addition of water and washed thoroughly. The washing also includes a 2-h wash with very dilute sulfuric acid to remove hydrogen sulfate esters that cause polymer instability.

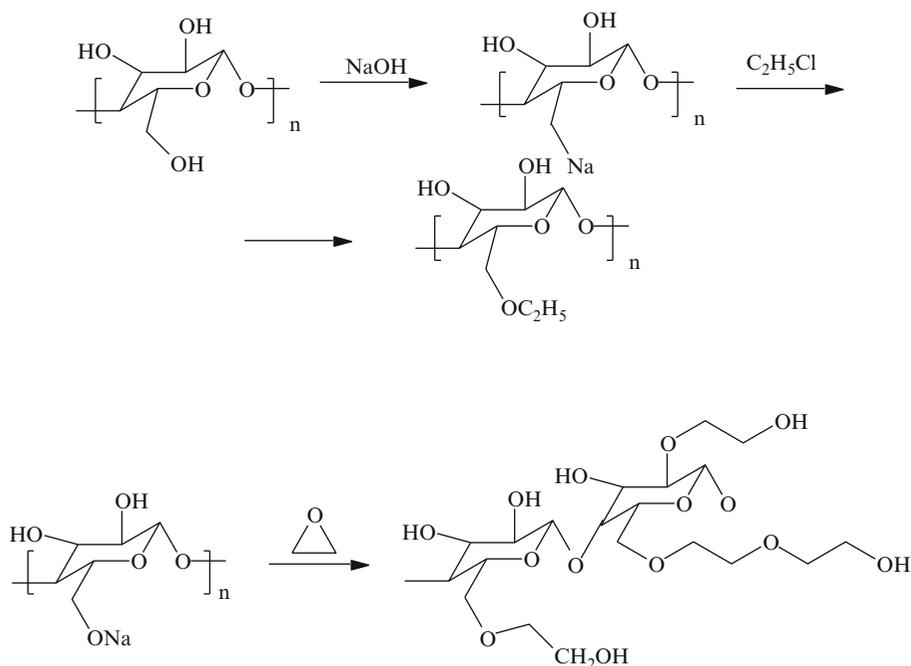
The process can be illustrated as follows:



Cellulose triacetate is also prepared by a heterogeneous process in the presence of benzene, a non-solvent. The triacetate that forms in both processes is hard to mold, but it can be used in films and fibers. The diacetate is more suited for plasticization and molding.

Many other esters of cellulose were prepared at various times, including some mixed esters. Various cellulose acetate-butyrate are manufactured today and are perhaps the best known of the mixed esters. They are synthesized in the same manner as cellulose acetate. Mixed anhydrides are used in esterification reactions catalyzed by sulfuric acid. The products are then slightly hydrolyzed. The butyric groups enhance flexibility and moisture resistance. The materials have the reputation of being tough plastics and are used in such applications as tool handles. Lower molecular weight grades are also used in surface finishes.

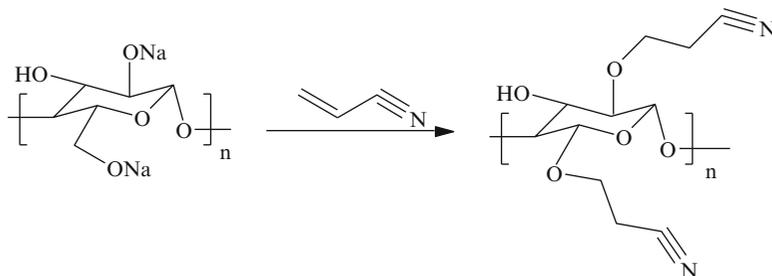
Several *cellulose ethers* are also prepared commercially. The original patents for preparation of cellulose ethers date from 1912. In spite of that, cellulose ethers never attained the industrial importance of cellulose esters. The ethers are prepared by reacting alkali cellulose with an alkyl halide or with an epoxide:



Typical commercial ethers are methyl, ethyl, hydroxyethyl, hydroxypropyl, carboxy-methyl, aminoethyl, and benzyl.

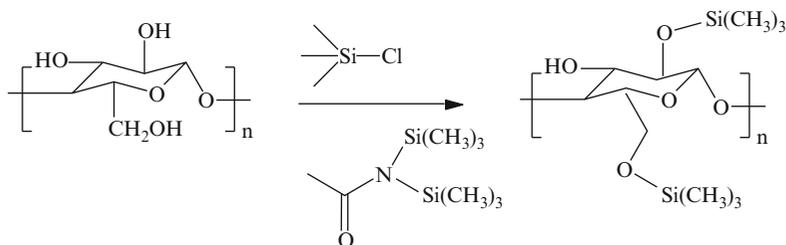
Ethyl cellulose is used industrially as a plastic similarly to cellulose acetate. The water-soluble ethers, like methyl, carboxymethyl, and hydroxyethyl, are used as thickeners in foods and in paper manufacturing.

Cellulose can be reacted with acrylonitrile to form a cyanoethylether. The Michael condensation takes place with alkali cellulose:

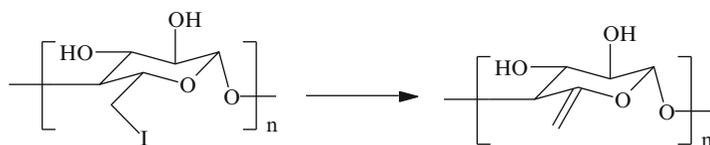


Cyanoethylated cellulose does not appear to be used commercially in any quantity.

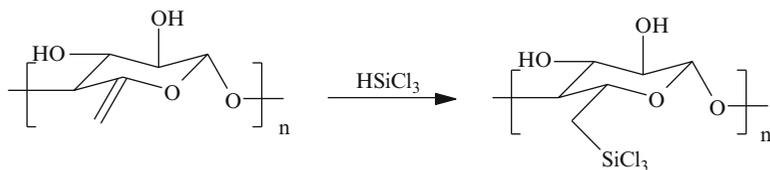
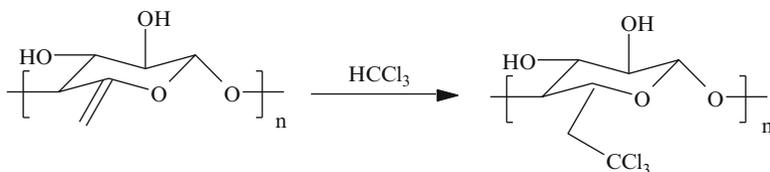
Very stable silyl ethers form when cellulose is treated with trimethyl chloro-silane or with bis(trimethylsilyl)-acetamide [15]:



Some interesting approaches to cellulose modification are possible via formations of double bonds in the glucopyranosine unit at the 5,6 positions [16]. This is accomplished by dehydro-halogenating a previously formed 6-iodocellulose:

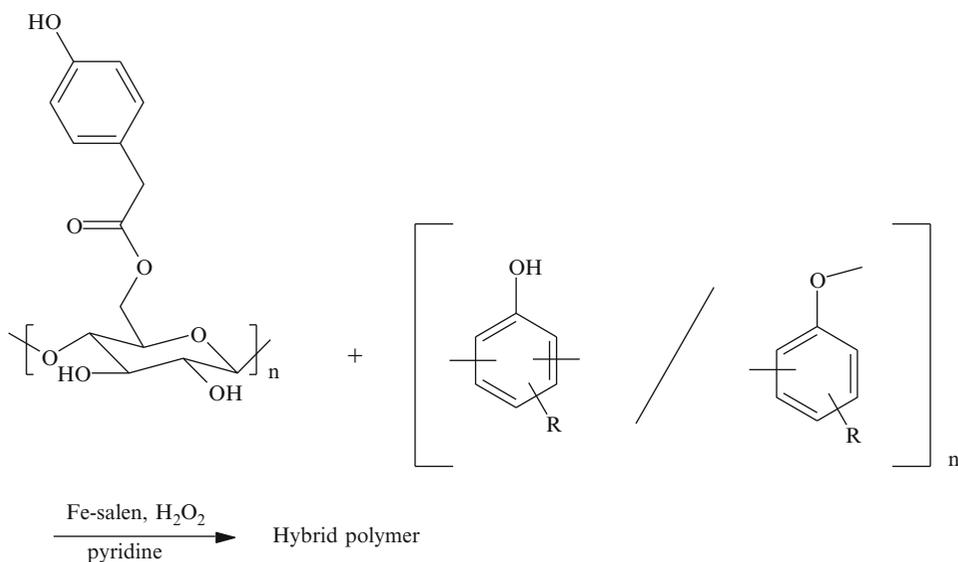


The resultant unsaturated compound can be converted into a number of derivatives. Examples of some of them are:



Other compounds that can be added across the double bonds are carbon tetrachloride, phosphorus trichloride, and methyl alcohol. Many graft copolymers of cellulose were reported. Some are described in Chap. 9.

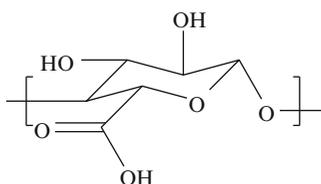
In wood, cellulose is present with lignin, a natural phenolic polymer, described in Sect. 8.3. Kobayshi and coworkers [16] grafted phenolic resins onto cellulose to form an artificial wood polymer.



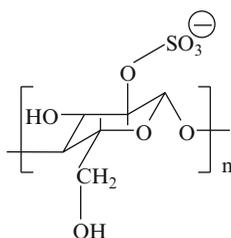
The reaction was catalyzed by a complex of iron with *N,N'*-ethylene bis(salicylidene amine) as well as a horseradish peroxidase enzyme to carry out oxidative coupling of phenols using hydrogen peroxide as an oxidizing agent. The product is a new type of plastic.

8.2.4 Miscellaneous Polysaccharides

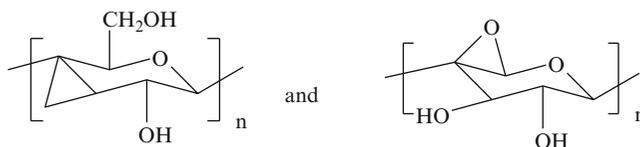
Other polysaccharides found in nature include *alginic acid* that is isolated from certain brown seaweeds [17]. The monomers of this polymer, similar to cellulose, are linked *trans* or β to each other, through the 1,4 positions:



A sulfate group bearing polysaccharide is isolated from another seaweed that is red in color. This polymer is called *carrageenan*. It consists of two fractions [17]. The first one has the galactose units linked though 1 and 3 or 1 and 4 carbons. A sulfate group is found at carbon 2 on some units:

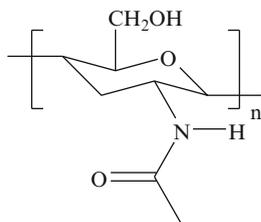


The second fraction has the some galactose units linked 1 and 4 and others have ether group linking carbons 3 and 6:



A similar polysaccharide is also obtained from seaweeds that is called *agar*. It is similar in structure, but has less sulfate groups per chain.

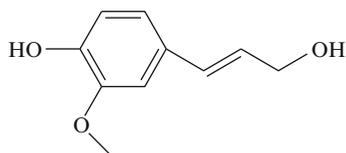
Crab and shrimp shell wastes are an abundant source of *chitin*, a nitrogen atom-containing polysaccharide:



The polymer can be deacetylated to yield an amine group bearing polysaccharide.

8.3 Lignin

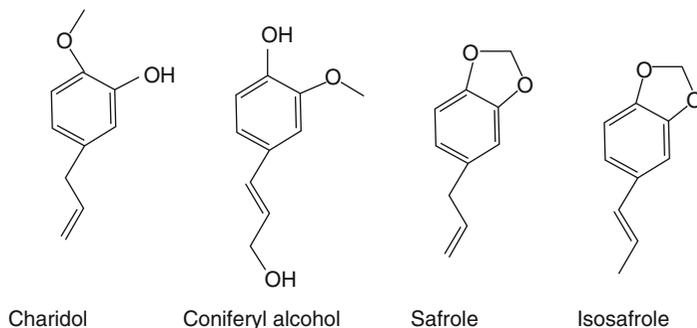
These polymers are also constituents of wood (about 25–30%) [18, 19]. It is uncertain what the molecular weights of the polymers are as the materials are quite complex in structure. The extraction processes of lignin result in considerable loss of molecular weights. The structures of lignin vary, depending upon the source. Generally, they are considered to be polymers of coniferyl alcohol:



An idealized picture of lignin that formed from coniferyl alcohol was published by Freudenberg [20]. It appears reasonable, however, that some lignins might, perhaps, also form in different trees, from other compounds not coniferyl alcohol, but related to it and also found in woods. Also it appears plausible that several of such compounds, including coniferyl alcohol, actually participate together in lignin formation, depending upon the species of wood. Figure 8.1 shows the chemical structures of some of these compounds.

Many attempts were made to convert lignin to a useful material for coatings and adhesives. Only very limited success, however, has been achieved. A reaction product with formaldehyde can be used as a wood adhesive. In addition, lignin obtained from wood pulping by the sulfate process (as a sulfonate) has been utilized to a limited extent as an asphalt extender and as an oil-well drilling mud additive.

Fig. 8.1 Compounds that occur in various woods and might, perhaps, participate in formation of lignin



8.4 Polyisoprene

Natural rubber is polyisoprene [21]. It is produced commercially from the sap of trees called *Hevea brasiliensis* and sometimes referred to as *Hevea rubber*. These trees yield a latex containing approximately 35% rubber hydrocarbon and 5% nonrubber solids, like proteins, lipids, and inorganic salts. The remaining 60% of the latex is water. The hydrocarbon polymer consists of 97% *cis*-1,4 units, 1% *trans*-1,4 units, and 2% 3,4 units, in a head to tail structure. Molecular weights of naturally occurring polyisoprene range from 200,000 to 500,000. A variety of shrubs and small plants, including some weeds, like dandelion and milkweed also contain polyisoprene in their sap. The *guayule* shrub, which grows in Mexico and in southern United States, is a good potential source of natural rubber. Work is now going on in various places to cultivate this shrub for potential rubber production.

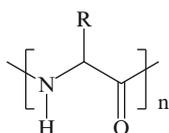
An almost all *trans*-1,4 polymer called *gutta-percha* is found in the exudations of various trees of the genus *Palaquium*, *Sapotaceae*, and *Habit*. The molecular weights of these polymers range from 42,000 to 100,000. *Balata* and *chicle*, also mainly *trans*-1,4-polyisoprenes, are found in saps of some plants in West Indies, Mexico, and South America.

Chapter 9 deals with various reactions of polymers including those of natural and synthetic rubber. That includes vulcanization of rubber. While there are very many commercial applications of the *cis* isomer, *gutta-percha* utilization is limited to wire coatings, impregnation of textile belting, and as a component of some varnishes. Its use is limited, because it is considerably harder than natural rubber.

8.5 Proteins

These materials are building blocks of animal tissues [22, 26, 28, 31]. To a lesser extent they are also found in vegetable sources. Because the major constituents of animal bodies, including skins, hairs, and blood, are proteins, they are of much greater interest to the biochemists. Nevertheless, some proteins are important commercial materials. These include animal glues, silk, and wool. It is beyond the scope of this book, however, to render a thorough discussion of the proteins. For that reason, only some basic principles are presented here.

Proteins are naturally occurring polyamides, polymer of α -amino acids. The structure can be illustrated as follows:



Because R represents many different groups, many different combinations of α -amino acids are possible and the proteins are very complex molecules. The arrangement or sequence of amino acids in proteins is referred to as their *primary structure*. The amide linkage is referred to in biochemistry as the *peptide linkage* or the *peptide group*. A dipeptide then is a compound consisting of two amino acids, a tripeptide of three, etc. *Polypeptide* refers to proteins, though the term is often reserved for lower molecular weight fractions, usually less than 10,000. Many proteins are monodisperse. This distinguishes them from many other naturally occurring polymers, such as polysaccharides, that are polydisperse.

8.5.1 α -Amino Acids

Twenty-five known naturally occurring amino acids were isolated from various proteins by hydrolysis. All but one of them, glycine, possess an asymmetric carbon. Table 8.1 lists the naturally occurring amino acids and gives their structures [26, 28, 31].

Among the above shown amino acids, a certain number are known as *essential amino acids*. They are not synthesized by human bodies and must be ingested for human metabolism.

All the optically active amino acids (that means all except glycine) have an L configuration. In addition, all amino acids exist as zwitterions.

8.5.2 Structures and Chemistry of Proteins

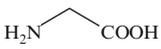
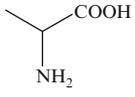
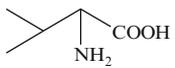
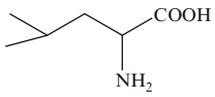
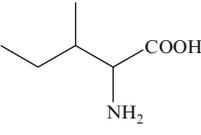
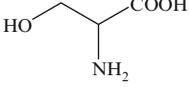
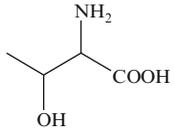
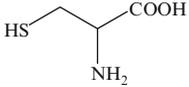
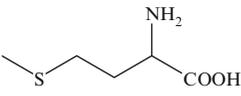
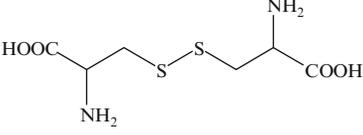
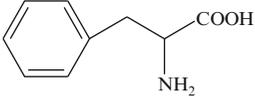
Proteins can be separated into two major groups, *fibrous proteins* and *globular proteins*, depending upon their shapes. The fibrous proteins are long molecules that function as structural materials in animal tissues. Hydrogen bonding holds these water insoluble molecules together to form extended coiled chains. To this group belong *collagen*, protein of the connecting tissues; *myosin*, protein of the muscles; *keratin*, protein found in hair, nails, horns, and feathers; and *fibroin*, protein of silk fibers.

Globular proteins are held by strong intramolecular hydrogen bonds in spherical or elliptical forms. Their intermolecular forces are weak and they are soluble in water and in dilute salt solutions. To this group of proteins belong enzymes, many hormones, egg albumin, and hemoglobin.

Some proteins also contain a non-peptide portion that is attached chemically to the polyamide chain. The non-peptide moieties are called *prosthetic groups*, and the proteins with such groups are called *conjugated proteins*. Examples are hemoglobin and myoglobin that consist of polypeptide portions with iron–porphyrin prosthetic groups attached. This particular prosthetic group, called *heme*, is illustrated in Fig. 8.2. There are also a number of proteins that are associated with a nucleic acid. They are known as *nucleoproteins*.

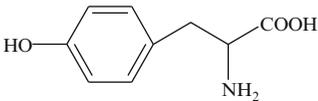
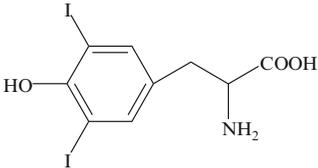
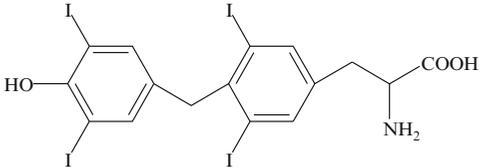
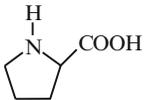
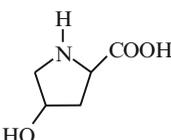
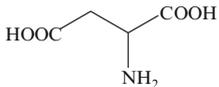
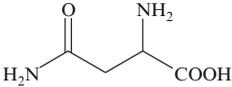
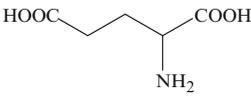
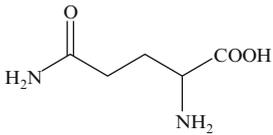
Numerous studies of protein structures have shown that the common conformations of the protein chains (fibrous) can be either as an α -helix, β -sheets, or random coils [26]. The steric arrangement or the conformations of the proteins are referred to as the *secondary structure*, while the composition of α -amino acids in the polypeptide chains is called the *primary structure* [26]. Based on X-ray crystallography data, Pauling et al. [24] deduced that an α -helix type configuration is formed because it accommodates hydrogen bonding of each nitrogen to a carbonyl oxygen (see Fig. 8.3). It allows space for all bulky substituents in amino acids and stabilizes the structure. The α -helix is probably the most important secondary structure in proteins [26]. The two α -helix illustrations are after Pauling et al. [24]. The one on the left shows right-handed helix. It is interesting to note that an α -helix conformation may

Table 8.1 Naturally occurring amino acids [26, 28–31]

Name	Structure	Optical rotation
Glycine		(+)
Alanine		(+)
Valine		(+)
Leucine		(-)
Isoleucine		(+)
Serine		(-)
Threonine		(-)
Cysteine		(-)
Methionine		(-)
Cystine		(-)
Amino acids with aromatic groups		
Phenylalanine		(-)

(continued)

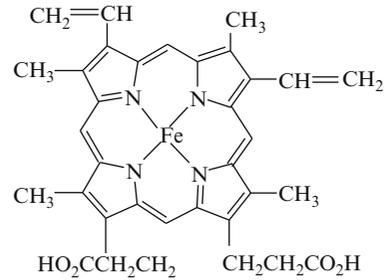
Table 8.1 (continued)

Name	Structure	Optical rotation
Tyrosine		(-)
Diiodotyrosine		(+)
Thyroxine		(+)
Amino acids with heterocyclic structures		
Proline		(-)
Hydroxyproline		(-)
Acidic amino acids		
Aspartic acid		(+)
Asparagine		(-)
Glutamic acid		(+)
Glutamine		

(continued)

Table 8.1 (continued)

Name	Structure	Optical rotation
Basic amino acids		
Lysine		(+)
Hydroxylysine		(-)
Arginine		(+)
Tryptophane		(-)
Histidine		(-)

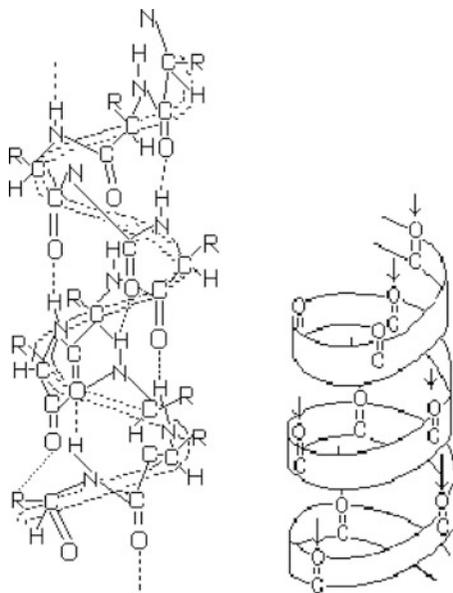
Fig. 8.2 Prostete group
heme

also occur in water solutions. This is due to van der Waal interactions [25], because water molecules interfere with hydrogen bonding that holds the helix together, as shown in Fig. 8.3.

Not all proteins, however, form helical structures. If the substituent groups on the amino acids are small, as found in silk fibroin, then the polypeptide chains can line up side by side and form sheet-like arrangements. The chains tend to contract to accommodate hydrogen bonding and form pleated sheets. This is called *β -arrangement*. Such an arrangement can be parallel and antiparallel. The identity period of the parallel one is 6.5 Å and that of the anti-parallel 7.0 Å.

The secondary structures of proteins do not describe completely the arrangement of these macromolecules. There may, for instance, be sections that may exhibit some irregularity. Or, some sections may be linked chemically by sulfur–sulfur bonds of cystine groups. There may also be areas

Fig. 8.3 α -Helix structure of proteins



where the folding of the helix is such that it allows hydrogen bonding between distant sites. The overall, three-dimensional picture of a protein structure is referred to as the *tertiary structure*. Disruption of the tertiary structure in proteins is called *denaturation*. When the protein is composed of more than a single peptide chain, the arrangement is called a *quaternary structure*. This association results from non-covalent interactions.

There is a relationship between the primary structures, or the amino acid content of many proteins, and the secondary structures [27]. The helical contents are inversely proportional to the amount of serine, threonine, valine, cysteine, and proline in the molecule. Conversely [28], valine, isoleucine, serine, cysteine, and threonine are non-helix-forming amino acids. Proline, due to its specific configuration, actually disrupts the helical structure when it is present in the polypeptide [29]. In addition, proteins that are composed of low ratios of polar to nonpolar amino acids have a tendency to aggregate [30]. Also, the globular protein, will, in an aqueous environment, tend to form shapes with nonpolar groups located inside the structure. This is due to the thermodynamic nature of the hydrophobic side chains. The polar ones, on the other hand, tend to be located outside, toward the water [31].

To date, much more information is available on some proteins than on others. Some of the more thoroughly explored proteins will be mentioned below.

Keratins are proteins that are found in wool, hair, fur, skin, nails, horns, scales, feathers, etc. They are insoluble because the peptide chains are linked by disulfide bonds [32, 33]. Many keratins contain coils of α -helices [34–36]. Some keratins, however, were found to consist of complicated β -helical structures. This apparently has not been fully explained. Wool keratin was shown to range in molecular weight from 8,000 to 80,000 [37]. The extensibility of α -keratins is believed to be due to the helical structures. The extent of keratin hardness (in claws, horns, and nails) is believed to be due to the amount of sulfur links.

Silk fibers, which are obtained from the secretion of the silkworm, are double filaments that are enclosed by a coating of a gum (sericin) as they are secreted [40]. The amino acid sequence of the silk protein was shown to be (glycine–serine–glycine–alanine–glycine–alanine)_n. The polypeptide chains are bound into antiparallel pleated β -sheet structures by hydrogen bonding [31, 39, 42]. The structures are also held together by van der Waal forces [31, 38].

The protein of skin and extracellular connective tissues in animals is *collagen*. The polymer is rigid and cross-linked. Mild hydrolysis disrupts the rigid secondary valence forces and produces gelatin [26]. The fundamental unit of collagen exists as a triple helix [41]. Three left-handed helices twist together to form a right-handed threefold super helix [31]. Collagen is composed mainly of glycine, proline, and hydroxyproline. Some other amino acids are also present in minor amounts.

A protein that is similar to collagen is *elastin*, which is present in elastic tissues, such as tendons and arteries. Hydrolyses of elastin, which has rubber-like properties, however, do not yield gelatin. Mildly hydrolyzed elastin can be fractionated into two proteins [26].

Among the most studied globular proteins are *myoglobin* and *hemoglobin*. Myoglobin consists of a single chain of 153 amino acid residues and a prosthetic group that contains iron, called *heme*. Myoglobin polypeptides have eight helical segments that consist of right-handed α -helices that are interrupted by corners and non-helical regions. The overall shape resembles a pocket into which the heme group just fits. The pocket is hydrophobic because all but two side groups are nonpolar. The heme group's two carboxylic acids protrude at the surface and are in contact with water [43]. The hemoglobin is similar to myoglobin but more complex [44]. There are four heme groups enclosed in the hemoglobin structure. Detailed conformational analysis has shown that hemoglobin is built up from 2×2 myoglobin-like subunits, α_2 and β_2 [45, 46].

Casein is present in several animal and vegetable sources. Commercially, however, casein is primarily obtained from milk that contains about 3% of this protein. The polymer is isolated either by acid coagulation or with the help of enzymes obtained from animal stomachs. It is very heterogeneous. The molecular weight of a large portion of bovine casein is between 75,000 and 100,000. It consists of two components, α and β . Casein belongs to groups of proteins that are identified as *phosphoproteins* because the hydroxyl residues of the hydroxy amino acids are esterified with phosphoric acid.

One other group of proteins that has so far not been fully identified is *glycoprotein*. This group of proteins contains a prosthetic group that is either a carbohydrate or a derivative of a carbohydrate. Glycoproteins are found in mucous secretions.

Very special proteins are called *enzymes*. These are biological catalysts. Their primary function is to increase the rate of reactions in organisms and they are found in all living systems. Many enzymes, like *pepsin* or *trypsin*, are relatively simple proteins. Others are conjugated proteins containing prosthetic groups often known as *coenzymes*. Because of their extreme importance to biochemists, enzymes and their actions are being investigated extensively. The full structures of several enzymes have been determined. One such enzyme is *lysozyme*.

Lysozyme enzymes occur in many species of plants and animals and the chemical behavior may differ. The enzyme found in egg white has a peptide chain consisting of two sections, approximately equal in size. The two sections are separated by a deep cleft. This enzyme performs its function by binding the substrates within this cleft with hydrogen bonds. The substrate is then hydrolyzed with the aid of glutamine (35th amino acid) and aspartine (52nd amino acid). Egg lysozymes primary structure contains 129 amino acid residues. The polymer is a single polypeptide chain that is cross-linked at four places by disulfide bonds [47].

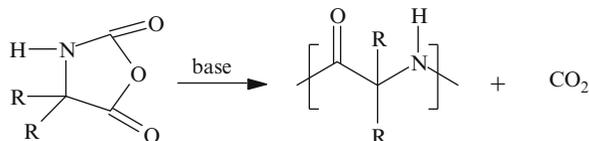
In addition, it was demonstrated [72] that the secondary structure of an enzymic protein is essential to protein's catalytic activity. Also, it was shown that this structure remains intact in neat organic solvents [72]. The molecules, however, are denatured in water-organic solvent mixtures. The α -helix of lysozyme, for instance, when the enzyme is crystalline or dissolved in neat acetonitrile, 35% of it is an α -helix, but in pure water that value is 23%. In a 60:30 mixture by volume of acetonitrile and water, it is reduced to 13% [72].

Some of the uncertainty about the transition state of the reaction of some enzymes, like β -phosphoglucomutase-catalyzed transfer of a phosphoryl group to a substrate in sugar metabolism, was resolved recently. Allan and Dunaway demonstrated that by means of ^{19}F nuclear magnetic resonance that the transition state involved a bipyramidal oxyphosphorane intermediate [72].

8.5.3 Synthetic Methods for the Preparation of Polypeptides

Studies of protein structures and their functions in nature or mode of actions, as in the case of enzymes, are only part of various investigations. Much effort is also put into syntheses of different polypeptide. Such polymers can actually be formed from mixture of various amino acids by simply heating them together. The products, however, are complex polymeric materials with random distribution of amino acids and do not resemble any naturally occurring materials.

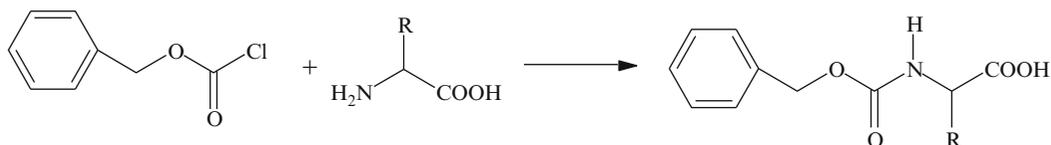
Base catalyzed ring opening polymerization reactions of *N*-carboxy- α -amino acid anhydrides also result in formations of polypeptides:



(for the mechanism of reaction see Chap. 5) [48]. Over the years, many polypeptides were synthesized by this reaction. These, however, were homopolymers of individual amino acids. Copolymerization leads only to block copolymers. Ability to form random copolymers with controlled sequences of amino acids, which would match naturally occurring proteins, appears to be beyond reach by this reaction [49, 50].

Duplication of naturally occurring polypeptides is needed, however, to understand the details of structures that lead to biological activities. One of the early works consisted of assembling 23 amino acids to form synthetic pig corticotropin [43]. The molecules were built stepwise [43].

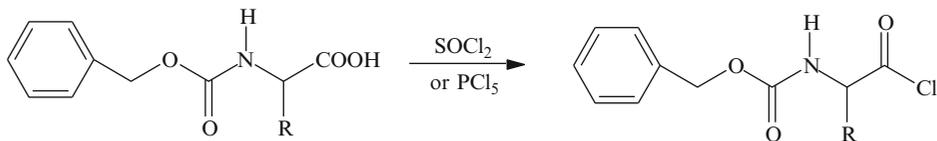
One technique used in these syntheses is to protect the terminal amino nitrogen by forming protective derivatives that can subsequently be easily cleaved. This is often done by converting them to amide groups:

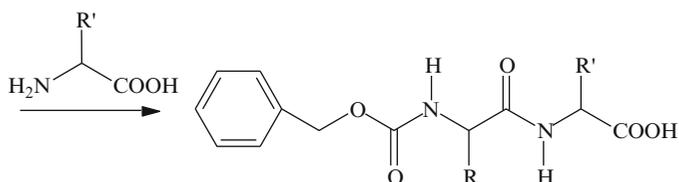


p-Toluenesulfonyl chloride is used in the same manner. It is also possible to form imides by reactions with phthalic anhydride:

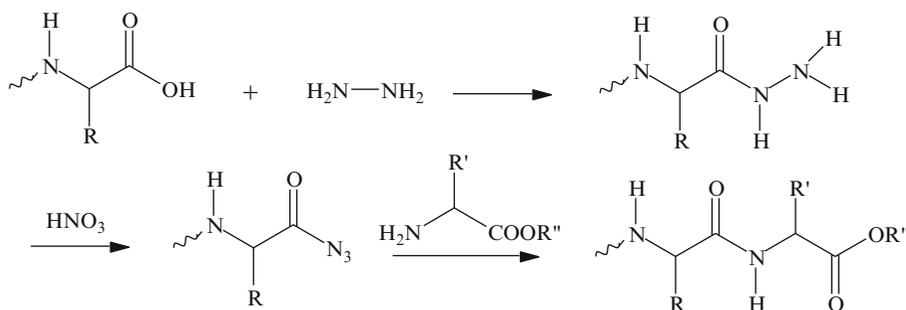


The condensations can be carried out by a number of different techniques [26, 28]. A few of them will be shown below. One is to carry out amino acyl halide reactions:

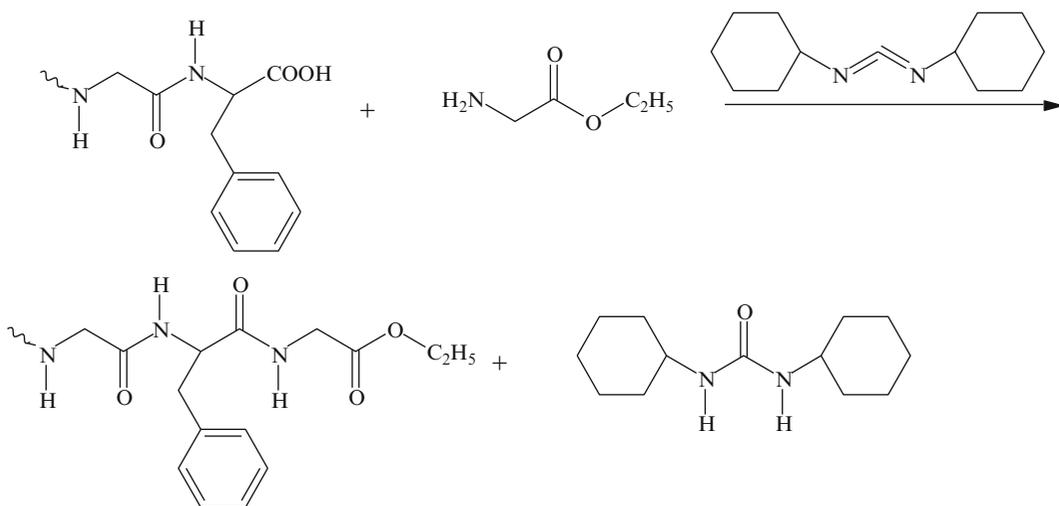




The Schotten–Baumann reaction is used in many peptide syntheses. It is usually carried out in the presence of common bases to remove the halogen acid. Another reaction that is also utilized often is an acid azide condensation:

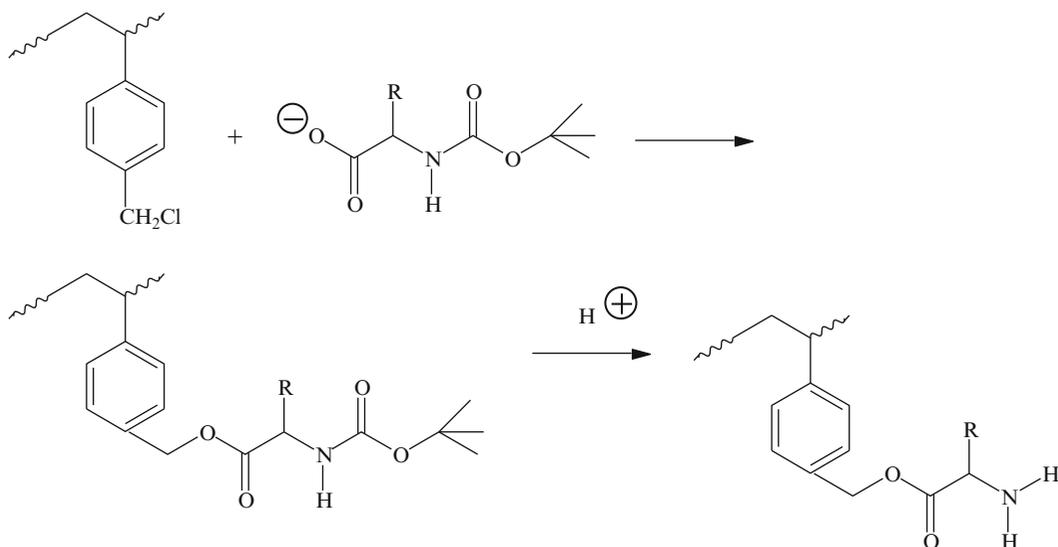


A unique way of coupling carboxylic acids with an amine groups is by using an *N,N'*-dicyclohexyl carboxy diimide method. This can be illustrated as follows:



In addition to the above mentioned, rather painstaking, techniques of polypeptide syntheses, a very elegant technique was developed by Merrifield [53]. This **solid phase peptide synthesis** automates the reaction sequences. The method makes use of an insoluble cross-linked polymer substrate with pendant reactive groups for attachment of peptide chains. Chloromethylated polystyrene microgels are often used (see Chap. 9 for more discussions on the use of chloromethylated polystyrene for

reactions of polymers). The chloromethyl moieties serve as the initiating sites for formation of the polypeptides:

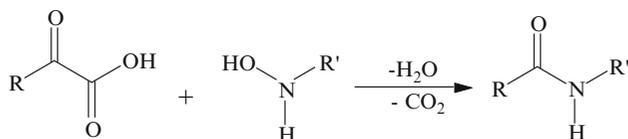


A new amino acid with a protective group can now be added. The sequence of additions can be controlled and repeated many times to build up the desired polypeptide chain. Unwanted by-products of the syntheses are washed away or filtered off before each new step.

This method lends itself so well to automation that automatic peptide synthesizers are now available commercially. One automatic peptide synthesizer was employed, for instance, in the synthesis of ribonuclease, an enzyme. In another instance, an enzyme, ferredoxin that consists of 55 amino acid residues was synthesized [26].

Most recent approaches to protein syntheses include use of templates for spontaneous self-assembly of multiple copies of a derivatized peptide [70]. The resultant structure, however, is not a conventional linear-chain protein. Instead, oxime bonds are formed between amino-oxyacetyl groups on the peptides and aldehyde groups on the template. The method is claimed to have many potential applications.

Bode et al. [70] reported a new method for synthesis of peptide oligomers. The reaction creates amide linkages between α -keto carboxylic acids and *N*-alkylhydroxylamines.



8.5.4 Chemical Modification of Proteins

Proteins have been utilized commercially from ancient times, either in their naturally occurring form or modified in some manner. Use of silk and wool fibers, for instance, goes back a very long time. Many animal glues, prepared from bones and hides of cattle or sheep, have also been around for a very long time. Today such glues are being replaced rapidly by synthetic materials. Those that are still

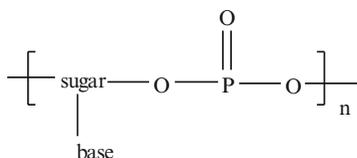
manufactured are usually formed by steaming the bones and the hides under pressure and then treating them with hot water in several cycles. This degrades the collagen and make is soluble. The aqueous solution is concentrated by vacuum evaporation of the water. The material that gels is dried and pulverized. Milder hydrolysis yields gelatin that is used commercially in foods.

Casein, the milk protein (less readily available casein from vegetable sources is hardly ever used), is also used in adhesives. Here too, synthetics are gradually taking over. At one time it was used to produce a fiber and a plastic that was formed by cross-linking with formaldehyde. The cross-linking reaction was carried out by immersing the proteins in a formaldehyde solution (4–5%) at 55–65°C for long periods of time, such as days and even months, depending upon the size of the article. The cross-linking reaction involved pendant amino groups and is quite similar to the reactions of urea- and melamine-formaldehyde resins (see Chap. 7). Some condensation and formation of methylene bridges may also involve amide nitrogens. It does not appear likely that casein fibers or plastics are still being produced anywhere.

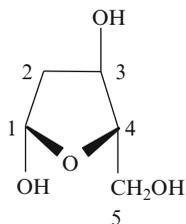
Extensive research work has gone into modification of proteins, not for commercial applications but for academic reasons. Thus, for instance, Frances et al. developed a new reaction that introduces single reactive ketones or aldehydes at the N-terminal groups of protein when the proteins are mixed with pyridoxal phosphate [44]. The researchers also developed a palladium-catalyzed allylic alkylation that attaches long lipid tails to proteins, a process that can be used to customize the solubility of enzymes, antibodies, viral capsids, and other proteins.

8.6 Nucleic Acids

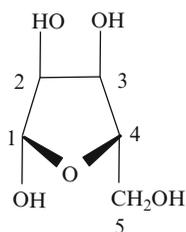
These are protein-bound polymers that are essential in many biological processes. They perform such functions as directing the syntheses of proteins in living cells and constitute the chemical basis of heredity [56, 57]. The polymers are polyphosphate esters of sugars that contain pendant heterocyclic amines, called “bases”:



There are two principle types of nucleic acids with two different sugars. One is **D-2-deoxyribose** found in **deoxyribonucleic acid (DNA)**:

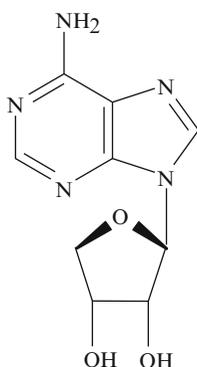


The other one *D-ribose* is found in *ribonucleic acids (RNA)*:

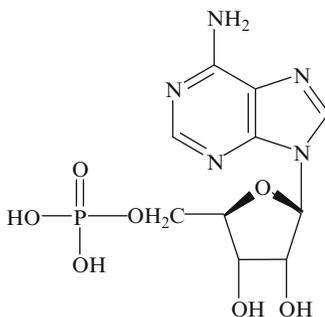


The sugars are in the furanose form. They are linked through the hydroxyl groups on carbons 3 and 5 as phosphate esters. The heterocyclic amine “bases” are attached at carbon 1, replacing the hydroxyl group.

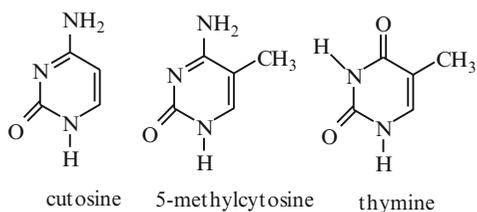
A sugar molecule with a base attached to it is referred to as a *nucleoside*:

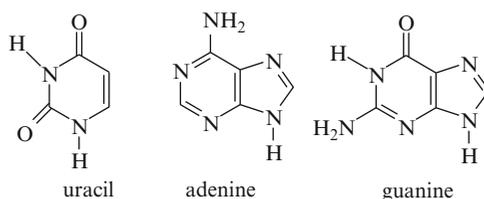


A nucleoside esterified with phosphoric acid is called a *nucleotide*:



All the heterocyclic amines that occur in nucleic acids (DNA and RNA) are derivatives of either pyrimidine or purine. These are:



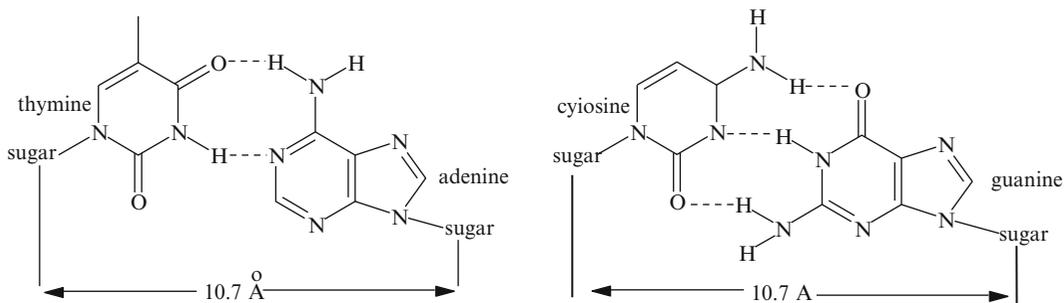


The naming of nucleosides depends upon the sugars. Thus, adenine attached to ribose is called adenosine. When it is attached to deoxyribose, it is called deoxyadenosine.

Hydrolysis of nucleoproteins separates the acids from the proteins. Further hydrolysis yields the components of nucleic acids, namely sugars, bases, and phosphoric acid. The nucleic acids differ from each other, depending upon the source, in chain lengths, sequences, and distributions of bases. Just like in the proteins, the primary structure of nucleic acids is determined by partial and sequential hydrolysis.

8.6.1 DNA and RNA

Deoxynucleic acids have been isolated from all types of living cells and it was established that their main function is to carry genetic information [57]. These are very high molecular weight polymeric materials. Some were found to be as high as 100 million. Analyses of DNA structures show that the numbers of adenine bases are always the same as the number of thymine bases. Also, the numbers of guanine bases always equal the numbers of cytosines. Based on the information from various analyses and an X-ray investigation of the structure, Watson and Crick concluded that the secondary structure of DNA must be a double helix [58]. Two separate right-handed helical chains wind around each other and are held together by hydrogen bonding between base pairs. The bases that are paired off are adenine with thymine and guanine with cytosine:

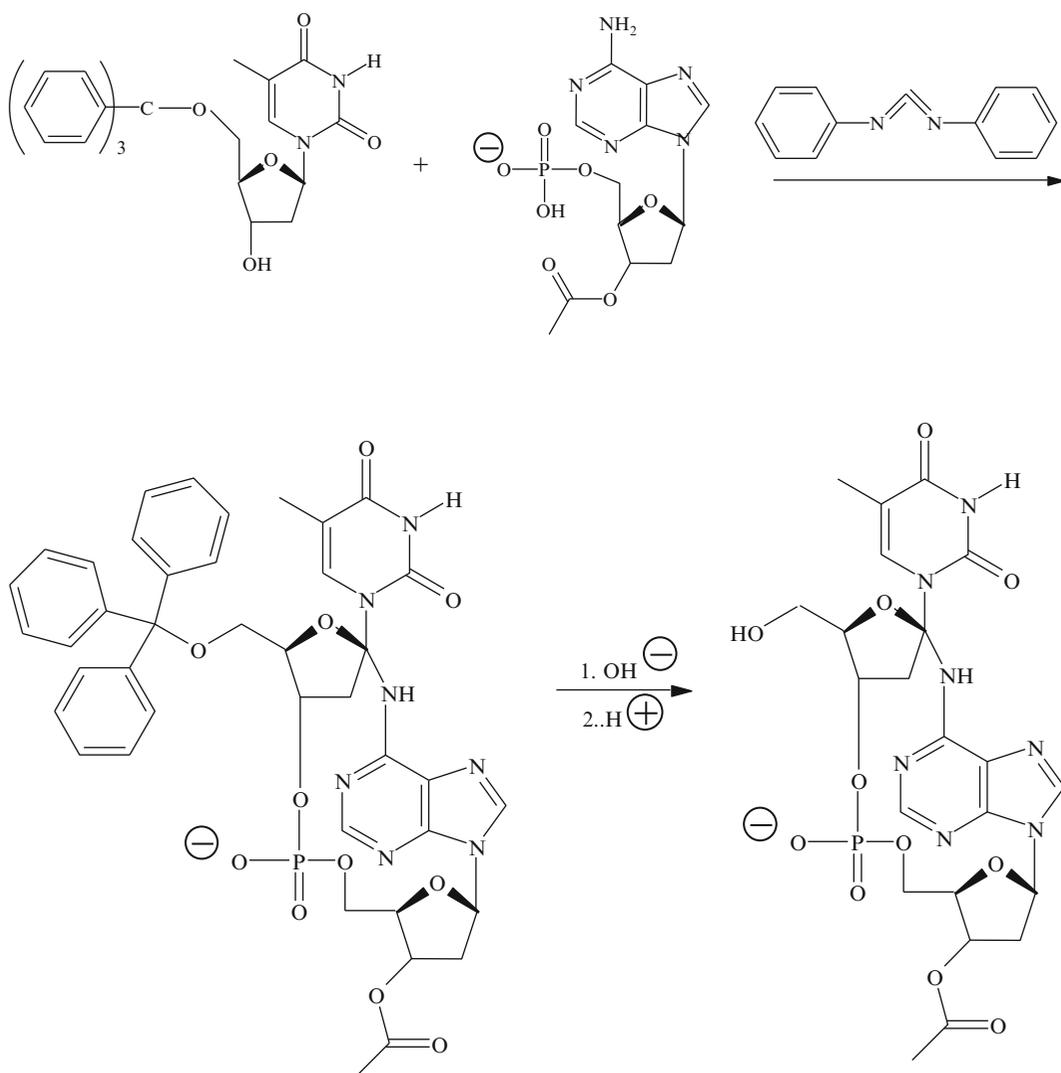


The base pairs are extended perpendicularly toward the center and the deoxyribose-phosphate ester chains are located on the outside of the helix. The two strands are antiparallel to each other. One turn of the helix corresponds to ten nucleotide pairs, 34 Å in length. The width of the helix is 20 Å. Evidence was presented that some DNAs in their native forms are cyclic [59] and may even occur as two interlocking rings. While most known DNA molecules form a right-handed helix, a left-handed helix can be prepared synthetically in the laboratory [52]. It was speculated that in some instances left-handed helices may exist in nature and have a biological function [53]. These DNA conformations were named Z-DNAs because the backbones zigzag down the molecule.

There is less information about the secondary structures of RNAs. It is known that the RNA molecules are lower in molecular weight than are the DNA molecules. In addition, it is known that there are three main types of RNAs in living cells. These are *ribosomal* RNA (r-RNA), *transfer* RNA (t-RNA), and *messenger* RNA (m-RNA). The molecular weights of the three forms on the average are about 1,000,000, 25,000, and 500,000, respectively. RNA molecules, with the help of hydrogen bonding, take three-dimensional cloverleaf structures [54]. The molecule's three-dimensional shape also assumes an L-shape, into which the cloverleaf is bent.

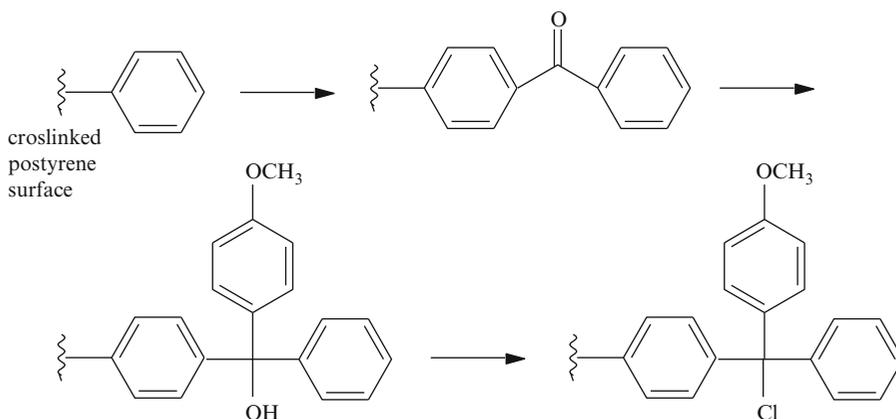
8.6.2 Synthetic Methods for the Preparation of Nucleic Acids

Over the last 20–30 years, methods were developed to synthesize short deoxyribonucleotide chains [57]. One synthetic procedure can be illustrated as follows:



The bulky triphenylmethyl moiety functions to block the 5' hydroxyl groups and is removed when necessary. The same is true of the acetyl portion that also serves to block the 3' hydroxyl position. The product can be used for further expansion of the chain.

Another approach to the syntheses of nucleic acids is to use polymeric supports as in the syntheses of polypeptides. The preparation of protecting groups for attachment to carbon 5 of deoxyribose on the surface of cross-linked polystyrene can be illustrated as follows [57]:

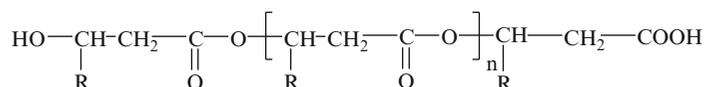


Another protective group that has been used is dimethoxy trityl. The carbon 3 of deoxyribose has been protected with phosphoramidate. Benzoyl groups are used to protect the adenine and guanine bases. Lately, in place of cross-linked polystyrene, controlled pore glass supports have become popular.

Commercial synthesizing machines are available today for polynucleotide syntheses. These are similar to the synthesizers used in polypeptide syntheses.

8.7 Polyalkanoates

Many bacteria are a potential source of naturally occurring polyesters, mainly *poly(β-hydroxyalkanoate)s* with a general structure



when the polymer is poly(β -hydroxybutyrate) $\text{R} = \text{CH}_3$ [69]. The material is found in the form of hard crystalline granules in many bacterial cells. The most common one, poly(β -hydroxybutyrate), was discovered back in the 1920s and identified as a polymer of D-(–)- β -hydroxybutyric acid. In the native state this polymer may reach molecular weights of 1,000,000 or higher. It forms a compact right-handed helix with a twofold screw axis and a repeat unit of 5.96 Å. Because poly(β -hydroxybutyrate) is stereoregular, it is highly crystalline. The substitution in the β -position makes it thermally unstable. This limits its use in plastics. It was found, however, that oxygen starvation of bacterial cultures results in formation of a copolymer of β -hydroxybutyric acid with β -hydroxyvaleric acid instead of a homopolymer. Further investigations showed that as many as 11 different β -hydroxy acid constituents are present in different naturally occurring polyalkanoates, depending upon the bacterial source and conditions of growth. Today, a family of products, marketed

under the trade name of Biopol, is available commercially with a range of properties, such as melting point, toughness, flexibility, and others. The melting points range from 80 to 180°C.

It was reported that *Pseudomonas oleovorans* microorganism can be forced to produce a thermo-plastic elastomer by growing it on a substrate containing sodium octanoate [71]. The product is poly (β -hydroxy octanoate). It contains crystalline regions that act as physical cross-links.

Also, addition of poly(ethylene glycol) of molecular weight 200 to cultivation media of *Alcaligenes eutrophus* during polymer formation, where the carbon source used is 4-hydroxybutyrate, affects the type of ester that it produces [73]. Addition of this glycol in amounts from 0 to 2% by weight results in increased amounts of 4-hydroxybutyrate incorporation from 66 to 86 mol.% into the produce, poly(3-dihydroxyalkanoate). When, however, the amount of the glycol is increased to 4%, the amount of incorporation of the 4-hydroxybutyrate decreases to 64%. The product then also contains a diblock copolymer of poly(3-dihydroxyalkanoate) and poly(ethylene glycol) [73].

Review Questions

Section 8.1

1. List the six main categories of naturally occurring polymers.
2. Draw the chemical structures of the repeat units of each category of naturally occurring polymers.

Section 8.2

1. Describe hemicellulose. This should include an explanation of what xylan, galactan, araban, and plant gums.
2. In discussing starches, explain what are amylose and amylopectin. Explain and draw structures.
3. Discuss cellulose. How does cellulose differ from starch?
4. What is cellobiose? Draw the structure and give the chemical name.
5. What is regenerated cellulose? Explain what is Chardonnet silk, Cuprammonium rayon, and viscose rayon and how they are prepared.
6. Discuss the chemistry of cellulose nitrates. How are they prepared and used?
7. Discuss the chemistry of cellulose acetate. How is it prepared and used? Describe mixed cellulose esters.
8. Discuss the chemistry of cellulose ethers.
9. Show the reaction of cellulose with acrylonitrile.
10. Iodocellulose can be dehydrohalogenated to form double bonds in the polymer. This can be used to form new derivatives. Give two examples.
11. Draw the structures of alginic acid and chitin.

Section 8.3

1. Discuss the chemistry of lignin, drawing the structure of coniferyl alcohol. Can you think of a useful product from lignin?

Section 8.4

1. Describe natural rubber. How is it obtained? What is the chemical structure?
2. What are gutta-percha, balata, and chicle? Explain.

Section 8.5

1. Explain what is meant by polypeptides.
2. Explain the difference between fibrous proteins and globular proteins.
3. What are nucleoproteins? What is a prosthetic group? Give an example.
4. Explain what is meant by a secondary structure of a protein and an α -helix.
5. What is meant by a tertiary structure of a protein?
6. What is an enzyme? How does it function?
7. Discuss with the aid of chemical equations the synthetic routes to polypeptides.
8. Discuss chemical modifications of proteins for commercial purposes.

Section 8.6

1. What is the basic structure of a unit in nucleic acids?
2. How do the sugars differ in DNA from RNA?
3. Draw the structures of a nucleoside and a nucleotide.
4. Discuss the syntheses of nucleic acids.

Recommended Reading

K. Kamide, *Cellulose and Cellulose Derivatives*, Elsevier, Amsterdam, 2005.

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