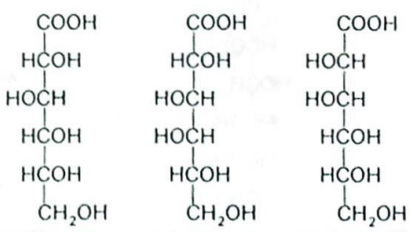
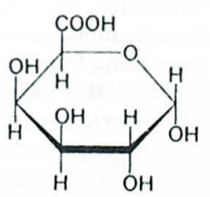
2.5.3 OXIDATION–REDUCTION

Carbohydrates may be classified as either reducing or nonreducing sugars. The reducing sugars, which are more common, are able to function as reducing agents because free, or potentially free, aldehyde groups, as in the cyclic hemiacetal forms, are present in the molecule. This aldehyde group is readily oxidized to the carboxylic acid at neutral pH by mild oxidizing agents and enzymes. This property is utilized in detecting and quantitating monosaccharides, especially glucose, in biological fluids such as blood or urine. The monocarboxylic acid that is formed is known as an aldonic acid (e.g., gluconic acid from glucose). The structures of several of these are shown.



In the presence of a strong oxidizing agent like HNO_3, both the aldehyde and the primary alcoholic function will be oxidized to yield the corresponding dicarboxylic or aldaric acid (e.g., galactaric acid).

One of the more important oxidation products of monosaccharides is the monocarboxylic acid obtained by the oxidation of only the primary alcoholic group, usually by specific enzymes, to yield the corresponding uronic acid (e.g., galacturonic acid). Such acids are components of important heteropolysaccharides found in nature.



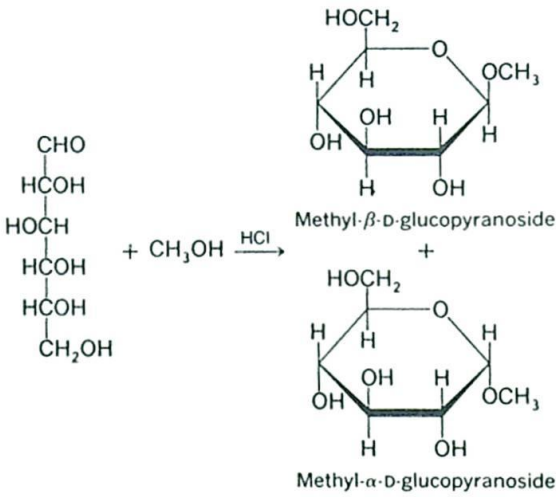
α-D-Galacturonic acid

The aldehyde and ketone groups of monosaccharides may be reduced nonenzymically (with hydrogen or $NaBH_4$) or with enzymes to yield the corresponding sugar alcohols. Thus, D-glucose when reduced yields D-sorbitol, and D-mannose produces D-mannitol. Sorbitol is found in the berries of many higher plants, especially in the *Rosaceae;* it is a crystalline solid at room temperature but has a low melting point. D-Mannitol is found in algae and fungi. Both compounds are soluble in H_2O and have a sweet taste.

2.5.4 GLYCOSIDE FORMATION

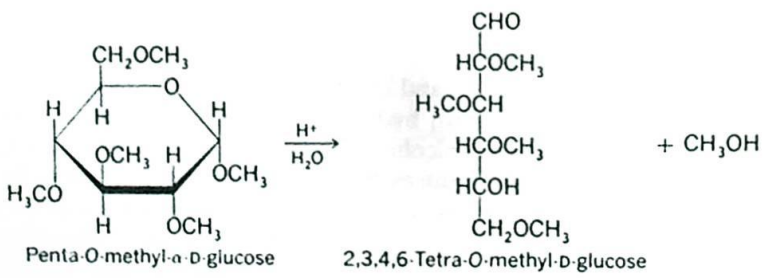
One of the most important properties of monsaccharides is their ability to form glycosides. Consider as an example the formation of the methyl glycoside of glucose. When D-glucose in solution is treated with methanol and HCl, two

compounds are formed. Determination of their structure has shown that these two compounds are the diastereomeric methyl α- and β-D-glucosides. These glucosides, and glycosides in general, are acid labile but are relatively stable at neutral and alkaline pH. Since the formation of the methyl glycoside converts the hemiacetal into an acetal group, the glycoside is not a reducing sugar and does not show the phenomenon of mutarotation.



When an alcoholic hydroxyl group on a second sugar molecule reacts with the hemiacetal (or hemiketal) hydroxyl, the resulting glycoside is a disaccharide. The bond between the two sugars is known as a **glycosidic bond.** Polysaccharides are formed by linking together a large number of monosaccharide units with glycosidic bonds.

Although the anomeric hydroxy group of sugars may be methylated with ease, as in the formation of methyl glycosides just described, methylation of the remaining hydroxyl functions requires much stronger methylating agents. Nevertheless, the remaining four hydroxyl groups of methyl-α-D-glucopyranoside can be reacted with methyl iodide or dimethyl sulfate to yield the pentamethyl derivative. Such compounds, in turn, are useful in determining the ring structure of the parent sugar as in the following example:



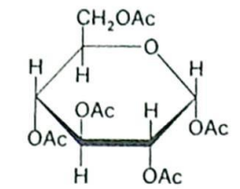
Penta-O-methyl-α-D-glucose

2,3,4,6-Tetra-O-methyl-D-glucose

The methyl group on the hemiacetal carbon, being a glycosidic methyl, is readily hydrolyzed by acid. The remaining methyl groups, being methyl ethers, are not. Therefore, treatment of the pentamethylglucose derivative pictured here with dilute acid at 100°C will yield the 2,3,4,6-tetra-*O*-methyl-D-glucose. Treatment of the pentamethyl derivative in which the sugar is in a furanose ring yields 2,3,5,6-tetra-*O*-methyl-D-glucose instead.

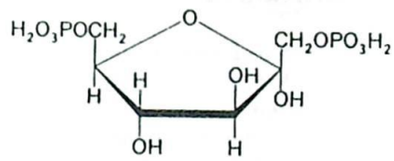
2.5.5 ESTER FORMATION

The alcoholic groups of carbohydrates may be esterified in both nonenzymatic and enzymatic reactions. Thus, when α-D-glucopyranose is treated with acetic anhydride, all the hydroxyl functions are acetylated to yield the penta-*O*-acetyl glucose pictured here. These acetyl groups, being esters, can be hydrolyzed either in acid or alkali.



Penta-O-acetyl-α-D-glucose
(Ac = CH_3—C(=O)—)

An important type of carbohydrate ester encountered in intermediary metabolism is the phosphate ester. Such compounds are formed by the reaction of the carbohydrate with biological phosphorylating reagents such as adenosine triphosphate (ATP) in the presence of an appropriate enzyme. An example is fructose-1,6-bisphosphate.

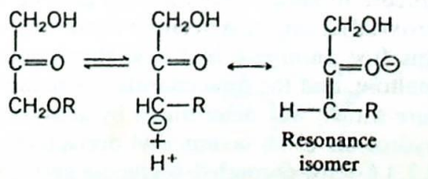


α-D-Fructose-1,6-bisphosphoric acid

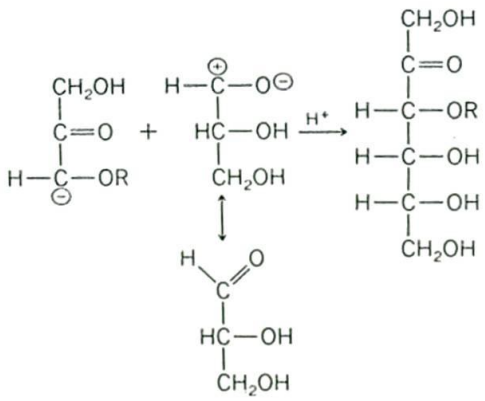
The correct name of the nonionized form of this compound is α-D-fructofuranose-1,6-bisphosphoric acid. Such phosphate esters are relatively strong acids with values of approximately 2.1 and 7.2 for pK_{a1} and pK_{a2}. Thus, at neutral pH, the sugar phosphates are anions and are normally referred to by the name of the anion, that is, fructose-1,6-bisphosphate.

2.5.6 ALDOL CONDENSATION

Another important reaction that is typical of carbohydrates and occurs frequently in biochemistry is the aldol condensation (or its reverse, the aldol cleavage). This reaction depends on the acidity of the hydrogens (α-hydrogens) on the carbon atom adjacent to a carbonyl group and the ability of the ionized ion



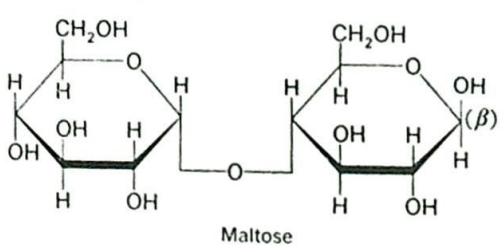
to be stabilized by resonance. The enolate ion is then capable of acting as a nucleophile and can attack the aldehyde group of a second sugar molecule.



As shown above, two trioses can condense in an aldol condensation to yield a hexose. In the process, a new chiral center is produced. In theory, two hexoses with either an R or S configuration on carbon 4 would be produced. In metabolism, an enzyme assists in the formation of the enolate ion, and only one of the two possible diasteromers would be formed.

2.6 DISACCHARIDES

The oligosaccharides (see page 26 for definition) most frequently encountered in nature are disaccharides that on hydrolysis yield two moles of monosaccharides. Among the disaccharides encountered is the sugar maltose; this sugar is obtained as an intermediate in the hydrolysis of starch by enzymes known as amylases. In maltose, one molecule of glucose is linked through the hydroxyl group on the C-1 carbon atom in a glycosidic bond to the hydroxyl group on the C-4 of a second molecule of glucose.



Maltose

The glycosidic linkage between the two glucose residues is designated as $\alpha(1 \rightarrow 4)$ to specify that the anomeric carbon involved in the glycosidic bond has the α-configuration and that it is linked to the 4-position of the second glucose molecule. This second glucose moiety possesses a free anomeric hydroxyl that can exist in either the α- or β-configuration (the β-isomer is shown); this free anomeric hydroxyl thus confers the property of mutarotation on maltose, and the disaccharide is a reducing sugar. That maltose has the structure shown was determined by analyzing the two products obtained on acid hydrolysis of its *octa*methyl derivative. The fully methylated maltose yields 2,3,4,6-tetra-*O*-methyl-D-glucose and 2,3,6-tri-*O*-methyl-D-glucose on hydrol-