

Carbohydrates

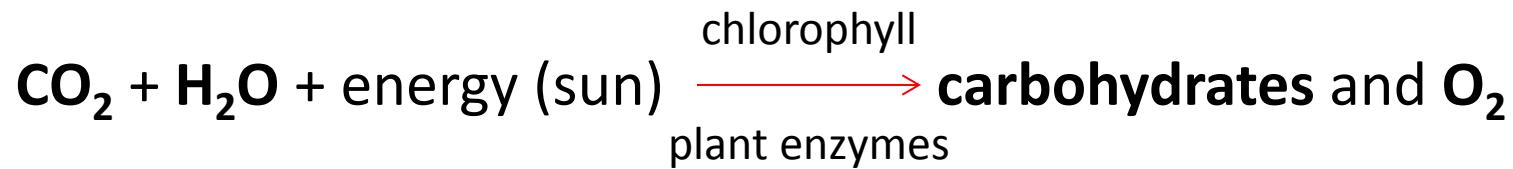
Chapter 18

Biochemistry – an overview

- **Biochemistry** is the study of chemical substances in living organisms and the chemical interactions of these substances with each other.
- Biochemical substances are found within living organisms, and are divided into two groups:
 - Bioinorganic substances include water and inorganic salts
 - Bioorganic substances include lipids, carbohydrates, proteins and nucleic acids

Occurrence and function of carbohydrates

- **Carbohydrates** are the most abundant form of bioorganic molecule, accounting for about 75% of a plant's dry mass.
- Plants produce carbohydrates from CO_2 and H_2O during photosynthesis:



Carbohydrates usually have the general formula $\text{C}_a(\text{H}_2\text{O})_b$ where a and b are whole numbers.
Example, in **glucose**, a and b are = 6: $\text{C}_6\text{H}_{12}\text{O}_6 = \text{C}_6(\text{H}_2\text{O})_6$
In **lactose** ($\text{C}_{12}\text{H}_{22}\text{O}_{11}$), a = 12 and b = 11

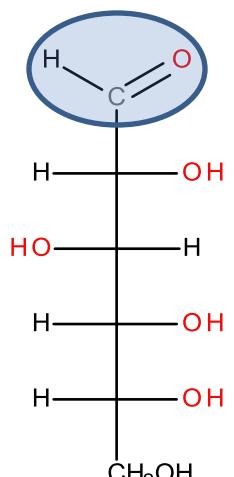
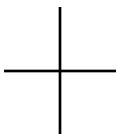
Occurrence and function of carbohydrates

- Carbohydrates have the following functions in the human body:
 1. Provide energy through oxidation
 2. Provide stored energy (in the form of glycogen)
 3. Supply materials for the synthesis of other biochemical substances
 4. Form part of the structural framework for DNA and RNA molecules
 5. When linked to lipids, they form structural components of cell membranes
 6. When linked to proteins, they participate in cell-cell and cell-molecule recognition processes

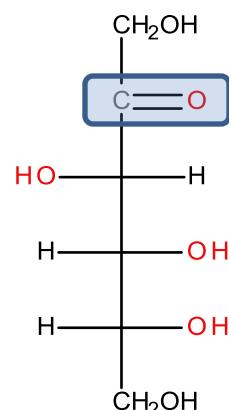
Classification of carbohydrates

- Carbohydrates are classified by structure as *polyhydroxy aldehydes* or *polyhydroxy ketones*, or compounds that yield either of these upon hydrolysis.

Fischer projection
each “cross” is a
carbon center



Glucose
a polyhydroxyaldehyde



Fructose
a polyhydroxyketone

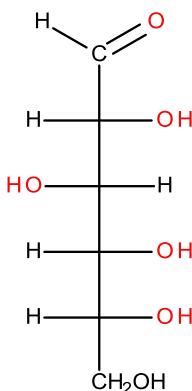
(Fischer projections)

Classification of carbohydrates

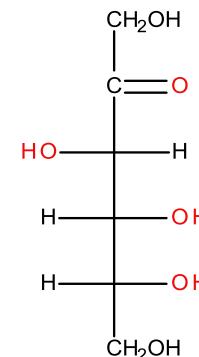
Monosaccharides

- Carbohydrates are classified *on the basis of size* as monosaccharides, oligosaccharides, or polysaccharides.
- **Monosaccharides** contain a single polyhydroxy aldehyde or polyhydroxy ketone unit.
- They can't be broken down into simple units by *hydrolysis reactions*.
- They tend to be crystalline solids, and water-soluble.

Examples of monosaccharides



Glucose
a polyhydroxyaldehyde

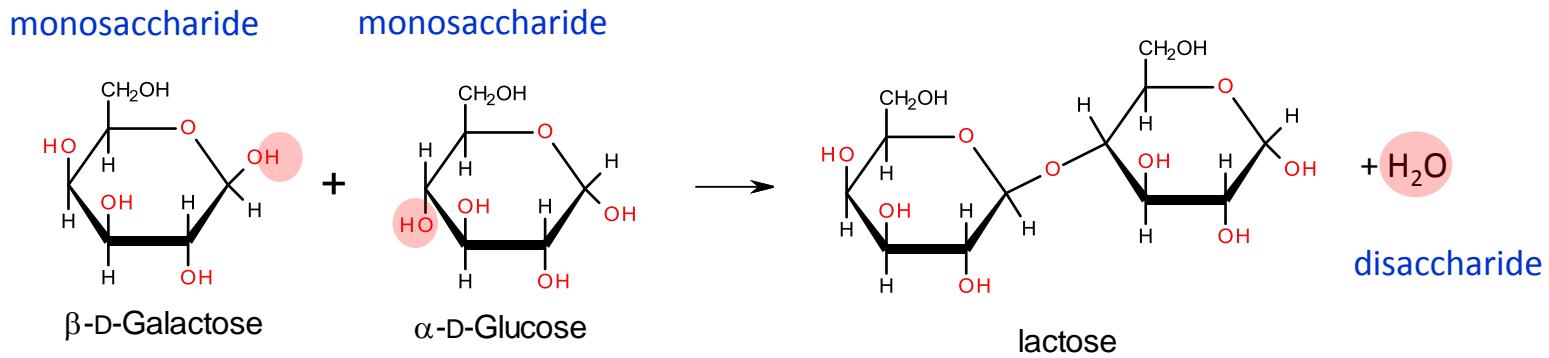
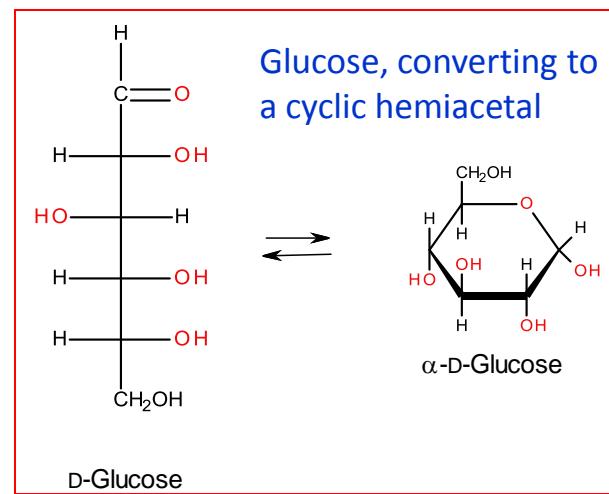
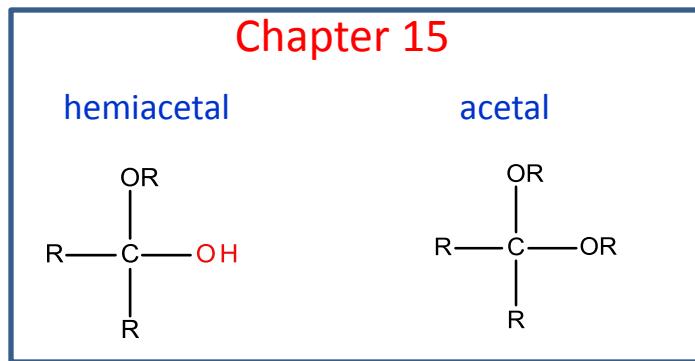


Fructose
a polyhydroxyketone

Classification of carbohydrates

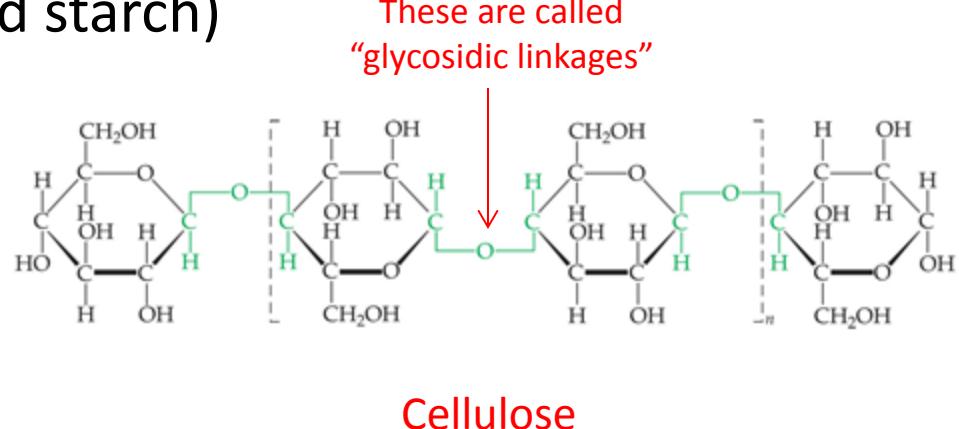
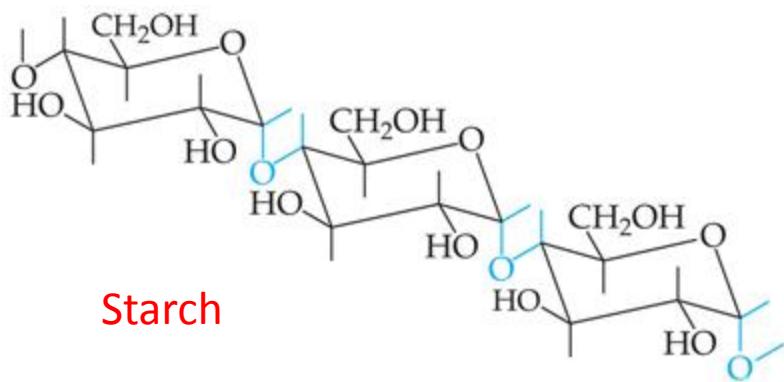
Disaccharides

- Two monosaccharides can link together to form a **disaccharide** (e.g. lactose).
- The reaction that links them together is another example of a condensation reaction.



Classification of carbohydrates

- **Oligosaccharides** are carbohydrates that possess two to ten monosaccharide units covalently bound to one another. Disaccharides (two units) tend to be crystalline and water-soluble (e.g. sucrose, lactose)
- **Polysaccharides** are polymeric carbohydrates that contain many monosaccharide units covalently bound together. Unlike monosaccharides (and disaccharides) these are not water-soluble (cellulose and starch)



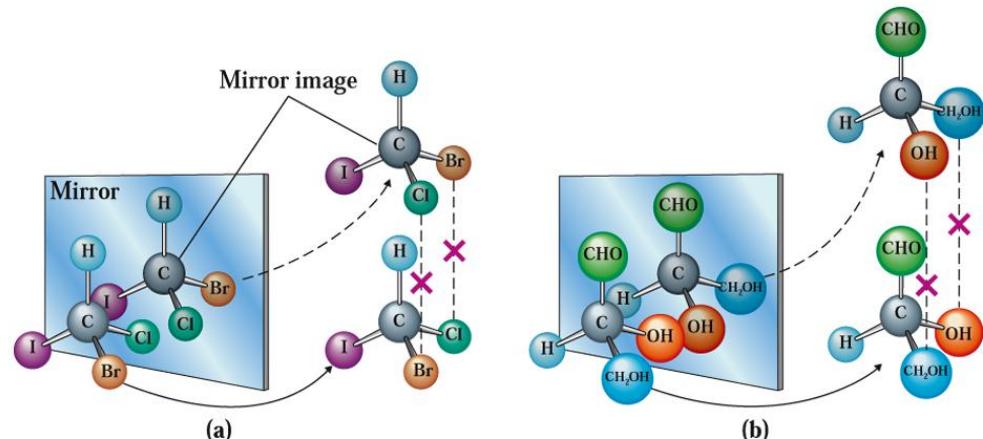
Chirality: handedness in molecules

- “Handedness” is a feature that an object possesses by virtue of its symmetry. When an object has a handedness (e.g. right- or left-), its mirror image cannot be superimposed upon it (the mirror image and object are **non-superimposable**)
- Non-superimposable means that the image of the original object will not be able to be made to overlap with the object, point-for-point as an exact duplicate.



Chirality: handedness in molecules

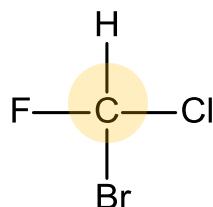
- Certain molecules possess this same symmetry feature. Molecules that have one or more tetrahedral centers that involve bonds to four different atoms/groups possesses a handedness.
- This kind of atom (center of asymmetry) is called a **chiral center**, and molecules that possesses one or more chiral centers are **chiral***.



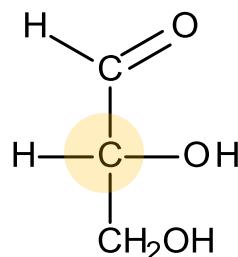
*Exception: in cases where chiral centers are present in a molecule that has a plane of symmetry: these are called meso structures and they are not chiral.

Chirality: handedness in molecules

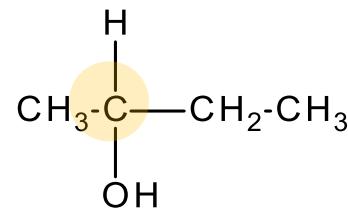
- Some examples of chiral molecules:



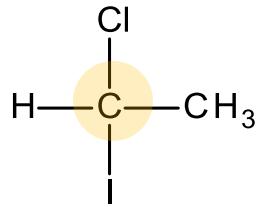
Bromochlorofluoromethane



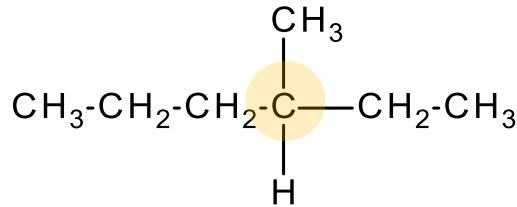
Glyceraldehyde



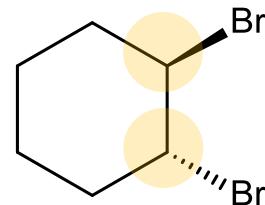
2-Butanol



1-Chloro-1-iodoethane



3-Methylhexane

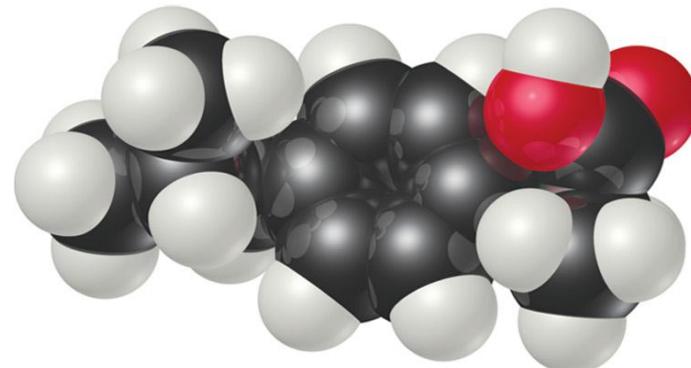
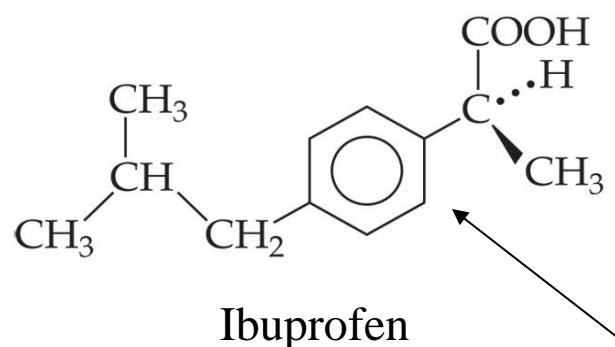


trans-1,2-Dibromocyclohexane

Chirality: handedness in molecules

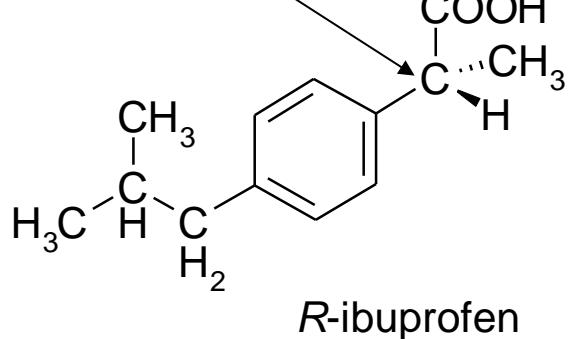
- So, it is possible for molecules to possess more than one chiral center.
- The human body's chemistry will often exhibit different responses to each mirror image form of a chiral molecule.
- Naturally occurring monosaccharides are almost always “right-handed” and amino acids are left-handed.

Chirality: handedness in molecules



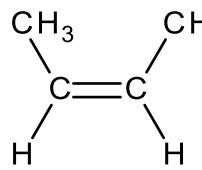
These two structures are only different in the placement of the -CH₃ and -H groups on this carbon.

Many pharmaceutical substances possess chiral centers.

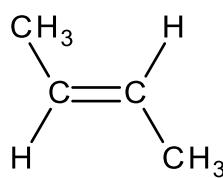


Stereoisomerism: enantiomers and diastereomers

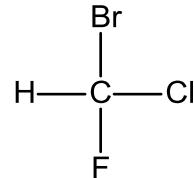
- We have seen several kinds of isomerism so far. One general class (constitutional isomers) consist of molecules that possess different atom-to-atom connectivity.
- **Stereoisomers** (e.g. *cis*-, *trans*-) do not differ in their atom-to-atom connectivities, but only in the orientations of the atoms in space (with respect to an inflexible bond)
- Chiral molecules are another example of stereoisomers.
- Two structural features make stereoisomerism possible:
 - Structural rigidity, or
 - The lack of symmetry in a molecule



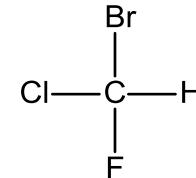
cis-



trans-

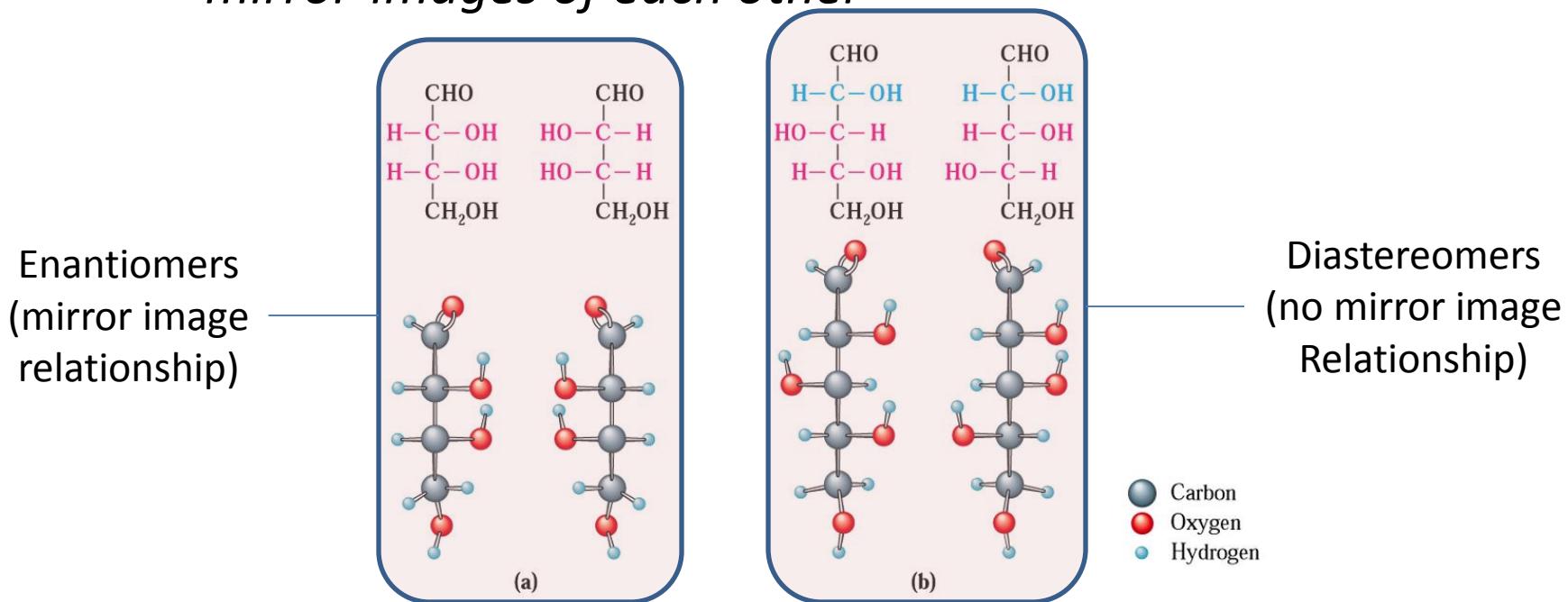


enantiomers



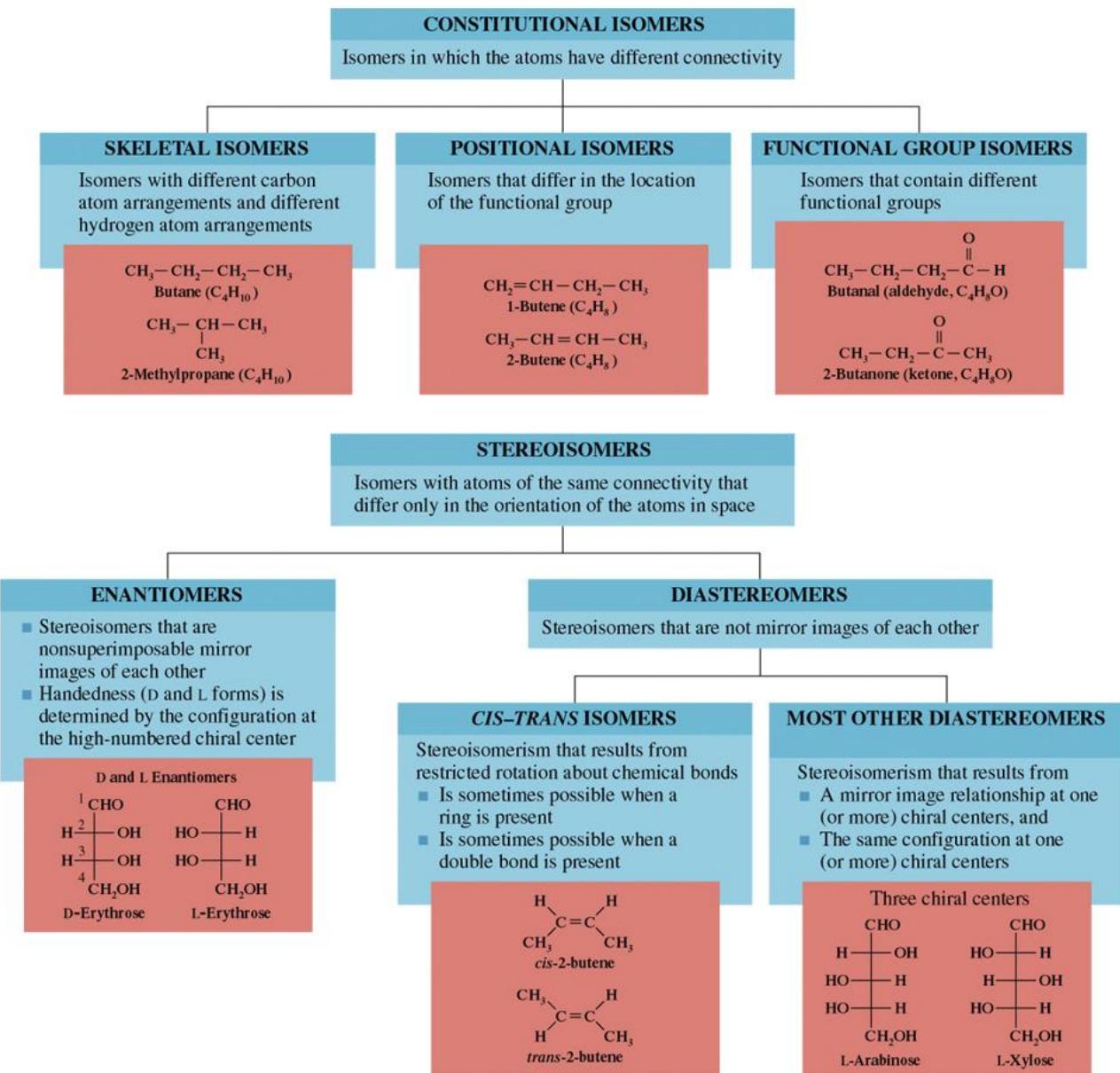
Stereoisomerism: enantiomers and diastereomers

- Stereoisomers may be divided into two groups:
 - Enantiomers are stereoisomers whose molecules are *non-superimposable mirror images* of each other
 - Diastereomers are stereoisomers whose molecules are *not mirror-images of each other*



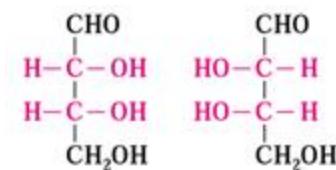
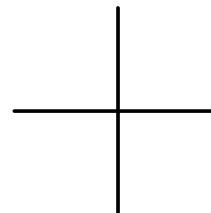
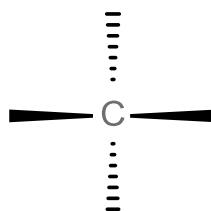
Stereoisomerism: enantiomers and

- Thus, because cis- and trans-isomers do not have a mirror-image relationship, they are not enantiomers, but are diastereomers.

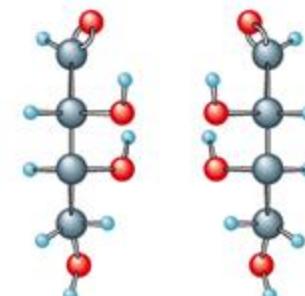


Designating handedness using Fischer projection formulas

- A Fischer projection formula is a two-dimensional structural notation for showing the spatial arrangement of groups around the chiral centers in molecules.
- Chiral centers (typically carbon atoms) are represented as the intersections of vertical and horizontal lines.
 - Vertical lines represent bonds to groups directed into the printed page
 - Horizontal lines represent bonds that are directed toward the viewer

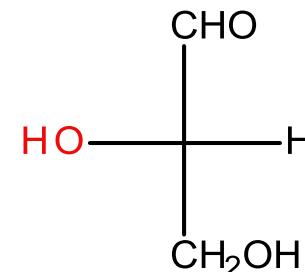
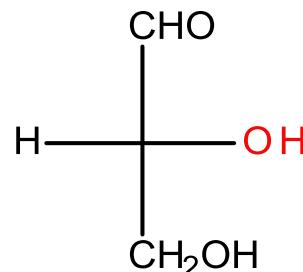
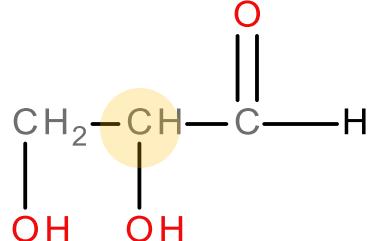


Carbon
Oxygen
Hydrogen



Designating handedness using Fischer projection formulas

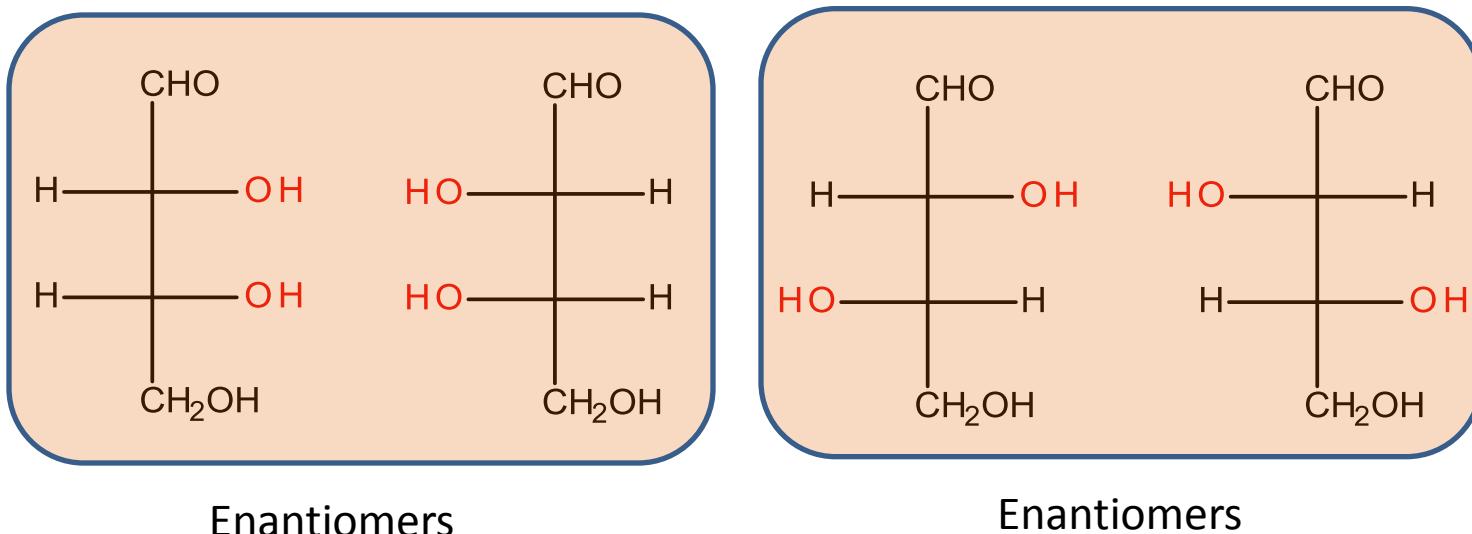
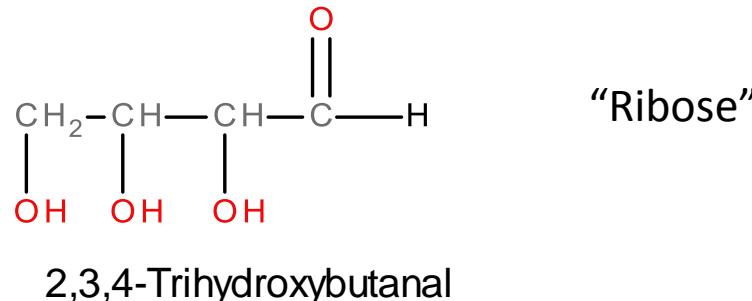
- A molecule like glyceraldehyde (2,3-Dihydroxypropanal) can be represented as follows:



- In the Fischer projection diagram, the aldehyde group is shown at the top (as CHO) (assigned position #1 in the molecule)
- The “D” enantiomer is the structure with the OH substituent on the right-hand side, and the “L” enantiomer has the OH group on the left side.

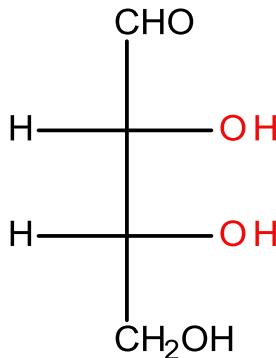
Designating handedness using Fischer projection formulas

- For monosaccharides involving more than one chiral center, the structures are drawn with the aldehyde/ketone carbon at the top end.
- Carbons are numbered from the top-down.

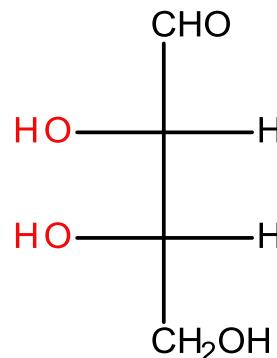


Designating handedness using Fischer projection formulas

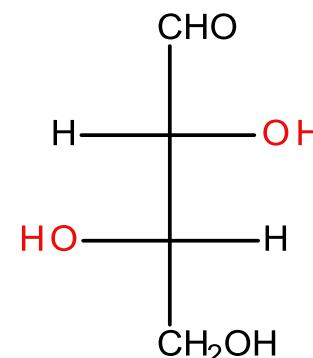
- The structures shown have the following relationships:
 - a** and **b** are enantiomers
 - c** and **d** are enantiomers
 - c** and **d** are diastereomers of **a**
 - c** and **d** are diastereomers of **b**



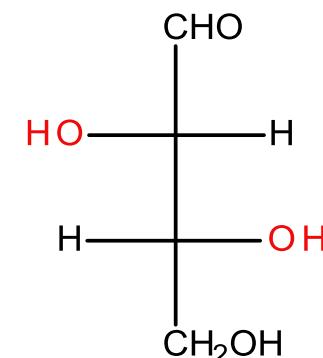
a



b



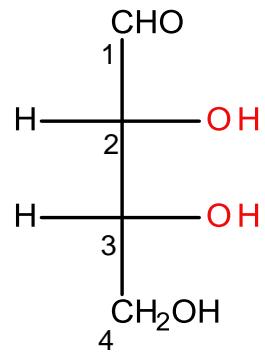
c



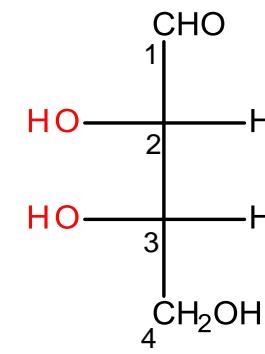
d

Designating handedness using Fischer projection formulas

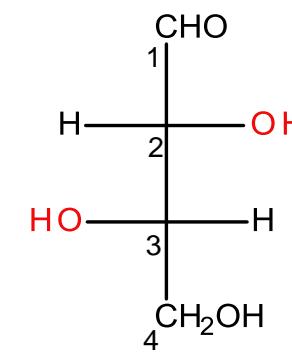
- For assigning “handedness”, the terms D and L are used. This is assigned by considering the placement of the OH group on the highest-numbered chiral carbon.
- If the OH group on the highest-numbered chiral center is on the center’s right side, the compound is labeled “D”
- If the OH group on the highest-numbered chiral center is on the center’s left side, the compound is labeled “L”



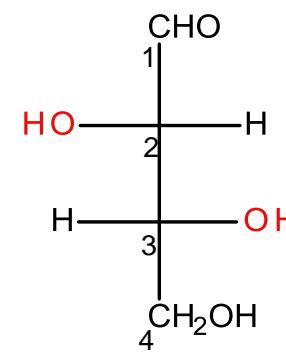
D-isomer



L-isomer



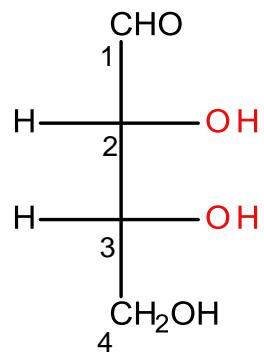
L-isomer



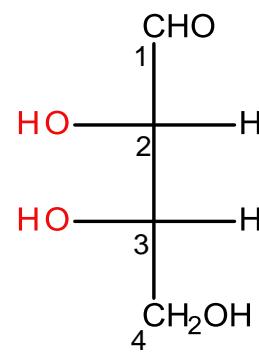
D-isomer

Designating handedness using Fischer projection formulas

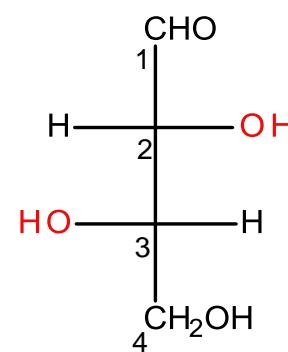
- The term, **epimer**, means diastereomers whose molecules differ in their configuration at one chiral center.



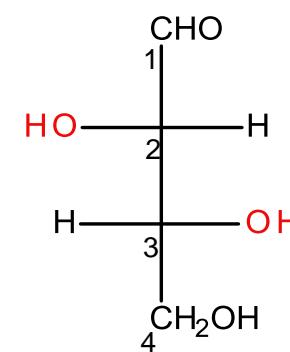
D-isomer



L-isomer



L-isomer

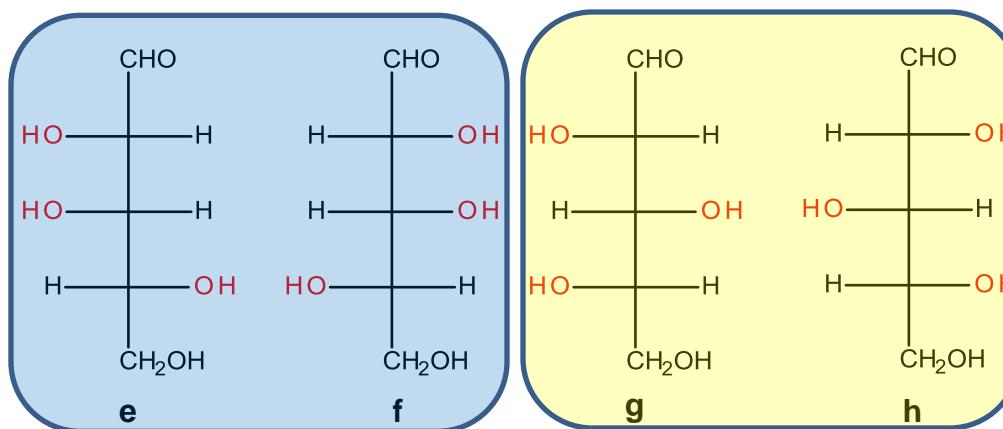
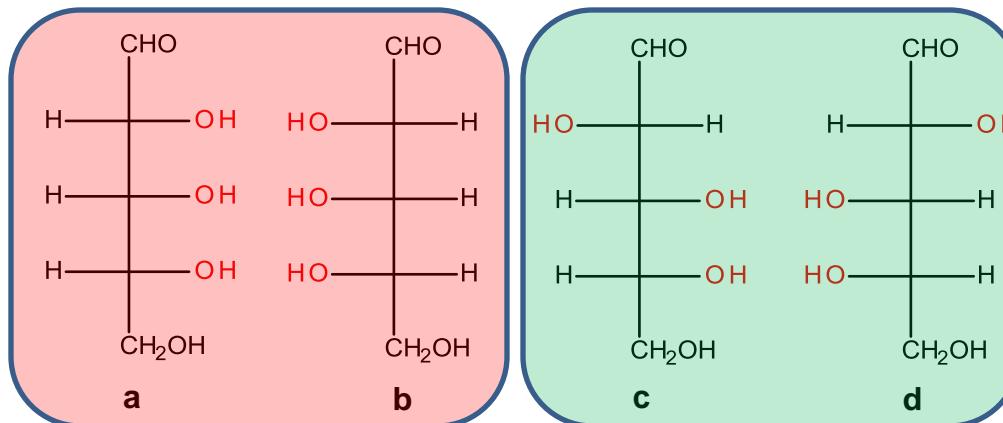


D-isomer

Designating handedness using Fischer projection formulas

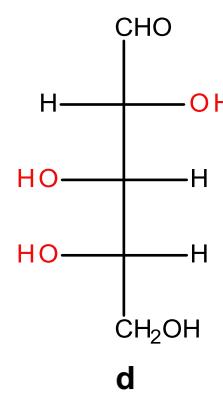
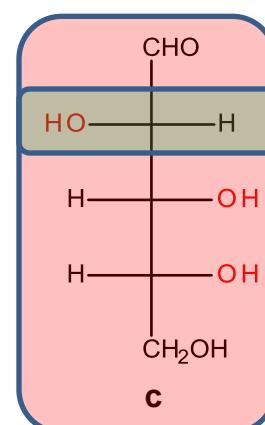
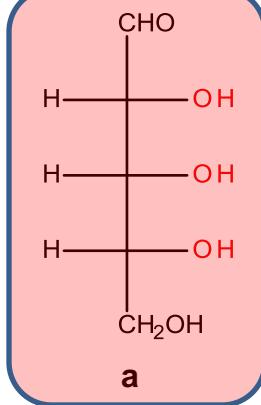
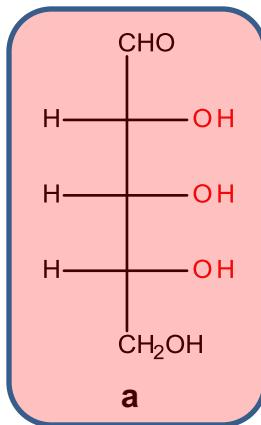
- In general, molecules that possess “n” chiral centers may exist in a maximum of 2^n possible stereoisomeric forms. (In some cases, a molecule’s symmetry might make this number less than 2^n)

Enantiomers

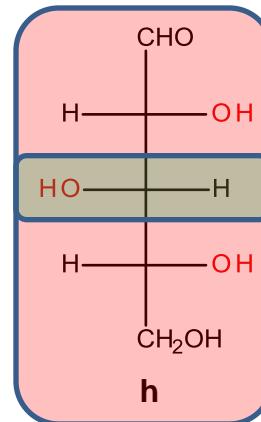
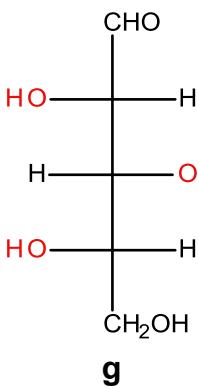
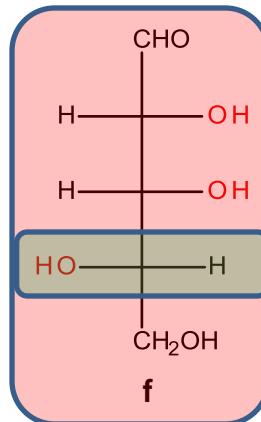
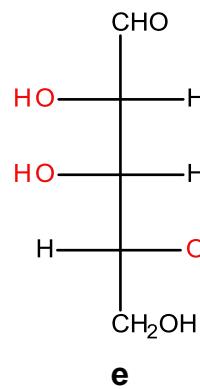


Designating handedness using Fischer projection formulas

- In general, molecules that possess “n” chiral centers may exist in a maximum of 2^n possible stereoisomeric forms. (In some cases, a molecule’s symmetry might make this number less than 2^n)



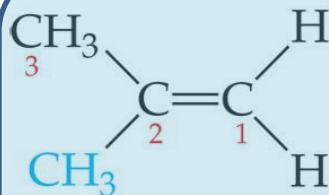
Epimers



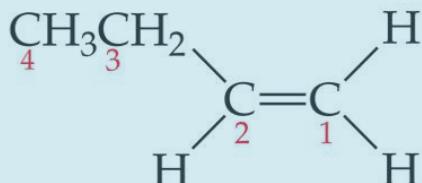
Properties of enantiomers

- We saw throughout the organic section of this course that constitutional isomers differ in their chemical and physical properties.
- They have different melting points, boiling points, and may have different water-solubility.

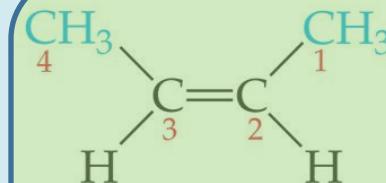
diastereomers



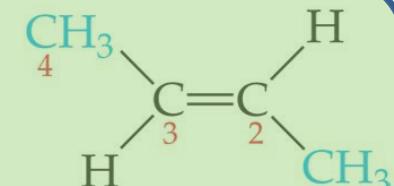
Methylpropene
bp -7°C



1-Butene
bp -6°C



cis-2-Butene
bp $+4^\circ\text{C}$



trans-2-Butene
bp $+1^\circ\text{C}$

- Even diastereomers show differences in their physical and chemical properties.

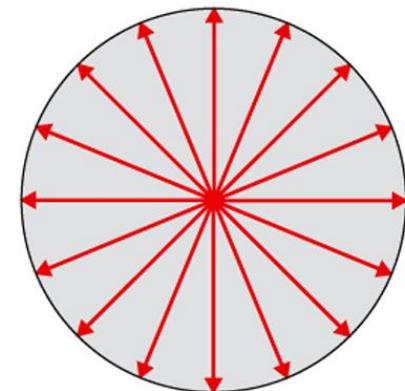
Properties of enantiomers

- Enantiomers show identical chemical and physical properties in an achiral environment. They will have the same boiling and melting points, same solubility, etc.
- They do, however, exhibit different behavior in two situations:
 - Their interactions with plane-polarized light
 - Their interactions with other chiral substances

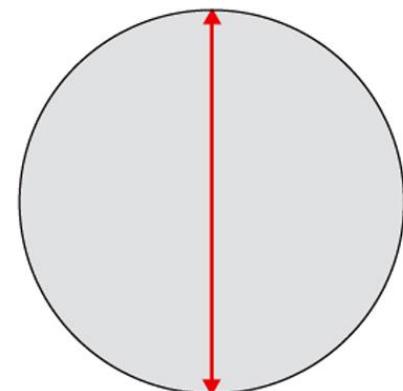
Properties of enantiomers

Interaction of enantiomers with plane-polarized light

- Plane-polarized light is light that has had all components except one removed by a polarizer, so that light waves travel in one plane only.
- Enantiomers are called **optically active isomers** because they are able to rotate a beam of plane-polarized light, either clockwise (to the right) or counterclockwise (to the left).
- Enantiomers rotate plane-polarized light in this manner in opposite directions, and to the same degree.



(a) Ordinary (unpolarized) light

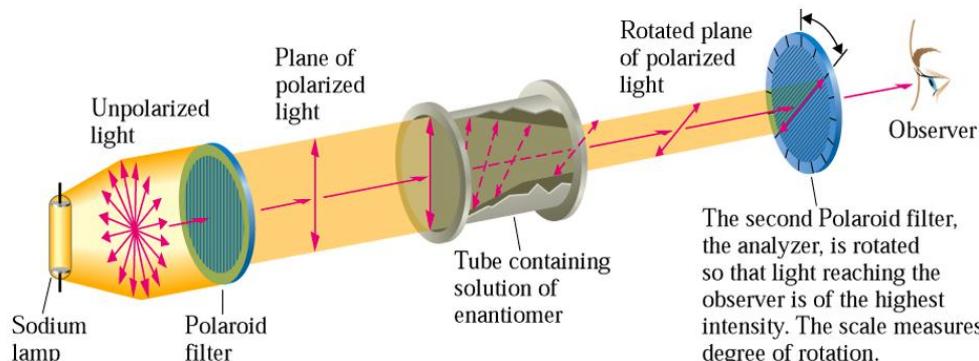


(b) Plane-polarized light

Properties of enantiomers

Dextrorotatory and levorotatory compounds

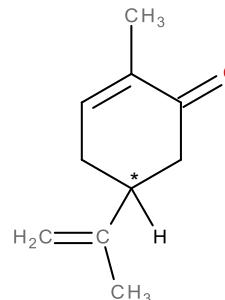
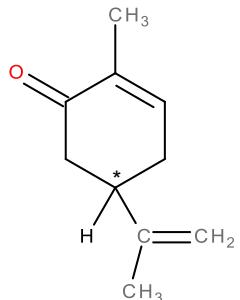
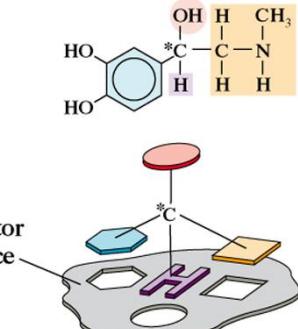
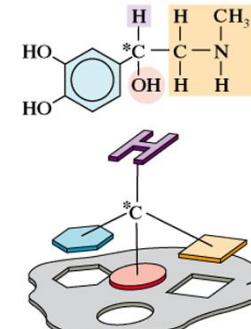
- Optically active compounds are able to rotate plane-polarized light.
- A compound that rotates a beam of plane-polarized light to the right (clockwise) is called **dextrorotatory**, and this is indicated by a “+” notation that follows the D- or L- part of the compound’s name.
- A compound that rotates a beam of plane-polarized light to the left (counterclockwise) is called **levorotatory**, and this is indicated by a “-” notation that follows the D- or L- part of the compound’s name.



Important: the handedness of an optically active compound, indicated by its D- or L- label, and the direction of rotation (left or right) of plane-polarized light are not connected.
In order to determine whether a compound is dextrorotatory or levorotatory, its effect on the rotation of plane-polarized light must be tested.

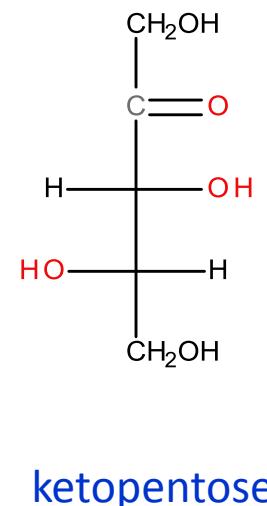
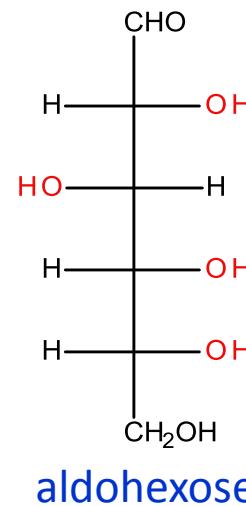
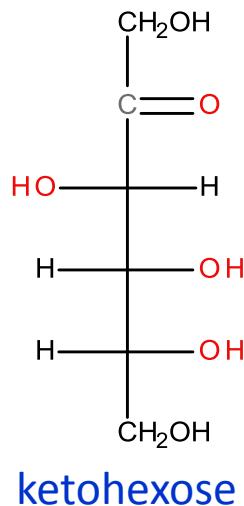
Interactions between chiral compounds

- Only in a chiral environment will enantiomers exhibit different physical and chemical properties.
 - Enantiomers have identical boiling/melting points – these values are dependent on intermolecular forces, which are the same since enantiomers possess the same functional groups.
 - Enantiomers have the same solubility in achiral solvents, but different solubilities in a chiral solvent.
 - Reaction rates involving chiral reactants are the same when the second reactant is achiral, but differ when the other reactant is chiral.
 - Because receptor sites in the body are chiral, the response of the body to two enantiomers will differ, sometimes dramatically.



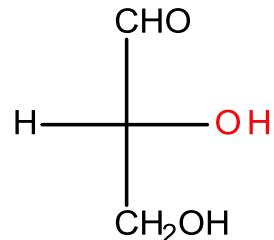
Classification of monosaccharides

- We saw that saccharides are polyhydroxy aldehydes or polyhydroxyketones.
- Monosaccharides tend to possess between three to seven carbon atoms, and may be classified as **aldose** or **ketose**, depending on the functional group (aldehyde/ketone) that is present.
- A monosaccharide that possesses three carbons and an aldehyde group is called an aldotriose, while a six-carbon polyhydroxyketone would be called a ketohexose.

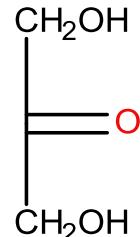


Classification of monosaccharides

- Monosaccharides and disaccharides are often called sugars (because they taste sweet).
- The simplest sugars are glyceraldehyde and dihydroxyacetone.
- Note: dihydroxyacetone is not a chiral molecule.



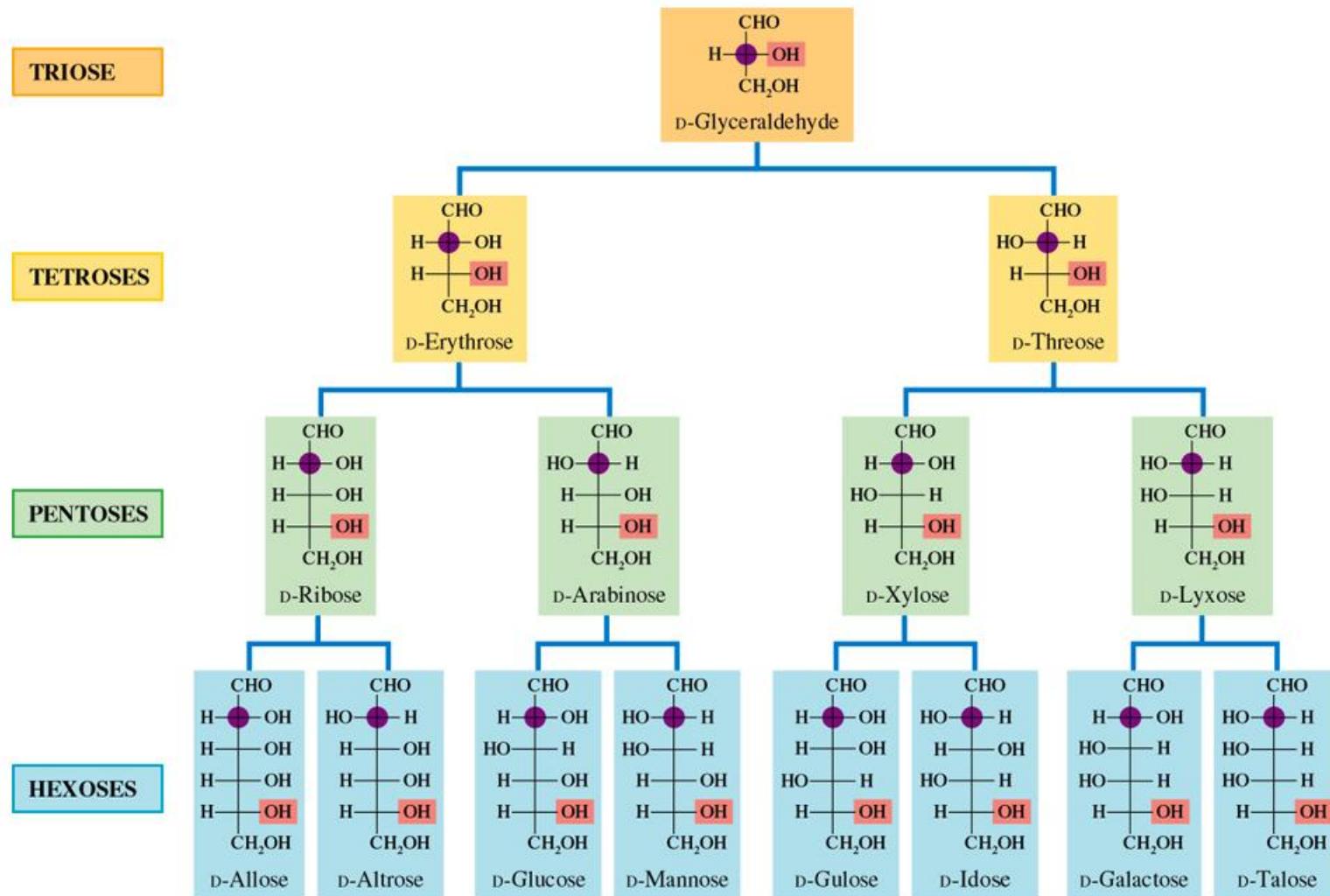
D-Glyceraldehyde
(2,3-Dihydroxypropanal)



1,3-Dihydroxyacetone

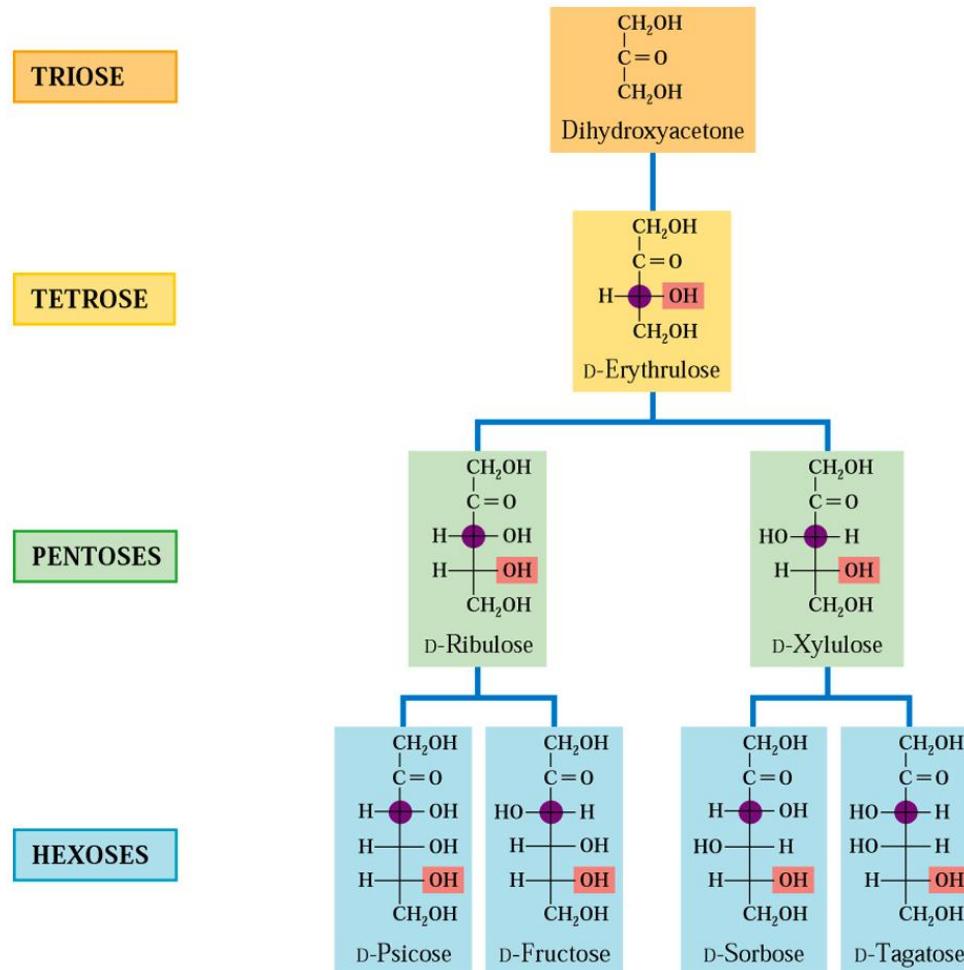
Classification of monosaccharides

polyhydroxyaldehydes



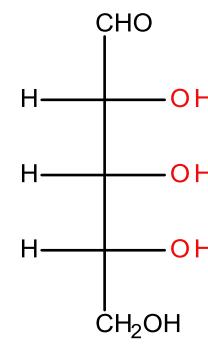
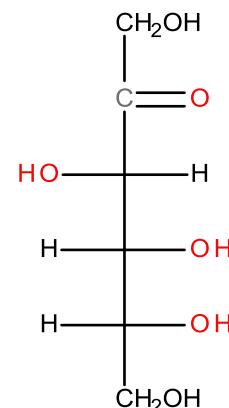
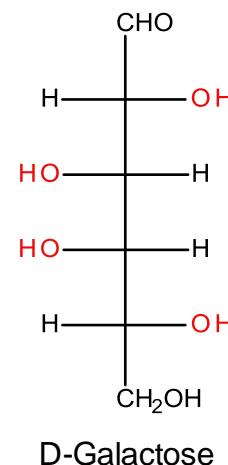
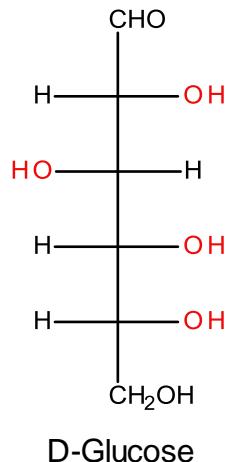
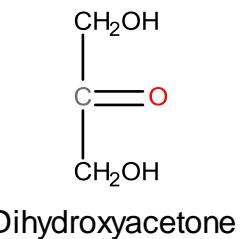
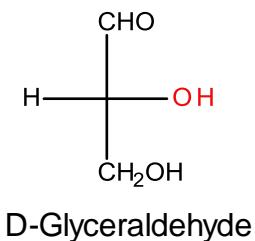
Classification of monosaccharides

polyhydroxyketones



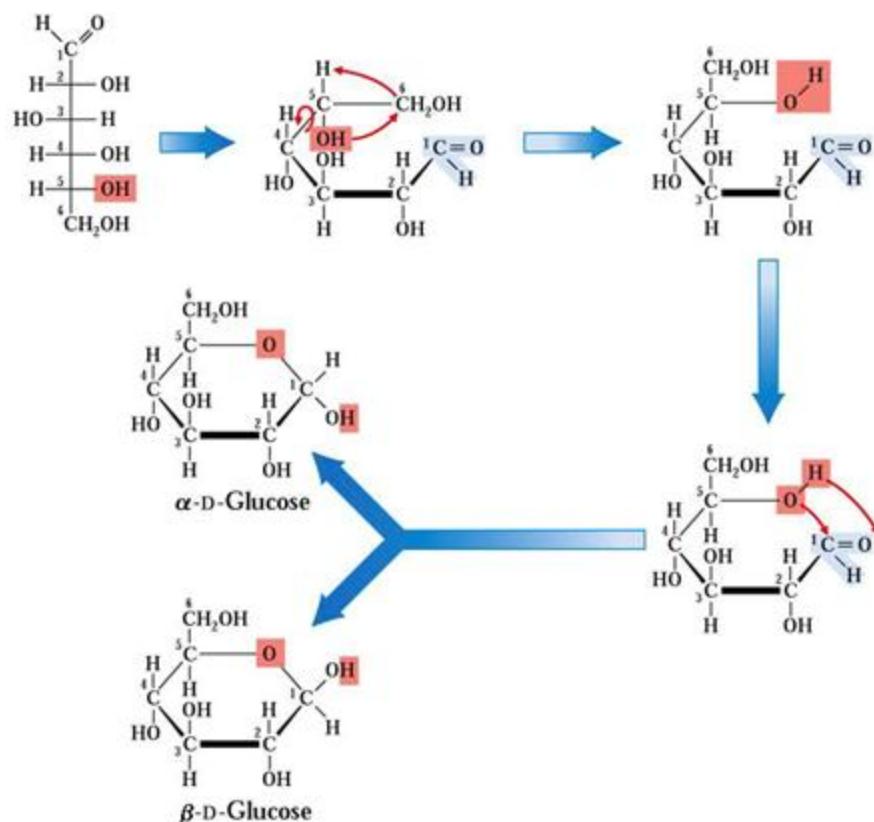
Biochemically important monosaccharides

- These are six monosaccharides that are especially important in metabolic processes



Cyclic forms of monosaccharides

- We saw back in chapter 15 that glucose can form a cyclic hemiacetal. In fact, this form of glucose is more predominant than the straight chain form:



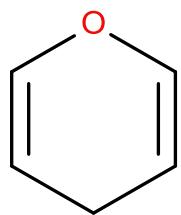
α -D-Glucose \rightleftharpoons open chain \rightleftharpoons β -D-Glucose

37% less than 0.01% 63%

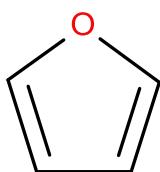
The difference between α - and β -D-Glucose is the position of the OH group on the hemiacetal carbon with respect to the CH_2OH group

Cyclic forms of monosaccharides

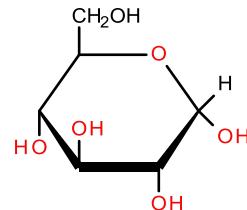
- Aldoses form rings that have the same number of members in the ring as there are carbons in the sugar.
- Ketoses form rings that have one fewer members than the number of carbons in the sugar.
- Cyclic monosaccharides containing six members are called pyranoses, similar to the cyclic ether, pyran.
- Five-membered cyclic monosaccharides are called furanoses, like the cyclic ether furan.



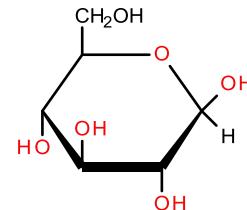
Pyran



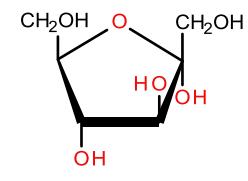
Furan



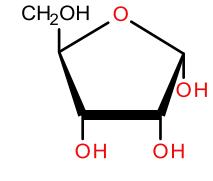
α -D-Glucose
 α -D-Glucopyranose



β -D-Glucose
 β -D-Glucopyranose



α -D-Fructose
 α -D-Fructofuranose

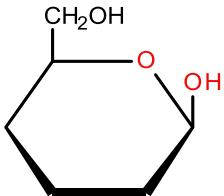
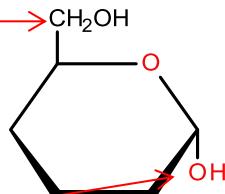


α -D-Ribose
 α -D-Ribofuranose

Haworth projection formulas

- The “edge-on” cyclic forms of monosaccharides are represented by Haworth projection formulas.
- In these formulas, the oxygen of the ring is in the upper right (6-membered rings) or top (5-membered rings).
- The placement of the CH_2OH group (above or below the ring) determines the D- or L- label.
- The α - or β -label is determined by the position of the OH on the hemiacetal carbon with respect to the CH_2OH group; same side of ring: β ; opposite sides of ring: α .

CH_2OH up = D



hemiacetal OH
opposite face of
ring: α

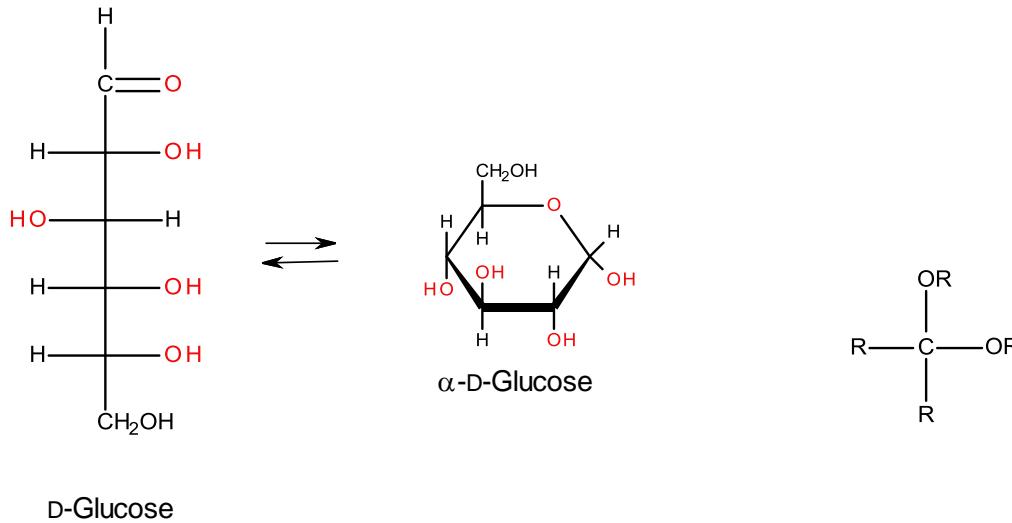
α -D-monosaccharide

β -D-monosaccharide

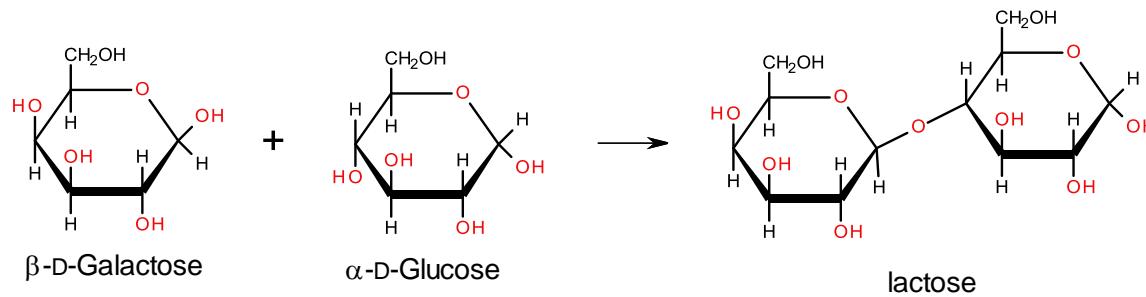
α -L-monosaccharide

Haworth projection formulas

- Comparing the straight chain and cyclic forms of monosaccharides, the OH groups that are located on the right of a chiral center point down in the cyclic form.



D-Glucose



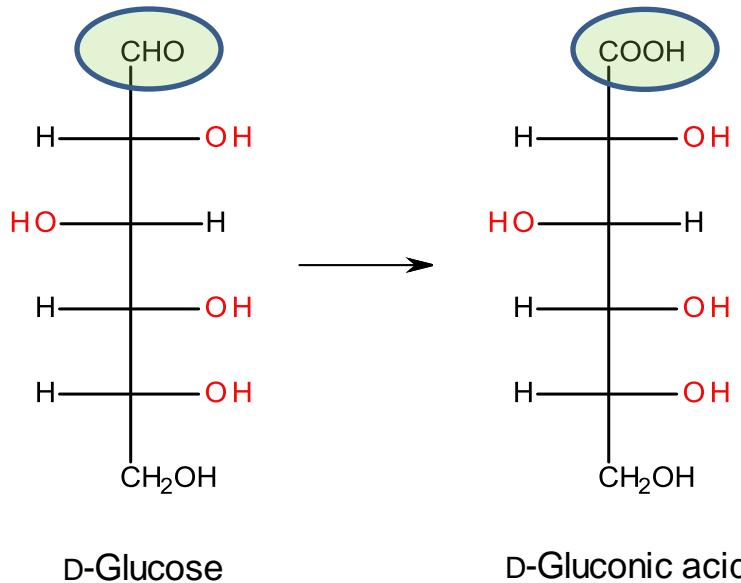
Reactions of monosaccharides

- The reactions of monosaccharides includes the following reactions:
 - Oxidation to acidic sugars
 - Reduction to sugar alcohols
 - Glycoside formation (hemiacetal → acetal)
 - Phosphate ester formation (esterification)
 - Amino sugar formation

Reactions of monosaccharides

Oxidation to produce acidic sugars

- Monosaccharide oxidation can yield three different kinds of acid sugars:
 - Weak oxidizing agents like Tollens' reagent and Benedict's solution oxidize the aldehyde end of an aldose structure to yield aldonic acids.

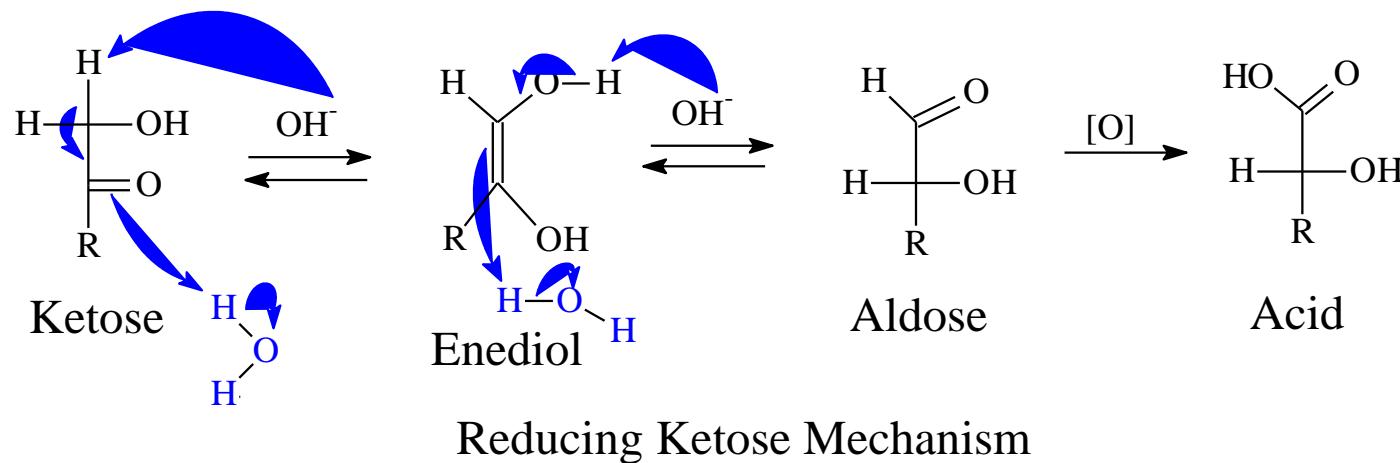


- In these reactions, the aldehyde reduces the Tollens'/Benedict's reagent, and so it (the aldose) is called a reducing sugar.

Reactions of monosaccharides

Oxidation to produce acidic sugars

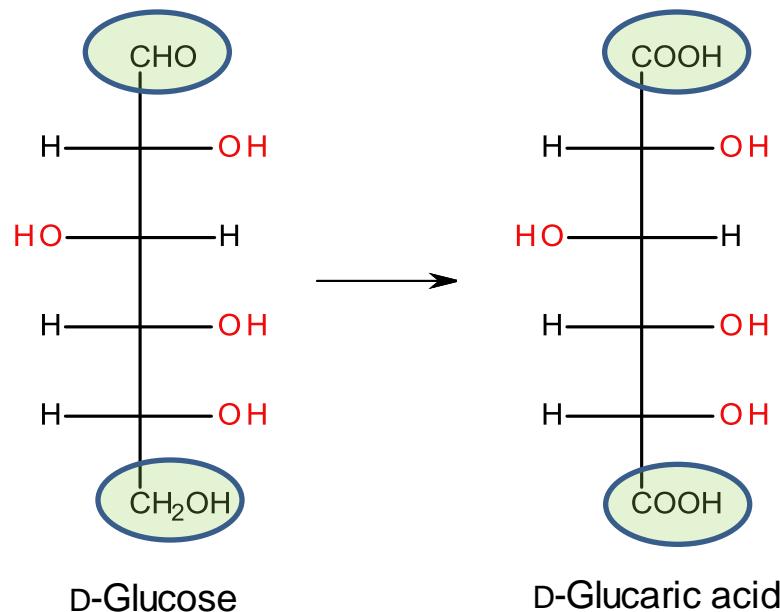
- Under basic conditions, ketones can also react with Tollens'/Benedict's reagents, not because the ketone becomes oxidized (can't oxidize a ketone), but because it can rearrange under basic conditions to an aldehyde (enol-keto isomerization):



Reactions of monosaccharides

Oxidation to produce acidic sugars

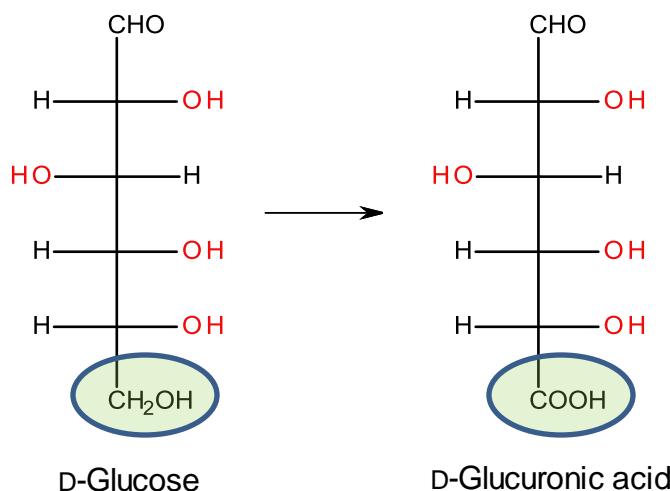
- Strong oxidizing agents can oxidize both ends of a monosaccharide, yielding a dicarboxylic acid called an **aldaric acid**:



Reactions of monosaccharides

Oxidation to produce acidic sugars

- It is possible for enzymes to oxidize the primary alcohol end of the monosaccharide *without oxidizing the aldehyde end*, to yield **alduronic acids**:

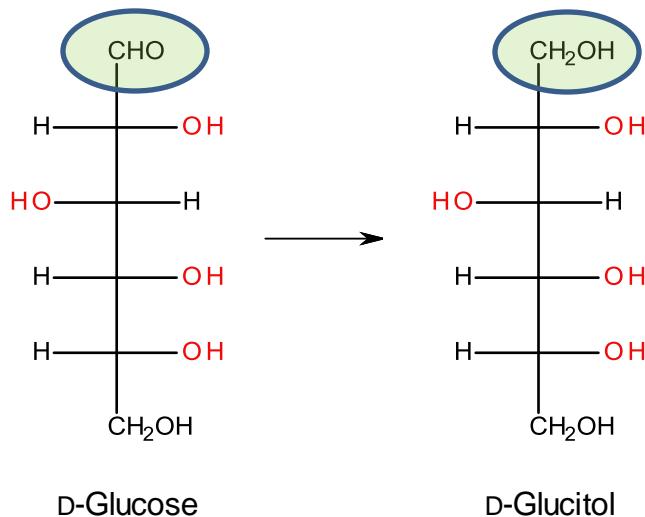


(This is really hard
to do in the lab)

Reactions of monosaccharides

Reduction to produce sugar alcohols

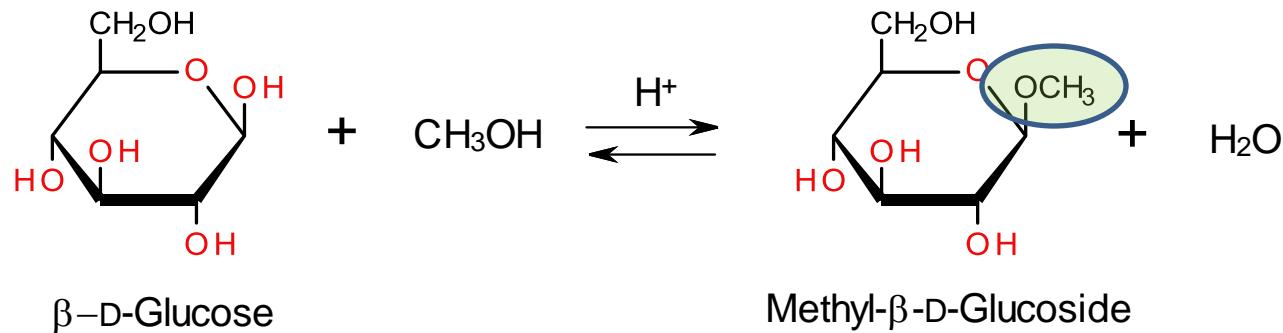
- The aldehyde/ketone groups of monosaccharides can undergo reduction to yield alcohol groups. The product is called a **sugar alcohol**:



Reactions of monosaccharides

Glycoside formation

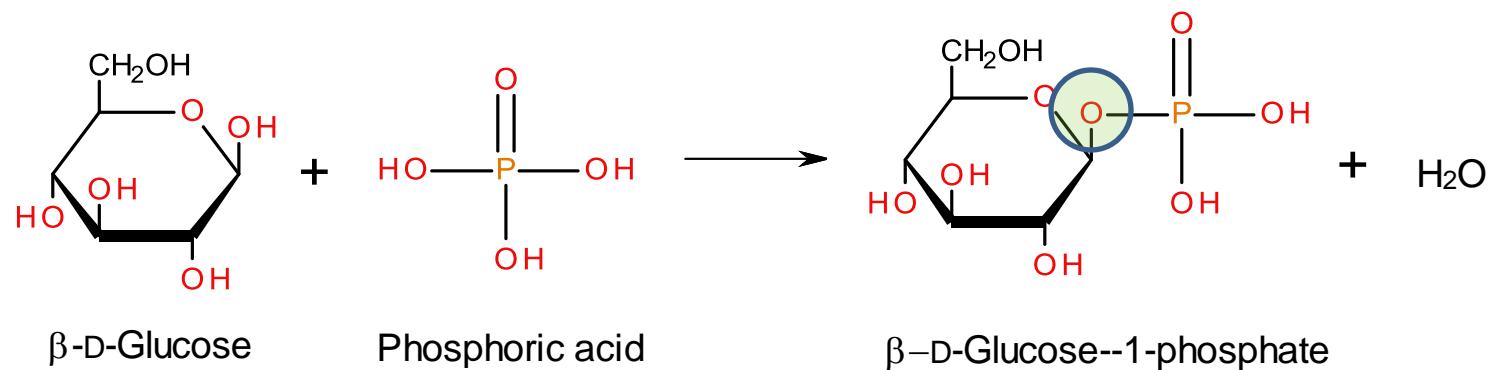
- Glycosides are acetals that form when cyclic hemiacetal forms of monosaccharides react with alcohols. The glycoside that results from glucose is called a glucoside:



Reactions of monosaccharides

Phosphate ester formation

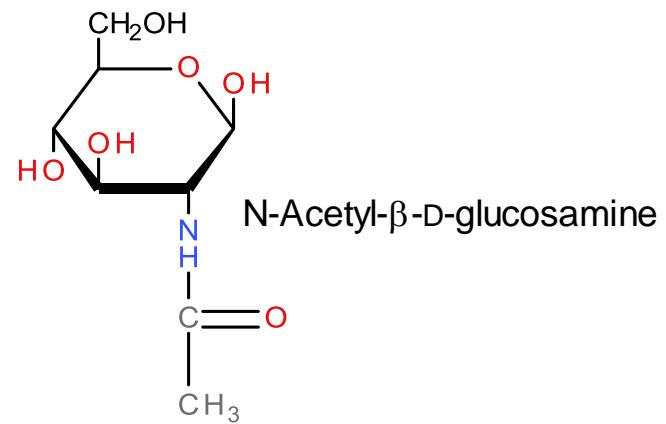
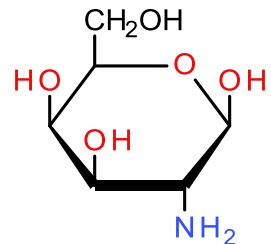
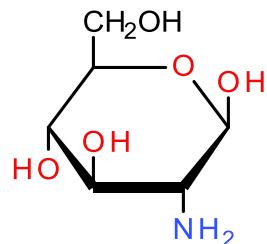
- The hydroxyl group of a monosaccharide may take place in an esterification with phosphate to produce an inorganic ester. These reactions are important in metabolic processes.



Reactions of monosaccharides

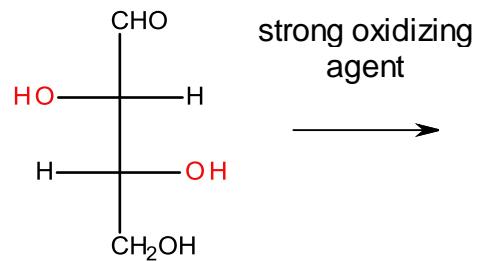
Amino sugar formation

- Amino sugars have one of their OH groups replaced with an NH₂ group. In naturally occurring amino sugars, the OH group on C-2 is replaced:

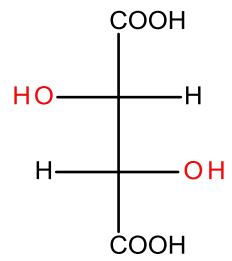


Reactions of monosaccharides

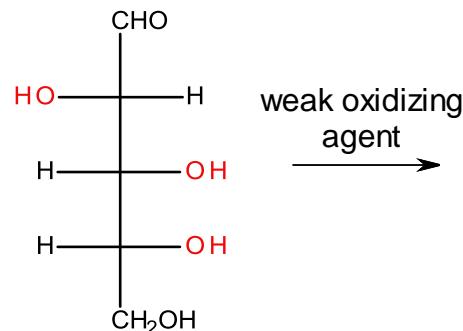
- Indicate the products when the following monosaccharides are reacted as follows:



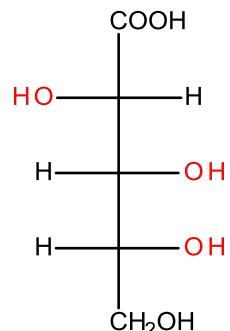
strong oxidizing agent



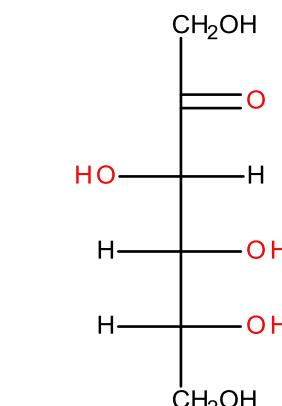
an aldarcic acid



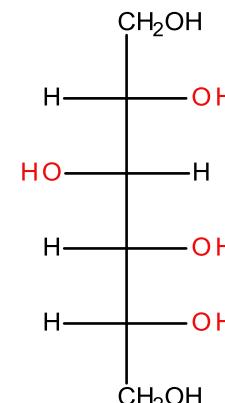
weak oxidizing agent



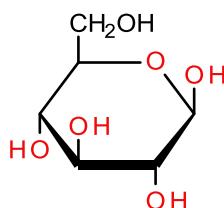
an aldonic acid



H₂, catalyst



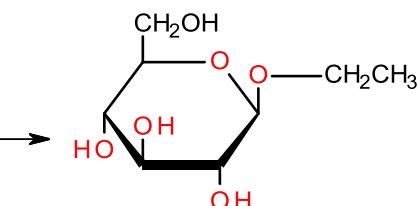
a sugar alcohol



β-D-Glucose



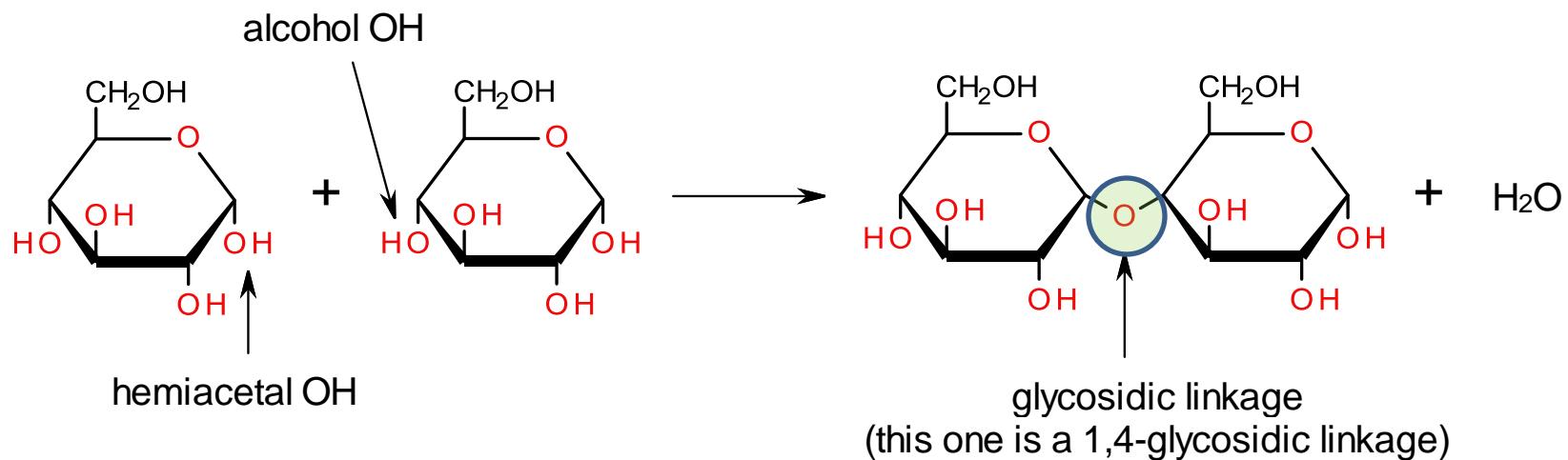
H⁺



Ethyl-β-D-Glucoside
(a glycoside)

Disaccharides

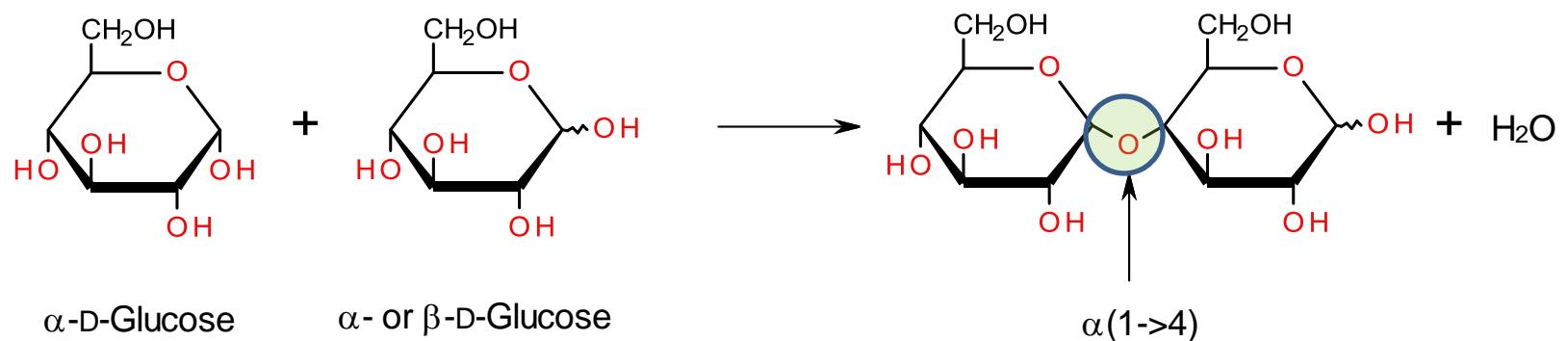
- Carbohydrates in which two monosaccharides are bonded through a glycosidic linkage are called disaccharides. In forming the glycoside-type bond, one monosaccharide acts as a hemiacetal and the other as an alcohol:



Disaccharides

Maltose

- Maltose is formed by reaction of two D-glucose units, one of which must be α -D-glucose.

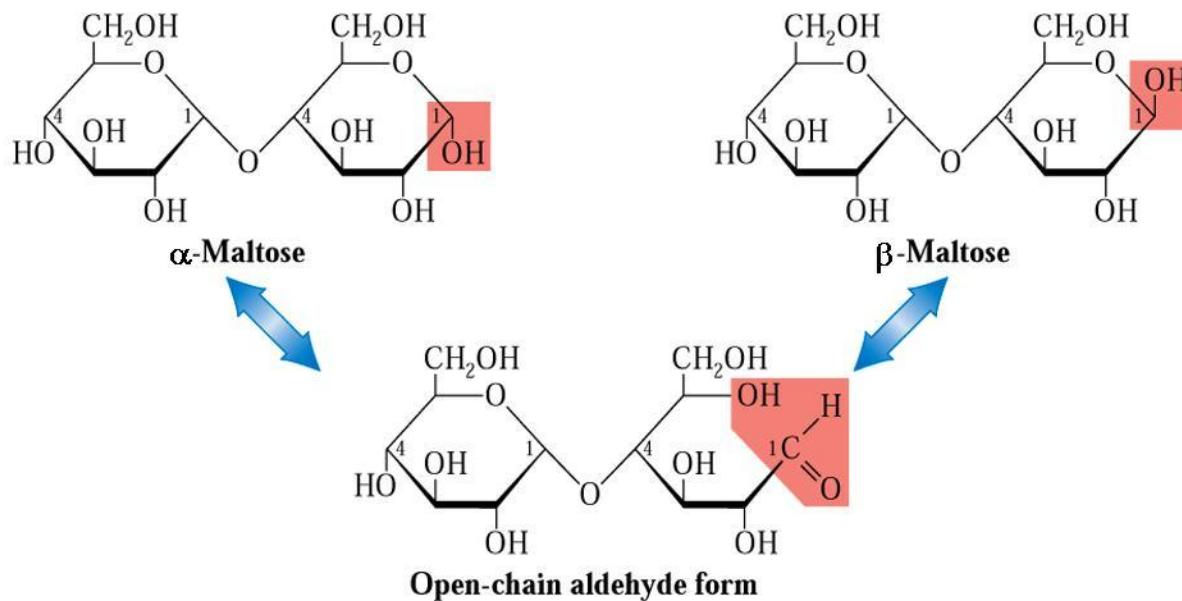


- The body breaks down maltose to glucose with the aid of the enzyme maltase.

Disaccharides

Maltose

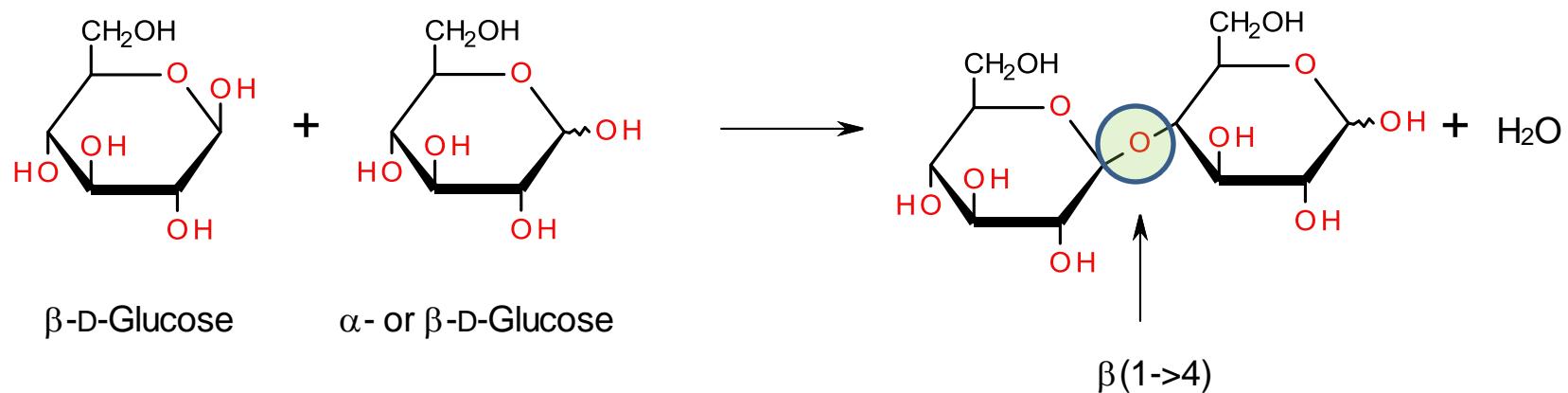
- Because the glucose unit on the right can open up (at the hemiacetal group) and close, maltose exists as three equilibrium forms. The open-chain form can react with Tollens/Benedict's reagent, and is thus a reducing sugar.



Disaccharides

Cellobiose

- Cellobiose contains two D-glucose monosaccharide units also, but unlike maltose, one must be of the β -configuration. This results in a $\beta(1 \rightarrow 4)$ configuration.

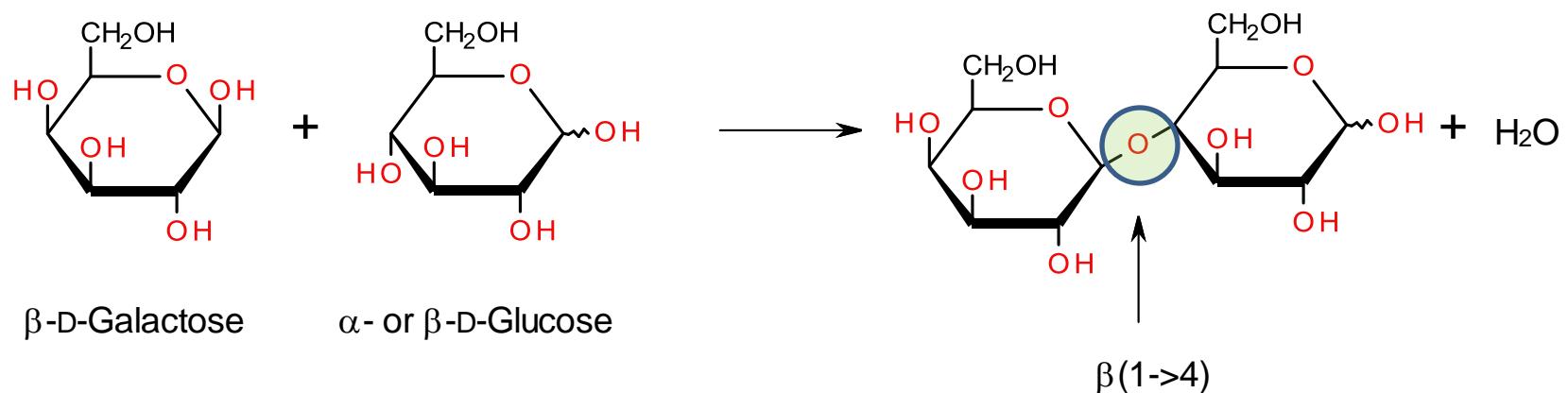


- Cellobiose is also a reducing sugar, but the human body lacks the enzyme required to break it down into glucose, so cellobiose can't be digested.

Disaccharides

Lactose

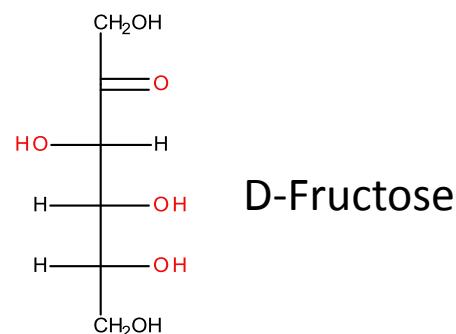
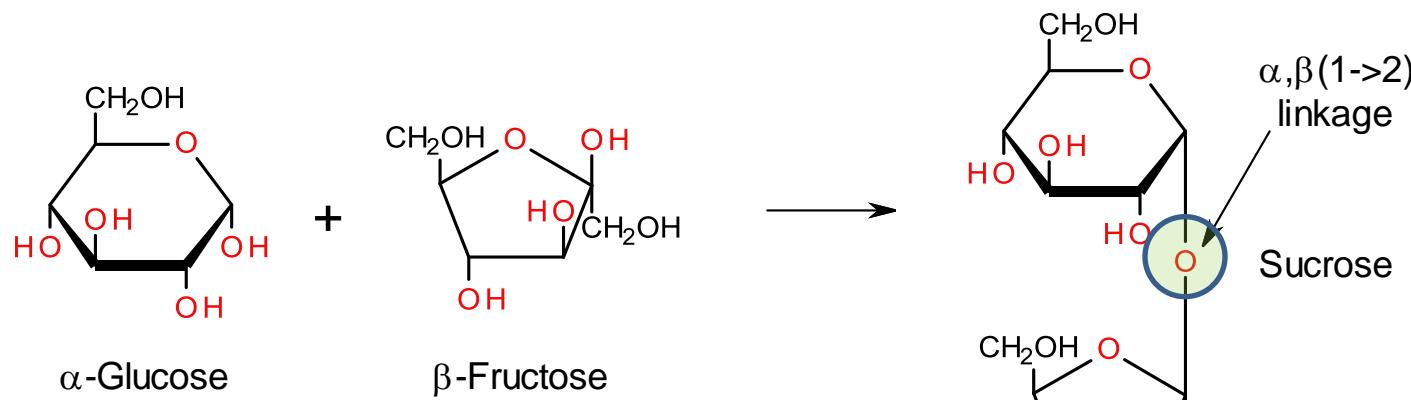
- In lactose, a β -D-galactose unit and a D-glucose unit are joined through a $\beta(1 \rightarrow 4)$ glycosidic linkage.



Disaccharides

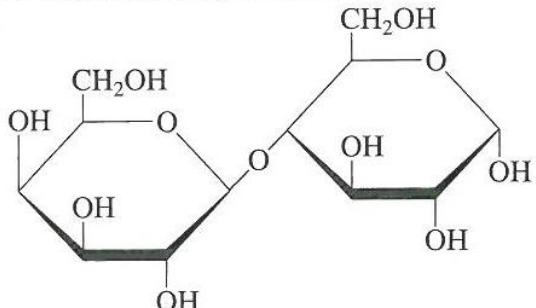
Sucrose

- Sucrose is the most abundant of all disaccharides, and is formed through a combination of D-glucose and D-fructose in a $\alpha,\beta(1\rightarrow2)$ glycosidic linkage:

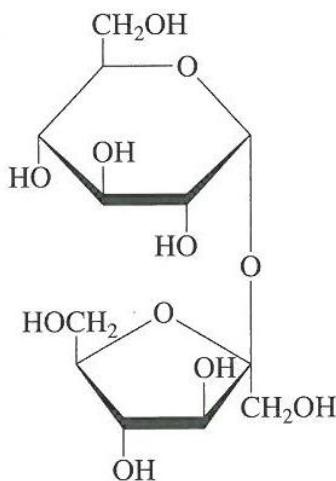


18.98 What type of glycosidic linkage [$\alpha(1 \rightarrow 4)$, etc.] is present in each of the following disaccharides?

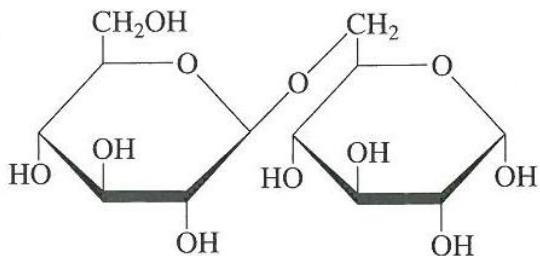
a.



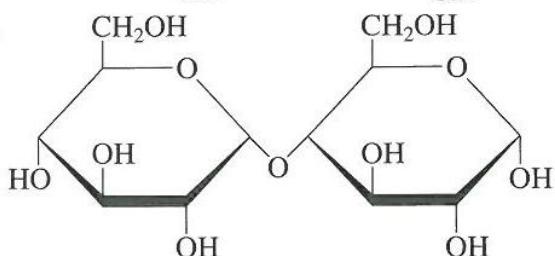
b.



c.



d.



Of these disaccharides, which are reducing sugars?