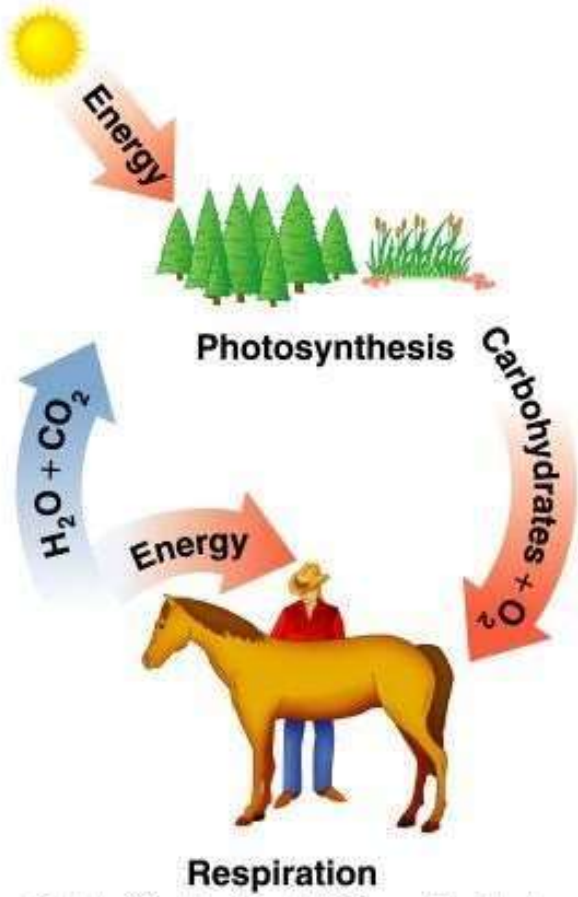
SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES
Sathy Main Road, SNS Kalvi Nagar,
Saravanampatti Post, Coimbatore - 641 035,
Tamil Nadu.

Chemistry of carbohydrates

Introduction

- Carbohydrates (or saccharides) consist of only carbon, hydrogen and oxygen
- Carbohydrates come primarily from plants, however animals can also biosynthesize them
- The "Carbon Cycle" describes the processes by which carbon is recycled on our planet
- Energy from the sun is stored in plants, which use photosynthesis to convert carbon dioxide and water to glucose and oxygen
- In the reverse process, energy is produced when animals oxidize glucose during respiration

Carbon cycle



Timberlake, *General, Organic, and Biological Chemistry.* Copyright © Pearson Education Inc., publishing as Benjamin Cummings

Definition

- Carbohydrates – poly hydroxy aldehydes or poly hydroxy-ketones of formula $(CH_2O)_n$, or compounds that can be hydrolyzed to them.

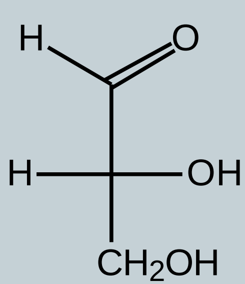
Classification of Monosaccharides

- Monosaccharides have 3-8 carbons in a chain, with one carbon in a carbonyl group, and the other carbons attached to c groups

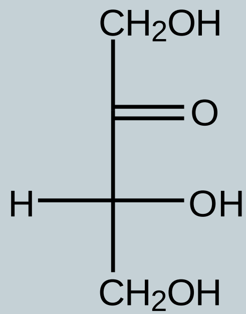
  - An **aldose** has the carbonyl C_1 (an aldehyde)

  - A **ketose** has the carbonyl on C_2 (a ketone)

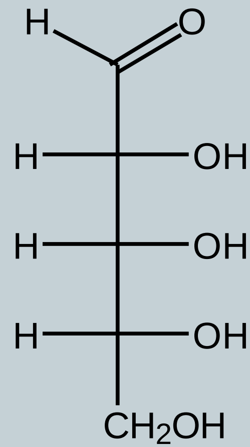
  -The number of carbons is indicated as follows: triose (3 C's), tetrose (4 C's), pentose (5 C's), hexose (6 C's)



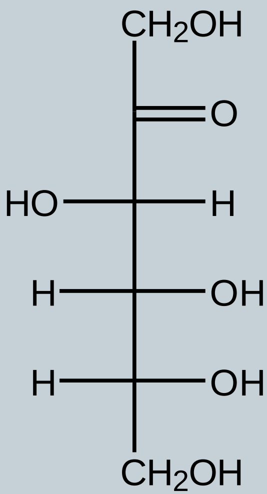
Glyceraldehyde
(aldotriose)



Erythrulose
(ketotetrose)



Ribose
(aldopentose)



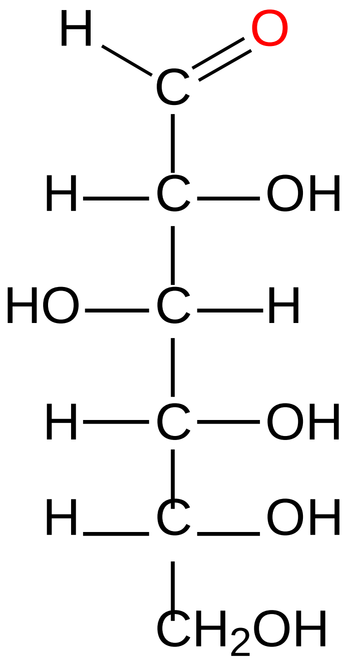
Fructose
(ketohexose)

Types of carbohydrates

- Monosaccharides – carbohydrates that cannot be hydrolyzed to simpler carbohydrates; eg. Glucose or fructose.
- Disaccharides – carbohydrates that can be hydrolyzed into **two** monosaccharide units; eg. Sucrose, which is hydrolyzed into glucose and fructose.
- Oligosaccharides – carbohydrates that can be hydrolyzed into a few monosaccharide units.
- Polysaccharides – carbohydrates that are polymeric sugars; eg Starch or cellulose.

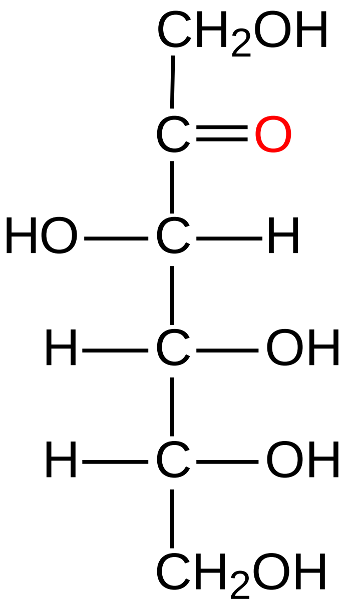
Aldoses and ketoses

Aldoses (e.g., glucose) have an aldehyde group at one end.



D-glucose

Ketoses (e.g., fructose) have a keto group, usually at C2.



D-fructose

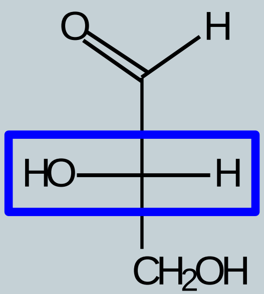
Monosaccharides

- Monosaccharides are classified by their number of carbon atoms

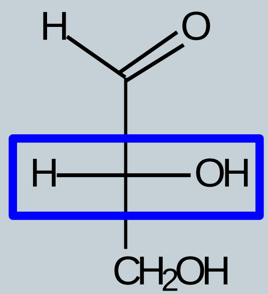
Name	Formula
Trios e	$C_3H_6O_3$
Tetros e	$C_4H_8O_4$
Pentose	$C_5H_{10}O_5$
Hexose	$C_6H_{12}O_6$
Heptose	$C_7H_{14}O_7$
Octose	$C_8H_{16}O_8$

D and L Sugars and Fischer Projections

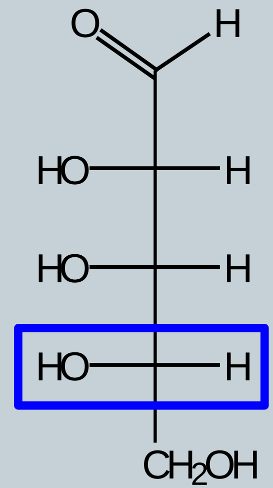
- Monosaccharides are chiral compounds (have stereoisomers)
  - Each monosaccharide has two enantiomeric forms
- The D and L classifications are based on glyceraldehyde
  - Each enantiomer refracts plane-polarized light in equal magnitude but opposite direction
  - In glyceraldehyde, L rotates light to the left and D to the right (however, this is not true for all sugars)
- L-glyceraldehyde has the hydroxyl group on the left, and D-glyceraldehyde has the hydroxyl group on the right
- **Fischer projection:** a two dimensional representation for showing the configuration of tetrahedral stereo centers



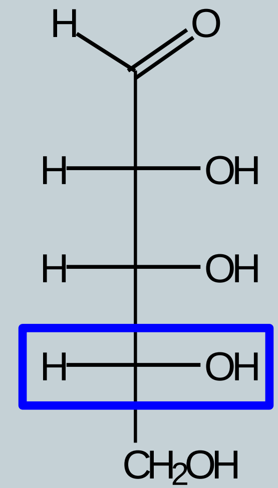
L-Glyceraldehyde



D-Glyceraldehyde



L-Ribose

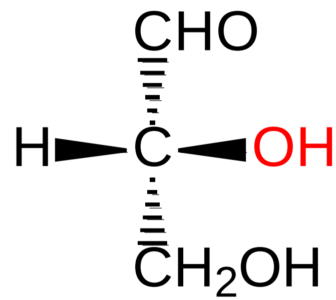


D-Ribose

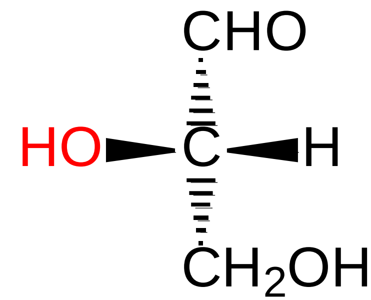
D vs L Designation

D & L designations are based on the configuration about the single asymmetric C in glyceraldehyde.

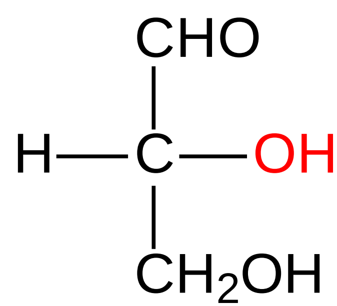
The lower representations are Fischer Projections.



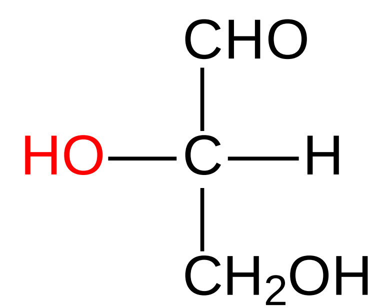
D-glyceraldehyde



L-glyceraldehyde



D-glyceraldehyde

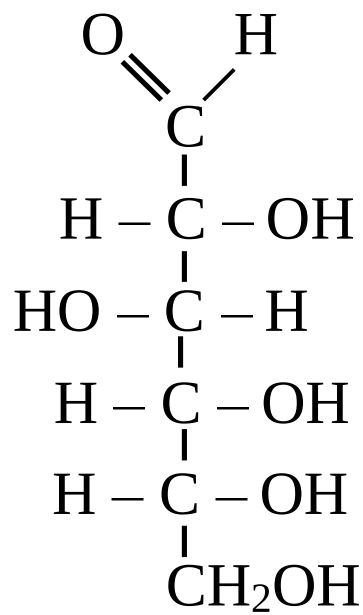


L-glyceraldehyde

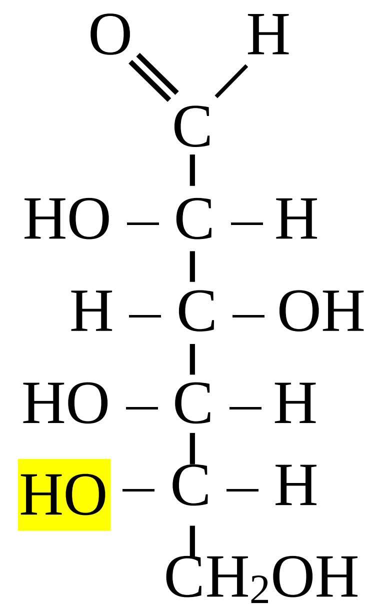
Sugar Nomenclature

For sugars with more than one chiral center, **D** or **L** refers to the asymmetric **C** farthest from the aldehyde or keto group.

Most naturally occurring sugars are D isomers.

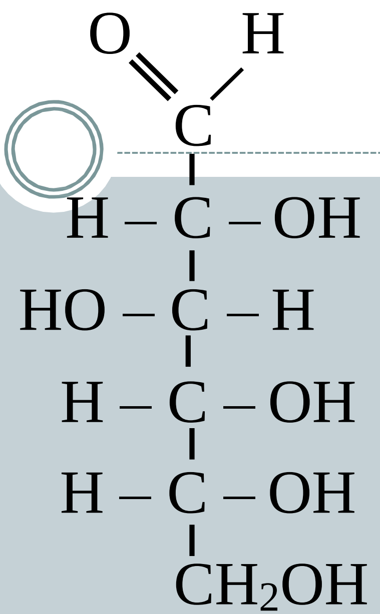


D-glucose

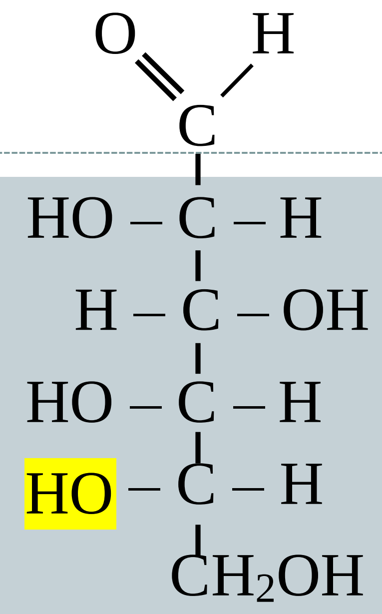


L-glucose

D & L sugars are mirror images of one another.



D-glucose



L-glucose

The number of stereoisomers is 2^n, where n is the number of asymmetric centers.

The 6-C aldoses have 4 asymmetric centers. Thus there are 16 stereoisomers (8 D-sugars and 8 L-sugars).

Three Important Monosaccharides

- **D-Glucose** is the most common monosaccharide

  - Primary fuel for our cells, required for many tissues

  - Main sources are fruits, vegetables, corn syrup and honey

  - Blood glucose is maintained within a fairly small range

  - Some glucose is stored as glycogen, excess is stored as fat

- **D-Galactose** comes from hydrolysis of the disaccharide lactose

  - Used in cell membranes of central nervous system

  -Converted by an enzyme into glucose for respiration (lack of this enzyme causes *galactosemia,* which can cause retardation in infants if not treated by complete removal from diet)

- **D-Fructose** is the sweetest carbohydrate

  - Converted by an enzyme into glucose for respiration

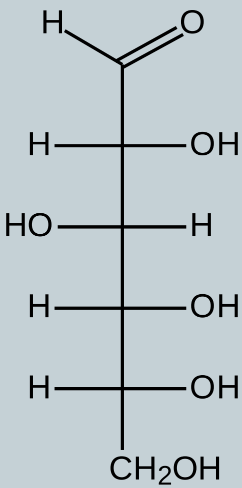
  - Main sources are fruits and honey

  - Also obtained from hydrolysis of the disaccharide sucrose

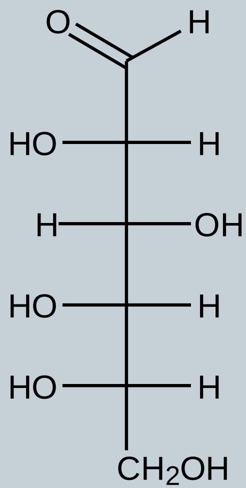
Structures of Glucose, D-Galactose and D-Fructose

- Note that in nature, only the D enantiomers of sugars are used
- What is the relationship between D-glucose and L-glucose?
- What is the relationship between D-glucose and D-galactose?
- What is the relationship between D-glucose and D-fructose?

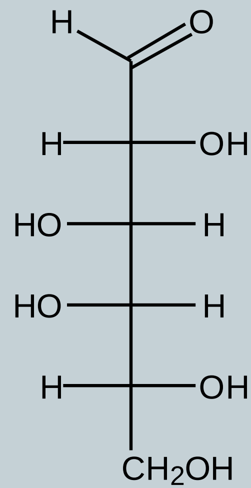
(enantiomers, diastereomers and constitutional isomers)



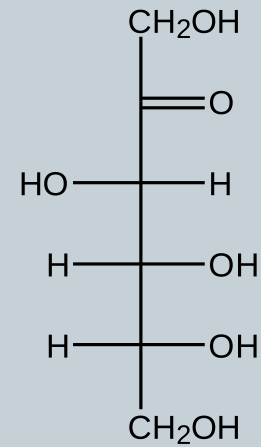
D-Glucose



L-Glucose



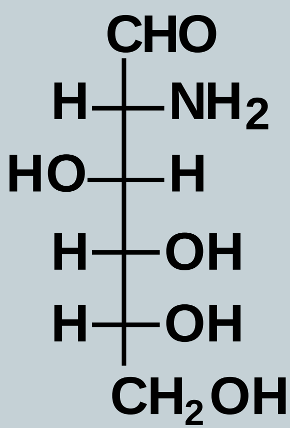
D-Galactose



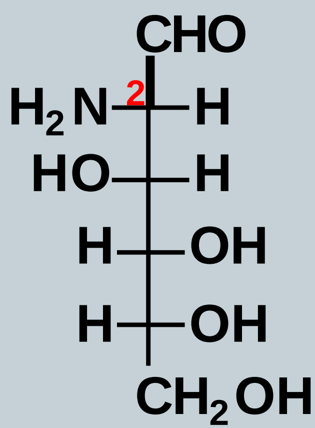
D-Fructose

Amino Sugars

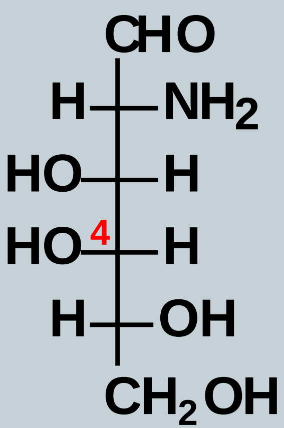
- Amino sugars contain an $-NH_2$ group in place of an -OH group
  - only three amino sugars are common in nature: D-glucosamine, D-mannosamine, and D-galactosamine



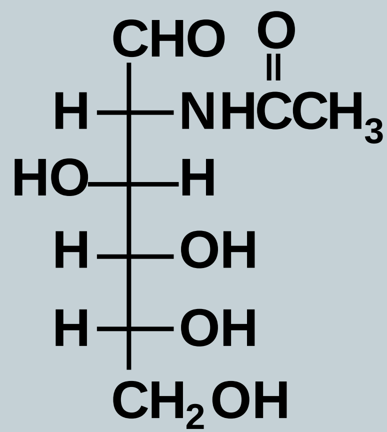
D-Glucosamine



D-Mannosamine (C-2 stereoisomer of D-glucosamine



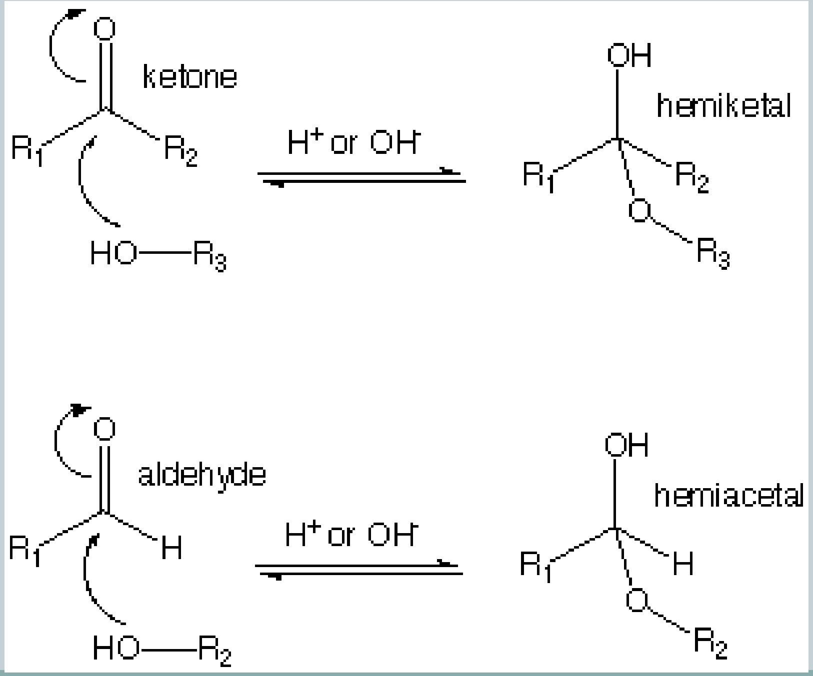
D-Galactosamine (C-4 stereoisomer of D-glucosamine)



N-Acetyl-D-glucosamine

Hemi acetal formation

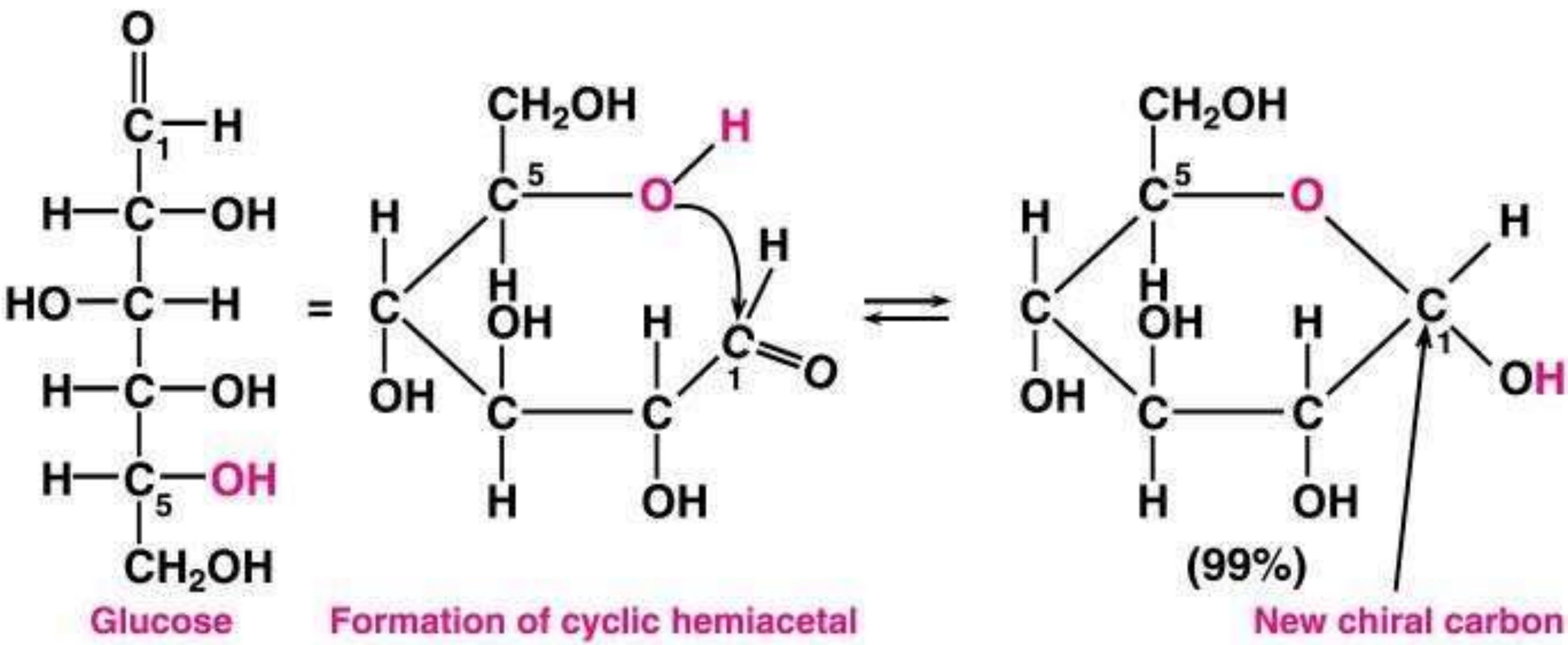
- Aldehydes and ketones react with Alcohol to give adducts called **hemi acetals** (*hemi*, Greek, half).
- These hemi acetals are intermediates on the way to acetals.
- Both acids and bases catalyze this process.



Cyclic Structures of Monosaccharides

- If the alcohol and aldehyde or ketone are in the same molecule, a cyclic hemiacetal is formed
- Monosaccharides in solution are in **equilibrium between the open-chain and ring forms**, and exist primarily in the ring form

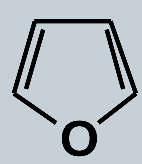
  (Why does the 6-membered ring form, instead of a smaller one?)



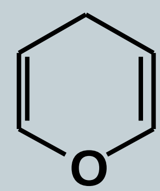
O
C
1
H
H
C
OH
HO
C
H
H
C
OH
H
C
5
OH
CH2OH
=
CH2OH
5
O
H
H
H
C
H
OH
H
C
1
O
OH
C
C
H
OH
CH2OH
5
O
H
H
H
C
1
OH
OH
H
OH
H
OH
(99%)
Glucose
Formation of cyclic hemiacetal
New chiral carbon

Alpha and beta structures

- In the terminology of carbohydrate chemistry,
  - β means that the -OH on the anomeric carbon is on the same side of the ring as the terminal $-CH_2OH$
  - α means that the -OH on the anomeric carbon is on the side of the ring opposite from the terminal $-CH_2OH$
  - a six-membered hemiacetal ring is called a pyranose, and a five-membered hemiacetal ring is called a furanose



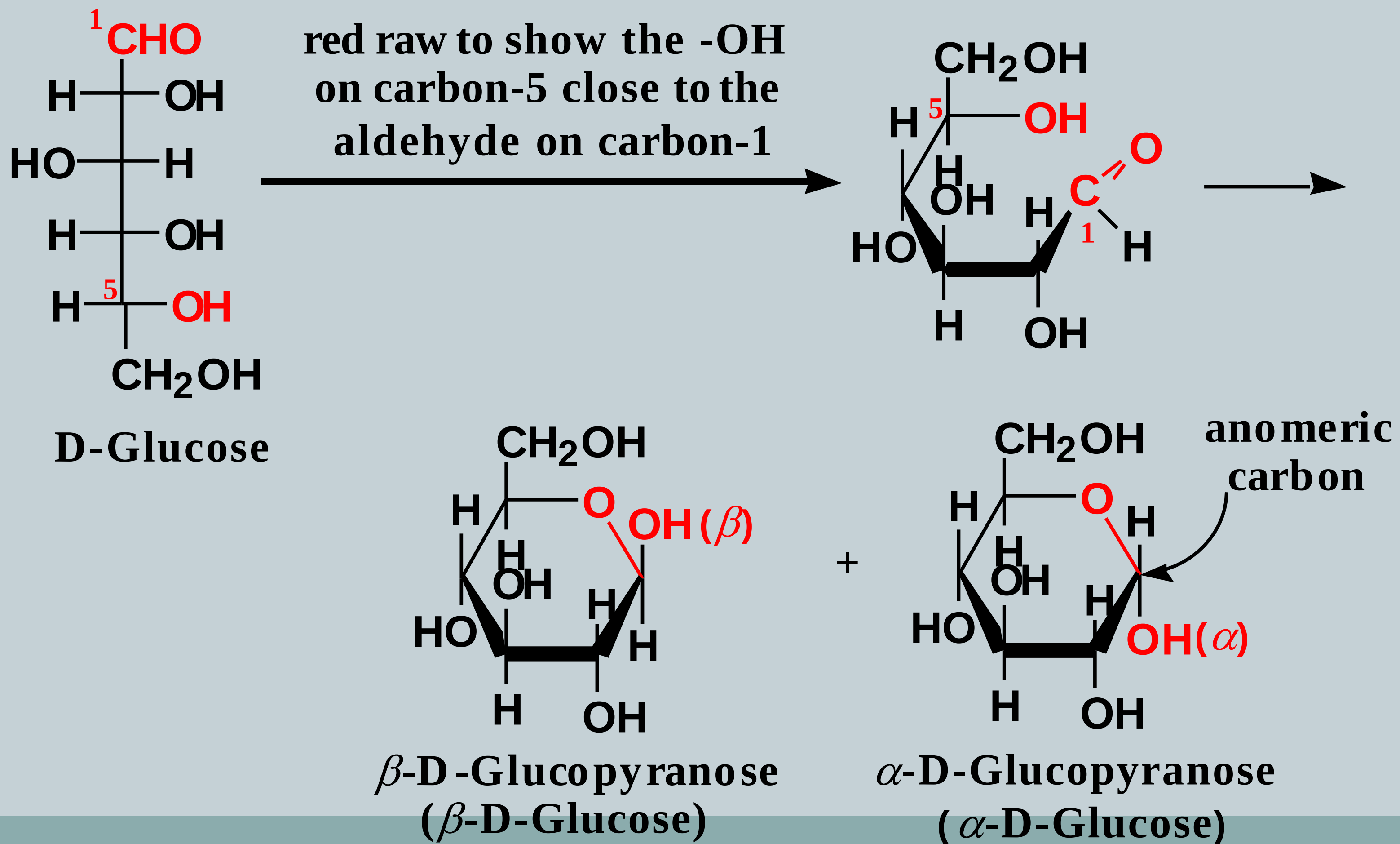
Furan



Pyran

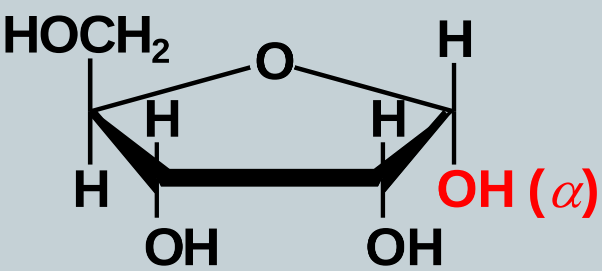
Haworth Projections

- D-Glucose forms these cyclic hemiacetals

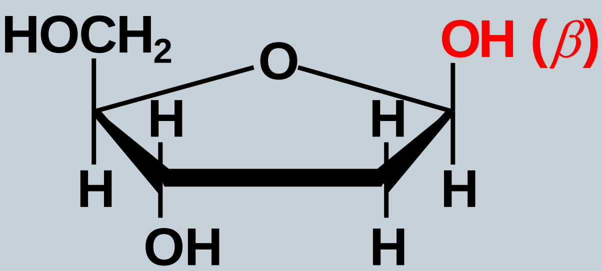


Haworth Projections

- Aldo pentoses also form cyclic hemi acetals
- the most prevalent forms of D-ribose and other pentoses in the biological world are furanoses



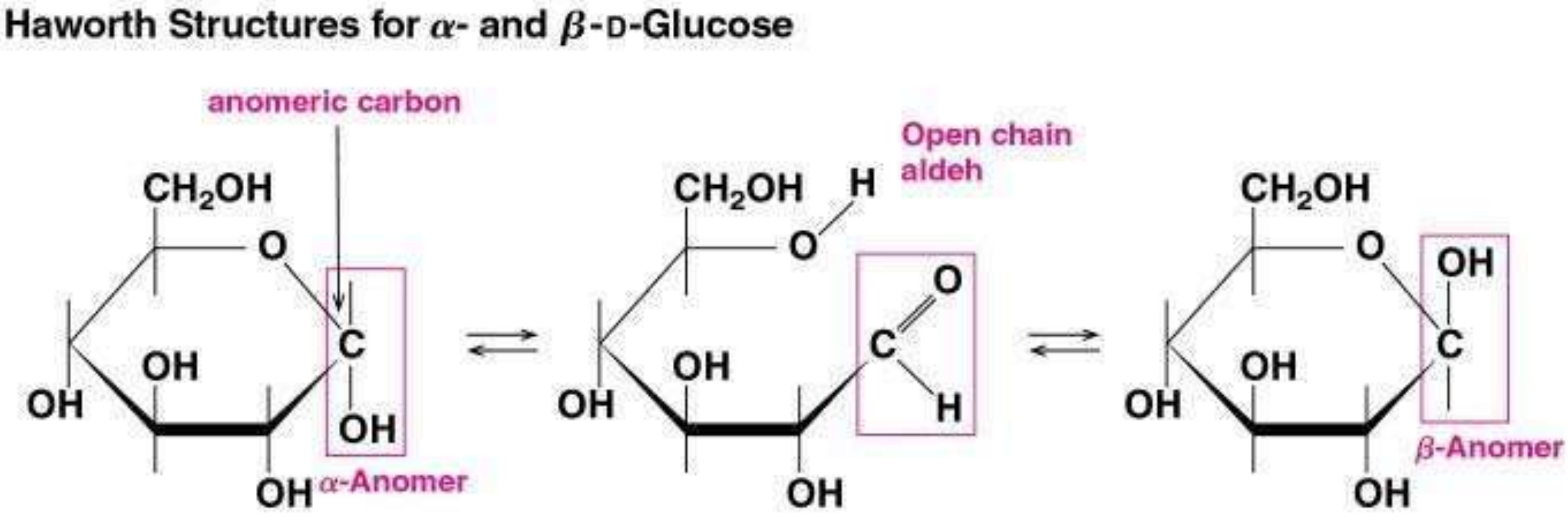
α-D-Ribofuranose
(α-D-Ribose)



β-2-Deoxy-D-ribofuranose
(β-2-Deoxy-D-ribose)

Mutorotation

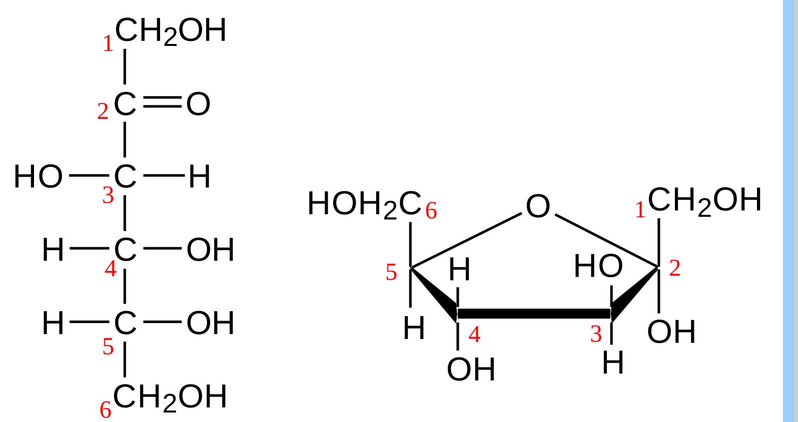
- When in solution, monosaccharides exist in equilibrium between the alpha and beta forms
- Each form is in equilibrium with the open-chain form (the process by which it goes back and forth is called mutorotation)
- Each time the chain closes, it can go to either form, although it turns out that beta forms more often (64% for glucose)



α-D-Glucose (36% in equilibrium mixture)

D-Glucose open-chain (trace)

β-D-Glucose (64% in equilibrium mixture)

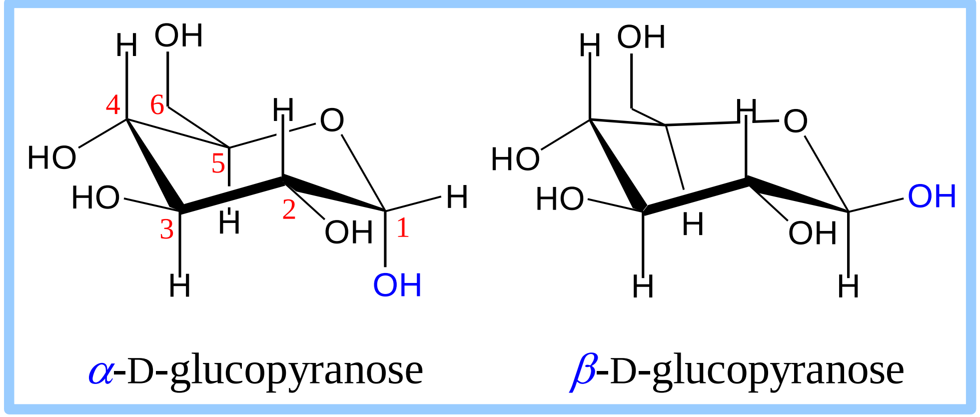


D-fructose (linear) α-D-fructofuranose

Fructose forms either

- a 6-member pyranose ring, by reaction of the C2 keto group with the OH on C6, or
- a 5-member furanose ring, by reaction of the C2 keto group with the OH on C5.

Chair Conformations

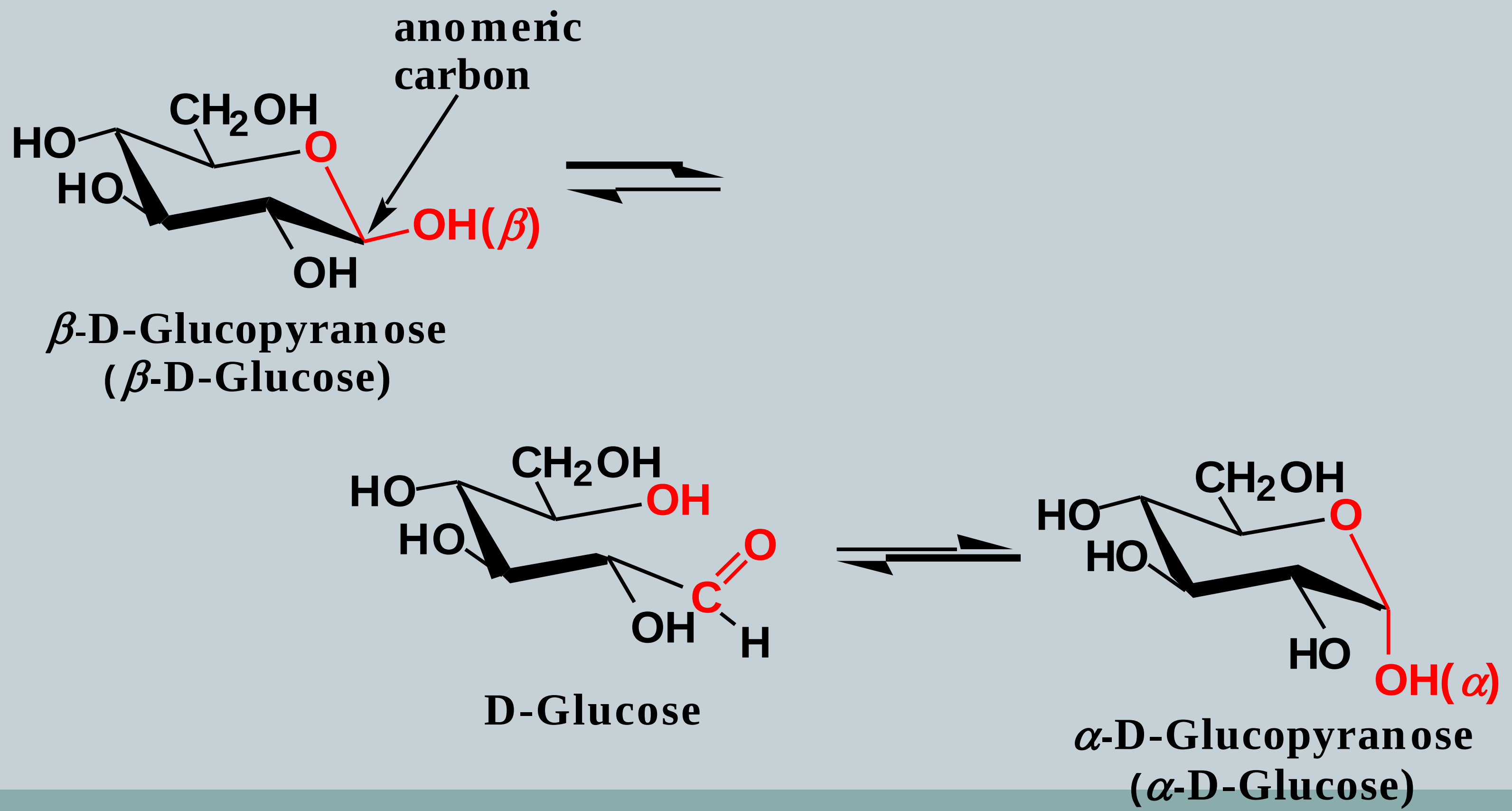


Because of the tetrahedral nature of carbon bonds, pyranose sugars actually assume a "chair" or "boat" configuration, depending on the sugar.

The representation above reflects the chair configuration of the glucopyranose ring more accurately than the Haworth projection.

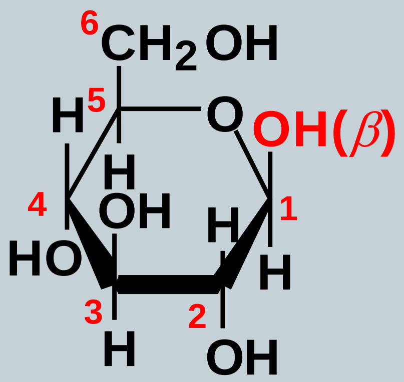
Chair Conformations

- For pyranoses, the six-membered ring is more accurately represented as a **chair conformation**

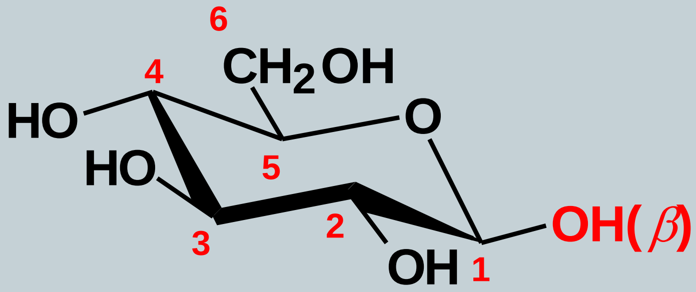


Chair Conformations

- in both a Haworth projection and a chair conformation, the orientations of groups on carbons 1- 5 of *β*-D-glucopyranose are up, down, up, down, and up

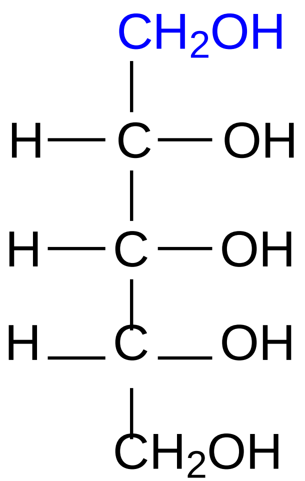


β-D-Glucopyranose (Haworth projection)

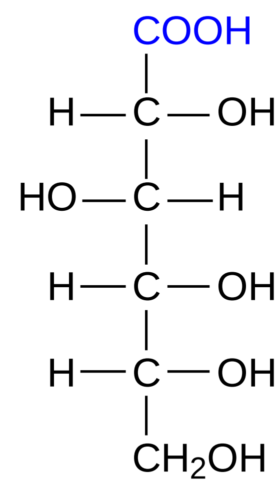


β-D-Glucopyranose (chair conformation)

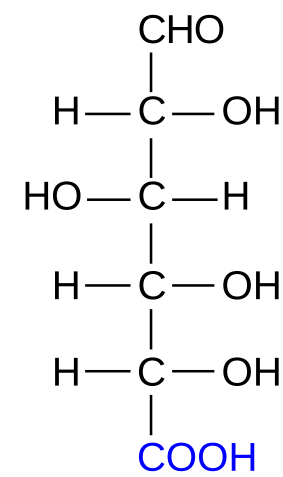
Sugar derivatives



D-ribitol



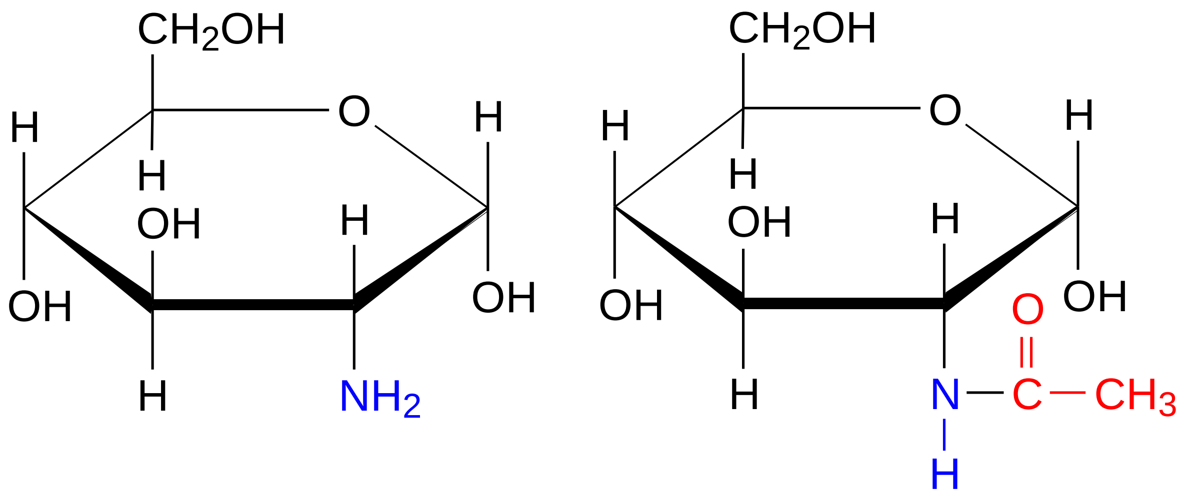
D-gluconic acid



D-glucuronic acid

- sugar alcohol - lacks an aldehyde or ketone; e.g., ribitol.
- sugar acid - the aldehyde at C1, or OH at C6, is oxidized to a carboxylic acid; e.g., gluconic acid, glucuronic acid.

Sugar derivatives

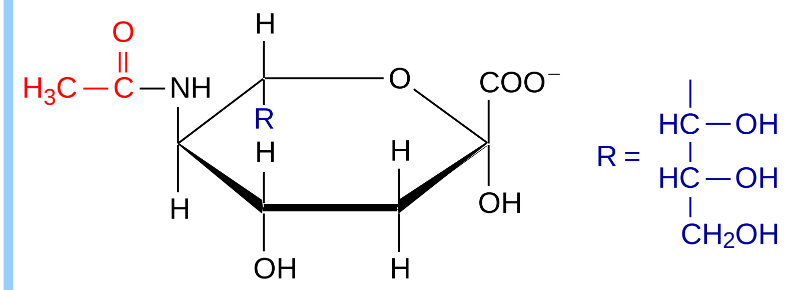


α-D-glucosamine

α-D-*N*-acetylglucosamine

amino sugar - an amino group substitutes for a hydroxyl. An example is glucosamine.

The amino group may be acetylated, as in *N*-acetylglucosamine.



N-acetylneuraminate (sialic acid)

N-acetylneuraminate (N-acetylneuraminic acid, also called sialic acid) is often found as a terminal residue of oligosaccharide chains of glycoproteins.

Sialic acid imparts negative charge to glycoproteins, because its carboxyl group tends to dissociate a proton at physiological pH, as shown here.

Identification tests

Reducing sugar – a carbohydrate that is oxidized by Tollen's, Fehling's or Benedict's solution.

Tollen's: Ag^{+} → Ag (silver mirror)

Fehling's or Benedict's: Cu^{2+} (blue) → Cu^{1+} (red ppt)

These are reactions of aldehydes and alpha-hydroxyketones.

All monosaccharides (both aldoses and ketoses) and **most*** **disaccharides** are reducing sugars.

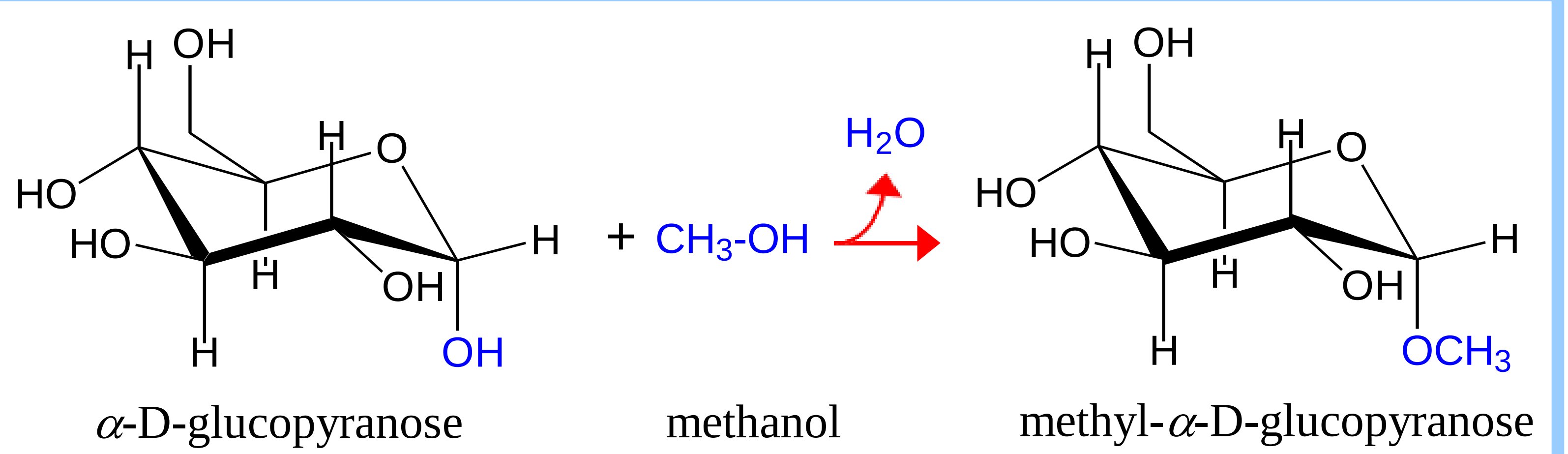
*Sucrose (table sugar), a disaccharide, is not a reducing sugar.

Glycosidic Bonds

The anomeric hydroxyl and a hydroxyl of another sugar or some other compound can join together, splitting out water to form a glycosidic bond:

R-OH + HO-R' → R-O-R' + H_2O

E.g., methanol reacts with the anomeric OH on glucose to form methyl glucoside (methyl-glucopyranose).



Disaccharides

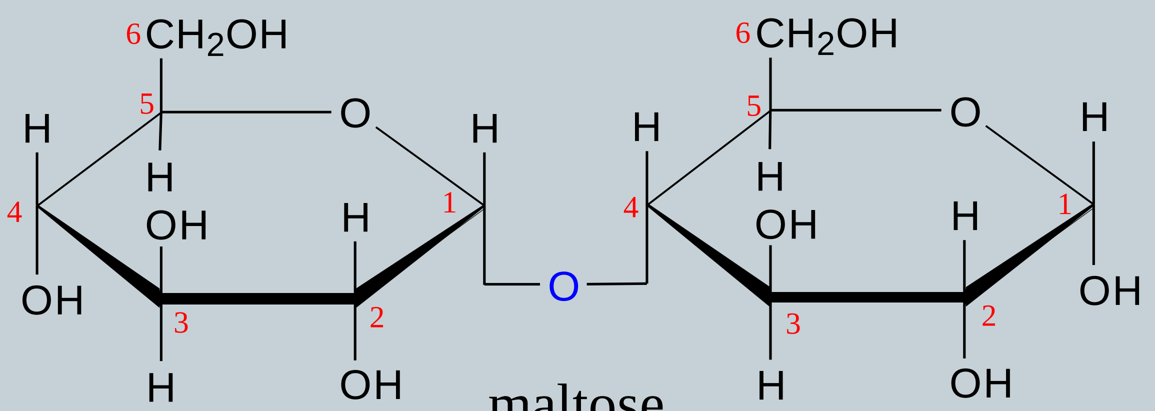
- Two monosaccharide units are linked by a glycosidic bond through hydroxyl groups

- Three most popular disaccharides
- Maltose, Lactose , Sucrose

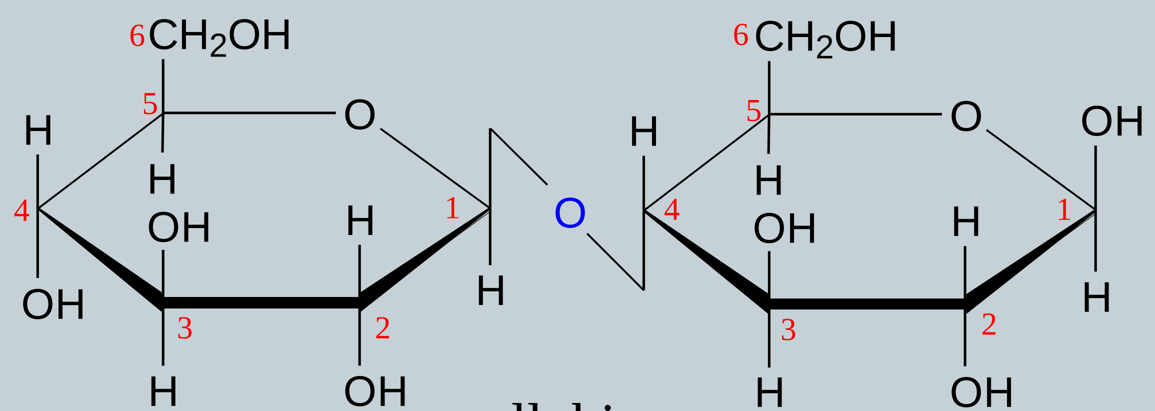
Maltose

- **Maltose**, a cleavage product of starch (e.g., amylose), is a disaccharide with an $\alpha(1 \rightarrow 4)$ glycosidic link between C1 - C4 OH of 2 glucoses.
- It is the α anomer (C1 O points down).

- **Cellobiose**, a product of cellulose breakdown, is the otherwise equivalent β anomer (O on C1 points up).
- The $\beta(1 \rightarrow 4)$ glycosidic linkage is represented as a zig-zag, but one glucose is actually **flipped over** relative to the other.

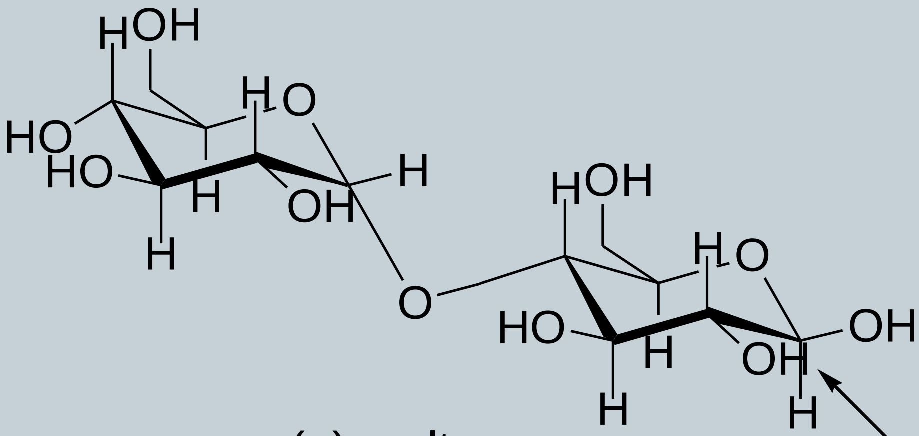


maltose



cellobiose

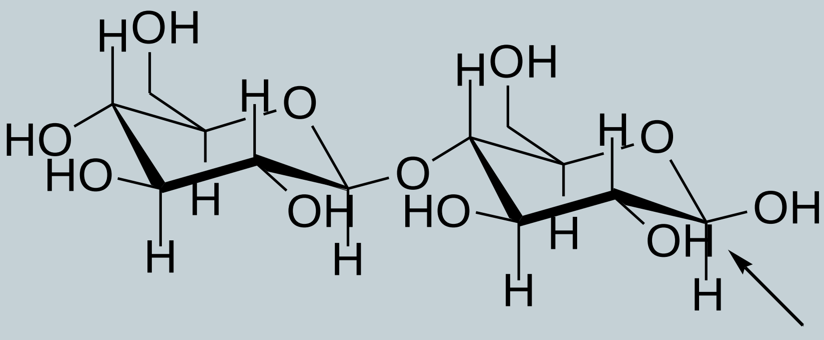
- Maltose can also undergo mutarotation because it has a free anomeric hydroxyl group
- So, it will show reducing properties and can be identified using Tollen’s or Fehling’s solution



two glucose units
alpha C-1 to C-4

(+)-maltose

reducing sugar



two glucose units
beta C-1 to C-4

reducing sugar

(+)-cellobiose

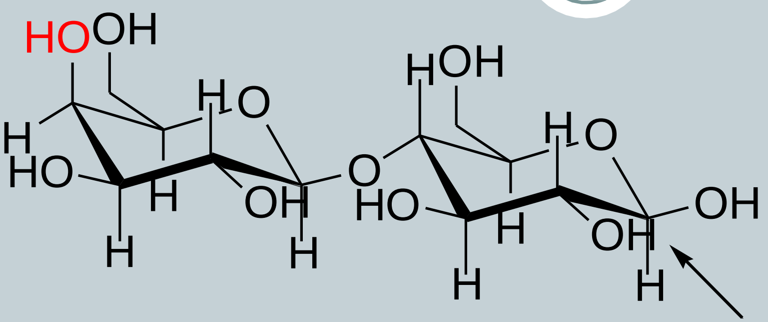
Sucrose

- Common table sugar, has a glycosidic bond linking the anomeric hydroxyls of glucose & fructose.

- Because the configuration at the anomeric C of glucose is α (O points down from ring), the linkage is $\alpha(1\rightarrow2)$.
- The full name of sucrose is α-D-glucopyranosyl-$(1\rightarrow2)$-β-D-fructopyranose.)

Lactose

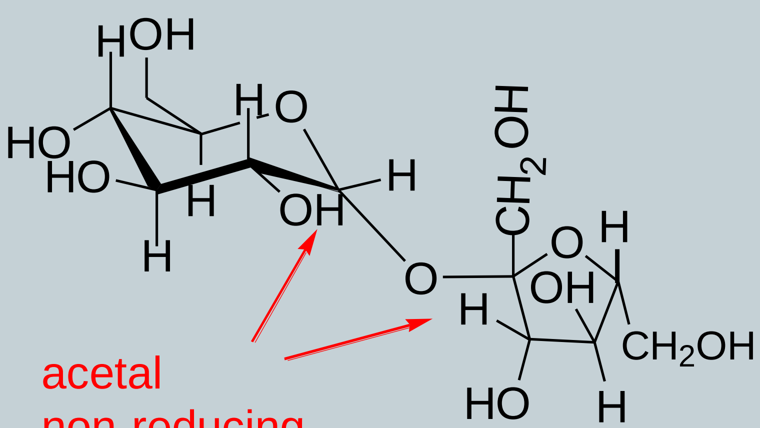
- **Lactose**, milk sugar, is composed of galactose & glucose, with $\beta(1\rightarrow 4)$ linkage from the anomeric OH of galactose.
- Its full name is β-D-galactopyranosyl-$(1\rightarrow 4)$-α-D-glucopyranose



galactose beta C-1
to C-4 glucose

(+)-lactose

reducing sugar



glucose alpha C-1
to beta C1 fructose

acetal
non-reducing

(+)-sucrose

Lactose intolerance

- Usually, lactation period of mammals can be extended up to maximum of four years
- After that, they will stop producing lactose digesting enzymes
- But humans have developed the ability to digest lactose genetically over the time during evolution, into a certain extent
- However, around 25% of human population is unable to digest lactose completely due to genetic reasons
- Most of others experience certain levels of lactose intolerance when consumed in high quantities

- If, more lactose is consumed than can be digested
  - lactose molecules attract water
    - cause floating, abdominal discomfort, diarrhea
  - intestinal bacteria feed on undigested lactose
    - produce acid and gas