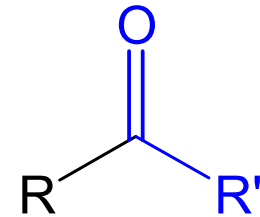
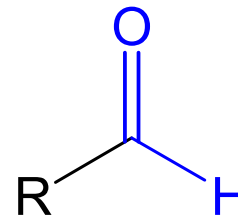
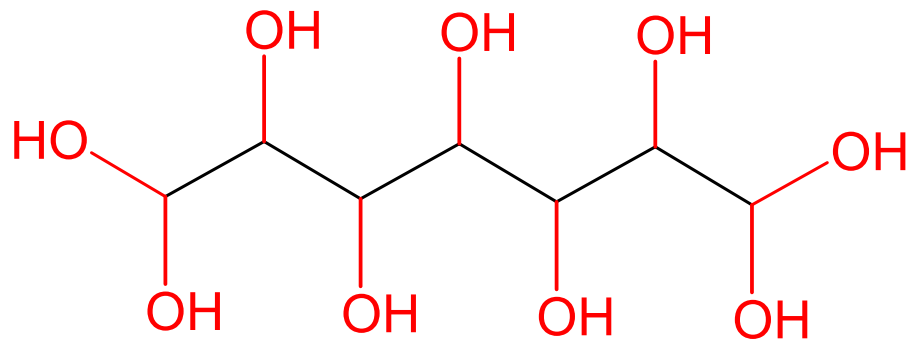


# Poly(Saccharides)

What is a saccharide (mono vs. di vs. poly), ether linkage, sugar,

# Carbohydrate Structures

- All common carbohydrates have the generic form  $C(H_2O)_n$  with  $n \geq 4$
- “hydrates of carbon”
- Polyhydroxy aldehydes or polyhydroxy ketones

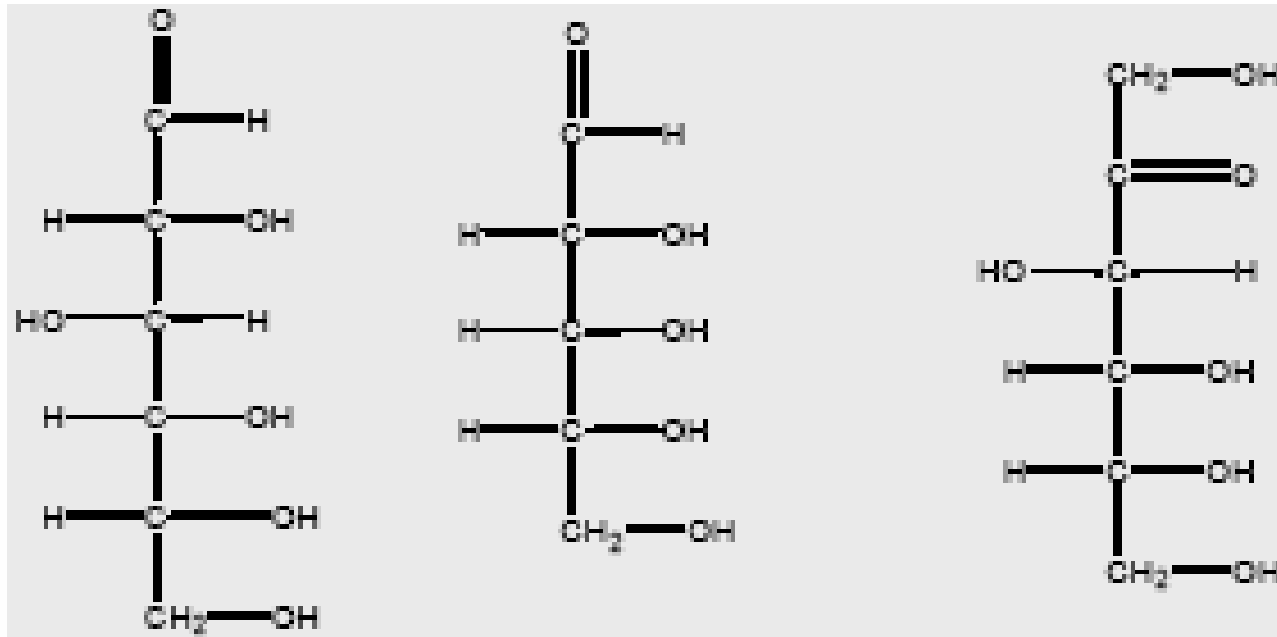


# Carbohydrates

- Most abundant organic constituents of plants-cellulose
- Important source of chemical energy for living organisms-sugar and starch
- In plants and animals important constituents for supporting tissues-chitin, wood, cotton and flax.

# Monosaccharide

- **Monosaccharide - a simple carbohydrate most commonly consisting of three to six carbon atoms.**
- Glucose, Ribose and Fructose are examples

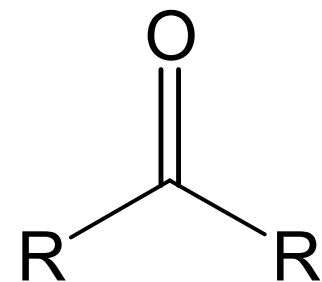
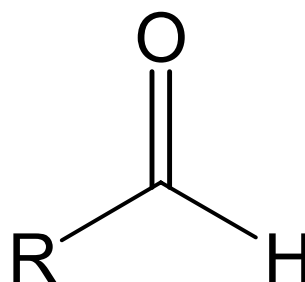


# Classification of Monosaccharides

- 1) The number of carbon atoms present in the molecule
- 2) Whether they contain an aldehyde or ketone group
- 3) Sucrose-ordinary table sugar
- 4) Fructose-sugar in fruit and honey
- 5) Glucose-primary sugar in blood
- 6) Maltose-malt sugar

# Naming - General

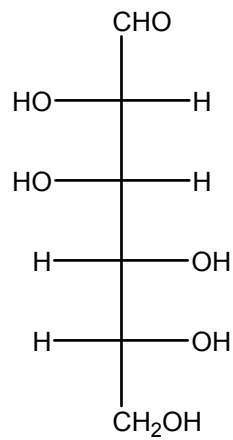
- Carbohydrates can be aldoses or ketoses.
- R is the polyhydroxy part.
- If it has an aldehyde then the prefix is aldo-
- If it has a ketone then the prefix is keto-
- All sugars end in -ose.



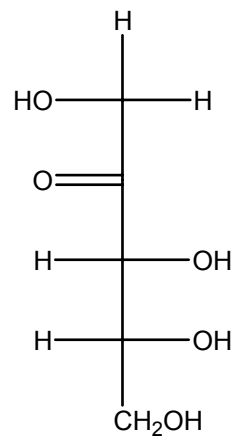
# Classes of sugars

| # of Cs  |         | aldehyde    | ketone      |
|----------|---------|-------------|-------------|
| <b>3</b> | triose  | aldotriose  | ketotriose  |
| <b>4</b> | tetrose | aldotetrose | ketotetrose |
| <b>5</b> | pentose | aldopentose | ketopentose |
| <b>6</b> | hexose  | aldohexose  | ketoheptose |
| <b>7</b> | heptose | aldoheptose | ketoheptose |

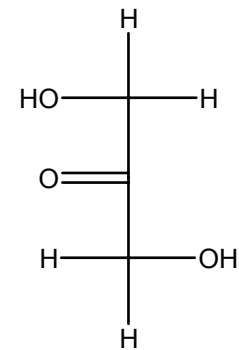
# Name that sugar!



An aldohexose  
Actually Mannose



A ketopentose



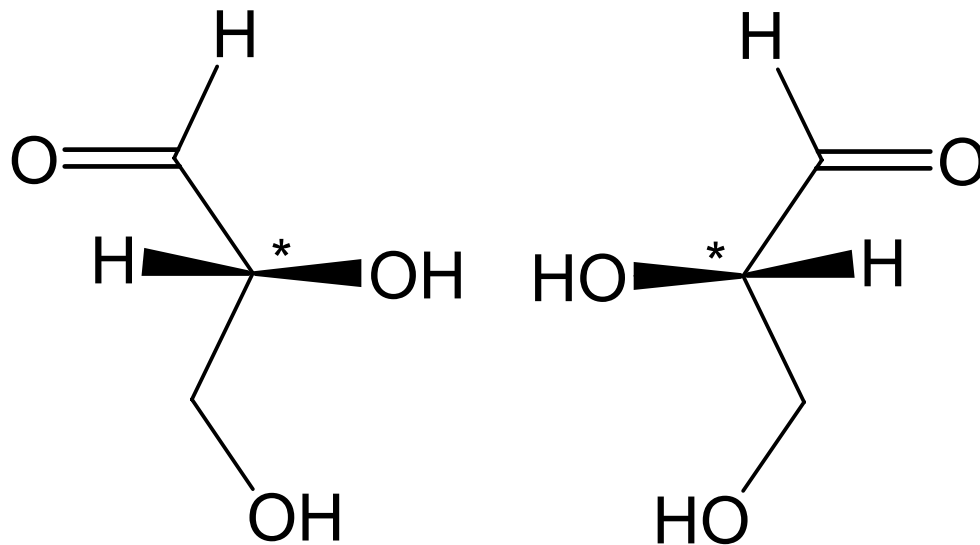
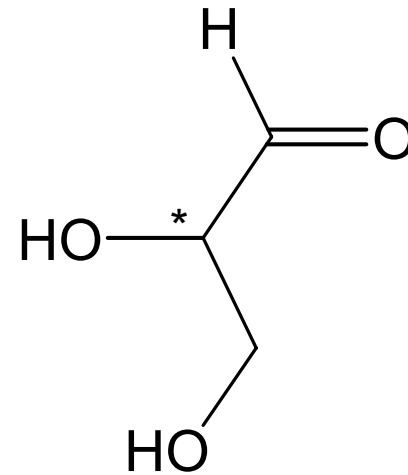
A ketotriose

# Saccharides

- Saccharides with the same structural formula can differ because they form different isomers
  - Aldo-ketal forms
  - Stereochemistry
  - Linear and ring forms (for  $n > 5$ )
    - common saccharides are  $n=5$  (furanose) and  $n=6$  (pyranose) rings
  - Anomeric forms
  - Chair and boat forms

# Simplest monosaccharide

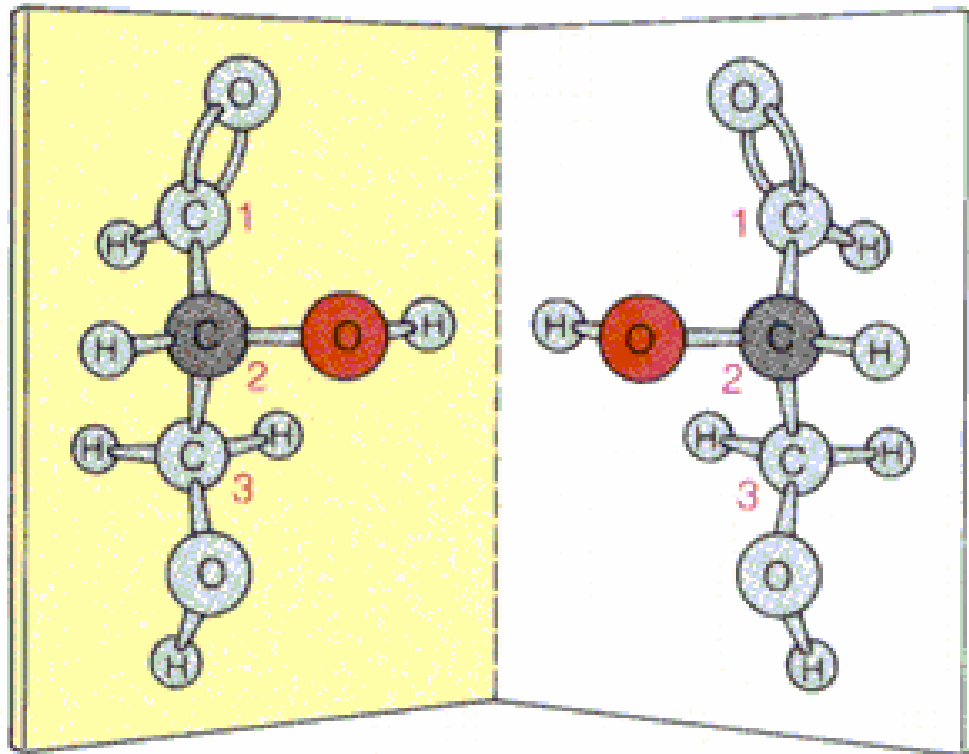
- Glyceraldehyde- an aldotriose



(R)-(+)-glyceraldehyde

(S)-(-)-glyceraldehyde  
© Caroline L. Schauer

# D- and L-glyceraldehyde



D-Glyceraldehyde

L-Glyceraldehyde

From [Matthews, van Holde, Ahern](#)  
"Biochemistry" © Caroline L. Schauer

- The designation 'D-' or 'L-' is old nomenclature but still used widely in biochemistry
- It originally described whether the compound rotated a plane of polarised light to the right (D for dextro) or left (L for left)

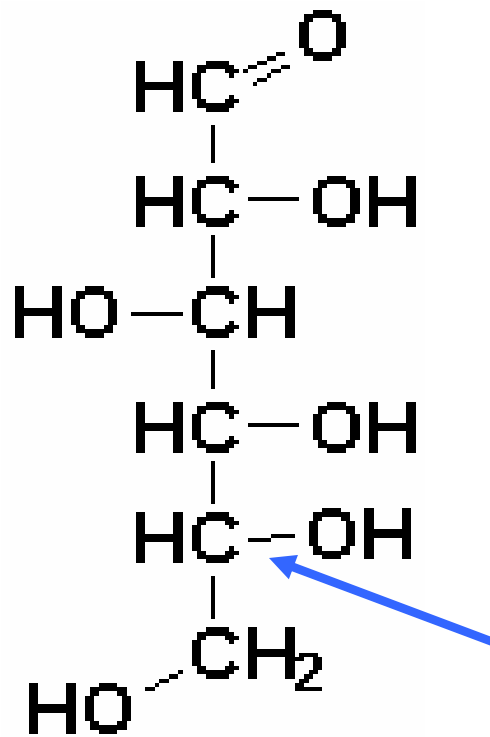
# Just to make things more confusing

- M. A. Rosanoff of NYU in 1906 determined
- (+)-glyceraldehyde is actually D-(+)-glyceraldehyde
- (-)-glyceraldehyde is actually L-(-)-glyceraldehyde
- This designation sets the configuration standards for all monosaccharides
- If the penultimate carbon is similar to D-(+)-glyceraldehyde then it gets the D designation same for L

# Fischer projections

- German chemist Emil Fischer (1852-1919) identified the stereoisomers for the aldohexoses in 1894.
- He received the 1902 Nobel Prize for chemistry for his work
- **Remember** this is only 12 years after the proposal of van't Hoff that carbon is tetrahedral
- Fischer's work was proven unequivocally by Bijvoet's absolute configuration determination in 1951

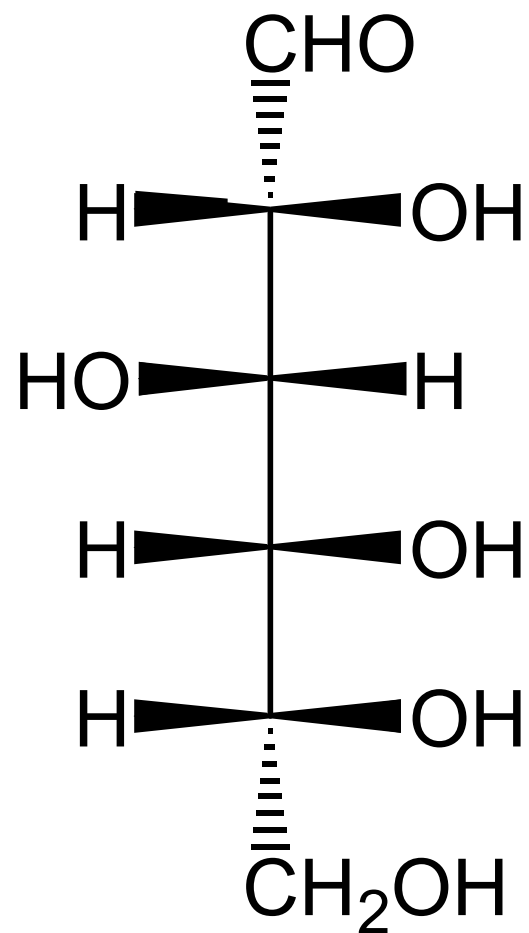
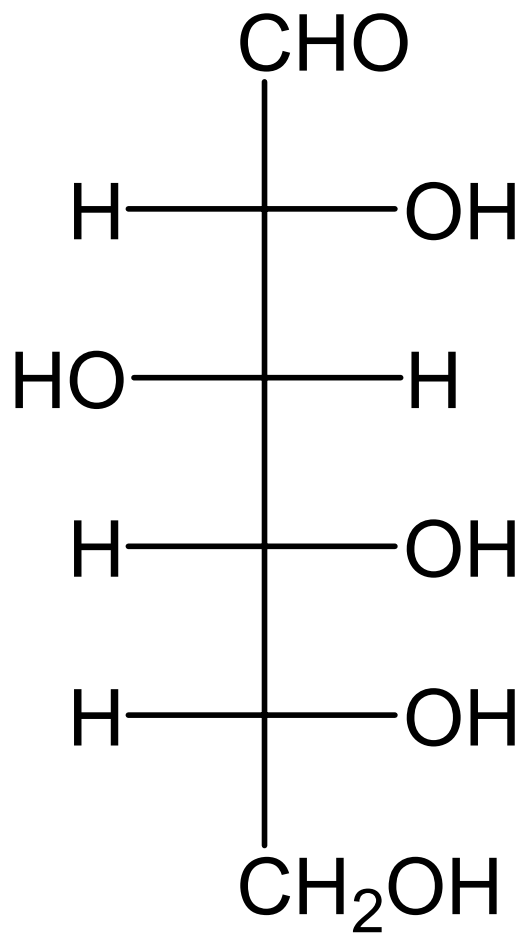
# Fischer Projections

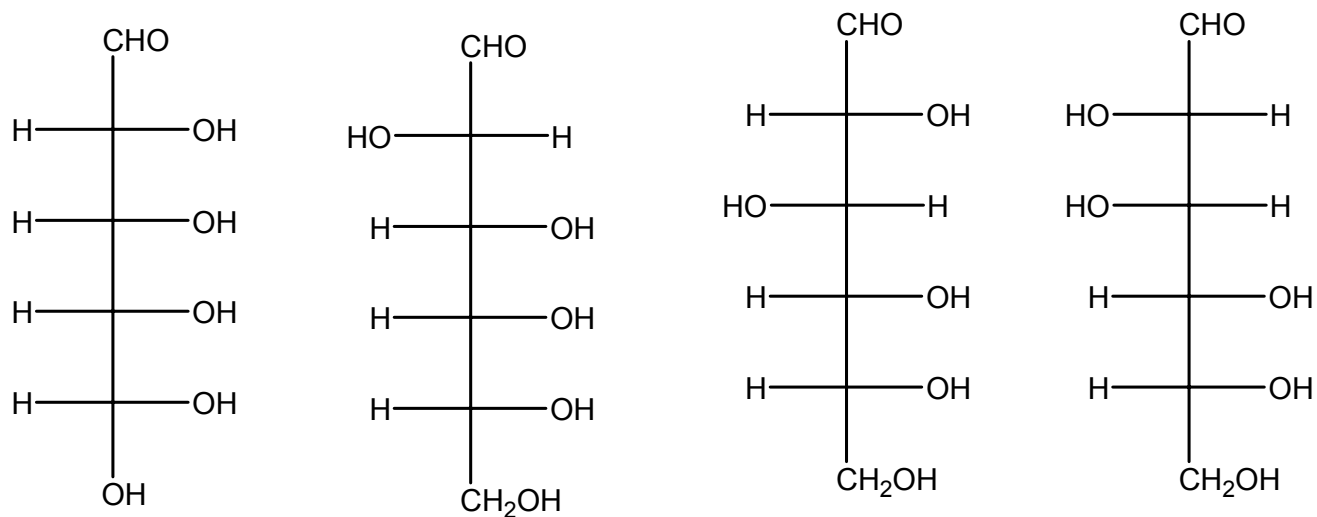


**Glucose**

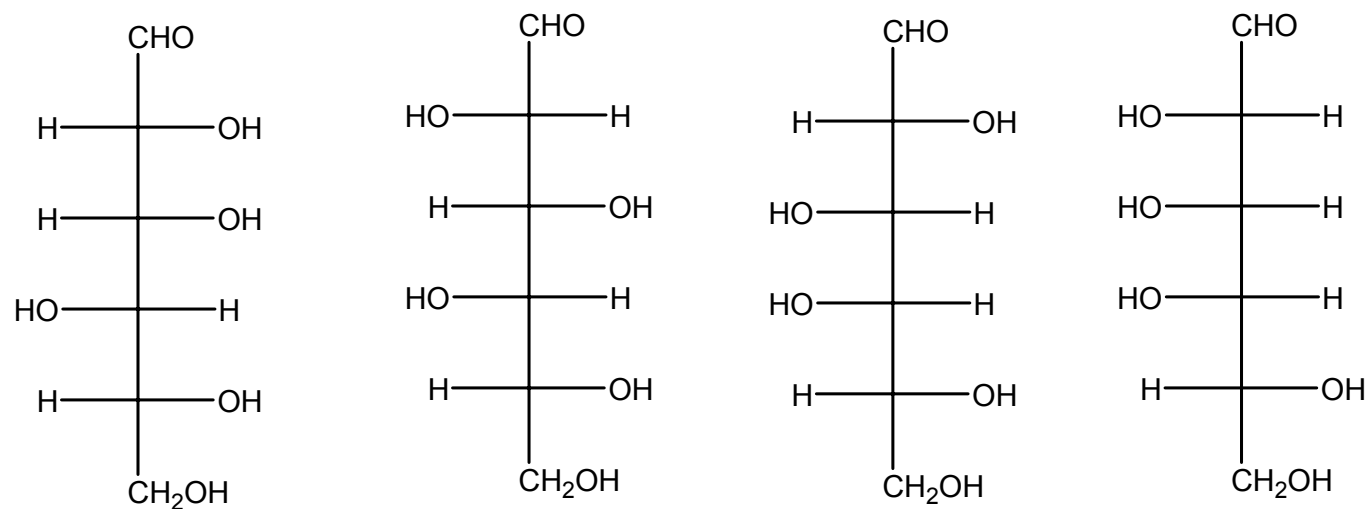
- Projections of monosaccharides are oriented with the carbonyl group at the top; the chiral carbon farthest from the carbonyl group is drawn with its hydroxyl to the right for the D form and to the left for the L form
- Chiral carbon, D-form
- This is D-glucose!

# Projections to 3-D





D-Allose D-Altrose D-Glucose D-Mannose



D-Gulose D-Idose D-Galactose D-Talose

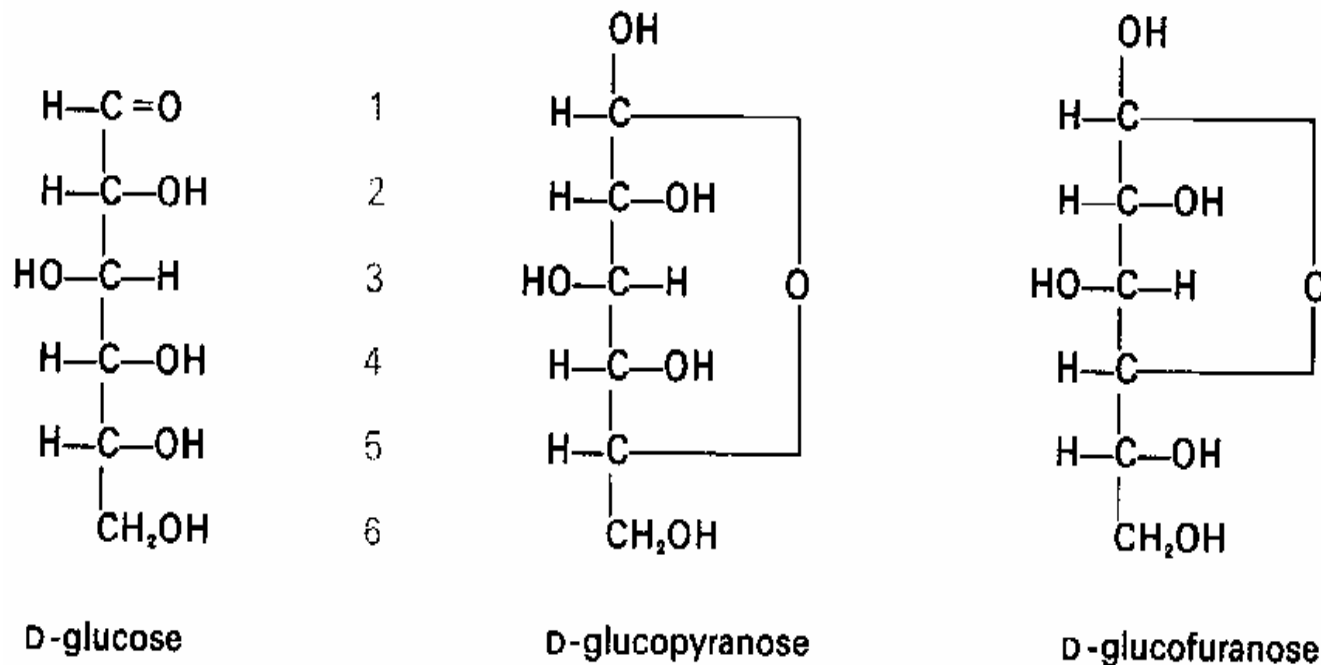
# Family tree of D-aldohexoses

- Most but not all naturally occurring aldoses are from the D family
- D-(+)-glucose most common
- D-(+)-galactose obtained from milk sugar
- L-(-)-galactose is found in the vineyard snail
- L-(+)-arabinose is found widely but D-(-)-arabinose is scarce
- Threose, lyxose, gulose and allose do not occur naturally but are synthetically made

# Lengthen or shorten monosaccharide

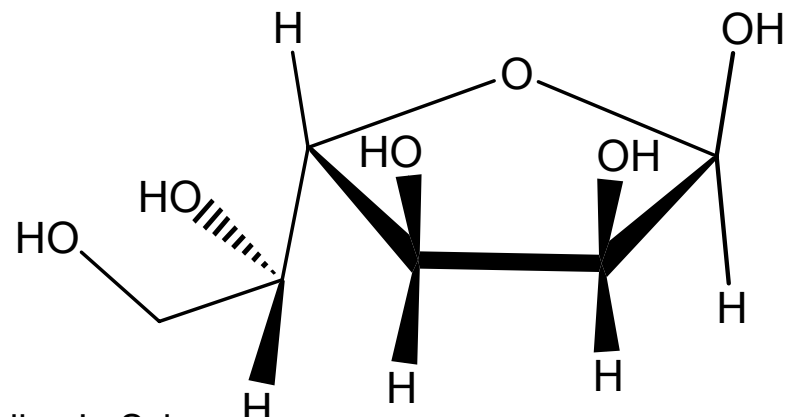
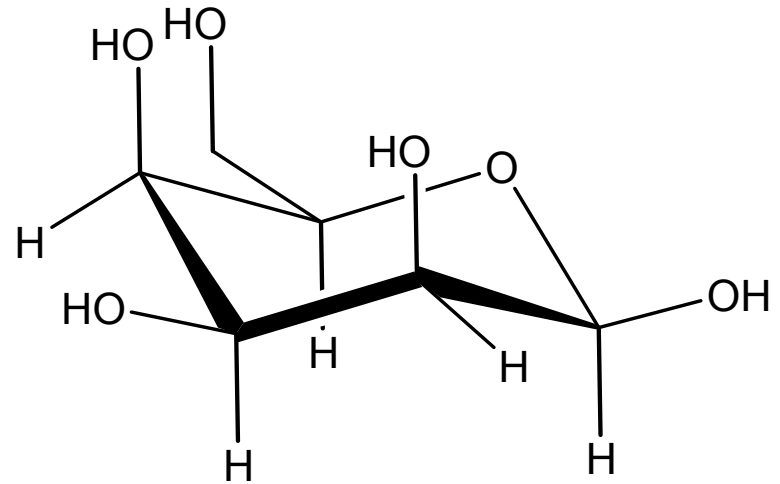
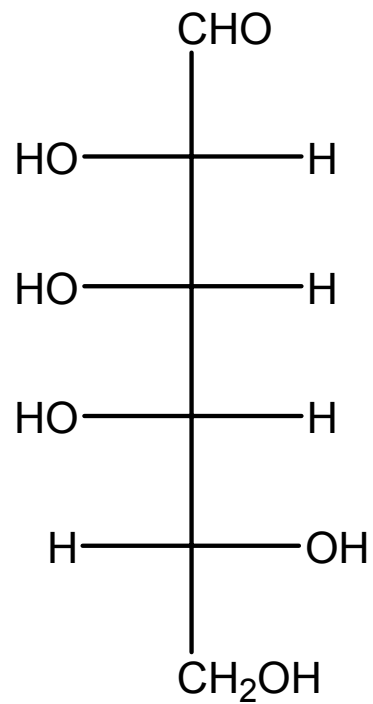
- Kiliani-Fischer synthesis (1885) lengthens the monosaccharide one C unit at a time through HCN and Ba(OH)<sub>2</sub>
- Ruff degradation (Otto Ruff 1871-1939) shortens the chain one unit at a time using Br<sub>2</sub> and H<sub>2</sub>O<sub>2</sub>

# Saccharide Ring Structures



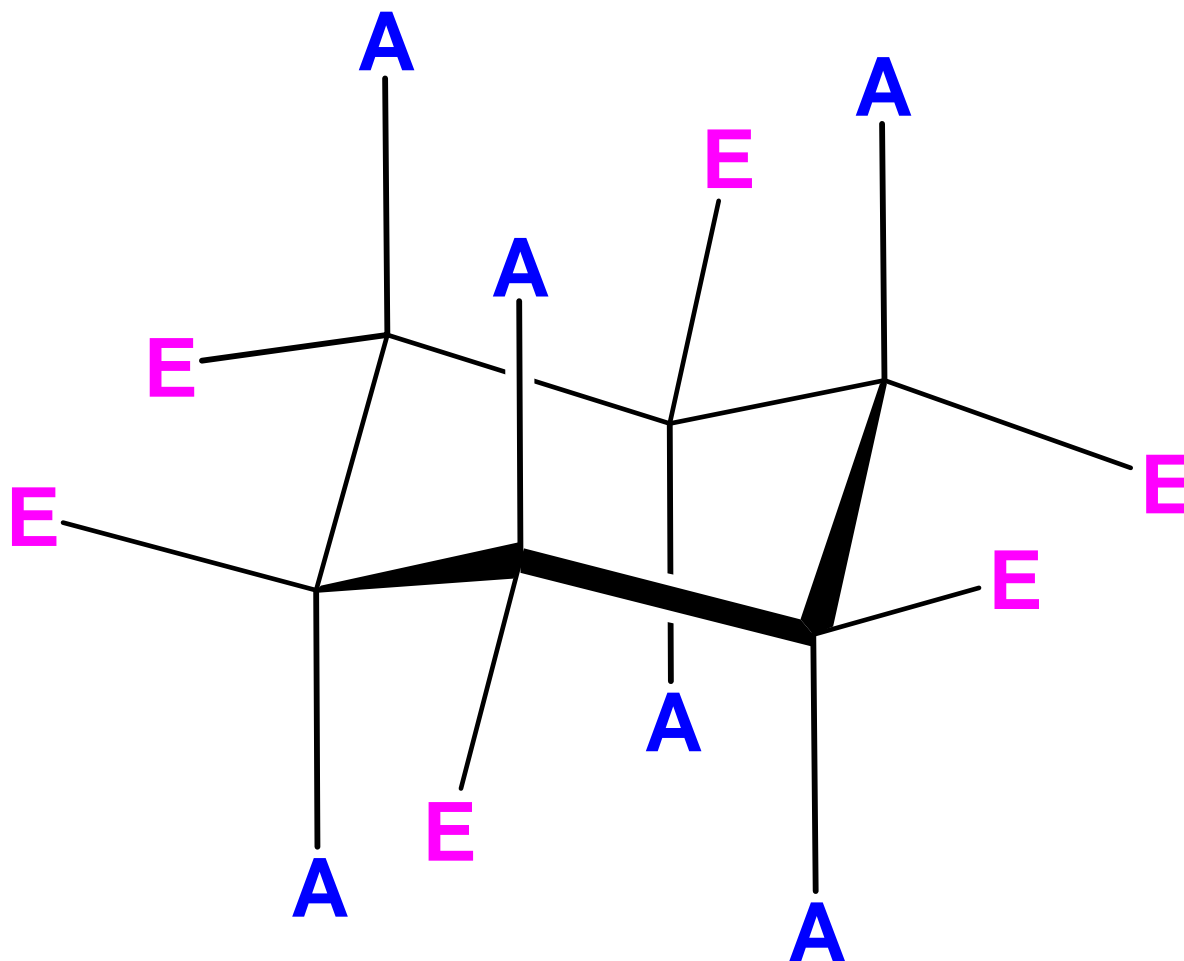
D-glucose an aldohexose can cyclise by forming a bond either between C1 and C5 to give a 6-membered pyranose ring or between C1 and C4 giving a furanose ring

# D-Talose



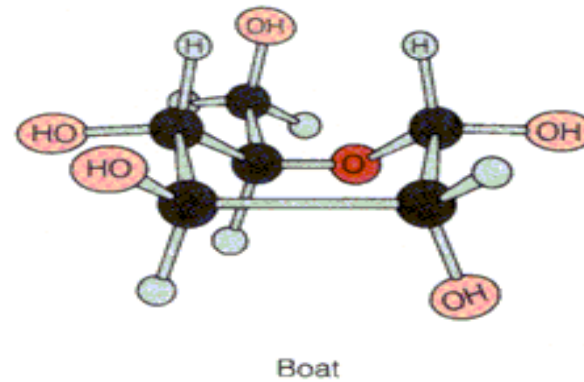
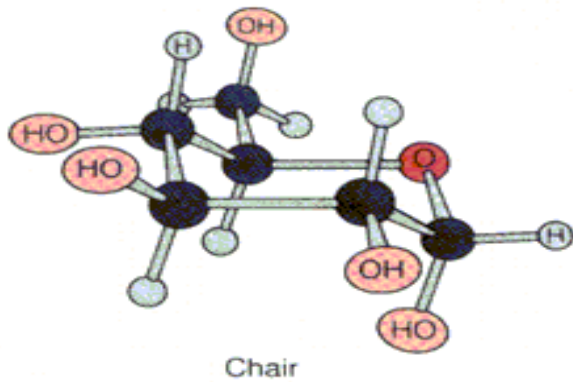
© Caroline L. Schauer

# Remember:



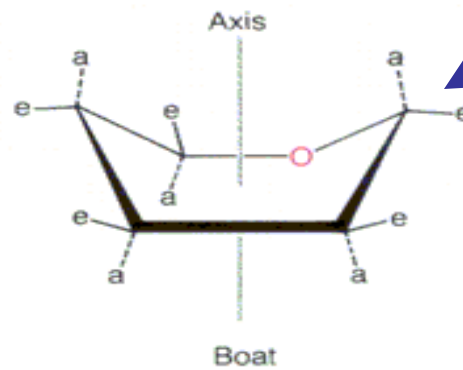
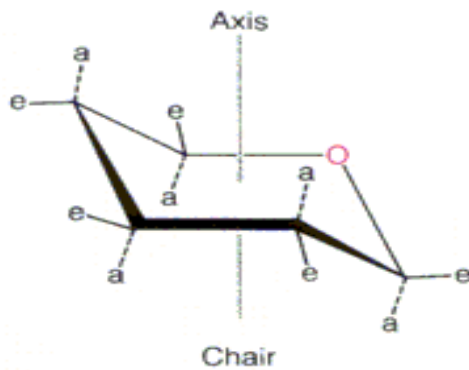
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# Chair and Boat Forms



(a)

• Chair form is lower energy = more stable



(b)

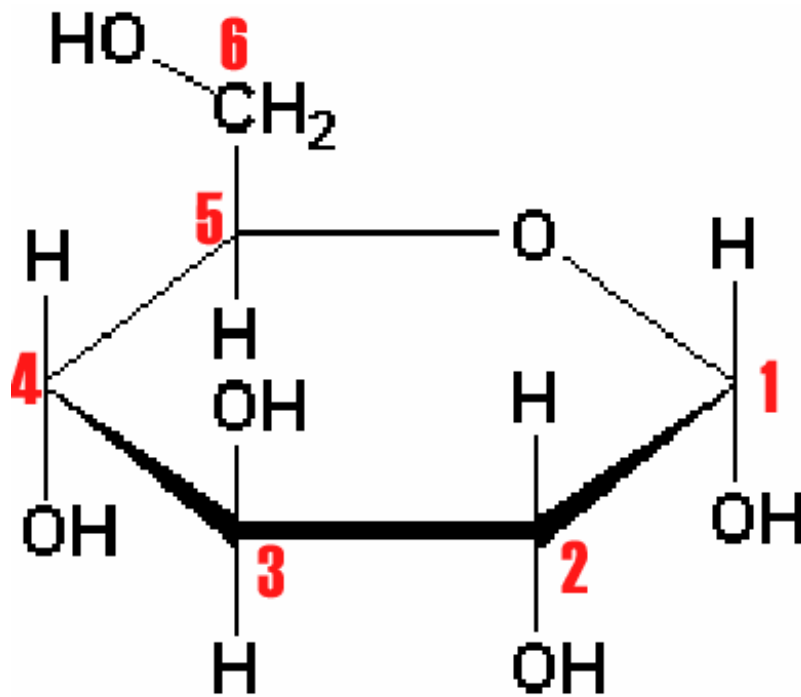
• Axial and equatorial substituents

From Matthews, van Holde, Ahern "Biochemistry"  
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# Haworth formulas

- W. N. Haworth, University of Birmingham
- 1926 with E.L. Hirst proved cyclic form of glucose acetals consist of a six membered ring
- Received the Nobel Prize 1937 for his work in carbohydrate chemistry

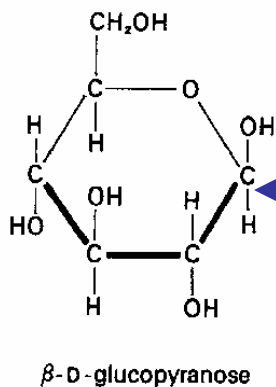
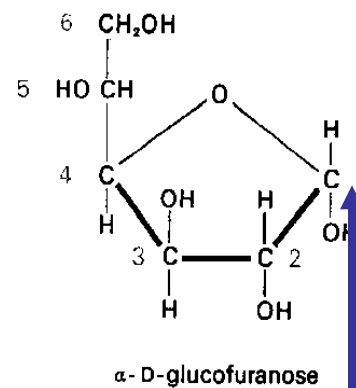
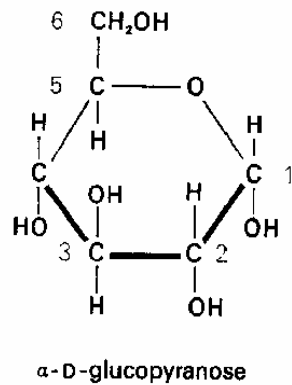
# Haworth Projection for Glucose



**Glucose**

- A Haworth projection is a planar representation of a cyclised monosaccharide
- C atoms are not shown
- Hydroxyls that are represented to the right of the chain in a Fischer projection are shown below the plane of the ring

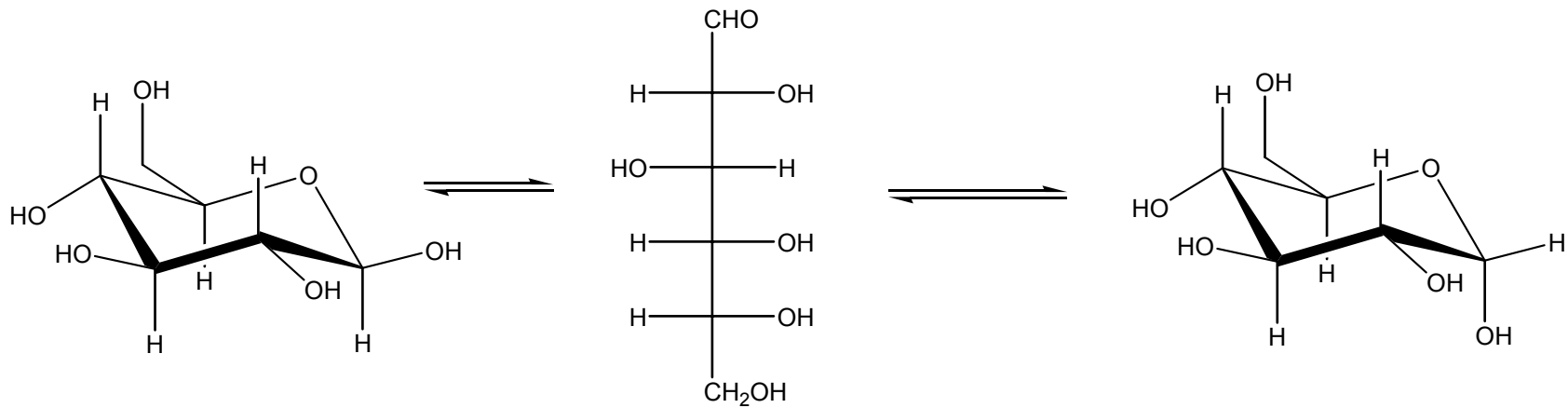
# Haworth Projections of Glucose Rings



Anomeric C

- From Fischer to Haworth the cyclization of a linear projection has two possible forms.
- The anomeric C (in this case C1) helps identify whether the sugar is in the  $\alpha$ - (OH- down) or  $\beta$ - (OH- up) configuration
- Anomers are capable of interconverting between positions by mutarotation

# Mutarotation



$\beta$ -D-(+)-glucopyranose  
Mp = 150°C;  $[\alpha]_D = +18.7^\circ$

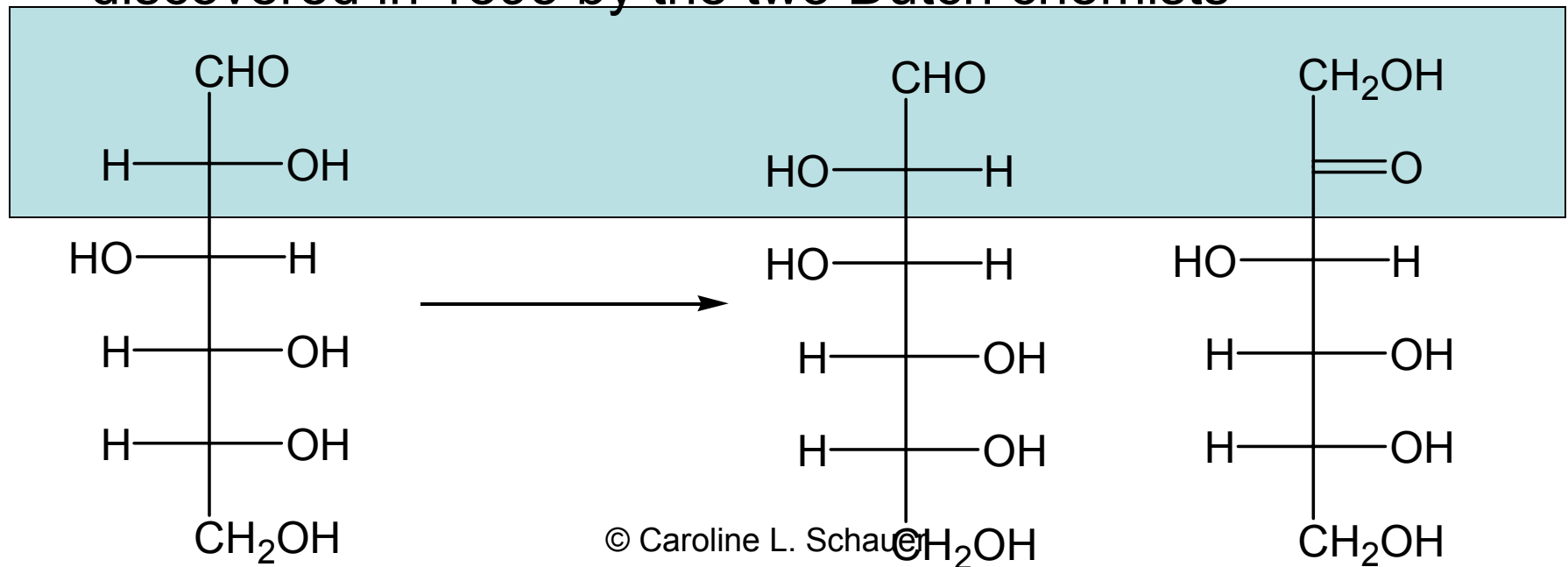
D-(+)-glucopyranose

$\alpha$ -D-(+)-glucopyranose  
Mp 146°C;  $[\alpha]_D = +112^\circ$

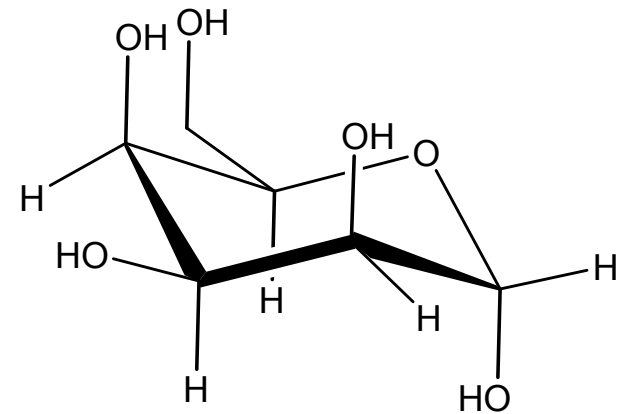
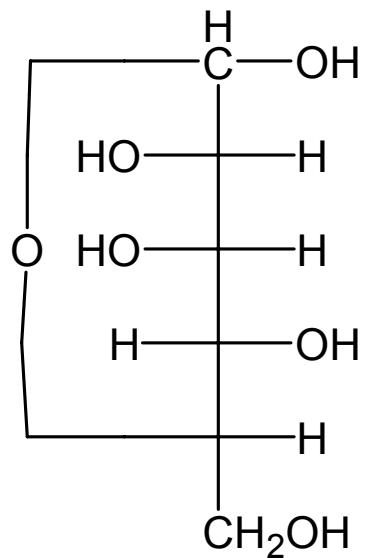
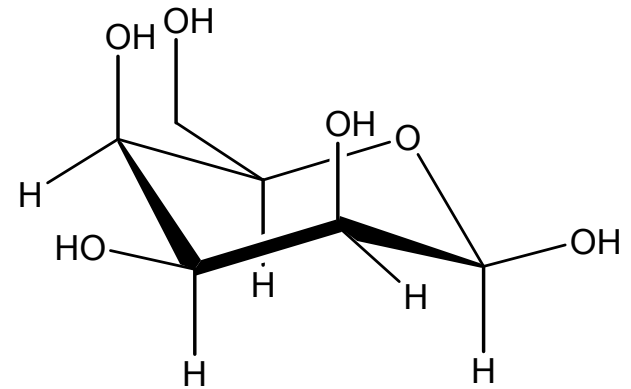
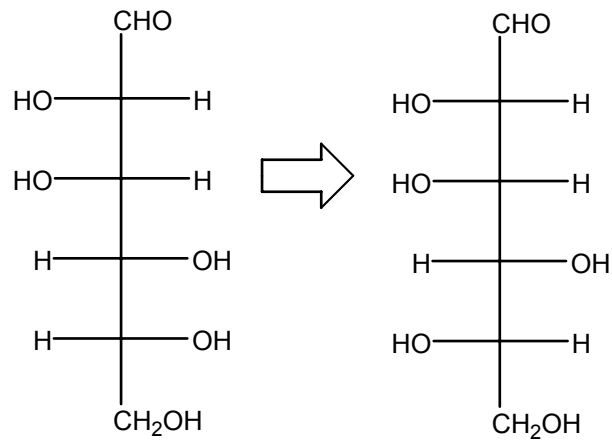
Equilibrates to  $[\alpha]_D = +52.7^\circ$   
© Caroline L. Schauer

# Enolization, tautomerization, Isomerization

- Dissolve in aqueous base causes enolizations
- Example D-glucose + Ca(OH)<sub>2</sub> is allowed to sit for several days- several products are isolated including D-fructose and D-mannose
- Lobry de Bruyn-Alberda van Ekenstein transformation discovered in 1895 by the two Dutch chemists



# Draw $\alpha$ -L-mannopyranose



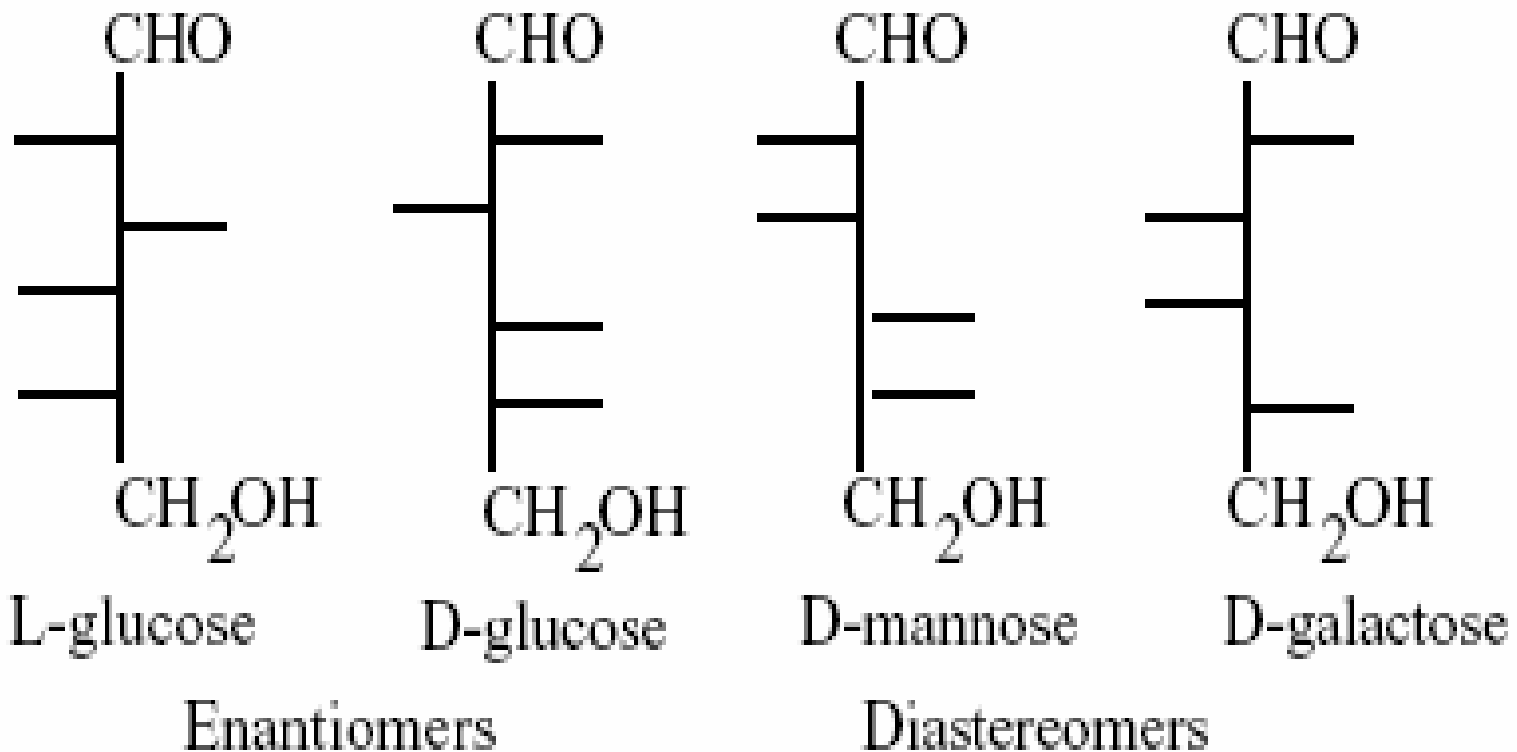
# Reminder Chirality

- The handedness of molecules is called chiral.
- A chiral object is an object that is not identical to its mirror image.
- Your hands are chiral objects. They are nonsuperimposable, they are not identical to their mirror image.

# Reminder Isomer vs. Stereoisomer

- Isomers - Two or more compounds having the same molecular formula but different arrangements of atoms.
- Stereoisomers - Compounds with the same structural formula but different spatial arrangements of atoms.
- **Molecules have handedness. Molecules can be right handed or left handed.**
- But how can they be different if they have the same structure?

# Enantiomers vs. Diastereomers



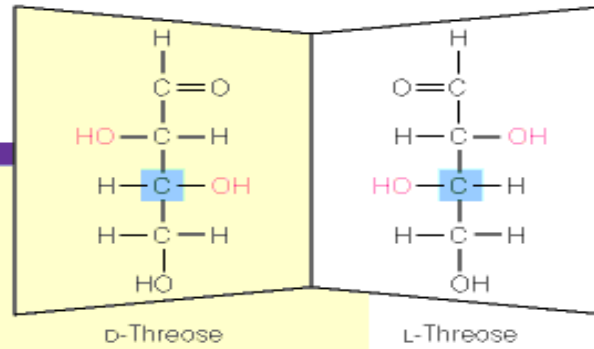
Anomers  $\alpha$  and  $\beta$  are diastereomers

# Saccharide Structures (Summary)

## Enantiomers

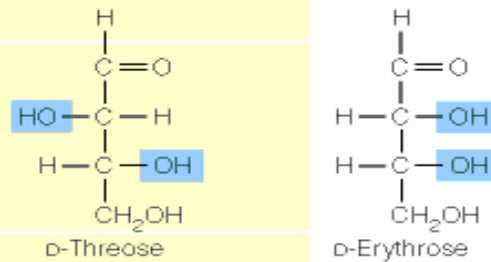
Stereoisomers that are mirror images of one another

The boxed asymmetric carbon (farthest from aldehyde) determines d/L designation



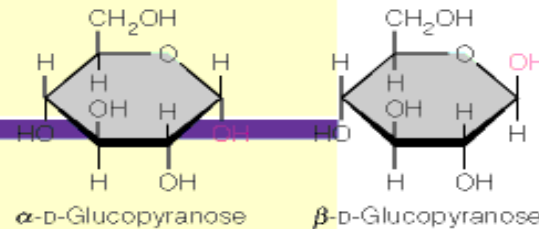
## Diastereomers

Stereoisomers that are not mirror images of one another



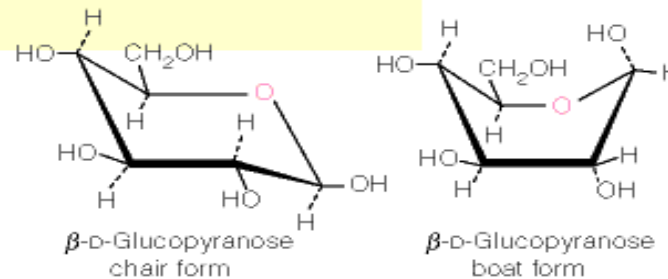
## Anomers

Stereoisomers that differ in configuration at the anomeric carbon



## Conformational isomers

Molecules with the same stereochemical configuration, but differing in three-dimensional conformation

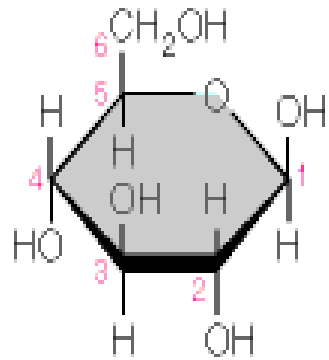


From Matthews, van Holde, Ahern  
"Biochemistry"

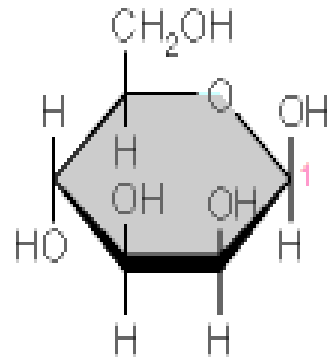
# Saccharide Rings - Summary

- Aldohexoses can cyclise to form **five-**membered (furanose) or **six-**membered (pyranose) ring structures
- Cyclisation creates a carbon with two possible orientations of the hydroxyl around it - this is the anomeric carbon
- Orientation of the -OH group at the anomeric C determines whether a sugar is in the  **$\alpha$ -** or  **$\beta$ -** forms
- These forms are called “**anomers**”

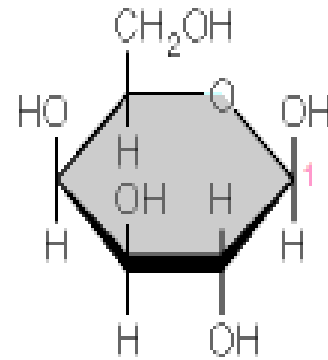
# Common Hexoses



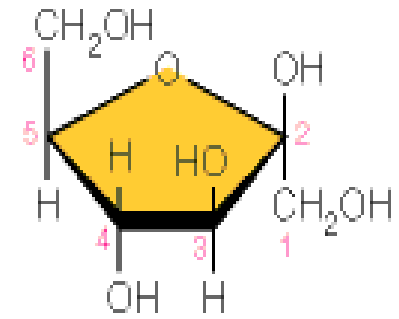
$\beta$ -D-Glucopyranose



$\beta$ -D-Mannopyranose



$\beta$ -D-Galactopyranose



$\beta$ -D-Fructofuranose

From Matthews, van Holde, Ahern "Biochemistry"

Glucose

Mannose

Galactose

Fructose

Glc

Man

Gal

Fru

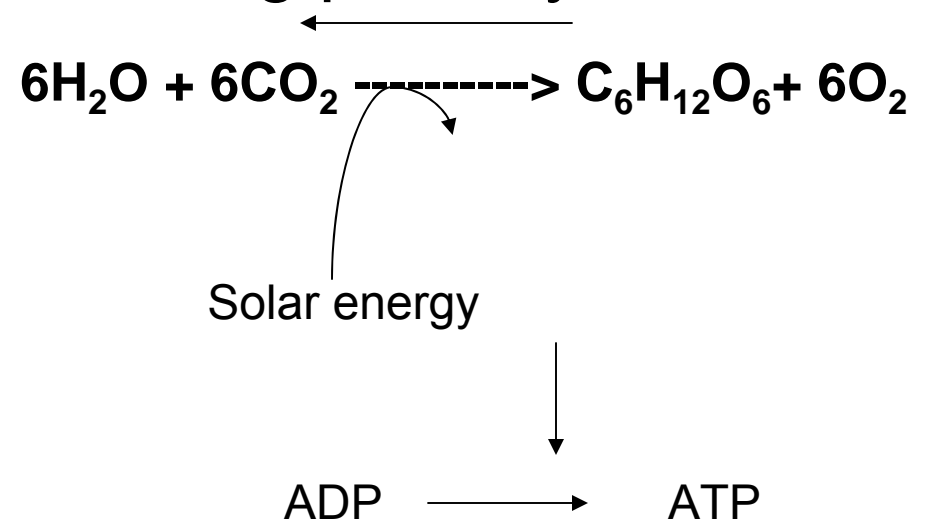
# Common Monosaccharides

| <u>Name</u>               | <u>Abbreviation</u> |
|---------------------------|---------------------|
| Arabinose                 | Ara                 |
| Fructose                  | Fru                 |
| Fucose                    | Fuc                 |
| Galactose                 | Gal                 |
| Glucose                   | Glc                 |
| Mannose                   | Man                 |
| Ribose                    | Rib                 |
| Xylose                    | Xyl                 |
| Glucuronic acid           | GlcUA               |
| Galactosamine             | GalN                |
| N-acetylgalactosamine     | GalNac              |
| N-acetylglucosamine (NAG) | GlcNac              |

# Natural synthesis

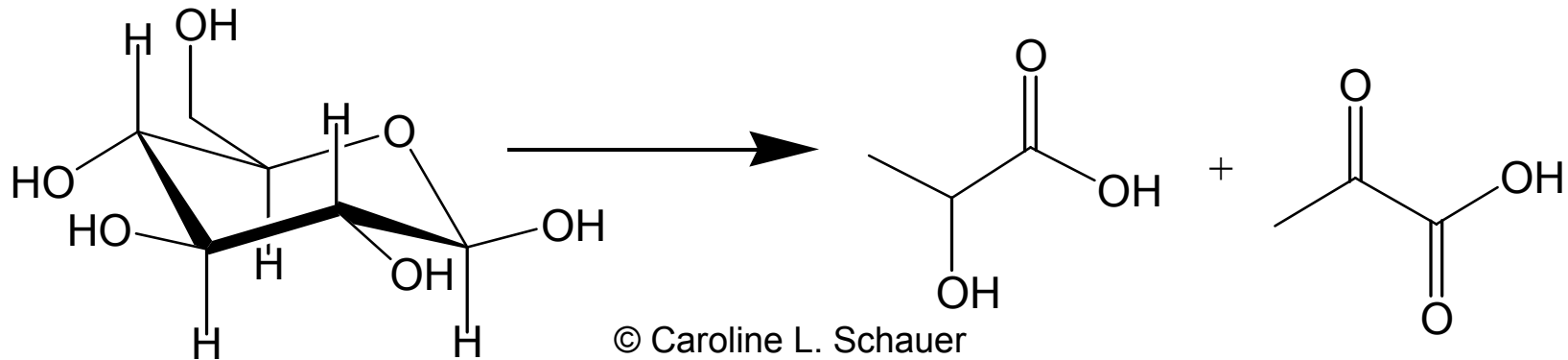
- Researchers have discovered that a known gene, PGC-1, activates the enzymes that generate glucose in the liver
- **gluconeogenesis** (literally “the birth of new glucose”).

- Carbohydrates are synthesized in plants using photosynthesis



# Glucose Oxidation

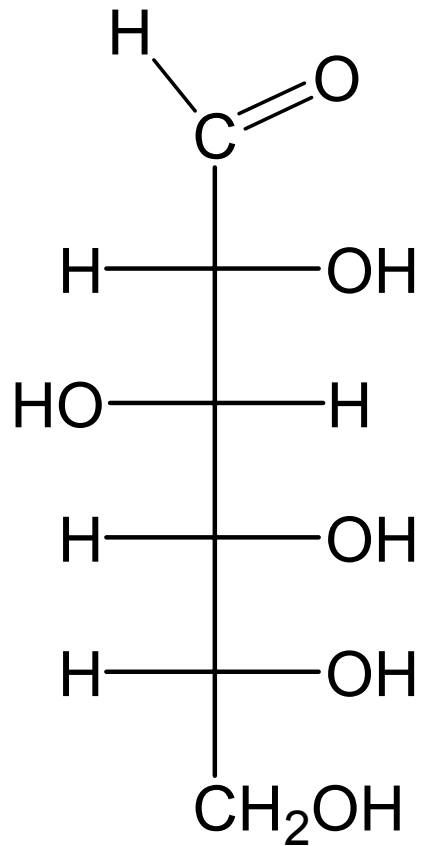
- Oxidation of glucose is known as **glycolysis**. Glucose is oxidized to either lactate or pyruvate.
- Under aerobic conditions, the dominant product in most tissues is pyruvate and the pathway is known as **aerobic glycolysis**.
- When oxygen is depleted, as for instance during prolonged vigorous exercise, the dominant glycolytic product in many tissues is lactate and the process is known as **anaerobic glycolysis**.



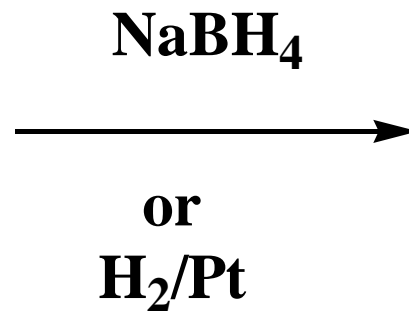
# Chemical Reactions for analysis

- **Reduction** (with borohydride) converts CHO to CH<sub>2</sub>OH (aldoses and ketoses give an alditol)
- glucose to glucitol (a.k.a. sorbitol)
- fructose gives glucitol *and* mannitol

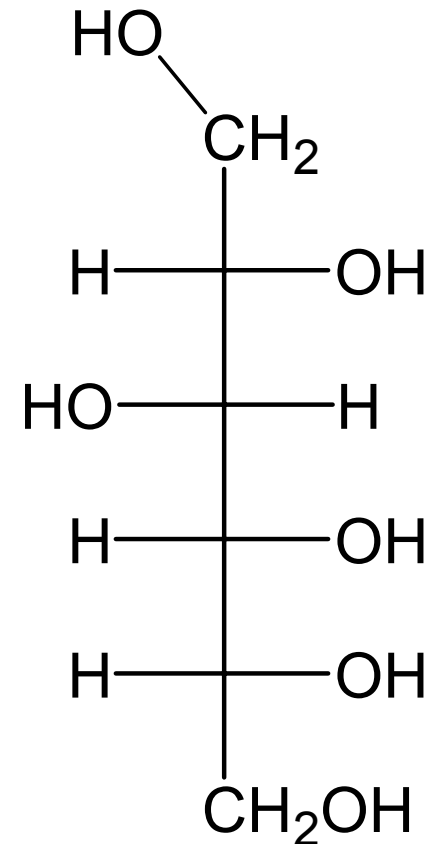
# Carbohydrate reduction



D-glucose



© Caroline L. Schauer



D-glucitol or D-sorbitol

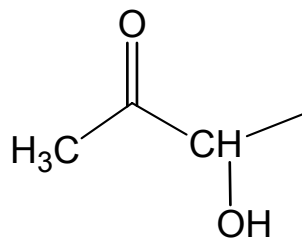
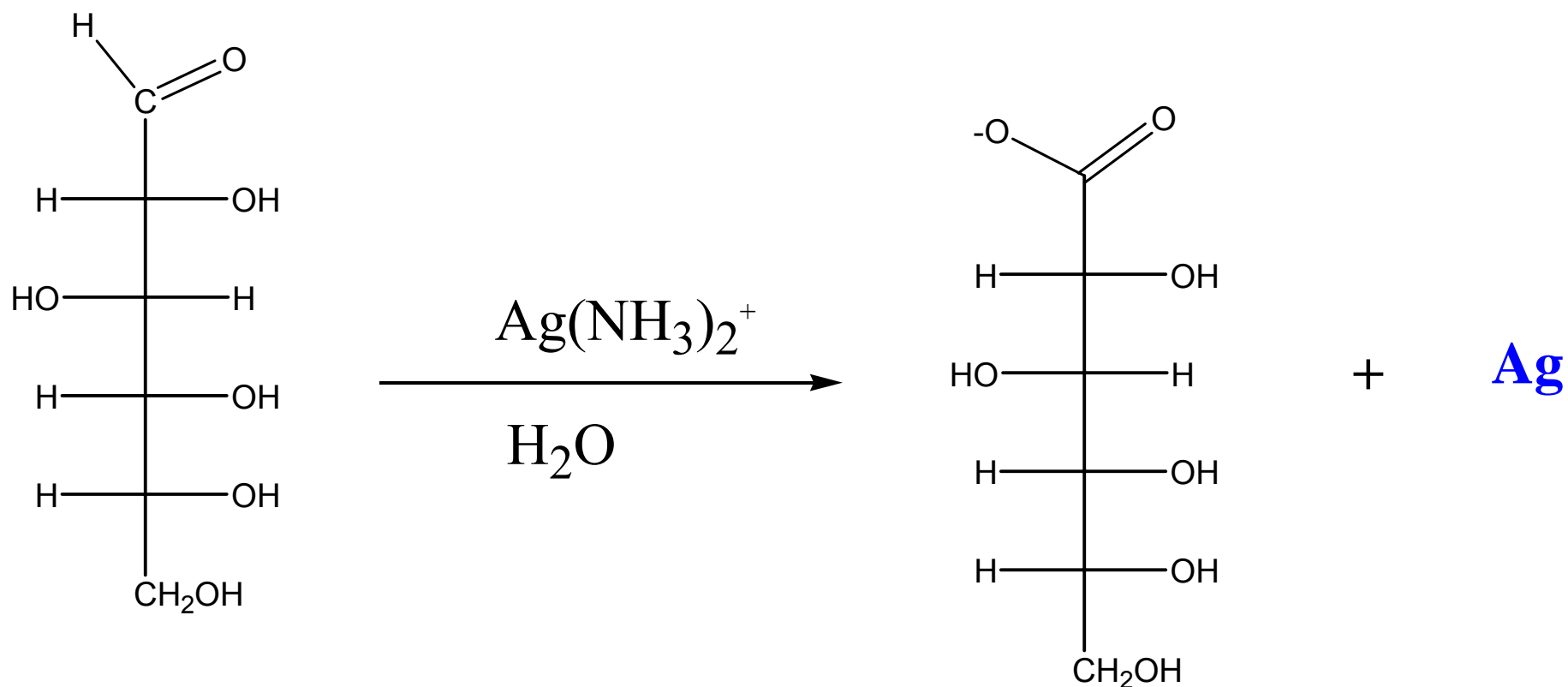
# Oxidation of Carbohydrates

- Benedict
- Tollens
- Bromine water
- Nitric acid
- Periodic acid

# Reactions for analysis

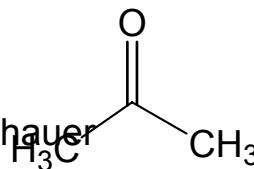
- **Oxidation**. Mild oxidation is often used to test for the **free C=O group** because with weak oxidizing reagents such as alkaline  $\text{Ag}^+$  (Tollen's Reagent) or alkaline  $\text{Cu}^{2+}$  (Fehling's or Benedicts- depending on the counter ion-Reagent) the products are the metallic Ag or the red insoluble  $\text{Cu}_2\text{O}$  both of which can be easily visualized.
- Sugars that give a positive response in these tests are called **REDUCING** sugars.

# Tollen's test for carbohydrates



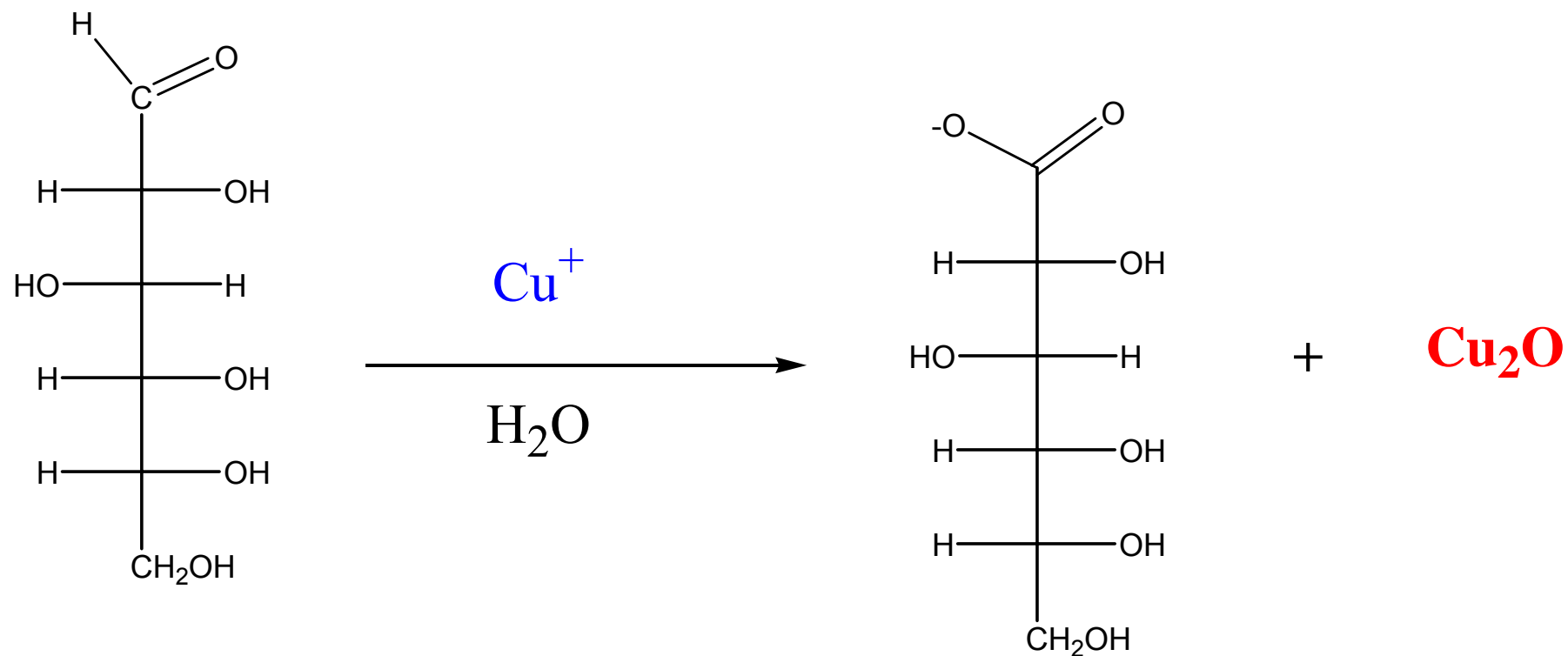
reaction

© Caroline L. Schauer



No reaction

# Fehling/Benedict's test

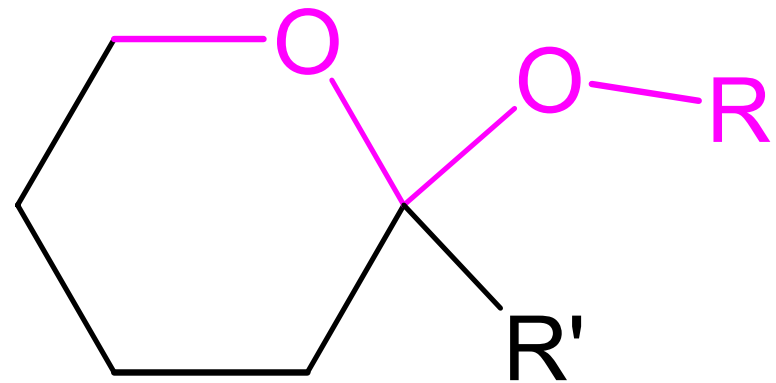
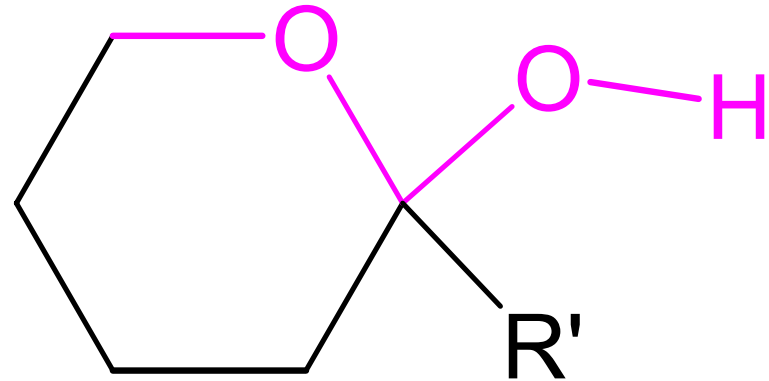


Cupric tartarate complex vs. Cupric citrate complex

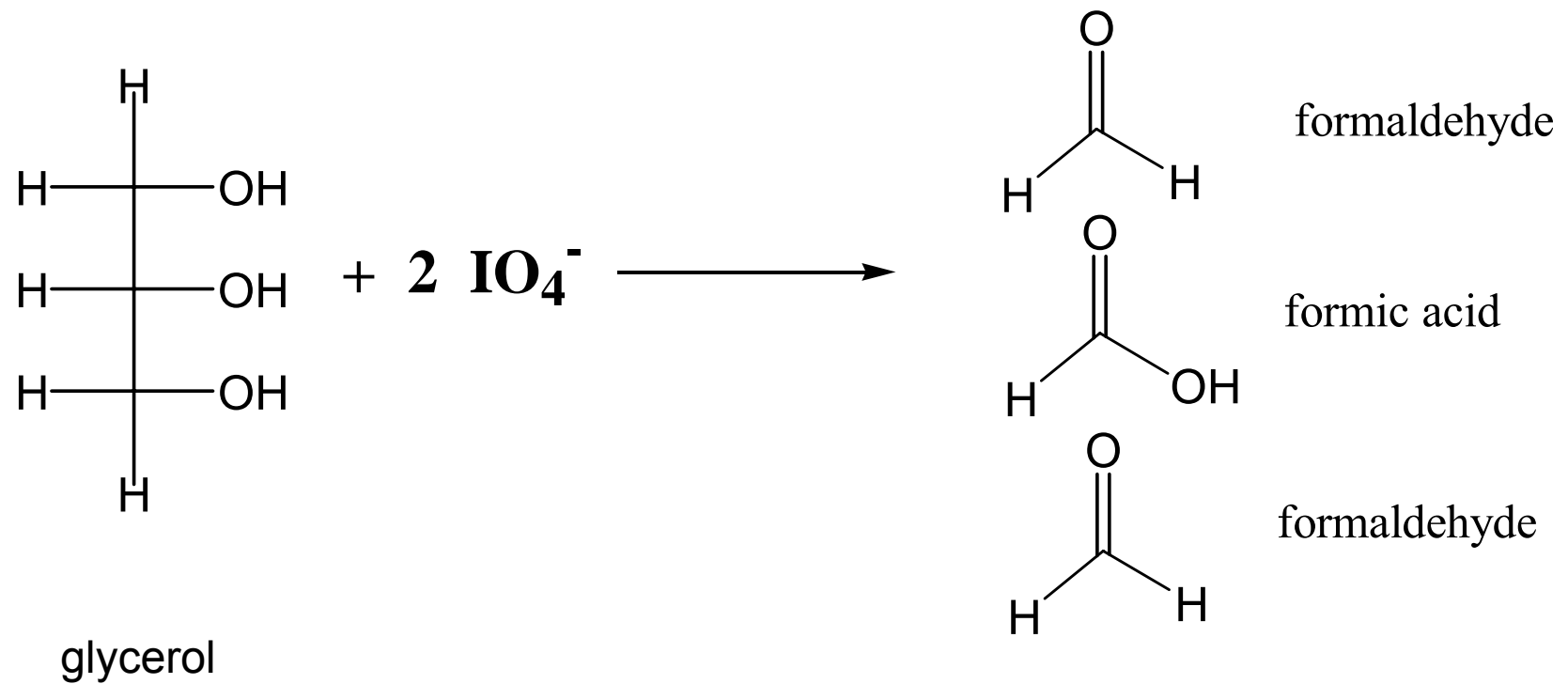
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# Reducing vs. non-reducing sugars

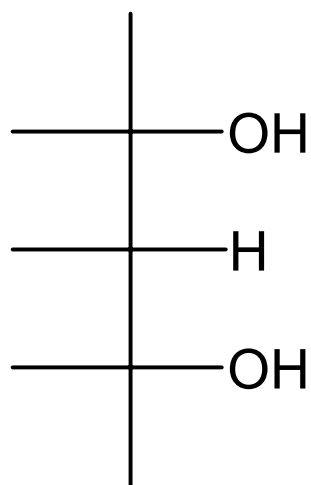
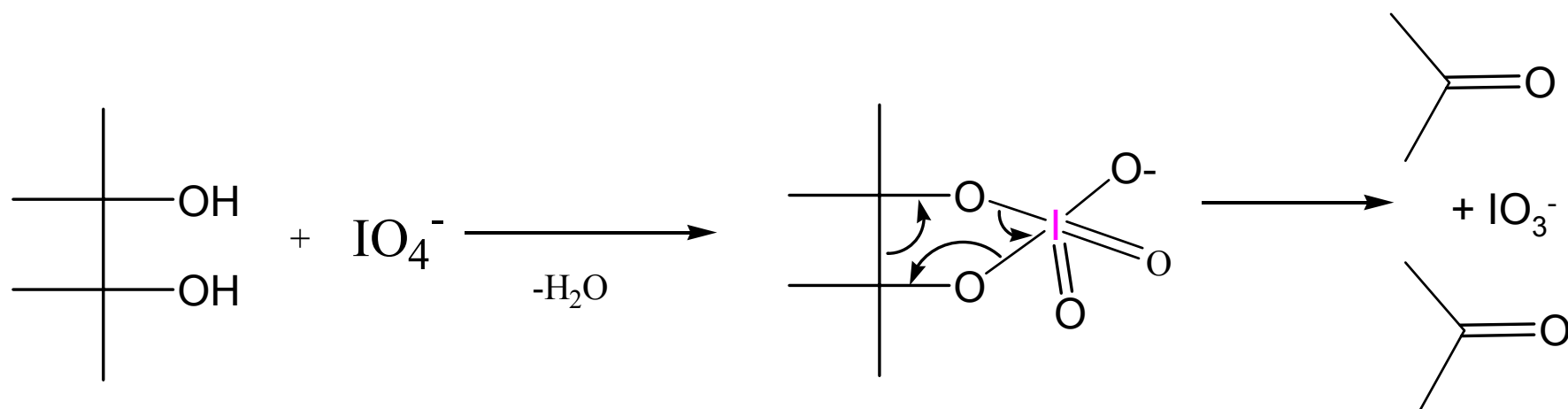
- R' equals H or  $\text{CH}_2\text{OH}$  = hemiacetal
- R equals alkyl or other sugar = acetal
- Hemiacetal is a reducing sugar
- Acetal is a non-reducing sugar



# Oxidative cleavage



# Mechanism for oxidative cleavage

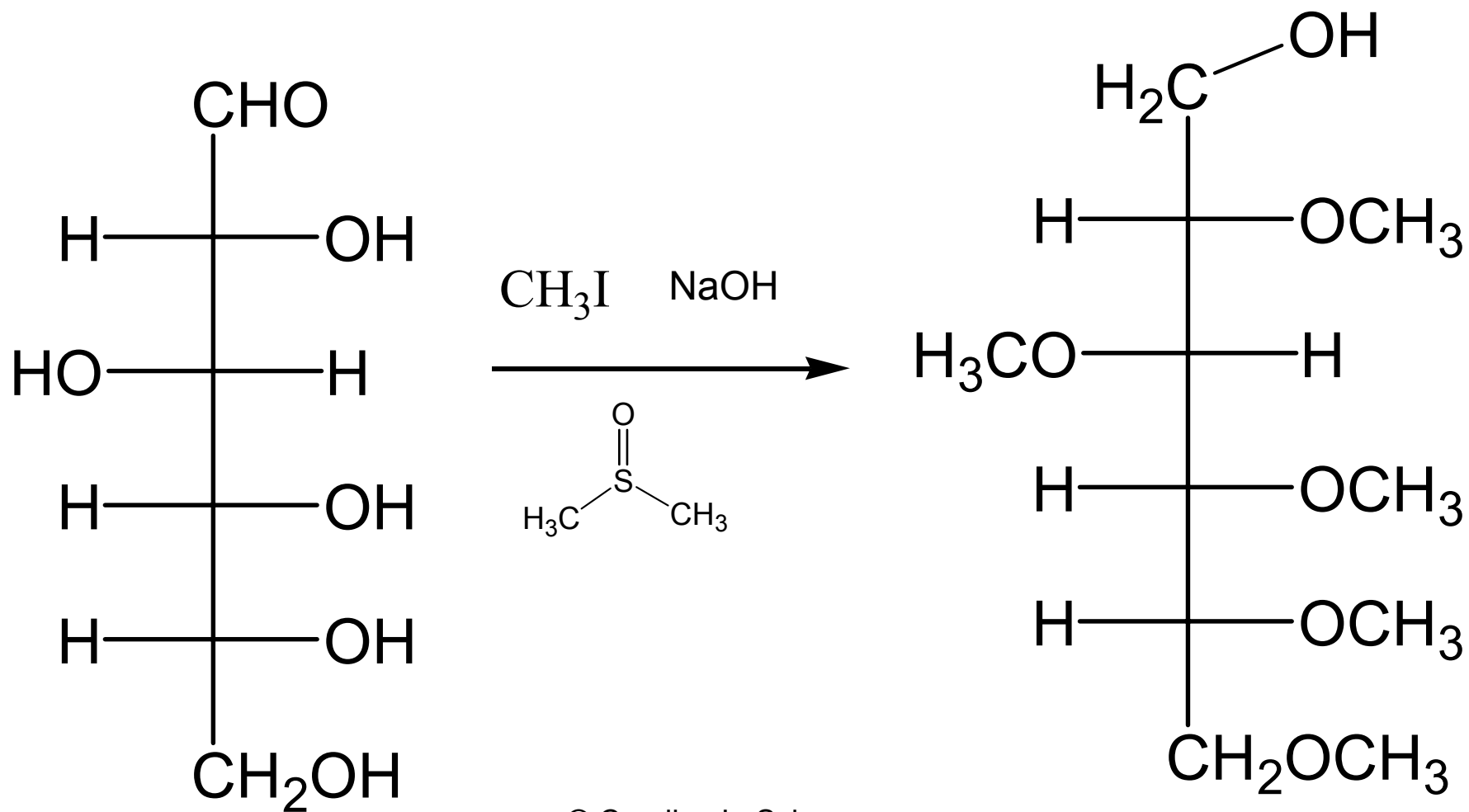


No cleavage!

# Reactions for structural analysis

- **Ether formation**: Base-induced reaction of all -OH's with **alkylating agents** e.g., methyl iodide,  $\text{CH}_3\text{I}$ , plus dimethyl sulfoxide,  $(\text{CH}_3)_2\text{S}=\text{O}$  (anion, scavenges proton) plus sodium hydride,  $\text{NaOH}$ , (catalyst; very strong base) to produce **methyl ether** (- $\text{OCH}_3$ ; -OH's react as strongly nucleophilic -O-).

# The ether link is very stable

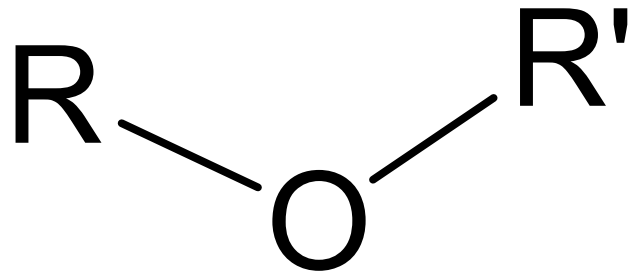


# Ether formation

- The oxygen at C1 also reacts (it is a hemiacetal) but the  $-OCH_3$  at C1 is atypical and hydrolyzes to  $-OH$  in dilute acid. Because of this the product from reaction of glucose is 2,3,4,5,6 **pentamethyl glucose**.
- Common protecting groups for carbohydrates are ethers, esters and acetals

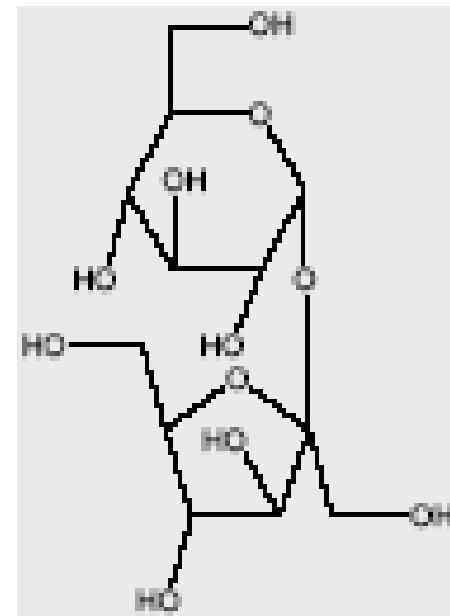
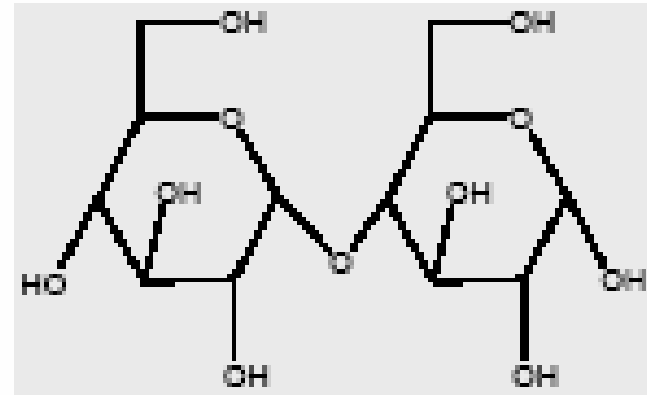
# From Mono to Di

- Carbohydrates that undergo hydrolysis and form two molecules are disaccharides
- Connected through ether linkage



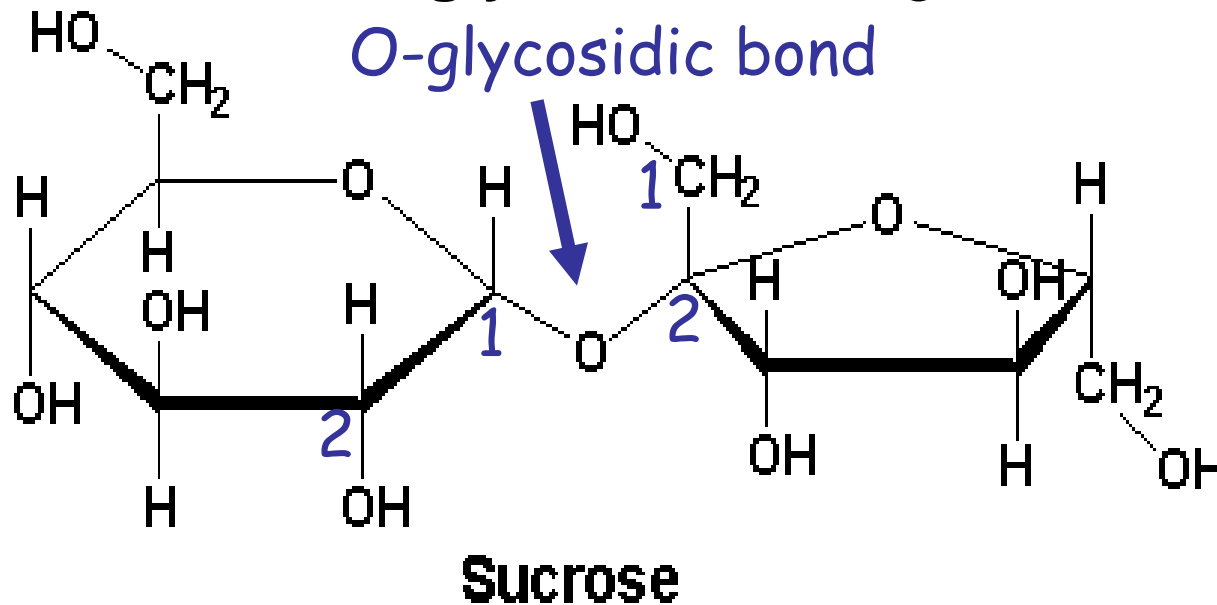
# Disaccharide

- **Disaccharide - A carbohydrate formed by the combination of two monosaccharides.**
- **The monosaccharides can be the same or different.**
- **Maltose and sucrose are examples of disaccharides.**



# Structure of Disaccharides

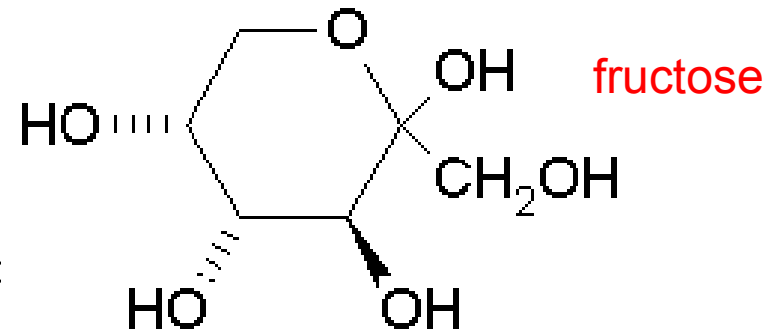
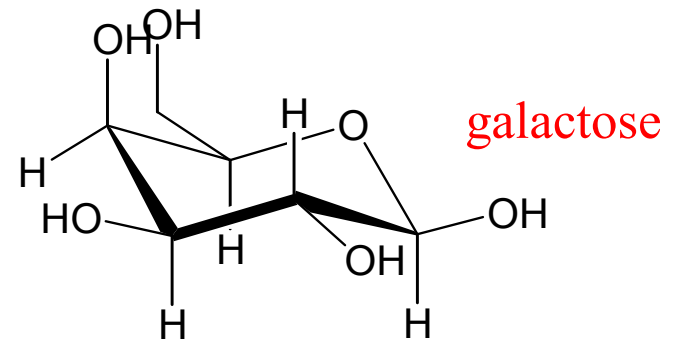
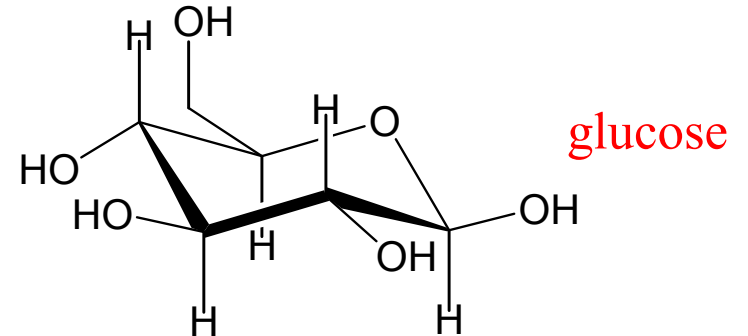
- Sugars are linked by an O-glycosidic bond
  - remember **N-glycosidic** linking bases to ribose



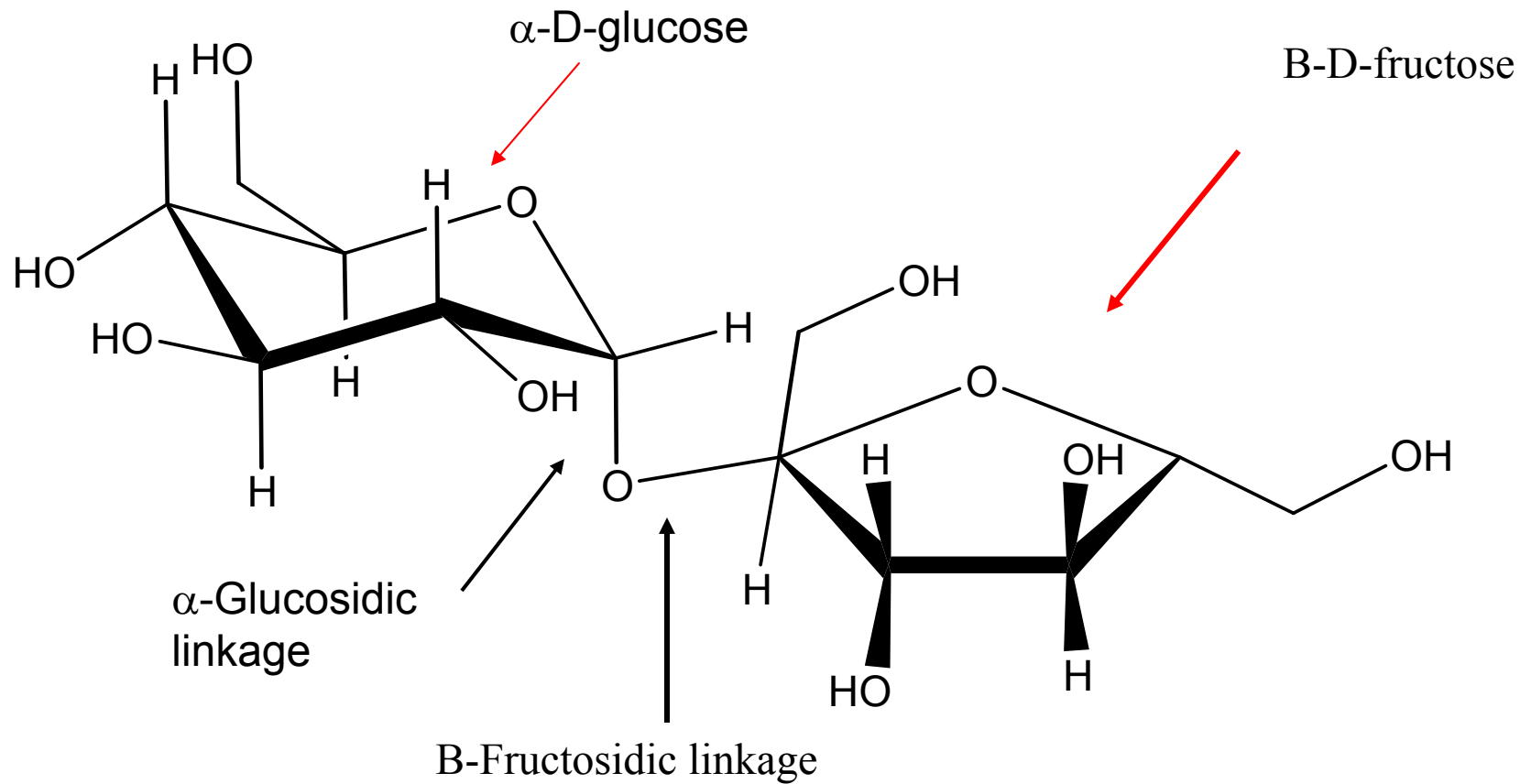
$\alpha$ -D-glucose (*pyranose*) 1,2 O-linked to  $\beta$ -D-fructose (*furanose*)

# Disaccharides

- **sucrose** - common table sugar = glucose + fructose
- **lactose** - major sugar in milk = glucose + galactose
- **maltose** - product of starch digestion = glucose + glucose



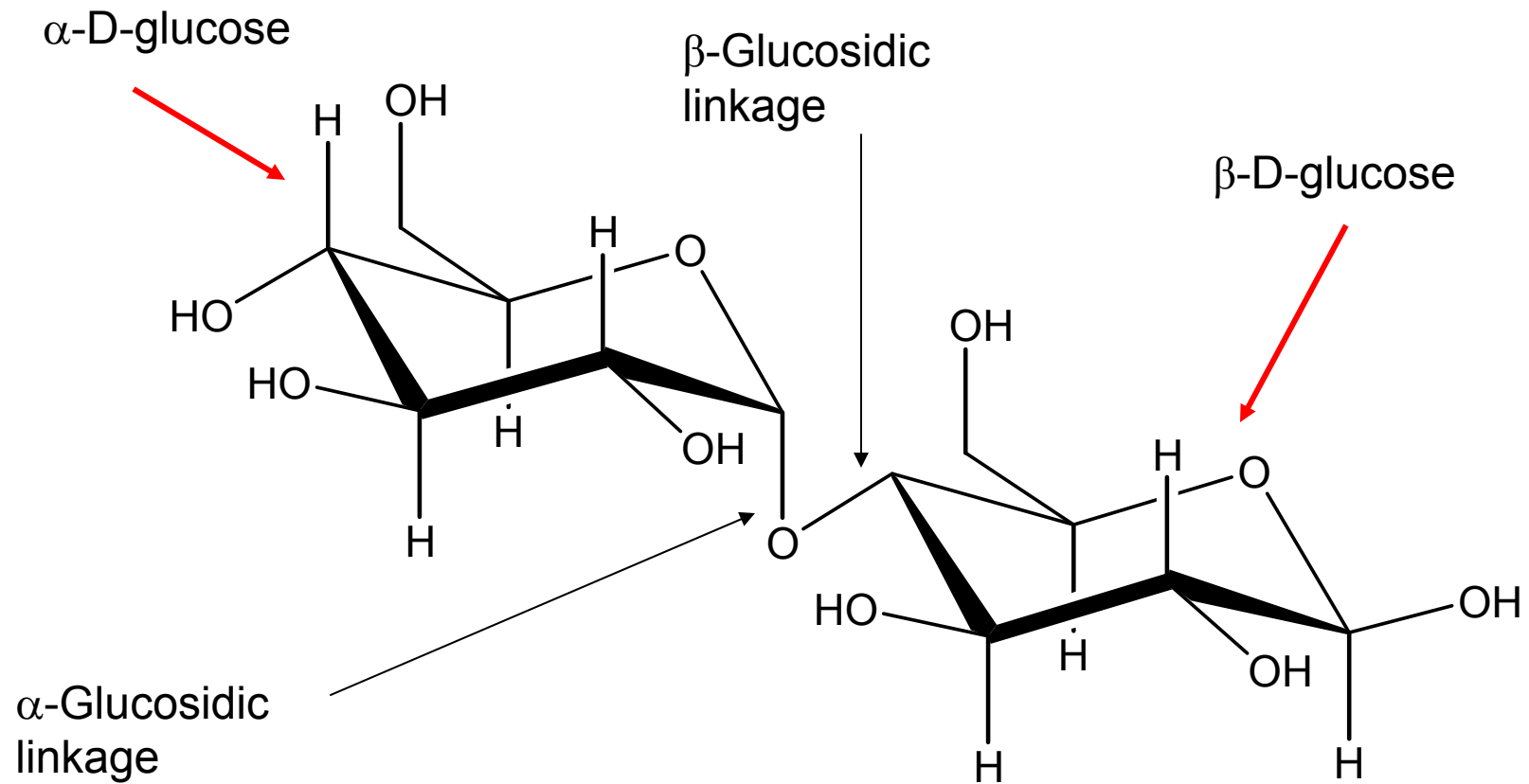
# (+)-Sucrose



# (+)-Sucrose

- $C_{12}H_{22}O_{11}$
- Acid catalyzation of 1 mol of sucrose yields 1 mol D-glucose and 1 mol D-fructose
- Non-reducing sugar negative Tollens and Benedict
- Does not undergo mutarotation

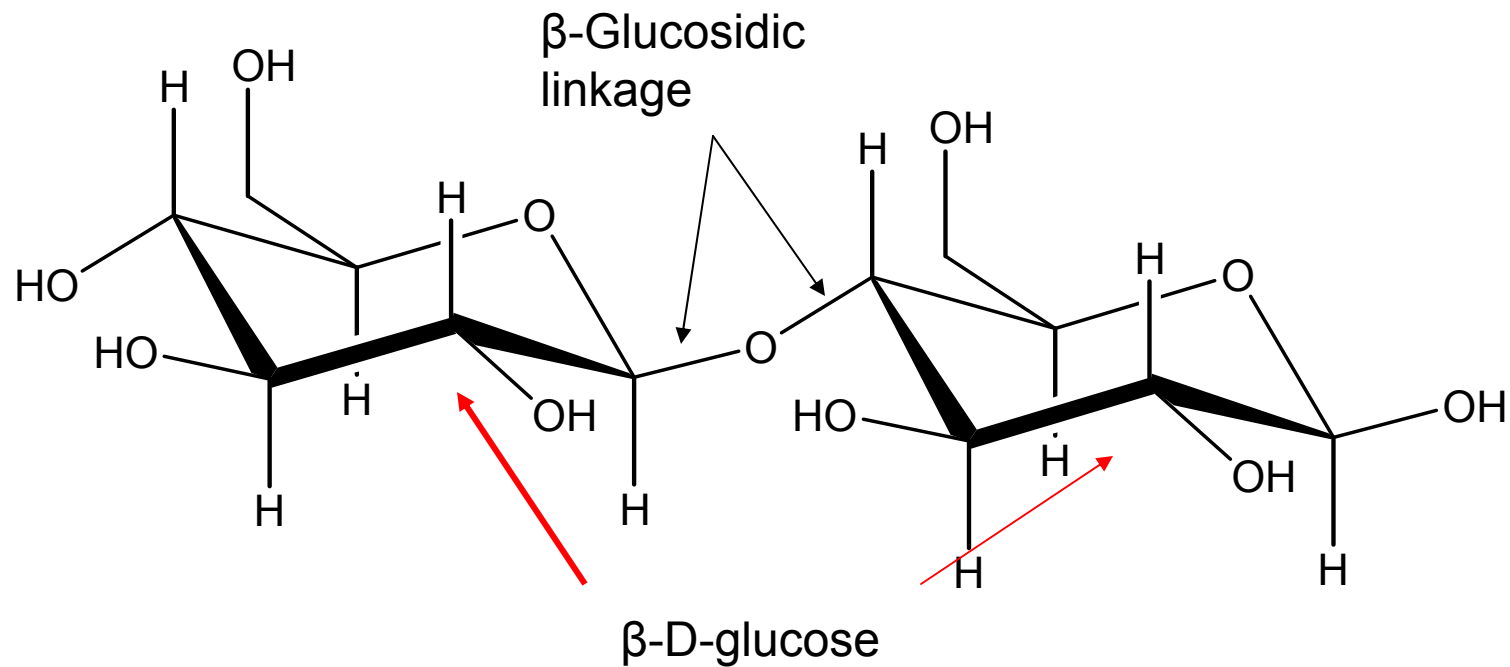
# (+)-Maltose



# Maltose

- $C_{12}H_{22}O_{11}$
- Acid-catalyzed hydrolysis yields 2 mol D-(+)-glucose
- Maltose is a reducing sugar
- Maltose undergoes mutarotation

# Partial Hydrolysis of cellulose

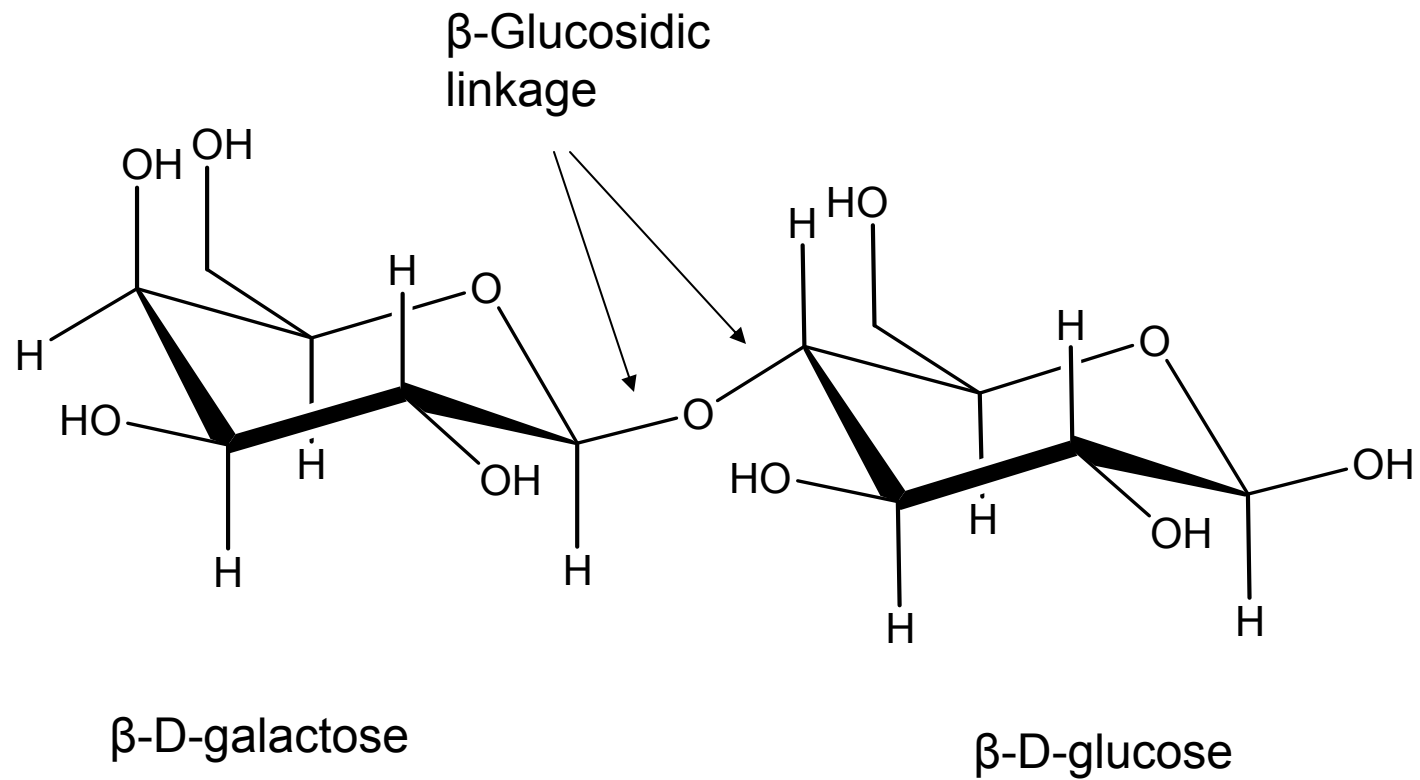


- Cellobiose  $C_{12}H_{22}O_{11}$
- Similar to Maltose except linkage

# Lactose

- In milk of humans, cows and most other mammals
- Reducing sugar
- Acid-catalyzed hydrolysis yields 1 mol D-glucose and 1 mol D-galactose

# Lactose



# End of lesson

- Sugars-or saccharides- are the most abundant bio-molecule on the planet.
- They are important in a number of biological roles. Most obviously you will know them as a major component of your diet.
- Insoluble sugars also function as structural material in the cell walls of plants and bacteria and in the connective tissue and cell coats of animals.
- Sugar polymers serve to lubricate skeletal joints. Sugars can be attached to proteins (in glycoproteins) and lipids (in glycolipids) and these *glycosylated* compounds serve (i) as antigenic sites; (ii) provide signals that determine the cellular localization of proteins and (iii) function as signals that allow cells to recognize each other and adhere in the formation of tissues and organs.

# $\beta$ -D-Glucose

