

# CARBOHYDRATES

- carbohydrates are the most abundant molecules found in nature
- these complex multifunctional compounds exhibit classic organic chemical behavior in the execution of myriad important biological applications

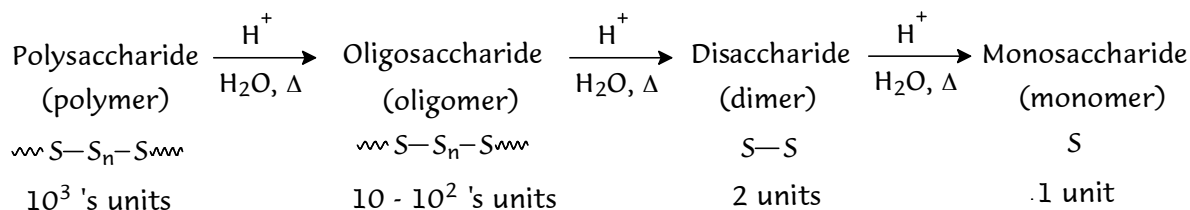
## CLASSIFICATION –

Original Definition ➤ hydrate of carbon,  $C_n(H_2O)_m$  (a common molecular formula)

Modern Definition ➤ a polyhydroxyaldehyde, a polyhydroxyketone or a compound which easily hydrolyzes to either of them

Saccharide, S ➤ a sugar unit (from Latin for *sweet*)

### Carbohydrate Hierarchy –



Monosaccharides & Disaccharides are commonly referred to as "*simple sugars*"

## I. MONOSACCHARIDES –

- the structural characteristics of monosaccharides are fundamental to all carbohydrates

### CLASSIFICATION –

- specific monosaccharides are usually referred to by their common names, but general classifications exist which are based on common structural features

#### A. Functional Group –

- every carbon in a monosaccharide is oxygenated (with a carbonyl =O or a hydroxyl -OH)
- monosaccharides can be classified according to the type of carbonyl group present:



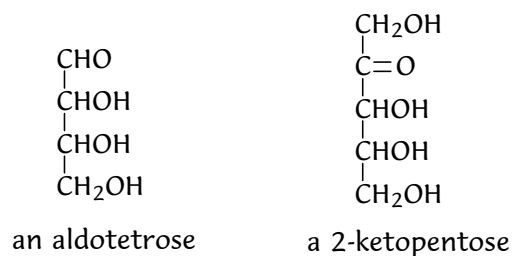
| <u>Functional Group</u>                                                               | <u>General Structural Formula</u>                                                                                                  | <u>Name</u> | <u>Prefix</u> | <u>Suffix</u> |
|---------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|-------------|---------------|---------------|
| $\begin{array}{c} \text{H} \\   \\ \text{R}-\text{C}=\text{O} \end{array}$ (Aldehyde) | $\begin{array}{c} \text{CHO} \\   \\ (\text{CHOH})_n \\   \\ \text{CH}_2\text{OH} \end{array}$                                     | Aldose      | aldo-         | -ose          |
| $\begin{array}{c} \text{R} \\   \\ \text{R}-\text{C}=\text{O} \end{array}$ (Ketone)   | $\begin{array}{c} \text{CH}_2\text{OH} \\   \\ \text{C}=\text{O} \\   \\ (\text{CHOH})_n \\   \\ \text{CH}_2\text{OH} \end{array}$ | Ketose      | keto-         | -ose          |

## B. Number of Carbons –

- monosaccharides can be classified according to the number of carbons present:

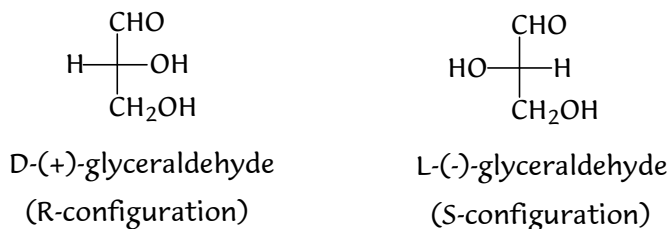
|          |        |         |         |        |         |       |
|----------|--------|---------|---------|--------|---------|-------|
| # C's =  | 3      | 4       | 5       | 6      | 7       | ..... |
| Name =   | triose | tetrose | pentose | hexose | heptose | ..... |
| (Suffix) |        |         |         |        |         |       |

EX. classify according to FG & #C's



## C. D & L Configuration –

- all CHOH group carbons in monosaccharides are stereocenters (C\*)
- the D/L configuration of all carbohydrates is based on the stereocenter contained in the simple aldotriose, glyceraldehyde



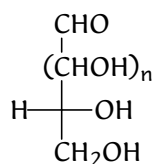
- all D-series sugars can be degraded to D-(+)-glyceraldehyde
- all L-series sugars can be degraded to L-(-)-glyceraldehyde



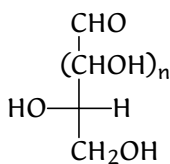
## Assigning the D/L Series Configuration –

- place the most oxidized carbon (C=O) closest to the "top" in a Fischer projection (FP)
- examine the configuration of the CHOH closest to the "bottom" (2<sup>nd</sup> to "last" C in the FP)

### -OH Right > D-Series

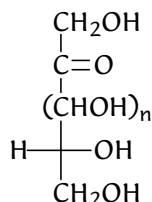


D-aldoses

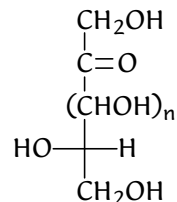


L-aldoses

### -OH Left > L-Series

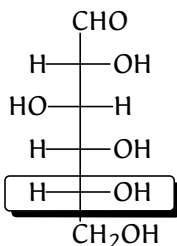


D-ketoses

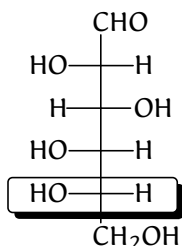


L-ketoses

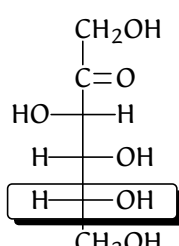
### EX's



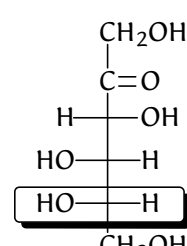
D-(+)-glucose



L-(-)-glucose



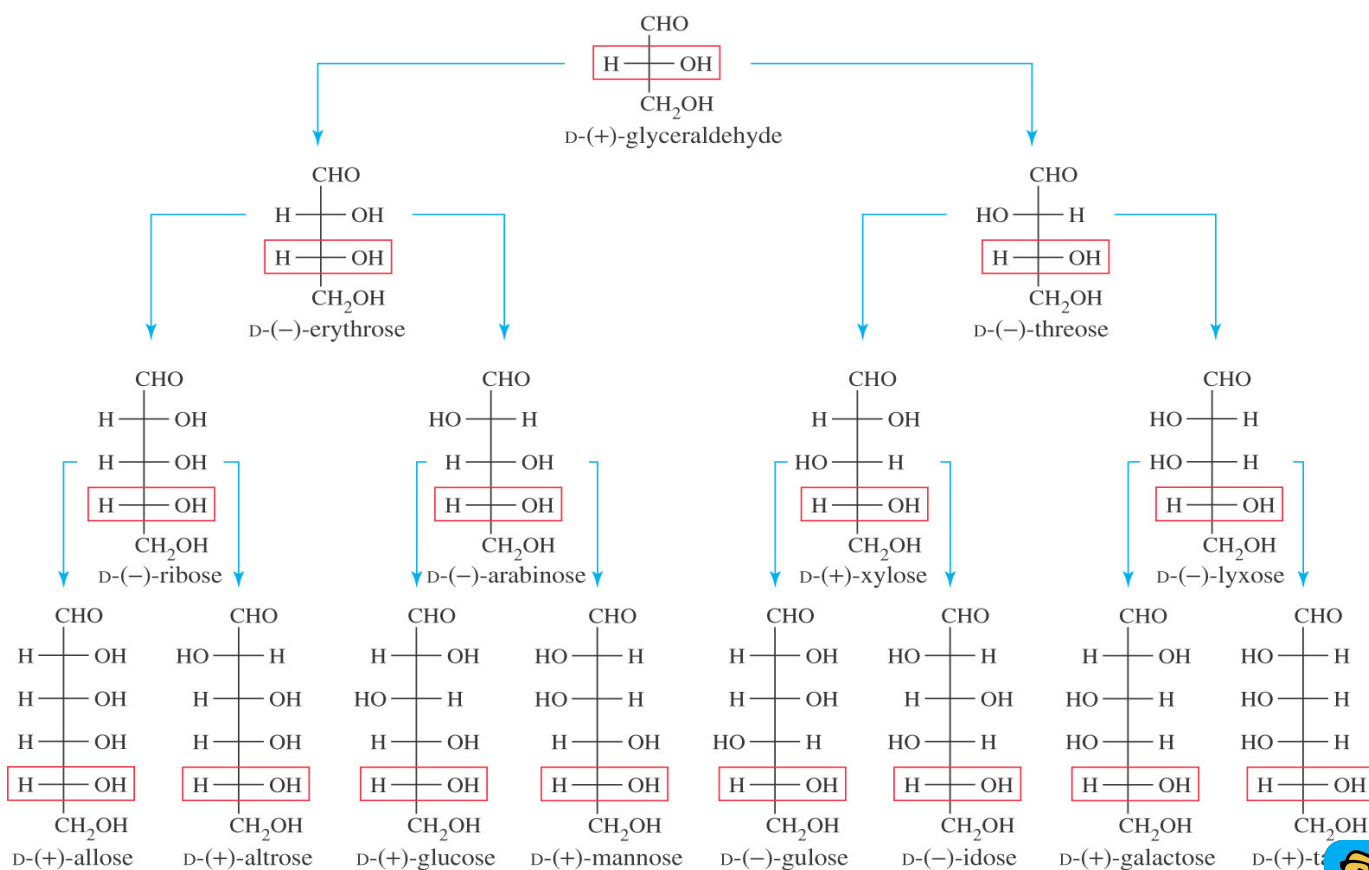
D-(-)-fructose



L-(+)-fructose

- most naturally occurring sugars are D-series

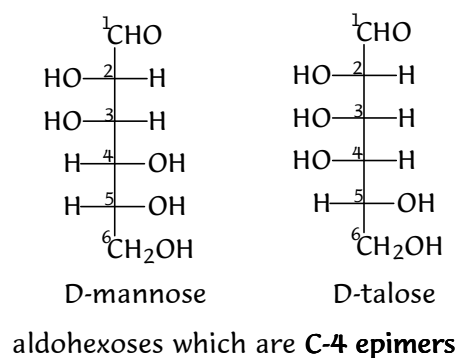
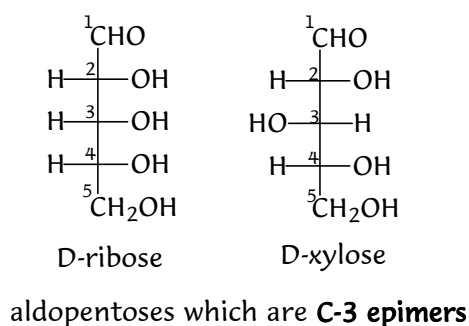
## Family of D-Aldoses



## EPIMERS –

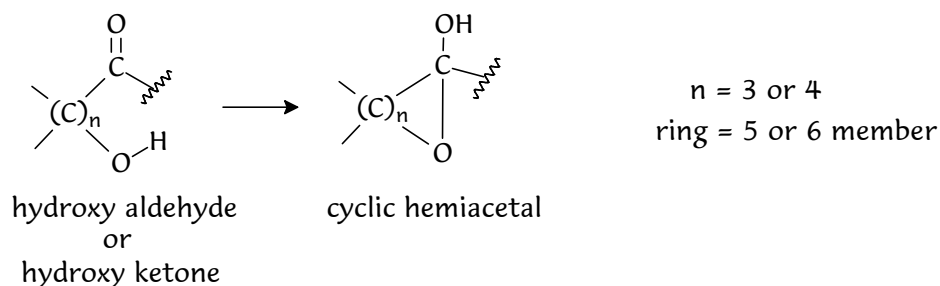
- a pair of sugars which differ in configuration at **one asymmetric carbon (C\*) only**
- while the unique configuration can exist at *any* stereocenter, the most common class of epimers differ in configuration at C-2 (in which case the carbon's number may be understood & omitted)
- epimers are a class of diastereomers (stereoisomers which are *not* mirror image enantiomers)
- the arrows in the family of D-aldoses (shown on previous page) relate pairs of C-2 epimers

### Other EX 's

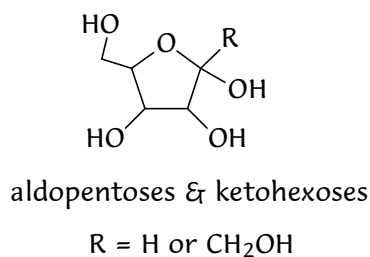
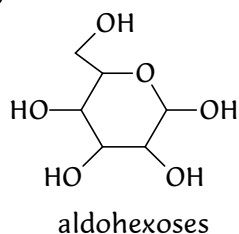


## CYCLIC STRUCTURES OF MONOSACCHARIDES –

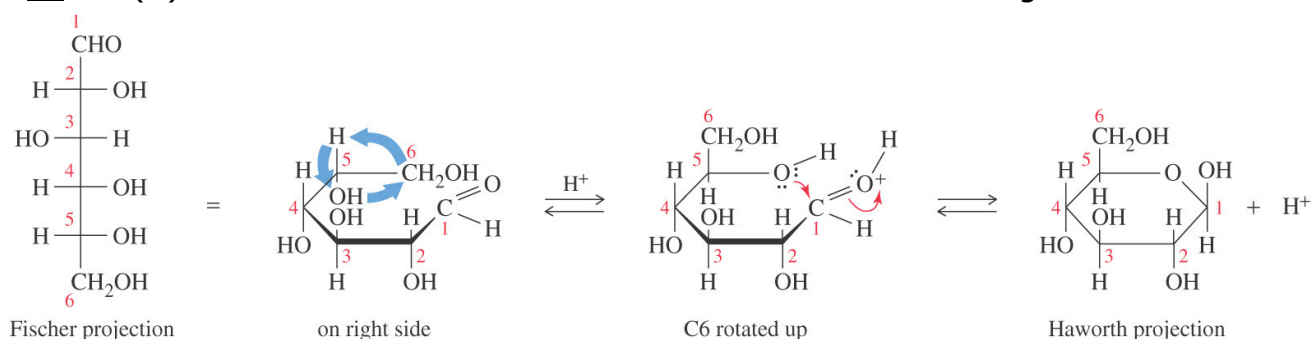
- recall that the intramolecular addition reaction of a  $\gamma$  or  $\delta$ -hydroxycarbonyl compound results in the formation of a cyclic hemiacetal



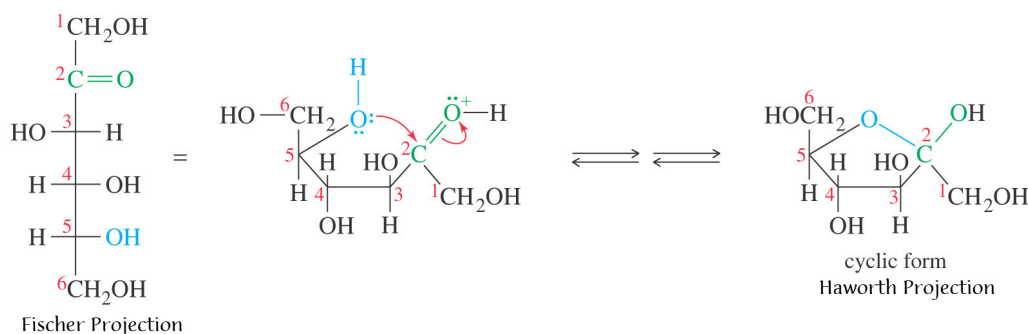
- monosaccharides exist predominately (>99%) in this more stable cyclic hemiacetal form
- aldohexoses form six-membered ring hemiacetals, while aldopentoses & ketohexoses form five-membered ring hemiacetals



**EX.** D-(+)-Glucose ➤ an aldohexose which forms a six-membered ring hemiacetal



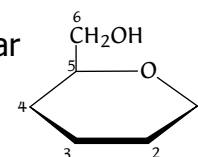
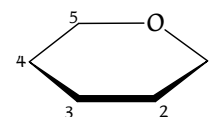
**EX.** D-(-)-Fructose ➤ a ketohexose which forms a five-membered ring hemiacetal



## Drawing Haworth Projection Formulas –

### Six-Membered Ring Hemiacetals –

- draw a flat cyclohexane with hemiacetal ring oxygen in the upper right corner
- the hemiacetal carbon is on the right side of the ring @ C-1
- number the ring clockwise from C-1 to C-5
- C-6 is the  $\text{-CH}_2\text{OH}$  group which points up in a D-sugar & down in an L-sugar



- the configurations @ C-2, C-3 & C-4 are determined from the following correlation:

### Fischer Projection

-OH *Right*

-OH *Left*

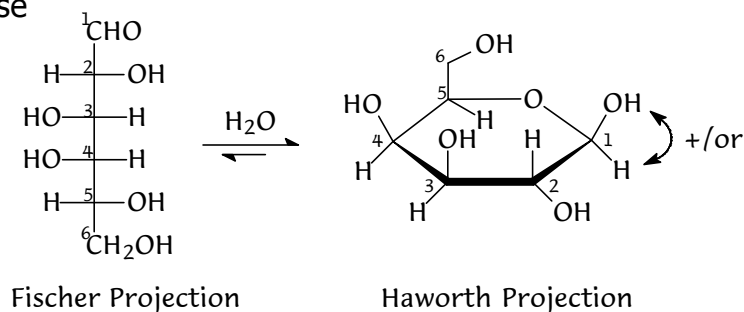
### Haworth Projection

-OH *Down*

-OH *Up*

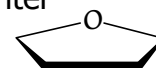
- the configuration @ C-1 is indeterminate (-OH can be either up or down)

EX. D-(+)- Galactose

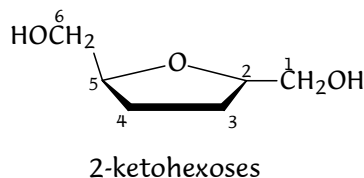
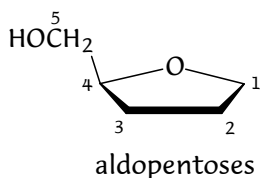


Five-Membered Ring Hemiacetals –

- draw a flat cyclopentane (pointing "back") with hemiacetal ring oxygen in the center
- the hemiacetal carbon is on the right side of the ring:



- @ C-1 in aldopentoses or @ C-2 in ketohexoses (C-1 is a -CH<sub>2</sub>OH)
- number the ring clockwise from C-1 to C-4 (aldopentoses) or C-2 to C-5 (ketohexoses)
- C-5 or C-6 is the -CH<sub>2</sub>OH group which points up in a D-sugar & down in an L-sugar



- the configurations @ C-2 & C-3 (aldopentoses) or @ C-3 & C-4 (ketohexoses) are determined from the following correlation:

Fischer Projection

-OH *Right*

-OH *Left*

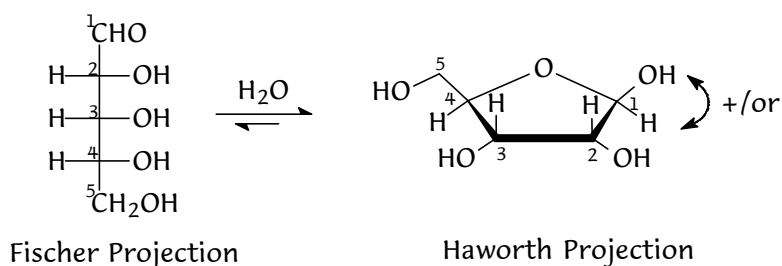
Haworth Projection

-OH *Down*

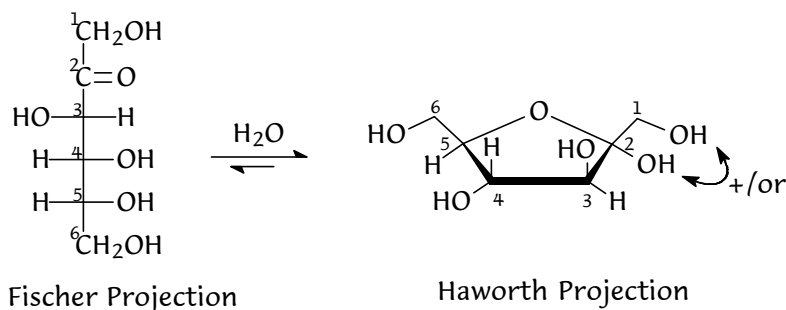
-OH *Up*

- the configuration @ C-1 (aldopentoses) or @ C-2 (ketohexoses) is indeterminate (-OH can be either up or down)

EX. D-(-)- Ribose ➤ an aldopentose



EX. D-(-)- Fructose ➤ a 2-ketohexose

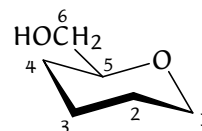


### Conformations of Six-Membered Ring Hemiacetals –

- the most stable cyclic hemiacetal form for aldohexoses is the **chair** conformer

#### Drawing Chair Conformers for Aldohexoses –

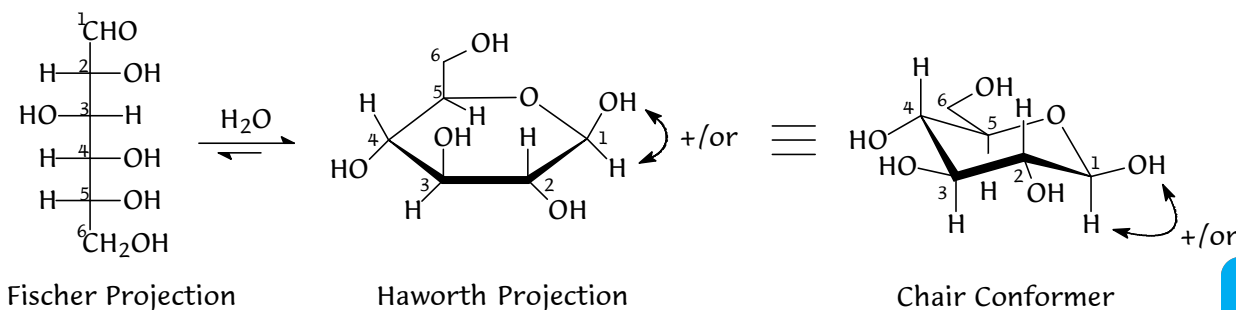
- arrange a chair with the hemiacetal carbon (C-1) pointing down on the right
- place the hemiacetal oxygen in the upper right position
- number the ring clockwise from C-1 to C-5
- C-6 is the  $\text{-CH}_2\text{OH}$  group which points up in a D-sugar & down in an L-sugar
- the configurations @ C-2, C-3 & C-4 are determined from the following correlation:



| <u>Fischer Projection</u> | <u>Haworth Projection</u> | <u>Chair Conformer</u> |
|---------------------------|---------------------------|------------------------|
| -OH <i>Right</i>          | -OH <i>Down</i>           | -OH <i>Down</i>        |
| -OH <i>Left</i>           | -OH <i>Up</i>             | -OH <i>Up</i>          |

- the configuration @ C-1 is indeterminate (-OH can be either up or down)
- the most stable aldohexose chair conformations will have the most equatorial -OH's

EX. D-(+)- Glucose

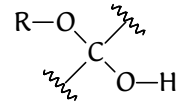


## Anomers –

- diastereomers resulting from the indeterminate configuration at the hemiacetal carbon (C-1 or C-2) where the -OH can point either up or down

### Anomeric Carbon –

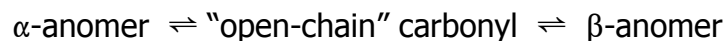
- the original carbonyl carbon (C=O) which reacts & becomes the cyclic hemiacetal carbon
- this position is C-1 in aldopentoses & aldohexoses and C-2 in ketohexoses
- it is the only carbon in the ring with two oxygens attached
- anomers are also a class of **epimers** (diastereomeric sugars with identical configurations at every stereocenter except one)
- anomers are distinguished as follows:



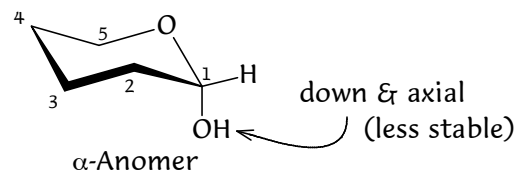
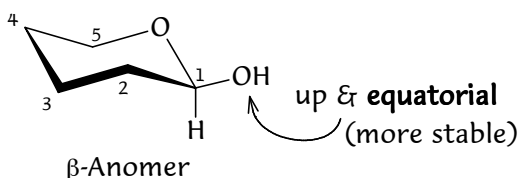
| <u>Name</u>              | <u>Configuration @ Anomeric Carbon</u> |
|--------------------------|----------------------------------------|
| $\alpha$ -Anomer (Alpha) | -OH <i>Down</i>                        |
| $\beta$ -Anomer (Beta)   | -OH <i>Up</i>                          |

## Mutarotation –

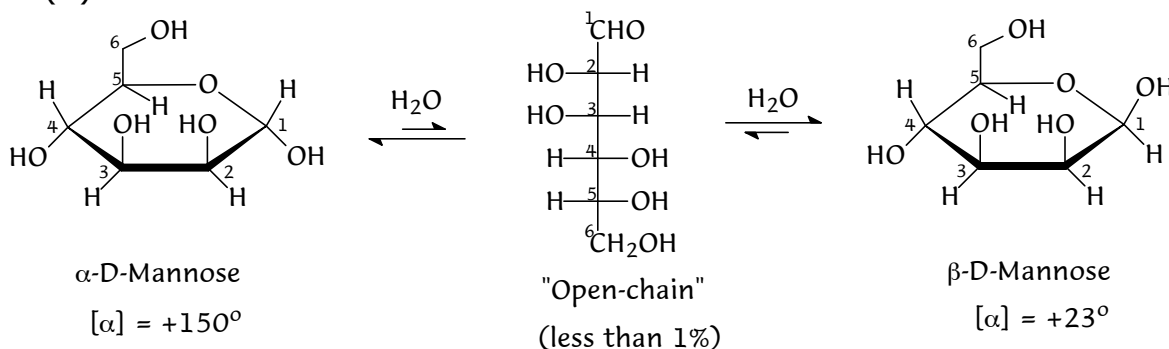
- because anomers are diastereomers, they have unique physical properties
- therefore, the specific rotation  $[\alpha]$  values for anomers will be different
- placing either the  $\alpha$ -anomer or the  $\beta$ -anomer in solution results in a “drift” of the specific rotation value  $[\alpha]$  to a **mutual** value between the values of the two anomers
- the phenomenon of mutarotation is the result of an equilibrium which exists between the  $\alpha$ -anomer & the  $\beta$ -anomer in solution:



- for aldohexoses, the mutarotation value is always **closer** to the value for the  $\beta$ -anomer
- this indicates that the equilibrium mixture contains more of the **more stable**  $\beta$ -anomer
- the  $\beta$ -anomer is more stable because the -OH on the anomeric carbon (C-1) is up & **equatorial**



### EX. D-(+)- Mannose



- after equilibrium has been established, the mutarotation value for D-(+)-mannose is:

$$[\alpha]_{\text{eq}} = +60^\circ \quad (\text{closer to the specific rotation value for the } \beta\text{-anomer})$$

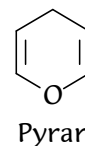
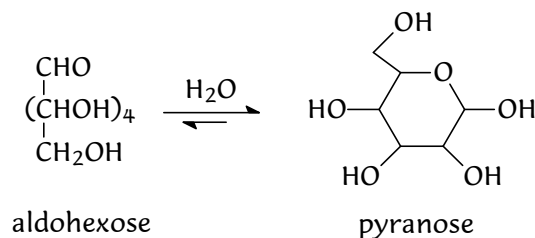
### Naming Cyclic Monosaccharides –

- sugars are classified and named according to hemiacetal ring size:

#### Pyranoses –

- six-membered ring hemiacetals (from *pyran*, a six-membered oxygen heterocycle)

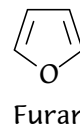
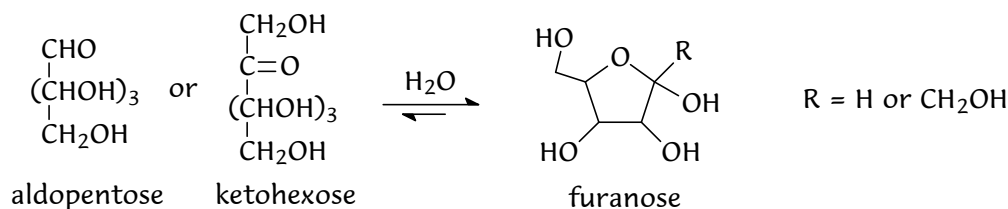
- pyranoses are the cyclic derivations of aldohexoses:



#### Furanoses –

- five-membered ring hemiacetals (from *furan*, a five-membered oxygen heterocycle)

- furanoses are the cyclic derivations of aldopentoses & ketohexoses:

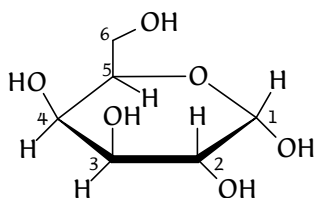


- the complete name of a specific monosaccharide in its cyclic hemiacetal form would include the prefix of that sugar's name:

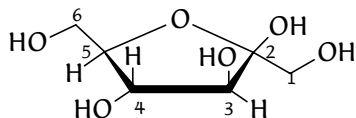
< $\alpha$  or  $\beta$ > - <D or L> - <sugar name prefix> - <pyran or furan> - ose



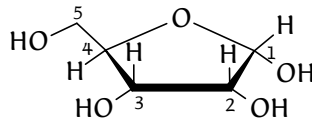
## EX's



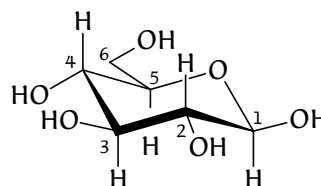
$\alpha$ -D-galactopyranose



$\beta$ -D-fructofuranose



$\alpha$ -D-ribofuranose



$\beta$ -D-glucopyranose

- students are responsible for knowing the structural formulas of the following monosaccharides:

D-(+)-Glyceraldehyde (an aldotriose)

D-(-)-Ribose (an aldopentose)

D-(+)-Glucose (an aldohexose)

D-(+)-Galactose (an aldohexose)

D-(+)-Mannose (an aldohexose)

D-(-)-Fructose (an ketohexose)

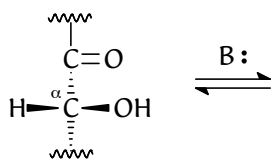
- only the Fischer projection formulas require memorization – the Haworth projection & chair conformer structural formulas are derived from the Fischer projection's pattern of -OH's
- note that there is no correlation between D/L (a drawing convention) & +/- (a physical property)
- students are only responsible for D & L structure (+ & - may be ignored)

## REACTIONS OF MONOSACCHARIDES –

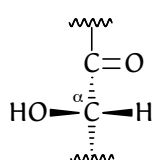
- because they are multifunctional compounds, monosaccharides exhibit the chemical behavior of three unique functional groups – carbonyls, alcohols & hemiacetals
- the small amount of "open-chain" carbonyl form present in the equilibrium accounts for the aldehyde/ketone reactions of monosaccharides

### A. Epimerization –

- a base-catalyzed process where the acidic alpha-hydrogen ( $\alpha$ -H) is removed & replaced, causing the configuration at the alpha-carbon ( $\alpha$ -C) to be racemized (creates epimers)



aldose or ketose

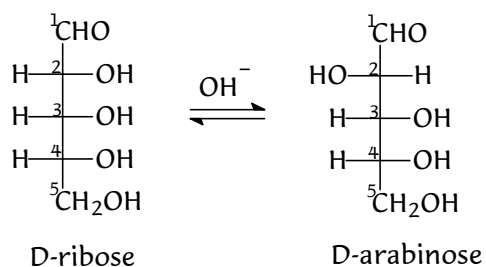


aldose or ketose



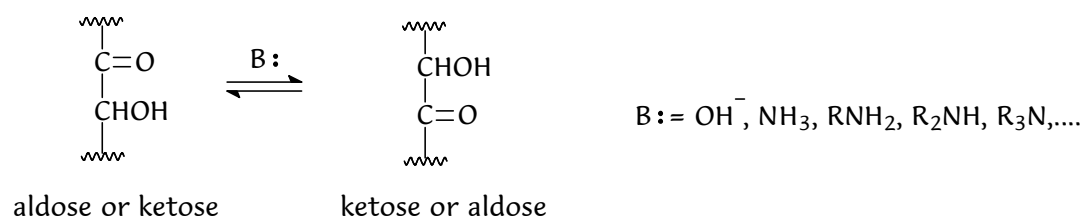
## Mechanism –

EX.



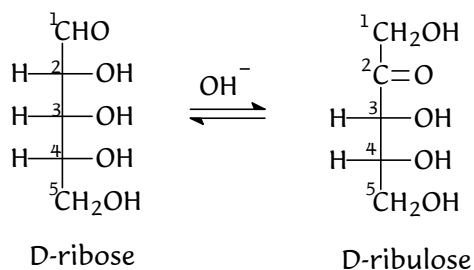
## **B. Eneidiol Rearrangement –**

- a base-catalyzed process where the carbonyl group migrates along the carbon chain
- note that aldoses & ketoses can thus interconvert under basic conditions



## Mechanism –

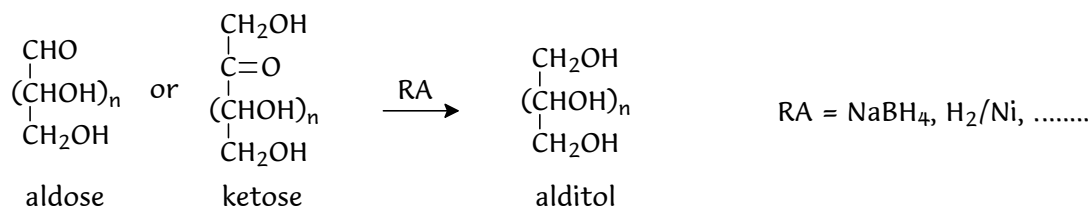
EX.



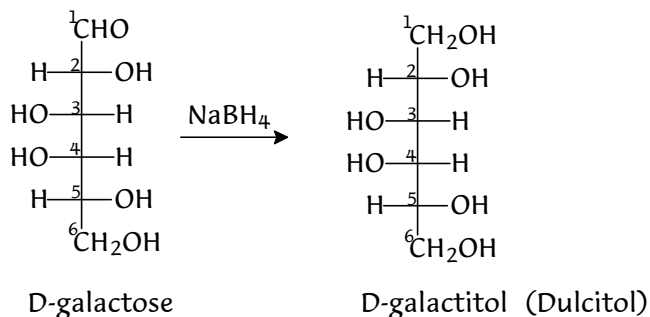
- under basic conditions, monosaccharides will undergo both epimerization & enediol rearrangement, resulting in complex product mixtures
- therefore, contact with alkaline reagents is mostly avoided

### C. Reduction –

- the small amount of “open-chain” carbonyl form present in the equilibrium allows for conversion of the carbonyl to an alcohol



EX.

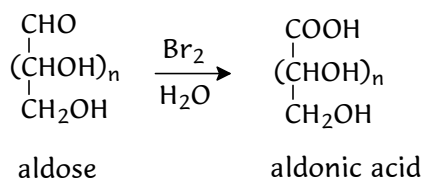


### D. Oxidation –

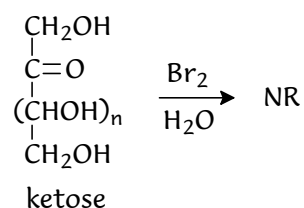
- different oxidizing agents produce different sugar derivatives:

#### 1) Bromine Water, Br<sub>2</sub>/H<sub>2</sub>O

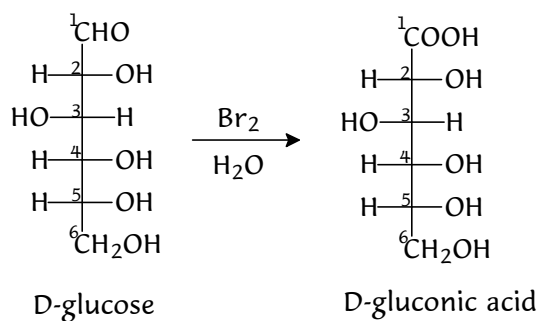
- only the aldehyde group of an aldose reacts:



- ketoses do not react:

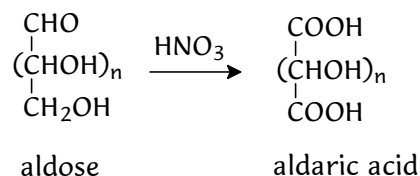


EX.

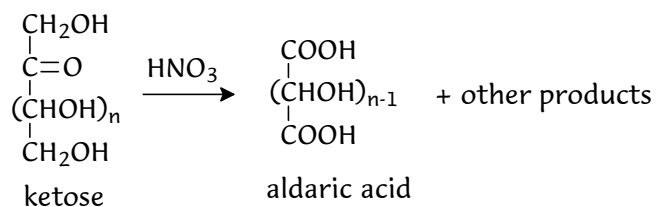


## 2) Nitric Acid, $\text{HNO}_3$

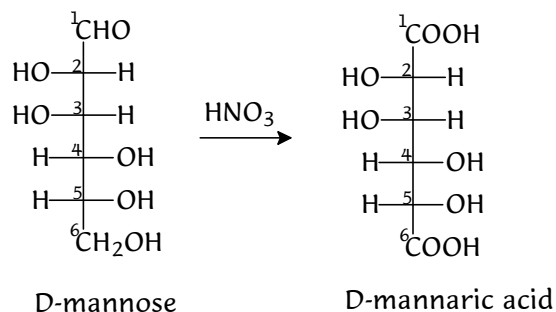
- both the aldehyde & primary alcohol groups of an aldose are oxidized:



- ketoses also react, giving more complex product mixtures:

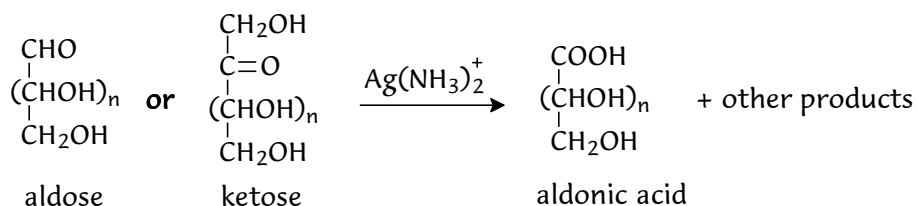


EX.



### 3) Tollen's Reagent, $\text{Ag}(\text{NH}_3)_2^+$

- Tollen's reagent provides a simple visible chemical test for aldehydes (a silver mirror is produced upon oxidation indicating a "positive test")
- other oxidizing agents, such as Fehling's & Benedict's solutions (copper(II) complexes) produce similar observable results with aldehydes (a red precipitate indicates a positive test)
- all of these reagents are strongly basic, and therefore cause epimerization & enediol rearrangement to occur with monosaccharides, resulting in complex product mixtures
- since enediol rearrangement converts ketoses to aldoses, ketoses are also ultimately oxidized & give positive tests, making them indistinguishable from aldoses:



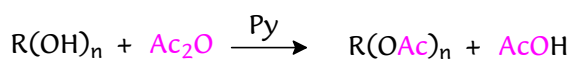
- while Tollen's reagent may not be useful for distinguishing aldoses from ketoses, it is useful for identifying a certain class of carbohydrates:

#### Reducing Sugars, RS –

- sugars which *reduce* Tollen's reagent (& related OA's), becoming oxidized themselves
- include all aldoses & ketoses (which equilibrate in the cyclic hemiacetal form)
- exist as anomers & exhibit mutarotation  $(\alpha\text{-anomer} \rightleftharpoons \beta\text{-anomer})$

### E. Ester Formation –

- all hydroxy groups in the monosaccharide react (like alcohols) with acid derivatives to produce ester groups



$\text{R}(\text{OH})_n$  = sugar, **all** OH's react, including hemiacetal OH

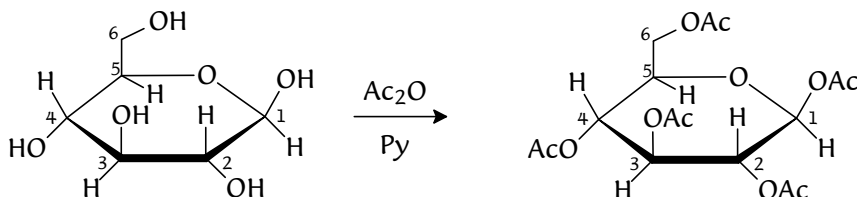
$\text{Ac} = \text{—}\overset{\text{O}}{\parallel}\text{C—CH}_3$  (acetyl group); other acyl groups possible

$\text{Ac}_2\text{O} = \text{CH}_3\text{—}\overset{\text{O}}{\parallel}\text{C—O—}\overset{\text{O}}{\parallel}\text{C—CH}_3$  (acetic anhydride); other acid derivatives possible

$\text{Py} =$   (pyridine); other bases possible

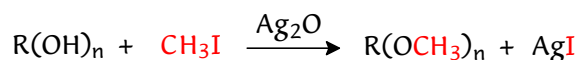


EX.



## E. Ether Formation –

- all hydroxy groups in the monosaccharide react (like alcohols) with alkyl halides to produce ether groups



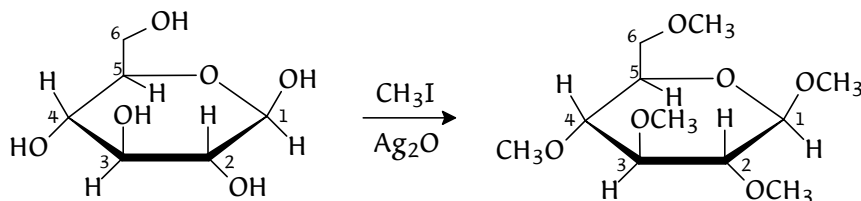
$R(OH)_n$  = sugar, **all** OH's react, including hemiacetal OH

$\text{CH}_3$  (Methyl) most common alkyl group; others possible

I (Iodo) most common leaving group; others possible

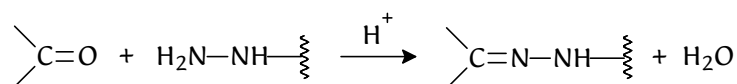
$\text{Ag}_2\text{O}$  (Silver oxide) most common base; others possible

EX.

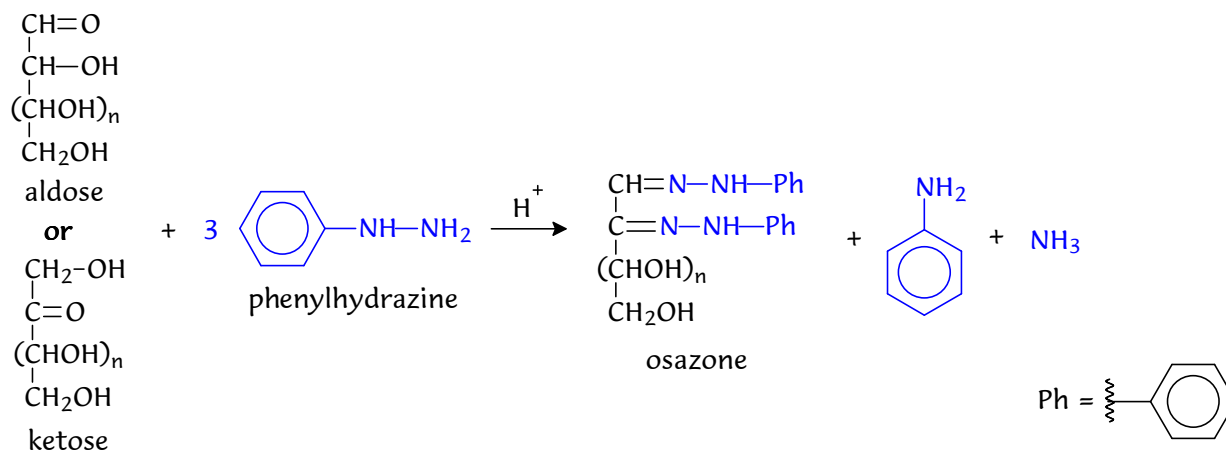


## F. Osazone Formation –

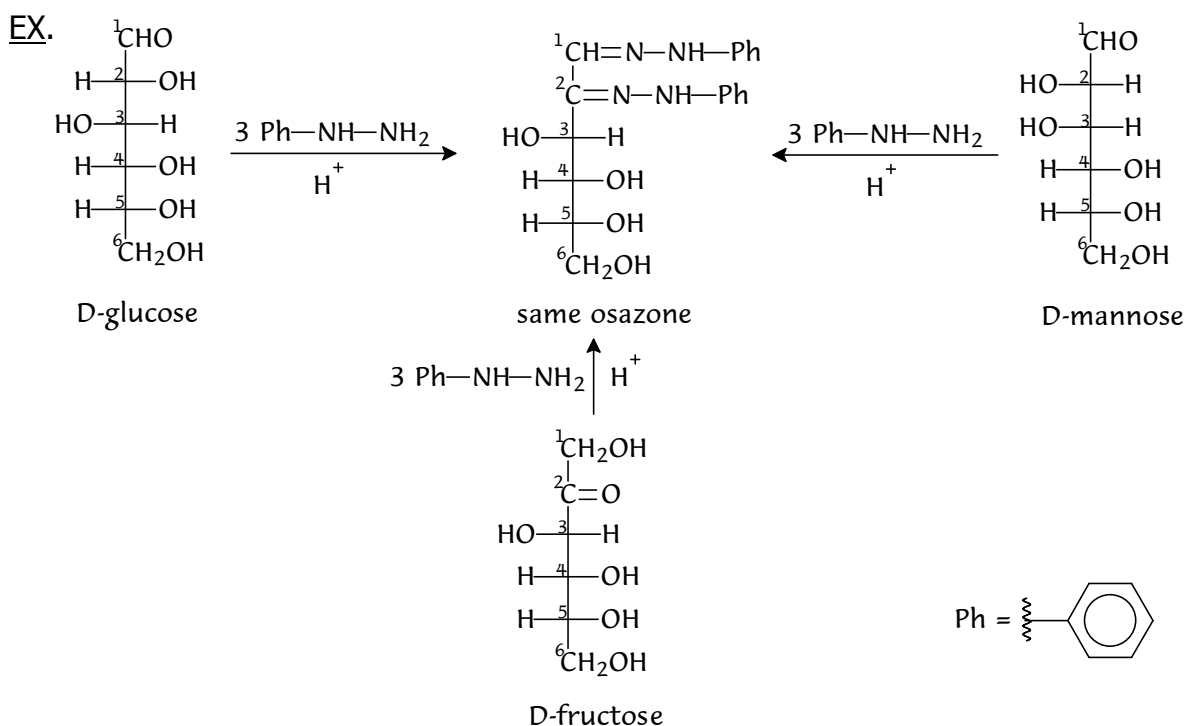
- recall the reaction of carbonyls with hydrazines to produce hydrazones:



- the first two carbons of both aldoses & ketoses react with phenylhydrazine to form a bis-hydrazone known as an osazone
- hydrazone formation at the first carbonyl group is followed by oxidation of the  $\alpha$ -carbon's hydroxyl group to a second carbonyl group which then forms the second hydrazone:

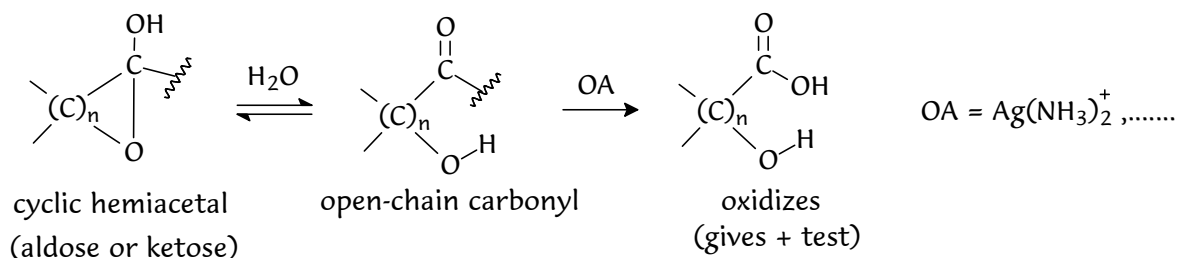


- any difference at C-1 or C-2 is lost in the formation of osazones
- thus, C-2 epimers will form the same osazones (as will related aldoses & ketoses)

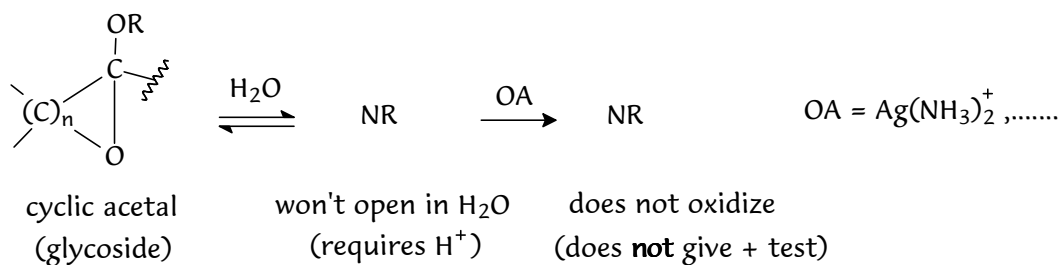


## G. Glycoside Formation –

- recall that Tollen's reagent (& related OA's) identify *reducing sugars*
- this distinguishes them from *nonreducing sugars* which do not give positive Tollen's tests
- this distinction is the result of the different functional groups present in these two cyclic monosaccharide classes:
  - the reducing sugar has a hemiacetal group which opens in water
  - the nonreducing sugar has an acetal group which does not open in water:

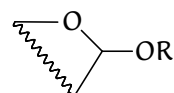


therefore; **reducing** sugars are **hemiacetals**



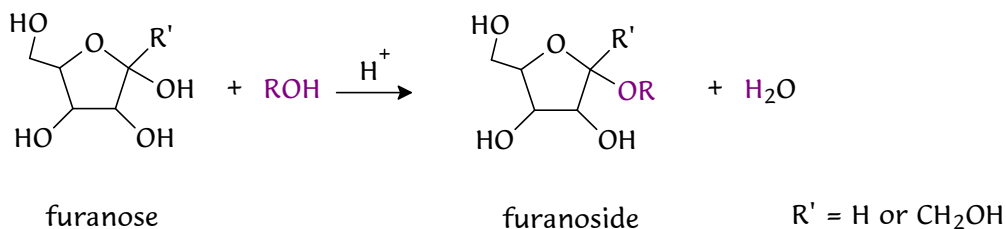
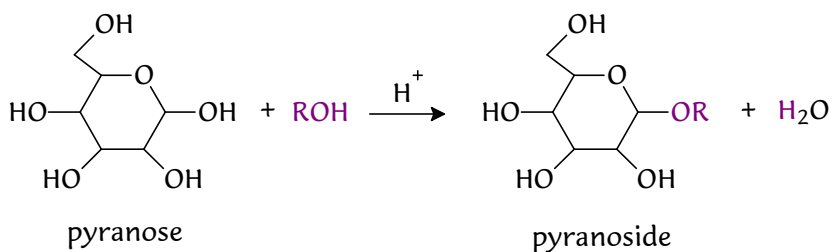
therefore; **nonreducing** sugars are **acetals** (glycosides)

- **Glycosides** are cyclic **acetal** forms of sugars



- they are prepared by the acid-catalyzed reaction of an alcohol with a pyranose or furanose

- note that only the anomeric (hemiacetal) carbon's hydroxyl group reacts under these conditions



ROH = CH<sub>3</sub>OH, CH<sub>3</sub>CH<sub>2</sub>OH, PhOH, another monosaccharide,.....

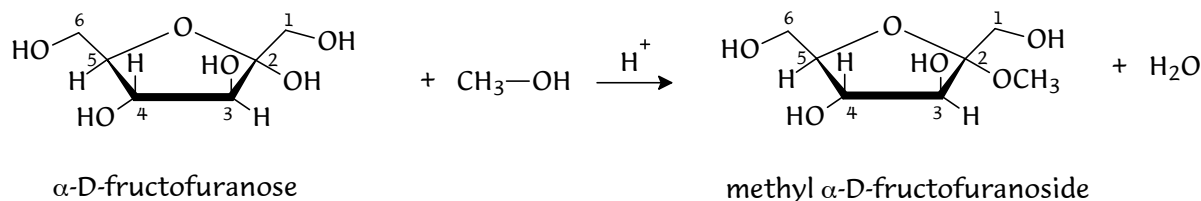
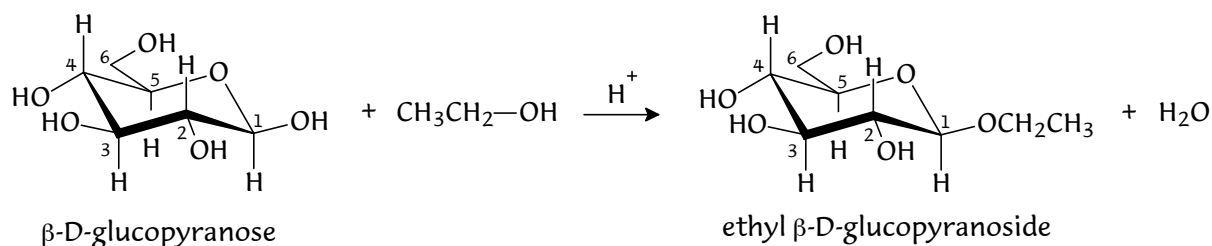
### Naming Glycosides –

- place R group (alkyl or aryl) name in front (separate word)

- change ending from **e** ⇒ **ide**



## EX's Preparation & naming of glycosides



- note the distinct contrast in chemical behavior between reducing & nonreducing sugars:

### Nonreducing Sugars, NRS –

- sugars which *do not* reduce Tollen's reagent (& related OA's)
- are glycosides (cyclic acetals)
- *do not* equilibrate in water with the "open-chain" carbonyl form
- *do not* exhibit anomerism or mutarotation  $\left( \alpha\text{-anomer} \nleftrightarrow \beta\text{-anomer} \right)$

## II. DISACCHARIDES –

- sugars composed of two monosaccharides connected in glycoside (acetal) linkages
- the glycosidic bond is formed between the anomeric carbon of the "first" monosaccharide unit & the hydroxyl group of the "second" monosaccharide unit
- disaccharides can be categorized according to the position of the hydroxyl group on the "second" monosaccharide unit making up the glycoside:

| <u>OH Position on 2<sup>nd</sup> MS Unit</u> | <u>Disaccharide Class</u> |
|----------------------------------------------|---------------------------|
| @ C-4                                        | 1→4' Glycoside            |
| @ C-6                                        | 1→6' Glycoside            |
| @ C-1                                        | 1→1' Glycoside            |
| @ C-2                                        | 1→2' Glycoside            |

- disaccharides can be categorized according to the configuration at the anomeric carbon of the first monosaccharide unit:

| <u>"OR" Position on Anomeric C of 1<sup>st</sup> MS Unit</u> | <u>Disaccharide Class</u>   |
|--------------------------------------------------------------|-----------------------------|
| Up                                                           | $\beta$ -Glycoside (beta)   |
| Down                                                         | $\alpha$ -Glycoside (alpha) |

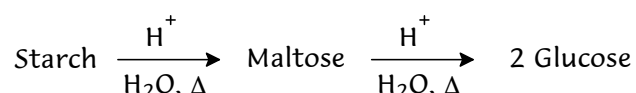
- typical monosaccharide units found in naturally occurring disaccharides are *glucose*, *galactose* & *fructose*

## A. 1→4' Glycosides –

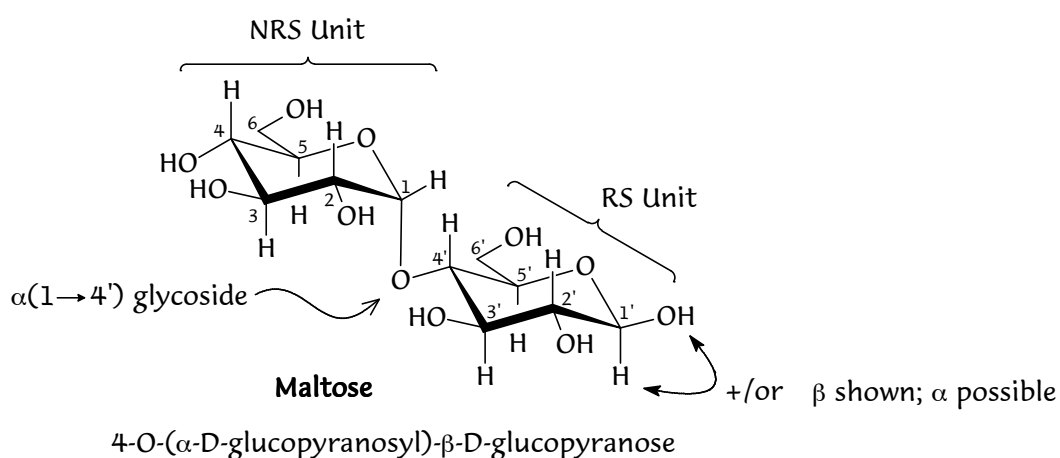
- these represent the most common naturally occurring disaccharides
- the anomeric carbon (C-1) of the first MS unit is connected through the C-4 OH of the second MS unit

### 1) Maltose –

- this disaccharide is a hydrolysis product of starch:

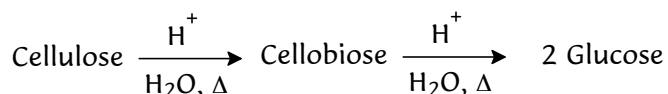


- maltose can be described as: **two glucose units in an  $\alpha(1 \rightarrow 4')$  glycoside** (glucoside)

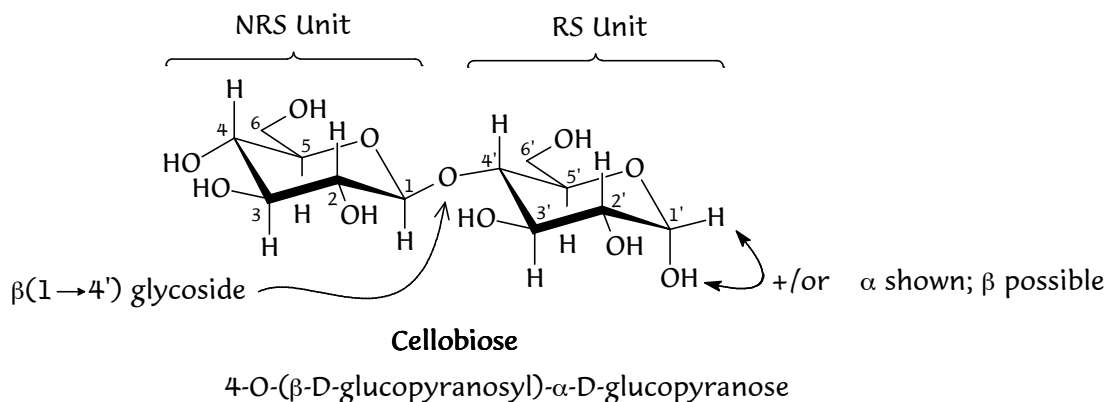


## 2) Cellobiose –

- this disaccharide is a hydrolysis product of cellulose:

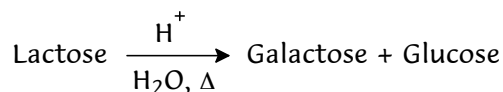


- cellobiose can be described as: **two glucose units in a  $\beta(1 \rightarrow 4')$  glycoside** (glucoside)

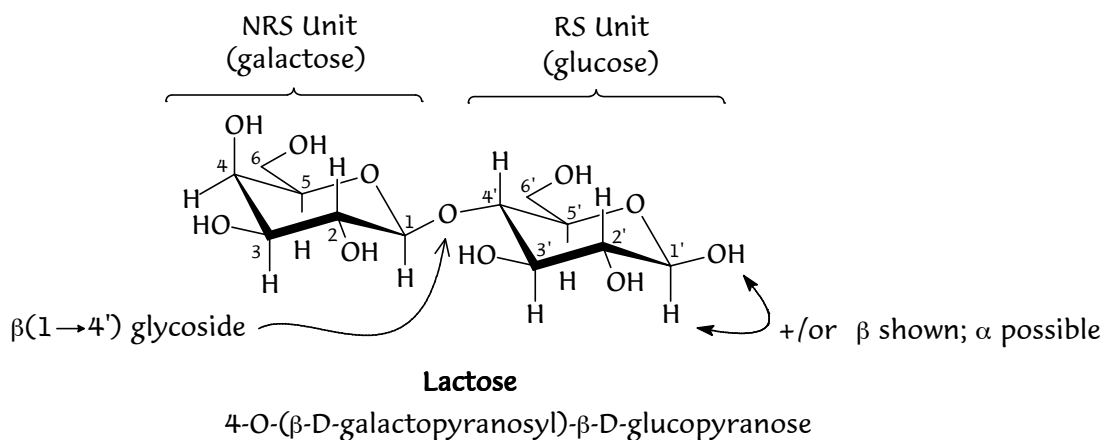


## 3) Lactose –

- a naturally occurring disaccharide found in the milk of mammals such as cows & humans
- lactose yields galactose & glucose upon hydrolysis:



- lactose can be described as: **galactose** (nonreducing) & **glucose** (reducing) **units in a  $\beta(1 \rightarrow 4')$  glycoside** (galactoside)

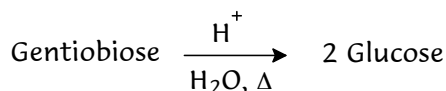


## B. 1→6' Glycosides –

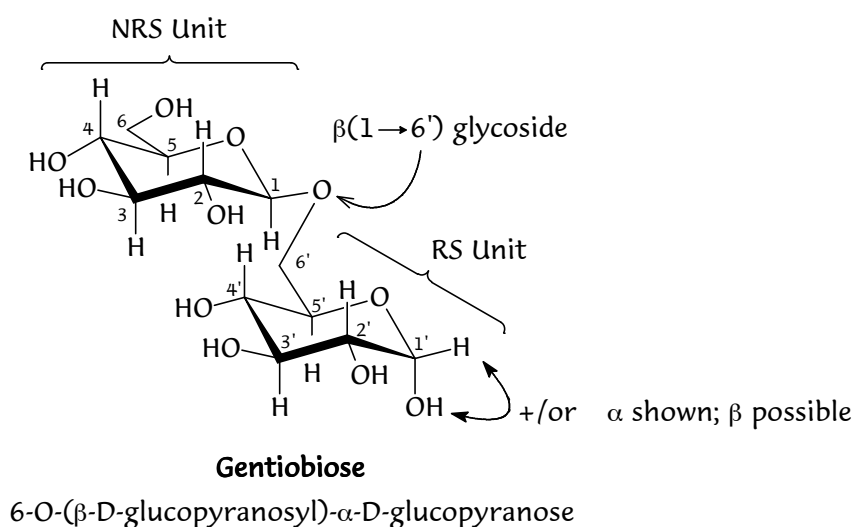
- the anomeric carbon (C-1) of the first MS unit is connected through the C-6 OH of the second MS unit

### Gentiobiose –

- this disaccharide is incorporated into crocin, the principle component of saffron



- gentiobiose can be described as: **two glucose units in a β(1→6') glycoside** (glucoside)

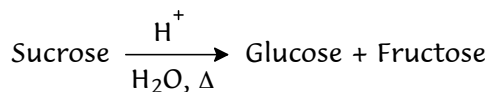


## C. 1→2' Glycosides –

- these compounds & their related 1→1' glycosides represent the *nonreducing disaccharides*
- the glycosidic linkage involves the anomeric carbons from both monosaccharide units

### Sucrose –

- a naturally occurring disaccharide found in sugar cane & sugar beets (table sugar)
- hydrolysis of sucrose yields glucose & fructose

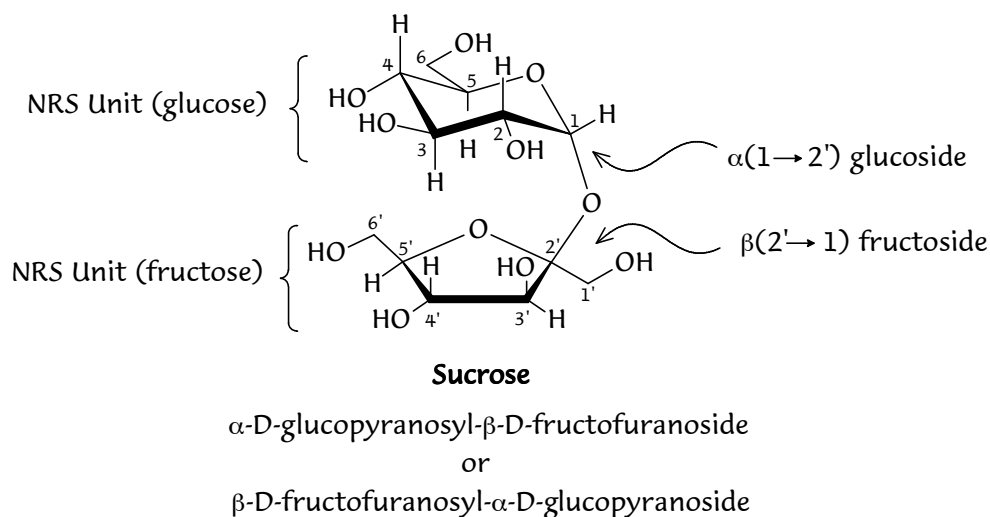


- sucrose can be described two ways:

**glucose & fructose units in an α(1→2') glycoside** (glucoside)

or; **fructose & glucose units in a β(2'→1) glycoside** (fructoside)





## Naming Disaccharides –

- the following systematic nomenclature method is used for disaccharides:

1) identify the hydroxyl oxygen making the glycosidic bond as a number prefix followed by O

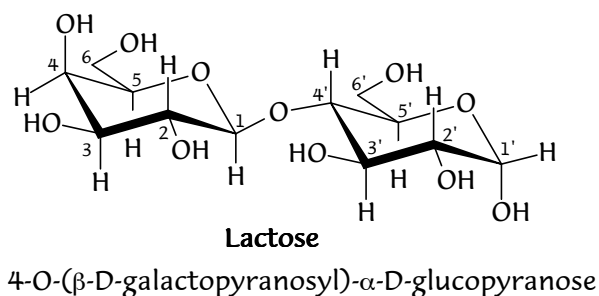
EX. 4-O- prefix indicates the RS unit's C-4 OH makes the glycoside

2) name the NRS unit (left), changing the ending from ose  $\rightarrow$  osyl

3) name the RS unit (right) as a normal cyclic monosaccharide & indicate the anomer present

- students are not responsible for common names of disaccharides

EX.



## III. POLYSACCHARIDES –

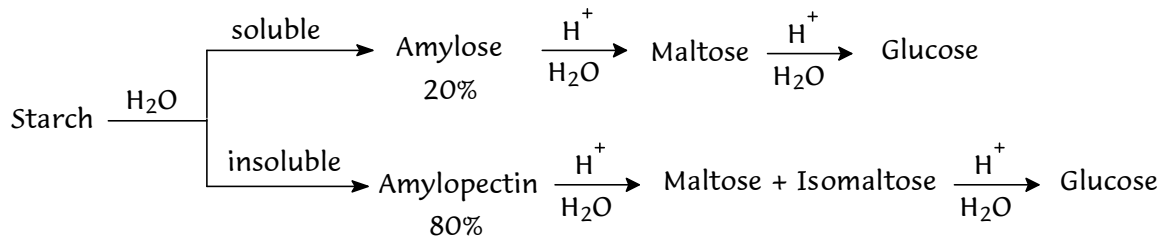
- macromolecules made up of long chains of monosaccharide units joined in glycosidic linkages

- the most common polysaccharides are polymers of glucose



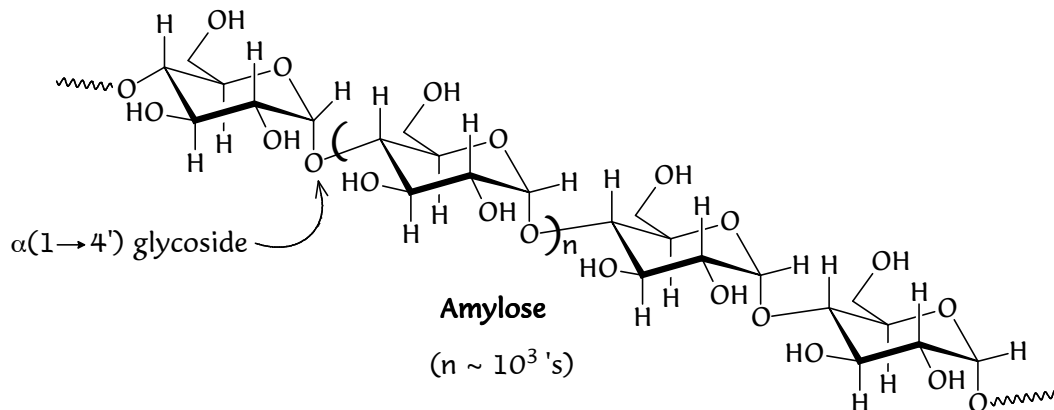
## A. Starch –

- the glucose (energy) storage form for plants
- starch contains two components, which are separable on the basis of water solubility



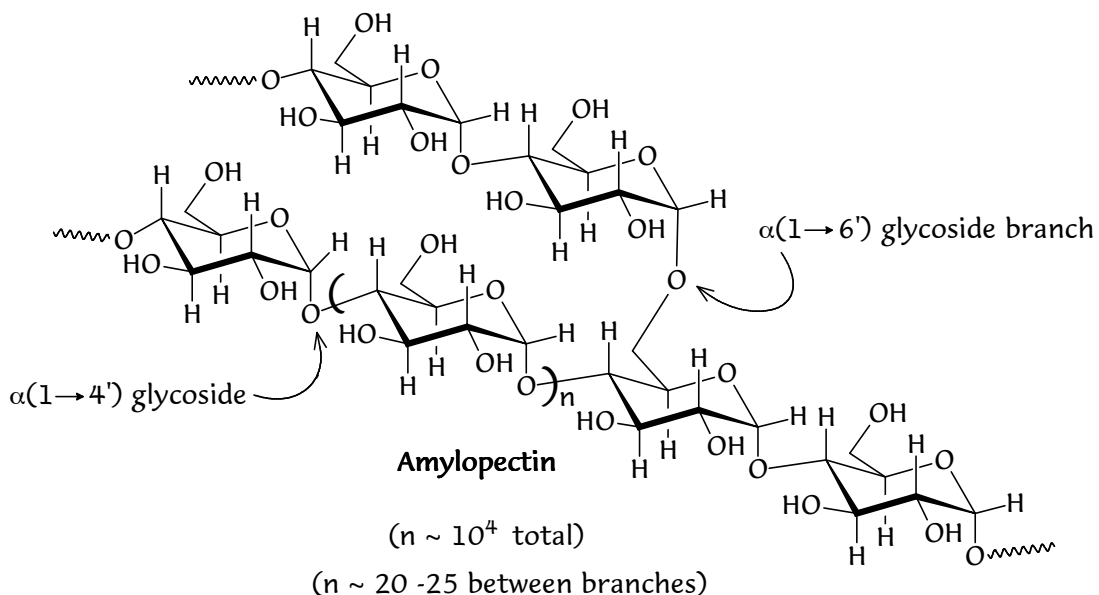
### 1) Amylose –

- a linear polymer of glucose units in  $\alpha(1 \rightarrow 4')$  glycosides (glucosides)



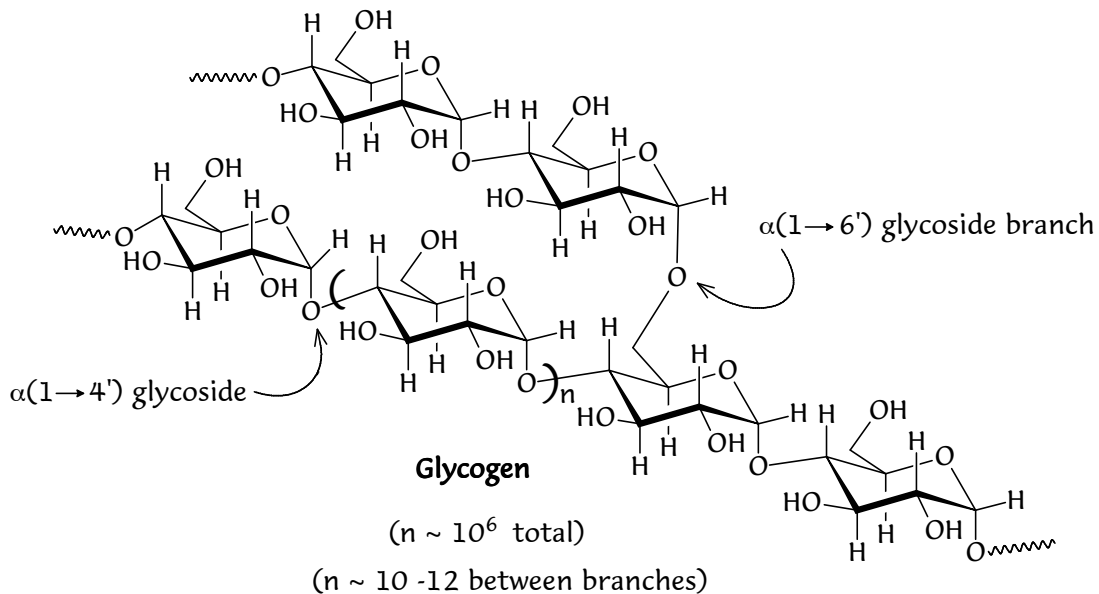
### 2) Amylopectin –

- a branched polymer of glucose units in  $\alpha(1 \rightarrow 4')$  glycosides with  $\alpha(1 \rightarrow 6')$  glycoside branches



## B. Glycogen –

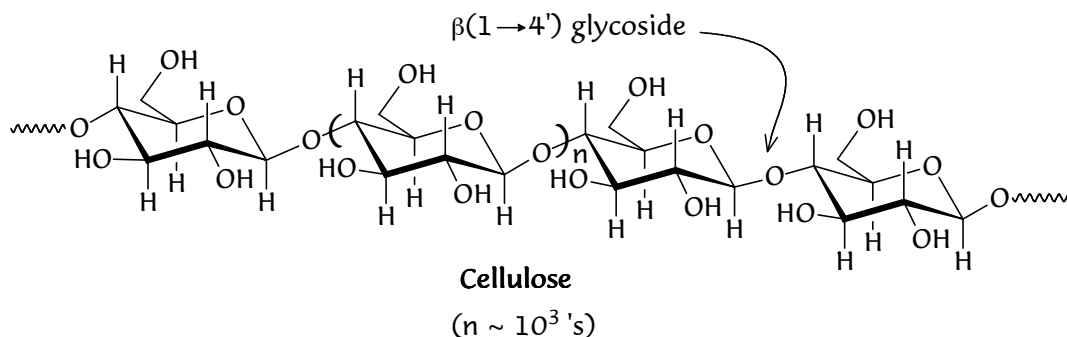
- the glucose (energy) storage form for animals
- a branched polymer of glucose units in  $\alpha(1\rightarrow4')$  glycosides with  $\alpha(1\rightarrow6')$  glycoside branches
- so; same as amylopectin, but more highly branched



- the increased branching in glycogen provides more available glucose “ends” to satisfy the greater metabolic demand of motile organisms

## C. Cellulose –

- the principal component of plant cell walls, providing the plant’s structural strength & rigidity
- a linear polymer of glucose units in  $\beta(1\rightarrow4')$  glycosides (glucosides)



- most organisms cannot digest cellulose because they lack the enzyme which catalyzes the hydrolysis of the  $\beta$ -glucoside