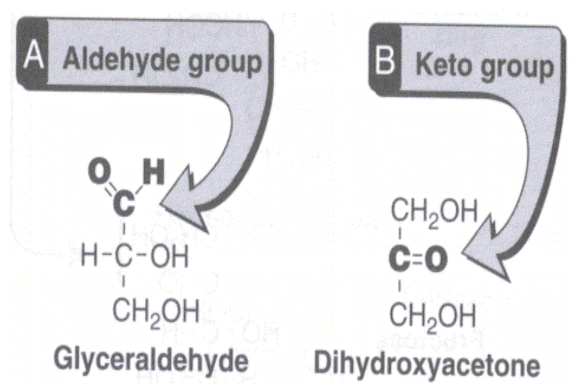
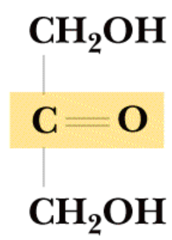
CARBOHYDRATES I

- Carbohydrates are based upon the general formula $C_n(H_20)_n$
  - As if they were hydrates of carbon (most abundant organic molecules in our biosphere)
- Functions of Carbohydrates
  - **Energy source** (glucose)
  - **Energy storage** (glycogen, starch)
  - **Carbon source** (pyruvate used to make Ile, Leu, Val, Ala)
  - **Structure/Protection** (chitin, cellulose, connective tissue)
  - **Recognition/Signaling** (Antibodies used for immune system recognition)
  - Can be **attached** to other **macromolecules** (glycoproteins and glycolipids)
- **Classes** of carbohydrates
  - monosaccharides (simple sugars like glucose)
  - disaccharides (sucrose)
  - trisaccharides
  - polysaccharides (oligosaccharides) (starch, cellulose, glycogen) – long chains of monosaccharides; chains of monosaccharides bridged through oxygen atoms – can be thousands long and can be branched
- Formula $\mathbf{C_n(H_20)_n}$ only holds for monosaccharides
  - one H_2O is eliminated when sugars are linked together to form disaccharides or higher polymers
- Common monosaccharides contain from 3 to 6 carbon atoms
  - these sugars are called trioses, tetroses, pentoses, hexoses
- **Monosaccharides** are either **aldehydes** or **ketones**
  - aldoses or ketoses
- Combining these terms describes the essential structure of sugars
  - glyceraldehyde is an aldotriose
  - glucose is an aldohexose
  - fructose is a ketohexose



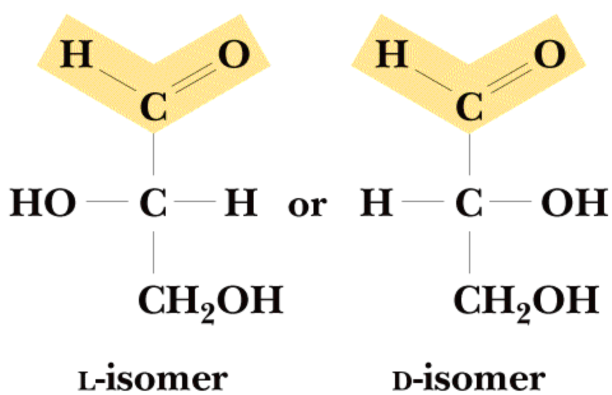
- For Aldoses and Ketoses – the name is based on the location of the carbonyl (C = O)
- The simplest **KETOSE** is **DIHYDROXYACETONE**



Dihydroxy-acetone

- Contains a **KETONE**
- Does **NOT** contain a **chiral** center
- Only monosaccharide that DOES NOT have a chiral center
  - Every other monosaccharide has at least one.
  - A sugar with n chiral centers can exist in 2^n different forms

- The simplest **ALDOSE** is **GLYCERALDEHYDE**



Glyceraldehyde

Contains an **ALDEHYDE** (yellow)

Contains a **CHIRAL** center:

- Carbon with 4 different groups bonded to it
- Because of the chiral center, has two **ENANTIOMERS** – non-superimposable mirror images
  - Called the **D and L forms**
  - **Almost ALL sugars are D**

- **<u>Isomers</u> = same chemical formula, different structure**
- **<u>Epimers</u> = isomers that differ at only one Carbon**
- **<u>Enantiomers</u> = isomers that are mirror images (D and L)**
- **<u>Anomers</u> = isomers that differ only at keto-/aldo carbon**

- These are the **Fischer Projections** for the two isomers of glyceraldehydes: Tell us stereochemistry. Tetrahedral carbon represented by two crossed lines.

Rules:
- Carbons are numbered from the top
- Most oxidized C (one with the most number of bonds to O goes at top (C1)
- Last carbon will ALWAYS be part of a CH_2OH group (Not CHIRAL)
- Vertical lines go into the page
- Horizontal lines come out of the page
- Crosses can also be the carbons
- Stereochemistry of the last CHIRAL carbon (2^{nd} to last C in chain) determines the stereochemistry of the sugar
- **If –OH is to the RIGHT → D-isomer**
- **If –OH is to the LEFT → L-isomer**

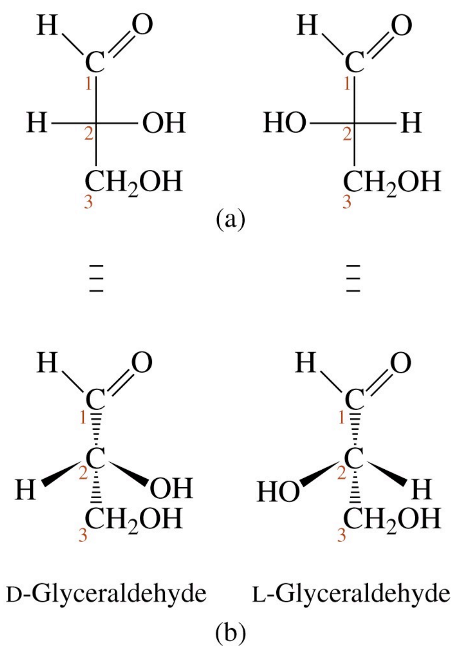
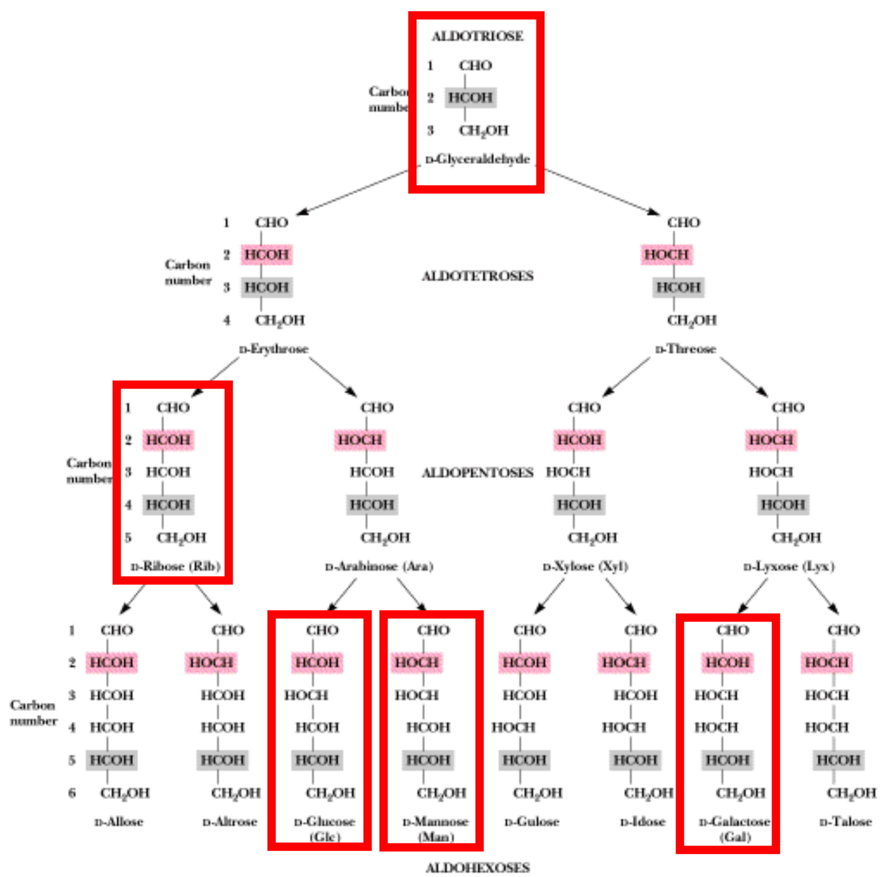
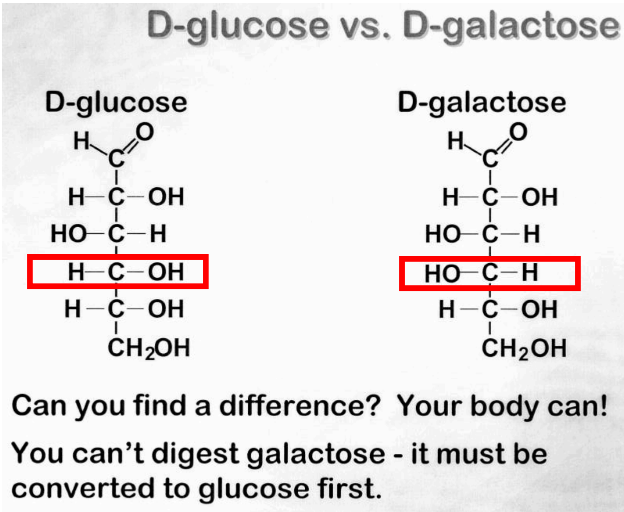


Figure 7-3 Concepts in Biochemistry, 3/e

- There are 15 D-aldose sugars of 3-6 carbons in length that have multiple chiral centers
- Note ALL have –OH to the right in the 2^{nd} to last position (last chiral centers) → D-aldoses
- Note how the positions at other chiral centers change
- All members of a row are **DIASTEREOMERS** of each other
- D-glucose, D-mannose and D-galactose are the most abundant aldohexose monosaccharides

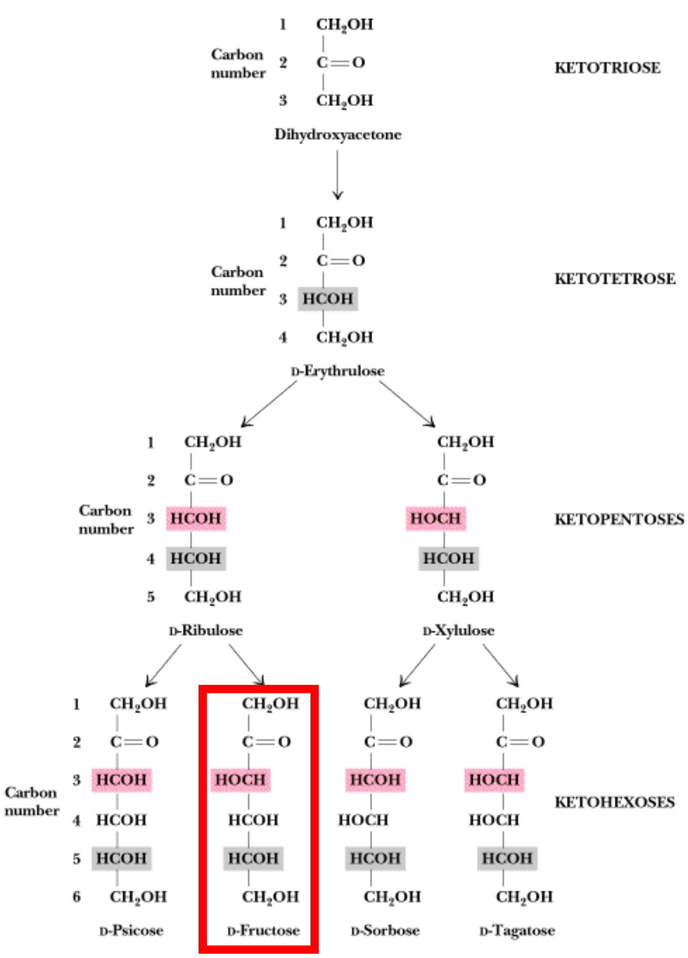


- D-mannose and D-galactose differ stereochemically from D-glucose at only 1 chiral center



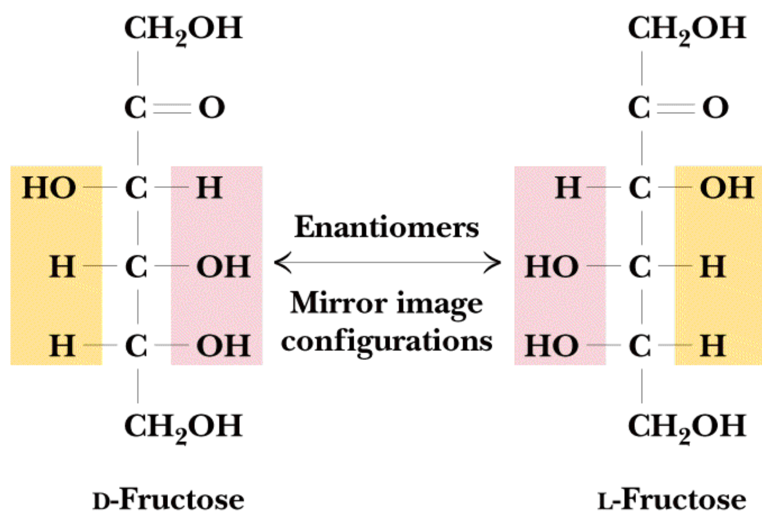
  - Therefore D-mannose and D-galactose are **EPIMERS** of glucose
  - D-galactose is a C-4 Epimer of D-glucose

Same rules apply for **KETOSES**:

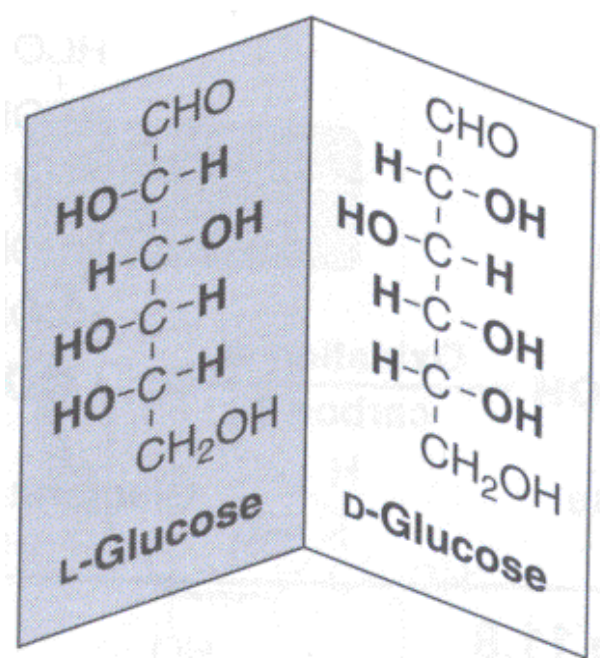


KNOW **D-FRUCTOSE**:

- A common sugar
- A ketohexose
- Sweetest of all sugars
- Similar in structure to D-glucose



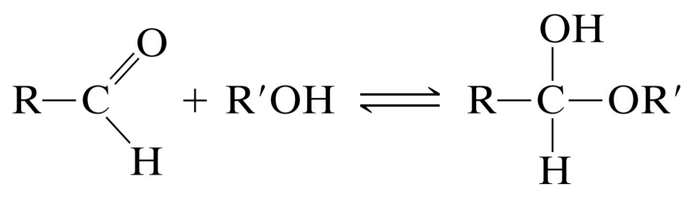
Enantionmers of Fructose: Note, in enantionmers the positions of ALL –OH change, not just the 2nd to last!



CYCLIZATION OF MONOSACCHARIDES

- In solution, monosaccharides are cyclic – especially C5 and C6 sugars
- Drawn as **HAWORTH PROJECTIONS** – Show all hydroxyls, oxygens, and hydrogens – no carbons
- **TWO CASES OF CYCLIZATION:**
    - **HEMIACETALS**:

Carbonyl reacting with hydroxyl group → addition product called <u>hemiacetal.</u> Carbon center bonded to one R-group, a H atom, an –OH and an –OR'.



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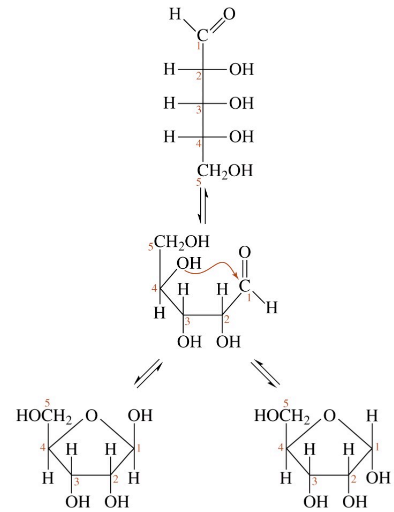

Figure 7-7a Concepts in Biochemistry, 3/e
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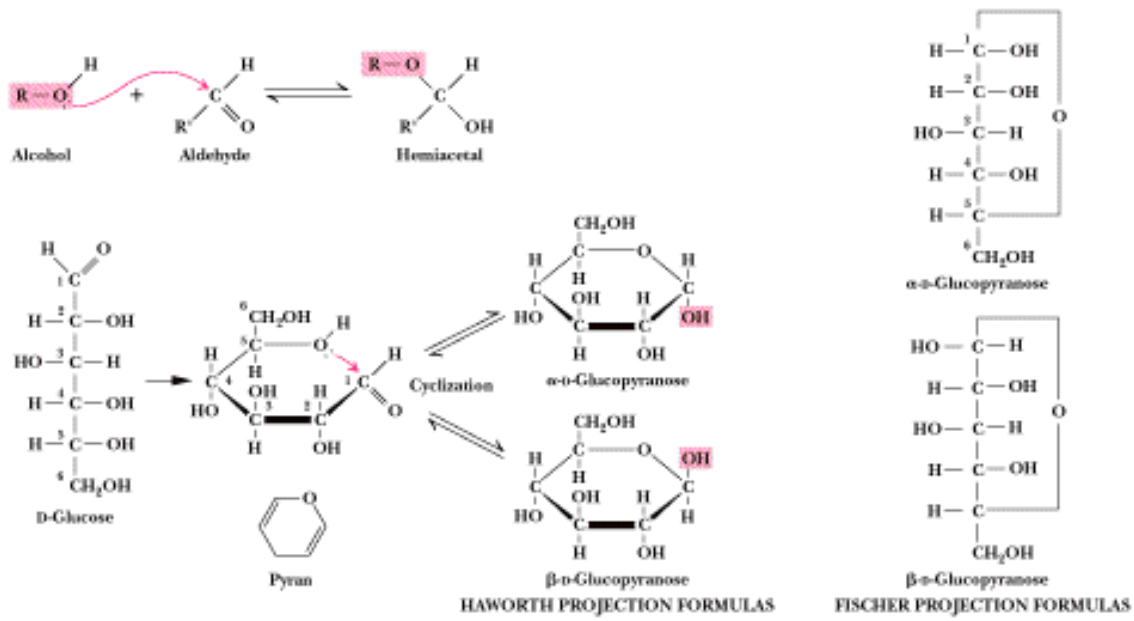
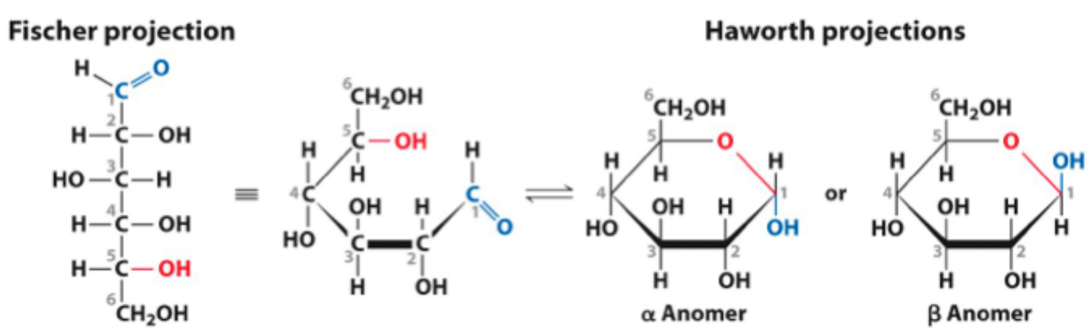


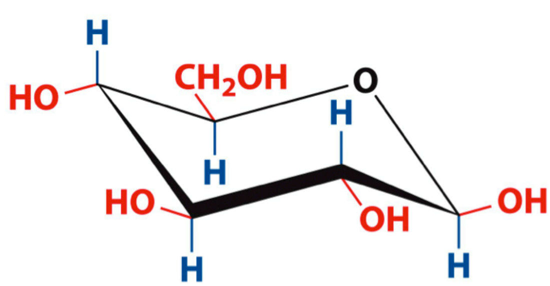


- In this example, C1 carbonyl group (aldehyde) interacts with alcohol on C5 to form a six membered ring, with C6 above the ring structure.
- Reaction called an **ALDOL CONDENSATION**
- Form a 5 or 6 membered ring
- The C1 carbonyl carbon becomes a new chiral center – a new C1 hydroxyl
- **New C1 hydroxyl = anomeric carbon**
  - The carbonyl carbon in the straight chain form
  - Carbon bonded to both the ring oxygen and a hydroxyl group in the cyclic form
- Hydroxyl group is either above or below the ring – **two forms α (alpha) and β (beta)**
  - For D-sugars:
    - **α-anomer**: hydroxyl group **BELOW** ring (down)
    - **β-anomer**: hydroxyl group **ABOVE** ring (up)

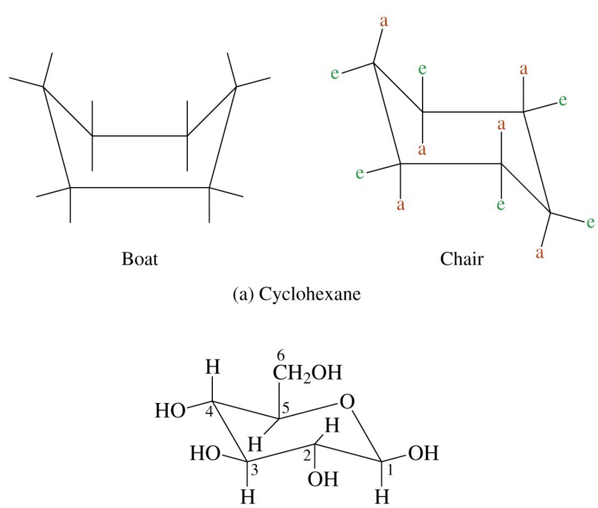
      "Beta get up for breakfast"

      ONLY ANOMERIC CARBON –OH is designated α or β

- **Going from FISCHER PROJECTIONS to HAWORTH:**
  - Numbering remains the same for the carbons
  - **If –OH is on the right → points DOWN in Haworth**
  - **If –OH is on the left → points UP in Haworth**
  - Terminal CH_2OH **ALWAYS** points **UP** relative to anomeric carbon in D sugars



Glucose



(a) Cyclohexane

(b) Glucose

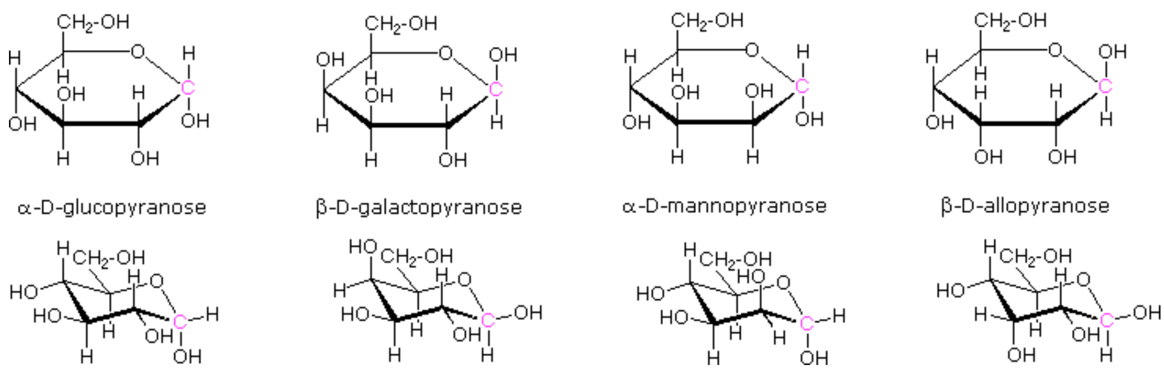
Figure 7-10 Concepts in Biochemistry, 3/e

a = axial position → bonds that extend straight above or below the plane of the ring

e = equatorial position → bonds that are pointed outward from the ring

Chair is the most STABLE conformation. Hydrogens are axial and larger substituents are equatorial – less opportunity for steric interactions.

Examples of Some Pyranose Forms of Hexoses

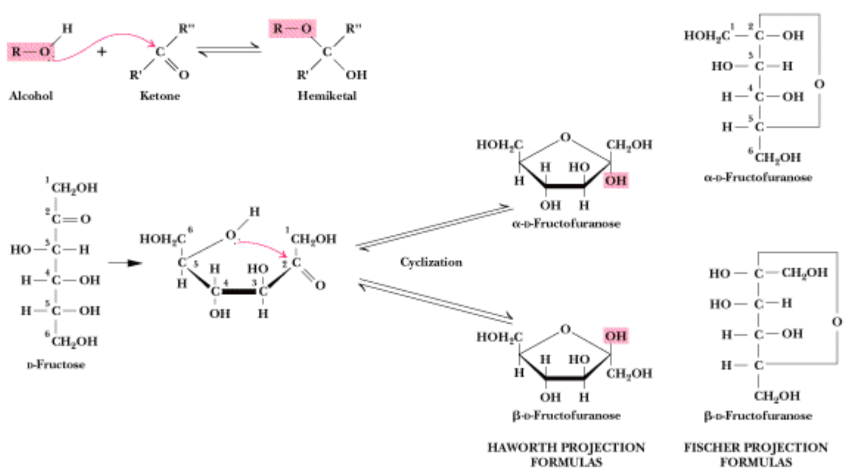


2. HEMIKETALS

$$\underset{\text{Ketone}}{R-\overset{\displaystyle O}{\overset{\|}{C}}-R'} + \underset{\text{Alcohol}}{R''OH} \rightleftharpoons \underset{\text{Hemiketal}}{R-\overset{\displaystyle OH}{\overset{|}{\underset{\underset{\displaystyle R'}{|}}{C}}}-OR''}$$

Hemiketal functional group includes a carbon center with 2 R-groups, an –OH and and an –OR'' group.

- Formed when C5 hydroxyl interacts with C2 carbonyl of a ketose
- Example: **D-fructose cyclization**



- Lone pair of electrons on –OH at position C5 attacks carbonyl at C2 forming the ring
- **Anomeric carbon is C2**

- Hemiketals also have **α and β anomers**
  - Depends on stereochemistry of –OH at **C2**
    - **Down = alpha**
    - **Up = beta**

- Note: Also have a CH_2OH at C1 – becomes the other group off of the anomeric C2 carbon

****IMPORTANT****

- Both condensations of hemiacetals and hemiketals are freely **reversible**
- In solution, there is rapid, free interconversion between the **α and β anomers** that necessarily passes through the **open chain** form
- Process called **MUTAROTATION**

MUTAROTATION

Mutarotation = interconversion between the α and β anomers

[Almost all monosaccharides in solution are in cyclized form]

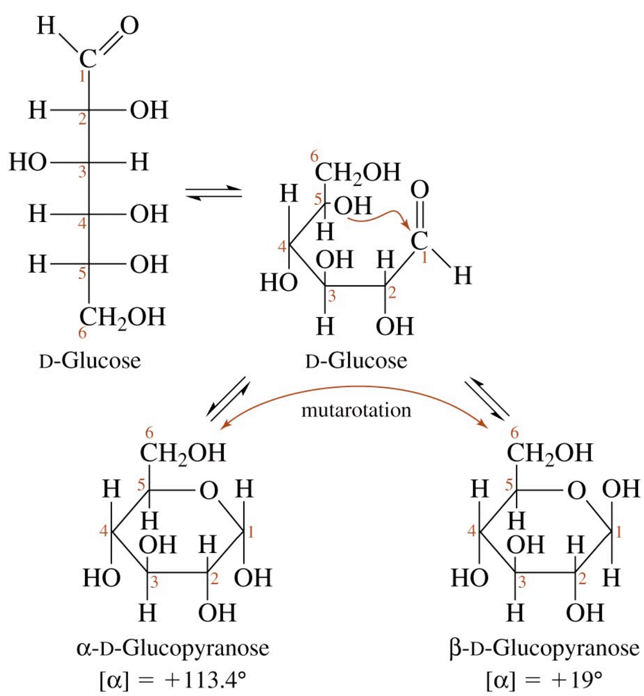
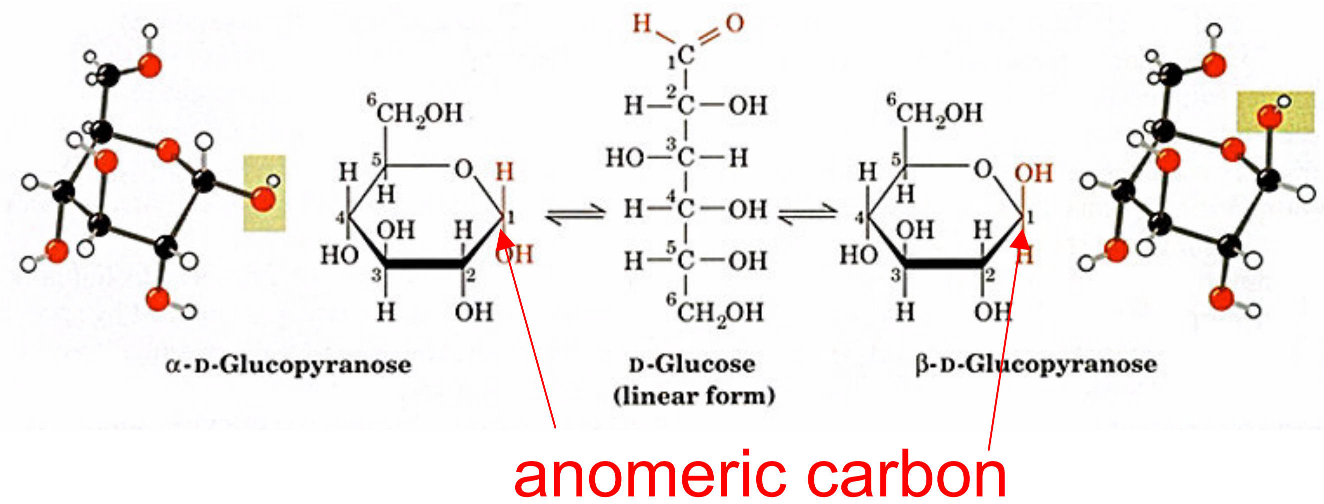


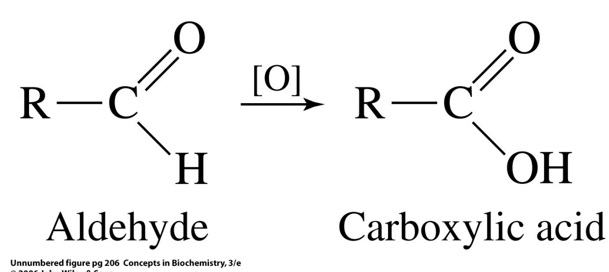
Figure 7-8a Concepts in Biochemistry, 3/e



– **REACTIONS OF MONOSACCHARIDES**

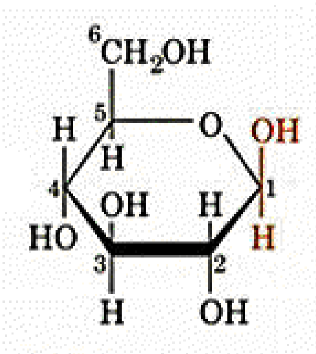
Because the cyclic and linear forms of aldoses and ketoses interconvert readily, these sugars undergo reactions typical of aldehydes and ketones.

- Biologically relevant reactions
- Those used to identify carbohydrates
- **1. OXIDATION-REDUCTION**
  - Complete **OXIDATION** of sugars supplies energy
  - Sugars that can be oxidized are called reducing sugars
  - Contain a **free** aldehyde group (found in open chain form)
  - A 2-ketose will open to give its 2-ketone form, which can tautomerize to an aldehyde and then be oxidized
  - All monosaccharides are reducing sugars
- Aldehyde in aldoses readily oxidized
- Ketoses isomerizes and get oxidized
  - **OPEN CHAIN FORM OF SUGAR GETS OXIDIZED**
  - **Due to equilibrium between open and cyclic form, more open chain form will be produced once the other has reacted.**



- Therefore, sugars **MUST** be able to open and close in ring form
- Therefore, reducing sugars **MUST** have a free ANOMERIC CARBON
- Free anomeric carbon = **REDUCING END**
- Sugars tested as reducing sugars in a test called the **TOLLENS TEST**
- Silver ammonia complex ion is the oxidizing agent (gets reduced)
- Sugar to be tested is the reducing agent (gets oxidized)

- DEMONSTRATION: The Silver Mirror Test
- **REMEMBER: The "Reducing End" of a sugar is the end with a free anomeric hydroxyl group**



The most reactive -OH.

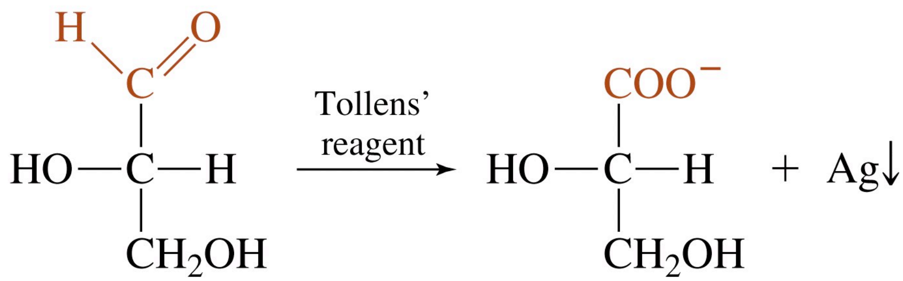


Figure 7-11a Concepts in Biochemistry, 3/e

Another oxidation carried out by an enzyme: Class of enzymes = Dehydrogenases

Sugar gets *oxidized* and the cofactor gets *reduced*.

Oxidation of glucose:

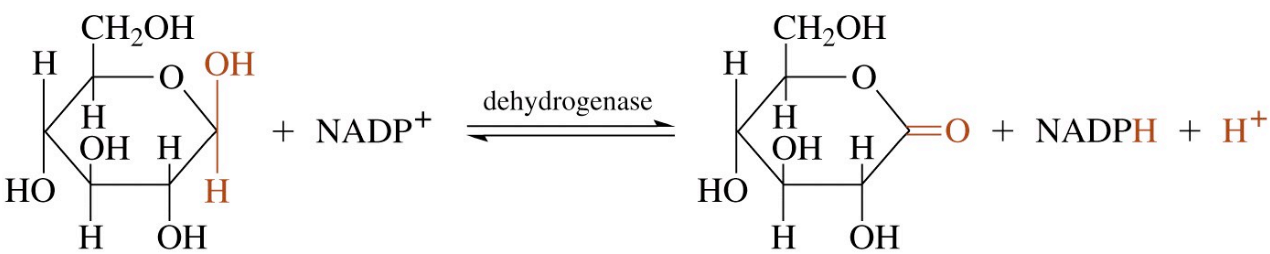


Figure 7-11c Concepts in Biochemistry, 3/e

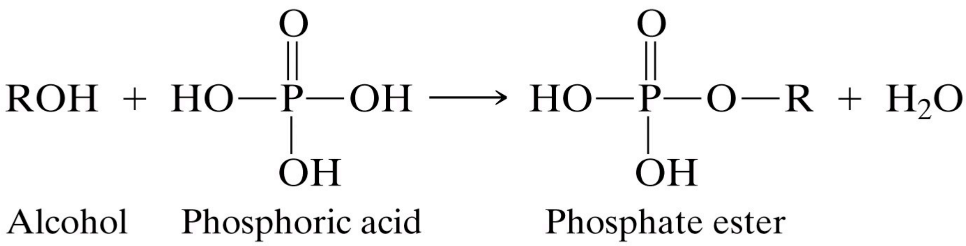
2. ESTERIFICATION:

Esters are formed by the reaction of alcohols (-OH) with acids.

$$\underset{\text{Alcohol}}{ROH} + \underset{\text{Acid}}{HOOCR'} \longrightarrow \underset{\text{Ester}}{R-O-\overset{\overset{\large O}{\|}}{C}-R'} + H_2O$$

Unnumbered figure pg 207a Concepts in Biochemistry, 3/e

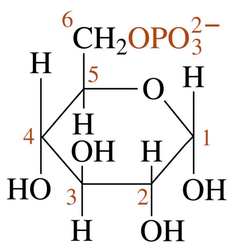
One of the most important biological esters is the <u>PHOSPHATE ESTER</u>. Performed in cells by transfer of a phosphoryl group from ATP to a carbohydrate hydroxyl – Catalyzed by <u>KINASES</u>



Unnumbered figure pg 207b Concepts in Biochemistry, 3/e

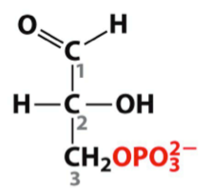
$$\text{D-glucose} + \text{ATP} \xrightleftharpoons{\text{hexokinase}} \text{D-glucose-6-phosphate} + \text{ADP}$$

Unnumbered figure pg 207c Concepts in Biochemistry, 3/e

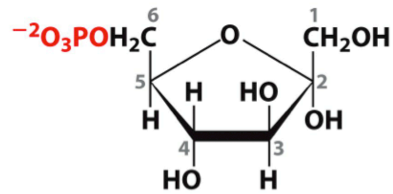


D-Glucose-6-phosphate

Figure 7-13a Concepts in Biochemistry, 3/e



Glyceraldehyde-3-phosphate



Fructose-6-phosphate

DISACCHARIDES

- Formed between monosaccharides via a glycosidic bond
- involves OH of anomeric carbon and any other OH
- In the reaction, lose elements of H_2O
- α (1→4)
    - α = alpha = configuration of anomeric carbon
    - 1 = number of anomeric carbon
    - →4 = denotes other carbon involved in glycosidic bond
- Anomeric carbon gets fixed/locked into either **α or β configuration** (**can't mutarotate**)
- Having lots of variation in monosaccharides and variation in how they are linked leads to many different disaccharides

- For example:

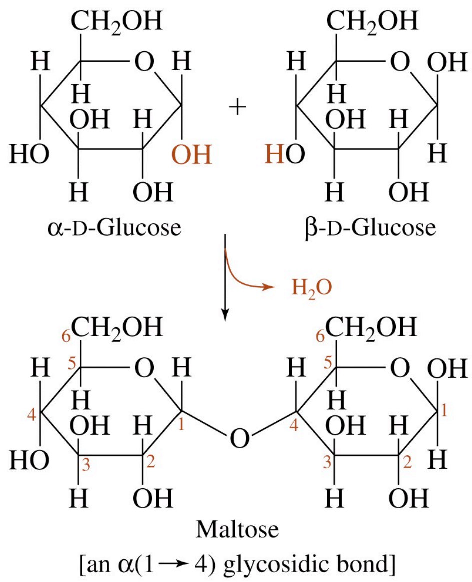


Figure 7-16 Concepts in Biochemistry, 3/e
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- **General format to describe a disaccharide is:**
1st Sugar name – OH type (Carbon # 1st sugar – Carbon # 2nd sugar) – 2nd Sugar name
(α or β)
[only if at anomeric carbon]

example: glucose α(1 → 4) glucose (how I name them! I also assume D-sugars)

This version of maltose also could be named more specifically:

α-D-glucopyrano<u>syl</u> (1 → 4) α–D-glucopyran<u>ose</u>

- **Should know the structures of:**
- **Cellobiose**
- **Sucrose**
- **Lactose**
- **Maltose**

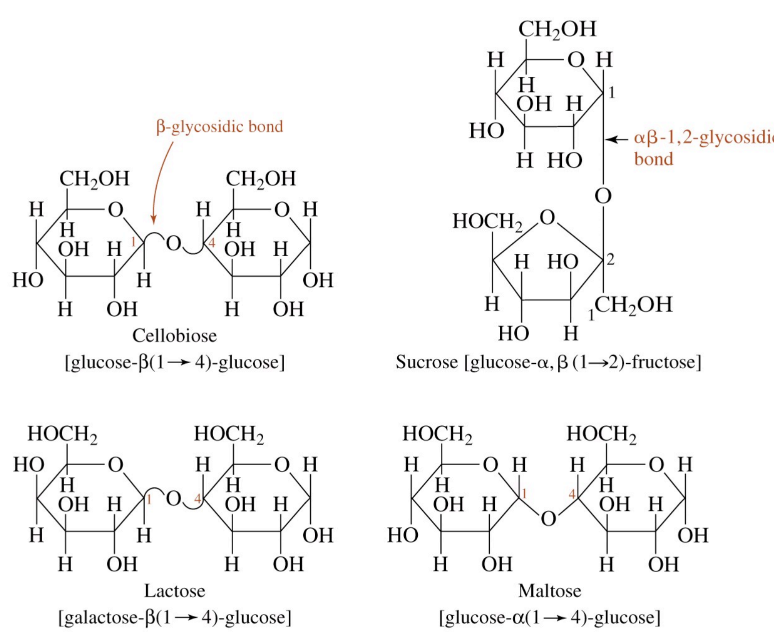

Figure 7-17 Concepts in Biochemistry, 3/e
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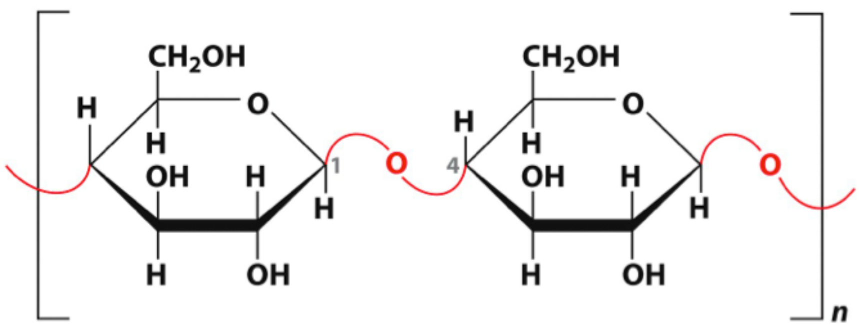
Table 7.2
Common disaccharides and their structural properties

Name	Monosaccharide Components	Type of Glycosidic Linkage
Maltose	Glucose, glucose	$\alpha(1 \rightarrow 4)$
Cellobiose	Glucose, glucose	$\beta(1 \rightarrow 4)$
Lactose	Galactose, glucose	$\beta(1 \rightarrow 4)$
Sucrose	Glucose, fructose	$\alpha,\beta(1 \rightarrow 2)$

Table 7-2 Concepts in Biochemistry, 3/e

- **Cellobiose**
  - 1st glucose is β-linked to the 4th carbon of another glucose
  - Not branched, on average has 10,000 – 15,000 glucose molecules
  - Very long straight chains that can bundle of parallel chains = fibrils
  - glucose β(1→4)glucose
  - β points up so draw the bond as curved or wavy line – Up from C1 and down from C4
  - forms planar, crystalline structure through lots of inter- and intra-molecular hydrogen bonding
  - Linked with oxygen



Cellulose – A Structural Polysaccharide

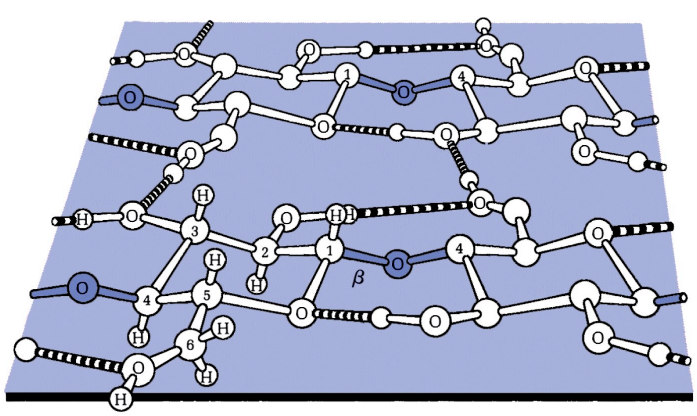
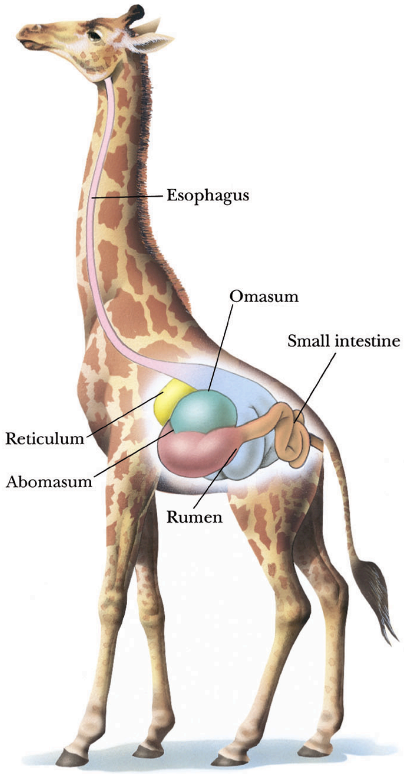
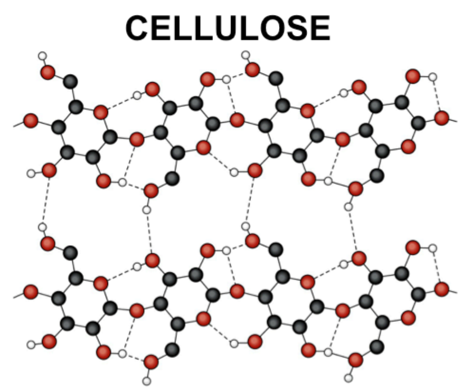


Figure 7-23b Concepts in Biochemistry, 3/e

- Cellobiose is the repeating unit in long polymers of **cellulose**, the major structural component of plants especially wood and plant fibers
- Humans do **NOT** have the capacity to digest cellobiose or cellulose

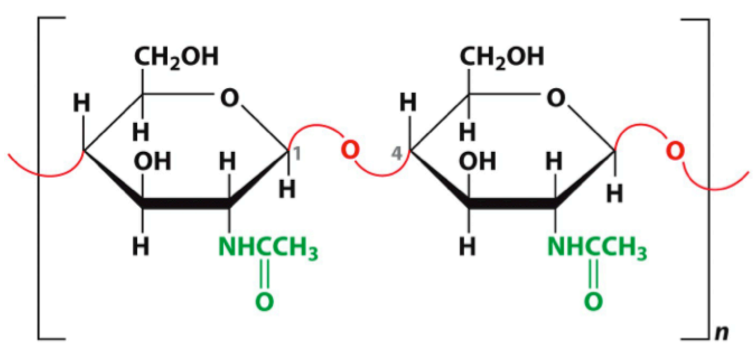


- Can't digest cellulose because we lack the enzyme **cellulase** that breaks β(1→4) linkages between glucose monomers
  - Ruminant animals (cattle, deer, giraffes, camels) CAN digest! Bacteria live in the rumen in GI tract and secrete **cellulase**.
  - Termites also have bacteria in digestive tract that secrete **cellulase** to digest wood fibers.



H-bonding between residues in same chain and adjacent chains results in a bundle of cellulose polymers that form an extended rigid fiber

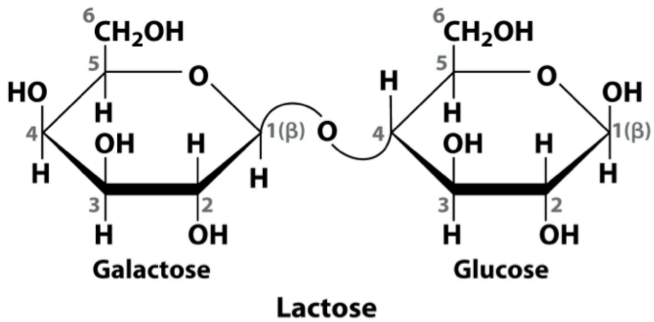
Another Structural Polysaccharide: CHITIN

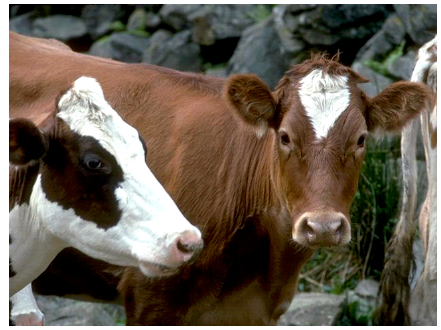


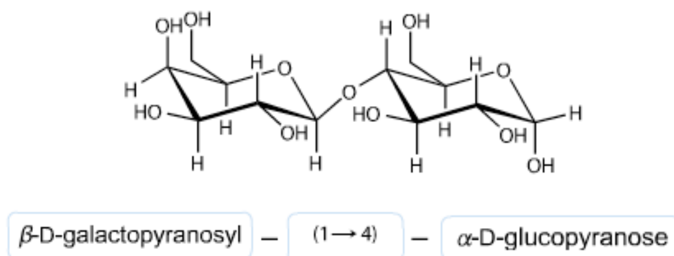
- Cellulose-like homopolymer
- Exoskeleton of insects and crustaceans, cell wall of many fungi
- β(1→4) linked glucose derivative: ***N*-acetylglucosamine** (glucosamine with an acetyl group linked to the amino group at C2)
- Modification allows for increased hydrogen bonding between adjacent polymers, giving the chitin-polymer matrix increased strength

Lactose:

- Galactose in a β(1→4) linkage with glucose
- Galactose is converted by the body to glucose and glucose used for energy
- Lactose IS digestible by most humans

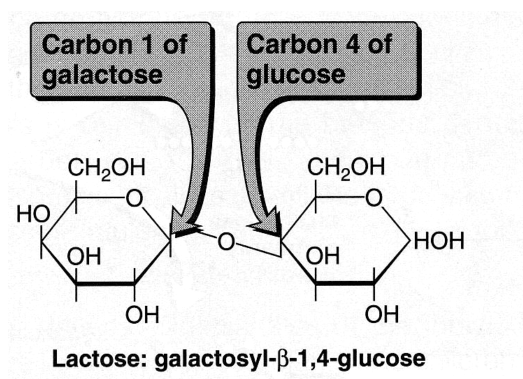






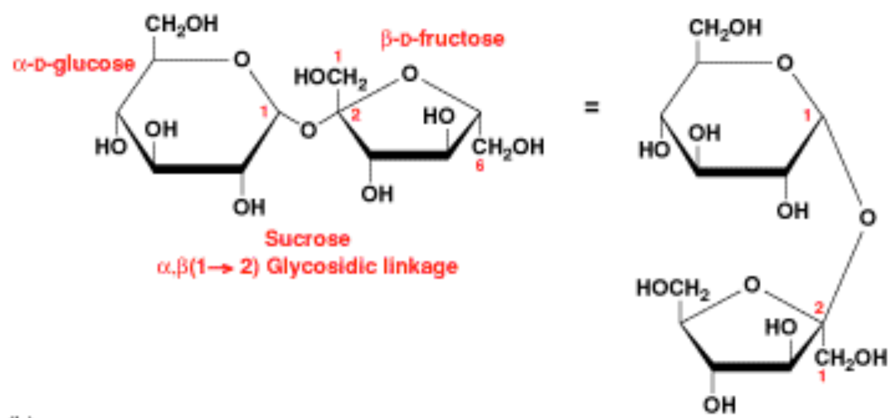
- Found in dairy products
- Enzyme **LACTASE** present in small intestine hydrolyzes lactose to <u>galactose</u> and <u>glucose.</u>

- 5% of people from Scandinavia and 90% of Asian adults suffer from <u>**lactose intolerance**</u> – deficiency in enzyme lactase.
    - For those with the deficiency:
    - o Lactose accumulates in small intestine
    - o Degraded by intestinal bacteria producing CO_2, hydrogen gas, and organic acids
    - o Presence of excess undigested lactose is harmful as well
    - o Both cause **symptoms**:
        - Bloating
        - Nausea
        - Cramping
        - Diarrhea
    - o **Treatment**:
    - • Avoid products containing lactose (dairy products)
    - • Use commercial products to hydrolyze lactose before consumption
        - • Add enzyme called β-galactosidase (e.g. lactaid milk)



Unnumbered figure pg 227 Concepts in Biochemistry, 3/e

- **Sucrose:**
  - Glucose in α,β (1→2) linkage with fructose (50% glucose:50% fructose)
  - NEEDS BOTH DESIGNATIONS! Both ANOMERIC CARBONS are involved in the linkage.



– (b)

- Anomeric carbon (C1) on glucose is linked to the anomeric carbon (C2) on fructose
- **BOTH** anomeric carbons are involved in glycosidic bonds
- Therefore, sucrose is **NOT** a reducing sugar
- **Sucrose, glucose and fructose most common natural sweeteners**
  - Corn syrup: glucose-heavy syrup made from corn starch - contains no fructose
  - High fructose corn syrup: Glucose in corn syrup is converted to fructose enzymatically. Mixed with corn syrup (glucose) to produce HFCS containing 55% fructose and 42% glucose. Larger sugar molecules called higher saccharides make up the remaining 3 percent of the sweetener.
  - In HFCS, the fructose and glucose are free and can be used by your body immediately. In sucrose they are linked by the glycosidic bond and must first be broken down enzymatically by your body before it can be used.

- **Humans can synthesize all the different sugars we need from glucose – we DON'T have to make a particular kind**
  - Also, our bodies can make glucose in many, many different ways
  - So, there is no <u>explicit</u> dietary need for sugars as long as we get enough calories
  - Sugars are so important that the body won't leave anything to chance!
  - Remember: for amino acids, there are essential and non-essential amino acids

Important things to consider when looking at a disaccharide:

1. Who are the two monosaccharides?

2. What anomer made the glycosidic bond?

3. Who is the reducing sugar (or is there one)?