Lecture 29 (12/2/20)

•Reading: Ch7; 247-257, 272-273

•Problems: Ch7 (text); 5,6,7,8,14,15,17
Ch7 (study-guide: applying); **3,4,6,8**
Ch7 (study-guide: facts); *2,4*

NEXT

•Reading: Ch7; 258-267
Ch10; 371-373

•Problems: Ch7 (text); 26,27,28
Ch7 (study-guide: applying); **2,5**
Ch7 (study-guide: facts); 6

Carbohydrates

A. Definition
B. Roles
C. Monosaccharides-Chemistry
   1. Chirality
      a. One or more asymmetric carbons
      b. Linear and ring forms
   2. Derivatives: the chemistry of carbohydrates
      a. Oxidation
         i. C1
         ii. C6
      b. Reduction
         i. C1/C2
         ii. Other carbons
      c. Ester formation
      d. Amino sugars
   3. Polymerization
      a. The Glycosidic Bond
      b. Non-covalent bonds in macro-molecular structure
D. Oligosaccharides
   1. Glycoproteins & glycolipids
   2. O-linked
   3. N-linked
   4. Sequence determination-ABO
E. Polysaccharides
   1. Polymers of glucose
   2. Polymers of disaccharides

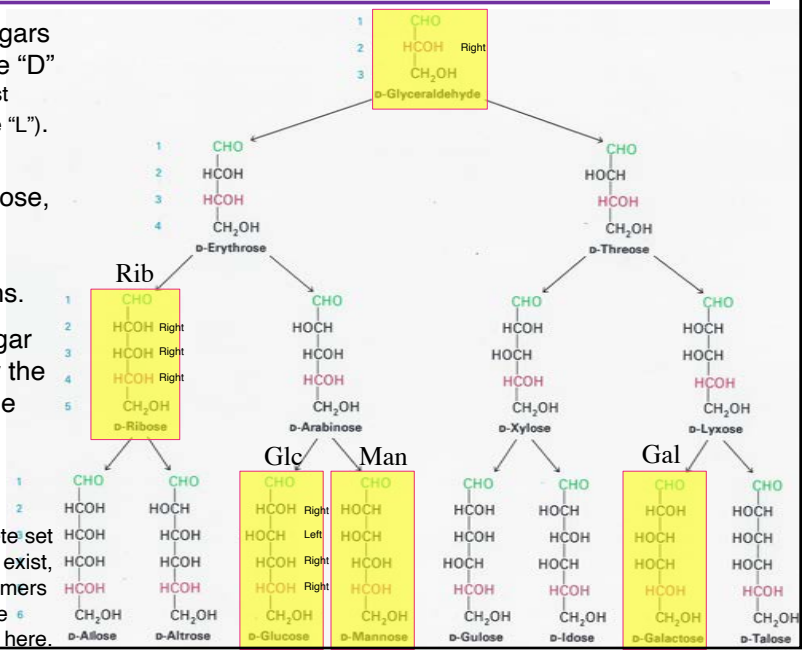
Carbohydrates

Nearly all sugars in biology are "D" (sort of like most amino acids are "L").

As you go to tetrose, pentose, etc., you are adding more chiral carbons.

A D- or L-sugar is defined by the chirality of the highest numbered carbon.

Another complete set of 15 L-aldoses exist, and are enantiomers of their D-aldose relatives shown here.

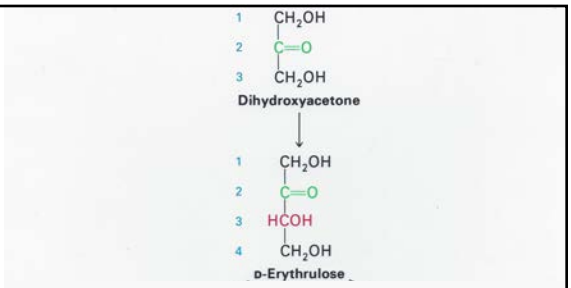


Carbohydrates

D-ketoses

The first chiral sugar is a tetrulose.

There is also another complete set of 7 L-ketoses exist, and are enantiomers of their D-ketose relatives shown here.



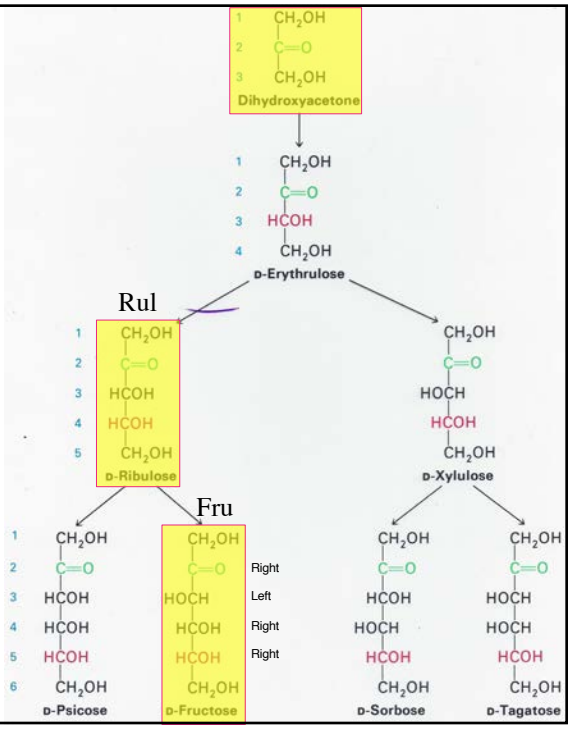
Carbohydrates

D-ketoses

The first chiral sugar is a tetrulose.

There is also another complete set of 7 L-ketoses exist, and are enantiomers of their D-ketose relatives shown here.

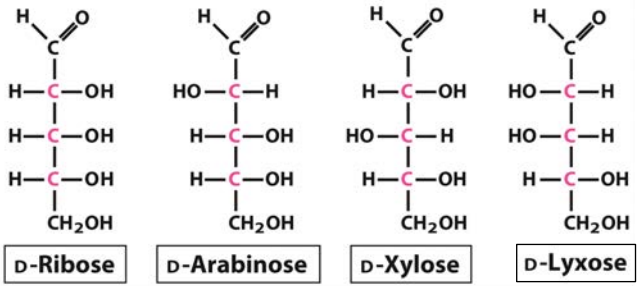
Fructose is the ketose form of glucose



Carbohydrates

Monosaccharides: Stereoisomer Nomenclature

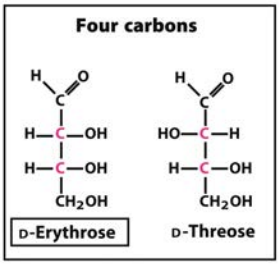
- Enantiomers
  - stereoisomers that are nonsuperimposable **complete** mirror images
  - Example: D-sugars & L-sugars
- Diastereomers
  - stereoisomers that are not complete mirror images
  - Diastereomers have different physical properties (e.g., water solubility)
  - Example:



Carbohydrates

Monosaccharides: Stereoisomer Nomenclature

- Epimers
  - Epimers are stereoisomers that differ at only **one** chiral center
  - Epimers are diastereomers; diastereomers have different physical properties (i.e., water solubility, melting temp)
  - Example:



  - Glc & Man (2 epimer); Glc & Gal (4 epimer); Rib & Ara; Rib & Xyl
- Anomers
  - Anomers have different chirality at carbon involved in ring formation

Carbohydrates

Monosaccharides: Stereoisomer Nomenclature

- D-Mannose and D-galactose are both epimers of D-glucose.
- D-Mannose and D-galactose vary at more than one chiral center and are diastereomers, but <u>not</u> epimers.

Left	Right
Left	Left
Right	Left
Right	Right

Carbohydrates

Monosaccharides: The most important sugars

- Glyceraldehyde and dihydroxyacetone are the simplest (3 carbon) aldose and ketose, respectively.
- Ribose (Rib) is the standard five-carbon sugar.
- Glucose (Glc) is the standard six-carbon sugar.
- Galactose (Gal) is an C4-epimer of glucose.
- Mannose (Man) is an C2-epimer of glucose.
- Fructose (Fru) is the ketose form of glucose.
- Ribulose (Rul) is the ketose form of ribose.

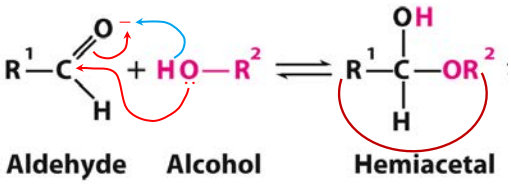
Need to know, recognize, draw, name, abbreviate

Carbohydrates

Monosaccharides: What are these "ring" forms?

- SUGARS WITH ≥5 CARBONS RAPIDLY AND STABLY FORM **RINGS** THROUGH HEMIACETAL (ALDOSES) AND HEMIKETAL (KETOSES) BONDS.

Hemiacetals



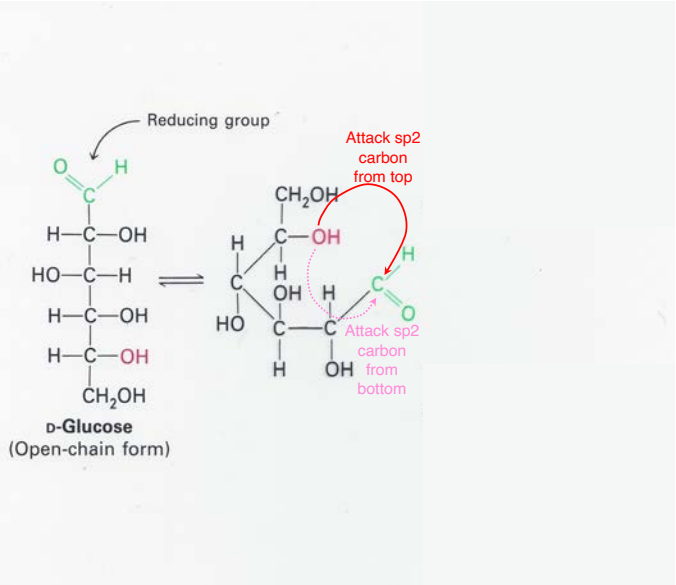
Not chiral

Chiral

- If the aldehyde (R1) and the alcohol (R2) are on the same molecule, you have a RING!
- Due to the oxygen, the ring is heterocyclic

Carbohydrates

Monosaccharides: What are these "ring" forms?

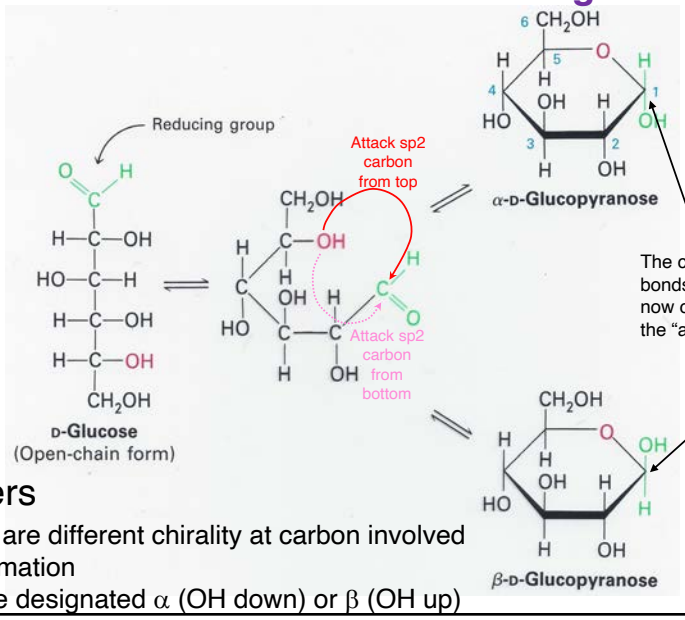


α

β

Carbohydrates

Monosaccharides: What are these "ring" forms?

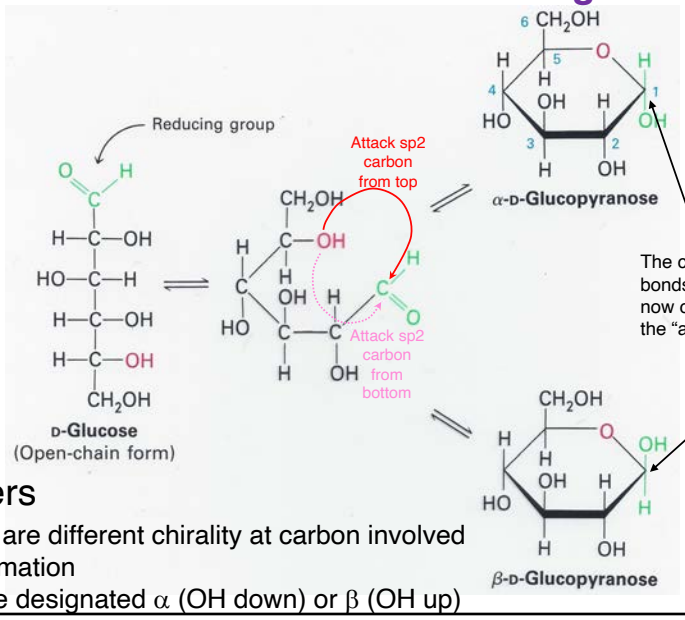


- Anomers
  - –Anomers are different chirality at carbon involved in ring formation
  - –These are designated α (OH down) or β (OH up)

*for D-sugars

Carbohydrates

Monosaccharides: What are these "ring" forms?



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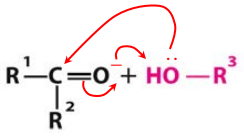
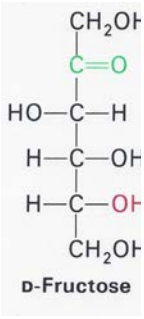
Carbohydrates

Monosaccharides: What are these "ring" forms?

Hemiketals





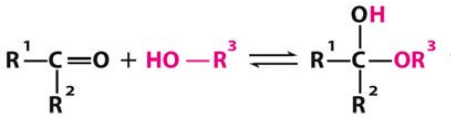
α (OH down) or β (OH up)

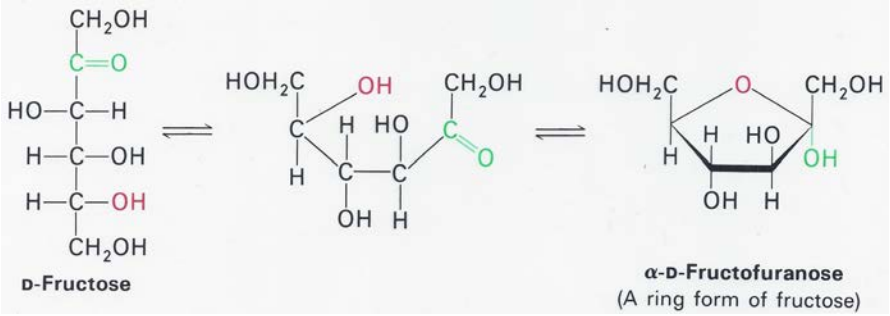
Besides the α & β, what is this pyran and furan?
Its all about which alcohols are used in these reactions.

Carbohydrates

Monosaccharides: What are these "ring" forms?

Hemiketals





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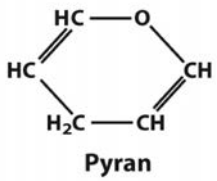
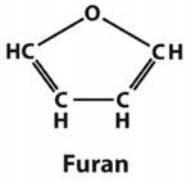
Carbohydrates

Monosaccharides: What are these "ring" forms?

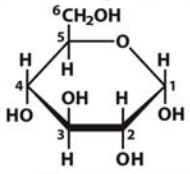
- Six-membered oxygen-containing rings are called pyranoses after the pyran ring structure.
- Five-membered oxygen-containing rings are called furanoses after the furan ring structure.



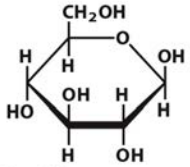
Pyran



Furan



α-D-Glucopyranose



β-D-Glucopyranose

Carbohydrates

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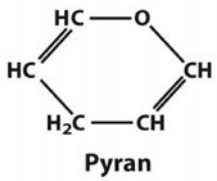
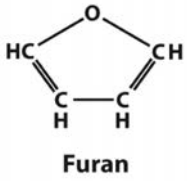
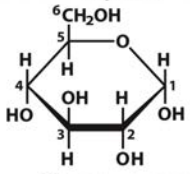
- Five-membered oxygen-containing rings are called furanoses after the furan ring structure.



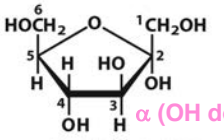
Pyran



Furan



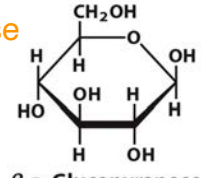
α-D-Glucopyranose



α (OH down)

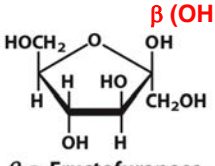
α-D-Fructofuranose

The way we are drawing these sugars is called a Haworth projection…..



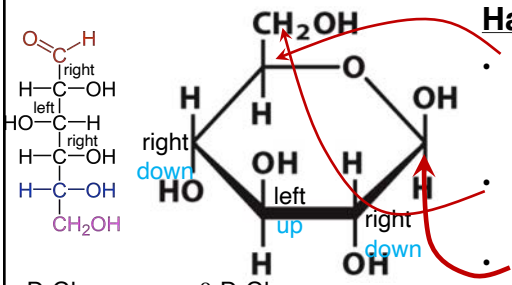
β-D-Glucopyranose

β (OH up)



β-D-Fructofuranose

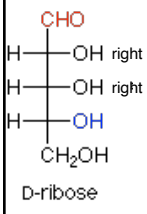
Carbohydrates



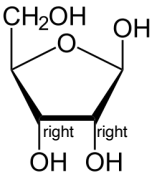
D-Glucose β-D-Glucopyranose

Haworth projections

- Highest carbon with hemiacetal/hemiketal alcohol in back; oxygen to right.
- If chiral (as for D-sugars), next highest carbon up if D, or down if L.
- The anomeric carbon is usually drawn on the right side.
- Other chiral carbons are down if right in Fisher projection and up if left in Fisher



D-ribose



β-D-Ribofuranose

- β-D-Glc pyranose goes up, down, up down, up as you go from C5 to C1
- β-D-Rib furanose goes up, down, down, up as you go from C4 to C1

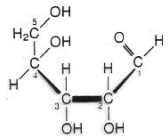
Carbohydrates

- Pentoses and hexoses readily undergo intramolecular cyclization.
- The former carbonyl carbon becomes a new chiral center, called the anomeric carbon.
- ALL forms are in equilibrium in solution
  Process is called "mutarotation"
  - When the former carbonyl oxygen becomes a hydroxyl group, the position of this group determines if the anomer is *α* or *β*.
  - If the hydroxyl group is on the opposite side (trans) of the ring as the CH_2OH moiety, the configuration is *α*.
  - If the hydroxyl group is on the same side (cis) of the ring as the CH_2OH moiety, the configuration is *β*.

Furan

Ring Forms (Anomers)

Pyran



D-Ribose

~56%

Carbohydrates

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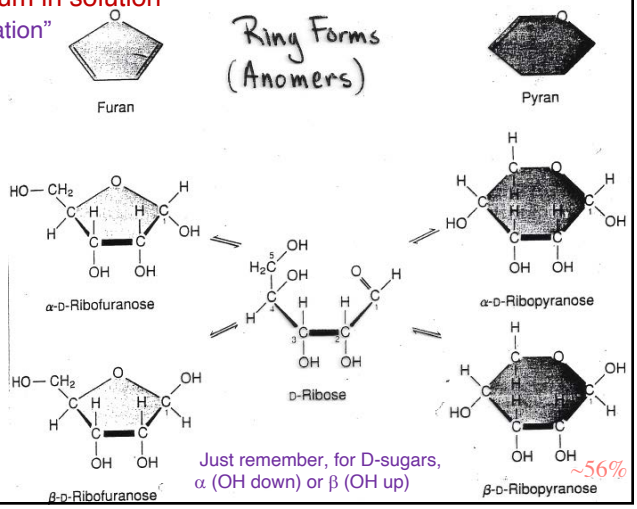
– If the hydroxyl group is on the same side (cis) of the ring as the CH_2OH moiety, the configuration is β.



Just remember, for D-sugars, α (OH down) or β (OH up)

Carbohydrates

Relative amounts of tautomeric forms for some monosaccharide sugars at equilibrium in water at 40°C[a]

Mono-saccharide	Relative Amount (%) α-Pyranose	β-Pyranose	α-Furanose	β-Furanose	Total Furanose
Ribose	20	56	6	18	24
Lyxose	71	29	[b]	[b]	<1
Altrose	27	40	20	13	33
Glucose	36	64	[b]	[b]	<1
Mannose	67	33	[b]	[b]	<1
Fructose	3	57	9	31	40

[a] In all cases, the open-chain form is much less than 1%. For data on other sugars, see S. J. Angyal, The composition and conformation of sugars in solution, *Angew. Chem.* 8:157–226(1969).

[b] Much less than 1%.

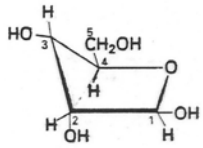
Why is the β-Glc more stable than α-Glc, and *visa versa* for Man?
to answer this, we need to look at **ACTUAL** structures.
These Haworth Projections are not the actual conformation…. What is?

Carbohydrates

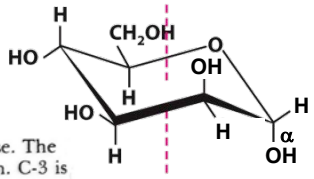
Actual Conformations of Cyclized Monosaccharides

- Cyclohexane rings have "chair" or "boat" conformations.

- Pyranose rings favor "chair" conformations.
- Multiple "chair" conformations are possible but require energy for interconversion (~46 kJ/mole).
- Furanose rings are envelopes



An envelope form of β-D-ribose. The C_3-*endo* conformation is shown. C-3 is out of plane on the same side as C-5.



Two possible chair forms of β-D-glucopyranose

We can understand why there is a 2:1 ratio of β:α glucose….. steric hindrance

AND why α–mannose is favored (2:1 ratio of α:β)

Carbohydrates

Monosaccharides: Chemistry

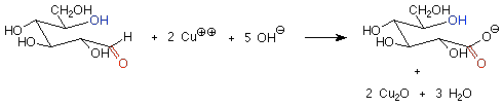
- **Chemical Features:**
  - Chirality
    - One or more asymmetric carbons
    - Linear and ring forms
  - Derivatives: the chemistry of carbohydrates
    - Oxidation
      - C1
      - C6
    - Reduction
      - C1/C2
      - Other carbons
    - Ester formation
    - Amino sugars
  - Polymerization
    - The Glycosidic Bond
    - Non-covalent bonds in macro-molecular structure

Carbohydrates

Monosaccharides: Derivatives

Oxidation: These make "sugar acids" or "acid sugars"

- Oxidation of aldehyde/ketone to acid ($2e^-$ loss); reaction from the C1 of aldoses
  - named as "onic" acids ("onate" for conjugate base)
  - these sugars can reduce Cu^{2+} to Cu^+ (Fehling's test) or Ag^+ to Ag^0 (Tollens' test)
  - Example: gluconic acid



$$CuSO_4 \rightarrow Cu^{2+} + SO_4^{2-}$$

Blue

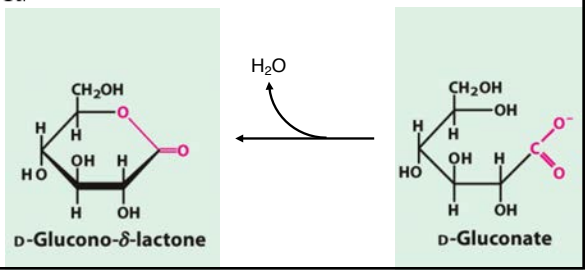
$$Cu^{2+} + \text{Reducing sugar} \rightarrow Cu^+$$

$$Cu^+ \rightarrow Cu_2O$$

Red (ppt)

This reaction is called Benedict's test

The copper is reduced and the sugar is oxidized. So, the sugar is called a **Reducing Sugar**. Reducing sugars have a free anomeric carbon.

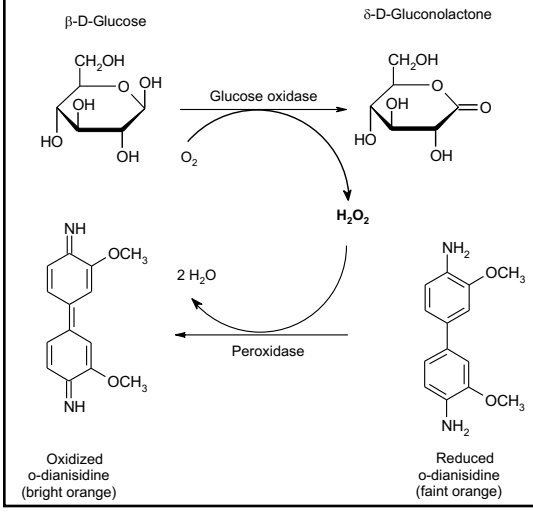


Carbohydrates

Monosaccharides: Derivatives

Oxidation: These make "sugar acids" or "acid sugars"

Colorimetric Glucose Analysis



- Enzymatic methods are used to quantify reducing sugars such as glucose.
  - The enzyme glucose oxidase catalyzes the conversion of glucose to glucono-δ-lactone and hydrogen peroxide.
  - Hydrogen peroxide oxidizes organic molecules into highly colored compounds.
  - Concentrations of such compounds is measured colorimetrically.
- Electrochemical detection is used in portable glucose sensors.

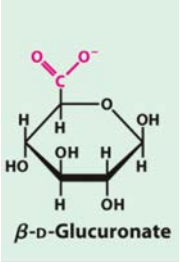
Carbohydrates

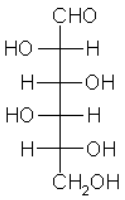
Monosaccharides: Derivatives

Oxidation: These make "sugar acids" or "acid sugars"

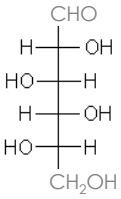
Oxidation of alcohol to acid ($4e^-$ loss)

- Reaction for C6 groups; normally aldoses as well
- Named as **ur**onic acids ("uronate" for conjugate base)
- Many L-sugars are Uronic acids
- Examples: D-glucuronic acid, L-iduronic acid

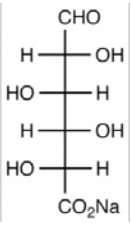




D-Idose



L-Idose



L-Iduronic acid

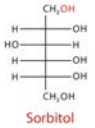
Carbohydrates

Monosaccharides: Derivatives

Reduction: These make "sugar alcohols" or "deoxysugars"

Reduction of aldehyde/ketone to alcohol ($2e^-$ gain)

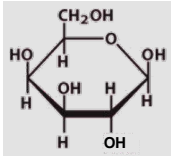
- Only carbon not already an alcohol is the anomeric carbon (C1/C2)
- Named as sugar **"ol"** or "itol"
- Examples: glycerol, mannitol, glucitol (sorbitol)



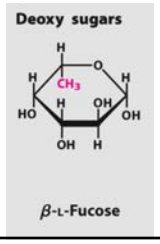
Reduction of alcohol carbon to methyl/methylene ($2e^-$ gain)

- Can react at any except the anomeric carbon
- Named as "x-deoxy"sugar with x being the reduced carbon
- Many are L-sugars, and have specific trivial names
- Examples: 2-deoxyribose, L-Fucose (Fuc) and L-Rhamnose (Rha)

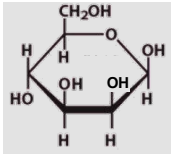
Fuc is also 6-deoxy L-Gal



β-D-Gal



Rha is also 6-deoxy L-Man



β-D-Man

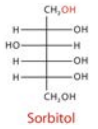
Carbohydrates

Monosaccharides: Derivatives

Reduction: These make "sugar alcohols" or "deoxysugars"

Reduction of aldehyde/ketone to alcohol ($2e^-$ gain)

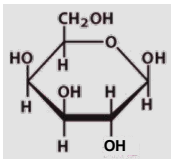
- Only carbon not already an alcohol is the anomeric carbon (C1/C2)
- Named as sugar **"ol"** or "itol"
- Examples: glycerol, mannitol, glucitol (sorbitol)

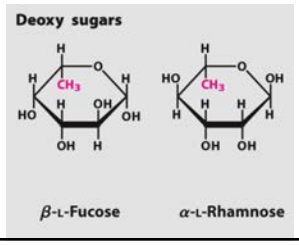

Sorbitol

Reduction of alcohol carbon to methyl/methylene ($2e^-$ gain)

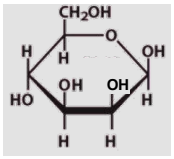
- Can react at any except the anomeric carbon
- Named as "x-deoxy"sugar with x being the reduced carbon
- Many are L-sugars, and have specific trivial names
- Examples: 2-deoxyribose, L-Fucose (Fuc) and L-Rhamnose (Rha)

Fuc is also 6-deoxy L-Gal


β-D-Gal



Rha is also 6-deoxy L-Man


β-D-Man

Carbohydrates

Monosaccharides: Chemistry

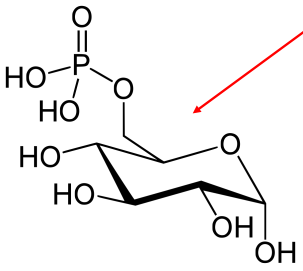
- **Chemical Features:**
  - Chirality
    - One or more asymmetric carbons
    - Linear and ring forms
  - Derivatives: the chemistry of carbohydrates
    - Oxidation
      - C1 -onic
      - C6 -uronic
    - Reduction
      - C1/C2 -tol
      - Other carbons deoxy-
    - Ester formation
    - Amino sugars
  - Polymerization
    - The Glycosidic Bond
    - Non-covalent bonds in macro-molecular structure

Carbohydrates

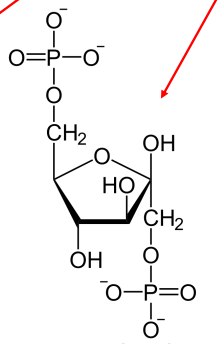
Monosaccharides: Derivatives

Esters: condensation of alcohol (sugar) and an acid

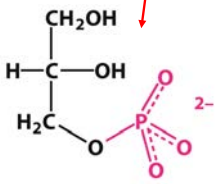
- Most important sugar esters use a phosphoric acid
  - These are called phospho-sugars or sugar phosphates
  - Examples: nucleotides, Glc 6-P, Fru 1,6-P_2, glycerol 3-phosphate



Glucose 6–phosphate



Fructose 1,6–bisphosphate



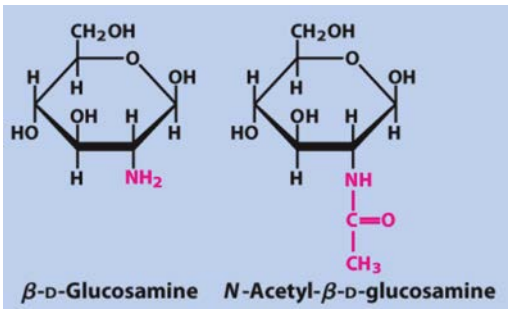
Glycerol 3-phosphate

Carbohydrates

Monosaccharides: Derivatives

Amines: condensation of alcohol (sugar) and ammonia

- These are called amino-sugars
- In biology, its ALWAYS at C2
- Often, the amino group will be further modified by an acetyl group (CH_3CO–) making an amide
- Named as sugar"amine" and when acetylated, the "N-acetyl" comes first. When abbreviation used "NAc" it comes after.
- Examples: glucosamine, N-acetyl-glucosamine (GlcNAc)

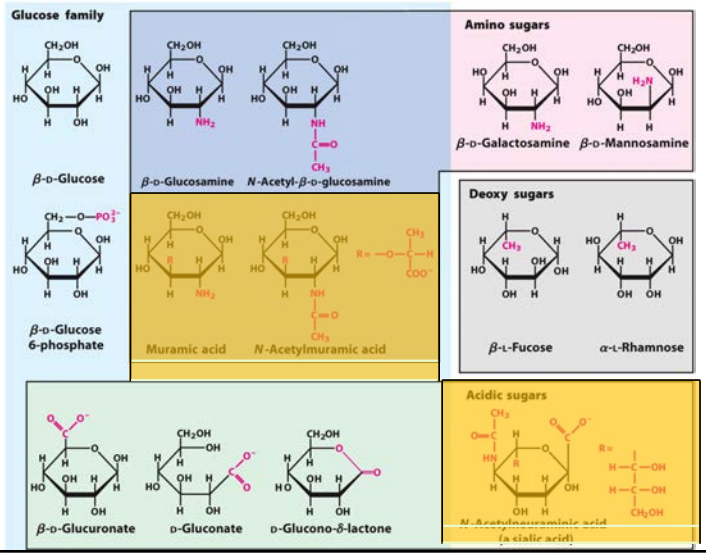


β-D-Glucosamine N-Acetyl-β-D-glucosamine (GlcNAc)

Carbohydrates

Monosaccharides: Derivatives

Important Hexose Derivatives

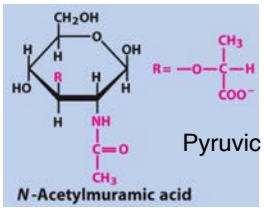


Carbohydrates

Monosaccharides: Derivatives

Muramic acid

Combined acid (C3) + amine (C2)



Pyruvic acid

Sialic Acid (Sia) (aka NeuNAc)

Combined acid (C1) + amine (C2)