

# Lecture 1,2, 3: Carbohydrates

## 1. Names, Structures, and Functional Groups

- Nomenclature
- Stereochemistry
- The Cyclic Form of Sugars

## 2. Reactions and Reactivity

- Glycosides and Acetals
- Oxidation and Reduction
- Functionalisation for Biology
- Carbohydrates in Synthesis

## 3. Disaccharides and Polysaccharides

- Maltose, Lactose and Sucrose
- Starch, Glycogen and Cellulose
- Blood Types and Sweetness

**What are carbohydrates:** carbohydrates are biological molecules consisting of CHO (Carbons and hydrate (H<sub>2</sub>O) carbon, hydrogens and oxygens). They are also known as sugars, sugar molecules are united because of the structural features they portray. They all have similar structural compounds. Carbohydrates are in equilibrium between ring and linear structures, for example glucose.

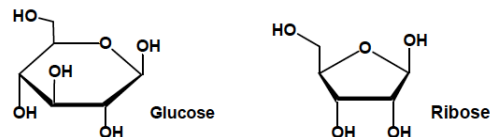
**Nomenclature:** we can name sugars according in 3 ways:

1. **By the number of carbon atoms:** We need to look for the suffix "-ose" to be a carbohydrate. We then apply the Greek numbering system to specify the number of carbons in the molecule.

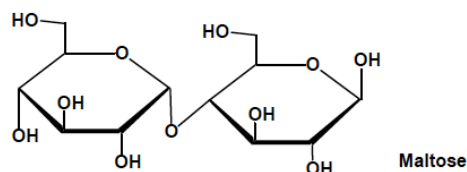
- Tri-ose
- Tetra-ose
- Pent-ose
- Hex-ose

2. **By number of bulk sugars:**

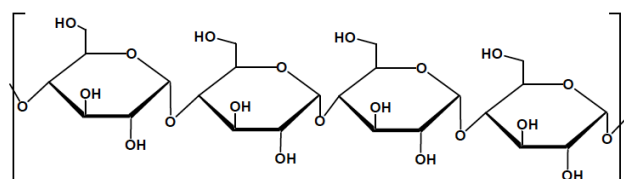
- Monosaccharide: contains a single sugar unit. Either a glucose or ribose.



- Disaccharide: contains 2 sugar units. E.g. maltose.



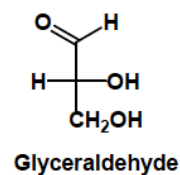
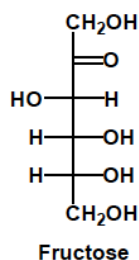
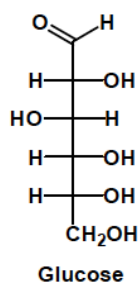
- Polysaccharide: contains many sugar units. E.g. starch.



3. **By their carbonyl functionality:** this is specific to linear chains because the cyclic form of the sugar does not contain a carbonyl functional group, rather hydroxyls and hemi-acetals. The sugar can either be a:

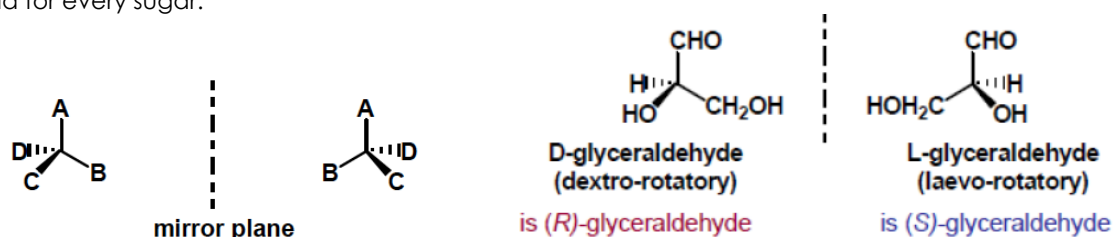
- **aldose:** Ald-ose, it contains an aldehyde functional group

- ketose:** Ket-ose. It contains a ketone functional group.



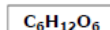
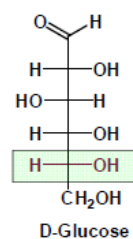
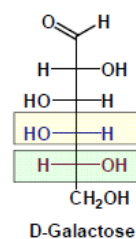
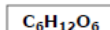
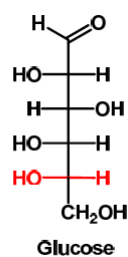
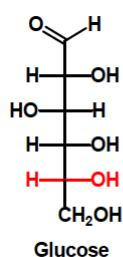
**Stereochemistry:** A carbon atom with 4 different groups attached is a stereocentre. carbohydrates can have many stereocentres and thus makes the molecule asymmetric or chiral. The molecule has mirror reflections which are not superimposable and thus is considered an enantiomer (optical isomers). we do not use R and S nomenclature for sugars but rather L/D. L-sugars rotate light to the left and D-sugars rotate light to the right. However, it is important to note that D-sugars are not necessarily R configured and L-sugars are not necessarily S configured.

For example, in the case of D-glyceraldehyde it is R configured and L-glyceraldehyde is S configured. This relationship does not hold for every sugar.

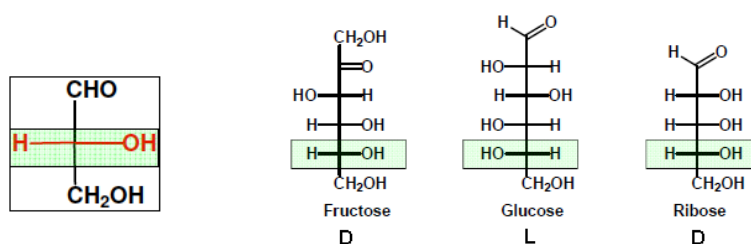


Note chirality: a molecule is said to be chiral if it is not superimposable on its mirror image. If a pair of molecules which are not identical but are mirror images of each other are called enantiomers. Almost all the properties of a pair of enantiomers are identical, melting point, IR spectra, <sup>1</sup>H NMR spectra, solubility. However, they differ in the direction of the rotation of polarised light (clockwise, or anticlockwise with the same degree).

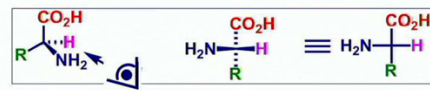
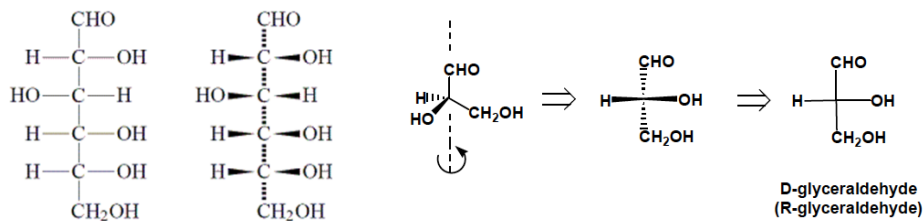
Note on drawing mirror images: we need to reverse every stereocentre of the molecule. If the OH group is pointing to the left, its mirror image will have it pointing to the right. However, if any other carbon atoms changes configuration to its mirror images they are called epimer. Epimers are diastereomers which are completely different molecules with different properties, different melting points, different NMR spectra, IR spectrum, etc.



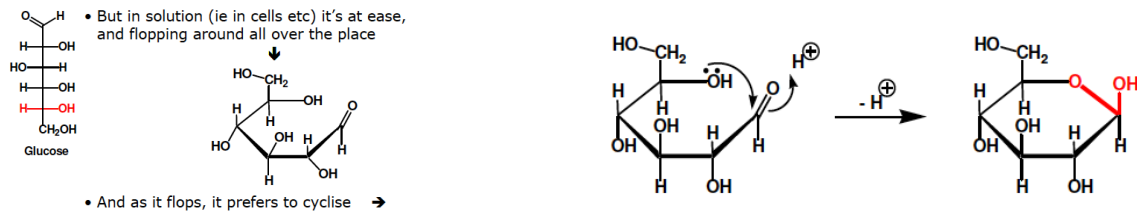
**Determining L/D stereochemistry of sugars:** everything is named with respects to D-glyceraldehyde. We can determine if a sugar has an L or D configuration from its linear and Fischer projections. If the second last carbon has its OH group to the right, then it is the D-isomer (points in the same projection as the D-glyceraldehyde). If the second last carbon has its OH group to the left, then it is a L-isomer.



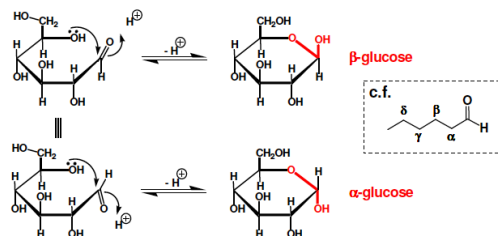
**Fischer projections:** the molecule is drawn as a cross. To draw Fischer projections begin with positioning the carbon of the aldehyde/Ketone as the first carbon and the carbon of the CH<sub>2</sub>OH as the last carbon at the bottom. Then, determine the absolute configuration, that is S or R in order to be able to determine what is coming out of the page and in which direction. Make sure to look right into the bonds between -H, -OH and -NH<sub>2</sub> groups. The horizontal bonds are wedged and vertical bonds are dashed.



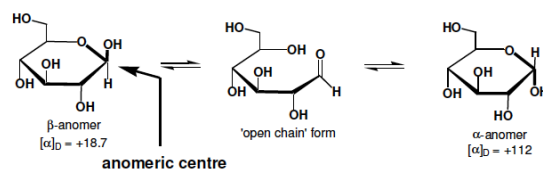
**The cyclization of Sugars:** 99.9% of glucose exist as rings when dissolved in water. Molecules such as glucose, have nucleophile and electrophile within its structure, as a result the linear structure can become cyclic. The OH is the nucleophile because it has a lone pair and the C=O is the electrophile because the carbon is electron deficient due to the higher electronegativity of the oxygen.



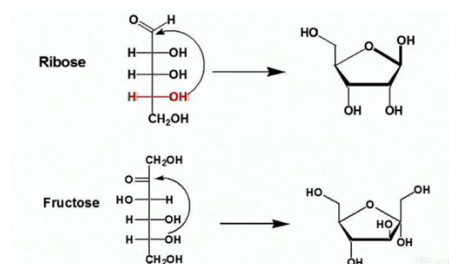
However, since the cyclisation is reversible and thus there is an equilibrium between different types of ring formation, 2 products can form since the the C=O group can be pointing above or below the ring. These are called anomers and they are diastereoisomers of cyclic forms of sugars differing only the configuration of the Carbon of the aldehyde. Alpha (think of fish in the sea, they swim down) and beta (birds fly up in the sky).



The conversion between  $\alpha$  and  $\beta$  is called mutarotation, the hemiacetal centres is referred to as the anomeric centre. However, these are not in 50-50% concentration, rather the most stable configuration will be the most abundant isomer.



this reaction also occurs in 5 membered rings:

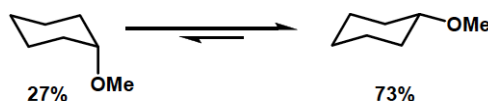


Note of stereochemistry of the ring from linear sugar: the stereochemistry of the starting linear sugar does not dictate the stereochemistry of the ring ( $\beta$  or  $\alpha$ ) rather you will get a mixture of products. L and D are for linear;  $\beta$  or  $\alpha$  are for cyclic.

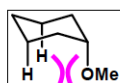
**The anomeric effect:** in general, any tetrahydropyran (a 6 membered ring with an oxygen in it, like glucose) ring bearing an electronegative substituent in the 2- position will prefer that substituent to be axial.

Anomers, although they are in equilibrium, they are not in 50-50% concentration, rather the most stable configuration will be the most abundant isomer. In normal molecules, this relates to the axial and equatorial confirmation of the groups of the sugar. However, the anomeric effect can be explained by stereoelectronic effects.

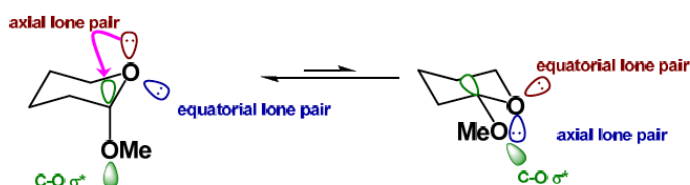
1. **Steric effects:** The most stable will be when the biggest groups adopts equatorial confirmation because it minimises steric effects and thus repulsions from neighbouring atoms.



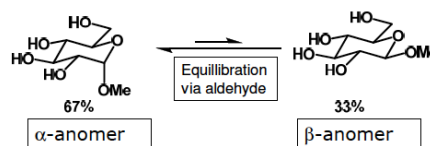
- Minimises adverse steric interactions:



2. **stereoelectronic effects:** the axial conformation allows a favourable orbital interaction between the 2 oxygens. The lone pair of electrons from the oxygen in the C–O–C bond, will interact with the antibonding orbital of the C–O group. So if the C-OMe group is axial, there is greater orbital interaction than compared to no orbital interaction when the C-OMe bond is equatorial. Although the OMe is axial, the stereoelectronic interaction outweighs the steric effects and hence has a greater stabilizing effect.



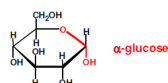
- The same does not apply when the ring contains an O:



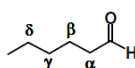
Note: only  $\alpha$  has the electronic stabilization effect, this is because the confirmation of the  $\alpha$ -glucose is completely parallel to the lone pair of the oxygen whereas the  $\beta$  is not completely parallel and thus not great overlap between the orbitals.

**The meaning of  $\alpha$ :** it is important to realise that  $\alpha$  can have 3 meanings:

1. for anomers of glucose where C1-OH is down (fish in the sea).

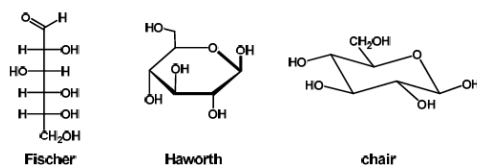


2. For the position of the carbon next to a carbonyl.



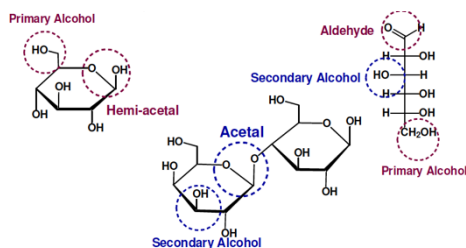
3. For optical rotation,  $[\alpha]_D$  or  $[\alpha]_L$ .

**Important molecular structures:** there are 3 important molecular structures we use for carbohydrates:



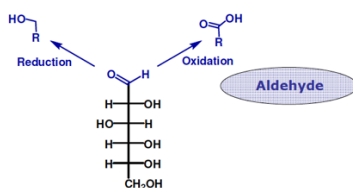
# Lecture 4: Reactions of Carbohydrates

**Reactions of Sugars:** the sugars contain many functional groups which can undergo reaction mechanisms:

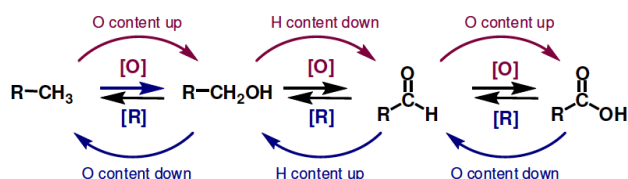


Although some reactions may involve the linear chain, we know that there is a 0.01% concentration in solution. Since the linear and ring structures are in equilibrium, by Le Chatelier's principle, consuming the linear structure, will drive the reaction to the formation of more linear structure. It may consume all the sugar and thus be no ring structures.

## Reactions from linear structures:



we need to understand reduction and oxidation by:

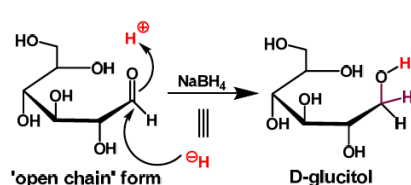
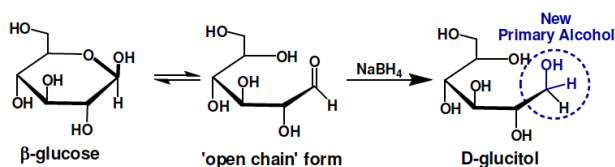


\* Increasing the oxygen content  
or Decreasing the hydrogen content = oxidation [O]

\* Decreasing the oxygen content  
or Increasing the hydrogen content = reduction [R]

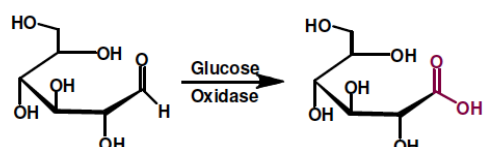
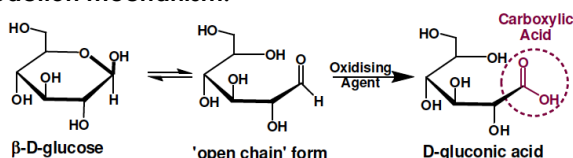
1. **Reduction of alditols:** this is an irreversible reaction. Since the reaction is in equilibrium between the ring and linear forms, by Le Chatelier's principle, consuming the linear structure will drive the reaction to a 100% yield. The type of sugar that is generated is called an alditol for all carbohydrates, but if it is glucose derivative it is called glucitol, if fructose it is fructitol, etc.

- **reagents:** we will use  $\text{LiAlH}_4$  (this is a stronger reducing agent) or  $\text{NaBH}_4$
- **Reaction mechanism:** the reducing agent acts as a nucleophile and attacks the electrophile (carbon in the  $\text{C}=\text{O}$  bond).

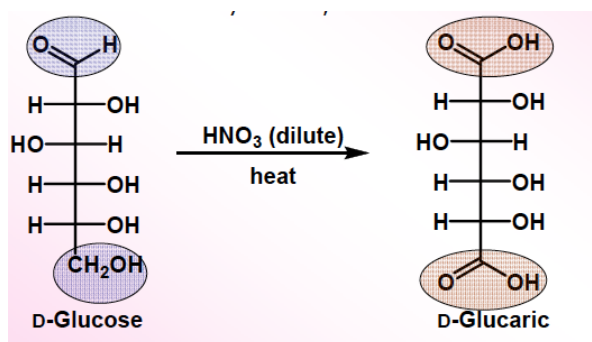


2. **Oxidation of aldonic acids:** this is an irreversible reaction. Since the reaction is in equilibrium between the ring and linear forms, by Le Chatelier's principle, consuming the linear structure will drive the reaction to a 100% yield. The product is called aldonic acid for all carbohydrates, but if it is a glucose derivative then it is called D-gluconic acid, etc.

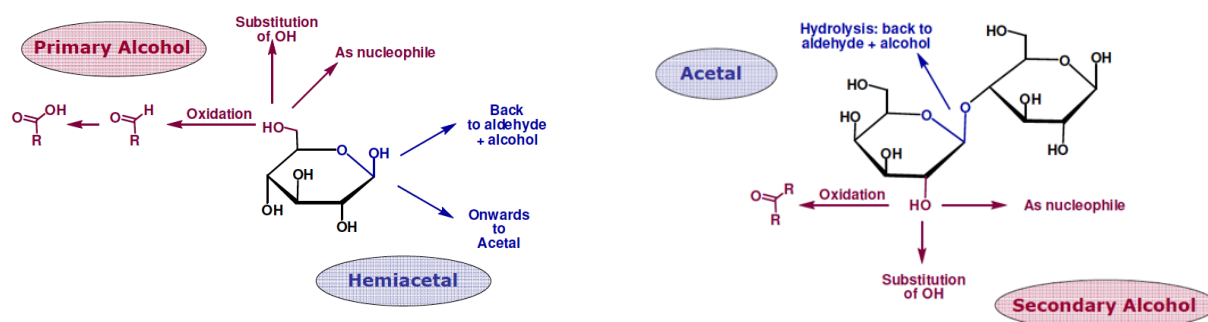
- **Reagents:** being selective is very hard since there are other primary alcohols which can be oxidized into aldehydes and carboxylic acids but in our body we have an enzyme which can oxidise the aldehyde selectively. Glucose oxidase. We can use  $\text{KMnO}_4$
- **Reaction mechanism:**



Note: this oxidation reaction can proceed until it form aldaric acid.

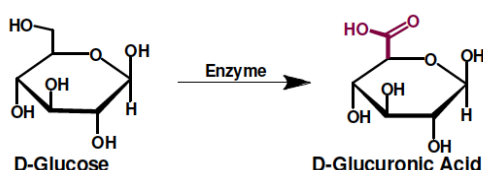


**Reactions from ring structures:** these reactions can proceed from a single ring or a disaccharides or many chains.



3. **Oxidation of uronic acids:** this is an irreversible reaction. Since the reaction is in equilibrium between the ring and linear forms, by le chatlier's principle, consuming the ring structure will drive the reaction to a 100% yield. the product is called uronic acid for all carbohydrates, but if it is glucose it is called D-glucuronic acid.

- **Reagents:** being selective is very hard since there are the secondary alcohols can also be oxidized into ketones but in our body we have an enzyme which can oxidise the primary alcohol selectively. Glucose oxidase.
- **Reaction mechanism:** the primary alcohol (C6) is oxidised to a carboxylic acid:
- **Role:** key component of connective tissue and important role in biochemical detox pathways (because of the attached carboxylic group is soluble in water, helps insoluble substance be excreted in the urine).



4. **Formation of glycosides (acetals):** this is an irreversible reaction. Since the reaction is in equilibrium between the ring and linear forms, by le chatlier's principle, consuming the ring structure will drive the reaction to a 100% yield. the product is called glycosides acid for all carbohydrates. The new bond (the acetal) is called a glycosidic bond.

- **Reagents:** We need an acid catalyse for the formation of an acetal but in our body we use enzyme to do this. We need a nucleophile, provided by the alcohol and the electrophile which is the hemiacetal.
- **Reaction mechanism:** there reaction forms the ring structure and then the hemiacetal is reaction with an alcohol which will yield an acetal. It undergoes S<sub>N</sub>1 mechanism, the hemiacetal is protonated and water leaves but the carboncation is resonance stabilised by the oxygen atom with the lone pairs so it is stable enough to exist.