

**CHEM 191****Module 4****Structures and reactions of biological molecules****Lecture 3****Chemistry of Carbohydrates:  
Monosaccharides – structure and reactions**

Lecturers: Dr Andrea Vernall  
Dr Eng Wui Tan

andrea.vernall@otago.ac.nz  
ewtan@chemistry.otago.ac.nz

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**Module 4 Lecture 3****Learning objectives****Learning Objectives:**

- Interpret Fischer projections, Haworth projections and 'chair' diagrams of monosaccharides
- Designate monosaccharides as D or L
- Understand the mechanism for hemiacetal formation (covered in lecture 2)
- Understand the equilibrium (mutarotation) between open chain and cyclic hemiacetal forms of monosaccharides
- Identify the anomeric carbon and assign the anomer stereochemistry as  $\alpha$  or  $\beta$
- Define and recognise a 'reducing sugar'

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## What are carbohydrates?

- An important class of naturally occurring compounds found in plant and animal matter
- *Most* carbohydrates have the formula  $C_m(H_2O)_n$  i.e. are 'hydrates' of carbon, hence the name 'carbohydrate', e.g. glucose  $C_6H_{12}O_6$  is equivalent to  $(C.H_2O)_6$ 
  - There are exceptions to the formula, e.g. deoxy sugars (lecture 9)

### Ingested in the diet, carbohydrates -

- Can provide energy and regulation of blood glucose
- Can spare the use of proteins and fats for energy
- Can provide dietary fibre

### Carbohydrates can also be synthesised and assembled *in vivo* -

- Ribose for nucleotide production
- Cell-surface carbohydrate-based polymers for adhesion and molecular recognition (*lecture 4*)
- Many important biochemical pathways

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## Classes of carbohydrates

- Carbohydrates are known as 'saccharides', from the Greek word *sákkharon* meaning 'sugar'
- Classified based on the number of saccharide units or sugars that cannot be broken down to more simple sugars

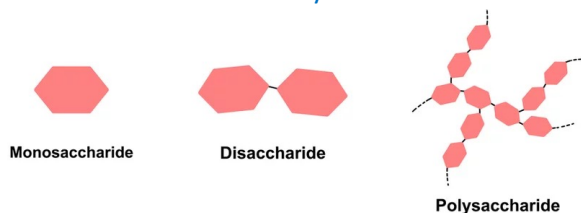
### • Di- to polysaccharides – covered in lecture 4

### • Today's lecture – monosaccharides

- Can not be broken down to more simple sugars
- Still called a 'carbohydrate'

### Monosaccharides include:

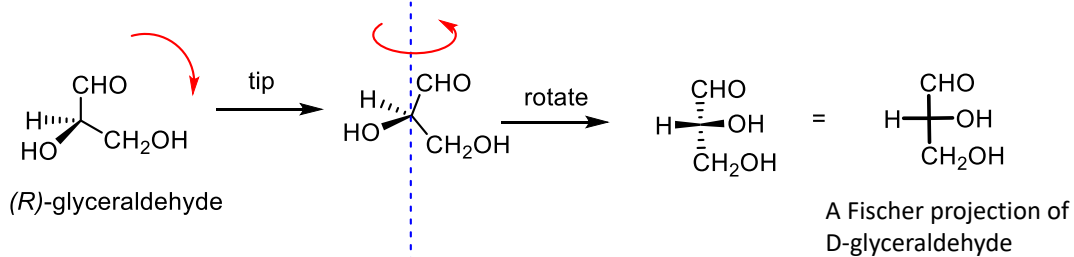
- polyhydroxy aldehydes – *aldoses* (most common form)
- polyhydroxy ketones – *ketoses*
- polyols – *alditols*
- polyhydroxy acids



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## Glyceraldehyde – the simplest aldose

- $C_3H_6O_3$
- Has a chiral carbon
- Drawing (R)-glyceraldehyde as a Fischer projection shows it is the D-form -



(R)-glyceraldehyde = D-glyceraldehyde; (S)-glyceraldehyde = L-glyceraldehyde

Most natural sugars are the D-isomer

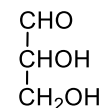
A Fischer projection represents a 2D drawing of a 3D chiral molecule about its stereocentre

..... let's look a Fischer projections more closely....

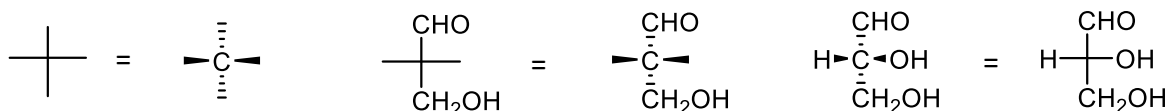
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## Fischer projection

asymmetric carbon  $\Rightarrow$



- 3D structures may be represented in a 2D shorthand form (Fischer projection)
- Chiral (or asymmetric) carbon represented as a cross piece
- For aldoses, drawn with the **aldehyde** at the top and  $\text{CH}_2\text{OH}$  at the bottom
- The **longest carbon chain** runs top-to-bottom on the page



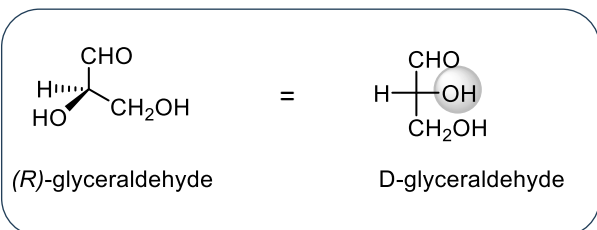
- In this orientation:
  - bonds up and down project into the page
  - bonds to the side project out from the page

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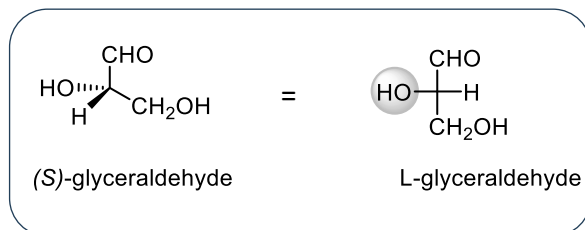
## Fischer projection – D and L nomenclature

Pages 1314-1316

- On the horizontal bonds:
  - If the non-hydrogen atom is pointing to the right it is the D-isomer
  - If pointing to the left it is L-isomer



OH to the right, **D-isomer**



OH to the left, **L-isomer**

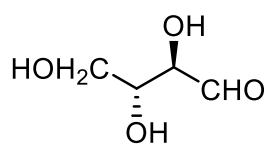
*Now let's look at how this nomenclature applies to larger monosaccharides with more carbons....*

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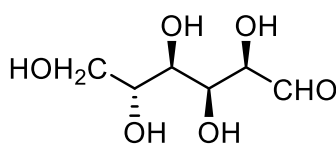
## Larger aldoses

Pages 1314-1316

- Aldoses may have varying numbers of carbons, e.g.



*D-erythrose*  
an aldotetrose  
4 carbons



*D-glucose*  
an aldohexose  
6 carbons

Hydrogens on carbons are still 'there' but omitted for clarity

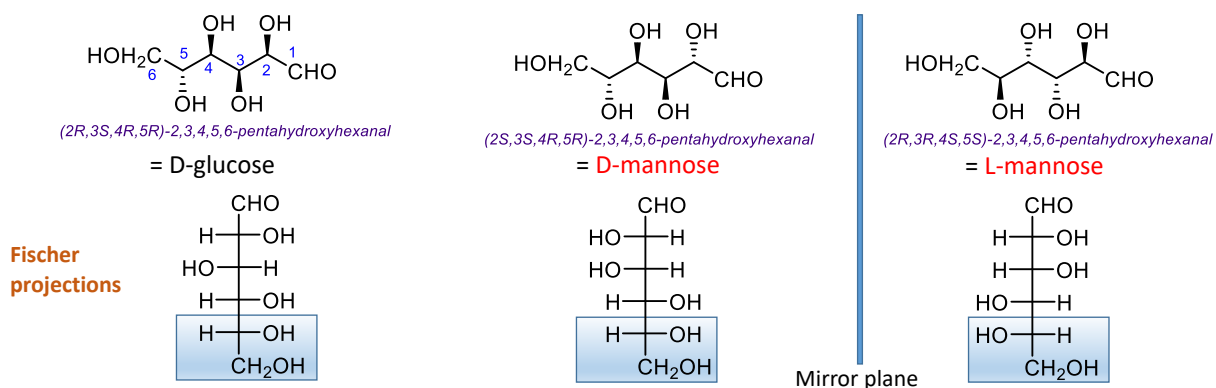
- As the number of carbons increases, the number of asymmetric (chiral) carbons and the numbers of possible stereoisomers increases
- An **aldohexose** with '*n*' asymmetric carbons has  $2^n$  possible stereoisomers, so for glucose this is  $2^4 = 16$

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## Aldohexoses

Pages 1314-1316

- Almost all natural monosaccharides are D-sugars (i.e. are the *D*-isomer)  
*But with multiple stereocentres in aldohexoses, which carbon do we look to for D/L?*
- It is just the chiral carbon **next to the CH<sub>2</sub>OH group** that defines D versus L
- The arrangements at other chiral carbons (C2, C3, C4, C5) give rise to **different sugar names**

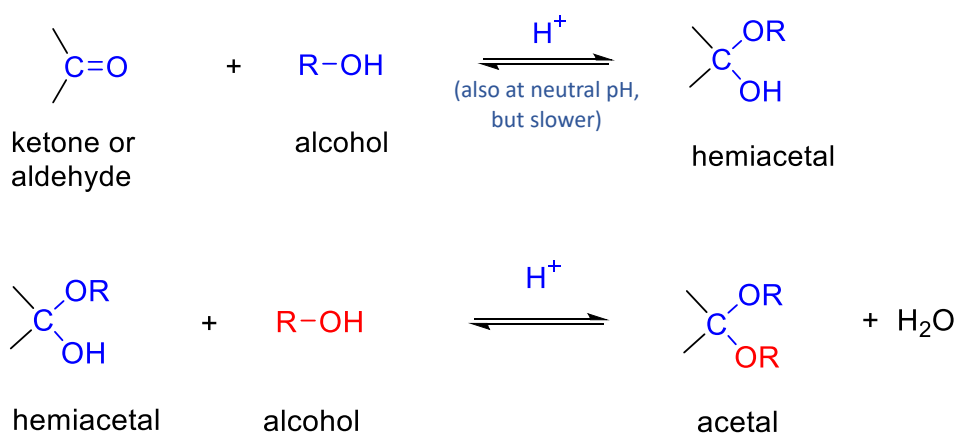


Homework – from the 3 sugars above, which are enantiomers? Which are diastereoisomers?

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## Hemiacetals and acetals

- The chemistry of carbohydrates is dominated by the chemistry of **hemiacetals** and **acetals**

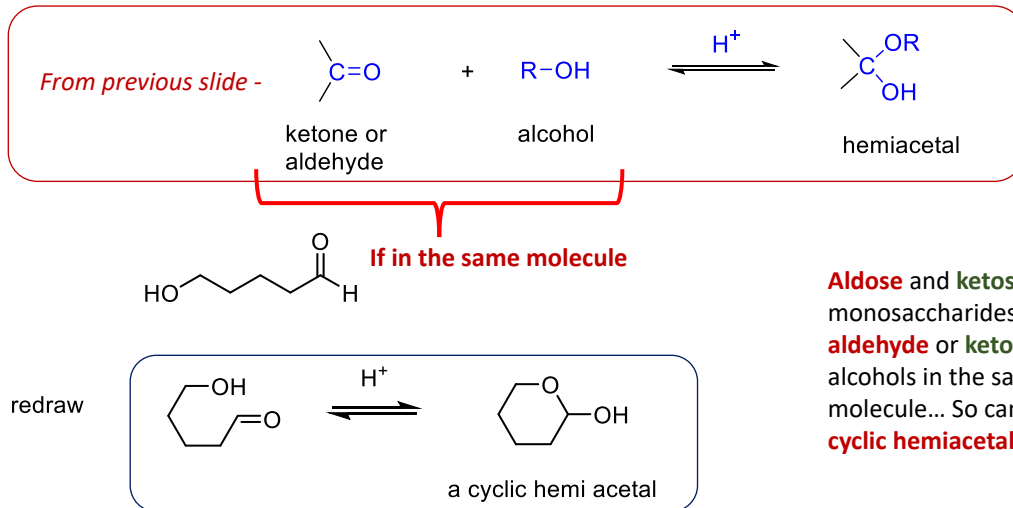


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## Cyclic hemiacetals

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- If the same molecule contains both the aldehyde and alcohol, then a **cyclic** hemiacetal can form

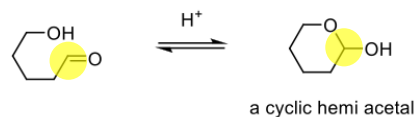


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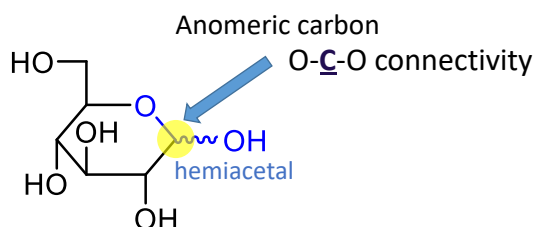
## The anomeric carbon

Pages 1317-1319

- The aldehyde/ketone carbon in the acyclic molecule turns into a **new stereocentre** in the cyclic molecule



- This carbon in the cyclic molecule is call the **anomeric carbon**



This way of drawing a sugar is called a **Haworth Projection**

- A way to visualize the stereochemistry of cyclic saccharides
- For monosaccharides, the anomeric carbon is on the RHS with the hemiacetal ring oxygen in the back right position

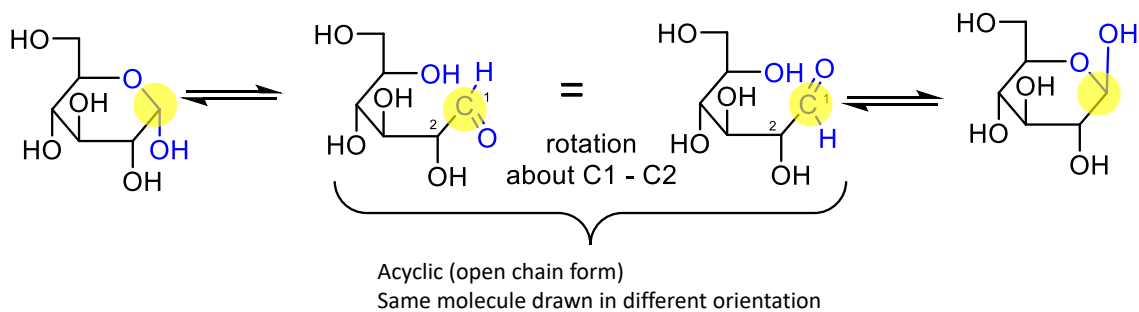
*What does the 'squiggly line' mean....? That there are two possible isomers at this position*

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## Acyclic form and cyclic hemiacetals are in equilibrium

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- Cyclic hemiacetal diastereoisomers exist in solution, in equilibrium via the 'open chain' form of the monosaccharide
- This equilibrium (i.e. interconversion of cyclic hemiacetal diastereoisomers) is called **mutarotation**

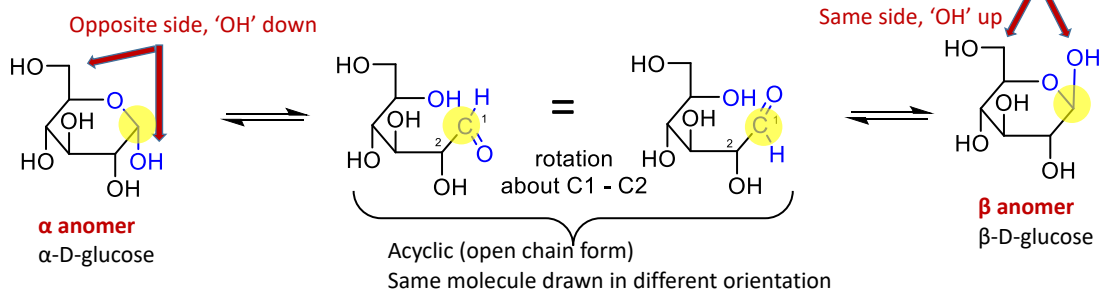


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## Cyclic hemiacetals – naming as the $\alpha$ or $\beta$ anomer

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- The cyclic hemiacetal diastereoisomers are called **anomers**
- The stereochemistry at the **anomeric carbon** (C1) is assigned as  $\alpha$  or  $\beta$



- $\alpha$  anomer - the OH is the **opposite side** to  $\text{CH}_2\text{OH}$ , the OH is 'down' in the Haworth projection
- $\beta$  anomer - the OH is the **same side** to  $\text{CH}_2\text{OH}$ , the OH is 'up' in the Haworth projection

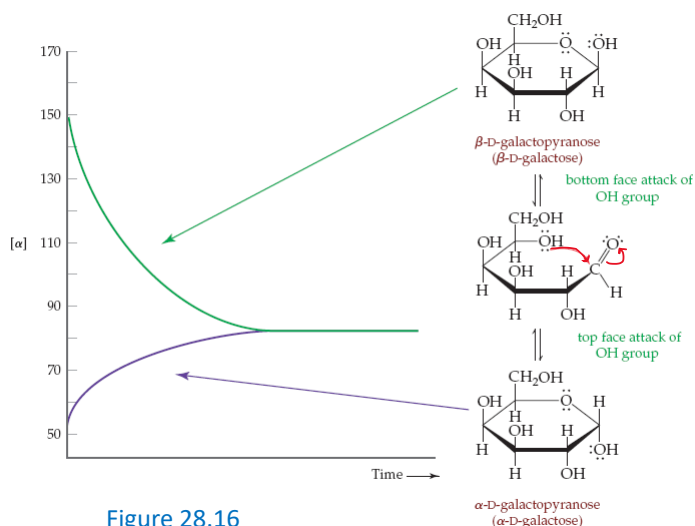
**How can we measure this equilibrium?** - Mutarotation is defined as a change in the optical rotation of a solution due to a change in the equilibrium between  $\alpha$  and  $\beta$  anomers

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## Measuring mutarotation

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Use **polarimetry** (*learnt in Module 3*) to measure specific rotation



1. Dissolve pure crystalline  $\beta$ -D-galactose in water, measuring **immediately** before any hemiacetal can turn into a straight chain form, gives **+151°**

2. The reaction starts, over time equilibrium is reached, the specific optical rotation stops changing, this is measured to be **+80°**

4. Knowing all this info the ratio at equilibrium is calculated to be **72:28  $\alpha$ : $\beta$  anomers.**

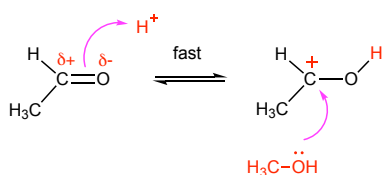
3. In a different experiment, start with pure crystalline  $\alpha$ -D-galactose, add water, measuring **immediately** before any hemiacetal can turn into a straight chain form, gives **+53°**, this also turns into **+80°** over time

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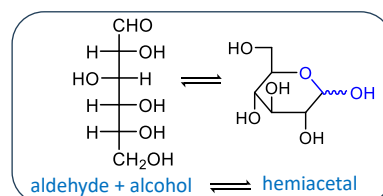
## Mutarotation mechanism

### Aldehyde + alcohol to hemiacetal

- In module 4 lecture 2 we learnt the mechanism for this in the presence of acid  $H^+$ , i.e. acid catalysed

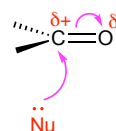


- The reaction *can still* occur in neutral conditions without acid with a 'weak' alcohol as the nucleophile, but it is much slower



### Hemiacetal to aldehyde + alcohol

- Essentially the exact reverse reaction of above
- Occurs faster with  $H^+$  catalysis but can occur slowly at neutral pH (mechanism not covered)
- Therefore in basic, neutral or acidic conditions, hemiacetals are **not stable** and are always in equilibrium with an aldehyde/ketone + alcohol



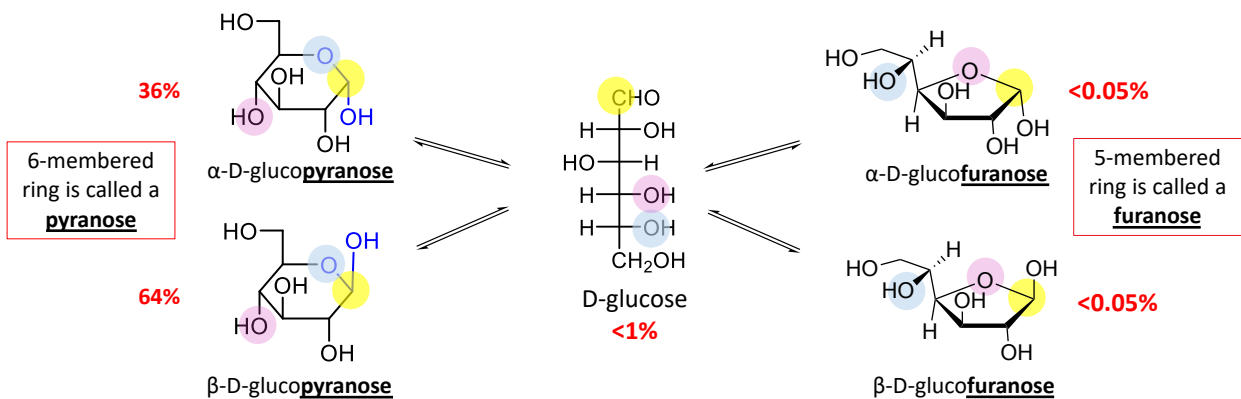
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## Different cyclic hemiacetal ring sizes can form

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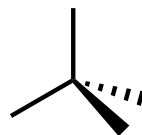
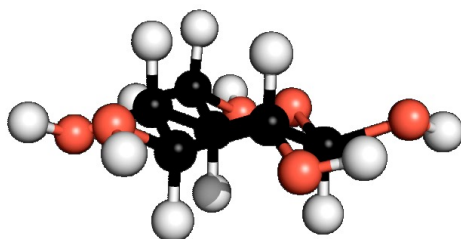
- For most hexose (C6) monosaccharides, cyclic hemiacetal forms dominate with the 'open chain' acyclic <1%.
- Different ring sizes of cyclic hemiacetals are possible
- Depending on the sugar, the 6 versus 5 membered ring may be favoured, e.g. D-glucose in solution:



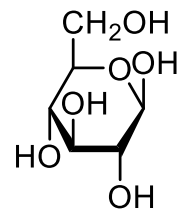
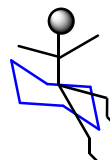
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## Chair representation of a sugar

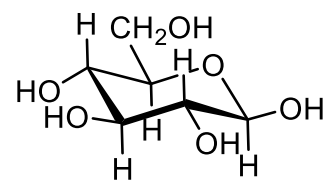
- The carbons in glucose are tetrahedral
- These ring systems are not flat



Piecing this together in a 6-membered ring gives a **chair**



β-D-glucopyranose



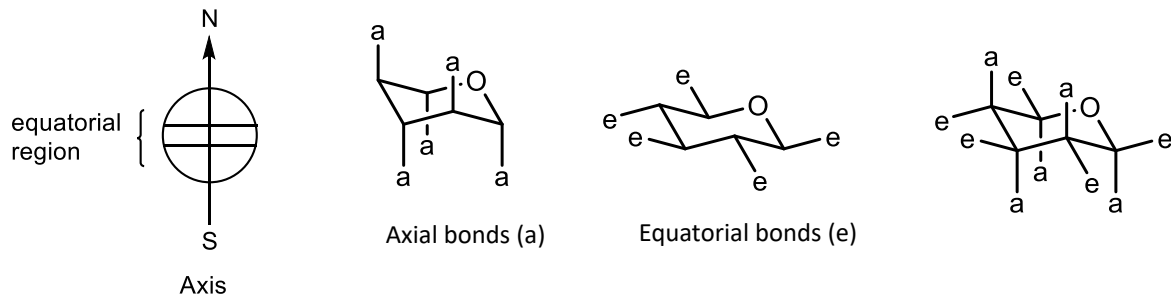
β-D-glucopyranose

The carbons all have tetrahedral geometry. This is a very stable structure.

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## Chair representation of a sugar

- As we will see in Lecture 4 with polysaccharides, usually large substituents (e.g. another sugar) are more stable in an 'equatorial' position

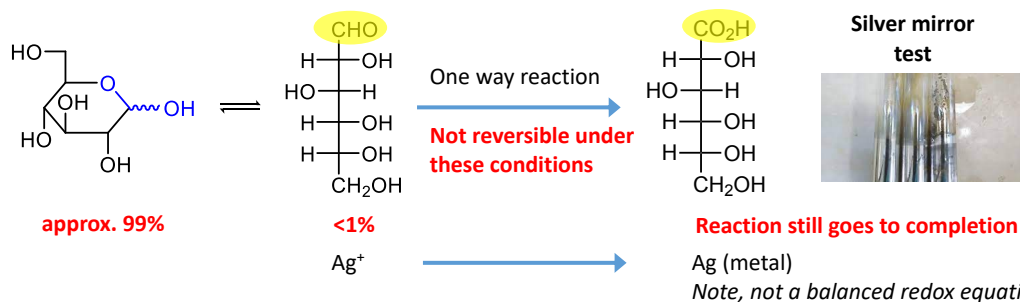


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## Reducing sugars

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- 'Reducing sugars' contain a functional group that can easily act as a *reducing agent* thereby is *itself oxidised*
- Even though most sugars exist predominantly in cyclic hemiacetal form(s), because this is an equilibrium with an **aldehyde**, any sugar with a cyclic hemiacetal is a **reducing sugar**



- As we will see in lecture 4, reducing sugars contain **hemiacetals**, while polysaccharides containing only **acetals** are much more stable and are **not** "reducing sugars".

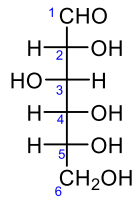
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## \* Homework \*

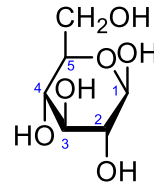
Practice interpreting/converting between the same sugar as a Fischer, Haworth and Chair.

e.g. make sure you are OK with going between the following ways of drawing sugars

Remember the difference between named sugars, e.g. shown here, is any stereochemistry at C-2, 3, 4 or 5 that is different

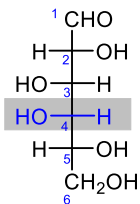


D-glucose open chain form

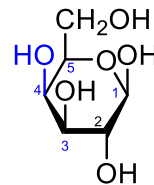


+ other cyclic anomer

$\beta$ -D-glucopyranose (cyclic form)



D-galactose open chain form



+ other cyclic anomer

$\beta$ -D-galactopyranose (cyclic form)