

Carbohydrates

CHE 2112

Carbohydrates

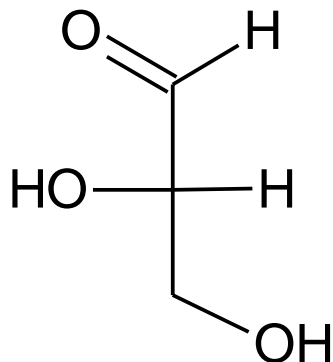
- Are polyhydroxy aldehydes or ketones and their derivatives
- Most conform to empirical formula $(\text{CH}_2\text{O})_n$

Classification

- 3 main groups - monosaccharide, disaccharides & polysaccharides.
- Sometimes 4th group known - oligosaccharides (2 to 10 monosaccharides)
- Oligosaccharides include Di, Tri, Tetra, and Penta,.....,Deca, - saccharides (*Give an example of each; Define a legume oligosaccharide and give three examples*)

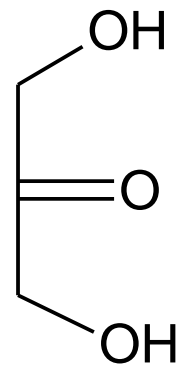
Monosaccharides

- Also called simple sugars
- Simplest carbohydrates
- Are aldehydes or ketones that have 2 or more hydroxyl groups
- Cannot be hydrolysed into simpler form
- Glyceraldehyde and dihydroacetone, with $n = 3$, are the smallest in this group.



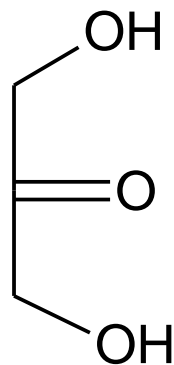
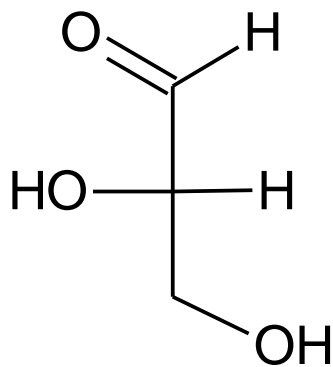
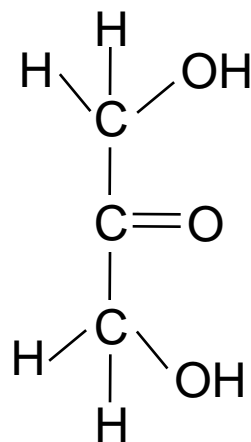
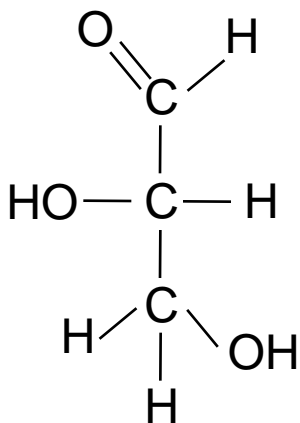
L - Glyceraldehyde

- An aldose
- Called an aldose because it is an aldehyde



Dihydroxyacetone

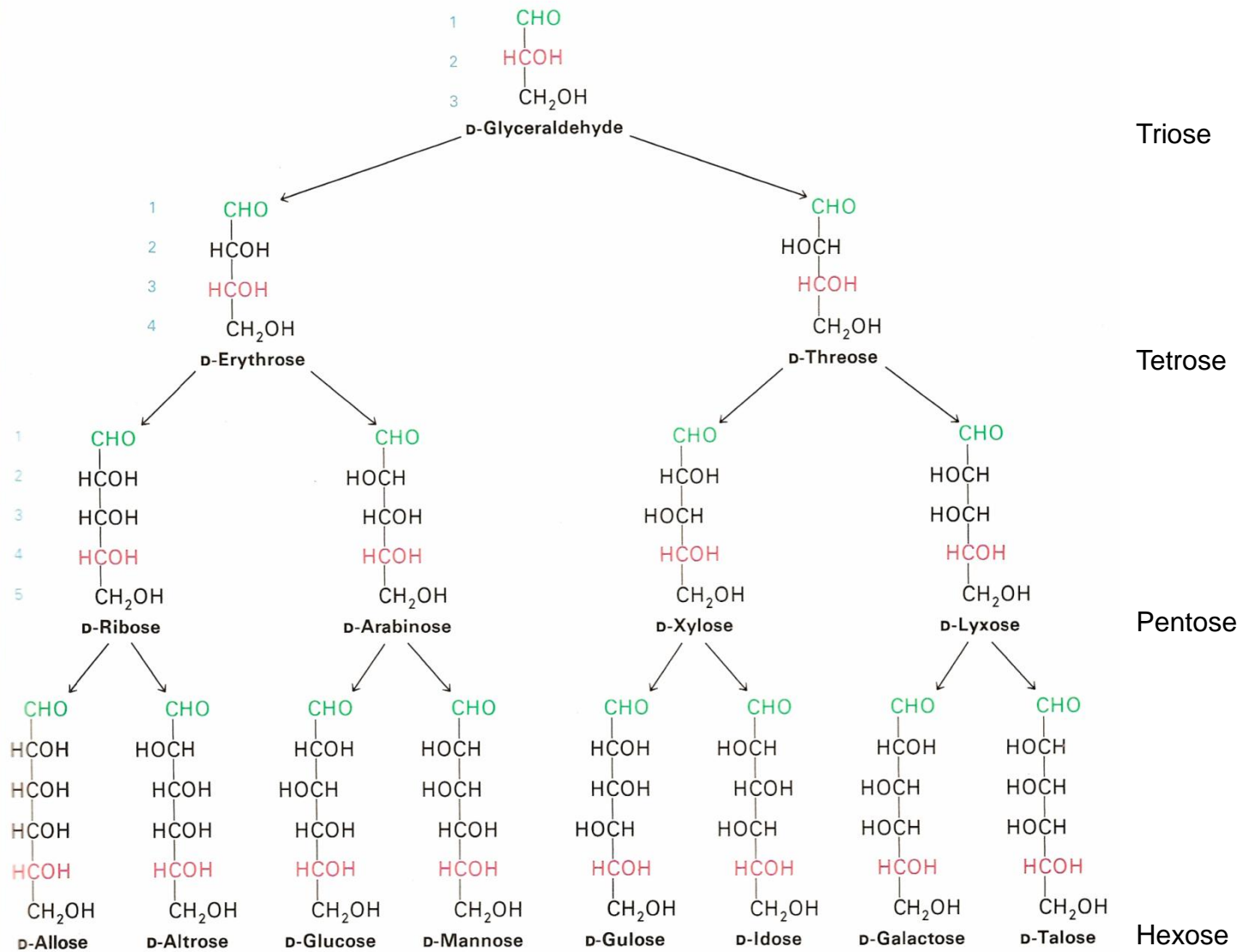
- A ketose
- Called a ketose because it is a ketone



L - Glyceraldehyde

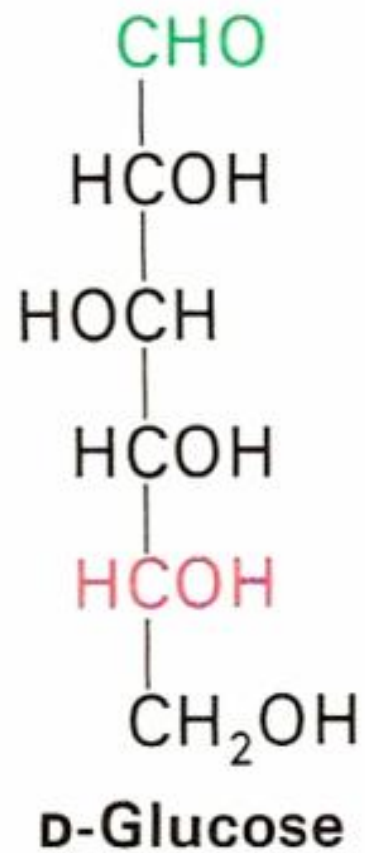
Dihydroxyacetone

- Depending on value of n in $(\text{CH}_2\text{O})_n$ or number of carbon atoms monosaccharides can be classified:-
 - $n = 3$ – triose
 - $n = 4$ – tetrose
 - $n = 5$ – pentose
 - $n = 6$ - hexose



Monosaccharide Isomerism

1. L and D Isomers (Use glucose as a model)
 - Orientation of H and OH around carbon atom adjacent to terminal primary alcohol determines whether the sugar is L or D (refer to preceding slide).
 - Most sugars / monosaccharides that occur in mammals are D – isomers.
 - Presence of asymmetric carbon makes them optically active.

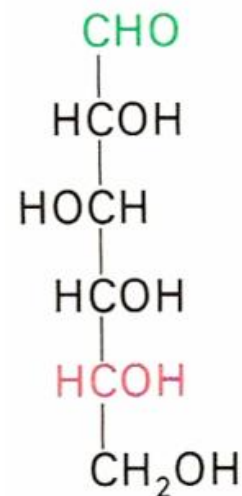
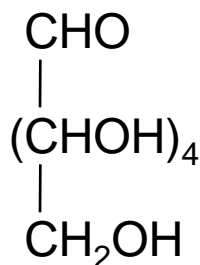
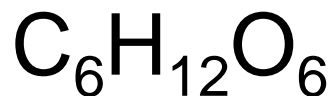


- Are able to rotate a beam of plane polarised light either to the Left or Right

- The left thus levorotatory or designated with a negative sign (-)
- Or to the right thus dextrorotatory or designated with a positive sign (+).
- Therefore a molecule could be designated as either D(-) or D(+) or L(-) or L(+).
- An equal concentration of D and L isomers result in a racemic mixture, which does not rotate plane polarised light, as the 2 isomers cancel each other.

Formulae of Glucose

- Molecular formula can be represented in various ways, revealing different levels of information at a glance



Molecular formula

Fittig Baeyer formula

Fischer Projection formula

- Functional groups

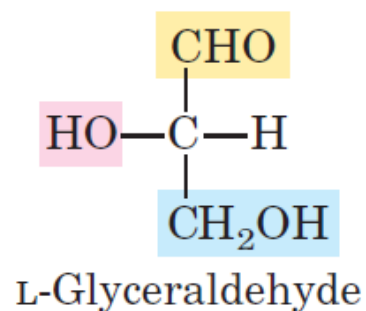
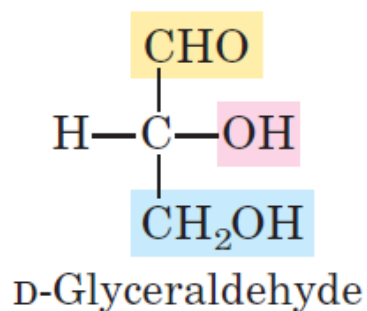
- 4 asymmetric carbons

- Work out total number of

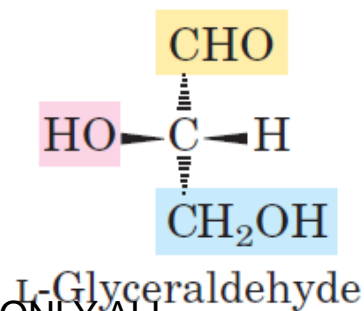
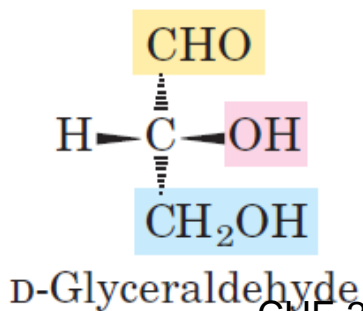
CHE 2112 2022 USE ONLY ALL isomers ($=2^n$)

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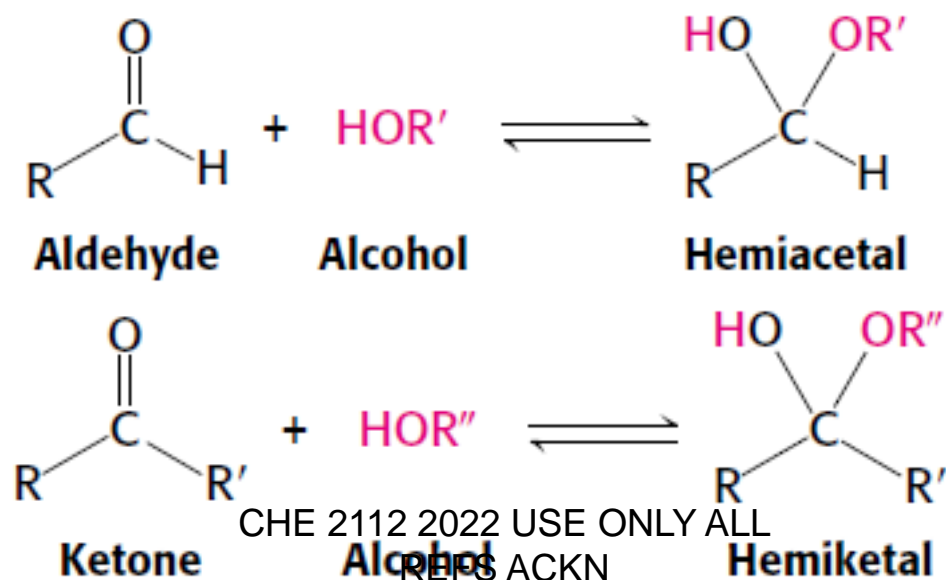
- Fischer projection perspective formula



Fischer projection formulas



- All these formulae representation fail to explain all the properties of glucose
- Sugars' aldehyde and ketone groups react with hydroxyl groups to form hemiacetals and hemiketals



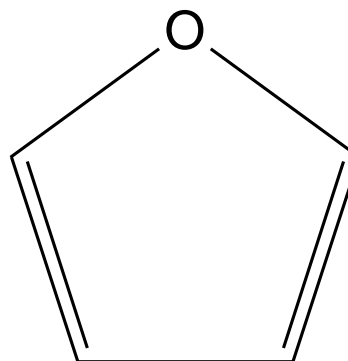
- Sugars with $n > 4$, aldehyde and ketone groups react with hydroxyl groups intramolecularly.
- This results in formation of 6-membered rings (pyranose) and 5-membered rings (furanose)
- 7 – membered rings are not possible due to molecular strains not allowing reaction between OH and CHO groups.

2. Pyranose and Furanose ring structures

- Monosaccharide form stable ring structures that are similar to pyran are called pyranose and those similar to furan are called furanose.
- Pyranoses sugars are more stable than furanoses sugars (pyranose formation has a ΔG° than that for furanose)

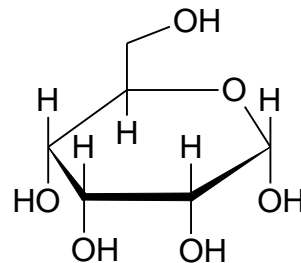


Pyran

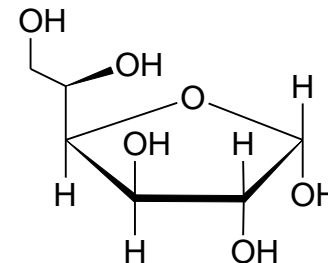


Furan

- These ring structures accounts completely for glucose's chemical properties

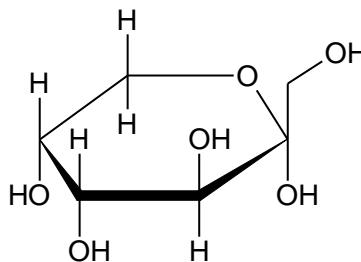


α -D-Glucopyranose
Or α -D-Glucose

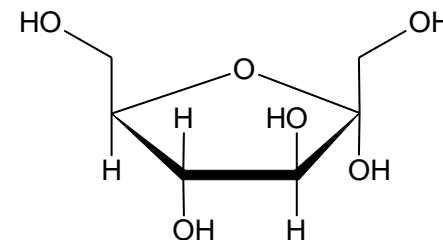


α -D-Glucofuranose

- Ketoses are also able to form ring structures



α -D-Fructopyranose



α -D-Fructofuranose

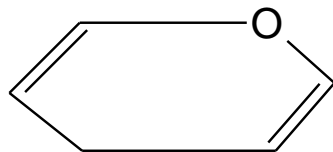
Haworth Perspective Formula

Groups on the right written down

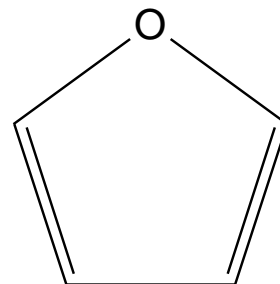
while groups on the left are

written up, except C₅

A

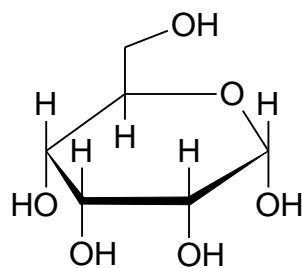


Pyran

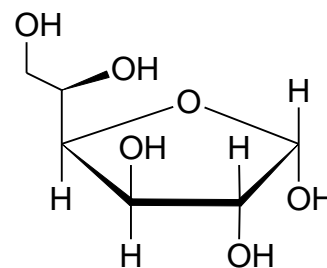


Furan

B



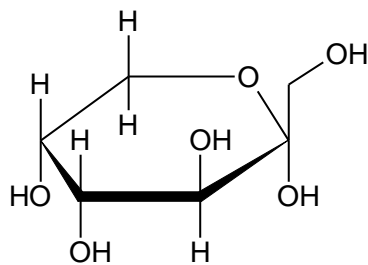
α -D-Glucopyranose



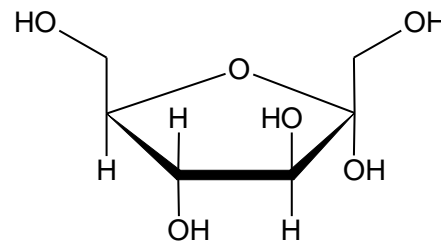
α -D-Glucofuranose

Or α -D-Glucose

C



α -D-Fructopyranose

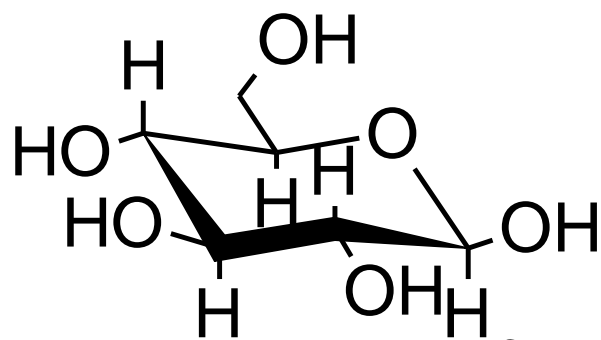


α -D-Fructofuranose

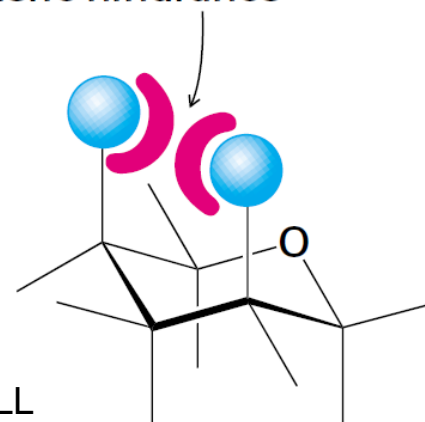
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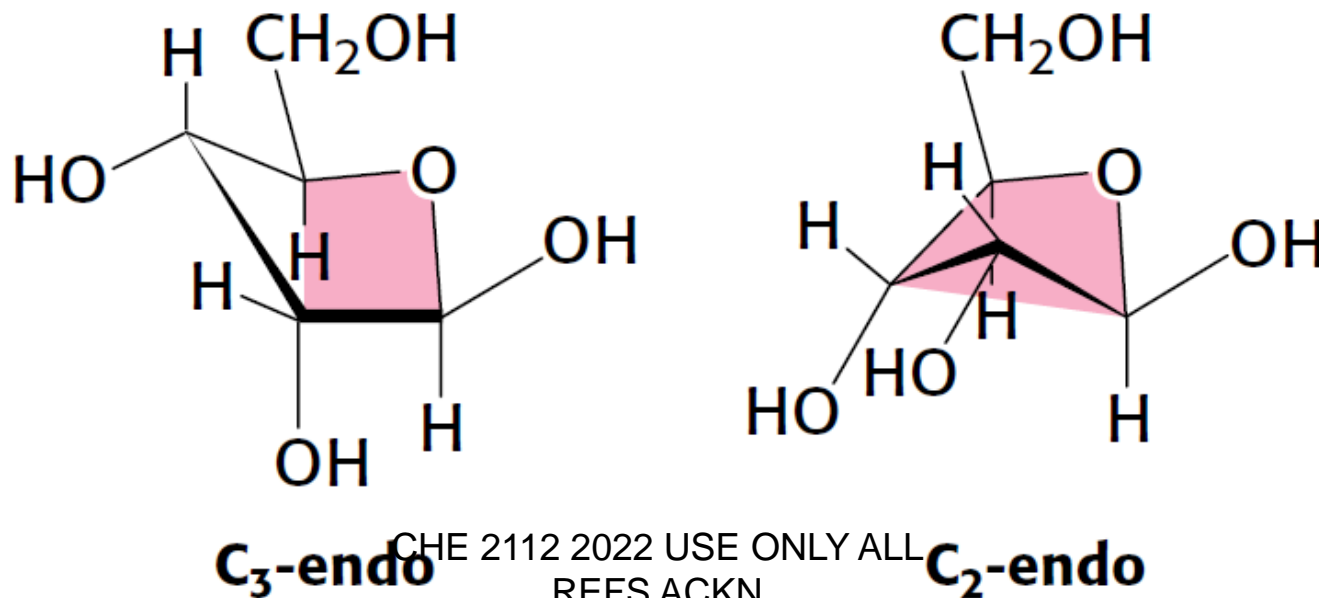
- Glucose solution exhibits 99 % in pyranose form and 1 % furanose form
- Glucose pyranose form has been found to be in the chair conformation with the larger substituents in the equatorial region as the chair conformation is energetically stable/favourable due to less hindrances



Steric hindrance



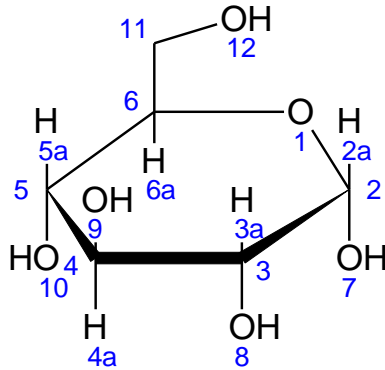
- Envelop confirmation of β -D- ribose
- C_2 – endo and C_3 – endo isomers exist due to changes in configuration at carbon atom 3 and 2.



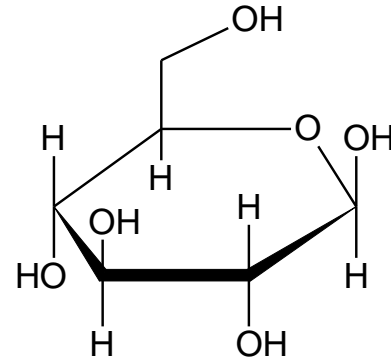
3. α and β anomers (Diastereoisomer)

- Cyclisation of linear glucose may result in α and β isomers due to the interchange of H and OH about carbon atom number 1 or anomeric carbon in the cyclic form.
- Isomerisation about carbon atom 1 or anomeric carbon result in a mixture of:-
 - 63% β -Glucopyranose
 - 36 % α -Glucopyranose
 - 1 % represented mainly by α - and β -Glucofuranose
- Inter-conversion or equilibrium result in optical rotation and interchange of H and OH about carbon atom 1 and is called **mutarotation**.

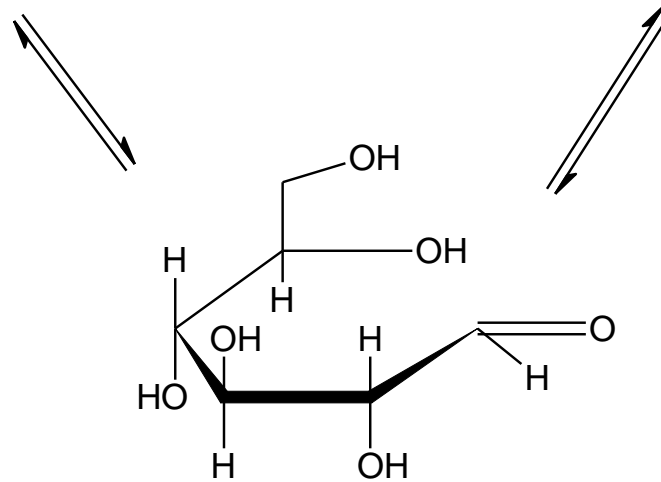
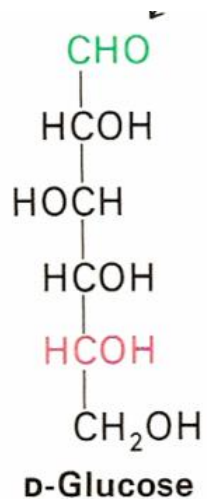
Mutarotation of Glucose



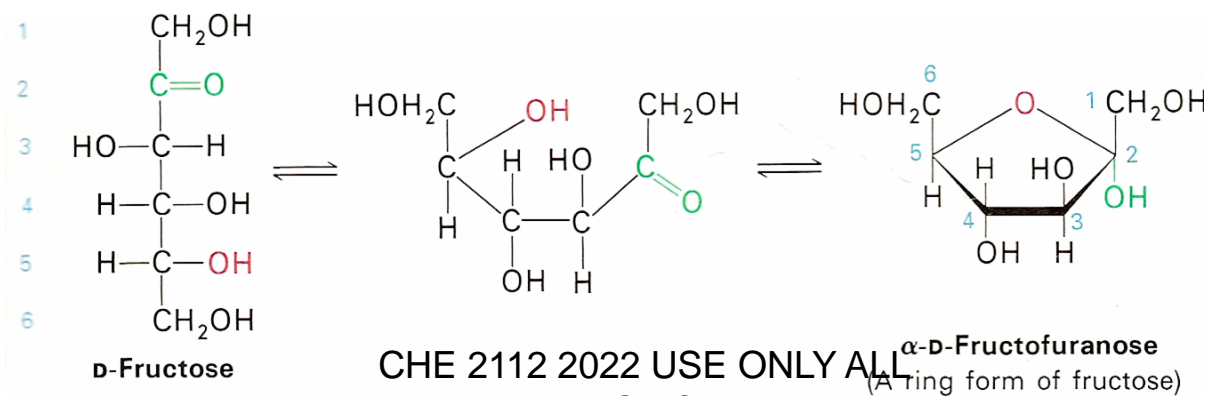
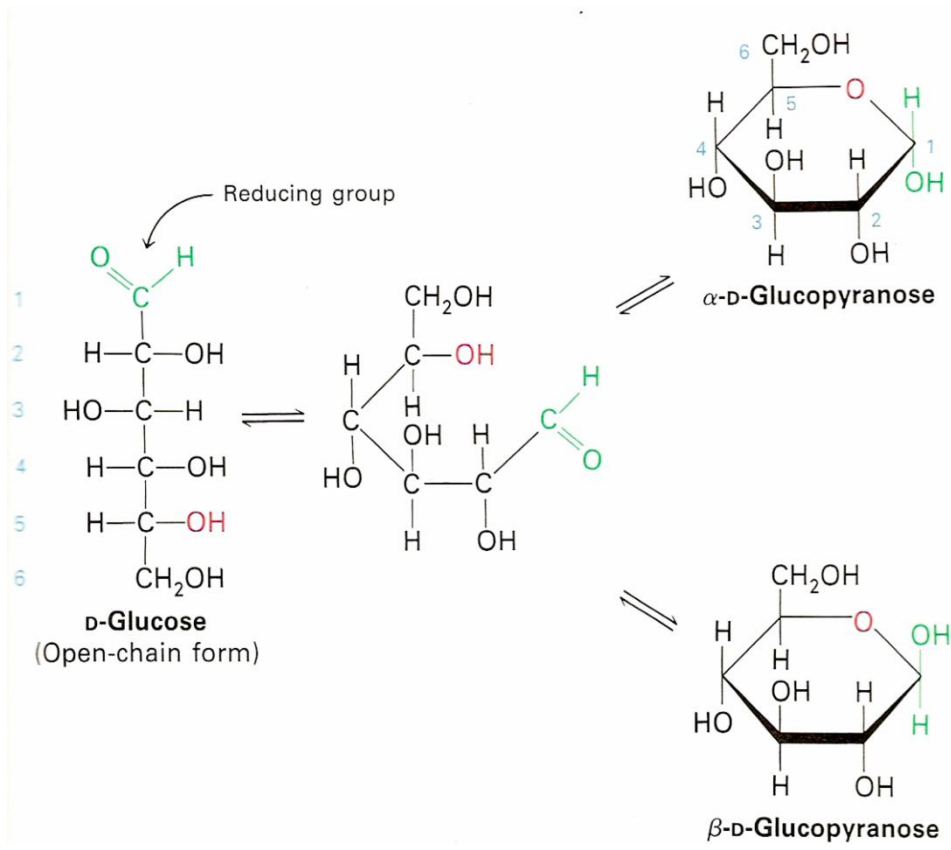
α -D-Glucopyranose



β -D-Glucopyranose

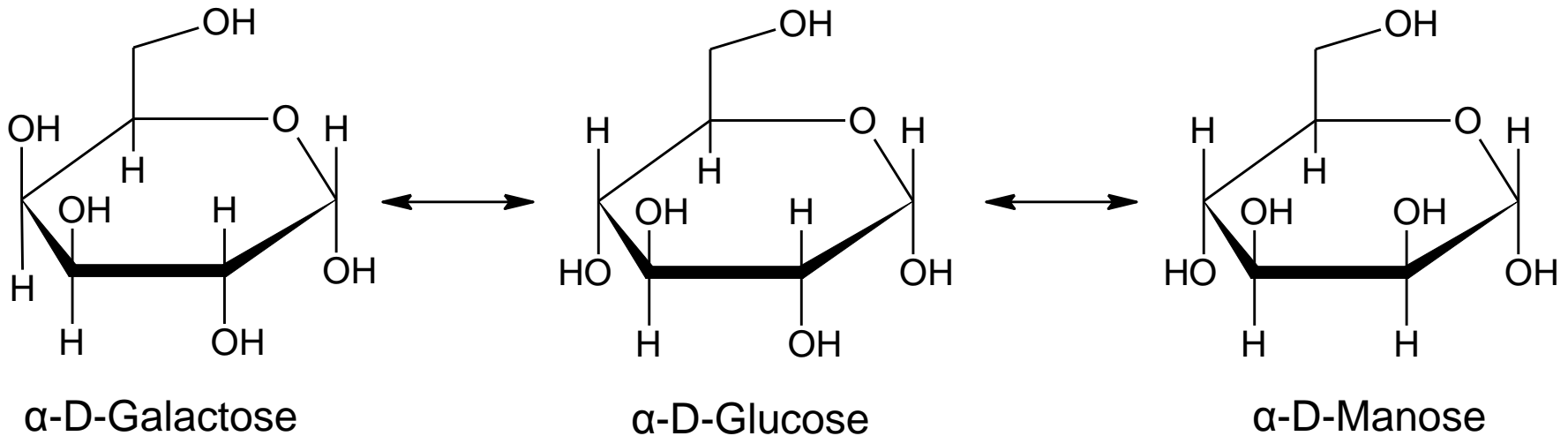


Acyclic Aldehyde form



4. Epimers

- Isomers of glucose differing in the position of H and OH at positions 2, 4, and 6 are called epimers.
- Epimers of glucose of biological importance are manose and galactose

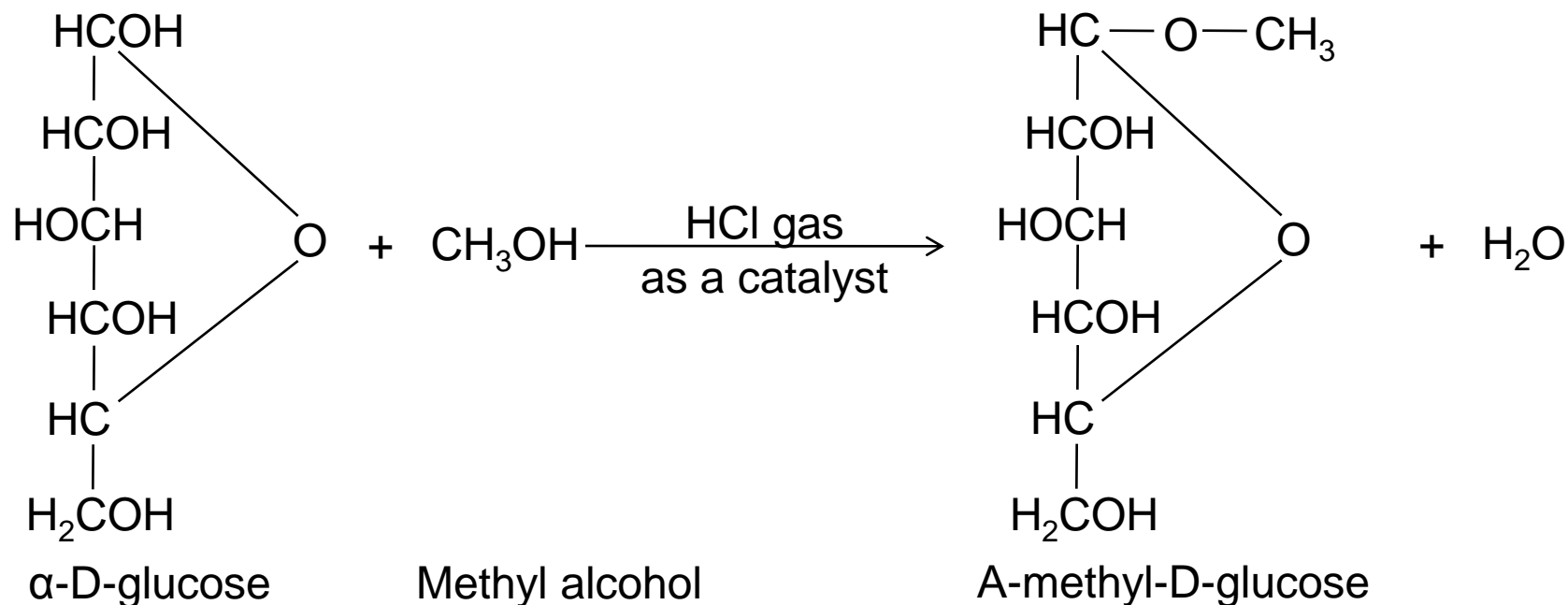


Chemical Properties

- Reactive groups in carbohydrates makes the reactive
- These are glycosidic OH, alcoholic OH and aldehyde (CHO)/ketone(C=O)
- α -form \leftrightarrow aldehyde/ketone form \leftrightarrow β -form
- Equilibrium shifts in favour of the reacting group

Rxn of Glycosidic OH group

- Reaction with alcohols

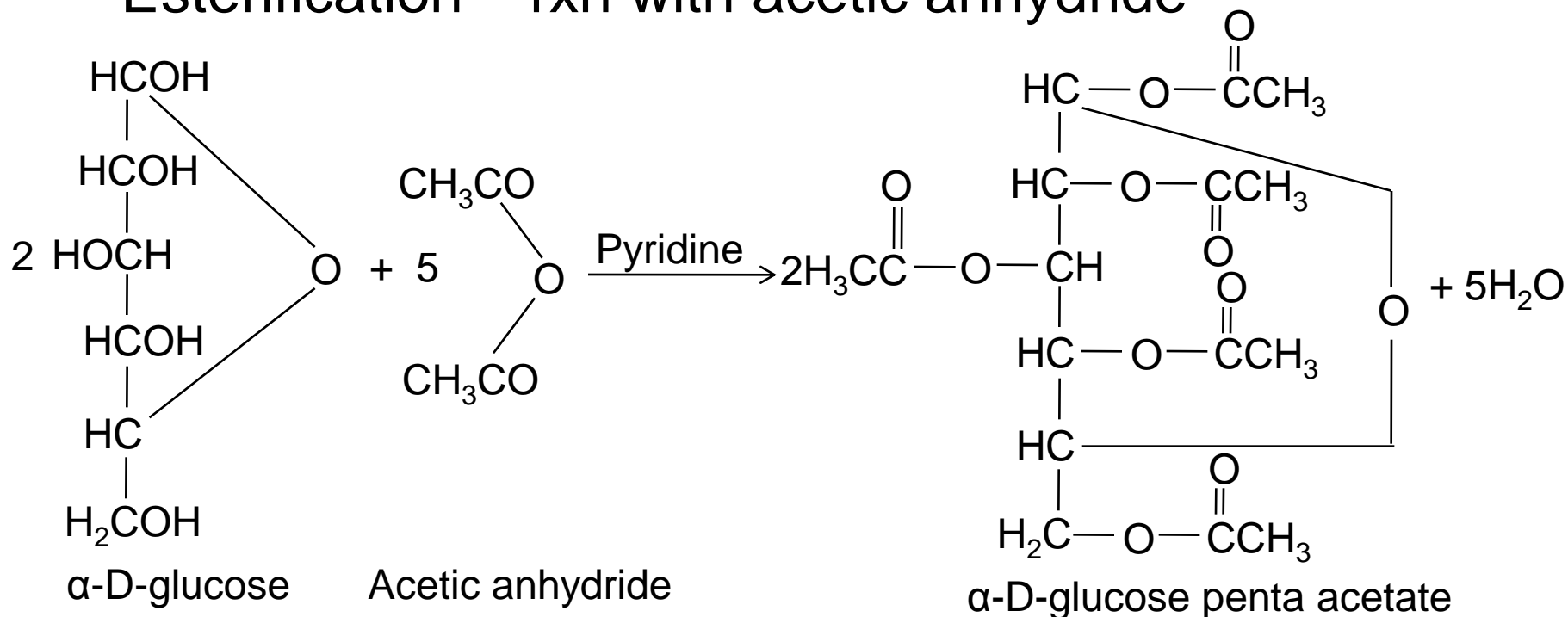


- Glycosidic OH reacts with alcohols to form α – and β -glycosides or acetals
- Glucose forms glucosides and fructose forms fructosides

- Glucosides or glycosides do not exhibit mutarotation as aldehyde group is in the acetal form
- These are used as medicaments

Rxn of Glycosidic & Alcoholic OH group

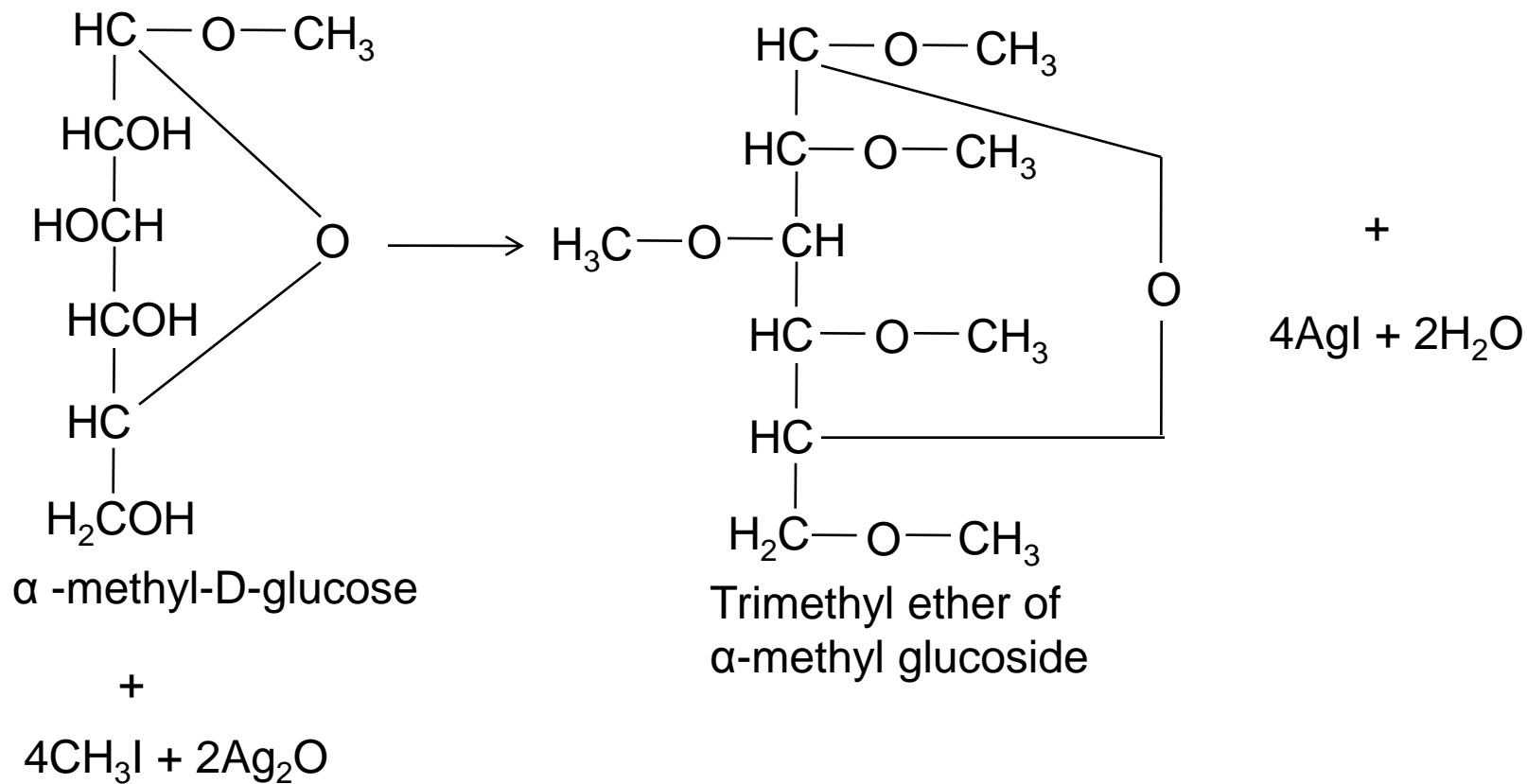
- Esterification – rxn with acetic anhydride



- Test for presence of alcohol groups in sugars to form esters
- Glucose forms a penta (5 OH groups) acetate derivative

Rxn of Alcoholic OH

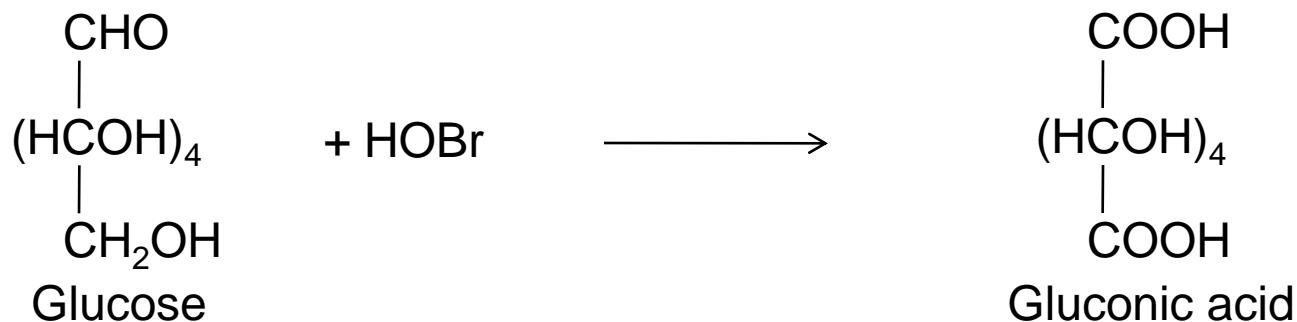
- Alcoholic OH of monosaccharides and disaccharides converted to ethers when reacted with methylating agents
- Glycosidic OH group of sugar first protected by R group (methyl group), before methylation



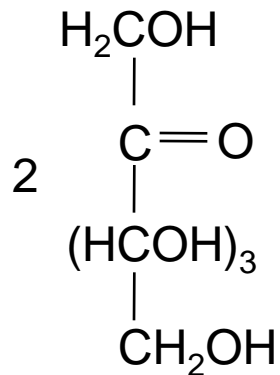
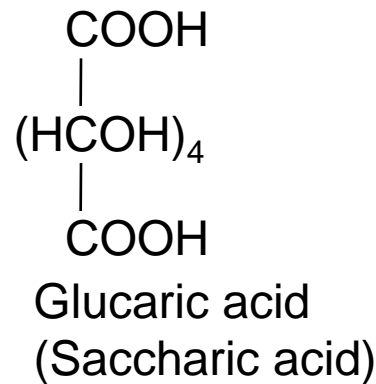
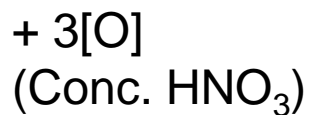
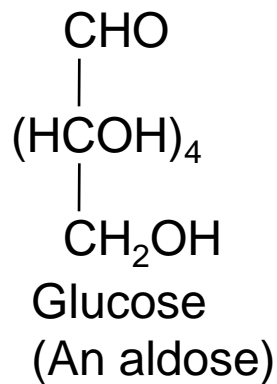
- Rxn used to determine which alcoholic OH groups are free for reaction

Rxns of both Alcoholic OH and CHO/C=O Groups

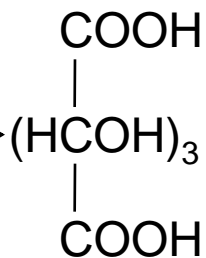
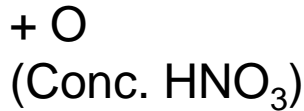
- Oxidation with Acids
 - Cyclic hemiacetal forms of sugars are in equilibrium with a small but finite amount of open chain aldehyde, they can easily be oxidised to carboxylic acids called aldonic acids
 - Certain oxidising agents oxidises OH to carboxylic groups
- a) Mild Oxidant, HOBr – Only aldehyde group converted to monocarboxylic acids
- Rxn used to differentiate Aldoses from ketoses



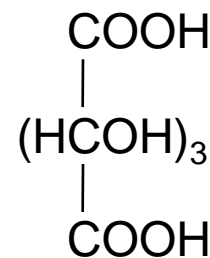
- b) Strong oxidants, HNO – aldehyde (ketone) and primary OH groups oxidised to dicarboxylic acids
- Aldoses oxidised to same number of carbon atoms while ketoses are oxidised to fewer numbers of carbon products



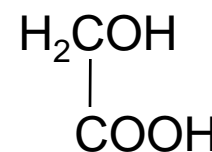
2



+



+



Fructose
(A ketose)

Trihydroxy
Glutaric acid

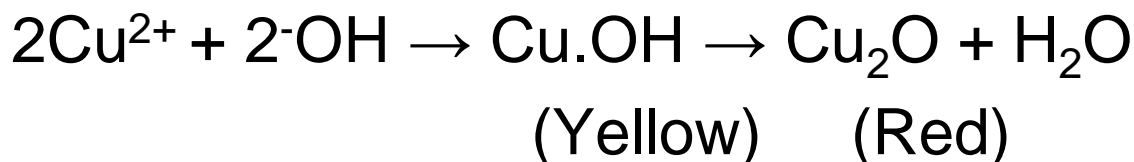
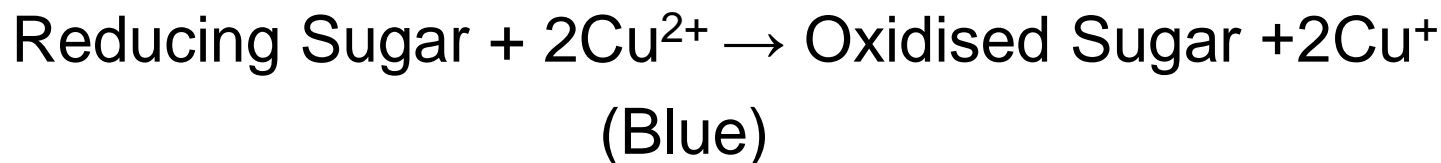
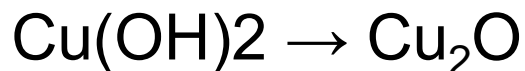
Tartaric acid

Glycolic acid

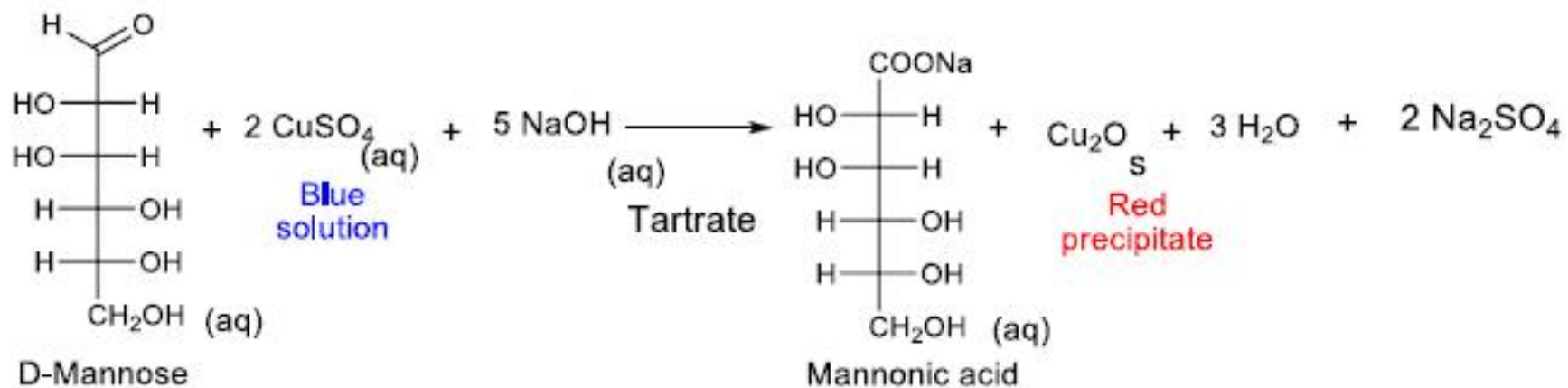
Rxns of CHO/C=O Groups

1. Oxidation with metal hydroxides

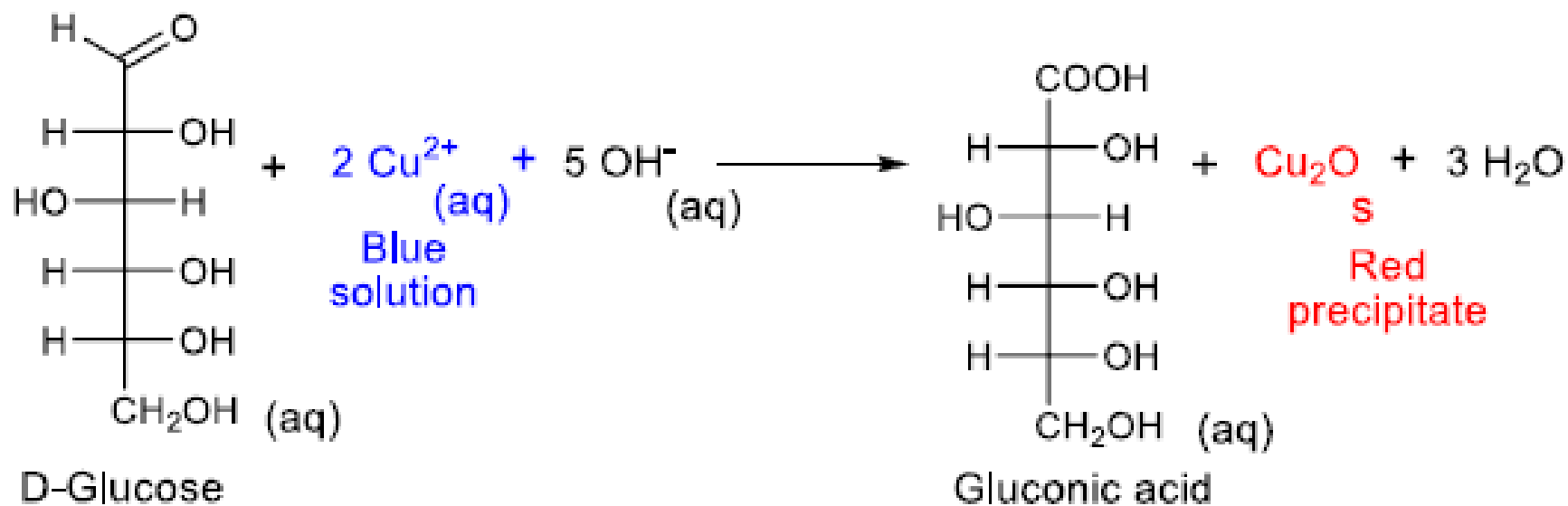
- $\text{Cu}(\text{OH})_2$, AgOH and $\text{Bi}(\text{OH})_3$ oxidise free CHO and C=O of mutarotating monosaccharides and disaccharides and get reduced



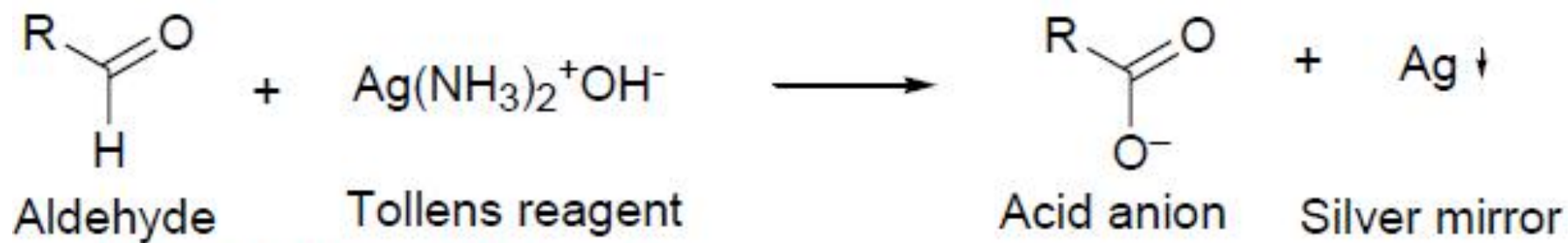
- **Fehling's reagent** (Equimolar of (a) 7% Cu.SO_4 & (b) 25% KOH /35% Potassium tartarate) on mixing the two forms a clear blue solution
- Test for reducing sugars
- Solution used in quantitative determination of sugars



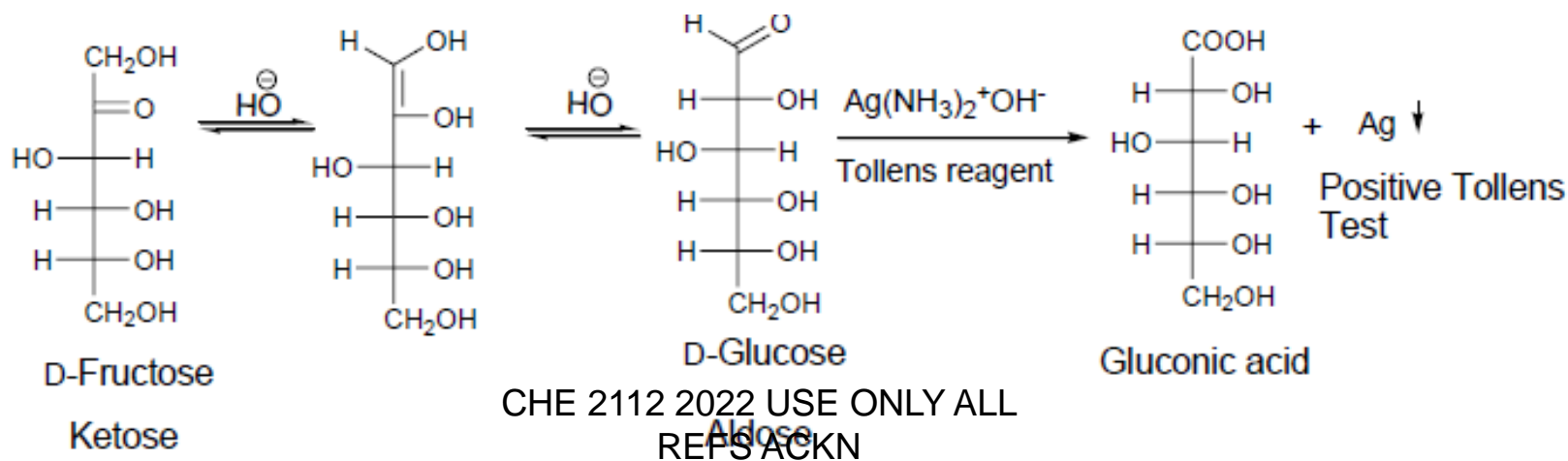
- **Benedict's Reagent** – ($\text{Cu}\cdot\text{SO}_4$, Na_2CO_3 & Sodium citrate)
- Variant of Fehling's reagent
- Qualitative determination of glucose in urine
- Alkaline solution of copper (II) sulphate as its citrate complex oxidizes aliphatic aldehydes, aldoses and ketoses to the corresponding carboxylic acid.
- Reducing sugars give a positive test result because the reduction of the metal is accompanied by oxidation of the sugar – hence called reducing sugars



- **Tollens reagent** - (silver(I) ammoniacal hydroxide)
- Oxidizes aldehydes to carboxylate ions.
- Ag(I) complex is soluble in ammonium hydroxide is reduced to metallic silver
- Metallic silver is insoluble in ammonium hydroxide, resulting in formation of a silver mirror on inside of test-tube



- Tollens test unable to differentiate between aldoses and ketoses but strongly basic solution of Tollens reagent promotes enediol rearrangements
- Basic conditions promotes open-chain form of ketoses being converted to aldoses, which give a +ve Tollens test. Hence Fructose gives a +ve result



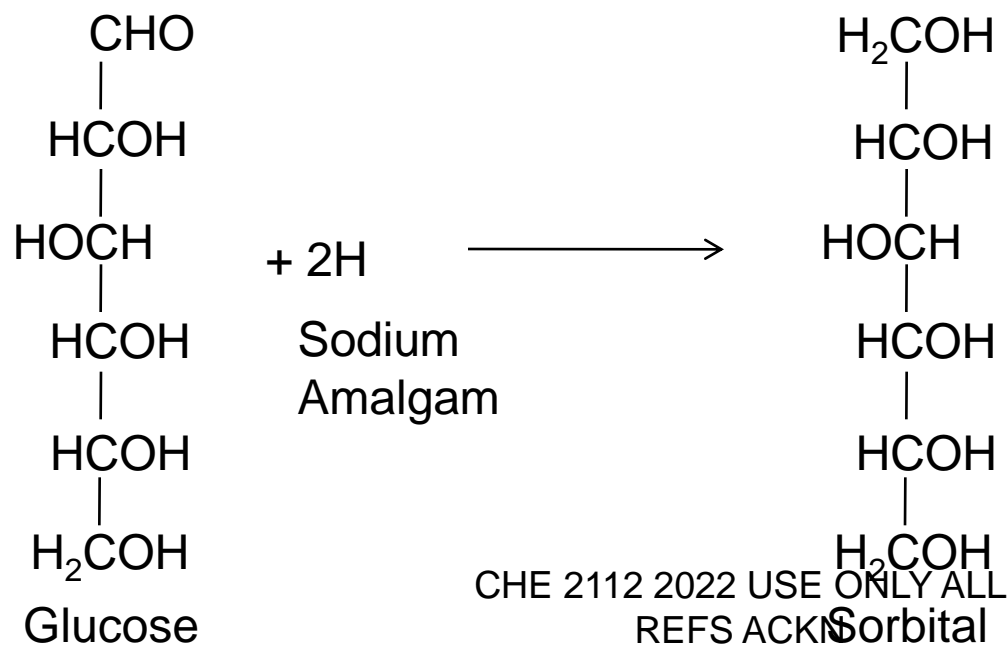
- **Barfoed's reagent** – (7% Copper acetate & 1% acetic acid)
- Used to differentiate monosaccharides from disaccharides
- Monosaccharides give a cuprous oxide ppt in dilute acid more quickly than disaccharides
- Monosaccharides are more active reducing agents than disaccharides

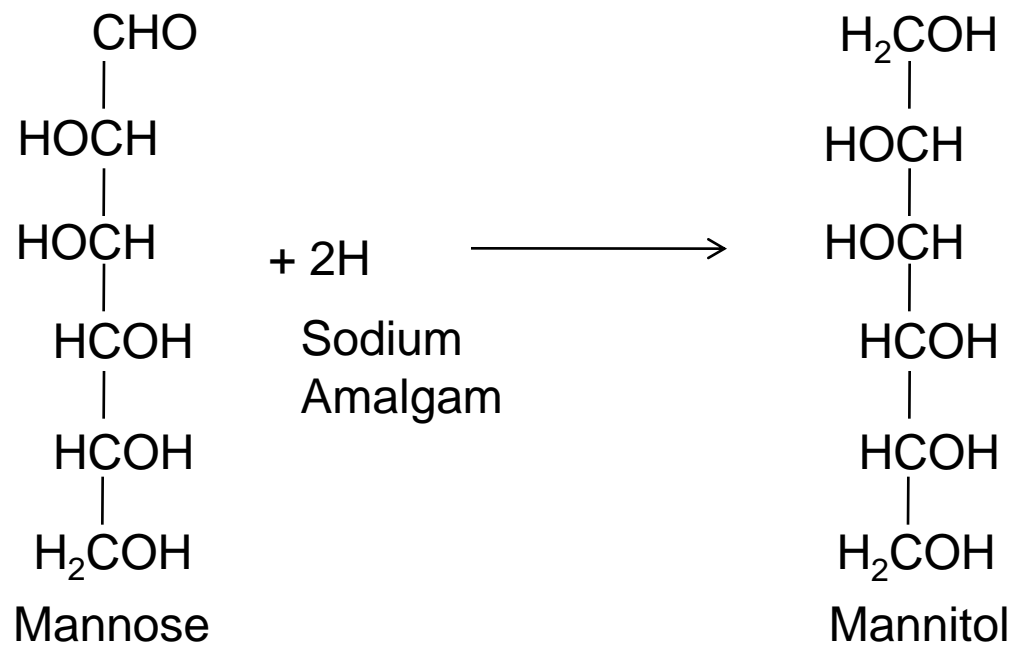
- **Molisch test** – (H_2SO_4 & α -naphthol as a phenol)
- Acid hydrolyses acetals and hence the most general of all test for carbohydrates
- Alkali conditions of earlier mentioned tests cause fragmentation of sugars to give a mixture of different chain length upon oxidation of the carbohydrate
- Thus earlier test are good for analytical methods than preparative methods

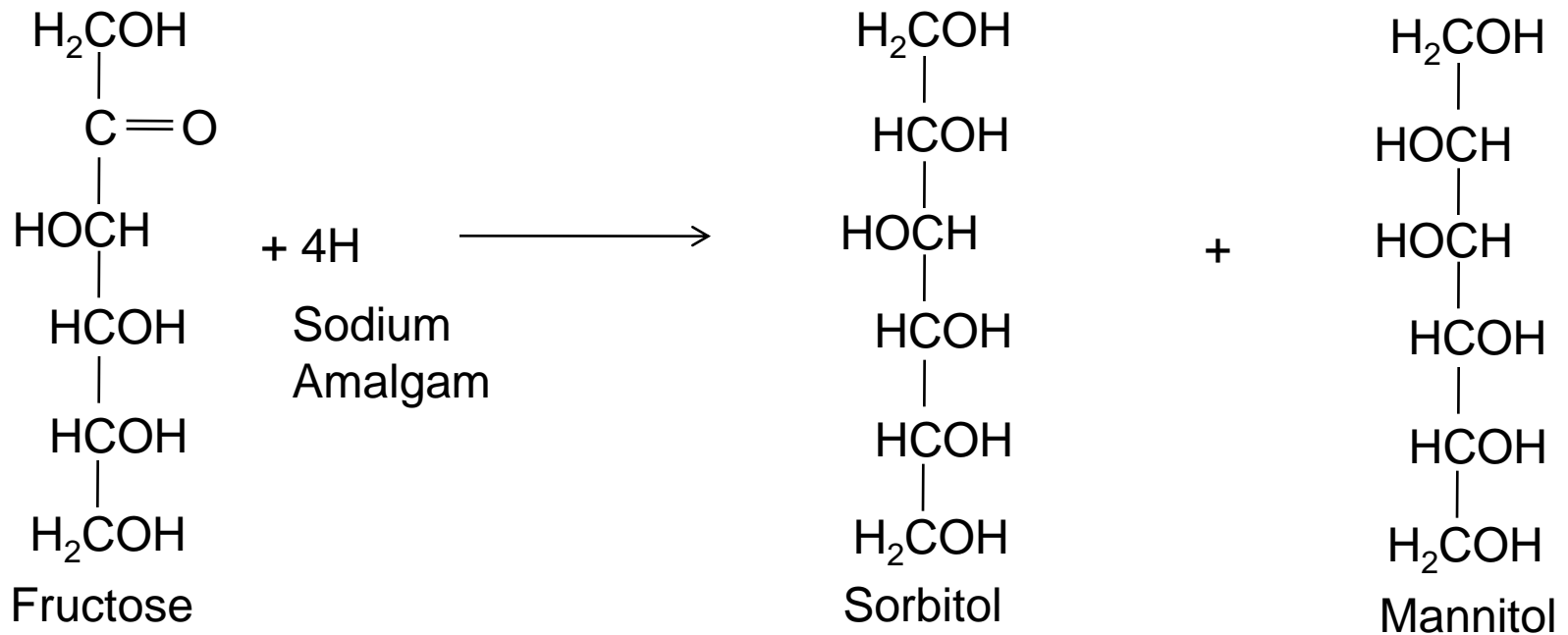
2. Reduction

a) With Sodium amalgam

- Monosaccharides reduced to corresponding alcohol.

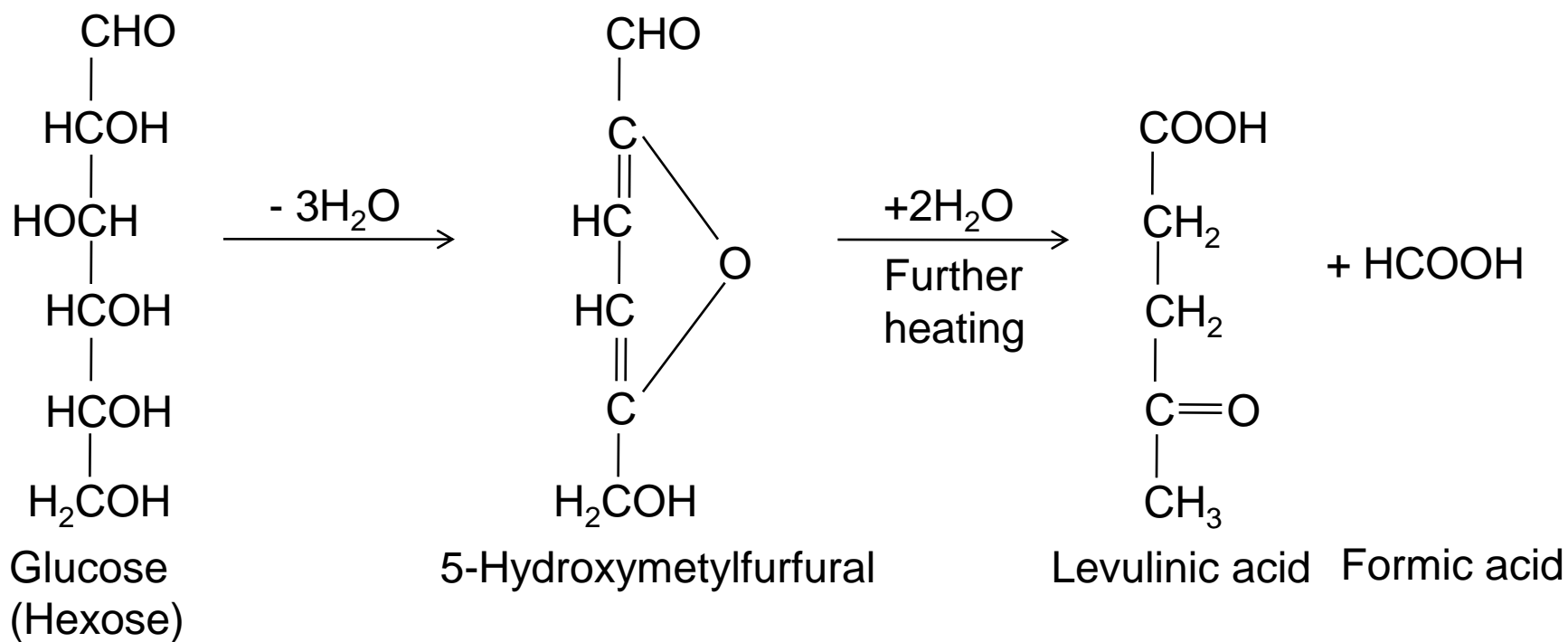


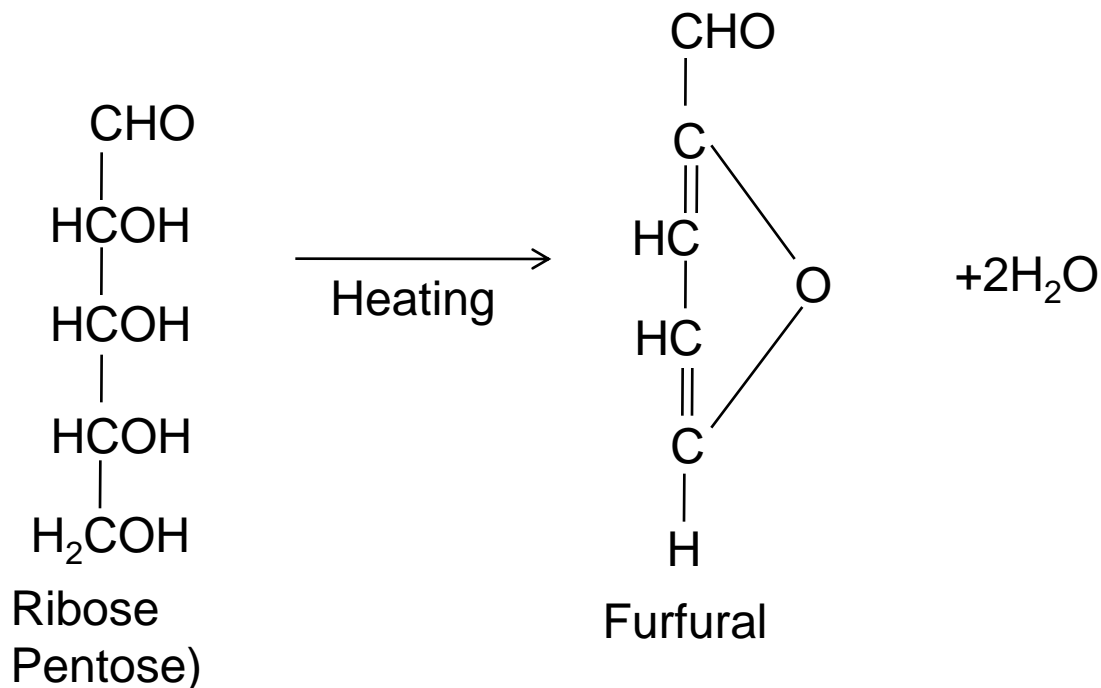




- Sorbitol and mannitol are used for manufacture of surface active agents and explosives

b) With strong mineral acids

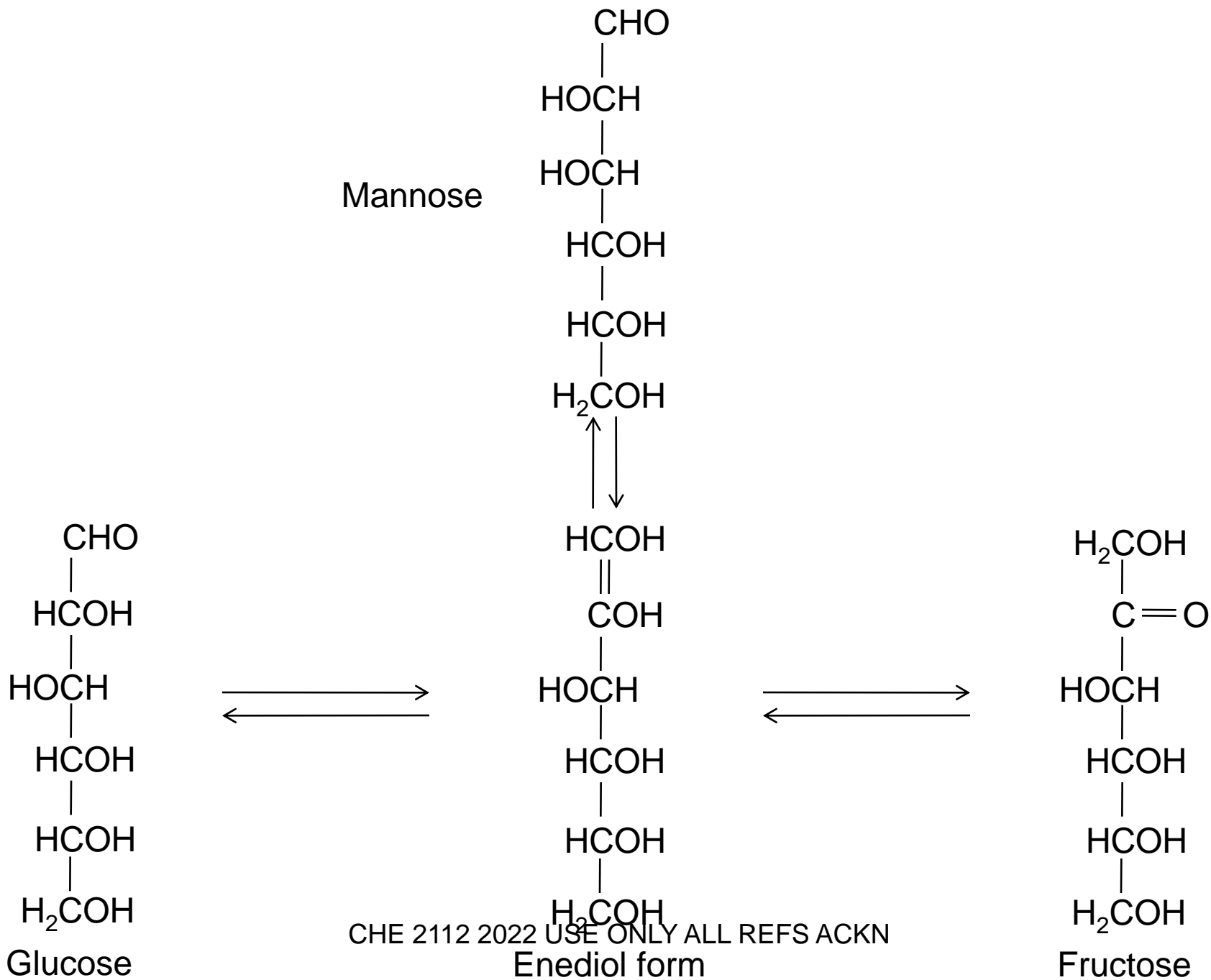




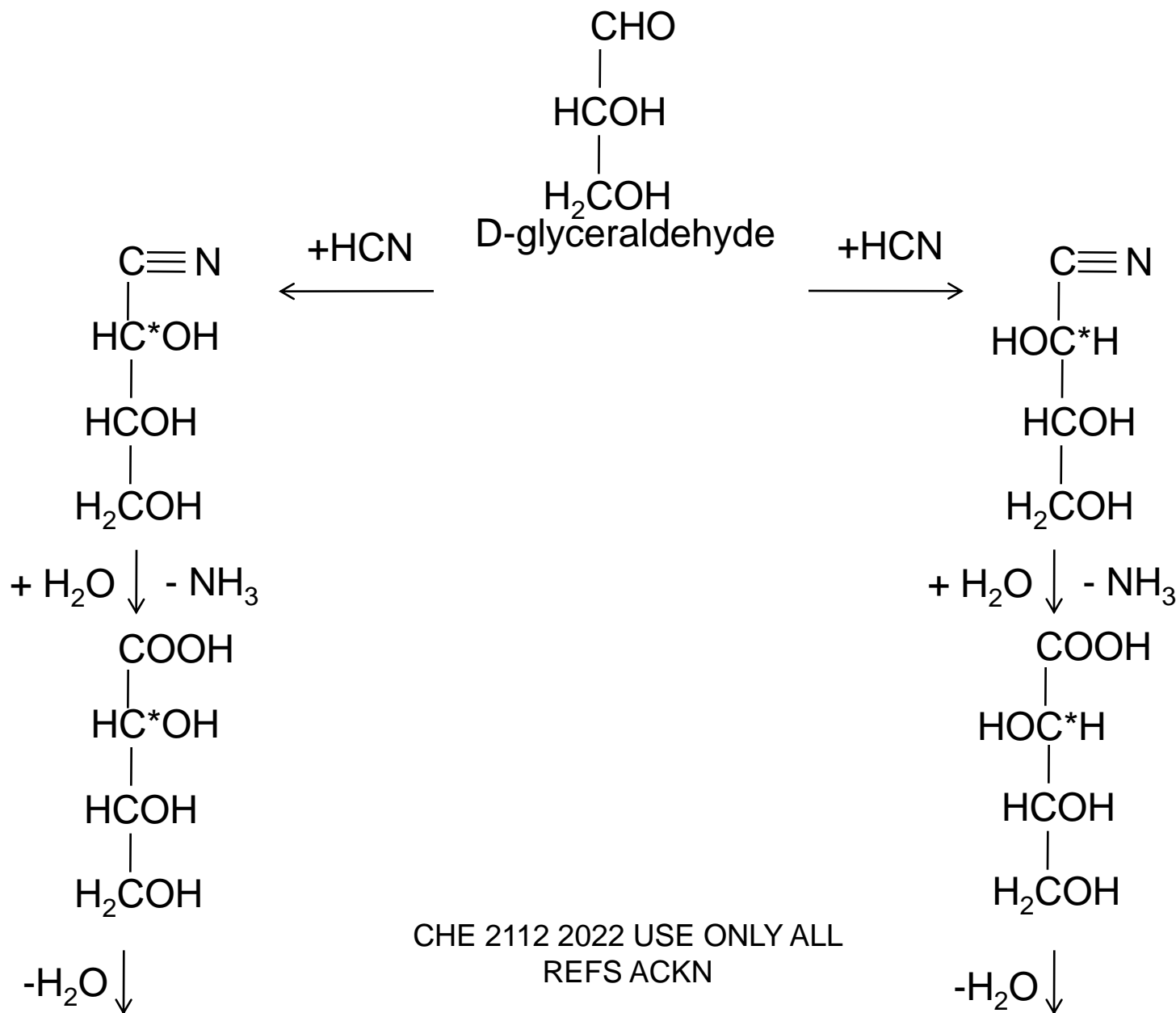
- Tetroses and Trioses do not undergo this reaction as they have fewer carbon atoms (less than 5) to form a furfural

c) With dilute alkalies

- Lobry De Bruyn-Alberda van Ekenstein transformation/rxn
- In weak alkaline solns of $\text{Ca}(\text{OH})_2$ and $\text{Ba}(\text{OH})_2$ at temperatures, glucose, mannose and fructose are interconvertible

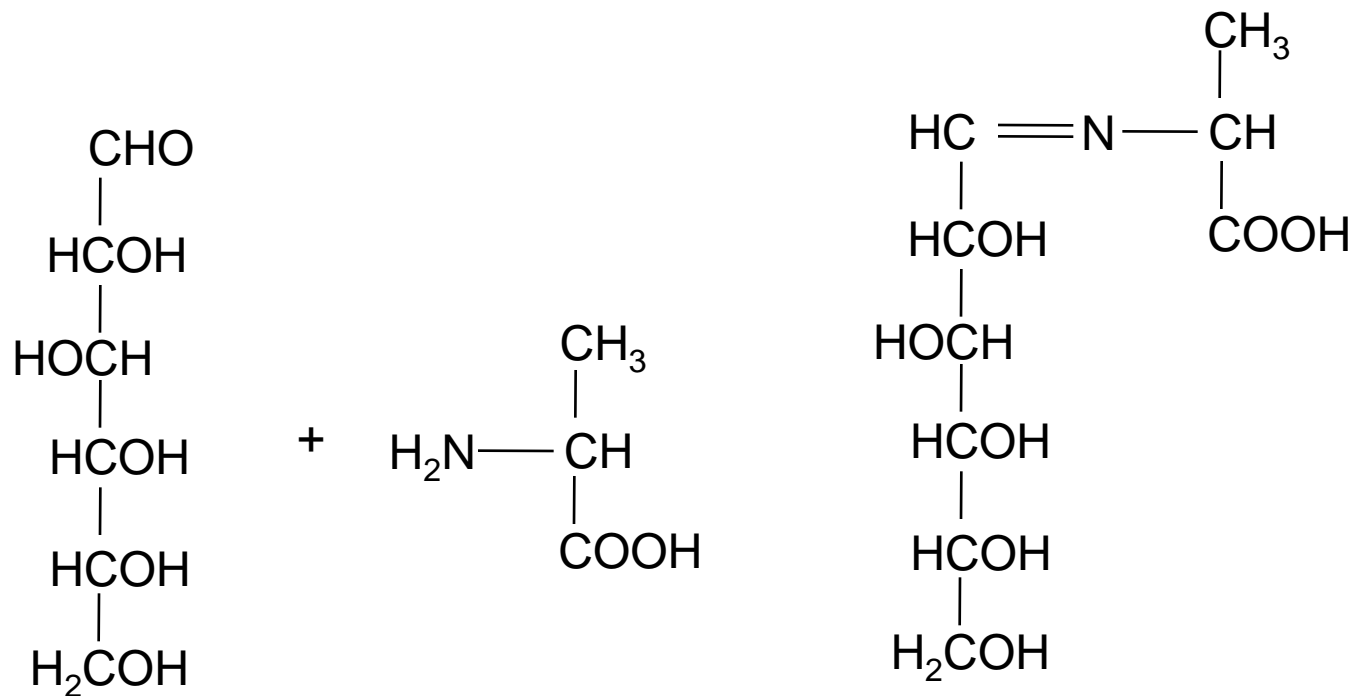


3. Rxn with Hydrogen cyanide (Kiliani Synthesis)
- Method for monosaccharide synthesis by chain elongation of the existing carbohydrate using 4 rxns:-
 - i. Cyanohydrin formation - Based on addition of HCN to carbonyl carbon of aldehyde or ketone to cyanohydrin
 - ii. Hydrolysis - Cyanohydrins hydrolysed to carboxylic acids
 - iii. Lactonisation - Carboxylic acids converted to γ -lactones or inner esters
 - iv. Reduction - Lactones reduced to corresponding aldoses containing 1 more carbon atom than the parent sugar



4. Rxn with Ala

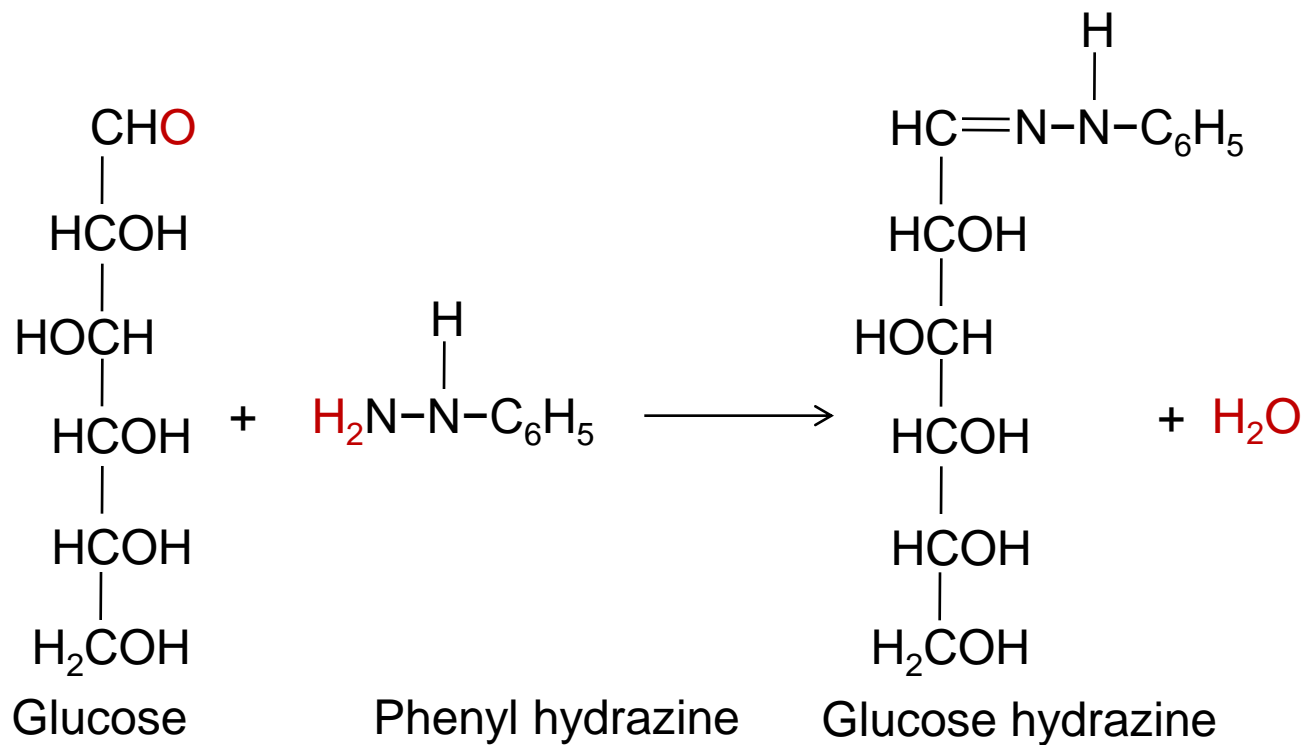
- Formation of schiff bases – Ala reacts with carbohydrates

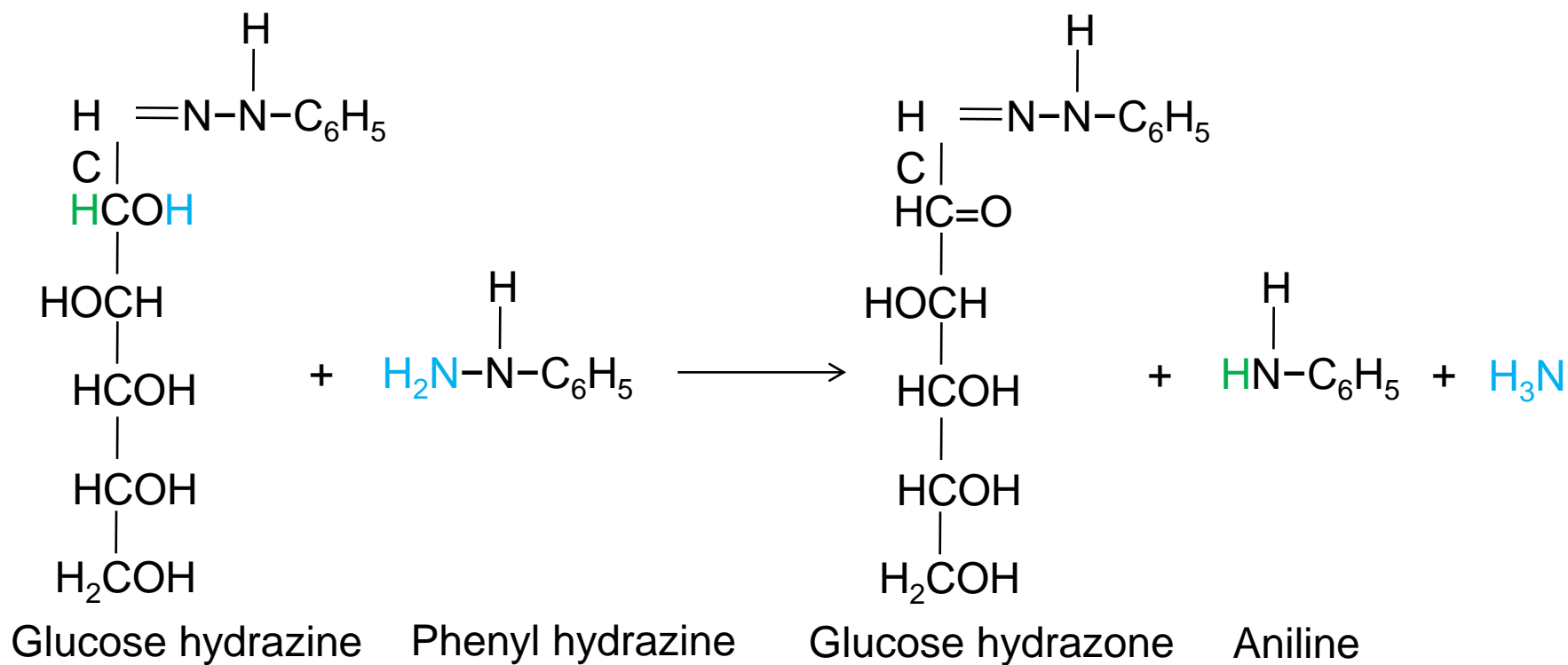


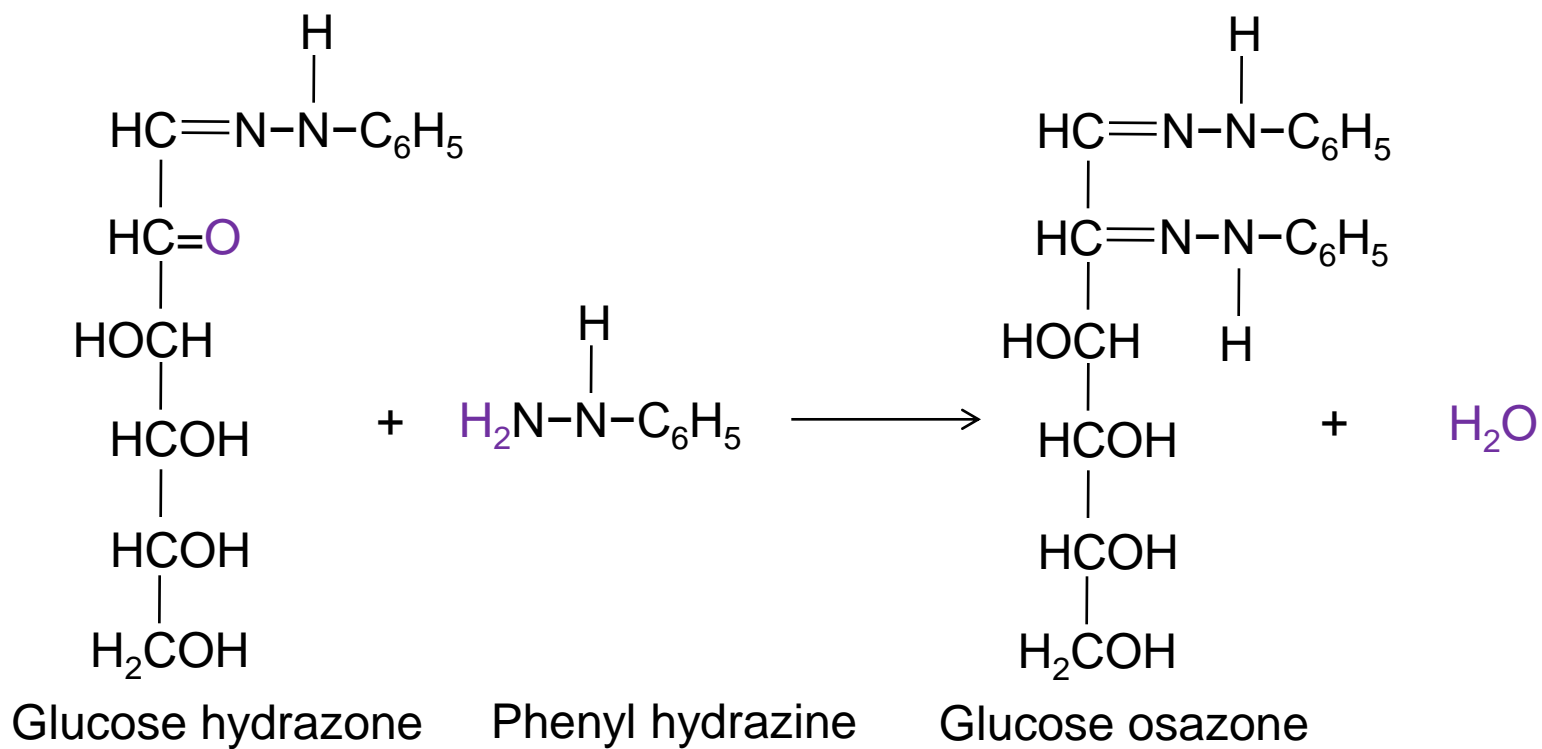
- Browning of bread during baking and other mixtures of carbohydrates and proteins thought to be due to formation of schiff bases as a result of the rxn between carbohydrate aldehyde group and amine groups of proteins

5. Reaction with Phenyl Hydrazine

- Involves the carbonyl carbon (aldehyde or ketone) and the adjacent carbon atom in the monosaccharide
- 3 mole of phenyl hydrazine are required to reduce the monosaccharide to react with aldehydes or ketones



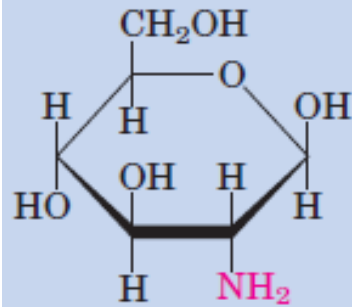




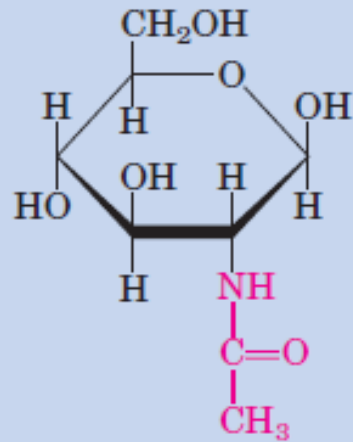
Osazones of mutarotating reducing sugars

- form yellow usually insoluble crystals
- have characteristic melting temperatures
- Hence used for identification of sugars
- Reducing disaccharides form crystals with specific shapes
- Glucose, fructose and mannose form the same osazone hence cannot be differentiated by this reaction

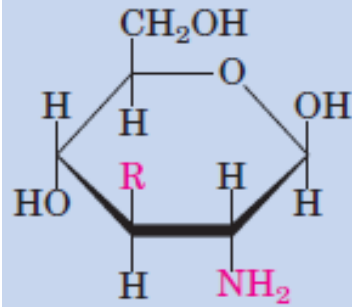
- **Sugar derivatives**
- Hydroxyl group in parent cpd replaced with another substituent, or carbon atom is oxidized to a carboxyl group
- Hydroxyl at C-2 of glucose, galactose & mannose, replaced with an amino group to give glucosamine, galactosamine & mannosamine, respectively
- Amino group is nearly always condensed with acetic acid, as in N-acetylglucosamine



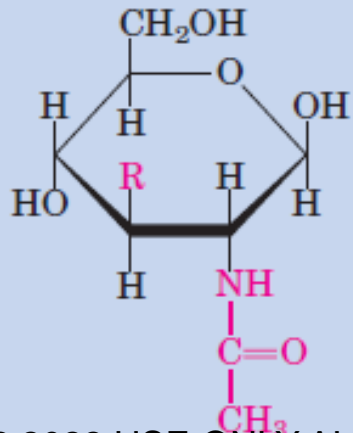
β -D-Glucosamine



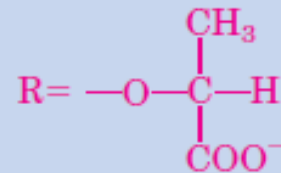
N-Acetyl- β -D-glucosamine



Muramic acid



N-Acetylmuramic acid



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- N-acetylglucosamine forms part of many structural polymers, including those of bacterial cell wall
- Bacterial cell walls also contain a derivative of glucosamine, N-acetylmuramic acid

Functions of monosaccharides

- Important metabolic intermediates e.g. in glycolysis, both in phosphorylated and unphosphorylated forms, for the generation of ATP
- Important constituents of nucleotides, nucleic acids, and many coenzymes e.g. NAD, NADP, flavoproteins. In this case it is mostly the pentoses.
- As glycosides they found in many drugs and spices
- As amino sugars are contained in several antibiotics e.g. erythromycins.