Carbohydrates

Carbohydrates are substances with the general formula $C_x(H_2O)_y$, and were called carbohydrates because they contained hydrogen and oxygen in the same proportion as in water. However, a number of compounds have been discovered which are carbohydrates by chemical behaviour, but do not conform to the formula $C_x(H_2O)_y$ e.g. 2-deoxyribose, $C_5H_{10}O_4$. It is also important to note that all compounds conforming to the formula $C_x(H_2O)_y$ are not necessarily carbohydrates e.g. formaldehyde, CH_2O.

All carbohydrates are polyhydroxy aldehyde or ketones or substances that yield on hydrolysis.

Carbohydrates are divided into two main classes sugar and polysaccharides. Sugars are crystalline substances with a sweet taste and soluble in water. Polysaccharides are more complex than the sugars, their molecular weights being far greater. Most of them are non-crystalline substances which are not sweet, and are insoluble or less soluble in water, than the sugar.

Sugars are subdivided into two major groups:

1. Monosaccharides: These are sugars which cannot be hydrolysed into smaller molecules. Their general formula is $C_nH_{2n}O_n$, where n is 2-10, and the most important are the pentoses and hexoses.

2. Oligosaccharides: These yield 2-10 monosaccharide molecules on hydrolysis.

Polysaccharides are carbohydrates which yield a mono-saccharide molecule on hydrolysis. The most widely spread polysaccharides have the general formula $(C_6H_{10}O_5)$ e.g. starch, cellulose etc.

Hexoses : ($C_6H_{12}O_6$).

The aldohexoses are important groups of monosaccharides, and their structure has been elucida as follows:

i. Analysis and MW determinations show the molecular formula of the aldohexoses is $C_6H_{12}O_6$

ii. When treated with Ac_2O, aldohexoses for the Penta-acetate. This indicates the presence of five hy groups.

iii. Aldohexoses form an oxime when treated hydroxylamine, and therefore contains a carbonyl group.

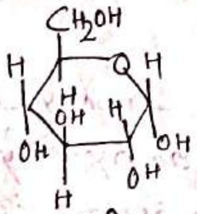
iv. When an aldohexose is oxidised with Br_2/water, a pentahydroxy-acid of formula $C_6H_{12}O_7$ is obtained. This indicates that the carbonyl group is present in an aldehydic group.

v. When reduced with conc. HI and red P at 100°C aldohexoses give a mixture of 2-iodohexane an n-hexane. This indicates that the six carbon atoms in an aldohexose are in straight chain.

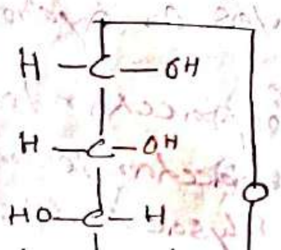
The foregoing reactions show that the structu of aldohexoses is

$$OCH\ CHOH\ CHOH\ CHOH\ CHOH\ CH_2OH$$

Although the foregoing evidence indicates an open-chain structure, there is further evidence which show that the sugars actually exist as six-membered rings in the solid state. The ring structure is hexagonal (I), but it is convenient to use planar formula (II)

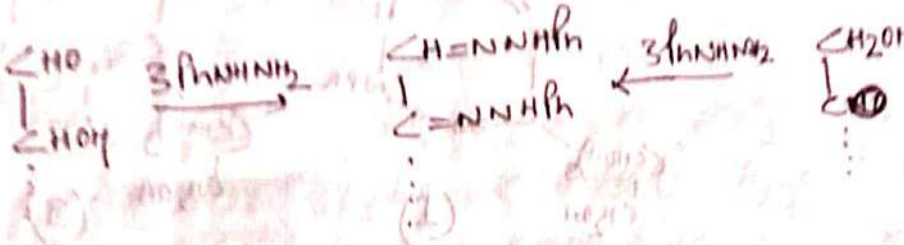


(I)

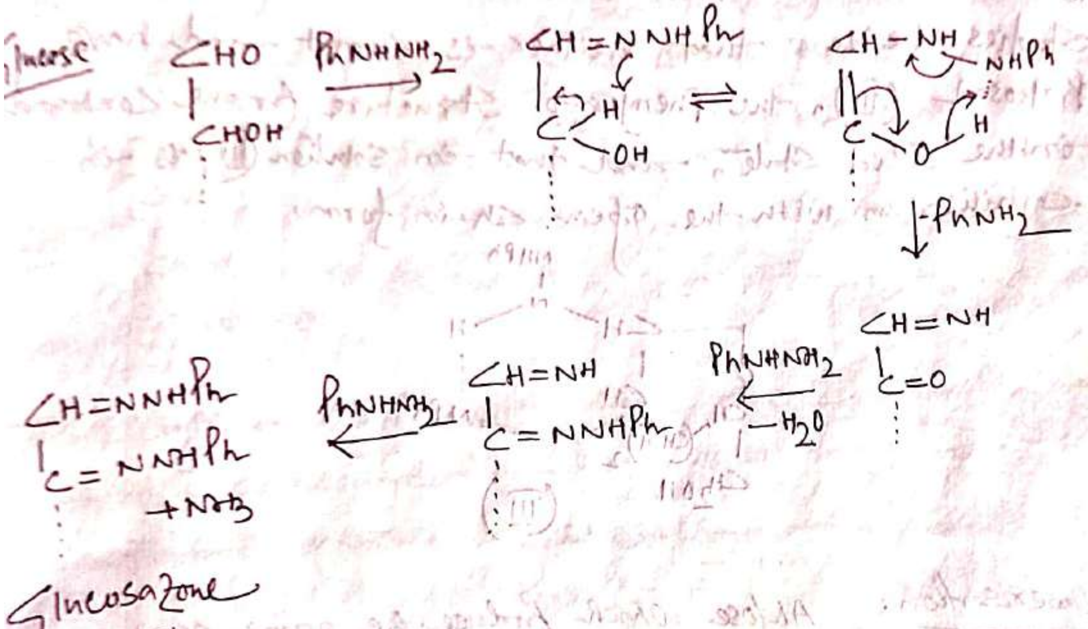


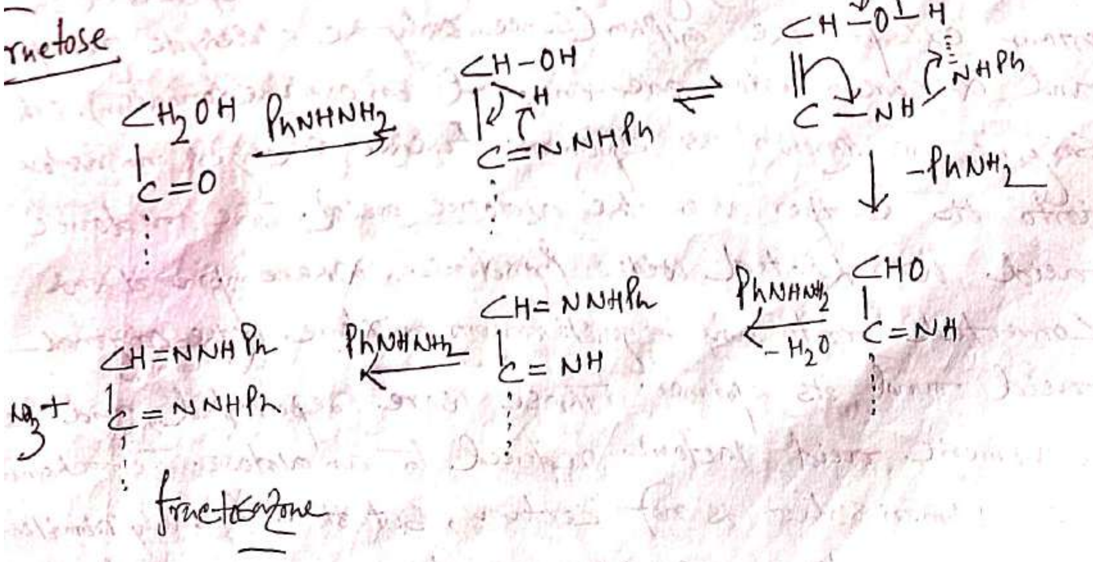
Reaction of glucose and fructose with Phenyl hydrazine:

Fischer showed that both aldose and Ketose react with excess of Phenyl hydrazine to form osazones, aniline and ammonia. The overall equation may be written

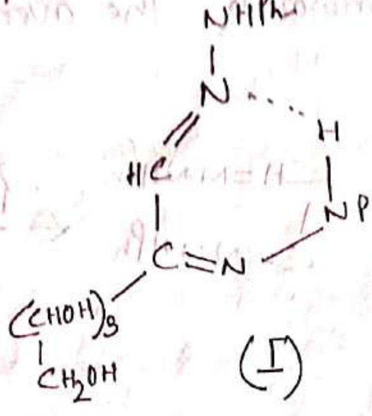


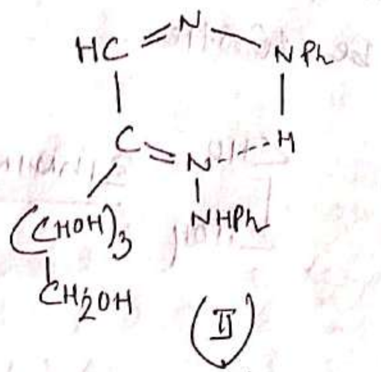
Mechanism:



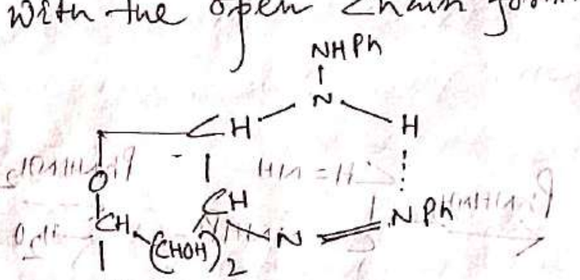


The failure to undergo further reaction has been expla
by stabilisation of the osazone by chelation, i.e. t
osazones have ring structures. Two alternatives (I) an
(II) were proposed.

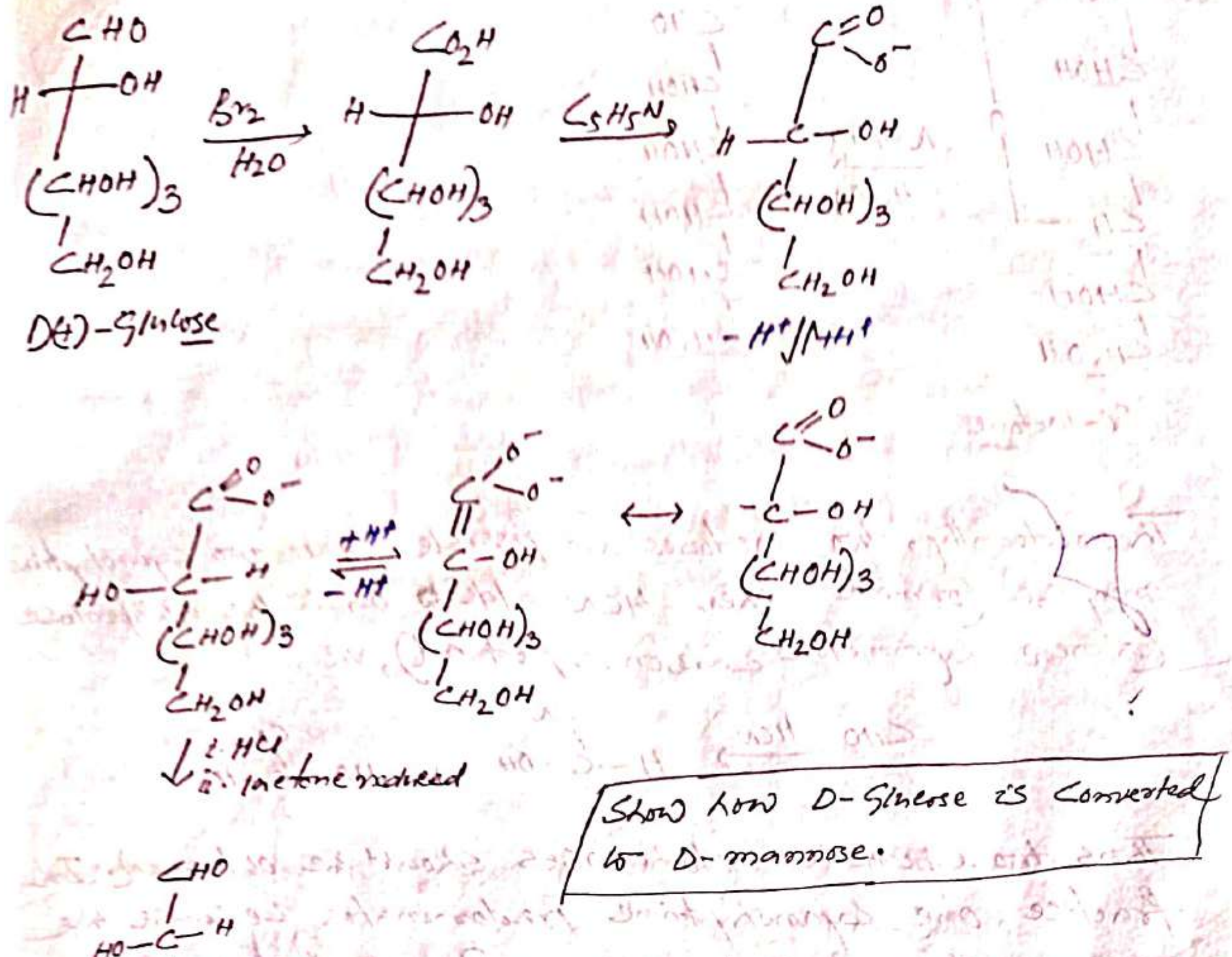

(I)


(II)

Mester believed that (I) was the correct structure, bu
Blair et al. from their chemical and i.r. and u.v. sp
studies, believe that neither is correct and have
proposed (III), the phenylazo structure for the compound
in the solid state, and that in solution (III) is in
equilibrium with the open chain form.


(III)

Epimerisation: Aldose which produce the same osazones mus
have identical configurations on all their asymmetric carb
atom except the alpha (since only the aldehyde group
and α-carbon atom are involved in osazone formation). Such
sugars are known as epimers. Fischer changed an aldose
into its emiper via the aldonic acid. The aldonic
acid was heated with pyridine, whereupon it was
converted into an equilibrium mixture of the original
acid and its epimer. These were separated, and the
epimeric acid lactone reduced to an aldose. The mechan
of epimerisation is not certain, but it is probably simil
to racemisation, e.g. epimerisation of glucose into manno

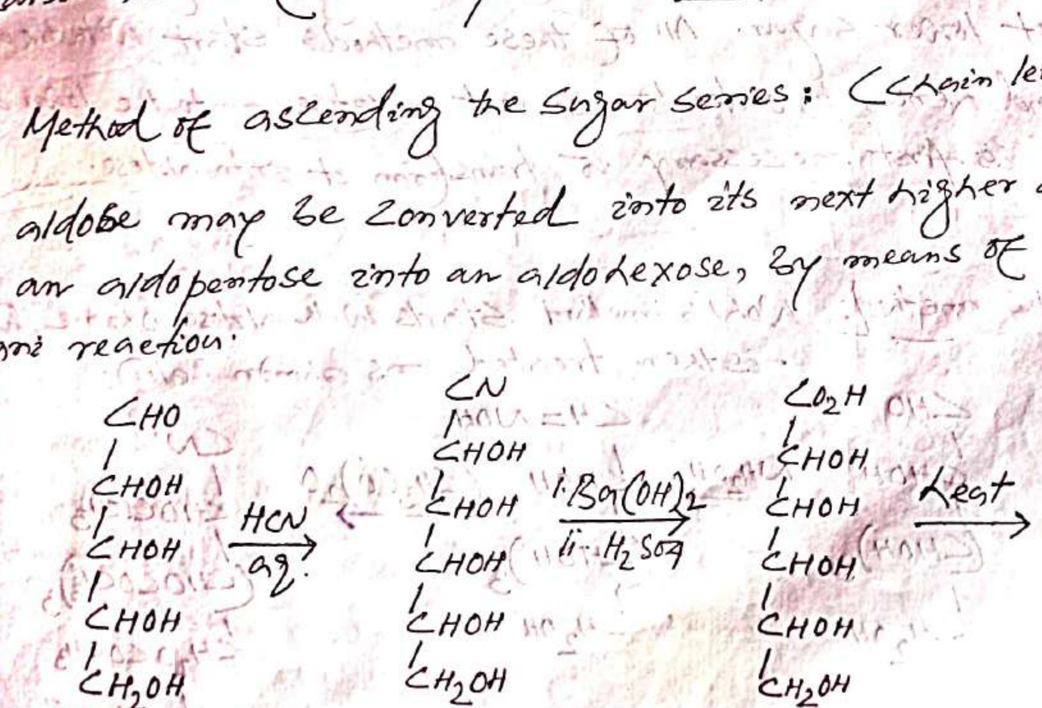


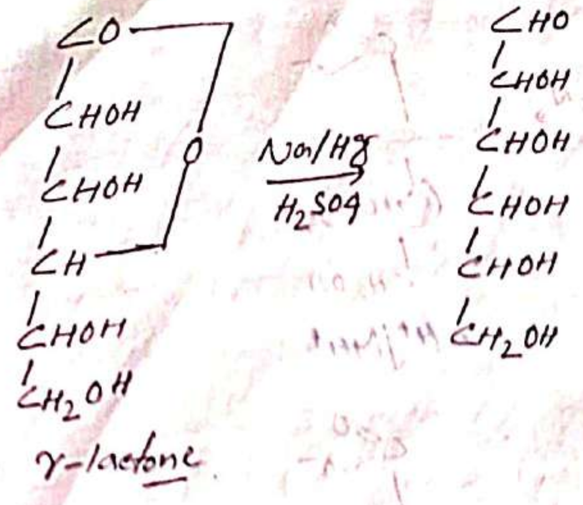
Show how D-glucose is converted to D-mannose.

This change of configuration of one asymmetric carbon atom in a compound containing two or more asymmetric carbon atom is known as epimerisation.

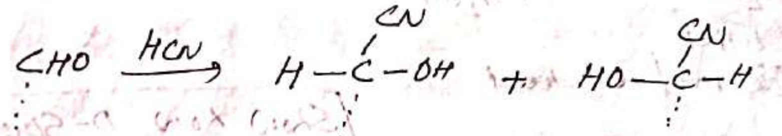
* Method of ascending the sugar series: (Chain lengthening

An aldose may be converted into its next higher aldose, e.g. an aldopentose into an aldohexose, by means of the Kiliani reaction.





Theoretically, two lactones are possible, since two cyanohy may be formed when HCN adds on to the aldopento (a new asymmetric carbon is produced), viz.,



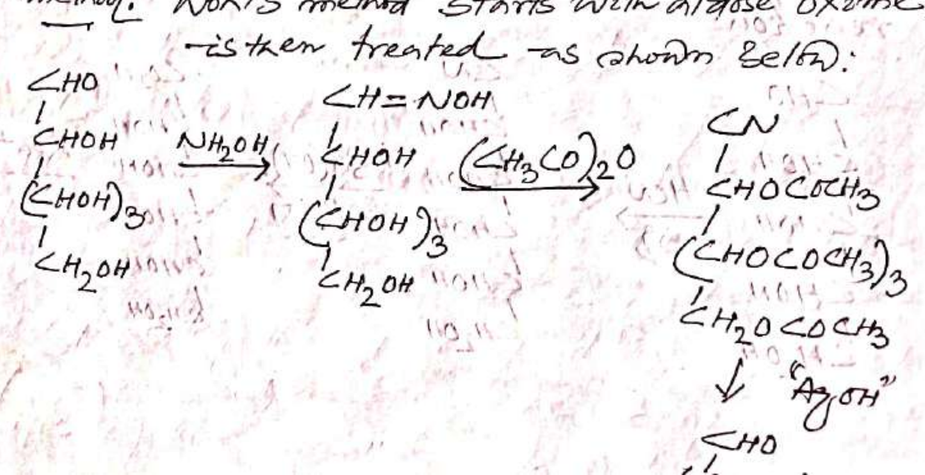
$$CHO \xrightarrow{HCN} H-\overset{CN}{C}-OH + HO-\overset{CN}{C}-H$$

Thus two epimeric aldohexoses should be obtained. In practice, one cyanohydrine predominates because the asymmetry present in the molecule produces diastereo face at the double bond. Hence the final product will be mainly one aldohexose, and very little of its epimer.

*Method of descending the sugar series (chain shortening).

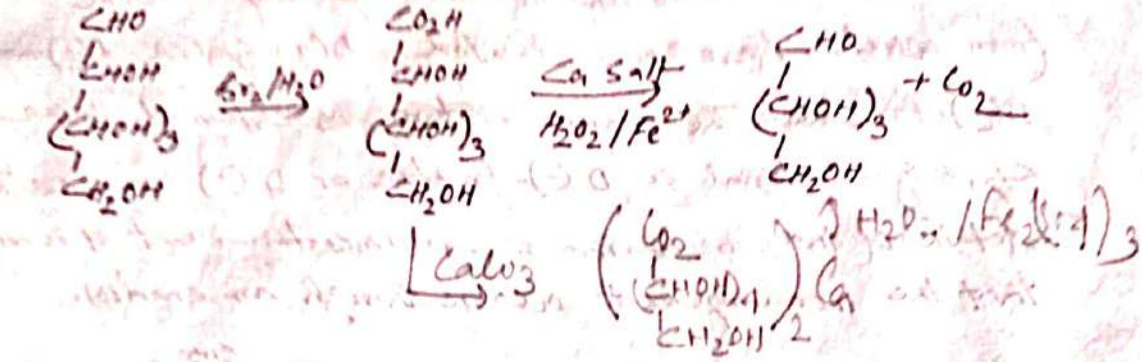
There are various methods of converting a sugar into the next lower sugar. All of these methods start with the aldose and hence, in order to convert a ketose into the lower aldose it is first necessary to transform it into aldose.

Wohl's method: Wohl's method starts with aldose oxime, which is then treated as shown below:



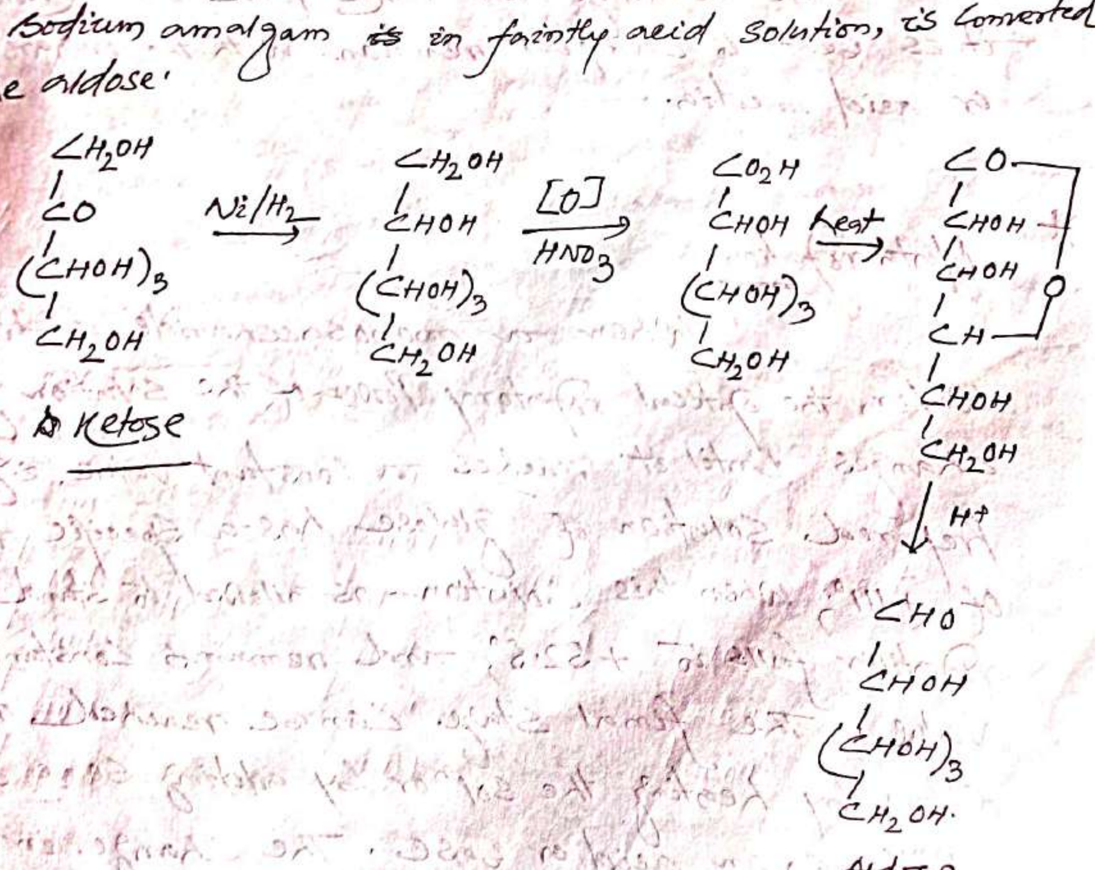
Ruff's method:

The aldose is oxidised (by bromine water) to the Corresponding aldonic acid; when the Calcium salt of this acid is treated with Fenton's reagent it is Converted into the lower aldose.



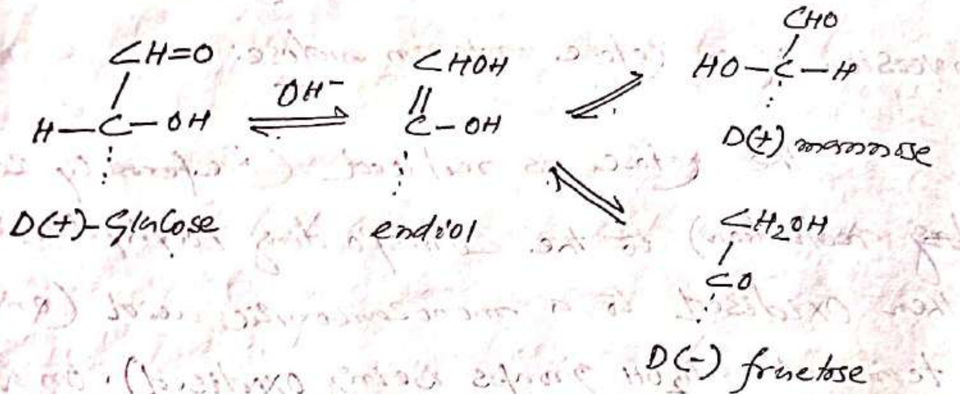
Conversion of a Ketose into an aldose:

The ketose is reduced (preferably by catalytic reduction) to the Corresponding polyhydric alcohol, which is then oxidised to a monocarboxylic acid (only one of the terminal CH$_2$OH groups being oxidised). On warming the acid is Converted into the γ-lactone which, on reduction with sodium amalgam is in faintly acid solution, is Converted into the aldose.



*

Lobry de Bruyn- Van Ekenstein rearrangement: When wa with concentrated alkali; Sugars first turn yellow, the brown and finally resinify. In the presence of dilu alkali or amines, sugars undergo rearrangement; e.g a dilute solution of glucose, in the presence of N is converted into an almost optically inactive so from which have been isolated D(+)-glucose, D(+)-m D(-)-fructose. The same mixture is obtained if the starting material is D(-)-fructose or D(+)-mannose. T details of the mechanism ~~is~~ are uncertain, but it is cer that the rearrangement occours through an enediol.



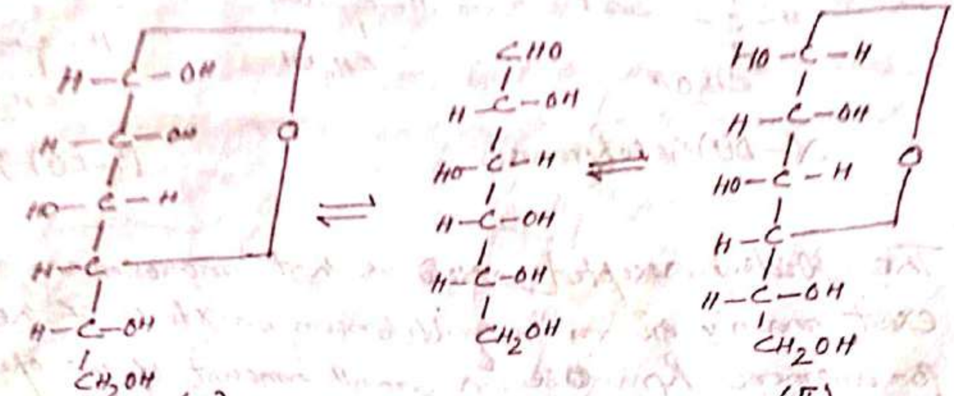
Since the rearrangement take place in alkaline media it is best to carry out reactions with the sugars in neutra or acid media.

*

Muta rotation:

When a monosaccharide is dissolved in water, the optical rotatory power of the solution gradually changes until it reaches a constant value, e.g. a freshly prepared solution of glucose has a specific rotation of +111°; when this solution is allowed to stand, the specifi rotation falls to +52.5°, and remains constant at this value. The final stage can be reached more rapidly either by heating the soln or by adding some catalyst wh may be an acid or base. The change in value of specific rotation is called mutarotatio

To account for mutarotation, Tollens suggested an oxide ring structure for D(+)-glucose, whereby two forms would be produced since, in the formation of the ring, another asymmetric carbon atom is produced. Tollens assumed that a five-membered was produced (I) and (II). The difficulty of this suggestion was that there is no experimental evidence for the existence of these two forms.



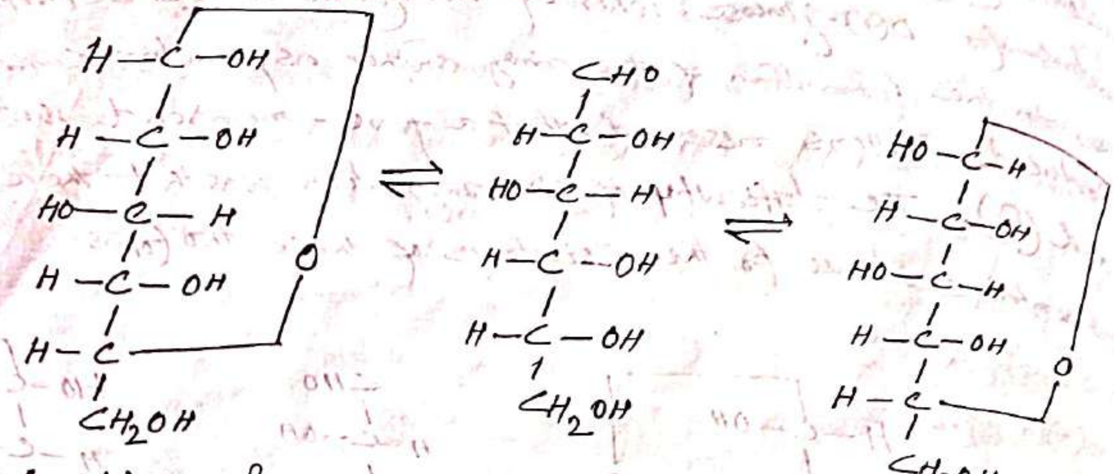
(I) (II)

Tanret, however isolated two isomeric forms of D(+)-glucose, thus apparently verifying Tollens' supposition. The two forms are called α- and β-D(+)-glucofuranose; (I) is the α-form and (II) the β.

Ring formation of a sugar is really hemiacetal formation, one alcohol group of the sugar forming a hemiacetal with the aldehyde group of same molecule, thus producing a ring structure. This equilibrium between the open and ring forms is an example of ring-chain tautomerism. The carbon atom in the chain tend to form a loop, and this results in the OH on C_4 and C_5 being very close to the CHO group. With ketoses, it is the OH group on C_5 or C_6 that is close to the CO group. In both aldoses and ketoses, therefore the geometry of the molecule is very favourable for hemiacetal formation.

Later work by Haworth, Hirst and their co-worker has shown that glucose (and other sugar) exist, not as a five-membered ring but as a six-membered ring, the two forms being α- and β-D(+)-glucopyranose. Such

Pairs of Stereoisomeric of any Sugar are Known as anom

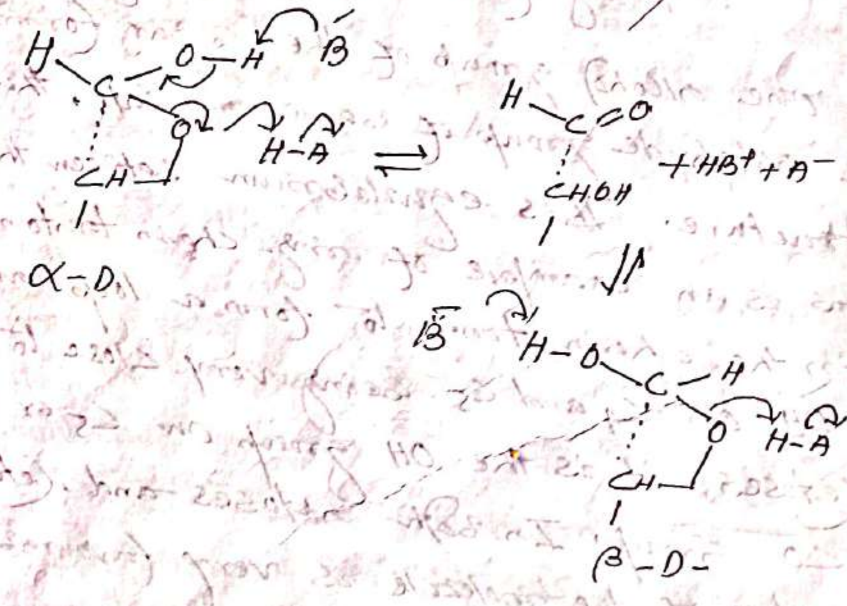


α-D(+) Glucopyranose

β-D(+) Glucopyranose

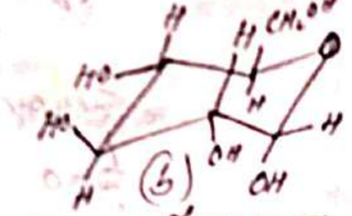
The widely accepted view is that monosaccharides in Solu exist mainly as an equilibrium mixture of the α- and β-anomeric pyranose, a small amount of the open chain fo together with small amounts of the α-and β-furanose.

The mechanism of mutarotation has been the subject of great deal of research, but it is Still uncertain. A widely accepted mechanism involves a concerted attack by a base and acid to produce the open-chain structure and then this recloses to the anomeric form.

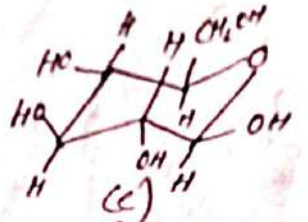


The cyclic structure of the sugars accounts for the following facts i. the existence of two isomers, e.g. α- and β-glucose. ii mutarotation iii. Glucose and other aldoses do not give certain characteristic reactions of aldehyde e.g. Schiff's reaction, do not form a bisulphite.

Reeves has shown that the conformation of α-D(+) glucopyranose is (b) and that of the β-anomer is (c). Both have the chair form, but in the former the glycosidic hydroxyl is axial and in the latter equatorial.



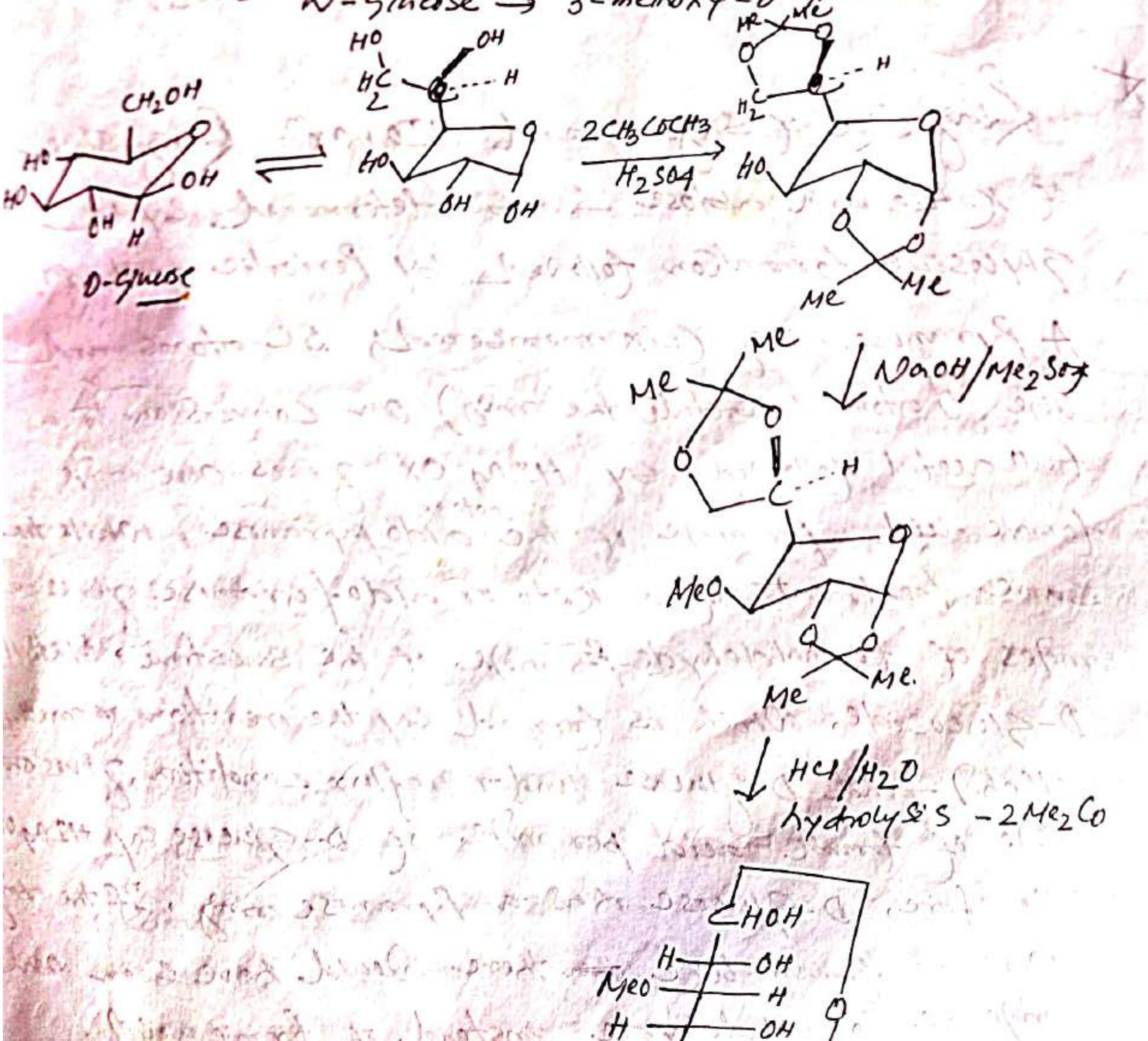
(b)
α-anomer



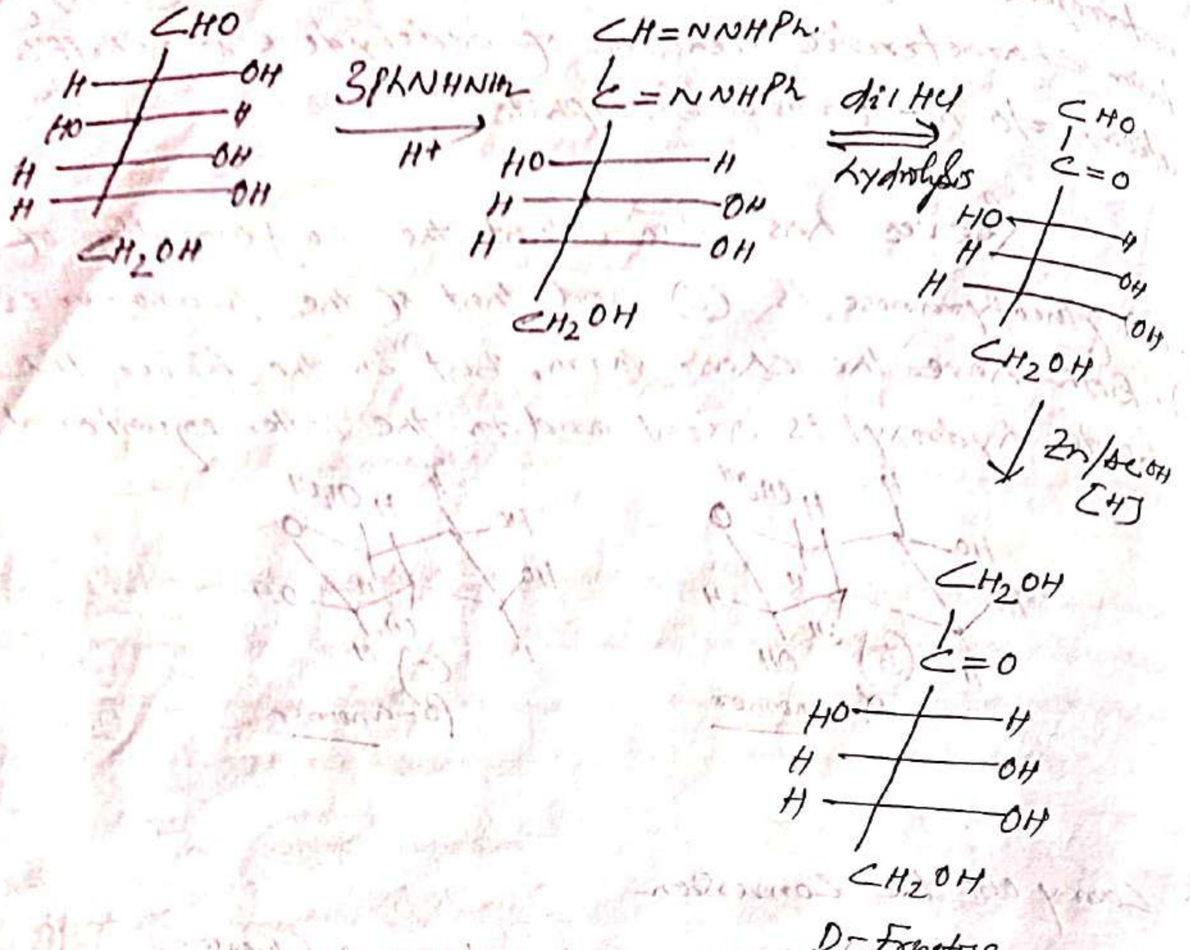
(c)
β-anomer

* Carry out the Conversion

i. D-Glucose → 3-methoxy-D-Glucose.



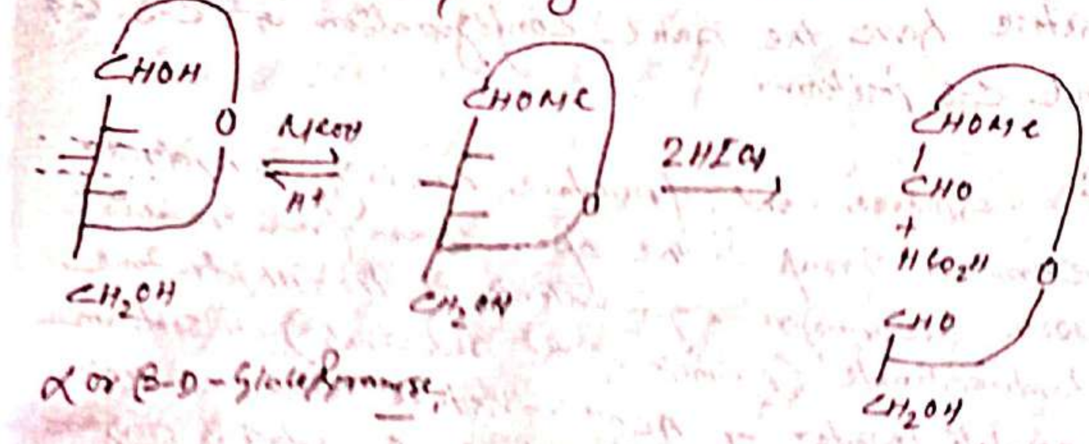
* Convert D-glucose to D-fructose.



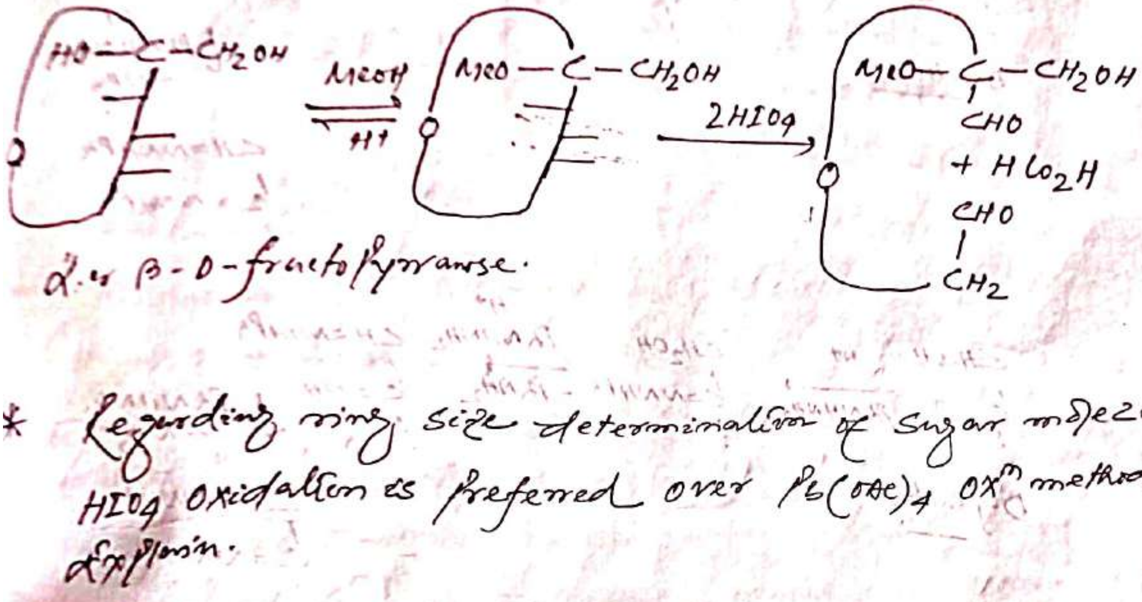
D-Fructose.

* Ring size of sugars and HIO_4 ox^n. Ring size of ketose and aldose can be determined by the glycoside formation followed by periodic acid ox^n. A pyranose ring (six membered; 5C atoms and one 'O' atom constitute the ring) on conversion to a full acetal followed by HIO_4 ox^n gives one mole formic acid per mole of the keto or aldo pyranose, while the same treatment of a keto or aldofuranose gives a moles of formaldehyde per mole of the substrate. Methyl D-glucoside, which is formed by the reaction of methyl alcohol and D-glucose under reflux condition, gives one mole of formic acid per mole of D-glucose by HIO_4 ox^n. Therefore, D-glucose has a pyranose ring. If the ring were a furan-like, ~~then~~ there would have been one mole of formaldehyde instead of formic

In the similar way ring size can also be determined.



α or β-D-Glucofuranose.



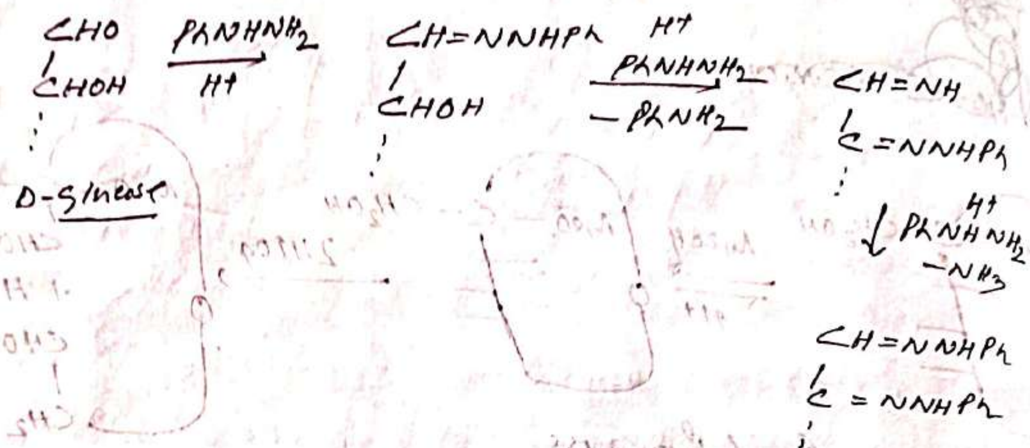
α or β-D-fructopyranose.

* Regarding ring size determination of sugar molecules, HIO_4 oxidation is preferred over $Pb(OAc)_4$ ox^{n} method. Explain.

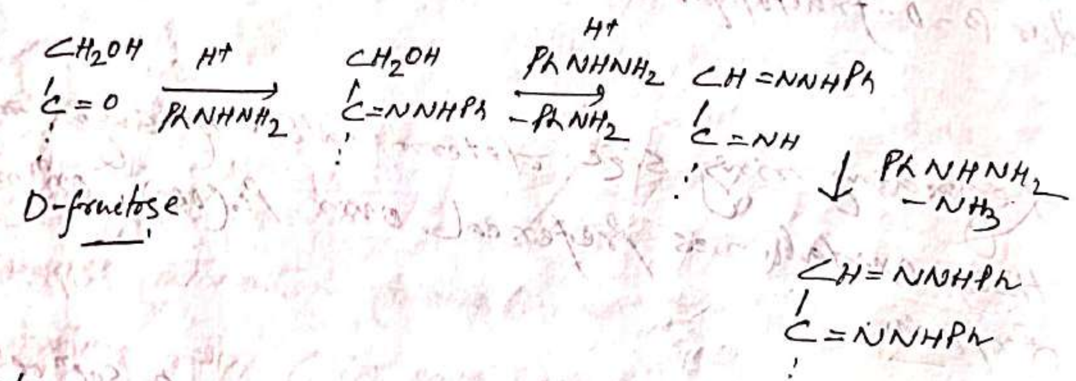
Ans An aqueous sol^{n} of HIO_4 or a sol^{n} of lead tetraacetate in organic solvent serves as remarkbly selective reagents for the cleavage of C-C bond of 1,2-diols. Compounds insoluble in water are cleaved with lead tetraacetate in an organic solvent more readily. Sugars being polyhydroxy carbonyl compounds or their condensation product, generally dissolves more readily in water rather than in an organic solvent. So to cleave the C-C bond of vicinal diols of sugar during ring size determination, an aqueous sol^{n} of HIO_4 was ~~added~~ generally used to an aqueous sol^{n} sugar for facile rep^{n}.

* How would you prove that D(+) glucose and D(-) fructose have the same configuration at C-3, C-4 and C-5 position.

Ans: Glucose and fructose having α-hydroxy carbonyl group in the open chain form react with free and/or equivalents of phenylhydrazine hydrochloride (per mole of the substrate) in sodium acetate/water or AcOH mixture at about 100°C to form dihydrazino derivatives of reducing sugars called osazones.



$$\underset{\text{D-glucose}}{\begin{matrix} CHO \\ | \\ CHOH \\ \vdots \end{matrix}} \xrightarrow[H^+]{PhNHNH_2} \begin{matrix} CH{=}NNHPh \\ | \\ CHOH \\ \vdots \end{matrix} \xrightarrow[-PhNH_2]{H^+,\ PhNHNH_2} \begin{matrix} CH{=}NH \\ | \\ C{=}NNHPh \\ \vdots \end{matrix} \xrightarrow[-NH_3]{H^+,\ PhNHNH_2} \begin{matrix} CH{=}NNHPh \\ | \\ C{=}NNHPh \\ \vdots \end{matrix}$$



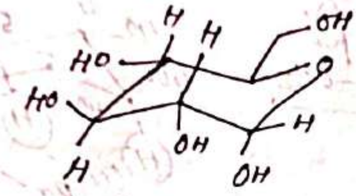
$$\underset{\text{D-fructose}}{\begin{matrix} CH_2OH \\ | \\ C{=}O \\ \vdots \end{matrix}} \xrightarrow[PhNHNH_2]{H^+} \begin{matrix} CH_2OH \\ | \\ C{=}NNHPh \\ \vdots \end{matrix} \xrightarrow[-PhNH_2]{H^+,\ PhNHNH_2} \begin{matrix} CH{=}NNHPh \\ | \\ C{=}NH \\ \vdots \end{matrix} \xrightarrow[-NH_3]{PhNHNH_2} \begin{matrix} CH{=}NNHPh \\ | \\ C{=}NNHPh \\ \vdots \end{matrix}$$

In this rexn only the carbonyl group and α-hydroxy group take part. The other groups and atom do not get affected through this rexn. Therefore C-2 epimeric reducing aldoses and C-2 isomeric ketoses having differences in carbonyl group in constitution or in configuration of the α-C and no other difference in configuration of other chiral carbon will give the same osazone. Since D(+) glucose and D(-) fructose gave the same osazone it can be conclude that they have same configuration at C-3, C-4 and C-5 position.

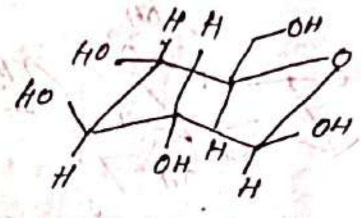
Define an anomer with a suitable example.?

ns:

An anomer is a type of geometric variation found in at certain atoms in carbohydrate molecules. An anomer is an epimer at the hemiacetal/acetal carbon in a cyclic saccharide, an atom called the anomeric carbon. The anomeric carbon is the carbon derived from the carbonyl carbon of the open chain form of the carbohydrate molecule. Anomerization is the process of conversion of one anomer to the other. As is typical for stereoisomeric compounds, different anomers have different physical properties melting points and specific rotations.



α-anomer

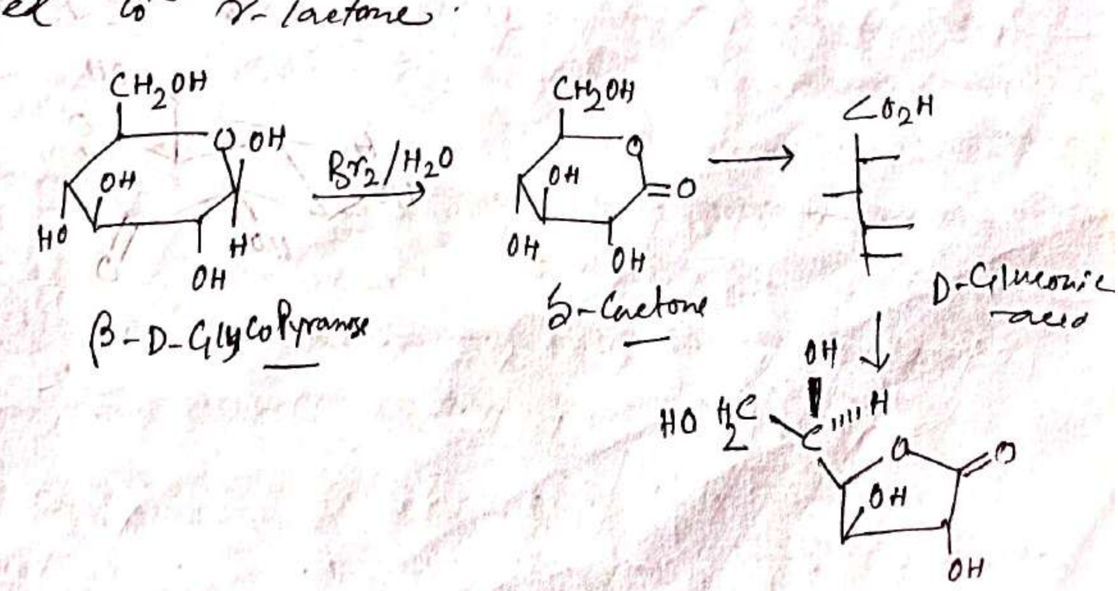


β-anomer

β-anomer of D-glucopyranoside undergoes oxidation with Br_2-H_2O at faster rate than that of α-anomer.

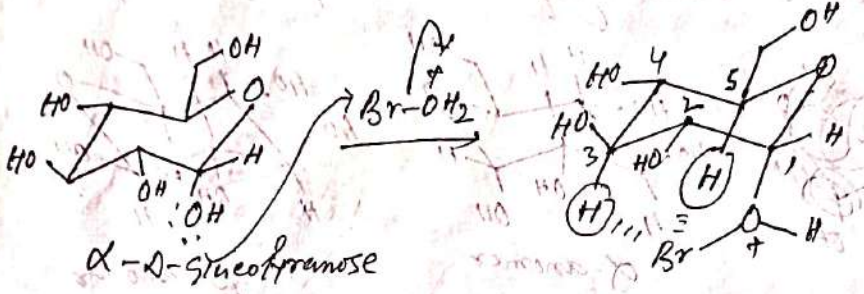
s

Bromine water being a mild oxidising agent, it xidises the carbonyl carbon atom of the aldoses in the emiacetal form to δ-lactone which via aldonic acid ets changed to γ-lactone.

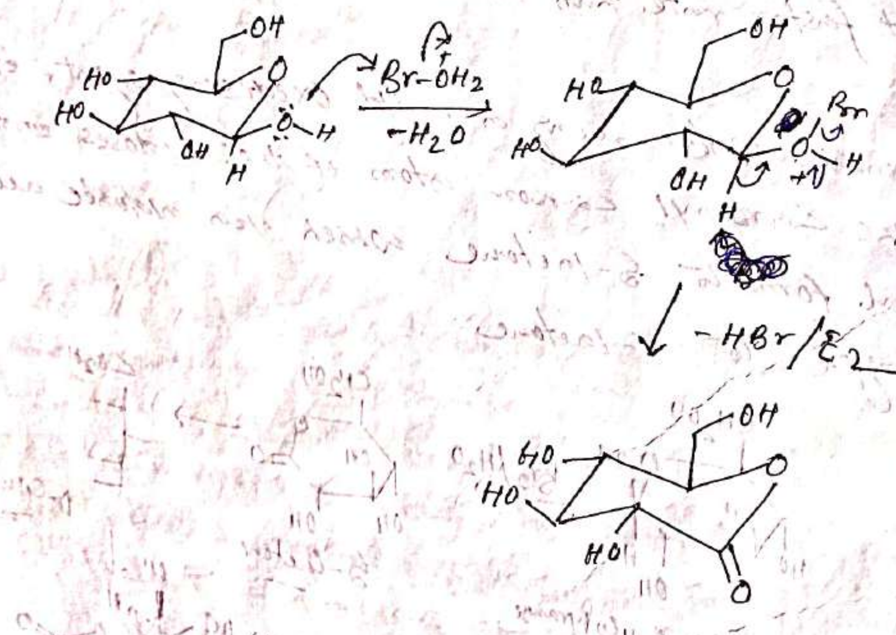


The Stereo electronic requirement for an E_2 reaction i the anti-periplanar arrangement of the two leaving grou In the case of β-D-glucose the stereoelectronic condition for the E_2 reaction involving C_1-H and O-Br is fulfilled. H of C_1 and Br of O-Br are the two leaving groups. In the case of α-D-glucose this ~~@~~ stereo electronic condition does not exist because of the 1,3-diax interaction involving C_1-O-Br/C_3-H and C_1-O-Br/C_5- as shown below:

$$Br_2 + H_2O \longrightarrow HOBr + HBr \longrightarrow H_2\overset{+}{O}-Br + Br^-$$



Since the stereo electronic conditions for the E_2 reaction is fulfilled in β-anomer it undergo Bromine-Water oxi ~~200~~ 250 times faster than α-anomer.



* How the absolute configuration of D(+)-Glucose has been established?

Ans: Haworth and Hirst by the classical oxidative degardation reaction were able to prove that naturally occurring D(+) glucose possesses a six-membered pyran-like ring structure. The flow-sheet for the sequential reactions is given below:

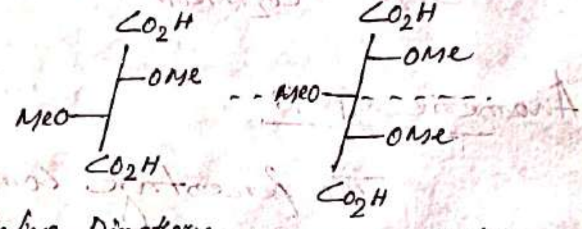
D(+) glucose $\xrightarrow[\text{reflux}]{MeOH/HCl}$ Methyl D-glucoside $\xrightarrow{NaOH/Me_2SO_4}$

Methyl tetra-O-methyl-D-glucoside

$\downarrow H_3O^+$

Tetra-O-methy-D-glucose

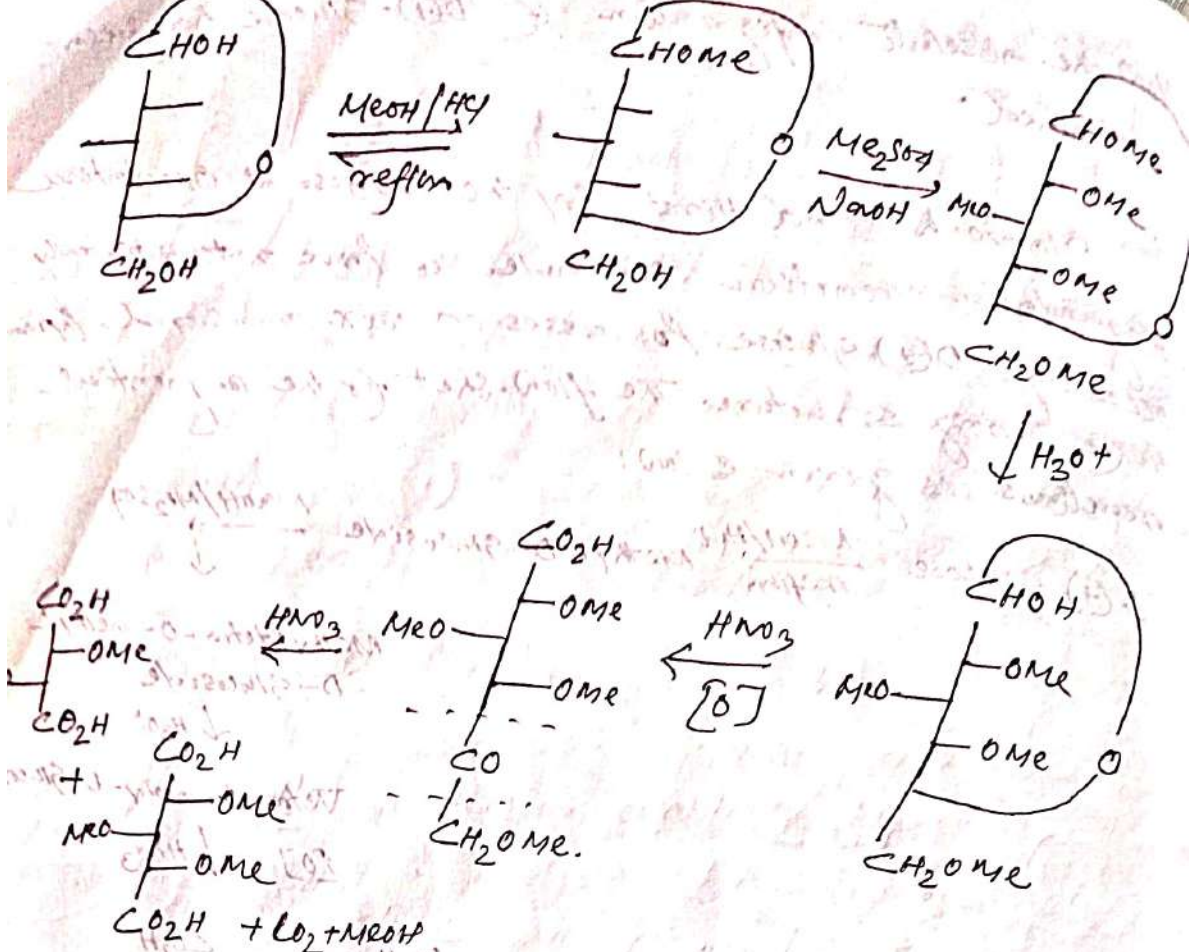
[O] $\downarrow HNO_3$



Op. active Dimethoxy Succinic acid + meso or Xylo trimethoxy glutaric acid

Since meso or Xylotrimethoxyglutaric acid is obtained as one of the products C-2 and C-4 must have the same configuration and C-3 may have the same or opposite configuration with respect to C-2 and C-4. Again if C-2, C-3 and C-4 had been the same configuration, the other product f oxidative degardation of tetra-O-methyl-D-glucopyranoside would have been meso-dimethoxy succinic acid. Since he product is optically active, we could easily say that C-2 nd C-4 have one and the same configuration and C-3 has a configuration ~~has~~ opposite to that of C-2 and C-4.

Haworth and Hirst from the above observatio orrectly predicts the absolute configuration of D(+) glucos

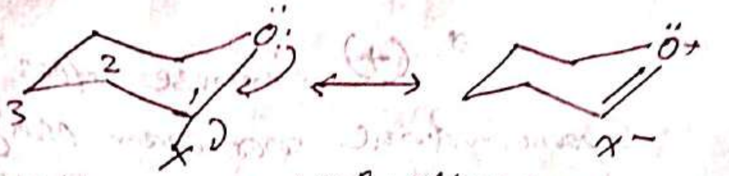


Anomeric effect:

The percentage composition of α-D- and β-D-glucoses in the aqueous medium shows that the conformati have different stabilities; the β-anomer is more stable than the α-anomer in the aqueous medium. But this is not the fact for all cases. There are a large number of examples in the carbohydrate chemistry where pyranose sugars with a strong electronegative substituent, such as halogens, alkox etc. at C_1 are more often more stable when the substituen has an axial orientation rather than equatorial one though the axial orientation of C_1-OH involves 1,3-diaxial strain. The phenomenon of extra preference for an axial orientati over the equatorial orientation of an electronegative substituent at the anomeric ^1C of a pyranose derivative — in solution is known as anomeric effect.

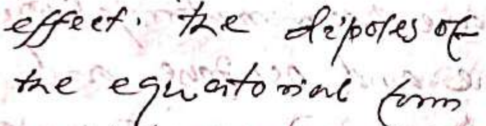
No fully convincing explanation for the anom effect has yet been obtained. It has been found that ther is always a non-bonding A.O with electron pair and the A.O. is anti-periplanar to the polar ano in compounds exhibiting ano called a stereoelectronic effect. The major contribution to the ~~stereoect~~ stereoelectronic factor of the anomeric effect comes from the interaction of the occupied 'p' orbital of the ring 'O' atom with the antibonding sigma (σ^*) orbital of the C-X bond (i.e. n-σ^* interaction; MO theory). According to the V.B. theory, it is a case of coupling effect of resonance and no-bond resonance involving the lone pair of e's of the ring 'O' atom and the axial C_1-X bond as shown below.

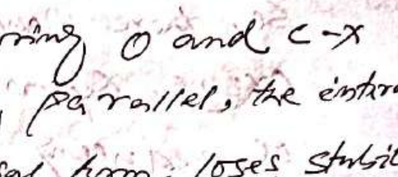
MO approach



V.B. approach

The fact that the anomeric effect increases with the decreasing dielectric constant of the solvent tells us that the dipole-dipole interaction also contributes to the anomeric effect. The dipoles of the ring O and C-X bond in the equatorial form being parallel, the interaction is very strong and the equatorial form loses stability while in the axial isomer, the two dipoles being divergent, the dipole-dipole interaction is weak and the axial form gets stability.





estion: i. β-D-Glucopyranose is more stable than β-D-~~Gluc~~ Galactopyranose - Explain

ii. The axial anomer of D(+) glucose pentaacetate is more stable than the equatorial anomer. Why?

Sucrose:

* Molecular formula → $C_{12}H_{22}O_{11}$

* On dilute acid hydrolysis or enzymatic hydrolysis of one molecule of (+) sucrose, one molecule of D(+) glucose and one molecule D(−) fructose are obtained. So (+) sucrose is a disaccharide formed by the condensation of D(+) glucose and D(−) fructose.

* (+) Sucrose does neither form oxime nor cyanohydrine nor even osazone by the reaction with NH_2OH or HCN or $PhNHNH_2$ respectively. Hence in the aqueous medium it has no free aldehydic and or ketonic carbonyl groups. It does not also mutarotate in any medium. Therefore, it ~~does~~ is neither a hemiacetal nor a hemiketal. If it were so, there would have been mutarotation, formation of oxime, cyanohydrine and osazone and the exhibition of reducing properties involving Felling's reagent, Tollen's reagent etc. Thus we conclude that the anomeric OH of D-glucose and that of D-fructose take part in the reaction to develop the full acetal (ketal).

At this stage two questions regarding the structure of (+) sucrose remain unsolved. (1) What is the nature of the linkage? Is that α, α or α, β or β, α or β, β.

(2) What are the size of the D-glucose ring and the D-fructose ring.

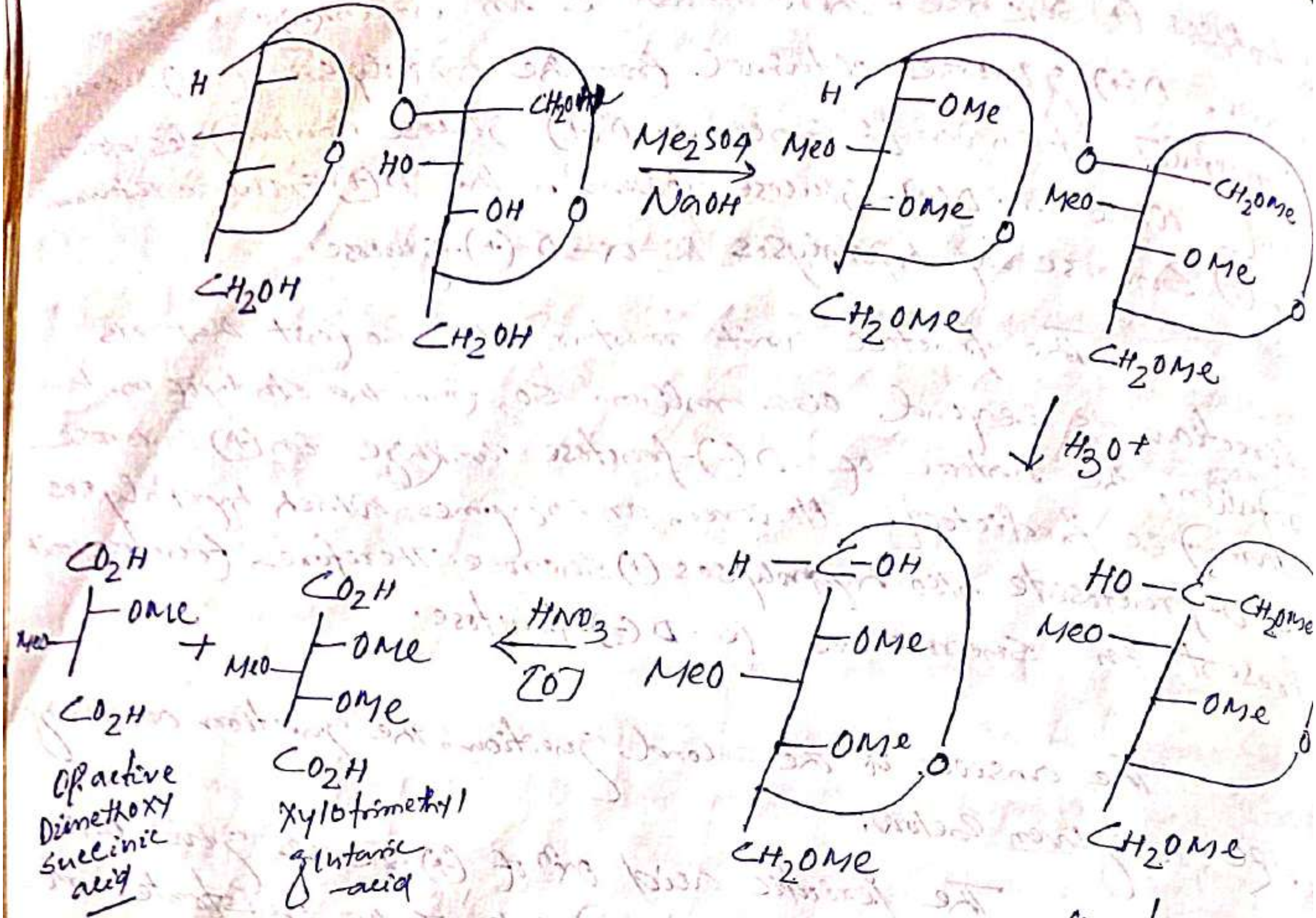
The answer to the first question is as follow: Maltase, an enzyme, which hydrolyses an α-linkage also hydrolyses (+) sucrose. Since enzymes are optically active highly stereospecific reagents and hydrolyses (+) sucrose, there must be an α-linkage in sucrose. Again, D(+) glucose obtained from the hydrolysis of (+) sucrose mutarotates downward; since α-D(+)-glucose mutarotates downward while β-D(+)-glucose upward, the D(+) glucose obtained from (+) sucrose by hydrolysis is α-D-(+)-glucose.

The fructose unit mutarotates so fast that its direction is beyond observation. So, from the study of mutarotation, the nature of D(-)-fructose linkage in (+) sucrose cannot be predicted. However, an enzyme which hydrolyses β-D-fructoside also hydrolyses (+) sucrose. Therefore, fructose unit present in sucrose is β-D(-)-fructose.

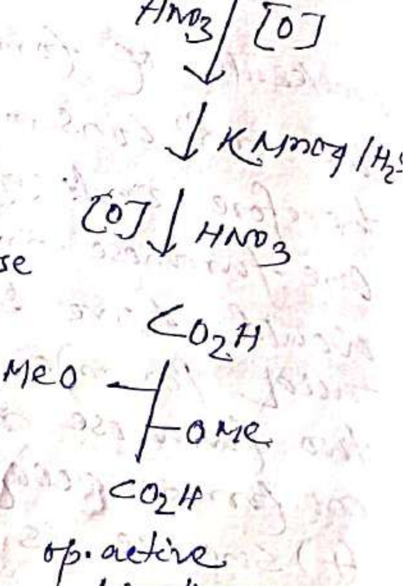
The answer to the second question, the question on ring size is given below:

The periodic acid ox^n of (+) sucrose gives one molecule of formic acid per molecule of the substrate and the rex^n consume three molecules of HIO_4. This reaction therefore indicates the presence of one pyranose ring and one furanose ring. If there were two pyranose rings, there would have been the formation of two molecule of formic acid per molecule of the substrate. Again, had there been two furanose ring in (+) sucrose, there would have been no formic acid in the ox^n products. So, one ring in (+) sucrose is pyranose and the other furanose.

The complete methylation of (+) sucrose by dimethyl sulphate (Me_2SO_4) and dilute NaOH sol^n followed by hydrolysis gives tetra-O-methyl-D-glucose and tetra-O-methyl-D-fructose. When these two compounds are subjected to the classical oxidative degardation as carried out by Haworth and Hirst show that tetra-O-methyl-D-fructose is 1,3,4,6-tetra-O-methyl-β-D-fructose and the tetra-O-methyl-D-glucose is 2,3,4,6-tetra-O-methyl-α-D-glucose. Therefore, the α-D-(+) glucose unit in (+) sucrose has a pyranose structure and that of β-D-(-)-fructose has a furanose structure. Hence (+) sucrose is α-D-glucopyranosyl-β-D-fructofuranoside or β-D-frucfuranosyl-α-D-glucopyranoside.



The isolation of meso or Xylotrimethoxy glutaric acid from the D-glucose and dimethoxy succinic acid ~~from~~ form the D-fructose unit tell us that the glucose and fructose units are D-glucopyranose and D-fructofuranose respectively.



Maltose

Molecular Formula → $C_{12}H_{22}O_{11}$

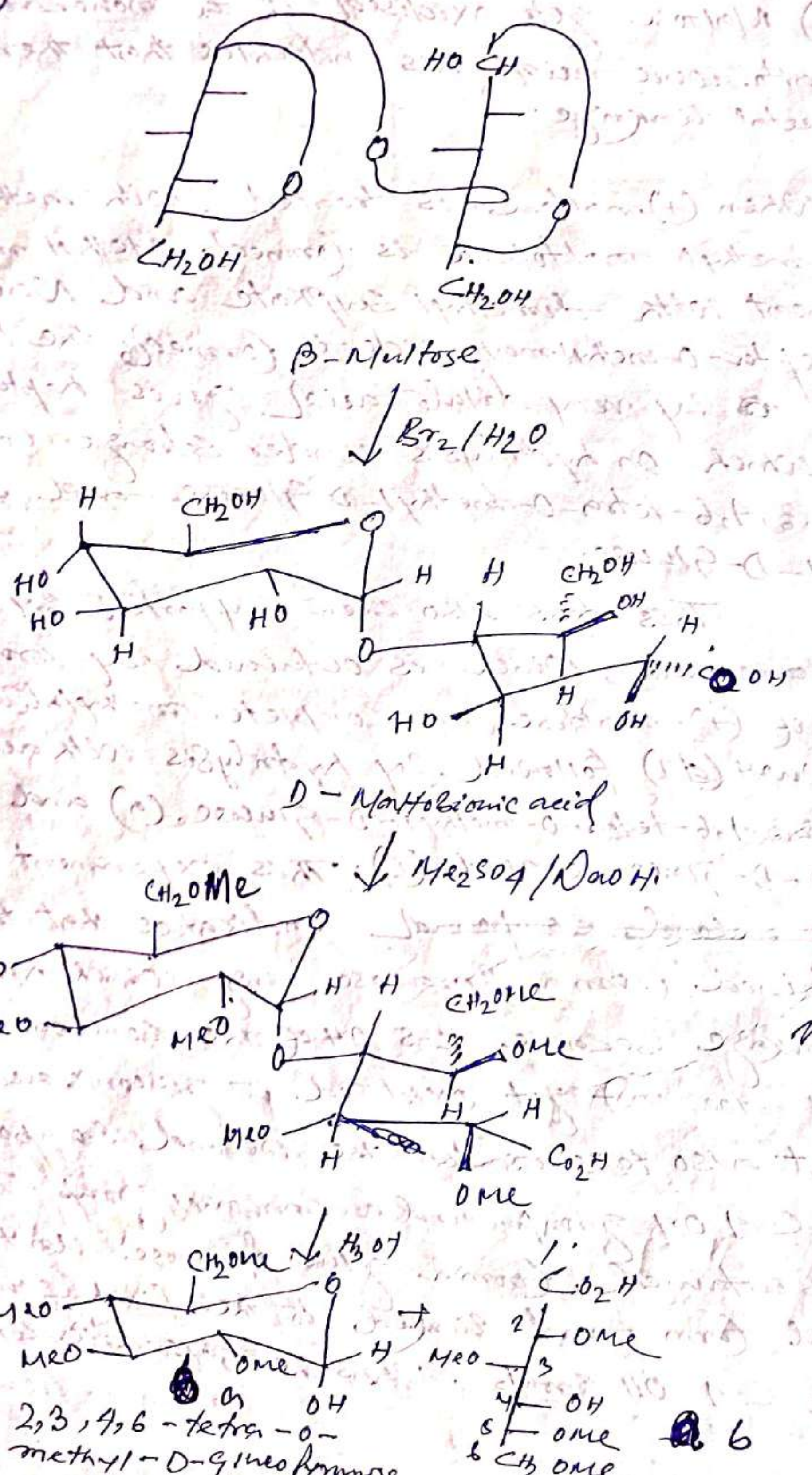
When one mole of (+) maltose is subjected to acid-catalysed hydrolysis, two moles of D-glucose are obtained. So it is a condensation product of two units of D-glucose. (+) Maltose reduces Fehling solution and Tollens reagent; it also mutarotates. Therefore, there is at least one hemiacetal linkage.

(+) Maltose gets oxidised to a monocarboxylic acid, D-maltobionic acid. This indicates that there is only one hemiacetal linkage.

When (+)maltose is treated with methyl alcohol and HCl, methyl maltoside is formed. Methyl maltoside on treatment with dimethyl sulphate and NaOH soln, methyl hepta-O-methylmaltoside is formed; the latter on hydrolysis by very dilute acid gives hepta-O-methyl maltose which on hydrolysis under stronger condition gives 2,3,4,6-tetra-O-methyl-D-glucose and 2,3,6-tri-O-methyl-D-glucose.

This has also been supported by the fact that D-maltobionic acid, which is obtained by bromine-water oxidation of (+)-maltose, on complete methylation with Me_2SO_4/NaOH (dil) followed by hydrolysis with acid catalyst, gives 2,3,4,6-tetra-O-methyl-D-glucose (a) and 2,3,5,6-tetra-O-methyl-D-gluconic acid (b). This experiment ~~also tells us that the second compound~~ indicates that the first product (a) is obtained from a pyranose ring which has a full acetal linkage because, C-5 OH of the compound (a) is free and it does not get oxidised to gluconic acid. This experiment also tells us that the second compound (b) bears a free C-4 OH group, and a carboxyl group. This is possible if this is obtained from a glucopyranose unit in the hemiacetal form and linked to the first glucose unit through its C-4 OH group. Thus the glycosidic linkage is formed by the reaction between anomeric OH of one D-glucopyranose and ~~a~~ C-4 OH of another D-glucopyranose, the latter unit is in hemiacetal form while the former is full acetal.

Lastly (+) maltose is hydrolysed by maltase an enzyme which hydrolyses α-glycosidic linkage and (+)-maltose does not hydrolyse by emulsin, which hydrolyses a β-glycosidic linkage. Therefore, (+) maltose contain an α-glycosidic linkage and no β-glycosidic linkage.



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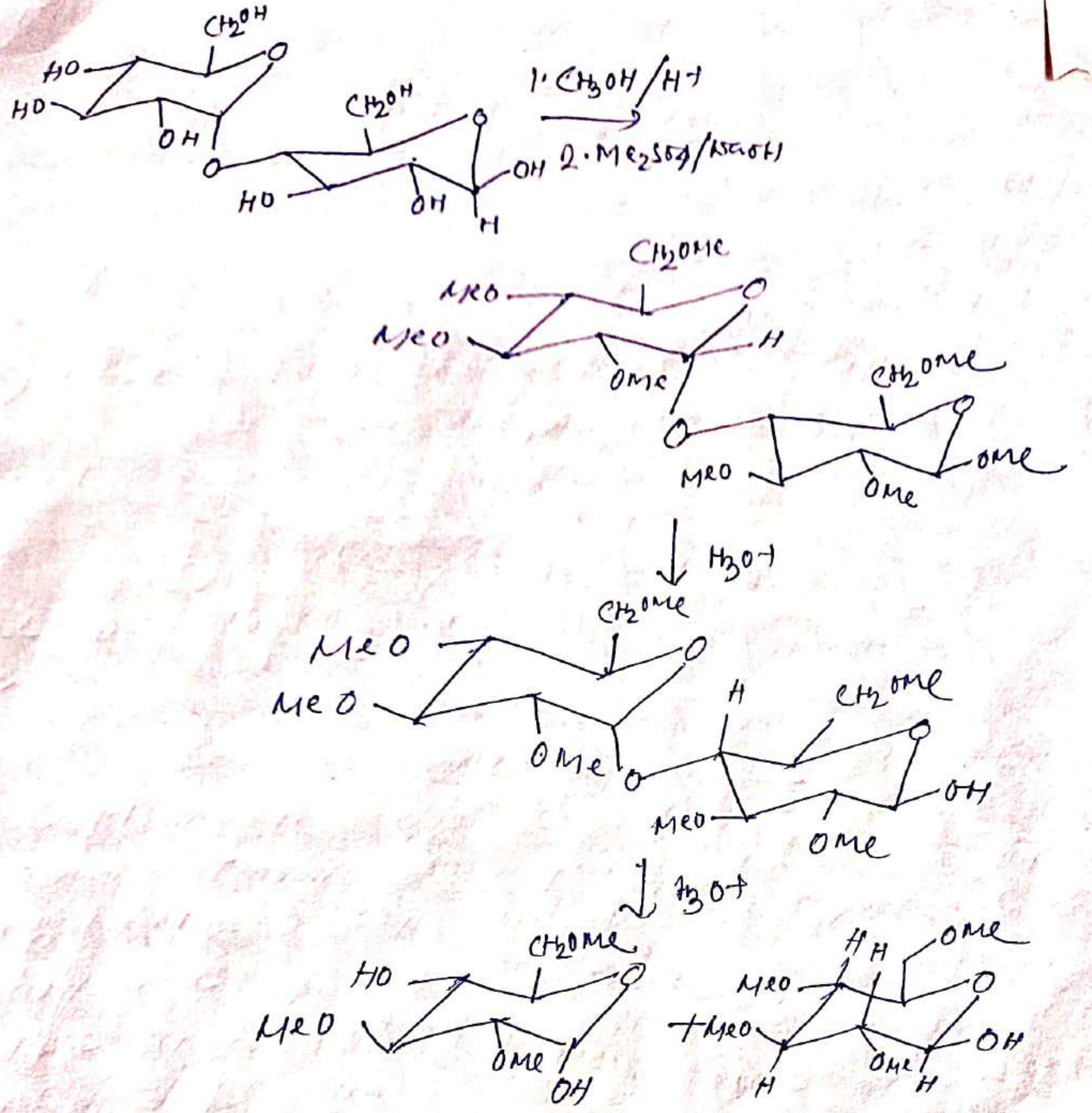
CH2OH
HO
HO
OH
O
CH2OH
O
OH
HO
OH
H
1. CH3OH/H+
2. Me2SO4/NaOH
CH2OMe
MeO
MeO
O
H
OMe
CH2OMe
O
O
OMe
MeO
OMe
H3O+
CH2OMe
MeO
MeO
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