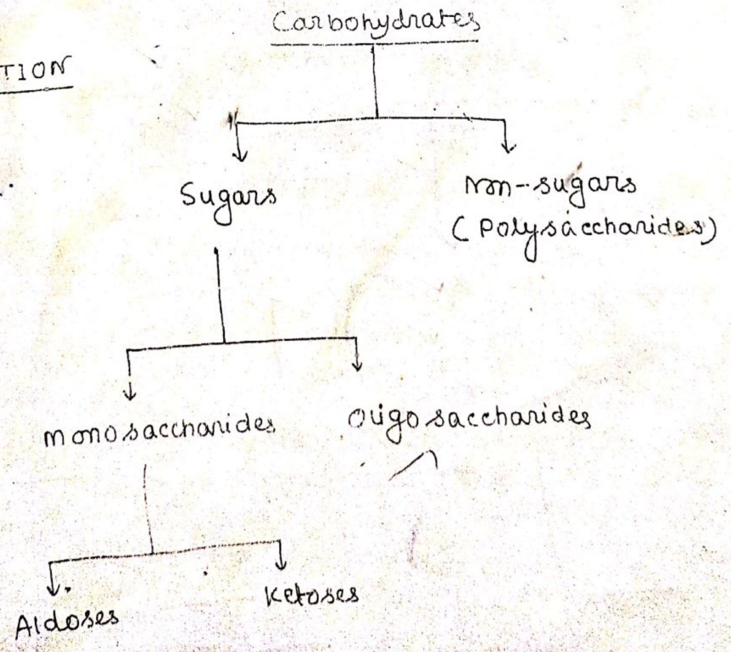
CARBOHYDRATES

Carbohydrates are substances with the general formula $C_x(H_2O)_y$ and were called Carbohydrates (hydrates of Carbon) 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; acetic acid, $C_2H_4O_2$; etc.

Thus; poly hydroxy-aldehydes or ketones that show optical isomerism are called Carbohydrates. All Carbohydrates are polyhydroxy-aldehydes or ketones or substances that yield these on hydrolysis.

CLASSIFICATION



- **Sugars** are sweet, crystalline substances and s in water. Their molecular weights are known an fixed for a particular compound.

- Polysaccharides are polymers of monosaccharides. most of them are non-crystalline substances which are not sweet, and are insoluble or less solubl in water, than the sugars. The polysaccharide ma be made up of a single type or different typ of monosaccharide units:- The two correspond polysaccharides are respectively known as homopol saccharide and heteropolysaccharide.

- Monosaccharides are sugars which can not b hydrolysed into smaller molecules. They may agai be classified according to the type of carbonyl gro and the number of carbon atoms in the molecu

A. Type of carbonyl:- ✓

✓ Aldoses – having aldeh gr

Ketoses:- having keto gr

B. number of carbon atoms:-

✓ Triose having 3-carbon atoms
✓ Tetrose having 4-carbon atoms
✓ Heptose having 7-carbon atoms

- oligosaccharides: These yield two to ten monosac -aride molecules on hydrolysis.

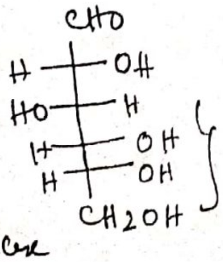
Reducing sugars: Carbohydrates that reduce Fehling's or Benedict's solutio

(an alkaline solution of cupric ion complexed with citrate ion) are known as reducing sugars. All monosaccharides, whether aldose or ketose are reducing sugars..

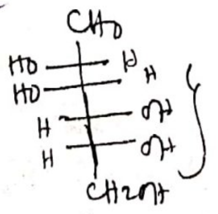
From the classification of the carbohydrates, ~~whether aldose or ketose are reducing~~ we see that monosaccharides are the simplest and ultimate carbohydrates and all others are considered as the condensation products of the monosaccharides. Furthermore, among the monosaccharides the pentoses and hexoses sugars are most important from the stand point of occurance and even between the two, the hexoses are important.

D/L sugar: These refer to the configuration of the lower most chiral carbon in a sugar. If the hydroxyl group is at the right in F.P.F then it will be D and if it at left it will be L.

Epimers: When two stereoisomers containing several asymmetric carbon atom differ only in the configuration of one of these stereocentres, they are said to be epimers. Both D-glucose and D-mannose have four asymmetric carbon atoms but they differ in configuration only at carbon 2, so they are epimers.



D- glucose



Mannose.

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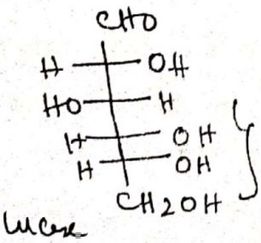
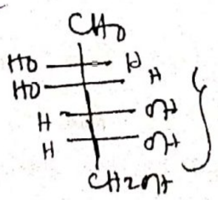


D- glucose



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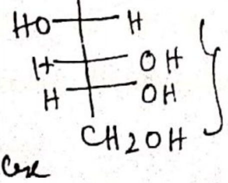
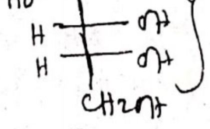


D- glucose



Mannose.

D(+)- Glucose, dextrose (grape-sugar), is found in ripe grapes, honey and most sweet fruits; it is also a normal constituent of blood, and occurs in the urine of diabetics. Commercially, pure D(+) glucose is manufacred by heating starch with dil HCl under pressure.

Structure elucidation:

a. Elemental analysis and molecular weight determination show that the molecular formula of gluc is $C_6H_{12}O_6$.

b. Complete reduction of glucose with concentrated H in presence of red phosphorus produces n-hexa as the major product. This indicates that the six carbon atoms in the glucose molecule form a consecu unbranched chain.

c. Glucose readily dissolve in water to give a neutra solution. This indicates that the glucose does not contain a carboxyl group ($-\overset{O}{\overset{\|}{C}}-O-$)

d. Glucose reacts with hydroxyl amine to form a mono or adds only one mole of HCN. These reactions indic the presence of either an aldehyde or a keto ($-\overset{O}{\overset{\|}{C}}-$) group but not both.

e. mild oxidation of glucose with Br_2/H_2O gives glucon acid, a monocarboxylic acid with molecular formu $C_6H_{12}O_7$. This indicates the presence of an aldehyd group only, the aldehyde group can be oxidised to an acid. Since the six carbon atoms in glucose form a consecutive unbranched chain, the aldehyde group must occupy one end of this chain.

Further oxidation of gluconic acid with nitric acid gives glucaric acid, a dicarboxylic acid with molecular formula $C_6H_{10}O_8$. This indicates the presence of a 1° alcohol group.

g. Glucose reacts with Ac_2O/Py to form glucose pentaacetate. This reaction indicates the presence of five hydroxyl group in a glucose molecule.

h. Organic compounds with hydroxyl groups attached to a single carbon atom are rare and those which are known usually lose water to produce a carbonyl group.

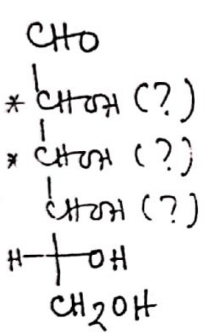
This suggest that in glucose molecule, each one of the five hydroxyl group is attached to a different carbon atoms.

From the above evidences we conclude that glucose is an aldohexose and can be represented, as the following structures

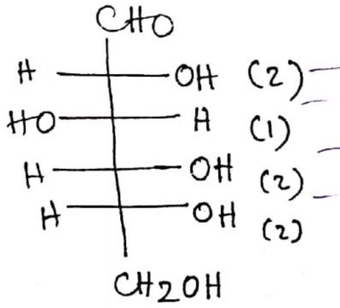
$$\boxed{OHC-(CHOH)_4-CH_2OH}$$

Configuration of monosaccharide

Although D/L system of stereochemical designatio is thoroughly enriched in the literature of Carbohydr chemisty, but it has the disadvange of specifying the Configuration of only one stereo centre, and it remains silent about the Configuration of oth stereocentres. Thus, say we have to write the Configuration of D(+) glucose, obviously we can wri it as

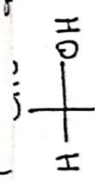


So either we have to memorise - he the mnemonic devise is (2122) for D(+ glucose

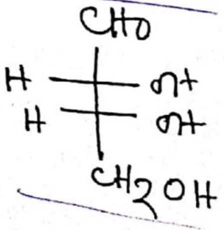


2 stands for OH
1 stands for H
— note the righ side in F. P. F. of D(+) glucose.

D(+) glyceraldehyde

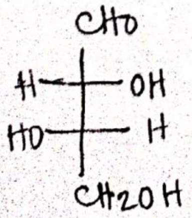


or we have to depend on their trivial name for example the Configuration of D(–) erythrose i.e. the erythro variety of aldotetrose is

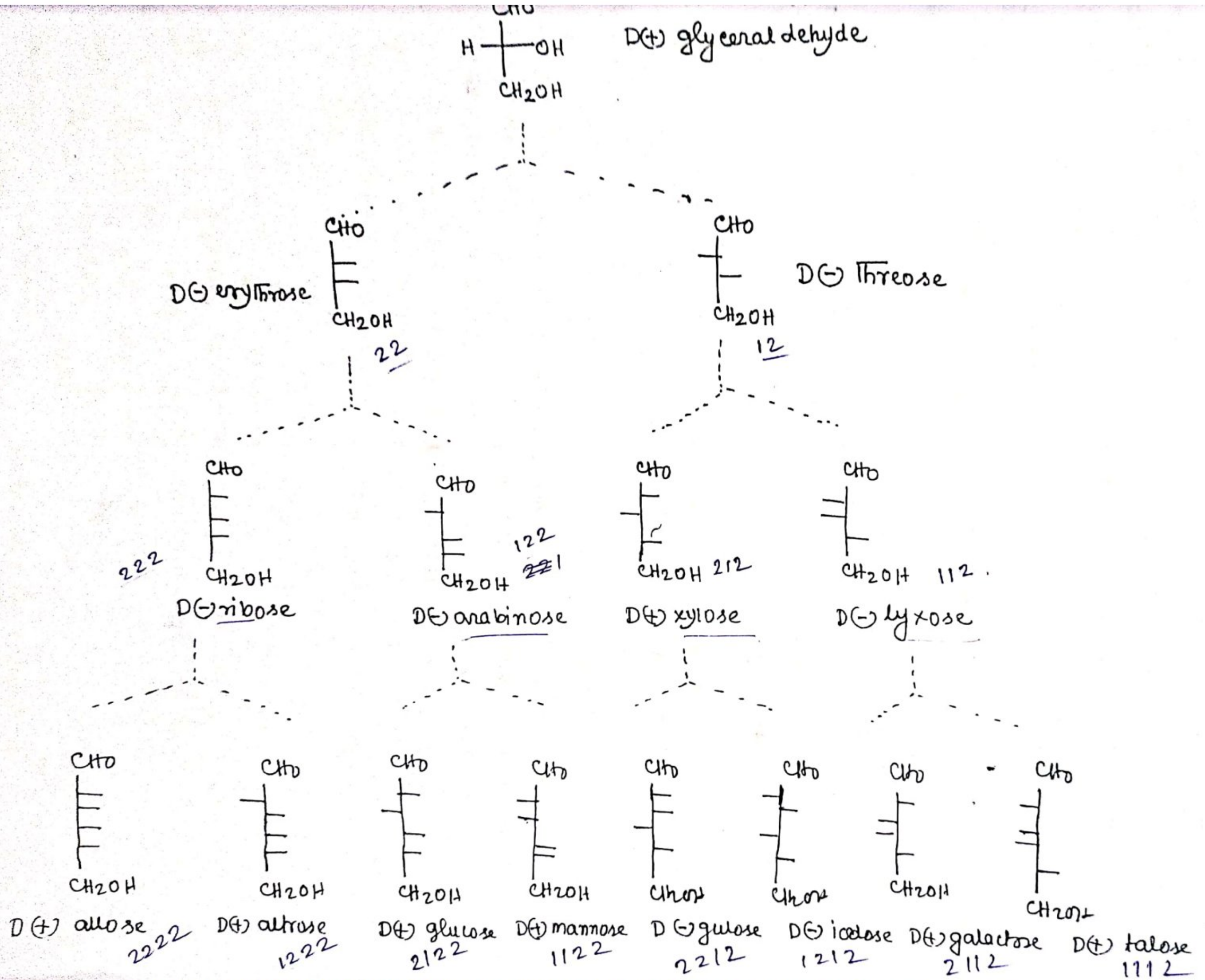


and

The Configuration of L(+) threose, The threo variety of aldotetrose is

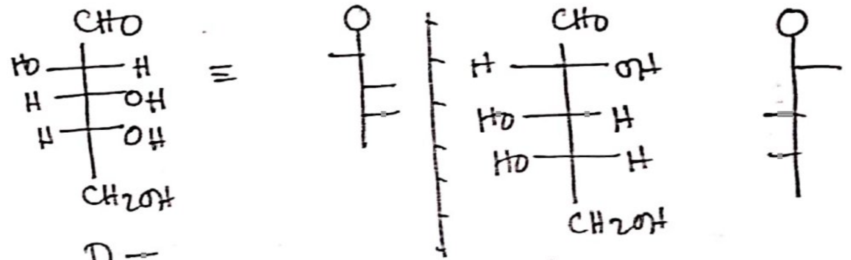


The arrangements of all the sugar in D-series are shown in the adjacent figure, Called the family tree of the sugars.


CHO
H
OH
CH2OH
D(+) glyceral dehyde
CHO
D(-) erythrose
CH2OH
22
CHO
D(-) Threose
CH2OH
12
CHO
CH2OH
222
D(-) ribose
CHO
CH2OH
122
~~221~~
D(-) arabinose
CHO
CH2OH 212
D(+) xylose
CHO
CH2OH 112.
D(-) lyxose
CHO
CH2OH
D(+) allose
2222
CHO
CH2OH
D(+) altrose
1222
CHO
CH2OH
D(+) glucose
2122
CHO
CH2OH
D(+) mannose
1122
CHO
CH2OH
D(-) gulose
2212
CHO
CH2OH
D(-) idose
1212
CHO
CH2OH
D(+) galactose
2112
CHO
CH2OH
D(+) talose
1112

The hexoses can be remembered with the phrase "All Altruists Gladly make Gum In Gallon Tanks". In this phrase the first two or three letters in each word correspond to the begining letters in the name of a sugar. The aldopentoses can be similarly remembered with the phrase "Ring All xylophones Loudly".

* D & L sugars are mirror images of each other



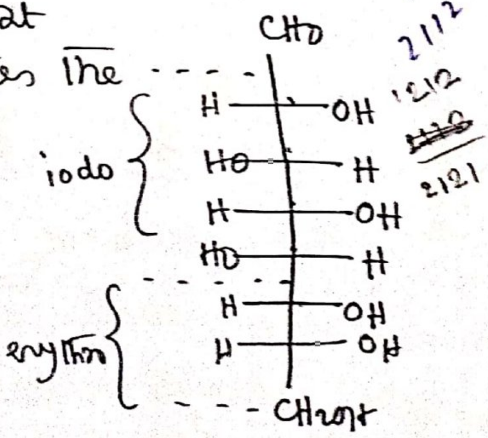
D-

L-

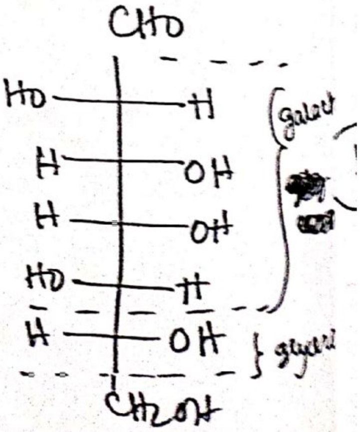
---

monosaccharides containing more than four asymmetric carbon atoms e.g, aldoheptose, aldo-octose etc. are named by using two prefixes derived from the lower sugars. Thus; one asymmetric carbon atom: glycero; two – erythro, threo; three – ribo, arabino, xylo, lyxo; four – allo, altro, gluco, manno, gulo, iodo, galacto, talo. The name to be assigned to the sugar is given by the prefix denoting four asymmetric carbon atoms which occur adjacent to C-1 (aldose) or C-2 (ketose) and by other prefix denoting the next group of asymmetric carbon atoms (up to four).

The prefix named last is that which denotes the 4 unit adjacent to the oxo group.



D-erythro-L-iodo octose



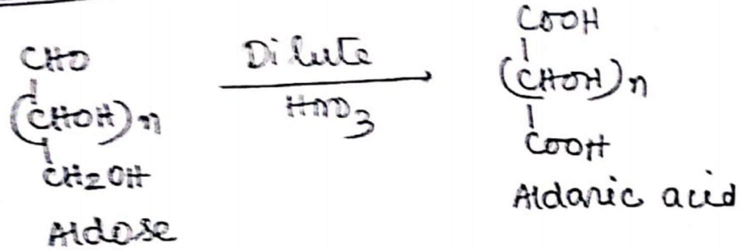
D-glycero-L-galacto heptose

DETERMINATION OF THE CONFIGURATION OF MONOSACCHARIDES.

Determination of the configuration of monosaccharides is based on the following important reactions.

1. Nitric acid oxidation

Dilute nitric acid oxidises both the $-CHO$ and the terminal $-CH_2OH$ groups of an aldose to $-COOH$ groups. These dicarboxylic acids are known as aldaric acids or saccharic acids

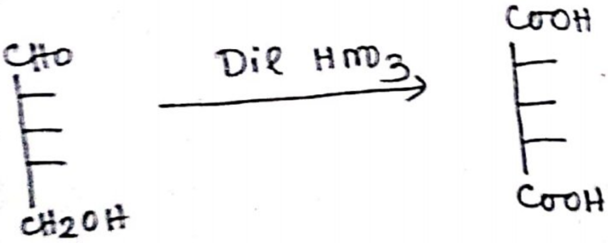


$$\underset{\text{Aldose}}{\begin{array}{c}CHO\\|\\(CHOH)_n\\|\\CH_2OH\end{array}} \xrightarrow[HNO_3]{\text{Dilute}} \underset{\text{Aldaric acid}}{\begin{array}{c}COOH\\|\\(CHOH)_n\\|\\COOH\end{array}}$$

This dilute nitric acid oxidation of an aldose is stereo-chemically very important.

ⓐ Through this reaction the aldose containing dissimilar stereogenic centres is converted to aldaric acid containing similar stereogenic centres. for example:

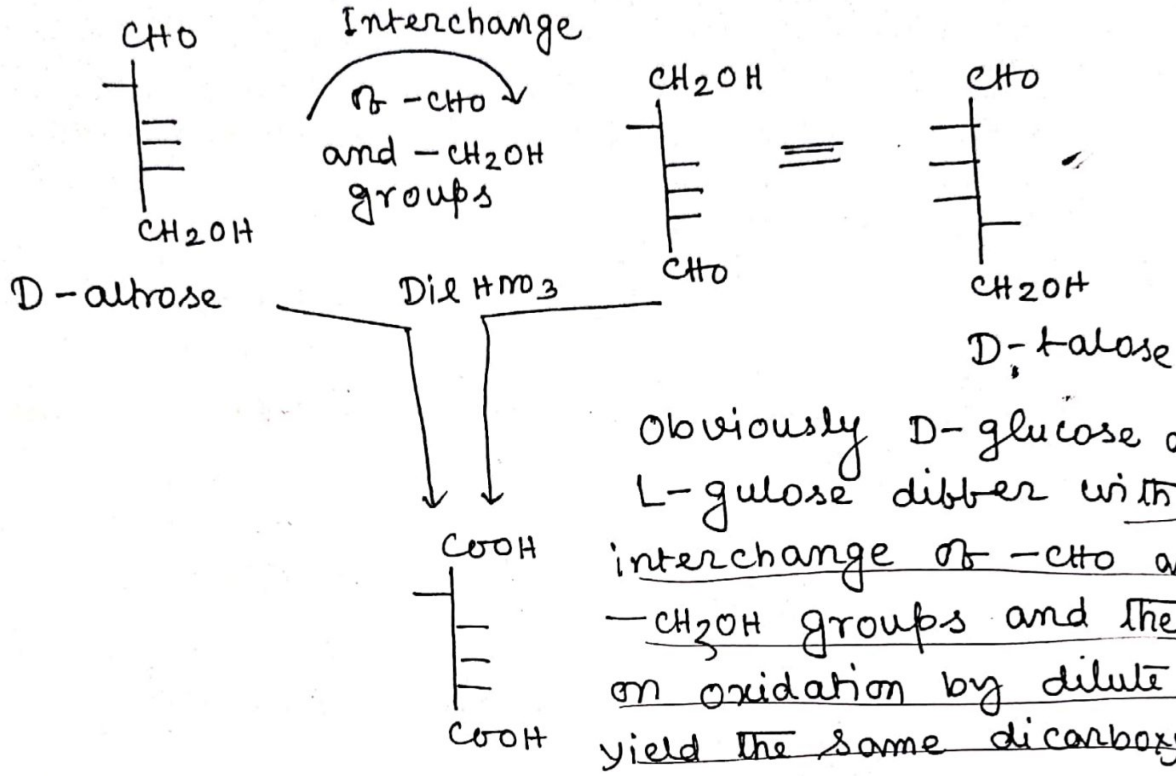
D-ribose
O.A.



Trihydroxy glutaric acid
O.I.

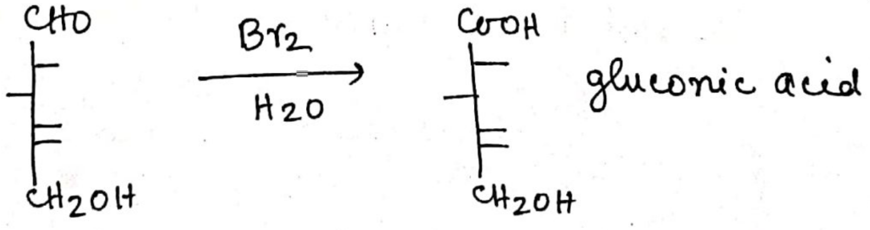
ⓑ Two aldoses differing with the interchange of $-CHO$ and $-CH_2OH$ groups on dilute HNO_3 oxidation will yield the same dicarboxylic acid. for example;

All altruists gladly make
Gum in Gallon Tanks.
2222
1222
2122
1122
2212
1212
2112
1112
11
2/1
manno
1212
Iodoes



Obviously D-glucose an L-gulose differ with interchange of -CHO an $-CH_2OH$ groups and these on oxidation by dilute H yield the same dicarboxyl acid.

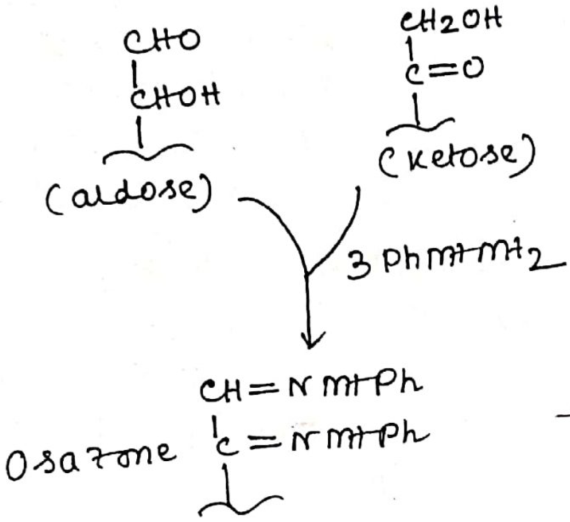
Mild oxidising reagents such as Br_2-H_2O or an al solution of iodine oxidise only the aldehyde grou to give aldonic acids. Thus glucose gives gluconic acid



The most noticeable difference between the glucose an the fructose is their behaviour towards oxidising age fructose is not oxidised by Br_2-H_2O or an alkali solution of iodine, and oxidation with HNO_3 gives a mixture of acids, each containing less than six carbon atoms.

2. OSAZONE FORMATION

When an aldose or a ketose is treated with excess phenyl hydrazine we get bis-1,2-phenyl hydrazone called osazone.

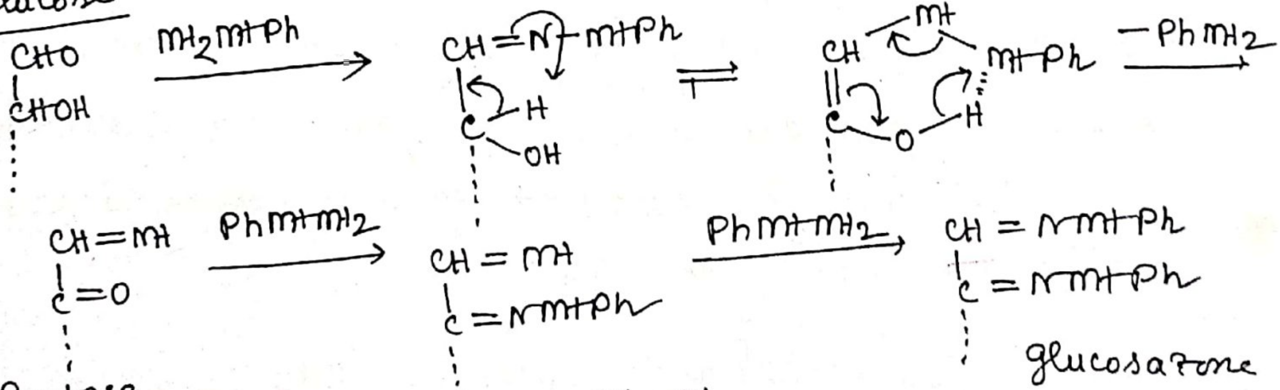


Since osazone formation involves the first two atoms C2 epimeric sugars give same osazone and aldohexoses & ketohexoses similar in configuration at C3, C4 & C5 atoms give identical osazone.

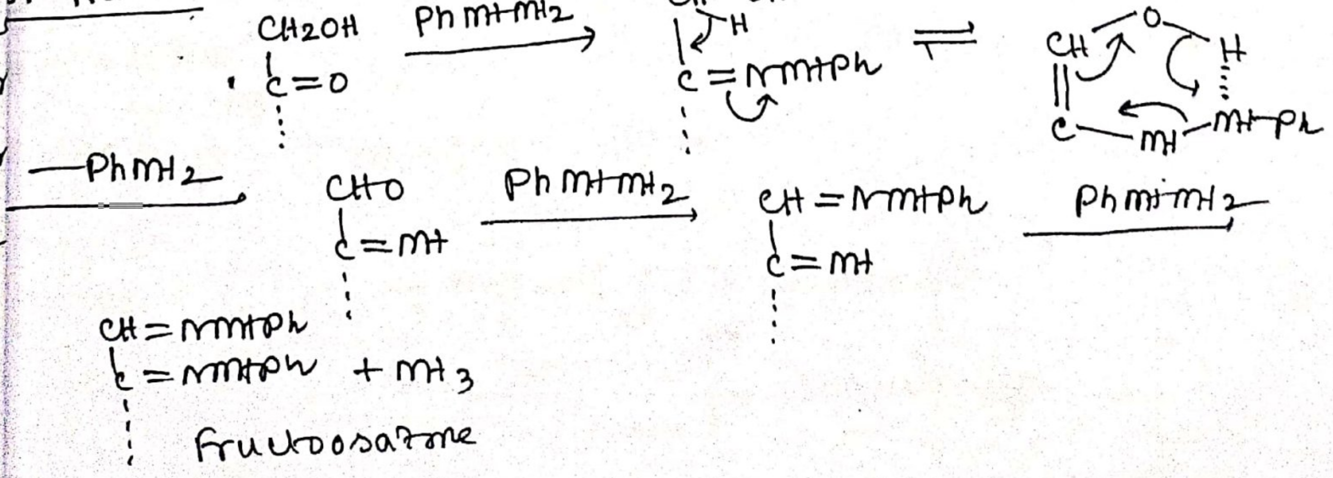
Pathway;

According to this mechanism, The first step is the formation of a phenyl hydrazone, which then undergo Amadori rearrangement.

glucose



fructose



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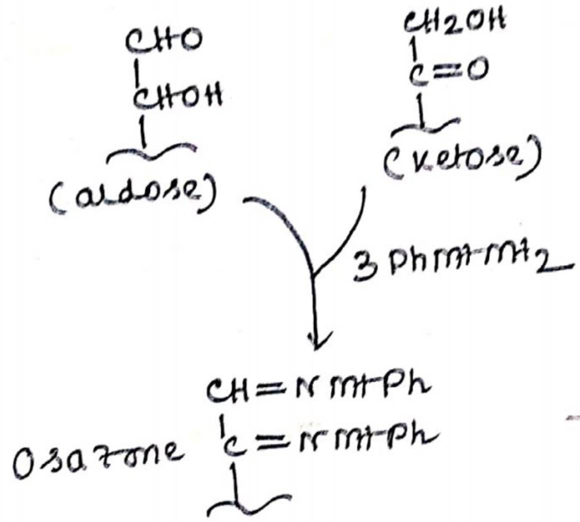

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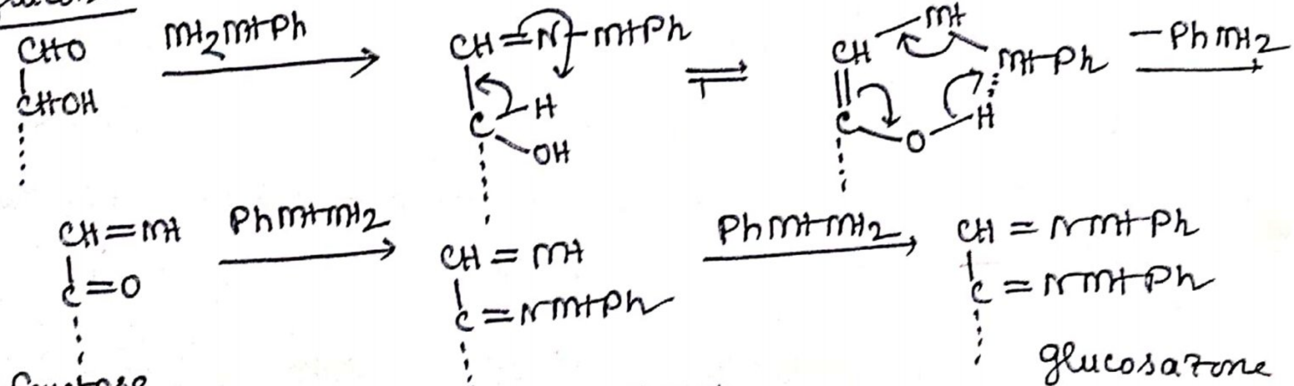
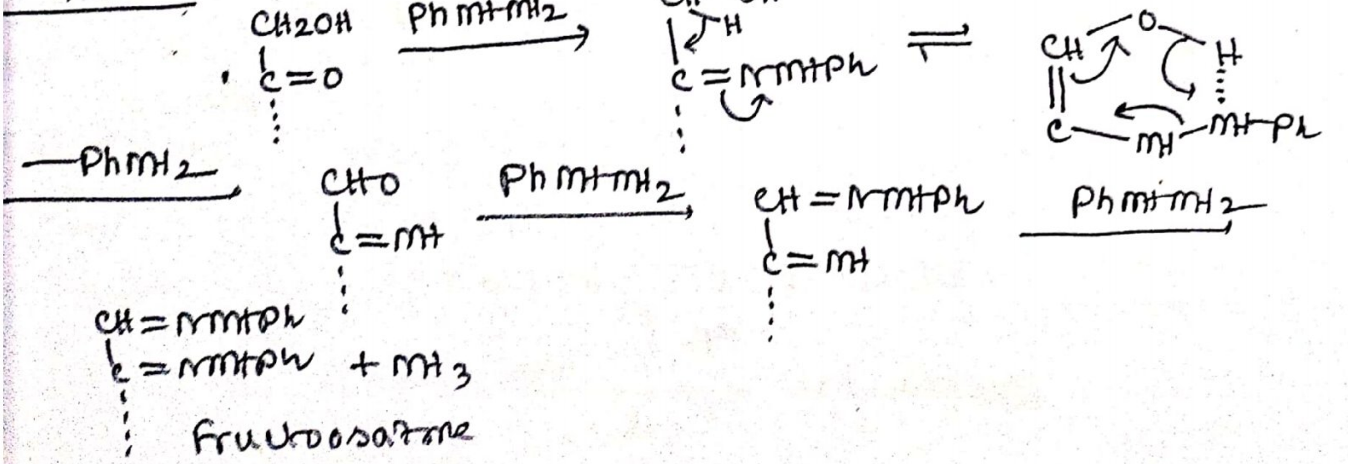
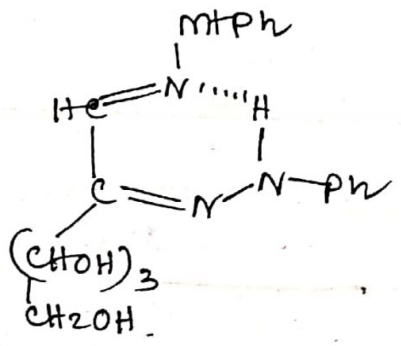
r glucose



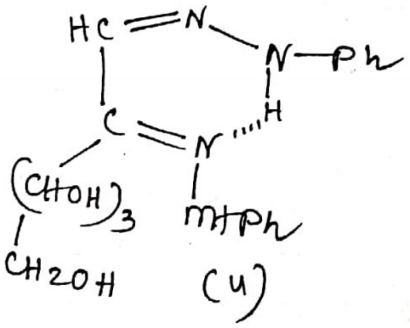
r fructose



Now the question is why only first two carbon atom should be involved in Amadori rearrangement. A first sight it might have been expected that the Amadori rearrangement could carry on down the chain to produce a hexaphenyl hydrazone. The failure to undergo further reaction has been explai by stabilisation of the osazone by chelation i. phenyl hydrazone have ring structure ① and (4).

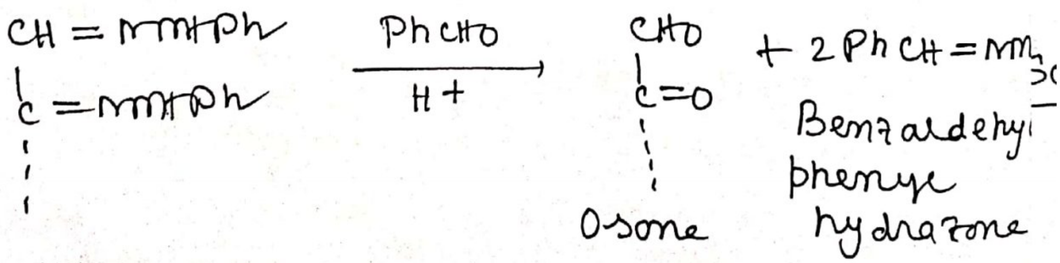


(1)



(4)

Osazones are yellow crystalline solids and ar used to characterise the sugars. Removal of both the phenyl-hydrazine groups yields dicarbony Compounds known as osones.



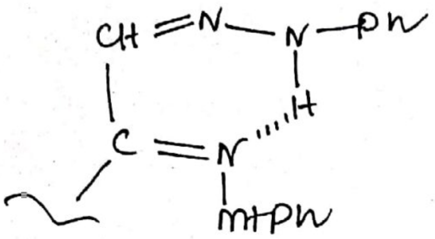
$$\begin{matrix} CH=NNHPh \\ | \\ C=NNHPh \\ \vdots \end{matrix} \xrightarrow[H^+]{PhCHO} \begin{matrix} CHO \\ | \\ C=O \\ \vdots \\ \text{Osone} \end{matrix} + 2PhCH=NN$$

Benzaldehyde phenyl hydrazone

Problem-1 : Complete the following

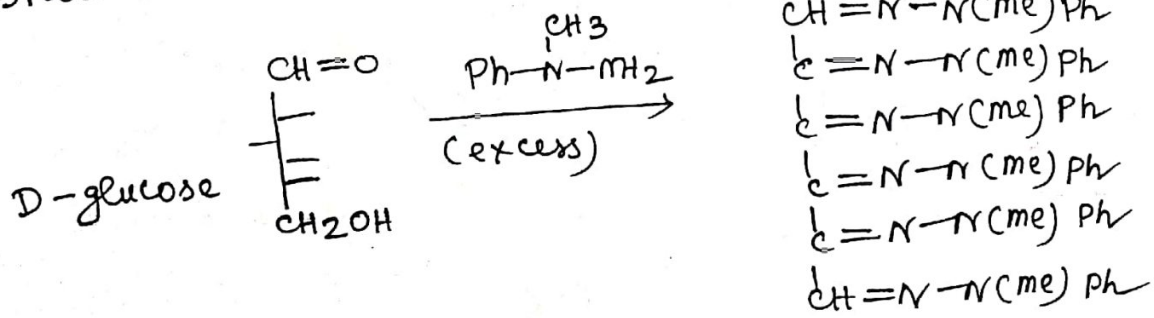
$$\text{D-glucose} \xrightarrow[\text{Excess}]{Ph\overset{me}{N}-NH_2} ?$$

We know that osazone is stabilised through intermolecular hydrogen bonding

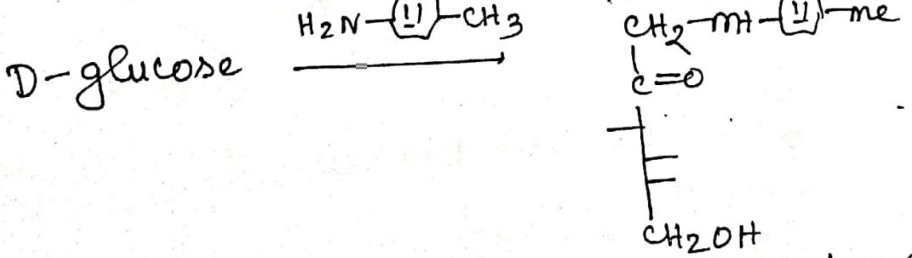


This hydrogen bonding disrupt the further reaction of phenyl hydrazine on the remaining part of the aldose chain through Amadori rearrangement.

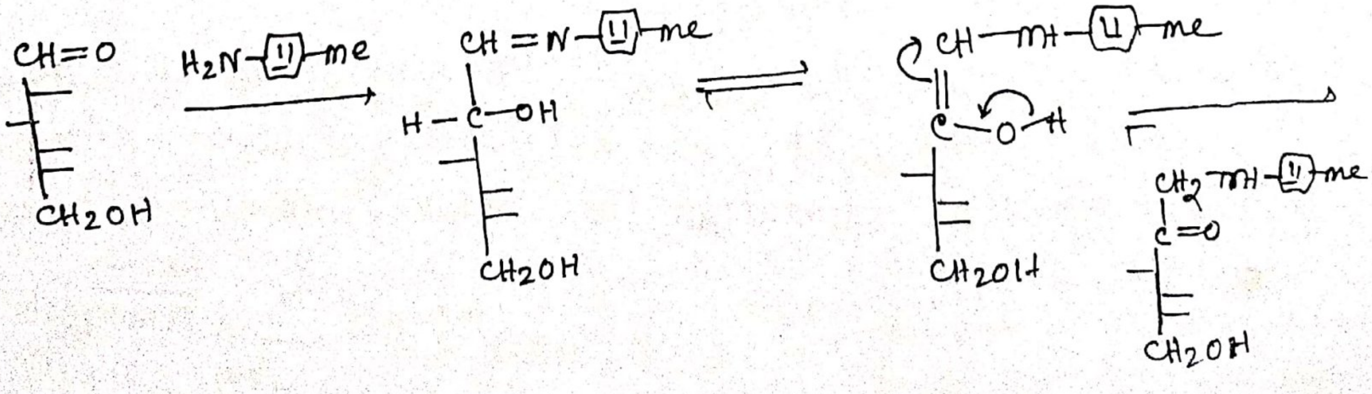
This explanation implies that if the hydrogen bonded N-H were replaced by a methyl group, the crucial hydrogen bond could not exist and further reaction of the osazone should be observed. Thus;



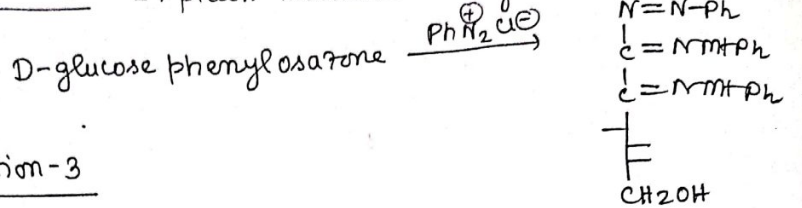
Problem-2: Explain mechanistically



Solution-2: The reaction can be explained by considering Amadori rearrangement in the following way

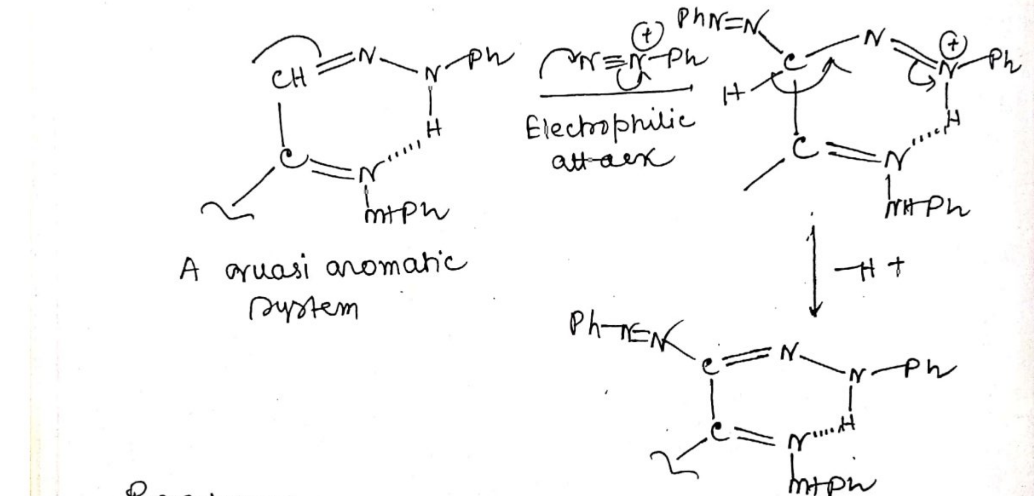


Problem-3 Explain mechanistically



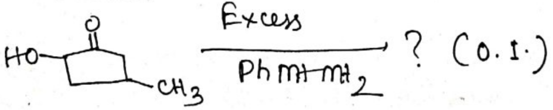
Solution-3

The reaction can be considered as electrophilic substi -on on a quasi aromatic system.



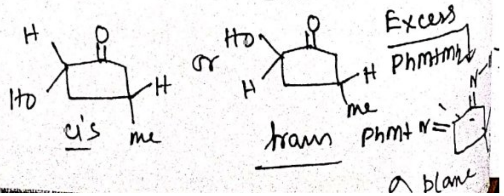
A quasi aromatic system

Problem-4 : Complete and explain the following obse -vation



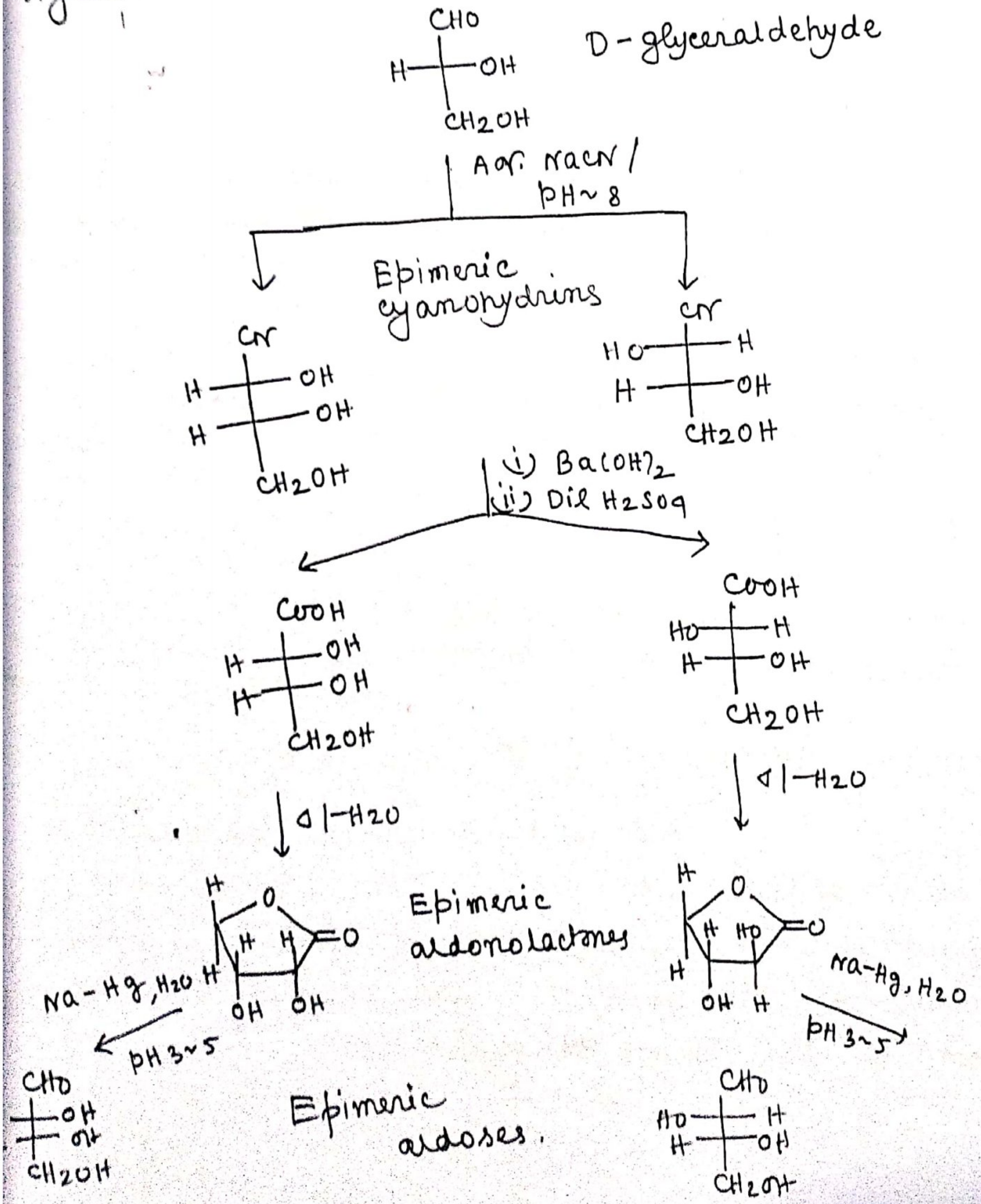
O.A. (cis or trans)

Solution-4: osazone formation is typical of α-hydro aldehydes and α-hydroxy ketones. Agai through osazone formation the stereocentre at α-Carb is lost. Thus;



3. Killiani– Fischer Synthesis:

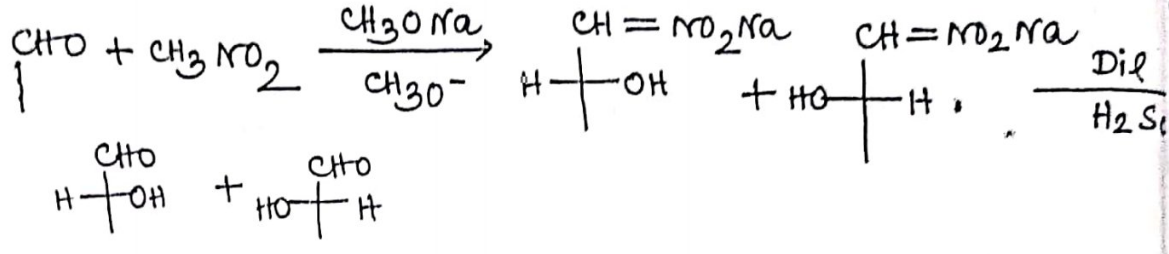
Killiani- fischer synthesis involves the Conversion of an aldose to next higher epimeric aldoses. we can illustrate the Killiani- Fischer synthesis with the synthesis of D-erythrose and D-Threose (aldotetroses) from D-glyceraldehyde (an aldotriose) in the following figure.



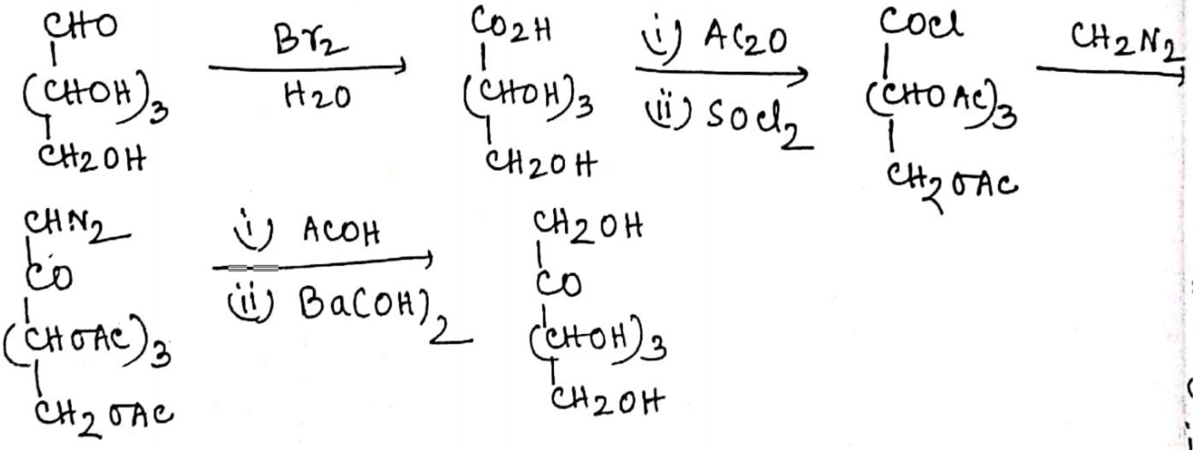
Scanned with CamScanner

Other methods:

There are now many other methods available for stepping up the sugars. Sowden et al. used nitromethane as follows



On the other hand, Wolform et al. have stepped up an aldose to a ketose with one more carbon atom by a modi Arndt-Eistert reaction

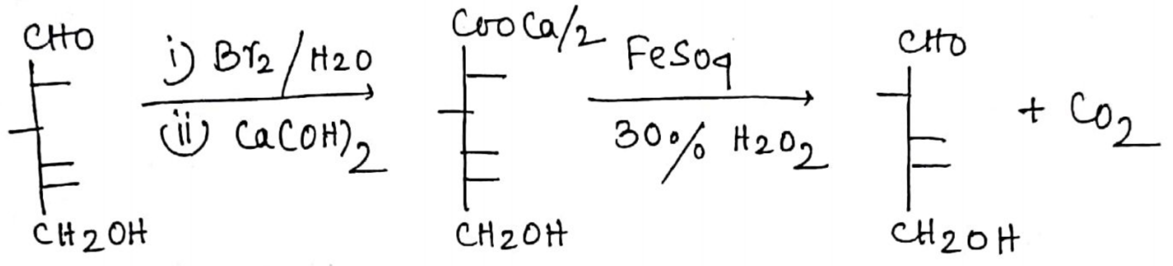


Decreasing the length of the aldose chain

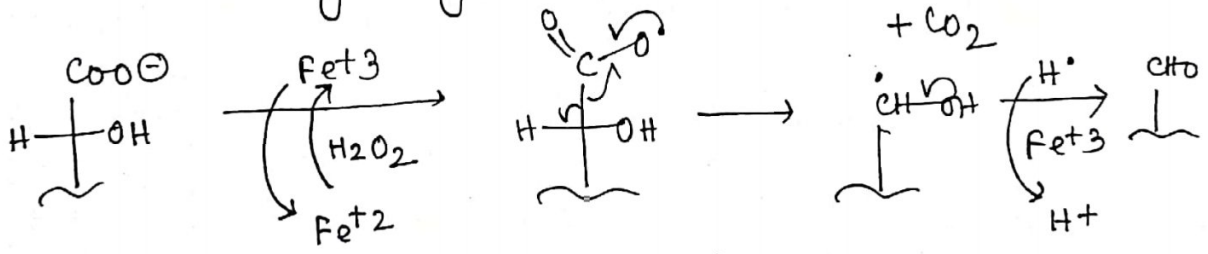
An aldose can be degraded to another aldose with one less carbon atom. In both degradations the aldehyde carbon is removed and carbon 2 of the original sugar becomes the aldehyd carbon of the lower sugar.

Ruff degradation

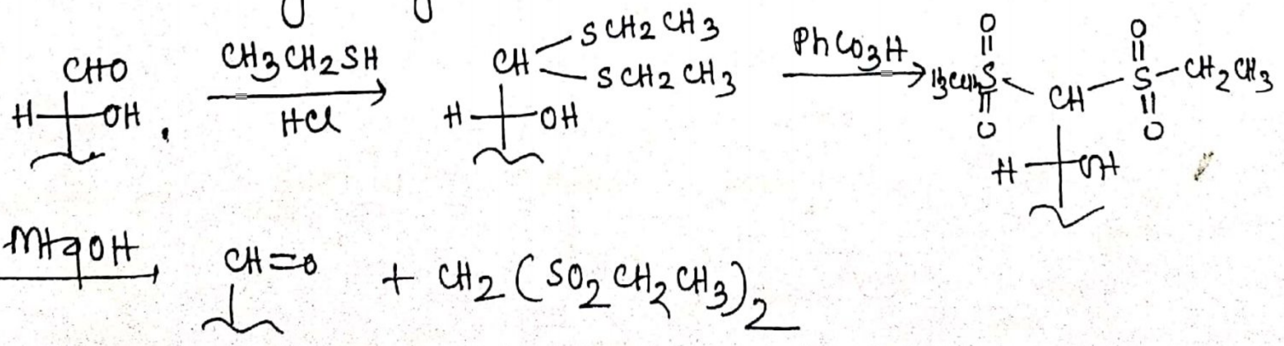
In the Ruff degradation, the aldose is oxidised by bromine water to the corresponding aldonic acid; when the calcium salt of this acid is treated with Fenton's reagent Fe^{+2}/H_2O_2 it is converted to lower aldose.



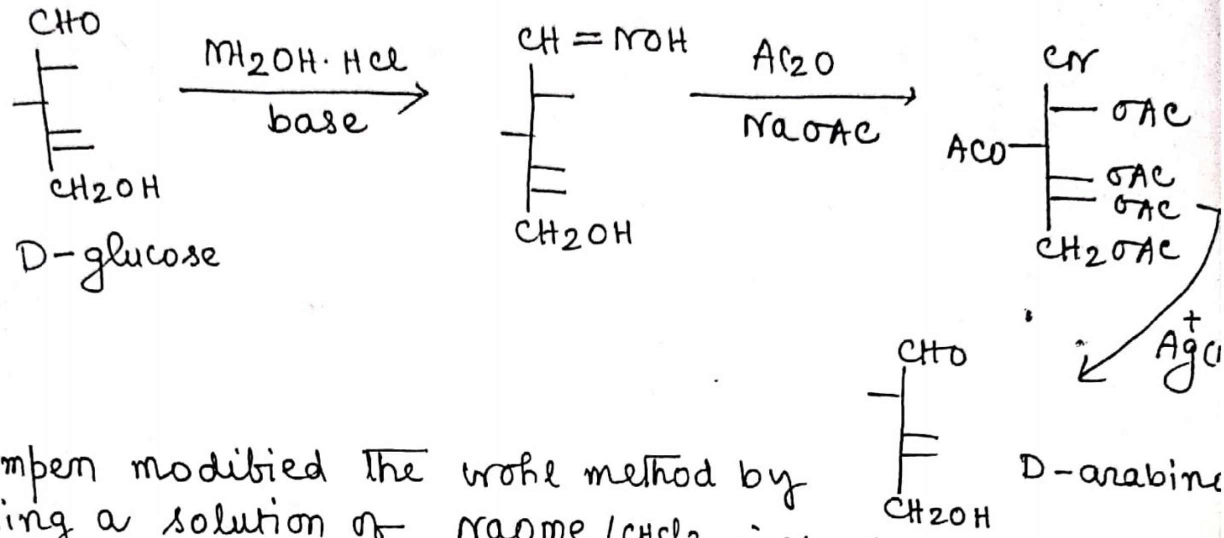
Oxidative decarboxylation of the calcium salt is believed to proceed via a free radical mechanism in the following way;



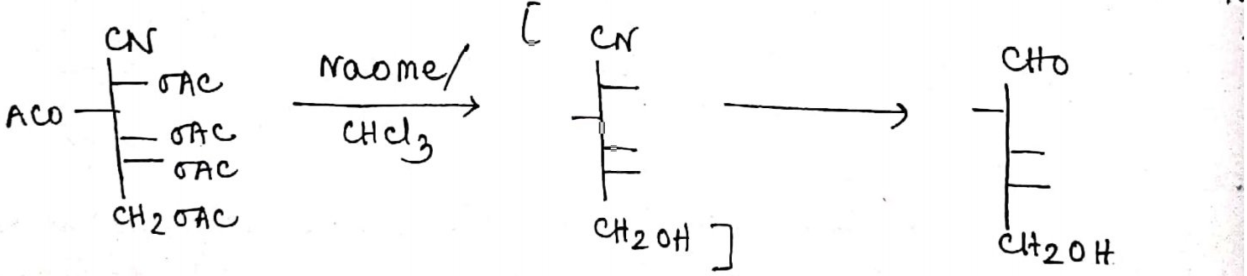
more recent methods of descending the sugars are also available. Thus macdonald have stepped down an aldose via the intermediate formation of thioacetal in the following way;



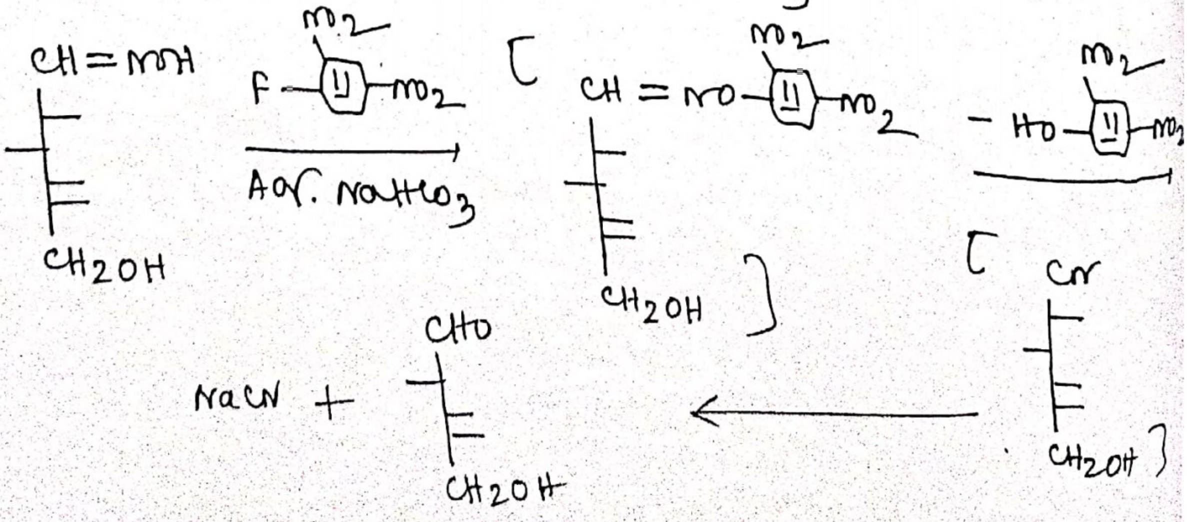
Wohl degradation



Zempen modified the wohl method by using a solution of NaOMe / $CHCl_3$ instead of an aqueous solution of ammonical silver nitra to remove hydrogen cyanide and the acetyl groups, and thereby increased the yield of pentose to 60~7



Again, weygand converted the oxime into lower ald by the treatment with 1-fluoro-2,4-dinitro benze in aqueous solution of $NaHCO_3$

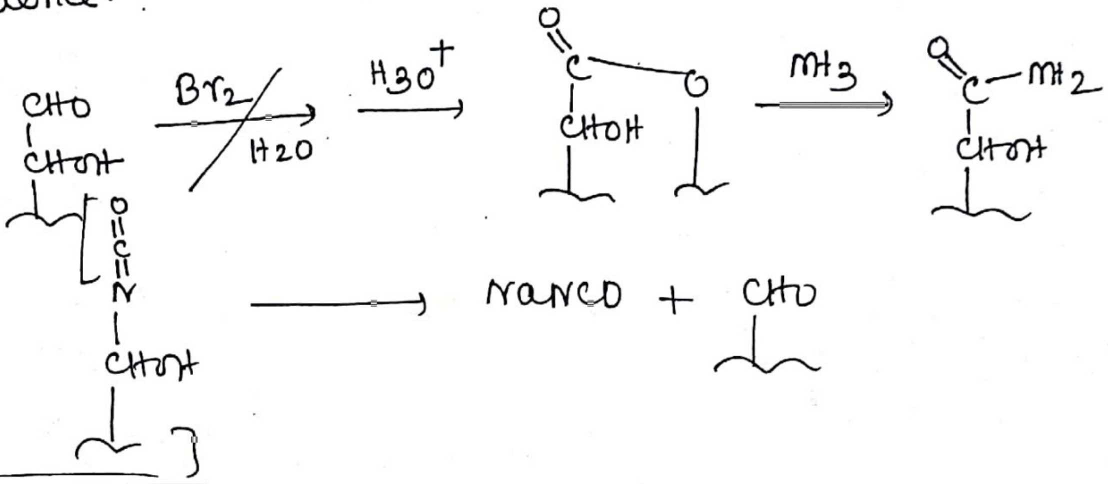


Problem: The following sequence of reactions, called the Weermann degradation, can be used to degrade an aldose to an aldose with one less carbon atom.

$$\text{Aldose} \xrightarrow[H_2O]{Br_2} \xrightarrow{H_3O^+} [A] \xrightarrow[\Delta]{NH_3} [B] \xrightarrow[NaOCl]{NaOH} \text{Aldose with one less carbon atom.}$$

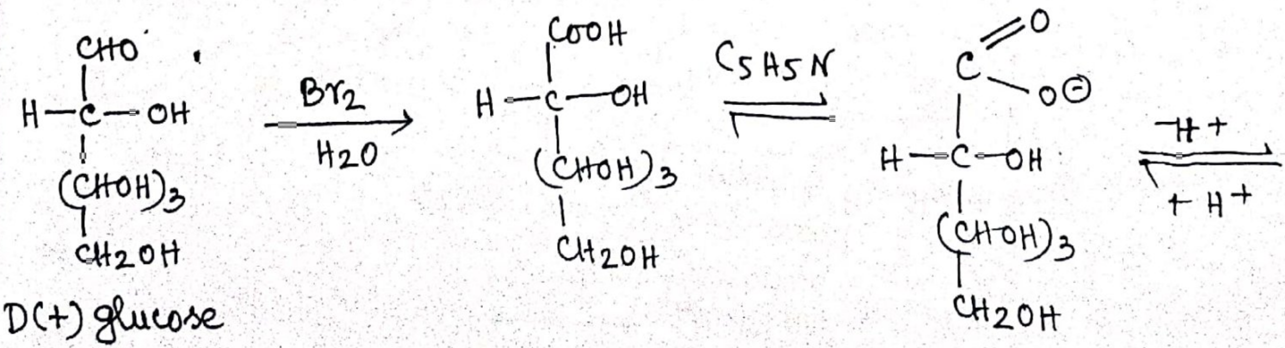
Explain what is happening in each step of this sequence.

Solution:

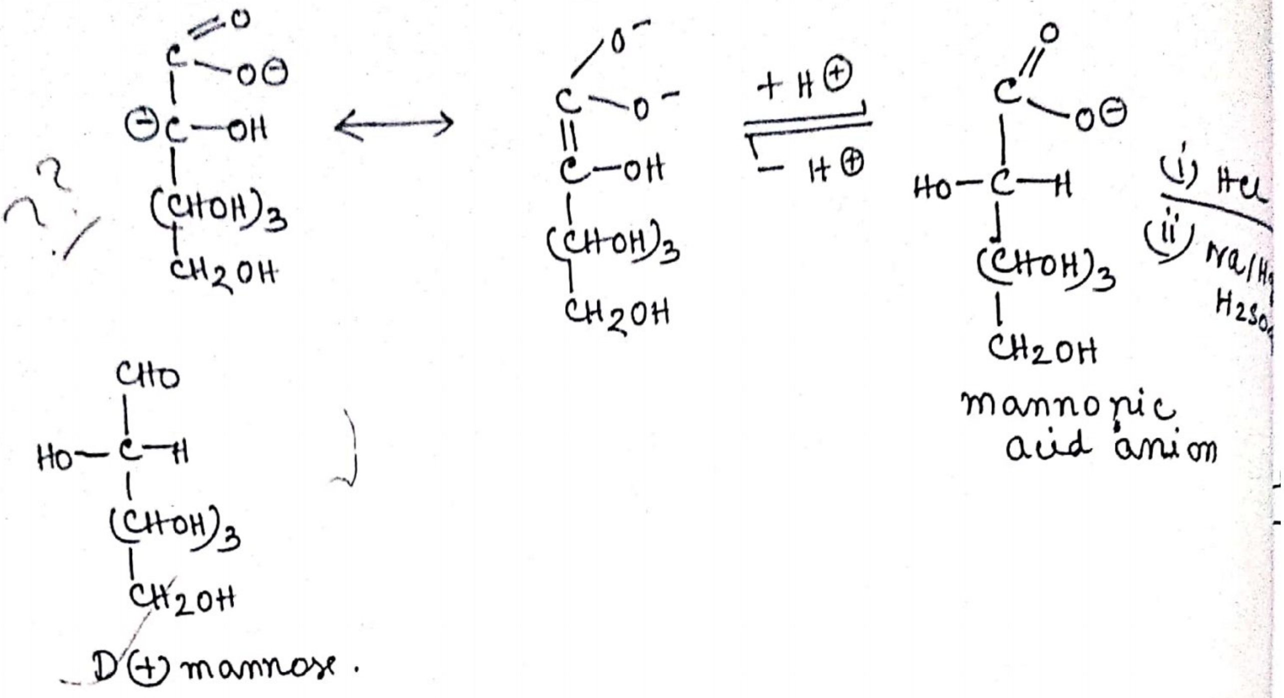


Epimerisation

Fischer changed an aldose into its epimer via the aldonic acid. The aldonic acid was heated with pyridine (or quinoline), 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. A probable mechanism is shown below.



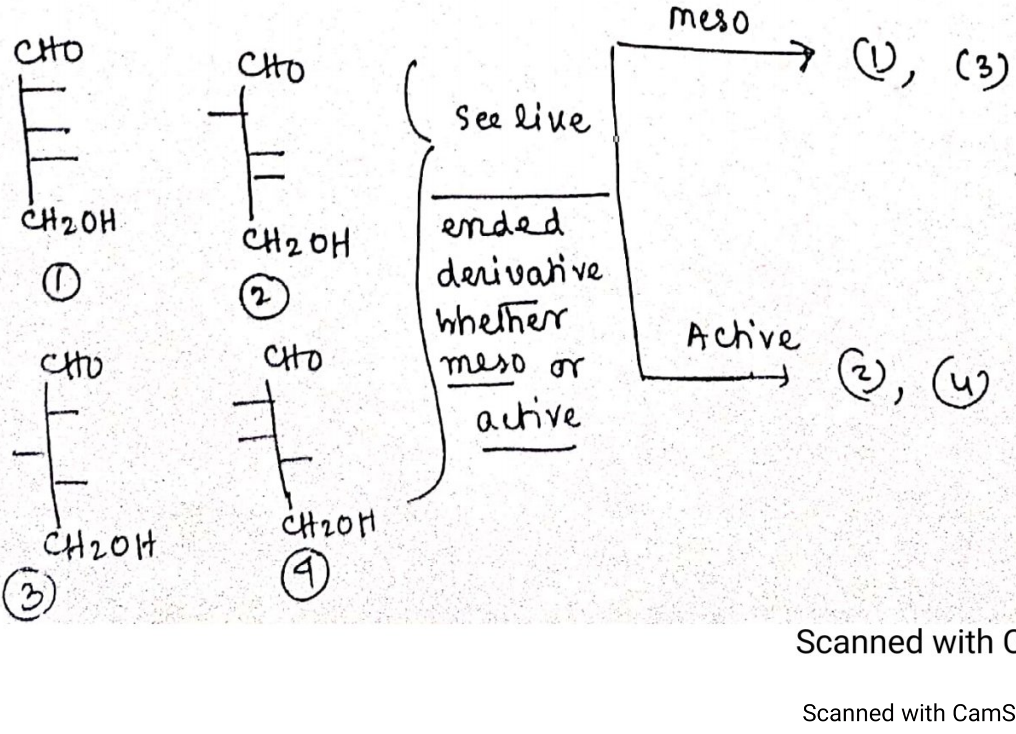
D(+) glucose



Determination of Structure:

Tetrose configuration :- See like ended derivative whether meso or not. If meso then ┼┼ and if not then Ho ┼┼ OH

Pentose Configuration



(1), (3)

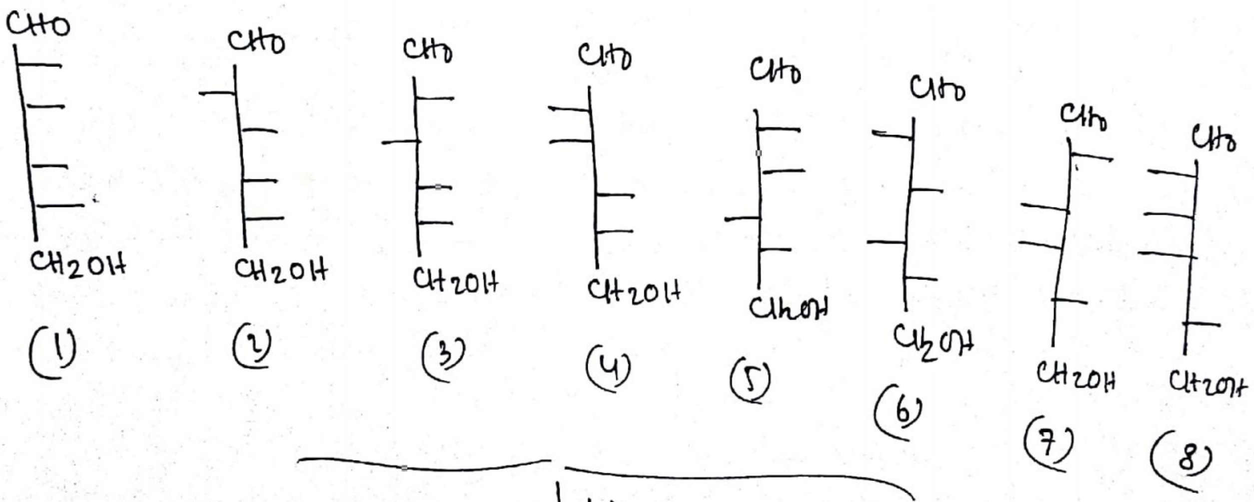
(2),(4)

step down to aldotetrose and see the like ended derivative

- meso: (1)
- Active: (3)

- meso: (2)
- Active: (4)

Hexose Configuration



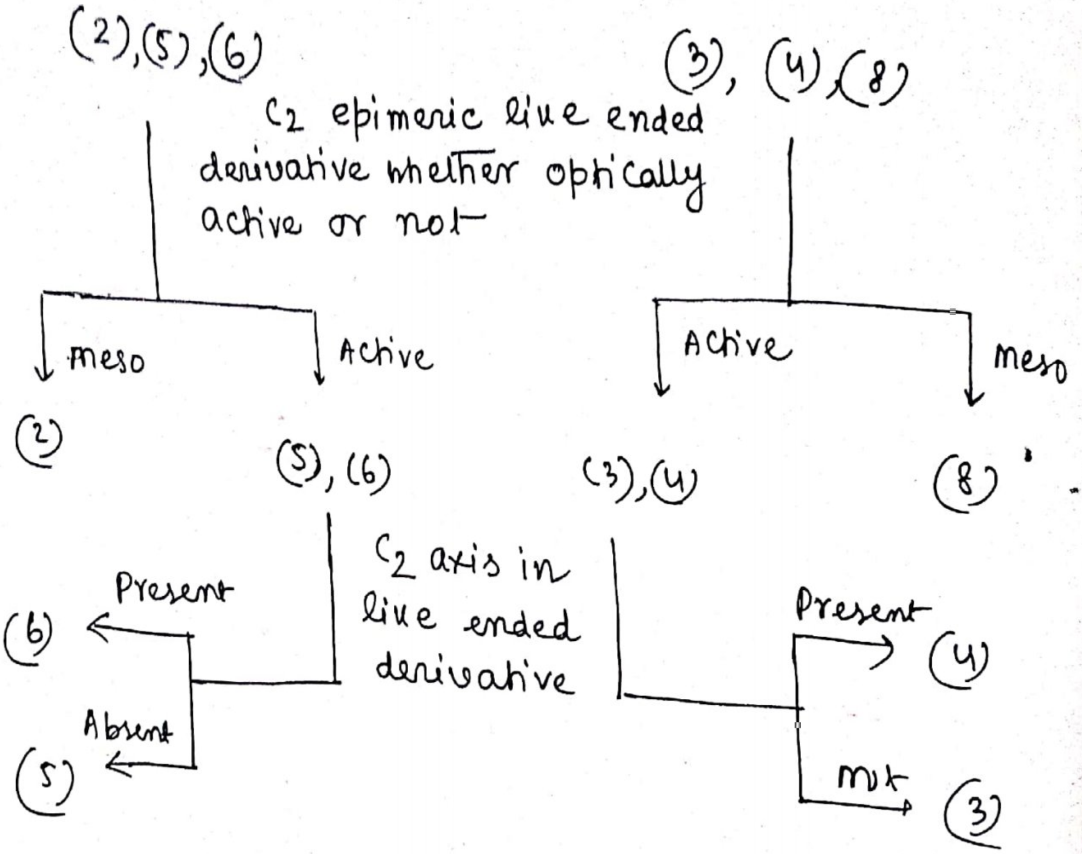
Like ended derivative

- meso: 1, 7
- Active: 2, 3, 4, 5, 6, 8

Step down to Aldopentose ~~deriva~~ and then see whether

- meso: (1)
- Active: (7)

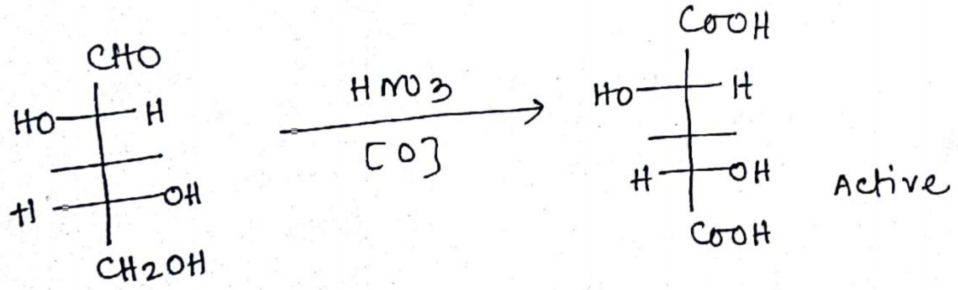
- meso: 2, 5, 6
- Active: 3, 4, 8


(2),(5),(6)
(3), (4),(8)
C_2 epimeric line ended derivative whether optically active or not
meso
Active
Active
meso
(2)
(5), (6)
(3),(4)
(8)
C_2 axis in line ended derivative
Present
(6)
Absent
(5)
Present
(4)
not
(3)

Configuration of D(+) Glucose: The Fischer's Proof

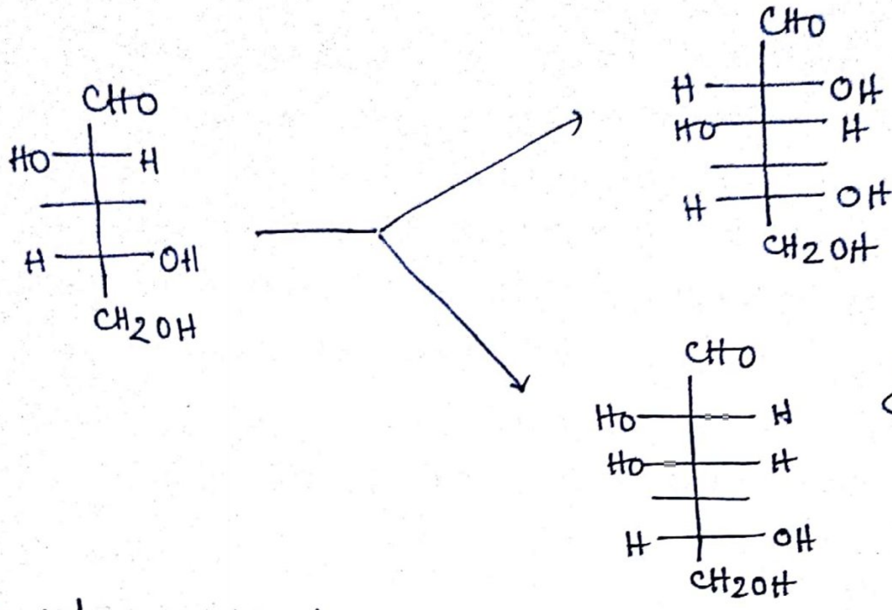
(+) Glucose was known to be an aldohexose; but as an aldohexose it could have any one of 16 possible configurations. The question was:- which configuration did it have? In 1888 Emil Fischer set out to find the answer to that question, and in 1891 announced the completion of a most remarkable piece of chemical research, for which he received the Nobel prize at 1902.. Let us follow Fischer's step in somewhat modified form to the configuration of D(+) glucose.

① upon oxidation by nitric acid (−) arabinose yields an optically active dicarboxylic acid. Since the −OH on the lowest chiral centre is arbitrarily placed on the right, this fact means that the −OH on the uppermost chiral centre is on the left.



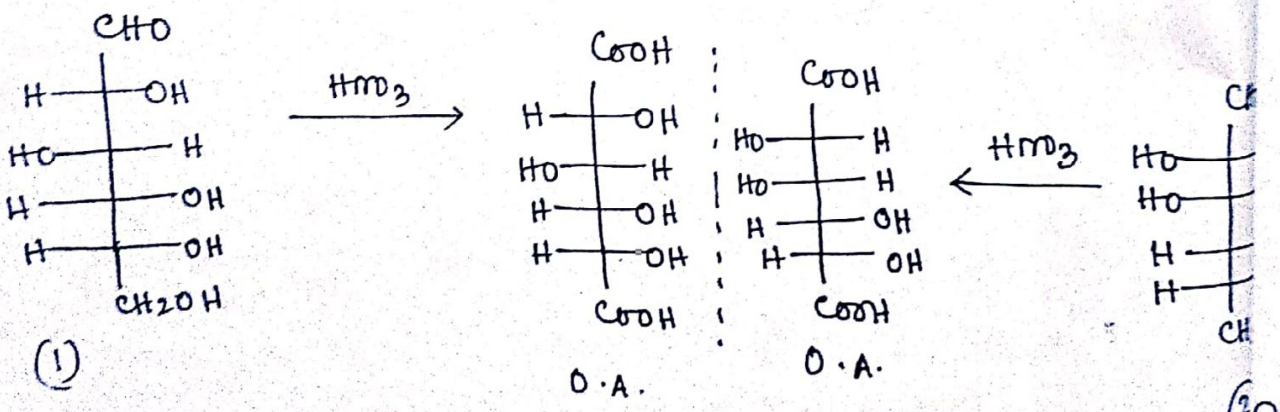
(−) Arabinose
(partial formula)

② (−) Arabinose is converted by the Kiliani Fischer synthesis into (+) glucose and (+) mannose. (+) glucose and (+) mannose give same osazone on treatment with $PhNHNH_2$; therefore (+) glucose and (+) mannose are epimers, differing only in configuration about C2 and have the same configuration about C-3, C-4 & C-5 as does (−) arabinose.

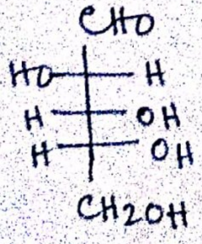


Stands for glucose and mannose.

③ upon oxidation by HNO_3, both (+) glucose and (+) mannose yield dicarboxylic acids that are optical active. This means that the —OH on C-4 is on the right as in ① and ②



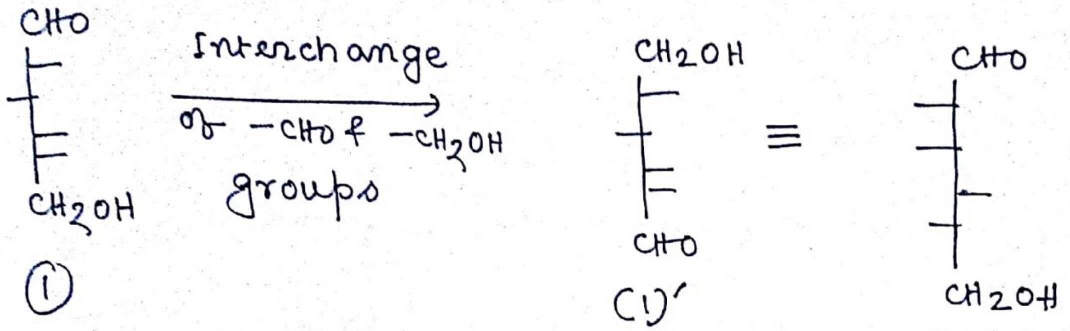
Thus (−) Arabinose must also have the —OH gr on the right and hence has configuration ③



③

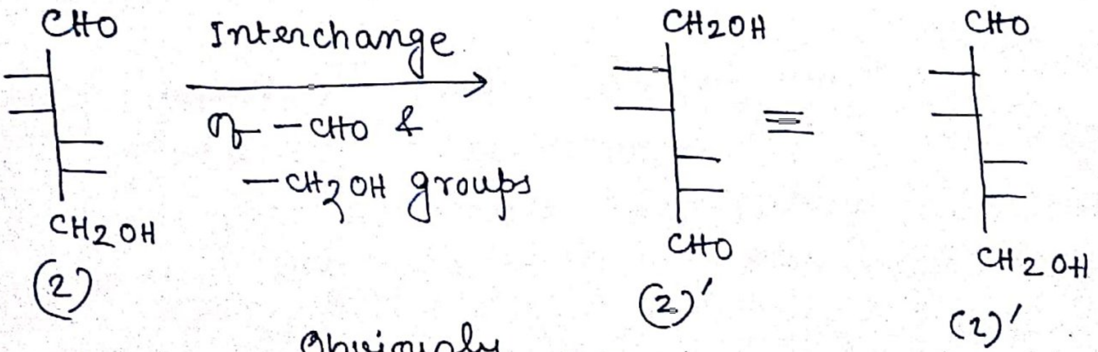
(+) Glucose and (+) mannose have configurations ① and ②, but one question remains ______ which compound has which configuration?

Now Fischer through his brilliant logic realised that if ~~A~~ the terminal — CHO and $-CH_2OH$ groups are interchanged in ① a new aldohexose will be formed.



Obviously 1 ≢ 1′

But if the terminal –CHO and $-CH_2OH$ groups are interchanged in ② the same aldohexose will be formed.



Obviously 2 ≡ 2′

Fischer carried out the end group interchange starting with (+) glucose and the product was the new aldohexose. This outcome proved that (+) glucose has the configuration ①. It was also established that ② as the configuration for (+) mannose and the new aldohexose (1)′ is (+) ~~glucose~~ gulose