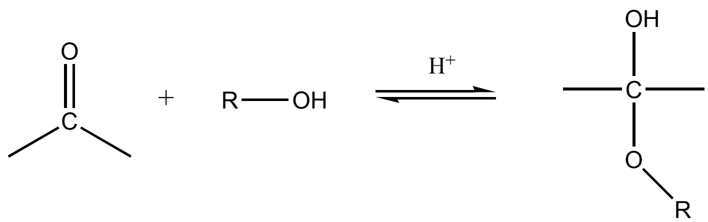
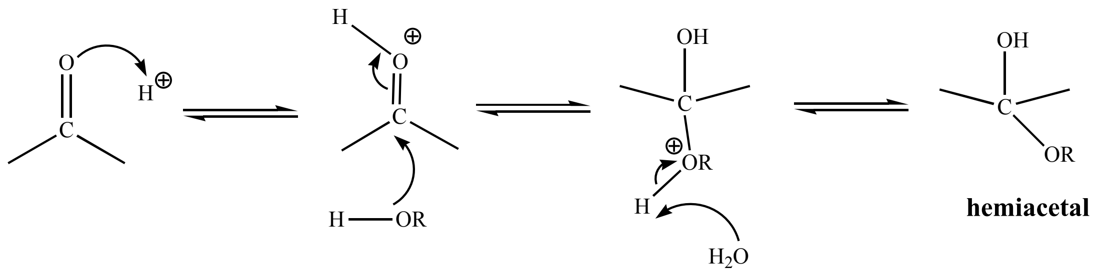
Carbohydrates- Hemiacetal Formation



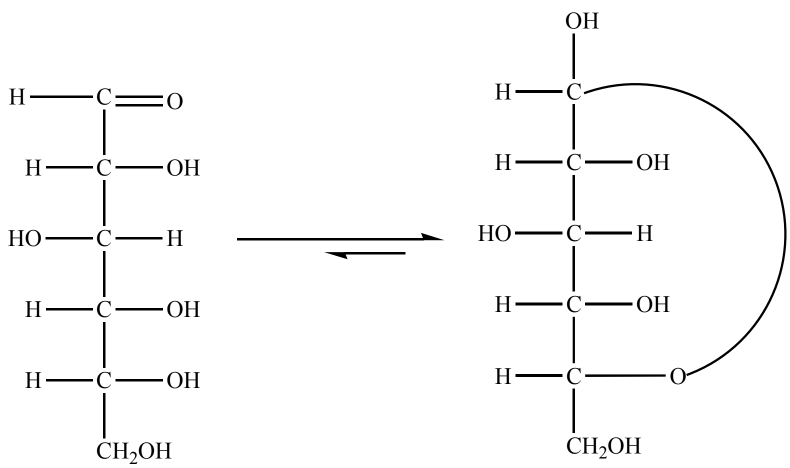
Mechanism



In nature, formations of 5- and 6-membered rings are favored, and if possible, a molecule will form such a ring when it can.

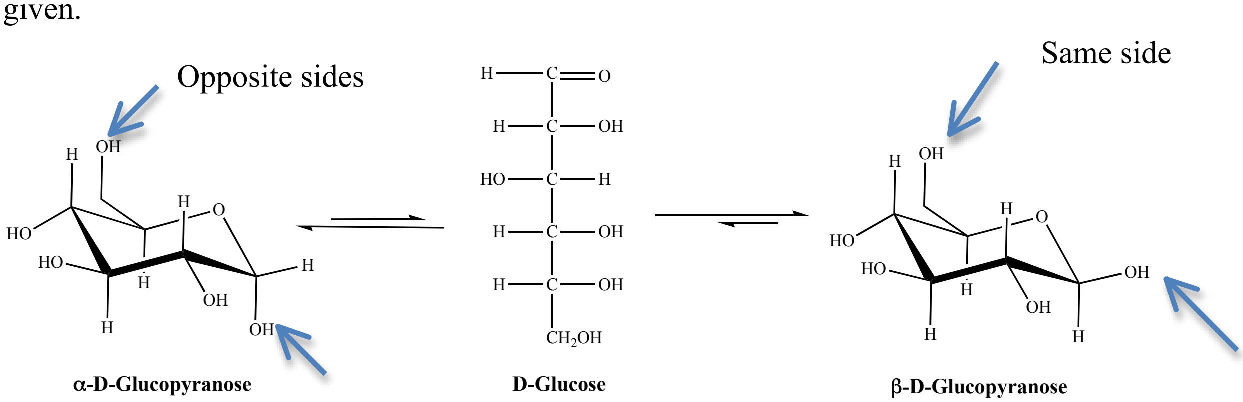
In sugars, the cyclic forms with 5-membered rings are called furanoses, and 6-member rings are called pyranoses. For most aldohexoses, the five membered furanose and six-membered pyranose can be formed. However, with D-glucose the six-membered pyranose usually predominates.

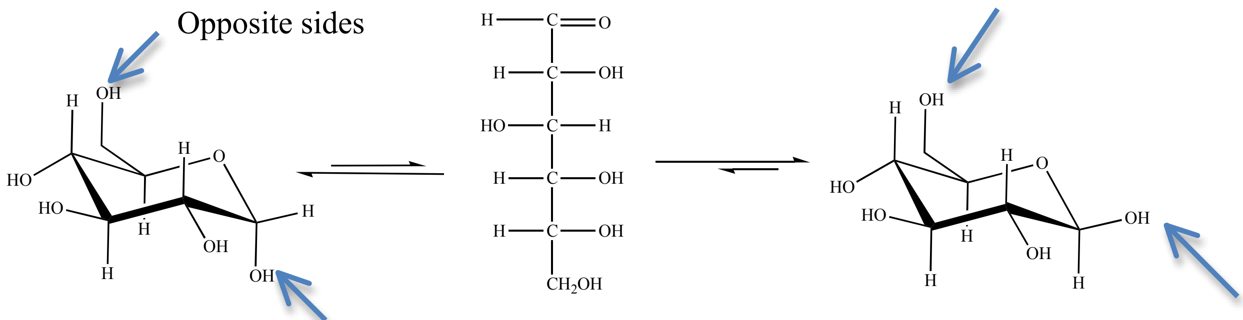
For example, glucose can react internally to form a hemiacetal (an intramolecular cyclization).



D-Glucose **hemiacetal**

The molecule exists predominantly in the cyclic form; however, it is still in equilibrium with a small amount of the acyclic form. The cyclic 6-membered rings exist in energy minimum chair forms (shown in figure below). This is also depicted in the handouts given.





α-D-Glucopyranose D-Glucose β-D-Glucopyranose

The cyclic forms are indicated in the name by combining the simple name of the sugar with “furanose” or “pyranose” to indicate the size of the ring. Therefore, glucose in its 6-membered ring form is called glucopyranose.

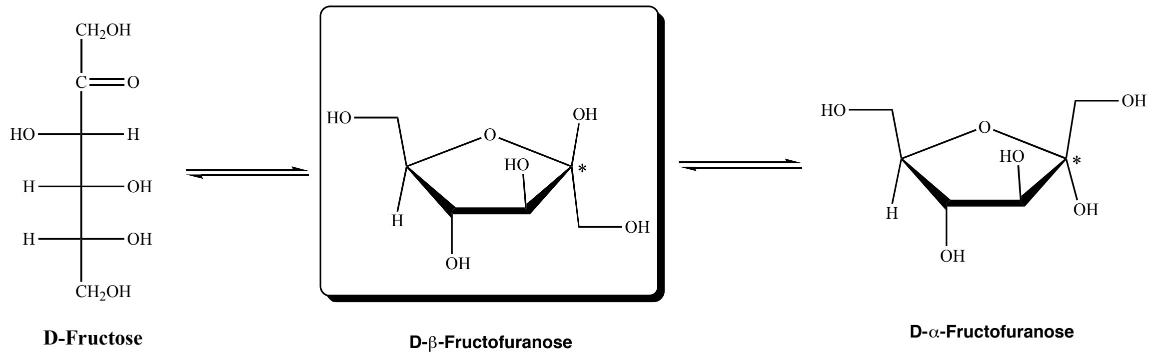
The intramolecular cyclization reaction creates a new stereogenic carbon that can be either R or S configuration, with OH group in equatorial or axial position. The terms ***α*** and ***β*** refer to position of OH at C1 relative to CH_2OH group of C6.

When the OH group attached to C1 is down relative to the CH_2OH group that is up (they are *trans* to each other), The configuration is ***α***. When they are on the same side (both are up), the configuration is ***β***.

The two stereoisomers are interconverting structural isomers called **anomers**. They differ only in stereochemistry at C1 position, which is known as the **anomeric carbon**.

The ***α*** and ***β*** anomers can equilibrate through the linear form.

Formation of a 5-membered ring is possible for D-glucose, but it exists predominantly as the 6-membered ring. Fructose, on the other hand, exists predominantly as 5-membered ring.

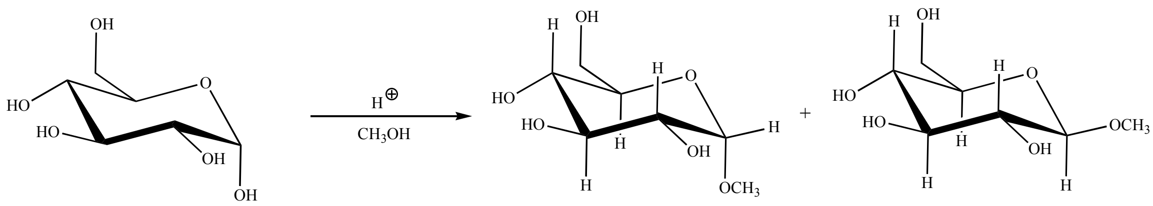


D-fructose is a ketohexose ("keto" since it contains ketone). Its cyclized form, D-fructofuranose is a hemiacetal since the anomeric carbon (marked by asterisk) has a free OH group and a OR group attached. An easy way to find the anomeric carbon is to find a carbon with 2 oxygen atoms attached directly.

*Is the fructofuranose highlighted in box an **α** or **β** sugar?*

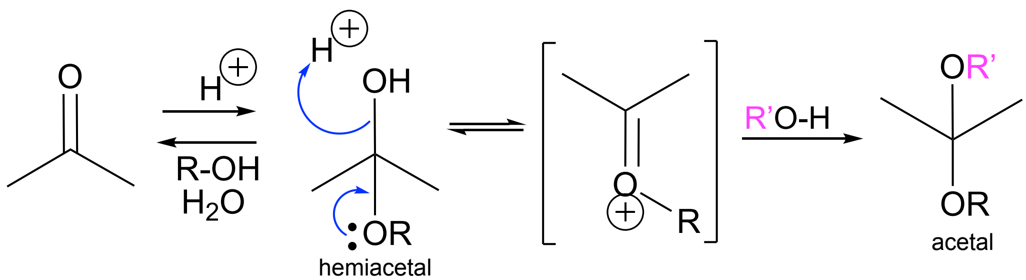
Answer: It is ***β***. The rule is to find the CH_2OH group (not on the anomeric carbon) and the OH substituent of the anomeric carbon, and see of they are on the same or opposite side. Since the OH group and the CH_2OH group are on the **same** side as each other, the ring is ***β***.

Acetal formation

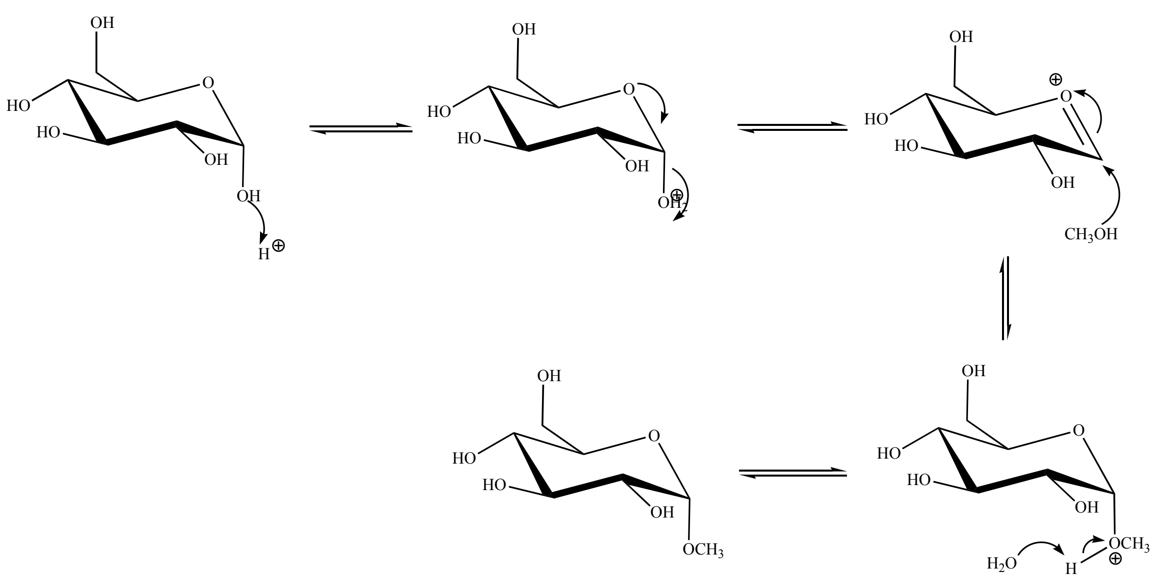


α-D-Glucopyranose α-D-Glucopyranoside (favored) β-D-Glucopyranoside (minor)

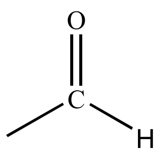
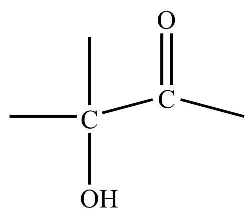
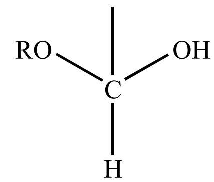
Treatment with dilute acid and alcohol converts only the OH at the anomeric position into an acetal called a glycoside. Specific glycosides are named by replacing the "ose" of the simple sugar's name with "oside". When glucopyranose is reacted, its product is called glucopyranoside.
The ***α*** anomer with the methoxy group in axial position is favored due to the anomeric effect (details about the anomeric effect is beyond the scope of this class).



Mechanism:

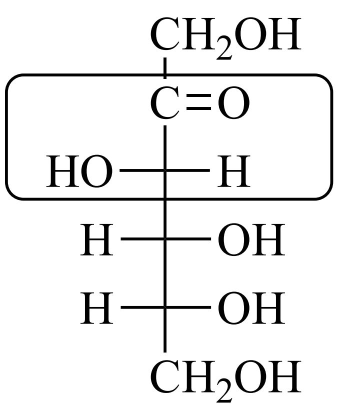


Reducing and non-reducing sugars
Usually, reducing sugars contain one of the three functional groups:

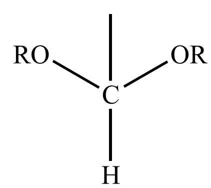




aldehyde **α-hydroxyketone** **hemiacetal**

The non-reducing sugars do NOT contain the above functionality, but may contain acetal functionality:
Example:



D-Fructose



acetal

Fructose is the sweetest sugar of all (sweetness index 180)

Is it a reducing or non-reducing sugar?
It is reducing since it contains a α-hydroxyl ketone group in open form and the cyclized form is a hemiacetal at anomeric position.