

**Course Code: CHEM3014**  
**Course Name: Organic Chemistry V**

**Unit: 4**  
**(Carbohydrate)**  
**(Lecture-Part 4)**

**For**  
**B.Sc. (Honours)**  
**Semester: VI**

**By**

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## Anomeric Effect

- An amide is more stable (less reactive) than a ketone because the  $p$  orbital of the N and the low-lying  $C=O$   $p^*$  of the carbonyl can lie parallel—they can overlap and electron density can move from nitrogen into the  $C=O$  bond, weakening  $C=O$ . (Evidence for this comes from the lower IR stretching frequency of an amide  $C=O$ , among other things.)
- Similarly,  $C-X$  bonds also have low-lying antibonding orbitals—the  $C-X$   $\sigma^*$ —so it is expected that molecule would be more stabilized if an adjacent heteroatom could donate electrons into this orbital like in case of amide. Take the generalized tetrahydropyran in the box above, for example, with  $X = Cl$ , say. This molecule is most stable if an oxygen lone pair can overlap with  $C-Cl$   $\sigma^*$ , like this.

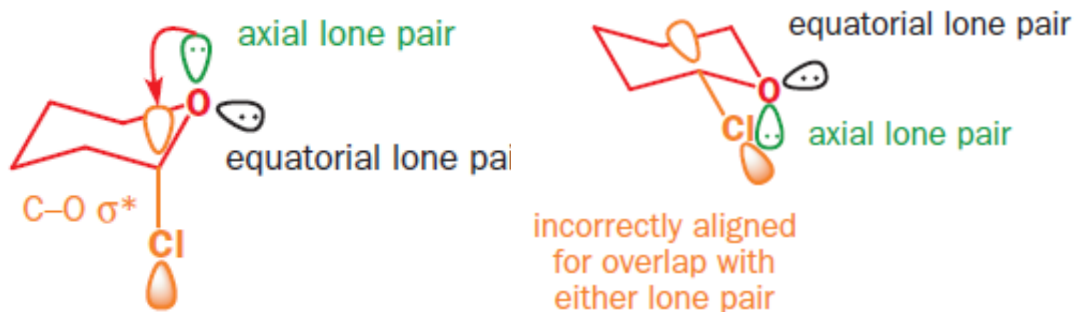
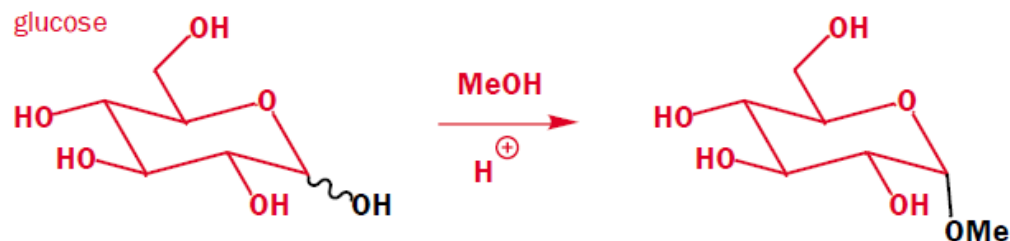


Figure 1: Explanation for Stabilization through anomeric effect.

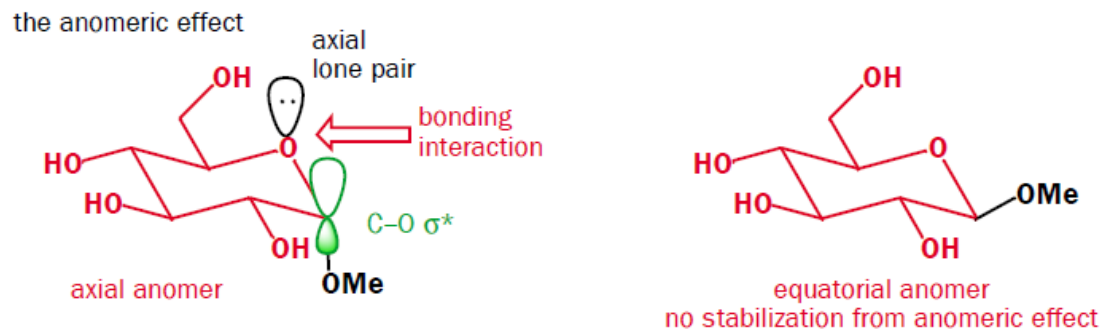


## Examples of Anomeric Effect

➤ Sugar's Shape could be fixed or locked through the formation of acetal. For example,



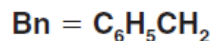
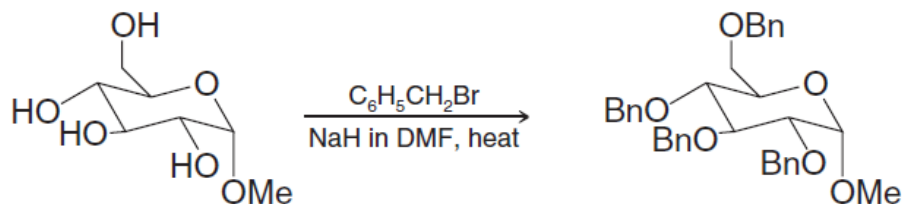
➤ Acetal formation is under thermodynamic control, so the axial compound must be the more stable. This is because of the anomeric effect—so called because this C atom is called the anomeric position and the acetal diastereoisomers are called anomers. The effect is a bonding interaction between the axial lone pair on the oxygen atom in the ring and the  $\sigma^*$  orbital of the OMe group.



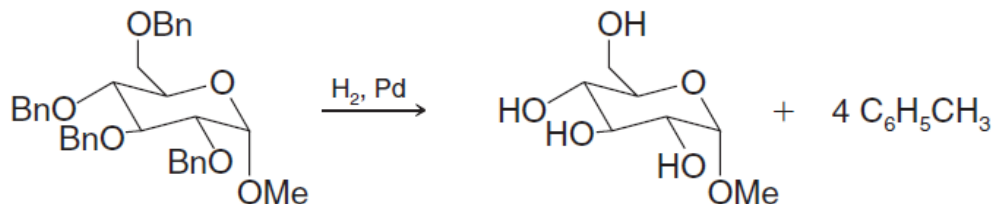
## Formation of Ethers

- *Benzyl ethers are commonly used to protect hydroxyl groups in sugars.*
- *Benzyl halides are easily introduced because they are highly reactive in  $S_N2$  reactions. Sodium or potassium hydride is typically used as the base in an aprotic solvent such as DMF or DMSO.*
- *The benzyl groups can later be easily removed by hydrogenolysis using a palladium catalyst.*

### Benzyl Ether Formation

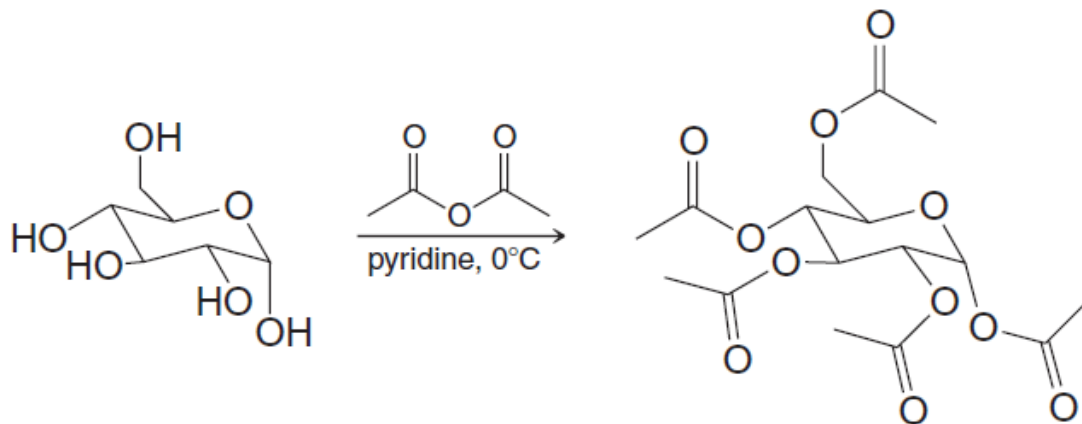


### Benzyl Ether Cleavage



## Formation of Esters

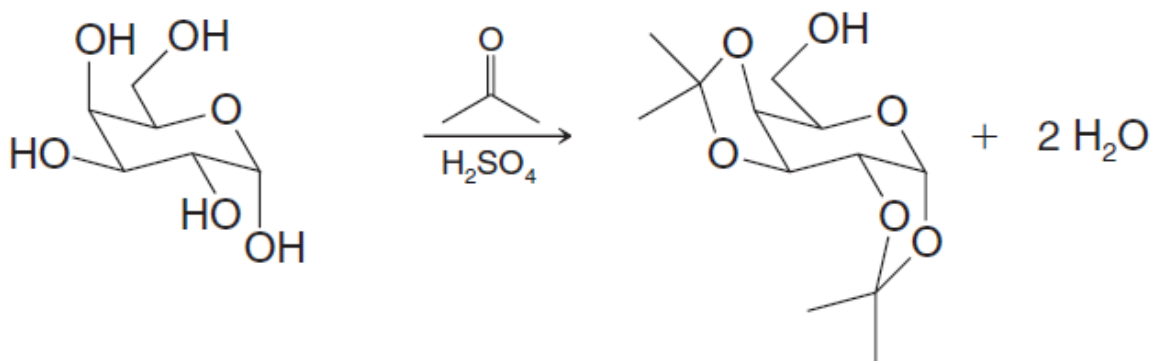
➤ Treating a monosaccharide with excess acetic anhydride and a weak base (such as pyridine or sodium acetate) converts all of the hydroxyl groups, including the anomeric hydroxyl, to ester groups.



➤ If the reaction is carried out at a low temperature (e.g., 0°C), the reaction occurs stereospecifically; the  $\alpha$  anomer gives the  $\alpha$ -acetate and the  $\beta$  anomer gives the  $\beta$ -acetate.

## Formation of Cyclic Acetals

- If the 1,2-diol is attached to a ring, as in a monosaccharide, formation of the cyclic acetals occurs only when the vicinal hydroxyl groups are *cis* to each other.
- For example,  $\alpha$ -D-galactopyranose reacts with acetone in the following way:



- Cyclic acetals are commonly used to protect vicinal *cis* hydroxyl groups of a sugar while reactions are carried out on other parts of the molecule.
- When acetals such as these are formed from acetone, they are called **acetonides**.

## ***Oxidation Reactions of Monosaccharides***

➤ *The following oxidation reactions would be discussed:*

(a) Reaction with Bromine Water: Formation of **Aldonic acids**

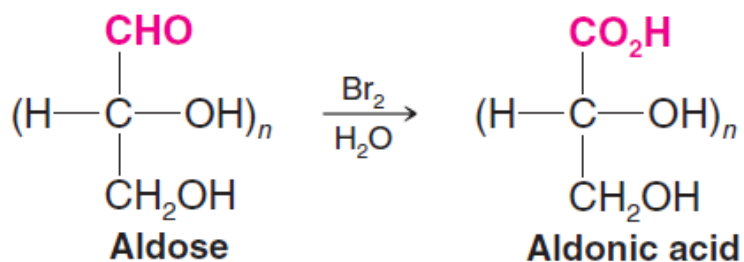
(b) Nitric Acid Oxidation: Formation of **Aldaric Acids**

(c) Periodate Oxidations: Oxidative Cleavage of Polyhydroxy Compounds



## Reaction with Bromine Water: Formation of Aldonic acids

➤ Bromine water is a general reagent that selectively oxidizes the CHO group to a CO<sub>2</sub>H group, thus converting an aldose to an **aldonic acid**.



➤ Bromine water specifically oxidizes the  $\beta$ -anomer, and the initial product that forms is a  **$\delta$ -aldonolactone**. This compound may then hydrolyze to an aldonic acid, and the aldonic acid may undergo a subsequent ring closure to form a  **$\gamma$ -aldonolactone**.

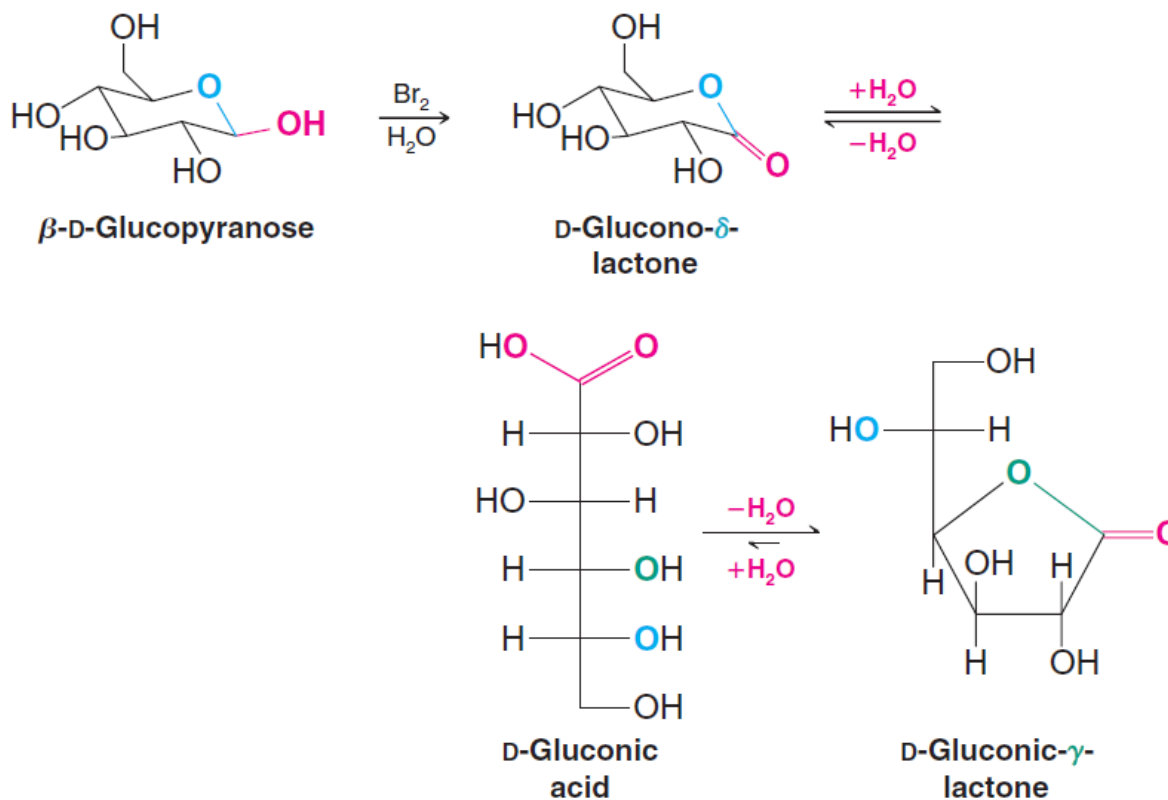
➤



## Reaction with Bromine Water: Formation of Aldonic acids

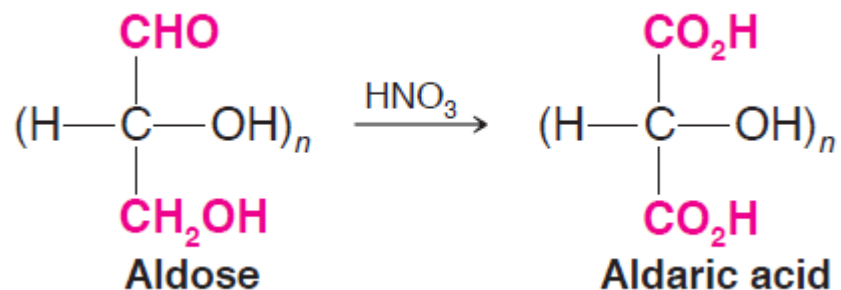
### ➤ Mechanism of oxidation using bromine water:

Bromine water specifically oxidizes the  $\beta$ -anomer, and the initial product that forms is a  $\delta$ -aldonolactone. This compound may then hydrolyze to an aldonic acid, and the aldonic acid may undergo a subsequent ring closure to form a  $\gamma$ -aldonolactone.



## Oxidation with Nitric Acid

➤ Dilute nitric acid—a stronger oxidizing agent than bromine water—oxidizes both the CHO group and the terminal CH<sub>2</sub>OH group of an aldose to CO<sub>2</sub>H groups, forming dicarboxylic acids are known as **aldaric acids**.



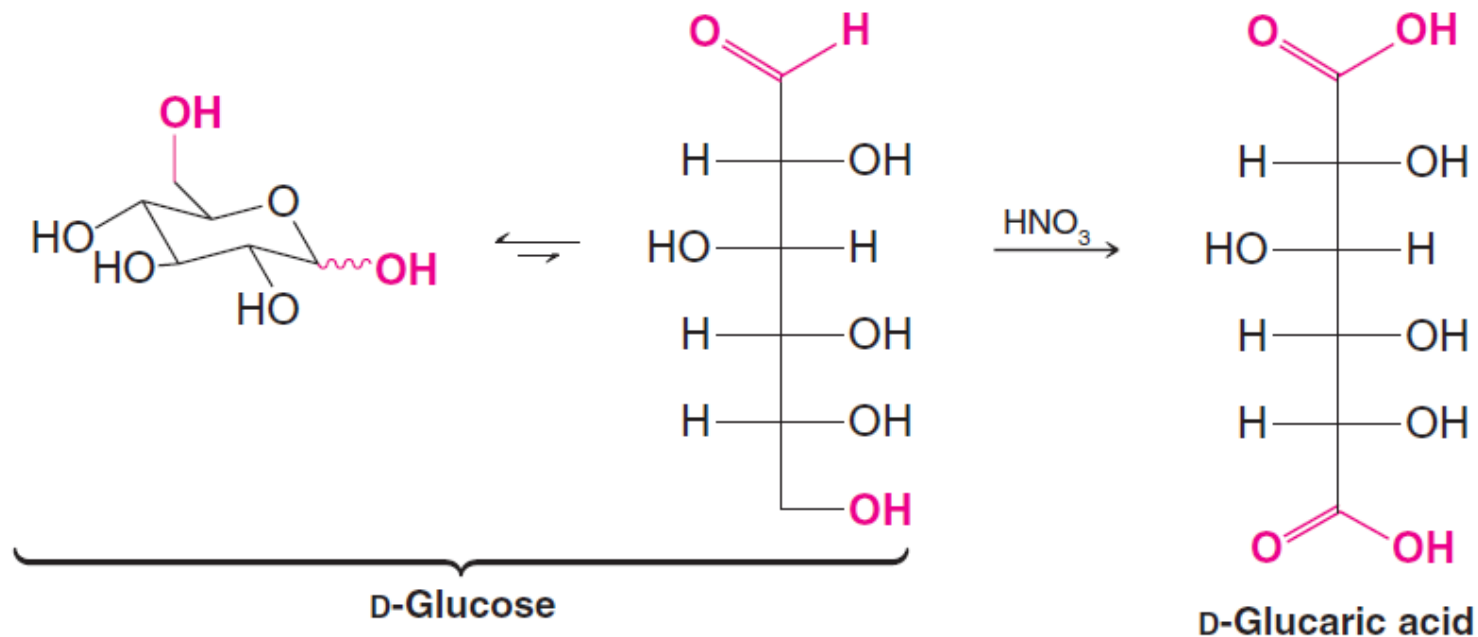
➤ It is not known whether a lactone is an intermediate in the oxidation of an aldose to an aldaric acid; however, aldaric acids form  $\gamma$ - and  $\delta$ -lactones readily.

➤ **Important to remember:**

Bromine water is a general reagent that **selectively oxidizes the CHO group** to a CO<sub>2</sub>H group, thus converting an aldose to an **aldonic acid** whereas Dilute nitric acid—a stronger oxidizing agent than bromine water—oxidizes **both the CHO group and the terminal CH<sub>2</sub>OH group** of an aldose to CO<sub>2</sub>H.

## Example of oxidation with Nitric Acid

➤ Glucose undergoes oxidation using nitric acid to form glucaric acid.



## Assignments

- Question 1: Write the open-chain structure for the aldaric acid (mannaric acid) that would be obtained by nitric acid oxidation of D-mannose.
- Question 2: Would you expect D-glucaric acid to be optically active?
- Question 3: What aldaric acid would you expect to obtain from D-erythrose?
- Question 4: D-Glucaric acid undergoes lactonization to yield two different  $\gamma$ -lactones. What are their structures?



## References

➤ *Student may also consult following study materials and books:*

1. *Chapter 22, Organic Chemistry (10<sup>th</sup> edition); Publisher: John Wiley & Sons, Inc. Authors: T. W. G. Solomons and C. B. Fryhle.*
2. *Chapter 16, 'Organic Chemistry'; Publisher: Oxford University Press; 2nd edition; Authors: Jonathan Clayden , Nick Greeves , Stuart Warren.*

*Rest of the topics of this unit will be discussed in next part of the lecture.*

***Stay Happy, Healthy and Safe!***

