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Assignment No: 02

Assignment Topic: General Method for Cyanohydrin Formation

Subject: Biochemistry

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Assignment Topic: General Mechanism for Cyanohydrin Formation

Aldehydes and ketones:

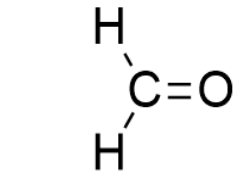
Definition of Aldehydes and ketones:

These are organic compounds containing carbonyl group (C=O) are called carbonyl compounds. Organic compound, any of a large class of chemical compounds in which one or more atoms of carbon are covalently linked to atoms of other elements, most commonly hydrogen, oxygen, or nitrogen. The few carbon-containing compounds not classified as organic include carbides, carbonates, and cyanides

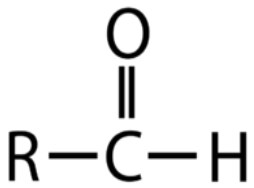
Aldehydes:

In aldehydes, the carbonyl group is bonded to at least one hydrogen atom. Its general formula is (RCHO).

For Example:



Formaldehyde

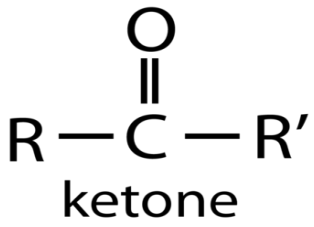


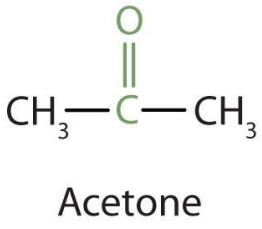
aldehyde

Ketone:

In ketones the carbonyl id bonded to two carbon atoms .Its general formula is (RCOR). The general formula of aldehydes and ketones is CnH2nO.

For Example:





Nucleophilic Addition Reactions of Aldehyde and Ketone:

Introduction:

Aldehydes and ketones undergo nucleophilic addition reactions, which are a reaction that occurs since the oxygen atom now has a negative charge; it can pick up a hydrogen ion from solution, forming alcohol on the carbonyl carbon.

Reasoning:

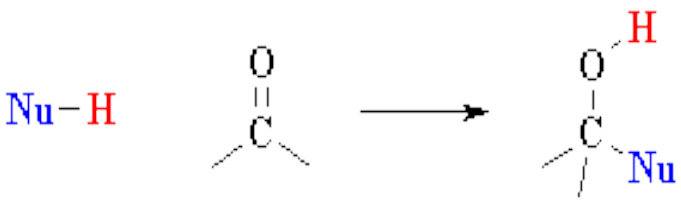
Carbonyl compounds have polarity. So they can be easily attacked by a Nucleophile or by the electrophile to give an addition product. These addition reactions can be catalyzed by both acids and bases.

Nucleophile Definition:

A nucleophile is a chemical species that donates an electron pair to form a chemical bond in relation to a reaction. All molecules or ions with a free pair of electrons or at least one pi bond can act as nucleophiles.

Or

Nucleophilic addition reactions are an important class of reactions that allow the interconversion of C=O into a range of important functional groups.



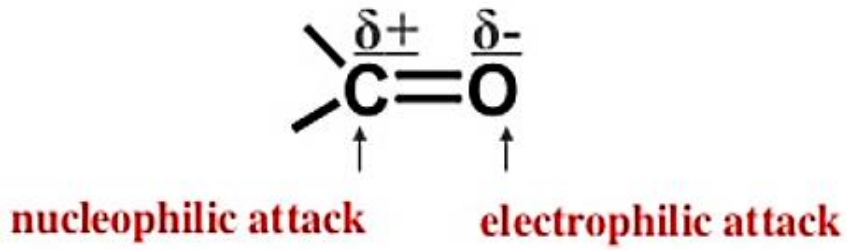
For Example:

Examples of nucleophiles are the halogen anions (I-, Cl-, Br-), the hydroxide ion (OH-), the cyanide ion (CN-), ammonia (NH3), and water.

Nucleophilic Addition Reaction:

- The carbonyl groups in aldehydes and ketones are polarized because of the difference in the electronegativity of carbon and oxygen.
- The carbon atom carries a partial positive charge while oxygen atom carries a partial negative charge.
- Aldehydes and ketones are susceptible to attack both by nucleophiles at the carbonyl carbon atom and by electrophiles at the oxygen atom.

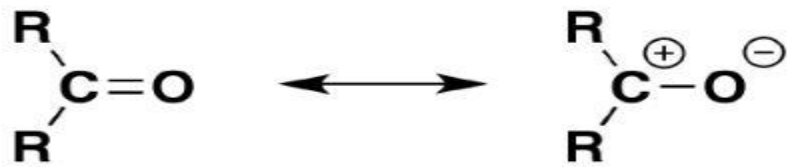
For Example:



Events in Nucleophilic Reaction:

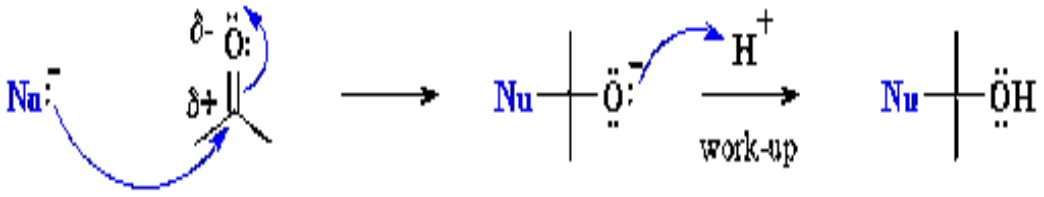
There are three fundamental events in a nucleophilic addition reaction:

1. Formation of the news bond between the nucleophile, Nu, to the electrophilic C of the C=O group.
2. Breaking of the p bond to the O resulting in the formation of an intermediate alkoxide.
3. Protonation of the intermediate alkoxide to give an alcohol derivative.



General Mechanism of Nucleophilic Addition reaction under basic Medium:

A bas catalyzed addition reaction takes place with a strong nucleophile. A general example is given below:



Nucleophilic Addition Reaction of HCN Cyanohydrin Formation:

Cyanohydrin Reaction:

A cyanohydrin reaction is an organic chemical reaction by an aldehyde or ketone with a cyanide anion or a nitrile to form a cyanohydrin. This nucleophilic addition is a reversible reaction but with aliphatic carbonyl compounds equilibrium is in favor of the reaction products.

General Properties of Cyanohydrin:

Here are the following properties for the formation of the Cyanohydrin:

- This cyanohydrin, also known as glycol nitrile, is a colorless liquid with a cyanide odor.
- It is soluble in water, alcohol, and diethyl ether.
- Equimolar amounts of 37% formaldehyde and aqueous hydrogen cyanide mixed with a sodium hydroxide catalyst at 2C for one hour give formaldehyde cyanohydrin in 79.5% yield.
- It is usually poisonous hence it is used in liquid form under the catalysts such as NaCN+ HCL.

General Formation of Cyanohydrin:

Cyanohydrins have the structural formula of R2C (OH) CN. The "R" on the formula represents an alkyl, aryl, or hydrogen. To form a cyanohydrin, a hydrogen cyanide adds reversibly to the carbonyl group of an organic compound thus forming a hydroxyalkanenitrile adducts (commonly known and called as cyanohydrins).

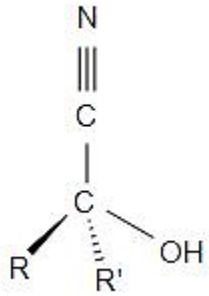


Fig 1.0 General structure of a cyanohydrin

Addition of Cyanohydrins:

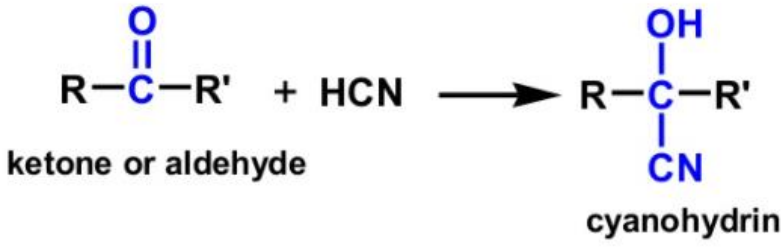
Cyanohydrins may be formed by the use of liquid HCN with a catalytic amount of sodium cyanide or potassium cyanide.

In aldehydes:

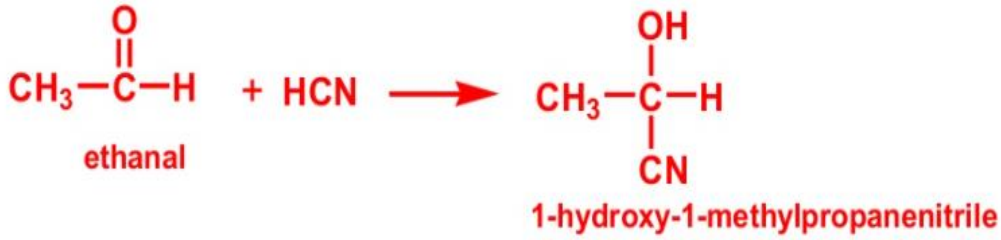
Hydrogen cyanide adds across the carbon-oxygen double bond in aldehydes and ketones to produce compounds known as hydroxynitriles.

For example: with ethanol (an aldehyde) you get 2-hydroxypropanenitrile.

Reaction:

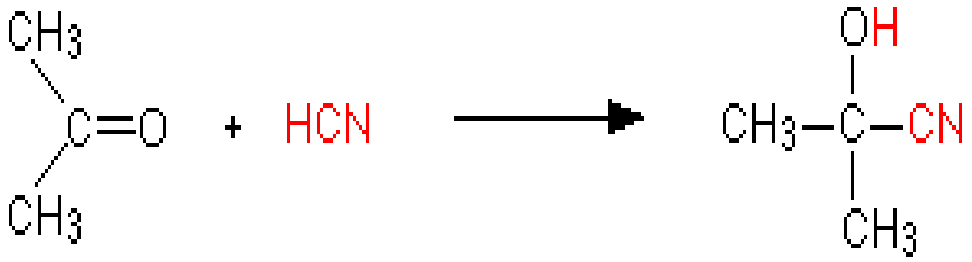


Example:



In ketones:

When the hydrogen cyanide are added into the ketones such as with propanone (a ketone) you get 2-hydroxy-2-methylpropanenitrile:



Precautions for this Reaction:

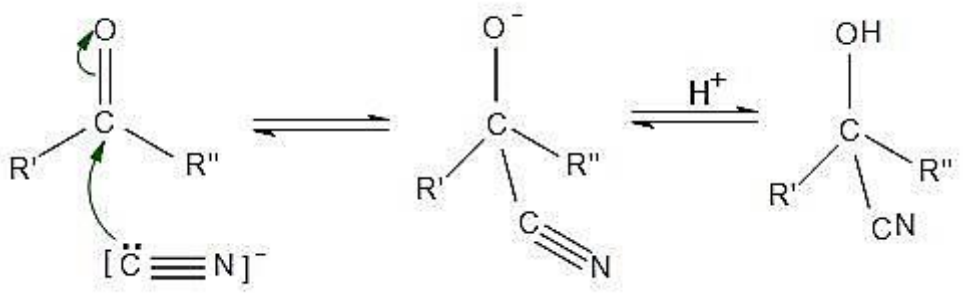
Here are the following precautions that should be taken in order to proceed to the formation of the cyanohydrin:

- The reaction isn't normally done using hydrogen cyanide itself, because this is an extremely poisonous gas.
- Instead, the aldehyde or ketone is mixed with a solution of sodium or potassium cyanide in water to which a little sulphuric acid has been added.
- The pH of the solution is adjusted to about 4 - 5, because this gives the fastest reaction.
- The solution will contain hydrogen cyanide (from the reaction between the sodium or potassium cyanide and the sulphuric acid), but still contains some free cyanide ions.
- This is important for the mechanism.

Mechanism for the Formation of Cyanohydrin:

Nucleophile attack is took place by the negatively charged carbon of cyanide ion at the carbonyl carbon of the aldehyde and ketone. Hydrogen cyanide itself is not a strong nucleophile and does not ionize to form cyanide to a significant extent. Thus, a source of cyanide ion such as NaCN or KCN is used .

The mechanism of this reaction is as follows:



The hydroxide ion liberated in the formation of cyanohydrin reacts with dissociated hydrogen cyanide and produces more cyanide ions, which in turn react with more carbonyl compound to form more cyanohydrins.

Conclusion:

The reactions also form part of the pharmaceutical preparation processes in industries and academia. The reaction helps in the formation of new complex organic chemicals. Therefore, nucleophilic addition reactions are central to organic chemistry.

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