5.7: NUCLEOPHILIC ADDITION OF HCN - CYANOHYDRIN FORMATION

OBJECTIVES

After completing this section, you should be able to

1. write an equation to describe the formation of a cyanohydrin from an aldehyde or ketone.
2. identify the cyanohydrin formed from the reaction of a given aldehyde or ketone with hydrogen cyanide.
3. identify the aldehyde or ketone, the reagents, or both, needed to prepare a given cyanohydrin.
4. write the detailed mechanism for the addition of hydrogen cyanide to an aldehyde or ketone.

KEY TERMS

Make certain that you can define, and use in context, the key term below.

- cyanohydrin

STUDY NOTES

For successful cyanohydrin formation it is important to have free cyanide ions available to react with the ketone or aldehyde. This can be achieved by using a salt (e.g. KCN or NaCN) or a silylated (e.g. Me_3SiCN) form of cyanide under acidic conditions or by using HCN with some base added to produce the needed CN^- nucleophile.

Hydrogen cyanide (HC≡N), adds reversibly to aldehydes and many ketones forming hydroxyalkanenitrile adducts commonly known and as **cyanohydrins**. Cyanohydrins have the structural formula of $R_2C(OH)CN$. The “R” on the formula represents an alkyl group, aryl group, or hydrogen.

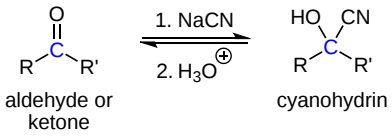
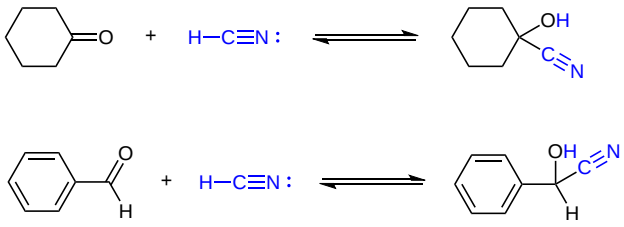


Figure 5.7.1: General Reaction of Cyanohydrin Formation

An important feature of cyanohydrin formation is that it requires a basic catalyst. Since hydrogen cyanide itself is a weak acid (pK_a = 9.25), the best results occur when a small amount of a strong base activates hydrogen cyanide by converting it to **cyanide ion (⁻C≡N)**, which can function as a carbon nucleophile. In the absence of base, the reaction does not proceed, or is at best very slow. Cyanohydrin formation is weakly exothermic, and is favored for aldehydes, and unhindered cyclic and methyl ketones.

EXAMPLE



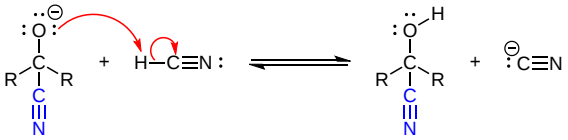
Hydrogen cyanide (HCN) is hazardous to handle because it is highly toxic. Therefore in many syntheses of cyanohydrins, HCN is created *in situ* by adding a strong acid to a mixture of sodium cyanide and the carbonyl compound, so that hydrogen cyanide is generated *in situ*. The amount of acid added should be insufficient to consume all the cyanide ion, therefore sufficiently alkaline conditions are maintained for rapid addition.

MECHANISM OF CYANOHYDRIN FORMATION

In the first step of the mechanism, the cyanide ion acts as a nucleophile and forms a C-C bond with the electrophillic carbonyl carbon. The two electrons in the carbonyl pi bond are pushed on to the electronegative oxygen forming a tetrahedral alkoxide ion intermediate. In the second step, the alkoxide ion is protonated by HCN which regenerates the cyanide ion.

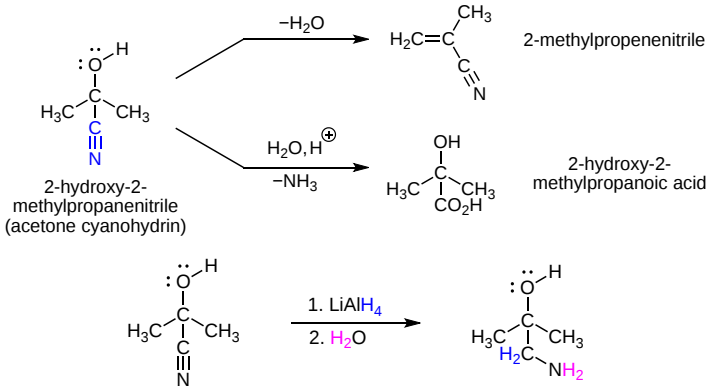
STEP 1: NUCLEOPHILIC ATTACK

STEP 2: PROTONATION



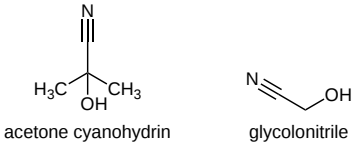
FURTHER CHEMISTRY OF CYANOHYDRINS

Cyanohydrin functional groups often prove useful because of the further chemistry that can be carried out due to the presence of a hydroxyl and a nitrile functionality. In particular, dehydration can convert the hydroxyl group into an alkene (Section 17.6). The nitrile can be converted into a carboxylic acid function group through reaction with a hot acidic aqueous solution (Section 20.7). Also, the nitrile can be reduced by the addition of $LiAlH_4$ to form a primary amine.



OTHER CYANOHYDRINS

Other interesting cyanohydrins are: **acetone cyanohydrin**, and **glycolonitrile**.

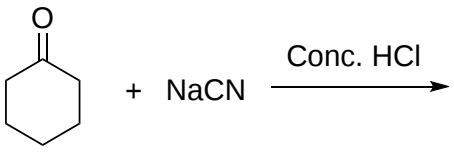


Acetone cyanohydrin has the structure, $(CH_3)_2C(OH)CN$, and is used in the production of methyl methacrylate (also known as acrylic). Glycolonitrile is an organic compound with the structural formula of $HOCH_2CN$, which is the simplest cyanohydrin that is derived by formaldehydes.

PROBLEMS

Complete the following reactions for cyanohydrins:

1)



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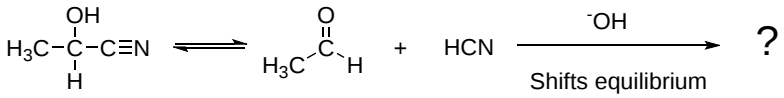
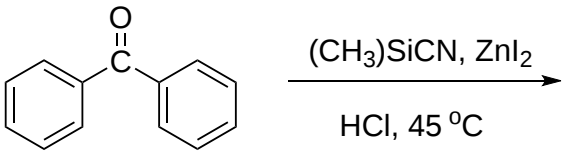


3) True or False: For a cyanohydrin to form, a *fast addition* of strong acid to cyanide salt is carried out to convert the salt into HCN.

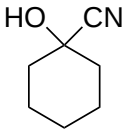
4) True or False: Cyanohydrin reactions are *irreversible*.

5) What is the product for the overall reaction?



ANSWERS

1)



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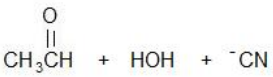

3) False, slow addition

4) False, reversible

5)