

*Notes on
Preparation and important reactions of nitro
compounds, nitriles, isonitriles*

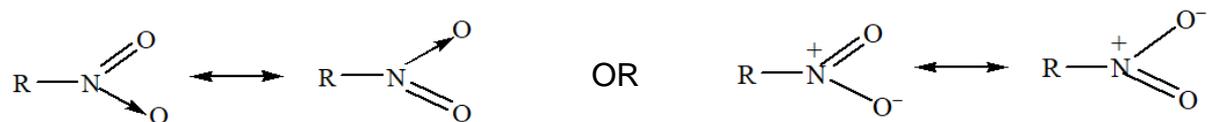


*By
Dr. Gangutri Saikia*

The structure of nitro compounds is originally written as:

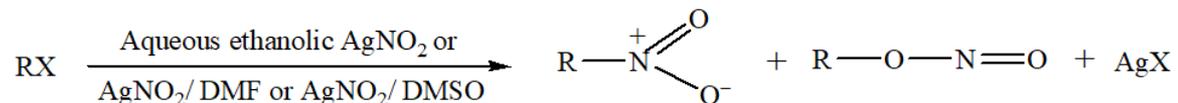
$$\text{R}-\text{N} \begin{array}{l} \text{// O} \\ \text{ \ O} \end{array}$$

They can be represented by the following resonating forms:



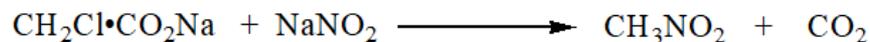
General methods of preparation:

1. From alkyl halide: By heating an alkyl halide with silver nitrite in aqueous ethanolic solution:

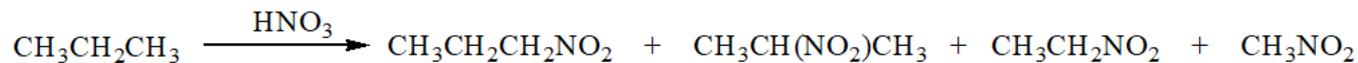
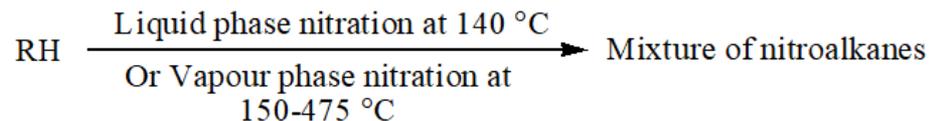


This method is only useful for the preparation of primary nitroalkane. Alkyl bromides and iodides get most satisfactory result, while chlorides react too slowly to be useful.

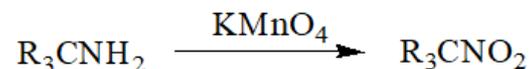
2. From sodium chloroacetate: Nitromethane may be prepared by boiling an aqueous solution of sodium nitrite with a halogeno acetic acid. This method has no value for preparing higher nitroalkane.



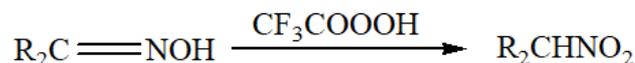
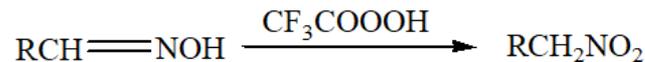
3. By nitration of alkanes: Direct nitration is an important industrial process. Two techniques are mainly involved in this process- liquid phase nitration and vapour phase nitration. In liquid phase nitration, the hydrocarbon is heated with concentrated nitric acid under pressure at 140 °C. Nitration under these conditions is always slow, and a large amount of polynitro compounds is produced. In vapour phase nitration, the hydrocarbon is heated with nitric acid or oxides of nitrogen at 150-475 °C. Vapour phase nitration is more satisfactory than liquid phase nitration.



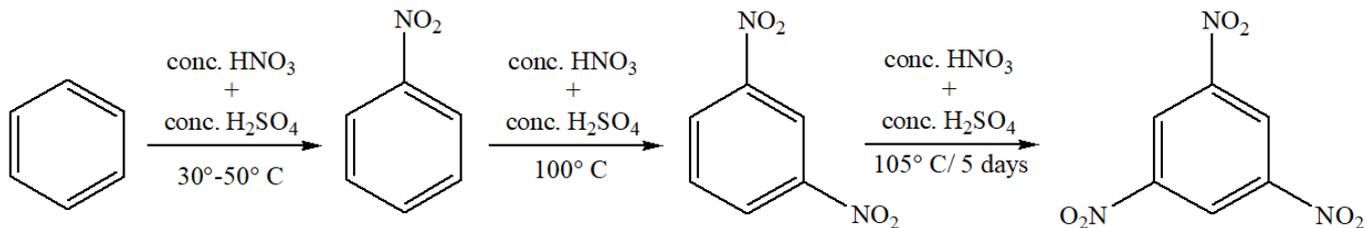
4. By oxidation of 3^o alkylamines: When 3^o alkylamines are oxidised by potassium permanganate, tertiary nitro compounds are obtained.



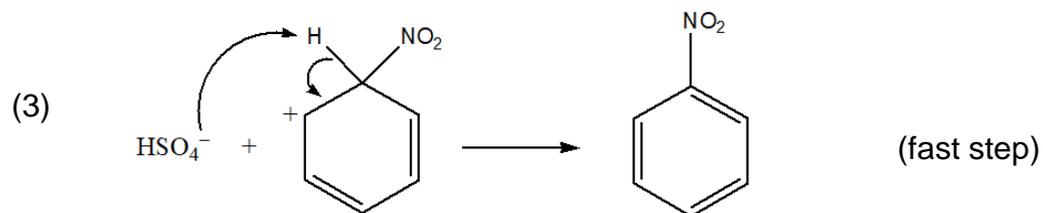
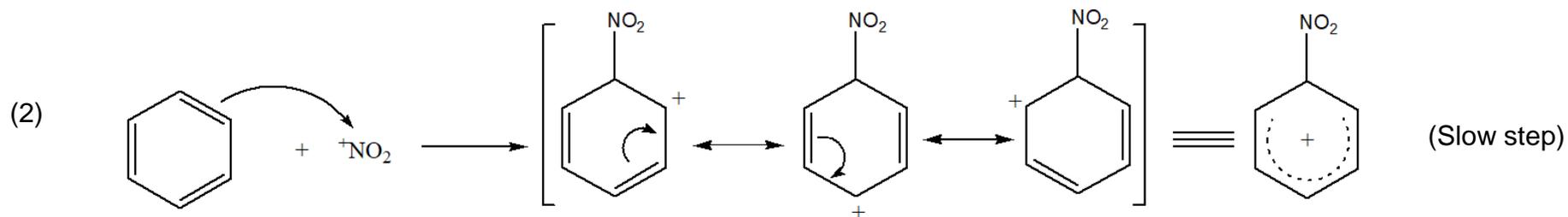
5. By oxidation of oximes: When aldoximes and ketoximes are oxidised by trifluoroacetic acid, 1^o and 2^o nitro compounds are formed, respectively.



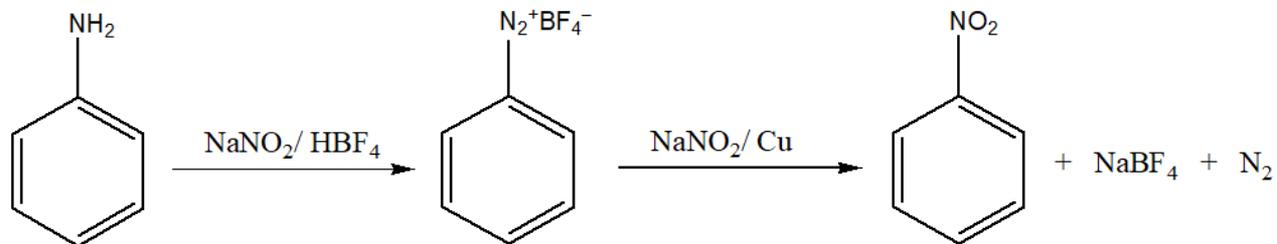
6. By nitration of aromatic compounds: Substitution of a H atom of an aromatic nucleus by a nitro group is called aromatic nitration. The reaction may be carried out with several nitrating agents such as conc. nitric acid in glacial acetic acid, nitric acid in water, conc. nitric acid in conc. sulphuric acid etc.



Mechanism:

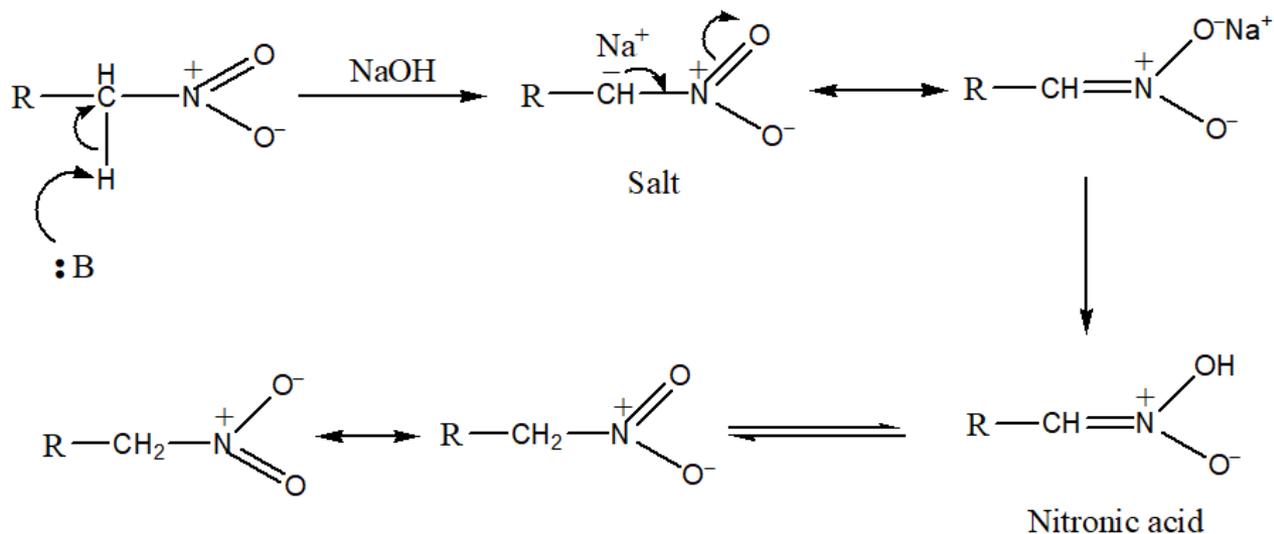


6. By arenediazonium compounds: When aromatic primary amines are diazotised with sodium nitrite and hydrogen borofluoride, thus formed arenediazonium salts are treated with copper powder and sodium nitrite to form nitroarenes.



Reactions of nitro compounds:

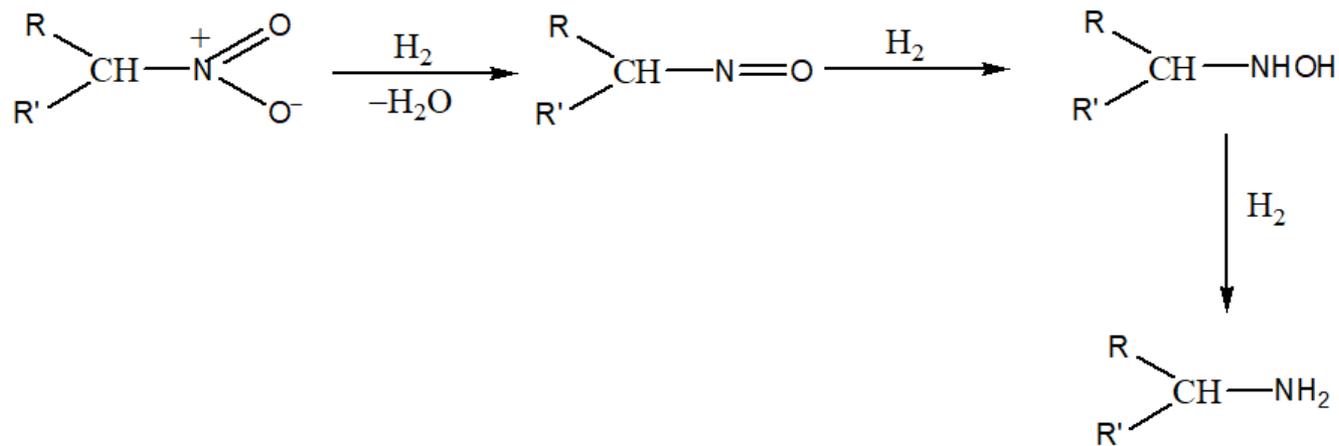
1. Salt formation reaction: Primary and secondary nitroalkanes are acidic in character due to the $-I$ effect of the nitro group. When treated with base, α -H of 1° and 2° nitroalkanes leave the species as proton, and a carbanion is formed.



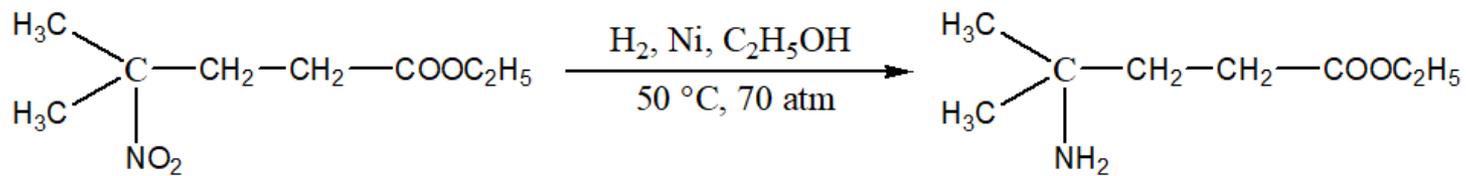
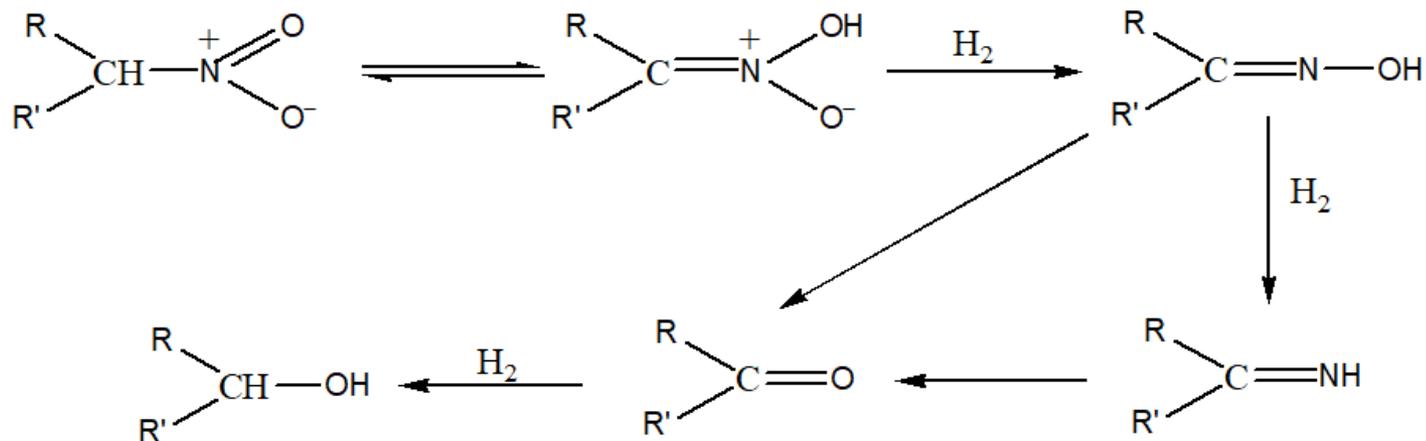
In presence of acid stronger than nitroalkane, proton is added to the salt of nitroalkane, at first nitronic acid is formed which then tautomerises to nitroalkane. The acidity of this tautomeric form is about as great as carboxylic acid. However, in equilibrium between nitro and tautomeric form, the latter remains in small amount, therefore aqueous solution of nitroalkane is slightly acidic.

2. Reduction of nitro group: Nitro group undergoes exceedingly easy reduction by many reagents. Both aromatic and aliphatic nitro groups are easy to reduce, often without affecting other functional groups. Nitro group behaves differently depending on whether it is bonded to a carbon having no hydrogen or bonded to a carbon having hydrogens. In latter case, tautomerism occurs which is reduced in different ways (**scheme II**) from those of the nitro group (**scheme I**).

Scheme I

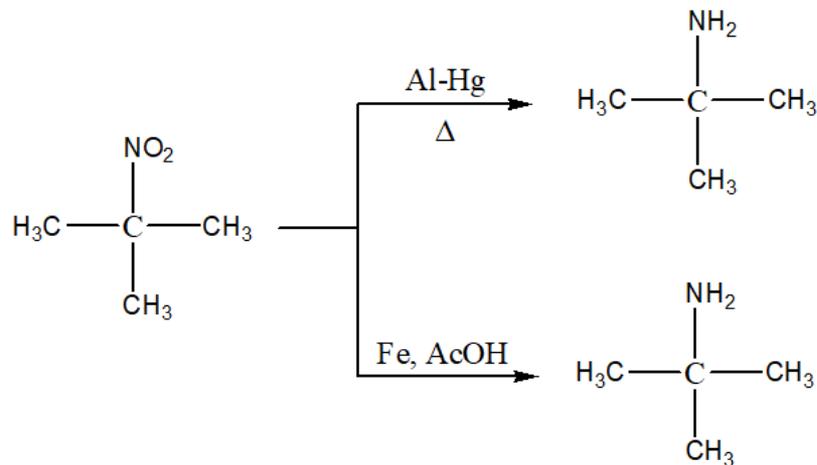


Scheme II

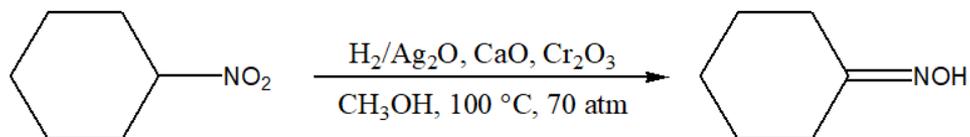
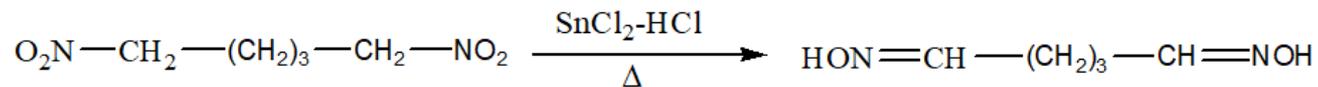


Reduction of aliphatic nitro compounds:

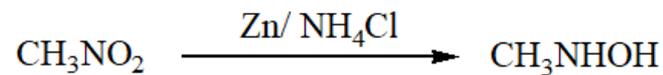
Aliphatic nitro compounds with nitro group on a tertiary carbon are reduced to amines with aluminium amalgam or iron/AcOH or catalytically.



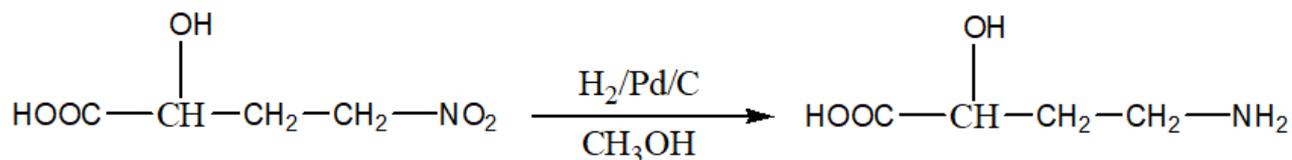
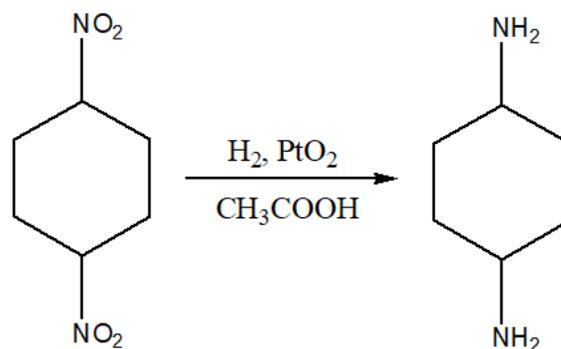
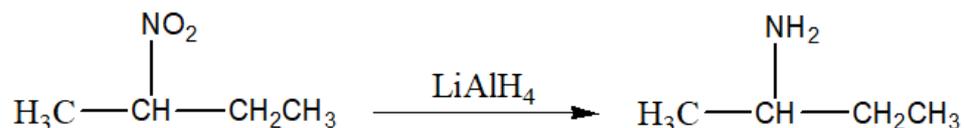
Generally primary nitro compounds are reduced to aldoximes and secondary to ketoximes by metal salts such as stannous chloride and chromous chloride. The same result is obtained by hydrogenation in presence of catalyst.



Catalytic reduction produces primary amine in acid solution, the yield with raney nickel catalyst is 90-100%. When the reduction is carried out in neutral solution, e.g., with zinc dust and ammonium chloride in aqueous or alcoholic solution, nitro compounds are converted into hydroxylamine derivatives.

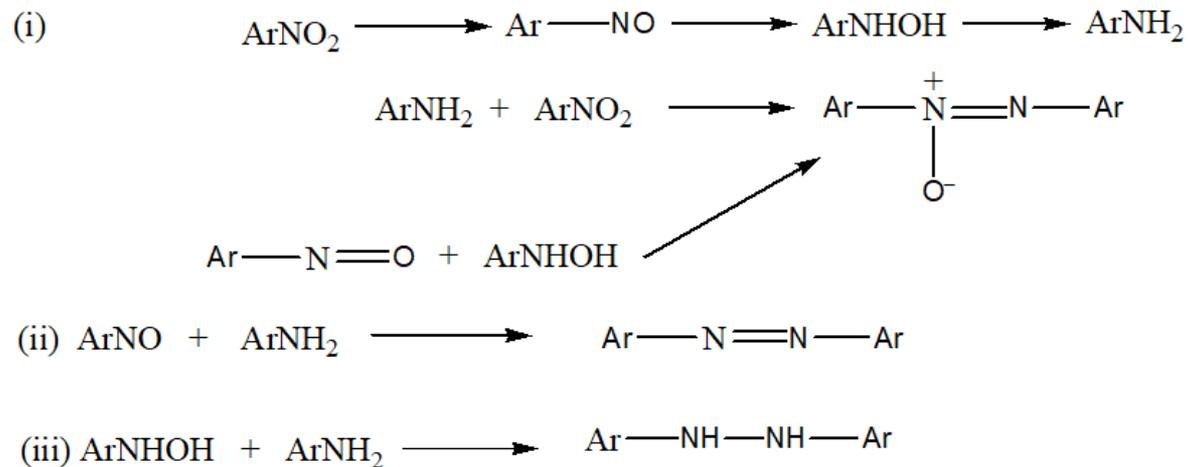


Lithium aluminium hydride and catalytic reduction with a transition metal catalyst are suitable methods for complete reduction of nitro group to give primary amines.

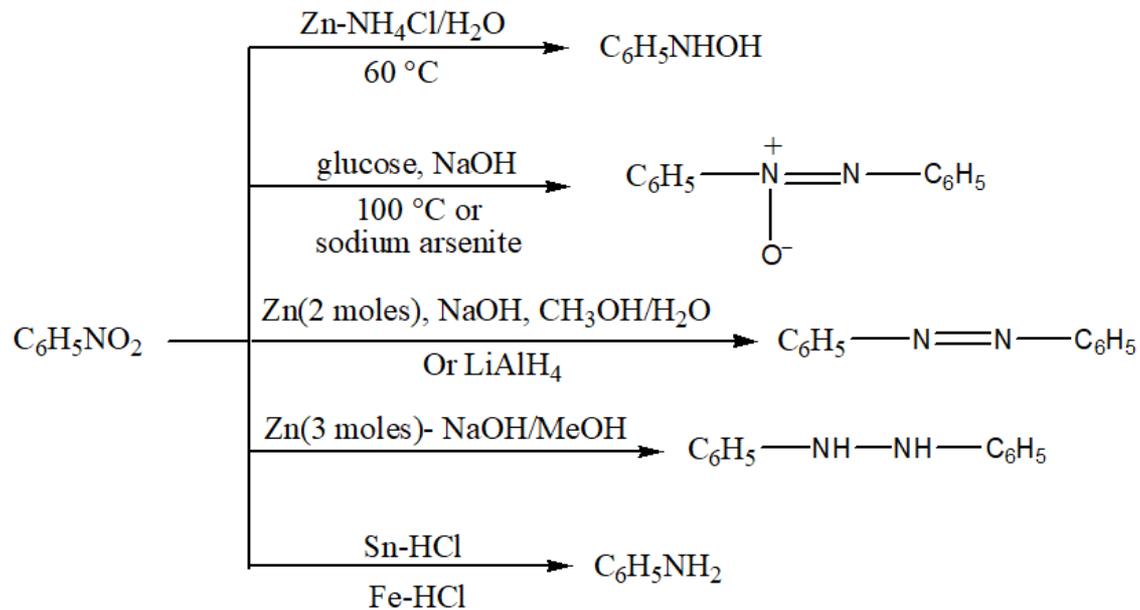


Reduction of aromatic nitro compounds:

The nitro group is readily converted into a series of functional groups of various degree of reduction.

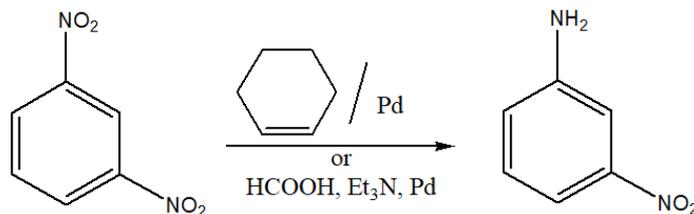


In neutral solution buffered with ammonium chloride, phenylhydroxylamine is the main product. In basic solution, using a weak reducing agent such as glucose, the intermediate nitrosobenzene reacts with phenylhydroxylamine to give azobenzene, with more powerful reducing agents converts into azobenzene and hydrazobenzene. Metal in acid solution brings about reduction to aniline.

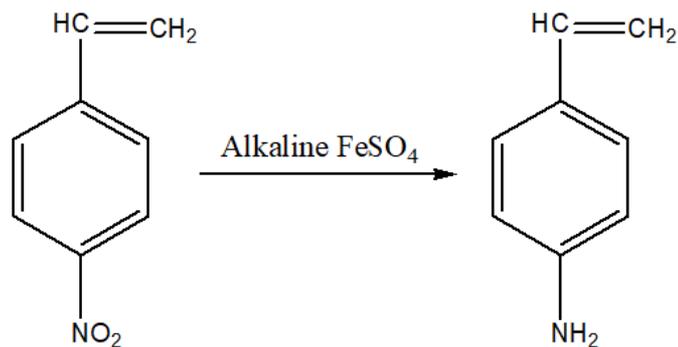


Selective reduction of nitro group:

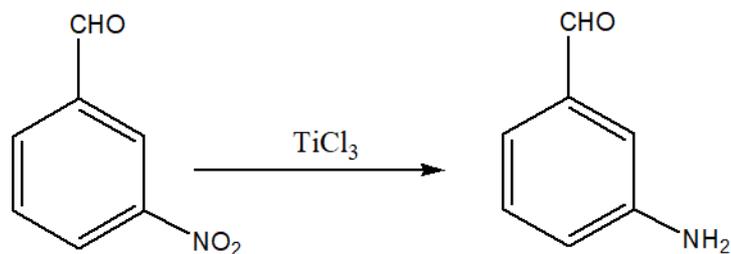
(1) Partial reduction of dinitro compound is accomplished by catalytic hydrogenation using Pd on carbon and cyclohexene or triethylammonium formate. Other reagents for this are titanium trichloride, hydrogen sulfide in pyridine and sodium or ammonium sulfide.



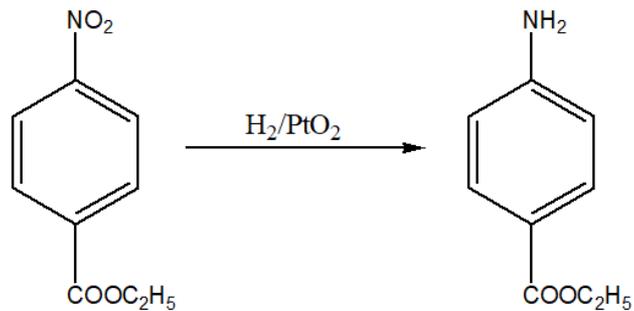
(2) To selectively reduce nitro group in presence of carbon-carbon multiple bonds in the side chain, alkaline ferrous sulphate is a reliable reagent.



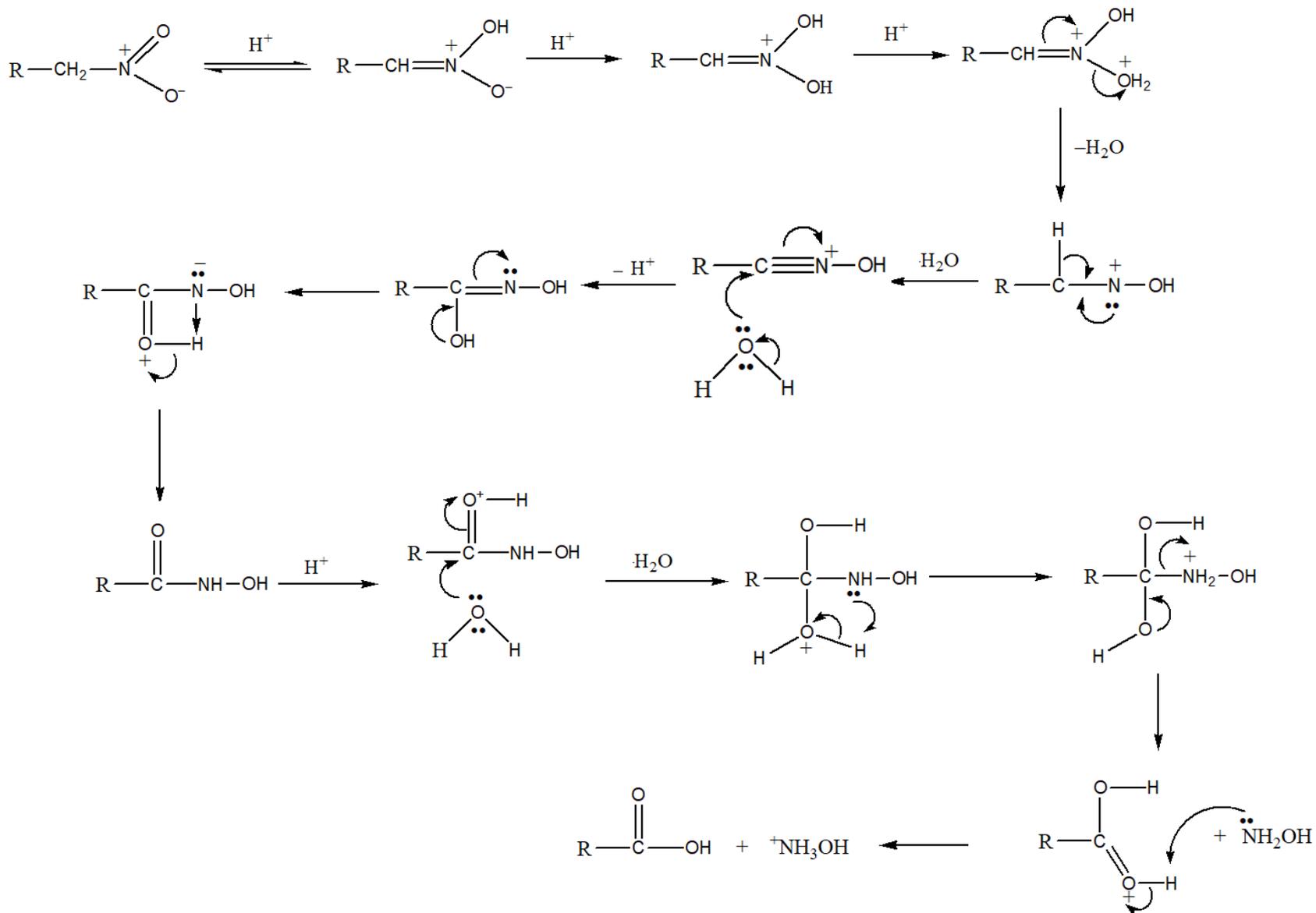
(3) Titanium trichloride is a very good reducing agent for nitro in presence of aldehyde group. SnCl₂-HCl can also be used.



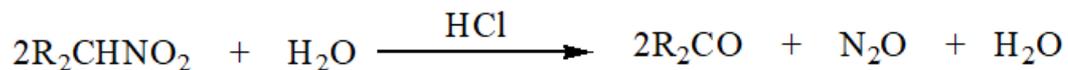
(4) Hydrogenation in presence of metal catalyst reduces only nitro group and has no effect on ester or carboxylic or hydroxy group.



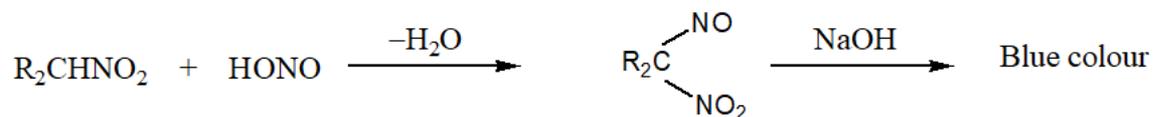
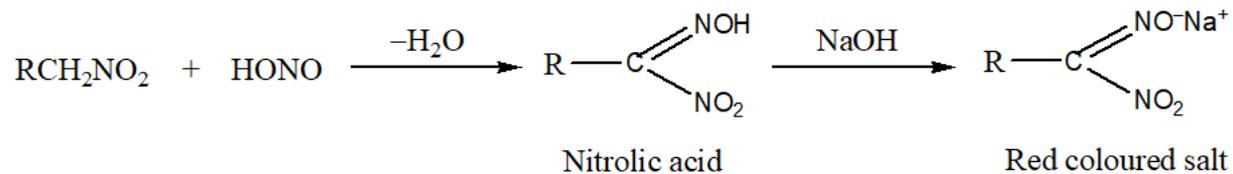
3. Hydrolysis of nitroalkane: Primary nitro compounds are hydrolysed by boiling hydrochloric acid or by 85 per cent sulfuric acid to a carboxylic acid and hydroxylamine. This is the most simple and cheapest process for the manufacture of hydroxylamine.



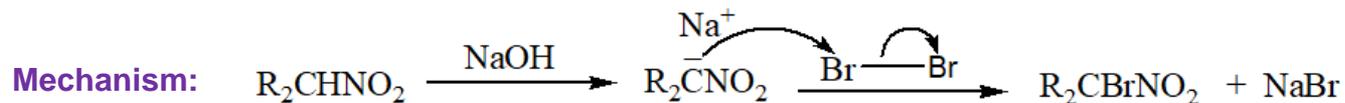
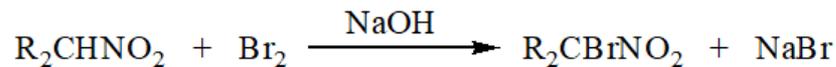
Secondary nitro compounds are hydrolysed by boiling hydrochloric acid to ketones and nitrous oxide. Tertiary nitro compounds are generally unaffected by hydrochloric acid due to the absence of any α -H.



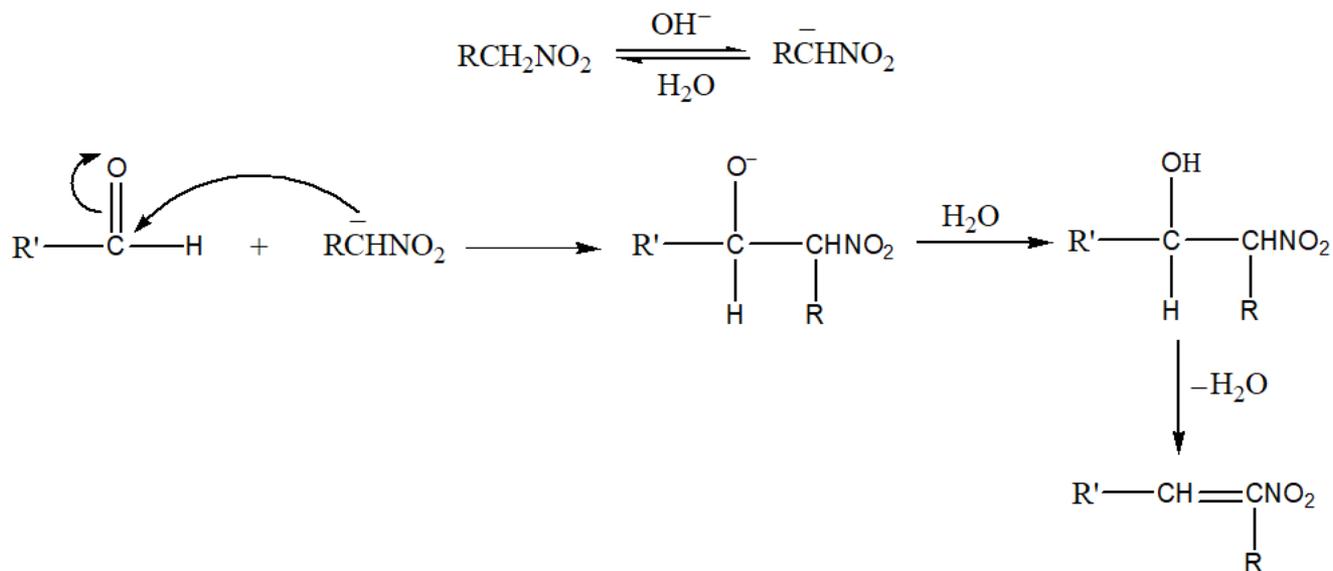
4. Reaction with nitrous acid: Primary nitroalkane reacts with nitrous acid to form nitrolic acid which dissolves in dilute aqueous sodium hydroxide and develops a red colour. A secondary nitroalkane reacts with nitrous acid to form pseudonitrole, it is a neutral blue compound which is insoluble in dilute aqueous sodium hydroxide solution, whereas tertiary nitroalkane does not undergo reaction with nitrous acid. This reaction is the basis of Victor Meyer's red, blue and white test.



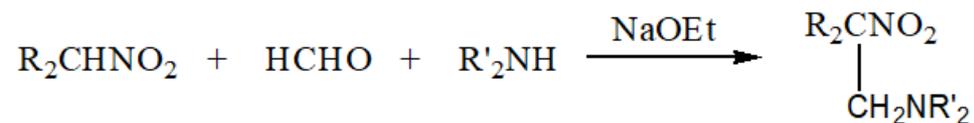
5. Bromination: Primary and secondary nitro compounds are readily halogenated in alkaline solution in the α - position only. Primary nitro compounds can form mono and dibromo derivatives, whereas secondary nitro compounds can only form monobromo derivative. Nitromethane is an exceptional which can form tribromo derivative.



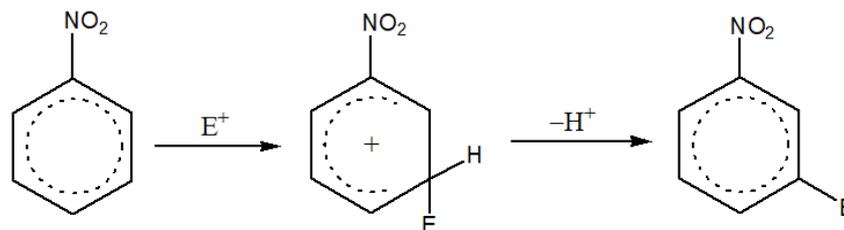
6. Condensation reaction with aldehydes: Owing to the presence of active α -hydrogen atoms, primary and secondary nitro compounds undergo condensation with aldehydes in presence of a base.



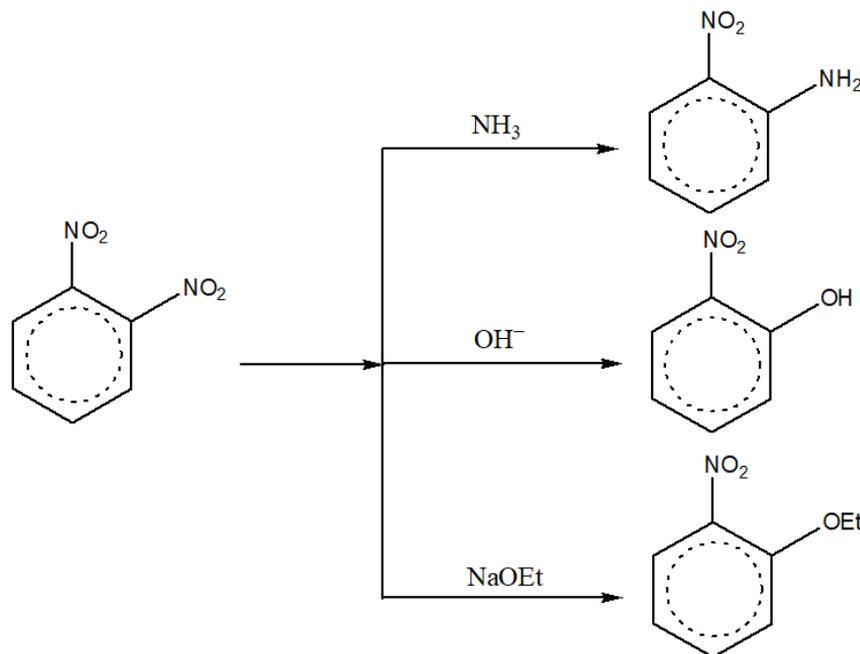
7. Mannich reaction: Primary and secondary nitro compounds also undergo Mannich reaction. This is the condensation between formaldehyde, ammonia or 1° or 2° amine and a compound containing at least one active hydrogen atom. The active hydrogen atom is replaced by an aminomethyl group or substituted aminomethyl group.



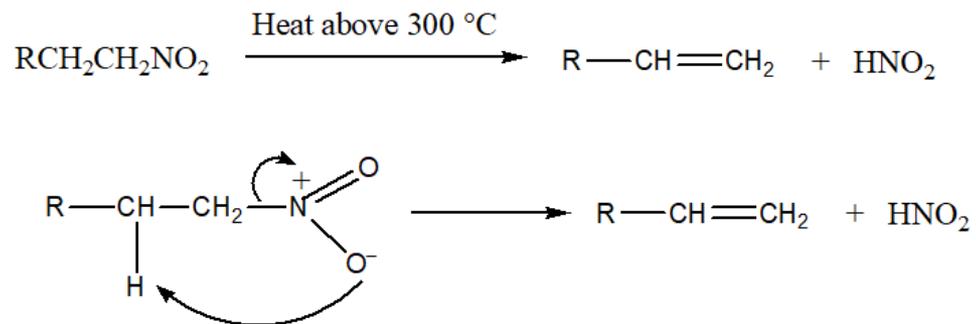
8. Electrophilic aromatic substitution of aromatic nitro compounds: Aromatic nitro compounds undergo electrophilic substitution reactions like halogenation, nitration, sulphonation etc.



9. Bimolecular nucleophilic substitution reaction: Aromatic nitro compounds undergo bimolecular nucleophilic substitution reactions.

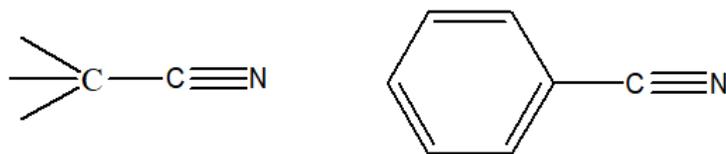


10. Action of heat: 1° and 2° nitroalkanes decompose on heating to form alkene.



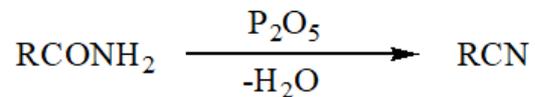
Nitriles (cyanides)

Cyano derivatives of alkanes and arenes are called alkanenitriles (alkyl cyanides) and arenenitriles (aryl cyanides), respectively. They are isomeric with isonitriles. Nitriles can be designated as RCN or ArCN where R and Ar represent alkyl and aryl groups, respectively.



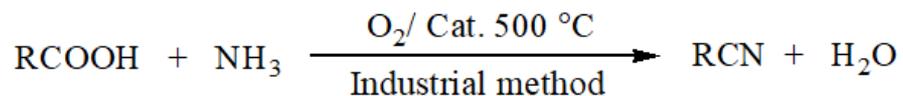
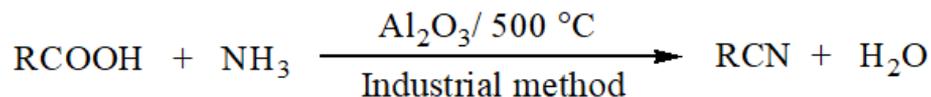
General methods of preparation:

1. By dehydration of acid amides with phosphorus pentoxide

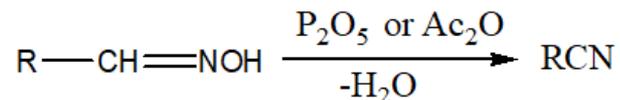


Amides may also be converted into cyanides by heating with phosphorus pentachloride or thionyl chloride.

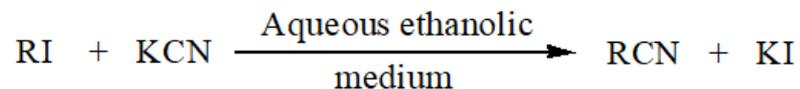
2. Cyanides are prepared industrially by passing a mixture of carboxylic acid and ammonia over alumina at 500 °C.



3. By dehydration of aldoximes with phosphorus pentoxide or with acetic anhydride.



4. The most convenient method is to heat an alkyl iodide with potassium cyanide in aqueous ethanolic solution; a small amount of isocyanide is also obtained.



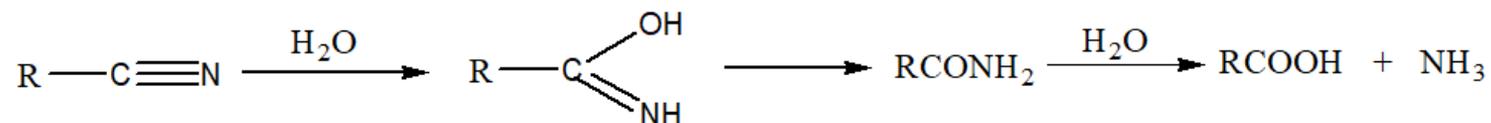
This method is satisfactory only if R is a primary or secondary alkyl group.

5. By interaction of a Grignard reagent and cyanogen chloride. This is the best method of preparing tertiary alkyl cyanides.

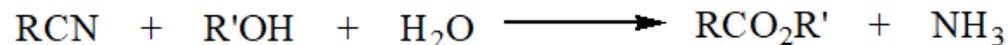


Reactions of nitrile compounds:

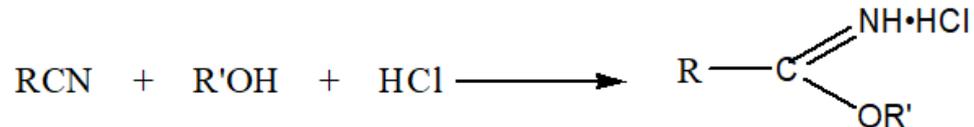
1. Hydrolysis of alkyl and aryl cyanides: The alkyl cyanides are hydrolysed by acids or alkalis to the corresponding acid via the intermediate formation of an amide.



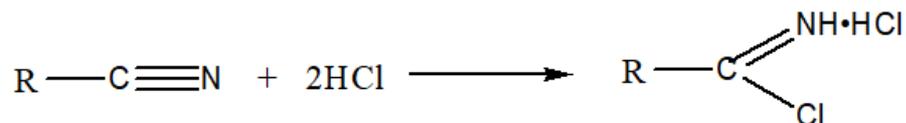
When a solution of alkyl cyanide in an alcohol is heated with concentrated sulphuric acid or hydrochloric acid, the ester is obtained as product.



On the other hand, if dry hydrogen chloride is passed into the solution of alkyl cyanide in anhydrous alcohol, the imidic ester hydrochloride is formed.

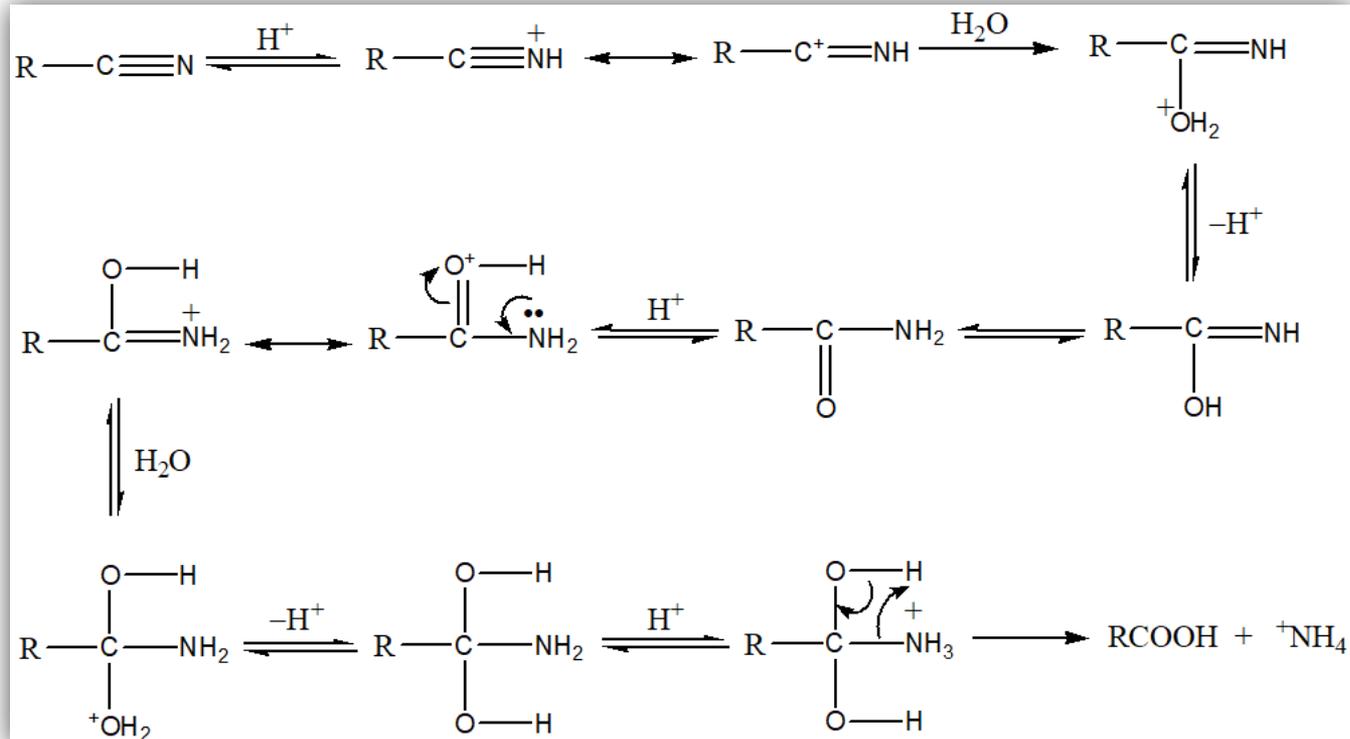


When an alkyl cyanide is treated with dry hydrochloric acid, the imidochloride is formed.

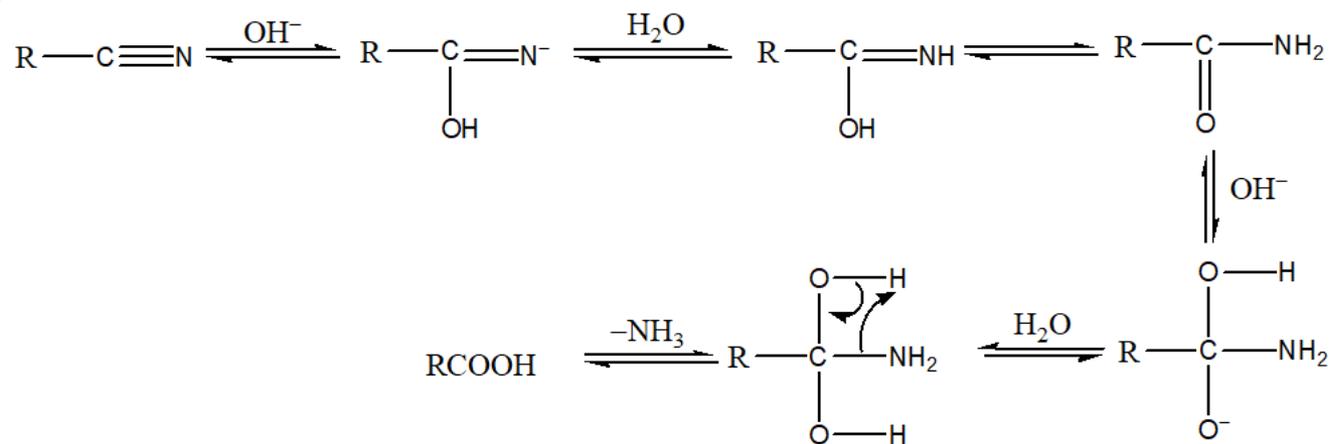


Mechanism:

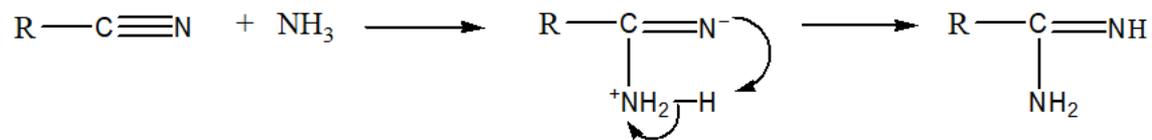
1. Acid catalysed hydrolysis of cyanides



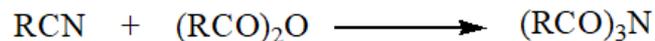
2. Base catalysed hydrolysis of cyanides



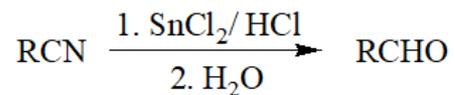
2. Alkyl cyanides combine with dry ammonia to form amidines.



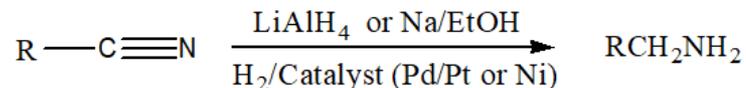
3. Alkyl cyanides combine with acid anhydride on heating to form tertiary acid amides.



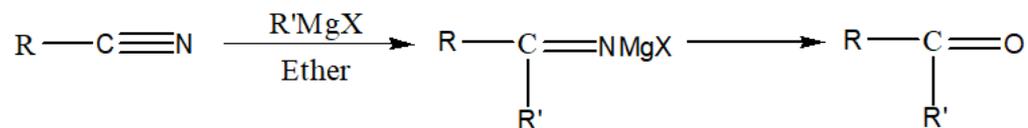
4. **Stephen's reaction:** When alkyl or aryl cyanides are reduced with stannous chloride and hydrochloric acid in ethereal solution, then the products are hydrolysed with water and the corresponding aldehydes are obtained as product. This reaction is known as Stephen's reaction.



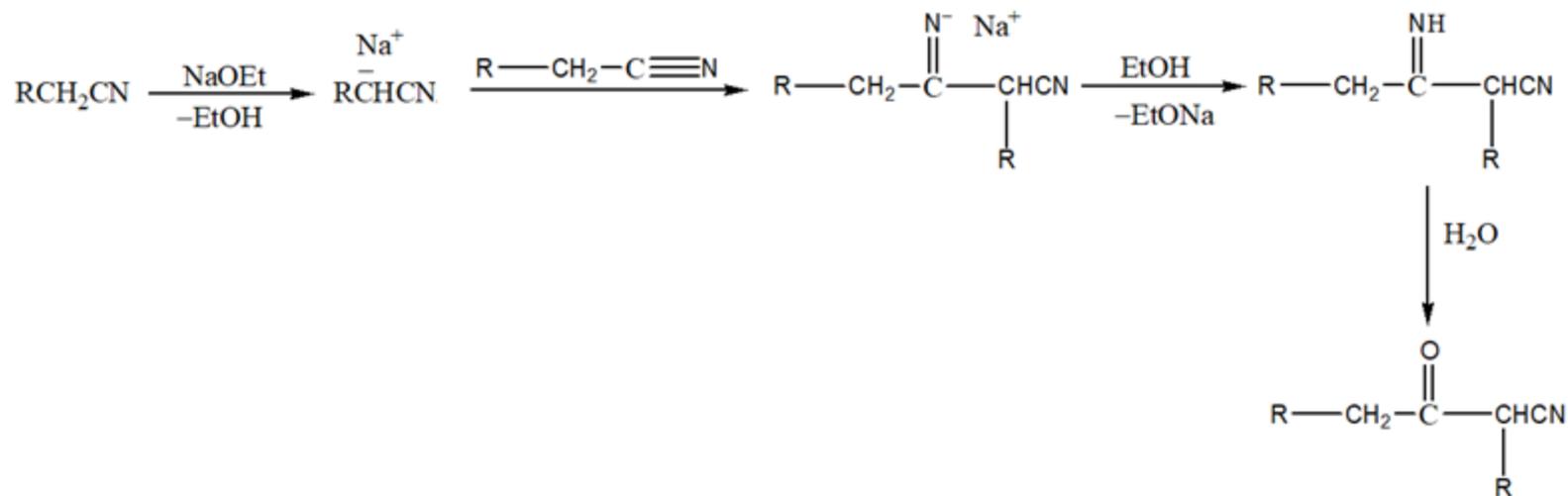
5. **Reduction of cyanides:** Catalytic hydrogenation or reduction with (i) LiAlH_4 /ether or (ii) Na/EtOH etc. reduces nitriles to primary amine.



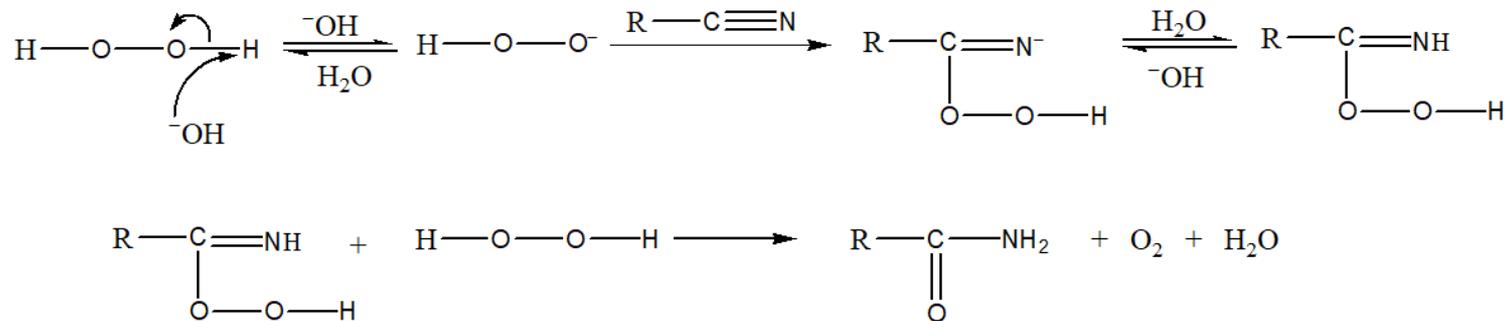
6. **Formation of ketones:** Grignard reagents add to nitriles and the addition products on hydrolysis give ketones.



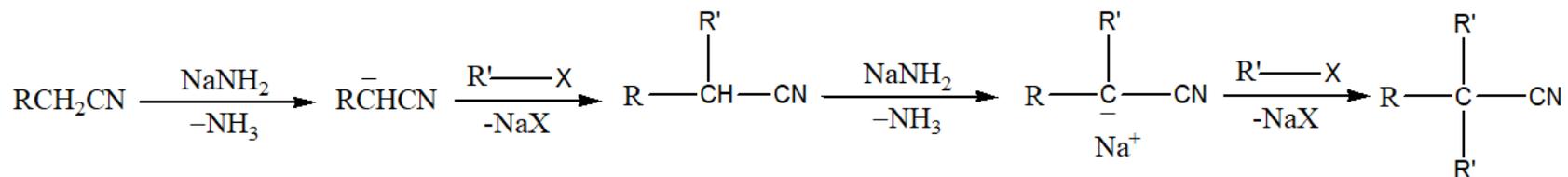
7. The Thorpe nitrile condensation: In presence of base (NaOEt) or metallic sodium, alkyl cyanides undergo condensation reaction to form iminonitrile in which α -carbon of one molecule is involved. The iminonitrile on treatment with water gives a β -ketonitrile.



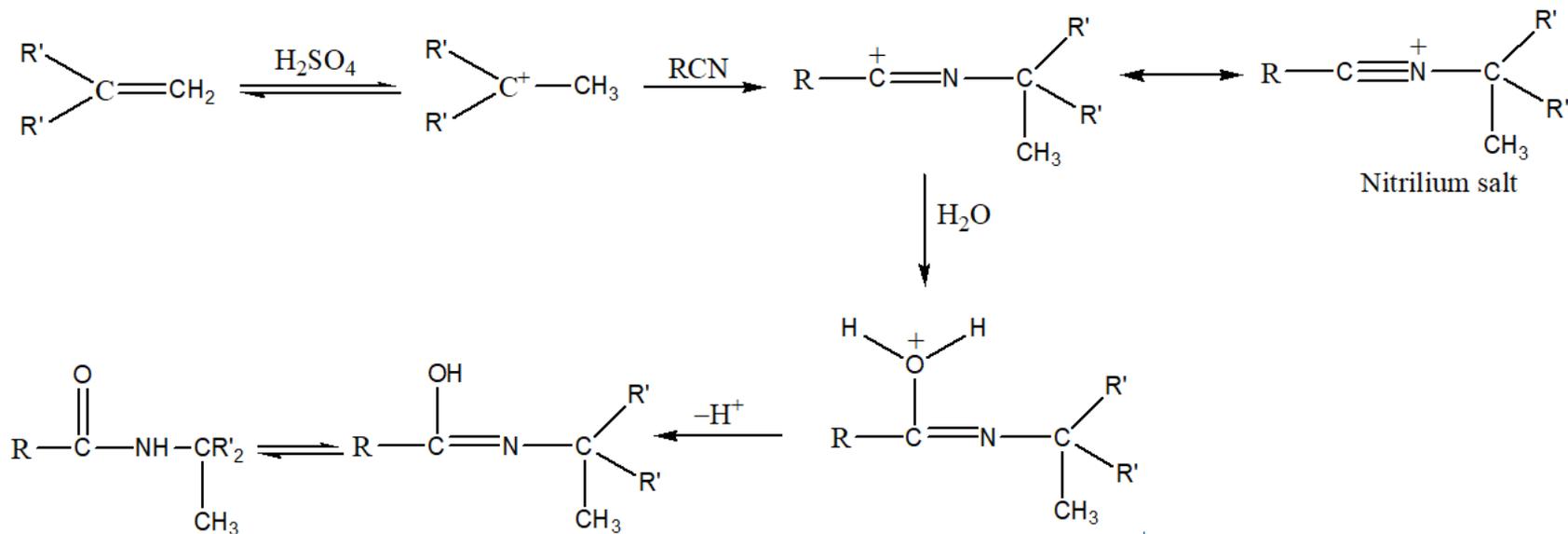
8. Hydrolysis of a nitrile to an amide: A primary nitrile can be hydrolysed to the amide in presence of alkaline hydrogen peroxide.



9. Alkylation: When a 1° or 2° nitrile is heated with alkyl halide and sodamide, α-H atoms get replaced by alkyl groups.



10. Addition of olefins: In presence of conc. H_2SO_4 , olefins add to nitriles to give nitrilium salts which on treatment with water gives N-t-alkylamide and the reaction is called Ritter reaction.



Isonitriles

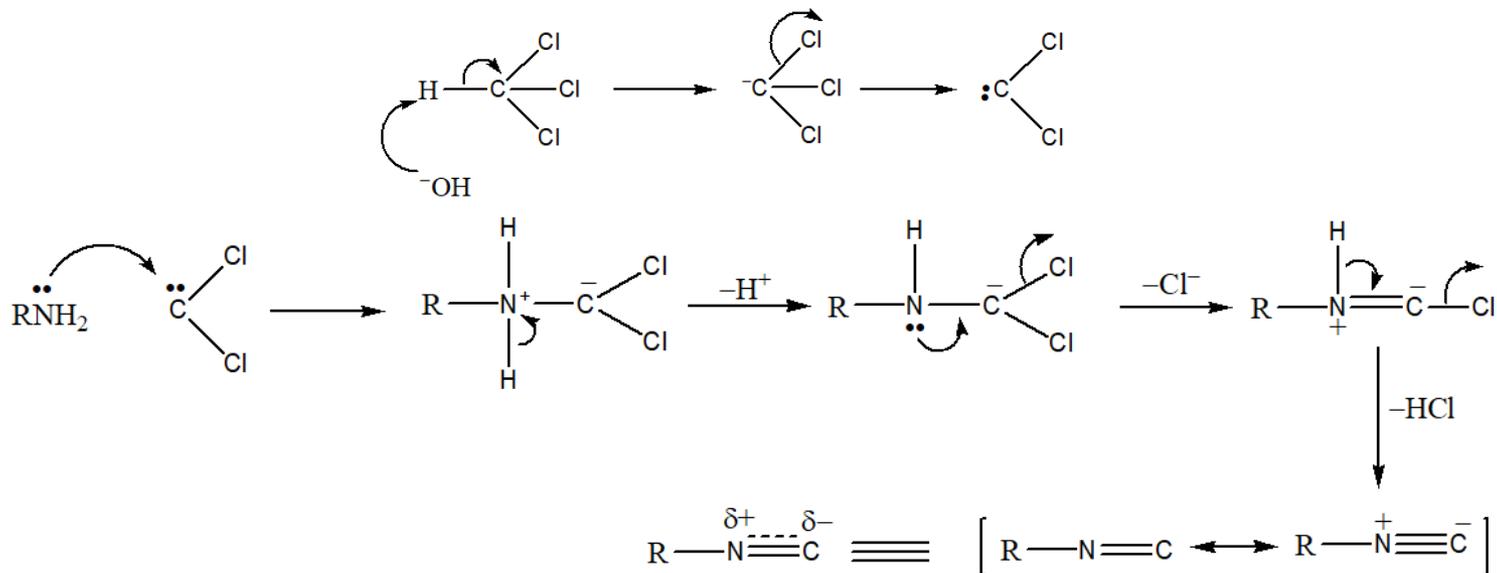
Isonitriles contain isocyano group ($\text{---}\overset{+}{\text{N}}\equiv\overset{-}{\text{C}}$). They are isomeric with nitriles. Isonitriles are also called isocyanides. They may be represented by RNC or ArNC.

General methods of preparation:

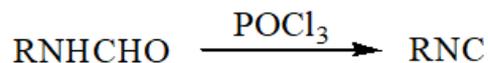
1. By heating an alkyl iodide with silver cyanide in aqueous ethanolic solution, a small amount of cyanide is also formed.



2. By heating a mixture of primary amine, aliphatic or aromatic, with ethanolic solution of potassium hydroxide and chloroform, an isonitrile forms and the reaction is popularly known as carbylamine reaction. Carbylamine is another name of isonitrile.

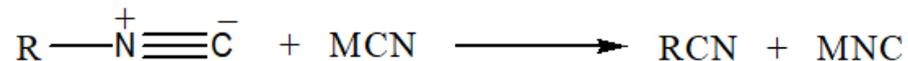


3. When N-alkyl formamides are dehydrated by phosphoryl chloride in presence of pyridine, alkyl isocyanides are formed.

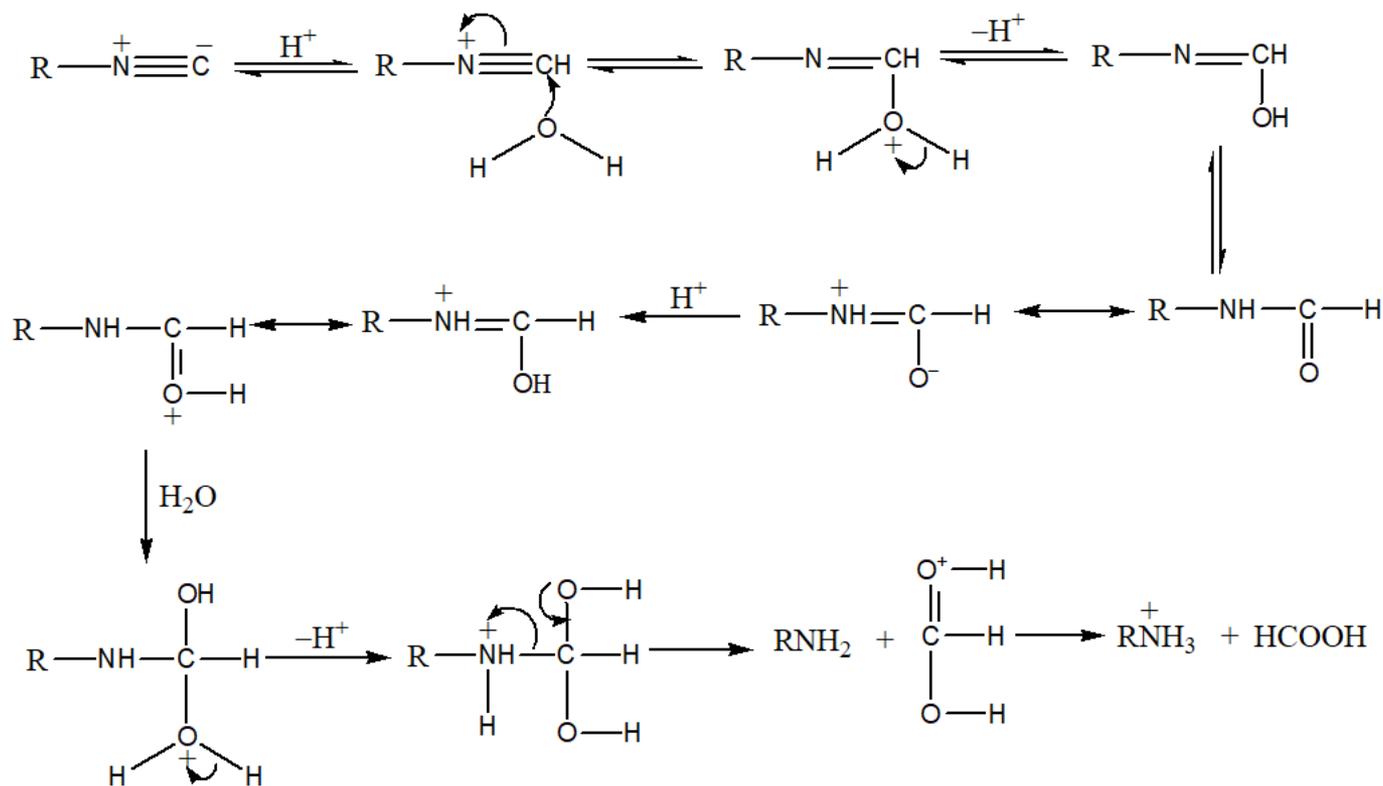


Reactions of isonitrile compounds:

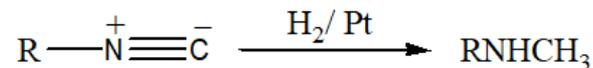
1. Reaction with metal cyanides: When isonitriles are heated with metal cyanides at 100 °C, the more stable nitriles are formed through nucleophilic displacement.



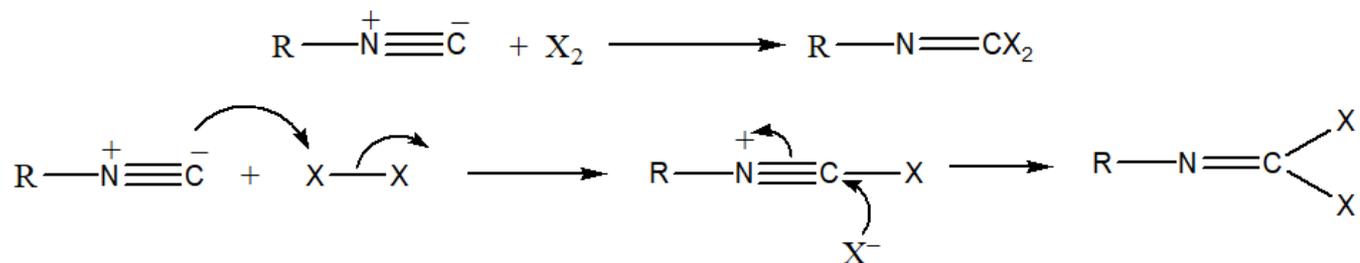
2. Hydrolysis of isonitriles: Isonitriles get hydrolysed by dilute acids readily to form 1° amines and formic acid. However, isonitriles do not get hydrolysed by alkalis.



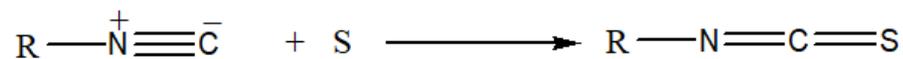
3. Reduction: Isonitriles are reduced catalytically to 2° methylamines. The reduction may also be carried out by dissolving metals.



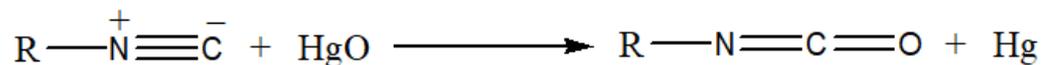
4. Addition of halogen: Isonitriles add on halogen to form alkyl and aryliminocarbonyl halides.



5. Addition of sulfur: Isonitriles react with sulfur to form isothiocyanates.



6. Addition of mercuric oxide: Isonitriles react with mercuric oxide to form isocyanates and metallic mercury.



7. Action of heat: When isonitrile compounds are heated for a long time, they rearrange to form cyanides.

