T.R.R GOVERNMENT DEGREE COLLEGE(A), KANDUKUR

DEPARTMENT OF CHEMISTRY

STUDY MATERIAL

II B.SC (Hons) CHEMISTRY

MAJOR-11 NITROGEN CONTAINING ORGANIC COMPOUNDS & SPECTROSCOPY

CLASS: SEMESTER-IV B. Sc. (HONS) CHEMISTRY

NAME OF THE FACULTY: Dr. K.V.PADMAVATHI

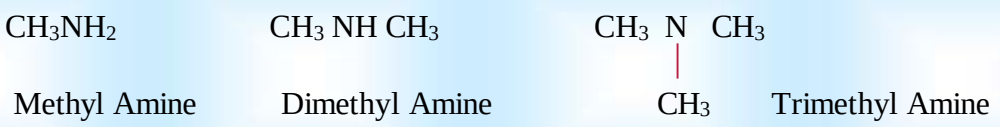
MAJOR-11: NITROGEN CONTAINING ORGANIC COMPOUNDS & SPECTROSCOPY

UNIT-I AMINES: (9 Hrs.)

Classification, chirality in amines (pyramidal inversion), preparations – Gabriel synthesis, Hoffmann- Bromamide reaction (with mechanism), reduction of amides and Schmidt reaction. Distinction between Primary, secondary and tertiary amines using Hinsberg's method and nitrous acid. Discussion of the following reactions with emphasis on the mechanistic pathway: Carbylamine reaction, Hoffmann's exhaustive methylation, Hofmann and Cope elimination.

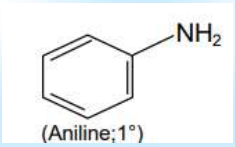
Diazonium Salts: Preparation and synthetic applications of diazonium salts including preparation of arenes, haloarenes, phenols, cyano and nitro compounds. Coupling reactions of diazonium salts (preparation of azo dyes).

Classification : Amines are the alkyl (or) aryl derivatives of NH_3. The general formula of amine is R_3N, where R is an alkyl (or) aryl group or hydrogen. In amines one or more Hydrogen atoms of ammonia are replaced by Alkyl or aryl groups.



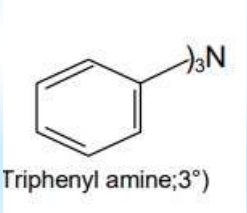
Amines are classified as primary, secondary (or) tertiary according to the number of groups attached to the nitrogen atom.

If one alkyl group has replaced one hydrogen atom of ammonia, it is primary amine



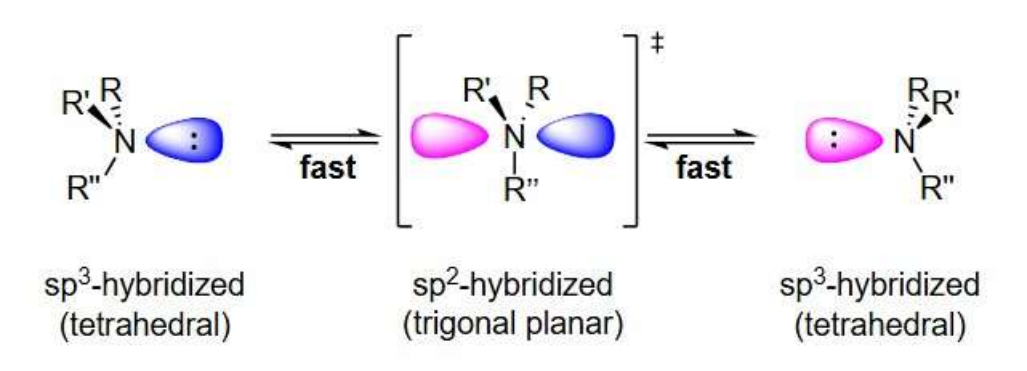
Similarly, if two hydrogens are replaced, it is secondary amine

and if all the three are replaced, it is tertiary amine



chirality in amines (pyramidal inversion): In Amines a nitrogen atom with 3 different groups and a lone pair (**:**N $R_1R_2R_3$) can be regarded as tetrahedral chiral centre with sp^3 hybridized. However, simple amines cannot be resolved into enantiomers. Due to nitrogen oscillates between two pyramidal shapes, passing through a trigonal-planar sp^2 transition state (This rapid interconversion is called "Pyramidal inversion")

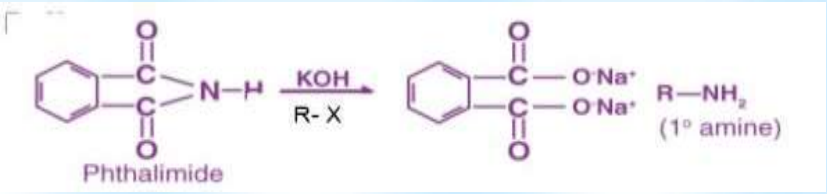
At room temperature this inversion has a very low energy barrier—about 20–25 kJ/mol and amine flips tens of thousands of times per second hence two configurations interconvert so rapidly, we never get stable enantiomers (racemizes rapidly)



In this transition state the lone pair orbital becomes a pure p-orbital perpendicular to the plane. The N–R σ orbitals lie in the plane.

However Quaternary Ammonium Salts (No lone pair),Rigid Cyclic Systems(Tröger's base), Three-Membered Rings (Aziridines) gives isolable enantiomers.

GABRIEL PHTHALIMIDE SYNTHESIS: The Gabriel Phthalimide Synthesis is a process primarily used for the preparation of pure primary aliphatic amines



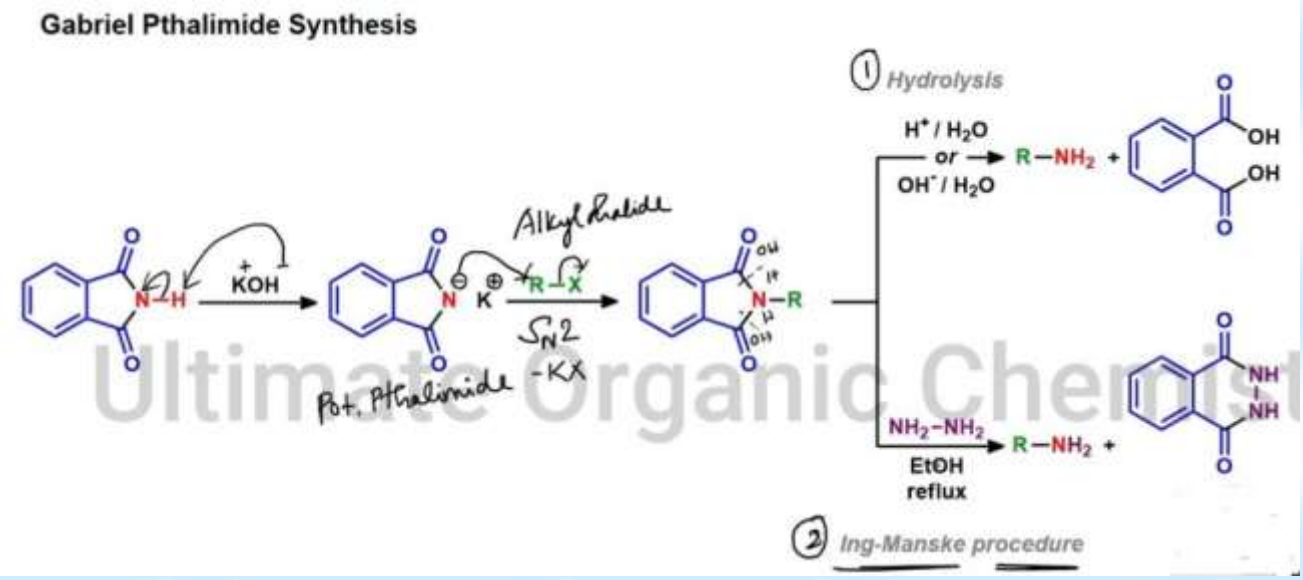
Mechanism of the Reaction

The mechanism proceeds through three main stages:

1. Formation of Potassium Phthalimide :The phthalimide, which contains an acidic hydrogen attached to the nitrogen atom due to the presence of two adjacent electron-withdrawing carbonyl groups. When treated with a base like ethanolic potassium hydroxide (KOH), the hydroxide ion (OH^-) removes this proton, resulting in the formation of potassium phthalimide

2. Nucleophilic Substitution (SN^2) : The potassium phthalimide acts as a nucleophile. It reacts with an alkyl halide (R−X) via an SN^2 mechanism. The nitrogen atom attacks the alkyl group, displacing the halide ion to form N-alkyl phthalimide

Alkaline Hydrolysis: A hydroxide ion attacks a carbonyl carbon, breaking the C−N bond and opening the phthalimide ring. A second hydroxide attack on the other carbonyl group releases the primary amine (R−NH 2) and leaves behind a salt of phthalic acid (potassium phthalate).
Ing-Manske Procedure: Instead of a base, hydrazine (NH 2 NH 2) is used. This is often preferred because it releases the amine more efficiently, forming a stable by product called phthalhydrazide

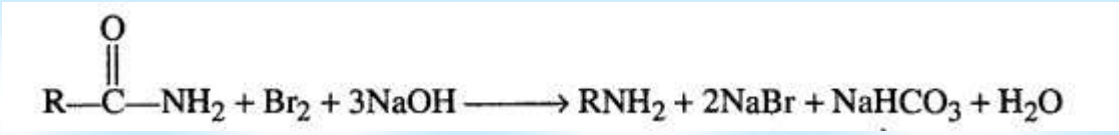


Important Points and Limitations

- Primary Amines Only: This reaction is specifically designed to produce primary aliphatic amines.
- SN^2 Dependency: Since the second step involves an SN^2 reaction, it works best with primary alkyl halides. Secondary halides react more slowly, and tertiary halides are generally unsuitable as they prefer elimination.
- No Aromatic Amines: You cannot use this method to synthesize aromatic amines like aniline. This is because aryl halides do not undergo SN^2 reactions
- Purity: The reaction is highly valued because it provides the primary amine in a very pure form, free from contamination by secondary or tertiary amines

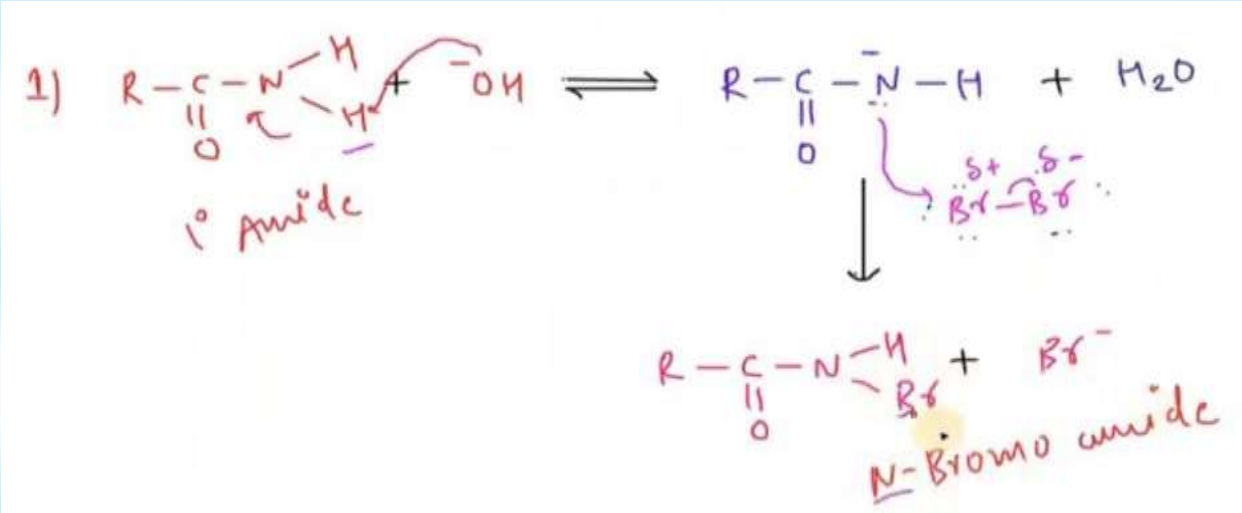
HOFFMANN- BROMAMIDE REACTION :

The Hoffmann Bromamide Reaction, also known as the Hoffmann rearrangement or Hoffmann degradation, is a chemical process where a primary (1◦) amide reacts with bromine (Br_2) and a base (like potassium hydroxide, KOH) to form a primary amine. This reaction is termed a "degradation" because the resulting amine contains one fewer carbon atom than the original amide due to the loss of the carbonyl group

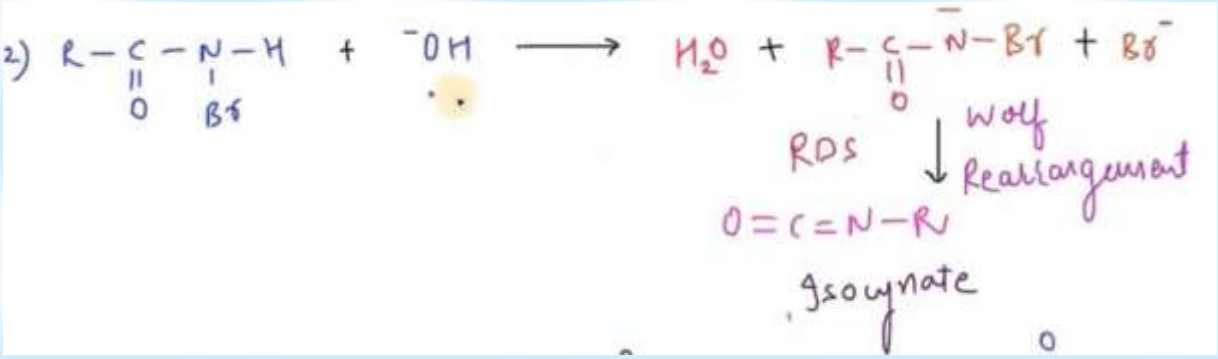


Mechanism of the Reaction

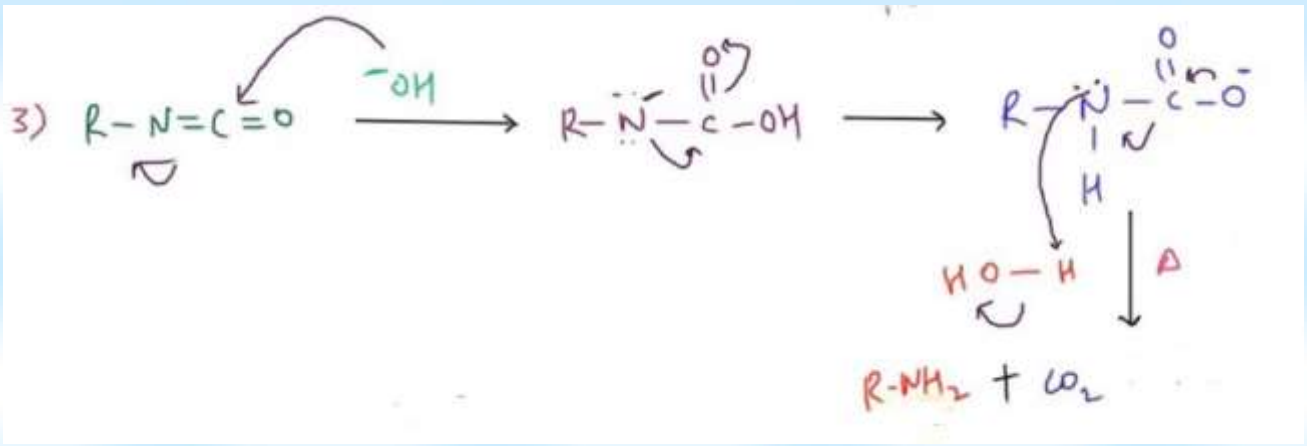
1. Formation of N-Bromo Amide: A hydroxide ion (OH^-) removes an acidic hydrogen from the nitrogen of the primary amide. The resulting negatively charged nitrogen attacks a bromine molecule, leading to the formation of an N-bromo amide



Wolff Rearrangement (Rate-Determining Step): A second equivalent of base removes the remaining hydrogen from the nitrogen atom of the N-bromo amide, creating another reactive anion. As the bromide ion (Br^-) departs, the alkyl group (R) migrates from the carbonyl carbon directly to the nitrogen atom. This simultaneous migration and loss of the leaving group is an intramolecular process and is the slowest step (rate-determining step) of the reaction. The rearrangement results in the production of an isocyanate intermediate (R−N=C=O)



Hydrolysis and Decarboxylation: Hydroxide ions attack the isocyanate, followed by an intramolecular hydrogen shift. Finally, carbon dioxide (CO_2) is released (which reacts with the base to form carbonates), leaving behind the primary amine ($R–NH_2$).

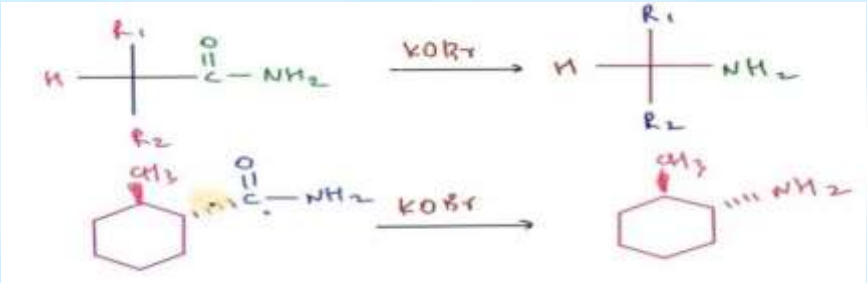


Important Characteristics and Insights

• Stoichiometry: For everyone mole of primary amide, the reaction consumes 1 mole of bromine (Br_2) and 4 moles of potassium hydroxide (KOH).

• Substrate Requirement: The reaction only works with primary amides. Secondary and tertiary amides cannot undergo this process because they cannot form the necessary isocyanate intermediate

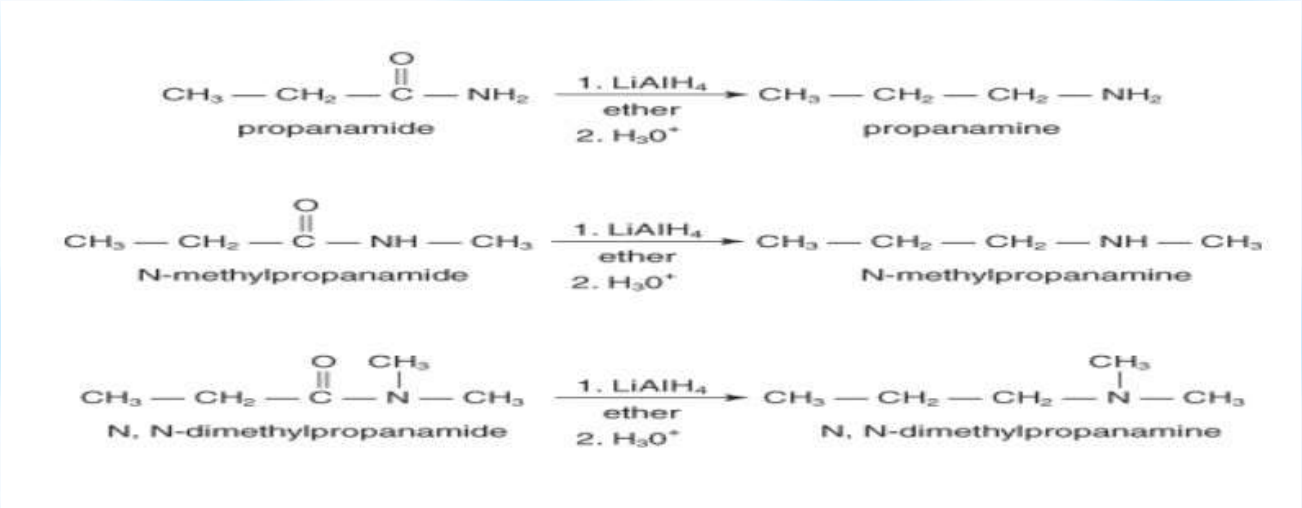
• Retention of Configuration: If the migrating alkyl group is optically active, its stereochemical configuration is retained.



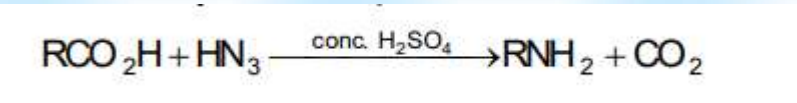
Migratory Aptitude: The rate of the reaction is enhanced by electron-donating groups (groups with a +M effect) attached to the migrating group. The more electron-rich the migrating group, the more effective the rearrangement.

REDUCTION OF AMIDES:

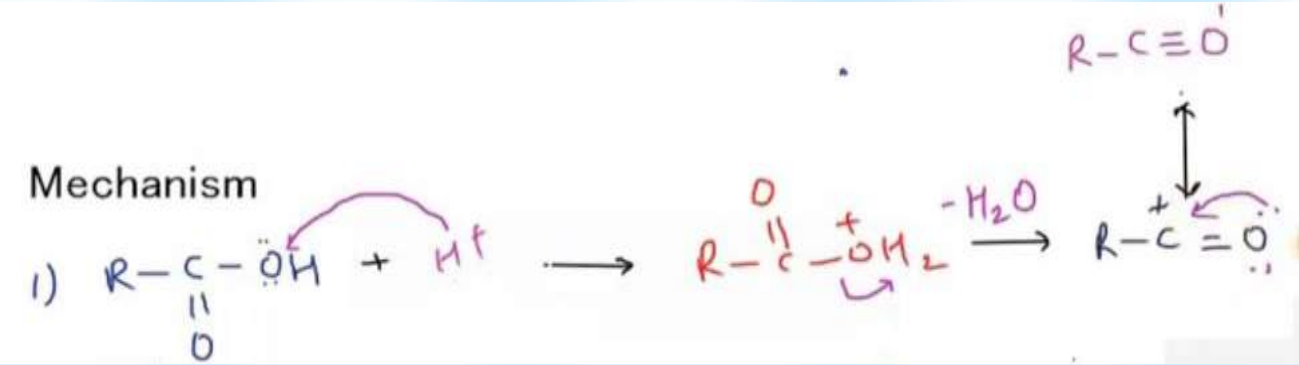
Amides yield primary amines on reduction by lithium aluminium hydride, while N-substituted and N, N-disubstituted amides produce secondary and tertiary amines, respectively.



SCHMIDT REACTION: The reaction of hydrazoic acid with carboxylic acids in the presence of concentrated mineral acids to give primary amines is called Schmidt reaction

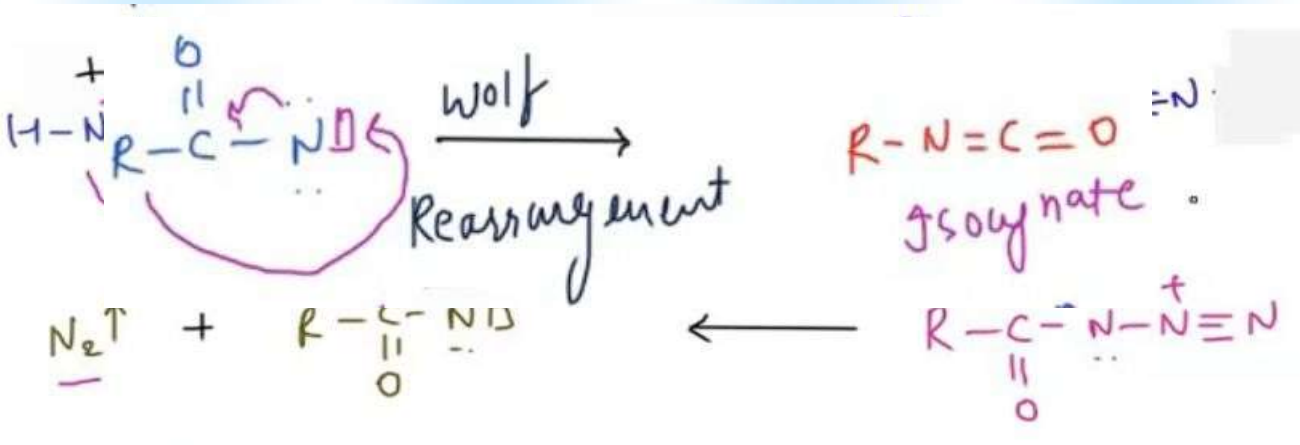


This mechanism begins with the formation of an acylium ion from the protonation of the carboxylic acid followed by the removal of water.

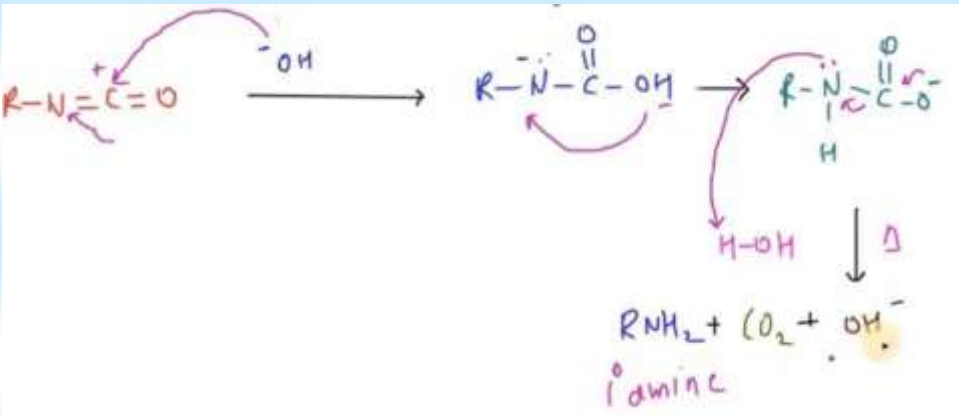


This acylium ion is now reacted with hydrazoic acid, leading to the formation of a protonated azido ketone and the removal of dinitrogen leading to the formation of nitrene intermediate

Now the R group undergo a Wolf rearrangement resulting in the migration of the carbon-nitrogen bond to form stable Isocyanate or carbamate



The Isocyanate undergoes basic hydrolysis leading formation of primary amine



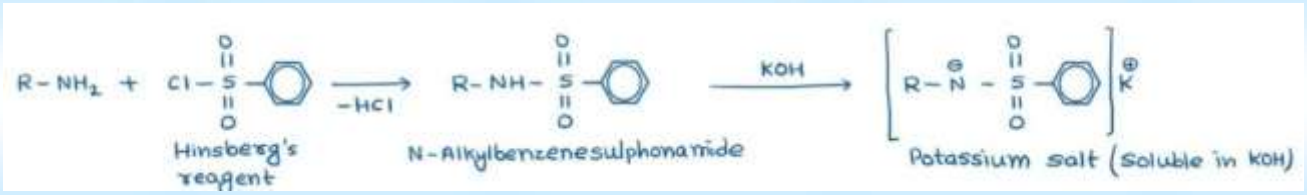
Important Characteristics and Insights

- The reaction is decarbonylative/decarboxylative: the carboxyl carbon is ultimately lost as CO_2, so a C_n acid gives a C_{n-1} amine
- The nitrogen source is hydrazoic acid (HN_3), and nitrogen gas (N_2) is evolved during rearrangement, which helps drive the reaction to completion.
- Product is a primary amine (RNH_2), not secondary or tertiary, because the new C–N bond forms via an isocyanate intermediate that hydrolyses and decarboxylates
- For carboxylic acids, there is no competition between different migrating groups, so the reaction is regioselective and directly yields a single primary amine
- Use is limited by the toxicity and explosiveness of hydrazoic acid, safety issues for strong acids

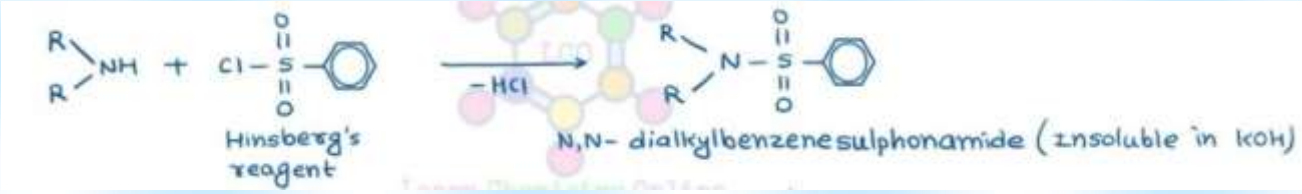
DISTINCTION BETWEEN PRIMARY, SECONDARY AND TERTIARY AMINES USING HINSBERG'S METHOD :

In this method, mixture of amines is treated with benzenesulphonyl chloride (Hinsberg reagent), followed by 5% aq. KOH solution.

The primary amine gives N- alkylbenzenesulphonamide which is soluble in 5% KOH solution.



The secondary amine yields N,N-dialkyl benzenesulphonamide which is insoluble in potassium hydroxide solution

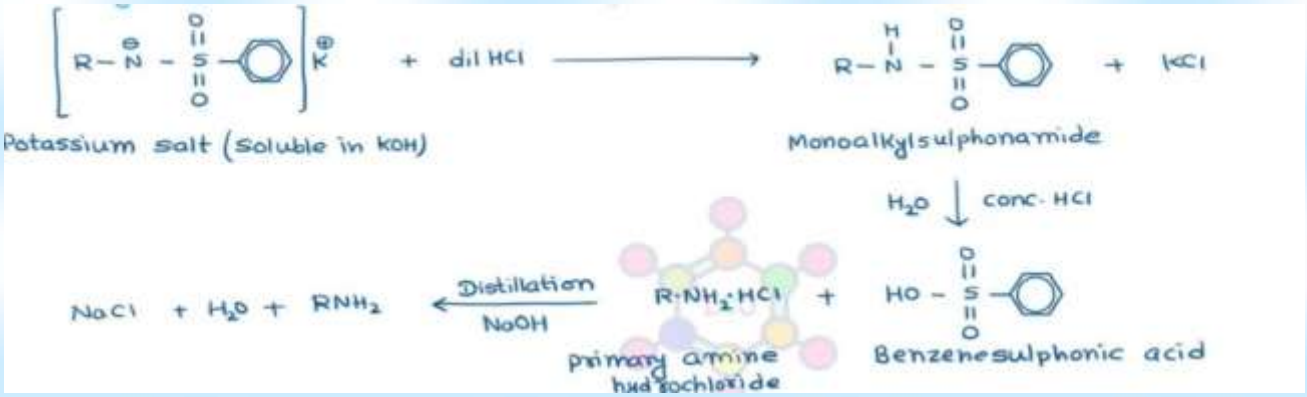


Tertiary amine does not react with the benzenesulfonyl chloride.

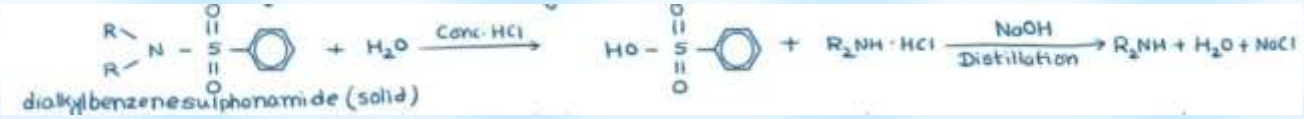
Recovery of amines:

The reaction mixture, so obtained, is extracted with ether. Tertiary amine and N.N-dialkylbenzenesulphonamide, being insoluble in water, pass into the ethereal layer while potassium mono-alkylsulphonamide remains in the aqueous layer. The two layers, aqueous and ethereal, are then separated.

Recovery of 1° amine from aqueous layer



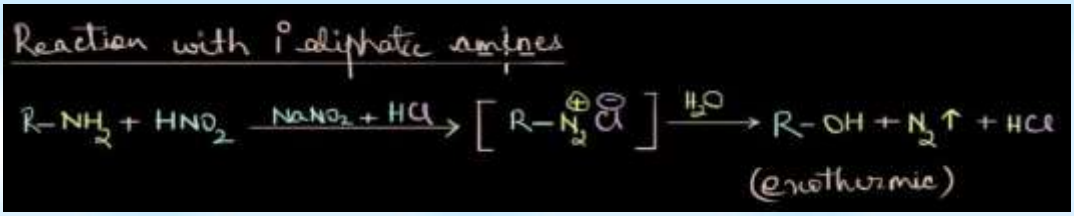
Recovery of 2° and 3° amine from ethereal layer: During fractional distillation of ethereal layer, ether distils first and then free tertiary amine distils over leaving behind solid dialkylbenzenesulphonamide.



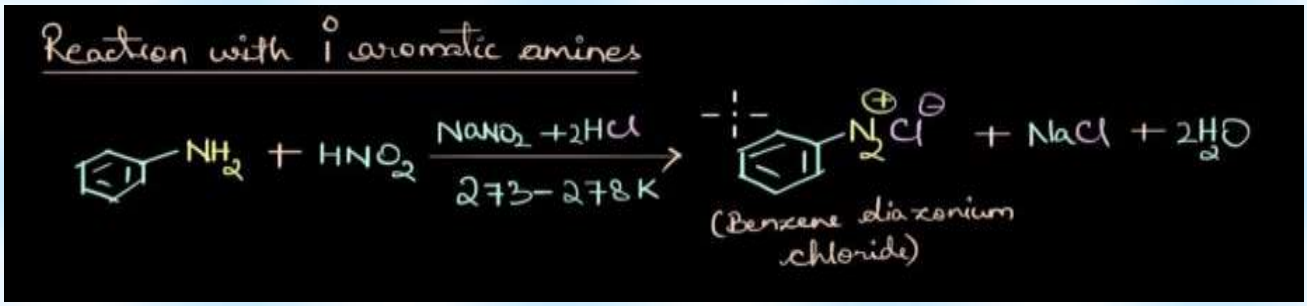
Note : Hinsberg's method is not suitable for higher primary amines because their monoalkyl - Sulphonamides are insoluble in alkali

DISTINCTION BETWEEN PRIMARY, SECONDARY AND TERTIARY AMINES USING NITROUS ACID

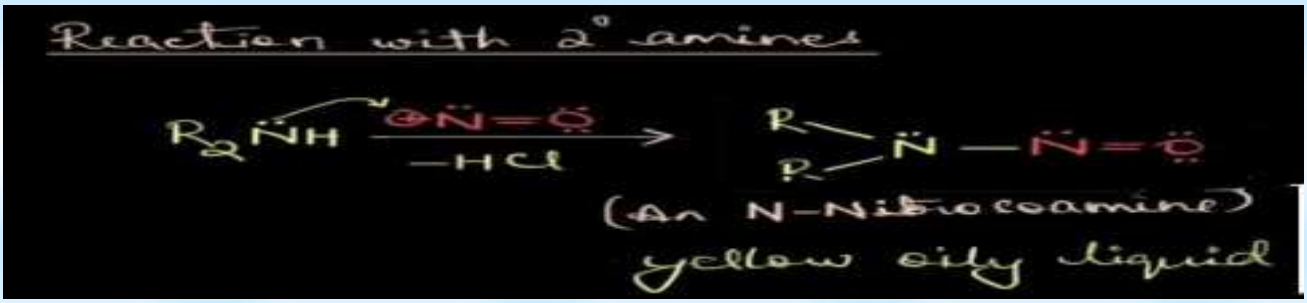
1° aliphatic amines reacts with Nitrous acid forms unstable diazoiumchloride which collapses to give alcohol and Nitrogen gas .This reaction is used for quantitative estimation of 1° aliphatic amines



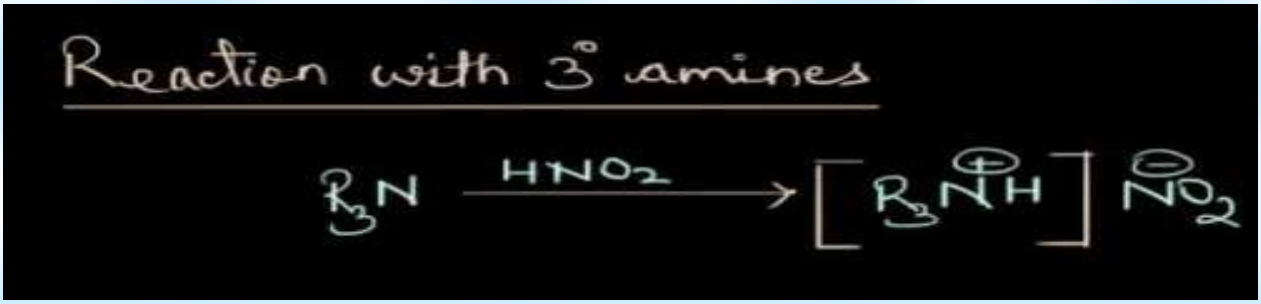
1° aromatic amines reacts with Nitrous acid forms stable Benzene diazoiumchloride which is stable at 0-5°C



2° aliphatic or aromatic amines reacts with Nitrous acid forms yellow-coloured oily substances



3° aliphatic or aromatic amines do not reacts with Nitrous acid forms only salts .no change is observed



Summary

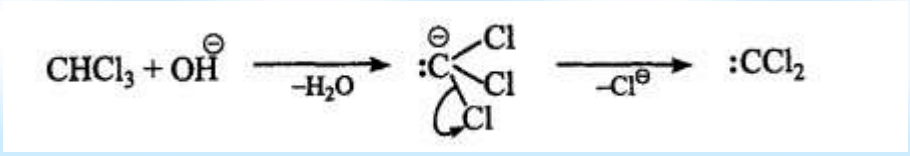
Type of amine	Reaction with nitrous acid	Observation
Aliphatic primary	Forms unstable alkyl diazonium salt	Vigorous effervescence of nitrogen gas
Aromatic primary	Forms stable aryl diazonium salt at low temperatures.	No effervescence, formation of aryl diazonium salt
Secondary	Forms N-Nitrosoamine	Yellow oily product
Tertiary	Forms ammonium nitrite salt	No observable changes

CARBYLAMINE REACTION : Alcoholic solution of primary amines (aliphatic and aromatic)react with chloroform and potassium hydroxide solution to yield isocyanides (carbylamines). This reaction has been used as a qualitative test for primary amines. The formation of isocyanides is readily noted by their characteristic foul smell , which can be easily detected. This reaction is used for the detection of primary amines in qualitative analysis

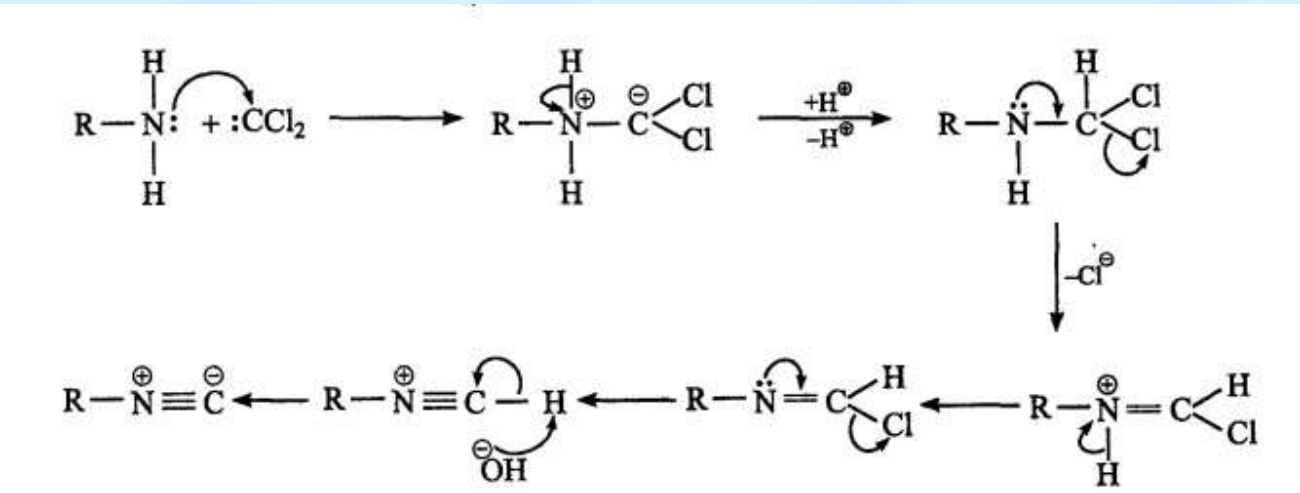
$$\underset{\text{Aniline}}{C_6H_5NH_2} + CHCl_3 + 3KOH \longrightarrow \underset{\text{Phenyl isocyanide}}{C_6H_5NC} + 3KCl + 3H_2O$$

Mechanism:

This reaction proceeds via the intermediate formation of dichloromethylene, which is produced from the chloroform in alkaline solution. Dichlorocarbene behaves as an electrophilic carbene because Cl withdraws electron density



Attack of the amine nitrogen on the carbene followed by loss of HCl yields the isocyanide.



HOFFMANN'S EXHAUSTIVE METHYLATION :

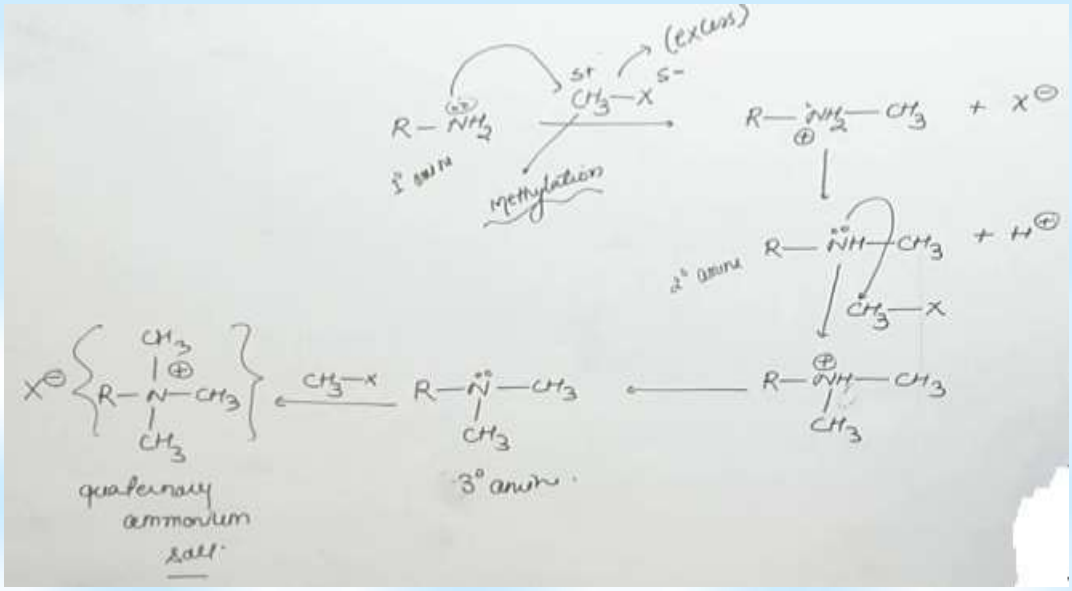
The reaction involves treating a primary amine with excess methyl iodide.

1° Amine (R-NH2) attacks CH_3I to give 2° amine (R-NH CH_3)

2° amine (R-NH CH_3) attacks CH_3I to give 3° amine (R-N $(CH_3)_2$)

3° amine (R-N $(CH_3)_2$) attacks CH_3I to give quaternary ammonium salt (R-N $(CH_3)_3)^+ I^-$

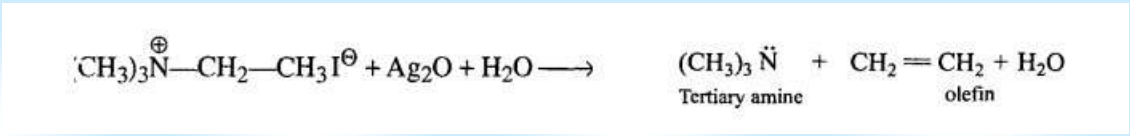
The reaction doesn't stop until the nitrogen has no lone pair left and carries a positive charge.



The Purpose of the Reaction : A neutral amine group (NH_2 or NR_2) is a very poor leaving group. It acts as a base, not a leaving group. By converting it into a Quaternary Ammonium Salt ($NR4^+$), the nitrogen becomes a better leaving group (neutral amine leaves upon elimination).This is used in Hofmann elimination reaction

HOFMANN ELIMINATION.

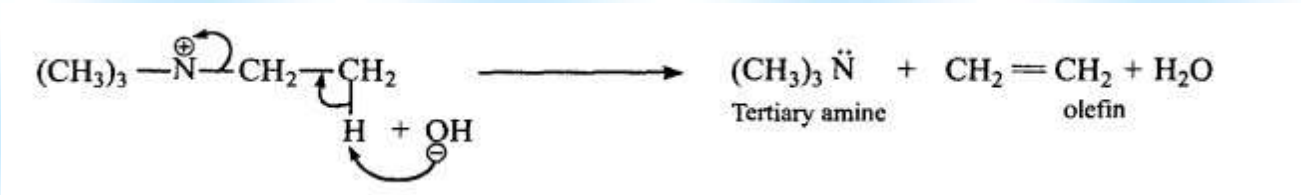
When tetraalkylammonium halide is heated with moist silver oxide, it gives quaternary ammonium hydroxide which is strongly basic like NaOH or KOH. Quaternary ammonium hydroxides on strong heating undergo ß-elimination to give an alkene, the reaction is called Hofmann elimination. The least substituted alkene is obtained as major product (in contrast to Saytzeff elimination)



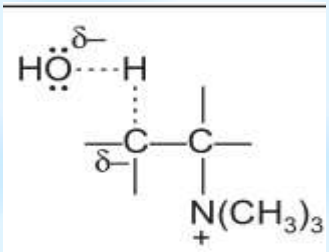
Hofmann Rule

When two possible alkenes are obtained by the elimination reaction then that alkene will be in good yield which contains minimum of alkyl groups or more no of hydrogens on doubly bonded Carbon-atoms i.e. less substituted or less stable alkene is major product.

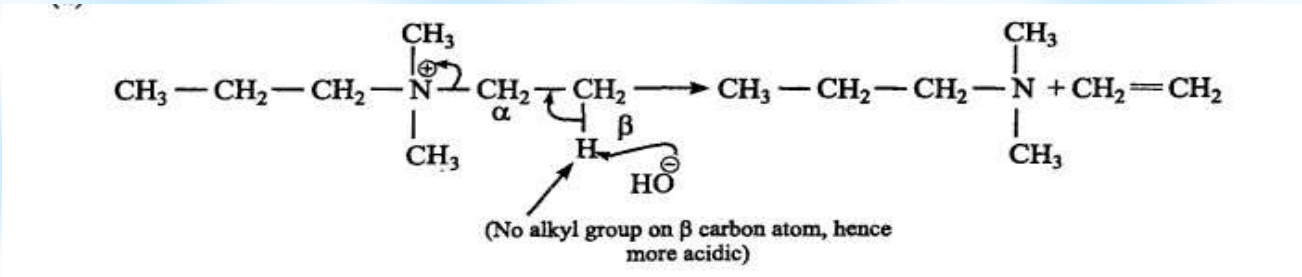
Mechanism: It is a E_2 Elimination is a second order reaction it is first order with respect to ammonium ion and in hydroxy ion. Thus the general mechanism is the hydroxide ion removes the hydrogen from the carbon, creating a double bond and separating the tertiary amine from rest of the molecule



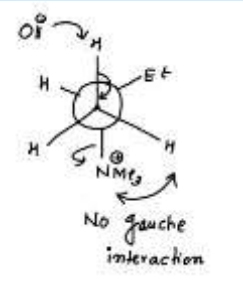
It involves carbanion like transition state



Why less substituted alkene or Hofmann product favours due to acidity of β hydrogens(β hydrogens with no alkyl groups are more acidic) and anti periplanarity of β hydrogens and $N^+(CH_3)_3$ stereochemical conditions

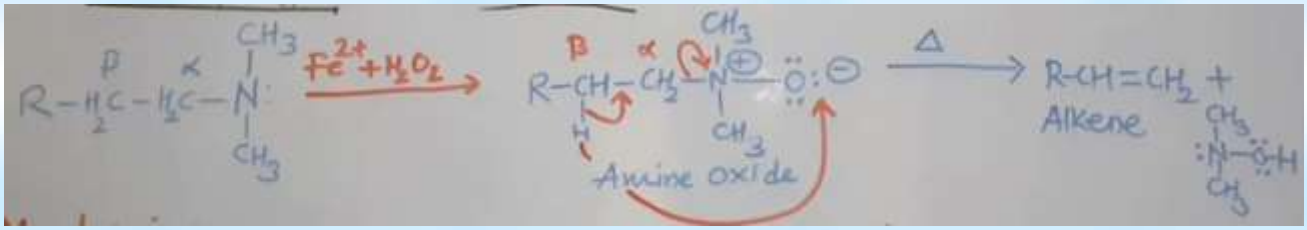


the stereochemical requirement is that the β hydrogen and $N^+(CH_3)_3$ are at 180° to avoid steric interactions

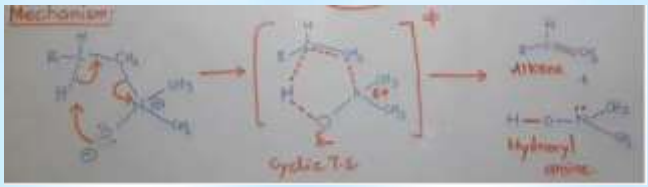


COPE ELIMINATION:

The Cope elimination is a thermal(150°C) elimination reaction used to convert amine oxides (N-oxides) into alkenes and dialkylhydroxylamines.



The reaction begins with a tertiary amine, which is treated with a peracid (such as m-CPBA or meta-chloroperbenzoic acid) or hydrogen peroxide (H_2O_2) This oxidation step creates the N-oxide. the Cope elimination proceeds through a five-membered cyclic transition state through Syn-Elimination , meaning the leaving group and the β-hydrogen must be on the same side of the molecule (syn-periplanar orientation). The reaction does not require an external base because the oxygen atom of the N-oxide itself acts as the base to grab the β-proton to give alkenes and dialkylhydroxylamines



- The Cope elimination is highly regioselective and generally yields the Hofmann product (the less substituted alkene)
- Polar Solvents like water or alcohols decrease the reaction rate because they form hydrogen bonds with the N-oxide, requiring higher temperatures
- Polar aprotic solvents such as DMSO or THF are preferred as they increase the rate of reaction, allowing it to occur at or near room temperature
- This reaction is stereospecific, starting material stereochemistry is retained in the product

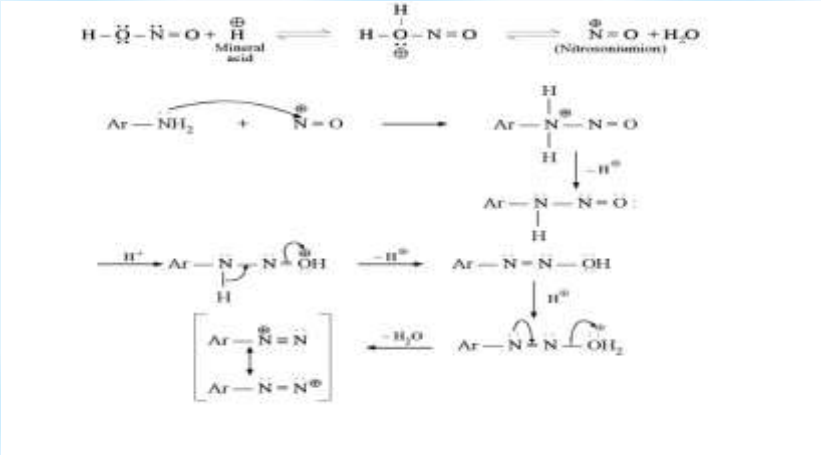
Preparation of Diazonium Salts:

Diazonium salts are aromatic organic compounds containing – N_2X group where X is halogen. The name diazo stands for two nitrogens. The word onium is obtained from ammonium as these compounds resemble ammonium salts in some respects.

Aromatic Diazonium salts ($Ar\ N^+_2\ X^-$) are highly reactive compounds which serve as intermediates in the synthesis of a wide variety of aromatic compounds

Diazonium salts are prepared by reaction between aromatic primary amine and nitrous acid obtained from sodium nitrite and dil. hydrochloric acid at 273-278K .

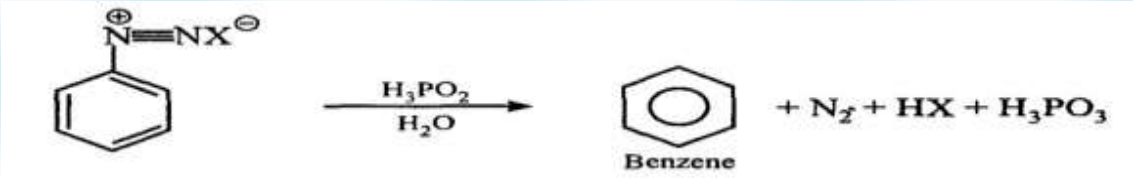
Mechanism of diazotisation. It is believed that the amine molecule undergoes nucleophilic attack by Nitrosonium ion obtained from nitrous acid.



Synthetic applications of Diazonium salts

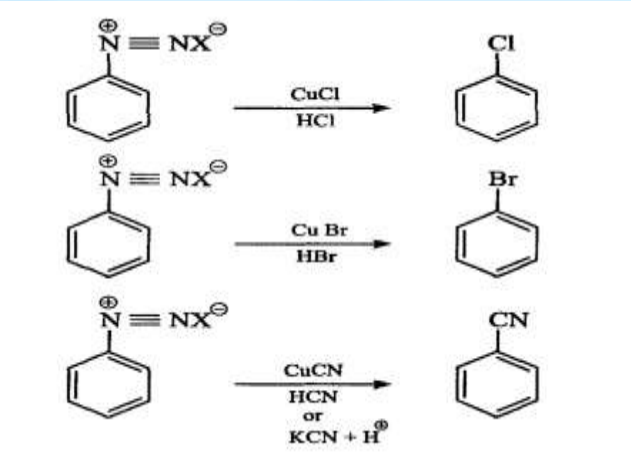
PREPARATION OF ARENES

The reaction of a diazonium salt with certain reducing agents, particularly hypo phosphorous acid (H_3P0_2), results in the replacement of the diazonium group by hydrogen to give arenes



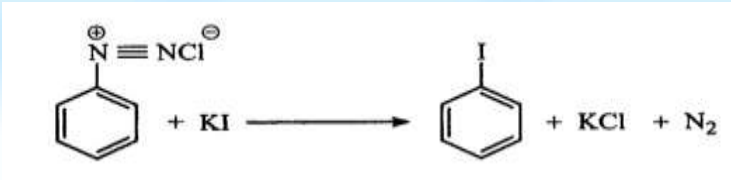
PREPARATION OF CHLORO, BROMO AND CYANO COMPOUNDS

Sandmeyer Reaction: The diazonium group can be replaced by chloro, bromo or a cyano group. The replacements proceed in the presence of the corresponding cuprous salts dissolved in corresponding halogen acids. The Sandmeyer reaction is not useful for the preparation of fluorides or iodides



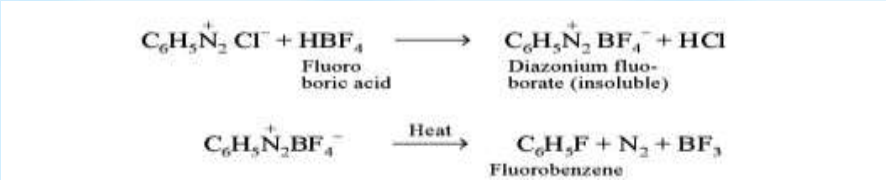
PREPARATION OF IODO COMPOUNDS

Solution of diazonium salt reacts with aqueous sodium or potassium iodide to give aryl iodides. This reaction is the most useful method of preparing aryl iodides including iodobenzene.



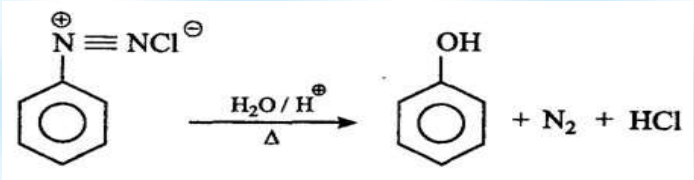
PREPARATION OF FLURO COMPOUNDS

Schiemann reaction : Aqueous HBF_4 precipitates diazonium cations as the relatively insoluble diazonium salts, diazonium fluoroborate. On gentle heating in absence of solvent they decompose to give aryl fluorides.



PREPARATION OF PHENOLS,

Heating of an aqueous acid solution of diazonium salt causes liberation of nitrogen and the formation of phenol.



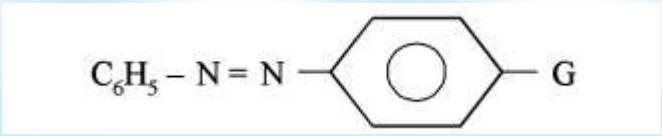
PREPARATION NITRO COMPOUNDS

substitution by nitro group is achieved by decomposing diazonium fluoborate with sodium nitrite solution in the presence of copper powder.

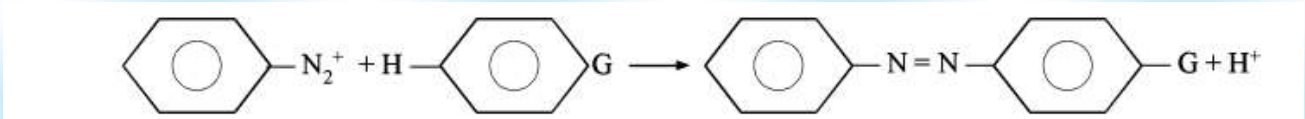
COUPLING REACTION

Diazonium salts which are electrophilic in nature attack aromatic amines and phenols (strong electron releasing groups like OH,NHR etc), preferably at the para position, to give azo compounds which are coloured (dye). This reaction is known as "coupling reaction" (N-N bond between two aromatic rings) and thousands . azo compounds have been synthesised by this method for use as synthetic dyes. Azo group creates extended conjugation thus lowering the HOMO–LUMO gap and absorbs visible light. Electron-donating substituents makes bathochromic shift (red shift) which gives deeper colours

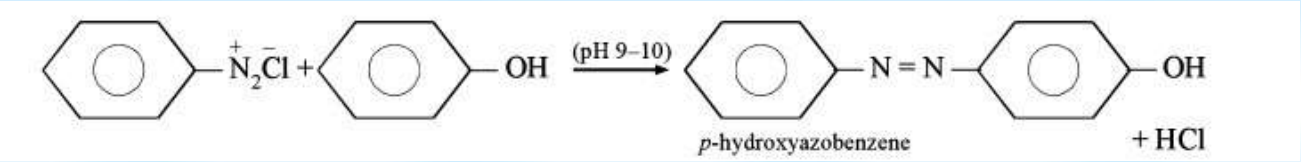
Their general formula is



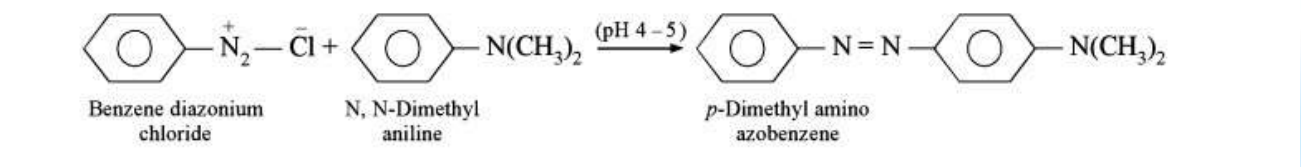
the coupling reaction in general may be written as



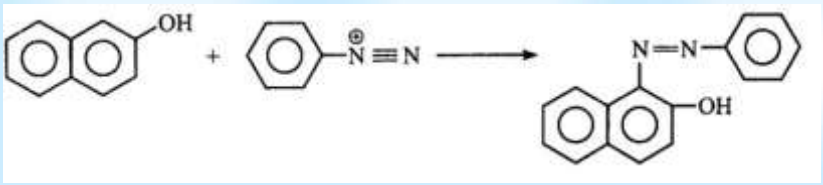
Coupling with phenol: Benzene diazonium salt reacts with phenol in weakly alkaline solution to form (orange dye) hydroxy azo compound.



Coupling with tertiary amine: This coupling takes place in acidic solution. Diazonium salt reacts with tertiary amine to form (yellow c dye) dialkylamino azo compound.



Coupling with β-naphthol: This coupling takes place in acidic solution. Diazonium salt reacts with β-naphthol to form (red dye) azo β-naphthol compound. The attack takes place in 1st carbon (ortho position) of the right ring which is more electron rich (C1-C2 more double bond character than C2-C3)



Note :

- P^H maintenance is important for coupling reactions for phenols slightly basic and for amines slightly acidic P^H shall be maintained to activate the reaction
- the coupling usually occurs at p-position with respect to activating group (NH_2, OH). In case the para position is occupied then the coupling may occur at o-position. If both the ortho and para positions are occupied, then generally the coupling does not take place

IMPORTANT QUESTIONS

UNIT–I : AMINES

Long Answer (10 Marks)

1. Explain the preparation of amines by Gabriel synthesis and Hoffmann bromamide reaction with mechanisms.

2. Define diazotization reaction ? How can you prepare Chloro, Fluoro and Iodo benzenes?

3. Distinguish between primary, secondary and tertiary amines using Hinsberg's method and nitrous acid test.

Short Answer (5 Marks)

4. Write a note on Schmidt reaction.

5. Explain Carbylamine reaction.

6. Write a note on Hofmann elimination.

7. Discuss Coupling reactions

MAJOR-11: NITROGEN CONTAINING ORGANIC COMPOUNDS & SPECTROSCOPY

UNIT- II :: Amino acids

(9 h)

Definition and classification of Amino acids into alpha, beta, and gamma amino acids. Natural and essential amino acids - definition and examples, classification of alpha amino acids into acidic, basic and neutral amino acids with examples. Methods of synthesis: a) from halogenated carboxylic acid, b) Gabriel Phthalimide synthesis c) Strecker's synthesis. Physical properties: Zwitter ion structure - salt like character - solubility, melting points, amphoteric character, definition of isoelectric point. Chemical properties: General reactions due to amino and carboxyl groups - lactams from gamma and delta amino acids by heating peptide bond (amide linkage). Structure and nomenclature of peptides and proteins.

Definition: Amino acids are organic compounds that contain at least one amino group ($–NH_2$) and at least one carboxyl group (–COOH) in the same molecule. They are the basic building blocks of proteins

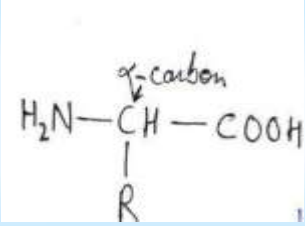
Physical properties of amino acids:-

- Amino acids are colourless salt like crystalline solids.
- They have high melting points and decompose before melting
- They are soluble in polar solvents but insoluble in organic solvents.
- Their aqueous solution exhibit dipole moments.

classification of Amino acids into alpha, beta, and gamma amino acids : Classification depends on where the amino group is attached next to the carboxyl group or with gap of one or two carbon groups

Alpha amino acids: $–NH_2$ group attached to the α-carbon (carbon next to –COOH) .

General formula R–CH(NH_2)–COOH . All protein amino acids are α-amino acids.



R= H ≈ Glycine

= CH3 ≈Alanine

= OH ≈ Serine

= CH2-SH ≈ Cysteine

β-Amino Acids: $–NH_2$ group on the β-carbon (second carbon from –COOH)

H_2N-CH_2CH_2 COOH → 2-Aminoethanoic arid or β-Amino Acid

γ-Amino Acids: $–NH_2$ group on the γ-carbon

H_2N- CH_2 CH_2 CH_2 COOH → 3-Aminoethanoic arid or γ -Amino Acid (GABA)

Natural (Non-Essential) amino acids : Out of 20 Amino acids 11 Natural Amino acids found in proteins of our body or living organisms. These can be synthesized by our body or living organisms from glucose intermediates, simple nitrogen sources. They are called non-essential not because they are unimportant, but because dietary supply is not compulsory under normal conditions. They are required for to remove toxins from the body and to produce red and white blood cells in the body . Six of these non-essential acids are also

known as “conditional,” meaning that the body may not be capable of producing enough of them when presented with inflammation or illness These are arginine, cysteine, glycine, glutamine, proline, and tyrosine

Examples: Glycine, Alanine, Valine, Lysine, Aspartic acid.

Essential amino acids : 9 Amino acids which are very important or essential for growth of humans and animals are called essential amino acids. These amino acids cannot synthesized by the human body and must be obtained from diet. They are essential not because they are the only amino acids required for human functioning, but because they are essential in the diet of the human. Lack of these amino acids in the diet may cause the disease Kwashiorkor (Oedema ,Growth failure,)

Sources: complete proteins such as eggs, milk, meat, fish, cereals , pulses

Examples: Histidine, Valine ,Leucine, Isoleucine, Lysine ,Methionine ,Phenylalanine ,Threonine and Tryptophan.

Classification of alpha amino acids into acidic, basic and neutral amino acids with examples:

Neutral Amino Acids: The amino acids in which equal number of Amino and Acid as are present

Ex: glycine. NH_2 -CH_2- COOH Equal No of NH_2 = Equal No of COOH

Basic Amino Acids: The amino acids in which a greater number of Amino groups than Acid group

No of NH_2 > No of COOH NH_2 -$(CH_2)_4$- CH- COOH (Lycine)

NH_2

Acidic Amino Acids: The amino acids in which a greater number of Acid groups than Amino group

No of COOH > No of NH_2 COOH- CH_2- CH- COOH (Aspartic Acid , Artificial Sweetener)

NH_2

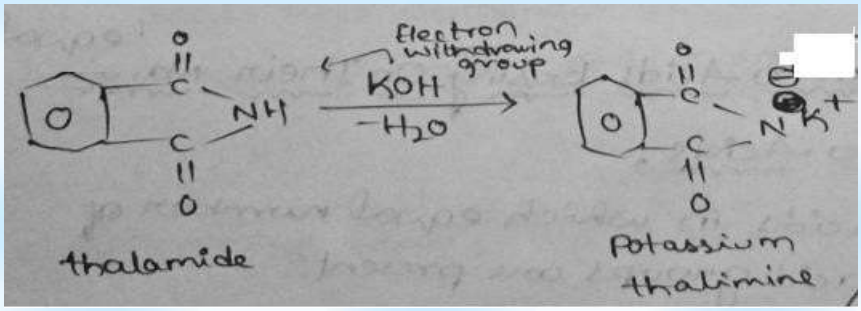
Methods of synthesis: a) from, b) c)

Halogenated carboxylic acid :Treatment of α Chloro or α Bromo acids with ammonia or ammonium hydroxide gives amino acids. A conc. solution of ammonia is needed to obtain a good yield of the amino acid

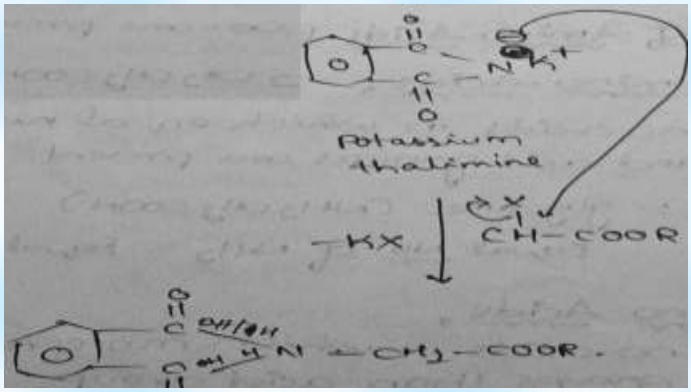
$$R\text{-}\underset{\displaystyle Cl}{\underset{|}{CH}}\text{-}COOH \xrightarrow{NH_3} R\text{-}\underset{\displaystyle NH_2}{\underset{|}{CH}}\text{-}COOH$$

Gabriel Phthalimide synthesis: In this method, potassium salt of phthalimide is made to react with an α - haloester and the product is hydrolyzed to get the amino acid.

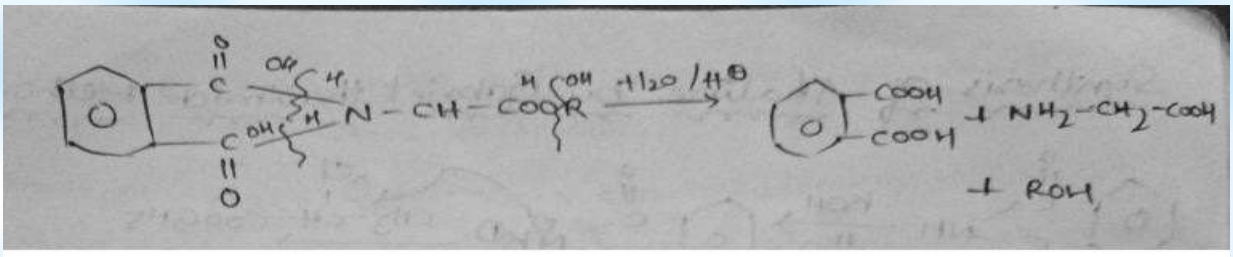
Pthalamide is reacted with potassium hydroxide to get potassium Pthalimide



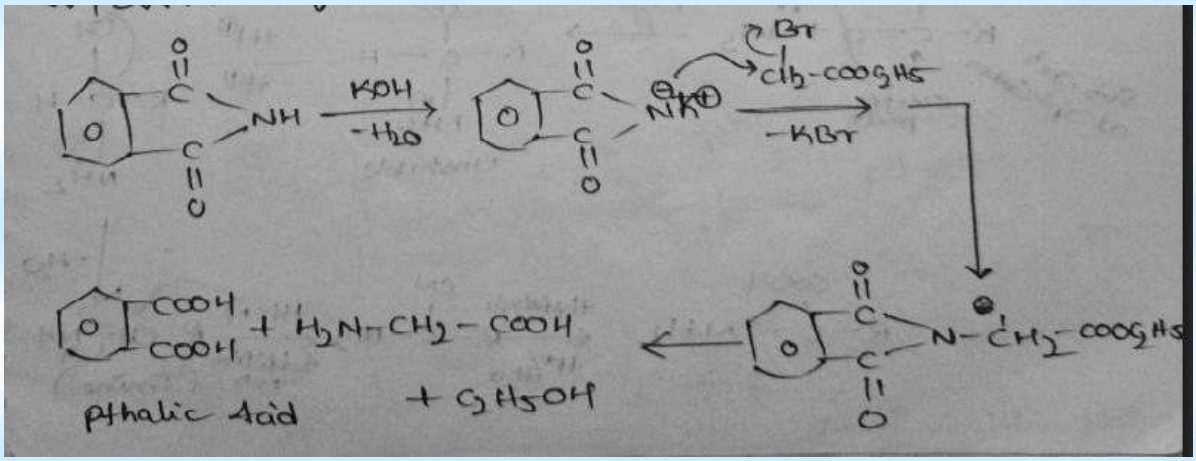
which attacks the α haloesters to get substituted Pthalimide



which on acidic hydrolysis gives Amino Acid

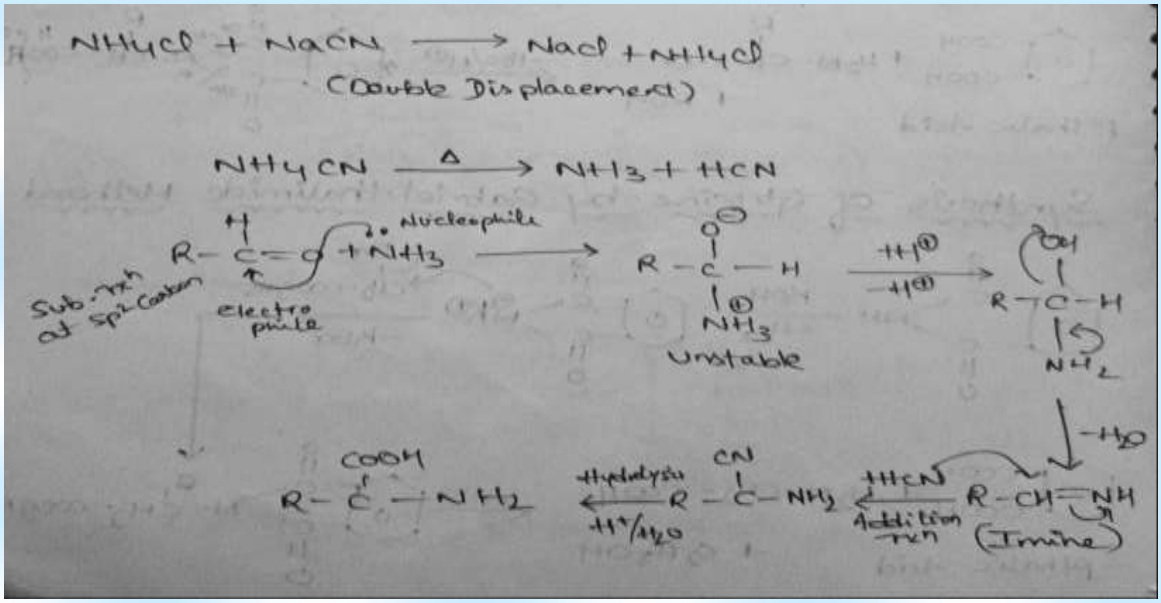


Synthesis Glycine Gabriel Pthalimide Method



Strecker's synthesis : In these successive reactions occurs between Aldehyde, NH_4Cl, NaCN to give α Amino acids

NH_4Cl and NaCN undergoes double decomposition to give NH_4CN witch on heating gives Ammonia and HCN the Aldehyde reacts with Ammonia to form imine this on addition with HCN followed by hydrolysis gives Amino Acid.



Zwitter ion structure -salt like character - solubility, melting points, amphoteric character:

It has been found that an amino acid molecule appears as a dipole, one end of it carrying positive charge and the other end with negative charge. Amino acids are amphoteric substances. In other words, they can exist as cations or anions. This property results from the presence of both an acidic (-COOH) and a basic (-NH2) functional groups. The dipolar ionic structure of amino acids can be represented as

NH_2-CH-COOH ↔ $^+NH_3$-CH-COO^-

R R

This is also called a Zwitter ion or Internal salt. There is no free amino or carboxylic group present in the molecule.

This is supported by the following evidence:

1. Amino acids are insoluble in non-polar solvents and soluble in polar solvents like water. This behaviour can be expected of the polar substances.
2. Amino acids are non-volatile crystalline solids, which melt at high temperature. This is quite like ionic substances which have high melting points and unlike amines and carboxylic acids which have low melting points.
3. They have high dipole moments indicating polar nature of the molecule.

4. Dissociation constant K_a and K_b, give us an idea about the acid and base strengths. Amino acids have very low values of K_a and K_b, indicating that the molecule does not possess these groups (NH_2 & COOH) in the normal forms

5. Spectroscopic studies of amino acids do not show bands characteristics of NH_2 & COOH groups

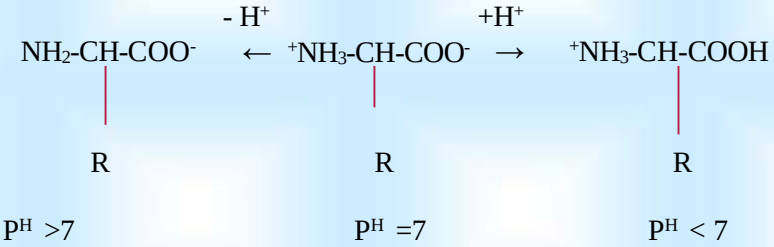
Definition of isoelectric point : As amino acids are polar in nature, they show electrical properties. On applying electrical field to the solution of an amine acid, they migrate to one or the other end electrode depending on the following factors

a) If the solution of amins aid is acidic. amino acid behaves as cation I so it migrates towards cathode (-vely charged electrode).

b) If solution is basic Amino acid behave as anion It will move towards Anode (+vely charged electrode)

At certain P^H of solution of amino acid, the cationic and anionic structures will be in equal concentrations and on parsing electricity we shall observe that there is no movement of amino acid.

"The P^H at which a particular Amino acid does not migrate under the influence of the electrical field is called isoelectric point"

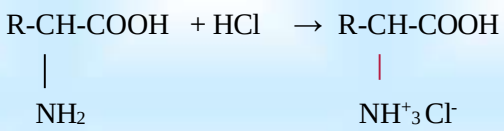


Electrophoresis is a process of separation and purification of compounds based on movement of charged particle (amins acid) in an electric field. Separation of mixture of amino acids can be brought about by electrophoresis.

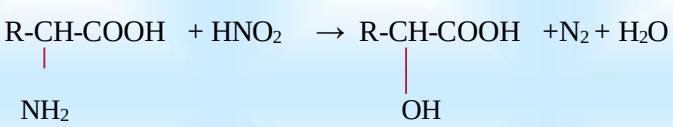
Isoelectric Point $P^I = \frac{Ka+kb}{2}$

Chemical properties: General reactions due to amino and carboxyl groups

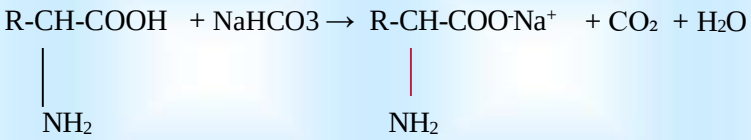
1. Basic nature:- Amino acids act as weak bases and hence react with strong mineral acids to form salts



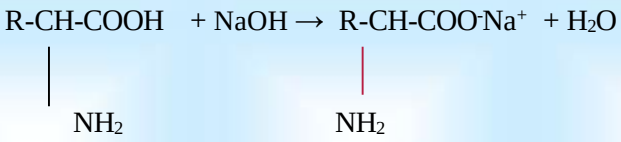
2. Action with Nitrous acid: This reaction forms a basis of well-known Van Slyke method for estimation of amino acids



3. Acidic nature : Amino acids show acidic character due to presence of a carboxylic group. This becomes by evolution of CO_2 when an aqueous solution of amino acid is treated with $NaHCO_3$

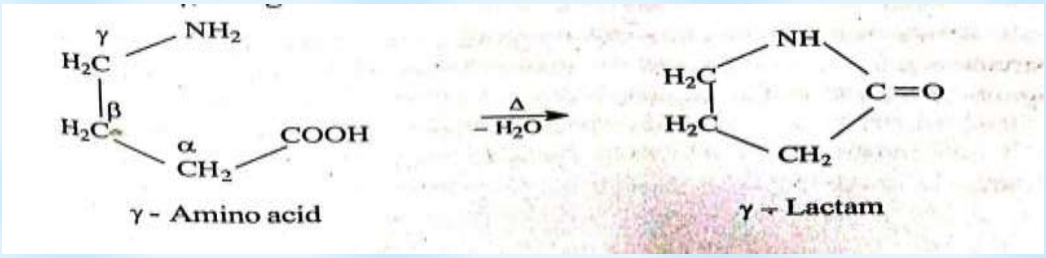


Amino acids react with base to form salts.

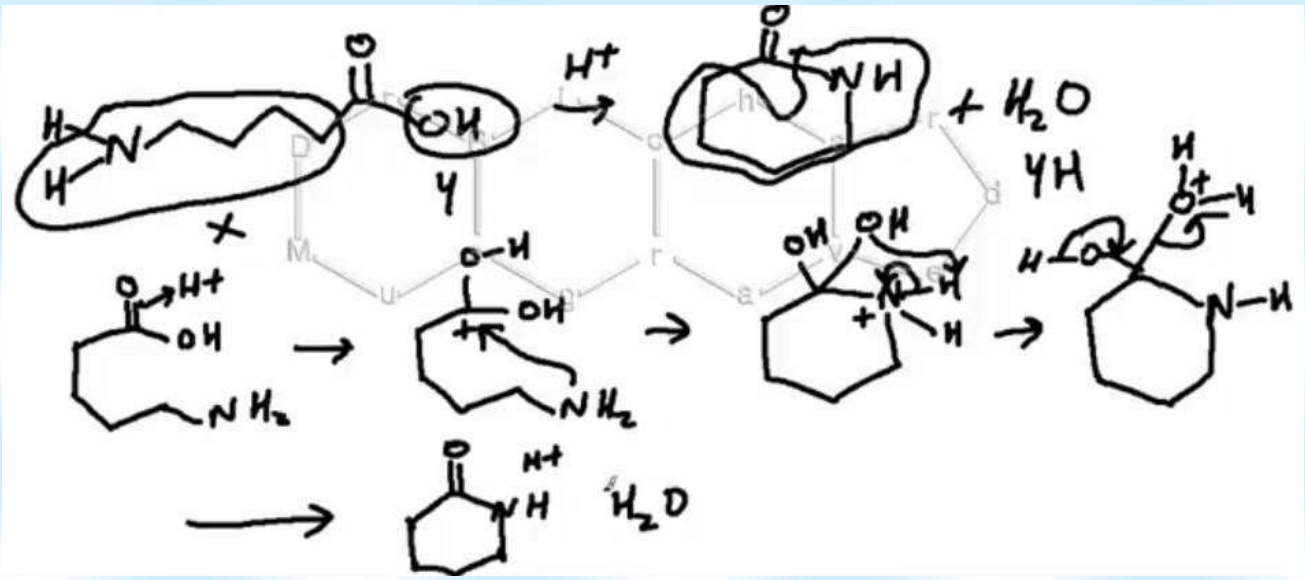


lactams from gamma and delta amino acids by heating : on heating γ and δ amino acids when heated, lose water form - COOH and NH, groups in the same molecule and cyclic amides are formed. The cyclic amides are called lactams. If the number of atoms in ring is 5 or 6, that ring will be stable. γ, δ rings are thus stable rings. They are highly stable at high temperatures, often exceeding 450–500°C.

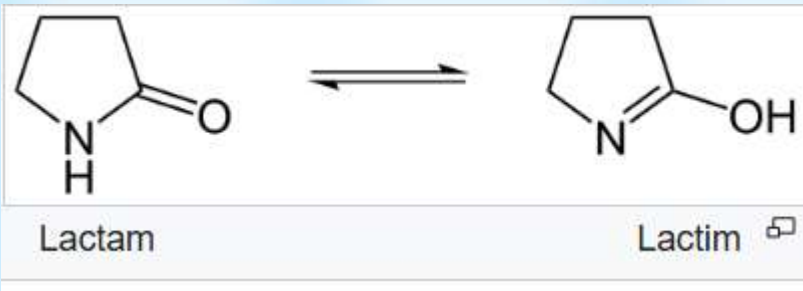
Antibiotics known as beta-lactams are used to treat and manage bacterial infections.



δ amino acids (5-aminopentanoic acids) readily cyclize to form 6-membered δ lactams (piperidones) through intramolecular amide formation, usually requiring activating agents like carbodiimides (e.g., DCC, HATU) to drive the condensation of the carboxylic acid and amine. .

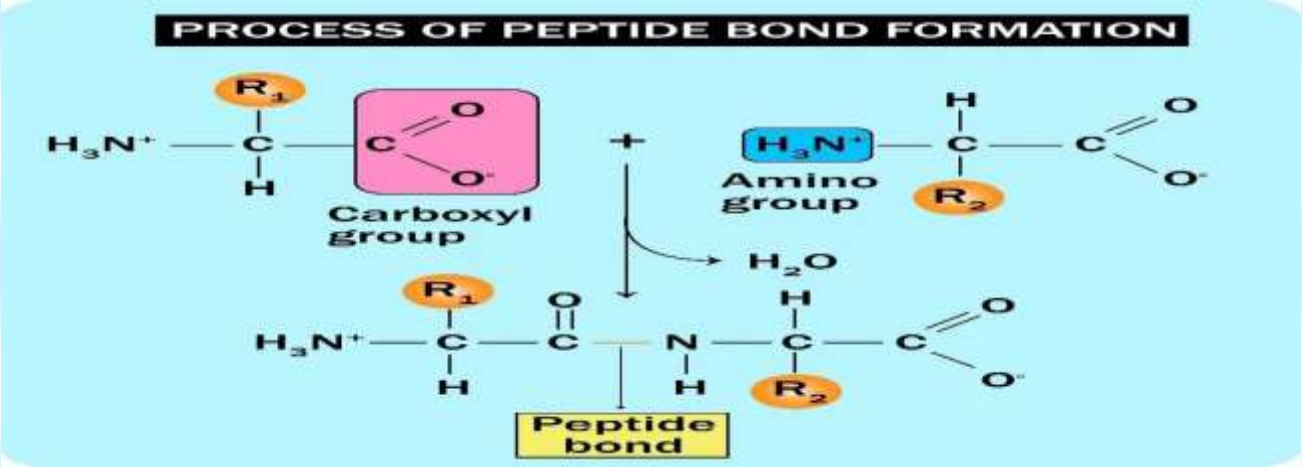


lactim is a cyclic imidic acid compound characterized by an endocyclic carbon-nitrogen double bond. They are formed when lactams undergo tautomerization

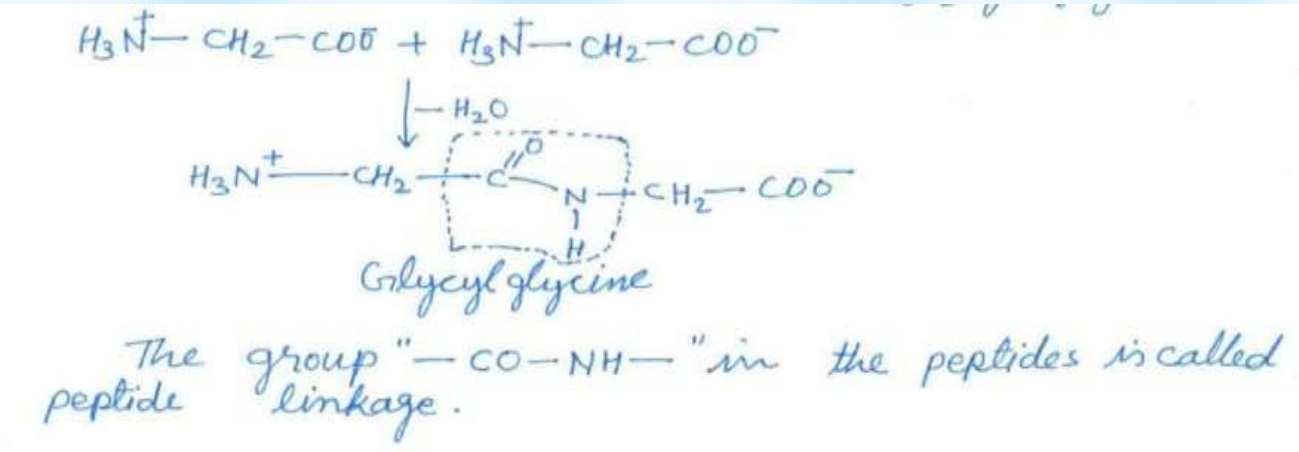


peptide bond (amide linkage). Structure and nomenclature of peptides

Peptides are amides obtained by interaction between the amino and carboxylic groups two or more amino acid molecules. When two amino acids join, they perform a "dehydration synthesis" (or condensation) reaction. The Carboxyl group of one amino acid reacts with the Amino group of the next .A molecule of water (H_2O) is released. The resulting covalent bond is called a Peptide Bond (-CONH-).



Two molecules of glycine, for example, combine to form ide substance known as glycyl glycine



The amide linkage in this type of polymer is called a peptide bond or a peptide linkage.

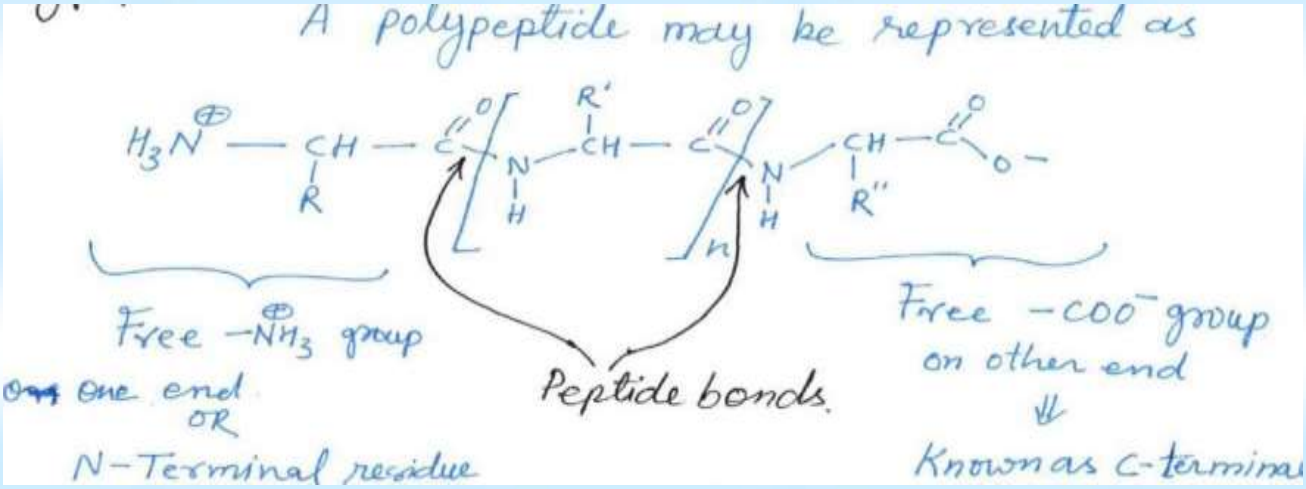
Structure and nomenclature of peptides: Peptides are classified as under

Dipeptide. A peptide obtained by the condensation of two amino acid molecules is called dipeptide.

Tripeptide. A peptide obtained by the condensation of three amino acid molecules is called tripeptide.

Tetrapeptide. A peptide obtained by the condensation of four amino acid molecules is called tetrapeptide.

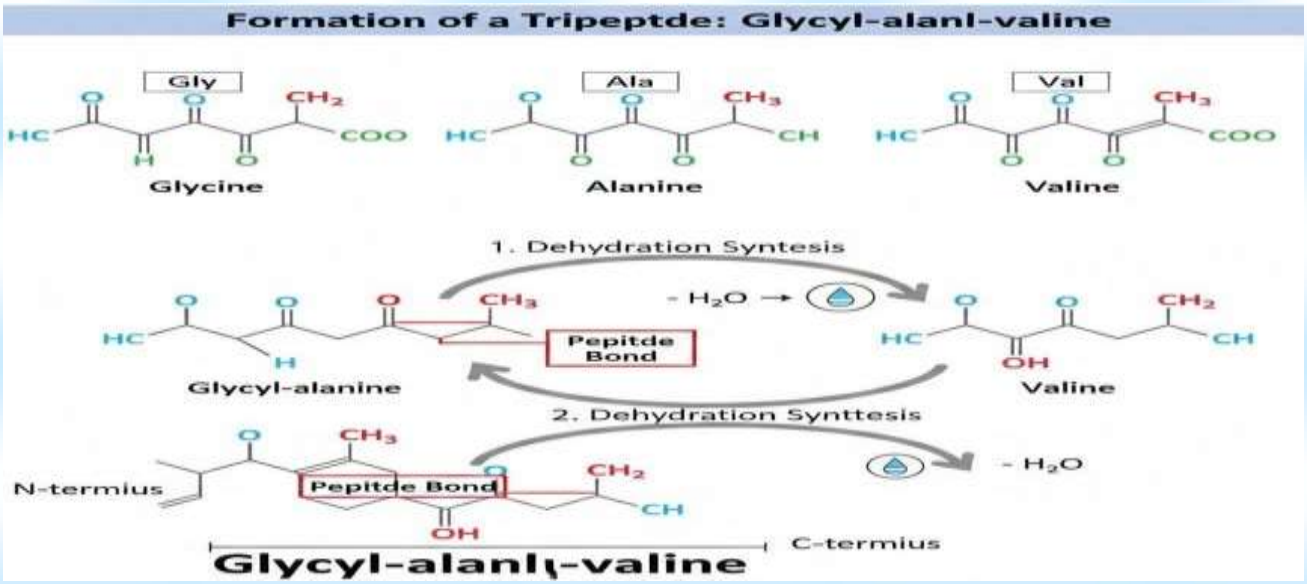
Polypeptide. A peptide obtained by the condensation of more than four amino acid molecules is called polypeptide. A polypeptide may be represented as



Nomenclature (Naming) Rules :When we name these chains, we follow a specific "left-to-right" logic:

Directionality: We always read from the N-terminus (the end with the free amino group) to the C-terminus (the end with the free carboxyl group). The "-yl" Suffix: For every amino acid in the chain except the last one, we change the ending of its name to -yl.

Example: A chain of Glycine + Alanine + Valine becomes Glycyl-alanyl-valine.

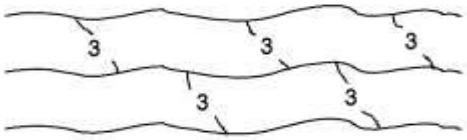


Structure and nomenclature of proteins:

A protein is typically a long polypeptide chain (often hundreds or thousands of amino acids long) that has folded into a specific, functional 3D shape. Proteins are complex organic compounds essential for growth and maintenance of life. These are nitrogenous compounds obtained from a-amino acids. They are the constituents of all living organisms and found in every part of plants and animals. They are present in muscles, skin, hair, nails, blood, tendons, and arteries. All proteins are mixed polymers of amino acids and as such all contain carbon, hydrogen, oxygen and nitrogen. Most contain Sulphur.

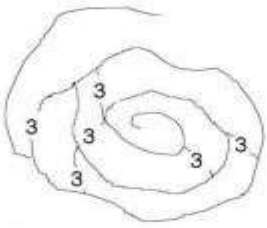
Proteins are classified into two types based on structure:

(a) Fibrous proteins. These proteins consist of thin linear molecules which lie side by side to form fibers. Intramolecular hydrogen bonding holds the peptide chain together. Fibrous proteins are insoluble in water.



Structure of fibrous proteins

Globular proteins. In these proteins, polypeptides are folded into compact spheroidal shapes. Intramolecular hydrogen bonding holds the peptide chain in shape in such proteins. These are soluble in water or aqueous solutions of acids and bases.



Structure of globular proteins

Nomenclature of Proteins : Naming full proteins is different from naming small peptides. Because they are so large, we don't name every single amino acid (like "glycyl-alanyl..."). Instead, Common Names, Most proteins have functional or historical names (e.g., Insulin, Hemoglobin, Keratin).

The "-ase" Suffix: If the protein is an enzyme (it speeds up a reaction), its name usually ends in -ase (e.g., Lactase, DNA Polymerase).

Subunit Naming: For Quaternary structures, subunits are often labeled with Greek letters (e.g., Hemoglobin has two α -chains and two β chains).

Denaturation. Proteins are very tender and delicate substances. When subjected to heat or action of acids or alkalis, they lose their biological activity. They are said to be denatured. This phenomenon in which the proteins lose their biological activity and other characteristics under the effect of temperature, is called denaturation.

The denatured proteins can be brought back to its original state by cooling the protein solution very slowly.This process is called renaturation. During denaturation, there is a rearrangement in the secondary and tertiary structure of the protein, but the primary structure remains unchanged .

QUESTION BANK

Long Answer Questions (10 Marks)

1. Describe any two methods for the synthesis of α-amino acids:

a) Gabriel phthalimide synthesis b) Strecker's synthesis

2. Discuss the physical properties of amino acids, with special emphasis on:

a) Zwitterion structure b) Isoelectric point

3. Explain the structure and naming of peptides and proteins and describe how the peptide bond is formed.

Short Answer Questions (5 Marks)

1. Define essential amino acids and give two examples.

2. Classify α-amino acids as acidic, basic, or neutral, with examples.

3. Explain how amino acids are prepared from halogenated carboxylic acids.

4. Describe the effect of heat on γ- and δ-amino acids, leading to lactam formation.

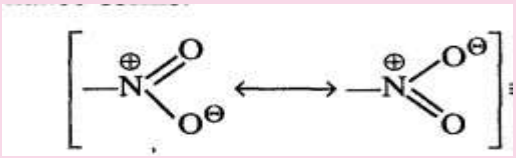
5. Define the isoelectric point and explain the amphoteric nature of amino acids.

UNIT- III :: Nitro hydrocarbons (9 h)

Nomenclature and classification, structure -Tautomerism of nitroalkanes leading to acid and keto form, Preparation of Nitroalkanes, reactivity - halogenation, reaction with HONO (Nitrous acid), Nef reaction and Mannich reaction and reduction.

INTRODUCTION : Nitroalkanes are nitro derivatives of hydrocarbons obtained by the replacement of a hydrogen atom by a nitro-group. The nitro-group is electronically similar to the carboxylate anion and can exist in two equivalent resonance forms.

STRUCTURE : Nitro group may be regarded as resonance hybrid of two equivalent contributing forms. The two resonating structures have equal energies. This imparts extra stability to the structure of nitro group.



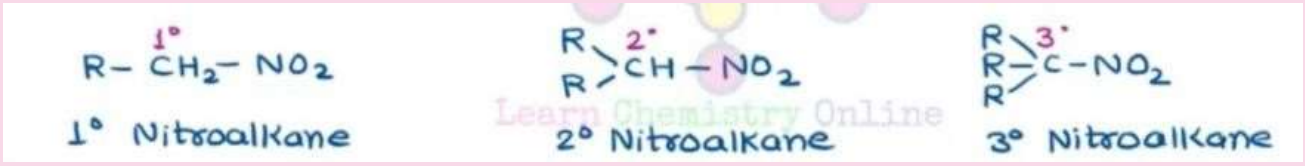
NOMENCLATURE : Nitro compounds are named by writing the word nitro before the name of parent Compound. Nitro compounds may be divided into two categories viz., aliphatic nitro compounds and aromatic nitro compounds. The nomenclature of compounds from both categories is given below

CH_3NO_2 Nitro Methane

$CH_3CH_2NO_2$ Nitro Ethane

$C_6H_5NO_2$ Nitro Benzene

CLASSIFICATION: Nitroalkanes are further classified as 1^0, 2° and 3^0 according as the Nitro group is attached to 1^0, 2° and 3^0 carbon atoms.



TAUTOMERISM OF NITROALKANES LEADING TO ACID AND KETO FORM :

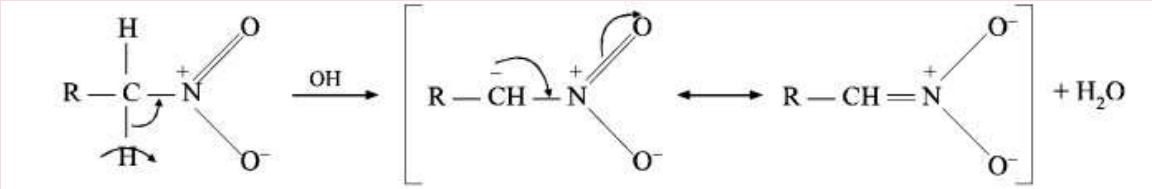
Tautomerism In solution the nitro form is in equilibrium with aci-nitro form. The aci-nitro form is acidic in nature and hence nitro methane is soluble in alkalis. Primary and secondary nitroalkanes exhibit tautomerism, the tautomeric forms being nitro form and aci-nitro form

Thus, Nitroalkanes containing α-hydrogen atom exhibit acidic behaviour and form salts with strong alkalis.

$$RCH_2NO_2 + NaOH \rightarrow [RCHNO_2]^-Na^+ + H_2O$$

Nitroalkanes containing α -hydrogens are much stronger acids than aldehydes, Ketones, esters, and nitriles.

Acidic nature of a-hydrogen containing nitroalkanes is due to the electron-withdrawing inductive effect (-I effect) of $-NO_2$ group. Also, the resulting anion, usually referred to as nitronate ion obtained after releasing one proton gets resonance stabilized.



PREPARATION OF NITROALKANES:

From alkyl halides: They are prepared by heating an alkyl halide with aqueous ethanolic solution of silver nitrite.

$$R\text{-}X + AgNO_2 \rightarrow R\text{-}NO_2 + AgX$$

This method is useful only for the preparation of primary nitroalkanes.

$$CH_3Br + AgNO_2 \rightarrow CH_3\text{-}NO_2 + Ag\ Br$$

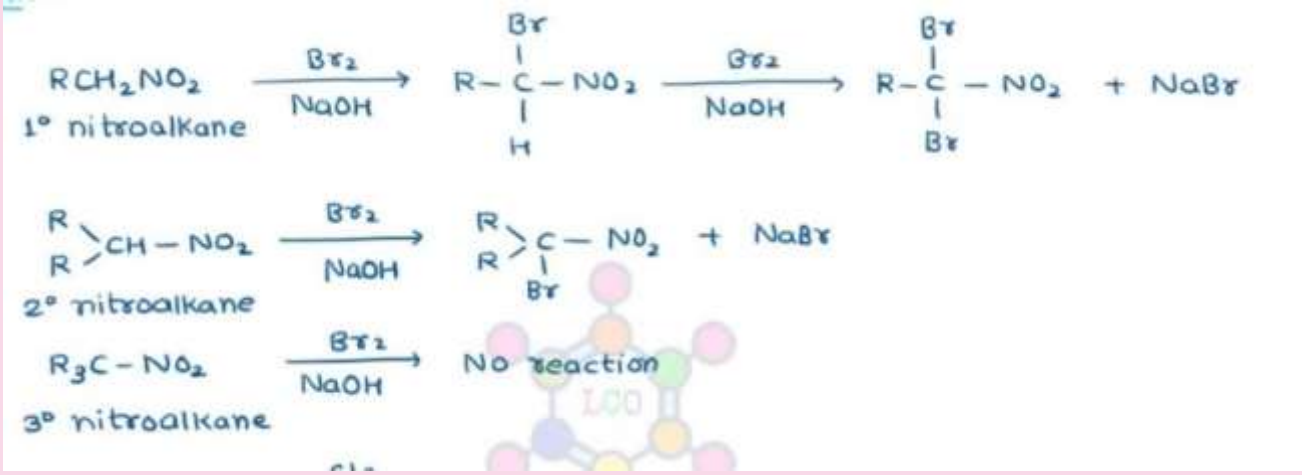
From alkanes: Higher alkanes can be readily nitrated with fuming nitric acid. However, the lower hydrocarbons can be nitrated only in vapor phase at higher temperature to give nitroalkanes.

$$n\text{-}C_6H_{14} + HN0_3 \rightarrow C_6H_{ll}NO_2 + H_2O$$

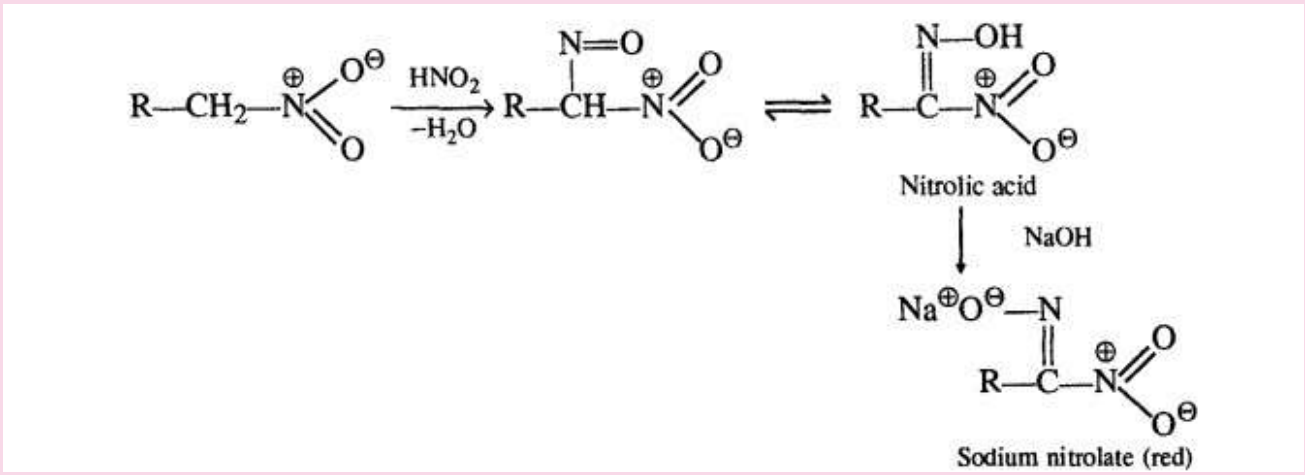
Oxidation of 3°-alkylamines: When tert-alkylamines are oxidised by KMn04, tert-nitroalkanes are formed. $KMnO_4$

$$(CH_3)_3CNH2 \xrightarrow{KMnO_4} (CH_3)_3C\ NO_2$$

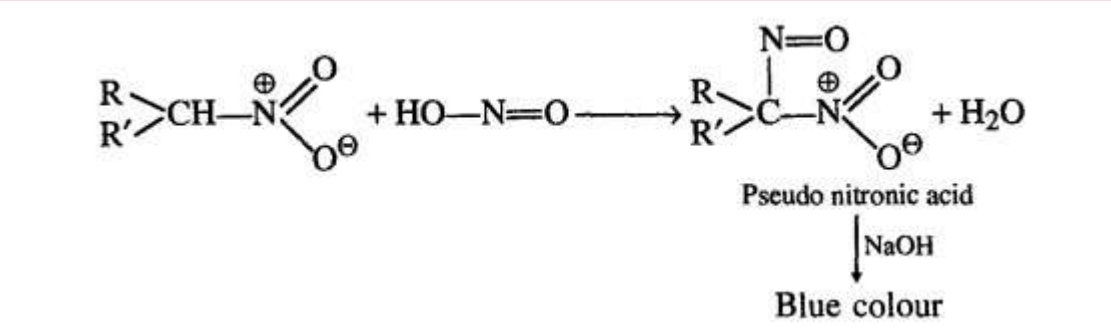
Halogenation: Primary and secondary nitroalkanes are readily halogenated with chlorine or bromine in the presence of base to form chloro or bromo nitroalkanes. During the reaction all α-hydrogens are replaced by halogens.



Reaction with HONO (Nitrous acid) : Nitroalkanes react with nitrous acid producing different . products depending upon the nature of nitro compound. (i) Primary nitroalkanes react with nitrous acid to form nitrolic acids, which gives a red colour with alkali.

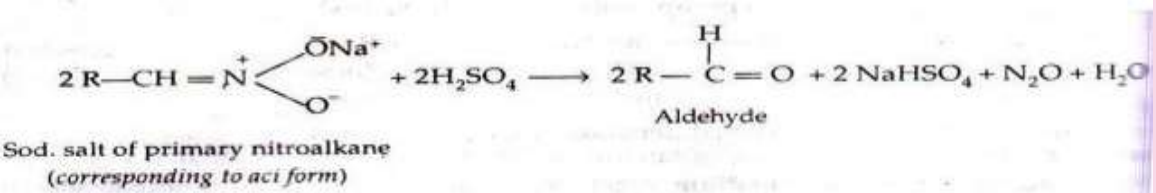


Secondary nitroalkanes produce pseudo nitrols. Pseudo nitrols give blue colour with alkali.

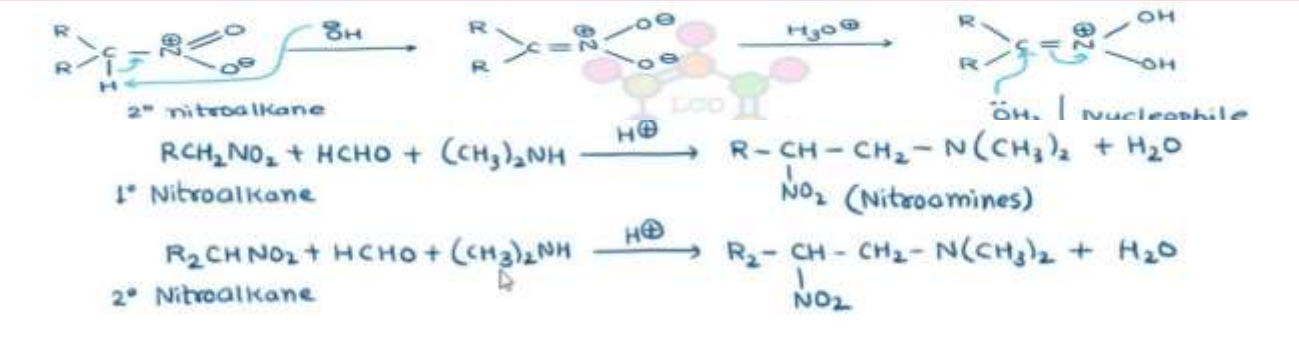


Tertiary nitroalkanes do not react with nitrous acid, as they do not contain a-hydrogen atom. This reaction can be used to distinguish between primary, secondary, and tertiary nitroalkanes.

Nef reaction : When sodium salts of primary and secondary nitro alkanes are hydrolysed with Con sulphuric acid aldehydes and ketones respectively are obtained. The reaction proceeds through aci nitro form of nitro alkanes. This reaction is known as Nef reaction. 1^0 nitroalkanes give aldehydes and 2° nitroalkanes give Ketone

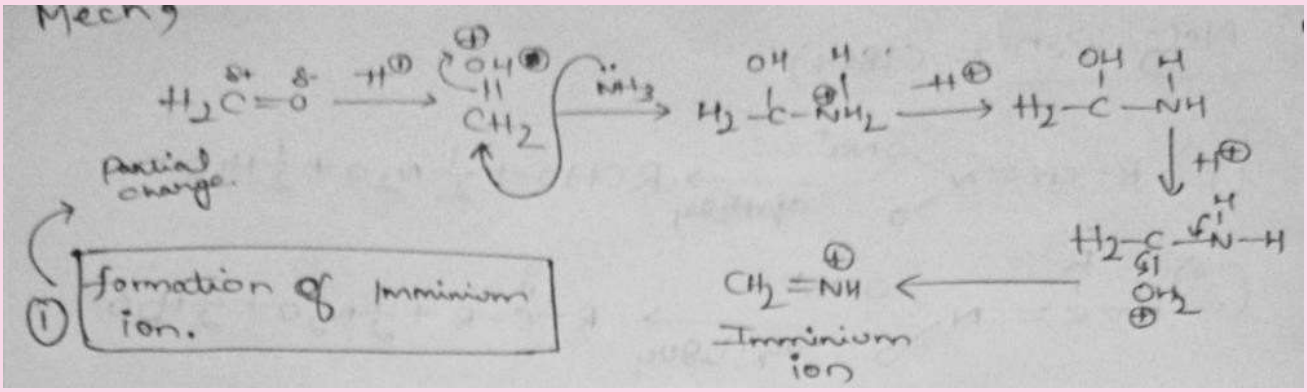


Nitroalkanes are first converted to their sodium salt and then hydrolyzed by concentrated sulphuric acid to aldehydes and ketones.

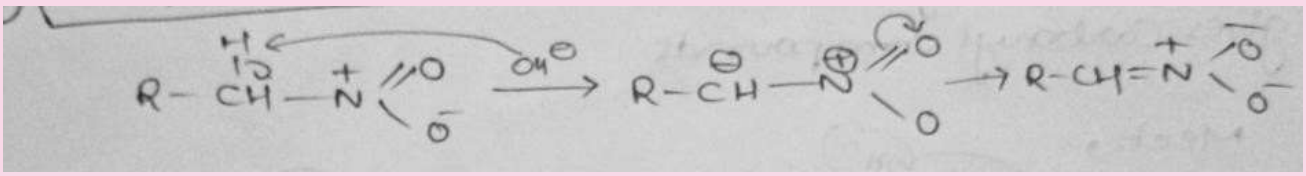


Mannich reaction : This is a condensation reaction which involves HCHO, Ammonia or a primary or secondary amine and a compound with at least one active hydrogen

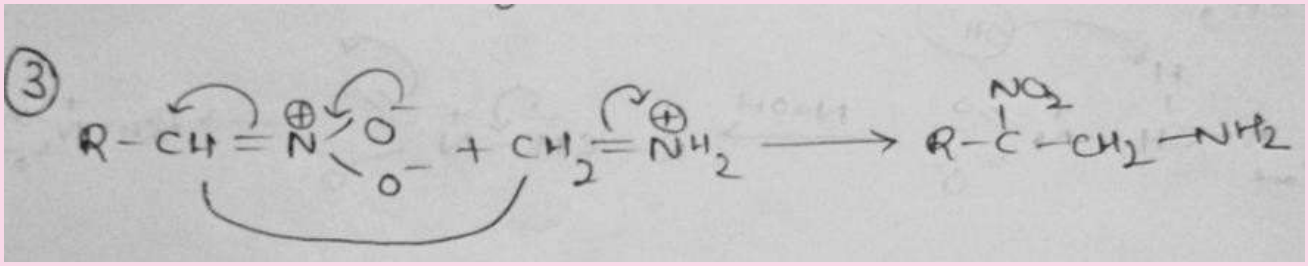
I step Formation of Iminium ion



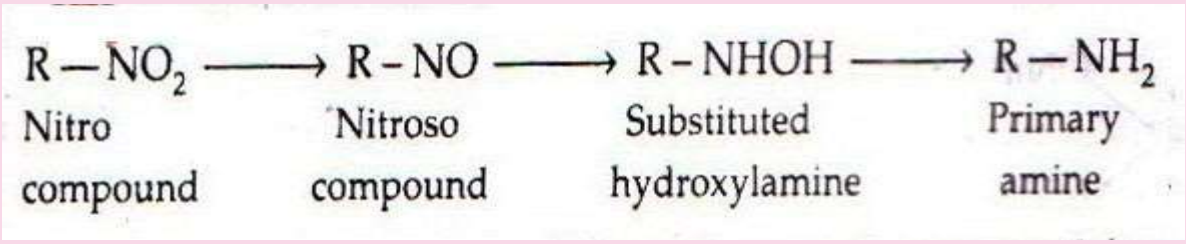
II step generation of Nitro anion



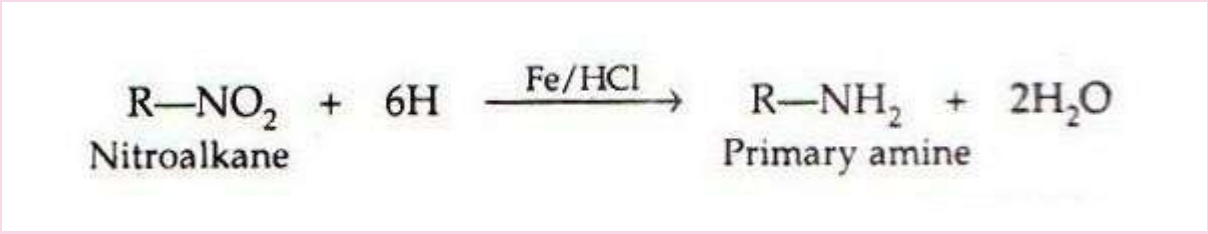
III step Anion of Nitroalkane attacks iminium ion to form Nitroamine



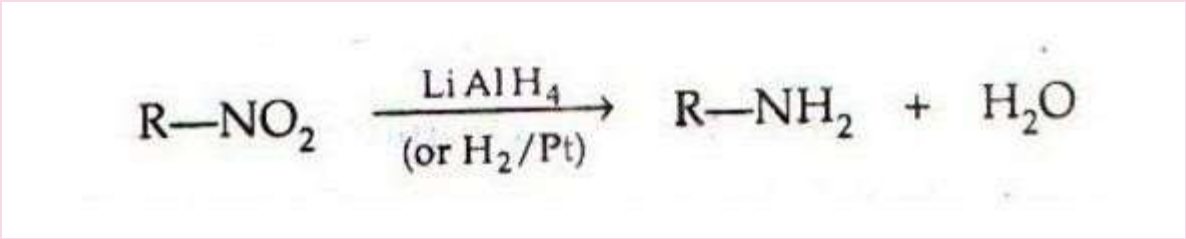
Reduction: Reduction of Nitroalkanes gives different products based on conditions The product obtained depend upon the nature of the reducing agent and $_{P}^{H}$ of the reaction medium.



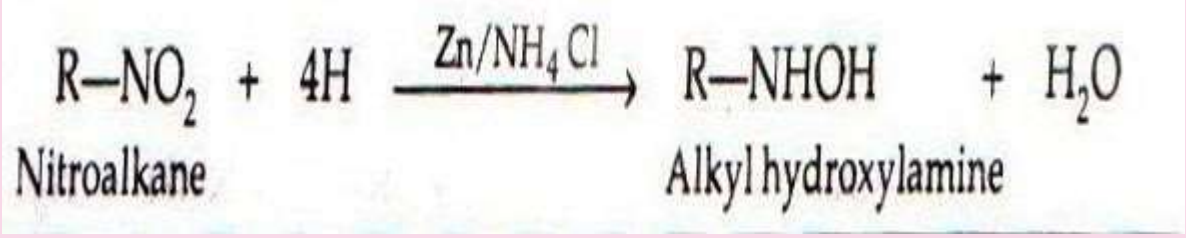
Acidic medium : primary amines are formed



Catalytic reduction: primary amines are formed



Neutral medium :hydroxyl amine derivative is obtained



QUESTION BANK FOR IMMORTANT QUESTIONS

Unit III: Nitro Hydrocarbons

Long Answer Questions (10 Marks)

1. Explain the tautomerism shown by nitroalkanes (acid form and keto form). Describe the Nef reaction.

2. Describe the general methods of preparing nitroalkanes and explain how they are reduced under different conditions.

3. Explain how nitroalkanes react with: Halogens and Nitrous acid (HONO)

Short Answer Questions (5 Marks)

1. Write a short note on the Mannich reaction.

2. Explain the Nef reaction with a chemical equation.

3. Describe the reaction of primary, secondary, and tertiary nitroalkanes with nitrous acid.

4. Explain the halogenation reaction of nitroalkanes.

MAJOR-11: NITROGEN CONTAINING ORGANIC COMPOUNDS & SPECTROSCOPY

UNIT- III :: Heterocyclic Compounds (9 h)

Introduction and definition: Simple five membered ring compounds with one heteroatom Ex. Furan, Thiophene and Pyrrole - Aromatic character – Preparation from 1, 4, -dicarbonyl compounds, Paul-Knorr synthesis. Properties: Acidic character of pyrrole – electrophilic substitution at 2 or 5 position, Halogenation, Nitration and Sulphonation - Diels Alder reaction in furan. Pyridine – synthesis - Aromaticity -Basicity - Comparison of basicity with pyrrole- Reactivity towards Nucleophilic substitution reaction (Chichibabin reaction).

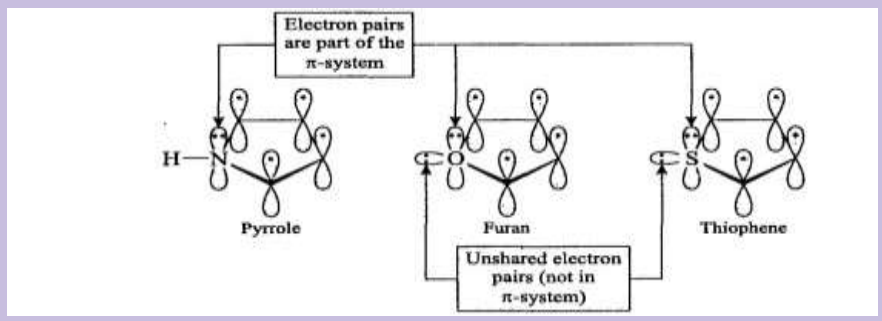
Introduction and definition : Heterocyclic compounds are those cyclic compounds in which one or more of the ring carbons are replaced by another atom. The non-carbon atoms in such rings are referred to as hetero atoms. The most common heteroatoms are Nitrogen, Oxygen and Sulfur

Many natural products of medicinal and biochemical importance are derivatives of heterocycles, e.g., RNA, DNA, chlorophyll, haemin, morphine, heroin, cocaine, penicillin's, cephalosporins, etc

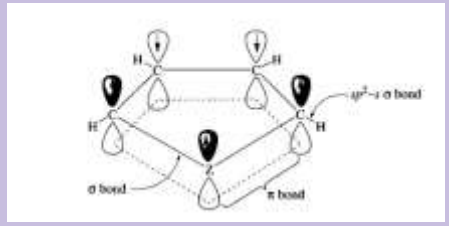
The three most common five-membered aromatic rings are furan, with an 0 atom , pyrrole, with an N atom and thiophene, with an S atom

Aromatic character:

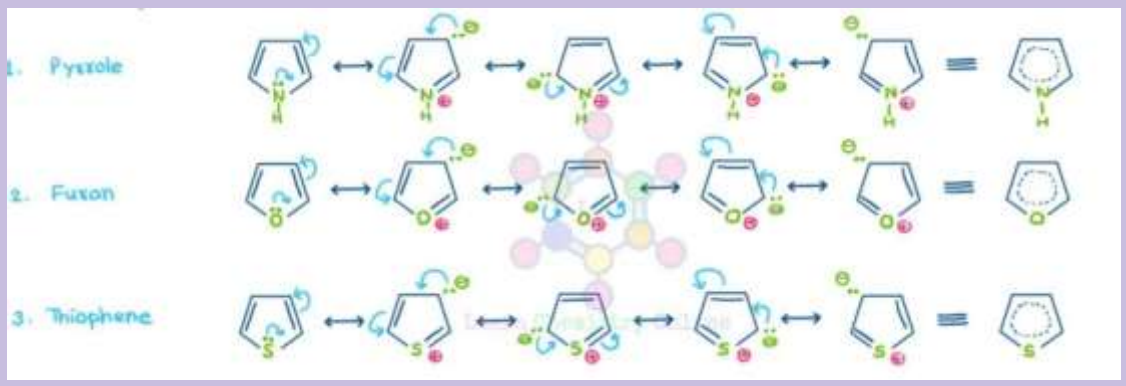
They have 4 C and 1 heteroatom, and all are sp^2 hybridized , sp^2 hybridization is planar, it makes a planar ring structure.



Each ring atom also contains unhybridized p orbital that is perpendicular to the plane of σ bonds (plane of ring). Here p orbitals are parallel to each other, so overlapping between p orbitals is possible.



the total no of nonbonding electrons is 6 (4 of four C, 2 from one N) They show resonance



These structures have charge separation whereas resonance structures of benzene do not involve charge separation. Due to these they are less aromatic than benzene

Evidence:- There are many evidence which support the above-mentioned delocalized structures or resonance structures

Bond length: The bonds of these compounds are intermediate in length between the normal single and double bond lengths for C-C, C-N, C-S and C-O bonds.

Dipole moment: If we compare dipole moments of these compounds with suitable reference compounds then this indicates delocalisation of e- pair into the ring

Huckel's rule : the 6 e- follows the Huckel's rule ie $4n + 2\pi = 4(1) + 2\pi = 6\pi$ electrons Hence, they are aromatic.

Relative aromatic character:- Aromatic character depends on electronegativity of the heteroatom .More electronegative atom will have a greater hold on the lone pair which will, be more localized. therefore, be less aromatic

The electronegativities of the heteroatoms are in the order

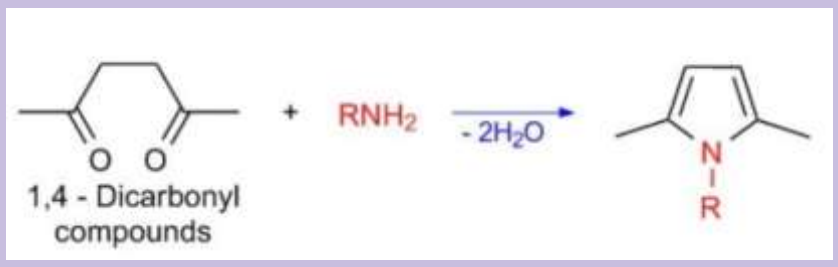
$$O > N > S$$

This means that oxygen has the least tendency to donate the electron pair to the aromatic sextet. So the aromatic character should be least in case of furan, followed Pyrrole and maximum for thiophene.

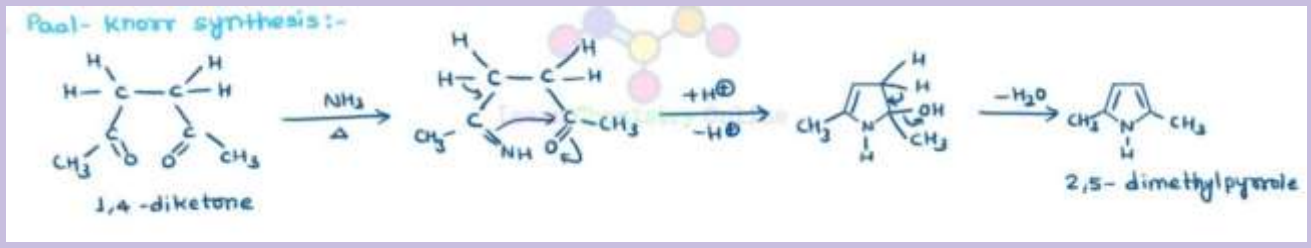
Thiophene > Pyrrole > Furan

Also Since S atom has empty 3d orbital ,hence it can give extra resonance structures and mor aromatic than others

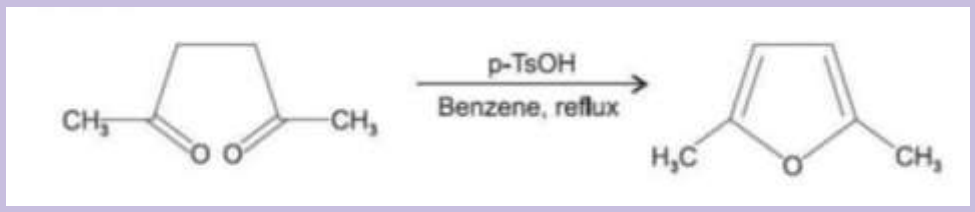
Pyrrole preparation from 1, 4, -dicarbonyl compounds, Paul-Knorr synthesis: 1,4 - Dicarbonyl compounds react with ammonia or primary amines to give pyrroles.



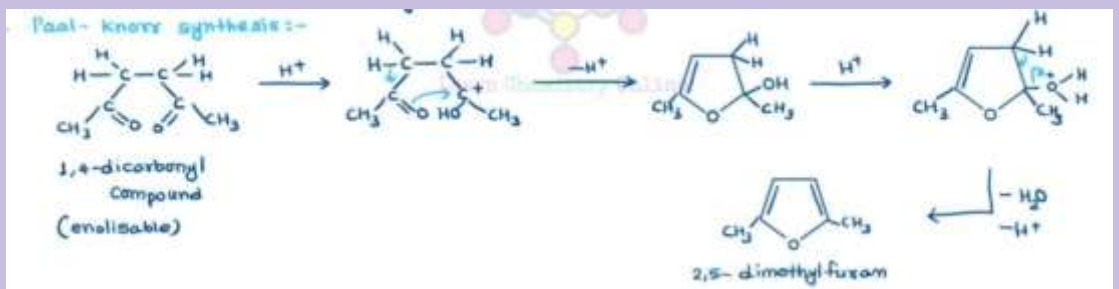
Mechanism: Successive nucleophilic additions of the amine nitrogen to each of the two carbonyl carbon atoms, imine formation and the dehydration gives pyrrole



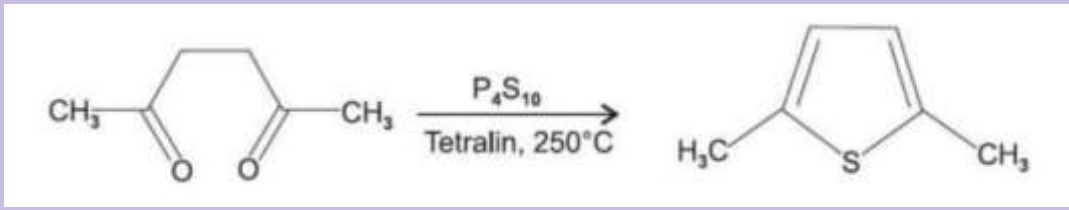
Furan preparation from 1, 4, -dicarbonyl compounds, Paul-Knorr synthesis: 1,4-Dicarbonyl compounds undergo cyclisation and dehydration in the presence of non-aqueous acidic medium usually p-toluene sulfonic acid (p-$CH_3C_6H_4SO_3H$) in benzene to yield furans. The other acid employed for this reaction are sulfuric acid, zine chloride, acetic anhydride, phosphorous pentoxide, or phosphoric acid.



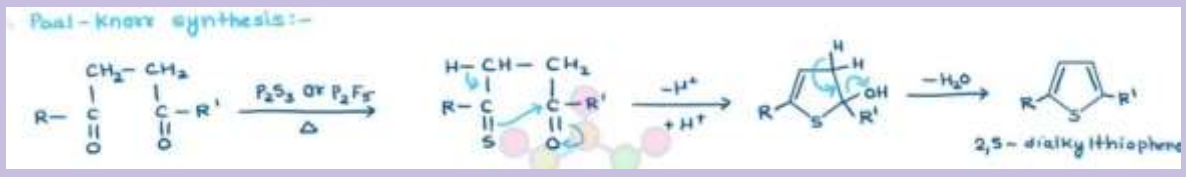
Mechanism: Successive protonation and deprotonation followed by dehydration gives furan



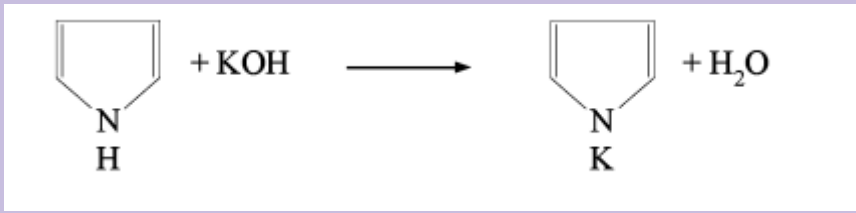
Thiophene preparation from 1, 4, -dicarbonyl compounds, Paul-Knorr synthesis: The condensation reaction of a 1,4-dicarbonyl compound with phosphorus pentasulfide gives thiophenes.



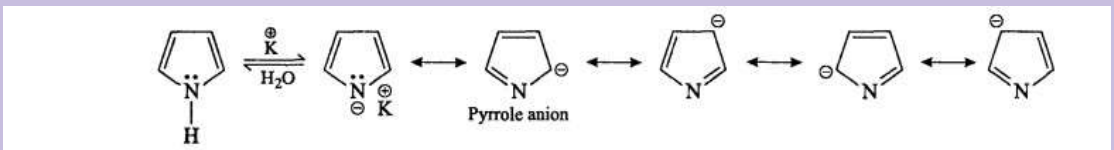
Mechanism: condensation reaction between 1,4-dicarbonyl compound and Sulphur followed by successive protonation and deprotonation and finally on dehydration gives thiophene



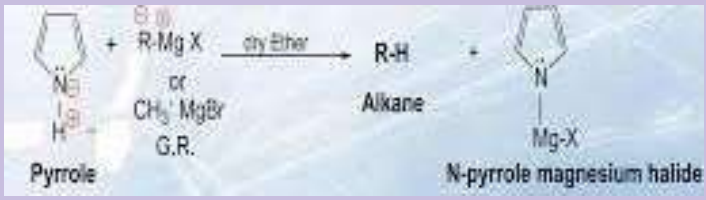
Acidic character of pyrrole: Due to participation of N lone pair in aromaticity, pyrrole has exceptionally strong acidic properties it shows resemblances to phenols and aromatic amines . The imino-hydrogen of pyrrole is replaceable by potassium, alkyl, or acyl groups. When pyrrole is heated with solid potassium hydroxide potassium pyrrole is formed,



and the pyrrole anion is stabilised by resonance. thus, pyrrole is acidic

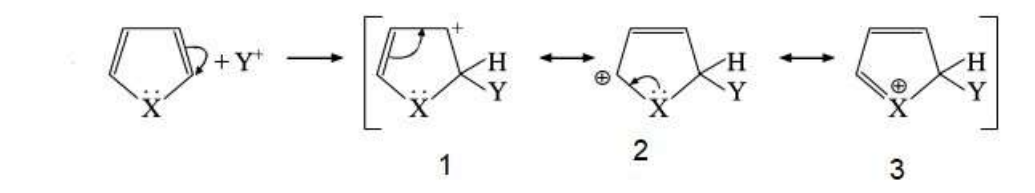


Further due to the acidic nature, pyrrole reacts with Grignard reagents to form pyrrolyl magnesium halide

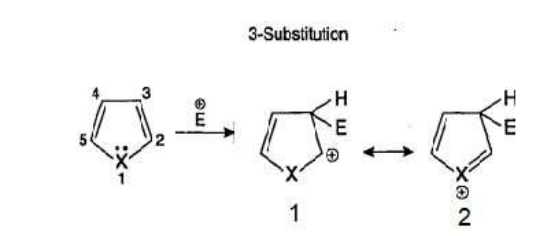


Electrophilic substitution at 2 or 3 position: Substitution takes place preferably at that position where the intermediate products is more stabilized. In the case of furan, thiophene and pyrrole, there are two positions 2 or 3 (α or β) where the substitution could take place.

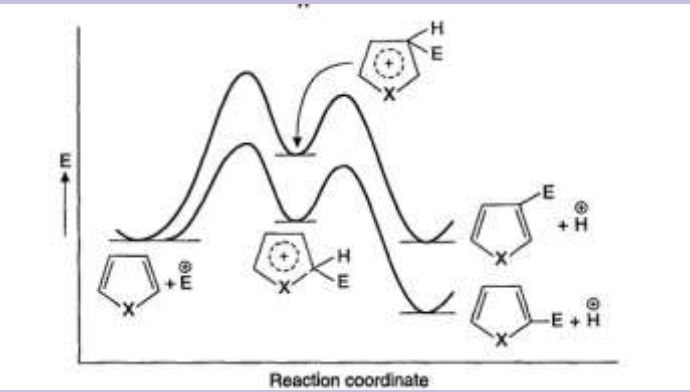
Substitution at 2 -position (or α -position) the intermediate products in case of substitution at x-position has three resonating structures are given below



Substitution at 3-position (or β-position) There are only two resonating structures for intermediate product in case of substitution at 3 -position



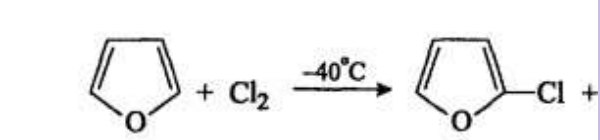
Electrophilic substitution preferentially at carbon 2 or α position because of the fact that the intermediate is more resonance stabilized 3 resonance structure than the 3 or β-position which has 2 resonance structure and carbocation (allylic carbocation) is more stabilized at 2 or α position .Hence substitution is preferred at 2 or α position



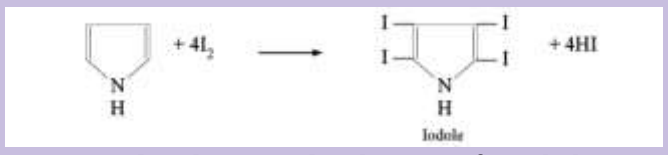
Energy diagram shows C 2 or α attack forms more stable intermediate than C3 or β Hence C2 preferred over C3 Also, C2 has larger HOMO than C3 ,it makes softer for electrophilic attack and it has long +ve charge separation over 4 atoms

The order of reactivity for electrophilic substitution is Pyrrole> Furan > Thiophene

Halogenation: Furan reacts readily with halogens. When the reaction is carried out at - 40°C following products are obtained

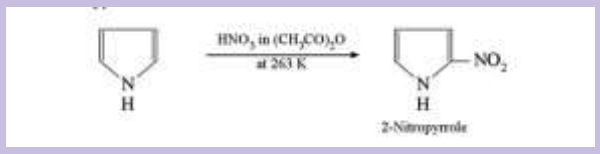


Pyrrole is extremely reactive towards electrophilic substitution with halogens, it reacts rapidly with iodine to give tetraiodopyrrole, which is used as substitute for Iodoform



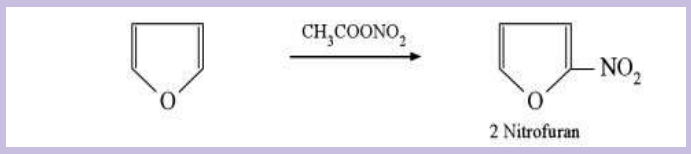
When thiophene is treated with Br_2 in the absence of any halogen carrier, the formation of 2, 5-dibromothiophene takes place

Nitration: With HNO_3 in acetic anhydride, pyrrole gives 2-nitropyrrole.

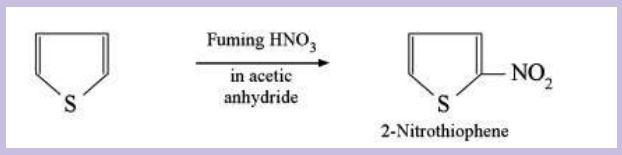


Since furan is acid sensitive, nonacidic reagents must be used for nitration and sulphonation reaction

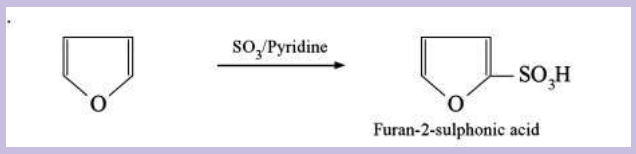
When furan is treated with acetyl nitrate, 2-nitrofuran is obtained



Thiophene when nitrated with fuming HNO_3 in acetic anhydride gives 2-nitro-thiophene.

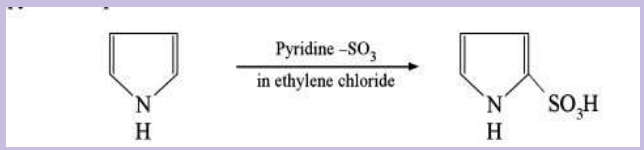


Sulphonation.: Furan upon sulphonation with pyridine & Sulphur trioxide forms Furan-2 sulphonic acid.

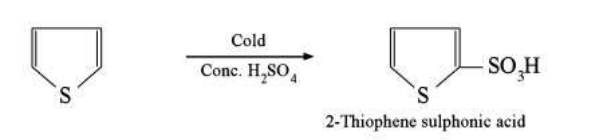


Since pyrrole is acid sensitive, nonacidic reagents must be used for sulphonation and nitration reactions.

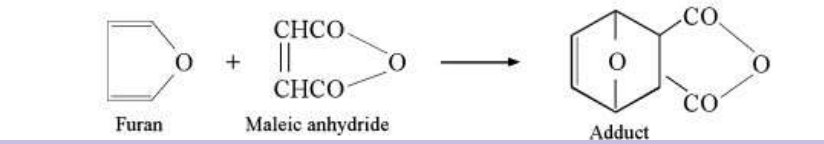
With pyridine – SO_3 mixture in ethylene chloride, pyrrole is sulphonated to give 2-pyrrole sulphonic acid.



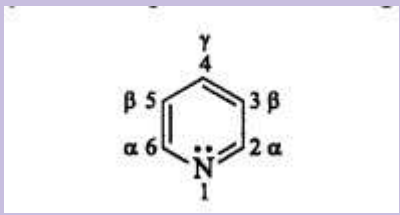
Sulphonation of thiophene with cold conc. H_2SO_4 gives 2-thiophene sulphonic acid.



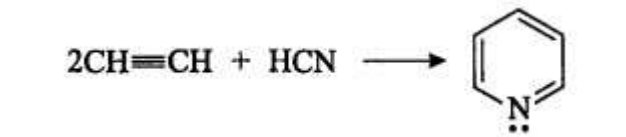
.**Diels-Alder reaction:** furan is least aromatic due to high electronegativity and behaves as a diene in Diels-Alder reaction. furan without having electron-withdrawing groups undergo 4+2 π cycloaddition reaction to give adducts .Furan is the only one heterocyclic compound that gives Diels-Alder product with stereochemistry.it gives exo product



Pyridine : Pyridine is an aromatic heterocyclic compound with Nitrogen containing six membered ring .also called "Azabenzene"



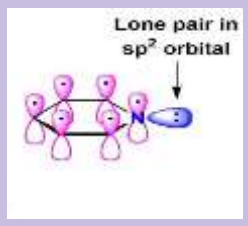
Synthesis : Pyridine is formed when mixture of acetylene and hydrogen cyanide is passed through red-hot tube.



Isolation from coal-tar:. The light oil fraction of coal-tar contains aromatic hydrocarbons and phenols besides pyridine and alkyl pyridines. The light oil fraction is thus heated with dil.H_2SO_4 which dissolves pyridine and other basic substances. This aqueous acid layer is neutralised using sodium hydroxide, when bases are liberated as a dark brown oily liquid. This oily layer is separated, and pyridine is obtained by fractional distillation.

Aromaticity : Pyridine features a planar hexagonal ring with five carbon atoms and one nitrogen at position 1.

All atoms are sp^2-hybridized, enabling p-orbital overlap for delocalization. The nitrogen has its lone pair in an sp^2 orbital in the ring plane, not participating in the π-system.

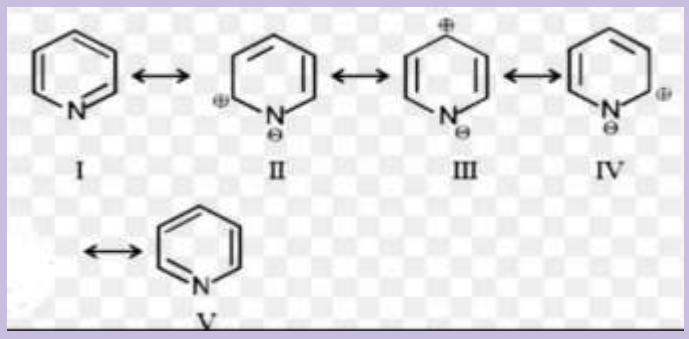


Pyridine meets all four key criteria for aromaticity

- cyclic structure
- planar conformation
- fully conjugated π-system
- follows Huckle's rule and 6 π-electrons (from three double bonds, each contributing 2)

Resonance occurs by shifting pi electrons in alternating double bonds around the ring, like benzene. But the nitrogen atom always maintains a single bond with its adjacent carbons and keeps its lone pair intact. Resonance structure with negative charge is on nitrogen and positive charge is on carbons are more significant.

The aromatic sextet is preserved in all resonance forms since the pi electrons remain delocalized over the ring.

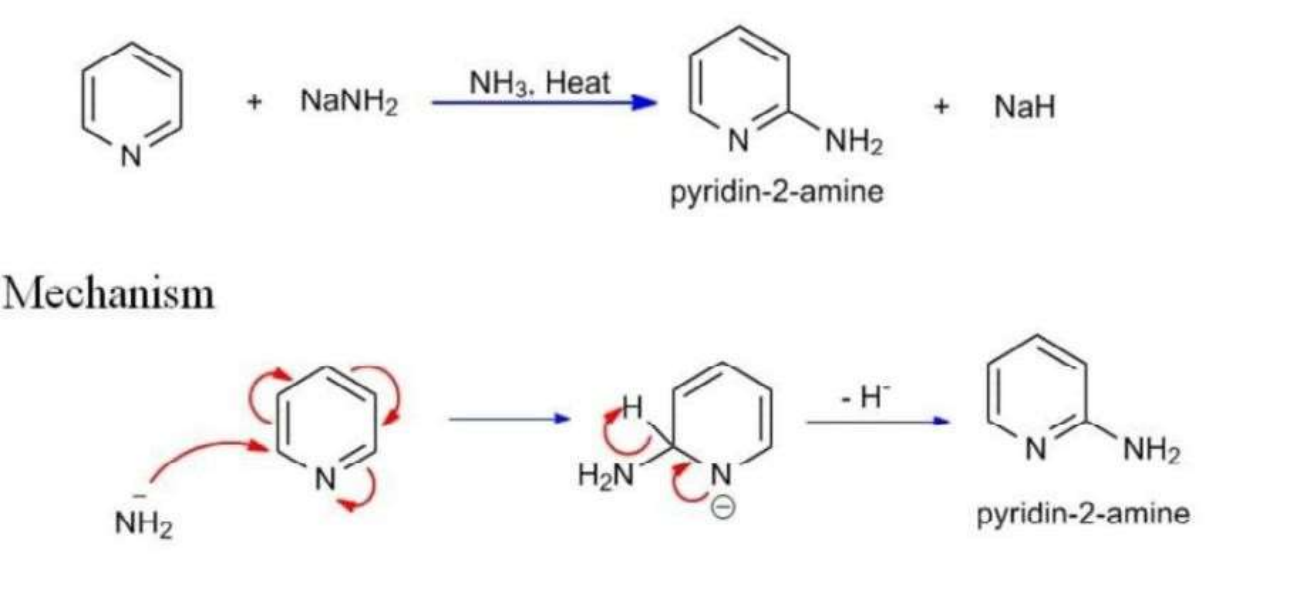


Basicity: Since Nitrogen atom carries a negative charge and the lone pair is completely available for protonation pyridine expected to be a very strong basic. but Pyridine less basic than alkylamine because the nitrogen atom in pyridine is sp^2 hybridized, it is more electron - withdrawing than nitrogen that is sp3 hybridized as in RNH_2

Comparison of basicity with pyrrole: Pyridine is more basic than pyrrole. Basicity depends on availability of lone pair of electrons . Pyridine Nitrogen have lone pair of electrons in same plane of pyridine hybridized orbitals plane .So it is not participating to resonance phenomena .Hence lone pair is readily available for acid-base reaction. Pyrrole Nitrogen have lone pair of electrons perpendicular to plane of Pyrrole unhybridized orbitals plane. it participates in resonance (delocalization of lone pair) .Hence not readily available for acid-base reaction.

As lone pair of Pyrrole of pyridine are readily available than pyrrole, Pyridine is more basic than pyrrole

Chichibabin reaction: Pyridine reacts with Sodamide at high temperatures undergoes Nucleophilic substitution reaction to give 2-aminopyridene . Since Nitrogen having -ve charge it attacked by position 2 than 3



QUESTION BANK

Unit IV: Heterocyclic Compounds

Long Answer Questions (10 Marks)

1. Explain the Paal–Knorr synthesis used to prepare furan, thiophene, and pyrrole from 1,4-dicarbonyl compounds.
2. Discuss the aromatic nature of pyrrole and its electrophilic substitution reactions, such as:

    a) Nitration b) Sulphonation c) Halogenation
3. Compare the basicity of pyridine with pyrrole and aliphatic amines. Explain the structure and aromaticity of pyridine.

Short Answer Questions (5 Marks)

1. Explain the Chichibabin reaction of pyridine.
2. Write a short note on the Diels–Alder reaction involving furan.
3. Explain why pyrrole shows acidic character.
4. Explain why electrophilic substitution in furan, pyrrole, and thiophene mainly occurs at the 2-position (or 5-position).
5. Describe the preparation of pyridine.

Unit V :: UV-Visible & IR Spectroscopy (9 h)

Selection rules for electronic spectra, types of electronic transitions in molecules, concept of chromophore and auxochrome, effect of conjugation in dienes and α,β unsaturated compounds. Woodward Fischer rules for calculating λmax of conjugated dienes and α,β unsaturated compounds.

Infrared spectroscopy - types of molecular vibrations - fingerprint region. IR spectra of alkanes, alkenes, and simple alcohols (inter and intra molecular hydrogen bonding), aldehydes, ketones, carboxylic acids, and their derivatives (effect of substitution on >C=O stretching absorptions).

Why does a molecule absorb light at all?

When UV or visible light hits the molecule, if the light carries *exactly* the right amount of energy, one electron gets promoted to an excited state. The wavelength at which this happens is recorded as an absorption peak. This is UV spectrum.

Selection Rules for Electronic Spectra : Not all transitions are allowed. For an electron to jump from one energy level to another, it must follow these rules

Spin Selection Rule: The spin of the electron must not change during the transition. Spin multiplicity MUST be conserved during electronic transition

Allowed: Singlet → Singlet (S → S) All electrons paired → ↑↓ → Net spin = 0

Forbidden: Singlet → Triplet (S → T) Two unpaired electrons with same spin → ↑↑ → Net spin = 1

When light hits a molecule, it cannot reverse electron's spin.

Laporte Selection Rule: The orbital angular momentum quantum number must change by exactly one (1) $\Delta l = \pm 1$

s → p ☑ ALLOWED ($\Delta l = +1$)

p → d ☑ ALLOWED ($\Delta l = +1$)

s → s ✗ FORBIDDEN ($\Delta l = 0$)

d → d ✗ FORBIDDEN ($\Delta l = 0$)

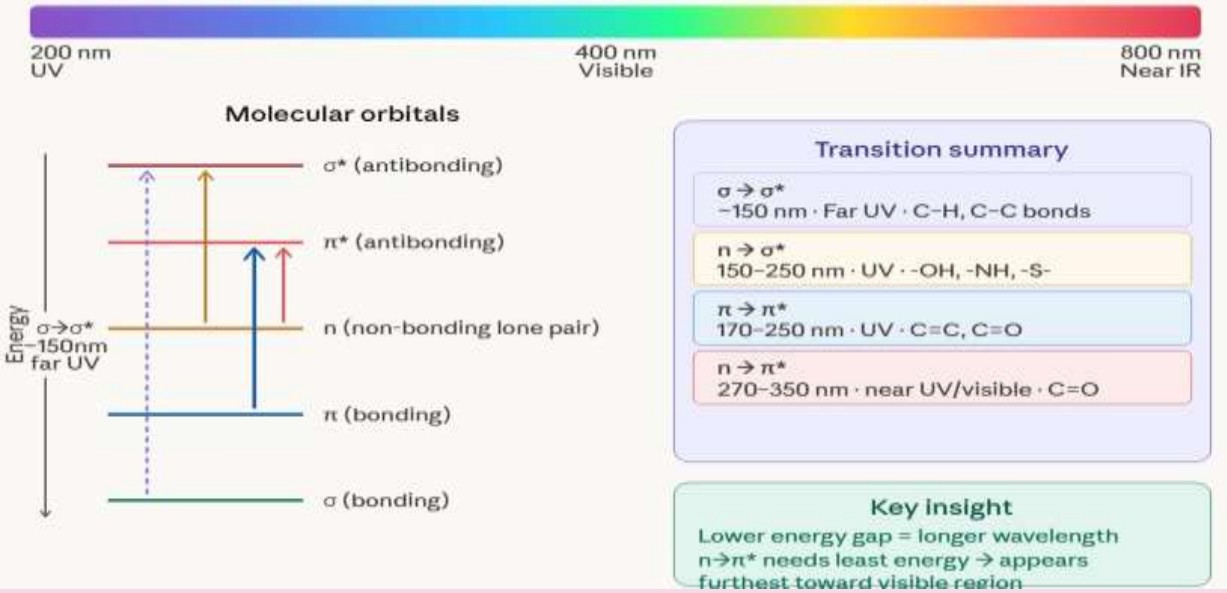
s → d ✗ FORBIDDEN ($\Delta l = +2$)

Laporte Selection Rule for Molecules : It applies for molecules with a center of symmetry Transitions must involve a change in symmetry

Allowed: g → u (gerade → ungerade)

Forbidden: g → g or u → u

Types of electronic transitions in molecules : The excitation of a molecule by absorption of radiation in the UV visible region involves promotion of its elections from a bonding or non-bolding (n) orbital to an antibonding orbital. There are bonding orbitals associated with σ or π for antibonding orbitals σ* or π* respectively. Non-bonding (n or p) orbitals are not associated with antibonding orbitals because non-bonding or lone pair of elections present in them do not form bonds



σ → σ* transition : This transition is associated bonding sigma orbital to anti bonding orbital . It is high energy which means very short wavelengths (~150 nm) process due to strong sigma bonds . λmax < 150nm these transitions are essentially invisible

Example : Hydrocarbons

n→ *σ transition:** Saturated compounds containing atoms (OH,NH_2) with lone pairs (non-bonding electrons) are capable of n→ *σ** transitions. These transitions usually need less energy than *σ* → *σ** transitions. They can be initiated by light whose wavelength is in the range 150 - 250 nm.

Example : Alcohols, Amines etc

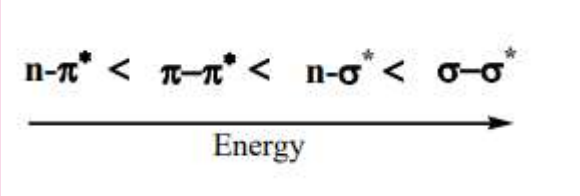
π → π ∗ transitions: molecules having π bonds like alkenes, alkynes, aromatic compounds electrons can excite from a π bonding molecular orbital to a π anti-bonding molecular orbital. This is called a π → π ∗ transition and is usually strong (high extinction coefficient).

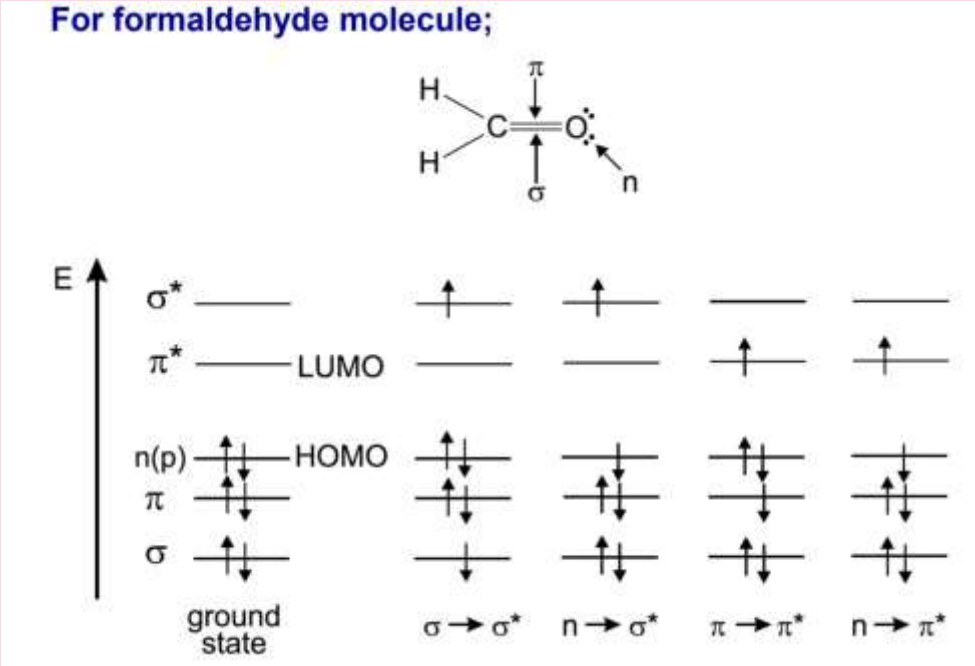
Example : Alkenes, Alkynes ,Benzene etc

n → π ∗ transitions: Lone pair electrons that exist on oxygen and nitrogen atoms may be promoted from their non-bonding molecular orbital to a π anti-bonding molecular orbital. This is called an n → π ∗ transition and requires less energy (longer wavelength) compared to a π → π ∗ transitions .

$n \rightarrow \pi *$ transition forbidden by symmetry but observed weakly due to The n orbital is **PERPENDICULAR** to the π* orbital. Poor spatial overlap and low extinction coefficient ε (10-100)

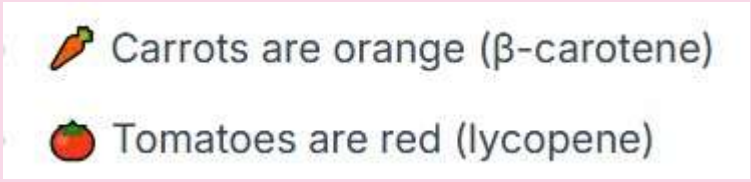
Example : Carbonyl compounds, Carboxylic acids ,Nitriles etc





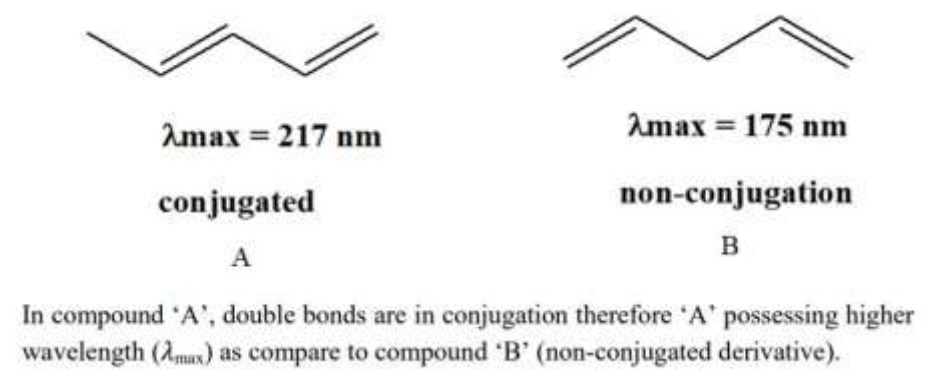
Chromophore: A Chromophore is a covalently unsaturated group functional group that absorbs light in the UV-Vis region mostly due to $\pi \rightarrow \pi *$ transitions. The term chromophore was previously used to denote a functional group of some other structural feature of which gives a colour to compound They need not produce visible color, if it absorbs UV, it's a chromophore.

Examples: C=C, C=O, N=N, NO_2. Nitro group is a chromophore because its presence in a compound gives yellow colour to the compound.



11 conjugated double bonds in each

Effect of Conjugation: When double bonds are conjugated (alternating single and double bonds C=C-C=C), the π electrons are delocalized over a larger space. A spread-out electron cloud has smaller energy gaps between HOMO and LUMO levels and can be excited by lower-energy (longer-wavelength) light. resulting λ_{max} increases (Red Shift Increases)



In compound 'A', double bonds are in conjugation therefore 'A' possessing higher wavelength (λ_{max}) as compare to compound 'B' (non-conjugated derivative).

Auxochrome: A Auxochrome is a saturated group (containing lone pair of electrons), that does not absorb light itself but, when attached to a chromophore, shifts the absorption to a longer wavelength (Red Shift) and increases intensity. They extend the conjugation through resonance

Examples: -OH, -NH_2, -Cl (groups with lone pairs). Benzene λ_{max} 225 When the auxo chrome – NH_2 group is attached to benzene ring. Its absorption changes from λ_{max} 225 to λ_{max} 280 nm due to participation of lone pair of electrons of Nitrogen into the ring by extending conjugation

Woodward- Fieser rules for calculating λmax of conjugated dienes and α,β unsaturated compounds

Woodward–Fieser used to estimate λmax (nm) of the $\pi \rightarrow \pi^*$ band for conjugated systems.

Conjugated dienes: 1) Choose the base value

Type of conjugated diene	Base value (nm)
Acyclic diene or heteroannular diene (double bonds in different rings)	214
Homoannular diene (both double bonds in the same ring)	253

2) Add increments (corrections) Add these to the base value:

Structural feature	Increment (nm)
Each alkyl substituent or ring residue on the conjugated system	+5
Each exocyclic double bond	+5
Each additional conjugated double bond beyond a diene (→ triene, tetraene, …)	+30

λ_{max} = Base Value + 5 (Alkyl or Ring residues)+ 5 (Exo Cyclic C = C)+30 (extended C=C)

Base Value Hetero Annular (2 Rings) = 214 nm

Ring residues = 3 X 5 = 15 nm

(C-C Single bond between Conjugated double bond)

Exocyclic bond = 5 nm

(Conjugated double bond has one outside ring)

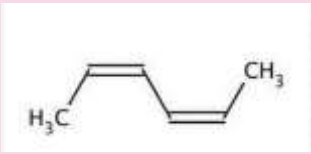
Total = 214+15+5 = 234 nm

1,3-Cyclohexadiene

Base Value: The compound contains a homoannular diene = 253 nm
(both double bonds in the same ring)

Substituents: There are no additional substituents to account for.

Calculation: λmax = 253 nm.



2,4-Hexadiene

Base Value: The parent system is an acyclic diene = 217 nm.

Substituents: There are two alkyl substituents attached to the diene = 2 X 5 = 10

Calculation: λmax = 217 + 10 = 227 nm

α,β-Unsaturated carbonyl compounds (enones)

1) Choose the base value

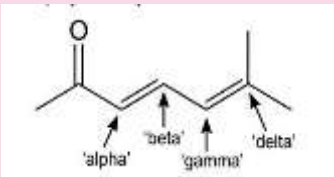
type of α,β-Unsaturated carbonyl	Base value (nm)
Acyclic enone or 6-membered ring enone	215
5-membered ring enone	222

2) Add increments (corrections) Add these to the base value:

Position (relative to C=O)	Increment (nm)
Each substituent (alkyl or ring residue) at α	+10
Each substituent (alkyl or ring residue) at β	+ 12
Each substituent (alkyl or ring residue) at γ	+ 18
Each exocyclic double bond	+5
Each additional conjugated double bond beyond a diene	+30

λ_{max} = Base Value +10 (α substituent)+ 12 (β substituent)+18 (γ substituent) +5 (Exo Cyclic C = C) + 30 (extended C=C)

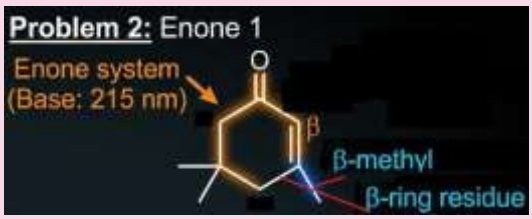
6-Methylheptadienone



Base Value for Acyclic enone base. = 215 nm
Extended Conjugation, =30,
(One extra double bond extending the system.)
δAlkyl Groups, = 2 × 18 nm).
(Two methyl groups at the δposition)

Total Calculated λmax = 215+ 30+ 36 = 281 nm

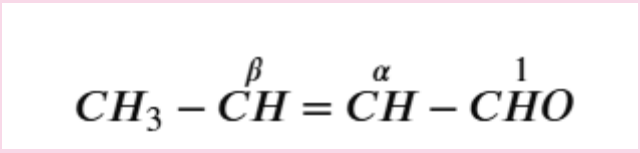
3 Methyl,5,5, dimethyl cyclohexenone



Base (6-ring enone) = 215 nm
β Alkyl (Methyl) = 12 nm
β Ring Residue = 12 nm

Total Calculated λmax = 215+ 12+ 12 = 239 nm

Crotonaldehyde



Base Value = 215 nm.
Substituents:
One alkyl substituent is present at β = 10 nm.
Calculation: λmax = 215 + 10 = 225 nm.