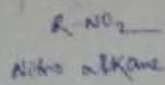


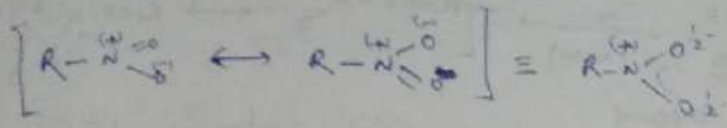
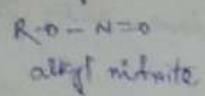
SEM IV STUDY MATERIAL

Amines and Nitro Compounds

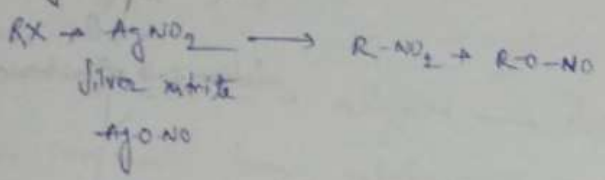
Nitro alkanes :-



Nitro compounds



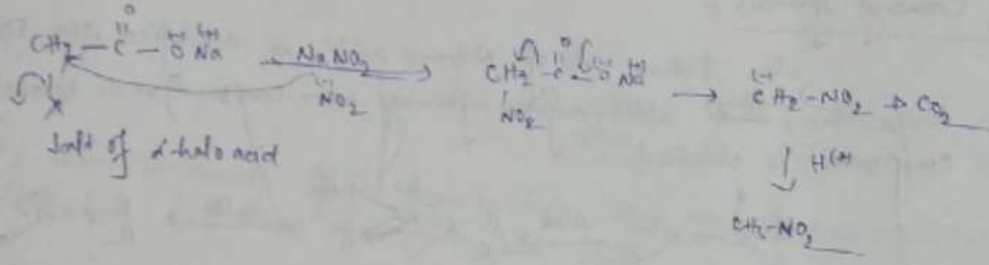
General methods of preparation :-



Primary alkyl halide \rightarrow nitroalkane - Major

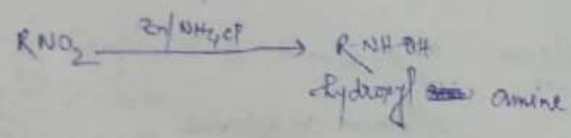
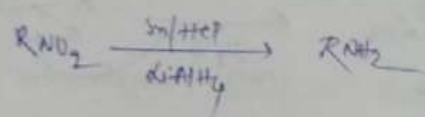
2° or 3° alkyl halide \rightarrow alkyl nitrite - Major

from salt of α -halo acid :-

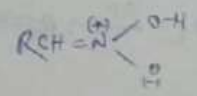
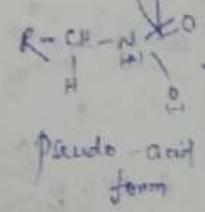


Reduction :-

Reduction :-

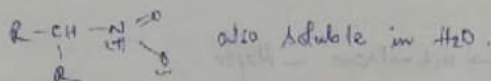
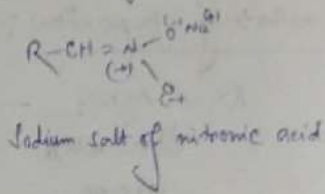
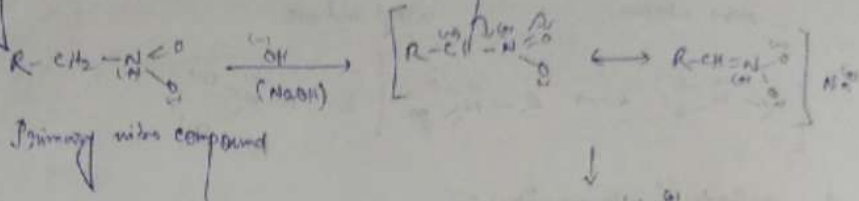


Primary and secondary nitro compounds containing α -H atom exhibit tautomerism,



The equilibrium is completely shifted towards left.

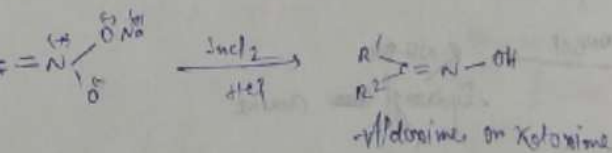
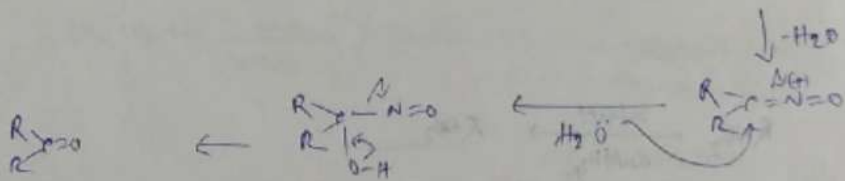
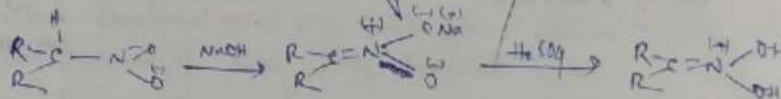
Nitro compounds dissolve in aq. NaOH to form salt. This is due to nitro compound with α -hydrogen atom exhibit some acidic properties.



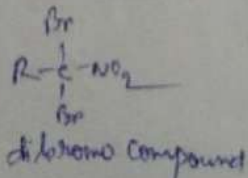
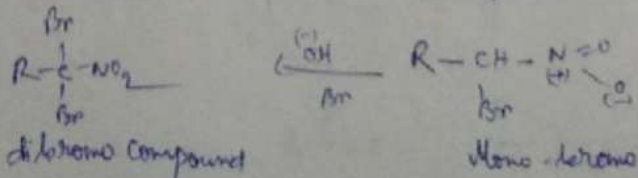
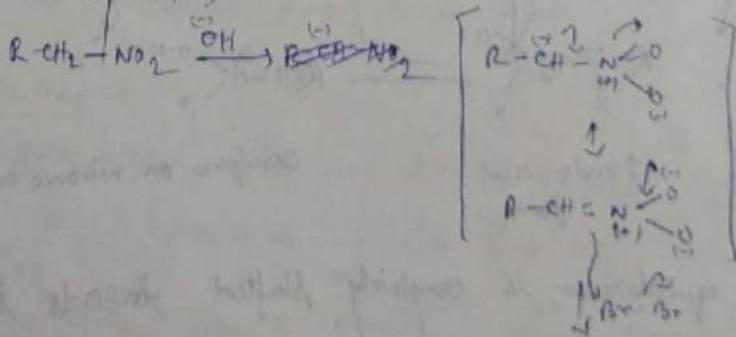
Tertiary nitro alkane would not react with NaOH because it has no α -H atom.

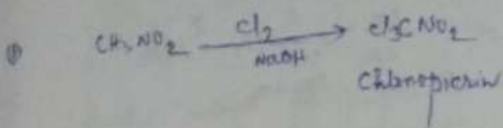
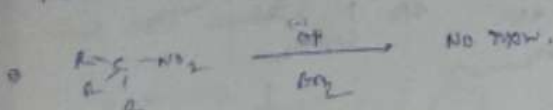
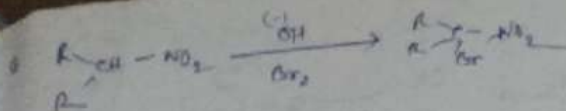
Nef Carbonyl Synthesis

When sodium salt of nitronic acid is acidified with 50% H_2SO_4 at room temperature, ~~then~~ ^{then} aldehyde from primary nitro compound or a ketone (secondary nitro compound) is obtained.

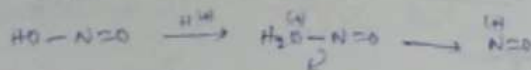


Halogenation of Nitro compounds

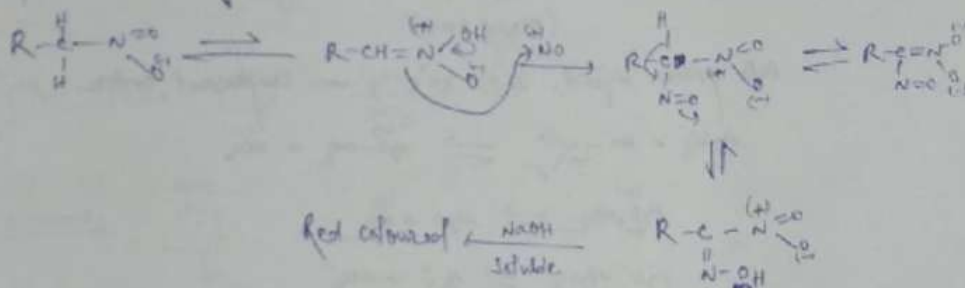




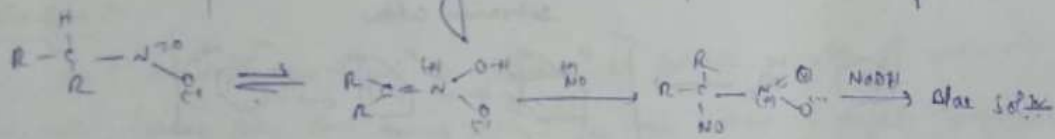
for with nitrous acid :-



Primary nitro compounds form nitrosic acid, these are crystalline substances which dissolves in NaOH to give red coloured soln.

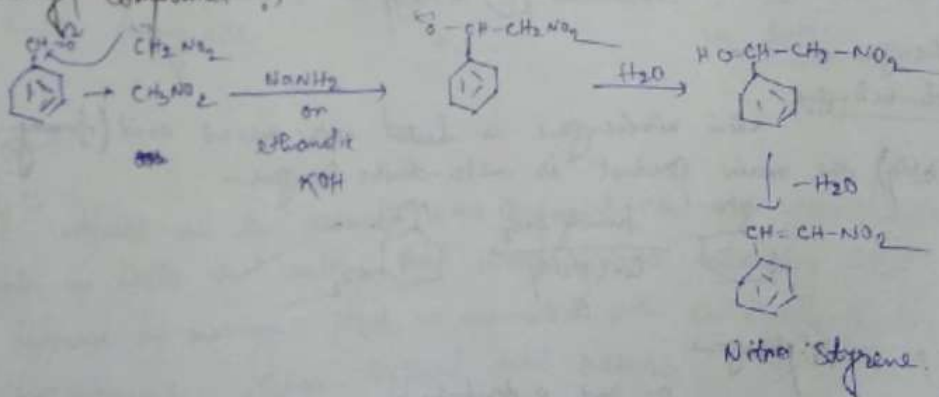


Secondary nitro compounds form pseudonitroles, these are colourless crystalline substance which dissolves in NaOH to give blue soln.

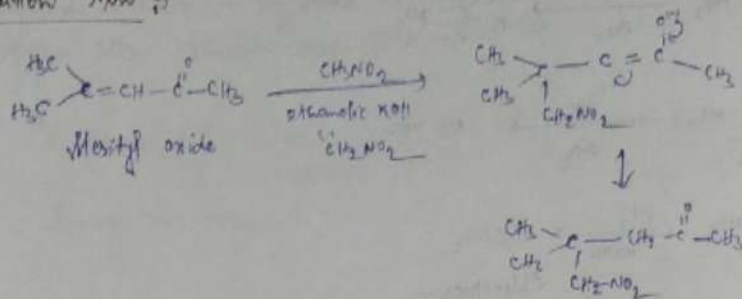


Tertiary nitroalkane $\xrightarrow{HNO_2}$ NO reaction.

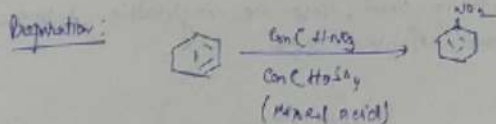
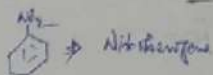
Now with Carbonyl Compound :-



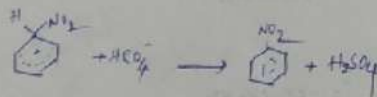
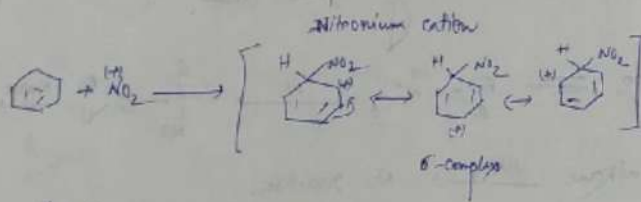
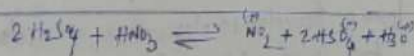
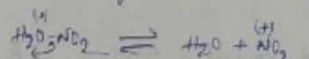
Michael addition rxn:



Aromatic Nitro compound:



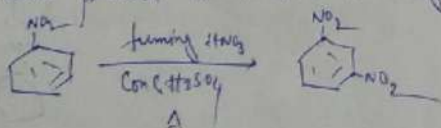
pale yellow liquid, b.p. = 211°C, unpleasant odor.



Dinitrobenzene \rightarrow

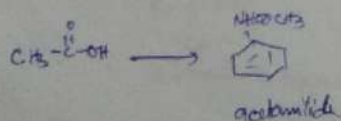
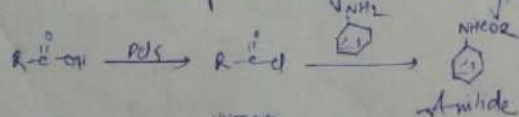
meta-dinitrobenzene:

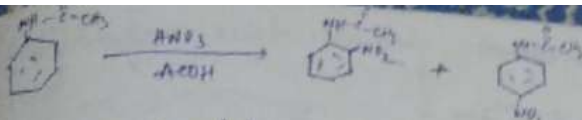
when nitrobenzene is treated with mixed acid (forming HNO_3 and $\text{Conc. H}_2\text{SO}_4$) the main product is meta-dinitrobenzene.



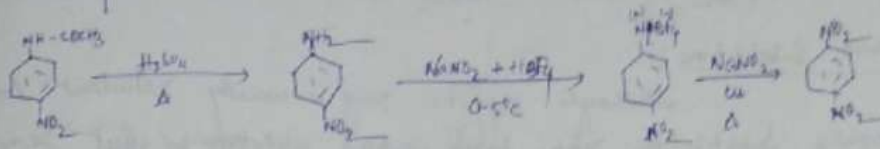
o- & p-dinitrobenzene:

o- and p-dinitrobenzene can be prepared by nitration of acetanilide,

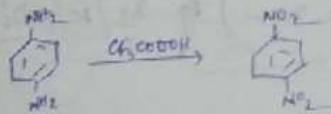
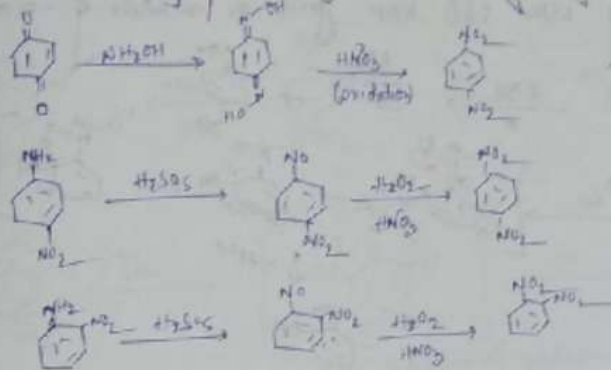




these are separated.



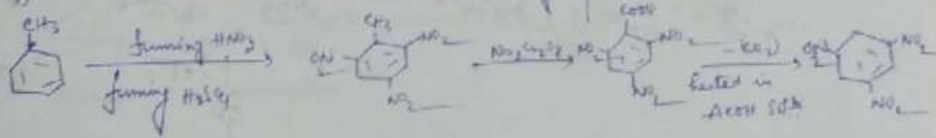
Another method for preparation of p-dinitrobenzene from p-nitroaniline



p-Phenylenediamine

1,3,5-trinitrobenzene :-

1,3,5-trinitrobenzene can be prepared by further nitration of meta-dinitrobenzene with fuming HNO_3 and fuming H_2SO_4 . The rxn takes 5 days to complete. It is very difficult to introduce the third nitro group.



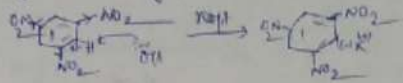
~~Physical Property :-~~

Physical Property :- Almost all the aromatic nitro compound are pale yellow substances. They are insoluble in water and melting point increases with increasing no. of $-NO_2$ groups. This increase in melting point is associated with the dipole-dipole attraction. Most of the nitrocompounds have typical bad odour.

Chemical Property :- Unlike primary and secondary aliphatic nitro-compounds, aromatic nitrocompounds have no $\alpha-H$ atoms. So they resemble tertiary nitro-compounds and not being acidic in nature.

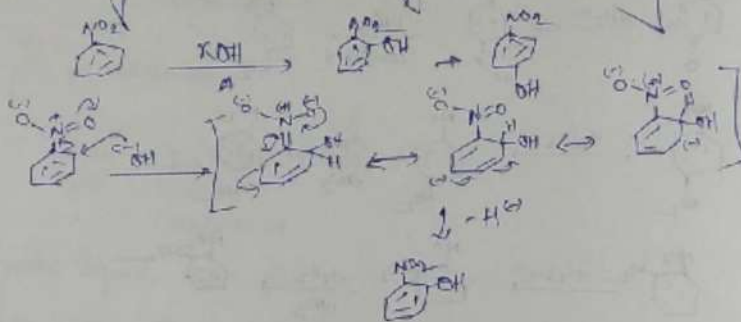
When two or more nitro groups are attached to the aromatic nucleus, they exert strong electron withdrawing effect on the ring, so much that it atom attached to the ring become active to nitro compound. often react with CH_3

eg alkali to give strongly coloured salt

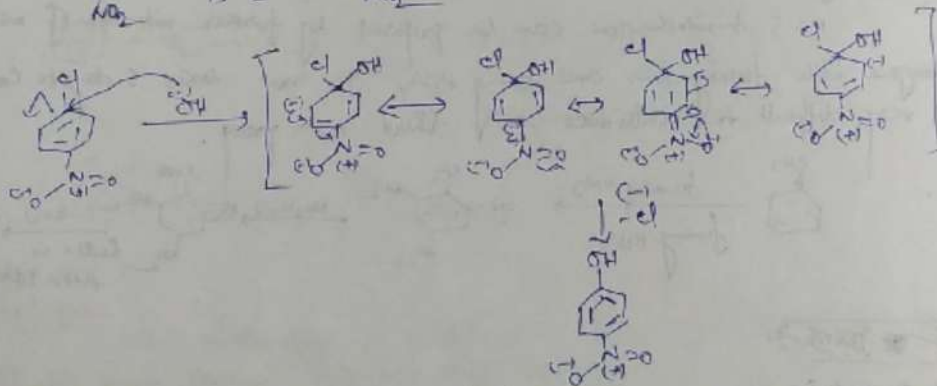
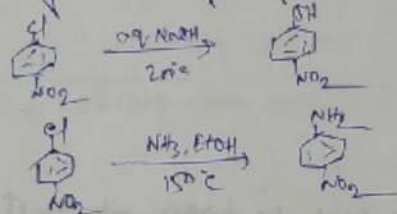


Nucleophilic Substitution

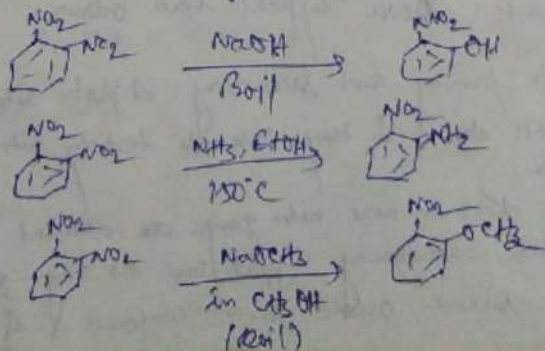
Although aromatic ring is usually reluctant toward nucleophilic substitution rxn, strong electron withdrawing effect (resonance) of nitro derivative do undergo nucleophilic substitution rxn easily. Even nitrobenzene on heating with solid KOH gives a mixture of -o and -p nitrophenols.



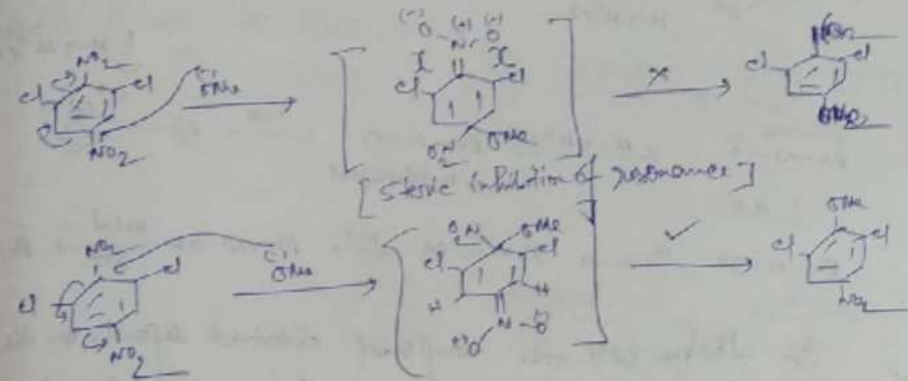
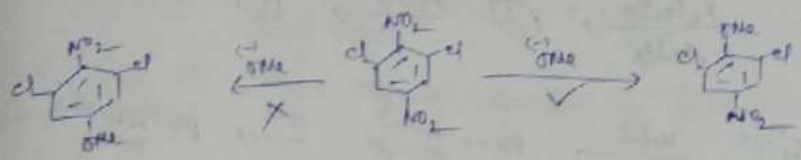
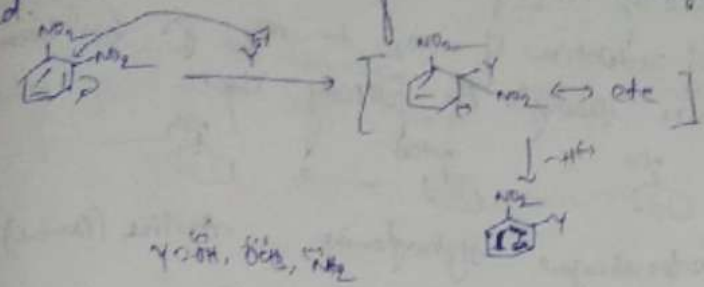
Presence of oxidizing agent facilitates the rxn [eg K₂[Fe(CN)₆]]



m-dinitrobenzene, although very similar to o & p dinitrobenzene but they differ in the following rxn. when o & p dinitrobenzene are boiled with aq NaOH, one -NO₂ gr is replaced by -OH group

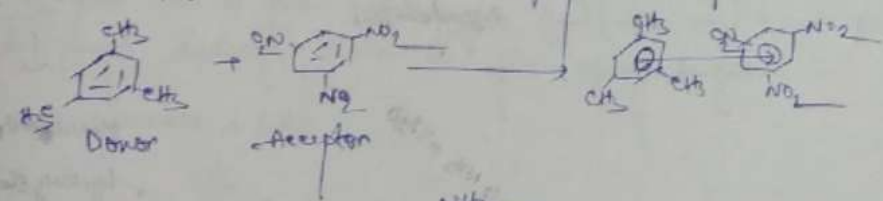


2 dinitrobenzenes react similarly. for m-dinitrobenzene it would be replaced.

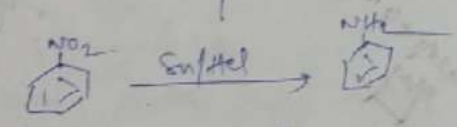


Charge transfer Complex

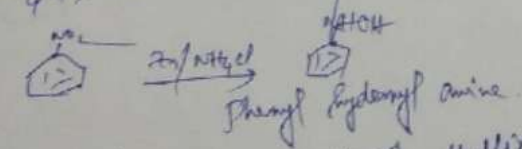
Many dyes and polynitrocompounds form complexes with other aromatic hydrocarbons, phenols etc. These complexes contain the component in 1:1 ratio and are slightly coloured.



Reduction



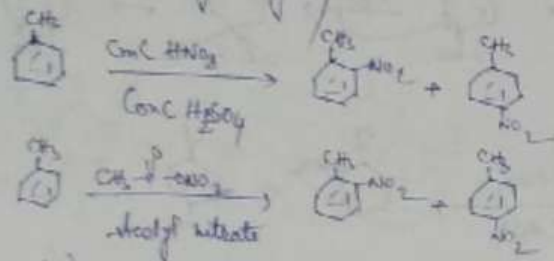
When reaction is carried out in a neutral solⁿ with Zn dust and aqueous NH₂Cl, the rxn stops at the hydroxylamine step.



This rxn forms the basis of Mulliken-Barker test for NO₂ groups. The rxn mixture is filtered and treated with Tollen's reagent. when a grey precipitate or metallic Ag is formed due to the reducing properties of hydroxyl amine, (C₆H₅NHOH).

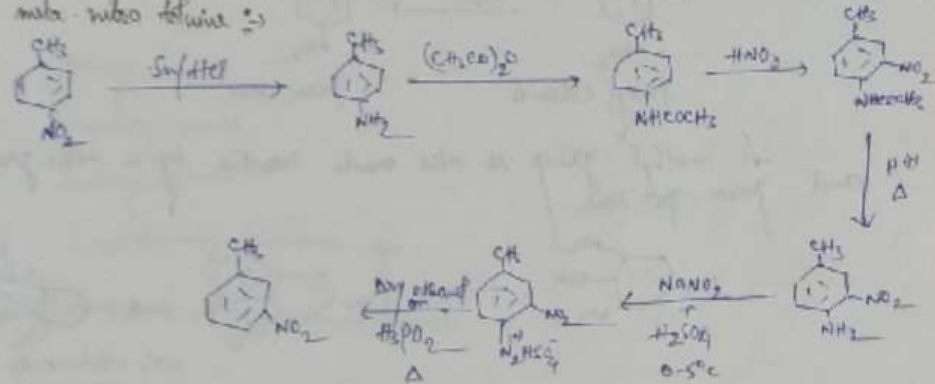
Nitrotoluenes :-

Benzene ring homologues are readily nitrated than benzene due to activating effect of its alkyl group



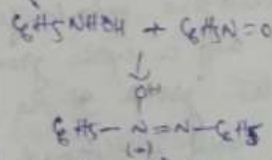
These two isomers may be separated by fractional distillation under reduced pressure.

Preparation of meta-nitro toluene :-

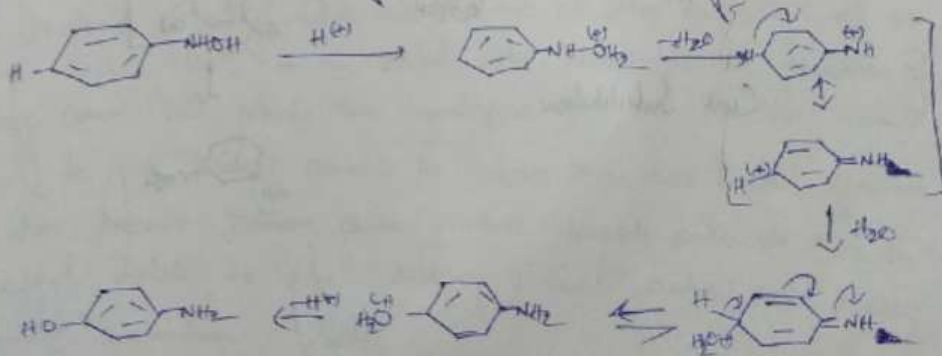


Phenyl hydroxyl amine :-

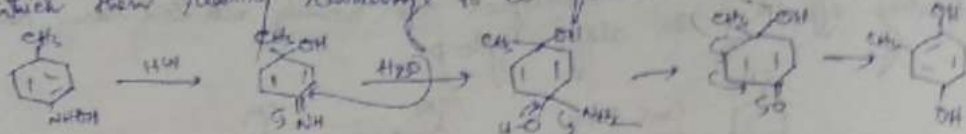
Phenyl hydroxyl amine is a powerful reducing agent, it reduces ammoniacal silver nitrate (Tollens' reagent) and ferric solution. It readily absorbs O_2 from air to form nitrosobenzene and this can react with unchanged phenyl hydroxyl amine to give azoxy benzene.



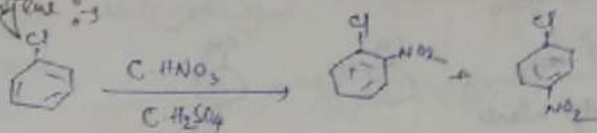
In dilute acid solution, phenyl hydroxyl amine rearranges to para amino phenol



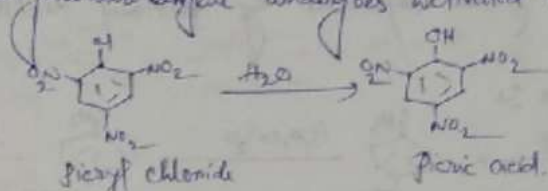
If p position is occupied by a methyl group, the rearrangement can still take place but in this case, ammonia is eliminated and a methyl quinoid is formed which then readily rearranges to a quinol.



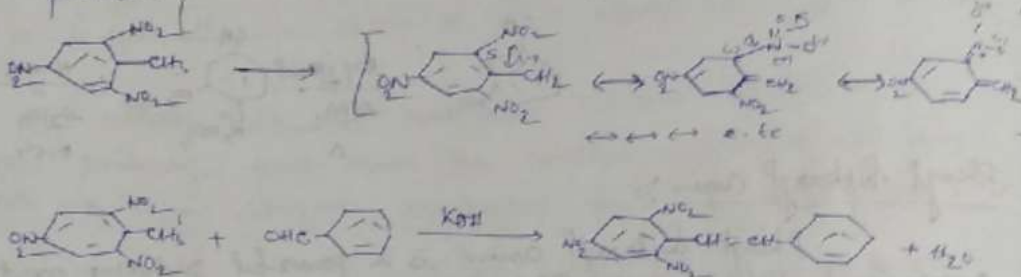
Halogenonitrobenzene \rightarrow



Halogenonitrobenzene undergoes activated nucleophilic substitution reaction.

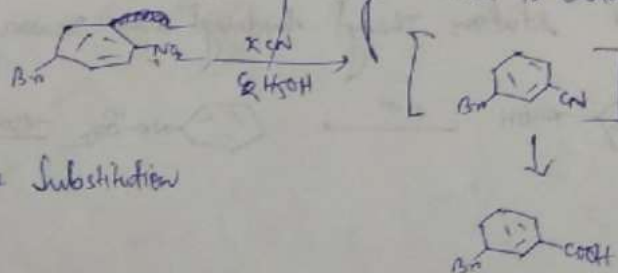


A methyl group is also made reactive by a nitro group in the ortho and para positions.



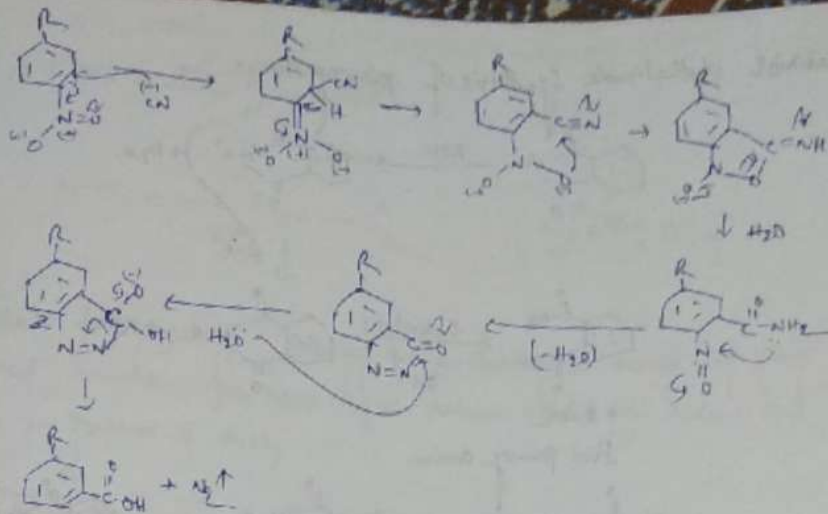
Von-Richter reaction \rightarrow

An example of nucleophilic substitution with rearrangement is Von-Richter reaction. When a halogeno nitrobenzene is heated with KCN at 150°C , the nitro group is expelled and a cyano group enters the ring ortho to the position occupied by nitro group. If the rxn is carried out in aq alkali, the corresponding acid is obtained.



Cine Substitution

Mechanism:

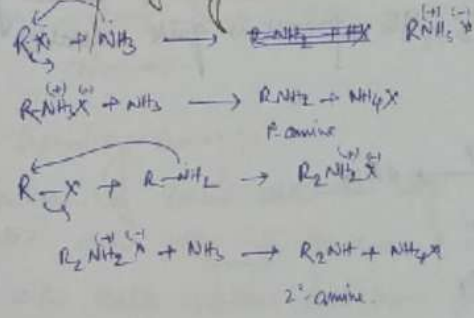


Amines:

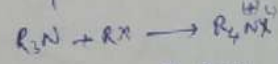
- RNH_2 : Primary amine
- R_2NH : Secondary amine
- R_3N : Tertiary amine
- R_4N^+ : Quaternary ammonium ion
- $(CH_3)_4N^+ Br^-$: Tetramethylammonium bromide

Methods of formation:

1) Hoffmann's ammonolysis of organic halide

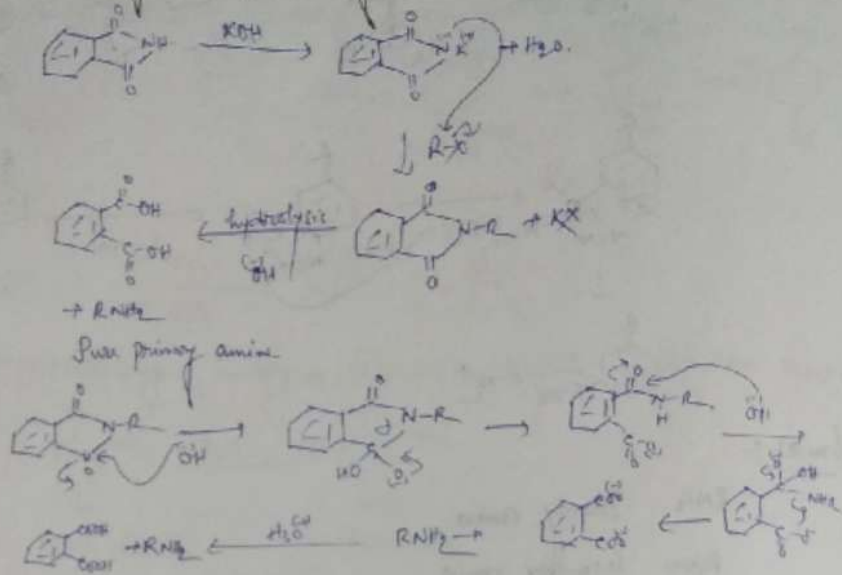


Similarly $\rightarrow R_3N$



Treatment of alkyl halide with ammonia at room temperature or on heating with $100^\circ C$ in a sealed tube, results in the formation of a primary amine salt which then undergoes acid-base reaction with ammonia to give primary amine. The above rxn has limited synthetic application, because primary amine product competes with NH_3 to react with alkyl halide to give salt of 2° and 3° amine and finally quaternary ammonium salts.

Catalytic phthalimide synthesis of primary amine :->

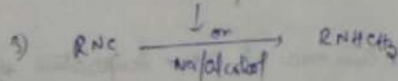
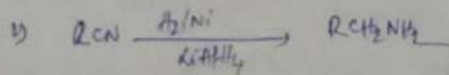
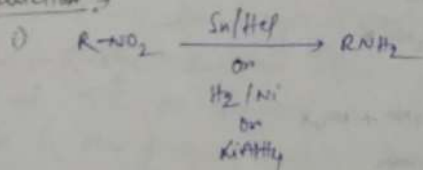


By ammonolysis of alcohol :->

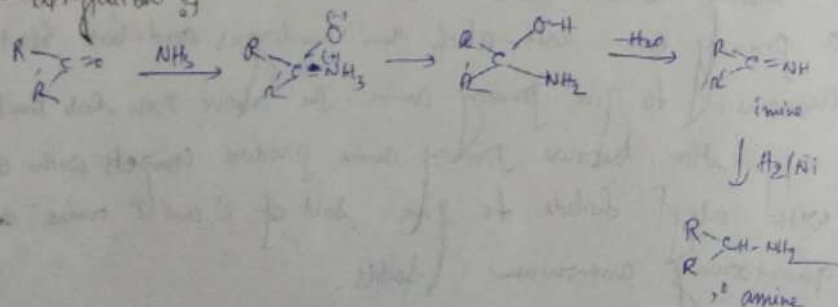


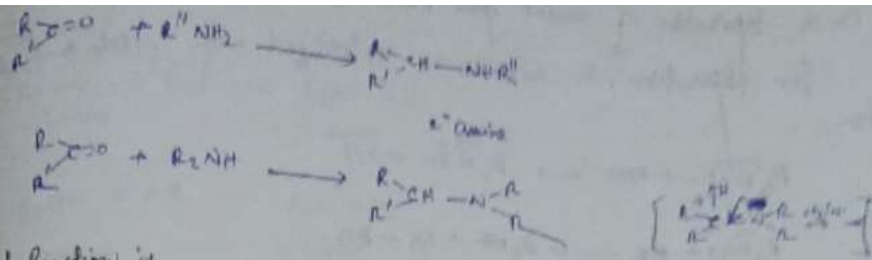
A mixture of primary, secondary and tertiary amines may be obtained by heating a mixture of alcohol and ammonia under pressure in the presence of catalyst Al_2O_3 . The process is quite suitable for preparation of tertiary amines.

By reduction :->



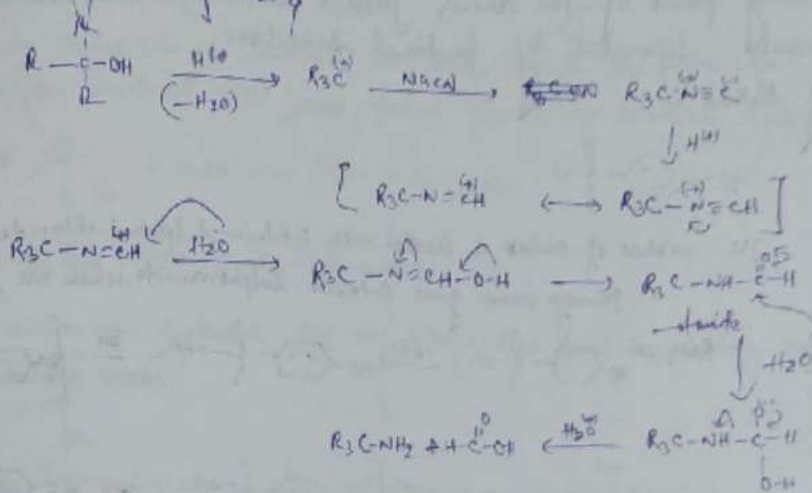
By reductive alkylation :->





Ritter Reaction :-

Method for preparing primary amine, containing a tertiary alkyl group
 The Ritter reaction involves the reaction of nitrile in presence of H₂SO₄

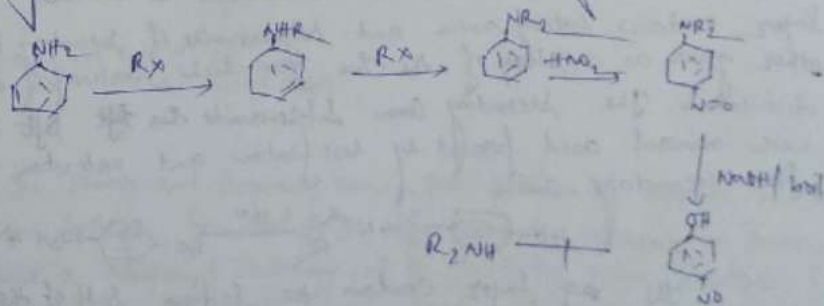


Reaction with Grignard reagent :-



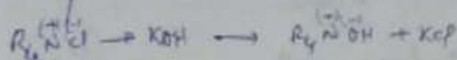
Preparation of Secondary amine :-

Aniline is treated with an alkyl halide and the product dialkyl aniline is treated with HNO₃ to produce p-nitroso-dialkyl aniline. It is then boiled with NaOH solution and then pure secondary amine and para-nitrosophenol are produced.



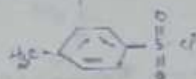
Distinction and separation of amines from their mixtures is

for separation, the mixture is neutralized with alkali and subjected to distillation.

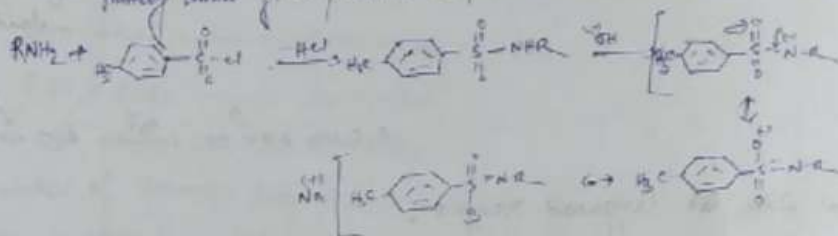


Primary, secondary and tertiary amines are distilled over leaving behind the quaternary ammonium compounds. The mixture of three amines are thus obtained as the distillation is then subjected to fractional distillation. If the boiling points of the amines present in the mixture are different, they are easily separated by fractional distillation.

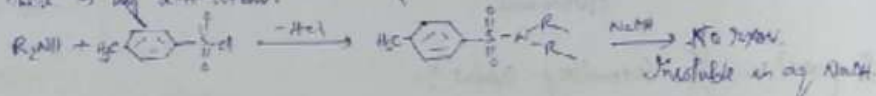
Hinsberg Method is



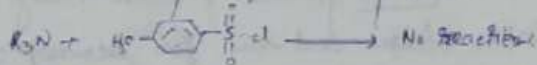
1) The mixture of amines is treated with p-toluenesulfonyl chloride followed by aqueous alkali. Primary amines give p-toluenesulfonamides, which are soluble in alkali.



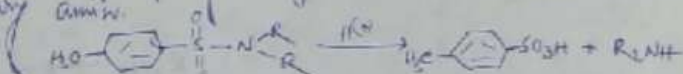
Secondary amines form N-toluenesulfonyl p-toluenesulfonamides, which are insoluble in alkali as there is no α -H-atom.



Tertiary amines remain unaffected on treatment with p-toluenesulfonyl chloride as there is no proton in tertiary amines.



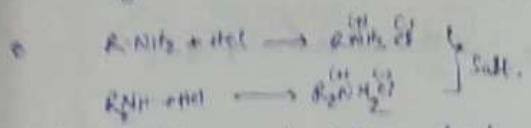
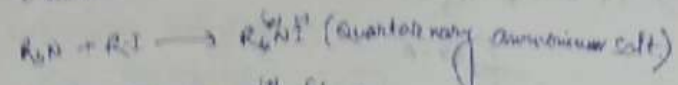
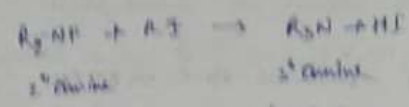
The alkaline mixture thus obtained is extracted with ether, the etheral layer contains tertiary amines and sulfonamide of secondary amines. Evaporation of ether gives a mixture of the two from which tertiary amines are obtained by distillation. The secondary amine sulfonamide that is left behind is treated with mineral acid followed by basification and extraction with ether liberates free secondary amines.



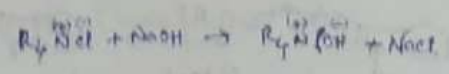
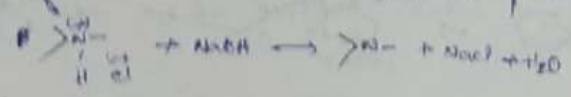
The aq. layer contains the sodium salt of the sulfonamide of primary amines. This is acidified with excess acid. This regenerates the sulfonamide, which is hydrolysed to the primary amines left (on heating the new mixture). Basification generates free primary amines which may be recovered by distillation or by extraction with ether.

Reaction of Amines :-

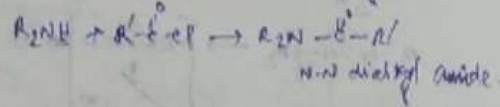
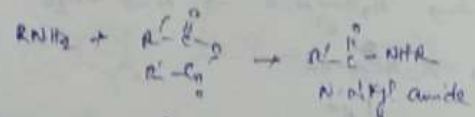
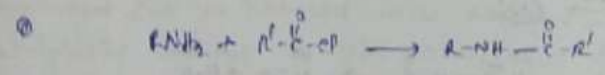
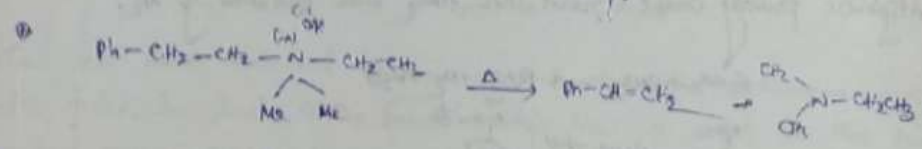
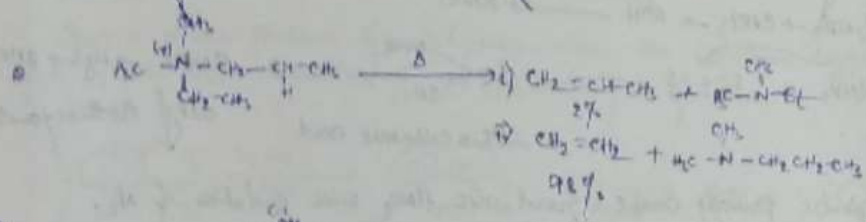
Alkylation of Amine



The ordinary amine salt on treatment with base, liberate free amine, but quaternary ammonium salt, on treatment with base, formed quaternary ammonium hydroxide.



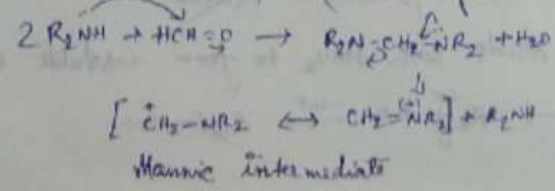
Quaternary ammonium hydroxide are very strong base, and on heating, they give alkene and tertiary amine.

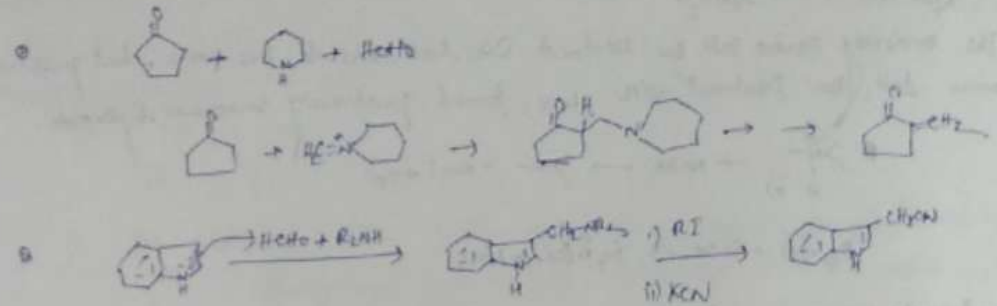
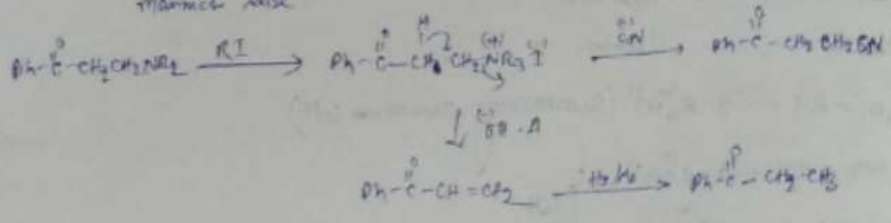
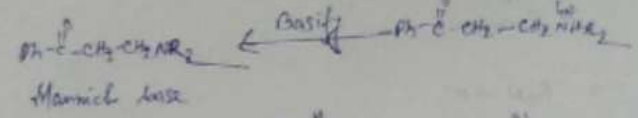
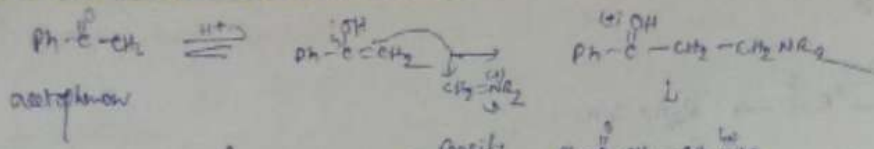


2nd

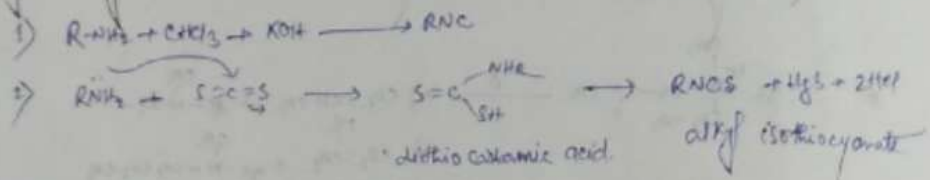
Mannich Reaction :-

The primary and secondary amine participate in the Mannich reaction. This is the condensation between formaldehyde or other aldehyde, ammonia or primary or secondary amine and a compound containing at least one active H atom. eg. ketone, keto ester, nitro-alkanes etc. The rxn is usually carried out in acid solution.





Reaction of primary amine:

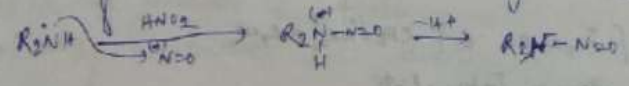


3) Aliphatic primary amine react with HNO_2 with evolution of N_2 .



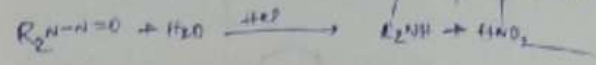
Aromatic diazonium chloride is stable due to aromatic conjugation but aliphatic diazonium chloride is not stable so produce alcohol depending on R, product may be isomeric alcohol, isomeric alkene.

Secondary amine reacts with HNO_2 to form insoluble oily nitrosamine

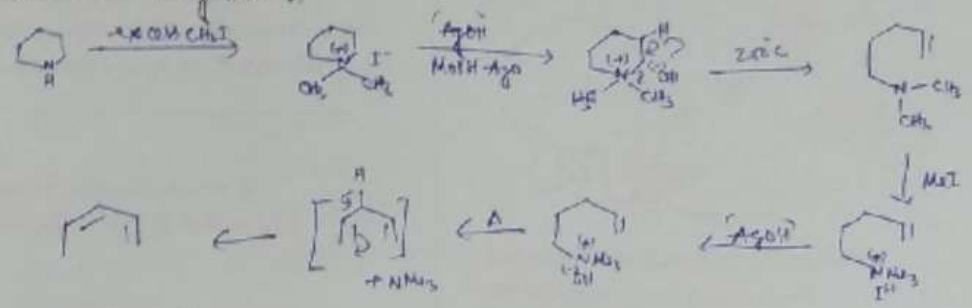


Nitrosamines are yellow neutral oils, which are steam volatile, show Lassaigne's test, and a few drops of conc. H₂SO₄. Nitrosamines form a green solution, which turns blue with aq. NaOH, then turns deep blue. This procedure may be used as a test for secondary amine. It is known as Heilmann's nitroso test.

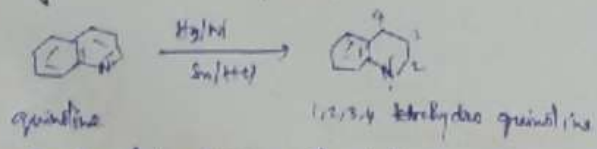
Nitrosamines are readily hydrolysed to the amine by boiling with dil. HCl.



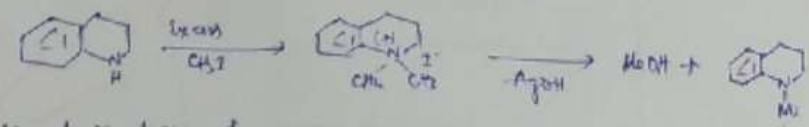
Hofmann exhaustive methylation:



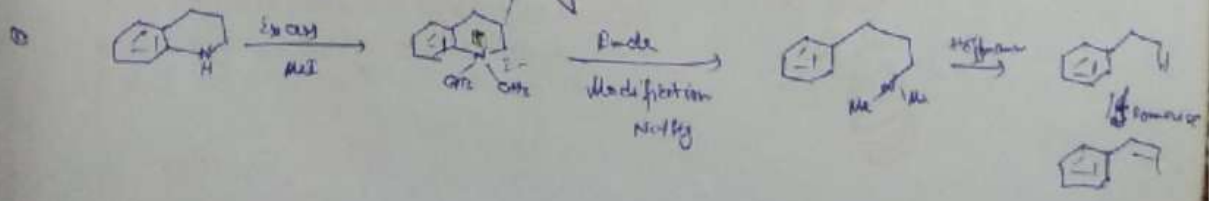
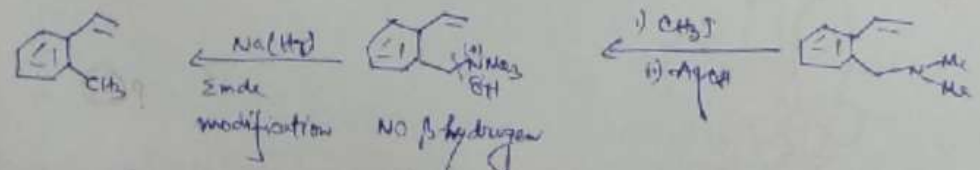
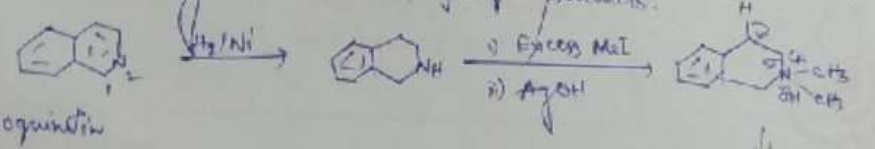
Emde degradation (modification)



In spite of the presence of a β -hydrogen atom, the Hofmann degradation is unsuccessful with the derivative of 1,2,3,4-tetrahydroquinoline.



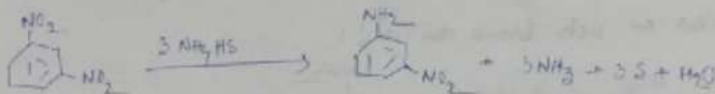
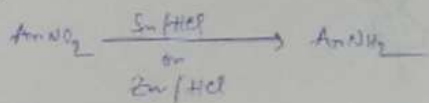
When the base does not contain a β -H atom, the exhaustive methylation method is also failed. In such cases, Emde modification is used. In this process, quaternary ammonium salt is reduced with Na(Hg) in aq. EtOH or with Na in dig. H₂ or catalytically reduced to give C-N bond fission products.



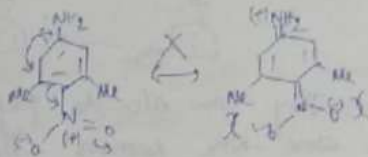
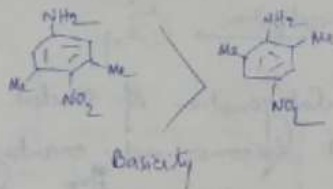
o-Aromatic Amine Compounds :-

- Primary : $ArNH_2$
 Secondary : Ar_2NH , $Ar-NHR$
 Tertiary : Ar_3N , Ar_2NR , $ArNR_2$

Preparation :-



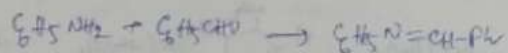
Basicity of aromatic amine :-



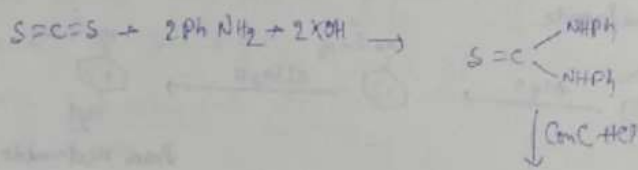
Steric inhibition of resonance

Chemical rxns :-

i) Aniline condenses with aromatic aldehyde to form anilines of Schiff's bases

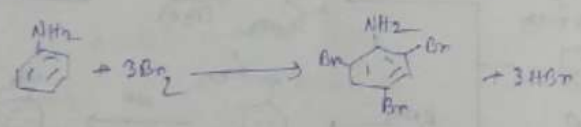


ii) when refluxed with ethanolic CS_2 and solid KOH , aniline forms N-N diphenyl thiourea.



\downarrow Conc. HCl
 C_6H_5NCS phenyl isothiocyanate

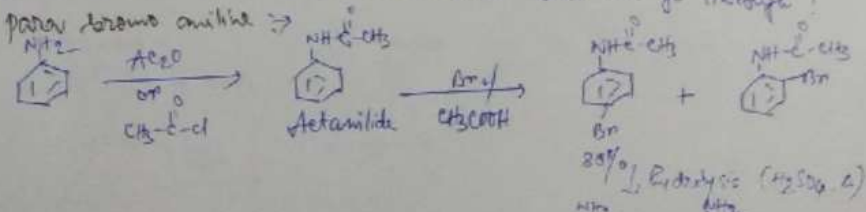
Halogenation :-



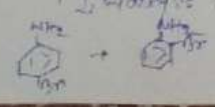
2,4,6-tribromo aniline (PPL)
 (Quantitative)

The yield is quantitative and so this rxn is used to estimate aniline. To introduce one Cl or Br atom, how could we go through?

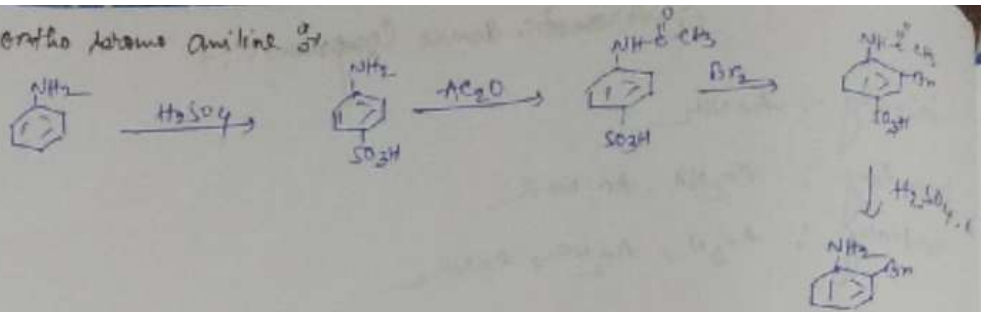
Preparation of para-bromo aniline :-



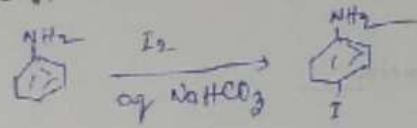
Can be separated by steam distillation to produce para-bromo aniline.



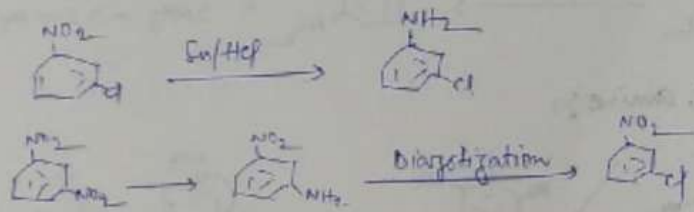
Preparation of ortho bromo aniline :-



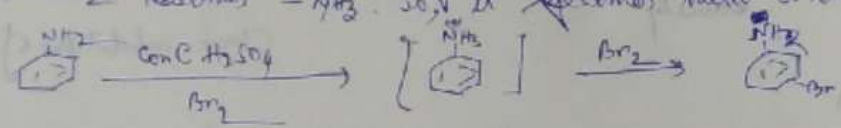
Para iodo aniline :-



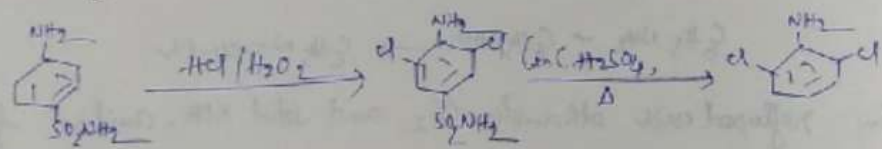
Meta chloro aniline or meta bromo aniline :-



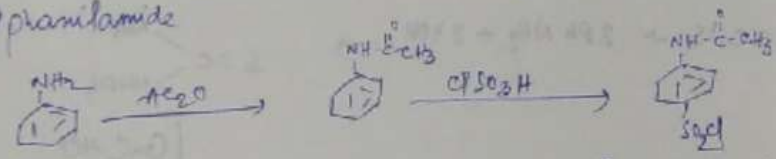
They can also be prepared by halogenation of aniline in conc H_2SO_4 . Here $-NH_2$ becomes $-NH_3^+$. So, it becomes meta orienting.



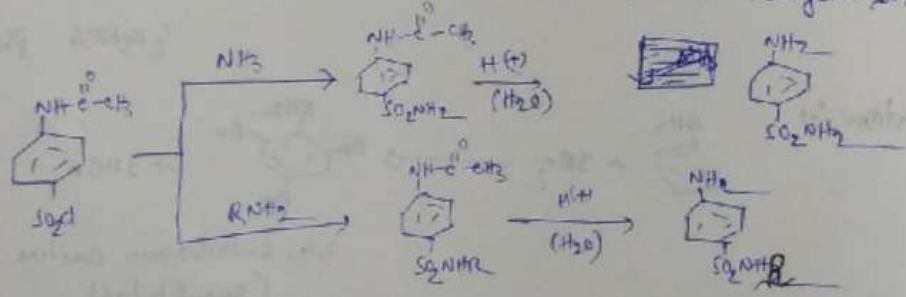
2,6 dichloro aniline :-



Sulpharamide

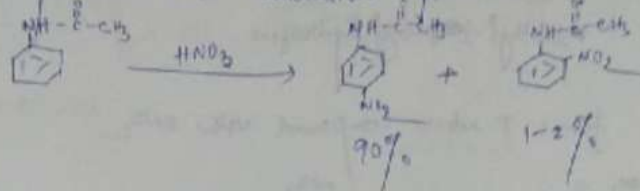


Para acetamide benzene sulphonic chloride

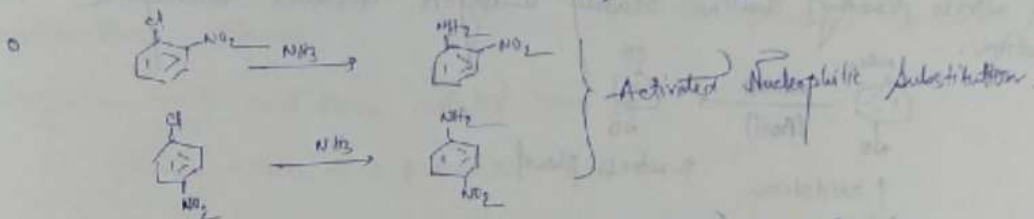
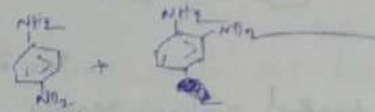


Nitro Anilines :-

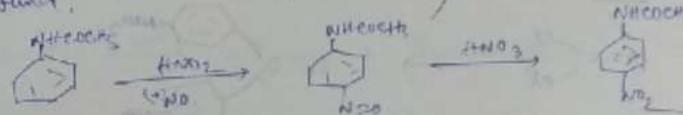
Direct nitration of aniline gives a complex mixture of mono, di and tri nitro compounds and oxidation product.



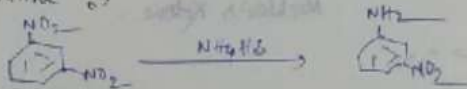
\downarrow H_2SO_4



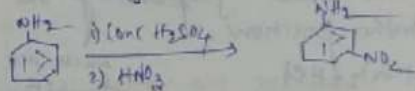
Nitration of aniline derivative is accelerated by HNO_2 . This is believed to be due to the formation of nitroso compound followed by oxidation to the nitro compound.



Meta nitro aniline :-

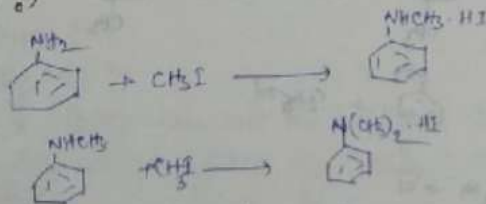


Meta nitro aniline may also be prepared by direct nitration of aniline in presence of $Conc. H_2SO_4$.

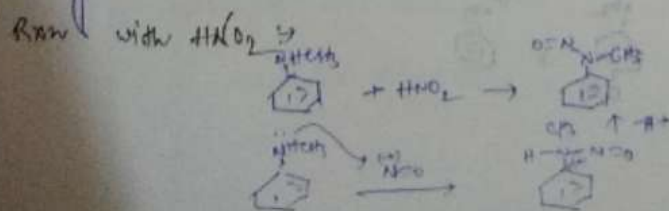


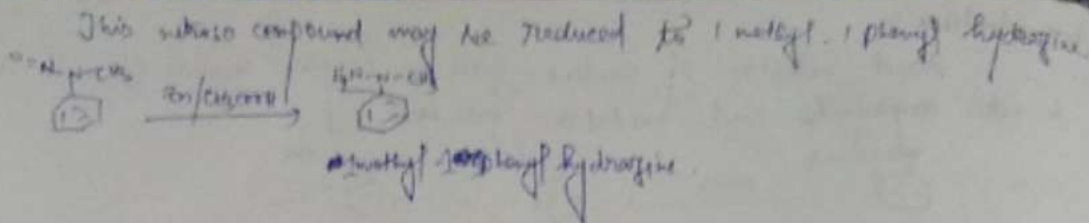
N-alkyl anilines :-

Preparation:

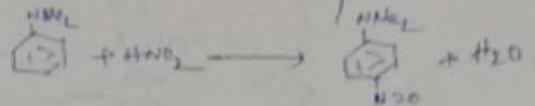


Monos alkyl anilines form pale yellow N-nitroso amines with HNO_2 and give Libermann's nitroso test.



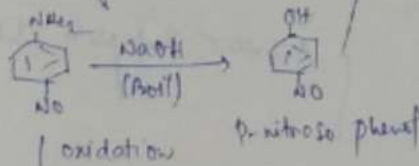


Dialkyl anilines forms p-nitroso compound with HNO_2

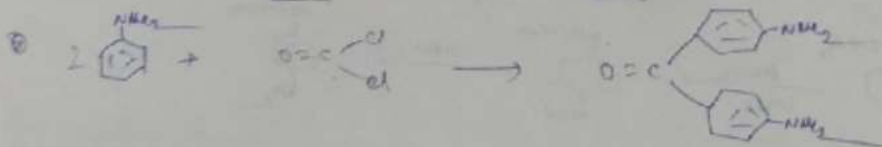
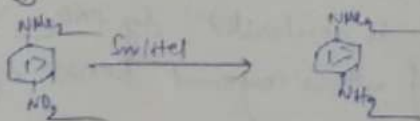


Para nitroso N,N-dimethylaniline

Para nitroso dimethyl aniline readily undergoes activated nucleophilic substitution.



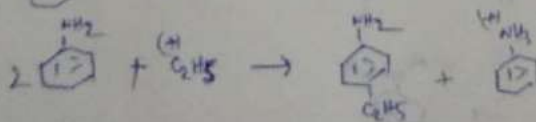
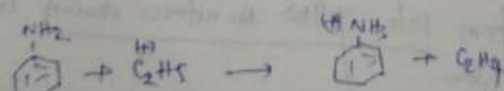
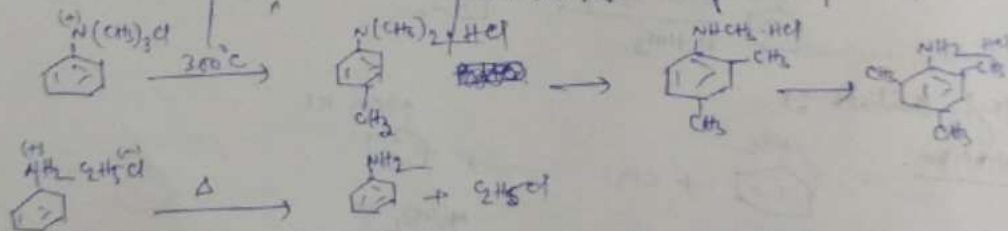
oxidation



Nichol's Ketone

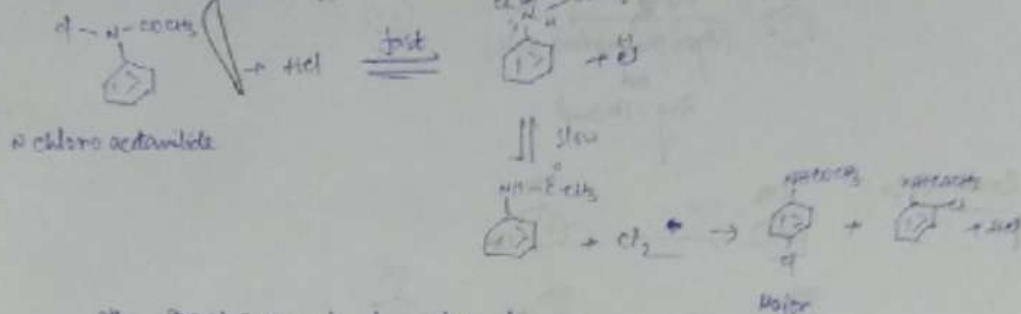
Hofmann-Martin rearrangement :-

Mono and dialkyl and quaternary compounds as their hydrochlorides undergo rearrangement on strong heating an alkyl group migrates from the N atom and enter preferentially the para position or if this is occupied the ortho position.



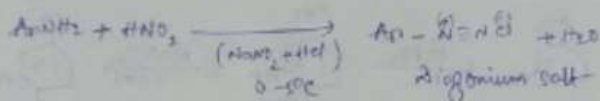
The Orton rearrangement is

chloramine rearrangement is

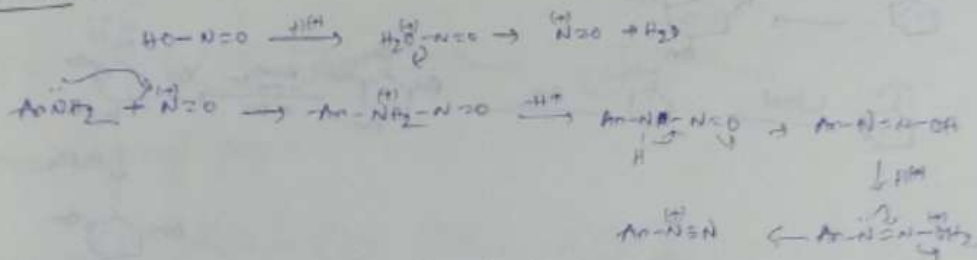


The rearrangement is intermolecular when HCl labelled with radioactive Cl_2 . The \parallel form chloroacetamide products contain some radioactive chlorine.

Diazonium salts and their related rxns:



Mechanism:

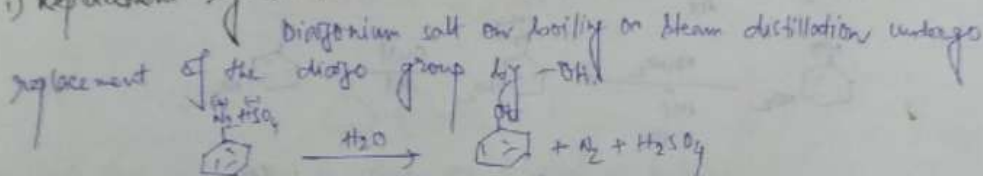


Row of Diazonium salt may be divided into two parts.

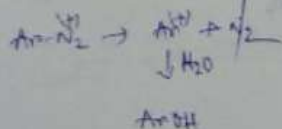
- 1) Row in which N_2 is liberated and the diazo group is replaced by some other univalent group.
- 2) Row in which N_2 atoms are retained.

Replacement rxn:

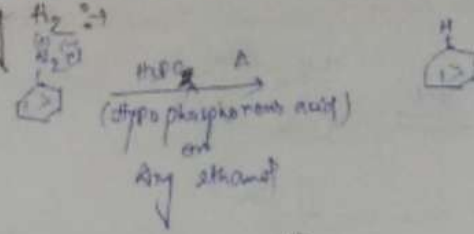
i) Replacement by $-OH$:



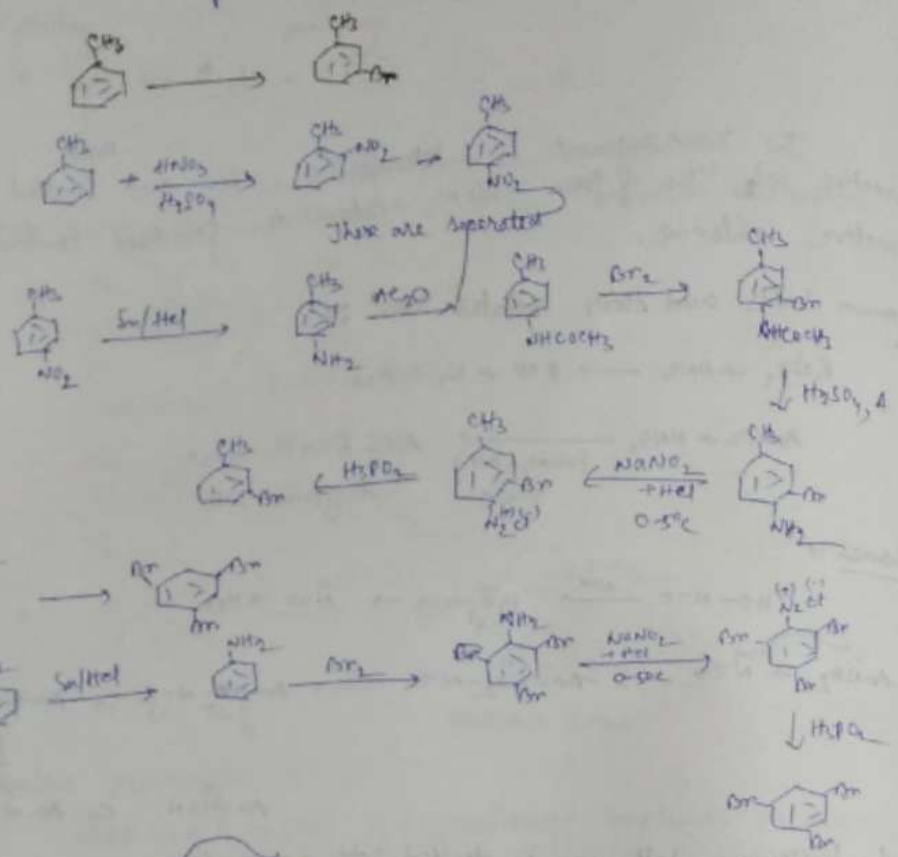
The rxn is nucleophilic



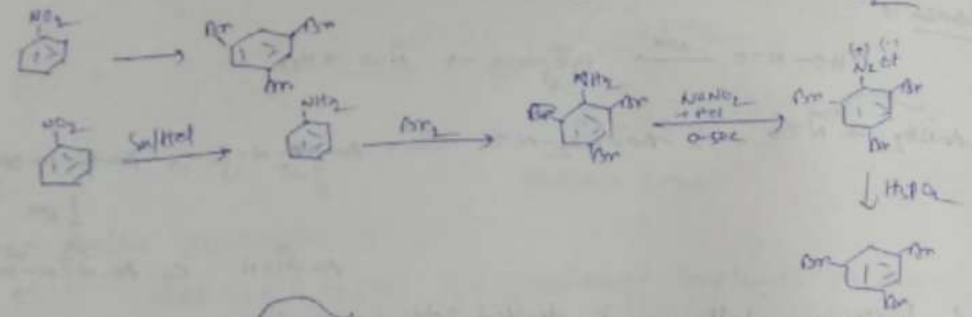
Replacement by $H_2 \Rightarrow$



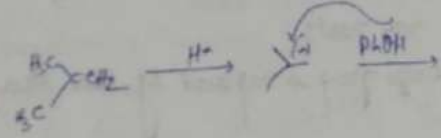
Convert \Rightarrow



ii

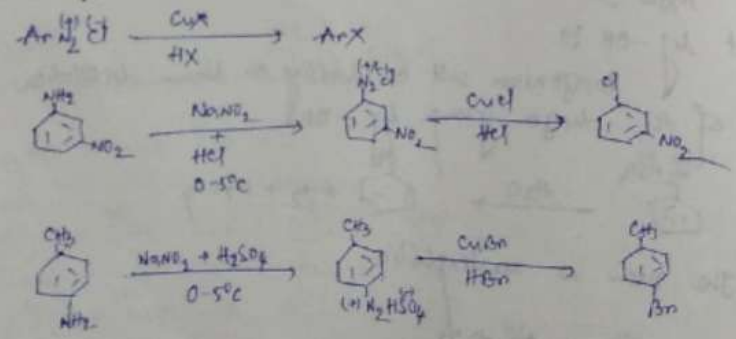


iii

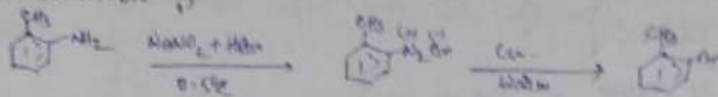


Replacement by halogen \Rightarrow

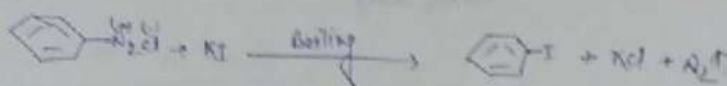
i) Sandmeyer reaction \Rightarrow



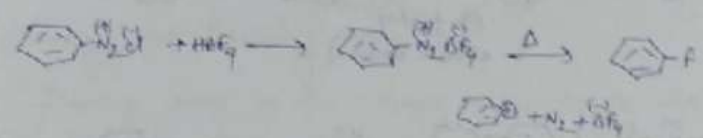
2) Gattermann reaction is



Sodo Compound:

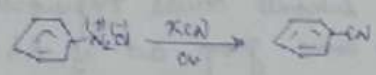


Fluoro Compound:

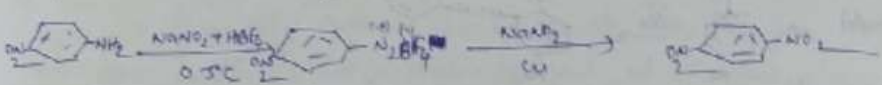


Replacement by cyano group:

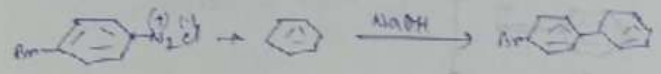
Sandmeyer reaction + Gattermann



Replacement by nitro group:

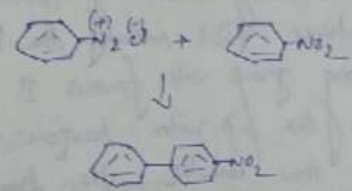


Replacement by aryl group:



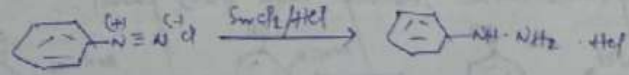
biarzenium salt, on heating with aromatic hydrocarbon, in presence of alkali, afford biaryl derivative.

Whatever the nature of the substituent in the second component, only para substitution always occurs predominantly. But some meta isomer is also formed.

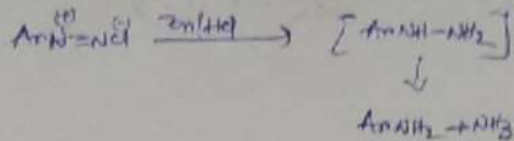


Row of diazonium salts in which the 'N' atoms are retained.

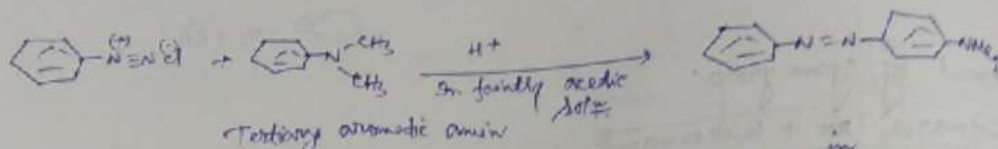
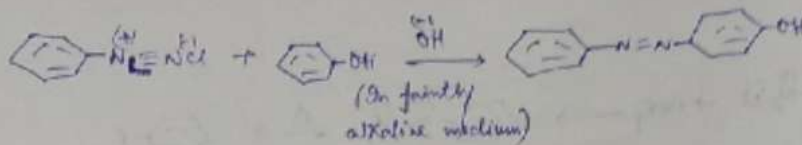
When reduced with SnCl_2/HCl diazonium chloride form phenyl hydrazine.



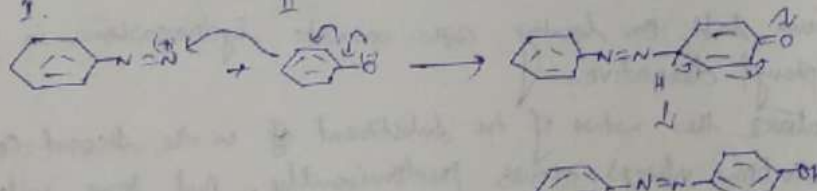
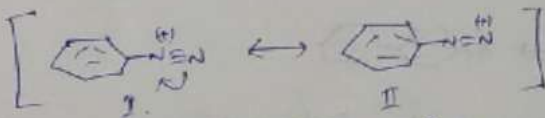
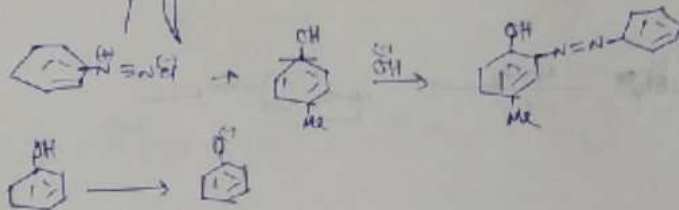
If vigorous reducing agent as for example Zn/HCl are used, the product is an aromatic amine.



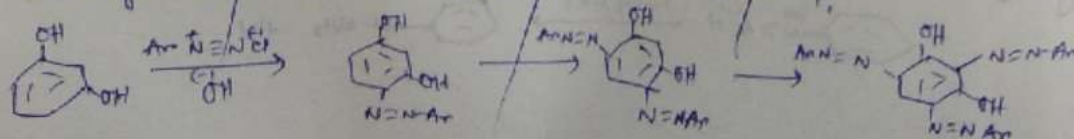
② Coupling rxn is



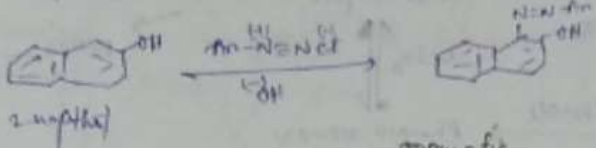
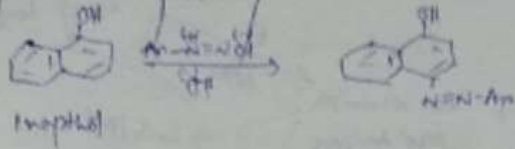
Coupling with benzene substrate occurs preferentially at the ortho position, to the hydroxyl or amine group. But if this is blocked then para coupling occurs.



Structure II is the reactive contributing resonating structure and any factor that increases its contribution will increase the reactivity of diazenium cation. Electron withdrawing group will favour II and electron releasing group will favour I. So the p nitro benzene diazenium cation is more reactive than p methyl ion under the same condition. Presence of another activating group in the meta position of phenol and on amine accelerates coupling eg. Resorcinol forms mono, bis and tris azo compounds more readily than does phenol.

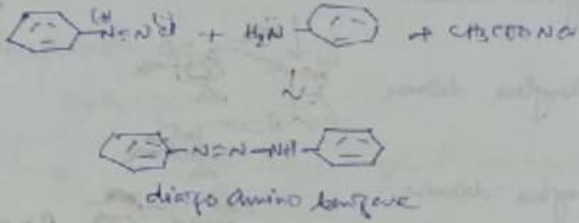


1 and 2 naphthol in ortho and para positions respectively couple with diazonium salt in the presence of

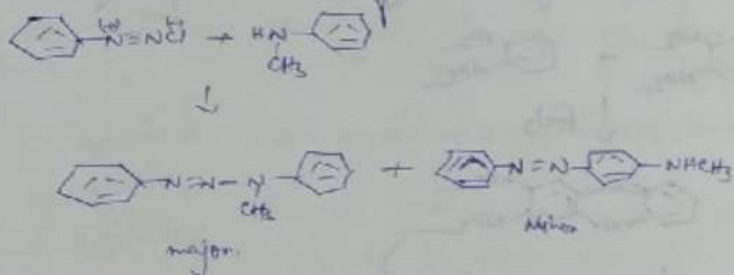


Coupling with primary and secondary amine:

Primary amine as for example aniline, couple with benzene diazonium chloride to form diazo amino benzene.



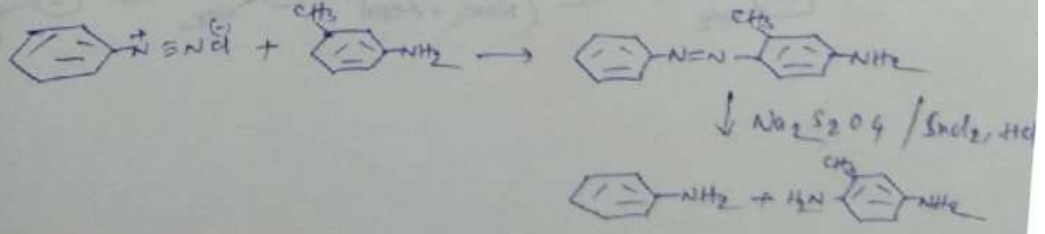
Secondary amine similarly couple with benzene diazonium chloride to form methyl diazo-amino benzene at the same time however C-azo coupling takes place and some methyl amino also benzene is formed.



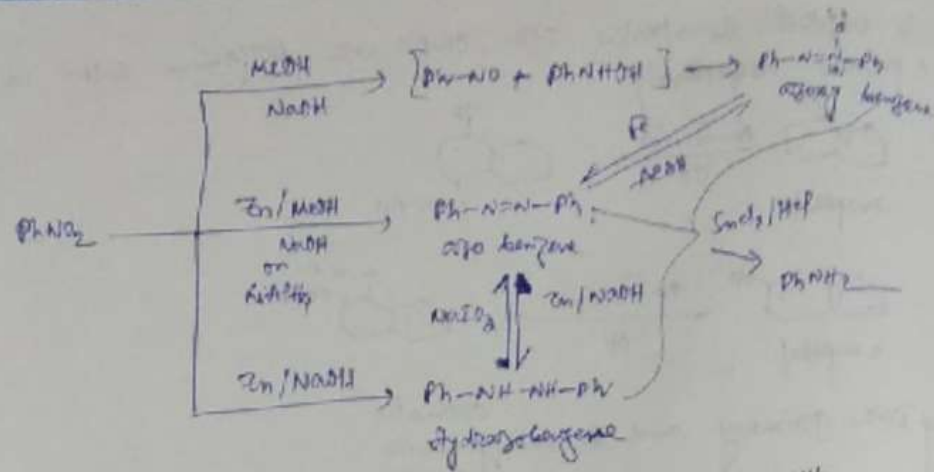
With tertiary amine, the formation of diazo amino compound is impossible, the amino azo compound is always formed by direct coupling in the para position.



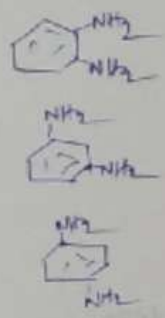
Reduction of azo compound with sodium hyposulphite or SnCl2/HCl offers a relative simple methods of preparing diamines (or amino phenol) in pure state.



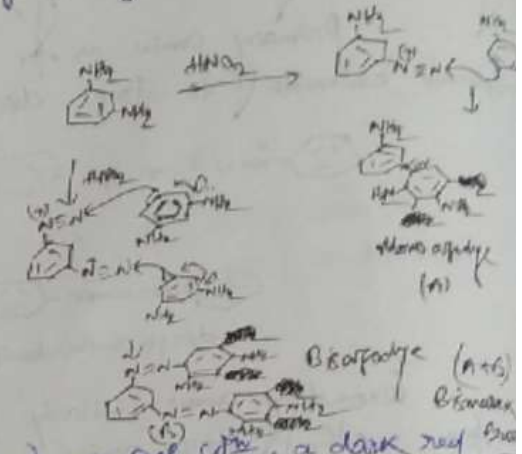
①



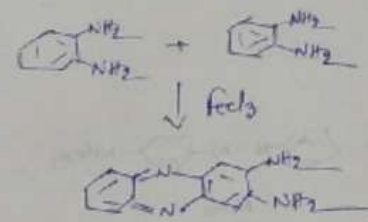
Diamines :-



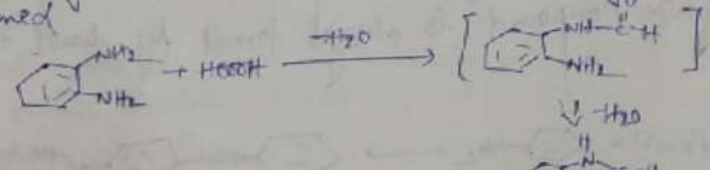
o-phenylene diamine
m-phenylene diamine
p-phenylene diamine



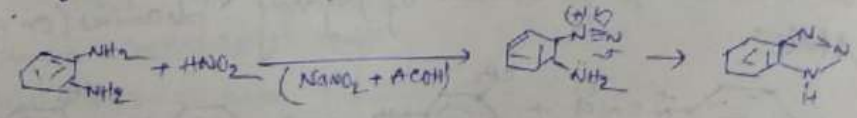
Reins when o-phenylene diamine is treated with FeCl₃ solⁿ, a dark red colour is produced due to formation of 2,2'-diaminodiphenylamine



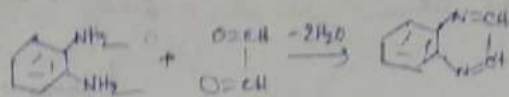
② when o-phenylene diamine is heated with organic acid, benzimidazole is formed



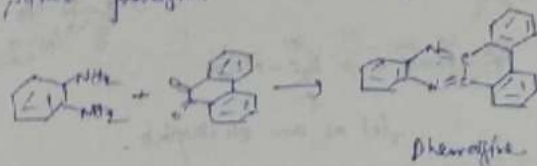
③ when o-phenylene diamine is treated with HNO₂, benz-triazole is formed.



o-phenylene diamine condenses with α -dicarbonyl compound to form quinoxaline

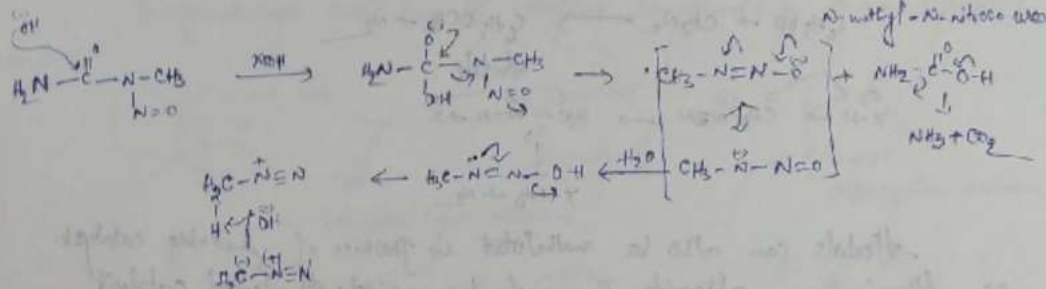
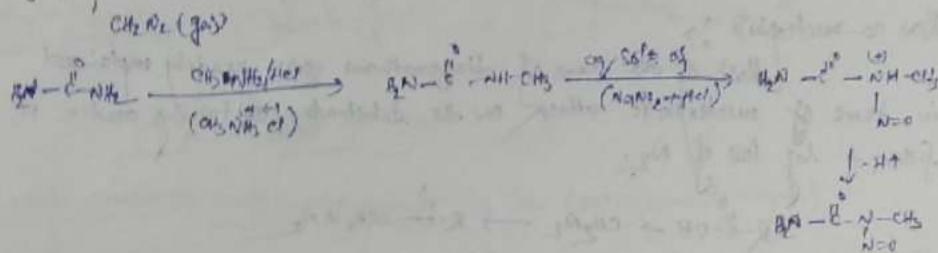


This rxn is used to identify ortho diamines. The α -dicarbonyl compound employed for this purpose is phthalic anhydride, resulting in the formation of a sparingly soluble quinoxaline

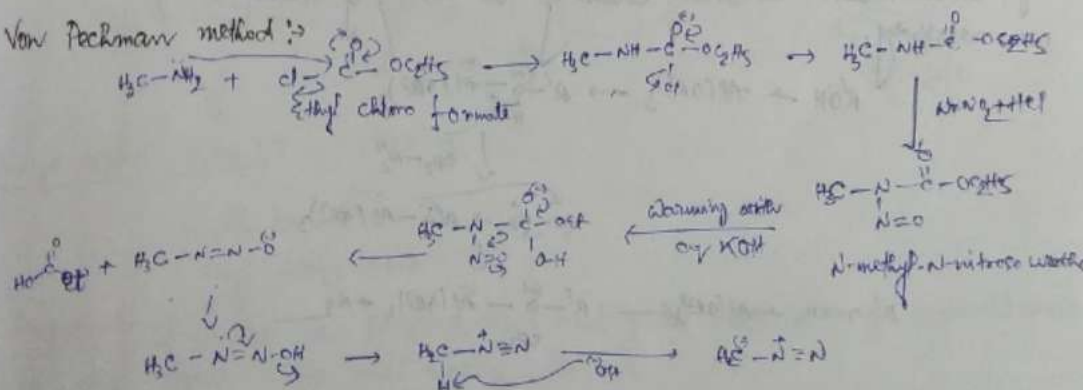


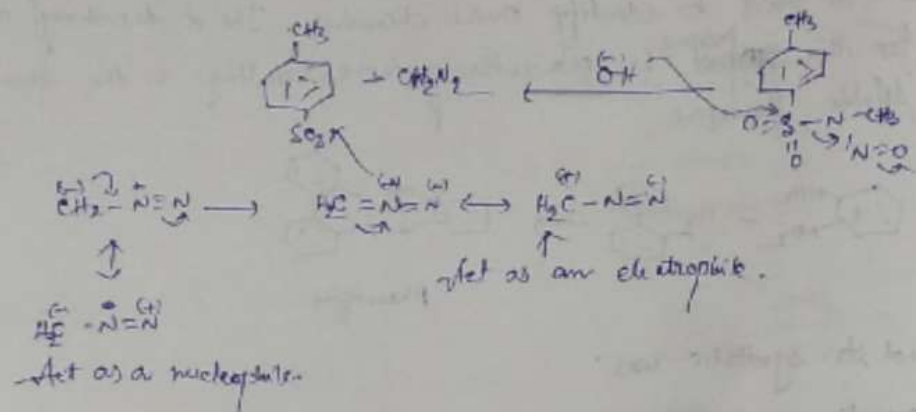
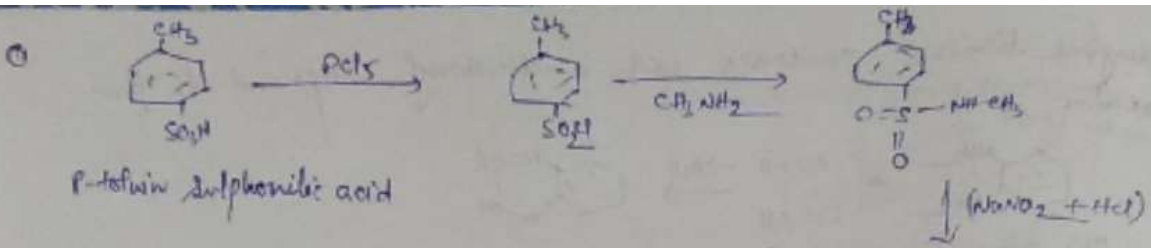
Diazomethane and its synthetic uses:

Methods of preparation:



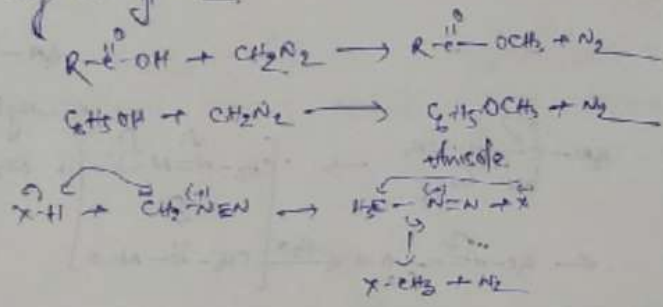
Von Peckmann method:



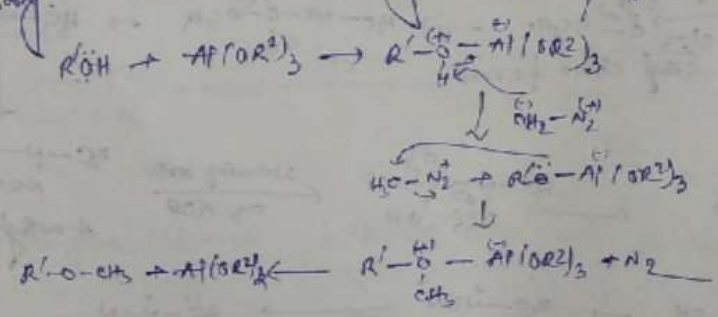


Reas :-

Reas as nucleophile :-
 Most of the reas of diazotization are readily explained in terms of nucleophilic attack on the substrate, containing acidic H, followed by loss of N_2 .

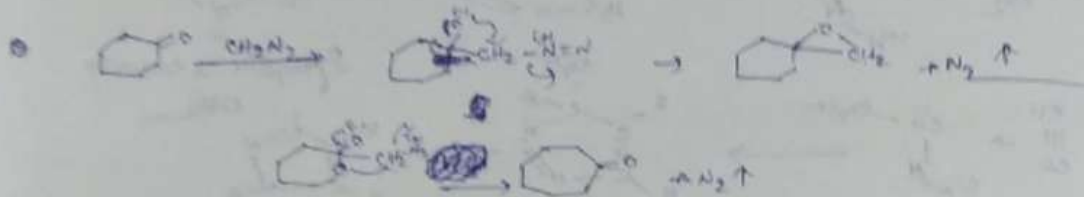
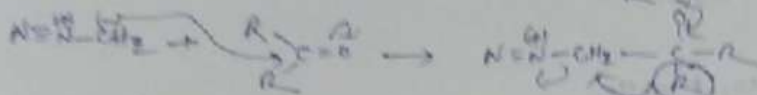
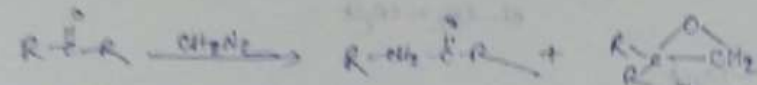
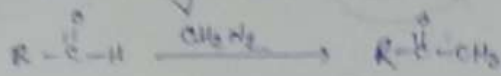


Alcohols can also be methylated in presence of suitable catalyst eg. Aluminium alkoxide. Because of low acidity of alcohol, catalyst are necessary.



Reaction with Carbonyl compound:

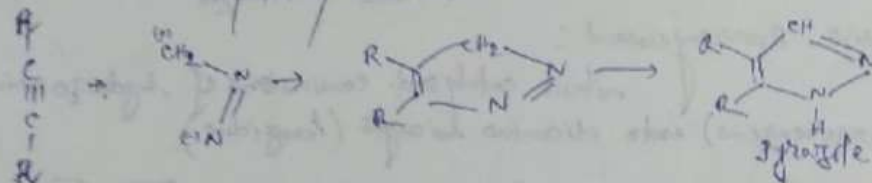
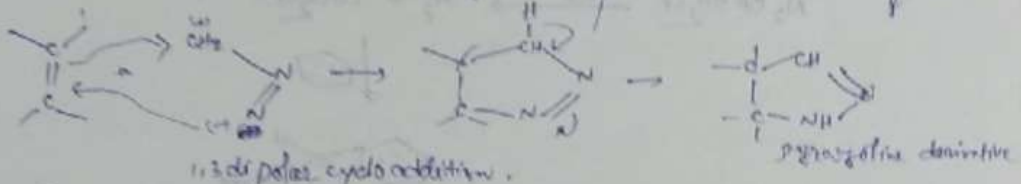
React with aldehyde to form methyl ketone, and with ketone to form higher homologues. In some cases an epoxide is formed and may be the predominant product.



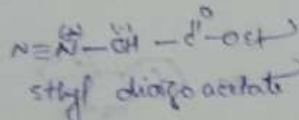
Amide-ester synthesis: Wolff rearrangement \rightarrow (see rearrangement chapter)

Diagonals add on to ethylene compounds to form pyrazoline derivative

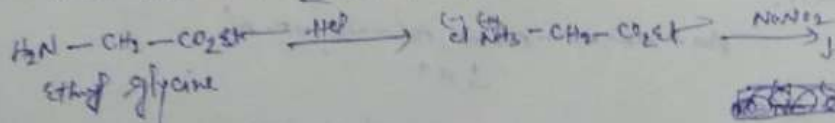
Derivative



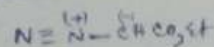
Diazo acetic ester \rightarrow



Preparation: May be prepared by treating a cooled soln of hydrochloride of ethyl glycine with cold $NaNO_2$ soln.

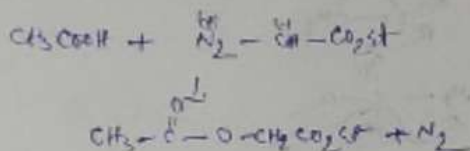
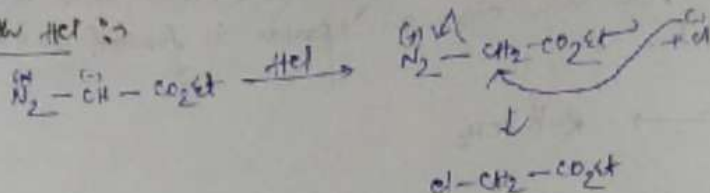


~~CH_3-CH_2-NH_2~~

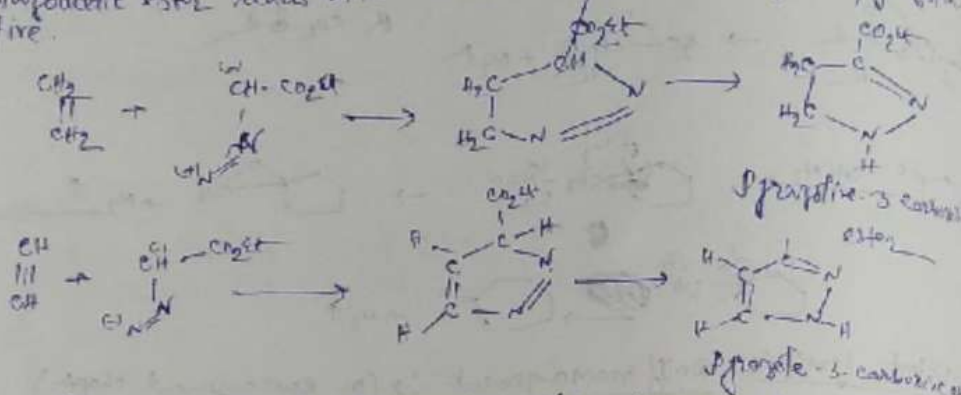


Reactions:

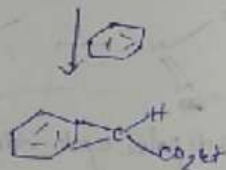
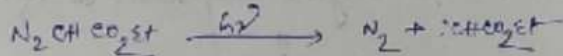
Reactions with HCl :



Diazooacetate ester reacts with ethelnic compounds to form pyrazole derivative.

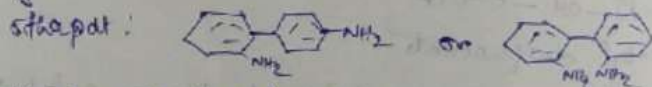
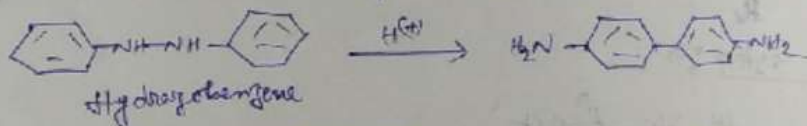


In some cases, diazoacetate ester decomposes to carbethoxy methylene

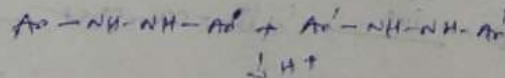


Benzidine Rearrangement:

Acid catalysed conversion of hydrozoarines (hydroazobenzene) into diamino biaryls (benzidine)



The rearrangement is intramolecular, no cross prod. is formed.



No cross prod.

Mechanism \Rightarrow

