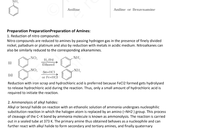
Amines

Amines are derivatives of ammonia (NH_3) in which one or more hydrogen atoms have been replaced by alkyl/aryl groups.

CLASSIFICATION: Amines are classified as primary (1°), secondary (2°) or tertiary (3°) according to the number of alkyl groups attached to the nitrogen atom.

STRUCTURE : The nitrogen atom in amine is sp^3 hybridised. The three hybrid atomic orbitals are involved in bonding with three other atoms (alkyl/aryl groups or hydrogen) and the unshared pair of electrons, giving the pyramidal structure as shown



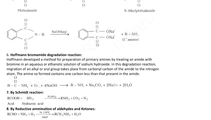
Nomenclature: In common system, an aliphatic amine is named by prefixing alkyl group to amine. In IUPAC system, it is named as alkanamine. Prefixes di and tri are used when two or three alkyl/aryl groups are attached to the same amine. For example, CH3NH2, is named as methanamine.

Structure	Common name	IUPAC name
CH_3-NH_2	Ethylamine	Ethanamine
$CH_3-CH_2-CH_2-NH_2$	n-Propylamine	Propan-1-amine
$CH_3-CH(CH_3)-CH_2-NH_2$	Isopropylamine	Propan-2-amine
$C_6H_5-NH_2$	Ethylphenylamine	N-Methylbenzenamine
$CH_3-N(CH_3)-C_6H_5$	Trimethylamine	N,N Dimethylbenzenamine
	Aniline	Benzenamine

Preparation Preparation/Preparation of Amines:

1. Reduction of nitro compounds:

Aliphatic and aromatic primary amines by passing hydrogen gas in the presence of finely divided nickel, palladium or platinum and also by reduction with metals in acidic medium. Nitroalkanes can also be similarly reduced to the corresponding alkanamines.



Reduction with iron scrap and hydrochloric acid is preferred because FeCl2 formed gets hydrolysed to release hydrochloric acid during the reaction. Thus, only a small amount of hydrochloric acid is required to initiate the reaction.

2. Ammonolysis of alkyl halides:

Alkyl or benzyl halide on reaction with an ethanolic solution of ammonia undergoes nucleophilic substitution reaction to form primary amine, secondary amine, tertiary amine and quaternary salt. Disadvantage of this 1° amine is that its ammonolysis reaction is known as polyamine. This reaction can be carried out in sealed tube at 373 K. The primary amine thus obtained behaves as a nucleophile and can react with the alkyl halide to form secondary and tertiary amines, and finally quaternary ammonium salt.

Thus amine can be obtained from the ammonium salt by treatment with a strong base:

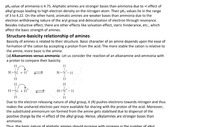
$R-CH_2-I + NaOH \rightarrow R-CH_2-NH_2 + CH_3OH + NaI$

Ammonolysis has the disadvantage of yielding a mixture of primary, secondary and tertiary amines and also a quaternary ammonium salt. However, primary amine is obtained as a major product by using a large excess of ammonia. The order of reactivity of halides with ammonia is : I > Br > Cl.

3. **Reduction of nitriles:**

Nitriles on reduction with lithium aluminium hydride (LiAlH4) or catalytic hydrogenation produce primary amines. Hydrogen gas in presence of a catalyst of nickel, platinum or palladium is used for catalytic hydrogenation. The reaction can be shown as

$R-C\equiv N \xrightarrow{LiAlH_4} R-CH_2-NH_2$ or $R-C\equiv N \xrightarrow{H_2/Ni} R-CH_2-NH_2$



4. **Reduction of amides:**

The amides on reduction with lithium aluminium hydride yield amines:

$R-C(=O)-NH_2 \xrightarrow{LiAlH_4} R-CH_2-NH_2$

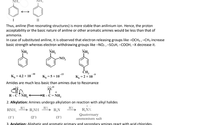
5. **Gabriel phthalimide synthesis:**

Gabriel synthesis is used for the preparation of primary amines. Phthalimide on treatment with alcoholic potassium hydroxide forms potassium salt of phthalimide which on heating with alkyl halides followed by alkaline hydrolysis produces the corresponding primary amine. Aromatic primary amines cannot be prepared by this method because aryl halides do not undergo nucleophilic substitution with the anion formed by phthalimide.

6. **Hofmann bromamide degradation reaction:**

Hoffmann developed a method for preparation of primary amines by treating an amide with bromine in an aqueous or ethanolic solution of sodium hydroxide. The reaction involves the migration of the alkyl or aryl group takes place from carbonyl carbon of the amide to the nitrogen atom. The amine so formed contains one carbon less than that present in the amide.

$R-C(=O)-NH_2 + Br_2 + 4NaOH \rightarrow R-NH_2 + Na_2CO_3 + 2NaCl + 2H_2O$



Physical Properties:

Methylamine, dimethylamine and trimethylamine are gases with fishy odour. Primary amines with three or more carbon atoms are liquid and still higher ones are solid. Aniline and other arylamines are usually colourless liquids with characteristic odour and are poisonous to breathe in.

Lower aliphatic amines are soluble in water because they can form hydrogen bonds with water molecules. However, solubility decreases with increase in molar mass of amines due to increase in number of hydrophobic alkyl groups. Amines are soluble in organic solvents like alcohol, ether and benzene.

Primary and secondary amines are engaged in intermolecular association due to hydrogen bonding which increases the boiling point of these amines. The order of boiling points of isomeric amines is 1° amine > 2° amine > 3° amine. The boiling point of primary amine is more than that of secondary amine as there are two hydrogen atoms available for hydrogen bond formation in 1°. Tertiary amines do not have intermolecular association due to the absence of

hydrogen atom available for hydrogen bond formation. Therefore, the order of boiling points of isomeric amines is as follows : Primary > Secondary > Tertiary.

Intermolecular hydrogen bonding in primary amines

Chemical Reactions:

Intermolecular association is essentially between nitrogen and hydrogen atoms and the presence of unshared pair of electrons over the nitrogen atom makes amines reactive. The number of hydrogen atoms attached to nitrogen atom also decides the course of reaction of amines; that is why primary, secondary and tertiary amines react in different manner with the reagents. Basicity of amines also

depends on the presence of unshared electron pair. Some of the reactions of amines are described below:

1. **Basic character of amines:**

Amines, being basic in nature, react with acids to form salts.

Amines react with water to leave the NH_2^- ion to form OH^- ion.

$R-NH_2 + H_2O \rightleftharpoons R-NH_3^+ + OH^-$

Lower the value of K_b or smaller the value of pK_b, stronger is the base.

pK_b value of ammonia is 4.75. Aliphatic amines are stronger bases than ammonia due to +ve effect of alkyl group which increases the electron density on the nitrogen atom. The pK_b value for methylamine is 3.36 and for ethylamine is 3.29. On the other hand, aromatic amines are weaker bases than ammonia due to the resonance withdrawing nature of the ring and also due to delocalisation of electron through resonance. Among the isomeric alkanamines, the inductive effects like ionisation effect, steric hindrance to solvation and the basic strength are in order:

Structure-basicity relationship of amines

The order of basicity of amines in the gas phase is the reverse of the order of basicity of amines in aqueous solution. The order of basicity of amines in the gaseous phase follows the expected order: tertiary amine > secondary amine > primary amine > NH_3. However, in aqueous solution, the order of basicity of amines is not in the expected order. Although the inductive effect of an alkyl group increases the electron density on the nitrogen atom and enhances its tendency to donate a lone pair of electrons to a Lewis acid, the stabilisation of the conjugate acid by electron-releasing effect of the alkyl group decreases the electron density on the nitrogen atom and hence decreases its tendency to donate a lone pair of electrons to a Lewis acid. The order of basicity of amines in aqueous solution is:

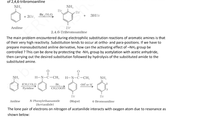
$(CH_3)_2NH > CH_3NH_2 > (CH_3)_3N > NH_3$

The order of basicity of amines with respect to the inductive effect, solvation effect and steric hindrance of the alkyl group which decides the lone pair availability on the nitrogen atom is:

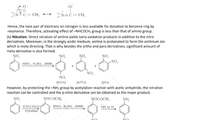
The order of basic strength in case of methyl substituted amines and ethyl substituted amines in aqueous solution is as follows:

$(CH_3)_2NH > CH_3NH_2 > (CH_3)_3N > NH_3$; $(C_2H_5)_2NH > C_2H_5NH_2 > (C_2H_5)_3N > NH_3$

2. **Alkylation:** Amines react with alkyl halides to form 1°, 2° and 3° amines and finally quaternary ammonium salt.



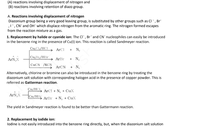
3. **Acylation:** Amines react with acyl halides, acid anhydrides or benzoyl halides to form 1°, 2° and 3° amides.



Amines also react with benzoyl chloride (C6H5CO). This reaction is known as **benzoylation.**

4. **Carbylamine reaction:** Aliphatic and aromatic primary amines on heating with chloroform and ethanolic potassium hydroxide form isocyanides or carbylamines which are foul smelling substances. This reaction is known as carbylamine test for primary amines. This test is not applicable to secondary amines or compounds that are not good as a test for primary amines.

$R-NH_2 + CHCl_3 + 3KOH \xrightarrow{\Delta} R-NC + 3KCl + 3H_2O$



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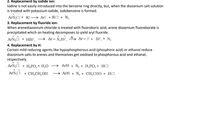


5. **Reaction with nitrous acid**

Three classes of amines react differently with nitrous acid which is prepared in situ from a mineral acid and sodium nitrite.

(i) **Aliphatic primary amines** react with nitrous acid to form aliphatic diazonium salts which being unstable, liberate nitrogen gas quantitatively and alcohols. Quantitative evaluation of nitrogen is used in estimation of amino acids and proteins.

$R-NH_2 + NaNO_2 + HCl \xrightarrow{273K} R-\overset{+}{N}\equiv N\,Cl^- + NaCl + 2H_2O \rightarrow R-OH + N_2 \uparrow + HCl$

(ii) **Aromatic primary amines** react with nitrous acid at low temperature (273-278 K) to form diazonium salt which is extremely stable.

$C_6H_5-NH_2 \xrightarrow{NaNO_2+HCl,\ 273-278K} C_6H_5-\overset{+}{N}\equiv N\,Cl^- + NaCl + 2H_2O$

Secondary and tertiary amines react with nitrous acid in a different manner

(iii) **Secondary aliphatic amines** react with nitrous acid to give **N-nitrosoamines** (N-nitroso amines) which is also known as **nitrosamines**. Reaction with primary and secondary amines to form substituteuredes.

(iv) Tertiary amines react with benzenesulphonyl chloride to form N-ethylbenzenesulphonyl amide.

The hydrogen attached to nitrogen in sulphonamide is strongly acidic due to the presence of strong electron withdrawing sulphonyl group. Hence, it is soluble in alkali.

(b) In the reaction with secondary amine, N,N-diethylbenzenesulphonamide is formed

Since N, N-diethylbenzenesulphonamide is not acidic, it does not react with alkali. Hence, it is not soluble in aqueous KOH.

(c) Tertiary amines do not react with benzenesulphonyl chloride.

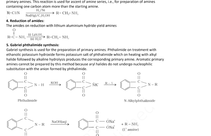
Hinsberg test: This test is used to distinguish primary, secondary and tertiary amines. Hinsberg reagent is used for the distinction of primary, secondary and tertiary amines and also for the separation of a mixture of amines. However, these deaz benzenesulphonyl chloride is replaced by p-toluenesulphonyl chloride.

6. **Electrophilic substitution:**

Due to resonance, Ortho- and para-positionsarch impact. So the ~NH2 group becomes centre of high electron density. Thus, it shows ortho and para-orientation in electrophilic aromatic substitution.

(i) **Bromination:** Aniline reacts with bromine water at room temperature to give a white precipitate of 2,4,6-tribromoaniline

The major problem encountered during electrophilic substitution reactions of aromatic amines is that of their very high reactivity. Substitution tends to occur at ortho- and para-positions. If we have to prepare the monosubstituted product, then the reactivity of the ~NH2 group has to be reduced or controlled ? This is done by protecting the ~NH2 group by acetylation with acetic anhydride, then carrying out the desired substitution followed by hydrolysis of the substituted amide to the substituted aniline.

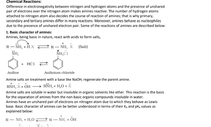


The base just of electrons on nitrogen of acetanilide interacts with oxygen atom due to resonance as shown below:

Hence, the lone part of electrons on nitrogen is less available for donation to benzene ring by resonance. Therefore, activating effect of ~NHCOCH3 group is less than that of amino group.

(ii) **Nitration:** Direct nitration of aniline yields tarry oxidation products in addition to the nitro derivatives because the ~NH2 group is susceptible to attack by the nitrating mixture. To avoid oxidation and to ensure smooth nitration, that is, safe because the nitro and para-isomers, significant amount of meta derivative is also formed.

However, by protecting the ~NH2 group by acetylation reaction with acetic anhydride, the nitration reaction can be controlled and the p-nitro derivative can be obtained as the major product.



(iii) **Sulphonation:** Aniline reacts with concentrated sulphuric acid to form anilinium hydrogensulphate which on heating at 453-473 K for 24 hours, rearranges to the para-aminobenzene sulphonic acid, commonly known as sulfanilic acid, as the major product.

Aniline does not undergo Friedel-Crafts reaction (alkylation and acylation) because its salt formation with aluminium chloride, the Lewis acid, which is used as a catalyst. Due to this, nitrogen of aniline carries positive charge and hence acts as a strong deactivating group for further reaction.

DIAZONIUM SALTS

Diazonium salts have the general formula $R-N_2^+X^-$ where R stands for an aryl group and X for an acid radical. They are prepared by diazotisation process. Primary aliphatic amines give unstable alcohols and stable for a short time orientation at low temperatures (273-278 K). The stability of arenediazonium ion is explained on the basis of resonance.

Method of Preparation Preparation/Preparation of Diazonium Salts:

Aromatic primary amine when treated with a cold and acidic solution of sodium nitrite kept at 273-278K forms a diazonium salt. The reaction mixture has to be kept in the presence of nitrous acid to avoid side reactions of diazonium salt with the unreacted amine. The diazonium salt is not generally isolated but is used immediately for preparation.

$C_6H_5NH_2 + NaNO_2 + 2HCl \xrightarrow{273-278K} C_6H_5-\overset{+}{N}\equiv N\,Cl^- + NaCl + 2H_2O$

Physical Properties:

Benzenediazonium chloride is a colourless crystalline solid. It is readily soluble in water and is stable in cold but reacts with water when warmed. It decomposes even in the dry state.

Benzenediazonium fluoroborate is water insoluble and stable at room temperature.

Chemical Reactions:

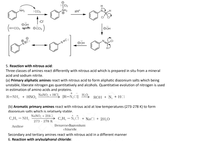
The reactions of diazonium salts can be broadly divided into two categories, namely reactions involving the retention of diazo group and reactions in which the diazo group is replaced by other groups.

A. Reactions involving displacement of nitrogen:

Diazonium group being a very good leaving group, is substituted by other groups such as F^-, Br^-, Cl^-, CN^- and OH- which displace nitrogen from the aromatic ring. The nitrogen formed escapes as molecular nitrogen gas.

1. Replacement by halide or cyanide ion: The Cl^-, Br^- and CN^- nucleophiles can be introduced in the benzene ring in the presence of Cu(I) ion. This reaction is called Sandmeyer reaction.

Alternatively, chlorine or bromine can also be introduced in the benzene ring by treating the diazonium salt solution with cold corresponding halogen acid in the presence of copper powder. This is referred as **Gattermann reaction**.



The yield in Sandmeyer reaction is found to be better than Gattermann reaction.

2. Replacement by iodide ion:

Iodine is not easily introduced into the benzene ring directly, but, when the diazonium salt solution is treated with potassium iodide, iodobenzene is formed.

$ArN_2^+Cl^- + KI \rightarrow ArI + N_2 + KCl$

3. Replacement by fluorine ion:

When arenediazonium chloride is treated with fluoroboric acid, arene diazonium fluoroborate is precipitated which on heating decomposes to yield aryl fluoride.

$ArN_2^+Cl^- + HBF_4 \rightarrow Ar-N_2^+BF_4^- \xrightarrow{\Delta} Ar-F + BF_3 + N_2$

4. Replacement by H:

Certain mild reducing agents like hypophosphorous acid (phosphinic acid) or ethanol reduce diazonium salts to arenes and themselves get oxidised to phosphorous acid and ethanal.

$ArN_2^+X^- + H_3PO_2 + H_2O \longrightarrow ArH + N_2 + H_3PO_3 + HX$

$ArN_2^+X^- + CH_3CH_2OH \longrightarrow ArH + N_2 + CH_3CHO + HX$

5. Replacement by hydroxyl group
When aqueous acid is added to diazonium salt solution is allowed to rise upto 283 K, the salt gets hydrolysed to phenol

$$Ar\overset{+}{N}_2Cl^- + H_2O \longrightarrow ArOH + N_2 + HCl$$

6. Replacement by $-NO_2$ group
When diazonium fluoroborate is heated with aqueous sodium nitrite solution in the presence of copper, the diazonium group is replaced by $-NO_2$ group.

B. Reactions involving retention of diazo-group coupling reactions

The azo products obtained have an extended conjugate system having both the aromatic rings joined through the –N=N–bond. These compounds are often coloured and are used as dyes. Benzene diazonium chloride reacts with phenol in which the phenol molecule at its para position is replaced by the –N=N–C$_6$H$_5$ group. The reaction of diazonium salt with phenol is called as coupling reaction. Similarly the reaction of diazonium salt with aniline yields p-aminoazobenzene. This is an example of electrophilic substitution reaction where diazonium ion acts as electrophile. For coupling reaction to occur, the ring must be activated by electron-releasing groups. Thus, where benzene ring highly activated and not with compounds like nitrobenzene where the ring is deactivated.