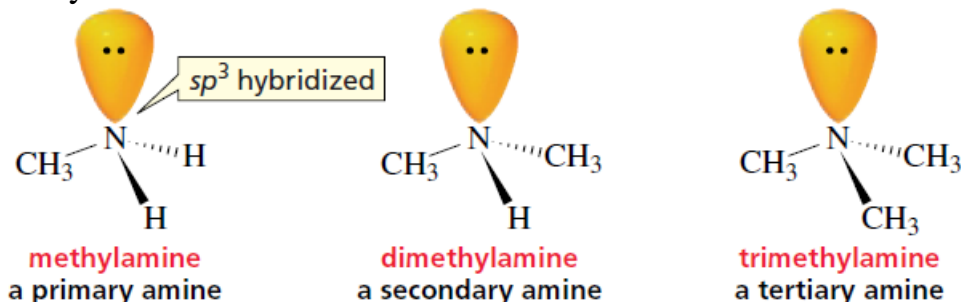


Amines and Diazonium salts

Primary, secondary and tertiary amines, general formula, structures and physical properties.

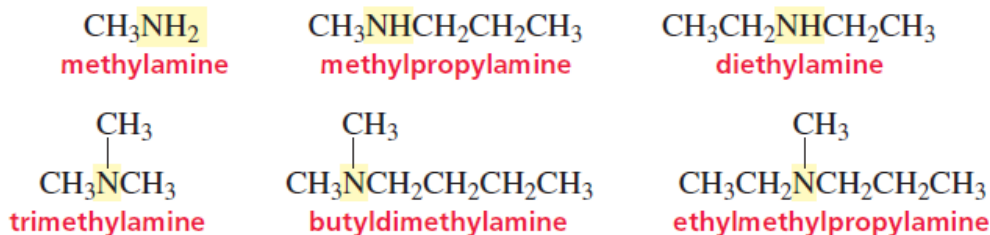
Amines are organic compounds in which one or more of the hydrogens of ammonia have been replaced by alkyl groups (derivatives of ammonia). In the same way that ROH and ROR are organic derivatives of water. Like ammonia amines contain a nitrogen atom with a lone pair of electrons, making amines both basic and nucleophilic.

Amines are classified into **primary, secondary and tertiary amines**. The classification depends on how many alkyl groups are bonded to the nitrogen. Primary amines have one alkyl group bonded to the nitrogen, secondary amines have two, and tertiary amines have three.

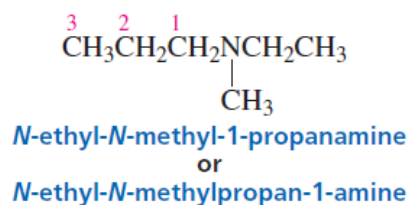
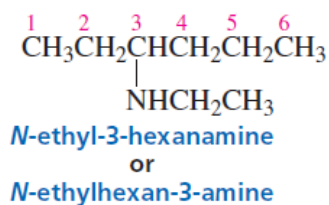
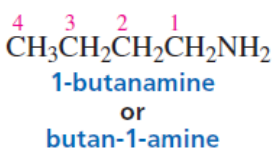


Nomenclature

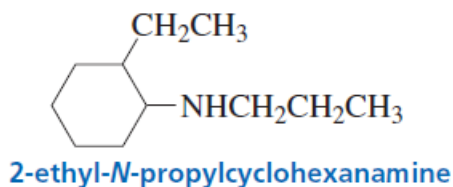
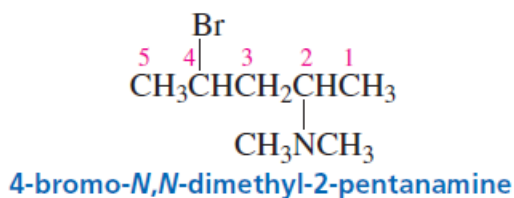
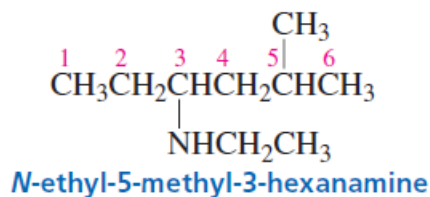
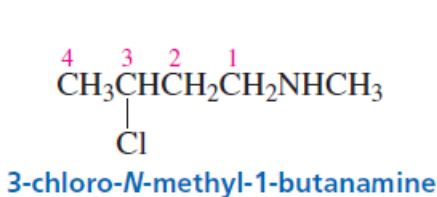
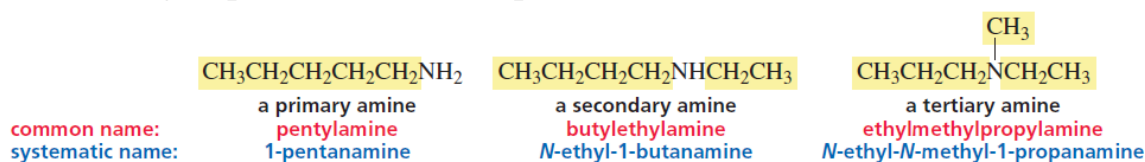
The common name of an amine consists of the names of the alkyl groups bonded to the nitrogen, in alphabetical order, followed by “amine.” The entire name is written as one word (unlike the common names of alcohols, ethers, and alkyl halides, in which “alcohol,” “ether,” and “halide” are separate words). common name



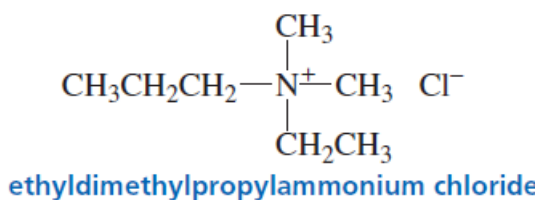
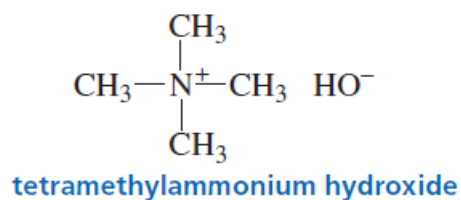
The IUPAC system uses a suffix to denote the amine functional group. The “e” at the end of the name of the parent hydrocarbon is replaced by “amine”—similar to the way in which alcohols are named. A number identifies the carbon to which the nitrogen is attached. The number can appear before the name of the parent hydrocarbon or before “amine.” The name of any alkyl group bonded to nitrogen is preceded by an “N” (in italics) to indicate that the group is bonded to nitrogen rather than to a Carbon: IUPAC name:



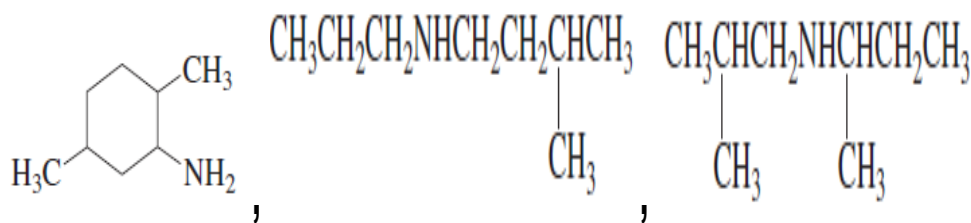
The substituents—regardless of whether they are attached to the nitrogen or to the parent hydrocarbon—are listed in alphabetical order, and then a number or an “*N*” is assigned to each one. The chain is numbered in the direction that gives the functional group suffix the lowest possible number.



Nitrogen compounds with four alkyl groups bonded to the nitrogen—thereby giving the nitrogen a positive formal charge—are called **quaternary ammonium salts**. Their names consist of the names of the alkyl groups in alphabetical order, followed by “ammonium” (all in one word), and then the name of the counter ion as a separate word.



Q1/ Give common and systematic names for each of the following compounds:



Q2/

Draw the structure of each of the following compounds:

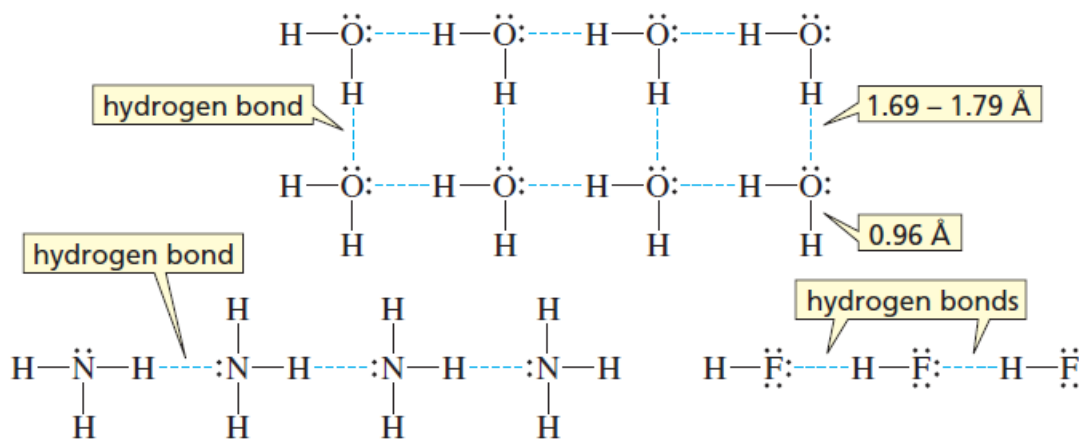
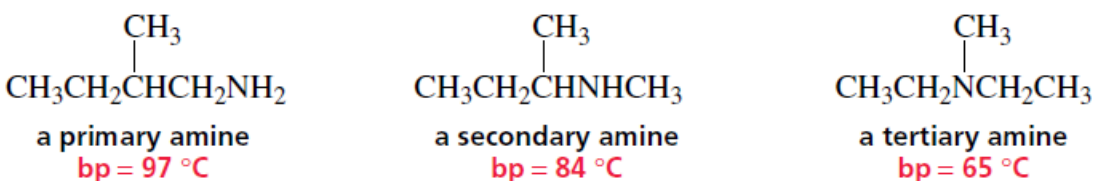
- | | |
|---|---------------------------------------|
| a. 2-methyl- <i>N</i> -propyl-1-propanamine | d. methyldipropylamine |
| b. <i>N</i> -ethylethanamine | e. <i>N,N</i> -dimethylpentan-3-amine |
| c. 5-methylhexan-1-amine | f. cyclohexylethylmethylamine |

Physical Properties

Generally, the boiling point of a compound depends on the strength of the attractive forces between the individual molecules. If the molecules are held together by strong forces, it will take a lot of energy to pull the molecules away from each other and the compound will have a high boiling point. In contrast, if the molecules are held together by weak forces, only a small amount of energy will be needed to pull the molecules away from each other and the compound will have a low boiling point. Amines can form hydrogen bonds. A hydrogen bond is a special kind of dipole–dipole interaction that occurs between a hydrogen that is bonded to an oxygen, a nitrogen, or a fluorine and the lone-pair electrons of an oxygen, nitrogen, or fluorine in another molecule.

The strongest hydrogen bonds are linear—the two electronegative atoms and the hydrogen between them lie on a straight line. Primary and secondary amines also form hydrogen bonds, so these amines have higher boiling points than alkanes with similar molecular weights. Nitrogen is not as electronegative as oxygen, however, which means that the hydrogen bonds between amine molecules are weaker than the hydrogen bonds between alcohol molecules. An amine, therefore, has a lower boiling point than an alcohol with a similar molecular weight. Because primary amines have two bonds, hydrogen bonding is more significant in primary amines than in secondary amines. Tertiary amines cannot form hydrogen bonds between

their own molecules because they do not have a hydrogen attached to the nitrogen. Consequently, if you compare amines with the same molecular weight and similar structures, you will find that primary amines have higher boiling points than secondary amines and secondary amines have higher boiling points than tertiary amines



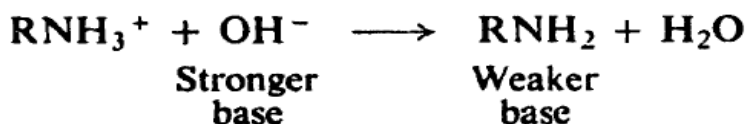
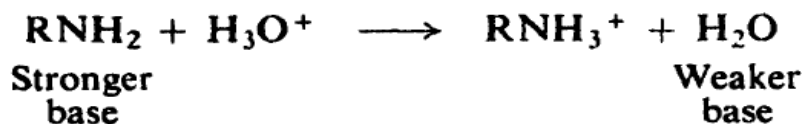
Low-molecular-weight amines are soluble in water because amines can form hydrogen bonds with water. Comparing amines with the same number of carbons, we find that primary amines are more soluble than secondary amines because primary amines have two hydrogens that can engage in hydrogen bonding. Tertiary amines, like primary and secondary amines, have lone-pair electrons that can accept hydrogen bonds, but unlike primary and secondary amines, tertiary amines do not have hydrogens to donate for hydrogen bonds. Tertiary amines, therefore, are less soluble in water than are secondary amines with the same number of carbons.

Structures and bonding in amines, basicity of amines.

Basicity and structure:

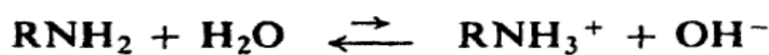
Amines are basic because they possess a pair of unshared electrons, which they can share with other atoms. These unshared electrons create an electron density around the nitrogen atom. The greater the electron density, the more basic the molecule,

amines are converted into their salts by aqueous mineral acids and are liberated from their salts by aqueous hydroxides. Therefore, amines are more basic than water and less basic than hydroxide ion:



Measuring of basicity

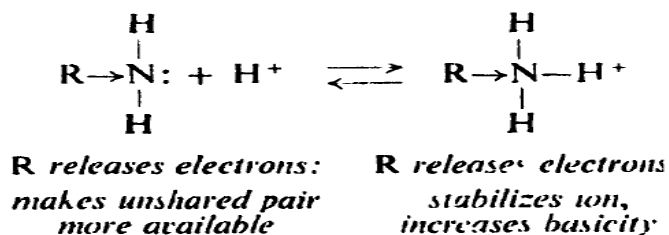
It is convenient to compare basicity of amines by measuring the extent to which they accept hydrogen ion from water; the equilibrium constant for this reaction is called a basicity constant, K_b .



$$K_b = \frac{[\text{RNH}_3^+][\text{OH}^-]}{[\text{RNH}_2]}$$

The larger the K_b , the stronger the base. aliphatic amines of all three classes have K_b 's of about 10^{-3} to 10^{-4} (0.001 to 0.0001); they are thus somewhat stronger bases than ammonia ($K_b = 1.8 \times 10^{-5}$). Aromatic amines, on the other hand, are considerably weaker bases than ammonia, having K_b 's of 10^{-9} or less.

Because basicity of amines is related to structure we shall compare the stabilities of **amines** with the stabilities of **their ions**; the more stable the ion relative to the amine from which it is formed, the more basic the amine.



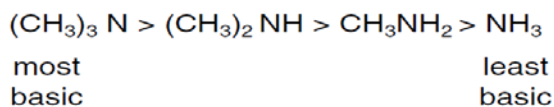
Aliphatic amine 1, 2, 3 and ammonia (Electronic and salvation factors):

An aliphatic amine is more basic than ammonia because the electron-releasing alkyl groups tend to disperse the positive charge of the substituted ammonium ion and therefore stabilize it in a way that is not possible for the unsubstituted ammonium ion. Thus an ammonium ion is stabilized by electron release in the

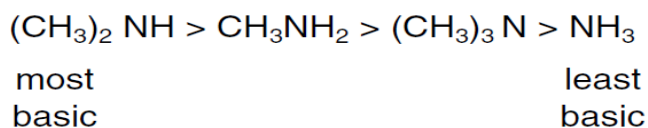
same way as a carbonium ion . From another point of view, we can consider that an alkyl group pushes electrons toward nitrogen, and thus makes the fourth pair more available for sharing with an acid.

(The differences in basicity among primary, secondary, and tertiary aliphatic amines are due to a combination of solvation and electronic factors.)

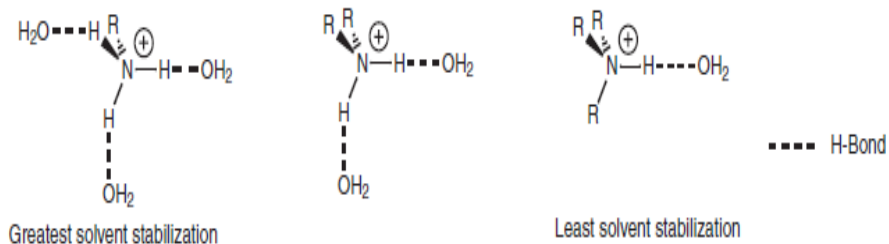
Groups that donate or supply electrons will increase the basicity of amines while groups that decrease the electron density around the nitrogen decrease the basicity of the molecule. For alkyl amines in the gas phase, the order of base strength is given below:

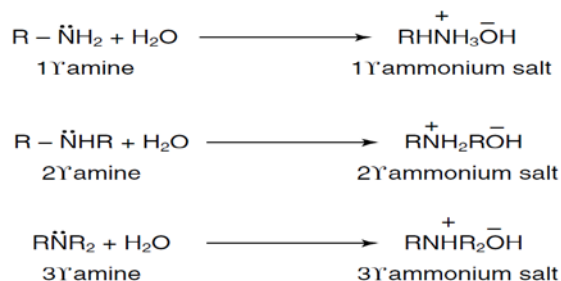


However, in aqueous solutions, the order of basicity changes.



The differences in the basicity order in the gas phase and aqueous solutions are the result of **solvation effects**. Amines in water solution exist as ammonium ions. In water, the ammonium salts of primary and secondary amines undergo solvation effects (due to hydrogen bonding) to a much greater degree than ammonium salts of tertiary amines. These solvation effects increase the electron density on the amine nitrogen to a greater degree than the inductive effect of alkyl groups.

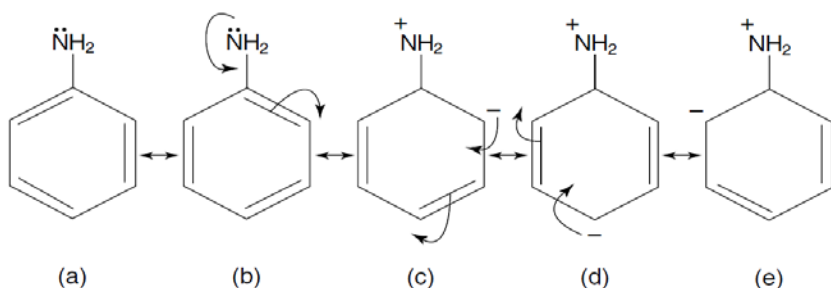




Arylamines :

Arylamines are weaker bases than cyclohexylamines because of resonance.

Aniline, a typical arylamine, exhibits the resonance structures shown in Figure below:

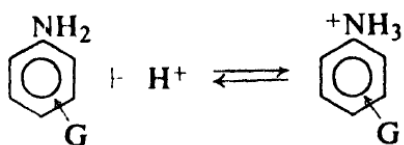


As structures **b** through **e** show, delocalization of the unshared electron pair occurs throughout the ring, making these electrons less available for reaction. As a result of this electron delocalization, the molecule becomes less basic.

Effect of substituents on basicity of aromatic amines

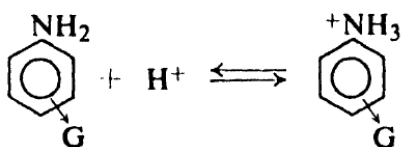
How is the basicity of an aromatic amine affected by substituents on the ring? an electron-releasing substituent like CH_3 increases the basicity of aniline, and an electron-withdrawing substituent like X or NO_2 decreases the basicity. These effects are understandable. Electron release tends to disperse the positive charge of the anilinium ion, and thus stabilizes the ion relative to the amine. Electron withdrawal tends to intensify the positive charge of the, anilinium ion, and thus destabilizes the ion relative to the amine.

Basicity of Aromatic Amines



*G releases electrons:
stabilizes cation,
increases basicity*

$G =$ $-\text{NH}_2$
 $-\text{OCH}_3$
 $-\text{CH}_3$



*G withdraws electrons
destabilizes cation,
decreases basicity*

$G =$ $-\text{NH}_3^+$
 $-\text{NO}_2$
 $-\text{SO}_3^-$
 $-\text{COOH}$
 $-\text{X}$

Q: Compare the basicities between the following pairs:

- 1- p-NH_2 and p-NH_3^+ aniline
- 2- pyridine and pyrrole
- 3- pyridine and piperidine
- 4- MeNHNa^+ and MeNH_2
- 5- CH_3CN , $\text{CH}_2=\text{NCH}_3$ and CH_3NH_2
- 6- $(\text{isoC}_3\text{H}_7)_3\text{N}(11)$ and $(\text{CH}_3)_3\text{N}(9.67)$

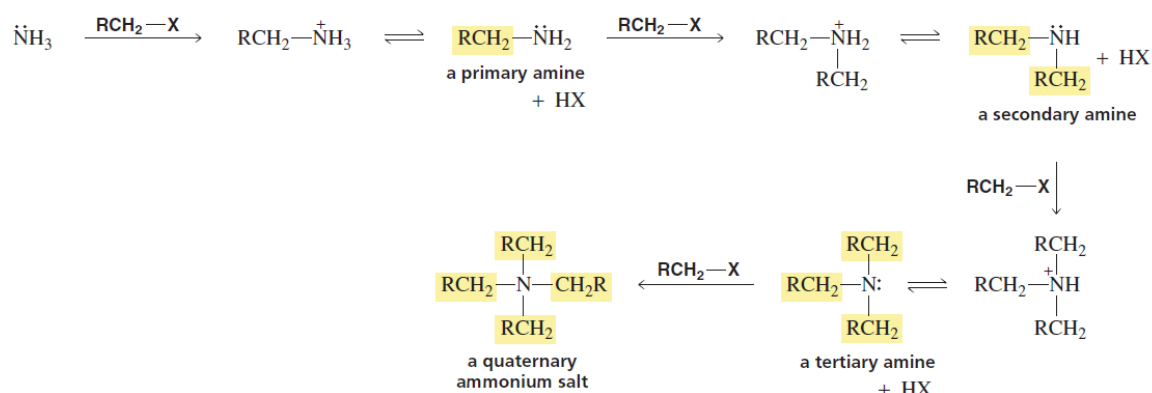
Preparations and reactions of amines:

A- Preparation of Amines

The alkylation of ammonia, Gabriel synthesis, reduction of nitriles, reduction of amides, reduction of nitro compounds, and reductive amination of aldehydes and ketones are methods commonly used for preparing amines.

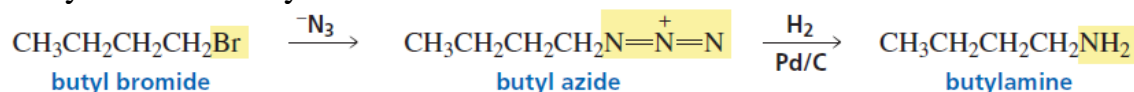
1-Alkylation of ammonia

The reaction of ammonia with an alkyl halide leads to the formation of a primary amine. The primary amine that is formed can also react with the alkyl halide, which leads to a di-substituted amine that can further react to form a tri-substituted amine. Therefore, the alkylation of ammonia leads to a mixture of products.



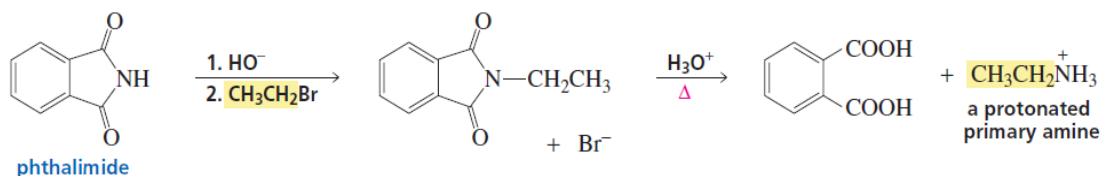
2- Reduction of alkylazides

You can best prepare a **primary amine** from its alkylazide by reduction or by the Gabriel synthesis.



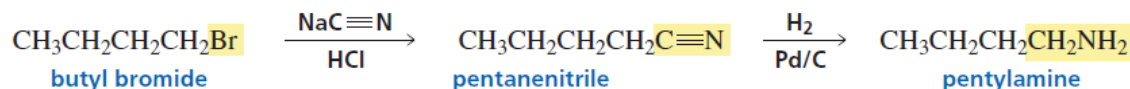
3- In the **Gabriel synthesis**, potassium phthalimide is reacted with an alkyl halide to produce an N-alkyl phthalimide. This N-alkyl phthalimide can be hydrolyzed by aqueous acids or bases into the primary amine.

Gabriel synthesis



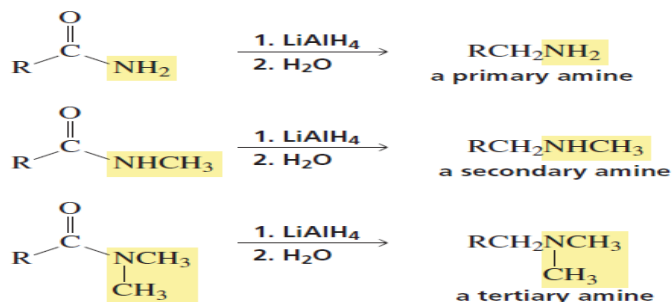
4- Reduction of nitriles

Nitriles can also be reduced to primary amines.



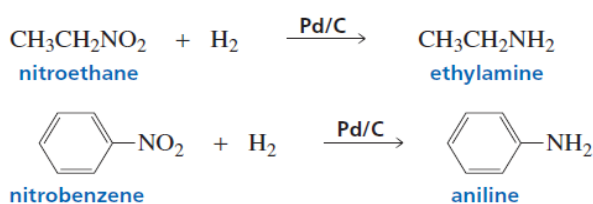
5- Reduction of amides

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



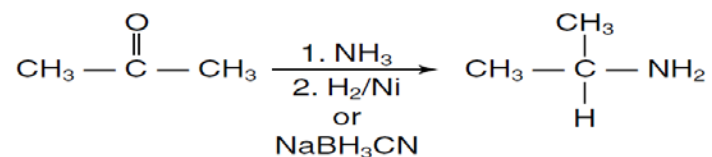
6- Reduction of nitro-compounds

A primary amine is obtained from the reduction of a nitroalkane, and an arylamine is obtained from the reduction of nitrobenzene.

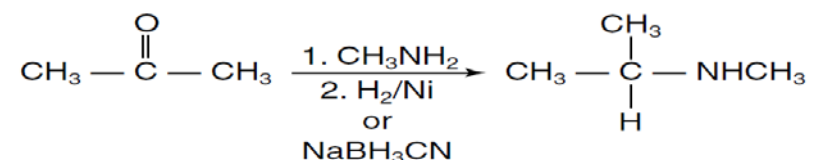


7-Reductive amination of aldehydes and ketones

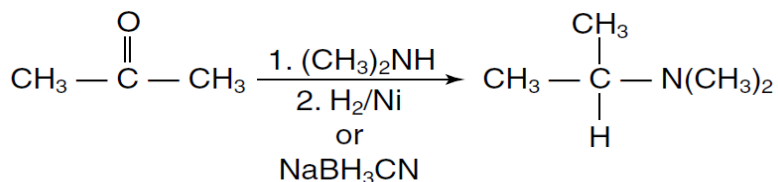
Aldehydes or ketones can be reduced by catalytic or chemical reductions in the presence of ammonia or primary or secondary amines, producing primary, secondary, or tertiary amines. The reaction of a ketone with ammonia, followed by catalytic reduction or reduction by sodium cyanoborohydride, produces a 1° amine.



N-substituted amines are produced by reaction of ketones with primary amines, followed by reduction.



N,N-disubstituted amines can be produced by reaction of 2° amines with ketones followed by reduction.(mechanism?)



B- Reactions of Amines

Due to the unshared electron pair, amines can act as both bases and nucleophiles.

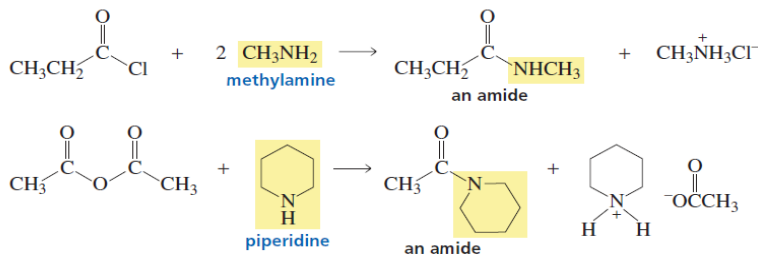
1-Reaction with acids

When reacted with acids, amines donate electrons to form ammonium salts.



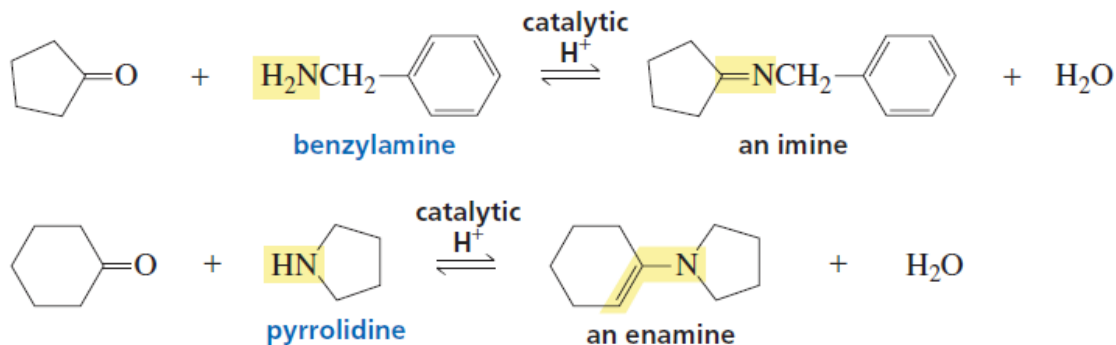
2- Reaction with acid halides

Acid halides react with amines to form substituted amides.



3- Reaction with aldehydes and ketones

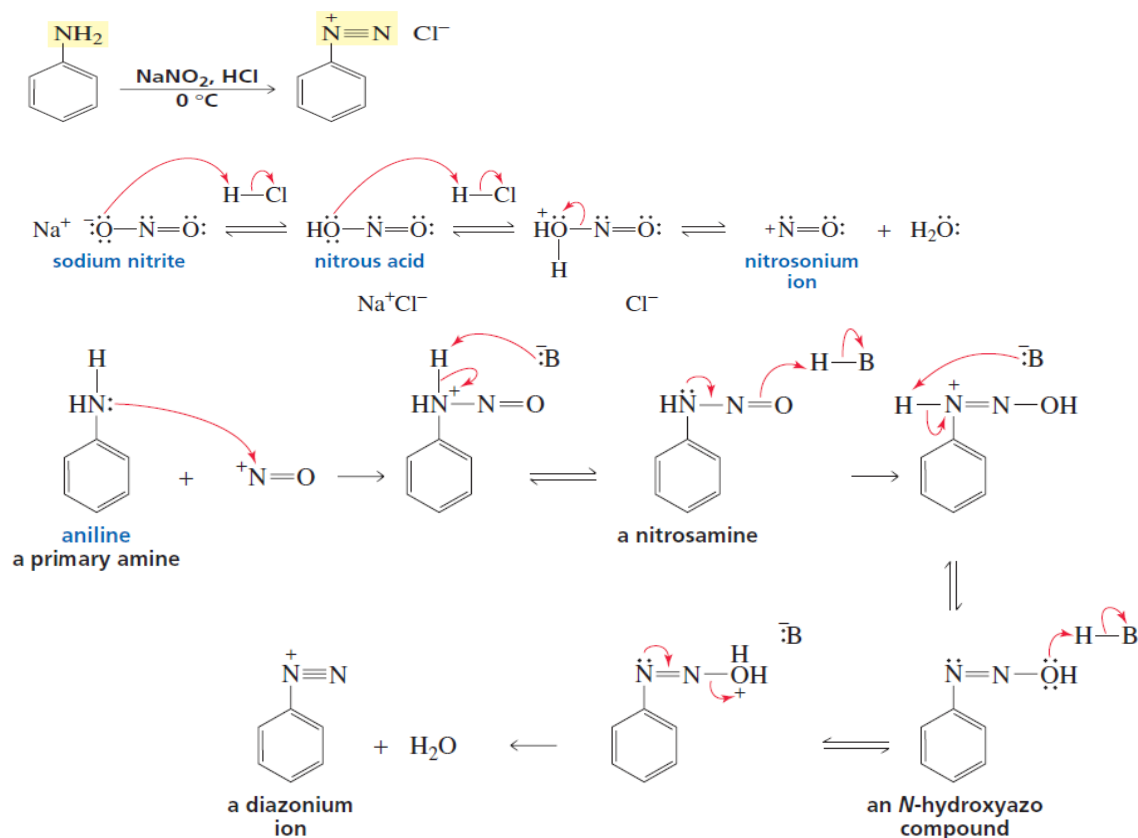
Aldehydes and ketones react with primary amines to give a reaction product (a carbinolamine) that dehydrates to yield aldimines and ketimines (Schiff- bases), and with secondary amines to form enamines (nucleophilic addition–elimination reactions).



Diazonium salts, preparation, replacement of nitrogen, coupling reactions, electrophilic aromatic substitution of anilines.

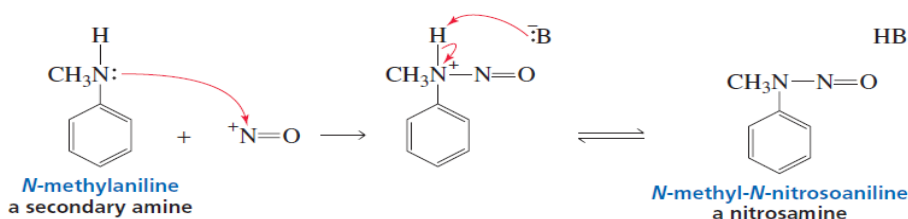
Diazonium salts. Preparation and reactions

When a primary **aromatic amine (not aliphatic?)**, dissolved or suspended in cold aqueous mineral acid, is treated with sodium nitrite, (to form HNO_2) gives a diazonium salt. Because nitrous acid is unstable, it is formed in situ, using an aqueous solution of sodium nitrite and HCl or HBr ; indeed, N_2 is such a good leaving group that the diazonium salt is synthesized at 0°C and used immediately without isolation. The large number of reactions undergone by diazonium salts may be divided into two classes: **replacement**, in which nitrogen is lost as N_2 , and some other atom or group becomes attached to the ring in its place; and **coupling**, in which the nitrogen is retained in the product. (The mechanism for conversion of a primary amino group to a diazonium salt is shown below:



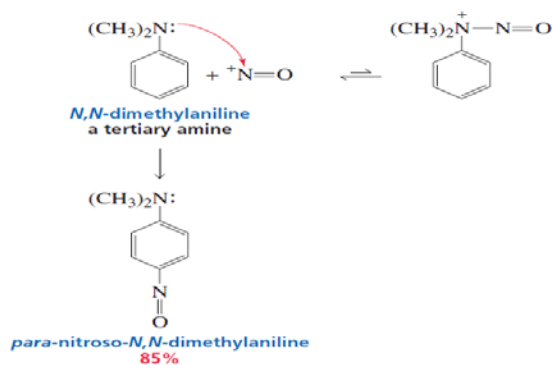
Secondary aryl and alkyl amines react with a nitrosonium ion to form nitrosamines rather than diazonium ions. The mechanism of the reaction is similar to that for the reaction of a primary amine with a nitrosonium ion, except that the reaction stops at the nitrosamine stage. The reaction stops because a secondary amine, unlike a

primary amine, does not have the second proton that must be lost in order to generate the diazonium ion.



The product formed when the nitrogen of a *tertiary* amine shares its lone pair with a nitrosonium ion cannot be stabilized by loss of a proton.

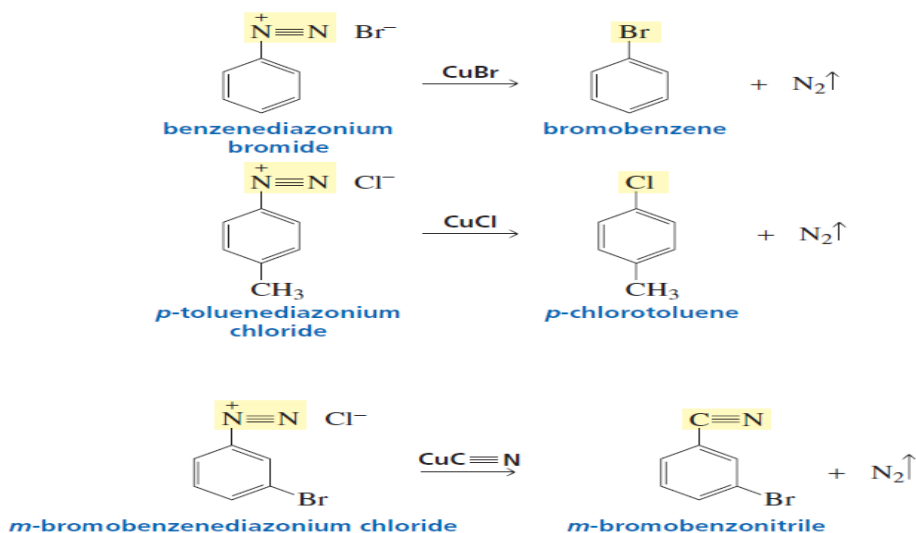
A tertiary aryl amine, therefore, can undergo an electrophilic aromatic substitution reaction with a nitrosonium ion. The product of the reaction is primarily the para isomer because the bulky dialkylamino group blocks approach of the nitrosonium ion to the ortho position.



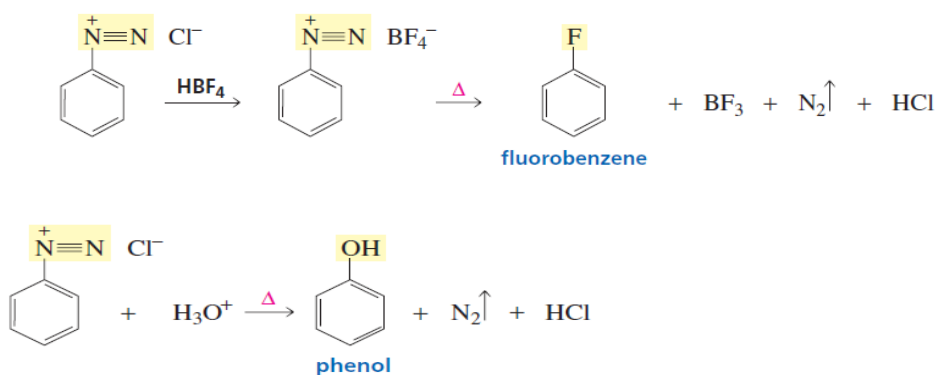
1- Replacement reaction : Sandmeyer reaction

Replacement of the diazonium group is the best general way of introducing F, Cl, Br, I, CN, OH, and H into an aromatic ring. Diazonium salts are valuable in synthesis not only because they react to form so many classes" of compounds, but also because they can be prepared from nearly all primary aromatic amines. Nucleophiles such as and will replace the diazonium group if the appropriate cuprous salt is added to the solution containing the arenediazonium salt. The reaction of an arenediazonium salt with a cuprous salt is known as a **Sandmeyer reaction**.

Sandmeyer reactions



Schiemann reaction

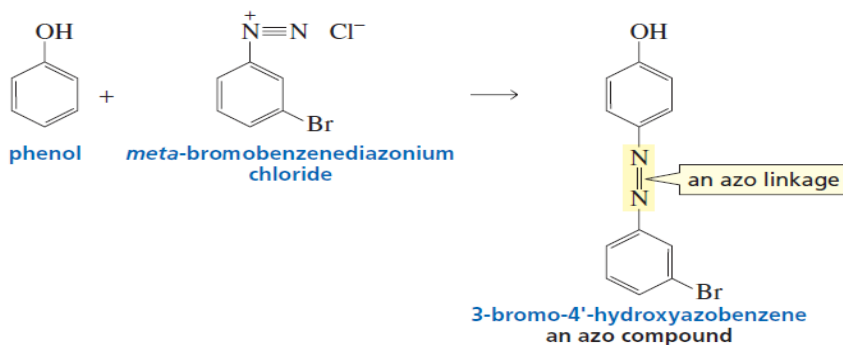


A hydrogen will replace a diazonium group if the diazonium salt is treated with hypophosphorous acid (H_3PO_2).

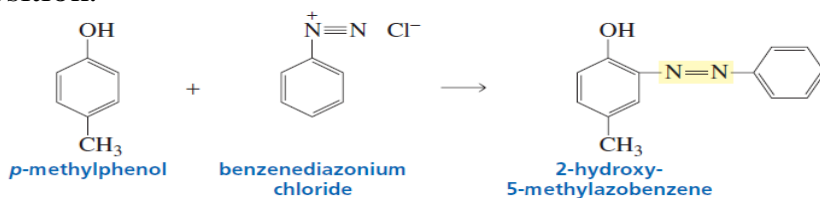


2- The Arenediazonium Ion as an Electrophile (Coupling reaction):

areediazonium ions can be used as electrophiles in electrophilic aromatic substitution reactions. Because an areediazonium ion is unstable at room temperature, it can be used as an electrophile only in electrophilic aromatic substitution reactions that can be carried out well below room temperature. In other words, only highly activated benzene rings (phenols, anilines, and *N*-alkylanilines) can undergo electrophilic aromatic substitution reactions with areediazonium ion electrophiles. The product of the reaction is an *azo compound*. The $-\text{N}=\text{N}-$ linkage is called an **azo linkage**. Because the electrophile is so large, substitution takes place preferentially at the less sterically hindered para position.

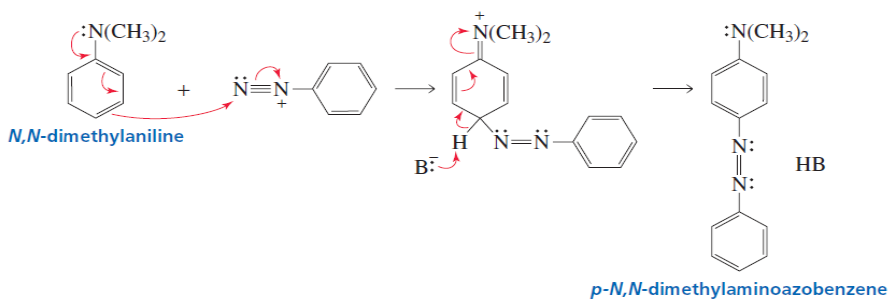


However, if the para position is blocked, substitution will occur at an ortho position.



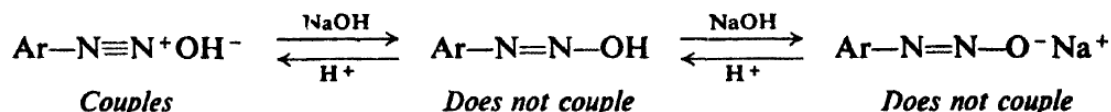
The mechanism for electrophilic aromatic substitution with an arenediazonium ion electrophile is the same as the mechanism for electrophilic aromatic substitution with any other electrophile.

mechanism for electrophilic aromatic substitution using an arenediazonium ion electrophile

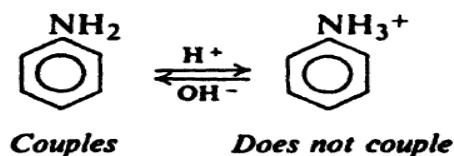


We have seen that azobenzenes are colored compounds because of their extended conjugation and are used commercially as dyes. The aromatic ring (Ar'H) undergoing attack by the diazonium ion must, in general, contain a powerfully electron-releasing group, generally OH, NR₂, NHR, or NH₂. Substitution usually occurs para to the activating group.

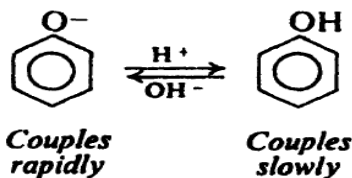
Typically, coupling with phenols is carried out in mildly alkaline solution, and with amines in mildly acidic solution. It is most important that the coupling medium be adjusted to the right degree of acidity or alkalinity. The electrophilic reagent is the diazonium ion, ArN₂⁺. In the presence of hydroxide ion, the diazonium ion exists in equilibrium with an un-ionized compound, Ar-N=N-OH, and salts (Ar-N=N-O⁻Na⁺) derived from it:



But what is the effect of high acidity on the amine or phenol with which the diazonium salt is reacting? Acid converts an amine into its ion, which, because of the positive charge, is relatively unreactive toward electrophilic aromatic substitution: much too unreactive to be attacked by the weakly electrophilic diazonium ion. The higher the acidity, the higher the proportion of amine that exists as its ion, and the lower the rate of coupling.



An analogous situation exists for a phenol. A phenol is appreciably acidic; in aqueous solutions it exists in equilibrium with phenoxide ion:

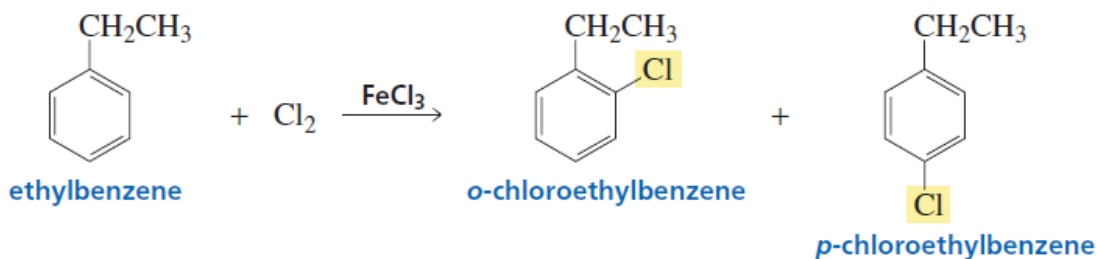


The fully developed negative charge makes O⁻ much more powerfully electron-releasing than OH; the phenoxide ion is therefore much more reactive than the un-ionized phenol toward electrophilic aromatic substitution. The higher the acidity of the medium, the higher the proportion of phenol that is un-ionized, and the lower the rate of coupling. In so far as the amine or phenol is concerned, then, coupling is favored by low acidity.

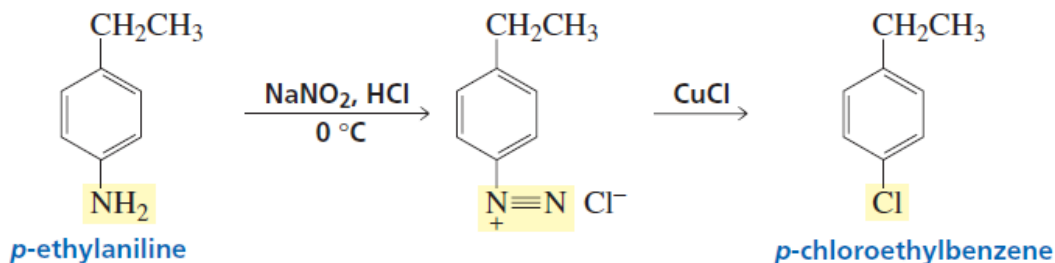
The conditions under which coupling proceeds most rapidly are the result of a compromise. **The solution must not be so alkaline that the concentration of diazonium ion is too low; it must not be so acidic that the concentration of free amine or phenoxide ion is too low.** It turns out that amines couple fastest in mildly acidic solutions, and phenols couple fastest in mildly alkaline solutions.

3- Electrophilic aromatic substitution and Syntheses using diazonium salts:

Amino groups are strongly activating, *o* and *p*-directing in electrophilic aromatic substitution reactions, so aromatic amines can be used as useful intermediates in the organic synthesis, a **Sandmeyer reaction** useful for preparation of different organic compounds. For example: chloro and bromo substituents can be placed directly on a benzene ring by halogenation, the Sandmeyer reaction can be a useful alternative., if you wanted to make *para*-chloroethylbenzene, chlorination of ethylbenzene would lead to a mixture of the *ortho* and *para* isomers.



However, if you started with *para*-ethylaniline and used a Sandmeyer reaction for chlorination, only the desired *para* product would be formed.



Examples :

