

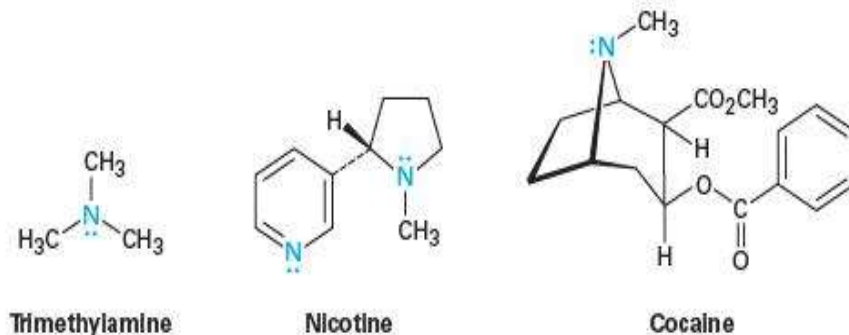
Amines: Naming and Physical Properties.

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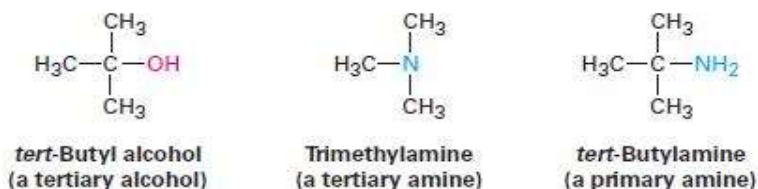
Amines are organic derivatives of ammonia in the same way that alcohols and ethers are organic derivatives of water. Like ammonia, amines contain a nitrogen atom with a lone pair of electrons, making amines both basic and nucleophilic. We'll soon see, in fact chemistry of amines depends on the presence of this lone pair of electrons.

Amines occur widely in all living organisms. Trimethylamine, for instance, occurs in animal tissues and is partially responsible for the distinctive odor of fish; nicotine is found in tobacco; and cocaine is a stimulant found in the leaves of the South American coca bush. In addition, amino acids are the building blocks from which all proteins are made, and cyclic amine bases are constituents of nucleic acids.

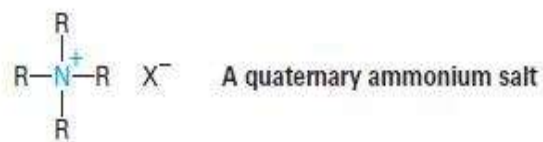


Naming Amines

Amines can be either alkyl-substituted (**alkylamines**) or aryl-substituted (**arylamines**). Although much of the chemistry of the two classes is similar, there are also substantial differences. Amines are classified as **primary (RNH_2)**, **secondary (R_2NH)**, or **tertiary (R_3N)**, depending on the number of organic substituents attached to nitrogen. Thus, methylamine (CH_3NH_2) is a primary amine, dimethylamine [$(CH_3)_2NH$] is a secondary amine, and trimethylamine [$(CH_3)_3N$] is a tertiary amine. Note that this usage of the terms **primary**, **secondary**, and **tertiary** differs from our previous usage. When we speak of a tertiary alcohol or alkyl halide, we refer to the degree of substitution at the alkyl carbon atom, but when we speak of a tertiary amine, we refer to the degree of substitution at the nitrogen atom.



Compounds containing a nitrogen atom with four attached groups also exist, but the nitrogen atom must carry a formal positive charge. Such compounds are called **quaternary ammonium salts**.



Primary amines are named in the IUPAC system in several ways. For simple amines, the suffix **-amine** is added to the name of the alkyl substituent. Phenylamine, $\text{C}_6\text{H}_5\text{NH}_2$, has the common name **aniline**.



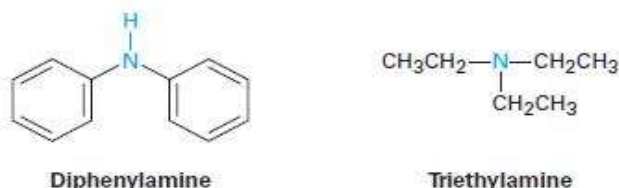
Alternatively, the suffix **-amine** can be used in place of the final **-e** in the name of the parent compound.



Amines with more than one functional group are named by considering the $-\text{NH}_2$ as an **amino** substituent on the parent molecule



Symmetrical secondary and tertiary amines are named by adding the prefix **di-** or **tri-** to the alkyl group.

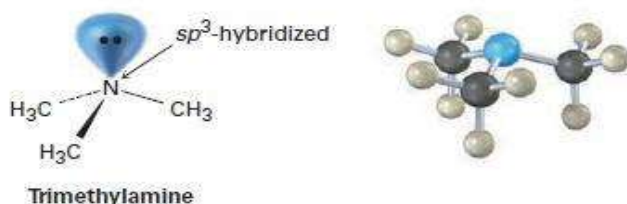


Unsymmetrically substituted secondary and tertiary amines are referred to as *N*-substituted primary amines. The largest alkyl group takes the parent name, and the other alkyl groups are considered *N*-substituents on the parent (*N* because they're attached to



Structure and Properties of Amines

The bonding in alkylamines is similar to the bonding in ammonia. The nitrogen atom is sp^3 -hybridized, with its three substituents occupying three corners of a regular tetrahedron and the lone pair of electrons occupying the fourth corner. As you might expect, the C-N-C bond angles are close to the 109° tetrahedral value. For trimethylamine, the C-N-C bond angle is 108° and the C-N bond length is 147 pm.



One consequence of tetrahedral geometry is that an amine with three different substituents on nitrogen is chiral. Unlike chiral carbon compounds, however, chiral amines can't be resolved because the two enantiomeric forms rapidly interconvert by a **pyramidal inversion**, much as an alkyl halide inverts in an S_N2 reaction. Pyramidal inversion occurs by a momentary rehybridization of the nitrogen atom to planar, sp^2 geometry, followed by rehybridization of the planar intermediate to tetrahedral, sp^3 geometry (**Figure 24-1**). The barrier to inversion is about 25 kJ/mol (6 kcal/mol), an amount only twice as large as the barrier to rotation about a C-C single bond.

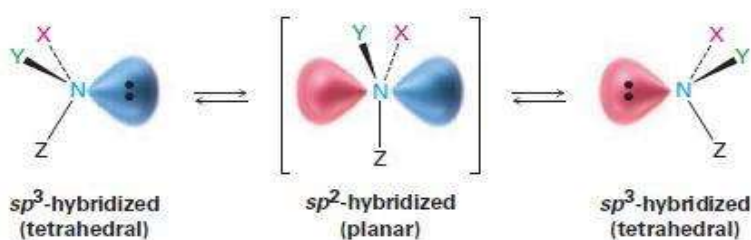
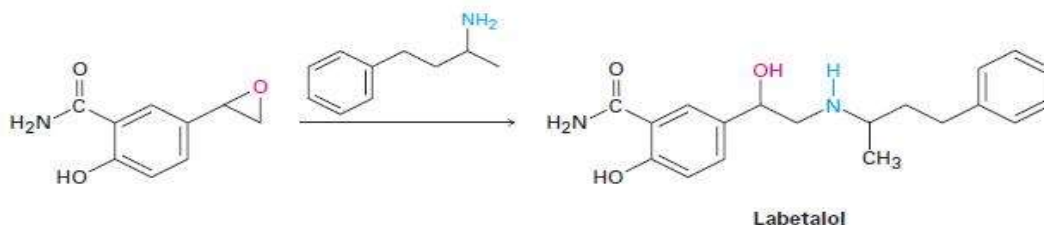
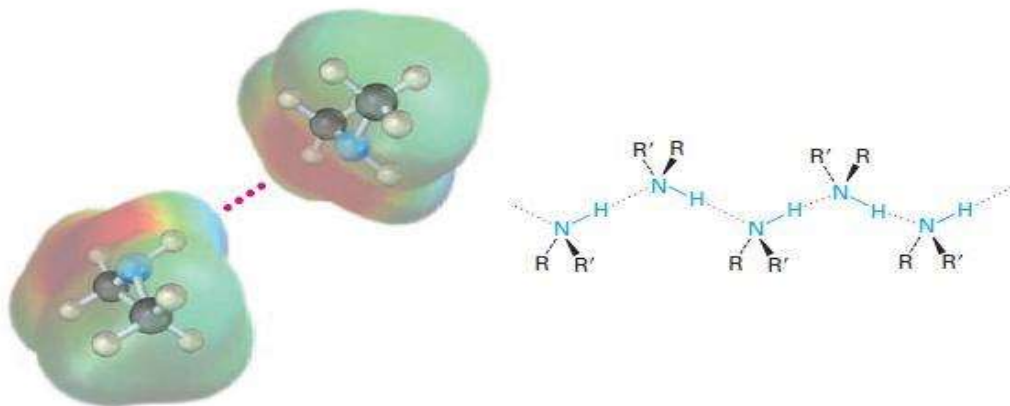


Figure 24-1 Pyramidal inversion rapidly interconverts the two mirror-image (enantiomeric) forms of an amine.

Alkylamines have a variety of applications in the chemical industry as starting materials for the preparation of insecticides and pharmaceuticals. **Labetalol**, for instance, a so-called *b*-blocker used for the treatment of high blood pressure, is prepared by S_N2 reaction of an epoxide with a primary amine. The substance marketed for drug use is a mixture of all four possible stereoisomers, but the biological activity results primarily from the (*R,R*) isomer.



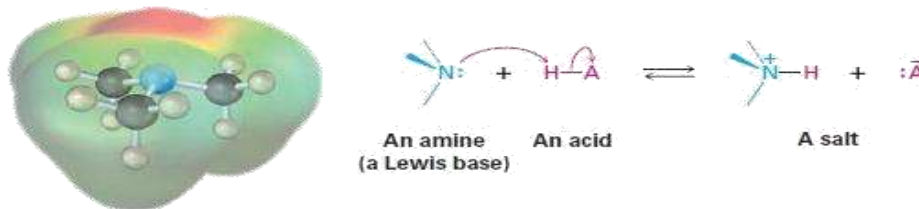
Like alcohols, amines with fewer than five carbon atoms are generally water-soluble. Also like alcohols, primary and secondary amines form hydrogen bonds and are highly associated. As a result, amines have higher boiling points than alkanes of similar molecular weight. Diethylamine (MW=73 amu) boils at 56.3 °C, for instance, while pentane (MW=72 amu) boils at 36.1 °C.



One other characteristic of amines is their odor. Low-molecular-weight amines such as trimethylamine have a distinctive fishlike aroma, while diamines such as cadaverine (1,5-pentanediamine) and putrescine (1,4-butanediamine) have the appalling odors you might expect from their common names. Both of these diamines arise from the decomposition of proteins.

Basicity of Amines

The chemistry of amines is dominated by the lone pair of electrons on nitrogen, which makes amines both basic and nucleophilic. They react with acids to form acid–base salts, and they react with electrophiles in many of the polar reactions seen in past chapters. Note in the following electrostatic potential map of trimethylamine how the negative (red) region corresponds to the lone pair of electrons on nitrogen.



Amines are much stronger bases than alcohols and ethers, their oxygen containing analogs. When an amine is dissolved in water, equilibrium is established in which water acts as an acid and transfers a proton to the amine. Just as the acid strength of a carboxylic acid can be measured by defining an acidity constant K_a , the base strength of an amine can be measured by defining an analogous **basicity constant K_b** . The larger the value of K_b and the smaller the value of pK_b , the more favorable the proton-transfer equilibrium and the stronger the base.

For the reaction



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

$$pK_b = -\log K_b$$

In practice, K_b values are not often used. Instead, the most convenient way to measure the basicity of an amine (RNH_2) is to look at the acidity of the corresponding ammonium ion (RNH_3^+). For the reaction



$$K_a = \frac{[\text{RNH}_2][\text{H}_3\text{O}^+]}{[\text{RNH}_3^+]}$$

$$\begin{aligned} \text{so } K_a \cdot K_b &= \left[\frac{[\text{RNH}_2][\text{H}_3\text{O}^+]}{[\text{RNH}_3^+]} \right] \left[\frac{[\text{RNH}_3^+][\text{OH}^-]}{[\text{RNH}_2]} \right] \\ &= [\text{H}_3\text{O}^+][\text{OH}^-] = K_w = 1.00 \times 10^{-14} \end{aligned}$$

$$\text{Thus } K_a = \frac{K_w}{K_b} \quad \text{and} \quad K_b = \frac{K_w}{K_a}$$







$$\text{and } pK_a + pK_b = 14$$

These equations state that the K_b of an amine multiplied by the K_a of the corresponding ammonium ion is equal to K_w , the ion-product constant for water (1.00×10^{-14}). Thus, if we know K_a for an ammonium ion, we also know K_b for the corresponding amine base because $K_b = K_w/K_a$. The more acidic the ammonium ion, the less tightly the proton is held and the weaker the corresponding base. That is, a weaker base has an ammonium ion with a smaller pK_a and a stronger base has an ammonium ion with a larger pK_a .

Weaker base smaller pK_a for ammonium ion

Stronger base larger pK_a for ammonium ion

Table 24-1 lists pK_a values of the ammonium ions from a variety of amines and indicates that there is a substantial range of amine basicities. Most simple alkylamines are similar in their base strength, with pK_a 's for their ions in ammonium then narrow range 10 to 11. Arylamines, however, are considerably less basic than alkylamines, as are the heterocyclic amines pyridine and pyrrole.

TABLE 24-1 Basicity of Some Common Amines					
Name	Structure	pK_a of ammonium ion	Name	Structure	pK_a of ammonium ion
Ammonia	<chem>NH3</chem>	9.26	Heterocyclic amine		
Primary alkylamine			Pyridine		5.25
Methylamine	<chem>CH3NH2</chem>	10.64	Pyrimidine		1.3
Ethylamine	<chem>CH3CH2NH2</chem>	10.75	Pyrrole		0.4
Secondary alkylamine			Imidazole		6.95
Diethylamine	<chem>(CH3CH2)2NH</chem>	10.98			
Pyrrolidine		11.27			
Tertiary alkylamine					
Triethylamine	<chem>(CH3CH2)3N</chem>	10.76			
Arylamine					
Aniline		4.63			

Basicity of Arylamines

Arylamines are generally less basic than alkylamines. Anilinium ion has $pK_a=4.63$, for instance, whereas methylammonium ion has $pK_a=10.64$. Arylamines are less basic than alkylamines because the nitrogen lone-pair electrons are delocalized by interaction with the aromatic ring's sp electron system and are less available for bonding to H^+ . In resonance terms, arylamines are stabilized relative to alkylamines because of their five resonance forms.



Much of the resonance stabilization is lost on protonation, however, so the energy difference between protonated and non-protonated forms is higher for arylamines than it is for alkylamines. As a result, arylamines are less basic. **Figure 24-3** illustrates this difference.

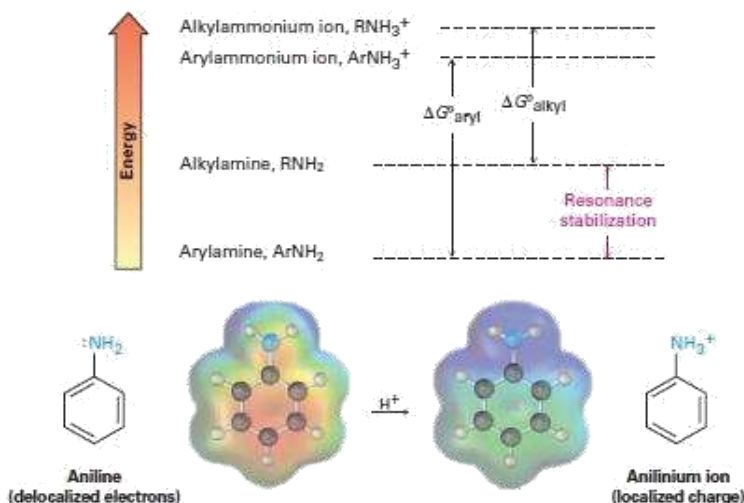


Figure 24-3 Arylamines have a larger positive ΔG° for protonation and are therefore less basic than alkylamines, primarily because of resonance stabilization of the ground state. Electrostatic potential maps show that lone-pair electron density is delocalized in the amine but the charge is localized in the corresponding ammonium ion.

Substituted arylamines can be either more basic or less basic than aniline, depending on the substituent. Electron-donating substituents, such as $-\text{CH}_3$, $-\text{NH}_2$, and $-\text{OCH}_3$, which increase the reactivity of an aromatic ring toward electrophilic substitution, also increase the basicity of the corresponding arylamine. Electron-withdrawing substituents, such as $-\text{Cl}$, $-\text{NO}_2$ and $-\text{CN}$, which decrease ring reactivity toward electrophilic substitution, also decrease arylamine basicity. **Table 24-2** considers only *p*-substituted anilines, but similar trends are observed for ortho and meta derivatives.

TABLE 24-2 Base Strength of Some *p*-Substituted Anilines

$$\text{Y}-\text{C}_6\text{H}_4-\text{NH}_2 + \text{H}_2\text{O} \rightleftharpoons \text{Y}-\text{C}_6\text{H}_4-\text{NH}_3^+ + \text{OH}^-$$

	Substituent, Y	$\text{p}K_a$		
<p>Stronger base</p> <p>Weaker base</p>	$-\text{NH}_2$	6.15	Activating groups	
	$-\text{OCH}_3$	5.34		
	$-\text{CH}_3$	5.08		
		$-\text{H}$	4.63	Deactivating groups
		$-\text{Cl}$	3.98	
		$-\text{Br}$	3.86	
		$-\text{CN}$	1.74	
	$-\text{NO}_2$	1.00		

