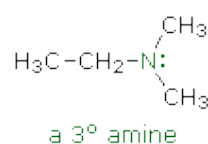
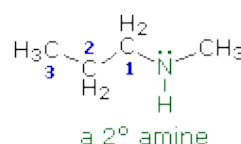
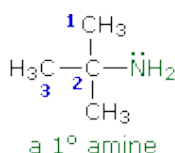
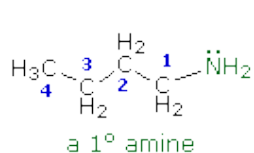


# Chemistry of Amines

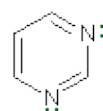
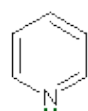
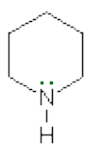
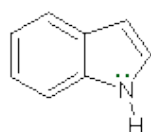
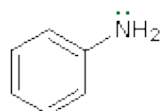
## Nomenclature and Structure of Amines :

In the IUPAC system of nomenclature, functional groups are normally designated in one of two ways. The presence of the function may be indicated by a characteristic suffix and a location number. This is common for the carbon-carbon double and triple bonds which have the respective suffixes **ene** and **yne**. Halogens, on the other hand, do not have a suffix and are named as substituents, for example:  $(\text{CH}_3)_2\text{C}=\text{CHCHClCH}_3$  is 4-chloro-2-methyl-2-pentene. If you are uncertain about the IUPAC rules for nomenclature you should review them now.

Amines are derivatives of ammonia in which one or more of the hydrogens has been replaced by an alkyl or aryl group. The nomenclature of amines is complicated by the fact that several different nomenclature systems exist, and there is no clear preference for one over the others. Furthermore, the terms primary ( $1^\circ$ ), secondary ( $2^\circ$ ) & tertiary ( $3^\circ$ ) are used to classify amines in a completely different manner than they were used for alcohols or alkyl halides. **When applied to amines these terms refer to the number of alkyl (or aryl) substituents bonded to the nitrogen atom**, whereas in other cases they refer to the nature of an alkyl group. The four compounds shown in the top row of the following diagram are all  $\text{C}_4\text{H}_{11}\text{N}$  isomers. The first two are classified as  $1^\circ$ -amines, since only one alkyl group is bonded to the nitrogen; however, the alkyl group is primary in the first example and tertiary in the second. The third and fourth compounds in the row are  $2^\circ$  and  $3^\circ$ -amines respectively. A nitrogen bonded to four alkyl groups will necessarily be positively charged, and is called a  $4^\circ$ -ammonium cation. For example,  $(\text{CH}_3)_4\text{N}^{(+)} \text{Br}^{(-)}$  is tetramethylammonium bromide.



IUPAC name	1-aminobutane	2-amino-2-methylpropane	1-methylaminopropane	dimethylaminoethane
CA name	butanamine	2-methyl-2-propanamine	N-methylpropanamine	N,N-dimethylethanamine
Common name	n-butylamine	tert-butylamine	methylpropylamine	ethyldimethylamine



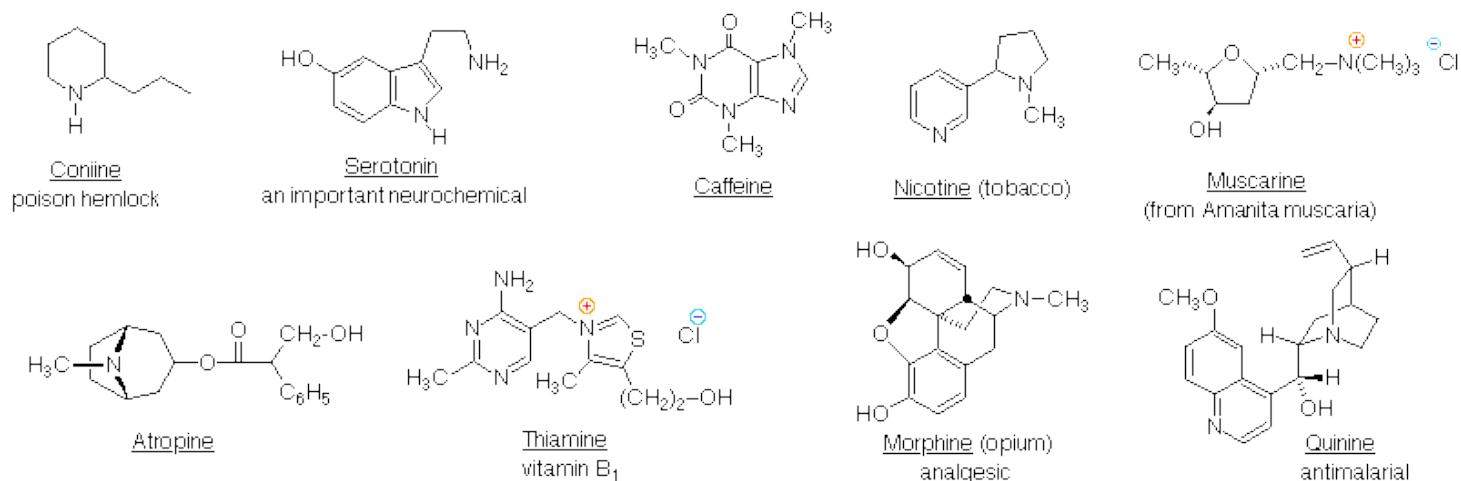
The IUPAC names are listed first and colored blue. This system names amine functions as substituents on the largest alkyl group. The simple  $-\text{NH}_2$  substituent found in  $1^\circ$ -amines is called an **amino group**. For  $2^\circ$  and  $3^\circ$ -amines a compound prefix (e.g. dimethylamino in the fourth example) includes the names of all but the root alkyl group.

The Chemical Abstract Service has adopted a nomenclature system in which the suffix **-amine** is attached to the root alkyl name. For 1<sup>o</sup>-amines such as butanamine (first example) this is analogous to IUPAC alcohol nomenclature (-ol suffix). The additional nitrogen substituents in 2<sup>o</sup> and 3<sup>o</sup>-amines are designated by the prefix **N-** before the group name. These CA names are colored magenta in the diagram. Finally, a common system for simple amines names each alkyl substituent on nitrogen in alphabetical order, followed by the suffix **-amine**. These are the names given in the last row (colored black).

Many aromatic and heterocyclic amines are known by unique common names, the origins of which are often unknown to the chemists that use them frequently. Since these names are not based on a rational system, it is necessary to memorize them. There is a systematic nomenclature of heterocyclic compounds, but it will not be discussed here.

## Natural Nitrogen Compounds

Nature abounds with nitrogen compounds, many of which occur in plants and are referred to as **alkaloids**. Structural formulas for some representative alkaloids and other nitrogen containing natural products are displayed below, and we can recognize many of the basic structural features listed above in their formulas. Thus, Serotonin and Thiamine are 1<sup>o</sup>-amines, Coniine is a 2<sup>o</sup>-amine, Atropine, Morphine and Quinine are 3<sup>o</sup>-amines, and Muscarine is a 4<sup>o</sup>-ammonium salt.

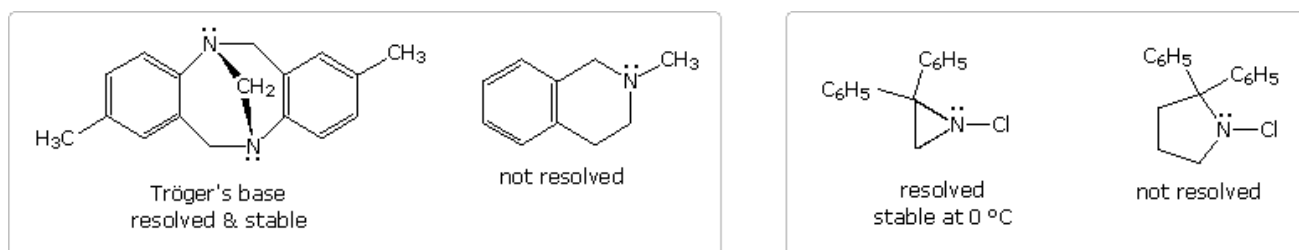


The reader should be able to recognize indole, imidazole, piperidine, pyridine, pyrimidine & pyrrolidine moieties among these structures. These will be identified by pressing the "Show Structures" button under the diagram.

Nitrogen atoms that are part of aromatic rings, such as pyridine, pyrrole & imidazole, have planar configurations (sp<sup>2</sup> hybridization), and are not stereogenic centers. Nitrogen atoms bonded to carbonyl groups, as in caffeine, also tend to be planar. In contrast, atropine, coniine, morphine, nicotine and quinine have stereogenic pyramidal nitrogen atoms in their structural formulas (think of the non-bonding electron pair as a fourth substituent on a sp<sup>3</sup> hybridized

nitrogen). In quinine this nitrogen is restricted to one configuration by the bridged ring system. The other stereogenic nitrogens are free to assume two pyramidal configurations, but these are in rapid equilibrium so that distinct stereoisomers reflecting these sites cannot be easily isolated.

It should be noted that structural factors may serve to permit the resolution of pyramidal chiral amines. Two examples of such 3<sup>o</sup>-amines, compared with similar non-resolvable analogs, are shown in the following diagram. The two nitrogen atoms in Tröger's base are the only stereogenic centers in the molecule. Because of the molecule's bridged structure, the nitrogens have the same configuration and cannot undergo inversion. The chloro aziridine can invert, but requires a higher activation energy to do so, compared with larger heterocyclic amines. It has in fact been resolved, and pure enantiomers isolated. An increase in angle strain in the sp<sup>2</sup>-hybridized planar transition state is responsible for the greater stability of the pyramidal configuration. The rough estimate of angle strain is made using a C-N-C angle of 60° as an arbitrary value for the three-membered heterocycle. To see these features Click on the Diagram.



Of course, quaternary ammonium salts, such as that in muscarine, have a tetrahedral configuration that is incapable of inversion. With four different substituents, such a nitrogen would be a stable stereogenic center.

## A Structure Formula Relationship

Recall that the molecular formula of a hydrocarbon (C<sub>n</sub>H<sub>m</sub>) provides information about the number of rings and/or double bonds that must be present in its structural formula. In the formula shown below a triple bond is counted as two double bonds.

$$\text{Rings} + \text{Double Bonds in a C}_n\text{H}_m \text{ Hydrocarbon} = \frac{(2n + 2 - m)}{2}$$

Compound	Molecular Formula	Revised Formula	Calculated Rings + C=Z
Coniine	C <sub>8</sub> H <sub>17</sub> N	C <sub>9</sub> H <sub>18</sub>	1
Nicotine	C <sub>10</sub> H <sub>14</sub> N <sub>2</sub>	C <sub>12</sub> H <sub>16</sub>	5
Morphine	C <sub>17</sub> H <sub>19</sub> NO <sub>3</sub>	C <sub>18</sub> H <sub>20</sub>	9

This molecular formula analysis may be extended beyond hydrocarbons by a few simple corrections. These are illustrated by the examples in the table above, taken from the previous

list of naturally occurring amines.

- The presence of oxygen does not alter the relationship.
- All halogens present in the molecular formula must be replaced by hydrogen.
- Each nitrogen in the formula must be replaced by a CH moiety.

Source : <http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/amine1.htm#aminom>