10.3: STRUCTURE AND PROPERTIES OF AMINES

> ◑ **OBJECTIVES**
>
> After completing this section, you should be able to
>
> 1. describe the geometry and bonding of simple amines.
> 2. explain why most chiral amines cannot be resolved into their two enantiomers.

> ⚲ **KEY TERMS**
>
> Make certain that you can define, and use in context, the key term below.
> - pyramidal inversion

> ⚲ **STUDY NOTES**
>
> Molecular models may help you to understand pyramidal inversion.

## BONDING, SHAPE, AND HYBRIDIZATION OF AMINES

The nitrogen atom in most amines is sp^3 hybridized. Three of the sp^3 hybrid orbitals form sigma bonds with the fourth orbital carrying the lone pair electrons. Single-bonded nitrogen is trigonal pyramidal in shape, with the non-bonding lone electron pair pointing to the unoccupied corner of a tetrahedron. Due to crowding by the lone pair electrons, the C-N-C bond angle between alkyl substituents on an amine is roughly 108° which is slightly less than the 109.5^o bond angle for a perfect tetrahedral geometry.
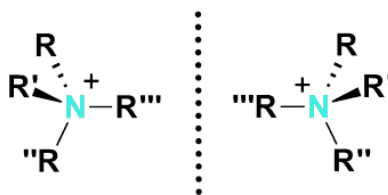

Trimethylamine
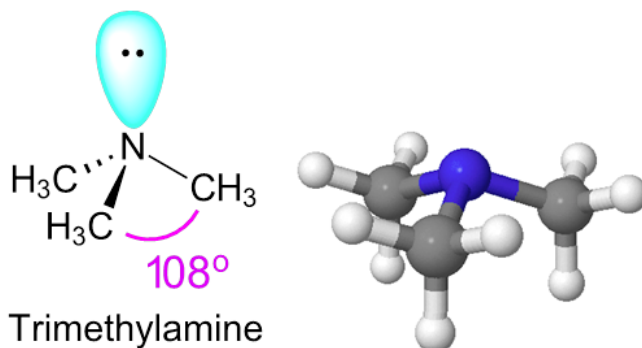
The C-N bonds (147 pm) of non-conjugated amines is shorter than C-C bond (154 pm) in alkanes, and longer than the C-O bond (143 pm) present in alcohols. This difference in bond length is expected given that the relative atom sizes are C > O > N.

CHIRALITY OF AMINES

Due to their tetrahedral configuration, amines with three different substituents are chiral. The R and S enantiomeric forms of a chiral amine cannot be resolved due to their rapid interconversion by a process called pyramidal or nitrogen inversion. During the inversion, the sp^3 hybridized amine momentarily rehybridizes to a sp^2 hybridized, trigonal planar, transition state where the lone pair electrons occupy a p orbital. The nitrogen then returns to a tetrahedral sp^3 hybridization causing the lone pair electrons to return to a sp^3 orbital on the opposite side of the nitrogen. During this process substituents invert to form the enantiomer. The thermodynamic barrier for this inversion (~25 kJ/mol) is low enough to allow rapid inversion at room temperature, leading to a mixture of interconverting R and S configurations. At room temperature a nitrogen atom exists as a racemic mixture of R and S configurations at equilibrium.
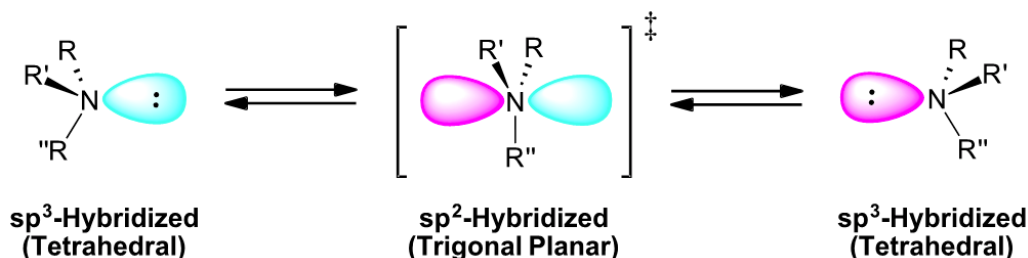
Quarternary amines lack lone pair electrons and therefore do not undergo pyramidal inversions. Quarternary amines with four different substituents are chiral and are readily resolved into separate enantiomers.


Enantiomers of a Chiral Quarternary Amine

BOILING POINT AND WATER SOLUBILITY

Methyl, dimethyl, trimethyl, and ethyl amines are gases under standard conditions. Most common alkyl amines are liquids, and high molecular weight amines are, quite naturally, solids at standard temperatures.

It is instructive to compare the boiling points and water solubility of amines with those of corresponding alcohols and ethers. The dominant factor here is hydrogen bonding, and the first table below documents the powerful intermolecular attraction that results from -O-H---O- hydrogen bonding in alcohols (light blue columns). Corresponding -N-H---N- hydrogen bonding is weaker, as the lower boiling points of similarly sized amines demonstrate. Alkanes provide reference compounds in which hydrogen bonding is not possible, and the increase in boiling point for equivalent 1º-amines is roughly half the increase observed for equivalent alcohols.
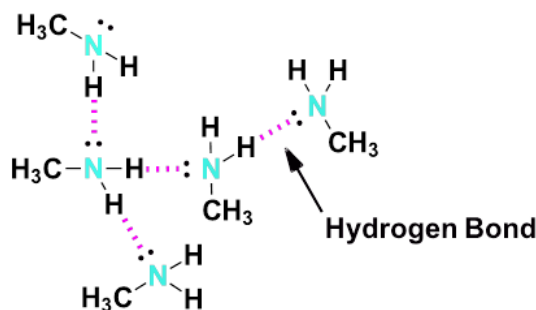
A Representation of the Hydrogen Bonding in Methyamine

Compound	CH_3CH_3	CH_3OH	CH_3NH_2	$CH_3CH_2CH_3$	CH_3CH_2OH	$CH_3CH_2NH_2$
Mol.Wt.	30	32	31	44	46	45
Boiling Point ºC	-88.6º	65º	-6.0º	-42º	78.5º	16.6º

The second table illustrates differences associated with isomeric 1º, 2º & 3º-amines, as well as the influence of chain branching. Since 1º-amines have two hydrogens available for hydrogen bonding, we expect them to have higher boiling points than isomeric 2º-amines, which in turn should boil higher than isomeric 3º-amines (no hydrogen bonding). Indeed, 3º-amines have boiling points similar to equivalent sized ethers; and in all but the smallest compounds, corresponding ethers, 3º-amines and alkanes have similar boiling points. In the examples shown here, it is further demonstrated that chain branching reduces boiling points by 10 to 15 ºC.
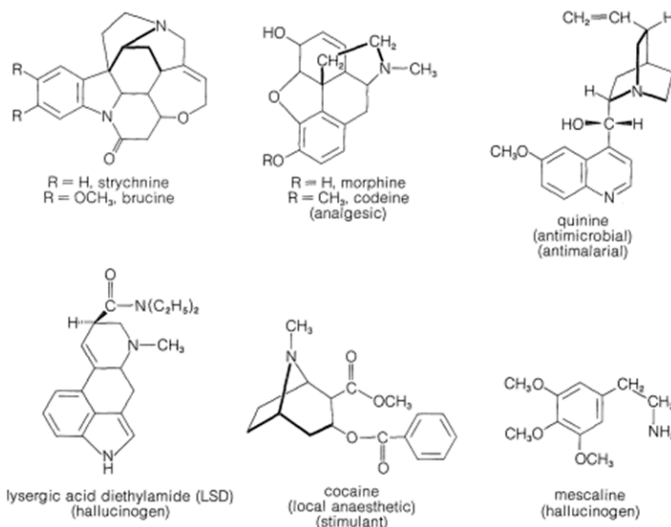
Compound	$CH_3(CH_2)_2CH_3$	$CH_3(CH_2)_2OH$	$CH_3(CH_2)_2NH_2$	$CH_3CH_2NHCH_3$	$(CH_3)_3CH$	$(CH_3)_2CHOH$	$(CH_3)_2CHNH_2$	$(CH_3)_3N$
Mol.Wt.	58	60	59	59	58	60	59	59
Boiling Point ºC	-0.5º	97º	48º	37º	-12º	82º	34º	3º

Most aliphatic amines display some solubility in water, reflecting their ability to form hydrogen bonds. Solubility decreases proportionally with the increase in the number of carbon atoms in the molecule – especially when the carbon atom number is greater than six. Aliphatic amines also display significant solubility in organic solvents, especially in polar organic solvents.

The water solubility of 1º and 2º-amines is similar to that of comparable alcohols. As expected, the water solubility of 3º-amines and ethers is also similar. The basicity of amines allows them to be dissolved in dilute mineral acid solutions, and this property facilitates their separation from neutral compounds such as alcohols and hydrocarbons by partitioning between the phases of non-miscible solvents.

NATURALLY OCCURRING AMINES

A large and widespread class of naturally occurring amines is known as alkaloids. The structures of the plant alkaloids are extraordinarily complex, yet they are related to the simple amines in being weak nitrogen bases. In fact, the first investigator to isolate an alkaloid in pure form was F. W. A. Sertürner who, in 1816, described morphine as basic, salt-forming, and ammonia-like. He used the term "organic alkali" from which is derived the name alkaloid. Alkaloids include compounds that may be classified as antimicrobial (quinine), as analgesics (morphine, codeine), as hallucinogens (mescaline, LSD), and as topical anesthetics (cocaine).

R = H, strychnine
R = OCH₃, brucine

R = H, morphine
R = CH₃, codeine
(analgesic)

quinine
(antimicrobial)
(antimalarial)

lysergic acid diethylamide (LSD)
(hallucinogen)

cocaine
(local anaesthetic)
(stimulant)

mescaline
(hallucinogen)

Certain amines and ammonium compounds play key roles in the function of the central nervous system as neurotransmitters and the balance of amines in the brain is critical for normal brain functioning. The amines acetylcholine chloride, adrenalin, and serotonin play important roles in nerve function in the human body.

acetylcholine chloride
(neurotransmitter)

adrenalin (epinephrine)

serotonin

(amine components of nerve action)
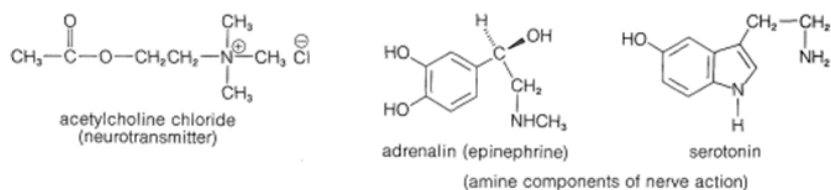
Most amines have "interesting" odors. The simple ones smell very much like ammonia. Higher aliphatic amines smell like decaying meat. The stench of rotting meat is due in part to two diamines: putrescine and cadaverine. They are made during the decarboxylation of the amino acids, ornithine and lysine, by bacteria.

Putrescine

Cadaverine
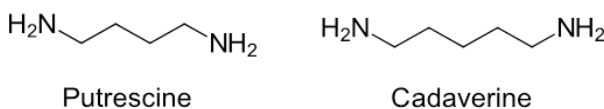
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