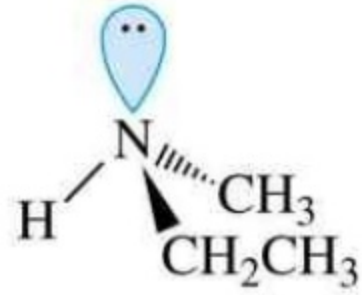
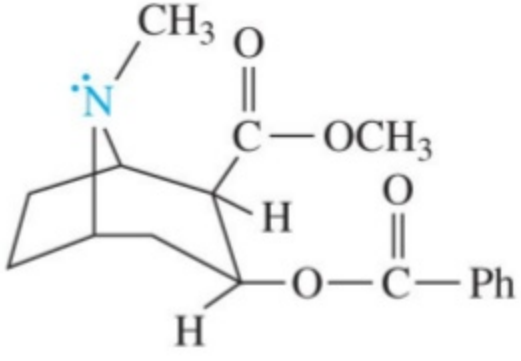
Organic Chemistry, 7th Edition
L. G. Wade, Jr.



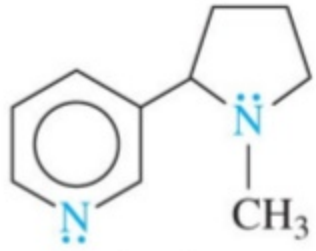
Chapter 19

Amines

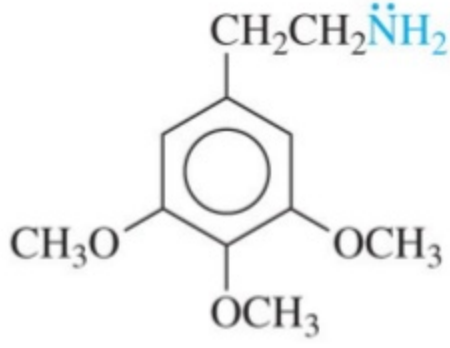
Biologically Active Amines



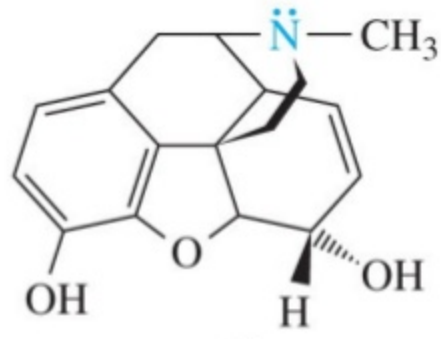
cocaine
in coca leaves



nicotine
in tobacco



mescaline
in peyote cactus



morphine
in opium poppies

- The alkaloids are an important group of biologically active amines, mostly synthesized by plants to protect them from being eaten by insects and other animals.
- Many drugs of addiction are classified as alkaloids.

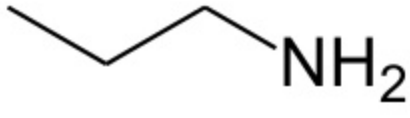
Biological Activity of Amines

- Dopamine is a neurotransmitter.
- Epinephrine is a bioregulator.
- Niacin, Vitamin B_6, is an amine.
- Alkaloids: nicotine, morphine, cocaine
- Amino acids

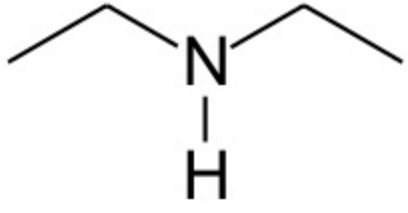
Classes of Amines

- ***Primary (1°)***: Has one alkyl group bonded to the nitrogen (RNH_2).
- ***Secondary (2°)***: Has two alkyl groups bonded to the nitrogen (R_2NH).
- ***Tertiary (3°)***: Has three alkyl groups bonded to the nitrogen (R_3N).
- ***Quaternary (4°)***: Has four alkyl groups bonded to the nitrogen and the nitrogen bears a positive charge(R_4N^+).

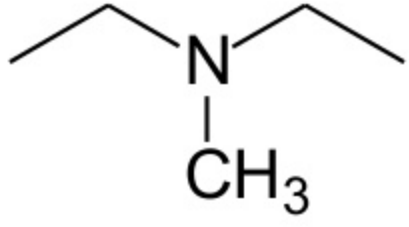
Examples of Amines



Primary
(1º)

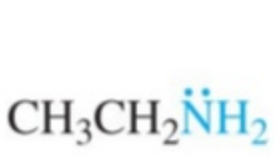


Secondary
(2º)

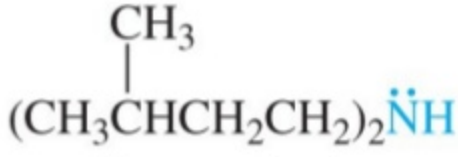


Tertiary
(3º)

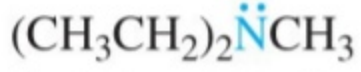
Common Names



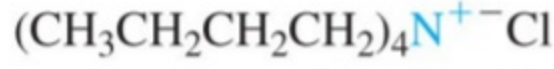
ethylamine



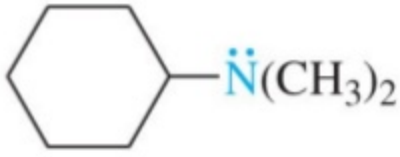
diisopentylamine



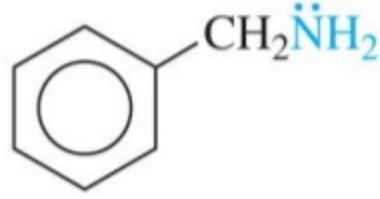
diethylmethylamine



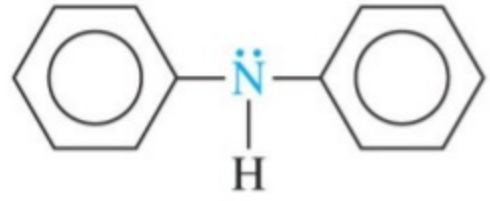
tetrabutylammonium chloride



cyclohexyldimethylamine

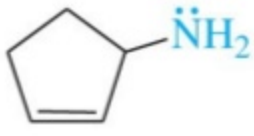


benzylamine

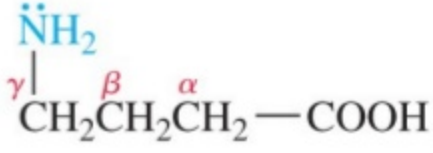


diphenylamine

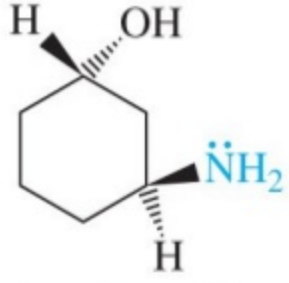
Amine as Substituent



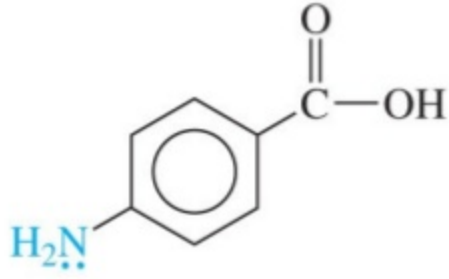
3-aminocyclopentene
(cyclopent-2-en-1-amine)



γ-aminobutyric acid
(4-aminobutanoic acid)



trans-3-aminocyclohexanol

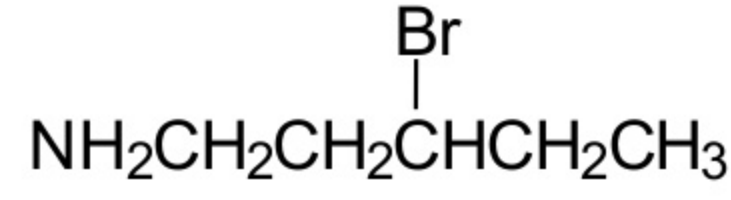


p-aminobenzoic acid (PABA)

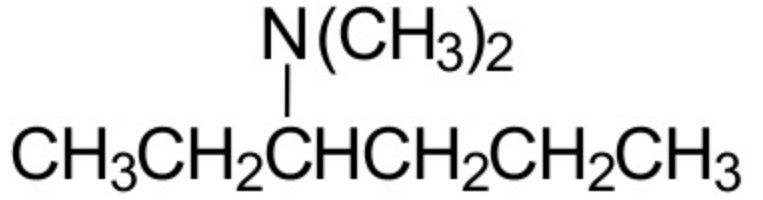
- On a molecule with a higher priority functional group, the amine is named as a substituent.

IUPAC Names

- Name is based on longest carbon chain.
- -*e* of alkane is replaced with -*amine*.
- Substituents on nitrogen have *N*- prefix.

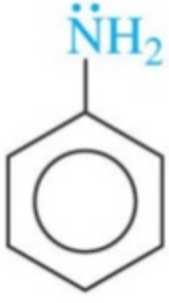


3-bromo-1-pentanamine

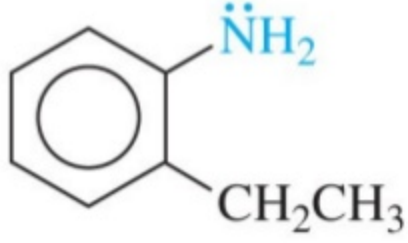


N,*N*-dimethyl-3-hexanamine

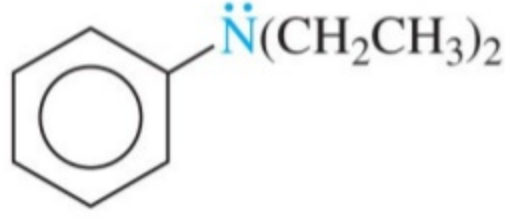
Aromatic Amines



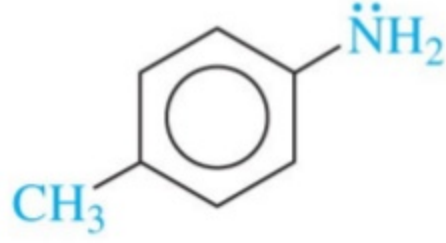
aniline



2-ethylaniline
or *o*-ethylaniline



N,*N*-diethylaniline



4-methylaniline
or *p*-toluidine

- In aromatic amines, the amino group is bonded to a benzene ring.
- Parent compound is called aniline.

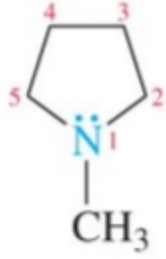
Heterocyclic Amines

When naming a cyclic amine the nitrogen is assigned position number 1.

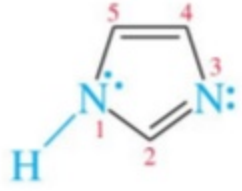
aziridine

pyrrole

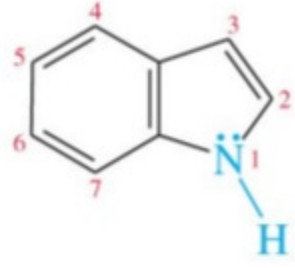
pyrrolidine



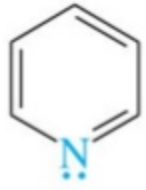
1-methylpyrrolidine
(*N*-methylpyrrolidine)



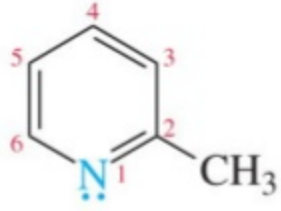
imidazole



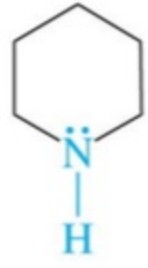
indole



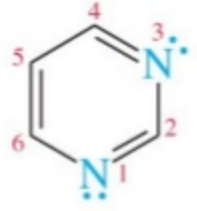
pyridine



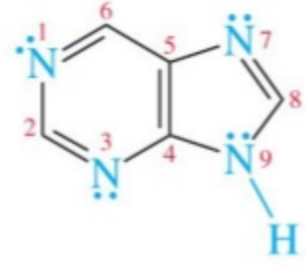
2-methylpyridine



piperidine

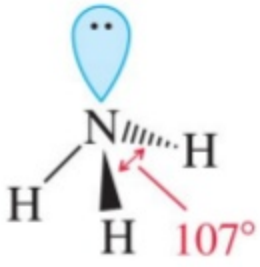


pyrimidine

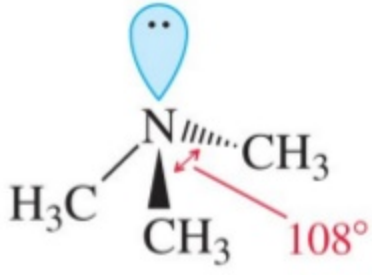


purine

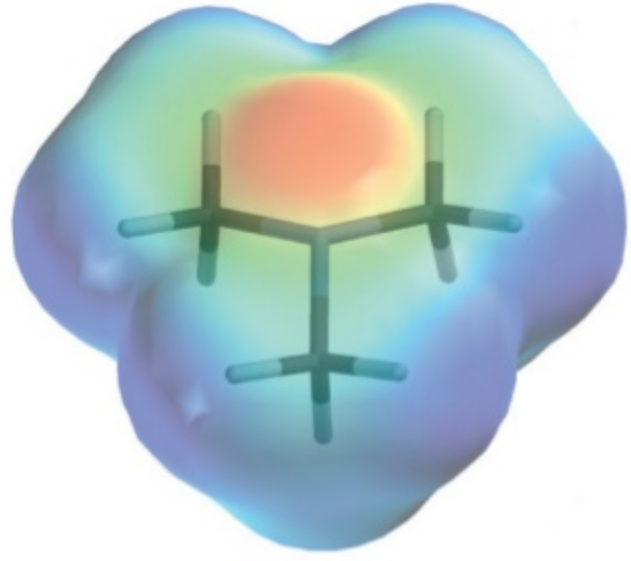
Structure of Amines



ammonia



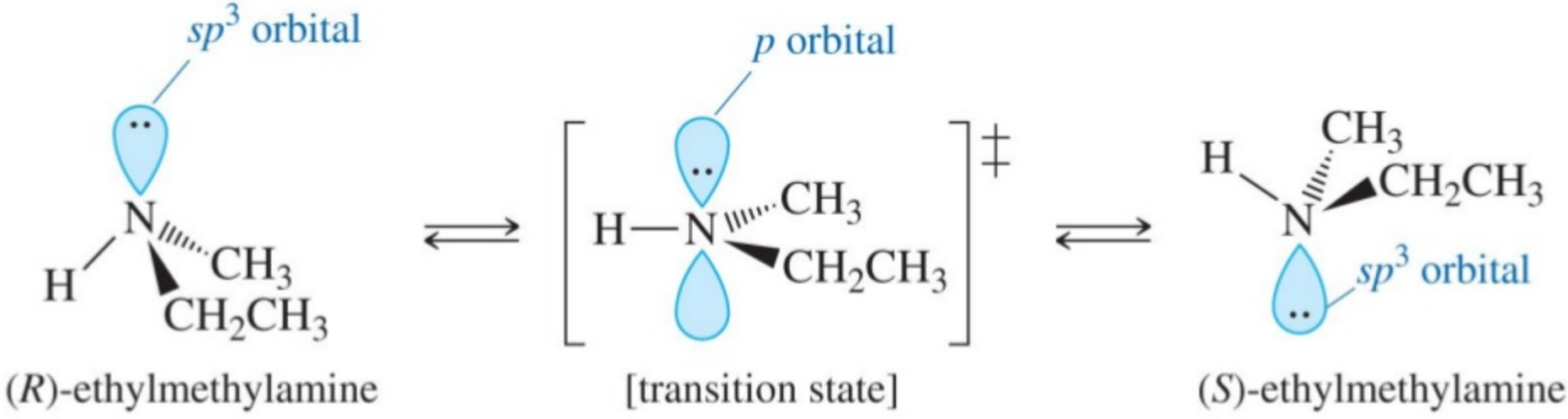
trimethylamine



electrostatic potential map for trimethylamine

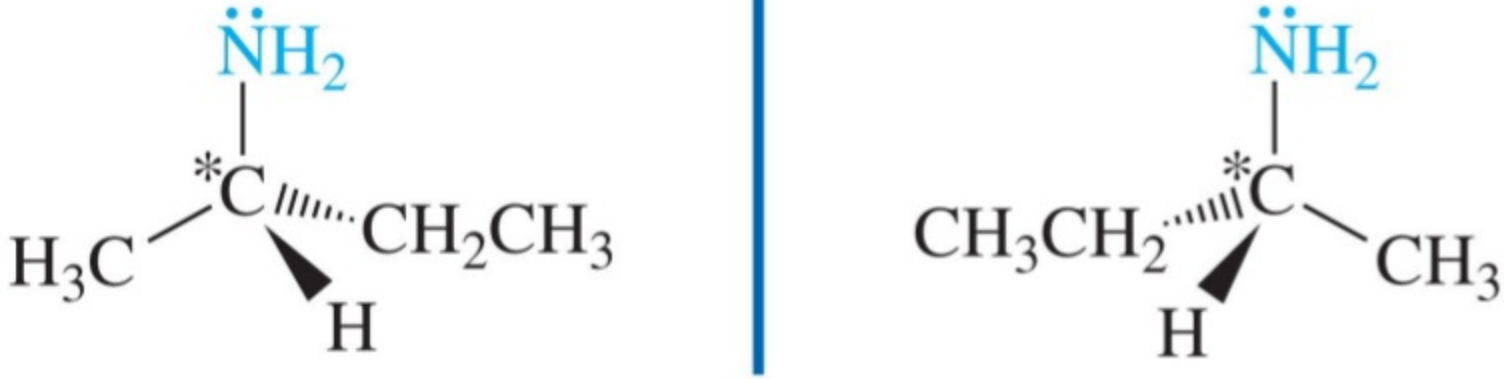
- Nitrogen is sp^3 hybridized with a lone pair of electrons.
- The angle is less than 109.5º.

Interconversion of Chiral Amines



- Nitrogen may have three different groups and a lone pair, but enantiomers cannot be isolated due to inversion around N.

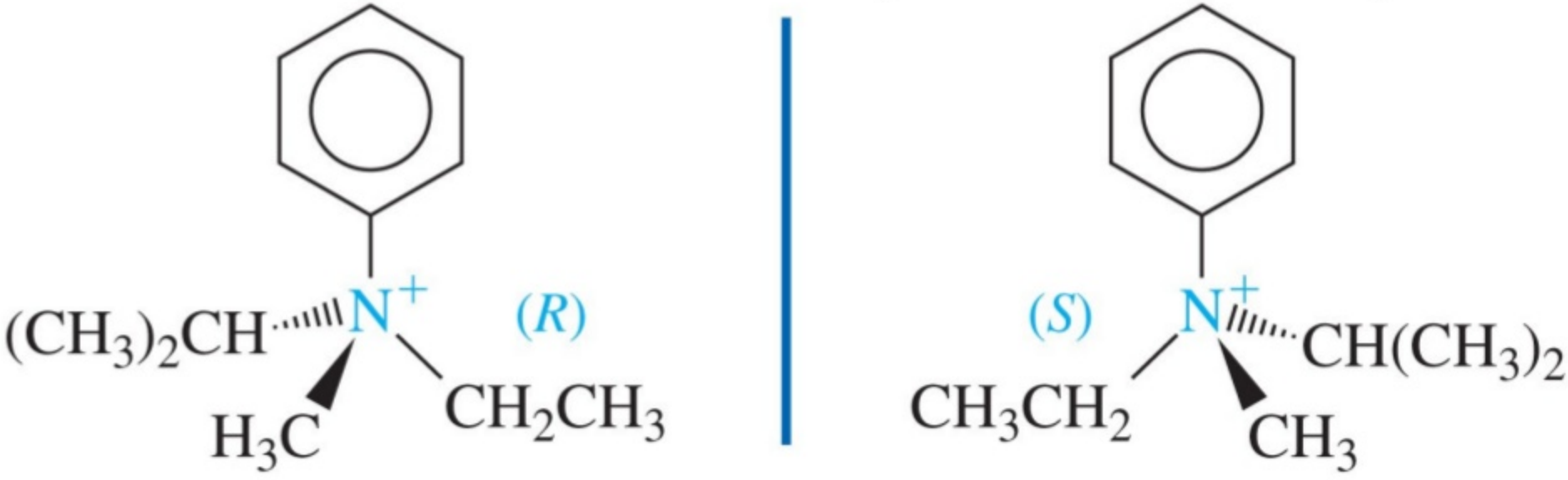
Chiral Amines



(*S*)-2-butanamine (*R*)-2-butanamine

- Amines whose chirality stems from the presence of chiral carbon atoms.
- Inversion of the nitrogen is not relevant because it will not affect the chiral carbon.

Chiral Amines (Continued)



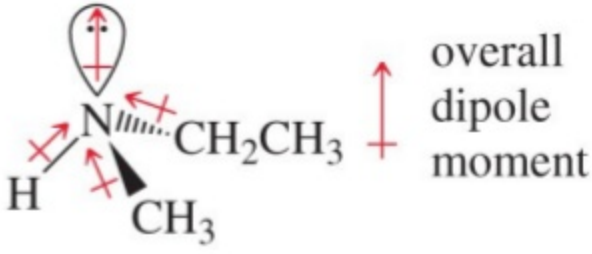
- Quaternary ammonium salts may have a chiral nitrogen atom if the four substituents are different.
- Inversion of configuration is not possible because there is no lone pair to undergo nitrogen inversion.

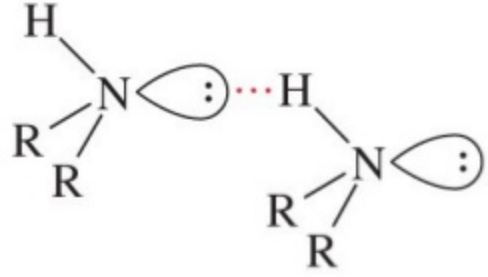
Chiral Cyclic Amines

(*R*)-1,2,2-trimethylaziridine (*S*)-1,2,2-trimethylaziridine

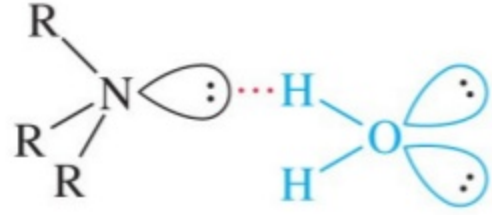
- If the nitrogen atom is contained in a small ring, for example, it is prevented from attaining the 120° bond angle that facilitates inversion.
- Such a compound has a higher activation energy for inversion, the inversion is slow, and the enantiomers may be resolved.

Boiling Points





1° or 2° amine:
hydrogen bond donor and acceptor



3° amine:
hydrogen bond acceptor only

- N—H less polar than O—H.
- Weaker hydrogen bonds, so amines will have a lower boiling point than the corresponding alcohol.
- Tertiary amines cannot hydrogen-bond, so they have lower boiling points than primary and secondary amines.

Solubility and Odor

- Small amines (< 6 Cs) are soluble in water.
- All amines accept hydrogen bonds from water and alcohol.
- Branching increases solubility.
- Most amines smell like rotting fish.

$NH_2CH_2CH_2CH_2CH_2CH_2NH_2$

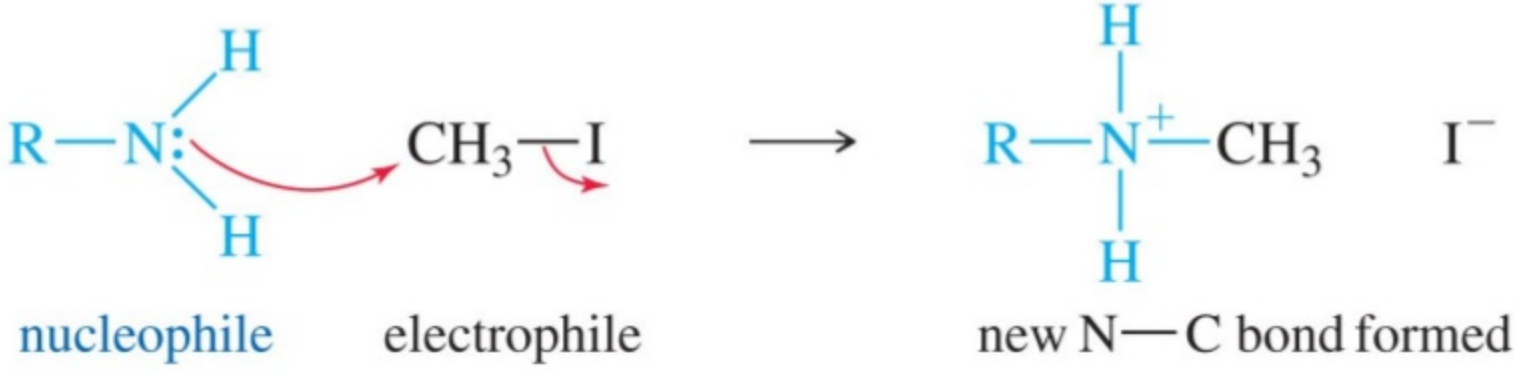
1,5-pentanediamine or cadaverine

Basicity of Amines

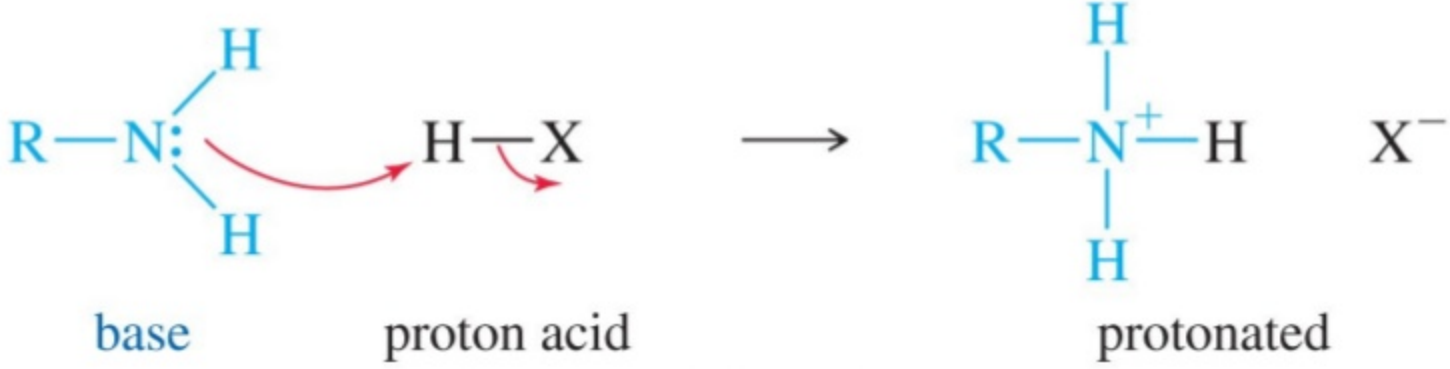
- Lone pair of electrons on nitrogen can accept a proton from an acid.
- Aqueous solutions are basic to litmus.
- Ammonia pK_b = 4.74
- Alkyl amines are usually stronger bases than ammonia.
- Increasing the number of alkyl groups decreases solvation of ion, so 2° and 3° amines are similar to 1° amines in basicity.

Reactivity of Amines

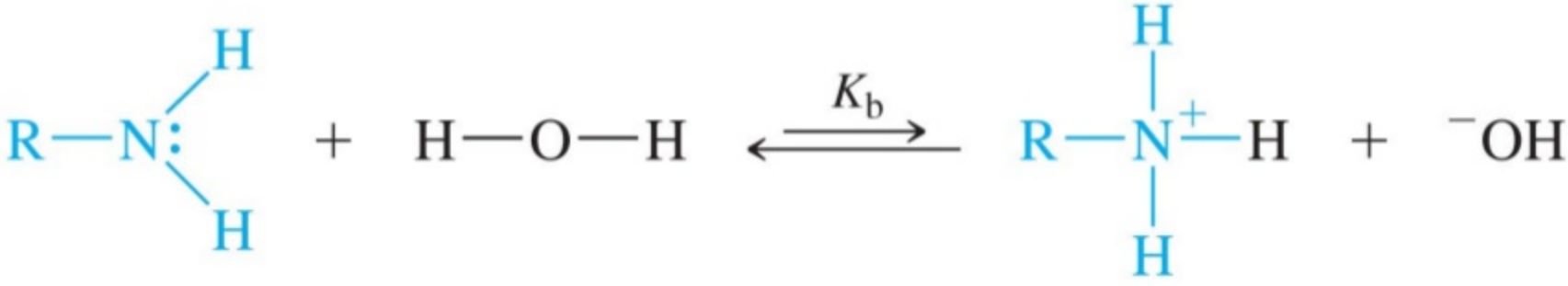
Reaction of an amine as a nucleophile



Reaction of an amine as a proton base



Base-Dissociation Constant of Amines



$$K_b = \frac{[RNH_3^+][^-OH]}{[RNH_2]} \qquad pK_b = -\log_{10} K_b$$

- An amine can abstract a proton from water, giving an ammonium ion and a hydroxide ion.
- The equilibrium constant for this reaction is called the ***base-dissociation constant*** for the amine, symbolized by K_b.