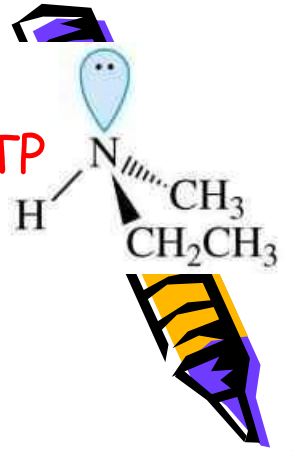

Aromatic amines

Prepared By:
Dr. Maulik D. Vaja
Associate Professor
PhD

SIPS

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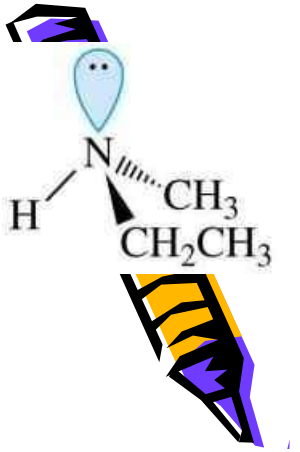
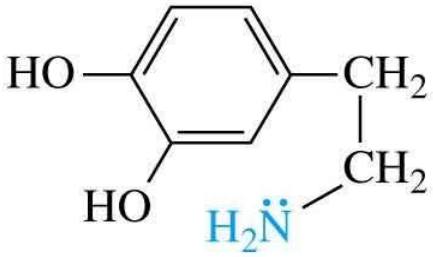
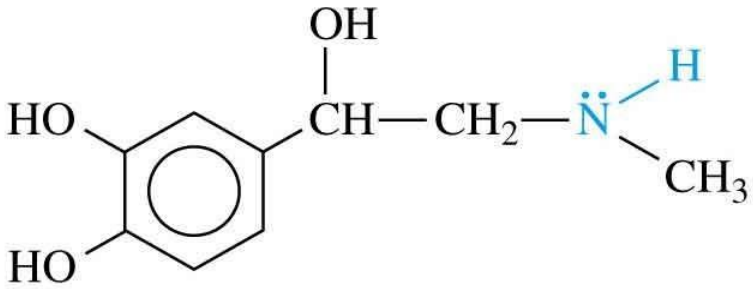
Introduction

- Organic derivatives of ammonia
- Many are biologically active.

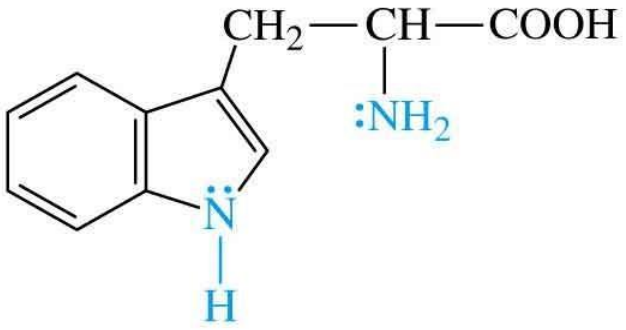




dopamine
a neurotransmitter

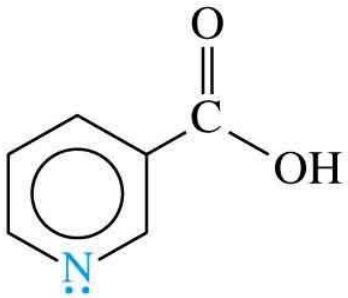


epinephrine
an adrenal hormone

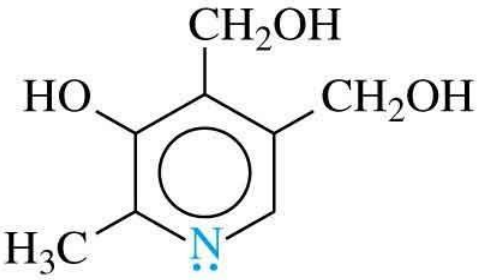


L-tryptophan
an amino acid

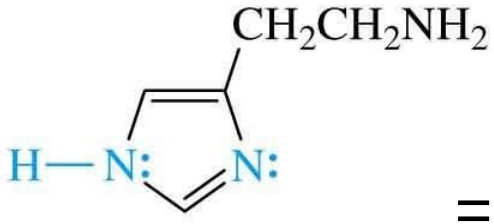
piperazine
kills intestinal worms



nicotinic acid
niacin, a vitamin



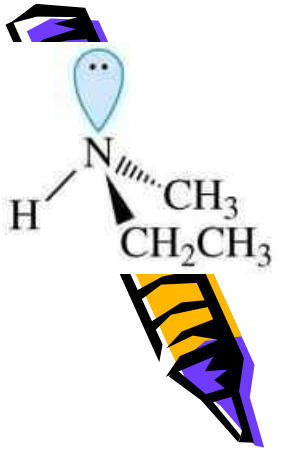
pyridoxine
vitamin B_6



histamine
dilates blood vessels

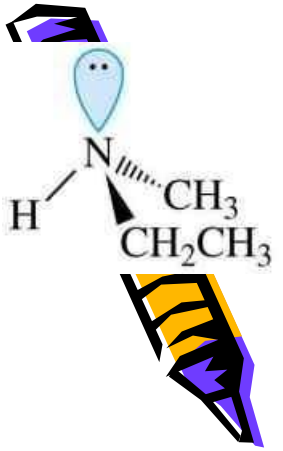
=>

Biological Activity

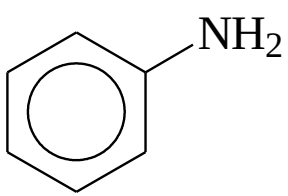


- Neurotransmitters: dopamine
- Bioregulators: epinephrine
- Vitamins: niacin, B_6
- Alkaloids: nicotine, morphine, cocaine
- Amino acids

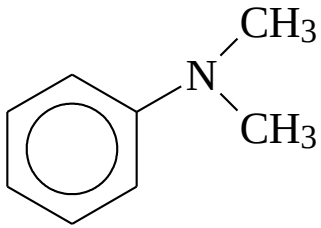
Aromatic Amines



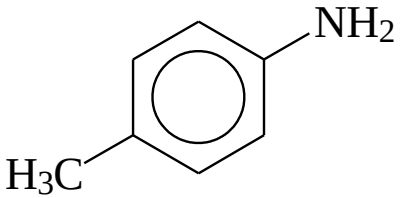
Amino group is bonded to a benzene ring. Parent compound is called aniline.



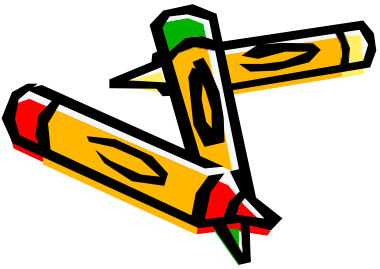
aniline



N,*N*-dimethylaniline



4-methylaniline or *p*-toluidine



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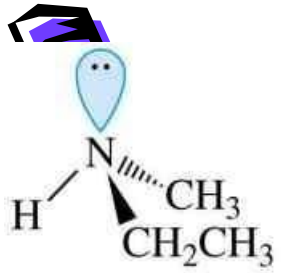
Basicity of Amines



- 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.

=>

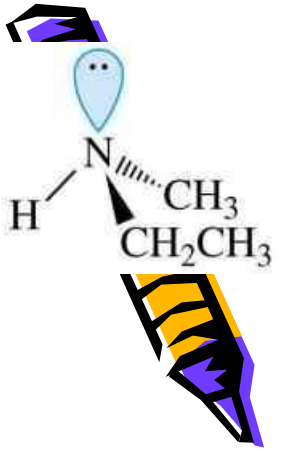
Basicity-Aliphatic Amines

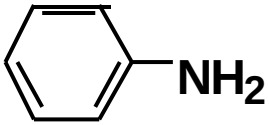
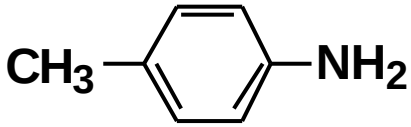
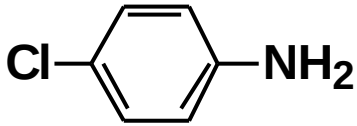
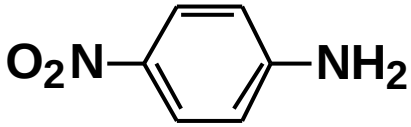
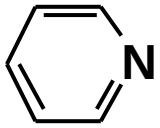
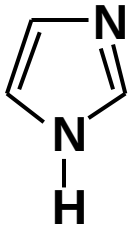
- Aliphatic Amines
  - note that $pK_a + pK_b = 14$

Amine	Structure	pK_a	pK_b
Ammonia Primary Amines	NH_3	9.26	4.74
methylamine	CH_3NH_2	10.64	3.36
ethylamine	$CH_3CH_2NH_2$	10.81	3.19
cyclohexylamine	$C_6H_{11}NH_2$	10.66	3.34
Secondary Amines			
dimethylamine	$(CH_3)_2NH$	10.73	3.27
diethylamine	$(CH_3CH_2)_2NH$	10.98	3.02
Tertiary Amines			
trimethylamine	$(CH_3)_3N$	9.81	4.19
triethylamine	$(CH_3CH_2)_3N$	10.75	3.25

Stronger bases

Basicity-Aromatic Amines

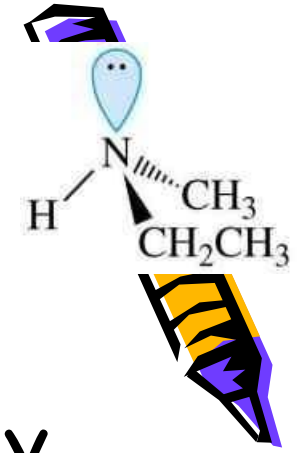


Amine	Structure	pK_a of Conjugate Acid
Aromatic Amines		
Aniline		4.63
4-Methylaniline		5.08
4-Chloroaniline		4.15
4-Nitroaniline		1.0
Heterocyclic Aromatic Amines		
Pyridine		5.25
Imidazole		6.95

Weaker bases

Intermediate

Basicity-Aromatic Amines



- Aromatic amines are considerably weaker bases than aliphatic amines.

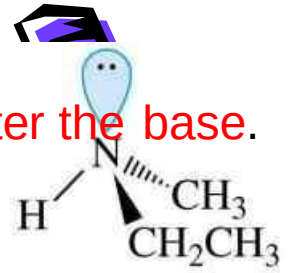
$pK_a = 10.66$

Cyclohexylamine — Cyclohexylammonium hydroxide

$pK_a = 4.63$

Aniline — Anilinium hydroxide

The greater the availability of the lone pair electrons on nitrogen, the greater the base.



In the old days, pK_b was a measure of base strength.

$Kb = [RNH_3^+] [OH^-] / RNH_2$ $\qquad pK_b = - \log K_b$

The stronger the base the lower the pK_b

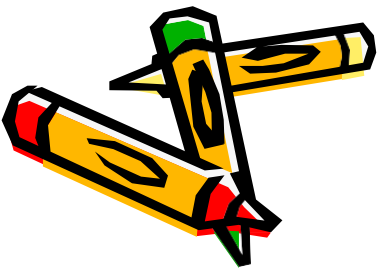
EFFECTS ON AMINE BASICITY

1. INDUCTIVE EFFECT - ALKYL SUBSTITUTION

$CH_3-NH_2 < CH_3-\underset{\displaystyle CH_3}{\underset{|}{N}}H$

METHYL GROUP INCREASES ELECTRON DENSITY ON N

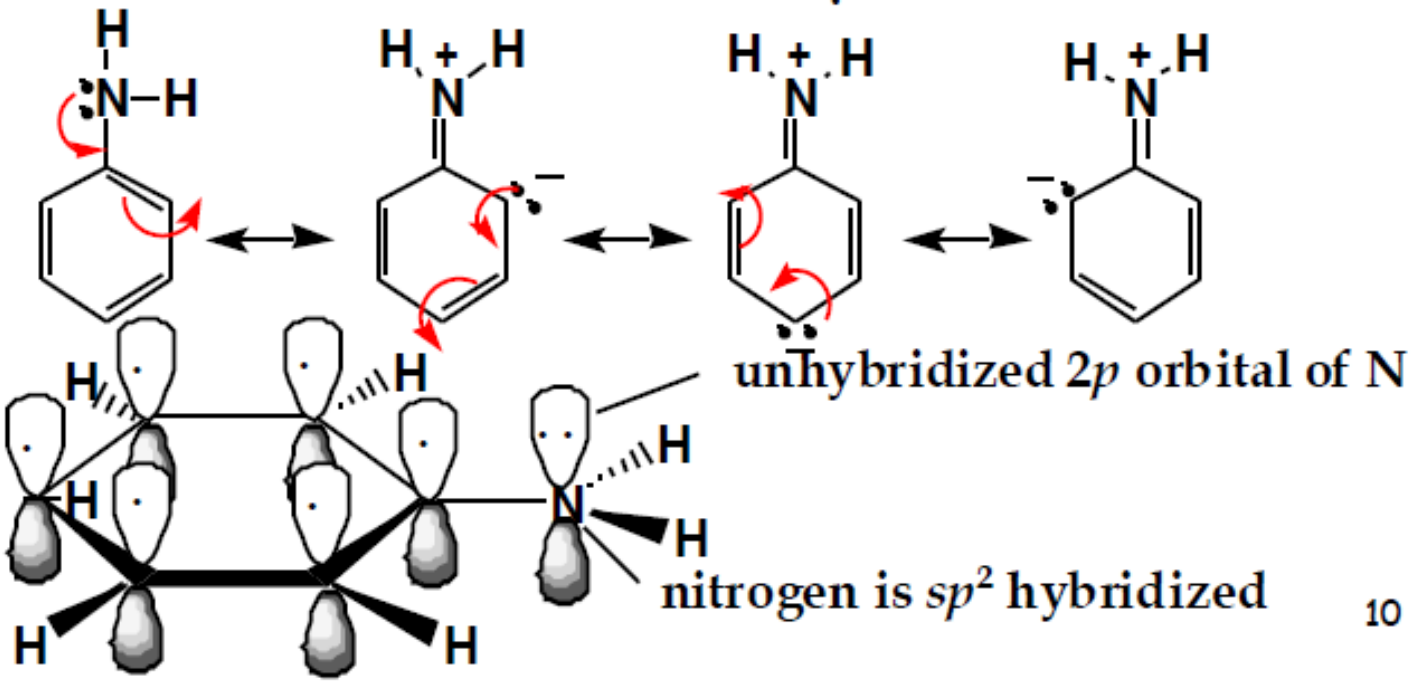
2 METHYLS ARE BETTER THAN ONE



WATCH OUT THREE METHYL GROUPS INCREASES BASICITY $pK_b = 4.26$ - Steric inhibition of solvation of HOH with the NH^+ of the R_3NH^+ cation.

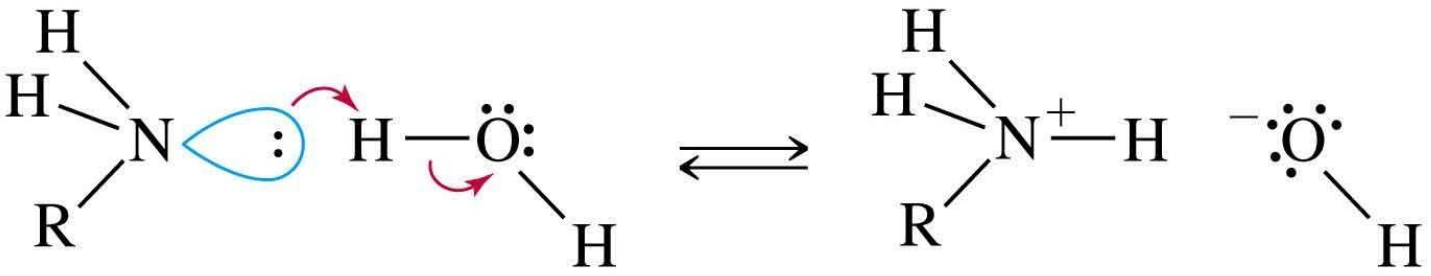
Basicity-Aromatic Amines

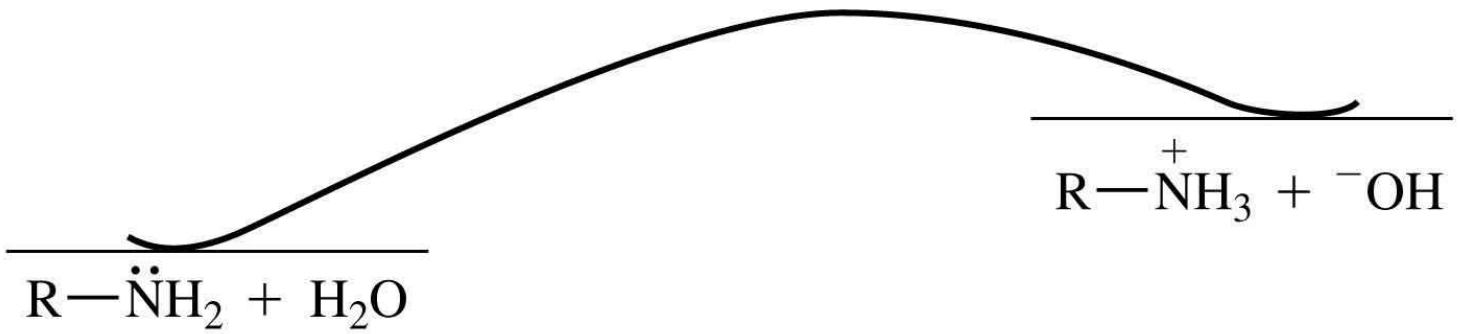
- Aromatic amines are weaker bases than aliphatic amines because of two factors:
  - Resonance stabilization of the free base, which is lost on protonation.



Energy Diagram

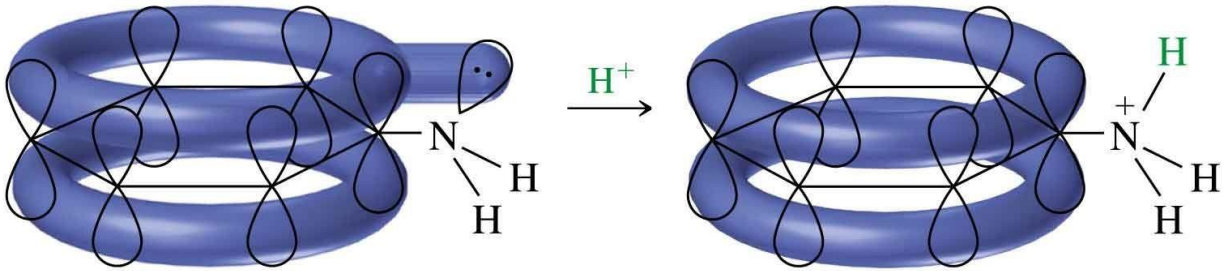
Alkyl groups are electron-donating and stabilize the cation.





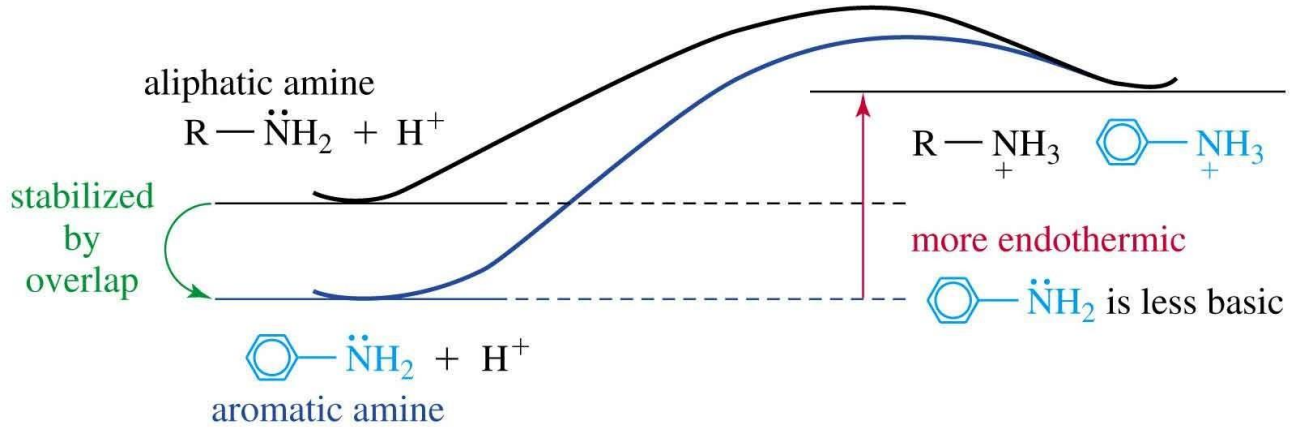
Resonance Effects

Any delocalization of the electron pair weakens the base.



aniline
stabilized by overlap with the ring

anilinium ion
no overlap is possible



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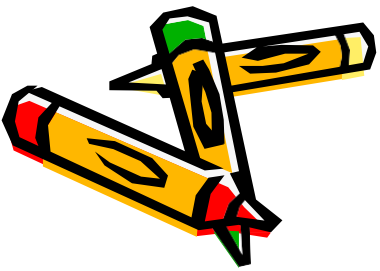
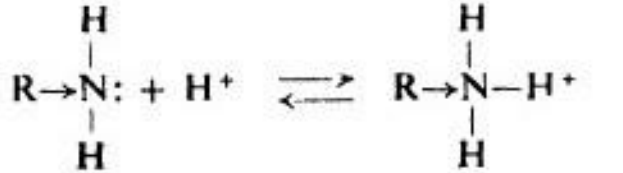
23.3 Structure and basicity

Let us see how basicity of amines is related to structure. We shall handle basicity just as we handled acidity: 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.

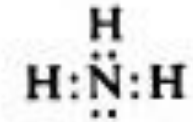
First of all, amines are more basic than alcohols, ethers, esters, etc., for the same reason that ammonia is more basic than water: nitrogen is less electronegative than oxygen, and can better accommodate the positive charge of the ion.

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 (Sec. 5.17). 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.)

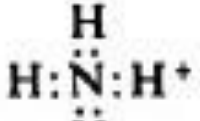




How can we account for the fact that aromatic amines are weaker bases than ammonia? Let us compare the structures of aniline and the anilinium ion with the structures of ammonia and the ammonium ion. We see that ammonia and the ammonium ion are each represented satisfactorily by a single structure:

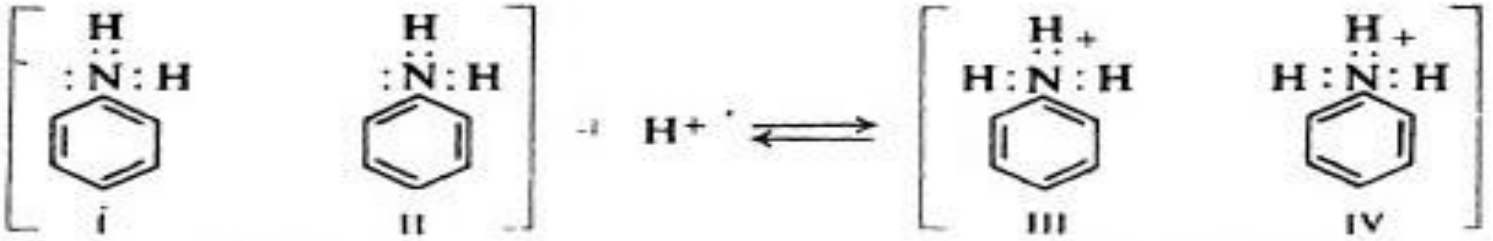


Ammonia



Ammonium ion

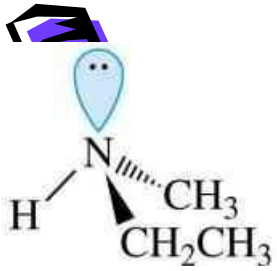
Aniline and anilinium ion contain the benzene ring and therefore are hybrids of the Kekulé structures I and II, and III and IV. This resonance presumably stabilizes

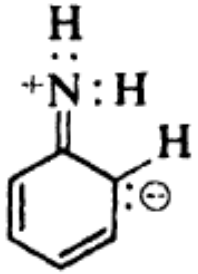


Aniline

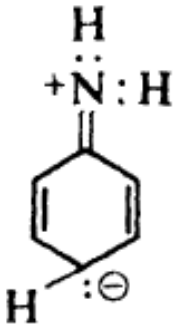
Anilinium ion

both amine and ion to the same extent. It lowers the energy content of each by the same number of kcal/mole, and hence does not affect the *difference* in their energy contents, that is, does not affect ΔG of ionization. If there were no other factors involved, then, we might expect the basicity of aniline to be about the same as the basicity of ammonia.

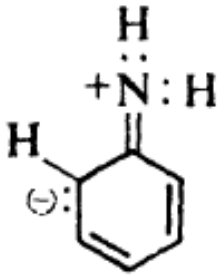




V



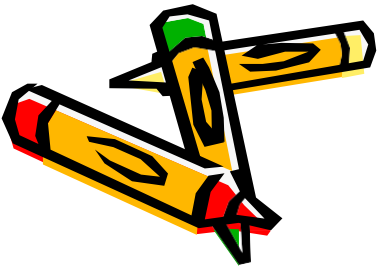
VI



VII

Contribution from the three structures V, VI, and VII stabilizes the amine in a way that is not possible for the ammonium ion; resonance thus lowers the energy content of aniline more than it lowers the energy content of the anilinium ion. The net effect is to shift the equilibrium in the direction of less ionization, that is, to make K_b smaller (Fig. 23.1). (See, however, the discussion in Sec. 18.11.)

The low basicity of aromatic amines is thus due to the fact that the amine is stabilized by resonance to a greater extent than is the ion.



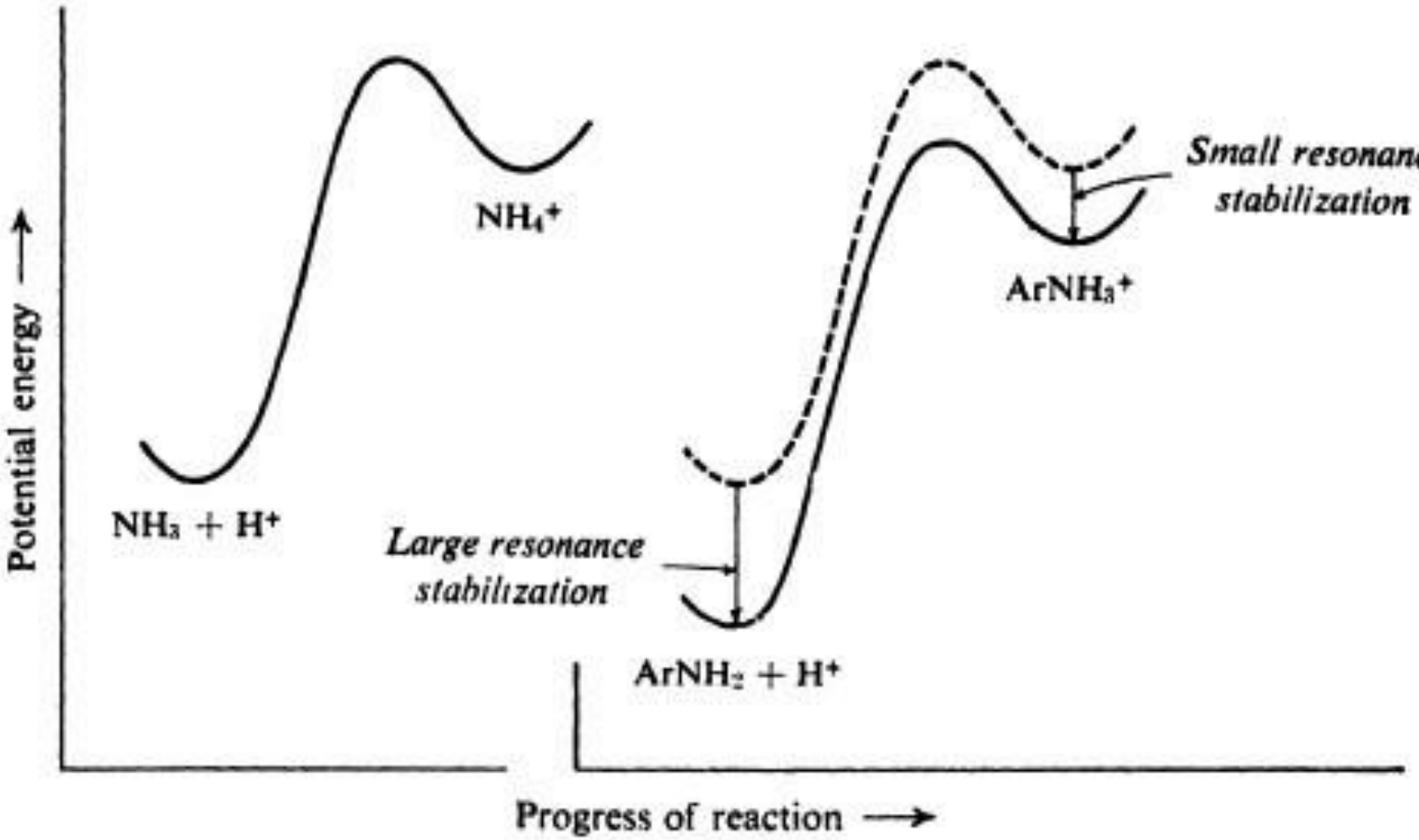


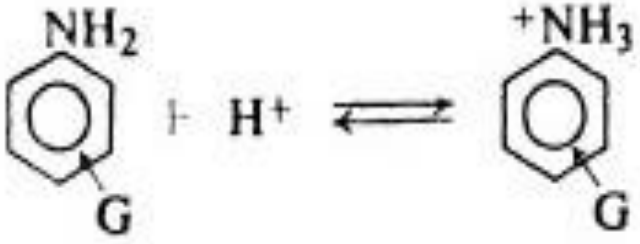
Figure 23.1. Molecular structure and position of equilibrium. Resonance-stabilized aromatic amine is weaker base than ammonia. (Plots aligned with each other for easy comparison.)

23.4 Effect of substituents on basicity of aromatic amines

How is the basicity of an aromatic amine affected by substituents on the ring?

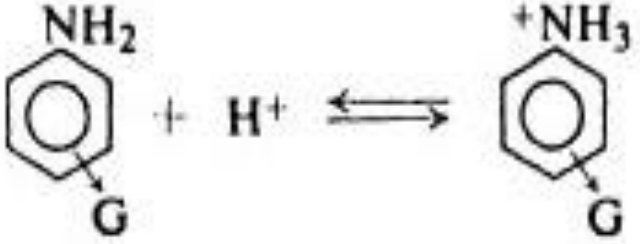
In Table 23.1 (p. 749) we see that an electron-releasing substituent like $-CH_3$ increases the basicity of aniline, and an electron-withdrawing substituent like $-X$ or $-NO_2$ decreases the basicity. These effects are understandable. Electron release tends to disperse the positive charge of the anilinium 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 = $-NH_2$
$-OCH_3$
$-CH_3$



G withdraws electrons
destabilizes cation,
decreases basicity

G = $-NH_3^+$
$-NO_2$
$-SO_3^-$
$-COOH$
$-X$

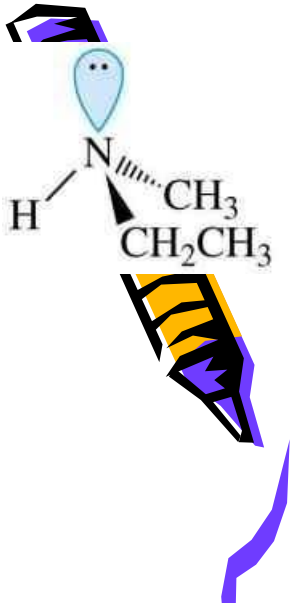
Basicity–Aromatic Amines

- The greater electron-withdrawing inductive effect of the sp^2-hybridized carbon of an aromatic amine compared with that of the sp^3-hybridized carbon of an aliphatic amine.

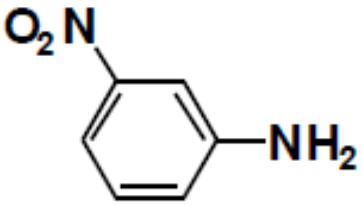
And note the effect of substituents

- Electron-releasing groups, such as alkyl groups, increase the basicity of aromatic amines.
- Electron-withdrawing groups, such as halogens, the nitro group, and a carbonyl group decrease the basicity of aromatic amines by a combination of resonance and inductive effects.

Example: Basicity-Aromatic Amines



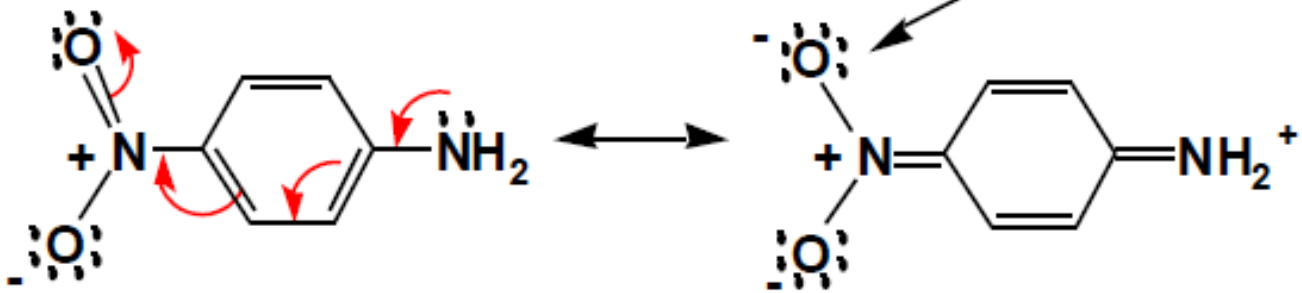
3-Nitroaniline is a stronger base than 4-Nitroaniline.



3-Nitroaniline
pK_a 2.47

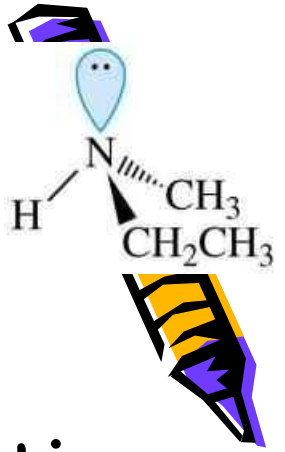
4-Nitroaniline
pK_a 1.0

delocalization of the nitrogen lone pair onto the oxygen atoms of the nitro group

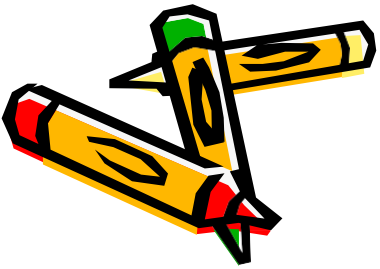


Cannot do this kind of resonance in 3 nitroaniline

Electrophilic Substitution of Aniline



- $-NH_2$ is strong activator, *o*-,*p*-directing.
- May trisubstitute with excess reagent.
- H^+ changes $-NH_2$ to $-NH_3^+$, a *meta*-directing deactivator.
- Attempt to nitrate aniline may explode.



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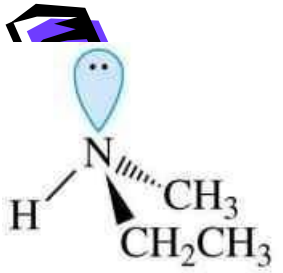
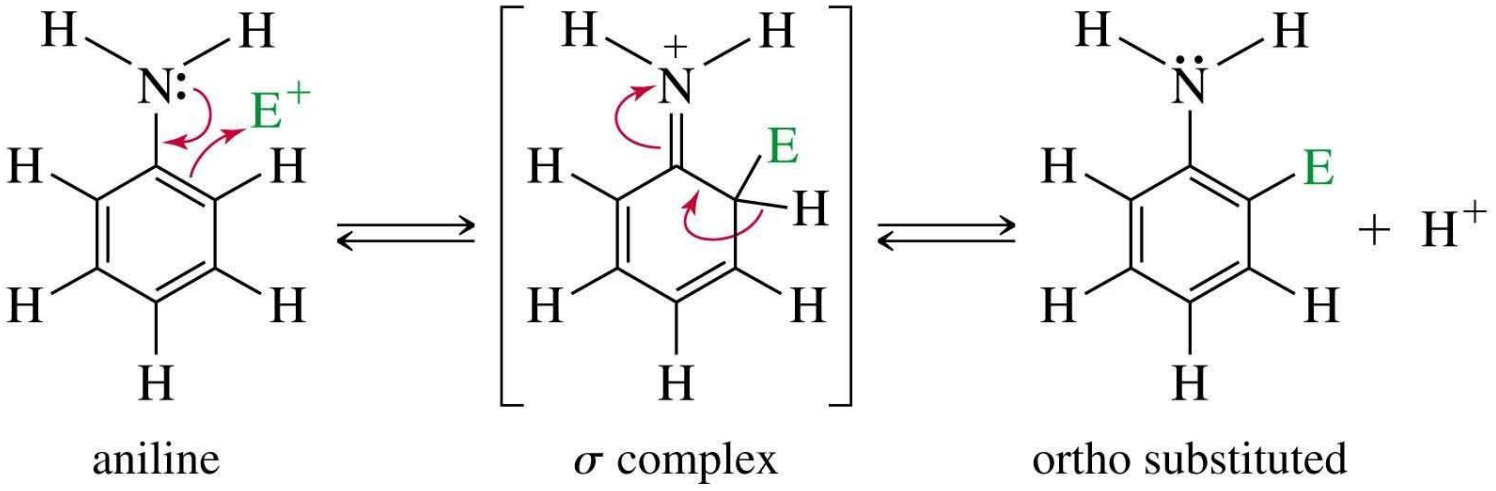
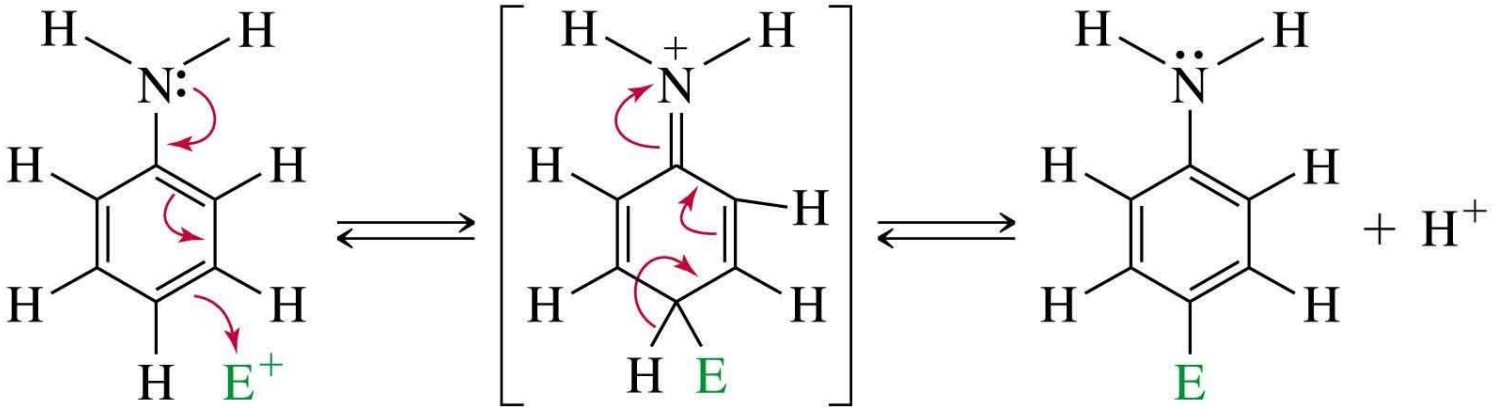
Aniline Substitution

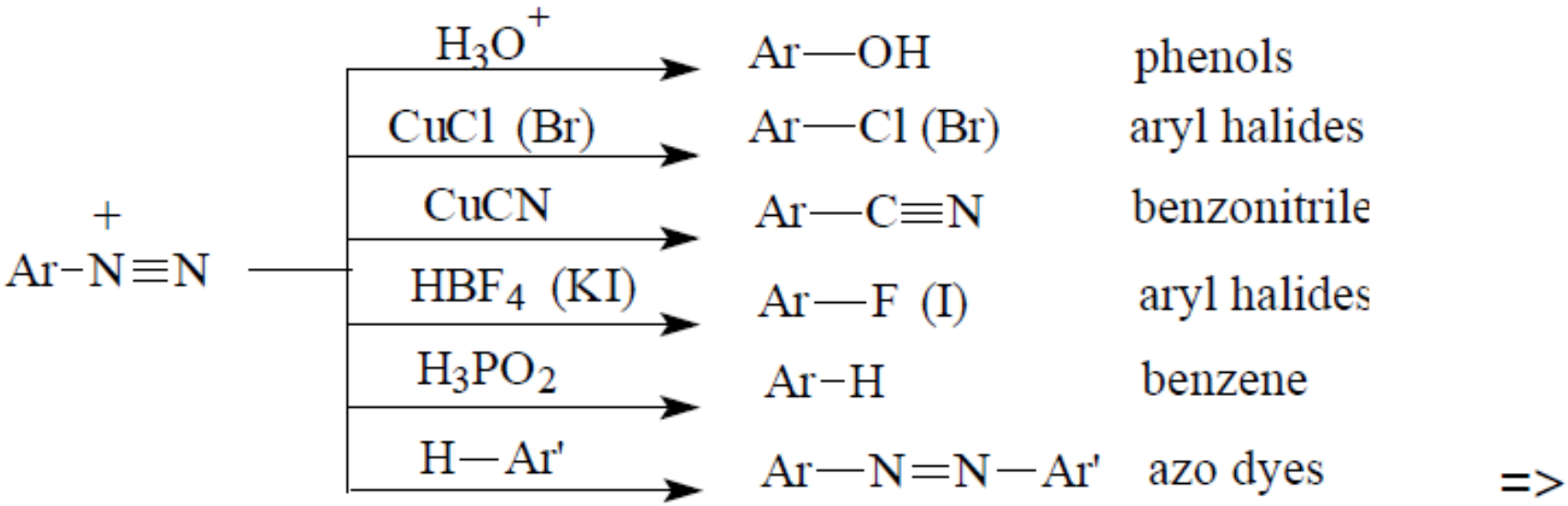






Arenediazonium Salts

- Stable in solution at 0°–10°C.
- Diazotizing reagent :- $NaNO_2 + 2HCl$
- The $-{}^{+}N{\equiv}N$ group is easily replaced by many different groups.
- Nitrogen gas, N_2, is a by-product.



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