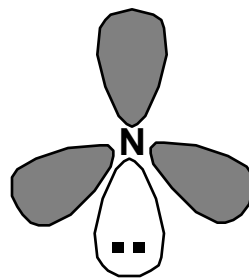
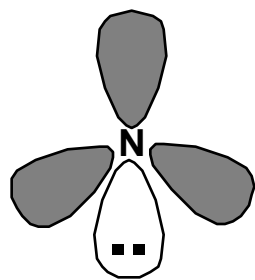
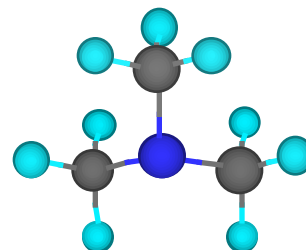
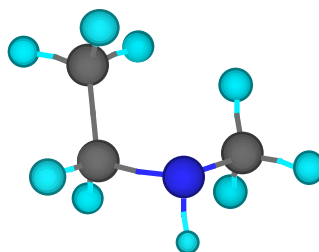
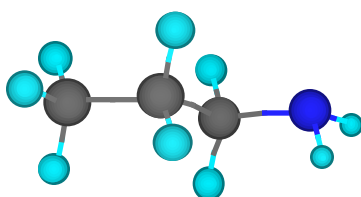


10



Amines



CHAPTER SUMMARY

10.1 Structure of Amines

Amines are derivatives of ammonia in which one or more hydrogens have been replaced by organic groups. Replacement of one hydrogen results in a **primary amine**. In a **secondary amine**, two hydrogens are replaced and in a **tertiary amine**, three hydrogens on ammonia are replaced. The nitrogen in alkyl amines is sp^3 hybridized, tetrahedral, and has bond angles of about 109° .

10.2 Nomenclature of Amines

A. Alkyl and Aromatic Amines

Common nomenclature of simple amines involves presenting the name of the alkyl group followed by the word amine (such as propylamine); this type of nomenclature is acceptable in IUPAC for simple amines. In **IUPAC nomenclature**, the name is based on the longest continuous chain of carbon atoms followed by the suffix -amine (such as 1-propanamine). Substituents on the carbon chain are located by a number; substituents on the nitrogen are located with N (such as N-methyl-1-propanamine). The simplest aromatic amine is **aniline**.

B. Unsaturated Amines

In **unsaturated amines**, the double bond or triple bond is named with the usual suffix (en and yn respectively) and located by a number.

CONNECTIONS 10.1 Nasal Decongestants, Diet Pills, and Stimulants

10.3 Physical Properties of Amines

Melting points and boiling points of amines generally increase with molecular weight. Because of **hydrogen bonding**, amines have higher than expected boiling points and lower molecular weight amines are water soluble. Amines with greater hydrogen bonding capacity have higher boiling points than those with similar molecular weight. Tertiary amines have no N-H bond and therefore cannot engage in hydrogen bonding; primary amines have two N-H bonds and secondary amines have two.

CONNECTIONS 10.2 Local Anesthetics and Cocaine

10.4 Basicity of Amines

A. Salt Formation

Basicity is the characteristic property of amines; the presence of a **non-bonding** electron pair on nitrogen makes amines **Lewis bases**.

Because of their basicity, amines react readily with strong mineral acids to form ammonium salts.

B. Expressing Relative Basicities of Amines: The Basicity Constant

Relative basicities are expressed using the **basicity constant, K_b** , which is defined as the concentrations of the ionized amine products in water (ammonium salt and hydroxide) divided by the concentration of the un-ionized amine. Larger K_b 's mean greater basicity. **pK_b** is the negative logarithm of K_b ; the smaller the pK_b the stronger the base.

C. Relationship of Structure and Basicity in Amines

1. **Electron-releasing groups** increase the availability of nitrogen's lone pair and, as a result, also increase the basicity of amines; **alkyl amines are more basic than ammonia.**

2. **Electron-withdrawing groups** decrease the availability of the non-bonding electron pair and decrease basicity; **amides are much less basic than ammonia.**

3. In aromatic amines, the non-bonding electron pair on nitrogen overlaps with the benzene pi-cloud by resonance; this decreases the availability of the lone pair and stabilizes the compound. As a result, **aromatic amines are considerably less basic than aliphatic amines.** Electron-donating groups on an aromatic amine increase availability of the non-bonding pair whereas electron-withdrawing groups decrease availability; as a result **electron-donating groups on an aromatic ring increase basicity and electron-withdrawing groups decrease basicity.** The effect of these groups is greatest at the ortho and para positions.

D. Expressing Basicity with Acidity Constants

Basicity can also be expressed with **acidity constants.** With amines, **K_a** defines the equilibrium in the direction of the ammonium salt ionizing to the free amine and hydronium ion in water. Since this is the opposite of the definition of K_b , small K_a 's and large pK_a 's mean strong basicity.

10.5 Amines as Nucleophiles: Alkylation by Nucleophilic Substitution

Alkylation involves treating ammonia or an amine with an alkyl halide. The amine, as a Lewis base with a non-bonding electron pair, is a good nucleophile and displaces the halide ion from the alkyl halide; the reaction is **nucleophilic substitution** with a neutral nucleophile. S_N2 reactions are common. Since alkylation tends to continue until four groups are bonded to the nitrogen, it has limited synthetic utility.

CONNECTIONS 10.3 Acetylcholine and Neuromuscular Blockade

10.6 Preparations of Amines by Reduction Reactions

A. Reduction of Aromatic Nitro Compounds

Amines can be synthesized by **reduction of nitro compounds** with hydrogen and platinum catalyst or with a tin and hydrochloric acid solution. Aromatic nitro compounds can be made by treating benzene or a benzene derivative with nitric and sulfuric acids.

B. Reduction of Nitriles

Nitriles can be reduced using hydrogen gas and nickel catalyst to produce amines.

C. Reduction of Amides

Lithium aluminum hydride is used to **reduce amides**. In both cases amines are the reduction products.

CONNECTIONS 10.4 Sulfa Drugs

10.7 Aromatic Diazonium Salts

A. Preparation

Upon treatment with sodium nitrite and hydrochloric acid at 0°C , primary aromatic amines can be converted to **aromatic diazonium salts**, an unstable species that is very useful in organic synthesis. Since a nitro group can be reduced to a primary amine, it is a synthetic precursor to a diazonium salt.

B. Replacement Reactions

Diazonium salts are quite useful in organic synthesis as the diazonium group can be easily replaced by fluorine, chlorine, bromine, iodine, cyanide, hydroxy, and hydrogen. In these **diazonium replacement reactions**, nitrogen gas is evolved.

C. Coupling Reactions

In **coupling reactions** of diazonium salts, nitrogen is retained and actually bonds to an activated aromatic ring in an **electrophilic aromatic substitution reaction**. This reaction is used to make **azo dyes**.

CONNECTIONS 10.5 Dyes and Dyeing

10.8 Heterocyclic Amines

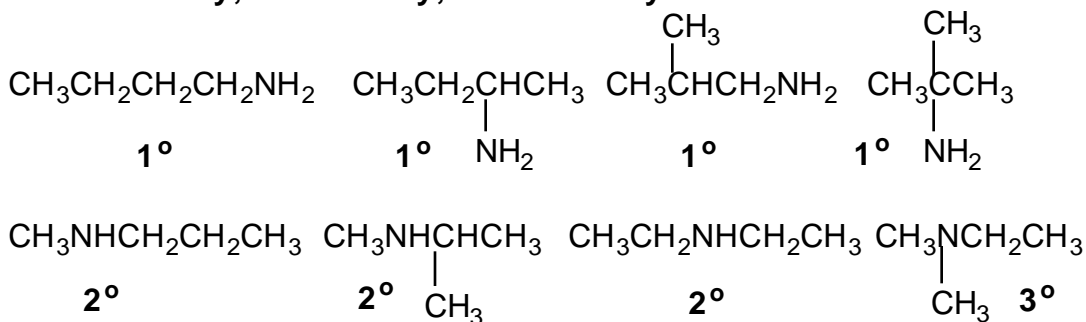
Heterocycles are cyclic compounds in which one or more of the ring atoms are not carbon.

A. Structure and Basicity of Heterocyclic Amines

Heterocyclic amines have nitrogen as one of the ring atoms. Although they are basic, their basicity can vary widely depending on structure and availability of nitrogen's non-bonding electron pair. Aromatic heterocyclic amines in which the nitrogen's non-bonding electron pair is part of the aromatic pi-cloud, the aromatic sextet, are much less basic than those in which it is not. If the nitrogen is involved in a "double bond", its lone pair is not in the pi cloud or part of the sextet.

B. Naturally Occurring Heterocyclic Amines: Alkaloids

Alkaloids are defined as plant-produced nitrogenous bases that have a physiological effect on humans. They are often classified according to the heterocyclic amine present in the structure. These include the following ring systems: pyrrolidine, pyrrole, piperidine, pyridine, quinoline, isoquinoline, indole, and purine.

SOLUTIONS TO PROBLEMS**10.1 Primary, Secondary, and Tertiary Amines****10.2 Nomenclature of Amines**

- (a) 1-nonanamine; (b) 2-hexanamine; (c) N,N-dimethyl-3-pentanamine;
 (d) N-ethyl-N-methyl-1-octanamine; (e) 2-ethyl-N-methylcyclohexanamine;
 (f) N-ethyl-N-methyl-3-nitroaniline

10.3 Nomenclature of Amines

Names of compounds in Problem 10.1 in order left to right.

First row: 1-butanamine; 2-butanamine; 2-methyl-1-propanamine;
 2-methyl-2-propanamine

Second row: N-methyl-1-propanamine; N-methyl-2-propanamine;
 N-ethylethanamine; N,N-dimethylethanamine.

10.4 Nomenclature of Amines

- (a) 2-penten-1-amine; (b) 5-methyl-3-hexyn-1-amine;
 (c) 2,4-hexadien-1,6-diamine; (d) N-methyl-3-penten-2-amine

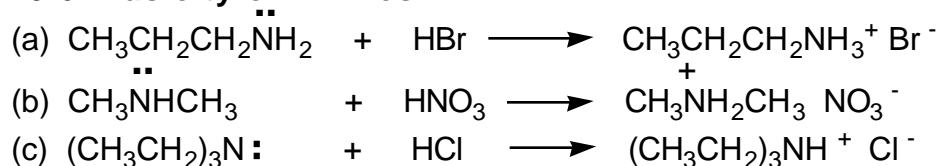
10.5 Physical Properties

(a) **ii < iii < i** These amines are isomers of one another. The differences in boiling point are determined by differences in hydrogen bonding capacity. ii is a tertiary amine with no N-H bonds and is incapable of hydrogen bonding. iii is a secondary amine with one N-H bond and i is a primary amine with two N-H bonds. The primary amine is most capable of hydrogen bonding and has the highest boiling point.

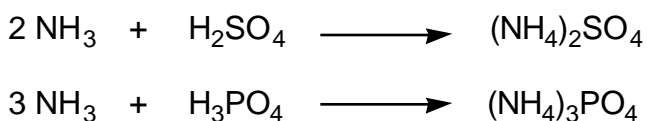
(b) **iii < iv < ii < i** These compounds have similar molecular weights. iii is non-polar and has no capacity for hydrogen bonding. iv and ii have N-H bonds

and can hydrogen bond; ii has a higher boiling point because it has two N-H bonds. i has an O-H bond and since this is much more polar than the N-H bonds, it hydrogen bonds more extensively and has the highest boiling point.

10.6 Basicity of Amines

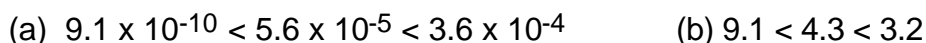


10.7 Ammonium Fertilizers



10.8 Basicity Constants

Constants are shown in increasing basicity.



10.9 Basicity Constants

(a) diethylamine; (b) triethylamine; (c) triethylamine; (d) p-methylaniline

10.10 Basicity of Amines

Arrangements are least basic to most basic.

(a) **ii < i < iii** Alkyl groups are electron-releasing and increase the availability of the lone pair of electrons on nitrogen. ii has no alkyl groups, i has one, and iii has two.

(b) **iii < ii < i** Carbon-oxygen double bonds are electron-withdrawing groups. They decrease the electron density around the nitrogen and lower the basicity. iii has two electron-withdrawing groups, ii has only one, and i has none.

(c) **v < iii < i < ii < iv** v has two electron-withdrawing groups, iii has one; these groups decrease lone pair availability and decrease basicity. i has neither releasing or withdrawing groups. ii has one electron-releasing group (alkyl) and iv has two; electron-releasing groups increase lone pair availability and increase basicity.

(d) $ii < iii < iv < v < i$ The amines with lowest basicity have an electron-withdrawing group (the carbon-oxygen double bond). The greater the distance of this group from the amine, the less effective. v has neither electron-releasing or electron-withdrawing groups, and i has an electron-releasing group which increases basicity.

10.11 Basicity of Amines

Arrangements are least basic to most basic.

(a) $i < ii < iii$ i and ii are both aromatic amines and are much less basic than iii which is an alkyl amine. Although ii is aromatic and not very basic, it does have a methyl group, an electron-releasing group, that increases basicity relative to the primary aromatic amine.

(b) $i < ii < iii$ The nitro group is electron-withdrawing and decreases basicity. It more effectively decreases basicity at ortho and para positions because of resonance; thus ii is more basic than i , because the nitro is meta in ii and cannot decrease basicity as effectively. iii has an electron-releasing group that increases basicity.

(c) $ii < i < iii$ ii has two withdrawing groups, i has one; electron-withdrawing groups decrease basicity. iii has an electron-releasing group that increases basicity.

(d) $ii < iii < i$ ii has an electron-withdrawing group attached directly to the nitrogen where it is most effective in decreasing lone pair availability and thus decreasing basicity. iii has an electron-withdrawing group but it is on the benzene ring, not right on the nitrogen. i has neither electron-releasing or withdrawing groups.

10.12 Expression of Basicity with Acidity Constants

Least to most basic for amines.

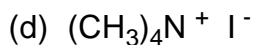
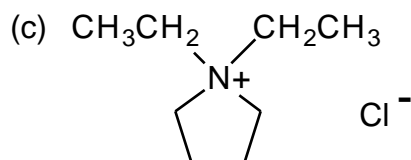
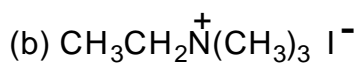
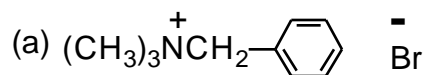
(a) $9.9 \times 10^{-10} < 8.3 \times 10^{-10} < 2.3 \times 10^{-11}$ (b) $5.25 < 9.81 < 10.74$

10.13 Expression of Acidity with Acidity Constants

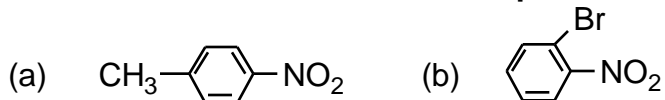
Least to most acidic for acids.

(a) $2.3 \times 10^{-11} < 8.3 \times 10^{-10} < 9.9 \times 10^{-10}$ (b) $10.74 < 9.81 < 5.25$

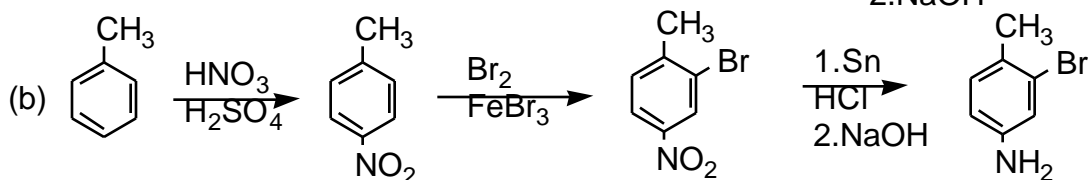
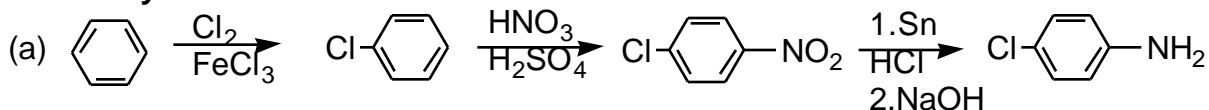
10.14 Alkylation of Amines by Nucleophilic Substitution



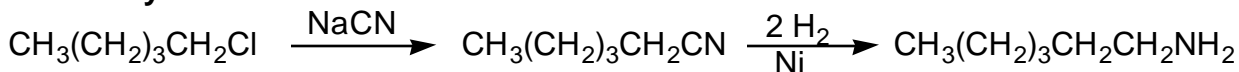
10.15 Reduction of Nitro Compounds



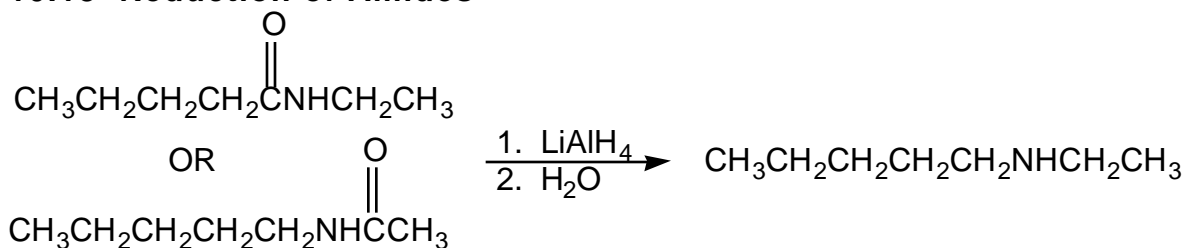
10.16 Synthesis of Amines



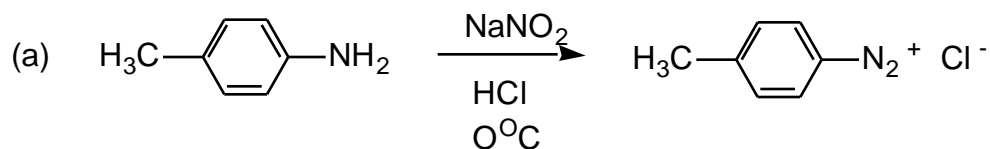
10.17 Synthesis of Amines

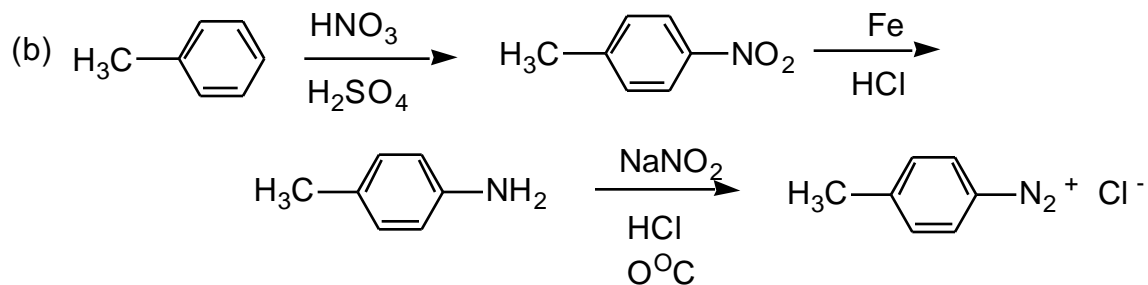


10.18 Reduction of Amides

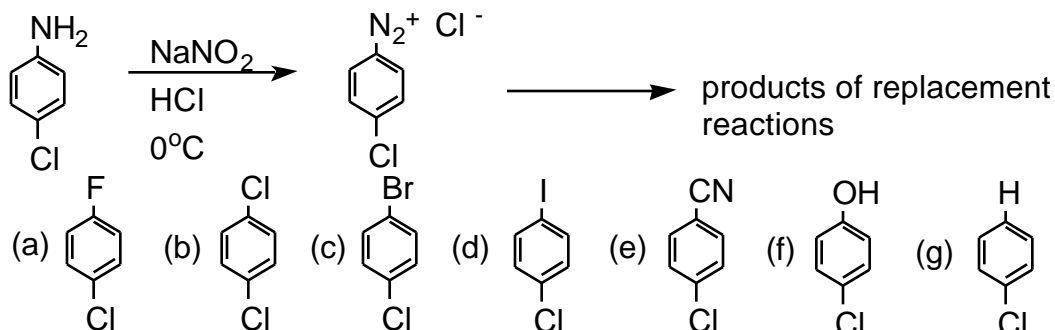


10.19 Preparation of Diazonium Salts

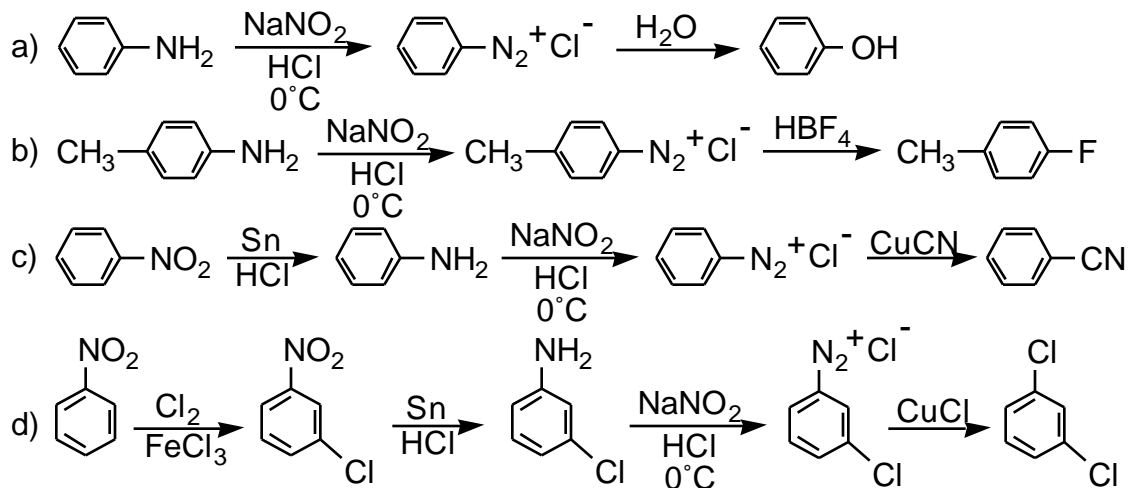




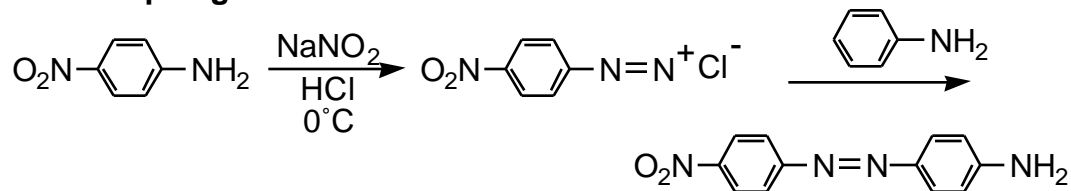
10.20 Diazonium Salt Replacement Reactions



10.21 Synthesis Using Diazonium Salts



10.22 Coupling Reactions of Diazonium Salts



10.23 Aromatic Heterocyclic Amines

Quinoline is aromatic. The ring system is planar and has a p-orbital on each carbon as a result of the "double bonds". There are a total of 6 pi electrons in the ring with the nitrogen. The non-bonding electron pair on nitrogen is not part of the aromatic sextet.

Indole is also aromatic. Two double bonds and the non-bonding electron pair of nitrogen comprise the aromatic sextet. There is a p-orbital on each carbon of the ring system as a result of the "double bonds". To allow aromaticity, the lone pair of electrons on nitrogen also exists in a p-orbital and is part of the aromatic sextet.

10.24 Aromatic Heterocyclic Amines

Isoquinoline is aromatic. The ring system is planar and has a p-orbital on each carbon as a result of the "double bonds". There are a total of 6 pi electrons in the ring with the nitrogen. The non-bonding electron pair on nitrogen is not part of the aromatic sextet.

Purine is also aromatic. Each ring is planar. Consider the five-membered ring first. Each atom has a p-orbital as a result of a "double bond" or, in the case of the NH, a p-orbital housing a non-bonding electron pair. There are six pi electrons, four from the "double bonds" and two from the lone pair of electrons on the NH. The lone pair of the other nitrogen is not part of the aromatic sextet. Now consider the six-membered ring. There are six pi electrons as a result of the three "double bonds" to complete the aromatic sextet. Neither of the nitrogens in this ring contributes its lone pair to the aromatic sextet.

10.25 IUPAC Nomenclature: Section 10.2A

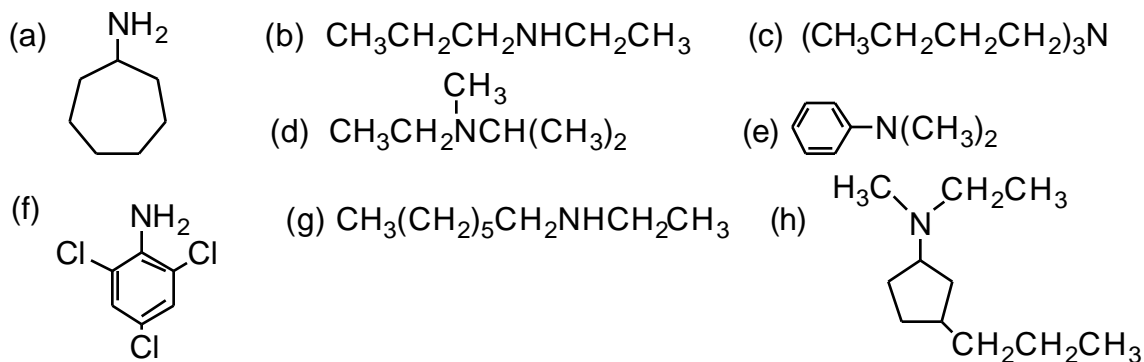
(a) 1-heptanamine; (b) 2-butanamine; (c) 1,8-octandiamine

10.26 IUPAC Nomenclature: Section 10.2A

(a) cyclohexanamine; (b) 4-methylcyclohexanamine;
(c) N-ethyl-4-methylcyclohexanamine; (d) p-methylaniline;
(e) N-ethyl-p-methylaniline; (f) N-ethyl-N-methylaniline;
(g) 2-bromo-N,N-diethyl-1-propanamine;
(h) 7,7-dimethyl-N,N-dipropyl-2-octanamine

10.27 IUPAC Nomenclature: Section 10.2B

- (a) 4-heptyn-1-amine; (b) 2-hexen-1-amine;
 (c) N-ethyl-2,4-hexadien-1-amine; (d) N,N-dimethyl-2-butyn-1-amine;
 (e) 3-cyclopenten-1-amine; (f) 3-methyl-3-cyclopenten-1-amine;
 (g) N,N-diethyl-3-methyl-3-cyclopenten-1-amine

10.28 IUPAC Nomenclature: Section 10.2A**10.29 Physical Properties:** Sections 2.9, 9.2, and 10.3

- (a) $\text{i} < \text{ii} < \text{iii} < \text{iv}$: increasing molecular weight in a homologous series
 (b) $\text{iii} < \text{i} < \text{ii}$: no hydrogen bonding in III; hydrogen bonding with OH is more effective than with NH because of increased bond polarity.
 (c) $\text{iii} < \text{ii} < \text{i}$: these compounds are isomers; the number of NH bonds increases from zero to two in this order and thus hydrogen bonding increases.
 (d) $\text{iii} < \text{ii} < \text{i}$: these compounds are isomers; the number of NH bonds increases from zero to two in this order and thus hydrogen bonding increases.

10.30 Physical Properties: Sections 2.9, 9.2, and 10.3

Methylamine has the lowest molecular weight and, though it has the most hydrogen bonding sites (two NH bonds), the low molecular weight gives it the lowest boiling point. Dimethylamine has one NH bond and can hydrogen bond and it is greater in molecular weight than methylamine. Although trimethylamine has the greatest molecular weight, it has no NH bonds and no hydrogen bonding; as a result it happens to fall in the middle. The boiling points of these compounds are close, they would be hard to predict, but they can be explained using hydrogen bonding and molecular weight.

10.31 Physical Properties: Section 2.9, 9.2, and 10.3

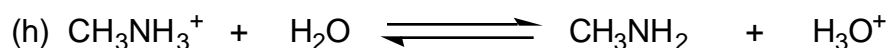
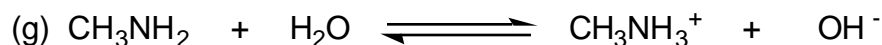
These compounds have similar molecular weights so that is not a factor. Pentane is non-polar and is incapable of hydrogen-bonding; this causes it to have the lowest boiling point. Butylamine has two NH bonds and diethylamine only one; the decreased ability to hydrogen bond gives diethylamine a lower boiling point. 1-butanol has an OH bond which is very polar and very effective in hydrogen bonding compared to amines; it has the highest boiling point as a result.

10.32 Basicity Constants: Section 10.4B

(a) $10^{-10} < 10^{-5} < 10^{-3}$; (b) $10 < 5 < 3$; (c) $11 < 6 < 3$; (d) $10^{-11} < 10^{-6} < 10^{-3}$

10.33 Acidity Constants: Sections 9.6A.1, 10.4D

(a) $10^{-12} < 10^{-8} < 10^{-3}$; (b) $10^{-3} < 10^{-8} < 10^{-12}$; (c) $12 < 8 < 3$;
 (d) $13 < 9 < 4$; (e) $4 < 9 < 13$; (f) $10^{-13} < 10^{-9} < 10^{-4}$

**10.34 Basicity of Amines:** Section 10.4C

(a) Propylamine is more basic than ammonia because the propyl group is an electron donating group and increases the electron availability around the nitrogen. (b) Diethylamine is more basic than ethylamine because it has two electron-donating groups (the ethyls) whereas ethylamine has only one; the electron-donating groups increase electron availability.

(c) Aniline is an aromatic amine. Its non-bonding electron pairs are pulled into the benzene ring by resonance making them less available to acids. This makes it much less basic than cyclohexylamine which is an alkylamine.

(d) Both are aromatic amines and are a lot less basic than alkyl amines. However, the N-methylaniline has an electron-donating group on the nitrogen (methyl) which increases electron availability and thus basicity.

(e) In N-phenylaniline, there are two benzene rings attached to the nitrogen. The non-bonding electron pair on nitrogen is drawn into both and this makes the compound less basic than aniline in which there is only one benzene ring.

(f) Chlorine is an electron-withdrawing group. As such it makes the non-bonding electron pair on nitrogen less available. As a result, aniline is more basic.

(g) Nitro groups are electron-withdrawing groups; they decrease electron availability and basicity. There are two nitro groups on 2,4-dinitroaniline so it is less basic than p-nitroaniline where there is only one.

(h) Chlorine withdraws electrons and decreases basicity; 2-chloropropanamine is less basic than propanamine for this reason.

(i) Both of these compounds have a chlorine which is an electron-withdrawing group and decreases basicity. In 3-chloropropanamine the chlorine is further away from the amine group than in 2-chloropropanamine and, because of this, it has a diminished effect. Thus 3-chloropropanamine is more basic.

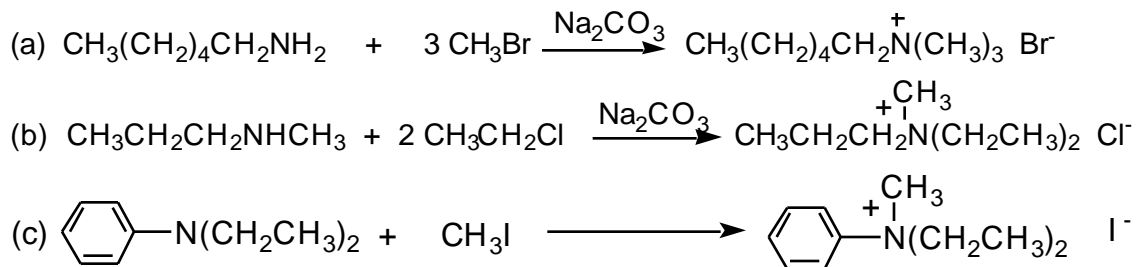
10.35 Acidity and Basicity of Phenol and Aniline: Sections 9.6A.2, and 10.4C.3

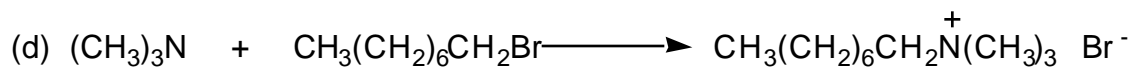
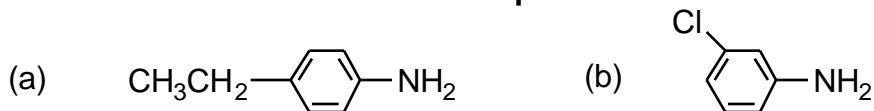
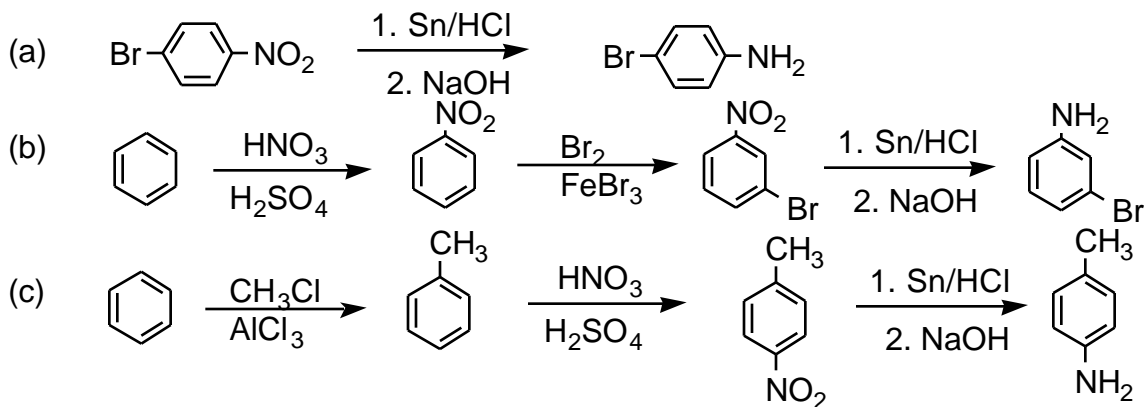
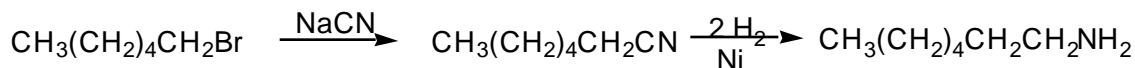
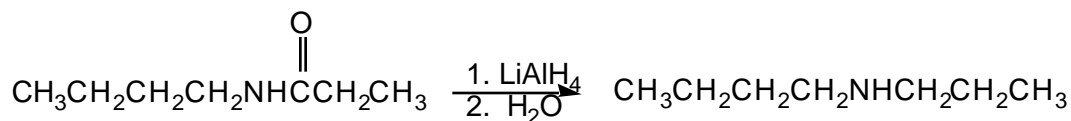
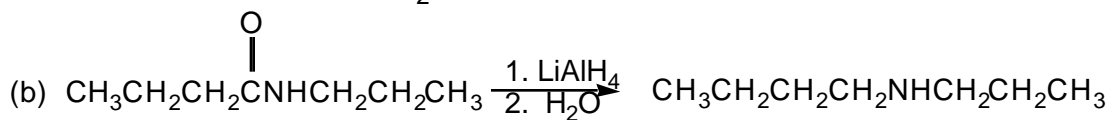
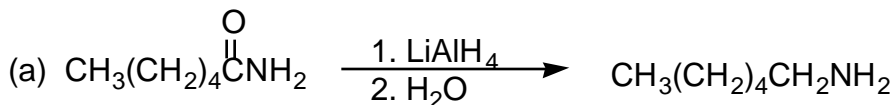
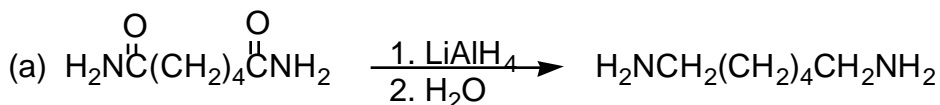
Phenols are more acidic than alcohols because one of the non-bonding electron pairs on oxygen is drawn into the benzene ring by resonance. This stabilizes the phenoxide ion that is formed upon ionization and thus the acidity of phenol is enhanced by the phenomenon. This same withdrawal of electrons by the benzene ring stabilizes aniline and decreases the availability of the non-bonding electron pair on nitrogen. Both effects decrease the basicity of aniline relative to alkyl amines.

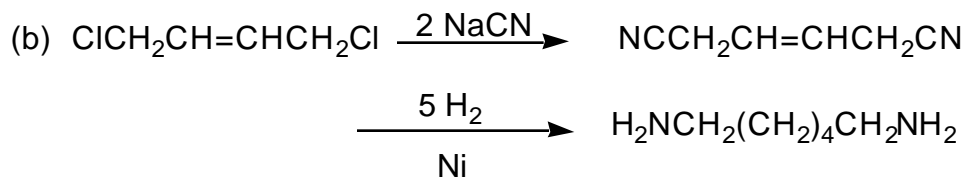
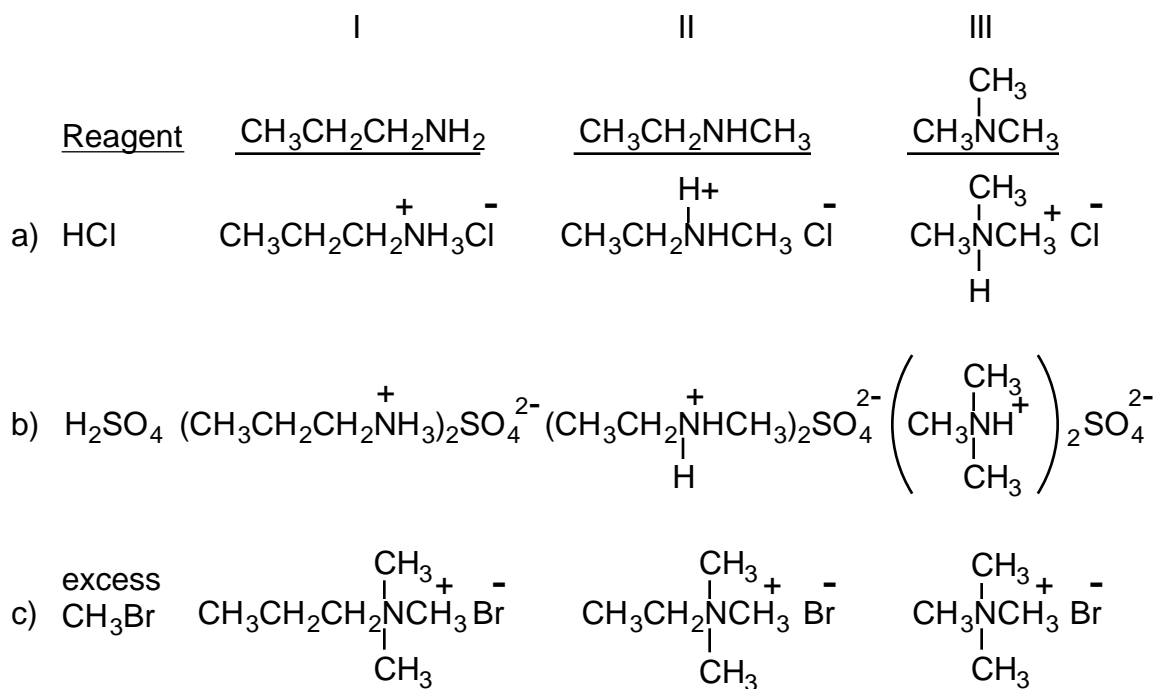
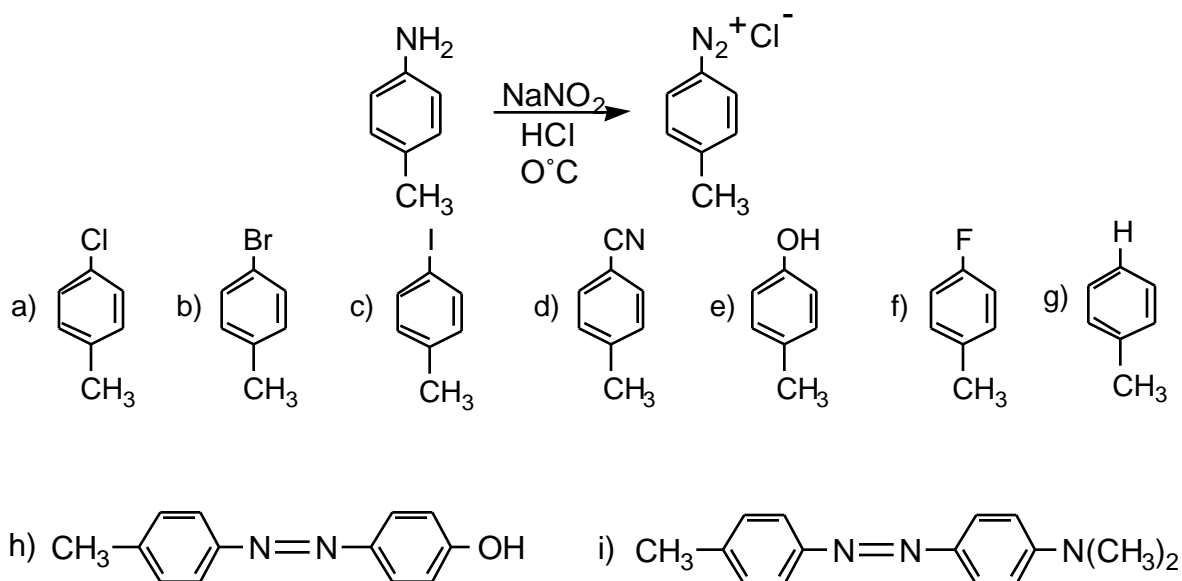
The withdrawal of electrons into the benzene ring makes both aniline and phenol more electron-rich. In electrophilic aromatic substitution, the ring is attacked by a positive electrophile; the more negative the ring, the more readily it reacts with an electrophile.

Please see the textbook references for the resonance structures and hybrids described.

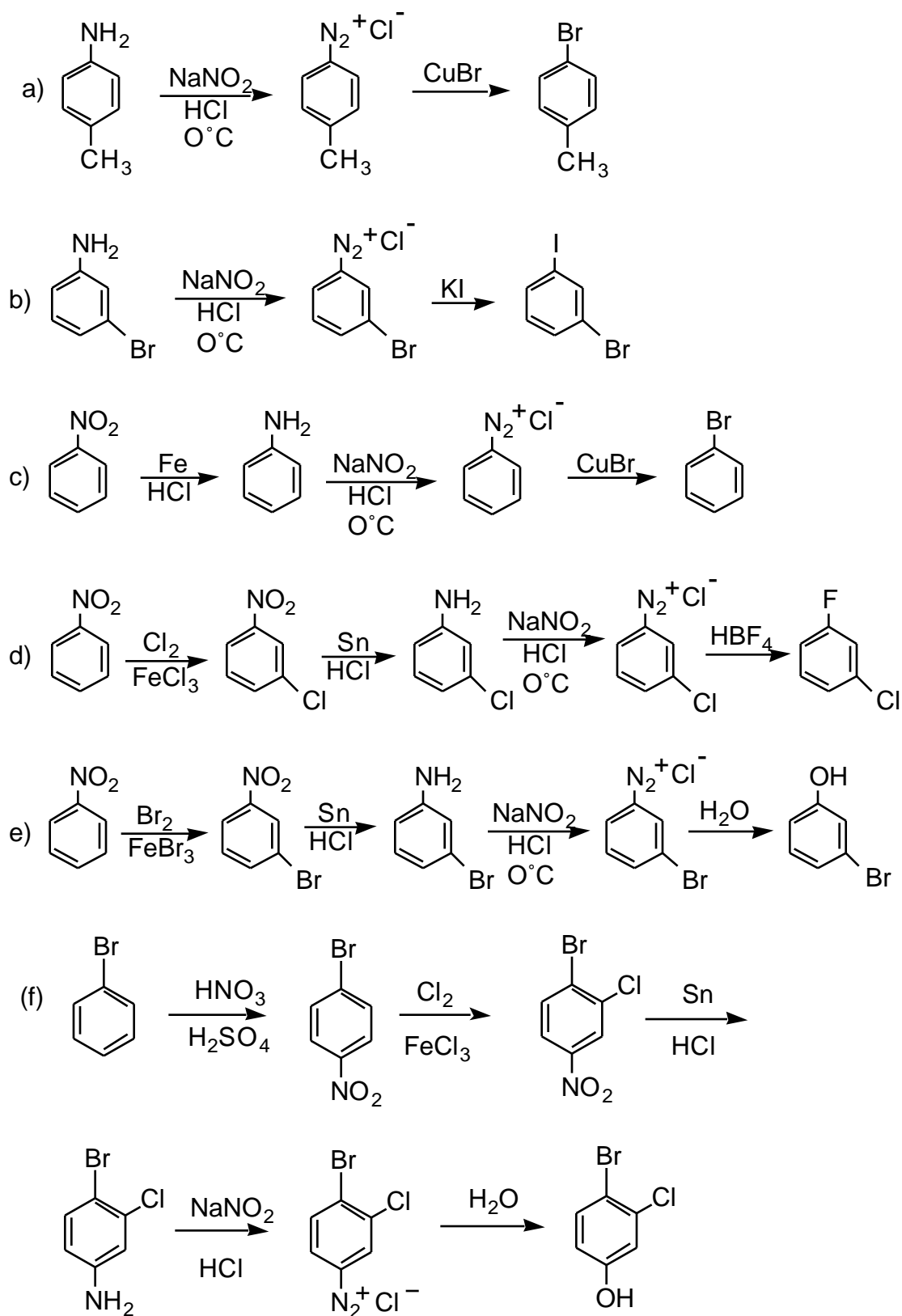
10.36 Alkylation of Amines: Section 10.5

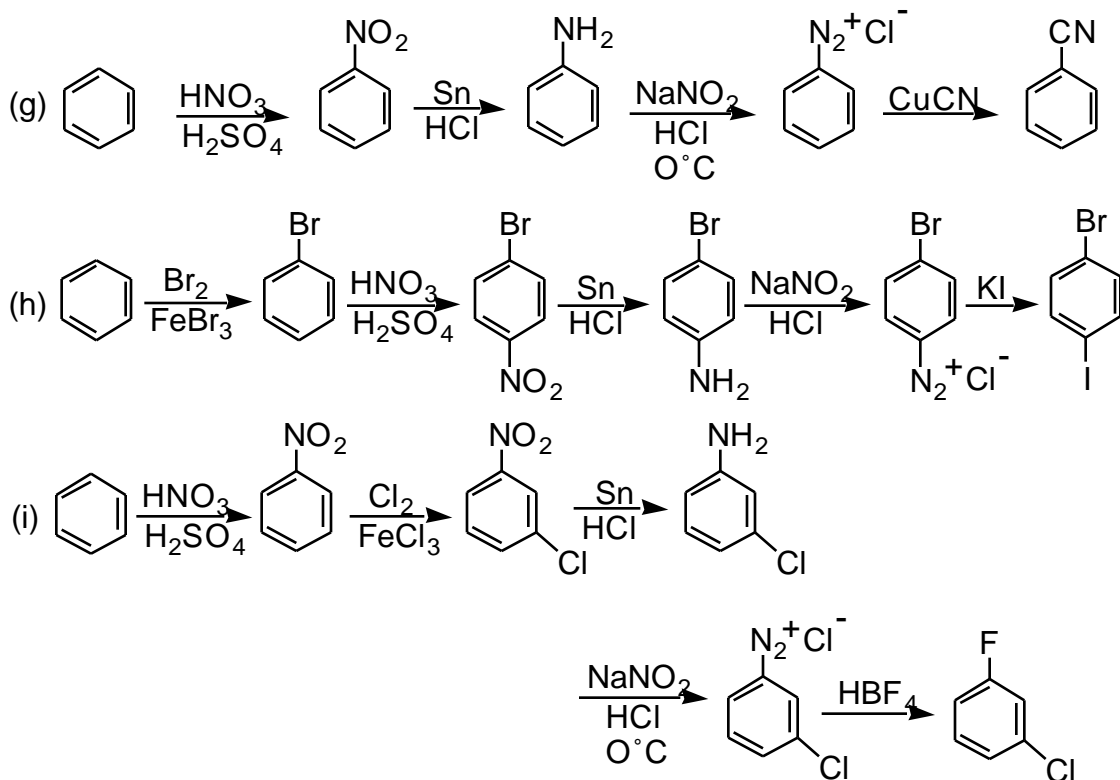



10.37 Reduction of Nitro Compounds: Section 10.6A

10.38 Reduction of Nitro Compounds: Sections 6.4 and 10.6A

10.39 Reduction of Nitriles: Sections 8.4 and 10.6

10.40 Reduction of Amides: Section 10.6C

10.41 Reductions to form Amines: Section 10.6


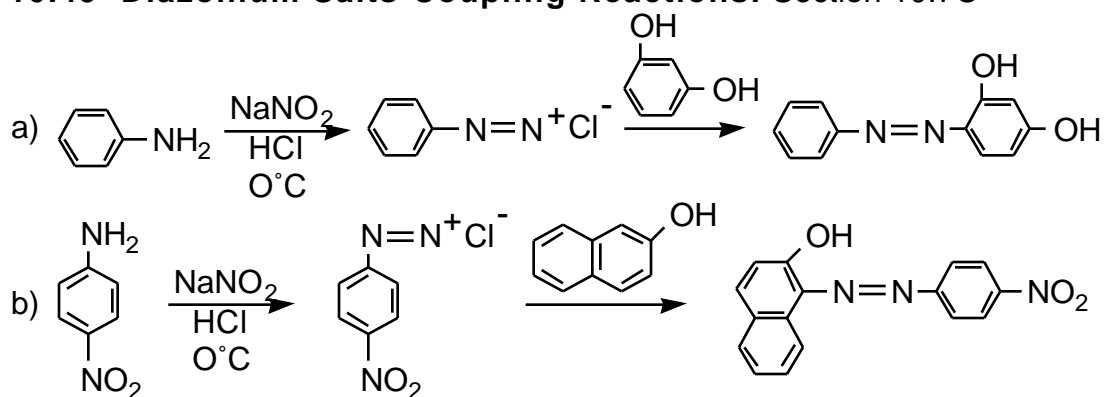

10.42 Reactions of Amines: Sections 10.5A and 10.6

10.43 Reactions of Diazonium Salts: Section 10.7


10.44 Syntheses Using Diazonium Salts: Sections 6.4 and 10.7





10.45 Diazonium Salts-Coupling Reactions: Section 10.7C



10.46 Basicity of Aromatic Amines: Section 10.8A

Both compounds need six pi-electrons in the ring system and a p-orbital on each ring atom to be aromatic. In each case there are two double bonds which provide four pi-electrons and four p-orbitals. The final p-orbital and two pi-electrons are provided by a nitrogen in each case. Visualize the nitrogen not involved in a double bond as housing its non-bonding electron pair in a p-orbital that overlaps with the others in the ring. Because of this overlap, this non-bonding electron pair is not as available to acids and the basicity is

drastically diminished. If an acid base reaction occurred, this electron pair would be used and the aromaticity destroyed, another factor that causes diminished basicity. In imidazole, there is a second nitrogen, the one involved in the double bond. Its non-bonding electron pair is not part of the pi-system as the double bond provides the p-orbital at that location and there already exists the aromatic sextet of electrons. Consequently, this electron-pair is much more available than that of the other nitrogen or the pair on the nitrogen in pyrrole and imidazole is four million times more basic than pyrrole.

10.47 Aromaticity of Heterocyclic Compounds: Section 10.8A

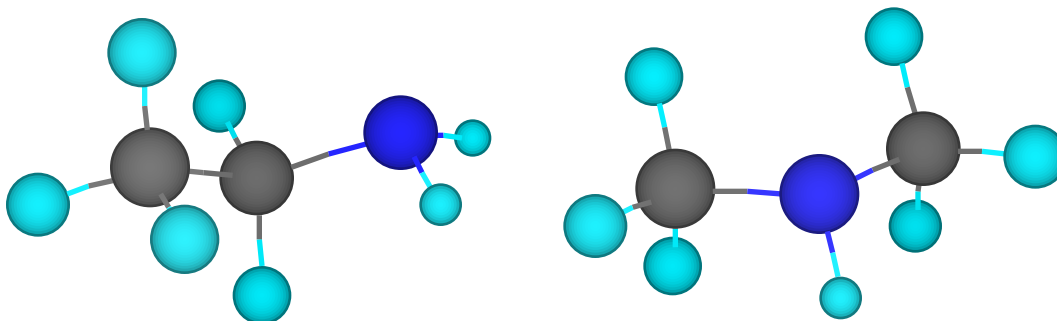
Both compounds are cyclic, planar, have a p-orbital on each ring atom, and have six pi-electrons. Four of the electrons and four of the p-orbitals come from the double bonds. The last p-orbital and the final two pi-electrons are a result of one of the non-bonding electron pairs on oxygen and sulfur existing in a p-orbital that overlaps with the others and completes the aromatic system.

10.48 Dyes: Connections 10.5

Chromophore and auxochrome groups are listed early in the Connections essay. Look for these along with extensive conjugation in the structures of dyes presented.

ACTIVITIES WITH MOLECULAR MODELS

1. Make models of a primary and a secondary amine of C_2H_7N .



2. Make models of the four isomers of C_3H_9N . What is the hybridization of each carbon and the nitrogen? How many non-bonding electron pairs are on the nitrogen? Identify primary, secondary and tertiary amines.

