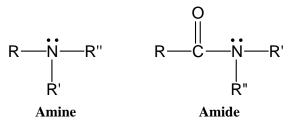


Nitrogen-Containing Functional Groups

• Nitrogen is in Group V of the periodic table, and in most of its compounds, it has three single bonds and one lone pair:



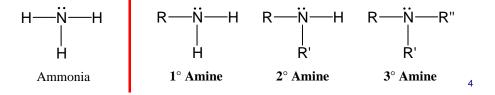
• In this chapter, we will take a look at two functional groups which contain nitrogen atoms connected to carbons: the **amines** and the **amides**.

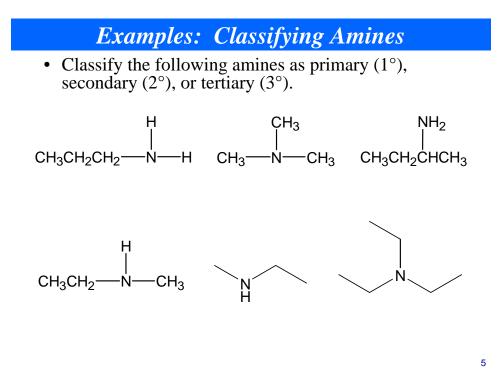


Classification and Nomenclature of Amines

Amines

- Amines and amides are abundant in nature. They are a major component of proteins and enzymes, nucleic acids, alkaloid drugs, etc. (*Alkaloids* are N-containing, weakly basic organic compounds; thousands of these substances are known.)
- Amines are organic derivatives of ammonia, NH₃, in which one or more of the three H's is replaced by a carbon group.
- Amines are classified as primary (1°), secondary (2°), or tertiary (3°), depending on how many carbon groups are connected to the nitrogen atom.



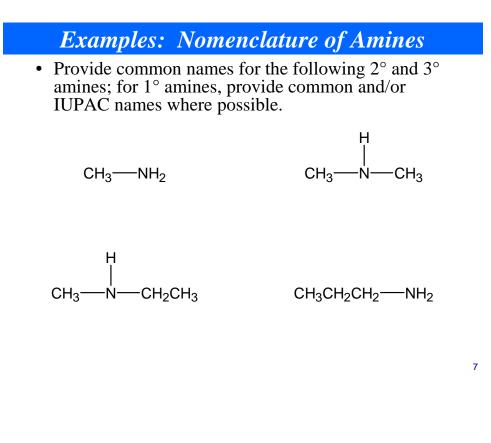


Nomenclature of Amines

- Simple 1°, 2°, and 3° amines: common (trivial) names are obtained by alphabetically arranging the names of the alkyl substituents on the nitrogen and adding the suffix -amine (e.g., ethylmethylamine).
- Amines in the IUPAC system: the "e" ending of the alkane name for the longest chain is replaced with –amine. The amine group is located by the position number. Groups that are attached to the nitrogen atom are located using "N" as the position number. More complex primary amines are named with —NH₂ as the *amino* substituent.
- Aromatic amines: named as derivatives of the parent compound aniline. Substituents attached to the nitrogen are indicated by using "N-" as the location number.

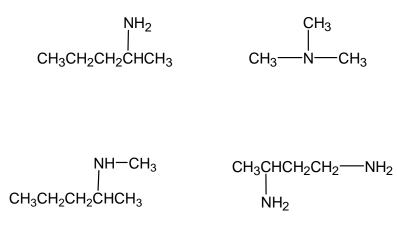
NH₂

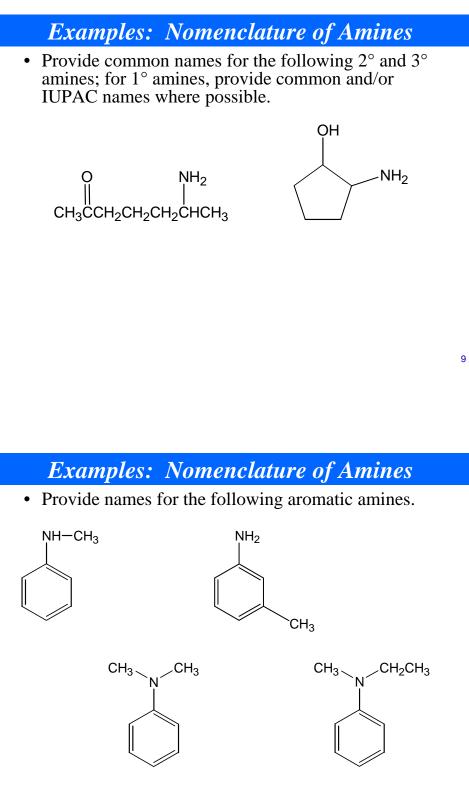
aniline 6



Examples: Nomenclature of Amines

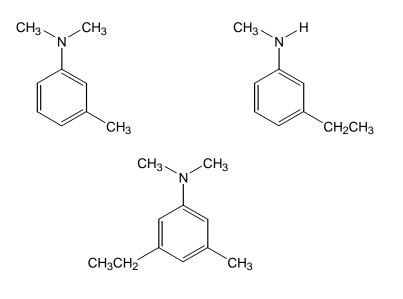
• Provide common names for the following 2° and 3° amines; for 1° amines, provide common and/or IUPAC names where possible.





Examples: Nomenclature of Amines

• Provide names for the following aromatic amines.



Examples: Nomenclature of Amines

• Draw structural formulas for the following molecules: - ethylisopropylamine

- tert-butylamine

- 2-pentanamine

Examples: Nomenclature of Amines

• Draw structural formulas for the following molecules: - N-methyl-2-propanamine

- 1,6-diaminohexane

- 3-amino-1-propanol

Examples: Nomenclature of Amines

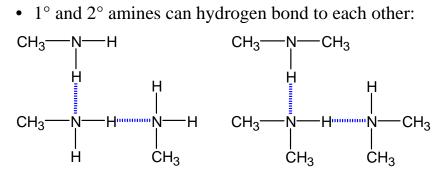
• Draw structural formulas for the following molecules: - N-methyl-2-chloroaniline

– N,3-diethylaniline

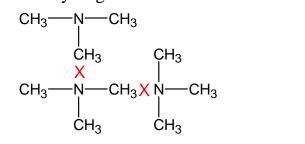
- N,N-dimethylaniline

Physical Properties of Amines

Physical Properties of Amines: H-Bonding



• 3° amines cannot hydrogen bond to each other:



Physical Properties of Amines: Boiling Points

- Nitrogen is less electronegative than oxygen, so the N—H bond is not quite as polar as the O—H bond.
 - Hydrogen bonds from N—H's are not as strong as those resulting from O—H's.
 - Hydrogen bonding between 1° and 2° amines is not as strong as those found in alcohols or carboxylic acids.
- 1° and 2° amines have lower boiling points than alcohols of similar molecular weight.
- 3° amines, since they do not hydrogen bond to each other, have boiling points similar to hydrocarbons of the same molecular weight.

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Physical Properties of Amines: Boiling Points

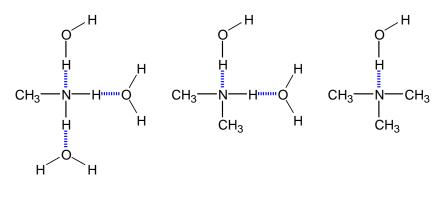
Boiling Point:

Carboxylic acid Alcohols 1°/2° Amines 3° Amines/Alkanes

Name	Molecular weight	Boiling point
Acetic acid	60.0 g/mol	118°C
1-propanol	60.1 g/mol	97°C
propyl amine	59.1 g/mol	48°C
ethylmethylamine	59.1 g/mol	36°C
trimethylamine	59.1 g/mol	2.9°C
butane	58.1 g/mol	-0.5°C

Physical Properties of Amines: Water Solubility

- 1°, 2°, and 3° amines can all form hydrogen bonds with water.
- Low-molecular weight amines are generally watersoluble.



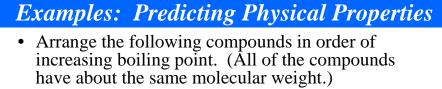
19

urine and bad breath

Physical Properties of Amines: Odor

- Low molecular-weight amines tend to have sharp, penetrating odors similar to ammonia
- Higher molecular-weight amines often smell like rotting fish, and are often found in decaying animal tissues.

CH ₃	$CH_2CH_2CH_2CH_2$	$CH_2CH_2CH_2CH_2CH_2$
ĊH ₃	NH ₂	NH ₂
Trimethylamine	1,4-Diaminobutane	1,5-Diaminopentane
Responsible for the	(Putrescine)	(Cadaverine)
odor of rotting fish	A poisonous oil present in rotting flesh; produced during the decomposition of the arrive acid arrining class	A poisonous, viscous liquid present in rotting flesh; produced during the
	the amino acid arginine; also partially responsible for the odor of urine and bad breath	decomposition of the amino acid lysine; also partially responsible for the odor of 20
		$\frac{20}{2}$



propanoic acid, diethylamine, 1-butanol, ethyldimethylamine

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Examples: Predicting Physical Properties

• Which member of each of the following pairs of compounds would you expect to have a higher boiling point?

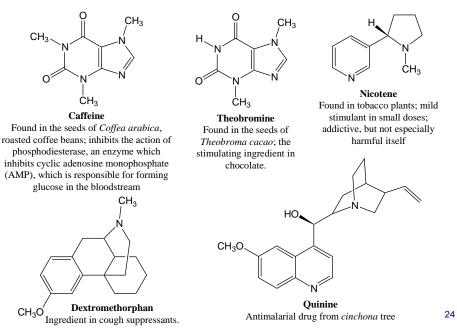
-2-aminopropane or 2-aminohexane

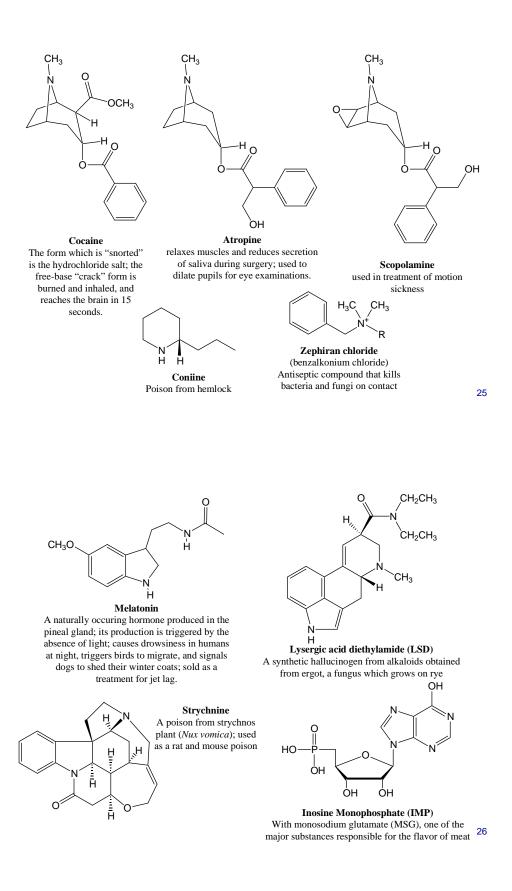
- triethylamine or 1-aminohexane

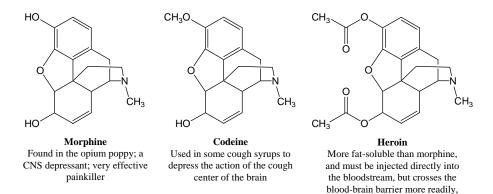
- propanoic acid or diethylamine
- -1-pentanol or 1-aminopentane

Some Important Alkaloids

Important Alkaloids



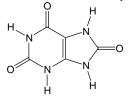




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Nitrogen Wastes

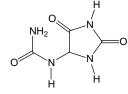
The disposal of waste nitrogen from the body is a problem which different species of animals have solved in different ways:



Uric acid

Birds, reptiles and insects excrete nigrogen wastes in the form of uric acid. Uric acid can be eliminated directly in the solid form, without being dissolved in water. It is produced in the body from foods and beverages rich in purines, such as claret and port. Lactic acid inhibits the removal of salts of uric acid in the urine; these salts instead deposit in the joints, causing gout. Dalmations have been bred to have black spots

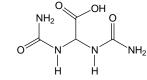
with no white hairs in them on their coats; however, the gene which determines the presence of white hairs is linked to the gene which codes the enzyme which breaks down uric acid into allantoin. Dalmations thus excrete uric acid instead of allantoin, and are very susceptible to gout.



Allantoin Most mammals contain enzymes which metabolyze uric acid into allantoin.



Urea is the major organic component of urine; about 25 g are excreted every day by humans. Cartilaginous fish and amphibians also excrete urea.



causing it to be more potent than morphine

Allantoic acid Marine vertebrates further metabolyze allantoin into allantoic acid.

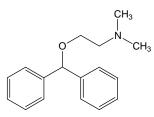
NH₄⁺ X[−] Marine invertebrates excrete ammonium salts.

Antihistamines

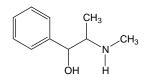


Histamine

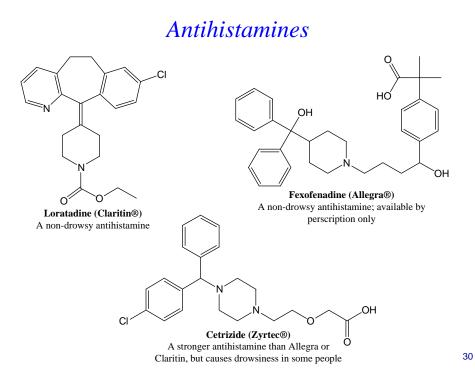
People who are allergic to pollen produce histamine, which causes blood vessels to dilate and leak, releasing fluid into surrounding tissues, causing watery eyes, sniffles, congestion, and other symptoms of hay fever (*allergic rhinitis*); also causes the symptoms of the common cold and swelling after insect bites.



Diphenylhydramine an *antihistamine*; active ingredient in Benadryl; sometimes used in sleeping pills



Ephedrine / Pseudoephedrine found in the Chinese ma-huang plant; a decongestant used in many cold remedies



Reactions of Amines

Bases

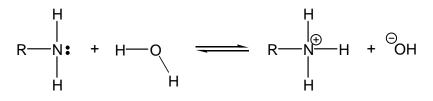
• A base takes a proton (H⁺) from another species. A base produces hydroxide ions, OH⁻, when dissolved in water:

 $\mathrm{B} \ + \ \mathrm{H_2O} \ \rightarrow \ \mathrm{BH^+} \ + \ \mathrm{OH^-}$

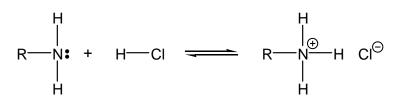
- A **strong base** is one that *completely dissociates* in water (i.e., every molecule of the acid splits apart).
- A weak base is one in which only a small percentage of the molecules are dissociated at any one time.
- Acidic solution: pH < 7.00 ([H₃O⁺] > [OH⁻])
- **Basic** solution: pH > 7.00 ([H₃O⁺] < [OH⁻])
- Neutral solution: pH = 7.00 ([H₃O⁺] = [OH⁻]) ₃₂

Chemical Properties of Amines: Basicity

• Amines are weak organic **bases**. They react with water to produce *alkylammonium ions* and hydroxide anions:

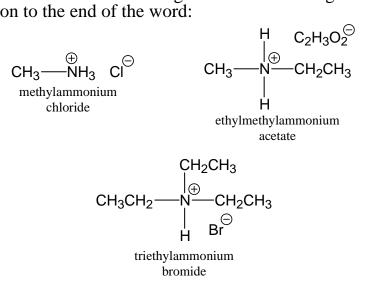


• and with acids to produce *alkylammonium salts*:



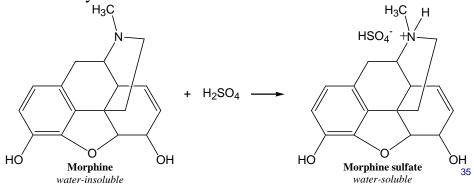
Alkylammonium Salts

• Salts of amines are named by changing "amine" to "ammonium" and adding the name of the negative ion to the end of the word:



Alkylammonium Salts

- Salts of amines are generally white crystalline solids with high melting points.
- The ionic charges makes these salts more soluble in water than the neutral amines. Many aminecontaining drugs are administered in the form of alkylammonium salts to increase their solubility in bodily fluids.



Chemical Properties of Amines: Basicity

• Ammonium salts may be converted back into neutral amines by a strong base:

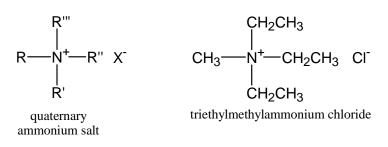
 $R-NH_3^+CI^- + NaOH \longrightarrow R-NH_2 + H_2O + NaCI$

• Thus, by adjusting the pH of the solution, it is possible to influence whether an amine is present in the neutral form or as its ammonium cation form:

$$R \xrightarrow{\text{acid}} R \xrightarrow{\text{(low pH)}} R \xrightarrow{\text{NH}_2} + H_2O \xrightarrow[high pH)} R \xrightarrow{\text{NH}_3} R \xrightarrow{\text{NH}_3} + OH$$

Quaternary Ammonium Salts

• In addition to salts of 1°, 2°, and 3° amines, it is possible to have amine cations which contain four alkyl groups attached to a nitrogen atom, which will *always* carry a positive charge, regardless of the pH of the surrounding solution. These are known as **quaternary ammonium salts**.



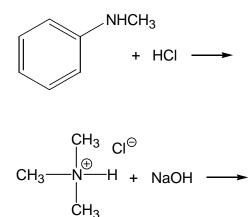
• These salts are present in many antiseptics and antibacterial agents.

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Examples: Basicity of Amines

• Complete the following reactions:

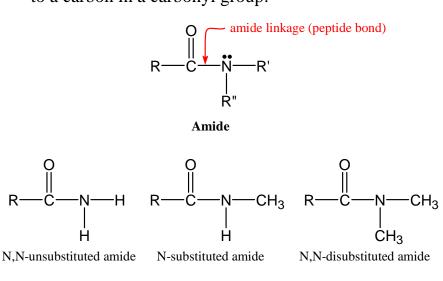
 $CH_3NH_2 + HCI \longrightarrow$



Amides

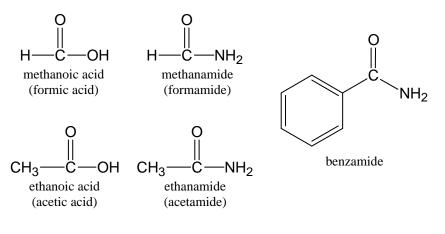
Amides

• **Amides** contain a nitrogen which is directly attached to a carbon in a carbonyl group:



Nomenclature of Amides

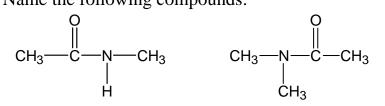
• Amides are named by changing the *-oic acid* ending of the corresponding carboxylic acid to **-amide**. If alkyl groups are attached to the nitrogen, they are named as N-alkyl substituents.

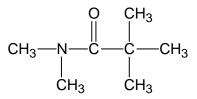


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Examples: Nomenclature of Amides

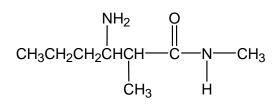
• Name the following compounds:





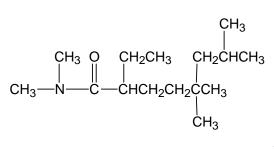
Examples: Nomenclature of Amides

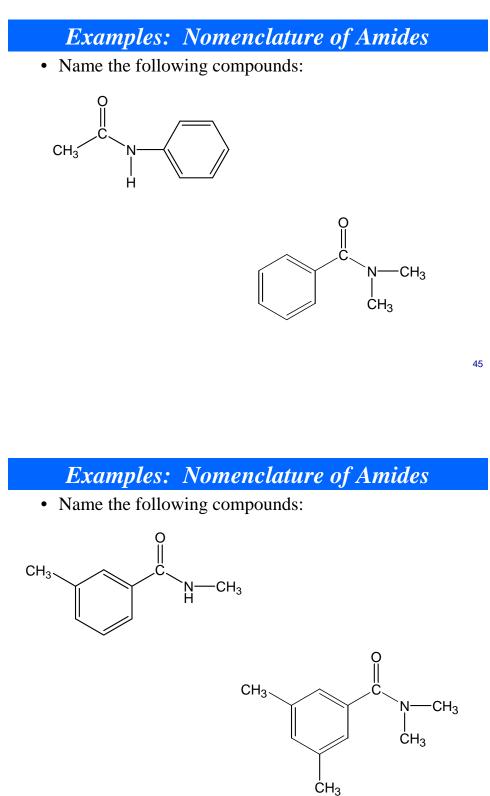
• Name the following compounds:



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 Examples: Nomenclature of Amides
Name the following compounds: CH₂CH₂ O CH₃





Examples: Nomenclature of Amides

• Draw structural formulas for the following molecules: - 2-methylpropanamide

- N,2,4-trimethylpentanamide

- N-ethyl-N-methylacetamide

Examples: Nomenclature of Amides

• Draw structural formulas for the following molecules: - N,2-diethylbenzamide

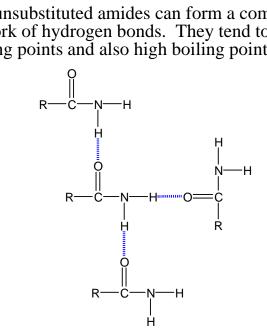
- N,N,2,3,4-pentamethylbenzamide

 $-N, N, 4, 4-tetramethyl but anamide \quad \mbox{(what's wrong with this name?)}$

Physical Properties of Amides

Physical Properties of Amides

• N,N-unsubstituted amides can form a complex network of hydrogen bonds. They tend to have high melting points and also high boiling points.



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Physical Properties of Amides

- N-substituted amides often have lower melting points and boiling points than N,N-unsubstituted amides because fewer hydrogen bonds can form.
- N,N-disubstituted amides cannot form hydrogen bonds, and have even lower melting points and boiling points.
- All amides can hydrogen bond with water, so low-molecular weight amides are water-soluble.

Boiling Point:

N,N-unsubstituted amides N-substituted amides N,N-disubstituted amides

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Examples: Predicting Physical Properties

• Arrange the following compounds in order of increasing boiling point. (All of the compounds have about the same molecular weight.)

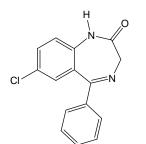
N-ethylethanamide

butanamide

N,N-dimethylethanamide

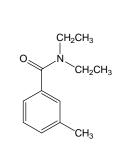
Important Amides

Important Amides

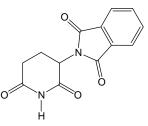


Diazepam (Valium) A benzodiazepene

tranquilizer; acts by enhancing the inhibitory neurotransmitter GABA; since it binds to the same protein as ethanol, combinations of valium and ethanol can be deadly

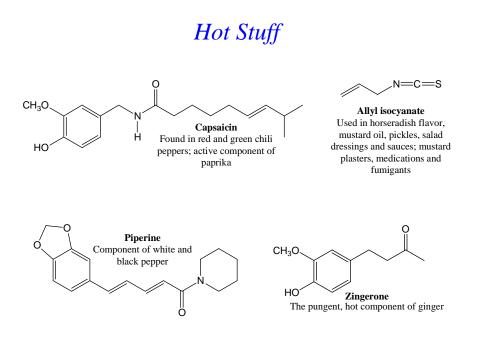


N,*N*-Diethyl-*m*-toluamide Active ingredient in OFF



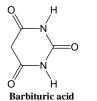
Thalidomide

Until 1956, a very popular, safe sedative; the largest market was for pregnant women who were experiencing morning sickness. However, it caused massive birth defects in women who used it in the early states of pregnancy, and was banned in Europe; it was never authorized for sale in the U.S.

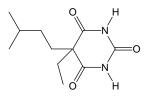


55

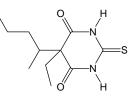
Barbiturates



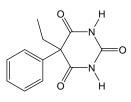
First synthesized by Adolf von Baeyer in 1864; barbiturates are soporifics, and are used as tranquilizers and anesthetics; many are also addictive, and overdoses can be fatal. (Other barbiturates include Seconal, Veronal, Phenobarbitol, Thiopental, Amobarbitol, etc.)



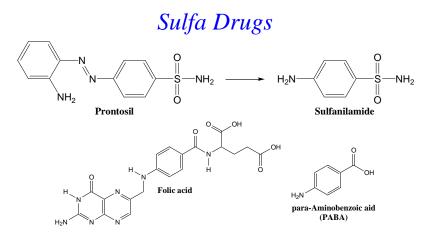
Amobarbital (Amytal) Used in the treatment of insomnia



Thiopental (Pentothal) An intravenous anesthetic



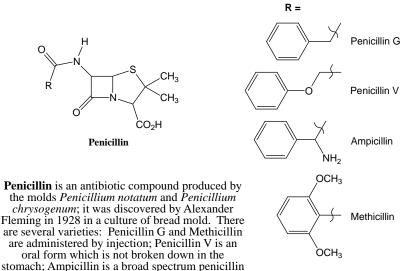
Phenobarbitol Anti-seizure medication, sedative



Sulfanilamide, the first antibiotic, was discovered by Gerhard Damagk (Nobel Prize, 1939), who observed the antibacterial action of the red dye Protonsil; further researched showed that it was the metabolic byproduct, sulfanilamide, which was the active form. It prevents bacteria from synthesizing folic acid, which they need in order to grow. Bacterial enzymes synthesize folic acid using *para*-aminobenzoic acid (PABA); sulfanilamide fits into the enzyme more tightly, blocking it from taking up PABA, and thus blocking folic acid synthesis. The bacterium cannot grow, and eventually dies. Humans obtain folic acid from their diet (an essential vitamin), so sulfa drugs do not harm people in this way (although they can cause allergic reactions).

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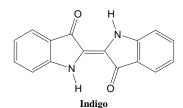
Penicillin

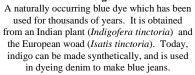


which can be administered by injection or orally

Molecules To Dye For

- **Dyes** are compounds that can be used to color other materials, such as clothing, paper, hair, etc.
- Many organic dyes contain a long series of double bonds that are close together. If the chain of double bonds is long enough, these molecules can absorb low-energy light in the visible region of the electromagnetic spectrum, resulting in colors that are visible to the human eye.





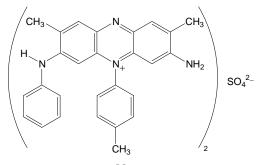


6,6'-dibromoindigo

Tyrian purple, or "royal purple," is a purple dye originally obtained from a species of mollusk (*Murex*) found near the cities of Tyre and Sidon in ancient Phoenicia. It took about 9,000 mollusk shells to obtain one gram of the dye, making it very expensive. This dye was used by royalty (hence the name "royal purple") and the Roman aristocracy.

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Molecules To Dye For

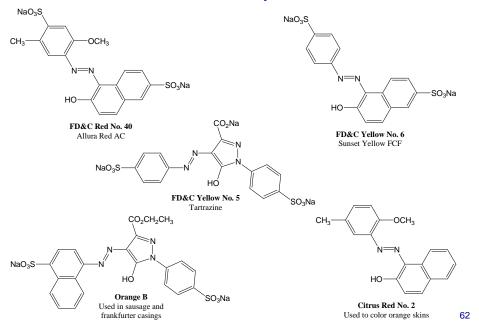


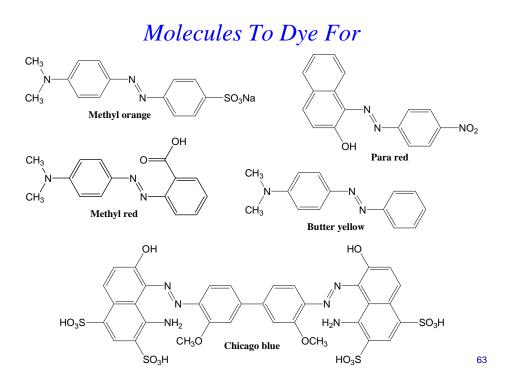
Mauve

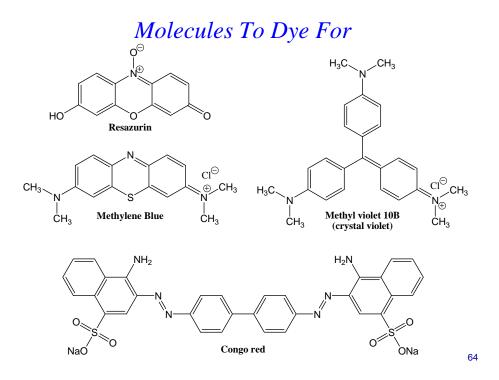
This is the first of the synthetic dyes. It was discovered by the 18-year-old English chemist William Henry Perkin in his home laboratory, while attempting to synthesize quinine (the only known treatment for malaria at that time). While cleaning up the sludge from one of his failed attempts, he noticed that the sludge was turning the water in his sink violet, and that cloth would pick up this purple color. Perkin patented his serendipitous discovery, and went into business making dyes, becoming so successful that he was able to retire at the age of 36 to focus his attention on chemical research.

FD&C Dyes These color additives are approved by the Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act (FD&C, 1938, amended 1997) for use in foods. NaO₃S SO3 SO₃Na ά FD&C Blue No. 2 NaO_3S SO₃Na Indigo Carmine, Indigotine FD&C Blue No. 1 Brilliant Blue FCF OH NaO 0 SO3 .CO₂Na NaO₃S .SO₃Na FD&C Red No. 3 Erythrosine FD&C Green No. 3 Fast Green FCF 61

FD&C Dyes





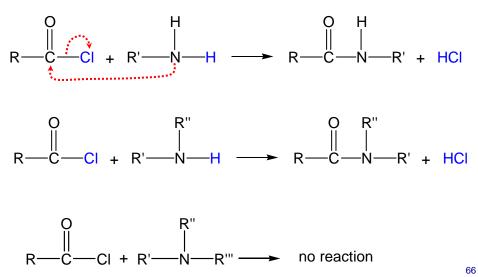


Reactions of Amides

Amide Formation

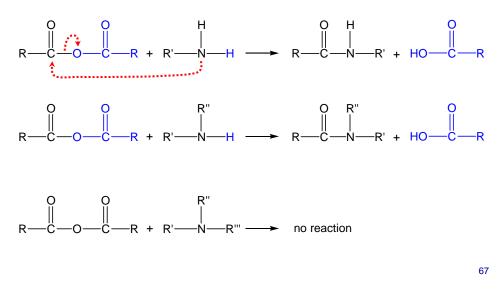
65

• Amides are formed when acid chlorides react with 1° or 2° amines; 3° amines cannot form amides:



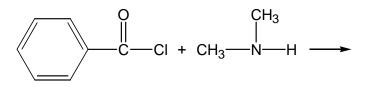
Amide Formation

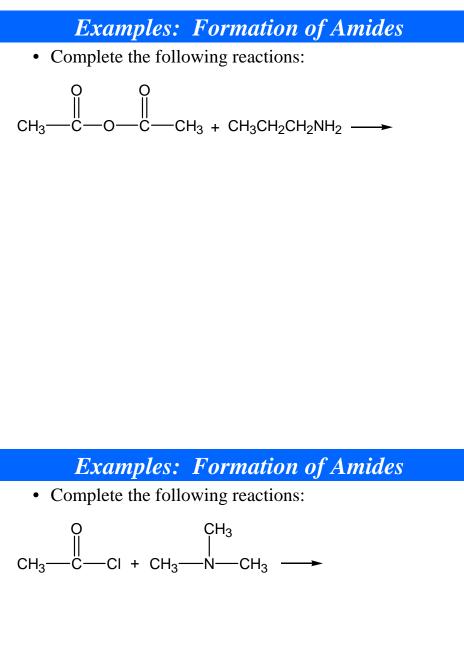
• Amides are also formed when acid anhydrides react with 1° or 2° amines.



Examples: Formation of Amides

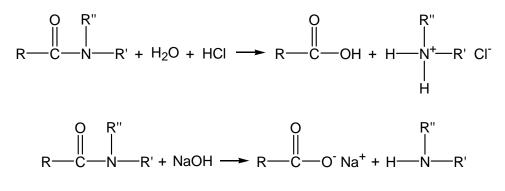
• Complete the following reactions:





Chemical Properties of Amides

- Unlike amines, amides are not basic.
- Amide hydrolysis can take place under acidic or basic conditions:



7	4
1	

Examples: Reactions of Amines and Amides

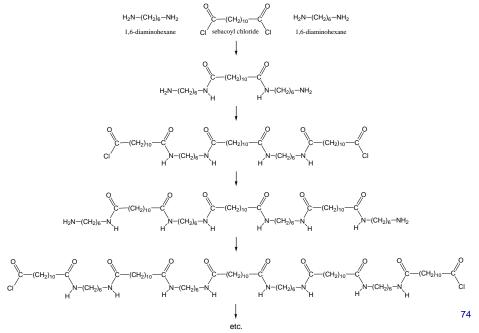
• Complete the following reactions:

$$\begin{array}{c} O \quad H \\ \parallel \quad \mid \\ CH_3 \longrightarrow C \longrightarrow N \longrightarrow CH_3 + H_2O + HCI \longrightarrow \end{array}$$

$$\begin{array}{ccc} O & H \\ \parallel & \parallel \\ CH_3 \longrightarrow C \longrightarrow N \longrightarrow CH_3 + NaOH \longrightarrow \end{array}$$

Condensation Polymers: Polyamides

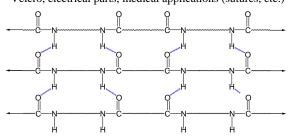
Condensation Polymers: Polyamides



Condensation Polymers: Polyamides \cap -(CH₂)₁₀-CI -(CH₂)₆--H ΝH--HN Nylon-6,12

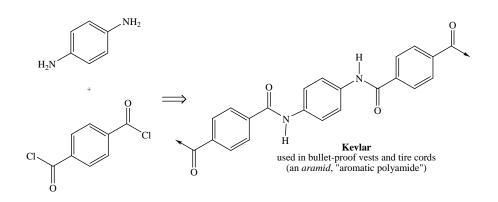
a polyamide

Discovered by Wallace Carrothers at DuPont in 1934; polymers average about 10,000 g/mol; 3 billion pound of Nylon made per year; 60% used for nylon fiber in home furnishings (carpet); also used in textile fibers, tire cord, rope, parachutes, paint brushes, Velcro, electrical parts, medical applications (sutures, etc.)

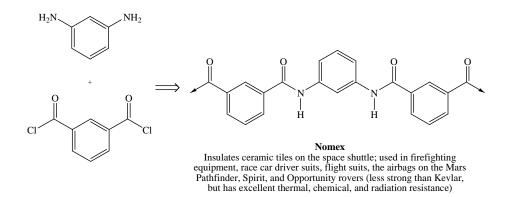


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Polyamides

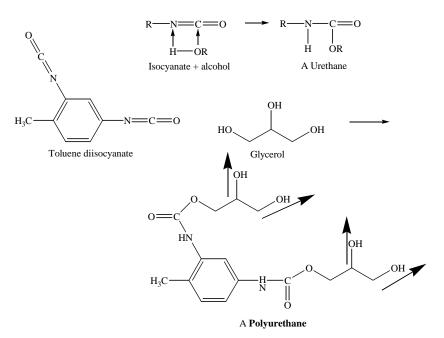


Polyamides



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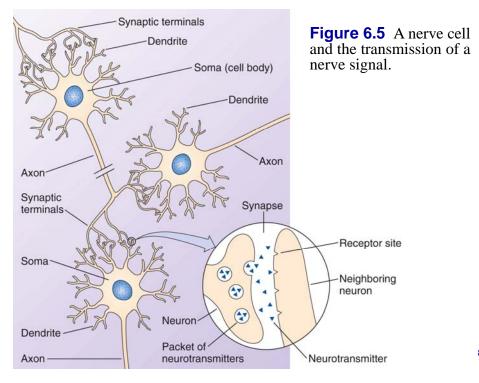
Polyurethanes

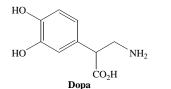


Neurotransmitters

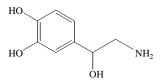
Neurotransmitters

- **Neurotransmitters** are small molecules that carry nerve impulses from one neuron to the next.
- Neurons consist of the main cell body (the **soma**), long stemlike projections (the **axons**), and short fibers connected to the soma (the **dendrites**).
- Neurons are not connected directly to each other, but are separated by a small gap called a **synapse**.
- When an electrical current originating in a neuron reaches the **synaptic terminals** at the end of the axon, the terminals release neurotransmitter molecules into the synapse; these molecules diffuse across the synapse and bind to receptors on the dendrites of the next neuron, stimulating an electrical current, which travels along that neuron until it reaches the next synapse, and so on until the nerve impulse reaches the brain.

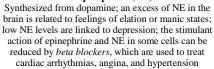


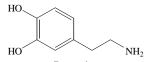


Synthesized from the amino acid tyrosine; used as a treatment for Parkinson's disease, which is caused by a breakdown of dopamine-based neurons that control the brain's motor system (dopamine cannot be administered directly because it does not cross the blood-brain barrier; however, the L-form of dopa does)



Norepinephrine (NE)





Dopamine Synthesized from dopa; used as a treatment for low blood pressure



Synthesized from the amino acid tryptophan; influences sleeping, body temperature, and sensory perception; drugs that mimic serotonin are used to treat depression, anxiety, and obsessive-compulsive disorder; serotonin blockers are used to treat migraine headaches and nausea resulting from chemotherapy 81

HO CH₃ HO ÓН Ĥ.

Epinephrine (Adrenalin) More important as a hormone than a neurotransmitter; synthesized in the adrenal glad; release of adrenalin into the bloodstream in response to pain, anger, or fear increases blood glucose levels, and provides a sudden burst of energy (fight-or-flight response); increases force of heart contractions (raising blood pressure); also a vasoconstrictor; used in local anesthetics to keep the anesthetic from being washed away

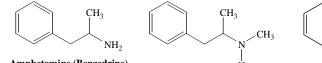
CH₃ CH₃ CH₂ Acetylcholine

 H_2N OH

Gamma-aminobutanoic acid (GABA) A inhibitory neurotransmitter

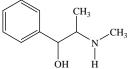
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Pheynlephrines and Amphetamines

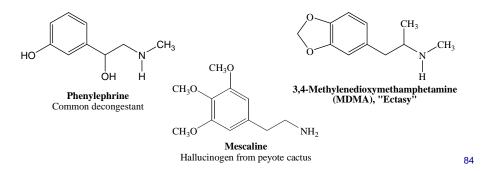


Amphetamine (Benzedrine) a powerful nervous stimulant; raises blood glucose levels, increases heart rate and blood pressure

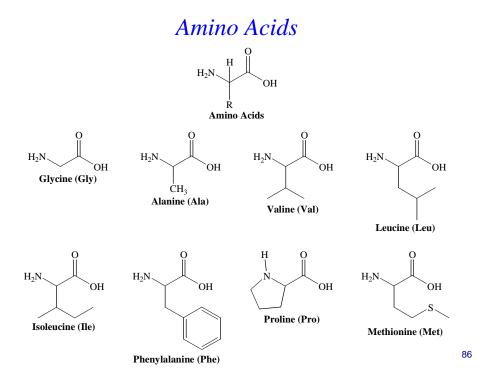
H N-Methylamphetamine (Methedrine, "speed") Also a powerful nervous stimulant

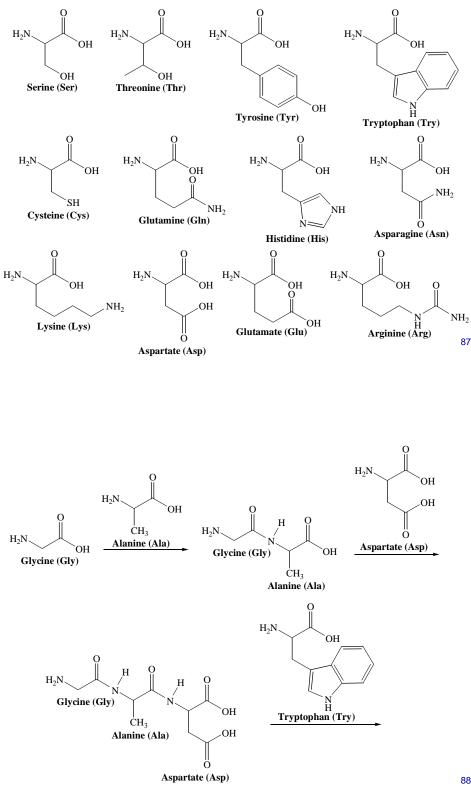


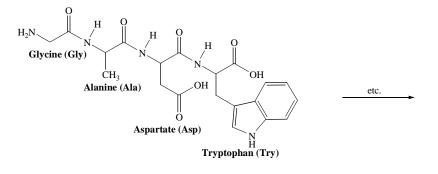
Ephedrine / Pseudoephedrine found in the Chinese ma-huang plant; a decongestant used in many cold remedies



Amino Acids and Proteins

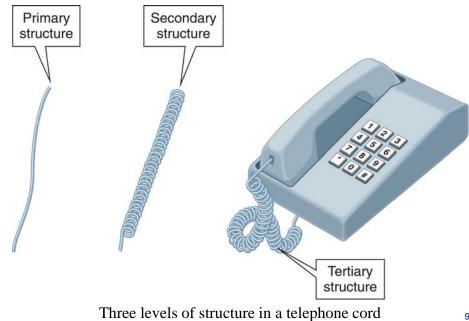




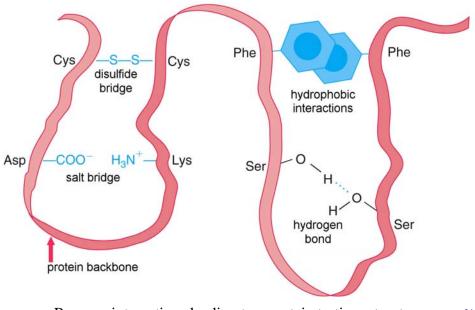


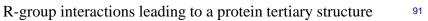
Gly—Ala—Asp -Try

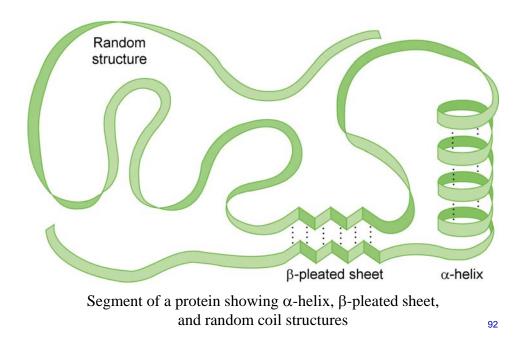
a **protein** (a polyamide) Instructions for making proteins are encoded in DNA.



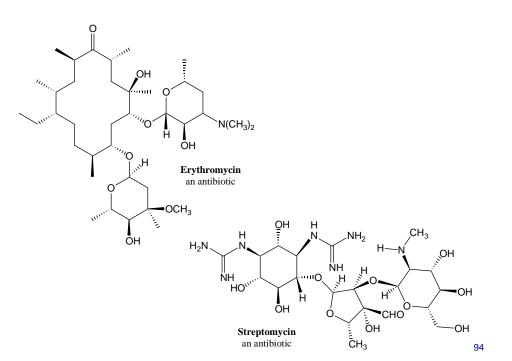
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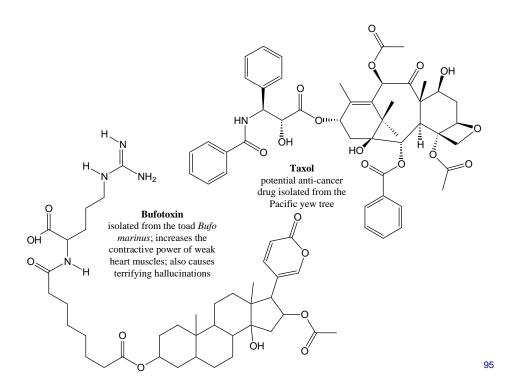


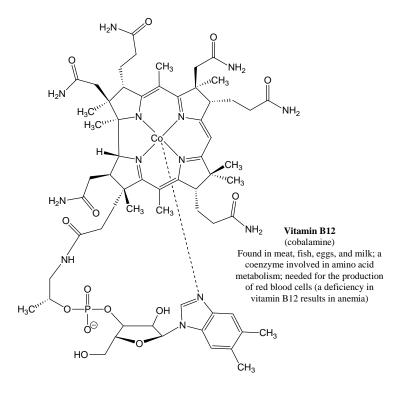


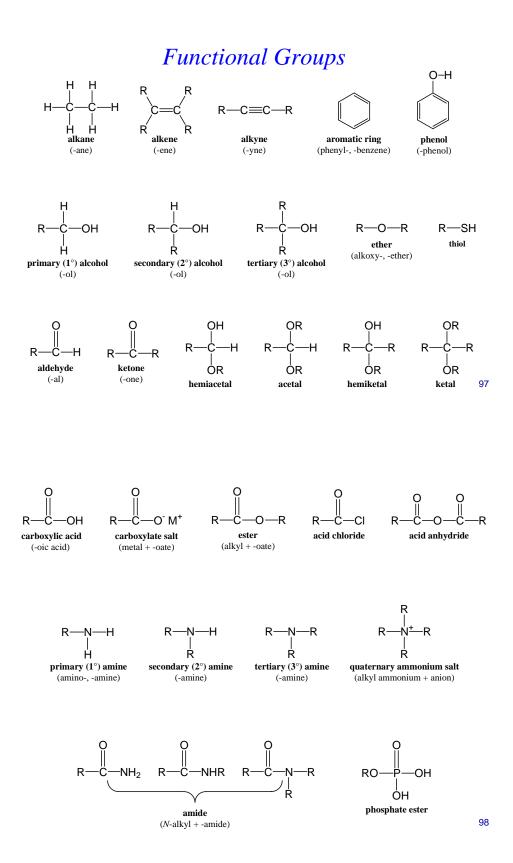


Some Hideously Complex Molecules



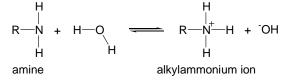




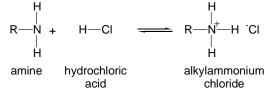


Reactions of Amines and Amides

1. Reaction of an amine with water to produce an alkylammonium ion.

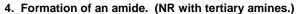


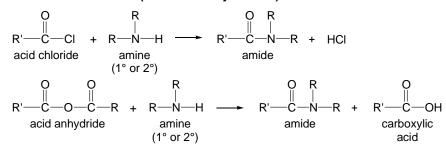
2. Reaction of an amine with acid to produce an alkylammonium salt.



3. Conversion of an alkylammonium salt back to an amine. $R-NH_3^+CI^- + NaOH \longrightarrow R-NH_2 + H_2O + NaCI$

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5. Hydrolysis of amides under acidic and basic conditions.

