

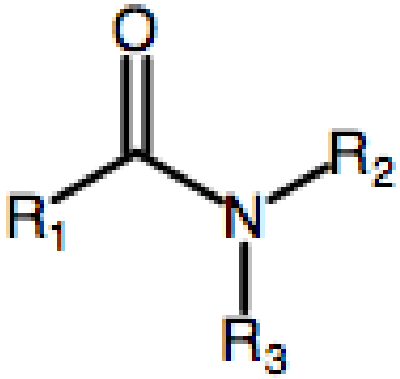
Chapter 15

Amines and Amides

Introduction

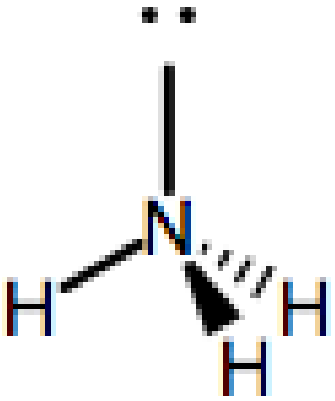
- Amines and amides contain one or more nitrogen atoms.
  - Amines have an amino group.

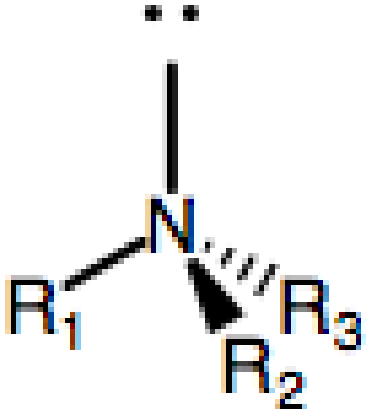
  - Amides are the product of reaction between an amine and a carboxylic acid derivative.



1. Amines: structure and properties

- **Amines** are organic derivatives of ammonia.
  - They are basic, like ammonia.
  - They are ammonia molecules with one or more of the hydrogens replaced by an organic group.

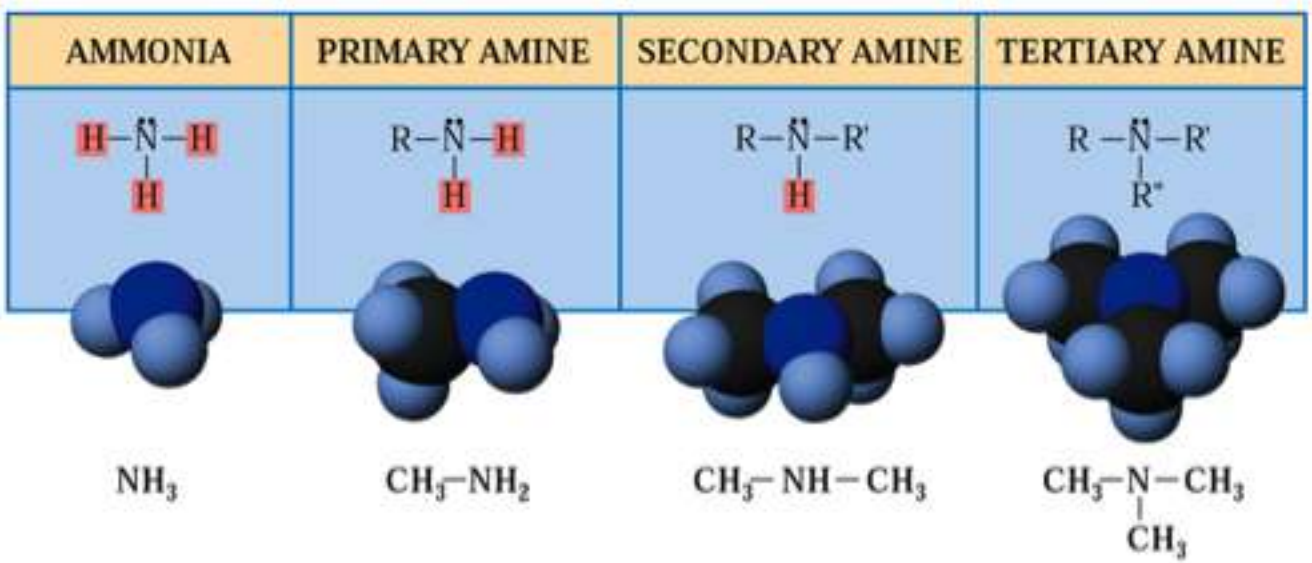




  - The amine structure is pyramidal, as is ammonia.
  - R may be a hydrogen or an aliphatic or aromatic organic group.

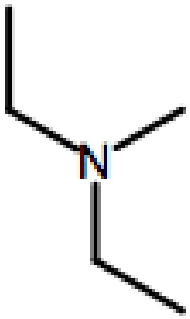
1. Amines: structure and properties

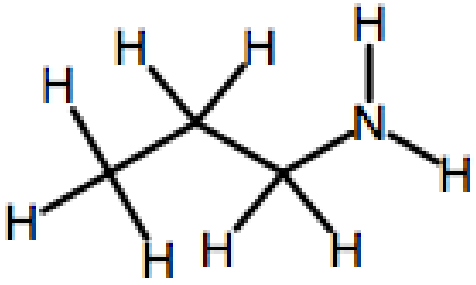
- Amines are classified by the number of carbons directly bonded to the nitrogen atom:
  - A primary amine has one: RNH_2 = 1°
  - A secondary amine has two: R_2NH = 2°
  - A tertiary amine has three: R_3N = 3°

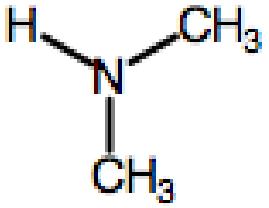


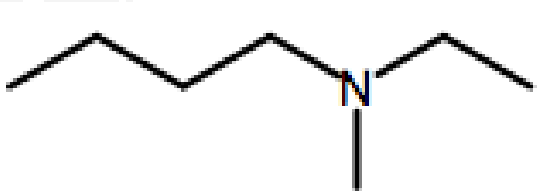
1. Amines: structure and properties

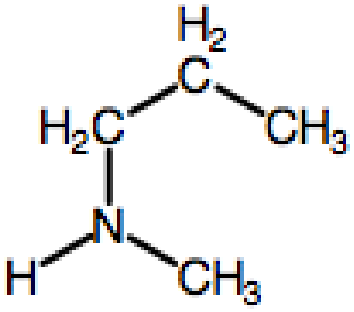
- Determine the classification of each of the following amines.











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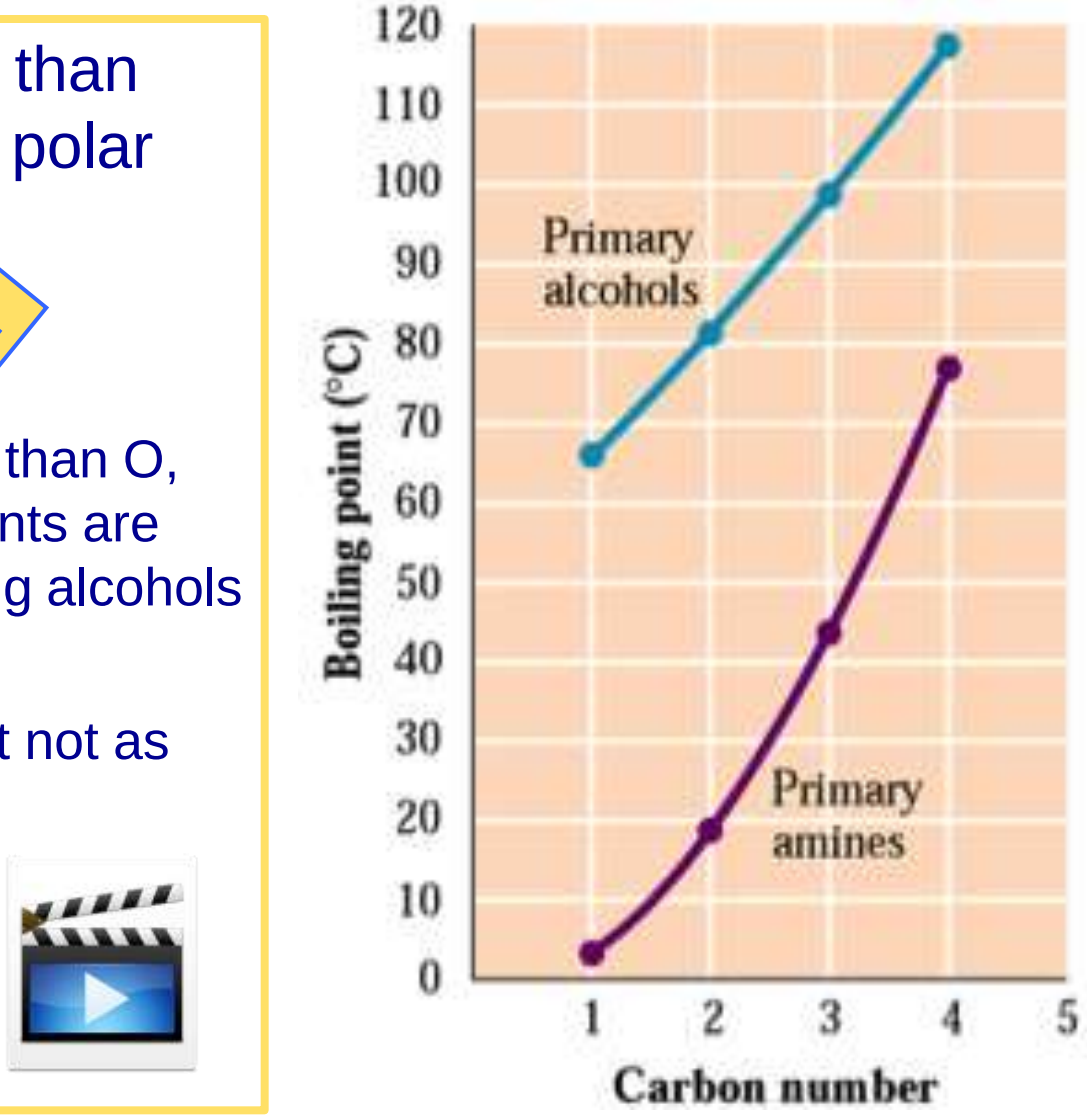
1. Amines: structure and properties

- Amines are more polar than hydrocarbons and less polar than alcohols.

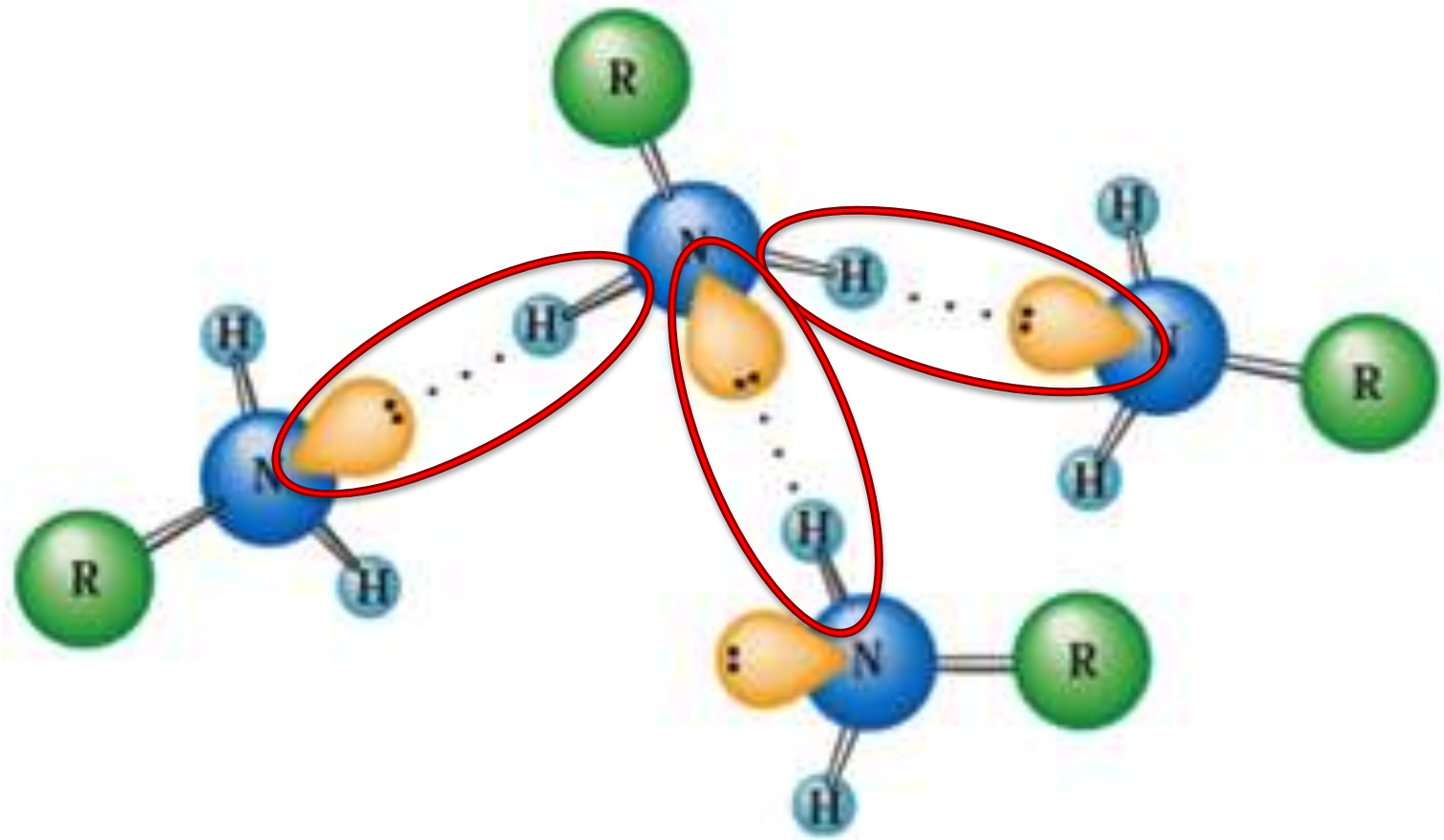
  - Because N is less polar than O, solubility and boiling points are lower than corresponding alcohols

  - H-bonds are formed, but not as strongly as with –OH.



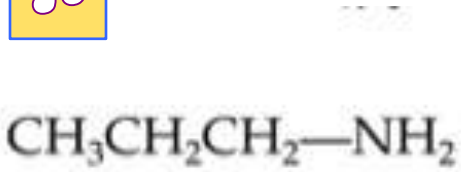
1. Amines: structure and properties

- Hydrogen bonding between primary amine molecules

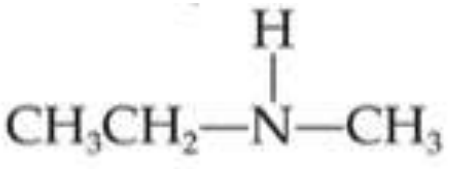


1. Amines: structure and properties

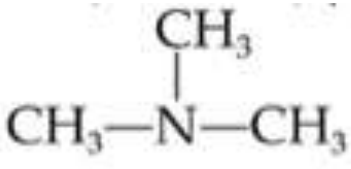
- Only primary and secondary amines can form intermolecular hydrogen bonds with themselves.



Propanamine
(propylamine)
M.W. = 59 g/mol
b.p. = 48.7° C



N-Methylethanamine
(ethylmethylamine)
M.W. = 59 g/mol
b.p. = 36.7° C



N,*N*-Dimethylmethanamine
(trimethylamine)
M.W. = 59 g/mol
b.p. = 2.9° C

- Boiling points for comparable molecular weight 1°, 2°, and 3° amines confirm this.

1. Amines: structure and properties

- Predict which compound in each pair will have the higher boiling point.
  - pentane or 1-butanamine
  - cyclohexane or 2-pentanamine
  - ethanamine or ethanol
  - butane or 1-propanamine
  - methanamine or water
  - N-methylethanamine or butane

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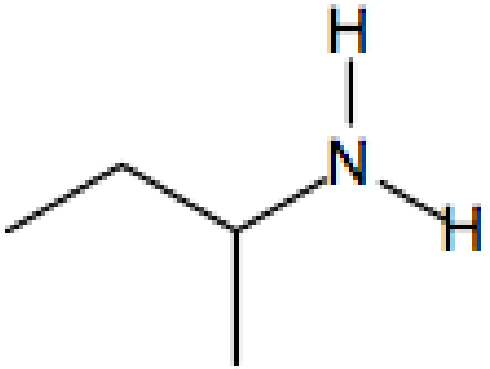
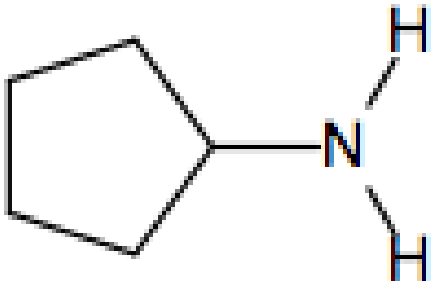
1. Amines: nomenclature

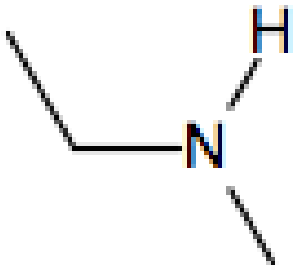
- Primary aliphatic amines
  - Find the longest continuous carbon chain containing the amine group to get the parent compound.
  - Drop the final –e of the parent name and add the suffix **-amine**.
  - Number the parent chain to give the amine carbon the lowest possible number.
  - Name and number all substituents as usual.
- Secondary and tertiary aliphatic amines
  - Add the prefix **N-alkyl** to the name of the parent for 2^o and 3^o amines.

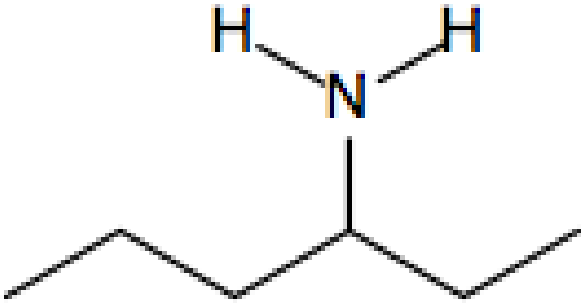
1. Amines: nomenclature

- Name each of the following amines.









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1. Amines: nomenclature

- Draw structures for the following amines.
  - 3-decanamine
  - N,N-dipropylbutanamine
  - N-ethylcyclohexanamine
  - 2-methyl-2-pentanamine
  - N-ethyl-2-heptanamine

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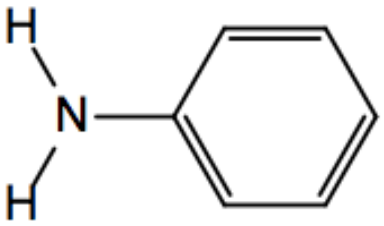
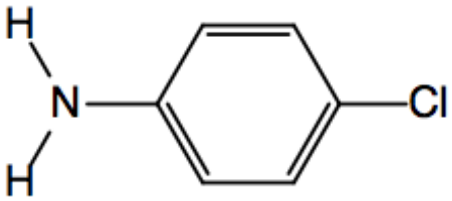
1. Amines: nomenclature

- The simplest aromatic amine is **benzenamine**, also called aniline.

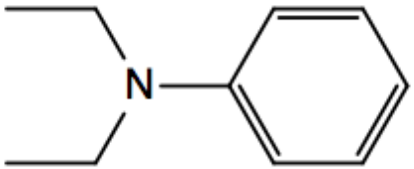


  - Substituents on the ring are numbered.



4-chlorobenzenamine

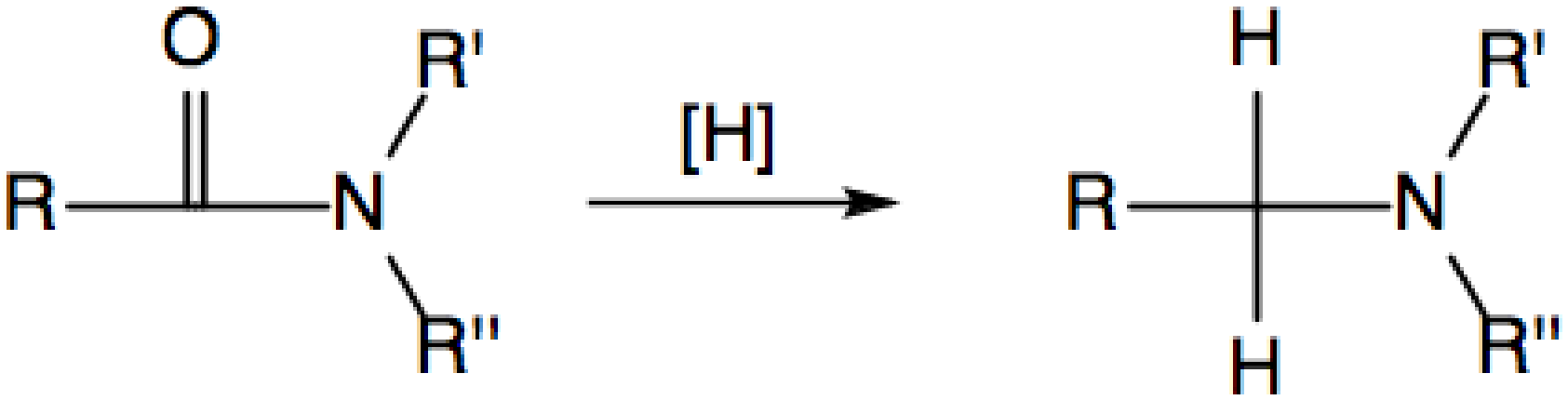
  - Groups attached to the nitrogen are labelled N-.



N,N-diethylbenzenamine

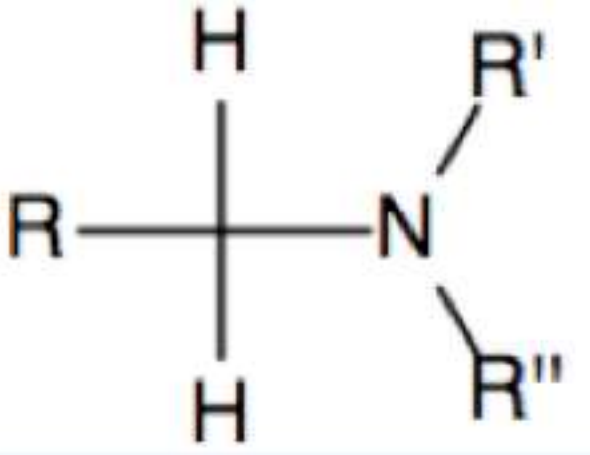
1. Amines: reactions

- Preparation of aliphatic amines is by reduction of amides.
  - Recall that reduction involves decreasing the number of bonds to oxygen and increasing the number of bonds to hydrogen.



amide ***amine***

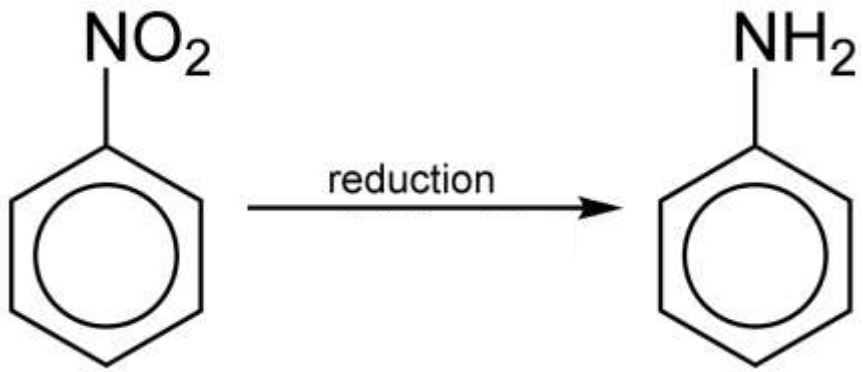
1. Amines: reactions



- If R’ = R” = H, a **primary amine** is produced.
- If R’ = H and R” = organic group, a **secondary amine** is produced.
- If R’ = R” = organic group, a **tertiary amine** is produced.

1. Amines: reactions

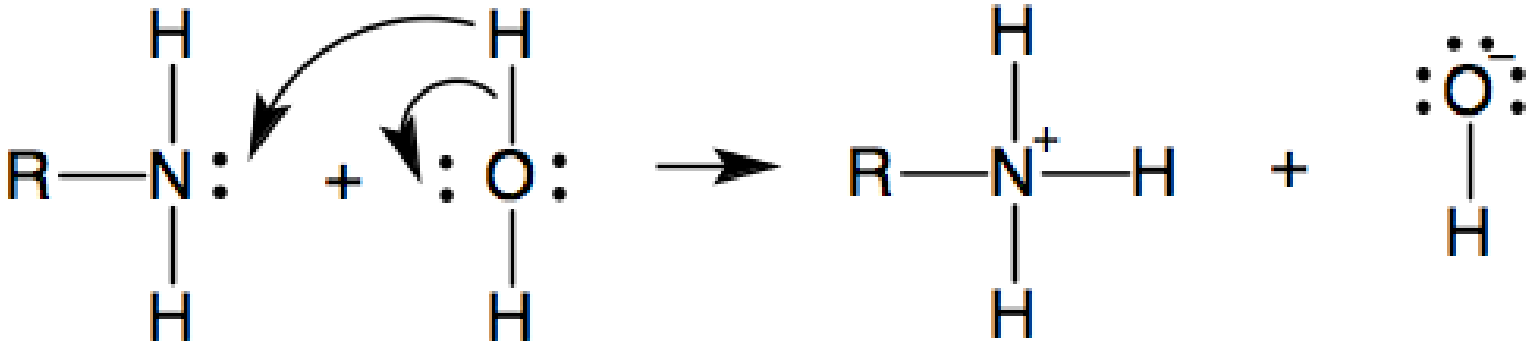
- Preparation of primary aromatic amines is by reduction of nitro compounds.



nitrobenzene ***aniline***

1. Amines: reactions

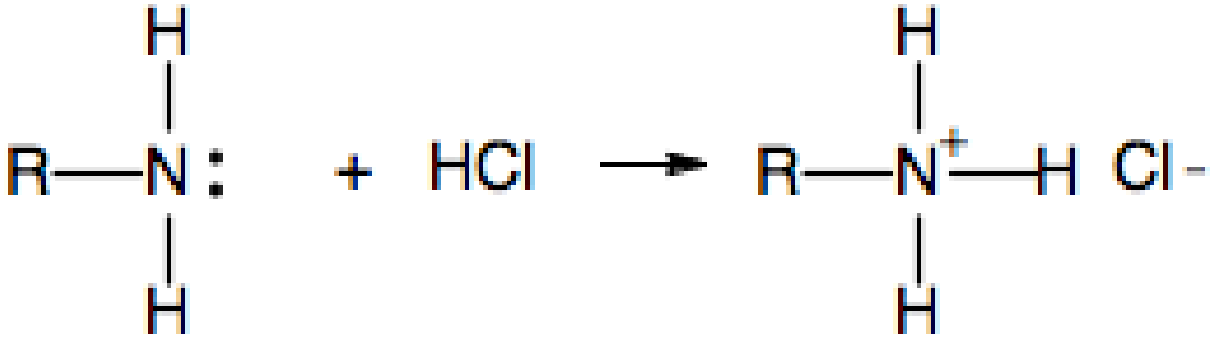
- Amines react as **weak bases** in aqueous solution.
  - "Weak" means only partially dissociated in solution.
  - "Base" means proton (H^+) acceptor.
  - Water acts as the proton donor (acid).



amine ***water*** ***alkylammonium ion*** ***hydroxide ion***

1. Amines: reactions

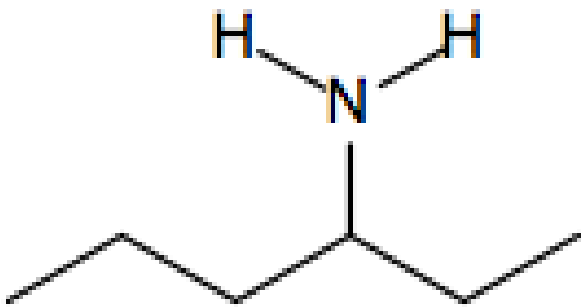
- When an amine (a base) is neutralized by an acid, an **alkylammonium salt** is produced.



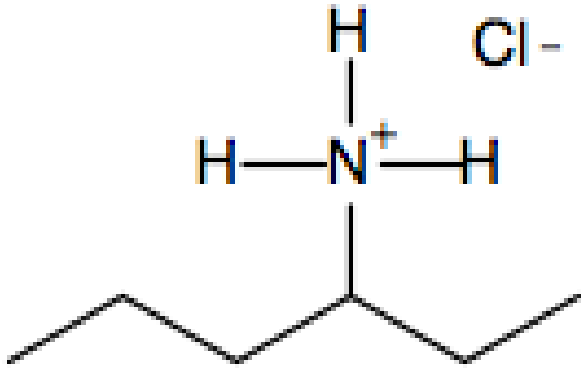
amine ***acid*** ***alkylammonium salt***

1. Amines: reactions

- Naming alkylammonium salts
  - Start with the name of the amine.
  - Replace the suffix –amine with –ammonium.
  - Add the name of the anion.



3-hexanamine



3-hexanammonium chloride

1. Amines: reactions

- What are the products of the following reactions?
  - $CH_3CH_2NHCH_3 + H_2O \rightarrow$
  - CH_3

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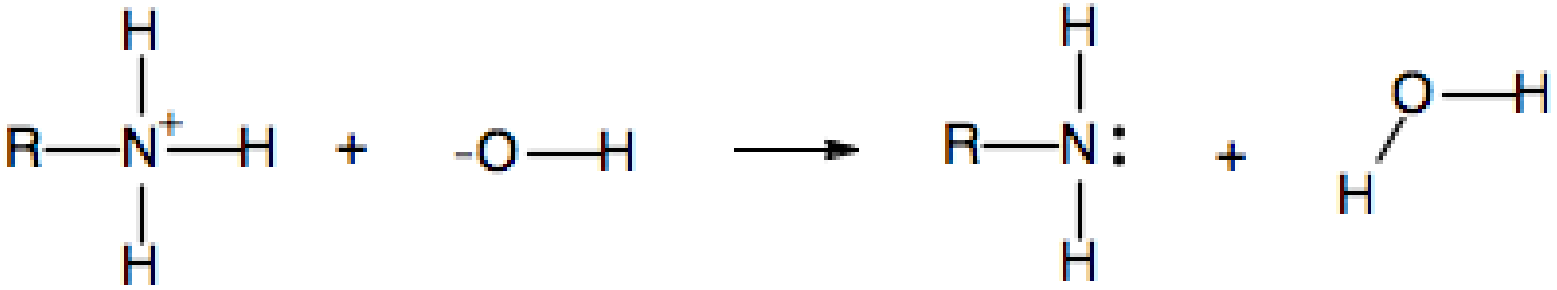
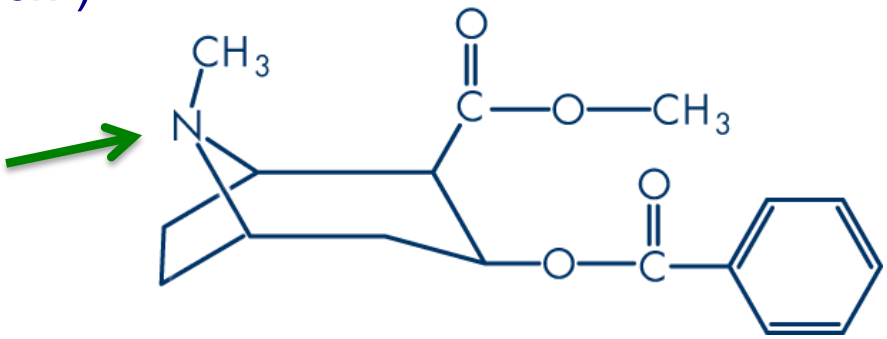
1. Amines: reactions

- An alkylammonium salt is the conjugate acid of the corresponding amine. Therefore, alkylammonium salts will react with hydroxide ions to produce the amine and water.

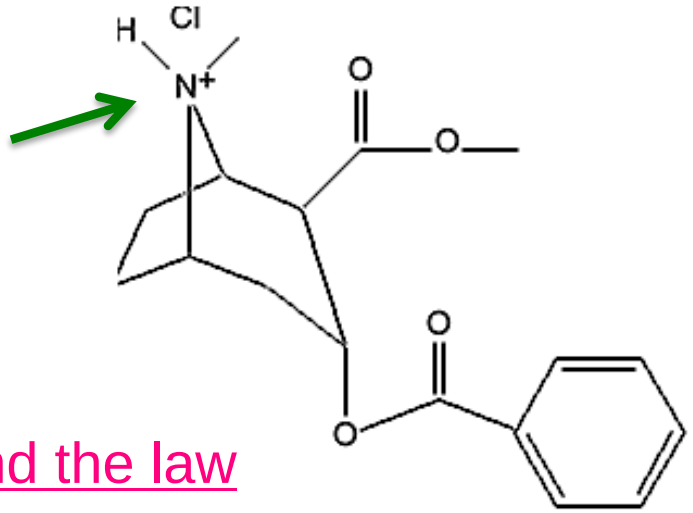


1. Amines: reactions

- Cocaine
  - Non-water-soluble amine (“crack”)



  - Water-soluble ammonium salt

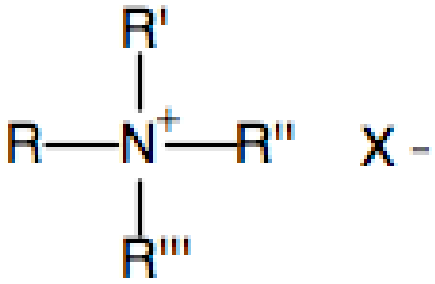


- Crack cocaine, powder cocaine, and the law
- Crack cocaine sentencing reform: the battle continues

1. Amines: quaternary ammonium salts

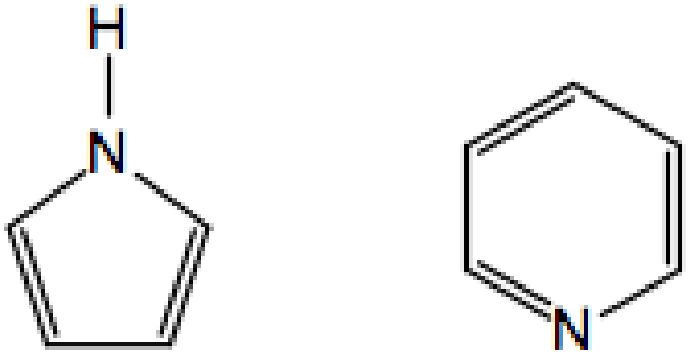
- Alkylammonium salts can be prepared from 1°, 2°, or 3° amines.
  - The nitrogen atom is bonded to three, two, or one hydrogen(s), respectively.

- In quaternary ammonium salts, the nitrogen is bonded to four organic groups.



2. *Heterocyclic amines*

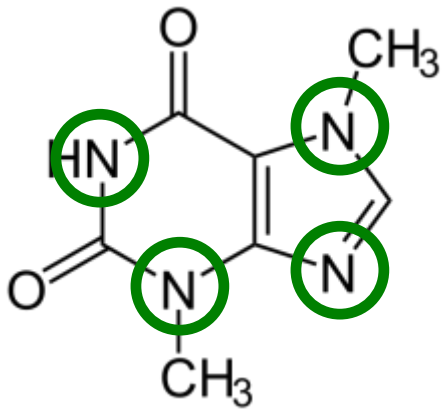
- A cyclic compound with at least one nitrogen within a ring structure is called a **heterocyclic amine**.



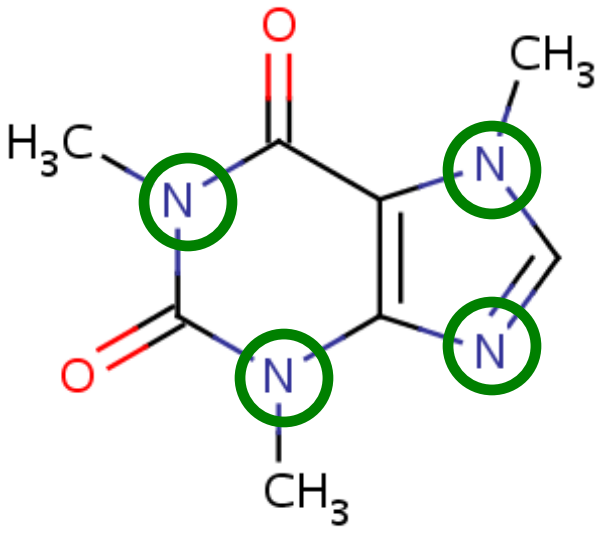
- Many heterocyclic amines are biologically important, or biologically active.
  - DNA, RNA, myoglobin, chlorophyll
  - LSD, cocaine, nicotine, strychnine

2. Heterocyclic amines

- Theobromine (3,7-dimethylpurine-2,6-dione)

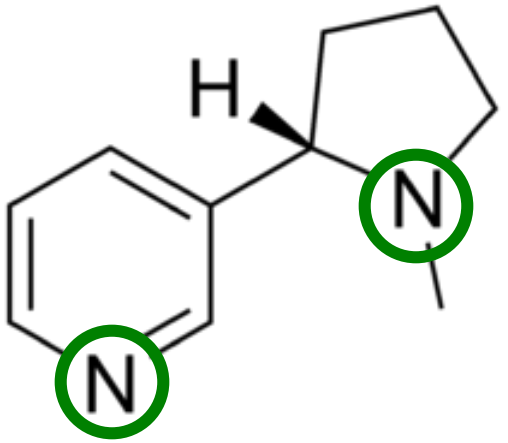


- Caffeine (1,3,7-trimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione-3,7-dihydro-1,3,7-trimethyl-1H-purine-2,6-dione)

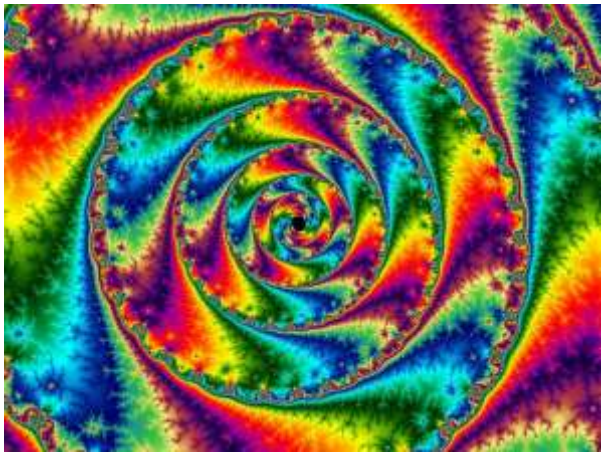


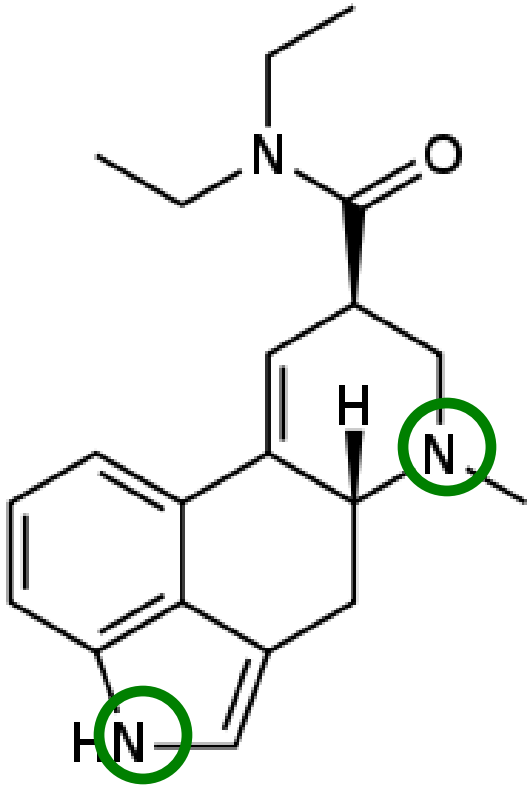
2. Heterocyclic amines

- Nicotine (3-[(2*S*)-1-methylpyrrolidin-2-yl]pyridine)



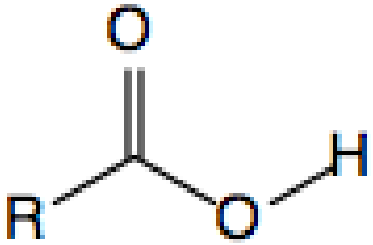
- LSD (9,10-didehydro-*N*,*N*-diethyl-6-methylergoline-8β-carboxamide)

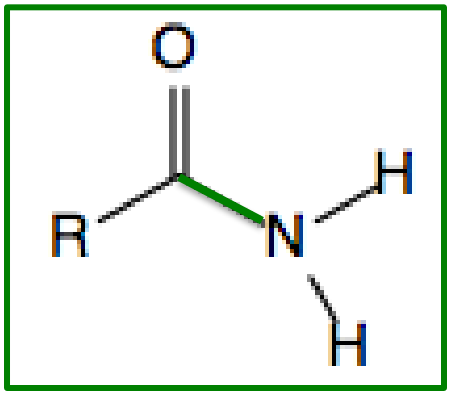


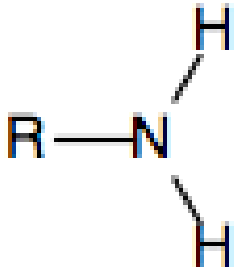


3. Amides

- In **amides**, an amino group ($-NH_2$) replaces the –OH group of carboxylic acids.



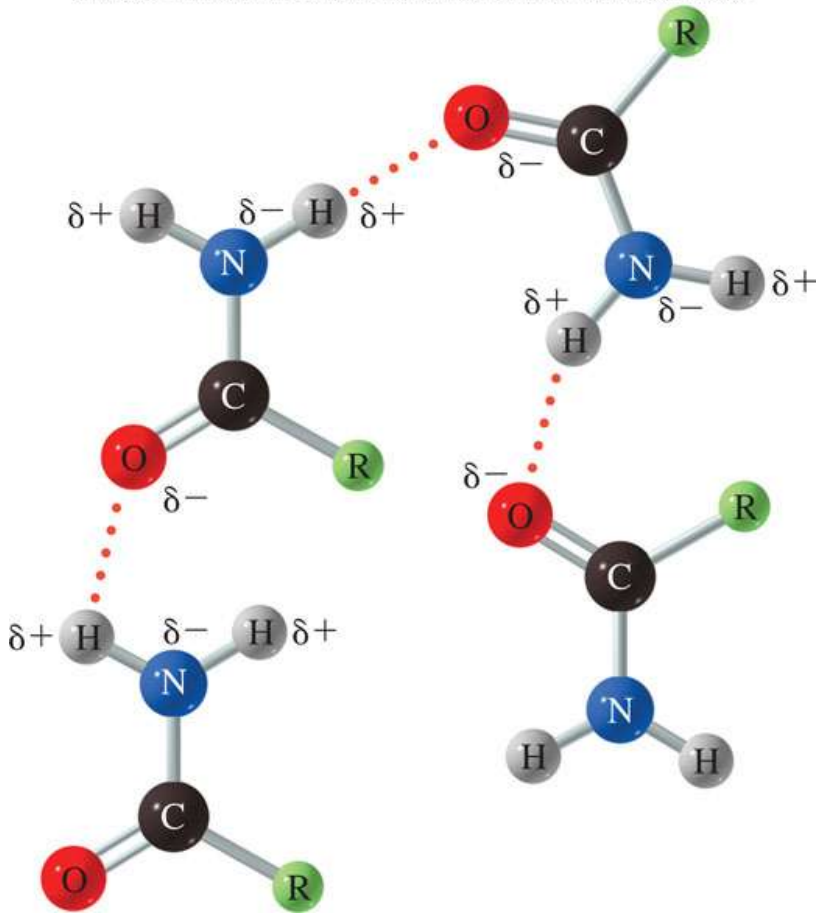




LINKS: ethanoic acid ethanamide ethanamine

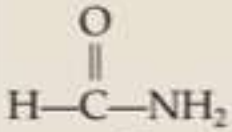
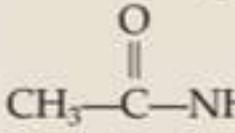
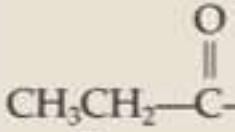
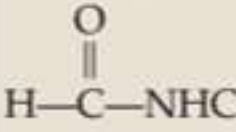
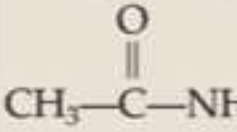
3. *Amides*

- Amides are (mainly) solids at room temperature and have very high boiling points.
- Simple amides are soluble in water.
- Amides do <u>not</u> behave like bases.



3. Amides

- Amides are named as alkanamides.
  - Name the carboxylic acid.
  - Replace the ***–oic acid*** ending with ***–amide***.
  - Alkyl groups attached to the nitrogen are named ***N-alkyl*** as a prefix.

Compound	I.U.P.A.C. Name
	Alkan*amide* (*-amide* replaces the *-oic acid* ending of the I.U.P.A.C. name of carboxylic acid)
	Methanamide
	Ethanamide
	Propanamide
	*N*-Methylmethanamide
	*N*-Methylethanamide

3. *Amides*

- Name the following compounds.

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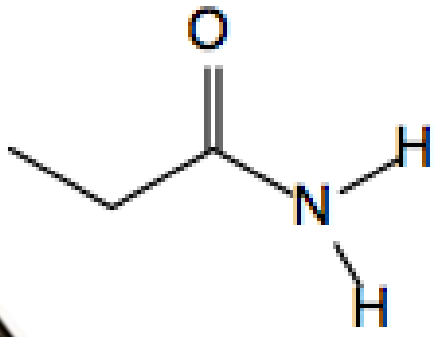
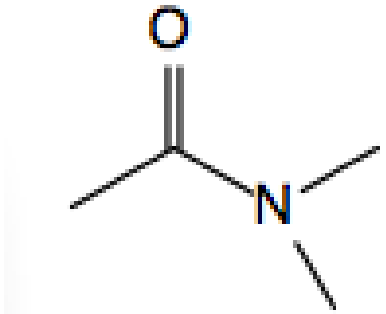
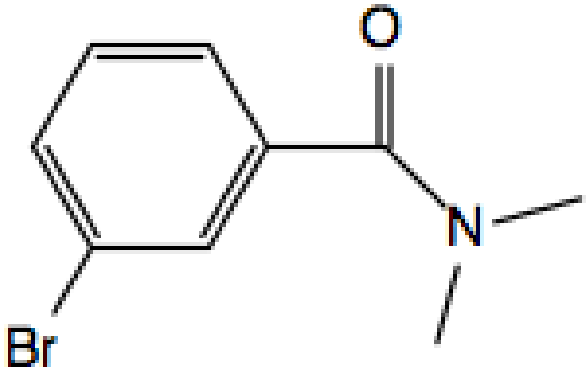






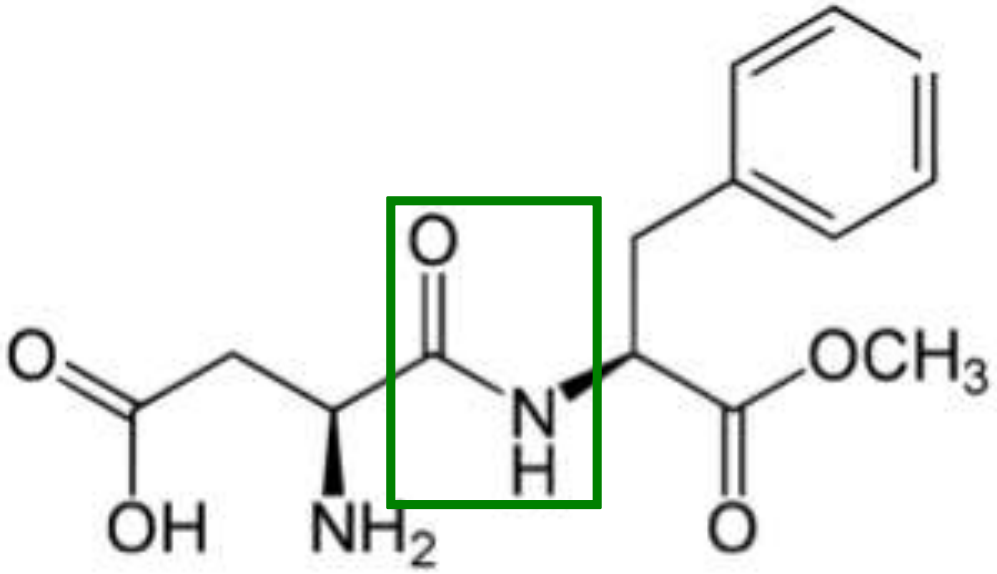
3. *Amides*

- Draw structures for the following compounds.
  - N-methylpropanamide
  - N,N-diethylbenzamide
  - 3-bromo-4-methylhexanamide

pencast

3. Amides

- Aspartame is an amide (among other things!):



Model

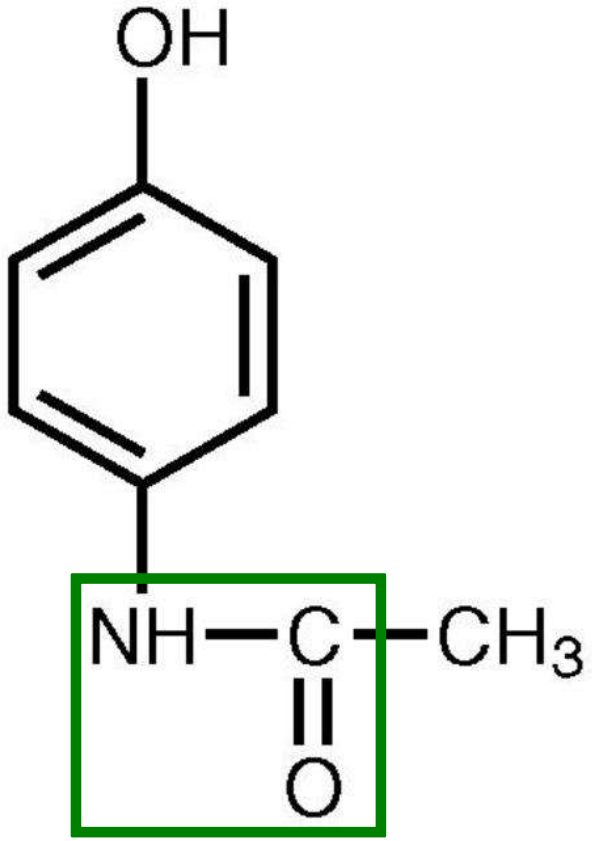
3-amino-3-[(1-methoxycarbonyl-2-phenyl-ethyl)carbamoyl]propanoic acid

3. Amides

- Acetaminophen is an amide (among other things!):

Model

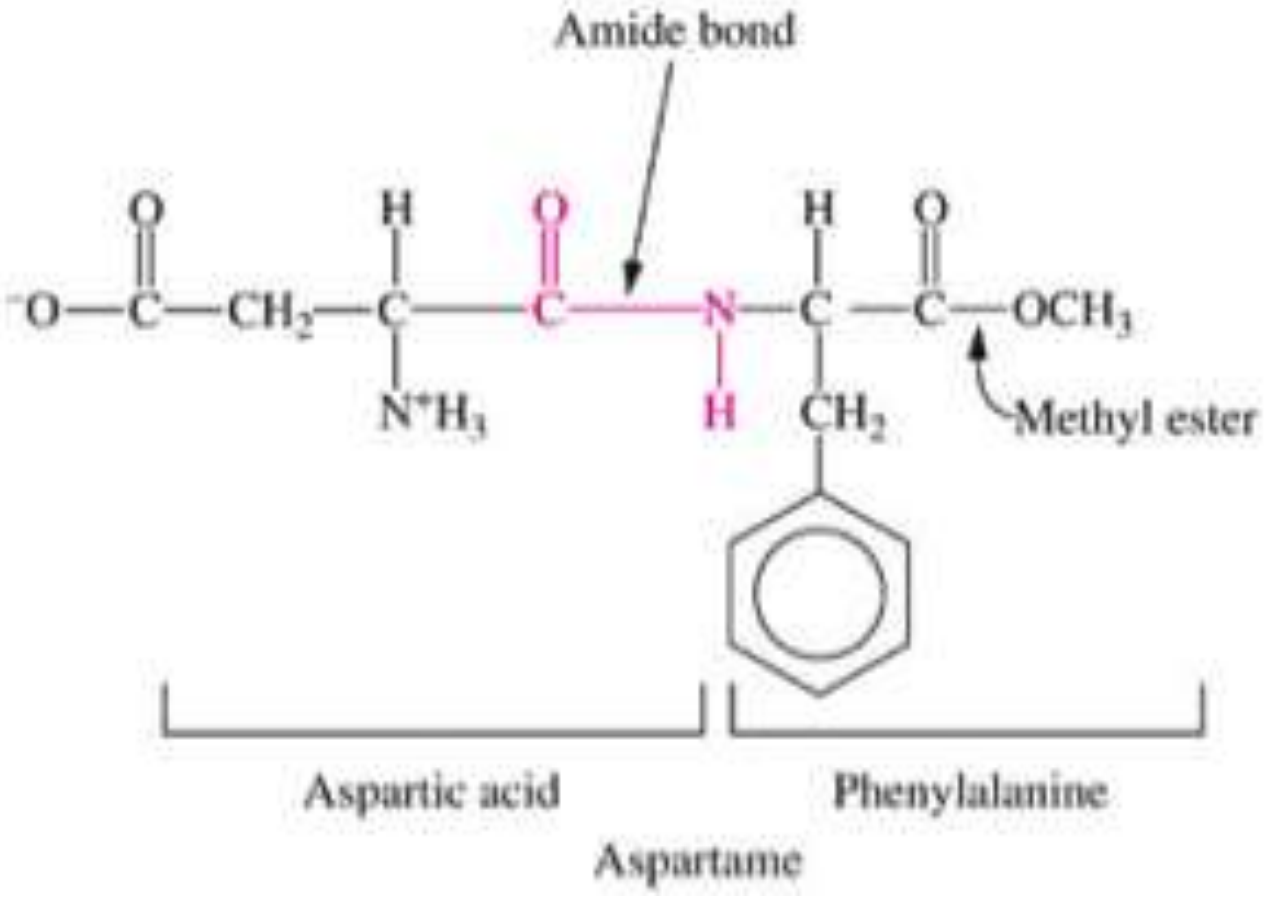
N-(4-hydroxyphenyl)ethanamide



3. Amides

- Aspartame

Model

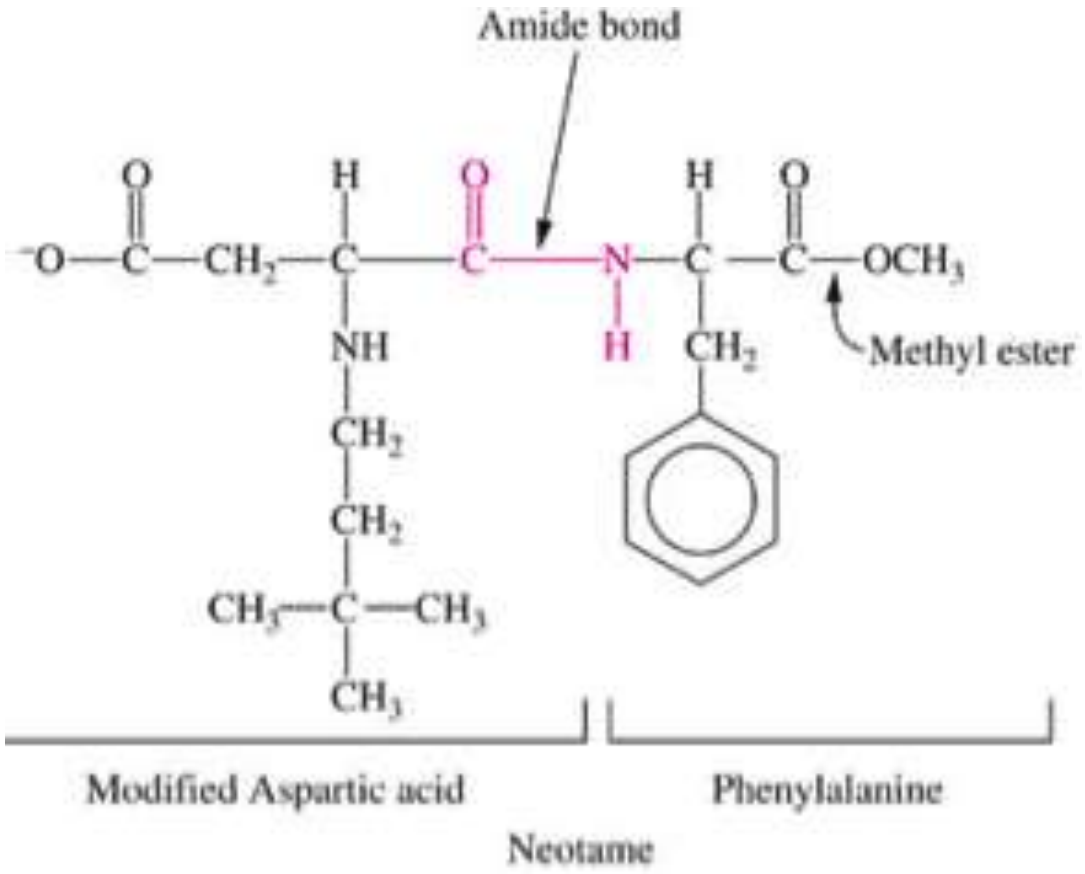


(3S)-3-amino-4-[[(2S)-1-methoxy-1-oxo-3-phenylpropan-2-yl]amino]-4-oxobutanoic acid

3. Amides

- Neotame

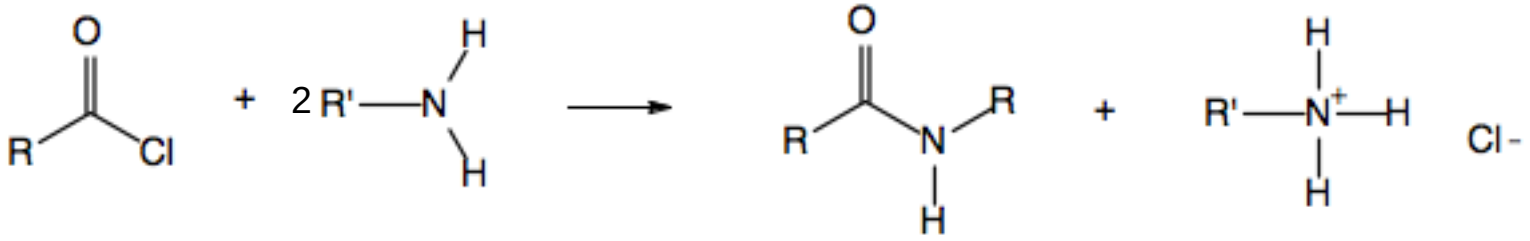
neotame™



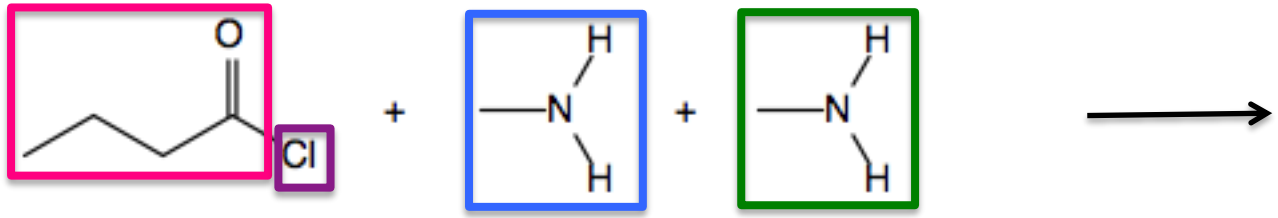
(3*R*)-3-(3,3-Dimethylbutylamino)-4-[[(1*R*)-2-methoxy-2-oxo-1-(phenylmethyl)ethyl]amino]-4-oxobutanoic acid

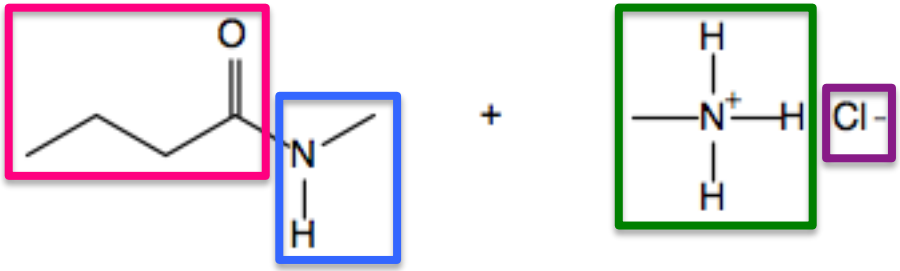
3. Amides

- Primary and secondary amines react with acid chlorides to produce amides.



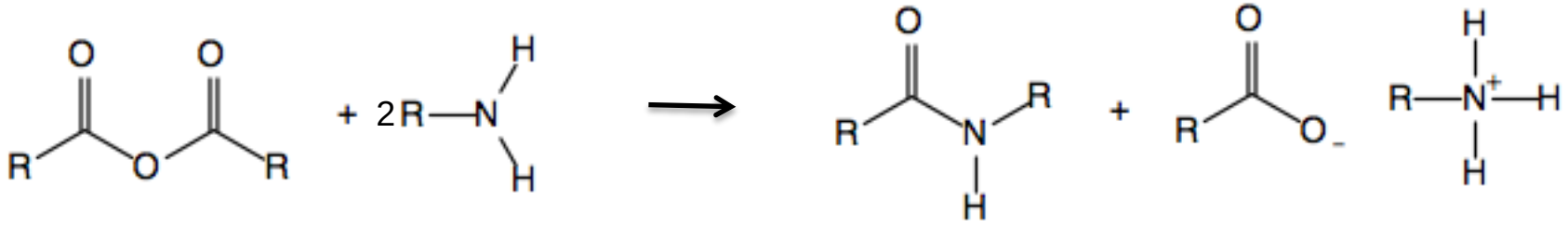
acid chloride ***amine*** ***amide*** ***alkylammonium chloride***



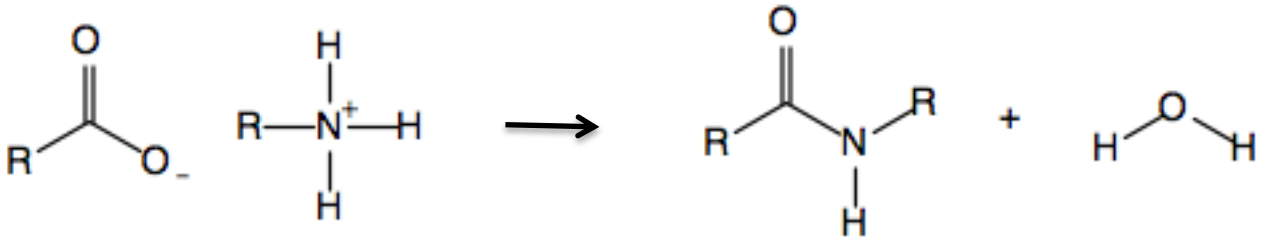


3. Amides

- Primary and secondary amines react with acid anhydrides to produce amides.



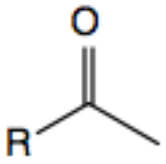
acid anhydride ***amine*** ***amide*** ***carboxylic acid salt***

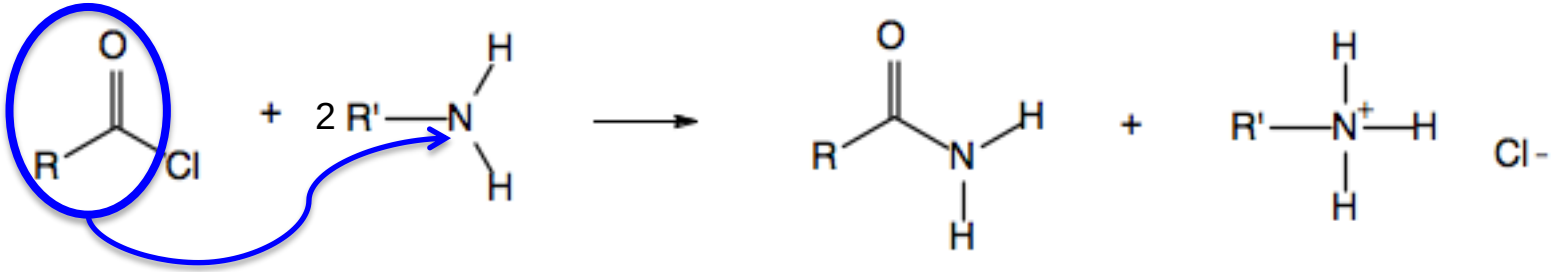


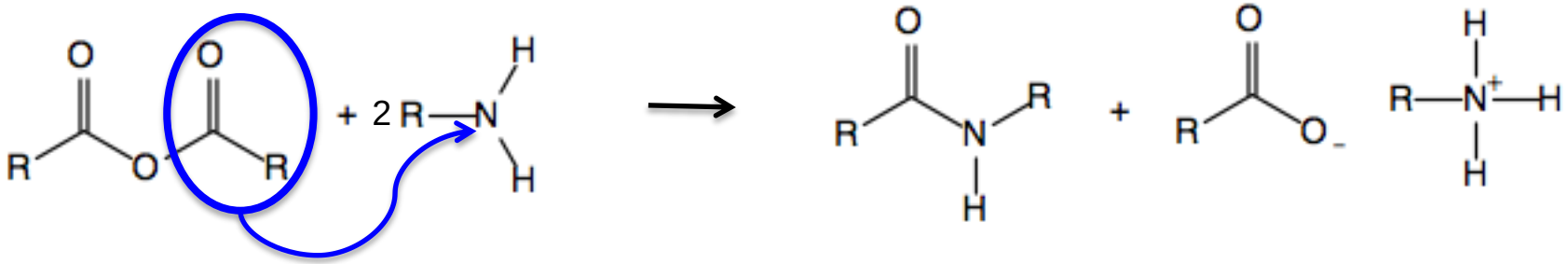
carboxylic acid salt ***amide*** ***water***

3. Amides

- Both reactions for preparation of amides involve an **acyl group transfer**.



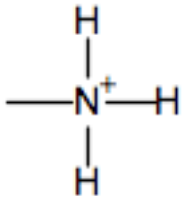




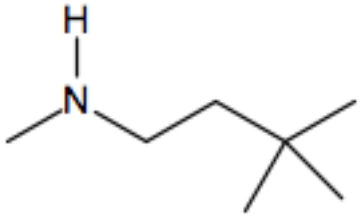
3. Amides

- Comparison of I.U.P.A.C. names for aspartame and neotame

(3S)-3-amino-4-[[(2S)-1-methoxy-1-oxo-3-phenylpropan-2-yl]amino]-4-oxobutanoic acid

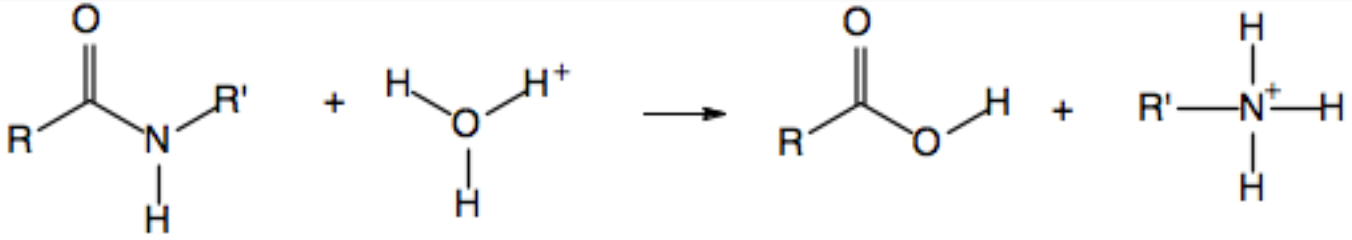


(3*R*)-3-(3,3-Dimethylbutylamino)-4-[[(1*R*)-2-methoxy-2-oxo-1-(phenylmethyl)ethyl]amino]-4-oxobutanoic acid

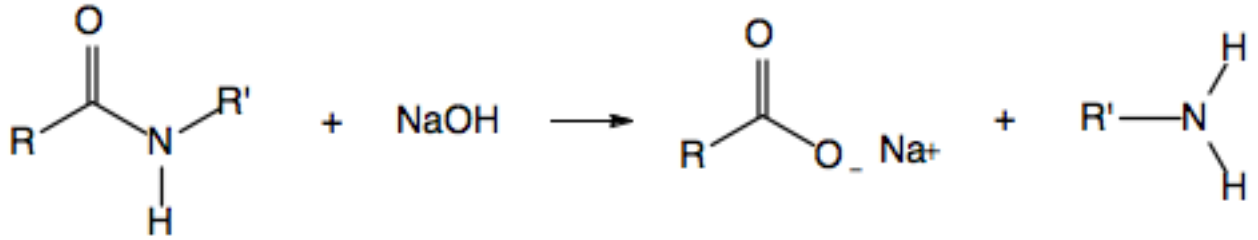


3. Amides

- Although the amide bond is difficult to break, hydrolysis of an amide is possible with heating in the presence of either a strong acid or a strong base.



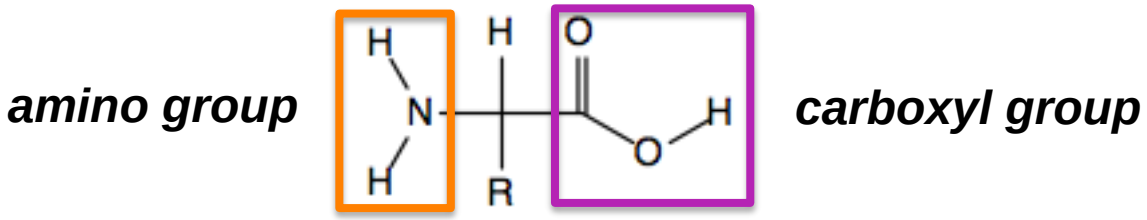
In strong acid: ***carboxylic acid + alkylammonium ion***



In strong base: ***carboxylic acid salt + amine***

4. Amino acids

- An **amino acid** is a combination of an amino group and a carboxyl group.



- Proteins are polymers of amino acids (chains of amides).