

CHAPTER 26: AMIDES AND AMINES

Organic and Biochemistry Supplement to Enhanced Introductory College Chemistry

by Gregory Anderson; Jen Booth; Caryn Fahey; Adrienne Richards; Samantha Sullivan Sauer; and David Wegman

Chapter Contents

- 26.1 Amines – Structures and Naming
- 26.2 Amines – Physical Properties
- 26.3 Heterocyclic Nitrogen Compounds
- 26.4 Basicity of Amines
- 26.5 Amides – Structures, Properties and Naming
- 26.6 Chemical Properties of Amines and Amides
- Chapter 26 – Summary
- Chapter 26 – Review
- Chapter 26 – Infographic descriptions

Except where otherwise noted, this OER is licensed under CC BY-NC-SA 4.0 (<https://creativecommons.org/licenses/by-nc-sa/4.0/>)

Please visit the web version of Organic and Biochemistry Supplement to Enhanced Introductory College Chemistry (<https://ecampusontario.pressbooks.pub/orgbiochemsupplement/>) to access the complete book, interactive activities and ancillary resources.

In this chapter, you will learn about:

- Amines: what are they? What is their chemical structure? What are the physical and chemical properties of these nitrogen containing compounds?
- Amides: what are they? What is their chemical structure? What are the physical and chemical properties of amides?

To better support your learning, you should be familiar with the following concepts before starting this chapter:

- Alkanes, Alkenes, and Alkynes (Chapter 20: Alkanes and Alkyl Halides and Chapter 22: Alkenes, Alkynes and Aromatics)
- Alcohols and Ethers (Chapter 23: Alcohols and Ethers)
- Aldehydes and Ketones (Chapter 24: Aldehydes and Ketones)
- Carboxylic Acids and Esters (Chapter 25: Carboxylic Acids and Esters)
- Functional Groups (Chapter 19.5: Families of Organic Molecules)

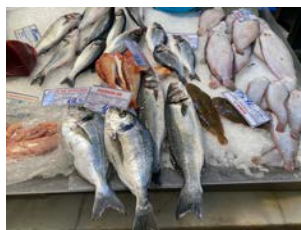


Figure 26.0a. The characteristic and unmistakable odour of fish is due to a mixture of simple alkylamines. (credit: Photo by Dudva, CC BY-SA 4.0)

By the end of this chapter, we will have seen all the common functional groups. Of those groups, carbonyl compounds and amines are the most abundant and have the richest chemistry. In addition to proteins and

nucleic acids, the majority of pharmaceutical agents contain amine functional groups, and many of the common coenzymes necessary for biological catalysis are amines.

Amines are organic derivatives of ammonia in the same way that alcohols and ethers are organic derivatives of water. Like ammonia, amines contain a nitrogen atom with a lone pair of electrons, making amines both basic and nucleophilic.

Amines occur widely in all living organisms. Trimethylamine, for instance, occurs in animal tissues and is partially responsible for the distinctive odour of fish; nicotine is found in tobacco; and cocaine is a stimulant found in the leaves of the South American coca bush. In addition, amino acids are the building blocks from which all proteins are made, and cyclic amine bases are constituents of nucleic acids.

Spotlight on Everyday Chemistry: Hay Fever

Many everyday chemicals and medications rely on the amine and amide functional groups. Infographic 26.0a. shows the applications of amines and amides to hay fever medication.

HAY FEVER & HAY FEVER MEDICATIONS

THE CAUSE
 TREE, GRASS & WEED POLLENS
 10-15% The percentage of the UK population affected by hay fever.
 90-95% The percentage of hay fever sufferers that are allergic to grass pollens.

THE ALLERGIC RESPONSE

- 1 Pollen exposure results in the body misidentifying it as a threat; antibodies are released to combat it.
- 2 The antibodies produced bind to two types of cell in tissues - mast cells and basophils.
- 3 These release several chemicals, including histamine, which produce an inflammatory response.
- 4 Symptoms of this response include a runny nose, itching, sneezing fits, and nasal congestion.

ANTIHISTAMINES FOR HAY FEVER
 CETIRIZINE
 LORATADINE
 Block histamine action, prevent most symptoms
 All oral formulations for treatment of hay fever are antihistamines. These bind to H₁ histamine receptors instead of histamine, preventing the effects produced by the allergic response - although they may not clear blocked noses.
 1ST GENERATION VS. 2ND GENERATION
 First generation antihistamines can cause undesirable effects, including sedation. Second generation are less likely to exhibit sedative effects, particularly loratadine. Peak levels of antihistamines are generally reached one hour after taking.
 Take when hay fever symptoms are expected, rather than when they have already started.
 This is because they cannot reverse the effects of histamine already binding to the H₁ receptors, and so will not provide relief.

SODIUM CROMOGLYCATE IN EYE DROPS
 SODIUM CROMOGLYCATE
 Prevents release of histamine
 Commonly used in eye drop solutions, sodium cromoglycate prevents hay fever symptoms by stabilising mast cells, and preventing them from releasing histamine. Unlike anti-histamines, it is effective at remedying itchy eyes even after symptoms have started.

CORTICOSTEROIDS
 BECLOMETHASONE
 Prevent the inflammatory symptoms of hay fever
 Prevent nasal symptoms more effectively than antihistamines, and also relieve itchy eyes. They act to reduce inflammation, rather than directly blocking or preventing the action of histamine.

NASAL SPRAY

© COMPOUND INTEREST 2016 - WWW.COMPOUNDCHEM.COM | Twitter: @compoundchem | Facebook: www.facebook.com/compoundchem
 This graphic is shared under a Creative Commons Attribution-NonCommercial-NoDerivatives International 4.0 licence.

Infographic 26.0a. Read more about “Hay Fever & Hay Fever Medications (<https://www.compoundchem.com/2014/06/20/hayfever/>)” by Andy Brunning / Compound Interest, CC BY-NC-ND, or access a text-based summary of infographic 26.0a [New tab].

Closely related to carboxylic acids and nitriles are the carboxylic acid derivatives, compounds in which an acyl group is bonded to an electronegative atom or substituent that can act as a leaving group in the nucleophilic acyl substitution reaction.

A chemical reaction shows the nucleophilic acyl substitution reaction of carboxylic acid derivative. The leaving group is denoted as Y.

Figure 26.0b. A nucleophilic acyl substitution reaction of carboxylic acid derivative. (credit: *Organic Chemistry (OpenStax)*, CC BY-NC-SA 4.0)

Many kinds of acid derivatives are known, one of those being amides. **Amides** are common in both laboratory and biological chemistry. Amides are molecules that contain nitrogen atoms connected to the carbon atom of a carbonyl group.

This figure shows three structures.

Two examples are provided. The basic structure has an H atom or R group bonded to a C atom which is double bonded to an O atom. The O atom has two sets of electron dots.

The C atom is bonded to an N atom which in turn is bonded to two R groups or two H atoms. The N atom has one set of electron dots.

The next structure includes acetamide, which has a methyl group bonded to a C atom with a doubly bonded O atom. The second C atom is also bonded to an NH₂ group. Hexanamide has a hydrocarbon chain of length 6 involving all single bonds. The condensed structure is shown here.

To the sixth C atom at the right end of the chain, an O atom is double bonded and an NH₂ group is single bonded.

Figure 26.0c. The image represents the functional groups for amides. It also shows two specific examples of amides. (credit: *Chemistry 2e (OpenStax)*, CC BY 4.0)

Watch Amines: Crash Course Organic Chemistry #46 – Youtube (12 min) (<https://youtu.be/Kzm61ubVQmE?>)

The table below outlines all organic compounds discussed thus far including their functional groups, formulas and names.

This table provides compound names, structures with functional groups in red, and examples that include formulas, structural formulas, ball-and-stick models, and names. Compound names include alkene, alkyne, alcohol, ether, aldehyde, ketone, carboxylic acid, ester, amine, and amide. Alkenes have a double bond. A formula is C_2H_4 which is named ethene. The ball-and-stick model shows two black balls forming a double bond and each is bonded to two white balls. Alkynes have a triple bond. A formula is C_2H_2 which is named ethyne. The ball-and-stick model shows two black balls with a triple bond between them each bonded to one white ball. Alcohols have an OH group. The O has two pairs of electron dots. A formula is C_2H_5OH which is named ethanol. The ball-and-stick model shows two black balls and one red ball bonded to each other with a single bond. There are four white balls visible. Ethers have an O atom in the structure between two R groups. The O atom has two sets of electron dots. A formula is $(C_2H_5)_2O$ which is named ethanal. The ball-and-stick model shows two black balls bonded to a red ball which is bonded to two more black balls. All bonds are single. There are five white balls visible. Aldehydes have a C atom to which a double bonded O and an H and an R are included in the structure. The O atom has two sets of electron dots. A formula is C_2H_3CHO which is named Ethanal. The ball-and-stick model shows two black balls bonded with a single bond and the second black ball forms a double bond with a red ball. There are three white balls visible. Ketones show a C atom to which a double bonded O is attached. The left side of the C atom is bonded to R and the right side is bonded to R prime. The O atom has two sets of electron dots. The formula is $C_3H_7COCH_3$ and is named methyl ethyl ketone. The ball-and-stick model shows four black balls all forming single bonds with each other. The second black ball forms a double bond with a red ball. There are five white balls visible. Carboxylic acids have a C to which a double bonded O and an OH are included in the structure. Each O atom has two sets of electron dots. A formula is C_2H_3COOH which is named ethanoic or acetic acid. The ball-and-stick model shows two black balls and one red ball forming single bonds with each other. The second black ball also forms a double bond with another red ball. Three white balls are visible. Esters have a C atom which forms a double bond with an O atom and single bond with another O atom which has an attached hydrocarbon group in the structure. Each O atom has two sets of electron dots. A formula is $C_4H_8O_2$ which is named ethyl acetate. The ball-and-stick model shows two black balls, a red ball, and two more black balls forming single bonds with each other. The second black ball forms a double bond with another red ball.

Figure 26.0d.
Summary of
Organic
Compounds
(credit: *Chemistry
2e (OpenStax)*, CC
BY 4.0)

Attribution & References

Except where otherwise noted, this page is adapted by Caryn Fahey from:

- “20.4 Amines and Amides” In *Chemistry 2e (Open Stax)* by Paul Flowers, Klaus Theopold, Richard Langley, R. Robinson & R. William, licensed under CC BY 4.0. Access for free at *Chemistry 2e (Open Stax)* (<https://openstax.org/books/chemistry-2e>)
- “Carboxylic Acid Derivatives: Why This Chapter?” In *Organic Chemistry (OpenStax)* by John McMurray, licensed under CC BY-NC-SA 4.0. Access for free at *Organic Chemistry (OpenStax)* (<https://openstax.org/books/organic-chemistry>)
- “15.0: Prelude to Organic Acids and Bases and Some of Their Derivatives” In *Basics of General, Organic, and Biological Chemistry (Ball et al.)* by David W. Ball, John W. Hill, and Rhonda J. Scott via LibreTexts, CC BY-NC-SA 4.0./ A LibreTexts version of *Introduction to Chemistry: GOB (v. 1.0)*, CC BY-NC 3.0.

26.1 AMINES - STRUCTURE AND NAMING

Learning Objectives

By the end of this section, you will be able to:

- Identify the general structure for an amine.
- Identify the functional group for amines.
- Determine the structural feature that classifies amines as primary, secondary, or tertiary.
- Use nomenclature systems to name amines.

Amines are molecules that contain carbon-nitrogen bonds. The nitrogen atom in an amine has a lone pair of electrons and three bonds to other atoms, either carbon or hydrogen. Various nomenclatures are used to derive names for amines, but all involve the class-identifying suffix *-ine* as illustrated here for a few simple examples:

Three structures are shown, each with a red, central N atom which has a pair of electron dots indicated in red above the N atoms. The first structure is labeled methyl amine. To the left of the N, a C H subscript 3 group is bonded. H atoms are bonded to the right and bottom of the central N atom. The second structure is labeled dimethyl amine. This structure has C H subscript 3 groups bonded to the left and right of the N atom and a single H atom is bonded below. The third structure is labeled trimethyl amine, which has C H subscript 3 groups bonded to the left, right, and below the central N atom.

Figure 26.1a. Examples of amines. (Credit: Chemistry 2e, OpenStax, CC BY 4.0)

In some amines, the nitrogen atom replaces a carbon atom in an aromatic hydrocarbon. Pyridine (Figure 26.1b.) is one such heterocyclic amine. A heterocyclic compound contains atoms of two or more different elements in its ring structure.

A molecular structure is shown. A ring of five C atoms and one N atom is shown with alternating double bonds. Single H atoms are bonded, appearing at the outside of the ring on each C atom. The N atom has an unshared electron pair shown on the N atom on the outer side of the ring. The N atom, electron dot pair, and bonds connected to it in the ring are shown in red.

Figure 26.1b. The illustration shows one of the resonance structures of pyridine. (Credit: Chemistry 2e, OpenStax, CC BY 4.0)

Classifying Amines

Amines can be either alkyl-substituted (alkylamines) or aryl-substituted (arylamines). Although much of the chemistry of the two classes is similar, there are also substantial differences. Amines are classified according to the number of carbon atoms bonded directly to the nitrogen atom. They are classified as primary (RNH_2), secondary (R_2NH), or tertiary (R_3N), depending on the number of organic substituents attached to nitrogen (Figure 26.1c.). A **primary (1°) amine** has one alkyl (or aryl) group on the nitrogen atom, a **secondary (2°) amine** has two, and a **tertiary (3°) amine** has three (Figure 26.1c.). Thus, methylamine (CH_3NH_2) is a primary amine, dimethylamine [$(\text{CH}_3)_2\text{NH}$] is a secondary amine, and trimethylamine [$(\text{CH}_3)_3\text{N}$] is a tertiary amine. Note that this usage of the terms *primary*, *secondary*, and *tertiary* differs from our previous usage. When we speak of a tertiary alcohol or alkyl halide, we refer to the degree of substitution at the alkyl carbon atom, but when we speak of a tertiary amine, we refer to the degree of substitution at the nitrogen atom (Figure 26.1d.).

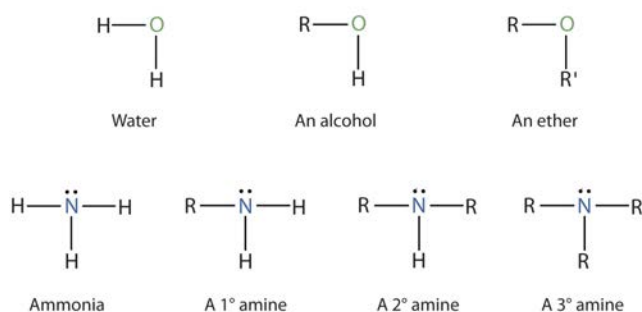


Figure 26.1c. The Structure of Amines Compared to Water, an Alcohol, and an Ether. (Credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0.)

Three structures show tertiary-butyl alcohol (a tertiary alcohol), trimethylamine (a tertiary amine) and tertiary butyl amine (a primary amine).

Figure 26.1d. Comparison of tertiary alcohol and tertiary amine. (Credit: Organic Chemistry, OpenStax, CC BY-NC-SA 4.0)

To classify alcohols, we look at the number of carbon atoms bonded to the *carbon atom* bearing the OH group, not the oxygen atom itself. Thus, although isopropylamine looks similar to isopropyl alcohol, the former is a *primary* amine, while the latter is a *secondary* alcohol (Figure 26.1e.).



Figure 26.1e. Comparison of an amine and an alcohol. (Credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0.)

Compounds containing a nitrogen atom with four attached groups also exist, but the nitrogen atom must carry a formal positive charge. Such compounds are called quaternary ammonium salts (Figure 26.1f.).

The structure of a quaternary ammonium salt, which is a nitrogen positive linked to four R groups and an X negative ion.

Figure 26.1f. Example of a quaternary salt. (Credit: *Organic Chemistry, OpenStax*, CC BY-NC-SA 4.0)

Naming Amines

Primary amines are named in two main ways using the IUPAC system. They can either be named as alkylamines or as alkanamines. Most 1° amines which are attached to linear alkanes, cycloalkanes, and alkyl groups with common names tend to be named as alkylamines.

Steps:

1. Identify the longest carbon chain bonded to the amine nitrogen.
2. The alkyl group is named as a substituent (prefix + alkyl).
3. The suffix amine is added to the end.

Primary also have several common names. You might recall that the aromatic phenylamine, $\text{H}_2\text{N}-\text{C}_6\text{H}_5$, has the common name *aniline* (Figure 26.1g.).

The structures of tertiary-butyl amine,
cyclohexylamine, and aniline. Aniline is enclosed in
square parentheses.

Figure 26.1g. Linear and ring structure examples of amines. (Credit: Organic Chemistry, OpenStax, CC BY-NC-SA 4.0)

Alternatively, primary amines tend to be named as alkanamines (Figure 26.1h.).

Steps:

1. Identify the longest carbon chain bonded to the amine nitrogen.
2. Identify the substituents.
3. Number the parent chain, giving the amine the lowest number.
4. Put all details together and ensure the substituents are in alphabetical order.

The structures of 4,4-dimethylcyclohexanamine and
1,4-butanediamine. 4,4-dimethylcyclohexanamine
has cyclohexane ring with two methyl groups on C4
and amine on C1. 1,4-butanediamine is four-carbon
chain with amines on C1 and C4.

Figure 26.1h. Examples of naming amines. (Credit: Organic Chemistry, OpenStax, CC BY-NC-SA 4.0)

Amines with more than one functional group are named by considering the $-\text{NH}_2$ as an *amino* substituent on the parent molecule (Figure 26.1i.).

The structures of 2-aminobutanoic acid,
2,4-diaminobenzoic acid and 4-amino-2-butanone.

The carbon atoms of 2-aminobutanoic acid and
4-amino-2-butanone are numbered explicitly.

Figure 26.1i. Examples of naming amines with more than one functional group. (Credit: Organic Chemistry, OpenStax, CC BY-NC-SA 4.0)

Symmetrical secondary and tertiary amines are named by adding the prefix *di-* or *tri-* to the alkyl group (Figure 26.1j.).

The structures of diphenylamine and
triethylamine. Diphenylamine has two benzene
rings linked to an N H group. Triethylamine has
a nitrogen atom linked to three ethyl groups.

Figure 26.1j. Examples of symmetrical secondary and tertiary amines. (Credit: Organic Chemistry, OpenStax, CC BY-NC-SA 4.0)

Unsymmetrically substituted secondary and tertiary amines are referred to as *N*-substituted primary amines. The largest alkyl group takes the parent name, and the other alkyl groups are considered *N*-substituents on the parent (*N* because they're attached to nitrogen) (Figure 26.1k.).

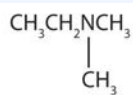
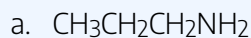
N,N-dimethylpropylamine has a nitrogen linked to
two methyl and a propyl group. N-ethyl-N-
methylcyclohexylamine has cyclohexane linked to a
nitrogen. This is connected to methyl and ethyl group.

Figure 26.1k. Examples of unsymmetrical secondary and tertiary amines. (Credit: Organic Chemistry, OpenStax, CC BY-NC-SA 4.0)

The common names for simple aliphatic amines consist of an alphabetic list of alkyl groups attached to the nitrogen atom, followed by the suffix *-amine*. (Systematic names are often used by some chemists.) The amino group (NH₂) is named as a substituent in more complicated amines, such as those that incorporate other functional groups or in which the alkyl groups cannot be simply named.

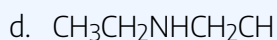
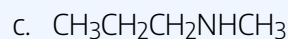
Example 26.1a

Name and classify each compound.



(Credit: Intro Chem: GOB (V. 1.0), CC BY-NC-SA 3.0.)

b.



Solution

1. There is only one alkyl group attached to the nitrogen atom, so the amine is primary. A group of three carbon atoms (a propyl group) is attached to the NH_2 group through an end carbon atom, so the name is propylamine.
2. There are two methyl groups and one ethyl group on the nitrogen atom. The compound is ethyldimethylamine, a tertiary amine.
3. There are two ethyl groups attached to the nitrogen atom; the amine is secondary, so the compound is diethylamine.
4. The nitrogen atom has a methyl group and a propyl group, so the compound is methylpropylamine, a secondary amine.

Exercise 26.1a

Draw the structure for each compound and classify.

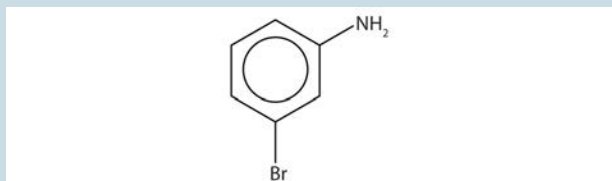
- a. isopropyldimethylamine
- b. dipropylamine

Check Your Answers:¹

Exercise & solution image source: Intro Chem: GOB (V. 1.0), CC BY-NC-SA 3.0.

Exercise 26.1b

Name this compound.



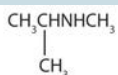
(Credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0.)

Check Your Answer:²

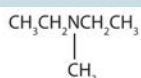
Exercise 26.1c

Name and classify each compound.

1.



2.

3. $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$ 4. $\text{CH}_3\text{CH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{CH}_3$

Check Your Answers:³

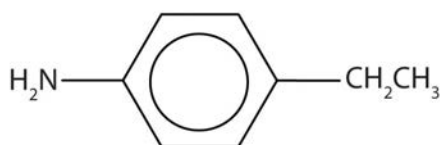
Exercise and image credits: *Introduction to Chemistry: GOB (V. 1.0)*, CC BY-NC-SA 3.0

Example 26.1b

Draw the structure for *p*-ethylaniline and classify.

Solution

The compound is a derivative of aniline. It is a primary amine having an ethyl group located *para* to the amino (NH₂) group.



(credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0).

Exercise 26.1d

Draw the structure for 2-amino-3-methylpentane.

Check Your Answer:⁴ **Exercise & solution image source:** *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0.

Attribution & References

Except where otherwise noted, this page is adapted by Caryn Fahey from:

- 20.4 Amines and Amides In *Chemistry 2e (OpenStax)* by Flowers, Paul., Theopold, Klaus., Langley, Richard., R. Robinson, William R., licensed under CC BY 4.0. Access for free at *Chemistry 2e (OpenStax)* (<https://openstax.org/books/chemistry-2e/>)
- “16.1: Classifying Amines” & “16.2: Naming and Drawing Amines” In *Map: Fundamentals of General Organic and Biological Chemistry (McMurry et al.)*, CC BY-NC-SA 3.0, a remixed version of *Basics of GOB (Ball et al.)*, CC BY-NC-SA 4.0 which is a LibreTexts version of *Introduction to Chemistry: GOB (v. 1.0)*, CC BY-NC-SA 3.0

- “24.1 Naming Amines” In *Organic Chemistry (OpenStax)* (<https://openstax.org/books/organic-chemistry/pages/1-why-this-chapter>) by John McMurry, CC BY-NC-SA 4.0. Access for free at *Organic Chemistry (OpenStax)* (<https://openstax.org/books/organic-chemistry/pages/1-why-this-chapter>)

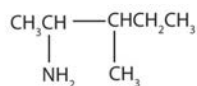
Notes

1. a. The name indicates that there are an isopropyl group (in red) and two methyl groups (in green) attached to the nitrogen atom; the



amine is tertiary.

- b. The name indicates that there are two propyl groups attached to the nitrogen atom; the amine is secondary. (The third bond on the nitrogen atom goes to a hydrogen atom.) $\text{CH}_3\text{CH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{CH}_3$
2. The benzene ring with an amino (NH_2) group is aniline. The compound is named as a derivative of aniline: 3-bromoaniline or m-bromoaniline.
3. 1) secondary amine, N-methylisopropylamine or methylisopropylamine 2) tertiary amine, N-ethyl-N-methylethylamine or diethylmethylamine 3) primary amine, butylamine, 4) secondary amine, n-propylpropylamine or dipropylamine



- 4.

Always start with the parent compound: draw the pentane chain. Then attach a methyl group at the third carbon atom and an amino group at the second carbon atom.

26.2 AMINES - PHYSICAL PROPERTIES

Learning Objectives

By the end of this section, you will be able to:

- Explain why the boiling points of primary and secondary amines are higher than those of alkanes or ethers of similar molar mass but are lower than those of alcohols.
- Compare the boiling points of tertiary amines with alcohols, alkanes, and ethers of similar molar mass.
- Compare the solubilities in water of amines of five or fewer carbon atoms with the solubilities of comparable alkanes and alcohols in water

Properties of Amines

Primary and secondary amines have hydrogen atoms bonded to an nitrogen atom and are therefore capable of hydrogen bonding (part (a) of Figure 26.2a.), although not as strongly as alcohol molecules (which have hydrogen atoms bonded to an oxygen atom, which is more electronegative than nitrogen). These amines boil at higher temperatures than alkanes but at lower temperatures than alcohols of comparable molar mass. For example, compare the boiling point of methylamine (CH_3NH_2 ; -6°C) with those of ethane (CH_3CH_3 ; -89°C) and methanol (CH_3OH ; 65°C). Tertiary amines have no hydrogen atom bonded to the nitrogen atom and so cannot participate in intermolecular hydrogen bonding. They have boiling points comparable to those of ethers (Table 26.2a.).

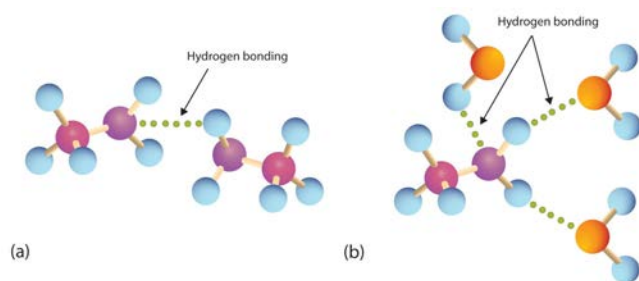


Figure 26.2a. Hydrogen Bonding. (a) Amine molecules are associated through hydrogen bonding. (b) An amine molecule can form a hydrogen bond with water molecules (credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0).

Table 26.2a. Physical Properties of Some Amines and Comparable Oxygen-Containing Compounds

Name	Condensed Structural Formula	Class	Molar Mass	Boiling Point (°C)	Solubility at 25°C (g/100 g Water)
butylamine	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$	1°	73	78	miscible
diethylamine	$(\text{CH}_3\text{CH}_2)_2\text{NH}$	2°	73	55	miscible
butyl alcohol	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$	—	74	118	8
dipropylamine	$(\text{CH}_3\text{CH}_2\text{CH}_2)_2\text{NH}$	2°	101	111	4
triethylamine	$(\text{CH}_3\text{CH}_2)_3\text{N}$	3°	101	90	14
dipropyl ether	$(\text{CH}_3\text{CH}_2\text{CH}_2)_2\text{O}$	—	102	91	0.25

Source: “15.11: Physical Properties of Amines” In *Basics of GOB Chemistry (Ball et al.)*, CC BY-NC-SA 4.0.

All three classes of amines can engage in hydrogen bonding with water (Figure 26.2a.). Amines of low molar mass are quite soluble in water; the borderline of solubility in water is at five or six carbon atoms (Table 26.2a.).

Spotlight on Everyday Chemistry: Hazards with Amines

Amines have “interesting” odours. The simple ones smell very much like ammonia. Higher aliphatic amines smell like decaying fish. Or perhaps we should put it the other way around: Decaying fish give off odorous amines. The stench of rotting fish is due in part to two diamines: putrescine and cadaverine. They arise from the decarboxylation of ornithine and lysine, respectively, amino acids that are found in animal cells.

Aromatic amines generally are quite toxic. They are readily absorbed through the skin, and workers must exercise caution when handling these compounds. Several aromatic amines, including β -naphthylamine (Figure 26.2b.), are potent carcinogens.

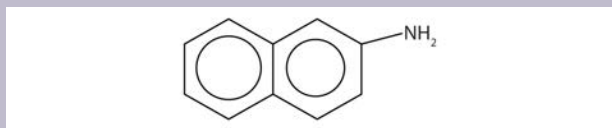
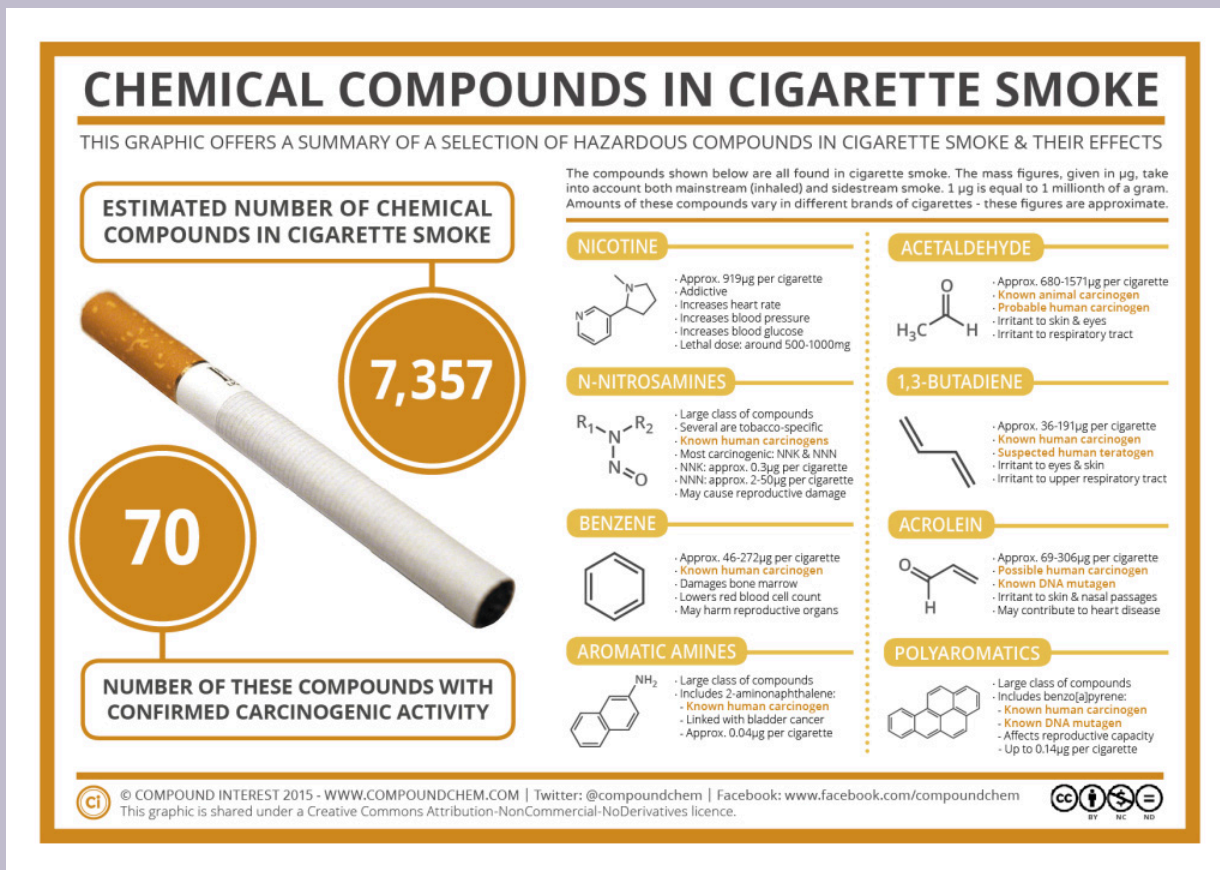


Figure 26.2b. Structure of beta-naphthylamine. (Credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0)

Cigarettes and cigarette smoke also have amine-based compounds. Read more in Infographic 26.2a.



Infographic 26.2a. Chemical compounds in cigarette smoke contain amines including aromatic amines. Read more about “The Chemicals in Cigarette Smoke & Their Effects (<https://www.compoundchem.com/2014/05/01/the-chemicals-in-cigarette-smoke-their-effects/>)” by Andy Brunning / Compound Interest, CC BY-NC-ND, or access a text-based summary of infographic 26.2a [New tab].

Exercise 26.2a

- Which compound has the higher boiling point, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$ or $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$? Explain.
- Which compound is more soluble in water, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ or $\text{CH}_3\text{CH}_2\text{NHCH}_2\text{CH}_3$? Explain.

Check Your Answers:¹

Spotlight on Everyday Chemistry: Scientist Dr. Nadine Borduas

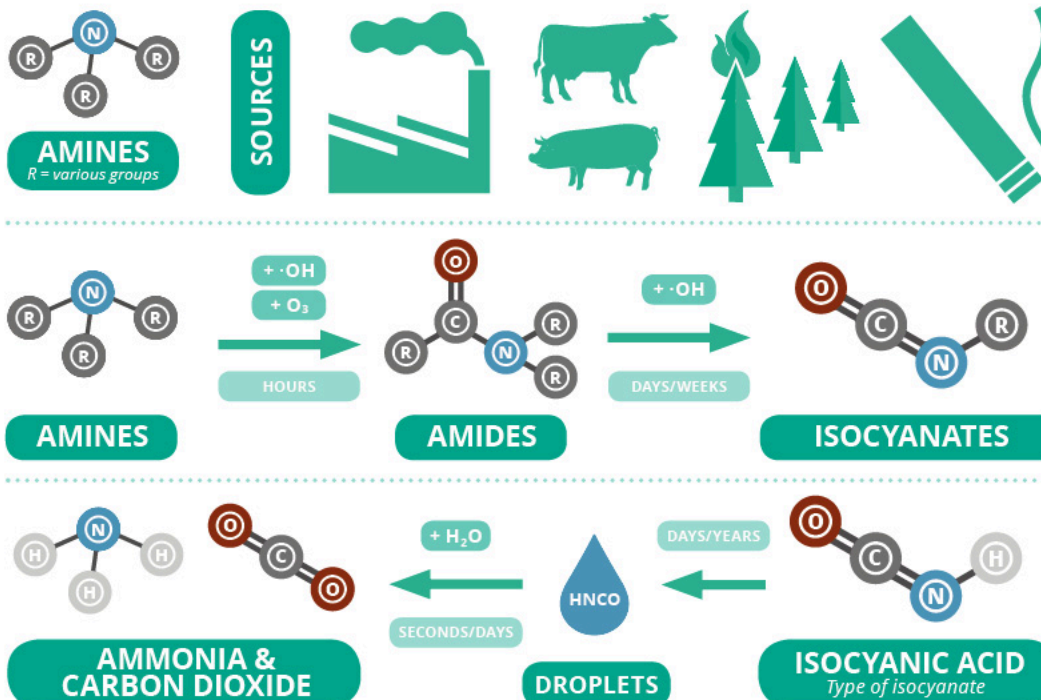
Research on nitrogen-containing amine compounds in the atmosphere is explained in Infographic 26.2b.



DR. NADINE BORDUAS
DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TORONTO

ORGANIC NITROGEN IN THE ATMOSPHERE

Organic nitrogen compounds enter our atmosphere from a variety of sources, both natural and industrial. What happens to these pollutants in the atmosphere is a question some chemists are trying to answer.



WHY DOES IT MATTER?

Ammonia reacts with chemicals in air to form particulates which can have human health issues, contribute to smog, and impact climate. Nitrogen deposition in soils can also affect ecosystems.



© COMPOUND INTEREST 2015 - WWW.COMPOUNDCHEM.COM
Shared under a CC Attribution-NonCommercial-NoDerivatives licence.



Attribution & References

Except where otherwise noted, this page is adapted by Caryn Fahey and Samantha Sullivan Sauer from

- “16.3: Properties of Amines” In *Map: Fundamentals of General Organic and Biological Chemistry* (McMurry et al.), CC BY-NC-SA 3.0, a remixed version of *Basics of GOB* (Ball et al.), CC BY-NC-SA 4.0 which is a LibreTexts version of *Introduction to Chemistry: GOB (v. 1.0)*, CC BY-NC-SA 3.0

Notes

1.
 1. $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$ because the nitrogen-to-hydrogen (N-H) bonds can engage in hydrogen bonding; $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ cannot engage in hydrogen bonding
 2. $\text{CH}_3\text{CH}_2\text{NHCH}_2\text{CH}_3$ because amines can engage in hydrogen bonding with water; alkanes cannot engage in hydrogen bonding

26.3 HETEROCYCLIC NITROGEN COMPOUNDS

Learning Objectives

By the end of this section, you will be able to:

- Understand how a heterocyclic compound differs from other cyclic hydrocarbons.
- Understand what an alkaloid is.
- Compare alkaloids to human health.

Heterocyclic Amines

Looking back at the various cyclic hydrocarbons discussed previously, we see that all the atoms in the rings of these compounds are carbon atoms. In other cyclic compounds, called **heterocyclic compounds** (Greek *heteros*, meaning “other”), nitrogen, oxygen, sulfur, or some other atom is incorporated in the ring. Many heterocyclic compounds are important in medicine and biochemistry. Some compose part of the structure of the nucleic acids, which in turn compose the genetic material of cells and direct protein synthesis.

Heterocyclic amines—compounds in which the nitrogen atom occurs as part of a ring—are also common, and each different heterocyclic ring system has its own parent name. The heterocyclic nitrogen atom is always numbered as position 1.

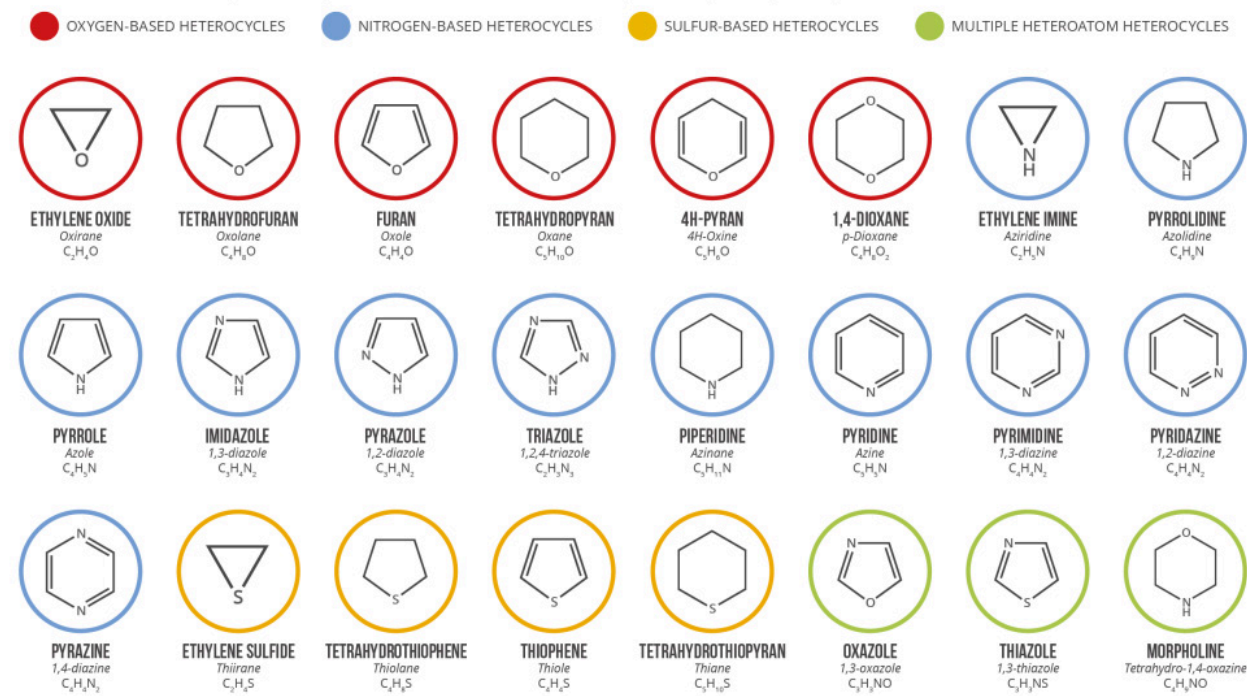
The structures of pyridine, pyrrole, quinoline, imidazole, indole, pyrimidine, pyrrolidine, and piperidine. The compounds are numbered from the nitrogen atom.

Figure 26.3a. Examples of heterocyclic amines. (Credit: Organic Chemistry, OpenStax, CC BY-NC-SA 4.0)

In addition to nitrogen heterocyclic rings, there are heterocyclic rings that contain oxygen and sulfur as well as nitrogen. Infographic 26.3a. shows the variety of heterocyclic rings in organic chemistry.

HETEROCYCLES IN ORGANIC CHEMISTRY

A HETEROCYCLE IN ORGANIC CHEMISTRY IS A RING OF CONNECTED ATOMS, WHERE ONE OR MORE OF THE ATOMS IN THE RING ARE ELEMENTS DIFFERENT FROM CARBON. HETEROCYCLES WITH OXYGEN, NITROGEN, AND SULFUR ARE THE MOST PREVALENT; SELENIUM, BORON, SILICON, ARSENIC & PHOSPHORUS CAN ALSO BE INCORPORATED.



© COMPOUND INTEREST 2014 - WWW.COMPOUNDCHEM.COM
Shared under a Creative Commons Attribution-NonCommercial-NoDerivatives licence.



Infographic 26.3a. Read more about “A Guide to Simple Heterocycles in Organic Chemistry (<https://www.compoundchem.com/2014/07/31/heterocycles/>)” by [Andy Brunning](#) / Compound Interest, CC BY-NC-ND, or access a text-based summary of infographic 26.3a [New tab].


Many heterocyclic amines occur naturally in plants. Like other amines, these compounds are basic. Such a compound is an **alkaloid**, a name that means “like alkalis.” Many alkaloids are physiologically active, including the familiar drugs caffeine, nicotine, and cocaine.

Spotlight on Everyday Chemistry: Scientist Gertrude B. Elion

Gertrude B. Elion won the 1988 Nobel Prize in Medicine for her work in medications. Many of the medications contain amine structures or heterocyclic rings. Read more in Infographic 26.3b.

TODAY IN CHEMISTRY HISTORY

23RD JANUARY – GERTRUDE B. ELION'S BIRTHDAY




GERTRUDE B. ELION

BORN

23 January 1918

DIED

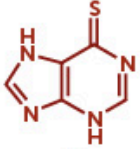
21 February 1999



1988

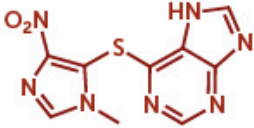
Elion was jointly awarded the 1988 Nobel Prize in Physiology or Medicine for work on the development of a number of drugs, based on biochemical differences between human and pathogen cells.

Working both alone and with George Hitchings, Elion discovered new drugs against a variety of diseases. Her name appears on 45 different patents and she was awarded 25 honorary doctorates.



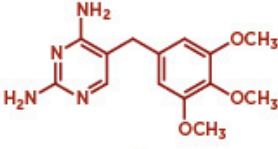
MERCAPTOPURINE

first treatment for leukemia



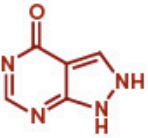
AZATHIOPRINE

to prevent transplant rejection



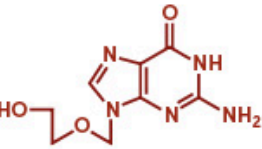
TRIMETHOPRIM

antibiotic



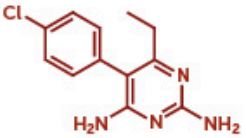
ALLOPURINOL

treatment for gout



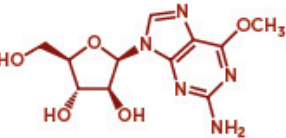
ACICLOVIR

antiviral for herpes infections



PYRIMETHAMINE


for malaria and toxoplasmosis



NELARABINE

treatment for cancer

© Andy Brunning/Compound Interest 2018 - www.compoundchem.com
 Shared under a Creative Commons Attribution-NonCommercial-NoDerivatives licence.



Infographic 26.3b. Read more about "Today in Chemistry History: Gertrude B Elion and drug discovery firsts (<https://www.compoundchem.com/2018/01/23/elion/>)" by Andy Brunning / Compound Interest, CC BY-NC-ND, or access a text-based summary of infographic 26.3b [New tab].

Three Well-Known Alkaloids

Caffeine (Figure 26.3b.) is a stimulant found in coffee, tea, and some soft drinks. Its mechanism of action is not well understood, but it is thought to block the activity of adenosine, a heterocyclic base that acts as a neurotransmitter, a substance that carries messages across a tiny gap (synapse) from one nerve cell (neuron) to another cell. The effective dose of caffeine is about 200 mg, corresponding to about two cups of strong coffee or tea. Infographic 26.3c. gives more details about coffee including why some brews are bitter.

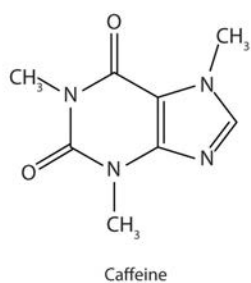
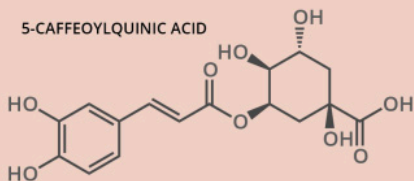


Figure 26.3b. Structural diagram for Caffeine (credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0).

THE CHEMISTRY OF COFFEE

WHY IS COFFEE BITTER?

5-CAFFEYOYLQUINIC ACID



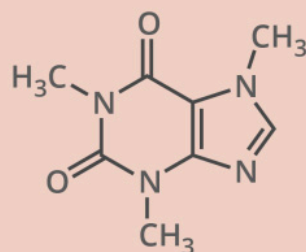
Chlorogenic acids account for up to 8% of the composition of unroasted coffee beans. More than 40 different varieties have been identified in green coffee beans, with 5-caffeoylquinic acid the most prevalent.

Chlorogenic acid content decreases when coffee beans are roasted, as they react to form quinolactones, phenylindanes & melanoidins. These contribute to flavour and bitterness.

3-CAFFEYOYLQUINIC-1,5-LACTONE



THE CAFFEINE CONTENT OF COFFEE



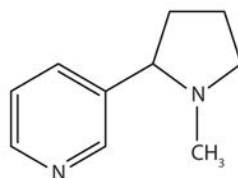
The caffeine content of coffee is variable but is approximately 100mg in a cup.

Caffeine works by blocking the action of a group of brain chemicals called adenosines, which work to naturally trigger tiredness.

The amount of caffeine in your bloodstream peaks 15 to 45 minutes after ingestion.

Infographic 26.3c. The Chemistry of Coffee. Read more about “Why is Coffee Bitter? – The Chemistry of Coffee (<https://www.compoundchem.com/2014/01/30/why-is-coffee-bitter-the-chemistry-of-coffee/>)” by Andy Brunning / Compound Interest, CC BY-NC-ND, or access a text-based summary of infographic 26.3c [New tab].

Nicotine (Figure 26.3c.) acts as a stimulant by a different mechanism; it probably mimics the action of the neurotransmitter acetylcholine. People ingest this drug by smoking or chewing tobacco. Its stimulant effect seems transient, as this initial response is followed by depression. Nicotine is highly toxic to animals. It is especially deadly when injected; the lethal dose for a human is estimated to be about 50 mg. Nicotine has also been used in agriculture as a contact insecticide.



Nicotine

Figure 26.3c. Structural diagram for Nicotine (credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0).

Cocaine (Figure 26.3d.) acts as a stimulant by preventing nerve cells from taking up dopamine, another neurotransmitter, from the synapse. High levels of dopamine are therefore available to stimulate the pleasure centers of the brain. The enhancement of dopamine action is thought to be responsible for cocaine's "high" and its addictive properties. After the binge, dopamine is depleted in less than an hour. This leaves the user in a pleasureless state and (often) craving more cocaine.

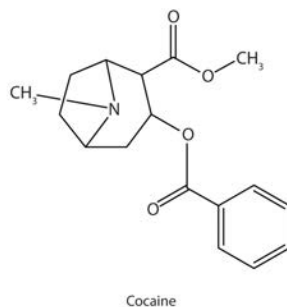


Figure 26.3d. Structural diagram for Cocaine (credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0).

Cocaine is used as the salt cocaine hydrochloride and in the form of broken lumps of the free (unneutralized) base (Figure 26.3e.), which is called *crack cocaine*.

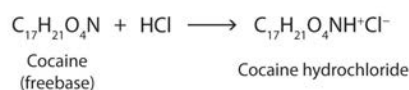


Figure 26.3e. Chemical reaction of Cocaine with Hydrochloric acid. (credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0).

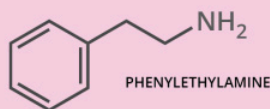
Because it is soluble in water, cocaine hydrochloride is readily absorbed through the watery mucous membranes of the nose when it is snorted. Crack cocaine is more volatile than cocaine hydrochloride. It vaporizes at the temperature of a burning cigarette. When smoked, cocaine reaches the brain in 15 s.

Spotlight on Everyday Chemistry: The Chemistry of Chocolate

Chocolate also has amine and heterocyclic compounds in it and one of these leads to toxicity in dogs. See Infographic 26.3d for more information.

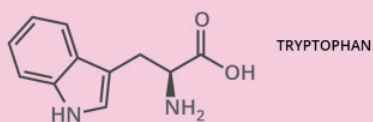
THE CHEMISTRY OF CHOCOLATE

IS CHOCOLATE AN APHRODISIAC?

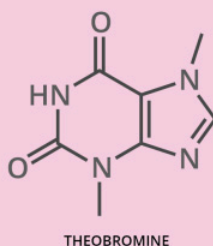


Phenylethylamine occurs naturally in the brain, and is often referred to as 'the love drug' due to its ability to produce feelings of well-being and contentment. It is also present in significant concentrations in chocolate, but since it is broken down after ingestion, it has been ruled out as causing a significant aphrodisiac effect.

Tryptophan is a chemical in the brain linked to the production of serotonin, the neurotransmitter that produces feelings of elation. It is present in chocolate, but only in small quantities, and it is unlikely that it causes any aphrodisiac effect.



WHY IS CHOCOLATE TOXIC TO DOGS?



Theobromine is a mild stimulant, similar in effect to caffeine, found in chocolate. This compound is harmless to humans at the levels found in chocolate - a fatal dose would require eating tens of kilograms of milk chocolate!

In cats & dogs, theobromine has a much more potent effect; small doses can lead to vomiting & diarrhoea, whilst as little as 50g of dark chocolate could kill a small dog.

© COMPOUND INTEREST 2014 - WWW.COMPOUNDCHEM.COM | Twitter: @compoundchem | Facebook: www.facebook.com/compoundchem
Photo: A Brunning. Graphic shared under a Creative Commons Attribution-NonCommercial-NoDerivatives licence.



Infographic 26.3d. Read more about "Toxicity & Aphrodisia – The Chemistry of Chocolate (<https://www.compoundchem.com/2014/02/13/toxicity-aphrodisia-the-chemistry-of-chocolate/>)" by Andy Brunning / Compound Interest, CC BY-NC-ND, or access a text-based summary of infographic 26.3d [New tab].

Attribution & References

Except where otherwise noted, this page is adapted by Caryn Fahey and Samantha Sullivan Sauer from

- "16.2: Naming and Drawing Amines" & "16.4: Heterocyclic Nitrogen Compounds" In *Map: Fundamentals of General Organic and Biological Chemistry* (McMurry et al.), CC BY-NC-SA 3.0, a remixed version of *Basics of GOB* (Ball et al.), CC BY-NC-SA 4.0 which is a LibreTexts version of *Introduction to Chemistry: GOB (v. 1.0)*, CC BY-NC-SA 3.0

26.4 BASICITY OF AMINES

Learning Objectives

By the end of this section, you will be able to:

- Name the typical reactions that take place with amines.

Like ammonia (NH_3), amines are weak bases due to the lone pair of electrons on their nitrogen atoms that can accept a proton from water to form substituted ammonium (NH_4^+) ions and hydroxide (OH^-) ions (Figure 26.4a.).

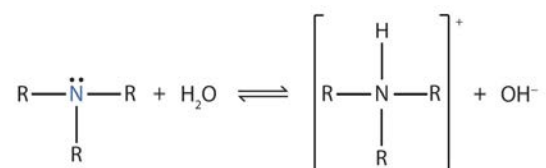


Figure 26.4a. Amines accepting protons from water to form ions (credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0).

As a specific example, methylamine reacts with water to form the methylammonium ion and the OH^- ion (Figure 26.4b.).

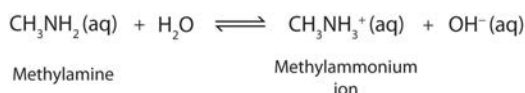


Figure 26.4b. Specific reaction of methylamine with water (credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0).

The basicity of an amine's nitrogen atom plays an important role in much of the compound's chemistry. Amine functional groups are found in a wide variety of compounds, including natural and synthetic dyes, polymers, vitamins, and medications such as penicillin and codeine. They are also found in many molecules

essential to life, such as amino acids, hormones, neurotransmitters, and DNA. For more information on DNA and its structure see Chapter 28.4 Nucleic Acids and DNA.

Nearly all amines, including those that are not very soluble in water, will react with strong acids to form salts soluble in water (Figure 26.4c.).

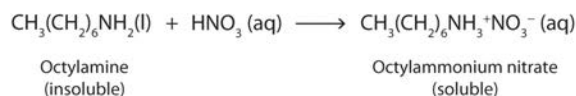


Figure 26.4c. An insoluble amine reacting with an acid to form a soluble salt (credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0).

Amine salts are named like other salts: the name of the cation is followed by the name of the anion.

Salts of aniline are properly named as *anilinium* compounds, but an older system, still in use for naming drugs, identifies the salt of aniline and hydrochloric acid as “aniline hydrochloride.” These compounds are ionic—they are salts—and the properties of the compounds (solubility, for example) are those characteristics of salts. Many drugs that are amines are converted to hydrochloride salts to increase their solubility in aqueous solution.

Example 26.4a

What are the formulas of the acid and base that react to form $[\text{CH}_3\text{NH}_2\text{CH}_2\text{CH}_3]^+\text{CH}_3\text{COO}^-$?

Solution

The cation has two groups—methyl and ethyl—attached to the nitrogen atom. It comes from ethylmethanamine ($\text{CH}_3\text{NHCH}_2\text{CH}_3$). The anion is the acetate ion. It comes from acetic acid (CH_3COOH).

Exercise 26.4a

What are the formulas of the acid and base that react to form $(\text{CH}_3\text{CH}_2\text{CH}_2)_3\text{NH}^+\text{I}^-$?

Check Your Answer:¹

Attribution & References

Except where otherwise noted, this page is adapted by Caryn Fahey from:

- “20.4: Amines and Amides” In *Chemistry 2e (Open Stax)* by Paul Flowers, Klaus Theopold, Richard Langley & William R. Robinson is licensed under CC BY 4.0. Access for free at Chemistry 2e (OpenStax).
- “16.5: Basicity of Amines” In *Map: Fundamentals of General Organic and Biological Chemistry (McMurry et al.)*, CC BY-NC-SA 3.0, a remixed version of *Basics of GOB (Ball et al.)*, CC BY-NC-SA 4.0 which is a LibreTexts version of *Introduction to Chemistry: GOB (v. 1.0)*, CC BY-NC-SA 3.0

Notes

1. tripropylamine and hydroiodic acid. Such reactions are common for stabilizing amine in medicine, cocaine and opioids. The nitrogen in this molecule becomes the central atom surrounded by three propyl carbon chains and the H^+I^- ions making the molecule net neutral overall.

26.5 AMIDES - STRUCTURES, PROPERTIES AND NAMING

Learning Objectives

By the end of this section, you will be able to:

- Identify the general structure for an amide.
- Identify the functional group for an amide.
- Name amides with common names.
- Name amides according to the IUPAC system.
- Compare the boiling points of amides with alcohols of similar molar mass.
- Compare the solubilities in water of amides of five or fewer carbon atoms with the solubilities of comparable alkanes and alcohols in water.

Amides are molecules that contain nitrogen atoms connected to the carbon atom of a carbonyl group. If the two remaining bonds on the nitrogen atom are attached to hydrogen atoms, the compound is a *simple amide*. If one or both of the two remaining bonds on the atom are attached to alkyl or aryl groups, the compound is a *substituted amide* (Figure 26.5a.).

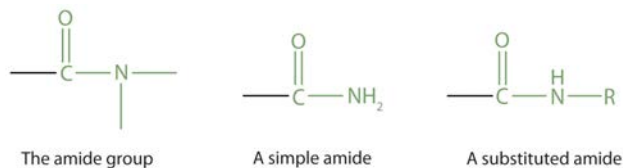


Figure 26.5a. Amide groups (Credit: *Introduction to Chemistry: GOB (V. 1.0)*, CC BY-NC-SA 3.0).

The carbonyl carbon-to-nitrogen bond is called an *amide linkage*. This bond is quite stable and is found in the repeating units of protein molecules, where it is called a *peptide linkage*.

Naming Amides

1. Primary amides are named by changing the name of the acid by dropping the -oic acid or -ic acid endings and adding -amide.
2. The carbonyl carbon is numbered carbon 1 on its location. It is not necessary to include the location number in the name because it is assumed that the functional group will be on the end of the parent chain.
3. Secondary amides are named by using an upper case N to designate that the alkyl group is on the nitrogen atom. Alkyl groups attached to the nitrogen are named as substituents. The letter N is used to indicate they are attached to the nitrogen.
4. Tertiary amides are named in the same way as secondary amides, but with two N's

Simple amides are named as derivatives of carboxylic acids. The *-ic* ending of the common name or the *-oic* ending of the International Union of Pure and Applied Chemistry (IUPAC) name of the carboxylic acid is replaced with the suffix *-amide* (Figure 26.5b.).



Figure 26.5b. Comparison of Formic acid and Formamide (Credit: *Introduction to Chemistry: GOB (V. 1.0)*, CC BY-NC-SA 3.0).

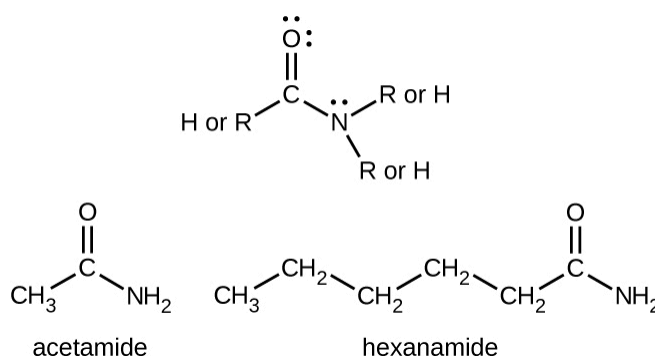


Figure 26.5c. Basic structure of an amide showcasing functional groups (credit: *General Chemistry 1 & 2*, CC BY 4.0).

Amides can be produced when carboxylic acids react with amines or ammonia in a process called **amidation**. A water molecule is eliminated from the reaction, and the amide is formed from the remaining pieces of the carboxylic acid and the amine (Figure 26.5d.) (note the similarity to formation of an ester from a carboxylic acid and an alcohol discussed in the previous section).

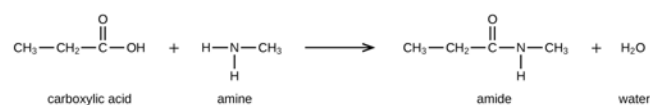


Figure 26.5d. Chemical reaction for formation of an amide (credit: *General Chemistry 1 & 2*, CC BY 4.0).

Example 26.5a

Give the IUPAC name for the following amides.

- $\text{CH}_3\text{CH}_2\text{C}=\text{O}(\text{NH}_2)$
- $\text{CH}_3\text{C}=\text{O}(\text{NH})\text{CH}_2\text{CH}_3$

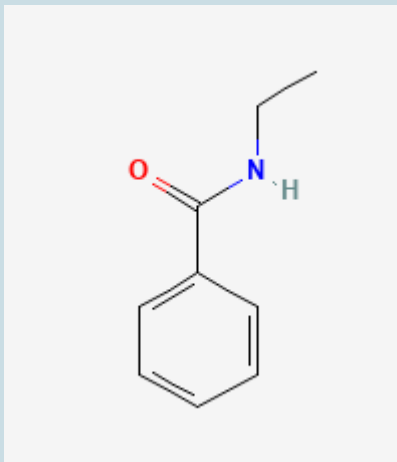
Solution

- propanamide (propionamide)
- N-ethylethanamide (N-ethylacetamide)

Exercise 26.5a

Write the IUPAC name for each of the following amides.

- $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{C}=\text{O}(\text{NH}_2)$
- $\text{CH}_3\text{CH}_2\text{CHClCH}_2\text{C}=\text{O}(\text{NH}_2)$

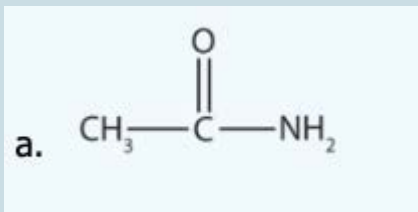


(credit: 2D
structure image of
CID 11959
(N-Ethylbenzamide
) via PubChem)

Check your answers: ¹

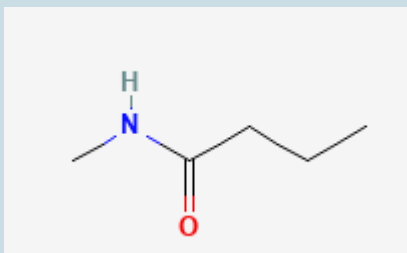
Exercise 26.5b

Name each compound with the common name, the IUPAC name or both.



(Credit:
*Introduction to
Chemistry: GOB (V.
1.0)*, CC BY-NC-SA
3.0).

b.



(credit: credit: 2D
structure image of
28774
(N-Methylbutyrami
de) via PubChem).

Check your answers: ²

The reaction between amines and carboxylic acids to form amides is biologically important. It is through this reaction that amino acids (molecules containing both amine and carboxylic acid substituents) link together in a polymer to form proteins.

PROTEINS AND ENZYMES

Proteins are large biological molecules made up of long chains of smaller molecules called amino acids. Organisms rely on proteins for a variety of functions—proteins transport molecules across cell membranes, replicate DNA, and catalyze metabolic reactions, to name only a few of their functions. The properties of proteins are functions of the combination of amino acids that compose them and can vary greatly. Interactions between amino acid sequences in the chains of proteins result in the folding of the chain into specific, three-dimensional structures that determine the protein's activity.

Enzymes are large biological molecules, mostly composed of proteins, which are responsible for the thousands of metabolic processes that occur in living organisms. Enzymes are highly specific catalysts; they speed up the rates of certain reactions. Enzymes function by lowering the activation energy of the reaction they are catalyzing, which can dramatically increase the rate of the reaction. Most reactions catalyzed by enzymes have rates that are millions of times faster than the non-catalyzed version.

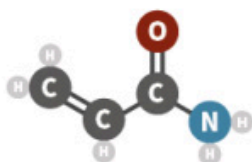
For more information on proteins see Chapter 28.3 Amino Acids, Proteins and Enzymes.

Spotlight on Everyday Chemistry: Acrylamide

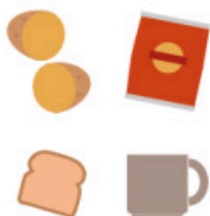
Acrylamide is found mainly in foods made from plants, that are high in carbohydrates and low in proteins. Examples of such foods include potato products, grain products or coffee. Acrylamide is more likely to build up when foods are cooked for longer periods of time or at higher temperatures. Acrylamide is known to cause cancer in experimental animals and is therefore a possible human carcinogen.

Chemical Concerns

DOES ACRYLAMIDE CAUSE CANCER?



ACRYLAMIDE

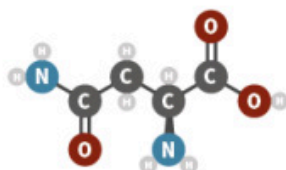


WHAT IS ACRYLAMIDE AND WHERE IS IT FOUND?

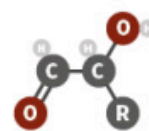
Acrylamide is a chemical formed by reactions that occur when carbohydrate-rich foods are cooked at high temperature. Low levels of it are found in foods including roast potatoes, toast, and potato chips. It's also found in roasted coffee beans and in cigarette smoke.

HOW DOES ACRYLAMIDE FORM IN FOODS?

When carbohydrate-rich foods are cooked at high temperature (above 120°C) amino acids can combine with reducing sugars (such as glucose) to form a range of products. The amino acid asparagine, combines with sugars to produce acrylamide. Higher temperatures and longer cooking times produce more acrylamide.



ASPARAGINE



REDUCING SUGAR

Acrylamide is classified as a probable human carcinogen; however, the amounts found in food are very low.

TOASTED BREAD



4.8 MICROGRAMS

(assumes 1 slice = 24 grams)

POTATO CRISPS



12.4 MICROGRAMS

(assumes packet = 32.5 grams)

AV. DAILY INTAKE



30 MICROGRAMS

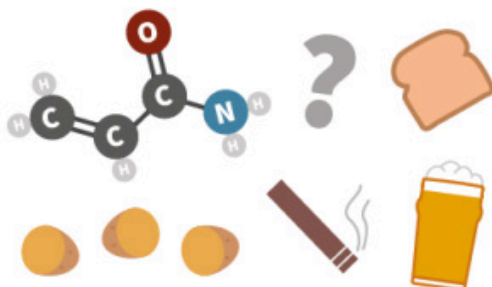
(assumes body weight = 75kg)

MAX. RECOMMENDED DAILY INTAKE



195 MICROGRAMS

(assumes body weight = 75kg)



SHOULD I BE WORRIED ABOUT ACRYLAMIDE?

Dietary levels of acrylamide are a minor concern for a small increased lifetime risk of cancer. This is based on animal studies – evidence for increased risk in humans is currently minimal. Increases in cancer risk associated with regularly drinking alcohol or smoking are much higher. The latest advice recommends cooking foods a little less brown to reduce acrylamide content.

IN SHORT: ACRYLAMIDE HASN'T BEEN DECISIVELY LINKED TO INCREASED CANCER RISK AT LEVELS FOUND IN COOKED FOODS



© Andy Brunning/Compound Interest 2017 - www.compoundchem.com
Twitter: @compoundchem | Facebook: www.facebook.com/compoundchem
Shared under a Creative Commons Attribution-NonCommercial-NoDerivatives licence



Infographic 26.5a. Infographic describing acrylamide and its possible increase in cancer risk. Read more about “Chemical Concerns – Does Acrylamide in Toast & Roast Potatoes Cause Cancer?” (<https://www.compoundchem.com/2017/01/24/acrylamide/>)” by Andy Brunning / Compound Interest, CC BY-NC-ND, or access a text-based summary of infographic 26.5a [New tab].

Watch Properties of Amides on YouTube (8 min). (https://youtu.be/b_1GoxLmDV4?)

Indigenous Perspectives: Hákarl (Iceland)

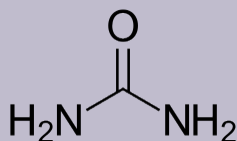


Figure 26.5e. The molecular structure of urea (credit: Image by NEUROtiker, PDM).

Hákarl is a fermented Greenland shark, which is the national dish of Iceland. The process of fermenting the shark is essential as fresh shark meat is poisonous as it contains urea (Figure 26.5e.) and trimethylamine oxide. See the **Day 13: Iceland: Hákarl infographic** (<https://www.compoundchem.com/2023advent/#day13>) for further information.

Physical Properties of Amides

With the exception of formamide (HCONH_2), which is a liquid, all simple amides are solids (Table 26.5a.). The lower members of the series are soluble in water, with borderline solubility occurring in those that have five or six carbon atoms. Like the esters, solutions of amides in water usually are neutral—neither acidic nor basic.

Table 26.5a. *Physical Constants of Some Unsubstituted Amides*

Condensed Structural Formula	Name	Melting Point (°C)	Boiling Point (°C)	Solubility in Water
HCONH ₂	formamide	2	193	soluble
CH ₃ CONH ₂	acetamide	82	222	soluble
CH ₃ CH ₂ CONH ₂	propionamide	81	213	soluble
CH ₃ CH ₂ CH ₂ CONH ₂	butyramide	115	216	soluble
C ₆ H ₅ CONH ₂	benzamide	132	290	slightly soluble

Source: “15.14: Physical Properties of Amides” In *Basics of GOB Chemistry* (Ball et al.), CC BY-NC-SA 4.0.

The amides generally have high boiling points and melting points. These characteristics and their solubility in water result from the polar nature of the amide group and hydrogen bonding (Figure 26.5f.). (Similar hydrogen bonding plays a critical role in determining the structure and properties of proteins, deoxyribonucleic acid [DNA], ribonucleic acid [RNA], and other giant molecules so important to life processes.

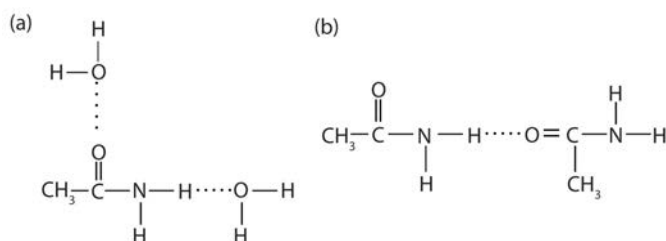


Figure 26.5f. Hydrogen Bonding in Amides. Amide molecules can engage in hydrogen bonding with water molecules (a). Those amides with a hydrogen atom on the nitrogen atom can also engage in hydrogen bonding (b). Both hydrogen bonding networks extend in all directions. (Credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0, edited by (Ball et al.), CC BY-NC-SA 4.0)

Spotlight on Everyday Chemistry: Urea

Urea (CO(NH₂)₂) is a diamide containing two amide groups joined by a carbonyl functional group. Urea is the main component of urine consisting of nitrogenous waste products from the metabolic breakdown of proteins. The liver produces enzymes which form urea which is then transported to the kidney's for removal from the body. Urea a colourless, odourless

solid which is highly soluble in water and when dissolved in water is neither acidic nor alkaline. Urea is widely used in fertilizers as a nitrogen source and is an important raw material for chemical industry.

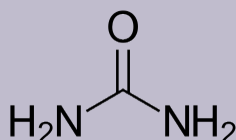


Figure 26.5g. The molecular structure of urea. (credit: Image by NEUROtiker, PDM).

Attribution & References

Except where otherwise noted, this page is adapted by Caryn Fahey from:

- “15.13: Amides- Structures and Names” & “15.14: Physical Properties of Amides” In Basics of General, Organic, and Biological Chemistry (Ball et al.) by David W. Ball, John W. Hill, and Rhonda J. Scott via LibreTexts, CC BY-NC-SA 4.0./ A LibreTexts version of *Introduction to Chemistry: GOB (v. 1.0)*, CC BY-NC 3.0.
- “18.4 Amines and Amides” In *General Chemistry 1 & 2* by Rice University, a derivative of *Chemistry (Open Stax)* by Paul Flowers, Klaus Theopold, Richard Langley & William R. Robinson and is licensed under CC BY 4.0. Access for free at *Chemistry (OpenStax)* (<https://openstax.org/books/chemistry/pages/1-introduction>)

References cited in-text

National Center for Biotechnology Information (2024). *PubChem Compound Summary for CID 11959, N-Ethylbenzamide* (<https://pubchem.ncbi.nlm.nih.gov/compound/N-Ethylbenzamide>). Retrieved February 7, 2024.

National Center for Biotechnology Information (2024). *PubChem Compound Summary for CID 28774, N-Methylbutyramide* (<https://pubchem.ncbi.nlm.nih.gov/compound/N-Methylbutyramide>). Retrieved February 7, 2024

Notes

1. a. pentanamide, b. 3-chloropentanamide, c. N-ethylbenzamide
2. a. acetamide (or ethanamide IUPAC), b. N-methylbutanamide

26.6 CHEMICAL PROPERTIES OF AMINES AND AMIDES

Learning Objectives

By the end of this section, you will be able to:

- Identify the typical reaction that amides undergo.
- Identify and describe the substances from which most amines and amides are prepared.
- Describe the preparation procedure for amines and amides.

Organic functional groups can be converted into other functional groups through reactions. A map of some of the more common reactions to convert functional groups can be found in Section 19.6 – General Reactions of Carbon in Infographic 19.6a.

Reactions of Amides

Generally, amides resist hydrolysis in plain water, even after prolonged heating. In the presence of added acid or base, however, hydrolysis proceeds at a moderate rate. In living cells, amide hydrolysis is catalyzed by enzymes. Amide hydrolysis is illustrated in Figure 26.6a.

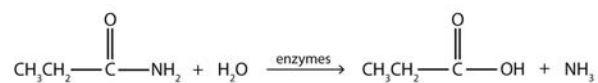


Figure 26.6a. Hydrolysis of an amide in acid solution actually gives a carboxylic acid and the *salt* of ammonia or an amine (the ammonia or amine initially formed is neutralized by the acid). Basic hydrolysis gives a salt of the carboxylic acid and ammonia or an amine. (Credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0)

Example 26.6a

Write the equation for the hydrolysis of each compound.

- butyramide
- benzamide

Solution

- a. The hydrolysis of a simple amide produces an organic acid and ammonia. Butyramide thus yields butyric acid and ammonia.

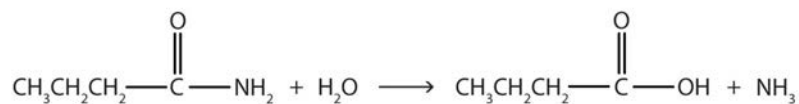


Figure 26.6b.
Solution for
reaction of
butyramide and
water.

- b. The hydrolysis of an amide produces an organic acid and ammonia. Benzamide thus yields benzoic acid and ammonia.

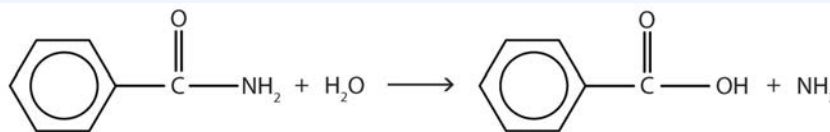


Figure 26.6c.
Reaction of
benzamide and
water.

Exercise and Image Source: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0

Exercise 26.6a

What are the products of the hydrolysis of an amide?

Check Your Answers:¹

Exercise 26.6b

When the amide $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CONH}_2$ is hydrolyzed in an NaOH solution, the products are $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}^- \text{Na}^+$ and NH_3 . What products are obtained when $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CONH}_2$ is hydrolyzed in an hydrochloric acid solution?

Check Your Answers:²

Formation of Amides

Amides can be produced when carboxylic acids react with amines or ammonia in a process called **amidation**. A water molecule is eliminated from the reaction, and the amide is formed from the remaining pieces of the carboxylic acid and the amine (note the similarity to formation of an ester from a carboxylic acid and an alcohol discussed in the previous section).

When a carboxylic acid reacts with ammonia (NH_3) a *primary amide* is formed. But the reaction is very slow at room temperature. Water molecules are split out, and a bond is formed between the nitrogen atom and the carbonyl carbon atom (Figure 26.6d.).



Figure 26.6d. (Credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0)

When a carboxylic acid reacts with primary or secondary amines, secondary or tertiary amides are produced, respectively (Figure 26.6e).



Figure 26.6e. Reaction of a carboxylic acid and amine produce an amide and water. (Credit: *Chemistry (OpenStax)*, CC BY 4.0)

Tertiary amines do not have a hydrogen attached to the nitrogen and therefore do not form amides when mixed with carboxylic acids. However, an acid-base reaction does occur with the amine accepting a proton (acts as a base) and the carboxylic acid donating a proton. In this case the ammonium and carboxylate salts are formed.

In living cells, amide formation is catalyzed by enzymes. Proteins, which make up all enzymes, are polyamides; they are formed by joining amino acids into long chains. In proteins, the amide functional group is called a *peptide bond*.

Carboxylic acids will react with alcohols and amines following a similar pattern. In both cases, the -OH group of the carboxylic acid will be replaced by a different group to form either an ester or an amide, with water formed as a by-product. When the reaction involves an alcohol, the -OH of the acid is replaced by the $\text{-OR}'$ of the alcohol (Figure 26.6f.). When the reaction involves an amine, the -OH of the acid is replaced by the -NH_2 , or $\text{-NHR}'$, or $\text{-NR}'_2$ of the amine (Figure 26.6g.).

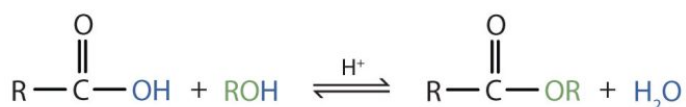


Figure 26.6f. Formation of an ester. (Credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0)



Figure 26.6g. Formation of an amide. (Credit: *Intro Chem: GOB (V. 1.0)*, CC BY-NC-SA 3.0)

Amides can also be prepared from the reaction of an acid chloride with ammonia. Refer to Section 25.3 Formation and Reactions of Carboxylic Acids where the formation of acid chlorides is discussed as well as their reaction with ammonia.

Formation of Amines

Reduction of Amides

Like other carboxylic acid derivatives, amides can be reduced by LiAlH_4 . The product of the reduction, however, is an amine rather than an alcohol (Figure 26.6h.). The net effect of an amide reduction is thus the conversion of the amide carbonyl group into a methylene group ($\text{C}=\text{O} \rightarrow \text{CH}_2$). This kind of reaction is specific to amides and does not occur with other carboxylic acid derivatives.

The reduction reaction of *N*-methyldodecanamide with lithium aluminum hydride followed by hydrolysis gives dodecylmethylamine (ninety-five percent). The carbonyl group is reduced to CH_2 .

Figure 26.6h. Reaction of an amide with lithium aluminum hydride and hydrolysis to form an amine (Credit: Organic Chemistry (OpenStax), CC BY-NC-SA 4.0).

Example 26.6b

Synthesizing an Amine from an Amide

How could you prepare *N*-ethylaniline by reduction of an amide with LiAlH_4 ?

The structure of *N*-ethylaniline, a derivative of aniline where an ethyl group replaces one of the hydrogen atoms of the amine.

Figure 26.6i. Reduction of an amide with lithium aluminum hydride to produce *N*-ethylaniline (Credit: Organic Chemistry (OpenStax), CC BY-NC-SA 4.0).

Strategy

Reduction of an amide with LiAlH_4 yields an amine. To find the starting material for synthesis of *N*-ethylaniline, look for a CH_2 position next to the nitrogen atom and replace that CH_2 by $\text{C}=\text{O}$. In this case, the amide is *N*-phenylacetamide.

Formula does not parse

Solution

The reaction shows the reduction of N-phenylacetamide using lithium aluminum hydride in ether followed by addition of water to form N-ethylaniline.

Figure 26.6j. Reduction of an amide with lithium aluminum hydride and hydrolysis to form an N-Ethylaniline. (Credit: *Organic Chemistry* (OpenStax), CC BY-NC-SA 4.0).

Reduction of Nitriles

Using lithium aluminum hydride (LiAlH_4), a nitrile can be reduced to a primary amine (Figure 26.6k.). The process to predict the product of a hydride reduction is shown in Figure 26.6l. (Farmer et al., n.d.).

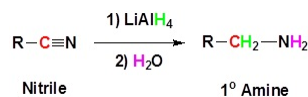


Figure 26.6k. Reduction of a nitrile to form a primary amine. (credit: *Organic Chemistry* (Morsch et al.), CC BY-SA 4.0.)

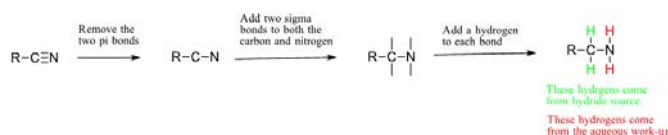
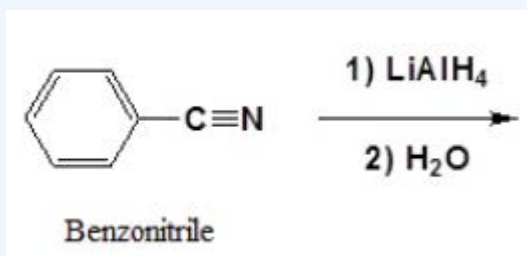


Figure 26.6l. Prediction of product of nitrile reduction (credit: *Organic Chemistry* (Morsch et al.), CC BY-SA 4.0).

Example 26.6c

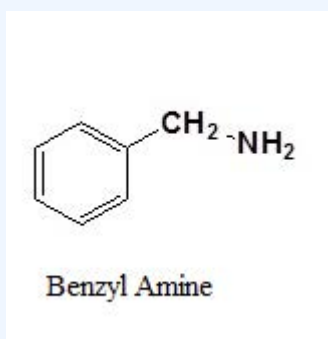
Write the product from this reaction.



(credit: *Organic Chemistry (Morsch et al.)*, CC BY-SA 4.0.)

Solution:

Following the process outlined in Figure 26.6l, the answer is



(credit: *Organic Chemistry (Morsch et al.)*, CC BY-SA 4.0.)

Source: Example 26.6c is adapted from “20.7: Chemistry of Nitriles” by Steven Farmer, Dietmar Kennepohl, Layne Morsch, William Reusch In *Organic Chemistry (Morsch et al.)*, CC BY-SA 4.0. / Image cut in two.

The formation of nitriles ($R-C\equiv N$) can be found in Section 25.3 – Formation and Reactions of Carboxylic Acids.

Alkylation of Ammonia

Another way to produce an amine is to react an alkyl halide (also called haloalkane) with ammonia. This reaction substitutes one hydrogen of the ammonia with the alkyl portion of the alkyl halide. It can be completed with ammonia to produce a 1° amine or with a 1° amine to produce a 2° amine or with a 2° amine to produce a 3° amine.

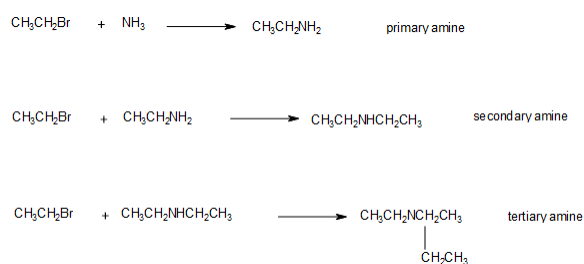
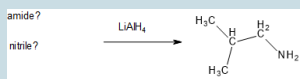


Figure 26.6m. Formation of primary amine from ammonia, secondary amine from primary amine, and tertiary amine from secondary amine through alkylation (credit: *Supplemental Modules*, CC BY-NC 4.0 / Adapted by Samantha Sullivan Sauer / Biovia Draw)

Exercise 26.6c

Write the structures of the amide and the nitrile that when reduced produce this amine.



(credit: Samantha Sullivan Sauer / Biovia Draw, CC BY-NC 4.0)

Check Your Answers:³

Source: Exercise 26.6c created by Samantha Sullivan Sauer, images drawn using Biovia Draw, CC BY-NC 4.0

Attribution & References

Except where otherwise noted, this page is written and adapted by Caryn Fahey and Samantha Sullivan Sauer from

- “15.16: Chemical Properties of Amides- Hydrolysis” In Basics of General, Organic, and Biological Chemistry (Ball et al.) by David W. Ball, John W. Hill, and Rhonda J. Scott via LibreTexts, CC BY-NC-SA 4.0./ A LibreTexts version of *Introduction to Chemistry: GOB (v. 1.0)*, CC BY-NC 3.0.
- “20.7: Chemistry of Nitriles” by Steven Farmer, Dietmar Kennepohl, Layne Morsch, William Reusch In *Organic Chemistry (Morsch et al.)*, CC BY-SA 4.0.

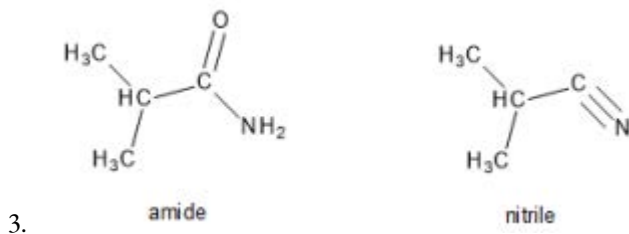
- “17.3: Reactions of Carboxylic Acids – Ester and Amide Formation” In *Map: Fundamentals of General Organic and Biological Chemistry (McMurry et al.)*, CC BY-NC-SA 3.0, a remixed version of *Basics of GOB (Ball et al.)*, CC BY-NC-SA 4.0 which is a LibreTexts version of *Introduction to Chemistry: GOB (v. 1.0)*, CC BY-NC-SA 3.0
- “21.7 Chemistry of Amides” In *Organic Chemistry (OpenStax)* by John McMurry, licensed under CC BY-NC-SA 4.0. Access for free at *Organic Chemistry (OpenStax)*.
- “Reaction of Alkyl Halides with Ammonia” by Jim Clark In *Supplemental Modules*, CC BY-NC 4.0

References cited in-text

Farmer, S., Kennepohl, D., Morsch, L., & Reusch, W. (n.d.). 20.7: Chemistry of Nitriles. In *Organic Chemistry (Morsch et al.)*. LibreTexts. CC BY-SA 4.0.

Notes

1. a carboxylic acid and ammonia or an amine
2. $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$ and NH_4Cl



CHAPTER 26 - SUMMARY

26.1 Amines – Structure and Naming

Amines are nitrogen-containing organic molecules derived from ammonia (NH_3). A primary (1°) amine (RNH_2) has one organic group bonded to the nitrogen atom, a secondary (2°) amine (R_2NH) has two organic groups bonded to the nitrogen atom, and a tertiary (3°) amine (R_3N) has three organic groups bonded to the nitrogen atom. A cyclic compound in which the ring contains one or more noncarbon atoms is called a heterocyclic compound. Alkaloids are heterocyclic amines found in many plants. Caffeine, nicotine, and cocaine are familiar alkaloids.

An amine is a derivative of ammonia in which one, two, or all three hydrogen atoms are replaced by hydrocarbon groups.

Amines are classified as primary, secondary, or tertiary by the number of hydrocarbon groups attached to the nitrogen atom. Amines are named by naming the alkyl groups attached to the nitrogen atom, followed by the suffix *-amine*.

26.2 Amines – Physical Properties

Primary and secondary amines have higher boiling points than those of alkanes or ethers of similar molar mass because they can engage in intermolecular hydrogen bonding. Their boiling points are lower than those of alcohols because alcohol molecules have hydrogen atoms bonded to an oxygen atom, which is more electronegative.

The boiling points of tertiary amines, which cannot engage in hydrogen bonding because they have no hydrogen atom on the nitrogen atom, are comparable to those of alkanes and ethers of similar molar mass.

Because all three classes of amines can engage in hydrogen bonding with water, amines of low molar mass are quite soluble in water.

26.3 Heterocyclic Nitrogen Compounds

Amines are bases; they react with acids to form salts. Salts of aniline are properly named as *anilinium* compounds, but an older system is used to name drugs: the salts of amine drugs and hydrochloric acid are called “hydrochlorides.” Heterocyclic amines are cyclic compounds with one or more nitrogen atoms in the ring.

26.4 Basicity of Amines

Amines are weak bases due to the lone pair of electrons on their nitrogen atoms. They can accept protons. Nearly all amines, including those that are not very soluble in water, will react with strong acids to form salts soluble in water.

26.5 Amides – Structures, Properties and Naming

Organic compounds containing a carbonyl group bonded to a nitrogen atom are amides, and the carbon-to-nitrogen bond is an amide linkage (or a peptide linkage). Most amides are colourless and odourless, and the lighter ones are soluble in water. Because they are polar molecules, amides have comparatively high boiling points and melting points. Amides are synthesized from carboxylic acids and NH_3 or amines. Amides are neutral compounds. They resist hydrolysis in water, but acids, bases, and enzymes catalyze the reaction.

Most amides are solids at room temperature; the boiling points of amides are much higher than those of alcohols of similar molar mass. Amides of five or fewer carbon atoms are soluble in water. Amides are prepared by the reaction of a carboxylic acid with ammonia or an amine.

26.6 Chemical Properties of Amines and Amides

The hydrolysis of an amide produces a carboxylic acid and ammonia. Primary amides are formed from the reaction of a carboxylic acid with ammonia. Secondary amides are formed from the reaction of a carboxylic acid and a primary amine. Tertiary amides are formed from the reaction of a carboxylic acid and a secondary amine. Amines are formed through the reduction of amides or the reduction of nitriles. Amines can also be formed through the alkyl halide substitution of ammonia or lower classed amines.

Attribution & References

Except where otherwise noted, this content has been adapted by Caryn Fahey and Samantha Sullivan Sauer from:

- 26.1 Summary -“15.18 End-of-Chapter Material” In *Introduction to Chemistry: General, Organic, and Biological (v. 1.0)*, CC BY-NC-SA 3.0 and “15.11 Amines: Structures and Names” In *Introduction to Chemistry: General, Organic, and Biological (v. 1.0)*, CC BY-NC-SA 3.0
- 26.2 Summary – “15.12 Physical Properties of Amines” In *Introduction to Chemistry: General, Organic, and Biological (v. 1.0)*, CC BY-NC-SA 3.0
- 26.3 summary – “15.13 Amines as Bases” In *Introduction to Chemistry: General, Organic, and Biological*

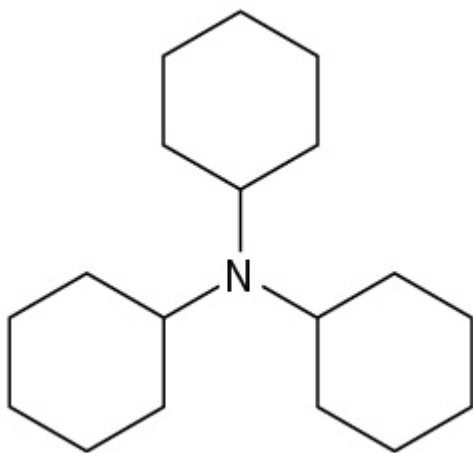
(v. 1.0), CC BY-NC-SA 3.0

- 26.4 summary – “11.10: Chemical Properties: Amines as Bases” In *USC Upstate: CHEM U109 – Chemistry of Living Things (Mueller)*, CC BY-NC-SA 4.0 license and was authored, remixed, and/or curated by LibreTexts.
- 26.5 summary – “18.15 Physical properties of amides“, “18.14 Amides: Structures and Names“, “18.16 Formation of Amides” and End-of-Chapter Material In *Introduction to Chemistry: GOB (v. 1.0)*, CC BY-NC 3.0
- 26.6 summary – “18.17 Chemical Properties of Amides: Hydrolysis” and written by Samantha Sullivan Sauer

CHAPTER 26 - REVIEW

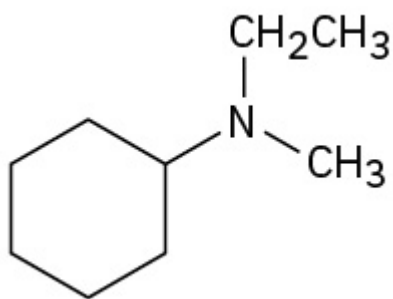
26.1 Amines – Structure and Naming

1. Draw the structure for each compound and classify.
 - a. ethylisopropylamine **Check answer**¹
 - b. diethylpropylamine
2. Name and classify each compound.
 - a. $\text{CH}_3\text{CH}_2\text{CH}_2\text{NH}_2$
 - b. $\text{CH}_3\text{CH}_2\text{NHCH}_2\text{CH}_3$
 - c. $\text{CH}_3\text{CH}_2\text{CH}_2\text{NHCH}_3$**Check answer**²
3. Draw the structure for each compound and classify.
 - a. isopropyldimethylamine . **Check answer**³
 - b. dipropylamine **Check answer**⁴
4. Name the following compounds.



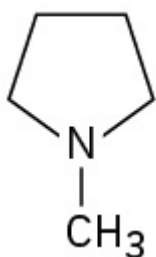
(credit: Organic Chemistry (OpenStax) (<https://openstax.org/books/organic-chemistry/pages/24-1-naming-amines>), CC BY-NC-SA 4.0)

- a. **Check answer**⁵



(credit: Organic Chemistry (OpenStax) (<https://openstax.org/books/organic-chemistry/pages/24-1-naming-amines>), CC BY-NC-SA 4.0)

b. **Check answer**⁶



(credit: Organic Chemistry (OpenStax) (<https://openstax.org/books/organic-chemistry/pages/24-1-naming-amines>), CC BY-NC-SA 4.0)

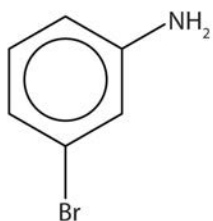
c. **Check answer**⁷

26.2 Amines – Physical Properties

- Which compound of each pair has the higher boiling point? Explain.
 - butylamine or pentane **Check answer**⁸
 - CH_3NH_2 or $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$ **Check answer**⁹
- Which compound is more soluble in water— $\text{CH}_3\text{CH}_2\text{CH}_3$ or $\text{CH}_3\text{CH}_2\text{NH}_2$? Explain. **Check answer**¹⁰

26.3 Heterocyclic Nitrogen Compounds

- Name this compound. **Check answer**¹¹



(credit:
Introduction to
Chemistry: GOB
(v. 1.0), CC BY-NC
3.0)

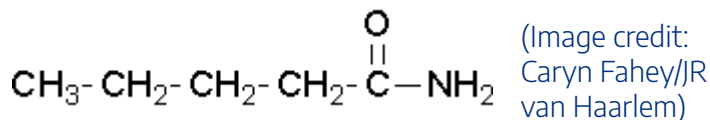
2. What is a heterocyclic compound? **Check answer**¹²

26.4 Basicity of Amines

1. Explain the basicity of amines. **Check answer**¹³
2. Contrast the physical properties of amines with those of alcohols and alkanes. **Check answer**¹⁴

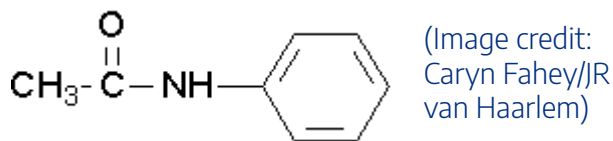
26.5 Amides – Structures, Properties and Naming

1. Draw a structure for the following compound: 3-chlorobenzamide. **Check answer**¹⁵
2. Try to name the following compound:



Check answer¹⁶

3. Try to draw a structure for the following compound: N,N-dimethylformamide. **Check answer**¹⁷
4. Try to name the following compound:



Check answer¹⁸

5. Try to draw a structure for N,N-dimethylformamide.

Check answer¹⁹

26.6 Chemical Properties of Amines and Amides

- Write the equation for the hydrolysis of each compound.
 - butyramide **Check answer**²⁰
 - benzamide **Check answer**²¹
- What are the products of the hydrolysis of an amide? **Check answer**²²
- When the amide $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CONH}_2$ is hydrolyzed in an NaOH solution, the products are $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}^-\text{Na}^+$ and NH_3 . What products are obtained when $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CONH}_2$ is hydrolyzed in a hydrochloric acid solution? **Check answer**²³

Links to Enhanced Learning

Create your own organic nomenclature quiz to identify, name and draw amines and amides using Organic Nomenclature [New tab] (<https://orgchem101.com/nom/en/index.php>). You can customize the types of questions you receive and get instant feedback.

Find a detailed video here for naming amines Khan Academy – Amines [New tab] (<https://www.khanacademy.org/science/organic-chemistry/amines-topic/naming-amines/v/amine-naming-introduction>)

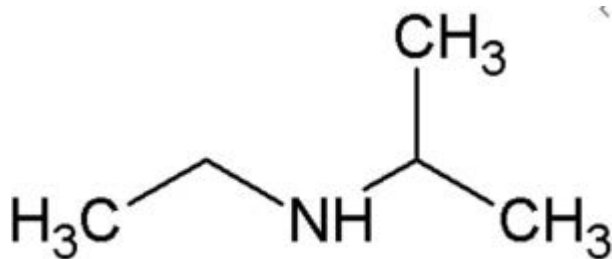
Attribution & References

Except where otherwise noted, this page (including images in solutions) is written and adapted by Caryn Fahey from:

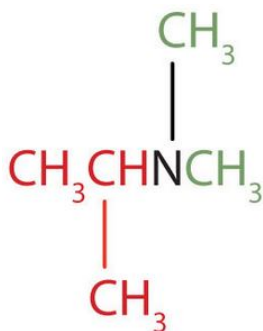
- “Amines: Structures and Names“, “Physical Properties of Amines“, “Amines: Structures and Names” and “Chemical Properties of Amides” In *Introduction to Chemistry: GOB (v. 1.0)*, CC BY-NC 3.0
- “Amines and Heterocycles” In *Organic Chemistry (OpenStax)* (<https://openstax.org/books/organic-chemistry/pages/1-why-this-chapter>) by John McMurry, CC BY-NC-SA 4.0. Access for free at *Organic Chemistry (OpenStax)* (<https://openstax.org/books/organic-chemistry/pages/1-why-this-chapter>)
- Images that are not marked otherwise are adapted from course materials by Caryn Fahey and JR van Haarlem
- Images in solutions are from the original source, except:

- 26.1 Question 1a: Image by Fran Ara, CC BY-SA 4.0
- 26.1 Question 3a: *Introduction to Chemistry: GOB (v. 1.0)*, CC BY-NC 3.0
- 26.5 Question 1, 3, 5: Caryn Fahey/JR van Haarlem
- 26.6 Question 1: *Introduction to Chemistry: GOB (v. 1.0)*, CC BY-NC 3.0

Notes

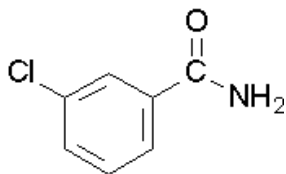


- a.
- a. There is only one alkyl group attached to the nitrogen atom, so the amine is primary. A group of three carbon atoms (a propyl group) is attached to the NH₂ group through an end carbon atom, so the name is propylamine, b. There are two ethyl groups attached to the nitrogen atom; the amine is secondary, so the compound is diethylamine, c. The nitrogen atom has a methyl group and a propyl group, so the compound is methylpropylamine, a secondary amine.



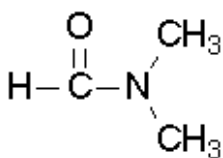
- The name indicates that there are an isopropyl group (in red) and two methyl groups (in green) attached to the nitrogen atom; the amine is tertiary.
- b. The name indicates that there are two propyl groups attached to the nitrogen atom; the amine is secondary. (The third bond on the nitrogen atom goes to a hydrogen atom.) $\text{CH}_3\text{CH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{CH}_3$
- tricyclohexylamine
- N-ethyl-N-methylcyclohexylamine
- N-Methylpyrrolidine
- butylamine because the N-H bonds can engage in hydrogen bonding; pentane cannot engage in hydrogen bonding
- $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$ because it has a greater molar mass than CH_3NH_2
- $\text{CH}_3\text{CH}_2\text{NH}_2$ because amines can engage in hydrogen bonding with water; alkanes cannot engage in hydrogen bonding
- The benzene ring with an amino (NH₂) group is aniline. The compound is named as a derivative of aniline: 3-bromoaniline or m-bromoaniline.
- Heterocyclic compounds are ring compounds with atoms other than carbon atoms in the ring.
- Amines have a lone pair of electrons on the nitrogen atom and can thus act as proton acceptors (bases).

14. The solubilities of amines are similar to those of alcohols; the boiling points of primary and secondary amines are similar to those of alcohols; the boiling points of tertiary amines, which cannot engage in hydrogen bonding because they do not have a hydrogen atom on the nitrogen atom, are comparable to those of alkanes.



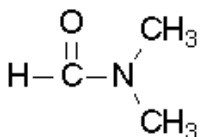
15.

16. pentamide



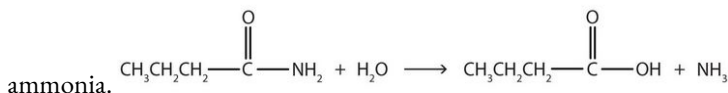
17.

18. N-phenylethanamide or N-phenylacetamide

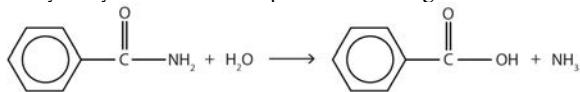


19.

20. The hydrolysis of a simple amide produces an organic acid and ammonia. Butyramide thus yields butyric acid and ammonia.



21. The hydrolysis of an amide produces an organic acid and ammonia. Benzamide thus yields benzoic acid and ammonia.



22. a carboxylic acid and ammonia or an amine

- 23.
- $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$
- and
- NH_4Cl

CHAPTER 26 - INFOGRAPHIC DESCRIPTIONS

Infographics used in Chapter 26

- 26.0a Hay Fever & Hay Fever Medications
- 26.2a The Chemicals in Cigarette Smoke & Their Effects
- 26.2b RTC Week 2015 – #3: Nitrogen-Containing Atmospheric Pollutants
- 26.3a A Guide to Simple Heterocycles in Organic Chemistry
- 26.3b Today in Chemistry History: Gertrude B Elion and drug discovery firsts
- 26.3c Why is Coffee Bitter? – The Chemistry of Coffee
- 26.3d Toxicity & Aphrodisia – The Chemistry of Chocolate
- 26.5a Chemical Concerns – Does Acrylamide in Toast & Roast Potatoes Cause Cancer?

26.0a Hay Fever & Hay Fever Medications

The cause of hay fever: trees, grass, weed pollens.

- 10-15% of the UK population is affected by hay fever.
- 90-95% of hay fever sufferers are allergic to grass pollen

The allergic response:

1. Pollen exposure results in the body misidentifying it as a threat; antibodies are released to combat it.
2. The antibodies produced bind to two types of cell in tissues – mast cells and basophils.
3. These release several chemicals, including histamine, which produce an inflammatory response.
4. Symptoms of this response include a runny nose, itching, sneezing fits, and nasal congestion.

Antihistamines for hay fever:

- Cetirizine and loratadine block histamine action, prevent most symptoms.

- Nasal sprays.

All oral formulations for treatment of hay fever are antihistamines. These bind to H₁ histamine receptors instead of histamine, preventing the effects produced by the allergic response – although they may be clear blocked noses.

First generation antihistamines can cause undesirable effects, including sedation. Second generation are less likely to exhibit sedative effects, particularly loratadine, Peak levels of antihistamines are generally reached one hour after taking.

Take when hay fever symptoms are expected, rather than when they have already started. This is because they cannot reverse the effects of histamine already binding to the H₁ receptors, and so will not provide relief.

Sodium cromoglycate prevents release of histamine. Commonly used in eye drop solutions, sodium cromoglycate prevents hay fever symptoms by stabilizing mast cells, and preventing them from releasing histamine. Unlike anti-histamines, it is effective at remedying itchy eyes even after symptoms have started.

Corticosteroids prevent the inflammatory symptoms of hay fever. Prevent nasal symptoms more effectively than antihistamines, and also relieve itchy eyes. They act to reduce inflammation, rather than directly blocking or preventing the action of histamine.

Read more about “Hay Fever & Hay Fever Medications [New tab] (<https://www.compoundchem.com/2014/06/20/hayfever/>)” by Andy Brunning / Compound Interest, CC BY-NC-ND

26.2a The Chemicals in Cigarette Smoke & Their Effects

- Estimated number of chemical compounds in cigarette smoke: 7,357.
- Number of these compounds with confirmed carcinogenic activity: 70

The compounds shown below are all found in cigarette smoke. The mass figures, given in μg , take into account both mainstream (inhaled) and sidestream smoke. 1 μg is equal to 1 million of a gram. Amounts of these compounds vary in different brands of cigarettes – these figures are approximate.

Nicotine:

- Approx. 9.19 μg per cigarette
- Addictive
- Increases heart rate
- Increases blood pressure
- Increases blood glucose
- Lethal dose: around 500-1000mg

N-Nitrosamines:

- Large class of compounds
- Several are tobacco-specific
- Known human carcinogens
- Most carcinogenic: NNK & NNN
- NNK: approx. $0.3\mu\text{g}$ per cigarette
- NNN: approx. $2\text{-}50\mu\text{g}$ per cigarette
- May cause reproductive damage

Benzene:

- Approx. $46\text{-}272\mu\text{g}$ per cigarette
- Known human carcinogen
- Damages bone marrow
- Lowers red blood cell count
- May harm reproductive organs

Aromatic Amines:

- Large class of compounds
- Includes 2-aminonaphthalene:
 - Known human carcinogen
 - Linked with bladder cancer
 - Approx. $0.04\mu\text{g}$ per cigarette

Acetaldehyde:

- Approx. $680\text{-}1571\mu\text{g}$ per cigarette
- Known animal carcinogen
- Probable human carcinogen
- Irritant to skin and eyes
- Irritant to respiratory tract

1,3-Butadiene:

- Approx. $36\text{-}191\mu\text{g}$ per cigarette
- Known human carcinogen

- Suspected human tetratogen
- Irritant to eyes and skin
- Irritant to upper respiratory tract

Acrolein:

- Approx. 69-306 μ g per cigarette
- Possible human carcinogen
- Known DNA mutagen
- Irritant to skin and nasal passages
- May contribute to heart disease

Polyaromatics:

- Large class of compounds
- Includes benzo[a]pyrene:
 - Known human carcinogen
 - Known DNA mutagen
 - Affects reproductive capacity
 - Up to 0.14 μ g per cigarette

Read more about “The Chemicals in Cigarette Smoke & Their Effects [New tab]

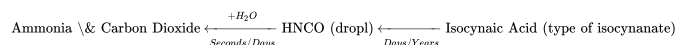
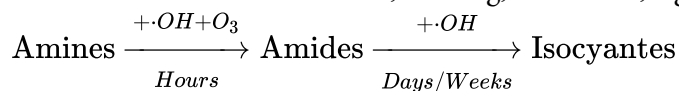
(<https://www.compoundchem.com/2014/05/01/the-chemicals-in-cigarette-smoke-their-effects/>)” by Andy Brunning / Compound Interest, CC BY-NC-ND.

26.2b RTC Week 2015 – #3: Nitrogen-Containing Atmospheric Pollutants

Dr. Nadine Borduas, department of chemistry at University of Toronto did research on how various nitrogen-containing amine compounds react when released into the atmosphere.

Organic nitrogen compounds enter our atmosphere from a variety of sources, both natural and industrial.

Amines: sources are: industrial, farming, forest fires, cigarette smoke. $R =$ various groups



Ammonia reacts with chemicals in air to form particulates which can have human health issues, contribute to smog, and impact climate. Nitrogen deposition in soils can also affect ecosystems.

Read more about “RTC Week 2015 – #3: Nitrogen-Containing Atmospheric Pollutants [New tab]

*(<https://www.compoundchem.com/2015/10/21/rtc-week-2015-3-nitrogen-containing-atmospheric-pollutants/>)”
by Andy Brunning / Compound Interest, CC BY-NC-ND*

26.3a A Guide to Simple Heterocycles in Organic Chemistry

A heterocycle in organic chemistry is a ring of connected atoms, where one or more of the atoms in the ring are elements different from carbon. Heterocycles with oxygen, nitrogen, and sulfur are the most prevalent; selenium, boron, arsenic and phosphorus can also be incorporated.

Heterocycles in organic chemistry

classes of heterocycles	Common name	Systematic names	Chemical formula
Multiple Heteroatom Heterocycles	Oxazole	1,3-oxazole	C_3H_3NO
Multiple Heteroatom Heterocycles	Thiazole	1,3-thiazole	C_3H_3NS
Multiple Heteroatom Heterocycles	Morpholine	Tetrahydro-1,4-oxazine	C_4H_9NO
Nitrogen-based Heterocycles	Ethylene Imine	Aziridine	C_2H_5N
Nitrogen-based Heterocycles	Pyrrolidine	Azolidine	C_4H_9N
Nitrogen-based Heterocycles	Pyrrole	Azole	C_4H_5N
Nitrogen-based Heterocycles	Imidazole	1,3-diazole	$C_3H_4N_2$
Nitrogen-based Heterocycles	Pyrazole	1,2-diazole	$C_3H_4N_2$
Nitrogen-based Heterocycles	Triazole	1,2,4-triazole	$C_2H_3N_3$
Nitrogen-based Heterocycles	Piperidine	Azinane	$C_5H_{11}N$
Nitrogen-based Heterocycles	Pyridine	Azine	C_5H_5N
Nitrogen-based Heterocycles	Pyrimidine	1,3-diazine	$C_4H_4N_2$
Nitrogen-based Heterocycles	Pyridazine	1,2-diazine	$C_4H_4N_2$
Nitrogen-based Heterocycles	Pyrazine	1,4-diazine	$C_4H_4N_2$
Oxygen-based Heterocycles	Ethylene oxide	Oxirane	C_2H_4O
Oxygen-based Heterocycles	Tetrahydrofuran	Oxolane	C_4H_8O
Oxygen-based Heterocycles	Furan	Oxole	C_4H_4O

Oxygen-based Heterocycles	Tetrahydropyran	Oxane	$C_5H_{10}O$
Oxygen-based Heterocycles	4H-Pyran	4H-Oxine	C_5H_6O
Oxygen-based Heterocycles	1,4-Dioxane	p-Dioxane	$C_4H_8O_2$
Sulfur-based Heterocycles	Ethylene Sulfide	Thiirane	C_2H_4S
Sulfur-based Heterocycles	Tetrahydrothiophene	Thiolane	C_4H_8S
Sulfur-based Heterocycles	Thiophene	Thiole	C_4H_4S
Sulfur-based Heterocycles	Tetrahydrothiopyran	Thiane	$C_5H_{10}S$

Read more about “A Guide to Simple Heterocycles in Organic Chemistry [New tab]

(<https://www.compoundchem.com/2014/07/31/heterocycles/>)” by Andy Brunning / Compound Interest, CC BY-NC-ND

26.3b Today in Chemistry History: Gertrude B Elion and drug discovery firsts

Gertrude B Elion born 23 January 1918 and died 21 February 1999. Elion was jointly awarded the 1988 Nobel Prize in Physiology or Medicine for work on the development of drugs, based on biochemical differences between human and pathogen cells. Working both alone and George Hitchings and she discovered new drugs against a variety of diseases. Her name appears on 45 different patents, and she was awarded 25 honorary doctorates.

Mercaptopurine, first treatment for leukemia; Azathioprine, to prevent transplant rejection; Trimethoprim, antibiotic; Allopurinol, treatment for gout; Aciclovir, antiviral for herpes infections; Pyrimethamine, for malaria and toxoplasmosis; Nelarabine, treatment for cancer.

Read more about “Today in Chemistry History: Gertrude B Elion and drug discovery firsts [New tab]

(<https://www.compoundchem.com/2018/01/23/elion/>)” by Andy Brunning / Compound Interest, CC BY-NC-ND,

26.3c Why is Coffee Bitter? – The Chemistry of Coffee

Chlorogenic acids account for up to 8% of the composition of unroasted coffee beans. More than 40 different varieties have been identified in green coffee beans, with 5-caffeoylquinic acid the most prevalent. Chlorogenic

acid content decreases when coffee beans are roasted, as they react to form quinolactones, phenylindanes and melanoidins. These contribute to flavour and bitterness.

The caffeine content of coffee is variable but approximately 100mg in a cup. Caffeine works by blocking the action of a group of brain chemicals called adenosines, which work to naturally trigger tiredness. The amount of caffeine in your bloodstream peaks 15 to 45 minutes after ingestion.

Read more about “Why is Coffee Bitter? – The Chemistry of Coffee [New tab] (<https://www.compoundchem.com/2014/01/30/why-is-coffee-bitter-the-chemistry-of-coffee/>)” by Andy Brunning / Compound Interest, CC BY-NC-ND

26.3d Toxicity & Aphrodisia – The Chemistry of Chocolate

Phenylethylamine occurs naturally in the brain, often referred to as ‘the love drug’ due to its ability to produce feelings of well-being and contentment. It is present in significant concentrations in chocolate, it is broken down during ingestion and is ruled out as causing significant aphrodisiac effect.

Tryptophan is a chemical in the brain linked to production of serotonin, the neurotransmitter that produces feelings of elation. It is present in small quantities in chocolate, it is unlikely that it causes any aphrodisiac effect.

Theobromine is a mild stimulant, similar to caffeine, found in chocolate. It is harmless to humans at levels found in chocolate and would require eating tens of kilograms of milk chocolate. However, theobromine has a more potent effect in cats and dogs; small doses can lead to vomiting and diarrhea and 50g of dark chocolate could kill a small dog.

Read more about “Toxicity & Aphrodisia – The Chemistry of Chocolate [New tab] (<https://www.compoundchem.com/2014/02/13/toxicity-aphrodisia-the-chemistry-of-chocolate/>)” by Andy Brunning / Compound Interest, CC BY-NC-ND

26.5a Chemical Concerns – Does Acrylamide in Toast & Roast Potatoes Cause Cancer?

Acrylamide is a chemical formed in reactions that occur when carbohydrate-rich foods are cooked at high temperature. Low levels of it are found in foods including roast potatoes, toast, and potato chips. It’s also found in roasted coffee beans and in cigarette smoke.

When carbohydrate-rich foods are cooked at high temperature (above 120 degree Celsius) amino acids can combine with reducing sugars (such as glucose) to form a range of products. The amino acid asparagine, combines with sugars to produce acrylamide. Higher temperatures and longer cooking times produce more acrylamide.

Acrylamide is classified as a probable human carcinogen; however, the amounts in food are very low:

- Toasted bread: 4.8 micrograms (assumes 1 slice is 24 grams)
- Potato chips: 12.4 micrograms (assumes packet is 32.5 grams)
- AV. daily intake: 30 micrograms (assumes body weight of 75kg)
- Max. Recommended daily intake: 195 micrograms (assumes body weight is 75kg).

Dietary levels of acrylamide are a minor concern for a small increased lifetime risk of cancer. This is based on animal studies -evidence for increased risk in humans is currently minimal. Increases in cancer risk associated with regularly drinking alcohol or smoking are much higher. The latest advice recommends cooking foods a little less brown to reduce acrylamide content.

In short: acrylamide hasn't been decisively linked to increased cancer risk at levels found in cooked foods.

Read more about “Chemical Concerns – Does Acrylamide in Toast & Roast Potatoes Cause Cancer? [New tab] (<https://www.compoundchem.com/2017/01/24/acrylamide/>)” by Andy Brunning / Compound Interest, CC BY-NC-ND

Attribution & References

Compound Interest infographics are created by Andy Brunning and licensed under CC BY-NC-ND

Except where otherwise noted, content on this page has been created as a textual summary of the infographics used within our OER. Please refer to the original website (noted below each description) for further details about the image.