Introductory Organic Chemistry

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An Introduction

Introductory Organic Chemistry is intended for use as a text in a single-term organic chemistry course as part of a one-year Introductory Chemistry course series, also known as a General, Organic and Biological Chemistry (GOB) course series. The text was produced with the specific objective of making an openly-available text for the course CH105 Introduction to Chemistry 2: Organic Chemistry at Central Oregon Community College. The audience for this book is likely to include students majoring in fields outside of the Sciences but who need or want some specific knowledge of the subdiscipline of Organic Chemistry. This will include students in pre-health fields, but also possibly students interested in Natural Resources, Agriculture or Business. The objective is to provide students with an exposure to core ideas of the subject without deep involvement in synthesis problems or organic mechanisms. *Introduction to Chemistry* is a derivative of the open text Organic Chemistry with a Biological Emphasis, by Timothy Soderberg, Associate Professor Emeritus at the University of Minnesota Morris. This text is cut back dramatically from what is offered by the Soderberg text, but includes sections of text and graphics drawn directly from that source.

Soderberg, Timothy, "Organic Chemistry with a Biological Emphasis Volume I" (2019). *Chemistry Publications*. 1. https://digitalcommons.morris.umn.edu/chem_facpubs/1

CHAPTER I

CHAPTER 1 THE ARCHITECTURE OF CARBON COMPOUNDS

1.0 The Architecture of Carbon Compounds

Learning Objectives

In this chapter, you will learn to

- identify organic compounds when provided with formulas
- explain the fantastic variety of known organic structures using explanations based on the atomic structure and bonding capabilities of carbon
- recognize and identify the presence of organic substances in everyday life

1.1 What is Organic Chemistry?

In the game "20 Questions," one player thinks of something and another is tasked with discovering what that thing is through a process of questioning. Up to 20 questions can be asked in an attempt to hone in on the answer. Frequently a questioner will ask "Animal, Vegetable, or Mineral?" early in the questioning, to narrow all the possible options down quickly. Of all the stuff in the universe, just about anything can be dropped into one of these categories.

Students of chemistry often are introduced quite early to a set of similarly broad categories: pure substances are classified as ionic, molecular (covalent) or metallic. Interestingly, these categories have some significant overlap with the categories from the 20 Questions: animals and vegetables are mostly composed of the elements carbon, hydrogen and oxygen and have other features characteristic of molecular substances. The materials they are made of can be burned in oxygen to yield carbon dioxide and water, and they may be present in any of three common physical states (solid, liquid, gas) under normal room conditions. They are mostly covalent in nature. In contrast, minerals typically contain metal as well as nonmetal elements and have features characteristic of ionic substances. They do not combust, they are usually solids under normal conditions and sometimes have recognizable crystalline structures. In certain conditions high heat can cause them to react to release pure metals–shiny, ductile and conductive materials that harden as they cool to form shiny solids.

General Contrasting Properties and Examples of Organic and Inorganic Compounds

Organic	**Hexane**	**Inorganic**	**NaCl**
low melting points	−95°C	high melting points	801°C
low boiling points	69°C	high boiling points	1,413°C
low solubility in water; high solubility in nonpolar solvents	insoluble in water; soluble in gasoline	greater solubility in water; low solubility in nonpolar solvents	soluble in water; insoluble in gasoline
flammable	highly flammable	nonflammable	nonflammable
aqueous solutions do not conduct electricity	nonconductive	aqueous solutions conduct electricity	conductive in aqueous solution
exhibit covalent bonding	covalent bonds	exhibit ionic bonding	ionic bonds

Given these general links, it may seem reasonable to think there might be some fundamental distinction between chemical substances that come from living things (animals and vegetables) and those that come from the rocky earth (mineral). Is the chemistry of living things fundamentally different than that of non-living things?

Not so long ago, people believed there was such a fundamental difference. This view called vitalism, that living and nonliving material was fundamentally different, was generally accepted within and outside of scientific circles through much of the 1700s.

Experimental evidence began to reveal inconsistencies between this view and reality, however. In 1828 a German chemist named Friederich Wohler provided what may have been the final blow to the idea: he took material from the non-living world and used it to produce urea, a known biochemical. The urea he produced was exactly the same stuff as the biologically sourced urea. They were indistinguishable.

Wohler's discovery wasn't planned. When he reacted silver cyanate and ammonium chloride he expected to get ammonium cyanate, as described by this equation:

$$AgOCN + NH_4Cl \rightarrow AgCl + NH_4OCN$$

But what he got was urea, NH_2CONH_2. Once he knew this the significance became clear.

And so the idea of vitalism faded, and chemistry continued to reveal in all kinds of ways that the universal basic building blocks of all matter were the same atoms, from the same elements, bonded together the same way no matter where a substance came from.

The elemental makeup of the living and nonliving materials was different in one way, however. The distribution of elements varied between them, with a wide variety of material from living sources full of carbon, hydrogen and oxygen. These "organic" materials were categorized in that way due to their relationship with life and nature. They gradually became defined by chemists in a more modern fashion: Organic chemistry is the chemistry of carbon compounds.

Nature is filled with chemical structures of many types, but in the chemistry of life we find an abundance of organic chemicals. Carbon has an outsized role to play in life, and thus in our chemical activities. Agriculture, manufactured goods from ag products (like textiles), and pharmaceutical products all are largely based on organic molecules. The petroleum industry, and all the products related to that, are also linked to organic chemistry because petroleum is a fossil fuel, produced in geologic processes from formerly living matter. In modern times these substances are the raw materials converted into a huge variety of plastics that we use in constructing the built world.

Chemists have found ways to alter and adjust organic structures in order to build all sorts of novel and interesting structures, through a process called synthesis. The versatility of organic chemistry is off the charts compared to most other elements, so organic chemistry has grown to a huge sub-field of chemistry and entire classes (such as this one) are taught on the subject.

Exercise 1.1.1

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https://openoregon.pressbooks.pub/introductoryorganic/?p=630#h5p-62

Exercise 1.1.2

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https://openoregon.pressbooks.pub/introductoryorganic/?p=630#h5p-33

Exercise 1.1.3

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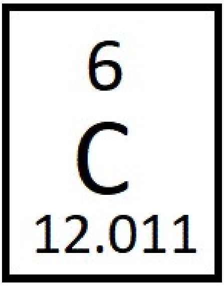
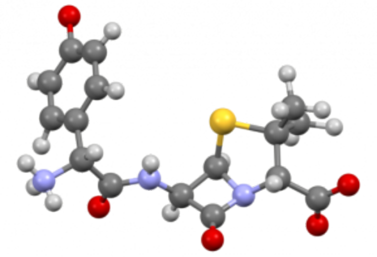
1.2 Why Carbon?



Carbon, atomic number 6, is an element with atoms that are small and relatively simple. The nucleus contains 6 positively-charged protons, and there are 6 electrons outside the nucleus distributed into two shells. The outer shell has four electrons that are held quite strongly by the electrostatic pull from the nucleus. So while a carbon atom can be ionized through either the gain or loss of electrons, it does not tend to do so. Carbon does however readily engage in covalent bonding, sharing electrons with neighboring atoms and forming tight associations with them. The four valence electrons in a carbon atom can do this by forming four single bonds, or by forming two single bonds and a double bond, by forming one single bonds and a triple bond, or by forming two double bonds.

Carbons covalently bond with one another, also, forming chains of various lengths, and rings. It readily bonds with other atoms such as oxygen, nitrogen and hydrogen, forming quite stable arrangements with these common elements as well.



Amoxicillin, C16H19N3O5S
Benjah-bmm27, Public domain, via Wikimedia Commons

The architecture of carbon structures is therefore fantastically varied. Small organic molecules might contain just one or two carbon atoms surrounded by other atoms. But the larger organic molecules can contain hundreds or thousands of carbons, linked with rings and bridges and other complex structures that fold into particular three-dimensional structures.

Carbon is a bit like a basic Lego building block. The 6-pin Lego is able to make lots of other connections, and also can make strong, stable connections. It has the features that make it an ideal basic building block for the construction of a wide variety of larger, complex shapes necessary for biological function. In a similar fashion Carbon can make 4 bonds, with varying geometry and generally stable structures.

Some Lego blocks are very limited in their use, while others are versatile for basic building. Carbon is like the classic 6 peg Lego in that it is a widely used building block in molecules.

No other element can quite do what carbon does: Silicon has the ability to form four bonds with other atoms but those bonds tend to be weak due to the additional electron shell in a silicon atom. Nitrogen has five valence electrons so generally only forms 3 single bonds, limiting its usefulness. Boron, similarly, does not make for a dependable, stable base structure.

Exercises 1.2.1-4

An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=628#h5p-5

CHAPTER II

CHAPTER 2 SORTING, CLASSIFYING AND NAMING ORGANIC COMPOUNDS

2.0 Sorting, Classifying and Naming Organic Compounds

Learning Objectives

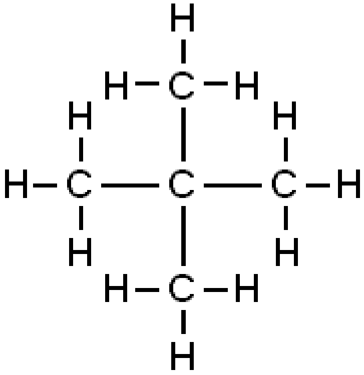
In this chapter you will learn to

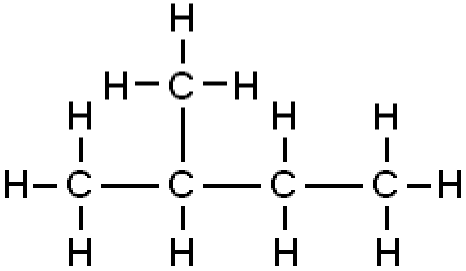
- draw and interpret organic structural formulas, condensed structural formulas, and line-bond formulas
- provide reasonably accurate names for some organic structures
- identify constitutional isomers from a set of chemical structures
- recognize and identify heteroatoms and functional groups

2.1 Drawing and Interpreting Organic Formulas

Organic molecules can be large and can contain multiple atoms of carbon, hydrogen and other elements. Their architecture can be complicated, with chains of various lengths and ring structures.

Consider the structures shown here:





Both of these structures are representations of organic molecules. Each contains 5 carbon atoms and 12 hydrogen atoms. But they look different, and it turns out they are: the properties of these substances are similar but not exactly the same.

The substance to the left has a boiling point of 9.5 °C, making it a gas at room temperature. The substance to the right has a boiling point of 28 °C, so it is a liquid at room temperature.

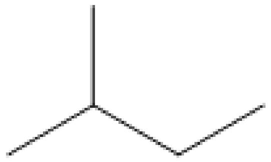
As we begin to consider and study organic molecules we very quickly are faced with this fact: molecular structures (showing the number and types of atoms in a molecule, such as H_2O) are inadequate to describe these substances.

In organic chemistry we make use of different types of formulas for this reason. There are several types, including

- **Structural formulas:** which show every atom with its elemental symbol and every bond drawn as a line. These look a lot like the Lewis Structures you probably learned to draw in Introductory Chemistry 1, but without the nonbonding electron pairs.
- **Condensed structural formulas:** similar to the structural formulas but without bonds shown to hydrogen atoms, so a carbon with 3 hydrogens attached becomes a CH_3. There are various levels of condensed, and there are some rules about how formulas are properly condensed. You will read these more often than write them since all these rules are challenging to learn.
- **Line-bond, also called Skeletal structures:** These are the hardest to learn but the quickest to draw of those described here. They are used extensively in chemical communication. In line-bond structures all bonds between carbons, and between carbons and other atoms except hydrogen are shown. Hydrogens are not included unless they are attached to something other than carbon. And the carbon atoms are shown without the elemental symbol. Instead the viewer recognizes carbon as present anywhere there is a vertex (pointed place) in the drawing, and at the end of a line.

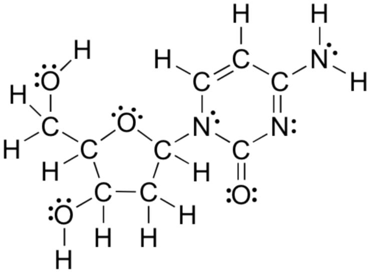
The structures above are shown as structural formulas, but could also be represented as condensed or line-bond structures. Can you tell which of the two structures is shown in the examples here?

$CH_3CH(CH_3)CH_2CH_3$



Common bonding patterns in organic structures

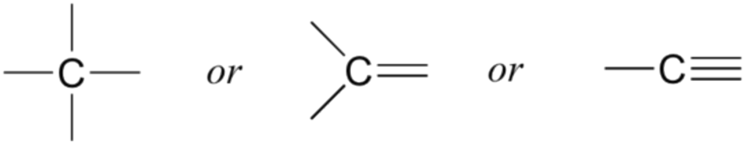
Drawing structural formulas is a good starting point for a novice organic chemist, and works when dealing with small, simple structures. But when you start dealing with larger structures it becomes increasingly difficult and time-consuming. Imagine trying to draw all atoms and bond every time you wanted to discuss the structure below, which is one small piece of DNA:



2'-deoxycytidine

Large molecules such as this are commonly considered in organic chemistry and biochemistry. In these situations Line-bond structures really help. To get good at drawing them accurately, you will first want to get familiar with some common bonding arrangements involving elements found frequently in organic molecules.

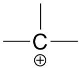
Let’s start with carbon. Carbon is said to be tetravalent, meaning that it tends to form four bonds. If you look at a variety of structures including carbon, you can see that nearly always each carbon atom has four bonding pairs of electrons, each represented as a line, surrounding it.



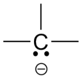
carbon usually has 4 bonds

This is a pattern that holds throughout most of the organic molecules we will see.

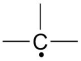
If a carbon has other electron arrangements in its valence shell (in other words, if it does not fulfill the octet rule), it will have a formal charge or exist as a radical:



3 bonds, no lone pair: carbocation



3 bonds + lone pair: carbanion

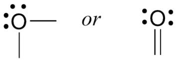


3 bonds + unpaired electron: carbon radical

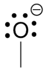
If you are able to quickly recognize these patterns (and the patterns described below for other atoms) it will help you tremendously as you learn more about organic chemistry.

The pattern for hydrogens is easy: hydrogen atoms have only one bond, and no formal charge. As a rule, all hydrogen atoms in organic molecules have one bond, and no formal charge.

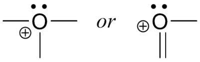
For oxygen, you will see an the atom bonding in three ways, all of which fulfill the octet rule.



neutral oxygen: 2 bonds + 2 lone pairs



negative formal charge: 1 bond + 3 lone pairs

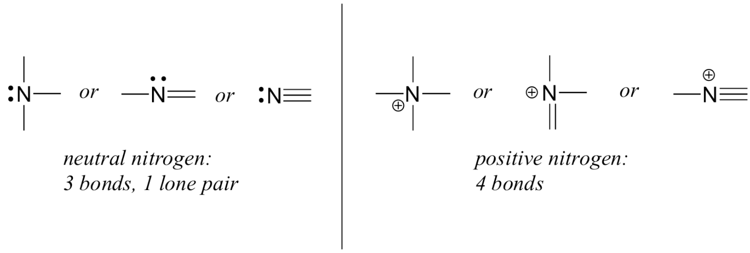


positive formal charge: 3 bonds + 1 lone pair

In most cases an oxygen atom has two bonds and two lone pairs, as in does in water. In this arrangement it will have a formal charge of zero. If it has one bond and three lone pairs, as in hydroxide ion, it will have a formal charge of-1. If it has three bonds and one lone pairit will have a formal charge of +1.

There are, again, some additional possibilities. However these three examples will account for virtually everything we see.

Nitrogen has two major bonding patterns, both of which fulfill the octet rule:

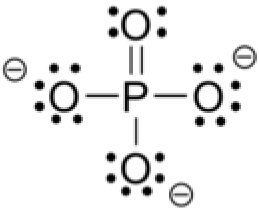


neutral nitrogen:
3 bonds, 1 lone pair

positive nitrogen:
4 bonds

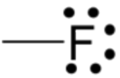
If a nitrogen has three bonds and a lone pair, it has a formal charge of zero. If it has four bonds (and no lone pair), it has a formal charge of +1. In a fairly uncommon bonding pattern, negatively charged nitrogen has two bonds and two lone pairs.

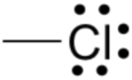
Two third row elements are commonly found in important organic molecules: sulfur and phosphorus. Although both of these elements have other bonding patterns that are relevant in laboratory chemistry, in a biological context sulfur almost always follows the same bonding/formal charge pattern as oxygen, while phosphorus is present in the form of phosphate ion (PO_4^{3-}), where it has five bonds (almost always to oxygen), no lone pairs, and a formal charge of zero. Remember that atoms of elements in the third row and below in the periodic table have ‘expanded valence shells’ with *d* orbitals available for bonding, and the the octet rule does not always apply.

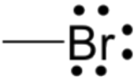


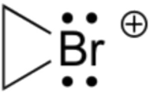
phosphate

Finally, the halogens (fluorine, chlorine, bromine, and iodine) are very important in laboratory and medicinal organic chemistry, but are less common in naturally occurring organic molecules. Halogens in organic compounds usually are seen with one bond, three lone pairs, and a formal charge of zero. Sometimes, especially in the case of bromine, we will encounter reactive species in which the halogen has two bonds (usually in a three-membered ring), two lone pairs, and a formal charge of +1.







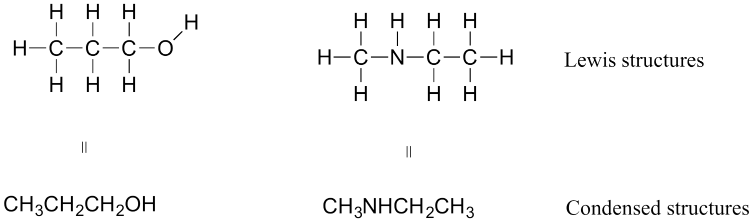


These rules, if learned and internalized so that you don't even need to think about them, will allow you to draw large organic structures, complete with formal charges, quite quickly.

Organic structure types often do not include lone pairs, since you can assume that the proper number of electrons are present around each atom to match the indicated formal charge (or lack thereof). Occasionally, though, lone pairs are drawn if doing so helps to make an explanation more clear.

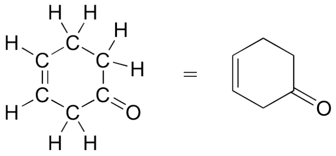
Using the 'line bond structure' convention

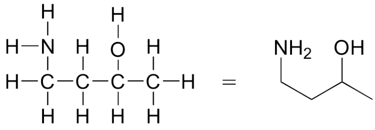
If you look ahead in this and other books at the way organic compounds are drawn, you will see that the figures are somewhat different from the Lewis structures you are used to seeing in your general chemistry book. In some sources, you will see **condensed structures** for smaller molecules instead of full structural formulas that include every bond:



More commonly, organic and biological chemists use an abbreviated drawing convention called **line-bond structures,** also sometimes called skeletal structures. The convention is makes it easier to draw molecules, but the convention does need to be learned.

Here is basically how it works: Carbon atoms are not depicted with their elemental symbol, but rather by a vertex (corner) or a free end of a bond. Open-chain molecules are usually drawn out in a 'zig-zig' shape. Hydrogens attached to carbons are generally not shown: rather, like lone pairs, it is assumed the person viewing the structure knows where they are. Hydrogens bonded to nitrogen, oxygen, sulfur, or anything other than carbon *are* shown, but are usually drawn without showing the bond. The following examples illustrate the convention.





The line-bond structures makes it much easier to see the basic structure of the molecule and the locations where there is something other than C-C and C-H single bonds. It can also be drawn quickly.

Sometimes, one or more carbon atoms in a line structure will be depicted with a capital C, if doing so makes an explanation easier to follow. *If you label a carbon with a C, you also must draw in the hydrogens for that carbon.*

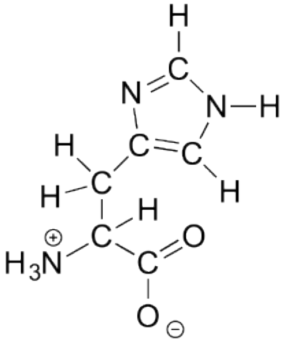
Exercise 2.1.1

A good way to test your understanding of the line structure convention is to see if you can accurately determine the number of hydrogen atoms in a molecule from its line structure. Do this for the structures here.

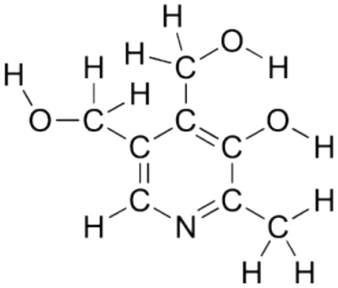
An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=639#h5p-35

Exercise 2.1.2

Draw line structures for histidine (an amino acid) and pyridoxine (Vitamin B_6).



histidine



pyridoxine
(Vitamin B_6)

Exercise 2.1.3

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Exercise 2.1.4

How many hydrogens are bonded to carbon at each hotspot (identified with a purple plus sign) on the structure shown below?

An interactive H5P element has been excluded from this version of the text. You can view it online here: *https://openoregon.pressbooks.pub/introductoryorganic/?p=639#h5p-6*

2.2 Naming Organic Compounds

Systematic Names

Chemists communicating about organic chemistry can use drawings in many situations, but in others the preference would be to describe substances with names. However there are millions of known, described organic substances. So providing each with an independent name, and learning a collection of such names, would be impossible. A solution to this difficulty exists in a system for naming, whereby a chemical is described by components of a name in such a way that the name contains enough information to translate the words back into a complete, unique structure.

Such a system has been devised by the International Union of Pure and Applied Chemistry (IUPAC, usually pronounced ***eye***-*you-pack*). While the IUPAC system is used frequently in conversation for smaller, simpler molecules, large and complex molecules such as many made by biological organisms end up with long and complicated names. However even these names are often used in official communication about such molecules. They can be written into documentation and are often easier to share than drawings. Unfortunately, public misunderstanding of how IUPAC names work has led to some association between complicated structure names and the health risks of exposure to a substance. This association is not at all real. Many natural substances, and substances that are very healthy to consume, have long and complicated systematic names.

The substance (Z)-3-hexenyl ethanoate sounds pretty unfriendly, but it is actually a principal component of the smell of fresh cut grass. The primary odor chemical in the fragrance of a rose is (2E)-3,7-Dimethyl-2,6-octadien-1-ol.

These names obviously would not be commonly used even by chemists discussing them at a cocktail party, but they are information-dense and in official communication provide an unequivocal link to a single chemical structure.

How to get a systematic name from a structure

To assign a name to a compound, begin by determining the **'parent chain'**, which is the longest straight chain of carbon atoms. On paper, you should be able to put a finger down on one end of the parent chain and trace through all carbons until you get to the end, without needing to lift your finger. We'll start with the simplest straight chain alkane structures.

If the parent chain is just one carbon long, the name is based on CH_4 which is called **methane.** For a two-carbon parent chain the name will be based on C_2H_6, which is **ethane**. The table below continues with the names of longer straight-chain alkanes. While rote memorization is generally not the best way to learn organic chemistry, it may be worth committing these to memory, as they are the basis for the rest of the IUPAC nomenclature system. With some practice they will become part of your functional vocabulary.

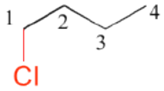
Names for straight-chain alkanes:

1 carbon: methane
2 carbons: ethane
3 carbons: propane
4 carbons: butane
5 carbons: pentane
6 carbons: hexane
7 carbons: heptane

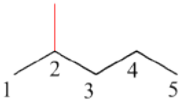
8 carbons: octane
9 carbons: nonane
10 carbons: decane

While many of these names share a Greek root with more familiar geometric shape names, some do not. For the first four, chemistry students often learn their order with the aid of the mnemonic (memory device) “Mice Eat Peanut Butter.”

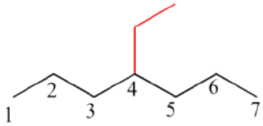
Substituents branching from the main parent chain are given a location signifier. This is done by providing the counted carbon number within the parent chain where the branch exists, with *the lowest possible numbers* being used. For example, notice below how the compound on the left is named 1-chlorobutane, *not* 4-chlorobutane. “1” designates the chlorine is attached at the first carbon in the parent chain. When the substituents are small carbon-containing, so-called **alkyl groups**, the terms **methyl**, **ethyl**, and **propyl** are used to identify them.



1-chlorobutane

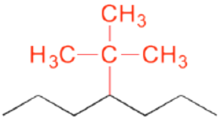


2-methylpentane

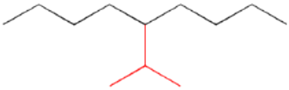


4-ethylheptane

Other common names for more complex alkyl groups are **isopropyl**, ***tert*-butyl** and **phenyl**. You may recognize how complicated the names could become, with multiple branches and non-carbon substituent groups all possible on large chains, etc.. In some situations this has caused a preference for common names to be used in casual talk or even among scientists, such as the names given for the amino acids shown below. Some common names, such as phenylalanine, include components of systematic names within them. No one can learn all the common names, and no one can learn all the rules for systematic names in a short period of time. For now we are learning bits and pieces, and learning how the system for nomenclature works.

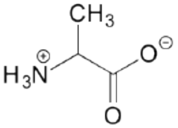


4-*tert*-butylheptane

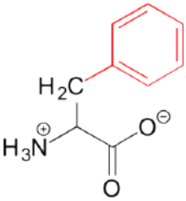


5-isopropylnonane

(non-IUPAC example):



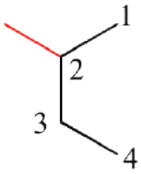
alanine
(an amino acid)



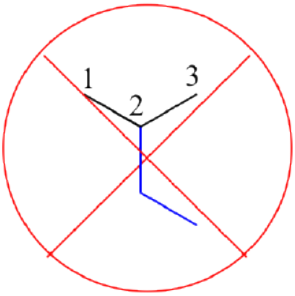
phenylalanine
(an amino acid)

The structure shown below is laid out on the page so that the longest continual carbon chain is oriented vertically. Structures that are presented this way can be confusing, leading to misinterpretation. In this case the structure could be accidentally named 2-ethylpropane (incorrect) instead of 2-methylbutane (correct).

Keep in mind the IUPAC name for straight-chain hydrocarbons is always based on the *longest possible parent chain*, which in this case is four carbons, not three. Especially if you are looking at large and complicated structures, it can get tricky to identify the parent chain, but it is the foundation of the name.



2-methylbutane

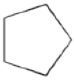


not 2-ethylpropane

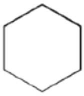
When carbons bond to form rings, the resulting cyclic alkanes are called cyclopropane, cyclobutane, cyclopentane, cyclohexane, and so on:

cyclopropane

cyclobutane

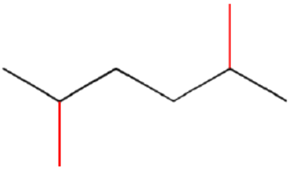


cyclopentane



cyclohexane

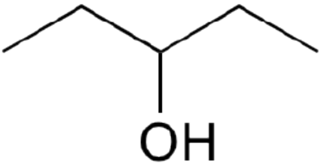
In cases where multiple copies of the same substituent are on a structure, the prefixes *di*, *tri*, and *tetra* are used.



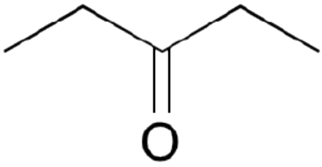
2,5-dimethylhexane

1,2,2,-trifluoropentane

We will learn more about functional groups soon. But for now, recognize that these recognizable groups of atoms show up in names as characteristic suffixes. Alcohols, for example, have '**ol**' appended to the parent chain name, along with a number designating the location of the alcohol group. Ketones are a functional group with a double bond to oxygen, designated in names by the suffix '**one**'.

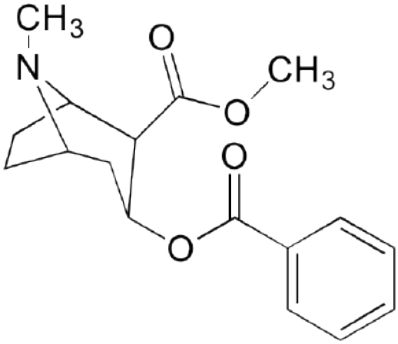


3-pentanol



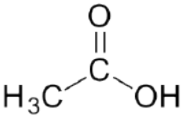
3-pentanone

All of the examples we have seen so far have been simple in the sense that only one functional group was present on each molecule. There are of course many more rules in the IUPAC system, and as you can imagine, the IUPAC naming of larger molecules with multiple functional groups, ring structures, and substituents can get very unwieldy very quickly. The drug cocaine, for example, has the IUPAC name 'methyl (1*R*,2*R*,3S,5S)-3-(benzoyloxy)-8-methyl-8-azabicyclo[3.2.1] octane-2-carboxylate.'

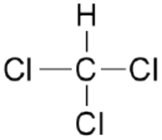


cocaine
(methyl (1*R*,2*R*,3*S*,5*S*)-3-(benzoyloxy)-8-methyl-8-azabicyclo[3.2.1] octane-2-carboxylate)

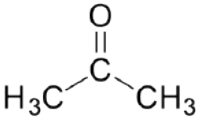
You can see why the IUPAC system is not used very much in biological organic chemistry – the molecules are just too big and complex. A further complication is that, even outside of a biological context, many simple organic molecules are known almost universally by their ‘common’, rather than IUPAC names. The compounds acetic acid, chloroform, and acetone are only a few examples.



acetic acid



chloroform



acetone

In biochemistry, nonsystematic names (like ‘cocaine’, ‘capsaicin’, ‘pyruvate’ or ‘ascorbic acid’) are usually used, and when systematic nomenclature is employed it is often specific to the class of molecule in question: different systems have evolved, for example, for fats and for carbohydrates. We will not focus very intensively in this text on IUPAC nomenclature or any other nomenclature system, but if you undertake a more advanced study in organic or biological chemistry you may be expected to learn one or more naming systems in some detail. If you are familiar with how naming systems work, you will be able to apply that general understanding to any specific system you need to learn.

Exercise 2.2.1

Look up the IUPAC names for acetic acid, chloroform, and acetone. One place you can find these is on Wikipedia, in the box of chemical information that is on the right side of the page. Wikipedia is quite reliable for this type of technical information. Other reliable sources for this kind of information include ChemSpider and PubChem.

Exercise 2.2.2

Attempt to draw line-bond structures of the following compounds, based on what you have learned about the IUPAC nomenclature system. If you can't do these now you probably will be able to do them in a few weeks. If you are unable to draw the line-bond structure, describe it in words.

a) methylcyclopentane

b) 5-methyl-1-hexanol ("-ol" indicates an alcohol, or -OH from carbon)

c) 2-methyl-2-butene ("-ene" indicates a carbon to carbon double bond)

Exercise 2.2.3

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=641#h5p-36

Exercise 2.2.4

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=641#h5p-37

Exercise 2.2.5

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https://openoregon.pressbooks.pub/introductoryorganic/?p=641#h5p-38

Exercise 2.2.6

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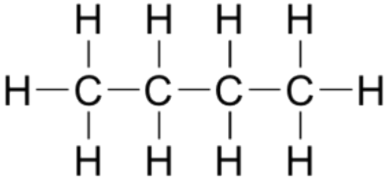
https://openoregon.pressbooks.pub/introductoryorganic/?p=641#h5p-63

2.3 Isomers

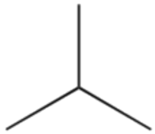
Constitutional isomers

Imagine you were asked to draw a structure for a compound with the molecular formula C_4H_{10}. This would not be difficult – you could simply draw:

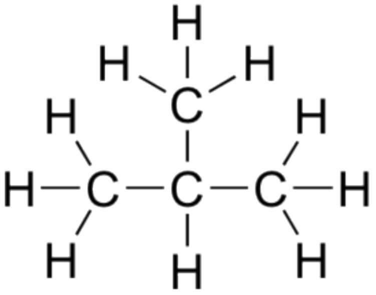
or



But when you compared your answer with that of a classmate, they may have drawn this structure:



or

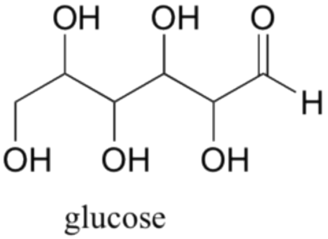


Who is correct? The answer, of course, is that both of you are. A molecular formula only tells you *how many* atoms of each element are present in the compound, not what the actual atom-to-atom connectivity is. There are often many different possible structures for one molecular formula.

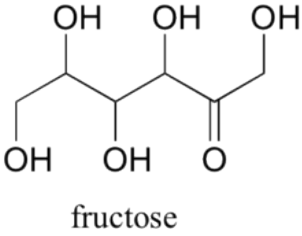
Compounds with this relationship: the same molecular formula but different connectivity, are called **constitutional isomers** (sometimes the term '**structural isomer**' is also used). The Greek term '*iso*' means 'same.'

The word isomer is a relational word, that describes the relationship between two things. It is similar in that sense to the word ‘cousin’ or ‘uncle.’ Being a cousin is not an identity essential to you, but describes your relationship to someone else. A substance can be an isomer *to something else*, but being an isomer is not an essential, internal characteristic.

Fructose and glucose, two kinds of sugar molecules, are related as constitutional isomers of one another. Can you figure out the molecular formula for each?



glucose



fructose

We will learn about other kinds of isomers including those that have the same molecular formula and the same connectivity in later chapters.

Exercise 2.3.1

How would you explain the difference between the structures of glucose and fructose? Would you make the explanation to a chemist (or fellow chemistry student) differently than you would make it to someone who doesn’t have any background knowledge of the subject?

Exercise 2.3.2

An interactive H5P element has been excluded from this

version of the text. You can view it online here: [*https://openoregon.pressbooks.pub/introductoryorganic/?p=643#h5p-41*](https://openoregon.pressbooks.pub/introductoryorganic/?p=643#h5p-41)

Exercise 2.3.3

Draw a constitutional isomer of ethanol, CH_3CH_2OH. If you are unable to draw it, explain it with words.

Exercise 2.3.4

An interactive H5P element has been excluded from this version of the text. You can view it online here: [*https://openoregon.pressbooks.pub/introductoryorganic/?p=643#h5p-42*](https://openoregon.pressbooks.pub/introductoryorganic/?p=643#h5p-42)

Exercise 2.3.5

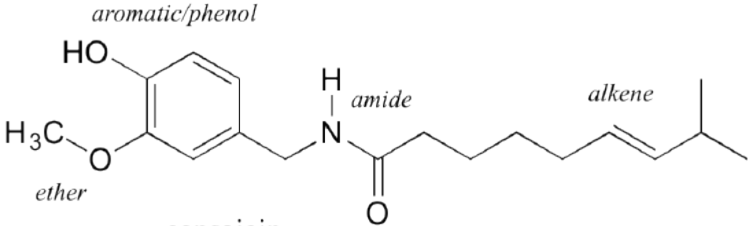
Draw as many constitutional isomers with the given molecular formula as you can, for each formula given. If you are unable to draw them, describe them with words.

a) C_5H_{12}
b) $C_4H_{10}O$
c) C_3H_9N

2.4 Heteroatoms and Functional Groups

Functional groups in organic compounds

Functional groups are structural units within organic compounds that are defined by specific bonding arrangements between specific atoms. Many, but not all, functional groups contain **heteroatoms:** atoms other than carbon and hydrogen. The structure below of capsaicin, the heat-sensation producing molecule in hot peppers, incorporates several functional groups, labeled in the figure and explained throughout this section.

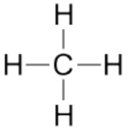


capsaicin

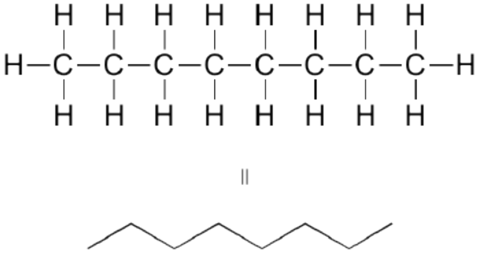
Functional groups *are the key structural elements that define how organic molecules act.* Our focus for now will be on drawing and recognizing each functional group, as depicted by structural formulas and line-bond structures. But as is implied by the name, functional groups are linked to the behavior of substances, their impact on properties of physical and chemical properties of substances. As the structural feature of a wing on an animal is associated with its ability to fly, functional groups on molecules are structural features that are associated with what those substances can do.

This section includes a quick tour through a collection of functional groups. You are not expected to know all of the details completely after one reading. The overview approach can help you appreciate the variety of structures within organic chemistry, and can help you begin to build a vocabulary. Later we will slow down and go through many of the most important of these groups again, in more detail.

The 'default' in organic chemistry (essentially, the *lack* of any functional groups) is described as **alkane**, characterized by single bonds between carbon and carbon, or between carbon and hydrogen. Methane, CH_4, is an alkane that is the combustible natural gas you may burn in your furnace to heat your home. Octane, C_8H_{18}, is an alkane which is a component of gasoline.

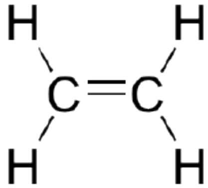


methane



octane

Alkenes (sometimes called **olefins**) have carbon-carbon double bonds, and **alkynes** have carbon-carbon triple bonds. Ethene is a gaseous alkene that serves as a cellular signal in fruits to stimulate ripening. Fruits that are sensitive to this signaling molecule can be placed in a paper bag along with an apple – the apple emits ethene gas, setting off the ripening process in the fruit. Commercial fruit packers can make use of this phenomenon by harvesting unripe fruits, then inducing ripening right before shipping to consumers. Ethyne, commonly called acetylene, is an alkyne used as a fuel in welding blow torches.

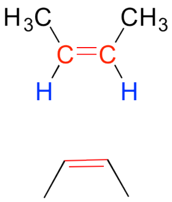


ethene
(an alkene)

ethyne
(an alkyne)

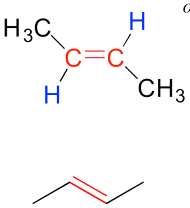
The bonding in alkenes is trigonal planar and the molecules are unable to rotate along the axis of the bond. The double bonds thus lead to 120 degree bond angles and a **planar triangular** geometry around the double bond. They are locked into one of two geometric configurations. These forms are given the descriptive names: ***cis*** or ***trans***. The *cis* and *trans* alkenes below are different molecules with different physical properties.

hydrogen atoms on same side



cis-alkene

hydrogen atoms on opposite sides

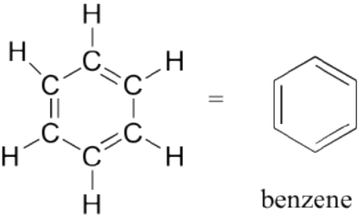


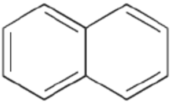
trans-alkene

In alkynes the geometry around the triple bond is linear (bond angles are 180°) and only one other atom can bond to the alkyne carbon, so while there is no rotation along the axis of the triple bond, such **geometric isomers** do not exist for this group.

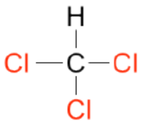
Alkanes, alkenes, and alkynes are all classified as **hydrocarbons**, because they are composed solely of carbon and hydrogen atoms. Alkanes are said to be **saturated hydrocarbons**, because the carbons are bonded to the maximum possible number of hydrogens – in other words, they are *saturated* with hydrogen atoms. The double and triple-bonded carbons in alkenes and alkynes have fewer hydrogen atoms bonded to them – they are thus referred to as **unsaturated hydrocarbons**.

The **aromatic** group is exemplified by benzene and naphthalene. Aromatic groups are planar (flat) ring structures, and are widespread in nature so you will see them frequently if you encounter chemical structures in biology classes or in biomedical work.

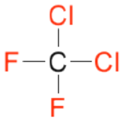

benzene


napthalene

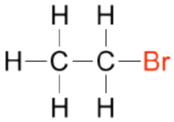
When the carbon of an alkane is bonded to one or more halogens, the resulting compound is called an **alkyl halide** or **haloalkane**. For many years chloroform, a haloalkane with the formula $CHCl_3$ was a commonly used solvent in the laboratory. This substance was also one of the earlier anesthetic drugs used in surgery. It's use is now highly restricted due to negative health effects, but it remains an important industrial chemical used in the production of PTFE (Teflon^{TM}). Chlorodifluoromethane was used as a refrigerant and in aerosol sprays until the late twentieth century, but its use was discontinued after it was found to have harmful effects on the ozone layer. Bromoethane is a simple alkyl halide often used in organic synthesis. Alkyl halides groups are quite rare in biomolecules.



trichloromethane
(chloroform)

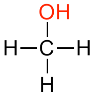


dichlorodifluoromethane
(Freon-12)

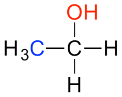


bromoethane

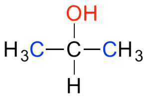
In the **alcohol** functional group, a carbon is single-bonded to an OH group (the OH group, by itself, is referred to as a **hydroxyl**). Except for methanol, all alcohols can be classified as primary, secondary, or tertiary. When the hydroxyl group is *directly* attached to an aromatic ring, the resulting group is called a **phenol**. The sulfur analog of an alcohol is called a **thiol** (from the Greek *thio*, for sulfur).



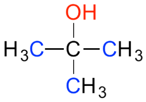
methanol



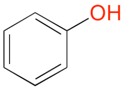
primary alcohol



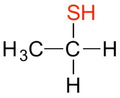
secondary alcohol



tertiary alcohol

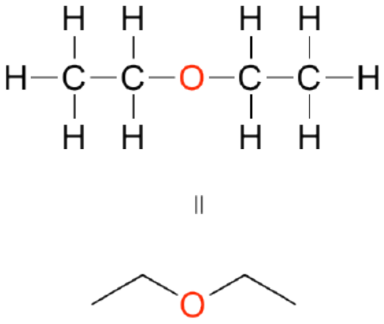


phenol

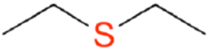


thiol

In an **ether** functional group, a central oxygen is bonded to two carbons. Below is the structure of diethyl ether, a common laboratory solvent and also one of the first compounds to be used as an anesthetic during operations. The sulfur analog of an ether is called a **thioether** or **sulfide**.



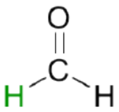
an ether



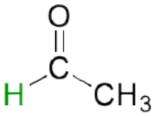
a sulfide

Amines are characterized by nitrogen atoms with single bonds to hydrogen and carbon. Just as there are primary, secondary, and tertiary alcohols, there are primary, secondary, and tertiary amines. Ammonia is a special case with no carbon atoms.

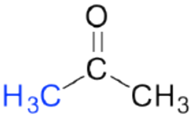
There are a number of functional groups that contain a carbon-oxygen double bond, which is commonly referred to as a **carbonyl**. **Ketones** and **aldehydes** are two closely related carbonyl-based functional groups that react in very similar ways. In a ketone, the carbon atom of a carbonyl is bonded to two other carbons. In an aldehyde, the carbonyl carbon is bonded on one side to a hydrogen, and on the other side to a carbon. The exception to this definition is formaldehyde, in which the carbonyl carbon has bonds to two hydrogens.



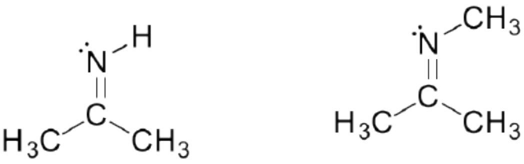
formaldehyde



an aldehyde

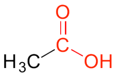


a ketone

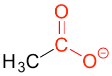


imines

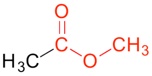
When a carbonyl carbon is bonded on one side to a carbon (or hydrogen) and on the other side to an oxygen, nitrogen, or sulfur, the functional group is considered to be one of the '**carboxylic acid derivatives**', a designation that describes a set of related functional groups. The eponymous member of this family is the **carboxylic acid** functional group, in which the carbonyl is bonded to a hydroxyl group. Other derivatives are carboxylic esters (usually just called **'esters'**) and **amides**. Other carboxylic acid derivatives also exist. Many are common in biology.



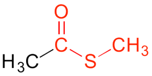
a carboxylic acid



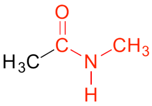
a carboxylate ion



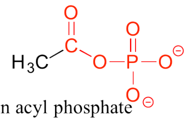
a carboxylic ester



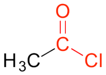
a thioester



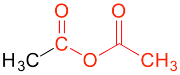
an amide



an acyl phosphate

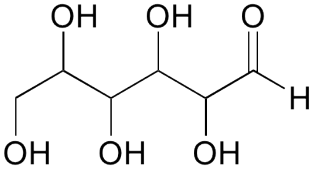


an acid chloride

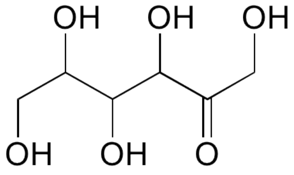


an acid anhydride

A single compound often contains several functional groups, particularly in biological organic chemistry. The six-carbon sugar molecules glucose and fructose, for example, contain aldehyde and ketone groups, respectively, and both contain five alcohol groups.

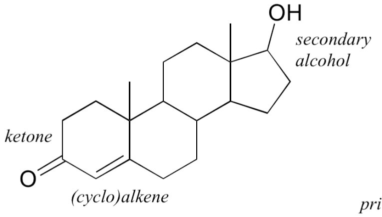


glucose

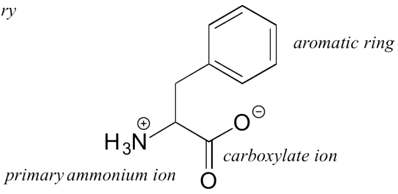


fructose

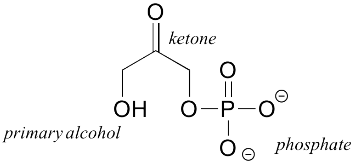
The hormone testosterone, the amino acid phenylalanine, and the glycolysis metabolite dihydroxyacetone phosphate all contain multiple functional groups, as labeled below.



testosterone



phenylalanine



dihydroxyacetone phosphate
(DHAP)

While not in any way a complete list, this section has covered most of the important functional groups that we will encounter in biological organic chemistry.

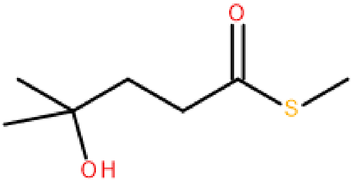
Exercise 2.4.1

An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=645#h5p-44

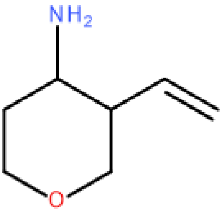
Exercise 2.4.2

Attempt to identify the functional groups (other than alkanes) in the following organic compounds. If you find alcohol or amine groups, identify them as primary, secondary, or tertiary.

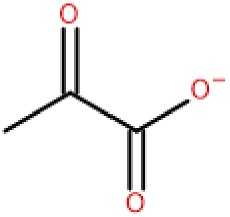
a)



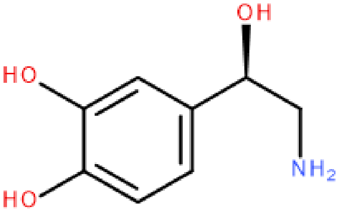
b)



c)



d)



Exercise 2.4.3

An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=645#h5p-43

As an add-on to the exercise above, write out a short explanation for how you went about identifying the secondary alcohol. What did you look at, or count, to figure this out?

Exercise 2.4.4

Draw one example each of compounds fitting the descriptions below, using line structures. If you can't draw them, describe them with words. Be sure to designate the location of all non-zero formal charges. All atoms should have complete octets (phosphorus may exceed the octet rule). There are many possible correct answers for these, so be sure to check your structures with your instructor.

a) a compound with molecular formula $C_6H_{11}NO$ that includes alkene, secondary amine, and primary alcohol functional groups

b) a molecule that includes aldehyde, secondary alcohol, and phosphate functional groups.

c) A compound with molecular formula C_6H_9NO that has an amide functional group, and does *not* have an alkene group.

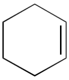
Functional Groups and Organic Nomenclature

As noted earlier, the presence of a functional group frequently shows up in the IUPAC name as a suffix. For alkanes, the names end in 'ane,' which indicates the absence of any functional group.

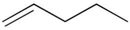
Alkenes are designated with an ‘ene’ ending, and when necessary the location and geometry of the double bond are indicated. Compounds with multiple double bonds are called dienes, trienes, etc.

$H_2C{=}CH_2$

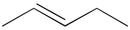
ethene



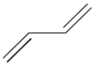
cyclohexene



1-pentene

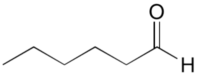


trans-2-pentene

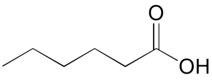


1,3-butadiene

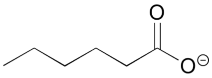
Some groups can only be present on a terminal carbon, and thus a locating number is not necessary: aldehydes end in ‘al’, carboxylic acids in ‘oic acid’, and their conjugate base carboxylates in ‘oate’.



hexanal



hexanoic acid



hexanoate

Other functional groups have their suffixes, as well, and some functional groups affect IUPAC names in more complex ways. Many molecules also have multiple functional groups on them, complicating the names further.

It is not crucial to learn the details now, but it is valuable to know that the suffix can often be used to identify the presence of a specific functional group on a molecule.

Exercise 2.4.5-9

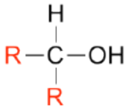
An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=645#h5p-46

Drawing abbreviated organic structures

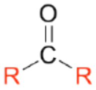
Often when drawing organic structures, chemists find it convenient to use the letter ‘R’ to designate part of a molecule outside of the region of interest. If we just want to refer in general to a functional group without drawing a specific molecule, for example, we can use ‘R groups’ to focus attention on the group of interest:

$R-CH_2OH$

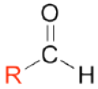
a primary alcohol



a secondary alcohol

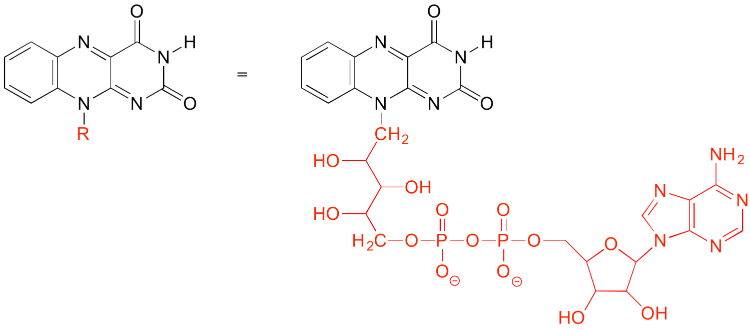


a ketone



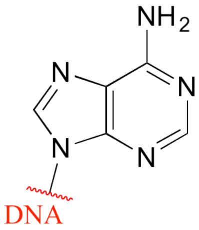
an aldehyde

The ‘R’ group is a convenient way to abbreviate the structures of molecules, especially when we are interested in something that is occurring specifically at one location on the molecule. For example, when considering the oxidation and reduction of the biologically-important flavin molecule, abbreviating the flavin structure helps a reader focus on the most important part of the molecule:

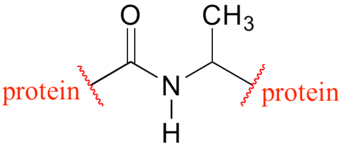


flavin adenine dinucleotide (FAD)

As an alternative, we can use a ‘break’ symbol to indicate that we are looking at a small piece or section of a larger molecule. This is used commonly in the context of drawing groups on large polymers such as proteins or DNA.

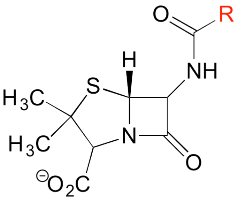


an adenine base in DNA

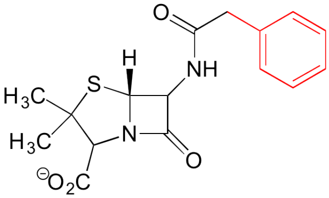


a small section of a protein

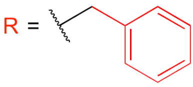
Finally, 'R' groups can be used to concisely illustrate a series of related compounds, such as the family of penicillin-based antibiotics.



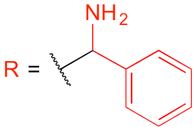
penicillin framework



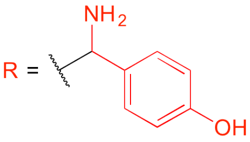
benzyl penicillin



benzyl penicillin



ampicillin



amoxicillin

Using abbreviations appropriately is very helpful to students interested in biology, because although many biomolecules are very large and complex (and take forever to draw!), usually we are focusing on just one small part of the molecule where a change is taking place. Abbreviations show up frequently in that context.

CHAPTER III

CHAPTER 3 CONNECTING STRUCTURES TO PROPERTIES

3.0 Connecting Structures to Properties

Learning Objectives

In this chapter you will learn to

- describe intermolecular forces: dipole-dipole interactions, Hydrogen bonding, and London forces
- look at a structure and determine which of these forces would have the greatest influence on the properties of that substance
- relate these intermolecular forces to observable properties including melting point, boiling point and solubility characteristics of a substance

3.1 Intermolecular Forces

Until now we have been focusing on understanding the covalent bonds that hold individual molecules together. We turn next to consider the subject of non-covalent interactions *between* molecules, or between different functional groups within a single molecule. The forces resulting in these interactions are called **intermolecular forces.** Along with ion-ion and ion-dipole forces they make up a set we might call noncovalent interactions.

Understanding these intermolecular interactions will allow us to explain differences in physical properties -such as boiling points, melting points, and solubility – between different organic compounds.

As you work through this section remember that these interactions are different than the covalent bonds that hold atoms together within a molecule. These interactions do not come from electron sharing, and they are individually much, much weaker than the covalent bonds which hold a molecule together. It is their aggregate effect that is important. Similar to how the individual hook and loop interactions of a piece of Velcro are weak, while the overall stickiness of a large piece of Velcro is strong, individual weak interactions between molecules in a sample can have an enormous effect on the characteristic of the substance in bulk.

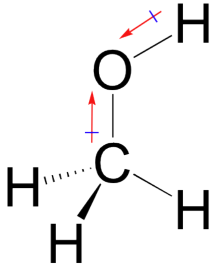
Dipoles


Linus Pauling's 1922 graduation portrait from Oregon Agricultural College, now Oregon State University.

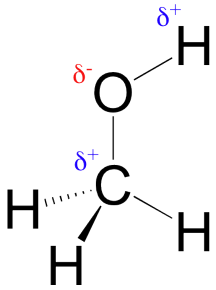
To understand the nature of intermolecular forces, we first must revisit covalent

bonds and delve into the subject of **dipoles**. Many of the covalent bonds that we have seen – between two carbons, for example, or between a carbon and a hydrogen –involve the approximately equal sharing of electrons between the two atoms in the bond. In these examples, the two atoms have approximately the same **electronegativity**. Linus Pauling, a famous chemist, Oregonian, and a key developer of these ideas, described electronegativity as "the power of an atom in a molecule to attract electrons to itself."

Quite often in organic chemistry we deal with covalent bonds between two atoms with different electronegativities, and in these cases the sharing of electrons is not equal. The more electronegative atom pulls the bonding electrons closer to its nucleus. In the carbon-oxygen bond of an alcohol, for example, the two electrons are held more closely to the oxygen than they are to the carbon, because oxygen is significantly more electronegative than carbon. The same is true for the oxygen-hydrogen bond, as hydrogen is much less electronegative than oxygen.



bond dipole arrows



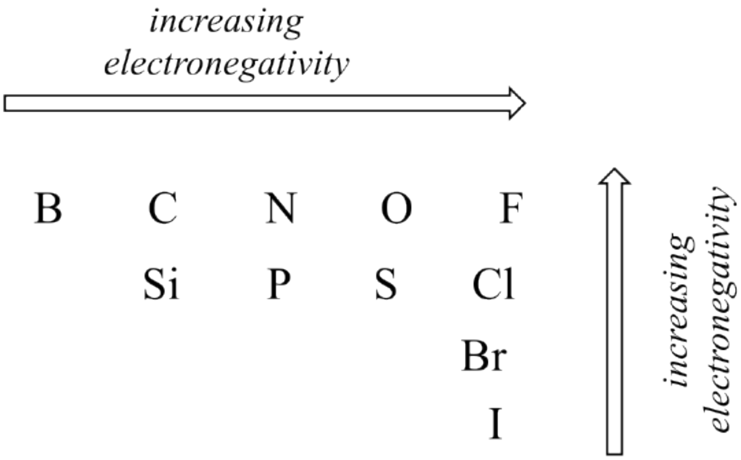
partial charge notation

The result of this unequal sharing is what we call a **bond dipole**, which exists in a **polar covalent bond**. The unequal sharing of the bonding electrons produces negative and positive ends, or poles, where electron density is lower (the positive pole) and higher (the negative pole). The resulting charges are called 'partial positive' and 'partial negative.' 'Partial' is used because these charges are not as great as the numeric charges we assign to elctrons (-1) or protons (+1).

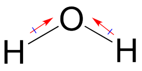
When dipoles are shown on chemical structures, the difference in electron density can be expressed using either of two types of notation. The Greek letter *delta* to denote the poles, with a plus (electron deficient) or minus (electron rich) sign is one way. The other uses 'dipole arrows', with a positive sign on the tail, to indicate the negative (higher electron density) direction of the dipole.

The degree of polarity in a covalent bond depends on the difference in electronegativity between the two bonded atoms. Electronegativity is a periodic trend: it increases going from left to right across a row of the periodic table of the elements, and also increases as we move up a column. Therefore, oxygen is more electronegative than nitrogen, which is in turn more electronegative than carbon. Oxygen is also more electronegative than sulfur. Fluorine, in the top right corner of the periodic table, is the most electronegative of the elements. Hydrogen is slightly less electronegative than carbon.

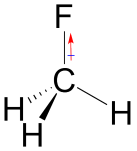
Periodic trends in electronegativity



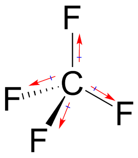
Most molecules contain both polar and nonpolar covalent bonds. Depending on the location of polar bonds and bonding geometry, molecules may posses a net polarity, called a **molecular dipole moment**. Water has a dipole moment that results from the combined dipoles of its two oxygen-hydrogen bonds. Fluoromethane also has a dipole moment.



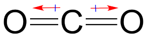
molecular dipole



molecular dipole



***no** molecular dipole*



***no** molecular dipole*

Tetrafluoromethane, however, has four polar bonds that pull equally in to the four corners of a tetahedron, meaning that although there are four individual bond dipoles there is no overall *molecular* dipole moment. Carbon dioxide also lacks a molecular dipole moment.

Dipole moments can be calculated, and are described with a value and the unit “D” for Debye. (Debye is pronounced so it would rhyme with “the spy.”)

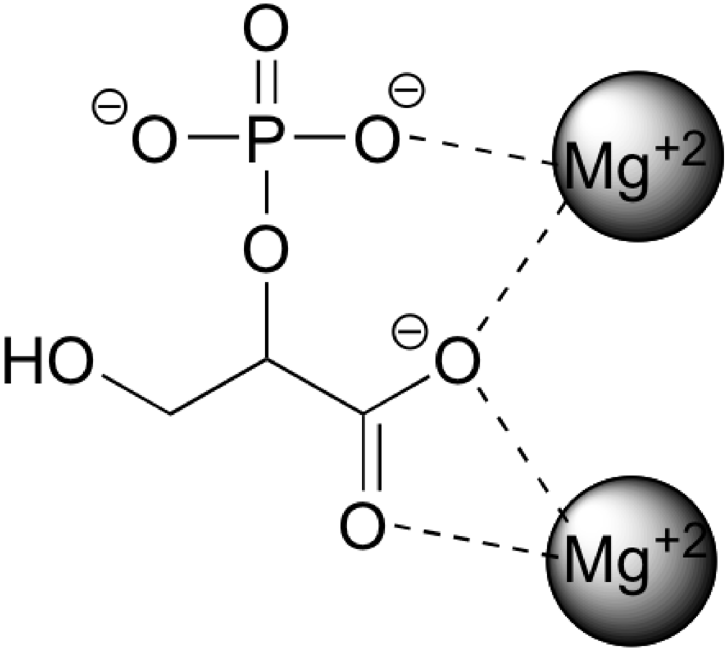
Exercise 3.1.1

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=652#h5p-49

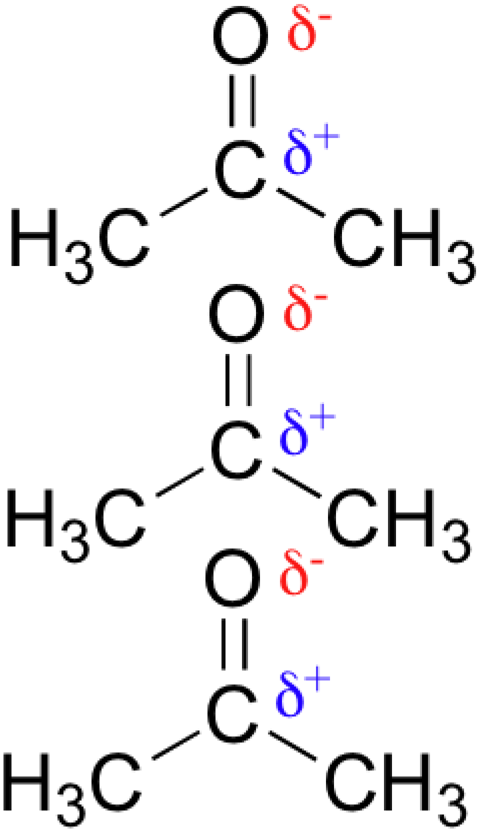
Types of intermolecular forces

Ion-ion, dipole-dipole and ion-dipole forces

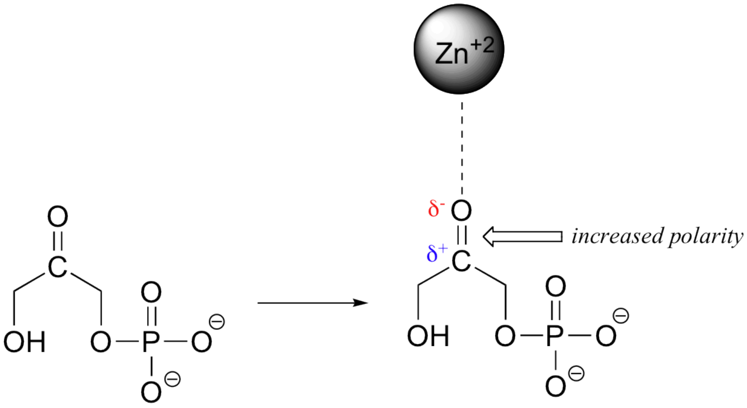
The strongest type of non-covalent interaction is between two ionic groups of opposite charge (an **ion-ion** or **charge-charge interaction**). For example, table salt is composed of sodium cations and chloride anions, held in a crystal lattice by ion-ion attractive interactions. One of the most common examples in biological organic chemistry is the interaction between a magnesium cation (Mg^{+2}) and an anionic carboxylate or phosphate group. The figure below shows a polyatomic anion named 2-phosphoglycerate interacting with two Mg^{+2} ions as it does in biological organisms, in the active site of an enzyme.



Polar molecules – those with a molecular dipole moment, such as acetone – can align themselves in such a way as to allow their respective positive and negative poles to interact with each other. This is called a **dipole-dipole interaction**.



When a charged species (an ion) interacts favorably with a polar molecule or functional group, the result is called an **ion-dipole interaction**. A common example of ion-dipole interaction in biological organic chemistry is that between a metal cation, most often Mg^{+2} or Zn^{+2}, and the partially negative oxygen of a carbonyl.

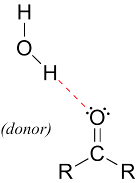


London dispersion forces

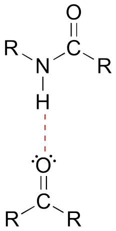
Nonpolar molecules such as hydrocarbons also are subject to weaker but still significant attractive intermolecular attractive forces. **London dispersion forces,** also called **van der Waal's forces** or **nonpolar interactions** result from the constantly shifting electron density in any molecule. Even a nonpolar molecule will, at any given moment, have a weak, short-lived dipole. This transient dipole will induce a neighboring nonpolar molecule to develop a corresponding transient dipole of its own, with the end result that a transient dipole-dipole interaction is formed. These forces are very weak, but in the absence of other intermolecular forces they do matter.

Hydrogen Bonding forces

Hydrogen bonds result from the interaction between a hydrogen bonded to a very electronegative heteroatom – specifically a nitrogen, oxygen, or fluorine – and lone-pair electrons on a nitrogen, oxygen, or fluorine a neighboring molecule or functional group. Because a hydrogen atom is just a single proton and a single electron, when it loses electron density in a polar bond it essentially becomes an approximation of a 'naked' proton, capable of forming an unusually strong noncovalent interaction with a lone pair on a neighboring electronegative atom.



hydrogen bonding between a ketone (acceptor) and water (donor)

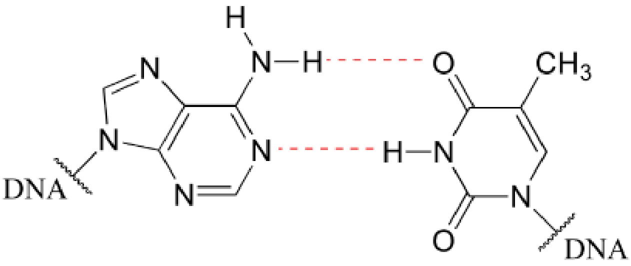


hydrogen bonding between a ketone (acceptor) and an amide (donor)

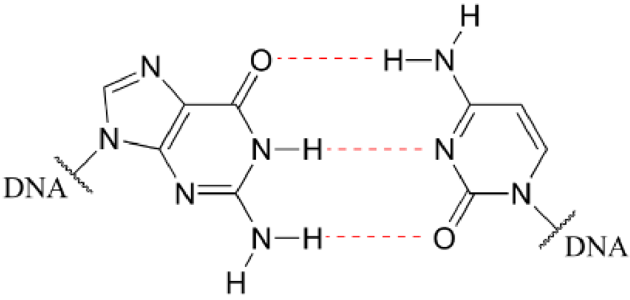
Hydrogen bonds are usually depicted with dotted lines in chemical structures. A group that provides a proton to a hydrogen bond is said to be acting as a **hydrogen bond donor**. A group that provides an oxygen or nitrogen lone pair is said to be acting as a **hydrogen bond acceptor**. Many common organic functional groups can participate in the formation of hydrogen bonds, either as donors, acceptors, or both. Water and alcohols, for example, can be both hydrogen bond donors and acceptors.

Hydrogen bonding has a huge importance in biology. Copying of DNA in the cell, for example, is based on very specific hydrogen bonding arrangements between DNA bases on complimentary strands: adenine pairs with thymine, while guanine pairs with cytidine:

A-T base pair:



G-C base pair:



Exercise 3.1.2

An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=652#h5p-64

Exercise 3.1.3

Draw figures that show the hydrogen bonds described below. If you are unable to draw them, describe them with words.

a) A hydrogen bond between methanol (donor) and water (acceptor).

b) A hydrogen bond between methanol (acceptor) and water (donor).

Relative Strength of Intermolecular Forces

In general, hydrogen bonding forces are stronger than dipole-dipole forces, but are also much weaker than covalent bonds. The strength of hydrogen bonds has enormous implications in biology.

Dipole-dipole interactions are somewhat weaker than Hydrogen bonding interactions.

Least powerful are the London dispersion forces that hold nonpolar substances together. These interactions occur all the time, but their effect is overshadowed by the more powerful intermolecular forces when a substance is capable of dipole-dipole interactions or Hydrogen bonding.

Exercise 3.1.4

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=652#h5p-68

3.2 Solubility

An understanding of the various types of noncovalent intermolecular forces allows us to explain many observable physical properties of organic compounds on a molecular level. One physical property that has links to intermolecular forces is solubility. Whether some organic substance will dissolve in a liquid solvent, and to what extent it will do so, is linked to the structures of the molecules making up this solute and the solvent.

Solubility

A lot of organic chemistry takes place in the solution phase. In the organic laboratory, reactions are often run in nonpolar or slightly polar solvents such as toluene (methylbenzene), dichloromethane, or diethyl ether. In recent years, much effort has been made to adapt reaction conditions to allow for the use of more environmentally friendly solvents such as water or ethanol, which are polar and capable of hydrogen bonding. So laboratory chemistry tends to occur in these environments.

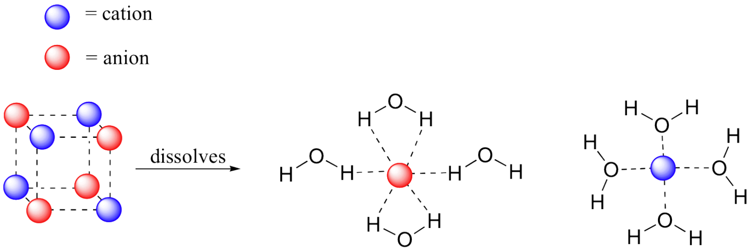
In biochemistry the solvent is of course water, but the microenvironment inside an enzyme’s active site – where the actual chemistry is going on – can range from very polar to very non-polar, depending on which amino acid residues on the enzyme surround the reactants.

Oil is insoluble in water and less dense, so it does not dissolve and floats on top of the surface. Source: User:Bitjungle, CC BY-SA *via Wikimedia Commons*

You have probably observed at some point in your life that oil does not mix with water, either in a puddle underneath a car with a leaky oil pan, or in a vinaigrette dressing bottle in the kitchen. The underlying reason for this insolubility (or immiscibility when we talk about liquids) is intermolecular forces that exist (or don't) between molecules within the solute, the solvent, and between the solute and solvent.

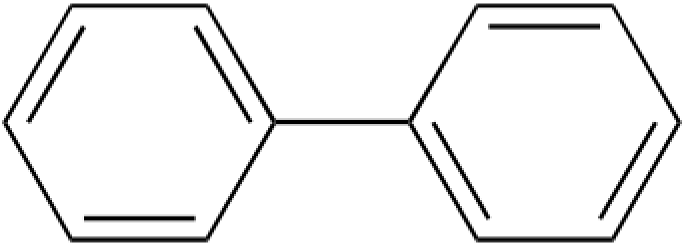
When considering the solubility of an organic compound in a given solvent, the most important question to ask ourselves is: How strong are the noncovalent attractive interactions between the compound and the solvent molecules? If the solvent is polar, like water, then a larger dipole moment, indicating greater molecular polarity, will tend to increase the solubility of a substance in it. If the solvent is non-polar, like the hydrocarbon hexane, then the exact opposite is true.

Imagine that you have a flask filled with water, and a selection of substances that you will test to see how well they dissolve in it. The first substance is table salt, or sodium chloride. This ionic compound dissolves readily in water. Why? Because water, as a very polar molecule, is able to form many ion-dipole interactions with both the sodium cation and the chloride anion, the energy from which is more than enough to make up for energy required to break up the ion-ion interactions in the salt crystal.



The end result, then, is that in place of sodium chloride crystals, we have individual sodium cations and chloride anions surrounded by water molecules – the salt is now *in solution*. Charged species as a rule dissolve readily in water: in other words, they are very **hydrophilic** (water-loving).

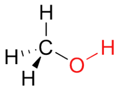
Biphenyl, like sodium chloride, is a colorless crystalline substance.



biphenyl

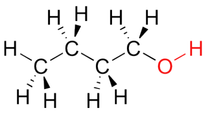
Biphenyl does not dissolve at all in water. Why is this? It is a very non-polar molecule, with only carbon-carbon and carbon-hydrogen bonds. It has some intermolecular forces bonding it to itself through nonpolar London dispersion forces, but it has no significant attractive interactions with very polar solvent molecules like water. Meanwhile the water molecules themselves are highly connected to one another through hydrogen bonding forces. Thus, the water tends to continue to engage in hydrogen bonding interactions with other molecules of its own kind, and very little is gained in terms of new biphenyl-water interactions. Water is a terrible solvent for nonpolar hydrocarbon molecules: they are very **hydrophobic** (water-fearing).

Next, you try a series of increasingly large alcohol compounds, starting with methanol (1 carbon) and ending with octanol (8 carbons).



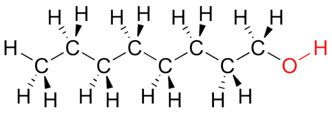
methanol

very soluble in water



butanol

slightly soluble in water



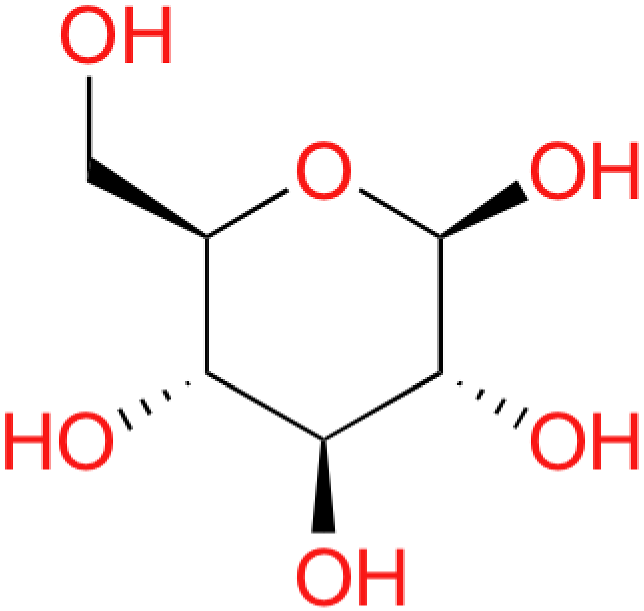
octanol

very insoluble in water

You find that the smaller alcohols – methanol, ethanol, and propanol – dissolve easily in water, at any water/alcohol ratio that you try. This is because the water is able to form hydrogen bonds with the hydroxyl group in these molecules, and the increased stability in the system due to formation of these water-alcohol hydrogen bonds is more than enough to make up for the lost stability from undoing the alcohol-alcohol (and water-water) hydrogen bonds. When you try butanol, however, you begin to notice that, as you add more and more to the water, it starts to form a layer on top of the water. Butanol is only sparingly soluble in water.

The longer-chain alcohols – pentanol, hexanol, heptanol, and octanol – are increasingly insoluble in water. What is happening here? Clearly, the same favorable water-alcohol hydrogen bonds are still possible with these larger alcohols. The difference, of course, is that the larger alcohols have larger nonpolar, hydrophobic regions in addition to their hydrophilic hydroxyl group. At about four or five carbons, the influence of the hydrophobic part of the molecule begins to overcome that of the hydrophilic part, and water solubility is lost.

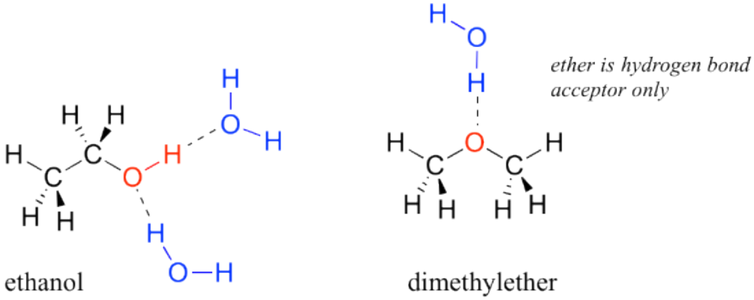
Now, try dissolving glucose in the water – even though it has six carbons just like hexanol, it also has five hydrophilic hydroxyl (-OH) groups that can engage in hydrogen bonding interactions, in addition to a sixth oxygen that is capable of being a hydrogen bond acceptor.



glucose

We have tipped the scales to the hydrophilic side, and we find that glucose is quite soluble in water.

We saw that ethanol was very water-soluble (if it were not, drinking beer or vodka would be rather inconvenient!) How about dimethyl ether, which is a constitutional isomer of ethanol but with an ether rather than an alcohol functional group? We find that diethyl ether is much less soluble in water. Is it capable of forming hydrogen bonds with water? Yes, in fact, it is –the ether oxygen can act as a hydrogen-bond acceptor. The difference between the ether group and the alcohol group, however, is that the alcohol group is both a hydrogen bond donor *and* acceptor.



The result is that the alcohol is able to form more energetically favorable interactions with the solvent compared to the ether, and the alcohol is therefore much more soluble.

'Like dissolves like' is a general rule for solubility frequently taught in chemistry classes. This phrase consolidates the patterns described above, and while it loses some of the explanation and is really general, it is helpful.

Coos Bay, Ore.(Feb 12, 1999)–Coast Guard helps avert environmental catastrophe after the bulk carrier New Carissa ran aground Feb. 4 one mile north of Coos Bay, Oregon and began to leak oil. The ship's remaining fuel was intentionally ignited to help prevent nearly 400,000 gallons of oil from reaching the shoreline. USCG photo by BANDROWSKY, VERONICA PA3

'Like' items are those that are more polar, or capable of hydrogen bonding or interacting with ions. Polar solvents will dissolve polar substances well, and also ionic ones. Nonpolar substances, in contrast, will not: but they will do a good job of dissolving things that are nonpolar.

Nonpolar solvents are less familiar to non-chemists, but in daily life they do sometimes help when it is necessary to dissolve something nonpolar. For instance, essential oils are oil solutions of fragrance molecules because the fragrance compounds are nonpolar and will not dissolve in water. Cleaning solvents also often are at least somewhat nonpolar, and help to dissolve and therefore remove nonpolar greasy contaminants from tools, bikes, and other places around the house. In the environment, oils tend to float on water and thus can cover wide areas rather than remain confined to a local spill. Small volumes of spilled hazardous materials that are nonpolar can contaminate vast areas.

Summary of factors contributing to water solubility

Evaluating a chemical structure to predict its solubility characteristics can be challenging. But consideration of these factors can often lead to predictions that match real observed behavior of substances:

A: How many carbons? All else being equal, more carbons means more of a non-polar/hydrophobic character, and thus lower solubility in water.

B: How many, and what kind of hydrophilic groups? The more, the greater the water solubility. In order of importance:

1. Anything with a **charged** group (eg. ammonium, carboxylate, phosphate) is almost certainly water soluble, unless has a vary large nonpolar group, in which case it will most likely be soluble in the form of micelles, like a soap or detergent.
2. Any functional group that can **donate a hydrogen bond** to water (e.g. alcohols, amines) will significantly contribute to water solubility.
3. Any functional group that can only **accept a hydrogen bond** from water (eg. ketones, aldehydes, ethers) will have a somewhat smaller but still significant effect on water solubility.
4. Other groups that contribute to polarity (eg. alkyl halides, thiols, sulfides) will make a small contribution to water solubility.

Watch for heteroatoms in molecules, which often are built into functional groups that contribute to molecular polarity, and thus water-solubility.

Exercise 3.2.1

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=654#h5p-69

Exercise 3.2.2

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Exercise 3.2.3

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version of the text. You can view it online here:
[*https://openoregon.pressbooks.pub/introductoryorganic/?p=654#h5p-71*](https://openoregon.pressbooks.pub/introductoryorganic/?p=654#h5p-71)

Exercise 3.2.4

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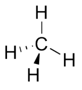
[*https://openoregon.pressbooks.pub/introductoryorganic/?p=654#h5p-51*](https://openoregon.pressbooks.pub/introductoryorganic/?p=654#h5p-51)

3.3 Melting points and Boiling Points

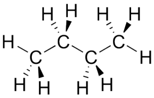
Boiling point and melting point

The observable melting and boiling points of different organic molecules provides an additional illustration of the effects of noncovalent interactions. The overarching principle involved is simple: *how strong are intermolecular forces within a pure sample of the substance*? Melting and boiling are processes in which these noncovalent attractive interactions are disrupted. The stronger the intermolecular attractive forces, the more energy that is required to break them apart. That energy is in the form of heat, e.g. a higher temperature must be reached for the melting or boiling to occur.

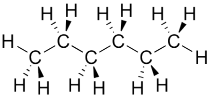
As a rule, larger molecules have higher boiling and melting points. Consider the boiling points of increasingly larger hydrocarbons. More carbons and hydrogens create a greater surface area possible for London forces, and thus higher boiling points. Below zero degrees Celsius (and at atmospheric pressure) butane is a liquid, because the butane molecules are held together by these forces. Above zero degrees, however, the molecules gain enough thermal energy to separate from one another and enter the gas phase. Octane, in contrast, remains in the liquid phase all the way up to 128°C, due to the increased influence of attractive London forces, made possible by the larger surface area of the individual molecules.



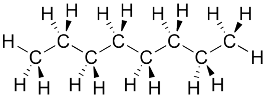
methane
bp = -164°C



butane
bp = 0°C



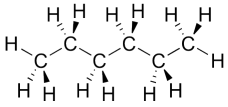
hexane
bp = 68°C



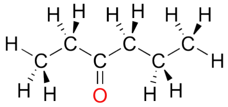
octane
bp = 128°C

The strength of intermolecular hydrogen bonding and dipole-

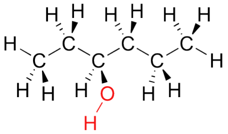
dipole interactions is reflected in higher boiling points. Look at the trend for hexane (London forces only), 3-hexanone (dipole-dipole interactions), and 3-hexanol (hydrogen bonding). In all three molecules, London forces are significant. The polar ketone group allows 3-hexanone to form intermolecular dipole-dipole interactions, in addition to the weaker London forces. 3-hexanol, because of its hydroxyl group, is able to form intermolecular hydrogen bonding interactions, which are stronger yet.



hexane
bp = 69°C



3-hexanone
bp = 123 °C



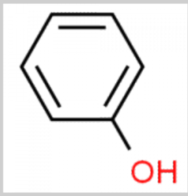
3-hexanol
bp =135°C

Of particular interest to biologists (and pretty much anything else that is alive on the planet) is the effect of hydrogen bonding in water. Because it is able to form tight networks of intermolecular hydrogen bonds, water remains in the liquid phase at temperatures up to 100 ^{O}C despite its small size. The world would obviously be a very different place if water boiled at 30 ^{O}C.

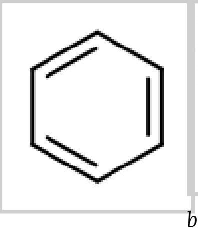
Exercise 3.3.1

An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=672#h5p-72

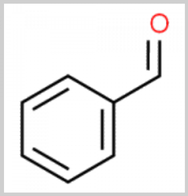
Wikipedia pages for these substances can be found through these links, for phenol, benzene, benzaldehyde and benzoic acid.



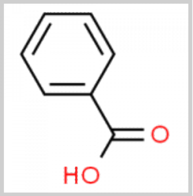
phenol



benzene



benzaldehyde

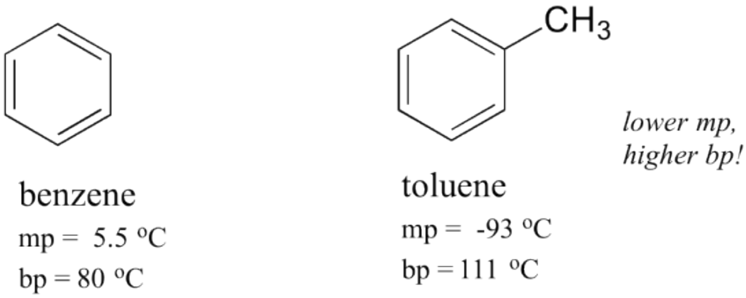


benzoic acid

By thinking about noncovalent intermolecular interactions, we can also predict relative melting points. All of the same principles apply: stronger intermolecular interactions result in a higher melting point. Ionic compounds, as expected, usually have very high melting points due to the strength of ion-ion interactions. Just like with boiling points, the presence of polar and hydrogen-bonding groups on organic compounds generally leads to higher melting points. The size of a molecule influences its melting point as well as its boiling point, again due to increased van der Waals interactions between molecules.

What is different about melting point trends versus boiling point or solubility trends, is the importance of a molecule's shape and its ability of pack tightly together. Picture yourself trying to make a stable pile of baseballs on the floor. It just doesn't work, because spheres don't pack together well – there is very little area of contact between each ball. It is very easy, though, to make a stack of flat objects like books.

The same concept applies to how well molecules pack together in a solid. The flat shape of aromatic compounds allows them to pack efficiently, and thus aromatics tend to have higher melting points compared to non-planar hydrocarbons with similar molecular weights. Comparing the melting points of benzene and toluene, you can see that the extra methyl group on toluene disrupts the molecule's ability to pack tightly, thus decreasing the cumulative strength of intermolecular van der Waals forces and lowering the melting point.



Note also that the boiling point for toluene is significantly above the boiling point of benzene! The key factor for the boiling point trend in this case is *size* (toluene has one more carbon), whereas for the melting point trend, *shape* plays a much more important role. This makes sense when you consider that melting involves 'unpacking' the molecules from their ordered array, whereas boiling involves simply separating them from their already loose (liquid) association with each other.

Exercise 3.3.2

Which would you expect to have the higher melting point: 2,3-dimethylbutane or hexane? Explain your reasoning.

Exercise 3.3.3

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=672#h5p-73

If you would like to review or learn about how the particles in solid, liquid and gas states move and interact, the animation below may be helpful. If you would like assistance viewing or working with the animation, talk with your instructor. The phase transitions (melting and boiling) discussed in this chapter are based on these ideas.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=672

CHAPTER IV

CHAPTER 4 THE HYDROCARBONS

4.0 The Hydrocarbons

Learning Objectives

In this chapter you will learn to

- classify structures that fall into the organic families named alkanes, alkenes, alkynes, and aromatic compounds
- give names for structures, and structures to accompany names for substances in these families
- describe the similarities and differences between constitutional isomers in this group of compounds

4.1 Alkanes, Alkenes, Alkynes and Aromatic Hydrocarbons

Anacortes, Washington Refinery

Hydrocarbons are used in a wide variety of applications, and on an enormous scale. They are sources from natural gas and crude oil, the fossil fuel substances taken from underground. These unrefined products are mixtures which are refined in industrial facilities to generate the raw materials used to produce everything from gasoline, to plastics, paints, and cosmetics.

Hydrocarbons are the simplest organic compounds, but they have interesting physiological effects. These effects depend on the size of the hydrocarbon molecules and the part of the body which is exposed to them.

Alkanes of low molar mass—those with from 1 to approximately 10 or so carbon atoms—are gases or light liquids that act as anesthetics. Inhaling these hydrocarbons in gasoline or aerosol propellants for their intoxicating effect is a major health problem that can lead to liver, kidney, or brain damage or to immediate death by asphyxiation by excluding oxygen. Accidental exposure to these fumes is also a danger in certain workplaces.

Swallowed, liquid alkanes do little harm while in the stomach. In the lungs, however, they cause "chemical" pneumonia by dissolving fatlike molecules from cell membranes in the tiny air sacs (alveoli). The lungs become unable to expel fluids, just as in pneumonia caused by bacteria or viruses. People who swallow gasoline or other liquid alkane mixtures should not be made to vomit, as this increases the chance of getting alkanes into the lungs. (There is no home-treatment antidote for gasoline poisoning; call a poison control center.)

Cream cosmetics often contain larger-molecule hydrocarbons. Clairechkim, CC BY-SA 4.0 *via Wikimedia Commons*

On skin, liquid alkanes with approximately 5–16 carbon atoms per molecule wash away natural skin oils and cause drying and chapping, while heavier liquid alkanes (those with approximately 17 or more carbon atoms per molecule) act as emollients (skin softeners). Such alkane mixtures as mineral oil and petroleum jelly can be applied as a protective barrier. Water and aqueous solutions such as urine will not dissolve such a film, which explains why petroleum jelly is used in diaper ointments. A similar protective barrier is set up in anti-chafing products marketed to athletes.

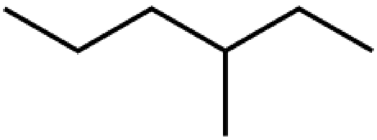
Alkenes, Alkynes and Aromatic hydrocarbons are a bit more reactive and have more complex chemical and physiological profiles. Their physical properties are quite similar to alkanes, however, since they are nonpolar due to the roughly equivalent electronegativities of carbon and hydrogen.

4.2 Names and Structures for Hydrocarbons

As we considered organic structures in the earlier portions of this book, alkanes were presented as examples because they are in many ways the simplest of organic molecules. And yet hydrocarbons can be very small or very large, can include straight chains of carbons or elaborate branching, and can have ring structures and even bridging carbons over rings. The alkenes and alkynes have double and triple bonds that produce new complexities in the structures, as well as reactivity. Then there is the issue of aromaticity, a phenomenon related to structure that is also common among hydrocarbon compounds.

Hydrocarbons are not simple!

You have already learned the basic naming conventions for small (1-10 carbon) straight chain and somewhat branched alkanes. These include a suffix 'ane' to indicate membership in the alkane family, the base of the name related to the number of carbons (e.g. 'hex' for a six-carbon parent chain) and indication of branching with a location for the branch and a name for it:



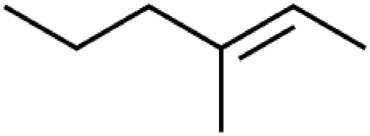
This is 3-methylhexane

Check your understanding by completing the questions in the short quiz here.

Exercise 4.2.1-3

An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=662#h5p-8

When faced with a structure containing a functional group such as an alkene, the name of the related alkane can be a good starting point. Most elements of the name will be the same, with the exception that the identity and location of the functional group itself needs to be conveyed somehow. For the alkenes, the suffix used is no longer 'ane,' but is now 'ene.' The location of the double bond is identified with a number. Count a parent chain that includes the alkene, counting from the end of the chain with the lowest possible number assignment given to the double bond. Then use the number of the carbon where the double bond is first encountered as the location indicator. Current IUPAC rules put the number immediately before the 'ene' suffix, but name changes are sometimes accepted rather slowly; it remains very common to see this number earlier in the name:



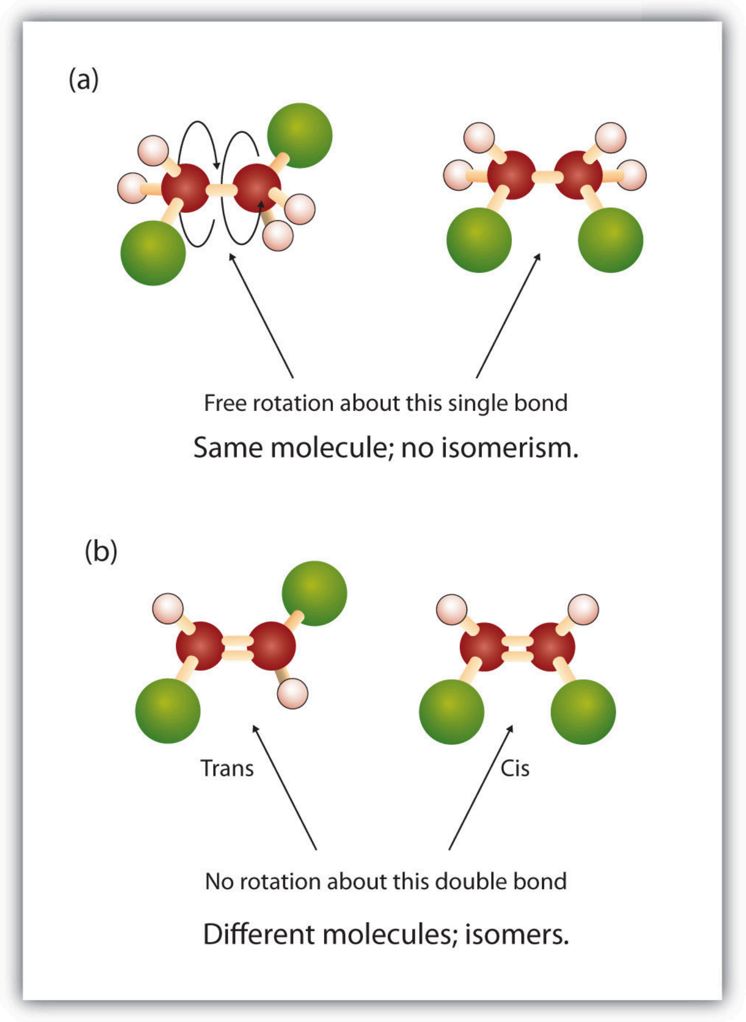
This is 3-methyl-hex-2-ene

Acceptable names for this molecule include 3-methylhex-2-ene and 3-methyl-2-hexene. IUPAC rules encourage placing the location identifier close to the feature at that location. The first name follows IUPAC rules to the letter. However these names can seem awkward even to chemists, and the second form is used frequently.

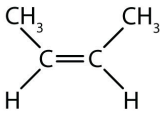
Other aspects of naming alkenes are identical to the process used for alkanes: the parent chain is indicated by the base name and the branches are numbered and named just as they are for alkanes.

Geometric Isomers in Alkenes

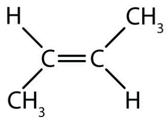
One other structural variation occurs with alkenes. The geometry of the carbon-carbon double bond is fixed, with no rotation along the axis of the double bond. Thus, two different isomers of a substance are often possible. Just like the structural isomers we have already considered, these are related but different compounds that have the same molecular formula. However, the geometric isomers are also the same in terms of their atom connectivity: each atom in the molecule has the same types of bonds (same connections) to its neighbors. The difference lies only in the 3-dimensional layout of the molecule.



The word prefixes ‘cis’ and ‘trans’ are commonly used to indicate which of the two geometric isomers is being identified.



cis-2-butene



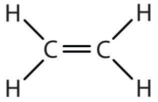
trans-2-butene

The ‘cis’ and ‘trans’ nomenclature is based on the parent chain: if the chain comes into the double bond on one side (long axis) of the double bond and leaves on the same side, it is a ‘cis’ isomer. If the parent chain leaves the double bond opposite where it came in, the isomer is termed ‘trans.’

IUPAC has a system for handling the distinction between these geometric isomers that uses the letters E and Z. For IUPAC, E and Z names are derived by applying a set of rules that rank the groups connected to each carbon of the double bond, and assign one with a higher priority than the other. By then following the trail of these groups, from higher priority atom through the two carbons of the double bond and out the other side, the arrangement can be identified and named. If these higher priority groups enter and exit the alkene on the same side (along the axis of the double bond) the molecule is described as ‘Z,’ short for zusammen, German for ‘together.’ If the groups enter and exit the double bond on opposite sides the structure is identified as ‘E’ for entgegen, meaning ‘opposite.’

Z and E isomers often correspond with cis and trans isomers, but not always, since the priority groups are usually but not always in the parent chain.

Note that alkenes at the end of a carbon chain will not exhibit this kind of isomerism, because the carbon at the end of the chain has two hydrogens on it:



Ethene and propene do not have cis and trans isomers because the carbon chains do not extend beyond the double bond. Any alkene with identical groups attached at the double bond similarly can not exist in a cis or trans form.

Why does this geometric distinction matter? The reason is because these isomers are different substances, and will have different characteristics. Specific isomers must be incorporated into pharmaceuticals containing alkenes, for instance, if they are to have the desired characteristics and not deleterious effects.

If you reconsider the structure above you should now recognize that it is one of these isomers. Since the parent chain comes into carbon 2 from below and exits from carbon three above the plane of the double bond, this is a trans isomer and could be better named as E-3-Methylhex-2-ene.

Remember these systematic names are coded information, and like any code it takes time and practice (and frequent errors along the way) to learn. With repeated use the code becomes familiar and you can become fluent in reading and understanding the names and structures.

You can practice naming some alkenes by completing the quiz here.

Exercise 4.2.4-6

An interactive H5P element has been excluded from this

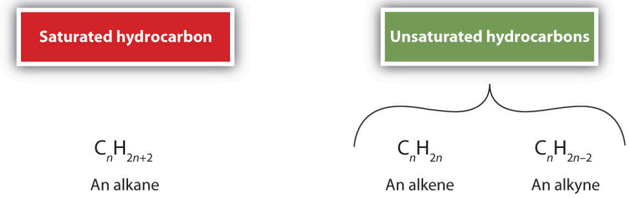
version of the text. You can view it online here: [*https://openoregon.pressbooks.pub/introductoryorganic/?p=662#h5p-9*](https://openoregon.pressbooks.pub/introductoryorganic/?p=662#h5p-9)

Alkynes are named similarly to alkenes but without the concern for designating cis or trans isomers.

Exercise 4.2.7-8

An interactive H5P element has been excluded from this version of the text. You can view it online here: [*https://openoregon.pressbooks.pub/introductoryorganic/?p=662#h5p-10*](https://openoregon.pressbooks.pub/introductoryorganic/?p=662#h5p-10)

An alkene or alkyne having one or more multiple (double or triple) bonds between carbon atoms is called unsaturated. This is because they have fewer hydrogen atoms than does an alkane with the same number of carbon atoms, as is indicated in the following general formulas:

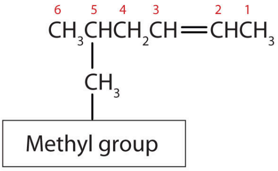


Summary of Naming Rules for Alkenes and Alkynes

The Rules for Naming Alkenes According to the International Union of Pure and Applied Chemistry (IUPAC) are summarized here:

1. The longest chain of carbon atoms *containing the double or triple bond* is considered the parent chain. It is named using the same stem as the alkane having the same number of carbon atoms but ends in *–ene* to identify it as an alkene. Thus the compound $CH_2{=}CHCH_3$ is *propene*. Alkynes are similarly indicated, using the suffix *-yne.*
2. If there are four or more carbon atoms in a chain, we must indicate the position of the double or triple bond. The carbons atoms are numbered so that the first of the two that are doubly or triply bonded is given the lower of the two possible numbers. The compound $CH_3CH{=}CHCH_2CH_3$, for example, has the double bond between the second and third carbon atoms. Its name is 2-pentene (not 3-pentene).

3. Substituent groups are named as with alkanes, and their position is indicated by a number. Thus,



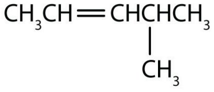
$$\overset{6}{CH_3}\underset{\underset{CH_3}{|}}{\overset{5}{C}H}\overset{4}{C}H_2\overset{3}{C}H{=}\overset{2}{C}H\overset{1}{C}H_3$$

   is 5-methyl-2-hexene. Note that the numbering of the parent chain is always done in such a way as to give the double bond the lowest number, even if that causes a substituent to have a higher number. *The double bond always has priority in numbering.*
4. For alkenes, identify the specific geometric isomer as

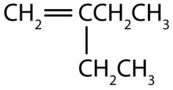
necessary by using the E or Z tag.

Worked Examples

Name each compound, without concerning yourself with E/Z designation.



$CH_3CH{=}CHCH(CH_3)CH_3$



$CH_2{=}C(CH_2CH_3)CH_2CH_3$

Solution

1. The longest chain containing the double bond has five carbon atoms, so the compound is a *pentene* (rule 1). To give the first carbon atom of the double bond the lowest number (rule 2), we number from the left, so the compound is a 2-pentene. There is a methyl group on the fourth carbon atom (rule 3), so the compound's name is 4-methyl-2-pentene.
2. The longest chain containing the double bond has four carbon atoms, so the parent compound is a *butene* (rule 1). (The longest chain overall has five carbon atoms, but it does not contain the double bond, so the parent name is not *pentene*.) To give the first carbon atom of the double bond the lowest number (rule 2), we number from the left, so the compound is a 1-butene. There is an ethyl group on the second carbon atom (rule 3), so the compound's name is 2-ethyl-1-butene.

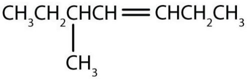
Exercise 4.2.9

Name this compound, without specifying which geometric isomer:

$CH_3CH_2CH_2CH_2CH_2CH{=}CHCH_3$

Exercise 4.2.10

Name this compound without specifying which geometric isomer:



$CH_3CH_2\underset{CH_3}{\underset{|}{C}H}CH{=}CHCH_2CH_3$

Just as there are cycloalkanes, there are *cycloalkenes*. These compounds are named like alkenes, but with the prefix *cyclo*– attached to the beginning of the parent alkene name.

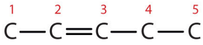
Worked Examples

Draw the structure for each compound.

1. 3-methyl-2-pentene
2. cyclohexene

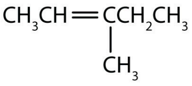
Solution

1. First write the parent chain of five carbon atoms: C–C–C–C–C. Then add the double bond between the second and third carbon atoms:



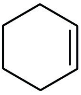
$\overset{1}{C}-\overset{2}{C}=\overset{3}{C}-\overset{4}{C}-\overset{5}{C}$

Now place the methyl group on the third carbon atom and add enough hydrogen atoms to give each carbon atom a total of four bonds.



$CH_3CH{=}\underset{CH_3}{\underset{|}{C}}CH_2CH_3$

2. First, consider what each of the three parts of the name means. *Cyclo* means a ring compound, *hex* means 6 carbon atoms, and –*ene* means a double bond.



Exercise 4.2.11

For each structure listed here, draw a line-bond structure. If you are unable to draw them, describe them in detail with words. Then check your drawing against a reliable source such as Wikipedia, ChemSpider or PubChem. Evaluate the length of the parent chain, the presence and location of branches, and for alkenes, also consider the issue of geometric (cis-trans) isomers.

2-ethyl-1-hexene

cyclopentene

2-methyl-2-pentene
2,3-dimethyl-1-butene
cyclohexene

5-methyl-1-hexene
3-ethyl-2-pentene

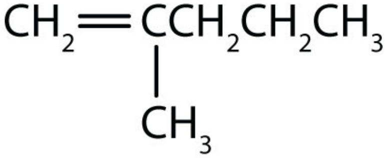
Exercise 4.2.12

Draw (Z)-4-methyl-2-hexene. If you are unable to draw it, describe it in detail with words. Why is it that the name for this compound requires a (Z) while 3-ethyl-2-pentene (from the prior exercise) does not?

Exercises 4.2.13-15

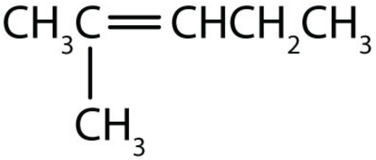
Name each compound according to the IUPAC system.

1.



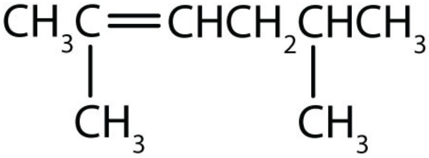
$$\mathrm{CH_2{=}\underset{\underset{\displaystyle CH_3}{|}}{C}CH_2CH_2CH_3}$$

2.

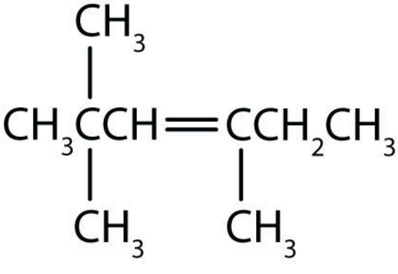


$$\mathrm{CH_3\underset{\underset{\displaystyle CH_3}{|}}{C}{=}CHCH_2CH_3}$$

3.



$$\mathrm{CH_3\underset{\underset{\displaystyle CH_3}{|}}{C}{=}CHCH_2\underset{\underset{\displaystyle CH_3}{|}}{C}HCH_3}$$

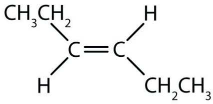


$$\mathrm{CH_3\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}CH{=}\underset{\underset{\displaystyle CH_3}{|}}{C}CH_2CH_3}$$

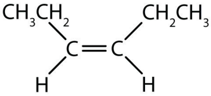
Exercises 4.2.16-19

Classify each compound as a cis isomer, a trans isomer, or neither.

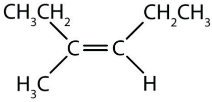
1.



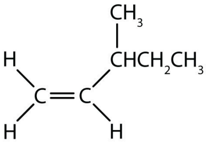
2.



3.



4.

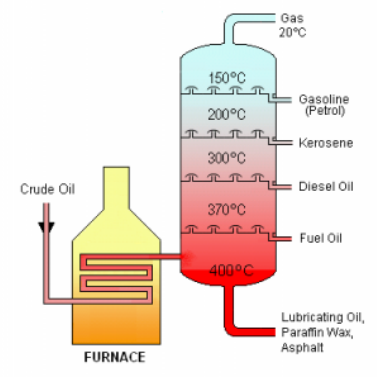


4.3 Properties of the Hydrocarbons

Hydrocarbons are nonpolar substances, with weak intermolecular forces. Their properties are influenced by the lack of strong intermolecular attractive forces. As a group they have relatively low melting and boiling temperatures, and they are poorly or not at all soluble in polar solvents, including water.

The sources of these substances for industry and commerce tend to be geologic deposits of gases (‘natural gas’) and the liquid oil, ‘crude oil.’ These substances along with the solid bitumen make up ‘petroleum,’ a word which in casual use is often used to describe just liquid material. These raw materials are processed in many ways, typically first by distillation to separate out the hydrocarbon components in them. Hydrocarbons are separated by boiling points in distillation, which corresponds to their molecular weights. Fractions containing mixtures of similarly-boiling substances are collected from the distillations, and then can be further refined and/or transformed into products of increasing value.

The lower molecular weight, small hydrocarbons are gases under normal conditions. Many are important substances industrially and in daily life. Methane, for instance, is the principle component of natural gas. It is a gaseous substance with a low boiling point and low reactivity except for its tendency to combust. The slightly larger alkanes ethane, propane and butane are also gases under normal environmental conditions. These also are important industrial feedstocks, and are often combusted to release energy.



Fractional Distillation Column for Separating Components of Crude Oil. By Users Psarianos, Theresa knott on en.wikipedia CC BY-SA 3.0, *https://commons.wikimedia.org/w/index.php?curid=*417182

With increased molecular size, the weak London forces operating between alkane molecules begin to provide enough intermolecular attraction for these substances to exist as liquids. Gasoline, for instance, is a complex mixture but consists mostly of alkanes with 5-8 carbons.

Somewhat larger hydrocarbons, while still liquid, are more viscous and have higher boiling points, and are used as kerosene and motor oil. Mineral oil ('baby oil') is also composed of alkanes in this group; petroleum jelly (Vaseline™) is similar.

At higher molecular weights, another fraction of alkanes are waxy solids. Blends of this distilled fraction of crude oil are sold as paraffin.

Note that all of the substances described here are obtained through mining: from the tapping of natural gas (methane) wells to the processing of liquid crude oil. These substances originated as dead material from living organisms that have been held and pressurized under the surface of the earth for geologic time spans. In these processes which occur in oxygen-poor environments, the production of hydrocarbons is favored over more oxidized organic compounds like alcohols.

The hydrocarbons are the raw materials used by enormous industries around the world. This includes the fossil fuel and gasoline industry, the plastics industry and the pharmaceutical and cosmetics industries, all of which make heavy use of oil and gas-derived materials. Our quality of life has been heavily impacted by these substances for better and for worse. At the moment these substances are inexpensive and readily-available materials that can be chemically altered to suit our needs, and we rely on them. Substituting for these materials is often difficult because there is no source of hydrocarbons as abundant, anywhere on earth. The geologic processes leading to the formation of petroleum occur in an oxygen-deficient environment, producing highly reduced carbons in these substances from decaying material. At the earth's surface, abundant oxygen leads to the production of compounds with more oxidized carbons.

The nonpolar nature of crude oil chemicals contributes to environmental problems associated with oil spills. Spilled crude oil floats at the surface of water. It streams outward over huge areas and thus impacts large areas near a spill. Nonpolar materials are not easily removed by water, since they do not dissolve in polar solvents, complicating cleanup.

Alkenes, alkynes and aromatic compounds exist in the complex mixtures we get from oil and gas, but these functional groups also show up in biological material at the surface of the earth. Alkenes and alkynes are prone to some reactions however, which means that they do not exist in stable forms in the environment to the same degree as alkanes.

Physical Properties of Some Selected Alkenes. Like alkanes they have low melting and boiling point temperatures.

IUPAC Name	Molecular Formula	Condensed Structural Formula
ethene	C_2H_4	$CH_2{=}CH_2$
propene	C_3H_6	$CH_2{=}CHCH_3$
1-butene	C_4H_8	$CH_2{=}CHCH_2CH_3$
1-pentene	C_5H_{10}	$CH_2{=}CH(CH_2)_2CH_3$
1-hexene	C_6H_{12}	$CH_2{=}CH(CH_2)_3CH_3$
1-heptene	C_7H_{14}	$CH_2{=}CH(CH_2)_4CH_3$
1-octene	C_8H_{16}	$CH_2{=}CH(CH_2)_5CH_3$

Synthetic Polymers

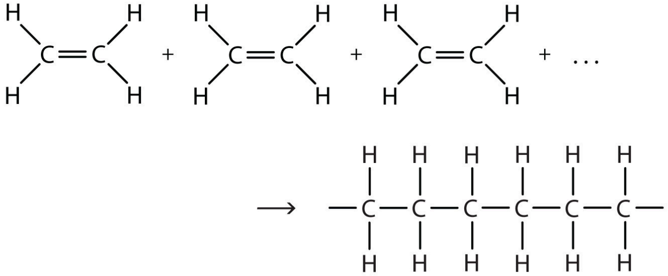
The most important commercial use of alkenes relates to *polymerizations*, reactions in which small molecules, referred to in general as monomers, are converted into enormous ones. These **polymers** are giant molecules formed by the combination of monomers in a repeating manner. A polymer is as different in characteristics from its monomer as a long strand of spaghetti is from a tiny speck of flour. For example, polyethylene, the familiar waxy material used to make plastic bags, is made from the monomer ethylene—a gas. Polyethylene is produced in astounding quantities: as of 2017, over 100 million tons were produced each year (source: Wikipedia).

The Production of Polyethylene

Polyethylene pellets are produced through the polymerization of gaseous ethene to produce the solid product. These pellets, called nurdles, are a commercial product which can be manipulated to form a wide variety of consumer products.

Nurdles of polyethylene can be melted and formed into sheets, bags, bottles, pipes, etc.. It can be mixed with other materials to manipulate the properties of the finished product so that it is harder or more flexible, colored or resistant to ultraviolet light. This versatility has made it immensely popular as a raw material.

Polyethylene is made by a chemical process called addition polymerization,in which monomers add to one another to produce a polymeric product that contains all the atoms of the starting monomers. Ethene molecules are joined together in long chains. The polymerization can be represented by the reaction of a few monomer units:

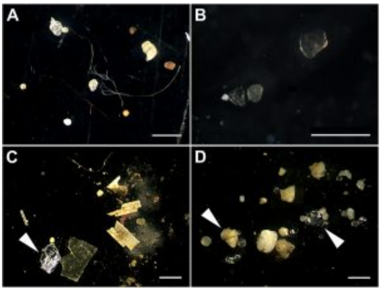


The bond lines extending at the ends in the formula of the product indicate that the structure extends for many units in each direction. Notice that all the atoms—two carbon atoms and four hydrogen atoms—of each monomer molecule are incorporated into the polymer structure.

Polyethylene is so stable that it exists in the environment for a very long time after disposal. With enormous production and such a long lifespan, plastic pollution (from polyethylene as well as other plastics) is increasingly concerning. The discovery of microplastics, which are minute bits of plastic material, in the environment in all kinds of remote environments and in the bodies of animals has led to increasingly worry about the impacts of our plastic use on our health and the health of the environment.

The scale of the problem is immense: More than half the compounds produced by the chemical industry are synthetic polymers. Most of this material resists chemical decomposition through natural processes.

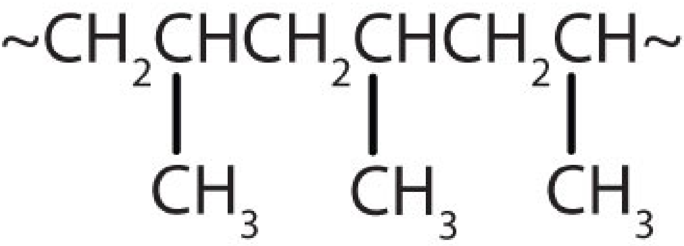
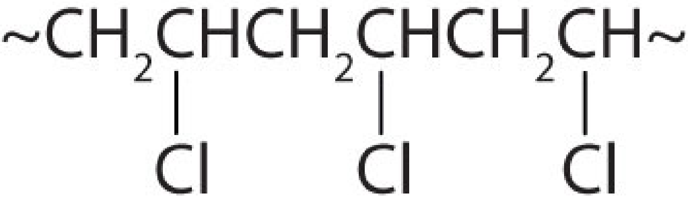
Polyethylene is not the only polymer produced at such a scale. Some other common addition polymers are listed in the table below. Many polymers are mundane (e.g., plastic bags, food wrap, toys, and tableware), but there are also polymers that conduct electricity, have amazing adhesive properties, or are stronger than steel but much lighter in weight. Specialized polymers are increasingly developed and selected for very specific purposes, such as medical applications.



Microplastics in freshwater ecosystems. By Martin Wagner et al. – Wagner et al. CC BY 4.0, *https://commons.wikimedia.org/w/index.php?curid=*39507778

This dental impression was made using polyvinyl siloxane, a polymer that quickly solidifies from a viscous liquid to a rubber-like solid. The materials are safe enough to use in someone's mouth. -public domain photo

Some Addition Polymers

Monomer	Polymer
$CH_2{=}CH_2$	$\sim CH_2CH_2CH_2CH_2CH_2CH_2\sim$
$CH_2{=}CHCH_3$	 $\sim CH_2\underset{\underset{CH_3}{\mid}}{CH}CH_2\underset{\underset{CH_3}{\mid}}{CH}CH_2\underset{\underset{CH_3}{\mid}}{CH}\sim$
$CH_2{=}CHCl$	 $\sim CH_2\underset{\underset{Cl}{\mid}}{CH}CH_2\underset{\underset{Cl}{\mid}}{CH}CH_2\underset{\underset{Cl}{\mid}}{CH}\sim$
$CF_2{=}CF_2$	$\sim CF_2CF_2CF_2CF_2CF_2CF_2\sim$

Many natural materials—such as proteins, cellulose and starch, and complex silicate minerals—are also polymers. But as natural products they tend to be subject to natural decay processes, breaking down chemically and by the action of microorganisms in the environment.

Exercise 4.3.1

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=664#h5p-53

4.4 Aromatic Hydrocarbons

Aromatic Compounds

Next we consider a class of hydrocarbons with molecular formulas like those of unsaturated hydrocarbons, but which react in different ways than the alkenes. For instance, while alkenes are prone to having new atoms and groups bond across the double bond (so-called 'addition' reactions) these compounds do not. These compounds are less prone to react, and when they do so they tend to substitute one atom or group for another at the functional group instead.

These compounds are said to be **aromatic.**

Benzene

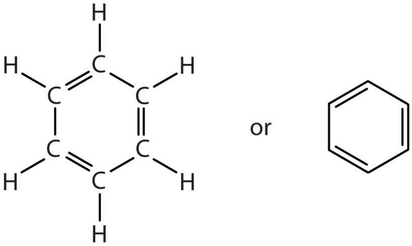
We start with the simplest of these compounds, composed of a ring of 6 carbons with one hydrogen attached to each, named benzene. Benzene is of great commercial importance, but its characteristics also include noteworthy negative health effects.

The formula for benzene, C_6H_6, seems to indicate that benzene has a high degree of unsaturation, and it is usually drawn with three double bonds. However, benzene does not react like an alkene. It does not, for example, react readily with bromine, which is a dependable reaction used to identify alkene double bonds in a sample. It is actually quite unreactive.

Benzene is a liquid that smells like gasoline, boils at 80°C, and freezes at 5.5°C, and dissolves many nonpolar substances. It was formerly used to decaffeinate coffee and was a significant component of many consumer products, such as paint strippers, rubber cements, and home dry-cleaning spot removers. It was removed from many product formulations in the 1950s, but remained in consumer products until the 1970s when it was associated with leukemia deaths.

Benzene is still important in industry as a precursor in the production of plastics (such as polystyrene (Styrofoam^{TM}) and nylon), drugs, detergents, synthetic rubber, pesticides, and dyes. It is used as a solvent for such things as cleaning and maintaining printing equipment and for adhesives such as those used to attach soles to shoes. Benzene is a natural constituent of petroleum products, but because it is a known carcinogen, its use as an additive in gasoline is now limited.

Benzene is typically drawn as a cyclic, hexagonal, planar structure of six carbon atoms with one hydrogen atom bonded to each. We can draw the structure with alternate single and double bonds, either as a full structural formula or as a line-bond formula:



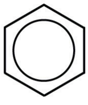
Experimental evidence, however, indicates that all six of the carbon-to-carbon bonds in benzene are equivalent. Each has the same bond length and strength as the others, and these bonds are neither as short and strong as typical alkene double-bonds, nor as long and weak as the single bonds we usually see in hydrocarbons.

The chemical properties of benzene don't match alkenes, nor do the measured bond characteristics. It just doesn't fit in with the alkenes. But aromaticity provides us with an explanation for these facts.

In the aromatic ring system of benzene, valence electrons are shared equally by all six carbon atoms. We describe the electrons are *delocalized*, or spread out, over all the carbon atoms. It is understood that each corner of the hexagon is occupied by one carbon atom, and each carbon atom has one hydrogen atom attached to it. The alternating double and single bonds around the ring actually are intermediate in length and strength between single C-C and double C=C bonds because of this delocalization.

The reactivity is also affected by this structure, so that atoms are not added to the carbons in the ring. Aromaticity provides a stability to the ring that alkenes do not have.

Sometimes, especially in pharmaceutical literature, you will see the benzene ring drawn with a circle inside the hexagon replacing the double bonds, in an attempt to convey the equivalence of the bonds within the ring:



Chemists generally aren't satisfied with this representation, however, for reasons we will not get into here. What is important to take away from the discussion of bonding in benzene is that the drawings we usually make of it don’t tell the entire story, and the explanation -called aromaticity, or aromatic character in the benzene ring- is connected to characteristics of compounds containing this feature. If you can spot a benzene ring, you will be able to more accurately predict the properties of substances from their formulas.

Why You Shouldn't Love the Smell of Gasoline

Pumping fuel at a gas filling station. By Tony Webster from Minneapolis, Minnesota, United States – Gas Pump, CC BY-SA 2.0, https://commons.wikimedia.org/w/index.php?curid=65977585

Once widely used as an organic solvent, benzene is now known to have both short- and long-term toxic effects. It is in gasoline, though in recent decades the amount of benzene in gas has been decreased to limit the chance of harmful exposure. It is a volatile liquid that can be taken into the lungs by simply standing nearby. The hoods over gas nozzles are designed to reduce this inhalation exposure for anyone operating a pump.

Inhaling large concentrations of benzene can cause nausea and even death due to respiratory or heart failure, while repeated exposure leads to a progressive disease in which the ability of the bone marrow to make new blood cells is eventually destroyed. This results in a condition called *aplastic anemia*, in which there is a decrease in the numbers of both the red and white blood cells.

Structure and Nomenclature of Aromatic Compounds

Historically, benzene-like substances were called aromatic hydrocarbons because they had distinctive aromas. Today, aromatic compounds include anythat contain a benzene ring or have the properties we associate with this group of compounds.

Aromatic compounds often are derivatives of benzene itself with substitution of other atoms and groups for one or more of the hydrogens on the ring. Other aromatic compounds are trickier to identify, but most contain 5 or 6-membered rings composed mostly of carbon, with alternating single and double bonds.

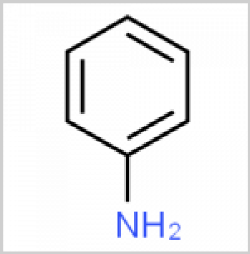
Some representative aromatic compounds and their uses are listed in the table, where the benzene ring is represented as C_6H_5.

Table Some Representative Aromatic Compounds

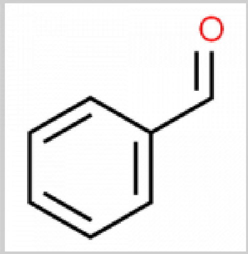
Name	**Structure**	**Typical Uses**
aniline	$C_6H_5–NH_2$	starting material for the synthesis of dyes, drugs, resins, varnishes, perfumes; solvent; vulcanizing rubber
benzoic acid	$C_6H_5–COOH$	food preservative; starting material for the synthesis of dyes and other organic compounds; curing of tobacco
bromobenzene	$C_6H_5–Br$	starting material for the synthesis of many other aromatic compounds; solvent; motor oil additive
nitrobenzene	$C_6H_5–NO_2$	starting material for the synthesis of aniline; solvent for cellulose nitrate; in soaps and shoe polish
phenol	$C_6H_5–OH$	disinfectant; starting material for the synthesis of resins, drugs, and other organic compounds
toluene	$C_6H_5–CH_3$	solvent; gasoline octane booster; starting material for the synthesis of benzoic acid, benzaldehyde, and many other organic compounds

In the International Union of Pure and Applied Chemistry (IUPAC) system, aromatic hydrocarbons such as those above are named as derivatives of benzene. In these structures, it is immaterial whether the single substituent is written at the top, side, or bottom of the ring: a hexagon is symmetrical, and therefore all positions are equivalent.

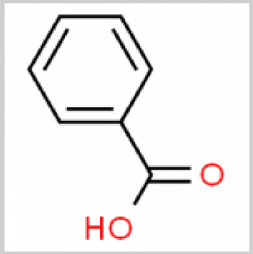
Structures of Some Benzene Derivatives



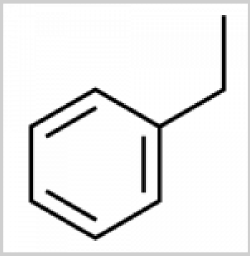
anilene



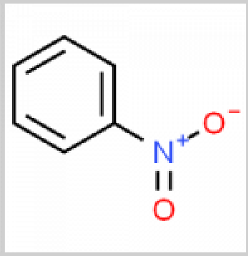
benzaldehyde



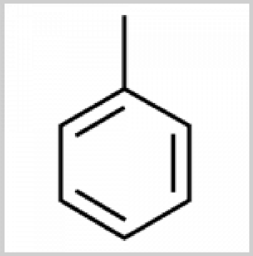
benzoic acid



ethylbenzene



nitrobenzene

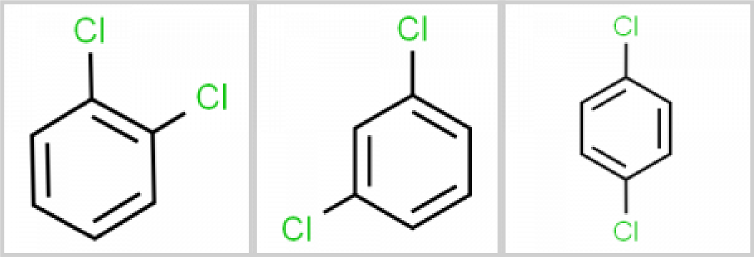


toluene

Although some compounds are referred to exclusively by IUPAC names, some are more frequently denoted by common names. Thus methylbenzene is usually called toluene, for instance.

When there is more than one substituent, the vertices of the hexagon are no longer equivalent, so we must designate the relative positions of substituent groups. There are three possible disubstituted benzenes, and we can use numbers to distinguish them. We start numbering at the carbon atom to which one of the groups is attached and count toward the carbon atom that bears the other substituent group by the shortest path.

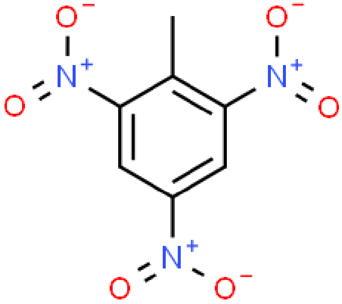
The Three Isomeric Dichlorobenzenes



1,2-dichlorobenzene *1,3-dichlorobenzene* *1,4-dichlorobenzene*

Common names are also used: the prefix *ortho* (*o*-) for 1,2-disubstitution, *meta* (*m*-) for 1,3-disubstitution, and *para* (*p*-) for 1,4-disubstitution.

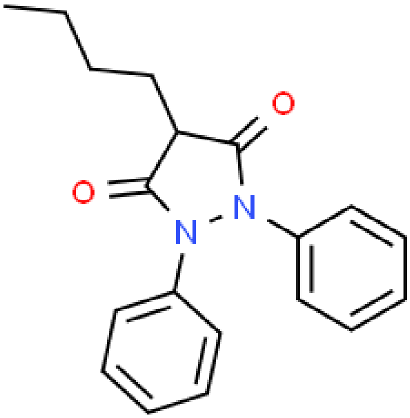
The nitro (NO_2) group is a common substituent in aromatic compounds. Many nitro compounds are explosive, for instance 2,4,6-trinitrotoluene (TNT).



trinitrotoluene, or TNT.

Sometimes an aromatic group is found as a substituent bonded to a nonaromatic entity or to another aromatic ring. The group of atoms remaining when a hydrogen atom is removed from an aromatic compound is called an aryl group. The most common aryl group is derived from benzene (C_6H_6) by removing one hydrogen atom (C_6H_5) and is called a *phenyl* group, from *pheno*, an old name for benzene.

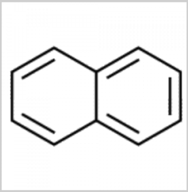
Phenylbutazone contains two of these phenyl groups. The drug, known commonly as “bute,” is a non-steroidal anti-inflammatory drug (NSAID) used in veterinary medicine. Its IUPAC name is 4-Butyl-1,2-diphenyl-3,5-pyrazolidinedione:

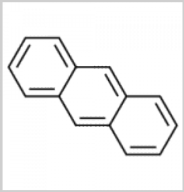


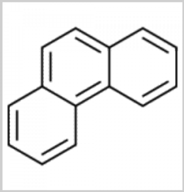
Can you identify the two phenyl groups that make up a portion of the molecule of phenylbutazone shown here?

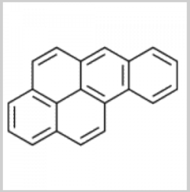
Polycyclic Aromatic Hydrocarbons

Some common aromatic hydrocarbons consist of fused benzene rings—rings that share a common side. These compounds are called polycyclic aromatic hydrocarbons (PAHs).


napthalene


anthracene


phenanthrene


benzo(a)pyrene

All the examples here can be isolated from coal tar. Naphthalene has a pungent odor you may recognize from mothballs. Anthracene is used in the manufacture of certain dyes.

The fourth example, benzo(a)pyrene, also forms during incomplete combustion, so it is a component of soot, auto and diesel exhaust, cigarette smoke and wood smoke. Our bodies metabolize it into compounds that react in well-understood ways with DNA, producing mutations that can develop into cancer. Benzo(a)pyrene is also produced during high temperature cooking, leading to associations between grilled and fried foods, especially meats, and cancer risk.

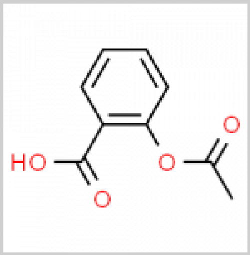
To Your Health: Polycyclic Aromatic Hydrocarbons and Cancer

The intense heating required for distilling coal tar results in the formation of PAHs. For many years, it has been known that workers in coal-tar refineries are susceptible to a type of skin cancer known as tar cancer. Investigations have shown that a number of PAHs are carcinogens. One of the most active carcinogenic compounds, benzopyrene, occurs in coal tar and has also been isolated from cigarette smoke, automobile exhaust gases, and charcoal-broiled steaks. It is estimated that more than 1,000 t of benzopyrene are emitted into the air over the United States each year. Only a few milligrams of benzopyrene per kilogram of body weight are required to induce cancer in experimental animals.

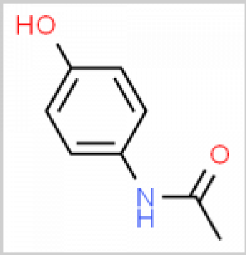
Biologically Important Compounds with Benzene Rings

Substances containing the benzene ring are common in both animals and plants, although they are more abundant in the latter. Plants can synthesize the benzene ring from carbon dioxide, water, and inorganic materials. Animals cannot synthesize it, but they are dependent on certain aromatic compounds for survival and therefore must obtain them from food. The essential amino acids phenylalanine, tyrosine, and tryptophan and vitamins K, B_2 (riboflavin), and B_9 (folic acid) all contain the benzene ring. Many important drugs also do.

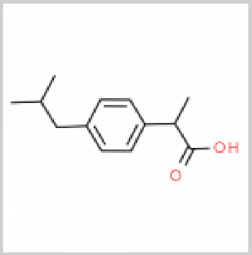
Some Drugs That Contain a Benzene Ring



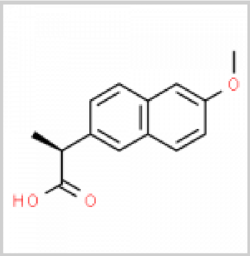
aspirin



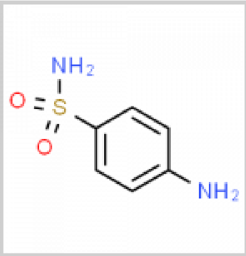
acetaminophen



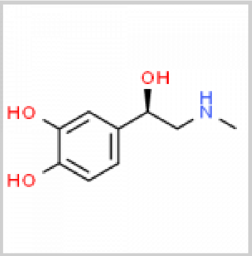
ibuprofen



naproxen



sulfanilamide

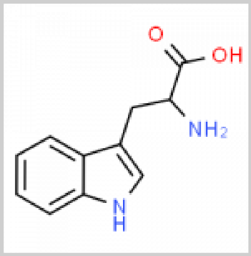


epinephrine

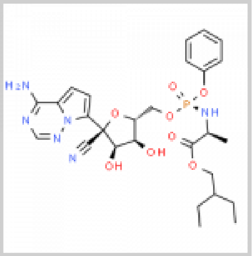
Heterocyclic compounds

Some cyclic compounds have an element other than carbon atoms in the ring. These compounds are called *heterocyclic compounds.* These substances are also sometimes aromatic, in which case they are called *heterocyclic aromatic compounds.*

Two examples are shown here. The first, smaller structure is tryptophan, an amino acid. The second, larger structure is that of Remdesivir, an antiviral drug developed by Gilead sciences and used as a treatment for COVID-19 during the firs part of the pandemic. Remdesivir has both the classic benzene ring “phenyl” group as well as a heterocyclic aromatic ring.



tryptophan



Remdesivir

Exercise 4.4.1

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https://openoregon.pressbooks.pub/introductoryorganic/?p=259#h5p-54

CHAPTER V

CHAPTER 5 ALCOHOLS, THIOLS, ETHERS AND AMINES

5.0 Alcohols, Thiols, Ethers and Amines

Learning Objectives

In this chapter you will learn to

- identify the functional groups alcohol, phenol, thiol, ether, and amine on organic chemical structures
- provide reasonably correct names when given structures, and draw structures when given names, for structures containing the functional groups above
- recognize the potential for hydrogen bonding in alcohols and amines and relate this to their physical properties (melting and boiling points, water solubility)
- explain the solubility and melting point changes that accompany amine protonation

5.1 Names and Structures for Alcohols, Thiols, Ethers, and Amines

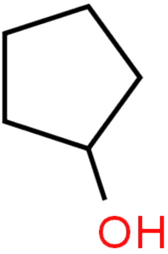
Now that we have learned quite a lot about the hydrocarbons, we are ready to venture into discussion of other organic families. Those described in this chapter include the alcohols, thiols, ethers and amines. Since these families include functional groups that contain heteroatoms, there will be some differences between them and the hydrocarbons. For each of the four groups considered here, as well as for additional organic families we will discuss later, we will organize our learning into several sections.

- identifying the functional group on a structure
- drawing from names, and naming structures
- explaining the physical properties of these substances, including discussion of melting points, boiling points, and solubility in water and other solvents

Interspersed throughout, you will be introduced to a few new ideas that may have specific relevance to the functional group under consideration. Reactivity is also related to organic families, but we are postponing that conversation until a bit later.

Alcohols

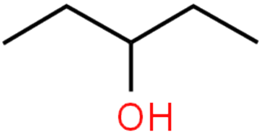
An alcohol can be recognized by the presence of the hydroxy or alcohol functional group on an organic molecule. Consider the structure shown below:



The oxygen and hydrogen connected to a carbon constitute the alcohol functional group. Atoms that are not carbon or hydrogen in organic molecules are often referred to as **heteroatoms**, where 'hetero' indicates 'other,' meaning an atom of an element other than carbon or hydrogen. When faced with a large molecule you wish to understand it is smart to first find the heteroatoms. They are indicators of functional groups, and in that role can have a strong influence on the properties of these substances.

Alcohol names are related closely to the names of the hydrocarbons they resemble, with key modifications. For instance, the molecule above without the hydroxy group would be named cyclopentane. The alcohol is named cyclopentanol.

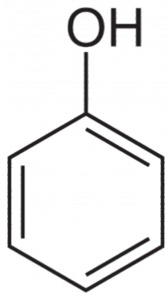
The '-ol' suffix may require a location signifier. When this is the case, provide a number that indicates the number of the carbon in the parent chain where the oxygen is attached. For cyclopentanol this is not necessary because there are not distinct carbons that are numbered. But in this example a number is required:



Numbering from either end of the parent chain (5 carbons) would identify carbon 3 as the point where the hydroxy (-OH) group connects to the chain. So the name of this alcohol is 3-pentanol. You may also see the more technically correct (according to IUPAC) pentane-3-ol, but this form of nomenclature has been slow to catch on in practice.

As with branches on an alkane, the number is assigned from whichever end of the parent chain produces the lowest possible number for the alcohol.

Aromatic rings with alcohol groups directly attached to them are different enough than non-aromatic ('aliphatic') alcohols to warrant their own names. Compounds containing this structure are named phenols, after the name of the substance below, which is the simplest of these aromatic alcohols, and is named phenol:



There are of course variations that make for extra challenge: branched hydrocarbon structures with alcohol groups and molecules with more than one functional group, for instance. Those issue can be dealt with later, once you have more experience.

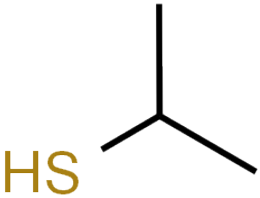
Exercise 5.1.1-2

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=676#h5p-11

Thiols

Thiols are substances that are structurally quite similar to alcohols, however they include Sulfur where Oxygen exists in an alcohol. The group -SH can be referred to as a thiol group. Occasionally the common name mercaptan is still used to describe members of this organic family.

Naming thiols involves a modification of the name of the corresponding hydrocarbon. In this case, rather than removing the '-ane' from an alkane name, the suffix changes to '-anethiol.' For instance:



is named 2-propanethiol.

These names will seem odd as you first learn them and you might find pronunciation unclear or difficult. That is normal. The names are designed to first convey structural information and only secondarily to be easy to speak.

Exercise 5.1.3

An interactive H5P element has been excluded from this version of the text. You can view it online here: *https://openoregon.pressbooks.pub/introductoryorganic/?p=676#h5p-12*

Ethers

Ethers are organic molecules that also contain oxygen. In this case, the oxygen is incorporated into a chain of carbons, so that it has two single-bond connections to two separate carbons. IUPAC rules for naming ethers involve naming one side of the ether as if it were a substituent group on the other carbons. This is somewhat complicated. Making matters worse for students, the systematic names for ethers are not used consistently by chemists. So common names, which utilize two separate words indicating each side of the ether, predominate:

This structure is named by IUPAC rules as Methoxybutane. The 'methoxy' portion describes a group that includes one carbon (and its hydrogens) and the oxygen, built onto a butane parent chain. The common name for this structure is methyl butyl ether.

What are students to do? Ask for clarification on the expectations for naming and drawing ether structures. You will be given guidance.

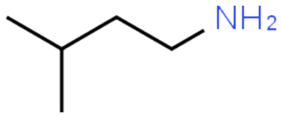
Exercise 5.1.4

An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=676#h5p-13

Amines

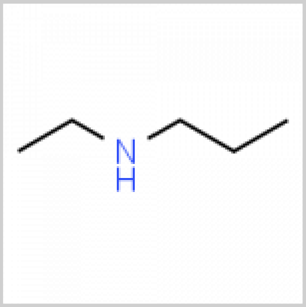
The amine functional group is composed of a nitrogen atom bonded to at least carbon by a single bond. Since nitrogen has 5 valence shell electrons it typically forms 3 bonds to other atoms and has one lone pair of electrons. Nitrogen atoms with one connection to carbon are called primary amines, those with two connections to carbons secondary amines, and those with three connections to carbon are tertiary amines.

The names of primary amines are formed by replacing the '-e' ending on an alkane name with '-amine.' As with other functional groups, the placement on the parent chain is noted with a number. For instance:

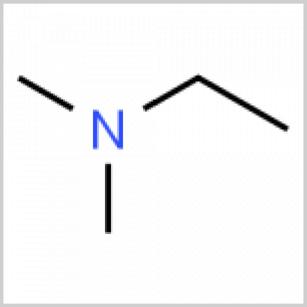


This is 3-methyl-1-butanamine. Note that the numbering is driven by the location of the functional group rather than the branch on the alkane. Functional groups nearly always have priority over other groups when locations are assigned in this way.

Secondary and tertiary amines, which have additional alkyl (carbon-based) groups attached to the nitrogen, are handled by adding a prefix describing the additional alkyl groups and indicating the location for attachment as 'N.' as demonstrated here:



N-ethylpropanamine



N,N-*dimethylethanamine*

Exercise 5.1.5

An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=676#h5p-14

Recall that hydrogen atoms are not shown in line-bond structures for hydrocarbons. When attached to heteroatoms, however, hydrogens are almost always shown explicitly on the structures.

The collection of rules governing naming is complex, since the structures of organic chemistry are so varied. It is not possible for anyone to learn to name everything, and even those who work as professional chemists for years still encounter situations where it is difficult for them to confidently assign a name to a structure (or a structure to a name). But the existence of the system is helpful, and provides an approach to organizing and making sense of the wide array of organic compounds that exist.

5.2 How Hydrogen-bonding Influences Properties

The presence of one or a group of heteroatoms on a molecule can have a huge effect on the properties of that substance. Much of the influence relates to the polarity of bonds between these heteroatoms and carbon. Organic structures often include elements from the upper right-hand corner of the periodic table in them. Oxygen, nitrogen, and other elements in that part of the table tend to have high electronegativity, producing polar bonds to carbon or hydrogen. When such groups are added to nonpolar hydrocarbon structures they usually impart some degree of polarity to the entire molecule, resulting in a molecular dipole moment. As you have already learned this produces intermolecular interactions in bulk samples of these substances, including dipole-dipole interactions as well as, in some cases, hydrogen bonding interactions.

These intermolecular interactions influence the melting point and boiling point temperatures of compounds, and also influence their solubility in water and other solvents. Compared to alkanes of similar size and structure, amines and alcohols especially (but to some extent, also thiols and ethers) have higher melting and boiling points. So under specific conditions (e.g. normal room temperature and pressure) they will more likely be liquids or solids. They also will tend to have lower vapor pressures, which describes how much of the substance escapes into the air at a given temperature, which correlates in some situations to their odor. Their solubility in polar solvents including water and small liquid alcohols (such as methanol, ethanol or 2-propanol) will be greater. Their solubility in nonpolar solvents, such as toluene, will be less than their nonpolar relatives.

Alcohols and amines (other than tertiary amines) both have the ability to engage in hydrogen bonding interactions. As described earlier, the structural requirements for this phenomenon to exist include:

- hydrogen attached to F, O, N, or Cl on a molecule (a highly polarized bond to the hydrogen)
- an electronegative atom with lone pair electrons: F, O, N, or another Group 17 element

The -OH and -NH groups on molecules in these families make hydrogen bonding possible, as both hydrogen-bond donor and hydrogen-bond acceptor atoms are present as part of the functional group itself. Hydrogen bond interactions are notably stronger than other dipole-dipole interactions, so these functional groups have especially strong intermolecular attractive forces and the substances have properties to match.

In ethers polar bonds do exist, and dipole-dipole interactions are in play. However in the ether functional group there is no ability to hydrogen bond completely. The carbon to oxygen bond is polarized, and the oxygen atom on an ether does have lone pair electrons. But there is no hydrogen attached to that oxygen, nor to any other highly electronegative atom.

In thiols we have an architecture that looks like the alcohols, but with sulfur standing in for the oxygen atom of an alcohol. Sulfur is much less electronegative than oxygen and bonds between that atom and hydrogen are much less polar than the oxygen-hydrogen bond of an alcohol. The result is a weak dipole-dipole interaction that can occur in thiols rather than the more powerful hydrogen bond of an alcohol. The properties of thiols are influenced somewhat by the -SH group, but the effect is modest compared to the effect of the hydroxy group on an alcohol.

The effects of intermolecular forces are nuanced, involving both the degree of polarity in functional groups and also the length and shape of the parent hydrocarbon chain itself. But in general, the more functional groups of these types exist in a structure the stronger their influences will be.

Exercise 5.2.1-3

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https://openoregon.pressbooks.pub/introductoryorganic/?p=678#h5p-77

Exercise 5.2.4

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Exercise 5.2.5

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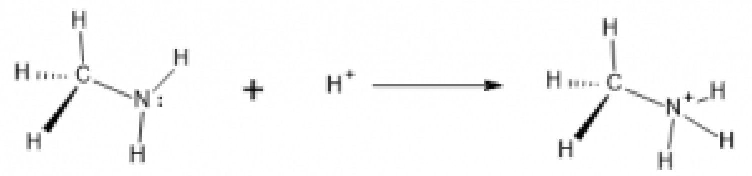
5.3 Amine Protonation

In amines, nitrogen is bonded to three other atoms (alkyl groups or hydrogens) and has a lone pair of nonbonding electrons. This lone pair produces a region of electron density on the nitrogen atom, which coupled with the electronegativity of nitrogen produces a partial-negative charge at that location. In samples containing amines there are intermolecular attractive forces between the amine nitrogen and other partially-positive or positive particles.

Bronsted-Lowry theory describes acids as Hydrogen ion (proton) donors. The hydrogen ion, H^+, is one type of positively-charged particle that can interact with an amine. By associating with the N and utilizing the lone pair for bonding, the amine can convert from an uncharged species to one that carried a positive charge. This takes the H+ from solution and incorporates it into a cation structure, called an ammonium ion:



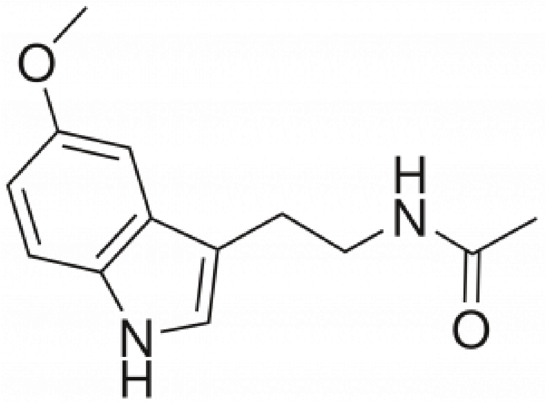
methylamine reacts with acid to produce methylammonium ion

Even at a neutral pH of 7, enough acid is available in solution for the ammonium ion to predominate. At lower pH, more acidic solutions it becomes almost the exclusive form.

Since the free, unprotonated amine is able to pick up or 'accept' a hydrogen ion in this reaction, the free amine (reactant above) is classified as a base. Various amines will exhibit this behavior to a greater or lesser degree, depending on the specific structures surrounding the amine functional group. For instance, molecules of aromatic amines with nitrogen attached are less commonly in the base form and are thus considered weaker bases.

Ammonium ions exhibit properties that clearly differ from the free, uncharged amine. These ions are more water soluble and can form ionic bonds with various anions to produce ionic substances that can be solid at room temperature. Most small unprotonated amines, by contrast, are liquids.

Amines are abundant in nature and appear very commonly in biologically-active molecules, whether those come from natural sources (like plants) or man-made ones (like pharmaceuticals). Liquid medicines are difficult to handle; producers and consumers alike appreciate the long shelf-stability and easy storage of drugs in the form of pills. Whereas an unprotonated amine may be an oily liquid under normal conditions, the corresponding ammonium ion is often part of an ionic solid which can be formed into a tablet. So pharmaceutical companies can use pH adjustment to help them formulate drugs into a better form. Also, the transport of drug molecules in the body will be influenced by water-solubility, so this solubility switch can be important for that reason, too.



Neurotransmitters and hormones frequently contain amines. This is melatonin, a hormone that regulates sleep-wake cycles.

Exercise 5.3.1

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https://openoregon.pressbooks.pub/introductoryorganic/?p=681#h5p-57

Exercise 5.3.2

Provide a description in your own words that explains why a substance that is soluble in water at pH=6 might be insoluble at pH=9.

CHAPTER VI

CHAPTER 6 CHIRALITY AND STEREOISOMERS

6.0 Chirality and Stereoisomers

Learning Objectives

In this chapter you will learn to

- identify chiral carbons in chemical structures
- recognize stereochemical designations in names
- explain how chirality affects the chemistry of substances in chiral systems, including in biology

6.1 Identifying Chiral Carbons

Introduction: Louis Pasteur and the discovery of molecular chirality

Louis Pasteur as a young man. Image: https://commons.wikimedia.org/w/index.php?curid=36413383 orig. from wellcomeimages.org

In 1848, a 25 year old chemist named Louis Pasteur made a startling – and some thought brash – claim to the scientific community. Pasteur was inexperienced, to say the least: he had only earned his doctorate the previous year, and had just started his first job as an assistant to a professor at the *Ecole normale superieure*, a university in Paris. Jean-Baptiste Biot, a highly respected physicist who had already made major contributions to scientific fields as diverse as meteorites, magnetism, and optics, was intrigued but unconvinced by Pasteur's claim. He invited the young man to come to his laboratory and reproduce his experiments.

Decades earlier, Biot had discovered that aqueous solutions of some biologically-derived substances, such as tartaric acid, quinine, morphine, and various sugars, were optically active: that is, the plane of polarized light would rotate in either a positive (clockwise, or right-handed) or negative (counter-clockwise, or left-handed) direction when passed through the solutions. Nobody understood the source of this optical property. One of the biological substances known to be optically active was a salt of tartaric acid, a compound found in abundance in grapes and a major by-product of the wine-making industry.

The compound was dextrorotatory in solution – in other words, it rotated plane-polarized light in the positive (right-handed, or clockwise) direction. Curiously, though, chemists had also found that another form of processed tartaric acid was optically *in*active, despite that fact that it appeared to be identical to the optically active acid in every other respect. The optically inactive compound was called '*acide racemique*', from the Latin *racemus*, meaning 'bunch of grapes'.

Louis Pasteur's claims had to do with experiments he said he had done with the 'racemic' acid. Jean-Babtise Biot summoned Pasteur to his laboratory, and presented him with a sample of racemic acid which he himself had already confirmed was optically inactive. With Biot watching over his shoulder, and using Biot's reagents, Pasteur prepared the salt form of the acid, dissolved it in water, and left the aqueous solution in an uncovered flask to allow crystals to slowly form as the water evaporated.

Pasteur in the laboratory. Wikimedia commons, public domain.

Biot again summoned Pasteur to the lab a few days later when the crystallization was complete. Pasteur placed the crystals under a microscope, and began to painstakingly examine their shape, just as he had done in his original experiments. He had recognized that the crystals, which had a regular shape, were asymmetric: in other words, they could not be superimposed on their mirror image. Scientists referred to asymmetric crystals and other asymmetric objects as being 'chiral', from the Greek word for 'hand'. Your hands are chiral objects, because although your right hand and your left hand are mirror images of one another, they cannot be superimposed. That is why you cannot fit your right hand in a left-handed glove.

More importantly, Pasteur had claimed that the chiral crystals he was seeing under the lens of his microscope were of two different types, and the two types were mirror images of each other: about half were what he termed 'right handed' and half were 'left-handed'. He carefully separated the right and left-handed crystals from each other, and presented the two samples to Biot. The eminent scientist then took what Pasteur told him were the left-handed crystals, dissolved them in water, and put the aqueous solution in a polarimeter, an instrument that measures optical rotation. Biot knew that the processed tartaric acid he had provided Pasteur had been optically inactive. He also knew that unprocessed tartaric acid from grapes had right-handed optical activity, whereas left-handed tartaric acid was unheard of. Before his eyes, however, he now saw that the solution was rotating light to the left. He turned to his young colleague and exclaimed, " *Mon cher enfant, j'ai tant aime ´les sciences dans ma vie que cela me fait battre le coeur*!' (My dear child, I have loved science so much during my life that this makes my heart pound!)

Hands are chiral objects, which are not superimposable despite having the same parts and connections. Chirality also exists at the molecular scale. By Daniel Sone https://commons.wikimedia.org/w/index.php?curid=24028610

Biot had good reason to be so profoundly excited. Pasteur had just conclusively demonstrated, for the first time, the concept of **molecular chirality**: molecules themselves – not just macroscopic objects like crystals – could exhibit chirality, and could be separated into distinct right-handed and left-handed 'stereoisomers'. Tying together ideas from physics, chemistry, and biology, he had shown that nature could be chiral *at the molecular level*, and in doing do he had introduced to the world a new subfield which came to be known as 'stereochemistry'.

About ten years after his demonstration of molecular chirality, Pasteur went on to make another observation with profound implications for biological chemistry. It was already well known that 'natural' tartaric acid (the right-handed kind from grapes) could be fermented by bacteria. Pasteur discovered that the bacteria were selective with regard to the chirality of tartaric acid: no fermentation occurred when the bacteria were provided with pure left-handed acid, and when provided with racemic acid they specifically fermented the right-handed component, leaving the left-handed acid behind.

Pasteur was not aware, at the time of the discoveries described here, the details of the structural features of tartaric acid at the molecular level that made the acid chiral, although he made some predictions concerning the bonding patterns of carbon which turned out to be remarkably accurate. In the more than 150 years since Pasteur's initial tartaric acid work, we have greatly expanded our understanding of molecular chirality. Put simply, stereochemistry is the study of how bonds are oriented in three-dimensional space. It is difficult to overstate the importance of stereochemistry in nature, and in the fields of biology and medicine in particular. As Pasteur so convincingly demonstrated, life itself is chiral: living things recognize different stereoisomers of organic compounds and process them accordingly.

So what, structurally, is a chiral object? The term **chiral**, from the Greek work for 'hand', refers to anything which exhibits 'handedness.' Your hands, of course, are the origin of this term as the prototypical chiral objects. But so are most gloves – you cannot fit your left hand into a right-handed glove, so gloves can come in right-handed and left-handed versions.

If you examine the origin of this handedness in any familiar object that is chiral, you'll find that the relationship between right and left-handed chiral objects are that they are mirror images of one another, and not **superimposable**.

Consider the example of a pair of garden gloves. If you place the right-handed glove over the top of the left-handed glove with the palm surfaces both facing downward, the thumbs point in opposite directions. If you orient the two gloves so the thumbs and fingers overlay one another, then the palms are facing opposite directions.

Also, if you hold the right-handed glove up before a mirror and imagine superimposing the glove with the glove's image in the mirror, the fingers will be aligned (all could lay over one another, thumb to thumb, etc.) but the palm surfaces will be on opposite sides. The image in the mirror is actually identical to a left-handed glove!

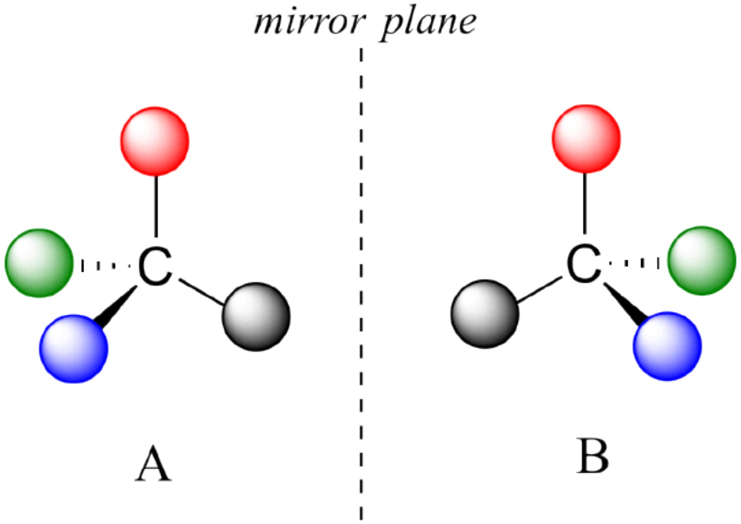
This same phenomenon occurs in any 'handed' object you interact with, and as Pasteur discovered, it also characterizes some objects at the molecular scale.

Another way to consider the phenomenon of chirality is to note that the gloves do not have an internal **mirror plane of symmetry**: you cannot find any way to slice straight through the glove in such a way that one piece of the glove is a mirror image of the other side. The 'slice' defines what is called a 'mirror plane,' which is a plane (2D flat surface). The symmetry we are searching for occurs when the two sides of the plane (two pieces of the glove) are mirror images of one another. *Chiral objects do not have such a plane of symmetry*.

A pair of pants, on the other hand is **achiral** – lacking chirality – because, if you ignore some details, you could slice through the pants and have two halves that are mirror images of one another. Where is that plane? It bisects the pants from the crotch through the waist, with one leg and half of the seat of the pants on each side. This is the internal mirror plane of symmetry. You don't need to buy pants in "right handed" or "left handed" versions, and the mirror image of a pair of pants could be superimposed over the originals.

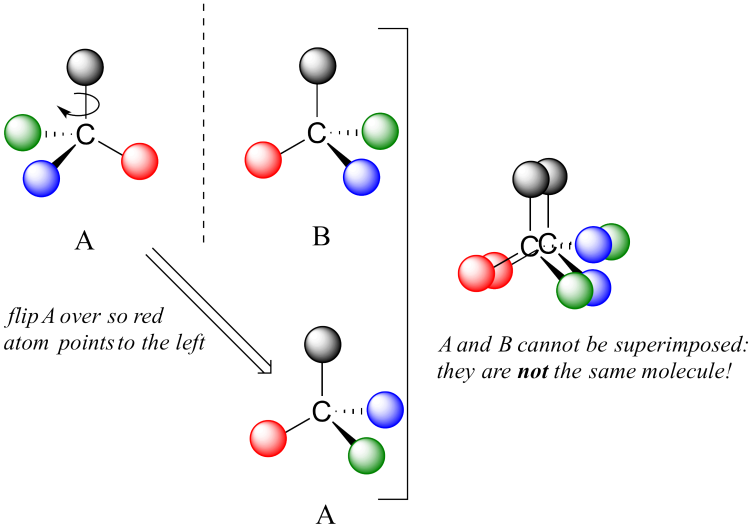
For Pasteur, Biot, and their contemporaries the *source* of chirality at the molecular level was at first undeciphered. It stood to reason that a chiral molecule is one that does not contain a plane of symmetry, and thus cannot be superimposed on its mirror image.

We now know much more about chemical structure. For molecules to have no internal mirror plane of symmetry, to not be superimposable on their mirror images, we know they must contain one or more **chiral centers.** These are almost always tetrahedral carbons with four different substituent groups around them. Consider the cartoon molecule A below: here we have four different substituents denoted by balls of four different colors around a carbon:



The mirror image of A, which we will call B, is drawn on the right side of the figure. Notice that every point on A lines up with the same point on B: in other words, if you looked at A in the mirror, you would see B as the image.

If we could simply slide structure A to see if it is superimposable with B, laying the carbon on A over the top of the carbon on B, we would also be able to align the black and red balls but not the blue and green ones. The blue sphere on A (left) would overlap the green sphere on B, and the green sphere on A would overlap the blue sphere on B.



flip A over so red atom points to the left

*A and B cannot be superimposed: they are **not** the same molecule!*

A is not superimposable on its mirror image (B), thus by definition A is a chiral molecule. It follows that B also is not superimposable on *its* mirror image (A), and thus it is also a chiral molecule.

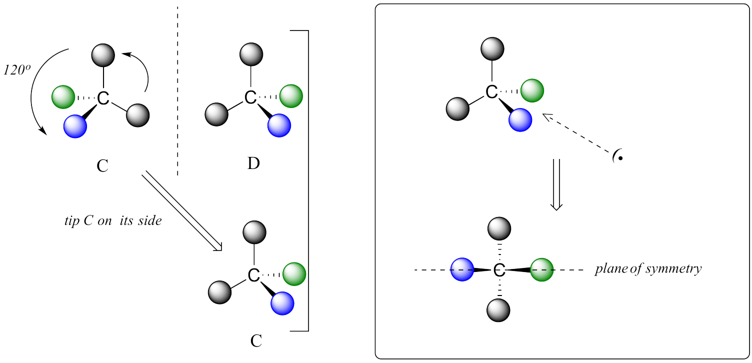
Notice also that neither A nor B has an *internal* plane of symmetry. There is no way to slice through these molecules so that the two portions are mirror images of one another.

The relationship between molecules A and B is that of **stereoisomers**: molecules which share a molecular formula and also same connectivity to other groups, but which have *a different arrangement of atoms in three-dimensional space*. There are two types of stereoisomers: enantiomers and diastereomers. **Enantiomers** are pairs of stereoisomers which are mirror images of each other: this describes molecules A and B. A chiral molecule will always have one and *only* one enantiomer: the word enantiomer describes one member of a pair of molecules, and the term implies a relationship to the other compound.

Enantiomers have identical physical properties (melting point, boiling point, density, and so on). However, enantiomers do differ in how they interact with polarized light and they may also interact in very different ways with other chiral molecules – proteins, for example. They are different chemical substances, though similar in many ways.

The other type of stereochemical relationship is that of a diastereomer. **Diastereomers** are stereoisomers which are *not* mirror images of each other. These can occur under certain circumstances, such as when there are multiple chiral centers arranged in specific ways on a molecule. Diastereomers share molecular formulas and connectivity between atoms, but their physical properties differ from one another.

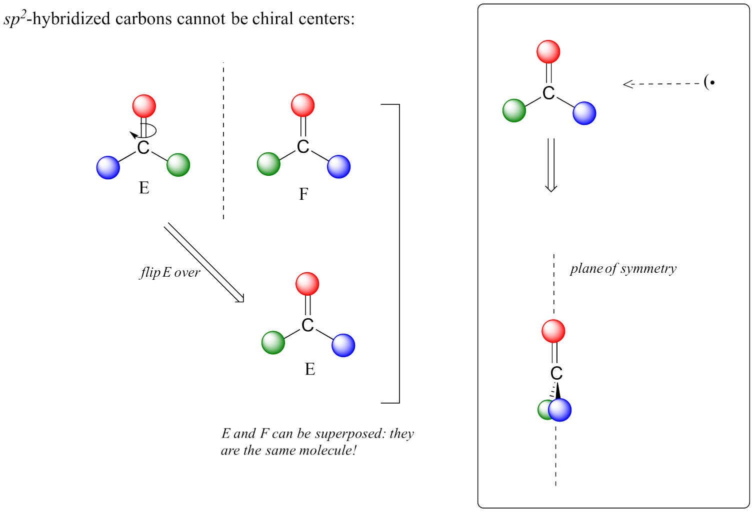
We defined a chiral center as a tetrahedral carbon with four different substituents. If, instead, a tetrahedral carbon has two identical substituents (two black atoms in the cartoon figure below), then while it still has a mirror image (*everything* has a mirror image, unless we are talking about a vampire!), it is superimposable on its mirror image.



C and D can be superposed: they are the same molecule!

The molecule has an internal plane of symmetry that passes through the central carbon and the green and blue spheres. Imagine slicing the molecule in half so that these 3 atoms are bisected: the two pieces would be mirror images of one another.

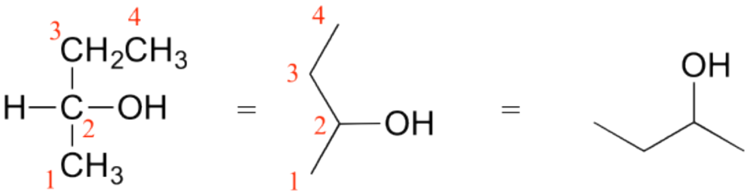
For these reasons we know the molecule is **achiral**. Using the same reasoning, we can see that a carbon with only three groups around it is also not a chiral center.



Notice that structure E can be superimposed on F, its mirror image – all you have to do is pick E up, flip it over, and it can completely overlay F. This molecule has an internal plane of symmetry, and is achiral.

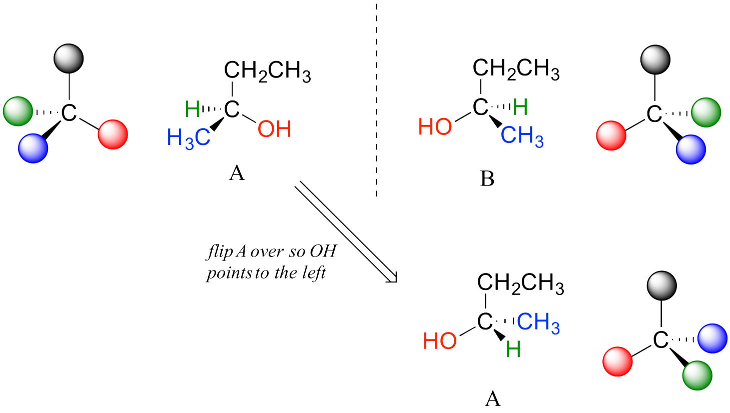
Let's apply our general discussion to real molecules. For now, we will limit our discussion to molecules with a single chiral center. It turns out that tartaric acid, the subject of our chapter introduction, has *two* chiral centers, making the situation with that molecule a bit more complex.

Consider 2-butanol, drawn in two dimensions below.



2-butanol
(drawn in 2D)

Carbon #2 is a chiral center: it has four bonds to other atoms and is tetrahedral, and each of the four things attached to it is different: a hydrogen, a methyl ($-CH_3$) group, an ethyl ($-CH_2CH_3$) group, and a hydroxyl (OH) group. If we put carbon 2 in the center of a 3-dimensional drawing and lay out the 4 groups around it, we can investigate the stereochemistry. To start we can connect the OH and ethyl groups with regular lines, and show the attachment to the methyl group with a solid wedge and the attachment to hydrogen with a dashed wedge. A mirror image of our first structure, with all the same groups, can also be drawn.

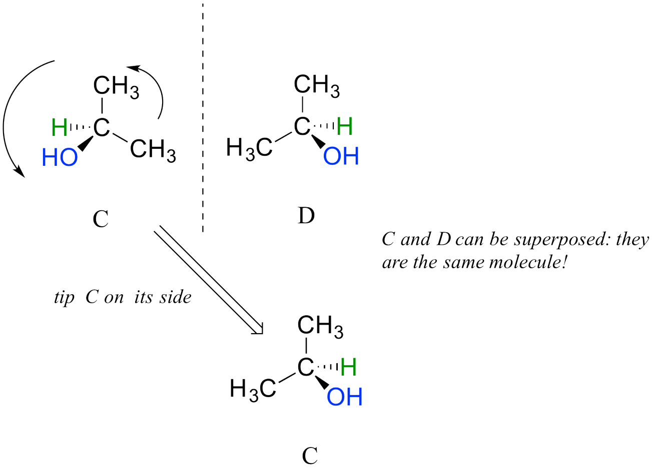


A and B cannot be superposed: they are both chiral, and are enantiomers

When we try to superimpose A onto B, we find that we cannot do it. A and B are both chiral molecules, and they are enantiomers of each other.

The substance 2-propanol, unlike 2-butanol, is *not* a chiral molecule. Carbon #2 is bonded to two identical substituents (methyl groups), not 4 different groups, and so it is not a chiral center. It has an internal mirror plane. Its mirror image is superimposable over the original.

2-propanol is achiral:

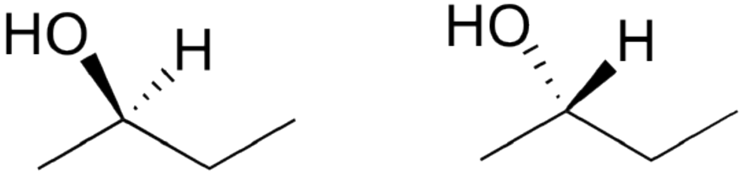


C and D can be superposed: they are the same molecule!

Notice that 2-propanol is superimposable on its own mirror image. Structures C and D here show two views of the same compound.

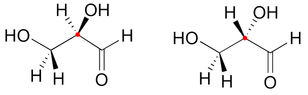
When we look at very simple molecules like 2-butanol, it is not too difficult to draw out the mirror image and recognize that it is not superimposable. However, with larger, more complex molecules, this can be a daunting challenge in terms of drawing and three-dimensional visualization. The easy way to determine if a molecule is chiral is simply to look for the presence of one or more chiral centers: molecules with chiral centers will often be chiral. We can not say 'always' here because it is possible to come up with exceptions to this rule.

Here's another trick to make your stereochemical life easier: if you want to draw the enantiomer of a chiral molecule, it is not necessary to go to the trouble of drawing the point-for-point mirror image, as we have done up to now for purposes of illustration. Instead, keep the carbon skeleton the same, and simply reverse the solid and dashed wedge bonds on the chiral carbon: that accomplishes the same thing. You should use models to convince yourself that this is true, and also to convince yourself that swapping *any two* *substituents* about the chiral carbon will result in the formation of the enantiomer.

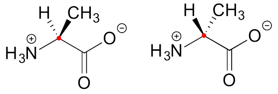


two enantiomers of 2-butanol

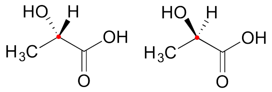
Here are four more examples of chiral biomolecules, each one shown as a pair of enantiomers, with chiral centers marked by red dots.



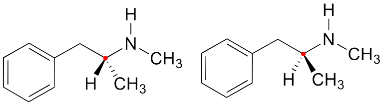
glyceraldehyde



alanine

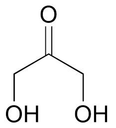


lactic acid

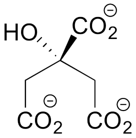


methamphetamine

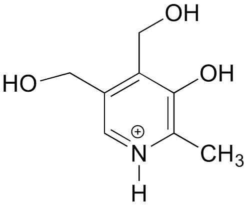
Here are some examples of ***achiral*** biomolecules – convince yourself that none of them contain a chiral center:



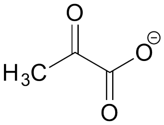
dihydroxyacetone



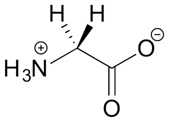
citrate



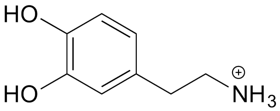
pyridoxine
(vitamin B_6)



pyruvate



glycine
(amino acid)



dopamine
(neurotransmitter)

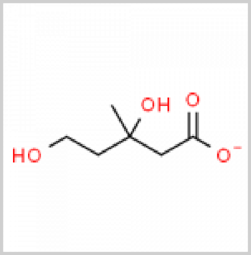
Can a chiral center be something other than a tetrahedral carbon with four different substituents? The answer to this question is 'yes' – however, these alternative chiral centers are very rare in the context of biological organic chemistry, and outside the scope of our discussion here.

Exercise 6.1.1

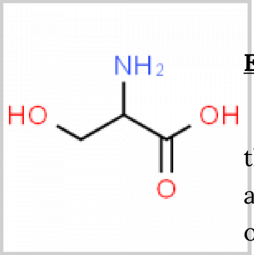
An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=693#h5p-78

Exercise 6.1.2

Locate all of the chiral centers (there may be more than one in a molecule). Remember, hydrogen atoms bonded to carbon usually are not drawn in the line structure convention – but they are still there.



mevalonate

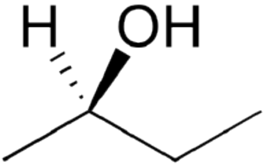


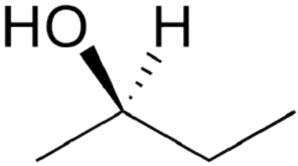
serine

Exercise 6.1.3

a) Select one of the named substances above that has at least one chiral center. Draw or describe it as a specific stereoisomer using the wedge convention introduced in this section. Then draw its enantiomer.

b) Are the two 2-butanol structures below enantiomers?





Exercise 6.1.4

An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=693#h5p-55

Exercise 6.1.5

On the web, look up the structures and IUPAC names for the over-the-counter analgesics known as Aspirin, Ibuprofen, Acetaminophen/Paracetamol, and Naproxen. Are you able to locate chiral carbons on any of these molecular structures?

6.2 Stereochemical Designations in Names and Structures

Nomenclature for distinguishing chiral isomers

Chemists need a convenient way to distinguish one stereoisomer from another. The **Cahn-Ingold-Prelog system** is a set of rules that allows us to unambiguously define the stereochemical configuration of any stereocenter, using the designations '**R** ' or '**S .**' The label 'R' comes from the Latin word *rectus*, suggesting 'right,' and is related to the Spanish words "derecha" and "derecho." S comes from the Latin *sinister*, which can be translated as 'left' ("sinistra" is "left" in Italian).

In an organic structure with chiral carbons, each chiral atom gets one of these designations. So the names for such compounds includes the letters. For instance:

(1S,2S)-2-methylamino-1-phenylpropan-1-ol

is the IUPAC name describing the structure of pseudoephedrine, which includes the designations of two chiral carbons at positions 1 and 2 on the parent chain. This substance is the active ingredient in the decongestant medication Sudafed^{TM}.

A step-wise method for accurately assigning an R/S designation to a chiral carbon:

Step 1: Assign priorities to the four substituents attached directly to the carbon. Priorities are based on the atomic number of the atom attached to the chiral carbon. If these are identical (a tie) other rules come into play. The highest priority substituent will be group number 1, others are numbered in decreasing order 2, 3 and 4.

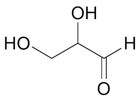
Step 2: Imagine a circle from 1 to 2 to 3.

Step 3: Determine the orientation of the #4 priority group. If it is oriented into the plane of the page (away from you), go to step 4a. If it is oriented out of the plane of the page (toward you) go to step 4b.

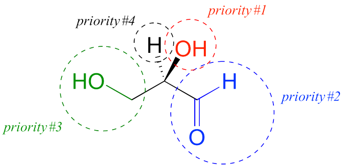
Step 4a: a clockwise circle as you move from group 1 to 2 to 3 corresponds to a carbon with the R configuration, while a counterclockwise circle corresponds to a carbon with the S configuration.

Step 4b: a clockwise circle in part 2 corresponds to the S configuration, while a counterclockwise circle corresponds to the R configuration.

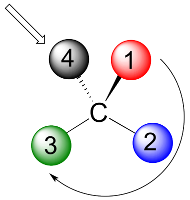
We'll use the 3-carbon sugar glyceraldehyde as an example.



glyceraldehyde



(*R*)-glyceraldehyde



clockwise = *R*

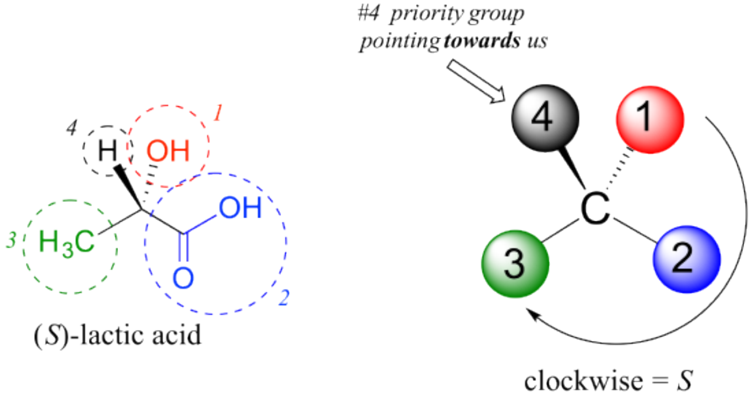
The first thing that we must do is to assign a **priority** to each of the four substituents bound to the chiral center. We first look at the atoms that are directly bonded to the chiral center: these are H, O (in the hydroxyl), C (in the aldehyde), and C (in the CH_2OH group).

Two priorities are easy: based on additional rules of the R/S system, hydrogen, with an atomic number of 1, is considered the lowest (#4) priority, and the hydroxyl oxygen, with atomic number 8, is priority #1. Carbon has an atomic number of 6. Which of the two 'C' groups is priority #2, the aldehyde or the CH_2OH? To determine this, the system instructs us to move one more bond away from the chiral center: for the aldehyde we have a *double* bond to an oxygen, while on the CH_2OH group we have a *single* bond to an oxygen. If the atom is the same, double bonds have a higher priority than single bonds. Therefore, the aldehyde group is assigned #2 priority and the CH_2OH group the #3 priority.

With our priorities assigned, we look next at the #4 priority group (the hydrogen) and see that it is pointed back away from us, into the plane of the page – thus step 4a from the procedure above applies. Then, we trace a circle defined by the #1, #2, and #3 priority groups, in increasing order. The circle is clockwise, which by step 4a tells us that this carbon has the ‘*R*’ configuration, and that this molecule is (*R*)-glyceraldehyde.

Its enantiomer, by definition, would be (*S*)-glyceraldehyde.

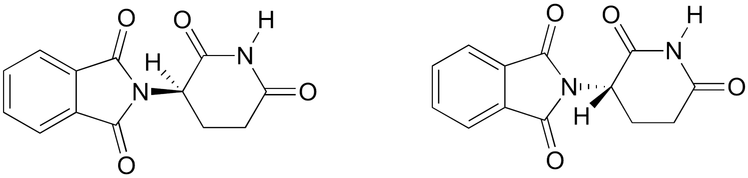
As another example, let’s look at one of the enantiomers of lactic acid and determine the configuration of the chiral center.



An Interactive model of (S)-alanine is available by following this link.

Clearly, H is the #4 substituent and OH is #1. Owing to its three bonds to oxygen, the carbon on the acid group takes priority #2, and the methyl group takes #3. The #4 group, hydrogen, happens to be drawn pointing *toward* us (out of the plane of the page) in this figure, so we use step 4b: The circle traced from #1 to #2 to #3 is clockwise, which means that the chiral center has the *S* configuration.

The drug thalidomide is an interesting – but tragic – case study in the importance of stereochemistry in drug design. First manufactured by a German drug company and prescribed widely in Europe and Australia in the late 1950's as a sedative and remedy for morning sickness in pregnant women, thalidomide was soon implicated as the cause of devastating birth defects in babies born to women who had taken it. Thalidomide contains a chiral center, and thus exists in two enantiomeric forms. It was marketed as a **racemic mixture**: in other words, a 50:50 mixture of both enantiomers.



two enantiomers of thalidomide

Although scientists are still not entirely sure how thalidomide works, experimental evidence suggests that it was actually the *R* enantiomer that had the desired medical effects, while the *S* enantiomer caused the birth defects. Even with this knowledge, however, pure (*R*)-thalidomide is not safe, because enzymes in the body rapidly convert between the two enantiomers..

Frances Kelsey is honored by then President Kennedy Photo: Unknown author – Public Domain, https://commons.wikimedia.org/w/index.php?curid=6424741

As a historical note, thalidomide was never approved for use in the United States. This was thanks in large part to the efforts of Dr. Frances Kelsey, a Food and Drug pharmacologist and physician, who, at peril to her career and resisting pressure, blocked its approval due to her concerns about the lack of adequate safety studies, particularly with regard to the drug's ability to enter the bloodstream of a developing fetus. Unfortunately, though, at that time clinical trials for new drugs involved widespread and unregulated distribution to doctors and their patients across the country, so families in the U.S. were not spared from the damage caused.

Kelsey's work and public awareness of it led directly to a strengthened process for drug approvals. This included passage of the Kefauver Harris Amendment, which required companies demonstrate the efficacy of new drugs, report adverse reactions to the FDA, and request consent from patients participating in clinical studies before approval and marketing.

Thalidomide is now back on the market, with strict safety measures enforced, for the treatment of multiple myeloma, graft vs. host disease, and some conditions related to leprosy. Disturbingly, control of the drug has been less than perfect in some parts of the world, leading to continuing problems, for instance in Brazil.

Exercise 6.2.1

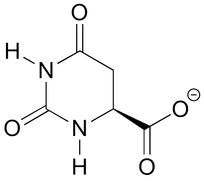
An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=695#h5p-59

Exercise 6.2.2

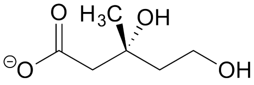
An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=695#h5p-60

Exercise 6.2.3

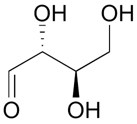
Determine the stereochemical configurations of the chiral centers in the biomolecules shown below.



dihydroorotate



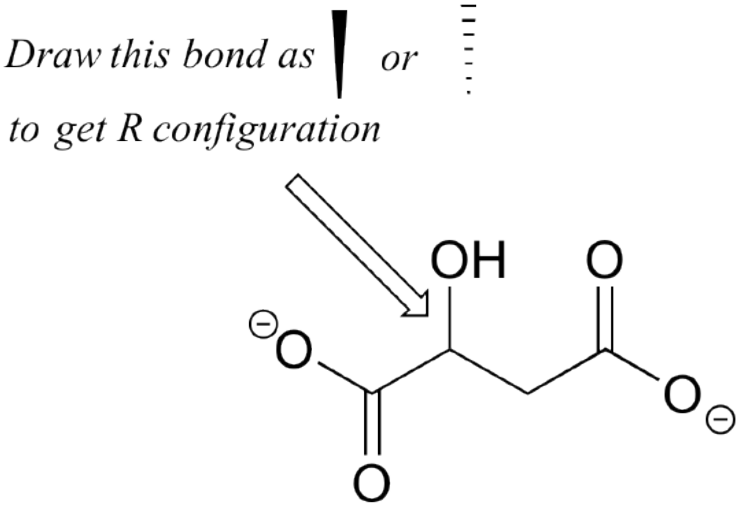
mevalonate



(D)-erythrose

Exercise 6.2.4

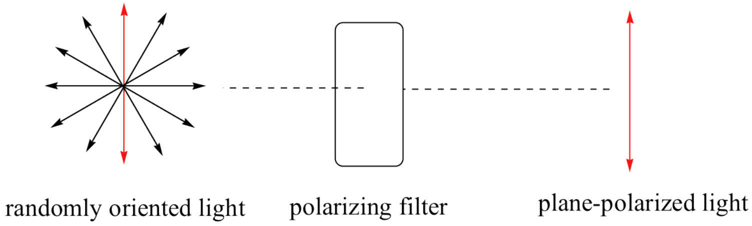
Should the (*R*) enantiomer of malate have a solid or dashed wedge for the C-O bond in the figure below?



(*R*)-malate

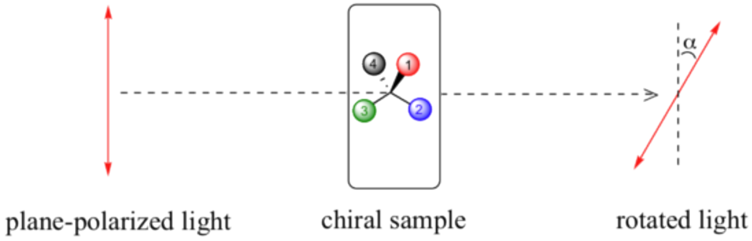
6.3 Chirality in Chemical, Environmental and Biological Systems

Chiral molecules, as we learned in the introduction to this chapter, have an interesting optical property. Physics teaches us that light waves can be described as oscillating electric and magnetic fields. In ordinary light, the oscillation is randomly oriented in an infinite number of planes. When ordinary light is passed through a polarizer, all planes of oscillation are filtered out except one, resulting in **plane-polarized light**.



This is the kind of polarizing filter that is used in anti-glare glasses and ski goggles.

A beam of plane-polarized light, when passed through a sample of a chiral compound, interacts with the compound in such a way that the angle of oscillation will rotate. This property is called **optical activity**.



If a compound rotates plane polarized light in the clockwise (+)

direction, it is said to be **dextrorotatory**, while if it rotates light in the counterclockwise (-) direction it is **levorotatory**. Under standardized laboratory conditions, the **specific rotation** of a pure chiral compound can be measured and used as a physical property characteristic of that specific substance. This is the specific rotation for that substance:

specific rotation:

$$[\alpha]_{\mathrm{D}}^{25} = \frac{\alpha_{\mathrm{obs}}}{lc}$$

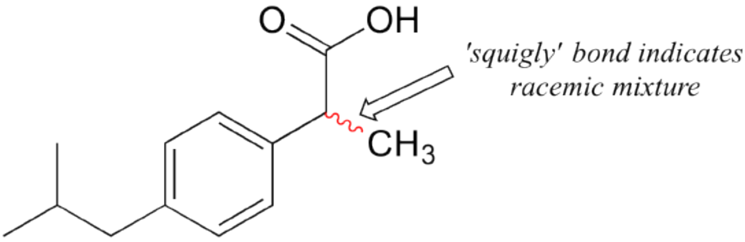
. . . where alpha$_{(obs)}$ is the observed rotation, *l* is the length of the path light must travel through the sample, and c is the concentration of the sample in grams per 100 mL.

A polarimeter is used to measure optical rotation. By Jerónimo Roure Pérez, CC BY-SA 4.0, *https://commons.wikimedia.org/w/index.php?curid=*59616417

The two enantiomers of a compound will always rotate plane-polarized light with an equal but opposite magnitude. (*S*)-ibuprofen, for example, has a specific rotation of +54.5^{o} (dextrorotatory) in methanol, while (*R*)-ibuprofen has a specific rotation of -54.5^{o}. *There is no relationship between chiral compound's R/S designation and the direction of its specific rotation because the R/S system is not experiment-based.* For example, the S enantiomer of ibuprofen is dextrorotatory, but the S enantiomer of glyceraldehyde is levorotatory.

A 50:50 mixture of two enantiomers (called a racemic mixture) will have no observable optical activity, because the equal amounts of two optical activities cancel each other out in the experimental situation.

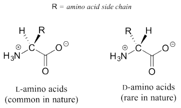
In a structural drawing, a 'squiggly' bond from a chiral center indicates a mixture of both R and S configurations.



(+/-) ibuprofen
(racemic)

Chiral molecules are often labeled according to whether they are dextrorotatory or levorotatory as well as by their *R/S* designation. For example, the pure enantiomers of ibuprofen are labeled (*S*)-(+)-ibuprofen and (*R*)-(-)-ibuprofen, while (±)-ibuprofen refers to the racemic mixture, which is the form in which the drug is sold to consumers.

All of the twenty natural amino acids except glycine have a chiral center at their alpha-carbon, which is the carbon that is next-door to the carbonyl carbon. Virtually all of the amino acids found in nature, both in the form of free amino acids or incorporated into peptides and proteins, have what is referred to in the biochemical literature as the 'L' configuration at this carbon:



R = *amino acid side chain*

L-amino acids
(common in nature)

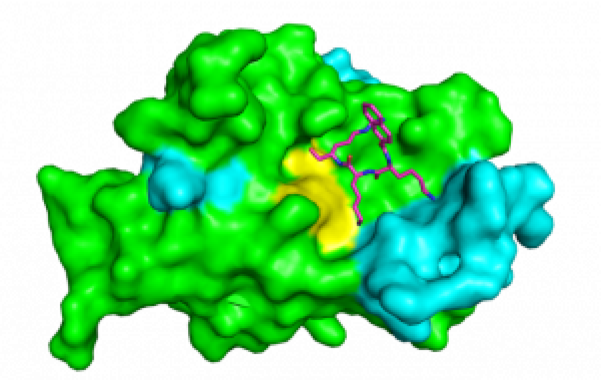
D-amino acids
(rare in nature)

It is unfortunate but true that biochemical literature often uses this alternative naming system, rather than sharing the R/S designations used in organic chemistry.

Chirality is everywhere in biology: in the proteins built from these chiral amino acids, in carbohydrates, in DNA, and in other organic molecules such as the signaling molecules such as neurotransmitters. Enzymes are themselves chiral, and so are able to distinguish between stereoisomers, catalyzing chemistry in some while not catalyzing chemistry in others.

While the small differences between enantiomers can be less important in a test tube, the differences matter in biological systems. This presents a great challenge to the pharmaceutical industry, which is often faced with the need to produce drugs that are specific stereoisomers because they are to be used in biological systems. Synthesizing these molecules exclusively, or separating them out from a mixture of stereoisomers can be enormously difficult. Chemical reactions occurring in test tubes and flasks without chiral reagents will produce a mixture of stereochemistry in the products. These substances are similar enough to the desired isomer that they can be very difficult to separate out.

The chemical reactions that occur within biological systems, on the other hand, are catalyzed by enzymes and produce specific stereoisomers. This is one reason the pharmaceutical industry has increased their use of fermentation and other biological production systems: they can circumvent the difficulty of separating stereoisomers if they can get a biologically-engineered microbe to produce a drug for them.



Enzymes bind very specifically, generally just one chiral isomer. This is a protease enzyme from West Nile Virus and shows the complex 3 dimensional shape of the binding site. Martin Stoermer, CC BY-SA 4.0 <https://creativecommons.org/licenses/by-sa/4.0>, via Wikimedia Commons

CHAPTER VII

CHAPTER 7 CARBONYL COMPOUNDS

7.0 Carbonyl Compounds

Learning Objectives

In this chapter you will learn to

- recognize structures that contain the functional groups aldehyde, ketone, carboxylic acid, ester, and amide
- provide names when given structures for simpler acids, aldehydes, ketones, and esters
- recognize certain characteristics of each of these organic families
- predict physical properties (including water solubility, melting and boiling points) for substances containing these functional groups

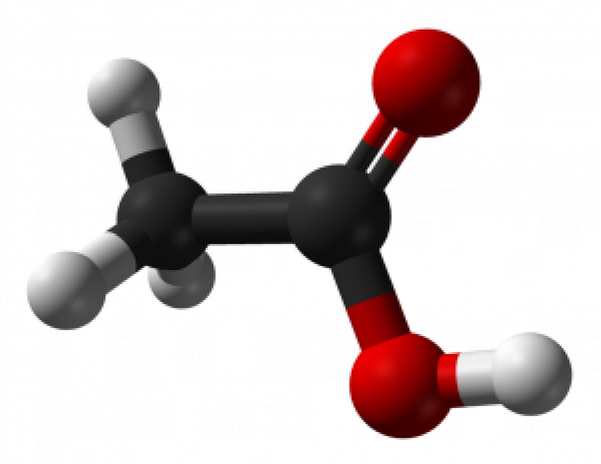
7.1 Aldehydes, Ketones, Carboxylic acids, Esters, and Amides

The Carbonyl Group

Double bonds between carbon and oxygen are common in nature. Organic families containing this arrangement of atoms are referred to as ‘carbonyl compounds,’ and the group itself is referred to as a ‘carbonyl group.’ Multiple organic families include this arrangement of atoms, and each has its own distinct characteristics. Included in the larger group of carbonyl compounds are the narrower families: aldehydes, ketones, carboxylic acids, esters, and amides. Others also exist.

The carbonyl group utilizes two of carbon’s four valence shell electrons for bonding, resulting in a trigonal planar arrangement around the carbon. As a result the bond angles between the carbonyl carbon and each of the other atoms it is attached to is 120 degrees. The carbon to oxygen bond is polar, with a partial positive charge at the oxygen. Additionally, that oxygen includes two nonbonding, lone pairs of electrons. This concentration of electron charge at the oxygen results in significant dipole-dipole interactions in samples of most carbonyl compounds.

Some carbonyl compounds may be able to engage in hydrogen bonding interactions as well, but not all do. So the families within this larger group have noticeable differences that relate to this fact.



Ethanoic acid, more commonly called acetic acid, is a carbonyl compound. This carboxylic acid is the acid present in vinegar.

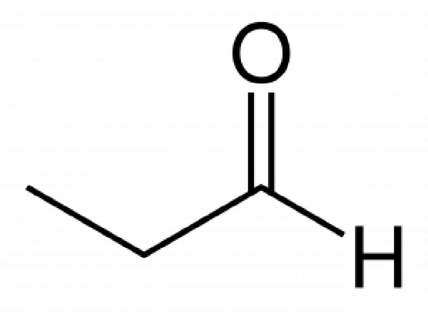
Exercise 7.1.1

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=699#h5p-61

7.2 Aldehydes and Ketones

Aldehydes

An aldehyde can be recognized by noting the presence of a carbonyl group at the end of a carbon chain. Consider the line-bond structure of the three carbon aldehyde 'propanal' here:



Hydrogen is shown explicitly on the aldehyde group for clarity, as it usually is. Note that because the aldehyde functional group includes both the double bond to oxygen and the hydrogen bonded to the carbonyl carbon, this group must exist at the end of the carbon chain: it requires 3 of 4 shared pairs of electrons from a carbon.

Aldehyde names are quite similar to the alcohols they resemble, with key modifications. For instance, the molecule above with a hydroxy group rather than an aldehyde group would be named 1-propanol. The suffix '-ol' given to an alcohol is replaced with the suffix '-al' to identify this is an aldehyde. The number becomes unnecessary because the aldehyde group can only be at position 1 on the parent chain. So it is not used.

In a branched aldehyde the parent chain begins at the carbonyl carbon. Naming structures with multiple functional groups can get tricky, but freely-available IUPAC rules provide guidance.

The presence of the aldehyde group can influence the properties of substances, due to the polarity that exists when this group is present. Aldehydes in mixtures with other substances can engage in hydrogen bonding as the oxygen can act as a hydrogen-bond acceptor. In pure samples, however, the aldehyde can not hydrogen-bond because there is no highly-polarized bond to a hydrogen. The hydrogen attached to the carbonyl is not very polarized, because the carbonyl carbon itself is electron deficient as a result of its bond to oxygen.

Exercise 7.2.1

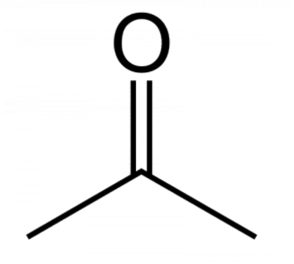
An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=1158#h5p-15

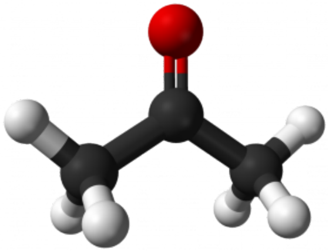
Exercise 7.2.2

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=1158#h5p-16

Ketones

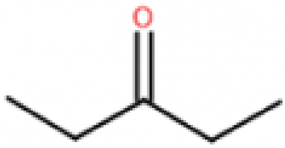
When a carbonyl exists within a chain of carbons the resulting structure is called a ketone. For instance here are three images representing the substance known by the common name 'acetone.' First is a line-bond structure, then a ball-and-stick style structure, and finally a picture of the substance as you would find it in the laboratory:

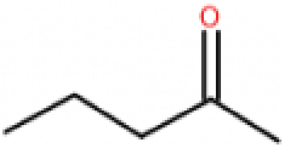




The ketone functional group includes a carbonyl carbon connected to two additional carbons. It is a carbonyl that is positioned within a chain of carbons.

Ketones are named using the suffix '-one.' Acetone has an IUPAC name of propanone. In larger ketones a location for the ketone group also needs to be included in the name, since multiple locations are possible:





What names would be given to each of the two compounds shown above? These two substances have very similar but distinct characteristics. Both have a molecular dipole, but other than the carbonyl itself both are entirely hydrocarbon, so they are just somewhat polar. Their physical properties including melting and boiling points are affected by this, as well as their ability to dissolve in various solvents.

So while similar in many ways, they are slightly different and are, in fact, different substances. They are structural isomers, and their names are 2-pentanone and 3-pentanone.

IUPAC rules guide us to number the parent chain so that the keto group the lowest possible number. Once the parent chain has its carbons numbered, any substituent groups are numbered accordingly.

Exercise 7.2.3

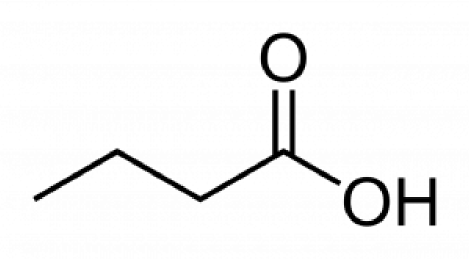
An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=1158#h5p-79

7.3 Carboxylic Acids

Carboxylic Acids

The carboxylic acid functional group includes a carbonyl carbon connected directly to an alcohol group, as shown below. Carboxylic acids are common in nature. Their properties are quite different from the other carbonyl compounds so far mentioned. Notably, as the name suggests, carboxylic acids are acidic.

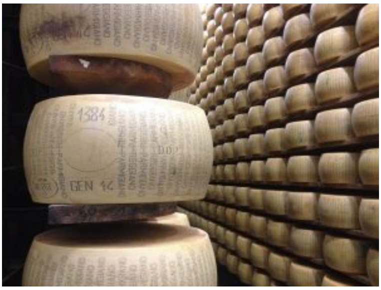
Many carboxylic acids are known by their common names, including lactic acid, citric acid, glutamic acid, and others. Systematic names for these substances also exist. They are modifications of the name of the corresponding hydrocarbons to include the suffix '-oic acid.' For instance:



This structure is butanoic acid.

As with some other organic families, common names are very frequently used with carboxylic acids and some are similar to, but not quite aligned with IUPAC rules. This is a difficulty for students, but sometimes enough information from the IUPAC system is included in a common name to allow you to decipher the structure.

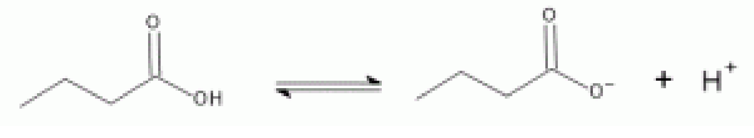
To illustrate, the carboxylic acid above is often called by its common name 'butyric acid.' Butyric comes from the ancient Greek word for butter, the source from which this compound was first isolated. Butyric acid is a breakdown product of the fats in milk that actually is associated with spoilage in butter and cheeses, and while it contributes to flavor in some foods (e.g. Parmesan cheese) also occurs in stale perspiration and vomit!



Ripe, aged cheeses have flavors that are influenced by the presence of butanoic acid, a smell that is pleasant in small amounts and distinctly unpleasant when concentrated.

Similar to the situation for aldehydes, the carboxylic acid group always exists at the end of the parent chain because the functional group requires 3 of 4 available valence electrons on the carbonyl carbon. The carbonyl carbon in these molecules is designated as carbon 1, so location signifiers are not required to pinpoint the location of a carboxylic acid group, unless a name is describing a complex substance with more than one of these groups on it.

Both oxygen atoms on the carbonyl carbon in a carboxylic acid are electronegative, drawing electron density away from surrounding atoms toward themselves. The hydrogen atom is acidic, due to the stability of the anion that exists when that hydrogen ion dissociates from the larger structure.



Carboxylic acids in water solution exist in an equilibrium between the acid and conjugate base states, shown here as the reactant and the anion product of this reaction. The double-headed arrow shown in the figure indicates the nature of this reaction is an equilibrium, with both forward and reverse reactions occurring to some degree. Carboxylic acids tend to be mostly in the reactant form at physiologic pH, with perhaps 5% of the substance in a deprotonated, anion form at any given moment.

This amount of acid added to a solution from this type of dissociation of a carboxylic acid, however, is significant in many contexts. For instance the acidity of ethanoic acid, also known as acetic acid, gives vinegar solutions their sour taste and contributes to their ability to retard the growth of undesirable organisms in pickles. Lactic acid in yogurt is another example of a carboxylic acid that has a big influence on its medium, as milk is converted by lactic-acid forming bacteria to kefir or yogurt.

Exercise 7.3.1

An interactive H5P element has been excluded from this version of the text. You can view it online here:
https://openoregon.pressbooks.pub/introductoryorganic/?p=1160#h5p-18

All of the substances in the interactive questions below are present in many ripe cheeses, including the famously funky cheese named Camembert.

By NJGJ – *photography by* NJGJ, CC BY 2.5, *https://commons.wikimedia.org/w/index.php?curid=1363259*

Exercise 7.3.2

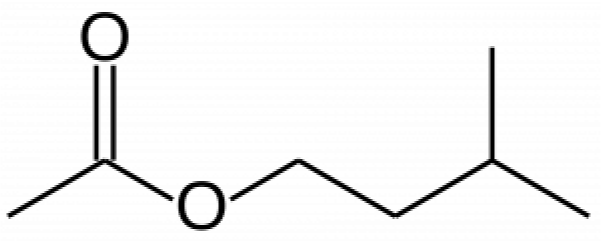
An interactive H5P element has been excluded from this version of the text. You can view it online here:

https://openoregon.pressbooks.pub/introductoryorganic/?p=1160#h5p-19

7.4 Esters and Amides

Esters

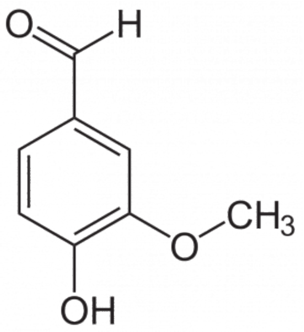
Esters are one type of carbonyl compound described as carboxylic acid derivatives. In this group the '-OH' group of a carboxylic acid has been replaced by a group containing a carbon-containing, '-OR' group. As an example:



This ester is 3-methylbutyl ethanoate. It is also known by its common name, isoamyl acetate. This substance is one of a few fragrance/flavor compounds that distinguish the flavor of banana, though it is also found in some other fruits. Artificial banana flavor, such as that used to make popular candy, is largely composed of this substance.

Note the carbonyl here, and the second oxygen atom connected directly to the carbonyl carbon. These structures look very similar to the carboxylic acid structures, but the properties of esters do not include acidity. Esters are thus unable to ionize, making them less water-soluble than carboxylic acids. And while un-ionized carboxylic acids are able to engage in intermolecular hydrogen bonding, esters are not. So esters are also less polar, and have lower melting and boiling points than their counterpart carboxylic acids.

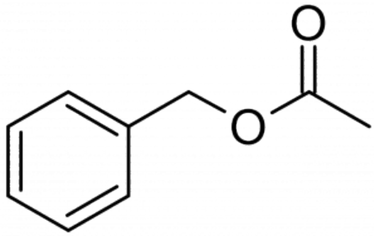
Many flavor and fragrance compounds from flowers and fruits are esters. Plant material is immensely complex, but individual esters separated out from plant extracts can be so characteristic of plant odors that people to identify their sources specifically. Plant fragrances in nature are often produced as animal attractants, and as animals we have evolved sensory organs that can identify the presence of these substances and enjoy many of them.



Vanillin is an aromatic ester that is a dominant fragrance/ flavor in processed vanilla beans.

The intermediate polarity of esters, coupled with their somewhat small (for an organic chemical) size means that many have low enough boiling points to have some of these molecules escape into the gas phase near their source. From where they are formed–from a flower or a piece of fruit–those molecules can drift into our noses.

Esters tend to be somewhat reactive, decomposing into other substances when heated or exposed to dramatic variations in pH. Cooking can alter the flavor of foods by contributing to the destruction of these compounds.



Benzyl ethanoate is an ester that contributes to the fragrance of strawberries. By Rbreidbrown – Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=92505251

The names of esters are based on two separate sections of these molecules, and unlike most IUPAC names are given as two separate words. The first is based on the organic structure beyond the carbonyl, '-methyl' or '-ethyl' etc.. In the case of our banana oil compound, this is the '3-methylbutyl' portion of the name. The second word in the name is derived from the carboxylic acid that would exist were we to remove the carbons beyond the carbonyl and replace them with a hydrogen. In the example here we have '-ethanoate,' which comes from 'ethanoic acid,' the two-carbon carboxylic acid.

Exercise 7.4.1

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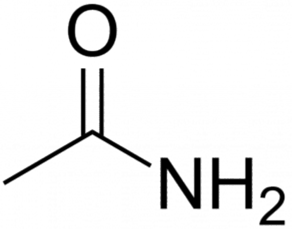
Amides

Amides are also carboxylic acid derivatives. These compounds have a carbonyl directly connected to a nitrogen. That nitrogen can be bonded to hydrogens or to additional carbons. The relationship between this group and the amines is suggested in the name “amide.”

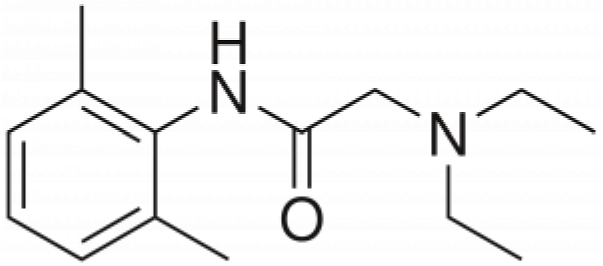
Naming can get quite complicated for amides, but the simplest amides are named based on the carboxylic acid they most closely resemble, with ‘-oic acid’ in the carboxylic acid name converted to ‘-amide.’

For instance, ethanamide looks like this:



Unfortunately for students, the IUPAC system is often cast aside for familiar names when chemists discuss amides. This substance is commonly called acetamide, a non-systematic, common name.

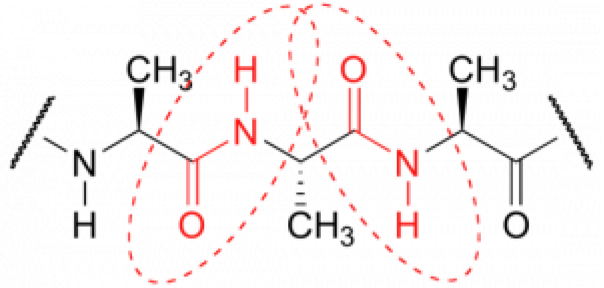
Amides have electronegative nitrogen atoms, with their lone pair electrons in a position close to the carbonyl group. This arrangement produces molecules with some polarity, but the degree of polarity in an amide is also influenced by what connects to the nitrogen itself. In short, polarity can vary a lot within this family of compounds. Ethanamide, shown above, can engage in hydrogen-bonding interactions, and has properties that reflect that. But the more highly substituted amides with additional carbons attached at the nitrogen are not able to do so, and have properties that correspond:



Lidocaine is a topical anaesthetic. It is an aromatic compound that contains an amide as well as an amine.

Resistance to rotation around the amide bond

Amides tend to share some electron density with the carbonyl unit itself, causing the C-N bond to exhibit some double-bond character. In particular, for amides located in the middle portion of larger molecules, these groups lock into a conformation illustrated below, resisting rotation around the carbon to nitrogen bond. This is similar to the lack of rotation we learned about in the carbon to carbon double bond (such as in cis-trans geometric isomers).



peptide bonds in a polypeptide

In 3-dimensional molecules and models, the amide adopts a planar (flat) configuration, and the flexiblity of the whole molecule is vastly reduced. This locked structure is occurs in multiple locations in proteins, where amino acids which bond to one another do so via amide linkages also known as peptide bonds. Larger structural features of proteins, such as the secondary structure units 'alpha helix' and 'beta sheet' frequently discussed in biochemistry, form in part because of this particular feature of the amide bonds within those proteins.

Exercise 7.4.2

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CHAPTER VIII

CHAPTER 8 FUNCTIONAL GROUPS AND REACTION PATTERNS

8.0 Functional Groups and Reaction Patterns

Learning Objectives

In this chapter you will learn to

- use functional group recognition to predict reactions of some organic substances
- write complete, balanced combustion reactions for hydrocarbons and alcohols
- write complete, balanced reactions describing the protonation of amines in acid
- explain the solubility and melting point changes that accompany amine protonation

8.1 Understanding Reactions

We have learned that the properties of organic substances can be understood by considering elements of their structures. As we have considered various families of organic chemicals we have connected physical properties such as melting and boiling points, and solubility, to the polarity of molecules and other elements of their structure.

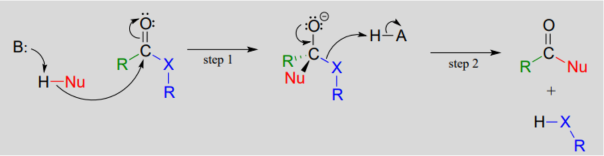
Similarly, chemical reactivity can also be related to organic families, with certain characteristic behavior of substances aligning with these categories. Characteristic reaction patterns include such examples as “substitution at the carbonyl” or “addition across a double bond.”

As with the patterns that exist for physical properties, the patterns that exist for chemical reactivity also have underlying explanations. Reactions, after all, require molecules to interact with one another, and those interactions will not be entirely random. For a reaction between two chemical species to occur, the following must happen:

- The species need to collide
- When they do, they need to be in a somewhat specific orientation, and
- They must have adequate energy when the collision occurs to induce changes in bonding

The so-called ‘productive collisions’ that result in reactions are more likely under certain conditions: higher concentrations of reactants, for instance, or higher temperatures which correspond with faster molecular motion (and harder collisions).

Chemists often use a form of mental model called a reaction mechanism to imagine the specific interactions that occur between reacting substances. In a mechanism, oppositely charged (or partially-charged) species will often come together, and like-charges will repel. The stability of species to exist on their own is evaluated so that the mechanism makes sense from that perspective. There are rules for proposing and writing good mechanisms and conventional approaches to doing so, including drawing curved arrows to indicate where areas of higher electron density 'go' through a multistep process.



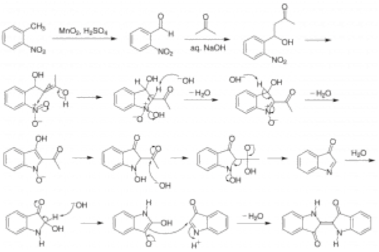
The mechanism for a Nucleophilic Acyl Substitution Reaction.

Mechanisms can be supported by experimental evidence, but they are often first built up from considerations of chemical structure that are theoretical, e.g. based on symbolic representations and shared understandings of how chemistry works. But no mechanism will be accepted in the face of evidence that is contrary to it.

Many, many reactions are understood both from practical experience and from mechanistic explanations. As an introduction to organic chemistry, the focus in this text will be on just a few example reactions. But hopefully the explanations given here will illuminate the ways that chemical reactivity relates to chemical structure. That is the underlying reason why certain organic families–molecules with specific functional groups–tend to react similarly.

The name 'functional group' indicates this, in its most essential sense. Molecules with a certain functional group will function (react) in a certain way.

Indigo cake. By David Stroe – Own work, CC BY-SA 3.0, *https://commons.wikimedia.org/w/index.php?curid=25102943*



A multistep mechanism describing one way to make synthetic indigo dye.

8.2 Combustion

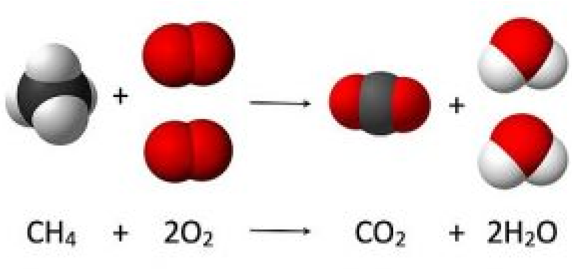
Our society depends on combustion reactions for providing some of our most basic needs: heat, light, and transportation. Additionally combustion reactions have strong cultural power for many people, who have grown up with the idea of a comforting hearth, backyard barbecues, campfires, and warm meals and drinks. Combustion reactions are perhaps among the most familiar of all chemical reactions, and yet we may go through life without giving much thought to their chemical nature.

Combustion provides heat, light, and for many of us a sense of comfort and security.

Through a chemical lens, combustion is the reaction of a fuel with oxygen, to produce heat and light as well as chemical products. While some combustion reactants are not carbon-based, the most familiar of these reactions involve organic fuels such as wood, coal, gasoline, and other carbon-based substances. The oxygen required for reaction is most commonly drawn from the air. When carbon compounds combust in this way the main products of the reaction are carbon dioxide and water. Natural materials are complex mixtures, so other products can also form, and even the combustion of the organic fuel itself can include some side reactions producing other products. These biproducts may not be abundant but can be very important if they are released into the environment. They can have negative impacts on human health and the environment. So can carbon dioxide, of course, as it is perhaps the most important of the greenhouse gases that human activity adds to the atmosphere.

Organic combustion fuels

Just about any molecule with some hydrocarbon can combust. Combustion involves the oxidation of the carbon in an organic molecule. The fuels that are burned on a large scale to provide energy for heat or electricity include the fossil fuels: natural gas, petroleum products, and coal. Natural gas is primarily methane, and combusts according to this reaction:



JyntoRobert A. RohdeJacek FHJynto, Public domain, via Wikimedia Commons

Other gaseous alkanes commonly used for fuel can be refined out of natural gas also, including ethane, propane, and butane.

Petroleum, also known as crude oil, is a liquid natural product with a composition that varies depending on the source. Petroleum is thus refined, leading to the production of many commercial products. Included in these are gasoline, kerosene, and fuel oil. While the specific equations describing the combustion of these substances varies based on the makeup of the reactant, the general pattern remains: fuel molecules react with molecular oxygen to produce carbon dioxide and water.

Coal, a solid fossil fuel, is also a mixture but combusts well due to the presence of hydrocarbons in the substance. Again, the substance we call coal is a mixture that varies depending on its source, but the combustion generally involves large hydrocarbon molecules, and the oxidation of those carbons through reaction with oxygen gas.

Among non-hydrocarbon fuels, ethanol has seen a lot of use. The development of ethanol as fuel in the United States occurred as new markets were sought for an abundance of starchy crop products, such as corn, during the past 50 years. Alcohols burn similarly to hydrocarbons, although the carbon within them is somewhat more oxidized to begin with. A consequence of this is that the energy yield per gram from combustion of alcohols tends to be somewhat lower than for hydrocarbons:

$$C_2H_5OH + 3\ O_2 \longrightarrow 2\ CO_2 + 3\ H_2O$$

Ethanol has been touted as a greener fuel than the non-renewable fossil fuels. However the production of ethanol from commodity crops like corn is itself fossil fuel dependent, and analyses have shown that the production of ethanol does not actually reduce overall fossil fuel use as much as it may first appear. Other biofuels such as biodiesel have struggled to gain market traction for similar reasons. The ideal renewable fossil fuel replacement requires a feedstock that can be produced and processed with few energy inputs.

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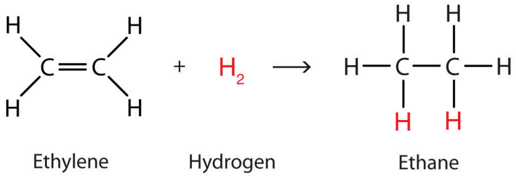
https://openoregon.pressbooks.pub/introductoryorganic/?p=729#h5p-22

8.3 Addition Reactions

Alkenes are valued mainly for their ability to participate in addition reactions,in which substituent groups join to hydrocarbon molecules at points of unsaturation—for this type of molecule, the double bonds. In these reactions one of the bonds in the double bond is broken. Each of the carbon atoms in the bond can then attach another atom or group while remaining joined to each other by a single bond.

Perhaps the simplest addition reaction is hydrogenation. This is a reaction in which hydrogen gas reacts at a carbon-to-carbon double or triple bond or a carbon-to-oxygen double bond to add hydrogen atoms to carbon atoms. In the laboratory this reaction can be facilitated with hydrogen (H_2) in the presence of a catalyst such as nickel (Ni) or platinum (Pt).



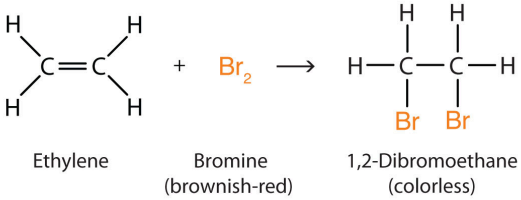
Note that the name 'addition' is apt here, since we take a reactant (ethene in this case) and add hydrogen to it, producing a single product (ethane). The carbon skeleton of the reactant is unchanged.

In one important application of this chemistry, hydrogenation is used to convert unsaturated vegetable oils to saturated fats. Hydrogenated fats, or partially-hydrogenated fats often appear on nutrition labels for processed foods such as crackers or chips.

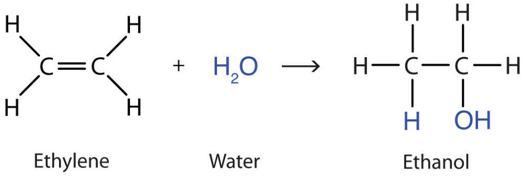
Hydrogenating foods in this way has several benefits: it removes a functional group on the fats that could react by oxidation to make products with off flavors. It also raises the melting points of the fats, changing the texture in ways that might be pleasing to consumers. It allows for higher temperature cooking for baked products, which can increase browning and improve flavor.

But there are also big drawbacks to chemical hydrogenation of fats in foods. During the process, cis double bonds can convert to the trans configuration during the reaction. Trans alkenes in fat molecules are associated with negative effects on cardiac health. Since consumers have largely rejected trans fats due to this, companies have shifted most of their hydrogenation to enzyme-catalyzed processes which yield only cis isomers.

Alkenes also readily undergo halogenation through addition, a reaction in which a halogen reacts at a carbon-to-carbon double or triple bond to add halogen atoms to carbon atoms. Indeed, the addition reaction with bromine (Br_2) can be used to test for alkenes in an uncharacterized sample of material. Bromine solutions are brownish red. When we add a Br_2 solution to an alkene, the color of the solution disappears because the alkene reacts with the molecular bromine (Br_2):

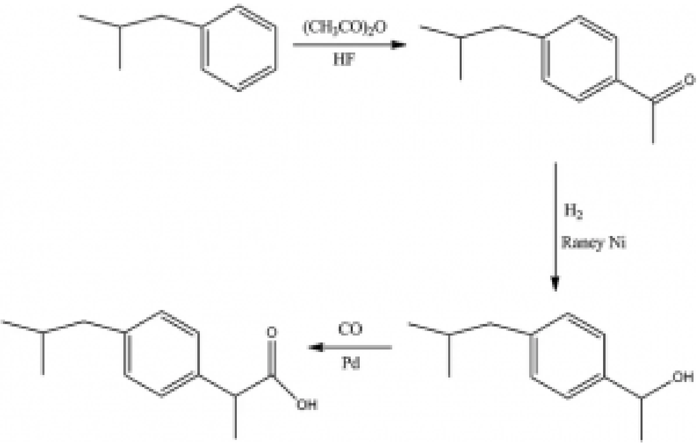


Another important addition reaction occurs between an alkene and water to form an alcohol. This reaction is called hydration, and represents the addition of water to a substance.



The practice of organic chemistry includes understanding, planning for and carrying out functional group transformations of these types. A knowledgeable organic chemist can link together reactions in order to build specific target molecules according to a plan.

Organic chemical synthesis has applications in many industries, from food to pharmaceuticals, adhesives and coatings, and more.



BHC greener ibuprofen synthesis: from Agee, B.M., Mullins, G. & Swartling, D.J. *Sustain Chem Process* 4, 8 (2016). *https://doi.org/10.1186/s40508-016-0052-y*

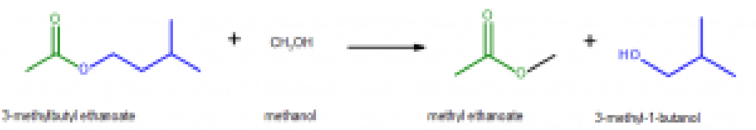
The three reactions steps in the above reaction sequence show the addition of hydrogen across a carbon-oxygen double bond in step 2. This reaction sequence is used to make Ibuprofen. The approach here replaced an older method that required six reaction steps and produced enormous quantities of waste. The synthesis here, from BHC (now part of the industrial chemical giant BASF) resulted in a Presidential Green Chemistry award for the company in 1997.

8.4 Reactions at the Carbonyl Carbon

Carbonyl compounds, containing the polarized carbon to oxygen double bond, exhibit several types of characteristic reactions. Some of these involve new bonds forming at the carbonyl carbon itself, with possible consequences for the carbon-oxygen bond. But a new bond to the carbonyl carbon can also initiate the disconnection of another group already attached there, resulting in the substitution of the new group for the leaving group.

There are lots of possible variations on these reactions we could consider. But to avoid overwhelming detail we will focus on a single example of this second type of reaction.

The reactants in this example include an ester (3-methylbutyl ethanoate) and an alcohol (methanol). The products of the reaction are a different ester (methyl ethanoate) and a different alcohol (3-methyl-1-butanol). In the course of the reaction the methoxy group from the reacting alcohol has been substituted for a portion of the original ester.



Note that portions of the original ester now exist in two separate molecules, and the methoxy group from the reacting alcohol shown in black is now incorporated into the product ester.

This substitution reaction is called a transesterification, indicating that the process starts with one ester and produces a different one.

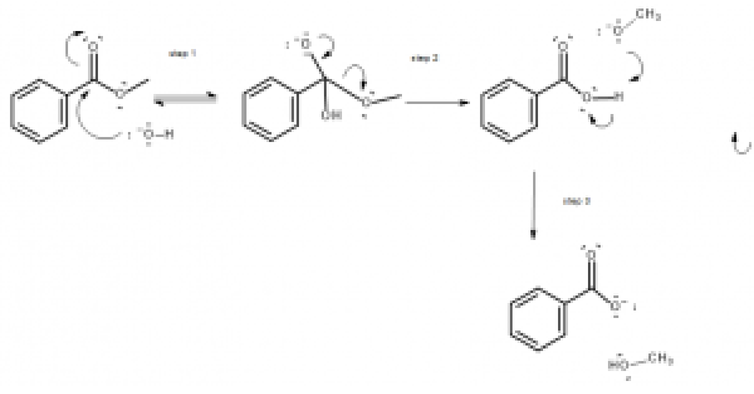
A mechanism for this reaction might involve an attack by the oxygen from the methanol at the carbonyl carbon. Considering that the oxygen atom on methanol carries a partial-negative charge, it is reasonable to imagine it would be attracted to the electron deficient, partially-positive carbonyl carbon. Once there the bond between those atoms can begin to form, but the carbonyl does not have the capacity to form another bond. As a result the blue 3-methyl-butoxy group disconnects as the new bond forms.

Substitution reactions of a variety of types occur widely in nature and in the laboratory. Substitution at a carbonyl carbon is common in biochemistry, with variations on this mechanism useful for explaining many important biological reactions: the phosphorylation and dephosphorylation of ATP involved in energy metabolism, the formation of amide bonds in protein formation, and the catalytic activity of important digestive enzymes all fall into this category.

Saponification

Saponification reactions are similar to transesterifications. In this case the reactant attacking an ester is not an alcohol, however, but a hydroxy anion (OH-).

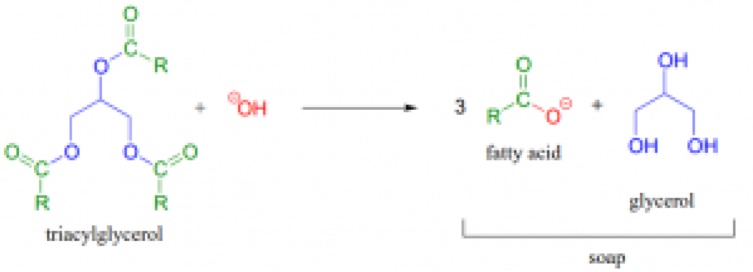
A reasonable mechanism for this process includes very similar steps to what we have considered above.



The mechanism includes an attack at the carbonyl carbon by the hydroxyl anion, and subsequently the disconnection of a group from the original ester.

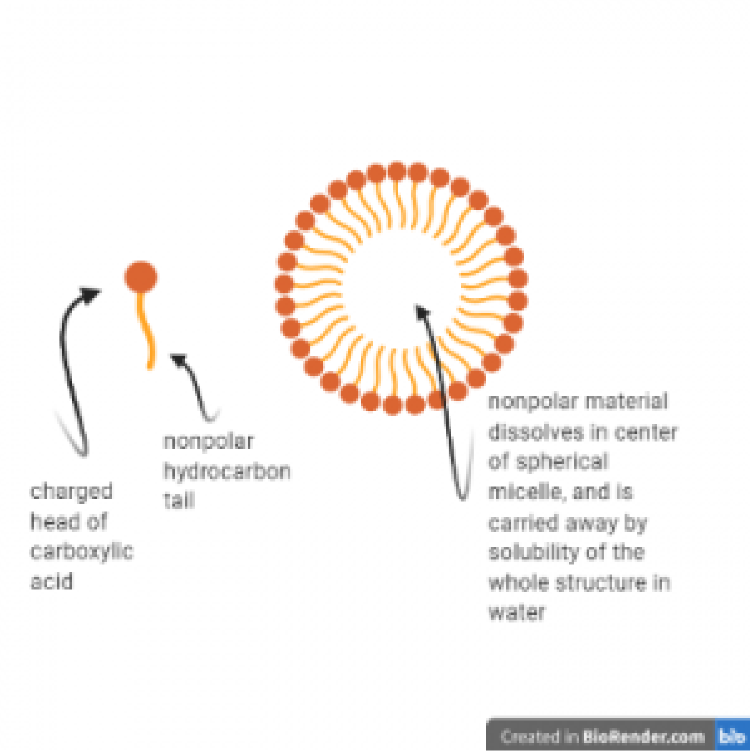
The result of this reaction is the formation of a carboxylic acid anion (the form of the carboxylic acid after it has lost its acidic hydrogen), and an alcohol.

Reactions of this type are called saponification, and include the chemistry that is used to convert fats and oils to soap:



This chemistry is used in modern industrial soap-making processes but also describes the chemistry carried out on a small scale, as cottage industry or in the home. Triacylglycerols are the main type of fat storage in both plants and animals, and are the predominant material in both animal tallow (rendered fat) and plant oils. Reacting these substances with lye (NaOH) solution produces fatty acids. These substances act as soap, forming micellar structures as shown below. Micelles have hydrophobic, nonpolar interiors that mix with and thus dissolve nonpolar substances they contact, such as fats. The outer portion of the micelle is soluble in water and is hydrophilic, however, due to the oxygens and charge. the entire micelle, with fatty cargo in tow, can be removed from surfaces and washed away in a soapy water solution.

In this way soap is able to remove nonpolar contaminants from dishes, fabric, and surfaces, including our bodies.


charged head of carboxylic acid
nonpolar hydrocarbon tail
nonpolar material dissolves in center of spherical micelle, and is carried away by solubility of the whole structure in water
Created in BioRender.com bio

CHAPTER IX

CHAPTER 9 HALOGENATED COMPOUNDS

9.0 Halogenated Compounds

Learning Objectives

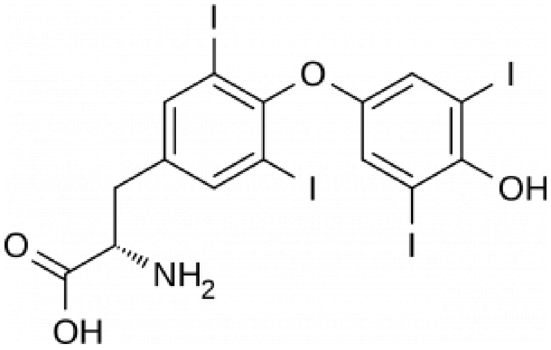
In this chapter you will learn to

- provide names when given structures, and draw structures from names of halogenated hydrocarbons
- evaluate the structures of halogenated alkanes to estimate their polarity, and the effects of this on their melting and boiling points, and water solubility

9.1 Names and Structures for Halogenated Compounds

Elements in Group 17 are named the Halogens. These elements are well known for their ability to gain electrons and form anions in ionic compounds. But halogens also readily engage in covalent bonding. They form diatomic molecules as elements, such as chlorine gas (Cl_2) and solid iodine (I_2). They also commonly engage in covalent bonding with carbon. When they do, the resulting substances are classified as halogenated organic substances, also known as alkyl halides.

Halogenated organic substances are not common in biological system, though they do exist. Iodine, for example, is an important part of the thyroid hormone molecules including thyroxine. Our dietary need for small amounts of iodine are due to the need our body has to make these hormones. The iodine comes from either iodated salt, or from exposure to iodine near salt water.



Structure of levothyroxine (T4), one of two similar compounds used for treatment of hypothyroidism.

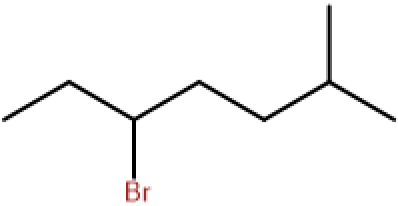
Halogenated hydrocarbons are useful in many industrial and consumer applications, so they are frequently synthesized. The halogenated alkene with the common name vinyl chloride (chloroethene) is the monomer that is used to produce polyvinyl chloride, or PVC plastic. PVC is abundant in the built environment, where it is used commonly for pipes such as sewers, for structural elements such as window frames in homes, and in carpets and flooring materials. PVC is also the base material for vinyl siding.

PVC is used frequently in construction, including the frame of this window.

Pharmaceuticals also frequently are halogenated organic compounds. Examples include the anti-anxiety drug Diazepam, which contains chlorine, and the antidepressant Fluoxetine, which contains fluorine. Pesticides and herbicides are also frequently organic molecules that contain halogen atoms.

Naming halogenated alkanes

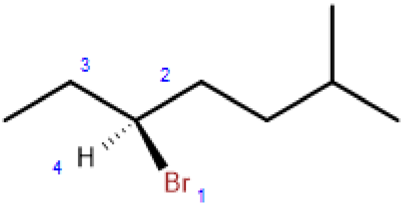
Consider this structure:



This halogenated alkane has a parent chain that is seven carbons long, so it will be named as a derivative of heptane. The halogen, bromine, might be assigned a location of 3, or a location of 5 if numbering from the opposite end of the chain. There is also a methyl group as a substituent on the chain. In this case IUPAC guides us to assign locations to give bromine the lowest possible number. So bromine is at position 3, the methyl group is at position 6, and the name is

3-bromo-6-methylheptane

Note that carbon 3 is surrounded by four different groups. This means that the carbon at that position can come in two alternative forms (R or S configured). Two stereoisomers of the substance, which are enantiomers, are possible. The structure below shows the S isomer:



The numbers (in blue) indicate the priority of each of the four groups surrounding the chiral carbon. Using this system one can determine this is the specific stereoisomer designated as S. The mirror image of this compound, R-3-bromo-6-methylheptane, will have very similar properties to this substance but will be noticeably different in the way it behaves in chiral systems: it will rotate plane-polarized light in the opposite direction from the S isomer, and it would have different effects in biological systems.

The name of this isomer is thus complete when the R or S designation is included: this is (S)-3-bromo-6-methylheptane.

Can you draw the enantiomer of this substance?

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version of the text. You can view it online here:
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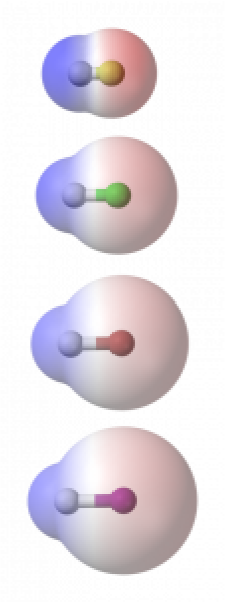
9.2 Properties of Halogenated Compounds

Halogenated Compounds have Varying Polarity



Varying polarity of H-X bonds. See text for details.

The electronegativity of halogens decreases from fluorine down the group, toward iodine. As a result the bonds between these elements and others vary in their polarity. The image at right shows computer generated electrostatic potential maps of a series of compounds formed between hydrogen and each of the halogens: Fluorine at the top, then Chlorine, Bromine, and finally Iodine.

The atomic sizes vary, so the H-F molecule appears quite small compared to H-I. Also notice the intensity of the translucent red and blue regions. These represent the electron clouds surrounding the nuclei, and the degree to which partial charges exist. The more intensely red a region the more electron-rich and negative the region; the more blue, the more electron-deficient and partially-positive the region. H-F has the most highly polarized of these bonds, with the brightest areas of red and blue color in the computer images.

Bonds between these halogen atoms and carbon would show a similar pattern, with the most polarized bonds occurring between carbon and fluorine. Molecules containing carbon to halogen bonds will thus have varied dipoles. In cases where fluorine or chlorine are present the molecular dipole moments can be quite large, altering the solubility of a compound in water, and affecting its melting and boiling points dramatically. In other arrangements the molecular dipole may be less, either due to less polar bonds to halogens or the arrangement of those atoms in the larger molecule.

For drug developers working with halogenated compounds, these differences are important.

Pharmaceutical compounds travel through the body very differently depending on their water solubility. That solubility relates to the molecular dipole moment. So the addition of halogens to these substances can alter the way a drug is absorbed and transported through a body. This is called the bioavailability of a drug. The best molecule is not worth much if it is unable to get to the organ or tissue where it needs to work.

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Drug companies know this and can experiment with alternative structures in order to improve bioavailability. Sometimes they can alter existing, somewhat effective drugs in their search for better alternatives. But they also need to consider the breakdown and excretion of these substances as well, which is also be affected by changes to water-solubility. None of the work is simple, but it is important. A whole area called pharmacokinetics is focused on the movement of drugs through the body.

CHAPTER X

CHAPTER 10 TOPICS: TOXICOLOGY, SAFETY AND HEALTH

1. 10.0 Safety, Hazards, and Risk

Learning Objectives

In this chapter you will learn to

- Consider risk in various situations as a product of hazard and exposure
- Find and interpret information about chemical hazards
- Consider the Hierarchy of Controls when thinking about reducing risk
- Recognize the links between personal safety and environmental safety

10.1 Risk, Hazard and Exposure

What does it mean to be in a safe workplace?

The activities that are carried out in laboratories vary widely. Even within the boundary of what we might call a 'chemical laboratory' many different types of things might go on: synthetic chemists may be running chemical reactions, analytical chemists may be working with instruments for analysis, and biochemists might be working with organisms or natural compounds that are poisons. Similar activities occur in other laboratory and production spaces as well. Lab work supports health care, agriculture, the food and textile industries, mining and manufacturing.

The work in these spaces may carry risks to the personal health of those working in that space, and/or to the greater environment. While the particular concerns relevant to a specific lab vary, workplace safety in all laboratories can be considered using general guidelines and concepts.

The field of **industrial hygiene** includes frameworks that are useful as we consider these issues, and has certain ways to describe and consider safety and environmental health. These ideas can cross over into other working environments beyond what we think of as laboratory work as well.

To begin, it makes sense to get a shared vocabulary around safety. Some fundamental terms to understand include:

Hazard is a characteristic of a substance or experience that links it to the possibility of doing harm to an individual or the environment. Both in and out of the laboratory we are faced with hazards every day.

Risk is related but different, in that it incorporates the likelihood that such harm will occur. Risk is often described as the product of hazard and exposure to the hazard.

Risk = Hazard x Exposure

It is always good to minimize risk. It is difficult/impossible to minimize hazard, since hazards are intrinsic, a characteristic of a substance or event.

Exercise 10.1.1-6

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://openoregon.pressbooks.pub/introductoryorganic/?p=741#h5p-80

Consider this familiar situation: Gasoline is a hazardous substance, which is not only dangerously reactive (flammable) but also highly toxic. Many of us don't worry much about these hazards, however, because we don't handle gas directly. We minimize risk by reducing exposure.

When we devise systems for handling a hazardous material like gasoline in order to reduce the risk to the public, gas station attendants, or the environment, we are working with what are called **controls**: methods to control risk. Controls are around us as we make our way through life. They come in various forms: some are more visible to us (like stop signs) while others are not (regulations that limit what type of vehicle can use the road). Many of these are not even recognized by us. For instance, the rules that govern the transportation of substances by train are many–and few people outside of that industry have taken the time to learn or pay attention to them.

We now will learn how to investigate hazardous materials, including how to think and communicate about the innate hazards associated with substances. Then we will turn our focus to controlling risk. The overall goal of this chapter is to give you a framework for thinking about hazard and risk so that you can work effectively and safely in potentially risky situations in chemical laboratories. The things you learn may also translate to other situations where there you encounter risks, as well.

10.2 Finding and Interpreting Information about Hazards

Hazard Communication

Remember**: *hazards are intrinsic, meaning they are fundamental characteristics of substances or activities. They are therefore not easy to reduce. Hazard Communication ("Haz Comm") can reduce risk in all situations where there is potential exposure to hazardous materials.***

Hazard communication ("Haz Comm") includes both interpreting and sharing information about hazards with others. There are regulatory laws that guide Haz Comm in the workplace. These laws have come from the collective experiences of many experts, and they guide us all toward good work practices. One form of Haz Comm closely connected to work with chemicals is **Safety Data Sheets (SDS)**, formerly known as Material Safety Data Sheets (MSDS). Chemical **labels** used to describe samples of hazardous chemicals on storage shelves or in the laboratory are also frequently encountered by chemists and chemistry students.

What is a Safety Data Sheet?

SIGMA-ALDRICH

Material Safety Data Sheet

Safety Data Sheets are available for commercially-available chemicals from suppliers of those substances. Their appearance may vary somewhat depending on the source, but they always contain:

The name, formula, physical and chemical properties of the material

The author/owner of the information on the document

Information for safe handling and storage of the material

Appropriate responses to emergencies involving the material

Toxicological properties of the material

This information is consistently found on SDS because the Occupational Safety and Health Administration (OSHA) operates based on federal laws requiring these documents, in order to protect the public. Federal OSHA maintains a specific list of information that must be included on SDS at this location:

https://www.osha.gov/Publications/HazComm_QuickCard_SafetyData.html

Pictograms

Any SDS you look at probably includes one or more pictograms communicating the type of hazard(s) associated with the material. Pictograms are supposed to be intuitively understandable. The pictograms convey the following messages about a material:

These pictograms indicate substances are:

Corrosive

Pressurized gas

Harmful

Explosive

Flammable

Oxidizer

Health hazard

Toxic

Toxic to environment

These pictograms are part of an international system for hazard communication called the **Globally Harmonized System (GHS).** Not long ago there was no such system, and various countries around the world had their own ways to communicate hazard. The GHS has made it possible for people around the world to communicate hazard with one another regardless of the language they use.

Hazard Statements

Hazard Statements are short statements that describe the hazards of a material a bit more specifically than the pictograms. They serve as useful guidance for making decisions about how to work with a hazardous substance. Find these statements on the SDS you have, and use them to determine which of the practices below would be potentially problematic for your chemical:

Practice	**Safe? Or possibly problematic?**
Storing the material in a glass bottle with a steel screw cap	
Transferring the material from one container to another without eye protection	
Portioning out small samples from a large stock in a small, confined room	
Adding the substance to water	
Heating a sample of the substance over an open flame	

Hazard statements can guide someone who is working with a

substance, or who has an accident while working with a substance. Imagine how they could help if:

…a small sample of this material was spilled and ended up dropping from the lab bench onto your foot

…you used some of this material and had 50 mL/50 g of excess (waste) to dispose of at the end of your work day?

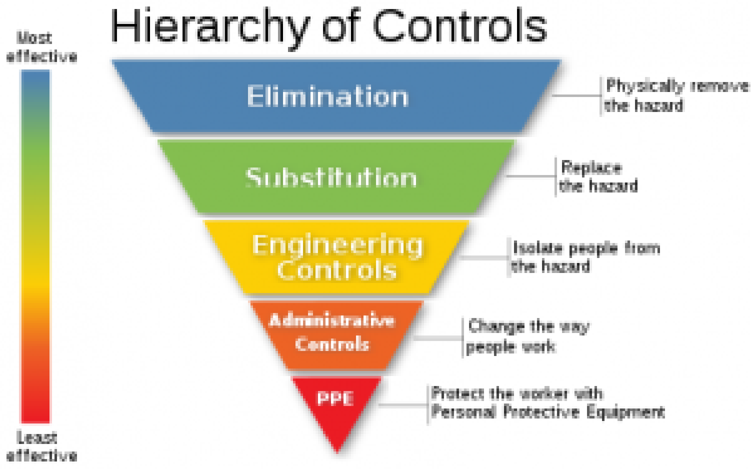
…you needed to find safe storage for this material for an extended period of time?

10.3 Hazard Controls

Hazard controls are practices or systems used to **minimize risk.** Effective controls minimize the potential for problems related to exposing individuals or the environment to a hazard. In the chemistry lab we think of most hazards as chemical hazards, though it is also common to encounter electric, slip/trip/fall, and fire hazards in this setting.

In work environments that are not primarily used as chemistry laboratories, the concept of controls is still useful. For instance, infection controls are a standard way of managing the risk to workers in hospitals, where individuals who carry infectious disease occupy a building with one another and a cadre of workers who move through the facility.

The national government agency **NIOSH (National Institute of Occupational Safety and Health)** developed a hierarchy of controls, such that the items at the top of the hierarchy are most effective at reducing risk.



Take a moment to reconsider the earlier example of risk to health and environment from the hazardous material, gasoline. Gasoline is highly flammable and is toxic by inhalation (breathing vapors) and through contact (skin contact or through contact with mucous membranes). How do we control the risk to health from exposure to this substance?

The most effective way to reduce your risk is by removing gasoline from your life (**Elimination**). But since many of us consider it an important substance to use, we protect ourselves by pumping it into our cars using special pumps that minimize our exposure to it. The pumps and our cars are engineered to isolate people from the hazard (an **Engineering control**). For those who work with gasoline all day, instructions to keep the hose pointed away from themselves are given (**administrative control).** These workers may also wear gloves or other protective clothing (**PPE**) to help them avoid exposure.

Note that in this example it is possible to identify a specific example of each type of control, with the exception of Substitution. Substitution would occur if gasoline were replaced with a different fuel that did not have the problematic hazards.

In the chemistry lab similar thinking is employed to minimize exposure to hazards, decreasing the risk of harm to students or workers who occupy and work in the lab.

Apply your understanding

For each example describing an adjustment to a lab procedure, identify which of the types of controls best describes the nature of the risk reduction:

Example	Type of control
Fume hoods are used to boil a substance that releases vapors that are hazardous by inhalation.	
Students are told to tie back their hair when working with a Bunsen burner.	
Concentrated hydrochloric acid (12M) is replaced with a more dilute solution (3M) to acidify a sample.	
One part of a lab procedure is removed since the learning objectives for the day can be met without it.	
Students are told to wear their safety glasses.	

The examples here demonstrate that controls on the bottom end of the hierarchy are not unimportant. However, for any hazard it is preferable to work at the top of the hierarchy to manage any particular hazard, if there is an option to do so. In the absence of satisfactory risk reduction from controls at the top of the hierarchy, we do often resort to things like PPE. Use of protective equipment is essential when the risks are real and the potential harm (damage to eyes and possible loss of vision in the case of eye protection) is great.

Engineering controls in a chemical laboratory often include air handling systems, the use of inert materials for benchtops and floors, placement of disposal areas and sinks near workers, and more.

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Administrative controls in the chemistry lab include expectations for behavior that

prohibits climbing, running, or throwing objects in the lab.

PPE used in the chemical laboratory always includes eye protection. Gloves, laboratory coats, face shields, hearing protection and insulated gloves are also frequently used.

10.4 Environmental Health

When we think about hazard and risk it is normal to immediately think of personal risk, e.g. Safety. However the environment is also affected by our activities, and can be unnecessarily put at risk by carelessness. As we consider risk controls we can also think about environmental risk.

One special consideration for environmental risk is **proper disposal of hazardous materials**. Making decisions about disposal is not simple, but general guidelines can still be useful:

- Treat everything as a hazardous material unless you know its effects.
- Know the fate of materials that go into the solid waste ("trash"), the public sewer, and into hazardous waste storage. Many materials put into the public sewer are reintroduced into the environment.
- Avoid mixing wastes if possible.
- Adhere to local and state regulations and ask before disposal if you don't know what to do.

The Environmental Protection Agency (EPA) and similar state institutions such as the Oregon Department of Environmental Quality (DEQ) govern waste handling and disposal. Laws are complex and evolving, but in general hazardous chemical wastes must be sorted, stored safely, and transported with great care to suitable disposal sites.

Many materials that are wastes in a laboratory can undergo operations to recover them for additional use. Others can be used safety as fuels, producing heat and electricity as they are combusted. Those that can not be put through these recycling or repurposing processes are usually placed in special hazardous waste landfills.

Responsible waste handling remains the responsibility of a waste generator in perpetuity. This law motivates waste producers to minimize the amount of waste they produce and to avoid unnecessarily hazardous wastes. Waste handling and disposal is also costly, which provides an additional incentive for businesses to be thoughtful about what, and how much waste they produce.

It is easy to judge waste producers, but we all contribute indirectly to the production of hazardous wastes. The materials we buy and consume come from the earth, and are transformed into useful substances through waste-producing processes. Some processes are certainly unnecessary and harmful, and should be curtailed or banned. But others are not easily avoided.

It is in our shared interest to be aware of and attentive to matters of waste production throughout the life cycle of the materials we use, and to produce as little waste as possible.

Where do chemicals end up when

- They are flushed down the drain?
- They are put into a trash can?
- They are put into a special waste jar?
- They are released to evaporate in the hood?

Appendix

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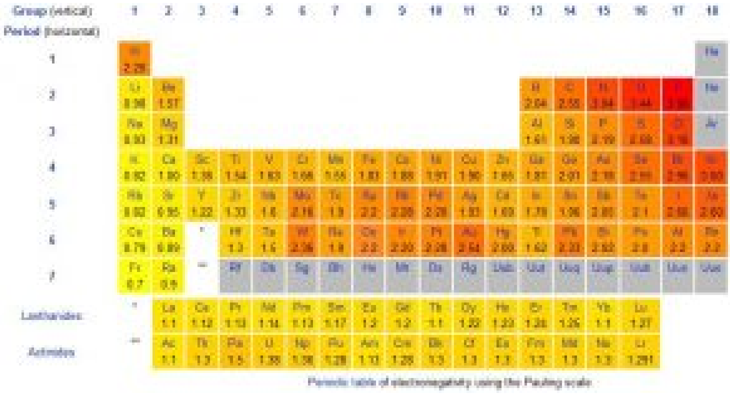
Electronegativities of the Elements, Pauling Scale



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Overview of the IUPAC System for Naming Organic Compounds

Rules (current as of December 2020) for organic nomenclature from the International Union of Pure and Applied Chemistry (IUPAC) can be found at

https://www.acdlabs.com/iupac/nomenclature/

Summary Rules for Naming Organic Compounds

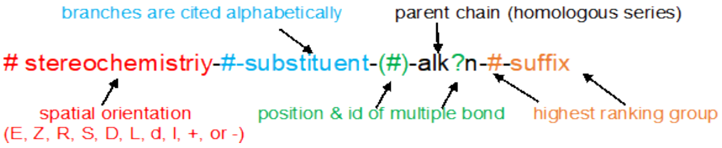
Taken from ChemLibre SCC Chem 420 text on Organic Chemistry

The International Union of Pure and Applied Chemistry (IUPAC) has established the rules of nomenclature of all chemical compounds. IUPAC nomenclature can also be called "systematic" nomenclature because there is an overall system and structure to the names. This section provides an overview of the general naming strategy and structure for organic compounds.

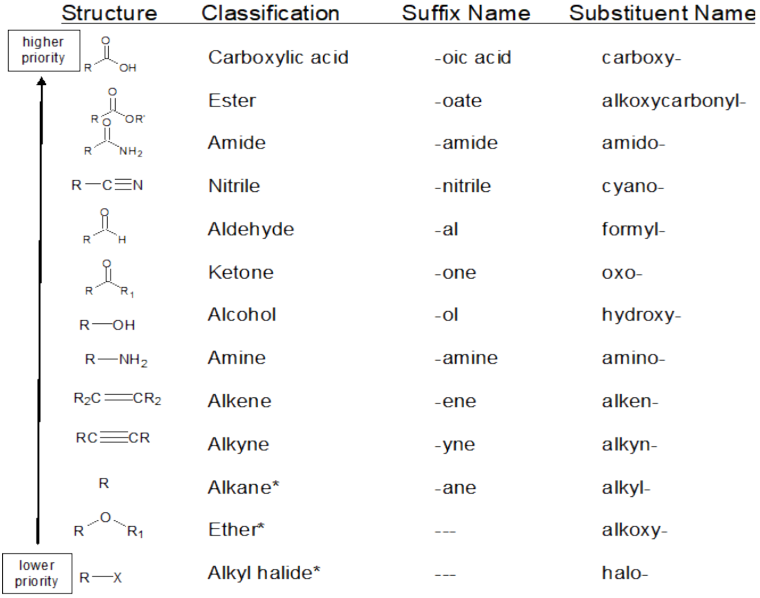
Naming organic compounds according to the IUPAC system requires up to four pieces of information

1. recognize & prioritize the functional group(s) present
2. identify & number the longest continuous carbon chain to give the highest ranking group the lowest possible number
3. cite the substituents (branches) alphabetically using the numbering determined above
4. recognize & classify any stereochemistry (E/Z, R/S, cis/trans)

With these four pieces of information, the IUPAC name is written using the format below. This same format applies to **ALL** the organic compounds.



Recognize and prioritize the Functional Group(s) Present



Structure	Classification	Suffix Name	Substituent Name
	Carboxylic acid	-oic acid	carboxy-
	Ester	-oate	alkoxycarbonyl-
	Amide	-amide	amido-
$R-C\equiv N$	Nitrile	-nitrile	cyano-
	Aldehyde	-al	formyl-
	Ketone	-one	oxo-
$R-OH$	Alcohol	-ol	hydroxy-
$R-NH_2$	Amine	-amine	amino-
$R_2C=CR_2$	Alkene	-ene	alken-
$RC\equiv CR$	Alkyne	-yne	alkyn-
R	Alkane*	-ane	alkyl-
	Ether*	---	alkoxy-
$R-X$	Alkyl halide*	---	halo-

*Same overall priority, prioritize by structure as described in the appendix

Identify & Number the Longest Continuous

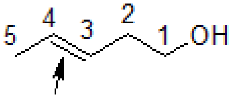
Carbon Chain with the Highest Priority Group

The longest continuous carbon chain (parent) is named using the Homologous Series, as well as any carbon branches. The suffixes and location within the name distinguish between the parent and the branches. Some of the homologous series names for saturated, straight-chain hydrocarbons are shown here, along with the substituent forms used when naming branches.

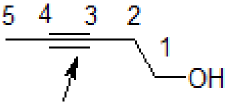
Parent chain length	Alkane base name	Substituent form
1 Carbon	Methane	Methyl
2 carbons	Ethane	Ethyl
3 carbons	Propane	Propyl
4 carbons	Butane	Butyl
5 carbons	Pentane	Pentyl
6 carbons	Hexane	Hexyl
7 carbons	Heptane	Heptyl
8 carbons	Octane	Octyl
9 carbons	Nonane	Nonyl
10 carbons	Decane	Decyl
11 carbons	Undecane	Undecyl
12 carbons	Dodecane	Dodecyl

When Alkenes and Alkynes have Lower Priority

The hydrocarbon suffixes differ in the letter preceeding the “n”. When alkenes and alkynes occur in compounds with higher priority functional groups, then the distinction between hydrocarbons is communicated with a single letter: “e”, or “y” for alkenes and alkynes, respectively, An example is shown below to illustrate the application of this rule.



pent-3-en-1-ol



pent-3-yn-1-ol

Cite the substituents (branches) alphabetically using the numbering determined above

Substituent forms above are used when naming simple branches off the parent chain. Additional branching does occur, naming guidelines for these situations are not introduced here.

Recognize and Classify Stereochemistry

Distinguishing spatial orientations of atoms (stereochemistry) are communicated at the beginning of the name using the appropriate symbols, such as E/Z, R/S, cis/trans, etc..

Atoms or groups are called *cis* or *trans* to one another when they project respectively on the same or on opposite sides of a reference plane identifiable as common among stereoisomers. The compounds in which such relations occur are termed *cis/trans*-isomers. For doubly bonded atoms, the reference plane contains these atoms and is perpendicular to the plane containing the doubly bonded atoms and the atoms directly attached to them.

In names of compounds, steric relationships around one or more double bonds can be designated by the stereodescriptors Z and/or E , assigned as follows. The sequence-rule-preferred atom or group attached to one of a doubly bonded pair of atoms is compared with the sequence-rule-preferred atom or group attached to the other of that doubly bonded pair of atoms; if the selected atoms are on the same side of the reference plane the italic capital letter Z is used as the stereodescriptor; if the selected atoms are on opposite sides, the italic capital letter E is used as the stereodescriptor. These stereodescriptors, placed in parentheses followed by a hyphen, normally precede the whole name; if the molecule contains several double bonds, then each stereodescriptor is immediately preceded by the lower or less primed locant of the relevant double bond.

Chiral centers are labelled as R or S preceded when necessary by appropriate locants.