Richard F. Daley and Sally J. Daley
www.ochem4free.com

Organic Chemistry

Chapter 0

Student's Guide to Success in Organic Chemistry

Chapter 0

Student's Guide to Success in Organic Chemistry

Chapter Outline

0.1 What is Organic Chemistry?
A brief history of the development of modern organic chemistry

0.2 Organic Chemistry in the Everyday World
Ways that organic chemistry impacts your everyday life

0.3 Organic Chemists are People Too
Stories about the people who made a couple of significant organic chemicals

0.4 Learning to Think Like a Chemist
An overview of how a chemist organizes learning organic chemistry

0.5 Developing Study Methods for Success
A guide to learning organic chemistry that is more than massive memorization including how you can succeed in organic chemistry by using the best study methods

Objectives

- ✓ Understand how organic chemistry impacts the world
- ✓ Learn how to think like an organic chemist so you can succeed in organic chemistry
- ✓ Adapt your own study methods to succeed in this class

“The horror of the moment,” the King went on, “I shall never, *never* forget!”

“You will though,” the Queen said, “if you don't make a memorandum of it.”

—Lewis Carrol

Welcome aboard! You are now at the launching point of a new adventure called Organic Chemistry. To succeed in this adventure, accept the intellectual challenge to look at things from a viewpoint that is perhaps different from any you have ever used before. By committing yourself to hard work and self-discipline, you are ready to make this adventure well worth the journey.

Organic chemistry is the study of the chemistry of the element carbon. What is it about carbon that makes this one element the focus of an entire branch of chemistry? Carbon atoms, unlike most other elements, form stable bonds to each other as well as to a wide variety of other elements. Carbon-containing compounds consist of chains and rings of carbon atoms—bonding in ways that form an endless variety of molecules. At this time, chemists have identified and/or synthesized more than ten million carbon-based compounds, and they add thousands of new organic molecules to this list every month.

0.1 What is Organic Chemistry?

The roots of chemistry go back into antiquity with the development of such techniques as metal smelting, textile dyeing, glass making, and butter and cheese preparation. These early chemical techniques were almost all-empirical discoveries. That is, someone either by accident or observation discovered them. They then passed this knowledge down from one generation to the next. For example, because copper is found in its free metallic state, it was first beaten into various implements. Later it was smelted, being perhaps one of the first metals to be separated from its ore.

Empiricism waned with the Greek philosophers who began the first systematic discussions of the nature of matter and its transformations. There were numerous philosophies and schools that grew up around those philosophers. One that is of particular interest to chemists is that of the atomists. Democritus (460-370 B.C.) elaborated much on the idea of atoms. He thought that atoms were solid particles and that atoms existed in a void but could move about and interact with each other; thus, forming the various natural systems of the world. However, Aristotle and Plato rejected the philosophy of atoms, and it wasn't until the early nineteenth century that Dalton proposed the beginnings of the modern atomic theory.

Socrates, Plato, and Aristotle had the greatest impact on Greek philosophy. Socrates felt that studying the nature of man and his relationships was much more important than studying the science of nature. He did benefit the later development of science by insisting that definitions and classifications be clear, that arguments be logical and ordered, and that there be a rational skepticism. Plato adopted the philosophy that there were four elements: fire, air, water, and earth. Aristotle added to those four elements four associated qualities: hot, cold, wet, and dry. He believed that each element possessed two of these qualities, as illustrated in Figure 0.1.

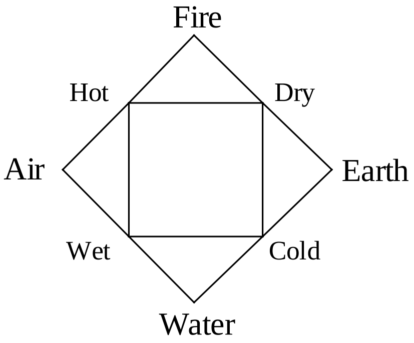


Figure 0.1. The relationship between the four elements and their associated qualities. This diagram frequently appears in alchemy literature.

According to this philosophy, one element might be changed (transmuted) into another element by changing its qualities. For example, earth was dry and cold, but it could be transmuted into fire by changing its qualities to hot and dry.

These theories remained important for nearly two thousand years. Of greatest significance was the scientific work that took place in Alexandria. Unfortunately, little of it was in the field of chemistry.

Alchemy is the philosophical and primitively empirical study of physical and chemical transformations.

It was in Alexandria, toward the end of the first century BC, that western **alchemy** began growing. Alchemy was a mixture of philosophy, religious, or spiritual, ideas, astrology, and empirical technical skills. Based on the theory that all matter consisted of fire, air, water, and earth with the associated qualities of hot, cold, wet and dry and that by changing the qualities of one form of matter you could change it to another form, the philosophers thought if they systematically changed matter from one form to another in time they could obtain the perfect metal. Not only were they working to form the perfect metal but also to form an elixir of life that would give them spiritual perfection.

From Alexandria, alchemy quickly spread throughout the Western world. For the next fifteen hundred years, its many practitioners persuaded wealthy patrons to support them in their research with the promise that unlimited wealth was just around the corner—just as soon as they could convert lead or iron into gold or silver.

Don't think that because alchemists promised to convert base materials into precious metals that they were just con-artists promising something for nothing. Many alchemists truly believed that somewhere in nature there existed a procedure that would form precious metals from base materials. As they worked to find this procedure, they learned much about science, although they were not scientists in a modern sense. What alchemy provided to science was the experimental base from which modern chemical theories arose.

Because alchemists promised impossible chemical feats and did not follow modern scientific methods, historians often call this time period the “dark age” of science. However, their logic was quite sound. Their goal to change matter from one form to another was the result of looking at the many dramatic changes they could see in nature. For example, in a fire, wood simply “disappeared” leaving a small amount of ashes. Thus, as the alchemists observed dramatic changes such as this, they reasoned that it should be as easy to make other sorts of changes—such as changing lead into gold. They had no way of knowing that converting lead to gold involved a totally different type of change than that of using fire to turn wood into ashes.

The move toward modern chemistry took a long time. Physics and medicine had provided an experimental base, but first the philosopher’s attitude toward nature had to change to a more inductive approach. That is, as René Descartes advocated, accept only those things that you can prove. Perhaps the biggest obstacle to modern chemistry was that of chemical identity. There was the need to replace the alchemist’s four elements with the understanding of atoms. Scientists needed to understand that the identity of a substance stayed the same even when that substance became a part of another substance. For example, copper is always copper even when mixed with zinc to form bronze, an alloy of copper. Robert Boyle (1627-1691) did much to do away with the view of the four elements, as well as to begin the study of gases (or air). Many scientists studied gases and isolated a number of pure gaseous compounds, but they all thought that these gases were either very pure air or very impure air. Antoine Lavoisier (1743-1794) finally moved chemistry into its own as a modern science with his recognition that oxygen was not just very pure air, it was a completely separate element.

Early in the nineteenth century, as modern chemistry began developing, chemists mostly ignored organic chemistry, viewing it as either medically or biologically related because nearly all the known organic compounds were derived from living organisms, both plant and animal. An exception to this was Lavoisier, who was very interested in organic chemistry and considered it to be a part of chemistry. He looked at some organic compounds and found that they all contained carbon.

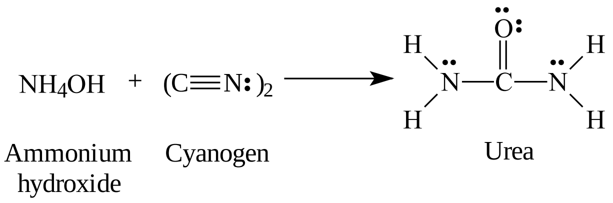
Because organic compounds were much more complex and unstable than the inorganic compounds being synthesized at the time, chemists had not knowingly prepared any and, in fact, thought that they were impossible to prepare. They believed that these compounds came only from living organisms. That is, the formation of the known organic compounds, such as urea, starches, oils, and sugar, required some “vital force” possessed by living organisms. Thus, organic chemistry became the study of compounds having a vital force, or **vitalism**. Some chemists felt that, because of the “vital force,” organic compounds did not follow the same rules that other compounds did.

Vitalism is the belief that the synthesis of organic compounds requires the “vital force” from some living organism.

Unaffected by the attitudes concerning organic chemistry, Michel Chevreul set out to study the composition of fats using the process of saponification, or soap making. In 1816, Chevreul separated soap into several pure organic compounds and found that these compounds were very different from the fat that he had started with. He had unwittingly dealt vitalism a major blow.

To do his work, Chevreul first made soap. He repeated the process many times making the soap from several sources of fat and alkali. Then, after he separated the soap from the glycerin, he separated the soap into its various fatty acids. He called these compounds fatty acids because he had isolated them from the soap, which he had prepared from animal fat. Previously people had not understood that a chemical reaction took place during the soap making process. They thought that soap was simply a combination of the fat and alkali. Unfortunately, other chemists took a long time to recognize the significance of Chevreul's work.

Another chemist that brought vitalism to its end was Friedrich Wöhler with his synthesis of urea in 1828—as he said, “without the use of a kidney”. The following reaction is the synthesis of urea using the starting material aqueous ammonium hydroxide and cyanogen.

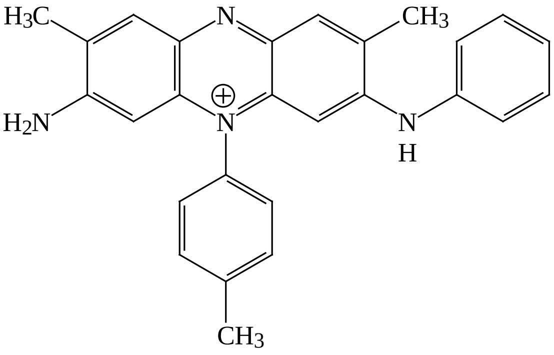


Wöhler’s goal was not to synthesize urea; he was trying to make ammonium cyanate (NH_4OCN), a compound he needed for his research. In fact, he may have become frustrated because he tried to make ammonium cyanate by several different routes. He tried reacting silver cyanate with ammonium chloride, reasoning that silver chloride is insoluble and would precipitate from solution. He tried reacting lead cyanate with ammonium hydroxide. Finally, he tried aqueous ammonium hydroxide and cyanogen. But, every attempt led to the same white crystalline substance that was *not* the desired product.

Wöhler made his mark in the annals of chemistry by deciding to identify this unknown substance. Once he identified it as urea, he also recognized the importance of his discovery. As he wrote in 1828 "[The] research gave the unexpected result . . . that is the more noteworthy inasmuch as it furnishes an example of the artificial production of an organic, indeed a so-called animal substance from inorganic materials."

Chevreul and Wöhler had forever altered the study of organic chemistry. As other chemists looked at the work that Chevreul and Wöhler had done, they saw that chemists could indeed synthesize compounds of carbon without a living organism. They then began making carbon compounds and studying them. Soon many chemists were achieving remarkable successes in the new art of the synthesis of organic compounds. Thus began the study of organic compounds.

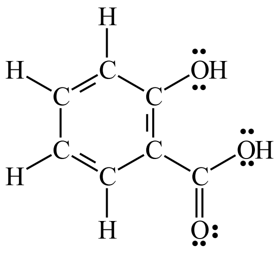
Inevitably, someone would take these new developments from the organic chemistry research laboratory and find ways to market them. William Henry Perkin was the first to do so. In 1856, at the age of 18, while on vacation from London's Royal College of Chemistry, Perkin was working in his home laboratory. While naively attempting to make quinine, a task not accomplished until 1944, he accidentally synthesized the dye now called Perkin's mauve. The next year, using money borrowed from his father, he built a factory and marketed the new dye. From there, he worked with coal tar and found that coal tar was a rich source of starting materials for a variety of new dyes.



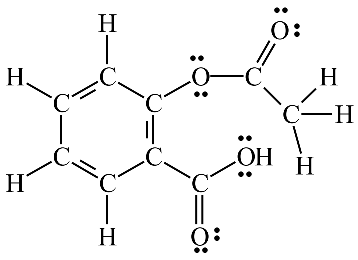
Perkin's mauve

Another step in the progress of organic chemistry was the drilling of the first oil wells in Pennsylvania in 1859. The oil pumped from those wells provided a new, cheap, and abundant source of carbon compounds. Today the petrochemical industry supplies the raw materials for thousands of different products including a variety of things from explosives and fuels to pharmaceuticals and agricultural chemicals.

In 1895, the Bayer Company of Germany established the pharmaceutical industry. Then in 1899, the company began marketing aspirin, as a result of the work of Felix Hoffmann. Hoffmann learned how to prepare aspirin from natural salicylic acid. For hundreds of years, people had chewed the bark of the willow tree to relieve minor pain. Willow tree bark contains the analgesic salicylic acid. Aspirin is superior to salicylic acid as an analgesic because it produces less irritation to the stomach and effectively treats the pain.



Salicylic acid



Aspirin

In the early days of chemistry, chemists learned a great deal about the simple compounds not usually found in living systems, but they learned very little about the organic compounds that are found in living systems. They were far too complex for the simple analytical tools available in the nineteenth century and the early twentieth century. Thus, progress was slow in understanding the chemistry of living systems. The subsequent development of powerful analytical tools allowed many insights into biologically important molecules and opened up new areas for scientific study.

0.2 Organic Chemistry in the Everyday World

Organic chemistry touches every aspect of your life. This includes such areas as the clothes you wear, the food you eat, and the car you drive. Common to each of these items are chemical compounds based on the element carbon. Organic chemistry has both positive and negative attributes, and organic chemistry involves you.

All living creatures, both plant and animal, consist largely of complex carbon-containing molecules. These molecules provide for the day-to-day operation and maintenance of each organism as well as for the continuance of the species. Interestingly, as chemists learned how to synthesize these complex molecules of life and the molecules that interact with them, organic chemistry came back to its roots. A part of the beginnings of organic chemistry was the study of compounds derived from the "organs" of living creatures—thus the name organic chemistry. Now the knowledge gained from that research provides the basis for healing the diseases of many of those organs.

Looking in a totally different direction for the presence of carbon atoms in your life, what can you find that is more commonplace than plastic? You use plastics, or polymers, virtually all day long from the "disposable" packaging of your bath toiletries to the sophisticated polymeric materials in your car and computer. The plastics that make up all these items are based on organic compounds. The polymer industry has impacted modern society more than any other industry.

The above discussion covers some of the positive contributions of organic chemistry. Unfortunately, however, organic chemistry has made some negative contributions to the world too. There is a wide variety of commercial products that do not readily degrade when discarded or that cause other sorts of environmental problems. In spite of their usefulness, plastics are among those products. Because of the negative side of plastic, and other products, chemistry has gained a bad reputation in modern society. Adding to this reputation are the unscrupulous entrepreneurs who inappropriately dump hazardous materials thus contaminating the soil, air, and water.

Few chemists and chemical companies intentionally market products that will cause harm to a customer or to the environment. Those that do usually are considering only how much profit they can make and may even cover up evidence showing harm from their product. In many cases, the problems with a product come to light after the product reaches the market—sometimes long after reaching the market. This may occur because the company simply did not thoroughly test its product. Also, the shortfall in testing is often in the areas where the customer uses the product in ways unrelated to its intended use. Most chemists and chemical industries are good citizens with sound environmental concerns.

So, besides being a consumer, how could you fit into organic chemistry? Are you good at thinking up new ideas or looking at old ideas in new ways? The marketplace always welcomes new products. Do you have a concern for the environment? There is a worldwide need for solutions to the multitude of environmental problems and to find new products to replace those products causing harm to the environment. Related to the environment are the needs for solutions to the many other problems of modern society. Have you always been one to ask, "Why?" and "How does it work?" Chemists have just begun to learn about chemistry. Perhaps you could do research in chemistry—just because it's there. Or you could use organic chemistry as an important foundation of your profession in medicine—either as a medical researcher or as a physician working with patients. Both biochemistry and many areas of biology depend heavily on a thorough understanding of organic chemistry. Biochemistry is the study of the molecules found in living organisms. Biology is increasingly directed to molecular biology, which is designed to learn more about living organisms by understanding the molecular processes of life.

0.3 Organic Chemists Are People, Too

At the root of all science, including organic chemistry, is people's unquenchable curiosity about the world and themselves. Everywhere are objects, living organisms, and events that people have had questions about. Scientists investigated these questions and discovered other questions. They investigated these new questions and found still more questions. Research, they learned, not only answers questions but uncovers new ones. Although scientists have learned many answers, they also have found that the answers to some questions must wait for the development of better investigative methods and tools. The job of scientists is to find answers to the multitude of questions about the world and to develop better methods and tools to answer the more and more sophisticated questions that they come up with along the way.

Because much of the world is based on the chemistry of carbon, organic chemists have provided many answers to the questions about the world. Many creative and curious people have been attracted to organic chemistry. The following stories illustrate the hard work and ingenuity of two such chemists.

In 1874, Othmer Zeidler reported the synthesis of DDT in his doctoral dissertation. Some years later, Paul Hermann Müller discovered the insecticidal properties of DDT and in 1948 received the Nobel Prize in Medicine and Physiology for his discovery. Today DDT has a bad reputation because of its persistence in the environment. Its intended use was to kill disease-bearing insects, but it also caused harm to a number of birds and animals. DDT is no longer used in most areas of the world, but in the 1940s it was a “magic bullet” that killed many disease-bearing insects and saved many hundreds of thousands of lives. During World War II, the military used DDT, but it was not available for civilian use until Frank Mayo happened to read about it.

Frank Mayo is an example of an ambitious person who, with determination and hard work, coupled with a sound chemical foundation, made an impact on society (See Friedman, *J. Chem. Educ.*, **1992**, 69, 362). Mayo attended Georgia Tech leaving just one semester from completing the three year degree in chemistry. He turned down a job offer for eighteen dollars per week because he thought he could earn more working on his father's farm.

A few years later he began manufacturing and marketing chlorine based bleaching compounds. In 1944, while looking for other products to manufacture, Mayo happened on an article in the *Atlanta Constitution* describing DDT and its uses. He became interested. DDT was available only to the military; but even there, it was available only in limited quantities. The article stated that the synthesis for DDT was classified. However, it did give one important clue—a brief mention of the original synthesis by Zeidler in Germany. That was just enough information for a determined chemist!

Mayo knew that usually graduate students published their doctoral dissertations four to six months after graduation. He also knew that Othmer Zeidler received his degree in May or June of 1874, so Mayo expected to find the published report in the renowned journal *Berichte der Deutschen Chemischen Gesellschaft* (Reports of the German Chemical Society) by October, 1874.

Mayo went to the Georgia Tech library but found they did not begin subscribing to *Berichte* until 1910. Nearby Emory University began in 1915. He next decided to try the University of Georgia library 75 miles away in Athens. Since his daughter Bebe was a student there, he phoned her and asked her to check the library for him.

She found that indeed the University of Georgia had the 1874 issues of *Berichte*, but they were in boxes stored in the attic of the library. Only after many delays and much persuasion did Bebe gain permission to look through the issues *Berichte* in the attic. The librarians were notably reluctant to get them out of storage for a freshman who was studying neither German nor Chemistry. Bebe examined the title pages of the 1874 volume of *Berichte* beginning with October. “Believe it or not,” says Mayo, “There it was, in the October issue.” Word for word in the unfamiliar German, Bebe copied the paper by hand, then she called her father.

Mayo rushed to Athens, only to arrive after visiting hours in the dormitory. They wouldn't even let a father see his daughter after visiting hours! He drove around the dormitory, parked under his daughter's window and honked the horn. Bebe placed the transcript in an envelope and threw it out the window. Carefully shielding the paper from the falling rain, he read Bebe's copy in the headlight of the car then immediately drove back to Atlanta. He had the synthesis of DDT!

The synthesis required three ingredients: chlorobenzene, sulfuric acid, and chloral. He already had the chlorobenzene and sulfuric acid, but he had no chloral. Ignoring the fact that it was midnight, he drove to the neighborhood druggist and asked for a pound of chloral. The sleepy druggist grumpily informed him that he needed a prescription, and that no physician was likely to give him a prescription for a pound of the stuff. The typical prescription for chloral was measured in minims (about 16 minims per milliliter).

Mayo explained the reason for wanting the chloral, and the druggist finally agreed to sell him a pound.

With the precious chloral in hand, Mayo went home to try to make DDT. He measured the chemicals into a fruit jar packed in ice, using a wooden kitchen spoon to stir the mixture. Twenty minutes later, floating white lumps covered the top of the liquid. He separated the solid from the mixture with a buttermilk strainer and dried the powder. Then he slept.

The next morning, he made up a 5% solution in mineral spirits and sprayed the laundry area of his basement. Fleas from his dogs infested the area. An hour later, he and his wife returned to the basement. “Not a flea jumped to my wife's ankles,” he said. “Nothing happened—no fleas! The fleas, formerly plentiful, were dead. Cockroaches were lying with their feet in the air as if waving good bye to me. I was a happy man.”

Mayo then built a plant to manufacture DDT. Because of the war, he could not buy the equipment he needed. However, being resourceful, he built his plant with scraps and old metal drums that most people would consider junk. Mayo made hundreds of thousands of pounds of DDT powder and DDT solutions in deodorized kerosene and shipped it all over the world. Because of the benefit DDT gave to people, Mayo received much praise. Later, problems showed up that scientists traced to DDT so he stopped making and selling it. Since the banning of DDT, insect born diseases are again on the rise, but because DDT causes damage to helpful animals, it is not an acceptable insecticide. So far no one has discovered a good substitute.

Are you ever heading in one direction with a particular project only to find it turning out differently than you had expected? Do you just junk the project, or do you find yourself trying to figure out what went wrong or how you can use the project some other way? Many of the great discoveries of chemistry were made because the chemist investigated the reasons for an unexpected result. That was the case for Roy J. Plunkett, a young Ph.D. chemist who graduated from Ohio State University in 1936.

Plunkett was working for DuPont attempting to find a non-toxic refrigerant. On April 6, 1938, he and his assistant, Jack Rebok, opened the valve on a cylinder of tetrafluoroethylene to begin an experiment. No tetrafluoroethylene came out. In fact, nothing came out, although the weight of the tank indicated it should be full. He pushed a wire into the valve to determine if it was blocked. The wire went in freely. Plunkett had no understanding of what was wrong, but instead of discarding the “empty” tank and getting another to continue his research, he decided to investigate. Sawing the tank open, he found it filled with a waxy white powder. The molecules of tetrafluoroethylene had reacted together to form a polymer, or plastic, that they called polytetrafluoroethylene.

No one had ever observed the polymerization of tetrafluoroethylene before, but somehow it had occurred inside an otherwise "empty" tank. What caused it? On further investigation, Plunkett found some iron oxide inside the tank and discovered that it had catalyzed the polymerization reaction. Plunkett and other DuPont investigators soon developed ways to make polytetrafluoroethylene.

This new polymer had some remarkable properties. It was inert—it would not react with either strong acids or strong bases. It was heat stable, and no solvent could dissolve it. It was also extremely slippery. In spite of these interesting properties, if it had not been for World War II, probably no one would have done anything with it. Tetrafluoroethylene was too expensive.

General Leslie R. Groves happened to hear about the new material and asked to test it. General Groves was in charge of the Manhattan Project, the group working to develop the atomic bomb. In their research, they used enriched uranium. To make the enriched uranium, they converted uranium to uranium hexafluoride, an extremely corrosive gas. The project needed a gasket material that was resistant to uranium hexafluoride, so DuPont made some gaskets and valves for Groves. The scientists at the Manhattan Project tested them and found them very resistant to uranium hexafluoride. DuPont manufactured Plunkett's polymer for the Manhattan Project under the name Teflon^{TM}.

Unlike DDT, Teflon's usefulness has stretched well beyond its wartime beginnings. Who hasn't used Teflon coated cookware? Of greater significance than the cookware is the fact that Teflon is a substance that the body does not reject. Thus, millions of people have benefited by receiving such things as artificial hips and knee joints or aortas and pacemakers made of Teflon. Another use of Teflon is in the space program. Space suits, wire and cable insulation, spaceship nose cones, and fuel tanks all use Teflon.

0.4 Learning to Think Like a Chemist

To learn to think like an organic chemist, you must first know how an organic chemist thinks. The following three points are an overview of their thought processes. Also, these three points are goals for you as you study this book. (1) Organic chemists learn the facts. (2) They use these facts to construct concepts by organizing the facts into a coherent picture. (3) As organic chemists learn new facts, they update their picture of concepts.

From the scientific viewpoint, facts are important because facts are the basis of science. A fact is an observation based on experimentation. Scientists, and that includes organic chemists, form their hypotheses based on the facts that they know about a certain topic. They make a speculation based on the hypothesis and do some experiments based on that speculation. These experiments lead to new facts, which lead to an updated hypothesis and further speculation and more experiments. Thus, the whole process in all sciences is designed to produce a coherent but expanding understanding of the universe.

Facts alone are not important to organic chemists. What is important is the way those facts fit together to form a coherent picture. Most organic chemists can produce an amazing variety of facts within the context of a particular concept. However, if asked to provide a list of the facts of organic chemistry, an organic chemist would probably be unable to produce a very impressive list. On the other hand, many beginning organic chemistry students can produce an amazing variety of facts on demand, but have little idea how they fit into a clear picture. A part of thinking like an organic chemist is to learn as many facts as you can about organic chemistry and, at the same time, to continually organize those facts in a way that allows you to synthesize new ideas. This method of learning can help you better understand and use the facts.

The important part of learning organic chemistry is the concepts you construct from the set of facts that you learn. Chemistry is, above all, a science. As a science, the only way to learn anything meaningful about organic chemistry is to work with the concepts. These concepts are not inviolable. They are subject to constant reconstruction and reinterpretation as you learn new facts. The authors of this book and your lecturer can only present the facts and provide you with the vehicle from which you can build your own understanding.

0.5 Developing Study Methods for Success

The key to your success in organic chemistry is in what you learn. Build your foundation to gain this knowledge by carefully studying the book and actively participating in the lectures. The more you apply your developing knowledge to understanding the design of the various organic syntheses and reaction mechanisms, the more you will grow in creativity as a student of organic chemistry.

Studying organic chemistry is like combining the elements of a foreign language class with the elements of a logic, or math, class. As with a foreign language, you must learn the vocabulary (names of compounds, chemical structures, reagents, and reactions), as well as the grammar (electron movements). As with a math class, you must understand the logic (reaction mechanisms). You combine these elements by practicing the grammar and vocabulary; then following the logic as you apply your knowledge to new situations (working the exercises in your book). Finally, you demonstrate your mastery of both the grammar and the logic (by doing well on the examinations your instructor writes).

To succeed in this class, you must develop a consistent knowledge base of concepts, theories, and techniques. In other words, what you learn in the early chapters is essential for your understanding of the material in later chapters. Failure to retain the things that you have studied will make learning organic chemistry seem overwhelming. When you study, make it your central objective to thoroughly understand the concepts, theories, and techniques being covered, then retain them. Could you repeat that, please? ***When you study, make it your central objective to thoroughly understand the concepts, theories, and techniques being covered, then retain them.*** These concepts, theories, and techniques are your knowledge base and the foundation for all of your continued efforts in learning organic chemistry.

Developing and maintaining your knowledge base of organic chemistry requires some learning strategies that are different from those used for many other classes. Primarily, learning organic chemistry requires consistent time, effort, and, most of all, thought. Organic chemistry has a reputation for being a difficult subject to master because it covers a lot of information and some students struggle over some of the concepts. Regular study diminishes this difficulty level. Some people can stuff in lists of facts in an all night cram, but few people can learn facts and the accompanying logic, then integrate those facts and the logic with previously learned facts and logic in a last minute effort. The most important move you can make on the road to success in organic chemistry is to establish a regular program of study.

Ideally, a schedule of regular study involves five steps.

Step 1 When your instructor assigns a new chapter, quickly read through it before your instructor lectures on it. Your goal is not to get everything from the chapter in this first reading but to get an overview of the main ideas.

Step 2 Immediately after the lecture, reread the material and work the in-text exercises. If you have difficulty with an exercise, then review your lecture notes and reread the material in that section. Be sure that you understand that section and can work the exercises before continuing.

Step 3 As you read and work the in-text exercises, begin memorizing the important facts from the chapter. Remember that memorizing facts is an essential part, but ***only*** a part, of success in organic chemistry.

Step 4 After you finish reading the chapter and working the in-text exercises; develop your logic skill by working the end of the chapter exercises.

Step 5 Prepare for the examination by working more of the end of chapter exercises. Your problem solving skills will show if you grasp what you have studied. Ask questions. Find someone who needs help and teach them what you have learned.

Problem solving in the real world of scientists seldom proceeds in the organized fashion that most textbook authors, classroom instructors, and scientists would have you think. Problem solving requires a lot of struggling, puzzling, trial-and-error, false starts, and dead ends. Chemists do not wait for divine inspiration to solve a problem. Instead, they write down what they know, then analyze and manipulate that information. When the next step becomes apparent, they take that step, then stop again to analyze and manipulate the new information. In this way chemists work toward a solution to the problem. As with them, so with you—the more problems you solve, the easier it will become to solve them.

There are two general strategies for problem solving. The most common form of problem solving is rote problem solving. With rote problem solving, you need to know only the proper formula to reach the correct answer. As long as you remember the formula and make no mistakes plugging in the facts and solving the formula, you will solve the problem correctly. This form of problem solving requires little understanding of the formula. Less common, but far more useful, is conceptual problem solving. Here you need to analyze and rearrange the statement of the problem to identify the underlying concepts involved. Once you identify the underlying concepts, you apply those concepts to the data and solve the problem.

Successful chemists use conceptual problem solving. To succeed as an organic chemistry student, you must also learn how to solve problems conceptually. Skill with conceptual problem solving requires much practice. When working the exercises in this book or those on your quizzes and examinations, seldom can you rely on "divine inspiration" for the solution. You must systematically dissect the exercise and apply the underlying principles of the particular concepts involved to find the solution. Even with this systematic work, many students find that, at first, they come up with the wrong answer to a problem. Don't let wrong answers discourage you; right answers will come more and more readily as you gain a larger foundation of principles and logic to work with.

The exercises in this book fit into three groups. The first group includes the exercises within the chapter. Work them as practice in learning the principles you have just read and to examine your grasp of those principles. The second group of exercises is the first few exercises at the end of the chapter. They are similar to those contained in the chapter. The final group of exercises are the remaining exercises at the end of the chapter. Many require that you synthesize a new idea from concepts in the current chapter or to integrate concepts from the current chapter with concepts from previous chapters. Work them to assist you in the integration of the material in the new chapter with the material you have previously learned.

The aim of this book is to provide you with the fundamentals of organic chemistry in a systematic, reasoned, and clear fashion. The field of organic chemistry is so broad that even a book of this size can give you only an overview of the subject. Within this overview look for the relationships of the various chemical reactions as they fit under the common reaction mechanisms. Have fun!

Key Ideas from Chapter 0

❏ Organic chemistry as a science is less than two hundred years old. However, in that brief time, it has made a major impact on the quality of life for most of the population of the world.

❏ Organic chemists develop an important strategy for learning organic chemistry. When a new fact is learned, it is integrated with the facts the chemist already knows. This new fact often alters the organic chemist's view of the discipline or provides some new insight into organic chemistry.

❏ Learning organic chemistry requires that you spend regular time learning the facts and working to develop a learning strategy similar to that of an organic chemist.

Richard F. Daley and Sally J. Daley
www.ochem4free.com

Organic Chemistry

Chapter 1

Atoms, Orbitals, and Bonds

Chapter 1

Atoms, Orbitals, and Bonds

Chapter Outline

1.1 The Periodic Table
A review of the periodic table

1.2 Atomic Structure
Subatomic particles and isotopes

1.3 Energy Levels and Atomic Orbitals
A review of the energy levels and formation of atomic orbitals

1.4 How Electrons Fill Orbitals
The Pauli Exclusion principle and Aufbau principle

1.5 Bond Formation
An introduction to the various types of bonds

1.6 Molecular Orbitals
Formation of molecular orbitals from the *1s* atomic orbitals of hydrogen

1.7 Orbital Hybridization
The VSEPR model and the three-dimensional geometry of molecules

1.8 Multiple Bonding
The formation of more than one molecular orbital between a pair of atoms

1.9 Drawing Lewis Structures
Drawing structures showing the arrangement of atoms, bonds, and nonbonding pairs of electrons

1.10 Polar Covalent Bonds
Polarity of bonds and bond dipoles

1.11 Inductive Effects on Bond Polarity
An introduction to how inductive and field effects affect bond polarity

1.12 Formal Charges
Finding the atom or atoms in a molecule that bear a charge

1.13 Resonance
An introduction to resonance

Objectives

- ✔ Know how to use the periodic table
- ✔ Understand atomic structure of an atom including its mass number, isotopes, and orbitals
- ✔ Know how atomic orbitals overlap to form molecular orbitals
- ✔ Understand orbital hybridization
- ✔ Using the VSEPR model, predict the geometry of molecules
- ✔ Understand the formation of π molecular orbitals
- ✔ Know how to draw Lewis structures
- ✔ Predict the direction and approximate strength of a bond dipole
- ✔ Using a Lewis structure, find any atom or atoms in a molecule that has a formal charge
- ✔ Understand how to draw resonance structures

> Concern for man and his fate must always form the chief interest of all technical endeavors. Never forget this in the midst of your diagrams and equations.
>
> —Albert Einstein

To comprehend bonding and molecular geometry in organic molecules, you must understand the electron configuration of individual atoms. This configuration includes the distribution of electrons into different energy levels and the arrangement of electrons into atomic orbitals. Also, you must understand the rearrangement of the atomic orbitals into hybrid orbitals. Such an understanding is important, because hybrid orbitals usually acquire a structure different from that of simple atomic orbitals.

When an atomic orbital of one atom combines with an atomic orbital of another atom, they form a new orbital that bonds the two atoms into a molecule. Chemists call this new orbital a molecular orbital. A molecular orbital involves either the sharing of two electrons between two atoms or the transfer of one electron from one atom to another. You also need to know what factors affect the electron distribution in molecular orbitals to create polar bonds. These factors include the electronegativity differences between the atoms involved in the bond and the effects of adjacent bonds.

1.1 The Periodic Table

The periodic table of the elements is a helpful tool for studying the characteristics of the elements and for comparing their similarities and differences. By looking at an element's position on the periodic table you can ascertain its electron configuration and make some intelligent predictions about its chemical properties. For example, you can determine such things as an atom’s reactivity and its acidity or basicity relative to the other elements.

Dmitrii Mendeleev described the first periodic table at a meeting of the Russian Chemical Society in March 1869. He arranged the periodic table by empirically systematizing the elements known at that time according to their periodic relationships. He listed the elements with similar chemical properties in families, then arranged the families into groups, or periods, based on atomic weight. Mendeleev’s periodic table contained numerous gaps. By considering the surrounding elements, chemists predicted specific elements that would fit into the gaps. They searched for and discovered many of these predicted elements, which led to the modern periodic table. A portion of the modern periodic table is shown in Figure 1.1.

The modern periodic table consists of 90 naturally occurring elements and a growing list of more than 20 synthetic elements. The elements in the vertical groups, or families, have similar atomic structures and chemical reactions. The elements in the horizontal groups, or periods, increase in atomic number from left to right across the periodic table.

Of all the elements the one of greatest importance to organic chemists is carbon (C). It is so important that many chemists define organic chemistry as the study of carbon and its interactions with other elements. Carbon forms compounds with nearly all the other elements, but this text considers only the elements of most concern to organic chemists. These elements are mainly hydrogen (H), nitrogen (N), oxygen (O), chlorine (Cl), bromine (Br), and iodine (I). Lithium (Li), boron (B), fluorine (F), magnesium (Mg), phosphorus (P), silicon (Si), and sulfur (S) are also significant.

1 H Hydrogen 1.01							2 He Helium 4.00
3 Li Lithium 6.94	4 Be Beryllium 9.01	5 B Boron 10.81	6 C Carbon 12.01	7 N Nitrogen 14.00	8 O Oxygen 16.00	9 F Fluorine 19.00	10 Ne Neon 20.18
11 Na Sodium 22.99	12 Mg Magnesium 24.31	13 Al Aluminum 26.98	14 Si Silicon 28.09	15 P Phosphorus 30.97	16 S Sulfur 32.06	17 Cl Chlorine 35.45	18 Ar Argon 39.95

Figure 1.1. Abbreviated periodic table with each element's atomic number, symbol, name, and atomic weight.

1.2 Atomic Structure

Protons, neutrons, and electrons are subatomic particles that make up the majority of atoms. Protons are positively charged, neutrons have no charge, and electrons are negatively charged.

To understand the elements of the periodic table, you must consider the subatomic particles that make up atoms. Atoms consist of three types of subatomic particles. These are **protons**, **neutrons**, and **electrons**. The protons and neutrons are located in the nucleus of the atom. The electrons fill "clouds" in the space surrounding the nucleus. Protons are positively charged, while electrons have a negative charge that is equal but opposite to the charge on the protons. As the name implies, neutrons are neutral. They have neither a positive nor a negative charge.

The number of protons in an atom identifies which element that atom is and gives that element its atomic number. The number of protons in the nucleus and the corresponding number of electrons around the nucleus controls each element's chemical properties. However, the electrons are the active portion of an atom when it chemically bonds with another atom. The electrons determine the structure of the newly formed molecule. Thus, of the three types of subatomic particles, electrons are the most important to your study of organic chemistry.

The ground state of an element is its lowest energy level.

Each element has more than one energy level. An element's lowest energy level is its **ground state**. In each element, the ground state of the atom contains a fixed and equal number of protons and electrons.

Isotopes are atoms with the same number of protons but with a different number of neutrons.

Mass number is the total number of neutrons and protons in the nucleus.

Many chemists refer to ^2H as deuterium and ^3H as tritium.

The number of protons in the atoms that make up a sample of a particular element is always the same, but the number of neutrons can vary. Each group of atoms of an element with the same number of protons is an **isotope** of that element. For example, hydrogen has three isotopes. The most common isotope of hydrogen contains a single proton, but no neutrons. This isotope has a **mass number** of 1. The atomic symbol for hydrogen is H, so the symbol for hydrogen's most common isotope is ^1H (read as "hydrogen one"). A very small portion of hydrogen, less than 0.1%, has one neutron and one proton in the nucleus. Its mass number is 2, and its symbol is ^2H. A third isotope of hydrogen has two neutrons and one proton. Its mass number is 3, and its symbol is ^3H. The ^3H isotope is radioactive with a half-life of 12.26 years. Because the ^3H isotope is radioactive, chemists use it to label molecules to study their characteristics or to follow their reactions with other molecules.

1.3 Energy Levels and Atomic Orbitals

An atomic orbital is the region of space where the electrons of an atom or molecule are found.

Electron density is a measure of the probability of finding an electron in an orbital.

The wave function is the mathematical description of the volume of space occupied by an electron having a certain amount of energy.

A node in an orbital is the place where a crest and a trough meet. At that point ψ is equal to 0 because it is neither positive nor negative.

In the early 1900s Niels Bohr developed the theory of an atom with a central nucleus around which one or more electrons revolved. From his model, chemists came to view **atomic orbitals** as specific paths on which the electrons travel about the nucleus. A common analogy is that of a miniature solar system with the electron "planets" in orbit around a nuclear "sun." Using quantum mechanics, Erwin Schrödinger showed this picture to be simplistic and inaccurate. In Schrödinger's model the orbitals of electrons are not like miniature solar systems, but are regions of **electron density** with the location and route of the electron described as probabilities.

Quantum mechanics describes orbitals by the mathematical **wave function** ψ (spelled psi and pronounced "sigh"). The wave function is useful here because orbitals have all the properties associated with waves on a body of water or sound waves. They have a crest and a trough (that is, they can be either positive or negative), and they have a **node**. There is zero probability of finding an electron at the node.

Use of Plus and Minus Signs

Do not confuse these positive and negative signs with ionic charges. They are the mathematical signs of the wave function. You will see their importance later in this chapter when you study bonding.

Now, apply these principles to a review of the energy levels and atomic orbitals of a simple atom. As you study organic chemistry, there are three energy levels, or shells, and five sets of atomic orbitals that are the most important for you to understand. These are the first, second, and third levels and the 1*s*, 2*s*, 2*p*, 3*s*, and 3*p* orbitals.

The 1*s* orbital, like all *s* orbitals, is spherically symmetrical. You can picture it shaped like a fuzzy hollow ball with the nucleus at the center. As you see in Figure 1.2, the probability of finding an electron decreases as the distance from the nucleus increases. The probability becomes zero at an infinite distance from the nucleus. The probability of finding an electron in an orbital at some distance from the nucleus is often called its electron density. The 1*s* orbital contains no nodes. Because the 1*s* orbital is closest to the nucleus and has no nodes, it has the lowest energy of all the atomic orbitals. Figure 1.3 is a representation of the 1*s* orbital.

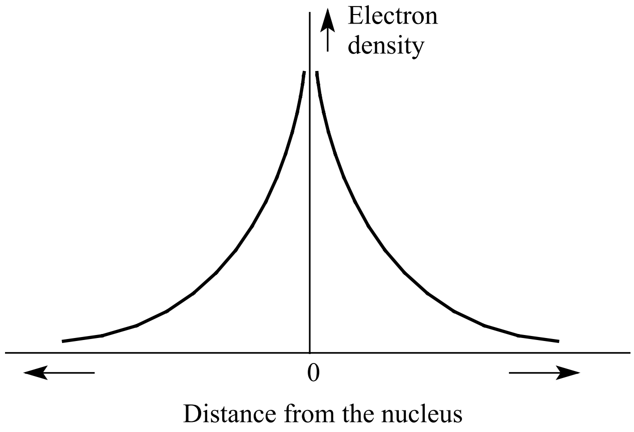


Figure 1.2. Graphical representation of the 1*s* atomic orbital.

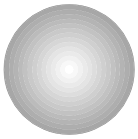


Figure 1.3. Representation of the 1*s* orbital.

The second level, or shell, of electrons contains two sets of orbitals: the 2*s* and 2*p* orbitals. The 2*s* orbital, like the 1*s*, is spherically symmetrical. However, its graphical representation does not have the simple exponential function shape of the 1*s* orbital. While some electron density is found close to the nucleus, most is farther from the nucleus past a node where there is no electron density. Figure 1.4 is a graphical representation of the 2*s* orbital and Figure 1.5 is a cross section through the 2*s* orbital.

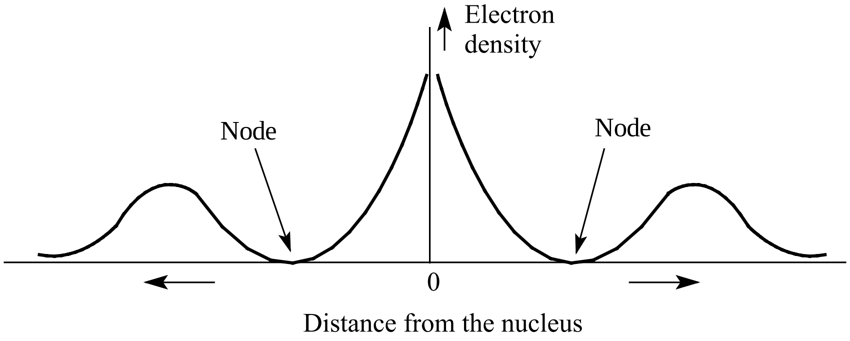


Figure 1.4. Graphical representation of the 2*s* atomic orbital. The 2*s* atomic orbital has a small region of electron density surrounding the nucleus, but most of the electron density is farther from the nucleus, beyond a node.

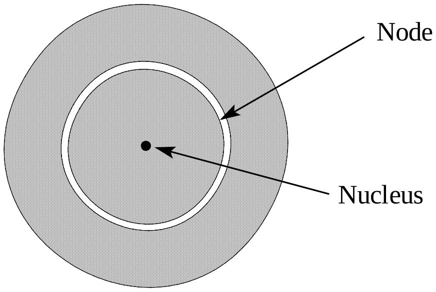


Figure 1.5. A cross section of the 2*s* atomic orbital.

A nodal plane is a plane between lobes of an orbital that has zero electron density.

Degenerate orbitals are two or more orbitals that have identical energies.

The three *p* orbitals in the second shell of electrons are totally different from the 1*s* and 2*s* orbitals. Each *p* orbital consists of a “teardrop” shape on either side of a **nodal plane** that runs through the center of the nucleus, as shown in Figure 1.6. The three 2*p* orbitals are oriented 90° from each other in the three spatial directions and have identical energies and shapes. Chemists call such orbitals **degenerate orbitals**. Figure 1.7 shows the spatial relationship of the three degenerate 2*p* orbitals. Figure 1.8 plots the electron density versus the distance from the nucleus for a *p* orbital. Because the electrons in the three 2*p* orbitals are farther from the nucleus than those in the 2*s* orbital, they are at a higher energy level.

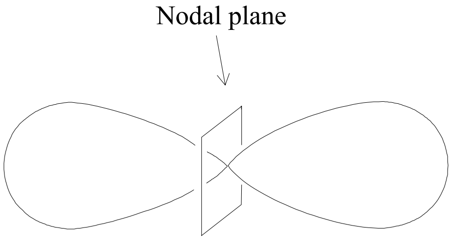


Figure 1.6. Representation of one of the 2*p* orbitals.

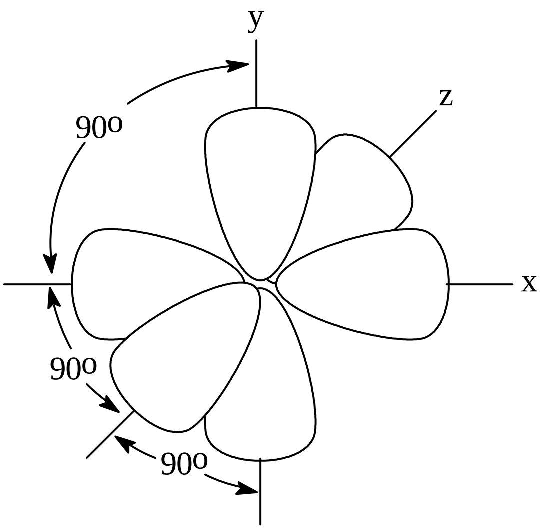


Figure 1.7. The three 2*p* orbitals are at 90° angles to one another. Here each is labeled with its orientation to the x, y, or z axis.

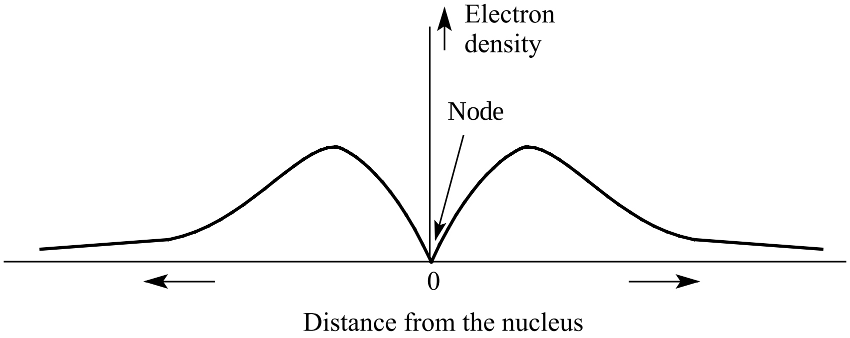


Figure 1.8. Graphical representation of a *p* orbital, showing that the node is at the nucleus.

The third energy level consists of nine orbitals. However, you only need to be familiar with the shapes of the *s* and *p* orbitals, because the orbitals beyond the 3*p* orbital are of less importance in the structure of organic molecules discussed in this book. The 3*s* and 3*p* orbitals resemble the 2*s* and 2*p* orbitals, respectively. Both third-level orbitals are larger than the second-level orbitals. The 3*s* orbital also adds another node, giving it a higher energy than the second-level orbitals.

Usually, the more nodes a wave function has the higher is its energy. In atoms with a number of electrons the energies of the atomic orbitals increases in the order of $1s < 2s < 2p < 3s < 3p$. Section 1.4 looks at how electrons fill these atomic orbitals.

1.4 How Electrons Fill the Orbitals

The Pauli Exclusion Principle states that an orbital, either atomic or molecular, can hold only two electrons.

According to the **Pauli Exclusion Principle**, each orbital contains a maximum of two electrons. These two electrons must have opposite values for the spin, which is generally indicated by showing the electrons as arrows pointing up (↑) or down (↓). When filled, the first shell (one 1*s* orbital) holds two electrons, the second shell (one 2*s* and three 2*p* orbitals) holds eight electrons, and the third shell (one 3*s*, three 3*p* orbitals, and five 3*d* orbitals) holds eighteen electrons.

The Aufbau principle states that each electron added to an atom must be placed in the lowest energy unfilled orbital.

The **Aufbau Principle** ("aufbau" means "building up" in German) explains the order in which the electrons fill the various orbitals in an atom. Filling begins with the orbitals in the lowest-energy, or most stable, shells and continues through the higher-energy shells, until the appropriate number of orbitals is filled for each atom. Thus, the 1*s* orbital fills first, then the 2*s*, followed by the 2*p* and the 3*s* orbitals. Figure 1.9 shows the energy relationships among the first three levels of orbitals.

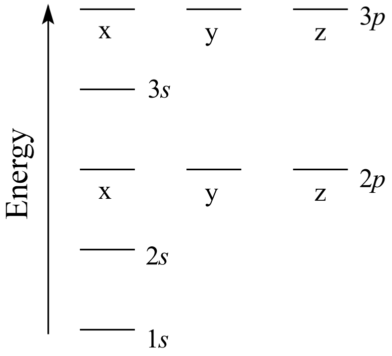


Figure 1.9. The relationship among the first three energy levels of atomic orbitals.

Hund's rule for degenerate orbitals states that each orbital must have one electron before any of them gets a second electron.

The three degenerate 2*p* orbitals require special consideration. **Hund's rule** states that each degenerate orbital, $2p_x$, $2p_y$, and $2p_z$, must first receive one electron before any of the orbitals can receive a second electron. For example, carbon has a total of six electrons. According to the Aufbau Principle, the 1*s*, 2*s*, and 2*p* orbitals contain two electrons each. However, according to Hund's Rule, the electrons in the $2p$ orbitals must go into two separate orbitals—arbitrarily designated as $2p_x$ and $2p_y$. Figure 1.10 illustrates carbon's electron configuration.

$$1s^2\ 2s^2\ 2p_x^{\,1}\ 2p_y^{\,1}$$

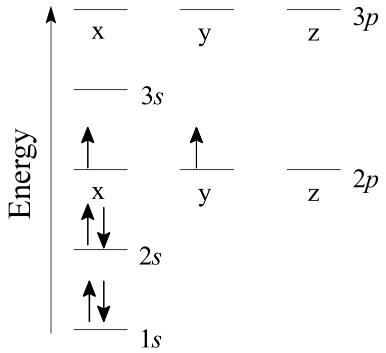


Figure 1.10. Hund's Rule applied to the filling of the atomic orbitals of carbon.

Exercise 1.1

Write a complete electron configuration for each of the eight third-row elements, Na through Ar.

This process of filling successive atomic orbital levels with electrons can be used to construct the entire periodic table. But the number of electrons in the outer shell determines the bonding that occurs between atoms. Section 1.5 looks at bonding of atoms.

1.5 Bond Formation

The valence shell of an atom is the highest energy shell that contains electrons.

Bonding is the joining of at least two atoms to form a molecule. The electrons in the **valence shell** are the active portion of an atom during bonding. In 1913, G. N. Lewis proposed several theories about how atoms combine to form molecules. The essence of his theories is that an atom with a filled outer shell of electrons is more stable than an atom with a partially filled outer shell. Therefore, bonds form between atoms such that each atom attains a filled outer shell. With a filled outer shell, an atom has the electron configuration of one of the noble gases—helium (He), neon (Ne), argon (Ar), krypton (Kr), xenon (Xe), and radon (Rn). This tendency of atoms to have a full outer shell is called the **Octet Rule.**

The Octet Rule states that an atom forms bonds that allow it to have the outer shell equivalent to the nearest noble gas.

Noble Gases

All the noble gases, except for He, have eight electrons in their outer shell. Helium has only two. Most atoms that you will encounter in organic chemistry follow the Octet Rule; that is, they form bonds that give eight electrons in their outer shells. Hydrogen is an exception to the Octet Rule, because it can only bond with two electrons. Because the elements that form organic compounds are largely located in the second row of the periodic table, the electron configuration of their atoms usually becomes that of neon. Neon has eight electrons in its outer shell.

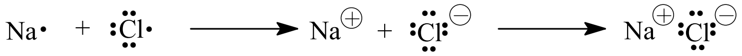
An ionic bond involves a transfer of electrons from one atom to another atom forming an electrostatic attraction between the atoms, or groups.

A covalent bond involves the sharing of electrons between two atoms to form a molecule.

Atoms that bond to attain noble gas configurations do so by forming either **ionic**[1] or **covalent bonds**. Ionic bonding usually takes place between elements positioned on opposite sides of the periodic table because they either have only one or two electrons in their valence shell or need only one or two more electrons to fill their valence shell. Covalent bonding takes place more among the elements in the center of the periodic table, as these elements have too many electrons in their valence shells to readily transfer from one atom to another.

An example of ionic bonding occurs between sodium and chlorine. Sodium has one electron in its valence shell, and chlorine has seven in its valence shell. When they react, sodium transfers its one valence electron to the valence shell of chlorine; thus, giving both a noble gas configuration. Sodium attains the configuration of neon, and chlorine that of argon. Below is a representation of this reaction using **Lewis structures**.

Lewis structures are schematic representations of the electron configuration of atoms and molecules in which each dot represents one valence electron.



By giving up its one valence electron, sodium becomes a positively charged ion. When chlorine accepts that electron, it becomes a negatively charged ion. An ion is an atom, or group of atoms, bearing a charge. Because they have opposite charges, $Na^{\oplus}$ and $Cl^{\ominus}$ attract each other; thus, forming an ionic bond. Such bonding is common with inorganic compounds, but seldom occurs in organic compounds.

A covalent bond involves the sharing of electrons between two atoms. For example, a hydrogen atom has a single unpaired electron.

---

[1] Usually, the word "bond" refers to the overlap of orbitals and the electron sharing between two atoms to form a molecule. In the strictest sense, ionic bonding is an inaccurate term. A more accurate term is ionic interaction. An ionic interaction involves electrostatic interactions with little or no electron sharing—the atoms are held together by their charges. However, this book uses the term "ionic bonding," because it allows for easier reading.

The noble gas configuration for hydrogen is that of helium, which has two electrons in the first shell (1*s*). When two hydrogen atoms form a bond, they share two electrons—one from each atom. Thus, both atoms, in effect, have a pair of electrons.

$$H\cdot + H\cdot \longrightarrow H{:}H$$

The ground state of a particular atom is the lowest energy level for that atom.

Covalent bonding is typically how organic compounds bond. The element of particular importance to organic chemists is carbon. In its **ground state** carbon has a total of four electrons in its valence shell (2*s* and 2*p* orbitals). The Octet Rule predicts that carbon will either give up or acquire four electrons in order to form stable compounds. Because of the great amount of energy required to transfer that many electrons, carbon forms covalent bonds by sharing its electrons.

A molecular orbital forms when two or more atomic orbitals overlap to form a bond.

A fundamental principle concerning electrons of atoms is that they reside in atomic orbitals. When atoms bond into molecules, **molecular orbitals** result. Molecular orbitals, regardless of the number of atoms involved, have many of the same properties of atomic orbitals. They fill with electrons beginning with the lowest energy levels, they have well-defined energy levels, and each orbital contains a maximum of two electrons. An additional characteristic of molecular orbitals is that each one may involve as few as two atoms or many atoms over a large part of the molecule.

1.6 Molecular Orbitals

The LCAO-MO method describes the shapes of molecular orbitals and is based on the atomic orbitals that form the molecular orbitals.

When looking at the way atoms combine to form molecules, scientists use the **Linear Combination of Atomic Orbitals–Molecular Orbital** method (LCAO-MO) to describe both the shapes of the molecular orbitals and the distribution of the electron density within those orbitals. The mathematics of the LCAO-MO method is beyond the scope of this book, but the primary concepts are not. The LCAO-MO method simply states that the shape of a molecular orbital is derived from the shape of the atomic orbitals that overlap to form that molecular orbital.

In-phase overlap is a constructive, or bonding, overlap of atomic orbitals.

Out-of-phase is a destructive, or antibonding, overlap of atomic orbitals.

As two atoms form a bond, they interact very much like waves on a lake. When two waves on a lake are traveling in the same direction and one overtakes the other, the amplitude of the new wave is greater than the amplitude of either of the two that created it. In contrast, when two waves are traveling in opposite directions, and they meet, as in the wakes of two boats, their amplitudes cancel each other. During bonding, atoms do the atomic equivalent—wave functions with the same sign overlap in an **in-phase overlap**, and wave functions of opposite signs overlap in an **out-of-phase overlap**.

With an in-phase overlap, the wave functions reinforce one another. This reinforcement increases the probability of finding the electrons in the region between the two nuclei. The molecular orbital that results from an in-phase overlap is a **bonding molecular orbital**. Figure 1.11 illustrates the formation of a bonding molecular orbital.

In a bonding molecular orbital two or more in-phase orbitals overlap to form a bond.

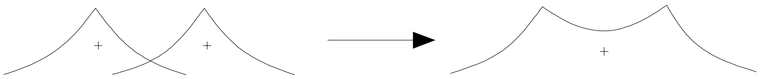


Figure 1.11. In-phase overlap of the 1*s* orbitals of two hydrogen atoms forming a bonding molecular orbital.

An out-of-phase overlap forms an **antibonding molecular orbital**. With an out-of-phase overlap, a node develops between the two nuclei. For each bonding molecular orbital that forms, an antibonding molecular orbital also forms. Figure 1.12 illustrates the formation of an antibonding molecular orbital.

An antibonding molecular orbital results from the out-of-phase overlap of two or more atomic orbitals.

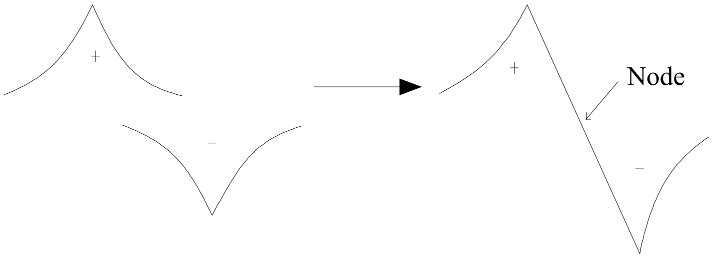


Figure 1.12. Out-of-phase overlap of the 1*s* orbitals of two hydrogen atoms forming an antibonding molecular orbital.

Usually, an antibonding molecular orbital contains no electrons because being occupied destabilizes the bond. However, in some systems the antibonding molecular orbitals are partially occupied. Generally, molecules at their lowest energy state have empty antibonding molecular orbitals. In most discussions of bonds, this book considers only the bonding and not the antibonding interaction.

To illustrate these concepts, examine the bond between two hydrogen atoms in a hydrogen molecule (H_2). The 1*s* atomic orbital of each hydrogen atom combines and generates the hydrogen—hydrogen molecular orbitals. Note in Figure 1.13 that a hydrogen molecule contains not one, but *two*, molecular orbitals.

According to the LCAO-MO method, whatever number of atomic orbitals combine to form molecular orbitals, the same number of molecular orbitals result. Therefore, orbitals are neither lost nor gained.

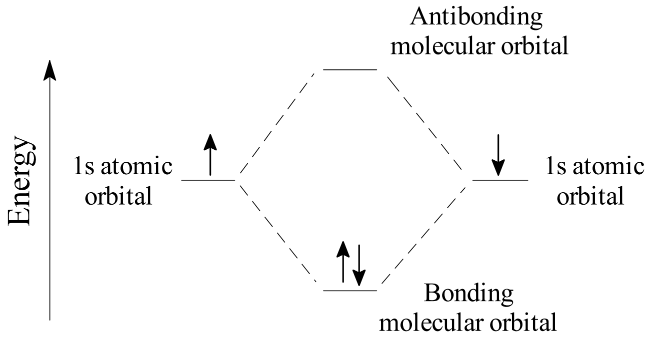


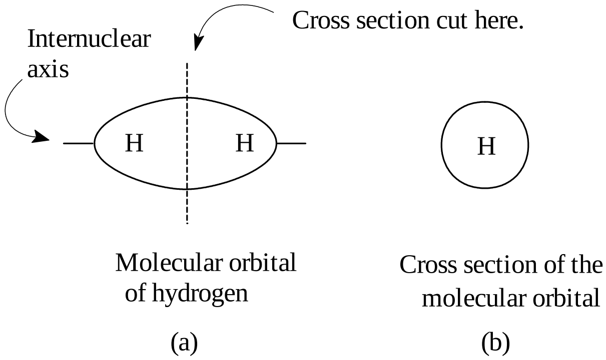
Figure 1.13. The two molecular orbitals of hydrogen generated by combining two 1*s* atomic orbitals. One of the molecular orbitals is bonding and lower in energy. The other is antibonding and higher in energy. The arrows represent the electrons involved in forming the bonding molecular orbital.

Why He_2 Does Not Form

A look at helium will help you see why antibonding molecular orbitals do not usually fill with electrons. Helium has a filled valence shell. In order for two helium atoms to bond, both the bonding and antibonding molecular orbitals would have to fill. This does not occur because there is no energy gain for He_2 as compared with He. Thus, He_2 does not form.

A bond possessing rotational symmetry has a circular cross section perpendicular to the bond.

Both the bonding and antibonding orbitals of hydrogen molecules have **rotational symmetry** about their internuclear axis. Chemists call orbitals with this type of symmetry σ (sigma) molecular orbitals. This symmetry is shown in Figure 1.14.



Molecular orbital of hydrogen

(a)

Cross section of the molecular orbital

(b)

Figure 1.14. (a) A hydrogen molecule showing the σ molecular orbital. (b) A cross section of the σ molecular orbital perpendicular to the internuclear axis.

To differentiate the antibonding from the bonding orbital, chemists add an asterisk to the σ, giving σ^* (sigma star).

A σ molecular orbital results from overlap of atomic orbitals along the internuclear axis.

Electrons prefer to occupy the orbital with the lowest possible energy state. For example, consider the electrons in the hydrogen molecule. The 1*s* atomic orbitals of two hydrogen atoms overlap and form the σ **molecular orbital** of the H_2 molecule. The σ orbital is lower in energy than the 1*s* orbitals of the hydrogen atoms. The antibonding molecular orbital, the σ^* orbital, is higher in energy than either the 1*s* orbitals or the σ orbital. Because the σ orbital has the lowest energy, both electrons in the hydrogen molecule reside there.

Bond length is the minimum distance between two nuclei connected by a molecular orbital.

As two atoms move closer together, the energy between them at first decreases. At the point of minimum energy between the nuclei of the two atoms, the molecular orbital forms, and the system releases energy. The distance of minimum energy between the two nuclei is the **bond length**. If the nuclei continue getting closer, the energy increases. Figure 1.15 shows how the energy between two atoms decreases until the atoms reach their state of minimum energy. Once two nuclei are bonded, they require energy to move apart again.

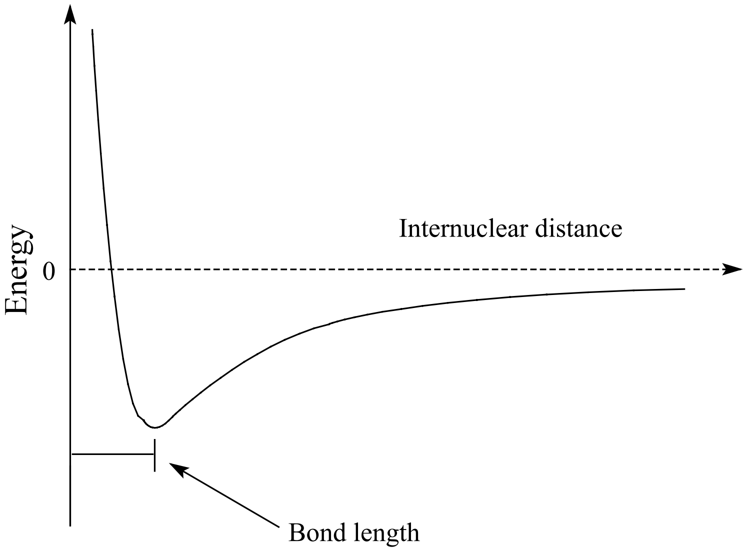


Figure 1.15. When two hydrogen atoms move into close proximity, they experience a change in energy. At the distance of the bond length, they achieve minimum energy. As the nuclei move apart, the energy of the interaction rapidly approaches zero, which it reaches at infinity.

Orbital overlap is how much an atomic orbital from one atom would extend over an atomic orbital from another atom, if the two atoms did not bond to form a molecular orbital.

For H_2, the distance between the two nuclei (the bond length) is 74 pm. At distances greater than this, the bond weakens because of reduced **overlap** between the 1*s* orbitals. At distances less than 74 pm, the repulsion between the two positively charged hydrogen nuclei increases substantially.

Exercise 1.2

Describe how Figure 1.15 would change in appearance a) for a weaker bond than H_2 and b) for a stronger bond.

Figure 1.15 shows that energy is released during the formation of the bond in a hydrogen molecule. Conversely, breaking that bond to reform hydrogen atoms requires an input of energy because the energy level of the hydrogen molecule is lower than the energy level of the two hydrogen atoms. Before hydrogen can bond with another element, such as carbon, the hydrogen—hydrogen bond in the hydrogen molecule must be broken. The **bond dissociation energy** for hydrogen is 104 kcal/mole[2].

The bond dissociation energy is the amount of energy required to break a bond.

In a homolytic bond dissociation, a bond breaks and each of the two atoms leaves with one of the two electrons from the bond.

Chemists use the bond dissociation energies of different bond types as a measure of the reactivity of those bonds. The higher the amount of energy required to break a bond, the stronger the bond is. A stronger bond reacts less readily than a weaker bond. Table 1.1 shows some representative bond dissociation energies. These bond dissociation energies are for the **homolytic** bond dissociation process.

Bond	Dissociation Energy, kcal/mole	Bond	Dissociation Energy, kcal/mole
H–H	104	H—F	136
F—F	37	H—Cl	102
Cl—Cl	57	H—Br	87.5
Br—Br	46	H—I	71.3
I—I	36	CH_3—H	103
C—F	108	CH_3CH_2—H	98
C—Cl	81	$(CH_3)_2CH$—H	94.5
C—Br	68	$(CH_3)_3C$—H	91
C—I	55.5	C=C—H	102
C—O	90	C≡C—H	125
C=O	257	C—C	88
O—H	105	C=C	163
		C≡C	200

Table 1.1. Some representative bond dissociation energies.

1.7 Orbital Hybridization

---

[2] In your General Chemistry course, you learned to use energy units in kilojoules. Organic chemists have not universally adopted the kilojoule unit. Thus, we have chosen to use the kilocalorie energy unit.

The development of the modern theory of organic chemistry began in the middle of the nineteenth century. At that time, the concept that all organic compounds contained carbon started replacing the theory of vitalism. Essential to the growth of organic chemistry was the work that determined the atomic structure of the carbon atom and how it bonded with other atoms.

Vitalism is discussed in Section 0.1, page 000.

When chemists learned that carbon frequently bonds with four other atoms, they thought the resulting molecule was square planar. That is, they thought all five atoms resided in a square plane with carbon in the center and the other four elements at the four corners. The discovery of methylene chloride (CH_2Cl_2) forced them to reevaluate this theory. Chemists had expected to see two different structures, or **isomers**, for methylene chloride, but they found only one. Figure 1.16 shows the two possible square planar isomers of methylene chloride.

Molecules that are isomers have the same number of each type of atom, but they are arranged differently.

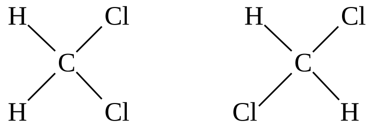


Figure 1.16. The two square planar isomers of methylene chloride.

Having only one structure meant the methylene chloride molecule was not square planar. In 1874, Jacobus H. van't Hoff and Joseph A. Le Bel proposed a three-dimensional tetrahedral structure for carbon compounds such as methylene chloride as shown in Figure 1.17. Initially, chemists scoffed at this theory. But gradually, through much discussion, they accepted it, even though no one proved it until the 1920s.

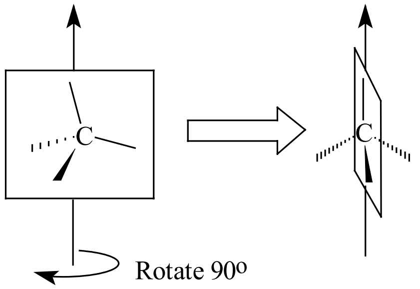


Figure 1.17. The tetrahedral structure of carbon. The wedge shaped line (◀) indicates a bond projecting in front of the page. The dashed line (┈┈) is a bond behind the page.

It was the development of the electron diffraction technique that allowed chemists to prove the tetrahedral structure of carbon. Electron diffraction measures the bond lengths and bond angles of compounds. As you may recall, bond length is the distance between two bonded nuclei. Bond angle, on the other hand, is the angle formed by the intersection of two covalent bonds at the atom common to them both. While using electron diffraction to study methane (CH_4), chemists discovered that the bond lengths and bond angles for all four C—H bond angles are identical. The bond angles measured 109.5°, instead of 90°, as was expected from the square planar theory. This measurement showed that methane was tetrahedral in shape. It also confirmed the tetrahedral shape suggested years before for methylene chloride. Figure 1.18 illustrates the actual structure of methylene chloride.

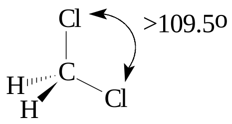


Figure 1.18. The actual structure of methylene chloride. Because the chlorines are larger than the hydrogens, they repel one another and the Cl—C—Cl bond angle is more than 109.5°.

Another problem challenging chemists at this time was how were carbon's electrons arranged? They knew that when an orbital contains only one electron, then bonding can occur with the electron in that orbital. The problem with carbon was that it had only two orbitals with one electron each, but yet carbon bonds with four atoms. The ground state of carbon has four valence electrons—two paired electrons and two unpaired electrons. These electrons are distributed among three different orbitals—two electrons in the 2*s* orbital and one electron each in the $2p_x$ and $2p_y$ orbitals. To resolve this problem, Linus Pauling pulled together all the ideas proposed by the various chemists and developed the concept of **orbital hybridization**. His concept of orbital hybridization also explained how carbon formed the measured bond angles of 109.5° rather than the expected 90°.

Orbital hybridization is a mathematical operation based on quantum mechanics that explains the geometry of a molecule.

Hybrid orbitals are the individual orbitals formed from hybridization.

The theory of orbital hybridization allows the wave functions of two atomic orbitals in the valence shell of an atom to "mix" and form new orbitals called **hybrid orbitals**. This book looks at the mixing of the *s* and *p* orbitals of carbon. Hybrid orbitals have a blend of the properties, shapes, and energy levels of both orbitals. There are two important benefits of orbital hybridization. Hybridized atoms form more bonds than do unhybridized atoms. Plus, bonds formed from hybridized orbitals are stronger and more stable than bonds formed by unhybridized orbitals. The hybrid orbitals of carbon combine the strong electron attracting ability of the *s* orbital and more electron density along the internuclear axis characteristic of the *p* orbitals.

Visualizing Hybridization

Hybridization is a theoretical explanation of how carbon and similar atoms bond. Being able to visualize the process of hybridization will help you understand what happens to carbon when it bonds with other atoms. Remember, as you move through this process, that the orbitals are always there—even when they are not occupied by electrons. To begin, set aside the electrons and hybridize, or "mix," the number of orbitals necessary to accomplish an octet; then distribute the electrons into the orbitals as needed for bonding. The rule of conservation of orbitals states that a molecule must have the same number of hybrid orbitals after hybridization and bonding as the atoms had before hybridization and bonding.

Not only does orbital hybridization enable carbon to bond to four other atoms, it also allows molecules like methane to obtain their tetrahedral shape. Because electron pairs strive to be as far apart from other electron pairs as possible, an atom bonded to four other identical atoms, as carbon is to the four hydrogens in methane, has bond angles of 109.5º. This arrangement places the four identical atoms, the hydrogens, toward the corners of a regular tetrahedron with the atom they are bonded to, the carbon, in the center. The bonding of carbon with four atoms that are not identical does change the angles somewhat, but the basic shape remains the same. The theory designed to explain the fact that electron pairs arrange themselves a maximum distance apart is called the **Valence Shell Electron Pair Repulsion (VSEPR) model**. VSEPR can be used to explain the shapes of the three hybridized orbitals.

The VSEPR model predicts the geometry of a molecule by arranging all orbitals at maximum distance from each other.

The three types of orbital hybridization considered important in organic chemistry are called *sp*, sp^2, and sp^3. These labels tell the number and the names of the orbitals involved in the hybridization. In *sp* hybridization two orbitals are involved, one *s* and one *p*. In sp^2 hybridization three orbitals are involved, one *s* and two *p* orbitals. And in sp^3 hybridization four orbitals are involved, one *s* and three *p* orbitals. Because hybridization blends all the characteristics of the *s* and *p* orbitals, the name of the new orbital indicates what proportion of each orbital is like an *s* orbital and what portion is like a *p* orbital. Each *sp* hybridized orbital has an equal blend of the characteristics of both the *s* and *p* orbitals. With sp^2 hybridization, each hybrid orbital bears 1/3 of the *s* orbital's characteristics and 2/3 of the *p* orbital's characteristics. Likewise, each orbital of an sp^3 hybridization has 1/4 of the characteristics of the *s* orbital and 3/4 of the characteristics of the *p* orbitals.

Another consideration with hybridization is the shape of the hybridized orbitals. The four hybrid sp^3 orbitals have a shape that is a combination of the *s* and *p* orbital shapes, as illustrated in Figure 1.19. Like the *p* orbitals, each sp^3 orbital has two lobes, but unlike the lobes of a *p* orbital, the two lobes are of unequal size. (The signs on the orbital lobes in Figure 1.19 and subsequent figures are the signs of the ψ wave function for those orbitals.) Therefore, for each orbital there is a greater electron density on one side of the nucleus than on the other. This unsymmetrical electron density allows for greater overlap—thus the formation of stronger bonds—than is possible with an unhybridized orbital. When the sp^3 orbitals participate in bond formation, it is the larger lobe that overlaps the orbital of the other atom. In the formation of methane, the overlap of the sp^3 orbital of carbon with the *s* orbital of hydrogen forms a σ bond very similar to the σ bond between two hydrogens. This type of bond is much more stable than that from the overlap of the *p* orbitals of an unhybridized carbon because of the greater overlap of the sp^3 orbitals as compared to the *p* or *s* orbitals.

Figure 1.20 shows the transformation of the orbital energy levels. Note that the four new hybrid orbitals all have the same energy level. This model explains why carbon forms four bonds to four other atoms and why these atoms are oriented in a tetrahedral fashion around carbon.

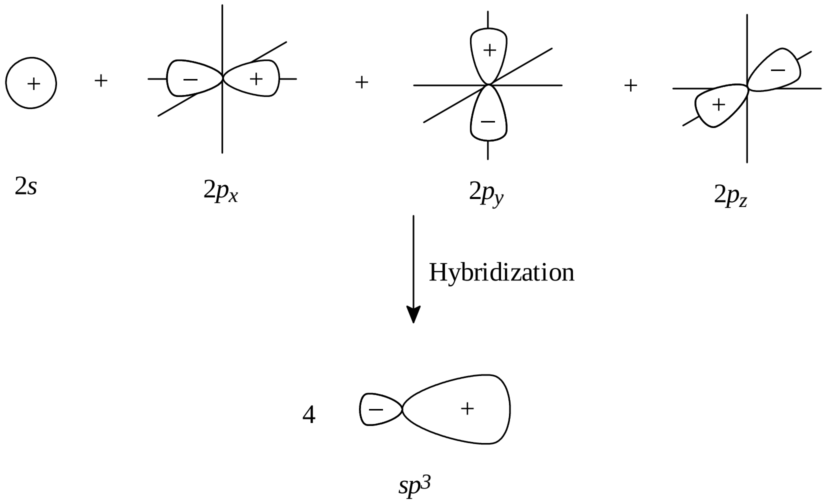


Figure 1.19. Mixing, or hybridization, of one *s* orbital with three *p* orbitals produces four sp^3 orbitals. Each of the sp^3 orbitals has 25% *s* character and 75% *p* character.

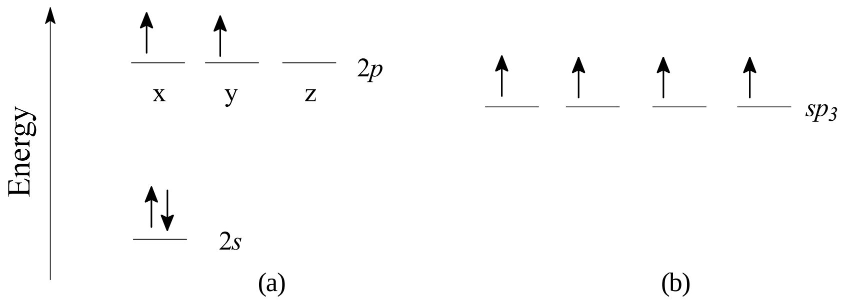


Figure 1.20. Electron configuration of carbon (a) before and (b) after hybridization. Note that the energy level of the hybrid orbitals is between that of the 2*s* and that of the 2*p* orbitals. The sum of the energies of the hybrid orbitals is equal to the sum of the energies of the unhybridized orbitals.

Thus, with methane (CH_4), each of the hydrogens is at one of the vertices of the tetrahedron and carbon is at the center.

Figure 1.21 illustrates the sp^3 hybrid orbitals. For clarity the figure shows only the large lobes of the hybrid orbitals. This arrangement allows the electrons in the orbitals to be as far apart as possible, as is called for by the VSEPR model. The tetrahedral structure allows the maximum possible distance between adjacent orbitals. The H—C—H bond angle in methane is 109.5^{o}. This tetrahedral orientation is characteristic of an sp^3 hybridized carbon.

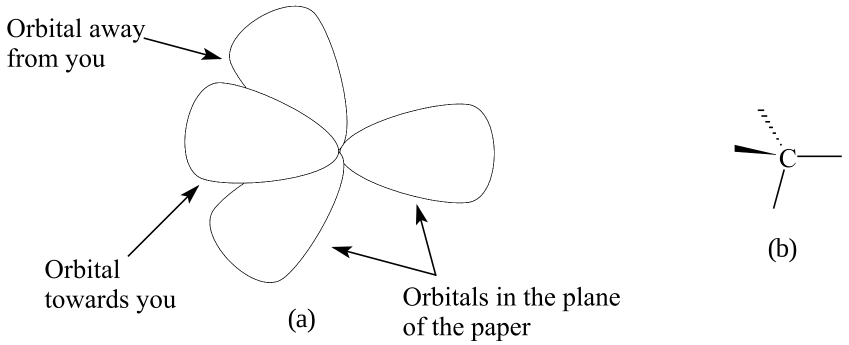


Figure 1.21. (a) Orbital hybridization arranges the sp^3 hybrid orbitals in a tetrahedron around the carbon enabling it to form four bonds with other atoms. The figure shows only the larger lobe of each sp^3 orbital. (b) The shorthand notation for an sp^3 hybridized carbon.

The overlapping of the four sp^3 hybrid orbitals of a carbon atom with the 1*s* orbitals of four hydrogen atoms forms the four carbon—hydrogen bonds of methane. Sigma bonds are the types of bond generated by the sp^3-s orbital overlap. A sigma bond has rotational symmetry about the internuclear axis.

Exercise 1.3

Consider an excited state of carbon in which one of the 2*s* electrons is promoted to the vacant 2*p* orbital. How would this state of carbon fail to account for the structure of methane?

Exercise 1.4

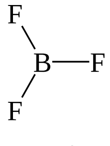
Ignoring any orbitals not in the valence shell how many orbitals are in each of the following molecules? How many are bonding, nonbonding, and antibonding? How many orbitals are occupied?

a) NH_3 b) H_2S c) HCl
d) CO_2 e) CH_3OH f) CH_3CH_3

Sample Solution

a) A molecule of ammonia (NH_3) consists of one nitrogen and three hydrogens. Each hydrogen has a 1*s* orbital in its valence shell, which they contribute to the bond. Nitrogen has one 2*s* and three 2*p* orbitals in its valence shell, which it contributes to the bond. The total number of atomic orbitals in the valence shells of these atoms is seven. The formation of ammonia allows nitrogen to follow the Octet Rule because the bonded nitrogen has eight electrons in its valence shell. Thus, four of the orbitals are filled—three as bonding molecular orbitals and one orbital with a lone pair of electrons. The other three orbitals are unfilled antibonding orbitals.

Boron trifluoride (BF_3) illustrates the second type of hybridization, *sp*^{2} hybridization. Structural studies indicate that boron has a triangular (trigonal planar) shape with three equivalent B—F bonds.



Boron trifluoride

Figure 1.22 shows the ground-state electron configuration of boron. This configuration does not account for the trivalent and trigonally bonded boron of BF_3. The best explanation is orbital hybridization. With hybridization, the 2*s* orbital combines with two of the 2*p* orbitals to give three equivalent *sp*^{2} hybridized orbitals, as shown in Figure 1.23. The VSEPR model explains why a set of *sp*^{2} hybrid orbitals adopts a planar trigonal shape with the orbitals pointed to the corners of an equilateral triangle and with angles of 120° between the orbitals. Figure 1.24 shows how the electron configuration of boron changes during hybridization.

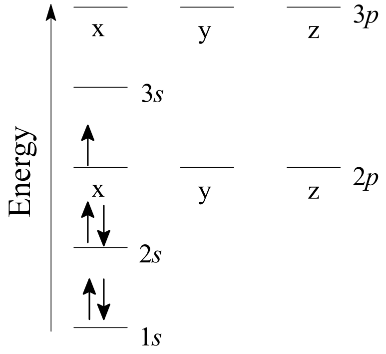


Figure 1.22. Orbital energy diagram for boron.

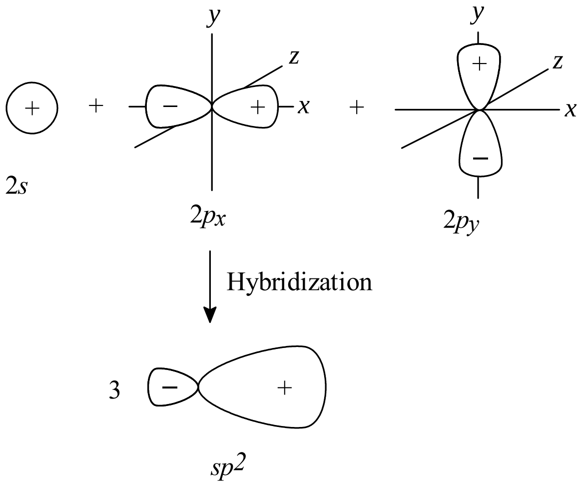


Figure 1.23. Mixing one *s* orbital with two *p* orbitals produces three sp^2 hybrid orbitals. Each orbital has 33.3% *s* and 66.7% *p* character.

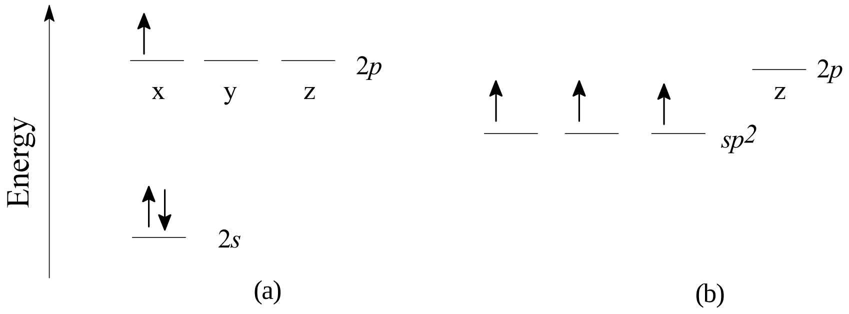
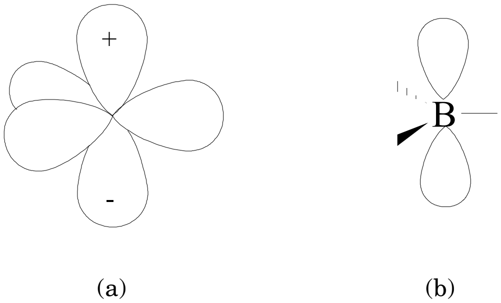


Figure 1.24. Electron configuration of boron (a) before and (b) after hybridization. Note that the energy level of the hybrid orbitals is between that of the 2*s* and that of the 2*p* orbitals.

Even after hybridization, the boron atom still has a vacant *p* orbital that was not involved in hybridization. This orbital orients itself at right angles to the three sp^2 orbitals. Figure 1.25 shows the orientation of the hybrid orbitals and the vacant unhybridized orbital.



(a) (b)

Figure 1.25. (a) The sp^2 hybrid orbitals of boron are in a planar triangle around the nucleus with an empty *p* orbital perpendicular to them. (b) The shorthand notation for sp^2 hybridized boron.

Exercise 1.5

What is the electron configuration of the valence electrons of a) an sp^2 hybridized carbon, b) an sp^2 hybridized nitrogen, and c) an sp^2 hybridized oxygen? For each of these, indicate the number of occupied and unoccupied orbitals and the hybridization of each orbital.

Sample solution

a) The electron configuration for an sp^2 hybridized carbon has one electron in each of three sp^2 hybrid orbitals and one electron in the 2*p* orbital.

Beryllium hydride (BeH_2) illustrates the third type of hybridization. Structural studies indicate that the H—Be—H bond angle is 180°. Thus, this molecule has a linear structure with 2 equivalent Be—H bonds. Figure 1.26 shows the ground state electron configuration for beryllium.

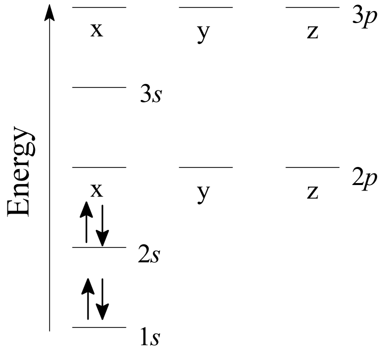


Figure 1.26. Electron configuration for the ground state of beryllium.

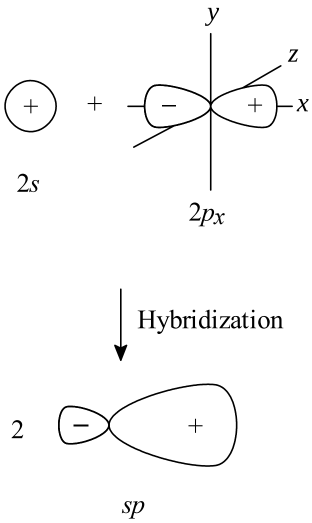


Figure 1.27. Hybridization of one *s* orbital with one *p* orbital produces two *sp* orbitals with 50% *s* character and 50% *p* character.

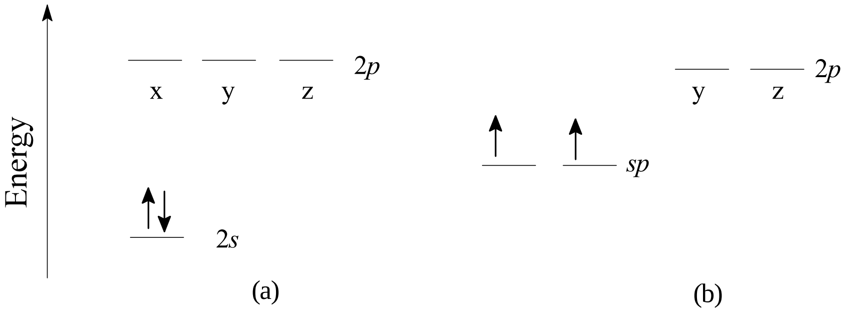


Figure 1.28. Electron configuration of beryllium (a) before and (b) after hybridization. Note that the energy level of the hybrid orbitals is between that of the 2*s* and that of the 2*p* orbitals.

To account for the structure of BeH_2, you need the theory of orbital hybridization. Figure 1.27 shows the hybridization of beryllium. One *s* orbital hybridizes with only one *p* orbital to obtain two *sp* hybrid orbitals. The VSEPR model places these *sp* hybridized orbitals at 180° from each other. Figure 1.28 shows how the electron configuration of beryllium changes during hybridization. Figure 1.29 shows that *sp* hybridized Be has two vacant, unhybridized *p* orbitals.

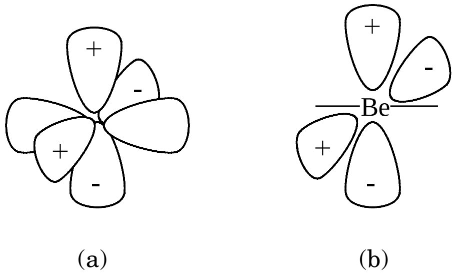


Figure 1.29. (a) The *sp* hybrid orbitals are on either side of the beryllium with empty *p* orbitals perpendicular to the *sp* orbitals. (b) The shorthand notation.

Remember that the drawings of the orbitals shown to this point are only schematic drawings. They are useful to help in understanding the hybridization process. In contrast, Figure 1.30 shows a contour plot of the shapes of the *sp* and sp^3 hybrid orbitals. Looking at these plots, you can more easily see the three-dimensional shapes of the orbitals as well as the varying size of the smaller lobe. The larger lobe is the “bonding” lobe of the orbital; the smaller one is not directly involved in bonding.

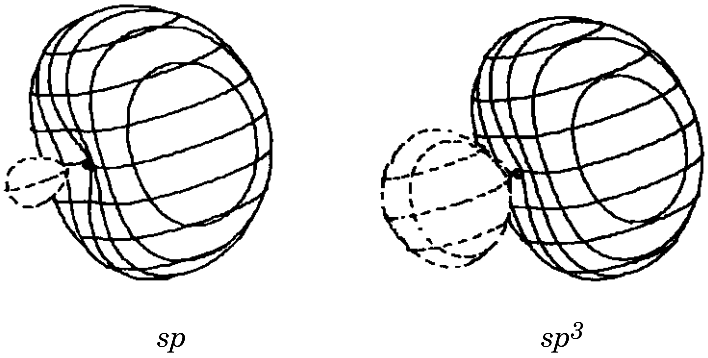
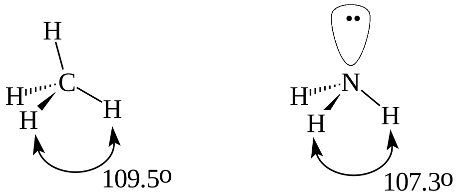
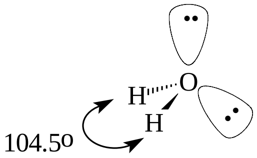


Figure 1.30. Three-dimensional perspective plots of *sp* and sp^3 hybrid orbitals.

So far you have learned about the spatial distribution of bonding molecular orbitals. Another factor that affects the shape of a molecule is the presence of nonbonding electron pairs. In general, a molecule with a pair of nonbonding electrons adopts a shape similar to a molecule with a bond in place of those electrons. For example, ammonia (NH_3) has three N—H bonds and a pair of nonbonding electrons. The structure is similar to that of methane (CH_4). The difference is that the nonbonding electrons have a greater repulsive influence than a pair of bonding electrons. Thus, even though both ammonia and methane have *sp*^{3} hybridization, the bond angles are slightly different. The H—C—H bond angle in methane is 109.5^o, but the H—N—H bond angle in ammonia is 107.3^o.



To predict the shape of an atom in a molecule, first determine the number of σ bonds plus the number of electron pairs in that atom. Once this is done, use the VSEPR model to predict the angles between the bonds and electron pairs. For example, the structure of water can be predicted using this approach. The oxygen of water has two σ bonds and two pairs of nonbonding electrons. The VSEPR model would predict a tetrahedral shape for water with the H—O—H bond angle about 109.5^o. Because there are two nonbonding pairs of electrons, the actual angle is somewhat smaller at 104.5^o.



Exercise 1.6

Predict the general shapes of the following molecules and ions. Indicate the hybridization of the central atoms.

a) PH_3 b) CCl_4 c) BH_3
d) $^{\ominus}BH_4$ e) BeF_2 f) $^{\oplus}CH_3$
g) SiH_4 h) $^{\ominus}:CH_3$ i) $^{\oplus}NH_4$

Sample Solution

d) According to the VSEPR model, the expected shape for $BH_4^{\ominus}$ is tetrahedral, so the central atom (B) must be sp^3 hybridized. This shape allows for a maximum distance between the four B—H bonds.

1.8 Multiple Bonding

With each of the three types of hybridization, the carbon not only exhibits a different kind of molecular shape, it bonds with a different kind of bond. An sp^3 hybridized carbon bonds with σ, or single, bonds. That is, each hybrid orbital contains only one pair of electrons, and the compound has a tetrahedral shape. Methane is an example of a compound with sp^3 hybridization.

An sp^2 hybridized carbon forms a double bond between itself and another atom. A double bond is a combination of one σ bond and one π (pi) bond and contains two pairs of electrons. The carbon has a trigonal planar shape. Ethylene ($CH_2{=}CH_2$) is an example of a carbon compound with sp^2 hybridization. Both carbons in ethylene are sp^2 hybridized and bonded to each other. Structurally, ethylene is flat with all six atoms in the same plane. Experimental evidence indicates that both the H—C—H and the H—C—C bond angles are 120°. Experimental evidence also indicates that the C—H bond length in ethylene is shorter than the C—H bond length in methane.

A π molecular orbital results when two orbitals overlap outside the internuclear axis.

The electron configuration of the two carbons of ethylene (see Exercise 1.5) indicates that there is a single electron in the unhybridized *p* orbital of each carbon. These two *p* atomic orbitals interact to form two new molecular orbitals, the π **molecular orbitals** (Figure 1.31). This bond, unlike the σ bond, is not oriented along the internuclear axis. Instead it is in a plane perpendicular to the plane formed by the trigonal carbons. Thus, there are two bonds between the carbons in the ethylene molecule.

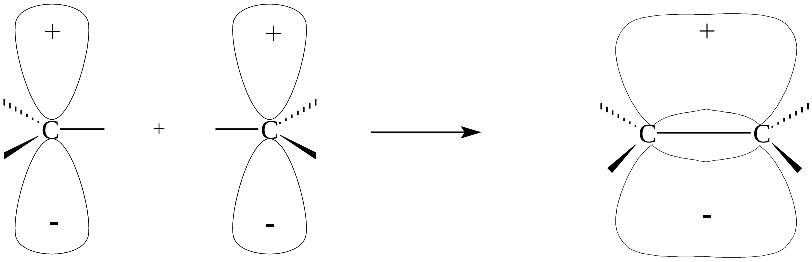


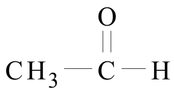
Figure 1.31. The *p* orbitals of two sp^2 hybridized carbons overlap to produce the π bond in ethylene.

Like σ molecular orbitals, π molecular orbitals have both bonding and antibonding orbitals. If the sign of the *p* lobes are the same (that is, if the two *p* orbitals are in phase with one another), as in Figure 1.31, the overlap forms a bonding π molecular orbital. If the two *p* orbitals are out of phase, then the overlap results in an antibonding π^* molecular orbital (for π^* read "pi star").

Similar to the *p* atomic orbitals from which it forms, a π molecular orbital has two lobes and a nodal plane through the axis between the two nuclei. The two lobes of electron density are above and below the nodal plane. The π bond, however, does not have the rotational symmetry of the σ bond.

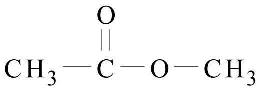
Exercise 1.7

Double bonds can also form between carbon and oxygen. Construct a molecular orbital picture for acetaldehyde and methyl acetate. Indicate approximate bond angles and the atomic orbitals that must overlap to form the molecular orbitals.



$CH_3-\overset{\overset{O}{\|}}{C}-H$

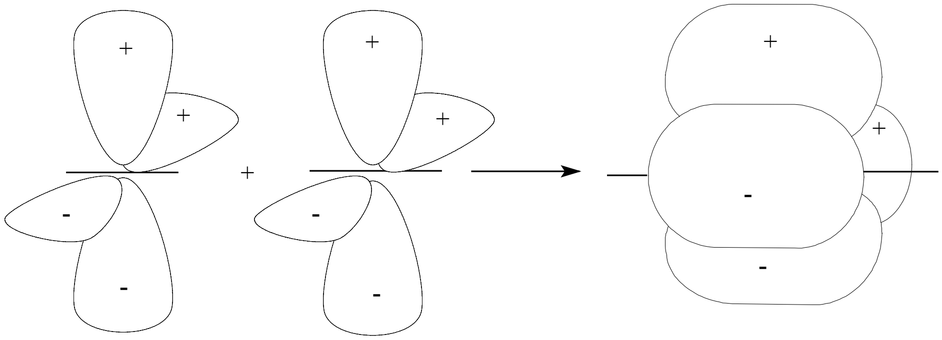
Acetaldehyde



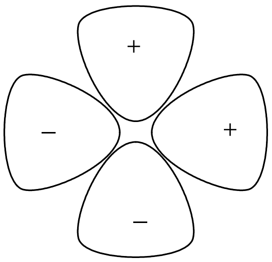
$CH_3-\overset{\overset{O}{\|}}{C}-O-CH_3$

Methyl acetate

An *sp* hybridized carbon forms a triple bond. A triple bond consists of three pairs of electrons shared between a carbon and another atom and is the combination of one σ and two π bonds. For example, both carbons in acetylene ($CH\equiv CH$) are *sp* hybridized. Experimental measurements show that the H—C—C bond angle is 180°. This angle gives acetylene a linear shape. Figure 1.32 (a) shows the interaction of the unhybridized *p* orbitals of two *sp* hybridized carbon to form the π bonds of acetylene. The view from the end of the acetylene molecule in Figure 1.32 (b) shows a nodal axis that coincides with the internuclear axis. The electron cloud of the two π bonds has a toroidal (doughnut-shaped) symmetry about the internuclear axis.



(a)



(b)

Figure 1.32. (a) The π molecular orbitals in acetylene are formed from overlap of the *p* orbitals of two *sp* hybridized carbon atoms. (b) The view of the π molecular orbitals along the internuclear axis.

Exercise 1.8

Acetonitrile has a triple bond between carbon and nitrogen. Construct a molecular orbital picture for acetonitrile. Indicate approximate bond angles and the atomic orbitals that must overlap to form the molecular orbitals.

$$CH_3{-}C{\equiv}N$$

Acetonitrile

1.9 Drawing Lewis Structures

As mentioned in Section 1.5, G. N. Lewis proposed the theory that an atom achieves its most stable electronic configuration when its valence shell is filled with electrons. Hydrogen requires two electrons. The elements in the second and third rows of the periodic table require eight electrons (the Octet Rule). Lewis proposed that during covalent bonding two atoms share one or more pairs of electrons and that each pair count as belonging individually to both atoms.

To help people visualize his theory, he developed a system that represents each electron in the valence shell of an atom by a dot (•) and each pair of electrons by a pair of dots (:). He placed these dots around the atomic symbol of the element. For example, he drew hydrogen and chlorine atoms like this:

H•

$$\cdot\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}\!:$$

He represented a bonding pair of electrons by either a pair of dots (:) or a dash (—) placed between the two atoms. He showed hydrogen and chlorine, for example, bonded to form hydrogen chloride like this:

A Lewis structure is a schematic representation of the bonds and nonbonding electrons in an ion or molecule.

Chemists call his method of representing atoms and molecules **Lewis structures**.

When drawing Lewis structures, use only the valence electrons and strive for an octet for each atom except hydrogen. Like helium, hydrogen's valence shell has only two electrons. Remember the conservation rule for orbitals and electrons—you must end up with the same number of both as when you started. A helpful tool that makes drawing Lewis structures easier is know how many bonds each of the commonly used elements usually forms.

The single dots represent unpaired electrons available for bonding, and the paired dots represent paired electrons available for bonding. For example, nitrogen bonds to three hydrogens with the nitrogen providing one electron to each hydrogen—nitrogen bond and each of the hydrogens providing one electron to the same bonds. When nitrogen bonds with three hydrogens, the valence shells of both the nitrogen and the hydrogens are filled. However, the nitrogen could also bond with an $H^{\oplus}$ ion by providing both electrons for the bond because the hydrogen ion has no electrons.

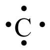
There are two steps to drawing a Lewis structure of a molecule. First, write the central atom of the molecule. Second, fit the other atoms around the central atom. If the molecule contains carbon, the carbon is the central atom. If the molecule contains a noncarbon other than hydrogen, the noncarbon is the central atom. If the molecule contains more than one noncarbon atom, the central atom is the first atom written in the formula, unless the first atom listed is a hydrogen. As you may remember from your course in general chemistry, a hydrogen at the start of the line structure of a non-carbon-containing molecule usually indicates a Brønsted-Lowry acid. In that case, set the hydrogen aside until the bonds for all the other atoms have been determined, then add that hydrogen at the appropriate place. When the formula for a carbon-containing molecule starts with a hydrogen, such as HCO_2H, the first hydrogen bonds to the carbon; the other hydrogen bonds to one of the oxygens.

Solved Exercise 1.1

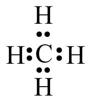
For each of the following compounds draw a Lewis structure showing all bonding and nonbonding electrons.

a) Methane (CH_4)

Solution: First, write a carbon with its appropriate four dots representing the four valence electrons.



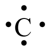
Then combine it with four hydrogens with each of their valence electrons to get methane.



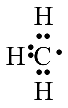
Next check the Lewis structure to make sure it contains the correct number of orbitals and electrons. Carbon has four identical valence shell orbitals, as the result of sp^3 hybridization, and each hydrogen atom has one. The carbon contributed four electrons and each hydrogen one electron, for a total of eight electrons. Methane has eight bonding electrons, and, as you see in the Lewis structure, the valence shell of each atom is full—two electrons for each hydrogen and eight for the carbon. The Lewis structure checks out.

b) Methanol, CH_3OH

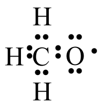
Solution: First, write a carbon with its appropriate four dots representing the four valence electrons.



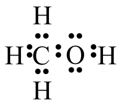
Then combine it with three hydrogens with its valence electron to get the methyl group.



Now add an oxygen with its six electrons.



Finally, add the last hydrogen to the oxygen.



Next check the Lewis structure to make sure it contains the correct number of orbitals and electrons. Carbon has four identical valence shell orbitals, as the result of sp^3 hybridization, and each hydrogen atom has one. The carbon contributed three electrons and each hydrogen one electron, for a total of six electrons. The final bond to carbon comes from the oxygen. Thus, carbon has a full octet of electrons. The oxygen has four nonbonding electrons and four bonding electrons. Each hydrogen has two bonding electrons. The Lewis structure checks out.

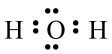
Exercise 1.9

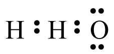
Show all the valence electrons as you write a Lewis structure for each of the following molecules.

a) H_2O b) PCl_3 c) I_2
d) CH_3Br e) NH_3 f) $AlCl_3$

Sample Solution

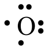
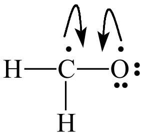
a) Oxygen is a member of Group VI of the periodic table; thus, it has six valence electrons. Hydrogen has one. There are two possible structures for a molecule with one oxygen and two hydrogens.

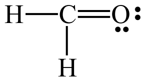




The left-hand structure is correct because it gives each atom a filled valence shell. Each hydrogen has two electrons, and the oxygen has eight. The structure on the right is incorrect because the central hydrogen has too many electrons in its valence shell (four) and the oxygen has too few (six).

Molecules with the greatest stability have all their electrons paired. Many times this requires that more than one bond form between two atoms. For example, look at formaldehyde (CH_2O). The central atom is carbon ($\cdot\overset{\cdot}{\underset{\cdot}{\mathrm{C}}}\cdot$). It combines with two hydrogens ($\mathrm{H}\cdot$)

and an oxygen () giving  . In this case, both the carbon and the oxygen have an unpaired electron. However, if these unpaired electrons pair, as indicated by the arrows, they form a second bond between carbon and oxygen. All four atoms now have gained their greatest stability, while maintaining the correct number of orbitals and electrons and fulfilling the Octet Rule. The completed Lewis Structure looks like this.

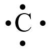


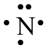
Exercise 1.10

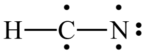
Write a Lewis structure, showing all valence electrons, for each of the following molecules.

a) CO_2	b) HCN	c) N_2
d) H_2S	e) SiO_2	f) CH_2NH

Sample Solution

b) First, write the carbon atom with its four valence electrons ().

Then add the hydrogen with its one electron () and the nitrogen with its five (). This gives the following structure:



However, this structure has four unpaired electrons—two on the carbon and two on the nitrogen. Pairing the electrons makes two additional covalent bonds and gives a Lewis structure with a carbon—nitrogen triple bond.

$H-C\equiv N:$

Now the structure satisfies all the rules for bonding.

1.10 Polar Covalent Bonds

In a polar bond the electron density of a molecular orbital is not equally distributed.

What you have learned so far is that a bond is either ionic or covalent. With ionic bonding an electron transfers from one atom to another. When the transfer occurs, one atom becomes a positively charged ion, and the other becomes a negatively charged ion. Then the bond forms as the two ions electrostatically attract each other. An ionic bond is the most extreme type of **polar bond**. Covalent bonds do not transfer electrons. Instead, the two atoms involved in the bond share electrons to form molecular orbitals. Two atoms that share electrons equally in a covalent bond are said to have **nonpolar bonds**.

A nonpolar bond has equal electron distribution in the molecular orbital.

Pauling defined electronegativity as "the power of the atom in a molecule to attract electrons to itself" and assigned each atom a number indicative of its ability to attract electrons.

However, few bonds in organic molecules are either completely ionic or completely covalent. Most fall somewhere on a continuum between the two. The **electronegativity** of the atoms involved in a bond determines the bond's position on this continuum. Linus Pauling developed the concept of electronegativity. These values of electronegativity range from 0 to 4. The most electronegative elements are in the upper right-hand corner of the periodic table. The least electronegative elements are in the lower left-hand corner. Figure 1.33 lists the electronegativities of the elements that are most important to organic chemists.

H 2.20						
Li 0.98	Be 1.57	B 2.04	C 2.55	N 3.04	O 3.44	F 3.98
Na 0.93	Mg 1.31	Al 1.61	Si 1.90	P 2.19	S 2.58	Cl 3.16
K 0.82	Ca 1.00					Br 2.96
						I 2.66

Figure 1.33. Electronegativities of the elements most important to organic chemists.

To determine where on the continuum between the completely ionic (polar) and the completely covalent (nonpolar) bonds a particular bond is, take the difference between the electronegativities of the two bonded atoms. If the difference is less than 1, that generally indicates that the bond is more covalent. If the difference is greater than 1.5, the bond is generally considered more ionic. Sodium chloride (NaCl) is a common example of a compound with a bond that is considered ionic. The electronegativity of Na is 0.93 and that of Cl is 3.16, giving a difference of 2.23. Methane is a common example of a compound whose bonds are considered covalent. The electronegativity of C is 2.55 and that of H is 2.20. The difference is 0.35.

Calling a bond covalent implies that the two bonded atoms equally share the electrons making up that bond. However, the only time that two atoms share electrons equally is when the two atoms have the same electronegativities, as do the two hydrogens in a hydrogen molecule. When two different atoms form a covalent bond, one atom attracts the electrons more strongly than the other does. This stronger attraction by one of the atoms prevents equal sharing between the atoms. It also creates a greater electron density around the atom with the higher electronegativity, giving it a partial negative charge and giving the atom with the lower electronegativity a partial positive charge. It is important to note that these partial charges are opposite and equal in magnitude. Chemists call this type of bond a **polar covalent bond**. Most bonds encountered in organic chemistry are polar covalent bonds. Hydrogen chloride (HCl) contains a covalent bond because the difference between the electronegativities of hydrogen and chlorine is 0.96. Because these are different elements and have different electronegativities, the bond is a polar covalent bond with the chlorine having the greater electron density due to its greater electronegativity. To indicate the partial charges on a polar covalent bond, chemists use δ^+ (partial positive charge) and δ^- (partial negative charge).

In a polar covalent bond the electrons in a molecular orbital are unequally distributed among the atoms of the orbital.

$$\overset{\delta^+}{\mathrm{H}}—\overset{\delta^-}{\mathrm{Cl}}$$

Bond dipole (μ) is the unit of measure that chemists use to describe the amount of polarity in a polar bond.

The **bond dipole** of a molecule is the product of the charge (e) and the distance (d) between the nuclei of the bonded atoms.

$$\mu = ed$$

The charge is the magnitude of either the positive or negative charge because, in a neutral molecule, the magnitude of both is equal. The value of the charge of an electron is 4.8 x 10^{-10} electrostatic units (esu), and bond lengths are typically in the range of 10^{-8} cm. Thus, molecular **dipole moments** are approximately 10^{-18} esu cm. The debye unit (D) is 1.0 x 10^{-18} esu cm and is named after Peter J. W. Debye, a Dutch chemist who pioneered in the study of polar molecules. Debye units simplify the reporting of dipole moments. Instead of reporting an experimentally determined dipole of 0.5 x 10^{-18} esu cm, using the debye unit shortens the measure to 0.5 D.

The dipole moment of a molecule is the measure of the polarity of an entire molecule.

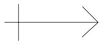
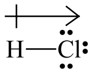
The symbol indicating the dipole moment of a molecule is . It is written with the Lewis structure of the molecule as follows:  $\overset{+\!\!\longrightarrow}{\mathrm{H}—\ddot{\underset{\cdot\cdot}{\mathrm{Cl}}}:}$ Note that the plus end is beside the element bearing the partial positive charge and the arrow end beside the element bearing the partial negative charge.

Table 1.2 lists the bond dipoles of some common types of bonds found in organic molecules. For simple molecules, such as HCl, the bond dipole is the same as the dipole moment of the molecule because there is only one bond in the molecule. For other, more complex molecules, the dipole moment is the vector sum of all of the bond dipoles for the molecule. To calculate the dipole moment of such molecules, chemists must consider the three-dimensional molecular structure. Thus, obtaining a dipole moment is very complicated for large molecules. However, having an understanding of the polarity of individual bonds will be very useful to you in understanding the chemical reactions you will study in later chapters of this book.

Bond	Bond Dipole, D	Bond	Bond Dipole, D
C—F	1.53	H—F	1.82
C—Cl	1.59	H—Cl	1.08
C—Br	1.48	H—Br	0.82
C—I	1.29	H—I	0.44
C—N	0.22	H—N	1.32
C—O	0.85	H—O	1.53
C—H	0.35		

Table 1.2. Selected bond dipoles.

Exercise 1.11

Draw the Lewis structure of each of the following molecules. For each bond in the molecule, indicate the direction of polarity. Also indicate whether each bond is covalent, polar covalent, or ionic.

a) HBr b) H_2O c) LiI
d) BrCl e) NH_3 f) KF

Sample solution

a) The electronegativity of H is 2.20 and that of Br is 2.96, giving a difference of 0.76. The molecule has a polar covalent bond with the positive end at hydrogen.

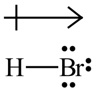


Table 1.2 shows that the dipole of the carbon—hydrogen bond is lower than the dipole of the carbon—oxygen bond and much lower than the dipoles of the carbon—halogen bonds. The low polarity of the C—H bond is important in the chemistry of organic molecules because the greater the polarity of a bond, the more reactive, or less stable, it is.

1.11 Inductive Effects on Bond Polarity

The inductive effect is the polarization of a bond by the atoms or groups of atoms attached to it.

In a molecule containing several different atoms, if one bond is polarized as a result of the high electronegativity of a constituent atom that bond increases the polarization of the other bonds adjacent to it. This is called an **inductive effect.** The inductive effect produces the strongest influence over the bonds immediately adjacent to the polarized bond and diminishes rapidly with distance. For example, the C—C bond in ethane (CH_3—CH_3) is completely nonpolar because it connects two equivalently bonded atoms. However, if you replace one of the hydrogens with a chlorine, forming chloroethane (CH_3—CH_2—Cl), the two carbon atoms are no longer equivalent. The higher electronegativity of the chlorine deprives the carbon to which it is bonded of some of its electron density; thus, creating a polarized bond. The polarized C—Cl bond effectively increases the apparent electronegativity of that carbon, and it compensates by drawing the electrons of its bond with the other carbon closer to itself. In other words, the polarized C—Cl bond of chloroethane polarizes the C—C bond through the inductive effect.

The field effect is the polarization of a bond by atoms or groups of atoms not directly bonded to the atoms connected by the polarized bond.

At this point it is important for you to consider a second effect, called the **field effect**. The field effect operates through space rather than through bonds like the inductive effect. The influence of this effect depends entirely on the three-dimensional structure of the molecule. Sometimes a molecule contains bonds that are separated by too many intervening atoms and bonds to interact with one another through the inductive effect. However, atoms of highly differing electronegativities can be brought close together as a result of the structure of the molecule, and the close proximity of two such atoms causes the same type of bond polarization as does the inductive effect.

Separating field effects and inductive effects experimentally is extremely difficult, as they accomplish the same result and reinforce each other. However, chemists have shown that the field effect is actually more important than the inductive effect. Because the effects have the same consequences and reinforce each other, chemists usually use the term field effect to refer to a combination of both effects.

1.12 Formal Charges

The formal charge is the positive or negative charge assigned to an atom in a Lewis structure.

When studying the pathways that organic reactions follow, you will deal frequently with charged molecular intermediates, called ions. Because chemical reactions usually take place at or near the site of charged atoms, you must know which particular atom, or atoms, bears the charge. The way to determine the charge-bearing atom in a molecule is to calculate the **formal charge** on each atom in that molecule. When calculating formal charges for the atoms, use the Lewis structure of the molecule as the basis of your calculation. Treat each electron in a covalent bond as if it belongs to both atoms that the bond joins. Assume that all the electrons that reside within the molecule do so in pairs. In Chapter 21, you will study some cases of unpaired electrons, but you will be told specifically when this occurs. Both electrons in any nonbonded pair belong to the atom next to which they are drawn—following the rules for drawing Lewis structures, of course.

Use the following formula to calculate formal charge:

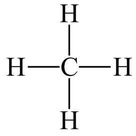
$$\begin{aligned}\text{formal charge} = {} & (\text{number of valence electrons}) \\ & -(\text{number of nonbonding electrons}) \\ & -\tfrac{1}{2}(\text{number of bonding electrons})\end{aligned}$$

Solved Exercise 1.2

Locate the formal charge in each of the following structures.

a) Methane, CH_4

Solution: First, draw the Lewis structure of methane:



Because all four of the carbon—hydrogen bonds are equivalent, calculate the formal charge only once. Each hydrogen has one valence electron, no nonbonding electrons, and two bonding electrons.

$$\text{Formal charge on hydrogen} = 1 - 0 - \tfrac{1}{2}(2) = 0$$

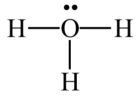
Carbon has four valence electrons and no nonbonding electrons. Because the carbon atom shares eight electrons with the four hydrogen atoms, it has eight bonding electrons.

$$\text{Formal charge on carbon} = 4 - 0 - \tfrac{1}{2}(8) = 0.$$

Thus, there are no formal charges in methane.

b) The hydronium ion, $H_3O^{\oplus}$

Solution: First, draw the Lewis structure of the hydronium ion:

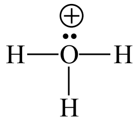


Because all three of the oxygen—hydrogen bonds are equivalent, calculate the formal charge for the hydrogens only once. Each hydrogen has one valence electron, no nonbonding electrons, and two bonding electrons.

Formal charge on hydrogen = 1 – 0 – ½(2) = 0

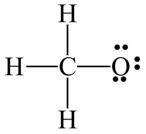
Oxygen has six valence electrons and two nonbonding electrons. Because the oxygen atom shares six electrons with the three hydrogen atoms, it has six bonding electrons.

Formal charge on oxygen = 6 – 2 – ½(6) = +1.



c) The methoxide ion, $CH_3O^{\ominus}$

Solution: First, draw the Lewis structure of the methoxide ion:



Because all three of the carbon—hydrogen bonds are equivalent, calculate the formal charge for the hydrogens only once. Each hydrogen has one valence electron, no nonbonding electrons, and two bonding electrons.

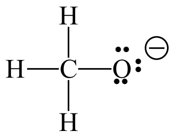
Formal charge on hydrogen = 1 – 0 – ½(2) = 0

Carbon has four valence electrons and no nonbonding electrons. Because the carbon atom shares six electrons with the three hydrogen atoms and two electrons with the oxygen atom, it has eight bonding electrons.

Formal charge on carbon = 4 – 0 – ½(8) = 0.

Oxygen has six valence electrons and six nonbonding electrons. Because the oxygen atom shares two electrons with one carbon atom, it has two bonding electrons.

Formal charge on oxygen = 6 – 6 – ½(2) = –1.



Calculating the formal charge on a bonded atom is the same as asking whether or not it has the same number of valence electrons available to it as it did when it was unbonded. For example, oxygen normally has six valence electrons. To be uncharged in a molecule, it must have six electrons as well.

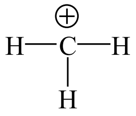
Exercise 1.12

Draw a Lewis structure for each of the following and determine whether any of the atoms bear formal charges.

a) CH_3F b) $CH_3OH_2^{\oplus}$ c) $CH_3^{\oplus}$ d) NH_3BF_3
e) $^{\ominus}$:CH_3 (the : indicates nonbonding electrons)
f) :CH_2 g) HNO_2

Sample solution

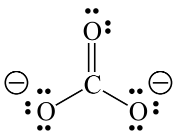
c) According to the conventions of drawing Lewis structures, carbon is the central atom.



Formal charge on hydrogen = 1 – 0 – ½(2) = 0
Formal charge on carbon = 4 – 0 – ½(6) = +1

1.13 Resonance

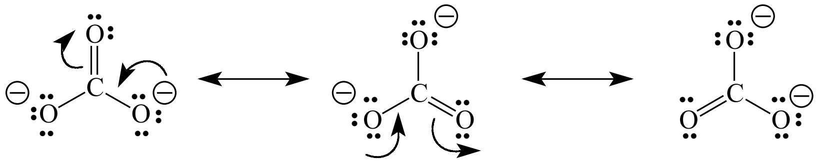
Some covalent molecules are impossible to represent satisfactorily with a single Lewis structure. The carbonate ion ($CO_3^{2\ominus}$) is an example. The following illustration seems to represent $CO_3^{2\ominus}$ accurately, according to the rules for drawing Lewis structures:



A Lewis structure also allows you to calculate the correct formal charges. Two of the oxygen atoms each bear a formal charge of –1, giving the ion a total charge of –2. However, experimental evidence demonstrates that this structure is not an accurate representation of the molecule. Instead, the evidence shows that the ion has three identical C—O bonds, that each O—C—O angle measures 120°, and that each of the three oxygens bears the same amount of negative charge.

What is needed is a structure that represents the electrons as being equally distributed among the three oxygen atoms. Lewis structures do not allow for this, so chemists developed another model. They call this model **resonance**. To represent a molecule in which there is resonance, as many structures as possible are drawn that differ only in the location of the pairs of electrons—for the carbonate ion there are three. In each structure, the atoms maintain the same relative positions.

With resonance, two or more Lewis structures that differ in the position of π and nonbonding electrons describe the same ion or molecule.



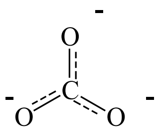
That is, the ion is not simply being rotated. The oxygen atoms are drawn in the same location in each structure, whereas the electrons are drawn showing all the possible positions that they might be in. A two-headed arrow (⟷) is the notation used to indicate resonance. This symbol does not mean that there is any kind of equilibrium, nor does it imply any kind of reaction.

Chemists frequently use **curved arrows** (↷) to indicate the direction of *electron movement*. In the resonance structures for the carbonate ion, the curved arrows show one pair of nonbonding electrons moving to become a new carbon—oxygen double bond, and a pair of bonding electrons from another carbon—oxygen double bond moving to become nonbonding. Understanding what curved arrows mean will help you to understand many of the reactions you will study in organic chemistry.

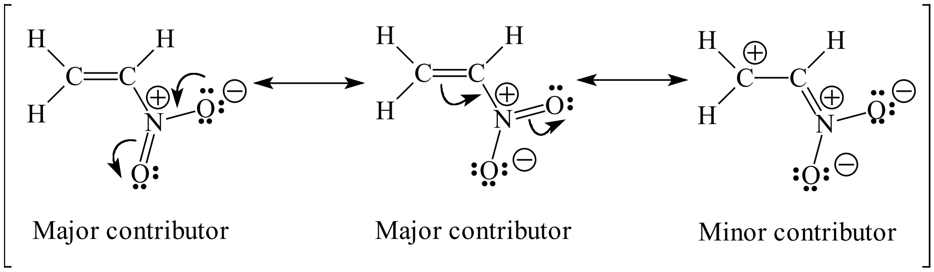
A curved arrow indicates the direction of electron movement. The arrowhead shows the destination of the electrons.

A resonance hybrid is the combination of the individual resonance contributors to the structure of a molecule.

Although three resonance structures are drawn for the carbonate ion, keep in mind that it has only one actual structure. That structure is a **resonance hybrid** of the three Lewis structures, which are called **resonance contributors**. None of the individual resonance contributors shown above actually exists. Also, the molecule that the resonance contributors illustrate is not a mixture of the different forms. There is only one actual molecule, and its properties are the weighted averages of the properties of the resonance contributors. With the carbonate ion, each oxygen bears 2/3 of a negative charge, and each carbon—oxygen bond has a bond length of 129 pm. This length is longer than a typical carbon—oxygen double bond (122 pm), but shorter than a typical carbon—oxygen single bond (143 pm). A more accurate drawing of the carbonate ion shows the bonds using a combination of solid and dashed lines indicating that the bonds fall somewhere between single and double bonds.



The three resonance contributors of the carbonate ion are equivalent. That is, they all have equal energy and contribute equally to the structure of the ion. But this is not always the case. For example, nitroethene (CH_2=$CHNO_2$) has three resonance contributors, but only two of them are equivalent; the third is different.



The first two structures are equivalent contributors to the resonance hybrid. Both have a double bond between nitrogen and one oxygen and a single bond between nitrogen and the other oxygen. Both have a positive charge on nitrogen and a negative charge on the oxygen with the single bond. The first two structures are important because the structures with the largest number of covalent bonds contribute most to the characteristics of the group. All three atoms also have noble gas configurations. Thus, these two resonance structures are the major contributors to the resonance hybrid of nitroethene.

The third structure has more charges and fewer bonds than the first two structures Plus one carbon does not have an octet. In the third structure, the carbon is positively charged, and both oxygens are negatively charged. The third contributor has a **separation of charge**. A molecule accomplishes separation of charge only with an expenditure of energy. These factors decrease the impact this structure has on the features of nitroethene, making it a minor contributor to the resonance hybrid.

Separation of charge occurs when two adjacent atoms have a plus and a minus charge that could be eliminated by the formation of a bond.

Writing resonance contributors requires a careful analysis of the Lewis structure for a molecule or ion. To write the resonance contributors, follow these rules:

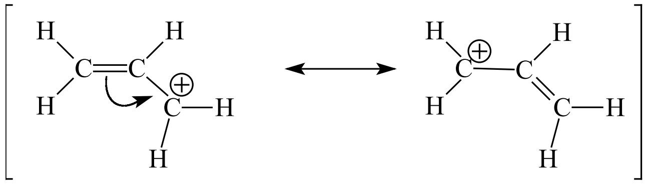
1. Only nonbonding and π bonding electrons change locations from one resonance contributor to another.
2. The atoms in the different resonance contributors remain in the same relative positions.
3. All resonance contributors must have the same number of paired and unpaired electrons.
4. Resonance contributors with atoms from the second period that have eight electrons around them are more important than those in which such atoms lack a full octet.
5. A resonance contributor with a greater number of covalent bonds is more important than one with a smaller number.
6. Because phosphorus and sulfur have empty *3d* orbitals, you can write structures with ten or more electrons about these atoms.
7. Resonance contributors with no separation of charge are more important than those with a separation of charge.
8. When a charge is present, the more important resonance contributor is the one with a negative charge on the most electronegative atom or a positive charge on the least electronegative atom.

Solved Exercise 1.3

For each of the following compounds, draw all important resonance contributors. Decide which resonance contributor, or contributors, is more important.

a) $H_2C{=}CH{-}CH_2^{\oplus}$

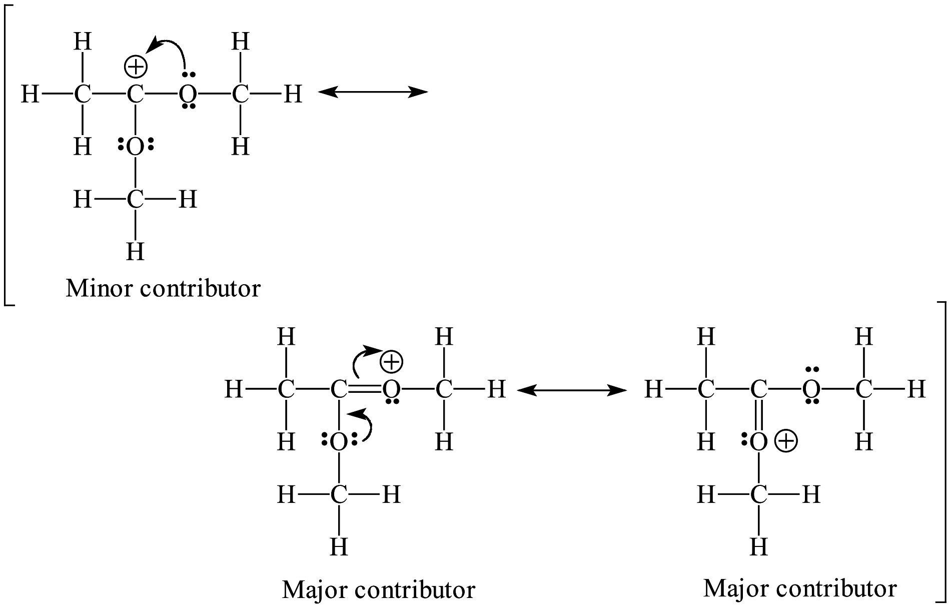
Solution: The resonance contributors are:



Both structures have octets on two of the carbon atoms and an incomplete octet on the third carbon atom. They have the same number of bonds and charges; thus, they are equivalent resonance structures.

b) $CH_3C(OCH_3)_2{}^{\oplus}$

Solution: First draw the resonance structures:



Minor contributor

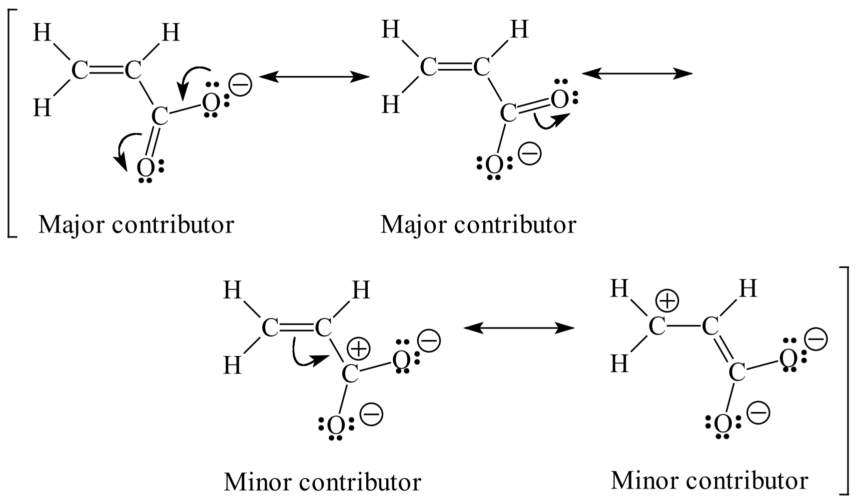
Major contributor

Major contributor

In the first structure one of the carbon atoms has only three bonds making it electron deficient. Both the second and third contributors have full octets on all the atoms; thus, they are equivalent.

c) $H_2C{=}CH{-}CO_2{}^{\ominus}$

Solution: First draw the resonance contributors:



The first two resonance contributors have equal numbers of bonding and nonbonding electrons and equal numbers of charges. Thus, they are equivalent structures. The third and fourth structures have an increase in the number of charges giving them higher energy levels. They are minor contributors to the structure of this anion.

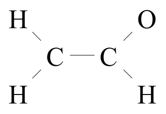
Exercise 1.13

Draw the Lewis structures of the following molecules or ions. Draw all important resonance contributors if the molecule is a resonance hybrid. Decide which contributor, or contributors, is more important.

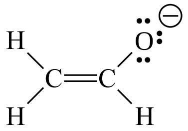
a) HNO_3
b) $CH_2CHO^{\ominus}$
c) CH_3NO_2
d) $SO_4{}^{2\ominus}$
e) CH_3NCO
f) CH_3SOCH_3

Sample Solution

b) First, note that there are a total of eighteen valence electrons available for the structure. The two carbons have four each, the three hydrogens have one each, the oxygen has six, and the negative charge represents one. Then, draw a Lewis structure.



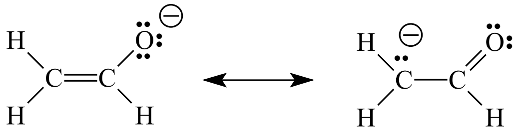
This structure accounts for ten of the eighteen valence electrons in the ion. Complete the structure, giving each atom a full valence shell of electrons.



Now confirm the formal charge on oxygen.

Formal charge = 6 – 6 – ½(2) = –1

The above structure is a valid Lewis structure for the molecule. Decide whether or not there are any valid resonance contributors by exploring ways of moving nonbonding and bonding electrons. This structure has two resonance contributors.



Finally, the more important contributor (see rule 8, page 000) is the one on the left.

Key Ideas from Chapter 1

- ❑ Electrons in atoms and molecules exist only in certain allowed energy states, called orbitals. These orbitals are regions of probability for finding an electron.
- ❑ An orbital has nodes, or regions, where there is no electron density. These nodes separate the electron wave peaks from the wave troughs or other peaks.
- ❑ The distribution of electron density in a given type of orbital has a characteristic arrangement in space. All *s* orbitals are spheres; all *p* orbitals have two lobes.
- ❑ Hybrid orbitals form by mixing atomic orbitals. The VSEPR model predicts the orientation of these hybrid orbitals in space.
- ❑ Bonds form when orbitals on different atoms overlap. Overlap of the 1*s* orbitals of two hydrogen atoms results in the formation of two molecular orbitals—one bonding and the other antibonding.

❑ The Aufbau Principle, Hund's Rule, and the Pauli Exclusion Principle determine the arrangement of electrons in both the atomic and molecular orbitals.

❑ Chemical compounds contain two types of bonds—ionic and covalent. In ionic compounds, electrostatic attraction holds the ions together. In covalent compounds, the atoms are held together by the sharing of electrons.

❑ When the second-row elements form chemical compounds, they tend to follow the Octet Rule. That is, each atom surrounds itself with eight electrons.

❑ Drawing a Lewis structure for a molecule requires that, as far as possible, each atom have an octet of electrons and that charge separation be minimized.

❑ In covalent compounds, atoms sometimes share electrons unequally and may give a molecule a dipole moment. A dipole moment is the vector sum of the dipoles of individual bonds.

❑ The formal charge convention assigns the total charge of a given chemical species to its constituent atoms. It also determines whether an uncharged species may have equal numbers of positive and negative charges present in the molecule.

❑ A single Lewis structure cannot always adequately represent an ion or molecule. For some cases, draw resonance structures by shifting nonbonding and/or π bonding electrons. The actual molecule is the weighted sum of its resonance contributors.

Supplementary Exercises

1.14 For each of the following compounds, tell whether the bonds are ionic or covalent. If covalent, show the polarity by drawing an arrow ($+\!\!\!\longrightarrow$) indicating the direction of the dipole.

a) CaF_2 b) NaH c) FCl d) SiH_4
e) BeF_2 f) NaI g) BH_3 h) PH_3

1.15 Draw Lewis structures for each of the following compounds showing all bonds, any nonbonding electrons present, and any formal charges.

a) $AlCl_3$
b) NF_3
c) H_2O_2
d) SO_2
e) CH_3NH_3Cl
f)CH_3CH_2OH
g) CH_3NHOH
h) CH_3SCH_3

1.16 Indicate which of the following molecules have a dipole moment. Using the geometry of orbital hybridization, draw a three-dimensional representation of the molecule and show the direction of the dipole for the molecule using an arrow (+⟶).

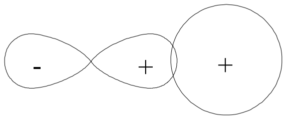
a) CCl_4
b) $CFBr_3$
c) CH_3NH_2
d) CH_3Cl
e) $CH_2{=}CHBr$
f) CH_3OCH_3
g) $CH_3CH{=}CH_2$
h) $CH_3CHClCH_3$

1.17 The compounds ICl and FCl have dipole moments that are similar in magnitude (0.7 D and 0.9 D) but opposite in direction. Specify the direction of each dipole moment. Explain your reasoning.

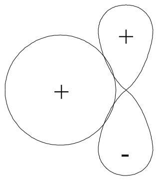
1.18 Sulfur dioxide has a dipole moment of 1.6 D. Carbon dioxide has a dipole moment of zero, even though the C—O bonds are more polar than the S—O bonds. Explain.

1.19 Two hydrogen atoms (H·) prefer to share electrons and form H_2 rather than forming $H^{\oplus}$ and $H{:}^{\ominus}$ by transferring an electron. Why?

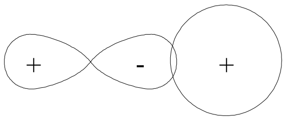
1.20 Below are three types of orbital overlaps. One is bonding, one is antibonding, and one is nonbonding. Which orbital overlap corresponds to which type of interaction? Explain.



A



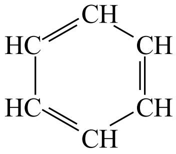
B



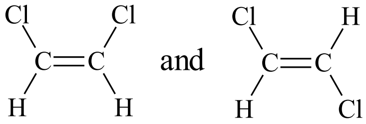
C

1.21 The hydrogen molecular ion, $H_2^{\oplus}$, is widely found in molecular clouds in interstellar space as a result of cosmic ray bombardment of H_2. Is the dissociation of this ion into a hydrogen atom (H•) and a hydrogen ion ($H^{\oplus}$) exothermic (releases energy) or endothermic (requires energy)?

1.22 Chemists took a number of years to deduce the structure of benzene. Given the experimental fact that all of the C—C bonds in benzene are equal in length, why is the structure shown below inaccurate? What is necessary to make a more accurate representation?

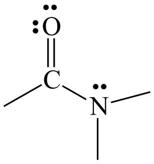


1.23 Two isomers of 1,2-dicholorethene can be differentiated by their dipole moments. One has a dipole moment μ = 1 D and the other μ = 0 D. Assign the dipole moments to the following structures:



Isomers of 1,2-dichloroethene

1.24 The structure of proteins depends on the amide functional group, shown below, because such groups make up the backbone of proteins. Resonance best explains the properties of the amide group. Write the three resonance contributors for the amide group. Discuss the relative stability of each contributor.

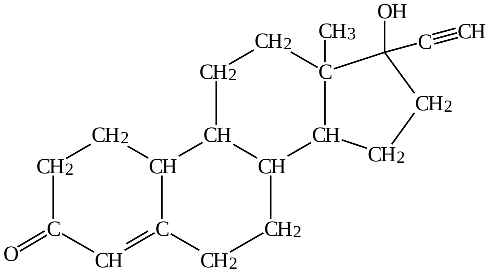


1.25 Draw the Lewis structures of isocyanic acid (HNCO) and cyanic acid (HOCN).

a) These structures are not resonance structures. Explain.

b) When either acid loses a proton, the same ion results. Explain.

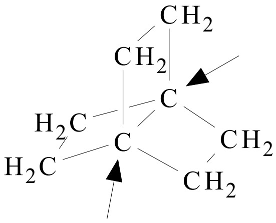
1.26 Norethindrone is an example of a molecule used in oral contraceptives. In this molecule, locate an example of each of the following types of atoms or bonds. (Ignore any bonds to hydrogen.)



Norethindrone

a) A nonpolar covalent bond.
b) A highly polarized covalent bond.
c) An *sp* hybridized atom.
d) An *sp*^{2} hybridized atom.
e) An *sp*^{3} hybridized atom.
f) A bond between atoms of different hybridizations.

1.27 Below is the complex molecule [2.2.2]propellane. Given the fact that the CH_2—C—CH_2 bond angle is 120°, what hybridization would you expect for the carbons designated by the arrows? What orbitals are involved in the bonding of those two carbons?



1.28 Imagine that the carbon atom of CH_2Cl_2 has some orbital hybridization other than *sp*^{3}. With this other hybridization, the compound has a planar structure placing the carbon at the center and the other four atoms at the corners of a square. Using this hybridization, the compound has more than one distinct structure.

a) How many structures are there? Draw them.

b) Suppose you have samples of each of these compounds. How would measurement of the dipole moment help you distinguish the isomers?

1.29 The van der Waals radius of sulfur is greater than that of an oxygen atom. How might that account for the fact that the H—S—H bond angle (92.2°) is less than the H—O—H bond angle (104.5°) of water? What orbitals from sulfur are involved in the bonds?

1.30 The C—O bond dipole is large—usually greater than 1.5 D. Surprisingly, carbon monoxide (CO) has a small dipole moment of 0.1 D. This fact puzzled chemists and led to many experiments and theoretical discussions. What explanation can you give?

a) Draw a Lewis structure for CO.

b) There are three resonance contributors for the structure of CO. Draw and analyze them for formal charge and whether or not each atom has an octet of electrons.

c) Carbon monoxide is highly toxic because it binds tightly to the iron ($Fe^{2\oplus}$) in hemoglobin and prevents oxygen transport by the hemoglobin. What does this tell you about the relative importance of the various resonance contributors for CO?

1.31 Allene has the structural formula $CH_2{=}C{=}CH_2$. What is the hybridization of each of the three carbon atoms? What orbitals are involved in the bonds of this molecule? What shape does the molecule have?

1.32 Consider the N—Br bond. Given the fact that nitrogen and bromine have nearly the same electronegativity (3.04 and 2.96), answer the following questions. Is the N—Br bond covalent, polar covalent, or ionic? Explain your answer. Is the N—Br bond a stable bond?

1.33 Account for the differences in bond length for the series of compounds in the table below:

Compound	C—Cl bond length, pm
H_3C—Cl	178
ClH_2C—Cl	177
Cl_2HC—Cl	176
FH_2C—Cl	176
Cl_3C—Cl	175
F_3C—Cl	172

1.34 Addition of an electron to a hydrogen molecule (H_2) leads to a very unstable hydrogen anion, $H_2^{\ominus}$. Why is this species unstable?

Richard F. Daley and Sally J. Daley
www.ochem4free.com

Organic Chemistry

Chapter 2

Introduction to Organic Nomenclature and Functional Groups

Chapter 2

Introduction to Organic Nomenclature and Functional Groups

Chapter Outline

2.1 Drawing Organic Structures
Drawing two-dimensional, condensed, and bond-line structures of organic compounds

2.2 Alkanes
An introduction to alkanes

2.3 Structural Isomerism
A look at compounds with the same molecular formula but with different structures

2.4 IUPAC Nomenclature
An introduction to the IUPAC rules of nomenclature

2.5 Naming Alkanes
An introduction to the systematic approach to naming alkanes

2.6 Naming Cycloalkanes
Systematic naming of cycloalkanes

2.7 Naming Complex Alkyl Groups
Systematic and common nomenclature of molecules with branched side chains

2.8 Functional Groups
A survey of organic functional groups

2.9 Naming Alkenes and Alkynes
Naming hydrocarbons with double and triple bonds

2.10 Naming Alkenes, Part II
Naming *cis* and *trans* alkenes

2.11 Arenes
Naming substituted benzenes

2.12 Organohalogens
Naming organic compounds containing one or more halogens

2.13 Using Molecular Formulas
Gaining information about the structure of a compound by examination of the molecular formula

Objectives

- ✔ Know how to draw the structure of an organic molecule
- ✔ Know how to draw the structure of an alkane from its name or to name an alkane from its structure
- ✔ Know how to draw and name cycloalkanes
- ✔ Recognize a functional group
- ✔ Know how to draw and name alkenes and alkynes
- ✔ Know how to draw and name alkyl substituted arenes
- ✔ Know how to name organohalogen compounds

> The Naming of Cats is a difficult matter,
> It isn't just one of your holiday games;
> At first you may think I'm as mad as a hatter
> When I tell you a cat must have THREE DIFFERENT NAMES.
> —T. S. Eliot

As the nineteenth century progressed, chemists discovered and synthesized more and more different compounds. The names they gave the compounds reflected their source or some property of the compound. Because of the difficulty of remembering the name of all these compounds, chemists knew they needed a systematic method for naming the compounds they were working with. The International Union of Pure and Applied Chemistry (IUPAC) committee took over the task of developing systematic rules of nomenclature. The first report of the IUPAC committee was presented in 1889. Since then, the IUPAC committee has continued studying nomenclature and releasing new rules as required. By using these rules, chemists, or you, can look at the name of a compound and draw its structure or look at the structure of a compound and write its name. Learning how to name and draw the structure of the various compounds is the first step in learning to speak the language of organic chemistry.

Heteroatoms are atoms other than carbon or hydrogen.

A functional group is the atom, or atoms, that are the center of reactivity of a molecule.

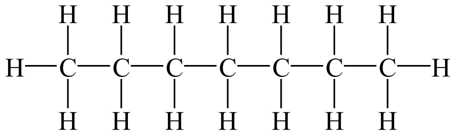
Chapter 1 presented organic chemistry as the chemistry of the carbon atom. However, many organic compounds contain other atoms besides carbon that contribute significantly to the physical and chemical properties of the compound. Chemists call these atoms **heteroatoms**, and the groups they form, **functional groups**. This chapter provides an overview of the rules for naming organic compounds. It also introduces the major functional groups that you will encounter as you study organic chemistry along with the rules of how to name them and draw their structures. The presence of heteroatoms radically changes the physical and chemical properties of the compounds to which they are bonded. In fact, the carbon—heteroatom bonds and the carbon—carbon multiple bonds are the main sites where chemical reactions take place.

Organic compounds are arranged into classes according to the particular functional groups that they contain. Members of each class of compounds share common chemical and physical characteristics. The names of organic compounds are assigned according to the class of the compound as determined by the functional groups. This chapter also shows how to draw the structural representations of these compounds.

2.1 Drawing Organic Structures

A two-dimensional structural formula of a hydrocarbon shows all of the atoms with all of their bonds in the plane of the page.

Molecules are actual, three-dimensional entities. Their structure is a major factor that determines their physical properties and the way one molecule interacts with another molecule. Because molecules are normally too small to see, chemists have devised ways to visually represent molecules. One way is by using a **two-dimensional structural formula** like that of the hydrocarbon heptane.



$$\begin{array}{ccccccccccccccccc} & & H & & H & & H & & H & & H & & H & & H & & \\ & & | & & | & & | & & | & & | & & | & & | & & \\ H & — & C & — & C & — & C & — & C & — & C & — & C & — & C & — & H \\ & & | & & | & & | & & | & & | & & | & & | & & \\ & & H & & H & & H & & H & & H & & H & & H & & \end{array}$$

Heptane

Hydrocarbons are compounds composed only of carbon and hydrogen atoms.

Hydrocarbons provide the backbone of all organic compounds. Each carbon atom in a hydrocarbon forms a total of four bonds. These bonds are combinations of single bonds with hydrogen atoms and single or multiple bonds with other carbon atoms.

A condensed structural formula includes all of the atoms but uses line bonds to emphasize the main structural characteristics of the molecule.

For molecules that contain a large number of atoms or complex structures, drawing every bond and every atom is time and space consuming. A common notation developed to abbreviate the drawing without sacrificing the clarity of the structure is the **condensed structural formula** shown below for heptane:

$$CH_3—CH_2—CH_2—CH_2—CH_2—CH_2—CH_3$$

Heptane

Taking out the lines representing the carbon—carbon bonds condenses this formula still more:

$CH_3CH_2CH_2CH_2CH_2CH_2CH_3$

Heptane

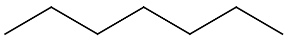
Heptane has five repeating —CH_2— groups, called methylene groups. Because many organic molecules have such repetitive groups, an even more condensed notation shows these repeating units. Using this notation, the formula for heptane is as follows:

$CH_3(CH_2)_5CH_3$

Heptane

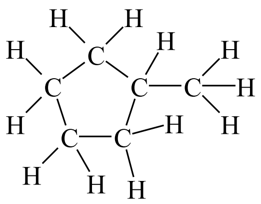
Bond-line formulas represent the carbon atoms as the intersection of lines and as line ends. You assume all the hydrogens needed to complete carbon's valences.

The **bond-line structural formula** is the notation that most organic chemists prefer to use. Bond-line formulas are easy to draw and quickly convey the essential structure of a molecule. Both the ends and the angles of the structure represent the carbon atoms. C—H bonds are not shown, but you should assume that the appropriate number of hydrogen atoms is present to complete the four bonds required by carbon to have its octet of electrons. The bond-line formula for heptane looks like this:



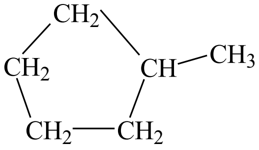
Heptane

Not all hydrocarbons are straight chains; many are rings. Chemists use the same structural formulas for them. Because the illustration of the two-dimensional structural formula of methylcyclopentane is so cluttered, it does not clearly show the ring.



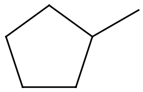
Methylcyclopentane

The condensed structural formula is clearer.



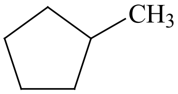
Methylcyclopentane

The bond-line structural formula is even clearer. Thus, chemists use it most frequently.



Methylcyclopentane

Often, chemists combine the bond-line and condensed notations to clarify a structure or emphasize specific features. This formula also represents methylcyclopentane.



Methylcyclopentane

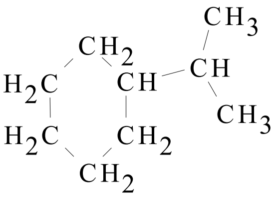
Exercise 2.1

Redraw each of the following condensed structural formulas using the bond-line notation.

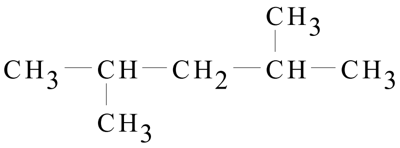
a) $CH_3CH_2CH_2CH_2CH_2CH_3$

b) $(CH_3)_2CH(CH_2)_4CH_3$

c)

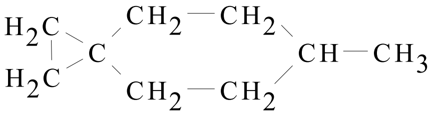


d)

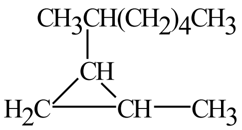


$$CH_3-\underset{\displaystyle CH_3}{\underset{|}{CH}}-CH_2-\overset{\displaystyle CH_3}{\overset{|}{CH}}-CH_3$$

e)

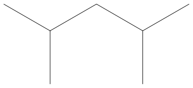


f)

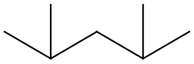


Sample solution

d)



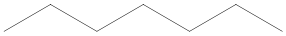
Chemists usually write the bond-line structural formula as shown above because this structure closely represents the actual structure of the molecule. In the molecule the carbons are sp^3 hybridized with 109.5° bond angles. The following notation is also a correct bond-line structural formula, but few chemists draw it this way because the bond angles are too small to represent the actual molecule.



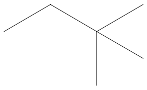
Exercise 2.2

Redraw each of the following bond-line structural formulas as condensed structures.

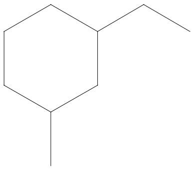
a)



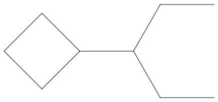
b)



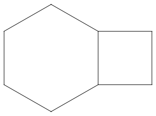
c)



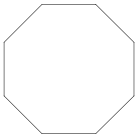
d)



e)



f)



Sample solution

b) $CH_3CH_2C(CH_3)_3$

2.2 Alkanes

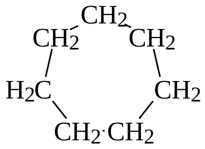
Each carbon atom in a saturated alkane forms bonds to four other atoms.

An unsaturated molecule has multiple bonds between some pairs of atoms in the molecule.

Of the various groups of organic compounds, alkanes have the simplest structure. Alkanes are hydrocarbons in which all the carbons form *sp*^{3} hybridized bonds; thus, each carbon atom bonds with four other atoms in the tetrahedral shape. Because each carbon atom in an alkane bonds to four other atoms, chemists say they are **saturated hydrocarbons**. Beginning in Chapter 13, you will study **unsaturated hydrocarbons**. Saturated hydrocarbons fall into two general types: alkanes and cycloalkanes. Alkanes have the general molecular formula C_nH_{2n+2}, and cycloalkanes have the general molecular formula C_nH_{2n}. The molecular formula for the seven-carbon alkane, heptane, is C_7H_{16}. The molecular formula for the seven-carbon cycloalkane, cycloheptane, is C_7H_{14}.

$CH_3CH_2CH_2CH_2CH_2CH_2CH_3$

Heptane



Cycloheptane

Chemists call alkanes with all the carbon atoms connected in a single continuous sequence normal alkanes. Other names for normal alkanes are linear and straight chain alkanes. However, don't let these names mislead you because, as you will learn in Chapter 3, carbon chains are actually twisted and kinked.

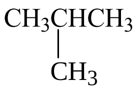
A series of molecules that differ by one carbon atom, but that are otherwise identical, is called a homologous series.

A succession of hydrocarbons that differ from each other by one methylene group (—CH_2—) is a **homologous series**. For example, the first three alkanes, methane (CH_3—H), ethane (CH_3CH_2—H), and propane ($CH_3CH_2CH_2$—H), are all members of a homologous series. Chemists often call each compound in a homologous series a homolog.

2.3 Structural Isomerism

Alkanes that contain up to three carbons form only the straight chain arrangement because that is the only way they can bond together. Alkanes that consist of more than three carbons have more than one possible molecular structure. For example, the molecular formula C_4H_{10} has two possible structural formulas.

$CH_3CH_2CH_2CH_3$



$$CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_3$$

Isomers are compounds with the same molecular formula but different molecular structures.

Stereoisomers have different three-dimensional structures, and constitutional isomers have different bond sequences.

Compounds with the same molecular formula but different molecular structures are called **isomers**. There are two categories of isomers: **stereoisomers** and **constitutional isomers**. The atoms that make up stereoisomers bond in the same order but differ in the spatial arrangement of those atoms. The only way you can distinguish between some stereoisomers is by examining their structures in three dimensions. Portions of Chapters 3 and 14, as well as all of Chapter 11, discuss stereoisomers in greater detail.

Constitutional isomers also contain the same atoms, but the order in which the atoms bond together is different in each isomer. The two structural formulas of C_4H_{10} are constitutional isomers. These two structural formulas represent completely different organic compounds—not only are their atoms bonded differently, but they have different physical properties. For example, the boiling point of $CH_3CH_2CH_2CH_3$ is –0.6°C, whereas the boiling point of $CH(CH_3)_3$ is –10.2°C.

As the number of carbons in a compound increases, so does the number of possible isomers. For the molecular formula C_5H_{12} there are three possible isomers and for C_6H_{14} there are five. For $C_{10}H_{22}$, however, there are a total of 75 isomers, for $C_{20}H_{42}$ there are over 300,000, and for $C_{40}H_{82}$ there are 6.35×10^{13}.

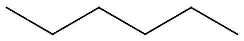
Exercise 2.3

Draw structural formulas for all isomers of the alkane C_6H_{14} using both the condensed and bond-line notations.

Sample solution

When drawing a set of structures for a particular molecular formula, it is important to follow an organized method. First draw the longest chain possible for the structure:

$CH_3CH_2CH_2CH_2CH_2CH_3$



Hexane

Once you've done this, shorten the chain by one carbon and draw a methyl branch on C2.

$CH_3CH_2CH_2\overset{\overset{CH_3}{|}}{C}HCH_3$

2-Methylpentane

Continue with this process, constantly double-checking for duplicates until there are no more structures to draw.

2.4 IUPAC Nomenclature

The development of a systematic approach to the naming of chemical compounds did not begin until near the end of the nineteenth century. Before that time, the names given to compounds reflected such things as their source or some property of the compound. Formic acid was distilled from some species of ants; thus, its name comes from the Latin word for ants, *formicae*. Ethyl alcohol was called grain alcohol because it was obtained from the fermentation of grains. Pure acetic acid was called *glacial* acetic acid because the laboratories of chemists were cold (glacier-like?) in the winter and pure acetic acid freezes just below room temperature. Thus, if the acid was pure, it was solid—glacial—in the winter.

Chemists still use these older, or common, names. In fact, many of the frequently used chemicals are known best by their common names. To help you become familiar with these common names, this book sometimes uses them. However, it is more important that you learn the systematized (IUPAC) rules of nomenclature.

The fundamental rule of chemical nomenclature is that *each different compound must have its own unique name*. The IUPAC system provides a unique name for each of the nearly 10 million known organic compounds, as well as the thousands of new compounds discovered or synthesized each year. The IUPAC rules are simple to learn and easy to use. With these rules you can readily write the name of any compound you might encounter or derive the structure of any given compound from its name.

Chemists adopted the IUPAC system of nomenclature for several reasons. First, chemists everywhere understand it. Second, they can readily adapt it to the indexing methods used for the chemical literature. Third, they can easily use it for computerized literature searching operations.

2.5 Naming Alkanes

The IUPAC method for naming a straight chain or unbranched alkane is as follows:

Step 1 Start with the prefix that indicates the number of carbons in the compound. The following compound has 8 carbons. The prefix for 8 carbons is oct–.

$$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_3$$

Step 2 Add the *–ane* ending. The name of the compound is octane.

The prefixes for most alkanes larger than four carbons come from Greek and Latin origin. Learning these prefixes is like learning to count in another language: one, two, three, four, five, six becomes meth–, eth–, prop–, but–, pent–, hex–. Table 2.1 lists the names for unbranched, sometimes-called normal, alkanes.

Name	Number of Carbon Atoms	Structure
Methane	1	CH_4
Ethane	2	CH_3CH_3
Propane	3	$CH_3CH_2CH_3$
Butane	4	$CH_3CH_2CH_2CH_3$
Pentane	5	$CH_3CH_2CH_2CH_2CH_3$ [or $CH_3(CH_2)_3CH_3$]
Hexane	6	$CH_3(CH_2)_4CH_3$
Heptane	7	$CH_3(CH_2)_5CH_3$
Octane	8	$CH_3(CH_2)_6CH_3$
Nonane	9	$CH_3(CH_2)_7CH_3$
Decane	10	$CH_3(CH_2)_8CH_3$
Undecane	11	$CH_3(CH_2)_9CH_3$
Dodecane	12	$CH_3(CH_2)_{10}CH_3$
Tridecane	13	$CH_3(CH_2)_{11}CH_3$
Tetradecane	14	$CH_3(CH_2)_{12}CH_3$
Pentadecane	15	$CH_3(CH_2)_{13}CH_3$
Hexadecane	16	$CH_3(CH_2)_{14}CH_3$
Heptadecane	17	$CH_3(CH_2)_{15}CH_3$
Octadecane	18	$CH_3(CH_2)_{16}CH_3$
Nonadecane	19	$CH_3(CH_2)_{17}CH_3$
Eicosane	20	$CH_3(CH_2)_{18}CH_3$
Heneicosane	21	$CH_3(CH_2)_{19}CH_3$
Doeicosane	22	$CH_3(CH_2)_{20}CH_3$
Trieicosane	23	$CH_3(CH_2)_{21}CH_3$
Triacontane	30	$CH_3(CH_2)_{28}CH_3$
Hentriacontane	31	$CH_3(CH_2)_{29}CH_3$
Dotriacontane	32	$CH_3(CH_2)_{30}CH_3$
Tritriacontane	33	$CH_3(CH_2)_{31}CH_3$
Tetracontane	40	$CH_3(CH_2)_{38}CH_3$

Name	Number of Carbon Atoms	Structure
Pentacontane	50	$CH_3(CH_2)_{48}CH_3$
Hexacontane	60	$CH_3(CH_2)_{58}CH_3$
Hectane	100	$CH_3(CH_2)_{98}CH_3$

Table 2.1. The names and structures of some unbranched alkanes.

Exercise 2.4

Name the following alkanes.

a) $CH_3CH_2CH_2CH_2CH_2CH_2CH_3$ b) $CH_3(CH_2)_9CH_3$
c) $CH_3(CH_2)_6CH_3$ d) $CH_3(CH_2)_{41}CH_3$

Sample solution

b) $CH_3(CH_2)_9CH_3$ has nine CH_2 groups and two CH_3 groups for a total of eleven carbons. The alkane chain with eleven carbons is undecane.

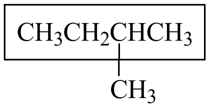
In a branched alkane the longest continuous chain of carbon atoms does not include all of the carbon atoms in the molecule.

Not all alkanes are unbranched; in fact, most are **branched**. Except for the shorter alkanes, which have only one or two different possible structures, branched alkanes have many different possible structures. Fortunately, the IUPAC system for naming branched alkanes makes it possible to distinguish between the many different structures. The following step-by-step description is used for naming branched alkanes:

A substituent is some group, other than hydrogen, attached to the longest chain of carbon atoms in a molecule.

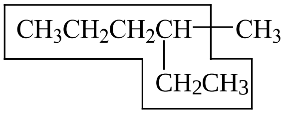
Step 1 Locate the longest continuous chain of carbon atoms.

a. This chain determines the compound's parent name. The parent name for the following compound is butane because the longest continuous chain contains four carbons. The box indicates the longest chain. The carbon—hydrogen group that is not a part of the parent chain is called a **substituent**.



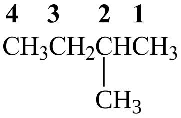
$$\boxed{CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_3}$$

b. The longest continuous chain is not always immediately obvious from the way the formula is written. For example, the following structure represents hexane because the longest chain contains six carbons. So, count the carbons carefully.



$$CH_3CH_2CH_2\underset{\substack{|\\ CH_2CH_3}}{C}H{-}CH_3$$

Step 2 Number the carbons in the parent chain beginning with the end of the chain nearest the substituent.



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

An alkyl group is any single carbon or carbon chain, along with their hydrogens, attached to the parent chain.

Step 3 Use these numbers to designate the position of the substituent, called an **alkyl group**, in the name of the compound.

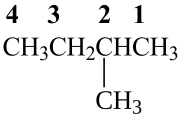
An alkyl group is an unbranched alkane with a hydrogen atom removed from the terminal, or end, carbon. To name the alkyl group, replace the *–ane* ending of the unbranched alkane with *–yl*. Thus, if you take one hydrogen from CH_4, it becomes —CH_3, and the name changes from methane to methyl. Table 2.2 illustrates this process with several additional examples.

Alkane	Name	Alkyl Group	Name
CH_3—H	Methane	CH_3—	Methyl
CH_3CH_2—H	Ethane	CH_3CH_2—	Ethyl
$CH_3CH_2CH_2$—H	Propane	$CH_3CH_2CH_2$—	Propyl
$CH_3CH_2CH_2CH_2$—H	Butane	$CH_3CH_2CH_2CH_2$—	Butyl
$CH_3CH_2CH_2CH_2CH_2$—H	Pentane	$CH_3CH_2CH_2CH_2CH_2$—	Pentyl

Table 2.2. Naming of alkyl groups.

Step 4 Now you have all the parts of the compound's name. Put them together in the following way.

a. Write down the number of the carbon from which the alkyl group branches. In the example it is carbon 2.

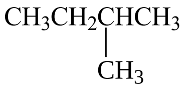


$$\overset{4}{C}H_3\overset{3}{C}H_2\underset{\substack{|\\ CH_3}}{\overset{2}{C}}H\overset{1}{C}H_3$$

b. Add a hyphen.

c. After the hyphen, place the name of the alkyl group. In this example, it is a methyl group.

d. Finally, add the name of the parent compound. In this example, the parent compound is butane. So the complete name is 2-methylbutane.



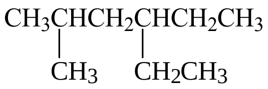
$$\begin{array}{l} CH_3CH_2\overset{}{C}HCH_3 \\ \quad\quad\quad\;\; | \\ \quad\quad\quad\;\; CH_3 \end{array}$$

2-Methylbutane

When naming a compound with two or more alkyl groups, follow the above steps with these additions:

Step 5 To name a molecule with multiple substituents use the following rules:

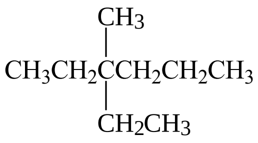
a. When numbering the parent chain, give each substituent a number that corresponds to its location on the longest chain by listing the groups alphabetically[1]. If a compound contains both an ethyl and a methyl group, list the ethyl before the methyl. The general form of such a name is #-alkyl-#-alkylalkane. As a specific example, the name of the following compound is 4-ethyl-2-methylhexane:



$$CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2\underset{\displaystyle CH_2CH_3}{\underset{|}{C}}HCH_2CH_3$$

4-Ethyl-2-methylhexane

b. If the two alkyl groups are on the same carbon, use the number of that carbon twice. For example, the following compound is called 3-ethyl-3-methylhexane:



$$CH_3CH_2\overset{\displaystyle CH_3}{\overset{|}{\underset{\displaystyle CH_2CH_3}{\underset{|}{C}}}}CH_2CH_2CH_3$$

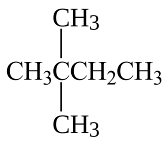
3-Ethyl-3-methylhexane

c. When multiple alkyl groups are identical, indicate this by the use of prefixes di–, tri–, tetra–, penta–, and so on with the alkyl group name. Also, every identical group must have a number with commas separating those numbers.

---

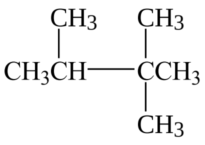
[1] Some handbooks also list groups by increasing size or complexity. For example, methyl would be listed before ethyl. However, alphabetical listing is the most commonly used system.

The general forms are #,#-dialkylalkane and #,#,#-trialkylalkane. When naming compounds with the prefixes of di–, tri–, and so on, do *not* alphabetize the prefixes. Thus, dimethyl follows triethyl. The following compounds are 2,2-dimethylbutane, 2,2,3-trimethylbutane, and 2,2,3,3-tetramethylbutane.



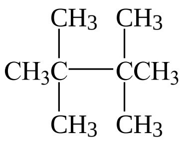
$CH_3\underset{CH_3}{\overset{CH_3}{C}}CH_2CH_3$

2,2-Dimethylbutane



$CH_3\overset{CH_3}{CH}{-}\underset{CH_3}{\overset{CH_3}{C}}CH_3$

2,2,3-Trimethylbutane



$CH_3\underset{CH_3}{\overset{CH_3}{C}}{-}\underset{CH_3}{\overset{CH_3}{C}}CH_3$

2,2,3,3-Tetramethylbutane

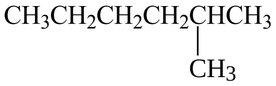
Exercise 2.5

Write the structural formulas and the IUPAC names for the nine isomers of C_7H_{16}. (*Hint*: It is helpful to name them as you go, to quickly eliminate duplication.)

Sample solution

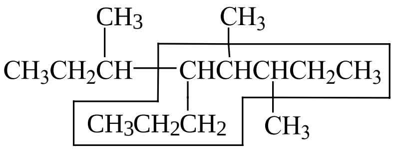
Starting with the simplest structures and working toward the more complex, the first two structures would be heptane and 2-methylhexane.

$CH_3CH_2CH_2CH_2CH_2CH_2CH_3$

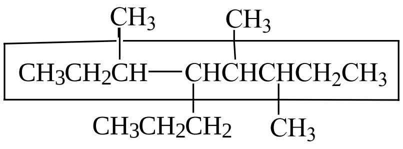


$CH_3CH_2CH_2CH_2\underset{CH_3}{CH}CH_3$

Step 6 If two or more chains compete for selection as the parent chain, choose the one with the smaller or simpler alkyl groups attached. This often means the greatest number of alkyl groups. For example, for the following structure, the lower chain has more and simpler attached groups than the upper chain even though the chains are both the same lengths:



$CH_3CH_2\overset{CH_3}{CH}{-}\underset{CH_3CH_2CH_2}{CH}\overset{CH_3}{CH}\underset{CH_3}{CH}CH_2CH_3$

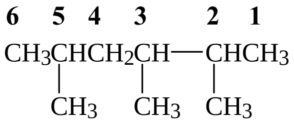


$$CH_3CH_2\overset{CH_3}{\overset{|}{C}}H—\underset{\underset{CH_3CH_2CH_2}{|}}{C}H\overset{CH_3}{\overset{|}{C}}H\underset{\underset{CH_3}{|}}{C}HCH_2CH_3$$

3,4,6-Trimethyl-5-propyloctane

Thus, the correct name for the structure is 3,4,6-trimethyl-5-propyloctane.

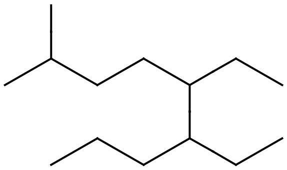
Step 7 When branching occurs an equal distance from either end of the longest chain, choose the name that gives the lower number at the first point of difference. Looking again at the previous structure, its name cannot be 3,5,6-trimethyl-4-propyloctane as it would give a higher number at the first point of difference. In the following structure numbering from the right end gives lower numbers than when numbered from the left end. Thus, the structure's name is 2,3,5-trimethylhexane and not 2,4,5-trimethylhexane.

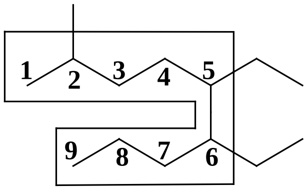


$$\overset{6}{CH_3}\overset{5}{\underset{\underset{CH_3}{|}}{C}H}\overset{4}{CH_2}\overset{3}{\underset{\underset{CH_3}{|}}{C}H}—\overset{2}{\underset{\underset{CH_3}{|}}{C}H}\overset{1}{CH_3}$$

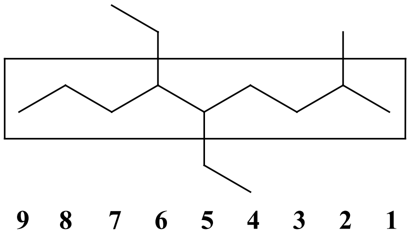
2,3,5-Trimethylhexane

The same principles apply to naming a compound when its bond-line formula is given. The colored screen on the right indicates the longest chain for the following compound.





The colored screen covers nine carbons. To simplify the way the drawing looks, redraw the longest chain straightened and number the carbon atoms as shown below.



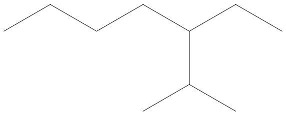
5,6-Diethyl-2-methylnonane

The name of this compound is 5,6-diethyl-2-methylnonane.

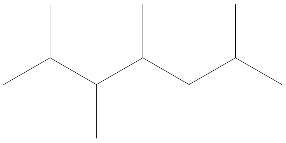
Exercise 2.6

Name each of the following alkanes using the IUPAC system.

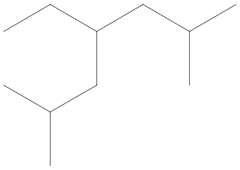
a)



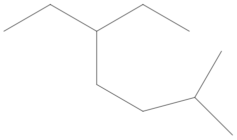
b)



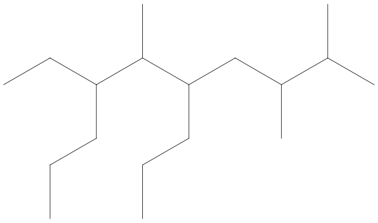
c)



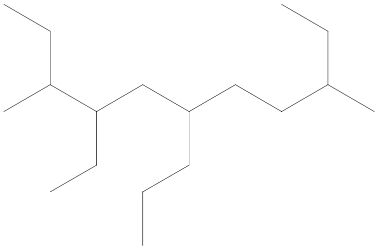
d)



e)

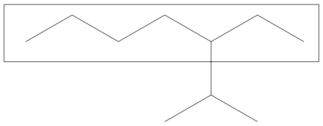


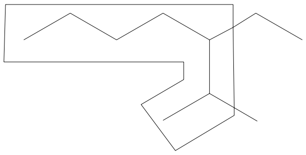
f)



Sample Solution

a) The longest chain has seven carbons, but there are two ways of counting them. The second way, shown on the right, is the preferred way because it has the smaller or simpler of attached groups. Thus, the compound is 3-ethyl-2-methylheptane.





A Summary of the Steps Used to Name an Alkane:

Step 1 Find the longest possible chain of carbon atoms. Name this chain based on the number of carbons in this chain. If there is more than one chain of the same length, choose the one with the simpler substituents.

Step 2 Number the carbons on the longest chain. Begin numbering from the end closest to a substituent on the chain.

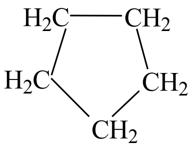
Step 3 Name any substituents using the alkane name for the number of carbons in the chain, changing the *–ane* suffix to *–yl*.

Step 4 List the names of the substituents alphabetically. Precede each substituent with a number and a dash. Immediately follow the last substituent by the name of the longest chain.

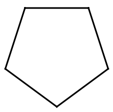
Step 5 If there are multiple instances of a substituent, list the substituent name with the prefix di–, tri–, etc., indicating the number of identical substituents. Number each substituent and separate the numbers with commas.

2.6 Naming Cycloalkanes

Cycloalkanes are hydrocarbons that have the general molecular formula C_nH_{2n} and in which some, or all, of the carbon atoms form a ring. The condensed structural and bond-line formulas for cyclopentane are as follows:



Condensed formula

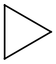


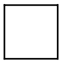
Bond-line formula

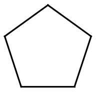
To name cycloalkanes, use the following steps.

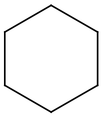
Step 1 Determine the parent name of the compound by counting the number of carbons in the ring. Use the same parent name for the ring that you would use for the normal alkane containing that number of carbons.

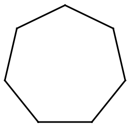
Step 2 Add the prefix *cyclo–* to the parent name.


Cyclopropane


Cyclobutane


Cyclopentane

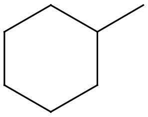

Cyclohexane


Cycloheptane

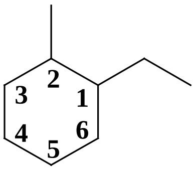
Step 3 Name any alkyl group substituents the same way that you name any other alkyl group.

Step 4 Determine the position of the alkyl group or groups on the ring.

a. For a ring with only one alkyl group attached, you do not need a number to designate the group's position. The carbon bearing a single group is always carbon number 1. For example, the following compound is methylcyclohexane:

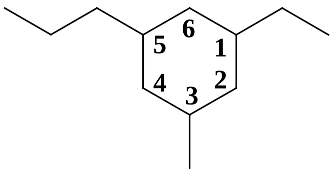

Methylcyclohexane

b. When a ring has more than one alkyl group attached, number the ring to give the lowest sum of numbers. If there are two groups, assign the number one to the first alkyl group alphabetically. Then count the shortest distance to the second substituent. With three or more substituents, determine a set of numbers to give the lowest sum of numbers. For example, the following compound is 1-ethyl-2-methylcyclohexane, not 1-ethyl-6-methylcyclohexane:



1-Ethyl-2-methylcyclohexane

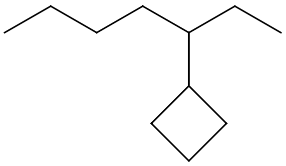
c. If the sum of numbers is identical either direction around the ring, then count towards the second group alphabetically on the ring. The following compound is 1-ethyl-3-methyl-5-propylcyclohexane:



1-Ethyl-3-methyl-5-propylcyclohexane

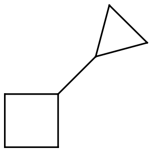
The more complex ring-containing alkanes need the following additional steps to name the compound.

Step 5 When the alkane chain is complex or has more carbons than the ring, name the ring as a substituent on the alkane chain. Follow the above steps for naming a normal alkane and for naming a cycloalkane. Call the ring a cycloalkyl group.



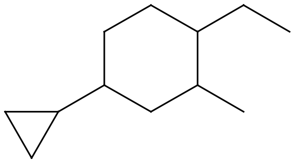
3-Cyclobutylheptane

Step 6 When one ring is attached to another ring, call the larger ring the parent compound. Use the above steps for naming the cycloalkane and cycloalkyl portions of the compound.



Cyclopropylcyclobutane

When naming molecules with a cycloalkyl substituent, consider the prefix *cyclo–* when alphabetizing.

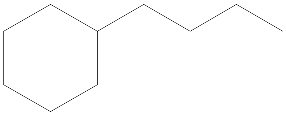


4-Cyclopropyl-1-ethyl-2-methylcyclohexane

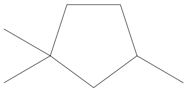
Exercise 2.7

Name the following cycloalkanes using the IUPAC system.

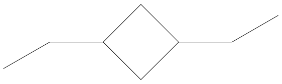
a)



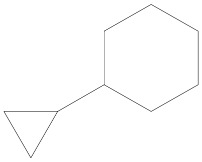
b)



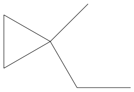
c)



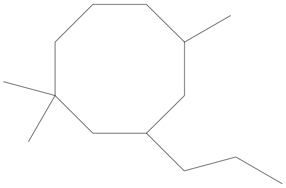
d)



e)



f)



Sample solution

a) To name the compound go through the steps covered in this section using only the ones that apply to this particular compound.

Step 1 Count the number of carbons in the ring. There are six. The parent name is hexane.

Step 2 Add the prefix *cyclo*– to the parent chain. This gives cyclohexane.

Step 3 Determine the name of the alkyl group. It has four carbons, so it is a butyl group.

Step 4 a) Determine the position of the substituent alkyl group on the ring. As there is only one, no number is required in the name.

These steps cover all the features of this compound. Its IUPAC name is butylcyclohexane.

2.7 Naming Complex Alkyl Groups

Because of the complexity of some alkyl groups, they are inconvenient to name following the steps covered in Sections 2.4 and 2.5. To name some of the simpler of these complex side chains, use the prefixes *n*–, iso, *sec*–, and *tert*–. While these prefixes are not a part of the IUPAC system, chemists commonly use them.

When using this system to name one of these complex alkyl groups, follow these steps.

Step 1 Use the IUPAC system to name the rest of the compound and to determine the position of the alkyl group.

Step 2 Count the number of carbons in the complex alkyl group to determine its name and use the appropriate prefix to show its arrangement.

a. The prefix *n*–

An alkyl group with one or two carbons forms only one possible isomer, so call it a methyl or ethyl group. An alkyl group with three or more carbons can form two or more possible isomers; thus, you need a way to show that the group is the straight chain isomer. The following structure illustrates the generalized structure of a straight chain alkyl group isomer. The values of *n* are 2 or more.

$$CH_3(CH_2)_n—$$

The prefix n– *is derived from the word* normal, *meaning an unbranched chain.*

Use the prefix ***n***– to name a straight chain isomer that contains three or more carbons. When naming molecules with the prefix *n*–, ignore the prefix when alphabetizing the name of the group. Two specific examples are the *n*-propyl and *n*-butyl groups.

$CH_3CH_2CH_2—$

n-Propyl group

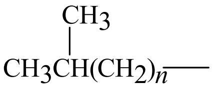
$CH_3CH_2CH_2CH_2—$

n-Butyl group

b. The iso prefix

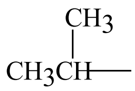
The iso prefix is not italicized because it is not separated from the name by a dash. The other prefixes are separated from the name by a dash and are italicized.

The prefix iso indicates a structure in which two methyl groups are bonded to the end of an alkyl side chain farthest from the point where the side chain bonds to the parent chain. The following structure illustrates a generalized structure for an isoalkyl group. The value of *n* is 0, 1, 2, or occasionally 3.

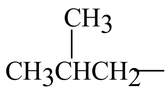


$$CH_3\overset{\overset{CH_3}{|}}{C}H(CH_2)_n—$$

Two specific examples of the iso structure are the isopropyl and the isobutyl groups. When naming molecules with an iso alkyl group, consider the prefix when alphabetizing the name of the group.


$CH_3\overset{CH_3}{\overset{|}{C}}H-$

Isopropyl group

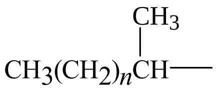

$CH_3\overset{CH_3}{\overset{|}{C}}HCH_2-$

Isobutyl group

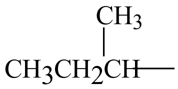
A secondary carbon bears two carbon—carbon bonds and is the carbon at the point where the group attaches to the main chain.

c. The prefix *sec*–

The prefix *sec*– indicates a structure in which the carbon that bonds the alkyl side chain to the parent chain bears a methyl group branch, making that carbon a **secondary** carbon. Following is the generalized structure of a *sec*-alkyl group. The value of *n* is 1, 2, or occasionally 3.


$CH_3(CH_2)_n\overset{CH_3}{\overset{|}{C}}H-$

A specific example is the *sec*-butyl group.


$CH_3CH_2\overset{CH_3}{\overset{|}{C}}H-$

sec-Butyl group

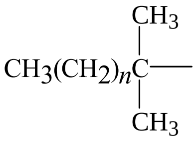
To name a molecule with a *sec*-alkyl group, ignore the prefix when alphabetizing the name of the group.

An exception to the use of the prefix *sec*– is when n=0. According to this system the name of the group should be *sec*-propyl. However, *sec*-propyl is not the accepted name for this group. Call the group isopropyl instead.

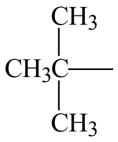
A tertiary carbon is the carbon at the point where the group attached to the main chain bears three carbon—carbon bonds.

d. The prefix *tert*–

The prefix *tert*– describes a structure in which the carbon that bonds the alkyl side chain to the parent chain bears two methyl group branches, making it a **tertiary** carbon. Below is the generalized structure for a *tert*-alkyl group. The value of *n* is 0, 1, or 2.

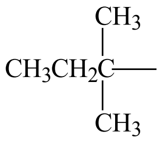

$CH_3(CH_2)_n\overset{CH_3}{\overset{|}{\underset{CH_3}{\underset{|}{C}}}}-$

Specific examples are the *tert*-butyl and *tert*-pentyl groups. As with the *n*– and *sec*– prefixes, ignore the *tert*– prefix when alphabetizing the name of the group.



$CH_3\underset{CH_3}{\overset{CH_3}{C}}—$

tert-Butyl group



$CH_3CH_2\underset{CH_3}{\overset{CH_3}{C}}—$

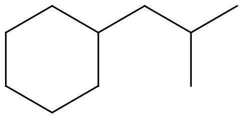
tert-Pentyl group
(Sometimes called a
tert-Amyl group)

Step 3 Write the name of the compound following this format:

#-prefix-alkylalkane

The following two step-by-step examples illustrate how to use this nomenclature system.

Step 1 Determine the parent chain. In this case the parent chain is a cyclohexane.

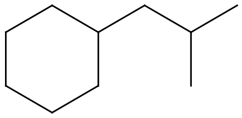


Step 2 Determine the position of the side chain. Because there is only one substituent on the ring its position number is 1. When writing the name of the compound, the position number is understood.

Step 3 Determine the side chain type. It is an iso group, because it has two methyl groups at the end of the side chain opposite the end bonded to the parent chain.

Step 4 Determine the name of the alkyl group by counting the number of carbons in the group. There are four, so it is a butyl group.

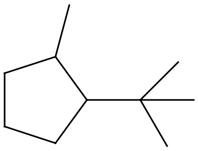
Step 5 Put all the parts of the name together in the following order: alkyl group prefix, alkyl group name, name of parent group. The name of this compound is isobutylcyclohexane.



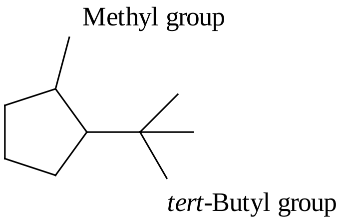
Isobutylcyclohexane

Example two is more complicated, but you follow the same steps.

Step 1 Determine the name of the parent chain. It is a ring structure that contains five carbons; thus, its name is cyclopentane.

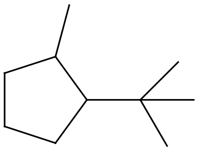


Step 2 Determine the names of the side chains. Because this compound contains two side chains, you must first know their names to alphabetize them so you can determine their positions. One is a methyl group; the other is a complex alkyl group. The complex alkyl group has four carbons and two methyl side groups attached to the carbon that is bonded to the ring, thus, it is a *tert*-butyl group.



Step 3 Determine the position of the two alkyl groups on the parent chain. Alphabetize the groups ignoring the prefix: *tert*–. The *tert*-butyl group comes first, and the methyl group comes next. Thus, the *tert*-butyl group's position is number 1, and the methyl group's position is number 2.

Step 4 Put all the names of parts together to get the name 1-*tert*-butyl-2-methylcyclopentane.

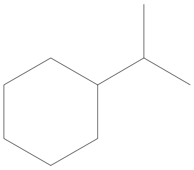


1-*tert*-Butyl-2-methylcyclopentane

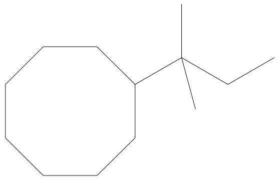
Exercise 2.8

Name the following compounds using the prefixes *n*–, iso, *sec*–, and *tert*–.

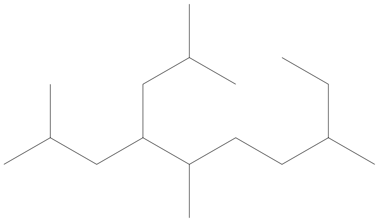
a)



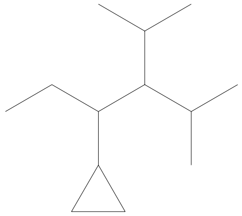
b)



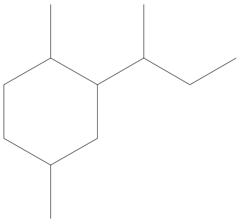
c)



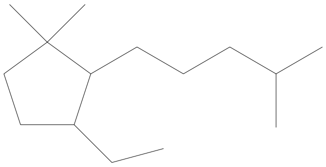
d)



e)



f)



Sample solution

b) To name this compound, follow these steps.

Step 1 Determine the name of the parent chain. In this case the parent chain is an eight-carbon ring, so the parent name is cyclooctane.

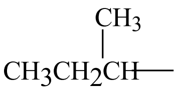
Step 2 Determine the name of the alkyl group side group. It has two methyl groups on the carbon bonding the group to the parent chain, thus, it is a *tert*– group. It has a total of five carbons, making the group a *tert*-pentyl group.

Step 3 When you put the names of all the parts of the compound together, you get the name *tert*-pentylcyclooctane.

Even though chemists use the *n*–, iso, *sec*–, and *tert*– prefixes, remember that they are not really a part of the IUPAC system. For these, and for even more complicated branched side chains, the

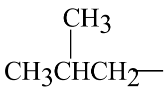
IUPAC nomenclature is the proper terminology. To name branched side chains using IUPAC system follow these steps.

Step 1 Find the longest chain of carbons starting with the carbon that bonds the alkyl chain to the parent chain.
Step 2 Number the carbons of the longest chain, beginning with C1 for the carbon at the point of attachment to the parent chain.
Step 3 Name and number any branches attached to the numbered side chain.
Step 4 When including the name of the branched side chain in the complete name of the compound, enclose the side chain name in parentheses. For example, the IUPAC name for the *sec*-butyl group is 1-methylpropyl and, when writing it as part of the name of the compound, enclose it in parentheses.



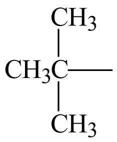
$$\mathrm{CH_3CH_2\overset{\displaystyle CH_3}{\overset{|}{C}}H-}$$

(1-Methylpropyl) group
(*sec*-Butyl group)



$$\mathrm{CH_3\overset{\displaystyle CH_3}{\overset{|}{C}}HCH_2-}$$

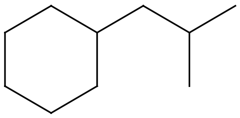
(2-Methylpropyl) group
(Isobutyl group)



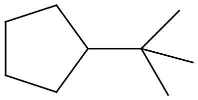
$$\mathrm{CH_3\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle CH_3}{\overset{|}{C}}}}-}$$

(1,1-Dimethylethyl) group
(*tert*-Butyl group)

Two examples using this nomenclature are as follows.



(2-Methylpropyl)cyclohexane



(1,1-Dimethylethyl)cyclopentane

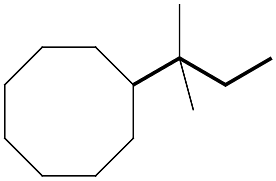
Exercise 2.9

Name the structures in Exercise 2.8 using the IUPAC system.

Sample solution

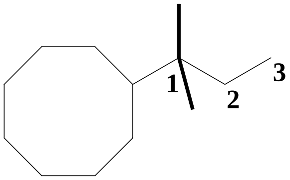
b) Name this compound the same way that you did when working Exercise 2.8, except substitute the following step for Step 2.

Step 2 Determine the name of the alkyl side chain.
a) Find the longest chain that begins with the carbon bonded to the ring. That chain includes three carbons, so it is a propyl group.



b) Number the chain. C1 is the carbon that bonds the alkyl group to the parent chain.

c) Name and number any groups attached to the longest chain. There are two methyl groups, and they are both bonded to C1.



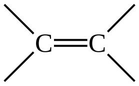
When you put the name together, you get (1,1-dimethylpropyl)cyclooctane.

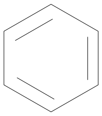
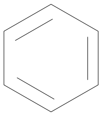
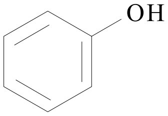
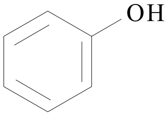
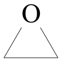
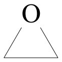
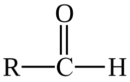
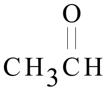
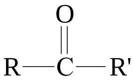
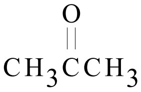
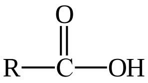
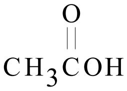
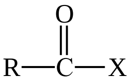
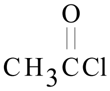
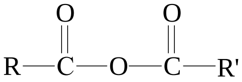
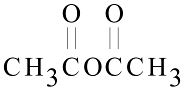
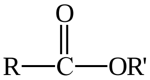
2.8 Functional Groups

The site of a functional group is the center of reactivity in a molecule. A functional group generally contains double or triple bonds and/or heteroatoms.

Alkanes are the simplest type of organic molecules, and they provide the backbone for many of the more complicated organic molecules, however, they are generally very unreactive. Possessing a **functional group** usually makes a molecule more reactive. Functional groups determine the types of chemical reactions that molecules will undergo and, to a large extent, the physical properties of the molecules to which they are attached.

Functional groups consist of carbon—carbon multiple bonds and/or carbon—heteroatom single and multiple bonds. Heteroatoms most commonly found in organic compounds are nitrogen, oxygen, sulfur, phosphorus, and the halogens. Table 2.3 lists the main functional groups with examples and their names. Subsequent sections in this and later chapters examine the nomenclature of the functional groups in detail.

Functional Group	Structure	Example	Name of Example
Double bond		$CH_2{=}CH_2$	Ethene or ethylene
Triple bond	$-C\equiv C-$	$CH\equiv CH$	Ethyne or acetylene

Functional Group	Structure	Example	Name of Example
Arene			Benzene
Organohalogen or alkyl halide	R—X (X = F, Cl, Br, or I)	CH_3CH_2Br	Bromoethane or ethyl bromide
Alcohol	R—OH	CH_3CH_2OH	Ethanol or ethyl alcohol
Thiol	R—SH	CH_3CH_2SH	Ethanethiol
Phenol			Phenol
Ether	R—O—R'	$CH_3CH_2OCH_2CH_3$	Ethoxyethane or diethyl ether
Epoxide			Epoxyethane or ethylene oxide or oxirane
Sulfide (or Thio ether)	R—S—R'	$CH_3CH_2SCH_2CH_3$	Diethyl sulfide
Amine	RNR'R'' (R' and R'' = H, alkyl, or aryl)	$CH_3CH_2NHCH_3$	N-Methylethanamine or ethyl methyl amine
Aldehyde	 $R-\overset{\overset{O}{\|}}{C}-H$	 $CH_3\overset{\overset{O}{\|}}{C}H$	Ethanal or acetaldehyde
Ketone	 $R-\overset{\overset{O}{\|}}{C}-R'$	 $CH_3\overset{\overset{O}{\|}}{C}CH_3$	Propanone or acetone
Carboxylic acid	 $R-\overset{\overset{O}{\|}}{C}-OH$	 $CH_3\overset{\overset{O}{\|}}{C}OH$	Ethanoic acid or acetic acid
Acyl halide	 $R-\overset{\overset{O}{\|}}{C}-X$ (X = Cl or Br)	 $CH_3\overset{\overset{O}{\|}}{C}Cl$	Ethanoyl chloride or acetyl chloride
Anhydride	 $R-\overset{\overset{O}{\|}}{C}-O-\overset{\overset{O}{\|}}{C}-R'$	 $CH_3\overset{\overset{O}{\|}}{C}O\overset{\overset{O}{\|}}{C}CH_3$	Ethanoic anhydride or acetic anhydride
Ester	 $R-\overset{\overset{O}{\|}}{C}-OR'$	 $CH_3\overset{\overset{O}{\|}}{C}OCH_2CH_3$	Ethyl ethanoate or ethyl acetate

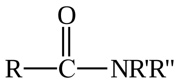
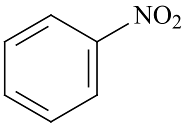
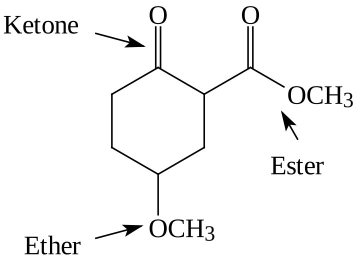
Functional Group	Structure	Example	Name of Example
Amide	 $\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}NR'R''}$ (R' and R" = H, alkyl, or aryl)	 $\mathrm{CH_3\overset{\overset{O}{\|}}{C}NHCH_2CH_3}$	N-Ethyl ethanamide or N-ethylacetamide
Nitrile	$\mathrm{R{-}C{\equiv}N}$	$\mathrm{CH_3C{\equiv}N}$	Ethanenitrile or acetonitrile
Nitro	$\mathrm{R{-}NO_2}$		Nitrobenzene

Table 2.3. The main functional groups in organic chemistry. The R stands for an alkyl group. An R' or R" stands for some alkyl group different than R.

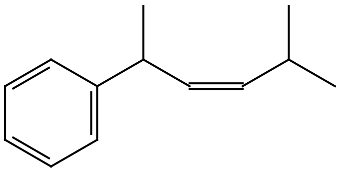
Consider the following example. It contains ether, ketone, and ester functional groups. Note that an ester contains portions that look like both the ether and the ketone. A common error that students make when learning functional group names is to call an ester a ketone-ether group.



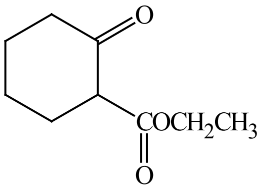
Exercise 2.10

Identify the functional groups present in each of the following molecules.

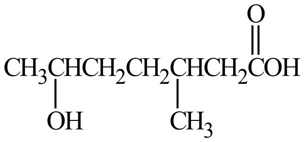
a)



b)

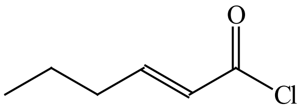


c)

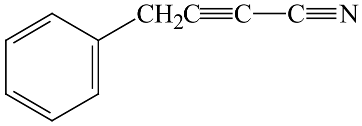


$CH_3\underset{OH}{\underset{|}{CH}}CH_2CH_2\underset{CH_3}{\underset{|}{CH}}CH_2\overset{O}{\overset{\|}{C}}OH$

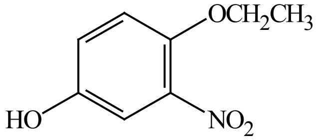
d)



e)

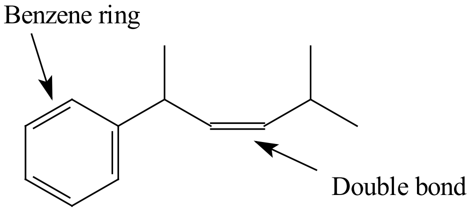


f)



Sample solution

a)



2.9 Naming Alkenes and Alkynes

Alkenes and cycloalkenes are hydrocarbons that have one or more carbon—carbon double bonds. The generalized molecular formula for alkenes is C_nH_{2n}. This formula is the same as the molecular formula for a cycloalkane; therefore, alkenes and cycloalkanes are constitutional, or structural, isomers.

Alkenes are occasionally referred to as olefins. Olefin is an old term meaning "oil forming" and comes from the fact that ethene, a gas, reacts with chlorine, a gas, to form an "oily" liquid product.

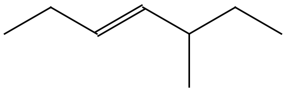
The way you name alkenes is quite similar to the way you name alkanes.

Step 1 Find the longest continuous chain of carbon atoms containing the double bond. This is the parent chain.
Step 2 Name this chain by replacing the —*ane* ending of the name of the alkane chain of the same length with —*ene*.
Step 3 Indicate the position of the double bond by numbering the parent chain from the end that gives the first carbon of the double bond the lowest number. Here are two examples that show how to number.

$CH_3CH_2CH{=}CH_2$
1-Butene
(not 3--butene)

$CH_3CH_2CH{=}CHCH_3$
2-Pentene
(not 3-pentene)

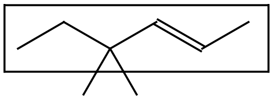
Because the double bond takes priority over other substituents in an alkene, sometimes the atoms of side chains and other functional groups must receive higher numbers than they otherwise would. For example, 5-methyl-3-heptene is the correct name for the following compound, not 3-methyl-4-heptene, even though the latter has a lower number for the methyl group.



5-Methyl-3-heptene

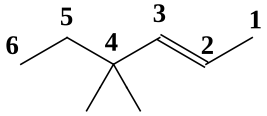
The following example shows step-by-step how to name an alkene.

Step 1 Find the longest chain of carbons containing the double bond. It contains six carbons.



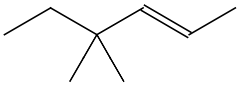
Step 2 Name the parent chain. Its name is hexene.

Step 3 Determine the position of the double bond in the parent chain. In this case, you number the parent chain from right to left because that gives the first carbon of the double bond the lowest number. The parent name is 2-hexene.



Step 4 Number and name the substituents. The compound has two methyl groups bonded to C4.

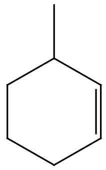
Step 5 Put together all the pieces of the name. The compound's complete name is 4,4-dimethyl-2-hexene.



4,4-Dimethyl-2-hexene

Naming cycloalkenes is similar to naming alkenes, except that you number the ring so that the double bond is *between* C1 and C2.

For example, the following compound is 3-methylcyclohexene, *not* 2-methylcyclohexene.



3-Methylcyclohexene

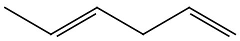
A type of organic compounds, called **polyenes**, contains two or more double bonds. For example, **dienes** have two double bonds, and **trienes** have three. To name a diene or a triene, follow the same steps for naming an alkene with these exceptions.

Polyene is the generalized name for a molecule that has more than one double bond. A diene is a molecule with two double bonds. A triene is a molecule with three.

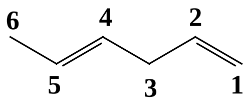
Step 1 Write the numbers indicating the locations of the double bonds separated by commas and followed by a hyphen.

Step 2 After the hyphen, write the parent name of the compound, changing the ending from —*ene* to —*diene*, if there are two double bonds, or —*triene*, if there are three, etc.

The following example demonstrates how to name a polyene.

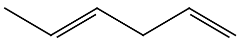


Step 1 Determine the length of the parent chain and the positions of the double bonds. The parent chain is six carbons long. There are two double bonds, and their positions are C1 and C4.



Step 2 Write the numbers of the locations of the double bonds followed by a hyphen: 1,4–.

Step 3 After the hyphen write the name of the parent chain with the –*diene* ending. The name of the compound is 1,4-hexadiene.



1,4-Hexadiene

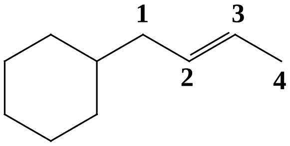
Special Types of Dienes

Two special types of dienes are the conjugated diene and the cumulated diene. In a conjugated diene, the double bonds are separated by only one single bond. In a cumulated diene, the double bonds share a carbon. Conjugated dienes are important because their chemical properties differ greatly from simple alkenes. Chapter 16 introduces conjugated dienes and their properties. Chapters 17 and 18 continue this study with benzene. The simplest conjugated diene is 1,3-butadiene, CH_2=CH—CH=CH_2. The simplest cumulated diene is 1,2-propadiene, CH_2=C=CH_2. 1,2-Propadiene is sometimes called allene.

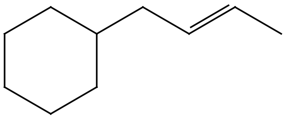
An alkenyl group is a side chain containing a double bond.

The generalized name for a side chain containing a double bond is **alkenyl**. Alkenyl side chain names are used when another name, especially a ring, would name a larger number of carbons in the molecule. To name an alkenyl side chain, use the same procedure that you use for naming an alkene with the following exceptions.

Step 1 Start numbering from the carbon that bonds the side chain to the parent chain.

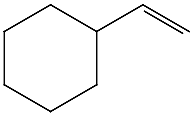


Step 2 When naming the side chain, use the —*enyl* suffix instead of —*ene*. Parentheses are often required so that you know the number belongs with the side chain.

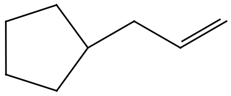


(2-Butenyl)cyclohexane

Many alkenyl side chains are better known by their common names than by their IUPAC names. Two of these are the ethenyl (CH_2=CH—) and 2-propenyl (CH_2=CHCH_2—) groups. Their common names are vinyl and allyl.



Vinylcyclohexane

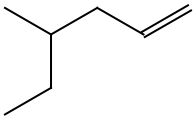


Allylcyclopentane

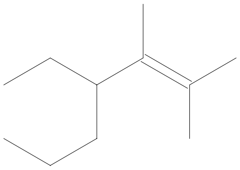
Exercise 2.11

Name each of the following molecules.

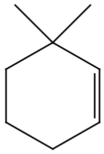
a)



b)

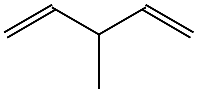


c)

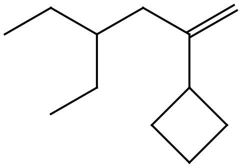


d) $CH_3(CH_2)_3CH{=}CH(CH_2)_3CH_3$

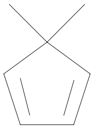
e)



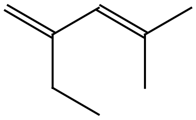
f)



g)



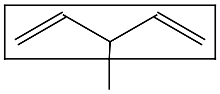
h)



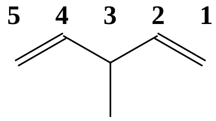
Sample solution

e) The following step-by-step process yields the correct answer.

Step 1 Determine which carbons make up the parent chain. There are five carbons with two double bonds, so the parent chain is a pentadiene.

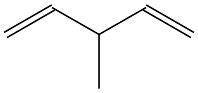


Step 2 Determine the positions of the double bonds. They are on C1 and C4.



Step 3 Determine the name and position of the side chain. It is a methyl group on C3.

Step 4 Put together all the parts. The name of the compound is 3-methyl-1,4-pentadiene.



3-Methyl-1,4-pentadiene

Alkynes are hydrocarbons that contain one or more carbon—carbon triple bonds.

Chemists often refer to **alkynes** as acetylenes from the common name of the simplest compound of this type, ethyne ($HC\equiv CH$), which is usually called acetylene. Follow these steps to determine the IUPAC name of an alkyne.

Step 1 Find the parent chain. As with alkenes, it must contain the triple bond. The parent chain contains five carbons.

$$CH_3CH_2C\equiv CCH_3$$

Step 2 Name the parent chain by substituting the —*yne* ending for the —*ane* ending of the parent carbon chain. The name of the parent chain is pentyne.

Step 3 Indicate the position of the triple bond by numbering the parent chain from the end that gives the first carbon of the triple bond the lowest number. The position of the triple bond is C2.

Step 4 Place the number of the position of the triple bond first, followed by a hyphen followed by the name of the parent chain. The name of the compound is 2-pentyne.

$$CH_3CH_2C\equiv CCH_3$$

2-Pentyne

Sometimes the parent chain of a molecule contains both a double bond and a triple bond. To name such a compound use the same procedure as you do for determining the parent chain. Then determine the position and name of each multiple bond with the following steps.

Step 1 Find the longest continuous chain containing both the double and triple bonds.

Step 2 Number the chain so that the multiple bonds get the lowest possible numbers.

Step 3 Number the position of the double bond on the parent chain. In the following example that is C1.

$$CH_2{=}CHCH_2C{\equiv}CCH_3$$

Step 4 Use the *—en* ending to indicate the name of the parent chain. The parent chain contains six carbons, so that gives the name hexen—.

Step 5 For the triple bond, use the *—yne* ending along with the number identifying the triple bond's position on the parent chain. Number the parent chain so that either the double or triple bond takes precedence over any other substituent, irrespective of whether the *—en* or *—yne* gets the lowest number. The name of the example compound is 1-hexen-4-yne.

$$CH_2{=}CHCH_2C{\equiv}CCH_3$$

1-Hexen-4-yne

However, when both groups could get the same number, the *–en* takes priority and receives the lower number.

$$CH_3CH{=}CHCH_2C{\equiv}CCH_3$$

2-Hepten-5-yne

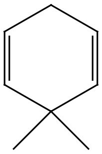
(*not* 5-Hepten-2-yne)

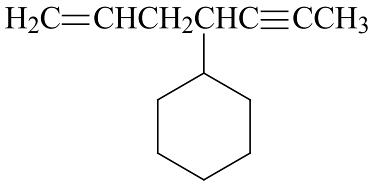
Exercise 2.12

Provide either the IUPAC name or a structural formula for the following compounds.

a) 5-methylcyclooctyne

b) 3-ethyl-2,4,4-trimethyl-2-octen-5-yne

c) 

d) 

$$H_2C{=}CHCH_2CHC{\equiv}CCH_3$$

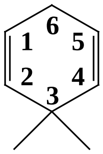
e) $CH_3C\equiv C—C\equiv C—C\equiv CCH_2CH_3$

Sample solution

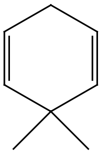
c) The following step-by-step process yields the name for this compound.

Step 1 Determine and name the parent chain. The parent chain is a ring with six carbons. It also contains two double bonds. Thus, the name of the parent chain is cyclohexadiene.

Step 2 Determine the positions of the double bonds. Remember that you want to number in such a way as to give the methyl groups their lowest possible number, too.



Step 3 Put the various parts together with commas separating the numbers and hyphens separating the numbers and words. The name of this compound is 3,3-dimethyl-1,4-cyclohexadiene.

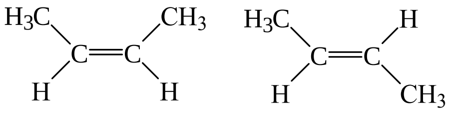


3,3-Dimethyl-1,4-cyclohexadiene

2.10 Naming Alkenes, Part II

Because alkenes do not rotate about the double bond they can exhibit ***cis-trans*** isomerism. For example, 2-butene has two possible stereoisomers. In one, both methyl groups are on the same side of the double bond; in the other, the methyl groups are on opposite sides of the double bond.

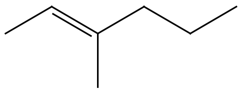
Cis *comes from a Latin word meaning "on the same side" and* trans *from the Latin word meaning "across".*



cis *trans*

The names for the two isomers of 2-butene are *trans*-2-butene and *cis*-2-butene.

For more complex structures, the *cis* or *trans* designation refers to the parts of the main carbon chain in which the double bond is found. For example, the following compound is *trans*-3-methyl-2-hexene because the substituents on the main chain have a *trans* relationship to each other.

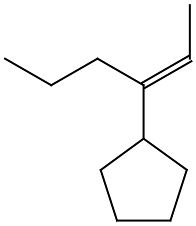


trans-3-Methyl-2-hexene

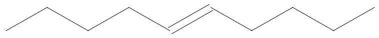
Exercise 2.13

Name each of the following molecules using IUPAC rules.

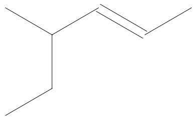
a)



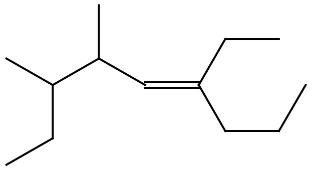
b)



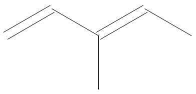
c)



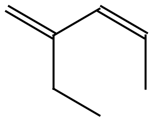
d)



e)



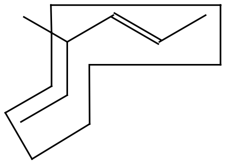
f)



Sample solution

c) To name this compound, follow these steps.

Step 1 Determine the parent chain. The longest chain that contains the double bond has six carbon atoms with the position of the double bond at C2. Thus, the parent chain is 2-hexene.



Step 2 The substituent is a methyl group on C4.

Step 3 The two substituents attached to the double bond are on opposite sides of the double bond and thus are *trans* to each other.

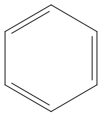
The name of this compound is *trans*-4-methyl-2-hexene.

2.11 Arenes

Arenes are cyclic hydrocarbons with alternating single and double bonds.

Aromatic hydrocarbons are arenes based on benzene.

Arenes are cyclic hydrocarbons that contain three single bonds and three double bonds conjugated in a six-carbon ring. Arenes are usually derived from benzene. Another commonly used name for arenes is **aromatic hydrocarbons**.



Benzene

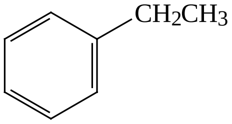
During the late 19th century, chemists isolated a number of other compounds similar to benzene. Among the similarities of these compounds was a distinctive pleasant odor. Because of this odor, chemists called this class of polyenes aromatic hydrocarbons. In time, aromatic hydrocarbons, or arenes, came to include all compounds that have the six-carbon ring structure drawn with alternating single and double bonds—whether or not they have the distinctive pleasant odor. Although arenes have double bonds, they are distinctly different from the common alkenes. Chemists call the chemical properties that are associated with the type of conjugation of double bonds found in arenes **aromaticity**.

Aromaticity refers to the special stability of benzene and benzene-like compounds. Chapter 17 explains this special stability.

The following steps are used for naming aromatic hydrocarbons.

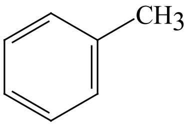
Step 1 Name aromatic hydrocarbons as **derivatives** of benzene. For example, ethylbenzene is a benzene ring with an ethyl group attached.

A derivative of benzene is a benzene ring with one or more other groups bonded to it.



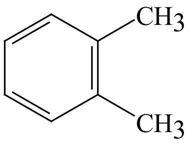
Ethylbenzene

Step 2 Not all benzene derivatives have the word benzene in their names. A number of these derivatives have their own unique names. For example, methylbenzene is more frequently known as toluene. Most of these unique names will be covered in more detail in Chapter 17.

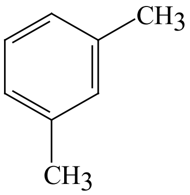


Toluene
(or Methylbenzene)

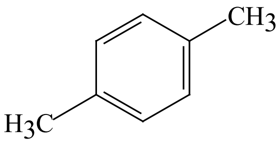
Step 3 When a benzene ring bears two side chains or groups, indicate their positions by numbering them or, as is more common, by using the prefixes *ortho*–, *meta*–, and *para*–, abbreviated as *o*–, *m*–, and *p*–. *Ortho*– indicates a 1,2-disubstituted benzene ring, *meta*– indicates 1,3, and *para*– names a 1,4 arrangement. Ignore the positions of the double bonds in the benzene ring when numbering the chains or groups. Number the ring so as to have the lowest sum of numbers, giving the first substituent the number 1.



1,2-Dimethylbenzene
or *o*-Dimethylbenzene
or *o*-Xylene



1,3-Dimethylbenzene
or *m*-Dimethylbenzene
or *m*-Xylene



1,4-Dimethylbenzene
or *p*-Dimethylbenzene
or *p*-Xylene

A benzene ring can be a functional group of a larger molecule. Its molecular formula is (C_6H_5—).

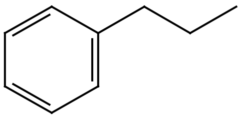
A phenyl group is a benzene ring substituent attached to the parent molecule.

Step 4 To name a benzene group as a side chain, call it a **phenyl group**. (Do not call a benzene ring functional group a benzyl group as would seem likely from the naming of the previous substituent groups. There is a benzyl substituent group, but its formula is $C_6H_5CH_2$—.)

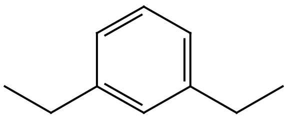
Exercise 2.14

Name each of the following aromatic hydrocarbons.

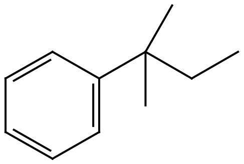
a)



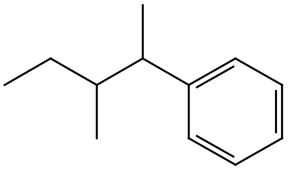
b)



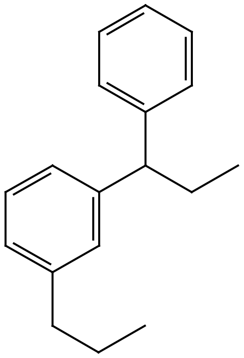
c)



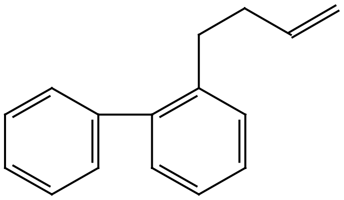
d)



e)



f)

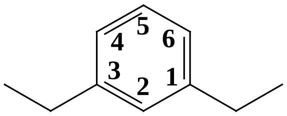


Sample solution

b) The following step-by-step process names this compound.

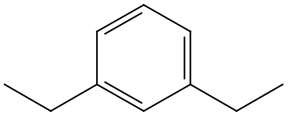
Step 1 Name the compound as a derivative of benzene. Thus, the parent name of the compound is benzene.

Step 2 Number the positions of the side chains to get the smallest total. Both are ethyl groups, so both are alphabetically the same, and either could receive the number one. Start with the ethyl on the right and number to the left to give the smaller total.



Step 3 Because the compound is a 1, 3 substituted benzene, you can call it by the *meta* prefix.

Step 4 Put the name together. The name is 1,3-diethylbenzene or *m*-diethylbenzene.



1,3-Diethylbenzene
or *m*-Diethylbenzene

2.12 Organohalogens

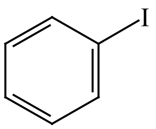
Except for Section 2.8, which presented a table listing the various functional groups important in organic chemistry, the preceding sections covered the naming of hydrocarbons, or organic compounds that contain only carbon and hydrogen. Section 2.12 introduces the nomenclature of those compounds that contain heteroatoms. Remember a heteroatom is any atom other than carbon or hydrogen in an organic molecule. Compounds with one or more halogen atoms are organohalogens. The halogens include fluorine (F), chlorine (Cl), bromine (Br), and iodine (I), with chlorine and bromine being the most common.

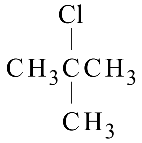
To name organohalogens, follow these steps.

Step 1 Consider organohalogens as substituted hydrocarbons. They have the same priority as alkyl groups in naming. Use the prefixes *bromo–*, *chloro–, fluoro–*, and *iodo–*.

Step 2 List any halogens alphabetically, along with any alkyl groups:

CH_3Cl





$$\begin{array}{c} Cl \\ | \\ CH_3CCH_3 \\ | \\ CH_3 \end{array}$$

Chloromethane Iodobenzene 2-Chloro-2-methylpropane

The rules are found in Section 2.5, page 000.

Common Names for Some Organohalogen Compounds

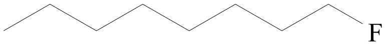
Most organohalogen compounds are named according to the standard IUPAC rules of nomenclature. The general form of the common name for many of these compounds is alkyl halide. Some examples are methyl chloride, isopropyl iodide, *sec*-butyl chloride, and *tert*-butyl bromide. There are a few compounds that do not follow this form. In most chemistry laboratories, the following names are used more often than the IUPAC names.

CH_2Cl_2	$CHCl_3$	CCl_4
Methylene chloride	Chloroform	Carbon tetrachloride

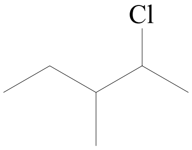
Exercise 2.15

Write a name for each of the following organohalogens.

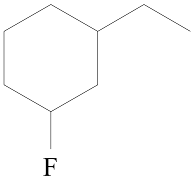
a)



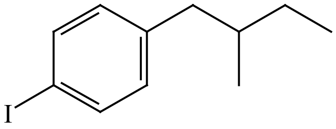
b)



c)

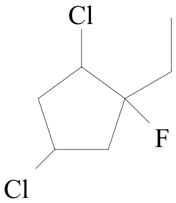


d)



e) $Br(CH_2)_3CH{=}CHCH_2CH_2CH_3$

f)

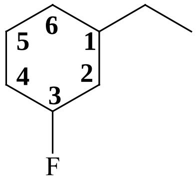


Sample solution

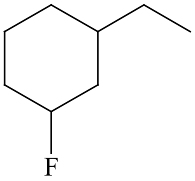
c) The following step-by-step analysis names this compound:

Step 1 Find the parent chain. The parent chain is a six-membered hydrocarbon. Its name is cyclohexane.

Step 2 Number the side chains. There are two, an ethyl group and a fluorine. Alphabetically ethyl comes first, so it gets the number one. Give the fluorine the number 3, not the number 5.



Step 3 Put the name together. The name of the compound is 1-ethyl-3-fluorocyclohexane.



1-Ethyl-3-fluorocyclohexane

2.13 Using Molecular Formulas

An acyclic structure has no rings.

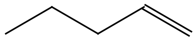
The molecular formula of a compound includes the chemical symbols of the various elements contained in one molecule of that compound and numbers that tell how many atoms of each element is present. However, using a molecular formula to draw a structural formula is not easy, as the molecular formula does not tell you what types of bonds are present or their locations. The generalized molecular formula for straight chain, or **acyclic**, alkanes is C_nH_{2n+2}. When the molecular formula for a compound differs from the alkane molecular formula having the same number of carbons, then you must account for the deviations. The most common deviations are a reduction in the number of hydrogen atoms or the addition of heteroatoms.

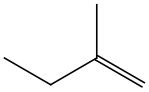
When a compound deviates from the parent molecular formula, consider first whether or not the compound is saturated. Remember a saturated hydrocarbon is one that has only single bonds and an unsaturated hydrocarbon is one that contains double or triple bonds. A special case is a compound that contains a ring. Although a

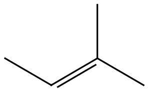
Two fewer hydrogens than are present in the parent formula indicate a unit of unsaturation.

cycloalkane is saturated, a compound with one ring has the same molecular formula as an acyclic compound with one double bond. A molecule with two fewer hydrogens than are found in its parent molecular formula has one **unit of unsaturation**. For example, one unit of unsaturation may correspond to a double bond between two atoms or to a ring. Two units of unsaturation may correspond to a triple bond between two atoms, two double bonds, two rings, or one ring and one double bond.

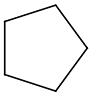
Pentane has the molecular formula C_5H_{12}. It is a saturated compound with no rings or double bonds. Another compound, with the formula C_5H_{10}, has the same number of carbons but two fewer hydrogens; thus, it has one unit of unsaturation. This means that it could contain one double bond or one ring. If the compound C_5H_{10} contains a double bond, it could be 1-pentene, 2-methyl-1-butene, 2-methyl-2-butene, or other possibilities.

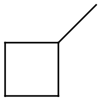

1-Pentene

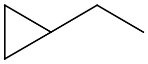

2-Methyl-1-butene


2-Methyl-2-butene

If it has a ring, it could be cyclopentane, methylcyclobutane, ethylcyclopropane, or other possibilities.


Cyclopentane


Methylcyclobutane


Ethylcyclopropane

As you can see, the molecular formula alone is not sufficient to determine whether or not a compound with a unit of unsaturation has a ring or a multiple bond. To make such a determination, you must obtain experimental evidence. You could get this evidence from chemical reactions or spectroscopy. In most cases, you need both types of additional data before you can assign the structure.

Exercise 2.16

Draw all possible structures having the molecular formula C_5H_{10}. Name them using the IUPAC system.

The presence of oxygen or sulfur in a molecular formula does not affect the determination of units of unsaturation. If a halogen is present, count it as equivalent to a hydrogen atom. A generalization that you can make is—compounds with four or more units of unsaturation are usually aromatic. However, for each nitrogen or phosphorus present, subtract one hydrogen before calculating the number of units of unsaturation. For example, to find the number of units of unsaturation the molecular formula C_4H_9N first subtract one hydrogen from the nine listed to yield eight. With four carbons, a saturated alkane has ten hydrogens. Thus, this molecule has one unit of unsaturation.

Exercise 2.17

How many units of unsaturation are present in each of the following molecular formulas?

a) C_8H_{14}
b) $C_6H_{13}N$
c) $C_5H_6Cl_2$
d) $C_6H_{12}O_6$

Sample solution

a) An acyclic alkane with eight carbons has 18 hydrogens ($2n + 2$ where $n = 8$). Since this formula has 14 hydrogens, it is “missing” 4 hydrogens so it has two units of unsaturation.

Key Ideas from Chapter 2

☐ Organic molecules have a skeleton of carbon atoms, often with functional groups attached.

☐ Hydrocarbons include only carbons and hydrogens. There are two classes of hydrocarbons: saturated and unsaturated. Saturated hydrocarbons are called alkanes and contain only single bonds. Unsaturated hydrocarbons are called alkenes, alkynes, or arenes and include both single and double or triple bonds.

☐ Homologs are hydrocarbons that differ from one another only in the number of methylene groups (—CH_2—) present.

☐ To name a saturated hydrocarbon:
  1. Find the longest chain of carbon atoms. This is the parent chain. Name it.
  2. Identify and alphabetize all the alkyl groups attached to the parent chain.

3. Number the carbon atoms in the parent chain so that the attached groups get the lowest possible numbers.

❑ A functional group is an atom or group of atoms bonded to a hydrocarbon that plays a major role in determining the physical and chemical properties of the compound.

❑ To name a molecule with a functional group:

1. Find the longest chain that includes the functional group.
2. Number that chain so that the functional group gets the lowest possible number.
3. Name all other groups alphabetically.

❑ A molecular formula gives information about the number of units of unsaturation in an organic compound. Use this information to assist you in determining the number of multiple bonds and/or rings in the molecule.

Richard F. Daley and Sally J. Daley
www.ochem4free.com

Organic Chemistry

Chapter 3

Molecular Conformations

Chapter 3

Molecular Conformations

Chapter Outline

3.1 Representing Three-Dimensional Molecules in Two Dimensions
Different methods for drawing a molecule in three dimensions

3.2 Dihedral Angles
Examination of the angles between atoms on adjacent atoms

3.3 The Conformations of Ethane
Rotation about the C—C bond in ethane

3.4 Conformational Analysis of Butane
Rotation about the C2—C3 bond in butane

3.5 Angle Strain in Cycloalkanes
The effect of bond angle strain on the stability of cycloalkanes

3.6 Conformations of Cyclohexane
The effect of bond angles on the shape of cyclohexane

3.7 Conformational Inversion of Cyclohexane
An examination of the various changes in the conformation of cyclohexane

3.8 Conformational Analysis of Monosubstituted Cyclohexanes
How a substituent affects the conformation of cyclohexane with a single substituent

3.9 Naming Stereoisomers
Naming *cis* and *trans* cycloalkanes

3.10 Conformational Analysis of Disubstituted Cyclohexanes
The effect of adding a second substituent to cyclohexanes

3.11 Conformations of Other Cycloalkanes
The shapes of cyclopropane, cyclobutane, and cyclopentane

3.12 Naming Polycyclic Ring Systems
Naming spiro and bicyclic ring systems

3.13 Stereochemistry of Polycyclic Ring Systems
Spiro, fused, and bridged bicyclic systems

Objectives

- ✔ Learn how to draw three-dimensional molecules in two dimensions and how to visualize three-dimensional molecules from two-dimensional representations
- ✔ Understand the conformational preferences in the structure of acyclic compounds
- ✔ Be able to name cycloalkanes, substituted cycloalkanes, and bicyclic compounds
- ✔ Know how ring size affects the stability of cycloalkanes
- ✔ Visualize the different conformations of cyclohexane
- ✔ Recognize how one or two substituents affect the conformation of cyclohexane
- ✔ Know the shapes of cyclopropane, cyclobutane, and cyclopentane
- ✔ Understand the various types of bicyclic compounds

> Full of nimble fiery and delectable shapes.
> —Shakespeare

The rotational symmetry of a σ bond (a carbon—carbon single bond) allows the atoms or groups of atoms connected by that bond to rotate about it. As a result of this kind of rotation, many molecules assume several different three-dimensional shapes. Chemists call these different shapes **conformations**. Some conformations of a particular molecule are more stable than others are. Knowing this will help you understand how many chemical reactions proceed.

Conformations are the shapes a molecule assumes by rotating about its bonds.

Conformational analysis is the examination of the positions a molecule takes and the energy changes it undergoes as it converts among its different conformations. This chapter covers in detail the conformational analysis of ethane, butane, and cyclohexane. It also gives an overview of other cyclic and polycyclic hydrocarbons.

Conformational analysis is the study of the effect of rotation on the properties of a molecule.

Because each of the various conformations of a molecule has different properties, the conformation the molecule normally adopts has a profound influence on its physical and chemical properties. Organic chemists use conformational analysis to understand the behavior of molecules in chemical reactions. Biochemists and molecular biologists also use conformational analysis to study the ways molecules interact with each other in living systems.

3.1 Representing Three-Dimensional Molecules in Two Dimensions

For a reaction to proceed the conformation of the individual molecules must allow them to collide at points where they will react. Conformational analysis visualizes the three-dimensional structures of various conformations. Because two-dimensional illustrations are limiting, invest in a set of molecular models and learn how to use them. Make a model of any molecule you are studying and twist the model back and forth into the molecule's various possible conformations. Continue manipulating the model until you have a thorough understanding of all the possible conformations. Working with a three-dimensional model set will help you learn to visualize molecular structures from a two-dimensional drawing.

Molecular models are an invaluable aid for visualizing the interactions between atoms in a molecule and in seeing how a chemical reaction proceeds. Even the most experienced chemist makes frequent reference to models in order to clarify questions of molecular structure. As you work your way through this text, using a molecular model set will make learning the material much easier.

A molecular model of ethane (CH_3CH_3) is shown in Figure 3.1. The white spheres represent the hydrogen atoms, and the black spheres represent the sp^3 hybridized carbon atoms. The lines connecting the spheres represent the bonds between the atoms. Make a model of ethane to help you visualize this structure in three dimensions.

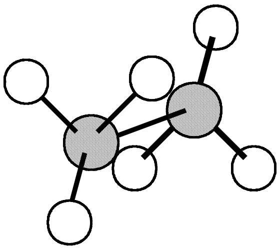
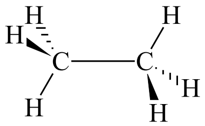


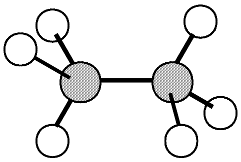
Figure 3.1. A ball-and-stick model of ethane.

A wedge-and-dash representation shows a three-dimensional molecule using wedges to show the bonds projecting toward you, dashed wedges to show the bonds projecting away from you, and lines to show the bonds in the plane of the page.

To represent the three-dimensional structures of molecules in two-dimensional drawings, chemists have developed two major types of notations. The one they use most frequently is the **wedge-and-dash** representation. In this example, compare the wedge-and-dash representation with the ball-and-stick model.



Wedge-and-dash representation

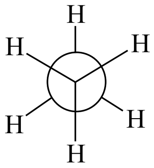


Ball-and-stick model

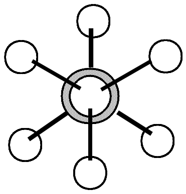
A wedge-and-dash representation shows the side of the carbon—carbon bond being drawn. The wedges (◀) represent bonds that project out of the plane of the paper toward you, the lines are bonds in the plane of the paper, and the dashed wedges (¦¦¦¦) represent bonds receding away from you behind the plane of the paper.

The Newman projection shows the relationships of groups bonded on adjacent carbon atoms.

The second type of two-dimensional notation used by chemists to represent structures is the **Newman projection**, which was devised by Professor Melvin S. Newman from Ohio State University. A Newman projection shows the two bonded carbons under consideration with one directly in front of the other.



Newman projection



Ball-and-stick model

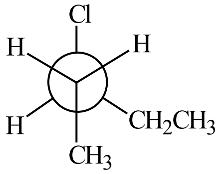
In a Newman projection the point represents the front carbon, the open circle represents the rear carbon, and the bonds connecting the other atoms with the carbons are shown emerging from the point and the circle. Be careful to clearly terminate the bond lines of the rear carbon atom at the perimeter of the circle.

These two structural representations illustrate different aspects of molecular geometry. The wedge-and-dash helps to visualize the molecule in three dimensions. The Newman projection shows the angles between atoms on adjacent carbons.

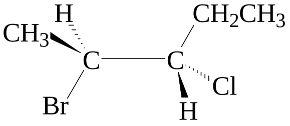
Exercise 3.1

Assign IUPAC names to each of the following structures and draw the other type of two-dimensional representation for each. Be careful to arrange the groups in exactly the same way, so you will be illustrating the same conformation.

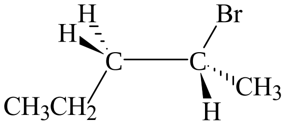
a)



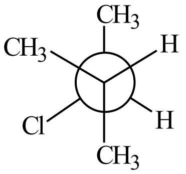
b)



c)

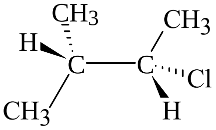


d)



Sample solution

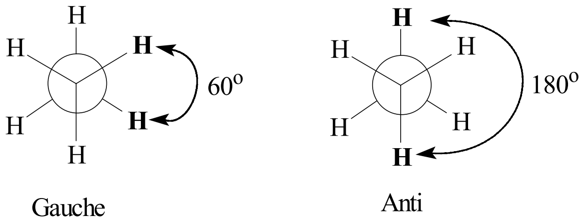
d) The IUPAC name is 2-chloro-3-methylbutane. You were shown the Newman projection so the wedge-and-dash representation is:



3.2 Dihedral Angles

The σ bond between two carbons permits the two carbons to rotate freely in relation to each other. With your molecular model of ethane, you can twist, or rotate, the carbons around the C—C bond to see the various conformations that ethane forms. Grasp a hydrogen from each CH$_3$ group, or in some way mark them, so you can remember which hydrogen in each CH$_3$ group is rotating in relation to the other. Turn your model so that you are looking at the carbons lined up one in front of the other. Then twist the marked hydrogens to match the Newman projections shown below. When the angle between two marked hydrogens is 60^{o}, chemists call this spatial relationship the **gauche** conformation. When the angle is 180^{o}, they call the relationship the **anti** conformation.

In the gauche spatial relationship, two substituents on adjacent carbons are 60^{o} apart in the Newman projection. In the anti spatial relationship they are 180^{o} apart.



In a staggered conformation, a bond on one carbon appears midway between the bonds on an adjacent carbon in a Newman projection.

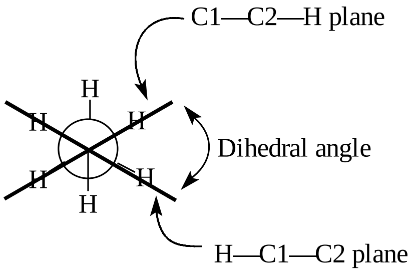
In an eclipsed conformation, a bond on one carbon is superimposed over one on the second in a Newman projection.

Dihedral angles are the angles between two bonds on adjacent atoms when you look at a Newman projection.

The definition of torsion is "twisting" of the bonds.

Chemists call a conformation that has only gauche or anti relationships **staggered**. Both of the structures drawn above are staggered. When the angles between adjacent substituents are 0°, the molecule is in an **eclipsed** conformation. Chemists talk of the atoms in ethane having either a gauche, anti, or eclipsed conformation. Keep in mind that ethane has an infinite number of additional conformations that differ from each other by infinitesimal increments of the angles between the two methyl groups.

The angles between the hydrogens on the two methyl groups of ethane are called the **dihedral**, or **torsional**, **angles**. The dihedral angle is the angle formed when one H—C1—C2 plane intersects with one C1—C2—H plane. Each conformation has a characteristic dihedral angle.



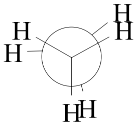
Understanding dihedral angles is an important part of conformational analysis.

Exercise 3.2

Using both a wedge-and-dash representation and a Newman projection, draw the eclipsed conformation of ethane.

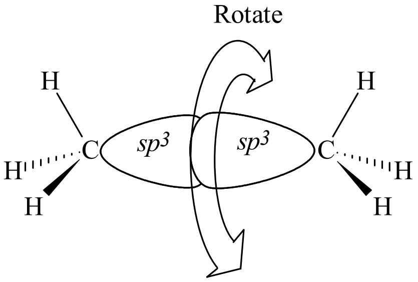
Sample solution

The Newman projection of eclipsed ethane looks like this:



Shapes of Alkanes

The basis for the shapes of alkanes is the ability of a carbon atom to *sp*^{3} hybridize with a tetrahedral geometry and four bonds. Each of these four bonds connects to either a carbon or a hydrogen atom. Also, each bond allows the free rotation of one atom with respect to the other. The following figure illustrates the rotation of one carbon with respect to the other carbon in ethane.



The linear overlap of two *sp*^{3} hybridized orbitals in the carbon—carbon σ bond in ethane allows the free rotation of one carbon with respect to the other.

Rotation about a single bond occurs relatively rapidly. For example, at room temperature, rotation around the C—C bond in ethane occurs millions of times a second. The reason for this rapid rotation, as suggested by molecular orbital theory, is a single bond has internuclear symmetry and therefore, no basis for hindered rotation. That is, a single bond has no preferred orientation of overlap, nor does it change in electron density because of rotation; thus, rotation should occur freely. However, experimental data published in the 1930s demonstrated that, contrary to theory, simple acyclic molecules, such as ethane, do have a small energy barrier of about 3-5 kcal/mole to free rotation about the carbon—carbon bond.

3.3 The Conformations of Ethane

Figure 3.2 is an energy diagram that shows how the internal energy of ethane changes as one of its methyl groups rotates with respect to the other. The plot shows the relative angle on the horizontal axis and the energy change on the vertical axis. Use your model of ethane as you look at this graph. Understanding the energy relationships it diagrams can help you later in understanding many chemical and physical processes.

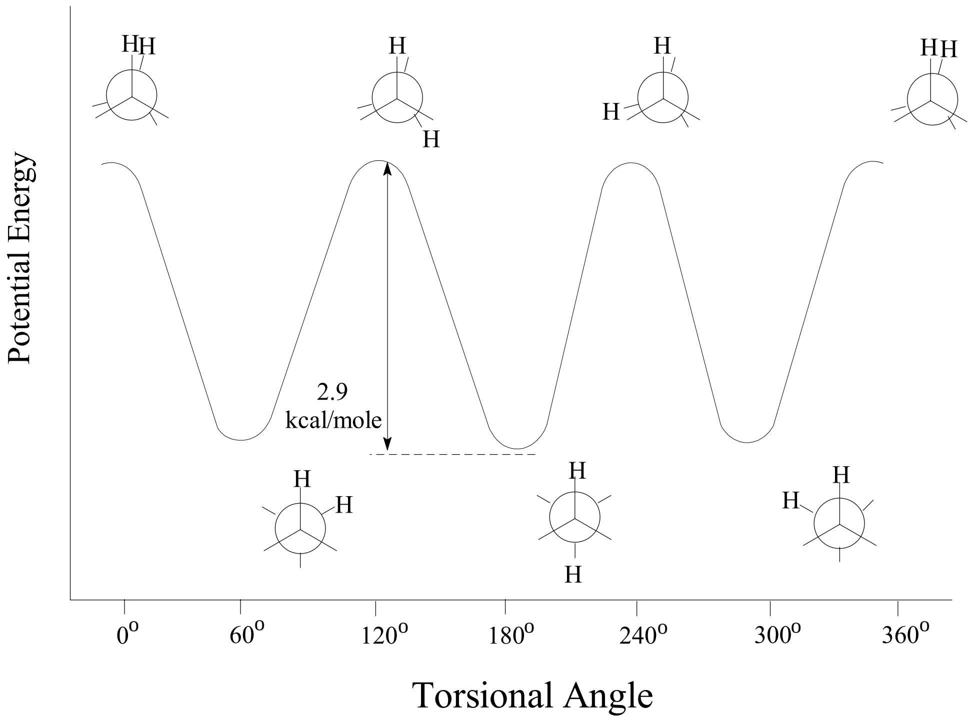


Figure 3.2. Energy diagram for rotation in ethane. Only two of the hydrogens are shown for clarity. For ethane, the rotational energy barrier is 2.9 kcal/mole.

Among the various conformations of ethane, the one with the least energy is the most stable. The graph in Figure 3.2 indicates that the staggered conformations are 2.9 kcal/mole lower in energy than the eclipsed conformations. The three staggered conformations correspond to the energy minima, and the three eclipsed conformations correspond to the energy maxima. Of course, distinguishing between the various eclipsed or staggered conformations is impossible because the hydrogens are all identical.

A staggered conformation of ethane is more stable than an eclipsed conformation because the staggered conformation maximizes the separation of the electron pairs in the molecular orbitals of the C—H bonds. In the eclipsed conformation, the hydrogens are closer; thus, the repulsions of the electron pairs are greater. Chemists call this increase of energy associated with eclipsed bonds on adjacent atoms **torsional strain**. Figure 3.3 illustrates the change in distance between the C—H bonds in the staggered and eclipsed conformations of ethane.

Torsional strain is the increase in energy due to eclipsing interactions in a molecule.

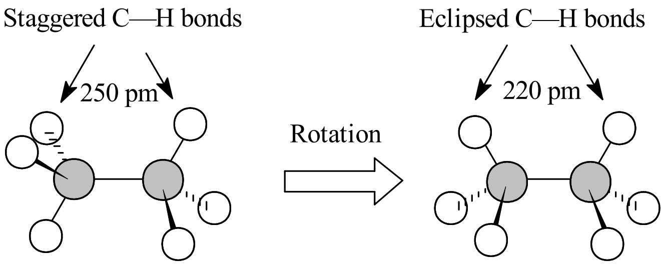


Figure 3.3. The C—H bonds of adjacent carbon atoms of ethane are closer together in the eclipsed conformation (220 pm) than in the staggered conformation (250 pm).

The energy barrier to rotation for different substituents varies with the size of the group on the molecule. Table 3.1 lists the sizes for substituents found in a variety of organic molecules. The larger the group on the molecule the closer that group will be to another group on an adjacent carbon atom. Consequently the barrier to free rotation increases.

Atom or Group	Size (pm)	Atom or Group	Size (pm)
H	120	Cl	180
N	150	Br	195
O	140	I	215
P	190	CH_3	200
S	185	CH_2	200
F	135		

Table 3.1. Selected van der Waals radii, measured in picometers (pm).

The van der Waals radius of an atom, or group of atoms, is the distance from the center of the electron cloud surrounding the atom or group to its outer edge.

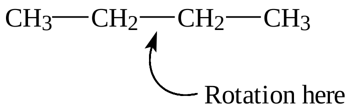
The van der Waals strain is a repulsion that arises when two groups come close to each other.

The van der Waals Radius and van der Waals Strain

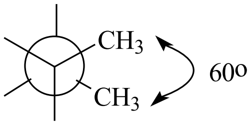
Every atom or group of atoms has a measure of size called its **van der Waals radius**. When two groups that are not bonded to each other get within close distance of their van der Waals radii, they begin repelling one another. The electrons surrounding one group repel the electrons surrounding the other group. The van der Waals radii indicate how close two groups can approach each other before these electron-electron repulsions occur. Chemists call such repulsion **van der Waals strain**. Table 3.1 has a list of the van der Waals radii of some selected atoms and groups that are important in organic chemistry.

3.4 Conformational Analysis of Butane

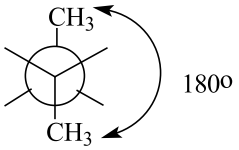
Make a model of butane and twist it into its different conformations as you read through this section. Consider only the conformations related to the rotation about the C2—C3 bond.



The structure of butane has two distinctly different staggered conformations. In one, the two methyl groups have a gauche conformation. In the other, the two methyl groups have an anti conformation. In the gauche conformation, the torsional angle between the two methyl groups is 60°. For the anti conformation, the two methyl groups have a torsional angle of 180°.



Gauche



Anti

The anti and gauche conformations of butane have an energy difference of 0.8 kcal/mole. The anti conformation is more stable than the gauche conformation because the two methyl groups are farther apart in the anti conformation. Thus, the anti conformation has less van der Waals strain than the gauche conformation. The van der Waals radius of a hydrogen atom is 120 pm, and that of a methyl group is 200 pm—nearly twice as large as a hydrogen. Because the methyl groups of butane are closer in the gauche conformation than they are in the anti, the compound has greater van der Waals strain in the gauche conformation. At 25°C, about three times as many butane molecules have the anti conformation as the gauche conformation.

Butane has two distinct eclipsed conformations about its C2—C3 bond. In one, the two methyl groups eclipse each other. In the second, each methyl group eclipses with a hydrogen atom. Both conformations have the same number of eclipsed bonds and the same amount of torsional strain. However, the methyl—methyl eclipsed conformation has significantly more van der Waals strain than does the methyl—hydrogen eclipsed conformation. The greater strain arises from the larger methyl groups that take up more space, and thus have more electron repulsion, than the hydrogens.

Eclipsed conformations of butane

Figure 3.4 shows the energy diagram for the different conformations of butane. As with ethane, the staggered conformations of butane are more stable than the eclipsed ones. Notice in the figure, however, that the staggered conformations of butane do not have the same energy level, nor do all the eclipsed conformations have the same energy level. The conformation with the greatest energy is the one with the methyl groups eclipsed; the conformation with the least energy is the one with the methyl groups anti. The energy difference of 6.1 kcal/mole between that maximum and minimum is the energy barrier for rotation about the C2—C3 bond in butane. It is higher than the 2.9 kcal/mole rotational energy of ethane because of the addition of the van der Waals strain to the torsional strain. Although rotation about the C2—C3 bond of butane is still a rapid process, it is much slower than the rotation about the C—C bond in ethane.

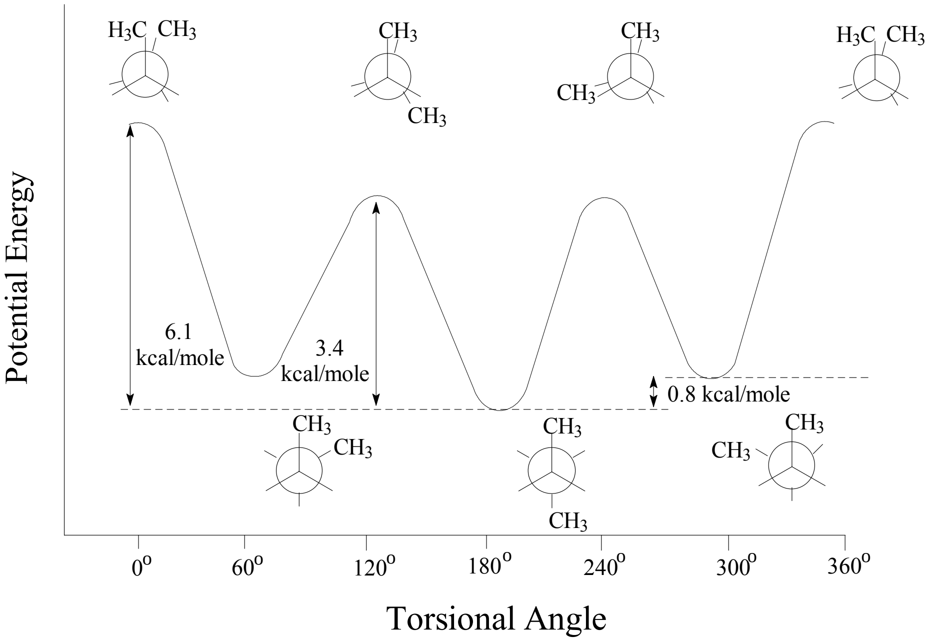


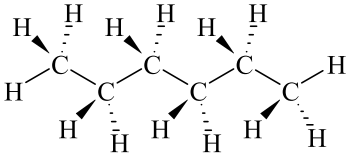
Figure 3.4. Energy diagram for rotation about the C—C bond between the second and third carbons in butane.

Exercise 3.3

a) Sketch an energy diagram for the rotation about the C1—C2 bond in propane. Clearly identify the conformation for each of the energy maxima and minima. Does this diagram look more like that of ethane or butane? Would you expect a higher rotational energy level for propane than for ethane or butane?
b) Repeat this for the C1—C2 bond in 1-iodopropane.

Conformations of Other Alkanes

For longer-chain alkanes, instead of viewing the molecules from the end in Newman projections, look at them from the side. The “carbon skeletons” tend to have a zigzag arrangement with all of the bonds staggered and all of the interactions between the groups anti. This completely anti conformation is the most stable conformation of all unbranched hydrocarbons.


Zigzag structure of hexane

3.5 Angle Strain in Cycloalkanes

In 1885, Adolph von Baeyer declared that the carbon skeletons of the cycloalkanes were planar. He stated that cyclopentane was the most stable of the cycloalkanes and based his belief on his observation that rings containing five or six carbons are the most common and the most stable in naturally occurring materials. From that observation, Baeyer suggested that cyclic stability relates to how closely the C—C—C angles come to 109.5°, the measurement of a tetrahedral angle. The C—C—C angles in cyclopentane come the closest, because the angles in a pentagon are 108°—almost a tetrahedral angle. The next closest are the 120° angles in cyclohexane. In polygons larger than a hexagon, the angles deviate more and more from the ideal tetrahedral angle. Thus, von Baeyer predicted that those cycloalkanes larger than cyclopentane would be increasingly strained and correspondingly less stable. For rings smaller than cyclopentane, he predicted a C—C—C bond angle of 60° for cyclopropane, which is a 49.5° deviation from the tetrahedral value, and of 90° for cyclobutane, a 19.5° deviation from the tetrahedral value. He called this destabilizing strain **angle strain**. That is, when the molecular orbitals of the bonding carbons cannot overlap end to end to form a tetrahedral angle, the bonds “bend,” causing strain.

Angle strain is the strain that occurs in a molecule when a bond angle is different from its optimum angle.

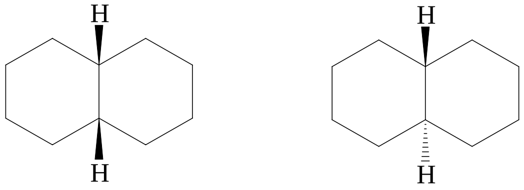
Just five years later, in 1890, Herman Sachse pointed out that cyclohexane, the most common naturally occurring cycloalkane and the most stable, could adopt a strain-free conformation, with normal tetrahedral bond angles, if the ring was nonplanar. Using molecular models, he showed that a nonplanar cyclohexane molecule would have two conformations, both without the ring strain that the von Baeyer theory predicted. He called the two isomers the C-form (or movable) and the Z-form (or rigid), because the models looked somewhat like the letters C and Z.

Exercise 3.4

Construct a molecular model of cyclohexane. Identify Sachse's C-form and Z-form. Draw the two forms.

As is often the case with young upstarts, after only a brief evaluation and a brief attempt to isolate the two structures, Sachse's proposed structures were largely ignored. Support of the planar structures, an inability to isolate Sachse's structures and von Baeyer's stature as a chemist meant Sachse was ignored. In 1918, however, E. Mohr suggested that Sachse might be correct. He pointed out that a nonplanar cyclohexane would have conformational mobility; thus, allowing the two forms to easily interconvert by rotating about their C—C bonds. Because they could interconvert so easily, the two forms could not be readily isolated. Although this was important, what finally confirmed Sachse's proposal was another of Mohr's suggestions: that decalin, a two-ring cycloalkane, existed in two forms that could interconvert only by breaking and reforming bonds. Finally, in 1925, Walter Hückel isolated the two postulated isomers of decalin.

For more on decalin see Section 3.11, page 000.



The two forms of decalin

Von Baeyer's theory is useful in that it identifies bond angle strain. Except for cyclopropane, all cycloalkanes are nonplanar. The shape that each molecule adopts is the one that minimizes the angle strain.

The heat of combustion is the energy given off when a substance is burned under controlled conditions.

Heat of Combustion

The most convenient method for determining the amount of angle strain within a molecule, and thereby accessing the molecule's thermodynamic stability, is by measuring its **heat of combustion**. All hydrocarbons burn. As they burn, they give off energy and produce water and carbon dioxide. These products, water and carbon dioxide, are the same for the combustion reaction of every hydrocarbon. The differences in the heats of combustion for a homologous series relate to the relative stabilities of the molecules. The following equation is the general form for the combustion of cycloalkanes:

$$C_nH_{2n} + (3n/2)O_2 \longrightarrow nH_2O + nCO_2$$

Table 3.2 lists the heats of combustion for various cycloalkanes, including the heat of combustion for both the whole molecule and each methylene (—CH_2—) group within the molecule. The heat of combustion for an individual methylene group is more important than the heat of combustion for the whole molecule, as the more stable molecules are those that have the lower heats of combustion per group. As you examine this table, note that the angle strain is lowest for cyclohexane, not cyclopentane as von Baeyer predicted. Note also that the angle strain per methylene group for rings of five or more carbons deviates little from approximately 1 kcal/mole.

Cycloalkane	Heat of Combustion (kcal/mole)	Number of Methylene Groups	Heat of Combustion Per Methylene Group (kcal/mole)	Angle Strain per Methylene Group (kcal/mole)
Cyclopropane	499.8	3	166.6	9.2
Cyclobutane	655.9	4	164.0	7.6
Cyclopentane	793.5	5	158.7	1.3
Cyclohexane	944.5	6	157.4	0
Cycloheptane	1108.2	7	158.3	0.9
Cyclooctane	1269.1	8	158.6	1.2
Cyclononane	1429.5	9	158.8	1.4
Cyclodecane	1586.0	10	158.6	1.2
Cyclopentadecane	2363.3	15	157.6	0.2
Normal Alkane			157.4	

Table 3.2. Heats of combustion of cycloalkanes.

3.6 Conformations of Cyclohexane

As noted in Section 3.5, there are two basic forms of the cyclohexane ring—initially called the C- and Z-forms. In current terminology, these forms are known as the **boat** and **chair conformations**. This section discusses which of these two structures is the more stable and why.

The boat is the C-form, and the chair is the Z-form.

In 1943, Odd Hassel of the University of Oslo established the chair form as the most stable conformation of cyclohexane. Later, Sir Derek Barton used Hassel's results in an analysis of chemical reactivity. For their work, Hassel and Barton shared the Nobel Prize in chemistry in 1969. Figure 3.5 shows a ball-and-stick model of the chair conformation. By using your imagination, you can see a lounge chair in this conformation.

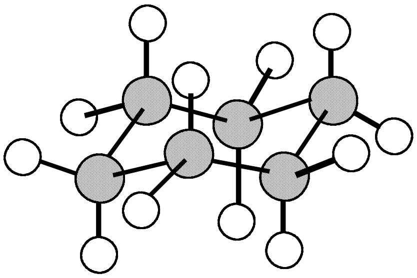


Figure 3.5. A ball-and-stick model of the chair form of cyclohexane.

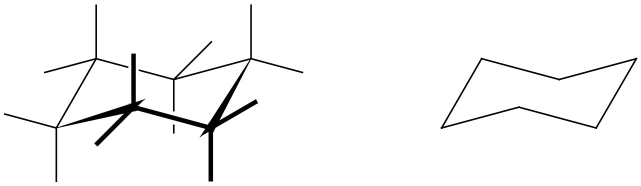
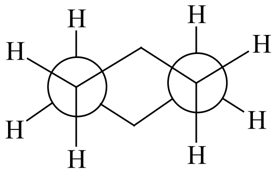


Figure 3.6. Bond line structural formulas for the chair form of cyclohexane. The structure on the left shows the positions of the hydrogens; the structure on the right shows only the C—C bonds.

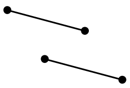
Using your model of cyclohexane, twist it into the chair conformation. Note that, unlike the drawings, cyclohexane is not a planar hexagon. When cyclohexane is in the chair conformation, any carbon you look at on the ring and the carbon opposite it is a part of the chair—either its back or its footrest. The chair form of cyclohexane is nearly free of angle strain. Because all the bonds are staggered, it is almost free from torsional strain as well. Looking along two of the C—C bonds in a Newman projection makes the staggered arrangement of the bonds in the chair form of cyclohexane more apparent. Compare your molecular model with the following representation:



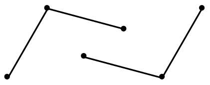
Newman projection of the chair form of cyclohexane

How to Draw a Chair Conformation of Cyclohexane

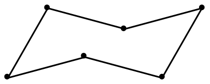
Drawing a chair conformation of cyclohexane is not difficult but does require some practice. The rules are quite simple. First, draw the "seat" of the chair. They are two slanted and slightly offset parallel lines.



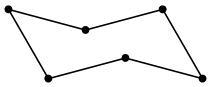
Next, draw two more parallel lines connecting the first lines with the “footrest” and “headrest” carbons.



Finally, add two more parallel lines connecting to the footrest and headrest carbons with the two lines of the “sides” of the chair to complete the ring.

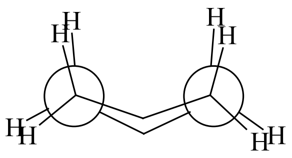


Of course, the chair can also be drawn as follows:



Practice these skills until you have mastered the art of drawing the chair structure. This skill is used throughout the book.

Now twist your model of cyclohexane into the boat form:



Newman projection of the boat form of cyclohexane

The bond angles are close to tetrahedral, so there is little angle strain, but the boat form of cyclohexane does have eclipsed bonds on four of its carbon atoms. This eclipsing produces a significant amount of torsional strain. More importantly, the close contact of the **“flagpole” hydrogens** at either end of the molecule destabilizes the boat conformation. Figure 3.7 shows a ball-and-stick model of the boat conformation.

The “flagpole” hydrogens are the two hydrogens that point upward and slightly toward each other from the two upturned ends of the boat.

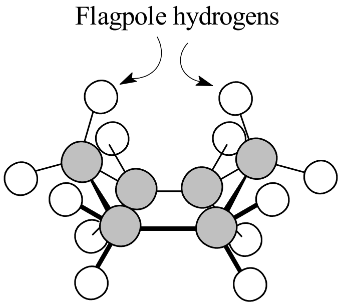


Figure 3.7. A ball-and-stick model of the boat form of cyclohexane with emphasis on the flagpole hydrogens.

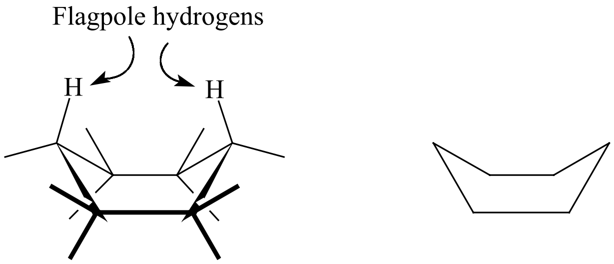


Figure 3.8. Bond-line structural formulas of the boat form of cyclohexane. The structure on the left shows the flagpole hydrogens.

These hydrogens are only about 180 pm apart, a distance that is closer than the sum (240 pm) of the van der Waals radii of two hydrogens. Thus, the van der Waals repulsions between the flagpole hydrogens add to the torsional strain. This torsional strain further increases the energy of the boat form. The boat form is 6.2 kcal/mole (see Figure 3.10) higher in energy than the chair form.

The twist or skew boat is slightly rotated to relieve the flagpole and eclipsing interactions of the boat.

A third conformation of cyclohexane is the **twist**, or **skew**, **boat** (see Figure 3.9). With your model still in the boat conformation, take the flagpole hydrogens and rotate, or twist, them in opposite directions from one another, so that instead of facing each other, they are more to the side. Twisting the flagpole hydrogens increases the distance between them and moves the eclipsed hydrogens farther apart. This relieves some of both the torsional strain and the van der Waals repulsion. The twist boat is 0.6 kcal/mole lower in energy than the boat conformation.

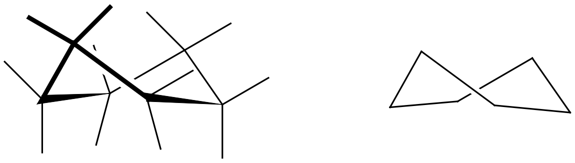
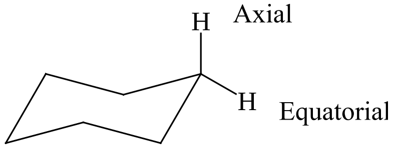


Figure 3.9. The twist boat form of cyclohexane.

At room temperature, ring flip occurs almost constantly. If it were possible to isolate the various conformations existing at a given instant, you would find some of each kind, but most molecules (more than 99%) would be in the chair conformation. This is due to the fact that the chair conformation is more stable than the boat conformation. Because most of the molecules are in the chair conformation most of the time, chemists know that when considering the physical and chemical properties of cyclohexane and its derivatives, they are thinking mostly of the chair conformation. This fact is significant to you, because this book uses cyclohexane derivatives frequently to illustrate reaction pathways.

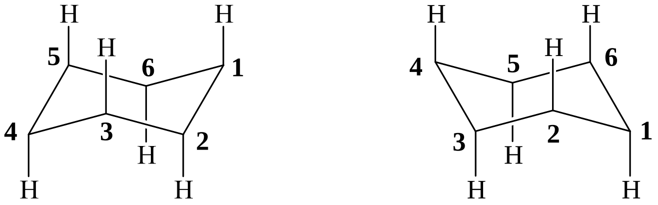
The chair conformation of cyclohexane has two distinct types of carbon—hydrogen bonds: **axial** and **equatorial**. Six of these bonds are axial and the other six equatorial, with one axial and one equatorial bond on each carbon.

Axial hydrogens point above and below the "plane" of the ring. Equatorial hydrogens are within the "plane" of the ring.



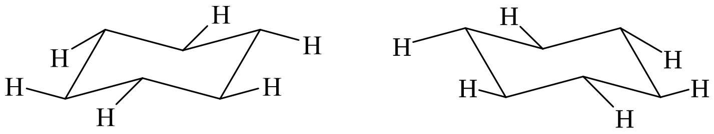
Drawing Substituents on a Chair Cyclohexane

Draw the axial bonds parallel to each other alternately up and down around the ring. That is, if you draw the axial bond to hydrogen on carbon 1 pointing up, draw it pointing down on carbon 2, up on carbon 3, and so on around the ring. Draw the bond up on carbon 1 if the bond angle points up and down if it points down.



Axial hydrogens on cyclohexane

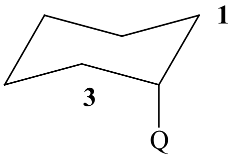
The equatorial hydrogens lie approximately in the plane formed by the ring of carbons and point out from the equator of the ring. (Keep in mind that the cyclohexane molecule does not lie in a flat plane, so the term equatorial fits rather loosely.) When a vertex of the ring points *down*, the equatorial hydrogen is *up* and away from the ring.



Equatorial hydrogens on cyclohexane

Exercise 3.5

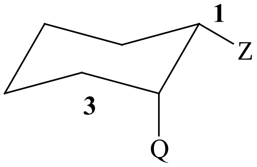
Using the following partial structure of cyclohexane, add a substituent, Z, to C1 to obtain each of the following relationships:



a)	gauche to Q	b)	anti to Q
c)	gauche to C3	d)	anti to C3

Sample Solution

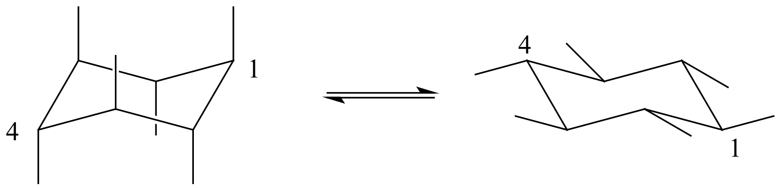
a) Substituent Z is gauche to Q when Z is in the equatorial position. The Z—C—C—Q torsional angle is 60^o.



3.7 Conformational Inversion of Cyclohexane

Ring inversion or the chair-boat-chair interconversion is the process where one chair form converts to another chair form of a molecule.

Through a process called **ring inversion**, or **chair-boat-chair interconversion**, one chair form of cyclohexane converts to another chair form of cyclohexane. That is, the back rotates down to become the footrest and the footrest opposite it on the ring rotates up to become the back. Use your model of cyclohexane to help yourself visualize this. Grasp one of the carbons in the back position in your right hand, call it C1, and grasp the carbon opposite it on the ring, which is in the footrest position and is C4, in your left hand.

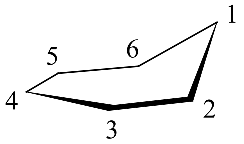


Ring flipping is another term for ring inversion.

Rotate C1, the back, down; then rotate C4, the footrest opposite it, up. In this process of **ring flipping**, the equatorial substituents become axial, and the axial substituents become equatorial. Also, all carbons in the back position move down to the footrest position, and all carbons that were in the footrest position move up to the back position. As you can see, when you rotate one of the C—C bonds in the ring, that rotation affects the relative positions of all the constituent atoms of that molecule.

In the half chair conformation the footrest of the chair forms a plane with the seat of the chair.

The process of ring inversion takes cyclohexane through a conformation called the **half-chair conformation**. The half-chair conformation exists at the point in the inversion process when the footrest carbon, C4, has rotated up to form a plane with carbons C2, C3, C5, and C6.



Half-chair conformation of cyclohexane

The position of C1, the back of the chair, is still, at this point, unchanged. This conformation is the transitional state between the chair and the twist boat forms.

At room temperature, this process of inversion goes on constantly. The half-life of a particular chair conformation of cyclohexane is approximately 10^{-5} seconds. That is, every 10^{-5} seconds half of the molecules in a given sample of cyclohexane undergo a ring flip.

The energy diagram in Figure 3.10 illustrates each step of ring flipping from one chair form to the other chair form and shows the variation in energy that accompanies the ring inversion. Use your molecular model of cyclohexane and follow the sequence.

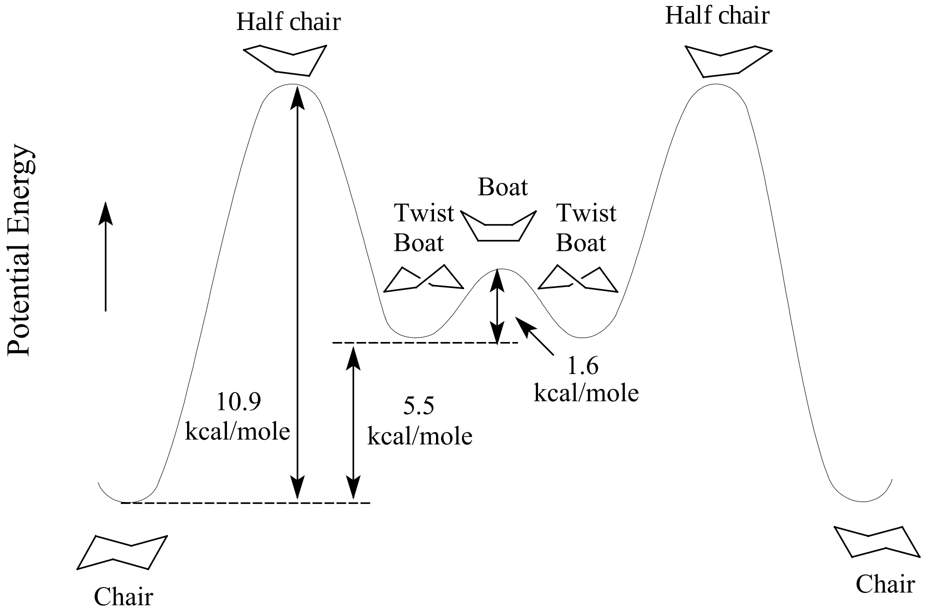
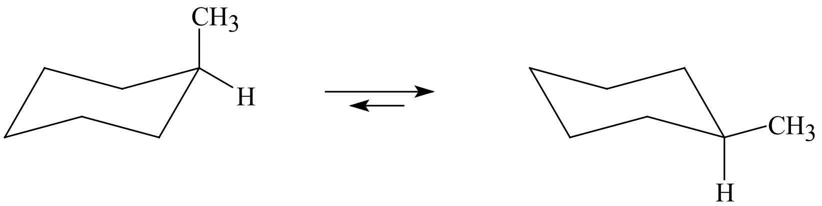


Figure 3.10. The energy diagram for the ring inversion of cyclohexane.

3.8 Conformational Analysis of Monosubstituted Cyclohexanes

The ring inversion, or ring flipping, that occurs in a molecule of cyclohexane takes place between two equivalent conformations. Thus, when a cyclohexane molecule flips between chair forms, the energy level for both forms is the same. However, if there is a substituent on the ring, the number of molecules in each conformation is different because the conformations are no longer equivalent. For example, if a hydrogen of cyclohexane is replaced with a methyl group to form methylcyclohexane, the two chair forms are different. In one the methyl group is equatorial, and in the other, it is axial.

The arrows between the two methylcyclohexanes indicate that the two conformations are not present in equal quantities. The conformation on the right is the more common conformation.



Methylcyclohexane

The two chair forms are not present in equal amounts. Experimental evidence shows that at room temperature approximately 95% of the methyl groups are equatorial. This preponderance is due to the differences in stability of the two conformations. In any equilibrium process, the most stable chemical species is present in greater quantities, and the chair form of methylcyclohexane having the equatorial methyl group is the more stable one.

To help you visualize why 95% of the methyl groups in a room-temperature sample of methylcyclohexane are in the equatorial position, make a model of methylcyclohexane and put the methyl group in an axial position on C1. As you see, an axial methyl group is quite close to the axial hydrogens on C3 and C5. When they are at their closest position, the hydrogens on the methyl group are less than 200 pm away from these axial hydrogens. Figure 3.11 illustrates the structure of methylcyclohexane.

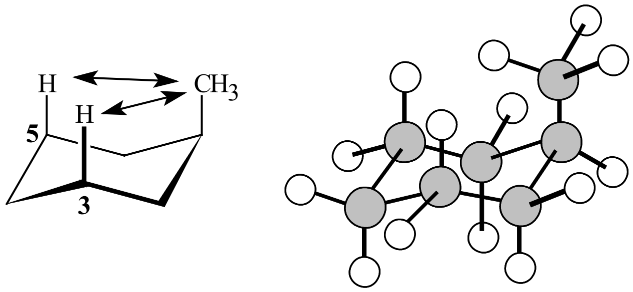
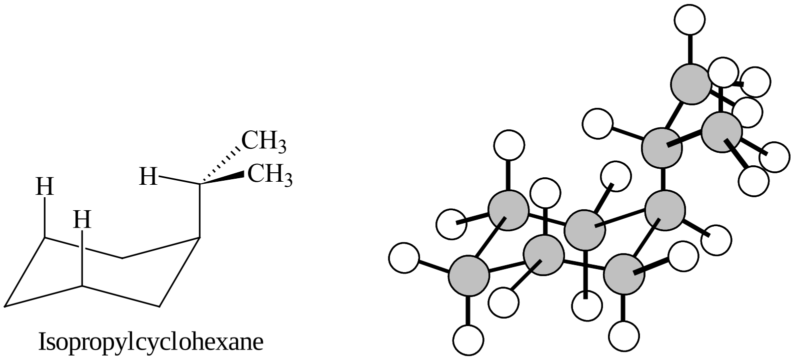


Figure 3.11. Bond-line and ball-and-stick model of methylcyclohexane with the methyl group axial.

This distance is less than the sum of the van der Waals radii for two hydrogens (240 pm), so the axial conformation of methylcyclohexane is destabilized by the strain of the van der Waals repulsive forces. The van der Waals repulsive forces arise when the electron clouds surrounding the atoms get close enough to repel one another.

Now rotate the methyl group to the equatorial position. Here all the hydrogens are in the axial positions, and the distance between them is about 400 pm, much greater than the combined van der Waals radii.

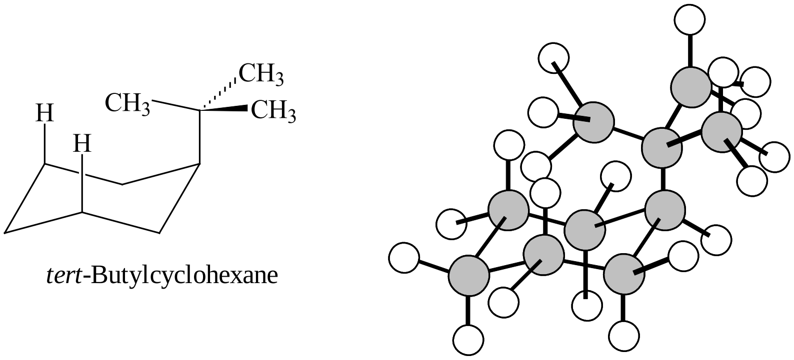
The stability of cyclohexanes having other axial substituents depends on the size of the substituent. For example, for fluorocyclohexane, about 40% of the molecules have fluorine in the axial position. When the substituent is an isopropyl group, about 3% of the molecules have the substituent in the axial position. This percentage is so similar to that for the methyl substituent that it might at first seem surprising because the isopropyl group is larger than the methyl group. However, the isopropyl group orients itself so that a hydrogen points toward the axial hydrogens on C3 and C5. This orients the two methyl groups away from the center of the molecule as shown in Figure 3.12.



Isopropylcyclohexane

Figure 3.12. Bond-line and ball-and-stick model of isopropylcyclohexane with the isopropyl group axial.

A *tert*-butyl group is so large that *tert*-butylcyclohexane exists almost entirely with this group in the equatorial position. In fact, the number of molecules with the *tert*-butyl group axial is too small to measure. The reason for so little ring flipping is that with the *tert*-butyl group in the axial position, one of its three methyl groups must point toward the axial hydrogens on C3 and C5. Figure 3.13 shows that the distance between the hydrogens in this methyl group and the axial hydrogens is only 50 pm, creating a large van der Waals strain.



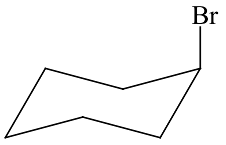
tert-Butylcyclohexane

Figure 3.13. Bond-line and ball-and-stick model of *tert*-butylcyclohexane with the *tert*-butyl group axial.

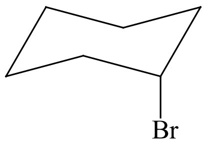
Solved Exercise 3.1

Draw a chair conformation of a cyclohexane ring with a bromine axial on the ring.

Solution: Draw the chair structure. Because the question does not specify the location of the axial substituent, there are six possible drawings. Three have the bromine axial and up, three axial and down. One of each is drawn below.



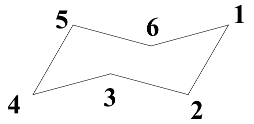
Axial and up



Axial and down

Exercise 3.6

Consider the chair conformation of the cyclohexane ring shown below, and answer the following questions. (**Note**: “Up” and “down” are relative to how the structure is drawn.)



a) Is a methyl group that is “up” at C5 axial or equatorial?

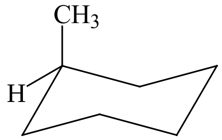
b) Is a *tert*-butyl group that is “down” at C1 more or less stable than one that is “down” at C4?

c) Which is more stable, a methyl group that is “down” at C3 or one that is “down” at C6?

d) Using the van der Waals radii (Table 3.1, page 000), place an iodine in its most stable position on C2.

Sample solution

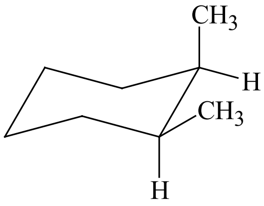
a) Placing the substituents on C5 indicates that a methyl that is up must be axial.



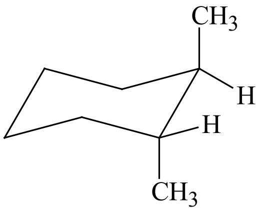
3.9 Naming Stereoisomers

Stereoisomers are isomers that have identical bond sequences but different spatial arrangements of their atoms.

Many compounds have isomers with identical bond sequences but different geometries. Chemists call these compounds **stereoisomers**. A number of cycloalkanes exist as stereoisomers. Cycloalkanes are less flexible than acyclic alkanes because the ring structure restrains the rotation about the C—C bonds. Because cycloalkanes are geometrically constrained, they have two sides: a “top” and a “bottom.” Thus, one compound of a pair of disubstituted cycloalkane stereoisomers will have the substituents on the same side of the ring, and the other compound will have the substituents on opposite sides of the ring. For example, there are two stereoisomers of the cyclohexane having methyl groups on adjacent carbon atoms. One stereoisomer has the methyl groups on the same side of the ring, and the other has two methyl groups are on opposite sides of the ring.



Methyl groups on the same side



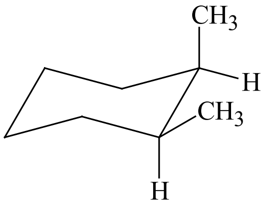
Methyl groups on opposite sides

To name stereoisomers, follow these steps:

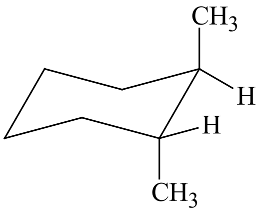
Step 1 Name the parent compound.
Step 2 Determine the names and positions of the substituents.
Step 3 If the isomer has both substituent groups on the same side of the ring, use the prefix *cis*- before the name of the compound.
Step 4 If the isomer has both substituent groups on opposite sides of the ring, use the prefix *trans*- before the parent name of the compound.

To name the example stereoisomers, follow these steps:

Step 1 The parent name is cyclohexane.
Step 2 Both substituents are methyl groups, and they are on carbons 1 and 2.
Step 3 Both methyl groups are on the same side of the ring in the first compound, so its name is *cis*-1,2-dimethylcyclohexane.
Step 4 The methyl groups are on opposite sides of the ring in the second compound, so its name is *trans*-1,2-dimethylcyclohexane.

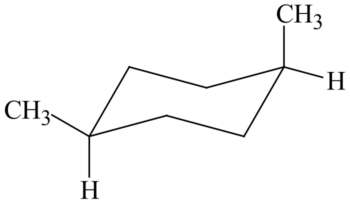


cis-1,2-Dimethylcyclohexane

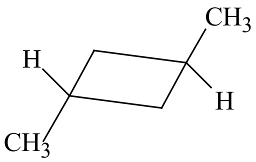


trans-1,2-Dimethylcyclohexane

Groups do not have to be on adjacent carbon atoms to be *cis* or *trans* on a ring, as the following examples demonstrate:



cis-1,4-Dimethylcyclohexane

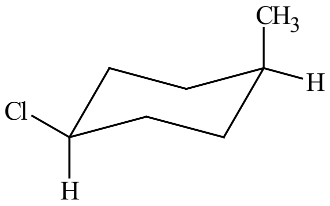


trans-1,3-Dimethylcyclobutane

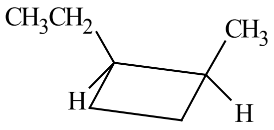
Exercise 3.7

Name each of the following using the IUPAC system.

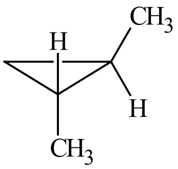
a)



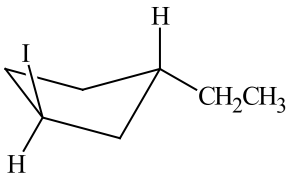
b)



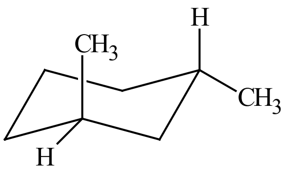
c)



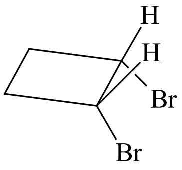
d)



e)



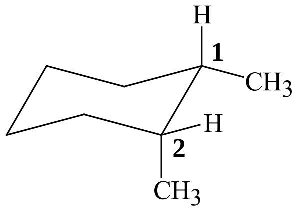
f)



Sample solution
d) *trans*-1-Ethyl-3-iodocyclopentane

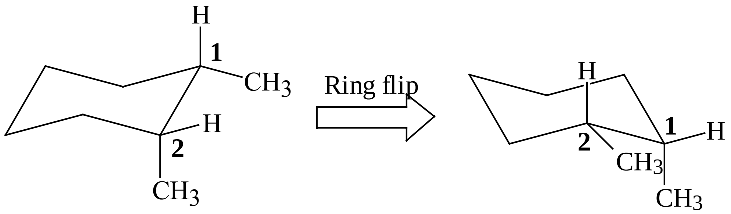
3.10 Conformational Analysis of Disubstituted Cyclohexanes

When a cyclohexane ring bears two substituents, the substituents occupy positions that are either on the same side or on opposite sides of the ring. To help yourself visualize this positioning, make molecular models of two cyclohexane rings and four methyl groups. Rotate both cyclohexane rings into the chair conformation. Choose a back carbon on one of the rings and call it C1. Replace the equatorial hydrogen on C1 with one of the methyl groups. Move to C2 and replace the axial hydrogen on that carbon with a methyl substituent. Both substituents are on the same side of the ring—one in the equatorial position and the other in the axial position.



cis-1,2-Dimethylcyclohexane

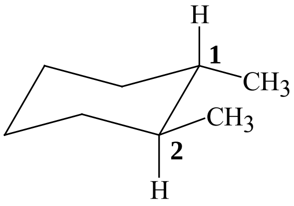
Because both substituents are on the same side of the ring, they are *cis* to each other. Flip your molecular model of *cis*-1,2-dimethylcyclohexane into the other chair conformation. Note that the methyl group on C1 is now in the axial position, and the methyl group on C2 is in the equatorial position.



cis-1,2-Dimethylcyclohexane

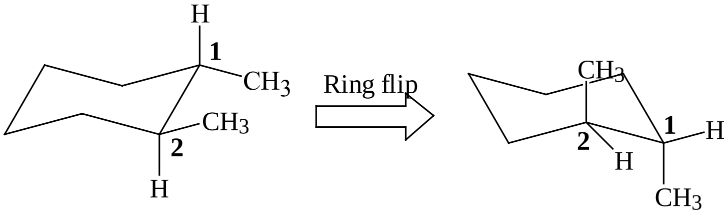
When two substituents on adjacent carbons in cyclohexane are *cis*, one is always axial and the other is always equatorial in either of the chair conformations of the molecule. Also, with a *cis* isomer of dimethylcyclohexane, both methyl groups point up from the carbon ring—straight up for the axial methyl and slightly up for the equatorial methyl, (Or, if you turn the model upside down, they both point down from the carbon ring).

Now take the other molecular model of cyclohexane. Locate one of the carbons, call it C1, and replace the equatorial hydrogen with a methyl group. Move to C2, and replace the equatorial hydrogen there with another methyl group. Note that both methyl groups are equatorial but on opposite sides of the ring, or in the *trans* conformation.



trans-1,2-Dimethylcyclohexane

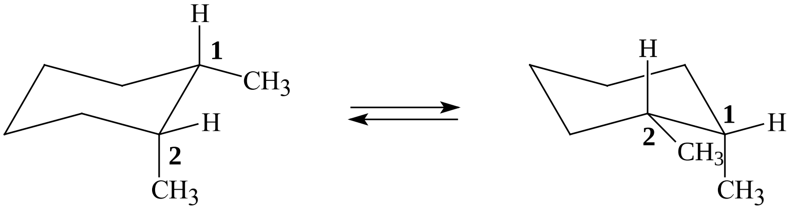
Flip your model of *trans*-1,2-dimethylcyclohexane into the other chair conformation. Note that both substituents are now in the axial positions.



trans-1,2-Dimethylcyclohexane

With a *trans* isomer of 1,2-dimethylcyclohexane, one methyl group always points up and the other always points down from the carbon ring.

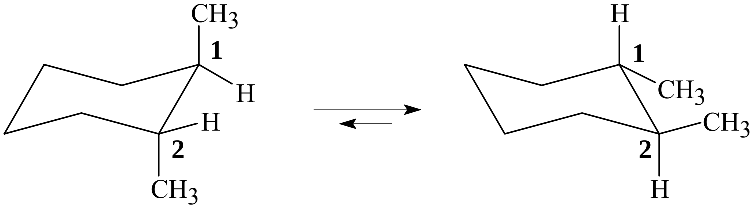
Stereoisomers have different stabilities. To understand the relationship between stereoisomerism and stability, look again at the *cis* and *trans* isomers of 1,2-dimethylcyclohexane in the chair conformations. The two conformations of *cis*-1,2-dimethylcyclohexane are equivalent—no matter which conformation you look at, each has one axial and one equatorial methyl group:



cis-1,2-Dimethylcyclohexane

Recall from Section 3.8 that the methyl group of methylcyclohexane is in the axial position less than 5% of the time because of van der Waals strain. From this you can surmise that *cis*-1,2-dimethylcyclohexane has some torsional strain, but how does it compare with that of the *trans* conformations?

The two conformations of *trans*-1,2-dimethylcyclohexane are not equivalent. In one conformation, both groups are axial; in the other, both are equatorial:



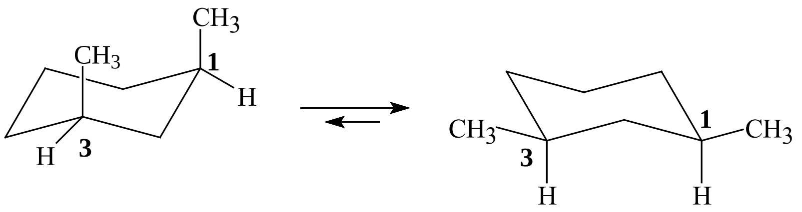
trans-1,2-Dimethylcyclohexane

The *trans* conformation with both methyl groups in the axial position constitutes only about 0.4% of the equilibrium mixture. Of the two conformations, the one with the methyl groups in the equatorial positions is definitely more stable. Thus, the *trans* stereoisomer is more stable than the *cis* stereoisomer[1]. The heats of combustion confirm that the *trans* stereoisomer is more stable, as the difference between the *cis* and the *trans* stereoisomers is 1.5 kcal/mole. A general rule is that any substituent on a cyclohexane ring that is equatorial is more stable than one that is axial.

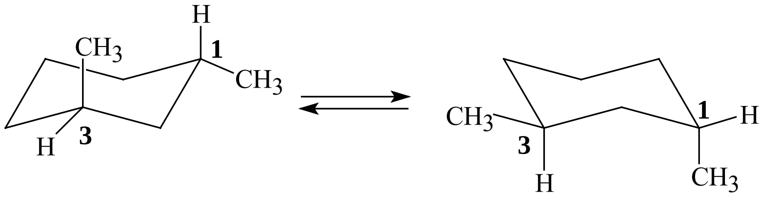
Now look at another constitutional isomer of dimethylcyclohexane: 1,3-dimethylcyclohexane. Both of these isomers have *cis* and *trans* stereoisomers. Make molecular models of the *cis* and *trans* stereoisomers of 1,3-dimethylcyclohexane.

---

[1] Remember that each stereoisomer has two conformations that are in equilibrium. These conformations cannot be separated. Although the diaxial *trans* conformation is much higher in energy than either *cis* conformation, the diaxial *trans* conformation is present only in small quantity. Thus, the *trans* isomer is more stable than the *cis*.



cis-1,3-Dimethylcyclohexane



trans-1,3-Dimethylcyclohexane

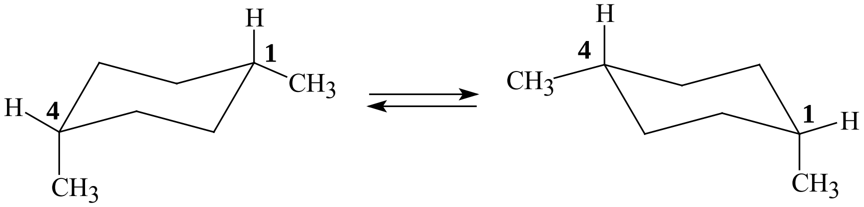
For ease of comparison, rotate both stereoisomers so that C1 is in the back position of the chair conformation. Remember that for a *cis* stereoisomer of a dimethylcyclohexane both substituents either point up or point down, and for a *trans* stereoisomer, when one points up, the other points down.

Now flip the two stereoisomers between their two chair conformations. The *cis* stereoisomer of 1,3-dimethylcyclohexane has one chair conformation in which both methyl groups are equatorial and another in which both methyl groups are axial. The *trans* stereoisomer has two equivalent chair forms, with one axial and one equatorial methyl group in each. Following the rule that equatorial groups are more stable than axial groups, the *cis* stereoisomer is more stable than the *trans* stereoisomer. Data on the heats of combustion show that the difference is 1.7 kcal/mole.

Solved Exercise 3.2

a) Draw both chair conformations of *cis*-1,4-dimethylcyclohexane. Determine which chair conformation is most stable.

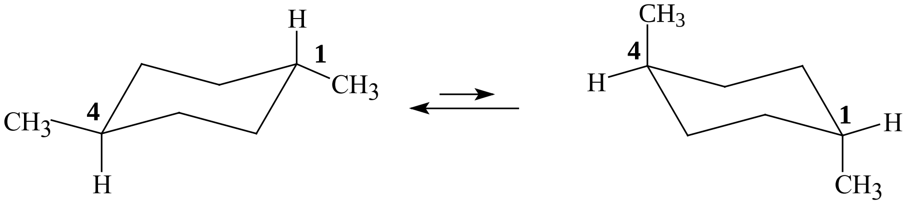
Solution: Notice that one methyl group is axial and the other is equatorial in either of the two conformations. Thus, they have the same energy level. To help visualize this, make a model.



cis-1,4-Dimethylcyclohexane

b) Repeat for the chair conformations of *trans*-1,4-dimethylcyclohexane.

Solution: In one conformation of the *trans* isomer, both methyl groups are equatorial, and in the other both methyl groups are axial. The conformation in which the two methyl groups are equatorial is much more stable than the one in which they are both axial.



trans-1,4-Dimethylcyclohexane

c) Which isomer is more stable?

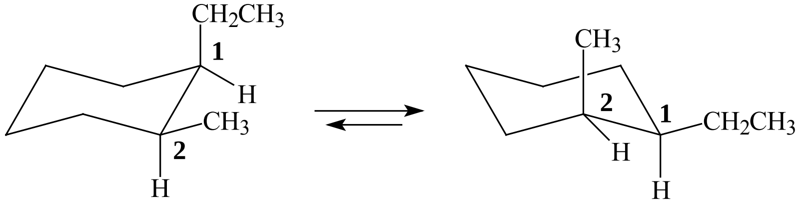
Solution: The *trans* isomer is more stable because in one conformation, both methyl groups are equatorial. Both *cis* conformations have an axial methyl group and thus are less stable. The difference in energy is about 1.7 kcal/mole.

To determine the more stable stereoisomer for a disubstituted cyclohexane having two different substituents, follow the same rules that you use for a disubstituted cyclohexane having two identical groups. An additional rule is the more stable stereoisomer has the chair conformation with the larger substituent group in the equatorial position. This rule is of the greatest significance for a cyclohexane ring bearing a *tert*-butyl group. A *tert*-butyl group is by far the largest group that is usually attached to a cyclohexane ring. It is so large that it essentially stops any ring flipping at room temperature; that is, it “fixes” the ring in one conformation. This fixing of the ring is especially useful to chemists studying the detailed pathways of organic chemical reactions, as the molecule is unable to flip from one conformation to another.

Solved Exercise 3.3

Draw the two conformations of *cis*-1-ethyl-2-methylcyclohexane. Determine which is more stable.

Solution: Draw the two conformations.



cis-1-Ethyl-2-methylcyclohexane

Both of these conformations have one group axial and one group equatorial. Because the ethyl group is slightly larger than the methyl group, the one with the ethyl group equatorial will have a slight preference.

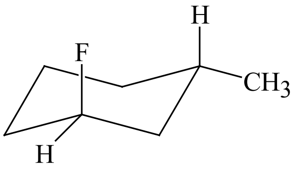
Exercise 3.8

Write the structural formula for the more stable conformation of each of the following compounds. [**Hint**: See Table 3.1 (page 000) for selected van der Waals radii.]

a) *trans*-1-Fluoro-3-methylcyclohexane
b) *cis*-1-Iodo-4-methylcyclohexane
c) *cis*-1-*tert*-Butyl-4-methylcyclohexane
d) *cis*-1,3,5-Trimethylcyclohexane

Sample Solution

a) The *trans* stereoisomer of a 1,3-disubstituted cyclohexane has one substituent axial and one equatorial. Because the van der Waals radius of fluorine is much smaller than that of a methyl group, in the most stable conformation, the fluorine is axial, and the methyl group is equatorial.



[Special Topic]

Computer Modeling

Computational chemistry is a new discipline in the field of chemistry. It began in a small way in the 1950s, but with the development of inexpensive and powerful computers in the 1980s, computational chemists have made significant contributions to chemical knowledge. Like other specialists in chemistry, computational chemists seek to understand chemical reactions, molecular structure, and chemical processes. Instead of using glassware and electronic instrumentation, their tools are computers and software.

Computational chemists predict the stability of chemical compounds, characterize their structures, and estimate the energy differences between their different energy states. In addition, they try to use these predictions to explain reaction pathways at the atomic level. In the long term, as chemists in the laboratory experimentally verify the results predicted by chemists on the computer, the computer models are refined and ultimately computer predictions can eliminate many time-consuming experiments.

The basis for the software tools of computational chemistry is empirical information. In the laboratory, chemists measure the properties of a number of molecules. They measure such things as the geometry of the molecules, their energy, charges or partial charges, and chemical reactivity. After they construct a database of these data, they analyze it to determine the mathematical relationships of the data. They then use these mathematical relationships to predict the values of those properties on new molecules. Next, they measure the properties of these new molecules in the laboratory, which either verifies the computational method or allows them to correct it. Because no one computational method yields accurate predictions in all cases, a number of computational methods have been developed. Understanding how the databases are constructed and the reliability of each computational method, chemists can choose the most appropriate method for a specific investigation understanding the limits of that method.

A typical molecular modeling program includes facilities for building and displaying two-dimensional representations of molecules. A well-defined structure is needed to calculate the properties of a molecule. This well-defined structure is a minimum energy conformation. The software has geometry optimizers to locate the nearest energy minimum to the structure the chemist drew. The local minimum is the lowest energy conformation nearest to the structure that was drawn. If, for example, the structure entered for cyclohexane looks more like a boat, the local minimum is a twist boat structure. Once a minimized structure is on the display, the bond or dihedral angles, bond lengths, and distances between different parts of a molecule can be measured. Various chemical properties—such as molecular orbitals, acidities, and chemical reactivity—can also be explored.

Exercises in this book marked with the 💻 symbol indicate that the exercise is a computational chemistry exercise.

💻**Exercise 3.9**

Construct a model of *cis*-1,3-dimethylcyclohexane with both methyl groups axial. Minimize this structure. Using the computer fill in the first column of the following table. Make a model with both methyl groups equatorial. Minimize this structure. Fill in the second column of the table below.

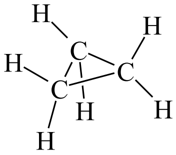
	cis-1,3-Dimethylcyclohexane	
Measurement	Axial methyl groups	Equatorial methyl groups
The CH_3—C1—H bond angle.		
The CH_3—C1—C2 bond angle.		
The distance between the two CH_3s.		

Are your results reasonable in light of the discussion of conformational preferences in Section 3.10? Why or why not?

3.11 Conformations of Other Cycloalkanes

Conformational analysis of rings smaller than cyclohexane is considerably simpler than conformational analysis of rings larger than cyclohexane. This is because the smaller rings have much less conformational mobility and thus fewer possible conformations.

The smallest possible ring size for a cycloalkane is a ring containing three carbons—cyclopropane. If you can make a molecular model of cyclopropane without breaking your models, do so. The three atoms in cyclopropane define a plane that has no possibility of conformational isomers. Because the C—C—C bond angle is 60°, well away from the ideal tetrahedral angle, the angle strain is large.



Cyclopropane

The data in Table 3.2 shows enormous bond angle strain that leads to a high heat of combustion. As a result of its high angle strain, cyclopropane is much less stable and, therefore, more reactive than the other cycloalkanes. With cyclopropane, the angle strain is of much greater importance than the torsional strain because all the hydrogens are eclipsed.

To achieve the maximum possible stability, the carbons in the cyclopropane ring overlap their bonding orbitals outside their internuclear axes. Unlike most carbon—carbon σ bonds, which are formed by overlap along the internuclear axis, the bonds in cyclopropane are formed by overlap at an angle that is slightly more than 20° outside the internuclear axis. See Figure 3.14. Chemists call these bonds "bent" bonds or sometimes "banana" bonds. Because the orbitals involved in forming the bent C—C bonds overlap outside the internuclear axes, the bonds are weaker than normal σ bonds.

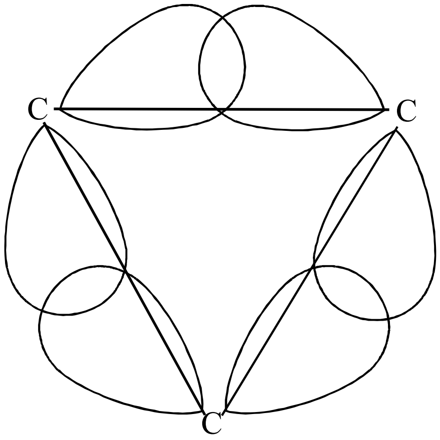
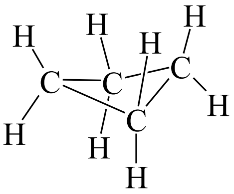


Figure 3.14. The orbitals that form the C—C bonds of cyclopropane do not lie along the internuclear axis. Chemists sometimes refer to these bonds as "bent," or "banana," bonds.

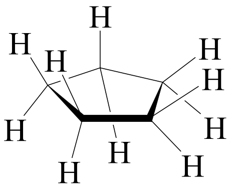
Cyclobutane has bent bonds similar to those in cyclopropane, but with considerably less bend. Again, make a model. Instead of overlapping 20° outside the internuclear axes, as in cyclopropane, cyclobutane's orbitals overlap about 7° outside the internuclear axes. In addition, cyclobutane adopts a folded conformation that relieves the torsional strain of the eclipsed hydrogens. In this conformation, one of the carbon atoms bends out of the plane of the other three by about 20°.



Folded conformation of cyclobutane.

Although this relieves the torsional strain, it does so at the expense of reducing the C—C—C bond angle from 90° to 88° for a planar cyclobutane.

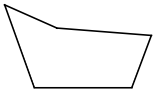
Now make a model of cyclopentane. The amount of bond angle strain in the planar conformation of cyclopentane is small, because the C—C—C bond angle for a regular pentagon is 108°—very close to the tetrahedral angle. However, the amount of torsional strain is substantial, because all the hydrogens around the ring are eclipsed.



Planar cyclopentane showing eclipsed hydrogens.

The shape of the envelope conformation of cyclopentane is like the chair conformation without the footrest.

A nonplanar conformation in which one atom moves out of the plane of the other four relieves some, but not all, of this torsional strain. Chemists call this conformation the **envelope form** of cyclopentane.



Envelope form of cyclopentane

With pseudorotation the conformational changes involve all of the atoms in the ring one at a time.

Each of the carbon atoms in cyclopentane moves out of the plane of the ring for a very short period of time in turn. This movement, known as **pseudorotation**, relieves the eclipsing of the hydrogen atoms at least part of the time. Equilibrium between the various conformations of cyclopentane occurs at rates comparable to the rates of rotation around the carbon—carbon bond of ethane.

Exercise 3.10

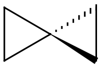
Which is more stable, *cis*- or *trans*-1,2-dimethylcyclopropane? Explain your answer.

3.12 Naming Polycyclic Ring Systems

Polycyclic compounds are compounds with two or more rings. Generally, these rings share one or more common atoms.

Spirocyclic molecules have two or more rings. Each pair of rings shares one common atom.

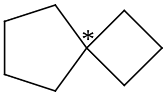
Cyclic compounds that contain more than one ring are **polycyclic compounds**. The simplest polycyclic compounds contain rings that share either one or two carbons. Molecules made up of two rings with only one common atom are **spirocyclic**. Spiro[2.2]pentane is an example of a spirocyclic compound.



Spiro[2.2]pentane

It gets the name pentane because it has a total of five carbon atoms in the two rings. The numbers between the square brackets ([ ]) do not indicate positions of substituents but rather the lengths of the carbon chains connected to the common atom.

To add to your nomenclature skills from Chapter 2, here is how to name a spiro compound. Make a molecular model of the following compound to visualize each step:



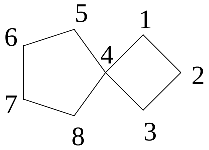
Step 1 Determine the parent name of the compound by counting the total number of carbons in the polycyclic ring. This compound has eight, so it is an octane.

Step 2 Identify the carbon that is shared by both rings. It is marked with an asterisk (*) in the example.

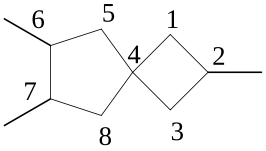
Step 3 Determine the numbers that belong in the brackets by counting from, but not including, the shared carbon around the larger ring and then around the smaller ring.

Step 4 Use the prefix *spiro*– to indicate that it is a spirocyclic compound. Thus, the name of this compound is spiro[4.3]octane.

Step 5 Count around the smaller ring and then the larger ring. Begin with a carbon adjacent to the shared carbon.



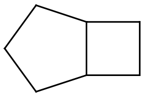
Step 6 Number the carbons first, then add any substituents. The following compound is 2,6,7-trimethylspiro[4.3]octane.



2,6,7-Trimethylspiro[4.3]octane

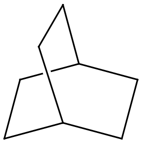
Bicyclic molecules are two rings sharing two atoms. These rings may be fused, sharing two adjacent atoms, or bridged, sharing atoms not adjacent to each other.

When two rings share two atoms, the compound is a **bicyclic compound**. The two types of bicyclic compounds are fused and bridged. A **fused bicyclic compound** has two rings joined by adjacent carbons. Make a model of bicyclo[3.2.0]heptane to help visualize a fused bicyclic compound.



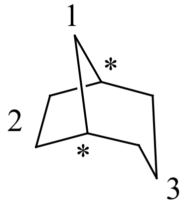
Bicyclo[3.2.0]heptane

In a **bridged bicyclic compound**, the shared carbons of the two rings are not adjacent carbons. Bicyclo[2.2.2]octane is an example of this type of compound.



Bicyclo[2.2.2]octane

Here is how to name a bicyclic compound. Make a molecular model of the following compound to visualize each step:



Step 1 Determine the parent name of the compound by counting the total number of carbons in the polycyclic ring. This compound has eight, so it is an octane.

Bridgehead carbons are those carbons shared by both rings in the molecule.

Bridges are the segments of rings between the bridgehead carbons.

Step 2 Identify the **bridgehead carbons**. They are marked by asterisks (*) above.

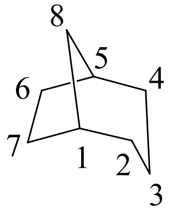
Step 3 Determine what numbers belong in the brackets.

a. Count the number of carbons in each **bridge** between the bridgehead atoms.

b. Arrange the numbers in decreasing order with periods between each number. For this compound, the longest bridge contains three carbons, the next longest two, and the shortest only one.

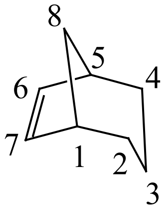
Step 4 Use the prefix *bicyclo–* to indicate that it is a compound containing two rings. Thus, the name of this example is bicyclo[3.2.1]octane.

Step 5 To number the carbons in a bicyclic compound, start with one bridgehead carbon and count around the longest bridge. Continue to the next longest bridge and finally to the smallest bridge.



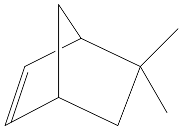
Bicyclo[3.2.1]octane

Step 6 After numbering the carbons, *then* add any substituents. This is true even for compounds with functional groups that would otherwise have high-priority numbering. For example, if there is a double bond between C6 and C7 in the previous compound, call it bicyclo[3.2.1]-6-octene.



Bicyclo[3.2.1]-6-octene

Compounds with equal length bridges are numbered so that the highest priority substituent is given the lowest number. For example, the following compound is 5,5-dimethylbicyclo[2.2.1]-2-heptene.

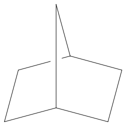


5,5-Dimethylbicyclo[2.2.1]-2-heptene

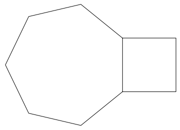
Exercise 3.11

Name each of the following compounds.

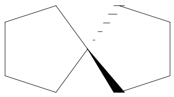
a)



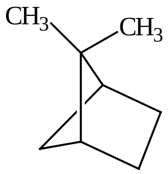
b)



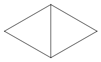
c)



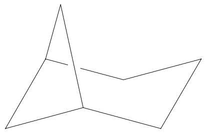
d)



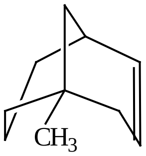
e)



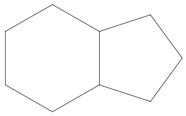
f)



g)



h)

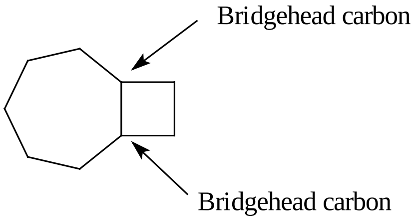


Sample Solution

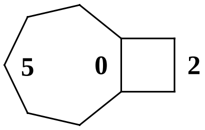
b) To name this compound, use the steps for naming a bicyclic compound.

Step 1 Determine the name of the parent compound by counting all the carbons. There are nine, so the parent name is nonane.

Step 2 Identify the bridgehead carbons.



Step 3 Determine the numbers that go in the brackets by counting the number of carbons in each bridge and arranging them in decreasing order. The longest chain has five carbons, the next longest has two, and the shortest none. Thus, the numbers are [5.2.0].

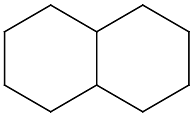


Step 4 Use the prefix *bicyclo*–.

The name of the compound is bicyclo[5.2.0]nonane.

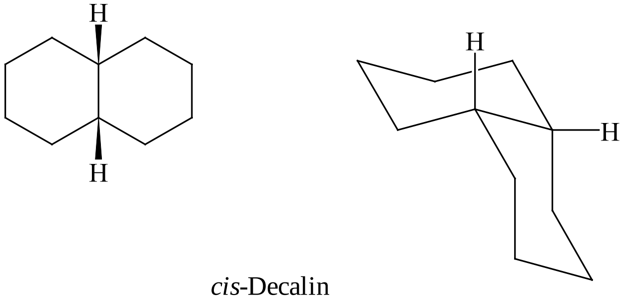
3.13 Stereochemistry of Polycyclic Ring Systems

The rings in a bicyclic compound can be joined in more than one way, forming stereoisomers. For example, the bicyclic compound decalin has two stereoisomers.

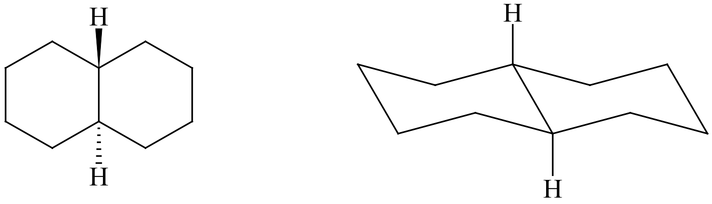


Decalin
(Bicyclo[4.4.0]decane)

Make models of *cis*- and *trans*-decalin (bicyclo[4.4.0]decane).



cis-Decalin



trans-Decalin

The stereochemistry of *cis*- and *trans*-decalin is essentially the same as that of *cis*- and *trans*-1,2-dimethylcyclohexane (Section 3.9) if you visualize one of the rings in decalin as a cyclohexane and the other ring as two substituents on the first ring. That is, you must temporarily ignore the other atoms of the second ring.

The two rings of *cis*-decalin undergo ring flips, just like *cis*-1,2-dimethylcyclohexane. However, in *trans*-decalin, the two rings cannot flip between alternate chair conformations; they must always stay with the carbons equatorial to each other. To understand this, first remember that an equatorial substituent of a *trans* stereoisomer becomes axial after a ring flip, and vice versa. Try doing a ring flip with your *trans*-decalin—be careful, don't break your models! Now detach a C—C bond in one of the rings, and do a ring flip on the other ring. Both C—C bonds from the ring junction are axial, and the distance between the two positions is much too great for bonding to occur between them.

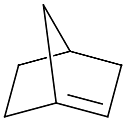
Exercise 3.12

a) Using your molecular model set, construct a model of bicyclo-[3.1.0]hexane. Is the ring junction *cis* or *trans*? Can the other ring junction exist? (Don't break your models!)
b) What is the smallest value of *n* to make a bicyclo[*n*.1.0]alkane with that *trans* ring junction? What is the smallest value of *n* for a bicyclo[*n*.*n*.0] alkane with a *trans* ring junction?

Cyclohexene and other small cycloalkenes always have a *cis* double bond. Make a model of *trans*-cyclohexene to better understand why. The bond angles around the C=C double bond are such that with only four other carbons in the ring it is difficult to form a ring from one side of the double bond C1 to the other side of the double bond C2. To do so introduces a great amount of strain on the π bond—any rotation of the bond reduces the efficiency of the overlap of the *p* orbitals, thus, producing a weaker bond. The smallest *trans*-cycloalkene stable enough to be isolated is *trans*-cyclooctene. However, it does have a strain energy of about 10 kcal/mole, when compared to *cis*-cyclooctene.

Bredt's rule states that a bridged bicyclic molecule with small rings cannot have a double bond involving one of the bridgehead carbons.

According to **Bredt's Rule**, a bicyclic compound with a double bond to a bridgehead carbon that is a part of a small ring is unstable. Bicyclo[2.2.1]-1(2)-heptene, an example of a compound that incorporates a *trans*-cyclohexene ring and illustrates Bredt's Rule, is so unstable that no one has ever isolated it. (Note the -1(2)- portion of the name. This states that the double bond is between C1 and C2.)



Bicyclo[2.2.1]-1(2)-heptene

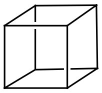
Attempt to make a model of it, but note the impossibility of connecting the bridge consisting of only one carbon to the double bond. Also, the sp^2 hybridized carbon at the bridgehead cannot be planar in this structure.

[SIDEBAR]

Higher Polycyclic Structures

Chemists have long been fascinated with imagining, synthesizing, and studying molecules whose structures have some particularly attractive symmetry, or reminds the chemist of some familiar or not so familiar object, or simply intrigues the chemist. Sometimes there is a rational justification for making such a molecule; at other times, perhaps, it is synthesized for the same reason people climb mountains—because it is there.

Consider the structure of pentacyclo[$4.2.0.0^{2,5}.0^{3,8}.0^{4,7}$]octane:



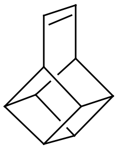
Pentacyclo[$4.2.0.0^{2,5}.0^{3,8}.0^{4,7}$]octane

Because its enchanting symmetry had intrigued chemists for years, there was great excitement when, in 1964, Philip Eaton's research group at the University of Chicago successfully synthesized it. This eight-carbon structure deserves its descriptive euonym (a name well suited to the person, place, or thing) cubane.

Chemists often give euonyms to the molecules they synthesize. They do so because euonyms are much easier to say than IUPAC names—even chemists like doing things the easy way. Compare saying “cubane” with saying “pentacyclo[$4.2.0.0^{2,5}.0^{3,8}.0^{4,7}$]octane”. The name cubane also allows you to visualize the shape of the molecule much more readily than does the IUPAC name.

A wide variety of euonyms represent not only geometrical shapes, but other things as well like musical instruments, persons, mechanical devices, animals, and many other items. Some names have obvious origins; others don't.

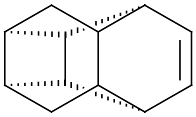
Another euonym that brings to mind the structure it names is basketene:



Basketene

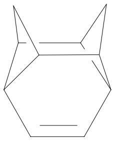
The research group of Satoru Masamune at the University of Alberta first synthesized this molecule in 1966. It received its name from its obvious similarity to a basket. Not to mention that basketene is far easier to say than pentacyclo[. . .]decene. For practice, you might try filling in the numbers for the IUPAC name. Beware: it isn’t easy.

Here's an example bound to become a favorite of animal lovers. The structure of tetracyclo[$4.4.0.0^{2,9}.0^{5,8}$]-3-decene is often drawn as follows:

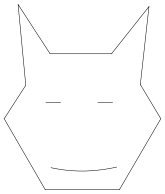


Tetracyclo[$4.4.0.0^{2,9}.0^{5,8}$]-3-decene

To help yourself visualize the molecule, make a model. The basis for its descriptive euonym becomes much more apparent if you rotate the structure by 90º.



After redrawing it, and taking a little artistic license, it becomes the smiling face of a cat.



Thus, this molecule was given the name *felicene (felis* is Latin for cat) in the research group of Andrew Gilbert at England's University of Reading in 1976.

Key Ideas from Chapter 3

❏ Wedge-and-dash representations and Newman projections are both ways of visualizing three-dimensional molecules in two dimensions.

❏ As atoms or groups of atoms that are connected by carbon—carbon single bonds rotate relative to each other, different conformations result. Conformations differ only in the spatial arrangement of the atoms.

❏ There are an infinite number of conformations for any carbon—carbon single bond, but this book covers only the two extremes:

the staggered and eclipsed forms. In the staggered form, the torsional angle between attached groups is at 60°. In the eclipsed form, it is at 0°.

❑ A staggered conformation of ethane or butane has a lower rotational energy than the eclipsed conformation.

❑ Except for cyclopropane, all cycloalkanes have nonplanar rings. The nonplanar conformations relieve the torsional strain that would result from eclipsed substituents and the angle strain that would be present in the planar form.

❑ The most stable form of cyclohexane is the chair conformation. In this form, the molecule has both axial and equatorial substituents. Cyclohexane undergoes a chair-boat-chair ring flip in which the axial substituents become equatorial, and vice versa.

❑ Cyclohexanes with axial substituents are less stable than those with the same substituents equatorial, because of unfavorable interactions among axial substituents.

❑ Spirocyclic compounds are those in which two rings share a common atom.

❑ Bicyclic compounds contain two rings that share two or more common atoms. If the common atoms are adjacent (there is a bond between the bridgehead carbons), the compound is a fused bicyclic compound. If the common atoms are not adjacent (there is no bond between the bridgehead carbons), the compound is a bridged bicyclic compound.

❑ Small cyclic alkenes are stable only when they contain a *cis* double bond. A *trans*-cycloalkene is unstable unless the ring has eight or more carbons.

Richard F. Daley and Sally J. Daley
www.ochem4free.com

Organic Chemistry

Chapter 4

Physical Properties of Organic Compounds

Chapter 4

Physical Properties of Organic Compounds

Chapter Outline

4.1 Phases of Matter
A review of the common phases of matter: solid, liquid, and gas

4.2 Melting and Freezing Points
Factors affecting the melting and freezing points of a compound

4.3 Boiling Points
Factors affecting the boiling point of a compound

4.4 Solubility
Why a compound is soluble in a given solvent

4.5 Density
Factors affecting the density of a compound

Objectives

✔ Understand what the terms *solid*, *liquid*, and *gas* mean at the molecular level

✔ Know how the symmetry and conformation of an organic structure affect its melting point

✔ Understand how a functional group affects the melting point of a compound

✔ Know how structure and functional groups affect the boiling point of a compound

✔ Recognize the molecular features that affect the solubility of a compound

✔ Know what molecular features affect the density of a compound

✔ Be able to rank compounds in order based on the physical properties discussed

“Contrariwise,” continued Tweedledee, “if it was so, it might be; and if it were so, it would be: but as it isn't, it ain't. That's logic.”

—Lewis Carroll

The physical properties of a compound include such things as its color, odor, refractive index, density, solubility, melting point, and boiling point. The exact values of the physical properties of a compound depend on its molecular structure. All the physical properties of a compound correlate with its molecular structure. Although chemists cannot examine the structure of a compound and predict the exact values for these physical properties, they can look at two compounds with similar structures and determine which has the higher melting or boiling point. By knowing the structure of a compound, a chemist can also choose a better solvent to extract or recrystallize the compound.

Knowledge of physical properties—such as solubilities, melting or boiling points, and density—will assist you in making judgments about the practical aspects of the isolation and purification of new molecules. This translates into doing better laboratory work. Understanding how molecules interact physically leads to a better understanding of how they interact in a chemical reaction. This chapter shows you how to use the molecular structure to predict qualitatively the physical properties of compounds. You can qualitatively predict physical properties because they relate to differences in intermolecular forces.

4.1 Phases of Matter

Matter ordinarily exists in four phases: solid, liquid, gas, and plasma. Plasma is a high-temperature phase not encountered in the typical organic chemistry laboratory and thus not considered in this book. Most pure chemical compounds exist in each of these phases. The phase of a compound at a particular moment depends on its temperature and pressure. For example, water at 1 atmosphere pressure is a solid below 0°C, a liquid from 0°C to 100°C, and a gas above 100°C. The temperatures at which a compound makes the transitions between phases are unique for each compound. These temperatures are a measure of some of the unique physical properties of that compound.

Because you have studied solids, liquids, and gases from your earliest years of school, you already know many facts about them. The goal for this section is to look at solids, liquids, and gases from the organic chemistry point of view—to cover their characteristics and to define any terms that are important in organic chemistry.

Consider a hypothetical ideal compound as it makes its transition through each phase. For simplicity's sake, assume that each molecule of this compound is spherical. A sphere is a simple shape that is easy to visualize with minimal **intermolecular** interactions (interactions between molecules)

Intermolecular interactions are interactions between molecules.

Starting at some low temperature, the compound is a solid. There are two extremes of solid forms: the **crystalline form** and the **amorphous form**. Because nearly all solid organic compounds are in the crystalline form, this book does not discuss the amorphous form. Spheres pack easily into an **ordered matrix**, thus, the idealized solid is a crystal. Envision this crystalline form by considering a box full of identically sized marbles. The box's size is such that one layer of marbles fits exactly in the bottom. The consecutive layers of marbles then fit on top of each other in an ordered set of layers. Figure 4.1 illustrates such a regular ordered matrix of molecules in a crystalline solid.

In the crystalline form the molecules pack together into a three-dimensional matrix.

In the amorphous form the molecules pack together in an irregular pattern.

An ordered matrix is a regular array of particles with each particle surrounded by the same arrangement of particles as any other particle.

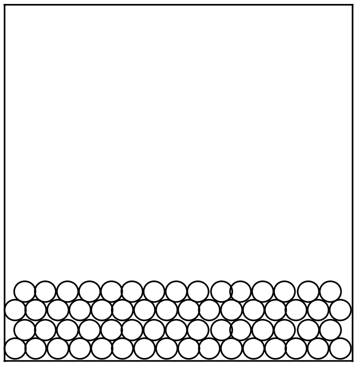


Figure 4.1. Idealized spherical molecules ordered in a very regular fashion in the crystalline form of the solid phase.

The intermolecular attractive forces hold the molecules in place in the crystal lattice. The stronger these forces are, the greater the energy that is required to break down the crystal lattice. When you apply sufficient heat to a solid, the crystalline structure of that solid breaks down.

Fusion is the transition between the solid and liquid phases.

As you heat a solid, it undergoes a transition from the solid phase to the liquid phase. Chemists call this transition **fusion** and the characteristic temperature at which a compound undergoes fusion its **melting point**. In the liquid phase the molecules are no longer packed in an ordered matrix. There is more disorder, but still a definite boundary between the liquid and its surroundings. Figure 4.2 illustrates the liquid phase using the idealized compound.

The melting point of a compound is the temperature at which fusion occurs.

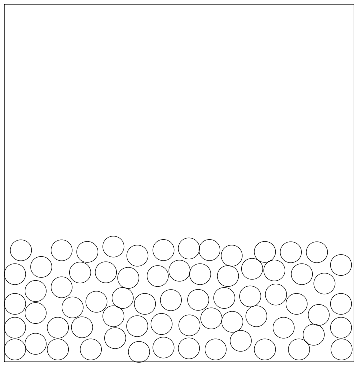


Figure 4.2. The liquid phase has less order than the solid phase. The organization and orientation of the molecules are more random.

Vaporization is the transition between the liquid and gas phases.

The boiling point of a compound is the temperature at which vaporization occurs.

As you continue to increase the temperature, the compound undergoes another transformation. It moves from its liquid phase to its gas phase. Chemists call the process of going from the liquid phase to the gas phase **vaporization**. The characteristic temperature at which a compound undergoes vaporization is its **boiling point**. In its gas phase a compound has even more disorder than it has in its liquid phase. There is little intermolecular interaction because the molecules now have enough energy to counteract these forces. Since there is so little intermolecular interaction, the molecules move freely, filling all the available space. There is no obvious boundary between the molecules of the gas and its surroundings. Figure 4.3 illustrates the gas phase using the idealized compound.

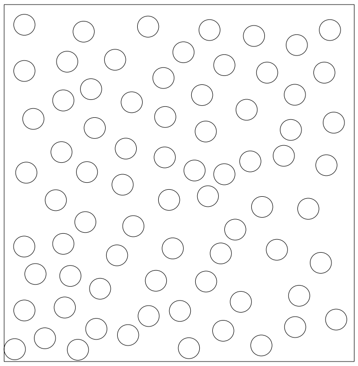


Figure 4.3. The gas phase is in even more disorder than the liquid phase. The molecules have little intermolecular interaction.

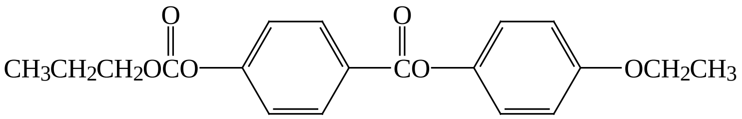
[Sidebar]

Liquid Crystals

A liquid crystal is a material showing characteristics of both a liquid and a crystal.

A mesophase shows behavior that is intermediate between two phases.

In a **liquid crystal**, the individual molecules have restricted mobility. They are more ordered than in a true liquid but less ordered than in a crystalline solid; thus, they are in an intermediate state. Because of this intermediate state, the liquid crystalline state is often called a **mesophase**. In general, materials that exhibit liquid crystallinity have rigid rod- or disk-like shapes.



Liquid crystal between 55°C and 87°C

A liquid crystal contains many small regions, each with a million or so molecules, with a preferred orientation for the molecules. Thus, even though the molecules in a liquid are in constant motion, the molecules in a particular region are all aligned with each other. On a larger scale, many regions of preferred orientation exist, but these regions are randomly oriented with respect to one another.

With nematic ordering, the molecules order themselves along their long axes.

With smectic ordering, not only do the molecules order themselves along their long axes, but they also have a layering tendency.

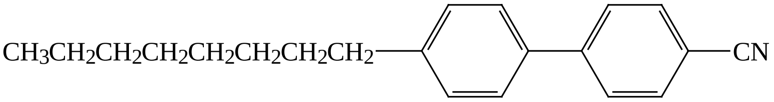
Liquid crystals are found in two types of ordering: the **nematic form** and the **smectic form**. Figure 4.4 illustrates both types of ordering. Weak intermolecular forces produce nematic ordering, but stronger intermolecular forces produce smectic ordering. Stronger intermolecular forces also produce larger regions of order in the liquid.

(a) Nematic form of a liquid crystalline material.

(b) Smectic form of a liquid crystalline material.

Figure 4.4. Schematic comparison between (a) the nematic form and (b) the smectic form of a liquid crystalline material.

An example of a liquid crystal is 4’-octyl-4-cyanobiphenyl.



4'-Octyl-4-cyanobiphenyl
Liquid crystal at room temperature

At room temperature it adopts the smectic form. Figure 4.5 is a scanning tunneling microscope image clearly showing the smectic alignment of the molecules.

(NEED PERMISSION FOR FIGURE 1A FROM REF BELOW)

Figure 4.5. A scanning tunneling microscope image of the ordering of the molecules of 4'-octyl-4-cyanobiphenyl. (from Smith and Horber, et.al., *Science*, 7/7/89, p43)

Liquid crystals are widely used in electronic displays because an external force, such as an electric field, increases the size of the ordered regions. Liquid crystals with large ordered regions have different optical properties than liquid crystals with small ordered regions. Most significantly, the large ordered regions become visible. Some watches and computer displays have a sealed container of liquid crystals. The surface of the container has a pattern of transparent electrodes. Depending on which electrodes are powered, a pattern of dots, lines, or symbols appears comprising the information visible on the display.

4.2 Melting Points

The melting point of a compound is the temperature at which the compound's solid and liquid phases are in equilibrium when the temperature is being increased.

Melting occurs as a result of applying sufficient heat to a solid so that it moves from its solid phase to its liquid phase. The temperature at which this transformation takes place is the compound's **melting point**. Each compound has a specific melting point; thus, when working with an unknown solid compound or a known solid compound whose purity is in doubt, one important measurement that chemists often take is the compound's melting point. Fortunately, taking a melting point is relatively easy to do. They then use this temperature to help identify the unknown solid compound or to verify that the compound is impure.

Freezing Points

The freezing point of a compound is the temperature at which the compound's solid and liquid phases are in equilibrium when the temperature is being decreased.

Not only does a compound have a melting point, it also has a **freezing point**. The freezing point of a compound is the temperature at which a compound's solid and liquid phases are in equilibrium when the compound is moving from its liquid phase to its solid phase. (Note that the direction of temperature change for freezing is opposite to the direction of temperature change for melting.) The melting point and the freezing point for a compound are the same temperature. Although freezing is a process that commonly occurs, chemists seldom use freezing points because controlling the cooling process is more difficult than controlling the heating process. Chemists do use freezing points for compounds that freeze at or near room temperature. When working with a liquid compound, they usually find its boiling point. Section 4.3 discusses boiling points.

Four factors that influence a compound's melting point are symmetry, polarity, hydrogen bonding, and molecular weight. Before looking at those factors, here is some information that you need to keep in mind about solids. As you learned in Section 4.1, a crystalline solid is composed of molecules arranged in a regular pattern. To arrange themselves in this pattern, the molecules normally have the same *conformation* and the same specific *orientation* relative to each other. Figure 4.6 shows a hypothetical crystalline solid. Above the solid are molecules A and B. They are both the same as the molecules in the solid, but neither molecule A nor molecule B can fit into the crystalline lattice. Molecule A has an incorrect conformation; and although molecule B has the correct conformation, it has an incorrect orientation.

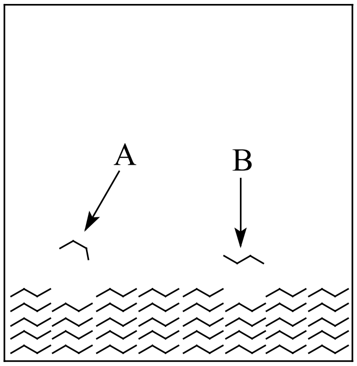
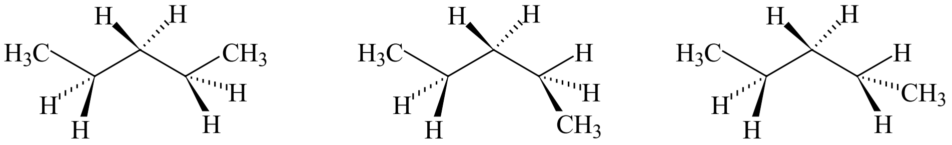


Figure 4.6. Molecule A has the wrong conformation to fit into the crystalline structure. Molecule B has the wrong orientation.

A symmetrical molecule has a regular shape—spherical, cubical, cylindrical, etc.

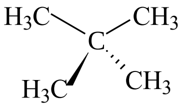
The more **symmetrical** a molecule is, the better it fits into a crystalline structure, and the higher is its melting point. Because molecules must have a similar conformation to form a crystalline lattice, any molecules with the "wrong" symmetry do not easily fit into the growing crystal. For example, consider the following isomeric compounds—pentane with a melting point of –130°C and 2,2-dimethylpropane with a melting point of –17°C. Pentane exists in a large variety of conformations that are similar in energy to each other. Below are three of its many possible staggered conformations.



Some conformations of pentane

Because the rotational energy barrier for the various conformations of pentane is very low, pentane exists as a mixture of conformations except at a very low temperature. Thus, pentane does not readily form a solid. It favors the liquid phase over the solid phase in the solid-liquid equilibrium.

In contrast to the conformational mobility of pentane, 2,2-dimethylpropane has only one conformation of the carbon skeleton:

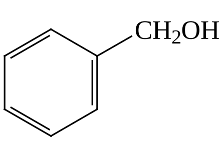


2,2-Dimethylpropane
m.p. -17°C

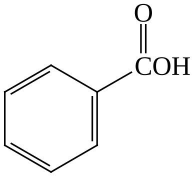
All the hydrogen atoms of 2,2-dimethylpropane are equivalent, and the molecule has a very high level of symmetry. This symmetry means that each molecule has the "right" conformation to form a crystal. Also, this symmetry increases the probability that each molecule has the correct orientation to fit into a growing crystal. Thus, 2,2-dimethylpropane readily forms a crystalline lattice. It favors its solid form in the solid-liquid equilibrium and requires a higher temperature than pentane to convert from its solid form to its liquid form.

In a polar molecule one or more bonds exhibit bond dipoles, and generally the molecule has a dipole moment.

Another important factor contributing to the melting point of a compound is its **polarity**. The more polar a compound is, the stronger are its intermolecular attractions and the higher is its melting point. For example, benzyl alcohol melts at –15°C whereas benzoic acid melts at 122°C.



Benzyl alcohol
m.p. -15°C

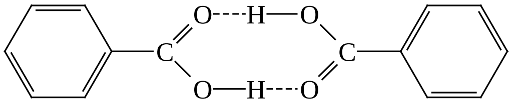


Benzoic acid
m.p. 122°C

A dimer is an association between two molecules that are held together by hydrogen bonds.

Hydrogen bonds form between polar oxygens in one molecule and acidic hydrogens in another. Section 4.3, page 000 discusses them in more detail.

Both compounds are polar, but the intermolecular attractions of benzoic acid are much stronger than those of benzyl alcohol, as is shown by the fact that benzoic acid forms a relatively stable **dimer**. This dimer is held together by attractions, called **hydrogen bonds**, between the polar oxygens and the acidic hydrogens of the carboxylic acid functional groups. Hydrogen bonds influence the melting point of a solid, but they influence the boiling point of a liquid even more (see Section 4.3.)



Dimer of benzoic acid

The molecular weight of a molecule is the sum of the atomic weights of all of the atoms in that molecule.

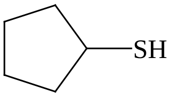
The **molecular weight** of a compound influences its melting point. As the molecular weight increases in a homologous series of compounds, so does the melting point. The reason the melting point increases with the weight is that it takes more energy to separate larger molecules from a crystalline structure than it takes to separate smaller ones. Although the increase in melting point holds true over a long series, other factors at times override the effects of molecular weight for molecules of similar size. Two of these factors are symmetry and hydrogen bonding. For example, because methane molecules are symmetrical and pack into a crystalline lattice better than propane molecules do, methane's melting point (–182.5 °C) is seven degrees *higher* than propane's (–189.7 °C) despite its lower molecular weight.

Exercise 4.1

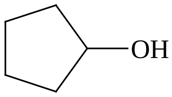
a) One stereoisomer of 1,4-dibromocyclohexane has a melting point of 113°C; the other isomer melts below 0°C. Draw both structures and assign melting points to the structures. Justify your choice.

b) Which has the higher melting point, hexane or cyclohexane? Explain your choice.

c) Cyclopentanethiol has a markedly *lower* melting point than cyclopentanol even though it has a higher molecular weight. Explain.



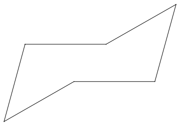
Cyclopentanethiol



Cyclopentanol

Sample solution

b) Cyclohexane has the higher melting point because it is more symmetrical and packs more readily into a crystal lattice. Hexane has many more conformations and thus is less likely to fit into a crystalline structure.



Cyclohexane

Hexane

4.3 Boiling Points

An important physical property of a liquid is its boiling point, which is the transformation point of a compound from its liquid phase to its gas phase. The definition of boiling point is the temperature at which the **vapor pressure** of a liquid equals the external (atmospheric) pressure above that liquid.

The vapor pressure of a compound is the pressure exerted by the vapor above the compound's surface.

When considering the boiling points for a homologous series of molecules, molecular weight is an important factor. Table 4.1 lists the boiling points for several common homologous series. As you look at the table, notice that within a series the boiling points quickly increase. For each series, the boiling point shows a fairly regular increase of 20-30°C with each additional CH_2 group in the chain. Also, the boiling points vary drastically based on the functional group that the molecule contains.

Number of Carbons in R	Boiling Points (°C)			
	R—H	R—Cl	R—OH	R—COOH
1	–160	–24	65	101
2	–89	12	78	118
3	–42	47	97	141

Number of Carbons in R	Boiling Points (ºC)			
	R—H	R—Cl	R—OH	R—COOH
4	0	78	117	164
5	36	98	138	186
6	69	134	157	206
7	98	160	176	223
8	126	183	195	240
9	151	203	213	254

Table 4.1. Comparative boiling points for several selected homologous series.

The molecules in the liquid phase are still close enough to each other that their physical interactions are similar to the physical interactions that occur between the same molecules in their solid phase. Although the interactions in the liquid phase are far more random, and thus generally weaker, than in the solid phase, they still occur and are important. In the gas phase, the molecules are so far apart that the intermolecular interactions are much weaker and are generally of little importance. Except for highly polar substances, such as carboxylic acids, there are essentially no interactions between most molecules in the gas phase.

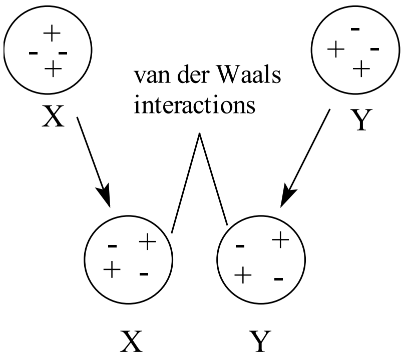
The interactions between molecules are the result of attractions between those molecules. These attractions fit into three different categories: van der Waals forces, dipolar attractions, and hydrogen bonding. The energies associated with these interactions are small compared to those associated with chemical bonds, but for a collection of molecules, they are significant.

When a pair of molecules approach each other, the nonbonded electrons on one molecule tend to attract the partially positive atoms on the other molecule. These attractive forces increase until they reach a maximum at intermolecular distances between 200 and 400 pm. At distances closer than this, the molecules tend to repel one another because their electrons repel one another. The actual distances at which the molecules begin to repel one another is the sum of the van der Waals radii of the two groups. The average distance between molecules in the liquid phase is in the range of 200-400 pm.

A complementary polarization occurs when a temporary dipole in one molecule induces a similar dipole in another molecule.

The van der Waals forces, also called London dispersion forces, are intermolecular attractions arising from complementary polarizations.

To understand what happens with these attractive forces, consider two nonpolar molecules, X and Y. Keep in mind that the distribution of electrons in these molecules is continually fluctuating. As the two molecules approach each other, they experience a mutual attraction, and any polarization in molecule X induces a **complementary polarization** in molecule Y. Chemists call this attraction **van der Waals forces** or **London dispersion forces**.

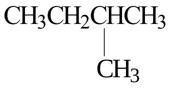


van der Waals forces, which are sometimes called induced polarizations or induced dipoles, are only temporary and are constantly changing because the electron distribution within each molecule rapidly fluctuates. When the polarization in one molecule changes, it influences a neighboring molecule, which in turn influences another neighboring molecule. The net effect is that all neighboring molecules are attracted to each other. The magnitude of van der Waals forces is based on the number of electrons in the molecules and how many of those electrons participate in these induced dipole-dipole interactions.

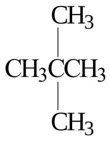
For a low polarity liquid to boil, it must overcome the van der Waals forces. The major factor in the magnitude of these forces is the shape of the molecule. Highly branched molecules have a more spherical shape and smaller van der Waals attractions. Unbranched molecules have more surface area that can be involved in intermolecular interactions and higher van der Waals attractions because they can pack closer. You can see this effect in the boiling points of the following three isomers: pentane, 2-methylbutane, and 2,2-dimethylpropane.

$CH_3CH_2CH_2CH_2CH_3$

Pentane
b.p. 36°C


$\mathrm{CH_3CH_2\underset{\underset{CH_3}{|}}{C}HCH_3}$

2-Methylbutane
b.p. 28°C

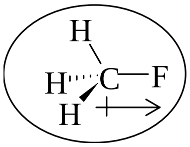

$\mathrm{CH_3\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}CH_3}$

2,2-Dimethylpropane
b.p. 9°C

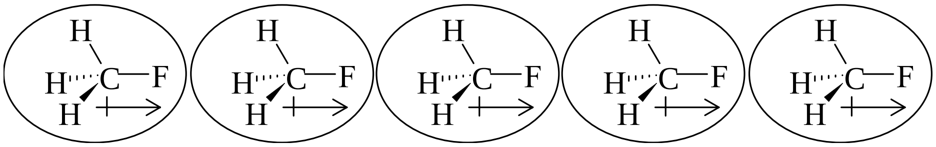
Individual van der Waals forces are very weak. However, a typical molecule can participate in so many polarization interactions that the van der Waals forces are among the most important of the intermolecular forces in the liquid phase. They are the only forces possible for nonpolar molecules.

Dipolar attractions are due to the uneven distribution of electrons in the covalent bonds that form between two atoms with differing electronegativities, thus creating a permanent dipole.

The second category of attractions that occurs between molecules is **dipolar attractions**. Molecules with permanent dipoles have dipolar attractions because of the charge polarization in their bonds. The interactions between molecules with permanent dipoles are similar to the van der Waals interactions between molecules with induced dipoles. The only difference is that the dipoles are permanent. Methyl fluoride illustrates the interaction of molecules with a permanent dipole. Methyl fluoride has a very polar C—F bond with a partial positive charge on the carbon and a partial negative charge on the fluorine atom:



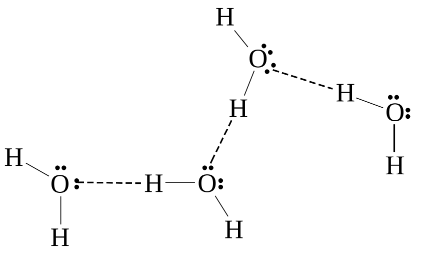
In the liquid form, many other molecules of methyl fluoride surround each individual molecule of methyl fluoride. All these molecules tend to line up with the negative end of one dipole associated with the positive end of another:



As with van der Waals forces, molecules with dipole attractions require energy to overcome these forces. The dipolar forces raise the boiling point of methyl fluoride above that of a comparable compound without electronegative substituents. For example, methyl fluoride and ethane, have similar molecular weights, but methyl fluoride boils at –78°C whereas ethane boils at –89°C.

Hydrogen bonding is an interaction between the hydrogen bonded to an electronegative atom (the hydrogen bond donor) and an atom with a nonbonding pair of electrons (the hydrogen bond acceptor).

The third category of interactions that affects the boiling point is **hydrogen bonding**. Hydrogen bonding is a type of weak bonding interaction that involves a **hydrogen bond donor** and a **hydrogen bond acceptor**. A hydrogen bond donor is a molecule containing a hydrogen attached to an electronegative atom. The most common electronegative atoms in organic molecules are oxygen and nitrogen. A hydrogen bond acceptor is a molecule containing an atom with a nonbonding pair of electrons. The best hydrogen bond acceptors in organic molecules are also oxygen and nitrogen.



Hydrogen bonding in water

The strongest hydrogen bonds are with the O—H group. Weaker hydrogen bonds form with N—H bonds. Much weaker still are the hydrogen bonds formed with S—H and P—H bonds. The strength of an individual hydrogen bond is roughly 5 kcal/mole, much smaller than the typical covalent bond strengths of 80-100 kcal/mole. Hydrogen bonds are stronger than dipolar interactions, which are about 1-2 kcal/mole.

Of the three types of attractive forces, hydrogen bonding is the strongest. Hydrogen bonding substantially raises the boiling points of the compounds in which it occurs. For example, the isomeric compounds dimethyl ether and ethanol have widely different boiling points due to hydrogen bonding in ethanol.

$CH_3—O—CH_3$

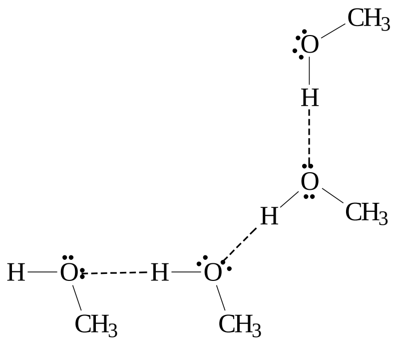
Dimethyl ether
b.p. -23°C

$CH_3CH_2—O—H$

Ethanol
b.p. 78°C

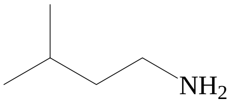
Dimethyl ether has no hydrogen atoms attached to the oxygen, so no hydrogen bonding is possible. However, ethanol has a hydrogen attached to the oxygen, so hydrogen bonding occurs.

Chemists consider hydrogen bonding a very weak or partial bonding between an oxygen of one molecule and a hydrogen of another. This bonding causes aggregations, or groupings, of molecules much like those resulting from dipolar attractions. However, these molecular aggregations possess much more stability than those resulting from dipolar interactions.

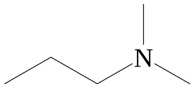


Hydrogen bonding in methanol

Similar aggregations of molecules occur with amines. However, the boiling point differences of isomeric amines are less dramatic than for isomeric compounds of oxygen. For example, 3-methyl-1-butanamine boils at 95-96°C whereas *N*,*N*-dimethylpropanamine boils at 65°C.



3-Methyl-1-butanamine
b.p. 95-96°C



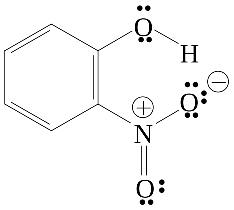
N,*N*-Dimethylpropanamine
b.p. 65°C

The electronegativity of N is 3.04 and O is 3.44.

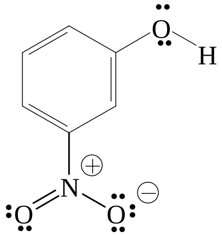
The smaller difference in boiling points suggests that hydrogen bonds with N—H bonds are weaker than hydrogen bonds with O—H bonds. The N—H bonds are less polar because nitrogen has a lower electronegativity than oxygen. The hydrogen bonds are weaker because the hydrogen end of the dipole in the N—H bond is less positive than that in the O—H bond.

Intramolecular interactions occur between different parts of the same molecule.

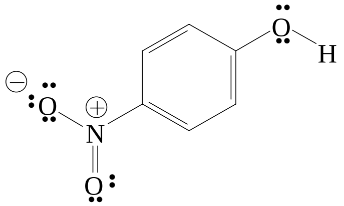
The previous discussion considers intermolecular hydrogen bonding. An additional factor comes into effect when two functional groups in one molecule participate in hydrogen bonding. The resultant **intramolecular** hydrogen bond is much more important than an intermolecular hydrogen bond in determining the properties of the molecule. For example, 2-nitrophenol has a much lower boiling point than either of its isomers, 3-nitrophenol or 4-nitrophenol.



2-Nitrophenol
b.p. 215^{o}C

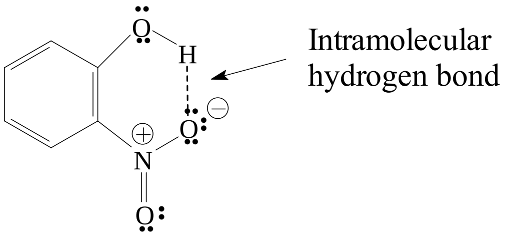


3-Nitrophenol
b.p. 263^{o}C



4-Nitrophenol
b.p. 279^{o}C

2-Nitrophenol forms an intramolecular hydrogen bond between the hydrogen of the O—H bond and one of the oxygens in the NO_2 group. This intramolecular hydrogen bond prevents an intermolecular hydrogen bond from forming. Thus, boiling requires much *less* energy for the 2-nitrophenol isomer than for the 4-nitrophenol isomer because there are no strong intermolecular forces to overcome in going from the liquid phase to the gas phase.



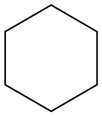
2-Nitrophenol
b.p. 215^{o}C

2-Nitrophenol represents a category of compounds in which intramolecular hydrogen bonding forms either a stable five- or six-membered ring. Section 3.5, page 000 discusses the relative stability of rings of various sizes. Because of this stability, they form more readily than rings of any other size. Any process that can result in a five- or six-membered ring is favored over one yielding another ring size. Expect to see this pattern repeatedly in your study of organic chemistry.

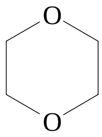
Section 3.5, page 000, discusses the relative stability of rings of various sizes.

Exercise 4.2

a) There is a 20^{o}C difference in the boiling points of cyclohexane and 1,4-dioxacyclohexane (commonly called 1,4-dioxane). Which boils higher? Explain.

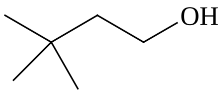


Cyclohexane

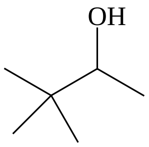


1,4-Dioxacyclohexane
(1,4-Dioxane)

b) Which has the higher boiling point, 3,3-dimethyl-1-butanol or 3,3-dimethyl-2-butanol? Explain.

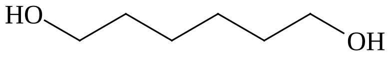


3,3-Dimethyl-1-butanol

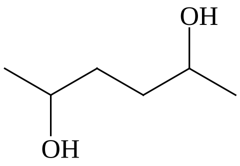


3,3-Dimethyl-2-butanol

c) 1,6-Hexanediol has a boiling point of 250^{o}C; 2,5-hexanediol has a boiling point that differs from this by 33^{o}C. What is the boiling point of 2,5-hexanediol? Explain.



1,6-Hexanediol



2,5-Hexanediol

Sample solution

(a) Cyclohexane is a nonpolar compound. Therefore, the only intermolecular attractions that must be overcome for it to boil are van der Waals forces. 1,4-Dioxane has four polar C—O bonds, so it participates in some dipolar attractions. Because of these added intermolecular attractions, 1,4-dioxane boils at a higher temperature.

4.4 Solubility

Most chemical reactions take place in solution. That is, the **solutes**, or the reagents that you want to react, are uniformly mixed with, or dissolved in, the solvent. There are two types of solutions: **single-phase solutions** and **multiple-phase solutions**. In a single-phase, or homogeneous, solution all the solutes are **soluble** in the same solvent. Reactions take place best in single-phase solutions. This

In a single-phase solution all solutes dissolved in the solution are soluble in the same solvent.

In a multiple-phase solution there are two or more mutually insoluble solvents present.

uniform distribution allows a higher rate of reaction between the reactants because they have a greater amount of contact with each other. Single-phase solutions also allow you to control the solution concentrations and reaction conditions. Multiple-phase mixtures are mixtures in which the individual solutes are not soluble in the same solvent, thus, you must use more than one solvent. Each solvent then forms a different layer in the mixture. In multiple-phase mixtures, the reactants have less contact with each other so that the rate of reaction is generally slower than in a single-phase solution.

One compound is soluble in another compound when both form one phase without either pure compound being separately visible.

One compound is soluble in another as a result of the various intermolecular forces present in both compounds. These intermolecular forces are van der Waals forces, hydrogen bonding, and polarity. Molecular weight also plays a part in the solubility of a compound. The higher the molecular weight the lower the solubility. A compound dissolves in a solvent when the interactions between the compound and the solvent are either similar in strength or stronger than those interactions between molecules in the compound to be dissolved. There are also correlations between the molecular structure of the compounds and their solubility. A simple rule of thumb for estimating solubility is: A compound dissolves most easily in a solvent that is structurally similar to itself. The phrase “structurally similar” means that the solvent and the solute are similar types of molecules. For example, polar solutes or solvents mix with other polar solutes or solvents and nonpolar solutes or solvents mix with other nonpolar solutes or solvents, but polar solutes or solvents do not generally mix with nonpolar solutes or solvents.

Water is highly polar making it an excellent solvent for ionic compounds and small polar organic molecules. If an ethyl group replaces one of the hydrogens in water, the result is ethanol, a solvent that has a substantially reduced polarity. Ethanol actually has both a polar and a nonpolar end. Although ethanol participates in hydrogen bonding and thus is a moderate solvent for salts and highly polar molecules, it also has van der Waals forces, making it a good solvent for a variety of organic molecules as well. Ethanol is too polar, however, to readily dissolve many low-polarity substances. Replacing both hydrogens in water with ethyl groups produces diethyl ether. Diethyl ether is only moderately polar. It acts as a hydrogen bond acceptor and so is a poor solvent for salts. However, it is a good solvent for a variety of both polar and nonpolar organic molecules.

Water is a poor solvent for low polarity compounds, such as gasoline. Gasoline, a mixture of alkanes, will not dissolve in water. All attempts to dissolve gasoline in water, or water in gasoline, result in a two-phase solution with the gasoline floating on the water. Gasoline won't dissolve in water for several reasons. (1) The molecular structures of the two substances are different. Gasoline, a mixture of hydrocarbons, is nonpolar, and water is highly polar. (2) The molecular weights of the hydrocarbons are much larger in comparison to water. (3) The van der Waals forces between the molecules of gasoline are much stronger than they are in water. With water, primarily hydrogen bonding and secondarily dipolar attractions determine its intermolecular interactions. Both hydrogen bonding and dipolar attractions are stronger than van der Waals forces. Thus, gasoline does not dissolve in water because such a solution would reduce the number of stronger interactions. With gasoline and water, there is an unfavorable solvent-solute interaction.

Solubility is dependent on the temperature of the solution. In general, the higher the temperature the higher the solubility of a solute in a given solvent. For example, the solubility of benzoic acid in water is 1.7 g/L at 0°C; it increases to 68.0 g/L at 95°C. Figure 4.7 shows a plot of the solubility of benzoic acid in water versus temperature. Note that the solubility of benzoic acid increases rapidly as the temperature increases above75°C.

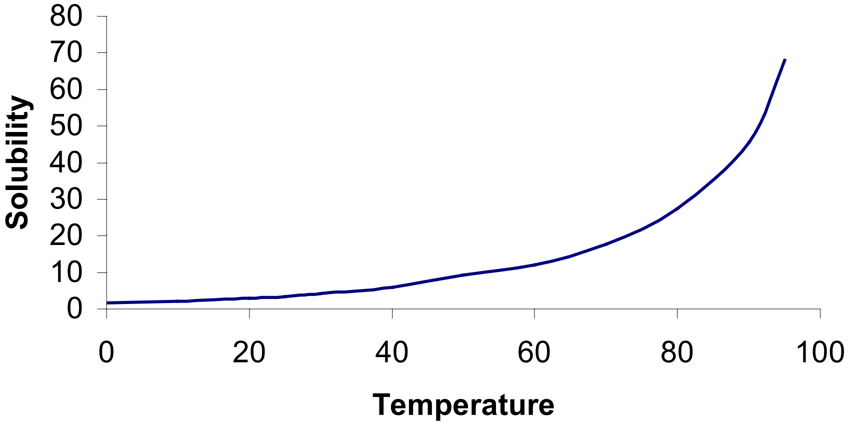


Figure 4.7. A plot of the solubility of benzoic acid in water versus the temperature of the solution.

Recrystallization

A common laboratory purification technique is recrystallization. To begin, dissolve a solid compound in a minimum quantity of a hot solvent. On cooling, crystals of the original molecule form. The ideal solvent is one that does not dissolve the solute very well at low temperatures, but dissolves it readily at its boiling point. In general, the best solvent has a slightly lower polarity than the solute and thus the intermolecular interactions of solute with solvent are weaker than the intermolecular interactions of the solute. At higher temperature the solute becomes more soluble. Another useful characteristic for the solvent is a low boiling point, which makes it easier to remove solvent traces from the purified solute crystals. Finally, a good solvent should be a better solvent for any impurities than it is for the desired compound.

Table 4.2 summarizes the solubility trends for several common solvents and solutes.

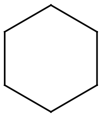
	Solvent			
Solute	Water H_2O	Ethanol CH_3CH_2OH	Diethyl ether $(CH_3CH_2)_2O$	Pentane $CH_3(CH_2)_3CH_3$
NaCl	+	s	-	-
Ethanoic Acid	+	+	+	+
2-Propanone	+	+	+	+
2-Decanone	-	+	+	+
2-Propanol	+	+	+	+
2-Decanol	-	+	+	+
Glycerol (1,2,3-Propanetriol)	+	+	s	s
Chloromethane	s	+	+	+
1-Chloropropane	-	+	+	+

Symbols used: + = soluble, s = slightly soluble, - = insoluble

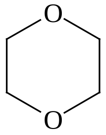
Table 4.2. Solubility trends.

Exercise 4.3

a) Is cyclohexane more or less soluble in water than 1,4-dioxacyclohexane (more commonly called 1,4-dioxane)? Explain.

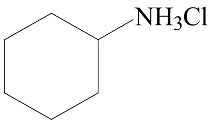


Cyclohexane

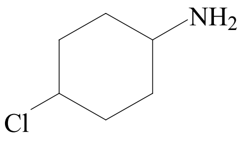


1,4-Dioxacyclohexane
(1,4-Dioxane)

b) Which of the two following compounds is more soluble in pentane? (Hint: Be sure to draw a Lewis structure of each.)

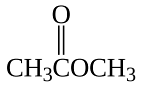


Cyclohexyl ammonium chloride



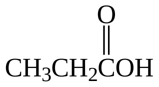
4-Chlorocyclohexanamine

c) Is methyl acetate more or less soluble in pentane than is propanoic acid? Explain.



$CH_3\overset{\overset{O}{\|}}{C}OCH_3$

Methyl acetate



$CH_3CH_2\overset{\overset{O}{\|}}{C}OH$

Propanoic acid

Sample solution

a) Cyclohexane is much less soluble in water than is 1,4-dioxane. The four C—O bonds of 1,4-dioxane are available for dipolar attractions and act as hydrogen bond acceptors.

[SIDEBAR]

Surfactants

When chemists hear the word “surfactant,” they first think of soaps or detergents. Although soaps and detergents are the most familiar of the **surfactants**, they are not the only ones. There are different kinds of surfactants—many of which have commercial uses. Even your body produces surfactants.

A surfactant is a molecule where one end of the molecule is soluble in one solvent and the other end of the same molecule is soluble in a different solvent. Surfactant is an acronym derived from the words surf*ace* act*ive* a*gent.*

A surfactant is one of a class of chemical structures with a “dual personality” in respect to solubility. Surfactants are usually large molecules. One end is soluble in water; the other end is soluble in the typical organic solvents. This dual solubility is due to a highly polar segment at one end of the molecule and a nonpolar segment at the other end.

Now look at soaps and detergents. A typical soap is the sodium or potassium salt of a long-chain carboxylic acid. Potassium stearate, $CH_3(CH_2)_{16}COOK$, is a soap molecule. The “head” of the molecule, the ionic portion, is water-soluble; the “tail” of the molecule, the hydrocarbon chain, is water-insoluble. Chemists call the head the **hydrophilic portion** of the molecule and the tail the **hydrophobic portion**.

Hydrophilic means “water-loving.” Hydrophobic means “water-hating.”

Adding a soap molecule to water results in the formation of small agglomerations of molecules with long hydrophobic tails. These tails are dissolved in one another and the polar portions pointing outward into the water. These agglomerations are called **micelles**. Figure 4.8 illustrates the structure of a micelle.

A micelle is an agglomeration of molecules that contain polar and nonpolar portions with one set of portions “dissolved” in one another and the other set of portions “dissolved” in the solvent.

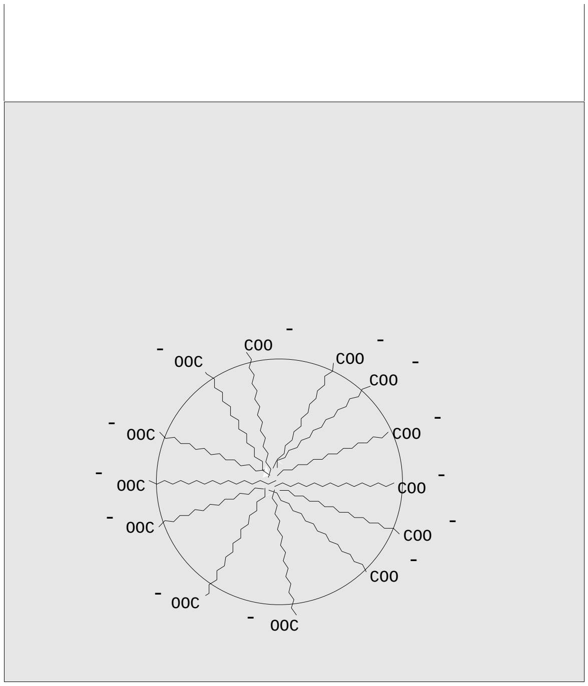


Figure 4.8. Soap molecules form a micelle in water.

When you wash your skin or clothing, you want to remove two basic types of materials: dry particles and grease. Usually, you can readily rinse dry particles off. Washing grease off is much harder because it is insoluble in water. Here the surfactants in soap help. The tails of the soap molecules are a solvent for the grease. So they dissolve the grease. The heads of the soap molecules project out of the grease particle. Because the heads are soluble in water, they dissolve in the water, and the water carries the soap and the grease away. The interaction of the ionic ends of the surfactant molecules with the surrounding water holds the micelles suspended in the water (see Figure 4.8). The suspended micelles form an **emulsion** of the grease-soap solution and water.

An emulsion is a suspension of small droplets of one liquid in another liquid in which it is normally insoluble.

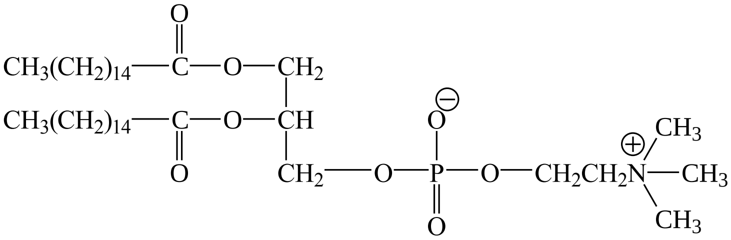
A difficulty with soaps is that they don't work well in **hard water**. The most common cations in hard water are calcium, magnesium, and iron ions. When you put soap into hard water, a precipitate of calcium, magnesium, or iron salts forms from an interaction of the cations with the carboxylate ions in the soap. This precipitate is the “bathtub ring” that you must scrub from your tub after you bathe using soap in hard water.

Hard water has any of the possible metal cations other than sodium or potassium ions dissolved in it.

To solve this problem, chemists have developed a variety of surfactants with more soluble calcium or magnesium salts. One is sodium dodecanyl sulfate (sodium lauryl sulfate), $CH_3(CH_2)_{11}OSO_3^{\ominus}$ $Na^{\oplus}$. The textile industry uses sodium lauryl sulfate as a detergent. It is also used as a **wetting agent** in photography and toothpaste. In an aqueous solution, a wetting agent works by lowering the surface tension of the solution below that of pure water.

A wetting agent causes a solvent to adhere to, or wet, a surface better than it does when the solvent is pure.

A very important surfactant that lowers the surface tension of a solution is found in the transfer of oxygen to the bloodstream. This surfactant is necessary for life itself. A complex mixture of lipids and water coats the interior of the lungs. Simply described, this mixture consists of an aqueous solution of diapalmitoylphosphatidylcholine (DPPC), whose molecules have a hydrophilic head and a hydrophobic tail.



Dipalmitoylphosphatidylcholine
(DPPC)

DPPC lowers the surface tension of the interior of the lungs, thereby increasing the rate of oxygen absorption. Polluted air and, particularly, cigarette smoke reduce the ability of the lungs to produce DPPC and thus inhibit the transfer of oxygen into the body.

DPPC also keeps your lungs inflated. DPPC coats the inside of the alveoli in your lungs and this coating lowers the surface tension on the inside of the alveoli. Outside the alveoli is the blood, which has a much higher surface tension. This difference in surface tension pulls the alveoli into a spherical shape.

Before birth, the fetus makes some respiratory-type movements, but its lungs remain collapsed. Immediately after birth the infant makes several strong inspiratory movements, and the lungs expand. The surfactant in the lining of the lungs keeps them inflated. However, when an infant is born before the surfactant system is functional, their lungs will not properly inflate or remain inflated. This problem, called hyaline membrane disease, is especially serious for premature infants who don't have a functional surfactant system. To help fight this condition, premature infants are given surfactants until their own surfactant system begins to function properly.

4.5 Density

Density is the mass of some substance per unit volume of that substance.

An extraction is the transfer of a solute from one solvent to a better one.

For liquids, **density** is usually measured as the number of grams per milliliter—expressed as g/mL. Density is a useful tool in the laboratory. Its most common use is in **extractions**, the transfer of a solute from one solvent to a better one. To do an extraction, choose a solvent that is better than the one the solute is currently dissolved in. The two solvents must be insoluble in one another. Then shake the two together and separate them. Because you know the density of each solvent and which solvent best dissolves the solute, you know which one to keep. You may also use density, as you do boiling or melting points, to help identify unknown liquids.

Density of Solids

You can easily estimate the relative density of many organic liquids, but you cannot do so as readily with solids because the density of a solid depends on too many factors. Two generalizations that relate to the density of solids are: organic solids typically have lower densities than inorganic solids, and nonionic solids typically have lower densities than ionic solids. Beyond these generalizations, this book does not consider the density of solids.

Selected van der Waals radii, are listed in Table 3.1, page 000.

The density of an organic liquid depends on three factors: the molecular weight of the substance, the ratio of the number of heavy atoms to the number of carbons in the molecule, and how well the molecules pack together. The first two factors are very closely related because, when determining the density of a liquid, there is more to the picture than just the molecule's actual weight. Of greater importance is the ratio of the number of heavy atoms to carbon atoms in the molecule. For example, the van der Waals radius of a methyl group is 200 pm, and the van der Waals radius of a bromine atom is 195 pm. The formula weight of a methyl group is 15, and the atomic weight of the bromine is 80. Bromine weighs more than five times as much as the methyl group, yet it takes up a smaller volume of space. This leads to a dramatic increase in density for bromine compared to a methyl group. Thus, when you compare the two in compounds pentane and 1-bromobutane, for example, you find that both compounds have nearly the same molecular volume, but the density of pentane is 0.62 g/mL, and that of 1-bromobutane is 1.27 g/mL.

This type of difference holds true for any set of molecules with similar sizes—the molecule with the heavier atoms is the molecule with the higher density. For example, cyclohexane and cyclohexane-d_{12} (in which all of the hydrogens have been replaced with deuterium, ^{2}H) have densities of 0.78 and 0.89 g/mL respectively.

The third factor that determines a liquid's density is how efficiently its molecules pack together. The closeness of packing depends on how readily each molecule fits into an aggregation of molecules. For example, hexane, with a density of 0.66 g/mL, has many more stable conformations than does cyclohexane, with a density of 0.78 g/mL. Cyclohexane packs more efficiently because it is more symmetrical than hexane.

Intermolecular attractions affect the packing efficiency of a molecule. The greater these attractions, the more readily the molecules pack together. Dipolar attractions and, especially, hydrogen bonding increase the density of a liquid. For example, compare the isomers diethyl ether and 1-butanol. Diethyl ether, which has van der Waals and dipolar attractions, has a density of 0.71 g/mL. 1-Butanol, which has hydrogen bonding in addition to van der Waals and dipolar attractions has a density of 0.81 g/mL.

$CH_3CH_2OCH_2CH_3$
Diethyl ether
0.71 g/mL

$CH_3CH_2CH_2CH_2OH$
1-Butanol
0.81 g/mL

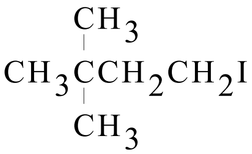
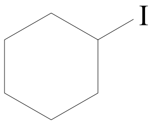
Chemists often perform extractions using a two-phase liquid system consisting of water and some organic liquid. They use an estimate of the density of the organic liquid relative to that of water. They work with estimates rather than precise densities because that is all they need to know to decide which layer is which. Here is a rule for estimating the densities of molecules relative to water. Any molecule containing bromine, iodine, or multiple chlorine atoms (e.g., $CHCl_3$) has a density greater than that of water (1 g/mL). All other organic solvents generally have a density less than that of water. This rule, of course, is less effective for large molecules. In a large molecule, the functional group becomes less important, and all the physical properties tend to converge to the same values. Table 4.3 illustrates how chain length affects densities. Note that the density changes rapidly for molecules containing between two and ten carbons, but above ten carbons, the density does not change very much.

	Chain Length				
Functional Group	2	6	10	14	18
Alkane	0.509	0.660	0.730	0.763	0.789
1-Amino	0.683	0.766	0.783	0.818	0.822
1-Chloro	0.898	0.879	0.870	0.866	0.864
1-Phenyl	0.783	0.814	0.830	0.834	Solid
Ethyl ester	0.900	0.871	0.865	0.857	0.852

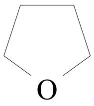
Table 4.3. The effect of changing chain length on the density of liquids containing various functional groups.

Exercise 4.4

Predict which compound of the following pairs has the higher density.

a) 
$CH_3C(CH_3)_2CH_2CH_2I$ or 

b) Bromotrifluoromethane or Tribromofluoromethane

c)  or $CH_3CH_2OCH_2CH_3$

Sample solution

b) Tribromofluoromethane has a much higher density than bromotrifluoromethane because it has three bromine atoms and bromotrifluoromethane has only one.

Key Ideas from Chapter 4

☐ The four phases of matter are solid, liquid, gas, and plasma.

☐ A sample compound in its gas phase has no definite shape or volume. In its liquid phase, it has volume but no specific shape. In its solid phase, it has both volume and shape.

☐ The molecular structure determines a compound's physical properties. Chemists are not yet able to correlate molecular structure with physical properties quantitatively.

☐ Intermolecular forces are the primary factors that determine the physical properties of a compound. These forces include van der Waals forces, dipolar interactions, and hydrogen bonding.

☐ The melting point of a compound is the temperature at which the compound's solid phase is in equilibrium with its liquid phase.

☐ The boiling point of a compound is the temperature at which its liquid phase is in equilibrium with its gas phase.

☐ Momentary dipolar attractions between adjacent nonpolar molecules cause van der Waals forces.

☐ A carbon bonded to some atom of different electronegativity results in a polar bond. Polar bonds cause dipolar interactions.

☐ The interaction between a hydrogen that is attached to an electronegative atom and the nonbonding electrons of an atom in another molecule results in hydrogen bonding.

☐ If the intermolecular forces between solute and solvent are as strong or stronger as the attractions between molecules of the solute or the solvent itself, then the solute will be soluble in the solvent.

☐ The atomic weights of the atoms of a molecule contribute to the density of that molecule. When a molecule has a relatively large number of heavy atoms, its density is high.

☐ Another factor that determines the density of a compound is the strength of its intermolecular attractions. The stronger the intermolecular attractions, the higher the density.

☐ The larger the molecule, the less important are any functional groups in determining that molecule’s physical properties.

Richard F. Daley and Sally J. Daley
www.ochem4free.com

Organic Chemistry

Chapter 5

Acid-Base Theory

Chapter 5

Acid-Base Theory

Chapter Outline

5.1 Acids and Bases
A comparison of the Arrhenius, Brønsted-Lowry, and Lewis theories of acids and bases

5.2 Acid and Base Strength
A review of pH and K_a

5.3 Hard and Soft Acids and Bases
An introduction to hard and soft acid-base theory

5.4 Organic Acids and Bases
Molecular characteristics of organic acids and bases

5.5 Relative Acidity and Basicity
Estimating relative acidity and basicity

5.6 Substituent Effects on Acidity and Basicity
Inductive effects on acid and base strength

Objectives

- ✓ Be familiar with the Arrhenius, Brønsted-Lowry, and Lewis theories of acids and bases
- ✓ Recognize the orbitals that are involved in an acid-base reaction
- ✓ Know the relationship between acid strength and the value of pK_a
- ✓ Understand the relationship between polarizability and the hardness or softness of an acid or base
- ✓ Predict the stability of a chemical bond using the hard-soft acid base theory
- ✓ Recognize whether an organic functional group is an acid or a base
- ✓ Predict the relative acid or base strength of two organic compounds
- ✓ Understand how the presence of a particular functional group affects the acid or base strength of another functional group

> I hope no body will offer to dispute whether an *Acid* has points or no, seeing every ones experience does demonstrate it, they need but to taste an *Acid* to be satisfied of it, for it pricks the tongue like anything keen, and finely cut … An *Alkali* is a terrestrous and solid matter, whose *pores* are figured after such a manner that the *Acid* points entering them do strike and divide whatsoever opposes their motion.
>
> —Nicholas Lemery
> "A Course in Chymistry"
> London (1686)

As you work with chemical reactions in organic chemistry, you will find that you can classify nearly all of them as acid-base reactions. The key to understanding organic chemical reactions is knowledge of acids and bases. When considering a reaction, you need to ask three questions: Where's the acid? Where's the base? How can the acid react with the base? The goal for this chapter is to introduce you to ways that answer these questions.

Whether a molecule acts as an acid or a base in a chemical reaction largely depends on its characteristics. There are three significant molecular characteristics that affect acidity and basicity. The most important is the compound's primary functional group. A second factor is the inductive effect caused by the presence of additional functional groups. A third is the delocalization, or resonance effects, of the electrons in a molecule.

Showing Charges on Atoms

When you learned to write ions in your introductory chemistry course, you learned to put the charges after the formula of the ion. For example, you wrote the hydroxide ion as $OH^{\ominus}$. In organic chemistry it is important to know *which* atom in an ion bears the charge. For example, the oxygen in the hydroxide ion has the negative charge. In this book the hydroxide ion is written as $^{\ominus}OH$ to remind you that the oxygen has the negative charge. Other examples of familiar ions written in this manner are $^{\oplus}NH_4$, $^{\ominus}CH_3$, and $NO_3^{\ominus}$. For these three ions, you know immediately that the charges are on N, C, and O respectively.

5.1 Acids and Bases

Three major definitions of acids and bases have influenced the thinking of chemists. In 1884, Svante Arrhenius formulated the first of these definitions. Then, in 1923, independently of each other, Johannes N. Brønsted and Thomas M. Lowry developed the second. The third definition grew from Gilbert Newton Lewis's theory of covalent bonding, which he proposed in 1916.

The first definition, proposed by Svante Arrhenius in his doctoral dissertation, was so revolutionary that he was almost denied his Ph.D. However, in 1903, he received the Nobel Prize in chemistry for his theory. His theory states that a stable ionic compound that is soluble in water will break down, or dissociate, into its component ions. This dissociation, or ionization, of a compound in water, leads to Arrhenius' definition of an acid and a base. An acid is a substance that, when added to water, increases the concentration of hydronium ions, $H_3O^{\oplus}$. Because Arrhenius regarded acid-base reactions as occurring only in water, he frequently called the hydronium ion a hydrogen ion, $H^{\oplus}$. An $H^{\oplus}$ ion is a proton, or a hydrogen that is electron-deficient. Thus, a base is a substance that, when added to water, increases the concentration of hydroxide ions, $^{\ominus}OH$. The following statements summarize his definition.

An Arrhenius acid is a source of $H^{\oplus}$ ion.
An Arrhenius base is a source of $^{\ominus}OH$ ion.

The Arrhenius acid-base theory provided a good start toward understanding acid-base chemistry, but it proved much too limited in its scope.

Brønsted and Lowry developed a more general acid-base definition than that of Arrhenius. Although they considered reactions other than those that take place in aqueous solutions, they still said acids were molecules that donate a hydrogen ion—such as HCl and H_2SO_4. However, they broadened the definition of bases to include any compound that accepts a proton. The basis of their acid-base definition is that in a reaction a proton transfers between reactants. Thus, acids involving a transfer of $H^{\oplus}$ ions are sometimes called proton acids. According to the Brønsted-Lowry definition, an acid is any molecule or ion that donates a proton to another molecule or ion, and a base is any molecule or ion that receives that proton. The following statements briefly summarize the Brønsted-Lowry definition.

A Brønsted-Lowry acid is a proton donor.
A Brønsted-Lowry base is a proton acceptor.

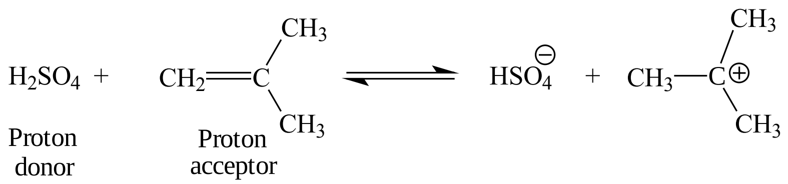
An example of the Brønsted-Lowry definition is the reaction between hydrogen chloride and sodium hydroxide:

$$\underset{\substack{\text{Proton}\\\text{donor}}}{HCl} + \underset{\substack{\text{Proton}\\\text{acceptor}}}{NaOH} \longrightarrow NaCl + H_2O$$

In this reaction, HCl is the acid because it is the source of protons, or hydrogen ions; NaOH is a base because the hydroxide ion is the proton acceptor. The following reactions further illustrate the Brønsted-Lowry acid-base definition.

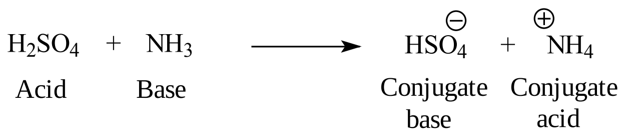
$$\underset{\substack{\text{Proton}\\\text{donor}}}{H_2SO_4} + \underset{\substack{\text{Proton}\\\text{acceptor}}}{NH_3} \longrightarrow HSO_4^{\ominus} + \overset{\oplus}{N}H_4$$

$$\underset{\substack{\text{Proton}\\\text{donor}}}{HCl} + \underset{\substack{\text{Proton}\\\text{acceptor}}}{CH_3CH_2NH_2} \longrightarrow Cl^{\ominus} + CH_3CH_2\overset{\oplus}{N}H_3$$



When an acid and a base react with each other, the reactants and products are in equilibrium with each other. Note the two-way arrows. They indicate that this is an equilibrium reaction. That is, the reactants on the left side of the equation are reacting and forming product, and the products on the right side are *also* reacting and forming the starting reactants. Chemists call the acid and base on the right side of the equation the **conjugate acid** and **conjugate base**. The reaction below is labeled to show the conjugate acid and conjugate base.

A conjugate acid-base pair consists of the acid and base products that result from an acid-base reaction.



A hydrogen of sulfuric acid (H_2SO_4) is the acid, and the nitrogen of ammonia (NH_3) is the base. They react to form the hydrogen sulfate anion ($HSO_4^{\ominus}$) and the ammonium ion ($NH_4^{\oplus}$). The ammonium ion is the conjugate acid of ammonia. The bisulfate ion is the conjugate base of the sulfuric acid.

The hydrogen sulfate ($HSO_4^{\ominus}$) anion is also called the bisulfate ion.

Like Brønsted and Lowry, G. N. Lewis defined acids and bases in a broader scheme than Arrhenius did. Lewis noted that there are a number of reactions that look like acid-base reactions but do not involve the transfer of a proton. Instead, they involve the interaction of a pair of nonbonding electrons. From that observation, he defined an acid as a molecule that forms a covalent bond by accepting a pair of electrons and a base as a molecule that forms a covalent bond by donating a pair of electrons. Below is a simplified statement of the Lewis definition of acids and bases.

A Lewis acid is an electron-pair acceptor.
A Lewis base is an electron-pair donor.

Reconciling the Acid-Base Theories

To prevent confusion over the terms *acceptor* and *donor*, stop and look at the three definitions of acids and bases. Keep in mind that although all three definitions consider the same concept, they do so from different viewpoints. Arrhenius and Brønsted-Lowry look at acids and bases from the viewpoint of proton transfers. Lewis looks at them from the viewpoint of electron pairs. The two viewpoints mesh when you remember that a proton is a positive hydrogen ion that has no electron, and is thus capable of accepting a pair of electrons.

Solved Exercise 5.1

The following compounds can act either as a Brønsted-Lowry acid or a Lewis acid. Show the reactive site in each compound and the structure of the conjugate base that results from a reaction with base $A^{\ominus}$. Determine whether the compound is a Brønsted-Lowry acid or a Lewis acid.

a) CH_3OH

Solution
Both the oxygen and the carbon have full valence shells and both have at least one hydrogen as a source of protons. However, oxygen is much more electronegative than carbon, so a negative charge on oxygen is more stable than a negative charge on carbon. Thus, the O—H bond is the reactive site and a stronger Brønsted-Lowry acid than is the C—H bond.

$$\underset{\text{Acid}}{CH_3OH} + \underset{\text{Base}}{A^{\ominus}} \rightleftharpoons \underset{\substack{\text{Conjugate}\\\text{base}}}{CH_3O^{\ominus}} + \underset{\substack{\text{Conjugate}\\\text{acid}}}{HA}$$

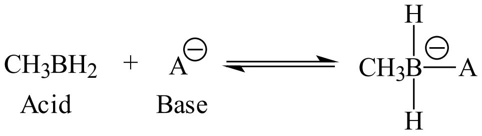
b) CH_3NH_2

Solution
Nitrogen is much more electronegative than carbon, so a negative charge on nitrogen is more stable than a negative charge on carbon. Thus, the N—H bond is a stronger Brønsted-Lowry acid than is the C—H bond.

$$\underset{\text{Acid}}{CH_3NH_2} + \underset{\text{Base}}{A^{\ominus}} \rightleftharpoons \underset{\substack{\text{Conjugate}\\\text{base}}}{CH_3\overset{\ominus}{N}H} + \underset{\substack{\text{Conjugate}\\\text{acid}}}{HA}$$

c) CH_3BH_2

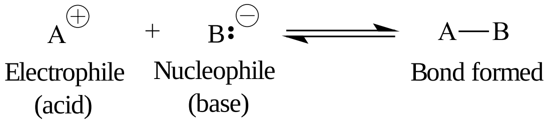
Solution
Because boron is electron deficient with only six electrons in its valence shell, it will react before any bonds to hydrogen are broken. Thus, the boron is the reactive site, and it acts as a Lewis acid.

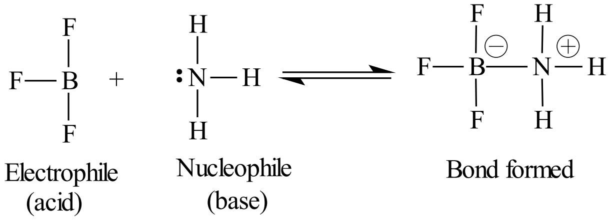


$$\underset{\text{Acid}}{CH_3BH_2} + \underset{\text{Base}}{A^{\ominus}} \rightleftharpoons CH_3\overset{\ominus}{B}H_2{-}A$$

In the formation of a new chemical bond, an electrophile accepts electrons, and a nucleophile donates electrons.

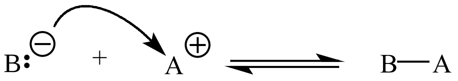
Because a Lewis acid accepts a pair of electrons, chemists call it an **electrophile**, from the Greek meaning "lover of electrons." They call the base a **nucleophile**, or "lover of nuclei," because it donates the electrons to a nucleus with an empty orbital. In a chemical reaction, a nucleophile seeks a nucleus, or a positive charge, and an electrophile seeks electrons, or a negative charge. Fundamental to organic chemistry is the fact that nearly all the reactions that you will study are reactions of an acid with a base or, more commonly, of an electrophile with a nucleophile.

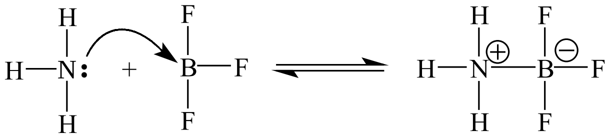




Curved arrows are introduced in Section 1.13, page 000.

Chemists use a curved arrow () to show electron movement. A curved arrow points from the electron-rich reactant, the base or nucleophile, toward the electron-poor reactant, the acid or electrophile. Rewriting the previous two reactions using a curved arrow shows the movement of electrons. In each reaction, a pair of nonbonding electrons from a nucleophile reacts with an electrophile to form a bond.





Exercise 5.1

Use curved arrows to write the acid-base reaction of a hydrogen ion with a hydroxide ion.

Acids and Bases versus Electrophiles and Nucleophiles

In organic chemistry, the terms *acid* and *electrophile* are formally synonymous, but informally, they have evolved different shades of meaning. The term *acid* has come to mean a proton donor and the term *electrophile* has come to mean an electron pair acceptor. Similarly, the term *base* has come to mean a proton acceptor, and the term *nucleophile* has come to mean an electron pair donor. However, from time to time, the dividing line between the two sets of terms becomes fuzzy. For example, chemists may call the same group of atoms a base or a nucleophile depending on the chemical environment of that group. Probably the most useful generalization is that the difference between a base and a nucleophile is in how they react. In organic reactions, a base generally reacts with a proton, and a nucleophile generally reacts with a positively charged or electron-deficient carbon. An electron-deficient carbon is a carbon with an unfilled octet in its valence shell.

All chemical reactions involve orbital interactions. The orbital description of a reaction can help you understand how chemical reactions occur. As you study the various reactions presented in this book, think about the orbitals involved in the reactions. Figure 5.1 is a molecular orbital picture of ammonia reacting with boron trifluoride to form a new bond. Ammonia is a base with a pair of nonbonding electrons. The nitrogen of ammonia is sp^3 hybridized. Boron trifluoride is an acid with an incomplete octet of electrons. The boron is sp^2 hybridized with an empty p orbital. The reaction occurs when an sp^3 orbital of ammonia overlaps with the empty p orbital of boron trifluoride. In the process, the boron becomes sp^3 hybridized. With this overlap the two molecules form a new bond.

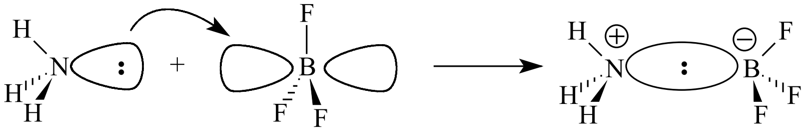


Figure 5.1. The orbitals involved in the acid-base reaction of NH_3 and BF_3.

Exercise 5.2

Show the orbitals involved in the acid-base reaction of a hydrogen ion with a hydroxide ion.

Being able to identify an acid or base is important. Of equal importance is the ability to recognize how the structure of that acid or base affects its strength. The rest of this chapter is devoted to helping you acquire the tools to do so. With these tools, you can predict the outcome of chemical reactions. Much of the rest of the material in this book depends on your ability to recognize acids and bases and their relative strengths.

5.2 Acid and Base Strength

The strength of a Brønsted-Lowry acid or base depends on the extent to which it ionizes in water. Although there are numerous solvents besides water, chemists discuss acid and base strength in relation to water because they use it so widely as a solvent. Chemists use the **autoionization** of pure water to determine the values for the concentrations of acidic and basic solutions. Autoionization is the reaction of two molecules of water with each other to give a hydronium ion, $H_3O^{\oplus}$, and a hydroxide ion, $^{\ominus}OH$.

Autoionization is a process by which one molecule of a compound reacts with another molecule of the same compound in an acid-base reaction.

$$H_2O + H_2O \rightleftharpoons H_3O^{\oplus} + {}^{\ominus}OH$$

For this reaction, the amount of autoionization is extremely slight—at 25^{o}C, it is 10^{-7} M (moles/liter). The concentrations of $H_3O^{\oplus}$ and $^{\ominus}OH$ are equal; that is, both measure 10^{-7} M. Chemists call this a neutral solution. If you add a compound that is more acidic than water, you increase the concentration of $H_3O^{\oplus}$ ions and make the solution acidic. If you add a compound that is more basic than water, you increase the concentration of $^{\ominus}OH$ ions and make the solution basic.

The product of the $H_3O^{\oplus}$ and $^{\ominus}OH$ concentrations in water is equal to 10^{-14} and is a constant, K_w. Chemists define K_w with the following equation.

$$K_w = [H_3O^{\oplus}][{}^{\ominus}OH] = 1.00 \text{ x } 10^{-14}$$

Because the concentrations of $H_3O^{\oplus}$ and $^{\ominus}OH$ are equal in a neutral solution, you can easily calculate the concentration of both:

When performing a concentration calculation, replace the chemical species listed within the brackets, [$^{\ominus}$OH], for example, with that species' molar concentration.

$$[H_3O^{\oplus}] = [{}^{\ominus}OH] = 1.00 \text{ x } 10^{-7} \text{ M}$$

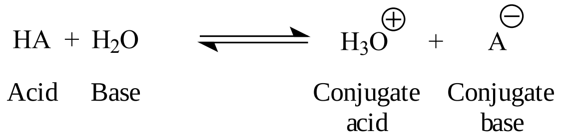
Because the product of the two concentrations is a constant, K_w, when one concentration increases, the other must decrease. For example, if you add $^{\ominus}OH$ ions to water the concentration of the $H_3O^{\oplus}$ decreases by whatever amount is necessary for the product of the two concentrations to still equal 10^{-14}.

Because the hydronium ion concentrations can span a very wide range of values, from greater than 1 M down to less than 10^{-14} M, chemists measure the concentration of $H_3O^{\oplus}$ on a logarithmic scale called pH. The pH values give the hydronium ion concentration of a solution. Therefore, measuring the pH of a solution is a means of quantifying the acidity of that solution. Chemists define this measurement as the negative logarithm (base 10) of the $H_3O^{\oplus}$ concentration, represented by the following equation:

$$pH = -\log_{10}[H_3O^{\oplus}]$$

For simplicity, this book will normally refer to the $H_3O^{\oplus}$ ion as the $H^{\oplus}$ ion from now on. If an equation shows the $H^{\oplus}$ ion present in aqueous solution, remember that it is actually the $H_3O^{\oplus}$ ion.

This equation shows the general reaction of an acid in water:



$$\underset{\text{Acid}}{HA} + \underset{\text{Base}}{H_2O} \rightleftharpoons \underset{\text{Conjugate acid}}{H_3O^{\oplus}} + \underset{\text{Conjugate base}}{A^{\ominus}}$$

Note that this reaction is an equilibrium. Most acid-base reactions are equilibrium reactions because the reactants only partly ionize. Strong acids and bases ionize completely in water. Weak acids and bases ionize only partly in water. An acidic, aqueous solution is any solution with a concentration of hydrogen ions greater than 10^{-7} M. Similarly, a basic solution is any solution with a concentration of hydroxide ions greater than 10^{-7} M.

To determine the relative strength of an acid or a base, you need to find out how much the acid or the base ionizes, or dissociates, in water at equilibrium. The equilibrium constant, K_e, gives this information and is defined as follows:

$$K_e = \frac{[H_3O^{\oplus}][A^{\ominus}]}{[HA][H_2O]}$$

However, because water is the solvent and its concentration is essentially constant, a more meaningful value for acid ionization comes from multiplying the equilibrium constant by the water concentration:

$$K_a = K_e[H_2O] = \frac{[H_3O^{\oplus}][A^{\ominus}]}{[HA]}$$

An acid dissociation constant expression is the equilibrium expression without the solvent concentration.

Chemists call K_a the **acid dissociation constant**. The value of K_a specifies the strength of the acid. The stronger the acid, the larger the amount of dissociation and the larger the concentration of $H_3O^{\oplus}$ ions. Thus, the stronger the acid, the larger the value of K_a. Strong acids completely dissociate in water and have large dissociation constants. Most organic compounds are weak acids and have dissociation constants in the range from 10^{-2} to 10^{-60}.

Because acids have such a large range of values for their dissociation constants, chemists often convert those values to a logarithmic scale, similar to pH. The following equation defines this scale:

$$pK_a = -\log_{10} K_a$$

Solved Exercise 5.2

Calculate the value of K_a and pK_a for water.

Solution
Below is the autoionization equation for water

$$H_2O + H_2O \rightleftharpoons H_3\overset{\oplus}{O} + \overset{\ominus}{O}H$$

and the K_a expression for water.

$$K_a = \frac{[H_3O^{\oplus}][^{\ominus}OH]}{[H_2O]}$$

The numerator of the K_a expression is the same as the expression for K_w:

$$K_w = [H_3O^{\oplus}][\,^{\ominus}OH] = 1.00 \text{ x } 10^{-14}$$

So, you can substitute $1.00 \text{ x } 10^{-14}$ for the numerator of the K_a expression. The $[H_2O]$ is the number of moles per liter of water and is calculated as follows.

$$[H_2O] = \frac{\text{Wt of 1 L of } H_2O}{\text{molecular weight of } H_2O} = \frac{1000 \text{ g/L}}{18 \text{ g/mol}} = 55.6 \text{ mol/L}$$

Substitute the values in the K_a expression and calculate:

$$K_a = \frac{[H_3O^{\oplus}][^{\ominus}OH]}{[H_2O]} = \frac{K_w}{[H_2O]} = \frac{1.00 \text{ x } 10^{-14}}{55.6} = 1.8 \text{ x } 10^{-16}$$

The value of pK_a for water is 15.7.

Strong acids generally have pK_a values around 0 or below, and most neutral organic acids have pK_a values greater than 2. Table 5.1 gives some values for a sampling of acids. A more complete listing is found in Appendix A. The pK_a values given are relative to water. Values higher than 18 and lower than –5 are estimates. Many of the values here and in the appendix will be useful to you as you learn organic chemistry. Mark the location of Appendix A for quick access.

Figure 5.2 is a graphical summary of pK_a values for some important categories of acids. It gives you an overview of the acid strengths of a variety of types of compounds.

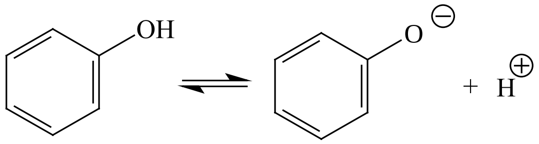
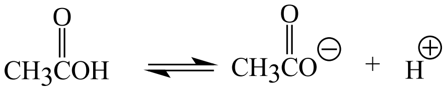
Acid Dissociation Reaction	pK_a
$CH_4 \rightleftharpoons {}^{\ominus}CH_3 + H^{\oplus}$	49
$CH_2{=}CH_2 \rightleftharpoons CH_2{=}\overset{\ominus}{C}H + H^{\oplus}$	44
$NH_3 \rightleftharpoons {}^{\ominus}NH_2 + H^{\oplus}$	36
$CH_2{=}CHCH_3 \rightleftharpoons CH_2{=}CH\overset{\ominus}{C}H_2 + H^{\oplus}$	35
$HC{\equiv}CH \rightleftharpoons HC{\equiv}C^{\ominus} + H^{\oplus}$	26
$H_2O \rightleftharpoons {}^{\ominus}OH + H^{\oplus}$	15.7
$CH_3OH \rightleftharpoons CH_3O^{\ominus} + H^{\oplus}$	15.1
	10.0
$H_2S \rightleftharpoons {}^{\ominus}SH + H^{\oplus}$	7.0
 $CH_3\overset{\overset{O}{\parallel}}{C}OH \rightleftharpoons CH_3\overset{\overset{O}{\parallel}}{C}O^{\ominus} + H^{\oplus}$	4.8
$HF \rightleftharpoons F^{\ominus} + H^{\oplus}$	3.2
$HNO_3 \rightleftharpoons NO_3^{\ominus} + H^{\oplus}$	–1.4
$H_3O^{\oplus} \rightleftharpoons H_2O + H^{\oplus}$	–1.7
$H_2SO_4 \rightleftharpoons HSO_4^{\ominus} + H^{\oplus}$	–5.2
$HCl \rightleftharpoons Cl^{\ominus} + H^{\oplus}$	–7.0
$HBr \rightleftharpoons Br^{\ominus} + H^{\oplus}$	–9.0
$HI \rightleftharpoons I^{\ominus} + H^{\oplus}$	–10

Table 5.1. Some pK_a values for various acids. See Appendix A for a more complete list of pK_a values.

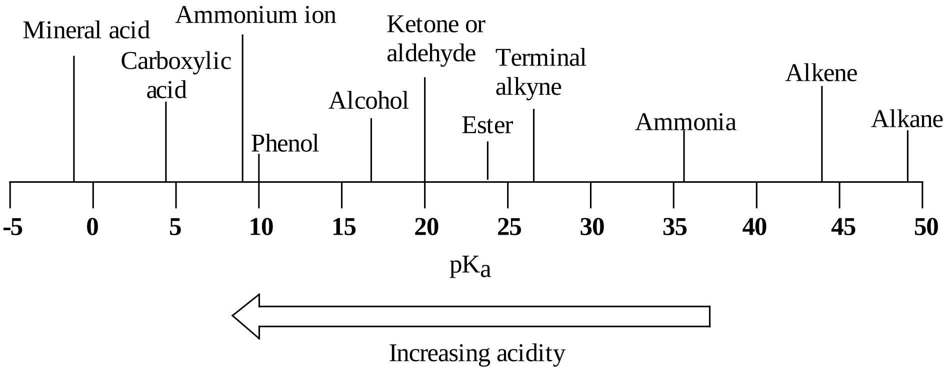


Figure 5.2. A graphical representation of pK_a values for some important categories of Brønsted-Lowry acids. Note that the value indicated for a functional group shows the most typical pK_a value for members of that group. For ketones, aldehydes, and esters, the pK_a is for the hydrogen on the carbon adjacent, or α, to the C=O double bond.

Exercise 5.3

Using the pK_a value given with each acid, calculate the pH of its aqueous solution.

a) 0.1 M CH_3COOH (p$K_a = 4.8$) b) 0.1 M H_2S (p$K_a = 7.0$)
c) 0.1 M CH_3CH_2SH (p$K_a = 10.6$) d) 0.1 M HCOOH (p$K_a = 3.7$)

Sample Solution

c) The pK_a is 10.6. The dissociation reaction is:

$$CH_3CH_2SH \rightleftharpoons CH_3CH_2S^{\ominus} + H^{\oplus}$$

Assume that the concentration of the acid is unchanged. You can make this assumption with less than 1% error if the pK_a is greater than 4 and the acid has one acidic proton. Use the K_a equation:

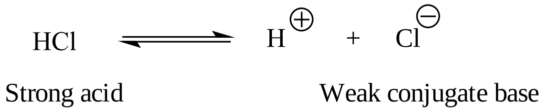
$$K_a = \frac{[H^{\oplus}][CH_3CH_2S^{\ominus}]}{[CH_3CH_2SH]}$$

Because you know the K_a of CH_3CH_2SH and since the concentrations of $H^{\oplus}$ and $CH_3CH_2S^{\ominus}$ are equal, the equation becomes:

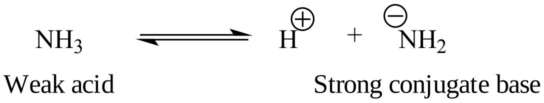
$$10^{-10.6} = \frac{x^2}{10^{-1}}$$

Solve for *x*. The result is a value of $10^{-5.8}$, or a pH of 5.8.

A strong acid always reacts to form a weak conjugate base, and a weak acid always reacts to form a strong conjugate base. This relationship exists because the stronger the Brønsted-Lowry acid, the more willing it is to give up a proton thus forming a more stable conjugate base. A more stable conjugate base is less willing to accept a proton. The following examples illustrate this relationship.



$$HCl \rightleftharpoons H^{\oplus} + Cl^{\ominus}$$



$$NH_3 \rightleftharpoons H^{\oplus} + {}^{\ominus}NH_2$$

The first reaction, the dissociation of HCl, may be familiar from your introductory chemistry course. At equilibrium, the right side is favored. The dissociation of NH_3, however, is very unlikely to occur because the amide ion (${}^{\ominus}NH_2$) is a very strong base. Thus, at equilibrium, the left side is favored.

Stability

Frequently, as you read and study chemistry, you will see the term *stable*. Chemists use this word in a comparative sense, saying that one chemical species is more stable than another chemical species. Seldom, if ever, do they use it in an absolute sense. Usually, when chemists compare one chemical species with another, the two have some similarities. In the previous example, the similarity is that both $Cl^{\ominus}$ and ${}^{\ominus}NH_2$ are bases. Experience shows that $Cl^{\ominus}$ is less reactive than ${}^{\ominus}NH_2$, so $Cl^{\ominus}$ is more stable.

The relationship between a base and its conjugate acid is similar to that of an acid and its conjugate base. Strong bases react to form weak conjugate acids, and weak bases react to form strong conjugate acids. The reasons for base strength are the opposite of the reasons for acid strength. For a Brønsted-Lowry base, the stronger the base, the *more* willing it is to accept a proton. For a Lewis base, the stronger the base, the *more* willing it is to give up electron pairs.

$$\overset{\ominus}{C}H_3 \quad + \quad H^{\oplus} \rightleftharpoons CH_4$$

Strong base Weak conjugate acid

$$NO_3^{\ominus} \quad + \quad H^{\oplus} \rightleftharpoons HNO_3$$

Weak base Strong conjugate acid

The reactants and products are usually in equilibrium in these reactions.

An extremely important concept in predicting the outcome of a reaction is that *the position of equilibrium is on the side of the weaker member of the acid-conjugate base (or base-conjugate acid) pair*. A strong acid or base is more reactive than a weak acid or base.

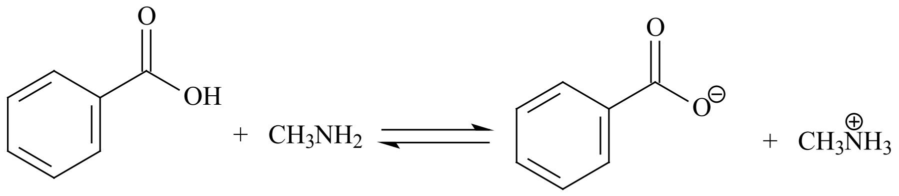
Exercise 5.4

For each of the following reactions identify the acid, base, conjugate acid, and conjugate base. Then, using the pK_a values from Appendix A, predict whether the position of equilibrium will favor the starting materials or the products.

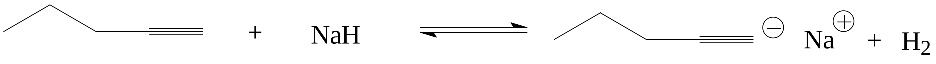
a)

$$CH_3OH \quad + \quad {}^{\ominus}NH_2 \rightleftharpoons CH_3O^{\ominus} \quad + \quad NH_3$$

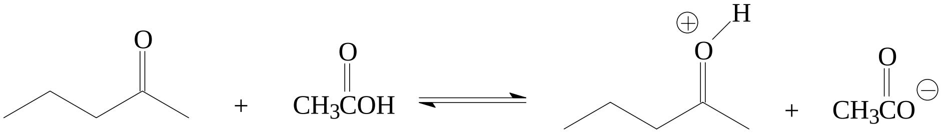
b)



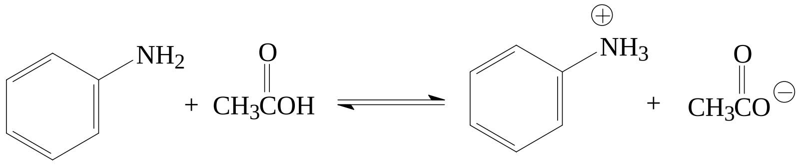
c)



d)



e)



Solution

a)

$$CH_3OH + {}^{\ominus}NH_2 \rightleftharpoons CH_3O^{\ominus} + NH_3$$

Acid	Base	Conjugate base	Conjugate acid
$pK_a = 15.1$			$pK_a = 36$

The conjugate acid is much weaker than the acid. Thus, the products are favored.

5.3 Hard and Soft Acids and Bases

The ease with which an acid-base reaction occurs depends on the strength of both the acid and the base. Strong acids and bases are generally more reactive than weak acids and bases. However, the direction of the reaction and the stability of the products often depend on another quality—the **hardness** or **softness** of the acid and base. Although chemists have not created a quantitative measure to describe the qualities that makes an acid or base hard or soft, they do describe them qualitatively. As you look at the following list of characteristics that describe hard and soft acids and bases, remember that an acid has an empty orbital and an unfilled valence shell, and a base has in its valence shell a pair of nonbonding electrons that is available for donation.

Hardness or softness is a qualitative measure of the reactivity of acids and bases. Hard or soft is independent of strength or weakness of acids and bases.

Soft Acids. For soft acids, the electron-pair acceptor atoms are large, have a low positive **charge density**, and contain unshared pairs of electrons in their valence shells. The unshared pairs of electrons are in the *p* or *d* orbitals. Also, soft acids have a high **polarizability** and a low electronegativity. In organic chemistry, the soft acids usually include only the halogens, phosphorus, and sulfur compounds.

Charge density is the volume of space occupied by a charge. A large ion has a lower charge density than a small ion does.

Polarizability means the ability of an atom to have a distorted distribution of electrons.

Hard Acids. For hard acids, the acceptor atoms are small, have a high positive charge density, and contain no unshared pairs of electrons in their valence shells. They have a low polarizability and a high electronegativity. The hydrogen ion is a good example of a hard acid.

Soft Bases. For soft bases, the donor atoms hold their valence electrons loosely. They have high polarizability, low negative charge density, and low electronegativity. Common soft bases are the cyanide ($^{\ominus}$CN) and iodide (I$^{\ominus}$) ions.

Hard Bases. For hard bases, the donor atoms are small, have a high negative charge density, and hold their valence electrons tightly. They have a low polarizability and a high electronegativity. The hydroxide ion is a good example of a hard base.

To visualize a polarizable atom, imagine that an atom is a large floppy ball and you are holding it cupped in both hands. The ball tends to be spherical, but, as you shift one hand higher than the other, it easily deforms. If you raise your left hand a little, the portion of the ball in your right hand becomes larger. Then, if you raise your right hand a little, the portion of the ball in your left hand becomes larger. A polarizable atom shifts its electron density from one part of the atom to another: at one instant, one portion of the atom has the higher electron density; then the next instant, another portion has the higher electron density.

Bond Polarity Versus Polarizability

Bond polarity differs from polarizability. In a polar bond, the more electronegative atom of the bonded pair pulls the bonding electrons toward itself. A polarizable atom or group can momentarily shift electron density from one portion of the atom or group to another.

For the concepts of hardness or softness of acids and bases to be of value to you, you must be able to differentiate between them. To do this, your most useful tool is the periodic table. A general rule is that hardness goes to softness moving from the top to the bottom on the periodic table because the size of the atoms increases with increasing numbers of electrons. A larger acid or base has a lower charge density and is more polarizable. For example, base softness in Group VII A on the periodic table decreases in this order: $I^{\ominus} > Br^{\ominus} > Cl^{\ominus} > F^{\ominus}$. Also, the elements on the left side tend to be acids, and elements on the right side tend to be bases. In this way, chemists approximately rank acids and bases in order of hardness or softness. Base softness within a period on the periodic table decreases in order of increasing electronegativity; for example, $^{\ominus}CH_3 > {}^{\ominus}NH_2 > {}^{\ominus}OH > F^{\ominus}$.

Hardness and softness are difficult to quantify. Rather than relying specifically on these types of sequences, chemists divide acids and bases into three groups: (1) hard acids or bases, (2) soft acids or bases, and (3) borderline acids or bases. Table 5.2 lists a few examples of each category.

Acids	**Type**	**Bases**
$H^{\oplus}$, $Li^{\oplus}$, $^{\oplus}CH_3$, $Na^{\oplus}$, $K^{\oplus}$, $Mg^{2\oplus}$,$Ca^{2\oplus}$, $Al^{3\oplus}$, BF_3, $AlCl_3$, $RCO^{\oplus}$, CO_2	*Hard*	H_2O, $^{\ominus}OH$, $F^{\ominus}$, $Cl^{\ominus}$, $^{\ominus}CH_3$, $^{\ominus}NH_2$, $RCOO^{\ominus}$, $CO_3{}^{2\ominus}$, ROH, $RO^{\ominus}$, NH_3, RNH_2
$Fe^{2\oplus}$, $Zn^{2\oplus}$, $Sn^{2\oplus}$, $Sb^{3\oplus}$, BR_3, SO_2, $R_3C^{\oplus}$, $NO^{\oplus}$	*Borderline*	$C_6H_5NH_2$, $N_3{}^{\ominus}$, $Br^{\ominus}$, $NO_2{}^{\ominus}$, $R^{\ominus}$
$Cu^{\oplus}$, $Ag^{\oplus}$, $Hg^{2\oplus}$, BH_3, I_2, Br_2, $:CH_2$ (carbenes)	*Soft*	$RS^{\ominus}$, $I^{\ominus}$, $^{\ominus}CN$, RCN, CO, C_6H_6, $^{\ominus}SH$, $H^{\ominus}$

Table 5.2. Some examples of hard and soft acids and bases. (R represents an alkyl group.)

$H^{\oplus}$ is a hard acid because it has no electrons and has a high positive charge density. The $H^{\ominus}$ ion is a soft base because it has a pair of electrons and only one proton, so it holds the electrons rather loosely. Thus, it is quite polarizable and soft.

Exercise 5.5

Classify each of the following chemical species as a hard, soft, or borderline acid or base.

a) $(CH_3)_3B$
b) $CH_3CH_2O^{\ominus}$
c) $(CH_3)_3Al$
d) AsH_3
e) $FeCl_3$
f) CH_3OH
g) $(CH_3)_3C^{\oplus}$
h) $(CH_3)_3C^{\ominus}$
i) $^{\ominus}SeH$
j) $(CH_3)_3N$
k) CH_3NH_2
l) $SnCl_2$

Sample solution

b) Oxygen is small and nonpolarizable and has a high electronegativity. Therefore, it is a hard base, making the alkoxide ion a hard base.

An important rule concerning acid-base reactions is that hard acids prefer to bond with hard bases, and soft acids prefer to bond with soft bases. This rule, often called the **HSAB Principle**, has nothing to do with acid or base strength, but merely states that a bond between a particular acid and a particular base has extra stability if both are either hard or soft. The HSAB Principle also helps to predict the outcome of an acid-base reaction. For example, the acyl group ($RCO^{\oplus}$) is a hard Lewis acid and forms stable combinations with hard Lewis bases such as $^{\ominus}NH_2$, $RO^{\ominus}$, and $Cl^{\ominus}$. In contrast, it forms

The HSAB principle is the preference for hard bases to form bonds with hard acids and soft bases to form bonds with soft acids.

Chapter 12, which begins on page 000, presents an application of the HSAB principle.

marginally stable or even unstable compounds with soft Lewis bases such as $RS^{\ominus}$ and $I^{\ominus}$.

Exercise 5.6

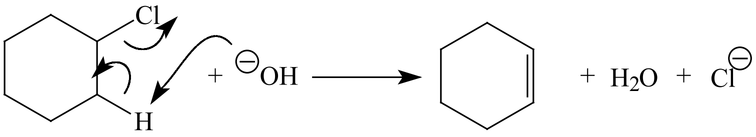
According to the HSAB Principle, which of the following chemical compounds would you expect to be stable (or only moderately reactive) and which would you expect to be unstable (or very reactive)?

a) AlI_3	b) CH_3COSH	c) NaH
d) $Mg(SH)_2$	e) $Hg(OH)_2$	f) CH_3Cl
g) AgF	h) $CuCH_3$	i) CuI
j) $HgCO_3$	k) CsOH	l) KCH_3

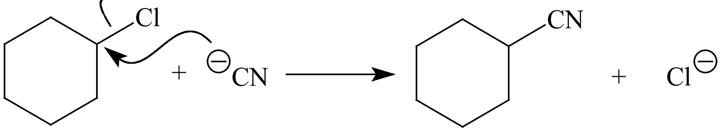
Sample solution

a) From Table 5.2, note that $Al^{3\oplus}$ is a hard acid, and $I^{\ominus}$ is a soft base. Thus, AlI_3 is either unstable or highly reactive.

Perhaps the most important application of the HSAB Principle is in determining whether a particular compound will act as a base or as a nucleophile. Generally, a soft base is a good nucleophile, and a hard base is a better base. Chapters 12 through 14 show this rule of thumb in action. The statement was made earlier that a nucleophile generally reacts with a positive or partially positive carbon, and a base generally reacts with a positive or partially positive hydrogen. This statement is a simplified form of the HSAB principle: $H^{\oplus}$ is a much harder acid than $C^{\oplus}$, so it tends to react with a harder base than $C^{\oplus}$ does. For example, chlorocyclohexane reacts with a hydroxide ion to remove a proton from the carbon adjacent to the carbon bearing the chlorine. This reaction forms a double bond.



On the other hand, chlorocyclohexane reacts with cyanide ion ($^{\ominus}CN$) to form a product containing a nitrile group.



The difference between these two reactions is that the hydroxide ion is a hard base, whereas the cyanide ion is a soft base. The hydroxide ion removes a proton; the cyanide ion reacts with the carbon bearing the chlorine to displace the chlorine.

Curved Arrows

A word of further explanation about curved arrows is appropriate here. As noted previously, curved arrows show the flow of electrons in reactions. As you look at the reaction of hydroxide ion with chlorocyclohexane, start following the arrows at the hydroxide ion. The first arrow points toward a hydrogen on the ring, forming a new H—OH bond. Simultaneously, the electrons in the C—H bond form a double bond, ejecting the chloride ion with its pair of electrons. In the second reaction, the cyanide ion reacts with the carbon bearing the chlorine to form a new C—C bond. At the same time the chloride ion leaves with its pair of electrons.

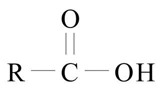
Thus far, this chapter has presented acids and bases in a broad sense. It covered the different theories of acidity and basicity and how to estimate their relative strengths. It also showed how acids and bases react with each other. Section 5.4 applies these concepts specifically to organic acids and bases.

5.4 Organic Acids and Bases

Organic acids and bases have acidic or basic functional groups and a carbon backbone.

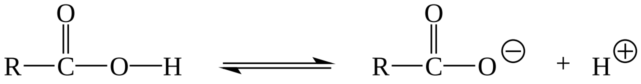
Section 5.4 moves from the broad spectrum of acids and bases in all areas of chemistry to the narrower topic of the organic acids and bases. **Organic acids** and **organic bases** are acids and bases that contain a carbon skeleton. Within these categories are a number of classes of neutral proton acids and bases (that is, uncharged acids and bases.) The first part of this section examines the three main types of neutral organic proton acids to see why they are acids and why they have widely different acid strengths. The second part looks at the two main types of neutral organic bases. The last part looks at positively charged carbon acids and negatively charged carbon bases.

Three main types of neutral organic Brønsted-Lowry acids are carboxylic acids, phenols, and alcohols. Each of these three functional groups has an —OH group. Each is acidic because of the electronegativity difference between the oxygen and the hydrogen involved in the O—H bond. The differences in acid strength of the three functional groups are due to the differences in stability of the conjugate base. The most acidic of the three groups are the carboxylic acids. Carboxylic acids are characterized by the presence of the carboxyl group:



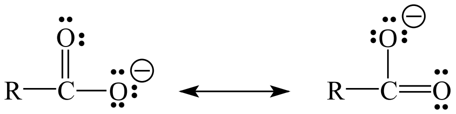
$$R-\overset{\overset{\displaystyle O}{\|}}{C}-OH$$

Carboxylic acids are among the most acidic of the neutral organic acids, but they are rather weak acids. For example, the pK_a of acetic acid, a common carboxylic acid, is 4.8, indicating that only a small portion of the molecules of acetic acid ionize in an aqueous solution. In contrast, mineral acids, such as HCl, with a pK_a of –7.0, and HNO_3, with a pK_a of –5.2, completely ionize in aqueous solutions. Although carboxylic acids are weaker than mineral acids, they are the strongest of the neutral organic acids that you will study.



$$R{-}\overset{\overset{\Large O}{\|}}{C}{-}O{-}H \rightleftharpoons R{-}\overset{\overset{\Large O}{\|}}{C}{-}O^{\ominus} + H^{\oplus}$$

The reason for the relative strength of the carboxylic acids is the conjugate base is resonance-stabilized, which makes it a weak base.

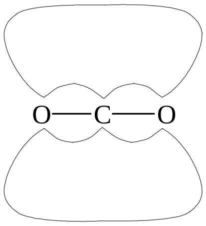


Carboxylate ion resonance

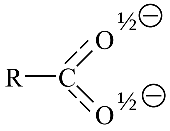
In the carboxylate ion the negative charge spreads over the two oxygen atoms as a resonance hybrid. This reduces the energy of the anion and makes the carboxylic acid more acidic.

Another way of visualizing the reason for the acid strength of carboxylic acids is to look at the molecular orbital system of the carboxylate ion. The carboxylate ion includes three *p* orbitals that contain a total of four electrons. The overlap of these three *p* orbitals results in a **three-centered π molecular orbital system**.

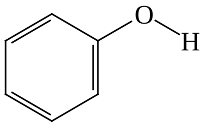
A three-centered π molecular orbital system is a π molecular orbital that includes three atoms. More examples are discussed in Chapter 16.



The carbon is joined to each oxygen atom by the equivalent of ½ of a π bond. Each oxygen atom bears ½ of the negative charge.

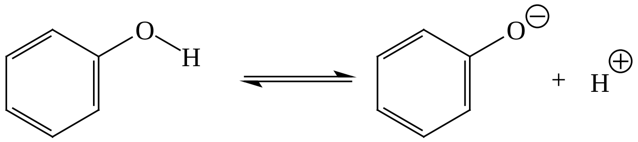


The second main type of neutral organic acids are the phenols. Phenols are much less acidic than carboxylic acids. An —OH group attached to an aromatic ring is characteristic of phenols:

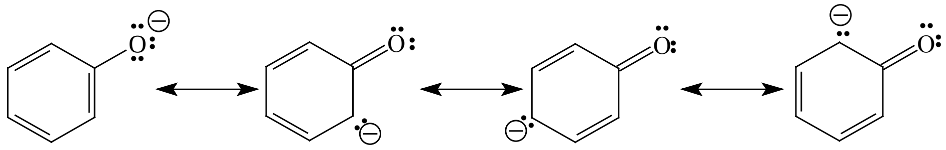


Phenol

Phenol has a pK_a of 10.0 in aqueous media, indicating that in water only a very small portion of it ionizes.



Phenols are moderately strong organic acids because their conjugate bases are resonance-stabilized. The aromatic ring is involved in resonance, which stabilizes the negative charge.



However, this stabilization is less significant than it is for carboxylic acids for two reasons: the resonance stabilization of the phenolate ion disrupts the aromaticity of the aromatic ring, and the resonance stabilization places a negative charge on the carbon atoms, which, when compared to oxygen, are not very electronegative.

The third type of neutral organic acids are alcohols. An —OH group attached to an alkyl group characterizes an alcohol:

The letter R is used in a chemical structure to represent a generalized alkyl group.

$$R{-}O{-}H$$

Alcohols are much less acidic than phenols. In fact, most alcohols have an acid strength slightly lower than that of water.

$$R{-}O{-}H \rightleftharpoons R{-}O^{\ominus} + H^{\oplus}$$

A typical alcohol has a pK_a of 15 to 18 in aqueous media, indicating only a very small amount of ionization. Alcohols have such a low acidity because there is no resonance stabilization of the conjugate base.

This section discusses only two of the many types of neutral organic bases: amines and ethers. The primary characteristic of neutral organic bases is they contain one or more pairs of nonbonding electrons. These pairs of electrons are available to donate to a Lewis acid or to accept a proton when the base is acting as a Brønsted-Lowry base. The more available the pair of electrons, often called a lone pair, the stronger the base. Any molecule with a lone pair of electrons can act as a base.

The most common of the organic bases are the amines. Amines are derivatives of ammonia (NH_3) and most are weak bases in aqueous media.

$$H_2O + \underset{\text{Methyl amine}}{CH_3NH_2} \rightleftharpoons \underset{\text{Methyl ammonium ion}}{CH_3\overset{\oplus}{N}H_3} + {}^{\ominus}OH$$

The pK_a of methyl ammonium ion is 10.6 meaning that the methyl ammonium ion is a relatively weak acid. Thus, methylamine is a moderately strong base.

Amines are stronger bases than other neutral organic bases because the nonbonding pair of electrons on the nitrogen is more available than nonbonding pairs of electrons on other neutral organic bases. The atoms that are found in these other neutral organic bases are oxygen, sulfur, or the halogens. Nitrogen holds its electrons less tightly than these other atoms, so its compounds are the stronger bases. Figure 5.3 illustrates the structure of an amine.

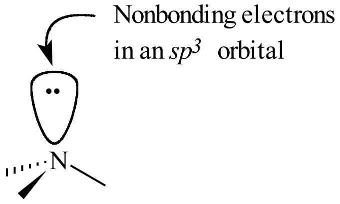
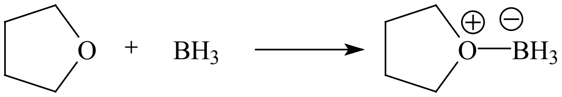


Figure 5.3. Structure of the amine nitrogen.

Ethers, the second type of neutral organic bases, have the general structure ROR′. Ethers are weak bases in aqueous media. In fact, they are so weak that they do not appreciably protonate, or accept a proton, even in 1 M HCl. The pK_a of the conjugate acid of ethyl ether is –3.8. A pK_a of this magnitude indicates that water is a better base than is an ether.

A complex is a type of molecule in which one of the atoms either donates or receives both electrons involved in the bond between that atom and an adjacent atom.

In nonaqueous media, ethers are good Lewis bases, forming stable **complexes** with Lewis acids. The ability to form stable complexes is extremely important in organic reactions. For example, in organic synthesis, chemists widely use the complex of BH_3 with the cyclic ether tetrahydrofuran:



A carbocation is a positively charged carbon atom. The carbon atom normally is sp^2 *hybridized.*

The third category of organic acids and bases discussed in this section are the positively charged acids and the negatively charged bases. Positively charged acids are electron-deficient. That is, they are organic acids that contain a carbon without an octet of electrons. The most significant electron-deficient organic acid is the **carbocation** (formerly called a carbonium ion). Carbocations are very reactive reaction intermediates, so chemists seldom observe them directly. A carbocation is a Lewis acid because, without a full octet of electrons, it is electron-deficient and "needs" electrons. As a result of this need for electrons, it reacts with the first available Lewis base—although it prefers a hard one because it is a hard acid. As Figure 5.4 shows, the positively charged carbon forms three *sp*^{2} hybridized bonds in a plane with an empty *p* orbital perpendicular to that plane. Chapter 12 examines nucleophilic substitution reactions that involve carbocations.

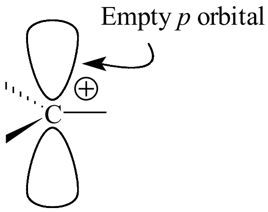


Figure 5.4. The structure of a carbocation.

Carbanions have a negatively charged carbon and are structurally similar to amines.

The negatively charged organic base discussed in this section is the **carbanion.** A carbanion has bonds to three other atoms and one pair of nonbonding electrons. The structure of a carbanion is much like the structure of an amine (See Figure 5.5). Because carbon is not very electronegative, it holds these nonbonding electrons loosely. Thus, a carbanion is a strong base. (Chapters 19 and 20 cover carbanion reactions extensively.)

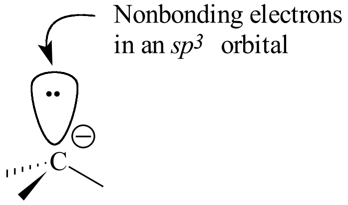


Figure 5.5. Carbanion structure.

Now that you have seen the various types of organic acids and bases, Section 5.5 examines the factors that modify the strength of the specific acids and bases.

5.5 Relative Acidity and Basicity

Each functional group has its own specific and measurable acidity or basicity. When you look at the groups involved in a chemical reaction, however, the values of their absolute strengths are of much less concern than their relative strengths. By knowing the relative strengths of the acids and bases on both sides of a reaction, you can accurately predict the direction of the equilibrium of that reaction. The direction of the equilibrium of a reaction moves from the stronger reactants toward the weaker reactants.

Because understanding acid-base concepts is the basis of organic chemistry, it is important that you be able to determine the relative acidity or basicity of various elements and groups. To do so, you must consider several factors. These factors include resonance, inductive forces, and electronegativity, topics covered in Chapter 1 and the HSAB Principle covered in this chapter.

Brønsted-Lowry Acid Strength

The strength of a Brønsted-Lowry acid depends on how much the acid dissociates to form protons and on the strength of the conjugate base that the acid forms. Among two or more Brønsted-Lowry acids in a reaction, the one that reacts to form the most stable, or weakest, conjugate base is the one that most readily releases a proton ($H^{\oplus}$) and is therefore the stronger acid. The strength of a Lewis acid depends on how strongly the acid attracts a pair of electrons. The strength of most bases, either

Brønsted-Lowry or Lewis bases depends on the availability of a pair of nonbonding electrons. The more loosely the base holds that pair of electrons, the stronger it is.

A helpful tool for predicting acid and base strength is the periodic table. By understanding the trends among the elements listed there, you can predict the relative acid and base strengths of the various functional groups. Also, you can predict the direction of a particular reaction and the stability of the products.

Consider the relative acid strengths of the Brønsted-Lowry hydrogen halide acids, HF, HCl, HBr, and HI. These four compounds differ only in the halogen bonded to the hydrogen. Their general ionization equation is:

$$\mathrm{HX} \rightleftharpoons \mathrm{H}^{\oplus} + \mathrm{X}^{\ominus}$$

This equation shows that the acid strength of each of these hydrogen halides is a measure of the ease of ionization of the H—X bond (X = a halogen). The stronger the bond, the weaker the acid. Understanding how to determine which H—X bond is stronger will allow you to predict the relative strength of each acid.

Determining which H—X bond is stronger requires consideration of the differences among the various halogens. Two significant differences between fluorine (F), the element at the top of the periodic table in the halogen family, and iodine (I), an element near the bottom are: F is more electronegative than I thus allowing F to hold its electrons more tightly. Also F is much smaller than I because F has fewer electrons. Being larger, I is more polarizable and therefore softer than F. The higher electronegativity of F would seem to result in a more stable ion, whereas, the softness of I means that the bond between I and the hard H is weaker than the bond between the hard F and the hard H. These predictions are obviously true as shown by the pK_a of the two acids: HF has a pK_a of 3.2, whereas HI is much stronger with a pK_a of –10.

Because a Brønsted-Lowry acid donates a proton ($H^{\oplus}$) to a base, the point of comparison for the relative strengths of the various acids is the atom, or group of atoms, to which the proton is attached. This atom or group of atoms bears the charge in the conjugate base. *The more stable the conjugate base, the higher the acid strength of the Brønsted-Lowry acid.* For example, HF with a pK_a of 3.2 is a much stronger acid than CH_4 with a pK_a of 49. This occurs because the F is more electronegative than C so F holds its electrons more tightly than C. Thus, the F anion is a weaker base than a C anion. Because F is a weaker base, it can donate a proton more readily than can C. Within a period on the periodic table, Brønsted-Lowry acidity increases from left to right: for example, $CH_4 < NH_3 < H_2O < HF$.

Compare the relative strengths of Lewis acids (MX_n) by looking at the positions of the elements represented by the X on the periodic table. Remember that a Lewis acid is an electron-pair acceptor. For Lewis acids, acid strength decreases going down the periodic table (for example, $BCl_3 > AlCl_3 > GaCl_3$.) This decrease in acid strength occurs because as the size of the atom represented by M increases, the attraction between the incoming electron pair and the nucleus weakens.

Brønsted-Lowry vs. Lewis Acid Strength

Note that Lewis acidity *decreases,* but Brønsted-Lowry acidity *increases* when going down the periodic table. These apparently opposite characteristics are not a contradiction. When measuring Lewis acidity, chemists compare the actual acid—the electron-deficient atom. For Brønsted-Lowry acidity, they do not compare the acidic atom because, in each case, it is the same—the proton. To determine the acidity of a Brønsted-Lowry acid, chemists look at how readily the acid gives up the proton. For example, when comparing the acidity of HF and HI, they compare only the relative ease with which $F^{\ominus}$ and $I^{\ominus}$ give up a proton. In this pair, the $F^{\ominus}$ ion is a hard base and forms a better bond with a hard $H^{\oplus}$ ion than does the soft $I^{\ominus}$ ion. Thus, HI is a stronger acid than HF.

Another factor to consider when comparing Lewis acids is the number of electron pairs required for the acid to fill its outer shell with electrons. Acids that require only one pair to complete that shell are stronger than those that require two. Adding one electron pair gives the electron-deficient atom a formal charge of –1; adding a second pair gives a formal charge of –2. Bringing in the second pair requires more energy because of the negative charge already present.

Solved Exercise 5.3

Determine whether the following pairs of acids are Lewis or Brønsted-Lowry acids and which one of the pair is the stronger acid. Justify your choice.

a) CH_3NH_2 and CH_3PH_2

Solution
CH_3NH_2 and CH_3PH_2 are Brønsted-Lowry acids. CH_3PH_2 is stronger because P is softer than N, so the P—H bond is weaker than the N—H bond.

b) $(CH_3)_3C^{\oplus}$ and $(CH_3)_3Si^{\oplus}$

Solution
$(CH_3)_3C^{\oplus}$ and $(CH_3)_3Si^{\oplus}$ are Lewis acids. $(CH_3)_3C^{\oplus}$ is stronger because C is more electronegative than Si, so C “needs” the electrons more.

c) $AlCl_3$ and BCl_3

Solution
$AlCl_3$ and BCl_3 are Lewis acids. BCl_3 is stronger because B is more electronegative than Al, so B “needs” the electrons more.

Exercise 5.7

Determine whether the following pairs of acids are Lewis or Brønsted-Lowry acids and which one of the pair is the stronger acid. Justify your choice.

a) CH_3SH and CH_3OH
b) NH_3 and PH_3
c) H_2Se and H_2S
d) AlH_3 and BH_3
e) $CH_3^{\oplus}$ and $SiH_3^{\oplus}$
f) HBr and HCl
g) HNO_3 and H_2SO_4
h) $NH_4^{\oplus}$ and $PH_4^{\oplus}$

Sample Solution

c) H_2Se and H_2S are Brønsted-Lowry acids. Because S and Se are both members of Group VIA on the periodic table, you must consider the softness of these atoms. Selenium is a softer base than sulfur and will more easily release a proton, so H_2Se is a stronger acid than H_2S.

The most important factor when determining the relative basicity of a set of compounds is the electronegativity of the element in each compound that contains a nonbonded pair of electrons. Basicity decreases for atoms with a pair of nonbonded electrons moving from left to right across the periodic table. Thus, $^{\ominus}CH_3$ is a stronger base than $F^{\ominus}$. Brønsted-Lowry basicity increases from the bottom to the top of the periodic table. Thus, the $F^{\ominus}$ ion is a stronger base than the $I^{\ominus}$ ion.

5.6 Substituent Effects on Acidity and Basicity

For more on the inductive effect see Section 1.11, page 000.

Various atoms or groups, when bonded to an acid or base, affect the acidity or basicity of that particular compound. As you recall from Chapter 1 chemists call this effect the inductive effect. For acids, if the substituent stabilizes the conjugate base, so that the ion forms more readily, it has increased the acidity of the acid; thus, making it stronger. Conversely, if the substituent destabilizes the conjugate base, so that the ion forms less readily, it has decreased the acidity of the acid. Because of its electronegativity, the substituent either draws the electrons toward itself or donates them to the acid functional group. For example, if the α **carbon** of a carboxylic acid has one or more strongly electron-withdrawing groups, the inductive effect is

An α carbon is the carbon adjacent to a functional group.

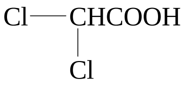
larger than without those groups. Compare ethanoic acid (commonly called acetic acid) with the chloroethanoic acids.

CH_3COOH

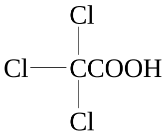
Ethanoic acid
$pK_a = 4.75$

$Cl—CH_2COOH$

Chloroethanoic acid
$pK_a = 2.86$


$Cl—CHCl—COOH$

Dichloroethanoic acid
$pK_a = 1.26$


$Cl—CCl_2—COOH$

Trichloroethanoic acid
$pK_a = 0.63$

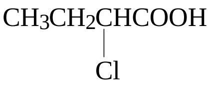
The effect on the acidity of each one is proportional to the number of substituents involved. The inductive effect is also proportional to the electronegativity of the substituent. The more electronegative the substituent, the lower the pK_a of the acid.

$F—CH_2COOH$	$Cl—CH_2COOH$	$Br—CH_2COOH$	$I—CH_2COOH$
Fluoroethanoic acid	Chloroethanoic acid	Bromoethanoic acid	Iodoethanoic acid
$pK_a = 2.59$	$pK_a = 2.86$	$pK_a = 2.90$	$pK_a = 3.17$

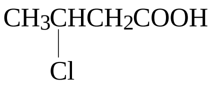
A final comparison illustrates how the effect diminishes with distance from the carboxyl functional group. The pK_a of the acid increases as the distance between the substituent and the carboxylic acid group increases.

$CH_3CH_2CH_2COOH$

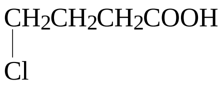
Butanoic acid
$pK_a = 4.82$


$CH_3CH_2CHClCOOH$

2-Chlorobutanoic acid
$pK_a = 2.86$


$CH_3CHClCH_2COOH$

3-Chlorobutanoic acid
$pK_a = 4.05$


$ClCH_2CH_2CH_2COOH$

4-Chlorobutanoic acid
$pK_a = 4.52$

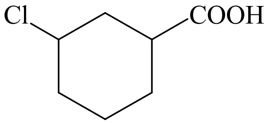
Exercise 5.8

Consider the following pairs of Brønsted-Lowry acids. Which member of each pair is the stronger acid? Why?

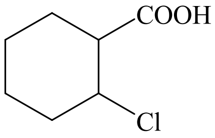
a) $CH_3O—CH_2—OH$ and $F—CH_2—OH$
b) $CH_3S—CH_2—COOH$ and $CH_3O—CH_2—COOH$
c) Cl_3CH and I_3CH

d) CH_3SH and CH_3OH

e)

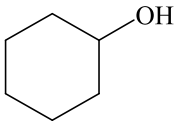


and

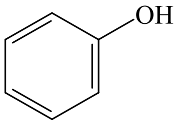


f) $CH_3CH_2NH_2$ and $CH_3CH_2PH_2$

g)



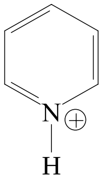
and



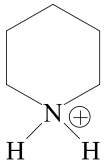
Sample Solution

d) To determine the difference in acidity between methanethiol and methanol, you must look at the difference in the hardness of the conjugate bases. The methoxide ion ($CH_3O^{\ominus}$) is a harder base than the thiomethoxide ion ($CH_3S^{\ominus}$). The hydrogen ion is a hard acid. As a result, the bond between the hard base, the methoxide ion, and the hydrogen ion is stronger than the bond between the thiomethoxide ion and the hydrogen ion. Therefore, methanethiol is the stronger acid.

With bases, hybridization is an important factor in the effect of substituents. For example, because ammonia and the amines are proton acceptors, any structural feature that reduces the availability of the nonbonding electrons on nitrogen also reduces the basicity of the compound. Consider the relative acidities of the pyridinium ion and the piperidinium ion:



Pyridinium ion
pK_a = 5.2



Piperidinium ion
pK_a = 11.1

This large difference in pK_a is due to hybridization—in pyridine, the nitrogen is sp^2 hybridized; in piperidine, it is sp^3 hybridized. Orbitals with more *s* character hold the nonbonding pair of electrons closer to the nucleus and, because the nitrogen in pyridine has more *s* character than the nitrogen in piperidine, the electrons are less available for donation to a hydrogen ion.

This effect is even more pronounced with an *sp* hybridized nitrogen. For example, protonated acetonitrile has a pK_a of –10. This value indicates that protonated acetonitrile is a rather strong acid making acetonitrile a rather weak base.

$$CH_3C\equiv\overset{\oplus}{N}-H$$

pK_a = –10
Protonated acetonitrile

A factor of less importance is the inductive effect of alkyl groups bonded to the nitrogen of amines. Alkyl groups donate electrons to cations and thus can help stabilize a positive charge on nitrogen. This effect is seen in the relative acidities of the conjugate acids ammonium and methylammonium ions:

$$\overset{\oplus}{N}H_4 \qquad CH_3\overset{\oplus}{N}H_3$$

pK_a = 9.4 pK_a = 10.6
Ammonium ion Methylammonium ion

The simple alkylamines are stronger bases than ammonia. Following the above line of reasoning you might expect that secondary amines would be even stronger bases and tertiary amines would be the strongest bases of all the amines. However, the effect of the solvent on the cation adds a complication. As the number of alkyl groups increases, so does the **steric crowding** around nitrogen. This crowding decreases the number of water molecules that can be involved in stabilizing the ion. As a result, trimethylamine is actually *less* basic than either dimethylamine or methylamine.

Steric crowding is where a reactive site is difficult to reach because of the alkyl groups surrounding it.

$$(CH_3)_2\overset{\oplus}{N}H_2 \qquad (CH_3)_3\overset{\oplus}{N}H$$

pK_a = 10.3 pK_a = 9.7
Dimethylammonium ion Trimethylammonium ion

Exercise 5.9

Consider the following pairs of bases. Which member of each pair is the stronger Brønsted-Lowry base. Why?

a) LiOH and LiSH
b) $(CH_3)_3N$ and $(CH_3)_3P$
c) CH_3OCH_3 and CH_3SCH_3
d) $^{\ominus}CH_3$ and $^{\ominus}SiH_3$

e) CH_3OCH_3 and $ClCH_2OCH_3$
f) $Cl_3C^{\ominus}$ and $I_3C^{\ominus}$
g) $CH_3O^{\ominus}$ and $CH_3S^{\ominus}$

Sample Solution

c) Because sulfur is softer than oxygen, it forms a weaker bond with hydrogen. Thus, dimethyl ether is the stronger base.

Key Ideas from Chapter 5

❏ According to the Brønsted-Lowry definition of acids and bases, an acid is a proton donor and a base is a proton acceptor.

❏ Acid strength is related to the stability of the acid’s conjugate base. The stronger the acid, the more stable is its conjugate base.

❏ A measure of acid strength is the value of the acid dissociation constant, K_a.

❏ According to the Lewis definition of acids and bases, an acid is an electron-pair acceptor and a base is an electron-pair donor.

❏ Lewis acids and bases can be classified as either hard or soft. The HSAB Principle states that hard acids prefer to bond with hard bases and soft acids prefer to bond with soft bases.

❏ The character of the acidic or basic functional group, as well as the inductive effect of any adjacent functional group, affects acid or base strength.

Supplementary Exercises

5.10 Arrange the following Brønsted-Lowry acids in order of increasing acidity. Justify your choices.

$$^{\oplus}NH_4 \quad H_2SO_4 \quad NH_3 \quad CH_3OH \quad CH_3COOH \quad CH_3SH$$

5.11 Rank the following compounds in order of increasing Brønsted-Lowry basicity. Justify your choices.

$$NH_3 \quad CH_3O^{\ominus} \quad ^{\ominus}OH \quad ^{\ominus}NH_2 \quad Cl^{\ominus} \quad CH_3S^{\ominus} \quad CH_3COO^{\ominus}$$

5.12 The pK_a of acetic acid is 4.8 and the K_a of benzoic acid is 6.3×10^{-5}. Calculate the K_a of acetic acid and the pK_a of benzoic acid. Which is the stronger Brønsted-Lowry acid?

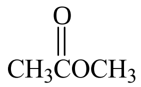
5.13 For each of the following compounds, identify the most acidic proton for reaction with a hydroxide ion ($^{\ominus}OH$). What factors are important to the stabilization of the conjugate base ion?

a) $HOCH_2COOH$

b) $HOCH_2CH_2SH$

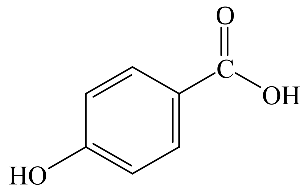
c) $CH_3CH_2NO_2$

d)

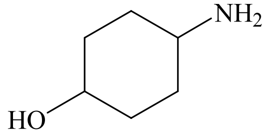


$CH_3\overset{\overset{\displaystyle O}{\|}}{C}OCH_3$

e)



f)



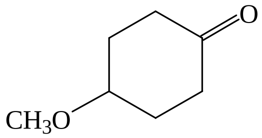
5.14 4.71 Grams of phenol were dissolved in water. Enough water was added to bring the volume to 500 mL and the pH was adjusted to 11.0. What is the concentration of the phenolate ion (the conjugate base of phenol)?

5.15 For each of the following compounds, identify the most basic atom for reaction with a proton ($H^{\oplus}$). What factors are important to the stabilization of the resulting cation?

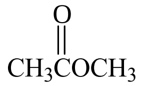
a) $CH_3OCH_2CH_2N(CH_3)_2$

b) $CH_3OCH_2CH_2SCH_3$

c)

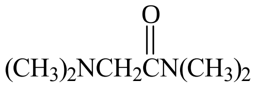


d)



$CH_3\overset{\overset{\displaystyle O}{\|}}{C}OCH_3$

e)



$(CH_3)_2NCH_2\overset{\overset{\displaystyle O}{\|}}{C}N(CH_3)_2$

5.16 Is a proton a Lewis acid, a Brønsted-Lowry acid, or both? Explain.

5.17 At a pH of 5.0, the amino acid glycine (H_2NCH_2COOH) exists in aqueous solution as an internal salt in which both the positive and negative ions are in the same molecule (a zwitterion). a) Suggest a structure for the zwitterion of glycine. b) What is the structure at pH 1.0? At pH 10.0?

5.18 Predict the products of the following acid-base reactions. Indicate the side favored by the equilibrium.

a) $HCl + CH_3COO^{\ominus} \rightleftharpoons$

b) $(CH_3)_2NH + {}^{\ominus}OH \rightleftharpoons$

c) $CH_3COOH + CH_3O^{\ominus} \rightleftharpoons$

d) $H_2SO_4 + (CH_3)_3N \rightleftharpoons$

e) $NH_3 + H_2O \rightleftharpoons$

f) $H_2SO_4 + CH_3OCH_3 \rightleftharpoons$

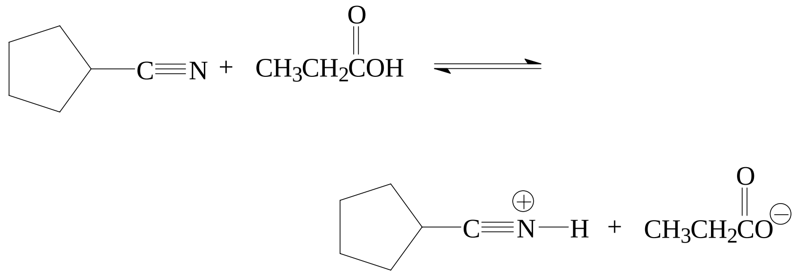
5.19 Draw resonance structures for aniline ($C_6H_5NH_2$) and its conjugate acid. Account for the fact that aniline is a weaker base than methylamine (CH_3NH_2).

5.20 An acid with more than one acidic proton has a different pK_a for each proton. For example, phosphoric acid (H_3PO_4) has the following pK_a values: $pK_{a1} = 2.1$, $pK_{a2} = 7.2$, and $pK_{a3} = 12.7$. Account for the large differences in these pK_a values.

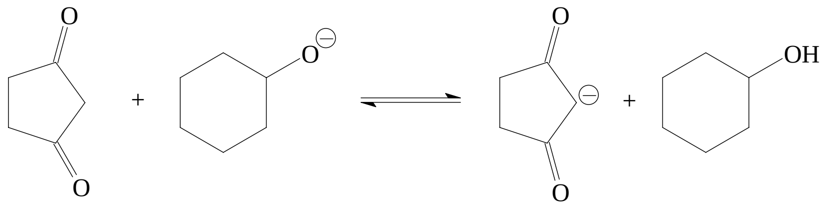
5.21 Predict whether CH_3CH_2OH is more acidic or less acidic than CF_3CH_2OH. Explain.

5.22 For each of the following reactions identify the acid, base, conjugate acid, and conjugate base. Then, using the pK_a values from Appendix A, predict whether the position of equilibrium will favor the starting materials or the products. (Hint: You may not find all the compounds in these reactions in Appendix A. However, they will be similar to compounds that are found there. Reason by analogy to come up with the correct results.)

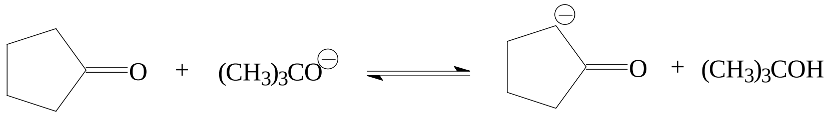
a)



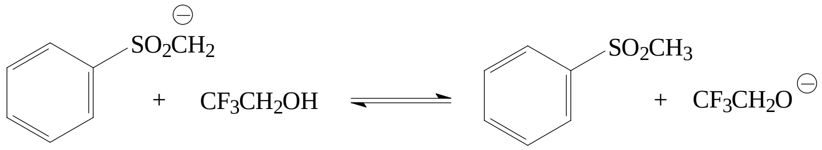
b)



c)



d)



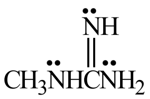
5.23 When chemists dissolve strong acids or strong bases in water, they observe a phenomenon known as the leveling effect. Because of the leveling effect they cannot measure differences in acidity for strong acids such as HCl ($pK_a = -7$) and H_2SO_4 ($pK_a = -5.2$) in water. They appear to have the same acidity. The same situation occurs with strong bases in water. a) Considering the leveling effect what is the strongest acid that can exist in water? b) What is the strongest base?

5.24 A mixture of aniline, benzoic acid, ethylene glycol, and naphthalene was shaken with equal volumes of aqueous sodium hydroxide and ethyl ether. The two layers were separated to give ether layer **A** and water layer **B**. Solution **A** was then extracted with an equal volume of dilute hydrochloric acid, and the layers were separated to give ether layer **C** and aqueous layer **D**. Solution **B** was made acidic with sulfuric acid, and the resulting solution extracted with an equal volume of ether. The layers were separated to give ether layer **E** and aqueous layer **F**. The procedure separated the four compounds. Show the distribution of the compounds in each of the layers **A** through **F**. (Hint: You will need to look up the structures and water solubilities of these four compounds in a chemical handbook. Consult Appendix A for pKa values. You may need to estimate some of these pKa values.)

5.25 Measures of acidity and basicity are relative values depending on the medium in which they are measured. For example, acetic acid is an acid when water is the solvent, but it acts as a base when 100% sulfuric acid is the solvent. Explain.

5.26 The pK_a of the conjugate acid of diphenylamine, $(C_6H_5)_2NH$, is 0.75. Is diphenylamine a strong or a weak base? Explain.

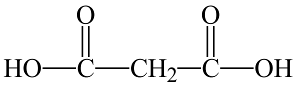
5.27 Guanidine protonates (has a hydrogen ion react with an electron pair) on any of its three nitrogen atoms. However, one is much more basic than the others and tends to protonate first. Draw resonance structures for the products of the protonation of each of the nitrogens. Which is the most stable; and thus, tends to protonate first? Justify your choice.



$CH_3\ddot{N}H\overset{\ddot{N}H}{\overset{\|}{C}}\ddot{N}H_2$

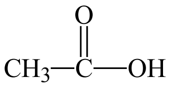
Guanidine

5.28 Malonic acid has two carboxylic acid groups and consequently undergoes two ionization reactions. The pK_a for the first ionization reaction is 2.9; the pK_a for the second is 5.7. For comparison, the pK_a for acetic acid is 4.8.



$HO-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-OH$

Malonic acid



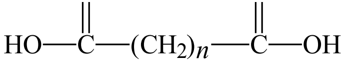
$CH_3-\overset{O}{\overset{\|}{C}}-OH$

Acetic acid

a) Show the first and second ionization reactions of malonic acid. Identify each with the appropriate pK_a value using pK_{a1} and pK_{a2}.

b) Why is the first pK_a of malonic acid lower than the pK_a of acetic acid, but the second pK_a higher than the pK_a of acetic acid?

c) Consider a series of dicarboxylic acids with the following general structure:

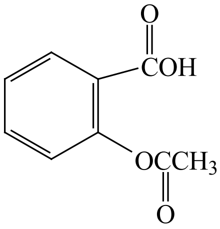


$HO-\overset{O}{\overset{\|}{C}}-(CH_2)_n-\overset{O}{\overset{\|}{C}}-OH$

How would you expect the difference between the first and second pK_a value to change as n increases? Briefly explain.

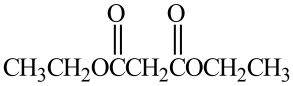
5.29 Ammonia is a weak acid with a pK_a of 35. Ammonia's conjugate base $^{\ominus}NH_2$, called the amide ion, is readily available as alkali metal compounds; for example, $LiNH_2$. Calculate the pH of 0.1 mole of lithium amide dissolved in 1 L of water. Calculate the pH of 0.1 mole of NaOH in 1 L of water. The solutions should have similar pH values. Why?

5.30 Acetylsalicylic acid (aspirin) has a pK_a of 3.5. The digestive fluids in the stomach have a pH of 2. The blood has a pH of 7. a) What is the predominant form (ionized or unionized) of aspirin in the stomach? b) What is the predominant form in the blood? c) What does this suggest about the passage of materials from the digestive tract to the bloodstream?

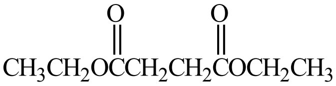


Aspirin

5.31 Diethyl propanedioate has a pK_a= 9.0; diethylbutanedioate has a pK_a = 21. Explain.

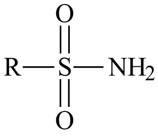

$CH_3CH_2O\overset{\overset{O}{\|}}{C}CH_2\overset{\overset{O}{\|}}{C}OCH_2CH_3$

Diethyl propanedioate


$CH_3CH_2O\overset{\overset{O}{\|}}{C}CH_2CH_2\overset{\overset{O}{\|}}{C}OCH_2CH_3$

Diethyl butanedioate

5.32 The hydrogen on the nitrogen of sulfonamides is quite acidic. Explain this observation. (Hint: Remember sulfur can have an expanded octet by placing electrons in the 3*d* orbital.)


$R-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}-NH_2$

A sulfonamide

Richard F. Daley and Sally J. Daley
www.ochem4free.com

Organic Chemistry

Chapter 6

Reaction Mechanisms
An Overview of Organic Chemistry

Chapter 6

Reaction Mechanisms An Overview of Organic Chemistry

Chapter Outline

6.1 Chemical Equilibria and Rates
A review of chemical equilibria

6.2 Equilibrium Thermodynamics
A review of the thermodynamics of equilibrium theory

6.3 Reaction Kinetics
The rate at which reactions occur

6.4 Reaction Profiles and Mechanisms
How a reaction profile relates to the reaction mechanism

6.5 Why Reactions Occur
A look at how polarity, electronegativity, and acidity/basicity affect a reaction.

6.6 Organic Reaction Terminology
The terminology organic chemists use to describe chemical reactions

6.7 Classification of Reagents in Organic Reactions
An introduction of typical nucleophiles and electrophiles used in organic reactions

6.8 Writing Reaction Mechanisms
The general operations used in writing reaction mechanisms

6.9 Substitution Reactions
An overview of the various types of substitution reactions

6.10 Addition Reactions
An overview of the various types of addition reactions

6.11 Elimination Reactions
An overview of the various types of elimination reactions

Objectives

- ✓ Review the concepts of equilibrium reactions
- ✓ Understand the relationship between rates of reactions and equilibrium
- ✓ Know what the reaction progress diagram tells about a reaction mechanism
- ✓ Become more proficient in using curved arrows to describe electron flow in a reaction
- ✓ Understand the relationship between a reaction profile and a reaction mechanism
- ✓ Know the descriptive terminology that applies to organic reactions
- ✓ Be able to write the generalized form of the five mechanistic operations used in writing reaction mechanisms
- ✓ Recognize when a reaction is substitution, elimination, or addition

> If you can think “mechanism” with reactions, then organic chemistry is yours!
>
> —Richard Daley

Chemical reactions and chemical synthesis are the “really interesting stuff” that organic chemistry is all about. But before you get to those things, you need to review some material from general chemistry that is pertinent to organic reactions and synthesis as well as learn some other basic information. The first half of this chapter is a review; the last half briefly previews the basic reaction types of organic chemistry. The goal for this preview is to provide you with a framework onto which you can organize new material as you learn it. Chapter 7 begins *the* detailed study of the reactions of organic chemistry.

6.1 Chemical Equilibrium and Rates

The study of reactions is the essence of much of organic chemistry. To understand reactions, you need to know how they occur, and knowing how they occur involves the study of reaction **equilibrium** and **rate**. An equilibrium equation has the following form:

The term equilibrium refers to reversible reactions.

The rate of a reaction is the speed that the concentrations of the reactants change per unit of time—usually stated as moles per liter per second.

$$\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C} + \mathrm{D}$$

Note that equilibrium does not imply an equality of concentrations of A and B relative to C and D but an equality of rates for the forward and reverse reactions.

In this reaction, the reactants, A and B, react to form the products, C and D; and, at the same time, the products, C and D, react to form the reactants, A and B. Equilibrium occurs when the rates of these two reactions are equal. An equilibrium is a state in which the forward and reverse reactions are continuous and simultaneous. The thermodynamics of the system determines whether the reactants or products are favored at equilibrium. The position of equilibrium favors the lowest energy state for the system.

Organic chemists view an equilibrium as favorable if a reasonable amount of product is present.

A mechanism is the step-by-step pathway that the reaction follows on its way from reactants to products. Section 6.5, page 000, begins the discussion of reaction mechanisms.

A number of factors affect the probability and the rate at which a reaction reaches a **favorable equilibrium**. The major factor is the **mechanism** that the reaction follows on its way from the reactants to the products. If the reaction pathway is thermodynamically favorable and if the products have less energy than the reactants, then the reaction can establish a favorable equilibrium. A secondary factor is the structure of the reactants. Other secondary factors are the reaction conditions, such as temperature and reactant concentrations. These secondary factors affect the rate at which a favorable equilibrium is established.

For a brief look at the effect of reaction conditions, consider the reaction of methane with chlorine:

$$CH_4 + Cl_2 \longrightarrow CH_3Cl + HCl$$

Chapters 3 and 11 provide the background for predicting reaction rates on the basis of structure.

Although this reaction moves toward a favorable equilibrium, its rate is easily controlled through regulating the reaction conditions. Mixed methane and chlorine gases, stored in the dark at room temperature, have no appreciable reaction even for extended time periods. However, if you either illuminate or heat the flask containing the mixture, a very rapid reaction immediately occurs. With other reactions, the rates at which the reactants attain a favorable equilibrium vary from imperceptibly slow to virtually instantaneous. By understanding these factors, not only can you control the rate of reaction, but you can also gain a better understanding of what happens—that is, what steps a reaction takes as it goes from reactants to products.

Writing an equilibrium equation in the form shown below indicates the specific rates at which the forward and reverse reactions proceed.

$$\mathrm{A} + \mathrm{B} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{C} + \mathrm{D}$$

If the rate at which A and B react to produce C and D is proportional to the concentrations of both A and B, then the following equation expresses the **rate law** for this reaction:

The rate law correlates the rate of the reaction with the concentrations of the reactants.

$$\text{rate}_1 = k_1[\mathrm{A}][\mathrm{B}]$$

But, if the concentration of A, for example, is doubled, then the rate of the reaction also doubles. The proportionality constant, k, also called the **rate constant**, is the measure of the actual rate of the reaction when all the reactants are at 1 mole/liter (1 M) concentrations at a given temperature. The rate constant has a definite value for each temperature. Large values of k indicate fast reaction rates, and small values of k indicate slow reaction rates.

The rate constant is the measure of the rate of the reaction when the reactants are present in solution at a concentration of 1 M.

To obtain the rate law for a reaction, chemists first measure the rate of that reaction experimentally for a number of concentrations. Then, using the data collected, they calculate the rate constant k_1. As you will see in Chapter 7 and later, if there is more than one possible pathway for the reaction to take, the rate law helps determine the correct steps by showing which reactants are involved in the **rate-limiting step** of that reaction. Reactants that appear in the rate law are those that react in the slowest step of the mechanism for the reaction system. These reactants are the rate-limiting reactants. For example, in the reaction of A and B, if the rate depends only on the concentration of B, you look for the step in the possible mechanism that is a reaction of B. Another possibility for a reaction where the rate depends only on the concentration of B is where the concentration of A is so much larger than the concentration of B that no dependence of rate on the concentration of A can be observed. If the reaction depends on the concentrations of both A and B, then you look for a mechanism where the rate-limiting step involves a reaction of both A and B.

The rate-limiting step of a reaction is the slowest, or highest energy, step in the reaction mechanism.

Just as the previous equation describes the rate law for the reaction of A and B, the following equation describes the rate law for the reaction of C and D:

$$\text{rate}_2 = k_2[\mathrm{C}][\mathrm{D}]$$

When rate_1 is equal to rate_2, the system is in equilibrium. In equilibrium, the concentrations of A, B, C, and D do not change with time. Molecules of A and B still react to produce C and D, and at the same time molecules of C and D react to form molecules of A and B.

However, because the rates of the forward and reverse reactions are the same, there is no *net* increase or decrease in the concentration of either set of molecules. Chemists state the relationship between the two rate laws for the forward and reverse reactions for the example equilibrium you've been considering in the following way:

$$k_1[\mathrm{A}][\mathrm{B}] = k_2[\mathrm{C}][\mathrm{D}]$$

The equilibrium constant is a mathematical quantity that describes the ratio of products to starting materials at equilibrium.

The **equilibrium constant**, K, is a property of a particular reaction at a specific temperature. K is independent of the initial concentrations of the reactants and products, although it does vary with temperature. To determine the equilibrium constant, calculate the quotient of the concentrations of the products and reactants at equilibrium using the following formula:

$$K = \frac{[\mathrm{C}]_{\mathrm{eq}}[\mathrm{D}]_{\mathrm{eq}}}{[\mathrm{A}]_{\mathrm{eq}}[\mathrm{B}]_{\mathrm{eq}}} = \frac{k_1}{k_2}$$

When a particular reaction reaches equilibrium, the actual concentrations of the reactants and products depend on their relative stabilities. The more stable one set is in comparison to the other, the higher is its concentration. That is, if the products are more stable than the reactants, then the reaction favors chemical compounds on the right and, at equilibrium, there is a higher concentration of products than reactants. Likewise, if the reactants are more stable than the products, the reaction favors the chemical compounds on the left, and there is a higher concentration of reactants than products.

An example of an equilibrium is the reaction of methyl chloride with hydroxide ion in water to produce methanol. Methyl chloride is a gas that is slightly soluble in water, forming solutions of about 0.1 M.

$$^{\ominus}\mathrm{OH} + \mathrm{CH_3Cl} \xrightleftharpoons{\mathrm{H_2O}} \mathrm{CH_3OH} + \mathrm{Cl}^{\ominus}$$

By substituting the concentrations of the reactants and products at equilibrium into the formula for the equilibrium constant and calculating, you get 10^{16} as the value of K.

$$K = \frac{[\mathrm{CH_3OH}][\mathrm{Cl}^{\ominus}]}{[^{\ominus}\mathrm{OH}][\mathrm{CH_3Cl}]} = 10^{16}$$

This large value of K indicates that the amount of methyl chloride present at equilibrium is very small and the reaction has gone to completion. That is, it proceeds almost completely to the right.

6.2 Equilibrium Thermodynamics

An equilibrium reaction tends to favor the side on which the substances have the greatest stability. Stability here refers to the energy content of the reactants and products. The side of the equilibrium reaction that has the higher energy level is the less stable side, and thus is the more reactive side. Chemists call this energy **enthalpy**, ΔH°, or the heat of reaction. If the sign of ΔH° is negative, the reaction is exothermic—gives off energy as it proceeds. If it is positive, then the reaction is endothermic—needs an addition of energy in order to proceed.

Enthalpy involves the heating or cooling that takes place as a reaction progresses.

The superscript ^{o} in the ΔH^o annotation simply means that the measurement was taken at a standard temperature and pressure.

The **Gibbs standard free energy**, ΔG°, is, in thermodynamic terms, a reaction's move to equilibrium. Free energy is that part of the energy of a process that is available to do work. According to the Gibbs Standard Free Energy Principle, any **spontaneous change** that takes place within a reaction system leads to a lowering of the free energy of that system. The value of ΔG° for a reaction is the difference in energy content between the reactants and the products. A negative ΔG° indicates a favorable thermodynamic reaction. The more negative ΔG° is, the more favorable the reaction and the more energy is given off as it proceeds.

The Gibbs standard free energy is a measure of the energy absorbed or given off by a reaction.

Spontaneous change is the change within a reaction that continues on its own, after it has been started.

The following form of the Gibbs Standard Free Energy Principle is the equation that chemists use to determine the maximum amount of energy produced during a reaction:

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

This formula determines the Gibbs free energy by relating the changes in enthalpy, ΔH°, in **entropy**, ΔS°, and the temperature of the reaction. The only time a reaction occurs is when molecules of the reactants collide—provided that the collision has sufficient energy and the correct spatial orientation. Thus, the more restricted a molecule's motion, the more difficult it is for a reaction to occur and the more negative is its entropy. The formation of stronger bonds and greater freedom of motion gives a more negative value for ΔG° and a larger **driving force** for the reaction. A reaction always moves toward the point of the lowest Gibbs free energy.

Entropy is the amount of freedom of motion that a molecule or portion of a molecule has, as allowed by its physical structure.

The driving force of a reaction is a measurement of how much the Gibbs free energy decreases in that reaction.

For the reaction of methyl chloride with the hydroxide ion, $\Delta H^\circ = -18$ kcal/mole and $\Delta S^\circ = 13$ cal/deg/mole (often called entropy units or simply eu). Thus, the value of ΔG° at 25°C is –21.9 kcal/mole. The driving force is the difference in energy between the stronger C—O bond (90 kcal/mole) and the C—Cl bond (80.8 kcal/mole). Here, as in most reactions, the formation of stronger bonds is a major component of the driving force for the reaction.

A reaction profile shows the changes in energy level as a reaction progresses.

Figure 6.1 shows a **reaction profile** for the following hypothetical reaction:

$$A + B \rightleftharpoons C + D$$

A reaction profile is a visual representation of a reaction system. The vertical axis measures the energy relationships between the components of the system. The horizontal axis indicates the progress of the reaction and is sometimes called the reaction coordinate. Note that the energy level of A + B is higher than the energy level of C + D. The higher energy level of A + B means that A and B are less stable than C and D. The difference in energy levels between A + B and C + D is ΔG^o. The more negative ΔG^o is, the farther the reaction will go to the right.

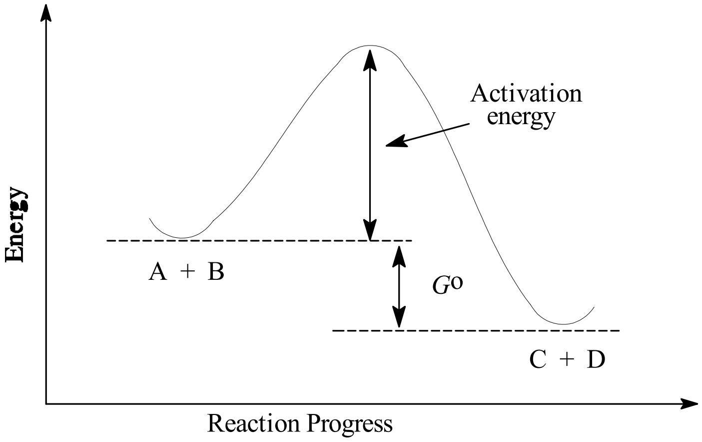


Figure 6.1. Reaction profile for reaction $A + B \rightleftharpoons C + D$.

The Gibbs Standard Free Energy, ΔG^o, is related to K, the equilibrium constant, by the following expression:

$$\Delta G^o = - RT \ln K$$

In units relevant to these calculations, the gas constant is 2.0 cal/deg•mole.

The Kelvin scale is a temperature scale where absolute zero, the coldest possible temperature, is designated as 0 K. For a temperature on the Celsius scale, simply add 273 to get the Kelvin temperature.

In this equation R is the **gas constant** and T is the absolute temperature measured on the **Kelvin** scale.

For the reaction of methyl chloride with hydroxide ion, ΔG^o is –22 kcal/mole—an exceptionally large value for an organic reaction. Plugging this value into the equation and solving for K yields a value of approximately 10^{16}, as calculated earlier.

Exercise 6.1

For the reaction $\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C} + \mathrm{D}$ assume that $\Delta H^{o} = -8$ kcal/mole and $\Delta S^{o} = -12$ eu.

a) Calculate the value of ΔG^{o} and the equilibrium constant if the reaction is carried out at 27°C (or 300 K). At 127°C (400 K)? At 227°C (500 K)?

b) Where would the equilibrium lie for each temperature?

c) Would the equilibrium be more favorable (i.e., give more of the products, C and D) at 77°C or at 177°C?

Sample solution

a) The value of ΔG^{o} at 127°C is calculated as follows:

$$\begin{aligned} \Delta G^{o} &= \Delta H^{o} - \mathrm{T}\Delta S^{o} \\ &= -8000 - (400 \times -12) \\ &= -3200 \text{ cal/mole} \end{aligned}$$

The value of K at that temperature is

$$\begin{aligned} \Delta G^{o} &= -\mathrm{RT} \ln K \\ \ln K &= \frac{\Delta G^{o}}{-\mathrm{RT}} \\ &= \frac{-3200}{-(2.0 \times 400)} \\ &= 4.0 \\ K &= e^{4.0} \\ &= 54.6 \end{aligned}$$

Assuming equal concentrations of A and B, the concentrations of C and D at equilibrium are equal. So the concentrations of each is the square root of the equilibrium constant. Thus, the concentrations of C and D are about 7.4 times ($54.6^{0.5}$) larger than the concentrations of A and B.

6.3 Reaction Kinetics

Reaction kinetics is the study of reaction rates, or speeds, and how they change under various conditions. Reaction kinetics data is used to establish the reaction mechanism for a reaction. After considering the thermodynamics of the reaction of methyl chloride with hydroxide ion in Section 6.2, you might think that the reaction should readily proceed from reactants to products. However, at room temperature, it does not. The reaction rate is so slow that even after

48 hours, the reaction has advanced only 10% of the way to equilibrium. When the thermodynamics of a reaction look favorable, yet the reaction does not proceed, chemists look at the kinetics of that reaction. Often favorable reaction thermodynamics are not enough to allow a reaction to proceed.

Activation energy is the minimum amount of energy required for a reaction to occur.

Methyl chloride reacts with a hydroxide ion so slowly at a room temperature because the energy barrier that the starting materials must overcome before they can react to form the products is so high. This barrier, often called the **activation energy**, E_a, appears in Figure 6.1 as a peak between the reactants and the products. In the reaction of methyl chloride with hydroxide ion, the activation energy is approximately 25 kcal/mole. When you consider that at room temperature all molecules have an average thermal energy of 0.6 kcal/mole, and that methyl chloride and hydroxide ion need approximately 25 kcal/mole to begin reacting, the difficulty in getting the reaction started is apparent. Therefore, for this reaction to proceed, heat must be added.

So, with an activation energy of 25 kcal/mole, what enables methyl chloride and hydroxide ions to react even to the extent of 10% in two days at room temperature? The measure of the thermal energy of a compound is a weighted average of all possible energies. The actual thermal energy for every molecule ranges from nearly zero to much, much higher than the average. Therefore, at any given time, some of the molecules have more than the required 25 kcal/mole, and these are the molecules that are reacting. Figure 6.2 illustrates the Boltzmann distribution function, the number of molecules present at any given thermal energy level, for three different temperatures. Most molecules in a sample at a particular temperature have an energy level close to the average energy, represented by the hump in the curve. Therefore, at room temperature only a minute fraction of the collisions between a methyl chloride molecule and a hydroxide ion have sufficient energy to result in a reaction.

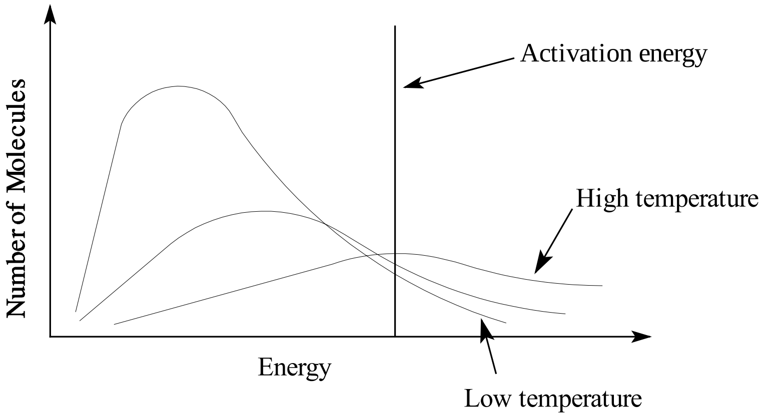


Figure 6.2. Boltzmann distribution function for three different temperatures. The energy of activation is shown. Note that as the temperature increases, the fraction of molecules with an energy greater than the activation energy increases.

Figure 6.2, shows that heating a molecule raises its average thermal energy. As a result, the fraction of molecules with sufficient energy to react increases, and the rate of reaction correspondingly increases. For example, the rate of reaction between CH_3Cl and $^{\ominus}OH$ is 25 times higher at 50°C than it is at 25°C. The general rule of thumb is that the rate for a reaction doubles when the temperature increases by 10°C.

The rate equation for the reaction between methyl chloride and hydroxide ion is as follows:

$$\text{rate} = k[CH_3Cl][\,^{\ominus}OH]$$

Because the rate of a reaction involves the change in concentration for a reactant or a product per unit of time, chemists usually express the rate as moles per liter per second, or M/s. Since they express the concentration as M, the rate constant, k, for this reaction must have the units of $M^{-1}\ s^{-1}$. The experimental value of k is $6 \times 10^{-6}\ M^{-1}\ s^{-1}$ at 25°C.

Rate Constant vs. Rate

Be careful not to confuse the terms *rate constant* and *rate*. The rate constant is a measure of how fast a reaction can occur when the reactants are brought together. The rate depends on the actual concentrations and the reaction conditions when they are brought together. It is like that hot sports car you've been dreaming about. That particular car has the potential of going 140 miles/hour, but because of external constraints—the highway patrol—you can only travel at the posted speed limit.

Exercise 6.2

Using the rate constant of $6 \times 10^{-6}\ M^{-1}\ s^{-1}$ for the reaction of methyl chloride with hydroxide ion, calculate the initial rate of reaction for each of the following concentrations. Compare that rate with the rates when the reaction is 50% and 90% complete.

a) 0.1M CH_3Cl and 0.1M $^{\ominus}OH$ b) 0.1M CH_3Cl and 1.0M $^{\ominus}OH$
c) 1.0M CH_3Cl and 0.1M $^{\ominus}OH$ d) 0.01M CH_3Cl and 0.01M $^{\ominus}OH$

Sample solution

(b) Using the rate equation for this reaction and substituting the numbers, you get the following initial rate:

$$\begin{aligned}\text{rate} &= (6 \times 10^{-6}\ \text{M}^{-1}\ \text{s}^{-1})(0.1\ \text{M})(1.0\ \text{M}) \\ &= 6 \times 10^{-7}\ \text{M/s}\end{aligned}$$

The concentrations at 50% completion are 0.05 M and 0.95 M; thus, you get the following rate, when the reaction is 50% complete:

$$\begin{aligned}\text{rate} &= (6 \times 10^{-6}\ \text{M}^{-1}\ \text{s}^{-1})(0.05\ \text{M})(0.95\ \text{M}) \\ &= 2.8 \times 10^{-7}\ \text{M/s}\end{aligned}$$

Note: A common error here is to assume that half of *both* reactants are used in the reaction. The reactant in lower concentration is the limiting reagent: you can never use more of a reagent in a reaction than can react with the limiting reagent. An advantage of having one reagent in excess is that the overall rate of reaction increases.

Reaction order describes the number of reagents present in the rate law—first-order for one reagent, second-order for two reagents, etc.

Reaction order is a term that chemists often use to describe the kinetics of a reaction. The reactions covered so far in this chapter are all second-order reactions. That is, the rate of the reaction depends on the concentrations of *two* reactants. A first-order reaction is a reaction whose rate is dependent on the concentration of only *one* reactant. The rate law for a first-order reaction is as follows:

$$\text{rate} = k[\text{A}]$$

A pseudo-first-order reaction is one where the second-order kinetics appears as first-order reactions.

When the concentration of one reactant in a second-order reaction is so high that it essentially does not change during the course of the reaction, chemists call the reaction a **pseudo-first-order reaction**. Such a reaction occurs, for example, in a solvolysis reaction when the reagent reacts with the solvent.

6.4 Reaction Profiles and Mechanisms

For any reaction to occur, the atoms involved must be converted from starting compounds to products. That is, the atoms must break their existing bonds and form new ones. The details of this kind of transformation are at the heart of organic chemistry, and basic to understanding these details is a knowledge of how the molecules change structurally during a reaction. One method of determining the structural changes is to plot the energy changes. Each possible configuration of the atoms, as they move from reactants to products, has an associated energy level. Because most reactions require existing bonds to be broken before, or concurrent with, new bonds being formed, the intermediate configurations generally have a higher energy level than the reactants or products do. As a reaction progresses, it forms a structure that has a maximum energy level for that reaction. Then, as the reaction continues forming the products, the energy level decreases until the products have been completely formed.

Figure 6.3, the reaction profile of the reaction between methyl chloride and hydroxide ion, shows the changes in energy as the reaction progresses. The point on the curve corresponding to the highest energy level represents the **transition state** of the reaction. The transition state is more unstable than either reactants or products, thus, it either continues on to form the products or returns to the reactants. The structure of the transition state is important because it shows how the molecules are interacting. In the reaction of hydroxide ion with methyl chloride, the transition state involves the formation of a bond between the OH and C, as the bond breaks between Cl and C. This structure, showing both bonds breaking and forming, is called an **activated complex**. An activated complex is generally written within brackets ([ ]) and with a double dagger (‡) superscript as shown in the figure.

The transition state of a reaction is a molecular complex intermediate between the reactants and the products and is the result of the reactants colliding and reacting.

An activated complex is the chemical species present at the transition state of a reaction.

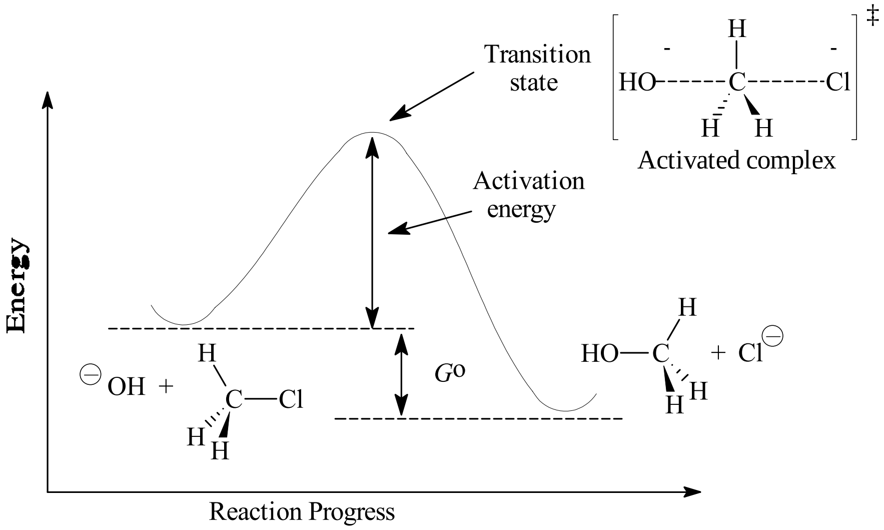
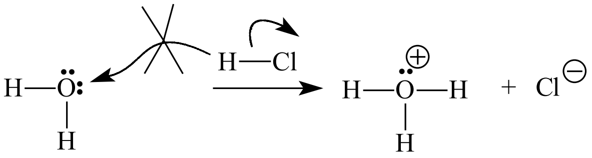
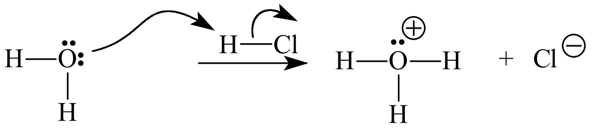


Figure 6.3. A reaction profile for the reaction of CH_3Cl with $^{\ominus}OH$.

Chemists use a mechanism to show all the steps in a reaction. Curved arrows (↷) are used in mechanisms to indicate what atoms or groups of atoms are reacting with each other. A curved arrow shows the direction of *electron movement*, as a bond breaks and a new bond forms. The standard convention used by chemists for drawing curved arrows shows electron flow from the electron-rich atom (Lewis base) to the electron poor atom (Lewis acid). For example, you might envision the protonation of water as occurring via the hydrogen ion approaching the water molecule and forming a bond. However, writing it in this way would be incorrect. The correct way is for a curved arrow to show the bond being formed by the oxygen donating electrons to the hydrogen ion. The head of the arrow indicates the number of electrons involved. An arrow with one barb, , indicates the movement of one electron. An arrow with two barbs, , indicates the movement of a pair of electrons.

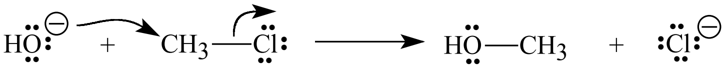


Incorrect use of curved arrows



Correct use of curved arrows

In the mechanism for the reaction of methyl chloride with hydroxide ion, an arrow with a double-barbed arrowhead indicates the movement of a pair of electrons. This mechanism shows that the nonbonding pair of electrons on the $^{\ominus}$OH attacks the carbon bearing the Cl, dislodging the Cl$^{\ominus}$ along with its electrons.



This type of reaction is known as an S_N2 (short for *S*ubstitution, *N*ucleophilic, Bimolecular) reaction. An S_N2 reaction is a single-step reaction with one transition state, as suggested by Figure 6.3. Chapter 12 explains the transition state of the S_N2 reaction in greater detail.

Methyl chloride and hydroxide ion react in one step; however, many reactions occur in more than one step. The reaction profile in Figure 6.4 represents a reaction that occurs in two steps. This reaction profile includes a **reaction intermediate** between two transition states. Some intermediates are sufficiently stable to be isolated and examined; others are so reactive that chemists can only infer their existence through cleverly designed experiments.

Reaction intermediates correspond to energy minima on the reaction progress diagram.

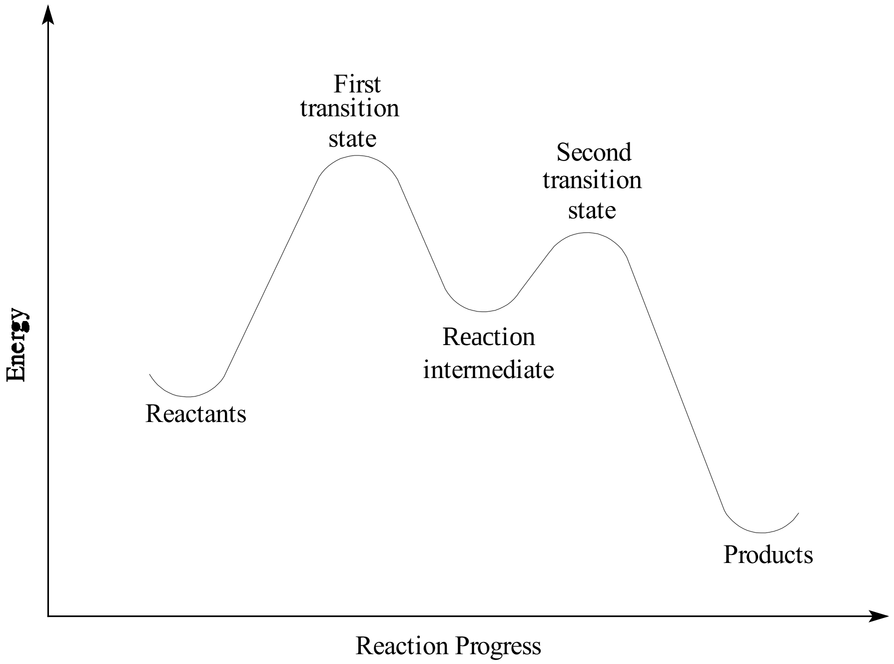


Figure 6.4. A reaction profile for an exothermic reaction with an intermediate product and two transition states.

Estimating the differences in the energy levels of the reactants, intermediates, and products can help you roughly predict the rate of a reaction. The general rule is that the less stable the transition state, the higher its energy and the slower its rate of reaction. This rule is important because the highest energy level on a reaction profile determines the overall reaction rate for that reaction. The step of the reaction involving the highest-energy transition state is the rate-limiting step.

In summary, think of a reaction mechanism as an accounting of the intermediates and transition states that occur in a reaction as it moves from the starting materials to the products. This book frequently uses reaction mechanisms because they help explain and classify the many reactions that make up organic chemistry. It also looks at the experimental details from which some of these mechanisms were deduced.

Exercise 6.3

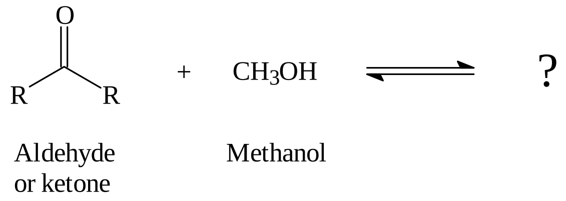
a) Construct a reaction profile for the following reaction:

$$X \underset{k_2}{\overset{k_1}{\rightleftharpoons}} Y \underset{k_4}{\overset{k_3}{\rightleftharpoons}} Z$$

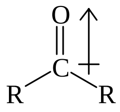
The relative stabilities are Z > X > Y, and the four rate constants are $k_3 > k_2 > k_1 >> k_4$.
b) Which is the rate-determining step in the reaction?

6.5 Why Reactions Occur

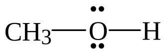
Most of the reactions discussed in this book are acid-base reactions. An essential skill for an organic chemist is to be able to look at the reactants of a reaction and to determine the strongest acid, the strongest base, and how the two will react. Chapter 5 introduces these concepts. Consider the reaction of an aldehyde or ketone with methanol. (The R groups in the following illustration represent either hydrogens or alkyl groups.)



The C=O bond in the aldehyde or ketone has a dipole moment with the positive end at the carbon of the C=O bond.



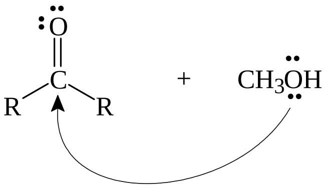
Because of this partial positive charge, the carbon is slightly electron deficient. Thus, the carbonyl carbon is a Lewis acid. The methanol has an electron rich site at the oxygen.



$$\mathrm{CH_3}-\underset{\cdot\cdot}{\ddot{\mathrm{O}}}-\mathrm{H}$$

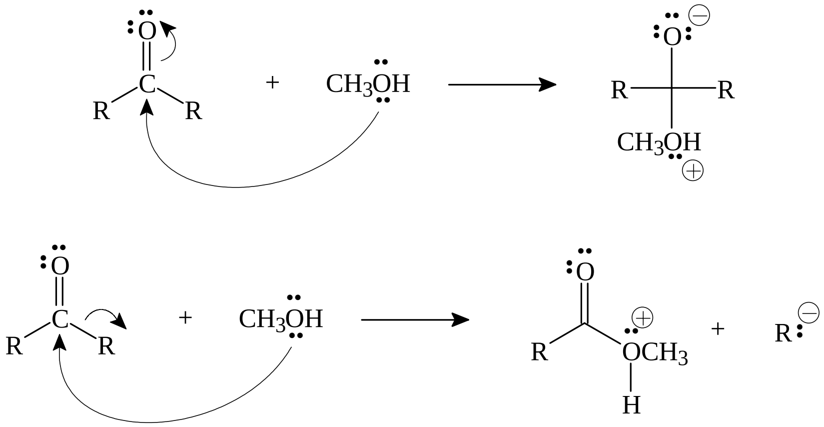
Thus, the methanol oxygen is a Lewis base.

When considering how these reactants might interact to form a bond, keep in mind that in an acid-base reaction the electrons from the base are donated to the acid to form a new bond. So the electron rich oxygen donates its electrons to the electron deficient carbon of the aldehyde or ketone forming a new bond.



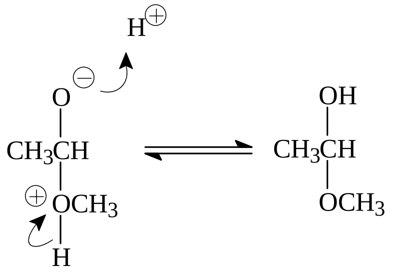
Even though the carbon is the positive end of the dipole, it has a full octet of electrons. Thus, a bond to the carbon must break at the same time as the new bond is forming.

Determine which bond (if any) will break in a reaction. This involves an important principle: the bond most likely to break is the one that will form the weakest acid or base in the product. The reaction of methanol with an aldehyde or ketone has two possible places. One is the π C–O bond, and the other is one of the C—R bonds.



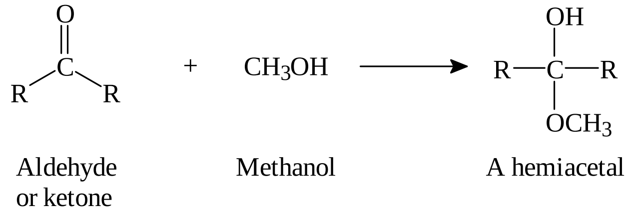
In these two possible reactions, the products have both positive and negative charges. In each case, the positive charge is on the oxygen of a methoxy group so they are at the same energy level. However, the negative charges are on different atoms. In the first possibility, the negative charge is on an oxygen and in the second, the negative charge is on either a carbon or hydrogen (the R group). From electronegativities, you would expect that oxygen (electronegativity = 3.44) would be a better base than either hydrogen (electronegativity = 2.20) or carbon (electronegativity = 2.55). Because of the electron affinity of oxygen, the first possibility is much more likely than the second one.

Finally, there is a proton transfer reaction in which the proton on the positively charged oxygen is lost and another is acquired for the negatively charged oxygen.

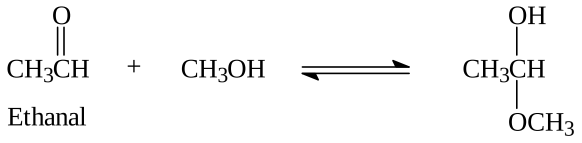


Proton transfer

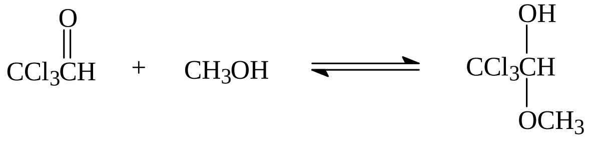
Thus the completed reaction is:



What would cause the reaction to give either a good or a poor yield of product? The first step of this reaction involves the acid-base reaction of an electron rich oxygen with an electron poor carbon. Anything that increases the electron density on the oxygen or decreases the electron density on the carbon will increase the yield of product. If one of the R groups on the ketone or aldehyde is electron withdrawing, the equilibrium constant (and thus the amount of product at equilibrium) increases. For example, adding 3 chlorine atoms to the methyl group of ethanal increases the equilibrium constant by 1.7×10^6.



$K_e = 1.5 \times 10^{-2}$

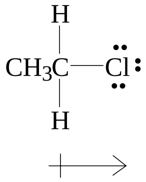


$K_e = 2.6 \times 10^{4}$

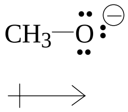
A second example is the reaction of chloroethane with methoxide ion.

$$CH_3CH_2Cl \quad + \quad CH_3O^{\ominus} \longrightarrow ?$$

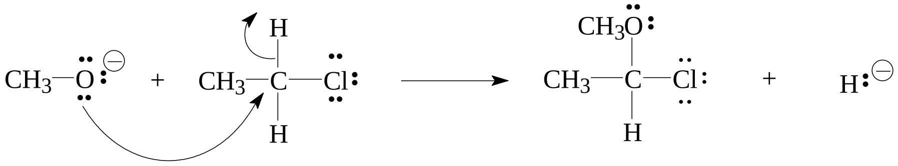
The C—Cl bond in chloroethane is a polar bond with the positive end of the dipole on the carbon end of the bond. Thus, the carbon is slightly electron deficient.

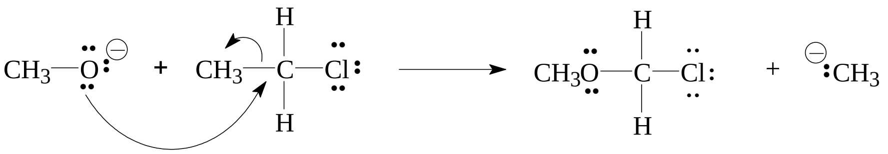


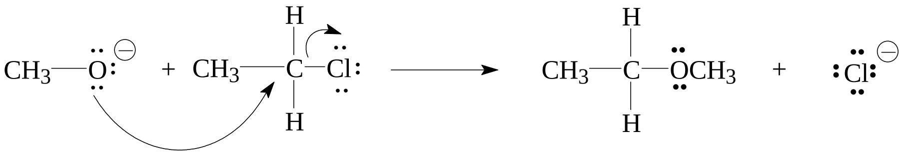
Because it bears a negative charge, the oxygen of the methoxide ion is the base in this reaction.



The acid-base reaction of the carbon bearing the chlorine with the oxygen of the methoxide ion is the preferred course for this reaction. However, the carbon bearing the chlorine already has a full octet so a bond must also be broken. There are three options for the bond to be broken:





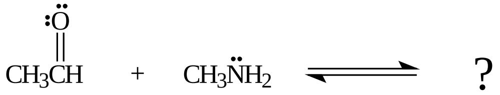


In the first option, a bond is broken to a hydrogen atom. In the second option, the bond to a carbon is broken and in the third to a chlorine atom. The difference in electronegativities between the three is hydrogen (2.20), carbon (2.55), and chlorine (3.16). The higher electronegativity of chlorine indicates that it is more stable with a negative charge than either hydrogen or carbon. Thus, the correct mechanism is the third option.

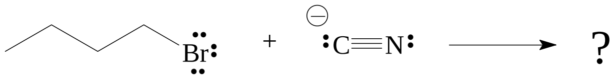
Exercise 6.4

For each of the following reactions identify the acidic and basic atoms. Predict how these atoms might react including bond forming and bond breaking.

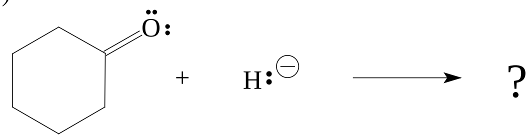
a)



b)

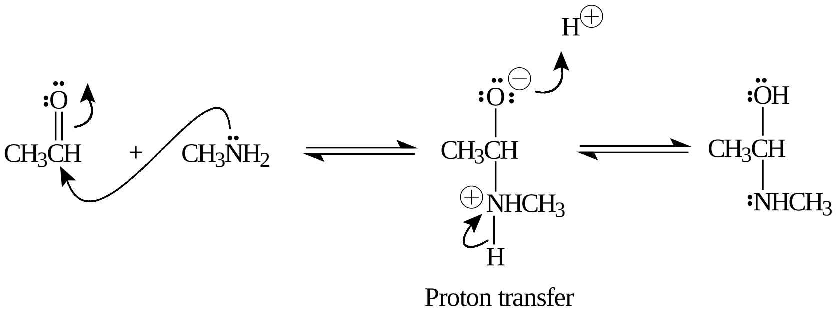


c)



Sample solution:

a)



6.6 Organic Reaction Terminology

A chemical reaction is initiated by mixing a set of reagents, which react to yield products.

The substrate in a reaction is the reagent whose reaction is of most interest to chemists.

The by-products of a reaction are those products not generally isolated and purified by chemists.

Section 6.6 defines several important words that organic chemists use when they talk about **chemical reactions**. A typical chemical reaction requires a set of **reagents**, which, in your introductory chemistry course, were called either reactants or starting materials and were placed on the left side of the arrow in a chemical equation. Organic chemists are mostly interested in those reagents that contain carbon. They call them **substrates**. **Products** are the substances that result from the reaction of the substrate with the other reagents and are placed on the right side of the arrow in a chemical equation. There are two categories of products: the product of interest and the **by-products**. The product of interest is the compound formed from the substrate. The by-products are any other products and are often of little interest to practicing organic chemists involved in synthesis.

By-Products

By-products are often "ignored" by organic chemists when they are converting some substrate into products using multiple steps. Writing these steps as transformations is the best way to easily convey the information involved with those steps. Including the by-products is inconvenient. However, when focusing on the reaction involved in one of those steps, then knowing what by-products are present and how they are formed is essential.

A transformation is the chemical reaction showing only the substrate, the other reagents, and the product of interest. The coefficients and by-products from the balanced equation are generally not shown.

When writing a chemical equation, organic chemists seldom use a complete balanced equation but instead write only a **transformation**. A transformation includes the substrate, the other reagents, and the products. It assumes both the by-products and coefficients. For example, consider the elimination reaction of *tert*-butyl bromide:

$$\underset{\substack{\textit{tert}\text{-Butyl}\\ \text{bromide}}}{(CH_3)_3CBr} + \underset{\substack{\text{Sodium}\\ \text{methoxide}}}{NaOCH_3} \longrightarrow \underset{\text{2-Methylpropene}}{(CH_3)_2C{=}CH_2} + \underset{\text{Methanol}}{CH_3OH} + \underset{\substack{\text{Sodium}\\ \text{bromide}}}{NaBr}$$

In this reaction, the process of interest to chemists is the conversion of the substrate, *tert*-butyl bromide, into the product, 2-methylpropene. The reagent, sodium methoxide, is important because it brings about the reaction, but the by-products, methanol and sodium bromide, are unimportant to organic chemists in their understanding of what happens in the reaction. Including them in the equation simply gets in the way of the significant part of the reaction. Thus, by rewriting the above equation as a transformation, chemists can see more clearly what happens:

$$\underset{\text{\textit{tert}-Butyl bromide}}{(CH_3)_3CBr} \xrightarrow{NaOCH_3} \underset{\text{2-Methylpropene}}{(CH_3)_2C{=}CH_2}$$

Note that the reagent sodium methoxide is written above the reaction arrow.

Using a transformation instead of a balanced equation can help you recognize the significant portion of a reaction and the reagents required to bring it about. However, because you do not write the by-products, you may find yourself forgetting about them. Remember that the by-products do exist and are important even though you do not write them in the transformation. Keep in mind all the chemical species that are present.

Solved Exercise 6.1

Rewrite each of the following equations as transformations.

a)

$$CH_3COCl + H_2O \longrightarrow CH_3COOH + HCl$$

Solution

Labeling the various substances is easy in this reaction. The substrate and product are the carbon-containing species.

$$\underset{\text{Substrate}}{CH_3COCl} + \underset{\text{Reagent}}{H_2O} \longrightarrow \underset{\text{Product}}{CH_3COOH} + \underset{\text{By-product}}{HCl}$$

After labeling the substrate and product, place them on opposite sides of the arrow and place the reagent on the arrow. You have written the transformation.

$$CH_3COCl \xrightarrow{H_2O} CH_3COOH$$

b)

$$CH_3COCl + CH_3OH \longrightarrow CH_3COOCH_3 + HCl$$

Solution

Labeling the various substances is more difficult with this example because both reactants are organic molecules. Later, when writing transformations, you will know more about the reactions than you know now, but a good rule of thumb is that the substrate and product are those molecules that most “resemble” each other.

$$\underset{\text{Substrate}}{CH_3COCl} + \underset{\text{Reagent}}{CH_3OH} \longrightarrow \underset{\text{Product}}{CH_3COOCH_3} + \underset{\text{By-product}}{HCl}$$

After you label the product and substrate, then write the transformation as follows:

$$CH_3COCl \xrightarrow{CH_3OH} CH_3COOCH_3$$

Exercise 6.5

For each of the following reactions, label the substrate, reagents, product, and by-products. Then rewrite each reaction as a transformation.

a)

$$(CH_3)_3COH + HCl \longrightarrow (CH_3)_3CCl + H_2O$$

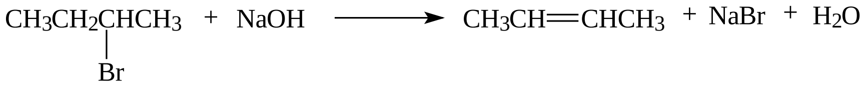
b)

$$SOCl_2 + CH_3CH_2OH \longrightarrow CH_3CH_2Cl + SO_2 + HCl$$

c)

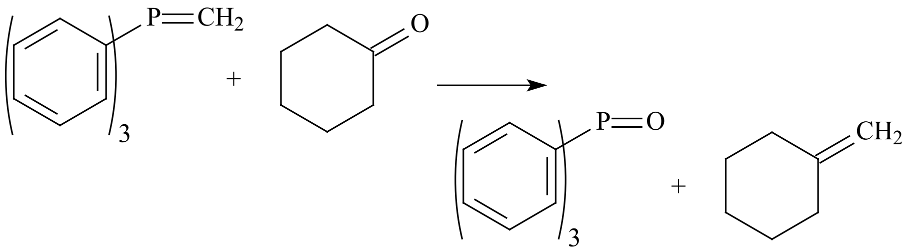
$$CH_3CONH_2 + H_2O \longrightarrow CH_3COOH + NH_3$$

d)

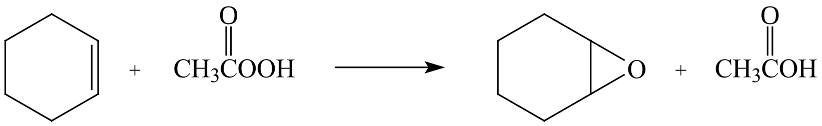


$$CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_3 + NaOH \longrightarrow CH_3CH{=}CHCH_3 + NaBr + H_2O$$

e)



f)



Sample Solution

a) First label the various substances:

$$\underset{\text{Substrate}}{(CH_3)_3COH} + \underset{\text{Reagent}}{HCl} \longrightarrow \underset{\text{Product}}{(CH_3)_3CCl} + \underset{\text{By-product}}{H_2O}$$

Then rewrite the equation as a transformation:

$$(CH_3)_3COH \xrightarrow{HCl} (CH_3)_3CCl$$

An example of a balanced equation is the following addition reaction of borane to an alkene. Note that the reaction includes a coefficient.

$$3\,CH_2{=}CH_2 + BH_3 \longrightarrow \underset{\text{Triethylborane}}{B(CH_2CH_3)_3}$$

Rewritten as a transformation, it looks like this:

$$CH_2{=}CH_2 \xrightarrow{BH_3} B(CH_2CH_3)_3$$

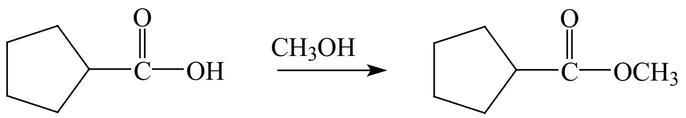
Exercise 6.6

Rewrite each of the following transformations as reactions, showing the balanced equation. Label the substrate, reagent(s), product, and by-product(s) in each balanced equation.

a)

$$CH_3CH_2Cl \xrightarrow{NaCN} CH_3CH_2CN$$

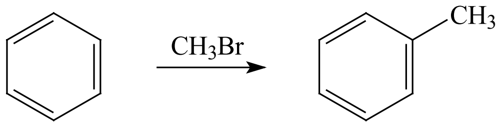
b)



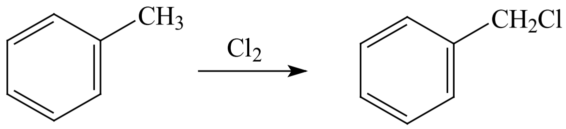
c)

$$CH_3CN \xrightarrow{H_2O} CH_3COOH$$

d)



e)



f)

$$CH_3CH_2CBr_2CH_3 \xrightarrow{NaOH} CH_3C{\equiv}CCH_3$$

Sample Solution

a) This reaction replaces —Cl with —CN.

$$\begin{array}{ccccccc} CH_3CH_2Cl & + & NaCN & \longrightarrow & CH_3CH_2CN & + & NaCl \\ \text{Substrate} & & \text{Reagent} & & \text{Product} & & \text{By-product} \end{array}$$

The reaction conditions are the requirements for maximizing the yield of products for a particular reaction.

Many reactions require a particular set of **reaction conditions**, such as a specific temperature and the presence or absence of light or air. These conditions are usually shown above the reaction arrow. If a reaction needs heat to react, instead of showing the specific temperature, chemists sometimes place the symbol Δ above the reaction arrow. The Δ symbol generally means heat the reaction mixture to the boiling point of the solvent to reflux. Frequently, chemists show the presence of light by placing the symbol $h\nu$ above the reaction arrow.

To proceed properly, many reactions start with one reagent or set of reagents, then require the addition of another reagent or set of reagents at a later time. Some reactions need the addition of two, three, or even four sets of reagents. A transformation shows each successive addition of reagents with a number that indicates the order in which the reagents are added.

$$\text{Substrate} \xrightarrow[\text{2) Second reagents}]{\text{1) First reagents}} \text{Product}$$

Alternatively, a transformation may be written with separate arrows for each reagent in the order that it is added.

$$\text{Substrate} \xrightarrow{\text{First reagents}} \xrightarrow{\text{Second reagents}} \text{Product}$$

A catalyst is a reagent whose presence changes the rate or mechanism for the reaction but does not show in the balanced equation.

Often, a reaction requires a reagent that does not appear in the balanced equation. Chemists call this kind of reagent a **catalyst** because it is required to enable the reaction but does not undergo any permanent changes itself. Chemists place a catalyst over the reaction arrow in the transformation but not in the balanced equation. For example, the reaction in part d) of Exercise 6.5 requires the presence of a strong Lewis acid to proceed. Chemists often use $AlCl_3$. Another reaction, the bromination of benzene, goes best when an iron nail is added to the reaction container! Although many reactions require catalysts, Chapter 6 only mentions them; Chapters 7 and onward will examine the part catalysts play in reactions in more detail.

6.7 Classification of Reagents in Organic Reactions

Sections 6.9, 6.10, and 6.11 briefly introduce three significant categories of chemical reactions. Remember, however, that you can categorize most organic reactions as acid-base reactions. Thus, you need to learn as many ways as possible to tell which reactant is the acid and which is the base. You can also classify reagents in organic reactions as either electrophiles or nucleophiles. An electrophilic reagent reacts with electron-rich substrates. That is, an electrophile is a Lewis acid that reacts with a substrate that is a Lewis base. A nucleophilic reagent reacts with an electron-poor substrate and is a Lewis base. Table 6.1 lists representative nucleophiles and electrophiles.

Nucleophiles	Electrophiles
$^{\ominus}OH$, $CH_3O^{\ominus}$, $CH_3CH_2O^{\ominus}$, $^{\ominus}SH$, $CH_3S^{\ominus}$, $CH_3CH_2S^{\ominus}$, $^{\ominus}CN$, $I^{\ominus}$, $Br^{\ominus}$, NH_3, $^{\ominus}CH_3$, CH_3NH_2	$H^{\oplus}$, $Cl^{\oplus}$, $Br^{\oplus}$, $^{\oplus}CH_3$, BF_3, $^{\oplus}NO_2$

Table 6.1. Representative nucleophilic and electrophilic reagents.

6.8 Writing Reaction Mechanisms

A mechanism shows the flow of electrons as reactants are transformed to products.

This book presents organic chemical reactions according to their reaction **mechanism** type. The mechanism of a reaction is a visual description of the pathway that reacting molecules follow as they are transformed from starting materials to products. That is, as molecules react, they move directly to the product or through one or more intermediate steps. These steps may involve changes that either convert one functional group to another or rearrange the carbon skeleton. A reaction mechanism is a step-by-step written representation of those structural changes. Writing a reaction mechanism is like taking a series of snapshots of each intermediate step. Understanding organic reactions depends on being able to visualize the structural changes that take place along the reaction pathway and being able to write out the steps helps in the visualization process. By knowing the specific mechanisms that are representative of broad categories of reactions, you can develop a feeling for the essential details of the organic reactions, enabling you to predict the outcome of unfamiliar ones.

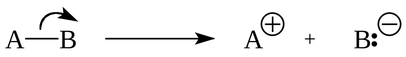
When writing a reaction mechanism for an organic reaction, you must show how the electron pairs flow in the reaction. The overall flow of electron pairs in a reaction can be broken down into five general operations and are discussed in this section. These five operations help you to link the reactant structure with the product structure. If you keep these five operations in mind when writing mechanisms, you will find it much easier to understand the electron flow in the reactions.

Using Sections 6.8 to 6.11

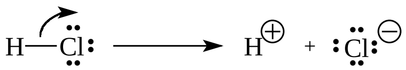
Do not attempt to memorize all of the reactions and reaction mechanisms in Sections 6.8 through 6.11. Many of the reactions in these sections are unfamiliar to you, and you do not have enough information to fully understand them. That understanding will come in later chapters. The goal for these sections is to give you the tools to understand and work with the various types of mechanisms. Pay particular attention to the electron flow in the examples given to develop your skills in writing mechanisms. So step back looking for trends and ideas, not for details. You will develop an understanding of the details in future chapters.

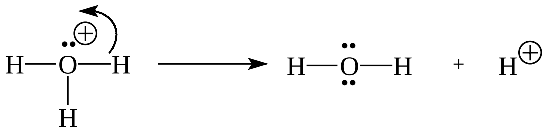
The heterolytic bond cleavage operation breaks a bond in such a way that one atom takes both electrons.

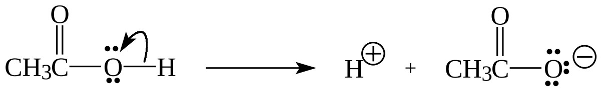
The first general operation used in mechanism writing is the **heterolytic bond cleavage operation**. Heterolytic bond cleavage takes place when the bond between two atoms breaks. One atom takes both electrons and becomes negatively charged while the other atom loses electrons and becomes positively charged.



Here are some examples of the heterolytic bond cleavage operation:

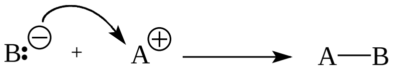




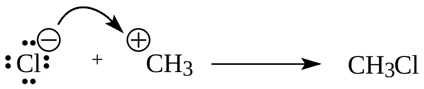


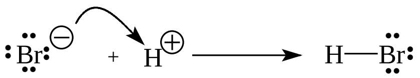
The heterogenic bond forming operation involves the formation of a bond between one atom with an empty orbital and another with a pair of nonbonding electrons.

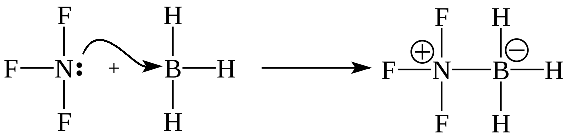
The second general operation is the **heterogenic bond forming operation**, which is the reverse of the heterolytic bond cleavage operation. An atom with a pair of electrons reacts with another atom having an empty orbital. The atom with the electrons becomes more positively charged while the atom with the empty orbital becomes more negatively charged.



Here are some examples of the heterogenic bond forming operation:

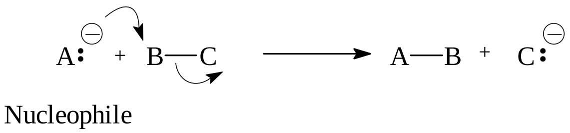




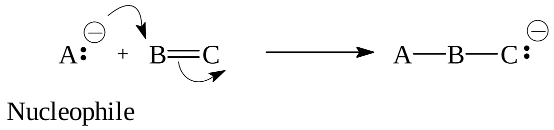


In a 1,3-electron pair displacement operation, one atom with a pair of nonbonding electrons forms a bond with a second atom and displaces a pair of bonding electrons to a third atom.

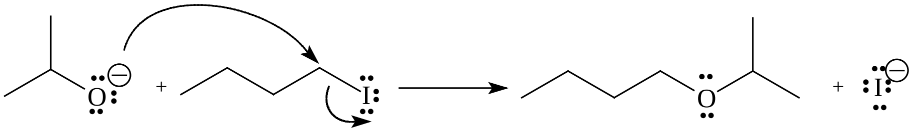
The third general operation is the **1,3-electron pair displacement operation**. This reaction involves an electron flow covering three atoms: an initiating electron-donating atom, the central atom, and an electron-accepting atom. Unlike the first two operations, there is no change in the net charge of the reacting system. However, the initiating atom becomes more positive and the displaced atom becomes more negative. The initiating electron-donor atom is normally called a nucleophile.

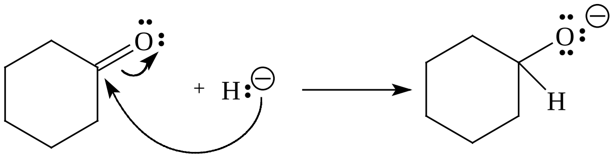


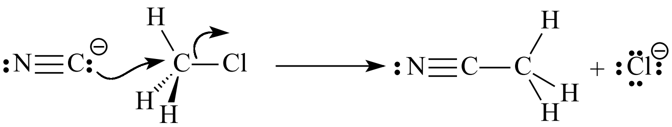
In addition to the bond-forming and bond-breaking process shown above, this general operation also fits the addition of a nucleophile to a double bond.



Some examples of the 1,3-electron pair displacement operation are shown below:

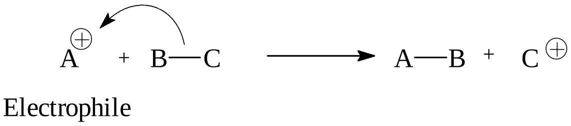




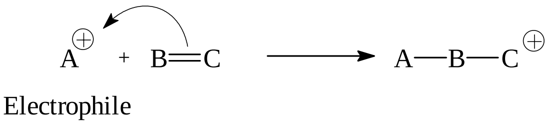


In a 1,3-electron pair abstraction operation, one atom with an empty orbital forms a bond with a second atom and removes a bond from a third atom.

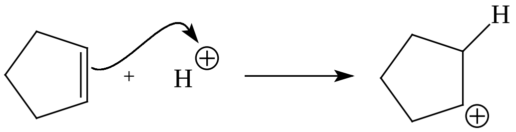
The fourth general operation is the **1,3-electron pair abstraction operation**. In this case, an electron-deficient species draws an electron pair from an electron-rich species, making another atom electron-deficient. The initiating atom becomes less positive, and the displaced atom becomes more positive. The initiating electron-acceptor atom is normally called an electrophile.

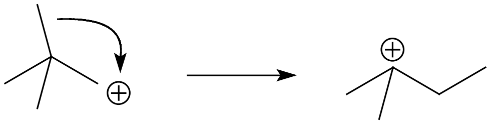


In addition to the bond-forming and bond-breaking process shown above, this fourth general operation also fits the addition of an electrophile to a double bond.



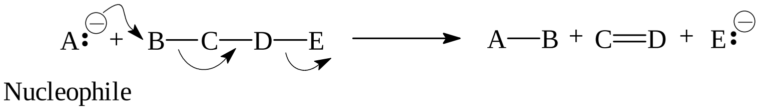
Following are some examples of the 1,3-electron pair abstraction operation:



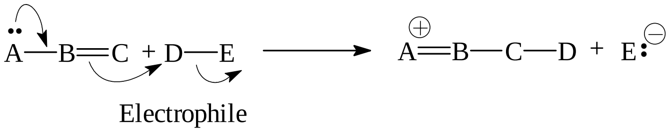


In a 1,5-electron pair displacement operation, one atom with a pair of nonbonding electrons forms a bond with a second atom and displaces a bonding electron pair to a third atom and then another to a fifth atom.

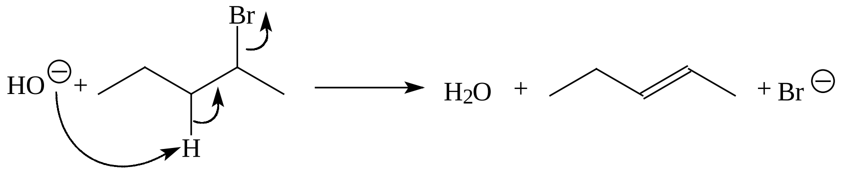
The fifth general operation is the **1,5-electron pair displacement operation**. This operation involves an electron flow covering five atoms: an initiating electron-donor atom, three central atoms, and an electron-acceptor atom. There is no change in the net charge of the reacting system. However, the initiating atom, the nucleophile, becomes more positive and the displaced atom becomes more negative.

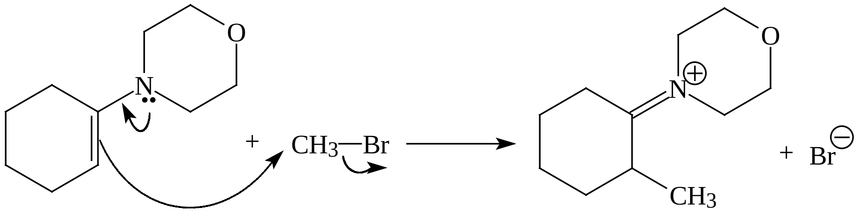


In addition to the bond-forming and bond-breaking process shown above, the fifth general operation also fits the addition of the electrophile (D) to a double bond.



Some examples of the 1,5-electron pair displacement operation are as follows:





Other operations are possible, but they do not occur in the reaction systems discussed in this book. Most organic reaction mechanisms, no matter how complex, can be written using these five operations. The next Sections 6.9, 6.10, and 6.11 use some specific reactions as examples to preview the three categories of reaction mechanisms covered in more detail in later chapters. In these sections, you will see how the five operations are used in some actual mechanisms.

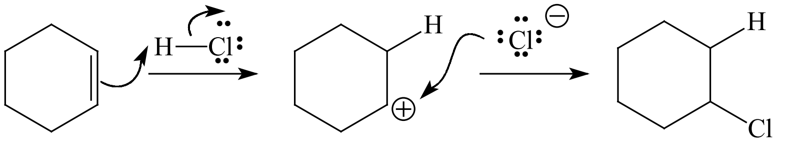
A Tip for Using Curved Arrows

When the mechanism of a reaction requires the use of multiple arrows, the tail of one arrow follows the head of the previous one. A common mistake of beginners is showing multiple arrows originating from or terminating at a single atom. Remember, the tail of a second arrow follows the head of the first and shows the direction of electron flow. When drawn this way, your arrow sequence will more likely be correct.

Solved Exercise 6.2

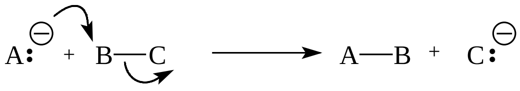
Identify the operations used in the following reaction mechanisms.

a)

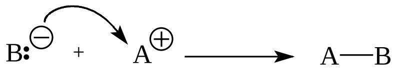


Solution

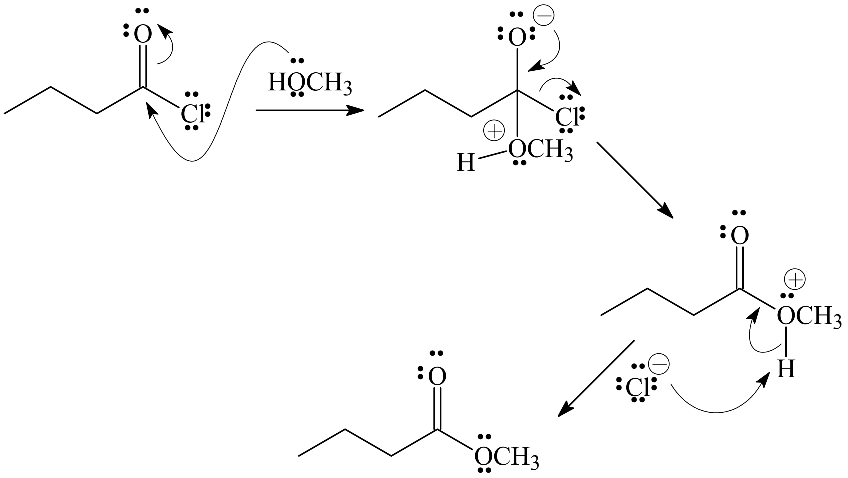
This mechanism has two steps. The first step is a 1,3-electron pair displacement operation. Compare it to the general operation description.



The second step is a heterogenic bond formation operation. Compare it to the general operation description.

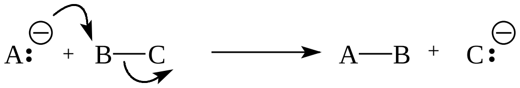


b)



Solution

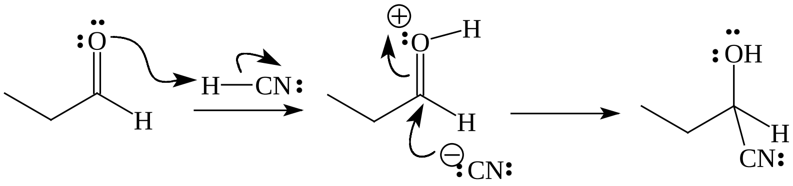
All three steps are 1,3-electron pair displacement operations.



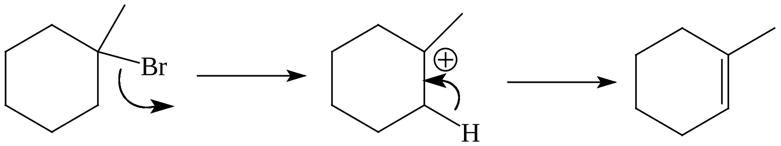
Exercise 6.7

Identify the general operation used in each step in the following mechanisms.

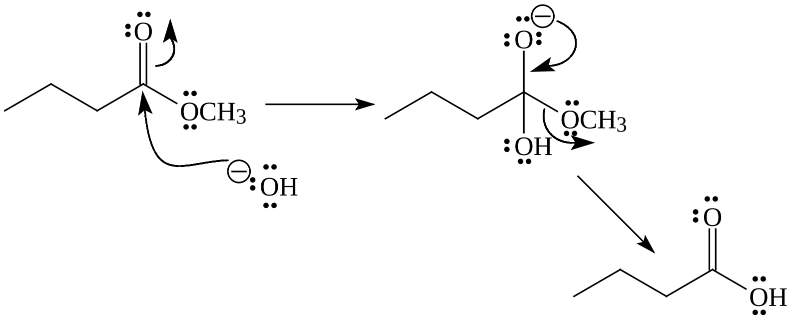
a)



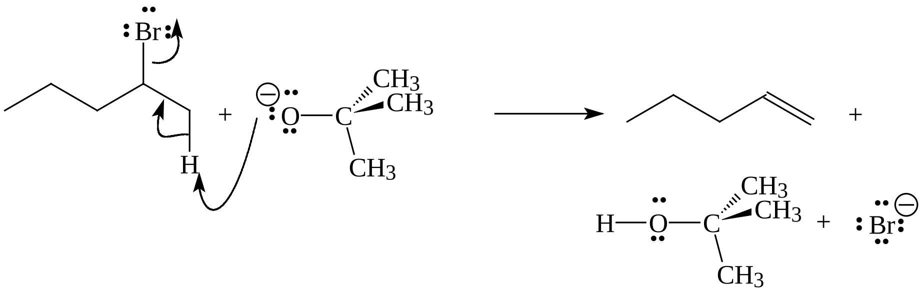
b)



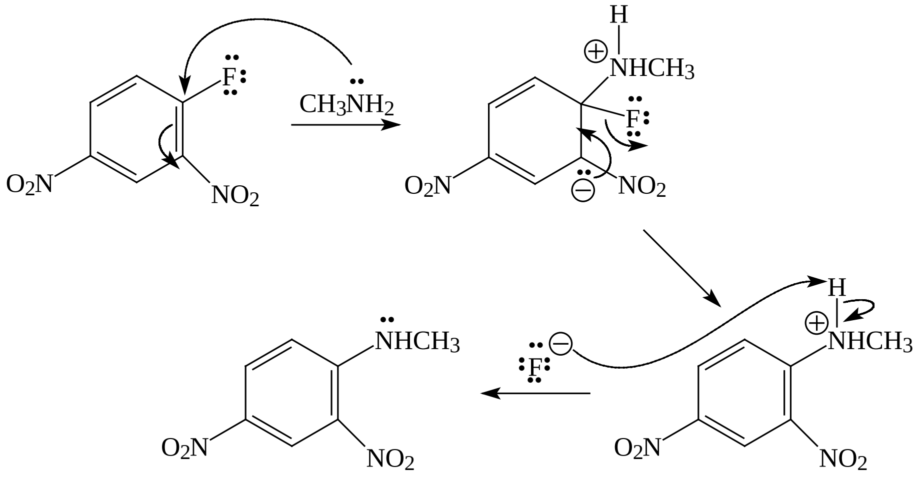
c)



d)



e)



Sample solution

b) The first step is a heterolytic bond cleavage operation; the second step is a 1,3-electron pair abstraction operation.

6.9 Substitution Reactions

Substitution, addition, and elimination refer to whether atoms are changed, added, or removed from a molecule. Rearrangement changes the carbon skeleton of a molecule.

The three categories of reaction mechanisms are **substitution**, **addition**, and **elimination** reactions. Some chemists add a fourth category, **rearrangement**, although a rearrangement reaction is simply a combination of the basic three categories that operates on the carbon skeleton of an organic compound. This section begins a preview of these mechanism types with a discussion of substitution reactions. The goal for this preview is to give you a framework for much of the rest of the book. You may be tempted to try to extract too much detail from this preview; as you study, you should try to see the ideas behind the reactions presented instead of concentrating on the details. Later chapters will cover each mechanism type in detail.

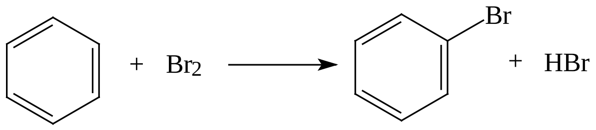
A substitution reaction is a type of reaction in which one atom, or a group of atoms, from the reagent replaces or substitutes itself for one atom or a group of atoms on the substrate. The substitution takes place at either a saturated or an unsaturated carbon atom. The following reactions are examples of substitution reactions.

(1) 

$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}Cl + CH_3OH \longrightarrow CH_3\overset{\overset{\displaystyle O}{\|}}{C}OCH_3 + HCl$$

(2) $CH_3Br + {}^{\ominus}OH \longrightarrow CH_3OH + Br^{\ominus}$

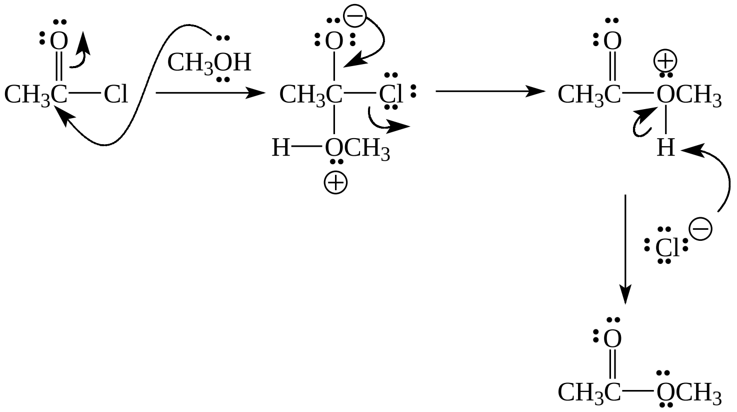
(3) $(CH_3)_3CBr + H_2O \longrightarrow (CH_3)_3COH + HBr$

(4) 

In a nucleophilic substitution, the reagent is a nucleophile (base).

In an electrophilic substitution, the reagent is an electrophile (acid).

Although each of these reactions is similar because each is a substitution reaction, they represent the different mechanistic pathways that substitution reactions can take. The first three reactions are **nucleophilic substitutions**. In a nucleophilic substitution reaction, the reagent is a Lewis base, and the substrate is a Lewis acid. The fourth reaction is an **electrophilic substitution**. In an electrophilic substitution reaction, the reagent is a Lewis acid and the substrate is a Lewis base. The first example reaction, the reaction of CH_3COCl (ethanoyl chloride or acetyl chloride) with CH_3OH (methanol), is a nucleophilic substitution reaction at the unsaturated carbon of a carbonyl group. The nucleophile adds to the carbonyl carbon, forming a tetrahedral intermediate. This intermediate then loses an atom or group of atoms, forming the product.



A concerted mechanism is a one-step mechanism in which all bond breaking and bond forming occurs simultaneously.

Figure 6.3 is found on page 000.

Figure 6.4 is found on page 000.

The term S_N2 means Substitution, Nucleophilic, Bimolecular. This is a concerted mechanism with a rate depending on both substrate and reagent concentrations.

The pathway for the second example reaction, the reaction of methyl bromide with a hydroxide ion, proceeds through a **concerted mechanism**. That is, the reaction has no intermediates between the starting materials and products. Because there are no intermediates, the reaction profile for this reaction looks similar to that shown in Figure 6.3. (The other three reactions proceed through an intermediate, so their reaction profiles look much like the one in Figure 6.4.)

As you consider this mechanism, note that the hydroxide ion attacks and reacts with the substrate, methyl bromide, on the side of the molecule opposite the bromine. The bromine is the atom that leaves the substrate. This attack causes the substrate to invert, much like an umbrella turning inside out in the wind. Figures 6.5 and 6.6 show two ways of illustrating this reaction. In both figures, the mechanism is seen as an 1,3-electron pair displacement operation. Chemists call a nucleophilic substitution that proceeds through a concerted mechanism an **S_N2 reaction**. S_N2 reactions are one of the most common types of organic reactions. Chapter 12 covers them in greater detail.

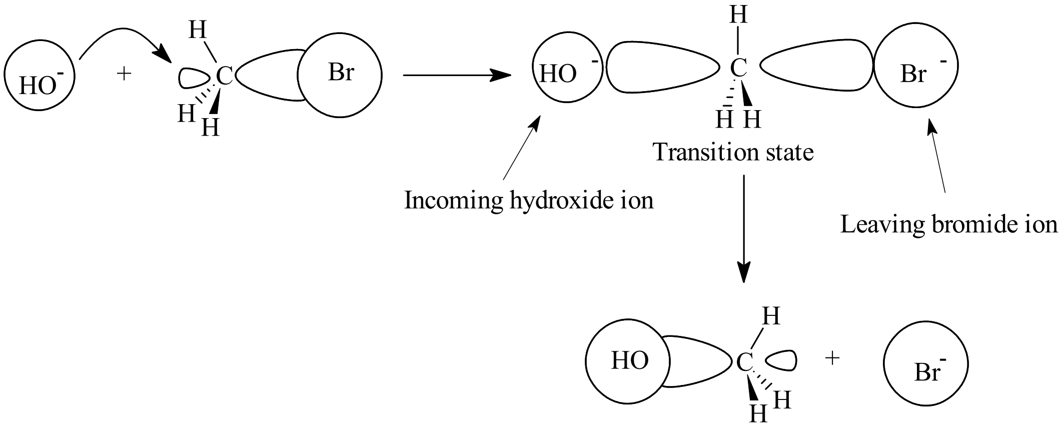


Figure 6.5. Orbitals on the carbon involved in the reaction of hydroxide ion with methyl bromide.

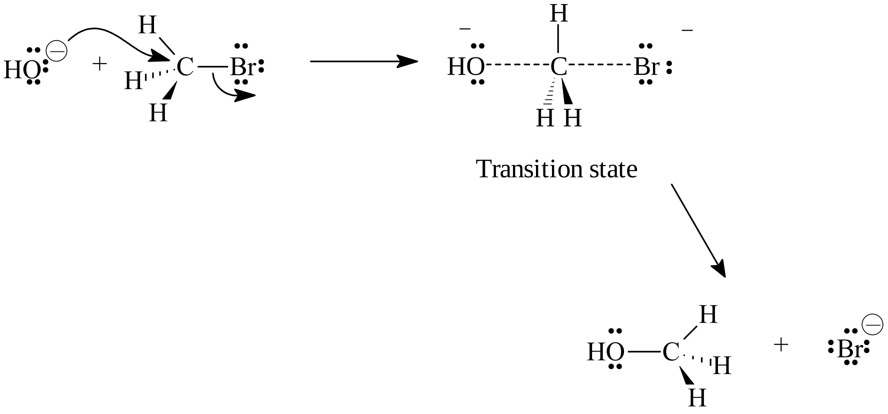
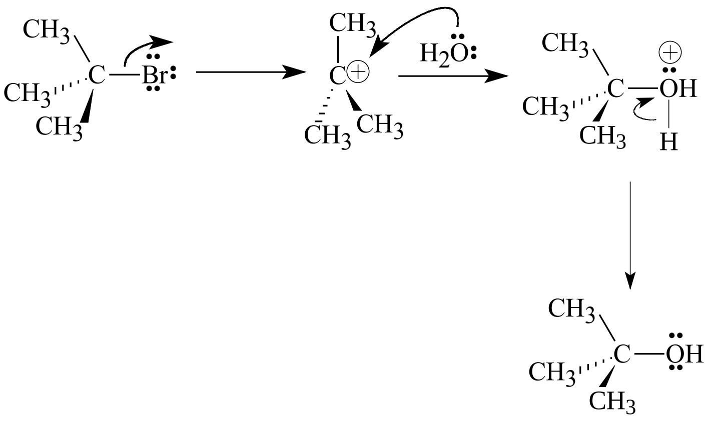


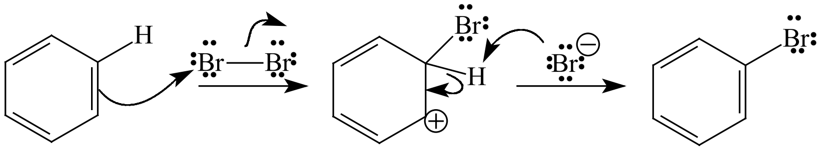
Figure 6.6. Standard mechanistic representation of the reaction of hydroxide ion with methyl bromide. Notice that this is an 1,3-electron pair displacement operation.

The term S_N1 means Substitution, Nucleophilic, Unimolecular. This is a stepwise mechanism with a rate that depends on the substrate concentration.

The third example of a substitution reaction, the reaction of $(CH_3)_3CBr$ (*tert*-butyl bromide) with water, is an **S_N1 reaction**. Chapter 12 also discusses these reactions. S_N1 reactions proceed through an intermediate that has a positively charged carbon. The intermediate is planar and reacts with the nucleophile from either side. This mechanism involves a heterolytic bond cleavage operation followed by a heterogenic bond forming operation.

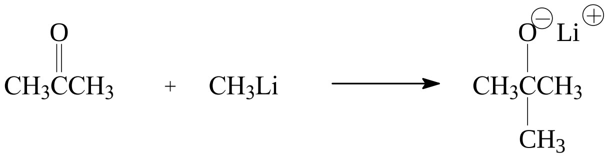


The final example reaction, the reaction of benzene with Br_2, is an electrophilic substitution. In an electrophilic substitution, the substrate (in this case the benzene) supplies the electrons to the bond being formed. The example reaction, an electrophilic aromatic substitution, involves an intermediate called a σ complex, which is a highly stabilized carbocation. Both steps in this mechanism are 1,3-electron pair displacement operations.

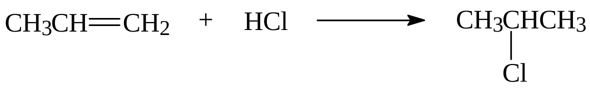


6.10 Addition Reactions

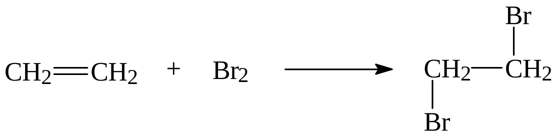
In an addition reaction, atoms or groups of atoms from the reagent add to the substrate generally without losing any atoms from the substrate. Thus, the product gains atoms from the reagent without losing any atoms from the substrate. The substrate for an addition reaction is an unsaturated molecule, that is, a molecule with either a double or a triple bond. An unsaturated molecule is the only type of molecule that can accept additional atoms or groups of atoms from a reagent without exceeding the maximum number of groups allowed by carbon. Addition reactions take place very readily because σ bonds are stronger than π bonds. The following are some examples of addition reactions:

(1) 

$$CH_3\overset{O}{\overset{\|}{C}}CH_3 + CH_3Li \longrightarrow CH_3\underset{\underset{CH_3}{|}}{\overset{\overset{O^{\ominus}\,Li^{\oplus}}{|}}{C}}CH_3$$

(2) 

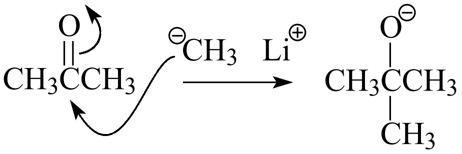
$$CH_3CH{=}CH_2 + HCl \longrightarrow CH_3\underset{\underset{Cl}{|}}{C}HCH_3$$

(3) 

$$CH_2{=}CH_2 + Br_2 \longrightarrow \underset{\underset{Br}{|}}{CH_2}{-}\overset{\overset{Br}{|}}{CH_2}$$

A nucleophilic addition is the reaction of an electron-rich reagent with an electron deficient substrate.

Each of these examples illustrates a different addition pathway from the substrate to the product. The reaction of CH_3COCH_3 (acetone) with CH_3Li is an example of a **nucleophilic addition** to a C=O double bond. Because of the difference in electronegativity between the carbon and the oxygen, the electrons are unevenly distributed in the bond. Thus, the carbon is slightly electron-deficient—has a slight positive charge—and is susceptible to attack by a nucleophile. This mechanism also involves a 1,3-electron pair displacement operation followed by a heterogenic bond forming operation.



$$CH_3\overset{O}{\overset{\|}{C}}CH_3 \quad {}^{\ominus}CH_3\ \ Li^{\oplus} \longrightarrow CH_3\underset{\underset{CH_3}{|}}{\overset{\overset{O^{\ominus}}{|}}{C}}CH_3$$

An electrophilic addition is the reaction of an electron deficient reagent with an electron-rich substrate.

The next two examples are **electrophilic additions** to alkenes. Each of the two reactions proceeds through the addition of an electrophile to the double bond, followed by reaction with a nucleophile. In the first reaction, the electrophile is the hydrogen ion, $H^{\oplus}$; in the second, it is the bromine ion, $Br^{\oplus}$. Each of these reactions adds a positive electrophile to the electron-rich double bond. Figure 6.7 illustrates the mechanism of the addition of HCl to propene. The first step of the mechanism is an electron pair displacement operation; the second step is a heterogenic bond forming operation.

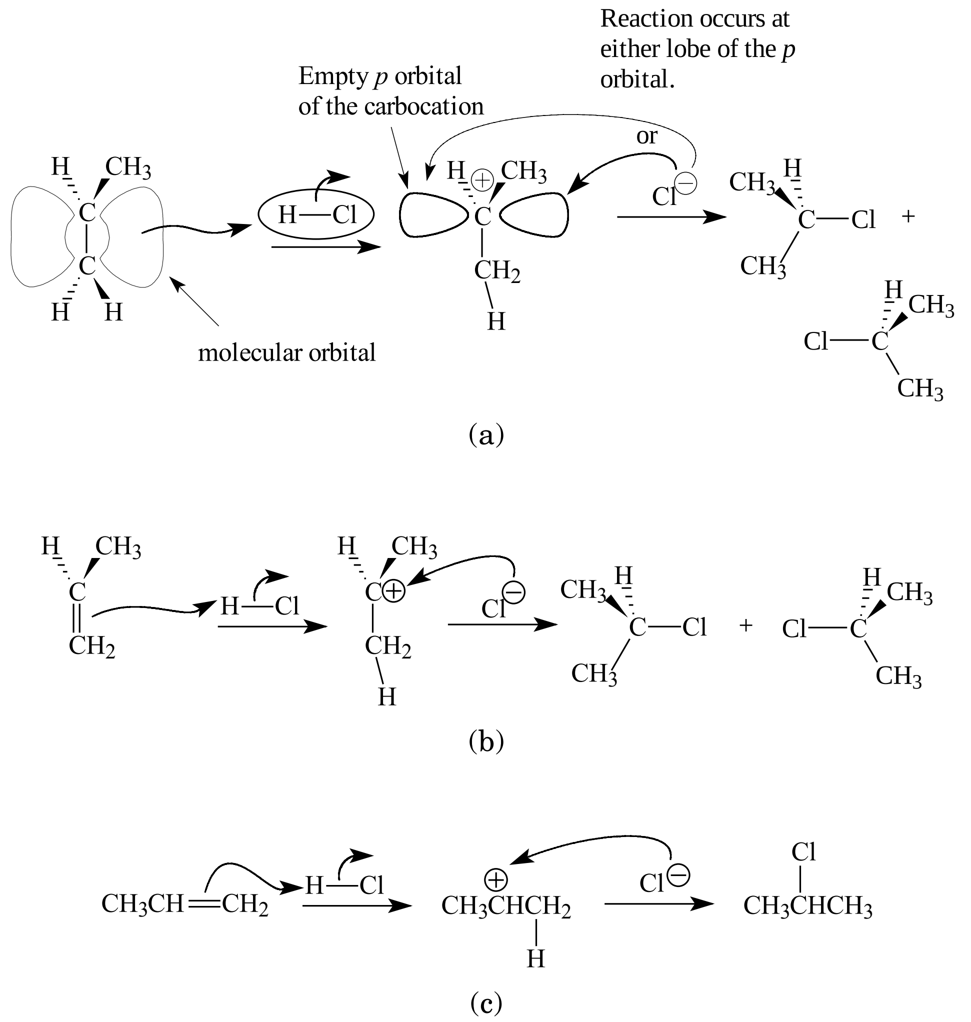
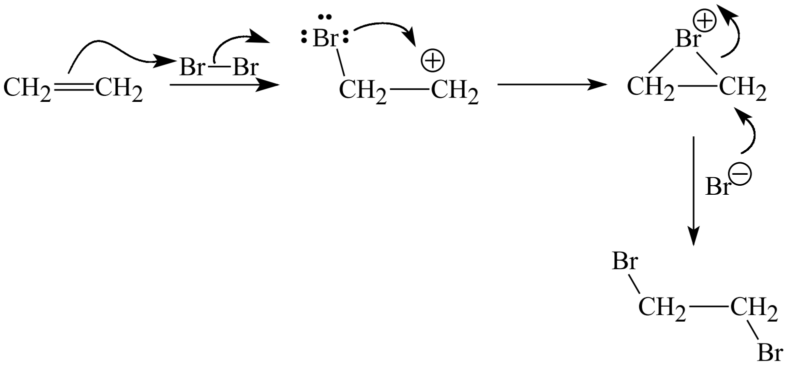


Figure 6.7. The addition of HCl to a double bond. (a) A picture of the orbitals involved in the reaction. (b) A three-dimensional drawing of the mechanism. (c) A standard mechanistic representation.

The difference between the reaction of propene with HCl and the reaction of ethene with Br_2 is the bromine has nonbonding electrons that it donates to stabilize the intermediate cation, whereas the hydrogen from HCl does not. As noted in Section 6.9, a carbocation permits a reaction with a nucleophile from either side, but here the bromonium ion effectively blocks one side of the molecule. Thus, the nucleophile can only add anti, or opposite, to the bromine already present. This mechanism involves a 1,3-electron pair displacement operation followed by a heterogenic bond forming operation.



6.11 Elimination Reactions

An elimination reaction is the opposite of an addition reaction. Whereas an addition reaction adds atoms to a compound, doing away with a multiple bond, an elimination reaction removes two atoms or two groups of atoms from the substrate, giving the product a multiple bond or, in some cases, causing it to form a ring. The atoms may leave the substrate from adjacent carbons or from carbons some distance apart. The following examples illustrate **1,2-eliminations**, that is, reactions in which the atoms leave from adjacent carbons of the substrate:

A 1,2-elimination involves loss of atoms from adjacent atoms in the substrate.

(1) $(CH_3)_3COH \xrightarrow[2)\ ^{\ominus}OH]{1)\ H_3O^{\oplus}} (CH_3)_2C{=}CH_2 + H_2O$

(2)

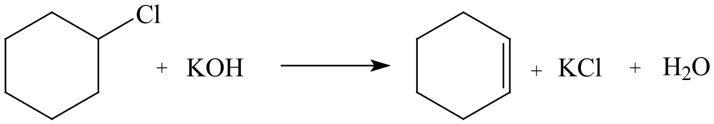
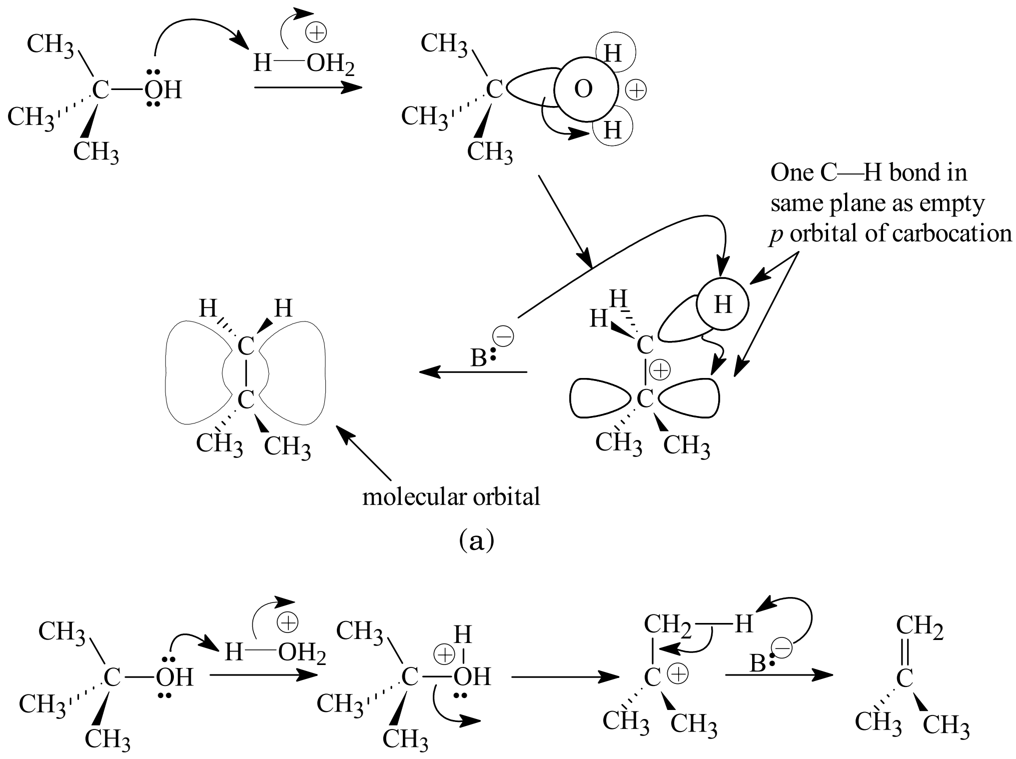


Figure 6.8 shows the mechanism of the first elimination example, the reaction of $(CH_3)_3COH$ (*tert*-butyl alcohol) with acid. This mechanism involves an electron pair abstraction operation, followed by a heterolytic bond cleavage operation and then a 1,5-electron pair displacement operation.



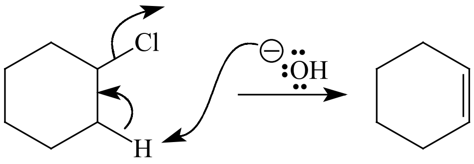
(a)

(b)

Figure 6.8. The elimination of water from *tert*-butyl alcohol. (a) The molecular orbitals involved in the reaction. (b) A standard mechanistic representation.

Some elimination, addition, and substitution reactions go through a carbocation intermediate. The carbocation intermediate often makes these reactions competitive with each other. For example, look at the first elimination example (the reaction of *tert*-butyl alcohol with acid), the third substitution example (the reaction of *tert*-butyl bromide with water), and the first addition example (the reaction of propene with HCl). All three reactions go through a carbocation intermediate. By careful choice of reagents, substrates, and reaction conditions, chemists control which reaction type occurs. The determining factor between the addition and elimination reactions is the substrate; between the elimination and substitution reactions, the nucleophile is the determining factor. Using an acid such as sulfuric acid or phosphoric acid brings about an elimination reaction; using an acid such as hydrochloric acid brings about a substitution reaction. Chapters 12, 14 and 15 examine the carbocation mechanism in greater detail.

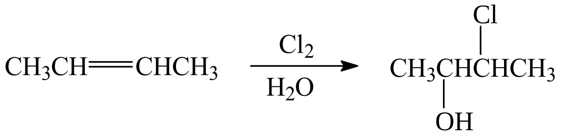
The second elimination reaction example (the reaction of chlorocyclohexane with KOH) is similar to the first substitution reaction example (the reaction of bromomethane with $^{\ominus}$OH) in that it has a concerted mechanism. Recall that a concerted reaction is one that passes through no intermediates between the starting materials and products. The second elimination example and the first substitution example are often competitive with one another because of their similar mechanisms and similar reaction conditions. Chapters 12, 14, and 15 cover those concepts in more detail. With the elimination reaction, a strong base initiates the reaction. As soon as a hydrogen on the carbon adjacent to the leaving group starts to leave, the carbon bearing that hydrogen begins to change from *sp*^{3} hybridization to *sp*^{2} hybridization. The change in hybridization occurs because the elimination of two atoms, in this case a chlorine and a hydrogen, allows an overlap between the *p* orbitals to form a bond. This mechanism is an example of a 1,5 electron pair displacement operation.



Exercise 6.8

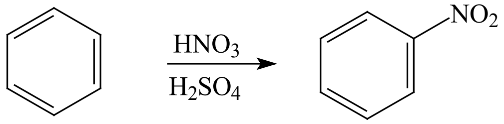
Each of the following reactions is a substitution, addition, or elimination reaction. Assign the correct type to each reaction.

a)

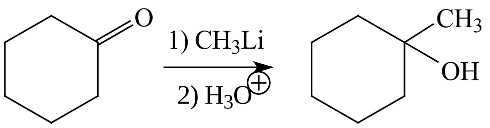


$$CH_3CH{=}CHCH_3 \xrightarrow[H_2O]{Cl_2} \underset{\displaystyle OH}{CH_3CH}\overset{\displaystyle Cl}{CHCH_3}$$

b)



c)



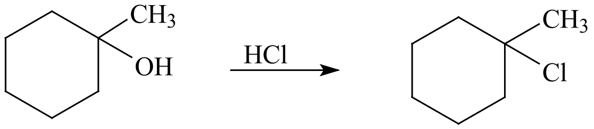
d)

$$CH_3CH{=}CH_2Br \xrightarrow{^{\ominus}OH} CH_3C{\equiv}CH$$

e)

$$CH_3CH_2CH_2\overset{\oplus}{N}(CH_3)_3 \quad ^{\ominus}OH \longrightarrow CH_3CH{=}CH_2 + (CH_3)_3N$$

f)



Sample solution

c) Addition reaction

Key Ideas from Chapter 6

- ❏ For a reaction to have any practical application, it must proceed at a reasonable rate. Adjusting the temperature of the reaction mixture so that the fraction of molecules with an energy content equal to, or above, the energy of activation often brings about a reasonable rate.

- ❏ The relative free energies of the molecules involved in a reaction determine their positions in the chemical equilibrium. The equilibrium moves toward the most stable molecule.

- ❏ Reactants often form products via unstable species called transition states. Among reactions, the smaller the differences in the energy levels between reactants and transition states the faster the reaction rate.

- ❏ The slowest step of a multistep reaction mechanism governs the rate of that reaction. The transition state is involved in the step with the highest energy of activation.

- ❏ A curved arrow symbolizes the electron movement in a reaction. This curved arrow shows the formal flow of electrons as the bonds form or break. A double barb arrow shows the movement of an electron pair. A single barb arrow shows the movement of a single electron.

- ❏ A chemical reaction involves the substrate, other reagents, product, and by-products.

- ❑ Organic chemists often do not write a balanced equation for a chemical reaction; instead they write a transformation. A transformation shows only what changes occur in the substrate as it reacts with the reagent to form the product.

- ❑ Most organic reagents fall into two categories: electrophiles and nucleophiles. An electrophile is a Lewis acid. A nucleophile is a Lewis base.

- ❑ A reaction mechanism is written using some combination of five types of operations: heterolytic bond cleavage, heterogenic bond formation, 1,3-electron pair displacement, 1,3-electron pair abstraction, and 1,5-electron pair displacement.

- ❑ All organic reactions can be classified as substitution, addition, or elimination reactions. Each of these categories has a number of different reaction mechanisms.

- ❑ In a substitution reaction, an incoming atom or group of atoms replaces a leaving atom or group of atoms.

- ❑ In an addition reaction, pairs of atoms or groups of atoms add to a multiple bond.

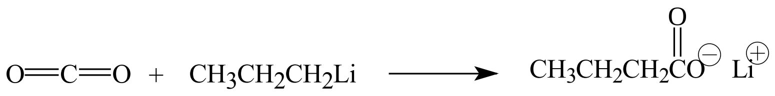
- ❑ In an elimination reaction, a pair of atoms or group of atoms leaves the substrate. The substrate then forms a multiple bond or forms a cyclic structure.

- ❑ Addition, elimination, and substitution reactions may proceed through a nucleophilic or electrophilic mechanism.

Supplementary Exercises

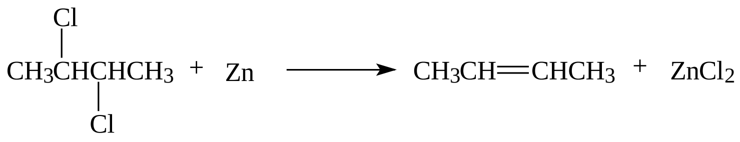
6.9 Classify each of the following reactions as substitution, addition, or elimination. Then rewrite each equation as a transformation.

a)



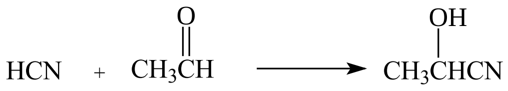
$$O{=}C{=}O \; + \; CH_3CH_2CH_2Li \longrightarrow CH_3CH_2CH_2\overset{\overset{\displaystyle O}{\|}}{C}O^{\ominus}\;Li^{\oplus}$$

b)



$$CH_3\overset{\displaystyle Cl}{\overset{|}{C}}H\underset{\displaystyle Cl}{\underset{|}{C}}HCH_3 + Zn \longrightarrow CH_3CH{=}CHCH_3 + ZnCl_2$$

c)

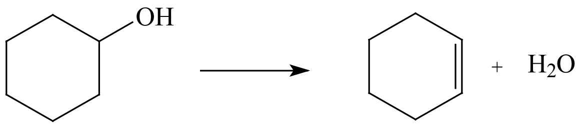


$$HCN + CH_3\overset{O}{\overset{\|}{C}}H \longrightarrow CH_3\overset{OH}{\overset{|}{C}}HCN$$

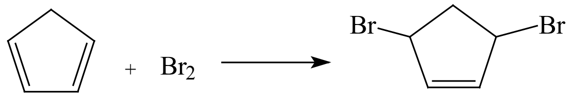
d)

$CH_3CH_2OH + CH_2{=}CHCN \longrightarrow CH_3CH_2OCH_2CH_2CN$

e)



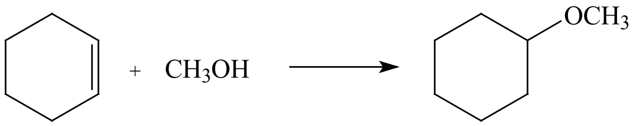
f)



g)

$CH_3SH + CH_3CH_2Br \longrightarrow CH_3SCH_2CH_3$

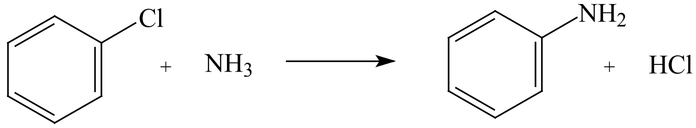
h)



i)

$H_2O + (CH_3)_2C{=}CH_2 \longrightarrow (CH_3)_3COH$

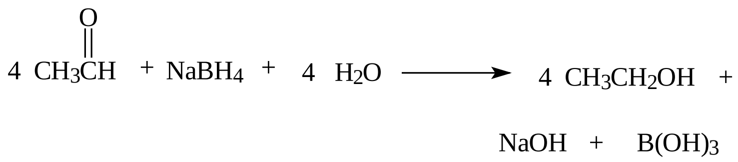
j)



k)

$$CH_3OCH_3 + 2\ HBr \longrightarrow 2\ CH_3Br + H_2O$$

l)



$$4\ CH_3\overset{\overset{O}{\|}}{C}H + NaBH_4 + 4\ H_2O \longrightarrow 4\ CH_3CH_2OH + NaOH + B(OH)_3$$

6.10 Hydrocarbon A, C_6H_{10}, reacts with hydrogen and platinum to produce methylcyclopentane, C_6H_{12}. In another reaction, hydrocarbon A reacts with bromine in carbon tetrachloride to produce $C_6H_{10}Br_2$.

a) Suggest structure(s) for A.

b) Write a transformation for each reaction described. If A has more than one structure, select and write the chemical equations for only one.

c) Do you have sufficient information to propose a unique molecular structure for A? Explain.

6.11 What value must ΔG^o have for the following equilibrium reaction to go 99% to completion at 25^oC?

$$A + B \rightleftharpoons C + D$$

6.12 Adding HBr to 2-butene produces a single product with the molecular formula C_4H_9Br. Adding HBr to 1-butene can produce two different products, depending on the reaction conditions; these also have the molecular formula C_4H_9Br. Suggest structures for each of the reaction products from both 1- and 2-butene.

6.13 1-Methylcyclohexene reacts with HCl to form 1-chloro-1-methylcyclohexane, compound C ($C_7H_{13}Cl$). When compound C reacts with water, compound D ($C_7H_{14}O$) slowly forms. a) Propose a structure for D. b) Write balanced chemical equations for the two reactions. c) Rewrite these reactions to transformations. d) Classify each step as a substitution, addition, or elimination reaction.

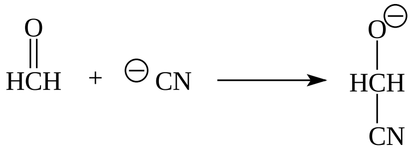
6.14 An unknown alcohol **E** (C_3H_8O) produces compound **F** when heated with an acid. Compound **F** produces a different alcohol, **G**, when reacted with an aqueous acid. Bromine adds to compound F to produce compound **H** ($C_3H_6Br_2$). a) Write the structures of compounds E through H. b) Write balanced chemical equations for the reactions. c) Rewrite the reactions to transformations. d) Classify each step as a substitution, addition, or elimination reaction.

6.15 Classify each of the following reactions as addition, elimination, or substitution. Use curved arrows to show the movements of the electrons as the starting materials are converted to products. Classify the type of operation for each step in the mechanism.

a)

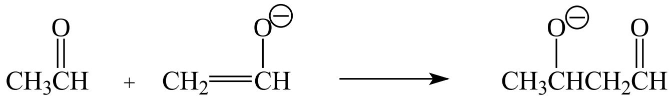
$$CH_3Cl + I^{\ominus} \longrightarrow CH_3I + Cl^{\ominus}$$

b)



$$HC(=O)H + {}^{\ominus}CN \longrightarrow HCH(O^{\ominus})(CN)$$

c)



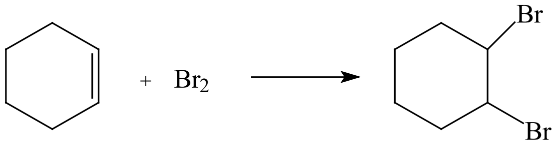
$$CH_3CH{=}O + CH_2{=}CH{-}O^{\ominus} \longrightarrow CH_3CH(O^{\ominus})CH_2CH{=}O$$

d)

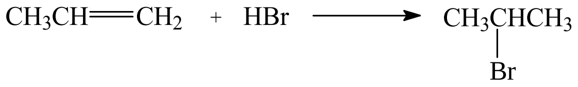
$$CH_2{=}CH_2 + H_2O \xrightarrow{H^{\oplus}} CH_3CH_2OH$$

(Note: The H$^{\oplus}$ is a catalyst for this reaction.)

e)



f)



$$CH_3CH{=}CH_2 + HBr \longrightarrow CH_3CH(Br)CH_3$$

6.16 Examine the nucleophilic substitution reaction between hydroxide ion and methyl bromide. Experiments show that the angle of attack between the hydroxide ion and the C—Br bond is very close to 180°. Consider the molecular orbital picture of methyl bromide (review Chapter 1) and explain why the angle of attack is 180°.

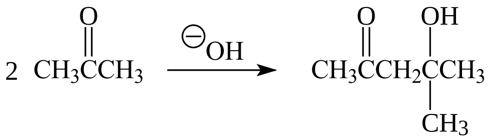
6.17 For the reaction of compounds A and B, rate = k[A][B]. If A and B have equal concentrations at the start of the reaction and rate = 1, what is the rate of the reaction at 50% completion?

6.18 Consider the elimination reaction between methoxide ion and *tert*-butyl bromide to form 2-methyl-1-propene. Experimental data shows that the leaving atoms, hydrogen and bromine, react best when they are anti to one another. Consider the molecular orbital picture of *tert*-butyl bromide, and then propose a reason why this is true. The rate of elimination is much slower when the hydrogen and the bromine are eclipsed. Why? Does this agree with the molecular orbital picture?

6.19 At 25°C the following reaction goes 5% to completion. (Hint: Please note that this reaction has the form

$$2\ A \xrightarrow{\text{Catalyst}} B$$

Thus, the equilibrium expression is $K_e = \frac{[B]}{[A]^2}$)

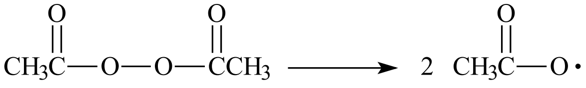


$$2\ CH_3\overset{\overset{O}{\|}}{C}CH_3 \xrightarrow{^{\ominus}OH} CH_3\overset{\overset{O}{\|}}{C}CH_2\underset{\underset{CH_3}{|}}{\overset{\overset{OH}{|}}{C}}CH_3$$

Determine the value of ΔG^o for the reaction.

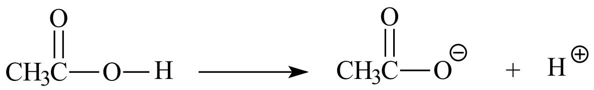
6.20 If the Gibbs free energy difference between the anti conformation of butane and the eclipsed conformation is 6.1 kcal/mole calculate the amount of eclipsed butane present in 1 mole of butane at equilibrium at 25°C.

6.21 When heated, the oxygen-oxygen bond of acetyl peroxide cleaves homolytically.



$$CH_3\overset{\overset{O}{\|}}{C}—O—O—\overset{\overset{O}{\|}}{C}CH_3 \longrightarrow 2\ CH_3\overset{\overset{O}{\|}}{C}—O\cdot$$

On the other hand, the oxygen-hydrogen bond of acetic acid cleaves heterolytically.



$$CH_3C(=O)—O—H \longrightarrow CH_3C(=O)—O^{\ominus} + H^{\oplus}$$

Why does one cleave homolytically and the other heterolytically?

6.22 An organic chemist attempted to prepare methanol labeled with ^{18}O ($CH_3—^{18}OH$) by dissolving 0.1 mole of $Na^{18}OH$ in 500 mL of distilled water and adding 0.1 mole of CH_3Br. The methanol that was produced contained almost no labeled oxygen. Explain this result.

6.23 For the reaction

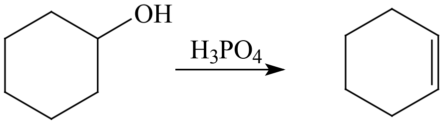
$$CH_3Cl + H_2O \longrightarrow CH_3OH + HCl$$

at 25°C the value of $\Delta H^o = –7.3$ kcal/mole and $\Delta S^o = 0.3$ eu. Calculate ΔG^o and the value of the equilibrium constant. On which side of the reaction does the equilibrium lie?

6.24 Using a rate constant of $6.0 \times 10^{-6}\ M^{-1}\ s^{-1}$, calculate the rate at the beginning of the reaction of 0.01 M CH_3Cl with 0.1 M $^{\ominus}OH$. Then, using this calculated rate and assuming a constant rate, determine the time required for the reaction to go 10% to completion and determine the rate of reaction at this point. Repeat this for 20% completion.

6.25 Unlike the reaction of hydroxide ion with methyl chloride, the reaction of hydroxide ion with *tert*-butyl chloride proceeds in two steps. The first step involves a heterolytic bond cleavage of the C—Cl bond followed by reaction with the hydroxide ion. Using curved arrows, propose a mechanism for this reaction. For each step of the mechanism, specify the type of general operation used.

6.26 When heated in the presence of a catalytic amount of phosphoric acid, cyclohexanol loses water to become cyclohexene. This reaction is a dehydration of an alcohol. The acid acts as a catalyst.



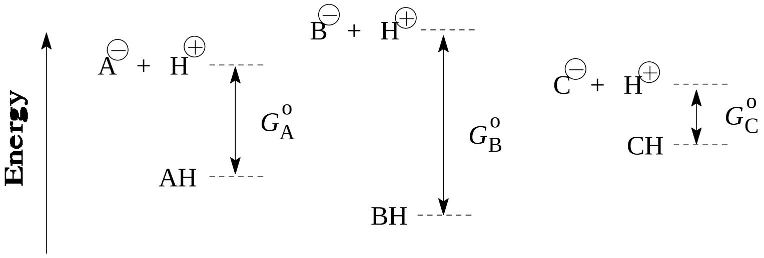
a) What type of reaction is this?

b) ΔS^o for this reaction is 41.1 eu and ΔH^o is 11.3 kcal/mole. Calculate the equilibrium constant for this reaction at 25°C (298 K). What is the position of the equilibrium?

c) Write a mechanism for this reaction. Label each step with the operation used.

d) No products form at room temperature. Cyclohexene forms only after the reaction mixture is heated. Which step of this reaction has the highest energy of activation?

6.27 Consider the energy relationships between these three hypothetical acids:



a) Which acid is the most thermodynamically stable?

b) Which acid is the most acidic?

c) Which has the most stable conjugate base?

6.28 Chloromethane can react with water instead of hydroxide ion to give methanol as the product.

a) Write an equation for the reaction of chloromethane with water.

b) The mechanism is essentially identical to the one for the reaction of chloromethane with hydroxide ion. Write a detailed mechanism. What operations are used in writing this mechanism?

c) What is the rate equation for this reaction?

d) Chloromethane is a gas. When bubbled through water, it forms a solution with a concentration of 3×10^{-3} mol/L. Assuming that the solution density is 1 g/mL, what is the concentration of water in the solution? Can you observe a change in the concentration of the water? Write the rate equation for these conditions.

e) Because there is essentially no change in the concentration of water, chemists call this reaction a pseudo first-order reaction. The rate constant is $k_1 = 3 \times 10^{-10}$ s^{-1}. For a first-order reaction, the time for half of the remaining reactant to react is $t_{1/2} = 0.693/k$. Calculate the half-life, in days, of an aqueous solution of chloromethane.

6.29 Ionic compounds generally have very high boiling points. However, when heated, some ammonium halides vaporize quite readily. Vaporization occurs with $RNH_3^{\oplus}\ Cl^{\ominus}$ but not with $R_4N^{\oplus}\ Cl^{\ominus}$. Explain. (Hint: Alkyl ammonium halides are the products of an acid/base equilibrium and tetraalkyl ammonium halides are the products of a substitution reaction.)

6.30 The symbol ΔG^{o} is used for the Gibbs free energy for the reaction $A \longrightarrow B$, and the symbol $\Delta G^{\ddagger}$ is the Gibbs free energy for the reaction $A \longrightarrow$ transition state. The following table gives the Gibbs free energy values for the steps in the sequence $L \longrightarrow M \longrightarrow N \longrightarrow O$.

Reaction	ΔG^{o} kcal/mole	$\Delta G^{\ddagger}$ kcal/mole
$L \longrightarrow M$	5	15
$M \longrightarrow N$	10	20
$N \longrightarrow O$	–10	5

a) Draw an energy profile for this series of steps using the energy values shown above.

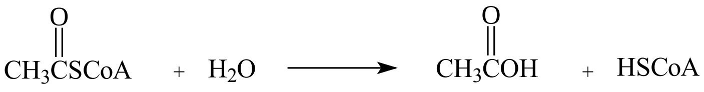
b) Mark the positions of L, M, N, and O on the diagram.

c) Mark the transition state(s) in the diagram with a ‡.

d) Which is the rate-controlling step in the reaction sequence?

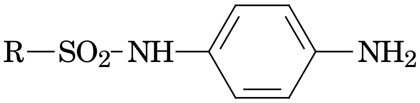
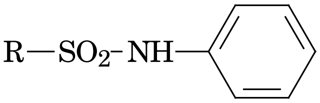
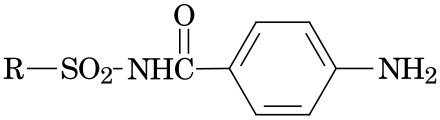
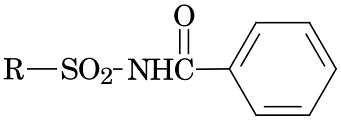
e) Determine the free energy, ΔG^{o} and the free energy of activation, $\Delta G^{\ddagger}$, for the sequence.

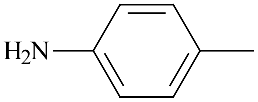
6.31 Acyl group transfer is very important in metabolic processes. Representative of this reaction is the hydrolysis of acetyl coenzyme A, acetyl CoA. The reaction proceeds through an addition followed by an elimination reaction. Write a mechanism for the reaction of acetyl CoA with water. What general operations are used in this mechanism?



$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}SCoA + H_2O \longrightarrow CH_3\overset{\overset{\displaystyle O}{\|}}{C}OH + HSCoA$$

6.32 Sulfonamides are quite acidic (see exercise 5.32). The biological activity of sulfa drugs, an important class of sulfonamides, depends on the pK_a of the compound. In the following table, the term C_r represents the minimum molar concentration needed to cause bacteriostasis of E. *coli* under standard conditions. From the data in the table, would you conclude that the active form of a sulfa drug is anionic, cationic, or nonionic?

Sulfa drug*	pK_a	C_r
$R—SO_2—NH_2$	10.43	20.0
	10.22	5.0
	9.60	3.0
	5.20	0.5
	4.57	0.3

* R represents 

Richard F. Daley and Sally J. Daley
www.ochem4free.com

Organic Chemistry

Chapter 7

Nucleophilic Additions to the Carbonyl Group

Chapter 7

Nucleophilic Additions to the Carbonyl Group

Chapter Outline

Objectives

- ✔ Extend your knowledge of IUPAC rules of nomenclature to the naming of carbonyl compounds
- ✔ Write the general mechanism for nucleophilic addition to a ketone or aldehyde
- ✔ Understand how the structure of the molecule containing a carbonyl group affects the reaction with a nucleophile
- ✔ Be familiar with the reactions of hydrogen cyanide with carbonyl groups
- ✔ Know the reactions of oxygen, nitrogen, hydrogen, and carbon nucleophiles with carbonyl groups
- ✔ Be familiar with the concepts of organic synthesis
- ✔ Understand the Wittig reaction

And it's time to turn out on the old trail, our
own trail, the out trail,
Pull out, pull out, on the Long Trail—the trail
that is always new!
- Rudyard Kipling

Chapter 6 gave you a broad overview of some of the fundamental concepts you need to understand organic chemistry. Some of these concepts were new. Others you covered in your general chemistry course and reviewed from the viewpoint of organic chemistry.

Chapter 7 starts the examination of the major types of reactions in organic chemistry grouped according to their mechanisms. The mechanistic pathway that a reaction follows determines its reaction type. Looking at reactions by their reaction mechanism allows you to relate seemingly different chemical reactions.

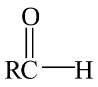
This chapter examines one of the three mechanistic pathways of the carbonyl group—the addition reaction. The carbonyl (C=O) group is possibly the most important functional group in organic chemistry. Seven different functional groups contain the carbonyl structure, and three mechanistic pathways operate on them. Chapters

8, 19, and 20 discuss the other two. Because aldehydes and ketones are the only carbonyl functional groups that commonly undergo addition reactions, this chapter looks at the numerous types of addition reactions that they undergo.

7.1 Naming Carbon—Oxygen Double Bonds

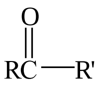
Perhaps the most chemically versatile functional group is the **carbonyl** group. There are three general types of carbonyl groups: aldehydes, ketones, and carboxylic acids and their derivatives. Here are their structural formulas.

A carbonyl group contains a carbon—oxygen double bond (C=O).



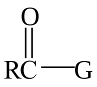
$RC(=O)H$

Aldehyde



$RC(=O)R'$

Ketone



$RC(=O)G$

Carboxylic acids
and
Carboxylic acid derivatives

With an aldehyde, the end carbon of a hydrocarbon chain is double bonded to an oxygen and single bonded to a hydrogen. A frequently used abbreviation for an aldehyde is —CHO in a condensed structure. To name an aldehyde, use the following steps.

When naming a carbonyl group, remember R stands for any alkyl group, and G stands for some group in which the atom bonded to the carbonyl group is a non-carbon atom. The G could represent a carboxylic acid (—OH), an ester (—OR), an anhydride (—OCOR), an amide (—NR_2), or an acid halide (halogen atom).

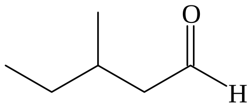
Step 1 Determine the name of the parent compound.

Step 2 For straight chain alkanes, drop the final *–e* of the alkane name and add the suffix *–al*. Call the compound by the name *alkanal*. For example, the following structure is butanal.

$CH_3CH_2CH_2CH(=O)$ is often written as $CH_3CH_2CH_2CHO$

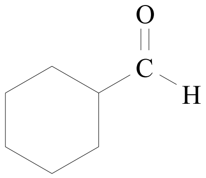
Butanal

Step 3 To number the substituents, assume the carbon of the aldehyde functional group is carbon number 1 because it bonds to the end of the parent chain. Omit the number 1, but number the other substituents. For example, the following structure is 3-methylpentanal.



3-Methylpentanal

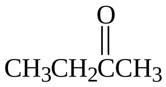
Step 4 For an aldehyde group attached to a ring, or if another functional group has priority, use the suffix *–carbaldehyde* (sometimes the suffix *–carboxaldehyde* is used) to name the compound. For example, the following compound is cyclohexanecarbaldehyde.



Cyclohexanecarbaldehyde

As with all carbonyl groups, ketones have an oxygen double bonded to a carbon, but in this case the carbonyl group is between two alkyl groups. To name a ketone, use the following steps.

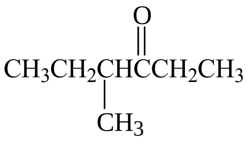
Step 1 Determine the name of the parent compound.
Step 2 Drop the final *–e* of the alkane name and then add the suffix *–one*, giving the name *alkanone*.
Step 3 Because the oxygen bonds to the parent chain somewhere in the middle, indicate its position with a number. Be sure the carbonyl group gets the lowest possible number. For example, the following compound is 2-butanone, not 3-butanone.



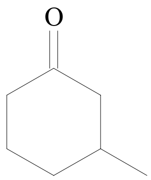
$CH_3CH_2\overset{O}{\overset{\|}{C}}CH_3$

2-Butanone

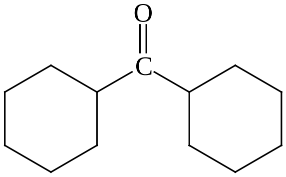
Step 4 You may also name a ketone by naming the two alkyl groups on either side of the carbonyl group as substituents, followed by the word *ketone*, that is, an alkyl alkyl ketone. For example, 2-butanone is often called ethyl methyl ketone. Note that the two alkyl groups are named alphabetically.
Step 5 When another functional group has priority over the ketone name, regard the oxygen as a substituent, designating it as such with the prefix *oxo–*.



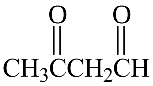
$CH_3CH_2\underset{CH_3}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}CH_2CH_3$



4-Methyl-3-hexanone 3-Methylcyclohexanone



Dicyclohexyl ketone



$\mathrm{CH_3\overset{\overset{O}{\|}}{C}CH_2\overset{\overset{O}{\|}}{C}H}$

3-Oxobutanal

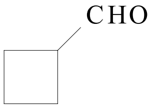
Exercise 7.1

Name each of the following compounds using IUPAC rules.

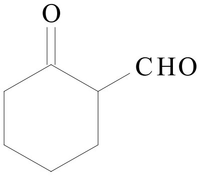
a) $CH_3(CH_2)_{16}CHO$

b) OHCCHO

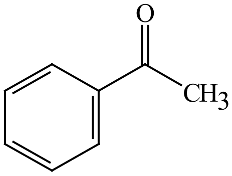
c)



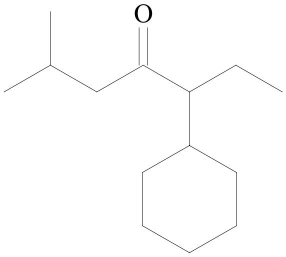
d)



e)



f)



Sample solution

e) 1-Phenylethanone. This compound is commonly called acetophenone.

Carboxylic acids (—COOH) are present in, or are derived from, many natural substances. Thus, they were one of the earliest types of organic compounds experimented with by ancient chemists. Ethanoic acid (common name: acetic acid or vinegar), distilled from sour wine, was one of the earliest organic compounds isolated in pure form. A carboxylic acid is an oxygen double bonded to a carbon that is bonded to a hydrogen or an alkyl group and also to a hydroxy group (—OH). Name carboxylic acids by following these steps. Notice how similar they are to the steps used to name aldehydes.

Step 1 Determine the parent name of the compound.

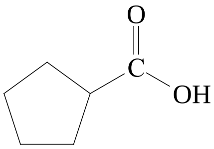
Step 2 For straight chain alkanes, drop the *–e* of the alkane name and add the suffix *–oic acid* to the parent name of the molecule. For example, the following molecule is pentanoic acid.

$$CH_3CH_2CH_2CH_2\overset{\overset{\Large O}{\|}}{C}OH$$

Pentanoic acid

Step 3 To number substituents, assume that the carbon bearing the carboxylic acid functional group is carbon 1 of the parent compound. Omit the number 1, but number the substituents. For example $(CH_3)_2CHCH_2COOH$ is 3-methylbutanoic acid.

Step 4 When the carboxylic acid group bonds to a ring, do not drop the *–e* before adding the suffix *–carboxylic acid* to the ring name.

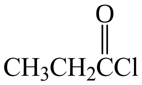


Cyclopentanecarboxylic acid

Some common carboxylic acid names are formic acid for methanoic acid, acetic acid for ethanoic acid, and benzoic acid for benzenecarboxylic acid.

Carboxylic acids form a number of derivatives that are common chemical compounds. These derivatives form by replacing the hydroxy group bonded to the carbonyl group with another heteroatom or group. The replacement groups include halogens (mostly Cl and Br), which form *acyl halides*; carboxylate (RCOO—) groups, which form *carboxylic anhydrides*; alkoxy (RO—) groups, which form *esters*; and amino ($—NR_2$) groups, which form *amides*. Each of these groups has a specific way of naming.

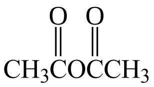
To name acyl halides, add the suffix *–oyl* to the parent name of the compound followed by a separate word for the halogen atom.



$$CH_3CH_2\overset{\overset{\Large O}{\|}}{C}Cl$$

Propanoyl chloride

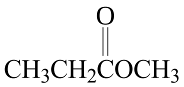
To name a carboxylic anhydride, use the appropriate carboxylic acid name then replace the word *acid* with the word *anhydride*.



$$CH_3\overset{\overset{O}{\parallel}}{C}O\overset{\overset{O}{\parallel}}{C}CH_3$$

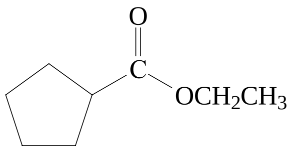
Ethanoic anhydride
(usually acetic anhydride)

To name esters of carboxylic acids, first name the alkyl group bonded to the oxygen followed by the name of the carboxylic acid using the suffix *–oate* to replace the *–oic acid*. Name esters as alkyl alkanoates.



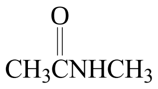
$$CH_3CH_2\overset{\overset{O}{\parallel}}{C}OCH_3$$

Methyl propanoate



Ethyl cyclopentanecarboxylate

To name amides, replace the final *–e* of the parent name with the suffix *–amide*. Name the alkyl groups of secondary and tertiary amides as substituents to the parent compound name by adding the letter *N* to show that the group is bonded to the nitrogen atom. Name the amides of formic, acetic, and benzoic acids in the same way.



$$CH_3\overset{\overset{O}{\parallel}}{C}NHCH_3$$

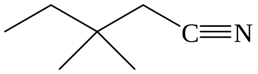
N-Methylethanamide
(usually *N*-methylacetamide)

Chemists often consider *nitriles* ($-C\equiv N$) as derivatives of carboxylic acids because they convert so easily to acids, and they are made from amides. When naming a nitrile, follow these steps.

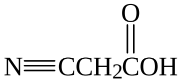
Step 1 Determine the parent name.
Step 2 Add the suffix *–nitrile* to the parent name.
Step 3 To number substituents, include the carbon of the nitrile group when counting carbons for substituent positions.
Step 4 Use the prefix *cyano–* when the nitrile group is a substituent group.

$CH_3CH_2CH_2C\equiv N$

Butanenitrile



3,3-Dimethylpentanenitrile



$N\equiv CCH_2\overset{\overset{\displaystyle O}{||}}{C}OH$

Cyanoethanoic acid

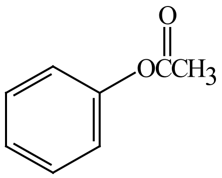
Exercise 7.2

Name each of the following compounds using IUPAC rules.

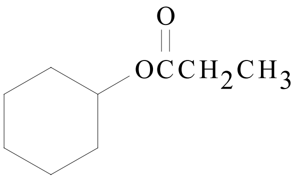
a) $(CH_3)_3CCOOH$

b) $HCON(CH_3)_2$

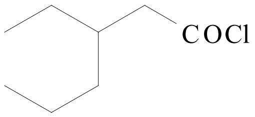
c)



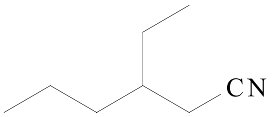
d)



e)



f)

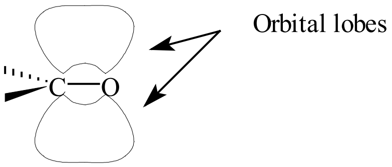


Sample solution

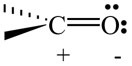
c) The compound is an ester derived from a two carbon carboxylic acid. Thus, the IUPAC name is phenyl ethanoate.

7.2 Reactivity of the Carbonyl Group

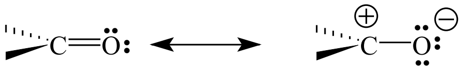
The structure of a carbonyl group is typical for groups involved in *sp*^{2} hybridized bonding. The hybridized carbonyl carbon is at the center of a planar group of atoms. Bonded to the *sp*^{2} hybridized carbon is an oxygen and two other groups—all three are σ bonded to the carbon. Above and below the plane of the three groups are the two orbital lobes of the π bond.



Because the oxygen is more electronegative than the carbon, it possesses the greater share of the electron density of both the σ and π bonds. Thus, the carbon has a partial positive charge, and the oxygen a partial negative charge. The difference in electronegativity between the carbon and oxygen gives the carbonyl group polarity.



The carbonyl group has two resonance structures:



The resonance contributor on the left is the major contributor, because both the carbon and the oxygen have a full octet of electrons and the carbonyl carbon in the resonance contributor on the right is electron-deficient. However, the structure on the right is significant because it emphasizes the polar nature of the carbonyl group.

A nucleophilic addition reaction involves the reaction of a nucleophile (base) with an electron-deficient center.

The polarity of the carbonyl group gives it two possible modes of reaction in a **nucleophilic addition reaction**. In one mode, the electron-deficient carbon reacts first with a nucleophile in a 1,3-electron-pair displacement operation (Figure 7.1) to form an intermediate. This intermediate then reacts with an electrophile in a heterogenic bond forming reaction to form the final product.

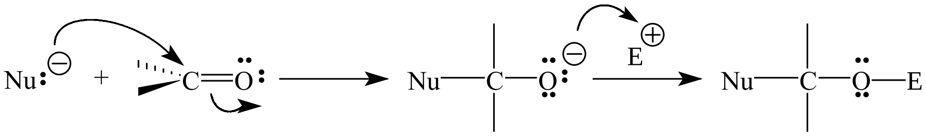


Figure 7.1. The first step is a nucleophilic addition to a carbonyl group followed by a reaction with the electrophile. The first mechanism step is a 1,3-electron pair displacement operation followed by a heterogenic bond forming operation.

In the second mode, the electron-rich oxygen reacts first with an electrophile in a heterogenic bond forming operation (Figure 7.2), then with the nucleophile in a 1,3-electron pair displacement operation to form the final product.

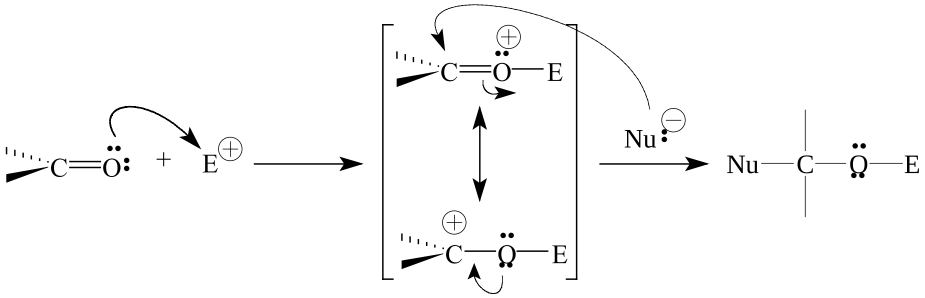


Figure 7.2. The first step is the reaction of an electrophile with the carbonyl oxygen followed by addition of the nucleophile. The square brackets indicate a reaction intermediate with two resonance structures. The first mechanism step is a heterogenic bond forming operation step followed by a 1,3-electron pair displacement operation.

Which pathway that the addition takes depends on the nature of the reagent and the reaction conditions. When the reaction conditions are basic, the nucleophile first adds to the carbonyl carbon (Figure 7.1). Then an electrophile, often a proton from the solvent, transfers to the oxygen (Figure 7.2). When the reaction conditions are acidic, the sequence reverses. First, the proton transfers to the oxygen (Figure 7.2), and then the nucleophile adds to the carbonyl carbon (Figure 7.1). The conjugate acid of the carbonyl group (Figure 7.2) is more likely to undergo a nucleophilic addition than is the carbonyl group itself. Thus, even a nucleophile that is not very reactive with a carbonyl reacts readily with the conjugate acid. Of the seven functional groups containing a carbonyl group, only aldehydes and ketones commonly undergo nucleophilic addition. The remaining five carbonyl functional groups undergo nucleophilic substitution, which is the topic of Chapter 8.

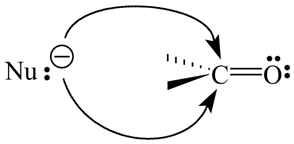
With a nucleophilic addition, aldehydes react more readily than ketones. Aldehydes are more reactive due to both electronic and structural effects. Electronically, the carbonyl group of the aldehyde bears only one electron-donating alkyl group, whereas the ketone bears two. An alkyl group is a weak electron donor, but it is a stronger electron donor than a hydrogen. Thus, the carbonyl carbon of an aldehyde has a lower electron density and is more electrophilic than the carbonyl carbon of a ketone.

Steric effects are the factors that measure the structural accessibility of a particular reaction site.

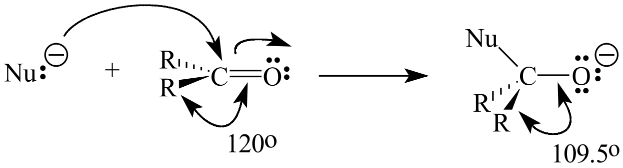
A sterically crowded, blocked, or hindered molecule has large groups adjacent to the reactive site blocking access of the reactant. A sterically open or unhindered molecule does not have large groups near the reactive site.

Structurally, the important considerations are the **steric effects.** If the reaction site is less accessible due to the large size of adjacent groups, then it is **sterically blocked**, or **sterically crowded**. If the reaction site is accessible to the reagent, then it is **sterically open**. When determining the steric effects of a molecule, examine it relative to another molecule. For example, pentanal is more sterically open than 3-pentanone. Use the terms **hindered** and **unhindered** synonymously with sterically blocked and sterically open.

Here is how the steric effects of a carbonyl group affect the reactivity of aldehydes versus ketones. Because the carbonyl group is planar, incoming nucleophile groups can approach the carbonyl from either side of the plane with equal probability.



With the formation of a fourth bond to the carbonyl carbon, the hybridization changes from sp^2 to sp^3. Consequently, the bond angles change from 120° to 109.5°, and the carbon atom becomes more crowded. Because the aldehyde has one alkyl group, and one hydrogen atom, it is more open sterically than the ketone with its two alkyl groups.



Also, the bulkier the R group, the slower is the rate of reaction. For example, the rate of reaction when R is a *tert*-butyl is much slower than when R is a methyl group.

7.3 Guide For Learning Organic Reactions

With Chapter 7, you begin adding reactions to the framework of mechanism types that Chapter 6 introduces. This section describes how this and future chapters are set up. It also gives you some guidelines for studying. Early in each chapter, the fundamental mechanism discussed in that chapter is presented. Nucleophilic addition reactions take two mechanism modes. Figures 7.1, and 7.2 on page 000 show both mechanistic modes. Study both modes. Try to find the underlying principles of acid-base chemistry that make the mechanism work.

Succeeding sections then present one or more specific reactions that follow the fundamental mechanism. Each section includes the generalized reaction and mechanism for that reaction type followed by one or more specific chemical examples. To study this material, strive to understand the generalized reaction and its mechanism. Consider how it relates to the fundamental mechanism given at the beginning of the chapter. Look at the examples and determine how they relate to the mechanism. Write a mechanism for one or more of the specific examples and compare it to the mechanism contained in the chapter. Then work the exercises using that particular reaction type.

As you study each of the reaction types, learn the answers to all of the following four questions:

1. What mechanistic operations describe the electron flow from the substrate and reagents through any intermediates to form the product?

2. Given the substrate, reagent(s), and a set of reaction conditions, what is the expected product?

$$\text{Substrate} \xrightarrow[\text{Conditions}]{\text{Reagents}} ?$$

3. Given both a substrate and a product, what reagents and reaction conditions favor the transformation?

$$\text{Substrate} \xrightarrow{?} \text{Product}$$

4. Given a product, reagent(s), and a set of reaction conditions, what is a probable substrate?

$$? \xrightarrow[\text{Conditions}]{\text{Reagents}} \text{Product}$$

The last three questions require that you *thoroughly* understand how a particular reaction type occurs. The fourth question focuses on the electron flow, or mechanism, of a substrate as it converts into a product. Reaction mechanisms are the key to your understanding of organic chemistry. Knowing the mechanism of a reaction allows you to generalize your knowledge about organic chemistry and to predict the outcome of a new reaction with confidence.

Retrosynthetic analysis literally means backward synthetic analysis. As chemists propose a synthesis, they usually work backwards from the target to the substrate molecules.

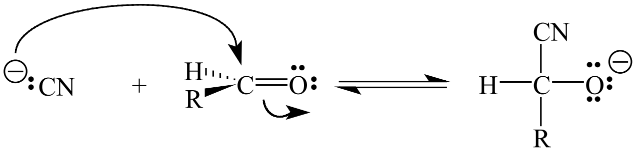
Being able to answer these four questions allows you to use the **retrosynthetic analysis** technique. This chapter and Chapter 15 discuss retrosynthetic analysis. To use retrosynthetic analysis, take the target molecule and search through the reactions you know to choose a reasonable precursor, which then becomes the new target molecule. Then search again through the reactions you know until you find a precursor for this new target molecule. Repeat this analysis until you find a readily available substrate. This approach allows you to logically plan the construction of a new molecule or to propose a new synthesis for existing molecules.

7.4 The Cyanohydrin Reaction

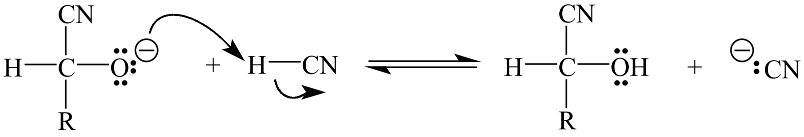
In the cyanohydrin reaction, HCN reacts with a carbonyl group to form an α hydroxy nitrile.

One of the simplest nucleophilic additions to the carbonyl group is the **cyanohydrin reaction**. In this reaction hydrogen cyanide, HCN, adds to a carbonyl group to produce a 2-hydroxy nitrile. Below is the generalized cyanohydrin reaction.

The mechanism for a cyanohydrin reaction shows that a cyanide ion, which is the nucleophile, reacts with the carbonyl carbon in a 1,3-electron pair displacement operation to produce an unstable intermediate anion.



Because the intermediate is a stronger base than the $^{\ominus}$CN ion, it abstracts a proton from the HCN molecule to form the cyanohydrin and another $^{\ominus}$CN ion. This step is a 1,3-electron pair displacement operation.



Exercise 7.3

The addition of HCN to a carbonyl group is a second order reversible reaction. The rate of a second order reaction depends on the concentrations of two reagents. The following equation expresses the rate for this reaction:

$$\text{rate} = k[\text{RHC=O}][^{\ominus}\text{CN}]$$

a) What is the rate-limiting step for the reaction?

b) What does this tell you about the role of the proton in the reaction?

c) The equilibrium constant for the addition of HCN to 2-propanone is 32 at 27°C. At equilibrium, are the products or the reactants found in higher quantity?

d) What is the ΔG^{o} of this reaction (see Section 6.2)?

HCN is a very weak acid (pK_a=9.1), so it ionizes only slightly. That is, at equilibrium only a few hydrogen and cyanide ions are present. Because of this low ionization, the reaction of the cyanide ion with the carbonyl group is relatively slow, but the reaction with the proton is relatively rapid. The rate law (see Exercise 7.3) for this reaction shows the concentrations of both the carbonyl group and the cyanide ion. Because the rate depends on the concentration of two reactants, the addition of HCN to an aldehyde or ketone is a second order reaction.

Exercise 7.4

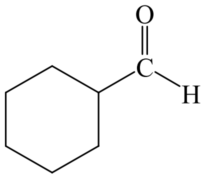
Using the data, and your answers from Exercise 7.3, sketch a reaction profile for this reaction. Propose structures for all intermediates.

Because HCN is such a weak acid, it is a very poor source of cyanide ion nucleophiles. The rate of reaction with pure HCN is very low. However, the addition of a source of cyanide ions to the reaction flask causes a dramatic increase in the rate of reaction. Arthur Lapworth discovered this effect in 1903. Lapworth assumed that the reaction was ionic in nature and proposed a reaction mechanism remarkably similar to the above mechanism. His proposal was an extraordinary accomplishment considering that Lewis' theory of bonding was more than ten years in the future. Lapworth was one of the originators of the mechanistic view of organic chemistry.

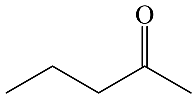
Exercise 7.5

Write a transformation for the conversion of each of the following compounds with HCN.

a)



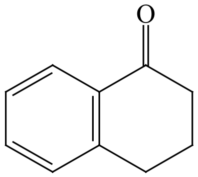
b)



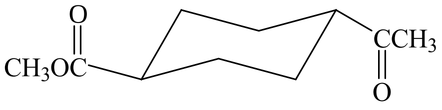
c) 2-Butenal

d) $CH_3CH_2OCH_2CH_2CH_2CHO$

e)

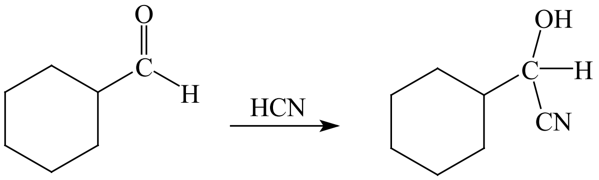


f)



Sample solution

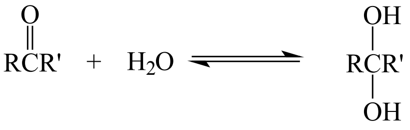
a)



7.5 Addition of Water and Alcohols

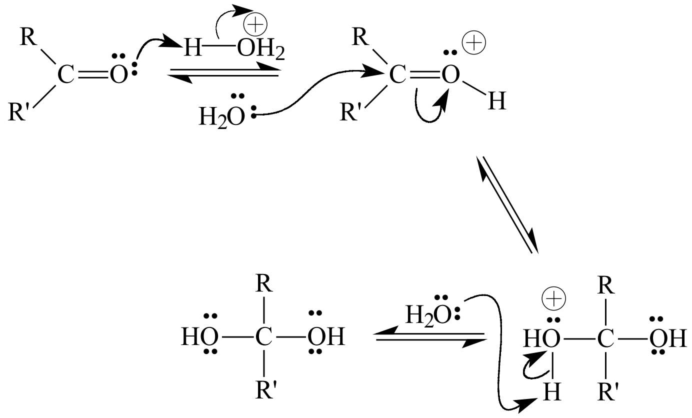
A hydrate is a compound that contains two —OH groups bonded to the same carbon.

The nucleophilic addition reaction of the carbonyl group in aldehydes and ketones with water is a rapidly reversible equilibrium reaction that produces a class of compounds known as **hydrates**.



$$R\overset{\overset{\displaystyle O}{\|}}{C}R' + H_2O \rightleftharpoons R\overset{\overset{\displaystyle OH}{|}}{\underset{\underset{\displaystyle OH}{|}}{C}}R'$$

The acid-catalyzed reaction mechanism has three steps. The first step involves the protonation of the carbonyl oxygen in a 1,3-electron pair displacement operation. The next step is a nucleophilic attack by the water on the carbonyl carbon, and the last step is the loss of a proton to form the hydrate. The last two steps are also 1,3-electron pair displacement operations.



The position of equilibrium for the nucleophilic addition of water to aldehydes and ketones depends on the size and the number of groups attached to the carbonyl carbon. As the carbonyl group becomes increasingly hindered, the position of equilibrium favors the substrate. Generally, an aldehyde is more hydrated at equilibrium than a ketone. Table 7.1 lists the equilibrium constants for the hydration of some common aldehydes and ketones.

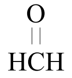
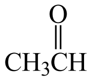
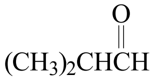
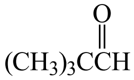
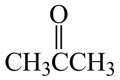
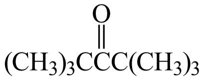
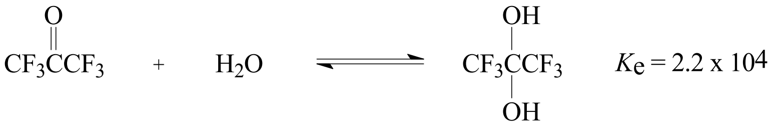
Carbonyl Compound	K_e (at 25°C)	% Reaction (at equilibrium)
 $\mathrm{H}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{H}$	41	99.95
 $\mathrm{CH_3}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{H}$	1.8×10^{-2}	50
 $\mathrm{(CH_3)_2CH}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{H}$	1.2×10^{-3}	32
 $\mathrm{(CH_3)_3C}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{H}$	4.0×10^{-3}	20
 $\mathrm{CH_3}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_3}$	2.5×10^{-5}	0.14
 $\mathrm{(CH_3)_3C}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{C(CH_3)_3}$	3.1×10^{-8}	1.7×10^{-4}

Table 7.1. Effect of group size on the equilibrium constant for the hydration of various carbonyl compounds.

The data in Table 7.1 show that K_e and the percentage of reaction to form the hydrate decreases as the size of the groups attached to the carbonyl carbon increases. This result is due mainly to steric hindrance. However, a second factor is the electronic effect of the alkyl groups attached to the carbonyl carbon. Because an alkyl group is weakly electron-donating, it tends to reduce the partial positive charge on the carbonyl carbon, thereby lowering its reactivity.

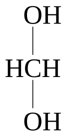
Acetone is the common name for 2-propanone.

A strong electron-withdrawing substituent attached to the carbonyl group shifts the position of equilibrium to the product. For example, consider $-CF_3$, a strong electron-withdrawing group. The negative end of the dipole moment for each of the three C—F bonds is the fluorine atom. Three such bonds create a large partial positive charge on the carbon atom, which, in turn, attempts to withdraw more electron density from the carbonyl group. **Acetone** has only a minute amount of hydration in contrast to hexafluoroacetone, which is almost completely hydrated.



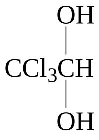
$$CF_3\overset{\overset{O}{\|}}{C}CF_3 + H_2O \rightleftharpoons CF_3\underset{OH}{\overset{OH}{C}}CF_3 \qquad K_e = 2.2 \times 10^4$$

Most hydrates are so unstable that they cannot be isolated. Two that are stable enough to isolate are the hydrate of methanal (formaldehyde) and the hydrate of trichloroethanal (chloral). Formaldehyde is a gas at room temperature (b.p. –21°C), but chemists use it as a 37% aqueous solution of the hydrate. In aqueous solution they call it formalin. Formalin is often used to preserve biological specimens. The reaction of chloral with water has a large equilibrium constant of 3×10^4. When isolated as a stable solid, its melting point is 57°C. Chloral is a hypnotic or sedative—the "knockout drops" or "Mickey Finn" of film and literature.



$$H\underset{OH}{\overset{OH}{C}}H$$

Formalin

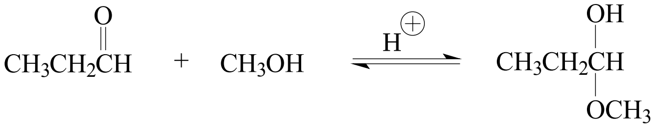


$$CCl_3\underset{OH}{\overset{OH}{C}}H$$

Chloral hydrate

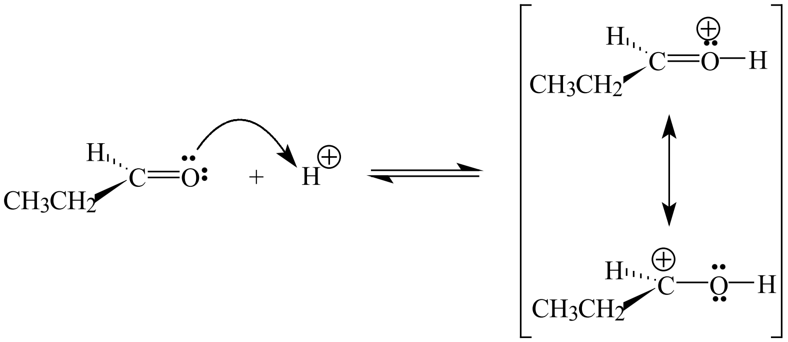
Hemiacetals are compounds containing one —OH group and one —OR group bonded to the same carbon.

A reaction equivalent to a hydration takes place between an aldehyde or ketone and an alcohol. This reaction involves one mole each of an alcohol and an aldehyde or ketone. The product is one of a class of compounds known as **hemiacetals**.

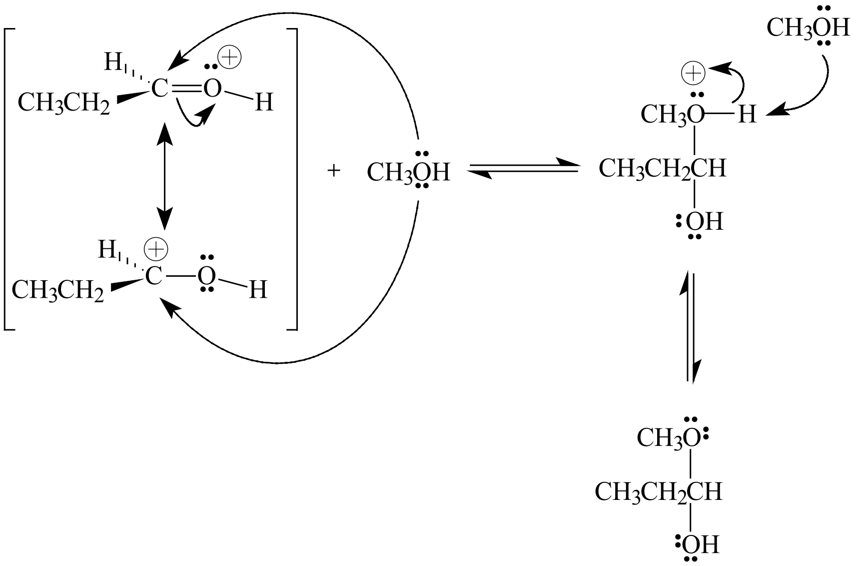


1-Hydroxypropyl methyl ether
A Hemiacetal
(64%)

As with hydrate formation, hemiacetal formation is a reversible process. Hemiacetal formation follows a similar three-step reaction mechanism to a hydrate formation. The first step in an acid-catalyzed reaction is the protonation of the carbonyl oxygen in a heterogenic bond forming operation. The protonation of the carbonyl oxygen enhances the electrophilicity of the carbonyl carbon.



Next, the nucleophilic oxygen of the alcohol adds to the carbonyl carbon of the resonance hybrid in a 1,3-electron pair displacement operation. The reaction consumes a proton to initiate the reaction, then releases a proton at the end of the sequence.

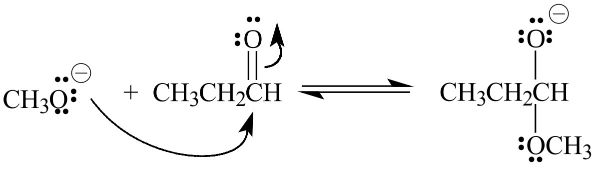


Resonance in the Protonated Aldehyde

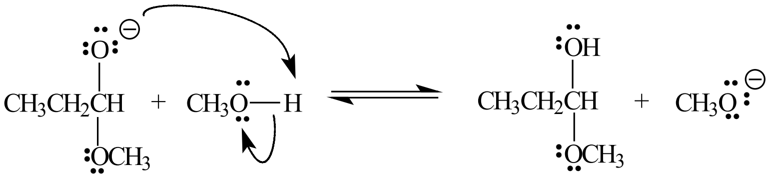
Remember that the protonated aldehyde is a resonance hybrid. The actual structure is neither of the structures shown in the brackets but a hybrid of both. However, the top structure more closely represents the structure of the hybrid. In that structure each atom has an octet of electrons. In the lower structure the carbonyl carbon has only six electrons.

Hemiacetal formation is also base-catalyzed. Many different bases are effective, but the one most commonly used is the hydroxide ion. The first step in the mechanism forming the methyl hemiacetal of propanal with a base catalyst is the reaction of hydroxide ion with methanol forming the methoxide ion.

The methoxide ion adds to the carbonyl group of propanal forming the anion of the hemiacetal.



Finally, the hemiacetal anion reacts with a molecule of methanol generating another methoxide ion and the product hemiacetal.

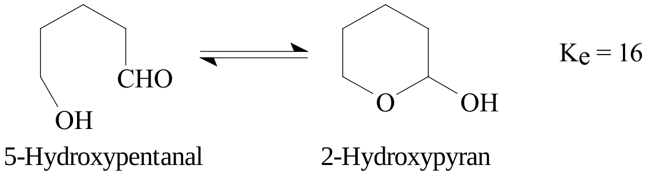


Exercise 7.6

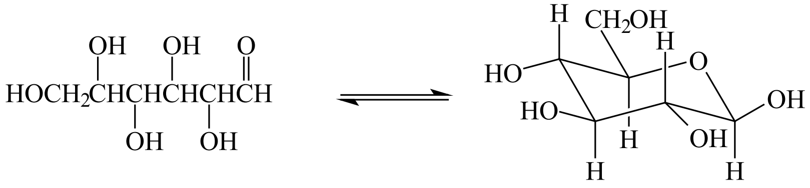
Propose a mechanism for the base-catalyzed formation of the hydrate of propanal with water.

For more on ring size stability, see Section 3.5, page 000.

Most hemiacetal formation reactions are not energetically favorable, so you must add energy (heat) for the reaction to occur. The equilibrium constant for most hemiacetal reactions is less than one, with the exception of reactions that form five- or six-membered cyclic hemiacetals. These reactions proceed without added energy because of the stability of five- and six-membered rings. For example, the equilibrium constant for the formation of 2-hydroxypyran from 5-hydroxypentanal is approximately 16.



Cyclic hemiacetals occur in natural compounds. For example, glucose contains a six-membered cyclic hemiacetal. Glucose makes this ring by forming the hemiacetal with the —OH group on carbon 5 of a straight chain form of glucose. Because of the stability of six-membered rings, the reaction always takes place on carbon 5 of glucose to allow the ring formation even though the molecule has an —OH group on every carbon from C2 to C6 in glucose.



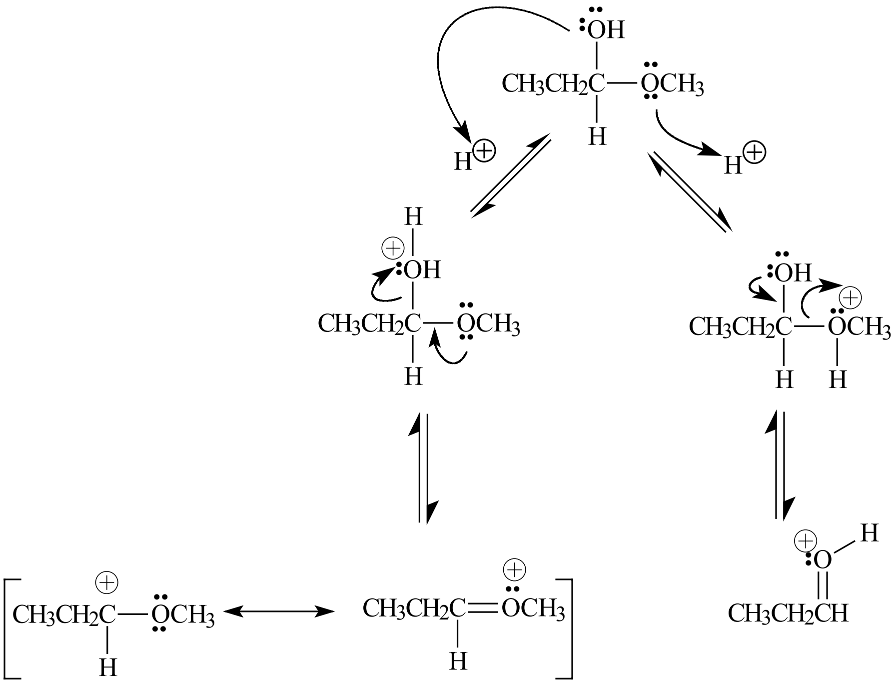
Open chain form

Cyclic form

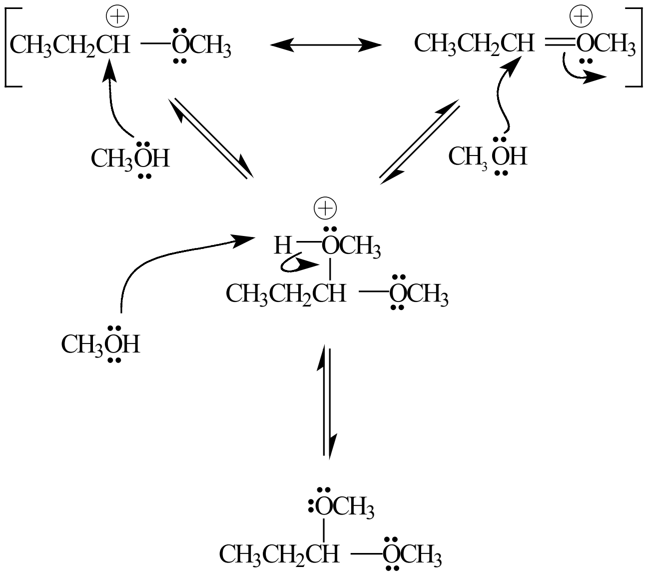
Glucose

When you add two moles of alcohol plus a catalytic quantity of acid to the carbonyl group of an aldehyde or ketone, a compound called an **acetal** forms. The reaction sequence for acetals involves two steps. In the first step, the reaction forms a hemiacetal. In the second step, the hemiacetal reacts with the second alcohol molecule. To react with the second alcohol molecule, the catalytic hydrogen ion first adds to one of the oxygens of the hemiacetal in a heterogenic bond forming operation. It can add to either oxygen. If it adds to the oxygen bonded to the hydrogen, as illustrated by the path on the left, the reaction leads to loss of water and a carbocation. If it adds to the oxygen bonded between the two carbons, as illustrated by the path on the right, the reaction leads to a loss of the alcohol and the regeneration of the original carbonyl compound.

Acetals are compounds containing two —OR groups bonded to the same carbon.



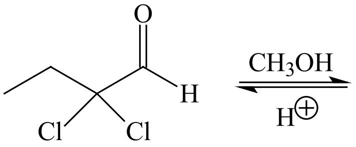
After the resonance-stabilized cation forms, it reacts with a molecule of alcohol to produce the acetal. The operation on the left in the following mechanism is a heterogenic bond forming operation. The operation on the right is a 1,3-electron pair displacement operation. Removal of the proton is a 1,3-electron pair displacement operation.



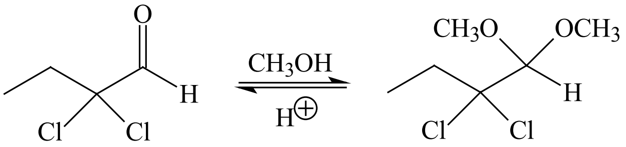
Solved Exercise 7.1

Predict the major product of each of the following reactions. Does the equilibrium favor the products or substrates?

a)

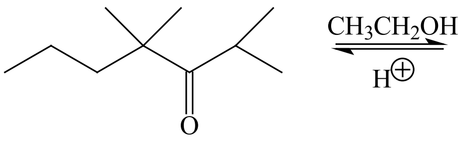


Solution
The product of this equilibrium is the dimethyl acetal.



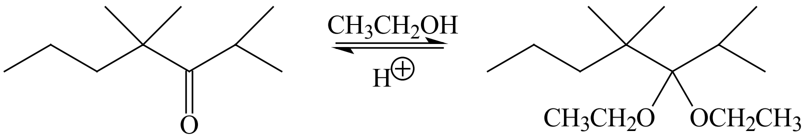
The product is favored by two considerations: 1) the substrate is an aldehyde that favors the formation of acetal, and 2) the aldehyde has electron-withdrawing chlorine atoms bonded to the carbon adjacent to the carbonyl group. These chlorine atoms withdraw electron density from the already partially positive carbonyl carbon making it even more reactive with a nucleophile.

b)



Solution

The product of this equilibrium is the diethyl acetal.

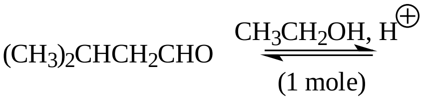


The starting material is favored because of two considerations: 1) the substrate is a ketone that does not form an acetal as readily as an aldehyde, and 2) the methyl groups on carbons 2 and 4 increase the crowding around the carbonyl group making the acetal formation unfavorable.

Exercise 7.7

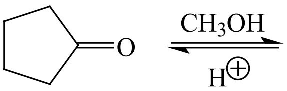
Predict the major products for each of the following reactions and whether the equilibrium favors the products or the substrates.

a)

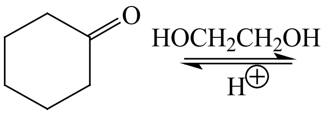


$$(CH_3)_2CHCH_2CHO \xrightleftharpoons[\text{(1 mole)}]{CH_3CH_2OH,\ H^{\oplus}}$$

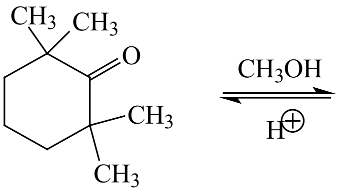
b)



c)



d)



e)

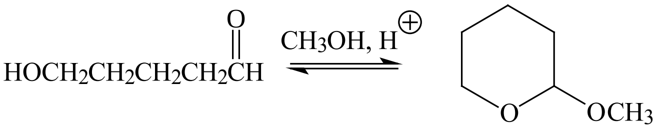
$$HOCH_2CH_2CH_2CH_2CHO \xrightleftharpoons[\text{(excess)}]{CH_3OH,\ H^{\oplus}}$$

f)

$$(CH_3)_3CCH_2CH_2CH_2CH(OCH_2CH_3)_2 \xrightleftharpoons{H_3O^{\oplus}}$$

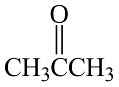
Sample solution

e) This reaction forms a cyclic acetal so the equilibrium position favors the product.



Exercise 7.8

Explain the observation that ethyl pyruvate forms an acetal faster than does acetone.



$CH_3\overset{O}{\overset{\|}{C}}CH_3$

Acetone

$CH_3\overset{O}{\overset{\|}{C}}\text{-}\overset{O}{\overset{\|}{C}}OCH_2CH_3$

Ethyl pyruvate

7.6 Reaction with Nitrogen Nucleophiles

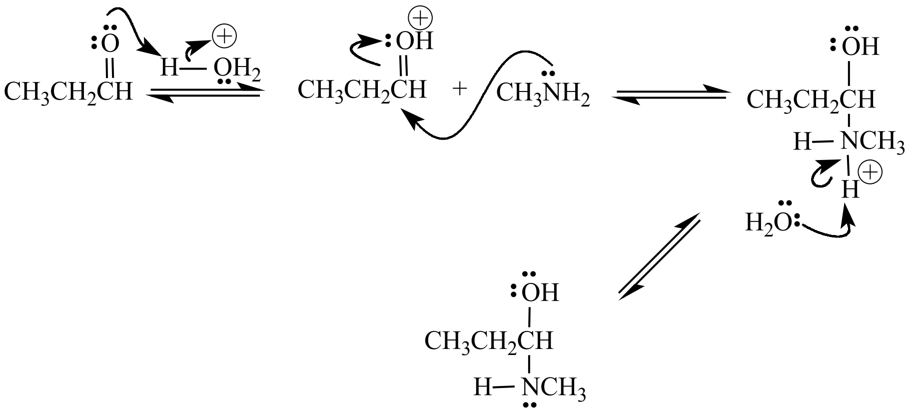
When aldehydes and ketones react with primary amines, they produce a class of compounds that contain a carbon—nitrogen double bond called **imines,** or sometimes **Schiff bases**.

An imine or Schiff base contains a carbon—nitrogen analog of a carbonyl group.

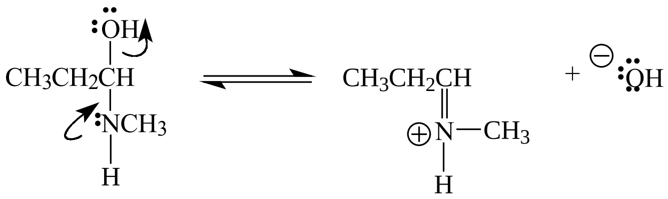
$$CH_3CH_2\overset{\overset{O}{\|}}{C}H + CH_3NH_2 \longrightarrow CH_3CH_2\overset{\overset{NCH_3}{\|}}{C}H + H_2O$$

N-Methyl-1-propanimine
(63%)

Although many imines lack stability, they are important intermediates in many reactions. The first step in the formation of an imine is a nucleophilic addition to the carbonyl carbon. In the next step, a proton transfers to the oxygen.

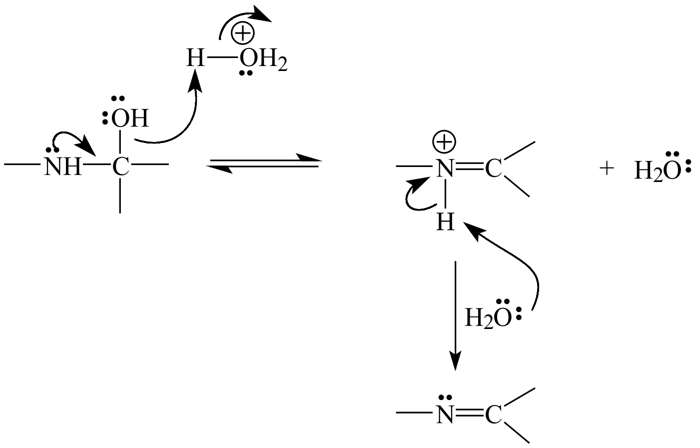


The reaction requires acid catalysis in a solution with a pH between 3 and 5. Outside this range, the rate of the reaction slows down markedly. At a high pH, the third step is the rate-limiting step in the reaction sequence.

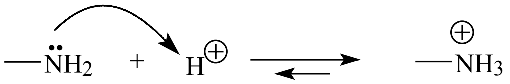


This elimination step proceeds slowly because of the charge separation in the products and because the number of charged species changes from substrate to product. The substrate is uncharged and the products both bear a charge. When the number of charged species increases from reactants to products, the reaction requires more energy than if there is no change in the number of charged species.

When the pH of a reaction is in the range of 3 to 5, the solution contains sufficient protons to protonate the —OH group. The —OH group then leaves as water. Within this pH range, this step requires much less energy than it does outside this pH range. Also, the reaction takes less energy because there is no change in the number of charged species.

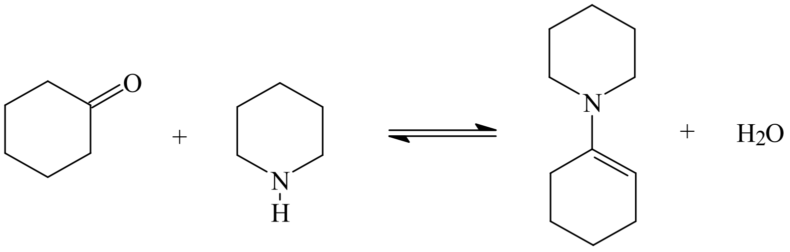


When the solution has a low pH, protonation occurs at the amine itself. In this case, the amine is not a nucleophile because the nitrogen no longer has a nonbonding pair of electrons. Without that pair of electrons, addition to the carbonyl group can not take place.



An enamine contains an amine nitrogen bonded to a carbon—carbon double bond.

Secondary amines (R_2NH) react as nucleophiles with ketones and aldehydes to form a group of compounds called **enamines.** The structure of enamines differs from imines in that when they dehydrate (eliminate water), they produce a stable compound containing a carbon—carbon double bond.

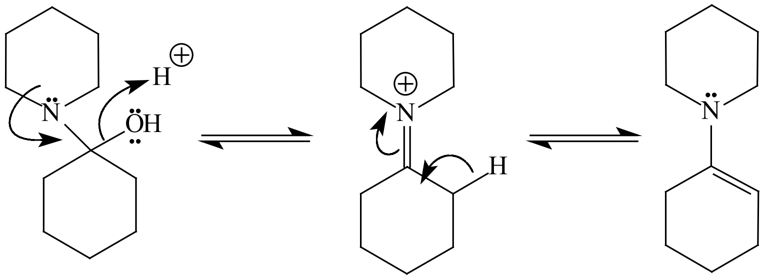


Cyclohexanone

Piperidine
(Secondary amine)

N-(1-Cyclohexenyl)piperidine
(Enamine)
(79%)

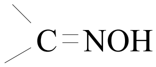
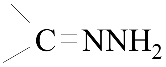
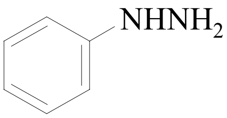
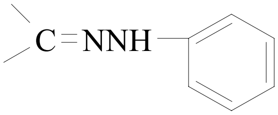
The reaction starts as the nucleophile reacts with the carbonyl group to form the intermediate carbinolamine. Next, the carbinolamine dehydrates (loses water). Because the nitrogen has no hydrogens, an adjacent carbon atom loses a hydrogen. The loss of this hydrogen results in the formation of a double bond.



Carbinolamine 1-Piperidinocyclohexene

Enamines are very useful reaction intermediates. Chapter 19 covers them in more detail. In addition to the reactions that form enamines and imines, several other reagents containing nucleophilic nitrogen react with aldehyde and ketone substrates. Table 7.2 lists several examples. For a long time, chemists have used these reactions to identify unknown aldehydes or ketones because the products are usually relatively insoluble solids and have sharp melting points. Extensive tables of these melting points have been compiled to aid chemists in the identification of unknown aldehydes and ketones. Although many students are still expected to use melting points to identify unknown compounds, modern research chemists typically rely on **spectroscopic** means of identification. Spectroscopy is covered in detail in Chapters 9 and 10.

Spectroscopic means of identification includes probing a molecule using infrared radiation, radio waves, magnetic fields, and electron beams.

Nucleophile	Product
NH_2OH (Hydroxylamine)	 (An oxime)
NH_2NH_2 (Hydrazine)	 (A hydrazone)
 (Phenylhydrazine)	 (A phenylhydrazone)

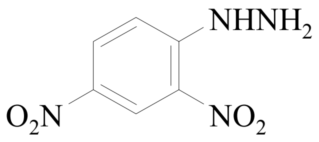
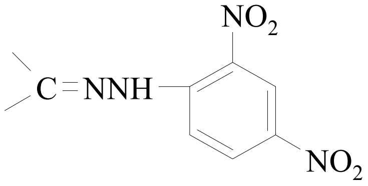
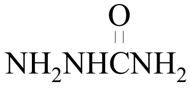
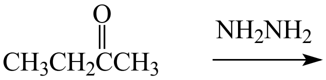
Nucleophile	Product
 (2,4-Dinitrophenylhydrazine)	 (A 2,4-Dinitrophenylhydrazone)
 $NH_2NH\overset{O}{\overset{\parallel}{C}}NH_2$ (Semicarbazide)	 $>C{=}NNH\overset{O}{\overset{\parallel}{C}}NH_2$ (A semicarbazone)

Table 7.2. Reactions of aldehydes and ketones with some derivatives of ammonia.

Exercise 7.9

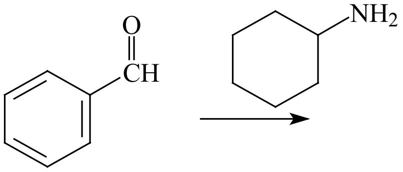
Predict the major products for each of the following reactions.

a)

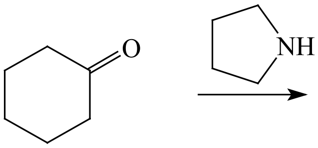


$$CH_3CH_2\overset{O}{\overset{\parallel}{C}}CH_3 \xrightarrow{NH_2NH_2}$$

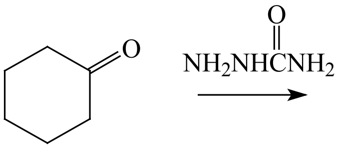
b)



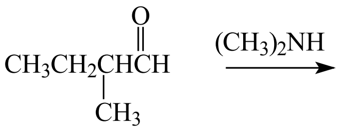
c)



d)



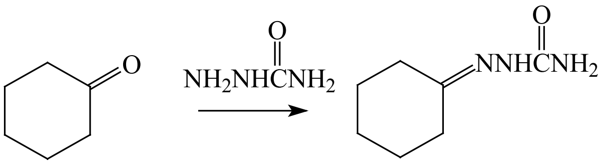
e)



$$\mathrm{CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}H\overset{\displaystyle O}{\overset{\|}{C}}H \xrightarrow{(CH_3)_2NH}}$$

Sample solution

d)



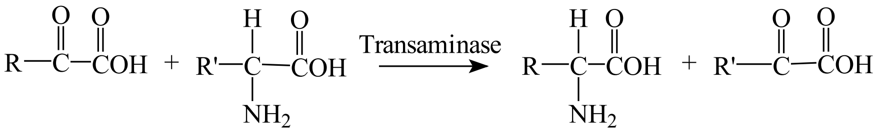
[Sidebar]

Biochemical Transamination

Many naturally occurring biochemical reactions resemble reactions done by organic chemists with two notable differences. 1) Naturally occurring biochemical reactions consistently progress at reasonable rates and have good yields at the temperature of the organism. 2) Most naturally occurring biochemical reactions are stereospecific. That is, they produce only one stereochemical isomer.

A very important reaction that occurs in many biochemical systems is the synthesis of amino acids. As the biochemical system synthesizes amino acids, the process follows the pathway of **transamination.** Along the transamination pathway the amine group transfers from the starting amino acid to a ketoacid, thus forming another amino acid. It makes this transfer via an imine intermediate. The transformation requires a catalyst, and the catalyst used comes from a class of enzymes called transaminases. An enzyme is a type of protein molecule that catalyzes specific chemical transformations. There are more than 50 different transaminases known—each catalyzing the reaction of one amino acid to another. The fundamental reaction for the formation of amino acids is the following reaction:

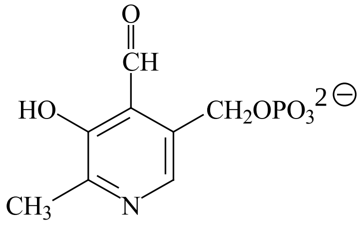
A transamination reaction transfers an amine group from one molecule to another.



$$\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}\overset{O}{\overset{\|}{C}}OH + R'{-}\underset{NH_2}{\underset{|}{\overset{H}{\overset{|}{C}}}}{-}\overset{O}{\overset{\|}{C}}OH \xrightarrow{Transaminase} R{-}\underset{NH_2}{\underset{|}{\overset{H}{\overset{|}{C}}}}{-}\overset{O}{\overset{\|}{C}}OH + R'{-}\overset{O}{\overset{\|}{C}}{-}\overset{O}{\overset{\|}{C}}OH}$$

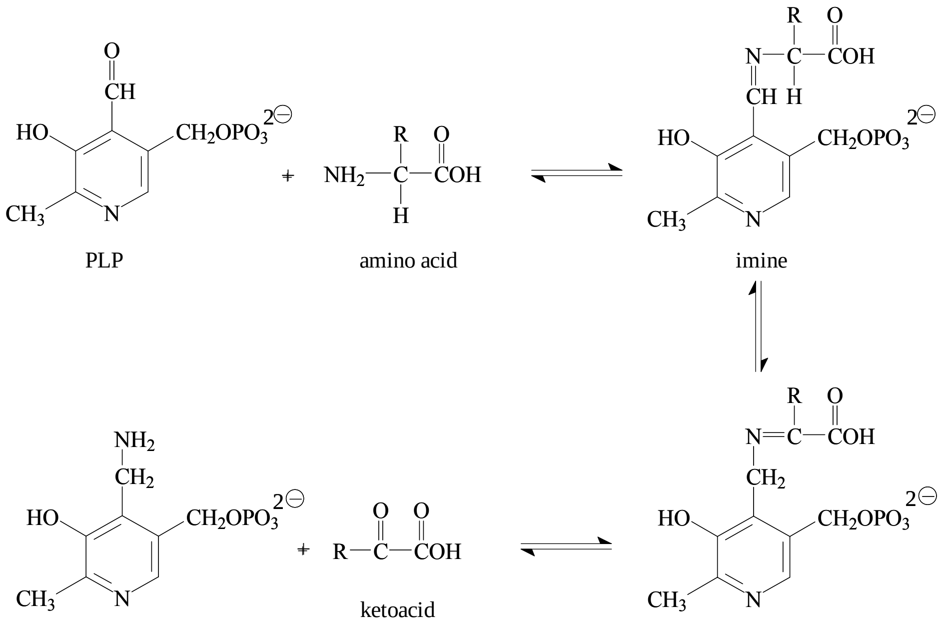
A coenzyme is a small non-protein organic molecule that enzymes often require for activity.

All transaminase enzymes have the same **coenzyme**, pyridoxal phosphate (PLP). The organism derives PLP from vitamin B_6.



Pyridoxal phosphate (PLP)

Although the fundamental reaction shows a simple transfer of an amino acid group from one molecule to another, the process itself is not so simple. It first goes through an imine isomer to form the new amine. Then in a subsequent reaction with a different ketoacid, it goes back though the same route, in reverse order, forming another imine isomer. Finally, it forms the new amino acid.

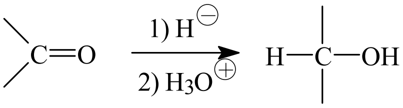


The carbonyl group of PLP forms the imine with the nitrogen of the amino acid. This imine then hydrolyzes to form the ketoacid. The transaminase enzyme is the proton source that catalyzes the reaction. Pyridoxal phosphate is the carrier for the amino group from one reactant to another.

7.7 Reaction with Hydride Nucleophile

In a typical organic reduction reaction, two hydrogen atoms add to the π bond of a multiple bond.

Reduction reactions are another term that chemists use when talking of addition reactions. In reduction reactions two hydrogens bond directly to the carbon and oxygen of the carbonyl group forming an alcohol. Chemists often reduce carbonyl groups via the nucleophilic addition of the hydride ion ($H^{\ominus}$). The following transformation shows the general pattern for a reduction reaction with a hydride ion:



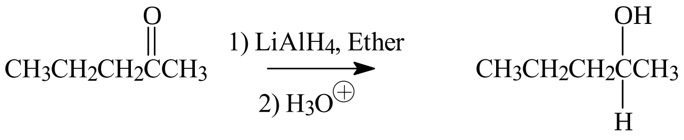
Aldehyde or ketone

Alcohol

A complex metal hydride contains two metallic atoms per molecule and is a source of hydride ($H^{\ominus}$) ions.

A **complex metal hydride** usually delivers the hydride ion to the carbonyl carbon in a reduction reaction. Two examples of complex metal hydrides are lithium aluminum hydride ($LiAlH_4$) and sodium borohydride ($NaBH_4$). Chemists commonly use both of these compounds to reduce carbonyl groups to alcohols.

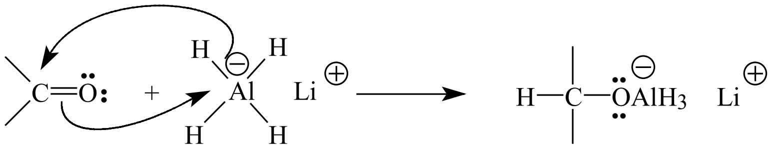
Lithium aluminum hydride is a very reactive and very powerful reagent capable of reducing many organic functional groups. When using lithium aluminum hydride as the reducing agent, chemists carry out the reaction in a solution of anhydrous tetrahydrofuran or diethyl ether. They can not use a water solution because the lithium aluminum hydride reacts violently with the water liberating hydrogen gas. The hydrogen then ignites due to the high heat of reaction. The following is an example of the desired reaction:



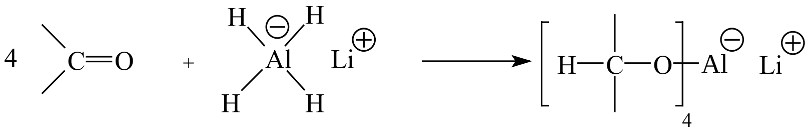
$$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[2)\ H_3O^{\oplus}]{1)\ LiAlH_4,\ Ether} CH_3CH_2CH_2\overset{OH}{\underset{H}{C}}CH_3$$

2-Pentanol
(91%)

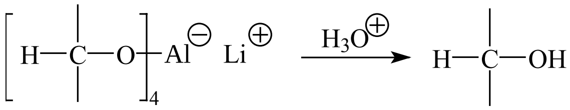
The key step in this reaction is the transfer of the hydride ion from the lithium aluminum hydride to the carbonyl carbon. Because aluminum hydride (AlH_3) is a Lewis acid, it acts as an electrophile, increasing the carbon's reactivity.



The reaction moves through the above step four times—once for each hydride ion. Thus, one mole of $LiAlH_4$ reduces four moles of ketone or aldehyde.



Finally, hydrolysis yields the alcohol.



Unfortunately, lithium aluminum hydride is not very selective. As well as reducing aldehydes and ketones, it reduces a variety of other functional groups. For example, it reduces carboxylic acid derivatives, nitriles, and nitro groups. Sodium borohydride ($NaBH_4$) is much less reactive. Because sodium borohydride is less reactive, it is more selective and normally reduces only aldehydes and ketones. When using sodium borohydride, chemists carry out the reduction in an aqueous alcohol in the presence of a hydroxide ion.

To understand why sodium borohydride is more selective, compare an ester with an aldehyde and how they react with sodium borohydride. An ester is a carboxylic acid derivative. It has one carbon and two oxygens bonded to the carbonyl carbon, whereas the aldehyde has one carbon, one hydrogen, and one oxygen bonded to the carbonyl carbon.

$R\overset{O}{\overset{\|}{C}}H$

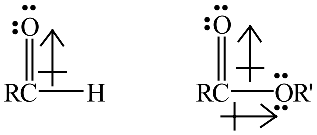
Aldehyde

$R\overset{O}{\overset{\|}{C}}OR'$

Ester

For more on inductive effects, see Section 1.11, page 000.

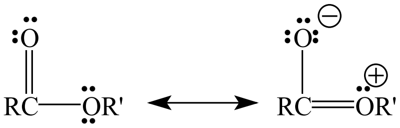
The two groups have significantly different inductive effects. Because oxygen has the strongest comparative electronegativity of the various groups, you would expect the carbonyl carbon of the ester, with two oxygens, to have a greater partial positive charge than the aldehyde with its one oxygen. The following diagram compares the two molecules and their dipoles.



Inductive effects

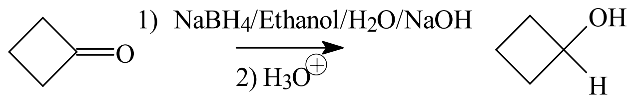
A higher partial positive charge should make the carbonyl carbon of the ester more susceptible to nucleophilic addition than the aldehyde. However, experiments show that the ester is *less* susceptible to a reaction and is thus less reactive.

Because inductive effects don't account for the observed reactivities of esters and aldehydes or ketones, consider the influence of resonance effects on the ester. The nonbonding electron pairs on the ester oxygen atoms donate electron density to the carbonyl carbon—especially with the singly bonded oxygen. No such resonance effects can occur in aldehydes. Thus, when you combine the inductive and resonance effects, the ester carbonyl carbon actually has a smaller partial positive charge than the aldehyde carbonyl carbon.

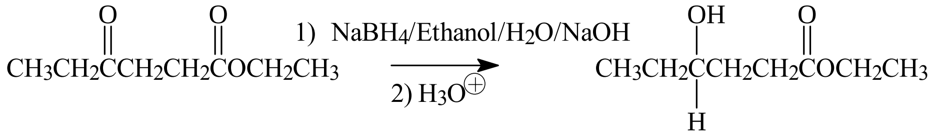


Resonance effect

Because sodium borohydride is less reactive than lithium aluminum hydride, it reduces aldehydes and ketones in the presence of esters, or other types of carbonyl groups, without reducing the other groups as well. Sodium borohydride also is much easier to handle in the laboratory than lithium aluminum hydride. Reactions can be run in water with ethanol added as needed to dissolve the substrate. Since sodium borohydride reacts with acid, base is added to make sure that it will only react with the substrate.



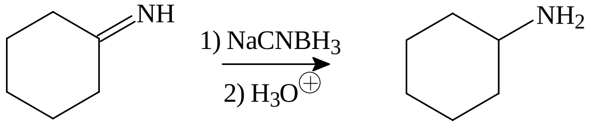
Cyclobutanol
(96%)



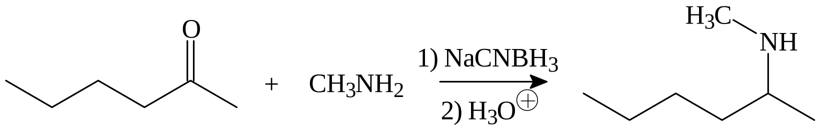
$$CH_3CH_2\overset{O}{\overset{\|}{C}}CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3 \xrightarrow[2)\ H_3O^{\oplus}]{1)\ NaBH_4/\text{Ethanol}/H_2O/NaOH} CH_3CH_2\underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{C}}CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3$$

Ethyl 4-hydroxyhexanoate
(87%)

An even milder reducing agent than sodium borohydride is sodium cyanoborohydride ($NaCNBH_3$), which will not reduce most carbonyl groups. Instead it reduces an imine group forming an amine. A common use for sodium cyanoborohydride is in the reaction of an amine with a ketone to form a substituted amine.



Cyclohexanamine
(98%)

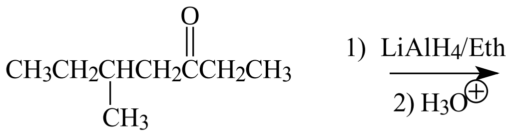


N-Methyl-2-hexanamine
(81%)

Exercise 7.10

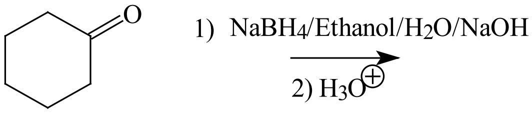
Predict the major products for each of the following reactions.

a)

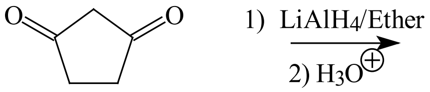


$$CH_3CH_2\underset{\underset{CH_3}{|}}{C}HCH_2\overset{O}{\overset{\|}{C}}CH_2CH_3 \xrightarrow[2)\ H_3O^{\oplus}]{1)\ LiAlH_4/\text{Ether}}$$

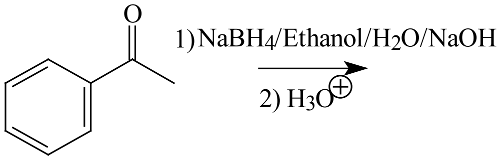
b)



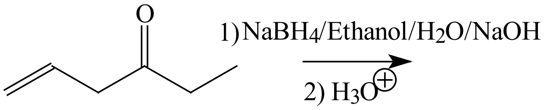
c)



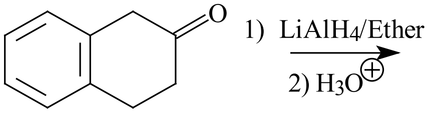
d)



e)

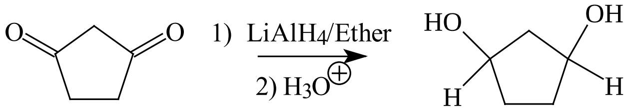


f)



Sample Solution

c)



7.8 Carbon Nucleophiles

In organometallic compounds, the carbon of the organic group is bound to a metal atom.

Organometallic compounds contain polar covalent bonds between a carbon atom and a metal atom. Because the metals are less electronegative than the carbon, the carbon is the negative end of the dipole. These covalent bonds possess enough polarity to make the carbon nucleophilic.

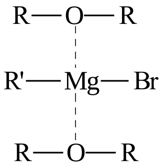
A Grignard reagent has the structure RMgX (X=Br,Cl,I) and is the product of the reaction of an alkyl halide and magnesium in an ether solvent.

An organometallic reagent of particular significance is the **Grignard reagent**, which Victor Grignard developed in 1902. Grignard received the Nobel Prize in chemistry in 1912 for his work. A Grignard reagent is an organomagnesium halide with the structure R—Mg—X and is the product of a reaction between magnesium metal and an alkyl halide.

$$CH_3CH_2CH_2Br \xrightarrow[\text{Ether}]{\text{Mg}} CH_3CH_2CH_2MgBr$$

Propylmagnesium bromide

Diethyl ether is the most common solvent used for a Grignard reaction because the ether donates a pair of electrons to the electron deficient magnesium. The formation of the ether-Grignard reagent complex is required for the magnesium to readily react with the alkyl halide. Without the ether, Grignard reagents do not readily form.



$$\begin{array}{c} R—O—R \\ \vdots \\ R'—Mg—Br \\ \vdots \\ R—O—R \end{array}$$

Ether-Grignard reagent complex

The reaction environment must contain no acidic hydrogen atoms. That includes no water, alcohols, amines, or carboxylic acids. Acidic hydrogen atoms protonate the carbon bearing the magnesium atom, thus preventing the formation of the Grignard reagent. The Grignard reagent is a strong base that reacts with these acidic functional groups to form a weaker base. Like most proton transfer reactions, Grignard reagents react more rapidly with a proton donor than with any other functional groups. Because of the sensitivity of Grignard reagents to acidic protons, chemists do not use any group containing acidic hydrogen atoms, and they carefully dry the diethyl ether to remove all traces of water.

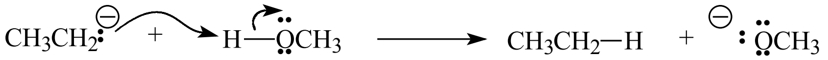
Solved Exercise 7.2

Write a mechanism for the reaction of ethyl magnesium bromide with methanol.

Solution

A counter ion is, in this case, a positively charged ion that is required to balance the negatively charged ion involved in the reaction.

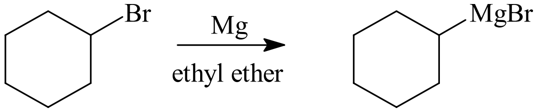
In the following mechanism, the ${}^{\oplus}MgBr$ is not shown because the Grignard reagent has significant ionic character; therefore the ${}^{\oplus}MgBr$ is considered a **counter ion**. The methoxide ion interaction with the ${}^{\oplus}MgBr$ is even more ionic.



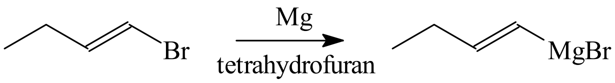
$$CH_3CH_2^{\ominus} + H-\ddot{O}CH_3 \longrightarrow CH_3CH_2-H + {}^{\ominus}:\ddot{O}CH_3$$

The alcohol is a much stronger acid than the alkane, and the Grignard reagent is a much stronger base than the alkoxide ion. Thus, the reaction proceeds to the right, the side of the weaker acid-base pair.

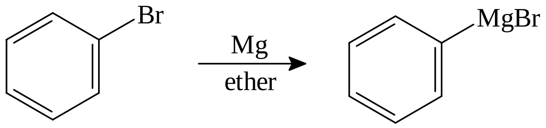
Grignard reagent formation occurs with primary, secondary, or tertiary alkyl halides, as well as with vinyl and aryl halides. Chlorine, bromine, or iodine work well as the halogen, but fluorine does not. Organofluorides generally are not reactive. The following reactions are examples of the Grignard reaction:



Cyclohexylmagnesium bromide



1-Butenylmagnesium bromide

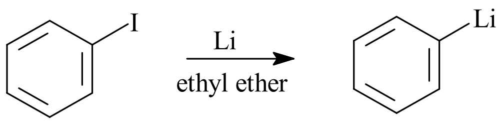


Phenylmagnesium bromide

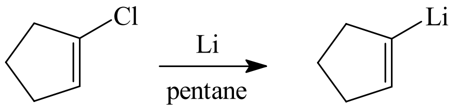
Lithium, like magnesium, reacts with a variety of halides to form organolithium reagents. Unlike the Grignard formation, organolithium reagent formation does not require an ether solvent for the reaction to proceed. However, you must use anhydrous reaction conditions.

$$CH_3CH_2CH_2CH_2Br \xrightarrow[\text{hexane}]{\text{Li}} CH_3CH_2CH_2CH_2Li$$

Butyl lithium



Phenyl lithium

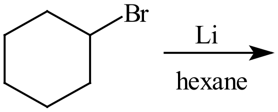


1-Cyclopentenyl lithium

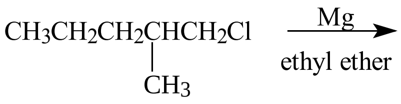
Exercise 7.11

Predict the major products for each of the following reactions.

a)

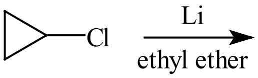


b)

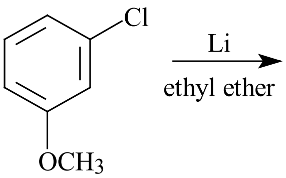


$$CH_3CH_2CH_2\underset{CH_3}{\underset{|}{C}}HCH_2Cl \xrightarrow[\text{ethyl ether}]{Mg}$$

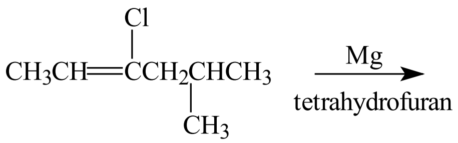
c)



d)

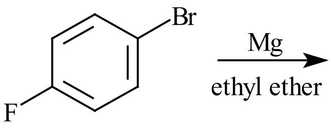


e)



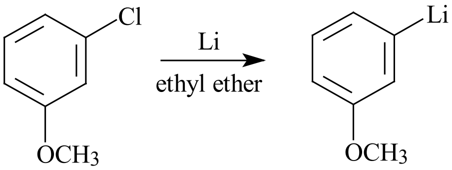
$$CH_3CH{=}\overset{\displaystyle Cl}{C}CH_2\underset{\displaystyle CH_3}{CH}CH_3 \xrightarrow[\text{tetrahydrofuran}]{Mg}$$

f)



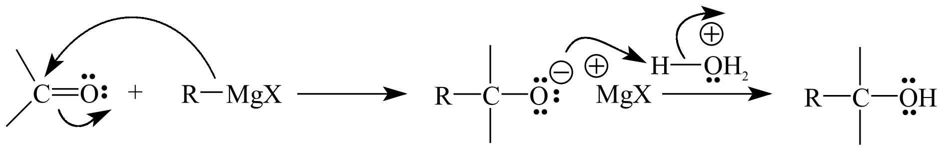
Sample solution

d)

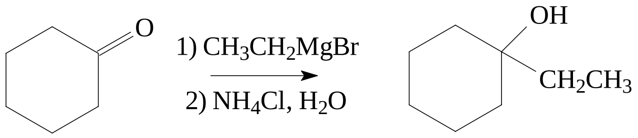


Grignard reagents and organolithium compounds are strong nucleophiles. Thus, they are strong bases. Both undergo a variety of similar reactions, but their most useful reaction is as a nucleophile with carbonyl compounds. Organolithium compounds usually react more readily than Grignard reagents, but because of this increased reactivity, they are more difficult to make and to handle. Chemists usually prefer Grignard reagents to organolithium compounds. When the carbonyl is of low reactivity, then the greater reactivity of the organolithium compounds makes them invaluable.

In a nucleophilic addition reaction, the carbon nucleophile of the organometallic compound reacts with the carbon electrophile of the carbonyl group to produce an alkoxide.

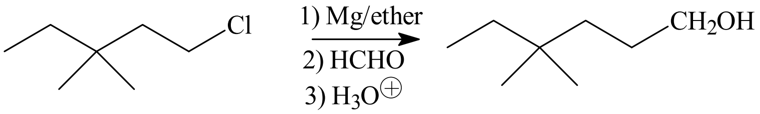


Then, hydrolysis of the alkoxide with a dilute acid produces the alcohol. When the product is a tertiary alcohol, chemists frequently use saturated aqueous ammonium chloride solution to protonate the alkoxide to form the alcohol. Tertiary alcohols readily react with acids to eliminate water and produce alkenes. Thus, aqueous NH_4Cl works well as a mildly acidic solution to neutralize the basic reaction mixture.



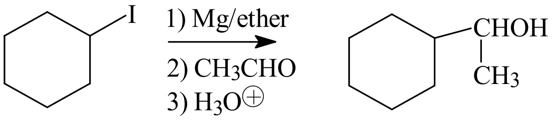
1-Ethylcyclohexanol
(74%)

Grignard reagents produce primary, secondary, or tertiary alcohols depending on the carbonyl group used. Formaldehyde (HCHO) produces a primary alcohol.



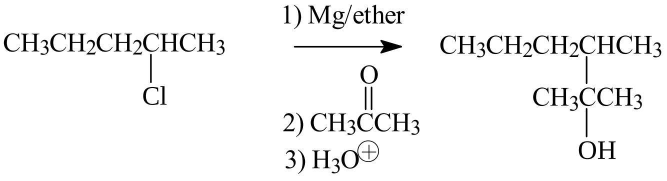
4,4-Dimethyl-1-hexanol
(68%)

Other aldehydes produce secondary alcohols.



1-Cyclohexylethanol
(55%)

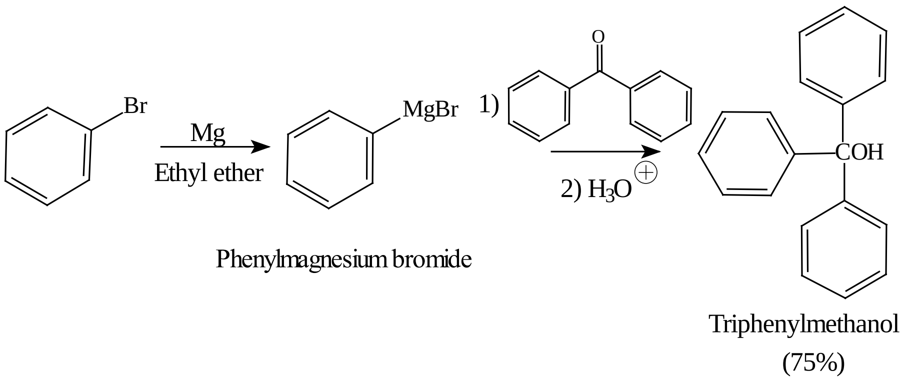
And ketones produce tertiary alcohols.



$$CH_3CH_2CH_2\underset{\substack{|\\Cl}}{C}HCH_3 \xrightarrow[\substack{2)\ CH_3\overset{\substack{O\\ \|}}{C}CH_3\\ 3)\ H_3O^{\oplus}}]{1)\ Mg/ether} CH_3CH_2CH_2\underset{\substack{|\\ CH_3\underset{\substack{|\\OH}}{C}CH_3}}{C}HCH_3$$

1,1,2-Trimethyl-1-pentanol
(74%)

Synthesis of Triphenylmethanol



Phenylmagnesium bromide

To 97 mg (4 mmol) of magnesium turnings in a dry reaction flask, add 1 mL of anhydrous ether. Dissolve 660 mg (4.2 mmol) of bromobenzene in 1.5 mL of anhydrous ether. Add about 0.1 mL of the bromobenzene solution to the flask containing the magnesium. If the reaction does not start immediately, crush the magnesium with a glass rod. The mixture becomes cloudy and gets warm when the reaction has started. Over a period of several minutes add the remaining bromobenzene maintaining a gentle reflux. If the boiling becomes too vigorous, stop the addition until it slows down. The reaction is complete when most or all of the magnesium has reacted. Use this solution of Grignard reagent immediately for the next step.

Triphenylmethanol

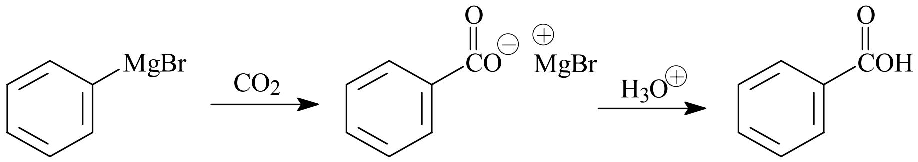
To a dry flask, add 728 mg (4 mmol) of benzophenone and dissolve in 2 mL of anhydrous ethyl ether. As you rapidly stir the Grignard solution, add the benzophenone solution dropwise. This reaction is exothermic, so do not add the benzophenone too fast or the reaction reflux can become too vigorous. A red color appears during the addition of the benzophenone. When the red color disappears, the reaction is complete. Formation of a precipitate is normal. Cool the reaction mixture in ice and slowly add 4 mL of 3M hydrochloric acid. The precipitate should dissolve after thorough mixing of the acid with the reaction mixture. Remove the aqueous layer and shake the ether layer with an equal volume of saturated sodium chloride solution. This removes most of the water and excess acid. Separate the layers and dry the ether layer with calcium chloride. Shake the tube for 5 to 10 minutes to complete the drying. Filter out the solid and wash the solid with a small amount of ether. Evaporate the ether. Grind the crystals with ice cold petroleum ether to remove the biphenyl by-product. Recrystallize with 2-propanol. The expected yield of triphenylmethanol is 780 mg (75%). Its melting point is 162-164°C.

Discussion Questions

1. Technical grade ethyl ether often contains ethanol (CH_3CH_2OH) as an impurity. What is the effect on the course of the reaction of using technical ether as a solvent for the benzophenone? If there is an effect, what alternate products are formed?
2. A Grignard reagent requires an ether to form from the alkyl halide and magnesium. This is because a complex of two moles of ether per mole of Grignard reagent forms. Propose a structure for this complex. Why do you think this complex forms?
3. Chemists typically observe formation of a white solid during the addition of benzophenone to the solution of phenylmagnesium bromide. Propose a structure

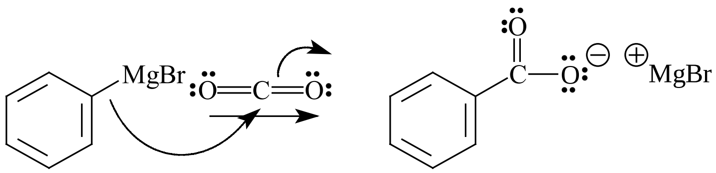
for this material. Why does the addition of aqueous hydrochloric acid dissolve the precipitate?

Carbon dioxide has a structure similar to a carbonyl group. In fact, it is really *two* carbonyl groups sharing one carbon atom (O=C=O). Thus, you must exclude atmospheric carbon dioxide from the reaction vessel during a Grignard reaction. However, reaction with carbon dioxide is a valuable technique for the synthesis of carboxylic acids containing one more carbon than the original alkyl halide.



Benzoic acid
(86%)

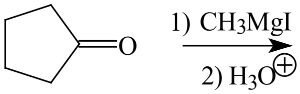
The mechanism of the reaction with CO_2 is parallel to the reaction with a carbonyl group.



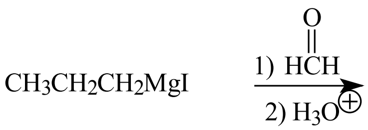
Exercise 7.12

Predict the major products for each of the following reactions.

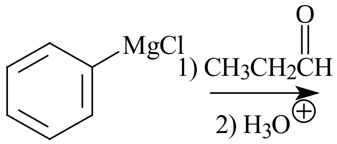
a)



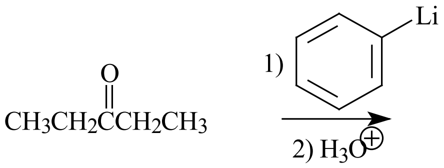
b)



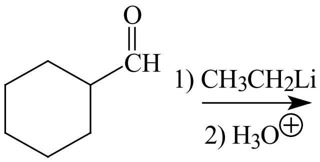
c)



d)

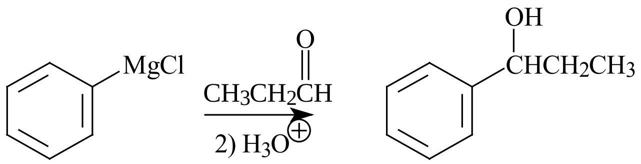


e)



Sample solution

c)



7.9 Organic Synthesis

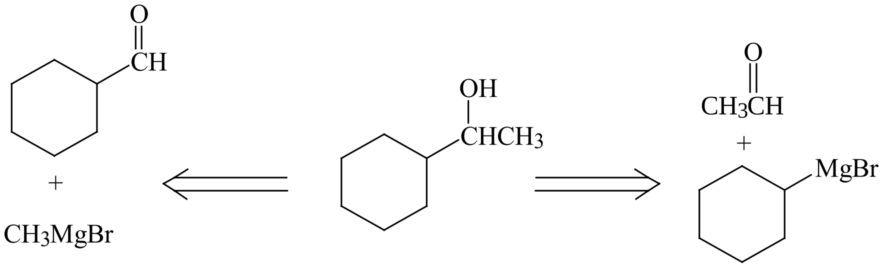
Organic synthesis is the technique of making an organic molecule via one or more steps from another organic molecule.

A major activity for many organic chemists is the synthesis of new organic molecules. In fact, much of the remainder of this book discusses the **organic syntheses** of various types of compounds. The ultimate goal of organic synthesis is to devise a sequence of reactions that prepares a specific product in the most efficient, shortest, and least expensive pathway. In practice, most organic syntheses are compromises among these factors. In industrial synthesis, cost is the primary factor, whereas in the laboratory accomplishing the goal is the major concern. Thus, a compound may have several widely varying methods of synthesis depending on whether it is a laboratory synthesis or an industrial synthesis.

When synthesizing an alcohol, a common starting material is an aldehyde or ketone. Hydride reduction of the carbonyl results in an alcohol with the same number of carbon atoms and the same carbon skeleton. A Grignard synthesis prepares an alcohol with an increased number of carbon atoms.

For example, consider the synthesis of 1-cyclohexylethanol, a secondary alcohol. A retrosynthetic analysis of the 1-cyclohexylethanol molecule shows that there are two possible combinations of Grignard reagents and carbonyls that result in this product. The arrow below ($\Longleftarrow$) is called a **retrosynthesis arrow**. A retrosynthesis arrow reads "is synthesized from." The following retrosyntheses show that 1-cyclohexylethanol is synthesized from either cyclohexanecarboxaldehyde and a methyl Grignard or a cyclohexyl Grignard and ethanal.

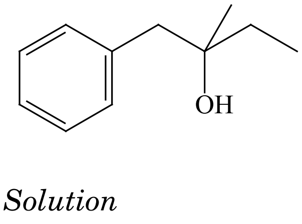
A retrosynthesis arrow shows synthetic ideas *rather than synthetic* details. *The retrosynthesis arrow points from the target molecule to the substrate molecule(s).*



One approach requires cyclohexanecarboxaldehyde, and the other requires ethanal (acetaldehyde). Either of the Grignard reagents shown above, methyl magnesium bromide or cyclohexyl magnesium bromide, are synthesized from readily available organohalogens. Although both approaches proceed readily and give the alcohol in good yield, ethanal is more readily available in most chemistry stockrooms than cyclohexanecarboxaldehyde.

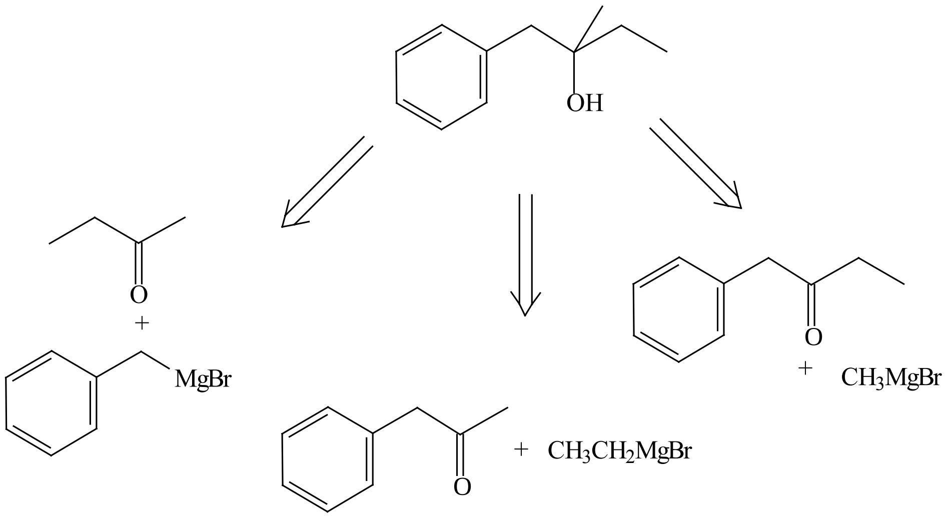
Solved Exercise 7.3

Show a synthesis for the following compound.



Solution

The synthesis of a tertiary alcohol can be accomplished with either a Grignard reagent or an organolithium reagent. Each of the three bonds between the carbon bearing the alcohol and the three alkyl groups can be synthesized by a different combination of an organometallic reagent with a carbonyl group. The following retrosynthesis shows the use of Grignard reagents, although, organolithium reagents can be substituted.

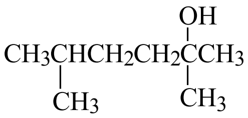


Exercise 7.13

Show a preparation of each of the following alcohols by the addition of the appropriate Grignard reagent or organolithium compound to a carbonyl compound.

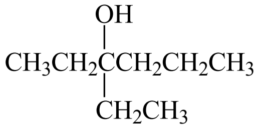
a) $CH_3CH_2CH_2CH_2OH$

b)



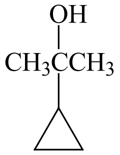
$CH_3\underset{CH_3}{C}HCH_2CH_2\overset{OH}{\underset{CH_3}{C}}CH_3$

c)

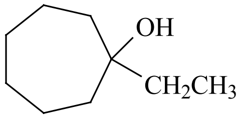


$CH_3CH_2\overset{OH}{\underset{CH_2CH_3}{C}}CH_2CH_2CH_3$

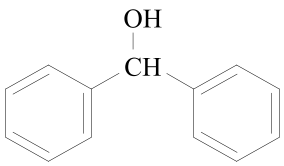
d)



e)

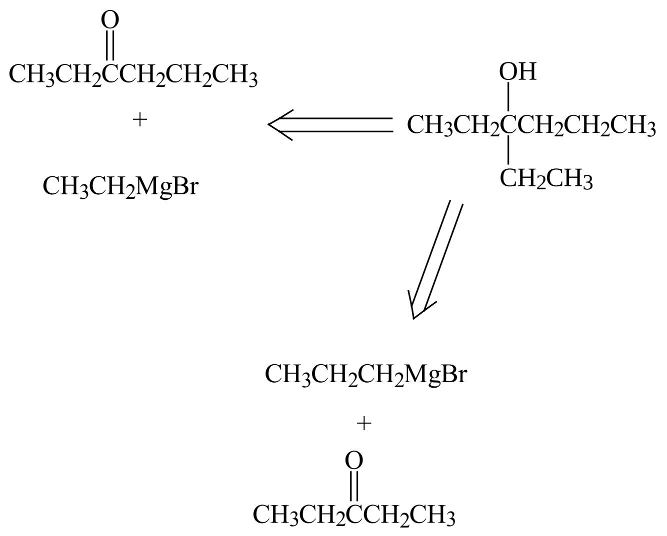


f)



Sample solution

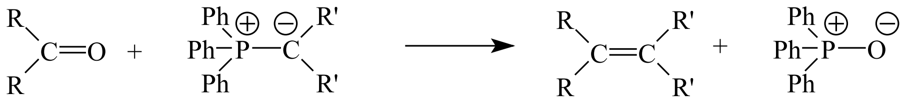
c) The synthesis of 3-ethyl-3-hexanol has two possible answers.



7.10 The Wittig Reaction

In 1954 Georg Wittig discovered a method that converts the carbonyl group of an aldehyde or ketone to a C=C double bond. For his work he received the 1979 Nobel Prize in chemistry. This method, called the Wittig reaction, involves the nucleophilic addition of a phosphorus-stabilized carbanion to a ketone or aldehyde. An elimination of the phosphorus then gives the alkene.

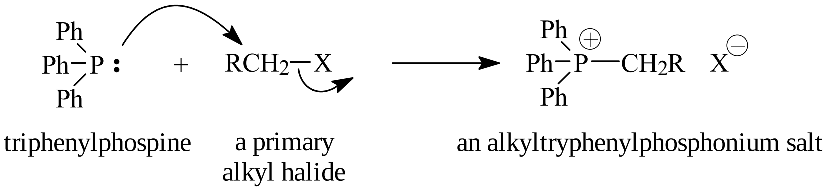
The abbreviation Ph is a common one for a phenyl group.



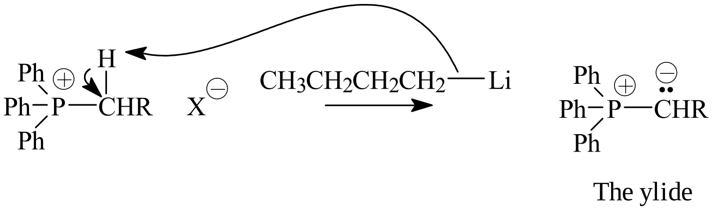
Phosphorus ylide

An ylide is a molecule that contains two adjacent charged atoms. One atom has a positive charge and the other a negative charge.

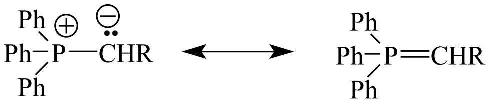
A phosphorus-stabilized carbanion, an **ylide**, has a negatively charged carbon and a positively charged phosphorus adjacent to each other. Some ylides have a sulfur atom instead of the phosphorus. The net charge of the ylide is zero. The preparation of a phosphorus ylide involves a two step reaction of triphenylphosphine and an alkyl halide. In the first step, the nucleophilic phosphorus attacks the saturated carbon bearing the halogen atom. The halogen-bearing carbon is usually a primary carbon. The product is an alkyltriphenylphosphonium salt.



In the second step, treatment of this salt with a strong base—usually butyl lithium—removes a proton from the carbon attached to the phosphorus atom. The result is the ylide.

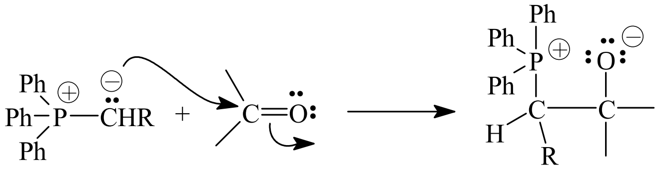


The ylide is a resonance hybrid with two resonance structures. One structure has charges on the phosphorus and the carbon. The other has a double bond between the phosphorus and the carbon. The second resonance structure, as shown on the right below, has ten electrons in the valence shell of the phosphorus. Phosphorus permits ten electrons in its valence shell because two of them can occupy empty 3*d* orbitals. The π bond is weak because of the involvement of the 3*d* orbital, so it makes only a small contribution to the structure of the ylide.



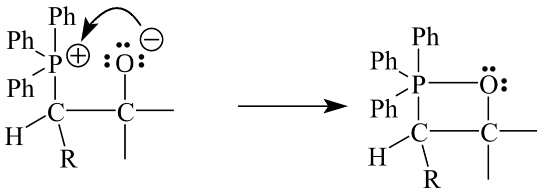
A betaine is a compound with charged heteroatoms bonded to adjacent carbon atoms.

When converting the carbonyl into an alkene, the ylide and the aldehyde or ketone react in a typical nucleophilic addition reaction. The reaction first produces an intermediate called a **betaine**.

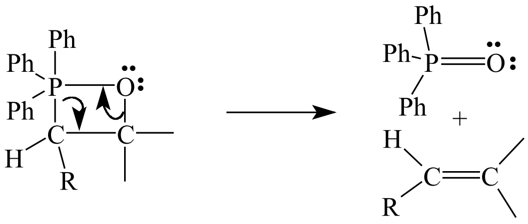


A betaine

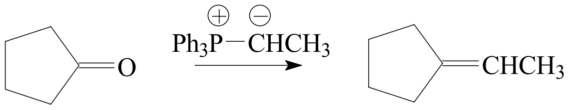
Because of the close proximity of the positively charged phosphorus and the negatively charged oxygen and because a phosphorus—oxygen bond is strong, the phosphorus and the oxygen immediately bond to form a four-membered ring.



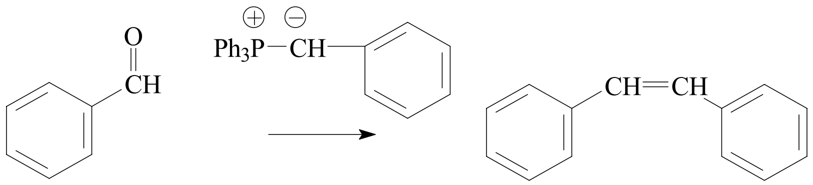
The ring rapidly collapses giving an alkene and triphenylphosphine oxide. Triphenylphosphine oxide is an exceptionally stable molecule and is usually insoluble in the reaction mixture. The stability of triphenylphosphine oxide and its insolubility in the reaction mixture provides the energy ("driving force") for the reaction.



The following are some examples of the formation of carbon—carbon double bonds using the Wittig reaction. Where possible, this reaction produces mixtures of *cis* and *trans* geometric isomers.

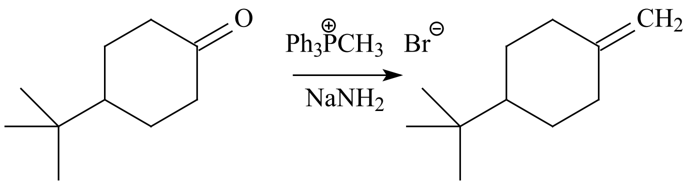


Ethylidinecyclopentane
(86%)



1,2-Diphenylethene
(78%)

Synthesis of Methylene-4-*tert*-butylcyclohexane

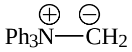


Methylene-4-*tert*-butylcyclohexane
(80%)

In a dry flask place a magnetic stirring bar and 1.28 g (4 mmol) of triphenylphosphonium bromide-sodium amide mixture (“instant ylide”). Add 4 mL of freshly distilled tetrahydrofuran. Stir the mixture for 15 minutes. During this time, the solution should become bright yellow—a color typical of an ylide solution. Add 0.4 g (2.7 mmol) of 4-*tert*-butylcyclohexanone and stir at room temperature for an additional 90 minutes. At the end of the time, add 4 mL of 25% aqueous sodium hydroxide solution. Transfer the reaction mixture to a separatory funnel. Carefully rinse the reaction flask with three 8 mL portions of ethyl ether. Add 10 mL of 0.1M HCl and agitate the solutions. Separate the layers and extract the aqueous layer with three additional 20 mL portions of ethyl ether. Dry the combined ether solutions using anhydrous sodium sulfate. Evaporate the ether. Prepare a chromatography column with 16 g of basic alumina. Dissolve the crude product with 2 mL of a 9:1 mixture of petroleum ether (60-80^{o}C):methylene chloride. Place this solution on the column and elute with 30 mL of the same solvent mixture. Carefully evaporate the solvent. The yield of product is 330 mg (80%), mp 48-51^{o}C.

Discussion Questions

1. Heteroatoms other than P can stabilize the negative charge on C to yield an ylide. For example, a nitrogen ylide has the structure:



$$\overset{\oplus}{Ph_3N}-\overset{\ominus}{CH_2}$$

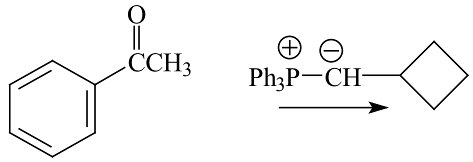
   Why are there no resonance structures for a nitrogen ylide analogous to the ones for a phosphorus ylide?
2. Separation of two compounds using column chromatography depends on the polarity of the substrate. Do you expect that alumina (Al_2O_3) will interact more strongly with 4-*tert*-butylcyclohexanone or methylene-4-*tert*-butylcyclohexane? Why?

Exercise 7.14

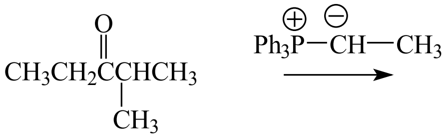
Predict the major products for each of the following reactions.

a)

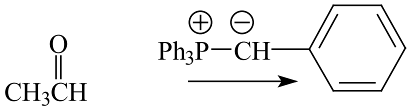
b)



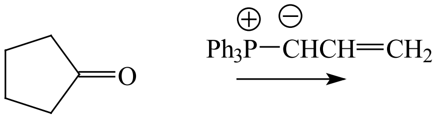
c)



d)

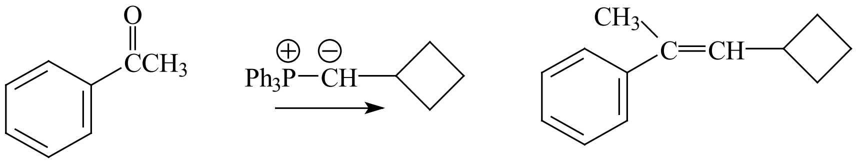


e)



Sample Solution

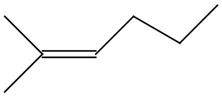
b)



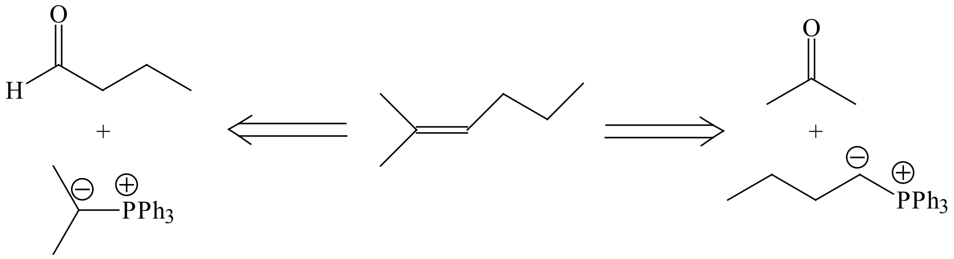
The Wittig reaction is a valuable synthetic tool because it provides a pathway for the synthesis of a wide variety of alkenes. Solved exercise 7.4 shows the synthesis of 2-methyl-2-hexene using the Wittig reaction. To determine the required reagents, first divide the target molecule into two fragments at the double bond. Add the carbonyl oxygen to the carbon of one fragment and the alkyl halide to the other fragment. Because triphenylphosphine is large, use the least hindered side for the alkyl halide. Also, ylide formation seldom works well with anything but a methyl or a primary halide.

Solved Exercise 7.4

Show a synthesis for the following compound.



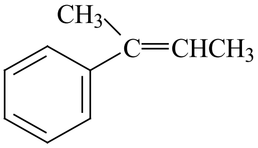
Solution
This synthesis involves the preparation of a Wittig reagent that reacts with a carbonyl compound. The synthesis follows two possible pathways. One is a Wittig reagent synthesized from 2-chloropropane and the other is a Wittig reagent synthesized from 1-chlorobutane. The pathway on the right below would give a better yield of product than the one on the left because the right hand Wittig reagent is prepared from a primary alkyl halide.



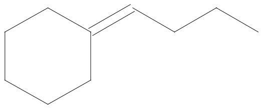
Exercise 7.15

Show the route you would use to prepare the following alkenes in the highest yield by the addition of the appropriate phosphorus ylide to a carbonyl compound.

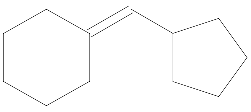
a)



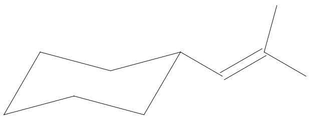
b)



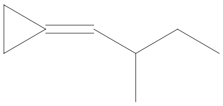
c)



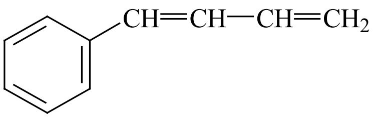
d)



e)

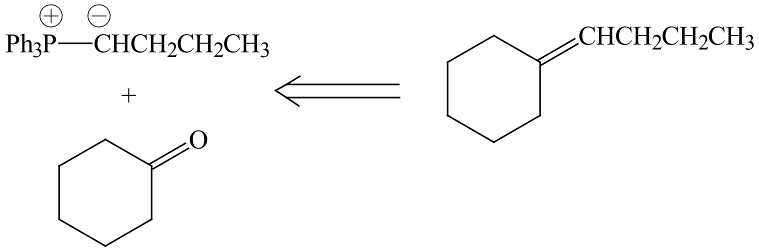


f)



Sample solution

b) This problem has two possible solutions, but the following solution prepares the ylide from 1-bromobutane, a primary alkyl halide. Of the two possible solutions, it gives a better yield.



Key Ideas from Chapter 7

❑ The carbonyl group consists of a carbon and an oxygen with one σ and one π bond between the two atoms. The group is polar: the carbon bears a partial positive charge and the oxygen bears a partial negative charge.

❑ The carbonyl group undergoes two modes of reaction: 1) nucleophilic addition to the carbonyl carbon followed by the reaction of the oxygen with an electrophile or 2) electrophilic addition to the carbonyl oxygen followed by reaction of the carbon with a nucleophile.

❑ In the cyanohydrin reaction, a cyanide ion nucleophile reacts with the carbonyl carbon. Then a hydrogen ion adds to the oxygen.

❑ Water adds to a carbonyl group to form a hydrate.

❑ One mole of an alcohol adds to a carbonyl group to form a hemiacetal.

❑ Two moles of an alcohol add to a carbonyl group to form an acetal.

❑ The position of equilibrium in reactions forming hydrates, hemiacetals, or acetals depends on steric and electronic factors—the larger the groups attached to the carbonyl, the smaller the amount of product at equilibrium. Electron-withdrawing groups α to the carbonyl carbon increase the amount of product at equilibrium.

- ☐ When forming a cyclic hemiacetal or a cyclic acetal with the —OH group attached to the ring, the size of the ring that forms in the reaction influences the position of the equilibrium.
- ☐ Primary nitrogen nucleophiles react with a carbonyl to produce a carbon—nitrogen double bond (an imine).
- ☐ Secondary nitrogen nucleophiles react with a carbonyl group to produce an enamine.
- ☐ A reduction reaction of aldehydes and ketones involves the addition of two hydrogens to a carbonyl group. $LiAlH_4$ and $NaBH_4$ often provide the hydride ion used in the reduction.
- ☐ Carbon nucleophiles from Grignard reagents (RMgX) and organolithium compounds (RLi) also add to carbonyl groups.
- ☐ Organic synthesis, an important activity of organic chemists, is the process of making a new organic molecule from other known, and often simpler, molecules. Chemists work from the desired target to starting materials in a process called retrosynthetic analysis.
- ☐ The Wittig reaction involves the addition of a phosphorus ylide to a carbonyl group to form a double bond. A phosphorus ylide has a negatively charged carbon and a positively charged heteroatom adjacent to one another with a net zero charge for the molecule.

Richard F. Daley and Sally J. Daley
www.ochem4free.com

Organic Chemistry

Chapter 8

Nucleophilic Substitution on the Carbonyl Group

Chapter 8

Nucleophilic Substitution on the Carbonyl Group

Chapter Outline

8.1 The Acyl Transfer Mechanism
The mechanism that transfers an acyl group from a leaving group to the nucleophile

8.2 Water and Alcohol Nucleophiles
The reaction of oxygen nucleophiles with carboxylic acid derivatives

8.3 Halide and Carboxylic Acid Nucleophiles
The reaction of halogen and carboxylic acid nucleophiles with carboxylic acid derivatives

8.4 Reaction with Nitrogen Nucleophiles
The reaction of nitrogen nucleophiles with carboxylic acid derivatives

8.5 Reaction with the Hydride Nucleophile
The reaction of hydride nucleophiles with carboxylic acid derivatives

8.6 Carbon Nucleophiles
The reaction of carbon nucleophiles with carboxylic acid derivatives

8.7 Nitriles
The reactions of oxygen, hydride, and carbon nucleophiles with the nitrile functional group

8.8 The Baeyer-Villiger Oxidation
The conversion of a ketone or aldehyde to a carboxylic acid derivative

8.9 Solving Mechanistic Problems
The use of experimental data to formulate a mechanistic interpretation for a chemical reaction

Objectives

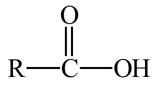
- ✔ Write the acyl transfer mechanism
- ✔ Understand how oxygen, nitrogen, hydride, and carbon nucleophiles react with carboxylic acid derivatives
- ✔ Recognize the similarity of nitriles with carboxylic acid derivatives
- ✔ Know the reaction of nitriles with oxygen, hydride, and carbon nucleophiles
- ✔ Become familiar with how experimental data is interpreted mechanistically
- ✔ Be familiar with Baeyer-Villiger Oxidation

Science is the knowledge of consequences, and dependence of one fact upon another.

—Thomas Hobbes

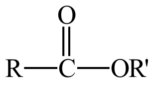
The beginning of a new chapter implies the beginning of a new set of concepts. However, the concepts covered in this chapter are a continuation of those included in Chapter 7. Chapter 7 presented nucleophilic *addition* to a carbonyl group; this chapter looks at the nucleophilic *substitution* of a carbonyl group. The reaction mechanisms of both are fundamentally the same. The big difference between the two is that instead of the nucleophile adding to the double bond between the carbonyl carbon and the oxygen, as it does in a nucleophilic addition, the nucleophile substitutes itself for one of the groups bonded to the carbonyl carbon in a nucleophilic substitution.

Although the mechanism of a nucleophilic substitution is essentially the same as a nucleophilic addition, aldehydes and ketones do not undergo nucleophilic substitution reactions because they do not have the required electronegative leaving group. Carboxylic acids and their derivatives have such a leaving group. The carbonyl carbon in the carboxylic acid family bonds to at least one other electronegative group besides the carbonyl oxygen. These electronegative groups usually are oxygen, nitrogen, or a halogen. Five functional groups make up the carboxylic acid family. They are carboxylic acids, esters, amides, acyl halides, and carboxylic anhydrides.



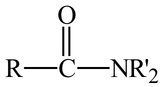
$$\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}OH}$$

Carboxylic acid



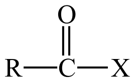
$$\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}OR'}$$

Ester



$$\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}NR'_2}$$

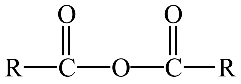
Amide



$$\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}X}$$

Acyl halide

(X = Cl, Br)

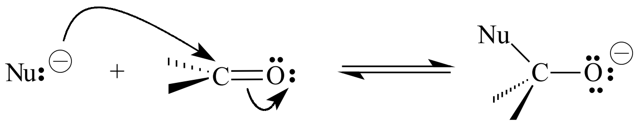


$$\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}O{-}\overset{\overset{O}{\|}}{C}{-}R}$$

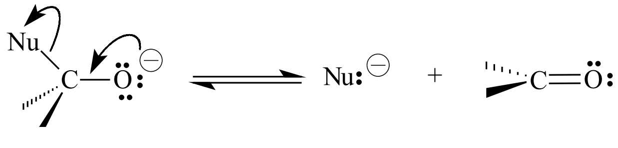
Carboxylic anhydride

8.1 The Acyl Transfer Mechanism

As you learned in Chapter 7, nucleophilic addition reactions are reversible reactions with the position of equilibrium dependent on the strength of the nucleophile. The stronger the nucleophile, the more the equilibrium favors the product.

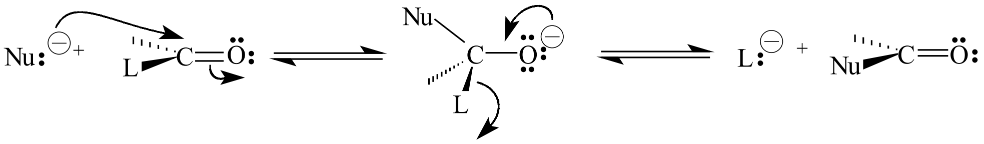


The mechanistic picture of the reverse reaction involves the loss of the nucleophile to re-form the original carbonyl compound.



A nucleophilic substitution at the carbonyl group of a carboxylic acid, or a carboxylic acid derivative, combines these two steps. But in a nucleophilic substitution, the group that leaves is the electronegative group that was bonded to the carbonyl carbon. Thus, the result of a nucleophilic substitution reaction is a carbonyl compound that is *different* from the starting carbonyl compound. A nucleophilic substitution reaction involving a carbonyl group is often called an **acyl transfer reaction**, and it follows this mechanism.

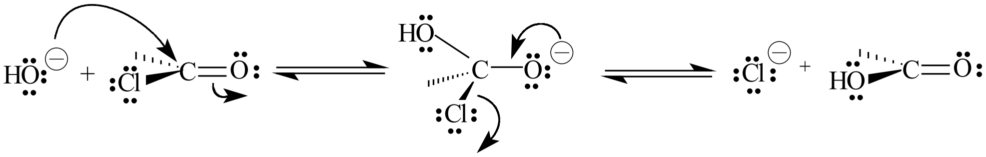
An acyl transfer is a reaction in which a nucleophile displaces a less electronegative group on the carbonyl group.



A leaving group, abbreviated "L" in the general acyl transfer mechanism, is the group displaced by the incoming nucleophile.

The ease with which a **leaving group** leaves a compound is inversely proportional to its basicity. Thus, the more basic the leaving group, the less readily it leaves. A stronger base is more willing to donate its electron pair to an electrophile that, in this case, is the carbonyl carbon. In the carboxylic acid family, the leaving group (the electronegative group bonded to the carbonyl carbon) is a base, but is generally a weaker base than the nucleophile. For example, the acyl transfer reaction works well with an acyl halide because the halide ion is a weak base. Thus, an acyl halide has a very good leaving group. Conversely, acyl transfer reactions do not occur with aldehydes and ketones because the leaving group, either a hydride or a carbanion, is generally too strong a base to be a good leaving group.

Not only is the leaving group a base, but the attacking nucleophile is also a base. With a nucleophilic substitution, a major consideration is the relative base strength of the nucleophile in comparison to the leaving group. Because the leaving groups in the carboxylic acid family are weak bases, they are stable anions. For example, the —OH group easily replaces the —Cl group. However, a —Cl group does not readily replace an —OH group. Thus, in a reaction between a strong basic nucleophile and a weaker basic leaving group in the acyl halide, the equilibrium favors the product.



The concept of a leaving group is fundamental to many areas of organic chemistry. Numerous reactions have a leaving group. In reactions with a leaving group, the behavior of the leaving group significantly affects the course of the reaction.

The reactivity of the various members of the carboxylic acid family relates to the stability of the leaving group. Acyl halides and anhydrides have the most stable leaving group, so they are the most reactive towards a substitution reaction. Esters and carboxylic acids have intermediate stability; thus, they have only intermediate reactivity. Amide leaving groups are the least stable; thus, amides are the least reactive carboxylic acid derivative. In general, the rule for reactivity is*: the more stable the leaving group, the more reactive the carboxylic acid derivative.*

Exercise 8.1

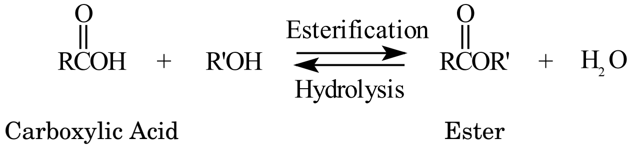
In a nucleophilic substitution reaction, what are the leaving groups for each of the carboxylic acid derivatives: acyl chlorides, anhydrides, esters, amides, and carboxylic acids? Relate the stability of these leaving groups to the reactivity of the carboxylic acid derivative.

8.2 Water and Alcohol Nucleophiles

An esterification reaction forms an ester functional group.

In a hydrolysis of an ester, the ester reacts with water to form a carboxylic acid and an alcohol.

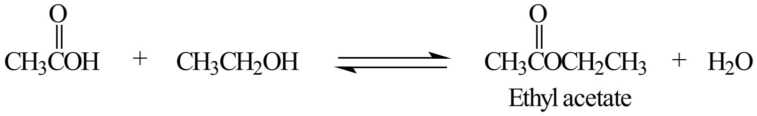
Esterification is the nucleophilic substitution reaction that converts a carboxylic acid, or a carboxylic acid derivative, to an ester. The reaction involves the substitution of a hydroxy group in the carboxylic acid with an alkoxy group from an alcohol. The reverse reaction, called a **hydrolysis,** is the substitution of an alkoxy group with a hydroxy group.



$$\mathrm{R}\overset{\overset{\displaystyle O}{\|}}{\mathrm{C}}\mathrm{OH} + \mathrm{R'OH} \underset{\text{Hydrolysis}}{\overset{\text{Esterification}}{\rightleftharpoons}} \mathrm{R}\overset{\overset{\displaystyle O}{\|}}{\mathrm{C}}\mathrm{OR'} + H_2O$$

Some of the earliest investigators into the nature of chemical equilibrium studied the interconversion of esters and acids. Marcellin Berthelot and Leon Saint-Gilles, in 1860, first published some rate studies on the formation and hydrolysis of ethyl acetate. In 1879, Cato Guldberg and Peter Waage formulated the equilibrium expression for the reaction.

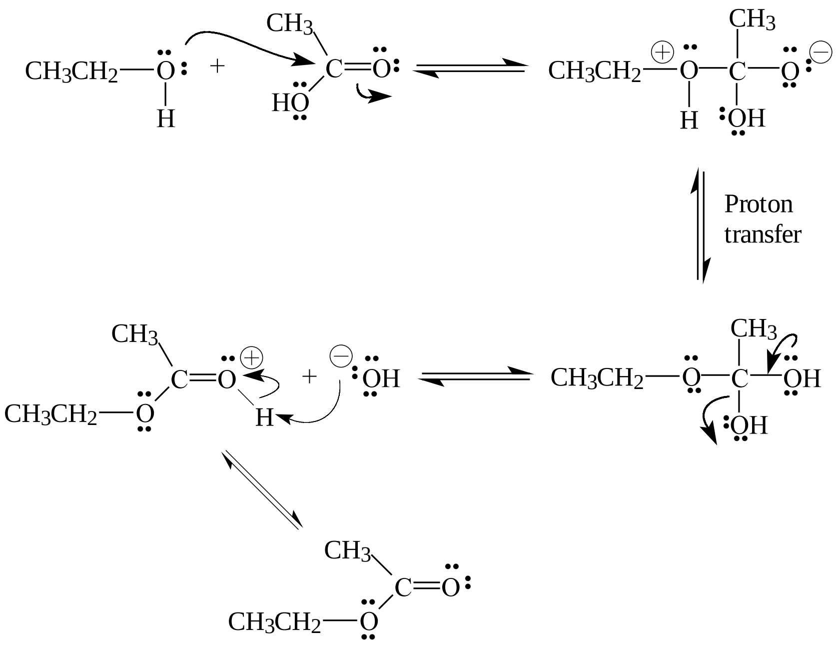
Equilibrium constants for esterification reactions are relatively small. The reaction of acetic acid with ethanol has an equilibrium constant of 4.



$$CH_3\overset{\overset{\displaystyle O}{\|}}{\mathrm{C}}OH + CH_3CH_2OH \rightleftharpoons CH_3\overset{\overset{\displaystyle O}{\|}}{\mathrm{C}}OCH_2CH_3 + H_2O$$

Looking at the pK_a values for the nucleophile and leaving group helps you to understand this equilibrium constant. Ethanol has a pKa of 16.3 and water 15.7. Because they are so similar, there is little thermodynamic preference between the substrate and product.

The mechanism for this reaction follows the generalized reaction mechanism shown in Section 8.1.



In the first step, the nucleophilic oxygen of the alcohol attacks the carbonyl carbon. In the second step, the proton bonded to the oxygen from the alcohol transfers to the oxygen that was the carbonyl oxygen. This proton transfer requires a base, like water, to remove the proton from one oxygen and move it to another. In the third step, the intermediate compound loses a hydroxide ion; thus, forming an ester with the carbonyl protonated. In the final step, the hydroxide ion removes the proton from the carbonyl group.

Exercise 8.2

For an esterification reaction consisting of a mixture of 0.5 moles each of ethanol and acetic acid in 1 liter of solution, give the amount of ethyl acetate present at equilibrium. Now increase the amount of ethanol to 5 moles. What is the amount of ethyl acetate present at equilibrium for this new mixture?

By altering the reaction conditions of a reaction, you change the equilibrium position of that reaction. By changing the equilibrium position of a reaction, you control which product forms in the greater amount. In an esterification reaction, chemists want to maximize the amount of ester obtained by the reaction. To do this, they change the reaction conditions by using one of the following two approaches. They remove one, or both, of the products as they form, particularly the water, or they add an excess of one reactant.

An azeotrope is a mixture of liquids that do not dissolve in each other with a constant boiling point and composition.

To remove the water from an esterification reaction, chemists usually use distillation. In the commercial distillation process, the result of the distillation is an **azeotropic mixture**. The azeotrope for the reaction of acetic acid and ethanol boils at 70°C and consists of 83% ethyl acetate, 8% ethanol, and 9% water. Because the ethyl acetate is largely insoluble in the mixture, chemists simply separate it from the mixture and purify it. Then they purify the ethanol from the water and recycle the alcohol. The laboratory process is very similar to the commercial process. Chemists reflux the mixture using a trap to remove the denser water. The apparatus returns the water-insoluble layer of ethyl acetate to the reaction flask for collection at the end of the reaction. See Figure 8.1.

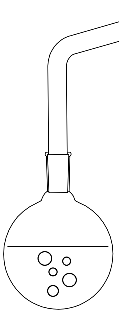


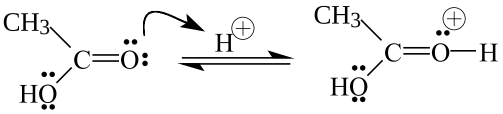
Figure 8.1. Use of a trap in an azeotropic distillation. As the distillate fills the trap, the lower layer stays in the trap and the upper layer overflows back into the reaction flask.

The Fischer esterification reaction uses a catalytic quantity of acid to promote reaction of the carboxylic acid with the alcohol.

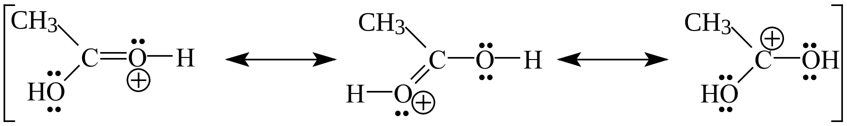
Because the hydroxide ion is a poor leaving group, chemists increase the rate of esterification by adding catalytic quantities of acid to the reaction mixture. The acid protonates the leaving group, allowing a water molecule to leave. This method, known as **Fischer esterification,** forms a wide variety of esters.

The presence of an acid catalyst in a Fischer esterification greatly increases the reactivity of the carbonyl group. The addition of an acid protonates the carbonyl oxygen, thus enhancing the carbon's reactivity to a nucleophile.

See Section 7.6, page 000, for a discussion of the resonance and inductive effects in an ester.

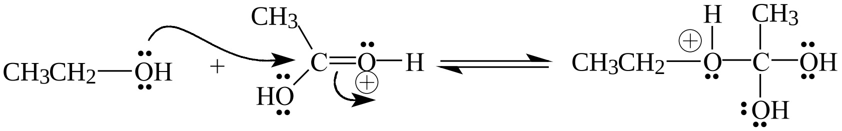


The protonated carboxylic acid is resonance-stabilized.

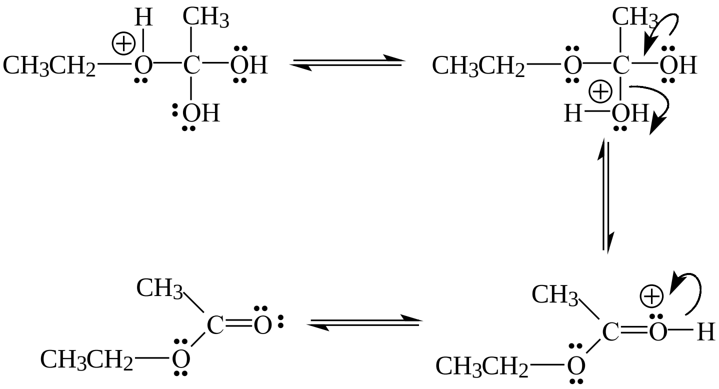


Because resonance allows several atoms to bear the partial charge, the ion has more stability and less reactivity than protonated aldehydes and ketones. The first two resonance contributors are equal in energy, but the third is only a minor contributor to the resonance.

The protonated carboxylic acid then adds the alcohol to form the hydrate of an ester.

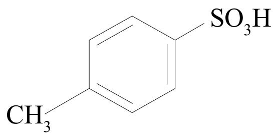


After a proton transfers from the alkoxy group to a hydroxy group, the intermediate loses water to form the ester. In the process the hydrated ester also loses a proton from the hydroxy group.



Chemists commonly use concentrated acids like sulfuric, *p*-toluenesulfonic, or phosphoric acid as the catalyst. Dilute aqueous solutions of acids are used only occasionally. Because esterification is a reversible reaction, adding water with the acid would drive the reaction the wrong way and decrease the yield of product.

Toluenesulfonic acid is the most popular choice because it is a very strong acid and because it is soluble in organic solvents.



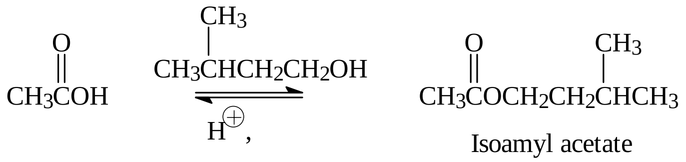
p-Toluenesulfonic acid

p-Toluenesulfonic acid is a strong acid because its conjugate base is resonance-stabilized with the negative charge distributed over all three of the oxygens bonded to the sulfur.

The Fischer method of esterification works well for most primary alcohols as they are not very sterically hindered. However, secondary and tertiary alcohols are more sterically hindered and usually have lower equilibrium constants and lower concentrations of the ester at equilibrium. To deal with these difficulties, chemists first convert the carboxylic acid to the acid chloride—the chloride is a good leaving group. The acid chloride then rapidly forms the ester in a reaction with an alcohol.

The synthesis of acid chlorides is discussed in Section 8.3, page 000.

Synthesis of Isoamyl Acetate (Banana Oil)



$$CH_3\overset{O}{\overset{\|}{C}}OH \xrightleftharpoons[H^{\oplus},]{CH_3\overset{CH_3}{\overset{|}{C}}HCH_2CH_2OH} CH_3\overset{O}{\overset{\|}{C}}OCH_2CH_2\overset{CH_3}{\overset{|}{C}}HCH_3$$

Isoamyl acetate

(72%)

To a reaction flask, add 265 mg (3 mmol) of 3-methyl-1-butanol, 960 mg (16 mmol) of acetic acid, and 100 mg of Amberlyst® 15 ion exchange resin. This resin provides a convenient source of acid catalyst. Add a boiling stone or magnetic stir bar. Reflux the reaction mixture for at least 1 hour. Cool to room temperature. Filter the cool mixture to remove the ion exchange resin. Prepare a chromatography column from a slurry of 8 mL of methylene chloride and 2g of silica gel. Add 2 g of potassium carbonate to the top of the silica gel. Drain the methylene chloride from the column until the solvent level just reaches the top of the potassium carbonate layer. Transfer the reaction mixture to the column using 1 mL of methylene chloride. Drain the column again until the solvent just reaches the potassium carbonate. Wash the resin and reaction flask with 1 mL of methylene chloride and add to the column. Drain the column again. Finally, complete the product elution, or washing, with 2 mL of additional methylene chloride and drain the column. Combine all the methylene chloride solvent portions and evaporate under a stream of air or nitrogen in the hood. The expected yield of ester is 280 mg (72%); the boiling point is 141-143°C.

Discussion Questions

1. In this reaction the molar ratio of alcohol:acid is 0.003:0.016. Why is such a large excess of acid used in this reaction?
2. What is the function of the potassium carbonate in the chromatography column?
3. Using the above procedure as a model, outline the synthesis expected to produce 500 mg of cyclohexyl acetate.

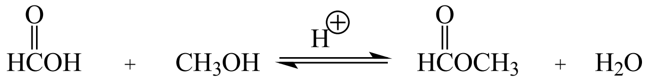
Exercise 8.3

Show the use of the Fischer esterification reaction in the synthesis of the following esters.

a) Ethyl benzoate b) $CH_3COOC_6H_5$
c) Methyl methanoate d) Methyl cyclopentanecarboxylate

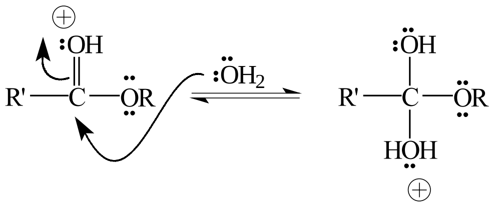
Sample solution

c) This is preparation of methyl methanoate (sometimes called methyl formate) from methanoic acid (HCOOH) and methanol (CH_3OH) with a catalytic quantity of acid.

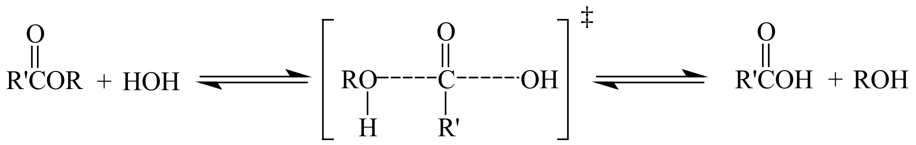


$$\mathrm{H\overset{O}{\overset{\|}{C}}OH} + \mathrm{CH_3OH} \xrightleftharpoons{\mathrm{H}^{\oplus}} \mathrm{H\overset{O}{\overset{\|}{C}}OCH_3} + \mathrm{H_2O}$$

As chemists worked with ester hydrolysis reactions, they came up with two possible mechanisms for the reaction. First, they proposed the formation of the tetrahedral intermediate that occurs in an esterification reaction. In this proposed intermediate, the nucleophile *and* the leaving group bond to the same carbon. However, no one had ever actually isolated and identified this intermediate.



A suggested alternate reaction mechanism involved the following transition state. This mechanism seemed much simpler than the mechanism with the tetrahedral intermediate.



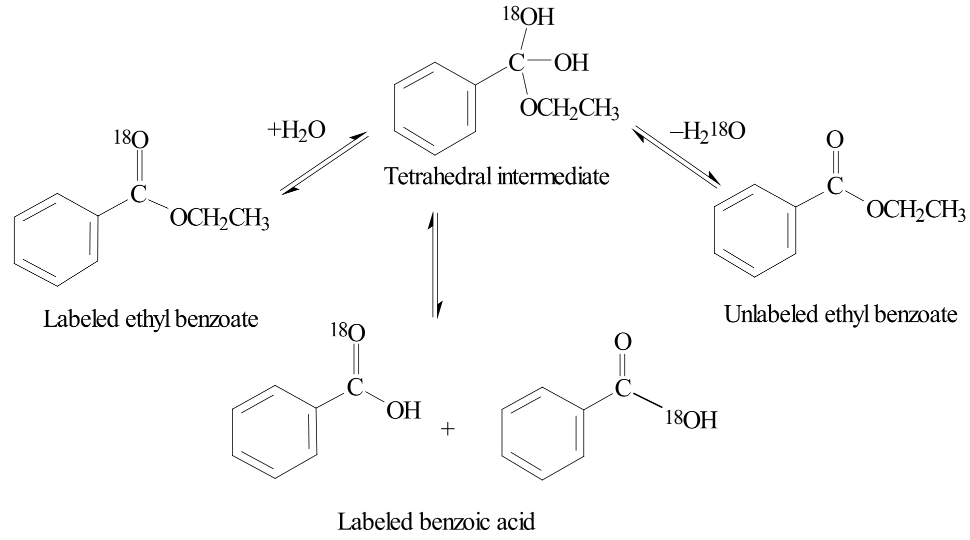
To decide which of these two possibilities actually happens, chemists carefully designed an experiment. As they planned, they compared the two mechanisms. In the intermediate of the first mechanism, the carbonyl oxygen becomes singly bonded to the carbonyl carbon, and in the transition state of the second mechanism, it remains doubly bonded to the carbonyl carbon. Thus, they wanted their experiment to follow what happens to the carbonyl oxygen. To provide evidence for the first mechanism, they needed a way to show that the carbonyl oxygen did not stay doubly bonded to the carbonyl carbon all the way through the reaction. Conversely, to provide evidence for the second mechanism, they needed a way to show that the carbonyl oxygen did stay doubly bonded to the carbonyl carbon throughout the reaction.

Isotopic labeling is synthesizing a molecule so that one or more of its atoms has a higher concentration of a specific isotope than occurs naturally. The isotopes that chemists commonly use for isotopic labeling are ^{2}H, ^{13}C, ^{14}C, ^{15}N, and ^{18}O. Each of these isotopes occurs in less than 1% concentration in natural sources.

The principle of microscopic reversibility states that the forward and reverse reactions occur through the same set of intermediates and the same reaction conditions.

To follow the carbonyl carbon, they first prepared an ester with a marked carbonyl oxygen using a technique called **isotopic labeling**. They then followed the marked oxygen through a hydrolysis reaction. (Remember? The reaction goes through the same steps for either an esterification or a hydrolysis—just in reverse order. This is called the **principle of microscopic reversibility**.)

The ester they prepared was ethyl benzoate. As they ran the ester synthesis, they labeled the carbonyl oxygen with ^{18}O. Then they reacted the ethyl benzoate with unlabeled H_2O. As the hydrolysis proceeded, they removed samples and isolated the ester. A portion of the ester had no labeled oxygen, indicating that some of the marked carbonyl oxygen had undergone an exchange of oxygen with the unlabeled water. The only way for this exchange to occur was for the reaction to proceed through an intermediate in which the carbonyl oxygen was no longer doubly bonded. The only reasonable way for an exchange of labels to occur is through the tetrahedral intermediate of the first proposed mechanism.

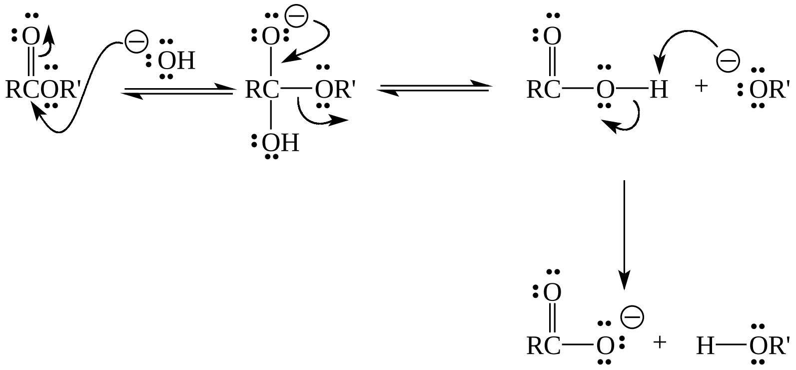


Chemists concluded that ester hydrolysis is the reverse reaction of the formation of an ester. In an ester hydrolysis, the ester reacts with an excess of water and an acid catalyst. The thermodynamics of the reaction requires that the reverse reaction proceed through the same set of intermediates (in reverse order) as the forward reaction. Of course, that also assumes identical reaction conditions. These reaction requirements illustrate the principle of microscopic reversibility.

Exercise 8.4

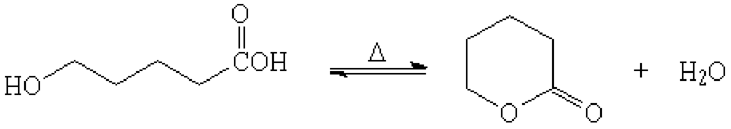
A proposed experiment to distinguish between the two mechanisms for the hydrolysis of an ester might be to label the *other* oxygen in the ester. Write a mechanism for the hydrolysis of ethyl benzoate with the ethoxy oxygen labeled with ^{18}O using both mechanisms above. Would this help to confirm one mechanism or the other? Why or why not?

Base assisted ester hydrolysis follows much the same pathway as acid catalyzed hydrolysis. With base, the first step is the reaction of an ester in a nucleophilic reaction of the base at the carbonyl carbon. This is followed by loss of the alkoxide ion. Finally, a proton exchange leaves the alcohol and the carboxylate anion product. Little reverse reaction takes place because the alcohol is too weak of a nucleophile to react with the carboxylate anion. Because of the lack of a reverse reaction chemists prefer using the base assisted ester hydrolysis to the acid-catalyzed hydrolysis.



A lactone is a cyclic ester in which the atoms of the ester functional group are part of the ring.

Lactones are cyclic esters. The formation of five- or six-membered lactone rings occurs from compounds containing a hydroxy group and a carboxylic acid group.



5-Hydroxypentanoic acid

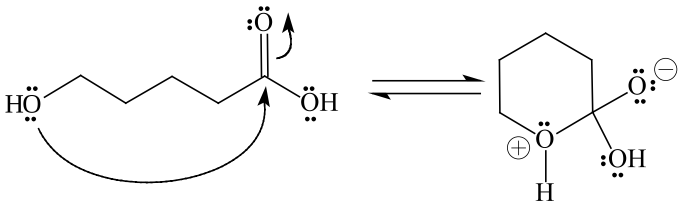
5-Hydroxypentanoic acid lactone
(δ-Valerolactone)
(86%)

In these reactions the equilibrium is more favorable than other reactions of alcohols and carboxylic acids. There is a preference for five- and six-membered rings because those ring sizes are low in ring strain and thus quite easy to form. This is a theme you will see repeatedly throughout organic chemistry.

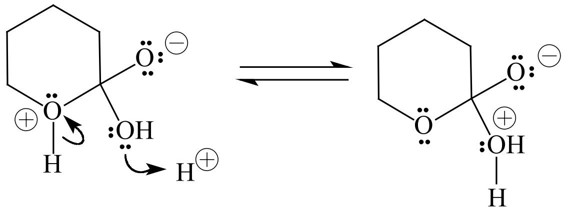
Solved Exercise 8.1

Write a mechanism showing the formation of 5-hydroxypentanoic acid lactone.

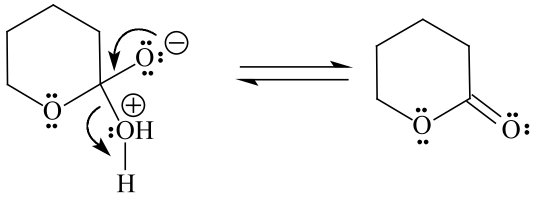
Solution
The first step in the mechanism is a 1,3-electron pair displacement reaction initiated by the —OH group on C5 on the carbonyl carbon.



The next step in the mechanism is a proton transfer, moving a proton from one oxygen to another.



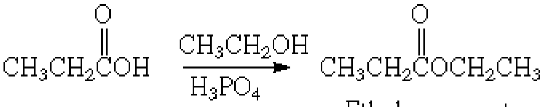
The loss of the —$^{\oplus}OH_2$ group from the cyclic intermediate formed above produces the final product.



The reactions of both water and an alcohol with other members of the carboxylic acid family are mechanistically identical to the reaction described in **Solved Exercise 8.1**. Water and alcohols react very rapidly with acyl halides and almost as fast with anhydrides. In both cases the leaving group is a very stable anion. It is either a halide or carboxylate ($RCOO^{\ominus}$) anion.

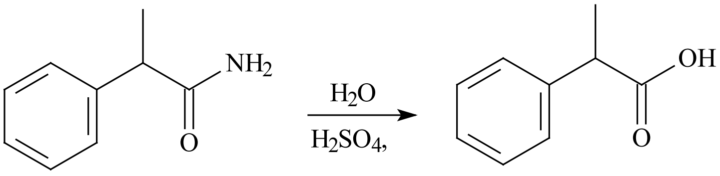
Amides are much less reactive than any of the other carboxylic acid derivatives. Hydrolysis of an amide with either an acid or a base requires heat and a longer reaction time than does an ester when producing a carboxylic acid.

Some examples of the reaction of carboxylic acid derivatives with water and alcohols are following.

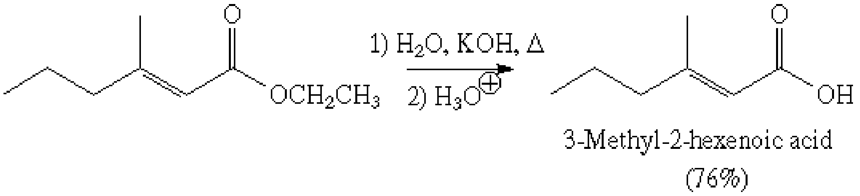


$$CH_3CH_2\overset{\overset{O}{\|}}{C}OH \xrightarrow[H_3PO_4]{CH_3CH_2OH} CH_3CH_2\overset{\overset{O}{\|}}{C}OCH_2CH_3$$

Ethyl propanoate
(79%)



2-Phenyl propanoic acid
(87%)

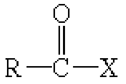


Exercise 8.5

Write a mechanism for the hydrolysis of acetamide (CH_3CONH_2) in aqueous acid.

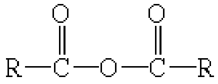
8.3 Halide and Carboxylic Acid Nucleophiles

Acyl halides and anhydrides are the most reactive members of the carboxylic acid family of derivatives because they have the most stable leaving groups. The leaving group for an acyl halide is a halide anion (e.g., $Cl^{\ominus}$), and the leaving group for an anhydride is a carboxylate anion ($RCOO^{\ominus}$).



Acyl halide

$$R-\overset{O}{\overset{\|}{C}}-X$$



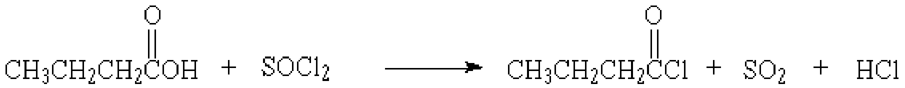
Anhydride

$$R-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-R$$

The leaving group of an acyl halide is the conjugate base of a very strong acid ($pK_a < 1$). In comparison, the leaving group of an anhydride is the conjugate base of a much weaker acid ($pK_a \sim 5$). Thus, the position of equilibrium for nucleophilic substitution is more favorable for an acyl halide than for an anhydride. Because of their reactivity, chemists usually synthesize either acyl halides or anhydrides as reactive intermediates rather than end products.

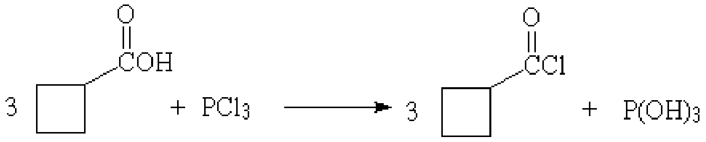
The only acyl halides that chemists generally use are the acyl chlorides. Acyl bromides and acyl iodides are more expensive to make, more unstable as compounds, and more difficult to handle than are the acyl chlorides, so they give little advantage over acyl chlorides. Chemists use acyl fluorides even less than acyl bromides and acyl iodides.

To synthesize acyl chlorides from carboxylic acids, chemists use either thionyl chloride, $SOCl_2$, or one of the phosphorus chlorides, PCl_3 or PCl_5. All of these reagents are the acid halides of an inorganic acid.

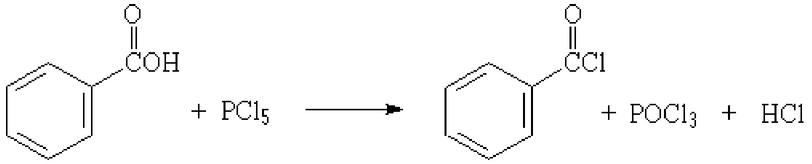


$$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OH + SOCl_2 \longrightarrow CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}Cl + SO_2 + HCl$$

Butanoyl chloride
(89%)

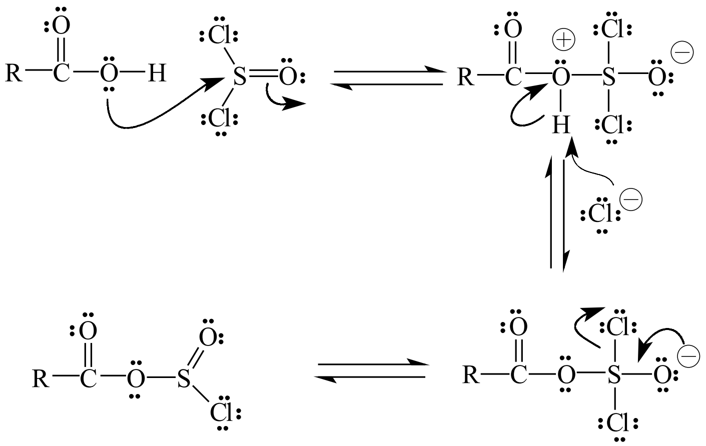


Cyclobutanecarbonyl chloride
(92%)

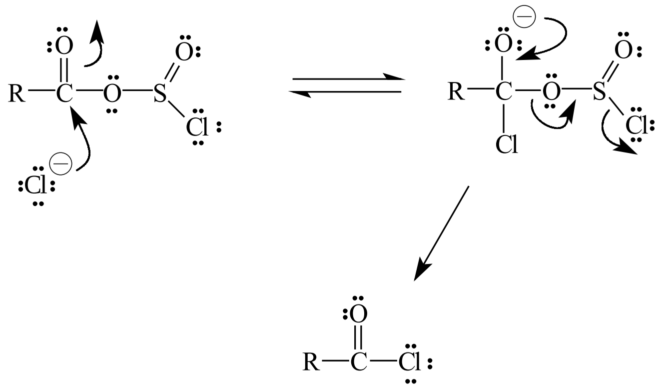


Benzoyl chloride
(98%)

The following reaction of a carboxylic acid with thionyl chloride shows the mechanism for the preparation of an acyl halide. The reaction first produces a mixed anhydride consisting of the organic acid and the inorganic acid chloride. Note that this mechanism is an equivalent of a nucleophilic substitution reaction on the sulfur oxygen double bond.



The reaction then follows a typical nucleophilic substitution on the carbonyl.

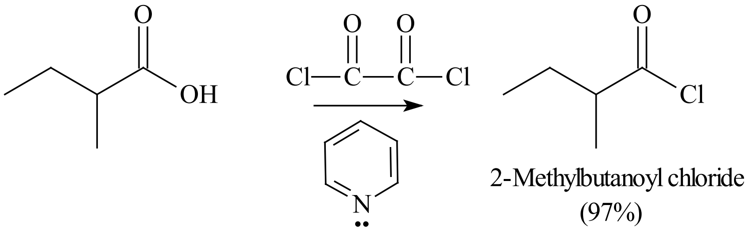


As the reaction progresses, the sulfur leaves as SO_2, and the second chloride leaves as HCl. Because both of these products are gasses, they readily bubble out of the reaction solution. Once the evolution of the gasses stops, the chemist distills the excess thionyl chloride (b.p. 76°C) from the reaction mixture leaving relatively pure acyl chloride. Because of the ease of reaction, chemists prefer thionyl chloride as the reagent for the preparation of acid chlorides. This reaction substitutes the —OH group of the original carboxylic acid with a Cl, an extremely good leaving group. The compound is now ready to act as an intermediate in another reaction.

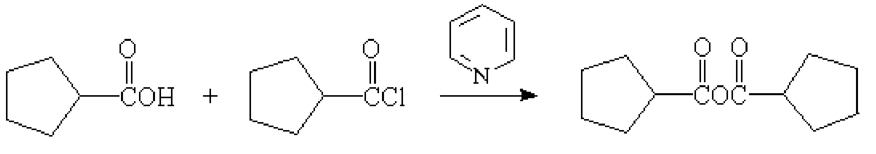
Exercise 8.6

Write a detailed mechanism for the reaction of butanoic acid with phosphorus trichloride.

Oxalyl chloride (ClCOCOCl) is fast becoming the reagent of choice for the synthesis of acyl chlorides. It is easier to handle and use than thionyl chloride or the phosphorus chlorides. Like thionyl chloride, the by-products are CO_2, CO, and HCl.

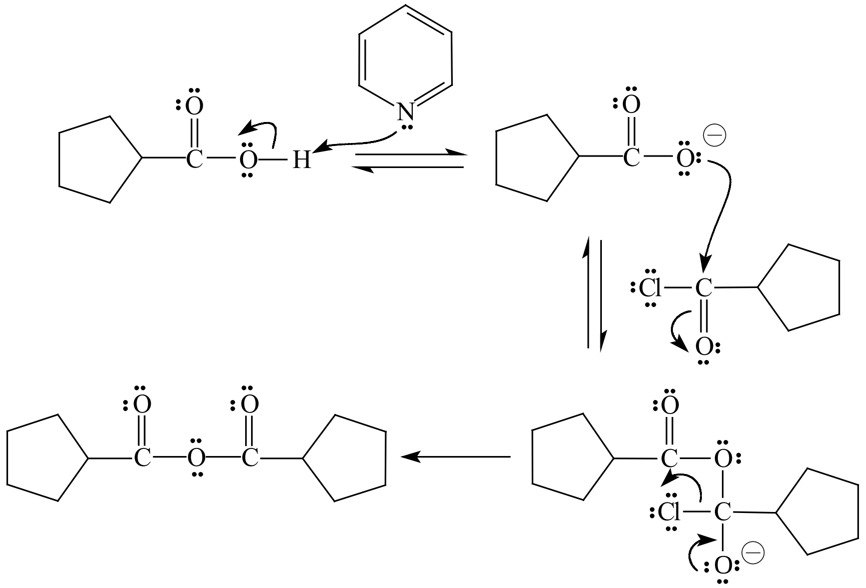


Chemists make only a limited number of anhydrides because acyl halides are more readily available and more reactive than the anhydrides. Also, most subsequent reactions involving anhydrides use only one of the two acyl groups. That means half of a potentially expensive, or scarce, starting material must be discarded. However, preparing anhydrides is simple. The preparation involves the reaction of an acyl halide with a carboxylic acid in the presence of a non-nucleophilic base such as pyridine.

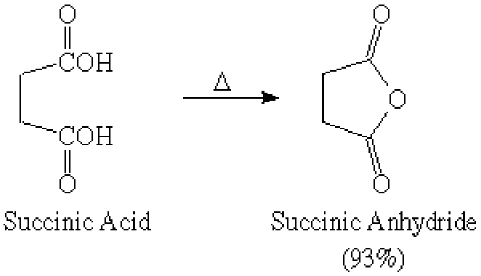


Cyclopentanecarboxylic anhydride
(95%)

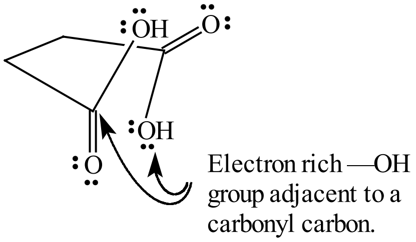
The mechanism for the formation of an anhydride is another example of the acyl transfer mechanism. A weak base, like pyridine, reacts with the acidic proton of the carboxylic acid forming a carboxylate anion. The negatively charged oxygen reacts with the carbonyl carbon of the acyl halide. The resulting tetrahedral intermediate loses a chloride ion forming the anhydride.



Heating two molecules of a carboxylic acid together to form an anhydride with loss of a molecule of water seems like a plausible reaction pathway. However, simply heating the carboxylic acids does not produce an anhydride, except when the reaction can form a five- or six-membered ring.

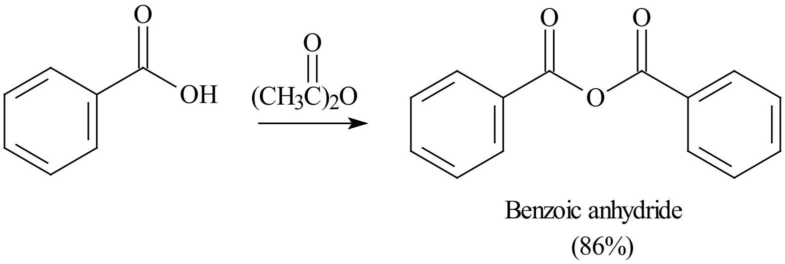


Beyond the heating, two important factors in the formation of five- and six-membered cyclic anhydrides are the stability of those sized rings and the proximity effect. For example, an important conformation of succinic acid and glutaric acid (pentanedioic acid) brings the two carboxylic acid groups close together—much closer than is normal for two separate molecules. Thus, the apparent concentration of the carboxylic acid group is very high, pushing the equilibrium towards completion of the reaction. As shown below, the —OH groups of succinic acid are close to the electron deficient carbonyl carbons.



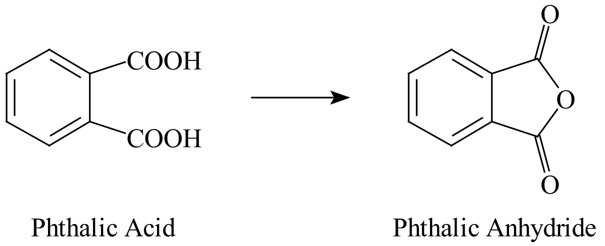
An anhydride exchange reaction involves reacting an available anhydride with a carboxylic acid to form a new anhydride.

Many anhydrides form via an **anhydride exchange**. An anhydride exchange involves heating the relatively inexpensive acetic anhydride with a carboxylic acid. Because acetic acid boils at a lower temperature than nearly all other carboxylic acids, it distills from the reaction mixture to make the equilibrium more favorable.



Exercise 8.7

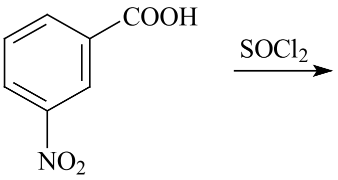
Propose a mechanism for the thermal dehydration of phthalic acid (benzene-1,2-dicarboxylic acid) to its anhydride.



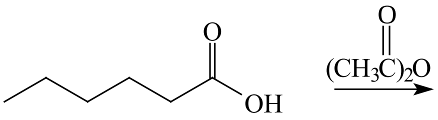
Exercise 8.8

Predict the major products of each of the following reactions.

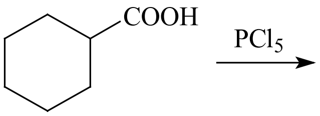
a)



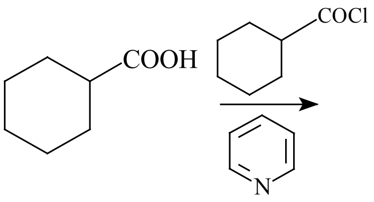
b)



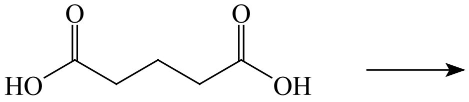
c)



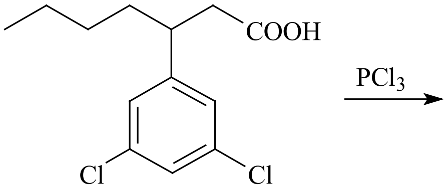
d)



e)

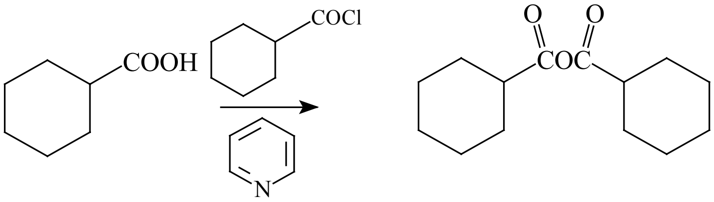


f)



Sample Solution

d)



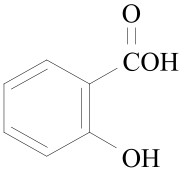
[SIDEBAR]

Aspirin and Acetaminophen

Aspirin and acetaminophen are two examples of compounds known as analgesics. An analgesic is a painkiller. There are two classes of analgesics: (1) those that act at the site of the pain and (2) those that act on the central nervous system to modify the brain's processing of the pain signals.

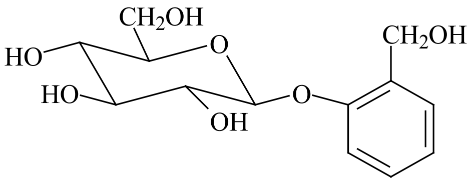
Analgesics that act on the brain generally alter the mood and become addictive. Examples of addictive analgesics are morphine, codeine, and heroin. Analgesics that act on the site of the pain do not alter the mood directly nor are they addictive. Examples of non-addictive analgesics are aspirin and acetaminophen.

Many of the milder non-addictive analgesics on the market are derivatives of salicylic acid.



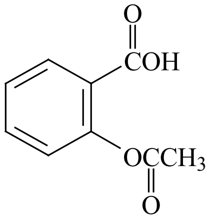
Salicylic acid

At first, chemists derived salicylic acid from the glycoside salicin. A glycoside consists of a non-sugar organic molecule attached to some sugar. Salicin is a naturally occurring substance found in the bark of the sweet, or white, willow tree (*Salix alba*).



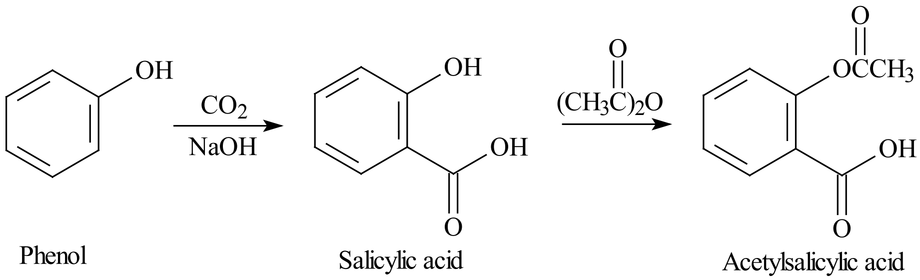
Salicin

From the time of the ancient Greeks, people have used willow bark preparations as pain relievers. Because these willow bark preparations were very bitter, they were typically used externally. In addition, taking salicylic acid internally also caused a number of side effects. However, converting salicylic acid to acetylsalicylic acid takes care of most of the side effects. Acetylsalicylic acid was marketed as aspirin in 1899.

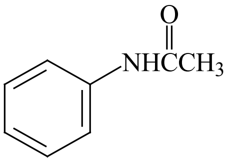


Acetylsalicylic acid
(Aspirin)

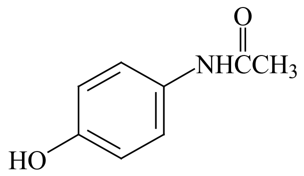
The synthesis of aspirin starts with phenol. Phenol is reacted with CO_2 to form salicylic acid. Then salicylic acid is reacted with acetic anhydride to form acetylsalicylic acid.



Acetaminophen is not a naturally occurring substance. It was only by accident that chemists discovered its analgesic properties. This accident occurred when a pharmacist added acetanilide to a patient's prescription by mistake.

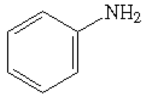


Acetanilide



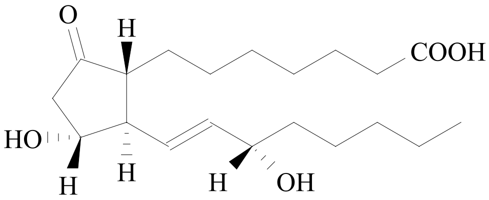
Acetaminophen

The structure of aniline is:



Acetanilide is toxic. In a person's body, part of the acetanilide converts to acetaminophen, accounting for its analgesic properties, but another portion converts to **aniline**, which is toxic. With the discovery of acetaminophen's analgesic properties, chemists began looking for some less toxic way of providing acetaminophen to the body.

The molecular shapes of aspirin and acetaminophen are quite similar. Because of this similarity, the enzyme *prostaglandin cyclooxygenase* recognizes both, allowing both to inhibit its function. Prostaglandin cyclooxygenase aids the body in the production of prostaglandins, and prostaglandins possess a remarkable variety of actions. One of the body processes involving prostaglandins is the modification of the signals, particularly pain signals, transmitted across the synapses. Another possible process may be the dilation of blood vessels that cause the pain associated with headaches, if the vessels are within the skull, or with the pain associated with migraines, if the vessels are external to the skull. Analgesics such as aspirin and acetaminophen inhibit the synthesis of these prostaglandins; thus, inhibiting the transmission of pain or the dilation of the blood vessels.

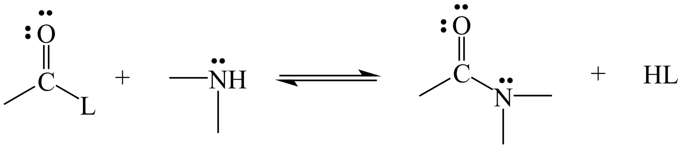


A typical prostaglandin (PGE_1)

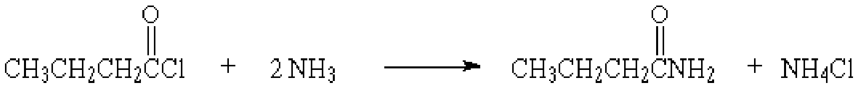
8.4 Reaction with Nitrogen Nucleophiles

The nitrogen nucleophiles studied most in carbonyl chemistry are ammonia (NH_3), primary amines (RNH_2), and secondary amines

(R_2NH). All react with carboxylic acid and its derivatives to produce amides.

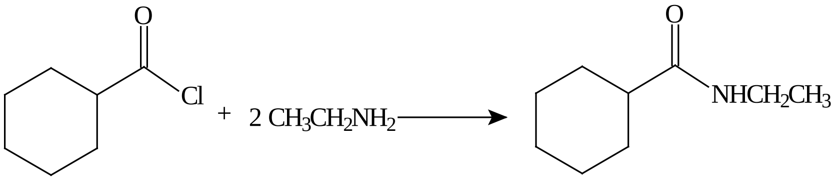


The most common method used to prepare amides is the reaction of a carboxylic acid or an acyl halide with ammonia or an amine. This procedure gives excellent yields of product with the addition of an extra mole of the amine, or a mole of some other base that is less nucleophilic than the amine. This extra base neutralizes the hydrogen halide that the reaction produces.



$$\mathrm{CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}Cl + 2\,NH_3 \longrightarrow CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}NH_2 + NH_4Cl}$$

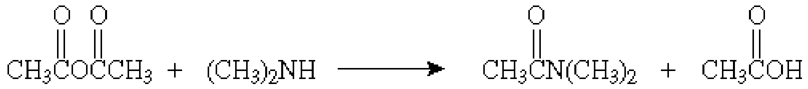
Butanamide
(99%)



N-Ethylcyclohexanecarbamide
(97%)

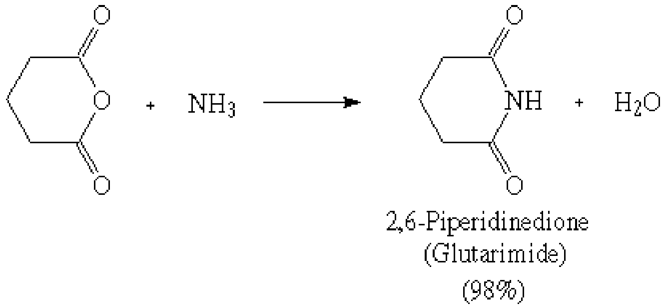
$+\ \mathrm{CH_3CH_2\overset{\oplus}{N}H_3\ \ Cl^{\ominus}}$

Acid, or acyl, anhydrides react in similar ways to acyl halides, but are less reactive.

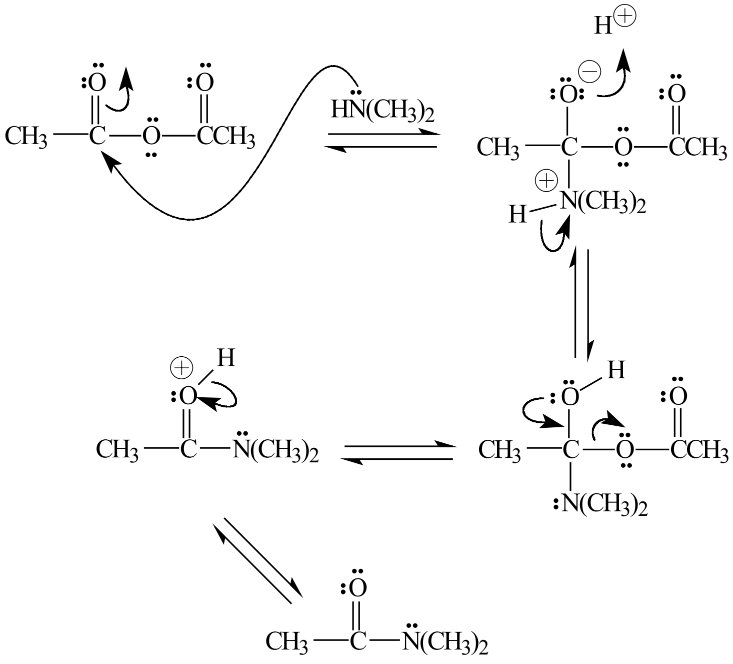


$$\mathrm{CH_3\overset{\overset{O}{\|}}{C}O\overset{\overset{O}{\|}}{C}CH_3 + (CH_3)_2NH \longrightarrow CH_3\overset{\overset{O}{\|}}{C}N(CH_3)_2 + CH_3\overset{\overset{O}{\|}}{C}OH}$$

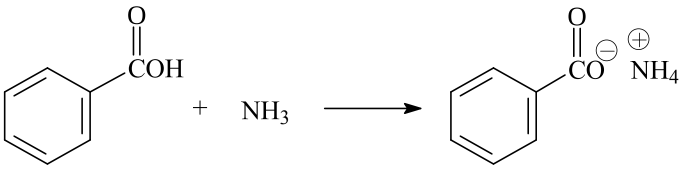
N,*N*-Dimethylethanamide
(85%)



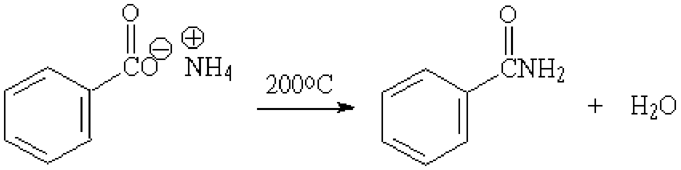
The mechanism for the formation of an amide by the reaction of an amine with an acid anhydride is similar to the mechanisms presented earlier. The amine nitrogen reacts with a carbonyl carbon to form a tetrahedral intermediate. The tetrahedral intermediate loses a carboxylate ion to form the amide.



Amides can also be synthesized from the direct reaction of an amine with a carboxylic acid. In this reaction, the amine forms a salt with the carboxylic acid because the amine is a good base.



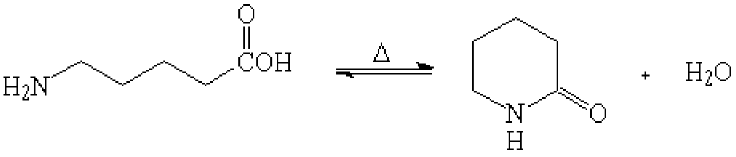
The water is then removed from the ammonium salt to produce the corresponding amide. Dehydration requires a high temperature. This type of thermal dehydration is useful in industrial synthesis, but chemists seldom use it in the laboratory. It is easier and cheaper to control a high temperature synthesis on an industrial scale than on a laboratory scale.



Benzamide
(79%)

A lactam is a cyclic amide in which the atoms of the amide functional group are part of the ring.

Lactams are cyclic amides. These five- and six-membered rings form easily from compounds that contain an amino group and a carboxylic acid group. The equilibrium reaction of a lactam is more favorable than the other reactions of amines and carboxylic acids.



5-Aminopentanoic acid lactam
(2-Piperidone)
(64%)

Exercise 8.9

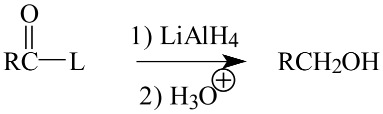
Propose a mechanism for the reaction of ammonia with acetic anhydride.

8.5 Reaction with the Hydride Nucleophile

Chapter 7 discusses the reactivity of lithium aluminum hydride and sodium borohydride, two complex metal hydrides, with aldehydes and ketones. These two compounds also react with the carbonyl group of the carboxylic acid family. Lithium aluminum hydride is much more reactive than sodium borohydride but, because of its decreased reactivity, sodium borohydride is much more selective than lithium aluminum hydride. The usual course of reaction of these complex

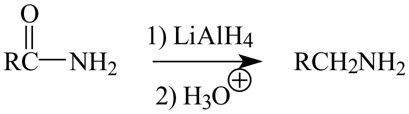
See Section 7.7, page 000 for a discussion of the relative reactivities of sodium borohydride and lithium aluminum hydride.

metal hydrides with a carboxylic acid is a reduction reaction. This reduction reaction is a two step process. The hydride first initiates a nucleophilic substitution followed by the loss of the leaving group to form an aldehyde or ketone. A second hydride reacts with this ketone or aldehyde to form an alcohol. The lithium aluminum hydride reduction reaction of all carboxylic acid derivatives, except the amides, forms primary alcohols.



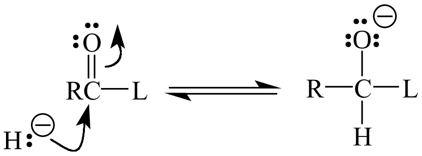
$$\mathrm{R}\overset{\overset{\displaystyle O}{\|}}{\mathrm{C}}-\mathrm{L}\ \xrightarrow[\text{2) } H_3O^{\oplus}]{\text{1) } LiAlH_4}\ RCH_2OH$$

Amides react with $LiAlH_4$ to form amines.

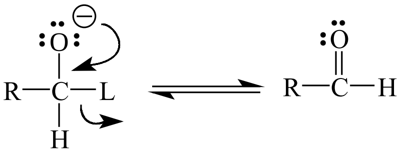


$$\mathrm{R}\overset{\overset{\displaystyle O}{\|}}{\mathrm{C}}-NH_2\ \xrightarrow[\text{2) } H_3O^{\oplus}]{\text{1) } LiAlH_4}\ RCH_2NH_2$$

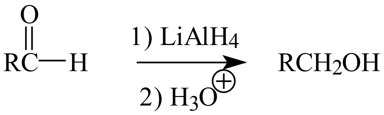
A reduction reaction proceeds in two steps. The first step is the now familiar reaction of the nucleophile with the electrophilic carbonyl carbon. In this case, the nucleophile is a hydride ion.



The tetrahedral intermediate is unstable, so the leaving group departs. The tetrahedral intermediate then forms an aldehyde, because the leaving group is a weaker base than the hydride ion.

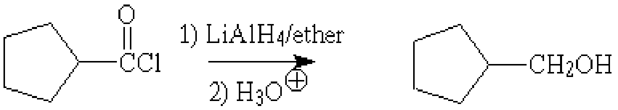


In the second step, the aldehyde immediately reacts to form an alcohol because the aldehyde is *more* reactive than the starting carboxylic acid derivative. The aldehyde intermediate reacts so rapidly with $LiAlH_4$ to form the alcohol that it is impossible to isolate the aldehyde.

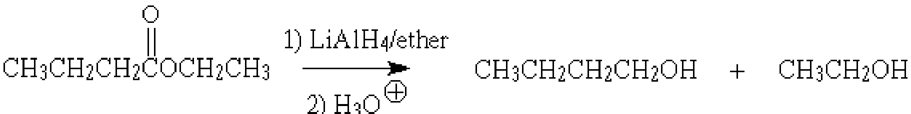


$$\overset{\displaystyle O}{\overset{\|}{RC}}{-}H \xrightarrow[2)\ H_3O^{\oplus}]{1)\ LiAlH_4} RCH_2OH$$

In practice, chemists start the reaction in anhydrous ethyl ether. After the reaction proceeds for a period of time, they add aqueous acid to protonate the conjugate bases of the products. Here are examples of the reaction of lithium aluminum hydride with an acyl halide and an ester.



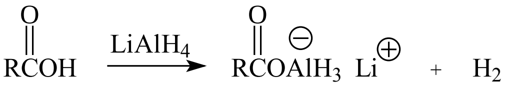
Cyclopentylmethanol
(71%)



$$CH_3CH_2CH_2\overset{\displaystyle O}{\overset{\|}{C}}OCH_2CH_3 \xrightarrow[2)\ H_3O^{\oplus}]{1)\ LiAlH_4/ether} CH_3CH_2CH_2CH_2OH + CH_3CH_2OH$$

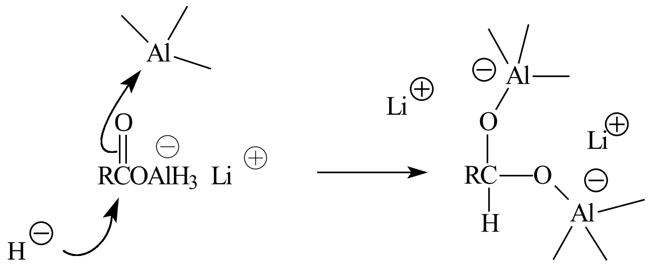
1-Butanol
(92%)

When lithium aluminum hydride reacts with a carboxylic acid in an acid-base reaction, the hydride ion is a strong base. The hydride ion reacts with the acidic hydrogen in an exothermic reaction to produce hydrogen gas. In the process, the carboxylic acid consumes one hydride from the $LiAlH_4$.

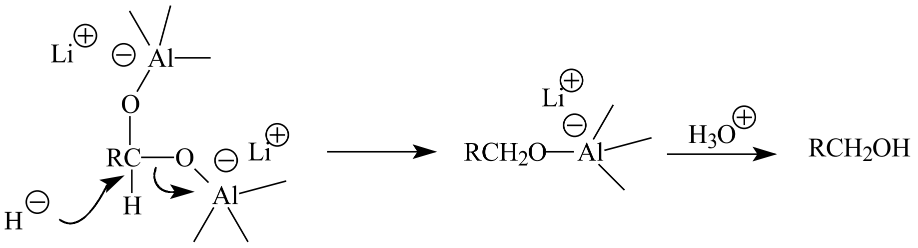


$$R\overset{\displaystyle O}{\overset{\|}{C}}OH \xrightarrow{LiAlH_4} R\overset{\displaystyle O}{\overset{\|}{C}}O\overset{\ominus}{Al}H_3\ Li^{\oplus} + H_2$$

This reaction produces a negatively charged ion. Any subsequent reduction reaction involving the carbonyl group of the product requires a nucleophile strong enough to react with the carbonyl carbon despite the negative charge of the product above. Lithium aluminum hydride is strong enough to react with the carbonyl carbon, but there is a complication. The initial product is usually insoluble in the reaction mixture, thus, the rate of reaction with the hydride ion is greatly reduced.

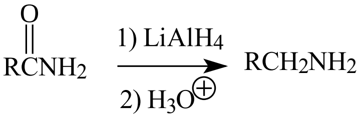


Next, the reaction mixture is treated with dilute aqueous acid to produce an alcohol product.



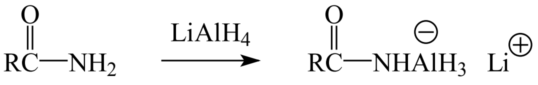
Because of the insolubility of the negatively charged ion and the subsequent slowness of reaction, chemists find it much easier to convert the carboxylic acid to a methyl or ethyl ester before reduction with a hydride. Converting to a methyl or ethyl ester also produces a better yield.

The reduction reaction of an amide with lithium aluminum hydride produces an amine.



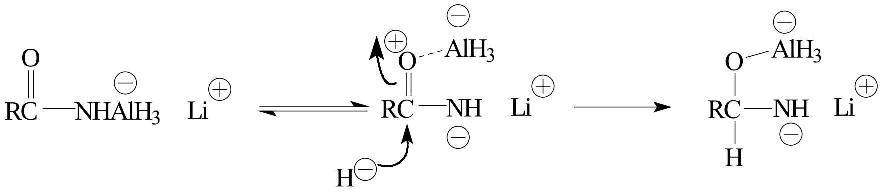
$$RC(=O)NH_2 \xrightarrow[2)\ H_3O^{\oplus}]{1)\ LiAlH_4} RCH_2NH_2$$

The mechanism for this transformation is not well known, but chemists widely agree that it follows a pathway via an imine. As with the reduction of carboxylic acids, the first step is an acid-base reaction between a hydride and a proton on the nitrogen to form hydrogen and an amide salt.

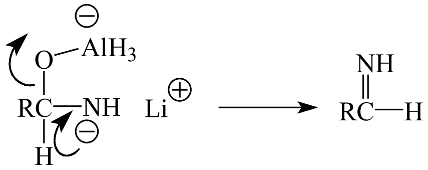


$$RC(=O)—NH_2 \xrightarrow{LiAlH_4} RC(=O)—\overset{\ominus}{N}HAlH_3\ \ Li^{\oplus}$$

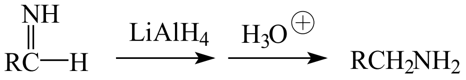
The amide salt rearranges; thus, allowing for a subsequent reaction with the hydride. This reaction forms the tetrahedral intermediate.



Because oxygen is a better leaving group than nitrogen, the intermediate loses oxygen to form an imine.

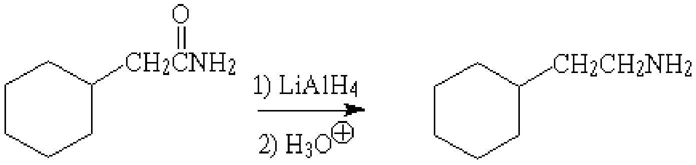


Then, because the imine is more reactive than an aldehyde, it reduces to the amine as soon as it forms.

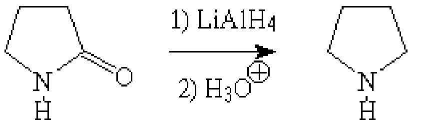


$$RCH{=}NH \xrightarrow{LiAlH_4} \xrightarrow{H_3O^{+}} RCH_2NH_2$$

This reaction is an excellent synthesis of amines as it easily produces a variety of amines. Following are some examples.



2-Cyclohexylethanamine
(95%)

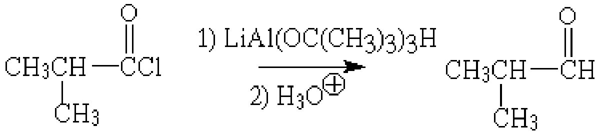


Pyrrolidine
(81%)

Chemists have found a way to prepare an aldehyde from an acyl halide. They commonly use lithium tri-*tert*-butoxyaluminum hydride ($LiAl(OC(CH_3)_3)_3H$). First, they synthesize $LiAl(OC(CH_3)_3)_3H$ by adding *tert*-butyl alcohol to $LiAlH_4$.

$$\mathrm{LiAlH_4 \;+\; 3\;(CH_3)_3COH \longrightarrow LiAl(OC(CH_3)_3)_3H \;+\; 3\;H_2}$$

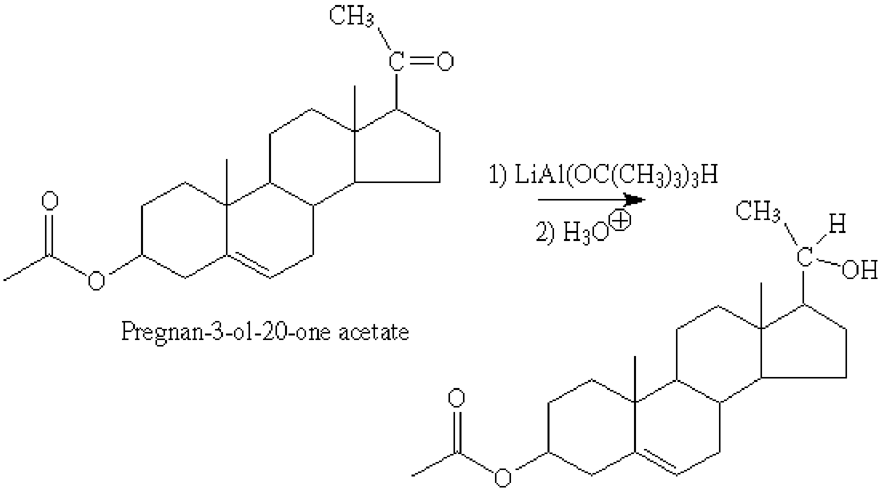
In this reaction the bulky *tert*-butoxy groups replace three of the original four hydrides. The product, lithium tri-*tert*-butoxyaluminum hydride, is much less reactive and more selective as a reducing agent than is lithium aluminum hydride. It is more selective because the *tert*-butoxy groups are very large, making the transfer of the hydride more difficult than with $LiAlH_4$. In addition, the oxygens of the *tert*-butoxy groups are electron withdrawing which deactivates the hydride. After completing the synthesis of lithium tri-*tert*-butoxyaluminum hydride, the chemists react it with an acyl halide to get an aldehyde. This procedure, developed by H. C. Brown of Purdue University, gives good yields of aldehydes from a variety of acyl chlorides.



$$\mathrm{CH_3CH(CH_3)\!-\!\overset{O}{\overset{\|}{C}}Cl \xrightarrow[2)\ H_3O^{\oplus}]{1)\ LiAl(OC(CH_3)_3)_3H} CH_3CH(CH_3)\!-\!\overset{O}{\overset{\|}{C}}H}$$

2-Methylpropanal
(74%)

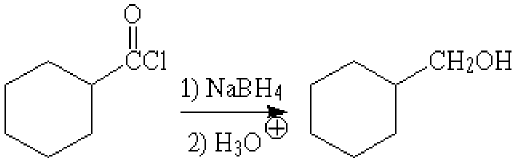
The use of lithium tri-*tert*-butoxyaluminum hydride allows selective reduction of one carbonyl group in a complex molecule containing more than one carbonyl group. For example, pregnan-3-ol-20-one acetate, a steroid molecule, contains both a ketone and an ester. Because of the selectivity of lithium tri-*tert*-butoxyaluminum hydride, only the ketone is reduced.



Pregnan-3-ol-20-one acetate

3-Acetoxypregnanediol
(73%)

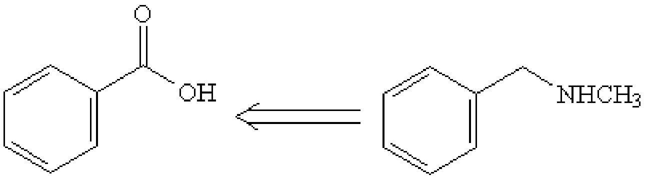
Sodium borohydride is a much weaker hydride donor than lithium aluminum hydride. The only carboxylic acid derivatives that sodium borohydride reduces are the acyl halides.



Cyclohexylmethanol
(86%)

Solved Exercise 8.2

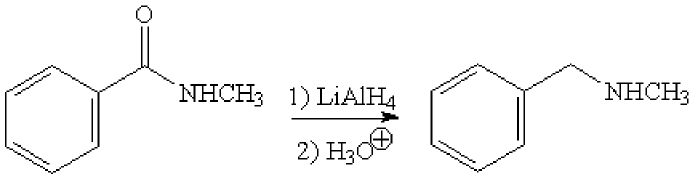
Propose a synthesis of the *N*-methylbenzyl amine from benzoic acid.



Benzoic acid

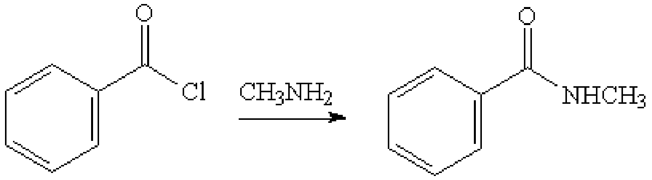
N-Methylbenzyl amine

Solution
The only method for synthesizing an amine from a carboxylic acid is via an amide that is reduced by $LiAlH_4$. *N*-Methylbenzamide reacts with $LiAlH_4$ to produce *N*-methylbenzyl amine.



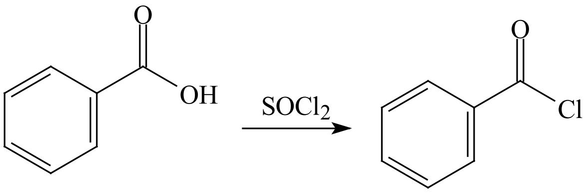
N-Methylbenzamide *N*-Methylbenzyl amine

N-Methylbenzamide is prepared, in turn, by a reaction of benzoyl chloride with methylamine.



Benzoyl chloride *N*-Methylbenzamide

Benzoyl chloride is synthesized from benzoic acid by reaction with thionyl chloride.

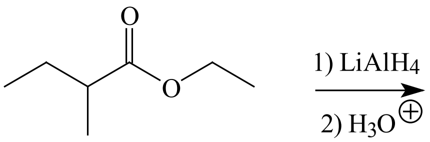


Benzoic acid Benzoyl chloride

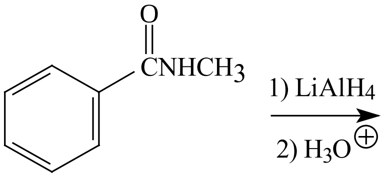
Exercise 8.10

Predict the major products of each of the following reactions.

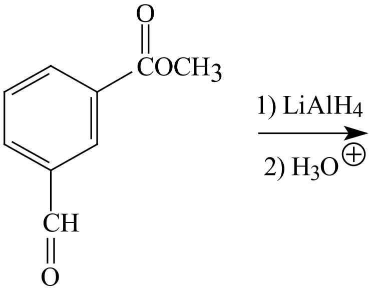
a)



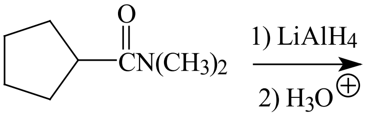
b)



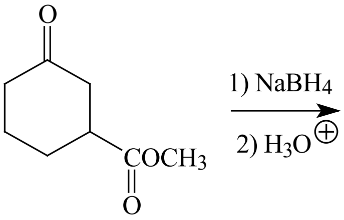
c)



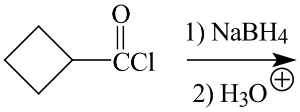
d)



e)

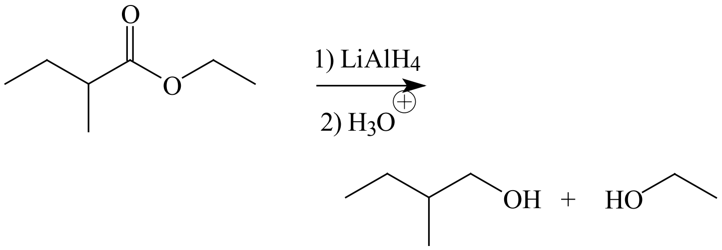


f)



Sample Solution

a)

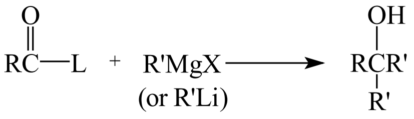


8.6 Carbon Nucleophiles

Section 7.8 begins on page 000.

Section 7.8 introduces organometallic reagents as a major source of carbon nucleophiles in reactions that involve carbonyl groups and shows how they react with aldehydes and ketones. This section discusses organometallic reactants in reactions with the carbonyl group of carboxylic acids and their derivatives. With these reactions, chemists commonly use Grignard and organolithium reagents. Both reagents react readily with members of the carboxylic acid family.

The reactions of organometallic reagents with carboxylic acids and carboxylic acid derivatives illustrate the concept of selectivity in organic reactions. When organometallic reagents react with carboxylic acids and carboxylic acid derivatives, they form one of two possible products depending on the organometallic reagent and the substrate. Organomagnesium compounds and organolithium compounds react with carboxylic acid derivatives to form alcohols.



$$\mathrm{R\overset{\overset{O}{\|}}{C}{-}L} + \underset{\text{(or R'Li)}}{\text{R'MgX}} \longrightarrow \mathrm{R\overset{\overset{OH}{|}}{\underset{\underset{R'}{|}}{C}}R'}$$

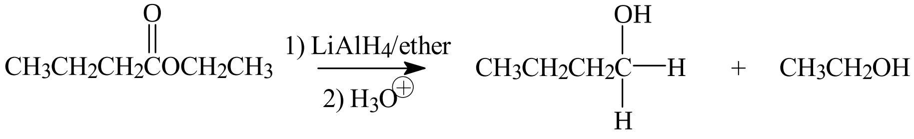
Organolithium compounds, but not Grignard reagents, react with carboxylic acids to form aldehydes or ketones.

$$\mathrm{R\overset{\overset{O}{\|}}{C}{-}OH} + \text{R'Li} \longrightarrow \mathrm{R\overset{\overset{O}{\|}}{C}R'}$$

Of the reactions that form alcohols, the ones involving acyl halides and anhydrides have limited synthetic utility due to their rapid reaction rates. Depending on the structure of the substrate, the reactions also tend to give many undesirable side reactions.

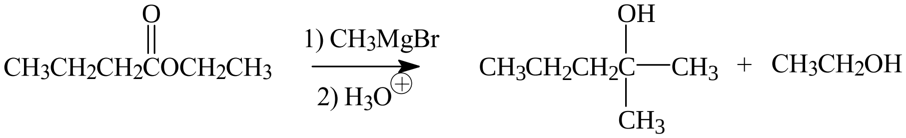
See Section 8.5, page 000 for the reaction of metal hydrides with carboxylic acid derivatives..

Esters react with Grignard reagents in much the same way that they react with metal hydrides. To see this similarity, compare the following reactions:



$$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3 \xrightarrow[2)\ H_3O^{\oplus}]{1)\ LiAlH_4/ether} CH_3CH_2CH_2\underset{H}{\overset{OH}{C}}-H + CH_3CH_2OH$$

1-Butanol
(92%)

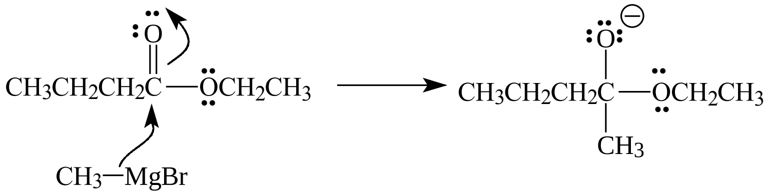


$$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3 \xrightarrow[2)\ H_3O^{\oplus}]{1)\ CH_3MgBr} CH_3CH_2CH_2\underset{CH_3}{\overset{OH}{C}}-CH_3 + CH_3CH_2OH$$

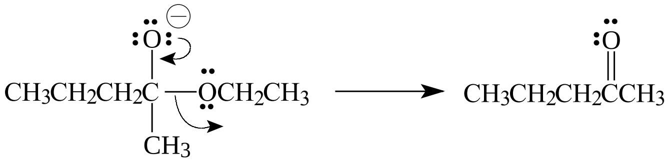
2-Methyl-2-pentanol
(85%)

The first is the reaction of an ester, ethyl butanoate, with lithium aluminum hydride. This reaction produces 1-butanol via the addition of two hydrides to the carbonyl carbon. The second reaction involves the same ester, ethyl butanoate, but it is treated with a Grignard reagent, methyl magnesium bromide. This reaction produces 2-methyl-2-pentanol by adding two methyl groups to the carbonyl carbon.

The mechanisms for both reactions are very similar. For example, compare the following reaction for the ester and Grignard reaction with the mechanism for the ester and hydride reaction shown in Section 8.5. The first step in the ester Grignard reaction is the addition of the nucleophilic carbon to the carbonyl group forming a tetrahedral intermediate.

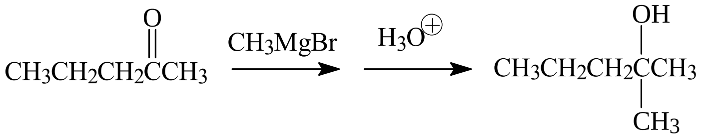


The ethoxy group is the best leaving group because it is a weaker base than the alkyl groups. Thus, the intermediate loses the ethoxy group and forms 2-pentanone.



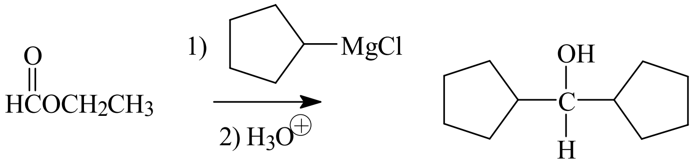
As with the hydrides, the reaction does not stop here. The 2-pentanone then reacts with *another* mole of the Grignard reagent to form the alkoxide which, after acidification, produces the final alcohol product. Ketones are much more reactive than the starting esters towards reaction with a Grignard reagent. Thus, the 2-pentanone reacts as soon as it forms. It usually is impossible to isolate the ketone intermediate.

Section 7.8, page 000, presents the mechanism for the reaction of a ketone with a Grignard reagent.

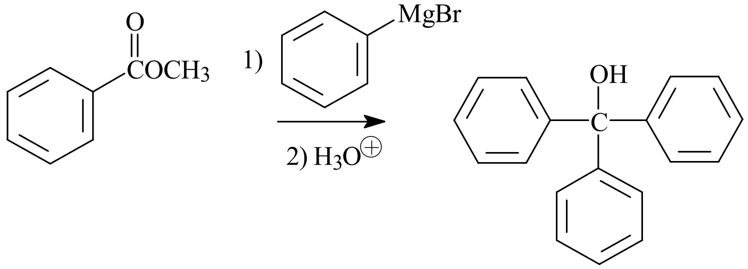


2-Methyl-2-pentanol
(85%)

Following are two other examples of this reaction.



Dicyclopentylmethanol
(94%)

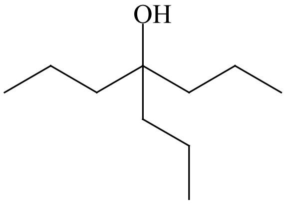


Triphenylmethanol
(89%)

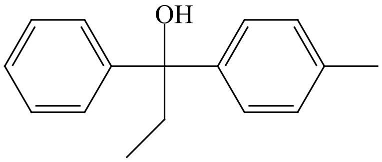
Solved Exercise 8.3

Consider the structures of the following tertiary alcohols. Some cannot be prepared by a Grignard reagent reaction with an ester. Which ones cannot? For those that can be prepared from an ester, what ester and Grignard reagent should be used?

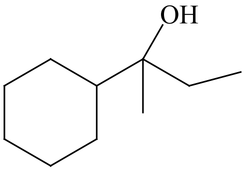
1)



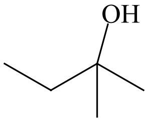
2)



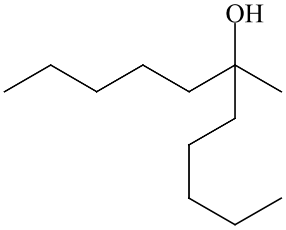
3)



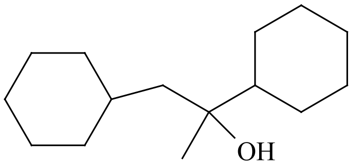
4)



5)

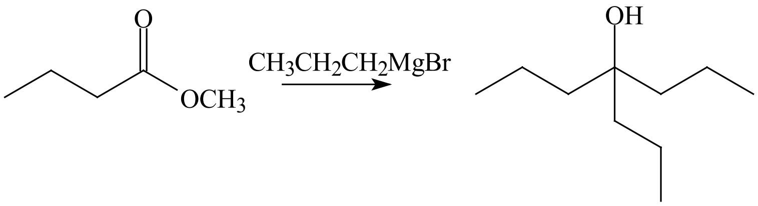


6)

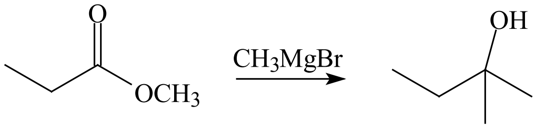


Solution

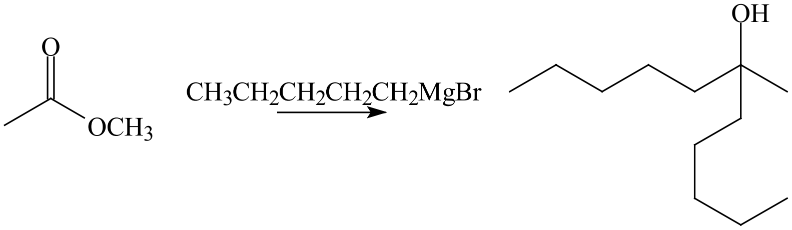
Two of the substituents must be the same to produce a tertiary alcohol by a Grignard reagent reacting with an alcohol. Alcohols 1, 4, and 5 can be synthesized in this way because they have two identical substituents.
Prepare compound 1 by reaction of propyl magnesium bromide with methyl butanoate.



Prepare compound 4 by reaction of methyl magnesium bromide with methyl propanoate.



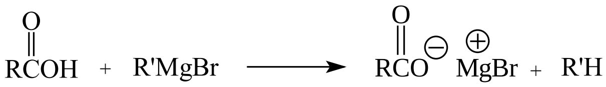
Prepare compound 5 by reaction of pentyl magnesium bromide with methyl acetate.



Exercise 8.11

Organolithium reagents react with esters in a similar manner to Grignard reagents. Predict the product formed from the reaction of ethyl lithium with methyl benzoate. Write a mechanism for this reaction.

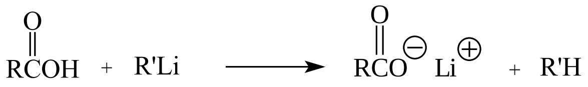
Some organometallic reagents react with carboxylic acids to form aldehydes and ketones. However, with Grignard reagents, the reaction is not very effective. The reaction proceeds very rapidly, producing a carboxylate salt that is insoluble in solution. The reaction usually stops at this point. Even in the presence of a large excess of Grignard reagent, only small amounts of the alkyl group add to the carbonyl group.



$$\mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{OH} + \mathrm{R'MgBr} \longrightarrow \mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{O}^{\ominus}\ \overset{\oplus}{\mathrm{MgBr}} + \mathrm{R'H}$$

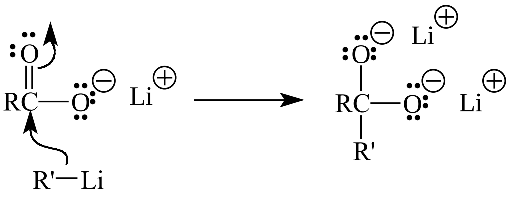
Because of the rapidity of this reaction, a Grignard reagent cannot react with another functional group when a carboxylic acid is present, even if the additional functional group is more reactive.

On the other hand, an organolithium reagent is more nucleophilic than a Grignard reagent. Thus, it is much more successful in taking a reaction with a carboxylic acid to the completion of the aldehyde or ketone formation. When mixed, the carboxylic acid and organolithium reagent immediately react to form a lithium salt much like the Grignard reagent.



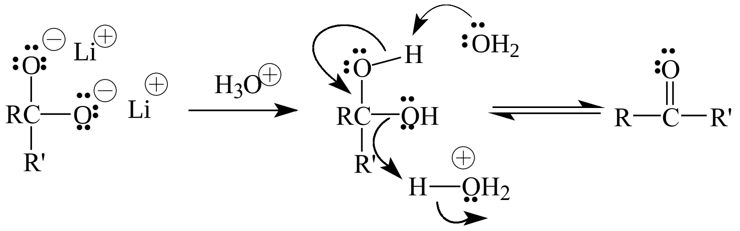
$$R\overset{O}{\overset{\|}{C}}OH + R'Li \longrightarrow R\overset{O}{\overset{\|}{C}}O^{\ominus}\ Li^{\oplus} + R'H$$

However, the reaction doesn't stop there. The organolithium compound has sufficient reactivity to add to the carbonyl group to form a dianion. An organolithium reagent is sufficiently reactive to react with a negatively charged species.



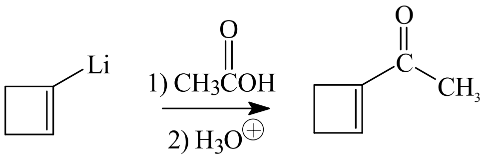
For more on hydrates, see Section 7.4, page 000.

After protonation, the dilithium salt forms an unstable hydrate of a ketone, which rapidly loses water to form a ketone.



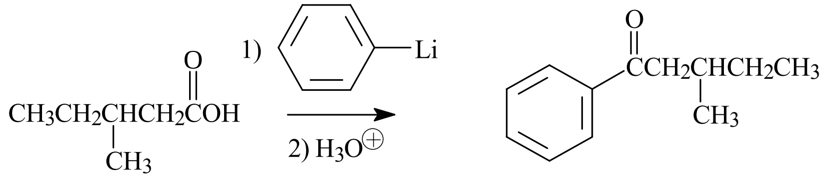
A reaction between a carboxylic acid and an organolithium reagent is very useful, as it directly converts the carbonyl group of a carboxylic acid to the carbonyl group of a ketone. This is a useful reaction in that it can readily form an unsymmetrical ketone.

The above conversion of a carboxylic acid to a ketone works well with all carboxylic acids except those with some other functional group that reacts with the lithium reagent. The following are two examples of organolithium and carboxylic acid reactions.



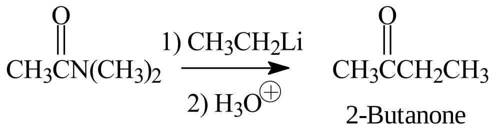
1-Cyclobutenyl methyl ketone

(67%)



3-Methyl-1-phenyl-1-pentanone
(79%)

Amides also react with organometallic compounds. When the amide has two alkyl groups on the nitrogen, the reaction forms a ketone.



$$CH_3\overset{O}{\overset{\|}{C}}N(CH_3)_2 \xrightarrow[2)\ H_3O^{\oplus}]{1)\ CH_3CH_2Li} CH_3\overset{O}{\overset{\|}{C}}CH_2CH_3$$

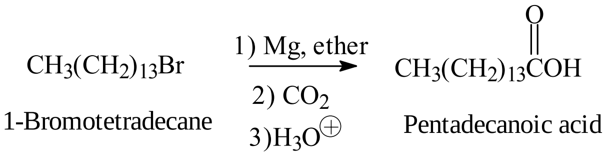
2-Butanone
(74%)

The presence of one or more hydrogens on the nitrogen complicates the reaction, because they are sufficiently acidic to react with both Grignard reagents and organolithium reagents, thus preventing the reaction from forming the ketone.

Solved Exercise 8.4

Fatty acids are long chain carboxylic acids found in a variety of biochemical sources. Most fatty acids contain an even number of carbon atoms. Those containing an odd number of carbon atoms are relatively rare. Propose a synthesis of pentadecanoic acid from myristic acid (tetradecanoic acid). (Needed information from Chapter 12: Reacting 1-tetradecanol with concentrated HBr accomplishes the synthesis of 1-bromotetradecane.)

Solution
This exercise requires that you propose a synthesis of a carboxylic acid by adding a carbon atom to the original molecule. The Grignard synthesis of a carboxylic acid is the best method to accomplish this purpose.

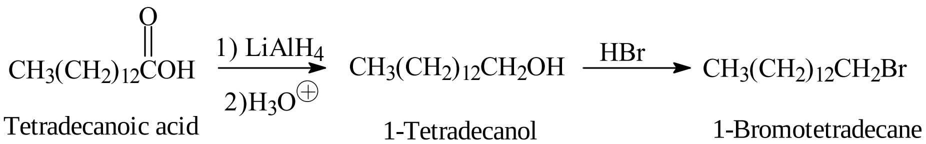


$$CH_3(CH_2)_{13}Br \xrightarrow[2)\ CO_2\quad 3)H_3O^{\oplus}]{1)\ Mg,\ ether} CH_3(CH_2)_{13}\overset{O}{\overset{\|}{C}}OH$$

1-Bromotetradecane

Pentadecanoic acid

Because you are told that 1-bromotetradecane is synthesized from 1-tetradecanol, completion of the synthesis requires making 1-tetradecanol. This is accomplished by reducing the original acid with $LiAlH_4$.



$$CH_3(CH_2)_{12}\overset{\overset{O}{\|}}{C}OH \xrightarrow[2)H_3O^{\oplus}]{1)\ LiAlH_4} CH_3(CH_2)_{12}CH_2OH \xrightarrow{HBr} CH_3(CH_2)_{12}CH_2Br$$

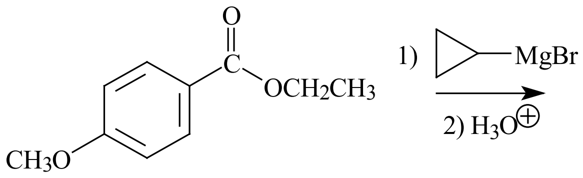
Tetradecanoic acid (Myristic acid) 1-Tetradecanol 1-Bromotetradecane

You could obtain a better yield of product by first synthesizing the ethyl ester of myristic acid and then reducing the ester with $LiAlH_4$. To review the reasons for this, see Section 8.5.

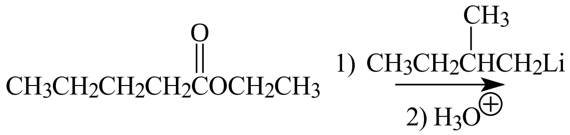
Exercise 8.12

Predict the major products of each of the following reactions.

a)

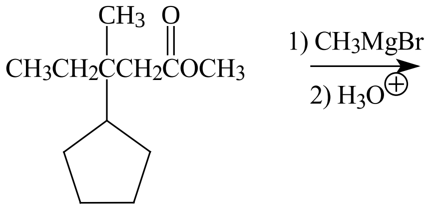


b)

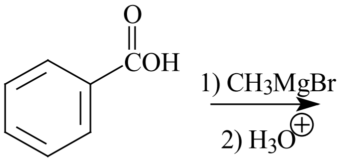


$$CH_3CH_2CH_2CH_2\overset{\overset{O}{\|}}{C}OCH_2CH_3 \xrightarrow[2)\ H_3O^{\oplus}]{1)\ CH_3CH_2\overset{\overset{CH_3}{|}}{C}HCH_2Li}$$

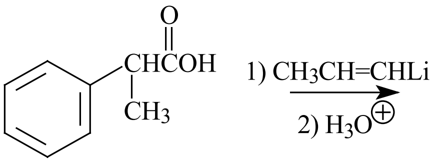
c)



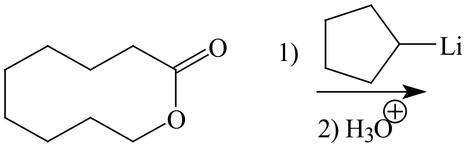
d)



e)

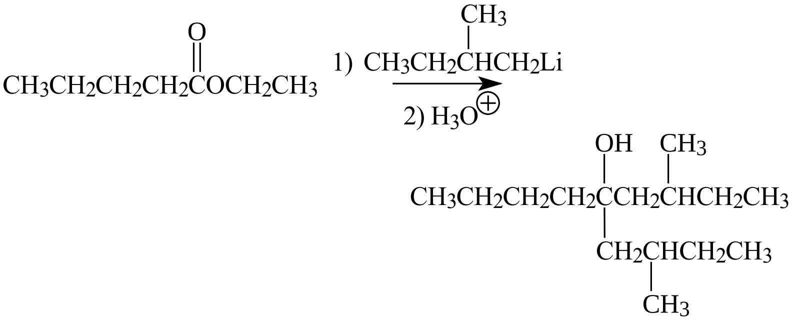


f)



Sample Solution

b)

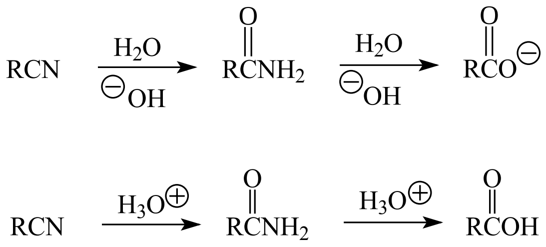


$$CH_3CH_2CH_2CH_2\overset{\overset{\displaystyle O}{\|}}{C}OCH_2CH_3 \xrightarrow[2)\ H_3O^{\oplus}]{1)\ CH_3CH_2\overset{\overset{\displaystyle CH_3}{|}}{C}HCH_2Li} CH_3CH_2CH_2CH_2\underset{\underset{\displaystyle CH_2\underset{\underset{\displaystyle CH_3}{|}}{C}HCH_2CH_3}{|}}{\overset{\overset{\displaystyle OH}{|}}{C}}CH_2\overset{\overset{\displaystyle CH_3}{|}}{C}HCH_2CH_3$$

8.7 Nitriles

Chemists often consider nitriles ($RC\equiv N$) carboxylic acid derivatives because, in terms of reactivity, a nitrile greatly resembles a carbonyl group. Nitriles readily hydrolyze to form amides or carboxylic acids and carboxylic acid derivatives. Also, nitriles are easy to synthesize (Chapter 12). Thus, the hydrolysis of nitriles is one of the primary methods that chemists use to prepare carboxylic acids and carboxylic acid derivatives.

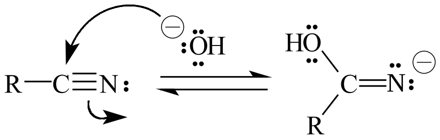
When forming a carboxylic acid from a nitrile, chemists hydrolyze the nitrile by adding water to it along with either an acid or a base catalyst. If they use mild reaction conditions, the hydrolysis stops at the amide. If they use more vigorous conditions, the amide hydrolyzes and forms the carboxylic acid. More vigorous reaction conditions include higher concentrations of the acid or the base and the addition of heat.



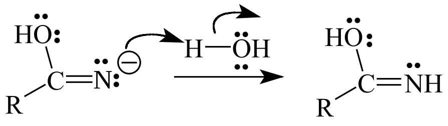
$$RCN \xrightarrow[{}^{\ominus}OH]{H_2O} RC(=O)NH_2 \xrightarrow[{}^{\ominus}OH]{H_2O} RC(=O)O^{\ominus}$$

$$RCN \xrightarrow{H_3O^{\oplus}} RC(=O)NH_2 \xrightarrow{H_3O^{\oplus}} RC(=O)OH$$

To hydrolyze the nitrile with a base, the mechanism begins with a nucleophilic attack of the hydroxide ion on the electrophilic carbon of the nitrile group.



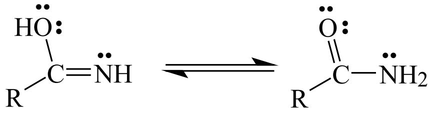
This product then rapidly picks up a proton from a molecule of water to produce an unstable isoamide and regenerates the hydroxide catalyst.



Isoamide

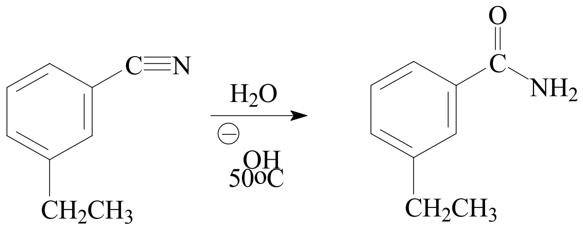
Because isoamides are unstable, they rapidly **isomerize** to form the amide. They isomerize by transferring a proton from the oxygen to the nitrogen. This transfer is accompanied by the shift of the π bond.

To isomerize a compound means to change the molecular structure from one atomic sequence to another.



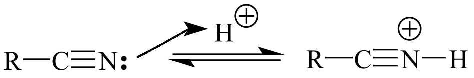
A tautomerism usually involves the shift of a hydrogen and a π bond. More on tautomerism in Section 19.1, page 000.

The equilibrium here is far to the right. Chemists call this rapid interconversion of functional groups a **tautomerism.**

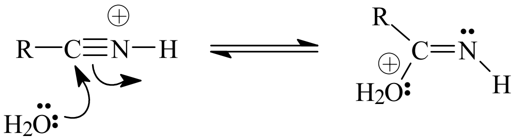


3-Ethylbenzamide
(91%)

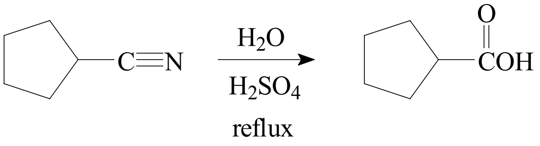
When an acid is the catalyst, the reaction begins with protonation of the nitrile nitrogen.



This reaction has an unfavorable equilibrium because the nitrogen is not very basic, so it does not protonate easily. Base strength depends on the ability of the atom to donate a pair of electrons, and that ability depends on which orbital holds the electrons. With a nitrile, an *sp* hybrid orbital holds the nonbonding electrons of the nitrogen. As discussed in Chapter 1, an *sp* hybrid orbital is closer to the nucleus than a *p* orbital, an sp^2, or an sp^3 hybrid orbital. Thus, an electron pair in an *sp* orbital is closer to the nucleus than an electron pair in an sp^2 orbital or an sp^3 orbital and is less available to act as a base. After the nitrile nitrogen is protonated, water adds via a nucleophilic addition to the carbon of the nitrile. Then, the intermediate loses a proton and tautomerizes to form the amide.

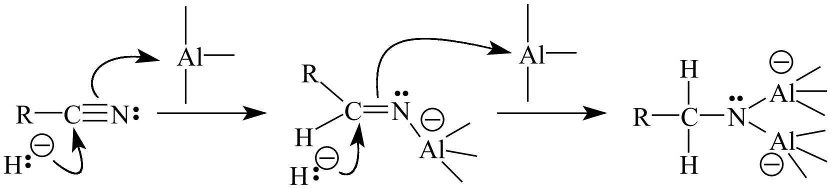


Because the nonbonding electron pair is in the *sp* orbital, the reaction requires heat to proceed. This additional heat also increases the rate of hydrolysis of the amide. The increased rate of amide hydrolysis makes isolating the amide from the acid-catalyzed reaction very difficult.

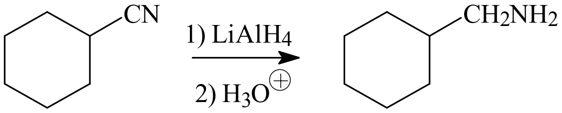


Cyclopentanecarboxylic acid
(84%)

Hydride addition to nitriles is a method that chemists use to synthesize primary amines. As the reaction proceeds, it moves through two successive additions of hydride from lithium aluminum hydride to the carbon of the nitrile.

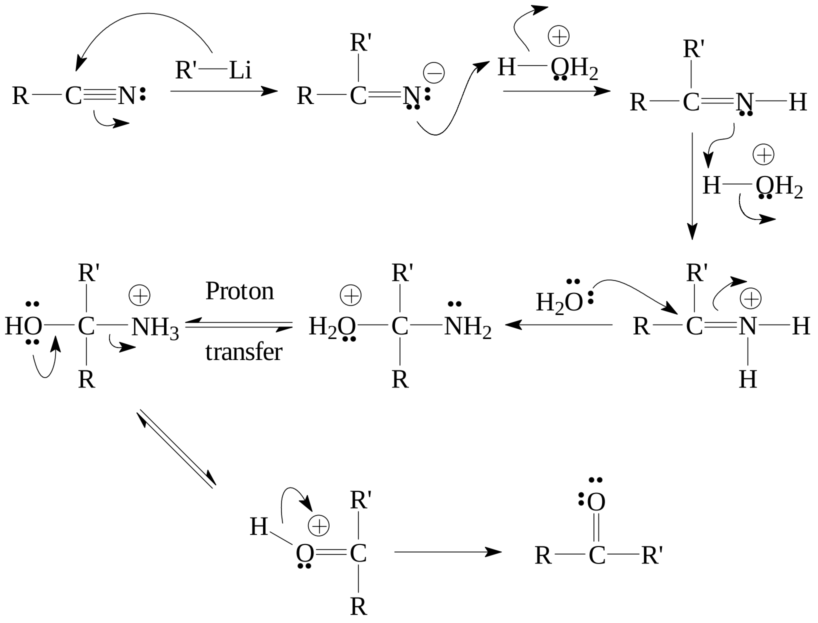


The strength of lithium aluminum hydride as a hydride nucleophile makes possible the second hydride reaction with the negatively charged imine intermediate. Finally, addition of water to the dianion hydrolyzes it to the primary amine.

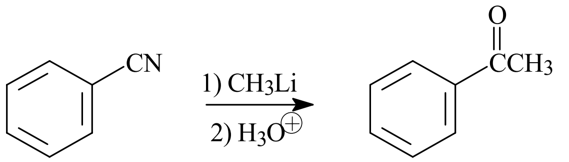


Cyclohexylmethanamine
(94%)

In another type of reaction, nitriles react with Grignard reagents and organolithium reagents to produce ketones. When the reaction involves an organometallic reagent and a nitrile, only one molecule of the organometallic reagent reacts with the nitrile. Neither a Grignard reagent nor an organolithium reagent is sufficiently nucleophilic to react with the intermediate iminium ion ($C{=}N^{\ominus}$) formed in the reaction, thus allowing protonation of the iminium ion to form an imine. The imine then hydrolyzes to form a ketone.



The following is an example of this reaction:

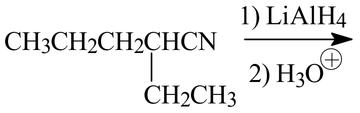


Methyl phenyl ketone
(Acetophenone)
(87%)

Exercise 8.13

Predict the major products of each of the following reactions.

a)



$$\mathrm{CH_3CH_2CH_2\underset{\displaystyle |\atop CH_2CH_3}{CH}CN \xrightarrow[2)\ H_3O^{\oplus}]{1)\ LiAlH_4}}$$

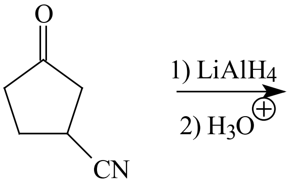
b)

$$\mathrm{CH_3CH_2CH_2CH_2CN \xrightarrow[50^{o}C]{H_2O,\ ^{\ominus}OH}}$$

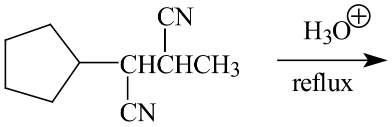
c)

$$CH_3CH_2CH_2CH_2CN \xrightarrow[2)\ H_3O^{\oplus}]{1)\ CH_3Li}$$

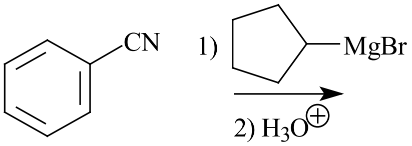
d)



e)

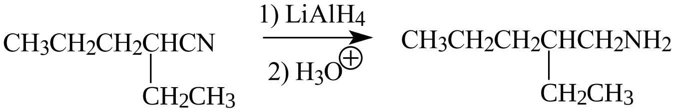


f)



Sample Solution

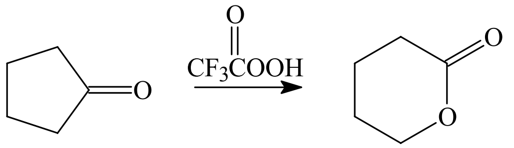
a)



$$CH_3CH_2CH_2\underset{CH_2CH_3}{\underset{|}{C}}HCN \xrightarrow[2)\ H_3O^{\oplus}]{1)\ LiAlH_4} CH_3CH_2CH_2\underset{CH_2CH_3}{\underset{|}{C}}HCH_2NH_2$$

8.8 The Baeyer-Villiger Oxidation

The Baeyer-Villiger reaction, named for the two German chemists who discovered it in 1899, is useful for converting a ketone to an ester. It works best when converting a symmetrical ketone to an ester or a cyclic ketone to a lactone.

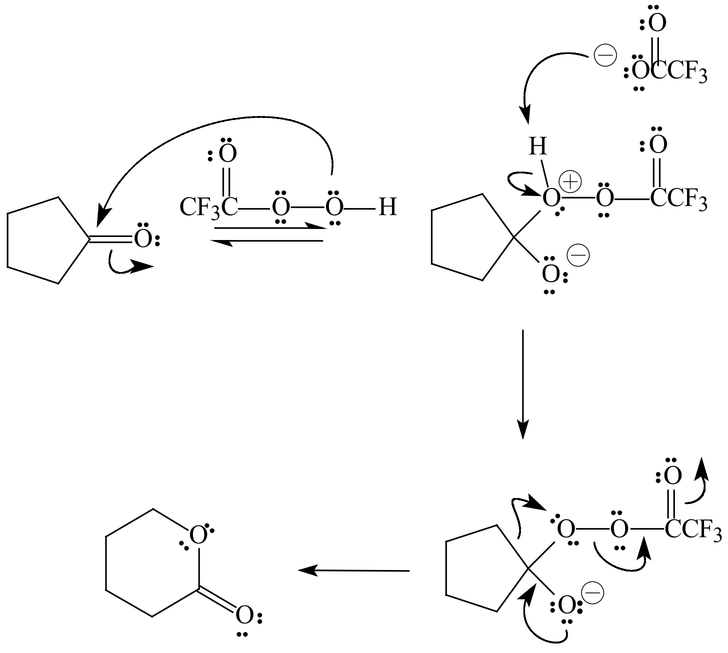


5-Hydroxypentanoic acid lactone

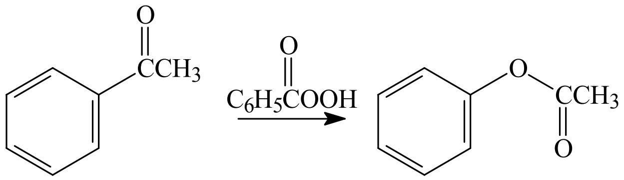
(76%)

The proposed mechanism for the Baeyer-Villiger oxidation reaction involves the nucleophilic addition of trifluoroperacetic acid (CF_3COOOH) or persulfuric acid (H_2SO_5) to the carbonyl carbon of the ketone. After the tetrahedral intermediate forms, a carbon adjacent to the carbon—trifluoroperacetic acid bond **migrates** its bond from the carbon—trifluoroperacetic acid bond to an oxygen of the peracid. Simultaneous with the bond migration, the carboxylate anion departs and the ester forms.

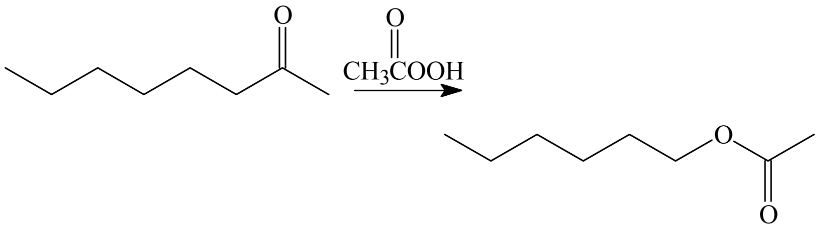
A bond migration is the movement of a bond from one atom to another, usually adjacent, atom.



The Baeyer-Villiger reaction works well on a variety of substrates, including the following:



Phenyl ethanoate
(Phenyl acetate)
(72%)



Hexyl ethanoate
(Hexyl acetate)
(62%)

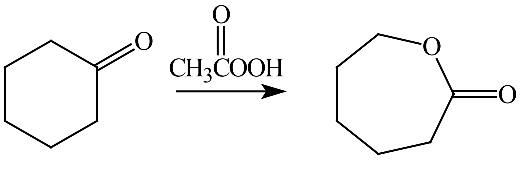
The migratory aptitude of a group is its tendency to move from one site in the molecule to another during a reaction where migration can occur.

Unlike the symmetrical ketone used as the substrate to illustrate the mechanism of the Baeyer-Villiger reaction, both ketones used as substrates in the examples are unsymmetrical. Even though they are unsymmetrical, each reaction gives only one major product. The selectivity of the reaction occurs because different groups have a different tendency to migrate to the oxygen. Studies of the Baeyer-Villiger reaction, as well as of other reactions with groups that migrate, show that the **migratory aptitude** for groups is H > *tert*-alkyl > secondary alkyl ~ benzyl ~ phenyl > primary alkyl > methyl. In all cases the migration takes the electron pair along with the group that migrates. The migratory aptitude parallels the base strength of the migrating group. The more basic the group, the more difficult it is for that group to migrate. The greater the difference between the two groups of an unsymmetrical ketone, the greater the selectivity shown in the reaction product.

Exercise 8.14

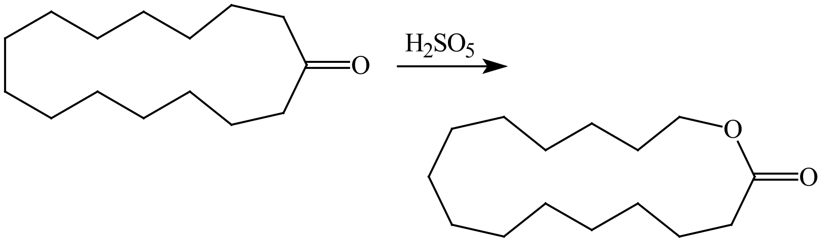
What is the major product formed in the Baeyer-Villiger reaction of 2-methylcyclohexanone?

Industry uses the Baeyer-Villiger reaction for the synthesis of various commercially useful products. One example is the synthesis of the lactone of 6-hydroxyhexanoic acid—its common name is caprolactone. Caprolactone is widely used as a starting material for some types of polyesters.



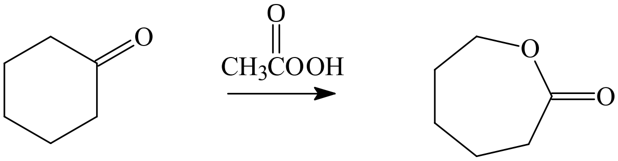
Caprolactone
(91%)

Another industrial synthesis makes large ring lactones. Perfume manufacturers value these lactones because a number of them are commonly used for musk fragrances. A simple one, extracted from the roots of *Angelica archangelica*, shows the synthesis of musk fragrances.



Lactone of 15-hydroxypentadecanoic acid
(84%)

Synthesis of Caprolactone



Caprolactone
(91%)

To 2.84 mL (12 mmol) of 32% peracetic acid solution, add 890 mg (9.1 mmol) of cyclohexanone. Stir the reaction mixture at room temperature for at least 24 hours. Add 10 mL of ethyl ether and wash the solution with 5 mL of saturated sodium bicarbonate solution three times to remove unreacted peracid as well as any acetic acid formed in the reaction. Dry the ether solution with anhydrous sodium sulfate and evaporate the ether. Fractional distillation of the product under reduced pressure produces 920 mg (89%) of caprolactone. The bp is 96-98^{o}C at 10mm pressure.

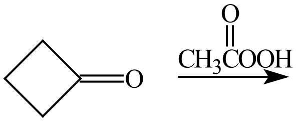
Discussion Questions

1. Propose a mechanism showing the formation of the acetic acid by-product in this reaction.
2. In oxygen, caprolactone undergoes a ring opening reaction to form an acyclic polymer. A polymer is a molecule consisting of a long chain of identical subunits. In this polymer, each subunit is derived from caprolactone and is connected by an ester functional group. Propose a structure for this polymer.

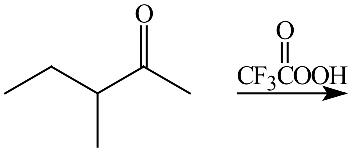
Exercise 8.15

Predict the major products of each of the following reactions

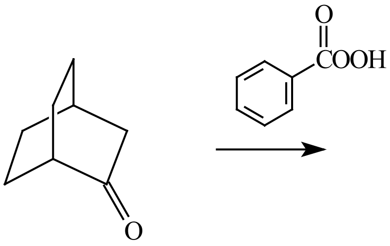
a)



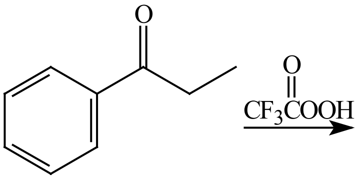
b)



c)

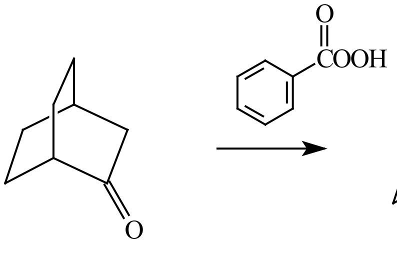


d)



Sample Solution

c)



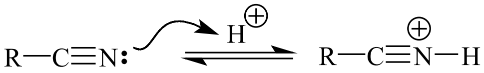
8.9 Solving Mechanistic Problems

A significant activity of organic chemists, and organic chemistry students, is proposing reasonable reaction mechanisms. When chemists discover a new reaction or identify an unexpected reaction product, they propose a mechanism for the transformation of the starting materials to the products. When chemists want to synthesize a previously unsynthesized molecule, or when they want to synthesize a molecule by an untried route, they propose reaction mechanisms to establish an experimental route for these syntheses. Whenever possible, they propose the reaction mechanism for a new reaction by finding an analogy with a known reaction or reaction mechanism.

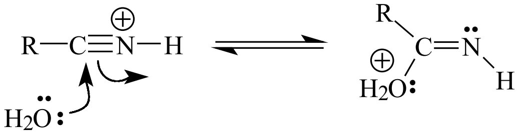
In Chapter 6, you surveyed the major types of mechanisms and in Chapters 7 and 8 you examined two of them in some detail. In this section, you will see how to actually *use* mechanisms by investigating a case study that involves mechanisms. As a part of this case study, you will examine a proposed mechanism for a reaction not covered previously in this book.

Before looking at the case study, an important principle for you to consider is that almost all the reactions covered in this book fit under the classification of acid-base reactions. Thus, answering the following two questions: 1) “Where is the acid?” and 2) “Where is the base?” allows you to more readily propose a mechanism for a particular reaction. Use the following sequence when proposing a mechanism for a reaction. Identify the atoms that probably act as the acid and the base. Use your information about how acids and bases interact and plan a step-by-step way that this acid and base would likely react together.

For example, look at an acid-base reaction that you are already familiar with—the acid-catalyzed hydrolysis of a nitrile. Answer the questions: Where is the acid? Where is the base? The $H^{\oplus}$ is the acid because it is electron deficient. The nitrogen of the nitrile is the base because it has a pair of nonbonding electrons. How does this acid and base react together? First, the $H^{\oplus}$ protonates the nitrogen.

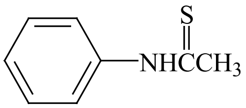


Then, because the protonation step enhanced the electrophilicity of the carbon atom, the nucleophile (water) attacks the nitrile carbon.



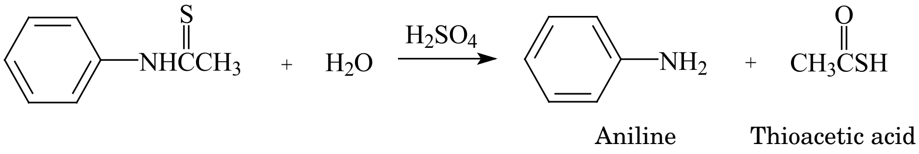
The product of this attack then loses a proton from the oxygen to form a neutral compound. This product is an isoamide, which is a tautomer of an amide.

Now consider the case study. The experimental evidence described here is the actual work done by John T. Edward and Sin Cheong Wong at McGill University (*J. Am. Chem. Soc.*, **1979**, 101, 1807). This work involved an acid-catalyzed hydrolysis of thioacetanilide.

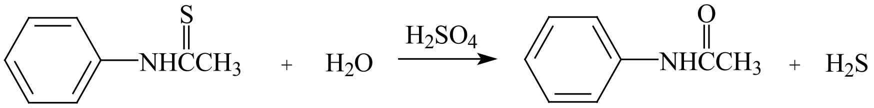


Thioacetanilide

Edward and Wong found that this reaction gives two different product mixtures and that the determining factor, as to which product mixture they obtained, depended on the sulfuric acid concentration. With a 48% concentration of sulfuric acid, 100% of the product was an aniline and thioacetic acid mixture.



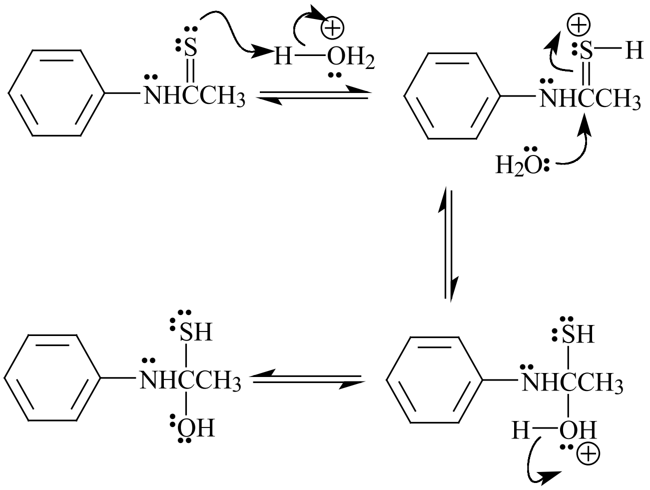
With a 3% concentration of sulfuric acid, more than half the product was acetanilide and hydrogen sulfide. The remaining product was aniline and thioacetic acid, showing that only part of the reaction followed the above pathway.



Acetanilide

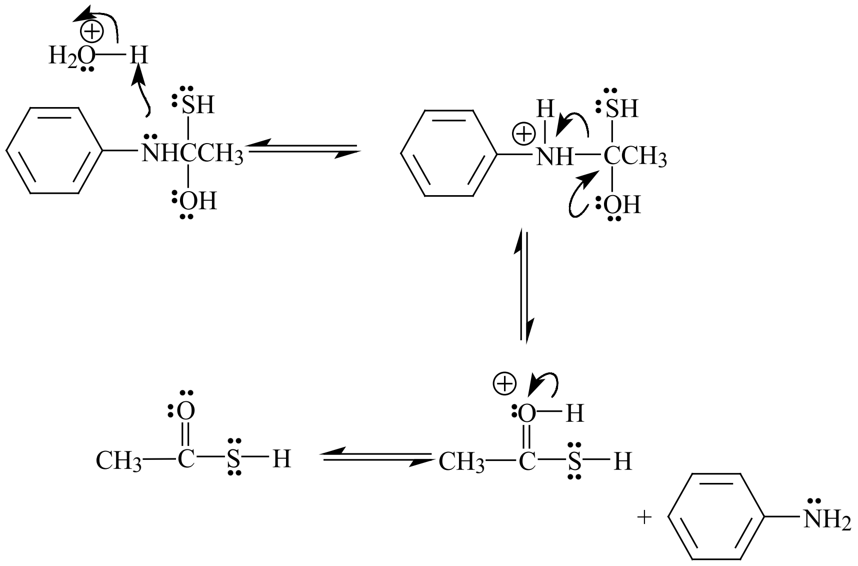
As they changed the concentration of sulfuric acid, they found that the ratio between these two reactions changed predictably. They also found that when they increased the temperature, they increased the amount of product (aniline and thioacetic acid) from the first reaction.

With this data and with your knowledge of acid-base theory and reaction mechanisms, you are ready to propose a mechanism. Following the above sequence, decide which is the acid and which is the base. The acid is sulfuric acid and the base is either the nitrogen or sulfur of the thioacetanilide. Because the nitrogen is donating electron density to the carbon of the thiocarbonyl group it is less basic than the sulfur. Then, using reasoning by analogy, propose a mechanistic sequence similar to the hydrolysis of an amide for the first reaction. This sequence begins with the protonation of the sulfur in the thiocarbonyl group, followed by nucleophilic attack by the oxygen of water and loss of a proton to give a tetrahedral intermediate.

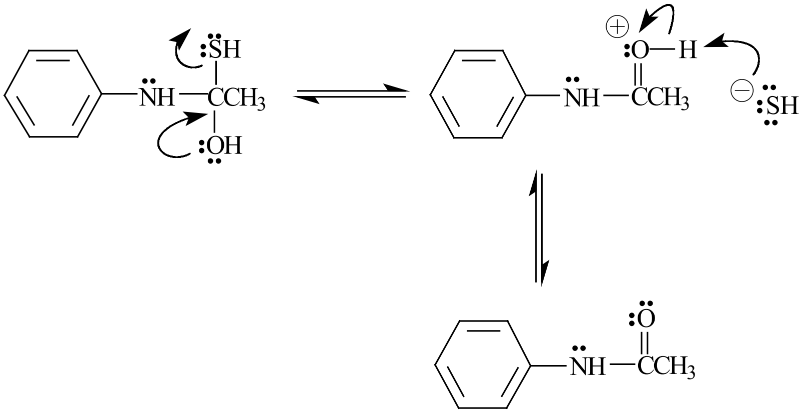


The tetrahedral intermediate has three possible protonation sites: the nitrogen, the sulfur, or the oxygen. Of these three, both sulfur and oxygen are weaker bases than nitrogen. In addition, protonation of the oxygen leads to the reverse reaction of the sequence shown above. Thus, protonation occurs on the nitrogen.

The protonation of the nitrogen atom of the tetrahedral intermediate makes the aniline molecule a good leaving group. This step forms thioacetic acid.



The second reaction follows the same mechanistic pathway until it reaches the *same* tetrahedral intermediate, but at low acid concentrations, little protonation occurs. Because the $^{\ominus}$SH is the conjugate base of a stronger acid than either of the other leaving groups, the loss of the $^{\ominus}$SH group (pK_a of H_2S is 7) is a lower energy path than the loss of either $^{\ominus}$OH (pK_a of H_2O is 15.7) or PhNH$^{\ominus}$ (pK_a of $PhNH_2$ is 25).



This pathway is *exactly* the reverse of the pathway for the initial formation of the tetrahedral intermediate, except that the sulfur leaves.

The only remaining question is, why does the change in acid concentration lead to different products? At low acid concentrations, only a small amount of protonation of the tetrahedral intermediate occurs. The group that leaves is the most stable anion. In this case, the leaving group is the $^{\ominus}$SH anion.

Increasing the acid concentration increases the likelihood that the tetrahedral intermediate will accept more than one proton from the acid. Then the question becomes, which protonated group is the better leaving group? The nitrogen, as well as the sulfur, and possibly the oxygen, are protonated at the higher acid concentrations. Preferential protonation on the nitrogen leads to a resonance-stabilized leaving group, which causes the carbon—nitrogen bond to break more easily.

Key Ideas from Chapter 8

❏ A nucleophilic substitution at the carbonyl group is identical to a nucleophilic addition to the carbonyl group, except that in the nucleophilic substitution, the nucleophile has some leaving group attached to the carbonyl carbon.

❏ A leaving group is an atom or group that departs from the substrate in a reaction.

❏ Leaving groups for nucleophilic substitutions on the carbonyl group generally include halides, carboxylate ions, hydroxides, alkoxide or amide ions or their conjugate acids.

❏ The mechanism for a nucleophilic substitution at the carbonyl group begins with an attack by the nucleophile at the carbonyl carbon. The substitution then proceeds through a tetrahedral intermediate, which loses the leaving group. Acid catalysis is common and the reaction takes place via a protonated carbonyl group.

❏ Hydrolysis of an ester is the reaction of the ester with water. Esterification is the reaction of a carboxylic acid and an alcohol. These reactions are the inverse of one another. The catalyst for this reaction is either an acid or a base. Usually, a base is the catalyst for the hydrolysis reaction, and an acid is the catalyst for the esterification reaction.

❏ Ester formation or hydrolysis is an equilibrium process in acid, but not in base. The basic hydrolysis is catalytic for the hydroxide ion. However, once the carboxylic acid is formed, it reacts with the hydroxide ion in solution.

❑ Amide hydrolysis follows the same pathway as esterification. However, amide formation requires a primary or secondary amine instead of the alcohol required by the esterification.

❑ A reaction of a carboxylic acid with $SOCl_2$, PCl_3, or PCl_5 generally produces an acyl halide.

❑ A reaction of an acyl halide with a carboxylic acid, or an anhydride exchange, synthesizes an acid anhydride.

❑ A reduction of a carboxylic acid derivative occurs by using $LiAlH_4$ as the reducing agent. All carboxylic acid derivatives, except the amides, produce alcohols from the carboxylate portion of the molecules. Amides produce amines.

❑ All carboxylic acid derivatives react with organolithium compounds. Depending on the leaving group, the reaction produces either a ketone or a tertiary alcohol . Carboxylic acids produce ketones; esters produce tertiary alcohols.

❑ Chemists usually consider nitriles as a part of the carboxylic acid family. Hydrolysis of a nitrile produces either an amide or a carboxylic acid. Hydrolysis proceeds either via an acid or a base catalysis.

❑ A reaction between a nitrile with a hydride donor produces a primary amine.

❑ A reaction between a nitrile and either a Grignard reagent or an organolithium compound produces a ketone.

❑ The Baeyer-Villiger reaction synthesizes an ester from a ketone. The reaction involves migration of a group with its electrons from the carbon to an oxygen. The migratory aptitude for migrating groups is H > *tert*-alkyl > secondary alkyl ~ benzyl ~ phenyl > primary alkyl > methyl.

❑ When solving a mechanism problem, look for an analogy among the mechanisms that you already know. Then draw the curved arrows to show the movement of electrons as the molecules react.

❑ If you can not find a clear analogy among the mechanisms you know, search for the most strongly acidic and basic atoms. Then using only previously studied methods, draw the curved arrows to show electron movement.

Richard F. Daley and Sally J. Daley
www.ochem4free.com

Organic Chemistry

Chapter 8-A

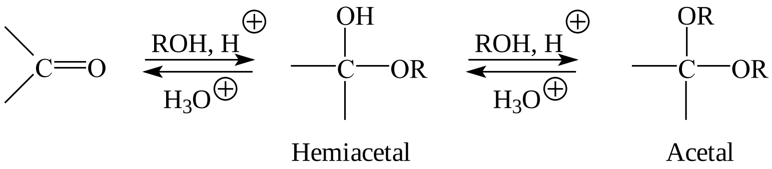
Reaction Summary I

A summary of the reactions learned in Chapters 7-8

Reaction Summary I

A summary of the reactions found in Chapters 7 and 8

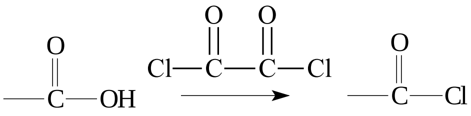
Acetal formation (Section 7.5, page 000)



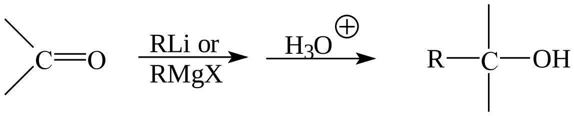
Acyl chloride synthesis via inorganic acid chlorides (Section 8.3, page 000)

Inorganic acid chloride = $SOCl_2$, PCl_3, or PCl_5

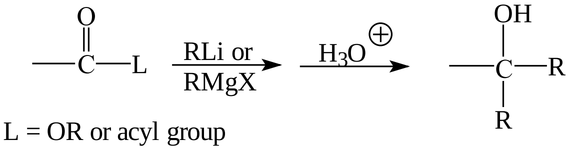
via oxalyl chloride (Section 8.3, page 000)

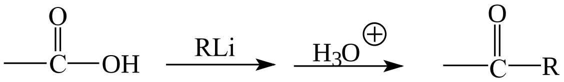


Addition of carbon nucleophiles to aldehydes and ketones (Section 7.8, page 000)

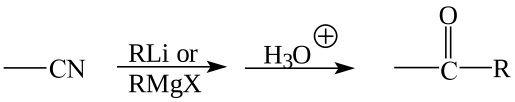


Addition of carbon nucleophiles to carboxylic acid derivatives (Section 8.6, page 000)

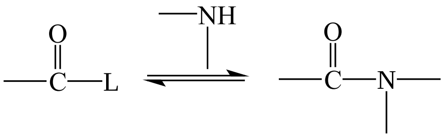

L = OR or acyl group



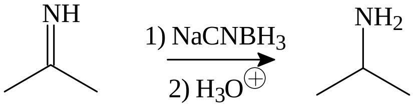
Addition of carbon nucleophiles to nitriles (Section 8.7, page 000)



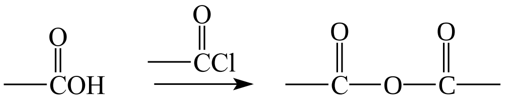
Amide synthesis (Section 8.4, page 000)


L = Cl or acyl group

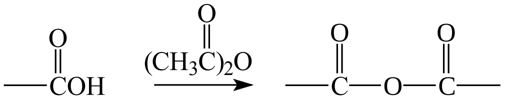
Amine synthesis (Section 7.7, page 000)



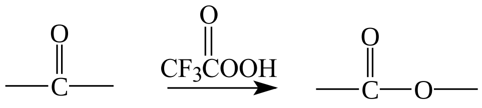
Anhydride synthesis (Section 8.3, page 000)



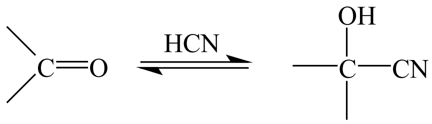
or



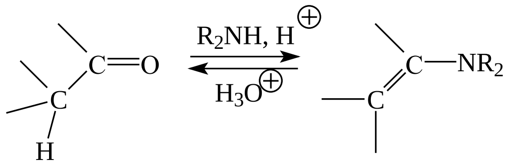
Baeyer-Villiger oxidation (Section 8.8, page 000)



Cyanohydrin reaction (Section 7.4, page 000)



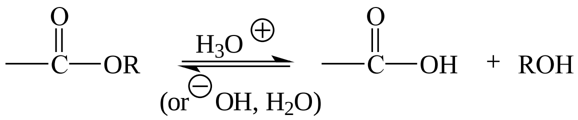
Enamine formation (Section 7.6, page 000)



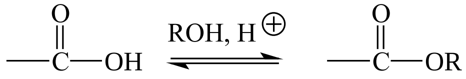
Ester synthesis (Section 8.2, page 000)

L = Cl, OH, or acyl group

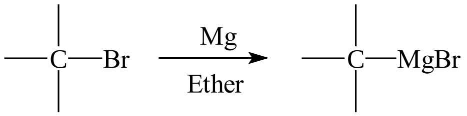
Ester hydrolysis (Section 8.2, page 000)



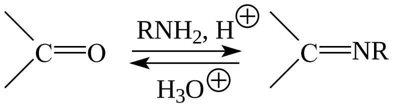
Fischer esterification (Section 8.2, page 000)



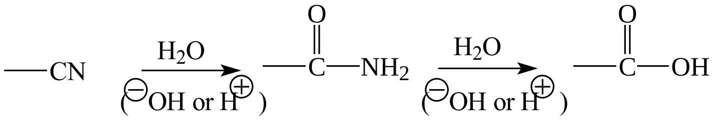
Grignard reagent formation (Section 7.8, page 000)



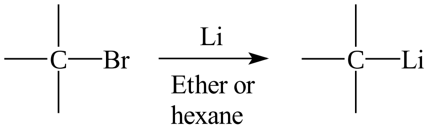
Imine formation (Section 7.6, page 000)



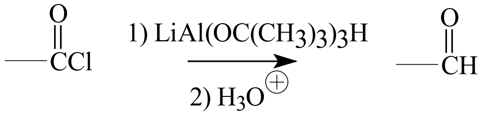
Nitrile hydrolysis (Section 8.7, page 000)

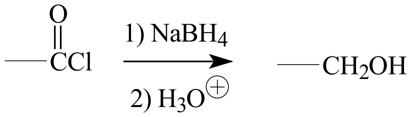


Organolithium reagents from alkyl halides (Section 7.8, page 000)

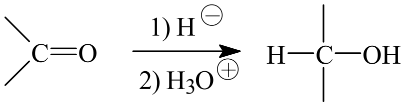


Reduction of acyl halides (Section 8.5, page 000)



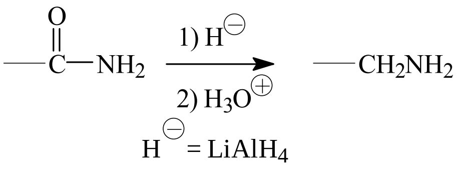


Reduction of a ketone or aldehyde (Section 7.7, page 000)

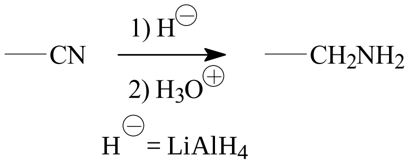


$H^{\ominus} = LiAlH_4$ or $NaBH_4$

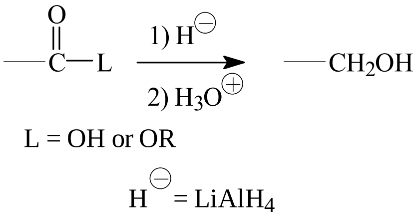
Reduction of an amide (Section 8.5, page 000)



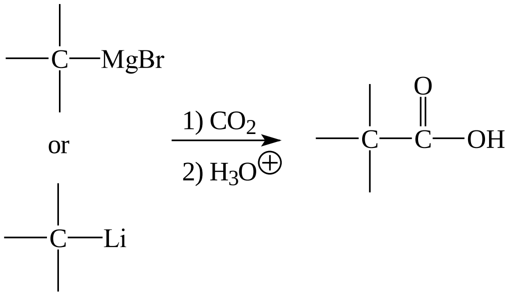
Reduction of a nitrile (Section 8.7, page 000)



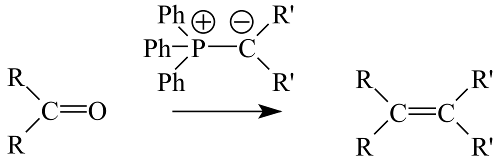
Reduction of carboxylic acids and esters (Section 8.5, page 000)



Synthesis of a carboxylic acid (Section 7.8, page 000)



Wittig reaction (Section 7.10, page 000)


R
R
C=O
Ph
Ph
Ph
P
C
R'
R'
R
R
C=C
R'
R'

Senthil Kumar's eBooks Collection - 2007

SD. Senthil Kumar,
Process Engineer,
senthilprocess@gmail.com