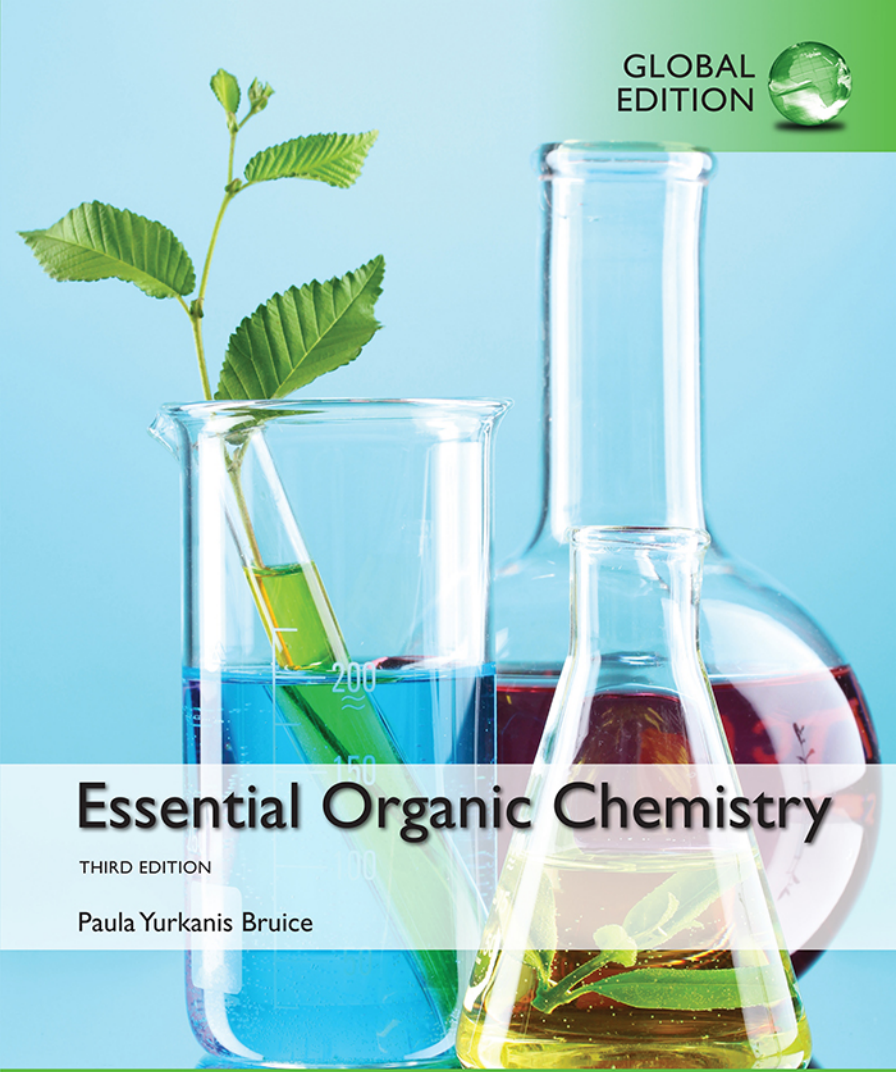
GLOBAL EDITION



Essential Organic Chemistry

THIRD EDITION

Paula Yurkanis Bruice

ALWAYS LEARNING

PEARSON

TO THE STUDENT

Welcome to the fascinating world of organic chemistry. You are about to embark on an exciting journey. This book has been written with students like you in mind—those who are encountering the subject for the first time. The book's central goal is to make this journey through organic chemistry both stimulating and enjoyable by helping you understand central principles and asking you to apply them as you progress through the pages. You will be reminded about these principles at frequent intervals in references back to sections you have already mastered.

You should start by familiarizing yourself with the book. Inside the front and back covers is information you may want to refer to often during the course. The list of Some Important Things to Remember and the Reaction Summary at each chapter's end provide helpful checklists of the concepts you should understand after studying the chapter. The Glossary at the end of the book can also be a useful study aid. The molecular models and electrostatic potential maps that you will find throughout the book are provided to give you an appreciation of what molecules look like in three dimensions and to show how charge is distributed within a molecule. Think of the margin notes as the author's opportunity to inject personal reminders of ideas and facts that are important to remember. Be sure to read them.

Work all the problems *within* each chapter. These are drill problems that you will find at the end of each section that allow you to check whether you have mastered the skills and concepts the particular section is teaching before you go on to the next section. Some of these problems are solved for you in the text. Short answers to some of the others—those marked with a diamond—are provided at the end of the book. Do not overlook the "Problem-Solving Strategies" that are also sprinkled throughout the text; they provide practical suggestions on the best way to approach important types of problems.

In addition to the *within-chapter* problems, work as many *end-of-chapter* problems as you can. The more problems you work, the more comfortable you will be with the subject matter and the better prepared you will be for the material in subsequent chapters. Do not let any problem frustrate you. If you cannot figure out the answer in a reasonable amount of time, turn to the *Study Guide and Solutions Manual* to learn how you should have approached the problem. Later on, go back and try to work the problem on your own again. Be sure to visit www.MasteringChemistry.com, where you can explore study tools, including Exercise Sets, an Interactive Molecular Gallery, and Biographical Sketches of historically important chemists, and where you can access content on many important topics.

The most important advice to remember (and follow) in studying organic chemistry is DO NOT FALL BEHIND! The individual steps to learning organic chemistry are quite simple; each by itself is relatively easy to master. But they are numerous, and the subject can quickly become overwhelming if you do not keep up.

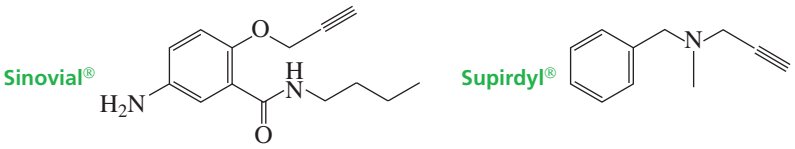
Before many of the theories and mechanisms were figured out, organic chemistry was a discipline that could be mastered only through memorization. Fortunately, that is no longer true. You will find many unifying ideas that allow you to use what you have learned in one situation to predict what will happen in other situations. So, as you read the book and study your notes, always make sure that you understand *why* each chemical event or behavior happens. For example, when the reasons behind reactivity are understood, most reactions can be predicted. Approaching the course with the misconception that to succeed you must memorize hundreds of unrelated reactions could be your downfall. There is simply too much material to memorize. Understanding and reasoning, not memorization, provide the necessary foundation on which to lay subsequent learning. Nevertheless, from time to time some memorization will be required: some fundamental rules will have to be memorized, and you will need to learn the common names of a number of organic compounds. But that should not be a problem; after all, your friends have common names that you have been able to learn and remember.

Students who study organic chemistry to gain entrance into professional schools sometimes wonder why these schools pay so much attention to this topic. The importance of organic chemistry is not in the subject matter alone. Mastering organic chemistry requires a thorough understanding of certain fundamental principles and the ability to use those fundamentals to analyze, classify, and predict. Many professions make similar demands.

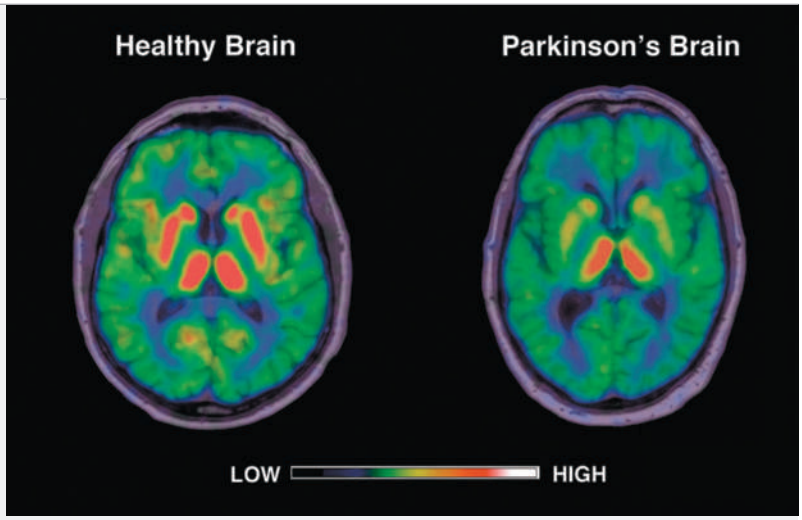
Good luck in your study. I hope you will enjoy studying organic chemistry and learn to appreciate the logic of this fascinating discipline. If you have any comments about the book or any suggestions for improving it, I would love to hear from you. Remember, positive comments are the most fun, but negative comments are the most useful.

Paula Yurkanis Bruice
pybruice@chem.ucsb.edu

only the company that holds the patent for a product can use the product's trade name for commercial purposes.

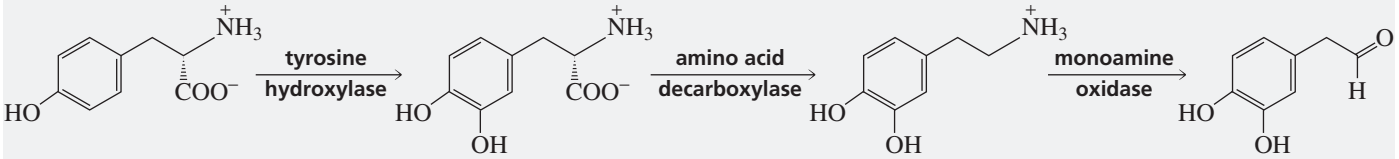


Synthetic Alkynes Are Used to Treat Parkinson's Disease

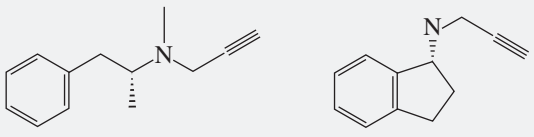


Parkinson's disease is a degenerative condition characterized by tremors. It is caused by the destruction of cells in the *substantia nigra*, a crescent-shaped region in the midbrain. These are the cells that release dopamine, the neurotransmitter that plays an important role in movement, muscle control, and balance. A neurotransmitter is a compound used to communicate between brain cells.

Dopamine is synthesized from tyrosine (one of the 20 common amino acids; Section 17.1). Ideally, Parkinson's disease could be treated by giving the patient dopamine. Unfortunately, dopamine is not polar enough to cross the blood–brain barrier. Therefore, L-DOPA, its immediate precursor, is the drug of choice, but it ceases to control the disease's symptoms after it has been used for a while.



Dopamine is oxidized in the body by an enzyme called monoamine oxidase. Two drugs, each containing a C≡CH group, have been developed that inhibit this enzyme, thus preventing the oxidation of dopamine and thereby increasing its availability in the brain. Both drugs have structures similar to that of dopamine, so they are able to bind to the enzyme's active site. (Recall that enzymes recognize their substrates by their shape; Sections 6.6 and 6.7.) Because these drugs form covalent bonds with groups at the enzyme's active site, they become permanently attached to the active site, thus preventing the enzyme from binding dopamine. Patients on these drugs continue to take L-DOPA, but now this drug can be taken at longer intervals and it can control the disease's symptoms for a longer period of time.



Selegiline was approved by the FDA first, but one of the compounds to which it is metabolized has a structure similar to that of methamphetamine (the street drug known as "speed"; page 169). So, some patients taking the drug experience psychiatric and cardiac effects. These side effects have not been found in patients taking rasagiline.

Notice that the name of most enzymes ends in "ase," preceded by an indication of what reaction the enzyme catalyzes. Thus, tyrosine hydroxylase puts an OH group on tyrosine, amino acid decarboxylase removes a carboxyl (COO^-) group from an amino acid (or, in this case, from a compound similar to an amino acid), and monoamine oxidase oxidizes an amine.

Why Are Drugs So Expensive?

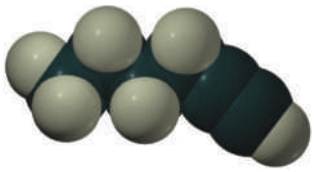
The average cost of launching a new drug is $1.2 billion. The manufacturer has to recover this cost quickly because the patent has to be filed as soon as the drug is first discovered. Although a patent is good for 20 years, it takes an average of 12 years to bring a drug to market after its initial discovery, so the patent protects the discoverer of the drug for an average of 8 years. It is only during the eight years of patent protection that drug sales can provide the income needed to cover the initial costs as well as to pay for research on new drugs.

Why does it cost so much to develop a new drug? First of all, the Food and Drug Administration (FDA) has high standards that must be met before a drug is approved for a particular use. An important factor leading to the high price of many drugs is the low rate of success in progressing from the initial concept to an approved product. In fact, only 1 or 2 of every 100 compounds tested become lead compounds. A lead compound is a compound that shows promise of becoming a drug. Chemists modify the structure of a lead compound to see if doing so improves its likelihood of becoming a drug. For every 100 structural modifications of a lead compound, only 1 is worthy of further study. For every 10,000 compounds evaluated in animal studies, only 10 will get to clinical trials.

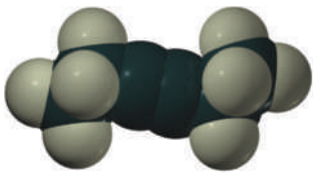
Clinical trials consist of three phases. Phase I evaluates the effectiveness, safety, side effects, and dosage levels in up to 100 healthy volunteers; phase II investigates the effectiveness, safety, and side effects in 100 to 500 volunteers who have the condition the drug is meant to treat; and phase III establishes the effectiveness and appropriate dosage of the drug and monitors adverse reactions in several thousand volunteer patients. For every 10 compounds that enter clinical trials, only 1 satisfies the increasingly stringent requirements to become a marketable drug.

6.10 THE NOMENCLATURE OF ALKYNES

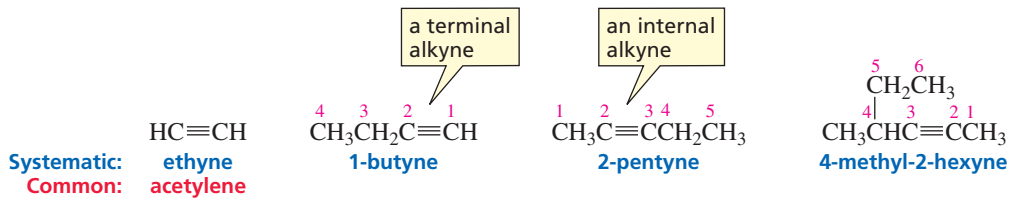
The systematic name of an alkyne is obtained by replacing the "ane" ending of the alkane name with "yne." Analogous to the way alkenes are named, the longest continuous chain containing the carbon–carbon triple bond is numbered in the direction that gives the functional group suffix as low a number as possible (Section 5.1). If the triple bond is at the end of the chain, the alkyne is classified as a **terminal alkyne.** Alkynes with triple bonds located elsewhere along the chain are **internal alkynes.**



1-hexyne
a terminal alkyne



3-hexyne
an internal alkyne



Acetylene is an unfortunate common name for an alkyne because its "ene" ending is characteristic of a double bond rather than a triple bond.

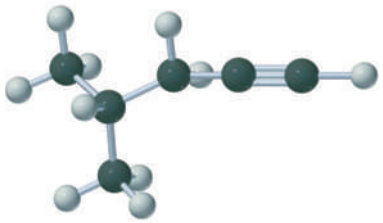
If counting from either direction leads to the same number for the functional group suffix, the correct systematic name is the one that contains the lowest substituent number. If the compound contains more than one substituent, the substituents are listed in alphabetical order.

A substituent receives the lowest possible number only if there is no functional group suffix, or if counting from either direction leads to the same number for the functional group suffix.

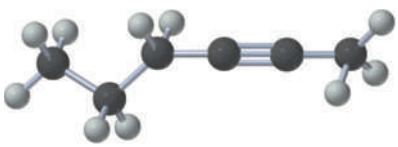
PROBLEM 16♦

Name the following:

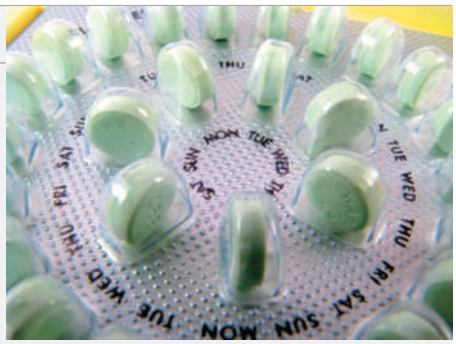
a.



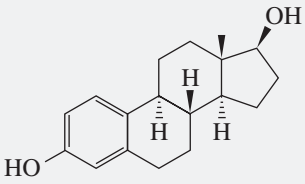
b.



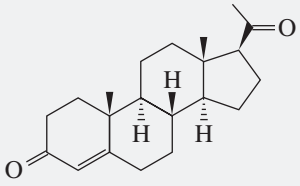
Synthetic Alkynes Are Used for Birth Control



Estradiol and progesterone are naturally occurring female hormones. Because of their skeletal ring structures, they are classified as steroids (Section 3.14). Estradiol is responsible for the development of secondary sex characteristics in women—it affects body shape, fat deposition, bones, and joints. Progesterone is critical for the continuation of pregnancy.

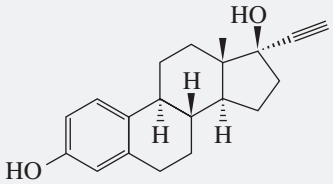


estradiol

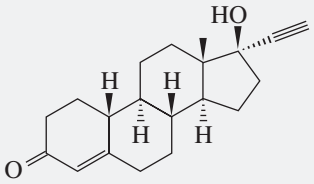


progesterone

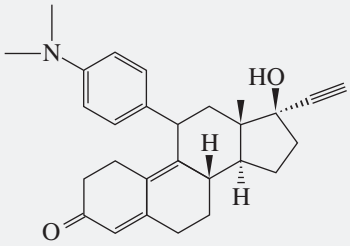
The four compounds shown next are synthetic steroids that are used for birth control; each contains an alkyne functional group. Most birth control pills contain ethinyl estradiol (a compound structurally similar to estradiol) and a compound structurally similar to progesterone (such as norethindrone). Ethinyl estradiol prevents ovulation, whereas norethindrone makes it difficult for a fertilized egg to attach to the wall of the uterus.



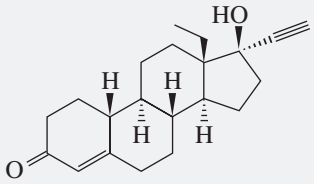
ethinyl estradiol



norethindrone
Aygestin®



mifepristone
RU-486
Mifegyne®



levonorgestrel
Norplant®

Mifepristone and levonorgestrel are also synthetic steroids that contain an alkyne functional group. Mifepristone, also known as RU-486, induces an abortion if taken early in pregnancy. Its name comes from Roussel-Uclaf, the French pharmaceutical company by which it was first synthesized, and from an arbitrary lab serial number. Levonorgestrel is an emergency contraceptive pill. It prevents pregnancy if taken within a few days of conception.

PROBLEM 17♦

Draw the structure for each of the following:

a. 1-chloro-3-hexyne **b.** cyclooctyne **c.** 4,4-dimethyl-1-pentyne

PROBLEM 18

Draw the structures for and name the seven alkynes with molecular formula C_6H_{10}.

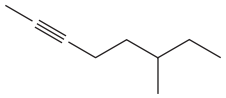
PROBLEM 19♦

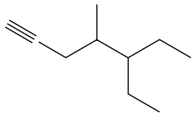
Name the following:

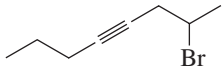
a. $BrCH_2CH_2C{\equiv}CCH_3$ **b.** $CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}HC{\equiv}C\underset{\displaystyle Cl}{\underset{|}{C}}HCH_2CH_3$ **c.** $CH_3CH_2\underset{\displaystyle CH_2CH_2CH_3}{\underset{|}{C}}HC{\equiv}CH$

PROBLEM 20♦

Name the following:

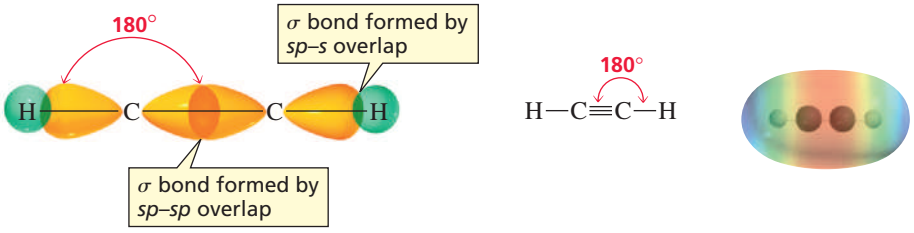
a. 

b. 

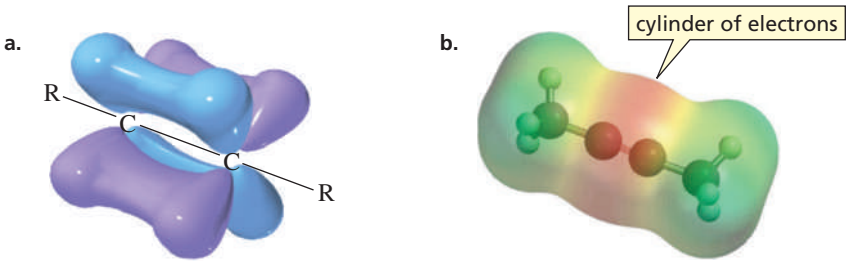
c. 

6.11 THE STRUCTURE OF ALKYNES

The structure of ethyne was discussed in Section 1.9, where we saw that each carbon is *sp* hybridized. As a result, each carbon has two *sp* orbitals and two *p* orbitals. One *sp* orbital overlaps the *s* orbital of a hydrogen, and the other overlaps an *sp* orbital of the other carbon. (The small lobes of the *sp* orbitals are not shown.) Because the *sp* orbitals are oriented as far from each other as possible to minimize electron repulsion, ethyne is a linear molecule with bond angles of 180°.



Other alkynes have structures similar to that of ethyne. Recall that the triple bond is formed by each of the two *p* orbitals on one *sp* carbon overlapping the parallel *p* orbital on the other *sp* carbon to form two π bonds (Figure 6.4). The end result can be thought of as a cylinder of electrons wrapped around the σ bond.



◀ Figure 6.4

(a) Each of the two π bonds of a triple bond is formed by side-to-side overlap of a *p* orbital of one carbon with a parallel *p* orbital of the adjacent carbon.

(b) The electrostatic potential map for 2-butyne shows the cylinder of electrons wrapped around the σ bond.

Also recall that a carbon–carbon triple bond is shorter and stronger than a carbon–carbon double bond, which in turn, is shorter and stronger than a carbon–carbon single bond, and that a π bond is weaker than a σ bond (Section 1.14).

Alkyl groups stabilize alkynes, just as they stabilize alkenes and carbocations (Sections 5.6 and 6.2, respectively). Internal alkynes, therefore, are more stable than terminal alkynes.

A triple bond is composed of a σ bond and two π bonds.

PROBLEM 21♦

What hybrid orbitals are used to form the carbon–carbon σ bond between the highlighted carbons?

a. $CH_3CH{=}CHCH_3$ **d.** $CH_3C{\equiv}CCH_3$ **g.** $CH_3CH{=}CHCH_2CH_3$

b. $CH_3CH{=}CHCH_3$ **e.** $CH_3C{\equiv}CCH_3$ **h.** $CH_3C{\equiv}CCH_2CH_3$

c. $CH_3CH{=}C{=}CH_2$ **f.** $CH_2{=}CHCH{=}CH_2$ **i.** $CH_2{=}CHC{\equiv}CH$

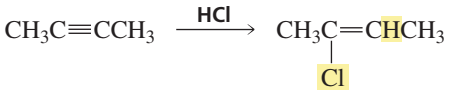
6.12 THE PHYSICAL PROPERTIES OF UNSATURATED HYDROCARBONS

All hydrocarbons—alkanes, alkenes, and alkynes—have similar physical properties. They are all insoluble in water but soluble in nonpolar solvents (Section 3.8). They are less dense than water and, like other homologous series, have boiling points that increase

with increasing molecular weight. Alkynes are more linear than alkenes, causing an alkyne to have stronger van der Waals interactions and, therefore, a higher boiling point than an alkene with the same number of carbons.

6.13 THE ADDITION OF A HYDROGEN HALIDE TO AN ALKYNE

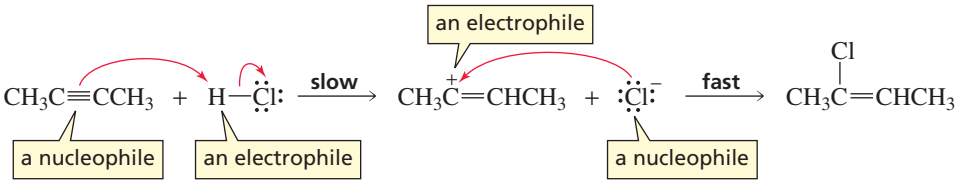
The cloud of electrons completely surrounding the σ bond makes an alkyne an electron-rich molecule. Alkynes therefore are nucleophiles, so they react with electrophiles. Thus alkynes, like alkenes, undergo *electrophilic addition reactions* because of their relatively weak π bonds. The same reagents that add to alkenes also add to alkynes. For example, the addition of hydrogen chloride to an alkyne forms a chloro-substituted alkene.



Moreover, the mechanism for electrophilic addition to an alkyne is similar to the mechanism for electrophilic addition to an alkene. For example, compare the mechanism for the addition of a hydrogen halide to an alkene shown in Sections 5.3 and 6.1 with the mechanism for the addition of a hydrogen halide to an alkyne shown below.

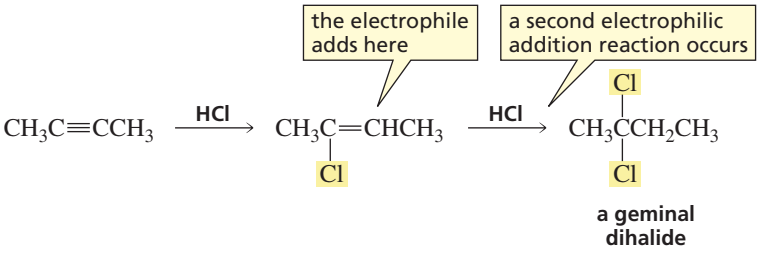
MECHANISM FOR THE ADDITION OF A HYDROGEN HALIDE TO AN ALKYNE

Recall that an arrowhead with a double barb signifies the movement of two electrons.

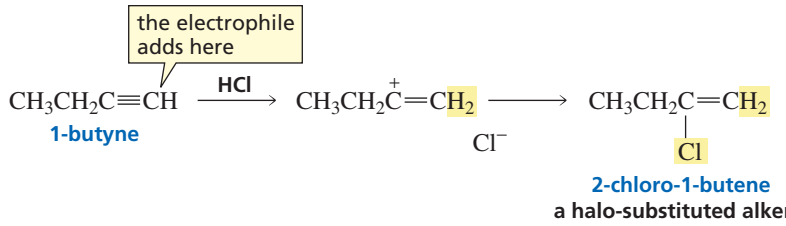


- The relatively weak π bond breaks because the π electrons are attracted to the electrophilic proton.
- The positively charged carbocation intermediate reacts rapidly with the negatively charged chloride ion.

The addition reactions of alkynes, however, have a feature that alkenes do not have: because the product of the addition of an electrophilic reagent to an alkyne is an alkene, a second electrophilic addition reaction can occur if *excess* hydrogen halide is present. In the second addition reaction, the electrophile (H^+) adds to the sp^2 carbon bonded to the most hydrogens—as predicted by the rule that governs electrophilic addition reactions (Section 6.3).

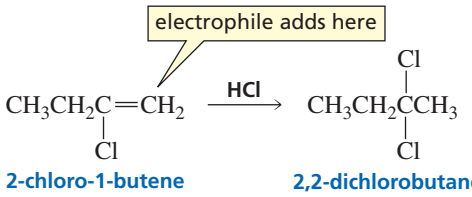


If the alkyne is a *terminal* alkyne, the H^+ will add to the *sp* carbon bonded to the hydrogen, because the *secondary* vinylic cation that results is more stable than the *primary* vinylic cation that would be formed if the H^+ added to the other *sp* carbon. (Recall that alkyl groups stabilize positively charged carbon atoms; see Section 6.2.)

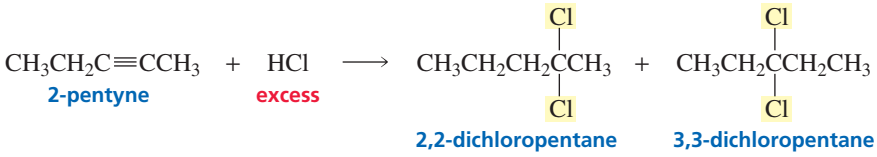


The electrophile adds to the *sp* carbon that is bonded to the hydrogen.

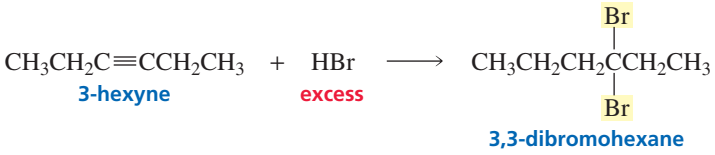
A second addition reaction will take place if excess hydrogen halide is present. Once again, the electrophile (H^+) adds to the sp^2 carbon bonded to the most hydrogens.



Addition of a hydrogen halide to an *internal* alkyne forms two products, because the initial addition of the proton can occur with equal ease to either of the *sp* carbons.



Note, however, that if the same group is attached to each of the *sp* carbons of the internal alkyne, only one product will be obtained.



PROBLEM 22♦

What is the major product of each of the following reactions?

a. $HC{\equiv}CCH_3 \xrightarrow{HBr}$ (excess)

b. $HC{\equiv}CCH_3 \xrightarrow[\text{excess}]{HBr}$

c. $CH_3C{\equiv}CCH_3 \xrightarrow[\text{excess}]{HBr}$

d. $CH_3C{\equiv}CCH_2CH_3 \xrightarrow[\text{excess}]{HBr}$

6.14 THE ADDITION OF WATER TO AN ALKYNE

In Section 6.4, we saw that alkenes undergo the acid-catalyzed addition of water. The product of the electrophilic addition reaction is an alcohol.