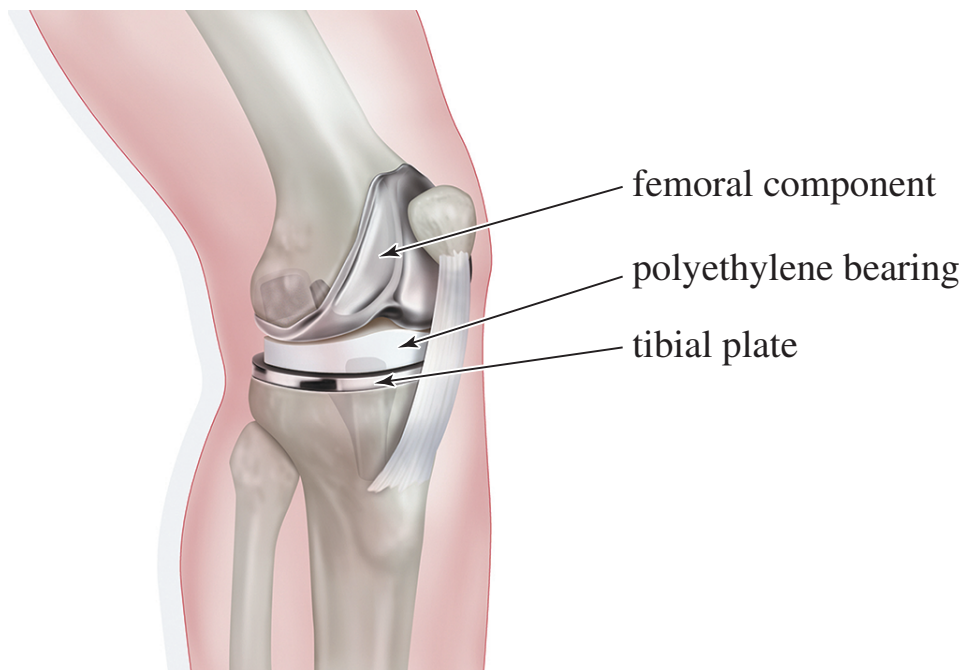


# 8

## Reactions of Alkenes



▲ Polyethylene provides a self-lubricating surface for movement of the metal parts of an artificial knee replacement. The highly cross-linked polyethylene used in these implants is fabricated to be exceptionally tough: It wears only about 0.1 mm per year. Polyethylene is compatible with the human body, and in most cases, it does not cause a foreign body reaction even after years of constant movement in the joint.

The alkene double bond is a gateway functional group. Alkene reactions lead to many other functional groups that lay the foundation for the rest of your study of organic chemistry. You can convert alkenes to alkyl halides, epoxides, alcohols, aldehydes, ketones, carboxylic acids, and other functional groups. The reactions of alkenes arise from the reactivity of their carbon–carbon double bonds. Organic chemists enjoy the challenge of taking a simple carbon–carbon double bond and manipulating it in all possible ways to produce other compounds, often mimicking biological reactions that occur in cells. This chapter covers the most common alkene reactions, including their mechanisms, reactivity, orientation, and stereochemistry.

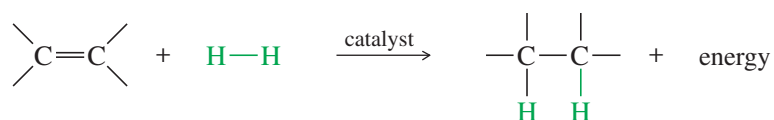
Most reactions of alkenes involve addition of atoms or groups across the double bond, with one atom or group adding to each end. By studying the typical mechanisms involved when reagents add to double bonds, you will be able to predict the outcomes of alkene addition reactions that you have not seen before. You will also find it easier to understand the mechanisms of addition reactions we see in other families of compounds.

### 8-1 Reactivity of the Carbon–Carbon Double Bond

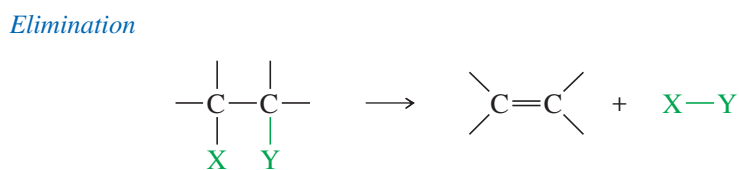
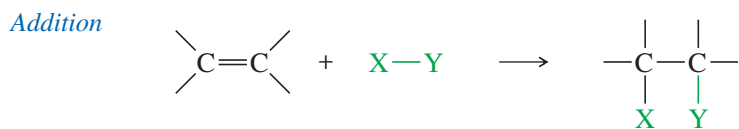
Because single bonds (sigma bonds) are more stable than pi bonds, the most common reactions of double bonds transform the pi bond into a sigma bond. For example, catalytic hydrogenation converts the C=C pi bond and the H–H sigma bond into two C–H sigma bonds (Section 7-8). The reaction is exothermic ( $\Delta H^\circ =$  about  $-80$  to  $-120$  kJ/mol or about  $-20$  to  $-30$  kcal/mol), showing that the product is more stable than the reactants.

### Goals for Chapter 8

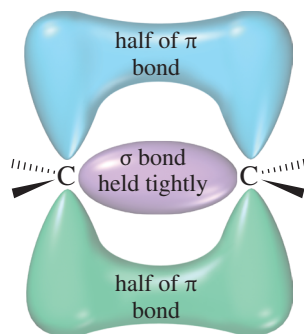
- 1 Explain why electrophilic additions are among the most common reactions of alkenes.
- 2 Predict the products of the reactions of alkenes, including the orientation of the reaction (regiochemistry) and the stereochemistry.
- 3 Propose mechanisms to explain the observed products of alkene reactions.
- 4 Use retrosynthetic analysis to solve multistep synthesis problems with alkenes as reagents, intermediates, or products.



Hydrogenation of an alkene is an example of an **addition**, one of the three major reaction types we have studied: addition, elimination, and substitution. In an addition, two molecules combine to form one product molecule. When an alkene undergoes addition, two groups add to the carbon atoms of the double bond and the carbons become saturated. In many ways, addition is the reverse of **elimination**, in which one molecule splits into two fragment molecules. In a **substitution**, one fragment replaces another fragment in a molecule.



Addition is the most common reaction of alkenes, and in this chapter, we consider additions to alkenes in detail. A wide variety of functional groups can be formed by adding suitable reagents to the double bonds of alkenes.



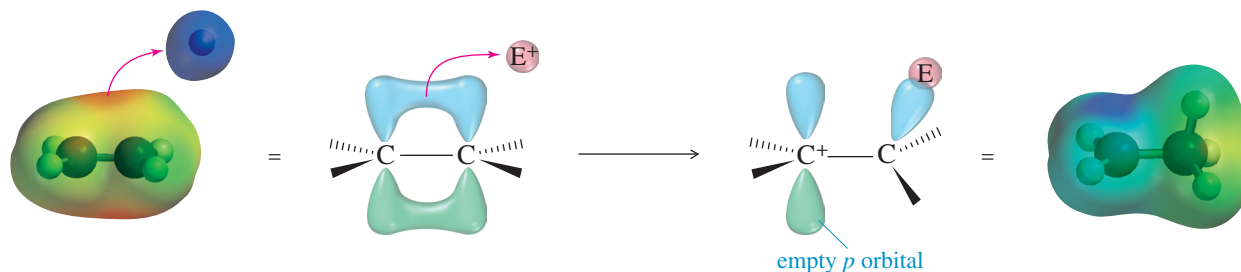
**FIGURE 8-1**  
The electrons in the pi bond are spread farther from the carbon nuclei and are more loosely held than the sigma electrons.

## 8-2 Electrophilic Addition to Alkenes

In principle, many different reagents could add to a double bond to form more stable products; that is, the reactions are energetically favorable. Not all of these reactions have convenient rates, however. For example, the reaction of ethylene with hydrogen (to give ethane) is strongly exothermic, but the rate is very slow. A mixture of ethylene and hydrogen can remain for years without appreciable reaction. Adding a catalyst such as platinum, palladium, or nickel allows the reaction to take place at a rapid rate.

Some reagents react with carbon–carbon double bonds without the aid of a catalyst. To understand what types of reagents react with double bonds, consider the structure of the pi bond. Although the electrons in the sigma bond framework are tightly held, the pi bond is delocalized above and below the sigma bond (Figure 8-1). The pi-bonding electrons are spread farther from the carbon nuclei, and they are more loosely held. A strong electrophile has an affinity for these loosely held electrons. It can pull them away to form a new bond (Figure 8-2), leaving one of the carbon atoms with only three bonds and a positive charge: a carbocation. In effect, the double bond has reacted as a nucleophile, donating a pair of electrons to the electrophile.

Most addition reactions involve a second step in which a nucleophile attacks the carbocation (as in the second step of the  $S_N1$  reaction), forming a stable addition product. In the product, both the electrophile and the nucleophile are bonded to the carbon atoms that were connected by the double bond. This reaction is outlined in Key Mechanism 8-1, identifying the electrophile as  $E^+$  and the nucleophile as  $Nuc^-$ . This type of reaction requires a strong electrophile to attract the electrons of the pi bond and generate a carbocation in the rate-limiting step. Most alkene reactions fall into this large class of **electrophilic additions** to alkenes.

**FIGURE 8-2**

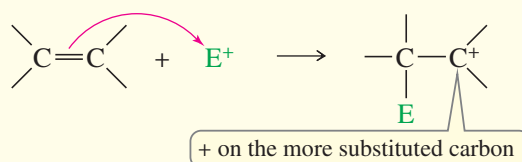
The pi bond as a nucleophile. A strong electrophile attracts the electrons out of the pi bond to form a new sigma bond, generating a carbocation. The (red) curved arrow shows the movement of electrons, from the electron-rich pi bond to the electron-poor electrophile.



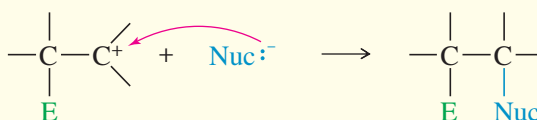
### KEY MECHANISM 8-1 Electrophilic Addition to Alkenes

A wide variety of electrophilic additions involve similar mechanisms. First, a strong electrophile attracts the loosely held electrons from the pi bond of an alkene. The electrophile forms a sigma bond to one of the carbons of the (former) double bond, while the other carbon becomes a carbocation. The carbocation (a strong electrophile) reacts with a nucleophile (often a weak nucleophile) to form another sigma bond. We symbolize the electrophile as  $E^+$  and the nucleophile as  $Nuc:^-$  because electrophilic additions often involve ionic reagents, with the electrophile having a positive charge and the nucleophile having a negative charge.

**Step 1:** Attack of the pi bond on the electrophile forms a carbocation.



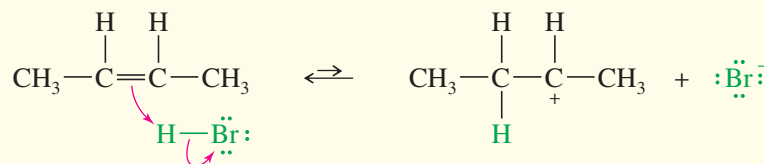
**Step 2:** Attack by a nucleophile gives the addition product.



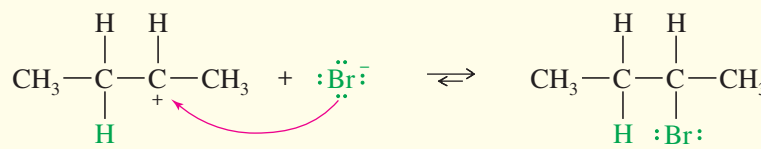
#### EXAMPLE: Ionic addition of HBr to but-2-ene

This example shows what happens when gaseous HBr adds to but-2-ene. The proton in HBr is electrophilic; it reacts with the alkene to form a carbocation. Bromide ion reacts rapidly with the carbocation to give a stable product in which the elements of HBr have added to the ends of the double bond.

**Step 1:** Protonation of the double bond forms a carbocation.



**Step 2:** Bromide ion attacks the carbocation.



**PROBLEM:** Explain why the + charge of the carbocation always appears at the carbon of the (former) double bond that has NOT bonded to the electrophile.

**TABLE 8-1**  
**Types of Additions to Alkenes**

	$\diagup \text{C}=\text{C} \diagdown$ Type of Addition [Elements Added] <sup>a</sup>	Product
$\xrightarrow[\text{[H}_2\text{O]}]{\text{hydration}}$	$\begin{array}{c} \text{H} \quad \text{OH} \\   \quad   \\ -\text{C}-\text{C}- \\   \quad   \end{array}$	$\xrightarrow[\text{[X}_2\text{], an oxidation}]{\text{halogenation}}$ $\begin{array}{c} \text{X} \quad \text{X} \\   \quad   \\ -\text{C}-\text{C}- \\   \quad   \end{array}$
$\xrightarrow[\text{[H}_2\text{]}, \text{ a reduction}]{\text{hydrogenation}}$	$\begin{array}{c} \text{H} \quad \text{H} \\   \quad   \\ -\text{C}-\text{C}- \\   \quad   \end{array}$	$\xrightarrow[\text{[HOX], an oxidation}]{\text{halohydrin formation}}$ $\begin{array}{c} \text{X} \quad \text{OH} \\   \quad   \\ -\text{C}-\text{C}- \\   \quad   \end{array}$
$\xrightarrow[\text{[HOOH], an oxidation}]{\text{dihydroxylation}}$	$\begin{array}{c} \text{OH} \quad \text{OH} \\   \quad   \\ -\text{C}-\text{C}- \\   \quad   \end{array}$	$\xrightarrow[\text{[HX]}]{\text{HX addition}}$ (hydrohalogenation) $\begin{array}{c} \text{H} \quad \text{X} \\   \quad   \\ -\text{C}-\text{C}- \\   \quad   \end{array}$
$\xrightarrow[\text{[O}_2\text{], an oxidation}]{\text{oxidative cleavage}}$	$\diagup \text{C}=\text{O} \quad \text{O}=\text{C} \diagdown$	$\xrightarrow[\text{[CH}_2\text{]}]{\text{cyclopropanation}}$ $\begin{array}{c} \text{H} \quad \text{H} \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \\ -\text{C}-\text{C}- \\   \quad   \end{array}$
$\xrightarrow[\text{[O], an oxidation}]{\text{epoxidation}}$	$\begin{array}{c} \text{O} \\ \diagdown \quad \diagup \\ -\text{C}-\text{C}- \\   \quad   \end{array}$	

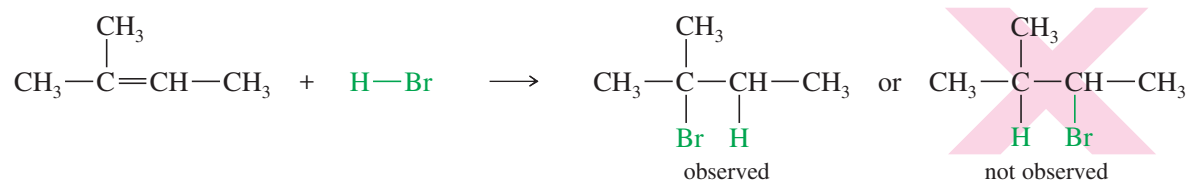
<sup>a</sup>These are not the reagents used, but simply the groups that appear in the product.

We will consider several types of additions to alkenes, using a wide variety of reagents: water, borane, hydrogen, carbenes, halogens, oxidizing agents, and even other alkenes. Most, but not all, of these will be electrophilic additions. Table 8-1 summarizes the classes of additions we will cover. Note that the table shows what elements have added across the double bond in the final product, but it says nothing about reagents or mechanisms. As we study these reactions, you should note the **regiochemistry** of each reaction, also called the *orientation of addition*, meaning which part of the reagent adds to which end of the double bond. Also note the *stereochemistry* when the reaction is stereospecific.

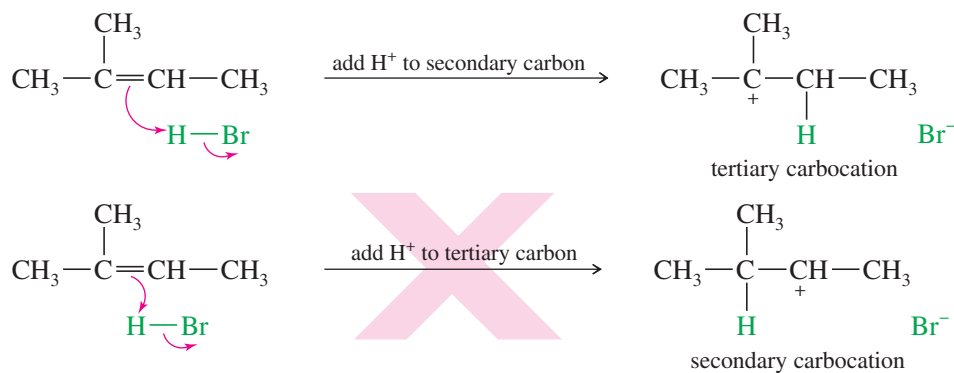
## 8-3 Addition of Hydrogen Halides to Alkenes

### 8-3A Orientation of Addition: Markovnikov's Rule

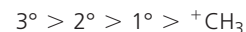
The simple mechanism shown for addition of HBr to but-2-ene applies to a large number of electrophilic additions. We can use this mechanism to predict the outcome of some fairly complicated reactions. For example, the addition of HBr to 2-methylbut-2-ene could lead to either of two products, yet only one is observed.



The first step is protonation of the double bond. If the proton adds to the secondary carbon, the product will be different from the one formed if the proton adds to the tertiary carbon.

**PROBLEM-SOLVING HINT**

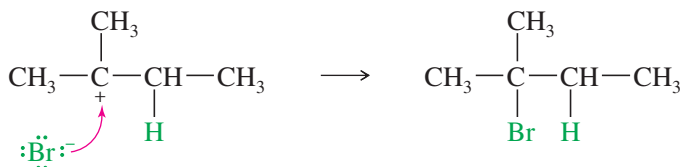
Stability of carbocations:



An electrophile adds to a double bond to give the most stable carbocation in the intermediate.

When the proton adds to the secondary carbon, a tertiary carbocation results. When the proton adds to the tertiary carbon atom, a secondary carbocation results. The tertiary carbocation is more stable (see Section 4-16A), so the first reaction is favored.

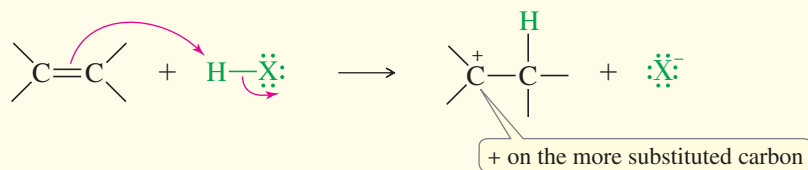
The second half of the mechanism produces the final product of the addition of HBr to 2-methylbut-2-ene.



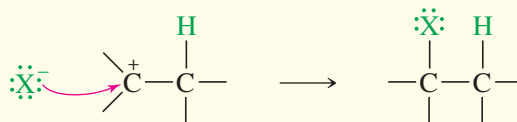
Note that protonation of one carbon atom of a double bond gives a carbocation on the carbon atom that was *not* protonated. Therefore, the proton adds to the end of the double bond that is *less* substituted to give the *more substituted carbocation* (the more stable carbocation).

**MECHANISM 8-2 Ionic Addition of HX to an Alkene**

**Step 1:** Protonation of the pi bond forms a carbocation.



**Step 2:** Attack by the halide ion gives the addition product.



(CONTINUED)

**EXAMPLE:** The ionic addition of HBr to propene shows protonation of the less substituted carbon to give the more substituted carbocation. Reaction with bromide ion completes the addition.

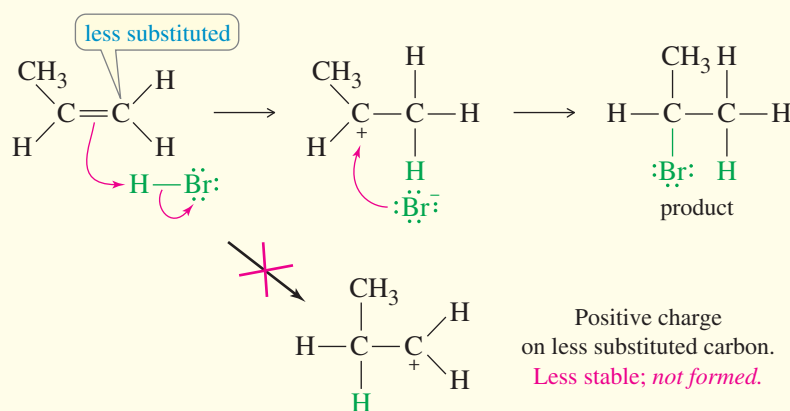


Figure 8-3 shows how addition of the proton to the less substituted end of the double bond gives the more substituted carbocation, which is more stable. Hammond's postulate predicts that the transition states resemble the carbocations, so the transition state leading to the more stable carbocation will be lower in energy than the one leading to the less stable carbocation. Therefore, the more highly substituted carbocation will be formed faster.

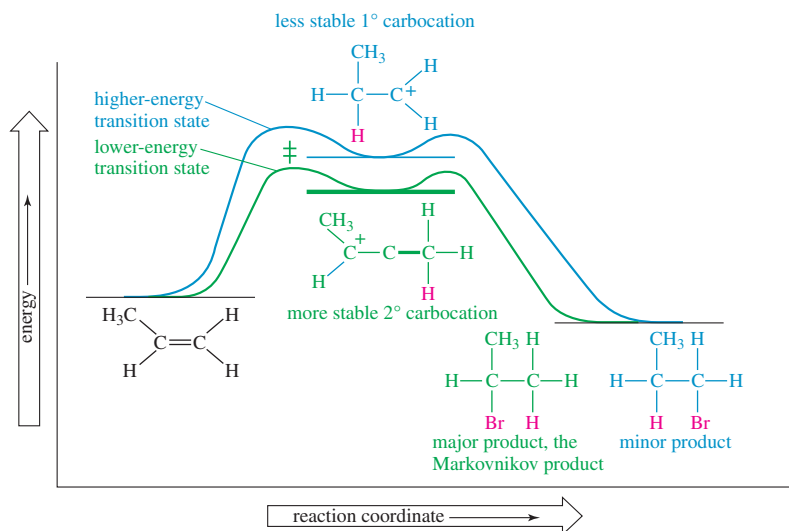
There are many examples of reactions where the proton adds to the less substituted carbon atom of the double bond to produce the more substituted carbocation. The addition of HBr (and other hydrogen halides) is said to be **regioselective** because in each case, one of the two possible orientations of addition results preferentially over the other.

**Markovnikov's Rule** A Russian chemist, Vladimir Markovnikov, first showed the orientation of addition of HBr to alkenes in 1869.

**MARKOVNIKOV'S RULE:** The addition of a proton acid to the double bond of an alkene results in a product with the acid proton bonded to the carbon atom that already holds the greater number of hydrogen atoms.

**FIGURE 8-3**

The reaction-energy diagram shows that the first step is rate-determining in the electrophilic addition to an alkene. The transition states resemble the intermediates (Hammond postulate), and the more highly substituted intermediate is formed faster because it has a lower-energy transition state leading to it. The more stable, more highly substituted intermediate generally leads to the Markovnikov product.



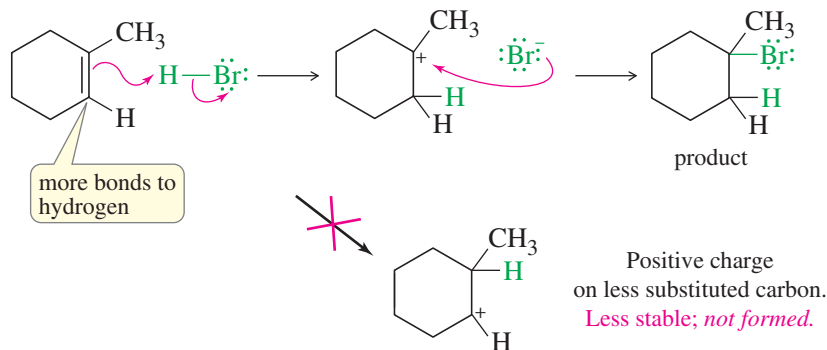


FIGURE 8-4

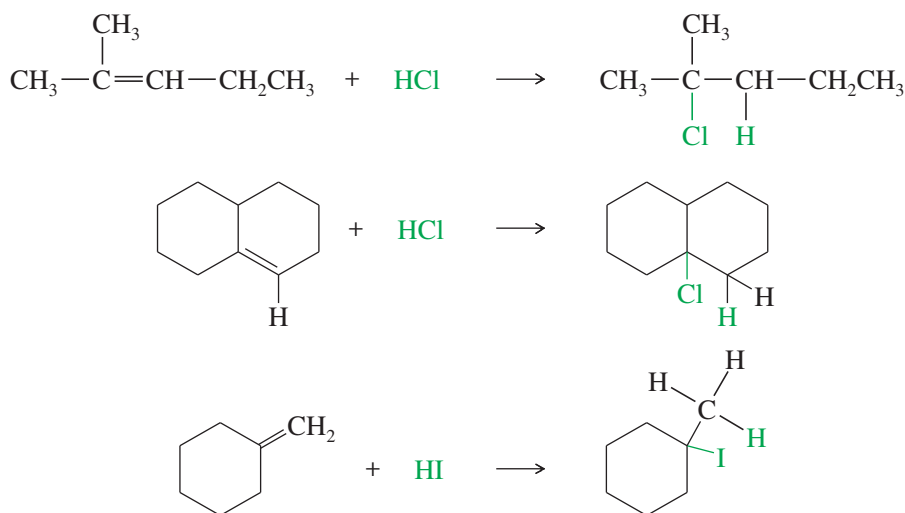
An electrophile adds to the less substituted end of the double bond to give the more substituted (and therefore more stable) carbocation.

This is the original statement of **Markovnikov's rule**. Reactions that follow this rule are said to follow **Markovnikov orientation** and give the **Markovnikov product**. We are often interested in adding electrophiles other than proton acids to the double bonds of alkenes. Markovnikov's rule can be extended to include a wide variety of other additions, based on the addition of the electrophile in such a way as to produce the most stable carbocation.

**MARKOVNIKOV'S RULE (extended):** In an electrophilic addition to an alkene, the electrophile adds in such a way as to generate the most stable intermediate.

Figure 8-4 shows how HBr adds to 1-methylcyclohexene to give the product with an additional hydrogen bonded to the carbon that already had the most bonds to hydrogen (one) in the alkene. Note that this orientation results from addition of the proton in the way that generates the more stable carbocation.

Like HBr, both HCl and HI add to the double bonds of alkenes, and they also follow Markovnikov's rule; for example,



#### PROBLEM-SOLVING HINT

The *orientation* or *regiochemistry* of an electrophilic addition is important when the reaction combines an unsymmetrical reagent with an unsymmetrical alkene. The first chemical species that reacts with the double bond is the electrophile ( $\text{H}^+$  in the case of adding HBr). Where the electrophile reacts determines where the second part of the reagent (the nucleophile,  $\text{Br}^-$  in this case) will react. Understanding the factors that determine where the electrophile reacts allows us to predict the products. This is the basis of Markovnikov's rule.

#### PROBLEM 8-1

Predict the major products of the following reactions, and propose mechanisms to support your predictions.

(a) pent-1-ene + HCl

(b) 2-methylpropene + HCl

(c) 1-methylcyclohexene + HI

(d) 4-methylcyclohexene + HBr

**PROBLEM 8-2**

- (a) When 1 mole of buta-1,3-diene reacts with 1 mole of HBr, both 3-bromobut-1-ene and 1-bromobut-2-ene are formed. Propose a mechanism to account for this mixture of products.
- (b) When 1-chlorocyclohexene reacts with HBr, the major product is 1-bromo-1-chlorocyclohexane. Propose a mechanism for this reaction, and explain why your proposed intermediate is more stable than the other possible intermediate.

**8-3B Free-Radical Addition of HBr: Anti-Markovnikov Addition**

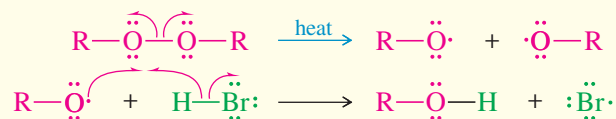
In 1933, M. S. Kharasch and F. W. Mayo found that some additions of HBr (but not HCl or HI) to alkenes gave products that were opposite those expected from Markovnikov's rule. These **anti-Markovnikov** reactions were most likely when the reagents or solvents came from old supplies that had accumulated peroxides from exposure to the air. Peroxides give rise to free radicals that initiate the addition, causing it to occur by a radical mechanism. The oxygen–oxygen bond in peroxides is rather weak, so it can break to give two alkoxy radicals.



Alkoxy radicals ( $\text{R}-\text{O}\cdot$ ) initiate the anti-Markovnikov addition of HBr. Radicals are electrophilic because they do not have octets. In most cases, a radical needs one more electron for its octet. When a radical reacts with a double bond, one electron from the pi bond fills the octet, leaving the other electron as a radical at the other end of the bond. The mechanism of this free-radical chain reaction is shown in Mechanism 8-3.

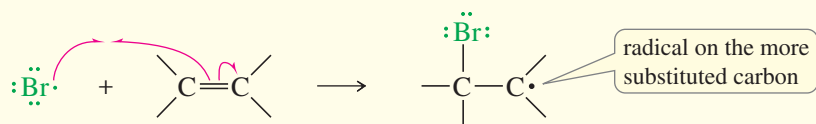
**MECHANISM 8-3 Free-Radical Addition of HBr to Alkenes**

Initiation: Formation of radicals.

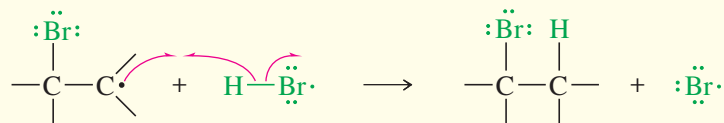


Propagation: A radical reacts to generate another radical.

**Step 1:** A bromine radical adds to the double bond to generate an alkyl radical on the more substituted carbon atom.



**Step 2:** The alkyl radical abstracts a hydrogen atom from HBr to generate the product and a bromine radical.

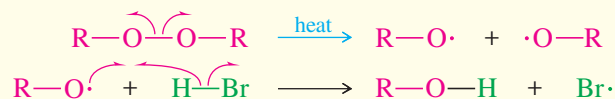


The bromine radical generated in Step 2 goes on to react with another molecule of alkene in Step 1, continuing the chain.

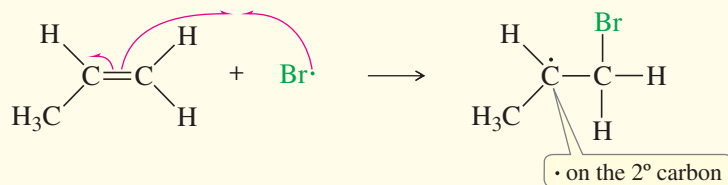
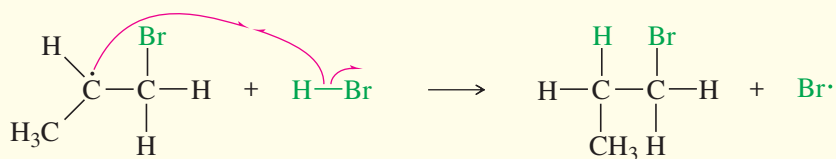


**EXAMPLE:** Free-radical addition of HBr to propene.

Initiation: Radicals are formed.

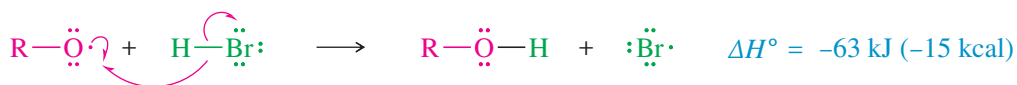


Propagation: A radical reacts to generate another radical.

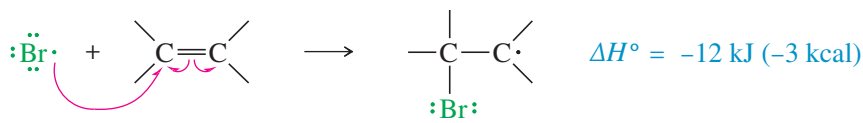
**Step 1:** A bromine radical adds to the double bond to generate an alkyl radical on the secondary carbon atom.**Step 2:** The alkyl radical abstracts a hydrogen atom from HBr to generate the product and a bromine radical.

The bromine radical generated in Step 2 goes on to react with another molecule of the alkene in another Step 1, continuing the chain.

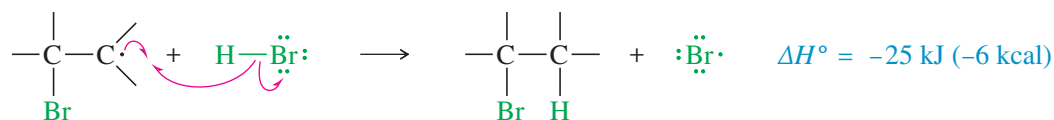
Let's consider the individual steps. In the initiation step, free radicals generated from the peroxide react with HBr to form bromine radicals.



The bromine radical lacks an octet of electrons in its valence shell, making it electron-deficient and electrophilic. It adds to a double bond, forming a new free radical with the odd electron on a carbon atom.

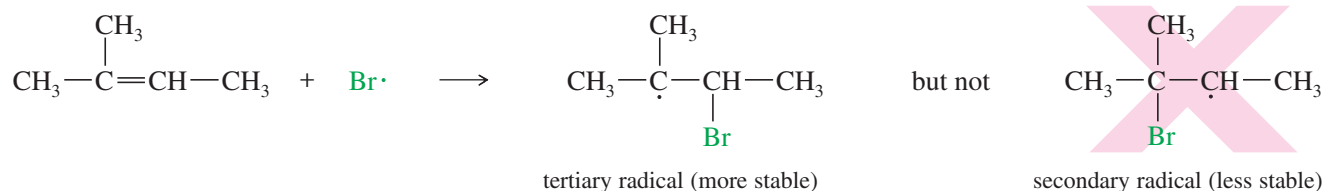


This free radical reacts with an HBr molecule to form a C—H bond and generate another bromine radical.

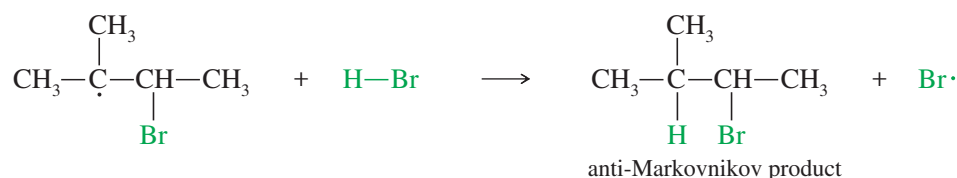


The regenerated bromine radical reacts with another molecule of the alkene, continuing the chain reaction. Both of the propagation steps are moderately exothermic, allowing them to proceed faster than the termination steps. Note that each propagation step starts with one free radical and ends with another free radical. The number of free radicals is constant, until the reactants are consumed, and free radicals come together and terminate the chain reaction.

**Radical Addition of HBr to Unsymmetrical Alkenes** Now we must explain the anti-Markovnikov orientation found in the products of the peroxide-catalyzed reaction. With an unsymmetrical alkene such as 2-methylbut-2-ene, adding the bromine radical to the secondary end of the double bond forms a tertiary radical.

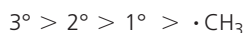


As we saw in the protonation of an alkene, the electrophile (in this case,  $\text{Br}\cdot$ ) adds to the less substituted end of the double bond, and the unpaired electron appears on the more substituted carbon to give the more stable free radical. This intermediate reacts with HBr to give the anti-Markovnikov product, in which H has added to the more substituted end of the double bond: the end that started with *fewer* hydrogens.



#### PROBLEM-SOLVING HINT

Stability of radicals:



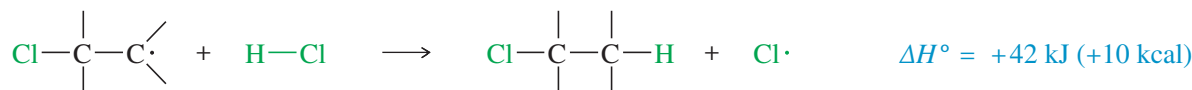
A radical adds to a double bond to give the most stable radical in the intermediate.

Note that *both* mechanisms for the addition of HBr to an alkene (with and without peroxides) follow our extended statement of Markovnikov's rule: In both cases, the electrophile adds to the less substituted end of the double bond to give the more stable intermediate, either a carbocation or a free radical. In the ionic reaction, the electrophile is  $\text{H}^+$ . In the peroxide-catalyzed free-radical reaction,  $\text{Br}\cdot$  is the electrophile.

Many students wonder why the reaction with Markovnikov orientation does not take place in the presence of peroxides, together with the free-radical chain reaction. It actually does take place, but the peroxide-catalyzed reaction is faster. If just a tiny bit of peroxide is present, a mixture of Markovnikov and anti-Markovnikov products results. If an appreciable amount of peroxide is present, the radical chain reaction is so much faster than the uncatalyzed ionic reaction that only the anti-Markovnikov product is observed.

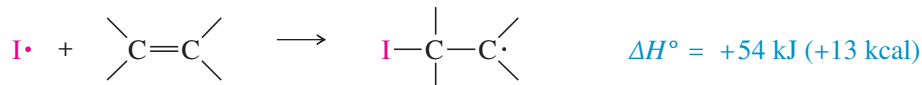
The reversal of orientation in the presence of peroxides is called the **peroxide effect**. It occurs only with the addition of HBr to alkenes. The peroxide effect is not seen with HCl because the second step, the reaction of an alkyl radical with HCl, is strongly endothermic.

Proposed free-radical addition of HCl fails:



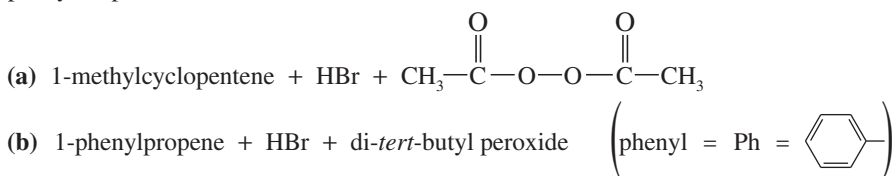
Similarly, the peroxide effect is not observed with HI because the reaction of an iodine atom with an alkene is strongly endothermic. Only HBr has just the right reactivity for each step of the free-radical chain reaction to take place.

Proposed free-radical addition of HI fails:



**PROBLEM 8-3**

Predict the major products of the following reactions, and propose mechanisms to support your predictions.

**PROBLEM-SOLVING HINT**

Remember to write out complete structures, including all bonds and charges, when writing a mechanism or determining the course of a reaction.

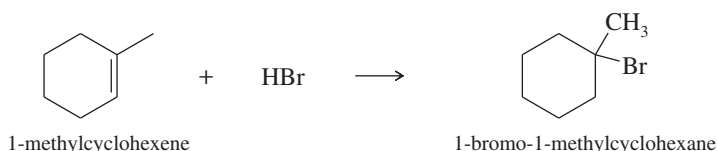
**SOLVED PROBLEM 8-1**

Show how you would accomplish the following synthetic conversions.

(a) Convert 1-methylcyclohexene to 1-bromo-1-methylcyclohexane.

**SOLUTION**

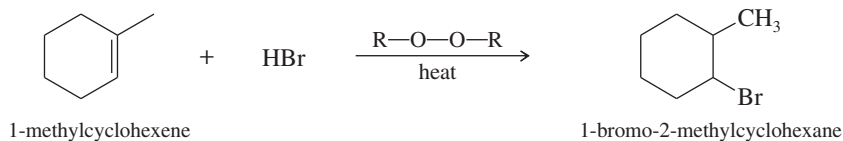
This synthesis requires the addition of HBr to an alkene with Markovnikov orientation. Ionic addition of HBr gives the correct product.



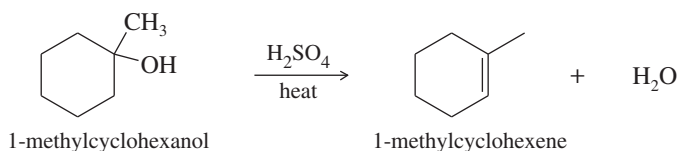
(b) Convert 1-methylcyclohexanol to 1-bromo-2-methylcyclohexane.

**SOLUTION**

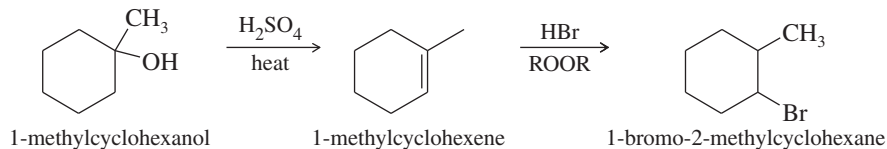
This synthesis requires the conversion of an alcohol to an alkyl bromide with the bromine atom at the neighboring carbon atom. This is the anti-Markovnikov product, which could be formed by the radical-catalyzed addition of HBr to 1-methylcyclohexene.



1-Methylcyclohexene is easily synthesized by the dehydration of 1-methylcyclohexanol. The most substituted alkene is the desired product.



The two-step synthesis is summarized as follows:

**PROBLEM 8-4**

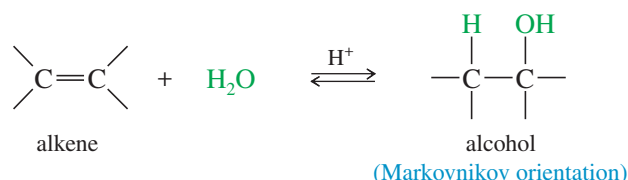
Show how you would accomplish the following synthetic conversions.

- (a) but-1-ene  $\longrightarrow$  1-bromobutane  
 (b) but-1-ene  $\longrightarrow$  2-bromobutane  
 (c) 2-methylcyclohexanol  $\longrightarrow$  1-bromo-1-methylcyclohexane  
 (d) 2-methylbutan-2-ol  $\longrightarrow$  2-bromo-3-methylbutane

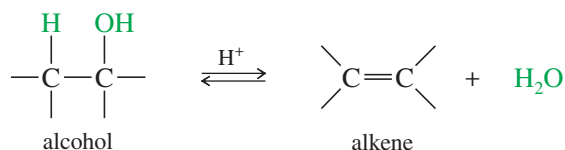
## 8-4 Addition of Water: Hydration of Alkenes

An alkene may react with water in the presence of a strongly acidic catalyst to form an alcohol. Formally, this reaction is a **hydration** (the addition of water), with a hydrogen atom adding to one carbon and a hydroxy group adding to the other. Hydration of an alkene is the reverse of the dehydration of alcohols we studied in Section 7-18.

### Hydration of an alkene



### Dehydration of an alcohol



For dehydrating alcohols, a concentrated dehydrating acid (such as  $\text{H}_2\text{SO}_4$  or  $\text{H}_3\text{PO}_4$ ) is used to drive the equilibrium to favor the alkene. Hydration of an alkene, on the other hand, is accomplished by adding excess water to drive the equilibrium toward the alcohol.

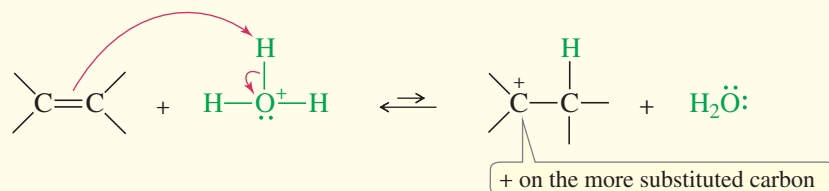
### 8-4A Mechanism of Hydration

The *Principle of Microscopic Reversibility* states that a forward reaction and a reverse reaction taking place under the same conditions (as in an equilibrium) must follow the same reaction pathway in microscopic detail. The hydration and dehydration reactions are the two complementary reactions in an equilibrium; therefore, they must follow the same reaction pathway. It makes sense that the lowest-energy transition states and intermediates for the reverse reaction are the same as those for the forward reaction, except in reverse order.

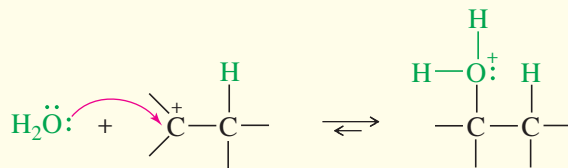
According to the Principle of Microscopic Reversibility, we can write the hydration mechanism by reversing the order of the steps of the dehydration (Section 7-18). Protonation of the double bond forms a carbocation. Nucleophilic attack by water, followed by loss of a proton, gives the alcohol.

## MECHANISM 8-4 Acid-Catalyzed Hydration of an Alkene

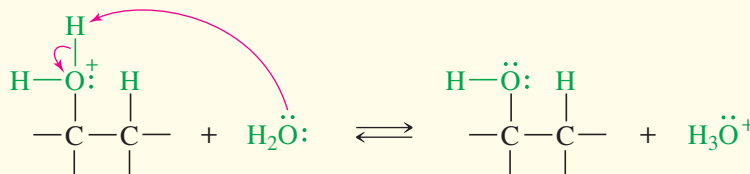
*Step 1:* Protonation of the double bond forms a carbocation.



**Step 2:** Nucleophilic attack by water gives a protonated alcohol.

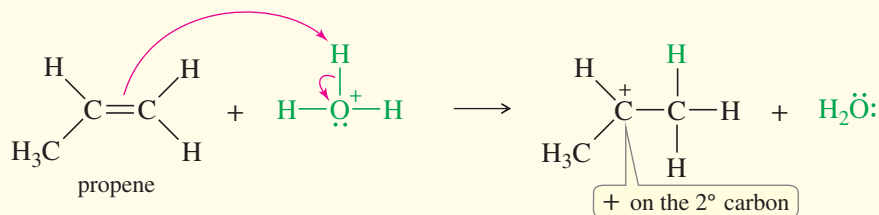


**Step 3:** Deprotonation gives the alcohol.

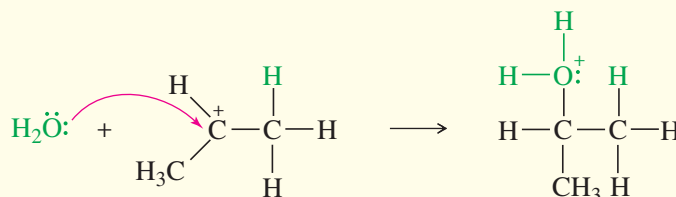


**EXAMPLE:** Acid-catalyzed hydration of propene.

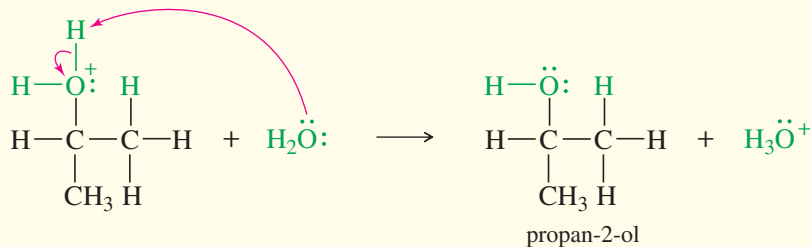
**Step 1:** Protonation of the double bond forms a secondary carbocation.



**Step 2:** Nucleophilic attack by water gives a protonated alcohol.



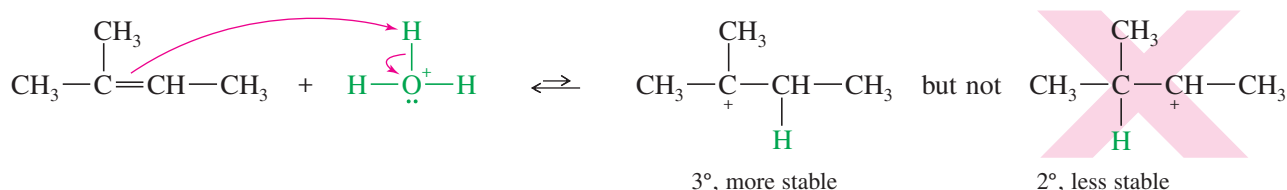
**Step 3:** Deprotonation gives the alcohol.



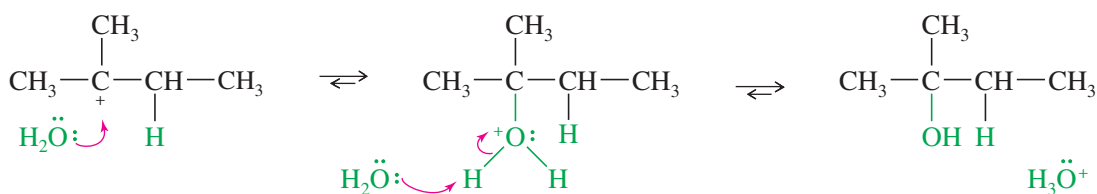
### 8-4B Orientation of Hydration

Step 1 of the hydration mechanism is similar to the first step in the addition of HBr. The proton adds to the *less* substituted end of the double bond to form the *more* substituted carbocation. Water attacks the carbocation to give (after loss of a proton) the alcohol with the —OH group on the more substituted carbon. Like the addition of hydrogen

halides, hydration is *regioselective*: It follows Markovnikov's rule, giving a product in which the new hydrogen has added to the less substituted end of the double bond. Consider the hydration of 2-methylbut-2-ene:

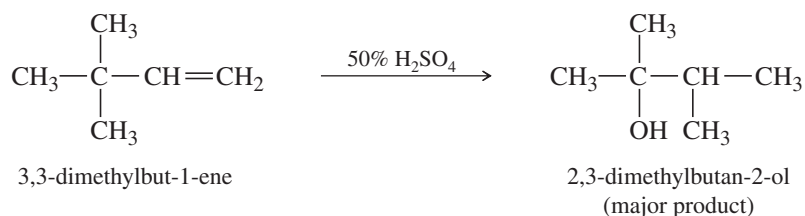


The proton adds to the less substituted end of the double bond, so the positive charge appears at the more substituted end. Water attacks the carbocation to give the protonated alcohol.



The reaction follows Markovnikov's rule. The proton has added to the end of the double bond that already had more hydrogens (that is, the less substituted end), and the —OH group has added to the more substituted end.

Like other reactions that involve carbocation intermediates, hydration may take place with rearrangement. For example, when 3,3-dimethylbut-1-ene undergoes acid-catalyzed hydration, the major product results from rearrangement of the carbocation intermediate.



### PROBLEM 8-5

Propose a mechanism to show how 3,3-dimethylbut-1-ene reacts with dilute aqueous  $\text{H}_2\text{SO}_4$  to give 2,3-dimethylbutan-2-ol and a small amount of 2,3-dimethylbut-2-ene.

### PROBLEM-SOLVING HINT

When predicting products for electrophilic additions, first draw the structure of the carbocation (or other intermediate) that results from electrophilic attack.

### PROBLEM 8-6

Predict the products of the following hydration reactions.

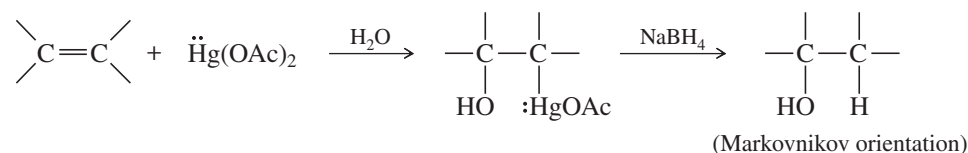
- 1-methylcyclopentene + dilute acid
- 2-phenylpropene + dilute acid
- 1-phenylcyclohexene + dilute acid

## 8-5 Hydration by Oxymercuration–Demercuration

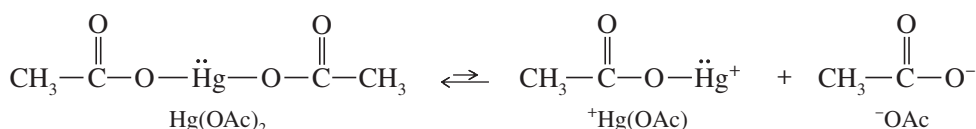
Many alkenes do not easily undergo hydration in aqueous acid. Some alkenes are nearly insoluble in aqueous acid, and others undergo side reactions such as rearrangement, polymerization, or charring under these strongly acidic conditions. In some cases, the overall equilibrium favors the alkene rather than the alcohol. No amount of catalysis can cause a reaction to occur if the energetics are unfavorable.

Oxymercuration–demercuration is another method for converting alkenes to alcohols with Markovnikov orientation. Oxymercuration–demercuration works with many alkenes that do not easily undergo direct hydration, and it takes place under milder conditions. No free carbocation is formed, so there is no opportunity for rearrangements or polymerization.

### Oxymercuration–Demercuration



The reagent for mercuriation is mercuric acetate,  $\text{Hg}(\text{OCOCH}_3)_2$ , abbreviated  $\text{Hg}(\text{OAc})_2$ . There are several theories as to how this reagent acts as an electrophile; the simplest one is that mercuric acetate dissociates slightly to form a positively charged mercury species,  $^+\text{Hg}(\text{OAc})$ .



**Oxymercuration** involves an electrophilic attack on the double bond by the positively charged mercury species. The product is a *mercurinium ion*, an organometallic cation containing a three-membered ring. In the second step, water from the solvent attacks the mercurinium ion to give (after deprotonation) an organomercurial alcohol. A subsequent reaction is **demercuration**, to remove the mercury. Sodium borohydride ( $\text{NaBH}_4$ , a reducing agent) replaces the mercuric acetate fragment with a hydrogen atom.

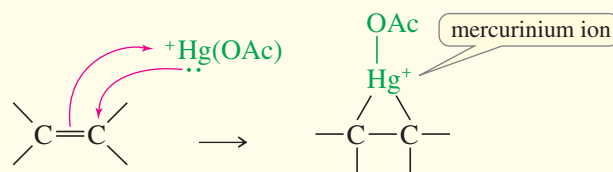
### Application: Toxicology

Mercury and its compounds were used for centuries as ingredients in antibacterial drugs, skin creams, and antiseptics. Mercury compounds are quite toxic, however. In the body, mercury combines with the thiol groups of critical enzymes, inactivating them. Mercury poisoning causes brain and kidney damage, often leading to death.

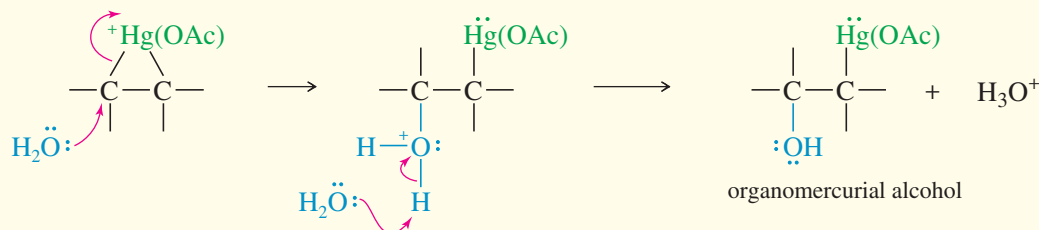
We cover these reactions using mercury-based reagents because they are particularly interesting and the concepts are useful. For example, oxymercuration–demercuration adds water to alkenes without the rearrangements that are common in the acid-catalyzed hydration. When possible, we prefer to use other, less toxic reagents.

## MECHANISM 8-5 Oxymercuration of an Alkene

**Step 1:** Electrophilic attack forms a mercurinium ion.

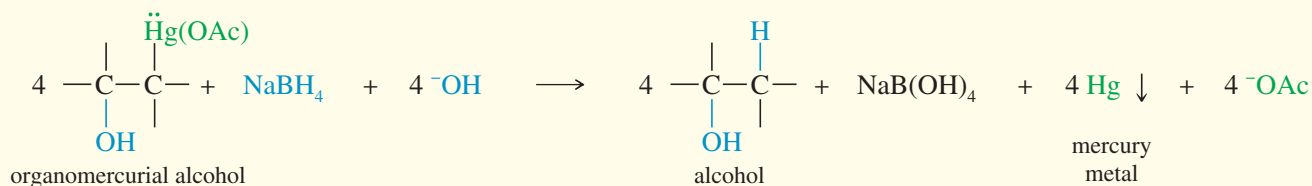


**Step 2:** Water opens the ring to give an organomercurial alcohol.



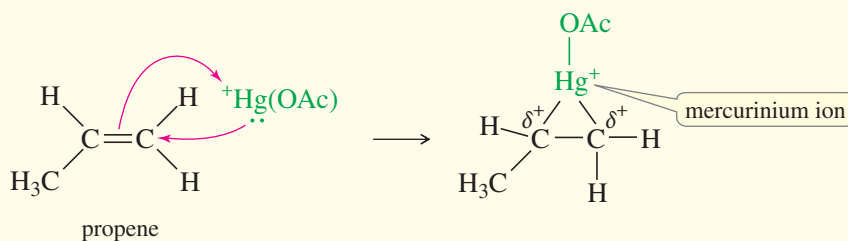
Demercuration replaces the mercuric fragment with hydrogen to give the alcohol.

(CONTINUED)

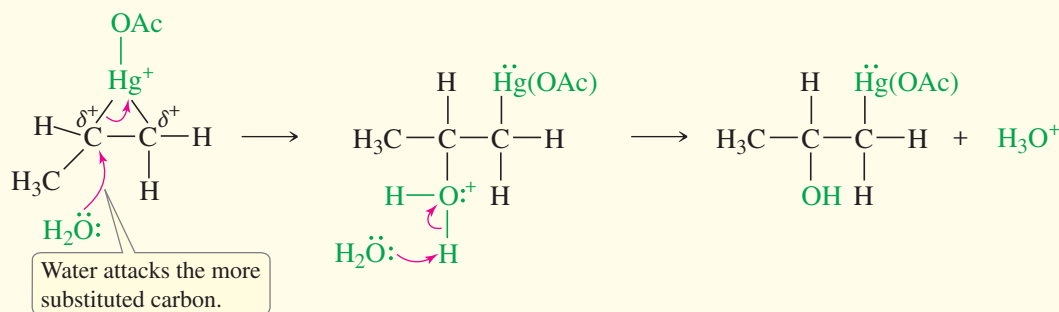


**EXAMPLE:** Oxymercuration–demercuration of propene.

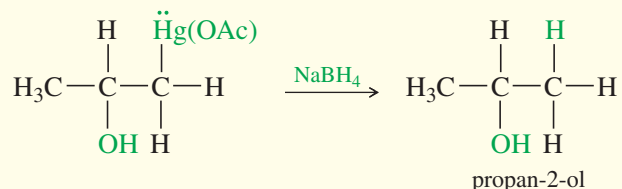
*Step 1:* Electrophilic attack forms a mercurinium ion.



*Step 2:* Water opens the ring to give an organomercurial alcohol.



Demercuration replaces the mercuric fragment with hydrogen to give the alcohol.

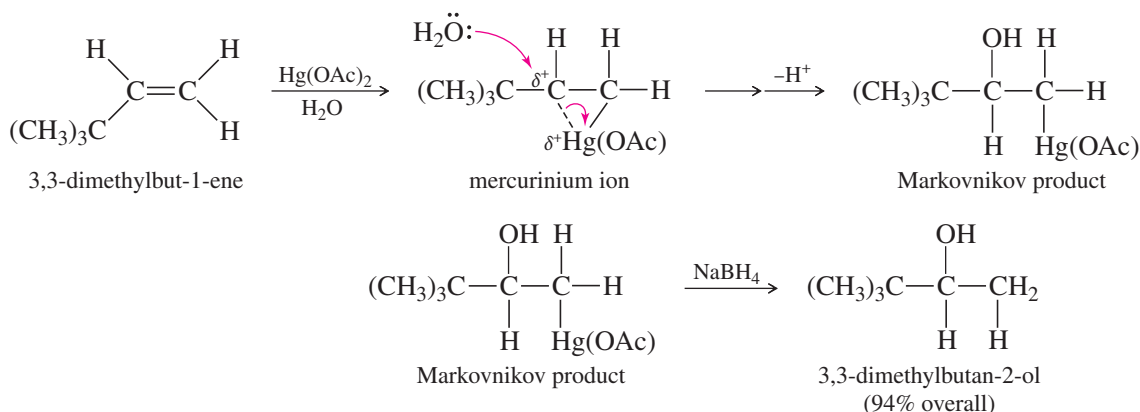


Oxymercuration–demercuration of an unsymmetrical alkene generally gives Markovnikov orientation of addition, as shown by the oxymercuration of propene in the preceding example. The mercurinium ion has a considerable amount of positive charge on both of its carbon atoms, but there is more of a positive charge on the more substituted carbon atom, where it is more stable. Attack by water occurs on this more electrophilic carbon, giving Markovnikov orientation. The electrophile,  $^+\text{Hg}(\text{OAc})$ , remains bonded to the less substituted end of the double bond. Reduction of the organomercurial alcohol gives the Markovnikov alcohol: propan-2-ol.

Similarly, oxymercuration–demercuration of 3,3-dimethylbut-1-ene gives the Markovnikov product, 3,3-dimethylbutan-2-ol, in excellent yield. Contrast this un-rearranged product with the rearranged product formed in the acid-catalyzed hydration of



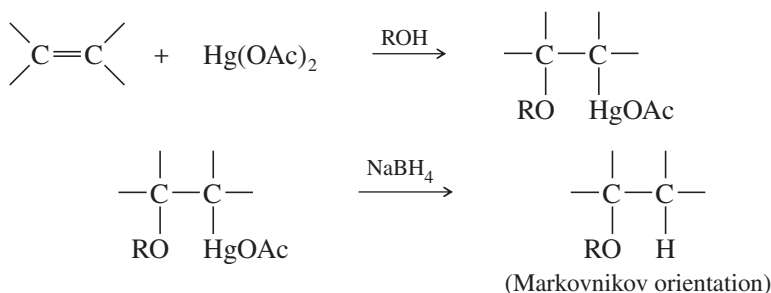
the same alkene in Section 8-4B. Oxymercuration–demercuration reliably adds water across the double bond of an alkene with Markovnikov orientation and without rearrangement.



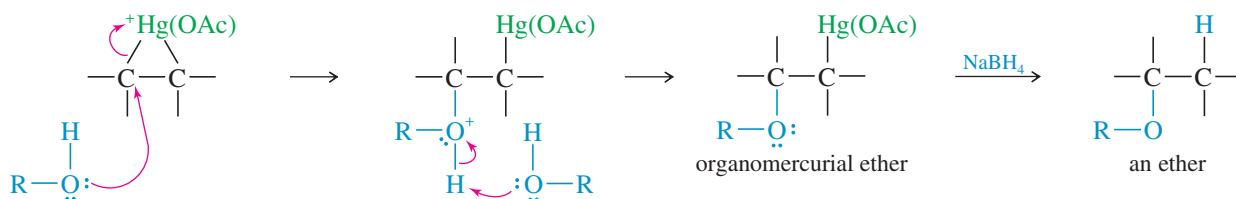
Of the methods we have seen for Markovnikov hydration of alkenes, oxymercuration–demercuration is most commonly used in the laboratory. It gives better yields than direct acid-catalyzed hydration, it avoids the possibility of rearrangements, and it does not involve harsh conditions. There are also disadvantages, however. Organomercurial compounds are highly toxic. They must be used with great care and then disposed of properly.

## 8-6 Alkoxymercuration–Demercuration

When mercuration takes place in an alcohol solvent, the alcohol serves as a nucleophile to attack the mercurinium ion. The resulting product contains an alkoxy ( $-\text{O}-\text{R}$ ) group. In effect, **alkoxymercuration**–demercuration converts alkenes to ethers by adding an alcohol across the double bond of the alkene.



As we have seen, an alkene reacts to form a mercurinium ion that is attacked by the nucleophilic solvent. Attack by an alcohol solvent gives an organomercurial ether that can be reduced to the ether.



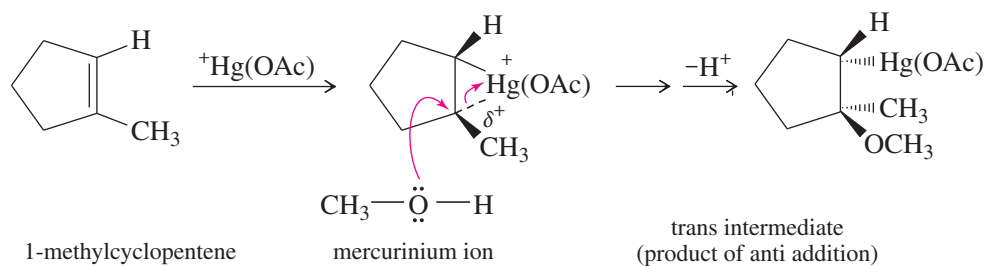
The solvent attacks the mercurinium ion at the *more* substituted end of the double bond (where there is more  $\delta^+$  charge), giving Markovnikov orientation of addition. The  $\text{Hg}(\text{OAc})$  group appears at the *less* substituted end of the double bond. Reduction gives the Markovnikov product, with hydrogen at the less substituted end of the double bond.

**SOLVED PROBLEM 8-2**

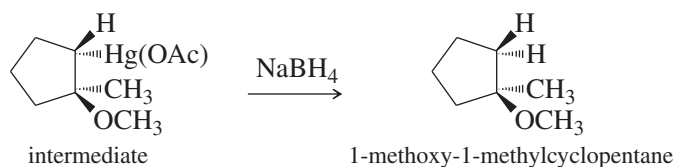
Show the intermediates and products that result from alkoxymercuration–demercuration of 1-methylcyclopentene, using methanol as the solvent.

**SOLUTION**

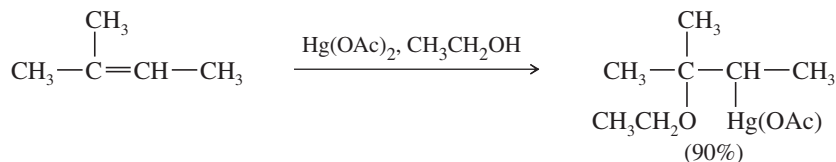
Mercuric acetate adds to 1-methylcyclopentene to give the cyclic mercurinium ion. This ion has a considerable amount of positive charge on the more substituted tertiary carbon atom. Methanol attacks this carbon from the opposite side, leading to *anti* addition: The reagents ( $\text{Hg(OAc)}$  and  $\text{OCH}_3$ ) have added to opposite faces of the double bond.



Reduction of the intermediate gives the Markovnikov product, 1-methoxy-1-methylcyclopentane.

**PROBLEM 8-7**

(a) Propose a mechanism for the following reaction.



(b) Give the structure of the product that results when this intermediate is reduced by sodium borohydride.

**PROBLEM 8-8**

Predict the major products of the following reactions.

- (a) 1-methylcyclohexene + aqueous  $\text{Hg(OAc)}_2$       (b) the product from part (a), treated with  $\text{NaBH}_4$   
 (c) 4-chlorocycloheptene +  $\text{Hg(OAc)}_2$  in  $\text{CH}_3\text{OH}$       (d) the product from part (c), treated with  $\text{NaBH}_4$

**PROBLEM 8-9**

Show how you would accomplish the following synthetic conversions.

- (a) but-1-ene  $\rightarrow$  2-methoxybutane      (b) 1-iodo-2-methylcyclopentane  $\rightarrow$  1-methylcyclopentanol  
 (c) 3-methylpent-1-ene  $\rightarrow$  3-methylpentan-2-ol

Explain why acid-catalyzed hydration would be a poor choice for the reaction in (c).

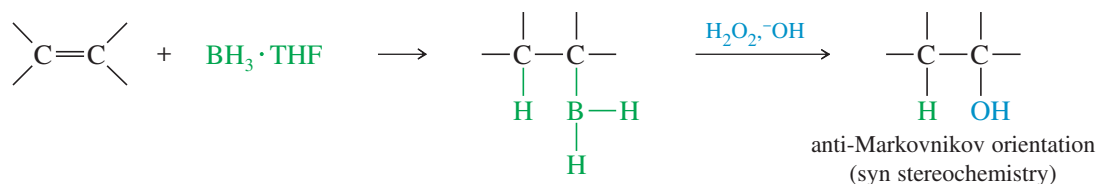
**8-7 Hydroboration of Alkenes**

We have seen two methods for hydrating an alkene with Markovnikov orientation. What if we need to convert an alkene to the anti-Markovnikov alcohol? For example, the following transformation cannot be accomplished using the hydration procedures covered thus far.



peroxide oxidizes the alkylborane to an alcohol. In effect, hydroboration–oxidation converts alkenes to alcohols by adding water across the double bond, with anti-Markovnikov orientation.

*Hydroboration–oxidation:*



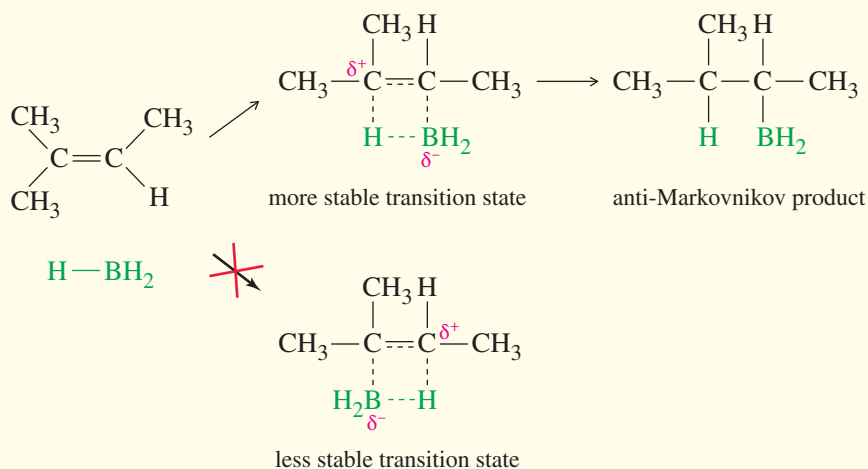
### 8-7A Mechanism of Hydroboration

Borane is an electron-deficient compound. It has only six valence electrons, so the boron atom in  $\text{BH}_3$  cannot have an octet. Acquiring an octet is the driving force for the unusual bonding structures (bridging hydrogens, for example) found in boron compounds. As an electron-deficient compound,  $\text{BH}_3$  is a strong electrophile, capable of adding to a double bond. This **hydroboration** of the double bond is thought to occur in one step, with the boron atom adding to the less substituted end of the double bond, as shown in Mechanism 8-6.

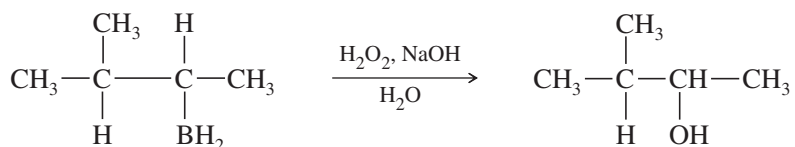
In the transition state, the electrophilic boron atom withdraws electrons from the pi bond, and the carbon at the other end of the double bond acquires a partial positive charge. This partial charge is more stable on the more substituted carbon atom. The product shows boron bonded to the less substituted end of the double bond and hydrogen bonded to the more substituted end. Also, steric hindrance favors boron adding to the less hindered, less substituted end of the double bond.

#### MECHANISM 8-6 Hydroboration of an Alkene

Borane adds to the double bond in a single step. Boron adds to the less hindered, less substituted carbon, and hydrogen adds to the more substituted carbon.



The boron atom is removed by oxidation, using aqueous sodium hydroxide and hydrogen peroxide ( $\text{HOOH}$  or  $\text{H}_2\text{O}_2$ ) to replace the boron atom with a hydroxy ( $-\text{OH}$ ) group. The oxidation does not affect the orientation of the product, because the anti-Markovnikov orientation was established in the first step, the addition of  $\text{BH}_3$ .



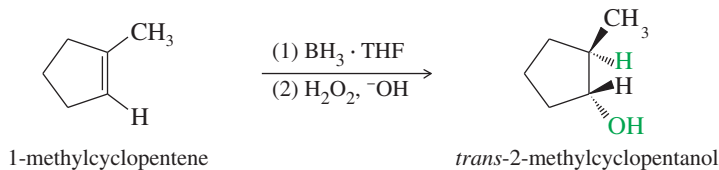
This hydration of an alkene by hydroboration–oxidation is another example of a reaction that does not follow the original statement of Markovnikov’s rule (the product is anti-Markovnikov), but still follows our understanding of the reasoning behind Markovnikov’s rule. The electrophilic boron atom adds to the *less* substituted end of the double bond, placing the positive charge (and the hydrogen atom) at the more substituted end.

### SOLVED PROBLEM 8-3

Show how you would convert 1-methylcyclopentanol to 2-methylcyclopentanol.

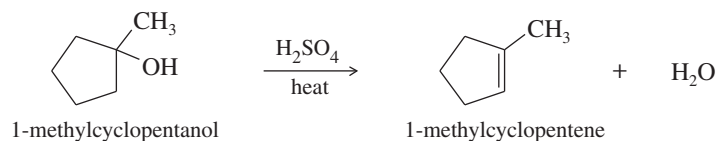
#### SOLUTION

Working backward, use hydroboration–oxidation to form 2-methylcyclopentanol from 1-methylcyclopentene. The use of (1) and (2) above and below the reaction arrow indicates individual steps in a two-step sequence.



The 2-methylcyclopentanol that results from this synthesis is the pure *trans* isomer. This stereochemical result is discussed in Section 8-7C.

1-Methylcyclopentene is the most substituted alkene that results from dehydration of 1-methylcyclopentanol. Dehydration of the alcohol would give the correct alkene.



### PROBLEM-SOLVING HINT

Work backward on multistep syntheses.

### PROBLEM 8-10

Predict the major products of the following reactions.

- |  |  |
|--|--|
| (a) propene + $\text{BH}_3 \cdot \text{THF}$             | (b) the product from part (a) + $\text{H}_2\text{O}_2/\text{OH}^-$ |
| (c) 2-methylpent-2-ene + $\text{BH}_3 \cdot \text{THF}$  | (d) the product from part (c) + $\text{H}_2\text{O}_2/\text{OH}^-$ |
| (e) 1-methylcyclohexene + $\text{BH}_3 \cdot \text{THF}$ | (f) the product from part (e) + $\text{H}_2\text{O}_2/\text{OH}^-$ |

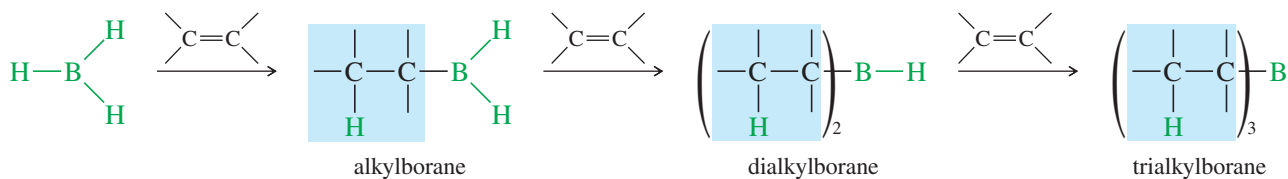
### PROBLEM 8-11

Show how you would accomplish the following synthetic conversions.

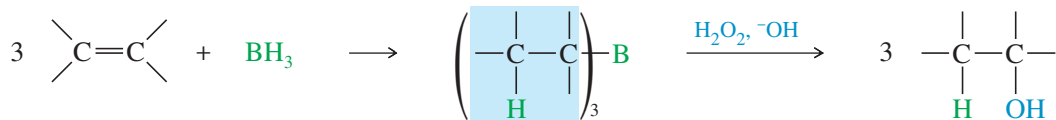
- |   |  |
|---|--|
| (a) but-1-ene $\rightarrow$ butan-1-ol                                | (b) but-1-ene $\rightarrow$ butan-2-ol |
| (c) 2-bromo-2,4-dimethylpentane $\rightarrow$ 2,4-dimethylpentan-3-ol |  |

## 8-7B Stoichiometry of Hydroboration

For simplicity, we have neglected the fact that 3 moles of an alkene can react with each mole of  $\text{BH}_3$ . Each B—H bond in  $\text{BH}_3$  can add across the double bond of an alkene. The first addition forms an alkylborane, the second a dialkylborane, and the third a trialkylborane.



### Summary

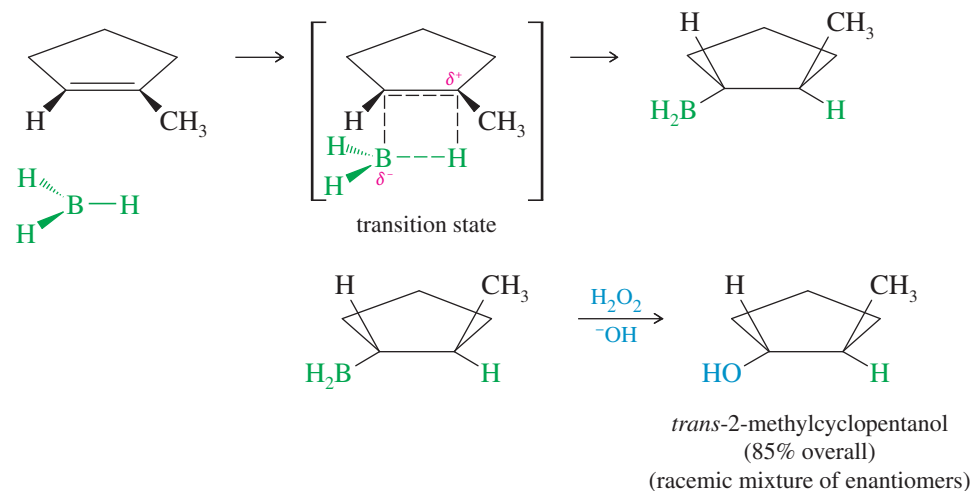


Trialkylboranes react exactly as we have discussed, and they oxidize to give anti-Markovnikov alcohols. Trialkylboranes are quite bulky, further reinforcing the preference for boron to add to the less hindered carbon atom of the double bond. Boranes are often drawn as the 1:1 monoalkylboranes to simplify their structure and emphasize the organic part of the molecule.

### 8-7C Stereochemistry of Hydroboration

The simultaneous addition of boron and hydrogen to the double bond (as shown in Mechanism 8-6) leads to a **syn addition**: Boron and hydrogen add across the double bond on the *same side* of the molecule. (If they added to opposite sides of the molecule, the process would be an **anti addition**.)

The stereochemistry of the hydroboration–oxidation of 1-methylcyclopentene is that boron and hydrogen add to the same face of the double bond (syn) to form a trialkylborane. Oxidation of the trialkylborane replaces boron with a hydroxy group in the same stereochemical position. The product is *trans*-2-methylcyclopentanol. A racemic mixture is expected because a chiral product is formed from achiral reagents.

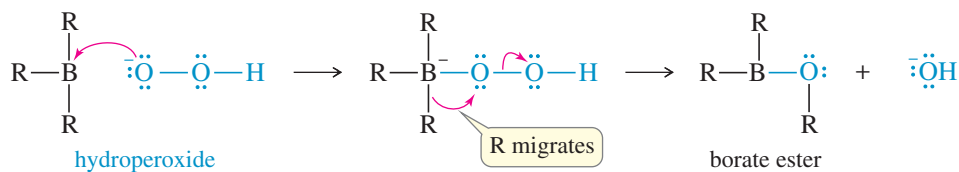


The second step (oxidation of the borane to the alcohol) takes place with retention of configuration. Hydroperoxide ion adds to the borane, causing the alkyl group to migrate from boron to oxygen. The alkyl group migrates with retention of configuration because it moves with its electron pair and does not alter the tetrahedral structure of the migrating carbon atom. Hydrolysis of the borate ester gives the alcohol.

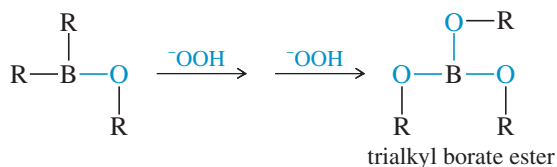
#### Formation of hydroperoxide ion



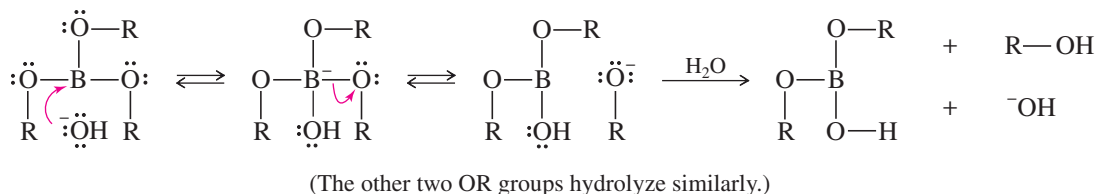
### Addition of hydroperoxide and migration of the alkyl group



### Twice more to oxidize the other two alkyl groups



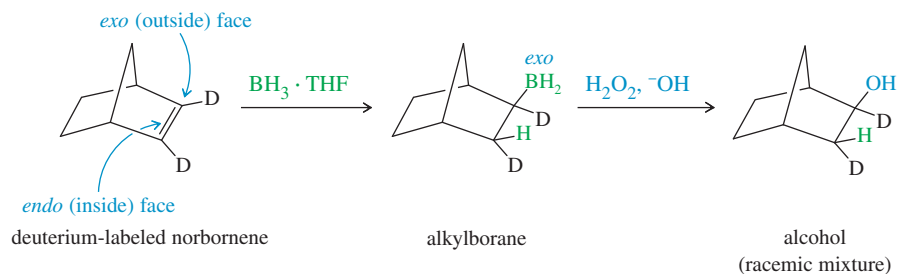
### Hydrolysis of the borate ester



Hydroboration of alkenes is another example of a **stereospecific reaction**, in which different stereoisomers of the starting compound react to give different stereoisomers of the product. Problem 8-14 considers the different products formed by the hydroboration-oxidation of two acyclic diastereomers.

### SOLVED PROBLEM 8-4

A norbornene molecule labeled with deuterium is subjected to hydroboration-oxidation. Give the structures of the intermediates and products.



### SOLUTION

The syn addition of  $\text{BH}_3$  across the double bond of norbornene takes place mostly from the more accessible outside (exo) face of the double bond. Oxidation gives a product with both the hydrogen atom and the hydroxy group in exo positions. (The less accessible inner face of the double bond is called the endo face.)

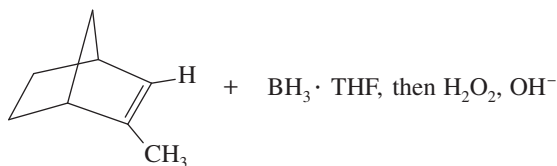
### PROBLEM 8-12

In the hydroboration of 1-methylcyclopentene shown in Solved Problem 8-3, the reagents are achiral, and the products are chiral. The product is a racemic mixture of *trans*-2-methylcyclopentanol, but only one enantiomer is shown. Show how the other enantiomer is formed.

**PROBLEM 8-13**

Predict the major products of the following reactions. Include stereochemistry where applicable.

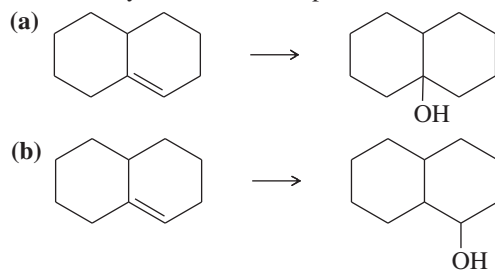
- (a) 1-methylcycloheptene +  $\text{BH}_3 \cdot \text{THF}$ , then  $\text{H}_2\text{O}_2$ ,  $\text{OH}^-$   
 (b) *trans*-4,4-dimethylpent-2-ene +  $\text{BH}_3 \cdot \text{THF}$ , then  $\text{H}_2\text{O}_2$ ,  $\text{OH}^-$   
 (c)

**PROBLEM 8-14**

- (a) When (*Z*)-3-methylhex-3-ene undergoes hydroboration–oxidation, two isomeric products are formed. Give their structures, and label each asymmetric carbon atom as (*R*) or (*S*). What is the relationship between these isomers?  
 (b) Repeat part (a) for (*E*)-3-methylhex-3-ene. What is the relationship between the products formed from (*Z*)-3-methylhex-3-ene and those formed from (*E*)-3-methylhex-3-ene?

**PROBLEM 8-15**

Show how you would accomplish the following transformations.



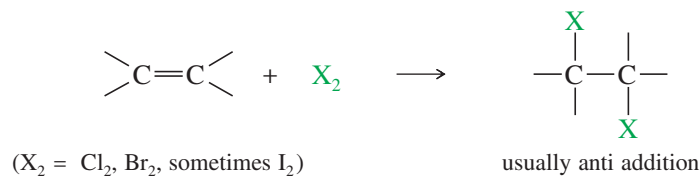
- (c) 1-methylcycloheptanol  $\rightarrow$  2-methylcycloheptanol

**PROBLEM 8-16**

- (a) When  $\text{HBr}$  adds across the double bond of 1,2-dimethylcyclopentene, the product is a mixture of the *cis* and *trans* isomers. Show why this addition is not stereospecific.  
 (b) When 1,2-dimethylcyclopentene undergoes hydroboration–oxidation, one diastereomer of the product predominates. Show why this addition is stereospecific, and predict the stereochemistry of the major product.

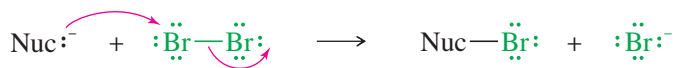
**8-8 Addition of Halogens to Alkenes**

Halogens add to alkenes to form vicinal dihalides.

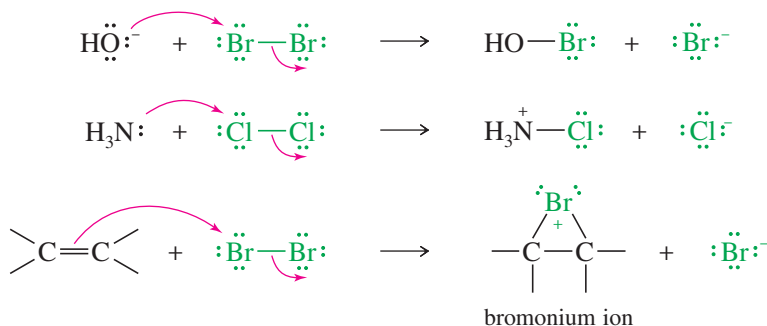
**8-8A Mechanism of Halogen Addition**

A halogen molecule ( $\text{Br}_2$ ,  $\text{Cl}_2$ , or  $\text{I}_2$ ) is electrophilic; a nucleophile can react with a halogen, displacing a halide ion:



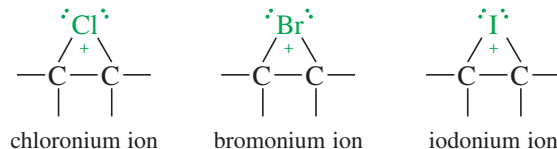


In this example, the nucleophile attacks the electrophilic nucleus of one bromine atom, and the other bromine serves as the leaving group, departing as bromide ion. Many reactions fit this general pattern; for example:

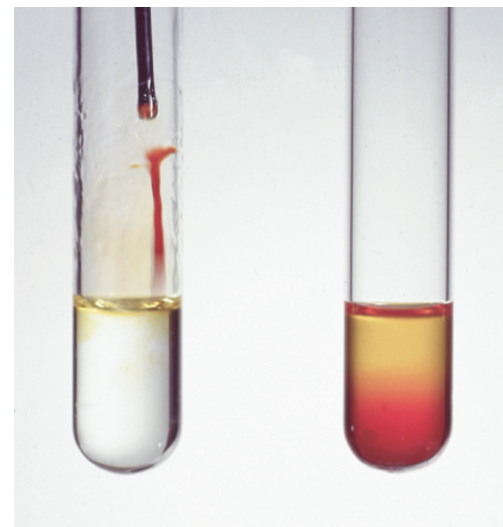


In the last reaction, the pi electrons of an alkene attack the bromine molecule, expelling bromide ion. A **bromonium ion** results, containing a three-membered ring with a positive charge on the bromine atom. This bromonium ion is similar in structure to the mercurinium ion discussed in Section 8-5. Similar reactions with other halogens form other **halonium ions**, including *chloronium ions* and *iodonium ions*.

#### Examples



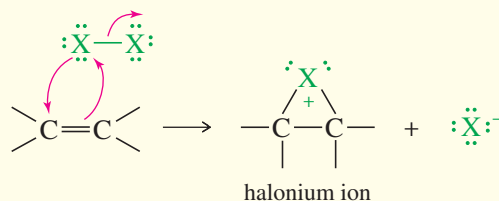
Unlike a normal carbocation, all the atoms in a halonium ion have filled octets. The three-membered ring has considerable ring strain, however, which, combined with a positive charge on an electronegative halogen atom, makes the halonium ion strongly electrophilic. Attack by a nucleophile, such as a halide ion, opens the halonium ion to give a stable product.



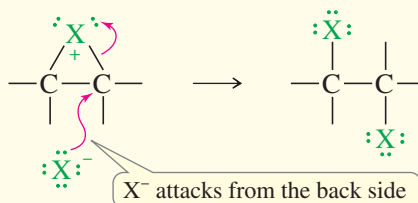
When a solution of bromine (red-brown) is added to cyclohexene, the bromine color quickly disappears because bromine adds across the double bond. When bromine is added to cyclohexane (at right), the color persists because no reaction occurs.

## MECHANISM 8-7 Addition of Halogens to Alkenes

**Step 1:** Electrophilic attack forms a halonium ion.



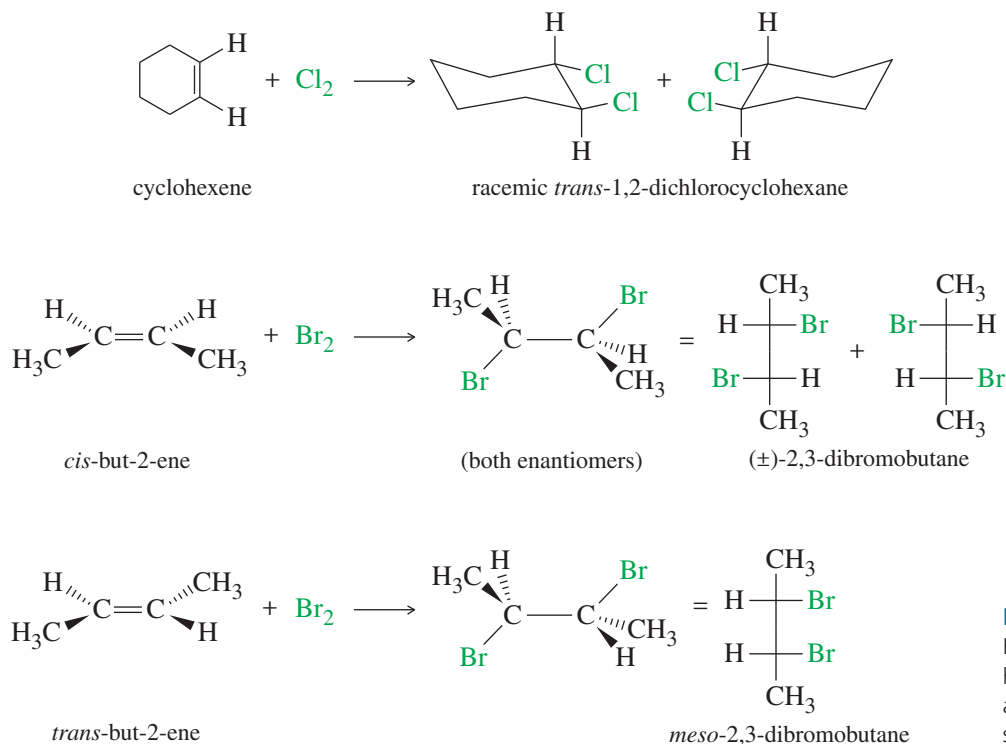
**Step 2:** The halide ion opens the halonium ion.



(CONTINUED)



Halogen addition is another example of a stereospecific reaction, in which different stereoisomers of the starting material give different stereoisomers of the product. Figure 8-5 shows additional examples of the anti addition of halogens to alkenes.



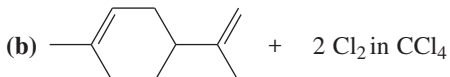
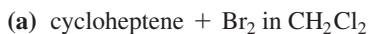
**FIGURE 8-5**  
Examples of the anti addition of halogens to alkenes. The stereospecific anti addition gives predictable stereoisomers of the products.

### PROBLEM 8-17

Give mechanisms to account for the stereochemistry of the products observed from the addition of bromine to *cis*- and *trans*-but-2-ene (Figure 8-5). Why are two products formed from the *cis* isomer but only one from the *trans*? (Making models will be helpful.)

### PROBLEM 8-18

Propose mechanisms and predict the major products of the following reactions. Include stereochemistry where appropriate.



### PROBLEM-SOLVING HINT

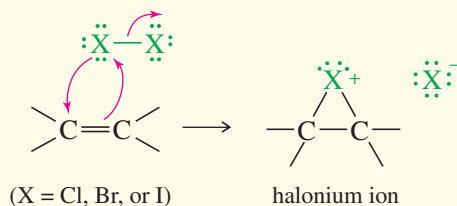
Models may be helpful whenever stereochemistry is involved. Write complete structures, including all bonds and charges, when writing mechanisms.

## 8-9 Formation of Halohydrins

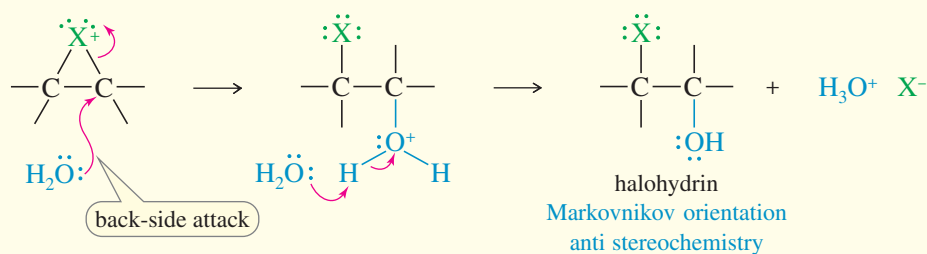
A **halohydrin** is an alcohol with a halogen on the adjacent carbon atom. In the presence of water, halogens add to alkenes to form halohydrins. The electrophilic halogen adds to the alkene to give a halonium ion, which is also electrophilic. Water acts as a nucleophile to open the halonium ion and form the halohydrin.

## MECHANISM 8-8 Formation of Halohydrins

**Step 1:** Electrophilic attack forms a halonium ion.

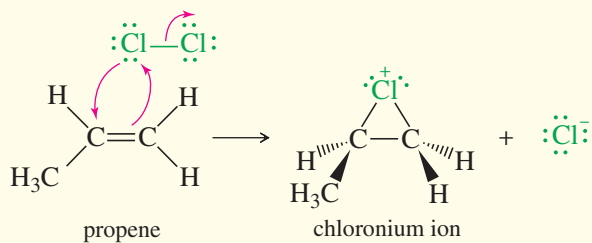


**Step 2:** Water opens the halonium ion; deprotonation gives the halohydrin.

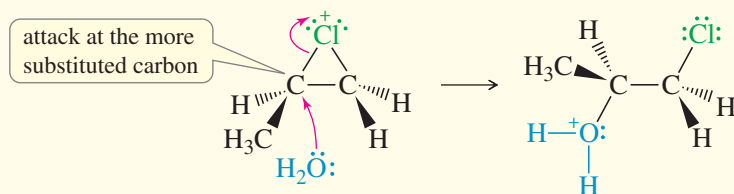


**EXAMPLE:** Addition of Cl<sub>2</sub> to propene in water.

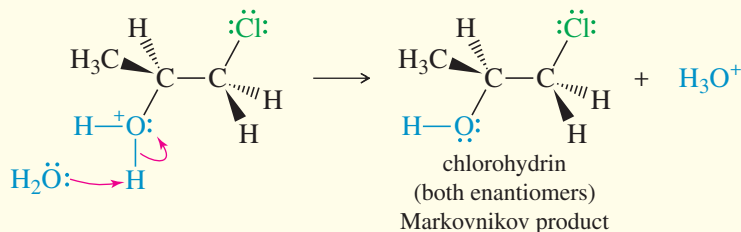
**Step 1:** Electrophilic attack forms a chloronium ion.



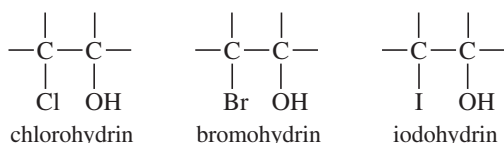
**Step 2:** Back-side attack by water opens the chloronium ion.



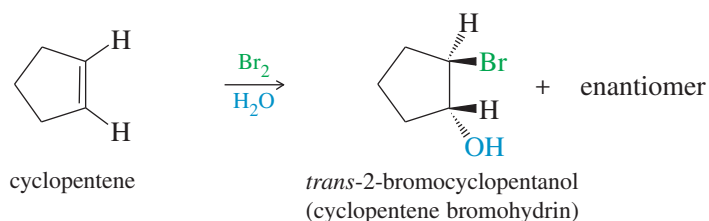
**Step 3:** Water removes a proton to give the chlorohydrin.



When halogenation takes place with no solvent or with an inert solvent such as carbon tetrachloride ( $\text{CCl}_4$ ) or chloroform ( $\text{CHCl}_3$ ), only the halide ion is available as a nucleophile to attack the halonium ion. A dihalide results. But when an alkene reacts with a halogen in the presence of a nucleophilic solvent such as water, a solvent molecule is the most likely nucleophile to attack the halonium ion. When a water molecule attacks the halonium ion, the final product is a halohydrin, with a halogen on one carbon atom and a hydroxy group on the adjacent carbon. The product may be a *chlorohydrin*, a *bromohydrin*, or an *iodohydrin*, depending on the halogen.



**Stereochemistry of Halohydrin Formation** Because the mechanism involves a halonium ion, the stereochemistry of addition is anti, as in halogenation. For example, the addition of bromine water to cyclopentene gives *trans*-2-bromocyclopentanol, the product of anti addition across the double bond.



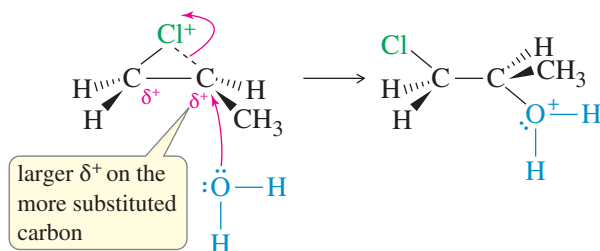
### PROBLEM 8-19

Propose a mechanism for the addition of bromine water to cyclopentene, being careful to show why the *trans* product results and how both enantiomers are formed.

**Orientation of Halohydrin Formation** Even though a halonium ion is involved, rather than a carbocation, the extended version of Markovnikov's rule applies to halohydrin formation. When propene reacts with chlorine water, the major product has the electrophile (the chlorine atom) bonded to the less substituted carbon of the double bond. The nucleophile (the hydroxy group) is bonded to the more substituted carbon.



The Markovnikov orientation observed in halohydrin formation is explained by the structure of the halonium ion intermediate. The two carbon atoms bonded to the halogen have partial positive charges, with a larger charge (and a weaker bond to the halogen) on the more substituted carbon atom (Figure 8-6). The nucleophile (water) attacks this more substituted, more electrophilic carbon atom. The result is both anti stereochemistry and Markovnikov orientation.



**FIGURE 8-6**

Orientation of halohydrin formation. The more substituted carbon of the chloronium ion bears more positive charge than the less substituted carbon. Attack by water occurs on the more substituted carbon to give the Markovnikov product.

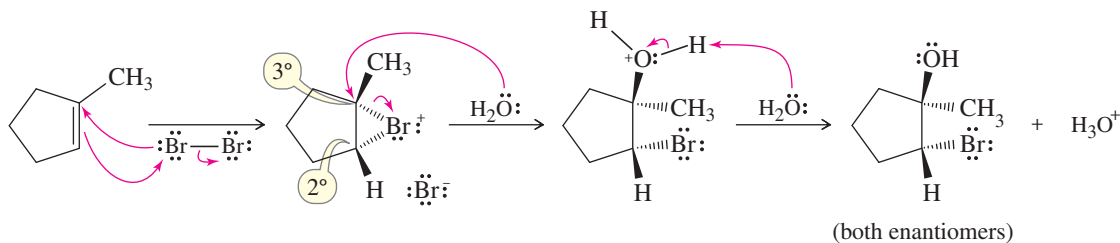
This halonium ion mechanism can be used to explain and predict a wide variety of reactions in both nucleophilic and non-nucleophilic solvents. The halonium ion mechanism is similar to the mercurinium ion mechanism for oxymercuration of an alkene, and both give Markovnikov orientation (Section 8-5).

### SOLVED PROBLEM 8-5

Propose a mechanism for the reaction of 1-methylcyclopentene with bromine water.

#### SOLUTION

1-Methylcyclopentene reacts with bromine to give a bromonium ion. Attack by water could occur at either the secondary carbon or the tertiary carbon of the bromonium ion. Attack actually occurs at the more substituted carbon, which bears more of the positive charge. The product is formed as a racemic mixture.

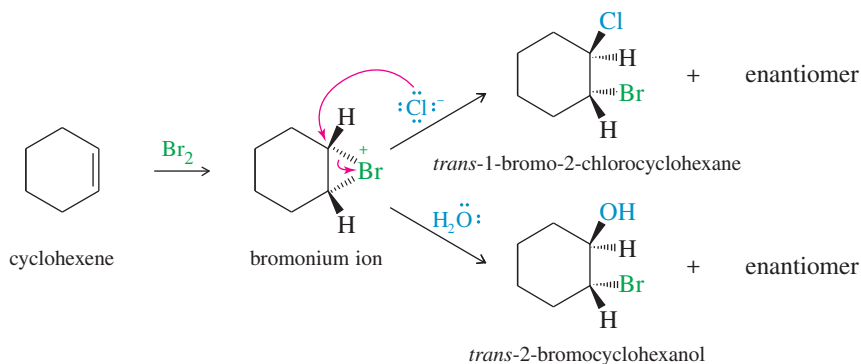


### SOLVED PROBLEM 8-6

When cyclohexene is treated with bromine in saturated aqueous sodium chloride, a mixture of *trans*-2-bromocyclohexanol and *trans*-1-bromo-2-chlorocyclohexane results. Propose a mechanism to account for these two products.

#### SOLUTION

Cyclohexene reacts with bromine to give a bromonium ion, which will react with any available nucleophile. The most abundant nucleophiles in saturated aqueous sodium chloride solution are water and chloride ions. Attack by water gives the bromohydrin, and attack by chloride gives the dihalide. Either of these attacks gives anti stereochemistry.



### PROBLEM 8-20

The solutions to Solved Problem 8-5 and Solved Problem 8-6 showed only how one enantiomer of the product is formed. For each product, show how an equally probable reaction forms the other enantiomer.

### PROBLEM 8-21

Predict the major product(s) for each reaction. Include stereochemistry where appropriate.

- (a) 1-methylcyclohexene +  $\text{Cl}_2/\text{H}_2\text{O}$                       (b) 2-methylbut-2-ene +  $\text{Br}_2/\text{H}_2\text{O}$   
 (c) *cis*-but-2-ene +  $\text{Cl}_2/\text{H}_2\text{O}$                       (d) *trans*-but-2-ene +  $\text{Cl}_2/\text{H}_2\text{O}$   
 (e) 1-methylcyclopentene +  $\text{Br}_2$  in saturated aqueous NaCl

**PROBLEM 8-22**

Show how you would accomplish the following synthetic conversions.

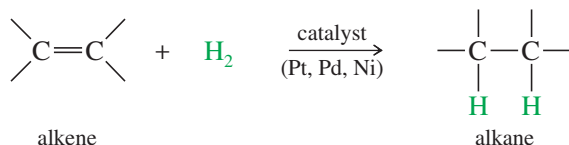
- (a) 3-methylpent-2-ene  $\rightarrow$  2-chloro-3-methylpentan-3-ol  
 (b) chlorocyclohexane  $\rightarrow$  *trans*-2-chlorocyclohexanol  
 (c) 1-methylcyclopentanol  $\rightarrow$  2-chloro-1-methylcyclopentanol

**PROBLEM-SOLVING HINT**

The opening of a halonium ion is driven by its electrophilic nature. The weak nucleophile attacks the carbon bearing more positive charge.

**8-10 Catalytic Hydrogenation of Alkenes**

Although we mentioned **catalytic hydrogenation** before (Sections 7-8A and 8-1), we now consider the mechanism and stereochemistry in more detail. Hydrogenation of an alkene is formally a reduction, with  $\text{H}_2$  adding across the double bond to give an alkane. The process usually requires a catalyst containing Pt, Pd, or Ni.



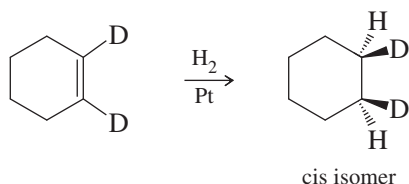
*Example*



For most alkenes, hydrogenation takes place at room temperature, using hydrogen gas at atmospheric pressure. The alkene is usually dissolved in an alcohol, an alkane, or acetic acid. A small amount of platinum, palladium, or nickel catalyst is added, and the container is shaken or stirred while the reaction proceeds. Hydrogenation actually takes place at the surface of the metal, where the liquid solution of the alkene comes into contact with hydrogen and the catalyst.

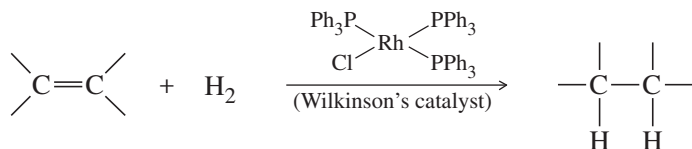
Hydrogen gas is adsorbed onto the surface of these metal catalysts, and the catalyst weakens the  $\text{H}-\text{H}$  bond. In fact, if  $\text{H}_2$  and  $\text{D}_2$  are mixed in the presence of a platinum catalyst, the two isotopes quickly scramble to produce a random mixture of  $\text{HD}$ ,  $\text{H}_2$ , and  $\text{D}_2$ . (No scrambling occurs in the absence of the catalyst.) Hydrogenation is an example of **heterogeneous catalysis**, because the (solid) catalyst is in a different phase from the reactant solution. In contrast, **homogeneous catalysis** involves reactants and catalyst in the same phase, as in the acid-catalyzed dehydration of an alcohol.

Because the two hydrogen atoms add from a solid surface, they add with **syn** stereochemistry. For example, when 1,2-dideuteriocyclohexene is treated with hydrogen gas over a catalyst, the product is the *cis* isomer resulting from *syn* addition (Figure 8-7).



One face of the alkene pi bond binds to the catalyst, which has hydrogen adsorbed on its surface. Hydrogen inserts into the pi bond, and the product is freed from the catalyst. Both hydrogen atoms add to the face of the double bond that is complexed with the catalyst.

Soluble homogeneous catalysts, such as *Wilkinson's catalyst*, also catalyze the hydrogenation of carbon-carbon double bonds.



The Parr hydrogenation apparatus shakes the reaction vessel (containing the alkene and the solid catalyst) while a pressurized cylinder supplies hydrogen.

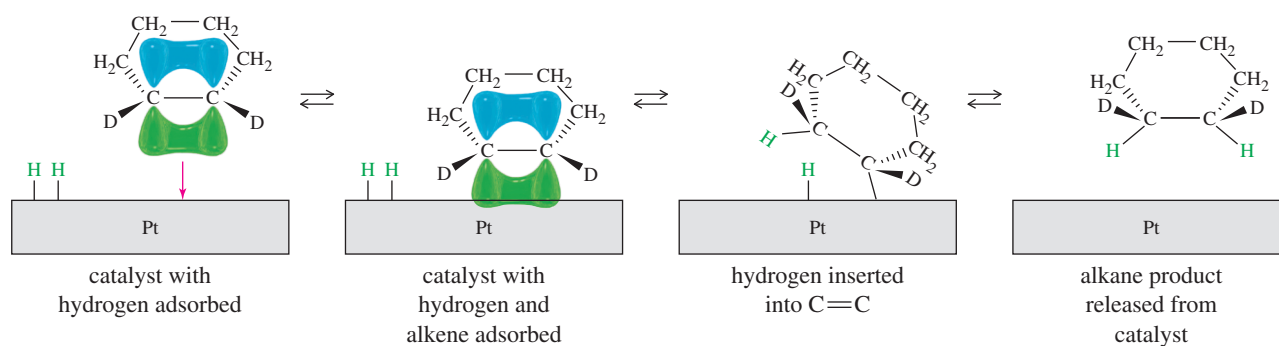


FIGURE 8-7

Syn stereochemistry in catalytic hydrogenation. A solid heterogeneous catalyst adds two hydrogen atoms to the same face of the pi bond (syn stereochemistry).

### Application: Trans Fats

The double bonds in naturally occurring vegetable oils are almost exclusively *cis*. Catalytic hydrogenation reduces some of the double bonds, raising the melting point and giving a white, creamy shortening that resembles lard. Catalytic hydrogenation is a reversible process, however, and some of the molecules undergo hydrogenation followed by dehydrogenation, leaving double bonds in random positions and often with *trans* stereochemistry. Our metabolism is not well equipped to deal with *trans* double bonds, and *trans* fats are associated with increased serum cholesterol levels and increased incidence of heart disease. The FDA has recently recommended the removal from food of all partially hydrogenated vegetable oils containing *trans* fats. Also see Section 25-3A.

Wilkinson's catalyst is not chiral, but its triphenylphosphine ( $\text{PPh}_3$ ) ligands can be replaced by chiral ligands to give chiral catalysts that are capable of converting optically inactive starting materials to optically active products. Such a process is called **asymmetric induction** or **enantioselective synthesis**. For example, Figure 8-8 shows a chiral ruthenium complex catalyzing an enantioselective hydrogenation of a carbon–carbon double bond to give a large excess of one enantiomer. Because the catalyst is chiral, the transition states leading to the two enantiomers of product are diastereomeric. They have different energies, and the transition state leading to the (*R*) enantiomer is favored. Ryoji Noyori and William Knowles shared the 2001 Nobel Prize in Chemistry for their work on chirally catalyzed hydrogenation reactions.

Enantioselective synthesis is particularly important in the pharmaceutical industry, because only one enantiomer of a chiral drug is likely to have the desired effect. For example, levodopa [(–)-dopa or *l*-dopa] is used in patients with Parkinson's disease to counteract a deficiency of dopamine, one of the neurotransmitters in the brain. Dopamine itself is useless as a drug because it cannot cross the “blood–brain barrier”; that is, it cannot get into the cerebrospinal fluid from the bloodstream. (–)-Dopa, on the other hand, is an amino acid related to tyrosine. It crosses the blood–brain barrier into the cerebrospinal fluid, where it undergoes enzymatic conversion to dopamine. Only the (–) enantiomer of dopa can be transformed into dopamine; the other enantiomer, (+)-dopa, is toxic to the patient.

The correct enantiomer can be synthesized from an achiral starting material by catalytic hydrogenation using a complex of rhodium with a chiral ligand called DIOP. Such an enantioselective synthesis is more efficient than making a racemic mixture, resolving it into enantiomers, and discarding the unwanted enantiomer.

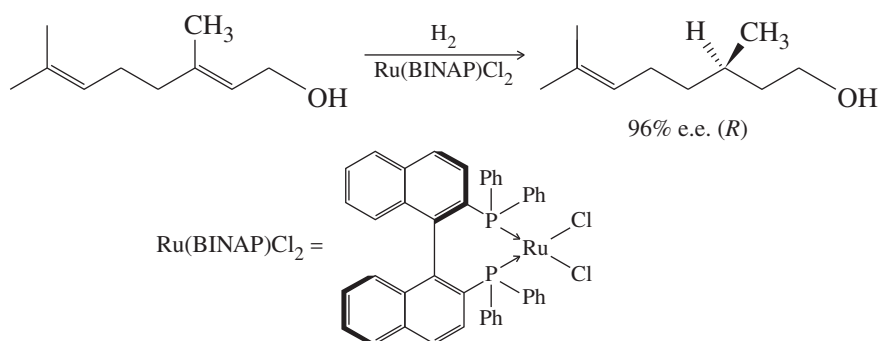
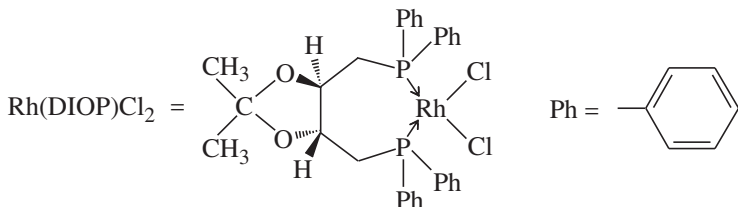
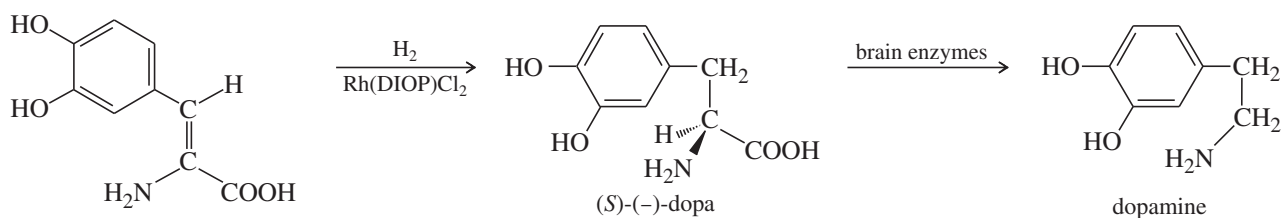


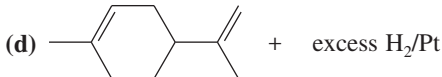
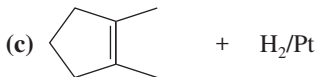
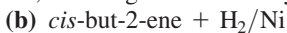
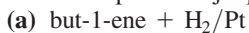
FIGURE 8-8

Chiral hydrogenation catalysts. Rhodium and ruthenium phosphines are effective homogeneous catalysts for hydrogenation. Chiral ligands can be attached to accomplish asymmetric induction, the creation of a new asymmetric carbon as mostly one enantiomer.



**PROBLEM 8-23**

Give the expected major product for each reaction, including stereochemistry where applicable.

**PROBLEM 8-24**

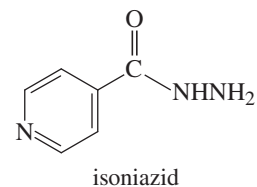
One of the principal components of lemongrass oil is *limonene*,  $\text{C}_{10}\text{H}_{16}$ . When limonene is treated with excess hydrogen and a platinum catalyst, the product is an alkane of formula  $\text{C}_{10}\text{H}_{20}$ . What can you conclude about the structure of limonene?

**PROBLEM 8-25**

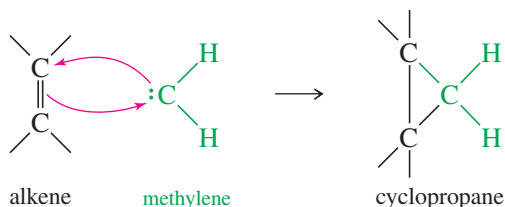
The chiral BINAP ligand shown in Figure 8-8 contains no asymmetric carbon atoms. Explain how this ligand is chiral.

**Application: Antibiotics**

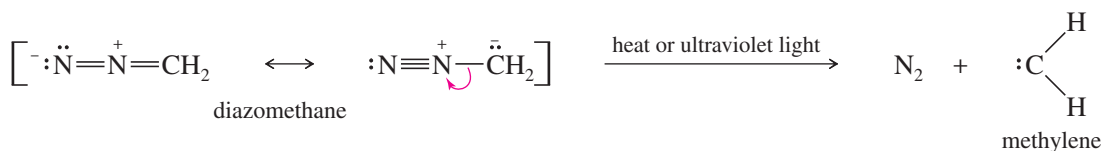
The enzymatic reduction of a double bond is a key step in the formation of a fatty acid that is ultimately incorporated into the cell wall of the bacterium that causes tuberculosis. The antituberculosis drug isoniazid blocks this enzyme, preventing reduction of the double bond. Without an intact cell wall, the bacteria die.

**8-11 Addition of Carbenes to Alkenes**

Methylene ( $:\text{CH}_2$ ) is the simplest of the **carbenes**: uncharged, reactive intermediates that have a carbon atom with two bonds and two nonbonding electrons. Like borane ( $\text{BH}_3$ ), methylene is a potent electrophile because it has an unfilled octet. It adds to the electron-rich pi bond of an alkene to form a cyclopropane.



Heating or photolysis of diazomethane gives nitrogen gas and methylene:



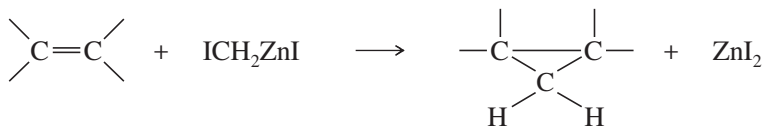
The methylene generated from diazomethane reacts with alkenes to form cyclopropanes, but diazomethane is very toxic and explosive, and the methylene generated is so reactive that it forms many side products. A safer and more reliable way to make cyclopropanes is with the Simmons–Smith reagent.

### 8-11A The Simmons–Smith Reaction

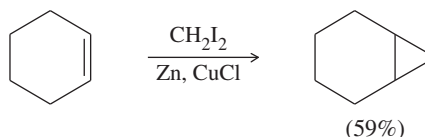
The **Simmons–Smith reagent**, named for the two DuPont chemists who discovered it, is made by adding methylene iodide to the “zinc–copper couple” (zinc dust that has been activated with an impurity of copper). The reagent probably resembles iodomethyl zinc iodide,  $\text{ICH}_2\text{ZnI}$ . This kind of reagent is called a *carbenoid* because it reacts much like a carbene, but it does not actually contain a divalent carbon atom.



The Simmons–Smith reagent adds to double bonds much like methylene ( $:\text{CH}_2$ ) would, except that the reagent is easier to use, is much more stable, and gives better yields without as many side reactions.



#### Example



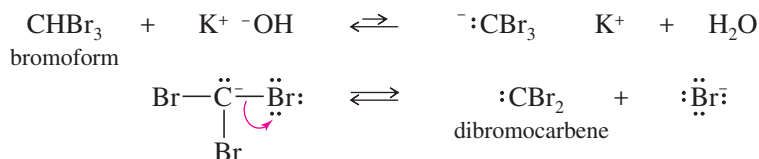
### PROBLEM 8-26

Predict the carbenoid addition products of the following reactions.

- (a) *trans*-hex-3-ene +  $\text{CH}_2\text{I}_2$ ,  $\text{Zn}(\text{Cu})$       (b) *cis*-hept-2-ene +  $\text{CH}_2\text{I}_2$ ,  $\text{Zn}(\text{Cu})$

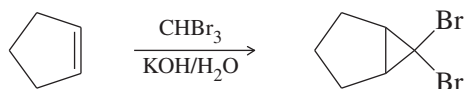
### 8-11B Formation of Carbenes by Alpha Elimination

Carbenes are also formed by reactions of halogenated compounds with bases. If a carbon atom has bonds to at least one hydrogen and to enough halogen atoms to make the hydrogen slightly acidic, it may be possible to form a carbene. For example, bromoform ( $\text{CHBr}_3$ ) reacts with a 50% aqueous solution of potassium hydroxide to form dibromocarbene.

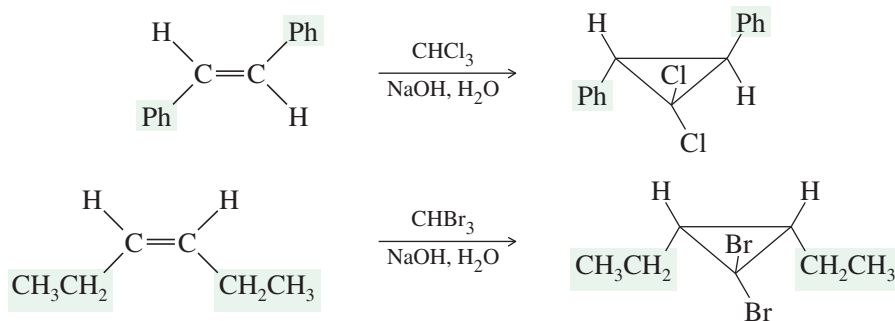


This dehydrohalogenation is called an **alpha elimination** ( $\alpha$  elimination) because the hydrogen and the halogen are lost from the same carbon atom. The more common dehydrohalogenations (to form alkenes) are called **beta eliminations** because the hydrogen and the halogen are lost from adjacent carbon atoms.

Dibromocarbene formed from  $\text{CHBr}_3$  can add to a double bond to form a dibromocyclopropane.



The products of these cyclopropanations retain any cis or trans stereochemistry of the reactants.

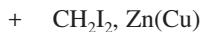
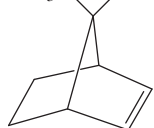


### PROBLEM 8-27

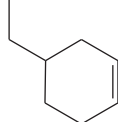
Predict the carbene addition products of the following reactions.

(a) cyclohexene +  $\text{CHCl}_3$ , 50%  $\text{NaOH}/\text{H}_2\text{O}$

(b) +  $\text{CH}_2\text{I}_2$ ,  $\text{Zn}(\text{Cu})$



(c) + 50%  $\text{NaOH}/\text{H}_2\text{O}$



### PROBLEM 8-28

Show how you would accomplish each of the following synthetic conversions.

(a) *trans*-but-2-ene  $\longrightarrow$  *trans*-1,2-dimethylcyclopropane

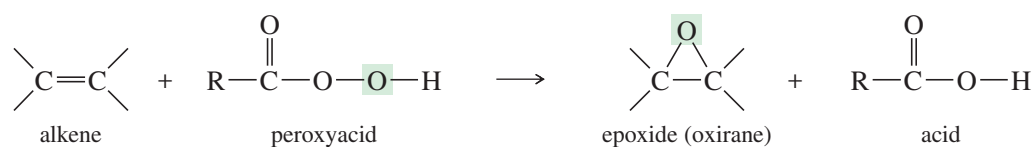
(b) cyclopentene  $\longrightarrow$

(c) cyclohexanol  $\longrightarrow$

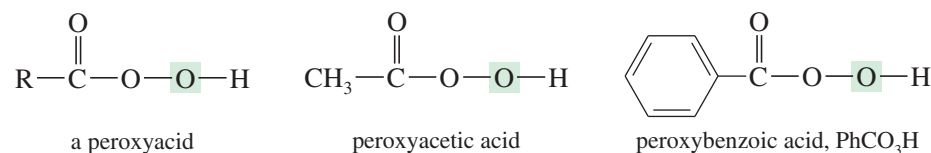
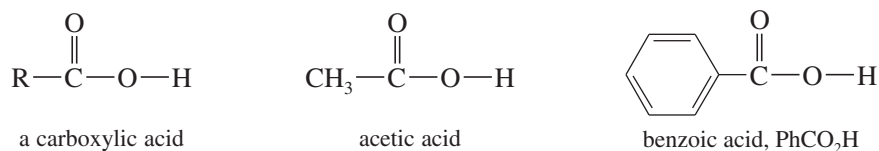
## 8-12 Epoxidation of Alkenes

Some of the most important reactions of alkenes involve oxidation. When we speak of oxidation, we usually mean reactions that form carbon–oxygen bonds. (Halogens are oxidizing agents, and the addition of a halogen molecule across a double bond is formally an oxidation as well.) Oxidations are particularly important because many common functional groups contain oxygen, and alkene oxidations are some of the best methods for introducing oxygen into organic molecules. We will consider methods for epoxidation, dihydroxylation, and oxidative cleavage of alkene double bonds.

An **epoxide** is a three-membered cyclic ether, also called an **oxirane**. Epoxides are valuable synthetic intermediates used for converting alkenes to a variety of other functional groups. An alkene is converted to an epoxide by a **peroxyacid**, a carboxylic acid that has an extra oxygen atom in a  $\text{—O—O—}$  (peroxy) linkage.



The **epoxidation** of an alkene is clearly an oxidation, because an oxygen atom is added. Peroxyacids are highly selective oxidizing agents. Some simple peroxyacids (sometimes called *peracids*) and their corresponding carboxylic acids are shown next.



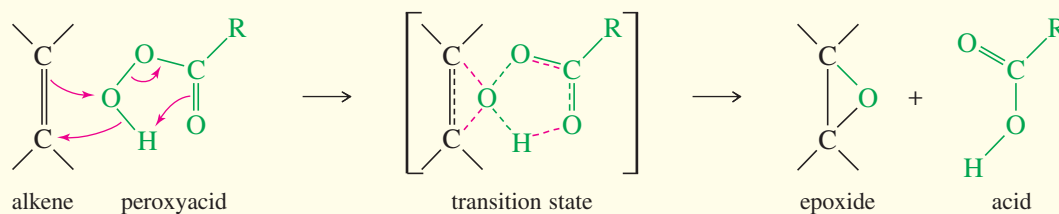
A peroxyacid epoxidizes an alkene by a concerted electrophilic reaction where several bonds are broken and several are formed at the same time. Starting with the alkene and the peroxyacid, a one-step reaction gives the epoxide and the acid directly, without any intermediates.

#### Application: Insecticides

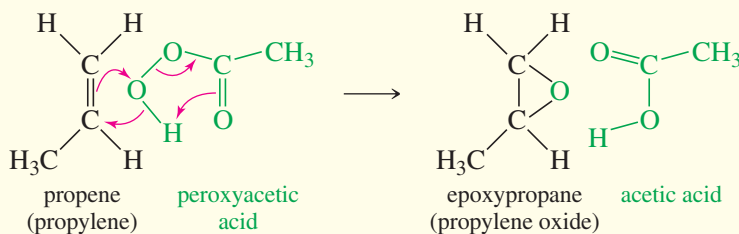
Epoxides are often found as components of natural products that plants use as defense mechanisms against insects. Typically, the epoxide reacts with critical cellular enzymes or DNA, preventing them from carrying out their normal functions. As a result, the insect is killed.

### MECHANISM 8-9 Epoxidation of Alkenes

Peroxyacids epoxidize alkenes in a one-step (concerted) process.

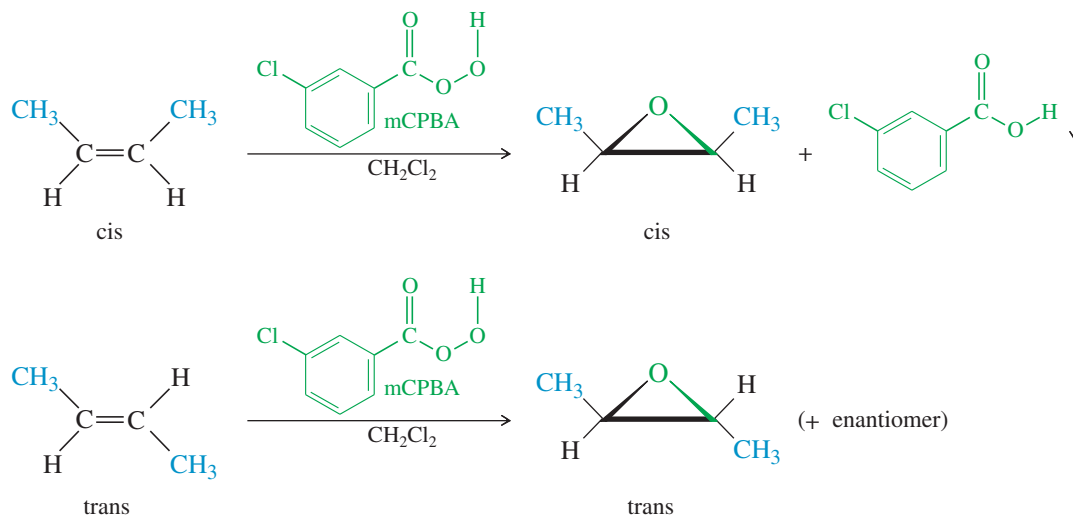


**EXAMPLE:** Epoxidation of propene by peroxyacetic acid.



Because the epoxidation takes place in one step, there is no opportunity for the alkene molecule to rotate and change its *cis* or *trans* geometry. The epoxide retains whatever stereochemistry is present in the alkene.

The following examples use *m*-chloroperoxybenzoic acid (mCPBA), a common epoxidizing reagent, to convert alkenes to epoxides having the same *cis* or *trans* stereochemistry. mCPBA is used for its desirable solubility properties: The peroxyacid dissolves, then the spent acid precipitates out of solution.

**PROBLEM 8-29**

Predict the products, including stereochemistry where appropriate, for the *m*-chloroperoxybenzoic acid epoxidations of the following alkenes.

- (a) *cis*-hex-2-ene                      (b) *trans*-hex-2-ene  
 (c) *cis*-cyclodecene                    (d) *trans*-cyclodecene

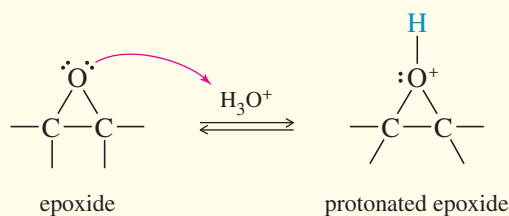
**8-13 Acid-Catalyzed Opening of Epoxides**

Most epoxides are easily isolated as stable products if the solution is not too acidic. Any moderately strong acid protonates the epoxide, however. Water attacks the protonated epoxide, opening the ring and forming a 1,2-diol, commonly called a **glycol**.

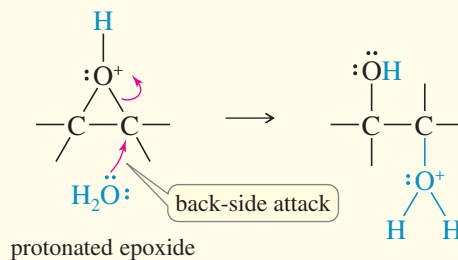
**MECHANISM 8-10 Acid-Catalyzed Opening of Epoxides**

The crucial step is a back-side attack by the solvent on the protonated epoxide.

**Step 1:** Protonation of the epoxide activates it toward nucleophilic attack.

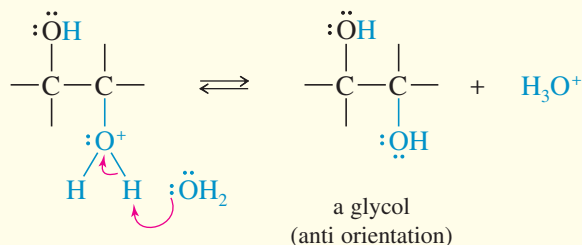


**Step 2:** Back-side attack by the solvent (water) opens the ring.



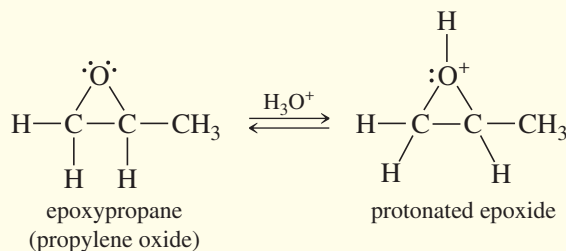
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**Step 3:** Deprotonation gives the diol product.

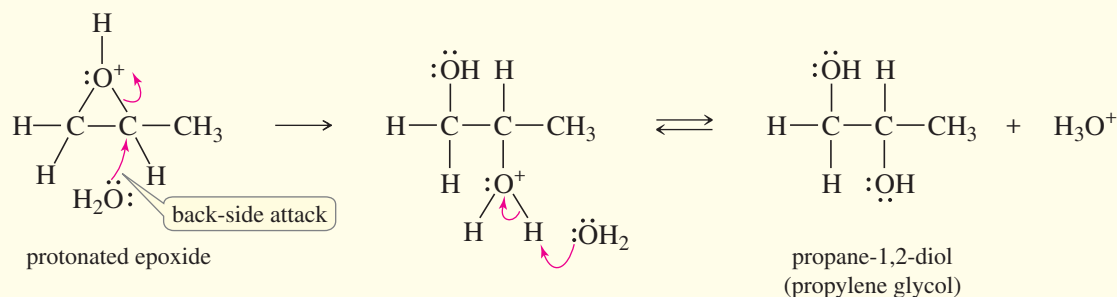


**EXAMPLE:** Acid-catalyzed hydrolysis of propylene oxide (epoxypropane).

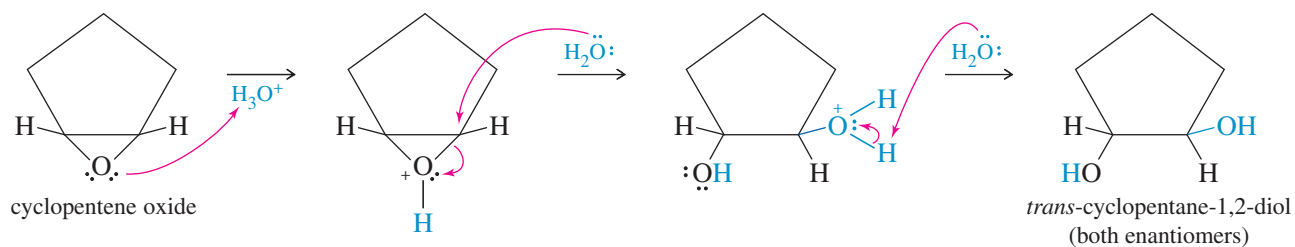
**Step 1:** Protonation of the epoxide.



**Steps 2 and 3:** Back-side attack by water, then deprotonation of the product.



Because glycol formation involves a back-side attack on a protonated epoxide, the result is anti orientation of the hydroxy groups on the double bond. For example, when 1,2-epoxycyclopentane (“cyclopentene oxide”) is treated with dilute mineral acid, the product is pure *trans*-cyclopentane-1,2-diol.



### PROBLEM 8-30

- Propose a mechanism for the conversion of *cis*-hex-3-ene to the epoxide (3,4-epoxyhexane) and the ring-opening reaction to give the glycol, hexane-3,4-diol. In your mechanism, pay particular attention to the stereochemistry of the intermediates and products.
- Repeat part (a) for *trans*-hex-3-ene. Compare the products obtained from *cis*- and *trans*-hex-3-ene. Is this reaction sequence stereospecific?

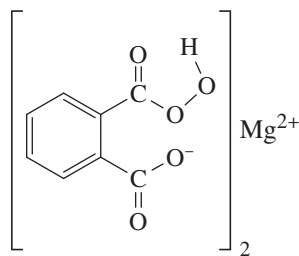
Epoxidation reagents can be chosen to favor either the epoxide or the glycol. Peroxyacetic acid is used in strongly acidic water solutions. The acidic solution protonates the epoxide and converts it to the glycol. Peroxybenzoic acids are weak acids that can be used in non-nucleophilic solvents such as carbon tetrachloride. *m*-Chloroperoxybenzoic acid in  $\text{CCl}_4$  generally gives good yields of epoxides. Figure 8-9 compares the uses of these reagents.

### Application: Biochemistry

The body oxidizes the alkene components of drugs and other substances to epoxides, which are then hydrolyzed to diols by an epoxide hydrolase enzyme. The more reactive epoxides are rapidly converted to water-soluble diols and eliminated in the urine. Epoxide hydrolase enzymes are sometimes used in organic synthesis to produce chiral diols.

### PROBLEM 8-31

Magnesium monoperoxyphthalate (MMPP) epoxidizes alkenes much like mCPBA. MMPP is more stable, however, and it may be safer to use for large-scale and industrial reactions. Propose a mechanism for the reaction of *trans*-2-methylhept-3-ene with MMPP, and predict the structure of the product(s).



Magnesium monoperoxyphthalate,  
MMPP

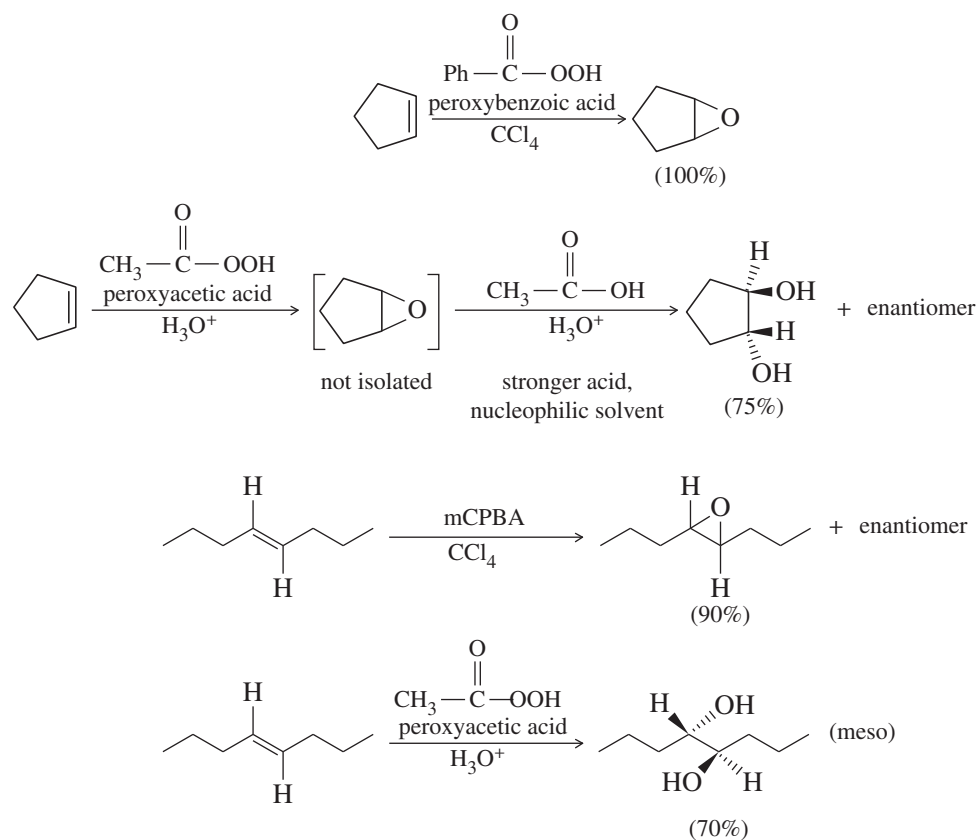


FIGURE 8-9

Reagents for epoxidation. Peroxyacetic acid is used in strongly acidic aqueous solutions. Alkenes are epoxidized, then opened to glycols in one step. Weakly acidic peroxyacids, such as peroxybenzoic acid or mCPBA, can be used in nonaqueous solutions to give good yields of epoxides.

**PROBLEM 8-32**

Predict the major products of the following reactions.

- cis*-hex-2-ene + mCPBA in chloroform
- trans*-hex-3-ene + peroxyacetic acid ( $\text{CH}_3\text{CO}_3\text{H}$ ) in water
- 1-methylcyclohexene + MMPP in ethanol
- trans*-cyclodecene + peroxyacetic acid in acidic water
- cis*-cyclodecene + mCPBA in  $\text{CH}_2\text{Cl}_2$ , then dilute aqueous acid

**PROBLEM 8-33**

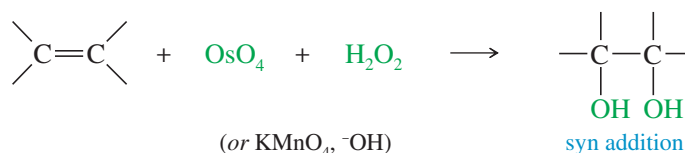
When 1,2-epoxycyclohexane (cyclohexene oxide) is treated with anhydrous HCl in methanol, the principal product is *trans*-2-methoxycyclohexanol. Propose a mechanism to account for the formation of this product.

**Application: Catalysis**

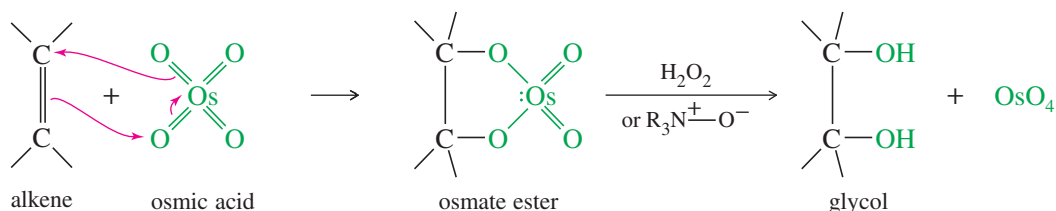
Older dihydroxylation procedures once used a full equivalent of  $\text{OsO}_4$  followed by a reducing agent such as  $\text{NaHSO}_3$  to reduce the osmate ester. These old procedures have been supplanted by methods using only catalytic amounts of  $\text{OsO}_4$ , an exceptionally toxic and expensive reagent.

**8-14 Syn Dihydroxylation of Alkenes**

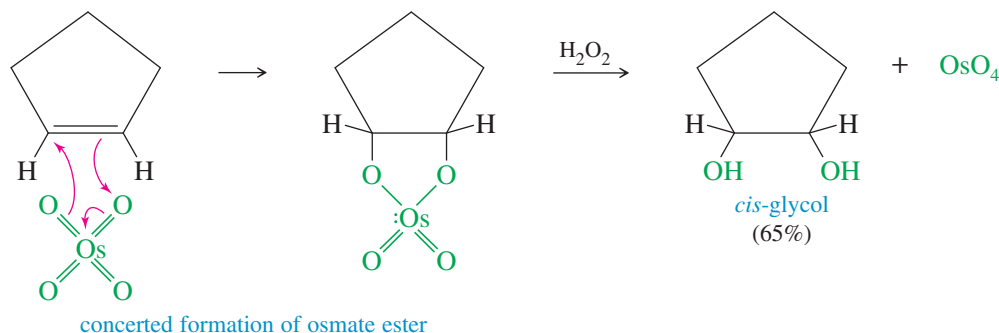
Converting an alkene to a glycol requires adding a hydroxy group to each end of the double bond. This addition is called **dihydroxylation** (or **hydroxylation**) of the double bond. We have seen that epoxidation of an alkene, followed by acidic hydrolysis, gives *anti* dihydroxylation of the double bond. Reagents are also available for the dihydroxylation of alkenes with *syn* stereochemistry. The two most common reagents for this purpose are osmium tetroxide and potassium permanganate.

**8-14A Osmium Tetroxide Dihydroxylation**

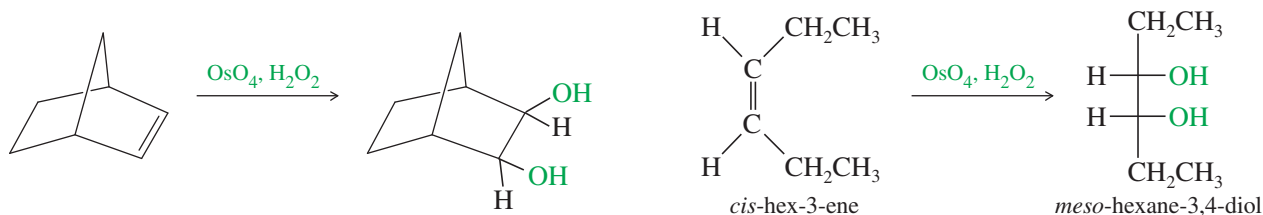
Osmium tetroxide ( $\text{OsO}_4$ , sometimes called *osmic acid*) reacts with alkenes in a concerted step to form a cyclic osmate ester. Oxidizing agents such as hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) or tertiary amine oxides ( $\text{R}_3\text{N}^+-\text{O}^-$ ) are used to hydrolyze the osmate ester and reoxidize osmium to osmium tetroxide. The regenerated osmium tetroxide catalyst continues to hydroxylate more molecules of the alkene.



Because the two carbon–oxygen bonds are formed simultaneously with the cyclic osmate ester, the oxygen atoms add to the same face of the double bond; that is, they add with *syn* stereochemistry. The following reactions show the use of  $\text{OsO}_4$  and  $\text{H}_2\text{O}_2$  for the *syn* dihydroxylation of alkenes.

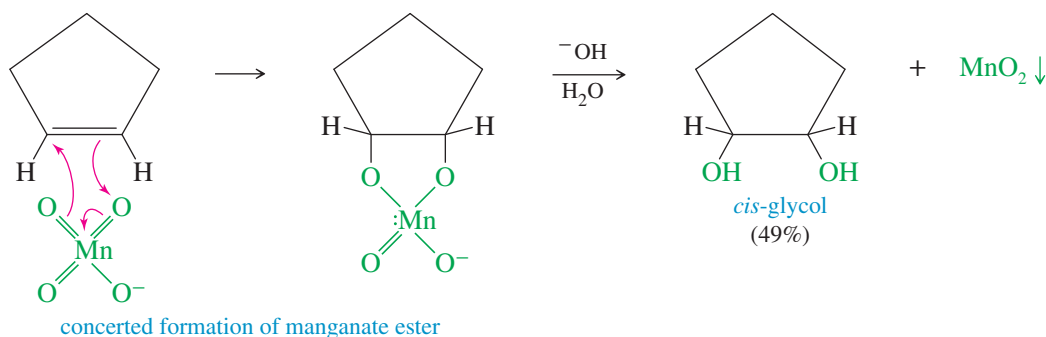






### 8-14B Permanganate Dihydroxylation

Osmium tetroxide is expensive, highly toxic, and volatile. A cold, dilute solution of potassium permanganate ( $\text{KMnO}_4$ ) also hydroxylates alkenes with syn stereochemistry, with slightly reduced yields in most cases. Like osmium tetroxide, permanganate adds to the alkene double bond to form a cyclic ester: a manganate ester in this case. The basic solution hydrolyzes the manganate ester, liberating the glycol and producing a brown precipitate of manganese dioxide,  $\text{MnO}_2$ .



In addition to its synthetic value, the permanganate oxidation of alkenes provides a simple chemical test for the presence of an alkene. When an alkene is added to a clear, deep purple aqueous solution of potassium permanganate, the solution loses its purple color and becomes the murky, opaque brown color of  $\text{MnO}_2$ . (Although there are other functional groups that decolorize permanganate, few do it as quickly as alkenes.)

### 8-14C Choosing a Reagent

To dihydroxylate an alkene with syn stereochemistry, which is the better reagent: osmium tetroxide or potassium permanganate? Osmium tetroxide gives better yields, but permanganate is cheaper and safer to use. The answer depends on the circumstances.

If the starting material is only 2 mg of a compound 15 steps along in a difficult synthesis, we use osmium tetroxide. The better yield is crucial because the starting material is precious and expensive, and little osmic acid is needed. If the dihydroxylation is the first step in a synthesis and involves 5 kg of the starting material, we use potassium permanganate. The cost of buying enough osmium tetroxide would be prohibitive, and dealing with such a large amount of a volatile, toxic reagent would be inconvenient. On such a large scale, we can accept the lower yield of the permanganate oxidation.

#### PROBLEM 8-34

Predict the major products of the following reactions, including stereochemistry.

- cyclohexene +  $\text{KMnO}_4/\text{H}_2\text{O}$  (cold, dilute)
- cyclohexene + peroxyacetic acid in water
- cis*-pent-2-ene +  $\text{OsO}_4/\text{H}_2\text{O}_2$
- cis*-pent-2-ene + peroxyacetic acid in water
- trans*-pent-2-ene +  $\text{OsO}_4/\text{H}_2\text{O}_2$
- trans*-pent-2-ene + peroxyacetic acid in water

**PROBLEM 8-35**

Show how you would accomplish the following conversions.

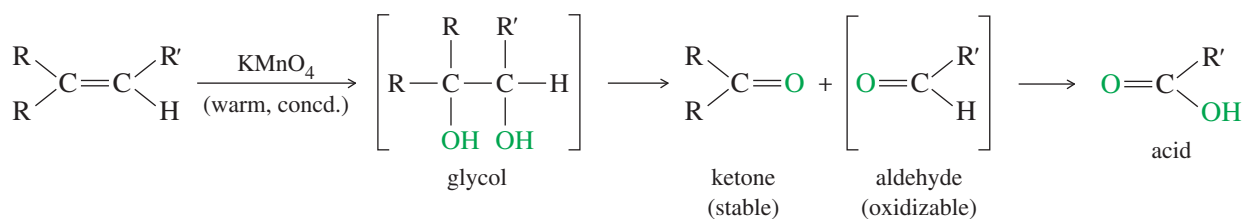
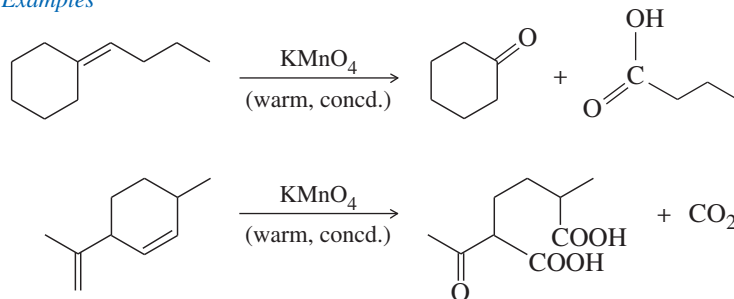
- (a) *cis*-hex-3-ene to *meso*-hexane-3,4-diol  
 (b) *cis*-hex-3-ene to (*d,l*)-hexane-3,4-diol  
 (c) *trans*-hex-3-ene to *meso*-hexane-3,4-diol  
 (d) *trans*-hex-3-ene to (*d,l*)-hexane-3,4-diol

**8-15 Oxidative Cleavage of Alkenes**

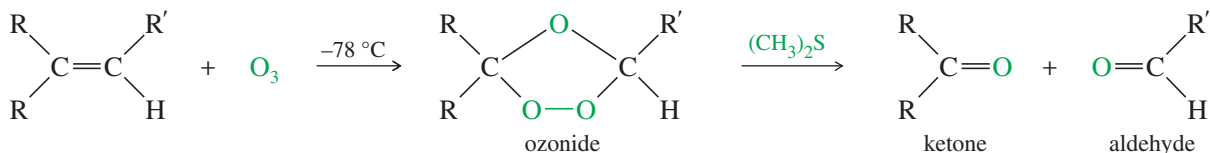
We just described two methods for oxidizing alkenes to glycols. Stronger conditions can further oxidize glycols to cleave the bond that was originally the double bond. Potassium permanganate and ozone are two of the most common reagents for such **oxidative cleavages**.

**8-15A Cleavage by Permanganate**

In a potassium permanganate dihydroxylation, if the solution is warm or acidic or too concentrated, oxidative cleavage of the glycol may occur. In effect, the double bond is cleaved to two carbonyl groups. The products are initially ketones and aldehydes, but aldehydes are oxidized to carboxylic acids under these strong oxidizing conditions. If the molecule contains a terminal =CH<sub>2</sub> group, that group is oxidized all the way to CO<sub>2</sub> and water.

*Examples***8-15B Ozonolysis**

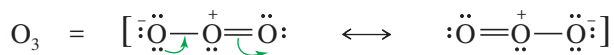
Like permanganate, ozone cleaves double bonds to give ketones and aldehydes. However, ozonolysis is milder, and both ketones and aldehydes can be recovered without further oxidation.



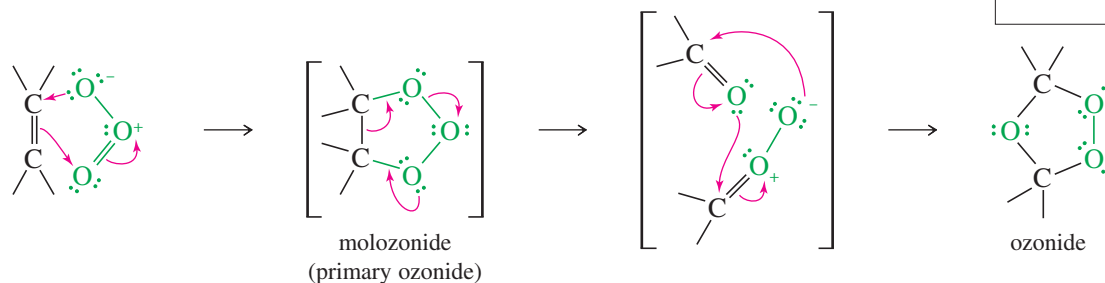
Ozone (O<sub>3</sub>) is a high-energy form of oxygen produced when ultraviolet light or an electrical discharge passes through oxygen gas. Ultraviolet light from the Sun converts oxygen to ozone in the upper atmosphere. This “ozone layer” shields Earth from some of the high-energy ultraviolet radiation it would otherwise receive.



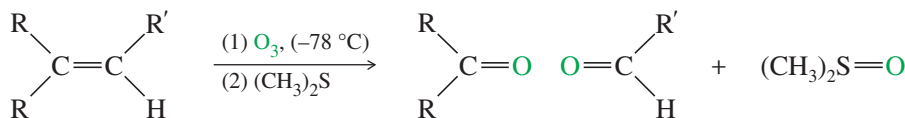
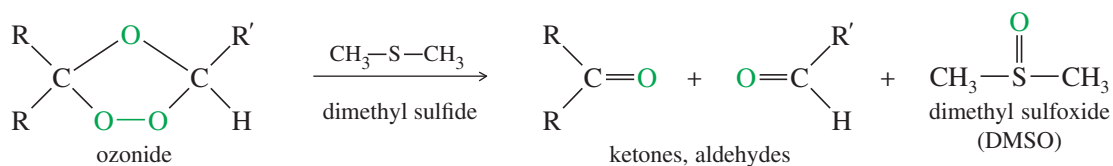
Ozone has 142 kJ/mol of excess energy over oxygen, and it is much more reactive. A Lewis structure of ozone shows that the central oxygen atom bears a positive charge, and that each of the outer oxygen atoms bears half a negative charge.



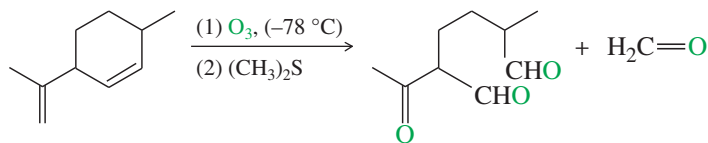
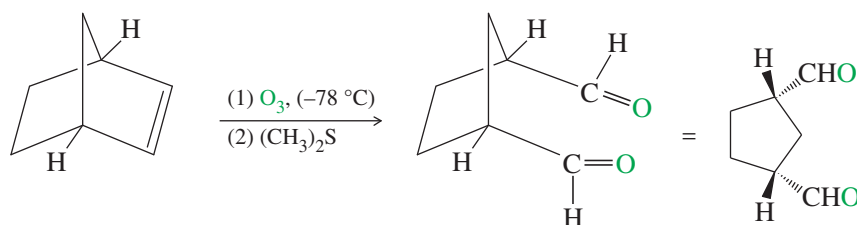
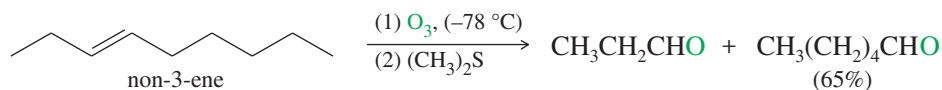
Ozone reacts with an alkene to form a cyclic compound called a *primary ozonide* or *molozonide* (because 1 mole of ozone has been added). This reaction is usually cooled with dry ice ( $-78^\circ\text{C}$ ) to minimize overoxidation and other side reactions. The molozonide has two peroxy ( $-\text{O}-\text{O}-$ ) linkages, so it is quite unstable. It rearranges rapidly, even at low temperatures, to form an ozonide.



Ozonides are not very stable, and they are rarely isolated. In most cases, they are immediately reduced by a mild reducing agent such as zinc or (more recently) dimethyl sulfide. The products of this reduction are ketones and aldehydes.



The following reactions show the products obtained from ozonolysis of some representative alkenes. Note how (1) and (2) are used with a single reaction arrow to denote the steps in a two-step sequence.

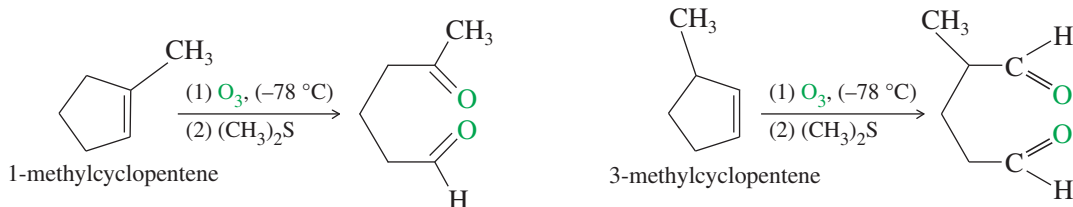


One of the most common uses of ozonolysis has been for determining the positions of double bonds in alkenes. For example, if we were uncertain of the position of the

#### Application: Air Pollution

Ozone is a powerful lung irritant, causing a cough, a sore throat, and tiredness. It can also increase a person's sensitivity to allergens. The mechanism may involve oxidation of the double bonds of the fatty acids that make up the surfactants and the membranes of the cells lining the bronchial airways and lungs.

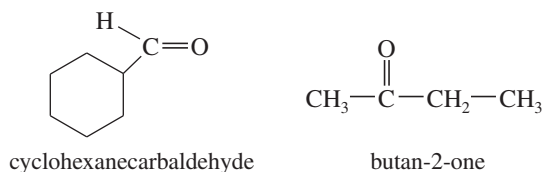
methyl group in a methylcyclopentene, the products of ozonolysis–reduction would confirm the structure of the original alkene.

**PROBLEM-SOLVING HINT**

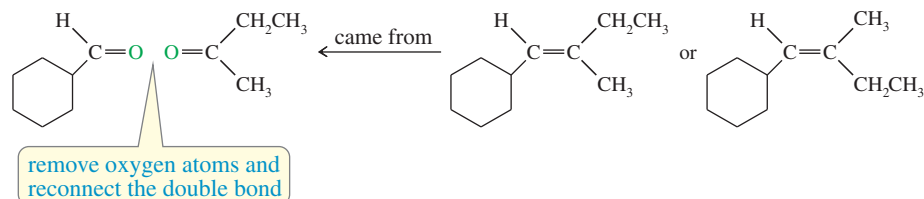
To predict the products from ozonolysis of an alkene, erase the double bond and add two oxygen atoms as carbonyl ( $\text{C}=\text{O}$ ) groups where the double bond used to be.

**SOLVED PROBLEM 8-7**

Ozonolysis–reduction of an unknown alkene gives an equimolar mixture of cyclohexanecarbaldehyde and butan-2-one. Determine the structure of the original alkene.

**SOLUTION**

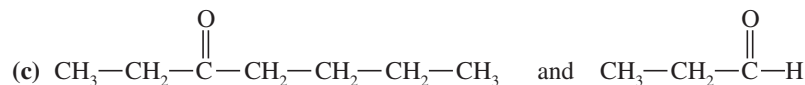
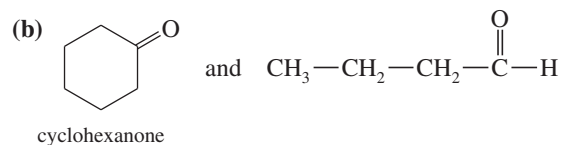
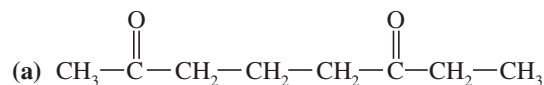
We can reconstruct the alkene by removing the two oxygen atoms of the carbonyl groups ( $\text{C}=\text{O}$ ) and connecting the remaining carbon atoms with a double bond. One uncertainty remains, however: The original alkene might be either of two possible geometric isomers.

**Application: Disinfectant**

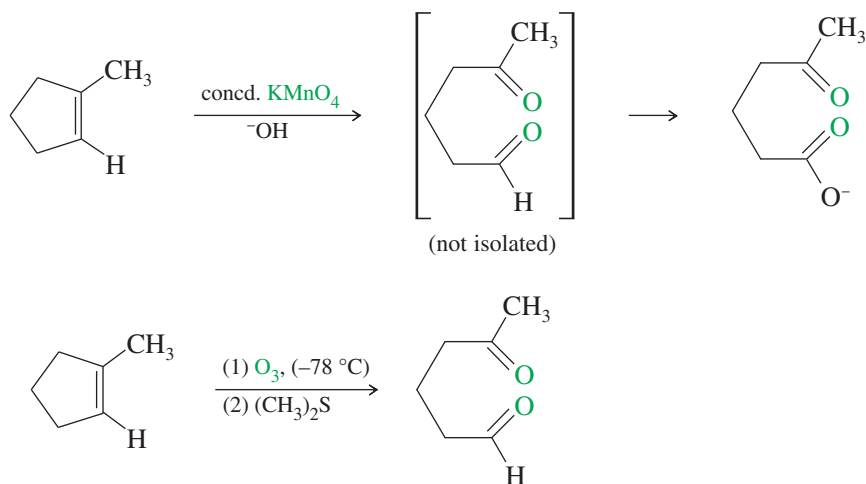
Ozone is a strong oxidizing agent that can be used instead of chlorine to disinfect the water in swimming pools. Ozone oxidizes organic matter, and it kills bacteria and algae. Ozone is used instead of chlorine because it can be generated on-site (rather than storing and using toxic chemicals such as chlorine gas or sodium hypochlorite) and because it doesn't produce as many harmful by-products.

**PROBLEM 8-36**

Give structures of the alkenes that would give the following products upon ozonolysis–reduction.

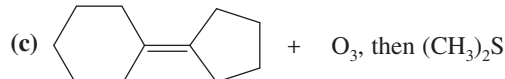
**8-15C Comparison of Permanganate Cleavage and Ozonolysis**

Both permanganate and ozonolysis break the carbon–carbon double bond and replace it with carbonyl ( $\text{C}=\text{O}$ ) groups. In the permanganate cleavage, any aldehyde products are further oxidized to carboxylic acids. In the ozonolysis–reduction procedure, the aldehyde products are generated in the dimethyl sulfide reduction step (and not in the presence of ozone), and they are not oxidized.

**PROBLEM 8-37**

Predict the major products of the following reactions.

- (a) (*E*)-3-methyloct-3-ene + ozone, then  $(\text{CH}_3)_2\text{S}$   
 (b) (*Z*)-3-methyloct-3-ene + warm, concentrated  $\text{KMnO}_4$



- (d) 1-ethylcycloheptene + ozone, then  $(\text{CH}_3)_2\text{S}$   
 (e) 1-ethylcycloheptene + warm, concentrated  $\text{KMnO}_4$   
 (f) 1-ethylcycloheptene + cold, dilute  $\text{KMnO}_4$

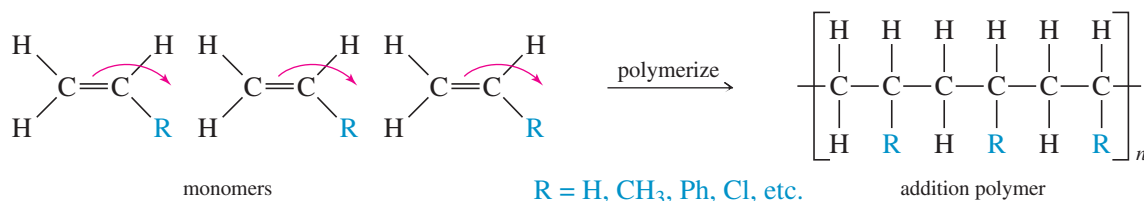
**PROBLEM-SOLVING HINT**

Three reagents oxidize the pi bond of an alkene but leave the sigma bond intact: (a) cold, dilute  $\text{KMnO}_4$ ; (b)  $\text{OsO}_4\text{-H}_2\text{O}_2$ ; and (c)  $\text{RCO}_3\text{H}$  epoxidation.

Two reagents break the double bond entirely, giving carbonyl groups: (a) warm, concentrated  $\text{KMnO}_4$  and (b)  $\text{O}_3$  followed by  $(\text{CH}_3)_2\text{S}$ .

**8-16 Polymerization of Alkenes**

A **polymer** is a large molecule composed of many smaller repeating units (the **monomers**) bonded together. Alkenes serve as monomers for some of the most common polymers, such as polyethylene, polypropylene, polystyrene, poly(vinyl chloride), and many others. Alkenes polymerize to give **addition polymers** resulting from repeated addition reactions across their double bonds.

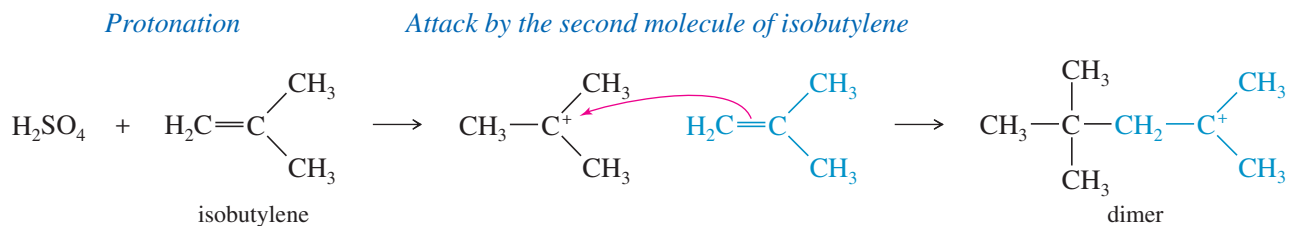


Addition polymers generally form by **chain-growth polymerization**, the rapid addition of one molecule at a time to a growing polymer chain. There is generally a reactive intermediate (cation, anion, or radical) at the growing end of the chain. The chain-growth mechanism involves addition of the reactive end of the chain across the double bond of the alkene monomer. The next sections show how this occurs with cations, radicals, and anions at the growing ends of the chains.

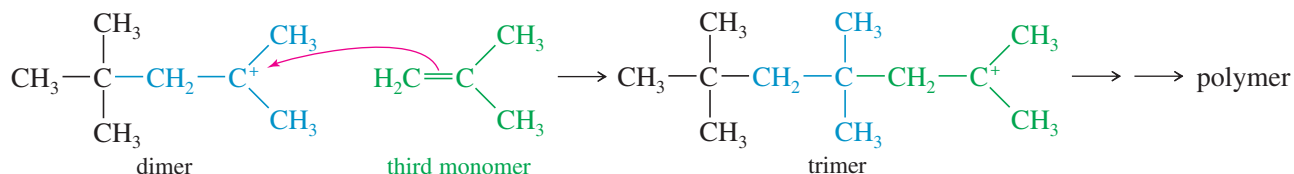
**8-16A Cationic Polymerization**

Alkenes that easily form carbocations are good candidates for **cationic polymerization**, which is just another example of electrophilic addition to an alkene. Consider what happens when pure isobutylene is treated with a trace of concentrated sulfuric acid. Protonation of the alkene forms a carbocation. If a large concentration of isobutylene is available, another molecule of the alkene may act as the nucleophile and attack the carbocation to form the *dimer* (two monomers joined together) and give another carbocation. If the conditions are right, the growing cationic end of the chain will keep adding

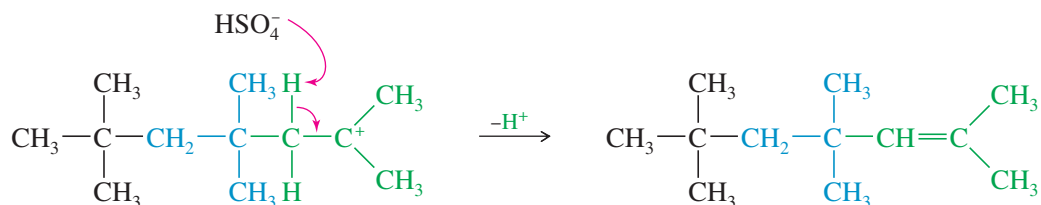
across more molecules of the monomer. The polymer of isobutylene is *polyisobutylene*, one of the constituents of *butyl rubber* used in inner tubes and other synthetic rubber products.



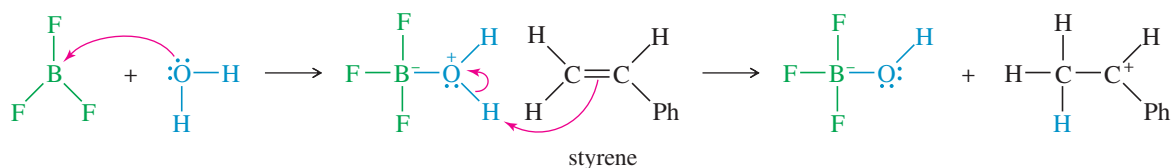
*Attack by a third molecule to give a trimer*



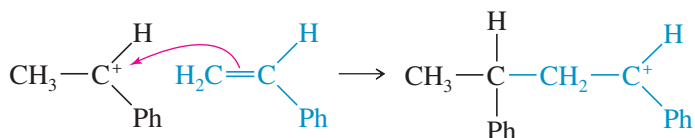
Loss of a proton is the most common side reaction that terminates chain growth:



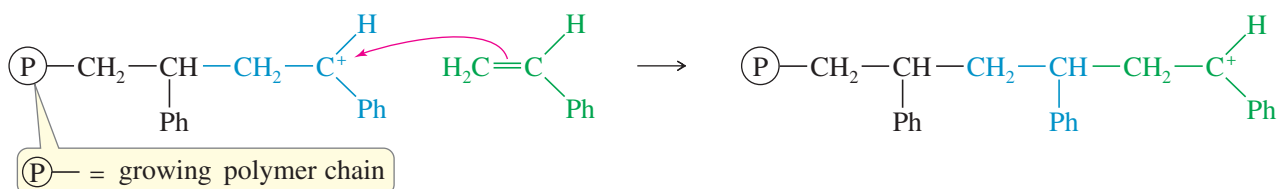
Boron trifluoride ( $\text{BF}_3$ ) is an excellent catalyst for cationic polymerization because it leaves no good nucleophile that might attack a carbocation intermediate and end the polymerization. Boron trifluoride is electron-deficient and a strong Lewis acid. It usually contains a trace of water that acts as a co-catalyst by adding to  $\text{BF}_3$  and then protonating the monomer. Protonation occurs at the less substituted end of an alkene double bond to give the more stable carbocation. Each additional monomer molecule adds with the same orientation, always giving the more stable carbocation. The following reaction shows the polymerization of styrene (vinylbenzene) using  $\text{BF}_3$  as the catalyst.



*First chain-lengthening step*

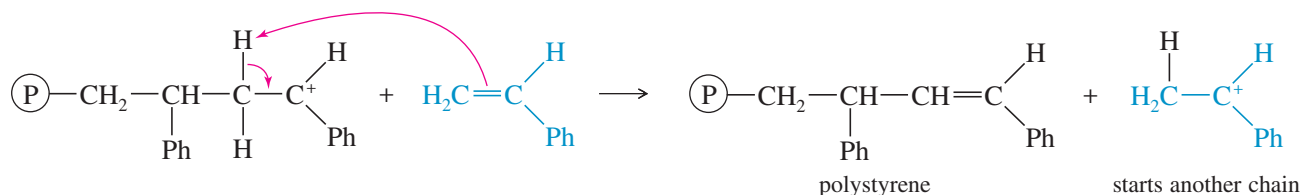


*After many steps, the polymerization continues*



The most likely ending of this  $\text{BF}_3$ -catalyzed polymerization is the loss of a proton from the carbocation at the end of the chain. This side reaction terminates one chain, but it also protonates another molecule of styrene, initiating a new chain.

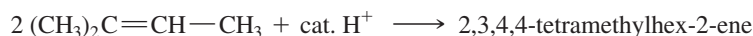
#### Termination of a polymer chain



The product of this polymerization is polystyrene: a clear, brittle plastic that is often used for inexpensive lenses, transparent containers, and Styrofoam<sup>®</sup> insulation. Polystyrene is also the major component of the resin beads that are used to make synthetic proteins. (See Section 24-11.)

#### PROBLEM 8-38

(a) Propose a mechanism for the following reaction.



(b) Show the first three steps (as far as the tetramer) in the  $\text{BF}_3$ -catalyzed polymerization of propylene to form polypropylene.

#### PROBLEM 8-39

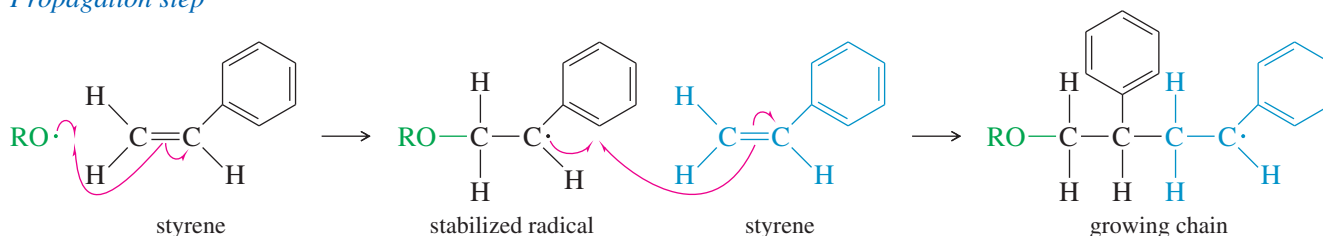
When cyclohexanol is dehydrated to cyclohexene, a gummy green substance forms on the bottom of the flask. Suggest what this residue might be, and propose a mechanism for its formation (as far as the dimer).

### 8-16B Free-Radical Polymerization

Many alkenes undergo **free-radical polymerization** when they are heated with radical initiators. For example, styrene polymerizes to polystyrene when it is heated to  $100^\circ\text{C}$  with a peroxide initiator. A radical adds to styrene to give a resonance-stabilized radical, which then attacks another molecule of styrene to give an elongated radical.

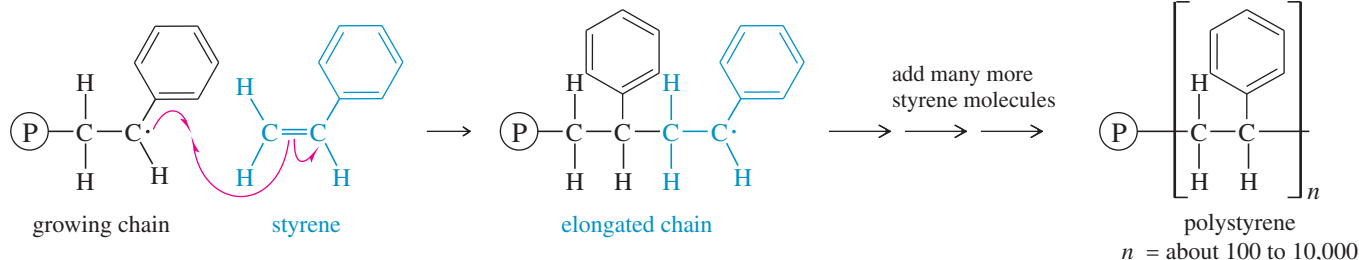


#### Propagation step



Each propagation step adds another molecule of styrene to the radical end of the growing chain. This addition always takes place with the orientation that gives another resonance-stabilized benzylic (next to a benzene ring) radical.

### Propagation step



Chain growth may continue with addition of several hundred or several thousand styrene units. Eventually, the chain reaction stops, either by the coupling of two chains or by reaction with an impurity (such as oxygen) or simply by running out of monomer.

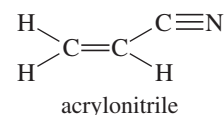
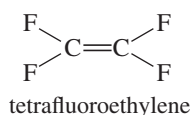
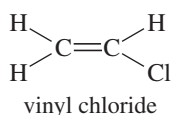
### PROBLEM 8-40

Show the intermediate that would result if the growing chain added to the other end of the styrene double bond. Explain why the final polymer has phenyl groups substituted on alternate carbon atoms rather than randomly distributed.

Ethylene is also polymerized by free-radical chain-growth polymerization. With ethylene, the free-radical intermediates are less stable, so stronger reaction conditions are required. Ethylene is commonly polymerized by free-radical initiators at pressures around 3000 atm and temperatures of about 200 °C. The product, called *low-density polyethylene*, is the material commonly used in polyethylene bags.

### PROBLEM 8-41

The structures of three monomers are shown. In each case, show the structure of the polymer that would result from polymerization of the monomer. Vinyl chloride is polymerized to “vinyl” plastics and PVC pipe. Tetrafluoroethylene polymerizes to Teflon<sup>®</sup>, used as non-stick coatings and PTFE valves and gaskets. Acrylonitrile is polymerized to Orlon<sup>®</sup>, used in sweaters and carpets.



### 8-16C Anionic Polymerization

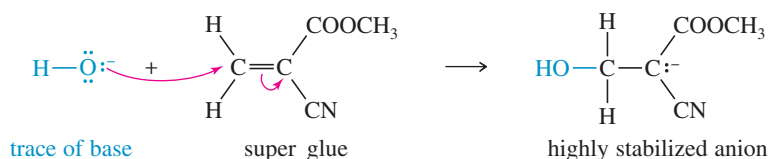
Like cationic polymerization, **anionic polymerization** depends on the presence of a stabilizing group. To stabilize anions, the double bond should have a strong electron-withdrawing group such as a carbonyl group, a cyano group, or a nitro group. Methyl  $\alpha$ -cyanoacrylate contains two powerful electron-withdrawing groups, and it undergoes nucleophilic additions very easily. If this liquid monomer is spread in a thin film between two surfaces, traces of basic impurities (metal oxides, for example) can catalyze its rapid polymerization. The solidified polymer joins the two surfaces. The chemists who first made this monomer noticed how easily it polymerizes and realized that it could serve as a fast-setting glue. Methyl  $\alpha$ -cyanoacrylate is sold commercially as “super” glue.



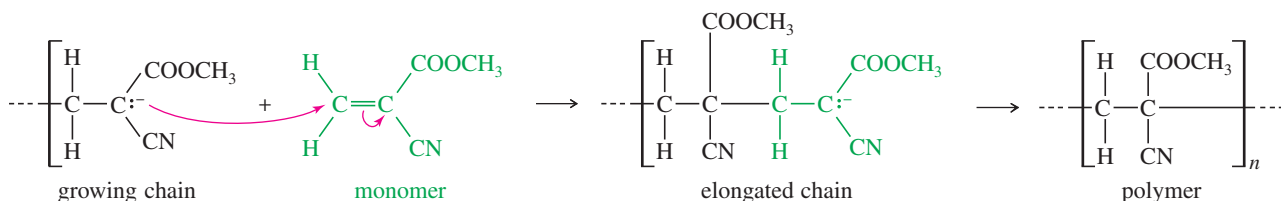
This 1949 DuPont promotional photo shows how a Teflon rod (on our right, in the model's left hand) resists a hot acid solution compared with a rod made from another plastic. In World War II, Teflon was used for insulation in aircraft wiring and for seals in the equipment used to enrich corrosive uranium hexafluoride.



## Initiation step

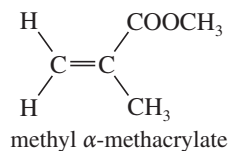


## Chain-lengthening step



## PROBLEM 8-42

Draw a mechanism for a base-catalyzed polymerization of methyl  $\alpha$ -methacrylate to give the Plexiglas<sup>®</sup> polymer.



## 8-17 Olefin Metathesis

The double bond is the strongest bond in an alkene, yet it is also the most reactive bond. Imagine how useful it would be if we could break molecules at their double bonds and reassemble them as we please. That is the goal of olefin metathesis. We can think of an alkene as two **alkylidene groups** ( $=\text{CHR}$ ) held together by the double bond, and mentally divide it up just like we divide the molecule when we go to name it as *E* or *Z* (Section 7-5B). **Olefin metathesis** is any reaction that trades and interchanges these alkylidene groups. The word *metathesis* comes from the Greek words *meta* (change) and *thesis* (position), meaning that the alkylidene groups change their positions in the products. Figure 8-10 shows the trading of alkylidene groups that takes place during olefin metathesis.

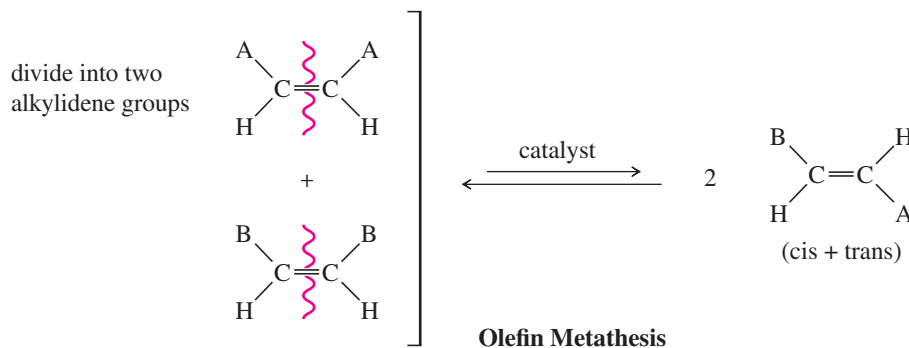


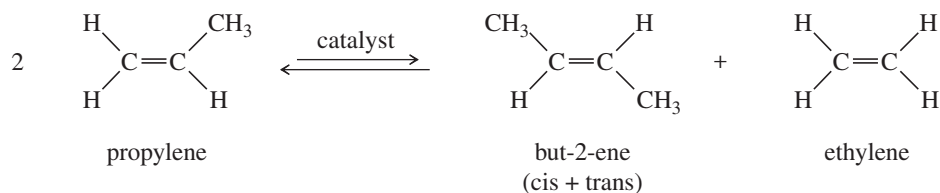
FIGURE 8-10

Olefin metathesis. During metathesis, the alkylidene groups of the reactant olefins trade partners and rearrange to give new combinations of alkenes in the products.

The 2005 Nobel Prize in Chemistry was awarded to Yves Chauvin (French Petroleum Institute), Robert Grubbs (Caltech), and Richard Schrock (MIT) for developing effective ways to induce alkenes to undergo metathesis.

### 8-17A Catalysts for Olefin Metathesis

Olefin metathesis was first observed in the 1950s, and was used in industry to convert propylene to a mixture of but-2-ene and ethylene. This *Phillips Triolefin Process* used an aluminum/molybdenum catalyst whose exact structure was unknown.



Around 1990, Richard Schrock developed versatile molybdenum and tungsten catalysts for olefin metathesis that tolerate a wide range of functional groups in the alkylidene fragments of the olefins. The Schrock catalyst shown in Figure 8-11a is now commercially available. The Schrock catalysts tend to be air- and moisture-sensitive, which limits their use in commercial processes.

In 1992, Robert Grubbs developed a ruthenium phosphine catalyst (Figure 8-11b) that is less sensitive to oxygen and moisture than the Schrock catalysts, and tolerates even more functional groups in the alkylidene fragments of the olefins. Both the Schrock and Grubbs catalysts have a metal atom that is double-bonded to an alkylidene ( $=\text{CHR}$ ) group. They can be symbolized  $[\text{M}]=\text{CHR}$ , where the  $[\text{M}]$  in brackets signifies that the metal atom has other ligands that fine-tune its reactivity.

**FIGURE 8-11**

(a) One of the Schrock molybdenum metathesis catalysts. (b) One of the Grubbs ruthenium metathesis catalysts.

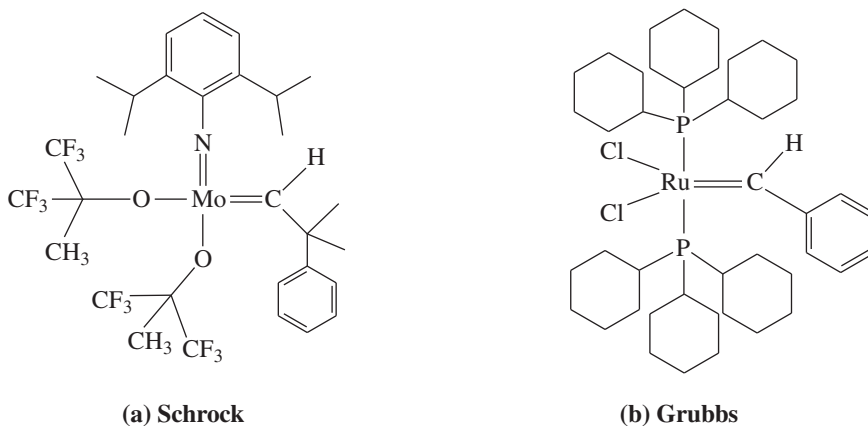


Figure 8-12 shows some examples of useful reactions that are catalyzed by the Schrock and Grubbs catalysts. One important aspect of these metathesis reactions is that they are all reversible, so they form equilibrium mixtures of the reactants and all possible products unless something is done to drive the reaction toward the desired products. The first two examples in Figure 8-12 use the most common method, formation of ethylene gas. Ethylene bubbles off as it forms, effectively driving the reaction to completion. The ring-opening metathesis polymerization is exothermic and naturally goes to products because the ring strain in the bicyclic norbornene is released when the ring opens to form the polymer.

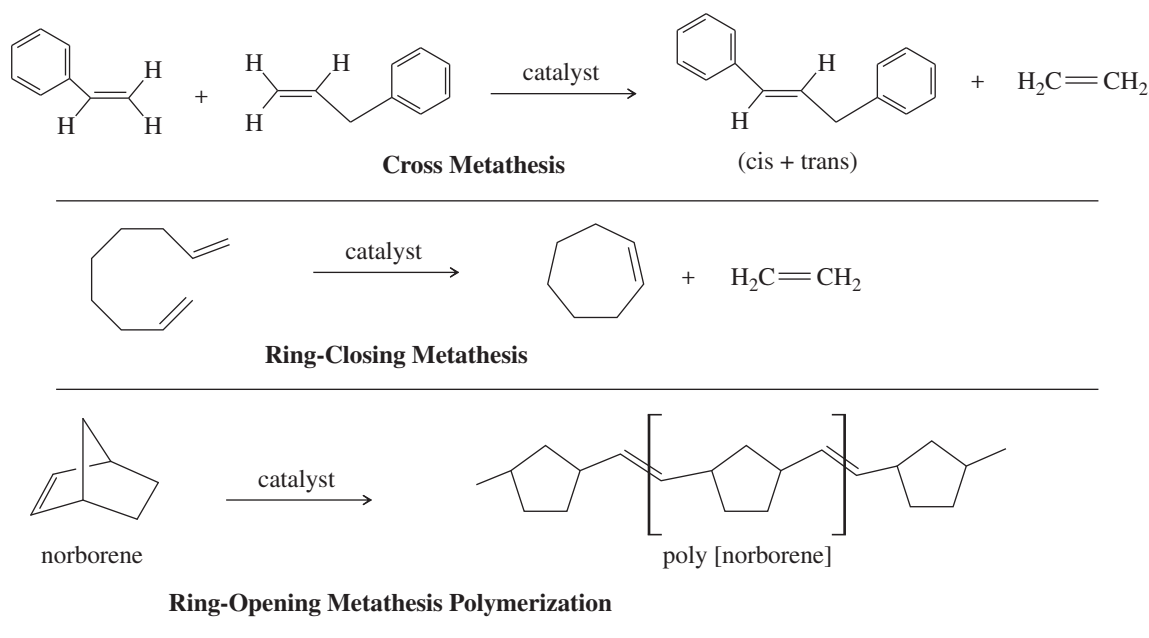
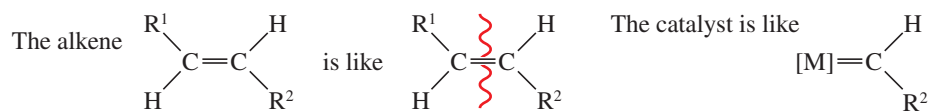


FIGURE 8-12

Useful examples of metathesis reactions.

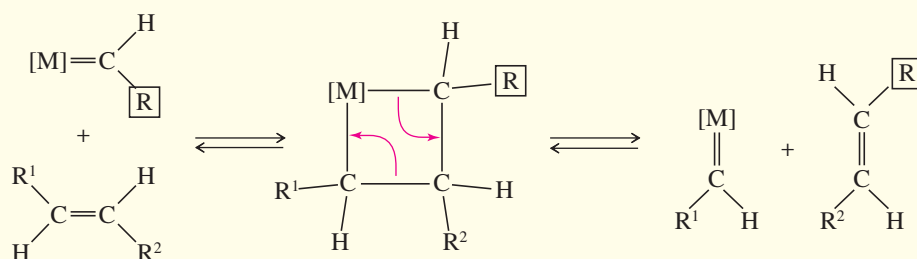
**8-17B Mechanism of Olefin Metathesis**

Several mechanisms were proposed to explain the catalytic metathesis reactions, but the mechanism published by Yves Chauvin in 1971 has come to be accepted as correct. We can think of an alkene as two alkylidene groups bonded together. Similarly, the Schrock and Grubbs catalysts are like a metal atom bonded to one alkylidene group.



Chauvin proposed that the metal-alkylidene catalyst forms an intermediate four-membered ring with an alkene, as shown in Mechanism 8-11. Then the ring breaks apart, either to give the starting alkene and catalyst or to give a new alkene that has traded one alkylidene group with the catalyst.

This mechanism allows the alkylidene groups to change partners back and forth with the catalytic metal until a thermodynamic equilibrium is reached. As we saw earlier, good yields of products result if there is an effective driving force (such as

**MECHANISM 8-11 Olefin Metathesis**

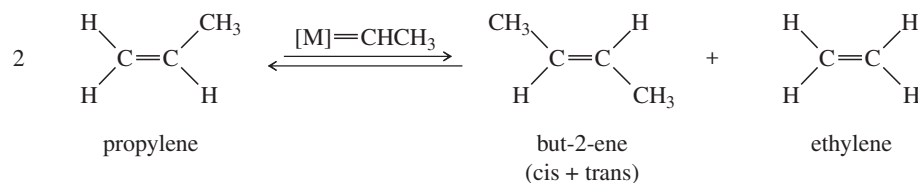


The omnivorous leafroller (OLR) feeds on a wide variety of fruits, vegetables, and ornamentals. Vineyards use pheromone traps to monitor the OLR populations and determine when control methods are needed.

formation of a gaseous by-product or release of ring strain) to push the equilibrium toward the desired products.

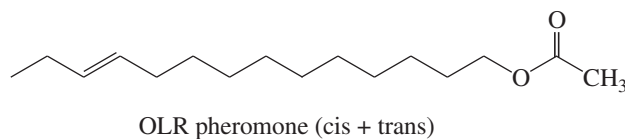
### PROBLEM 8-43

Propose a mechanism for the triolefin process using a metal alkylidene as the catalyst.



### PROBLEM 8-44

Show what reagents would be needed to synthesize the pheromone of the omnivorous leafroller (OLR) using olefin metathesis to assemble the molecule at the double bond.



## PROBLEM-SOLVING STRATEGY Organic Synthesis

Alkyl halides and alkenes are readily made from other compounds, and they are easily converted to other functional groups. This flexibility makes them useful as reagents and intermediates for organic synthesis. Alkenes are particularly important for industrial syntheses because they are inexpensive and available in large quantities from cracking and dehydrogenation of petroleum fractions.

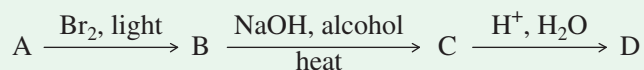
**Organic synthesis** is the preparation of desired compounds from readily available materials. Synthesis is one of the major areas of organic chemistry, and nearly every chapter of this book involves organic synthesis in some way. A synthesis may be a simple one-step reaction, or it may involve many steps and incorporate a subtle strategy for assembling the correct carbon skeleton with all the functional groups in the right positions.

Many of the problems in this book are synthesis problems. In some synthesis problems, you are asked to show how to convert a given starting material to the desired product. There are obvious one-step answers to some of these problems, but others may require several steps, and there may be many correct answers. In solving multistep synthetic problems, it is often helpful to analyze the problem backward: Begin with the desired product (called the *target compound*) and see how it might be mentally changed or broken down to give the starting materials. This backward approach to synthesis is called a **retrosynthetic analysis**.

Some problems allow you to begin with any compounds that meet a certain restriction. For example, you might be allowed to use any alcohols containing no more than four carbon atoms. A retrosynthetic analysis can be used to break down the target compound into fragments no larger than four carbon atoms; then those fragments could be formed from the appropriate alcohols by functional group chemistry.

The following suggestions should help you solve synthesis problems:

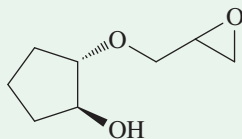
1. Do not guess a starting material and try every possible reaction to convert it to the target compound. Rather, begin with the target compound and use a retrosynthetic analysis to simplify it.
2. Use simple equations, with reagents written above and below the arrows, to show the reactions. The equations do not need to be balanced, but they should include all the reagents and conditions that are important to the success of the reaction.



3. Focus on the functional groups, because that is generally where reactions occur. Do not use any reagents that react with a functional group that you don't intend to modify.

In solving multistep synthesis problems, you will rarely be able to “see” the solution immediately. These problems are best approached systematically, working backward and considering alternative routes. To illustrate a systematic approach that can guide you in solving synthesis problems, we will work through the synthesis of a complex ether starting from alkenes. The problem-solving method described here will be extended in future chapters to multistep syntheses based on the reactions of additional functional groups.

A systematic retrosynthetic analysis begins with an examination of the structure of the product. We will consider the synthesis of the following compound from alkenes containing up to five carbon atoms.



**1. Review the functional groups and carbon skeleton of the target compound.**

The target compound is an ether. One alkyl group is a five-carbon cyclopentane ring with two oxygen atoms situated trans. The other group has three carbons containing a reactive epoxide ring.

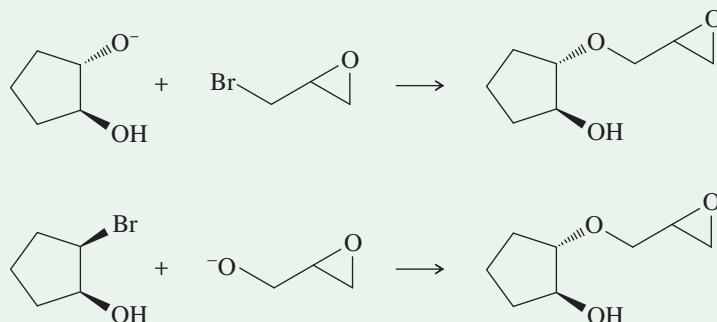
**2. Review the functional groups and carbon skeletons of the starting materials (if specified), and see how their skeletons might fit together in the target compound.**

The synthesis is to begin with alkenes containing up to five carbon atoms, so all the functional groups in the product must be derived from alkenes. Most likely, we will start with cyclopentene to give the five-carbon ring and propene to give the three-carbon chain.

**3. Compare methods for synthesizing the functional groups in the target compound, and select the reactions that are most likely to give the correct product.**

This step may require writing several possible reactions and evaluating them.

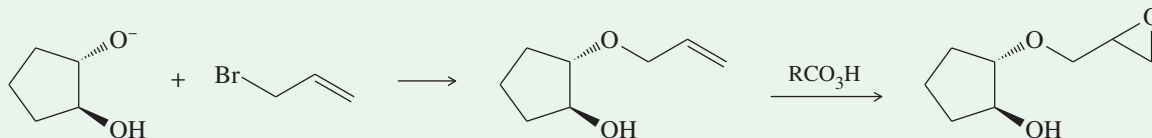
Ethers can be synthesized by nucleophilic reactions between alkyl halides and alkoxides (Section 6-9). The target compound might be formed by  $S_N2$  attack of an alkoxide ion on an alkyl halide in either of two ways shown below:



The first reaction is better because the  $S_N2$  attack is on a primary alkyl halide, while the second is on a secondary halide. Also, in the second reaction, the alkoxide might simply deprotonate the alcohol on the left and cause the reaction to fail.

**4. In general, reactive functional groups are best put into place toward the end of a synthesis.**

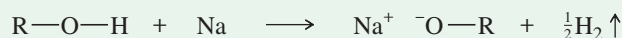
The target compound contains a reactive epoxide ring. Epoxides react with acids and bases, and the epoxide might not survive the crucial ether-forming reaction just shown. Perhaps the epoxide is best added after formation of the ether. That gives us the following final two steps in the synthesis:



**5. Working backward through as many steps as necessary, compare methods for synthesizing the reactants needed for the final step.**

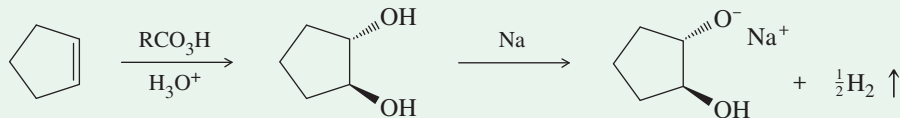
This process may require writing several possible reaction sequences and evaluating them, keeping in mind the specified starting materials.

Two reactants are needed to form the ether: an allylic halide and an alkoxide ion. Alkoxide ions are commonly formed by the reaction of an alcohol with sodium metal:

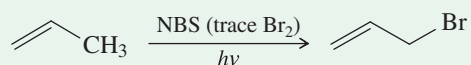


(continued)

The alkoxide needed to make the ether is formed by adding sodium to a trans diol as shown below. Trans diols are formed by epoxidation and hydrolysis of alkenes (Section 8-13).



The other piece we need is an allylic bromide. Allylic bromides are formed by allylic bromination of alkenes (Section 6-6B).



**6. Summarize the complete synthesis in the forward direction, including all steps and all reagents, and check it for errors and omissions.**

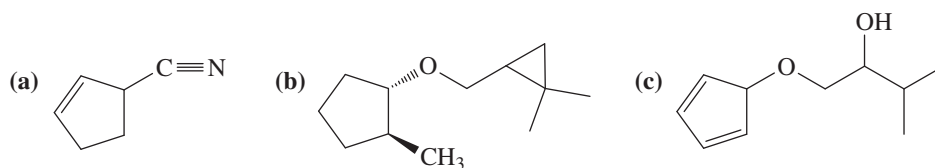
This summary is left to you as a review of both the chemistry involved in the synthesis and the method used to develop multistep syntheses.

**PROBLEM:** Summarize the synthesis outlined in the problem-solving strategy. This summary should be in the synthetic (forward) direction, showing each step and all reagents.

Problem 8-45 requires devising several multistep syntheses. As practice in working such problems, we suggest that you proceed in order through the five steps just outlined.

**PROBLEM 8-45**

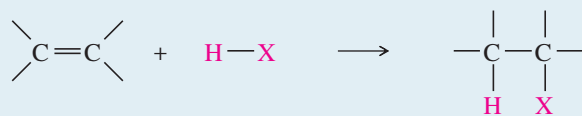
Show how you would synthesize each compound, starting with alkenes or cycloalkenes that contain no more than six carbon atoms. You may use any additional reagents you need.



**SUMMARY Reactions of Alkenes**

**1. Electrophilic Additions**

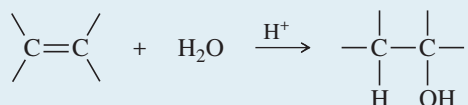
a. Addition of hydrogen halides (Section 8-3)



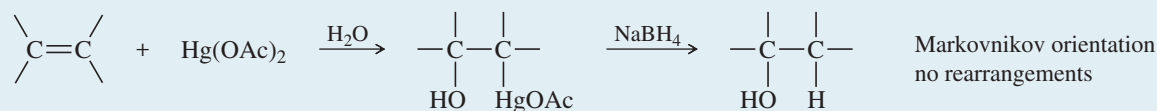
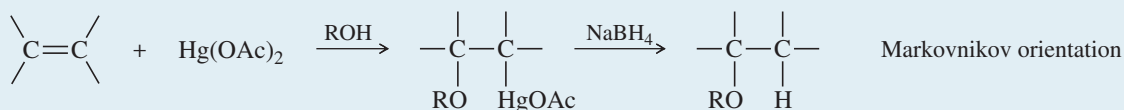
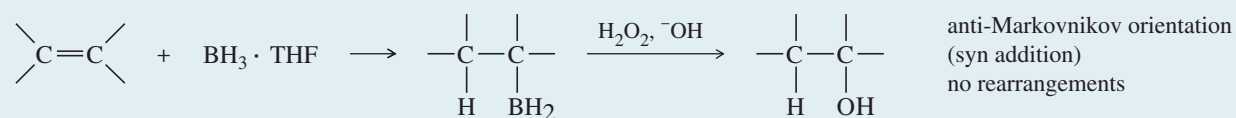
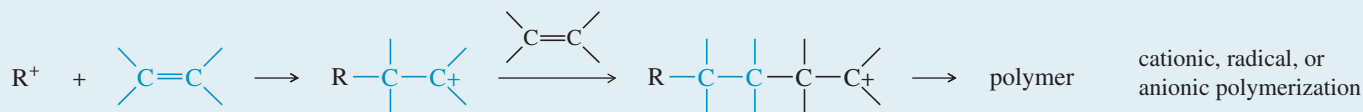
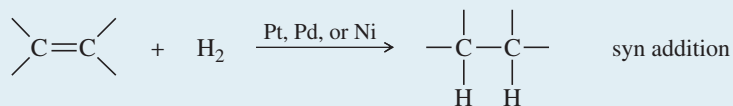
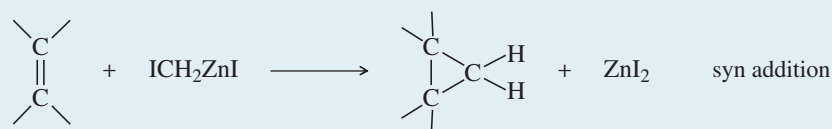
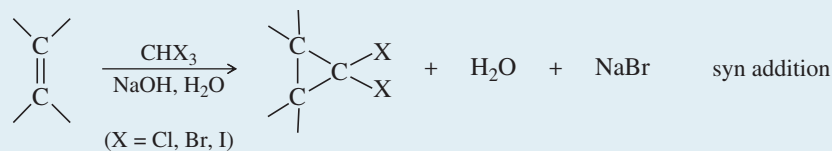
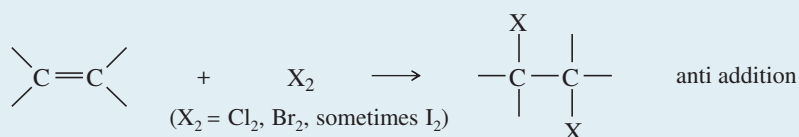
(HX = HCl, HBr, or HI)

works with HCl, HBr, and HI  
Markovnikov orientation  
(anti-Markovnikov  
with HBr and peroxides)  
Rearrangements are possible

b. Acid-catalyzed hydration (Section 8-4)



Markovnikov orientation  
Rearrangements are possible

c. *Oxymercuration–demercuration* (Section 8-5)d. *Alkoxymercuration–demercuration* (Section 8-6)e. *Hydroboration–oxidation* (Section 8-7)f. *Polymerization* (Section 8-16)2. *Reduction: Catalytic Hydrogenation* (Section 8-10)3. *Addition of Carbenes: Cyclopropanation* (Section 8-11)a. *Simmons-Smith Reaction*b. *Alpha elimination*4. *Oxidative Additions*a. *Addition of halogens* (Section 8-8)

(continued)









## GUIDE TO ORGANIC REACTIONS IN CHAPTER 8

Reactions covered in Chapter 8 are shown in red. Reactions covered in earlier chapters are shown in blue.

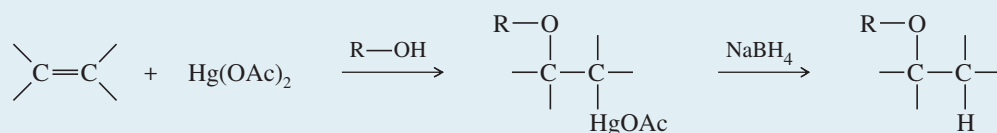
Substitution	Addition	Elimination	Oxidation/Reduction
<p>▶ Nucleophilic</p> <ul style="list-style-type: none"> <li>▶ at <math>sp^3</math> C (<math>S_N1</math>, <math>S_N2</math>) Ch 6, 10, 14, 22</li> <li>▶ at <math>sp^2</math> C (Nuc. Arom. Subst.) Ch 17, 19</li> <li>▶ at C=O (Nuc. Acyl Subst.) Ch 10, 11, 20, 21, 22</li> </ul> <p>▶ Electrophilic</p> <ul style="list-style-type: none"> <li>▶ at <math>sp^2</math> C (Elect. Arom. Subst.) Ch 17, 19</li> </ul> <p>▶ Radical</p> <ul style="list-style-type: none"> <li>▶ at <math>sp^3</math> C (alkane halogenation) Ch 4, 6, 16, 17</li> <li>▶ at <math>sp^2</math> C (Sandmeyer rxn) Ch 19</li> </ul> <p>▶ Organometallic</p> <ul style="list-style-type: none"> <li>▶ Gilman Ch 10, 17</li> <li>▶ Suzuki Ch 17</li> <li>▶ Heck Ch 17</li> </ul>	<p>▶ Nucleophilic</p> <ul style="list-style-type: none"> <li>▶ at C=O (Nuc. Addn.) Ch 9, 10, 18, 22</li> <li>▶ at C=C (conjugate addn.) Ch 22</li> </ul> <p>▶ Electrophilic</p> <ul style="list-style-type: none"> <li>▶ at C=C (Elect. Addn.) Ch 8, 9, 10</li> <li>▶ at C=C (Carbene Addn.) Ch 8</li> </ul> <p>▶ Radical</p> <ul style="list-style-type: none"> <li>▶ at C=C (HBr + ROOR) Ch 8</li> </ul> <p>▶ Pericyclic</p> <ul style="list-style-type: none"> <li>▶ cycloaddition (Diels-Alder) Ch 15</li> </ul> <p>▶ Oxidation</p> <ul style="list-style-type: none"> <li>▶ epoxidation Ch 8, 10, 14</li> </ul> <p>▶ Reduction</p> <ul style="list-style-type: none"> <li>▶ hydrogenation Ch 8, 9, 17, 18, 19</li> </ul>	<p>▶ Basic conditions (E2)</p> <ul style="list-style-type: none"> <li>▶ E2 dehydrohalogenation Ch 7, 9</li> <li>▶ tosylate elimination Ch 11</li> <li>▶ Hofmann elimination Ch 19</li> </ul> <p>▶ Acidic conditions (E1)</p> <ul style="list-style-type: none"> <li>▶ E1 dehydrohalogenation Ch 7</li> <li>▶ dehydration of alcohols Ch 11</li> </ul> <p>▶ Pericyclic (Cope elimination)</p> <ul style="list-style-type: none"> <li>▶ Ch 19</li> </ul>	<p>▶ Oxidation</p> <ul style="list-style-type: none"> <li>▶ epoxidation Ch 8, 10, 14</li> <li>▶ oxidative cleavage Ch 8, 9, 11, 17, 22</li> <li>▶ oxygen functional groups Ch 11, 18, 19, 20</li> </ul> <p>▶ Reduction</p> <ul style="list-style-type: none"> <li>▶ hydride reduction Ch 8, 10, 11, 17, 18, 19, 20, 21</li> <li>▶ hydrogenation Ch 8, 9, 17, 18, 19</li> <li>▶ metals Ch 9, 17, 18, 19</li> </ul>

This *Guide to Organic Reactions* will appear at the end of six of the chapters in which large numbers of new reactions are introduced. The purposes are to show the overview of major reaction categories, to indicate where that chapter's reactions fit in the larger scheme, and to serve as a study tool by indicating which reaction types are new and which have been previously covered. The new reactions in the current chapter will appear in **red type**. Those reactions that have been covered in previous chapters will appear in **blue type**. As you progress through *Organic Chemistry*, you will gradually see more reactions appear in blue type because you have previously covered them.

### Essential Terms

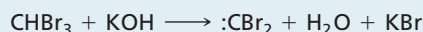
<b>addition</b>	A reaction involving an increase in the number of groups attached to the alkene and a decrease in the number of elements of unsaturation. (p. 360)
<b>anti addition:</b>	An addition in which two groups add to opposite faces of the double bond (as in addition of $Br_2$ ). (p. 380)
<b>electrophilic addition:</b>	An addition in which the electrophile (electron-pair acceptor) bonds to one of the double-bonded carbons first, followed by the nucleophile. (p. 360)
<b>syn addition:</b>	An addition in which two groups add to the same face of the double bond (as in osmium tetroxide <b>dihydroxylation</b> ). (p. 380)
<b>addition polymer</b>	A polymer that results from the addition reactions of alkenes, dienes, or other compounds with double and triple bonds. Most addition polymers form by a chain-growth process. (p. 403)
<b>alkoxy group</b>	( <b>alkoxyl group</b> ) ( $-O-R$ ) An alkyl group bonded through an oxygen atom, as in an ether. (p. 375)

**alkoxymercuration** The addition of mercuric acetate to an alkene in an alcohol solution, forming an alkoxymercurial intermediate. Demercuration gives an ether. (p. 375)



**alkylidene group** One of the carbon atoms at either end of a double bond, together with its two substituents. Most commonly =CH<sub>2</sub> or =CHR or =CR<sub>2</sub>. (p. 407)

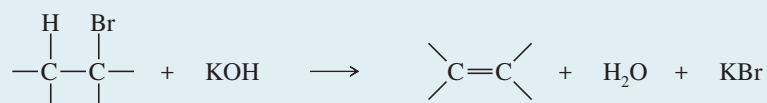
**alpha elimination** ( $\alpha$  elimination) The elimination of two atoms or groups from the same carbon atom. Alpha eliminations can be used to form carbenes. (p. 392)



**anionic polymerization** The process of forming an addition polymer by chain-growth polymerization involving an anion at the end of the growing chain. (p. 406)

**asymmetric induction** (**enantioselective synthesis**) The formation of an optically active product from an optically inactive starting material. Such a process requires the use of an optically active reagent or catalyst. (p. 390)

**beta elimination** ( $\beta$  elimination) The elimination of two atoms or groups from adjacent carbon atoms. This is the most common type of elimination. (p. 392)



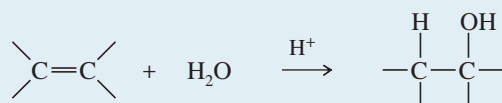
**carbene** A reactive intermediate with a neutral carbon atom having only two bonds and two nonbonding electrons. Methylene (:CH<sub>2</sub>) is the simplest carbene. (p. 391)

**cationic polymerization** The process of forming an addition polymer by chain-growth polymerization involving a cation at the end of the growing chain. (p. 403)

**chain-growth polymer** A polymer that results from the rapid addition of one monomer at a time to a growing polymer chain, usually with a reactive intermediate (cation, radical, or anion) at the growing end of the chain. Most chain-growth polymers are addition polymers of alkenes and dienes. (p. 403)

**demercuration** The removal of a mercury species from a molecule. Demercuration of the products of oxymercuration and alkoxymercuration is usually accomplished using sodium borohydride. (p. 373)

**dihydroxylation** (**hydroxylation**) The addition of two hydroxy groups, one at each carbon of the double bond; formally, an oxidation. (p. 398)



**epoxide** (**oxirane**) A three-membered cyclic ether. (p. 393)

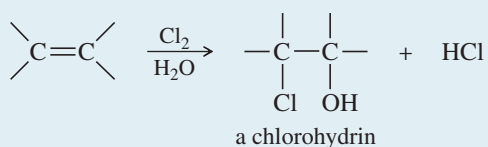
**epoxidation:** Formation of an epoxide, usually from an alkene. A peroxyacid is generally used for alkene epoxidations. (p. 394)

**free-radical polymerization** The process of forming an addition polymer by chain-growth polymerization involving a free radical at the end of the growing chain. (p. 405)

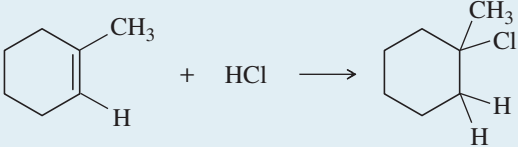
**glycol** A 1,2-diol. (p. 395)

**halogenation** The addition of a halogen (X<sub>2</sub>) to a molecule, or the free-radical substitution of a halogen for a hydrogen. (p. 382)

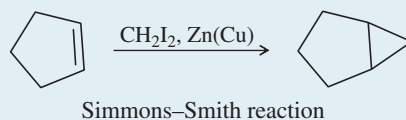
**halohydrin** A beta-haloalcohol, with a halogen and a hydroxy group on adjacent carbon atoms. (p. 385)



**halonium ion** A reactive, cationic intermediate with a three-membered ring containing a halogen atom; usually, a **chloronium ion**, a **bromonium ion**, or an **iodonium ion**. (p. 383)

<b>heterogeneous catalysis</b>	Use of a catalyst that is in a separate phase from the reactants. For example, a platinum hydrogenation catalyst is a solid, a separate phase from the liquid alkene. (p. 389)
<b>homogeneous catalysis</b>	Use of a catalyst that is in the same phase as the reactants. For example, the acid catalyst in hydration is in the liquid phase with the alkene. (p. 389)
<b>hydration</b>	The addition of water to a molecule. Hydration of an alkene forms an alcohol. (p. 370)
	$\begin{array}{c} \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \end{array} + \text{H}_2\text{O} \xrightarrow{\text{OsO}_4} \begin{array}{c} \text{HO} \quad \text{OH} \\   \quad   \\ -\text{C}-\text{C}- \\   \quad   \end{array}$
<b>hydroboration</b>	The addition of borane (BH <sub>3</sub> ) or one of its derivatives (BH <sub>3</sub> ·THF, for example) to a molecule. (p. 378)
<b>hydrogenation</b>	The addition of hydrogen to a molecule. The most common hydrogenation is the addition of H <sub>2</sub> across a double bond in the presence of a catalyst ( <b>catalytic hydrogenation</b> or <b>catalytic reduction</b> ). (p. 389)
<b>hydroxylation</b>	See <b>dihydroxylation</b> .
<b>Markovnikov's rule</b>	( <i>original statement</i> ) When a proton acid adds to the double bond of an alkene, the proton bonds to the carbon atom that already has more hydrogen atoms. (p. 365)
<b>Markovnikov's rule</b>	( <i>extended statement</i> ) In an electrophilic addition to an alkene, the electrophile adds in such a way as to generate the most stable intermediate. (p. 365)
	 <p style="text-align: center;">Markovnikov product</p>
<b>Markovnikov orientation:</b>	An orientation of addition that obeys the original statement of Markovnikov's rule; one that gives the <b>Markovnikov product</b> . (p. 365)
<b>anti-Markovnikov orientation:</b>	An orientation of addition that is the opposite of that predicted by the original statement of Markovnikov's rule; one that gives the <b>anti-Markovnikov product</b> . (p. 366)
<b>mCPBA</b>	( <i>meta</i> -chloroperoxybenzoic acid) A common reagent for epoxidizing alkenes. mCPBA dissolves in common solvents such as dichloromethane. As the epoxidation takes place, the <i>m</i> -chlorobenzoic acid by-product precipitates out of solution. (p. 394)
<b>metathesis</b>	( <b>olefin metathesis</b> ) Any reaction that trades and interchanges the alkylidene groups of an alkene. (p. 407)
	$\begin{array}{c} \text{R}^1 \quad \text{H} \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \\ \text{H} \quad \text{H} \end{array} + \begin{array}{c} \text{H} \quad \text{H} \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \\ \text{H} \quad \text{R}^2 \end{array} \xrightarrow{\text{Ru or Mo catalyst}} \begin{array}{c} \text{R}^1 \quad \text{H} \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \\ \text{H} \quad \text{R}^2 \end{array} + \text{H}_2\text{C}=\text{CH}_2$ <p style="text-align: center;">olefin metathesis      (cis + trans)      ethylene</p>
<b>monomer</b>	One of the small molecules that bond together to form a polymer. (p. 403)
<b>organic synthesis</b>	The preparation of desired organic compounds from readily available materials. (p. 410)
<b>oxidative cleavage</b>	The cleavage of a carbon–carbon bond through oxidation. Carbon–carbon double bonds are commonly cleaved by ozonolysis/reduction or by warm, concentrated permanganate. (p. 400)
<b>oxymercuration</b>	The addition of aqueous mercuric acetate to an alkene. (p. 373)
	$\begin{array}{c} \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \end{array} + \text{Hg}(\text{OAc})_2 \xrightarrow{\text{H}_2\text{O}} \begin{array}{c} \text{HO} \quad   \\   \quad   \\ -\text{C}-\text{C}- \\   \quad   \\ \text{HgOAc} \end{array} + \text{HOAc}$
<b>ozonolysis</b>	The use of ozone, usually followed by reduction, to cleave a double bond. (p. 400)
<b>peroxide effect</b>	The reversal of orientation of HBr addition to alkenes in the presence of peroxides. A free-radical mechanism is responsible for the peroxide effect. (p. 368)
<b>peroxyacid</b>	( <i>peracid</i> ) A carboxylic acid with an extra oxygen atom and a peroxy (—O—O—) linkage. The general formula is RCO <sub>3</sub> H. (p. 393)

<b>polymer</b>	A high-molecular-weight compound composed of many molecules of a smaller, simpler compound called the <b>monomer</b> . (p. 403)
<b>polymerization:</b>	The reaction of monomer molecules to form a polymer. (p. 403)
<b>regiochemistry</b>	The orientation of a chemical reaction on an unsymmetrical substrate. In additions to alkenes, the regiochemistry of the addition involves which part of the reagent adds to which end of an unsymmetrical alkene. (p. 362)
<b>regioselective reaction</b>	A reaction in which one direction of bond making or bond breaking occurs preferentially over all other directions. For example, the addition of HCl is regioselective, predicted by Markovnikov's rule. Hydroboration–oxidation is regioselective because it consistently gives anti-Markovnikov orientation. (p. 364)
<b>retrosynthetic analysis</b>	A method of working backward to solve multistep synthetic problems. (p. 410)
<b>Simmons–Smith reaction</b>	A cyclopropanation of an alkene using the carbenoid reagent generated from diiodomethane and the zinc–copper couple. (p. 392)



<b>stereospecific reaction</b>	A reaction that converts different stereoisomers of the starting material into different stereoisomers of the product. (p. 381)
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## Essential Problem-Solving Skills in Chapter 8

Each skill is followed by problem numbers exemplifying that particular skill.

- |   |   |
|---|---|
| <b>1</b> Use the extended version of Markovnikov's rule to predict the regiochemistry (orientation) of electrophilic additions to alkenes.  | Problems 8-46, 47, and 50                                     |
| <b>2</b> Show how to control the stereochemistry and regiochemistry (orientation) of additions to alkenes to obtain the products we want.   | Problems 8-47, 49, 50, 55, 61, 65, and 76                     |
| <b>3</b> Show how to control the hydration of alkenes to give alcohols with either Markovnikov or anti-Markovnikov orientation, depending on the reagents.                            | Problems 8-46, 49, 50, 51, and 79                             |
| <b>4</b> Predict the products of halogenations, oxidations, reductions, and cleavages of alkenes, including the orientation (regiochemistry) and the stereochemistry of the reaction. | Problems 8-46, 47, 48, 54, 55, 61, 65, 66, and 75             |
| <b>5</b> Predict the stereochemistry observed in the hydroboration, halogenation, and dihydroxylation reactions of alkenes.   | Problems 8-46, 50, 51, 55, and 66                             |
| <b>6</b> Propose logical mechanisms to explain the observed products of alkene reactions, including regiochemistry and stereochemistry.   | Problems 8-56, 57, 58, 59, 64, 67, 70, 71, 76, 77, 78, and 79 |
| <b>7</b> Use retrosynthetic analysis to solve multistep synthesis problems with alkenes as reagents, intermediates, or products.  | Problems 8-49, 50, 51, 55, and 61                             |
| <i>Problem-Solving Strategy: Organic Synthesis</i>  | Problems 8-49, 50, 51, 55, and 61                             |
| <b>8</b> Use clues provided by the products of reactions, such as ozonolysis, to determine the structure of an unknown alkene.  | Problems 8-48, 54, 55, 60, 61, 62, 63, and 68                 |
| <b>9</b> Show how metathesis interchanges the alkylidene (=CHR) groups in alkenes, forming new and different alkenes.   | Problems 8-46, 52, and 53                                     |
| <b>10</b> Given a particular monomer unit, draw the structure of the resulting polymer.   | Problems 8-72, 73, and 74                                     |

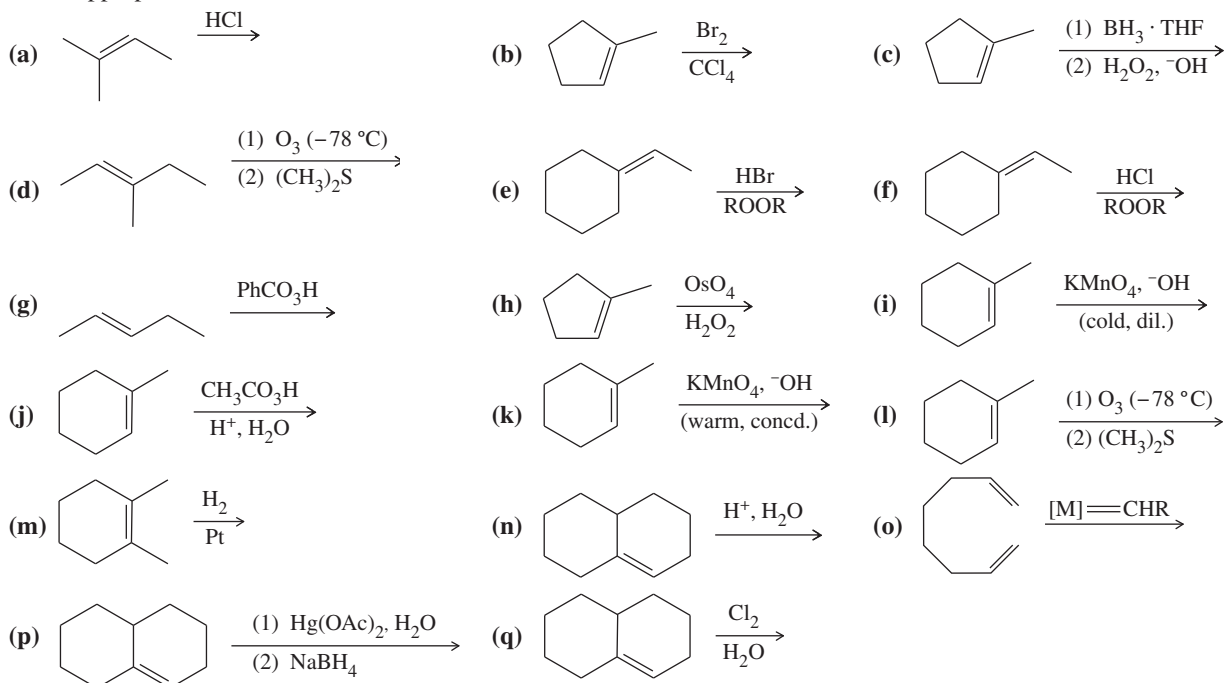
In studying these reaction-intensive chapters, students ask whether they should “memorize” all the reactions. Doing organic chemistry is like speaking a foreign language, and the reactions are your vocabulary. Without knowing the words, how can you construct sentences? Making flash cards often helps students learn the reactions.

In organic chemistry, the mechanisms, regiochemistry, and stereochemistry are your grammar. You must develop *facility* with the reactions, as you develop facility with the words and grammar you use in speaking. Problems and multistep syntheses are the sentences of organic chemistry. You must practice combining all aspects of your vocabulary in solving these problems.

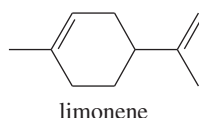
Students who fail organic chemistry exams often do so because they have memorized the vocabulary, but they have not practiced enough problems. Others fail because they think they can do problems, but they lack the vocabulary. If you understand the reactions and can do the end-of-chapter problems without referring to the chapter, then you should do well on your exams.

## Study Problems

**8-46** Predict the major products of the following reactions, and give the structures of any intermediates. Include stereochemistry where appropriate.

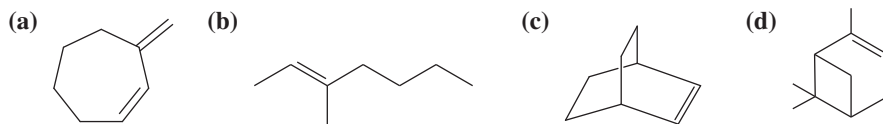


**8-47** Limonene is one of the compounds that give lemons their tangy odor. Show the structures of the products expected when limonene reacts with an excess of each of these reagents.

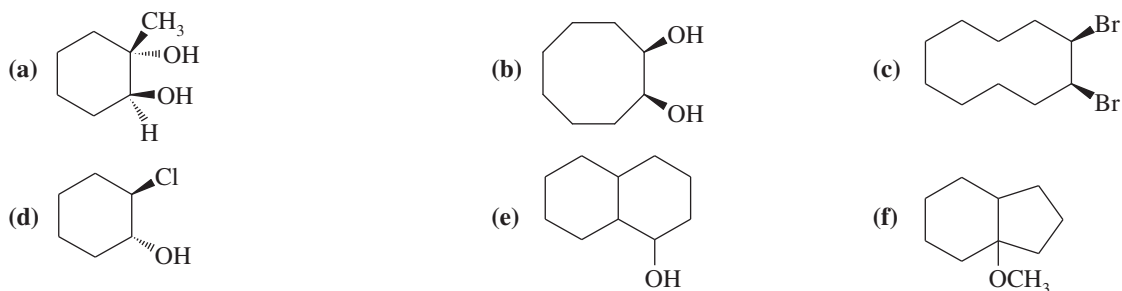


- borane in tetrahydrofuran, followed by basic hydrogen peroxide
- m*-chloroperoxybenzoic acid
- ozone, then dimethyl sulfide
- a mixture of osmic acid and hydrogen peroxide
- hot, concentrated potassium permanganate
- peroxyacetic acid in acidic water
- hydrogen and a platinum catalyst
- hydrogen bromide gas
- hydrogen bromide gas in a solution containing dimethyl peroxide
- bromine water
- chlorine gas
- mercuric acetate in methanol, followed by sodium borohydride
- $\text{CHBr}_3$  and 50% aq. NaOH

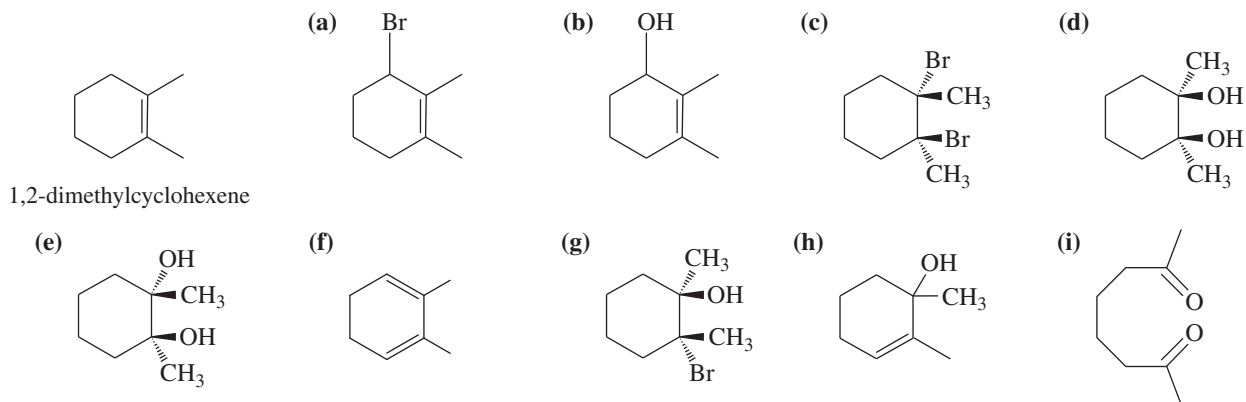
**8-48** Give the products expected when the following compounds are ozonized and reduced.



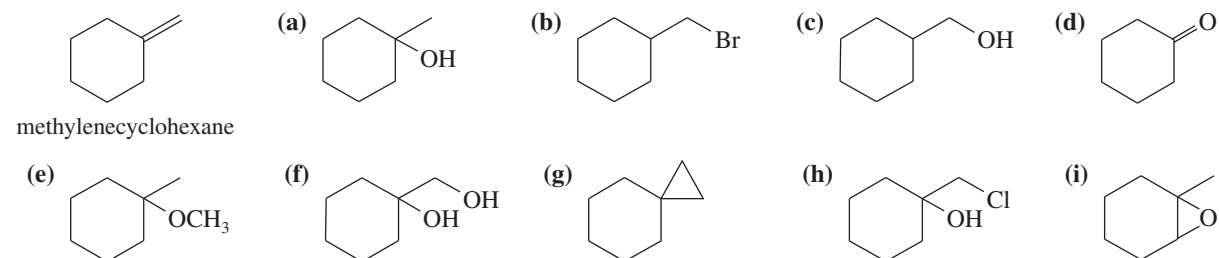
8-49 Show how you would make the following compounds from a suitable cyclic alkene.



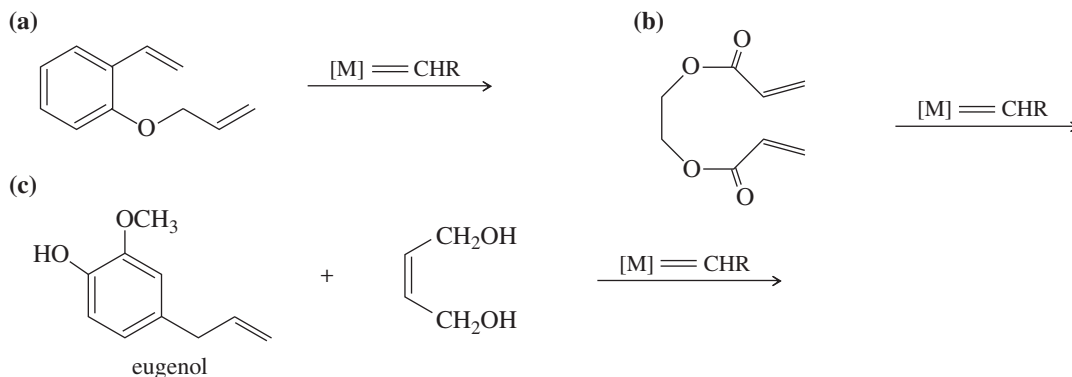
8-50 Using 1,2-dimethylcyclohexene as your starting material, show how you would synthesize the following compounds. (Once you have shown how to synthesize a compound, you may use it as the starting material in any later parts of this problem.) If a chiral product is shown, assume that it is part of a racemic mixture.



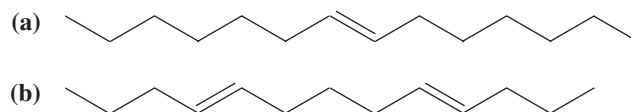
8-51 Show how you would synthesize each compound using methylenecyclohexane as your starting material.



8-52 Show what products you would expect from the following metathesis reactions, using the Schrock or Grubbs catalysts.

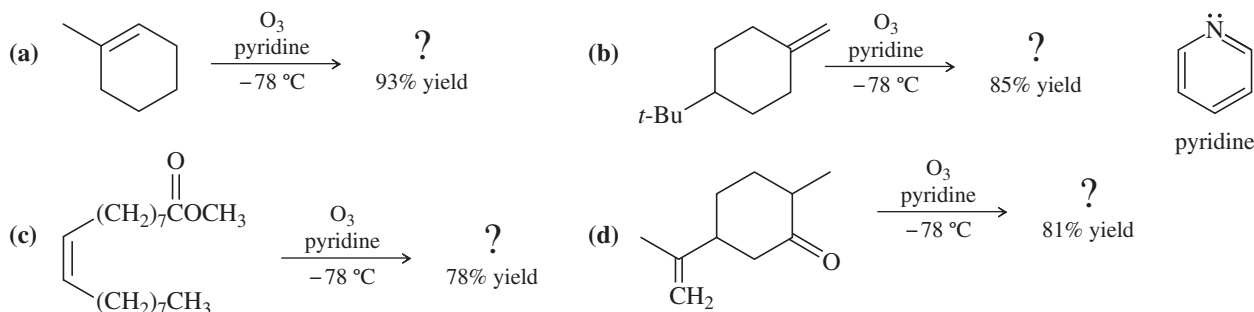


8-53 Show how you might use olefin metathesis to assemble the following alkenes from smaller units:

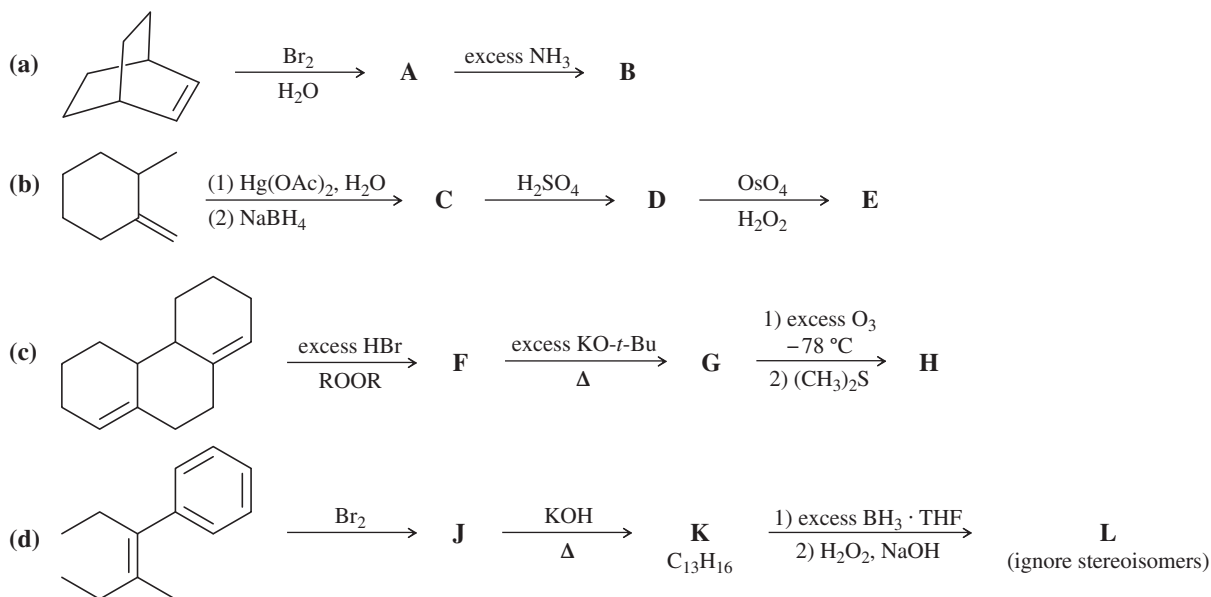




**8-54** Professor Patrick Dussault (University of Nebraska at Lincoln) has developed an alternative to the standard two-step ozonolysis procedure requiring reduction of the ozonide in a second step. He uses 2 to 3 equivalents of pyridine, a mildly basic organic solvent, in a one-step process (*Organic Letters*, **2012**, 14, 2242). Show the products you expect from the following examples.

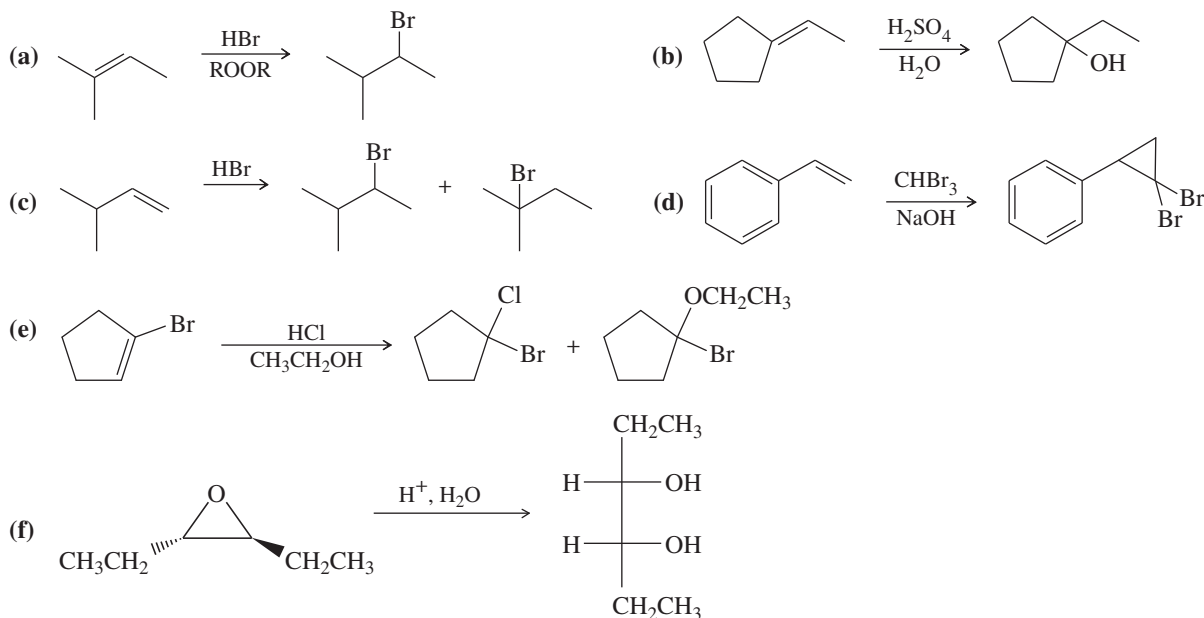


**8-55** Complete each synthesis by providing the structure of the major product at each step, including any important stereochemistry.

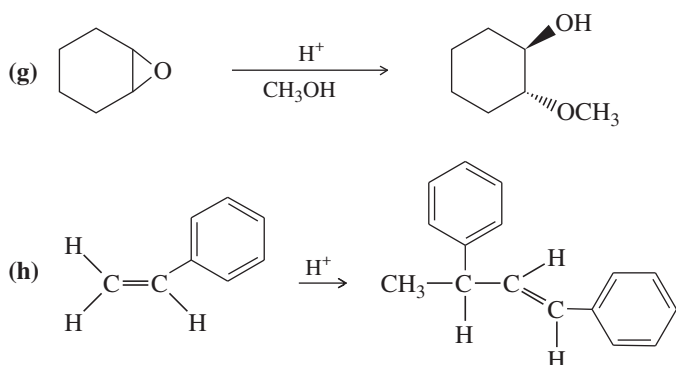


(Hint: Recall that benzene does not undergo most addition reactions.)

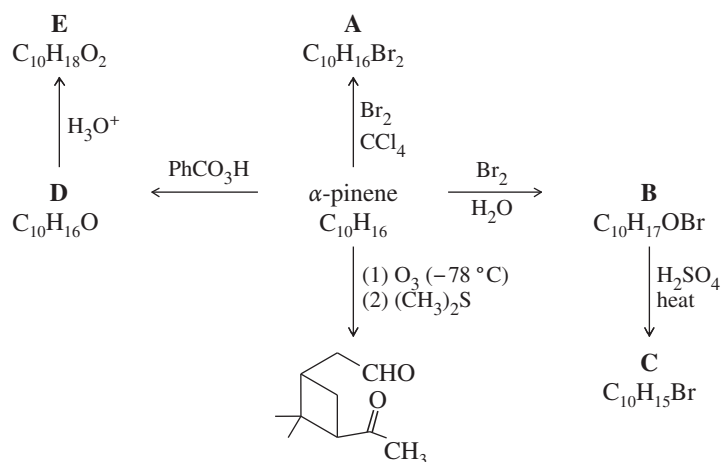
**8-56** Propose mechanisms consistent with the following reactions.



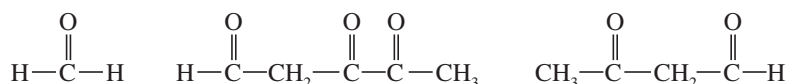
(continued)



- 8-57** Draw an approximate reaction-energy diagram showing the curves for the two possible pathways for ionic addition of HBr to 1-methylcyclohexene. (a) Formation of the major product, 1-bromo-1-methylcyclohexane, and (b) formation of the minor product, 1-bromo-2-methylcyclohexane. Point out how these curves show that 1-bromo-1-methylcyclohexane should be formed faster.
- 8-58** Cyclohexene is dissolved in a solution of lithium chloride in chloroform. To this solution is added one equivalent of bromine. The material isolated from this reaction contains primarily a mixture of *trans*-1,2-dibromocyclohexane and *trans*-1-bromo-2-chlorocyclohexane. Propose a mechanism to show how these compounds are formed.
- 8-59** Draw a reaction-energy diagram for the propagation steps of the free-radical addition of HBr to isobutylene. Draw curves representing the reactions leading to both the Markovnikov and the anti-Markovnikov products. Compare the values of  $\Delta G^\circ$  and  $E_a$  for the rate-limiting steps, and explain why only one of these products is observed.
- 8-60** Unknown **X**,  $C_5H_9Br$ , does not react with bromine or with dilute  $KMnO_4$ . Upon treatment with potassium *tert*-butoxide, **X** gives only one product, **Y**,  $C_5H_8$ . Unlike **X**, **Y** decolorizes bromine and changes  $KMnO_4$  from purple to brown. Catalytic hydrogenation of **Y** gives methylcyclobutane. Ozonolysis–reduction of **Y** gives dialdehyde **Z**,  $C_5H_8O_2$ . Propose consistent structures for **X**, **Y**, and **Z**. Is there any aspect of the structure of **X** that is still unknown?
- 8-61** One of the constituents of turpentine is  $\alpha$ -pinene, formula  $C_{10}H_{16}$ . The following scheme (called a “road map”) gives some reactions of  $\alpha$ -pinene. Determine the structure of  $\alpha$ -pinene and of the reaction products **A** through **E**.

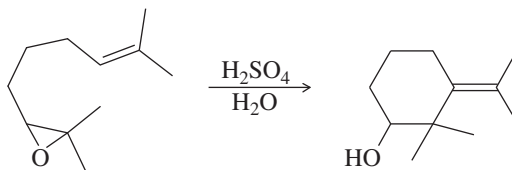


- 8-62** The sex attractant of the housefly has the formula  $C_{23}H_{46}$ . When treated with warm potassium permanganate, this pheromone gives two products:  $CH_3(CH_2)_{12}COOH$  and  $CH_3(CH_2)_7COOH$ . Suggest a structure for this sex attractant. Explain which part of the structure is uncertain.
- 8-63** In contact with a platinum catalyst, an unknown alkene reacts with three equivalents of hydrogen gas to give 1-isopropyl-4-methylcyclohexane. When the unknown alkene is ozonized and reduced, the products are the following:

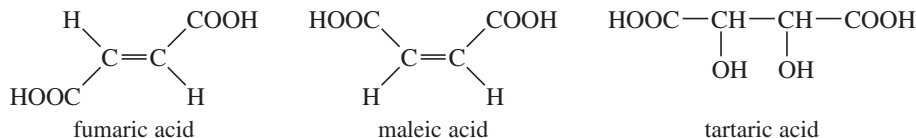


Deduce the structure of the unknown alkene.

\*8-64 Propose a mechanism for the following reaction.



8-65 The two butenedioic acids are called *fumaric acid* (trans) and *maleic acid* (cis). 2,3-Dihydroxybutanedioic acid is called *tartaric acid*.

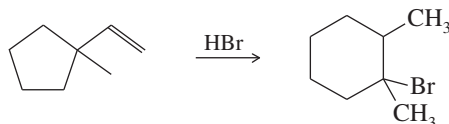


Show how you would convert

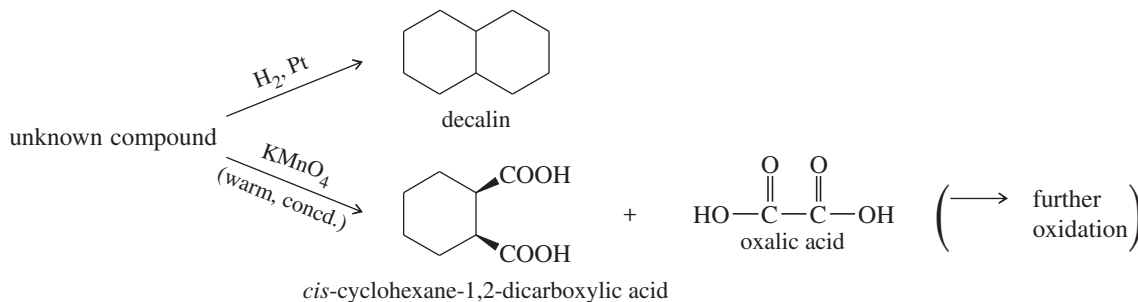
- (a) fumaric acid to ( $\pm$ )-tartaric acid.      (b) fumaric acid to *meso*-tartaric acid.  
 (c) maleic acid to ( $\pm$ )-tartaric acid.      (d) maleic acid to *meso*-tartaric acid.

8-66 The compound  $\text{BD}_3$  is a deuterated form of borane. Predict the product formed when 1-methylcyclohexene reacts with  $\text{BD}_3 \cdot \text{THF}$ , followed by basic hydrogen peroxide.

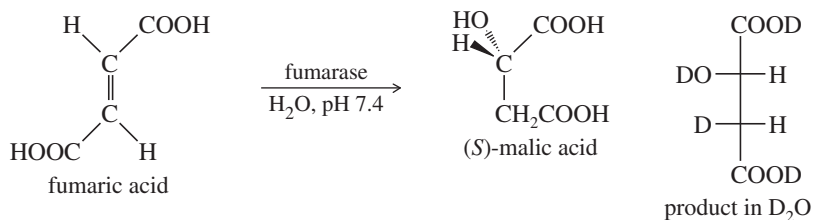
8-67 A routine addition of  $\text{HBr}$  across the double bond of a vinylcyclopentane gave a small amount of an unexpected rearranged product. Propose a mechanism for the formation of this product, and explain why the rearrangement occurs.



8-68 An unknown compound decolorizes bromine in carbon tetrachloride, and it undergoes catalytic reduction to give decalin. When treated with warm, concentrated potassium permanganate, this compound gives *cis*-cyclohexane-1,2-dicarboxylic acid and oxalic acid. Propose a structure for the unknown compound.

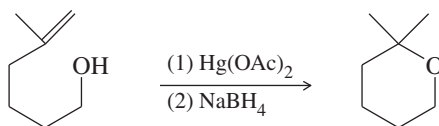


\*8-69 Many enzymes catalyze reactions that are similar to reactions we might use for organic synthesis. Enzymes tend to be stereospecific in their reactions, and asymmetric induction is common. The following reaction, part of the tricarboxylic acid cycle of cell respiration, resembles a reaction we might use in the laboratory; however, the enzyme-catalyzed reaction gives only the (*S*) enantiomer of the product, malic acid.



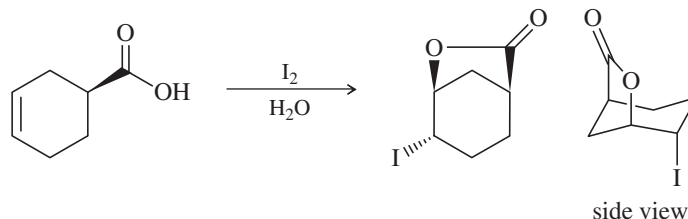
- (a) What type of reaction does fumarase catalyze?  
 (b) Is fumaric acid chiral? Is malic acid chiral? In the enzyme-catalyzed reaction, is the product (malic acid) optically active?  
 (c) If we could run the preceding reaction in the laboratory using sulfuric acid as the catalyst, would the product (malic acid) be optically active?  
 (d) Do you expect the fumarase enzyme to be a chiral molecule?  
 (e) When the enzyme-catalyzed reaction takes place in  $D_2O$ , the *only* product is the stereoisomer just pictured. No enantiomer or diastereomer of this compound is formed. Is the enzyme-catalyzed reaction a syn or anti addition?  
 (f) Assume that we found conditions to convert fumaric acid to deuterated malic acid using hydroboration with  $BD_3 \cdot THF$ , followed by oxidation with  $D_2O_2$  and  $NaOD$ . Use Fischer projections to show the stereoisomer(s) of deuterated malic acid you would expect to be formed.

- \*8-70 (a) The following cyclization has been observed in the oxymercuration–demercuration of this unsaturated alcohol. Propose a mechanism for this reaction.

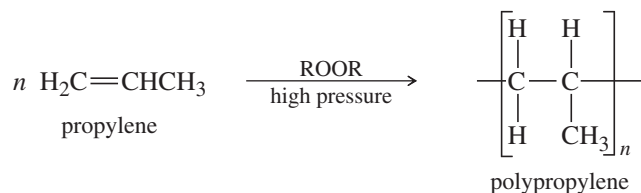


- (b) Predict the product of formula  $C_7H_{13}BrO$  from the reaction of this same unsaturated alcohol with bromine. Propose a mechanism to support your prediction.

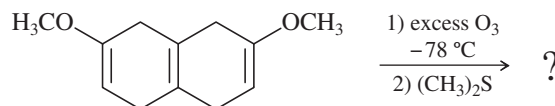
- 8-71 A graduate student attempted to form the iodohydrin of the alkene shown below. Her analysis of the products showed a good yield of an unexpected product. Propose a mechanism to explain the formation of this product.



- 8-72 Propose a mechanism for reaction of the first three propylene units in the polymerization of propylene in the presence of a peroxide.

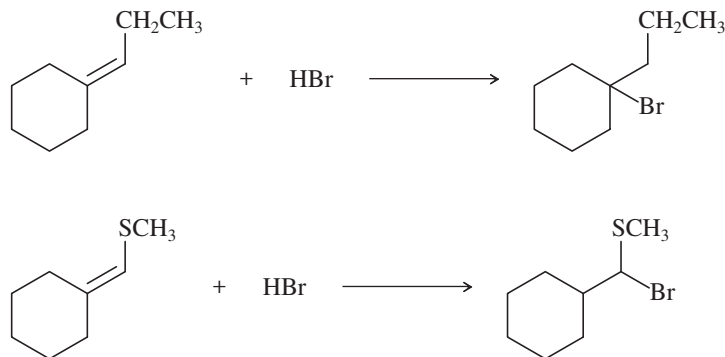


- \*8-73 When styrene (vinylbenzene) is commercially polymerized, about 1–3% of 1,4-divinylbenzene is often added to the styrene. The incorporation of some divinylbenzene gives a polymer with more strength and better resistance to organic solvents. Explain how a very small amount of divinylbenzene has a marked effect on the properties of the polymer.
- 8-74 The cationic polymerization of isobutylene (2-methylpropene) is shown in Section 8-16A. Isobutylene is often polymerized under free-radical conditions. Propose a mechanism for the free-radical polymerization of isobutylene.
- 8-75 Ozonolysis can be applied selectively to different types of carbon–carbon double bonds. The compound shown below contains two vinyl ether double bonds, which are electron-rich because of the electron-donating alkoxy groups. Ozone reacts more quickly with electron-rich double bonds and more slowly with hindered double bonds. At  $-78^\circ C$ , this compound quickly adds two equivalents of ozone. Immediate reduction of the ozonide gives a good yield of a single product. Show the expected ozonolysis product, and label the functional groups produced, some of which are not typical from ozonolysis of simple alkenes.



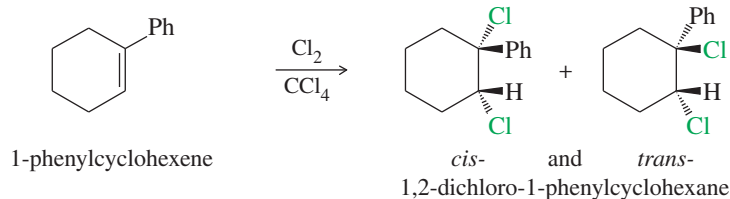
(continued)

8-76 Propose mechanisms to explain the opposite regiochemistry observed in the following two reactions.

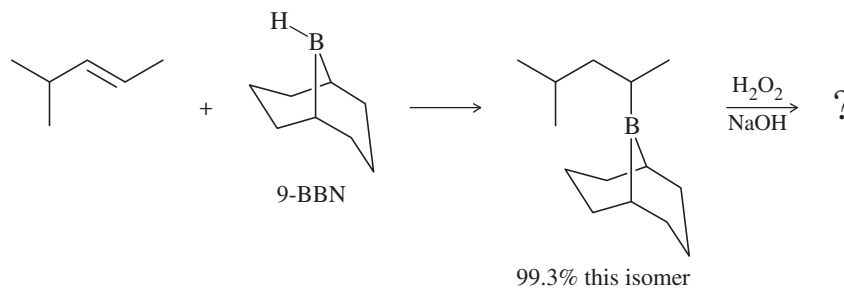


\*8-77 An inexperienced graduate student treated dec-5-ene with borane in THF, placed the flask in a refrigerator, and left for a party. When he returned from the party, he discovered that the refrigerator was broken and that it had gotten quite warm inside. Although all the THF had evaporated from the flask, he treated the residue with basic hydrogen peroxide. To his surprise, he recovered a fair yield of decan-1-ol. Use a mechanism to show how this reaction might have occurred. (*Hint*: The addition of  $\text{BH}_3$  is reversible.)

\*8-78 We have seen many examples where halogens add to alkenes with anti stereochemistry via the halonium ion mechanism. However, when 1-phenylcyclohexene reacts with chlorine in carbon tetrachloride, a mixture of the *cis* and *trans* isomers of the product is recovered. Propose a mechanism, and explain this lack of stereospecificity.



8-79 The bulky borane 9-BBN was developed to enhance the selectivity of hydroboration. In this example, 9-BBN adds to the less hindered carbon with 99.3% regioselectivity, compared with only 57% for diborane.



- (a) Show the two organic products generated when the trialkylborane is oxidized with  $\text{H}_2\text{O}_2/\text{NaOH}$ .  
 (b) 9-BBN is synthesized by adding  $\text{BH}_3$  across a symmetric, cyclic diene. What is the structure of the diene?