13

Radicals • Reactions of Alkanes

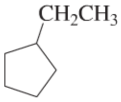
The world needs a renewable, nonpolluting, and economically affordable source of energy (see page 557).

Alkanes are widespread both on Earth and on other planets. The atmospheres of Jupiter, Saturn, Uranus, and Neptune contain large quantities of methane (CH_4), the smallest alkane, which is an odorless and flammable gas. The blue colors of Uranus and Neptune are the result of methane in their atmospheres (see page 28). Alkanes on Earth are found in natural gas and petroleum, which are formed by the decomposition of plant and animal material that have been buried for long periods of time in the Earth's crust, where oxygen is scarce. As a result, natural gas and petroleum are known as fossil fuels.

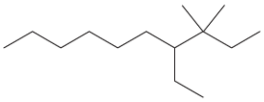
We have seen that there are three classes of hydrocarbons: *alkanes,* which contain only carbon–carbon single bonds; *alkenes,* which contain carbon–carbon double bonds; and *alkynes,* which contain carbon–carbon triple bonds. Because **alkanes** do not contain any double or triple bonds, they are called **saturated hydrocarbons,** meaning they are saturated with hydrogen. A few examples of alkanes are

$CH_3CH_2CH_2CH_3$

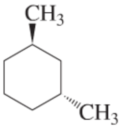
butane



ethylcyclopentane



4-ethyl-3,3-dimethyldecane



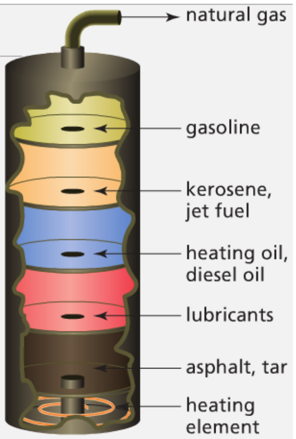
(*R*,*R*)-1,3-dimethyl-cyclohexane

13.1 ALKANES ARE UNREACTIVE COMPOUNDS

We have seen that the carbon–carbon double and triple bonds of *alkenes* and *alkynes* are composed of strong σ bonds and weaker π bonds and that, because of their relatively weak π bonds, alkenes and alkynes undergo electrophilic addition reactions (Sections 6.0 and 7.5).

Alkanes have only strong σ bonds. In addition, the electrons in the C—C and C—H σ bonds are shared equally by the bonding atoms, so none of the atoms in an alkane has any significant charge. This means that alkanes are neither nucleophiles nor electrophiles, so neither electrophiles nor nucleophiles are attracted to them. Alkanes, therefore, are relatively unreactive compounds. The failure of alkanes to undergo reactions prompted early organic chemists to call them *paraffins,* from the Latin *parum affinis,* which means "little affinity" (for other compounds).

Natural Gas and Petroleum



Natural gas is approximately 75% methane. The remaining 25% is composed of other small alkanes such as ethane, propane, and butane. In the 1950s, natural gas replaced coal as the main energy source for domestic and industrial heating in many parts of the United States.

Petroleum is a complex mixture of alkanes and cycloalkanes that can be separated into fractions by distillation. Natural gas is the fraction that boils off at the lowest temperature (hydrocarbons containing fewer than 5 carbons). The fraction that boils at somewhat higher temperatures (hydrocarbons containing 5 to 11 carbons) is gasoline; the next fraction (9 to 16 carbons) includes kerosene and jet fuel. The fraction with 15 to 25 carbons is used for heating oil and diesel oil, and the highest-boiling fraction is used for lubricants and greases. After distillation, a nonvolatile residue called asphalt or tar is left behind.

The 5- to 11-carbon fraction that is used for gasoline is actually a poor fuel for internal combustion engines. To become a high-performance gasoline, it requires a process known as catalytic cracking. Catalytic cracking converts straight-chain hydrocarbons that are poor fuels into branched-chain compounds that are high-performance fuels (Section 3.2). Originally, cracking (also called pyrolysis) required heating the gasoline to very high temperatures in order to obtain hydrocarbons with three to five carbons. Modern cracking methods use catalysts to accomplish the same thing at much lower temperatures.

Fossil Fuels: A Problematic Energy Source

Modern society faces three major problems as a consequence of our dependence on fossil fuels for energy. First, these fuels are a nonrenewable resource and the world's supply is continually decreasing. Second, a group of Middle Eastern and South American countries controls a large portion of the world's supply of petroleum. These countries have formed a cartel called the *Organization of Petroleum Exporting Countries* (*OPEC*) that controls both the supply and the price of crude oil. Political instability in any OPEC country can seriously affect the world's oil supply.

Third, burning fossil fuels—particularly coal—increases the concentration of CO_2 in the atmosphere; burning coal also increases the concentration of atmospheric SO_2. Scientists have established experimentally that SO_2 causes "acid rain," a threat to plants and, therefore, to our food and oxygen supplies (see page 53 and Section 2.2).

The concentration of atmospheric CO_2 at Mauna Loa, Hawaii, has been periodically measured since 1968. The concentration has increased 25% since the first measurements were taken, causing scientists to predict an increase in the Earth's temperature as a result of the absorption of infrared radiation by CO_2 (the *greenhouse effect*). A steady increase in the temperature of the Earth would have devastating consequences, including the formation of new deserts, massive crop failure, and the melting of glaciers with a concomitant rise in sea level. Clearly, what we need is a renewable, nonpolitical, nonpolluting, and economically affordable source of energy.

13.2 THE CHLORINATION AND BROMINATION OF ALKANES

Alkanes react with chlorine (Cl_2) or bromine (Br_2) to form alkyl chlorides or alkyl bromides. These **halogenation reactions** take place only at high temperatures or in the presence of light. (Irradiation with light is symbolized by *hν*.)

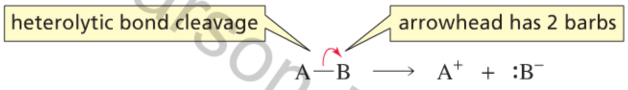
$$CH_4 + Cl_2 \xrightarrow[h\nu]{\Delta \text{ or}} \underset{\text{chloromethane}}{CH_3Cl} + HCl$$

$$CH_3CH_3 + Br_2 \xrightarrow[h\nu]{\Delta \text{ or}} \underset{\text{bromoethane}}{CH_3CH_2Br} + HBr$$

Halogenation and combustion (burning) are the only reactions that alkanes undergo (without the assistance of a metal catalyst). In a **combustion** reaction, alkanes react with oxygen at high temperatures to form carbon dioxide and water.

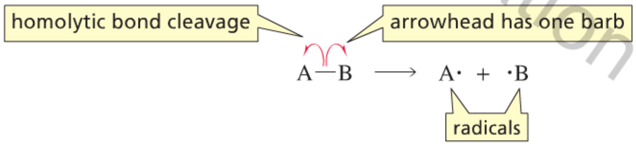
When a bond breaks so that both of its electrons stay with one of the atoms, the process is called **heterolytic bond cleavage** or **heterolysis.**

An arrowhead with two barbs signifies the movement of two electrons.



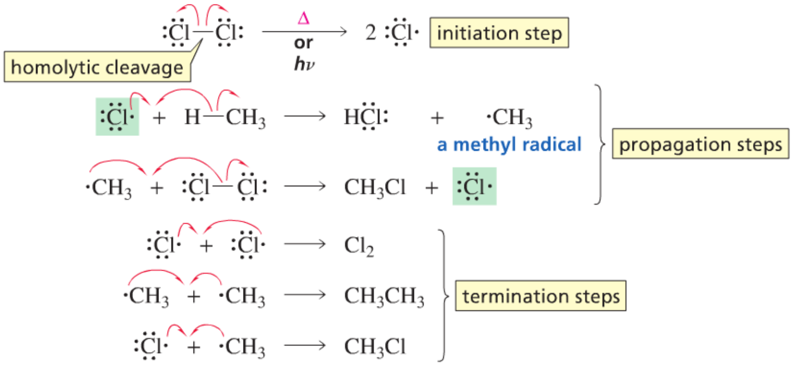
When a bond breaks so that each of the atoms retains one of the bonding electrons, the process is called **homolytic bond cleavage** or **homolysis.** Homolysis results in the formation of radicals. A **radical** (often called a **free radical**) is a species containing an atom with an unpaired electron. A radical is highly reactive because acquiring an electron will complete its octet.

An arrowhead with one barb—sometimes called a fishhook—signifies the movement of one electron.



The mechanism for the halogenation of an alkane is well understood. As an example, let's look at the mechanism for the monochlorination of methane. The monochlorination of alkanes other than methane has the same mechanism.

MECHANISM FOR THE MONOCHLORINATION OF METHANE



See the tutorial on page 590 for additional information on drawing curved arrows in radical systems.

- Heat or light supplies the energy required to break the Cl—Cl bond homolytically. This is the **initiation step** of the reaction because it creates radicals from a molecule in which all the electrons are paired.
- The chlorine radical formed in the initiation step removes a hydrogen atom from the alkane (in this case methane), forming HCl and a methyl radical.
- The methyl radical removes a chlorine atom from Cl_2, forming chloromethane and another chlorine radical, which can then remove a hydrogen atom from another molecule of methane.

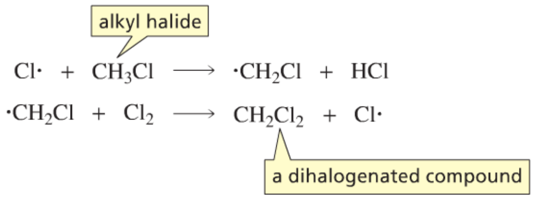
  Steps 2 and 3 are **propagation steps** because the radical created in the first propagation step reacts in the second propagation step to produce the radical that participates in the first propagation step. A propagation step is one that propagates the chain. Thus, the two propagation steps are repeated over and over. The first propagation step is the rate-determining step of the overall reaction.
- Any two radicals in the reaction mixture can combine to form a molecule in which all the electrons are paired. The combination of two radicals is called a **termination step** because it helps bring the reaction to an end by decreasing the number of radicals available to propagate the reaction. Any two radicals can combine, so a radical reaction produces a mixture of products.

Radical chain reactions have initiation, propagation, and termination steps.

Because the reaction has radical intermediates and repeating propagation steps, it is called a **radical chain reaction.** This particular radical chain reaction is called a **radical substitution reaction** because it substitutes a chlorine for one of the hydrogens of the alkane.

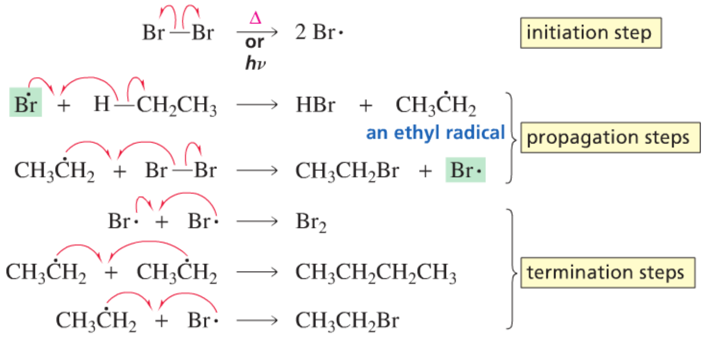
In order to maximize the amount of monohalogenated product formed, a radical substitution reaction should be carried out in the presence of excess alkane. Excess alkane in the reaction mixture increases the probability that the halogen radical will collide with a molecule of alkane rather than with a molecule of alkyl halide—even toward the end of the reaction, by which time a considerable amount of alkyl halide will have been formed.

If the halogen radical removes a hydrogen from a molecule of alkyl halide rather than from a molecule of alkane, a dihalogenated product will be obtained.



The bromination of alkanes has the same mechanism as the chlorination of alkanes.

MECHANISM FOR THE MONOBROMINATION OF ETHANE



Why Radicals No Longer Have to Be Called Free Radicals

At one time an "R" group was called a radical. For example, the OH substituent in CH_3CH_2OH was said to be attached to an ethyl radical. To distinguish this kind of ethyl radical from $CH_3\dot{C}H_2$, which has an unpaired electron and is not attached to a substituent, $CH_3\dot{C}H_2$ was called a "free radical"—it was free from attachment to a substituent. Now that we call "R" a *substituent* or a *group,* instead of a *radical,* we no longer need to call a compound with an unpaired electron a "free radical"; the word *radical* is now unambiguous.

PROBLEM 1

Show the initiation, propagation, and termination steps for the monochlorination of cyclohexane.

PROBLEM 2

Write the mechanism for the formation of tetrachloromethane (CCl_4) from the reaction of methane with $Cl_2 + h\nu$.

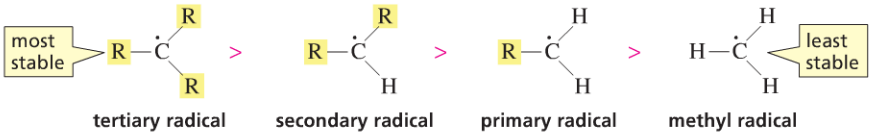
13.3 RADICAL STABILITY DEPENDS ON THE NUMBER OF ALKYL GROUPS ATTACHED TO THE CARBON WITH THE UNPAIRED ELECTRON

Radicals are classified according to the carbon that bears the unpaired electron. **Primary radicals** have the unshared electron on a primary carbon, **secondary radicals** have the unshared electron on a secondary carbon, and **tertiary radicals** have the unshared electron on a tertiary carbon.

Alkyl groups stabilize radicals the same way they stabilize carbocations—that is, by hyperconjugation (Section 6.2). Therefore, the relative stabilities of **primary, secondary,** and **tertiary alkyl radicals** follow the same order as the relative stabilities of primary, secondary, and tertiary carbocations.

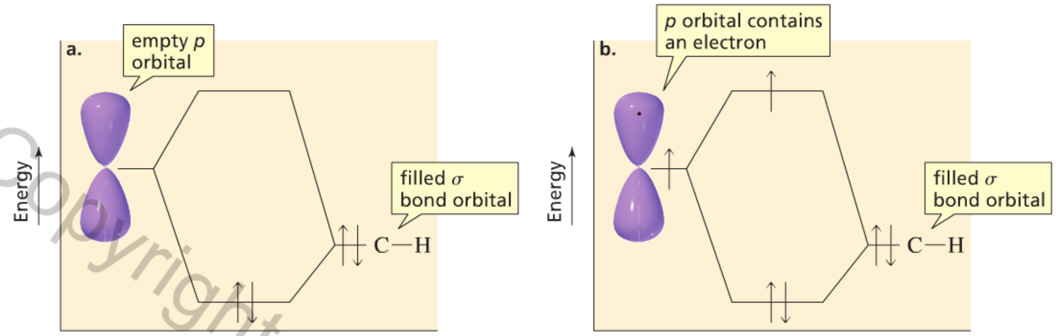
relative stabilities of alkyl radicals

Stability of alkyl radicals: 3° > 2° > 1°



The differences in the relative stabilities of the radicals are much smaller than the differences in the relative stabilities of the carbocations because alkyl groups do not stabilize radicals as well as they stabilize carbocations.

The MO diagrams in Figure 13.1 explain why alkyl groups stabilize carbocations better than they stabilize radicals. Stabilization of a carbocation results from overlap between a filled orbital of a C—H or C—C σ bond and an empty p orbital—a two-electron system (Figure 13.1a). In contrast, stabilization of a radical results from overlap between a filled orbital of a C—H or C—C σ bond and a p orbital that contains one electron—a three-electron system (Figure 13.1b).



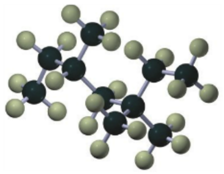
▲ **Figure 13.1**
MO diagrams showing the stabilization achieved when the electrons of an orbital of a C—H or C—C σ bond overlap with
(a) an empty *p* orbital
(b) a *p* orbital that contains one electron

Both electrons are in a bonding MO in the two-electron system, whereas one of the electrons has to go into an antibonding MO in the three-electron system. Overall, the three-electron system is stabilizing because there are more electrons in the bonding MO than in the antibonding MO, but it is not as stabilizing as the two-electron system, which does not have an electron in the antibonding MO. Consequently, an alkyl group stabilizes a carbocation about 5–10 times better than it stabilizes a radical.

PROBLEM 3♦

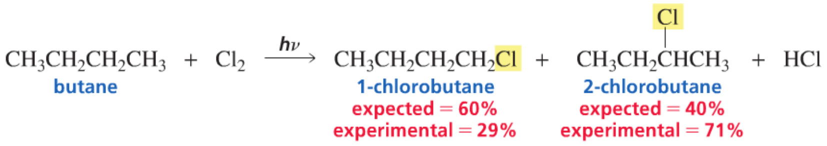
a. Which of the hydrogens in the following structure is the easiest for a chlorine radical to remove?

b. How many secondary hydrogens does the structure have?



13.4 THE DISTRIBUTION OF PRODUCTS DEPENDS ON PROBABILITY AND REACTIVITY

Two different alkyl halides are obtained from the monochlorination of butane. Substitution of a hydrogen bonded to one of the primary carbons produces 1-chlorobutane, whereas substitution of a hydrogen bonded to one of the secondary carbons forms 2-chlorobutane.



$$CH_3CH_2CH_2CH_3 + Cl_2 \xrightarrow{h\nu} CH_3CH_2CH_2CH_2Cl + CH_3CH_2\overset{Cl}{\overset{|}{C}}HCH_3 + HCl$$

butane

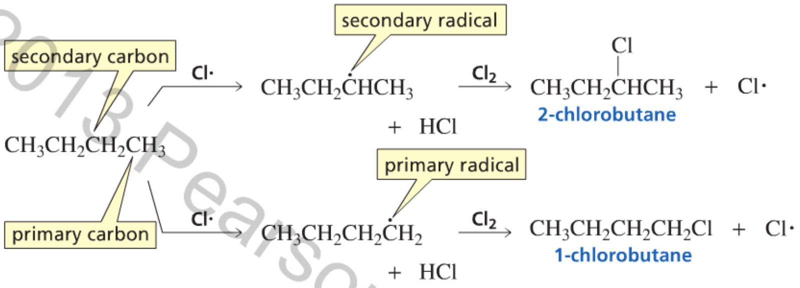
1-chlorobutane
expected = 60%
experimental = 29%

2-chlorobutane
expected = 40%
experimental = 71%

The expected (statistical) distribution of products is 60% 1-chlorobutane and 40% 2-chlorobutane because six of butane's 10 hydrogens can be substituted to form 1-chlorobutane, whereas only four can be substituted to form 2-chlorobutane.

When the reaction is carried out in the laboratory, however, the products are found to be 29% 1-chlorobutane and 71% 2-chlorobutane. In other words, the product distribution does not depend solely on the *probability* of a chlorine radical colliding with a primary or a secondary hydrogen.

Because more 2-chlorobutane is obtained than expected and *the rate-determining step of the overall reaction is removal of the hydrogen atom,* we can conclude that it is easier to remove a hydrogen atom from a secondary carbon to form a secondary radical than it is to remove a hydrogen atom from a primary carbon to form a primary radical.

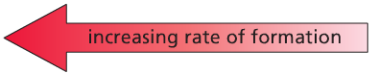


We should not be surprised that it is easier to form a secondary radical, because a secondary radical is more stable than a primary radical. The more stable the radical, the more easily it is formed, because the stability of the radical is reflected in the stability of the transition state leading to its formation (Section 6.3).

After experimentally determining the amount of each chlorination product obtained from various hydrocarbons, chemists were able to conclude that *at room temperature* it is 5.0 times easier for a chlorine radical to form a tertiary radical than a primary radical, and it is 3.8 times easier to form a secondary radical than a primary radical. The precise ratios differ at different temperatures. (How relative rates are determined experimentally is described in Problem 40.)

relative rates of alkyl radical formation by a chlorine radical at room temperature

tertiary	>	secondary	>	primary
5.0		3.8		1.0



Now we see that both *probability* (the number of hydrogens that can be removed that lead to the formation of a particular product) and *reactivity* (the relative rate at which a particular radical is formed) must be taken into account when determining the relative amounts of the products obtained from the radical chlorination of an alkane.

Both probability and reactivity must be taken into account when calculating the relative amounts of products.

relative amount of 1-chlorobutane	relative amount of 2-chlorobutane
number of hydrogens × relative reactivity	number of hydrogens × relative reactivity
$6 \times 1.0 = 6.0$	$4 \times 3.8 = 15$

The anticipated percent yield of each alkyl chloride (as a percentage of all the monochlorinated products) is calculated by dividing the relative amount of the particular product by the sum of the relative amounts of all the alkyl chloride products ($6 + 15 = 21$).

percent yield of 1-chlorobutane

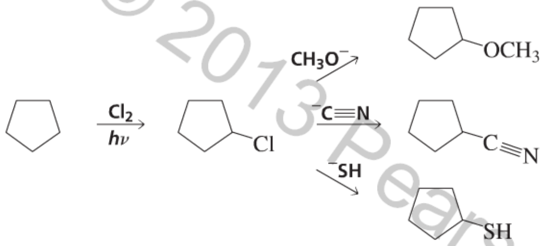
$$\frac{6.0}{21} = 29\%$$

percent yield of 2-chlorobutane

$$\frac{15}{21} = 71\%$$

Because the radical chlorination of an alkane can yield several different monosubstitution products as well as products that contain more than one chlorine atom, it is not the best method to use to synthesize an alkyl halide. The addition of a hydrogen halide to an alkene or the conversion of an alcohol to an alkyl halide are both much better ways to make an alkyl halide (Sections 6.1, 11.1, and 11.2).

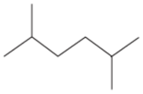
Radical halogenation of an alkane is still a useful reaction because it is the only way to convert an inert alkane into a reactive compound. And once the halogen is introduced into the alkane, it can be replaced by a variety of other substituents (Section 11.2).

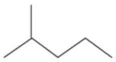


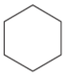
PROBLEM 4♦

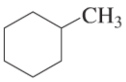
How many alkyl chlorides can be obtained from monochlorination of the following alkanes? Disregard stereoisomers.

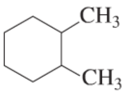
a. 

b. 

c. 

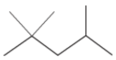
d. 

e. 

f. 

g. 

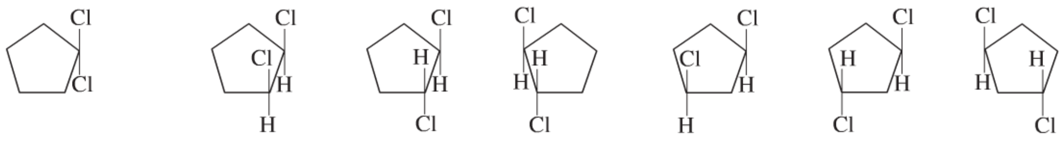
h. 

i. 

PROBLEM 5 Solved

If cyclopentane reacts with more than one equivalent of Cl_2 at a high temperature, how many dichlorocyclopentanes would you expect to obtain as products?

Solution Seven dichlorocyclopentanes could be obtained as products. Only one isomer is possible for the 1,1-dichloro compound. The 1,2- and 1,3-dichloro compounds have two asymmetric centers. Each has three stereoisomers because the cis isomer is a meso compound and the trans isomer is a pair of enantiomers.



1,1-dichloro compound

meso compound enantiomers

1,2-dichloro compounds

meso compound enantiomers

1,3-dichloro compounds

13.5 THE REACTIVITY–SELECTIVITY PRINCIPLE

The relative rates of radical formation by a bromine radical are different from the relative rates of radical formation by a chlorine radical. For example, at 125 °C, a bromine radical forms a tertiary radical 1600 times faster than a primary radical and it forms a secondary radical 82 times faster than a primary radical.

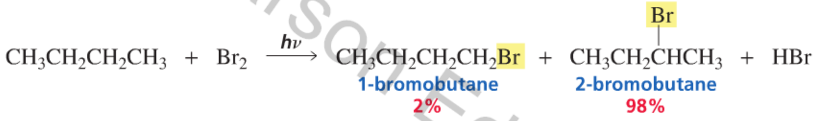
relative rates of alkyl radical formation by a bromine radical at 125 °C

tertiary	>	secondary	>	primary
1600		82		1

← increasing rate of formation

The differences in the relative rates of radical formation by a bromine radical are so great that the *reactivity factor* is vastly more important than the *probability factor* in determining the relative amounts of products obtained in a radical substitution reaction.

For example, the radical bromination of butane gives a 98% yield of 2-bromobutane, compared with a 71% yield of 2-chlorobutane obtained when butane is chlorinated (Section 13.4).


$$CH_3CH_2CH_2CH_3 + Br_2 \xrightarrow{h\nu} CH_3CH_2CH_2CH_2Br + CH_3CH_2\overset{\overset{\large Br}{|}}{C}HCH_3 + HBr$$

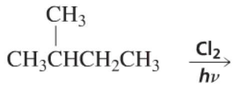
1-bromobutane 2%

2-bromobutane 98%

PROBLEM 6 Solved

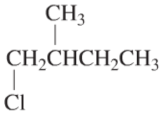
a. What is the major monochlorination product of the following reaction? Disregard stereoisomers.

b. What would be the anticipated percent yield of the major product (as a percentage of all the monochlorinated products)?


$$CH_3\overset{\overset{\large CH_3}{|}}{C}HCH_2CH_3 \xrightarrow[h\nu]{Cl_2}$$

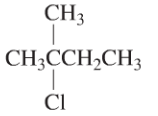
Solution

a. The relative amount of each product is determined by multiplying the number of hydrogens that can be removed that will lead to the formation of that product by the relative rate for formation of the radical. Thus, the major product is 2-chloro-3-methylbutane.


$$\underset{\underset{\large Cl}{|}}{CH_2}\overset{\overset{\large CH_3}{|}}{C}HCH_2CH_3$$

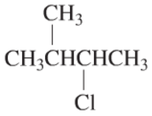
1-chloro-2-methylbutane

$6 \times 1.0 = 6$


$$CH_3\underset{\underset{\large Cl}{|}}{\overset{\overset{\large CH_3}{|}}{C}}CH_2CH_3$$

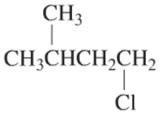
2-chloro-2-methylbutane

$1 \times 5.0 = 5$


$$CH_3\overset{\overset{\large CH_3}{|}}{C}H\underset{\underset{\large Cl}{|}}{C}HCH_3$$

2-chloro-3-methylbutane

$2 \times 3.8 = 7.6$


$$CH_3\overset{\overset{\large CH_3}{|}}{C}HCH_2\underset{\underset{\large Cl}{|}}{CH_2}$$

1-chloro-3-methylbutane

$3 \times 1.0 = 3$

b. The anticipated percent yield of the major product is obtained by dividing its relative amount by the relative amounts of all the alkyl halides produced in the reaction. The major product would be obtained in 35% yield.

$$6.0 + 5.0 + 7.6 + 3.0 = 21.6 \qquad \frac{7.6}{21.6} = 35\%$$

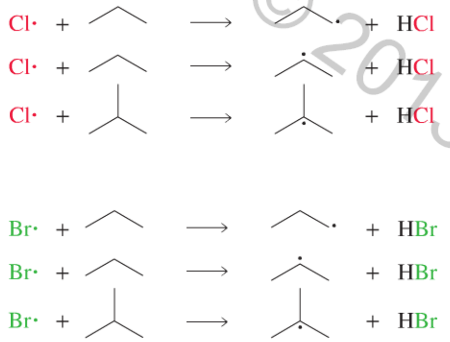
PROBLEM 7♦

a. What would be the major product of the reaction in Problem 6 if the alkane had reacted with Br_2 instead of with Cl_2? Disregard stereoisomers.

b. What would be the anticipated percent yield of the major product?

Why are the relative rates of radical formation so different when a bromine radical rather than a chlorine radical is used as the hydrogen-removing reagent?

To answer this question, we must compare the $\Delta H°$ values for forming primary, secondary, and tertiary radicals by a chlorine radical and by a bromine radical. These $\Delta H°$ values can be calculated using the bond dissociation energies in Table 5.1 on page 210.



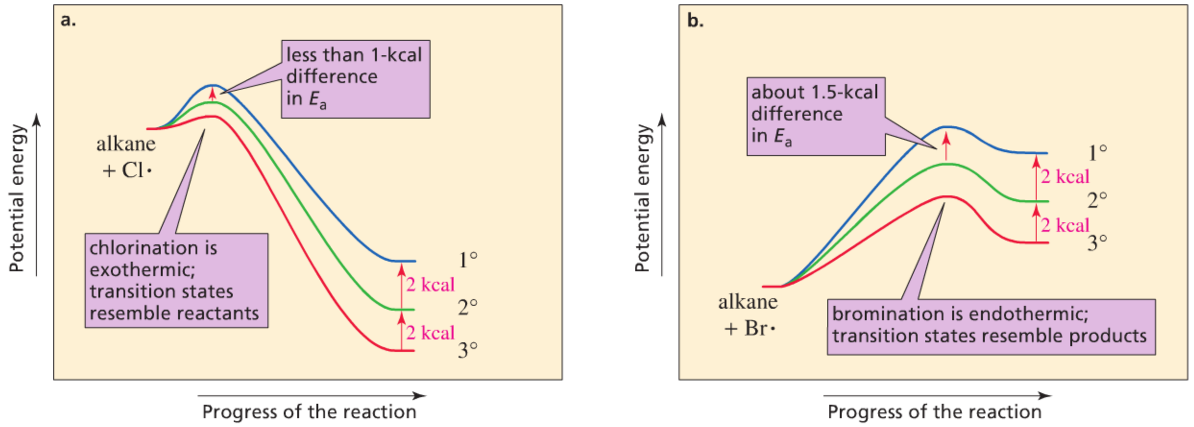
ΔH° (kcal/mol)	ΔH° (kJ/mol)
101 − 103 = −2	−8
99 − 103 = −4	−17
97 − 103 = −6	−25

ΔH° (kcal/mol)	ΔH° (kJ/mol)
101 − 87 = 14	59
99 − 87 = 12	50
97 − 87 = 10	42

ΔH° is equal to the energy of the bond being broken minus the energy of the bond being formed; Section 5.7.

We must also be aware that bromination is a much slower reaction than chlorination. The activation energy for removing a hydrogen atom by a bromine radical is about 4.5 times greater than that for removing a hydrogen atom by a chlorine radical.

Using the calculated $\Delta H°$ values and the experimental activation energies, we can draw reaction coordinate diagrams for formation of primary, secondary, and tertiary radicals by a chlorine radical (Figure 13.2a) and by a bromine radical (Figure 13.2b).



▲ **Figure 13.2**

(a) Reaction coordinate diagrams for formation of primary, secondary, and tertiary alkyl radicals by a chlorine radical. The transition states have relatively little radical character because they resemble the reactants.

(b) Reaction coordinate diagrams for formation of primary, secondary, and tertiary alkyl radicals by a bromine radical. The transition states have a relatively high degree of radical character because they resemble the products.

Because the reaction of a chlorine radical with an alkane to form a primary, secondary, or tertiary radical is exothermic, the transition states resemble the reactants (see the Hammond postulate, Section 6.3). The reactants all have approximately the same energy, so there is only a small difference in the activation energies for the formation of a primary, secondary, or tertiary radical.

In contrast, the reaction of a bromine radical with an alkane is endothermic, so the transition states resemble the products. Because there are significant differences between the energies of the product radicals—depending on whether they are primary, secondary, or tertiary—there are significant differences between the activation energies.

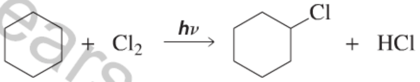
Therefore, a chlorine radical makes primary, secondary, and tertiary radicals with almost equal ease (Figure 13.2a), whereas a bromine radical has a clear preference for forming the easiest-to-form tertiary radical (Figure 13.2b). In other words, because a bromine radical is relatively unreactive, it is highly selective about which radical it forms. In contrast, the much more reactive chlorine radical is considerably less selective.

These observations illustrate the **reactivity–selectivity principle,** which states that *the greater the reactivity of a species, the less selective it will be.*

A bromine radical is less reactive and more selective than a chlorine radical.

The more reactive a species is, the less selective it will be.

Because chlorination is relatively nonselective, it is a useful reaction only when there is only one kind of hydrogen in the alkane.

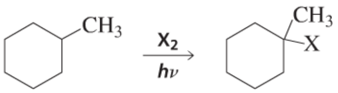


PROBLEM-SOLVING STRATEGY

Planning the Synthesis of an Alkyl Halide

Would chlorination or bromination of methylcyclohexane produce a greater yield of 1-halo-1-methylcyclohexane?

To solve this kind of problem, first draw the structures of the compounds being discussed.



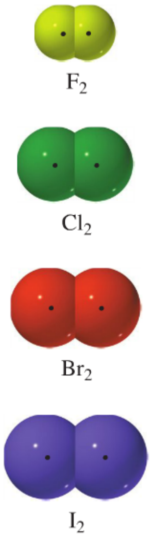
1-Halo-1-methylcyclohexane is a tertiary alkyl halide, so the question becomes, "Will bromination or chlorination produce a greater yield of a tertiary alkyl halide?" Because bromination is more selective, it will produce a greater yield of the desired compound. Chlorination will form some of the tertiary alkyl halide, but it will also form significant amounts of primary and secondary alkyl halides.

Now use the strategy you have just learned to solve Problem 8.

PROBLEM 8♦

a. Would chlorination or bromination produce a greater yield of 1-halo-2,3-dimethylbutane?
b. Would chlorination or bromination produce a greater yield of 2-halo-2,3-dimethylbutane?
c. Would chlorination or bromination be a better way to make 1-halo-2,2-dimethylpropane?

By comparing the ΔH° values for the sum of the two propagating steps in the monohalogenation of methane, we can understand why alkanes undergo chlorination and bromination but not iodination, and why fluorination is too violent a reaction to be useful.



Halogens

$$\mathrm{F}\cdot + \mathrm{CH_4} \longrightarrow \cdot\mathrm{CH_3} + \mathrm{HF} \qquad 105 - 136 = -31$$
$$\cdot\mathrm{CH_3} + \mathrm{F_2} \longrightarrow \mathrm{CH_3F} + \mathrm{F}\cdot \qquad 38 - 115 = -77$$
$$\Delta H^\circ = -108 \text{ kcal/mol} \quad (\text{or } -452 \text{ kJ/mol})$$

$$\mathrm{Cl}\cdot + \mathrm{CH_4} \longrightarrow \cdot\mathrm{CH_3} + \mathrm{HCl} \qquad 105 - 103 = 2$$
$$\cdot\mathrm{CH_3} + \mathrm{Cl_2} \longrightarrow \mathrm{CH_3Cl} + \mathrm{Cl}\cdot \qquad 58 - 84 = -26$$
$$\Delta H^\circ = -24 \text{ kcal/mol} \quad (\text{or } -100 \text{ kJ/mol})$$

$$\mathrm{Br}\cdot + \mathrm{CH_4} \longrightarrow \cdot\mathrm{CH_3} + \mathrm{HBr} \qquad 105 - 87 = 18$$
$$\cdot\mathrm{CH_3} + \mathrm{Br_2} \longrightarrow \mathrm{CH_3Br} + \mathrm{Br}\cdot \qquad 46 - 72 = -26$$
$$\Delta H^\circ = -8 \text{ kcal/mol} \quad (\text{or } -23 \text{ kJ/mol})$$

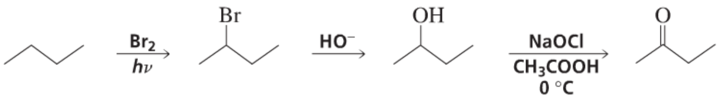
$$\mathrm{I}\cdot + \mathrm{CH_4} \longrightarrow \cdot\mathrm{CH_3} + \mathrm{HI} \qquad 105 - 71 = 34$$
$$\cdot\mathrm{CH_3} + \mathrm{I_2} \longrightarrow \mathrm{CH_3I} + \mathrm{I}\cdot \qquad 36 - 58 = -22$$
$$\Delta H^\circ = 12 \text{ kcal/mol} \quad (\text{or } 50 \text{ kJ/mol})$$

The fluorine radical is the most reactive of the halogen radicals—it reacts readily with alkanes ($\Delta H^\circ = -31$ kcal/mol), and the radical it produces reacts violently with F_2 ($\Delta H^\circ = -77$ kcal/mol). In contrast, the iodine radical is the least reactive of the halogen radicals. In fact, it is so unreactive ($\Delta H^\circ = 34$ kcal/mol) that it is unable to remove a hydrogen atom from an alkane. Consequently, it reacts with another iodine radical and reforms I_2.

PROBLEM 9 Solved

How could butanone be prepared from butane?

Solution We know that the first reaction has to be a radical halogenation because that is the only reaction that an alkane undergoes. Bromination will lead to a greater yield of the desired 2-halo-substituted compound than will chlorination because a bromine radical is more selective than a chlorine radical. A nucleophilic substitution reaction forms the alcohol, which forms the target molecule when it is oxidized.



PROBLEM 10

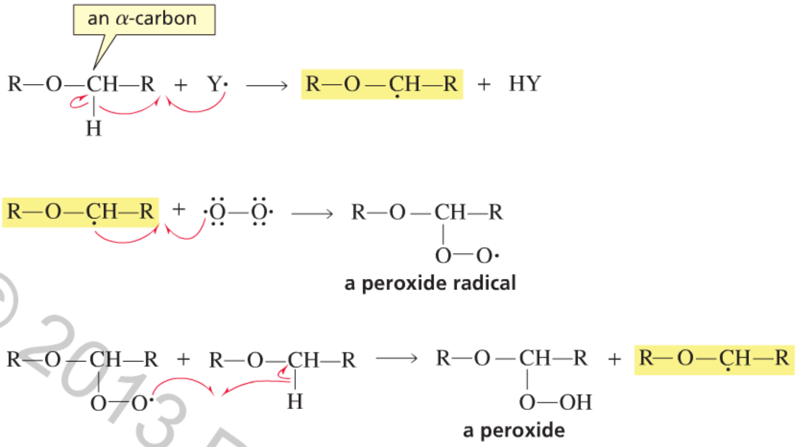
Show how the following compounds could be prepared from 2-methylpropane:

a. 2-bromo-2-methylpropane **b.** 2-methyl-2-propanol **c.** 2-methyl-1-propene

13.6 FORMATION OF EXPLOSIVE PEROXIDES

Ethers are a laboratory hazard because they form explosive peroxides by reacting with O_2 when they are exposed to air. We will see that this reaction is similar to the reaction that causes fats to become rancid (Section 13.11).

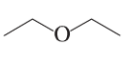
MECHANISM FOR PEROXIDE FORMATION



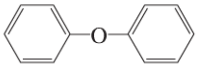
- A chain-initiating radical removes a hydrogen atom from an α-carbon of the ether. (The α-carbon is the carbon attached to the oxygen.) This is an initiation step because it creates the radical that is used in the first propagation step.
- The radical formed in the initiation step reacts with oxygen in a propagation step, forming a peroxide radical.
- In the second propagation step, the peroxide radical removes a hydrogen atom from an α-carbon of another molecule of ether to form a peroxide and regenerate the radical used in the first propagation step.

A **peroxide** is a compound with an O—O bond. Because an O—O bond is easily cleaved homolytically, a peroxide forms radicals that then can create new radicals—it is a **radical initiator.** Thus, the peroxide product of the preceding radical chain reaction can initiate another radical chain reaction—an explosive situation. To prevent the formation of explosive peroxides, ethers contain a stabilizer that traps the chain-initiating radical. Once an ether is purified (in which case it no longer contains the stabilizer), it has to be discarded within 24 hours.

PROBLEM 11♦

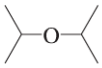


A



B

C

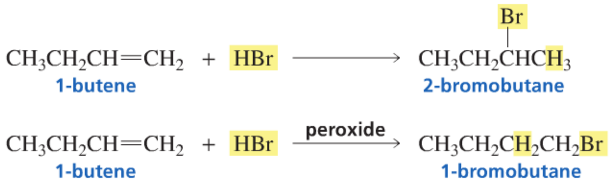


D

a. Which ether is most apt to form a peroxide? **b.** Which ether is least apt to form a peroxide?

13.7 THE ADDITION OF RADICALS TO AN ALKENE

The addition of HBr to 1-butene forms 2-bromobutane, because the electrophile (H^+) adds to the sp^2 carbon bonded to the most hydrogens (Section 6.4). If, however, you want to synthesize 1-bromobutane, then you need to find a way to make bromine an electrophile so it, instead of H^+, will add to the sp^2 carbon bonded to the most hydrogens.



$$CH_3CH_2CH{=}CH_2 + HBr \longrightarrow CH_3CH_2\underset{}{\overset{Br}{C}}HCH_3$$

1-butene 2-bromobutane

$$CH_3CH_2CH{=}CH_2 + HBr \xrightarrow{\text{peroxide}} CH_3CH_2CH_2CH_2Br$$

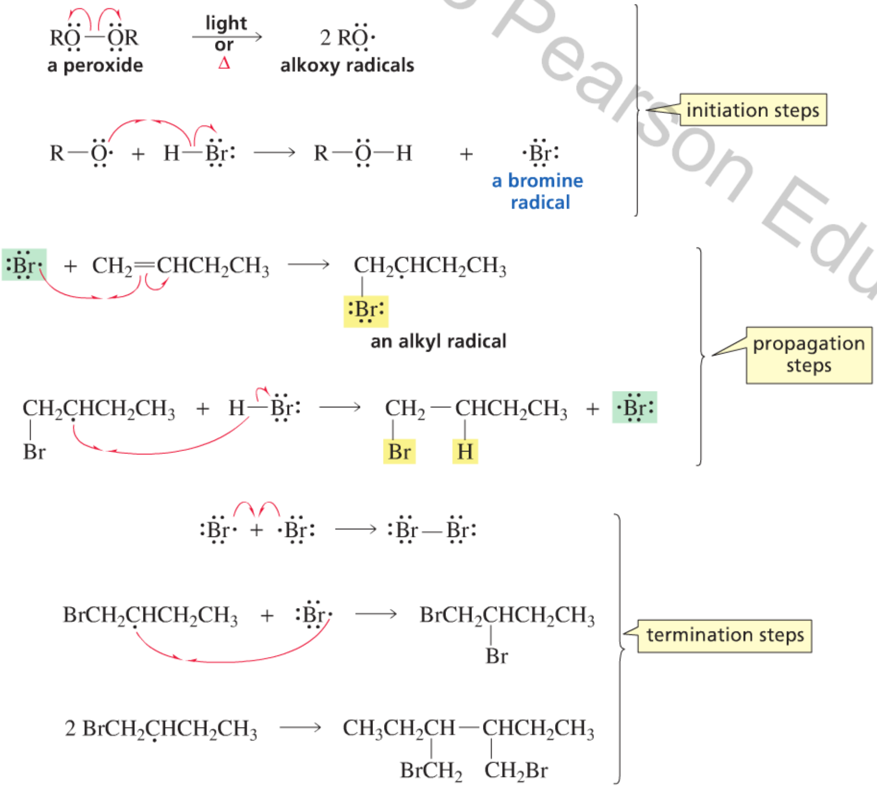
1-butene 1-bromobutane

The electrophile adds to the sp^2 carbon that is bonded to the most hydrogens.

If a peroxide (ROOR) is added to the reaction mixture, the product of the addition reaction will be the desired 1-bromobutane. Thus, the peroxide changes the mechanism of the reaction in a way that causes a bromine radical to be the electrophile.

The following mechanism for the addition of HBr to an alkene in the presence of a peroxide shows that it is a radical chain reaction with characteristic initiation, propagation, and termination steps:

MECHANISM FOR THE ADDITION OF HBr TO AN ALKENE IN THE PRESENCE OF A PEROXIDE



- The weak O—O bond of the peroxide readily breaks homolytically in the presence of light or heat to form alkoxy radicals. This is an initiation step because it creates radicals.
- The alkoxy radical completes its octet by removing a hydrogen atom from a molecule of HBr, thus forming a bromine radical. This too is an initiation step because it creates the radical that is used in the first propagation step.
- The bromine radical now seeks an electron to complete its octet. Because the π bond of an alkene is the weakest bond in the molecule, the bromine radical completes its octet by combining with one of the electrons of the π bond to form a C—Br bond. The second electron of the π bond is the unpaired electron in the resulting alkyl radical.

If the bromine radical adds to the *sp*^{2} carbon of 1-butene that is bonded to the most hydrogens, a secondary alkyl radical is formed. If the bromine radical adds to the other *sp*^{2} carbon, a primary alkyl radical is formed. *The bromine radical, therefore, adds to the* sp^2 *carbon that is bonded to the most hydrogens in order to form the more stable radical.*

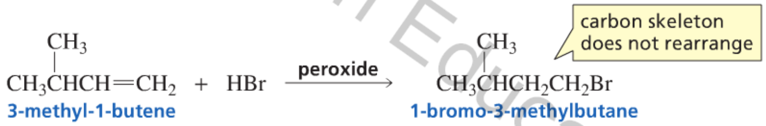
- The alkyl radical removes a hydrogen atom from another molecule of HBr to produce a molecule of the alkyl halide product and another bromine radical.

  The preceding two steps are propagation steps. As is characteristic of a pair of propagation steps, a radical (Br·) reacts in the first propagation step to form a radical that reacts in the second propagation step to regenerate the radical (Br·) that is the reactant in the first propagation step.
- The last three steps are termination steps.

Because the first species that adds to the alkene is a radical (Br·), the addition of HBr in the presence of a peroxide is called a **radical addition reaction.**

When HBr reacts with an alkene in the absence of a peroxide, the electrophile—the first species to add to the alkene—is H$^+$. In the presence of a peroxide, the electrophile is Br·. In both reactions, the electrophile adds to the *sp*^{2} carbon that is bonded to the most hydrogens in order to form the more stable intermediate, thereby following the general rule for electrophilic addition reactions.

The radical intermediate formed in the following reaction does not rearrange, because radicals do not rearrange as readily as carbocations do.



$$CH_3\overset{CH_3}{C}HCH{=}CH_2 + HBr \xrightarrow{\text{peroxide}} CH_3\overset{CH_3}{C}HCH_2CH_2Br$$

carbon skeleton does not rearrange

3-methyl-1-butene

1-bromo-3-methylbutane

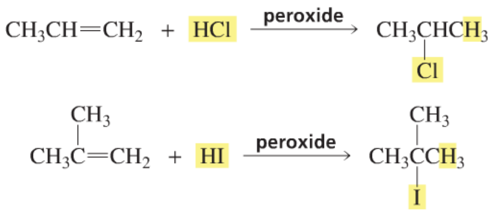
PROBLEM 12

Write out the propagation steps for the addition of HBr to 1-methylcyclohexene in the presence of a peroxide.

Without a *radical initiator* (in this case, peroxide), the radical reaction we have just described would not occur. Any compound that can readily undergo homolysis (dissociate to form radicals) can act as a radical initiator. We will encounter radical initiators again when we discuss polymers in Chapter 27.

While radical initiators cause radical reactions to occur, *radical inhibitors* have the opposite effect; they trap radicals as they are formed, thereby preventing reactions that depend on the presence of radicals. We will see how radical inhibitors trap radicals in Section 13.11.

A peroxide has no effect on the addition of HCl or HI to an alkene; the product that forms in the presence of a peroxide is the same as the product that forms in the absence of a peroxide.



$$CH_3CH{=}CH_2 + HCl \xrightarrow{\text{peroxide}} CH_3\underset{Cl}{C}HCH_3$$

$$CH_3\overset{CH_3}{C}{=}CH_2 + HI \xrightarrow{\text{peroxide}} CH_3\underset{I}{\overset{CH_3}{C}}CH_3$$

Why is the **peroxide effect** observed for the addition of HBr, but not for the addition of HCl or HI? This question can be answered by calculating the Δ*H*° for the two propagation steps in the radical chain reaction (using the bond dissociation energies in Table 5.1 on page 210).

$Cl\cdot + CH_2{=}CH_2 \longrightarrow ClCH_2\dot{C}H_2$ $\Delta H^\circ = 63 - 85 = -22$ kcal/mol (or -91 kJ/mol) exothermic

$ClCH_2\dot{C}H_2 + HCl \longrightarrow ClCH_2CH_3 + Cl\cdot$ $\Delta H^\circ = 103 - 101 = +2$ kcal/mol (or $+8$ kJ/mol) endothermic

$Br\cdot + CH_2{=}CH_2 \longrightarrow BrCH_2\dot{C}H_2$ $\Delta H^\circ = 63 - 72 = -9$ kcal/mol (or -38 kJ/mol)

$BrCH_2\dot{C}H_2 + HBr \longrightarrow BrCH_2CH_3 + Br\cdot$ $\Delta H^\circ = 87 - 101 = -14$ kcal/mol (or -59 kJ/mol)

exothermic

$I\cdot + CH_2{=}CH_2 \longrightarrow ICH_2\dot{C}H_2$ $\Delta H^\circ = 63 - 57 = +6$ kcal/mol (or $+25$ kJ/mol) endothermic

$ICH_2\dot{C}H_2 + HI \longrightarrow ICH_2CH_3 + I\cdot$ $\Delta H^\circ = 71 - 101 = -30$ kcal/mol (or -126 kJ/mol) exothermic

For the radical addition of HCl, the first propagation step is exothermic and the second is endothermic. For the radical addition of HI, the first propagation step is endothermic and the second is exothermic. Only for the radical addition of HBr are both propagation steps exothermic.

In a radical reaction, the steps that propagate the chain reaction compete with the steps that terminate it. Termination steps are always exothermic, because only bond making (and no bond breaking) occurs. Therefore, only when both propagation steps are exothermic can propagation compete successfully with termination. When HCl or HI adds to an alkene in the presence of a peroxide, any chain reaction that is initiated is then terminated rather than propagated because propagation cannot compete successfully with termination. Consequently, the radical chain reaction does not take place, and the only reaction that occurs is ionic addition (H^+ followed by Cl^- or I^-).

PROBLEM 13♦

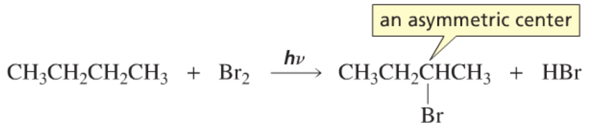
What will be the major product of the reaction of 2-methyl-2-butene with each of the following reagents?

a. HBr **b.** HCl **c.** HBr + peroxide **d.** HCl + peroxide

13.8 THE STEREOCHEMISTRY OF RADICAL SUBSTITUTION AND RADICAL ADDITION REACTIONS

We have seen that when a reactant that does not have an asymmetric center undergoes a reaction that forms a product with one asymmetric center, the product will be a racemic mixture (Section 6.16). Thus, the following *radical substitution reaction* forms a racemic mixture (that is, an equal amount of each enantiomer).

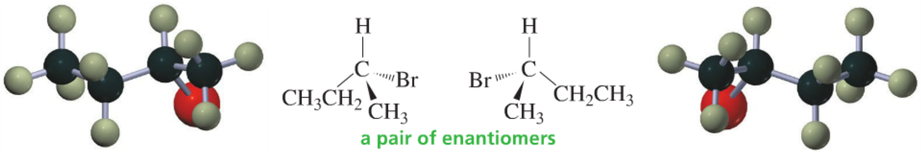
When a reactant that does not have an asymmetric center undergoes a reaction that forms a product with one asymmetric center, the product will be a racemic mixture.



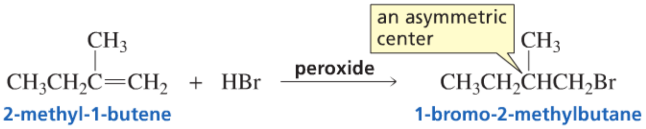
$$CH_3CH_2CH_2CH_3 + Br_2 \xrightarrow{h\nu} CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_3 + HBr$$

an asymmetric center

configuration of the products

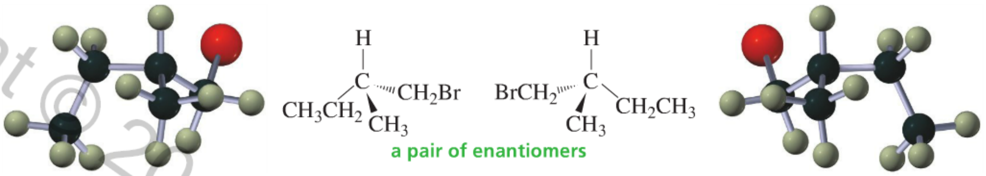


Similarly, the product of the following *radical addition reaction* is a racemic mixture:

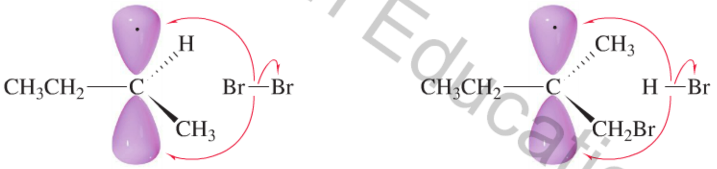


$$CH_3CH_2\overset{CH_3}{\overset{|}{C}}{=}CH_2 + HBr \xrightarrow{\text{peroxide}} CH_3CH_2\overset{CH_3}{\overset{|}{C}}HCH_2Br$$

configuration of the products



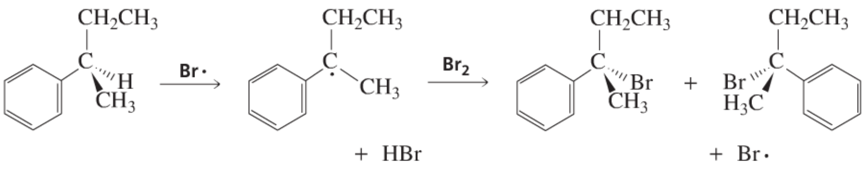
Both the radical substitution and radical addition reactions form a racemic mixture because both reactions form a radical intermediate, and the reaction of the intermediate determines the configuration of the products. The radical intermediate in the substitution reaction is formed when the bromine radical removes a hydrogen atom from the reactant; the radical intermediate in the addition reaction is formed when the bromine radical adds to one of the sp^2 carbons of the double bond.



radical intermediate in the substitution reaction **radical intermediate in the addition reaction**

The carbon that bears the unpaired electron in the radical intermediate is sp^2 hybridized, so the three atoms to which it is bonded lie in a plane (Section 1.10). Therefore, the incoming atom has equal access to both sides of the plane. Consequently, identical amounts of the *R* and *S* enantiomers are formed in both the substitution and addition reactions.

Identical amounts of the *R* and *S* enantiomers are also obtained if a hydrogen bonded to an asymmetric center is substituted by a halogen. Breaking the bond to the asymmetric center destroys the configuration at the asymmetric center and forms a planar radical intermediate. The incoming halogen has equal access to both sides of the plane, so a racemic mixture is formed.



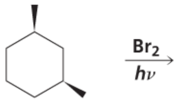
PROBLEM 14♦

a. What hydrocarbon with molecular formula C_4H_{10} forms only two monochlorinated products? Both products are achiral.

b. What hydrocarbon with the same molecular formula as in part **a** forms three monochlorinated products? One is achiral and two are chiral.

PROBLEM 15

Draw the stereoisomers of the major monobromination products obtained from the following reaction.



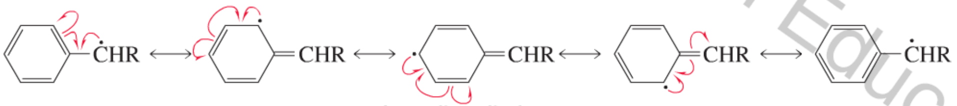
13.9 RADICAL SUBSTITUTION OF BENZYLIC AND ALLYLIC HYDROGENS

An **allylic radical** has an unpaired electron on an allylic carbon and, like an allylic cation, has two resonance contributors (Section 8.13).

$$R\dot{C}H{-}CH{=}CH_2 \longleftrightarrow RCH{=}CH{-}\dot{C}H_2$$

an allylic radical

A **benzylic radical** has an unpaired electron on a benzylic carbon and, like a benzylic cation, has five resonance contributors (Section 8.13).

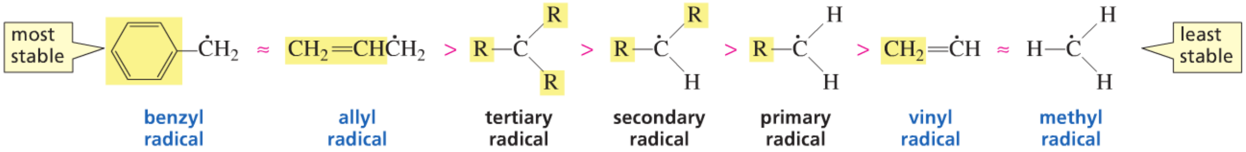


a benzylic radical

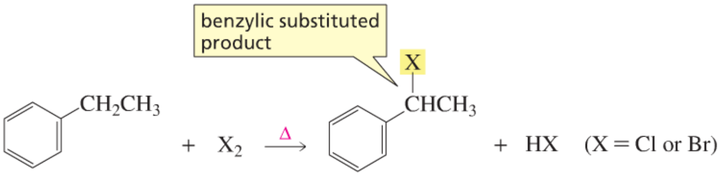
Because electron delocalization stabilizes a molecule (Section 8.6), allyl and benzyl radicals are both more stable than other primary radicals. They are even more stable than tertiary radicals.

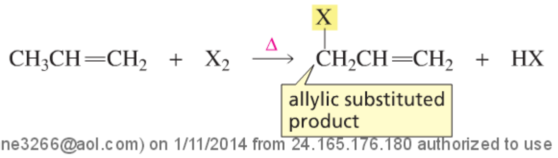
Electron delocalization increases the stability of a molecule.

relative stabilities of radicals



We know that the more stable the radical, the faster it can be formed. This means that a hydrogen bonded to either a benzylic carbon or an allylic carbon will be preferentially substituted in a halogenation reaction. Because bromination is more highly regioselective than chlorination, the percent of substitution at the benzylic or allylic carbon is greater for bromination.

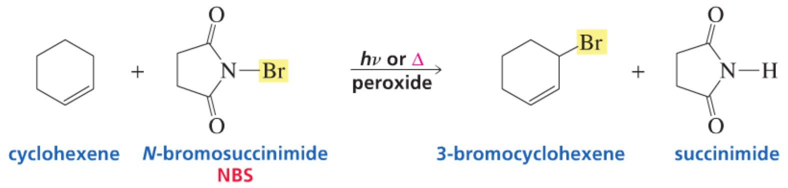




$$CH_3CH{=}CH_2 + X_2 \xrightarrow{\Delta} \overset{X}{C}H_2CH{=}CH_2 + HX$$

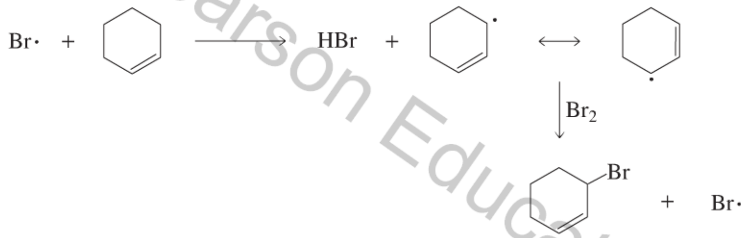
N-Bromosuccinimide (NBS) is frequently used to brominate allylic carbons because it allows a radical substitution reaction to be carried out in the presence of a low concentration of Br_2 and a low concentration of HBr. If a high concentration is present, addition of Br_2 or HBr to the double bond will compete with allylic substitution.

NBS is used to brominate allylic carbons.

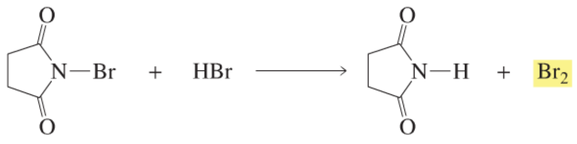


The bromination reaction begins with homolytic cleavage of the N—Br bond of NBS. This generates the bromine radical needed to initiate the radical reaction. Light or heat and a radical initiator such as a peroxide are used to promote homolytic cleavage.

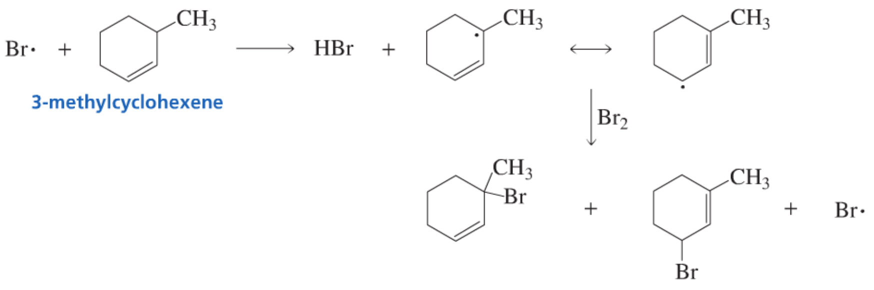
In the first propagation step, the bromine radical removes an allylic hydrogen to form HBr and an allylic radical. Notice that the allylic radical is stabilized by electron delocalization. The allylic radical reacts with Br_2 in the second propagation step, thus forming the allylic bromide and the chain-propagating bromine radical.



The Br_2 used in the second propagation step is produced in low concentration from a fast ionic reaction between NBS and the HBr that is produced in the first propagation step.



Even though there are two resonance contributors in the preceding reaction, only one substitution product (disregarding stereoisomers) is formed because the resonance contributors are mirror images. However, if the resonance contributors are not mirror images, then two substitution products (disregarding stereoisomers) are formed:



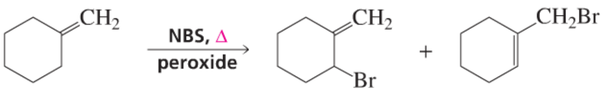
PROBLEM 16

a. How many stereoisomers are formed from the reaction of cyclohexene with NBS?

b. How many stereoisomers are formed from the reaction of 3-methylcyclohexene with NBS?

PROBLEM 17

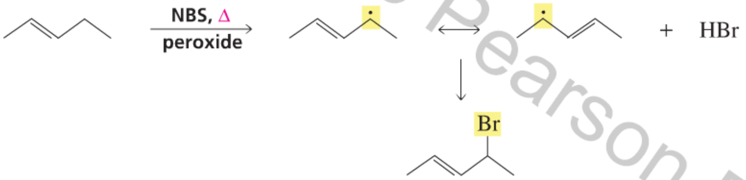
Two products are formed when methylenecyclohexane reacts with NBS. Show how each is formed.



PROBLEM 18 Solved

How many allylic substituted bromoalkenes are formed from the reaction of 2-pentene with NBS? Disregard stereoisomers.

Solution Because of the high selectivity of the bromine radical, it will remove a secondary allylic hydrogen from C-4 of 2-pentene much more easily than it will remove a primary allylic hydrogen from C-1. The resonance contributors of the resulting radical intermediate are mirror images, so only one bromoalkene is formed (ignoring stereoisomers).

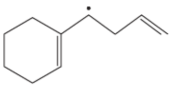


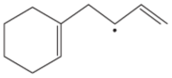
PROBLEM 19

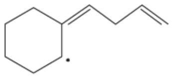
How many allylic substituted bromoalkenes are formed from the reaction in Problem 18 if stereoisomers are included?

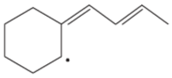
PROBLEM 20

Draw the resonance contributors for the following radicals:

a.


b.


c.


d.


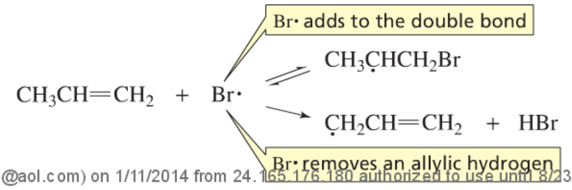
PROBLEM 21

a. Draw the major product(s) of the reaction of 1-methylcyclohexene with the following reagents, disregarding stereoisomers:

1. NBS/Δ/peroxide **2.** Br_2/CH_2Cl_2 **3.** HBr **4.** HBr/peroxide

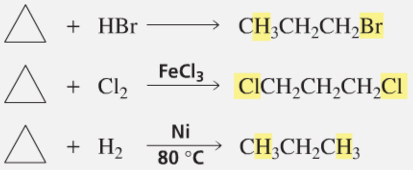
b. For each reaction, show what stereoisomers are obtained.

Why does the bromine radical generated from NBS remove an allylic hydrogen, whereas the bromine radical generated from HBr + peroxide adds to the double bond? The bromine radical can in fact do both. When NBS is used, however, there is little HBr present to complete the addition reaction after the bromine radical has added to the double bond. Because addition of a bromine radical to a double bond is reversible, the reactant is reformed and allylic substitution becomes the major reaction pathway.

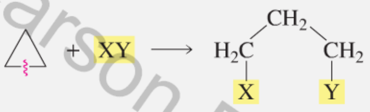


Cyclopropane

Although it is an alkane, cyclopropane undergoes electrophilic addition reactions as if it were an alkene. Cyclopropane is more reactive than propene toward the addition of acids such as HBr and HCl, but is less reactive toward the addition of Cl_2 and Br_2, so a Lewis acid ($FeCl_3$ or $FeBr_3$) is needed to catalyze halogen addition (Section 19.4).



It is the strain in the small ring that makes it possible for cyclopropane to undergo electrophilic addition reactions. Because of the 60° bond angles in its three-membered ring, the compound's sp^3 orbitals cannot overlap head-on. Thus, the C—C bonds in cyclopropane are considerably weaker than normal C—C bonds (see Figure 3.8 on page 125). Consequently, the three-membered ring undergoes a ring-opening reaction with electrophilic reagents.

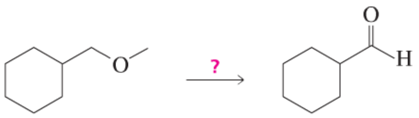


DESIGNING A SYNTHESIS III

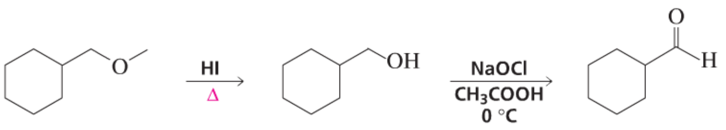
13.10 MORE PRACTICE WITH MULTISTEP SYNTHESIS

Now that the number of reactions with which you are familiar has increased, you can design the synthesis of a wide variety of compounds.

Example 1. Starting with the ether shown here, how could you prepare the aldehyde?

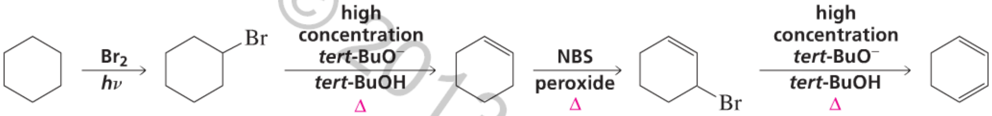


Heating the ether with one equivalent of HI forms a primary alcohol that, when oxidized, forms the desired aldehyde.

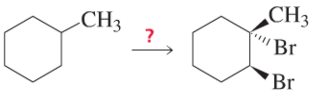


Example 2. Suggest a way to prepare 1,3-cyclohexadiene from cyclohexane.

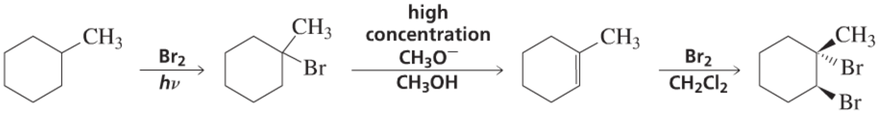
Deciding what the first reaction should be is easy, because the only reaction that an alkane can undergo is a radical substitution reaction with Cl_2 or Br_2. Next, an E2 reaction, using a high concentration of a strong and bulky base and carried out at a relatively high temperature to encourage elimination over substitution, will form cyclohexene. Radical bromination of cyclohexene forms an allylic bromide, which will form the desired target molecule by undergoing another E2 reaction.



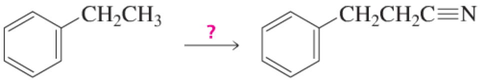
Example 3. Starting with methylcyclohexane, how could the following vicinal *trans*-dihalide be prepared?



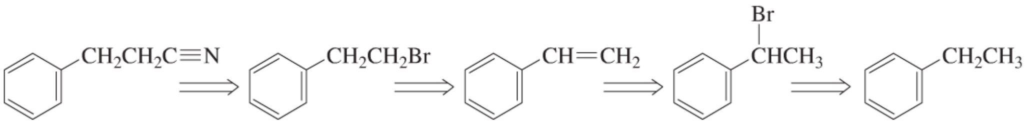
Again, since the starting material is an alkane, the first reaction must be a radical substitution. Bromination leads to selective substitution of the tertiary hydrogen. Under E2 conditions, tertiary alkyl halides undergo only elimination, so there will be no competing substitution product formed in the next reaction. A relatively unhindered base should be used to favor removal of a proton from the secondary carbon over removal of a proton from the methyl group. The final step is addition of Br_2; only anti addition occurs in this reaction, so the target molecule (along with its enantiomer) is obtained.



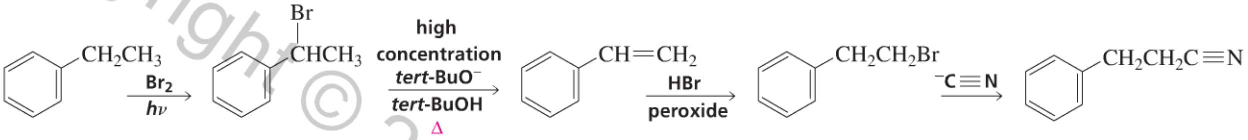
Example 4. Design a synthesis for the target molecule from the indicated starting material.



It is not immediately obvious how to carry out this synthesis, so let's use retrosynthetic analysis to find a way. The only method you know for introducing a C≡N group into a molecule is nucleophilic substitution. The alkyl halide for that substitution reaction can be obtained from the addition of HBr to an alkene in the presence of a peroxide. The alkene for that addition reaction can be obtained from an elimination reaction using an alkyl halide obtained by benzylic substitution.



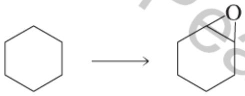
The reaction sequence can now be written in the forward direction along with the reagents required to carry out each step. Notice that a bulky base is used to encourage elimination over substitution.



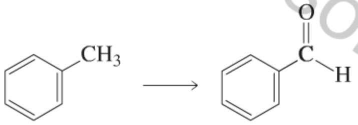
PROBLEM 22

Design a multistep synthesis to show how each of the following compounds could be prepared from the given starting material:

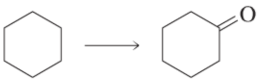
a.



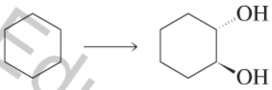
b.



c.



d.



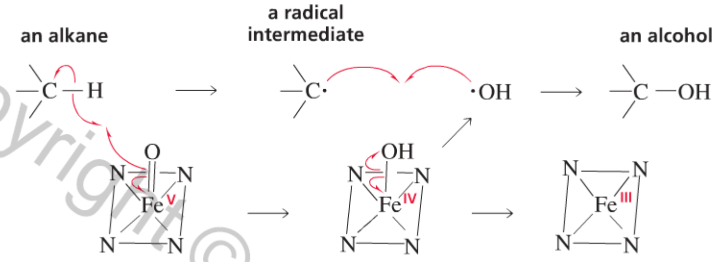
13.11 RADICAL REACTIONS OCCUR IN BIOLOGICAL SYSTEMS

Because of the large amount of heat or light energy required to initiate a radical reaction and the difficulty in controlling a chain reaction once it is initiated, scientists assumed for a long time that radical reactions were not important in biological systems. It is now widely recognized, however, that many biological reactions involve radicals. The radicals in these reactions, instead of being generated by heat or light, are formed by the interaction of organic molecules with metal ions. The radical reactions take place at the active sites of enzymes (Section 5.12). Containing the chain reaction at a specific site allows the reaction to be controlled.

Water-soluble (polar) compounds are readily eliminated by the body. In contrast, water-insoluble (nonpolar) compounds are not readily eliminated but, instead, accumulate in the nonpolar components of cells. For cells to avoid becoming "toxic dumps," nonpolar compounds that are ingested (such as drugs, foods, and environmental pollutants) must be converted into polar compounds that can be excreted.

A radical reaction carried out in the liver converts nonpolar hydrocarbons into less toxic polar alcohols by substituting an H in the hydrocarbon with an OH. The reaction is catalyzed by an iron-containing enzyme called cytochrome P_{450}.

A radical intermediate is created when $Fe^{V}{=}O$ removes a hydrogen atom from the alkane. Then $Fe^{IV}{-}OH$ dissociates homolytically into Fe^{III} and $\dot{O}H$, and the $\dot{O}H$ immediately combines with the radical intermediate to form the alcohol.



This reaction can also have the opposite toxicological effect. For example, studies found that when animals inhale dichloromethane (CH_2Cl_2), it becomes a carcinogen as a result of an H being substituted by an OH.

Decaffeinated Coffee and the Cancer Scare

Animal studies revealing that dichloromethane becomes a carcinogen when inhaled immediately led to a study of thousands of workers who inhaled dichloromethane daily. However, no increased risk of cancer was found in this group. (This shows that the results of studies done on humans do not always agree with the results of those done on laboratory animals.)

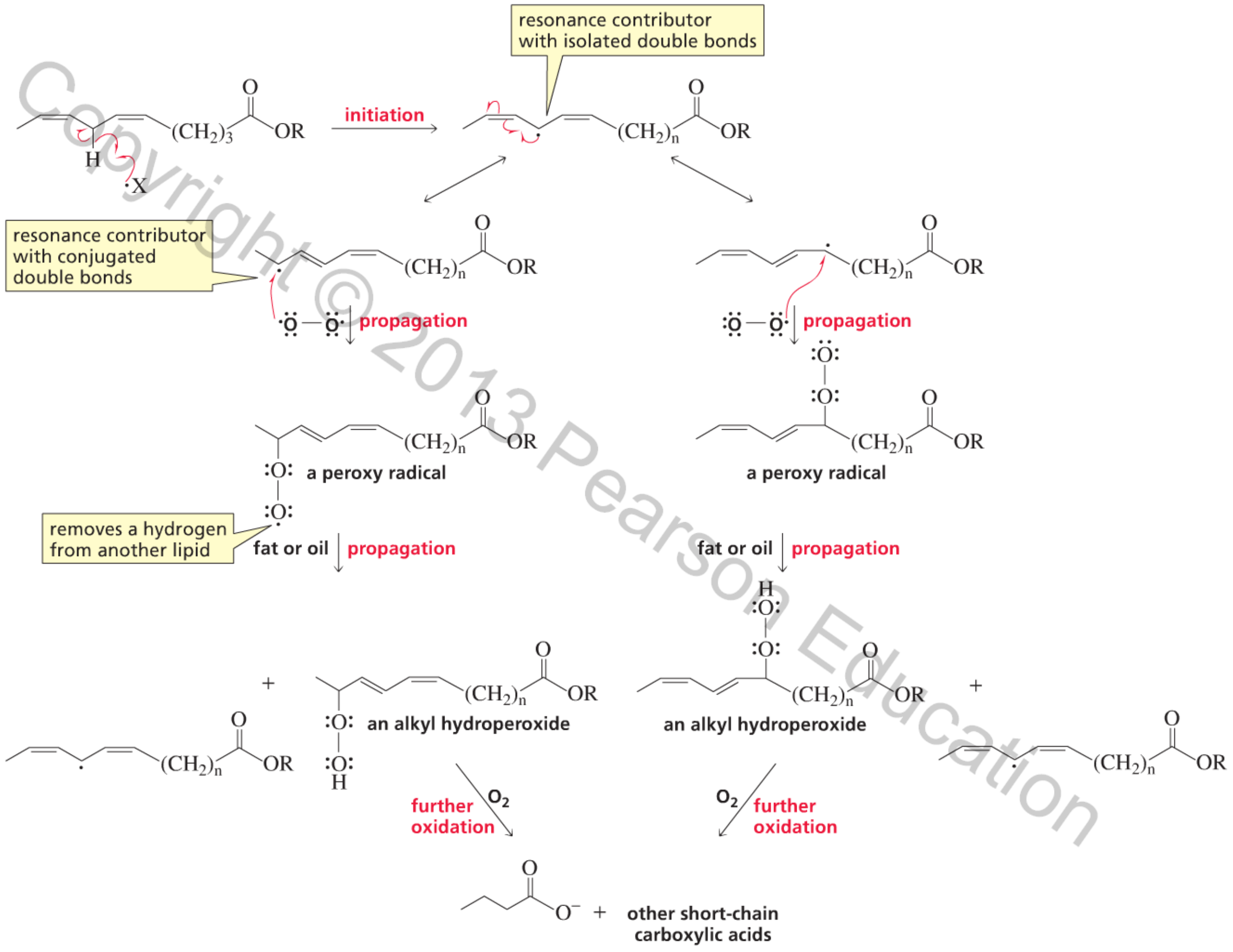
Because dichloromethane was the solvent used to extract caffeine from coffee beans in the manufacture of decaffeinated coffee, a study was done to see what happened to animals that drank dichloromethane. When dichloromethane was added to the drinking water given to laboratory rats and mice, researchers found no toxic effects, even in rats that had consumed an amount of dichloromethane equivalent to the amount that would be ingested by drinking 120,000 cups of decaffeinated coffee per day and in mice that had consumed an amount equivalent to drinking 4.4 million cups of decaffeinated coffee per day.

However, because of the initial concern, researchers sought alternative methods for extracting caffeine from coffee beans. Extraction by CO_2 at supercritical temperatures and pressures was found to be a better method because it extracts caffeine without simultaneously extracting some of the flavor compounds, as dichloromethane does. This was one of the first green (environmentally benign) commercial chemical processes to be developed. After the caffeine has been removed, the CO_2 can be recycled, whereas dichloromethane is not a substance that should be released into the environment (Section 7.12).

Fats and oils are easily oxidized by O_2 by means of a radical chain reaction to form compounds that have strong odors. These compounds are responsible for the unpleasant taste and smell associated with sour milk and rancid butter.

Fats and oils have double bonds ($-CH{=}CH-CH_2-CH{=}CH-$) that are separated by two single bonds. The mechanism for their oxidation by O_2 is shown next. Notice the similarity of this mechanism to that shown for peroxide formation in Section 13.6.

MECHANISM FOR THE OXIDATION OF FATS AND OILS BY OXYGEN

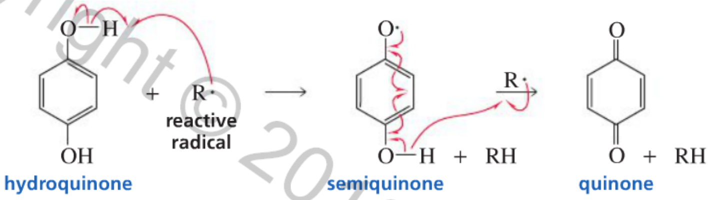


- In the initiation step, a radical removes a hydrogen atom from a methylene group that is flanked by two double bonds. This hydrogen is the one most easily removed because the resulting radical is relatively stable, since the unpaired electron is shared by three carbons.
- In the first propagation step, the radical created in the initiation step reacts with O_2, forming a peroxy radical.
- In the second propagation step, the peroxy radical removes a hydrogen atom from another molecule of fat or oil. The two propagation steps are repeated over and over.
- The alkyl hydroperoxide undergoes further oxidation to form butyric acid and other short-chain carboxylic acids.

The molecules that form cell membranes (Section 16.13) can undergo this same radical reaction, which leads to their degradation. Radical reactions in cells have been implicated in the aging process.

Clearly, unwanted radicals in cells must be destroyed before they damage the cells. Radical reactions can be prevented by **radical inhibitors,** compounds that destroy reactive radicals by converting them into unreactive radicals or into compounds with only paired electrons. Radical inhibitors are *antioxidants*—that is, they prevent oxidation reactions such as the one just shown.

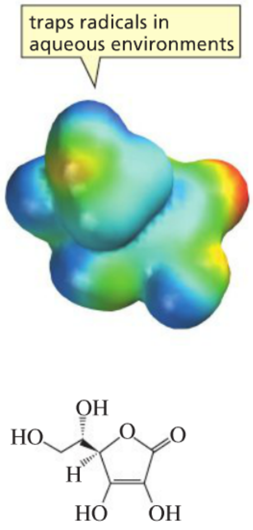
Hydroquinone is an example of a radical inhibitor. When hydroquinone traps a radical, it forms semiquinone, a radical that is stabilized by electron delocalization, so it is less reactive than other radicals. Moreover, semiquinone can trap another radical and form quinone, a compound whose electrons are all paired. Hydroquinones are found in the cells of all aerobic organisms.



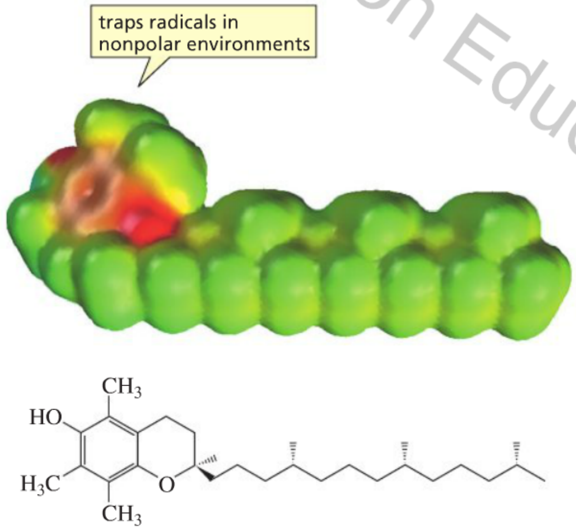
Because radicals are implicated in the aging process, many products are available that contain antioxidants.

Two other examples of radical inhibitors in living systems are vitamins C and E. Like hydroquinone, they form relatively stable (unreactive) radicals.

Vitamin C (also called ascorbic acid) is a water-soluble compound that traps radicals formed in the interior of cells and in blood plasma (both of which have aqueous environments).



vitamin C
ascorbic acid



vitamin E
α-tocopherol

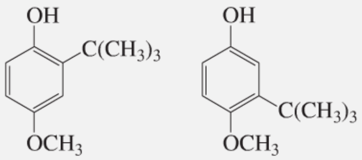
Vitamin E (also called α-tocopherol) is a fat-soluble compound that traps radicals formed in cell membranes, which are nonpolar. Vitamin E is the primary antioxidant for fat tissue in humans and is, therefore, important in preventing the development of atherosclerosis.

Why one vitamin functions in aqueous environments and the other in nonaqueous environments is apparent from their structures and their electrostatic potential maps; both show that vitamin C is a relatively polar compound and vitamin E is a nonpolar compound.

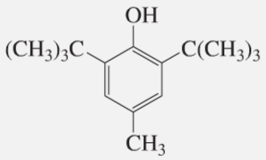
Nuts are a natural source of vitamin E.

Food Preservatives

Radical inhibitors found in food are known as *preservatives.* They preserve food by preventing radical chain reactions. Vitamin E is a naturally occurring preservative found in such things as vegetable oil, sunflower seeds, and spinach. BHA and BHT are synthetic preservatives that are added to many packaged foods. Notice that, like hydroquinone, vitamin E and all the synthetic preservatives are phenols.



butylated hydroxyanisole
BHA



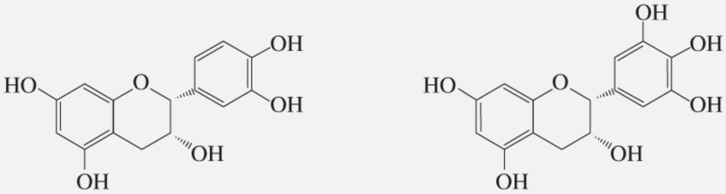
butylated hydroxytoluene
BHT

food preservatives

Is Chocolate a Health Food?

We have long been told that our diets should include lots of fruits and vegetables because they are good sources of antioxidants. Antioxidants protect against cardiovascular disease, cancer, and cataracts, and they are thought to slow the effects of aging. Chocolate is made up of hundreds of organic compounds, including high levels of antioxidants called catechins. (Catechins are also phenols.)

On a weight basis, the concentration of antioxidants in chocolate is higher than in red wine or green tea, and 20 times higher than in tomatoes. Another piece of good news for chocolate lovers is that stearic acid, the main fatty acid in chocolate, does not appear to raise blood cholesterol levels the way other saturated fatty acids do. Dark chocolate contains more than twice the level of antioxidants found in milk chocolate. Unfortunately, white chocolate contains no antioxidants.



catechins

PROBLEM 23

How many atoms share the unpaired electron in semiquinone?

PROBLEM 24

Using resonance structures, explain why a catechin is an antioxidant.

13.12 RADICALS AND STRATOSPHERIC OZONE

Ozone (O_3), a major constituent of smog, is a health hazard at ground level—it inflames the airways, worsens lung ailments, and increases the risk of death from heart or lung disease. In the stratosphere, however, a layer of ozone shields the Earth from harmful solar radiation, with the greatest concentrations lying between 12 and 15 miles above the Earth's surface.

In the stratosphere, ozone acts as a filter for biologically harmful ultraviolet light that otherwise would reach the surface of the Earth. Among other effects, short-wavelength ultraviolet light can damage DNA in skin cells, causing mutations that trigger skin cancer (Section 28.7). We owe our very existence to this protective ozone layer. According to current theories of evolution, life could not have developed on land without it. Instead, most if not all living things would have had to remain in the ocean, where water screens out the harmful ultraviolet light.

The ozone layer is thinnest at the equator and densest toward the poles. Since about 1985, scientists have noted a precipitous drop in stratospheric ozone over Antarctica. This area of ozone depletion, dubbed the "ozone hole," is unprecedented in the history of ozone observations. Scientists subsequently noted a similar decrease in ozone over Arctic regions; then, in 1988, they detected a depletion of ozone over the United States for the first time. Three years later, scientists determined that the rate of ozone depletion was two to three times faster than originally anticipated.

Polar stratospheric clouds increase the rate of ozone destruction. These clouds form over Antarctica during the cold winter months. Ozone depletion in the Arctic is less severe because the temperature generally does not get low enough for stratospheric clouds to form there.

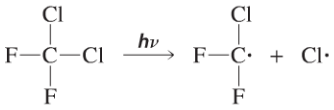
Strong circumstantial evidence implicated synthetic chlorofluorocarbons (CFCs)—alkanes in which all the hydrogens have been replaced by fluorine and chlorine—as a major cause of ozone depletion. These gases, known commercially as Freon, had been used extensively as cooling fluids in refrigerators and air conditioners. They were also once widely used as propellants in aerosol spray cans (deodorant, hair spray, and so on) because of their odorless, nontoxic, and nonflammable properties and because, being chemically inert, they do not react with the contents of the can. Now such use is banned and propane and butane are used as propellants instead.

The global agreement to phase out CFCs and other ozone-depleting agents seems to be working. The ozone layer is no longer depleting and it is hoped that it will regain its density by 2048.

Ozone is formed from the interaction of molecular oxygen with very short wavelength ultraviolet light.

$$O_2 \xrightarrow{h\nu} O + O$$
$$O + O_2 \longrightarrow \underset{\text{ozone}}{O_3}$$

Chlorofluorocarbons are stable until they reach the stratosphere. There they encounter wavelengths of ultraviolet light that cause the C—Cl bond to break homolytically, generating chlorine radicals.



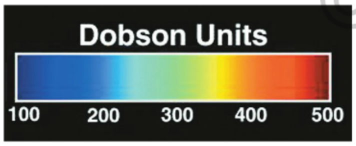
$$\mathrm{F{-}\overset{Cl}{\underset{F}{C}}{-}Cl} \xrightarrow{h\nu} \mathrm{F{-}\overset{Cl}{\underset{F}{C}}\cdot} + \mathrm{Cl\cdot}$$

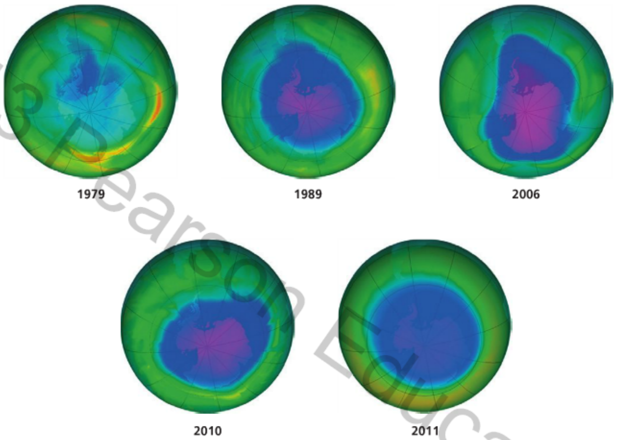
These chlorine radicals are the ozone-removing agents. They react with ozone to form chlorine monoxide radicals and molecular oxygen. The chlorine monoxide radical then reacts with more ozone to form chlorine dioxide, which dissociates to regenerate a chlorine radical. These three steps—two of which each destroy an ozone molecule—are the propagating steps that are repeated over and over. It has been calculated that a single chlorine atom destroys 100,000 ozone molecules!

$$Cl\cdot + O_3 \longrightarrow ClO\cdot + O_2$$

$$ClO\cdot + O_3 \longrightarrow \cdot ClO_2 + O_2$$

$$\cdot ClO_2 \longrightarrow Cl\cdot + O_2$$





The growth of the Antarctic ozone hole, located mostly over the continent of Antarctica, since 1979. The images were made from data supplied by total ozone-mapping spectrometers (TOMSs). The color scale depicts the total ozone values in Dobson units, with the lowest ozone densities represented by dark blue. (The ozone over a given area is compressed to 0 °C and 1 atm pressure, and the thickness of the slab is measured. 1 Dobson unit = 0.01 mm thickness.)

Artificial Blood

Clinical trials are underway to test the use of perfluorocarbons—alkanes in which all the hydrogens have been replaced by fluorines—as compounds to replace blood volume and mimic hemoglobin's ability to carry oxygen to cells and transport carbon dioxide to the lungs.

These compounds are not a true blood substitute, because blood performs many functions that artificial blood cannot. For example, white blood cells fight against infection and platelets are involved in blood clotting. However, artificial blood has several advantages in trauma situations until an actual transfusion can be done: it is safe from disease, it can be administered to any blood type, its availability does not depend on blood donors, and it can be stored longer than whole blood, which is good for only about 40 days.

SOME IMPORTANT THINGS TO REMEMBER

- **Alkanes** are called **saturated hydrocarbons**. Because they do not contain any carbon–carbon double or triple bonds, they are saturated with hydrogen.
- Alkanes are unreactive compounds because they have only strong σ bonds and atoms with no partial charges.
- In **heterolytic bond cleavage,** a bond breaks so that one of the atoms retains both of the bonding electrons; in **homolytic bond cleavage,** a bond breaks so that each of the atoms retains one of the bonding electrons.
- Alkanes undergo **radical substitution reactions** with chlorine (Cl_2) or bromine (Br_2) at high temperatures or in the presence of light to form alkyl chlorides or alkyl bromides. This substitution reaction is a **radical chain reaction** with **initiation, propagation,** and **termination steps.**
- The rate-determining step of a radical substitution reaction is removal of a hydrogen atom to form an alkyl radical.
- The relative rates of radical formation are benzylic $\sim$allyl $> 3° > 2° > 1° >$ vinyl $\sim$ methyl.
- Calculation of the relative amounts of products obtained from the radical halogenation of an alkane must take into account both probability and the relative rate at which a particular radical is formed.
- The **reactivity–selectivity principle** states that the more reactive a species is, the less selective it will be.
- A bromine radical is *less reactive* than a chlorine radical, so a bromine radical is *more selective* about which hydrogen atom it removes.
- Ethers form explosive peroxides when they are exposed to air.
- A **peroxide** is a **radical initiator** because it creates radicals.
- A **radical inhibitor** (an **antioxidant**) destroys reactive radicals by creating radicals that are less reactive or by creating compounds that have only paired electrons.
- **Radical addition reactions** are chain reactions with **initiation, propagation,** and **termination steps.**
- A peroxide reverses the order of addition of H and Br to an alkene because it causes $Br\cdot$, instead of H^+, to be the electrophile. The **peroxide effect** is observed only for the addition of HBr.
- If a reactant that does not have an asymmetric center undergoes a radical substitution or a radical addition reaction that forms a product with an asymmetric center, then a racemic mixture will be obtained.
- A racemic mixture is also obtained if a hydrogen bonded to an asymmetric center is substituted by a halogen.
- *N*-Bromosuccinimide (NBS) is used to brominate allylic carbons.
- Some biological reactions involve radicals formed by the interaction of organic molecules with metal ions. The reactions take place at the active sites of enzymes.
- Fats, oils, and membranes are oxidized by O_2 in a radical chain reaction.
- The interaction of CFCs with UV light generates chlorine radicals, which are ozone-removing agents.

SUMMARY OF REACTIONS

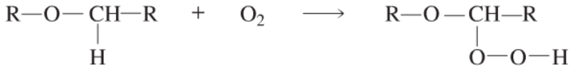
1. *Alkanes* undergo radical substitution reactions with Cl_2 or Br_2 in the presence of heat or light (Sections 13.2–13.5). The mechanisms of the reaction are shown on pages 558 and 559.

$$\underset{\text{excess}}{CH_3CH_3} + Cl_2 \xrightarrow{\Delta \text{ or } h\nu} CH_3CH_2Cl + HCl$$

$$\underset{\text{excess}}{CH_3CH_3} + Br_2 \xrightarrow{\Delta \text{ or } h\nu} CH_3CH_2Br + HBr$$

bromination is more selective than chlorination

2. A radical initiator removes a hydrogen atom from an α-carbon of an ether to form a peroxide (Section 13.6). The mechanism of the reaction is shown on page 568.

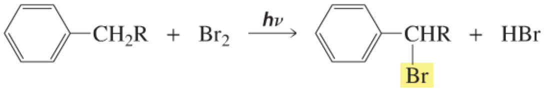


$$R{-}O{-}\underset{\displaystyle H}{\underset{|}{CH}}{-}R + O_2 \longrightarrow R{-}O{-}\underset{\displaystyle O{-}O{-}H}{\underset{|}{CH}}{-}R$$

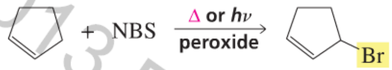
3. *Alkenes* undergo radical addition of hydrogen bromide in the presence of a peroxide (Br· is the electrophile; Section 13.7). The mechanism of the reaction is shown on page 569.

$$RCH{=}CH_2 + HBr \xrightarrow{\text{peroxide}} RCH_2CH_2Br$$

4. *Alkyl-substituted benzenes* undergo radical substitution at the benzylic position (Section 13.9).



5. *Alkenes* undergo radical substitution at allylic carbons. NBS is used for bromination at allylic carbons (Section 13.9). The mechanism of the reaction is shown on page 574.



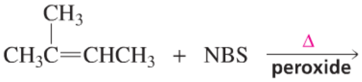
$$RCH_2CH{=}CH_2 + NBS \xrightarrow[\text{peroxide}]{\Delta \text{ or } h\nu} \underset{\substack{|\\Br}}{RCH}CH{=}CH_2 + RCH{=}CH\underset{\substack{|\\Br}}{CH_2} + HBr$$

PROBLEMS

25. Draw the product(s) of each of the following reactions, disregarding stereoisomers:

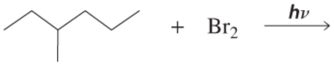
a. $CH_2{=}CHCH_2CH_2CH_3 + NBS \xrightarrow[\text{peroxide}]{\Delta}$

b.

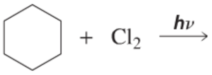


$$CH_3\overset{\substack{CH_3\\|}}{C}{=}CHCH_3 + NBS \xrightarrow[\text{peroxide}]{\Delta}$$

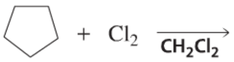
c.



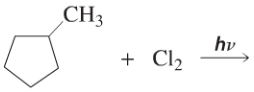
d.



e.



f.

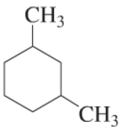


26. a. What alkane, with molecular formula C_5H_{12}, forms only one monochlorinated product when it is heated with Cl_2?

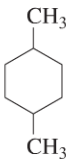
b. What alkane, with molecular formula C_7H_{16}, forms seven monochlorinated products (disregarding stereoisomers) when heated with Cl_2?

27. What is the major product that would be obtained from treating an excess of each of the following compounds with Cl_2 in the presence of light at room temperature? Disregard stereoisomers.

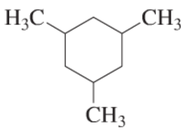
a.



b.



c.

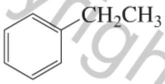


28. What would the answers be to Problem 27 if the same compounds were treated with Br_2 at 125 °C?

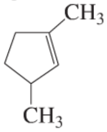
29. Draw the major product of each of the following reactions, disregarding stereoisomers:

a.  + NBS $\xrightarrow[\text{peroxide}]{\Delta}$

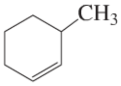
b.  + NBS $\xrightarrow[\text{peroxide}]{\Delta}$

c. 

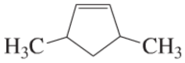
+ NBS $\xrightarrow[\text{peroxide}]{\Delta}$

d. 

+ NBS $\xrightarrow[\text{peroxide}]{\Delta}$

e. 

+ NBS $\xrightarrow[\text{peroxide}]{\Delta}$

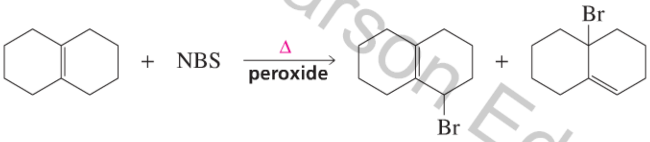
f. 

+ NBS $\xrightarrow[\text{peroxide}]{\Delta}$

30. When 2-methylpropane is monochlorinated in the presence of light at room temperature, 36% of the product is 2-chloro-2-methylpropane and 64% is 1-chloro-2-methylpropane. From these data, calculate how much easier it is to remove a hydrogen atom from a tertiary carbon than from a primary carbon under these conditions.

31. Iodine (I_2) does not react with ethane, even though I_2 is more easily cleaved homolytically than the other halogens. Explain.

32. Propose a mechanism to account for the products formed in the following reaction:



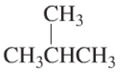
33. The deuterium kinetic isotope effect for the halogenation of an alkane is defined in the following equation, where X· = Cl· or Br·

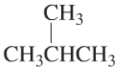
$$\textbf{deuterium kinetic isotope effect} = \frac{\textbf{rate of homolytic cleavage of a C—H bond by X·}}{\textbf{rate of homolytic cleavage of a C—D bond by X·}}$$

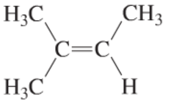
Predict whether chlorination or bromination would have a greater deuterium kinetic isotope effect.

34. **a.** How many monochlorination products could be obtained from the radical chlorination of methylcyclohexane? Disregard stereoisomers.
b. Which product would be obtained in greatest yield? Explain.
c. How many monochlorination products would be obtained if all stereoisomers are included?

35. Draw the alkyl halide that would be obtained in greatest yield. Include stereoisomers.

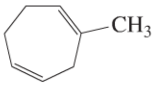
a. 
$\underset{\text{excess}}{CH_3\overset{CH_3}{\overset{|}{C}}HCH_3}$ + Cl_2 $\xrightarrow{h\nu}$

b. 
$\underset{\text{excess}}{CH_3\overset{CH_3}{\overset{|}{C}}HCH_3}$ + Br_2 $\xrightarrow{h\nu}$

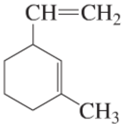
c. 

+ HBr $\xrightarrow{\text{peroxide}}$

d. 
$CH_2{=}CHCH_2CH_2\overset{CH_3}{\overset{|}{C}}{=}CH_2$ $\xrightarrow[\text{peroxide}]{\text{HBr}}$

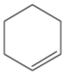
e. 

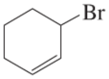
+ HBr $\xrightarrow{\text{peroxide}}$

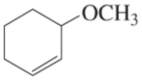
f. 

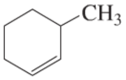
+ HBr $\xrightarrow{\text{peroxide}}$

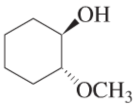
36. Starting with cyclohexane, how could the following compounds be prepared?

a. 

b. 

c. 

d. 

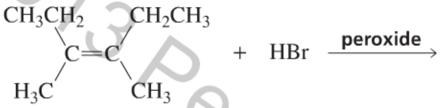
e. 

37. a. Propose a mechanism for the following reaction:

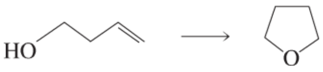
$$CH_3CH_3 + CH_3-\underset{CH_3}{\overset{CH_3}{C}}-OCl \xrightarrow{\Delta} CH_3CH_2Cl + CH_3-\underset{CH_3}{\overset{CH_3}{C}}-OH$$

b. Given that the $\Delta H°$ value for the reaction is −42 kcal/mol and the bond dissociation energies for the C—H, C—Cl, and O—H bonds are 101, 85, and 105 kcal/mol respectively, calculate the bond dissociation energy of the O—Cl bond.

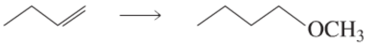
38. What stereoisomers would be obtained from the following reaction?



39. Using the given starting material and any necessary organic or inorganic reagents, indicate how the desired compounds could be synthesized:

a. 

c. 

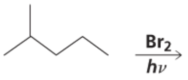
b. 

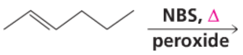
d. 

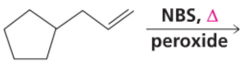
40. A chemist wanted to determine experimentally the relative ease of removing a hydrogen atom from a tertiary, a secondary, and a primary carbon by a chlorine radical. He allowed 2-methylbutane to undergo chlorination at 300 °C and obtained as products 36% 1-chloro-2-methylbutane, 18% 2-chloro-2-methylbutane, 28% 2-chloro-3-methylbutane, and 18% 1-chloro-3-methylbutane. What values did he obtain for the relative ease of removing a hydrogen atom from tertiary, secondary, and primary hydrogen carbons by a chlorine radical under the conditions of his experiment?

41. At 600 °C, the ratio of the relative rates of formation of a tertiary, a secondary, and a primary radical by a chlorine radical is 2.6 : 2.1 : 1. Explain the change in the degree of regioselectivity compared to what was found in Problem 40.

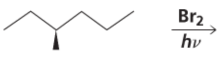
42. Draw the products of the following reactions, including all stereoisomers:

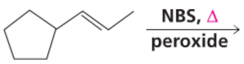
a. 

c. 

e. 

b. 

d. 

f. 

43. a. What five-carbon alkene will form the same product whether it reacts with HBr in the *presence* of a peroxide or with HBr in the *absence* of a peroxide?

b. Give three six-carbon alkenes that form the same product, whether they react with HBr in the *presence* of a peroxide or with HBr in the *absence* of a peroxide.

44 **a.** Calculate the $\Delta H°$ value for the following reaction:

$$\mathrm{CH_4} + \mathrm{Cl_2} \xrightarrow{h\nu} \mathrm{CH_3Cl} + \mathrm{HCl}$$

b. Calculate the sum of the $\Delta H°$ values for the following two propagation steps:

$$\mathrm{CH_3{-}H} + \cdot\mathrm{Cl} \longrightarrow \cdot\mathrm{CH_3} + \mathrm{H{-}Cl}$$
$$\cdot\mathrm{CH_3} + \mathrm{Cl{-}Cl} \longrightarrow \mathrm{CH_3{-}Cl} + \cdot\mathrm{Cl}$$

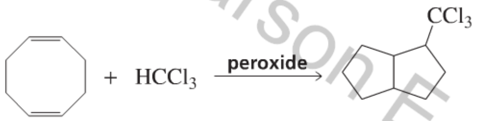
c. Why do both calculations give you the same value of $\Delta H°$?

45. A possible alternative mechanism to that shown in Problem 44 for the monochlorination of methane would involve the following propagation steps:

$$\mathrm{CH_3{-}H} + \cdot\mathrm{Cl} \longrightarrow \mathrm{CH_3{-}Cl} + \cdot\mathrm{H}$$
$$\cdot\mathrm{H} + \mathrm{Cl{-}Cl} \longrightarrow \mathrm{H{-}Cl} + \cdot\mathrm{Cl}$$

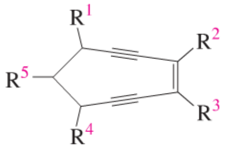
How do you know that the reaction does not take place by this mechanism?

46. Propose a mechanism for the following reaction:



47. Explain why the rate of bromination of methane decreases if HBr is added to the reaction mixture.

48. Enediynes are natural products with potent antitumor properties because they are able to cleave DNA (page 299). Their cytotoxic properties are due to the enediyne undergoing a cyclization to form a highly reactive diradical intermediate. The intermediate abstracts hydrogen atoms from the backbone of DNA, which triggers its damage. Draw the structure of the diradical intermediate.



an enediyne

TUTORIAL

Enhanced by MasteringChemistry®

DRAWING CURVED ARROWS IN RADICAL SYSTEMS

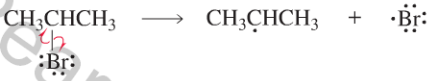
We have seen that chemists use curved arrows

1. to show how electrons move when going from a reactant to a product.
2. to show how electrons move when going from one resonance contributor to the next.

The two previous tutorials on drawing curved arrows showed the simultaneous movement of two electrons. The movement of two electrons is indicated by an arrowhead with two barbs. Electron movement in radical systems involves the movement of only one electron. The movement of a single electron is indicated by an arrowhead with one barb.

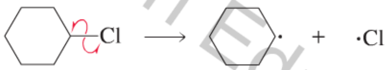
DRAWING CURVED ARROWS IN RADICAL REACTIONS

When a bond breaks in a way that allows each of the bonded atoms to retain one of the bonding electrons, an arrowhead with one barb is used to represent the movement of each of the single electrons.

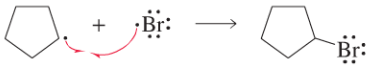


$$\underset{\displaystyle :\ddot{\underset{\cdot\cdot}{Br}}:}{CH_3CHCH_3} \longrightarrow CH_3\underset{\cdot}{C}HCH_3 + \cdot\ddot{\underset{\cdot\cdot}{Br}}:$$

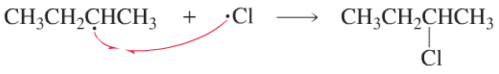
Sometimes, the lone pairs are not shown.



When a bond is formed using one electron from one atom and one electron from another, an arrowhead with one barb is used to represent the movement of each of the single electrons.



Sometimes, the lone pairs are not shown.

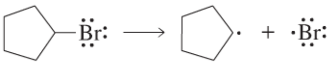


$$CH_3CH_2\underset{\cdot}{C}HCH_3 + \cdot Cl \longrightarrow CH_3CH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCH_3$$

PROBLEM 1 Draw curved arrows to show the movement of the electrons as the bond breaks.

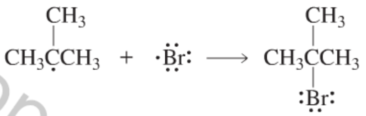
a. $CH_3CH_2—\ddot{\underset{\cdot\cdot}{Cl}}: \longrightarrow CH_3\dot{C}H_2 + \cdot\ddot{\underset{\cdot\cdot}{Cl}}:$

c. $CH_3\ddot{\underset{\cdot\cdot}{O}}—\ddot{\underset{\cdot\cdot}{O}}CH_3 \longrightarrow CH_3\ddot{\underset{\cdot\cdot}{O}}\cdot + \cdot\ddot{\underset{\cdot\cdot}{O}}CH_3$

b. 

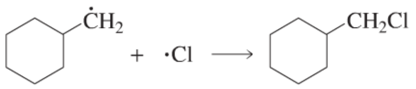
PROBLEM 2 Draw curved arrows to show the movement of the electrons as the bond forms.

a.



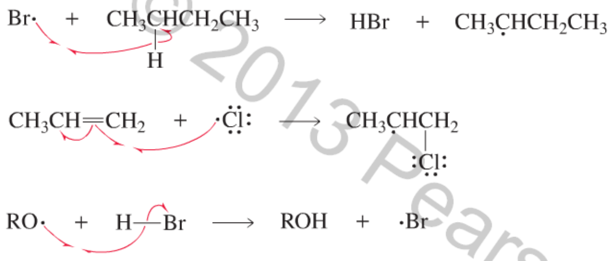
$CH_3\overset{CH_3}{\underset{\cdot}{C}}CH_3 + \cdot\ddot{Br}: \longrightarrow CH_3\overset{CH_3}{\underset{:Br:}{C}}CH_3$

c.



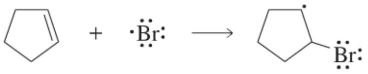
b. $\cdot Br + \cdot Br \longrightarrow Br_2$

Often one bond breaks and another bond forms in the same step.



PROBLEM 3 Draw curved arrows to show the movement of the electrons as one (or more) bond breaks and another bond forms.

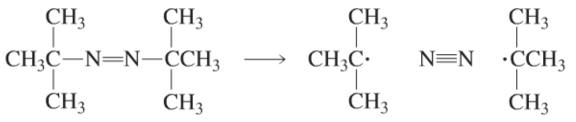
a.



b. $CH_3\underset{\cdot}{C}HCH_2CH_3 + H{-}Cl \longrightarrow CH_3CH_2CH_2CH_3 + \cdot Cl$

c. $CH_3\dot{C}H_2 + Br{-}Br \longrightarrow CH_3CH_2Br + \cdot Br$

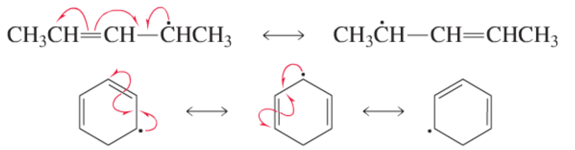
d.



$CH_3\overset{CH_3}{\underset{CH_3}{C}}{-}N{=}N{-}\overset{CH_3}{\underset{CH_3}{C}}CH_3 \longrightarrow CH_3\overset{CH_3}{\underset{CH_3}{C}}\cdot \quad N{\equiv}N \quad \cdot\overset{CH_3}{\underset{CH_3}{C}}CH_3$

DRAWING CURVED ARROWS IN CONTRIBUTING RESONANCE STRUCTURES THAT ARE RADICALS

The arrows that represent electron movement in resonance contributors of radicals have only one barb on the arrowhead because the arrow represents the movement of only one electron.



PROBLEM 4 Draw curved arrows to show the movement of the electrons as one resonance contributor is converted to the next.

a.

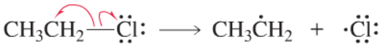

b.

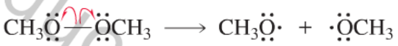

c.

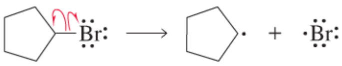

d.


ANSWERS TO PROBLEMS ON DRAWING CURVED ARROWS IN RADICAL SYSTEMS

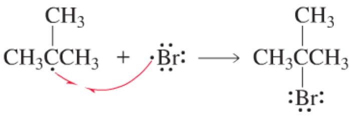
PROBLEM 1

a.


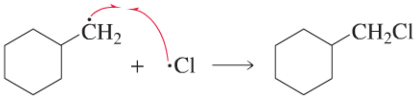
c.


b.


PROBLEM 2

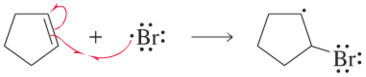
a.


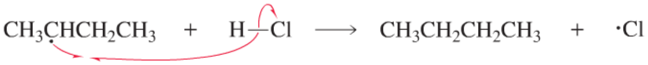
$$CH_3\overset{CH_3}{\dot{C}}CH_3 + \cdot Br \longrightarrow CH_3\overset{CH_3}{\underset{Br}{C}}CH_3$$

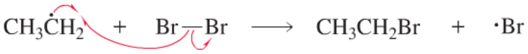
c.


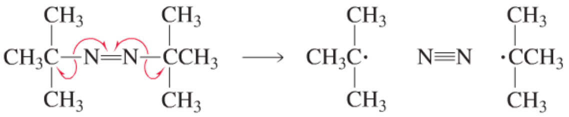
b.


PROBLEM 3

a.


b.


c.


d.


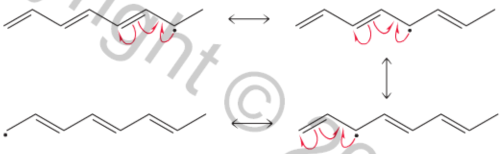
$$CH_3\underset{CH_3}{\overset{CH_3}{C}}—N=N—\underset{CH_3}{\overset{CH_3}{C}}CH_3 \longrightarrow CH_3\underset{CH_3}{\overset{CH_3}{C}}\cdot \quad N\equiv N \quad \cdot\underset{CH_3}{\overset{CH_3}{C}}CH_3$$

PROBLEM 4

a.

b.

c.



d.