

# Organic Chemistry, *Fourth Edition*

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## Chapter 15 Lecture Outline

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The University of Illinois - Springfield

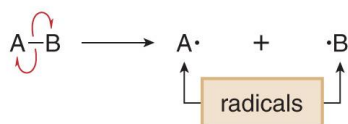
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### Radicals

- A small but significant group of reactions involve radical intermediates.
- A **radical** is a reactive intermediate with a single unpaired electron, formed by homolysis of a covalent bond.
- A radical contains an atom that does not have an octet of electrons.
- **Half-headed arrows** are used to show the movement of electrons in radical processes.

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## Structure of Radicals

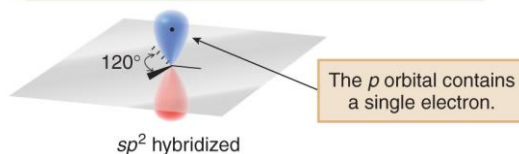
- Carbon radicals are classified as 1°, 2°, or 3°.
- A carbon radical is  $sp^2$  hybridized and trigonal planar, like carbocations.
- The unhybridized  $p$  orbital contains the unpaired electron and extends above and below the trigonal planar carbon.

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### Classification of carbon radicals



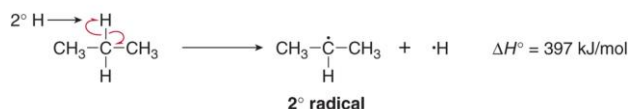
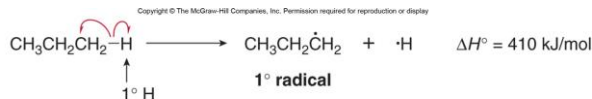
### The trigonal planar geometry of a carbon radical



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## Bond Dissociation Energies

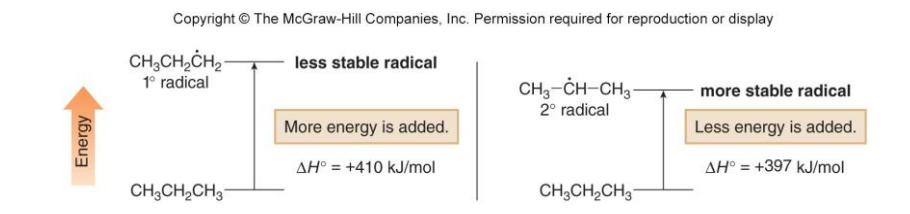
- **Bond dissociation energies** for the cleavage of C—H bonds are used to measure stability.
- They are determined by calculating the energy needed to break the bond into two radicals.
- Cleaving a stronger bond requires more energy.
- In the example below, the 2° radical is more stable than the 1° radical because less energy is required to produce it.



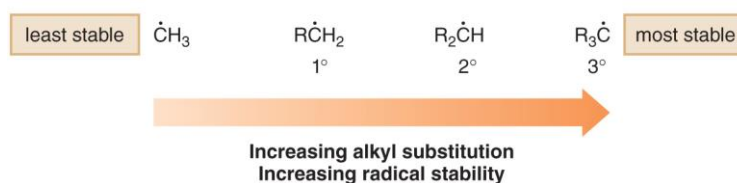
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# Stability of Radicals

Figure 15.1  
The relative stability of 1° and 2° carbon radicals



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## General Features of Radical Reactions

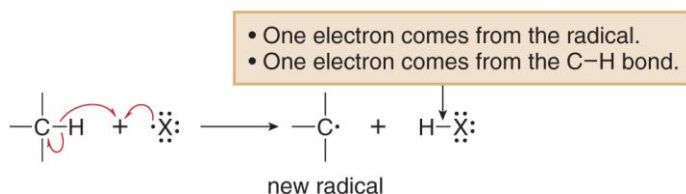
- Radicals are formed from covalent bonds by adding energy in the form of heat ( $\Delta$ ) or light ( $h\nu$ ).
- Some radical reactions are carried out in the presence of a radical initiator.
- Radical initiators, such as peroxides of general structure, RO-OR, contain an especially weak bond that serves as a source of radicals.
- Heating a peroxide readily causes homolysis of the weak O-O bond, forming two RO• radicals.
- Radicals undergo two main types of reactions—they react with  $\sigma$  bonds, and they add to  $\pi$  bonds.

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## Reaction of a Radical X• with a C–H Bond

- A radical X•, once formed, rapidly reacts with whatever is available, usually a stable  $\sigma$  or  $\pi$  bond.
- A radical X• abstracts a hydrogen atom from a C–H  $\sigma$  bond to form H–X and a carbon radical.

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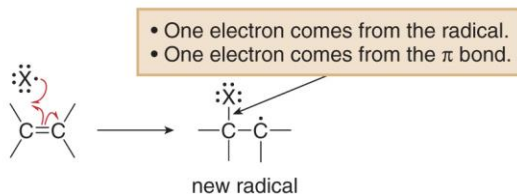


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## Reaction of a Radical X• with a C=C Bond

- A radical X• can also add to the  $\pi$  bond of a carbon–carbon double bond.

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- In either type of radical reaction (with a  $\sigma$  or  $\pi$  bond) a new radical is created.

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## Inhibition of Radicals by Molecular Oxygen

- Occasionally, two radicals react to form a sigma bond.
- An example is the reaction of a radical with oxygen (a diradical in its ground state electronic configuration).

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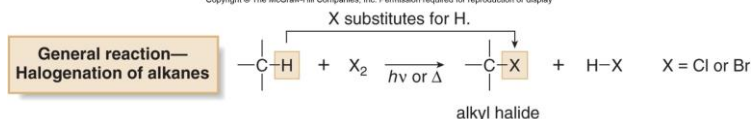
- Reaction with oxygen causes the reaction to slow down or stop, as X-O-O· radicals are not as reactive as halogen radicals.
- Compounds that prevent radical reactions from occurring are called **radical inhibitors** or **radical scavengers**.

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## Radical Halogenation of Alkanes

- In the presence of heat or light, alkanes react with halogens to form alkyl halides by a radical substitution reaction.
- Halogenation of alkanes is only useful with Cl<sub>2</sub> or Br<sub>2</sub>.
- Reaction with F<sub>2</sub> is too violent, and reaction with I<sub>2</sub> is too slow to be useful.

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## Halogenation of Alkanes—Mechanism

- Three facts about halogenation suggest that the mechanism involves radical, not ionic, intermediates:

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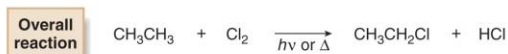
Fact	Explanation
[1] Light, heat, or added peroxide is necessary for the reaction.	<ul style="list-style-type: none"><li>• Light or heat provides the energy needed for homolytic bond cleavage to form radicals. Breaking the weak O–O bond of peroxides initiates radical reactions as well.</li></ul>
[2] O <sub>2</sub> inhibits the reaction.	<ul style="list-style-type: none"><li>• The diradical O<sub>2</sub> removes radicals from a reaction mixture, thus preventing reaction.</li></ul>
[3] No rearrangements are observed.	<ul style="list-style-type: none"><li>• Radicals do not rearrange.</li></ul>

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## Common Steps of Radical Reactions

- Radical halogenation has three distinct steps:

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- *Initiation:* Two radicals are formed by homolysis of a  $\sigma$  bond and this begins the reaction.
- *Propagation:* A radical reacts with another reactant to form a new  $\sigma$  bond and another radical.
- *Termination:* Two radicals combine to form a stable bond. Removing radicals from the reaction mixture without generating any new radicals stops the reaction.

- This type of mechanism that involves two or more repeating steps is called a **chain mechanism**.
- The most important steps of any chain mechanism including radical halogenation are the **propagation steps** which lead to product formation.

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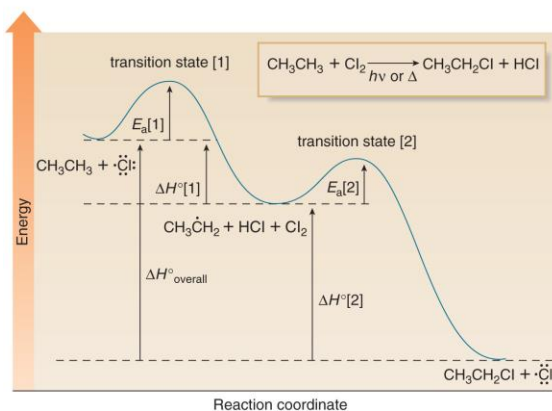


# Energy Diagram for Radical Propagation

Figure 15.4

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- Because radical halogenation consists of two propagation steps, the energy diagram has two energy barriers.
- The first step is rate-determining because its transition state is at higher energy.
- The reaction is exothermic because  $\Delta H^\circ_{\text{overall}}$  is negative.

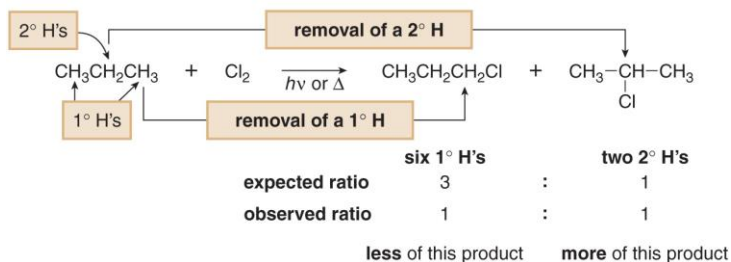


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## Product Mixture in Radical Chlorination

- Chlorination of  $\text{CH}_3\text{CH}_2\text{CH}_3$  affords a 1:1 mixture of  $\text{CH}_3\text{CH}_2\text{CH}_2\text{Cl}$  and  $(\text{CH}_3)_2\text{CHCl}$ .
- $\text{CH}_3\text{CH}_2\text{CH}_3$  has six  $1^\circ$  hydrogens and only two  $2^\circ$  hydrogens, so the expected product ratio of  $\text{CH}_3\text{CH}_2\text{CH}_2\text{Cl}$  to  $(\text{CH}_3)_2\text{CHCl}$  (assuming all hydrogens are equally reactive) is 3:1.

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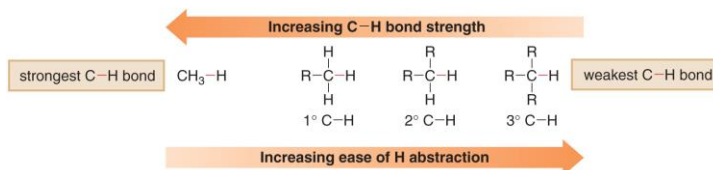
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## Radical Halogenation of Alkanes

- Since the observed ratio between  $\text{CH}_3\text{CH}_2\text{CH}_2\text{Cl}$  and  $(\text{CH}_3)_2\text{CHCl}$  is 1:1, the  $2^\circ$  C–H bonds must be more reactive than the  $1^\circ$  C–H bonds.

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- The weaker the C–H bond, the more readily the hydrogen atom is removed in radical halogenation.



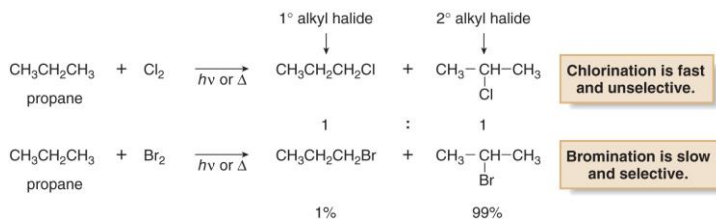
- Thus, when alkanes react with  $\text{Cl}_2$ , a mixture of products results, with more product formed by cleavage of the weaker C–H bond than you would expect on statistical grounds.

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## Chlorination vs Bromination

- Although alkanes undergo radical substitutions with both  $\text{Cl}_2$  and  $\text{Br}_2$ , chlorination and bromination exhibit two important differences.
  1. Chlorination is faster than bromination.
  2. Chlorination is unselective, yielding a mixture of products, but bromination is more selective, often yielding one major product.

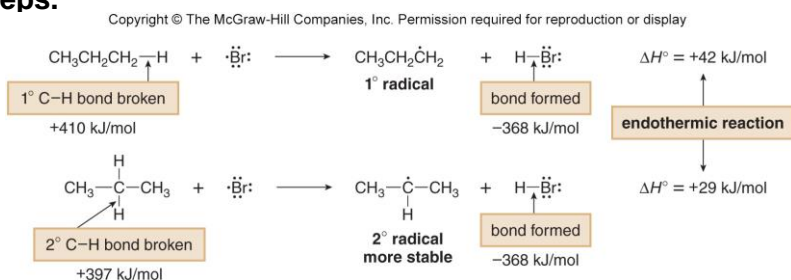
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## Energy of Halogenation

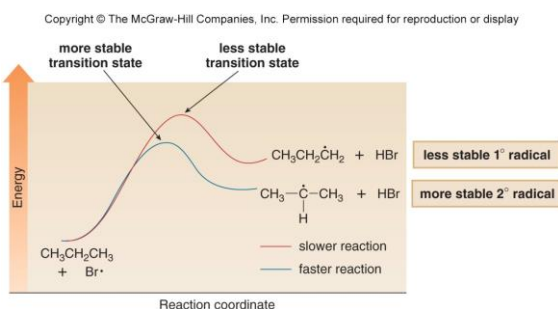
- The differences in chlorination and bromination can be explained by considering the relative energetics of their key propagation steps.
- Calculating  $\Delta H^\circ$  using bond dissociation energies reveals that abstraction of a  $1^\circ$  or  $2^\circ$  hydrogen by  $\text{Br}\cdot$  is endothermic.
- However, it takes less energy to form the more stable  $2^\circ$  radical, and this difference is more important in endothermic steps.



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## Energy Diagram for Endothermic Reaction—Bromination

Figure 15.5

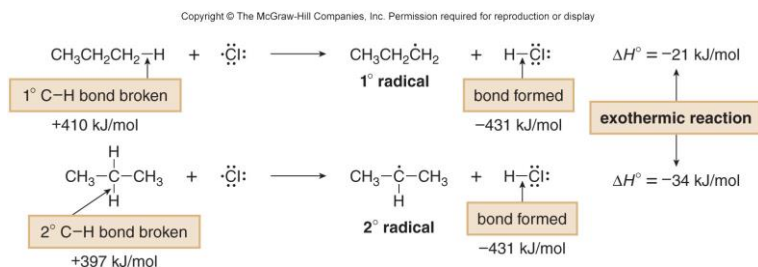


- The transition state to form the less stable  $1^\circ$  radical ( $\text{CH}_3\text{CH}_2\dot{\text{C}}\text{H}_2$ ) is higher in energy than the transition state to form the more stable  $2^\circ$  radical [ $(\text{CH}_3)_2\dot{\text{C}}\text{H}$ ]. Thus, **the  $2^\circ$  radical is formed faster.**
- **Because the rate-determining step is endothermic, the transition state resembles the products.**
- **The more stable radical is formed faster, and often a single radical halogenation product predominates.**

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## Energy of Radical Formation

- Calculating  $\Delta H^\circ$  using bond dissociation energies for chlorination reveals that abstraction of a  $1^\circ$  or  $2^\circ$  hydrogen by  $\text{Cl}\cdot$  is exothermic.

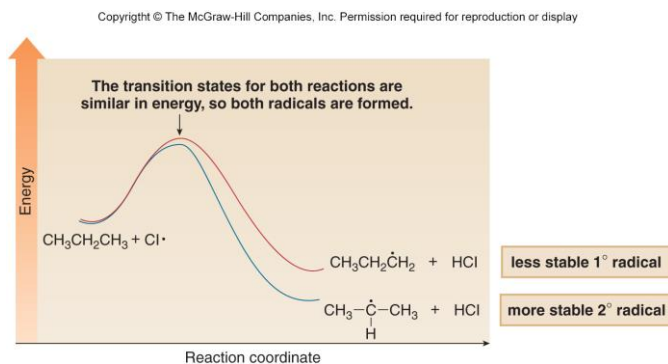


- Since chlorination has an exothermic rate-determining step, the transition state to form both radicals resembles the same starting material,  $\text{CH}_3\text{CH}_2\text{CH}_3$ .
- Thus, the relative stability of the two radicals is much less important, and both radicals are formed.

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## Energy Diagram for Exothermic Reaction—Chlorination

Figure 15.6



- Because the rate-determining step in chlorination is exothermic, the transition state resembles the starting material, both radicals are formed, and a mixture of products results.

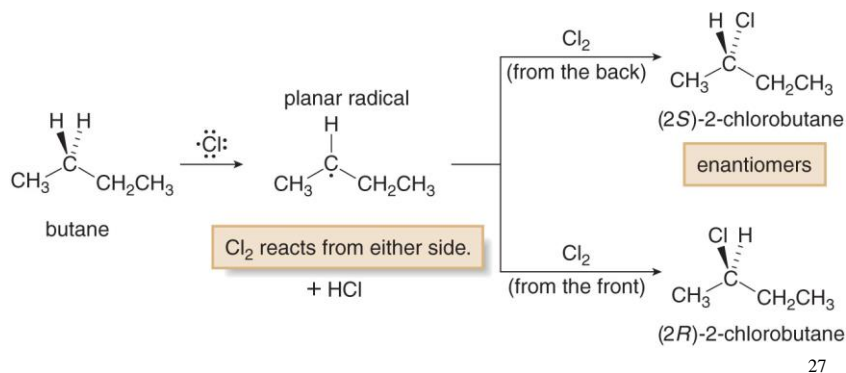
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## Racemates from Achiral Starting Material

- A racemic mixture results because the first propagation step generates a planar  $sp^2$  hybridized radical.
- $\text{Cl}_2$  then reacts with it from either side to form an equal amount of two enantiomers.

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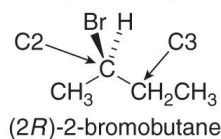


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## Stereochemistry from Chiral Starting Material

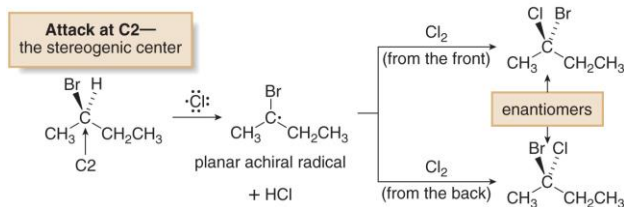
### Chlorination at the Chiral Center

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- Chlorination at C2 occurs at the stereogenic center.

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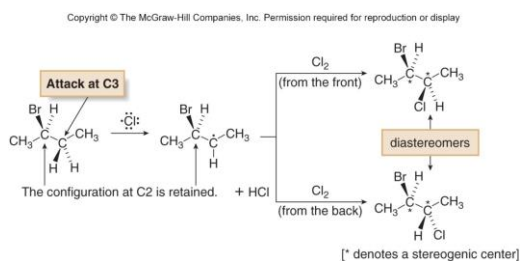
- Radical halogenation reactions at a stereogenic center occur with racemization.

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# Stereochemistry from Chiral Starting Material

## Chlorination Away from the Chiral Center

- Chlorination at C3 does not occur at the stereogenic center, but forms a new stereogenic center.
- Since no bond is broken to the stereogenic center at C2, its configuration is retained during the reaction.
- The trigonal planar  $sp^2$  hybridized radical is attacked from either side by  $Cl_2$ , forming a new stereogenic center.
- A pair of diastereomers is formed.



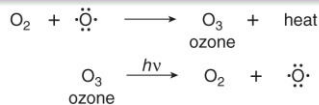
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## The Ozone Layer and CFCs

- Ozone is vital to life, and acts as a shield, protecting the earth's surface from harmful UV radiation.

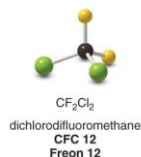
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### The synthesis and decomposition of O<sub>3</sub> in the upper atmosphere



- Current research suggests that **chlorofluorocarbons (CFCs)**, used extensively as refrigerants and propellants, are responsible for destroying ozone in the upper atmosphere.

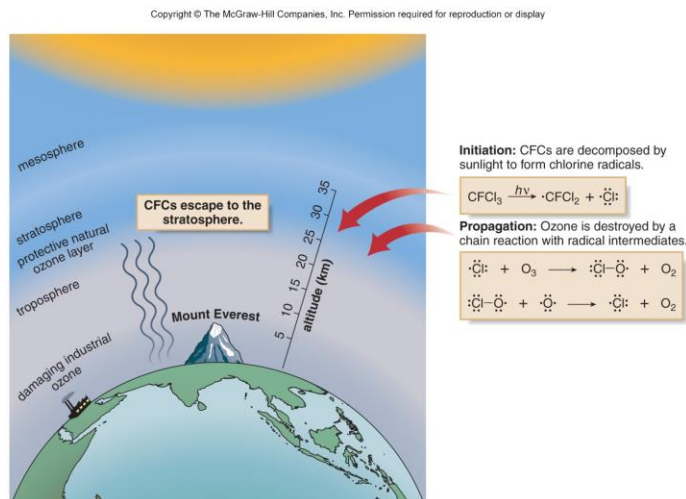
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# CFCs and the Destruction of the Ozone Layer

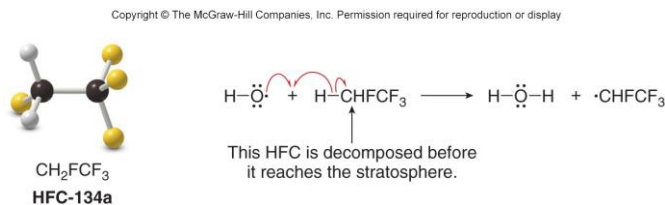
Figure 15.7



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## Alternatives to CFCs

- The overall result is that  $\text{O}_3$  is consumed as a reactant and  $\text{O}_2$  is formed.
- In this way, a small amount of CFC can destroy a large amount of  $\text{O}_3$ .
- New alternatives to CFCs are **hydrochlorofluorocarbons (HCFCs)** and **hydrofluorocarbons (HFCs)** such as  $\text{CH}_2\text{FCF}_3$ .
- These compounds are decomposed by  $\text{HO}\cdot$  before they reach the stratosphere and therefore, they do not take part in the radical reactions resulting in  $\text{O}_3$  destruction.

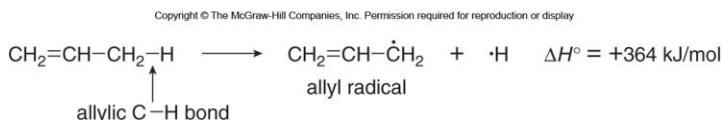


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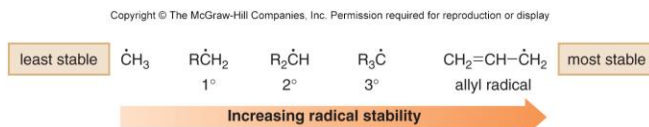


## Radical Halogenation at an Allylic Carbon

- An **allylic carbon** is a carbon adjacent to a double bond.
- Homolysis of the allylic C–H bond in propene generates an **allylic radical** which has an unpaired electron on the carbon adjacent to the double bond.



- The bond dissociation energy for this process is even less than that for a 3° C–H bond (91 kcal/mol).
- This means that an allyl radical is more stable than a 3° radical.

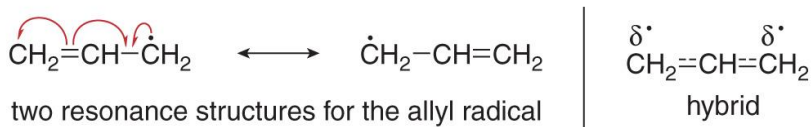


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## Stability of Allyl Radicals

- The allyl radical is more stable than other radicals because the  $\pi$  bond and the unpaired electron are delocalized.
- The “true” structure of the allyl radical is a hybrid of the two resonance structures.
- Delocalizing electron density lowers the energy of the hybrid, thus stabilizing the allyl radical.

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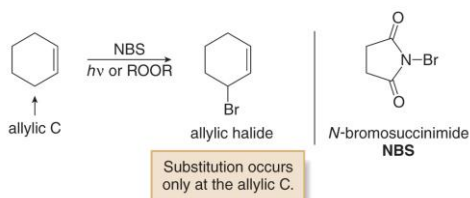


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## NBS—a Radical Bromination Reagent

- Because allylic C–H bonds are weaker than other  $sp^3$  hybridized C–H bonds, the allylic carbon can be selectively halogenated using NBS in the presence of light or peroxides.

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- NBS contains a weak N–Br bond that is homolytically cleaved with light to generate a bromine radical, initiating an allylic halogenation reaction.
- Propagation then consists of the usual two steps of radical halogenation.

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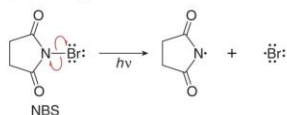
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### Mechanism 15.2 Allylic Bromination with NBS

#### Initiation

**Step [1]** Cleavage of the N–Br bond forms two radicals.



- The reaction begins with homolysis of the weak N–Br bond in NBS using light energy. This generates a  $Br\cdot$  radical that begins the radical halogenation process.

#### Propagation

**Steps [2] and [3]** One radical reacts and a new radical is formed in each step.



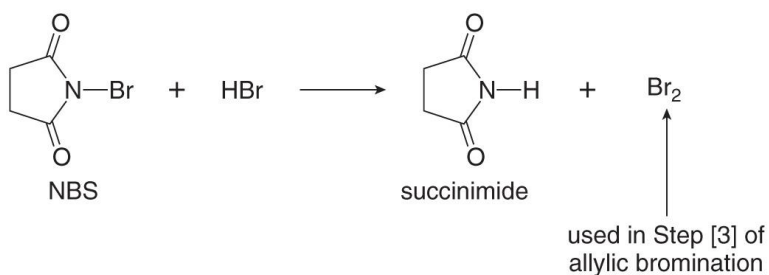
- The  $Br\cdot$  radical abstracts an allylic hydrogen atom to afford an allylic radical in Step [2]. (Only one Lewis structure of the allylic radical is drawn.)
- The allylic radical reacts with  $Br_2$  in the second propagation step to form the product of allylic halogenation. Because the  $Br\cdot$  radical formed in Step [3] is also a reactant in Step [2], Steps [2] and [3] repeatedly occur without the need for Step [1].

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## Formation of Bromine from NBS

- The HBr formed in Step [2] reacts with NBS to form a low concentration of  $\text{Br}_2$ .
- This is then used for halogenation in Step [3] of the mechanism.

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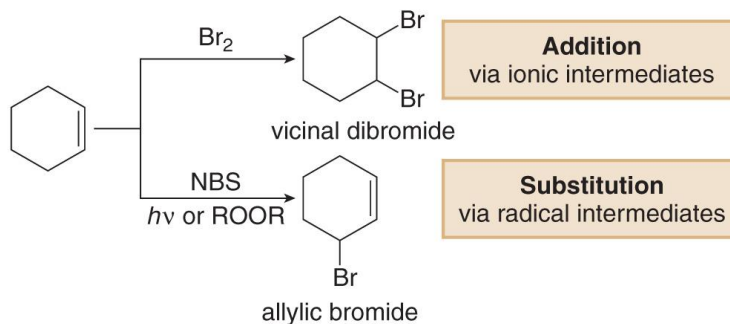


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## Radical vs Ionic Bromination

- An alkene with allylic C–H bonds undergoes two different reactions depending on the reaction conditions.
  - **Addition and Substitution**

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## Why NBS Favors Substitution Over Addition

A low concentration of  $\text{Br}_2$  (from NBS) favors allylic substitution over ionic addition to form the dibromide.

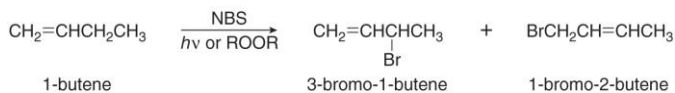
- The  $\text{Br}_2$  produced from NBS, present in very low concentrations, must first react with the double bond to form the bridged bromonium ion.
- The bridged bromonium ion must then react with more bromine (in the form of  $\text{Br}^-$ ) in a second step to form the dibromide.
- If concentrations of both intermediates—the bromonium ion and  $\text{Br}^-$  are low (as is the case here), the overall rate of addition is very slow, and the products of the very fast and facile radical chain reaction predominate.

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## Regiochemistry of Allylic Halogenation

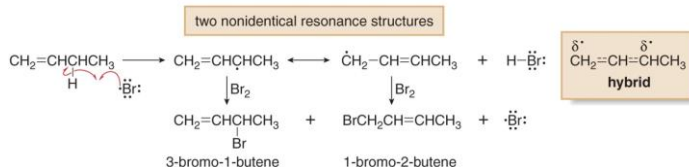
- Halogenation at an allylic carbon often results in a mixture of products.

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- A mixture results because the reaction proceeds by way of a resonance-stabilized radical.

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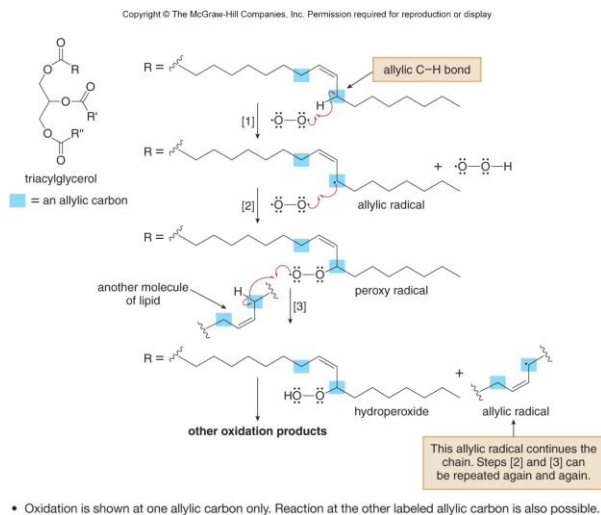


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# Oxidation of Unsaturated Lipids

- Oils are susceptible to allylic free radical oxidation.

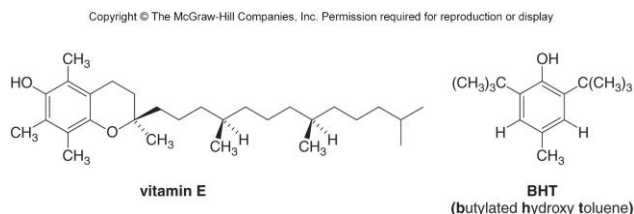
Figure 15.8



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## Antioxidants

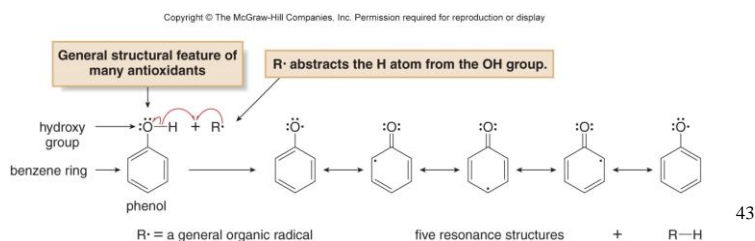
- An **antioxidant** is a compound that stops an oxidation reaction from occurring.
- Naturally occurring antioxidants such as vitamin E prevent radical reactions that can cause cell damage.
- Synthetic antioxidants such as **BHT—butylated hydroxy toluene**—are added to packaged and prepared foods to prevent oxidation and spoilage.
- Vitamin E and BHT are radical inhibitors, which terminate radical chain mechanisms by reacting with the radical.



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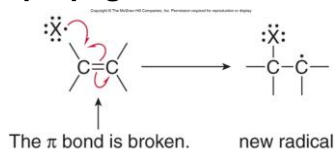
## Mechanism of Antioxidant Behavior

- To trap free radicals, both vitamin E and BHT use a hydroxy group bonded to a benzene ring—a general structure called a **phenol**.
- Radicals (R•) abstract a hydrogen atom from the OH group of an antioxidant, forming a new resonance-stabilized radical.
- This new radical does not participate in chain propagation, but rather terminates the chain and halts the oxidation process.
- Because oxidative damage to lipids in cells is thought to play a role in the aging process, many antiaging formulations contain antioxidants.

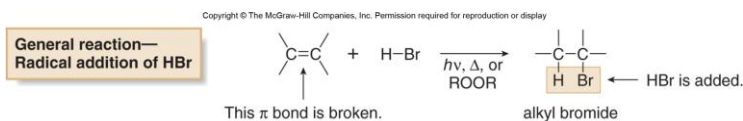


## General Radical Additions to Alkenes

- Electron rich alkenes react with electron deficient radicals.
- Radicals react with alkenes via radical chain mechanisms consisting of:
  - Initiation, propagation and termination steps



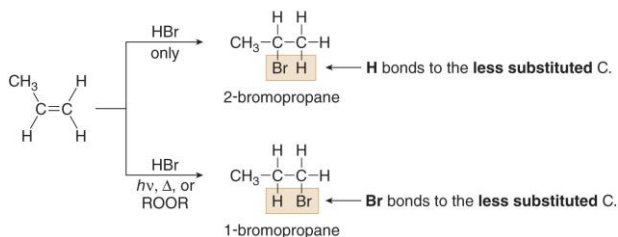
- HBr adds to alkenes to form alkyl bromides in the presence of heat, light, or peroxides.



# Radical Additions to Alkenes

- The regioselectivity of the addition to unsymmetrical alkenes is different from that for addition of HBr in the absence of heat, light, or peroxides.

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- The addition of HBr to alkenes in the presence of heat, light, or peroxides proceeds via a radical mechanism.

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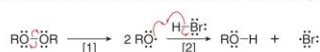
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## Mechanism 15.3 Radical Addition of HBr to an Alkene

### Initiation

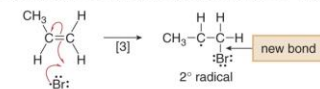
Steps [1] and [2] Abstraction of H from HBr occurs by a two-step process.



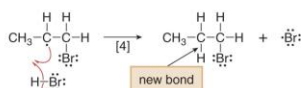
- With ROOR to initiate the reaction, two steps are needed to form Br·. Homolysis of the weak O–O bond of the peroxide forms RO·, which abstracts a hydrogen atom from HBr to form Br·.

### Propagation

Steps [3] and [4] The  $\pi$  bond is broken and the C–H and C–Br  $\sigma$  bonds are formed.



- The first step of propagation forms the C–Br bond when the Br· radical adds to the terminal carbon, leading to a 2° carbon radical.



- The 2° radical abstracts a H atom from HBr, forming the new C–H bond and completing the addition reaction. Because a new Br· radical is also formed in this step, Steps [3] and [4] occur repeatedly.

Repeat Steps [3], [4], [3], [4], and so forth.

### Termination

Step [5] Two radicals react to form a bond.



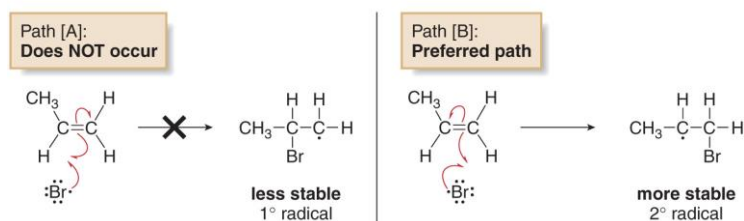
- To terminate the chain, two radicals (for example two Br· radicals) react with each other to form a stable bond, preventing further propagation via Steps [3] and [4].

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## Regiochemistry of Radical Addition to Alkenes

- In the first propagation step, the addition of  $\text{Br}\cdot$  to the double bond, there are two possible paths:
  1. Path [A] forms the less stable  $1^\circ$  radical.
  2. Path [B] forms the more stable  $2^\circ$  radical.
- The more stable  $2^\circ$  radical forms faster, so Path [B] is preferred.

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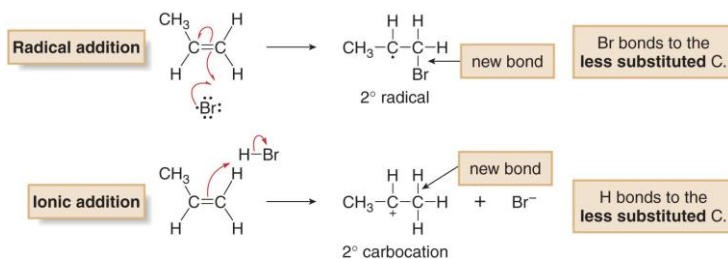


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## Radical vs Ionic Addition of HBr

- Depending on the reaction conditions, a different species initially reacts with the  $p$  bond accounting for the difference in regioselectivity.
  - Radical addition involves initial attack by a bromine radical.
  - Ionic addition involves initial attack by a proton.

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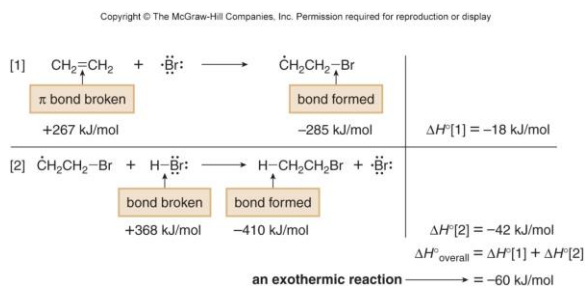
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## Energy Changes of Radical HBr Addition

- HBr adds to alkenes under radical conditions, but HCl and HI do not, due to differences in bond dissociation energies.
- Both propagation steps for HBr addition are exothermic, so propagation is exothermic (energetically favorable) overall.
- For addition of HCl or HI, one of the chain propagating steps is quite endothermic, and thus too difficult to be part of a repeating chain mechanism.

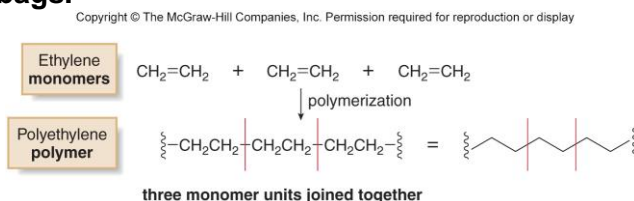
Figure 15.9



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## Polymers and Polymerization

- **Polymers** are large molecules made up of repeating units of smaller molecules called **monomers**.
- They include biologically important compounds such as proteins and carbohydrates, as well as synthetic plastics such as polyethylene, polyvinyl chloride (PVC) and polystyrene.
- **Polymerization** is the process of joining together of monomers to make polymers.
- For example, joining ethylene monomers together forms the polymer polyethylene, a plastic used in milk containers and plastic bags.

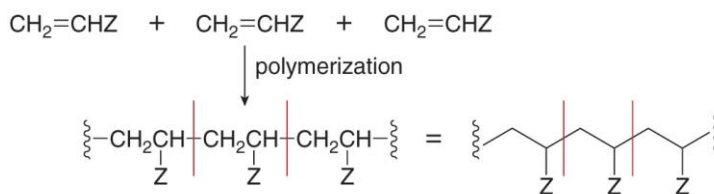


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## Polymers from Ethylene Derivatives

- Many ethylene derivatives having the general structure  $\text{CH}_2=\text{CHZ}$  are also used as monomers for polymerization.
- The identity of Z affects the physical properties of the resulting polymer.
- Polymerization of  $\text{CH}_2=\text{CHZ}$  usually affords polymers with Z groups on every other carbon atom in the chain.

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three monomer units joined together

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**Table 15.2** Common Monomers and Polymers Used in Medicine and Dentistry

Monomer	→	Polymer	Consumer product
$\text{CH}_2=\text{CHCl}$ vinyl chloride	→	 poly(vinyl chloride) PVC	 PVC blood bags and tubing
$\text{CH}_2=\text{CHCH}_3$ propene	→	 polypropylene	 polypropylene syringes
$\text{CF}_2=\text{CF}_2$ tetrafluoroethylene	→	 polytetrafluoroethylene Teflon	 dental floss

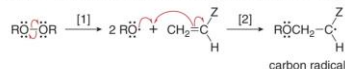
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### Mechanism 15.4 Radical Polymerization of $\text{CH}_2=\text{CHZ}$

#### Initiation

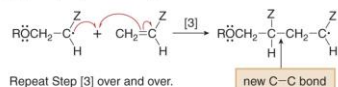
Steps [1] and [2] A carbon radical is formed by a two-step process.



- Chain initiation begins with homolysis of the weak O–O bond of the peroxide to form  $\text{RO}\cdot$ , which then adds to a molecule of monomer to form a carbon radical.

#### Propagation

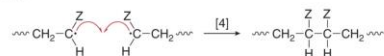
Step [3] The polymer chain grows.



- Chain propagation consists of a single step that joins monomer units together.
- In Step [3], the carbon radical formed during initiation adds to another alkene molecule to form a new C–C bond and another carbon radical. Addition always forms the more substituted carbon radical—that is, the **unpaired electron is always located on the carbon atom having the Z substituent**.
- This carbon radical reacts with more monomer, so that Step [3] occurs repeatedly, and the polymer chain grows.

#### Termination

Step [4] Two radicals combine to form a bond.



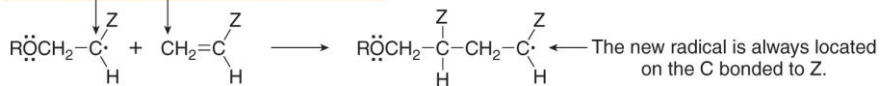
- To terminate the chain, two radicals combine to form a stable bond, thus ending the polymerization process.

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## Radical Polymerization

- In radical polymerization, the more substituted radical always adds to the less substituted end of the monomer, a process called **head-to-tail polymerization**.

The **more substituted radical** adds to the **less substituted end** of the double bond.



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