

Organic Chemistry Chapter 15: Radical Reactions

General Features of Radical Reactions

Two Common Reactions of Radicals

[1] Reaction of a Radical $X\cdot$ with a C – H Bond

A radical $X\cdot$ abstracts a hydrogen atom from a C – H σ bond to form H – X and a carbon radical.



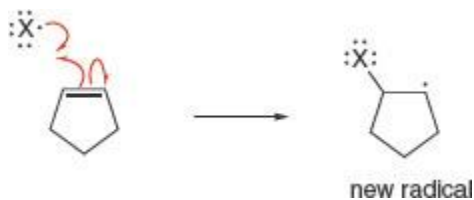
- One electron in H – X comes from the radical.
- One electron in H – X comes from the C – H bond.

This radical reaction is typically seen with the nonpolar C – H bonds of **alkanes**, which cannot react with polar or ionic electrophiles and nucleophiles.

[2] Reaction of a Radical $X\cdot$ with a C = C

A radical $X\cdot$ also adds to the π bond of a carbon—carbon double bond

Whenever a radical reacts with a stable single or double bond, a new radical is formed in the products.

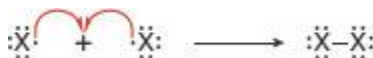


- One electron in C – X comes from the radical.
- One electron in C – X comes from the π bond.

Although the electron-rich double bond of an **alkene** reacts with electrophiles by ionic addition mechanisms, it also reacts with radicals because these reactive intermediates are also electron deficient.

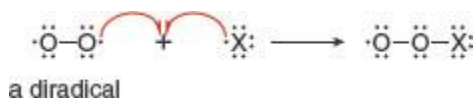
Two Radicals Reacting with Each Other

A radical, once formed, rapidly reacts with whatever is available. Usually that means a stable σ or π bond. Occasionally, however, two radicals come into contact with each other, and they react to form a σ bond.



- One electron in X – X comes from each radical.

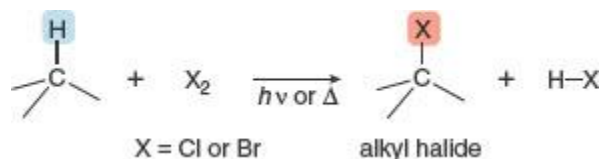
The reaction of a radical with oxygen, a diradical in its ground state electronic configuration, is another example of two radicals reacting with each other. In this case, the reaction of O_2 with $X\cdot$ forms a new radical, thus preventing $X\cdot$ from reacting with an organic substrate.



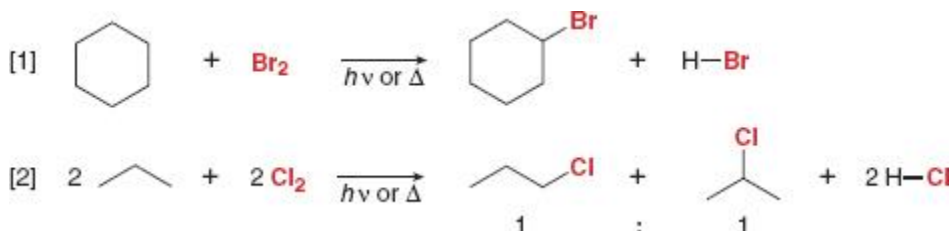
Compounds that prevent radical reactions from occurring are called *radical inhibitors* or *radical scavengers*.

Halogenation of Alkanes

In the presence of light or heat, alkanes react with halogens to form alkyl halides. Halogenation is a **radical substitution reaction**, because a halogen atom X replaces a hydrogen via a mechanism that involves radical intermediates.

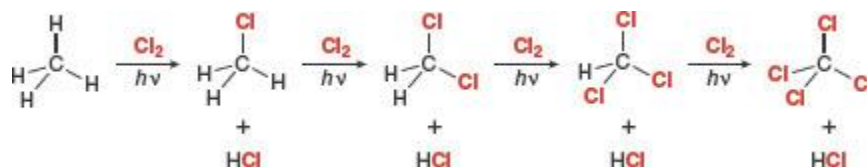


Halogenation of alkanes is useful only with Cl₂ and Br₂.



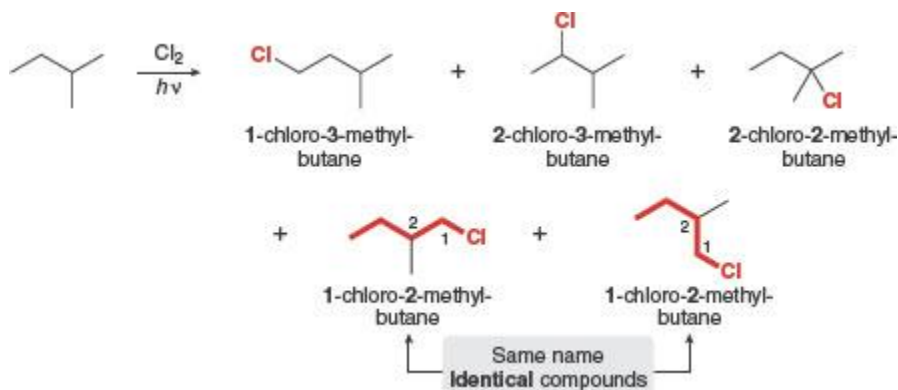
Monohalogenation—the substitution of a single H by X—can be achieved experimentally by adding halogen X₂ to an excess of alkane.

Complete halogenation of CH₄ using excess Cl₂



Sample Problem 15.1

Draw all the constitutional isomers formed by monohalogenation of (CH₃)₂CHCH₂CH₃ with Cl₂ and hν.



The Mechanism of Halogenation

Fact	Explanation
[1] Light, heat, or added peroxide is necessary for the reaction.	<ul style="list-style-type: none"> 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. The diradical O₂ removes radicals from a reaction

[2] O₂ inhibits the reaction.

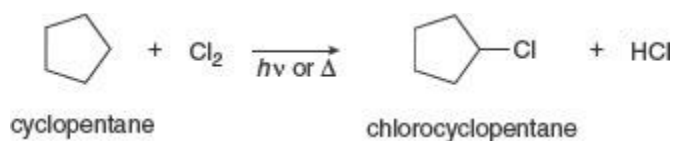
[3] No rearrangements are observed.

mixture, thus preventing reaction.

- Radicals do not rearrange.

The Steps of Radical Halogenation

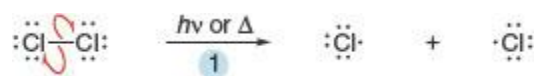
The chlorination of cyclopentane illustrates the **three distinct parts of radical halogenation** (Mechanism 15.1):



- **Initiation:** Two radicals are formed by homolysis of a σ bond and this begins the reaction.
- **Propagation:** A radical reacts with another reactant to form a new σ 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.

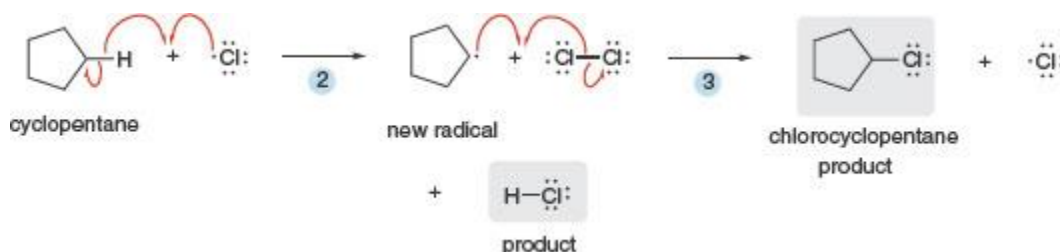
Mechanism 15.1 Radical Halogenation of Alkanes

Part [1] Initiation



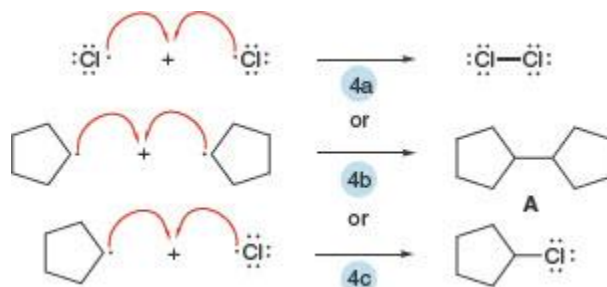
- **1** Bond cleavage forms two radicals. Homolysis of the weakest bond (Cl—Cl) requires light or heat and forms two chlorine radicals.

Part [2] Propagation



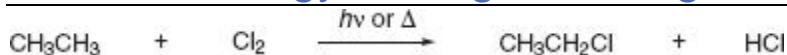
- **2** The Cl· radical abstracts a hydrogen from cyclopentane to form HCl (a reaction product) and a new carbon radical.
- **3** The carbon radical abstracts a chlorine atom from Cl₂ to form chlorocyclopentane (a reaction product) and Cl·. Because Cl· is a reactant in Step [2], Steps [2] and [3] can occur repeatedly without additional initiation (Step [1]).

Part [3] Termination

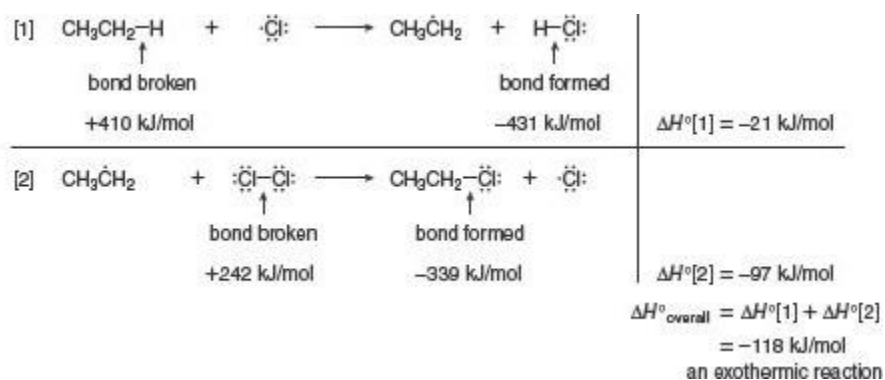


- **4** Termination of the chain occurs when any two radicals combine to form a bond.

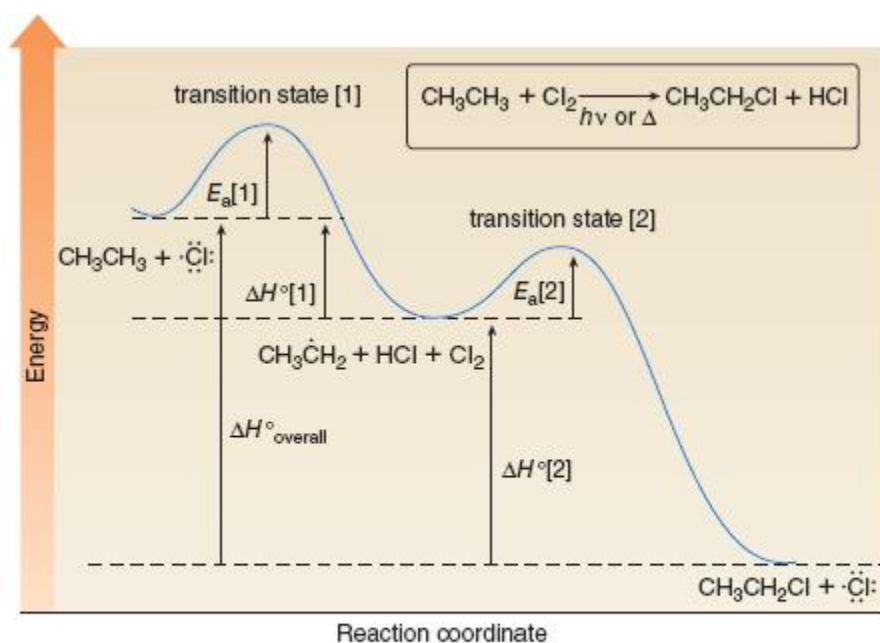
Energy Changes During the Chlorination of Ethane



Energy changes in the propagation steps during the chlorination of ethane

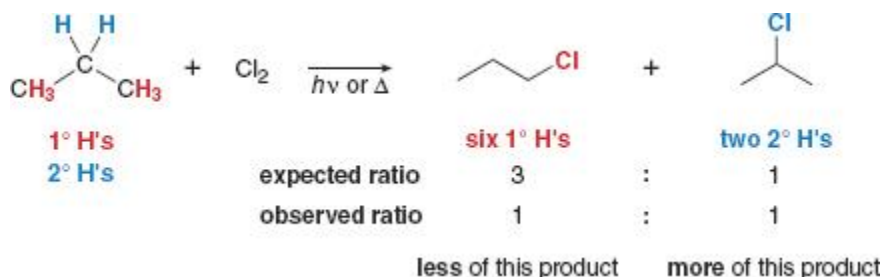


Energy diagram for the propagation steps in the chlorination of ethane

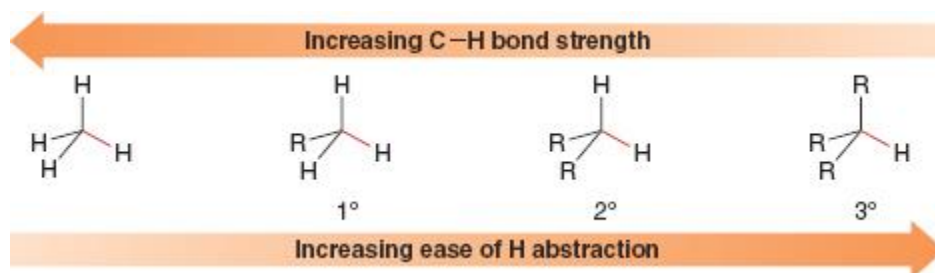


- Because radical halogenation consists of two propagation steps, the energy diagram has two energy barriers.
- The first step is rate-determining because its transition state is at higher energy.
- The reaction is exothermic because $\Delta H^\circ_{\text{overall}}$ is negative.

Chlorination of Other Alkanes

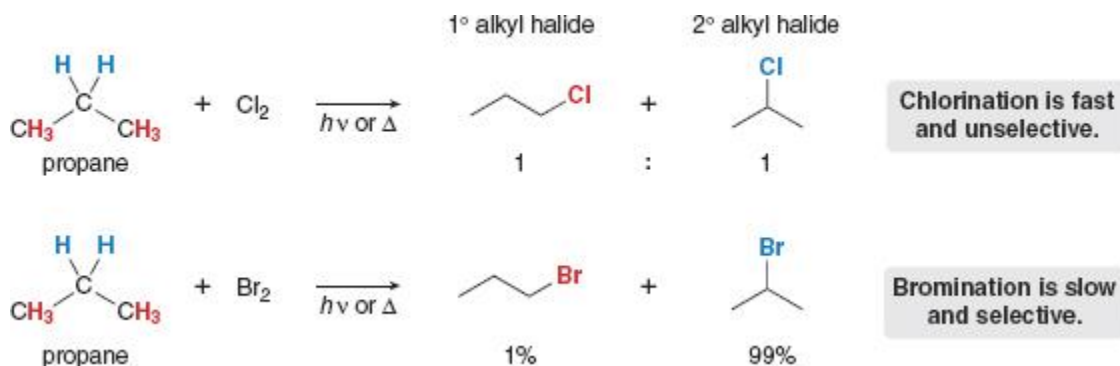


- The weaker the C – H bond, the more readily the hydrogen atom is removed in radical halogenation.



Chlorination Versus Bromination

- Chlorination is *faster* than bromination.
- Although chlorination is *unselective*, yielding a mixture of products, bromination is often *selective*, yielding one major product.

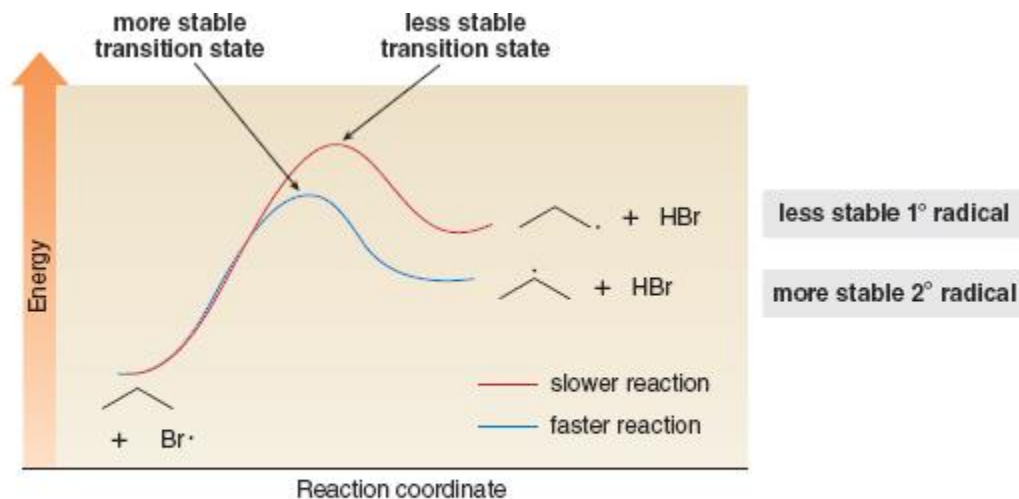
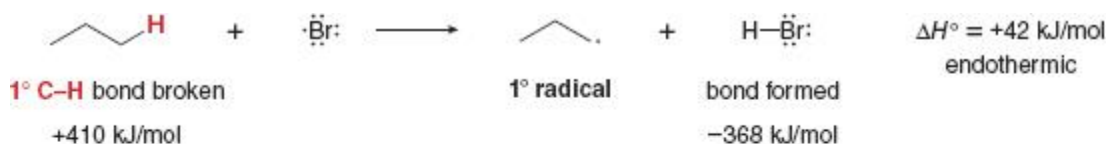


- In bromination, the major (and sometimes exclusive) product results from cleavage of the *weakest* C – H bond.

The rate-determining step in halogenation is the abstraction of a hydrogen atom by the halogen radical, so we must compare these steps for bromination and chlorination. Keep in mind:

- Transition states in endothermic reactions resemble the products. The more stable product is formed faster.
- Transition states in exothermic reactions resemble the starting materials. The relative stability of the products does not greatly affect the relative energy of the transition states, so a mixture of products often results.

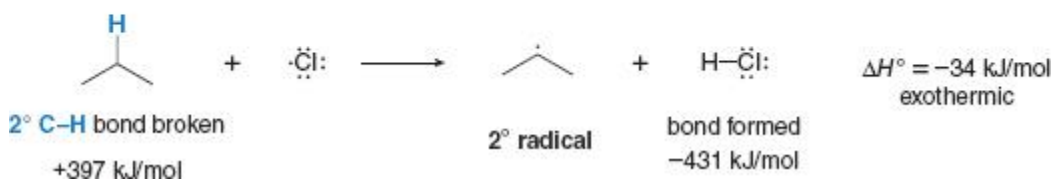
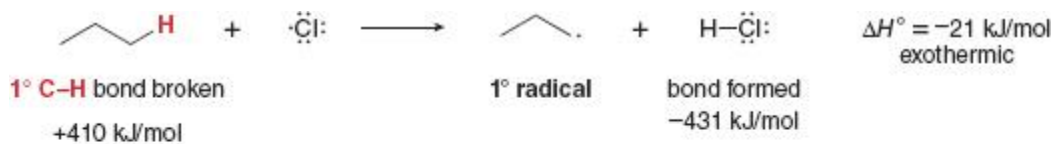
Bromination: $\text{CH}_3\text{CH}_2\text{CH}_3 + \text{Br}_2$



- The transition state to form the less stable 1° radical ($\text{CH}_3\text{CH}_2\text{CH}_2\cdot$) is higher in energy than the transition state to form the more stable 2° radical [$(\text{CH}_3)_2\dot{\text{C}}\text{H}$]. Thus, the 2° radical is formed faster.

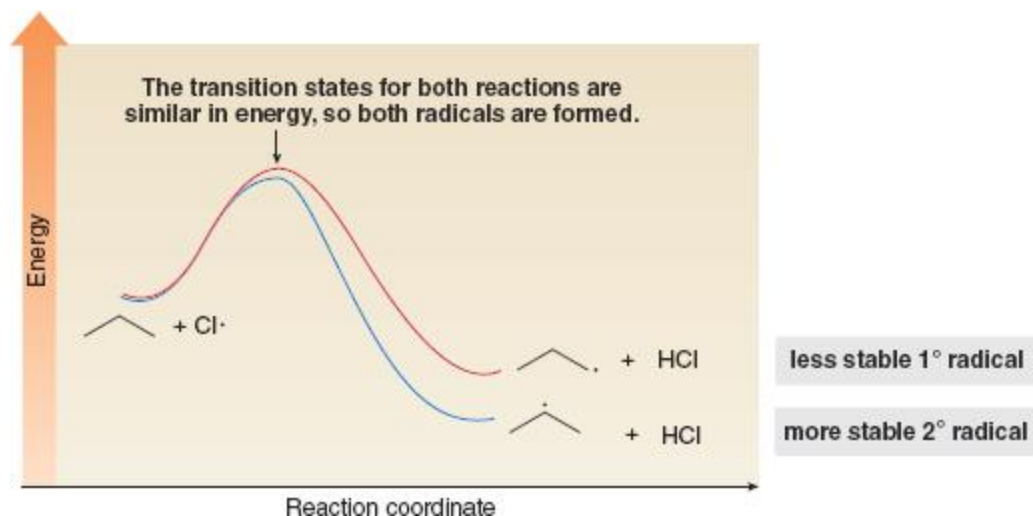
Conclusion: Because the rate-determining step in bromination is endothermic, the more stable radical is formed faster, and often a single radical halogenation product predominates.

Chlorination: $\text{CH}_3\text{CH}_2\text{CH}_3 + \text{Cl}_2$



Because the 1° and 2° radicals are converted to 1-chloropropane ($\text{CH}_3\text{CH}_2\text{CH}_2\text{Cl}$) and 2-chloropropane [$(\text{CH}_3)_2\text{CHCl}$], respectively, in the second propagation step, **both alkyl halides are formed in chlorination.**

Energy diagram for a nonselective exothermic reaction



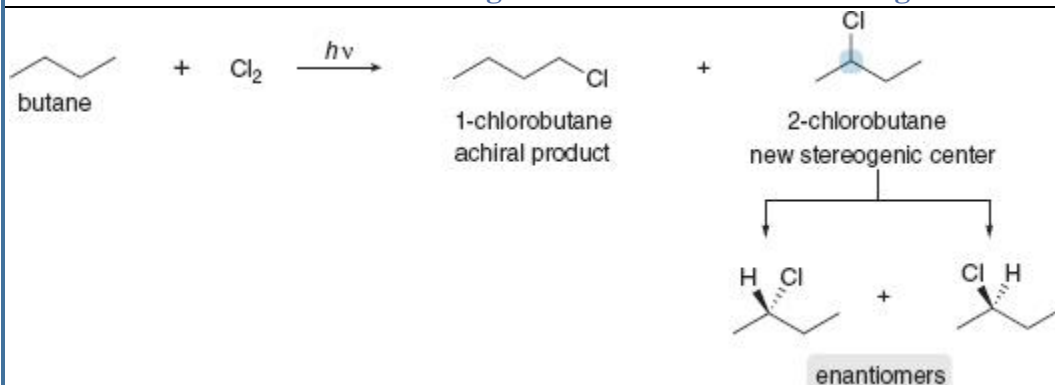
- **Conclusion:** Because the rate-determining step in chlorination is exothermic, the transition state resembles the starting material, both radicals are formed, and a mixture of products results.

The Stereochemistry of Halogenation Reactions

Table 15.1 Rules for Predicting the Stereochemistry of Reaction Products

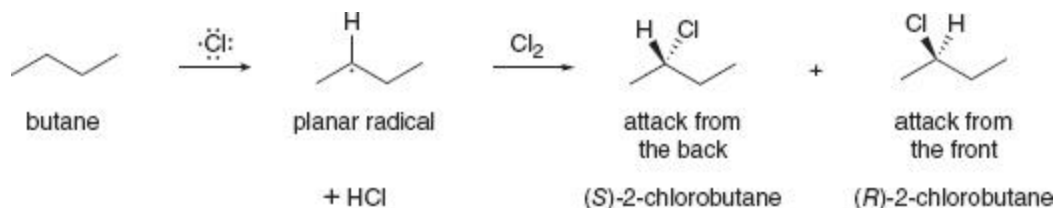
Starting material	Result
Achiral	<ul style="list-style-type: none"> • An achiral starting material always gives either an achiral or a racemic product.
Chiral	<ul style="list-style-type: none"> • If a reaction does not occur at a stereogenic center, the configuration at a stereogenic center is retained in the product. • If a reaction occurs at a stereogenic center, we must know the mechanism to predict the stereochemistry of the product.

Halogenation of an Achiral Starting Material

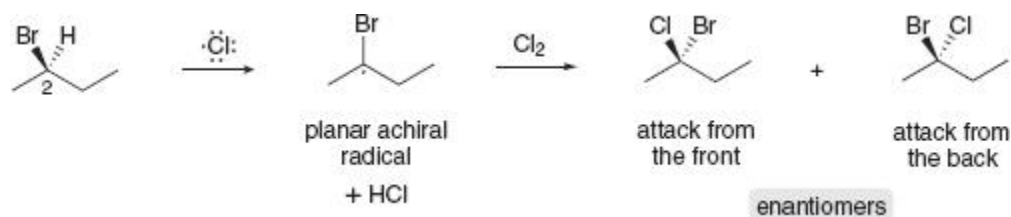


- 1-Chlorobutane (CH₃CH₂CH₂CH₂Cl) has no stereogenic center, so it is an **achiral** compound.
- 2-Chlorobutane [CH₃CH(Cl)CH₂CH₃] has a new stereogenic center, so an **equal amount of two enantiomers** must form—a **racemic mixture**.

- A racemic mixture results when a new stereogenic center is formed because the first propagation step generates a **planar, sp^2 hybridized radical**.
- Cl_2 then reacts with the planar radical from either the front or back side to form an equal amount of two enantiomers.

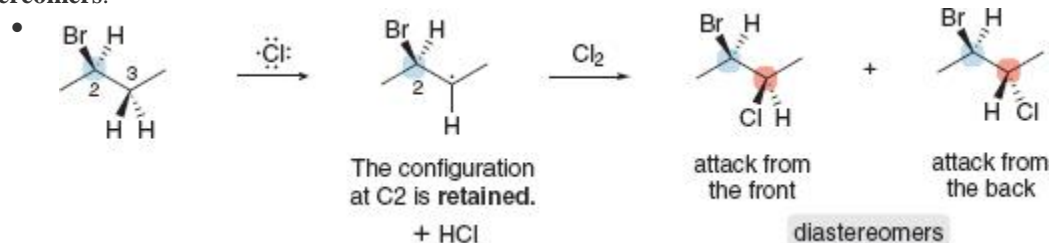


Halogenation of a Chiral Starting Material



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

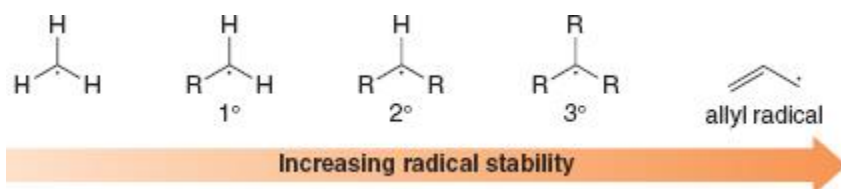
- **Chlorination at C3** does *not* occur at the stereogenic center, but it forms a new stereogenic center. Because no bond is broken to the stereogenic center at C2, **its configuration is retained** during the reaction.
- Abstraction of a hydrogen atom at C3 forms a trigonal planar sp^2 hybridized radical that still contains this stereogenic center.
- Reaction of the radical with Cl_2 from either side forms a new stereogenic center, so the products have two stereogenic centers: the configuration at C2 is the same in both compounds, but the configuration at C3 is different, making them **diastereomers**.



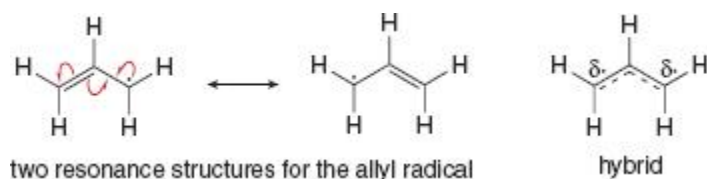
- Thus, four isomers are formed by chlorination of (R)-2-bromobutane at C2 and C3.
 - Attack at the stereogenic center (C2) gives a product with one stereogenic center, resulting in a mixture of enantiomers.
 - Attack at C3 forms a new stereogenic center, **giving a mixture of diastereomers**.

Radical Halogenation at an Allylic Carbon

- Allylic carbon—the carbon adjacent to a double bond.



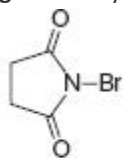
The position of the atoms and the σ bonds stays the same in drawing resonance structures. Resonance structures differ in the location of only π bonds and nonbonded electrons.



- The “true” structure of the allylic radical is a hybrid of the two resonance structures. In the hybrid, the π bond and the unpaired electron are delocalized.
- Delocalizing electron density lowers the energy of the hybrid, thus stabilizing the allylic radical.

Selective Bromination at Allylic C – H Bonds

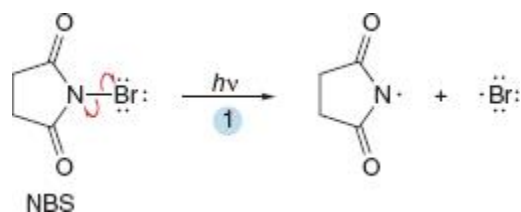
- Because allylic C – H bonds are weaker than other sp^3 hybridized C – H bonds, the **allylic carbon can be selectively halogenated** by using *N*-bromosuccinimide (**NBS**) in the presence of light or peroxides.



N-bromosuccinimide
NBS

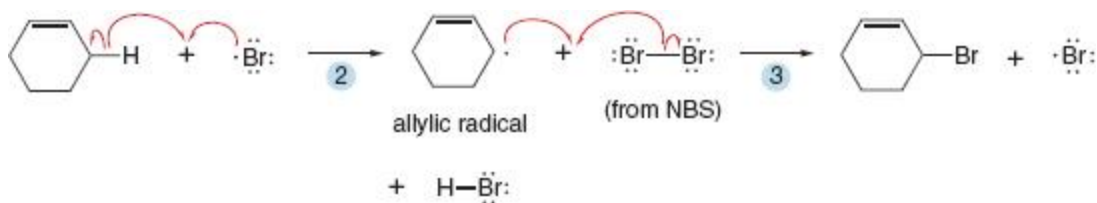
Mechanism 15.2 Allylic Bromination with NBS

Part [1] Initiation

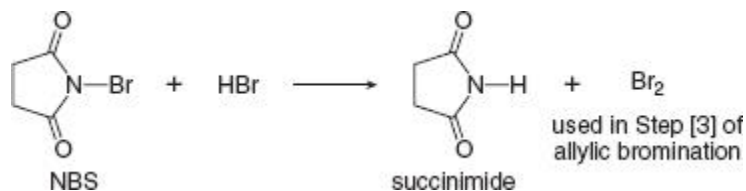


- 1 Homolysis of the weak N – Br bond with light energy forms a $\text{Br}\cdot$ radical that initiates radical halogenation.

Part [2] Propagation

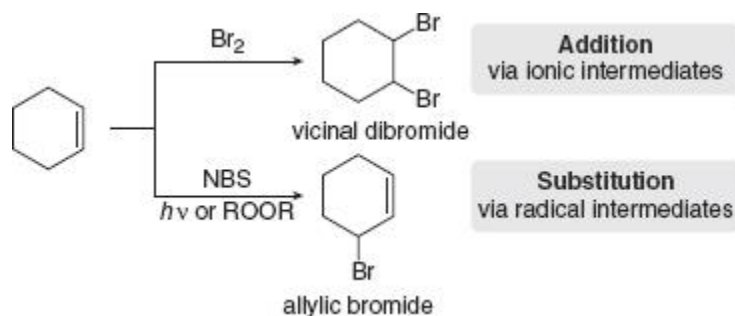


- **2** The Br• radical abstracts an allylic H to afford an allylic radical. (Only one resonance structure is drawn.)
- **3** The allylic radical reacts with Br₂ to form the allylic halide. The radical Br• formed in Step [3] can now react in Step [2], so Steps [2] and [3] can repeatedly occur without additional initiation.



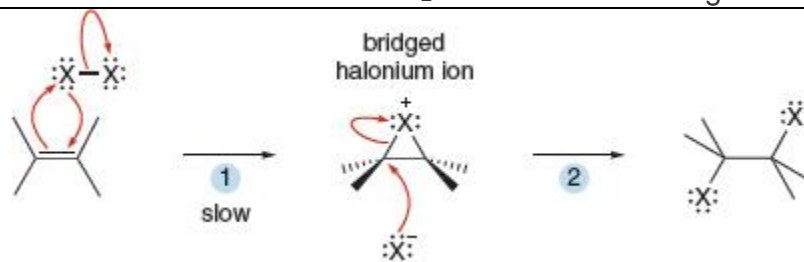
- A **low concentration of Br₂** (from NBS) **favors allylic substitution** (over addition) in part because bromine is needed for only *one* step of the mechanism.
- When Br₂ adds to a double bond, a low Br₂ concentration would first form a low concentration of bridged bromonium ion (Section 10.13), which must then react with more bromine (in the form of Br⁻) in a second step to form a dibromide.
- **If concentrations of both intermediates—bromonium ion and Br⁻—are low, the overall rate of addition is very slow.**

Thus, an alkene with allylic C – H bonds undergoes two different reactions depending on the reaction conditions.



- Treatment of cyclohexene with Br₂ (in an organic solvent like CCl₄) leads to **addition** via **ionic intermediates** (Section 10.13).
- Treatment of cyclohexene with NBS (+ *hν* or ROOR) leads to **allylic substitution**, via **radical intermediates**.

Mechanism 10.3 Addition of X₂ to an Alkene—Halogenation

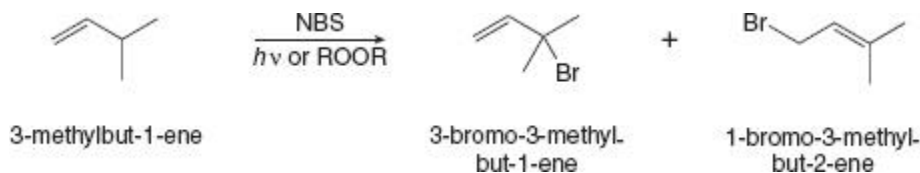


- **1** Four bonds are broken or formed to generate an unstable bridged halonium ion that contains a three-membered ring. The electron pair in the π bond and a lone pair on a halogen are used to form two new C – X bonds, and the X – X bond is cleaved.
- **2** Nucleophilic attack of X⁻ ring opens the bridged halonium ion and forms a new C – X bond.

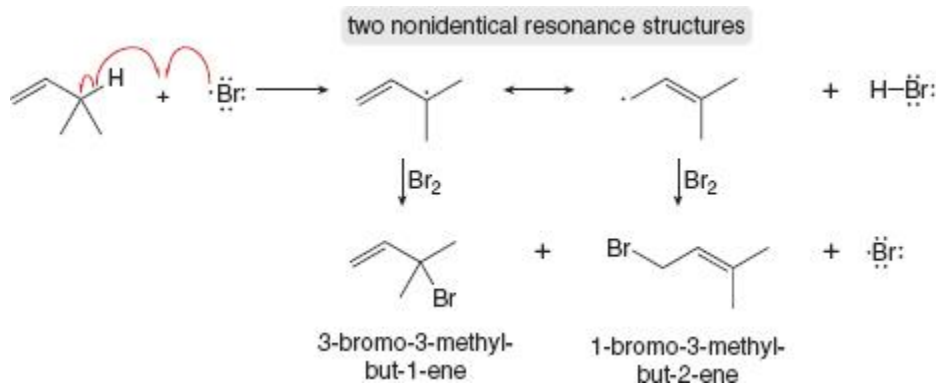
Bridged halonium ions resemble carbocations in that they are short-lived intermediates that react readily with nucleophiles. Carbocations are inherently unstable because only six electrons surround carbon, whereas **halonium ions are unstable because they contain a strained three-membered ring** with a positively charged halogen atom.



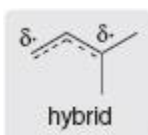
Product Mixtures in Allylic Halogenation



A mixture is obtained because the reaction proceeds by way of a **resonance-stabilized radical**. Abstraction of an allylic hydrogen from the alkene with a $\text{Br}\cdot$ radical (from NBS) forms an allylic radical for which **two different Lewis structures** can be drawn.

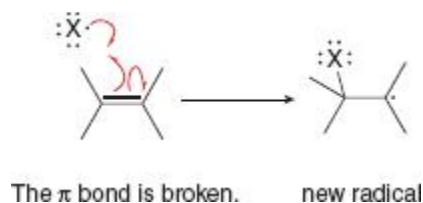


- Whenever two different resonance structures can be drawn for an allylic radical, two different allylic halides are formed by radical substitution.



Radical Addition Reactions to Double Bonds

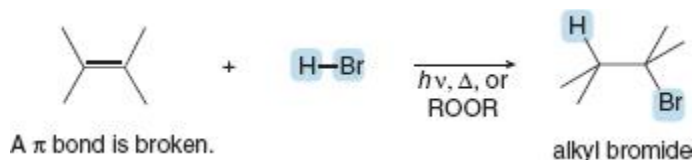
Because an alkene contains an electron-rich, easily broken π bond, it reacts with an electron-deficient radical.



Radicals react with alkenes via a radical chain mechanism that consists of **initiation**, **propagation**, and **termination** steps analogous to those discussed previously for radical substitution.

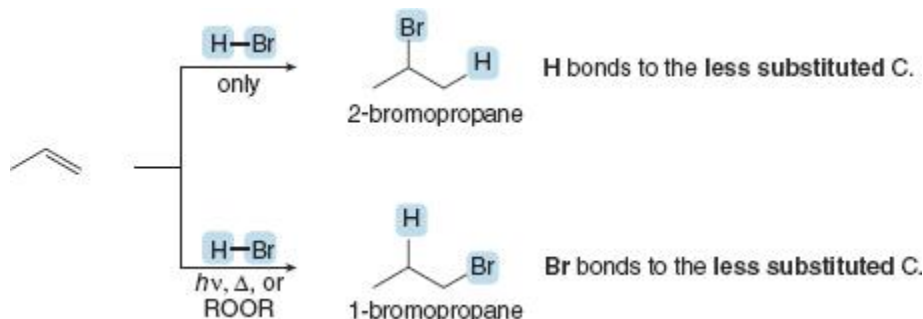
Addition of HBr

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



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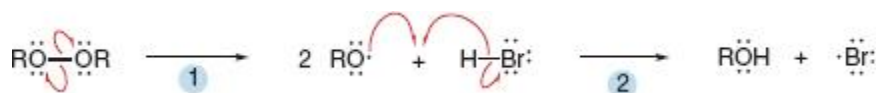
The regioselectivity of addition to an unsymmetrical alkene is *different* from the addition of HBr without added light, heat, or peroxides.



- HBr addition to propene *without* added light, heat, or peroxides gives 2-bromopropane: the **H atom is added to the less substituted carbon**. This reaction occurs via **carbocation** intermediates (Section 10.10).
- HBr addition to propene *with* added light, heat, or peroxides gives 1-bromopropane: the **Br atom is added to the less substituted carbon**. This reaction occurs via **radical** intermediates.

Mechanism 15.3 Radical Addition of HBr to an Alkene

Part [1] Initiation



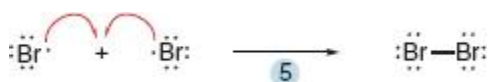
- 1-2** Initiation with ROOR occurs in two steps—homolysis of the weak O – O bond and abstraction of H to form a bromine radical.

Part [2] Propagation



- 3** Addition of $\text{Br}\cdot$ to the terminal carbon forms a 2° radical.
- 4** Abstraction of H from HBr forms a new C – H bond and a bromine radical, so Steps [3] and [4] can occur repeatedly.

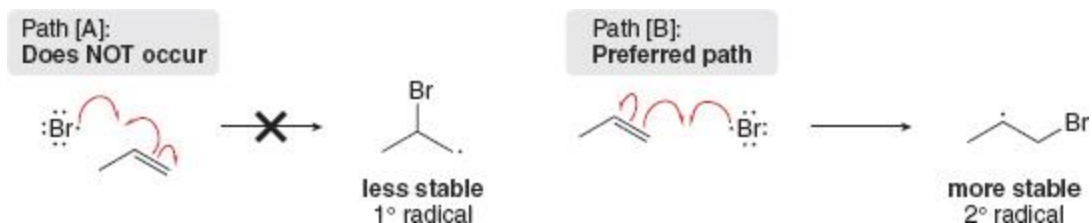
Part [3] Termination



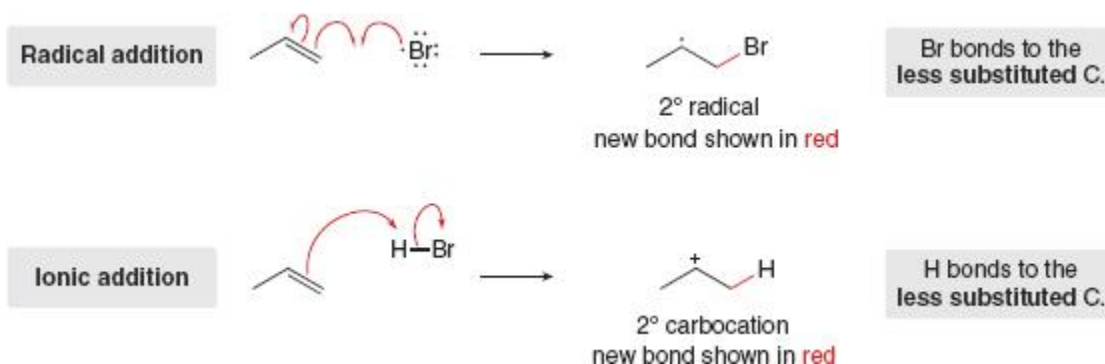
- 5** Termination of the chain occurs when any two radicals combine to form a bond.

The first propagation step (Step [3] of the mechanism, the addition of $\text{Br}\cdot$ to the double bond) is worthy of note. With propene there are two possible paths for this step, depending on which carbon atom of the double bond forms the new bond to bromine.

- Path [A] forms a less stable 1° radical whereas Path [B] forms a more stable 2° radical. **The more stable 2° radical forms faster**, so Path [B] is preferred.

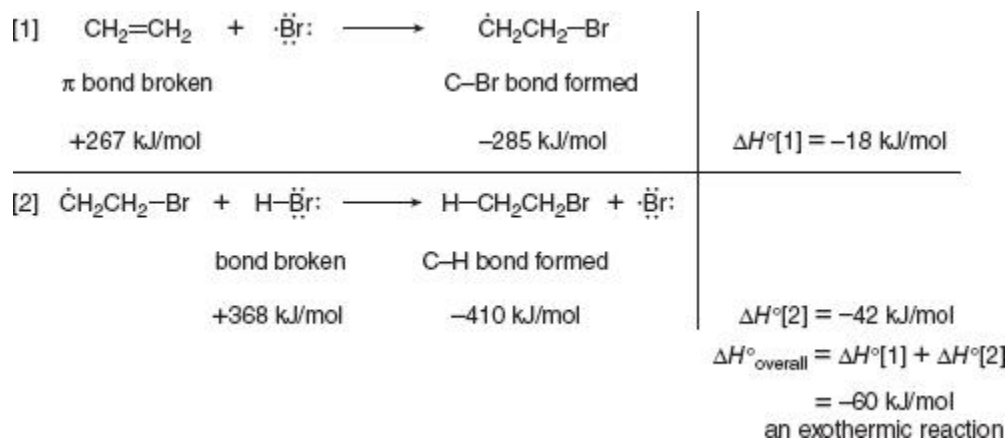


The mechanism also illustrates why the regioselectivity of HBr addition is different depending on the reaction conditions. In both reactions, H and Br add to the double bond, but the *order* of addition depends on the mechanism.



- In radical addition (HBr with added light, heat, or ROOR), $\text{Br}\cdot$ adds first to generate the more stable radical.
- In ionic addition (HBr alone), H^+ adds first to generate the more stable carbocation.

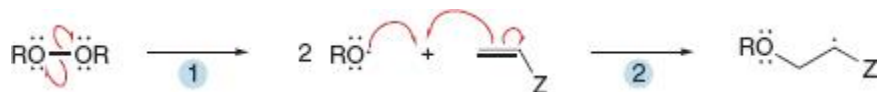
Energy Changes in the Radical Addition of HBr



Radical Polymerization

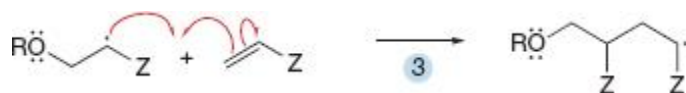
Mechanism 15.4 Radical Polymerization of $\text{CH}_2 = \text{CHZ}$

Part [1] Initiation



- **1-2** Initiation with ROOR occurs in two steps—homolysis of the weak O – O bond and addition of $\text{RO}\cdot$ to the alkene to form a carbon radical.

Part [2] Propagation



- **3** Chain propagation consists of a single step. The carbon radical adds to another alkene to form a new C – C bond and another carbon radical. Addition forms the radical with the unpaired electron on the atom with the Z substituent.

Part [3] Termination



- **4** Termination of the chain occurs when any two radicals combine to form a bond.

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.

