Chapter 10
Radical Reactions

What are radicals?

Radicals are intermediates with an unpaired electron

$$H\cdot \qquad Cl\cdot \qquad CH_3\cdot$$
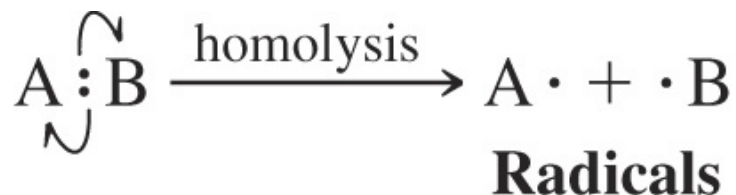
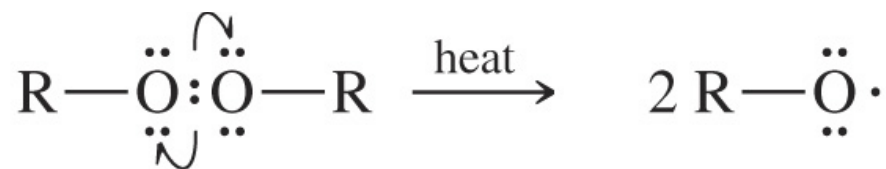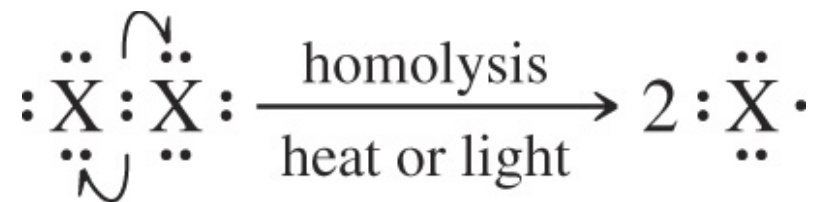**Hydrogen radical** **Chlorine radical** **Methyl radical**

♦ **Often called free radicals**

♦ **Formed by homolytic bond cleavage**

♦ **Radicals are highly reactive, short-lived species**

  ● **Half-headed arrows are used to the show movement of single electrons**

$$A : B \xrightarrow{\text{homolysis}} A\cdot + \cdot B$$

Radicals

Production of radicals

♦ **Usually begins with homolysis of a relatively weak bond such as O-O or X-X**

♦ **Initiated by addition of energy in the form of heat or light**

$$:\ddot{X}:\ddot{X}: \xrightarrow[\text{heat or light}]{\text{homolysis}} 2\ :\ddot{X}\cdot$$

$$R{-}\ddot{O}:\ddot{O}{-}R \xrightarrow{\text{heat}} 2\ R{-}\ddot{O}\cdot$$

Dialkyl peroxide   **Alkoxyl radicals**

Reactions of radicals

♦ **Radicals seek to react in ways that lead to the pairing of their odd electron thus completing a full octet.**

♦ **Reaction of a radical with any species that does not have an unpaired electron will produce another radical.**

  ● **Hydrogen abstraction is one way a halogen radical can react to pair its unshared electron**

$$:\ddot{X}\cdot \; + \; H:R \longrightarrow :\ddot{X}:H \; + \; R\cdot$$

Alkane   Alkyl
                          radical
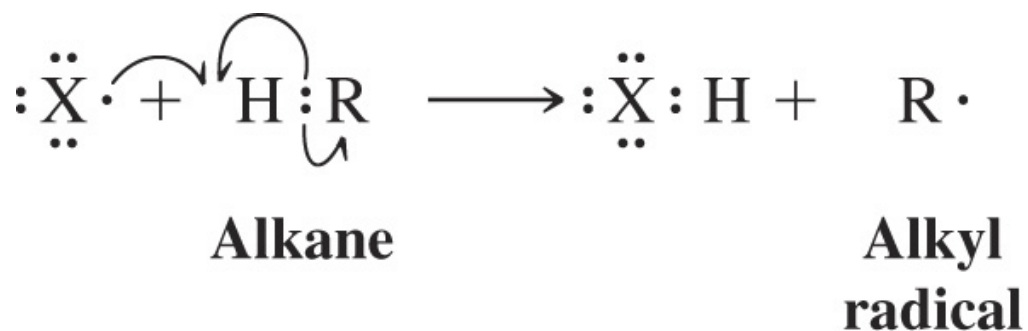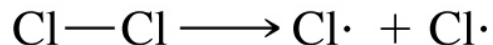
Electronic structure of the Methyl Radical
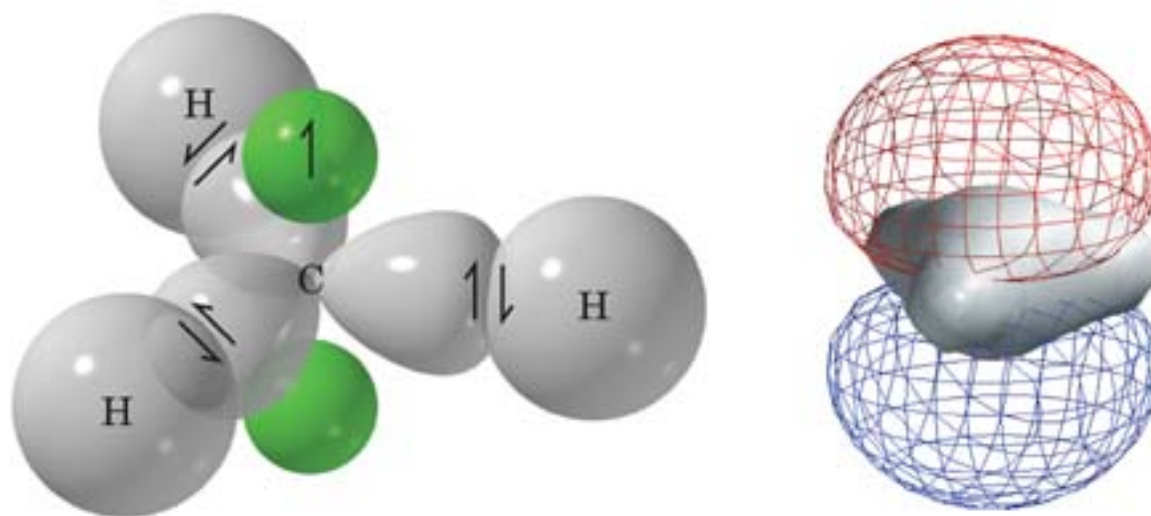
Bond Dissociation Energies

Atoms have higher energy (are less stable) than the molecules they can form

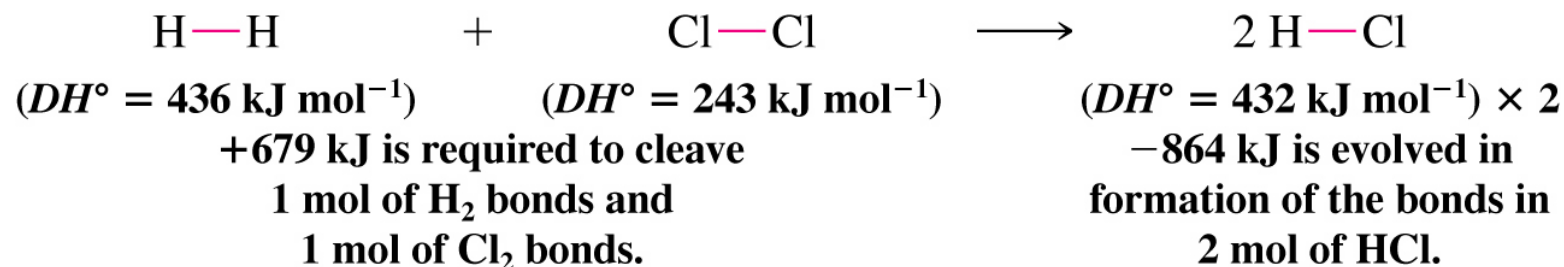**Breaking covalent bonds requires energy (*i.e.,* it is endothermic)**

$$H{-}H \longrightarrow H\cdot + H\cdot \qquad\qquad \Delta H^\circ = +436 \text{ kJ mol}^{-1}$$

$$Cl{-}Cl \longrightarrow Cl\cdot + Cl\cdot \qquad\qquad \Delta H^\circ = +243 \text{ kJ mol}^{-1}$$

Example of using Bond Dissociation Energies

Consider the reaction of H_2 with Cl_2

$$\text{H—H} \quad + \quad \text{Cl—Cl} \quad \longrightarrow \quad 2\,\text{H—Cl}$$

$(DH° = 436 \text{ kJ mol}^{-1})$ $(DH° = 243 \text{ kJ mol}^{-1})$ $(DH° = 432 \text{ kJ mol}^{-1}) \times 2$

+679 kJ is required to cleave 1 mol of H_2 bonds and 1 mol of Cl_2 bonds.

−864 kJ is evolved in formation of the bonds in 2 mol of HCl.

$$\Delta H° = (-864 \text{ kJ} + 679 \text{ kJ}) = -185 \text{ kJ} \quad \text{for 2 mol HCl produced}$$

Reaction is exothermic, more energy is released in forming the 2 H-Cl bonds of product than is required to break the H-H and Cl-Cl bonds of reactants

Table of bond dissociation energies in text, p. 460

		A:B ⟶ A· + B·		
Bond Broken (shown in red)	kJ mol^{-1}		Bond Broken (shown in red)	kJ mol^{-1}
H—H	436		$(CH_3)_2CH—Br$	298
D—D	443		$(CH_3)_2CH—I$	222
F—F	159		$(CH_3)_2CH—OH$	402
Cl—Cl	243		$(CH_3)_2CH—OCH_3$	359
Br—Br	193		$(CH_3)_2CHCH_2—H$	422
I—I	151		$(CH_3)_3C—H$	400
H—F	570		$(CH_3)_3C—Cl$	349
H—Cl	432		$(CH_3)_3C—Br$	292
H—Br	366		$(CH_3)_3C—I$	227
H—I	298		$(CH_3)_3C—OH$	400
$CH_3—H$	440		$(CH_3)_3C—OCH_3$	348
$CH_3—F$	461		$C_6H_5CH_2—H$	375
$CH_3—Cl$	352		$CH_2=CHCH_2—H$	369
$CH_3—Br$	293		$CH_2=CH—H$	465
$CH_3—I$	240		$C_6H_5—H$	474
$CH_3—OH$	387		$HC\equiv C—H$	547
$CH_3—OCH_3$	348		$CH_3—CH_3$	378
$CH_3CH_2—H$	421		$CH_3CH_2—CH_3$	371
$CH_3CH_2—F$	444		$CH_3CH_2CH_2—CH_3$	374
$CH_3CH_2—Cl$	353		$CH_3CH_2—CH_2CH_3$	343
$CH_3CH_2—Br$	295		$(CH_3)_2CH—CH_3$	371
$CH_3CH_2—I$	233		$(CH_3)_3C—CH_3$	363
$CH_3CH_2—OH$	393		HO—H	499
$CH_3CH_2—OCH_3$	352		HOO—H	356
$CH_3CH_2CH_2—H$	423		HO—OH	214
$CH_3CH_2CH_2—F$	444		$(CH_3)_3CO—OC(CH_3)_3$	157
$CH_3CH_2CH_2—Cl$	354			
$CH_3CH_2CH_2—Br$	294		$\overset{\overset{O}{\|\|}}{C_6H_5C}O—O\overset{\overset{O}{\|\|}}{C}C_6H_5$	139
$CH_3CH_2CH_2—I$	176		$CH_3CH_2O—OCH_3$	184
$CH_3CH_2CH_2—OH$	395		$CH_3CH_2O—H$	431
$CH_3CH_2CH_2—OCH_3$	355			
$(CH_3)_2CH—H$	413		$\overset{\overset{O}{\|\|}}{CH_3C}—H$	364
$(CH_3)_2CH—F$	439			
$(CH_3)_2CH—Cl$	355			

Relative stability of organic radicals

Compare the Bond Dissociation Energies for the primary and secondary hydrogens in propane

$$CH_3CH_2CH_2—H \longrightarrow CH_3CH_2CH_2· + H· \qquad \Delta H° = +423 \text{ kJ mol}^{-1}$$
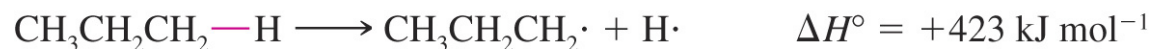
Propyl radical
(a 1° radical)

$$CH_3CHCH_3 \longrightarrow CH_3\overset{·}{C}HCH_3 + H· \qquad \Delta H° = +413 \text{ kJ mol}^{-1}$$

H

Isopropyl radical
(a 2° radical)

Diff = 10 kJ/mol

Since less energy is needed to form the isopropyl radical (from same starting material), the isopropyl radical must be more stable.

Relative Stability of organic radicals

Using the same table, the *tert*-butyl radical is more stable than the isobutyl radical

$$\Delta H^\circ = +400 \text{ kJ mol}^{-1}$$

tert-Butyl radical (a 3° radical)

Diff = 22 kJ/mol

$$\Delta H^\circ = +422 \text{ kJ mol}^{-1}$$
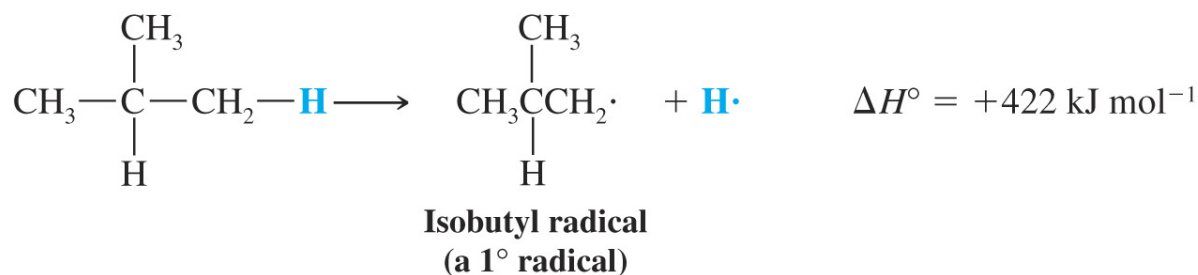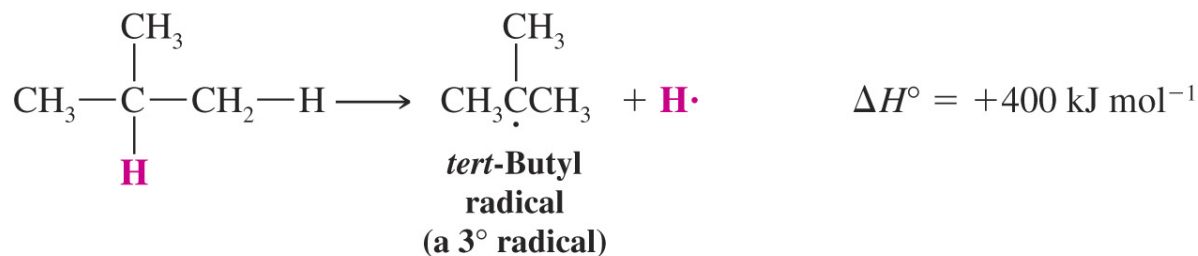
Isobutyl radical (a 1° radical)

Relative Stability of Free Radicals

The relative stabilities of carbon radicals follows the same trend as for carbocations

- **The more substituted radical is the more stable.**
- **The reason: Radicals are electron deficient, as are carbocations, and are therefore also stabilized by hyperconjugation.**

Tertiary > Secondary > Primary > Methyl
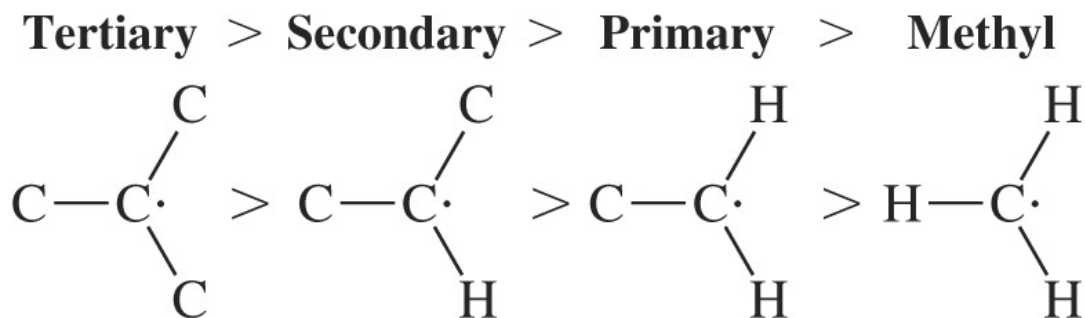
Energy diagrams for formation of radicals
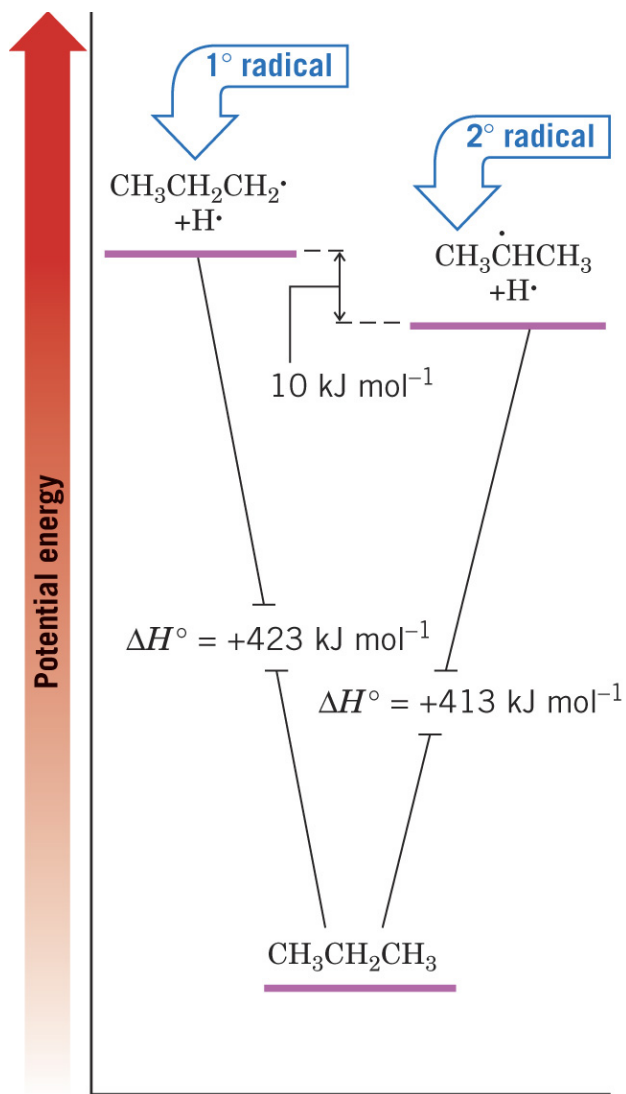
(a)
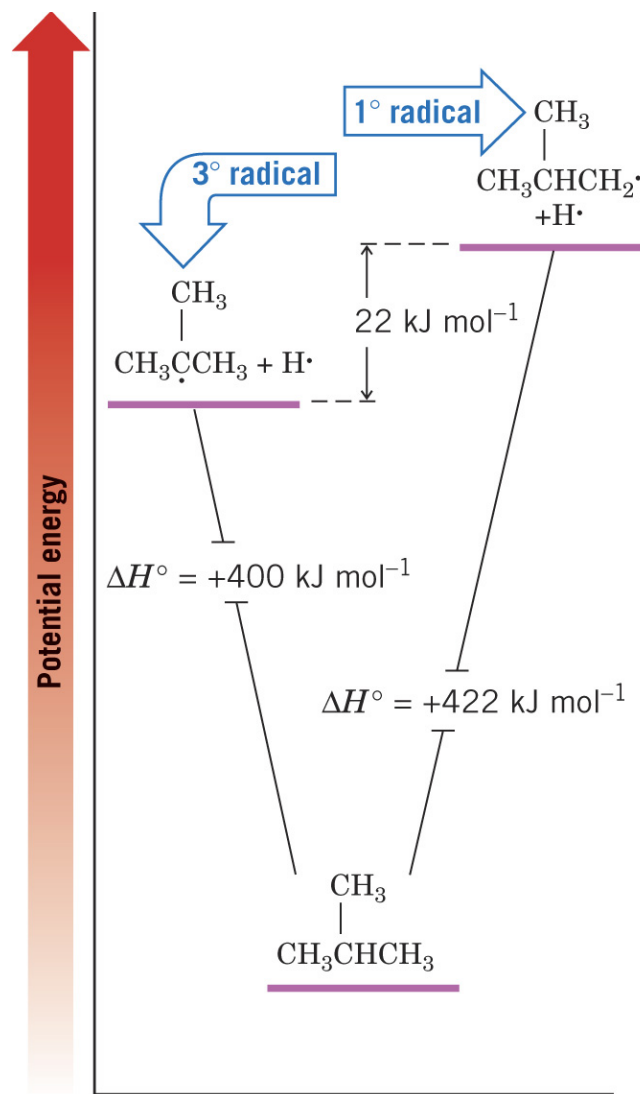
(b)

The Reactions of Alkanes with Halogens

Alkanes undergo substitution reactions with halogens (fluorine, bromine and chlorine). The reaction is initiated by heat or light

Methane + Halogen → Halomethane + Dihalomethane + Trihalomethane + Tetrahalomethane + Hydrogen halide

X = F, Cl, or Br

(The sum of the number of moles of each halogenated methane produced equals the number of moles of methane that reacted.)
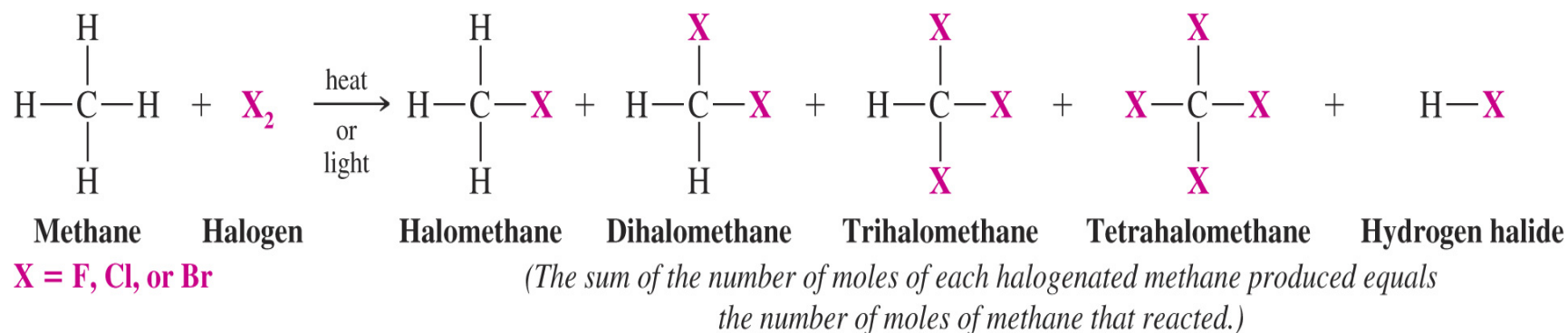
♦ **Free radical halogenation usually yields a mixture of halogenated compounds because all of the hydrogen atoms in an alkane are capable of substitution.**

♦ **Monosubstitution can be achieved by using a large excess of the alkane - so long as all hydrogens are equivalent.**

♦   **For example in CH_4, CH_3CH_3, cyclopentane**

♦   **(BUT NOT IN, for example, $CH_3CH_2CH_3$)**

Chlorination

♦ **Chlorination of higher alkanes leads to mixtures of all possible monochlorinated products (as well as more substituted products).**

$$CH_3CHCH_3 \xrightarrow[\text{light}]{\textbf{Cl}_2} CH_3CHCH_2\textbf{Cl} + CH_3CCH_3 + \text{polychlorinated} + H\textbf{Cl}$$

Isobutane   Isobutyl chloride (48%)   *tert*-Butyl chloride (29%)   (23%)
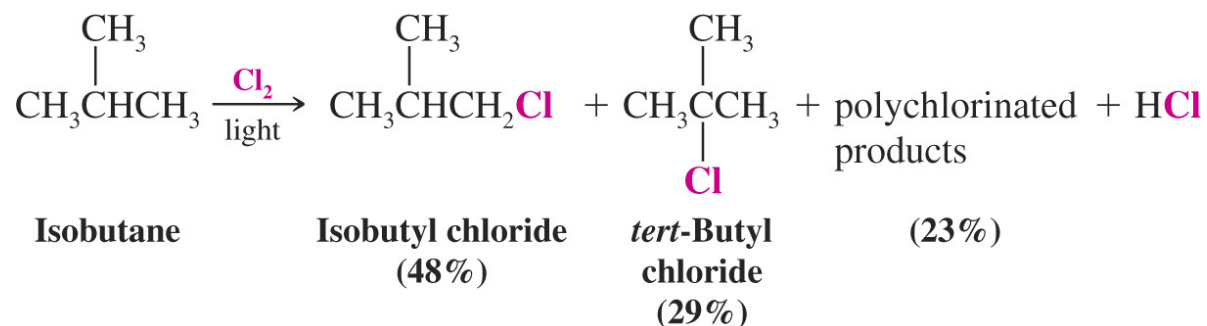
Chlorine is relatively unselective and does not greatly distinguish between the type of hydrogen it replaces.

NOTE: If there were no selectivity, the *t*-butyl chloride account for 1/9 of the product, whereas it is actually 2/3 meaning that there is a preference of about 5-fold.

Mechanism of Chlorination: a Chain Reaction

♦ **Chain Reactions have three distinct aspects:**

1. **Initiation**
2. **Propagation**
3. **Termination**

Initiation:

● **Chlorine radicals form when the reaction mixture is subjected to heat or light.**

Chain Initiation

$$\textit{Step 1} \quad Cl_2 \xrightarrow[\text{or light}]{\text{heat}} 2\,Cl\cdot$$
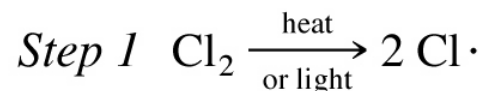
Recall that the Cl-Cl bond is relatively weak

Chlorination of Methane: Mechanism of Reaction

Propagation (2 steps which are repeated many times)

- A chlorine radical reacts with a molecule of methane to generate a methyl radical.
- The methyl radical reacts with a molecule of chlorine to yield chloromethane and forms another chlorine radical.
- The new chlorine radical reacts with another methane molecule, thus continuing the chain reaction.

Chain Propagation

$$Step\ 2\quad CH_4 + Cl\cdot \longrightarrow CH_3\cdot\ + H{-}Cl$$

$$Step\ 3\quad CH_3\cdot + Cl_2 \longrightarrow CH_3Cl + Cl\cdot$$
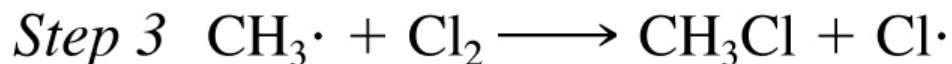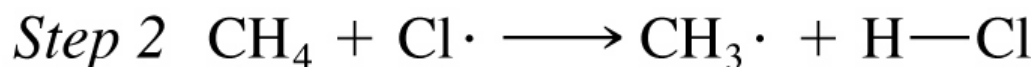
A single initiation step can lead to thousands of propagation steps, hence the term Chain Reaction

Electron flow in the mechanism

$$CH_4 + Cl_2 \xrightarrow[\text{or light}]{\text{heat}} CH_3Cl + HCl$$

Step 1 $:\ddot{C}l : \ddot{C}l: \xrightarrow[\text{or light}]{\text{heat}} :\ddot{C}l\cdot + \cdot\ddot{C}l:$

Step 2 $:\ddot{C}l\cdot + H : C-H \longrightarrow :\ddot{C}l:H + \cdot C-H$

Step 3 $H-C\cdot + :\ddot{C}l:\ddot{C}l: \longrightarrow H-C:\ddot{C}l: + \cdot\ddot{C}l:$
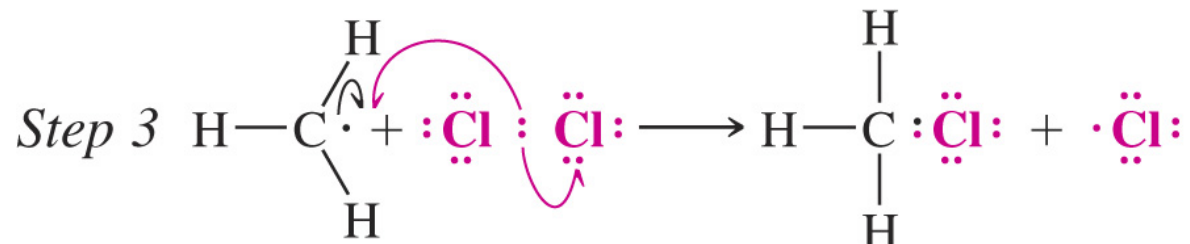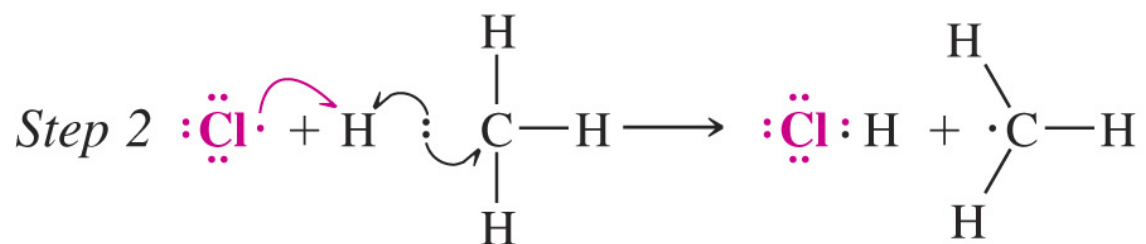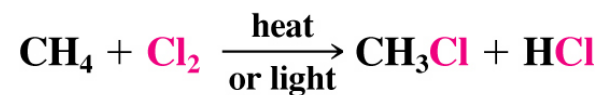
Termination:

Occasionally, the reactive radical intermediates are quenched by reaction pathways that do not generate new radicals.
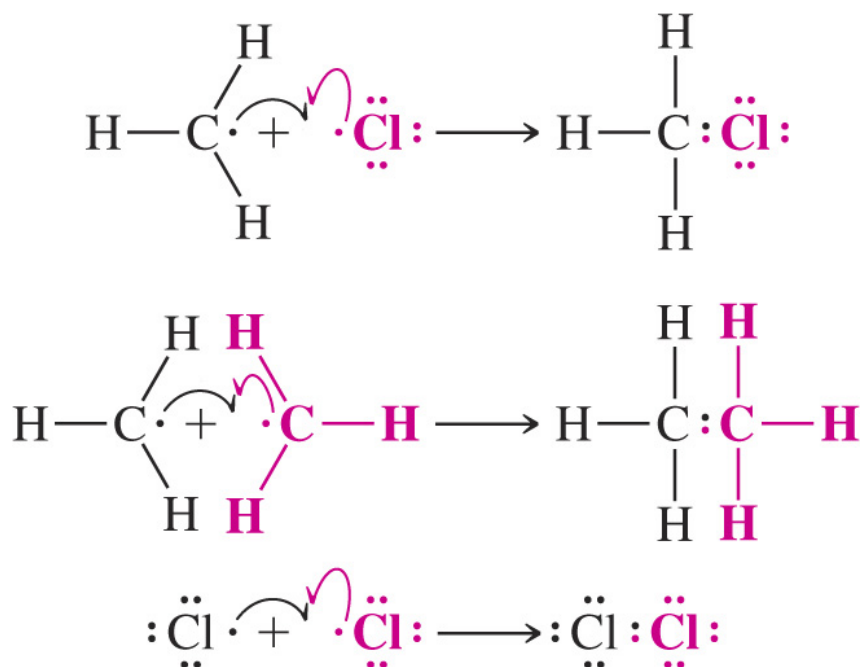
Therefore, the reaction of chlorine with methane requires constant irradiation to replace radicals quenched in chain-terminating steps.

Reaction of Methane with Other Halogens

The order of reactivity of methane substitution with halogens is: **fluorine > chlorine > bromine >> iodine**

Halogenation of Higher Alkanes

♦ **Monochlorination** of alkanes proceeds with **limited selectivity**.

- Tertiary hydrogens are roughly 5 times more reactive than primary.
- Secondary hydrogens are roughly 3.5 times more reactive than primary.

Chlorination occurs so rapidly it cannot distinguish well between types of hydrogen and so is not very selective.

$$CH_3CH_2CH_3 \xrightarrow[\text{light, 25°C}]{\textbf{Cl}_2} CH_3CH_2CH_2\textbf{Cl} + CH_3CHCH_3$$
$$| $$
$$\textbf{Cl}$$

Propane	1-Chloropropane (45%)	2-Chloropropane (55%)

$$
\begin{array}{c}
CH_3 \\
| \\
CH_3CHCH_3
\end{array}
\xrightarrow[\substack{\text{light} \\ 25°C}]{\textbf{Cl}_2}
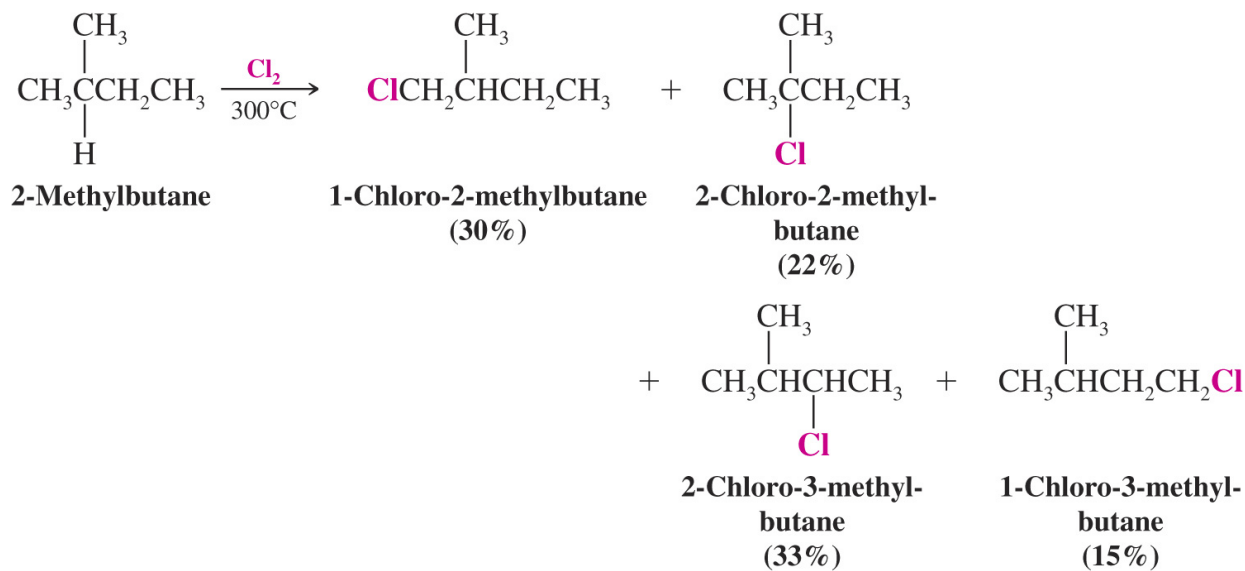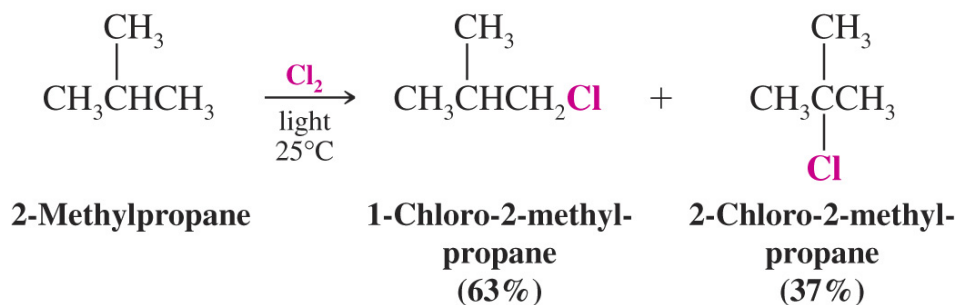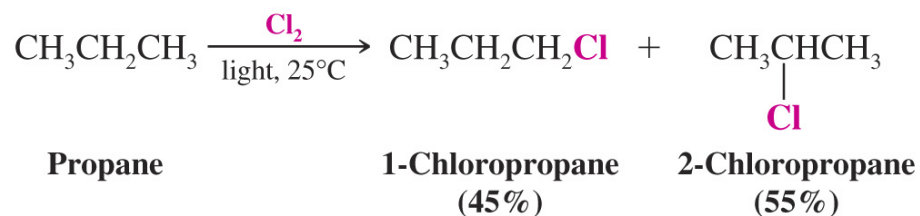\begin{array}{c}
CH_3 \\
| \\
CH_3CHCH_2\textbf{Cl}
\end{array}
+
\begin{array}{c}
CH_3 \\
| \\
CH_3CCH_3 \\
| \\
\textbf{Cl}
\end{array}
$$

2-Methylpropane   1-Chloro-2-methyl-propane (63%)   2-Chloro-2-methyl-propane (37%)

$$
\begin{array}{c}
CH_3 \\
| \\
CH_3CCH_2CH_3 \\
| \\
H
\end{array}
\xrightarrow[300°C]{\textbf{Cl}_2}
\begin{array}{c}
CH_3 \\
| \\
\textbf{Cl}CH_2CHCH_2CH_3
\end{array}
+
\begin{array}{c}
CH_3 \\
| \\
CH_3CCH_2CH_3 \\
| \\
\textbf{Cl}
\end{array}
$$

2-Methylbutane   1-Chloro-2-methylbutane (30%)   2-Chloro-2-methyl-butane (22%)

$$
+
\begin{array}{c}
CH_3 \\
| \\
CH_3CHCHCH_3 \\
| \\
\textbf{Cl}
\end{array}
+
\begin{array}{c}
CH_3 \\
| \\
CH_3CHCH_2CH_2\textbf{Cl}
\end{array}
$$

2-Chloro-3-methyl-butane (33%)   1-Chloro-3-methyl-butane (15%)

Useful Chlorinations

Chlorination is synthetically useful only when molecular symmetry limits the number of possible substitution products.

Neopentane
(excess)

Neopentyl chloride

Cyclohexane
(excess)

Chlorocyclohexane
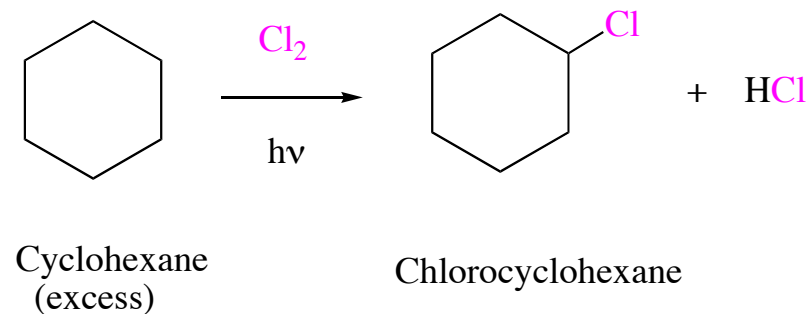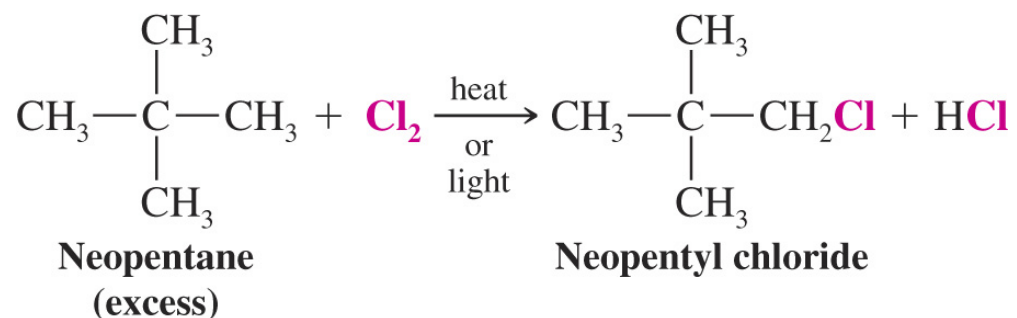
Is Fluorination Selective?

♦ **Fluorine shows almost no discrimination in replacement of hydrogens because it is so reactive**

♦ **It is so reactive that only perfluoro compounds (all H replaced by F) are formed *via* direct fluorination.**

Bromination

Bromination is the only halogenation that is controllable and selective.

Therefore, free radical bromination is the only practical method for halogenating alkanes.

>99%   <1%
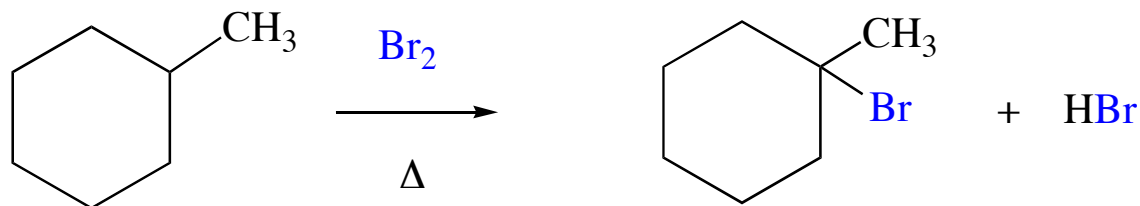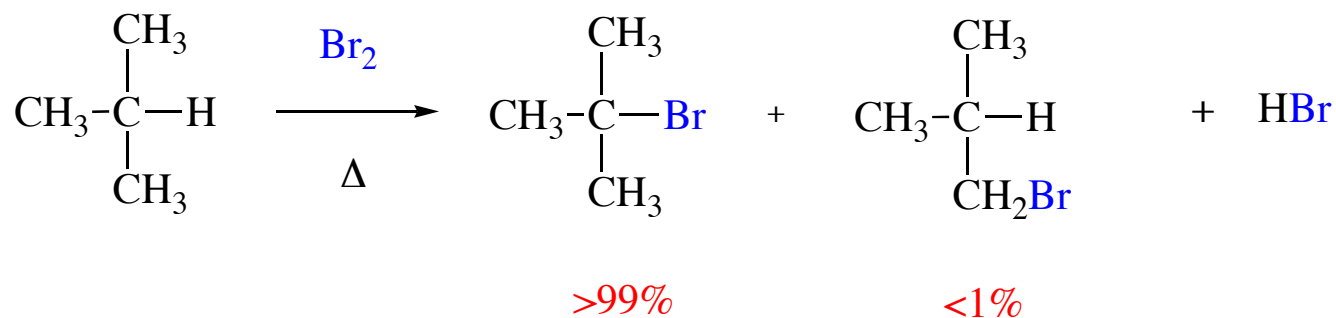
Summary of the Halogenation of Alkanes

Reactions that Generate Tetrahedral Stereogenic Carbons

♦ **A reaction of achiral starting materials which produces a product with a stereogenic carbon will produce a racemic mixture**
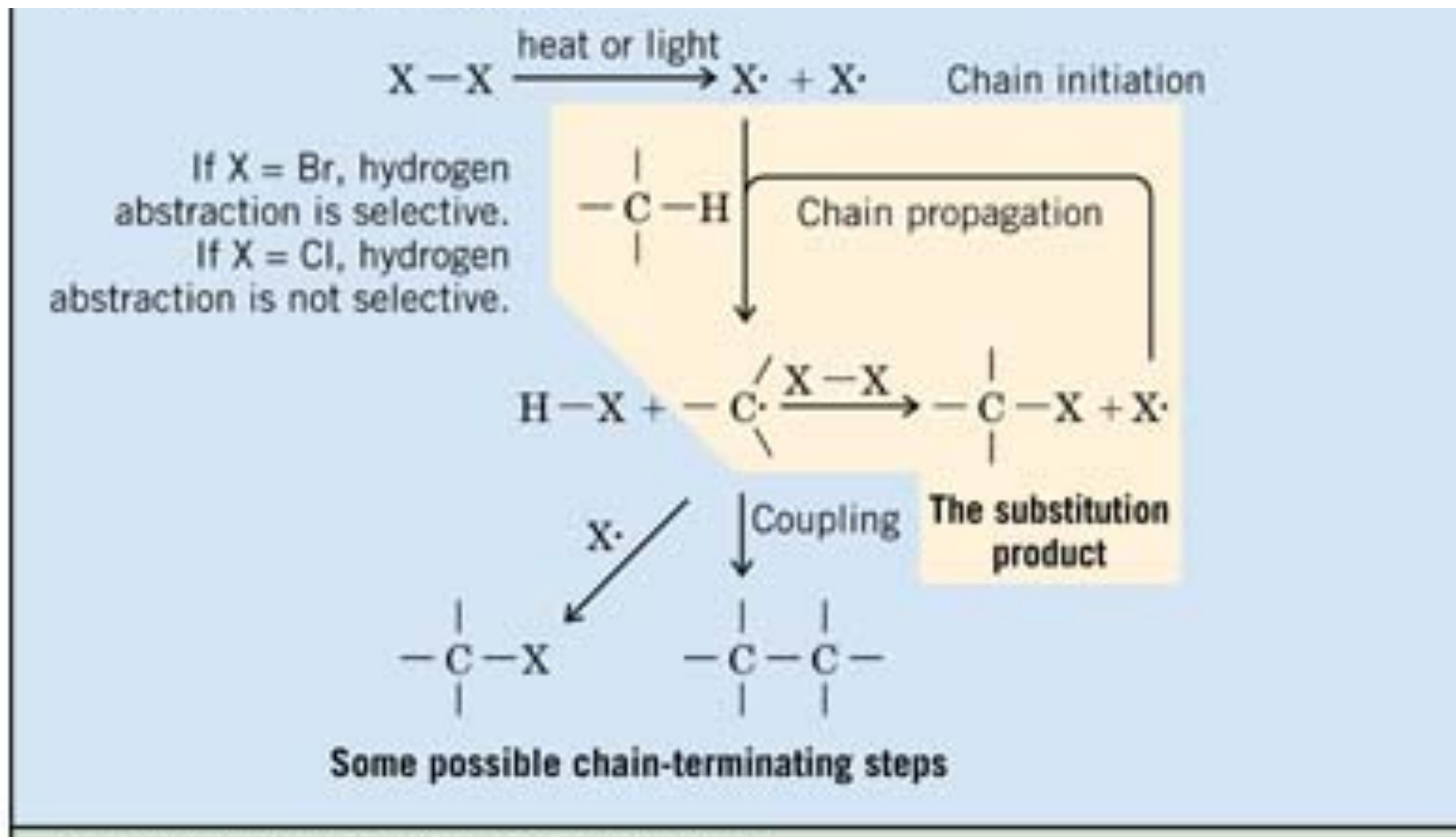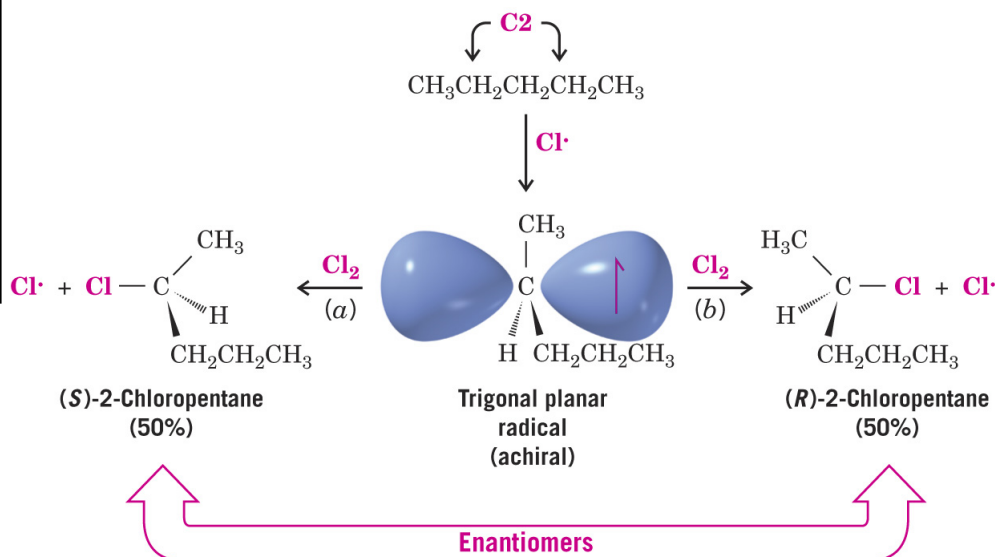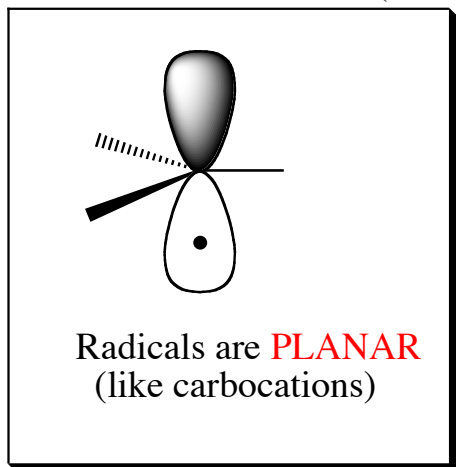
$$CH_3CH_2CH_2CH_2CH_3 \xrightarrow[\text{(achiral)}]{Cl_2} CH_3CH_2CH_2CH_2CH_2\mathbf{Cl} + CH_3CH_2CH_2\overset{*}{C}H\mathbf{Cl}CH_3$$

Pentane
(achiral)

1-Chloropentane
(achiral)

(±)-2-Chloropentane
(a racemic form)

$$+ CH_3CH_2CH\mathbf{Cl}CH_2CH_3$$

3-Chloropentane
(achiral)

Radicals are PLANAR
(like carbocations)

C2

$$CH_3CH_2CH_2CH_2CH_3$$

$$\downarrow Cl\cdot$$

$$Cl\cdot + Cl-\underset{CH_2CH_2CH_3}{\overset{CH_3}{\underset{|}{C}}}-H \xleftarrow{Cl_2 \; (a)} \underset{H \; CH_2CH_2CH_3}{\overset{CH_3}{C}} \xrightarrow{Cl_2 \; (b)} \underset{CH_2CH_2CH_3}{\overset{H_3C}{\underset{H}{C}}}-\mathbf{Cl} + Cl\cdot$$

(S)-2-Chloropentane
(50%)

Trigonal planar
radical
(achiral)

(R)-2-Chloropentane
(50%)

Enantiomers

Generation of a Second Stereogenic Carbon

♦ **When a molecule with one or more stereogenic carbons reacts to create another stereogenic carbon, two diastereomeric products are produced.**

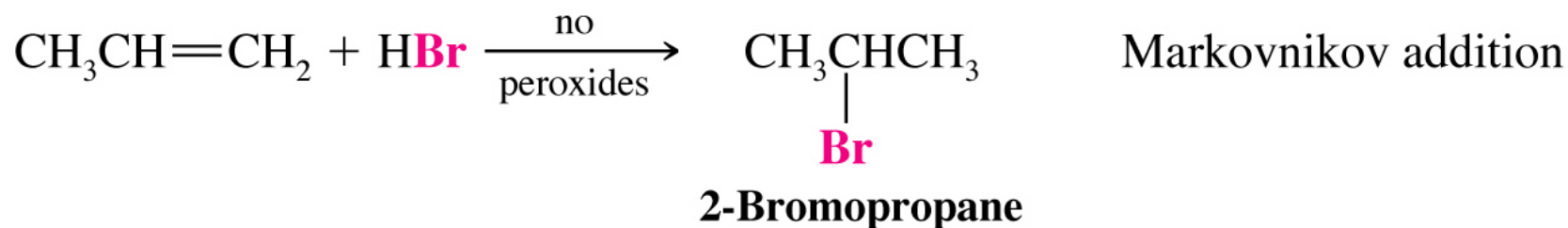 ● **The intermediate radical is chiral and and reactions on the two faces of the radical lead to two diastereomers.**
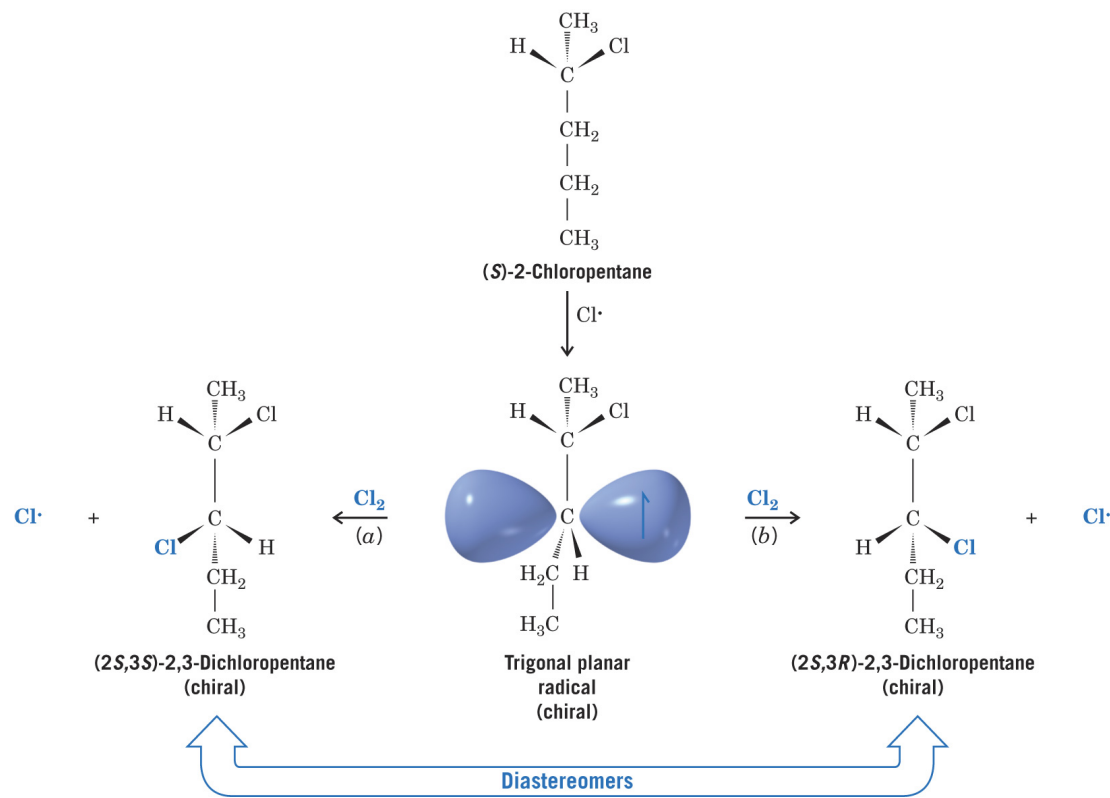
Anti-Markovnikov Addition of HBr to Alkenes

Addition of hydrogen bromide in the presence of peroxides gives anti-Markovnikov addition

$$CH_3CH = CH_2 + HBr \xrightarrow{\text{ROOR}} CH_3CH_2CH_2Br \qquad \text{Anti-Markovnikov addition}$$

1-Bromopropane

$$CH_3CH = CH_2 + HBr \xrightarrow[\text{peroxides}]{\text{no}} CH_3CHCH_3$$

$$|$$
$$Br$$

Markovnikov addition

2-Bromopropane

Works only for HBr: the other hydrogen halides do not give this type of anti-Markovnikov addition.

A Second Way That Radicals React

Besides abstracting a hydrogen atom

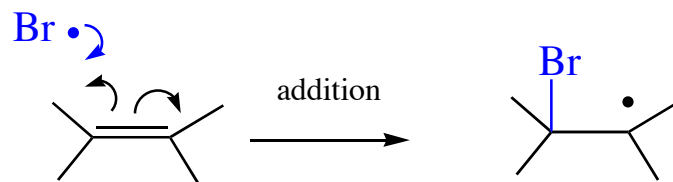Br •   H—R   ──abstraction──▶   Br—H   +   • R
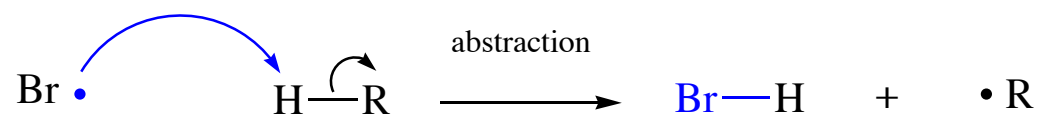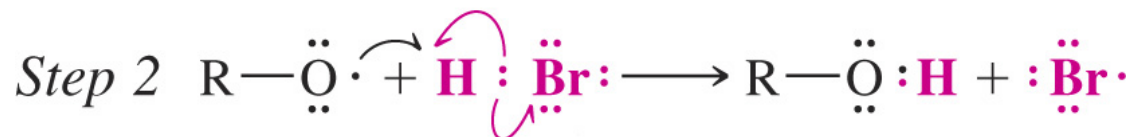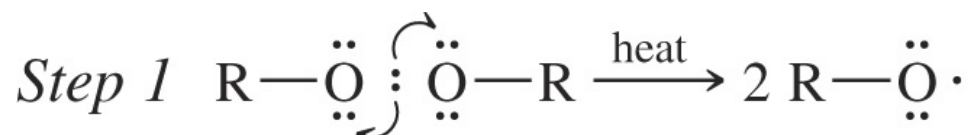
Radicals can add to the pi bond of an alkene

Br •   ──addition──▶   Br

Mechanism for the Anti-Markovnikov Addition of HBr

A free radical chain mechanism

Steps 1 and 2 of the mechanism are chain initiation steps which produce a **bromine radical**

Step 1 $\quad$ R—Ö ⦂ Ö—R $\xrightarrow{\text{heat}}$ 2 R—Ö ·

Step 2 $\quad$ R—Ö · + H ⦂ Br: $\longrightarrow$ R—Ö:H + :Br ·

In **step 3,** the first step of propagation, a bromine radical adds to the double bond to give the most stable of the two possible carbon radicals (in this case, a 2º radical)

- Attack at the 1º carbon is also less sterically hindered

Step 3 $CH_2\!\!=\!\!CHCH_3$ $\longrightarrow$ $CH_2\!-\!\overset{\bullet}{C}HCH_3$
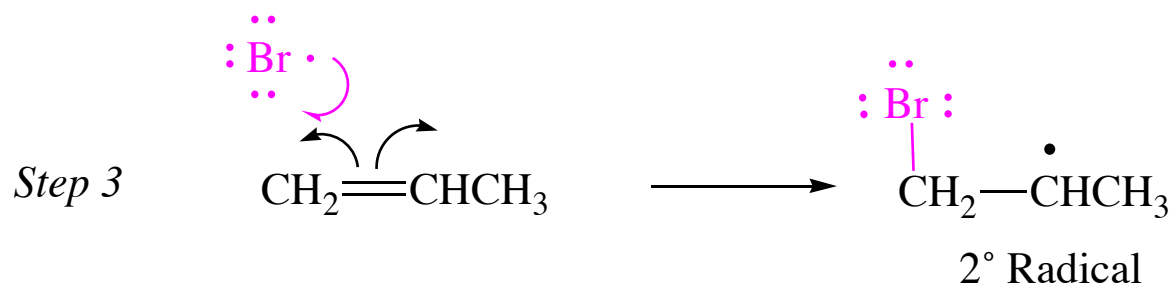
2° Radical

Step 4 regenerates a bromine radical

Step 4 $CH_2\!-\!\overset{\bullet}{C}HCH_3$ + H$-$Br: $\longrightarrow$ $CH_2\!-\!CHCH_3$ + · Br:
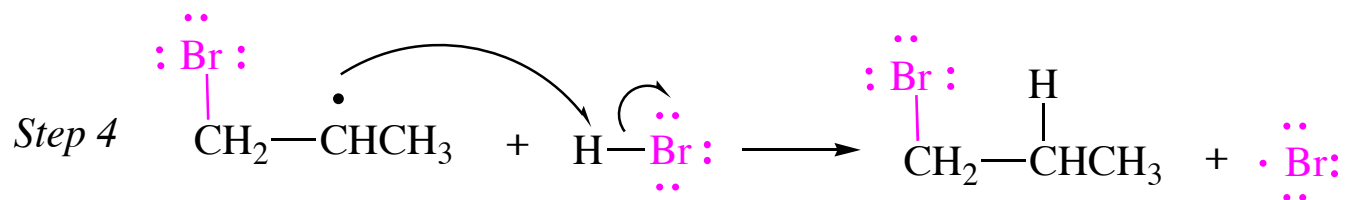
The new bromine radical reacts with another equivalent of alkene, and steps 3 and 4 repeat in a chain reaction

Controlling Addition of HBr to Alkenes

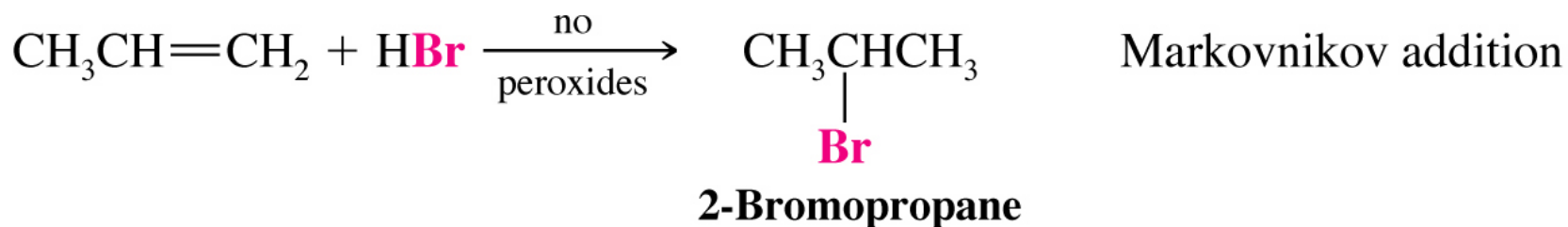Early studies of HBr addition gave contradictory results – sometimes Markovnikov addition and sometime anti-Markovnikov

$$CH_3CH=CH_2 + HBr \xrightarrow{\text{ROOR}} CH_3CH_2CH_2Br \quad \text{Anti-Markovnikov addition}$$

1-Bromopropane

$$CH_3CH=CH_2 + HBr \xrightarrow[\text{peroxides}]{\text{no}} CH_3CHCH_3 \quad \text{Markovnikov addition}$$

|
Br

2-Bromopropane

To favor "normal" addition, remove possible traces of peroxides from the alkene and use a polar, protic solvent.

To favor anti-Markovnikov addition, add peroxide and use non-polar solvent.

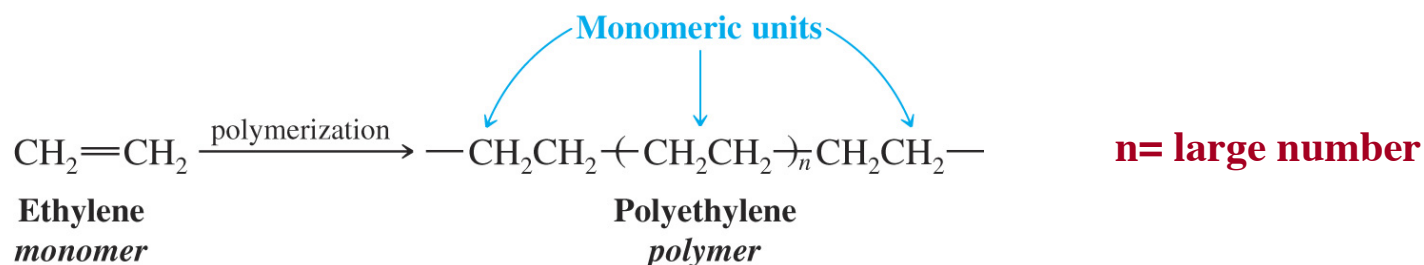Very useful for your synthetic tool box.

Radical Polymerization of Alkenes

**Polymers are macromolecules made up of repeating subunits**
- **The subunits used to synthesize polymers are called monomers**

Polyethylene is made of repeating subunits derived from ethylene
- **Polyethylene is called a chain-growth polymer or addition polymer**

$$CH_2{=}CH_2 \xrightarrow{\text{polymerization}} -CH_2CH_2(CH_2CH_2)_{n}CH_2CH_2-$$

Monomeric units

Ethylene *monomer*

Polyethylene *polymer*

n= large number

♦ **Polystyrene is made in an analogous reaction using styrene as the monomer**

$$CH_2{=}CH \xrightarrow{\text{polymerization}} -CH_2CH(CH_2CH)_{n}CH_2CH-$$

Styrene

Polystyrene
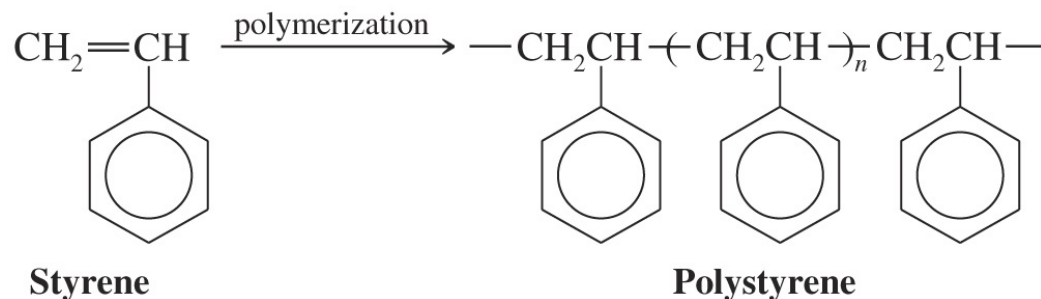
Initiator used to start a chain reaction mechanism

By using a very small amount of a diacyl peroxide is added to initiate the reaction only a few, but very long polymer chains are obtained.

Chain Initiation

$$Step\ 1\quad R-\overset{\overset{O}{\|}}{C}-O:O-\overset{\overset{O}{\|}}{C}-R \longrightarrow 2\ R:C-O\cdot \longrightarrow 2\ CO_2 + 2\ R\cdot$$
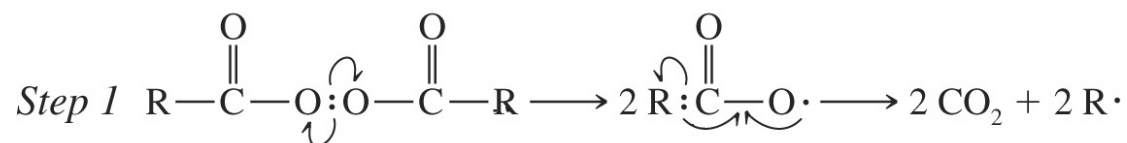
Diacyl peroxide

Produces an alkyl radical to initiate chain

$$Step\ 2\quad R\cdot + CH_2{=}CH_2 \longrightarrow R:CH_2-CH_2\cdot$$

The propagation step simply adds more ethylene molecules to a growing chain.

Chain Propagation

$$Step\ 3\quad R-CH_2CH_2\cdot + n\ CH_2{=}CH_2 \longrightarrow R{+}CH_2CH_2{)}_n CH_2CH_2\cdot$$

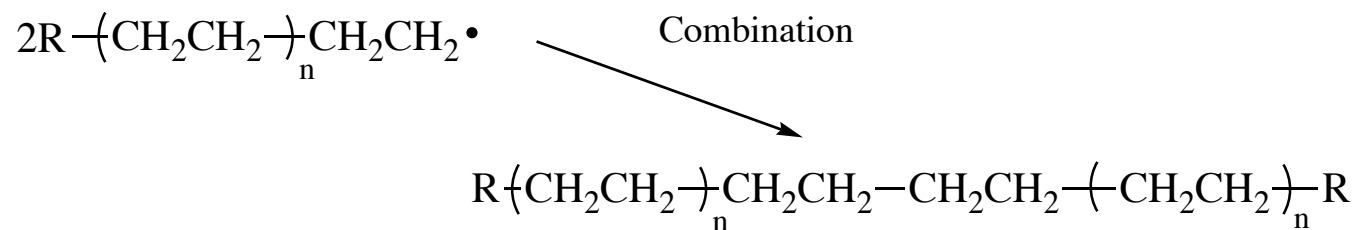## Chain termination

Chain growth will terminate if two radicals collide and combine.

Chain Termination

Step 4

$$2R\!-\!(CH_2CH_2)_n\!CH_2CH_2\bullet \xrightarrow{\text{Combination}}$$

$$R\!-\!(CH_2CH_2)_n\!CH_2CH_2\!-\!CH_2CH_2\!-\!(CH_2CH_2)_n\!R$$

Some Other Addition Polymers from Common Alkenes

Monomer	Polymer	Names
$CH_2{=}CHCH_3$	$-(CH_2{-}CH)_n$ | CH_3	Polypropylene
$CH_2{=}CHCl$	$-(CH_2{-}CH)_n$ | Cl	Poly(vinyl chloride), PVC
$CH_2{=}CHCN$	$-(CH_2{-}CH)_n$ | CN	Polyacrylonitrile, Orlon
$CF_2{=}CF_2$	$-(CF_2{-}CF_2)_n$	Polytetrafluoroethene, Teflon
CH_3 | $CH_2{=}CCO_2CH_3$	CH_3 | $-(CH_2{-}C)_n$ | CO_2CH_3	Poly(methyl methacrylate), Lucite, Plexiglas, Perspex

Note the regular alternation of the X groups, since the addition step always produces the more stable radical