Chapter 10
Radical Reactions

What are radicals?

Radicals are intermediates with an unpaired electron
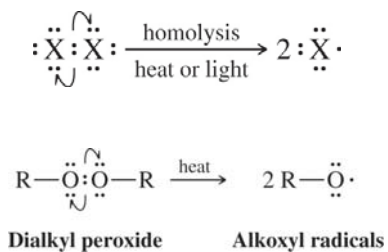
H·	Cl·	CH_3·
Hydrogen radical	**Chlorine radical**	**Methyl radical**

♦ **Often called free radicals**
♦ **Formed by homolytic bond cleavage**
♦ **Radicals are highly reactive, short-lived species**
  ● **Half-headed arrows are used to show movement of single electrons**

$$A\!:\!B \xrightarrow{\text{homolysis}} A\cdot + \cdot B$$
Radicals
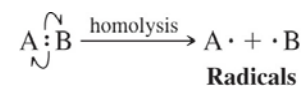
Production of radicals

♦ **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**

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

$$R—\ddot{O}\!:\!\ddot{O}—R \xrightarrow{\text{heat}} 2\,R—\ddot{O}\cdot$$
**Dialkyl peroxide**   **Alkoxyl radicals**

Reactions of radicals

♦ **Radicals seek to react in ways that lead to pairing of their unpaired electron and 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**

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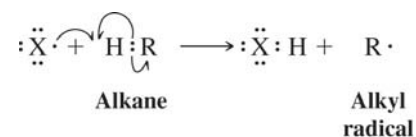
Electronic structure of methyl radical
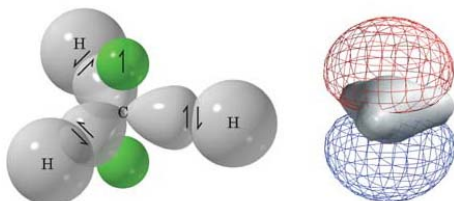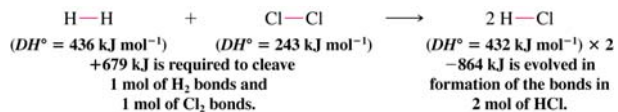

Bond Dissociation Energies

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

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

$$H—H \longrightarrow H\cdot + H\cdot \qquad \Delta H° = +436 \text{ kJ mol}^{-1}$$
$$Cl—Cl \longrightarrow Cl\cdot + Cl\cdot \qquad \Delta H° = +243 \text{ kJ mol}^{-1}$$

Example of using Bond Dissociation Energies

Consider the possible reaction of H_2 with Cl_2

$$H—H \quad + \quad Cl—Cl \quad \longrightarrow \quad 2\,H—Cl$$

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

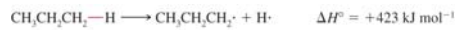$$\Delta H° = (-864 \text{ kJ} + 679 \text{ kJ}) = -185 \text{ kJ} \quad \text{for 2 mol HCl produced}$$

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

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Table of bond dissociation energies in text, p. 430

Relative stability of organic radicals

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

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

$CH_3CHCH_3 \longrightarrow CH_3CHCH_3 + H\cdot$ $\Delta H° = +413\ kJ\ mol^{-1}$
|
H
Isopropyl radical
(a 2° radical)

Diff = 10 kJ/mol

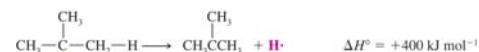**Since less energy is needed to form the isopropyl radical (from same starting material), the isopropyl radical must be more stable.**

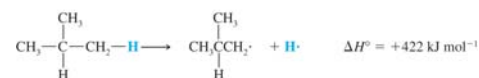## Relative Stability of organic radicals

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

CH_3 CH_3
| |
CH_3—C—CH_2—$H \longrightarrow CH_3CCH_3 + H\cdot$ $\Delta H° = +400\ kJ\ mol^{-1}$
|
H   *tert*-Butyl
                           radical
                           (a 3° radical)

Diff = 22 kJ/mol

CH_3 CH_3
| |
CH_3—C—CH_2—$H \longrightarrow CH_3CCH_2\cdot + H\cdot$ $\Delta H° = +422\ kJ\ mol^{-1}$
| |
H   H
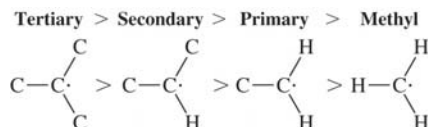   Isobutyl radical
                           (a 1° radical)

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.**
- **Radicals are electron deficient, as are carbocations, and are therefore also stabilized by hyperconjugation.**

Tertiary > Secondary > Primary > Methyl
       C   C   H   H
       | | | |
  C—C·   > C—C·   > C—C·   > H—C·
       | | | |
       C   H   H   H

Energy diagrams for formation of radicals
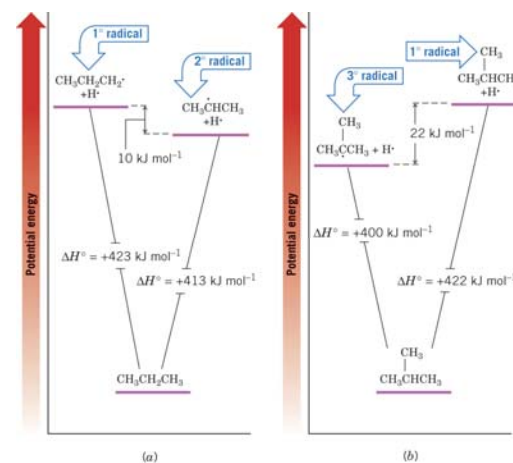
The Reactions of Alkanes with Halogens

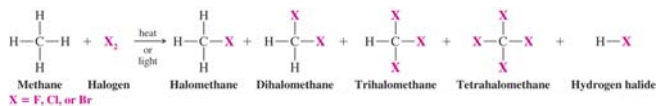**Alkanes undergo substitution reactions with halogens (fluorine, bromine and chlorine) initiated by heat or light**

♦ **Free radical halogenation can yield 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 monochlorinated product (and more substituted products)**
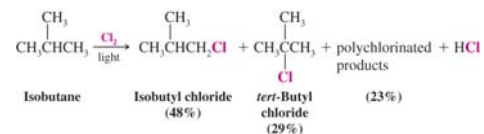
Chlorine is relatively unselective and does not greatly distinguish between the type of hydrogen it replaces.

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.
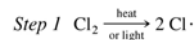

Mechanism of Chlorination: a Chain Reaction

♦ **The reaction mechanism has three distinct aspects:**
  1. **Initiation**
  2. **Propagation**
  3. **Termination**

Initiation – Step 1
  ● **Chlorine radicals form when the reaction mixture is subjected to heat or light.**

Chain Initiation

$$Step \ 1 \quad Cl_2 \xrightarrow[\text{or light}]{\text{heat}} 2 \ Cl\cdot$$

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 regenerates chlorine radical**
  ● **The new chlorine radical reacts with another methane molecule, continuing the chain reaction**

Chain Propagation

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

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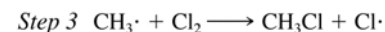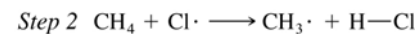
A single initiation step can lead to thousands of propagation steps, hence the term chain reaction

Electron flow in the mechanism

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

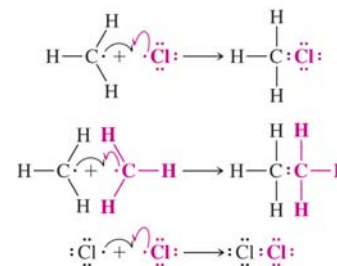Step 1 $:\ddot{C}l \frown \ddot{C}l: \xrightarrow[\text{or light}]{\text{heat}} :\ddot{C}l\cdot + \cdot\ddot{C}l:$

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

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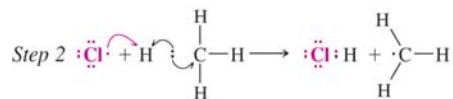
Termination

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.**

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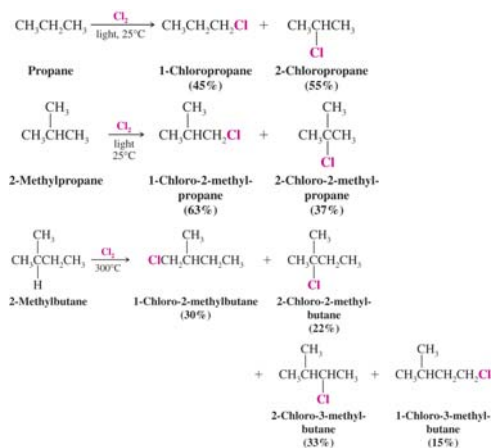
Useful Chlorinations

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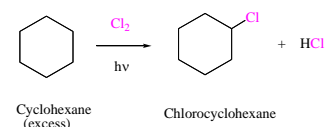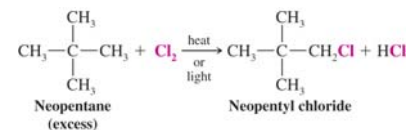
Is Fluorination Selective?

♦ **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.
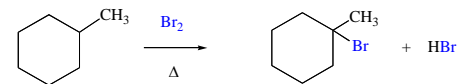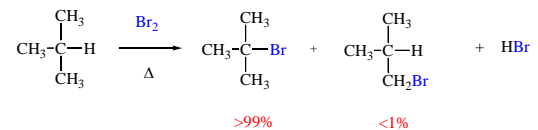
Reactions that Generate Tetrahedral Stereogenic Carbons

♦ A reaction of **achiral starting materials** which produces a product with a stereogenic carbon will produce a **racemic mixture**
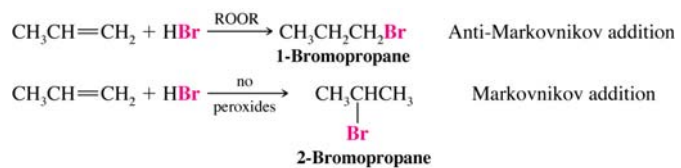
Radicals are PLANAR
(like carbocations)
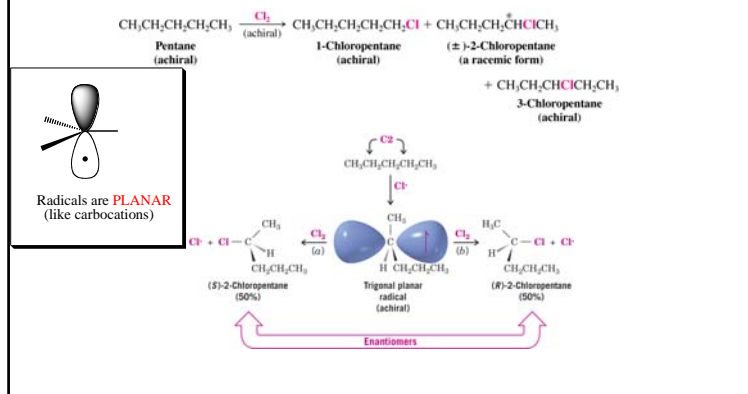
Generation of a Second Stereogenic Carbon

♦ **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.
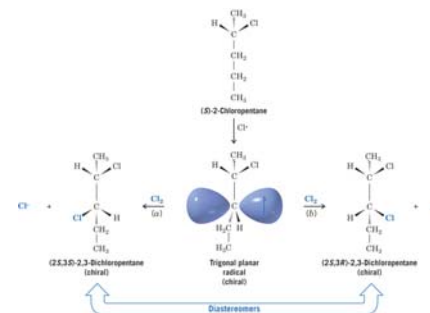
Anti-Markovnikov Addition of HBr to Alkenes

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

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

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

$Br \cdot$ $H{-}R$ $\xrightarrow{abstraction}$ $Br{-}H$ + $\cdot R$
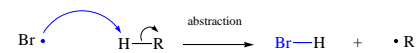
Radicals can add to the pi bond of an alkene

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

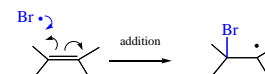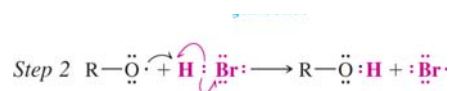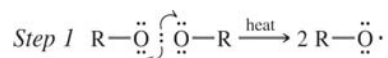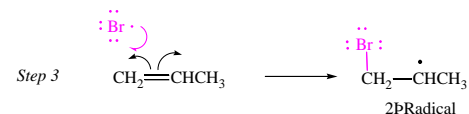*Step 2* $R-\ddot{O}\cdot + H:\ddot{B}r: \longrightarrow R-\ddot{O}:H + :\ddot{B}r\cdot$
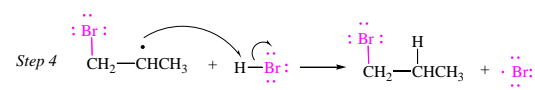

In **step 3,** the first step of propagation, a bromine radical adds to the double bond to give the most stable of the two possible carbon radicals (in this case, a 2º radical)
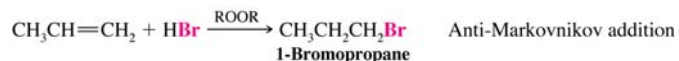- Attack at the 1º carbon is also less sterically hindered

Step 3 $:\ddot{B}r\cdot \quad CH_2{=}CHCH_3 \longrightarrow \overset{:\ddot{B}r:}{CH_2}-\overset{\cdot}{C}HCH_3$

2º Radical

Step 4 regenerates a bromine radical

Step 4 $\overset{:\ddot{B}r:}{CH_2}-\overset{\cdot}{C}HCH_3 + H-\ddot{B}r: \longrightarrow \overset{:\ddot{B}r:}{CH_2}-\overset{H}{C}HCH_3 + \cdot\ddot{B}r:$

The new bromine radical reacts with another equivalent of alkene, and steps 3 and 4 repeat in a chain reaction

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Controlling Addition of HBr to Alkenes

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

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

$CH_3CH{=}CH_2 + HBr \xrightarrow[peroxides]{no} CH_3\underset{Br}{C}HCH_3$ Markovnikov addition
2-Bromopropane

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

To favor anti-Mark, add peroxide and use non-polar solvent

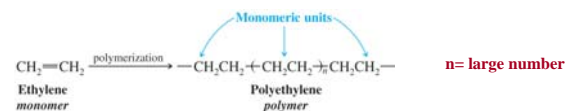Very useful for your synthetic tool box

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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

Monomeric units

$CH_2{=}CH_2 \xrightarrow{polymerization} -CH_2CH_2{\left(CH_2CH_2\right)_n}CH_2CH_2-$ **n= large number**

Ethylene monomer → Polyethylene polymer

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

$CH_2{=}CH \xrightarrow{polymerization} -CH_2CH{\left(CH_2CH\right)_n}CH_2CH-$

Styrene → Polystyrene
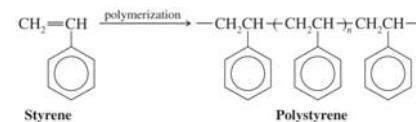
Initiator used to start a chain reaction mechanism

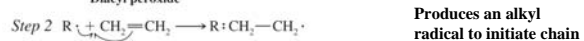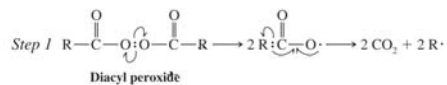**A very small amount of a diacyl peroxide is added to initiate the reaction so that few, but very long polymer chains are obtained**

Chain Initiation

Step 1 $R-\overset{O}{\overset{\|}{C}}-O\!:\!O-\overset{O}{\overset{\|}{C}}-R \longrightarrow 2\,R\!:\!\overset{O}{\overset{\|}{C}}-O\cdot \longrightarrow 2\,CO_2 + 2\,R\cdot$

Diacyl peroxide

Step 2 $R\cdot + CH_2\!=\!CH_2 \longrightarrow R\!:\!CH_2-CH_2\cdot$

Produces an alkyl radical to initiate chain

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

Chain Propagation

Step 3 $R-CH_2CH_2\cdot + n\,CH_2\!=\!CH_2 \longrightarrow R\!\!\left(CH_2CH_2\right)_{\!n}\!CH_2CH_2\cdot$

Chain termination

Chain growth can terminate by combination of two radicals.

Chain Termination

Step 4

$2R\!\!\left(CH_2CH_2\right)_{\!n}\!CH_2CH_2\cdot$ Combination

$R\!\!\left(CH_2CH_2\right)_{\!n}\!CH_2CH_2-CH_2CH_2\!\!\left(CH_2CH_2\right)_{\!n}\!R$
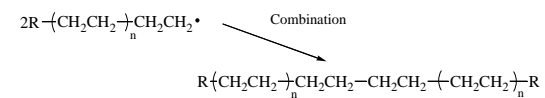
Some other addition polymers from common alkenes

Monomer	Polymer	Names
$CH_2\!=\!CHCH_3$	$\left(CH_2-CH\right)_n$, CH_3	Polypropylene
$CH_2\!=\!CHCl$	$\left(CH_2-CH\right)_n$, Cl	Poly(vinyl chloride), PVC
$CH_2\!=\!CHCN$	$\left(CH_2-CH\right)_n$, CN	Polyacrylonitrile, Orlon
$CF_2\!=\!CF_2$	$\left(CF_2-CF_2\right)_n$	Polytetrafluoroethene, Teflon
$CH_2\!=\!CCO_2CH_3$, CH_3	$\left(CH_2-C\right)_n$, CH_3 , 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

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Superglue

♦ **Some monomers can also be polymerized by nucleoophiles**

$$CH_2\!=\!C\begin{smallmatrix} CN \\ \\ CO_2CH_3 \end{smallmatrix}$$

Methyl α-cyanoacrylate