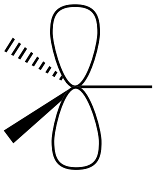
Lecture Notes
Chem 51B
S. King

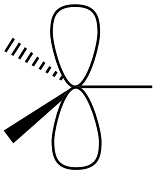
Chapter 15 Radical Reactions

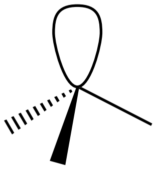
I. Introduction

A radical is a highly reactive intermediate with an unpaired electron. Radicals are involved in oxidation reactions, combustion reactions, and biological reactions.

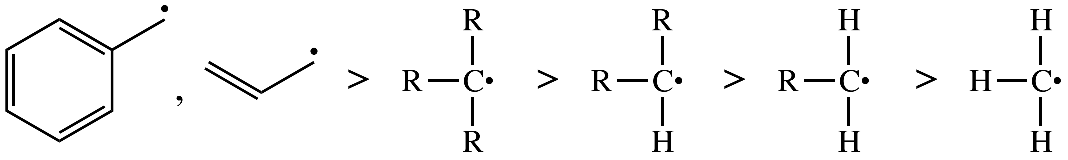
Structure: compare with: compare with:



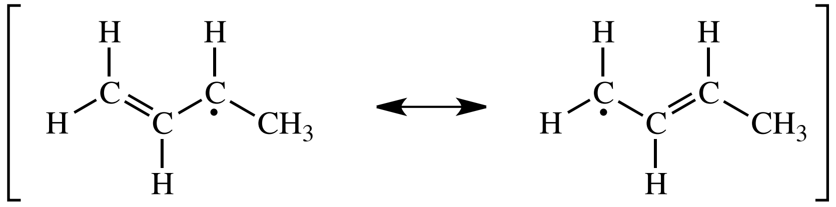




Stability: Free radicals and carbocations are both electron deficient and they follow a similar order of stability:



- like carbocations, radicals can be stabilized by resonance.



- unlike carbocations, *no rearrangements* are observed in free radical reactions.

Q. How are free radicals formed?
A. Free radicals are formed when bonds break ***homolytically***:

Look @ the arrow pushing:

Notice the fishhook arrow! It shows movement of a ***single electron***:

Compare with heterolytic bond cleavage:

A double-headed arrow shows movement of a ***pair of electrons***:

Nomenclature:

bromide ion **bromine atom** **Bromine (molecule)**

II. General Features of Radical Reactions

Radicals are formed from covalent bonds by adding energy in the form of heat or light (hν). Some radical reactions are carried out in the presence of radical initiators, which contain weak bonds that readily undergo homolysis. The most common radical initiators are peroxides (ROOR), which contain the weak O–O bond.

A. Common Reactions of Radicals:

Radicals undergo two common reactions: they react with σ-bonds and they add to π-bonds.

1. Reaction of a Radical X• with a C–H bond

A radical X• abstracts a H atom from a C–H bond to form H–X and a carbon radical:

2. Reaction of a Radical X• with a C=C bond

A radical X• also adds to the π-bond of a carbon-carbon double bond.

B. Radical Mechanisms

Radicals react *via* radical chain reactions. All radical chain reactions have **3 steps**:

1. Initiation step(s): The reactive intermediate is generated.
2. Propagation steps: The reactive intermediate reacts with a stable molecule to form another reactive intermediate, and the chain continues until the supply of reactants is exhausted or the reactive intermediate is destroyed.
3. Termination steps: Side reactions that destroy reactive intermediates and tend to slow or stop the reaction.

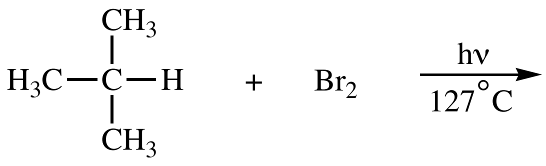
III. Halogenation of Alkanes

Chlorine or Bromine will react with alkanes in the presence of light or heat or added peroxide to give alkyl halides.

Example 1:

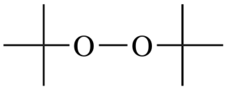
$$CH_4 + Cl_2 \longrightarrow \underset{80\%}{CH_3Cl} + \underset{10\%}{CH_2Cl_2} + CHCl_3 + CCl_4 + Cl_3CCCl_3$$

Example 2:



$$H_3C-\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}-H + Br_2 \xrightarrow[127^\circ C]{h\nu}$$

- Reaction with F_2 is too violent and reaction with I_2 is too slow to be useful.
- With an alkane that has more than one type of hydrogen atom, a mixture of alkyl halides may result.

weak bonds:	BDE (kcal/mole)
F—F	38
Cl—Cl	59
Br—Br	46
I—I	36
HO—OH	51
	38

☛ *This is a radical chain reaction:*

Mechanism for Example 1:

$$CH_4 + Cl_2 \longrightarrow CH_3Cl + CH_2Cl_2 + CHCl_3 + CCl_4 + Cl_3CCCl_3$$

1. **Initiation**: Radical formed

2. **Propagation**:

3. **Termination**: Radicals destroyed by recombining

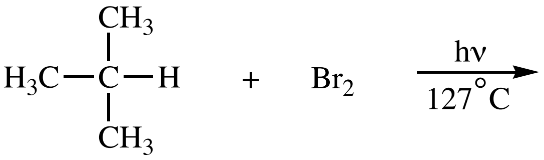
- *The reaction is carried out using a large excess of CH_4 to maximize formation of the monosubstituted product*

Competing propagation step:

- Free radical halogenation is ***not*** the best way to synthesize alkyl halides (*there are better ways)*, but, it is still useful because it is the ***only*** way to convert an inert alkane into a reactive compound!

One better way we know to synthesize alkyl chlorides:

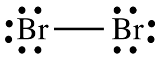
Mechanism for Example 2:



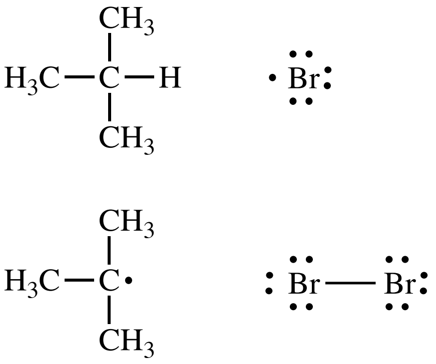
$$H_3C-C(CH_3)_2-H + Br_2 \xrightarrow[127^{\circ}C]{h\nu}$$

Mechanism:

1. **Initiation**: Radical formed

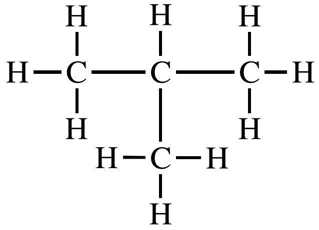


2. **Propagation**:



3. **Termination**: Radicals destroyed by recombining

A. Look at the selectivity in example 2:



Q: Why are no 1° H's abstracted?

A. You have to look at two factors:

1. Relative stability of the radicals formed:

2. Ease at which the different hydrogens are removed *(look at bond dissociation energies and* E_a*)*

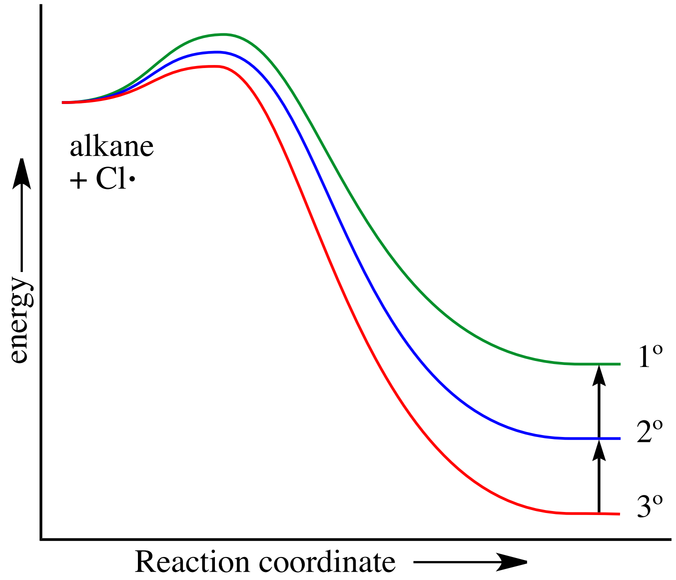
Look at the relative rates of hydrogen abstraction by halogen atoms:

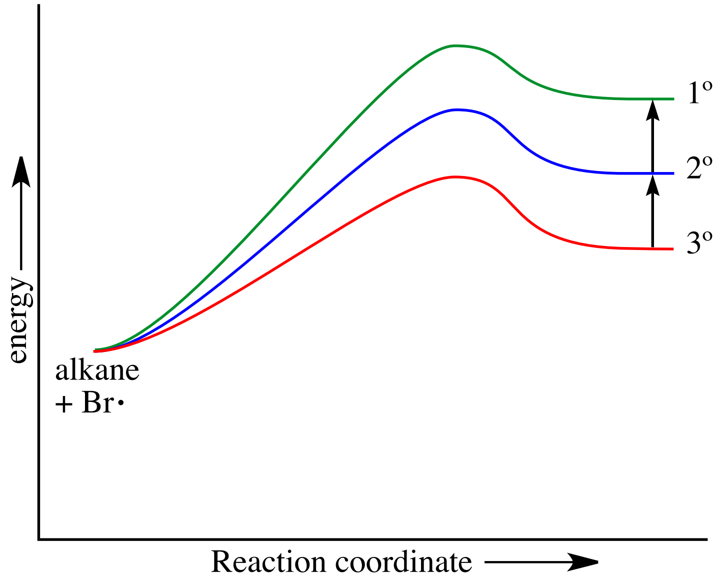
	1°	2°	3°
Br•			
Cl•			

Q. Why is the bromine atom so much more selective?

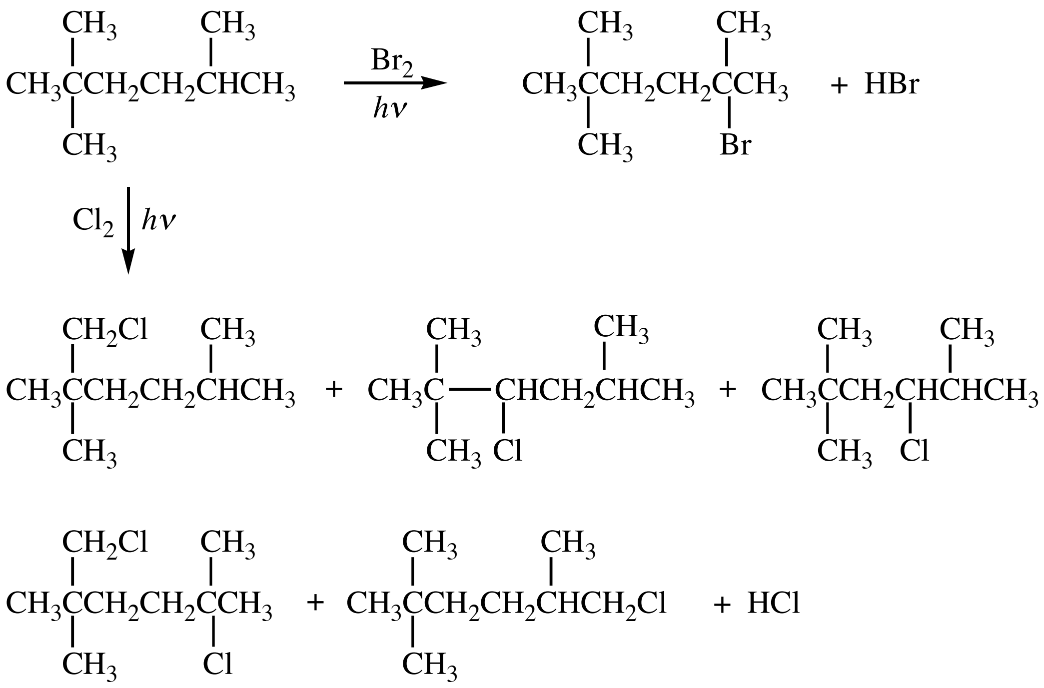
A. If you compare the transition states and activation energies for the abstraction of a hydrogen atom by a bromine radical *vs*. a chlorine radical you will find that:

1. Abstraction of a hydrogen atom by Br· is ***endothermic*** while abstraction of a hydrogen atom by Cl· is ***exothermic***.
2. The transition states for the endothermic bromination have a larger energy difference than those for exothermic chlorination, even though the energy difference of the products is the same in both reactants.





Example 3: This example shows the dramatic difference in selectivity in bromination *vs*. chlorination:



$$CH_3\underset{CH_3}{\overset{CH_3}{C}}CH_2CH_2\overset{CH_3}{C}HCH_3 \xrightarrow[h\nu]{Br_2} CH_3\underset{CH_3}{\overset{CH_3}{C}}CH_2CH_2\underset{Br}{\overset{CH_3}{C}}CH_3 + HBr$$

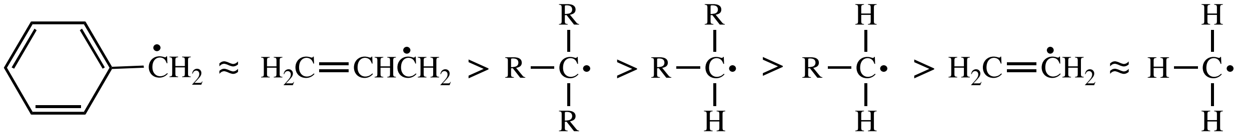
$$\downarrow Cl_2,\ h\nu$$

$$CH_3\underset{CH_3}{\overset{CH_2Cl}{C}}CH_2CH_2\overset{CH_3}{C}HCH_3 + CH_3\underset{CH_3}{\overset{CH_3}{C}}\text{—}\underset{Cl}{C}HCH_2\overset{CH_3}{C}HCH_3 + CH_3\underset{CH_3}{\overset{CH_3}{C}}CH_2\underset{Cl}{C}H\overset{CH_3}{C}HCH_3$$

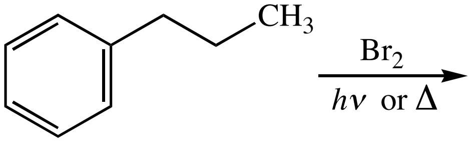
$$CH_3\underset{CH_3}{\overset{CH_2Cl}{C}}CH_2CH_2\underset{Cl}{\overset{CH_3}{C}}CH_3 + CH_3\underset{CH_3}{\overset{CH_3}{C}}CH_2CH_2\overset{CH_3}{C}HCH_2Cl + HCl$$

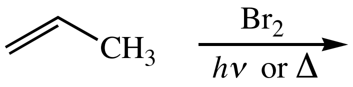
IV. Radical Substitution of Benzylic and Allylic Hydrogens

Recall that allyl and benzyl radicals are both more stable than tertiary radicals:

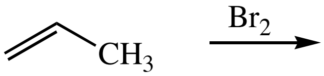


We know that the more stable the radical, the faster it can be formed, so a hydrogen bonded to either a benzylic or allylic carbon can preferentially be substituted in a halogenation reaction.

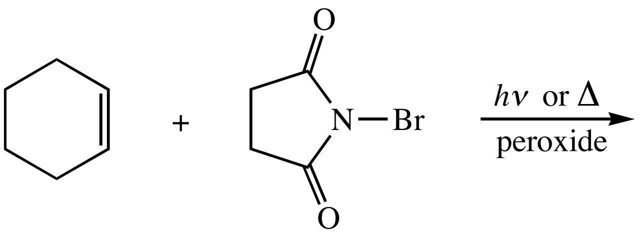


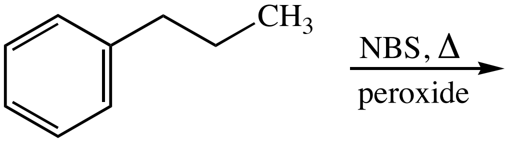


Complication: Bromine also adds to double bonds!



Solution: Use *N*-Bromosuccinimide (NBS) instead *(don’t use Br_2!)*





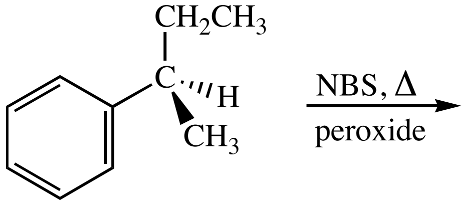
- NBS serves to provide a small steady state concentration of Br_2 so that addition to the double bond does not occur.

V. Stereochemistry of Radical Reactions

Because free radicals are planar and sp^2 hybridized, racemic mixtures are obtained in reactions that form a stereocenter:

$$CH_3CH_2CH_2CH_3 \xrightarrow[h\nu]{Br_2}$$

In addition, loss of optical purity will occur if substitution occurs at a chiral center.



VI. Radical Addition of HBr to an Alkene

The addition of HBr to 1-butene gives the Markovikov product, 2-bromobutane. If HBr is added in the presence of an alkyl peroxide, ROOR, the anti-Markovnikov product is formed:

$$CH_3CH_2CH{=}CH_2 \quad + \quad HBr \quad \longrightarrow$$

$$CH_3CH_2CH{=}CH_2 \quad + \quad HBr \quad \xrightarrow{ROOR}$$

- A peroxide reverses the order of addition because it changes the mechanism of the reaction, so that Br•, a radical, becomes the electrophile rather than H^+.

1. **Initiation**: Radical formed

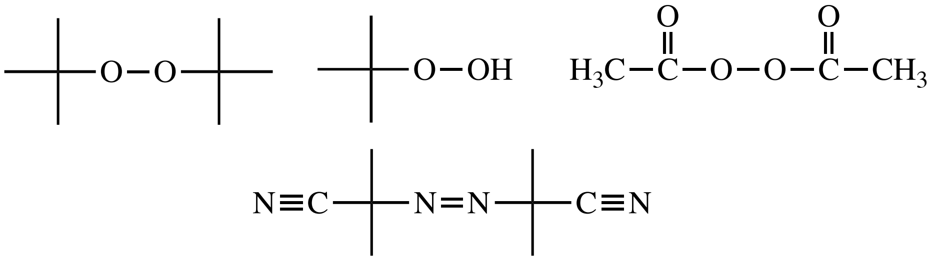
2. **Propagation**:

3. **Termination**: Radicals destroyed by recombining

- In the propagation step, Bromine adds to the sp^2 carbon of 1-butene that is bonded to the greater number of hydrogens to form a secondary radical, rather than adding to the other sp^2 carbon to form a primary radical. ***Why?***

- An alkyl peroxide is a *radical initiator* because it creates radicals. Without a peroxide, the preceding reaction would not occur. Radical initiators have weak bonds that readily undergo homolysis.

Some radical initiators:



Q: This **peroxide effect** occurs only with HBr, and not with HCl or HI. ***Why?***
A: If you calculate ΔH° for each reaction:

For radical addition of ***HBr:***

1st propagation step:

2nd propagation step:

For radical addition of ***HCl:***

1st propagation step:

2nd propagation step:

For radical addition of ***HI:***

1st propagation step:

2nd propagation step:

☛ For radical chain reactions, the steps that propagate the chain compete with termination steps. Termination steps are always exothermic because only bond making occurs.

When HCl or HI adds to an alkene in the presence of peroxide, any chain reaction that is initiated is terminated because propagation cannot compete with termination!

VII. Free-Radical Oxidations with Molecular Oxygen

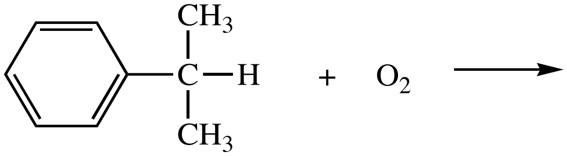
A. Autooxidation

When organic compounds are exposed to air, they react slowly with oxygen to give hydroperoxides - this is known as autooxidation, and it is responsible for the slow deterioration in air of foods, rubber, and paints.

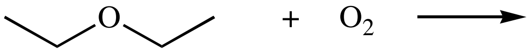
Compounds that are easily autooxidized are compounds that form especially stable radicals.

Examples:

Compounds with allylic or benzylic hydrogens:

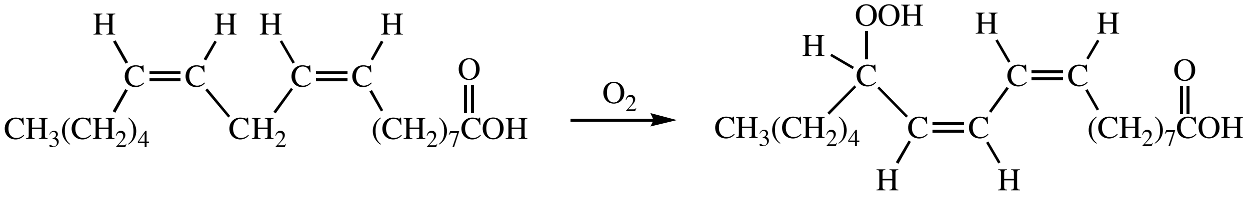


Compounds with hydrogen atoms on a carbon adjacent to an oxygen:

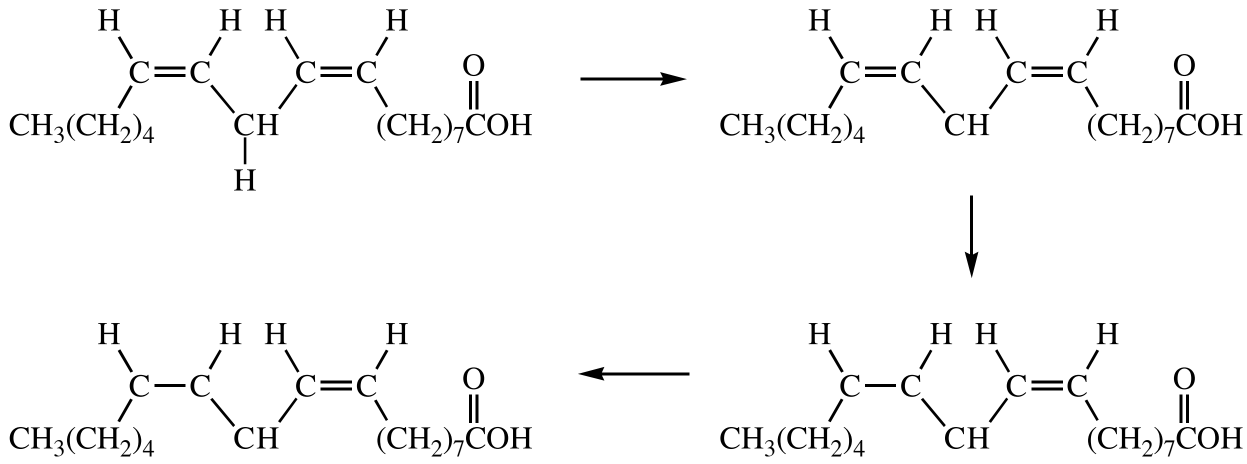


- Solvents such as diethyl ether which have been stored for some time contain hydroperoxides.
- Hydroperoxides are **unstable** compounds and may decompose violently when heated!

Polyunsaturated fats:



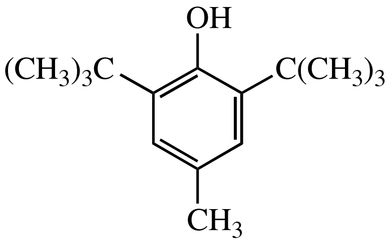
How??



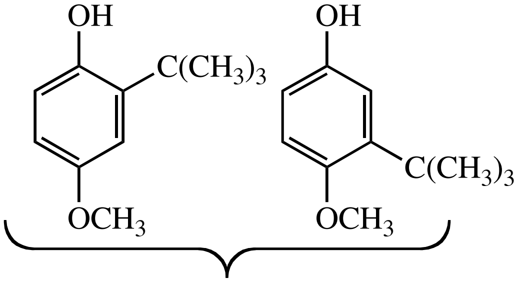
B. Preventing Autooxidation: Additon of Antioxidants (Free-Radical Scavengers)

Antioxidants are added to foods to retard spoilage or rancidity. They are free-radical scavengers.

Common Antioxidants:



BHT



BHA

BHA and BHT react with free radicals that are formed to make hindered phenoxy radicals which are unreactive and thus terminate free-radical chain reactions.