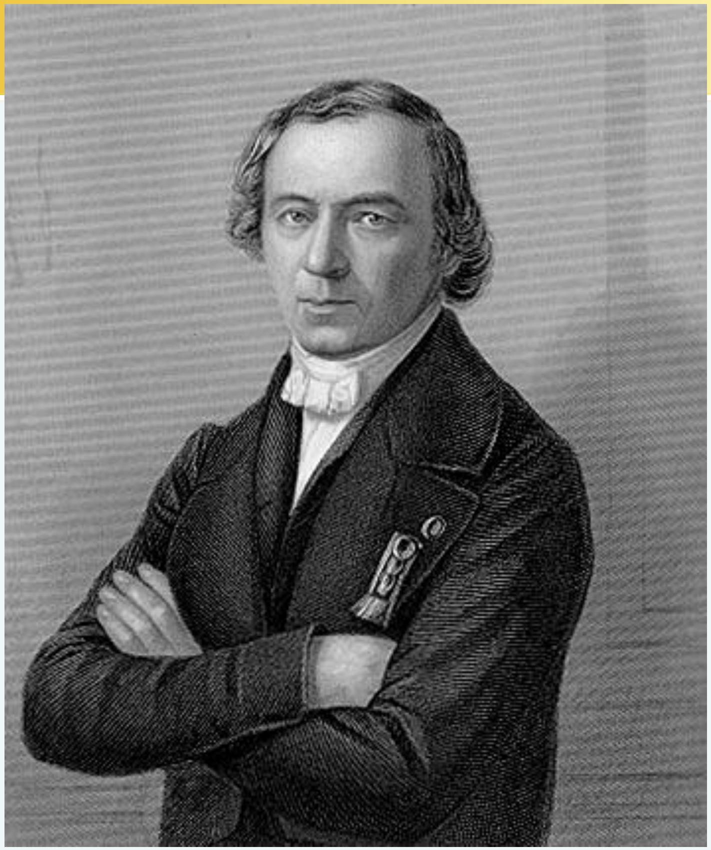
Radical Reactions

Substitution Theory



J. B. Dumas
(1800 -1884)

1838 - chlorination of acetic acid

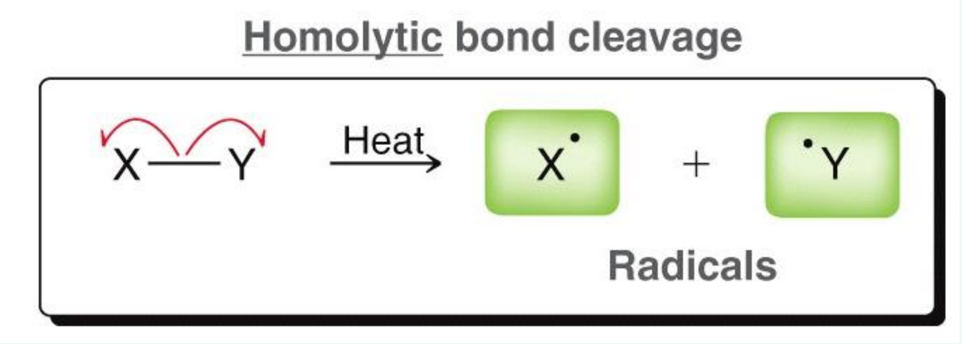
$$\underline{C}_4H_4O_2 + Cl_6 = \underline{C}_4HCl_3O_2 + H_3Cl_3$$

$$\underline{C} = 6, O = 16$$

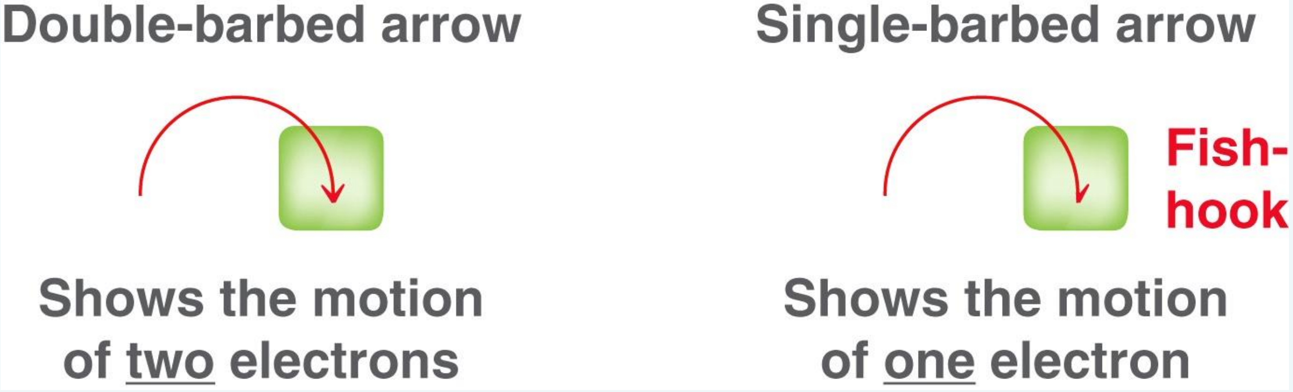
$$C_2H_4O_2 + 3Cl_2 = C_2HCl_3O_2 + 3HCl$$

11.1 Free Radicals

- Free radicals form when bonds break homolytically

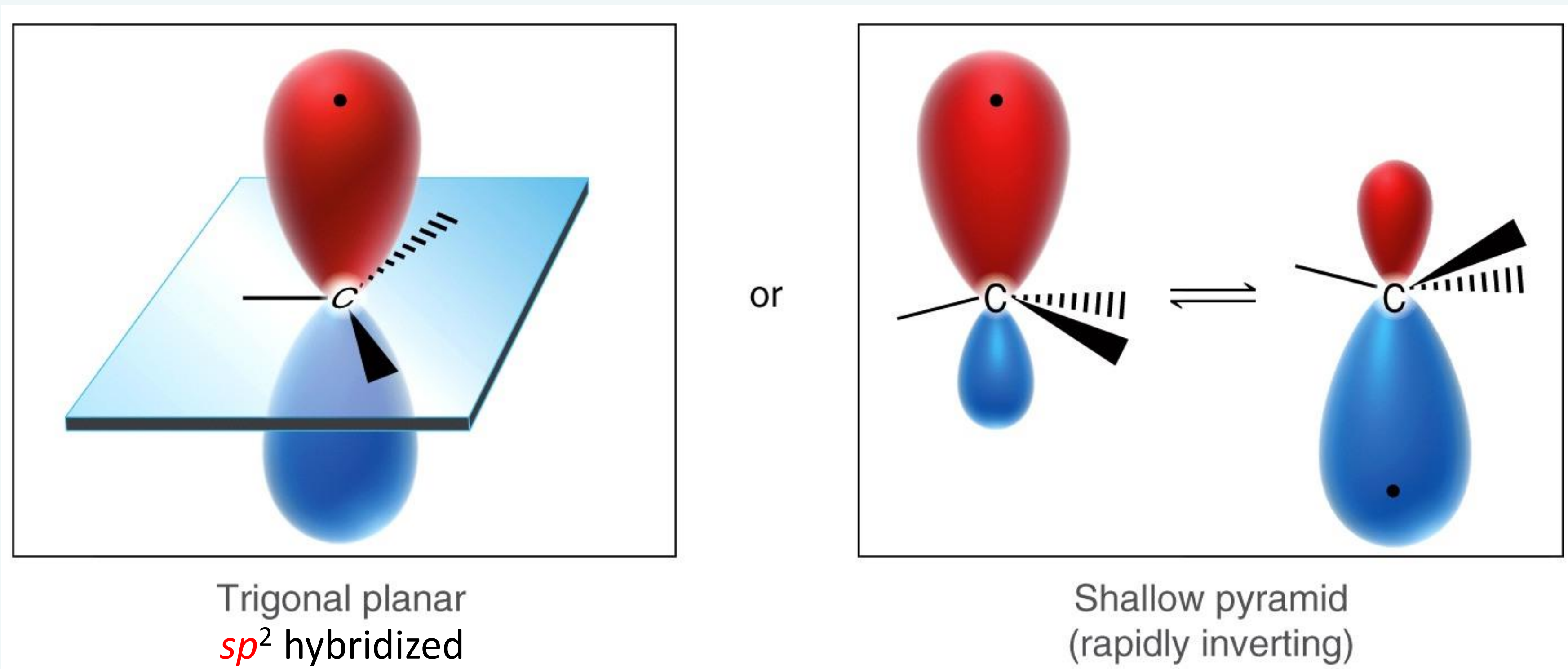


- Note the single-barbed or fishhook arrow used to show the electron movement



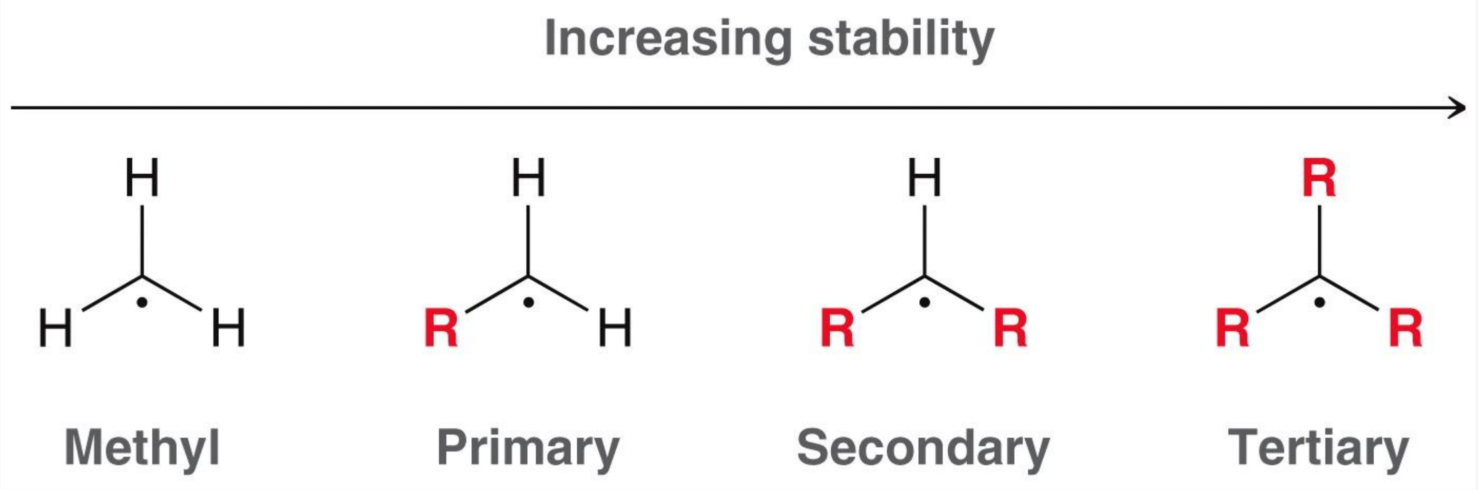
11.1 Free Radicals

- Free radicals can be thought of as *sp*^{2} hybridized or quickly interconverting *sp*^{3} hybridized



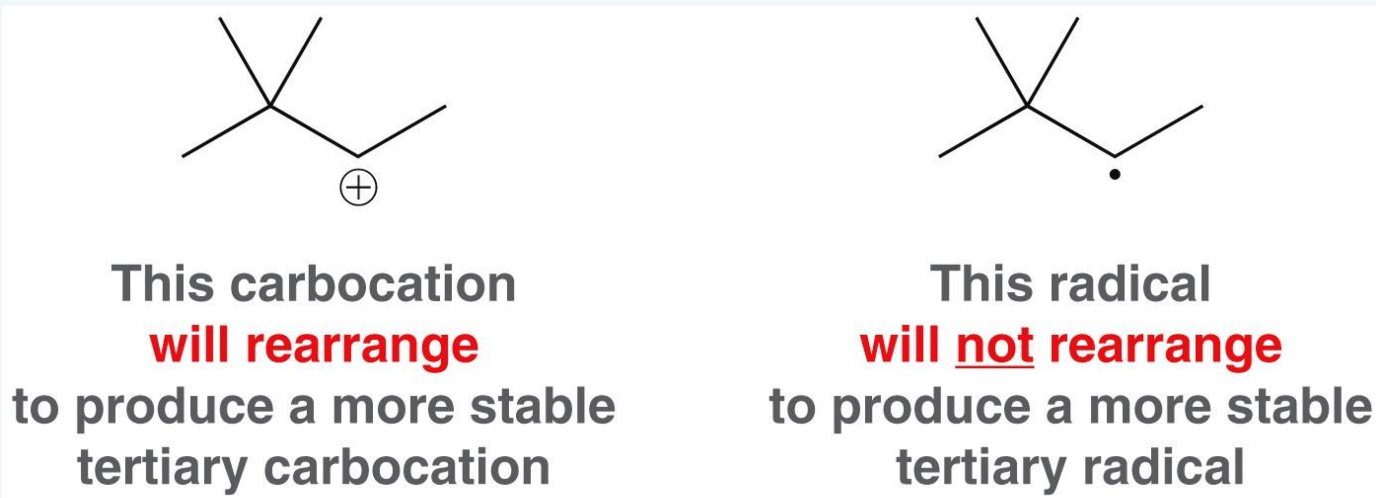
11.1 Free Radical Stability

- Free radicals do not have a formal charge but are unstable because of an incomplete octet
- Groups that can push (donate) electrons toward the free radical will help to stabilize it. WHY? HOW? Consider hyperconjugation



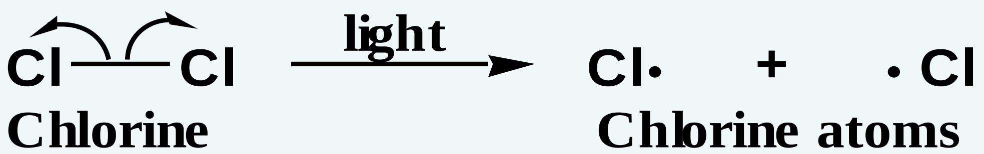
11.2 Radical Electron Movement

- Free radical electron movement is quite different from electron movement in ionic reactions
- For example, free radicals don't undergo rearrangement



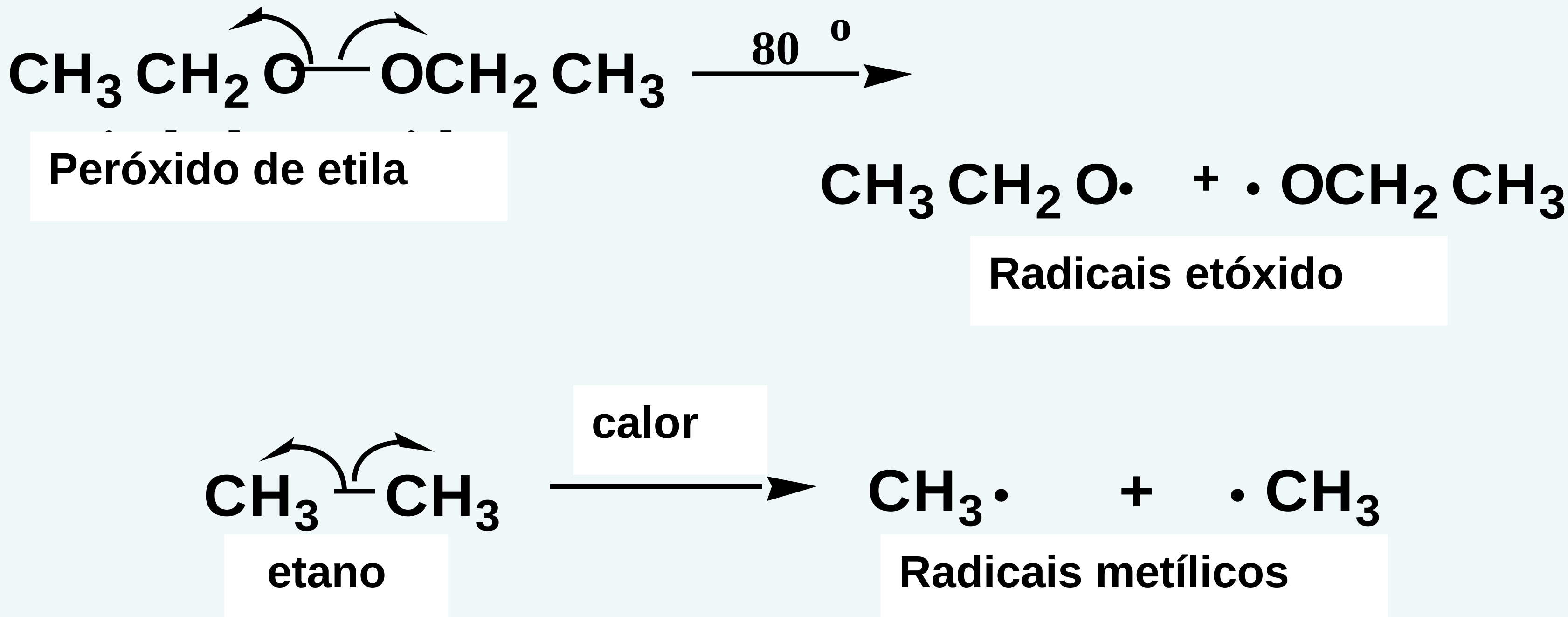
Mecanismo

- Um mecanismo radicalar em cadeia
- Radical: qualquer espécie química que contém um ou mais elétrons desemparelhados
- Radicais são formados por clivagem homolítica de uma ligação



  – uma seta em forma de anzol é usada para mostrar a mudança na posição de um único elétron

Formação de Radicais



- A ordem de estabilidade dos radicais alquílicos é $3^\circ > 2^\circ > 1^\circ >$ metila

Mecanismo

- Iniciação da cadeia: passo em uma reação radicalar em cadeia caracterizada pela formação de radicais de compostos não radicalares

Iniciação da cadeia

1. $Cl_2 \xrightarrow[\text{ou luz}]{\text{calor}} Cl\cdot + \cdot Cl$

Mecanismo

- Propagação da cadeia: passo em uma reação radicalar em cadeia caracterizada pela reação de um radical e uma molécula para formar um novo radical

Propagação da cadeia

2. $CH_3CH_3 + Cl\cdot \longrightarrow CH_3CH_2\cdot + HCl$

3. $CH_3CH_2\cdot + Cl_2 \longrightarrow CH_3CH_2Cl + Cl\cdot$

- Comprimento da cadeia, n: o número de vezes no ciclo que o passo de propagação repete-se numa reação em cadeia

Mecanismo

- Terminação da cadeia - passo em uma reação radicalar em cadeia que envolve destruição de radicais

Terminação da cadeia

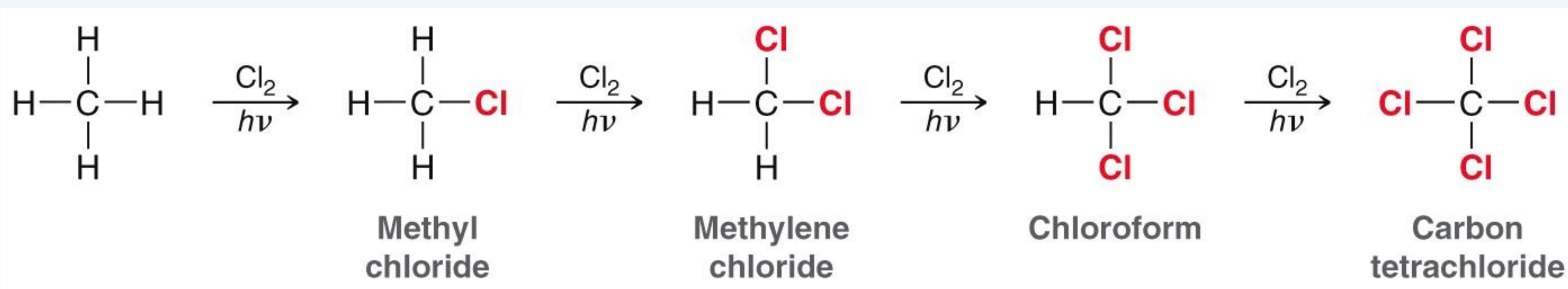
4. $2\ CH_3CH_2\cdot \longrightarrow CH_3CH_2CH_2CH_3$
5. $CH_3CH_2\cdot + \cdot Cl \longrightarrow CH_3CH_2Cl$
6. $Cl\cdot + \cdot Cl \longrightarrow Cl_2$

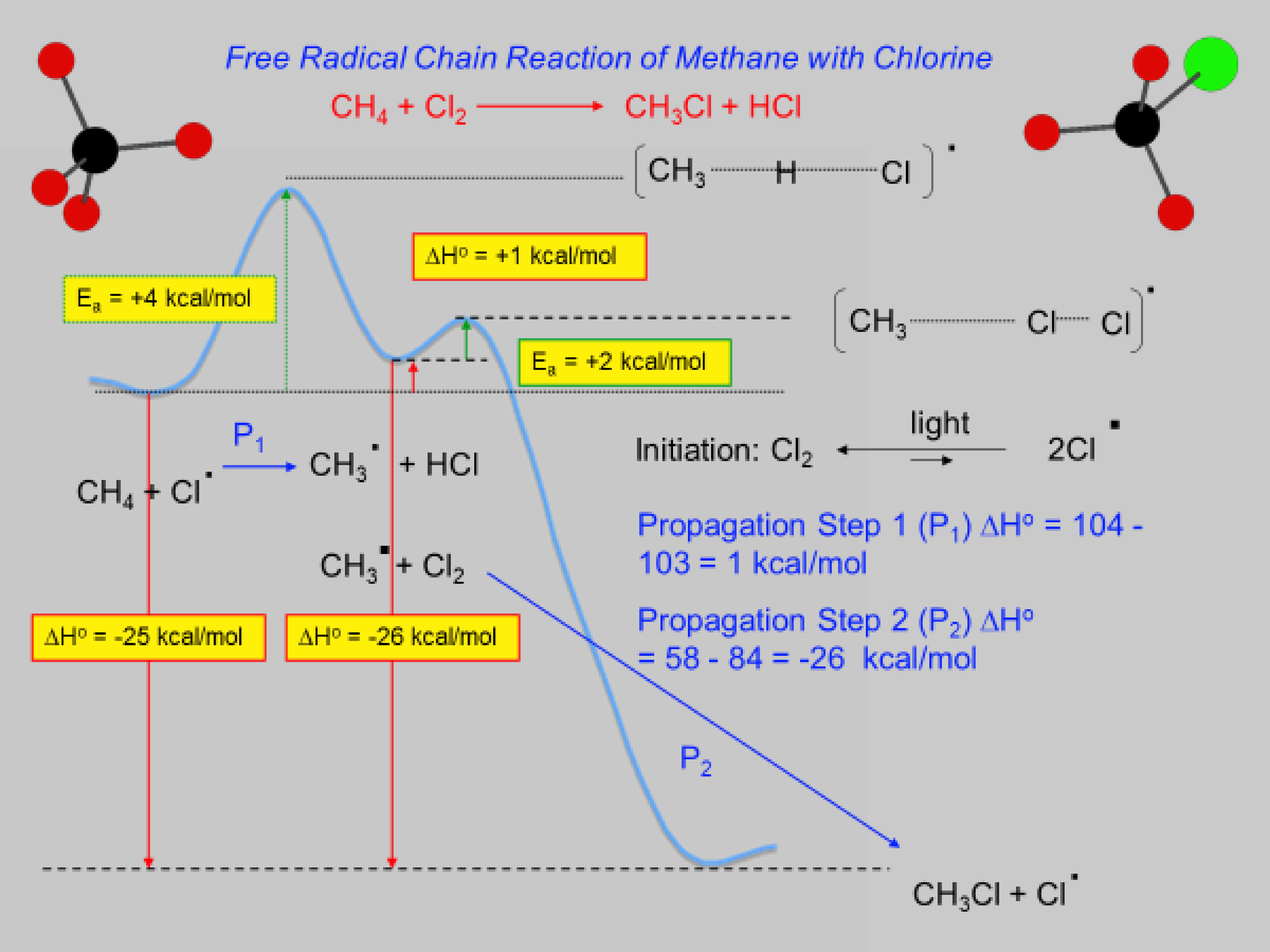
Propagação da cadeia

				ΔH° (kcal/mol)
Passo 2:				
CH_3CH_3 + $Cl\cdot$	$\longrightarrow$	$CH_3CH_2\cdot$ + HCl		
+100		-103		-3
Passo 3:				
$CH_3CH_2\cdot$ + Cl_2	$\longrightarrow$	CH_3CH_2Cl + $Cl\cdot$		
+59		-80		-21
CH_3CH_3 + Cl_2	$\longrightarrow$	CH_3CH_2Cl + HCl		-24

11.3 Chlorination of Methane

- Reactions that have self-sustaining propagation steps are called **chain reactions**
- **Chain reaction:** the products from one step are reactants for a different step in the mechanism
- Polychlorination is difficult to prevent, especially when an excess of Cl_2 is present.

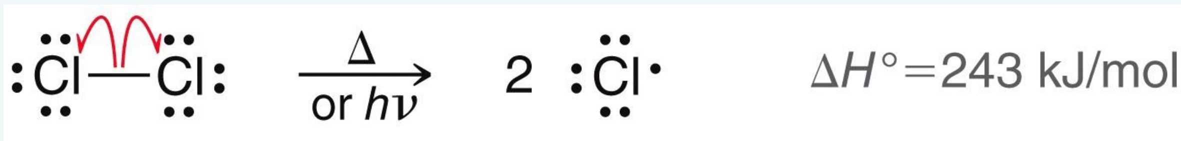


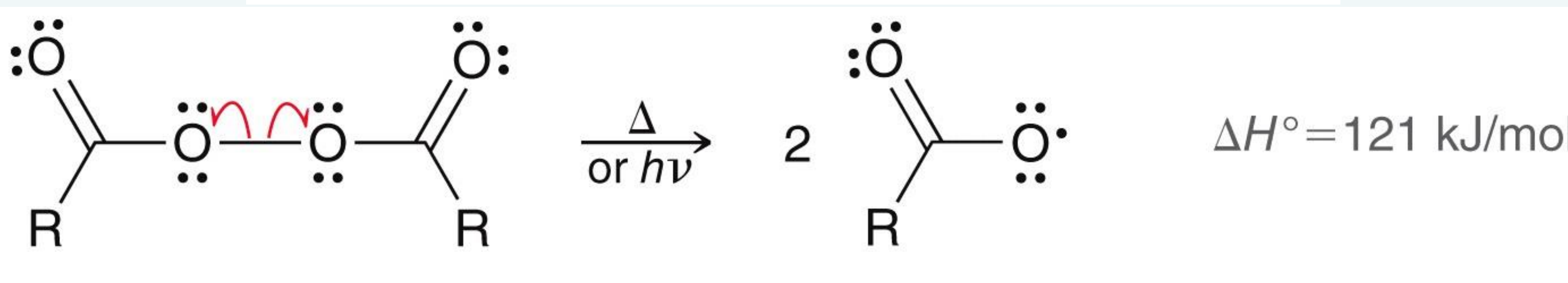


Free Radical Chain Reaction of Methane with Chlorine
CH4 + Cl2 → CH3Cl + HCl
[CH3 ····· H ····· Cl]•
ΔHº = +1 kcal/mol
Ea = +4 kcal/mol
[CH3 ····· Cl ···· Cl]•
Ea = +2 kcal/mol
P1
CH3• + HCl
CH4 + Cl•
Initiation: Cl2 ⇌ 2Cl• (light)
Propagation Step 1 (P1) ΔHº = 104 - 103 = 1 kcal/mol
CH3• + Cl2
ΔHº = -25 kcal/mol
ΔHº = -26 kcal/mol
Propagation Step 2 (P2) ΔHº = 58 - 84 = -26 kcal/mol
P2
CH3Cl + Cl•

11.3 Radical Initiators

- An initiator starts a free radical chain reaction



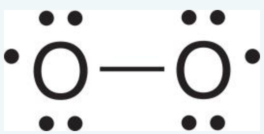


An acyl peroxide

- Which initiator above initiates reactions most readily? WHY?

11.3 Radical Inhibitors

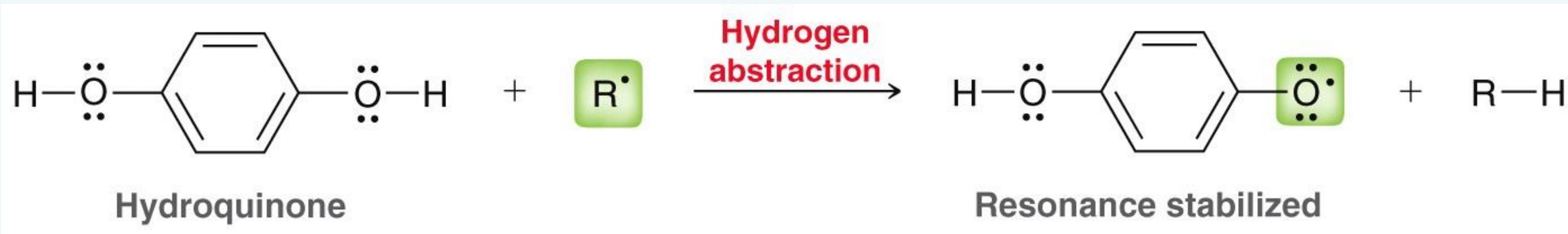
- Inhibitors act in a reaction to scavenge free radicals to stop chain reaction processes
- Oxygen molecules can exist in the form of a diradical, which reacts readily with other radicals. Use arrows to show the process

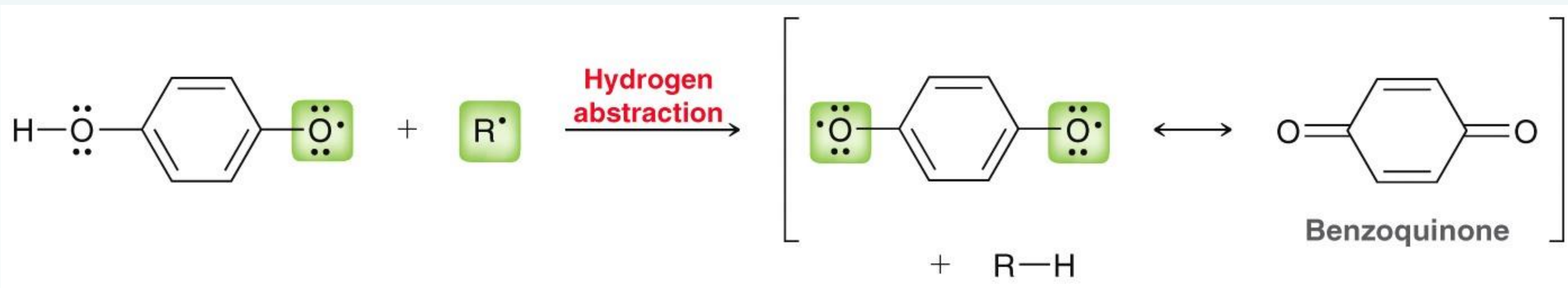


- How can reaction conditions be modified to stop oxygen from inhibiting a desired chain reaction?

11.3 Radical Inhibitors

- Hydroquinone is also often used as a radical inhibitor





Reactivity–Selectivity Principle

- The very reactive chlorine atom will have lower selectivity and attack pretty much any hydrogen available on an alkane
- The less reactive bromine atom will be more selective and tends to react preferentially with the easy targets, i.e. tertiary hydrogens

11.5 Halogenation Regioselectivity

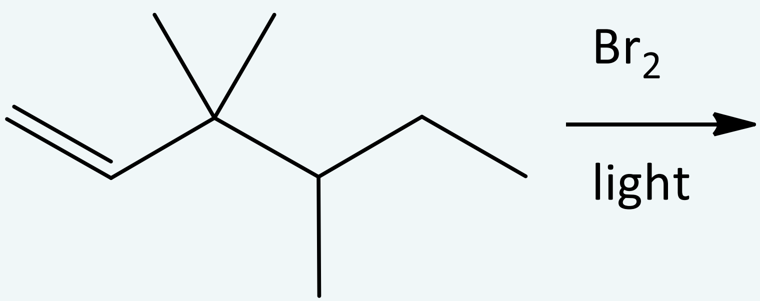
- Which process is least regioselective?

TABLE 11.2 THE RELATIVE SELECTIVITY OF FLUORINATION, CHLORINATION, AND BROMINATION

	PRIMARY	SECONDARY	TERTIARY
F	1	1.2	1.4
Cl	1	4.5	5.1
Br	1	82	1600

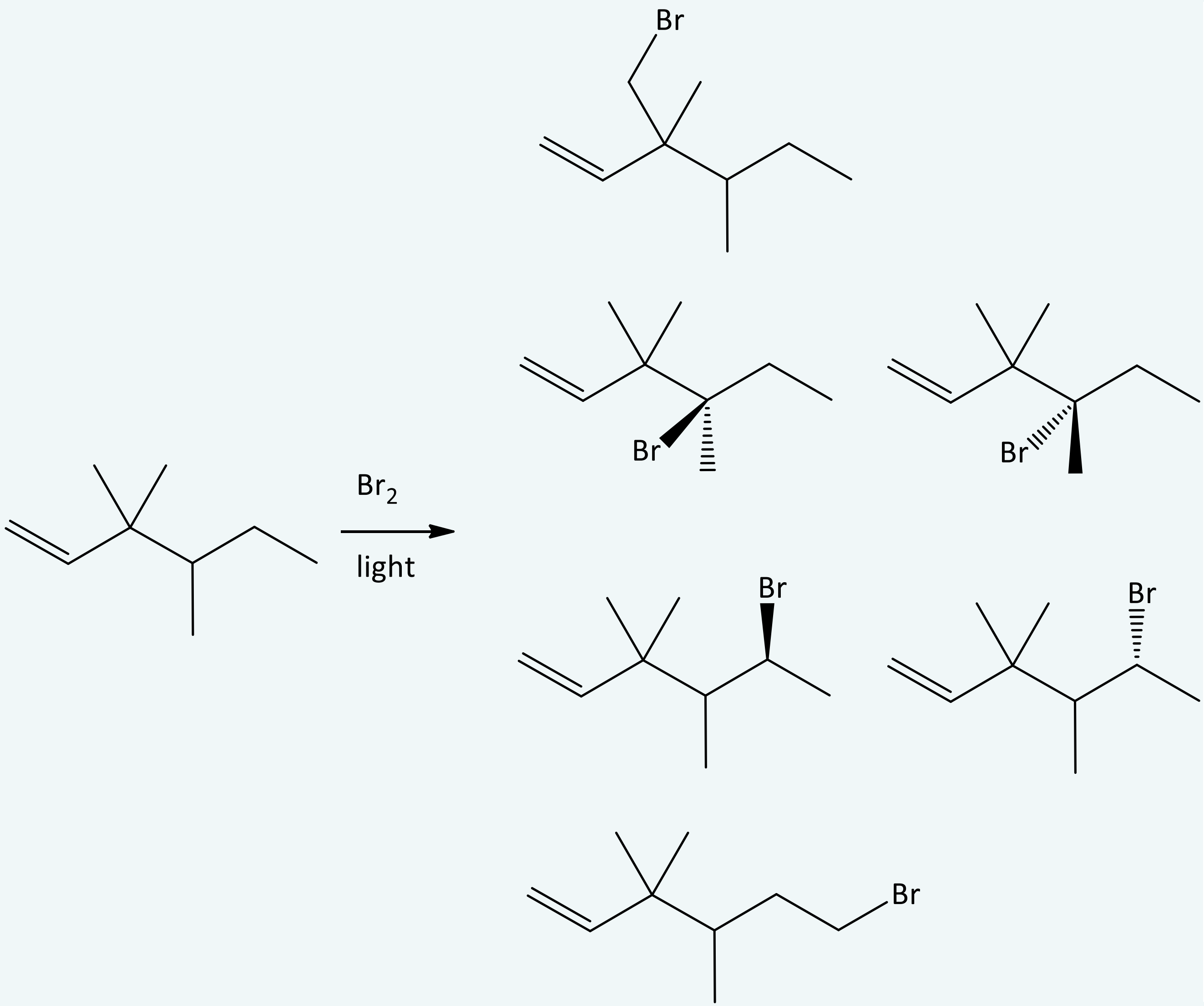
11.5 Halogenation Regioselectivity

- Ignoring possible addition products for now, draw the structure for EVERY possible monobromination product for the reaction below



- Rank the products in order from most major to most minor

11.5 Halogenation Regioselectivity



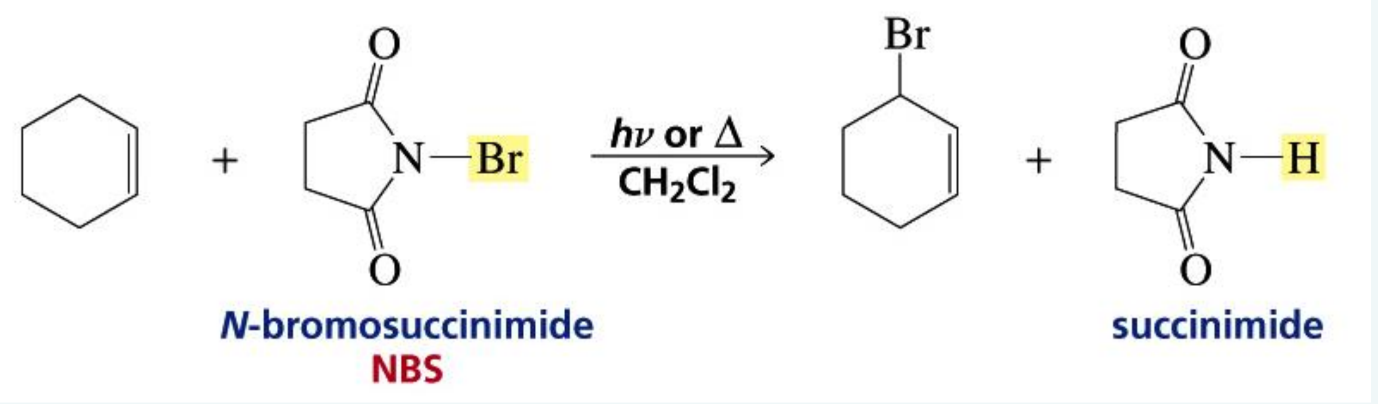
- Second least abundant product
- Most abundant product
- Second most abundant product
- Least abundant product

Radical Substitution of Benzylic and Allylic Hydrogens

- Electrophilic addition can be minimized by maintaining the halogen at a very low concentration
- Under these conditions, halogens can substitute for allylic and benzylic hydrogens

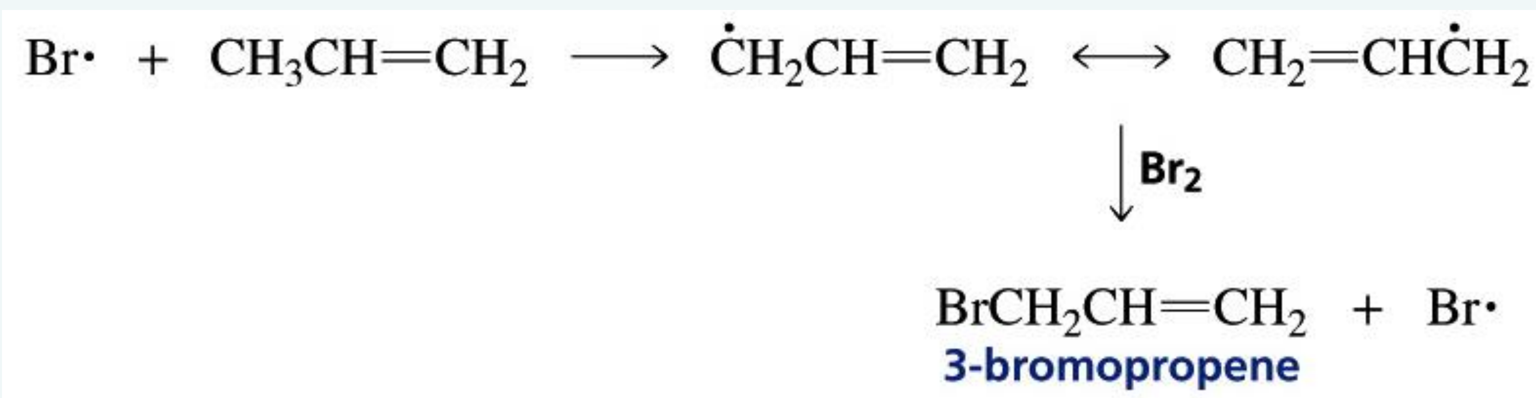
Radical Substitution of Benzylic and Allylic Hydrogens

- *N*-Bromosuccinimide (NBS) is a good reagent for supplying low concentrations of bromine radical



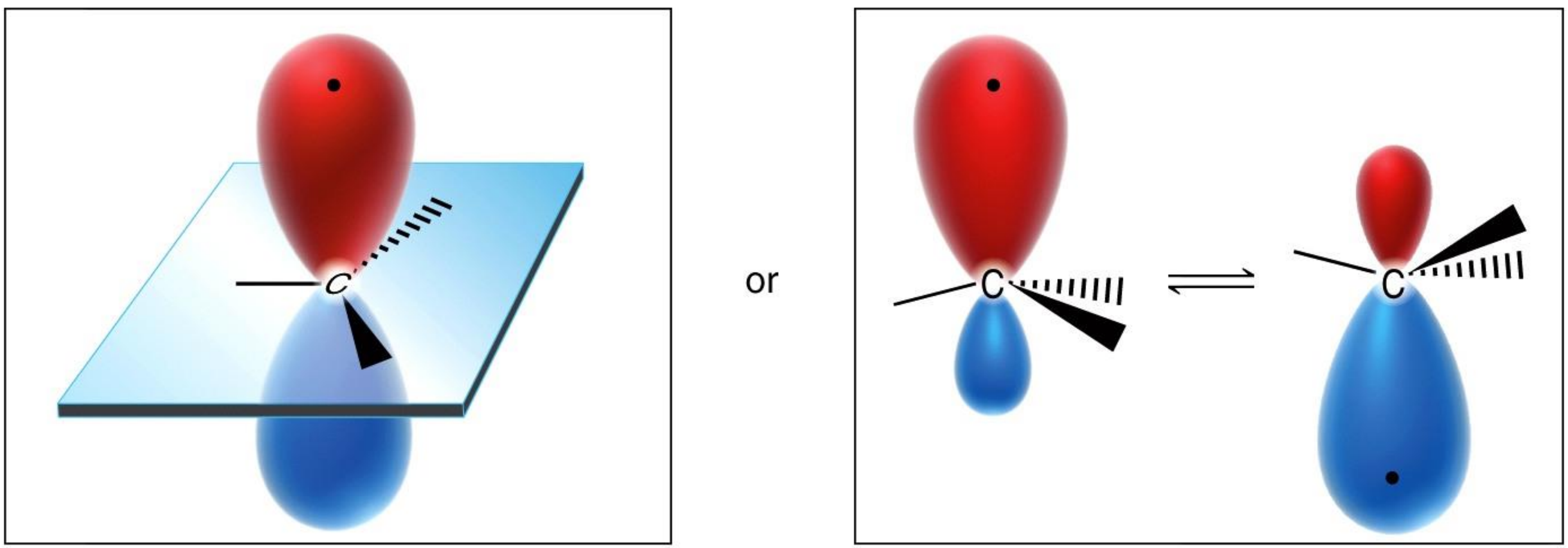
Radical Substitution of Benzylic and Allylic Hydrogens

- When a radical abstracts an allylic or benzylic hydrogen, a radical that is stabilized by resonance is obtained



11.6 Halogenation Stereochemistry

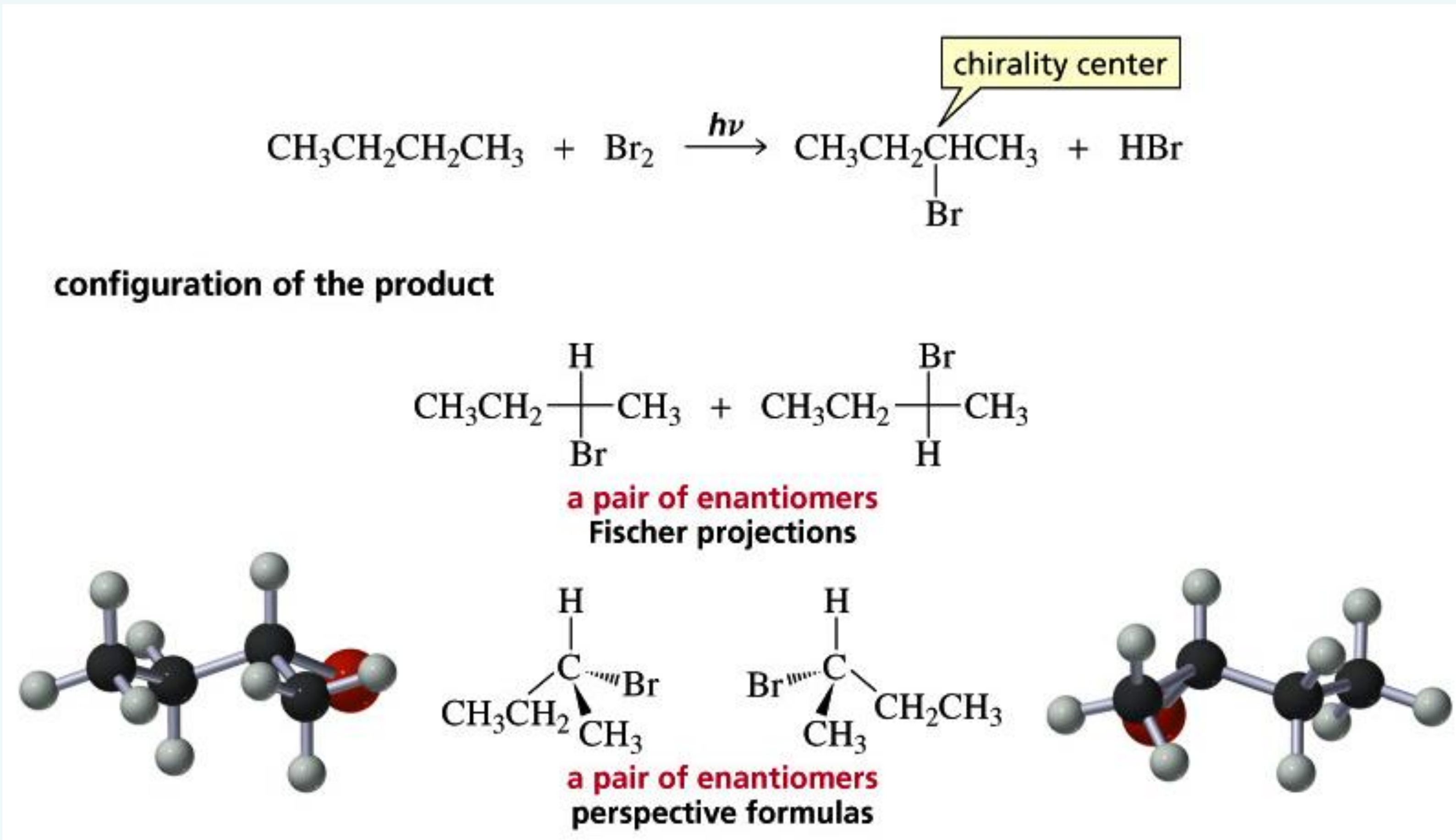
- Whether the free radical carbon is *sp*^{2} or a rapidly interconverting *sp*^{3}, the halogen abstraction will occur on either side of the plane with equal probability



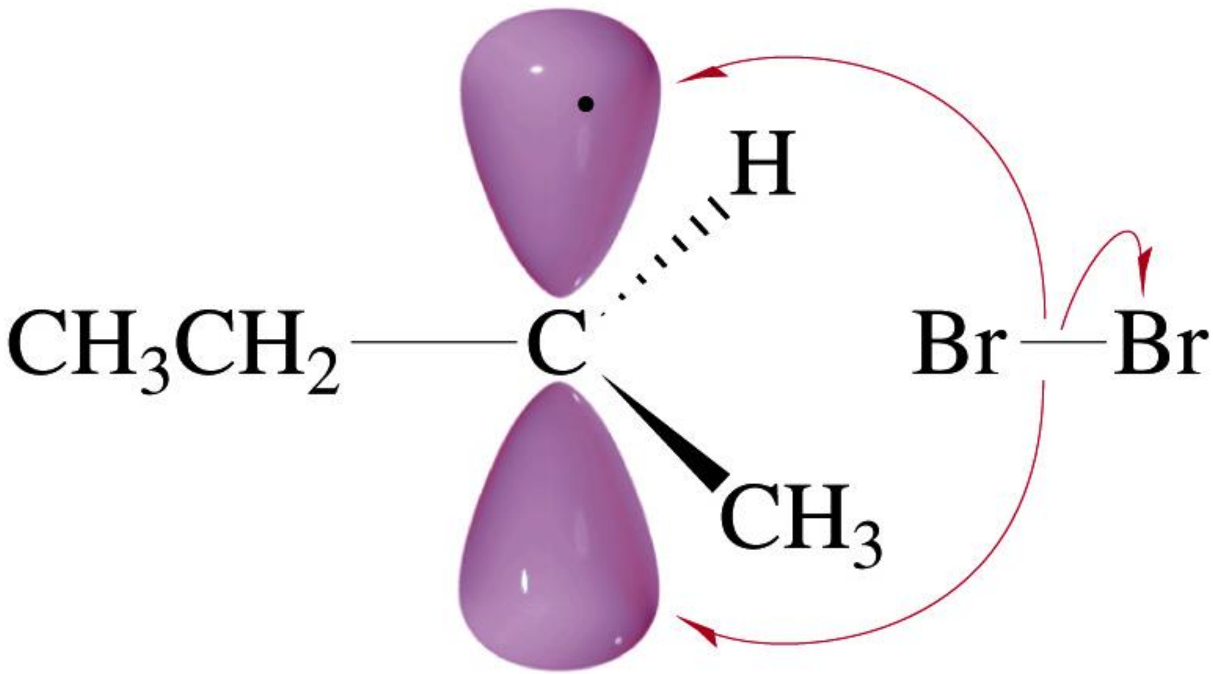
Trigonal planar
sp^2 hybridized

Shallow pyramid
(rapidly inverting)

Stereochemistry of Radical Substitution



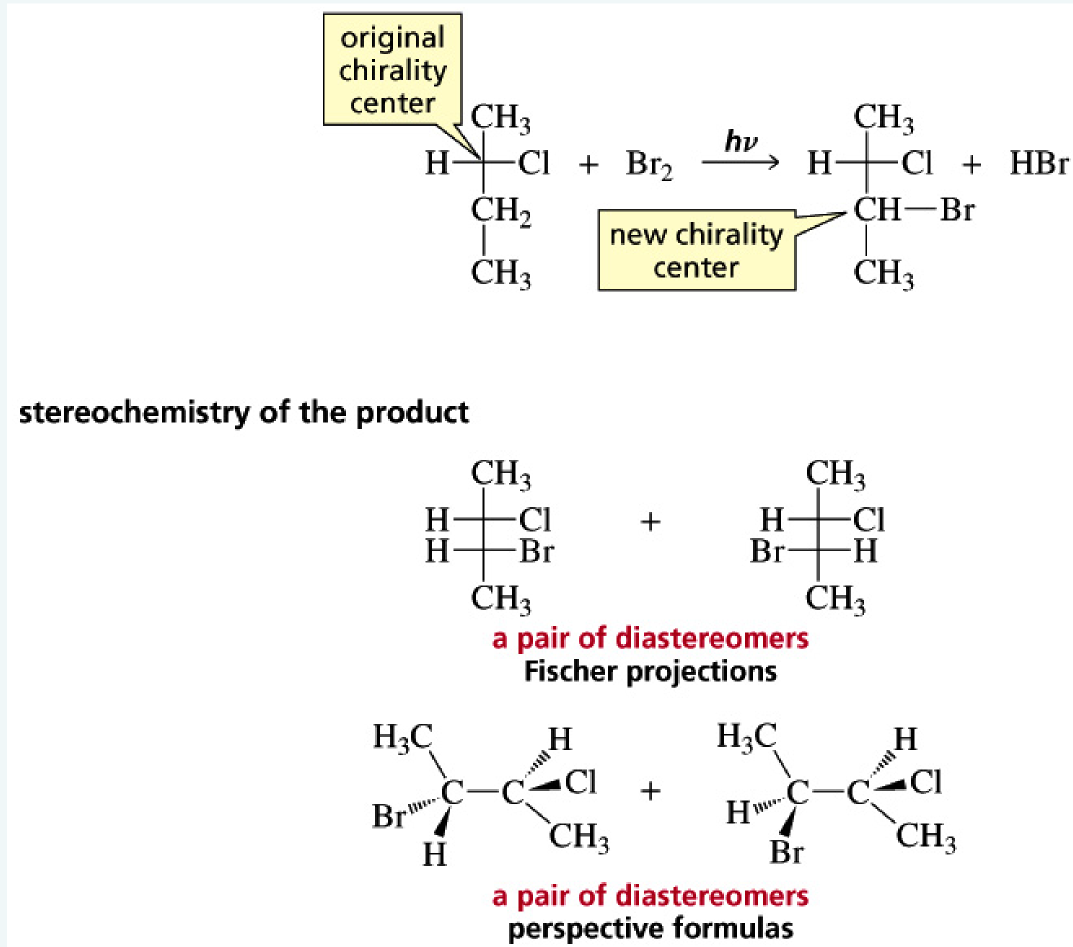
Stereochemistry of Radical Substitution



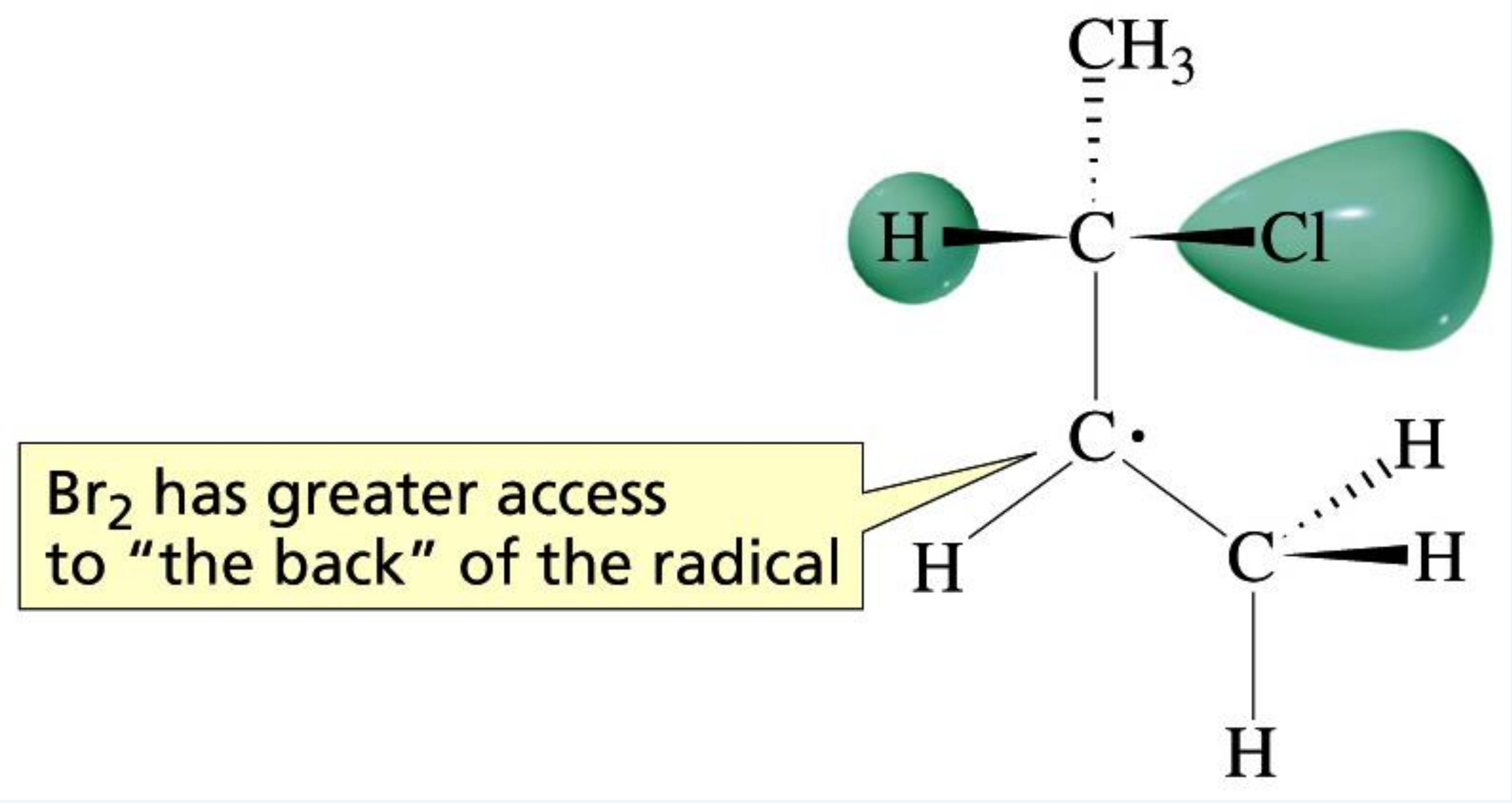
a radical intermediate

Stereochemistry of Radical Substitution

- If a chirality center already exists, it may affect the distribution of products
- A pair of diastereomers will be formed, but in unequal proportions

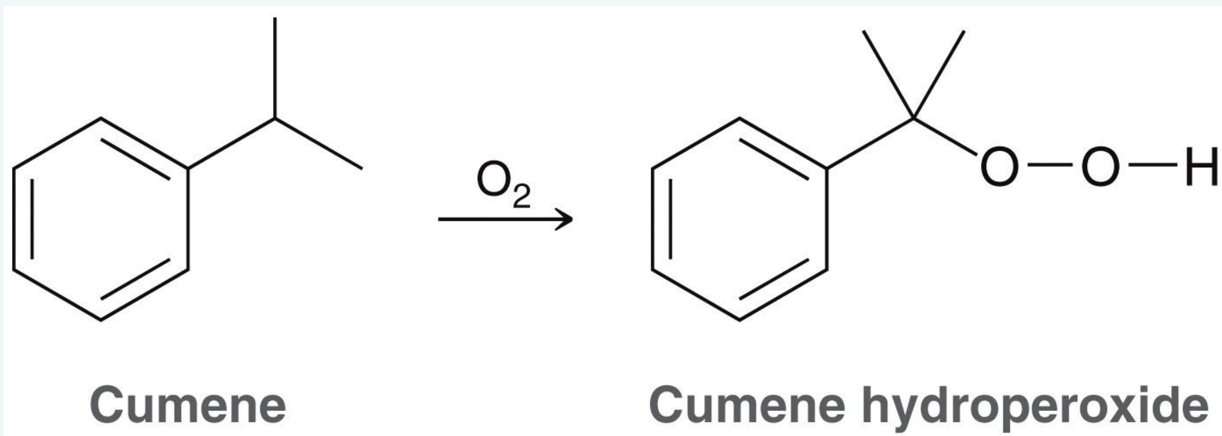


Stereochemistry of Radical Substitution



11.9 Autooxidation

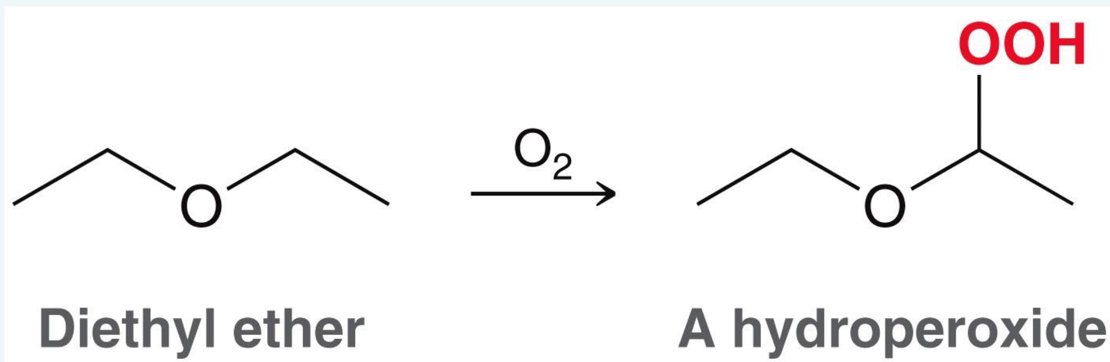
- Autooxidation is the process by which compounds react with molecular oxygen



- The process is generally very slow

11.9 Autooxidation

- Some compounds such as ethers are particularly susceptible to autooxidation



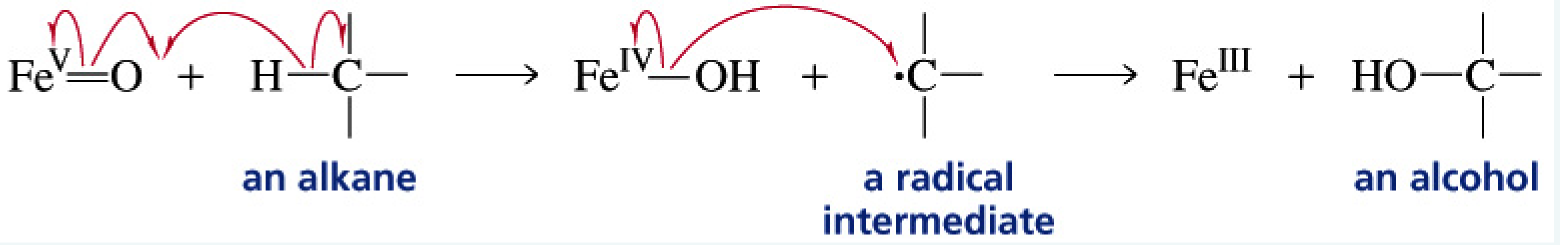
- Because hydroperoxides can be explosive, ethers like diethyl ether must not be stored for long periods of time
- They should be dated and used in a timely fashion

11.9 Autooxidation

- Light accelerates the autooxidation process
- Dark containers are often used to store many chemicals such as vitamins
- In the absence of light, autooxidation is usually a slow process
- Compounds that can form a relatively stable C• radical upon H abstraction are especially susceptible to autooxidation. WHY?
- Consider the autooxidation of compounds with allylic or benzylic hydrogen atoms

Radical Reactions in Biological Systems

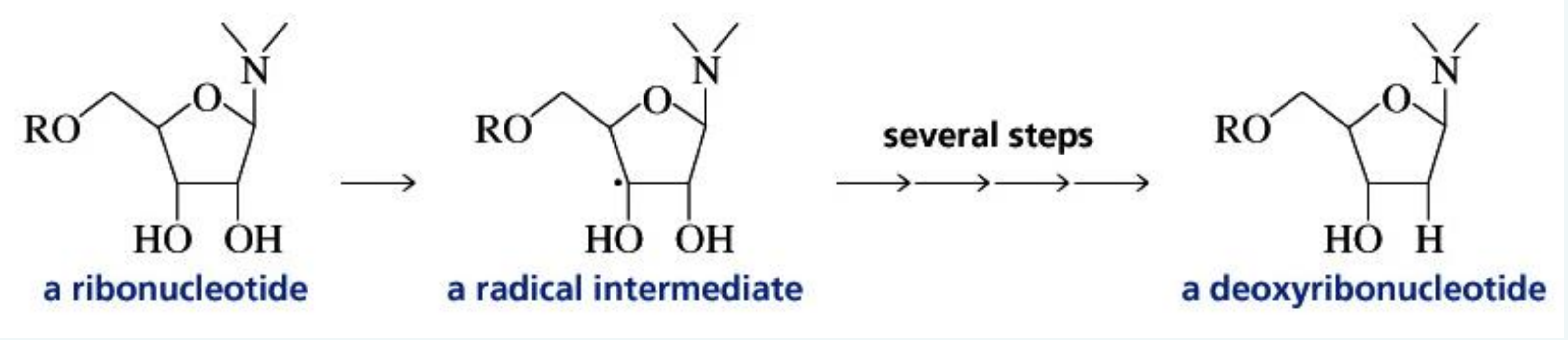
- Alkanes (toxic) are converted to alcohols (nontoxic) in the liver via a radical mechanism



- An iron-containing enzyme, cytochrome P_{450}, catalyzes the reaction

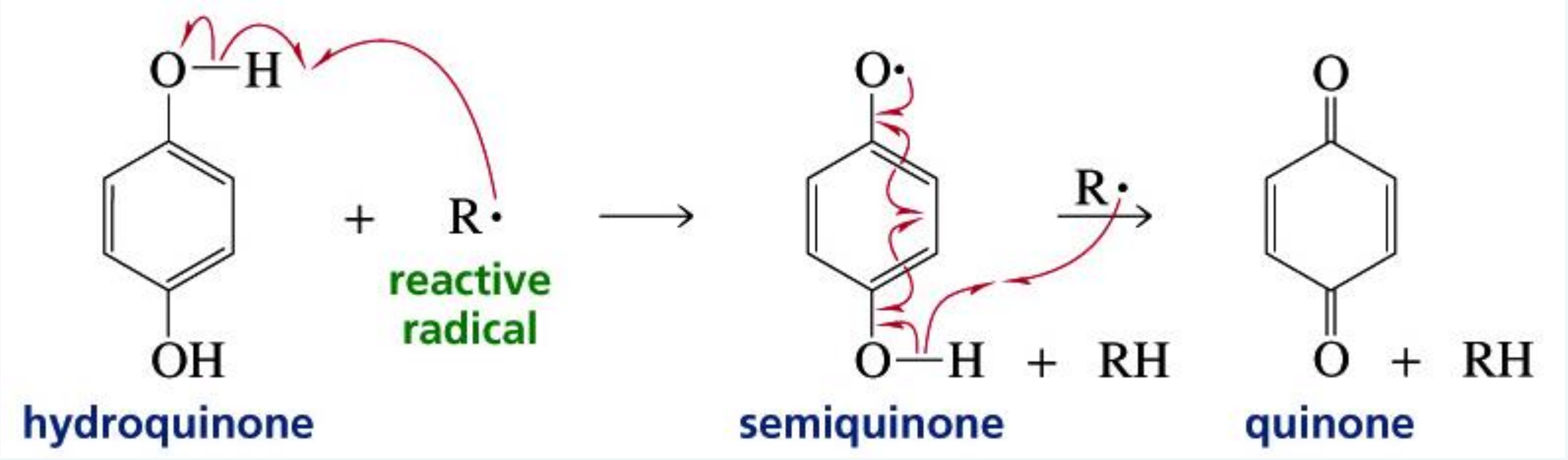
Radical Reactions in Biological Systems

- A radical reaction also is involved in the reduction of a ribonucleotide to a deoxyribonucleotide

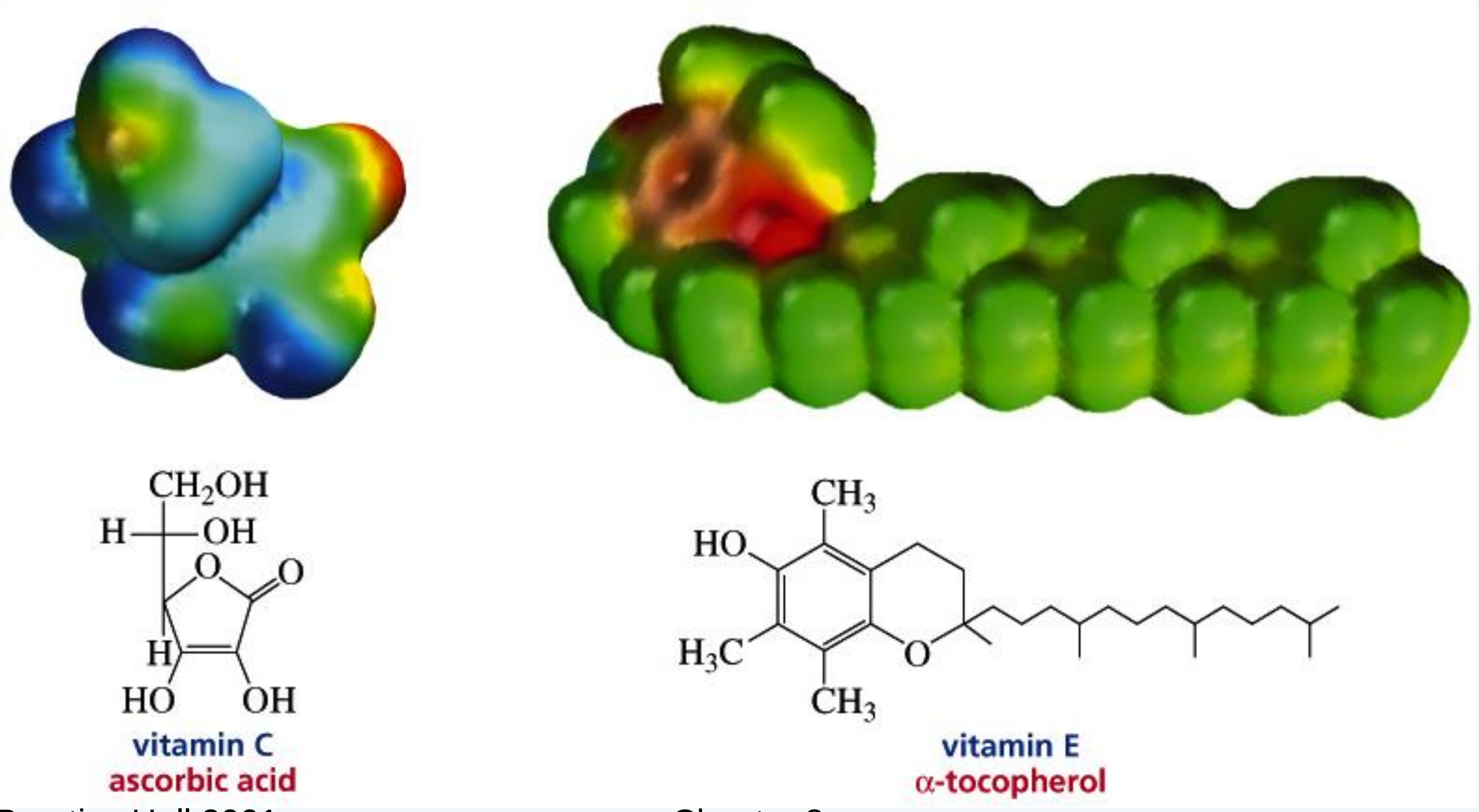


Radical Reactions in Biological Systems

- Protection from radical reaction is possible if a compound is present that reacts with the radical and forms a less reactive radical

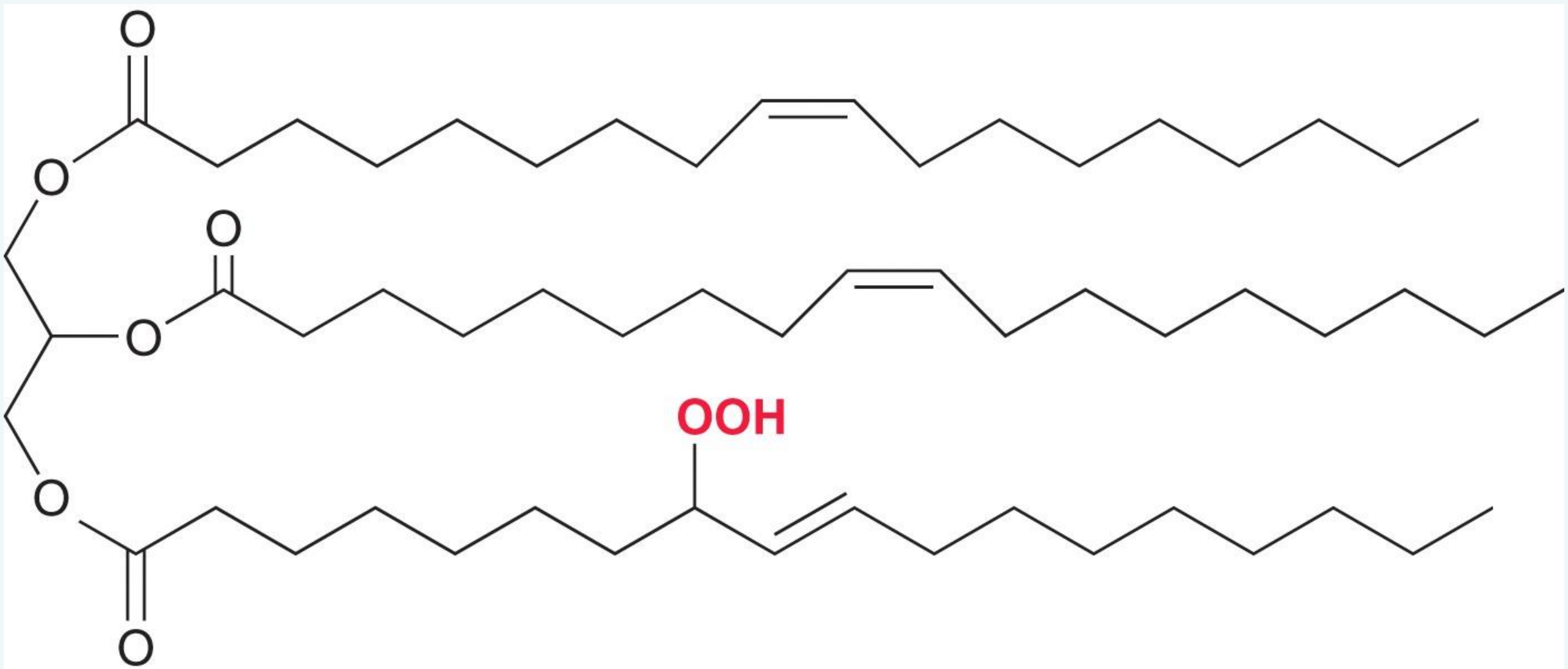


Radical Reactions in Biological Systems



11.9 Antioxidants

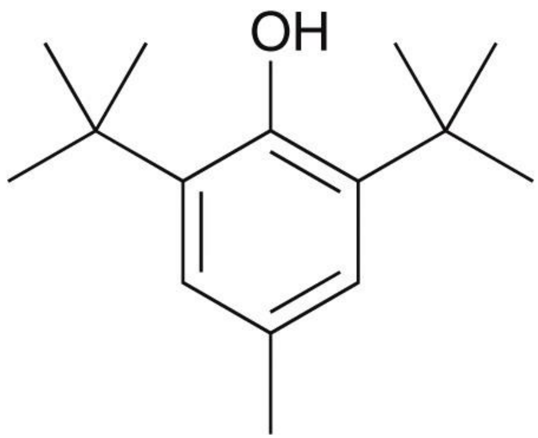
- Triglycerides are important to a healthy diet



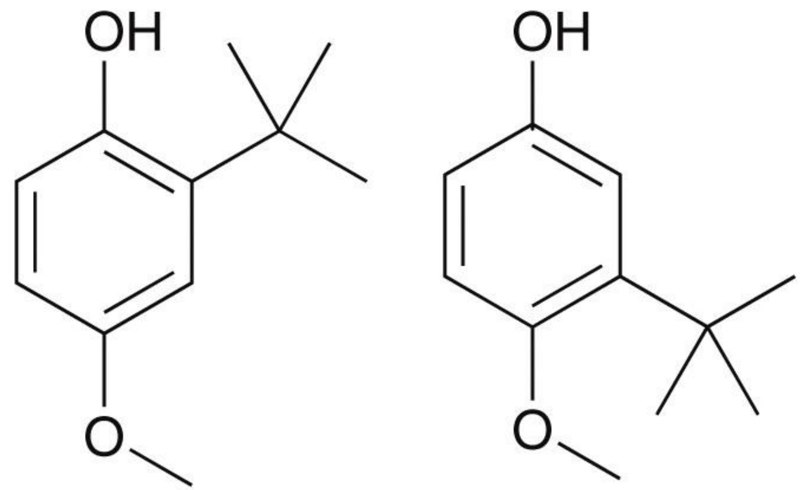
- Autooxidation can occur at the allylic positions causing the food to become rancid and toxic

11.9 Antioxidants

- Foods with unsaturated fatty acids have a short shelf life unless preservatives are used



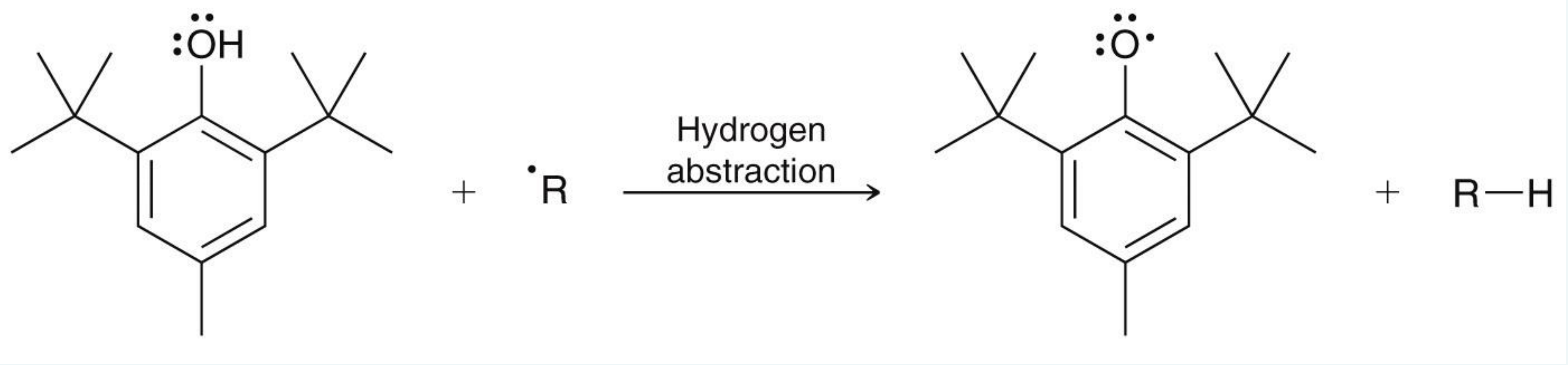
Butylated hydroxytoluene
(BHT)



Butylated hydroxyanisole
(BHA)

11.9 Antioxidants

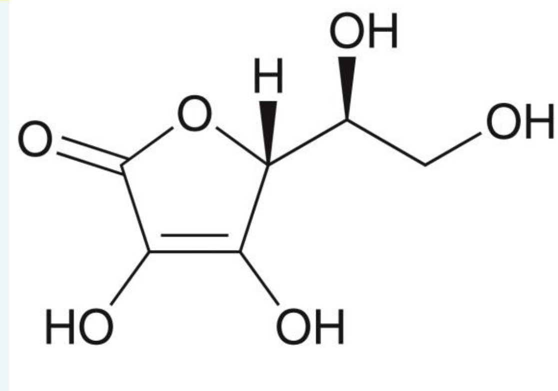
- Preservatives can undergo H abstraction to quench the C• radicals that form in the first step of autooxidation



- One molecule of BHT can prevent thousands of autooxidation reactions by stopping the chain reaction
- How does BHT's structure make it good at taking on a free radical? Consider resonance and sterics

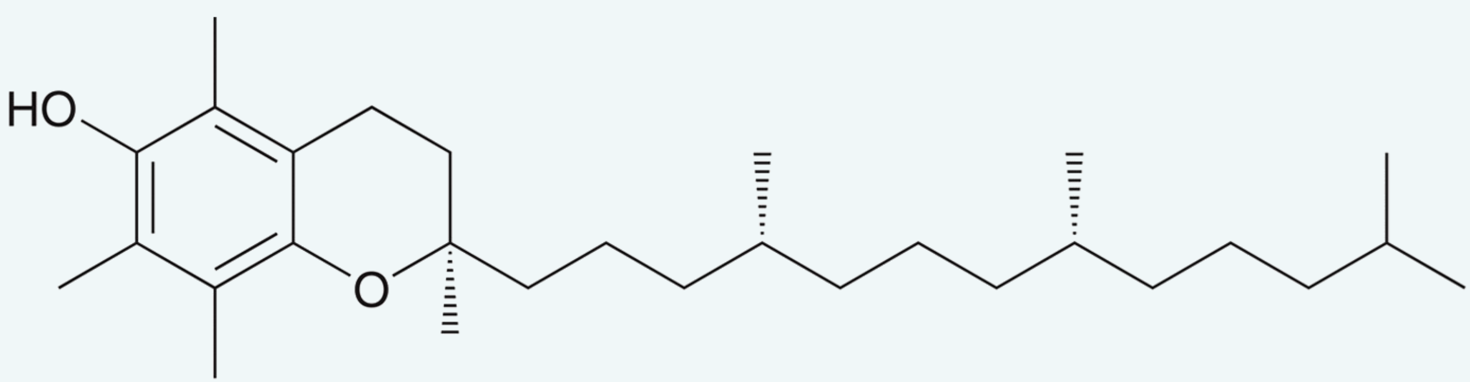
11.9 Natural Antioxidants

- Vitamins C is hydrophilic
- Vitamin E is hydrophobic
- What parts of the body do these vitamins protect?



Vitamin C

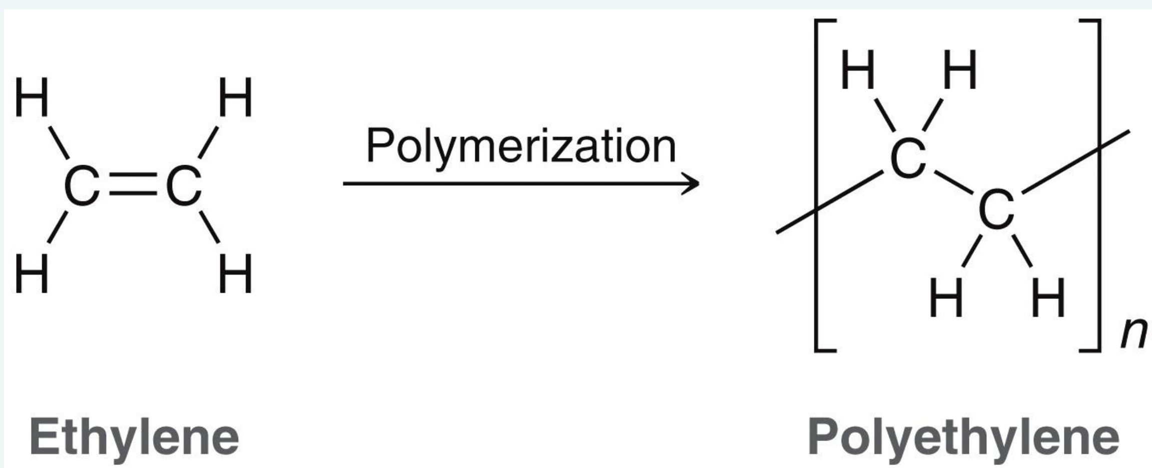
- For each vitamin, show its oxidation mechanism, and explain how that protects the body from autooxidation



Vitamin E

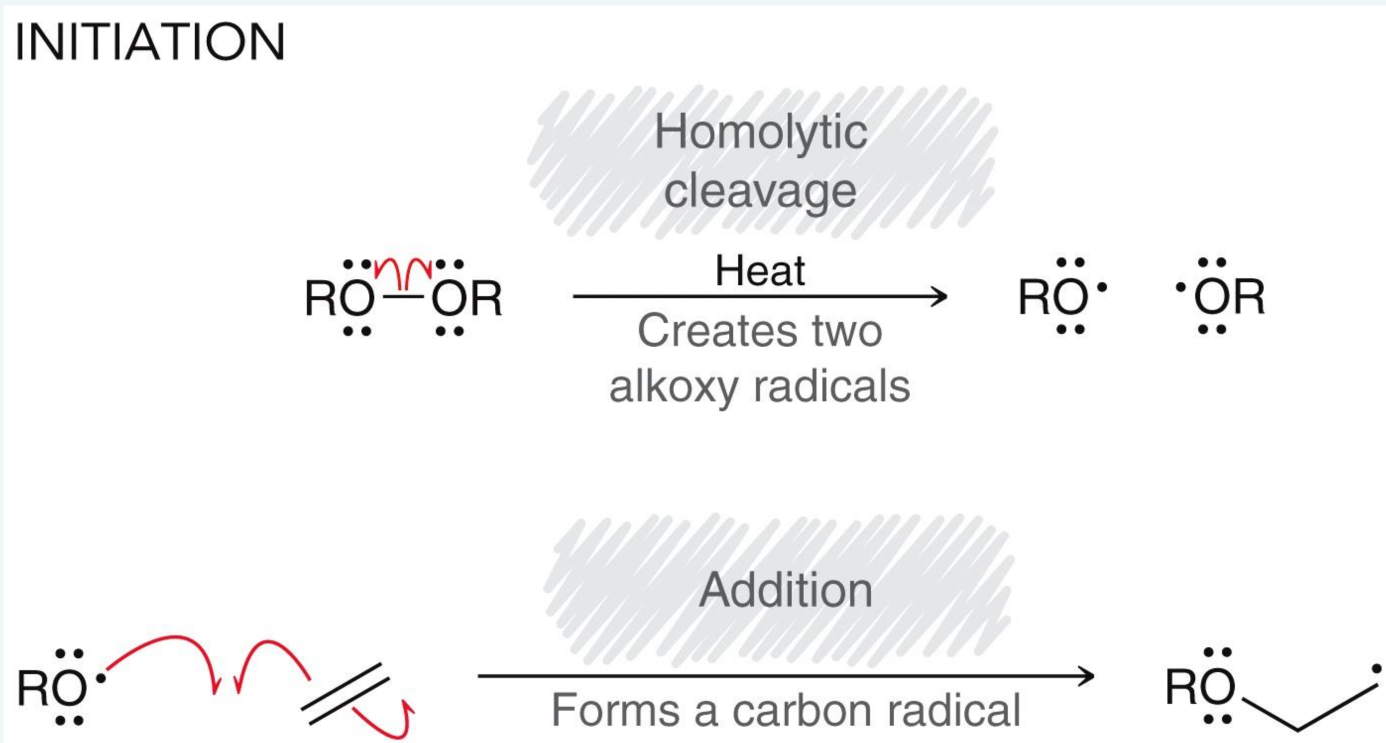
11.11 Radical Polymerization

- Free radical conditions are also frequently used to form polymers
- Recall that a polymerization process joins together many small units called monomers in a long chain



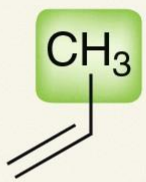
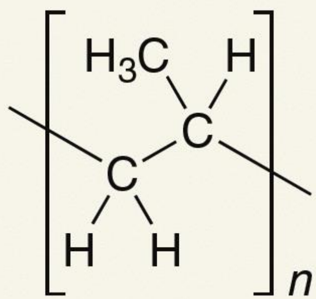
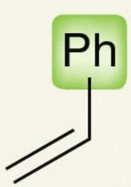
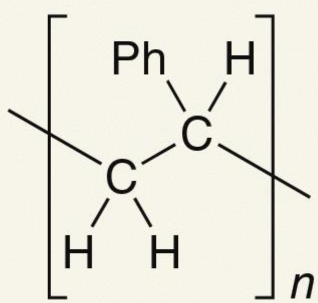
11.11 Radical Polymerization

- Radical polymerizations generally proceed through a chain reaction mechanism

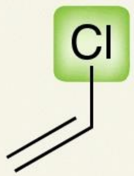
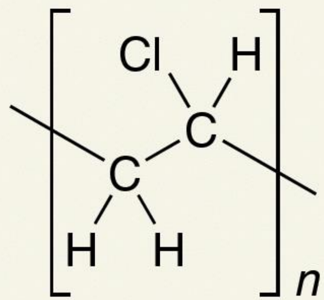
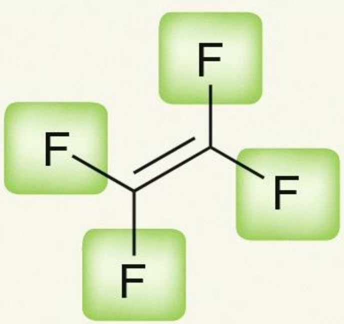
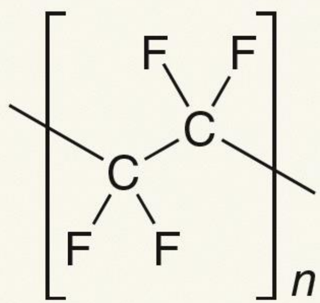


11.11 Radical Polymerization

- Many derivatives of ethylene are also polymerized

MONOMER	POLYMER	APPLICATION
 **Propylene**	 **Polypropylene**	Carpet fibers, appliances, car tires
 **Styrene**	 **Polystyrene**	Televisions, radios, Styrofoam

11.11 Radical Polymerization

MONOMER	POLYMER	APPLICATION
 Vinyl chloride	 Poly(vinyl chloride)	PVC piping for plumbing, CDs, garden hoses, raincoats, shower curtains
 Tetrafluoroethylene	 Teflon	Nonstick coating for frying pans