Radical Reactions & Mechanisms - Chapter 10 (Klein)

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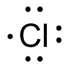
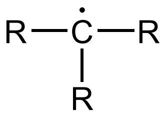


chlorine atom



carbon radical

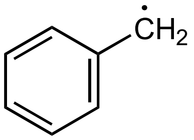
$R\cdot$

general radical

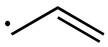
I. Introduction to Free Radicals (10.1)

- radicals have an unpaired electron (reactive intermediates)
- radical geometry is essentially planar (*sp*^{2} or rapidly inverting pyramidal)
- radicals are electron rich / deficient

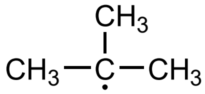
Radical stability



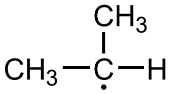
benzylic radical



allylic radical



3° radical



2° radical

$CH_3\text{-}\dot{C}H_2$

1° radical

$\dot{C}H_3$

methyl radical

- alkyl groups are polarizable (their electron density can be drawn toward missing octet)
- alkyl groups are inductively electron withdrawing / donating (called hyperconjugation)
- this is a stabilizing feature for the radical
- if INCREASE # of alkyl substituents, then ______________ stability

Overall radical stability: benzylic, allylic > 3° > 2° > 1° > methyl

II. Radical Mechanisms (10.2)

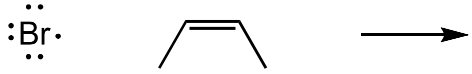
regular arrow  moves 2 electrons

fish-hook arrow  moves 1 electron

Common mechanisms:

$:\ddot{\underset{\cdot\cdot}{Cl}}-\ddot{\underset{\cdot\cdot}{Cl}}: \longrightarrow \;:\ddot{\underset{\cdot\cdot}{Cl}}\cdot \quad \cdot\ddot{\underset{\cdot\cdot}{Cl}}:$ *homolytic cleavage ("initiation" generates a radical)*

$:\ddot{\underset{\cdot\cdot}{Br}}\cdot \quad H-CH_2CH_3 \longrightarrow$ *atom abstraction (usually H, Cl or Br)*



addition to a pi bond

try SkillBuilders 10.1 & 10.3

III. Free-Radical Halogenation (10.3 - 10.6)

$$CH_4 \quad + \quad Cl_2 \xrightarrow[\text{heat }(\Delta)]{\text{light }(h\nu)\text{ or}} CH_3Cl \quad + \quad HCl$$

this is an important reaction to functionalize alkanes (add a FG)

A) Mechanism: a chain reaction (after initiation, there are two main steps* to form product)

Initiation (creates a radical)

$$:\underset{\cdot\cdot}{\overset{\cdot\cdot}{Cl}}-\underset{\cdot\cdot}{\overset{\cdot\cdot}{Cl}}: \xrightarrow{h\nu}$$

***Propagation steps** (one radical creates a new radical)

happens MANY times (tens of thousands)

1. $:\underset{\cdot\cdot}{\overset{\cdot\cdot}{Cl}}\cdot \quad H-CH_3 \longrightarrow$ *hydrogen atom abstraction*

2. *chlorine atom abstraction*

Also possible (but infrequent): **Termination steps** (destroys radicals)

- when any two radicals collide $R\cdot \quad \cdot R \longrightarrow$

this is a rare event...consider thermodynamics vs. kinetics

$$\underbrace{Cl\cdot \quad \cdot CH_3}_{\textit{present in small concentration}} \longrightarrow \underbrace{Cl-CH_3}_{\textit{accounts for a negligible amount of product!}} \qquad H_3C\cdot \quad \cdot CH_3 \longrightarrow \underset{\textit{other byproducts possible}}{CH_3CH_3}$$

- when a radical reacts with an "inhibitor"

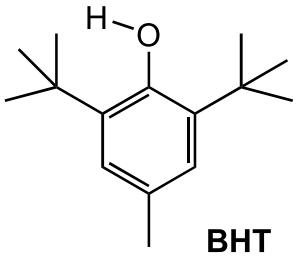
inhibitor + $R\cdot \longrightarrow$ inhibitor-R or inhibitor-H + $\cdot R \longrightarrow$ inhibitor$\cdot$ + RH

example: O_2 gas is a diradical, so radical reactions require an oxygen-free atmosphere

example: BHT (butylated hydroxytoluene) is a radical inihibitor because the chain reaction is stopped when a stable and hindered radical is formed.

Show the reaction of a radical with BHT (a hydrogen atom abstraction takes place). Use drawings to show why the product is so stable. You can use the abbreviation t-Bu in your drawings.

$R\cdot$ +



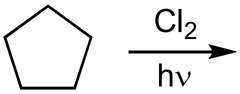
$\longrightarrow$

BHT

try SkillBuilder 10.4

Predict the major product for each of the following reactions (assume monohalogenation).

$CH_3CH_3 \xrightarrow[h\nu]{Br_2}$



Group work: provide a mechanism for the monochlorination of cyclopentane.
Begin with an initiation step, and then use propagation steps until the product is formed.

Consider: why does the chlorine radical abstract a H atom not a C group?
Estimate ΔH for competing propagation steps...

	bond broken	bond formed
$Br\cdot + H{-}CH_2CH_3 \longrightarrow H{-}Br + \cdot CH_2CH_3$		
$Br\cdot + H_3C{-}CH_3 \longrightarrow$ Br-CH3 $+ \cdot CH_3$		

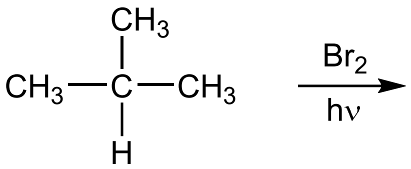
BDE (kcal/mol)	C-H 98	H-Br 88	C-C 90	C-Br 68

Thermodynamic considerations (strengths of bonds formed and bonds broken) also explain why reaction with F_2 and I_2 are not useful. Fluorination releases too much energy (explosive) and iodination forms very weak bonds so it is endothermic and unfavorable.

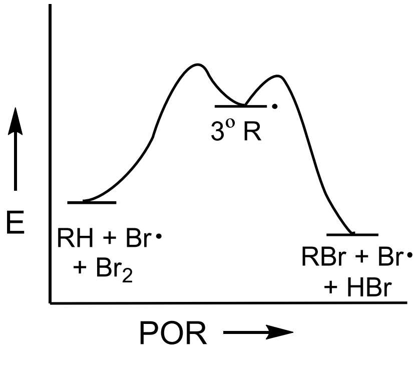
******Therefore, free-radical halogenation always replaces a H atom with a Cl or Br atom******

B) Regiochemistry of Free-Radical Halogenation (10.5)

Which site/region undergoes a reaction?



$CH_3-\overset{\displaystyle CH_3}{\underset{\displaystyle H}{C}}-CH_3 \xrightarrow[h\nu]{Br_2}$



** Bromination is very selective**

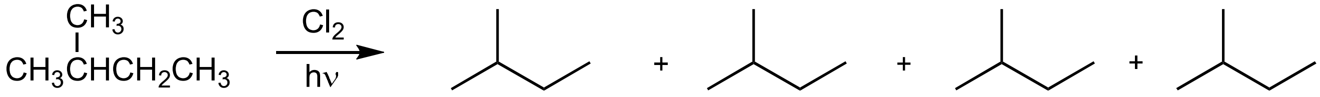
Site of reaction	1°	2°	3°
Relative rate			

- tertiary H atom is easier to remove
- tertiary radical is more stable than primary radical
- tertiary C-H bond is weaker (costs less energy to break)
- tertiary is *faster* reaction (lower E intermediate/TS)

try SkillBuilder 10.2

** Chlorination is less selective** (therefore statistics/#H's must be considered)

Site of reaction	1°	2°	3°
Relative rate			



$$\underset{}{CH_3\overset{CH_3}{\overset{|}{C}}HCH_2CH_3} \xrightarrow[h\nu]{Cl_2}$$

**** Bromination occurs at most substituted carbon, chlorination forms all possible products****

Consider: why is bromination more selective than chlorination?
See ΔH for the H atom abstraction step for both...

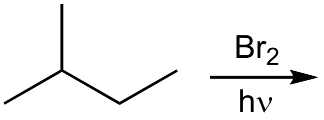
	bond broken	bond formed
$Br\cdot + H{-}CH_2CH_3 \longrightarrow H\text{-}Br + \cdot CH_2CH_3$		
$Cl\cdot + H{-}CH_2CH_3 \longrightarrow H\text{-}Cl + \cdot CH_2CH_3$		

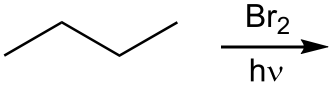
BDE (kcal/mol)	C-H 98	H-Br 88	H-Cl 103

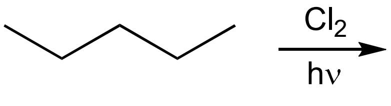
**The first propagation step for bromination is *endothermic* so it is slow and the transition states leading to the different intermediates (1°/2°/3°) are significantly different (primary is over 1600 times slower than tertiary).

**For chlorination, this step is *exothermic* so it is fast and does not discriminate about which hydrogen is abstracted. The transition states for chlorination at 1°/2°/3° sites are not significantly different, so the reaction rates are similar (primary is one-fourth the rate of teriary).

Predict the major product(s) for each reaction. Consider both regiochemistry and stereochemistry.





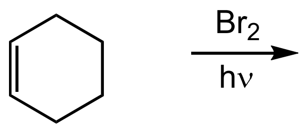


try SkillBuilders 10.5, 10.6

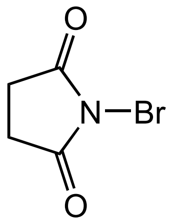
C) Allylic Halogenation (10.7)

But...consider reaction of Br_2 with alkene!

Predict the major product:

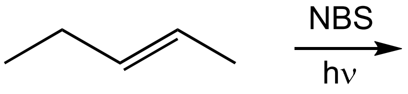


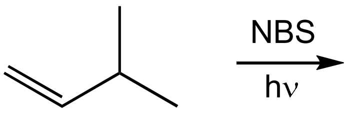
Avoid using Br_2 with an alternate source of Br•



N-bromosuccinimide

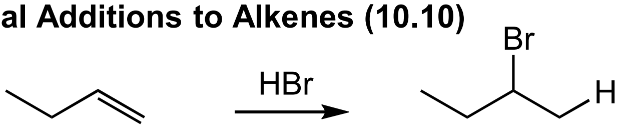
predict the major product(s):





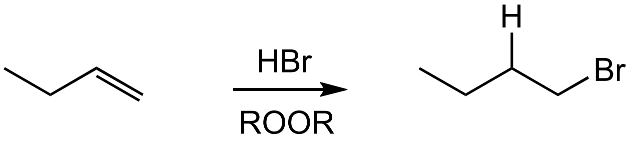
try SkillBuilder 10.7

IV. Radical Additions to Alkenes (10.10)



Markovnikov addition of HBr

Mechanism:



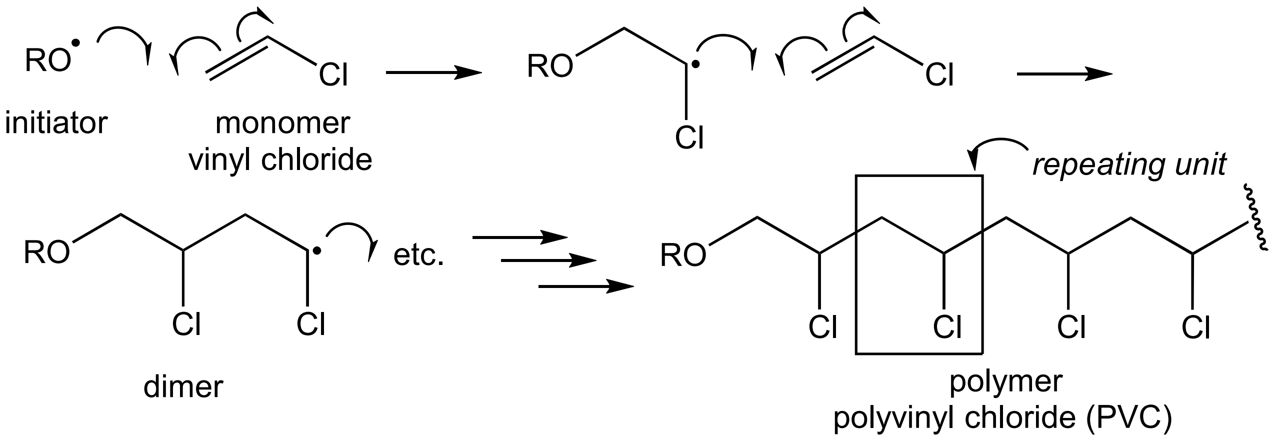
Presence of peroxides results in *ANTI-Markovnikov* addition of HBr

Mechanism:

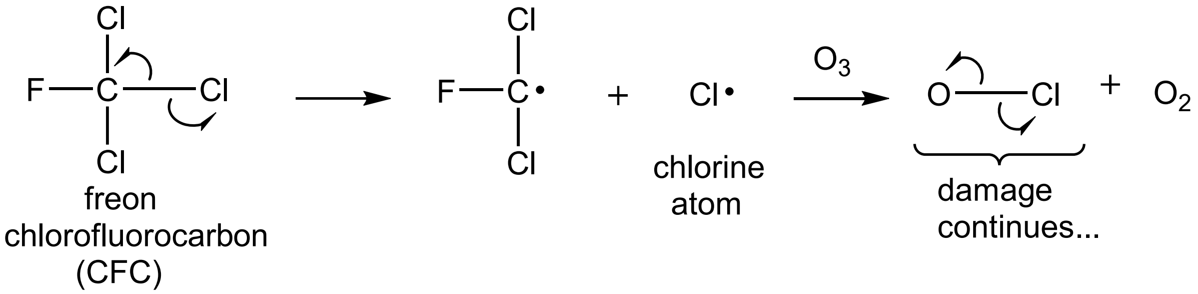
try SkillBuilder 10.8

V. Real-World Reactions (10.8, 10.9, 10.11, 10.12)

A. Polymerizations

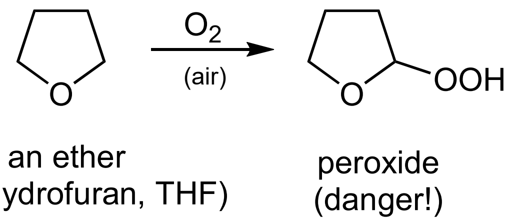


B. Ozone degradation



C. Autooxidation

(reaction with O_2)



- ethers (used as solvents) can become **explosive** if stored too long
- reaction is catalyzed by light so reagents are usually stored in dark bottles
- autooxidation also causes deterioration of food (rancid oil)
- preservatives (BHT, BHA) react with radicals and inhibit autooxidation

D. Antioxidants (prevent autooxidation)

sunlight exposure ⟶ **free radicals** ⟶ skin damage (cancer, wrinkles)

Antioxidants (vitamins E, K, C, β-carotene, preservatives!) behave as **radical scavengers** and consume free radicals. Anti-aging miracles? Doubtful...

VI. Synthetic Strategies (10.13)

Transform the given starting material to desired TM.