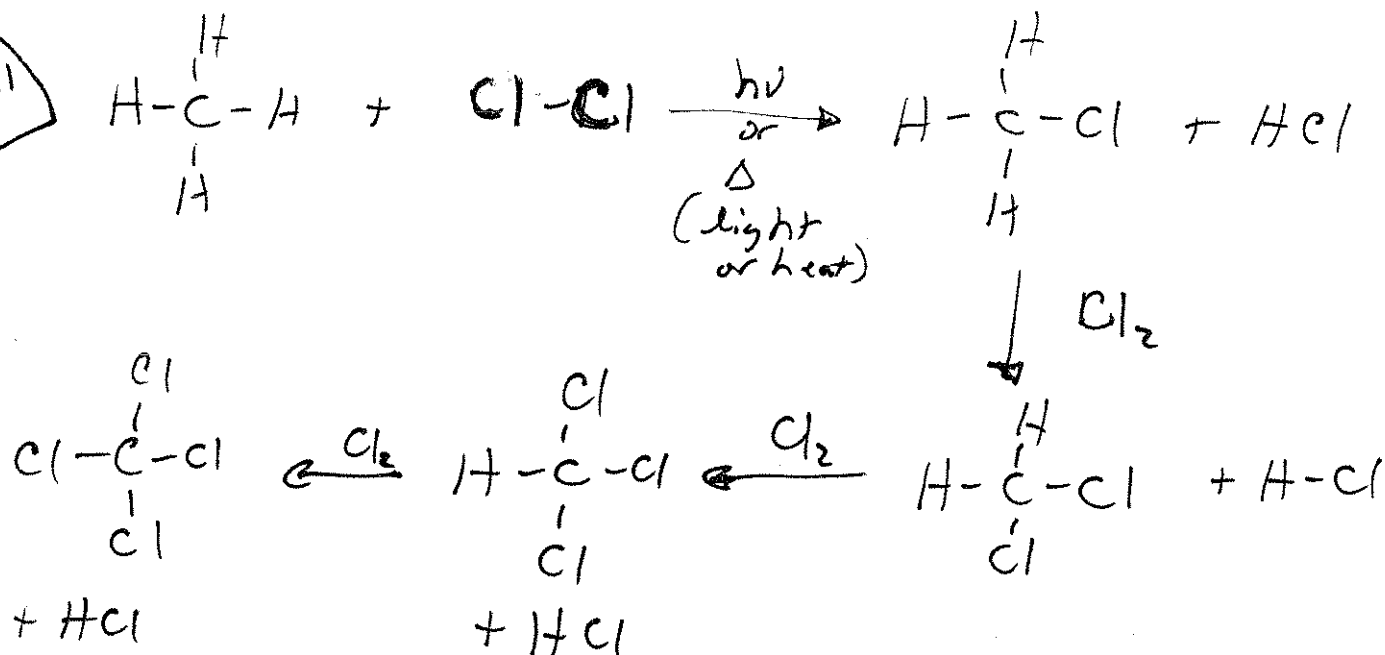


# Chapter 19: Free Radicals

## Chlorination of Alkanes (can also do bromination)

→ produces a mixture of chlorinated products

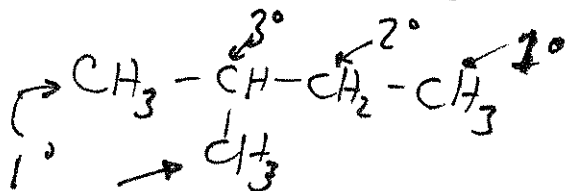
Free Radical Rxn

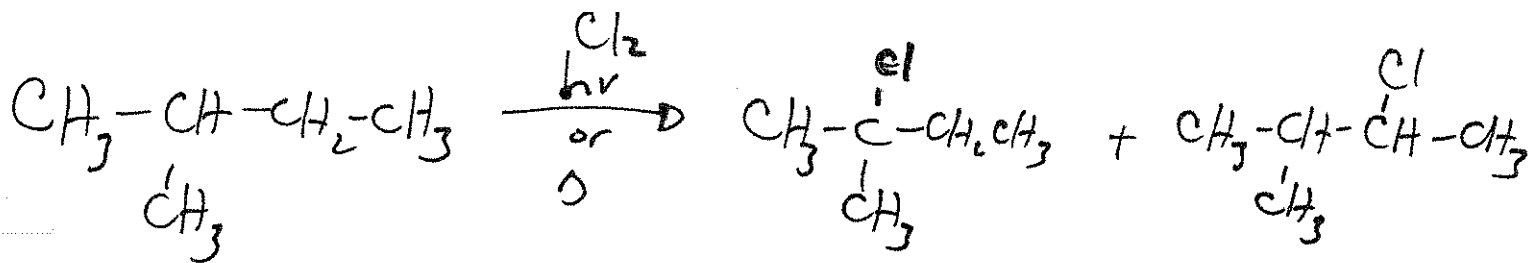


→ % composition of chlorinated products depends on ratio of alkane to Cl<sub>2</sub> (and other factors) - but will always get a mixture of products

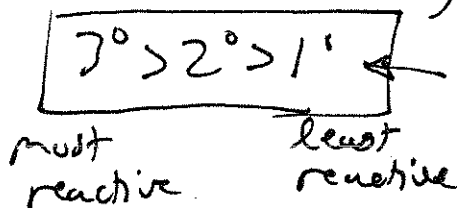
(hard to stop rxn at monochlorination pt)

- What if one has an alkane with different degrees of substitution (1°, 2°, 3° carbons) in a chlorination or bromination rxn? Which carbon is most reactive?

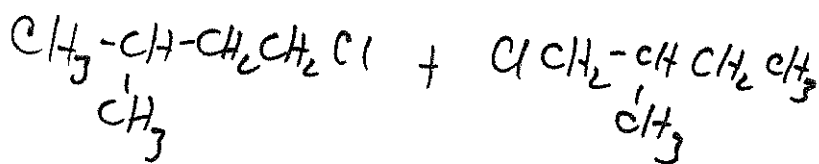




- Any hydrogen can be substituted w/ Cl, but reactivity of different carbons vary:



Why? Because  $3^\circ$  radical is more stable than  $2^\circ > 1^\circ$ .



(mixture of products)

→ not good for synthesis

## Free-Radical Reaction Mechanism (Bromination of Methane)

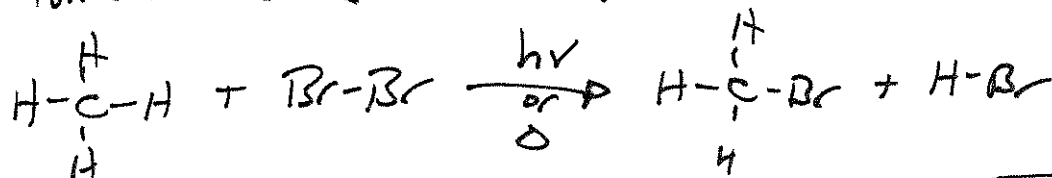
- Free radical
- Bromination rxn is more synthetically useful than chlorination (bromination is much more selective than

chlorination → will discuss why soon)

### 3 Steps

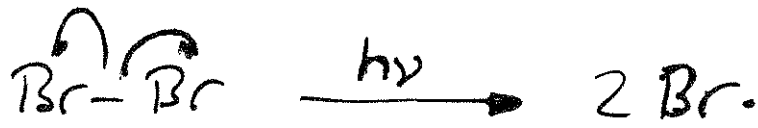
- 1) initiation: generation of a reactive intermediate
- 2) propagation: reactive intermediate reacts with a stable molecule to form another reactive intermediate (+ so on...)
- 3) termination: side rxns that stop the rxn

→ We will look at a free-radical chain rxn of methane with  $\text{Br}_2$  to form the monobrominated pdt.



# Mechanism

**Initiation** - split molecule of bromine by absorption of photon of light



homolytic cleavage

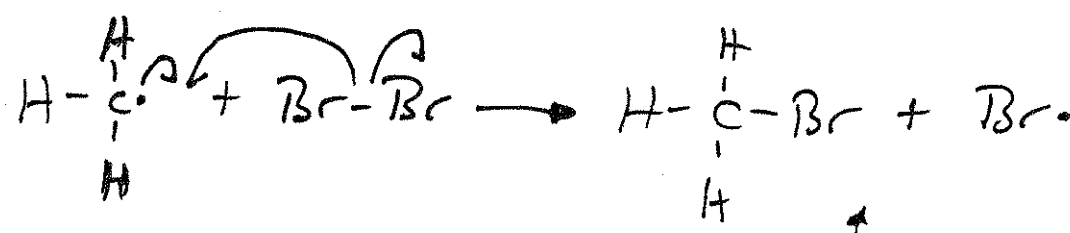
(heat can also cause homolytic cleavage)

## Propagation

**1st step**



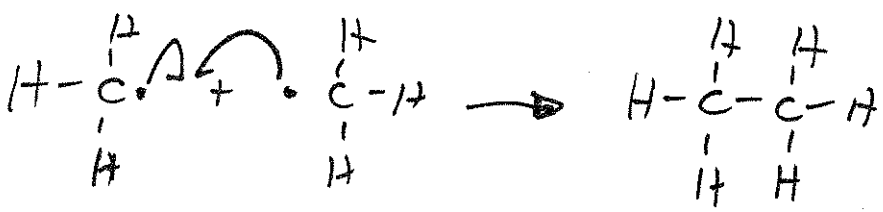
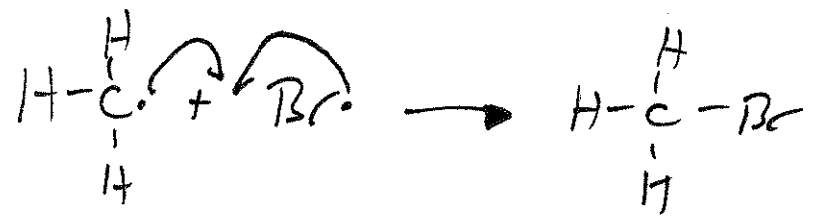
**2nd step**



(Chain continues)

## Termination Reactions

- breaks chain rxn cycle



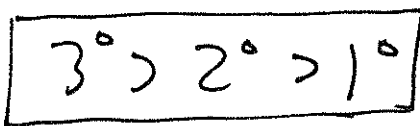
(or  $\text{H}-\underset{\text{H}}{\overset{\text{H}}{\text{C}}}\cdot + \text{Br}\cdot$  reacts with container wall  $\rightarrow \text{H}-\underset{\text{H}}{\overset{\text{H}}{\text{C}}}$  - wall or Br - wall)

- In free-radical chain reactions  $\rightarrow$  Conc. of radical is low, so the probability of propagation rxns much higher than termination rxns
- Free-radical rxns affected by the presence of inhibitors (sometimes called "free radical scavengers")
- Antioxidants (i.e. Vit. C + Vit. E) <sup>help to</sup> stop free-radical rxns that are initiated by  $O_2$  ( $\ddot{O}=\ddot{O} \leftrightarrow \cdot\ddot{O}-\ddot{O}\cdot$ )

oxygen diradical

remember

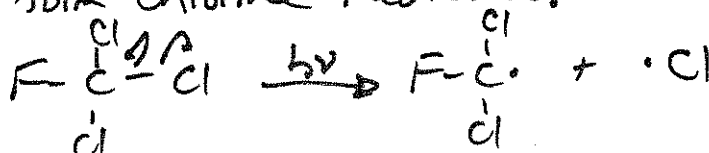
Stability of free-radicals



## Chlorination versus Bromination

- $\rightarrow$  bromination much more selective than chlorination. Why?
- Most chlorinations are exothermic while brominations are endothermic, allowing the relative stabilities of the alkyl radical to <sup>better</sup> dictate the regiochemistry with bromination rxns

$\rightarrow$  Chlorofluorocarbons (CFC's); released from air conditioners & drift up to the stratosphere where they react with UV light to form chlorine radicals.



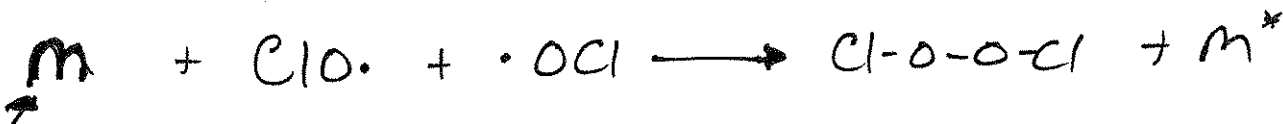
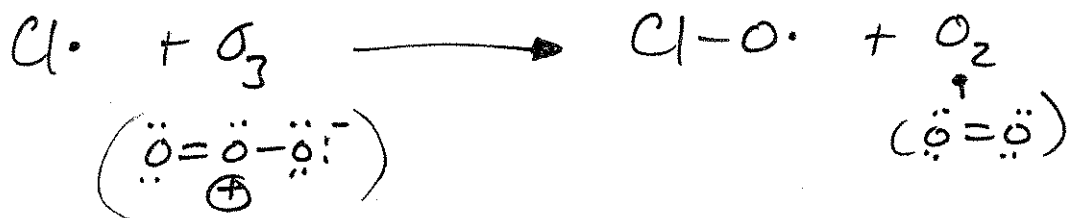
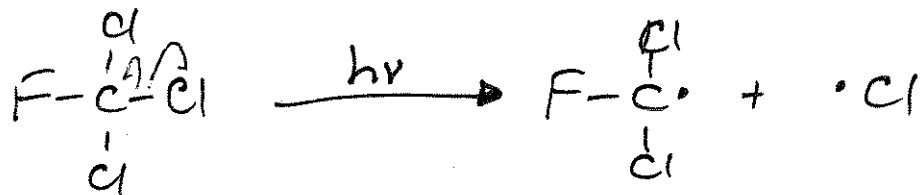
$\rightarrow$  CFC production now very limited

Why?

19-4

• CFC's were found to deplete ozone in the stratosphere which is necessary to protect life from harmful high energy UV light. (O<sub>3</sub> molecules absorb these rays)

**"The Ozone Hole"** → free radical mechanism



neutral molecule like N<sub>2</sub>; absorbs energy & releases in rxn



← reacts further w/ O<sub>3</sub>

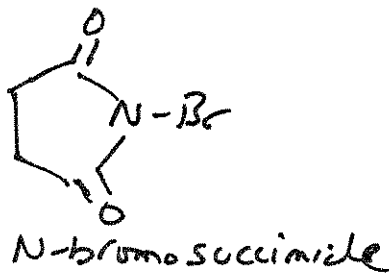
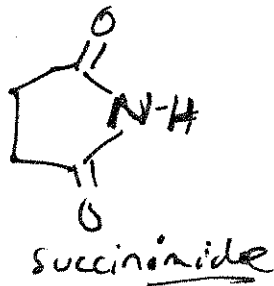
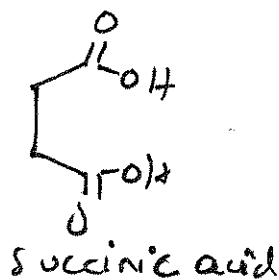


## Alkene Free-Radical Substitutions

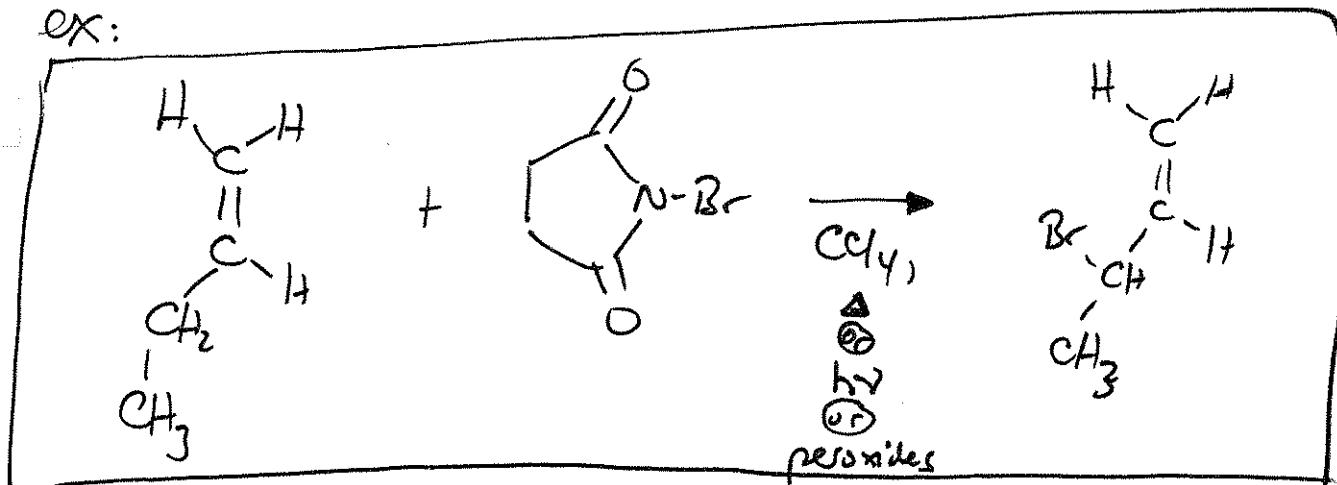
→ bromination of allylic position



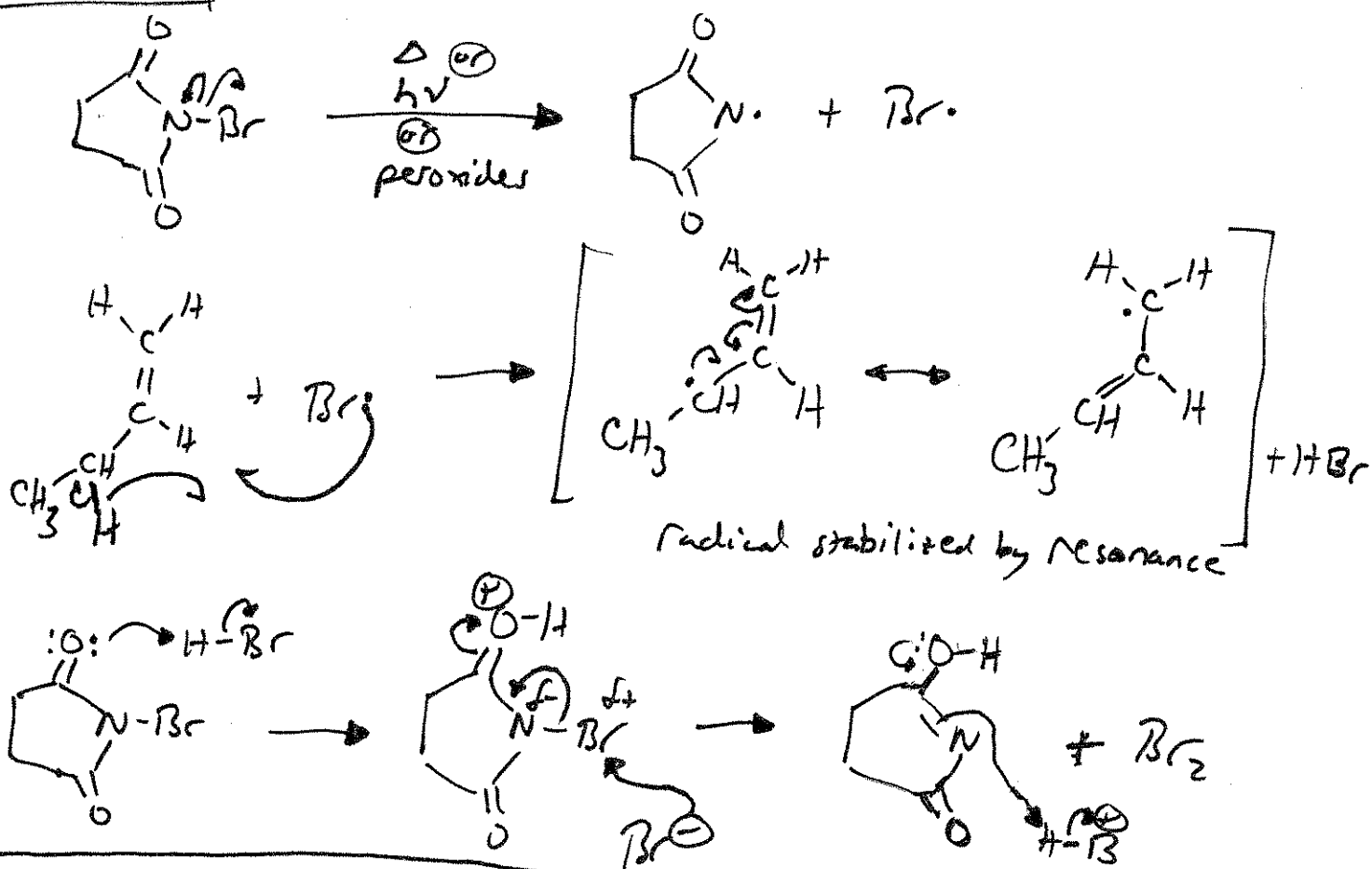
→ use N-bromosuccinimide (NBS)



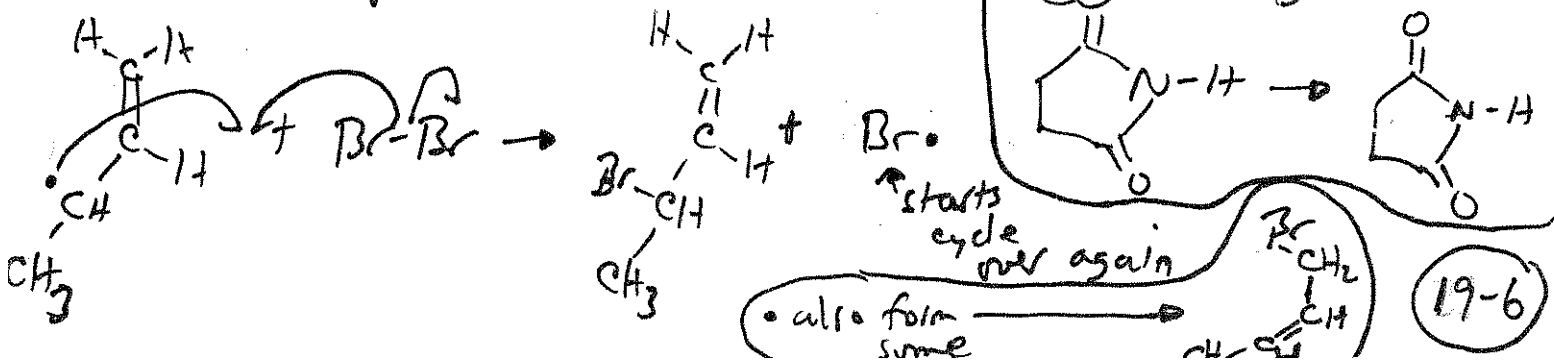
ex:



Mechanism

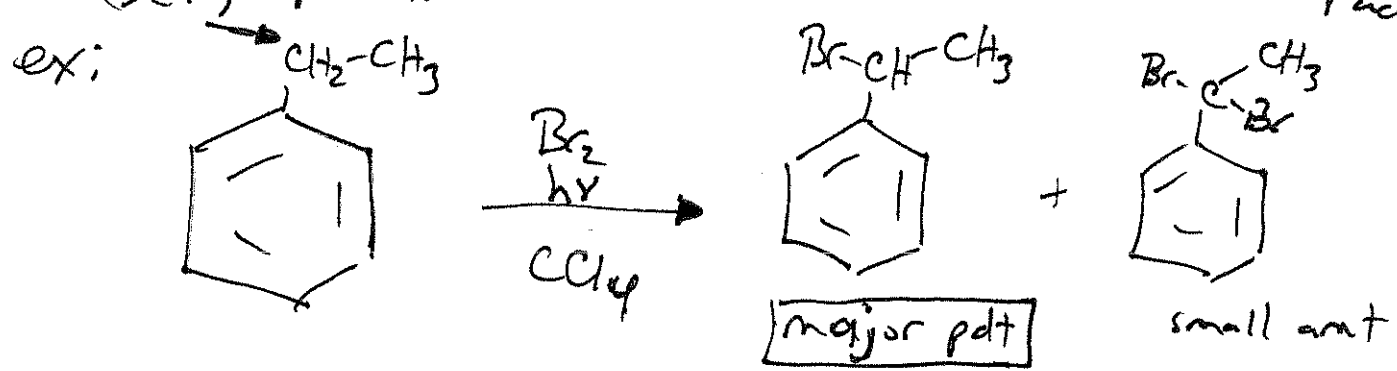


Now,  $Br_2$  reacts with allylic radical formed in 1<sup>st</sup> step

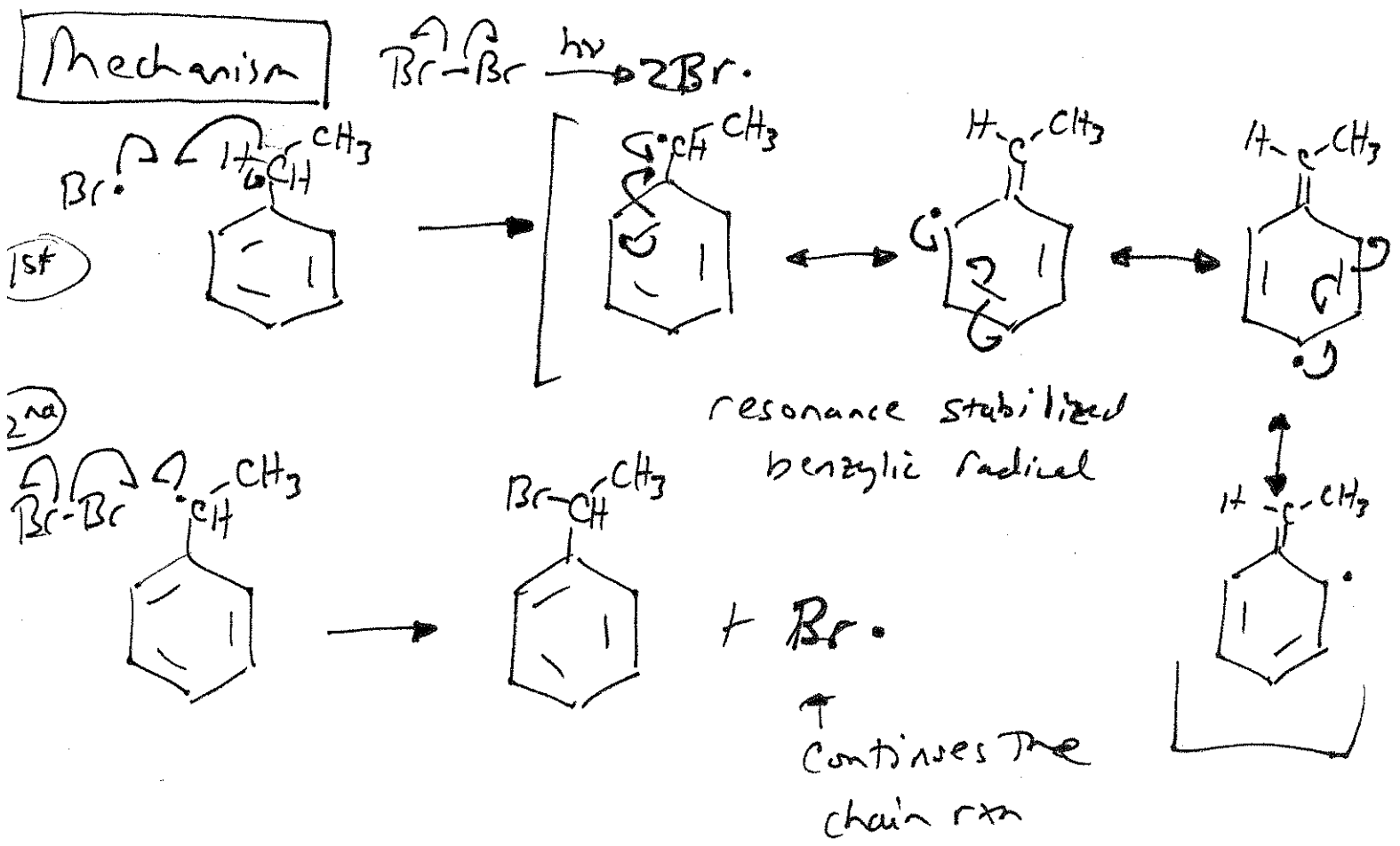


# Benzylic Free-Radical Halogenation

→ alkyl benzenes undergo free-radical halogenation at the benzylic position because abstraction of an H-atom (benzylic position) gives a resonance stabilized benzylic radical



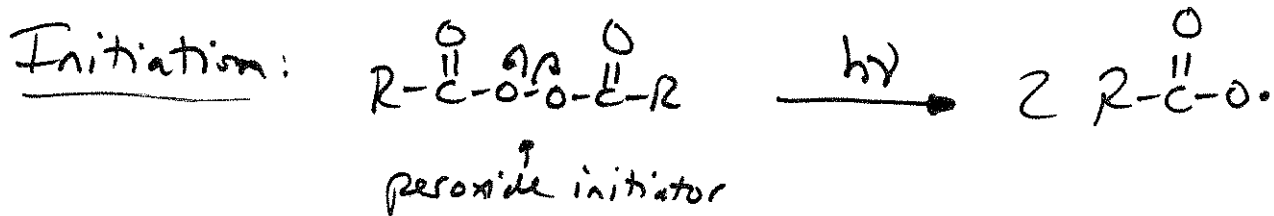
## Mechanism



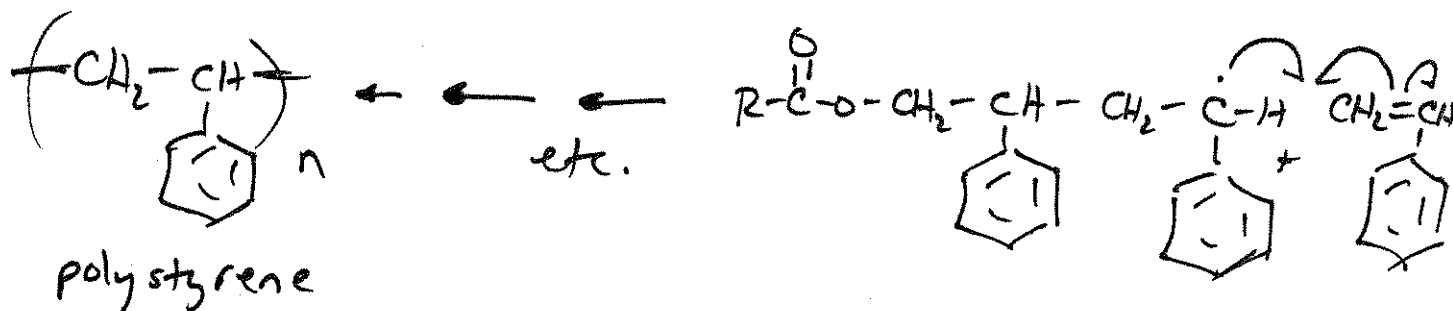
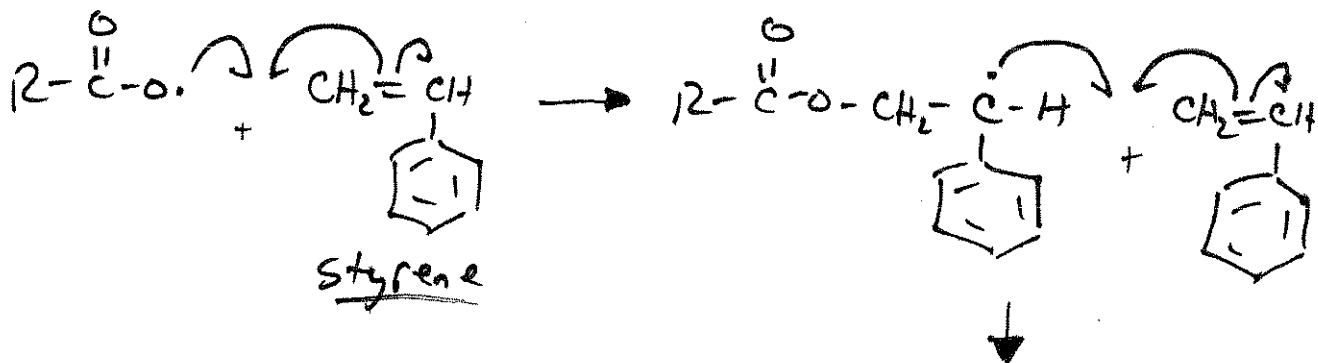
• Can also use NBS,  $CCl_4$ ,  $\Delta$  to do benzylic bromination

# Free-Radical Addition Reactions of Alkenes

## Polymerization - of styrene



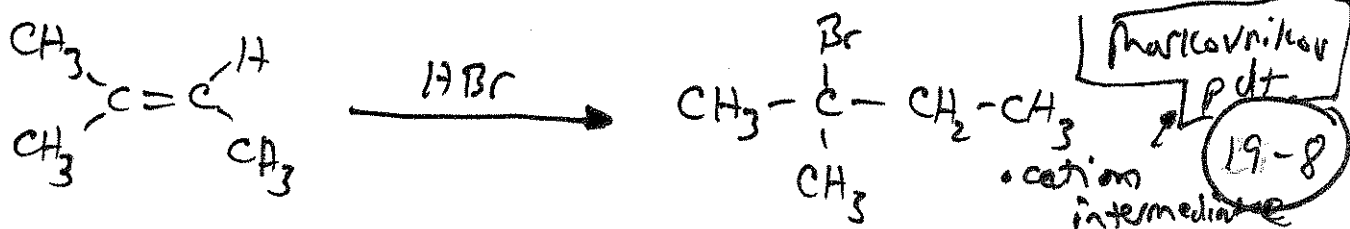
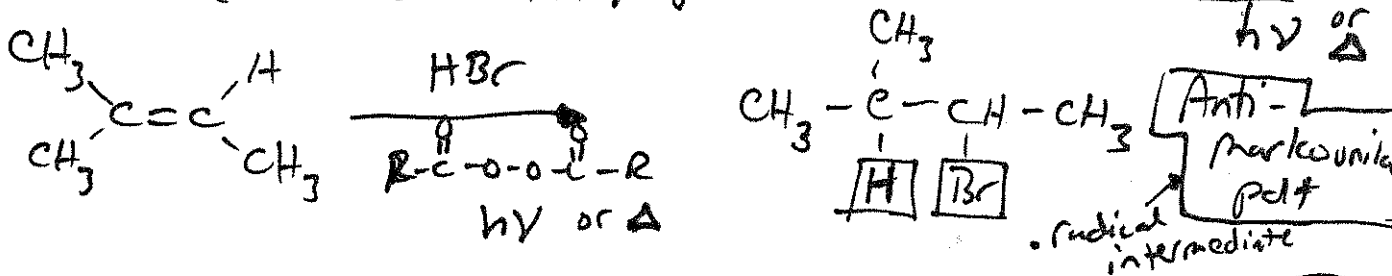
Propagation:



## Antimarkovnikov Addition of HBr $\rightarrow$ use HBr, alkene + peroxide

(see "One Small Step" p 783 in text)

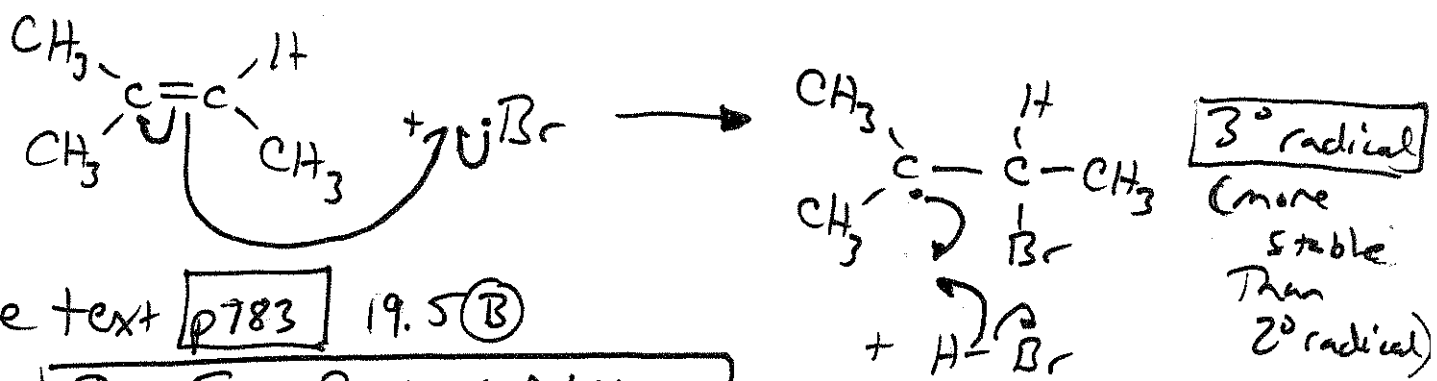
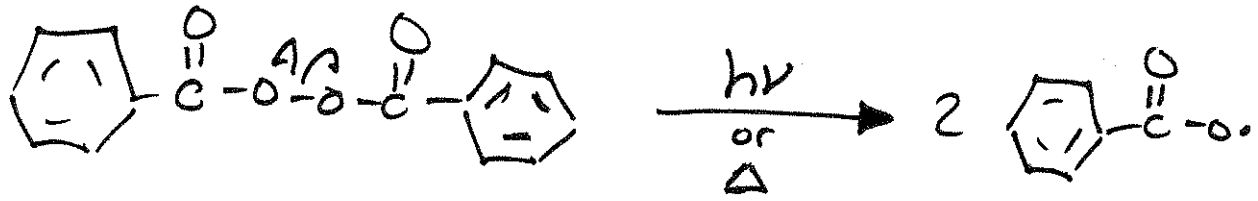
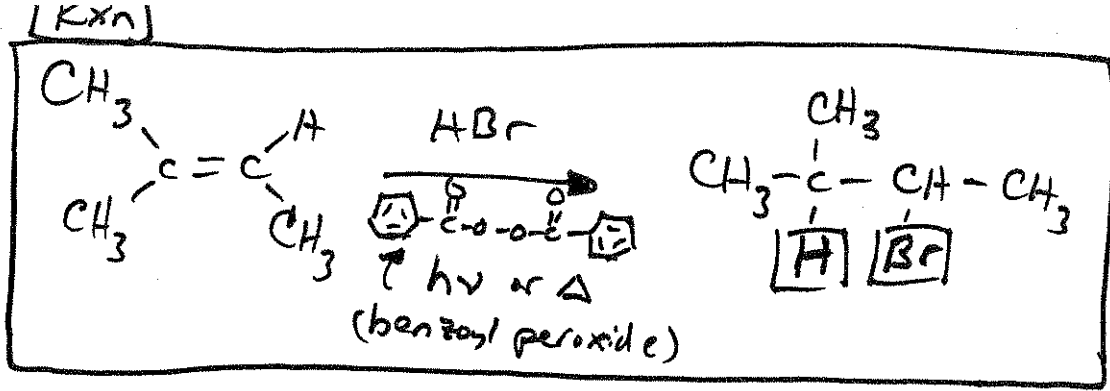
Compare with



19-8

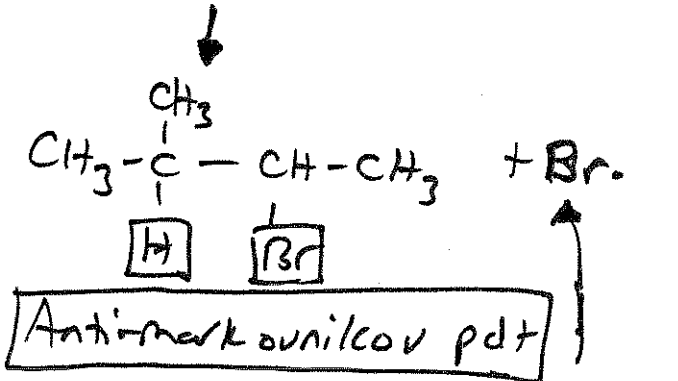


**Mechanism**

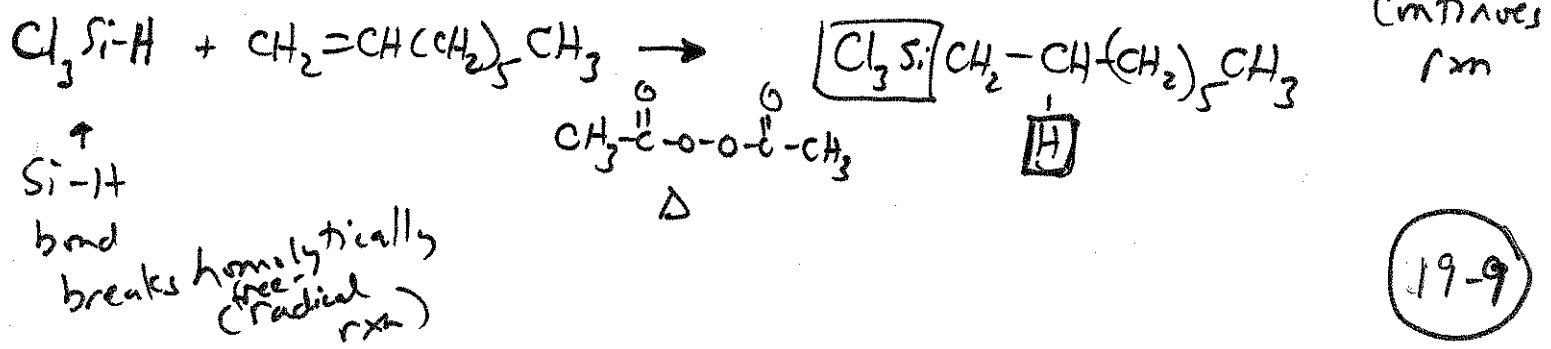


• See text p783 19.5(B)  
 → Other Free-Radical Additions to Alkenes

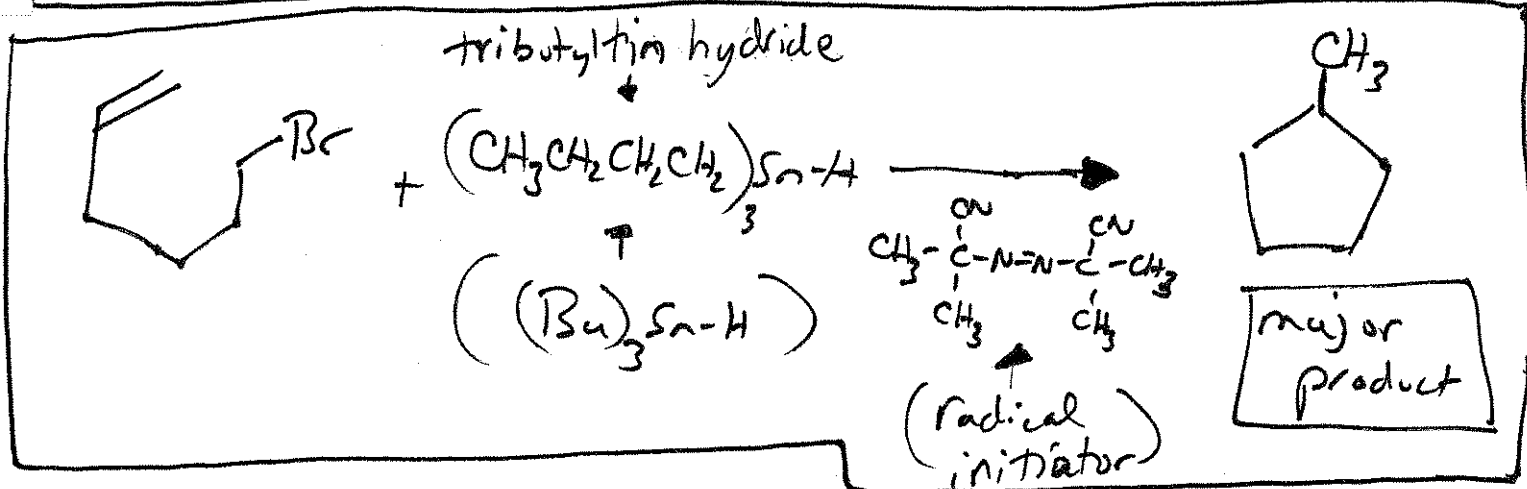
• Note similarity to Antimarkovnikov Addn of HBr rxn



ex:

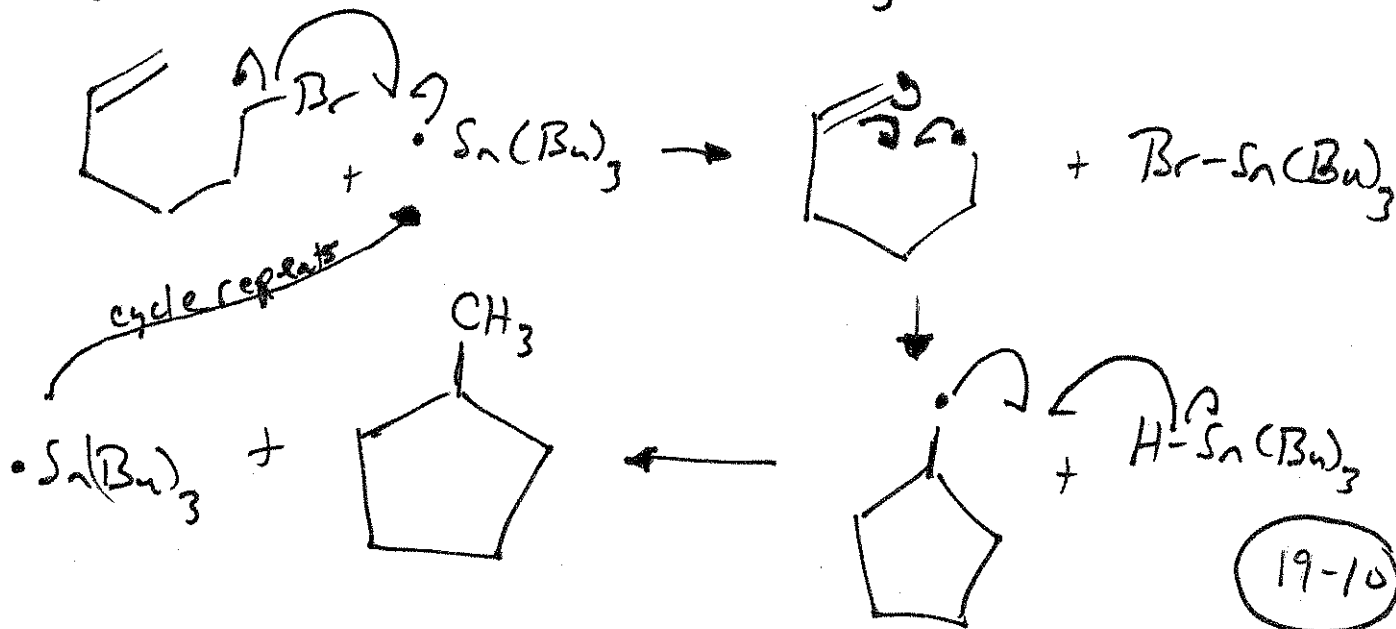
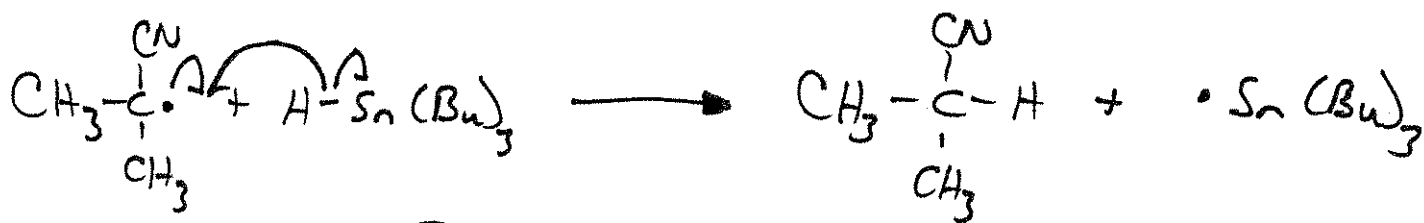
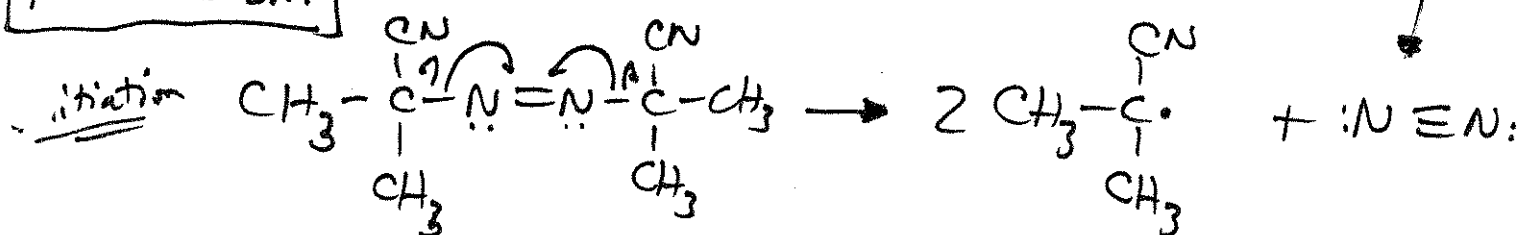


# Intramolecular Free-Radical Addition Reactions



- 5-membered rings favored over 6-membered rings in intramolecular free-radical addition rxns.

## Mechanism

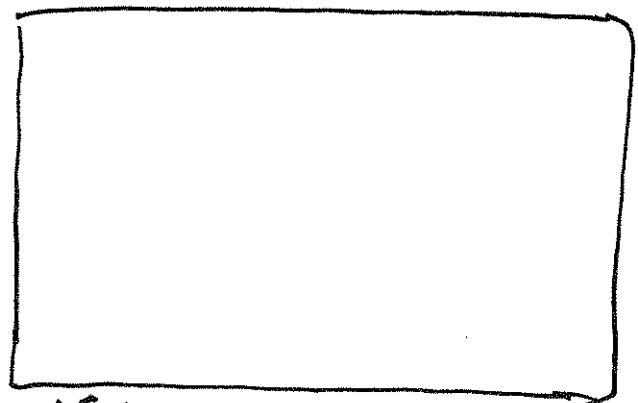
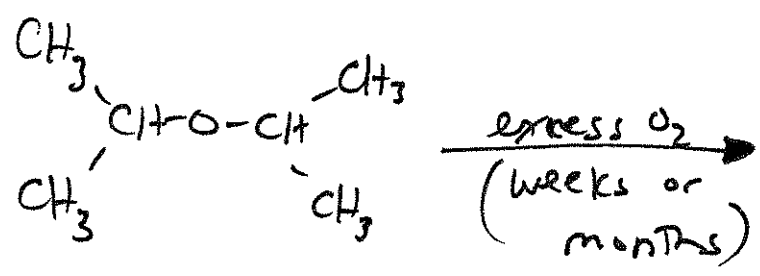
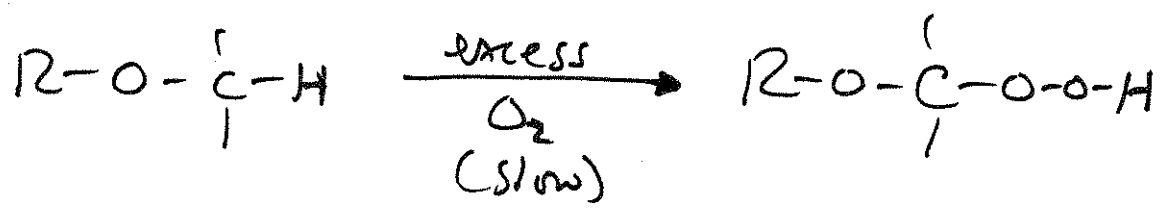


# Free-Radical Oxidations with Molecular Oxygen

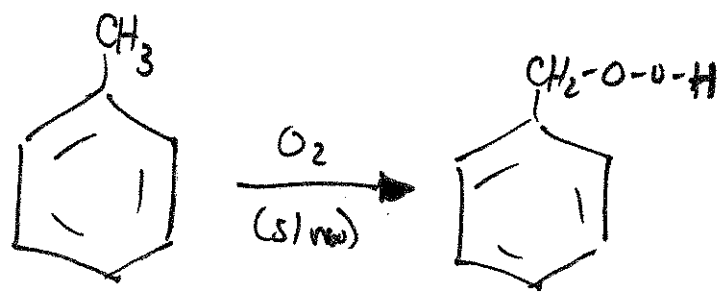
## Autoxidation

- Many organic compounds slowly react with  $O_2$  in the air
- Compounds that form free-radicals more easily more easily autooxidize because autooxidation goes thru a free-radical mechanism.

## Ethers

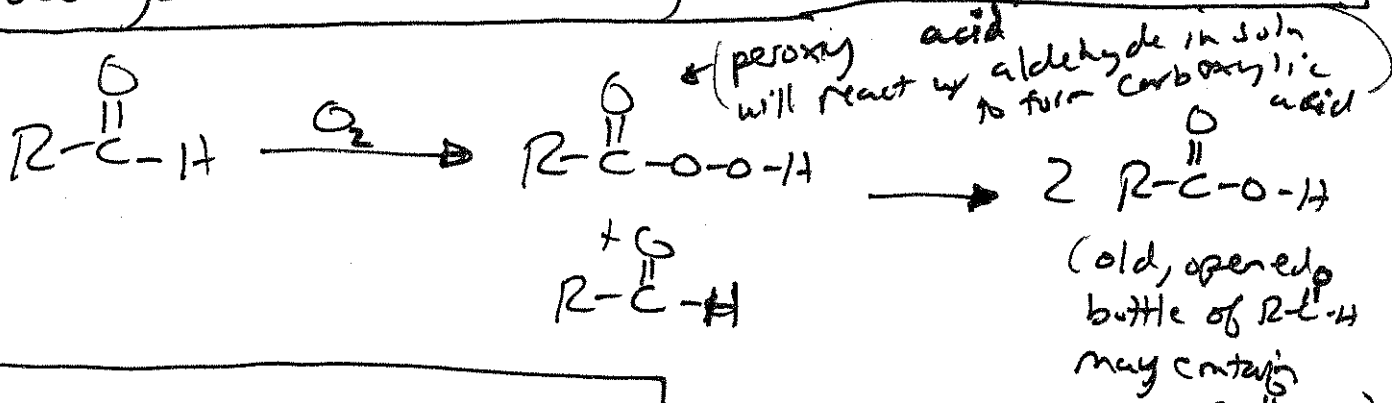


## Compounds with Benzylic Carbons



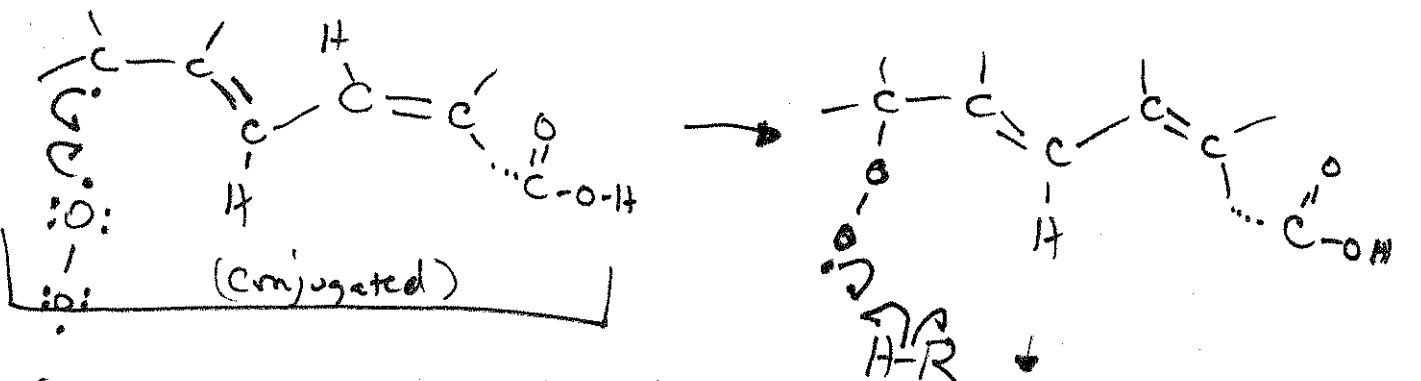
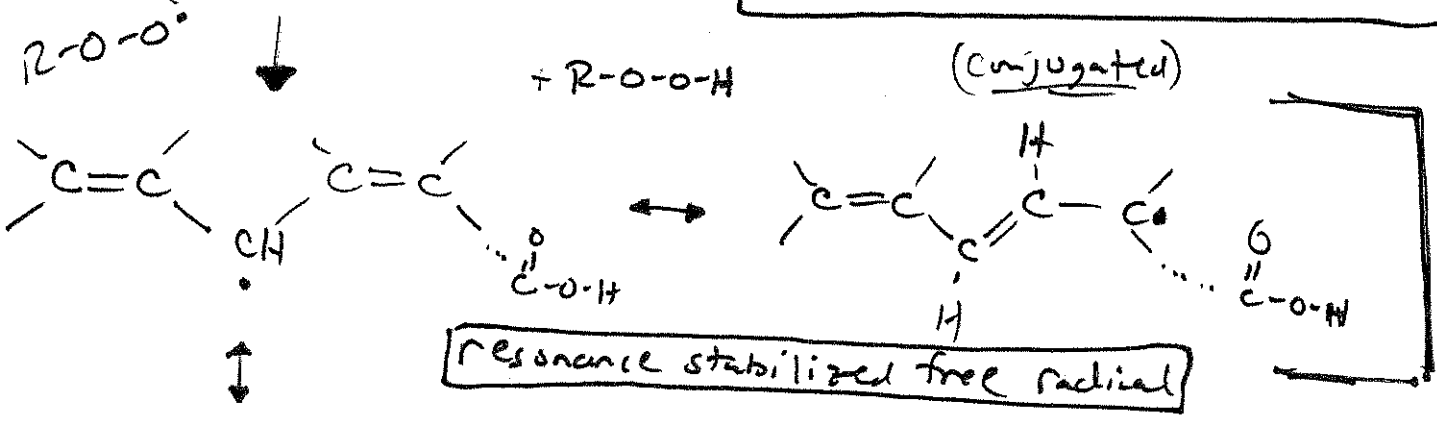
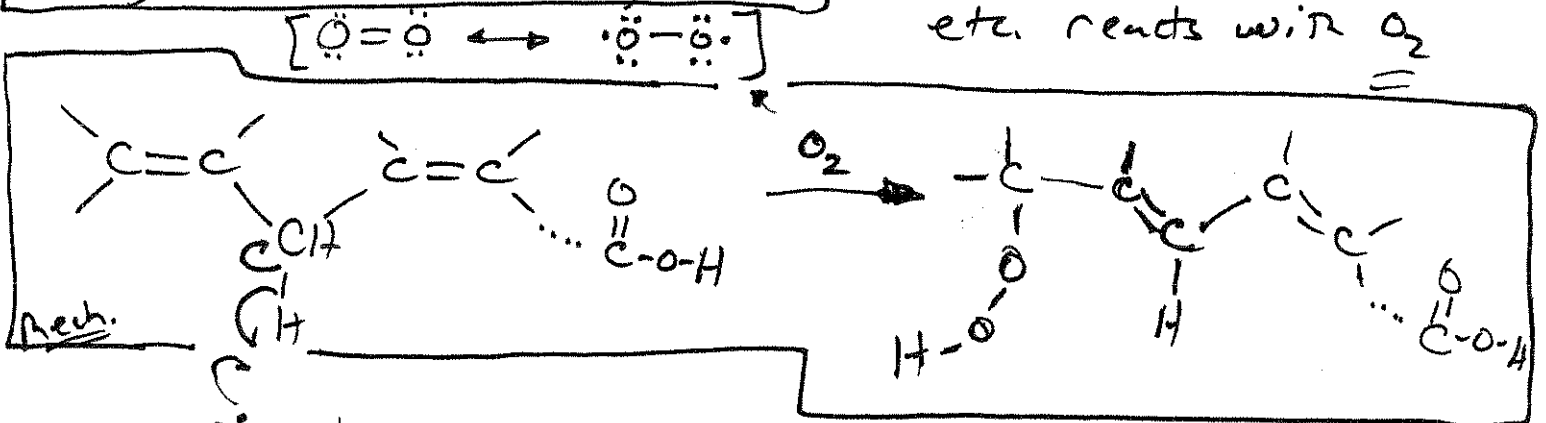
• if have open can of ether can contain peroxide autoxidation products → explosive if distilled to dryness

**Aldehydes  $\rightarrow$  Carboxylic Acids by Autooxidation**

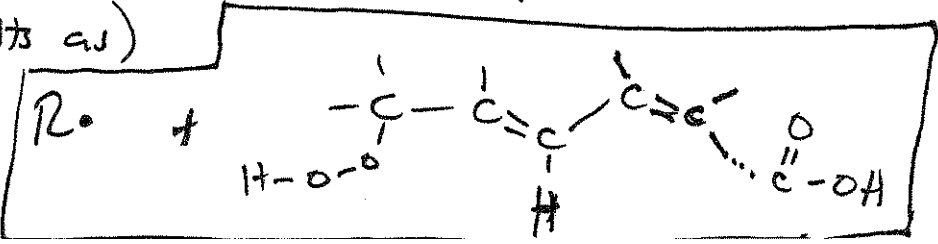


**Polyunsaturated Fatty Acids**

- in food, the body, etc. reacts with  $O_2$



Can get other ppts as well and crosslinking



- If have saturated fatty acid  $\text{CH}_3(\text{CH}_2)_n-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\text{H}$  autooxidation doesn't happen as readily. Why?

→ Sat'd fatty acids unable to form stabilized radicals

- Autooxidation responsible for oils going "rancid"

**Prostaglandins + Leukotrienes** - Polyunsaturated Carboxylic acids

→ very important biologically  
 play roles in • inflammation  
 • allergic rxns  
 • blood clotting etc...

• See text p 788-789 for structures

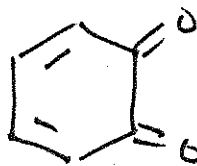
• Free-Radical Rxns involved in biosynthesis of some of these compounds

**Oxidation of Phenols**

**Quinones**



p-benzoquinone

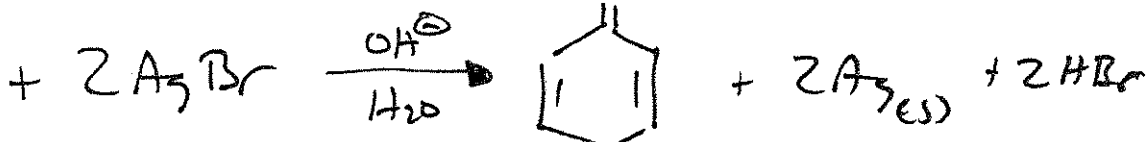


o-benzoquinone

Redox reaction

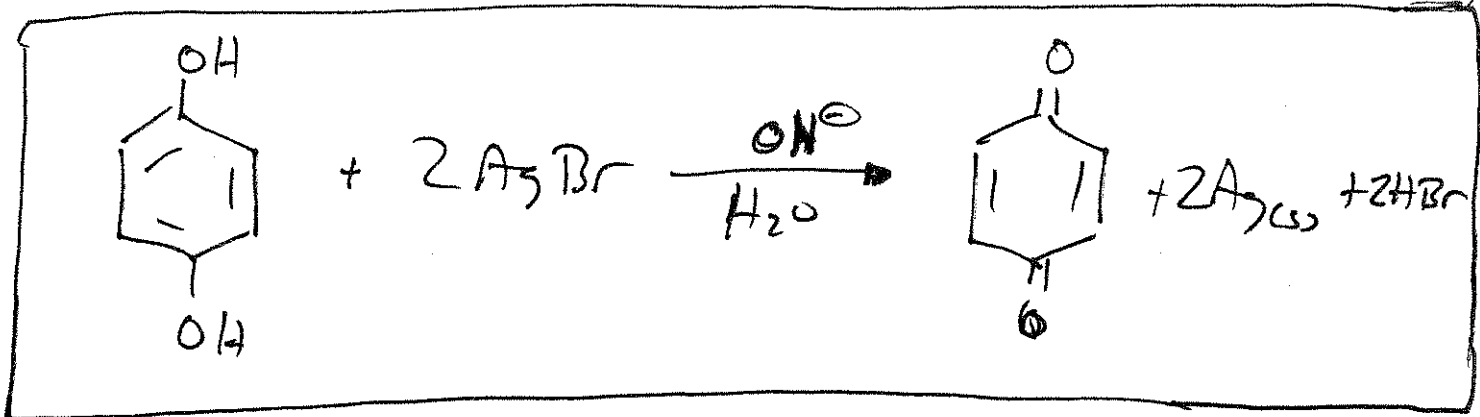


hydroquinone (diphenolic compd)



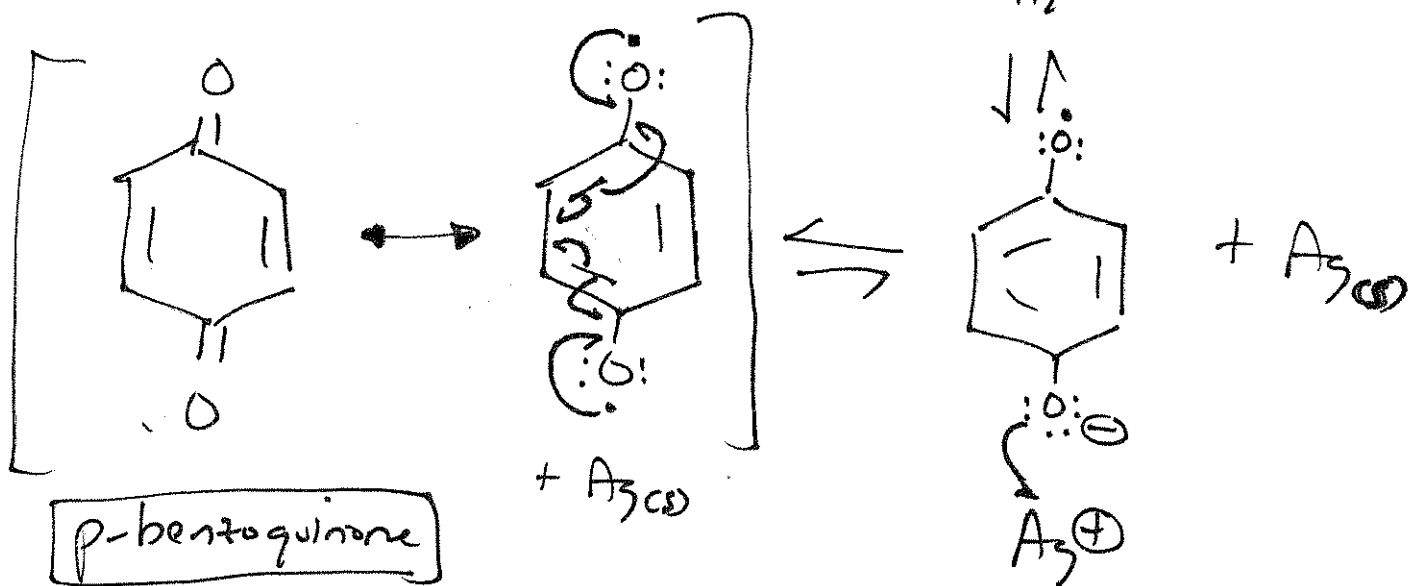
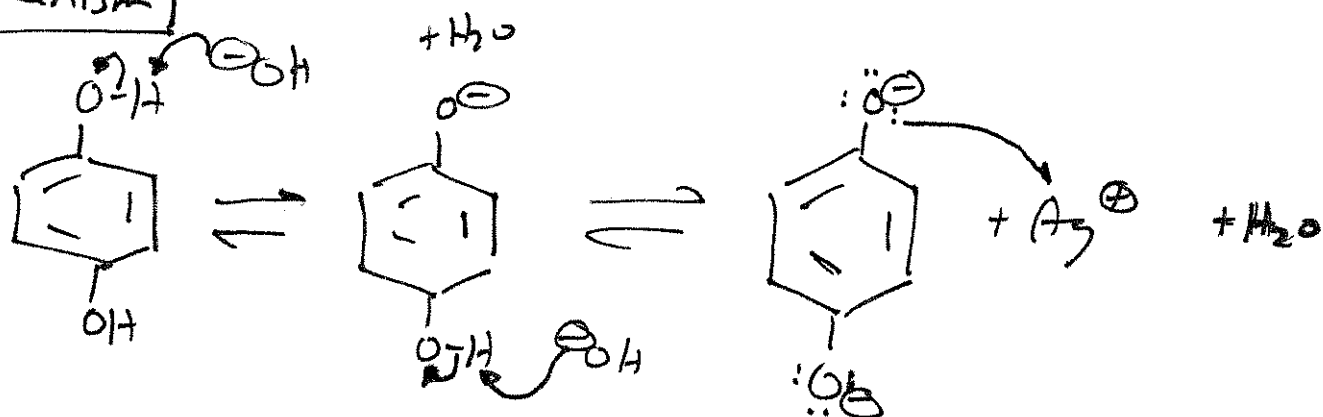
What's being oxidized + what's being reduced?

How does this happen?

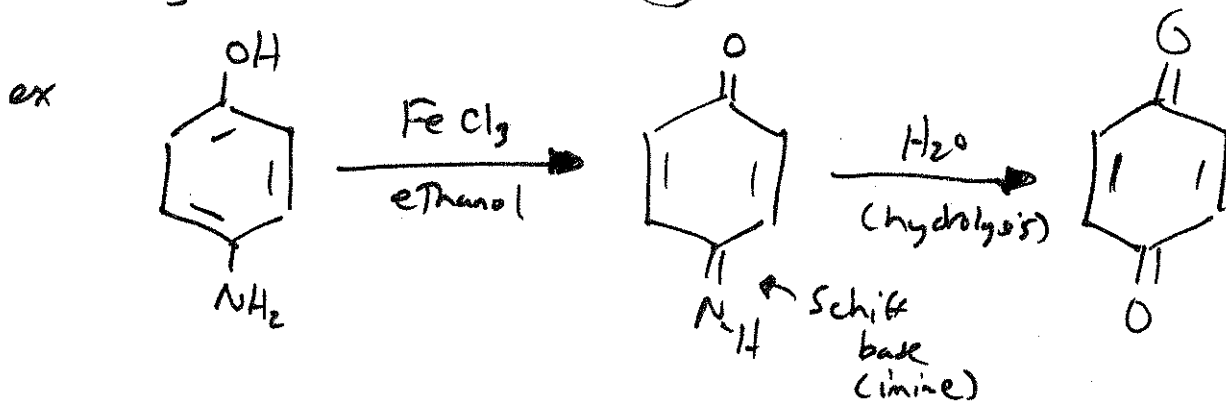


- hydroquinone being oxidized to quinone
- $\text{Ag}^+$  being reduced to  $\text{Ag}$
- goes thru a free-radical mechanism

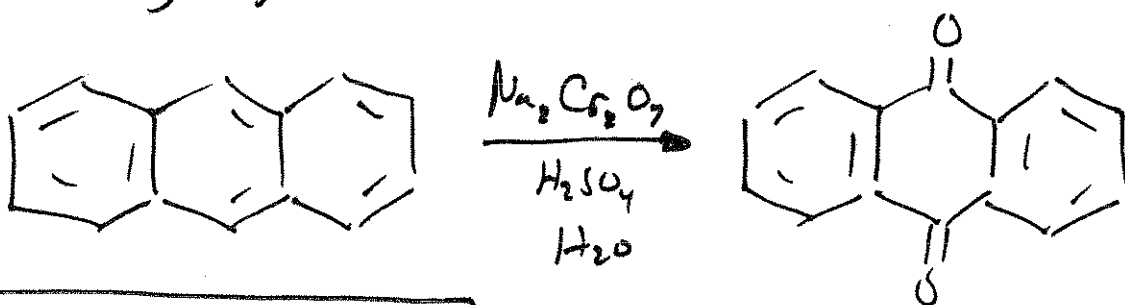
**Mechanism**



•  $FeCl_3$  - also an oxidizing agent

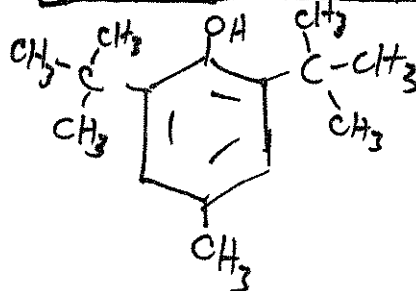
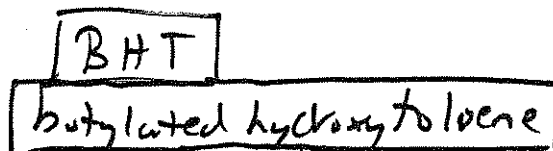
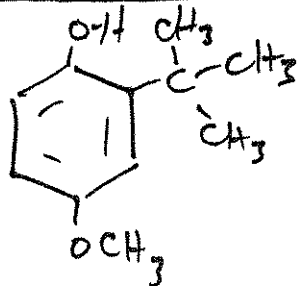
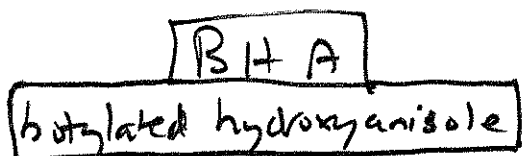


• fused ring systems can also be oxidized to quinones



## Phenols as Antioxidants

→ food preservatives are many times phenols



(Free-radical rxns)

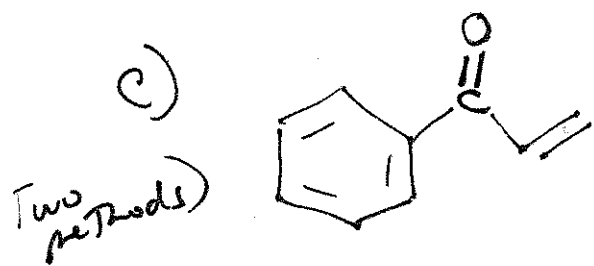
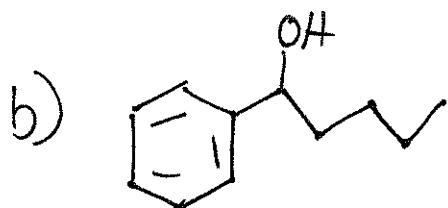
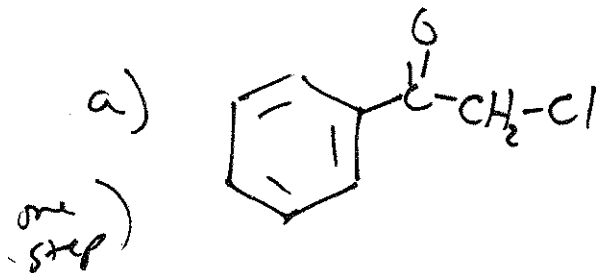
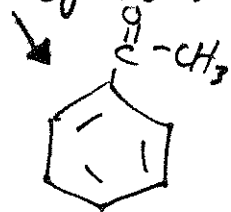
• many foods contain unsaturated fatty acids → oxidized by air + spoil  
+ oils

→ Phenols help stop free-radical chain rxns + prevent food spoilage. How?

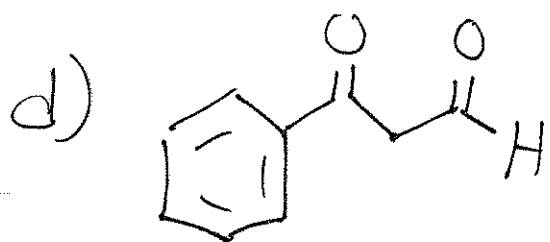
→ Makes a more stable free radical (because hindered + resonance stabilized) so won't react with alkenes

# Multistep Problems (End of Ch. 17, 18 + 19)

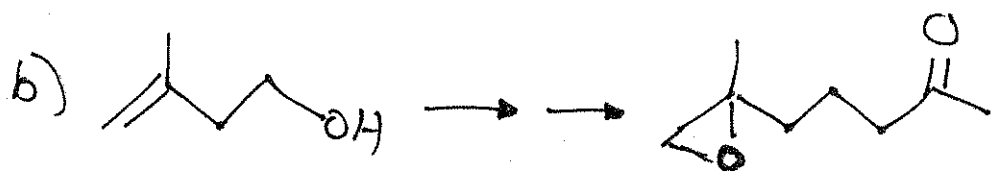
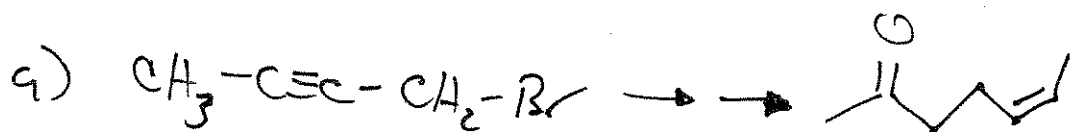
• Make the following compounds from acetophenone.







Make the following compounds from  $\text{CH}_3\text{-C(=O)-CH}_2\text{-C(=O)-OCH}_2\text{CH}_3$  and the given starting material.



• Show how you would convert alkene A into  $\alpha, \beta$ -unsaturated aldehyde B.  
(Harder one)

