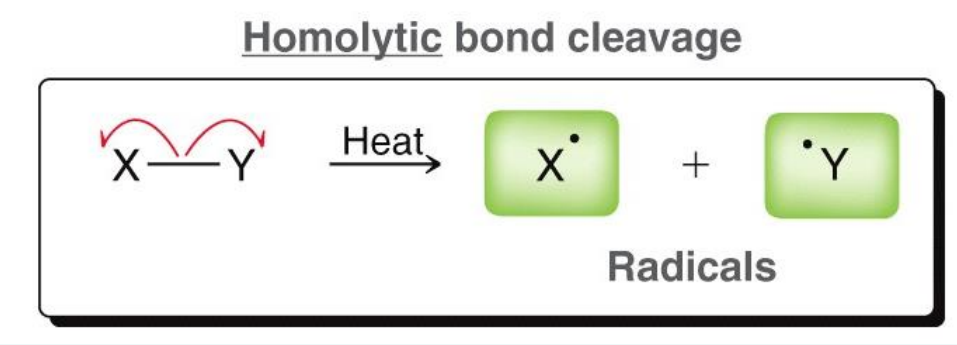
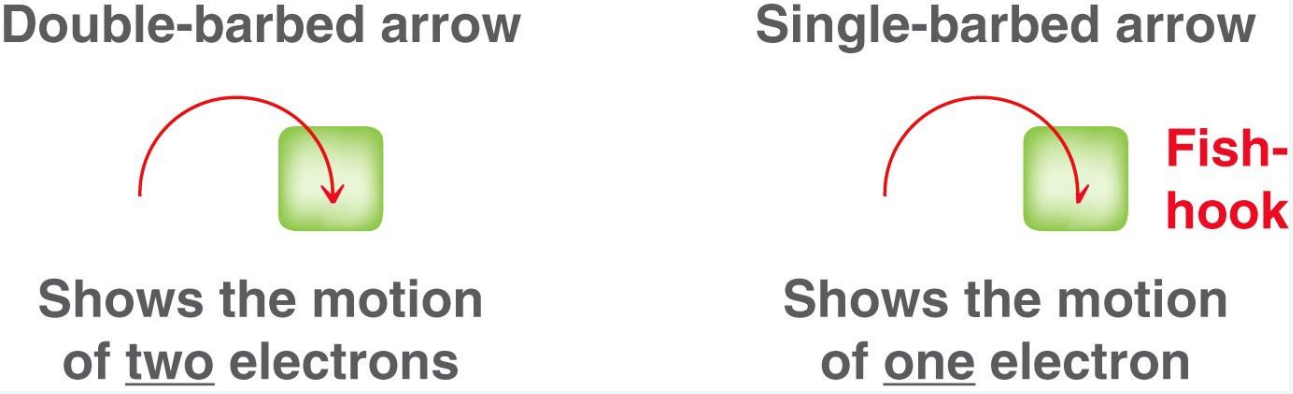
Radical Reactions

Free Radicals

- Free radicals form when bonds break homolytically

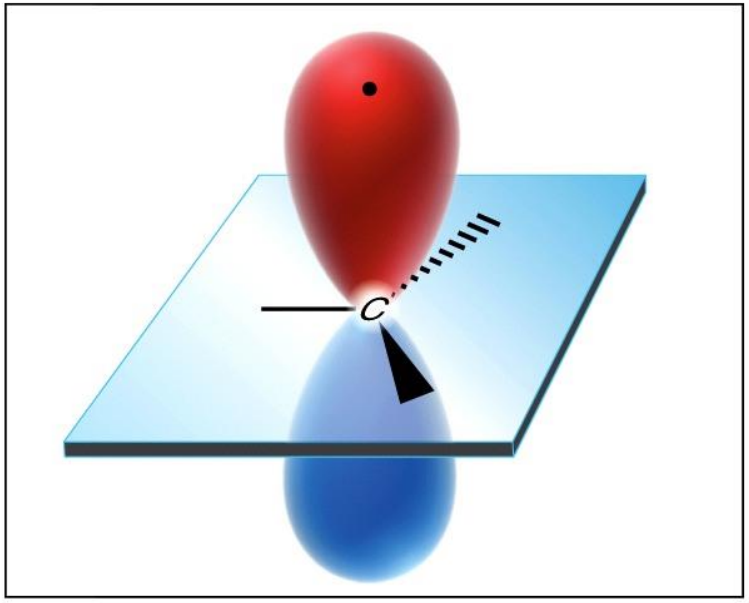


- Note the single-barbed or fishhook arrow used to show the electron movement



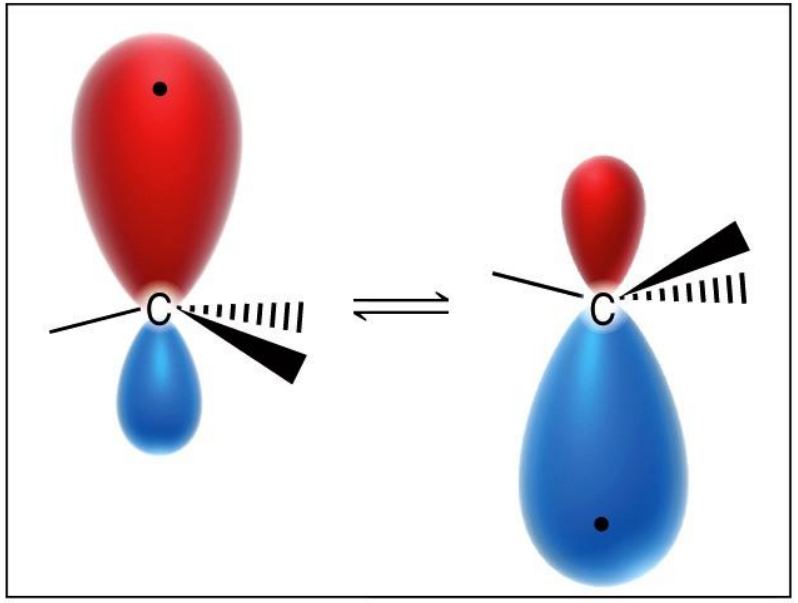
Free Radicals

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



Trigonal planar
sp^2 hybridized

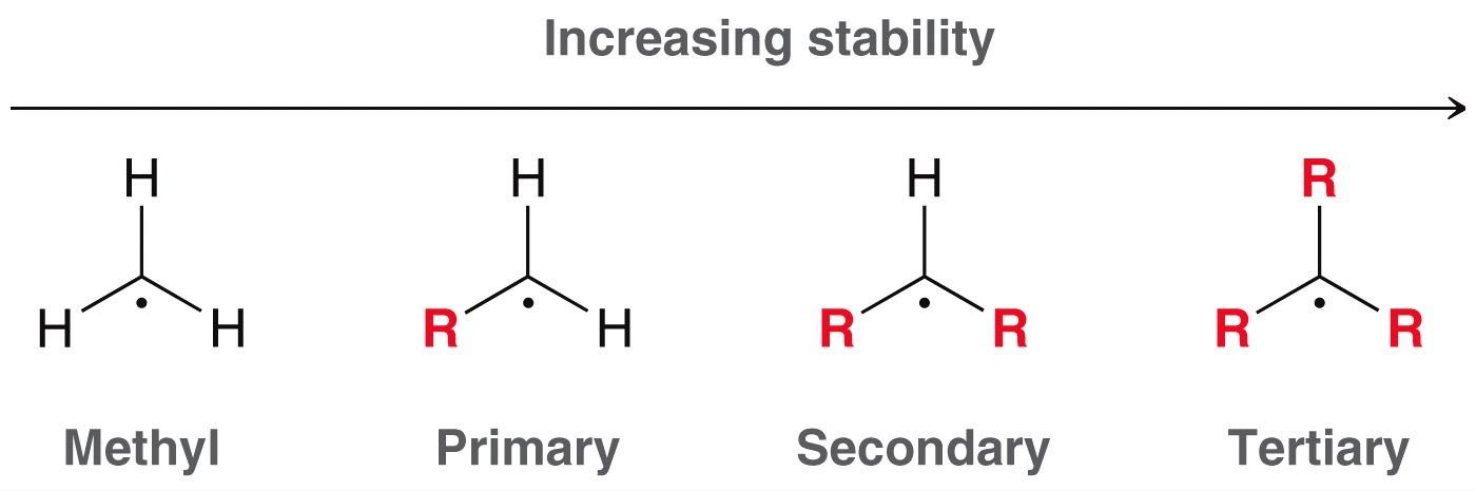
or



Shallow pyramid
(rapidly inverting)

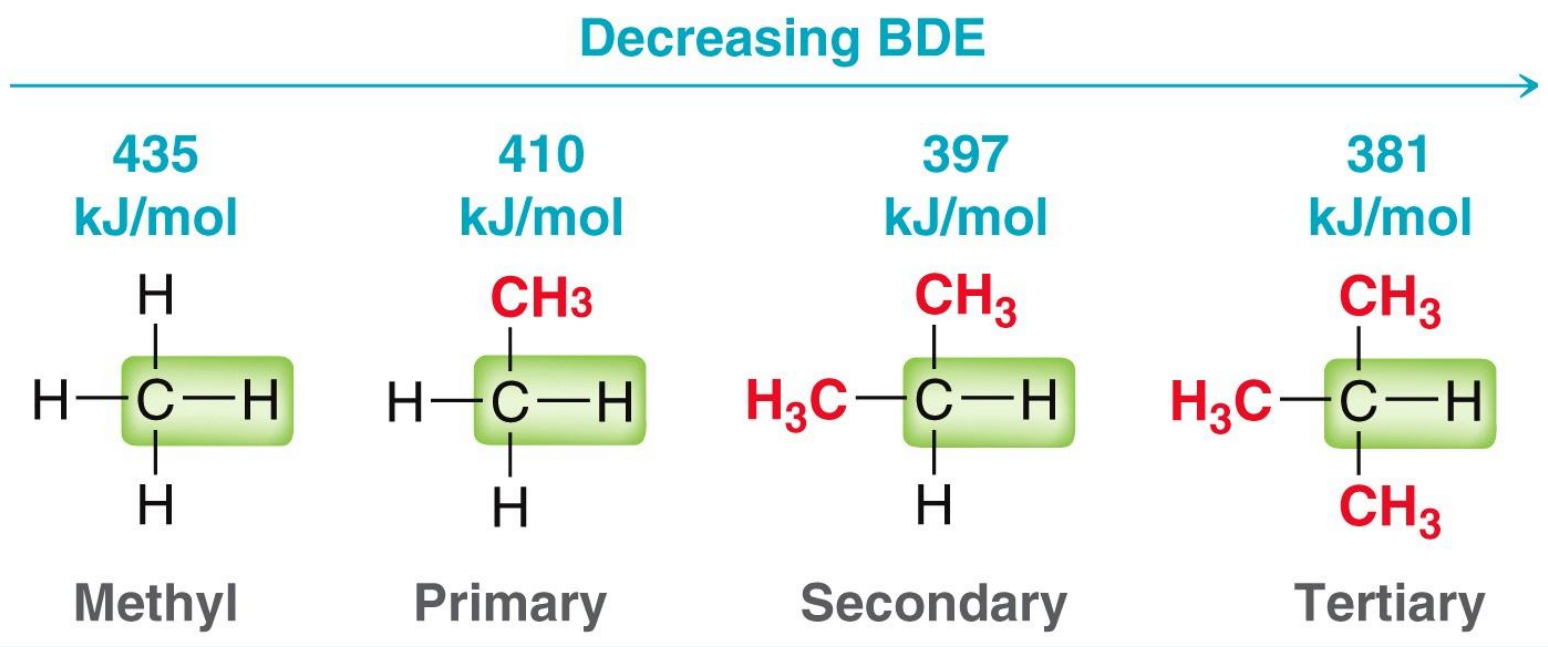
Free Radical Stability

- 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



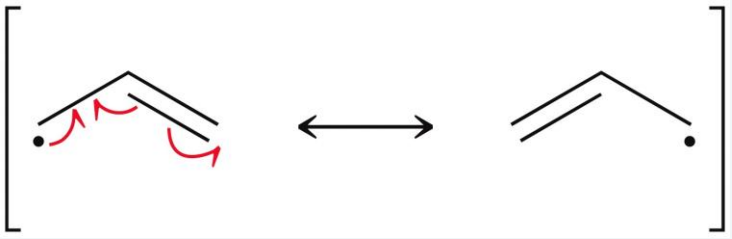
Free Radical Stability

- Use arguments that involve hyperconjugation and an energy diagram to explain the differences in bond dissociation energy below.



Free Radical Resonance

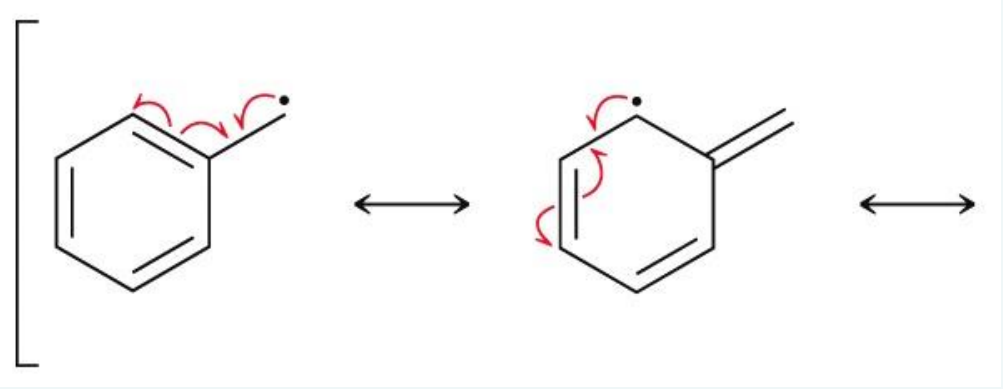
- Drawing resonance for free radicals using fishhook arrows show electron movement
- Remember, for resonance, the arrows don't ACTUALLY show electron movement. WHY?
- Draw the resonance hybrid for an allyl radical



- HOW and WHY does resonance affect the stability of the free radical?

Free Radical Resonance

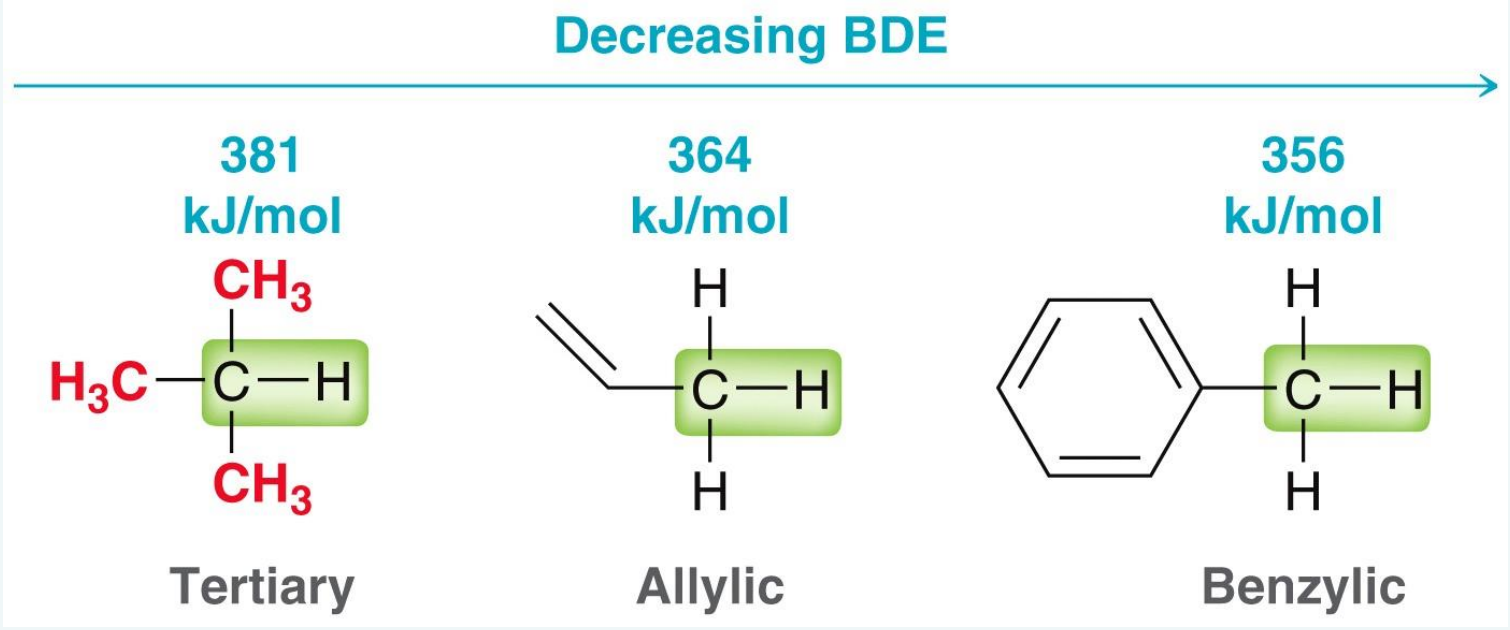
- The benzylic radical is a hybrid that consists of 4 contributors



- Draw the remaining contributors

Resonance Stabilization

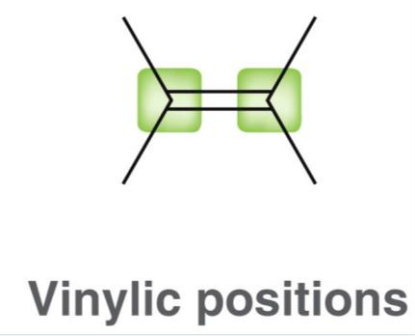
- How does resonance affect the stability of a radical? WHY?

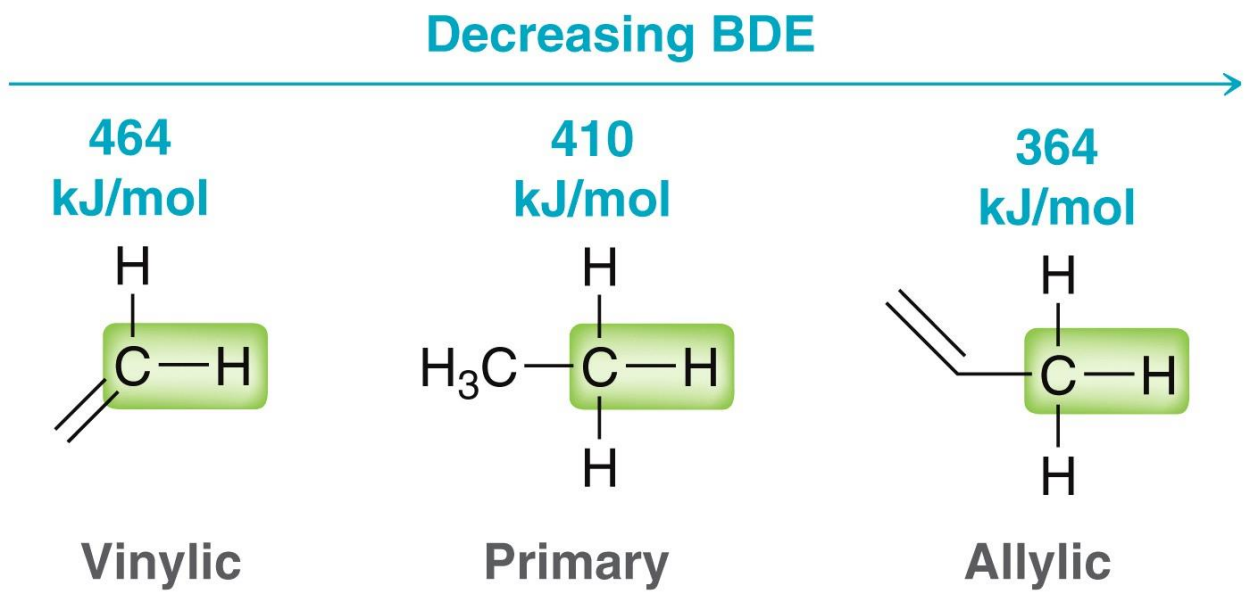


- What is a bigger factor, hyperconjugation or resonance?

Resonance Stabilization

- Vinylic free radicals are especially unstable

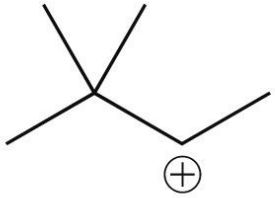




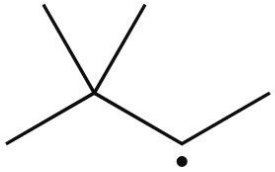
- No resonance stabilization
- What type of orbital is the vinylic free radical located in, and how does that affect stability?

Radical Electron Movement

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



This carbocation
will rearrange
to produce a more stable
tertiary carbocation

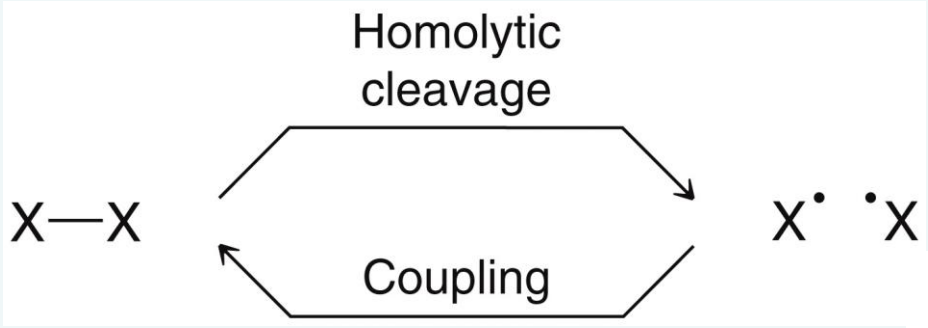


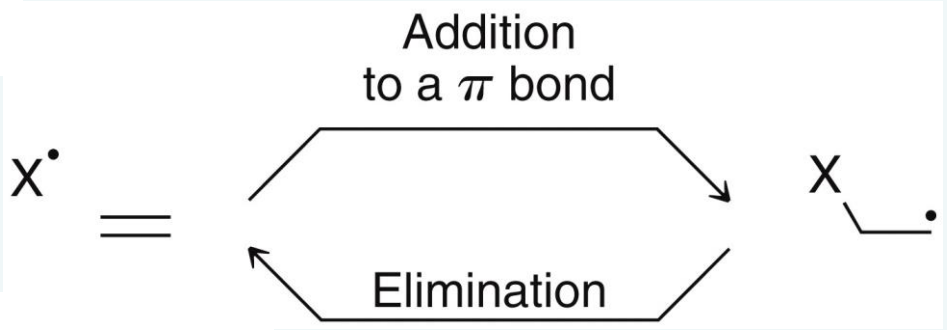
This radical
will not rearrange
to produce a more stable
tertiary radical

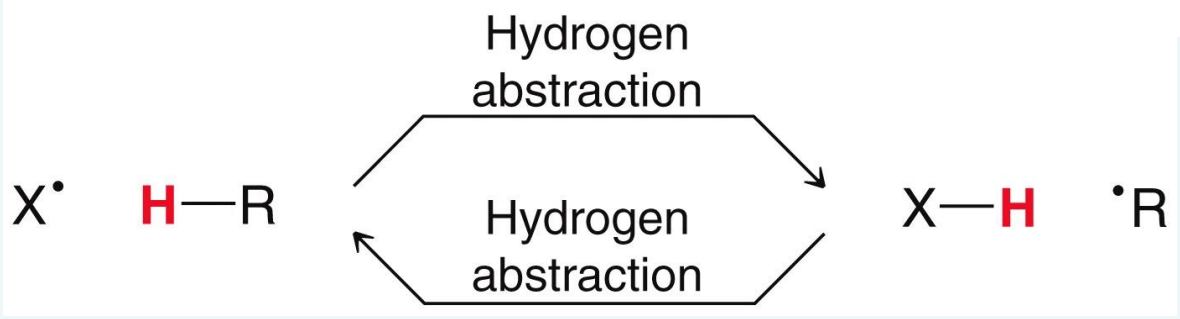
- There are SIX key arrow-pushing patterns that we will discuss

Radical Electron Movement

- Note the reversibility of radical processes





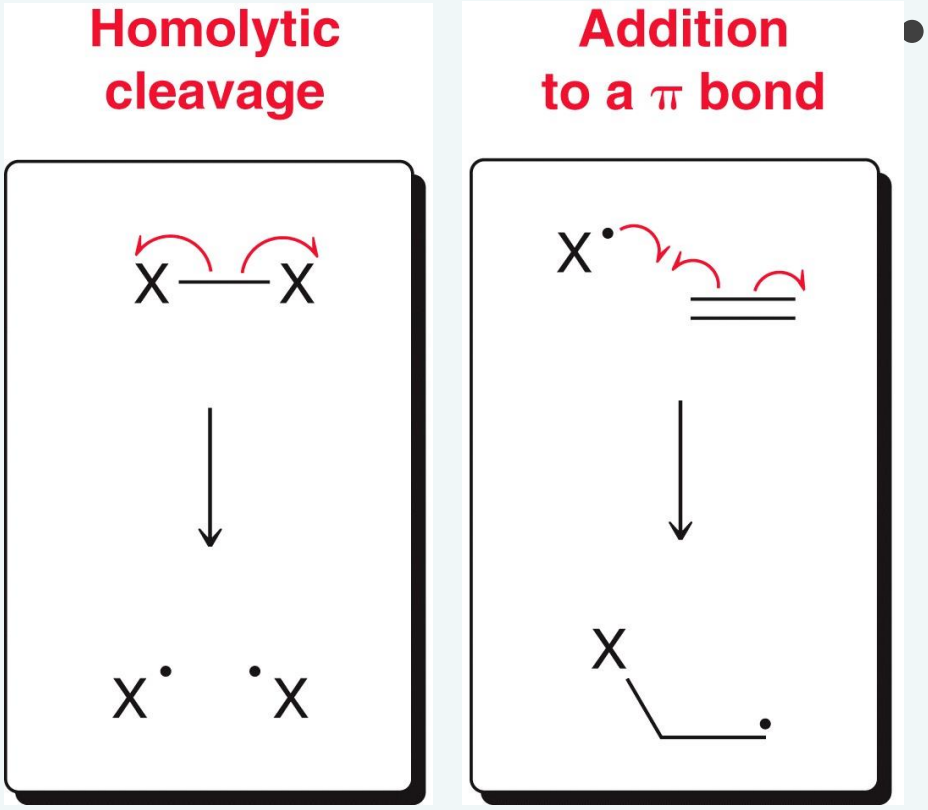


Radical Electron Movement

- Radical electron movement is generally classified as either initiation, termination, or propagation

Initiation Propagation

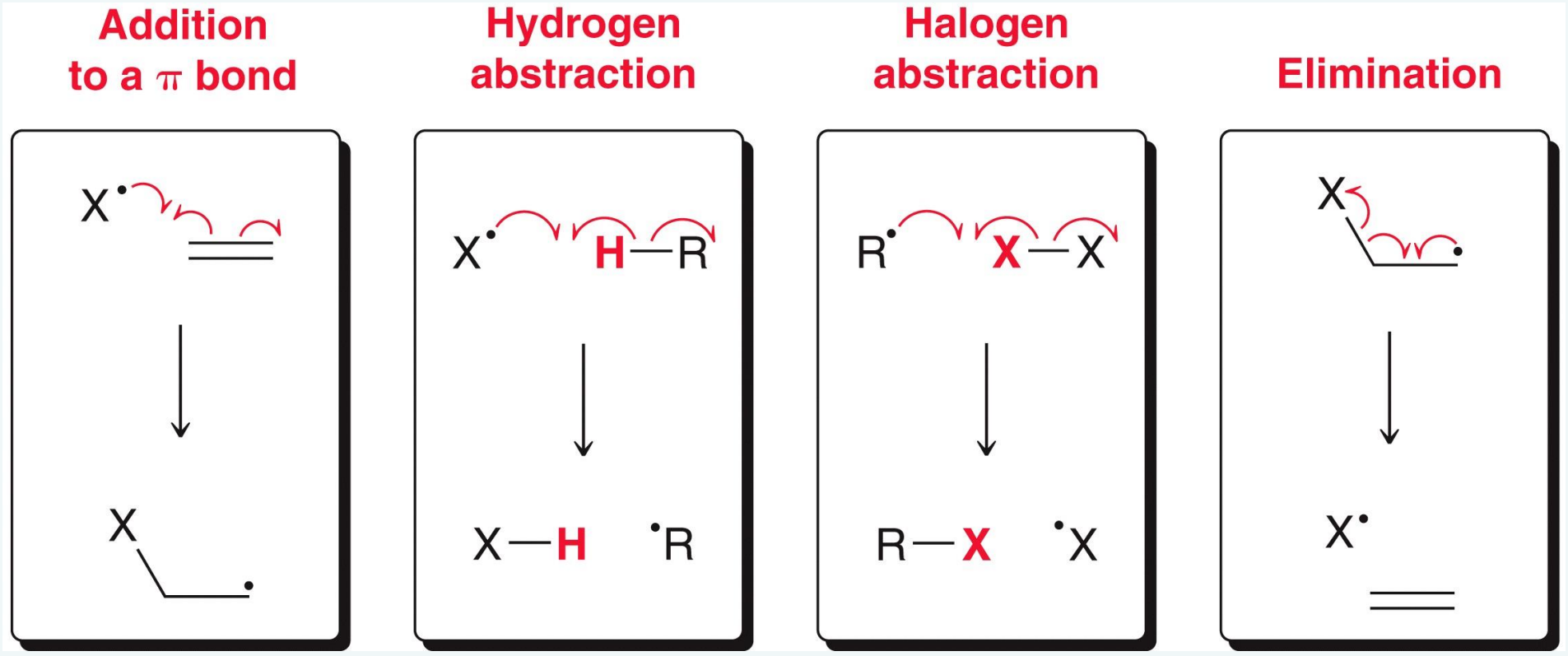
- **Initiation** occurs when radicals are created



- **Termination** occurs when radicals are destroyed

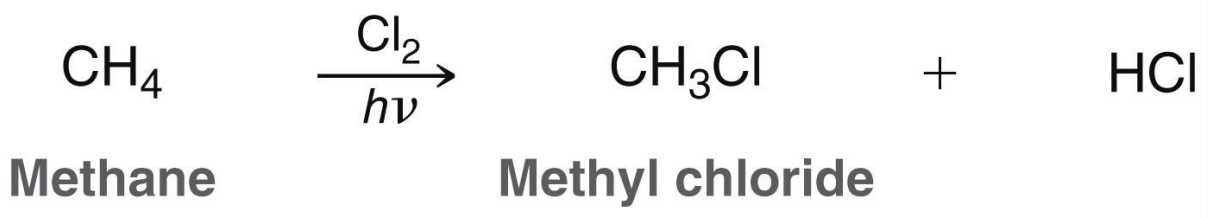
Radical Electron Movement

- **Propagation** occurs when radicals are moved from one location to another

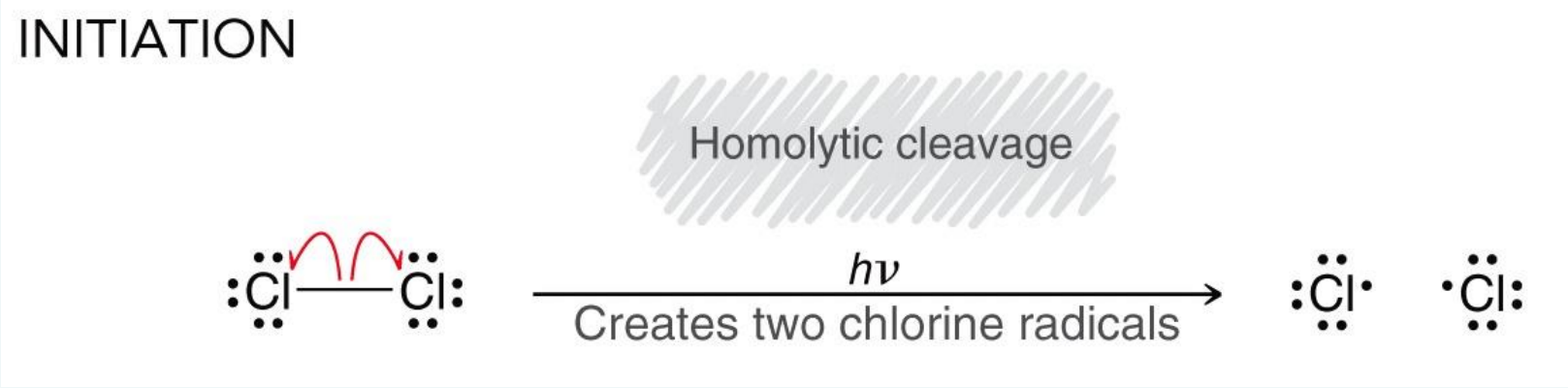


Chlorination of Methane

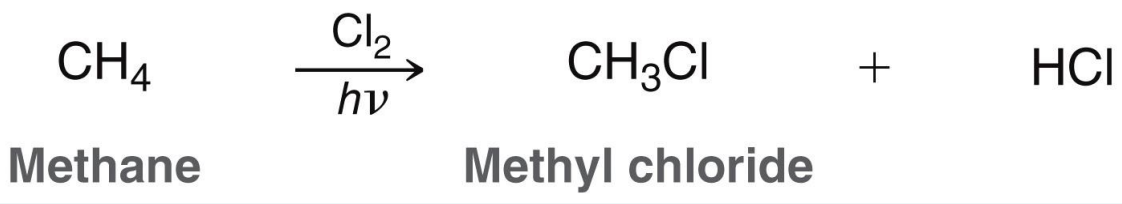
- Let's apply our electron-pushing skills to a reaction



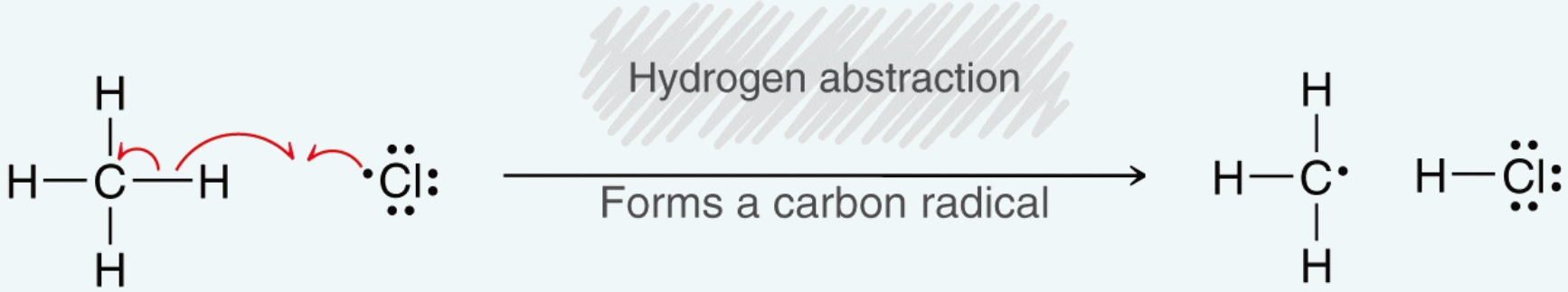
- We must consider each pattern for any free radical that forms during the reaction

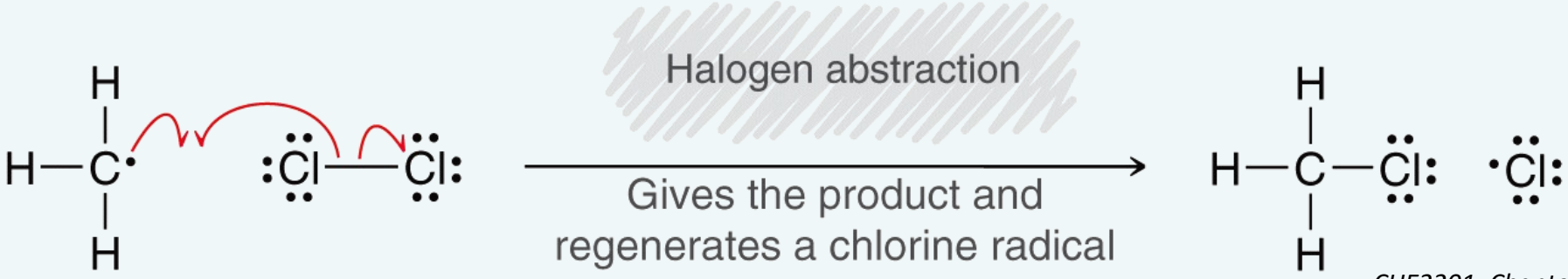


Chlorination of Methane

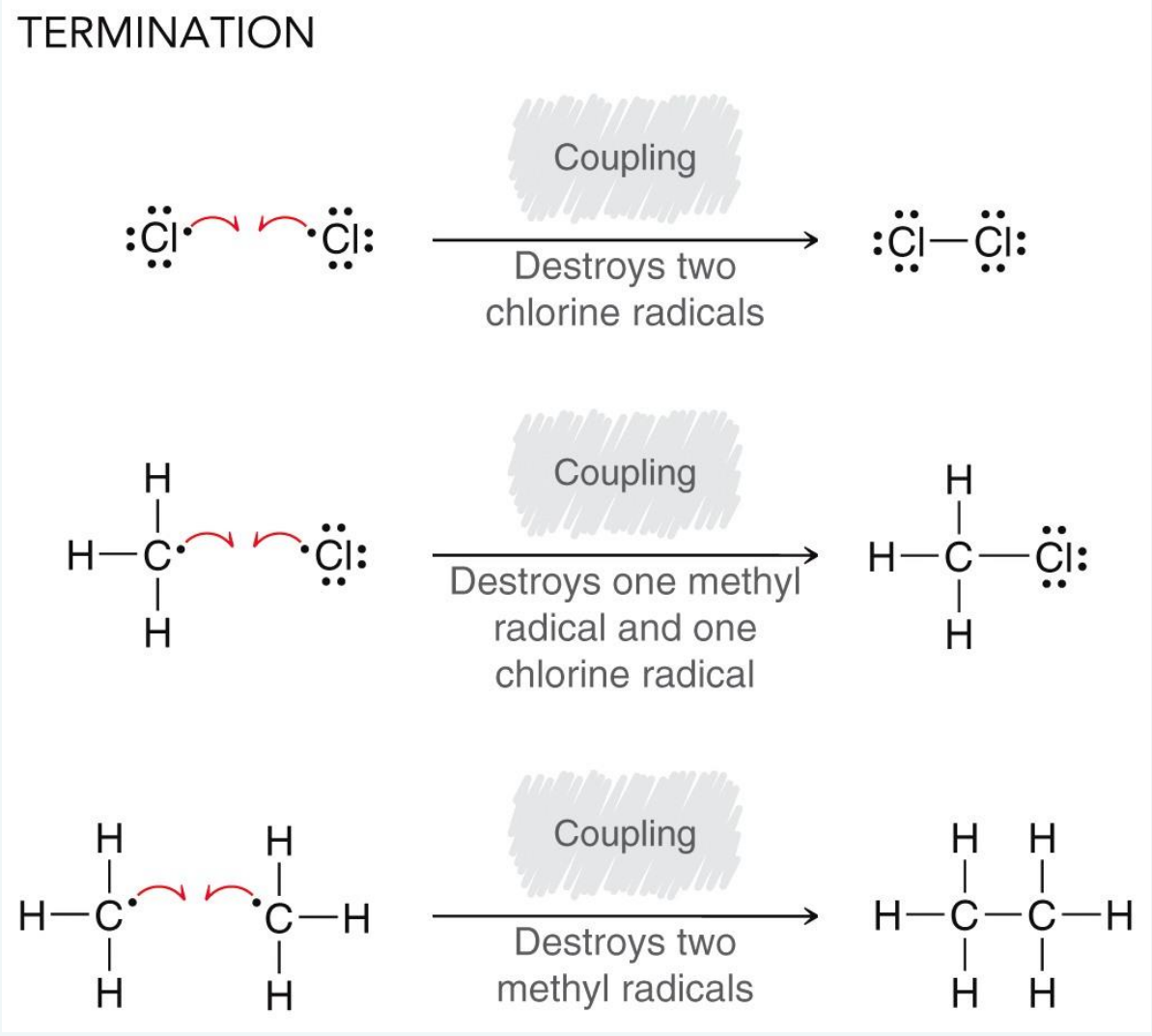


PROPAGATION



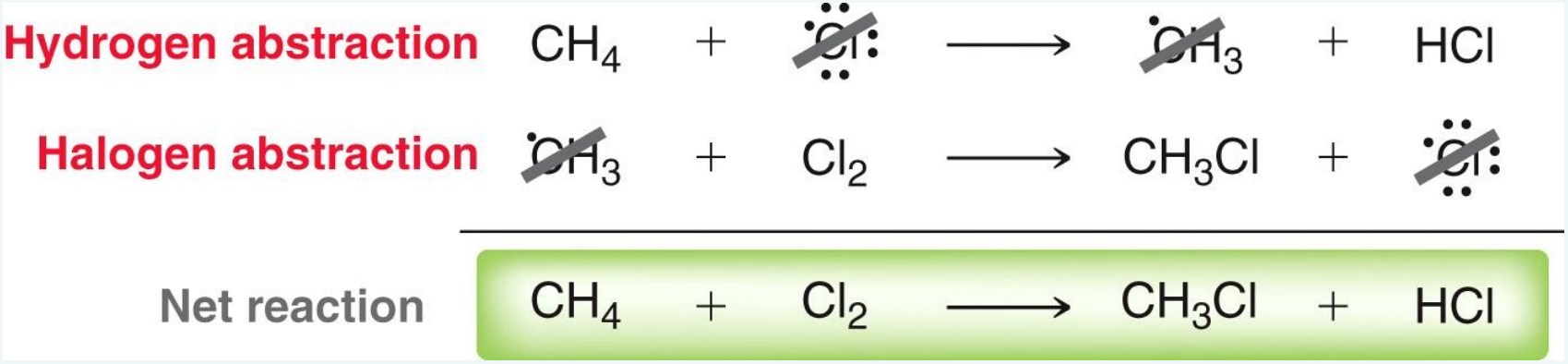


Chlorination of Methane



Chlorination of Methane

- The propagation steps give the net reaction

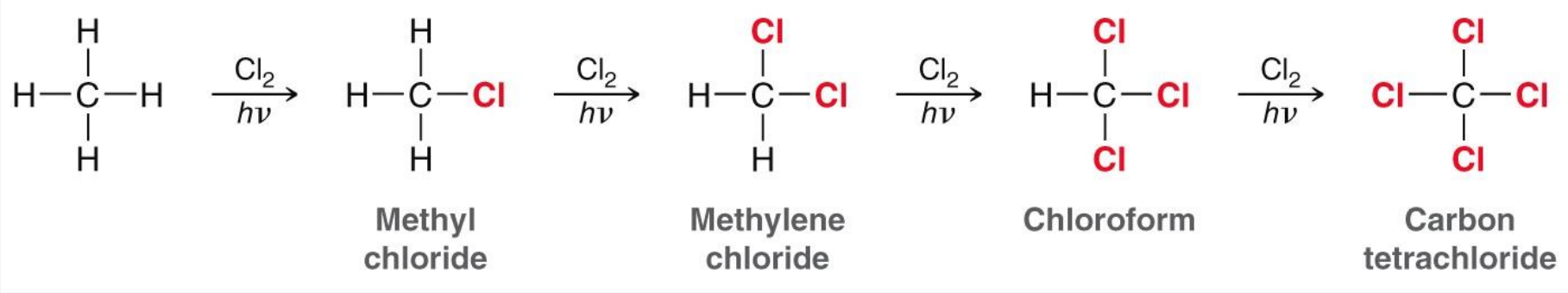


1. Initiation produces a small amount Cl• radical
2. H abstraction consumes the Cl• radical
3. Cl abstraction generates a Cl• radical, which can go on to start another H abstraction

- Propagation steps are self-sustaining

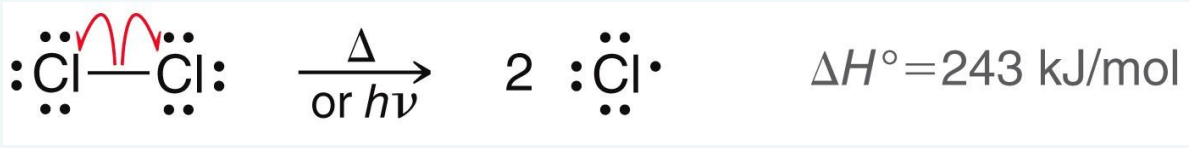
Chlorination of Methane

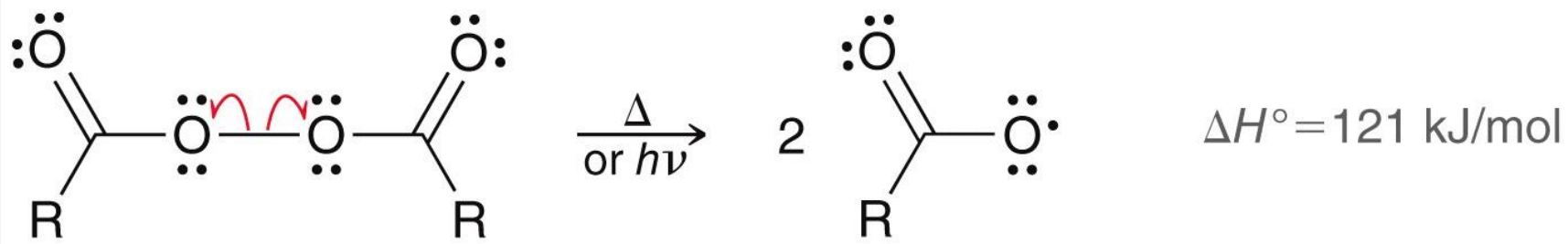
- Reactions that have self-sustaining propagation steps are called **chain reactions**
- **Chain reaction:** the products from one step are reactants for a different step in the mechanism
- Polychlorination is difficult to prevent, especially when an excess of Cl_2 is present.



Radical Initiators

- An initiator starts a free radical chain reaction



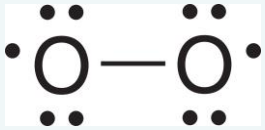


An acyl peroxide

- Which initiator above initiates reactions most readily? WHY?
- The acyl peroxide will be effective at 80 ° C

Radical Inhibitors

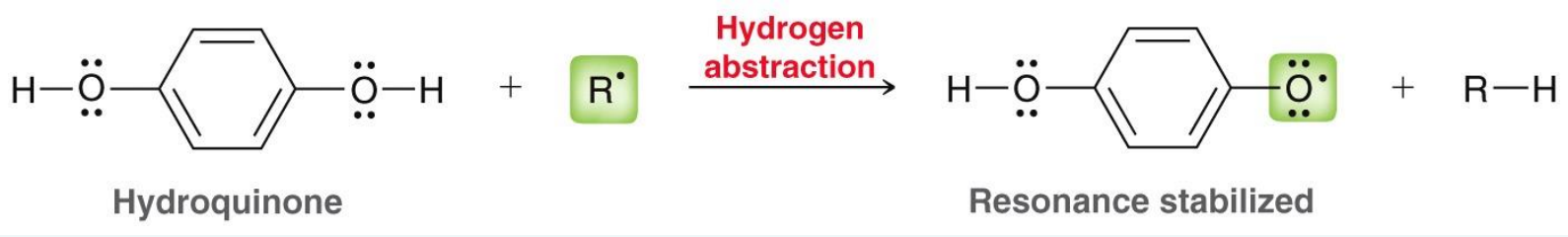
- Inhibitors act in a reaction to scavenge free radicals to stop chain reaction processes
- Oxygen molecules can exist in the form of a diradical, which reacts readily with other radicals. Use arrows to show the process

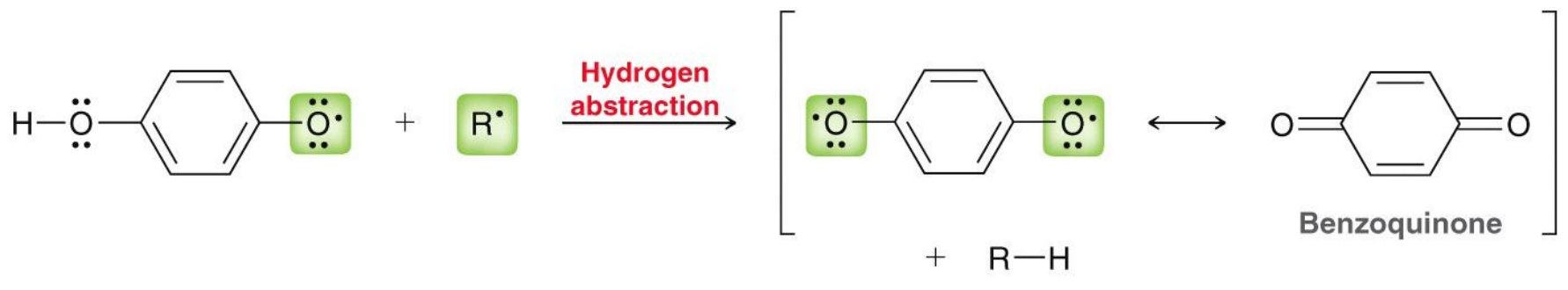


- How can reaction conditions be modified to stop oxygen from inhibiting a desired chain reaction?

Radical Inhibitors

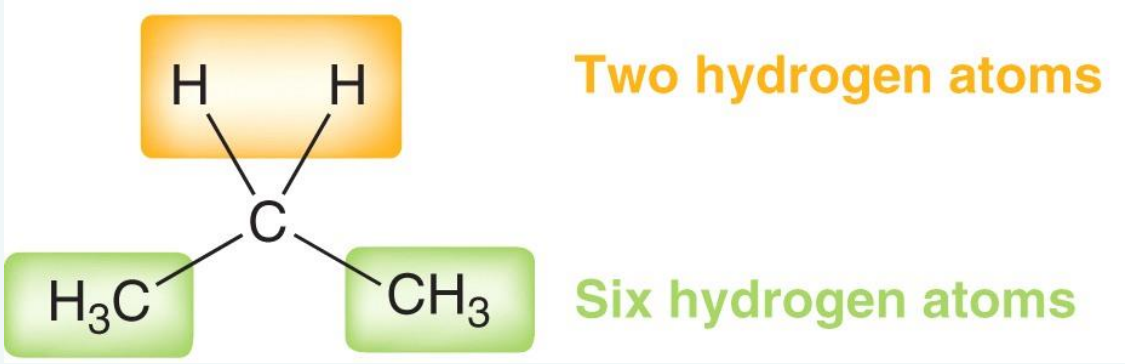
- Hydroquinone is also often used as a radical inhibitor



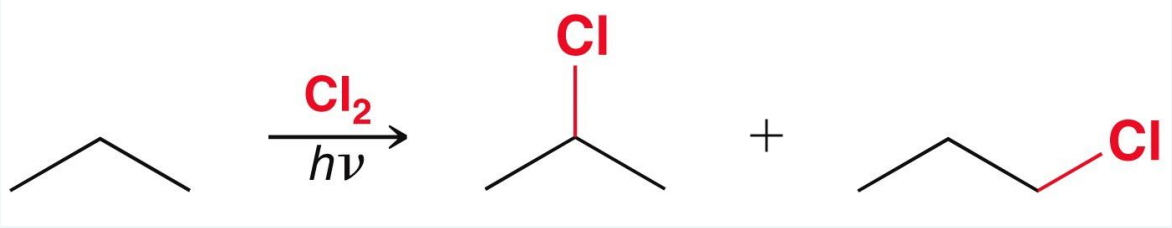


Halogenation Regioselectivity

- With substrates more complex than ethane, multiple monohalogenation products are possible

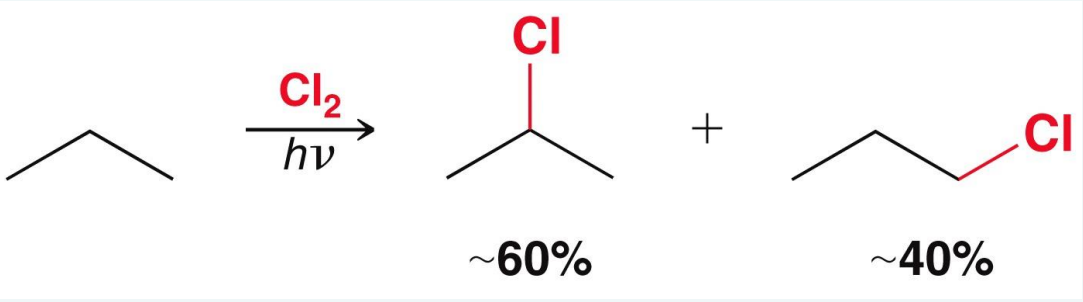


- If the halogen were indiscriminant, predict the product ratio?



Halogenation Regioselectivity

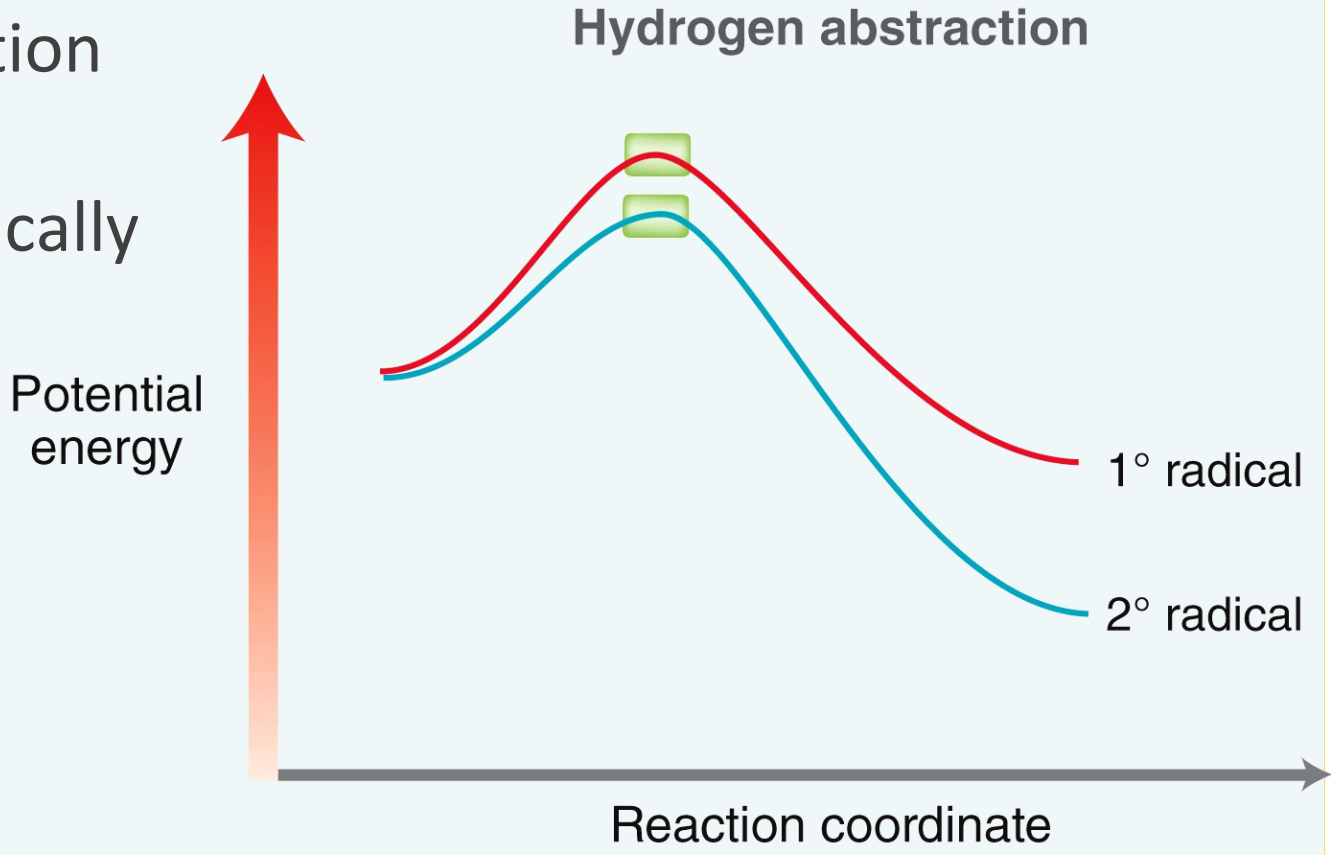
- For the CHLORINATION process, the actual product distribution favors 2-chloropropane over 1-chloropropane



- Which step in the mechanism determines the regioselectivity?

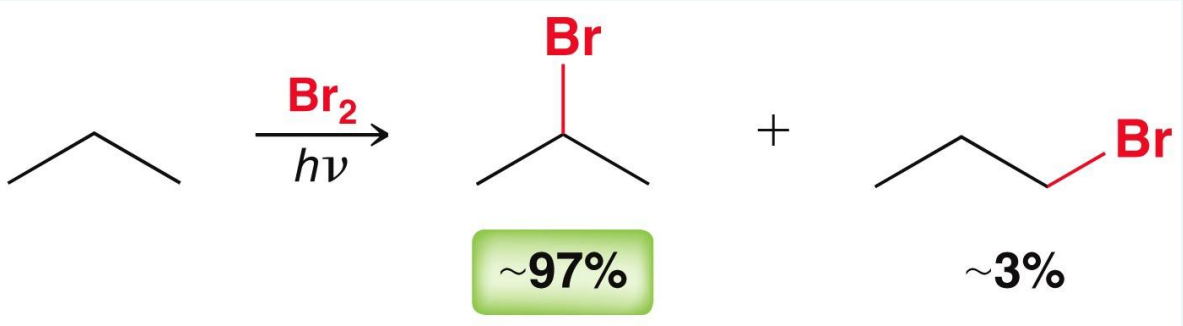
Halogenation Regioselectivity

- In one reaction, a 1° free radical forms, and in the other a 2° radical forms
- Is the chlorination process thermodynamically or kinetically controlled?



Halogenation Regioselectivity

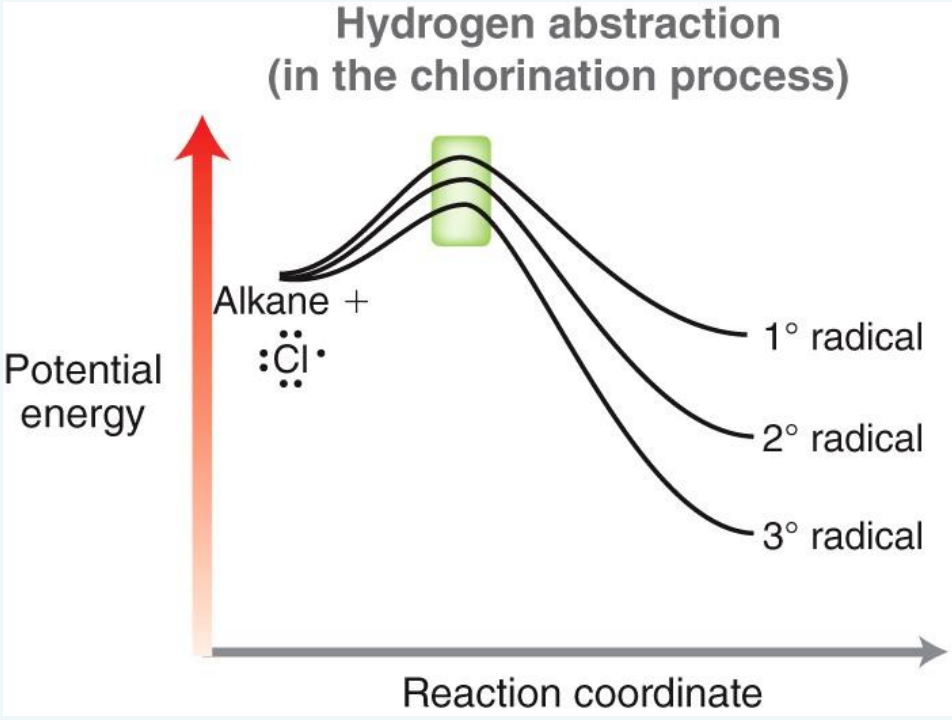
- For the BROMINATION process, the product distribution vastly favors 2-bromopropane over 1-bromopropane

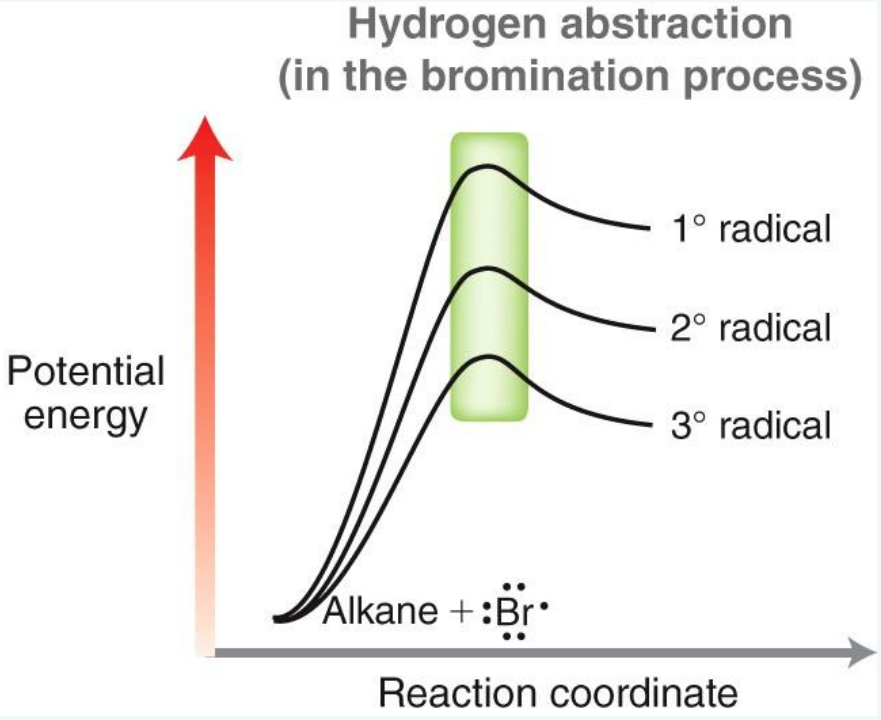


- Which step in the mechanism determines regioselectivity?

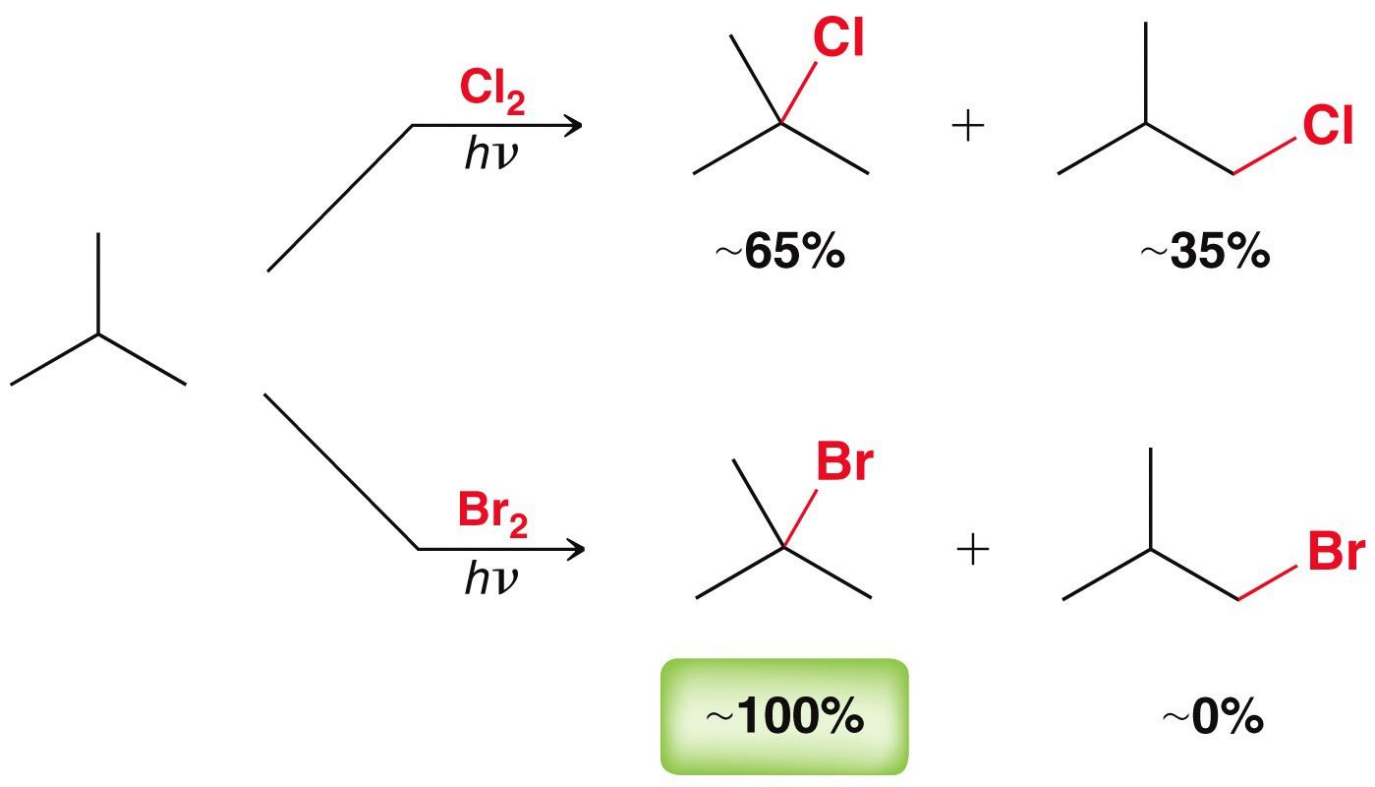
Halogenation Regioselectivity

- Which process is more regioselective? WHY?





Halogenation Regioselectivity



- Bromination at the 3° position happens 1600 times more often than at the 1° position

Halogenation Regioselectivity

- Which process is least regioselective?

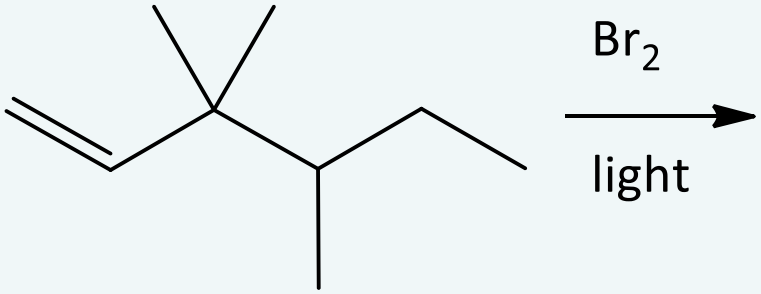
TABLE 11.2 THE RELATIVE SELECTIVITY OF FLUORINATION, CHLORINATION, AND BROMINATION

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

- What is the general relationship between reactivity and selectivity? WHY?

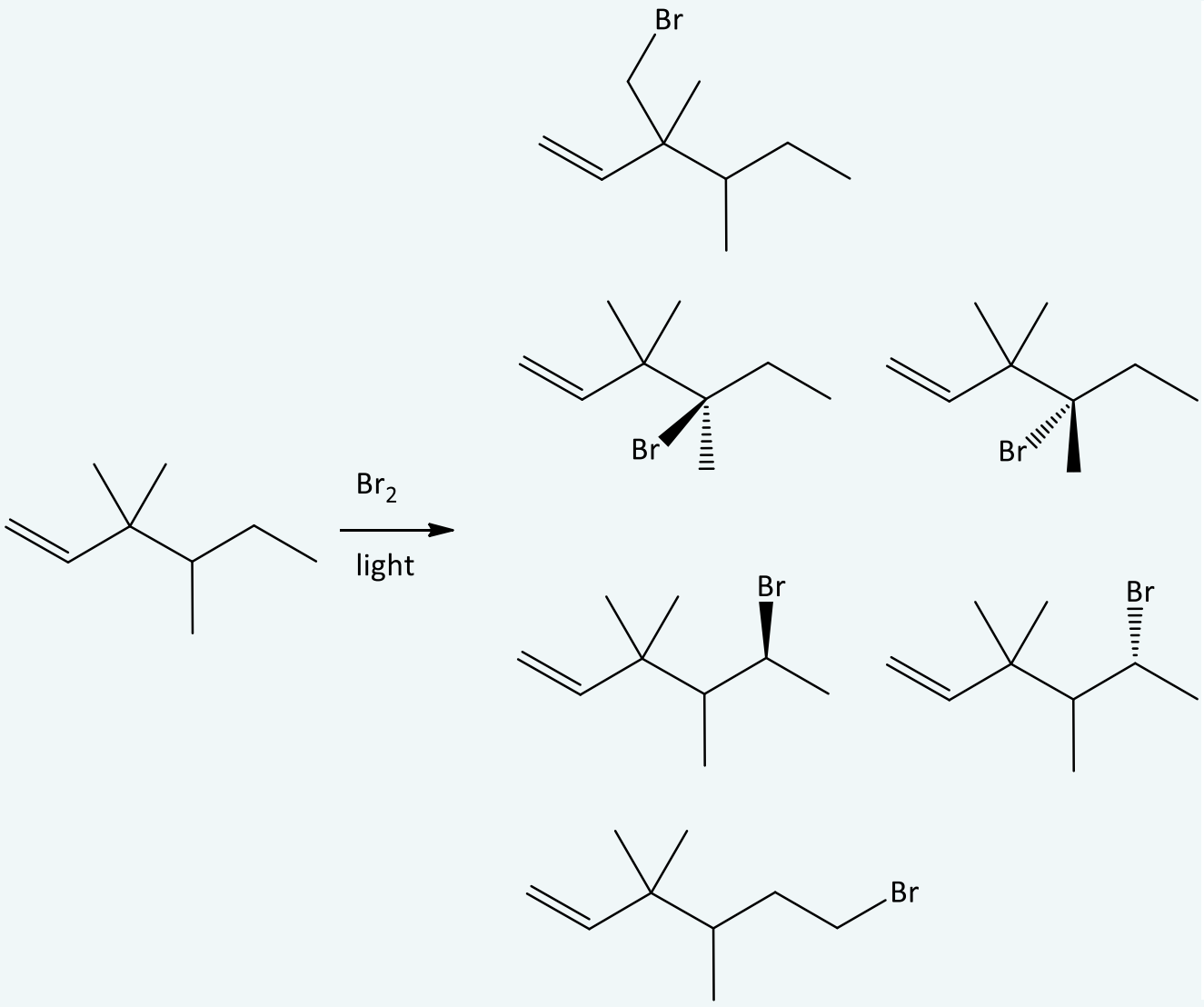
Halogenation Regioselectivity

- 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

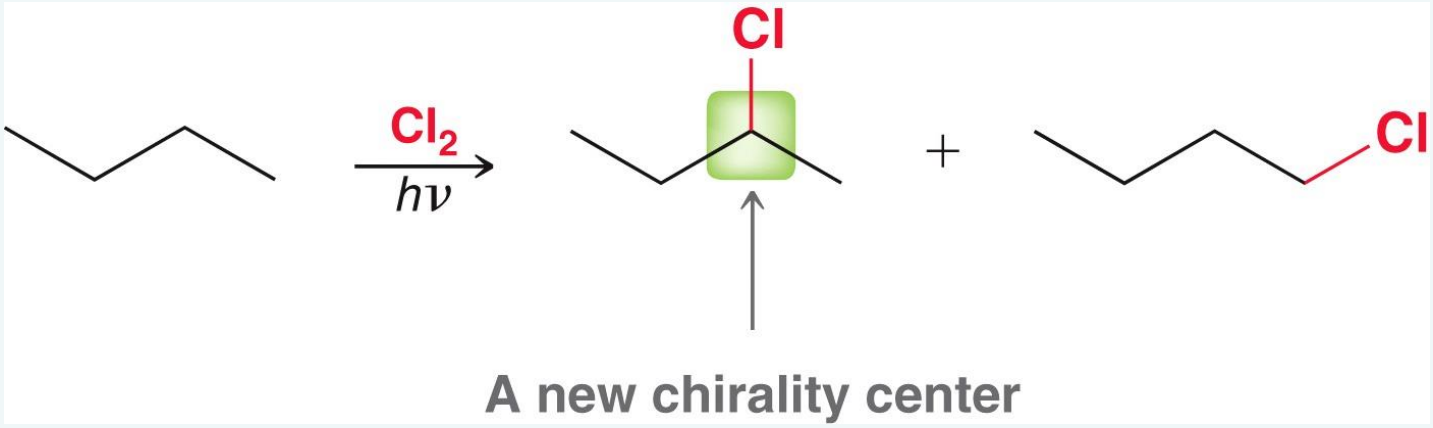
Halogenation Regioselectivity



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

Halogenation Stereochemistry

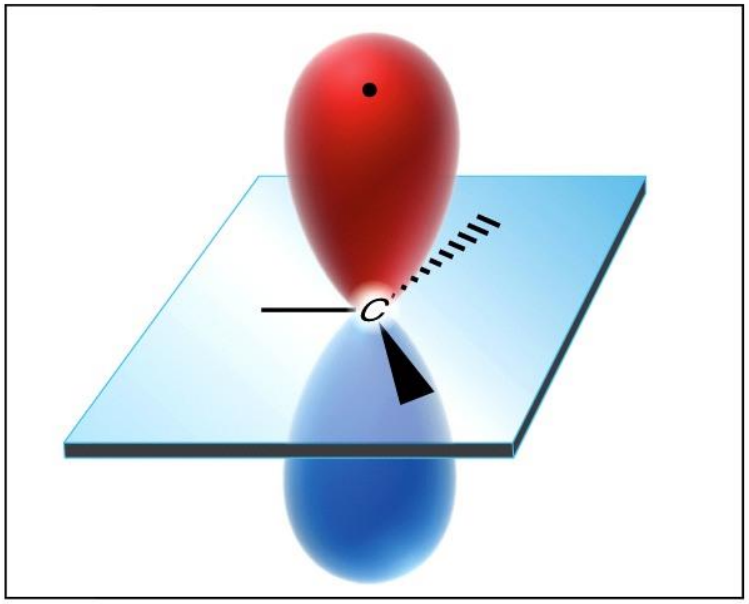
- The halogenation of butane or more complex alkanes forms a new chirality center



- 2-chlorobutane will form as a racemic mixture

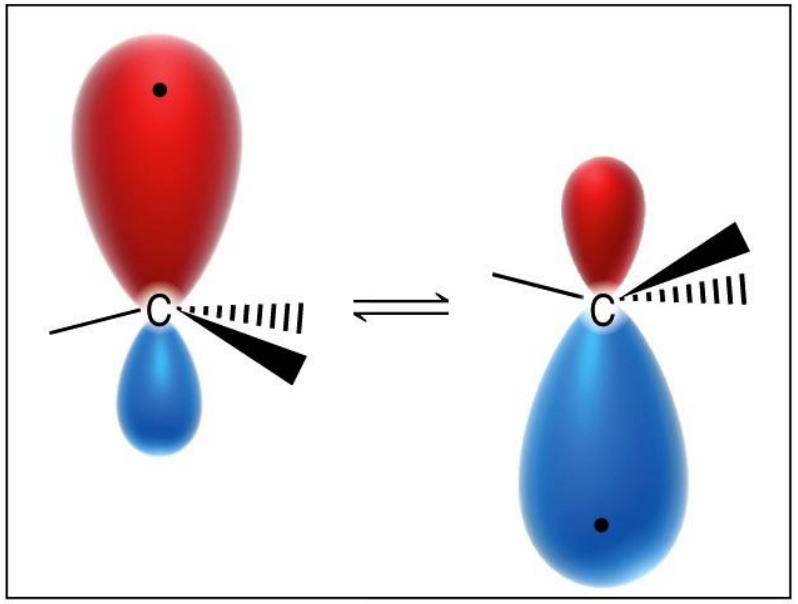
Halogenation Stereochemistry

- 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

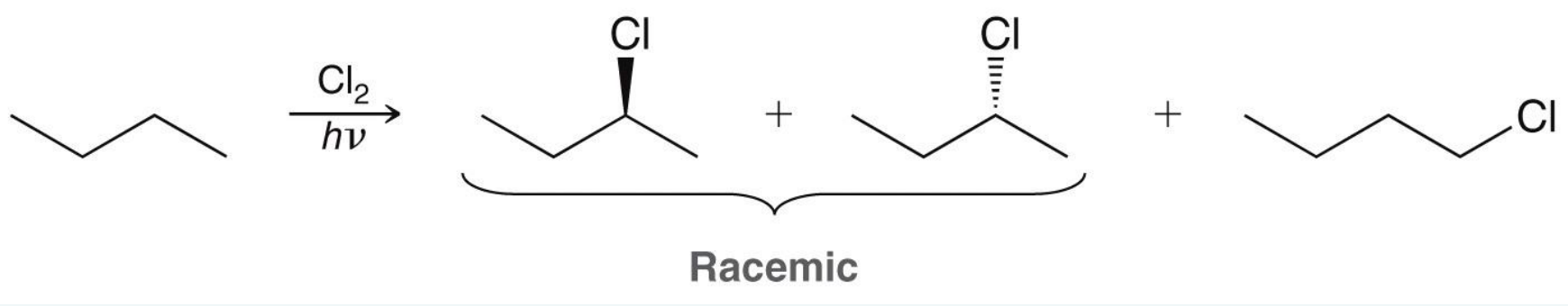
or



Shallow pyramid
(rapidly inverting)

Halogenation Stereochemistry

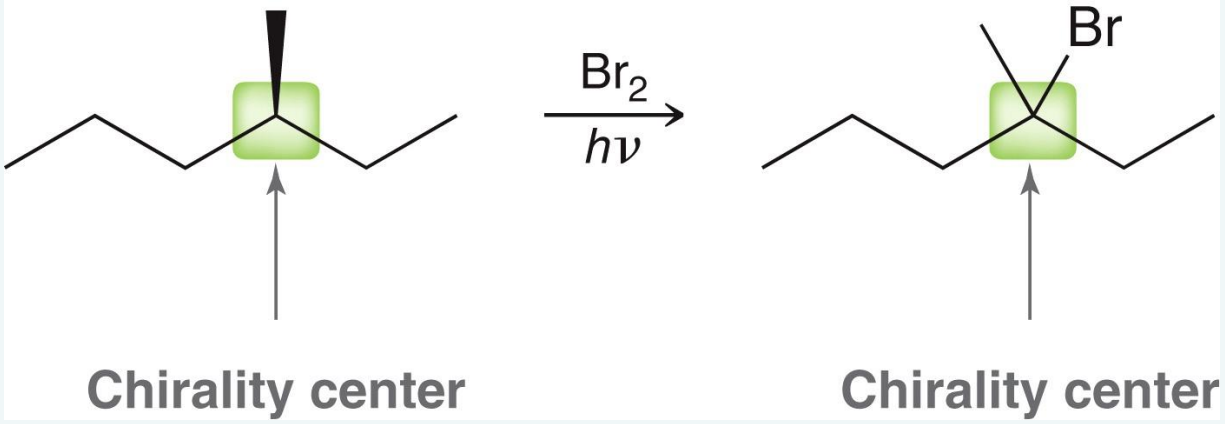
- Three monosubstituted products form in the halogenation of butane



- Draw all of the monosubstituted products that would form in the halogenation of 2-methylbutane including all stereoisomers

Halogenation Stereochemistry

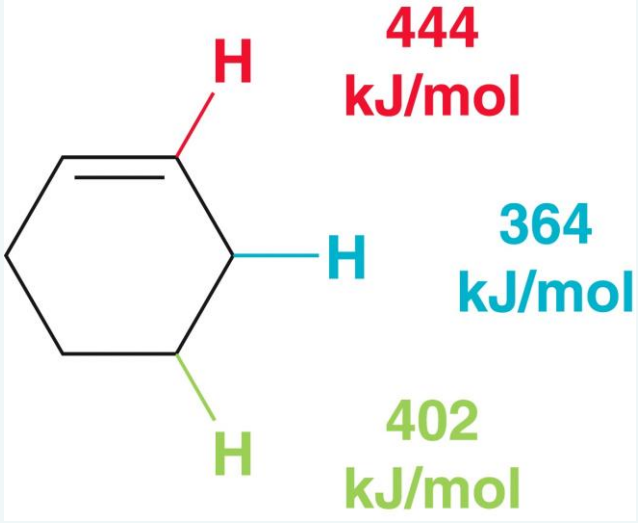
- In the halogenation of (*S*)-3-methylhexane, the chirality center is the most reactive carbon in the molecule. WHY?



- Name the product and predict the stereochemical outcome

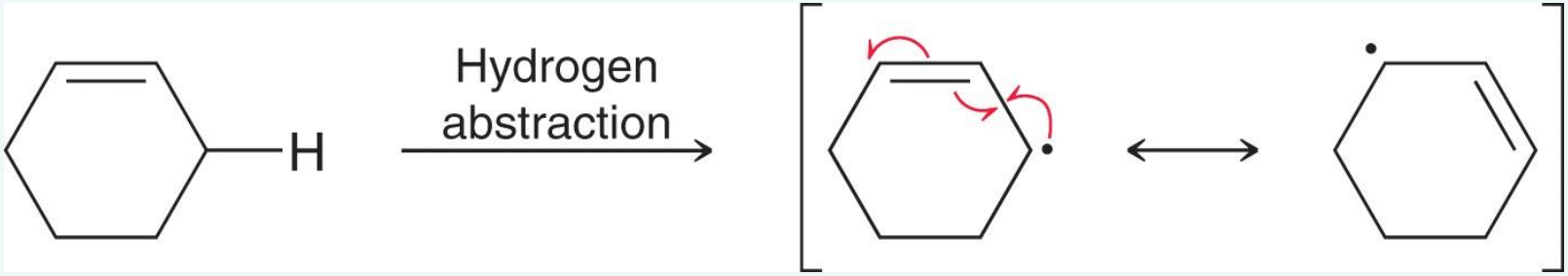
Allylic Halogenation

- When an C=C double bond is present it affects the regioselectivity of the halogenation reaction
- Given the bond dissociation energies below, which position of cyclohexene will be most reactive toward halogenation?

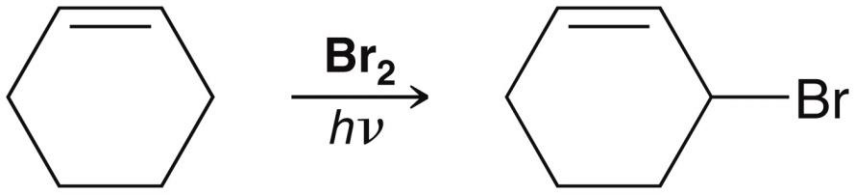


Allylic Halogenation

- When an allylic hydrogen is abstracted, it leaves behind an allylic free radical that is stabilized by resonance



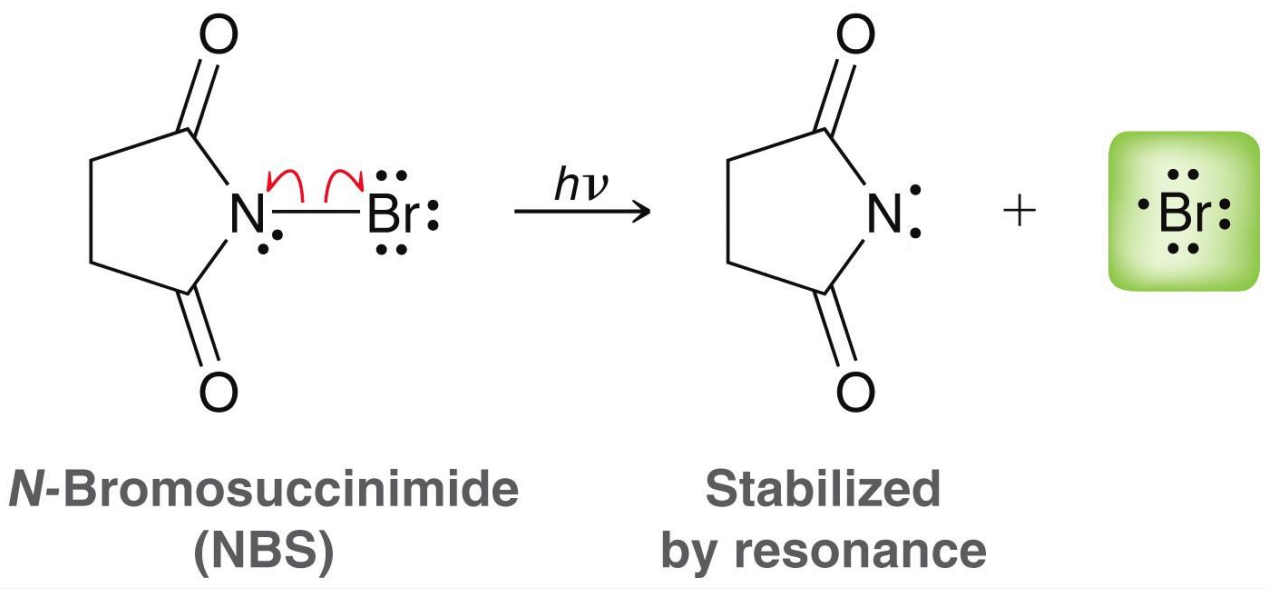
- Based on the high selectivity of bromination that we discussed, you might expect bromination to occur as shown below



- What other set of side-products is likely to form in this reaction? Hint: addition reaction

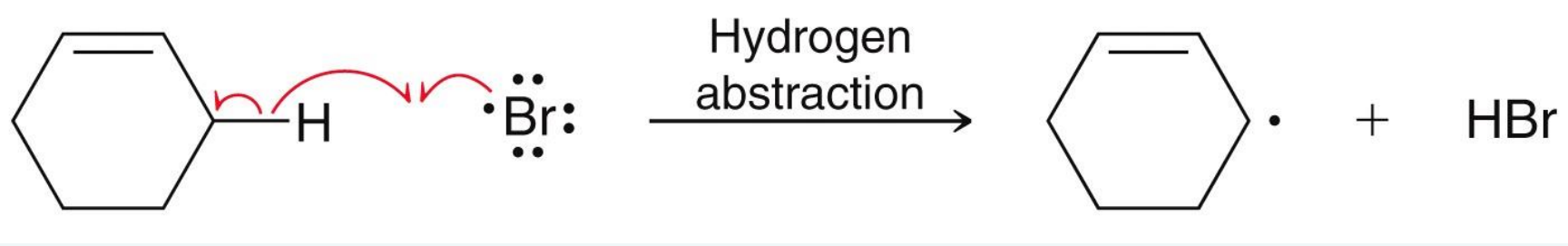
Allylic Halogenation with NBS

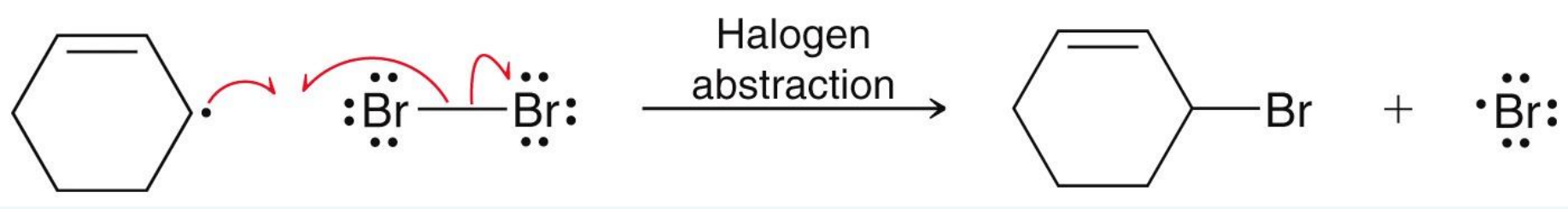
- To avoid the competing halogenation **addition** reaction, NBS can be used to supply Br• radicals



- Show how resonance stabilizes the succinimide radical
- Heat or light **initiates** the process

Allylic Halogenation with NBS

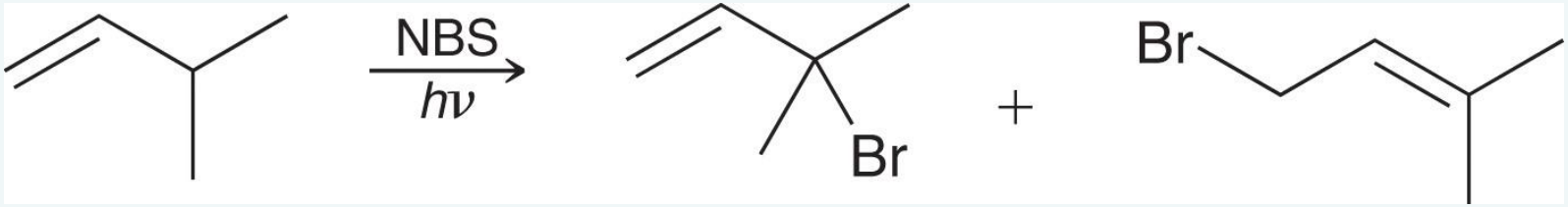




- Propagation produces new Br• radicals to continue the chain reaction
- Where does the Br-Br above come from? The amount of Br-Br in solution is minimal, so the competing addition reaction is minimized

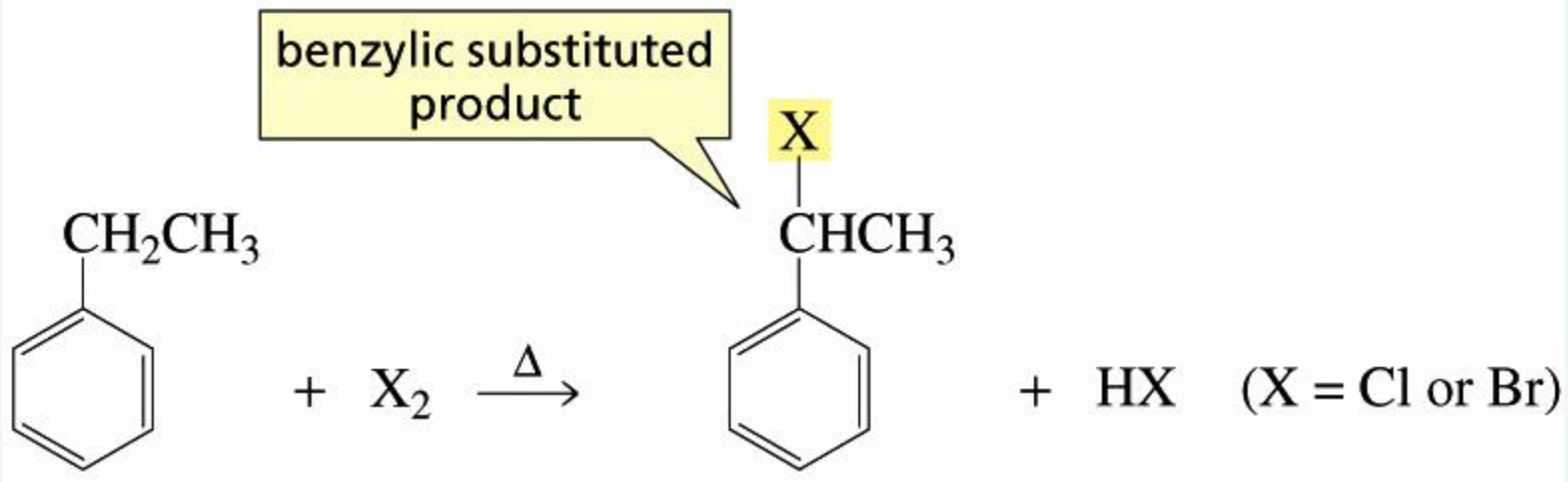
Allylic Halogenation with NBS

- Give a mechanism that explains the following product distribution. Hint: resonance



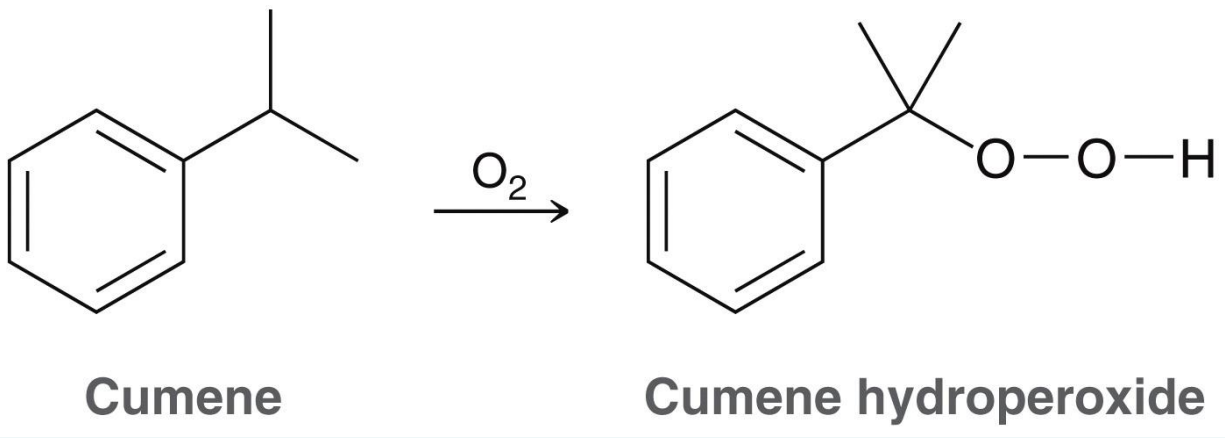
Radical Substitution of Benzylic and Allylic Hydrogens

- Benzylic and allylic radicals are even more stable than tertiary alkyl radicals
- It should be easy for a halogen radical to abstract a benzylic or allylic hydrogen



Autooxidation

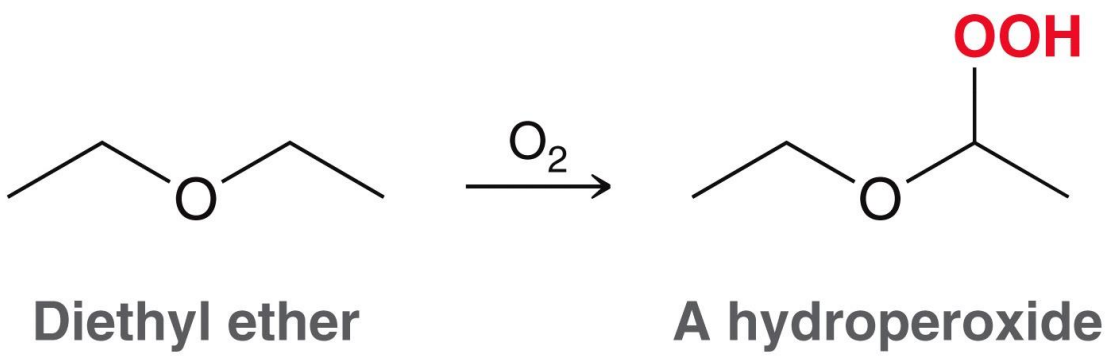
- Autooxidation is the process by which compounds react with molecular oxygen



- The process is generally very slow

Autooxidation

- Some compounds such as ethers are particularly susceptible to autooxidation



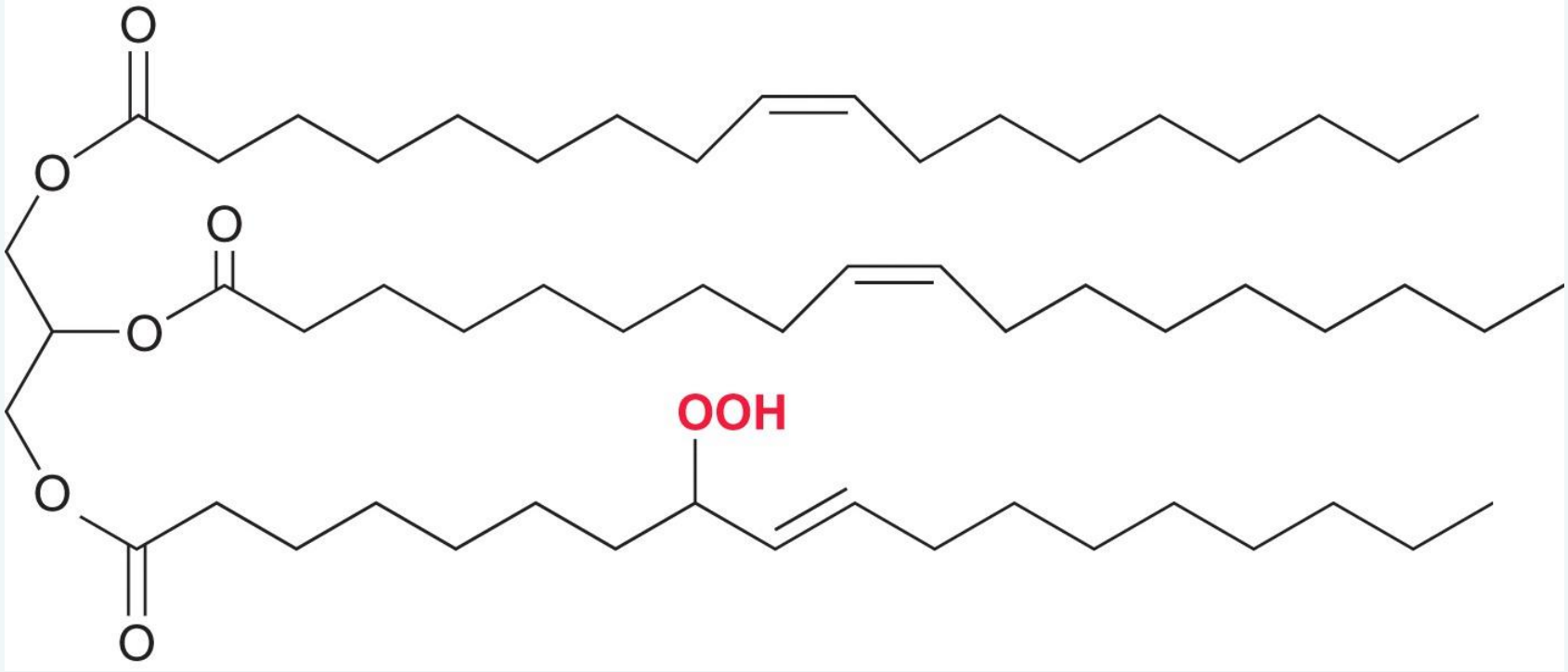
- Because hydroperoxides can be explosive, ethers like diethyl ether must not be stored for long periods of time
- They should be dated and used in a timely fashion

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

Antioxidants

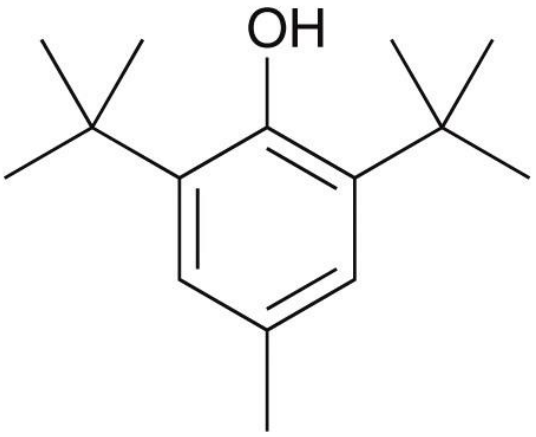
- Triglycerides are important to a healthy diet



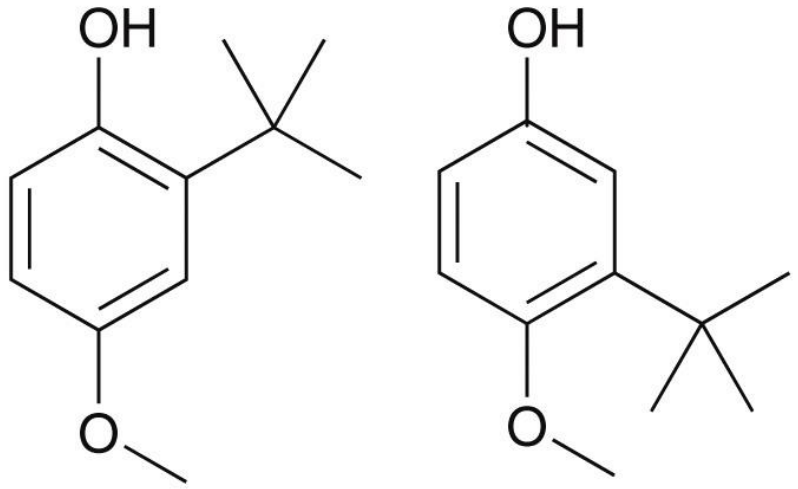
- Autooxidation can occur at the allylic positions causing the food to become rancid and toxic

11.9 Antioxidants

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



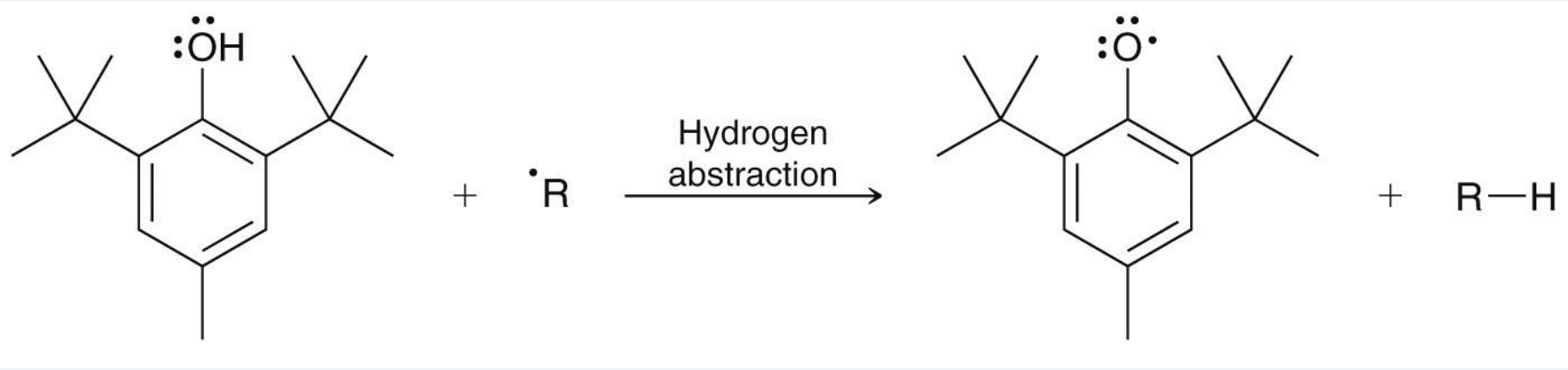
Butylated hydroxytoluene (BHT)



Butylated hydroxyanisole (BHA)

Antioxidants

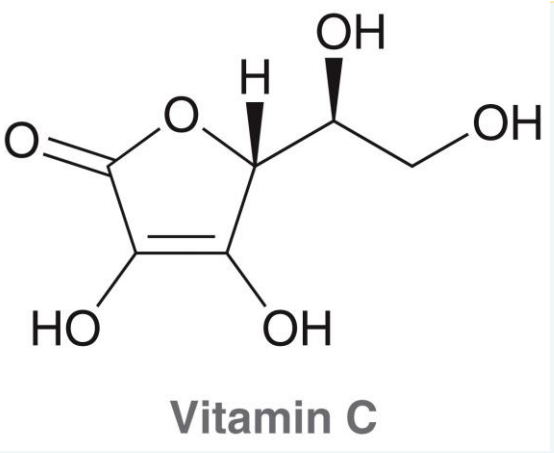
- Preservatives can undergo H abstraction to quench the C• radicals that form in the first step of autooxidation



- 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

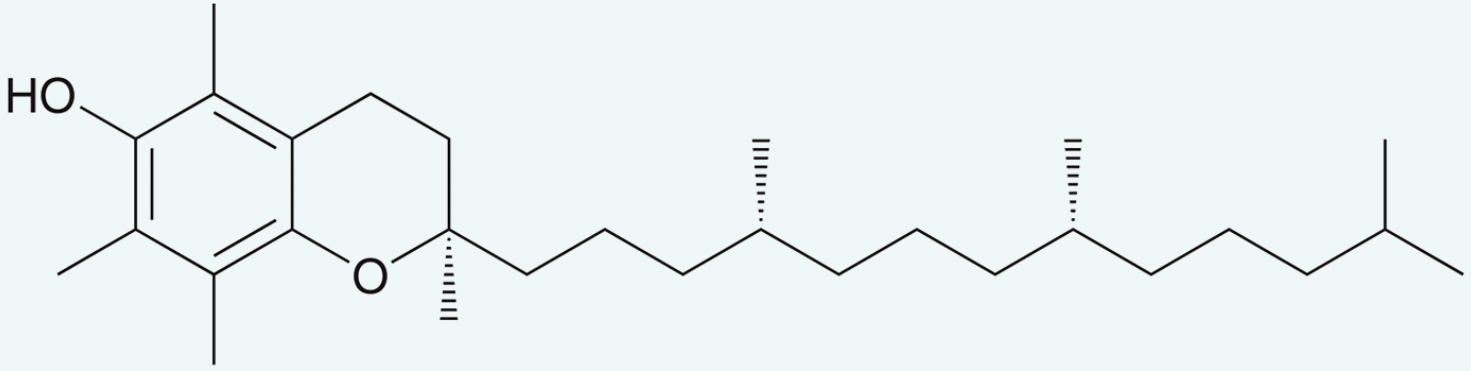
Natural Antioxidants

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



Vitamin C

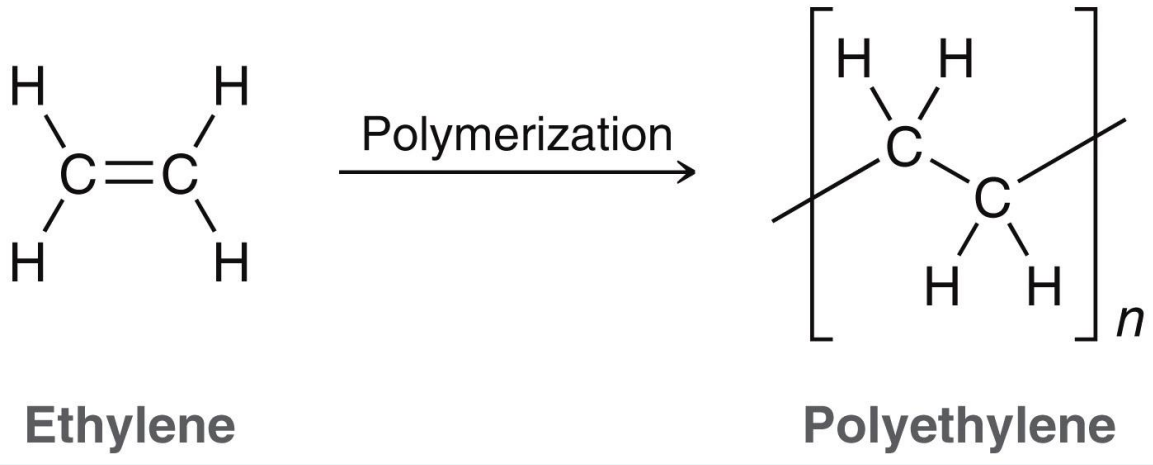
- For each vitamin, show its oxidation mechanism, and explain how that protects the body from autooxidation



Vitamin E

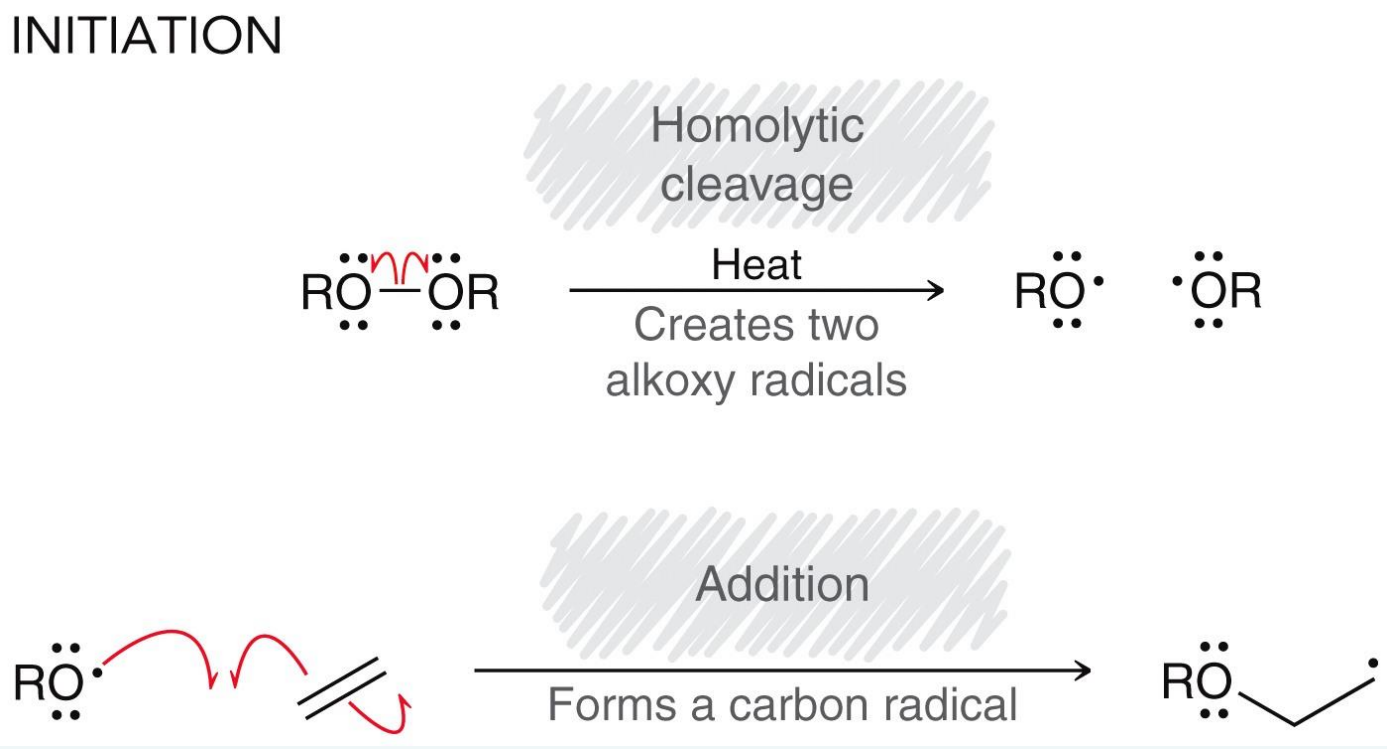
Radical Polymerization

- In chapter 9, we learned how some ionic polymerizations occur
- 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



Radical Polymerization

- Radical polymerizations generally proceed through a chain reaction mechanism



Radical Polymerization

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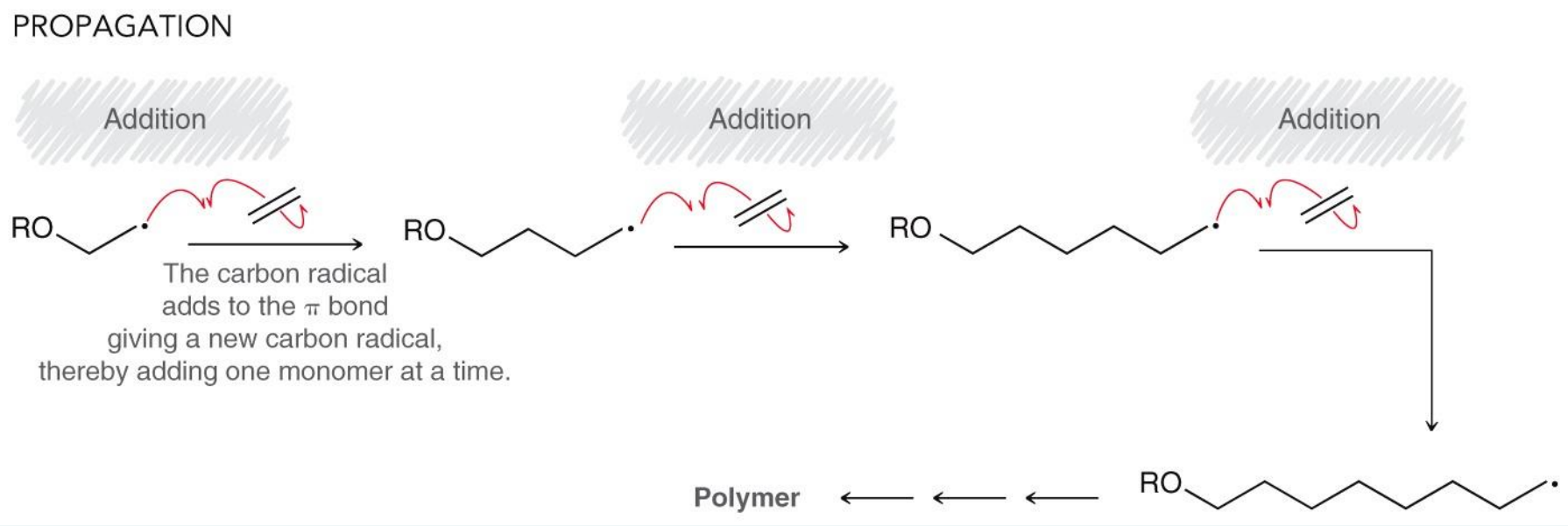
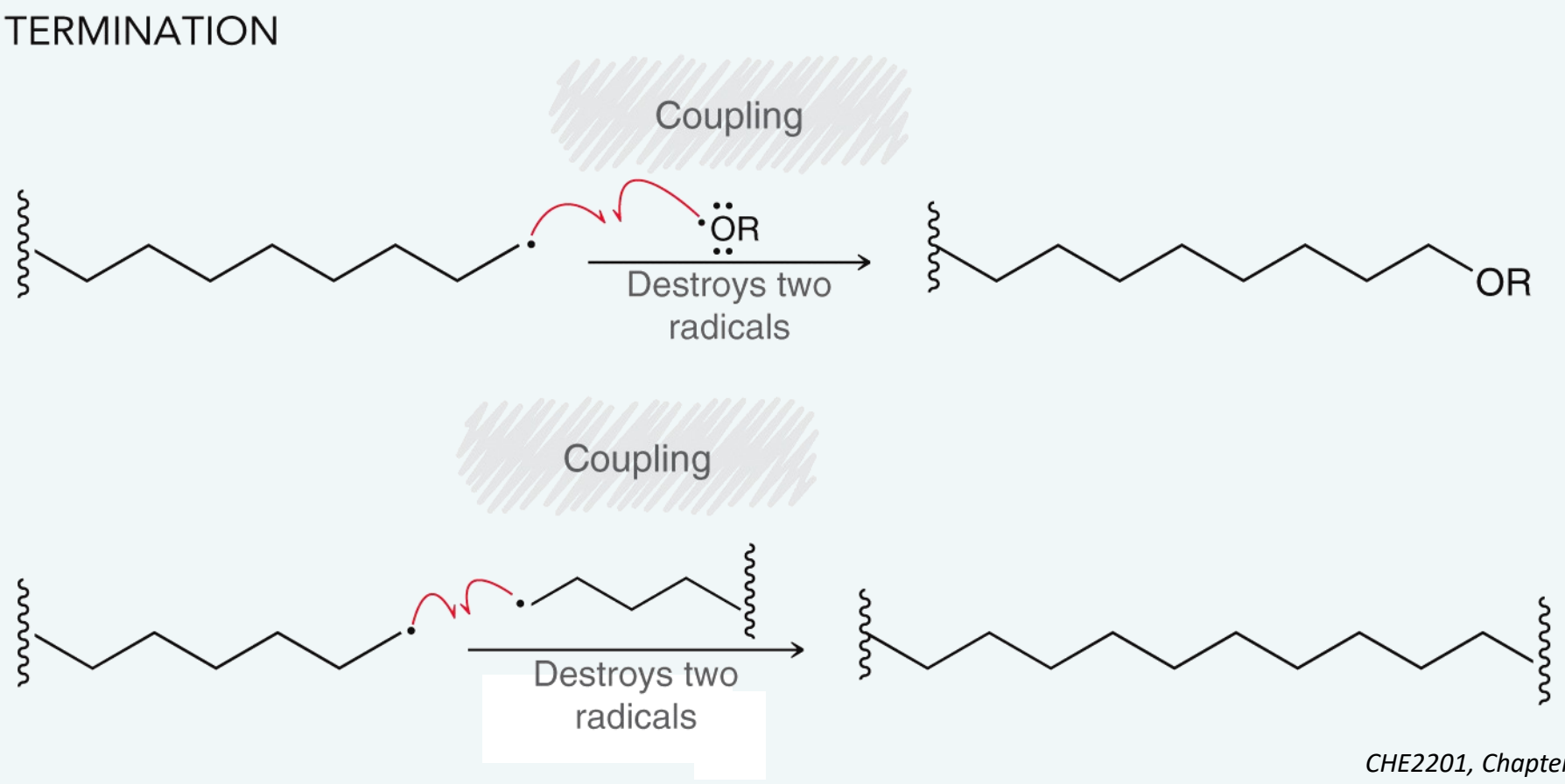


- Note how the sum of the propagation steps yields the overall reaction

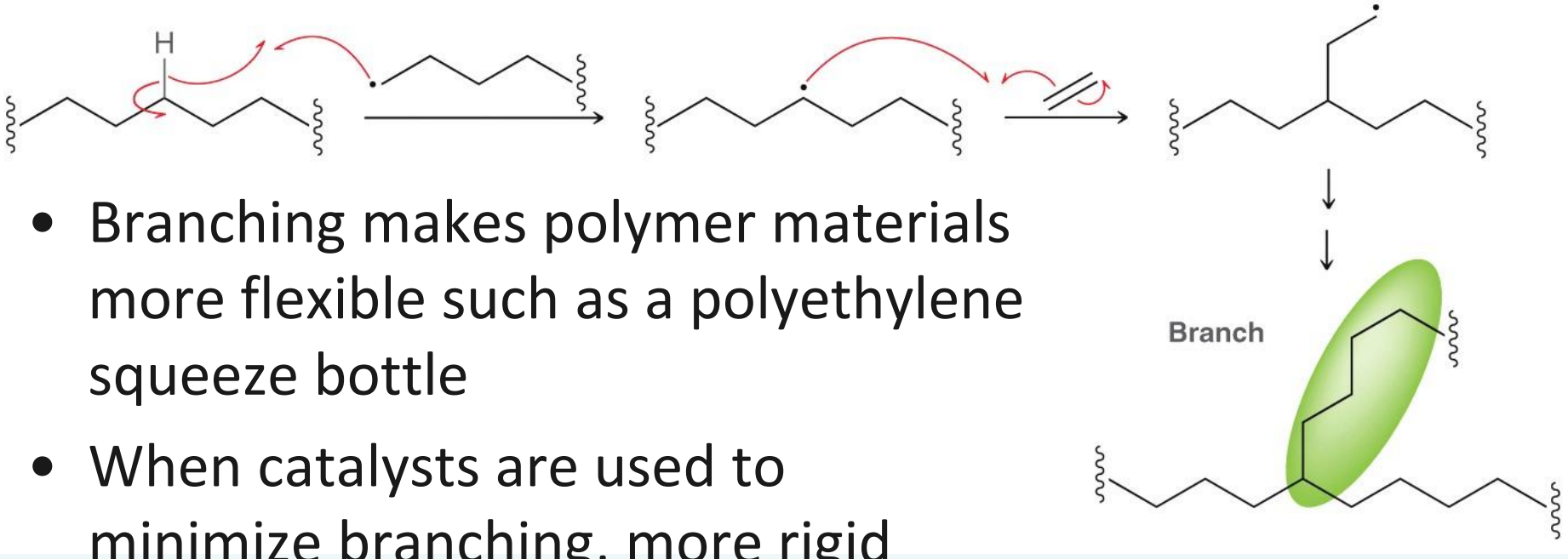
Radical Polymerization

- Radical polymerizations generally proceed through a chain reaction mechanism



Radical Polymerization

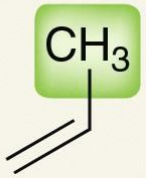
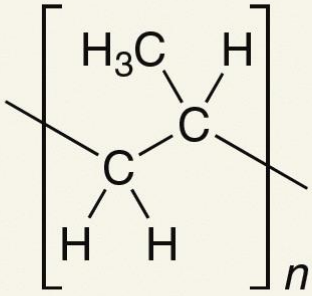
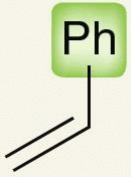
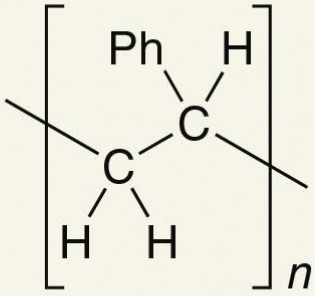
- Branching is common in some radical polymerizations



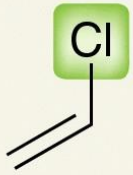
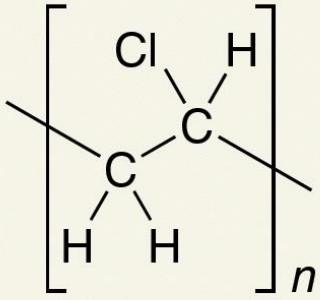
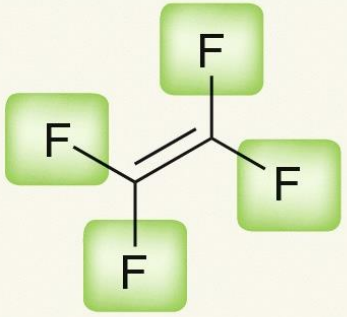
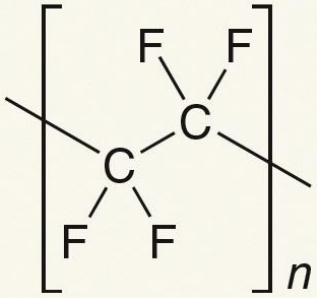
- Branching makes polymer materials more flexible such as a polyethylene squeeze bottle
- When catalysts are used to minimize branching, more rigid materials are produced such as the squeeze bottle cap
- Why does branching affect rigidity?

Radical Polymerization

- Many derivatives of ethylene are also polymerized

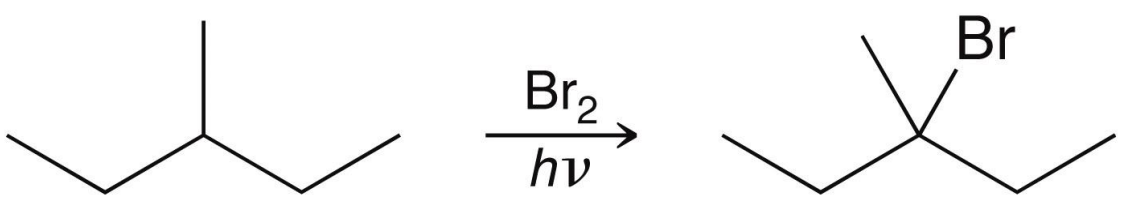
MONOMER	POLYMER	APPLICATION
 Propylene	 Polypropylene	Carpet fibers, appliances, car tires
 Styrene	 Polystyrene	Televisions, radios, Styrofoam

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

Synthetic Utility of Halogenation

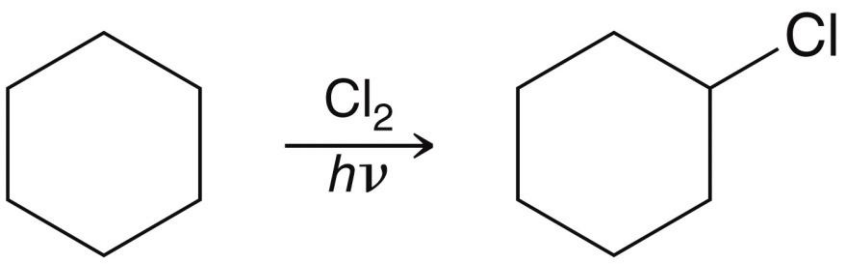
- Radical chlorination and bromination are both useful processes
- Recall that bromination is more selective.



- Temperature can be used to help avoid polysubstitution. HOW?

Synthetic Utility of Halogenation

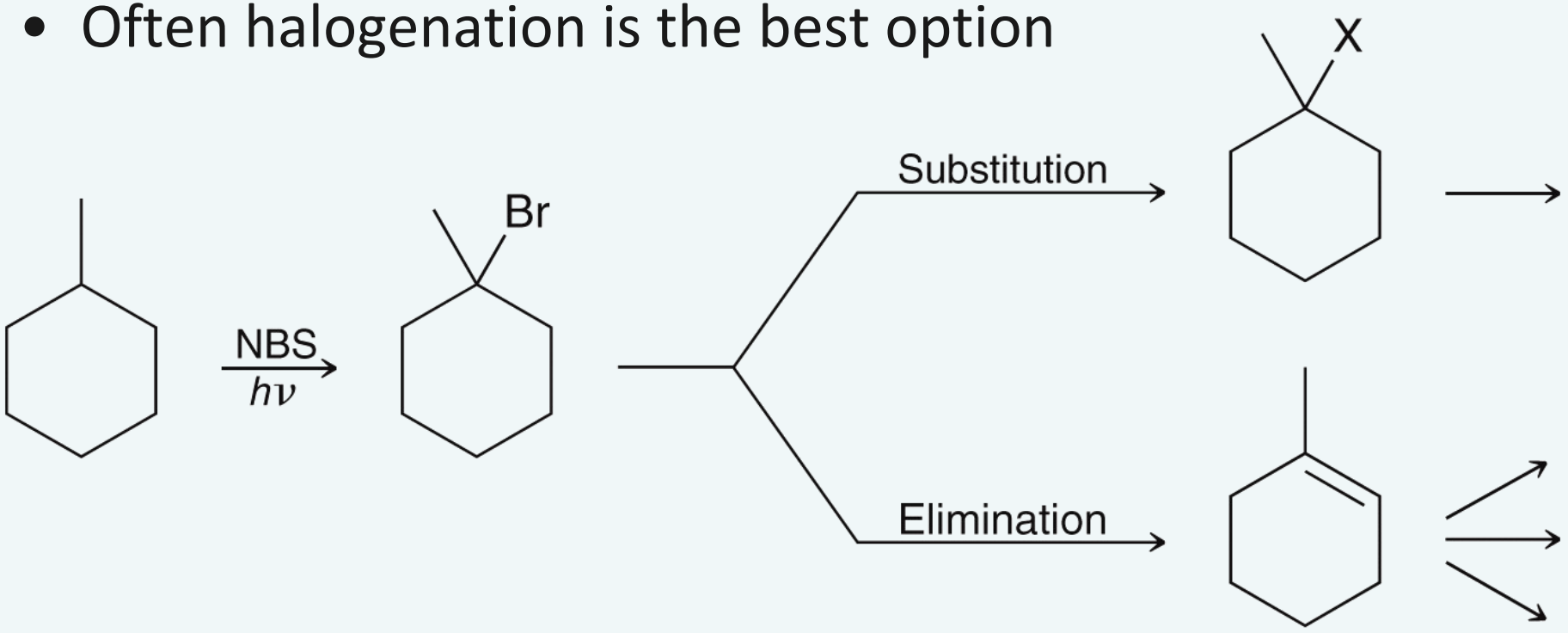
- Chlorination can be useful with highly symmetrical substrates



- It is difficult to avoid polysubstitution. WHY?
- The synthetic utility of halogenation is limited
  - Chlorination is difficult to control
  - Bromination requires a substrate with 1 site that is significantly more reactive than all others

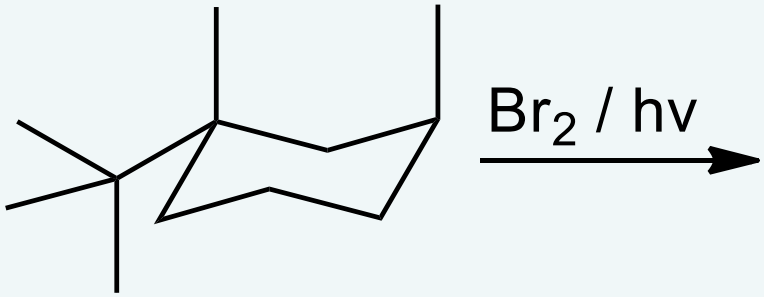
Synthetic Utility of Halogenation

- Synthesizing a target molecule from an alkane is challenging because of its limited reactivity
- Often halogenation is the best option



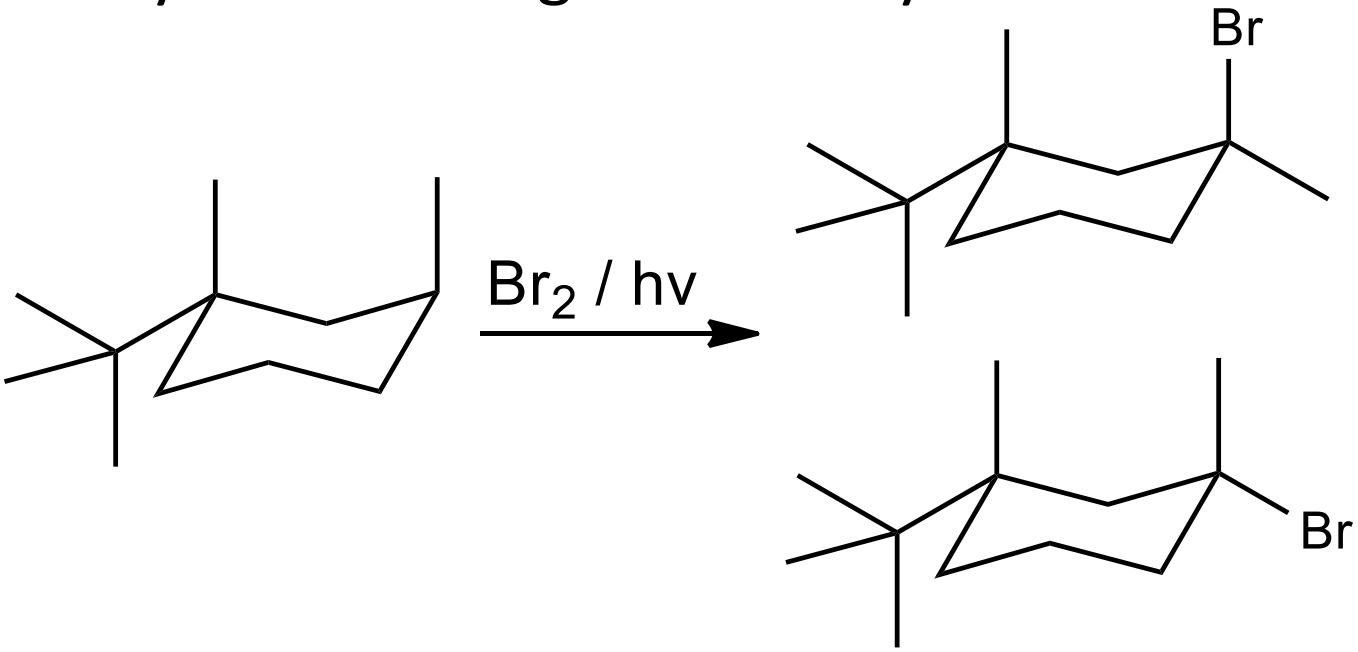
Additional Practice Problems

- Give the major product(s) for the reaction below. Carefully consider regiochemistry and stereochemistry.



Additional Practice Problems

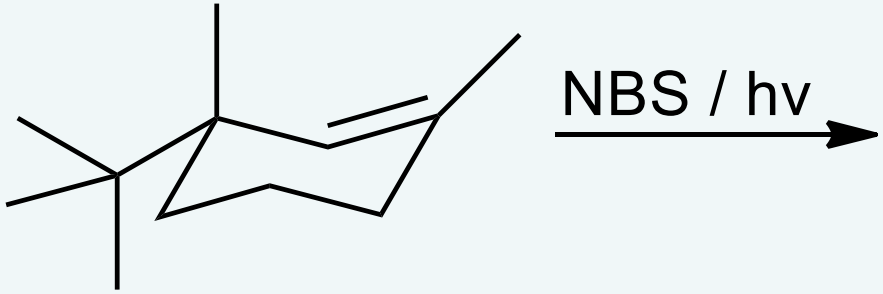
- Give the major product(s) for the reaction below. Carefully consider regiochemistry and stereochemistry.



There is only 1 tertiary center, so it should be where the majority of the reaction occurs, and although the text doesn't discuss, Br is less sterically hindering than CH_3, so it should occupy the axial position. If students place the Br in the equatorial position, that may also be an acceptable answer given the scope of the text content.

Additional Practice Problems

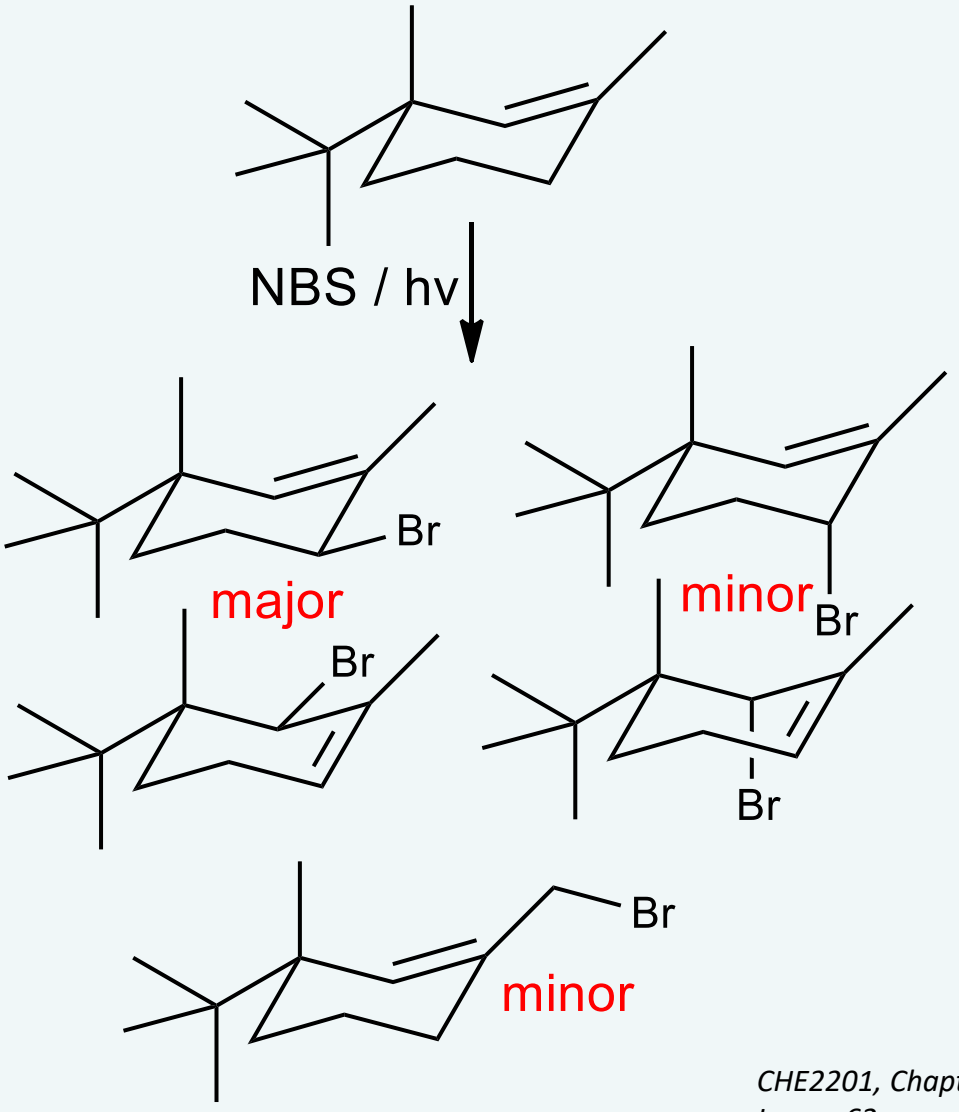
- Predict the major product for the reaction below and explain why NBS is preferred over Br_2.



Additional Practice Problems

- Predict the major product for the reaction below and explain why NBS is preferred over Br_2.

  Products form from both radical contributors once the free radical resonance hybrid forms. Equatorial substitution should be favored over axial. The primary free radical can also form because it is stabilized by resonance. NBS is preferred, because it will give much less addition side products.



Additional Practice Problems

- Draw the monomer necessary to synthesize the given polymer using a free radical mechanism.