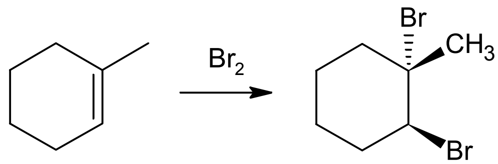
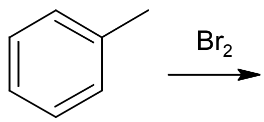
RADICALS

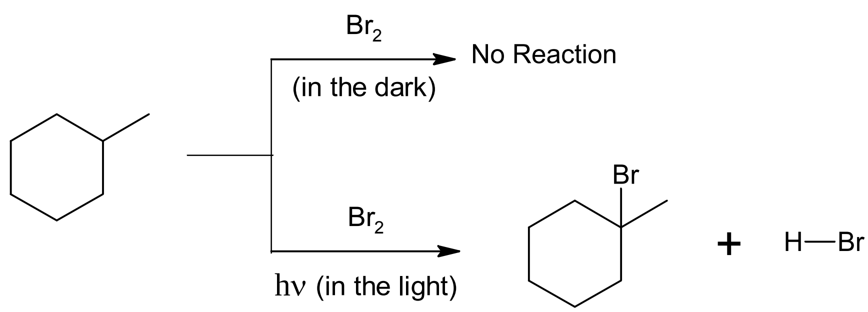
❖ Reactions with Br_2:



Addition to an alkene with Br_2

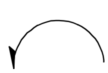


No reaction when an aromatic molecule is mixed with Br_2

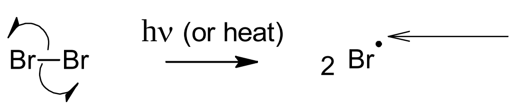


- During a demonstration by Dr. H, the reactants changed colors when held against light.
- This is a substitution reaction, but what kind?
  - S_N2 – No! There's no leaving group.
  - S_N1 – No! No leaving group.
  - EAS – No. The reactant is not aromatic.

❖ Mechanism:



This symbol is a *fishhook*, which has half of an arrow head. This means that only one electron is moving (instead of a pair of electrons)

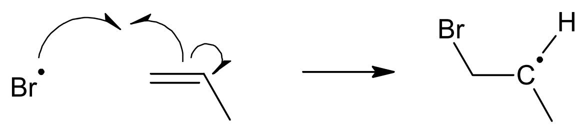


Unpaired electron, **free radical**, and open octet

- The Br—Br bond weakens with heat or light (it takes 46 kcal/mol to break it).
- Each electron in the bond goes to a different Br

❖ Three Fates of Radicals:

a) **Addition to pi bond**



The bromine radical and one electron from a pi bond form a new bond on the least substituted end of the alkene. The other electron in the pi bond is transferred to the more stable carbon atom (making a 2˚ radical).

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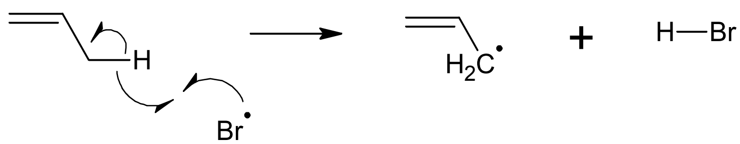
b) **Atom or group transfer**



The bromine radical and an electron from the C—H bond form a new bond, forming a new molecule, H—Br. The remaining electron in the C—H bond transfers onto to the attached carbon, making a carbon radical.

Hydrogen transfer is often preferred to transfer of a methyl group (even if the product is less stable). The removal of hydrogen from the molecule of CH_2CHCH_3 is called "***hydrogen abstraction.***"

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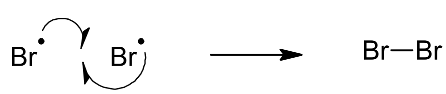
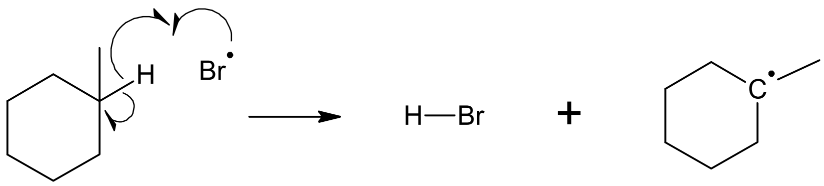
c) **Radical combination**



This step is rare because it is a *termination step* (see notes below—radicals are eliminated). Radicals are found in low concentrations and many times react with other molecules before radical combination can occur.

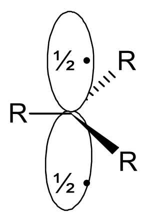
❖ Radical Structure and Stability



- Process of removing hydrogen from a molecule and forming a new radical is called **"hydrogen abstraction"**
- Is the given product (3˚ carbon radical) the best position for the radical?

- **Structure**

$R_3C\bullet$



sp^2 geometry

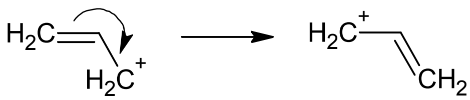
The electron density from the radical is distributed throughout the empty orbital.

- **Substituents**

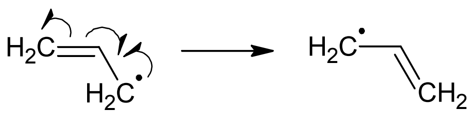
Carbocation stability:							**<u>Radical stability:</u>**						
$^+CH_3$ Methyl	<	$^+CH_2R$ 1˚	<	HC^+R_2 2˚	<	$^+CR_3$ 3˚	$\bullet CH_3$ Methyl	<	$\bullet CH_2R$ 1˚	<	$\bullet CHR_2$ 2˚	<	$\bullet CR_3$ 3˚

- Same trend for radical stability as for carbocation stability (more substituted carbon makes the more stable radical), but <u>making a medical radical isn't as impossible as making a methyl carbocation</u>. Methyl and 1˚ radicals exist!
    - o Carbon radicals aren't as electron-deficient as carbocations, so it is possible to form a methyl radical.

- **Resonance**

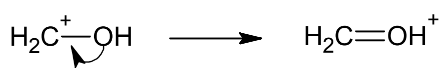


<u>Carbocation resonance with pi bonds</u>
The positive charge is delocalized by resonance and the pair of electrons forming the pi bond shift to the adjacent bond.

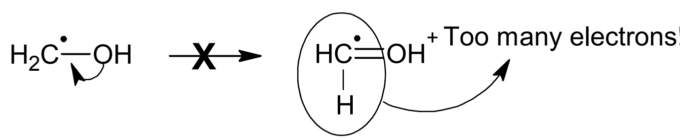


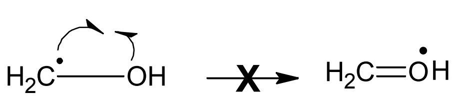
<u>Radical resonance with pi bonds</u>
An electron from the alkene forms a new bond with the carbon radical, leaving an electron to the carbon at the other end of the alkene.

<u>Carbocation resonance with lone pairs</u>
Transfer of cation from carbon to oxygen. Very good resonance contributor because the structure has full octets!



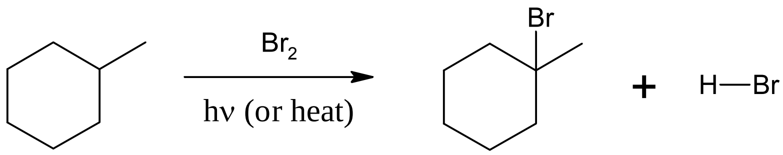
<u>Radical resonance with lone pairs</u>
NOT POSSIBLE! This mechanism would Give a carbon attached to <u>nine</u> electrons, which violates the octet rule.



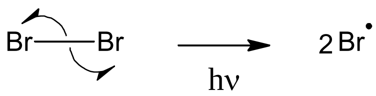


<u>Radical resonance → radical on oxygen</u>
BAD!! Will not happen this way.

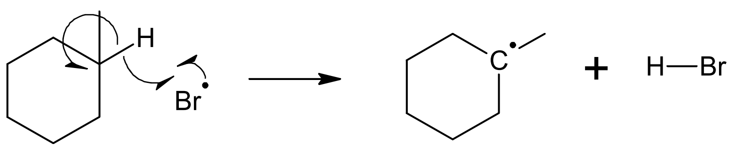
❖ Br_2 Radical Reaction Mechanism



Mechanism:

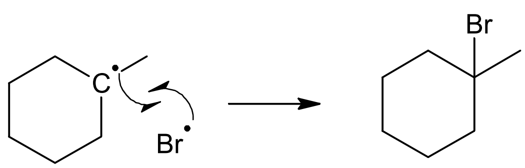


Initiation
Starts without radicals and produces radicals.



Radical intermediate is formed, now what? Three ways to get to the desired product:

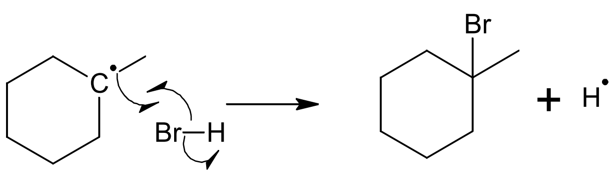
1.



Looks good, but there's a kinetics problem (the reaction would be too slow). As soon as the radicals are produced (Br•), they're consumed. So the probability of one radical finding another is very slim. **Not the best choice.**

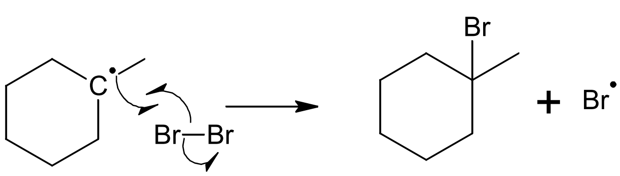
Termination
Radicals are consumed but not produced (going from radicals to no radicals)

2.



Unlikely. Br—H bond is strong and harder to break.

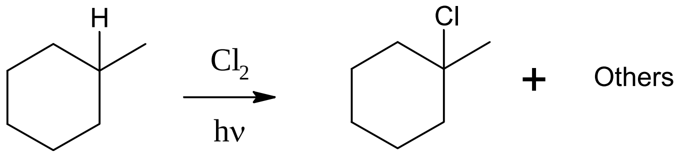
3.



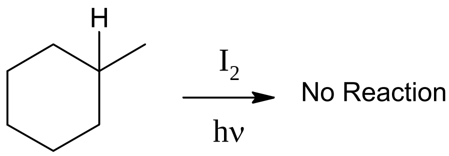
Br—Br is a weaker bond, so this is **more probable**. New radical (Br•) is formed, which will react with hydrogen on cyclohexane again, creating a *new* 3˚ radical. This is called a **"chain reaction": one or more mechanism steps repeated in a cycle.**

Propagation
A radical produces a new radical.

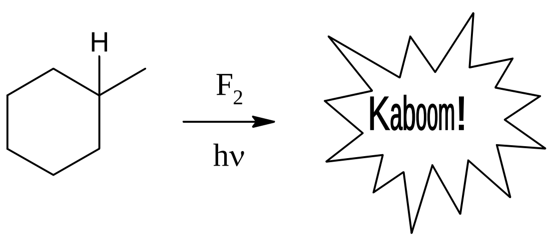
❖ Other Radical Halides



- Cl_2 is not selective at all



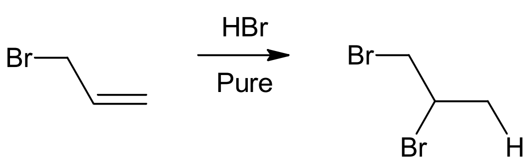
- I_2 bonds are weak, so atoms separate and form radicals easily
- I• is not reactive/is happy as a radical so it doesn't have energy to react



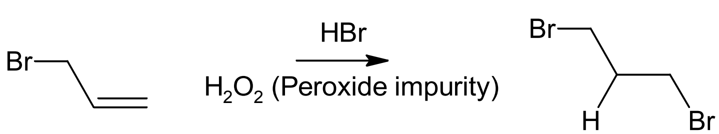
- F_2 is *extremely* reactive
- It will react with anything (hence the kaboom!)

- **The more reactive, the less selective** (F_2 is not selective at all, hence it is extremely reactive)

❖ H—Br and Alkenes



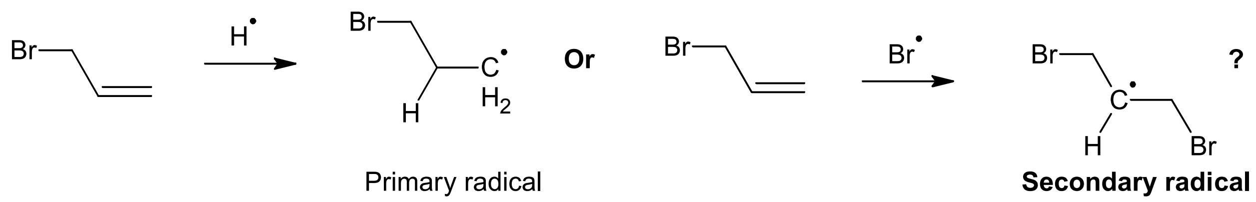
The product follows **Markovnikov's Rule** –
The hydrogen was added to the least substituted end of the alkene in pure HBr.



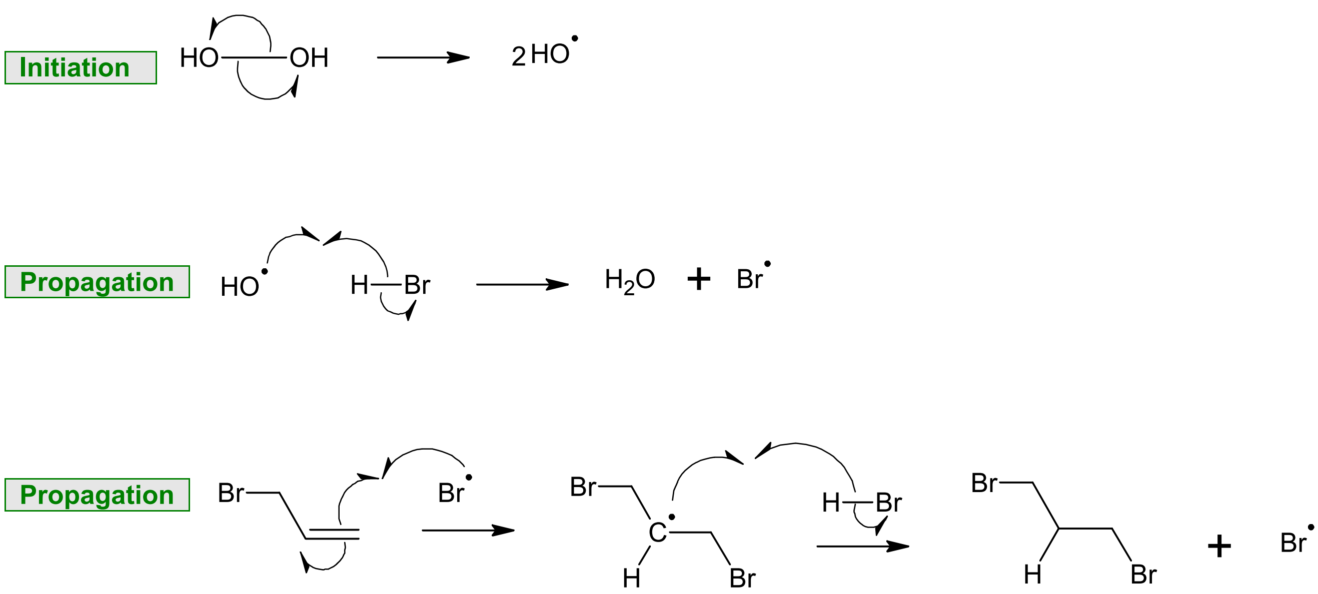
The product is **anti-Markovnikov –**
The hydrogen was added to the most substituted end of the alkene when the HBr solution was impure.

❖ H—Br Addition Mechanism in the Presence of Impurities

Which radical mechanism leads to the anti-Markovnikov product?



Mechanism:



- Therefore the **secondary radical intermediate** forms the *anti-Markovnikov* product in the presence of peroxide.
- This effect (peroxide impurities leading to anti-Markovnikov addition of a bromine) <u>only applies to **bromine**</u>!!
- HCl or HF add to an alkene according to Markovnikov's rule
- See *Practice Problems: Radicals* in the *Thinkbook,* problems 17-20 (pg.186) for more on this topic.

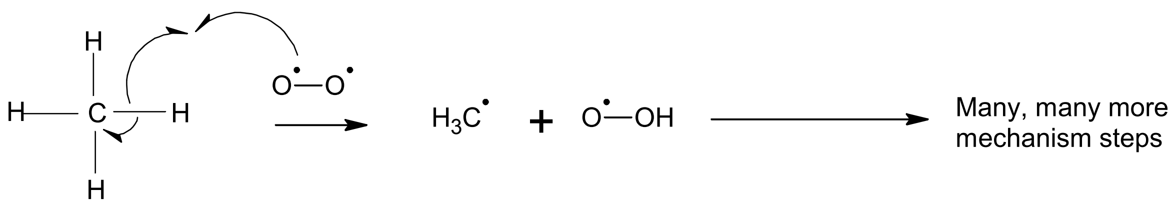
❖ Combustion

$$CH_4 + O_2 \longrightarrow CO_2 + H_2O + \text{energy}$$

Structure of O_2:

$O^{\bullet}\!-\!O^{\bullet}$ **A diradical,** **<u>NOT</u>** $\cancel{O=O}$ **double-bonded oxygen atoms.**

Mechanism:



❖ Biological Oxidation

$$O^{\bullet}\!-\!O^{\bullet} \xrightarrow{e^-} O^{\bullet}\!-\!O^-$$

- Product when an electron is added to an oxygen diradical is $O_2{\bullet}^-$, **<u>superoxide</u>**. Humans make about 10kg per year of this potentially cancerous molecule.

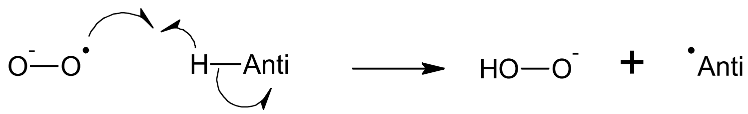
$$\text{DNA}-\text{H} \xrightarrow{O^{\bullet}-O^-} {}^{\bullet}\text{DNA} + \text{HO}-O^{\bullet}$$

$\Downarrow$

Fragment of DNA where hydrogen was abstracted can lead to cancer

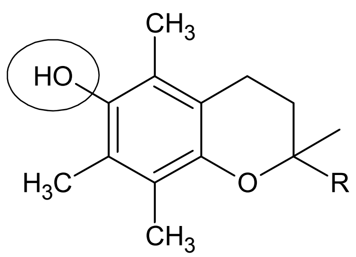
- When superoxide in the body reacts with DNA, it may pull of a hydrogen (abstract a hydrogen) from DNA, forming •OOH and a DNA radical.

❖ Antioxidants

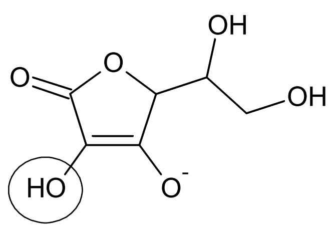


- Anti = antioxidant
- The antioxidant radical product is very favorable because of good resonance stabilization
- Antioxidants easily give up their hydrogen (through hydrogen abstraction) to superoxide because the product is stable (low energy). This prevents superoxide from affecting DNA and therefore prevents cancer.

2 important antioxidants:



Vitamin E (α – Tocopherol)
- Nonpolar
- Lipophilic
- Hydrogen that is circled is the one that is abstracted. Resulting radical is has very good benzene ring resonance.



Vitamin C
- Polar
- Hydrophilic
- Circled hydrogen gets removed to form a radical stabilized by resonance with pi bonds and lone pairs.

Fun facts – According to the USDA, the foods highest in antioxidant concentration are:

1. Small red beans
2. Wild blueberries
3. Red Kidney beans
4. Pinto beans
5. Cultivated Blueberries
6. Cranberries
7. Artichokes
8. Blackberries
9. Prunes
10. Raspberries
11. Strawberries
12. Red Delicious & Granny Smith apples
13. Pecans
14. Sweet cherries
15. Black plums
16. Russet potatoes
17. Black beans
18. Plums
19. Gala apples
20. Walnuts