



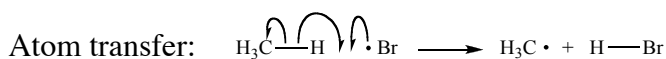
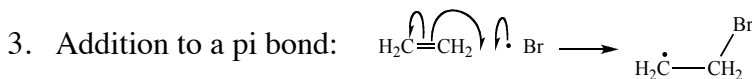
8. Briefly discuss the role of Freon, photolysis, and chain reactions in the depletion of atmospheric ozone.
9. (a) Draw the Lewis dot structure of nitric oxide (NO).  
(b) That nitric oxide is a biological signal molecule is surprising because of its reactivity. Briefly but clearly explain why nitric oxide is a reactive molecule.

### Concept Focus Questions Solutions

1. Illustrated definitions can be found at the Illustrated Glossary of Organic Chemistry available at the course web site.
- (a) Antioxidant: A molecule that prevents propagation of radical chain reactions initiated by oxygen-based free radicals such as molecular oxygen (O<sub>2</sub>) or hydroxyl radical (HO).
- (b) Bond dissociation enthalpy: The enthalpy required to cause homolytic bond cleavage. Commonly abbreviated as BDE. Also called by the less precise name bond dissociation energy.
- (c) Chain initiation: A step in a chain reaction characterized by the formation of reactive intermediates from non-radical or neutral molecules.
- (d) Chain propagation: A step in a chain reaction characterized by the reaction of a reactive intermediate and another molecule to give a new reactive intermediate and a new molecule.
- (e) Chain reaction: A reaction in which one or more mechanism steps are repeated indefinitely. *This term is usually reserved for radical reactions.*
- (f) Chain termination: A step in a chain reaction characterized by the consumption of reactive intermediates without the formation of new reactive intermediates.
- (g) Chlorofluorocarbon: A molecule composed only of chlorine, fluorine, and carbon. Commonly abbreviated as CFC.
- (h) Free radical: A species with one or more unpaired electrons.
- (i) Freon: The trade name for chlorofluorocarbons.
- (j) Heterolytic bond cleavage: Bond cleavage in such a way that the bonding electron pair is split unevenly between the bonded atoms and ions usually result.
- (k) Homolytic bond cleavage: Bond cleavage in such a way that the bonding electron pair is split evenly between the bonded atoms, and free radicals result.
- (l) Photochemistry: The study of chemical processes induced by absorption of light.

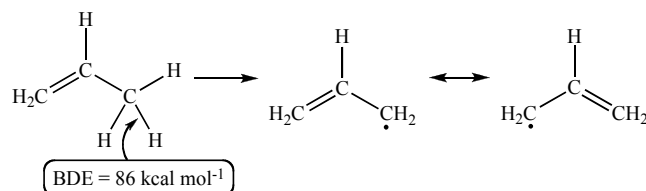
(m) Photolysis: A process in which a chemical reaction is brought about through interaction with light.

2. Free radicals are electrophilic because they have open octets.

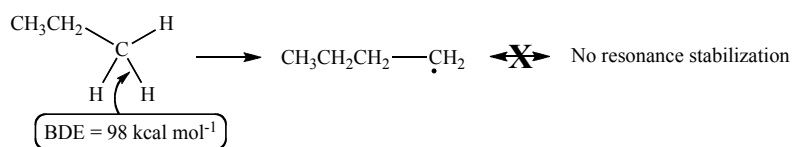


4. Radicals are electron deficient, much like carbocations. Therefore the same structural features that influence carbocation stability are expected to influence radical stability as well.

Resonance: A radical with resonance that can delocalize the electron deficiency is more stable (more easily formed; lower bond dissociation enthalpy) than a radical without resonance. Example: The allyl radical is easier to form than the propyl radical. (Compare the bond dissociation enthalpies.)

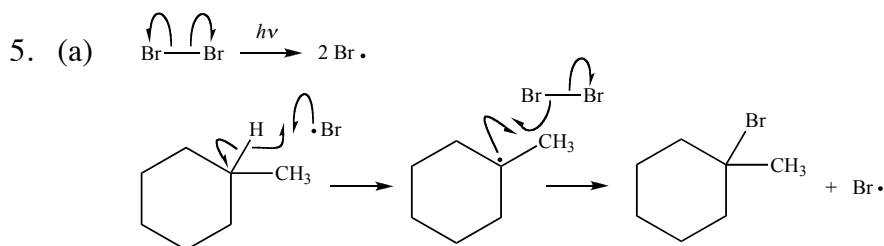


Allyl radical: resonance delocalization of the unpaired electron increases stability.



Propyl radical: no resonance delocalization of unpaired electron. Harder to form.

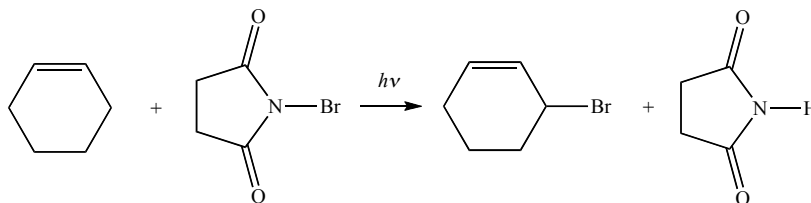
Number of substituents: Radicals are electron-deficient, and thus may be stabilized by electron donating groups such as alkyl groups. More highly substituted radicals are more stable, just like carbocations. Thus the order of radical stability is: methyl < primary < secondary < tertiary.



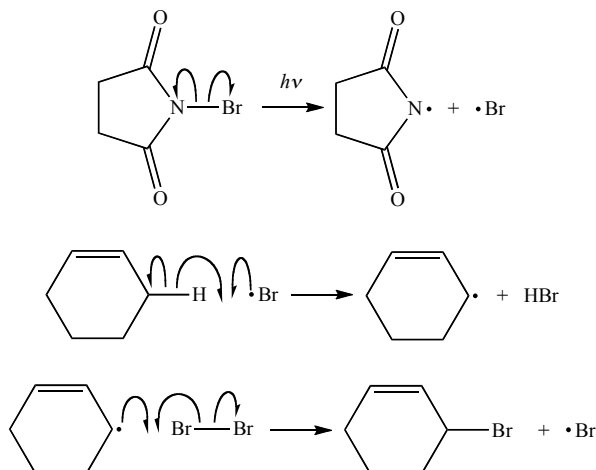
- (b) The mechanism step that determines which alkyl bromide is formed is the step in which the bromine radical abstracts a hydrogen atom from methylcyclohexane. Like other mechanism steps, this step proceeds to give the more stable reactive intermediate as the major product. A tertiary radical is the most stable radical that can result from hydrogen atom abstraction from methylcyclohexane. Reaction of this tertiary radical with molecular bromine in the next step leads to the formation of the observed tertiary bromide product.

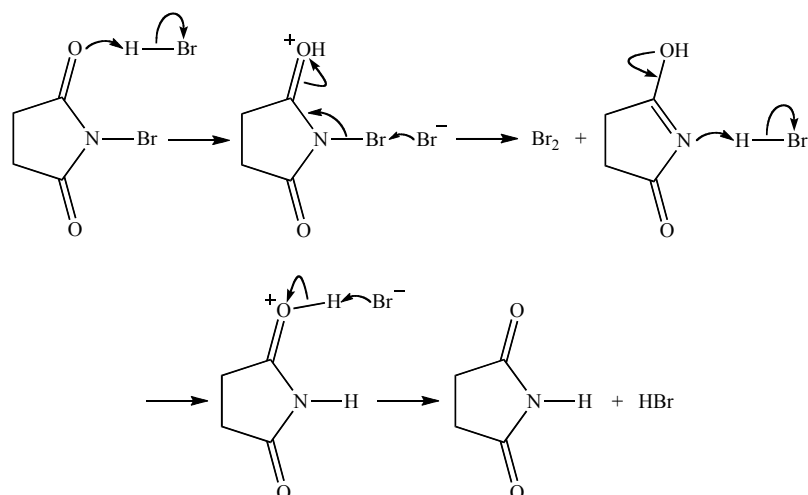
Any mechanism must be consistent with all the known facts of a reaction. It is known that most (but not all) radical reactions are chain processes. To account for this fact, the mechanism cannot end with the reaction of the tertiary radical with a bromine radical to form 1-bromomethylcyclohexane, as this is a termination step.

6. Reaction of cyclohexene with NBS (*N*-bromosuccinimide) in the presence of light results in allylic bromination:

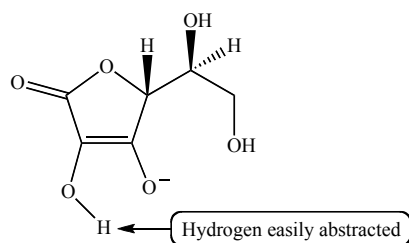


Mechanism:

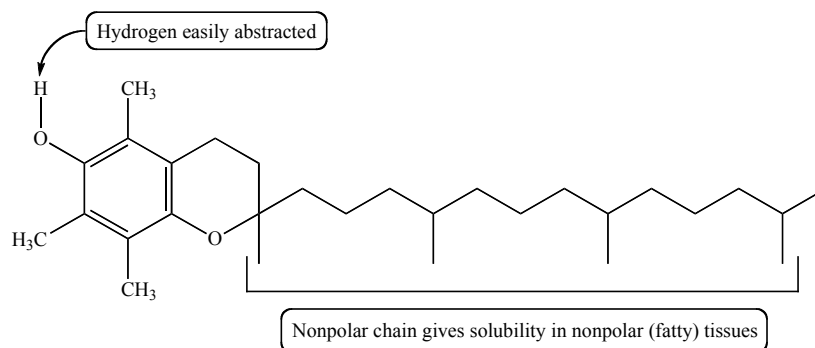




7. The most significant cellular free radicals are the hydroxyl radical ( $\text{HO}\cdot$ ) and superoxide ( $\text{O}_2^{\cdot-}$ ). Biological systems contain many molecules that are prone to damage by free radical chemistry. Free radical reactions may establish radical chains. One radical may thus result in damage to many biomolecules. Antioxidants intercept radical chains by providing hydrogen atoms that are easily transferred, leading to resonance-stabilized radical products. Because they react so readily with radicals, antioxidants consume radicals before these radicals can damage biomolecules. Abstraction of a hydrogen atom from an antioxidant forms a new radical, but because this new radical has significant resonance stability, it is unreactive, and the radical chain is interrupted (but not actually terminated). Two common biological antioxidants are vitamin C (ascorbic acid; water soluble due to a very polar structure with many sites for hydrogen bonding) and vitamin E ( $\alpha$ -tocopherol; fat soluble due to a long hydrocarbon chain).

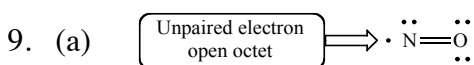


Vitamin C (ascorbate)



Vitamin E ( $\alpha$ -tocopherol)

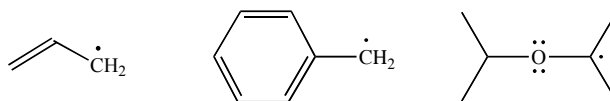
8. "Freon" is the trade name for a series of compounds containing only carbon, chlorine, and fluorine (chlorofluorocarbons, or CFCs) that were selected for use in a variety of applications such as refrigeration and as blowing agents due to their chemical inertness. When CFCs escape to the stratosphere, they can undergo photolysis (bond cleavage induced by light) from high-energy ultraviolet photons from the sun. These photons are normally absorbed by the ozone layer. CFC photolysis products convert ozone to oxygen, via a chlorine radical. The ozone destruction mechanism is a chain reaction, using chlorine radicals to convert ozone to oxygen, and generating new chlorine radical in the process. Because this is a chain reaction, photolysis of one CFC molecule can lead to the destruction of millions of molecules of ozone. A combination of a long atmospheric half-life (about 50 years for a typical CFC) and the small concentration of ozone in the stratosphere, CFCs represent a significant danger to the Earth's ozone layer.



- (b) Nitric oxide is reactive because the nitrogen atom has an unpaired electron and an open octet. It is a free radical. Free radicals are generally very reactive molecules with short lifetimes. This reactivity suggests that nitric oxide is not a very efficient messenger molecule (even though empirical evidence suggests otherwise).

### OWLS Problems

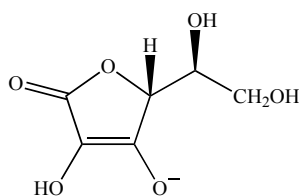
1. By this point in Chem 30A you probably have come to the conclusion that resonance influences many aspects of molecular structure and reactivity. This conclusion is also true for radicals, but radical resonance is a bit trickier than resonance involving shifts of electron pairs.
- (a) For each of the following radicals draw all of the significant resonance contributors (include curved arrows) plus the resonance hybrid.



- (b) Based on your resonance contributors, form a resonance contributor preference rule concerning the number of unpaired electrons. (Review resonance contributor preference rules from earlier in Chem 30A if necessary.)
2. Central to the mastery of radical chemistry is an understanding of the molecular structural features that influence radical stability. For each feature listed below briefly explain how it influences radical stability, make a brief comparison with carbocations, and provide a clear example.
- Number of carbons bonded to the carbon bearing the unpaired electron
  - Resonance with pi bonds
  - Resonance with lone pairs
  - Radical rearrangement

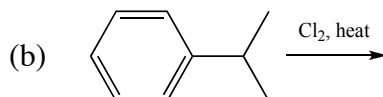
- (e) Inductive effects
- (f) Chain reactions

3. Draw the Lewis dot structure for superoxide, a potentially damaging radical produced by normal metabolic processes.
4. Much in the same way that carbocations have three common mechanism fates, radicals have three common mechanism fates as well.
  - (a) Use hydroxyl radical to illustrate the only radical fate that is also a termination step in a radical chain mechanism.
  - (b) Vitamin C is a naturally occurring hydrophilic antioxidant. At cellular pH it exists primarily as ascorbate (the conjugate base of ascorbic acid). Use superoxide and ascorbate anion to illustrate the remaining two radical fates.

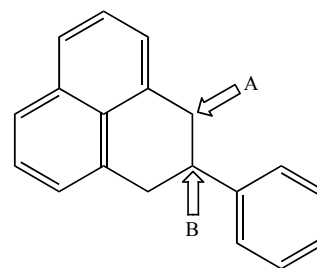


Ascorbate

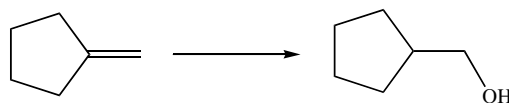
5. Provide the major products and corresponding mechanisms of these reactions.



6. When the molecule shown is reacted with  $\text{Br}_2$  in the presence of light, does bromination occur at carbon A or carbon B? Briefly explain your choice.

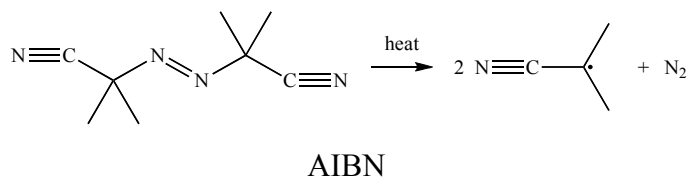


7. Consider the hydration reaction (addition of water) reaction shown below.
  - (a) List two different reactants that you have encountered in Chem 30 that cause this reaction to occur as written. Hint: both involve two sets of reactants.
  - (b) Give a mechanism for the reaction that involves radicals.

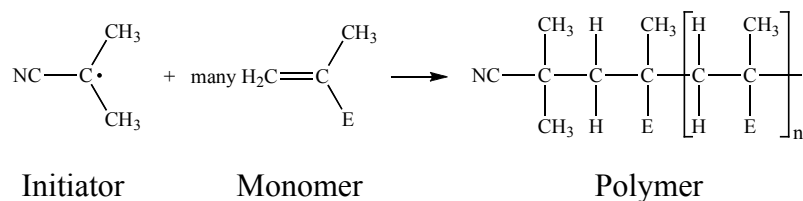


8. Radical polymerization is an industrial process used to prepare a wide variety of materials, especially plastics such as poly(methyl methacrylate), also called Plexiglas.

- (a) Azobis(isobutyronitrile) (AIBN) is sometimes used as a radical chain initiator. Heating it causes it to fragment, as shown below. Draw a curved arrow mechanism to show how this happens.

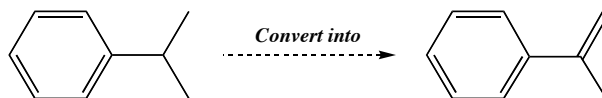


- (b) This radical then initiates a chain wherein many smaller molecules (called monomers) are covalently bonded to become one large molecule, called the polymer. Draw a curved arrow mechanism to show how this happens. The subscript  $n$  in the product indicates the the same molecular fragment in brackets is repeated many times. You do not need to include any termination steps in this mechanism. E = COOCH<sub>3</sub>.



The magnitude of  $n$  varies widely, from a few to millions, and is controlled by the conditions under which the monomer is polymerized. Plexiglas with different ranges of  $n$  has different physical properties such as hardness, brittleness, and melting point.

9. Suggest the reaction(s) necessary to convert cumene (isopropyl benzene) into 2-phenylpropene. Reactions from previous lecture topics are necessary.

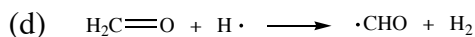
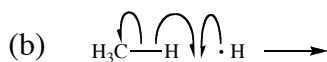
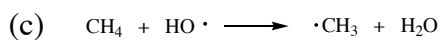
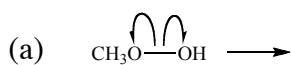


### Practice Problems

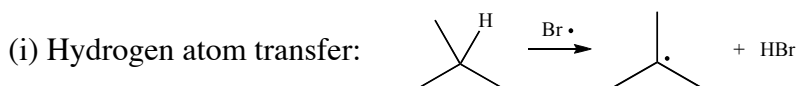
1. Draw the Lewis dot structure for the hydroxyl radical.
2. What is wrong with this statement: "I found an error in the Thinkbook. It says bromine atom when it really means bromine radical."
3. Why are radicals generally very reactive species?
4. Name the three fundamental free radical mechanism steps (fates) as discussed in lecture. Using H<sub>2</sub>C=CH<sub>2</sub> and bromine radicals as the only reactants, illustrate each of

these mechanism steps. Include the product and all curved arrows for each illustration. This question does not refer to initiation, propagation, and termination.

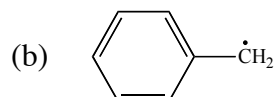
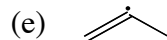
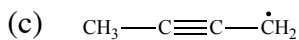
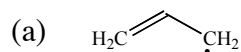
- Recall that molecular oxygen ( $O_2$ ) is best described as a diradical. Using only  $O_2$ , propene ( $CH_3CH=CH_2$ ), or products from reactions of these two molecules, name and illustrate the three fundamental radical mechanism steps.
- Using hydroxyl radical and isoprene (2-methyl-1,3-butadiene) as the only reactants in each case name and illustrate (using curved arrows) the three fundamental radical mechanism steps. If the reactants can illustrate the mechanism step in more than one way, draw the mechanism step that occurs most readily.
- The mechanism for the combustion of methane is very complex. Over 75 intermediates and 300 mechanism steps have been implicated. This is because the reaction occurs at high temperatures, which may allow processes that are otherwise unlikely at lower temperatures. Shown below are four incomplete steps in the mechanism. Complete these steps by adding the missing curved arrows or products.



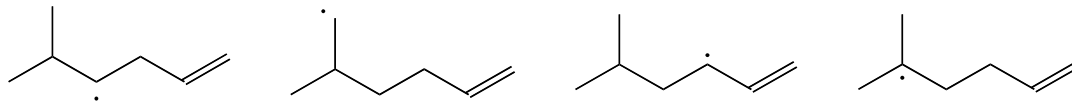
- When studying radical chemistry, students frequently ask why hydrogen atom transfers are common but methyl group transfers are rare. In other words, why is step (i) more favorable than step (ii)?



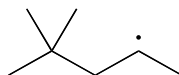
- For each radical shown below, draw all significant resonance contributors (including curved arrows, lone pairs, and formal charges), and the resonance hybrid.



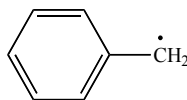
10. Rank these radicals according to stability. Briefly explain your reasoning.



11. Draw the structure of a radical with the same number of carbon atoms that is obviously more stable than the radical shown.



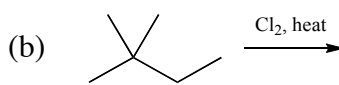
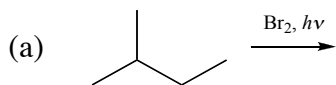
12. Draw the structure of a radical with the same number of carbon atoms that is obviously less stable than the benzyl radical shown.



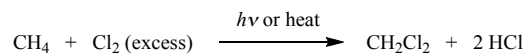
13. Many reactions involving carbocations, carbanions, or radicals occur readily at a benzylic carbon. Explain.

14. Complete the phospholipid side chain plus hydroxyl radical reaction scheme on the Radicals Lecture Supplement by adding the appropriate curved arrows for each mechanism step. Also include all significant resonance contributors. Label each mechanism step as a radical fate (addition to pi bond, etc.) as well as a radical chain step (initiation, etc.).

15. In each case, determine the major product and write a mechanism for its formation.



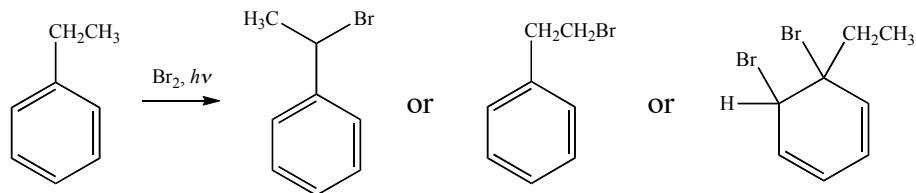
16. Dichloromethane (methylene chloride,  $\text{CH}_2\text{Cl}_2$ ) is a solvent used for a variety of laboratory and industrial processes, including the decaffeination of coffee. This solvent was replaced with supercritical  $\text{CO}_2$  when it was found that  $\text{CH}_2\text{Cl}_2$  might cause cancer in laboratory animals. Dichloromethane is produced by reaction of methane with chlorine and heat or light. Provide a mechanism for this reaction.



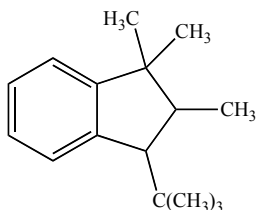
17. For the reaction shown below,

- Write a mechanism for the formation of the major product. Label each step in your mechanism with the name of the fundamental radical fate (from lecture) that describes it.
- Briefly explain your choice of major product.

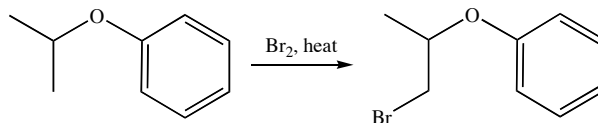
(c) Briefly explain how a single photon results in the formation of millions of molecules of the final product.



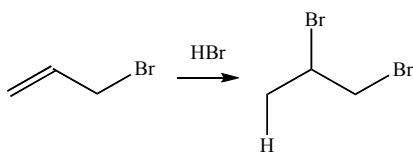
18. Suggest the major reaction product when the molecule shown below is reacted with  $Br_2$  in the presence of light.



19. The reaction shown below does not proceed as written. Draw the correct major product of this reaction, and briefly explain your reasoning.

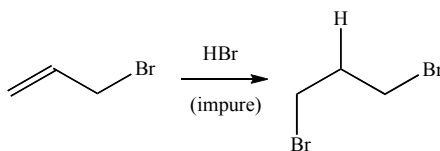


20. Recall that HBr undergoes electrophilic addition to alkenes. The product is formed in accordance to Markovnikov's Rule, and results from the more stable carbocation intermediate. Example:



Markovnikov addition

If the reactants are not carefully purified, the reaction might give an alternate isomer, or a mixture of products. Example:

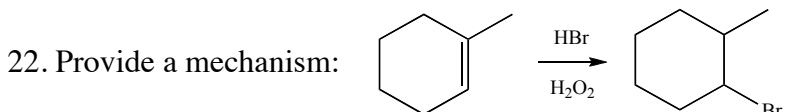


Anti-Markovnikov addition

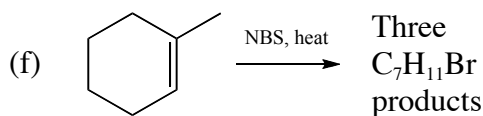
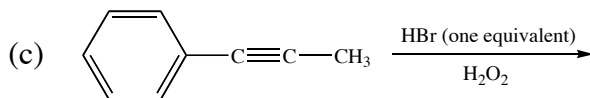
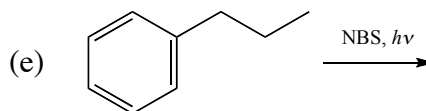
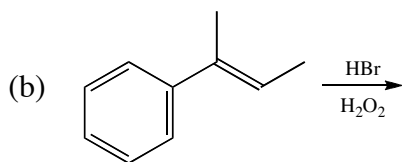
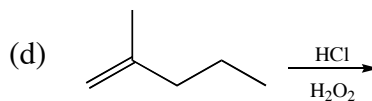
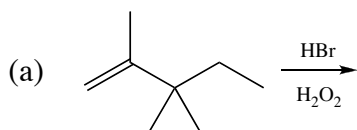
In 1933, Kharasch and Mayo (University of Chicago) reported that peroxide impurities such as hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) cause this change in products. Addition reactions to pi bonds that violate Markovnikov's Rule are called anti-Markovnikov.

- (a) Write a mechanism for the free radical reaction of allyl bromide with HBr in the presence of  $\text{H}_2\text{O}_2$ . Hint: Like the Br-Br bond, the O-O bond of  $\text{H}_2\text{O}_2$  is weak (bond dissociation energy is  $51 \text{ kcal mol}^{-1}$ ). The Lewis structure for hydrogen peroxide is H-O-O-H.
- (b) Conducting the reaction between allyl bromide and HBr in air can also cause anti-Markovnikov addition to occur. Explain.

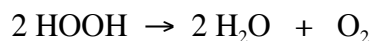
21. Carefully explain why the reaction of an alkene with HBr in the presence of peroxides gives a different product than the same reaction in the absence of peroxides. A mechanism can be used to justify your answer, but your mechanism must clearly show why these reaction conditions give different products.



23. Provide the organic product(s) of the following reactions.



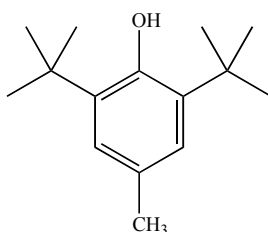
24. A 3% solution of hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) in water can be purchased at any drugstore. It is used to kill bacteria (an antibiotic) in fresh wounds. This solution has an expiration date because hydrogen peroxide slowly decomposes into water and oxygen:



It is the oxygen that provides the antibacterial effects of this solution, but normal decomposition is not fast enough to provide a sufficiently high concentration of oxygen. The body contains the enzyme peroxidase that converts  $\text{H}_2\text{O}_2$  to  $\text{O}_2$  much more quickly than noncatalyzed decomposition. This is the source of effervescence

when  $\text{H}_2\text{O}_2$  solution is poured over a wound.) Suggest a mechanism for the decomposition of  $\text{H}_2\text{O}_2$  into  $\text{H}_2\text{O}$  and  $\text{O}_2$ . Hint: The mechanism involves an uncommon radical event.

25. Very briefly outline the role chain reactions and antioxidants in the chemistry of free radicals in a living cell.
26. Briefly explain how ascorbic acid functions as a biological antioxidant. Your explanation must include at least one relevant mechanism step with curved arrows.
27. Antioxidants are added to food products to prevent discoloration and spoilage due to reactions of radicals present in the food and with oxygen in the air. Can the molecule shown below serve as such an antioxidant? Very briefly explain.

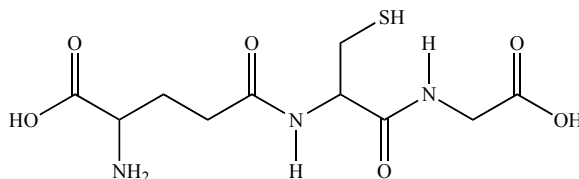


28. The reactions of superoxide radical anion with triglycerides such as the linoleic ester shown below have been implicated in the formation of arterial deposits leading to arteriosclerosis. Briefly describe how the reaction of one superoxide radical anion results in damage to many other molecules in the body.



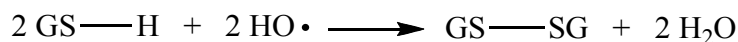
Linoleic ester

29. Name the three fundamental radical mechanism steps (not initiation, propagation, and termination). Illustrate each with curved arrows and using only superoxide radical anion and the generic linoleic ester from the previous question.
30. Glutathione (GSH) is another of many hydrophilic antioxidants.



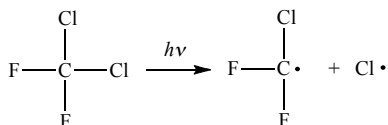
Glutathione (GSH)

Present in relatively high concentration in certain cells (up to 5 mM in liver cells), it protects against biological damage from reactive oxygen species such as hydroxyl radical by conversion to glutathione disulfide (GS-SG).

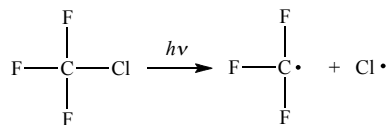


Write a mechanism for this reaction.

31. The 1995 Nobel Prize in Chemistry was awarded to Sherwood Rowland, Mario Molina, and Paul Crutzen for their work on the atmospheric chemistry of molecules containing only carbon, chlorine, and fluorine. Such molecules are called chloro-fluorocarbons, CFCs, or Freons (DuPont trade name). CFCs were implicated in the destruction of Earth's ozone layer by a free radical process. Photolysis of a carbon-chlorine bond initiates this chain reaction. For example:



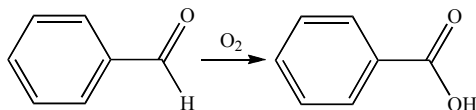
Photolysis of Freon-12



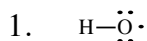
Photolysis of Freon-13

- (a) Which one of these CFCs is destroyed more quickly in the atmosphere (that is, which of these two reactions occurs more readily)? Briefly explain your reasoning.
- (b) Based on your logic for part (a), design a CFC that is degraded more quickly than the two shown above. Briefly explain your choice.
32. In your studies of organic and biochemistry you will encounter reactions that you have never seen before, for which you need to figure out the mechanism. You can do this by considering the bond changes necessary to convert the starting material into the product(s), and deciding on a reasonable set of curved arrows. In addition, consider the reactants: what have you seen them do in the past?

Autoxidation is the process in which a molecule reacts with oxygen to form a hydroperoxide (ROOH). Aldehydes are particularly susceptible to autoxidation, which converts them to carboxylic acids. Write the mechanism for autoxidation of benzaldehyde, shown below.



## Practice Problems Solutions



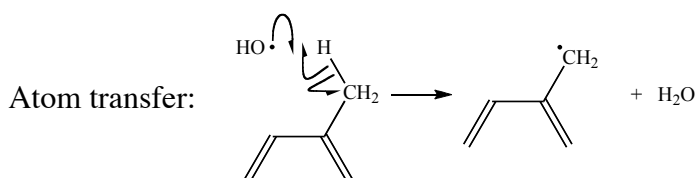
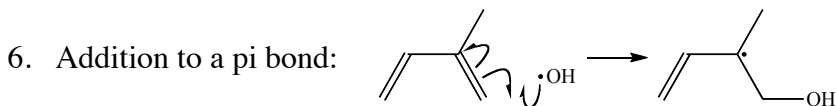
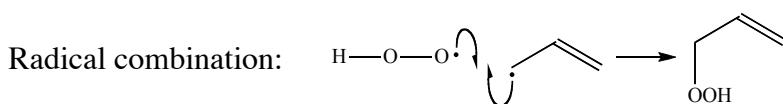
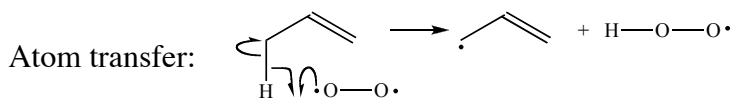
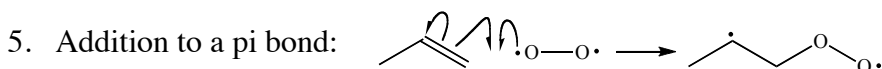
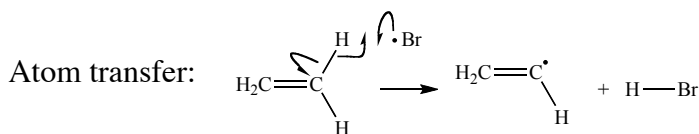
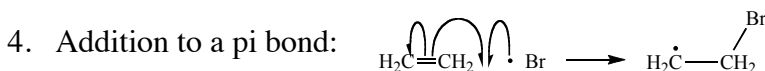
If you have difficulty with this basic skill, review the Lewis structure tutorial at the course web site ([web.chem.ucla.edu/~harding/tutorials/tutorials.html](http://web.chem.ucla.edu/~harding/tutorials/tutorials.html)).

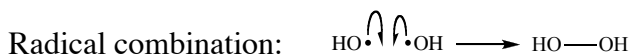
2. Looking at a periodic table we see that a bromine atom has seven valence electrons. Because this is an odd number, one of these electrons must be unpaired. Species that have one or more unpaired electrons are radicals, so a bromine atom is also a bromine radical.



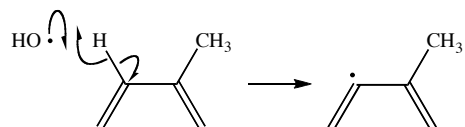
A bromine atom/radical

3. Free radicals are generally very reactive because they have a strong driving force to fill their open octets.

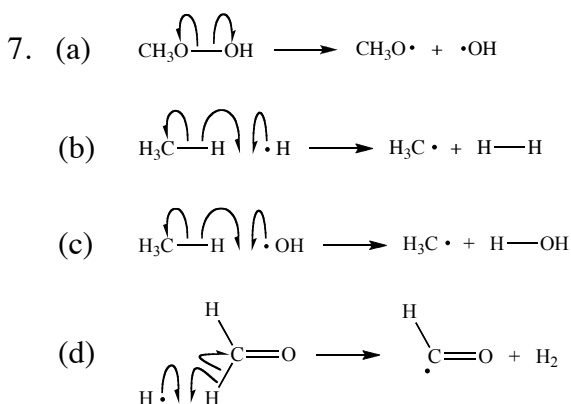




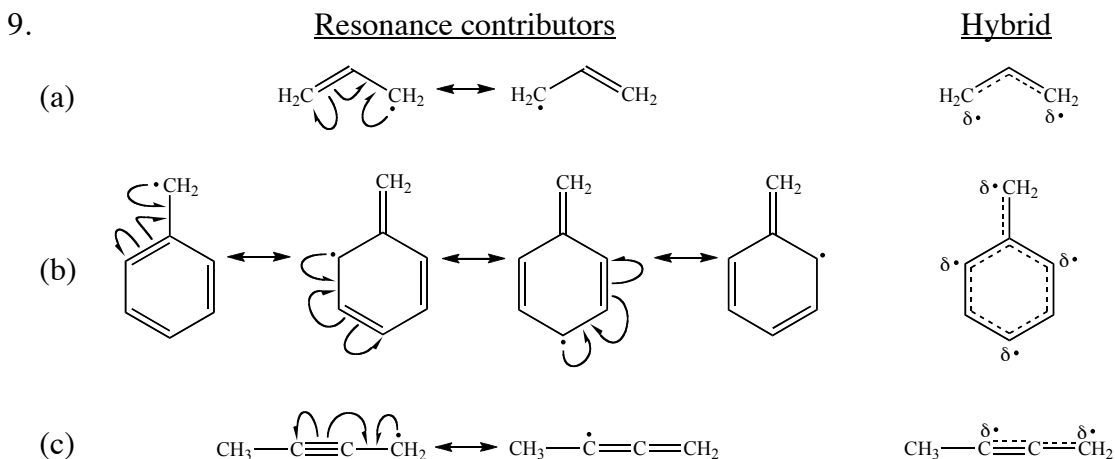
Students frequently ask why this atom transfer is not more likely:

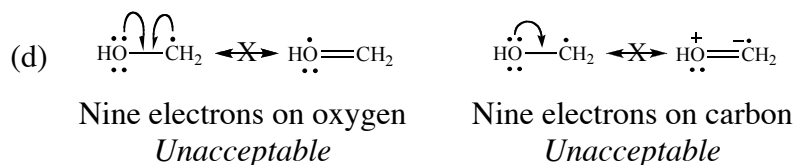


This atom transfer leads to a secondary vinylic radical with resonance stabilization. Just like carbocations, vinylic radicals are less stable than their nonvinylic counterparts. A secondary vinylic radical with resonance is no better than (and probably even less stable than) a primary nonvinylic radical with resonance. There are orbital alignment issues as well, which can be seen by exploring molecular models of the two radicals in question.



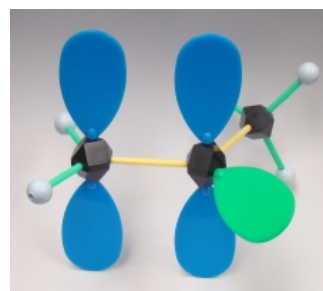
8. Hydrogen atom transfer leads to a tertiary radical whereas methyl transfer leads to a secondary radical. As we have seen so many times before, the reaction favors the mechanism step that leads to the more stable intermediate (or product if it is the last step of the mechanism). Since a tertiary radical is more stable than a secondary radical, hydrogen atom transfer is favored over methyl group transfer.



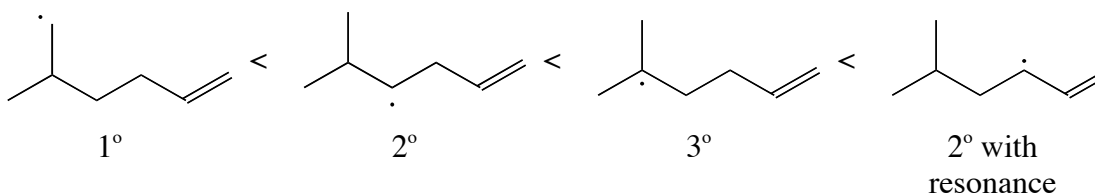


Conclusion:  $\text{H}\ddot{\text{O}}-\dot{\text{C}}\text{H}_2$  does not have significant resonance.

- (e) This radical does not have significant resonance because the  $sp^2$  orbital that contains the unpaired electron is perpendicular to the pi bond. Verify this with a model.

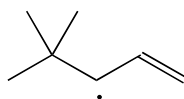


10. Radicals are electron deficient species. Resonance or electron-donating groups stabilize the carbon atom bearing the open octet in the same manner as carbocations. Thus, increasing the number of alkyl groups attached to the carbon with the open octet increases the stability of the radical. We cannot say for sure that degree of substitution outweighs resonance, so we cannot say for certain that a tertiary radical is more stable than an isomeric radical that is secondary and has resonance. However, we can apply the general assumption that resonance is usually the dominant effect. In this case our order of stability becomes:

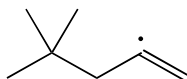


Computer modeling suggests the assumption concerning the weighting of substitution versus resonance effects to be correct.

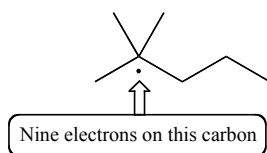
11. This radical is secondary, so any radical that is tertiary or is secondary and has resonance is more stable. The example below is secondary with resonance.



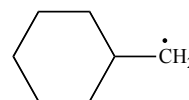
Avoid this common error: The secondary radical shown below does not have resonance, and is therefore not more stable.



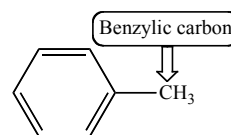
Avoid this common error #2: When this was given as an exam question, a significant number of students drew structures with nine electrons on carbon, or structures that did not have the same number of carbons as the given structure. Pay careful attention to what the question is asking!



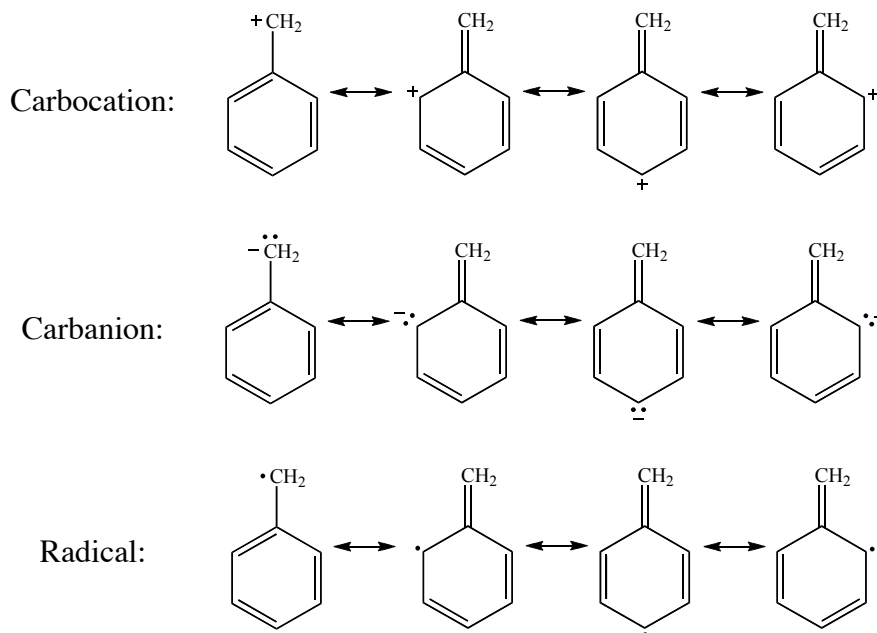
12. The given radical is primary with resonance, so any radical that is primary without resonance or secondary without resonance is less stable. One simple modification to achieve this is to remove the benzene ring.



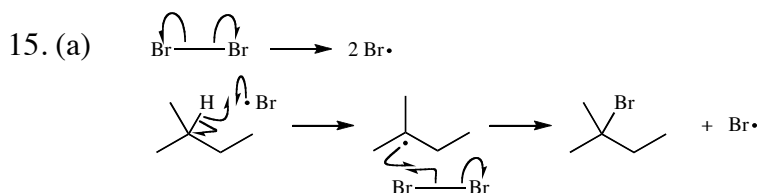
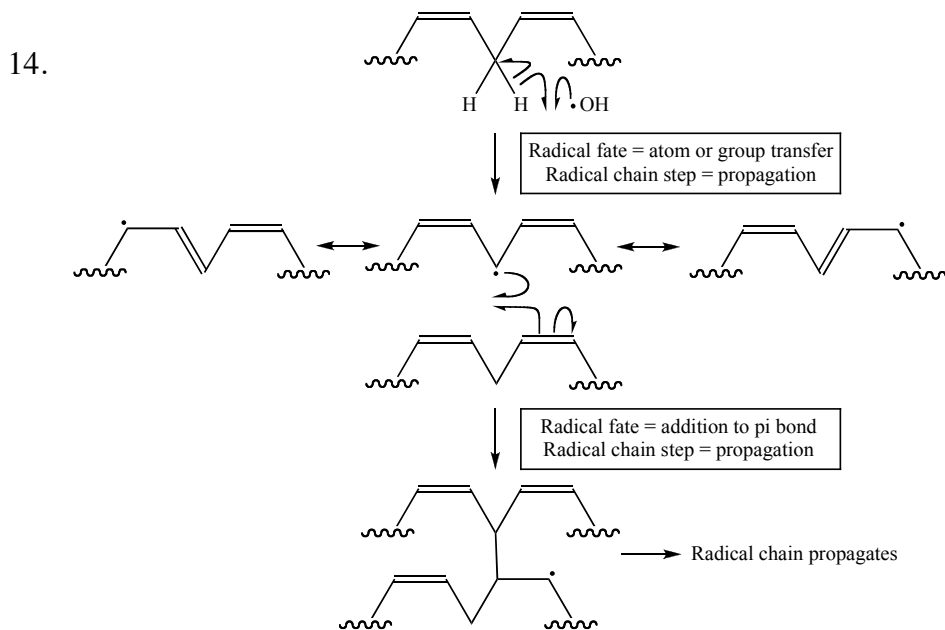
13. A benzylic carbon is a carbon atom directly bonded to a benzene ring, such as the methyl group carbon of toluene (PhCH<sub>3</sub>)



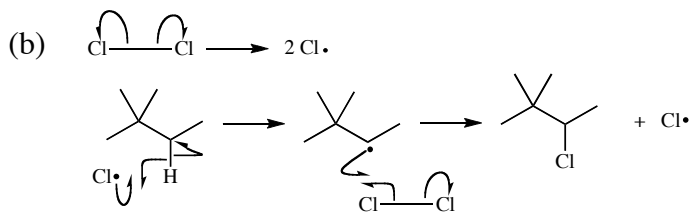
Many reactions involving carbocations, carbanions, or radicals occur readily at a benzylic carbon because resonance stabilization by the benzene ring allows these intermediates to form readily, as shown below.



Each reactive intermediate that can delocalize an open octet or lone pair (carbocation, carbanion, and radical) has four resonance contributors. The most significant of these is the contributor in which the pi electron cloud of the benzene ring is not disrupted. (The first contributor drawn in each case.) The net effect is that benzene ring resonance is about equal to allylic resonance.

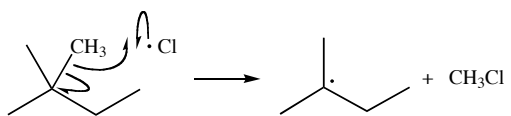


As an alternate last mechanism step, you may have considered showing the combination of a bromine radical and at the tertiary carbon radical to give the same reaction product. This radical combination is a termination step, not a chain propagation step. While it does give the observed product, it fails to explain the chain nature of the reaction. Since a reaction mechanism must be consistent with all the known facts and observations, the mechanism must include a final chain propagation step instead of a final chain termination step.

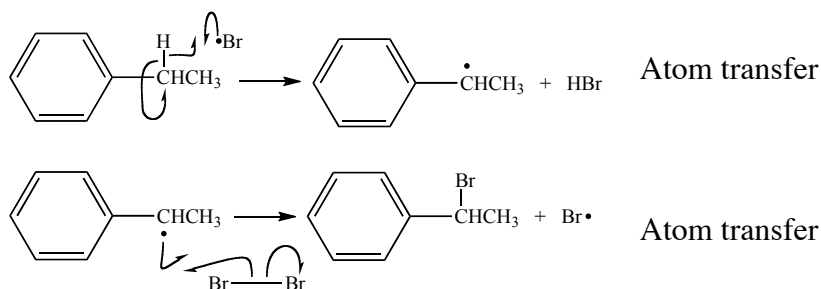
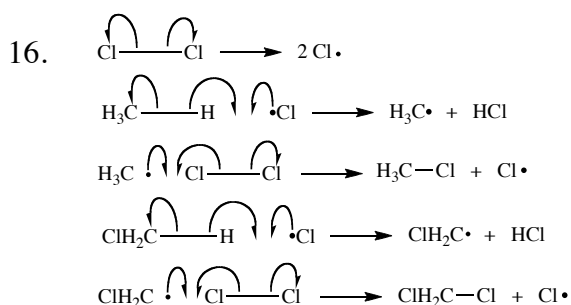


You may have drawn a different product (and corresponding mechanism) in which the chlorine radical abstracts a methyl group instead of a hydrogen atom.

This is a very reasonable idea because abstraction of hydrogen leads to a secondary radical whereas abstraction of methyl leads to a tertiary radical.

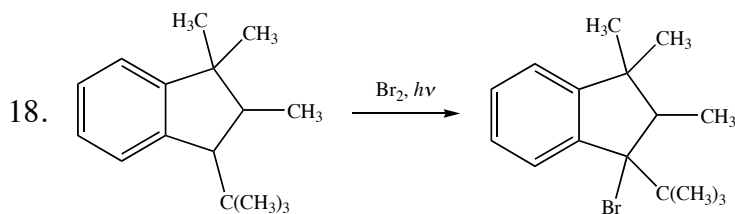


In this case the energy difference between a carbon-carbon and carbon-hydrogen bond is enough to favor the abstraction of hydrogen over methyl. (Steric effects may also have a role in this.) *Because of these factors, abstractions of single atoms are generally much more common than abstractions of groups of atoms.* (Review Practice Problem 8 for more on this.)

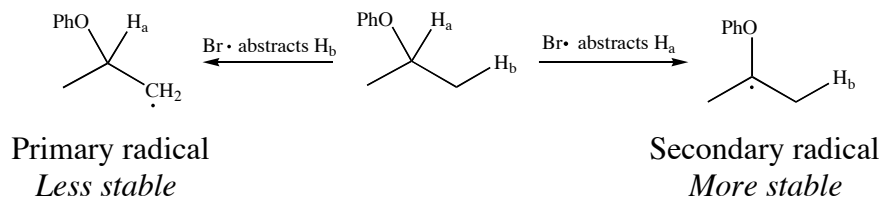


(b) The second step of the reaction mechanism controls which product isomer is formed. Atom transfer (abstraction) occurs so as to give the most stable radical product, which in this case is secondary with resonance. Reaction of this radical with  $\text{Br}_2$  in the final step leads to the observed product. The dibromo product is not formed, as its formation requires loss of aromaticity. Only powerful electrophiles can attack the benzene ring.

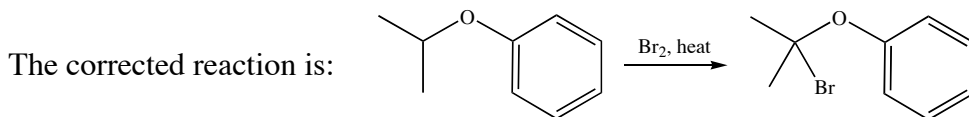
(c) One photon cleaves one molecule of  $\text{Br}_2$  into two  $\text{Br}\cdot$  radicals (first mechanism step). Each bromine radical produces one molecule of the product and one new bromine radical. This new bromine radical produces another molecule of product and another new bromine radical that...etc. A chain reaction results.



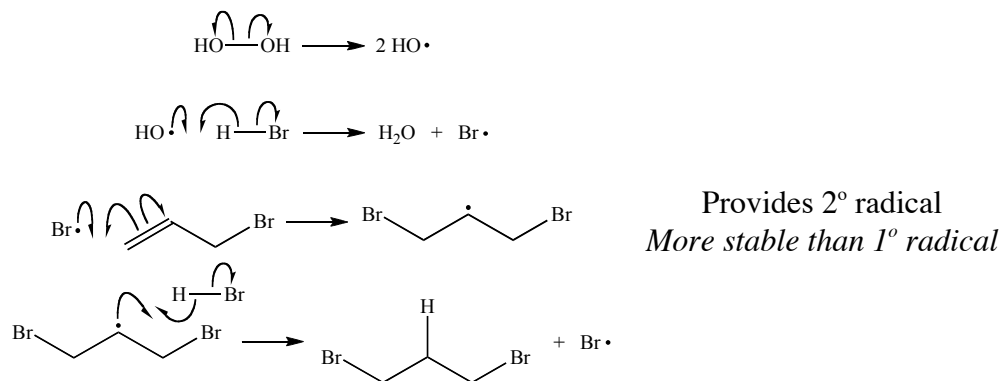
19. The mechanism step that determines which product isomer results in the one in which bromine radical abstracts a hydrogen atom:



Like every other mechanism step that produces a reactive intermediate such as a carbocation, carbanion, or radical, the most stable intermediate is favored. A secondary radical is more stable than a primary radical, so hydrogen atom abstraction forms the secondary radical.



20. (a) The presence of  $\text{H}_2\text{O}_2$ , with its weak O–O bond, strongly suggests this is a free radical reaction. The mechanism must account for the fact that the new C–Br bond is formed at the end of the chain. Recalling that electrophilic addition to an alkene occurs to give the more stable intermediate, we can achieve this goal by having a bromine atom attack the alkene pi bond. Bromine atoms can be generated from HBr by hydrogen atom transfer. Thus the mechanism is:



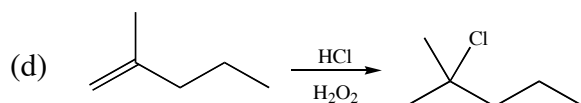
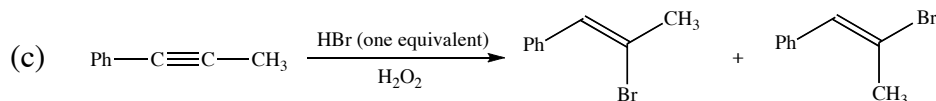
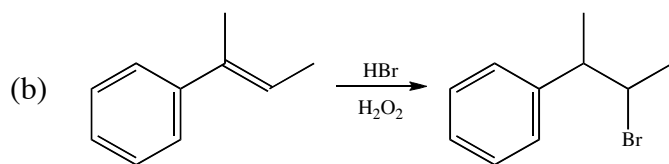
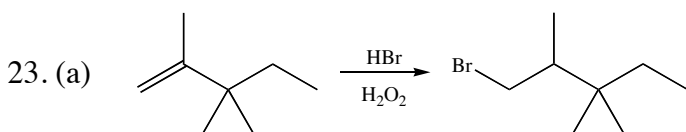
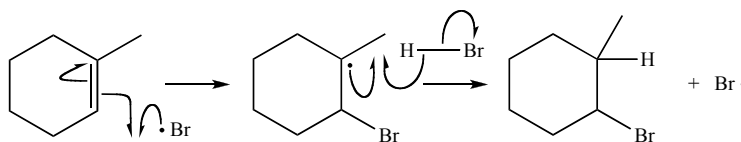
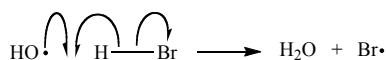
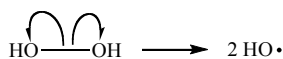
(b) Molecular oxygen is best described as a diradical. Being a radical, oxygen can initiate a radical reaction in the same way as hydroxyl radical. In the presence of air, the first step in the anti-Markovnikov addition of HBr to allyl bromide is the

reaction of  $O_2$  with HBr to form  $HOO\cdot$  (hydroperoxyl radical) and a bromine atom.

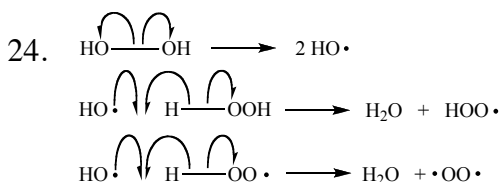
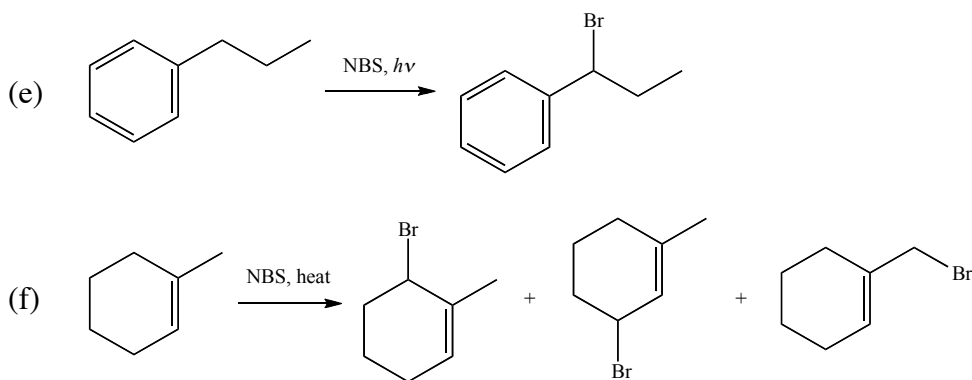
21. *In the presence of peroxides*, the electrophile is bromine radical. This electrophile adds to the alkene to form the more stable radical intermediate. This causes the bromine to become bonded to the least substituted carbon of what was the alkene.

*In the absence of peroxides*, when HBr attacks on an alkene the hydrogen end of HBr becomes attached to the least substituted end of the alkene to form the more stable carbocation. Capture of bromide ion by the carbocation then leads to the product in which the bromide atom is bonded to the carbon that was the more substituted end of the alkene.

22. The presence of molecular oxygen or peroxides (such as HO–OH) often, but not always, suggests the reaction mechanism involves radicals. For example the  $HOOH/NaOH$  step in the hydroboration-oxidation reaction is an anionic process involving  $HOO^-$ , and not radicals.

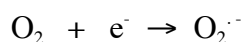


Reminder: The change in regioselectivity for electrophilic addition to a pi bond in the presence of a peroxide (“the peroxide effect”) occurs *only with HBr*. Other electrophiles such as HCl are immune to this effect.



Recall that molecular oxygen ( $O_2$ ) is best described as a diradical, with one unpaired electron on each oxygen atom.

25. Chain reaction: In a chain reaction, one or more mechanism steps are repeated indefinitely. A significant free radical in living cells is superoxide, produced by single electron reduction of molecular oxygen during normal cellular metabolic activities.

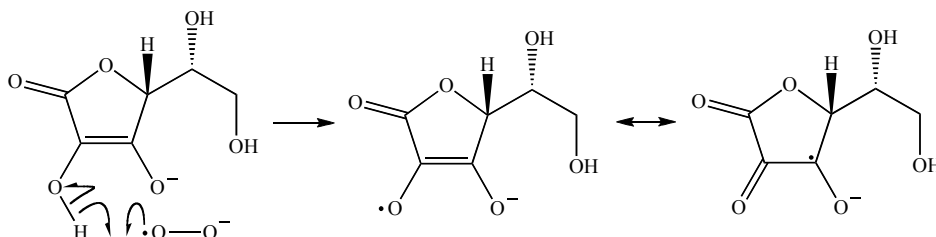


Superoxide can attack a biomolecule such as DNA by atom transfer or addition to a pi bond. If for example superoxide removes a hydrogen atom from DNA, then a new DNA radical results. This DNA radical can then attack another biomolecule, thus propagating the chain. Each biomolecule involved in this chain might be damaged. Thus, because of the chain nature of radical reactions, one superoxide can damage many biomolecules.

Antioxidant: An antioxidant is a compound that protects a cell from free radical damage. Examples are vitamin E (lipid-soluble) and vitamin C (water-soluble). Both of these molecules have a hydrogen atom that is readily removed, because the resultant antioxidant radical has significant resonance stabilization. Because this hydrogen atom is so readily removed, superoxide reacts more readily with an antioxidant than it does with a biomolecule such as DNA. In this way the antioxidant sacrifices itself to protect the biomolecules. The radical that results from hydrogen atom transfer from the antioxidant has significant resonance stabilization, so it is not

very reactive, and it does not attack other molecules. In this way the radical chain is interrupted (but not actually terminated).

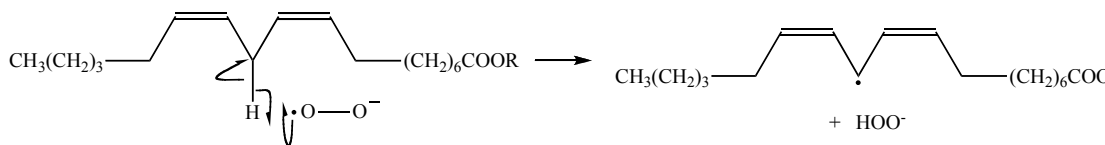
26. Free radicals such as superoxide can damage biomolecules by the usual radical reactions such as atom transfer. Ascorbate can also donate a hydrogen atom to superoxide:



The ascorbate radical that results has significant resonance stabilization, and thus not much driving force to react. This results in an interruption of the radical chain. This is not a termination of the radical chain because a radical (the ascorbate radical) is produced. However, because of its significant resonance stabilization, ascorbate radical is fairly unreactive, and the radical chain does not quickly propagate. Stopping the radical chain stops the damage cycle initiated by cellular free radicals. The ascorbate radical is then disposed through other means, probably by single electron reduction to ascorbate dianion, which is unreactive and flushed out of the cell.

27. The role of an antioxidant is to react with undesirable radicals such as superoxide radical anion, hydroxyl radical, or molecular oxygen more readily than these undesirable radicals can react with the material being protected. For this the antioxidant must have a hydrogen atom that can readily be removed by the undesirable radical, and the antioxidant radical that is formed must be of low reactivity so the radical chain process does not continue. Both antioxidant requirements are met if the antioxidant has a hydrogen atom whose removal leads to a resonance-stabilized radical. In the case of the compound shown above, removal of the hydroxyl hydrogen or the less sterically hindered methyl hydrogen leads to a radical that is readily stabilized by resonance with the benzene ring. Thus we conclude that this compound can serve as a useful antioxidant. (In fact, this compound is called BHT [**b**utylated **h**ydroxy**t**oluene] and was used for many years as a food preservative. Radical transfer occurs most readily at the hydroxyl hydrogen, probably driven by the relief of van der Waals crowding in that area of the molecule.)
28. Reaction of the linoleic ester with superoxide radical anion yields a new radical. This new radical can react with another biomolecule, perhaps another linoleic ester. This reaction product has a different structure than linoleic acid by itself, and perhaps cannot perform the normal biological roles of linoleic acid. Thus, the reaction with superoxide can cause damage. The reaction product is also a radical, which can react with another biomolecule, damaging it as well, and producing yet another new radical. This chain propagation process can thus result in the damage of many biomolecules, starting from just one superoxide radical anion.

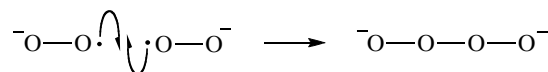
29. Atom transfer:



Addition to a pi bond:



Radical combination:



Radical combination of two superoxides is not likely, due to the weak oxygen-oxygen bond that is formed plus the close proximity of two negative charges in the product.



A radical combination step is usually rare, because radicals are usually present in low concentrations. However, the relatively high stability of glutathione radical (sulfur has a low electronegativity and large atomic radius) combined with its high concentration makes this step feasible.

31. (a) Both reactions afford a chlorine radical that results from homolytic cleavage of a C-Cl bond. The difference lies in the carbon radicals that are produced. These radicals differ only in the presence of a fluorine atom versus a chlorine atom. Fluorine is more electronegative than chlorine, so fluorine withdraws more electron density from the carbon, making the  $\text{CF}_3$  radical less stable than the  $\text{CF}_2\text{Cl}$  radical. Because the  $\text{CF}_3$  radical is less stable, it is formed more slowly. We predict therefore that Freon-13 degrades more slowly than Freon-12.

(b) Based on the logic of the previous answer, a Freon that produces a radical that is more stable than  $\text{CF}_2\text{Cl}$  radical degrades faster than Freon-12. Replacing one more fluorine atom with a chlorine atom affords Freon-11,  $\text{CFCl}_3$ . Photolysis of Freon-11 affords a  $\text{CFCl}_2$  radical. The  $\text{CFCl}_2$  radical is more stable than the  $\text{CF}_2\text{Cl}$  radical, so Freon-11 degrades more quickly than Freon-12. There are many other CFCs that can be envisioned that also degrade faster than Freon-12.

