Radical Reactions Non Lewis Acid/Base Mechanisms

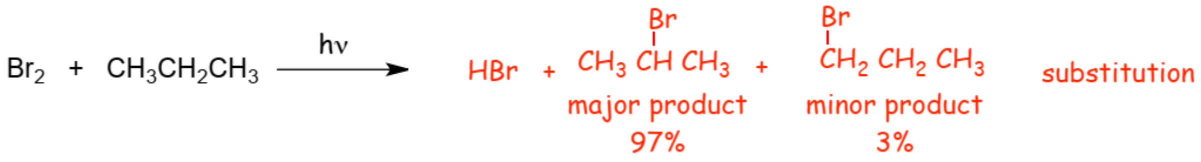
1 Photobromination

- Most reactions occur via Lewis acid/base mechanisms and involve **heterolytic cleavage** of bonds and **ionic** intermediates.
- Some reactions, however, involve **homolytic cleavage** of bonds and **radical** intermediates.

1.1 Photobromination of propane (as an example)

- Photobromination: "Photo-" means using light, specifically light (at an appropriate wavelength and energy)
- Bromination: means adding bromine to a structure, except that this is **very** sloppy language since the -Br must replace something, usually -H, in a **substitution** reaction

The reaction is:



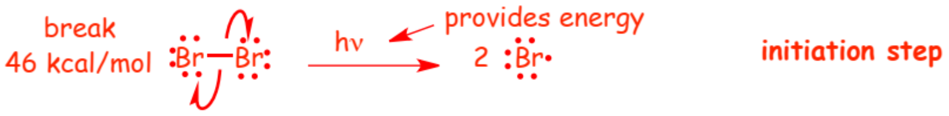
$$Br_2 + CH_3CH_2CH_3 \xrightarrow{h\nu} HBr + CH_3\overset{Br}{CH}CH_3 + \overset{Br}{CH_2}CH_2CH_3$$

- **Note:** the use of the notation hν = light (energy), compares to Δ = heat (thermal energy) the "ν" in hν is actually the Greek "nu", the Greek version of n that looks like a "curvy" v, and so we often just use the lowercase letter "v" in hν.

The mechanism - for formation of the major product

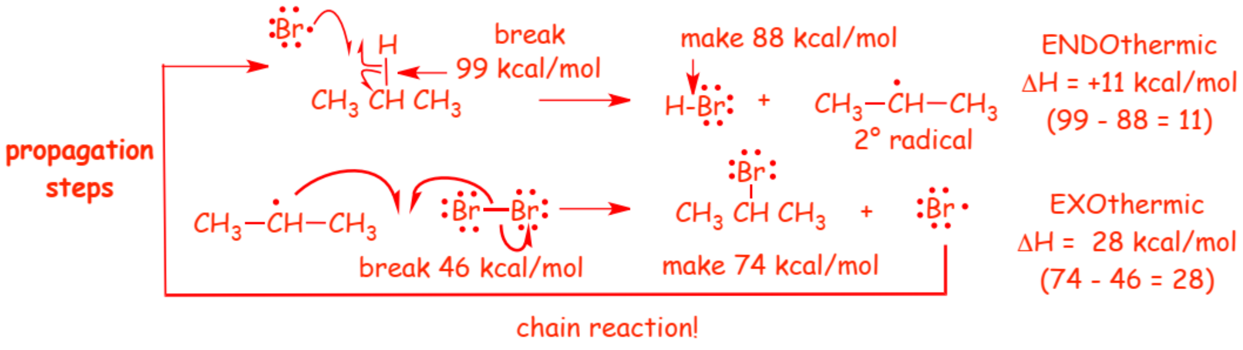
- Immediately we will see a difference compared to conventional Lewis acid/base mechanisms of, for example, alkene addition reactions. In radical mechanisms the steps are often **separately, not in a continuous "chain"**.
- At first sight this may appear confusing, but there are reasons for this, most importantly the mechanisms are usually not linear, **there are "branches"**, and, it is often useful to separate the steps to discuss them individually.
- **Note:** all bond cleavages are **homolytic**, and are described in terms of **bond dissociation energies.**

First: The **initiation** step



- We are about to see that this mechanism is a **chain** mechanism, the first (initiation) step **initiates** the chain.
- The light energy (hν) supplies the energy required >46 kcal/mol to homolytically break the Br-Br bond.

Next: The **propagation** steps



1st step endothermic by 11 kcal/mol
2nd step exothermic by 28 kcal/mol

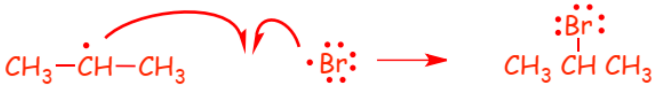
propagation steps overall
exothermic by 17 kcal/mol

- The first propagation step breaks a C-H bond and makes a weaker H-Br bond, the energy of the electrons goes **up**, this step is **endothermic**, the exothermicity is determined by the difference in the relevant BDEs.
- The second propagation step breaks a Br-Br bond and makes a stronger C-Br bond, the energy of the electrons goes **down**, this step is exothermic, the exothermicity is determined by the difference in the relevant BDEs.
- The second propagation step forms a Br atom, **that repeats the first of the propagation steps,** and thus continues in a **chain reaction.**
- The chain reaction is not a linear sequence of reaction steps, which is why we write these mechanisms this way.

Common termination steps

- The **chain reaction** continues until one of the radicals or atoms in the propagation steps does something else, in which case the chain is then broken, and with continued light irradiation, another chain starts.

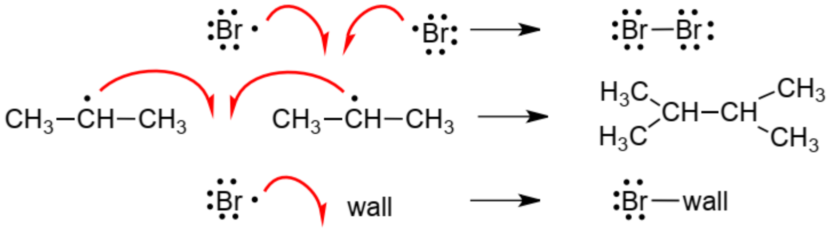
One termination step that breaks the chain is….



termination
not to be included in the mechanism

- Although this reaction does form the product, it is **not included** as part of the conventional mechanism, because it is **not a part** of the chain reaction and it is **much less probable** than the propagation steps that form the product because the concentration of the bromine atom and the propyl radical are so low that the probability of them colliding as shown here is rather low.

Other common termination steps are…….



- The "wall" is the reaction container wall, atoms and radicals are so reactive that if they collide with the container wall they may form a bond to one of the atoms at the container wall, such reactions are hard to describe using curved-arrow pushing since it is not clear which atoms of the container the radical/atom may react with.

Important: An initiation step is **not required** for every reaction!

- Initiation steps are actually quite rare, for every propagation step there is much less than one initiation step.
- The reaction is initiated with light, and the light intensity that is used is usually quite low, and so at any one time there are only a very few reactions being initiated.
- **However**, once the reaction is initiated, it can keep going with requiring another initiation because the Br atom that is formed in the second propagation step goes and starts another first propagation step in a chain reaction
- And so reaction can keep going without any initiation, until the chain terminates.
- **In fact**, if there were one initiation step for every propagation step there would be a huge buildup of Br atoms that would recombine, and then termination would then be a major step. In practice it is hard to get a light source that its intense enough to do this, and you don't need an intense light source anyway, because of the chain.

When you shine light on a mixture of alkane and Br_2, it is the Br_2 that absorbs the light energy, Br_2 is brownish colored, whereas alkanes have no color at all, this is why the first thing that happens if the light causing homolysis of the Br-Br bond, nothing can happen until bond homolysis.

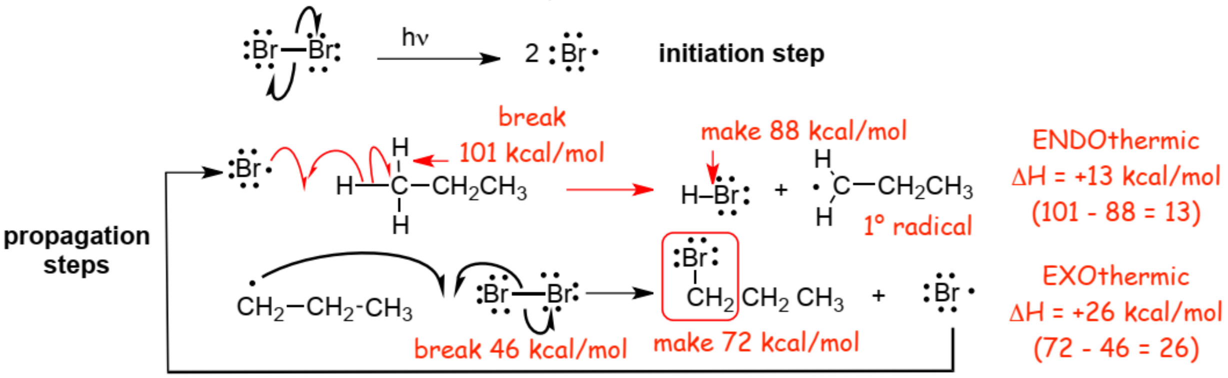
Now, the Br atom is surrounded by millions and millions of molecules, and, the light intensity is not high, which means that at any one time hardly any of the bromine molecules have actually absorbed light and split into atoms, and so the concentration of bromine atoms will be very low. Also, the bromine atoms are very reactive and they react almost as soon as they form, and so they never build up any significant concentration compared to the concentration of alkane molecules.

Because the concentration of the bromine atoms is very small, it is much more likely that the bromine atom will react with an alkane rather than recombine with another bromine atom, and this starts the chain reaction going. Of course, recombination of 2 bromine atoms could occur sometimes, and this will be a chain-terminating step, but each bromine atom is more likely to react with an alkane.

The alkyl radical is not attacked by a bromine atom, because again, the concentration of bromine atoms is much smaller than the concentration of unreacted bromine molecules, and so the radical reacts with a bromine MOLECULE (not atom) to form the product and another bromine atom, which then starts the cycle over again.

What Determines Which is the Major and Which Minor Product?

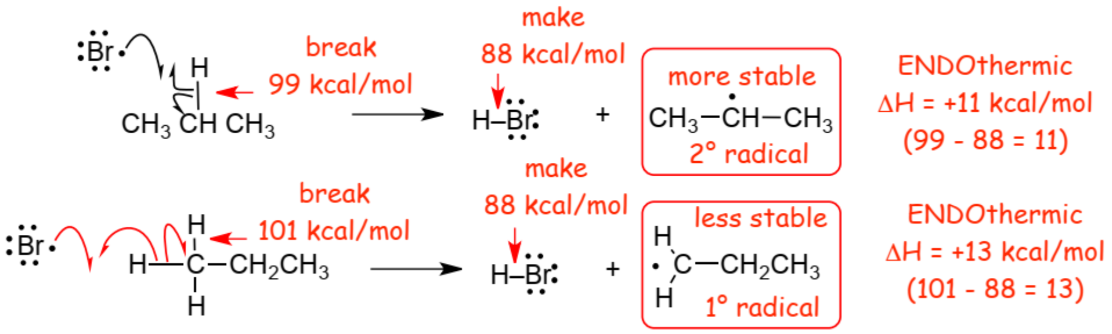
- **The mechanism** for formation of the **minor side** product.



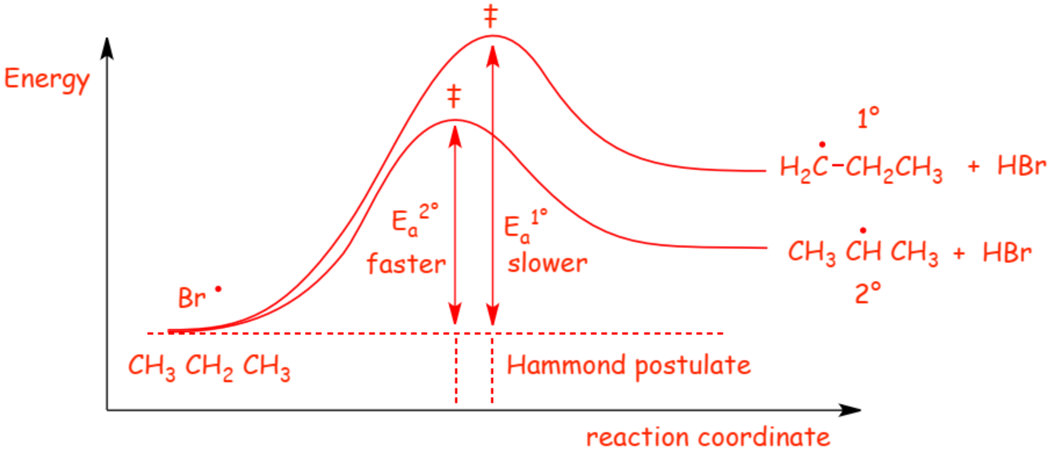
chain reaction!!!

- Termination steps are not shown, but are similar to those shown in the previous mechanism.
- The step that is **different** compared to the mechanism for the major product is the FIRST propagation step, that in this case forms a **primary** (1°) radical.

- **Now**, let's compare the enthalpies of the two steps that are **different** between the two mechanisms.
- The **faster** of these two will determine the **major product** of the reaction.



- According to the **Hammond Postulate**
- The reaction that proceeds via the **primary** radical (that forms the **minor side product**) is more endothermic, and therefore should have a higher Ea, a later transition state and should be slower
- The reaction that proceeds via the **secondary** radical (that forms the **major product**) is less endothermic, and therefore should have a lower Ea, an earlier transition state and should be faster.
- This is often called **The Reactivity/Selectivity Principle**

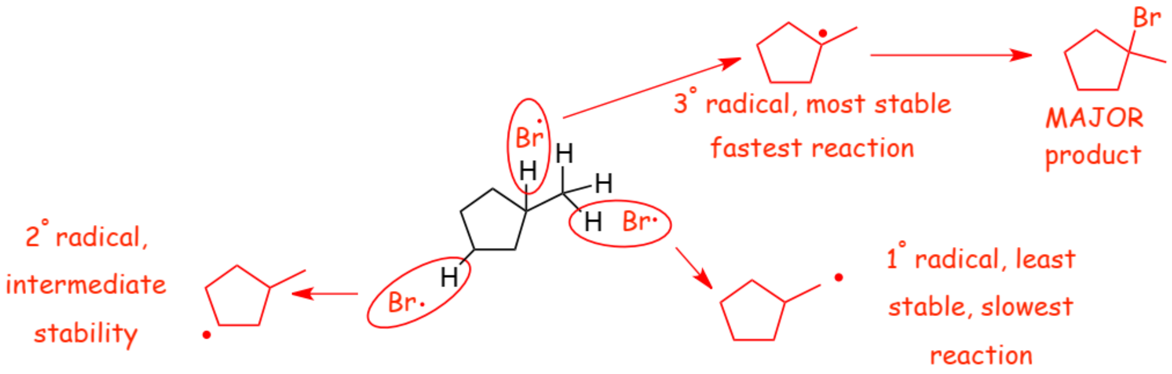


- There is a **large** difference in Ea when the reactions are **endothermic**, which results in a large difference in rate for endothermic reactions, resulting in high selectivity (reactivity/selectivity) even if the difference in endothermicity is not large.

1.2 Photochemical Bromination is a Useful Reaction

- What is the major product of the following reaction
- **Note** that organic chemical equations are often not fully balanced the emphasis is on the organic part of the reaction), **and**, usually only the major organic product is shown unless there is a particular reason to show other products:

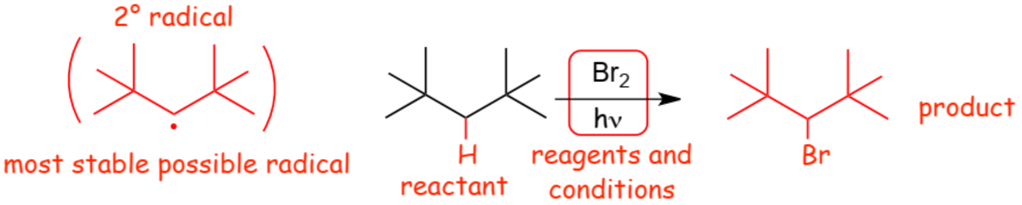
- How to we explain the formation of THIS major organic product, i.e., why substitution of the particular hydrogen atom indicated instead of one of the other 11 H atoms in the reactant structure?
- We **could** do the entire mechanism, and if we don't make a mistake, the **mechanism** is our **algorithm** for arriving at the correct product.
- **However**, by now we know that the critical intermediate in the mechanism is the radical that is formed by hydrogen atom abstraction by the bromine atom.
- We can use **heuristics** to "jump" to the critical part of the reaction, by only looking at all of the possible radical intermediates that could be made in this reaction:

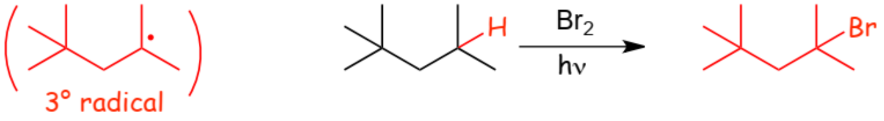


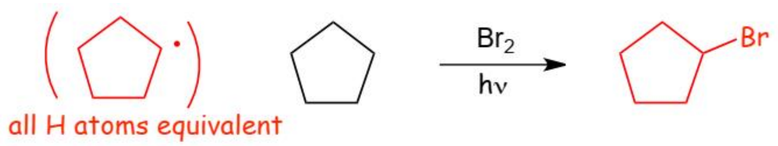
- The **tertiary** radical is the most stable radical we can make by doing a hydrogen atom abstraction reaction, this radical will be **formed fastest**, this radical gives the observed major organic product.

Example problems. Give the major organic products of the following reactions:

- **Each** reaction proceeds via the most stable radical intermediate (shown in parenthesis), since that is the intermediate that will be formed **fastest** (the reaction is **kinetically controlled.**
- Use **heuristics** to quickly determine the major organic product by identifying the most stable radical intermediate.



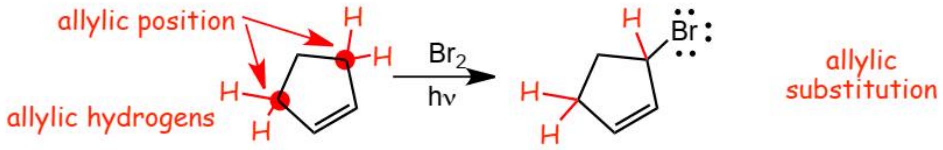




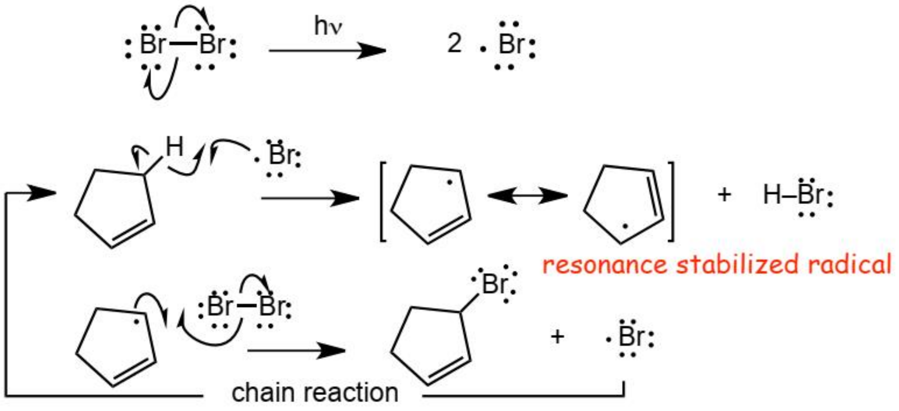
- Note however, that in practice this reaction is only really useful if there is an obvious radical site that is more stable that any others, otherwise there will be multiple products (see later).

2 Allylic Bromination

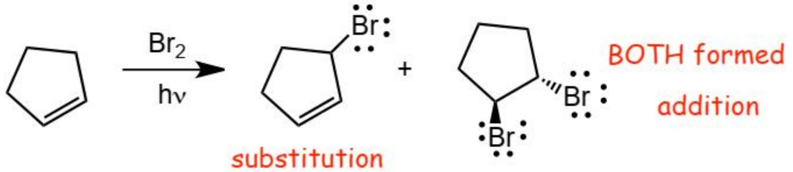
- **This reaction** should work, and it does…..



- This is substitution again of **one** of the four (in this case) allylic hydrogen atoms for -Br (if the reaction were run for longer times then more than one substitution would probably occur, care needs to be taken to properly control the reaction time and conditions).
- The reaction proceeds via the most stable radical intermediate, a resonance stabilized radical, as illustrated in the mechanism:

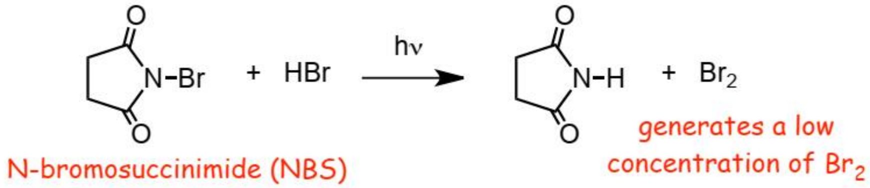


Wait a minute, didn't we just learn that Br_2 ADDS to C=C bonds?



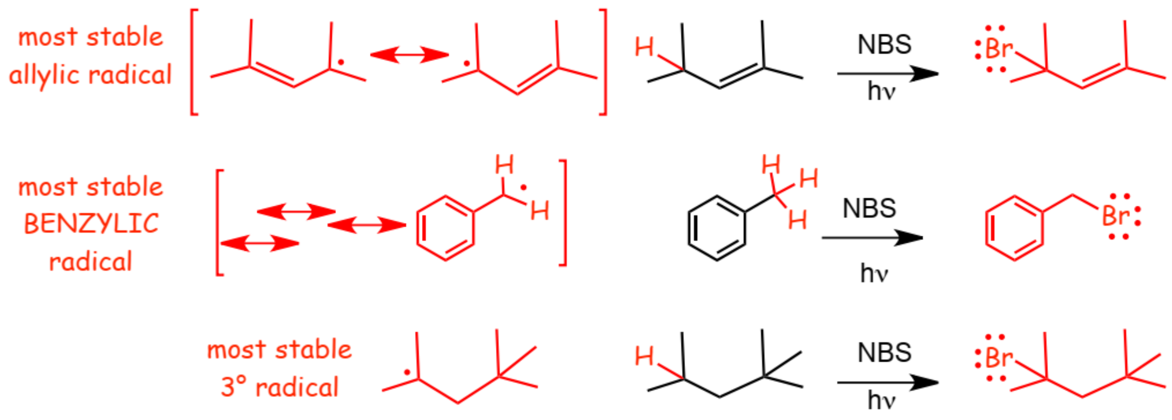
- Br_2 **does add** to C=C bonds, and it is difficult to ensure that substitution occurs without any addition.
- This problem can be **solved** by using a **very low** concentration of Br_2 to minimize addition to the alkene.

This Requires a New reagent!



- Using NBS, low concentrations of Br_2 are generated that can be photolyzed as usual to initiate the radical substitution reaction.
- The mechanism for formation of Br_2 from NBS is a bit obscure and uses H-Br that is often present as an **impurity**, for this reason we will not go into the mechanism of the NBS reaction.

Examples of Allylic Bromination



Some **heuristics** that you should expect to develop for these reactions:

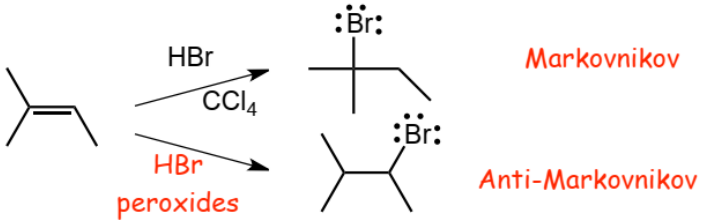
1) The reaction is substitution of -H for -Br and proceeds via a resonance stabilized RADICAL intermediate and therefore there will be no rearrangements.

2) NBS and light should be used instead of Br_2/light to avoid direct addition of Br_2 to the C=C bond.

- You can USE NBS/light to do **conventional** bromination of a simple alkane also.
- Use NBS and light as the reagents for allylic bromination, not Br_2 and light.
- Use **either** NBS/light OR Br_2/light for bromination of an alkane - **Most students will use NBS/light** for **all** radical brominations (radical substitutions) to avoid making mistakes with the choice of best reagents.

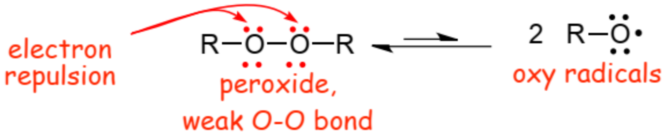
3 Anti-Markovnikov Addition of H-Br to an Alkene

- In the previous section we learned how to do Markovnikov addition of H-Br to a C=C double bond in an ionic Lewis acid/base mechanism.



- But what if we need the -Br atom on the **least** substituted carbon of the C=C bond? i.e., what if we want to do **Anti**-Markovnikov addition of H-Br to the alkene?
- This can be done using a **peroxide** as an addition **reagent** in a **radical mechanism**.
- Light turns out to be not the best way of initiating this reaction, because unlike Br_2, which is (slightly) colored and can interact with light, most alkenes and H-Br do not have any color, we need **another way** of generating radicals.

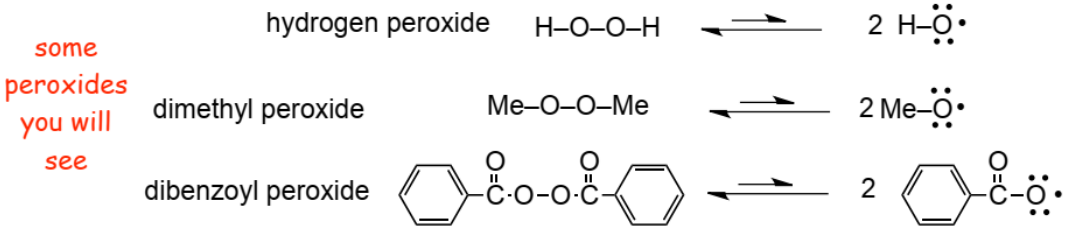
A New Reagent:



- the oxygen-oxygen bond is weak due to electron repulsion between the non-bonding pairs on the adjacent oxygen atoms, and even just with a small amount of thermal energy it is possible to break the bond by homolysis to generate two alkoxy radicals that can initiate a **radical chain mechanism.**

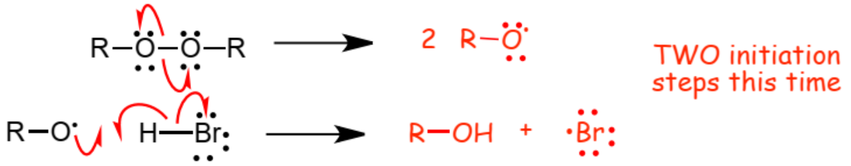
The O-O bond in the peroxide is also weak because the two oxygen atoms are smallish, which reduces the atomic orbital overlap, but that is beyond the scope if most general organic chemistry courses

- Unfortunately, there are several peroxides that can be used in this reaction, either a specific peroxide may be specified in the reaction or just a generic "peroxides" may be specified, you need to recognize these various ways of specifying peroxides and how they are used.

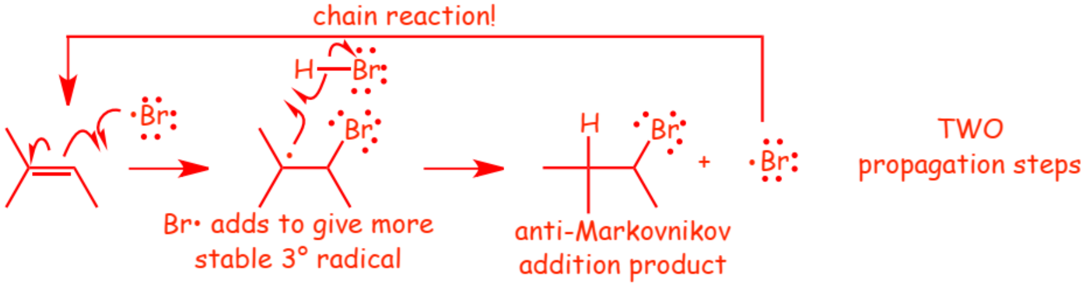


The Mechanism:

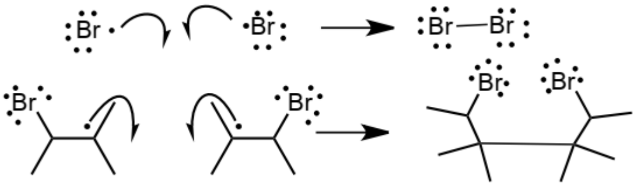
- As usual, radical mechanisms are not shown linearly step-by-step because they are often non-linear, in this case we have a non-linear **chain** mechanism again.
- There are **two initiation** steps this time:



- There are **two propagation steps:**

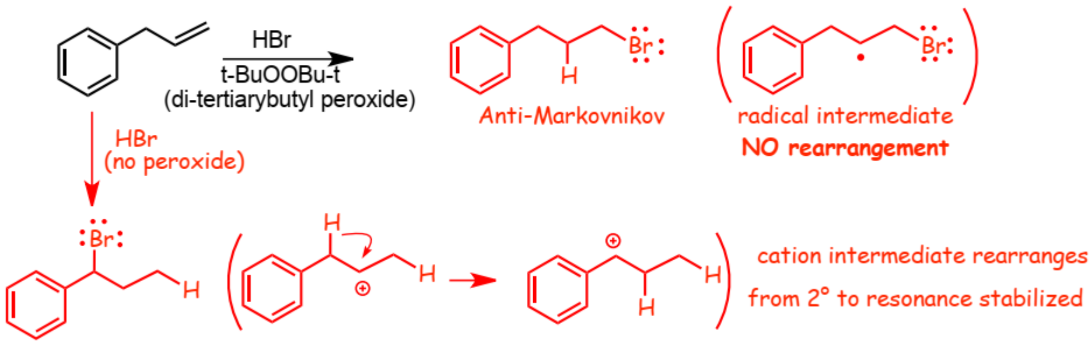


- And the usual termination steps, the following are examples (there are others, such as reaction with the wall).



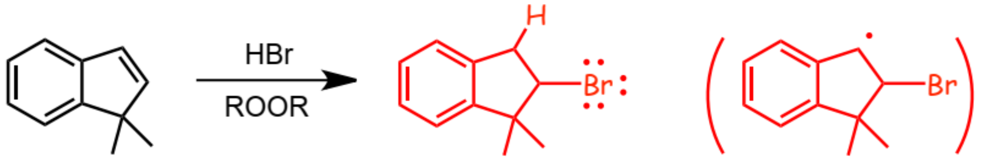
An Example Reaction

Compare the conventional Lewis acid/base reaction of an alkene with H-Br to the **radical reaction** that is initiated in the presence of peroxides:



- The presence of **peroxides** makes the **radical reaction** much faster than the Lewis acid/base reaction.
- The reaction is **regiospecific**, the -Br adds to the LEAST substituted "end" of the C=C bond, **Anti-Markovnikov**
- **Radicals do not rearrange** the same way that cations do, and so the addition is simple **Anti-Markovnikov** (no rearrangements).

Example Reaction:



most stable radical intermediate

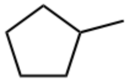
- This reaction is **not stereospecific**, because addition of a H atom to the intermediate carbon-centered radical can occur either from the "top" or the "bottom" equally, which means that the -H and -Br will be added both to the same side and also opposite sides, when stereoisomers can be formed (as in the case above), all isomers will be formed, which is why the structure above is shown with PLAIN bonds to both -Br and -H, it is not appropriate to use wedged/dashed bonds.

Some **heuristics** that you should expect to develop for this reactions:
1) These is an **addition** reaction of -H and -Br across the C=C bond
2) This reactions is **regiospecific Anti-Markovnikov addition** (-Br adds to most substituted end of the C=C bond where appropriate)
3) These reactions proceed via a **radical** intermediate and therefore there will be no rearrangements
4) These reactions are **not stereospecific**, if cis/trans-isomers can form they will form

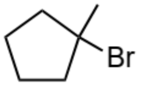
4 Reaction Summary

Do not start studying by trying to memorize the reactions here!
Work as many problems as you can, with this list of reactions in front of you if necessary, so that you can get through as many problems as you can without getting stuck on the reagents/conditions, and so that you can learn and practice solving reaction problems. Use this list **after** you have worked all of the problems, and just before an exam. By then you will have learned a lot of the reagents/conditions just by using them and you will only have to memorize what you haven't learned yet. Then do the following:

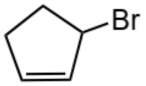
- Cover the entire page of reagents/conditions with a long vertical strip of paper, see if you can write down the reagents/conditions for each reaction, check to see which you get correct, if **completely** correct, circle Y, if incorrect or even slightly incorrect, circle N. In this way you keep track of what you know and what you don't know.
- Keep coming back to this list and so the same thing only for those reactions you circled N, until all are circled Y.
- Knowing the reagents/conditions on this page is **insufficient** to do well on an exam since you will ALSO need to recognize how to use and solve reaction problems in different contexts, this page **only** helps you to learn the reagents/conditions that you have **not yet** learned by working problems.



$\xrightarrow[h\nu]{Br_2}$ Y / N



$\xrightarrow[h\nu]{NBS}$ Y / N



$\xrightarrow[ROOR]{HBr}$ Y / N