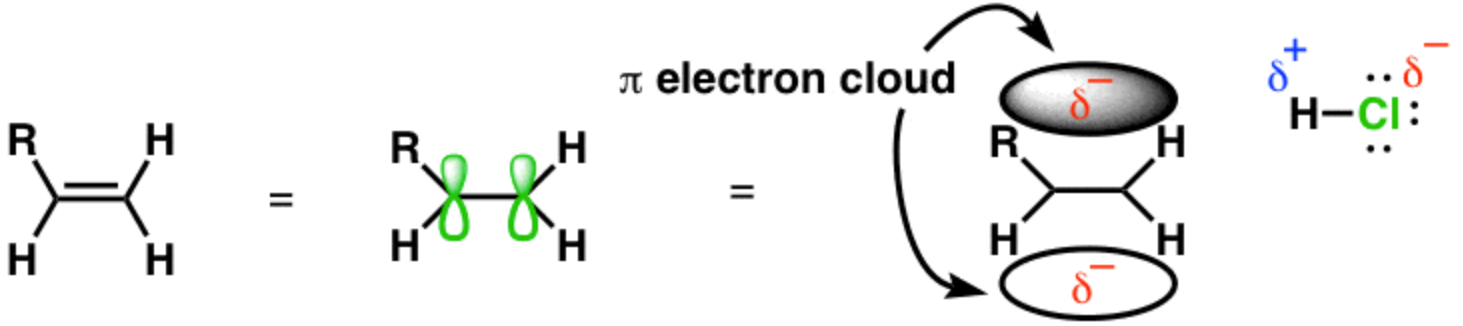
Alkene Reactions

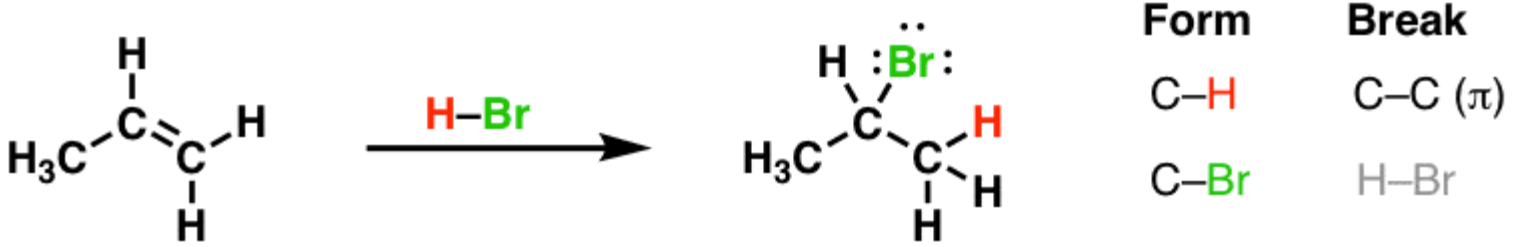
Electron distribution in alkenes and HCl



Electron flow occurs from electron-rich to electron poor

Addition Reactions: Elimination's Opposite

look at an experimental observation that dates back well over 140 years. In the late 1860's, the Russian chemist Vladimir Markovnikov made the following observation: alkenes treated with hydrobromic acid formed alkyl bromides.

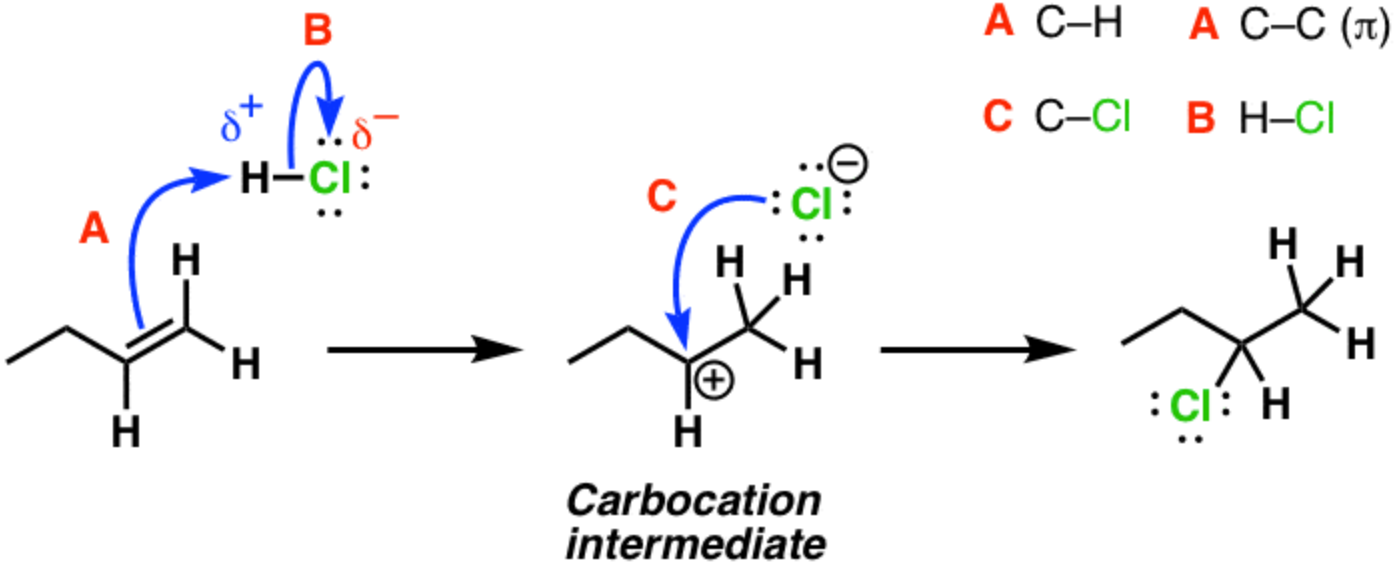


Form	Break
C–H	C–C (π)
C–Br	H–Br

Note the pattern of bond-forming and bond-breaking here: we're breaking a C-C π bond and forming a C-Br and C-H bond on adjacent carbons.

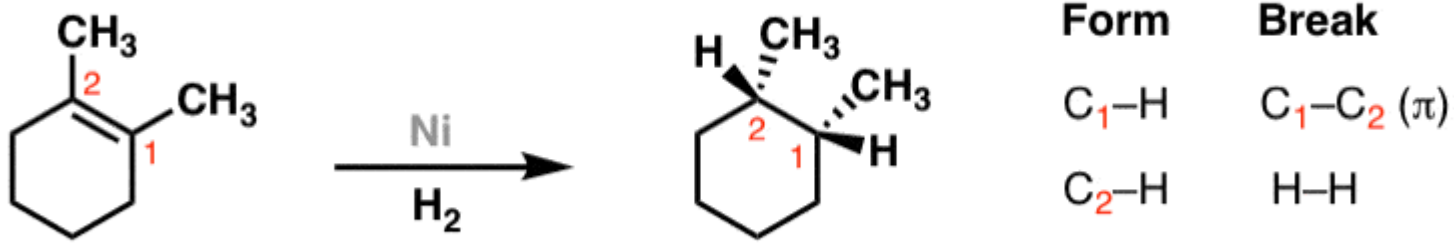
A hypothesis that fits all the facts:

Form	Break
A C–H	A C–C (π)
C C–Cl	B H–Cl



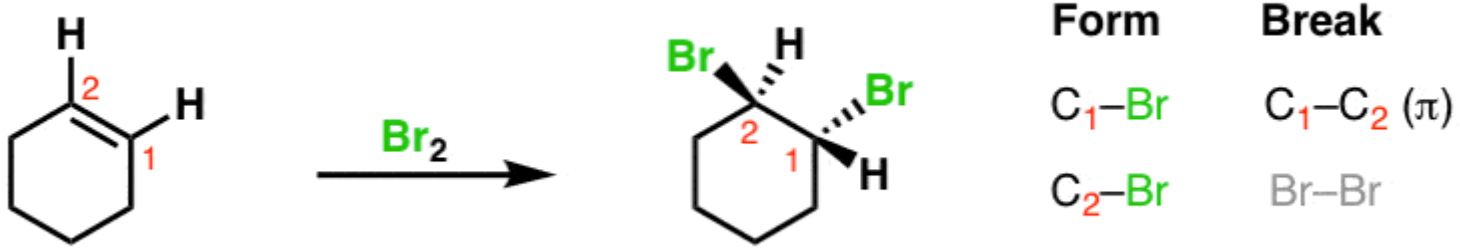
Carbocation intermediate

Here's another example. In the late 1800's it was discovered by French chemist Paul Sabatier that when alkenes are treated with hydrogen gas in the presence of finely divided nickel, the following reaction occurs:



Sabatier won the 1912 Nobel Prize in chemistry for the development of this reaction, which was subsequently found to occur with many different varieties of metal catalysts besides nickel, including palladium, platinum, and many other "late" metals. Again, note the pattern: breaking a C–C π bond and forming two C–H bonds on adjacent carbons. [Don't worry so much about the dashes and wedges for now – we'll get there in a later post].

Here's one last example. If you take an alkene (like cyclohexane, for instance) and add elemental (liquid) bromine, the following reaction occurs:

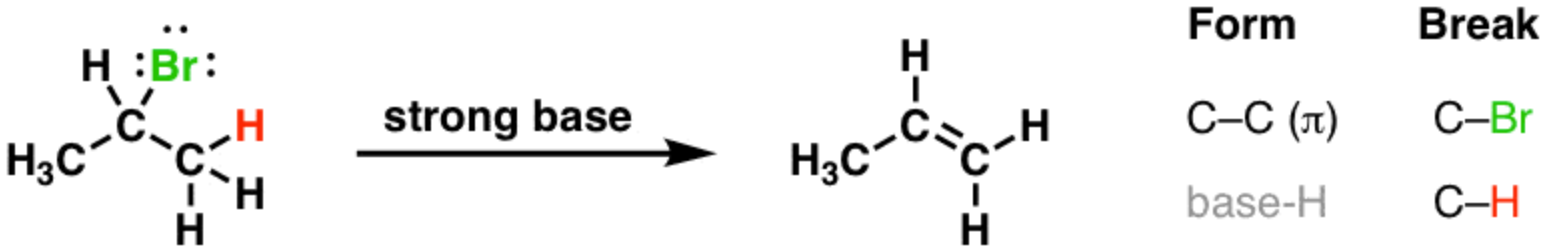


Form	Break
C_1–Br	C_1–C_2 (π)
C_2–Br	Br–Br

The Key Pattern Of All These Reactions Is That They Break A C–C Pi Bond And Form Two Single Bonds On Adjacent Carbons (The Exact Reverse Of Elimination)

Again, note the pattern – break C–C π [and Br-Br] and form C–Br bonds on adjacent carbons. [We'll deal with the dashes and wedges in subsequent posts – it's OK to just ignore them for now].

If you've got a really good memory, you might notice that this pattern is strangely familiar. If we go waaay back into the archives, we've seen a reaction that fits this pattern exactly…. but *in reverse!* It's our old friend the elimination reaction!



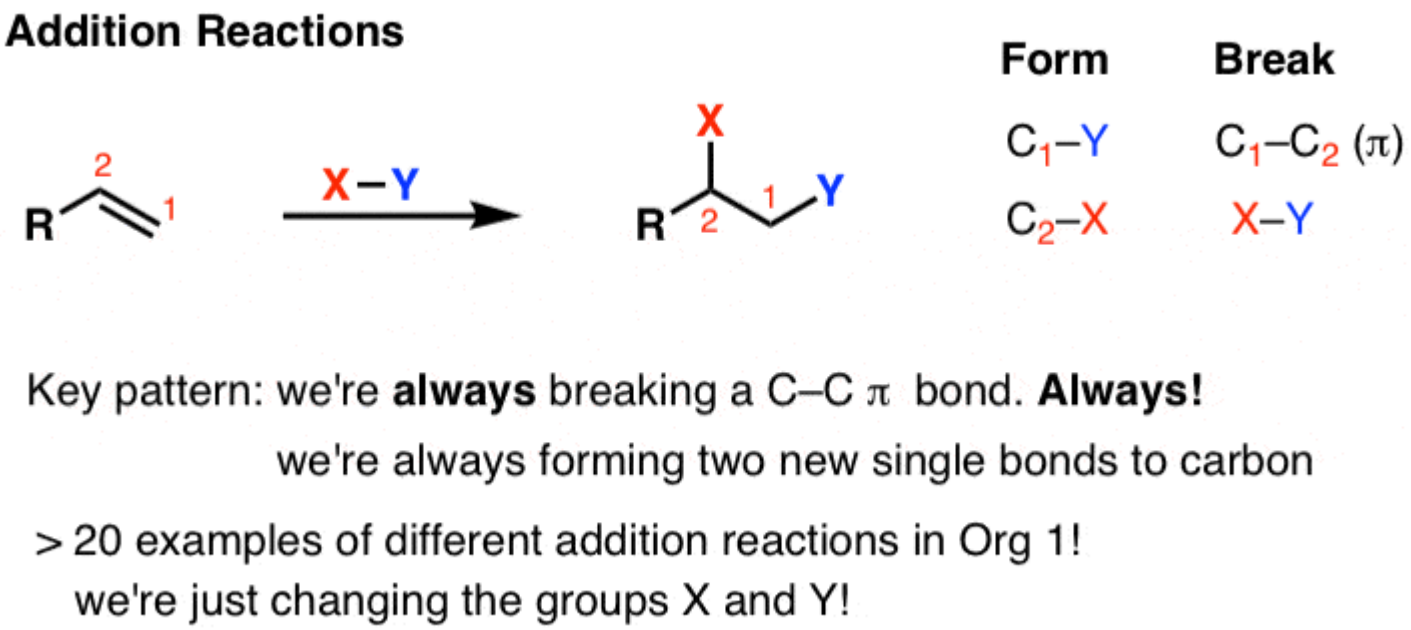
[I've left the "strong base" here as generic, but a typical example would be $NaOCH_3$ or $NaOCH_2CH_3$]

As we've previously seen, elimination reactions involve breaking two single bonds on adjacent carbons and forming a new C–C π bond. Notice how these two reactions (addition and elimination) achieve the exact opposite results here.

- In the addition reaction [the first reaction at the top of the page] , we're **forming** C-Br and C-H, and **breaking** C–C π [we're also breaking H-Br]
- In the elimination reaction, we're **breaking** C–Br and C–H, and **forming** C–C π [and forming a bond between the base and hydrogen]

The General Pattern For Addition Reactions

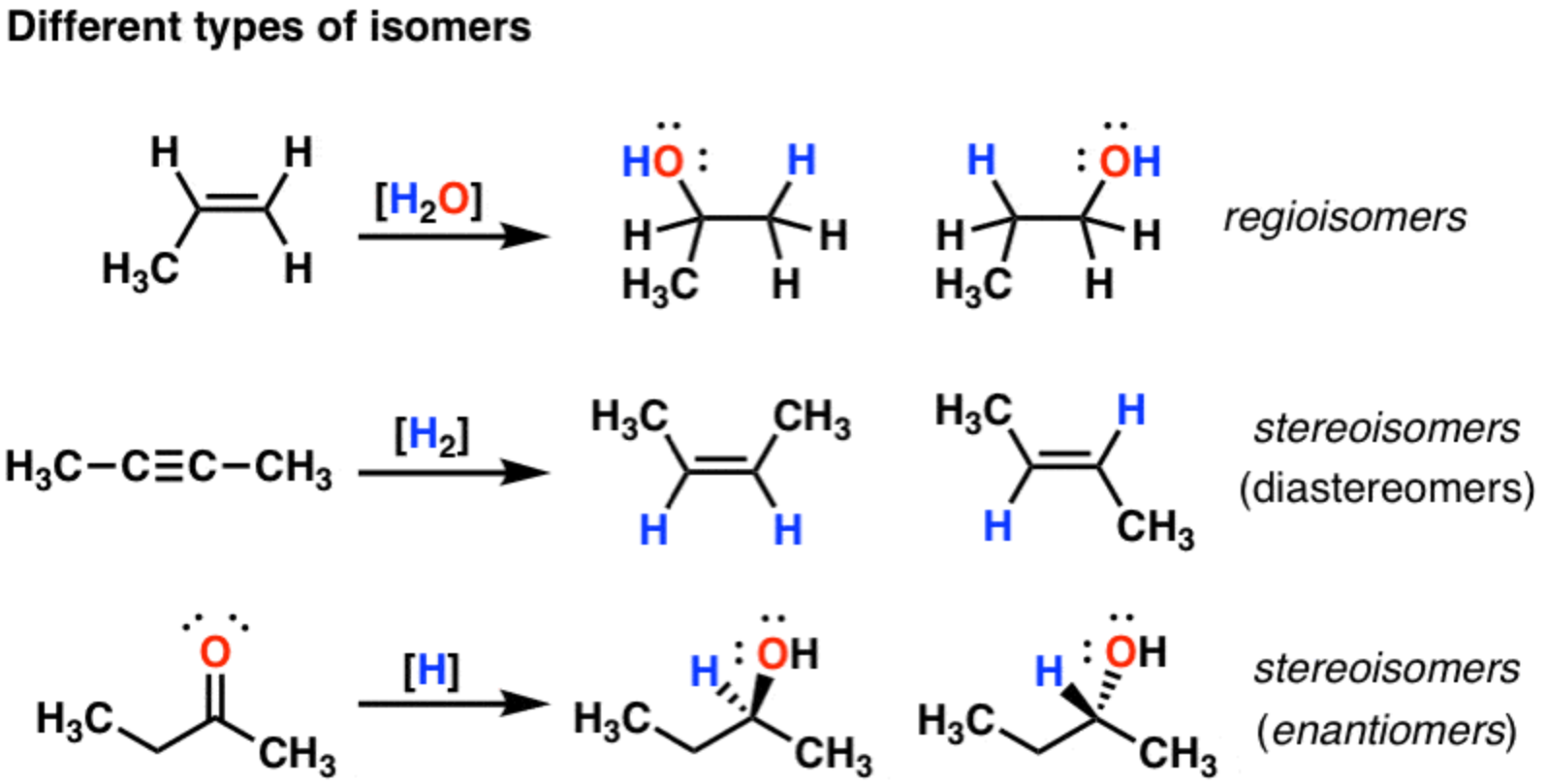
We can even generalize these patterns beyond this specific example of H-Br. Likewise, for addition reactions, the general pattern looks like this:



As we'll see , there are many, many more examples of addition reactions we'll see beyond the 3 examples we've seen here. But they all follow the same essential pattern. We'll always break a C-C π bond and we'll always be forming two new single bonds to carbon.

Selective vs. Specific

Many of the transformations you will encounter have the potential to create multiple products – isomers – from a single starting material. The reactions shown in the drawing, for instance (I've left the actual reactants vague) could each form a mixture of constitutional isomers (i.e. regioisomers), diastereomers, or enantiomers.



The potential of these reactions to produce multiple products is both a curse and an opportunity. It's a curse in that we have the potential to create multiple products, each of which have to be separated from each other. But it's an **opportunity** in that **if** we can develop reactions that can yield one isomer over the other (and vice versa) we have a very useful tool: we can start with a simple starting material – like an alkyne – and transform it into several complex products through a series of selective reactions. That's extremely powerful. (For that reason, I like to say that alkynes are like a blank canvas – you can decorate them many, many different ways).

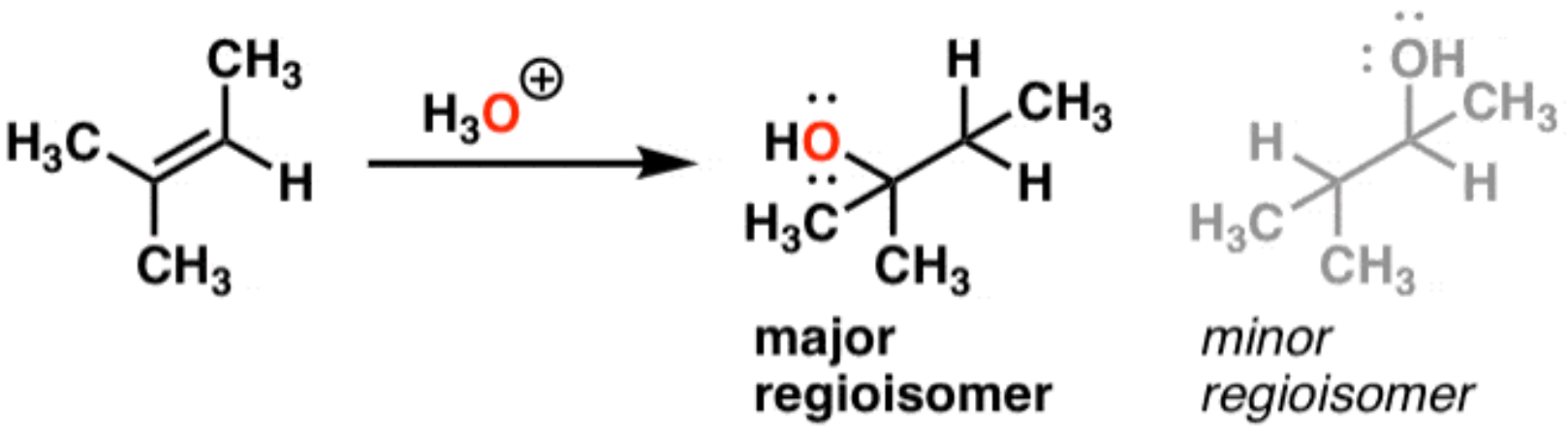
Here comes a part of organic chemistry terminology that can trip people up. We can have *selective* reactions and *specific* reactions. Selective means "mostly", or "almost all". Specific means "all". **"Selective" implies that there are factors which *favor* one product over the other, while "specific" is usually a sign that there's something inherent to the mechanism that leads to only <u>one</u> product.**

It might sound like semantics, but there's some disagreement on where to draw the line for "selective". For instance, is a reaction that gives you a 99:1 ratio selective or specific? I'm in the camp which believes that 99:1 is merely "highly selective". Specific reactions are 100:0 . I am always very careful not to use "specific" where "selective" would suffice. *The opinion of your instructor (or textbook) may vary.*

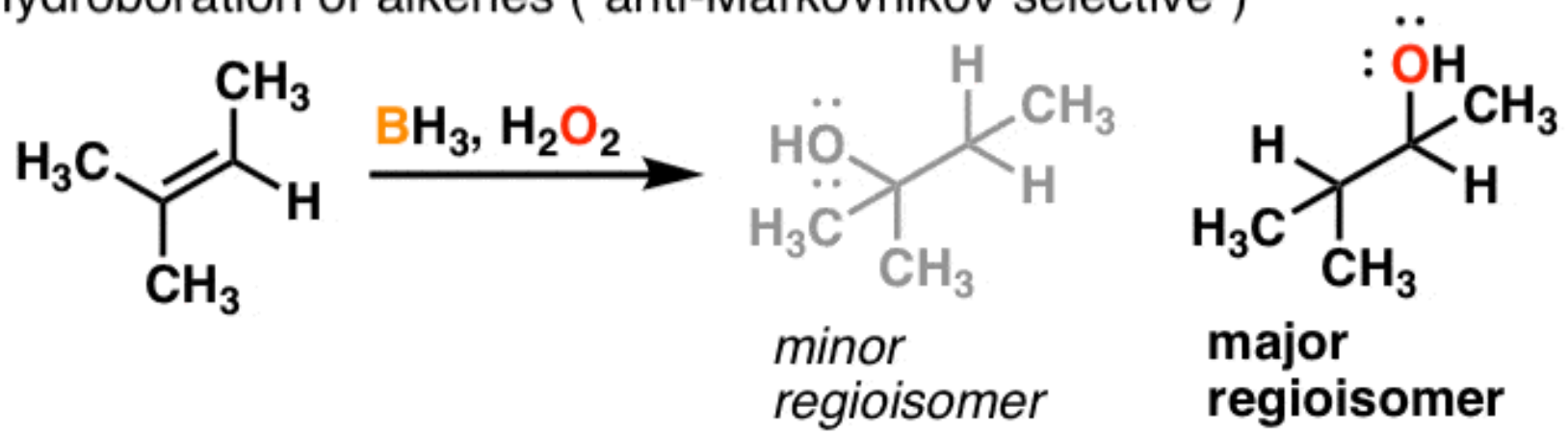
Let's look at some selective reactions:

Regioselective reactions

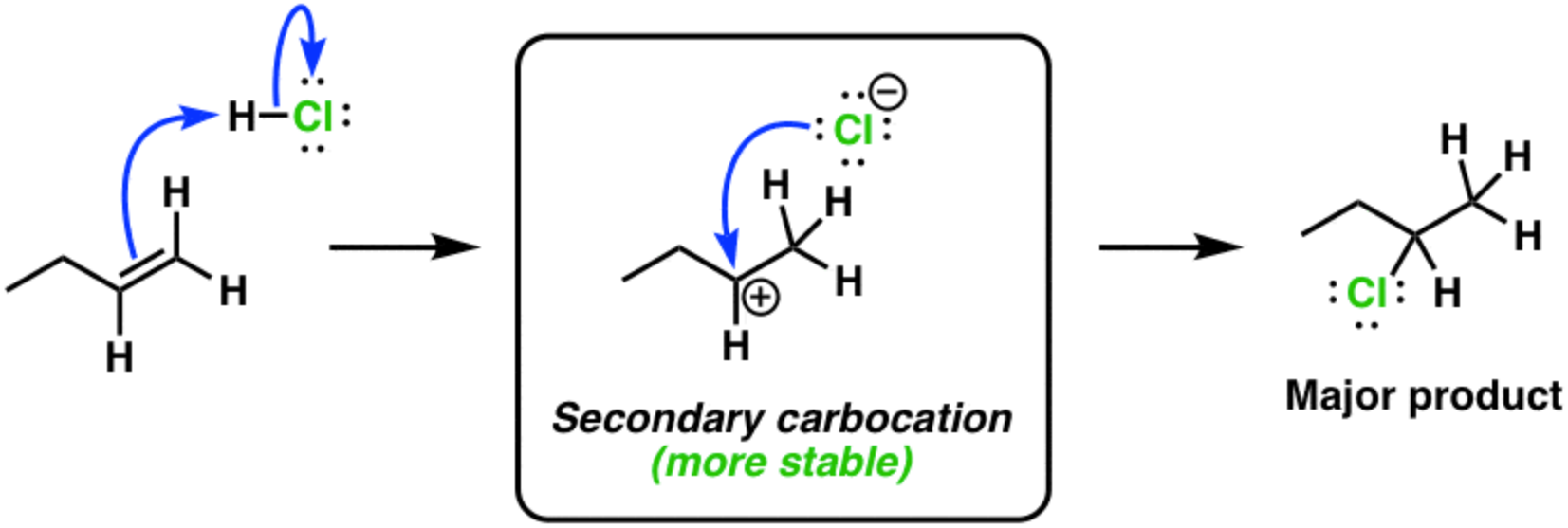
Hydration of alkenes with acid ("Markovnikov-selective")

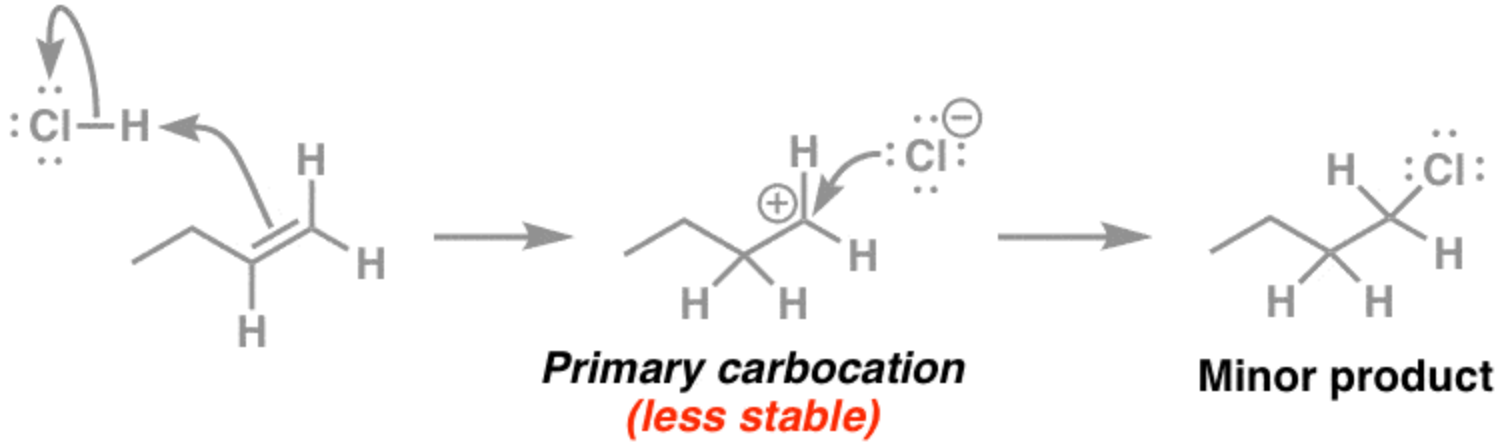


Hydroboration of alkenes ("anti-Markovnikov selective")

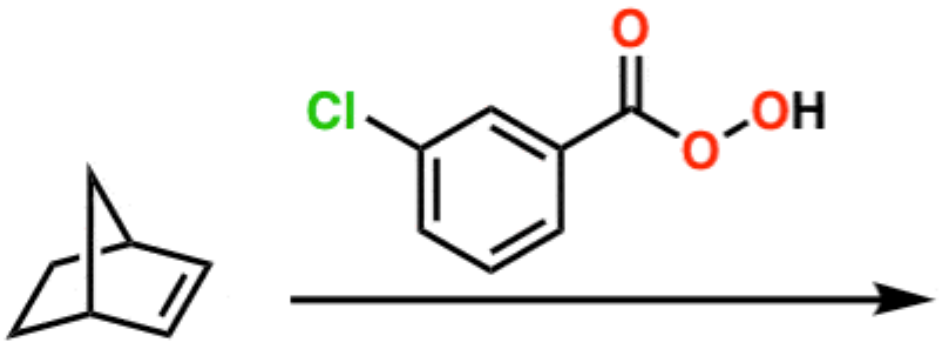


Regioselective reactions: This is where a starting material forms two (or more) structural isomers, and one predominates. A good example is Markovnikoff addition of water. The **major** product is where addition has occurred on the most substituted carbon. The mechanism doesn't rule out a small amount of the minor structural isomer. (Note that this reaction as shown, forms a 50:50 mixture of enantiomers. It is regioselective, but not enantioselective.) Hydroboration is another example of a regioselective reaction: it is highly selective for the less substituted alcohols. Like I said, some instructors might consider this reaction regiospecific, even if it is >99:1. I would make the case that it is merely highly regioselective.

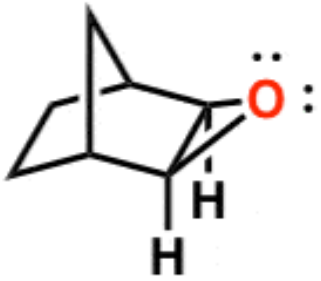

Secondary carbocation
(more stable)
Major product


Primary carbocation
(less stable)
Minor product

A stereoselective reaction

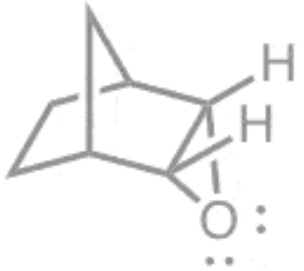


(Epoxidation using *m*-chloroperoxybenzoic acid, *m*-CPBA)



major stereoisomer

(attack on least hindered face)

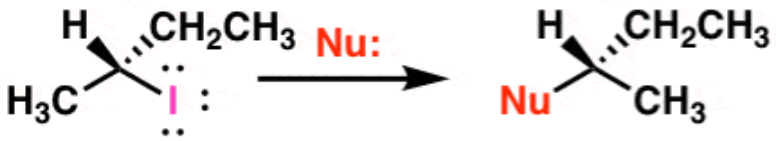


minor stereoisomer

Stereoselective reactions: An example of a stereoselective reaction is shown in the next drawing. In the 2.2.1 bicycle shown, attack of the per-acid from the top face is highly favored, which leads to dominant formation of the epoxide on the left. There is also a small amount of the epoxide on the right.

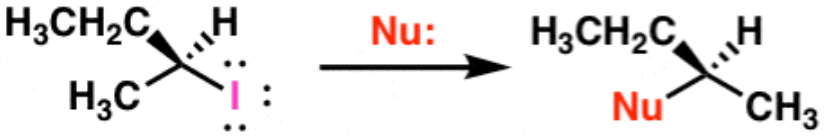
The S_N2 is a *stereospecific* reaction: a given starting material produces *only one* product

The S_N2 proceeds with *inversion*.



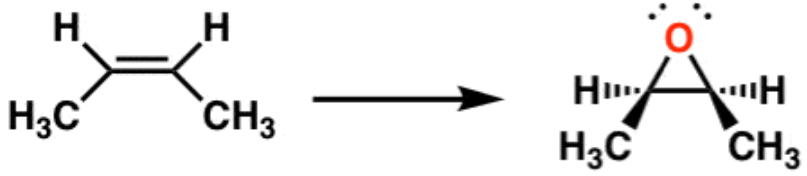
only product

(a 50:50 mixture of the two iodides will produce a 50:50 mixture of the two products)

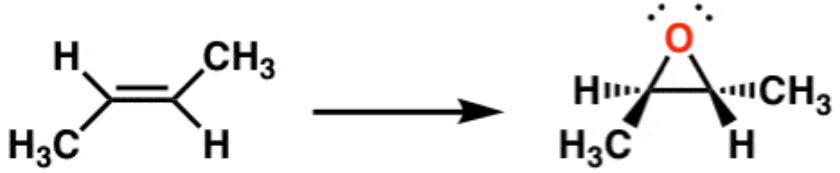


only product

Epoxidation is also stereospecific: *cis* alkenes give **only** *cis* products, and *trans* alkenes give **only** *trans* products.



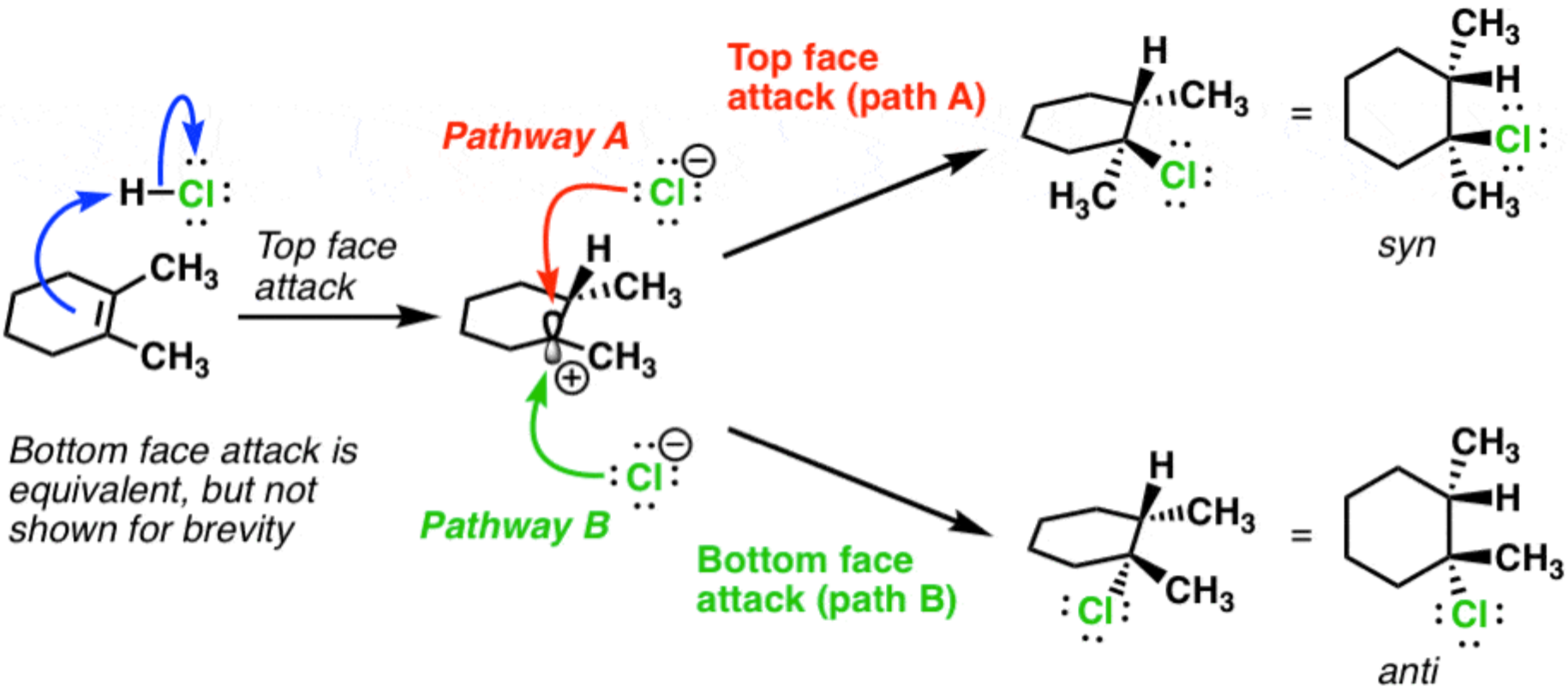
only product



only product

Other stereospecific reactions:
- Alkene bromination (gives *anti* dibromide)
- Hydroboration (hydrogen and boron are delivered *syn*)
- Hydrogenation (hydrogens are delivered *syn* to double bonds)
- E2 (proceeds through *anti* transition state)

A mixture of syn and anti products is consistent with a free carbocation, since the empty p-orbital can be attacked from either direction.



Note that the syn and anti products will not be formed in equal amounts, since the methyl group adjacent to the carbocation will shield the bottom face from attack to a greater extent than H will

Stereospecific reactions: A perfect example of a stereospecific reaction is shown in the third drawing. Because the SN2 proceeds through inversion (100%) a given starting material will produce the product with the inverted stereochemistry. The second starting material (the enantiomer of the one above) will produce the enantiomer (100%). Two different isomers go through the same reaction manifold to provide two different enantiomers. There is no "leakage" of one to the other.

There are actually quite a few examples of other stereospecific reactions. The hydroboration reaction is one (cis addition), as is catalytic hydrogenation (gives cis products), addition of bromine to double bonds (anti products), epoxidation, cyclopropanation, the Diels Alder, and more.

There are also reactions which are *enantioselective*. They aren't covered as much in Org 1/Org 2, but the 2001 Nobel prize in chemistry was given to Noyori, Sharpless, and Knowles for their development of some key enantioselective reactions. Some of the most cutting-edge organic chemistry going on at the moment is concerned with designing highly enantioselective reactions.

The concept of selectivity is not exclusive to one type of isomer. You can have a regioselective reaction that is not stereoselective (like the Markovnikoff addition of water to alkenes) as well as regioselective reactions that are also stereoselective (like hydroboration. In fact, enantioselective hydroborations have been developed, which are therefore regioselective, stereoselective (for the syn addition product) *and* enantioselective. It depends on what kind of isomers you can form from your substrate.

Regioselectivity In Alkene Addition Reactions

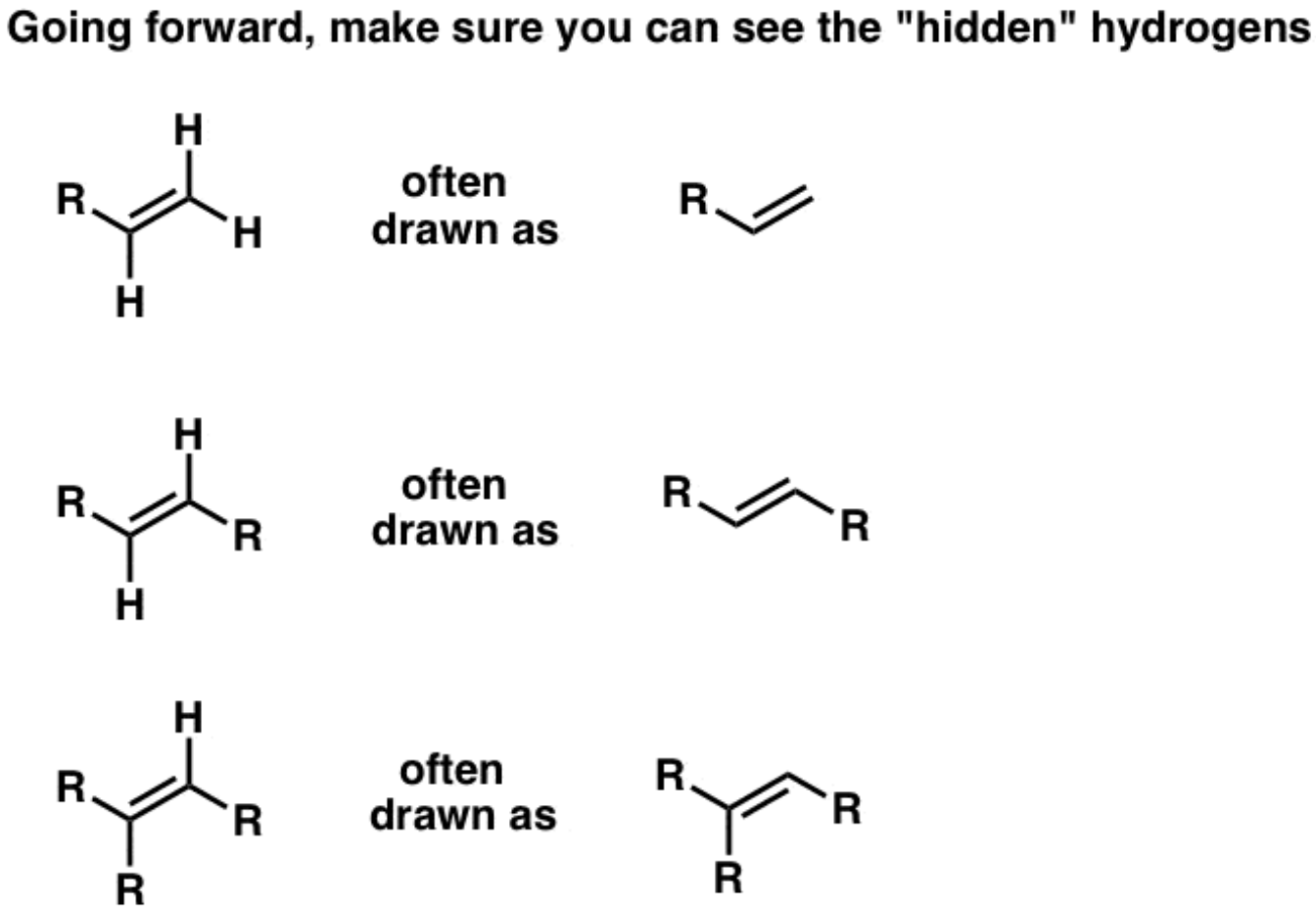
Alkene Addition Reactions: Regioselectivity

In the previous post on addition, we talked about the **key pattern of addition reactions** [break C-C π, form two new bonds to adjacent carbons] and how this is the exact **opposite** pattern of elimination reactions we went through earlier.

Since alkene addition reactions form bonds to ***two adjacent carbons,*** if the two new single bonds that are formed are to different atoms, we therefore have the potential to form **isomers**.

Make Sure You Can Recognize “Hidden” Hydrogens

Going forward, we’re going to use a lot of structure shortcuts. So it’s helpful to be able to see the “hidden” (or “implicit”) hydrogens that are present when you are looking at alkenes (and alkanes for that matter):



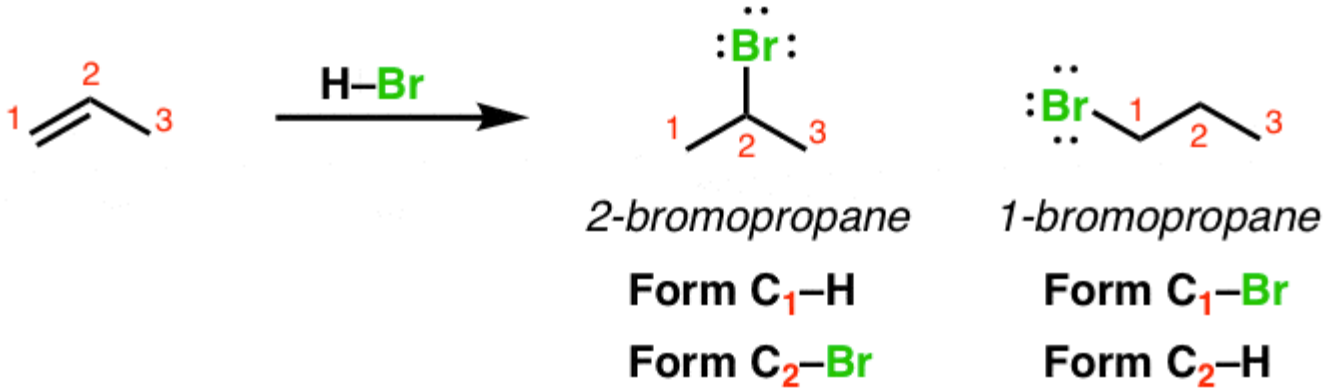
What Are "Regioisomers" ?

This post is all about one of the important consequences of reactions of alkenes that wasn't in effect for substitution and acid-base reactions: **regioselectivity.**

More on that in a sec. Think back to substitution reactions. When a substitution reaction occurs, normally what's happening is a swapping out of one bond for another on the **same carbon**. No adjacent atoms are involved [one exception, see Note 1].

With **addition reactions**, we have the potential to impact ***two adjacent carbons***. If the two new single bonds that are formed are to different atoms, we therefore have the potential to form **isomers**.

This reaction forms constitutional isomers



2-bromopropane

Form C_1–H

Form C_2–Br

1-bromopropane

Form C_1–Br

Form C_2–H

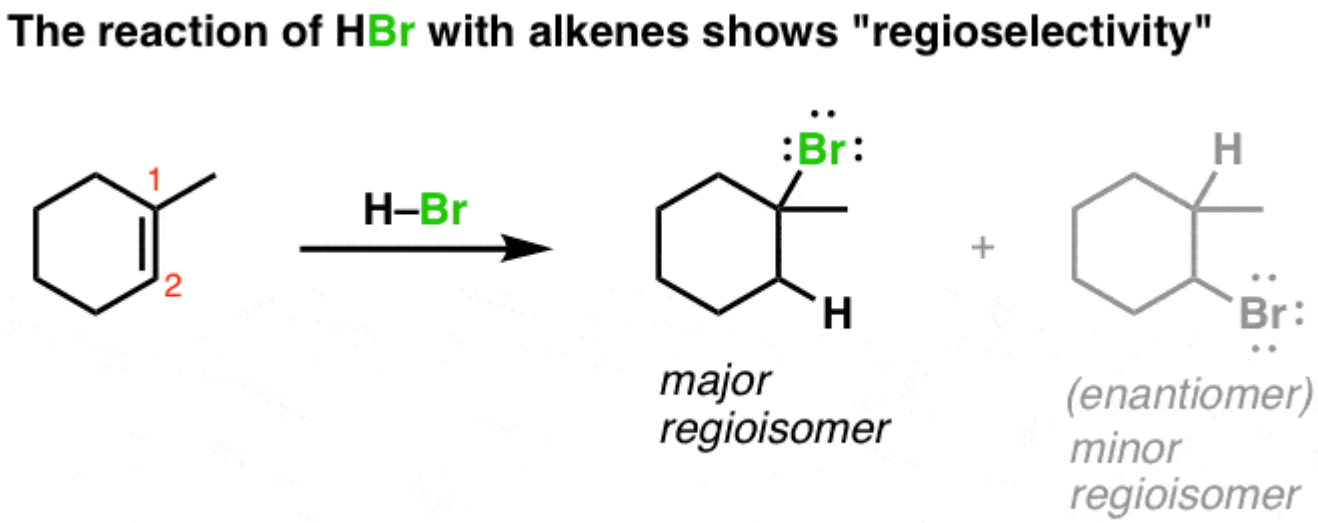
Since they arise from adding H and Br to different "regions" of the alkene, they are often called "regioisomers" in the context of addition reactions.

Notice how the two products drawn here? The product on the left is 2-bromopropane, and the product on the right is 1-bromopropane.

How are these compounds related to each other? They're **constitutional isomers** [same molecular formula, different connectivity]. In the context of addition reactions, however, there's another name we can use to describe the relationship between these molecules. Since H and Br add to a different region of the double bond in each case, these can also be called **regioisomers.**

Many Reactions Have A Strong Preference For Forming One "Regioisomer" Over The Other. This Property Is Called, "Regioselectivity".

As it turns out, it's very rare that two regioisomers are formed in equal yields. In fact, many reactions have a strong preference for forming one regioisomer over the other, a property called "**regioselectivity**". The addition of HBr to alkenes is a perfect example. As we'll see later, the structure of the alkene plays a key role in determining which product is favored.

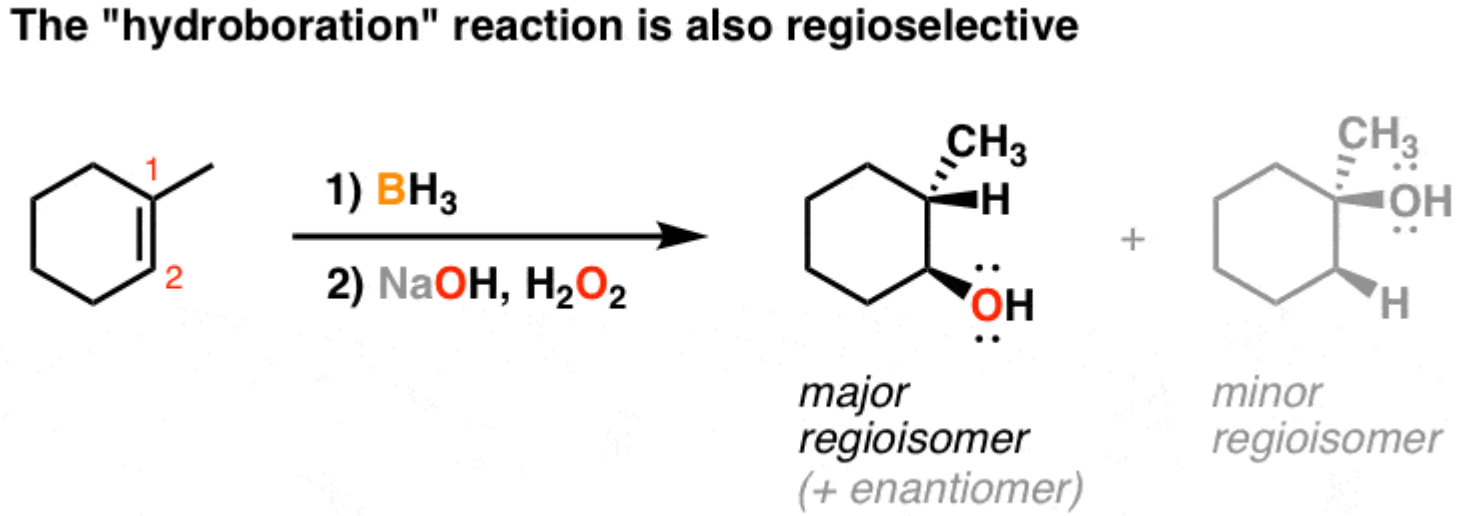


Note how in the major product, we have formed 1-bromo-1-methyl cyclohexane, and in the minor product, we form 2-bromo-1-methylcyclohexane.

If you don't understand how this reaction works right now, that's OK! In a subsequent post, we'll go through the "how" and "why" details. For now, just focus on the "what" – being able to see the bonds formed and broken, and recognize that these two products are isomers of each other.

Hydroboration: Another Example Of A "Regioselective" Reaction

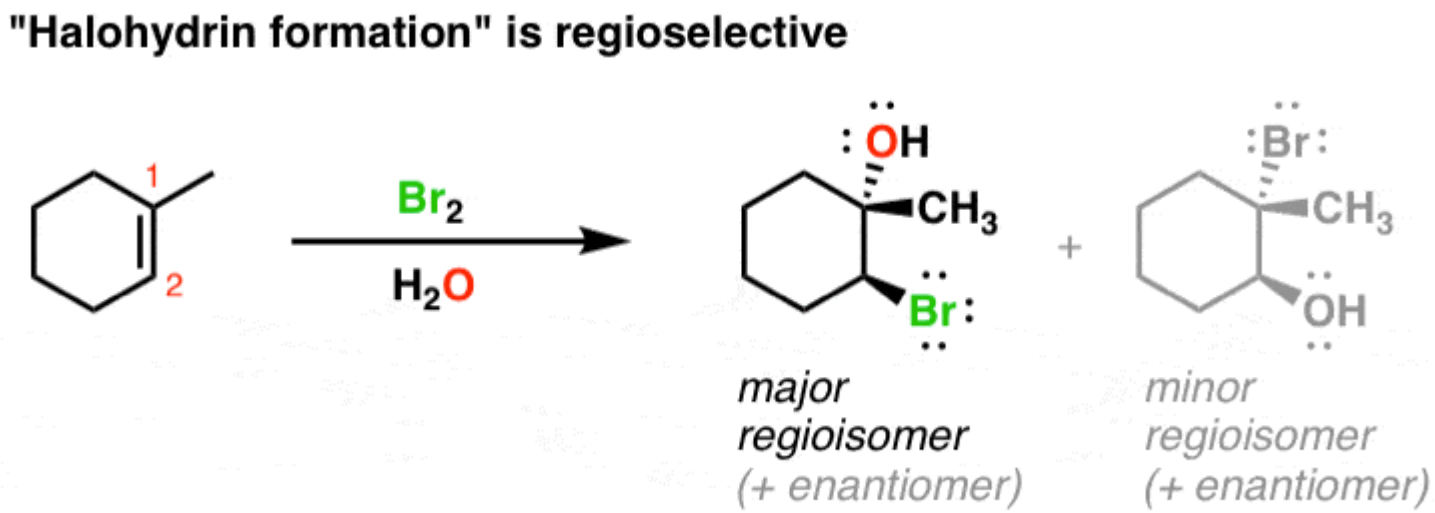
Here's an experimental result from a different reaction called "hydroboration", where we treat an alkene with borane (BH_3) and then sodium hydroxide and hydrogen peroxide. Again, we'll talk about the mechanism soon, but for now, focus on the bond patterns [again, don't need to worry about dashes/wedges for now either – all in good time].



Again note how we're forming regioisomers here. In this reaction, it's observed that the product on the left is formed in much higher yield than the product on the right. [The mechanism is covered here: Hydroboration of Alkenes – The Mechanism]

Formation Of “Halohydrins” Is Also Regioselective

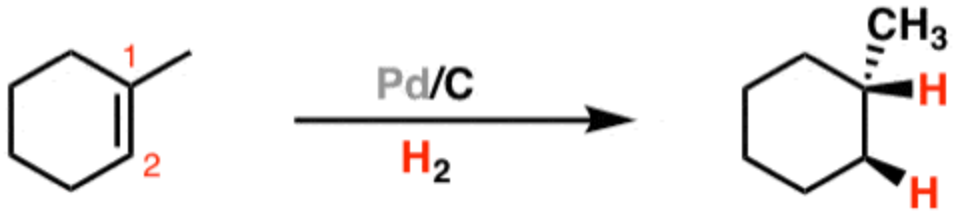
Here’s another example, in a reaction called “halohydrin formation”. Note the placement of the OH and the Br. See how they’re different? The product on the left is favored.



Not All Addition Reactions Produce Regioisomers

Not all addition reactions produce regioisomers. For example, "hydrogenation" – treatment of alkenes with a metal catalyst (palladium over carbon or Pd/C) and hydrogen gas – gives the following product. Since we're forming C-H bonds on both sides of the alkene, it's not possible to form regioisomers here.

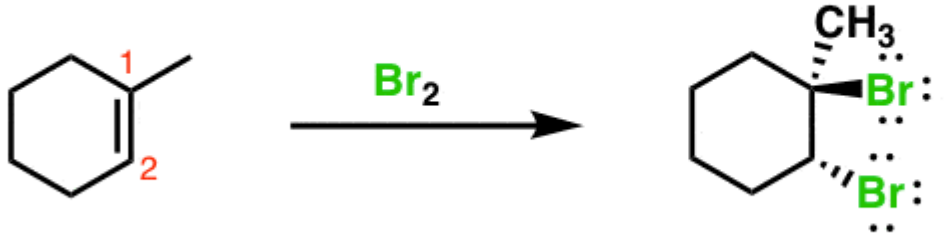
"Hydrogenation" of alkenes cannot form regioisomers



Only product

The same is the case for the addition of bromine (Br_2) to alkenes. Since we're forming C-Br on both carbons, regioselectivity isn't an issue here.

Similarly, bromination of alkenes cannot form regioisomers



(+ enantiomer)

Stereoselectivity In Alkene Addition Reactions: Syn vs Anti Addition

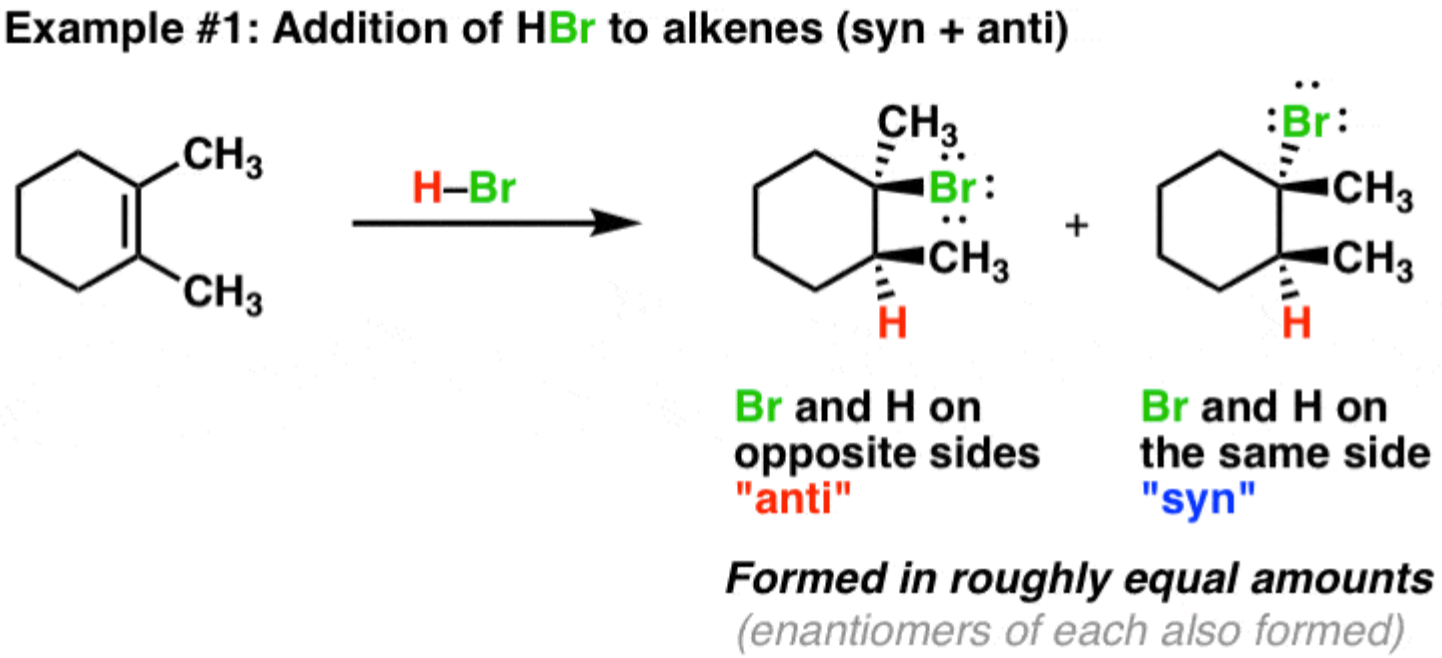
A Collection Of Observations That Nobody Predicted Ahead Of Time Until They Did The Experiment

Those three reactions we'll look at today are addition of HBr, bromination with Br_2, and hydrogenation with Pd-C and H_2. However, later we'll see that each of these reactions is characteristic of a particular "family" of reactivity for addition reactions. (The carbocation pathway, the "3-membered ring" pathway, and the "concerted" pathway)

Remember, these are results from *experiment.* They are *observations.* Without prior knowledge, it isn't possible to predict from first principles how they proceed – those who discovered these reactions in the late 1800's and early 1900's didn't know what we know now.

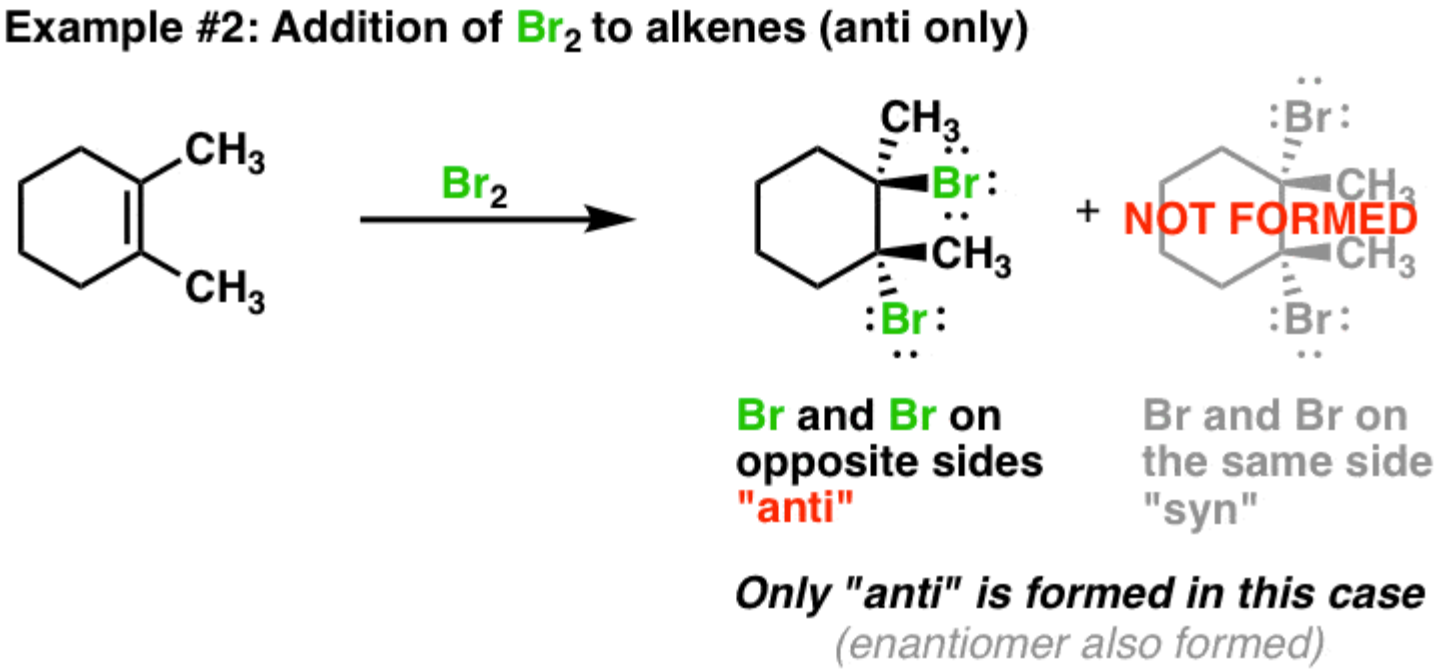
Addition Of H-Br To Alkenes Is Not Stereoselective, And Gives A Roughly Equal Mixture Of "Syn" And "Anti" Products

First example: let's take a cyclic molecule like 1,2-dimethylcyclohexene and treat it with hydrobromic acid (HBr). Here's what we get.



Addition Of Bromine (Br_2) To Alkenes Is Stereoselective, Giving "Anti" Addition Stereochemistry

Let's look at a different reaction next. When we treat an alkene with a halogen such as Br_2, (often in a halogenated solvent such as CH_2Cl_2 or CCl_4) we obtain the following product using 1,2-dimethylcyclohexene.

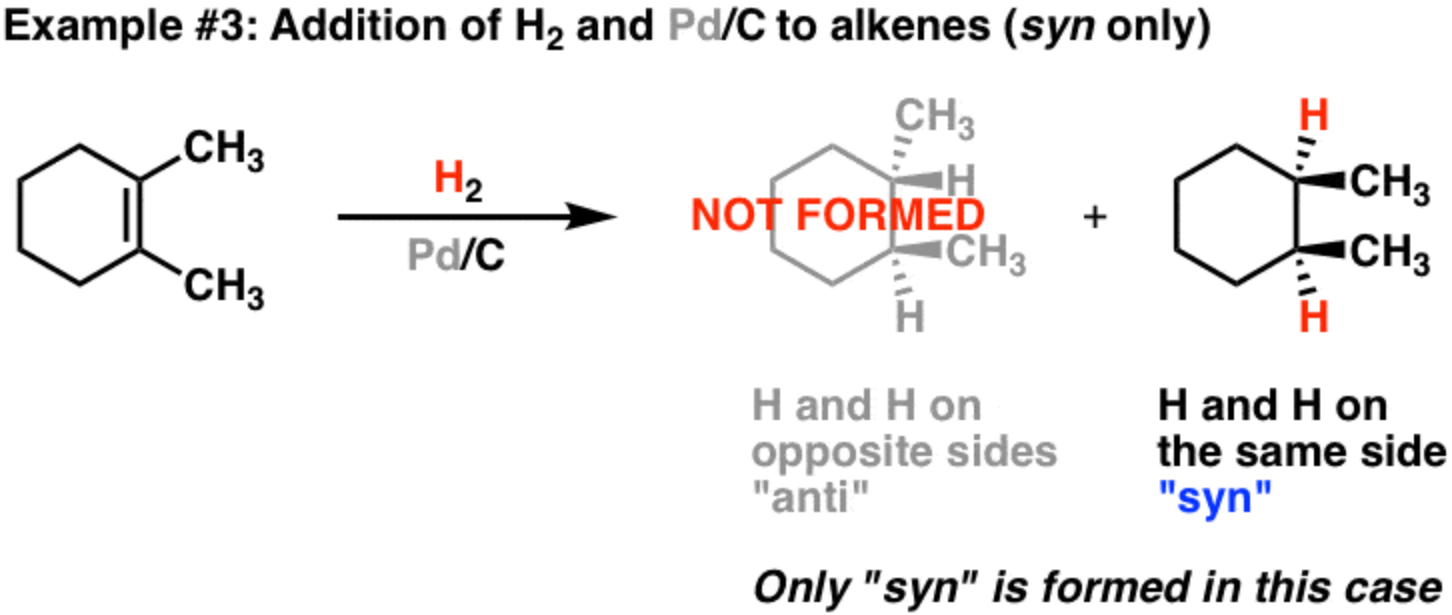


Again, pay attention to the dashes and wedges. Here, notice that we observe **only** the “anti” product and **none** of the “syn” product. In other words, the reaction is highly **selective** for one stereoisomer over the other. We could go even further and say that because of the complete absence of the “syn” product, the reaction is **stereospecific** for the “anti”. Only one type of stereoisomer is formed.

We’ll see that this pattern is observed for other reactants similar to Br_2. Again, any mechanism we propose will have to account for the fact that we **only** get the “anti” product and none of the “syn”.

Hydrogenation Of Alkenes With Pd-C and H_2 Is Selective For "Syn" Addition Stereochemistry

Finally, let's look at a third category of addition reaction. When 1,2-dimethylcyclohexane is treated with hydrogen gas and palladium catalyst (Pd-C), the result is as follows:



Notice how the only product of this reaction is the one where two hydrogens have added to the same face of the alkene ("syn" stereoselectivity). The product where hydrogens add to opposite faces is not observed. Again, this is an example of a highly **stereoselective** reaction. The mechanism will once again have to explain why we only obtain the syn product of this reaction and none of the anti product.

Summary: Stereoselectivity For Syn vs Anti Products In Alkene Addition Reactions

The key point from this post is to **pay close attention** to the stereochemistry of addition reactions.
There are three key categories of alkene reaction pathways:

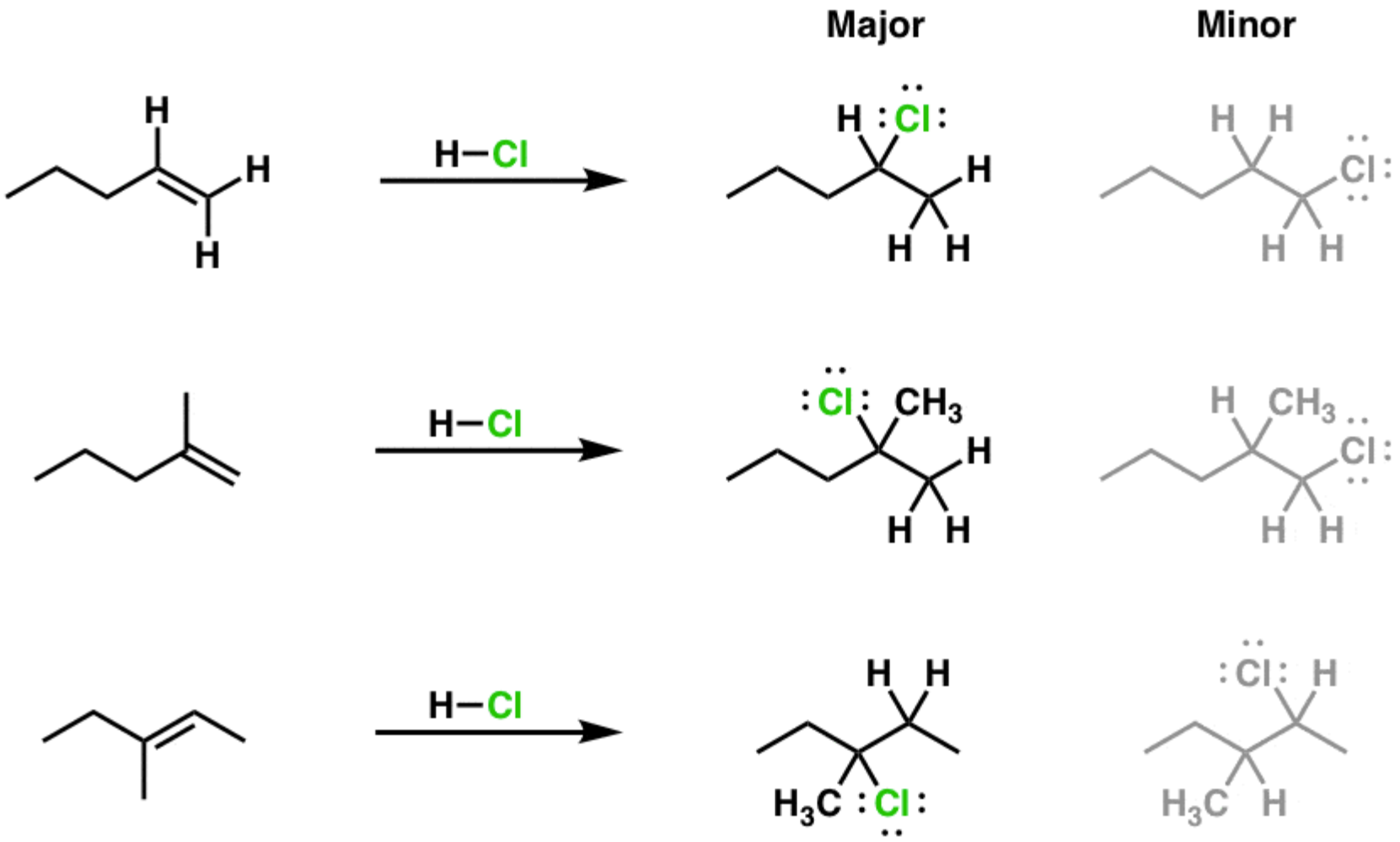
- an non-stereoselective mixture of syn vs anti products (e.g. H-Br to alkene)
- reactions that are stereoselective for the anti product (e.g. Br2 to alkene)
- reactions that are stereoselective for the syn product (e.g. Pd-C/H2 to alkene)

Different reagents can lead to very different stereochemical results – a point which is often tested for by organic chemistry instructors. Stereochemistry really is the key theme of Org 1!

Markovnikov Addition Of HCl To Alkenes

Having discussed the concepts of “regioselectivity” and “stereoselectivity” of alkene addition reactions, let’s go back to “regioselectivity” for a moment.
We said earlier that the reaction of HCl and HBr (among others) with alkenes is “regioselective”. In this post we give several examples of these regioselective reactions and trace them back to the observations of a Russian chemist in the 1880’s, Vladimir Markovnikov. (In the next post, we will show how these observations give us important clues about the mechanism of this reaction.)

What Is The Common Pattern In These Three Addition Reactions Of HCl To Alkenes?

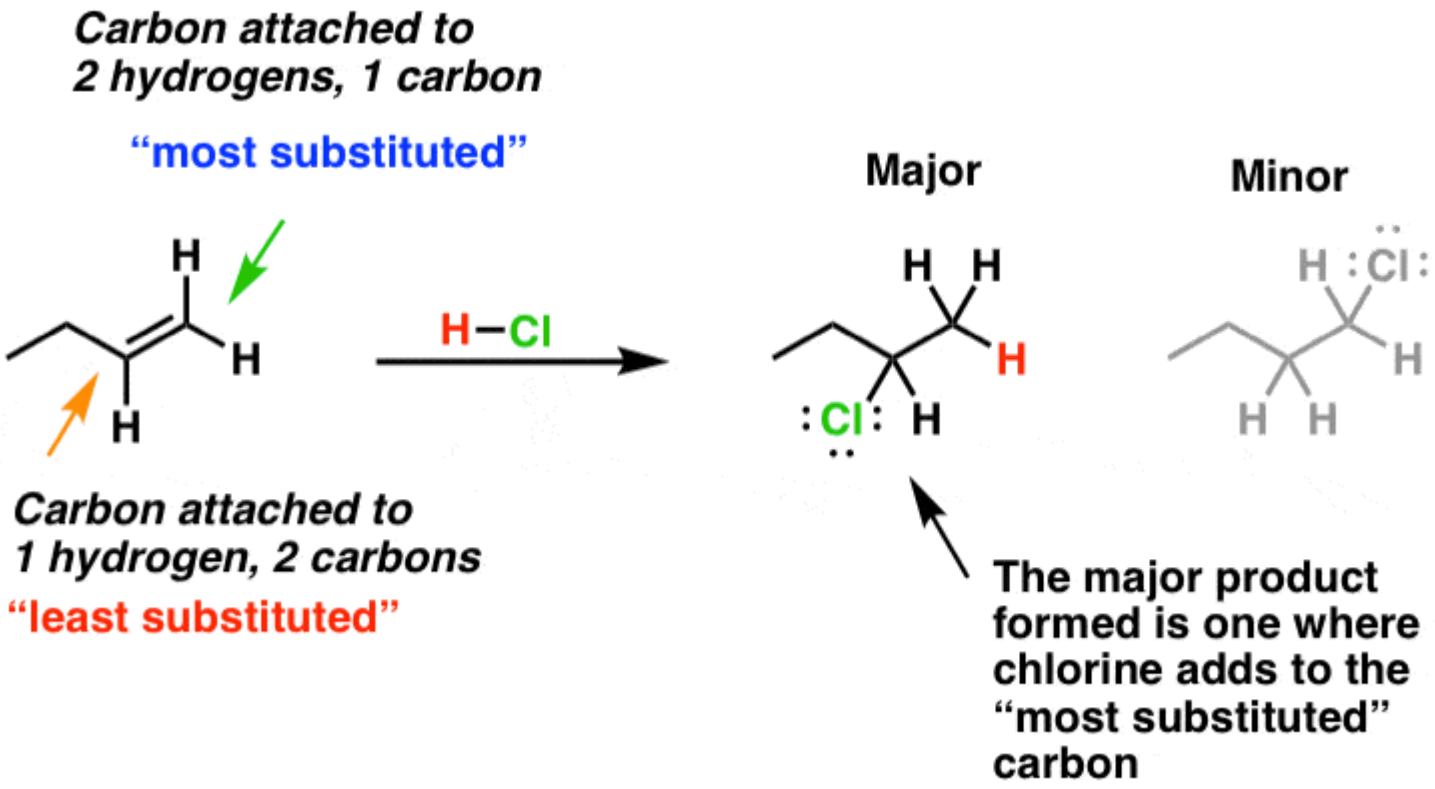


The Major Product Is The One Where Hydrogen Adds To The Carbon Of The Pi Bond With The Most Hydrogens

The major product in each case is always the one **where the hydrogen adds to the pi-bonded carbon with the most hydrogens, and the chlorine adds to the carbon with the fewest hydrogens.**

In other words, this reaction is **regioselective.**

To describe this, the term "most substituted" is often thrown around a lot, so here is a graphical explanation:



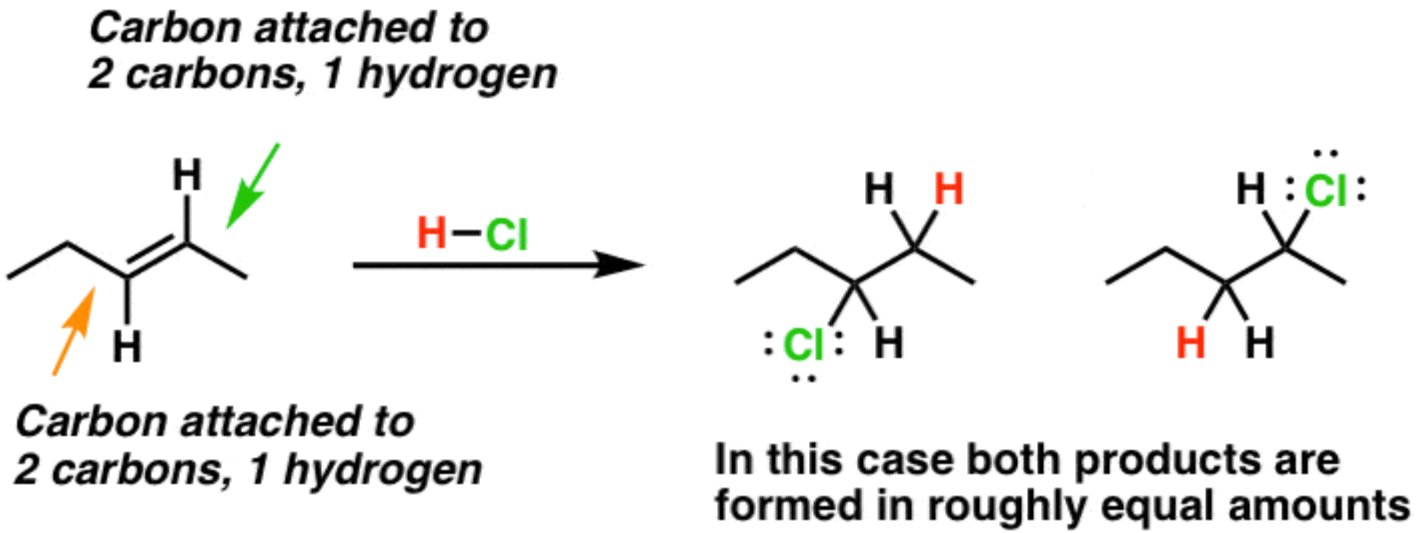
For our purposes,

- the "**most substituted**" carbon is the carbon of the alkene that is attached to the most carbons (or "fewer number of hydrogens", if you prefer).
- the "**less substituted**" carbon is the carbon of the alkene that is attached to the fewest carbons (or "greater number of hydrogens")

Addition Of HCl, HBr, And Other Acids To Alkenes Follows "Markovnikov's Rule"

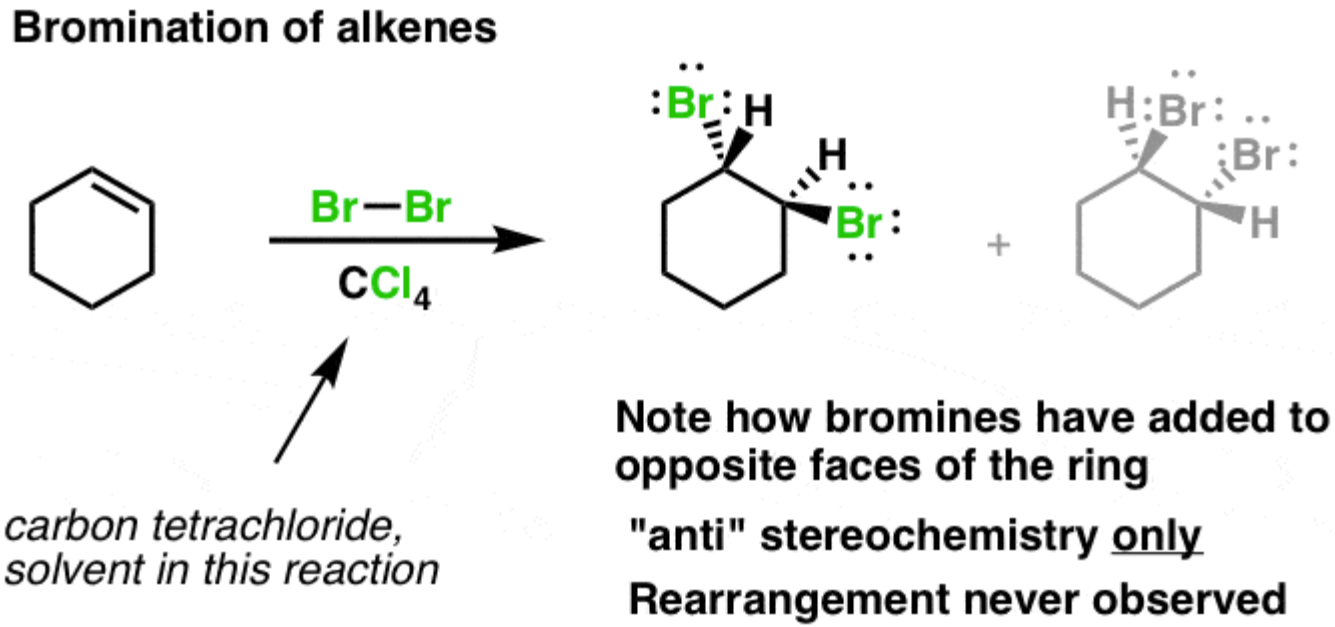
This pattern is not unique to the reaction of HCl with alkenes. It also applies to the reaction of HBr, HI, and other strong acids with alkenes. This empirical observation was first pointed out in 1870 by one Vladimir Markovnikov and this pattern of regioselectivity has become known as "Markovnikov's rule":

"*when an unsymmetrical alkene reacts with a hydrogen halide to give an alkyl halide, the hydrogen adds to the carbon that has the greater number of hydrogen substituents, and the halogen to the carbon having the fewer number of hydrogen substituents*"



Bromination of Alkenes Gives *anti* Products

1. Bromination Of Alkenes Observation #1: Only *anti* Products Are Observed



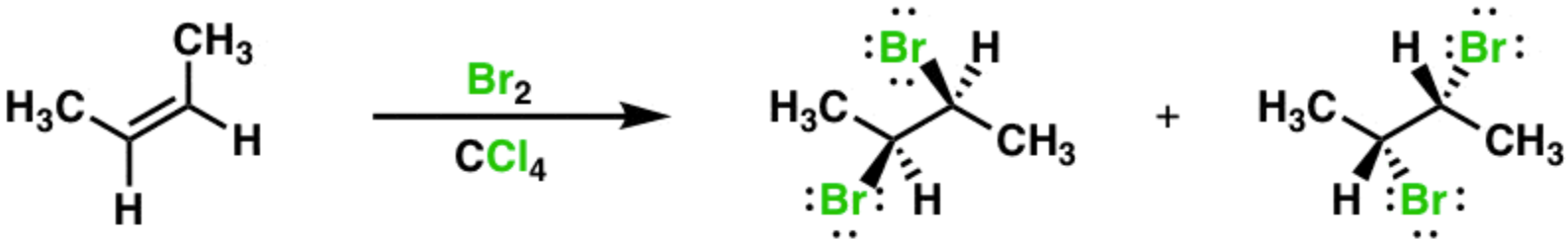
2. Bromination of Alkenes Observation #2: The Reaction Is Stereospecific

For instance if we treat cis-2-butene [aka (Z)-2-butene] with Br_2, we get a mixture of enantiomers.

But if we treat trans-2-butene, we only get a single product ("meso" 2,3-dibromobutane), which is itself a diastereomer of (S,S)-2,3-dibromobutane and (R,R)-2,3-dibromobutane.

These starting materials, *cis*-But-2-ene and *trans*-But-2-ene, which differ only in the configuration of the double bond, lead to stereoisomeric products. This type of process is given the name, stereospecific.

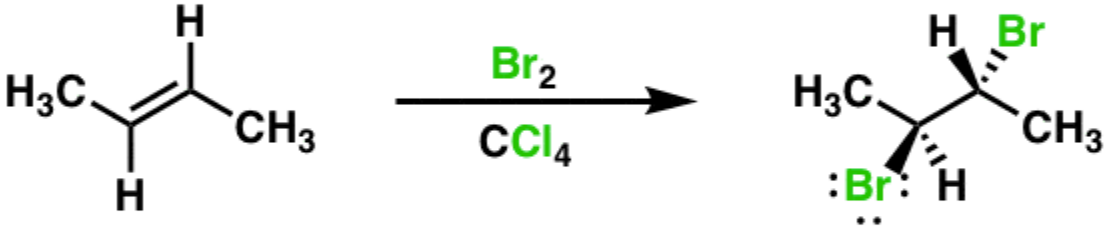
Cis and _Trans_ 2-butene give different products!



cis-2-butene

(*S,S*)-2,3-dibromobutane

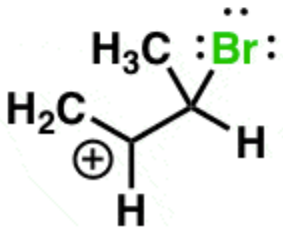
(*R,R*)-2,3-dibromobutane



trans-2-butene

one compound
meso-2,3-dibromobutane

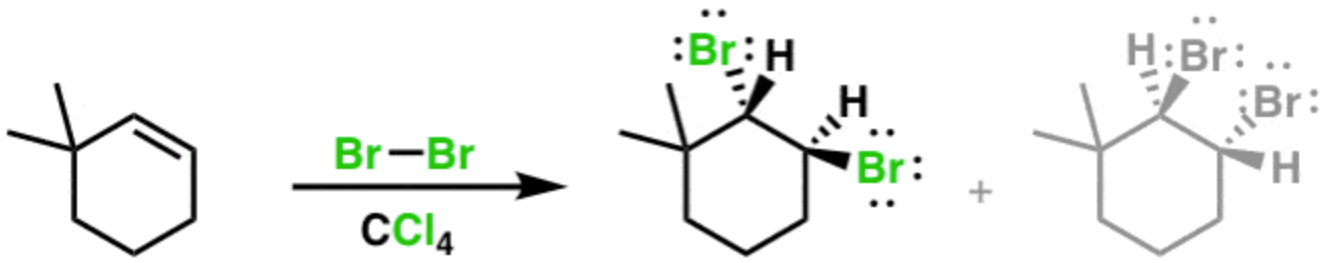
This is inconsistent with a carbocation intermediate



free rotation would allow for all possible 2,3-dibromobutane products from either isomer of 2-butene

3. Observation #3: Rearrangements Are Never Observed

Rearrangement does not occur in bromination reactions

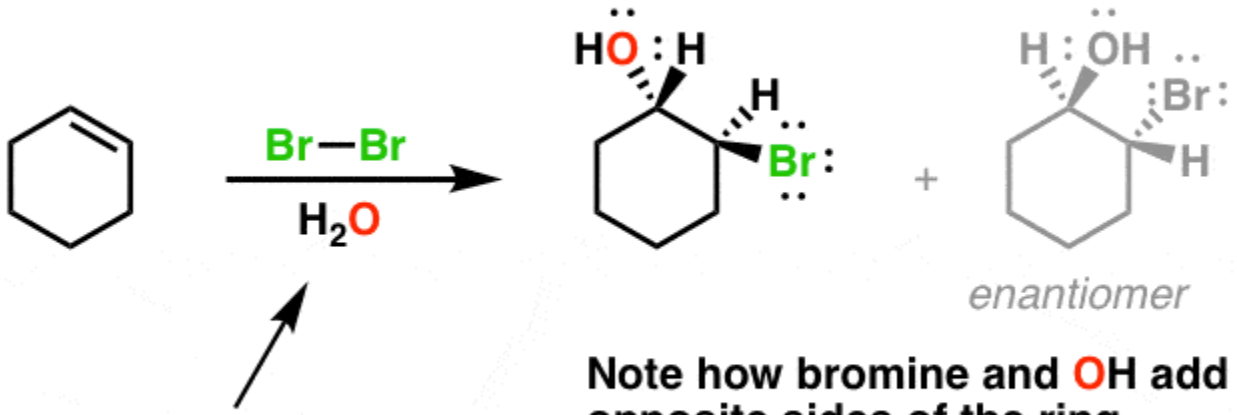


Rearrangement not observed

Argues *against* a carbocation intermediate

4. Observation #4: Certain Solvents Can Affect The Reaction Products

Bromination of alkenes in water

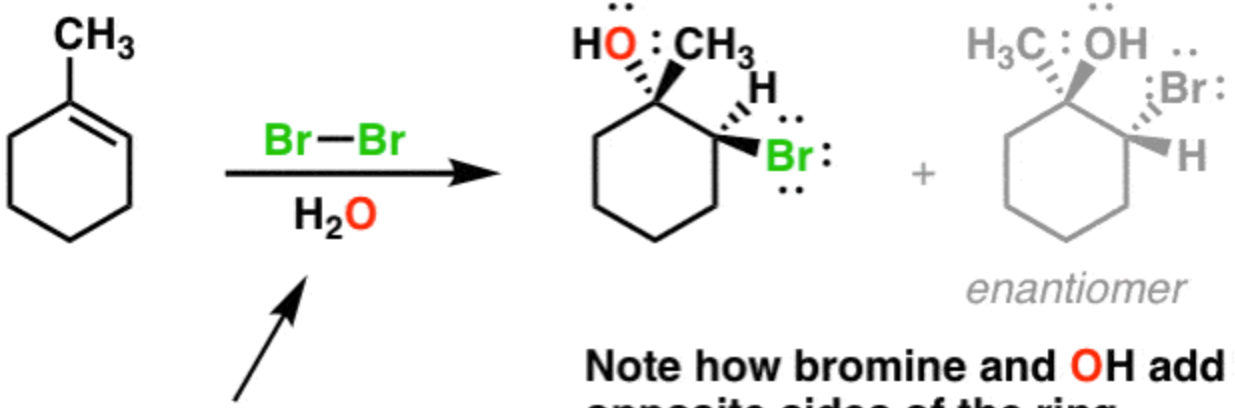


water is the solvent for this reaction

Note how bromine and OH add to opposite sides of the ring

"anti" stereochemistry only

Substituted alkenes

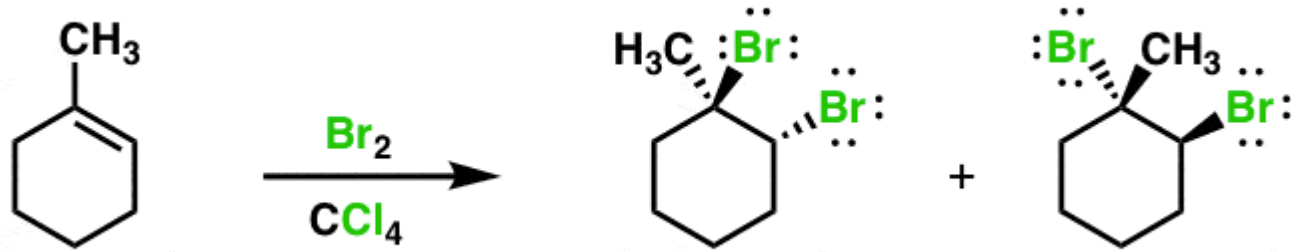


Note how bromine and OH add to opposite sides of the ring

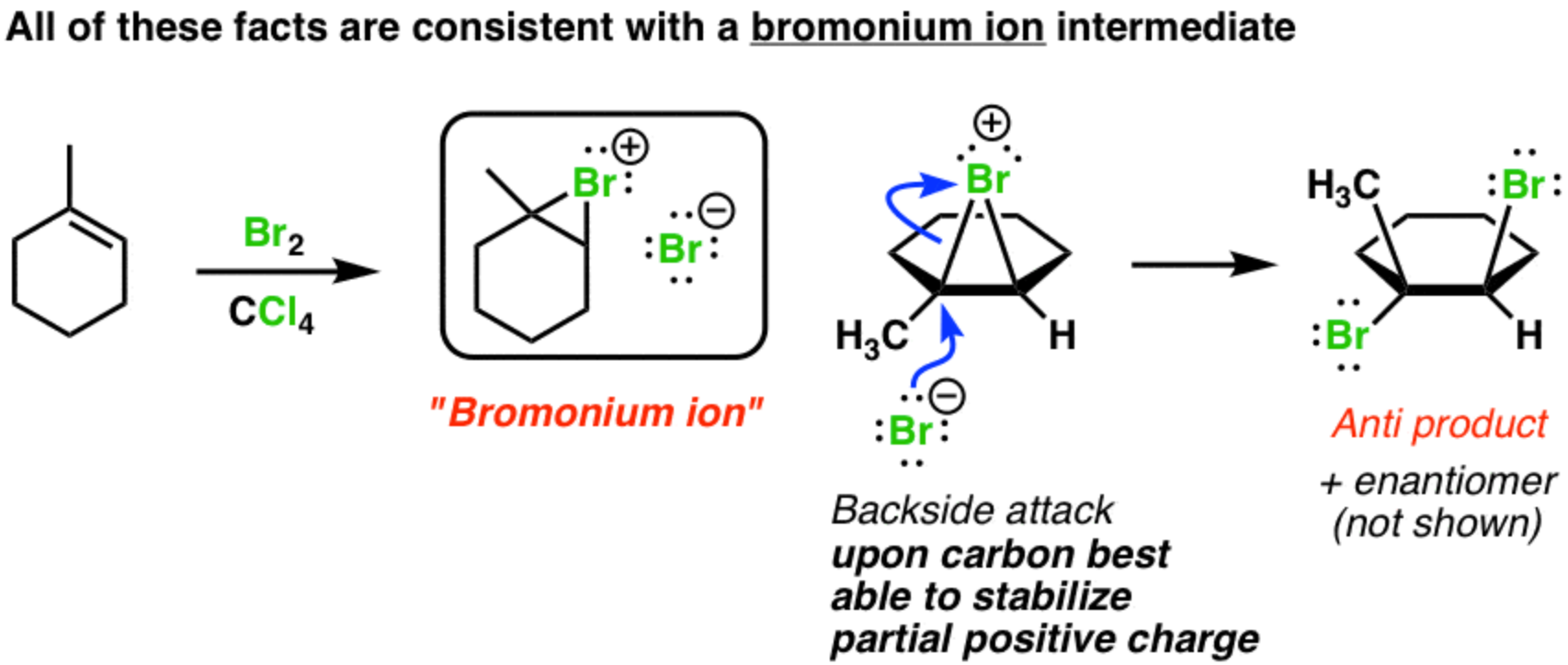
"anti" stereochemistry only

OH preferentially adds to most substituted carbon

1. It's stereoselective. The two atoms that form new bonds to carbon add to **opposite faces of the alkene** ("anti" stereoselectivity)
2. The reaction is *stereospecific* – (Z)-2-butene gives different product(s) than does (E)-2-butene (in fact, the products are stereoisomers of each other).
3. **No rearrangements** are observed, as they are for, say, the reactions of H-Cl with certain alkenes



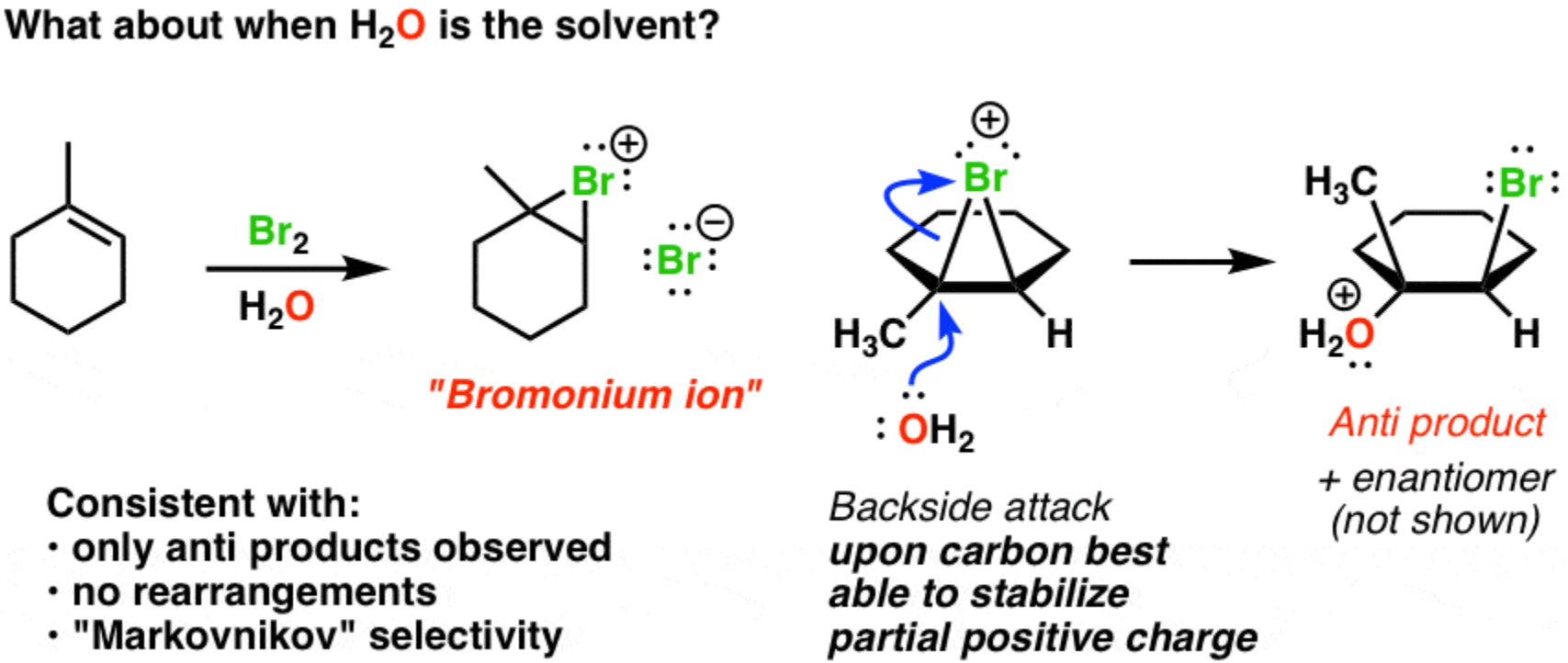
1. The Bromination Mechanism Proceeds Through A 3-Membered "Brominium Ion" Intermediate



[Worth noting: bromination of alkenes is technically an oxidation reaction, because each carbon goes from being bound to another carbon (0) to bromine (–1). The oxidation state of each carbon in ethene is +2; the oxidation state of each carbon in dibromoethane is +1.]

2. When Water Or Alcohols Are The Solvent, "Marknovnikov" Regioselectivity Is Observed In The Formation of Bromohydrins

If we use a solvent which can potentially act as a nucleophile such as water or an alcohol, the intermediate halonium ion can be "trapped" by solvent, giving rise to "halohydrin" products in the case where the solvent is water. Again, note that the water molecule attacks the most substituted carbon:



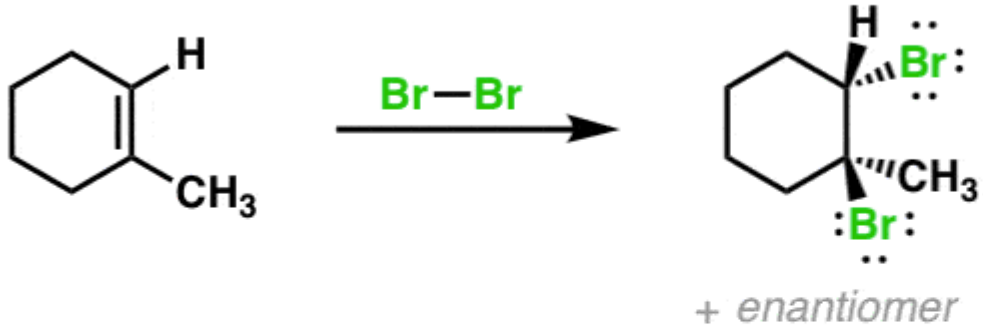
Why the most substituted carbon? Because that's the carbon best able to stabilize positive charge, and **since it has the most partial positive character, it will also be the most electrophilic of the two carbons.**

Alkene Addition Pattern #2: The “Three-Membered Ring” Pathway

The “Three-Membered Ring” Pathway In Alkene Mechanisms: Halogenation, Oxymercuration, Halohydrin Formation, and Acidic Epoxide Opening

1. Bromination of Alkenes: The Mechanism

Bromination of Alkenes



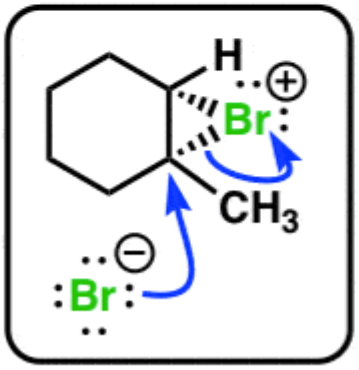
Stereochem

Anti

Regiochem

Markovnikov

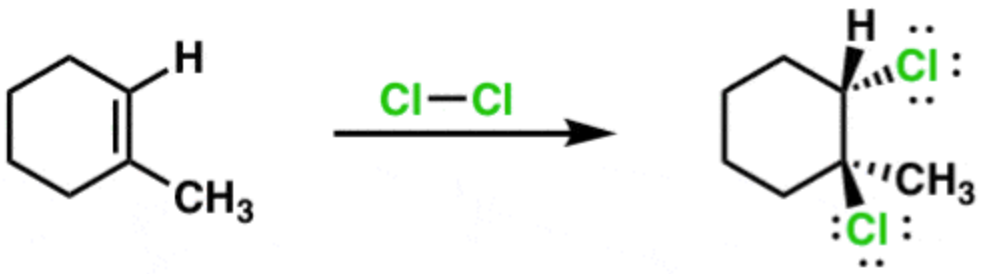
(although not relevant here)



via bromonium ion

2. Chlorination of Alkenes: The Mechanism

Chlorination of Alkenes



+ *enantiomer*

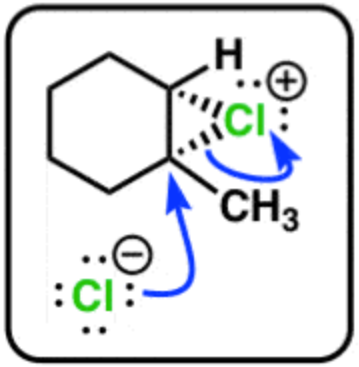
Stereochem

Anti

Regiochem

Markovnikov

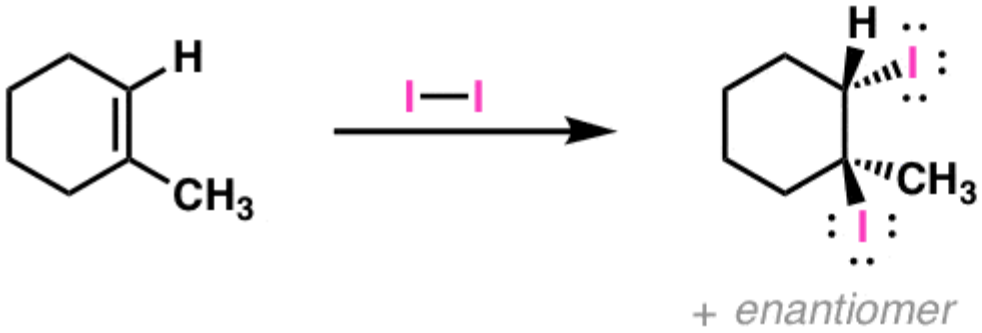
(although not relevant here)



via chloronium ion

3. Iodination of Alkenes: The Mechanism

Iodination of Alkenes



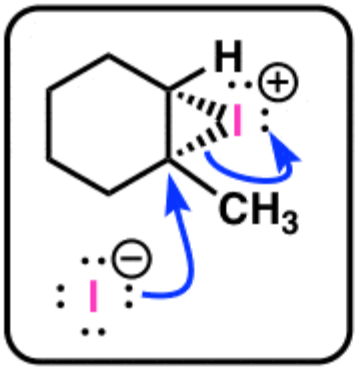
Stereochem

Anti

Regiochem

Markovnikov

(although not relevant here)

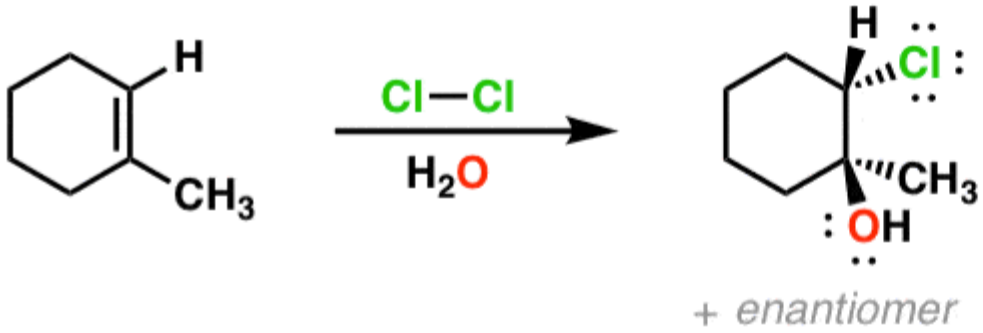


via iodinium ion

4. Chlorohydrin Formation: The Mechanism

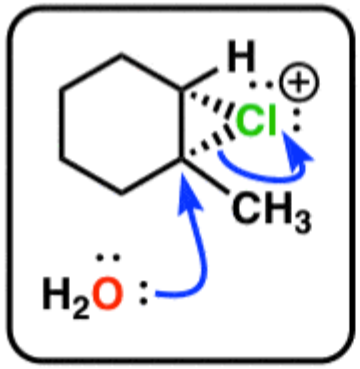
This also applies to reactions where the intermediate chloronium ion is trapped with solvent (water in this case). After deprotonation of R–OH+ to give R–OH, the product is referred to as a "chlorohydrin"

Chlorohydrin Formation



Stereochem *Anti*

Regiochem *Markovnikov*

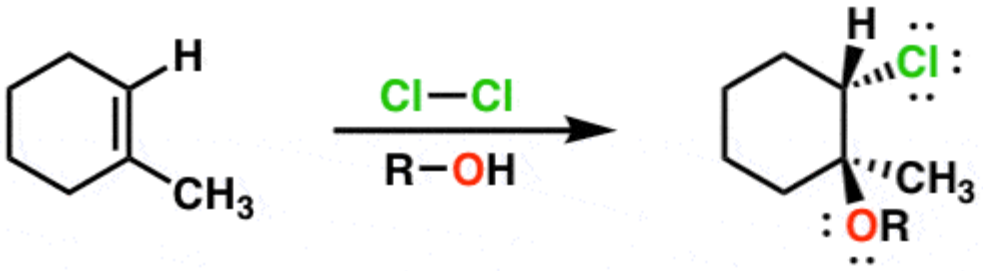


via chloronium ion

(skipping over bromohydrin and iodohydrin formation, which work exactly the same way...)

5. “Haloether” Formation: The Mechanism

Chlorohydrin Formation



+ enantiomer

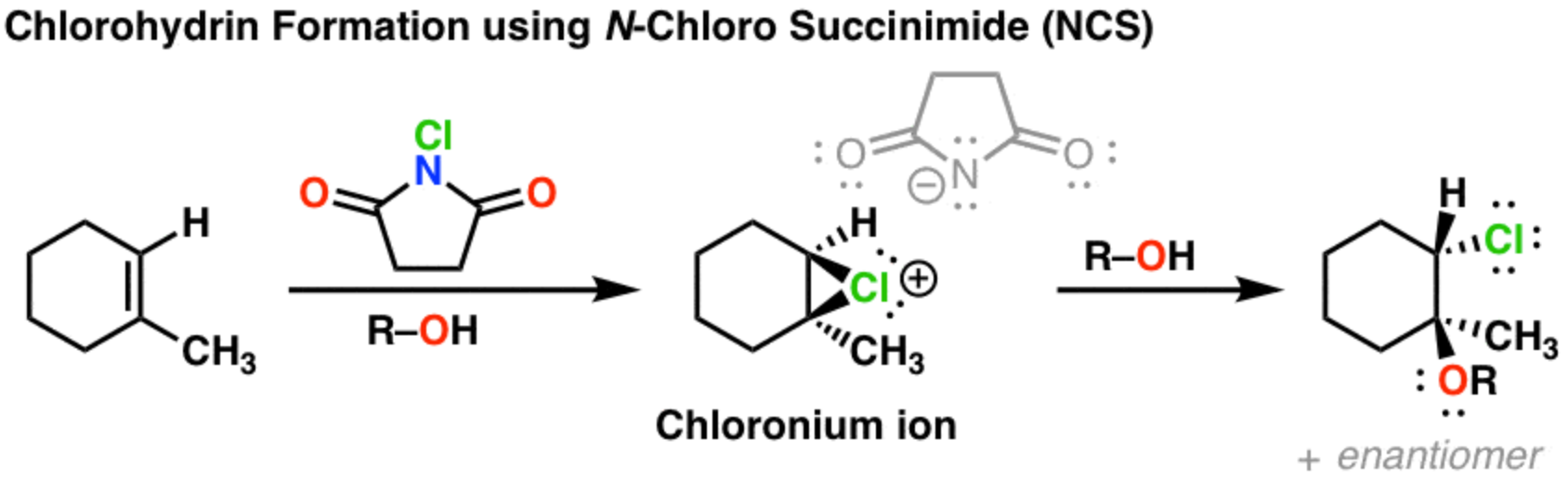
Stereochem	Regiochem
Anti	*Markovnikov*

also via chloronium ion

(same type of reaction works with Br_2 and I_2)

6. Chlorohydrin Formation Using *N*-Chloro Succinimide

A convenient source of "electrophilic" chlorine is the crystalline salt N-chlorosuccinimide (NCS), an innocuous appearing white crystalline solid. Alkenes react rapidly with NCS to form chloronium ions, which can then be intercepted to form a variety of useful products by analogy to those shown above. With the exception of this more convenient source of halogen, the reaction is otherwise the same. N-bromosuccinimide (NBS) and N-iodosuccinimide (NIS) likewise find use.

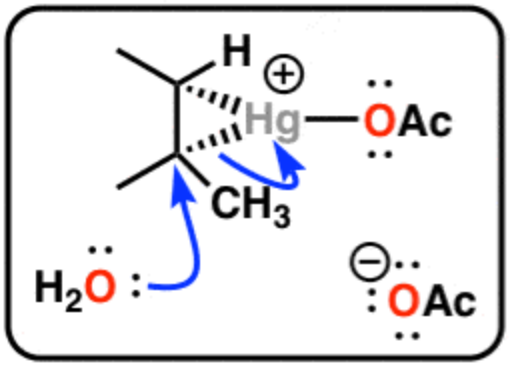


7. Oxymercuration: The Mechanism

When alkenes are treated with mercury (II) salts (such as mercuric acetate) in the presence of water or alcohols, we obtain products with the same pattern of stereochemistry and regiochemistry that we're accustomed to seeing by now. What's a likely intermediate here? A three-membered ring called the "mercurinium ion".

Oxymercuration

Stereochem	Regiochem
Anti	***Markovnikov***

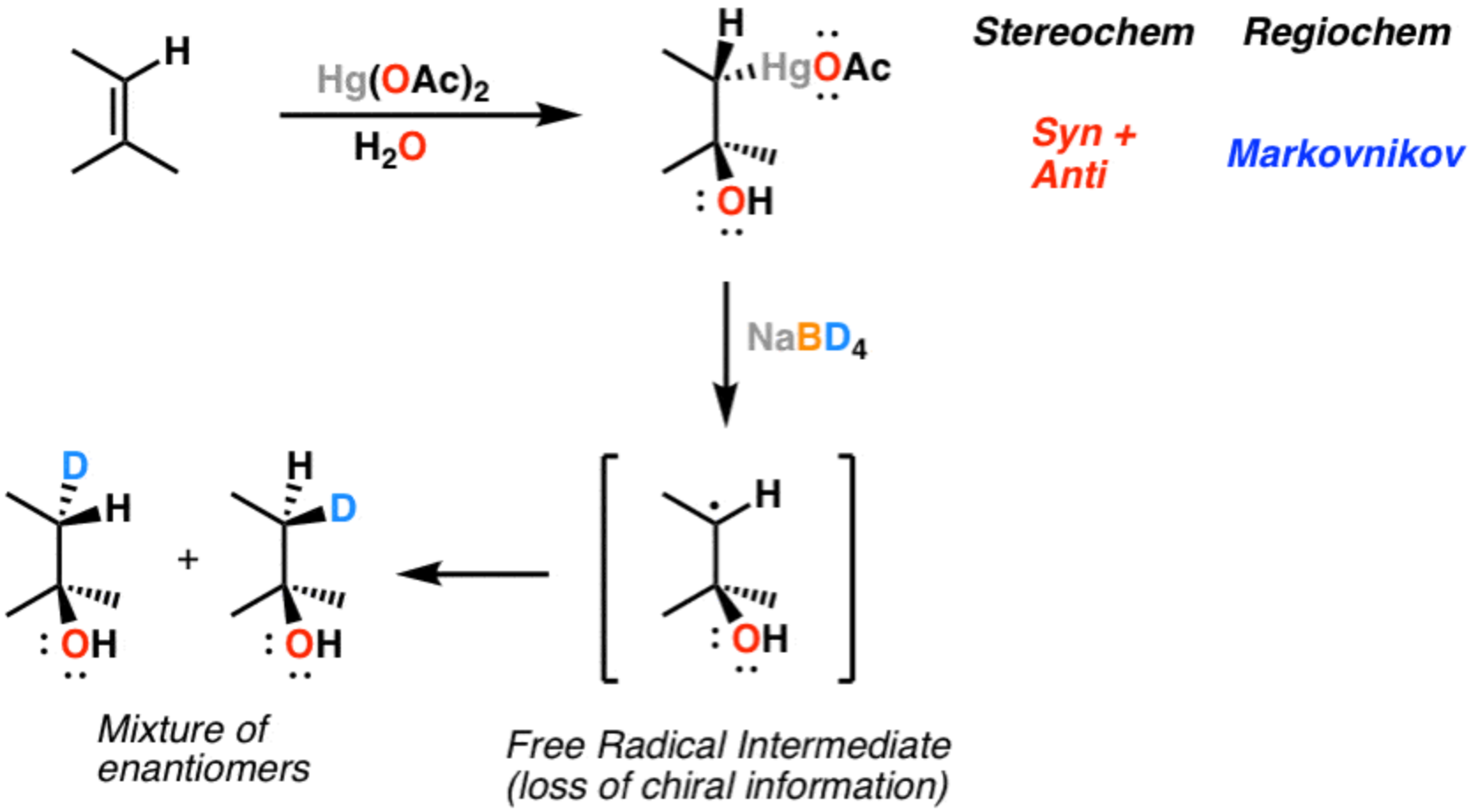


via mercurinium ion

8. Oxymercuration: The Reduction Step

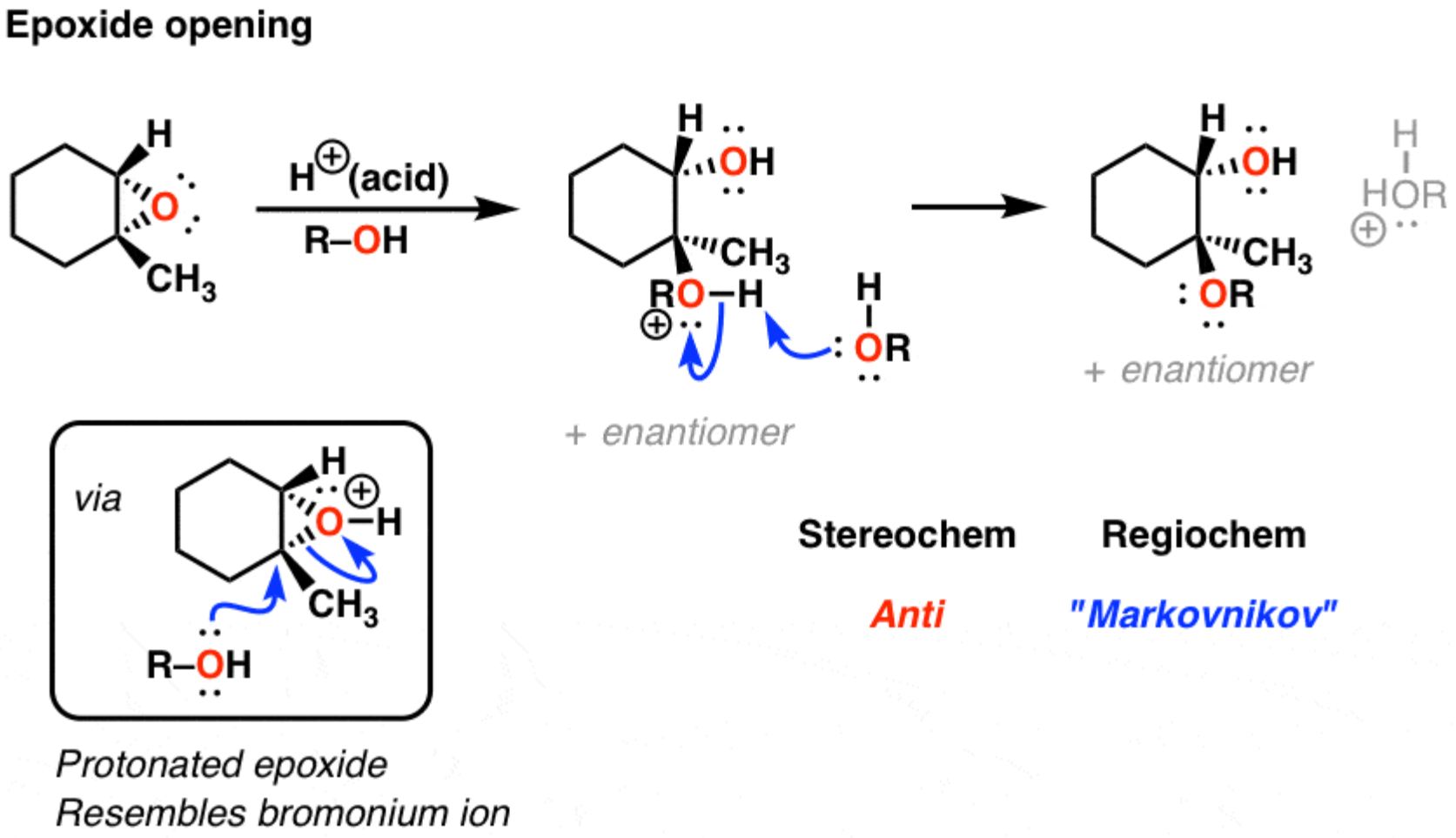
Organomercury compounds find very little application in themselves, but can be used as intermediates in subsequent reactions. To replace mercury with hydrogen, sodium borohydride (NaBH4) is added. In this case, rather than being “anti” , the stereochemistry of this reaction ends up being a wash: treatment with $NaBH_4$ leads to cleavage of the C-Hg bond and formation of a free radical.

Workup of oxymercuration involves loss of stereochemistry at carbon containing Hg



9. A Non-Obvious Cousin: Protonated Epoxides

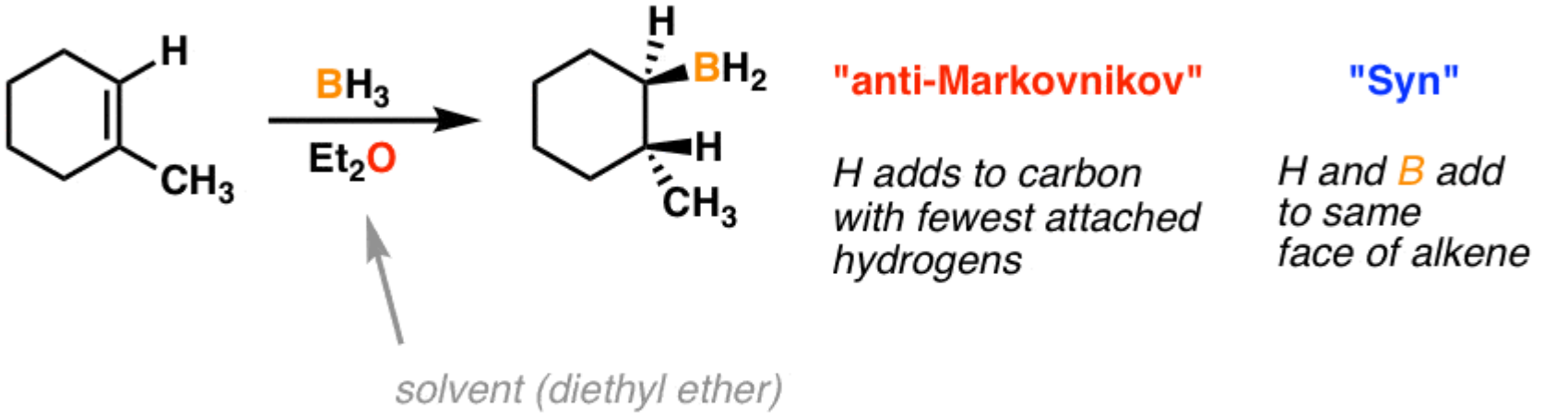
Treatment of an epoxide with acid leads to a positively charged intermediate that resembles a bromonium ion. As you might guess, the nucleophile attacks the backside of the most substituted carbon and the resulting product has anti stereochemistry.



1. Hydroboration – Oxidation of Alkenes

In the **carbocation pathway**, we saw reactions that proceed with "Markovnikov" regioselectivity, a mixture of "syn" and "anti" stereochemistry, and can be accompanied by rearrangements. In the **3 membered ring pathway**, the regiochemistry is also "Markovnikov", the stereochemistry is trans (anti), and the reaction proceeds through a 3 membered ring

Hydroboration of alkenes



Regiochemistry

"anti-Markovnikov"

H adds to carbon with fewest attached hydrogens

Stereochemistry

"Syn"

H and B add to same face of alkene

- No rearrangements observed
- Never observe incorporation of solvent

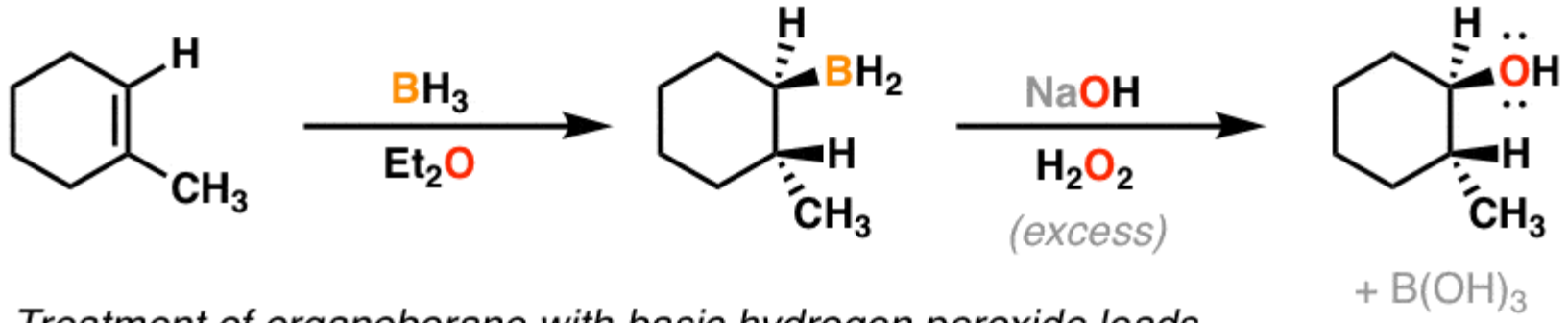
Inconsistent with a free carbocation or with an intermediate 3-membered ring

Note that the hydrogen is adding to the **more substituted** end of the carbon ("anti-Markovnikov") and the stereochemistry is **syn**.

5. The Resulting Organo-boranes Are Easily Oxidized To Alcohols With Basic Hydrogen Peroxide

This process is called “hydroboration-oxidation”. Note how the stereochemistry of the C-B bond is preserved in the C-O bond.

Hydroboration - oxidation



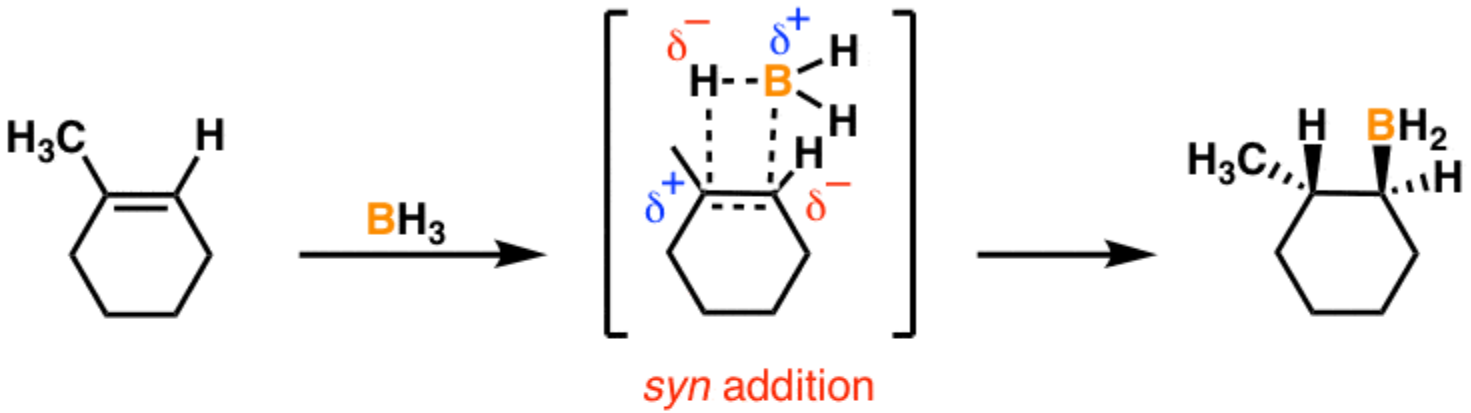
Treatment of organoborane with basic hydrogen peroxide leads to formation of an alcohol

Stereochemistry is preserved!

Hydroboration Oxidation of Alkenes Mechanism

1. Hydroboration Of Alkenes: A Proposed Mechanism

The Hydroboration Mechanism



- **Concerted transition state**

  C–H and C–B bonds are formed at approximately the same time

- **'Anti-Markovnikov' Regioselectivity**

  The most favored transition state allows the partially negative hydrogen atom to form a bond with the carbon atom best able to bear positive charge (the "most substituted" carbon of the alkene in most cases)

- **'Syn' Stereochemistry**

  In this concerted transition state, the C-H and C-B bonds are formed on the same side of the alkene (technical term: "suprafacial")

2. Why Does Hydroboration Exhibit So-Called "Anti-Markovnikov" Regioselectivity?

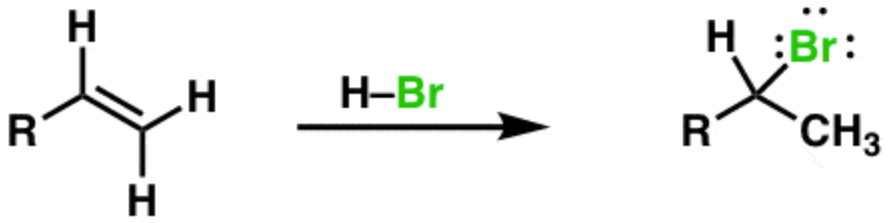
More on that "Anti-Markovnikov" Regioselectivity

In H–Cl and H–Br (among others), **Cl and Br are more electronegative than H**, so H bears a **partial positive charge**. Hence, hydrogen has ***electrophilic*** character This is borne out by the strong acidity of these species.

Electronegativity:

H	Cl	Br
2.2	3.2	3.0

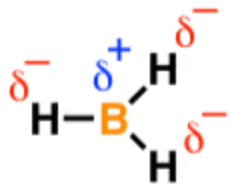
In the reaction of H-Br to alkenes (for example) hydrogen ends up attached to the least substituted carbon, and bromine ends up attached to the most substituted carbon



In BH_3, **boron is less electronegative than H.** So H bears a **partial negative** charge. Hence, hydrogen has ***nucleophilic*** character.

Electronegativity:

H	B
2.2	2.0



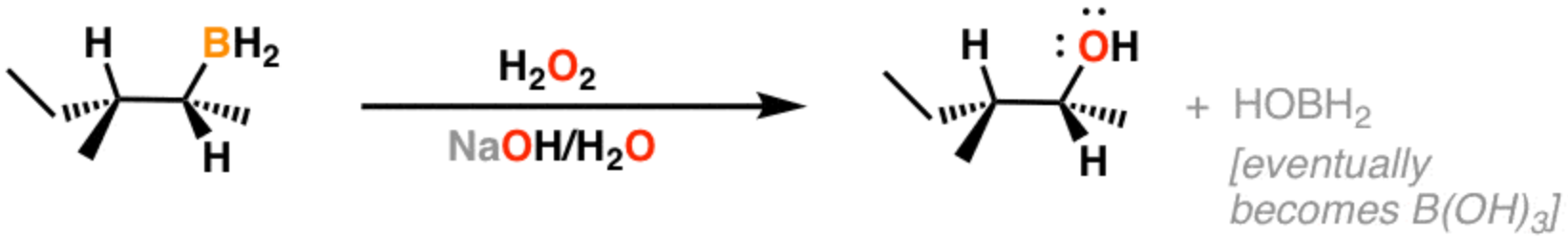
In this sense the more electronegative atom still ends up bonded to the "most substituted carbon"

The irony of all of this is that even though hydroboration is often thought of as that "exception" of a reaction which is anti-Markovnikov, it actually follows the **same principle** as the reactions we've encountered before: the more electronegative atom ends up bound to the carbon best able to stabilize positive charge. So there's actually no real "exception" at all here!

3. Hydroboration-Oxidation: How Does The Oxidation Work?

After hydroboration, treatment of the organo-borane with basic hydrogen peroxide leads to replacement of C-B with C-OH. Note that there is no change in stereochemistry; it has occurred with retention!

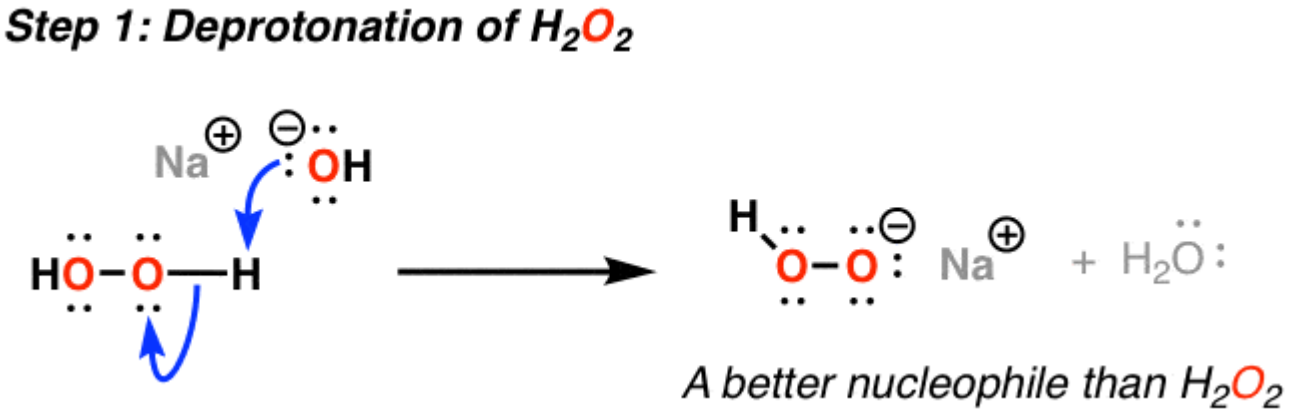
How does the oxidation step work?



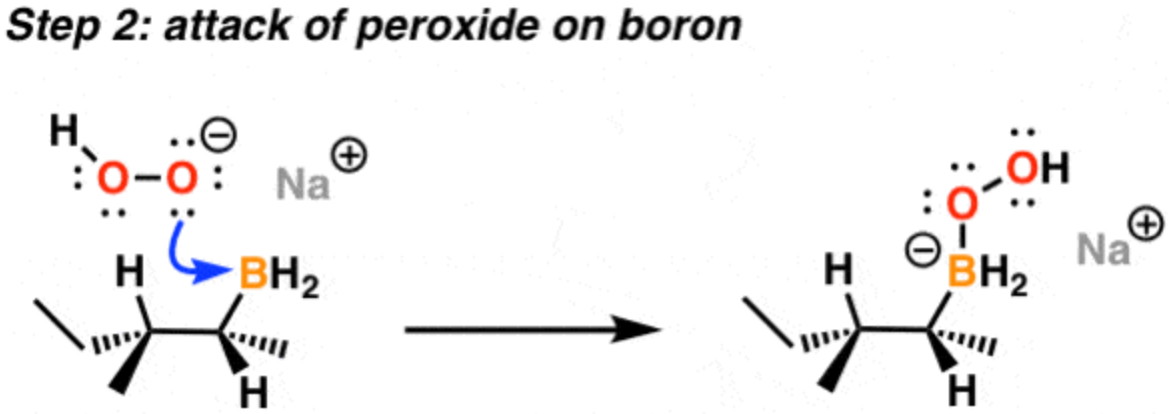
- **Stereochemistry at carbon is preserved**

4. Oxidation Steps 1 And 2: Deprotonation Of Hydrogen Peroxide, And Attack Of The Peroxide Ion On Boron

The first step here is deprotonation of hydrogen peroxide to give NaO-OH. Since the conjugate base is a better nucleophile, this speeds up the rate of the subsequent step.

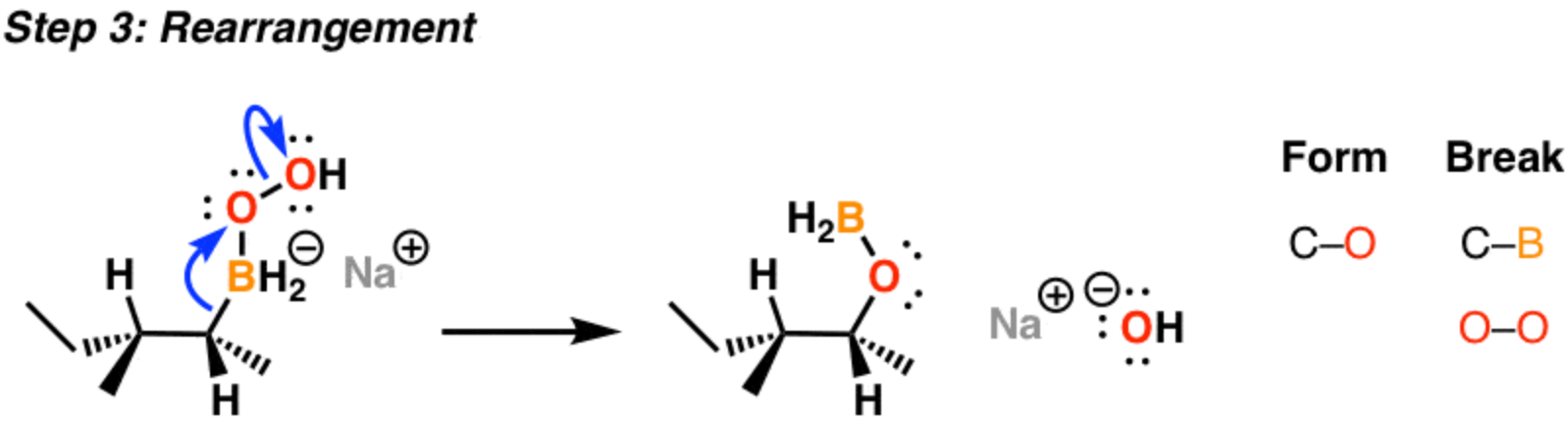


The next step is a simple Lewis acid-base reaction. The deprotonated peroxide anion then adds to the empty orbital of boron, forming a negatively charged boron species:



5. Oxidation Step 3: The Key Rearrangement Step

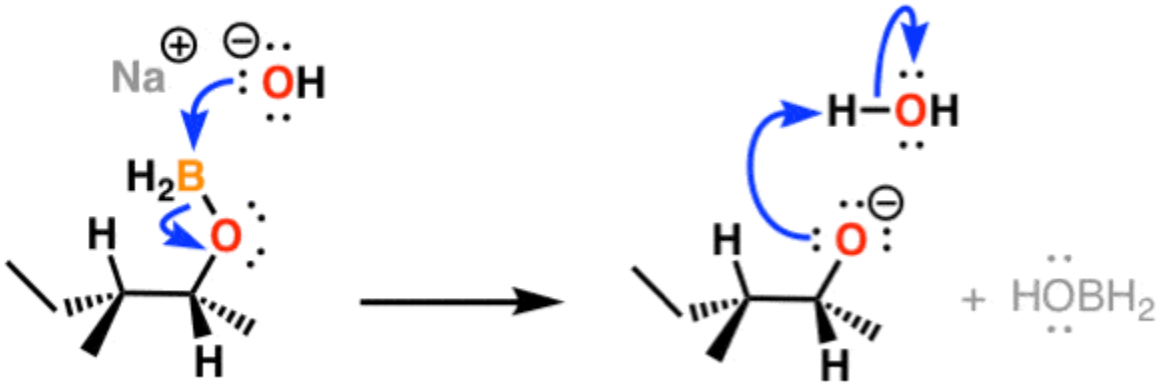
The next step often gives students difficulty. Here, the pair of electrons in the C–B bond migrates to oxygen, leading to breakage of C–B and formation of C–O, along with rupture of the O–O bond. It's very similar to 1,2-hydride and alkyl shifts we've seen previously, except that instead of migrating to the empty p orbital on a carbocation, the electron pair is essentially performing a "backside attack" on the σ* orbital of the weak O–O bond.
Note how the charge on boron goes from negative to neutral.



6. Oxidation Step 4: Cleavage Of The O–B Bond

The next step can be written several different ways. Hydroxide ion attacks the empty p orbital of boron, and the O–B bond breaks. Although drawn here as a "concerted" step, where bond formation accompanies bond breakage, it need not be so, since addition of hydroxide to boron does not violate the octet rule.
Finally the negatively charged oxygen is then protonated by water (the solvent).

Step 4: Attack of hydroxide on boron.... and Step 5: protonation of alkoxide



That sums up the key points of the hydroboration reaction.
In the next post, we'll go through some other reactions of alkenes that might not share the *exact* same mechanism as hydroboration, but share a similar pattern of stereochemistry that is also a result of "concerted" reactions.

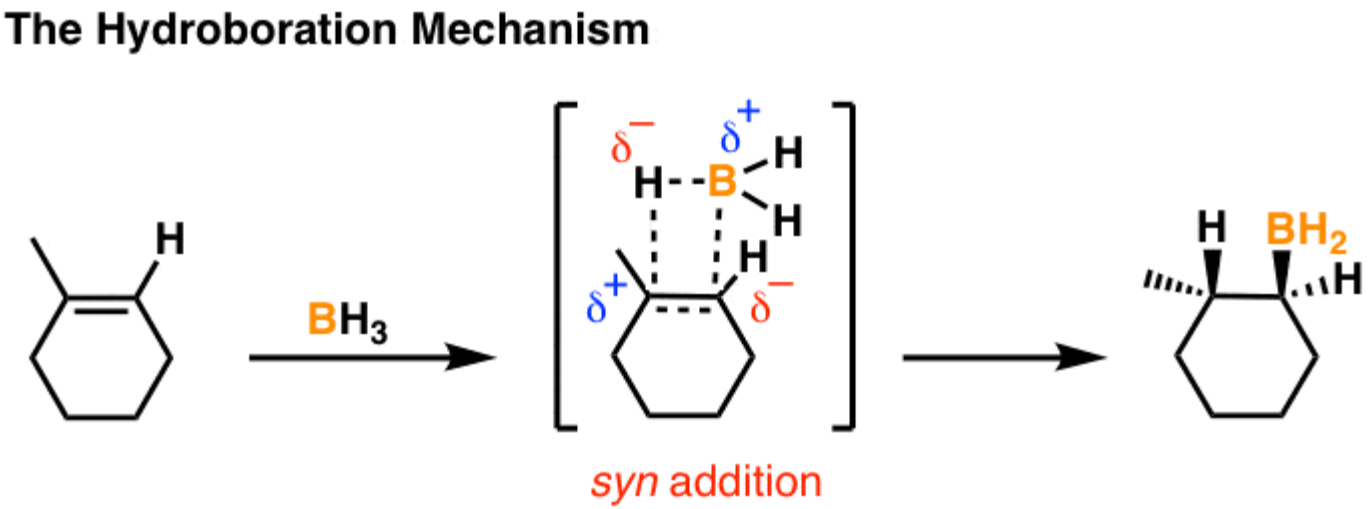
“Concerted” Mechanisms In Alkene Addition Reactions: Hydroboration, Hydrogenation, Epoxidation, Dihydroxylation, And Simmons-Smith Cyclopropanation.

In contrast to alkene addition reactions in the Carbocation Pathway and the 3-Membered Ring Pathway, we saw in the last two posts that hydroboration of alkenes is anomalous. The regioselectivity of the reaction is “anti-Markovnikov” and the stereochemistry of the addition is “syn“.

We also saw that the “syn” stereochemistry is due to the concerted nature of the mechanism proposed for this reaction.

1. Concerted Mechanisms In Alkene Addition Reactions

Just to review the previous post, here's a drawing of the transition state for the hydroboration of alkenes showing the concerted mechanism that results in *syn* addition.



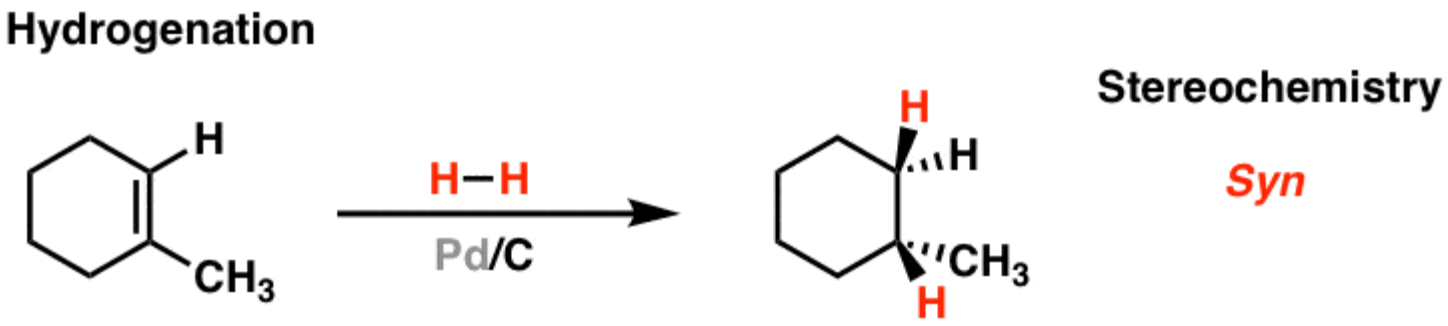
Several other reactions of alkenes that proceed through a concerted transition state are the following:

- Hydrogenation (Pd-C, H_2)
- Dihydroxylation (OsO_4)
- Epoxidation (RCO_3H ; *meta*-chloroperoxybenzoic acid, *m*-CPBA is a common reagent in this family)
- Cyclopropanation (CH_2I_2, Zn-Cu)
- Dichlorocyclopropanation ($CHCl_3$, KOH)

Although the exact mechanism of each reaction is not necessarily the same, each of these reactions does proceed through a **concerted** transition state and the stereochemistry of the addition is **syn**. One important thing to note here is that, unlike hydroboration, each of the reactions is adding identical atoms to each carbon of the alkene, **so the issue of "regioselectivity" is moot**.

The fact that the reaction products have these characteristics in common (if not the *exact* mechanism) still allows us to group them together as a loosely connected "family" – the "Concerted Pathway", if you will.

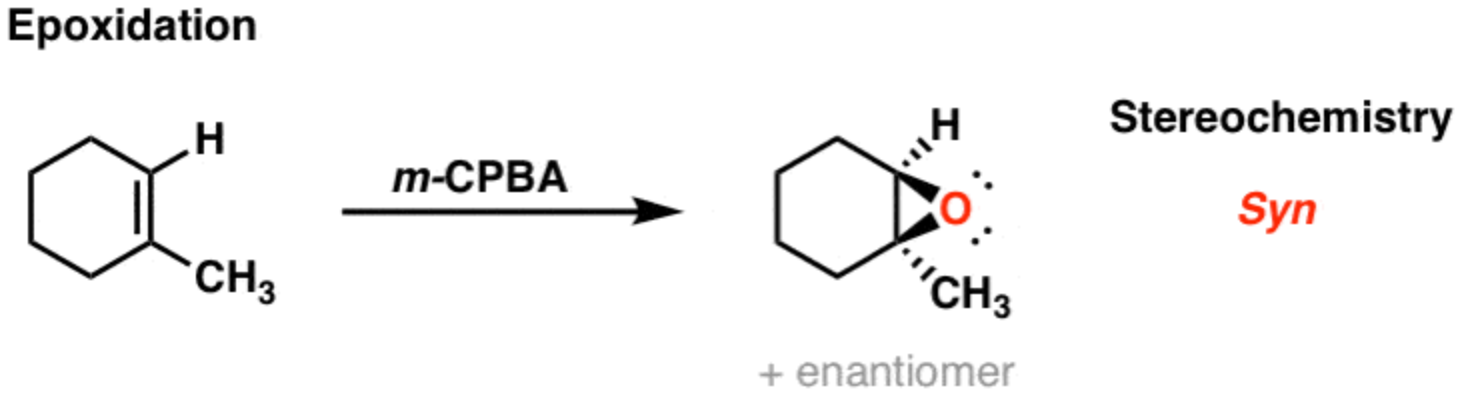
2. Hydrogenation Of Alkenes With H_2 And A Metal Catalyst Such As Pd-C



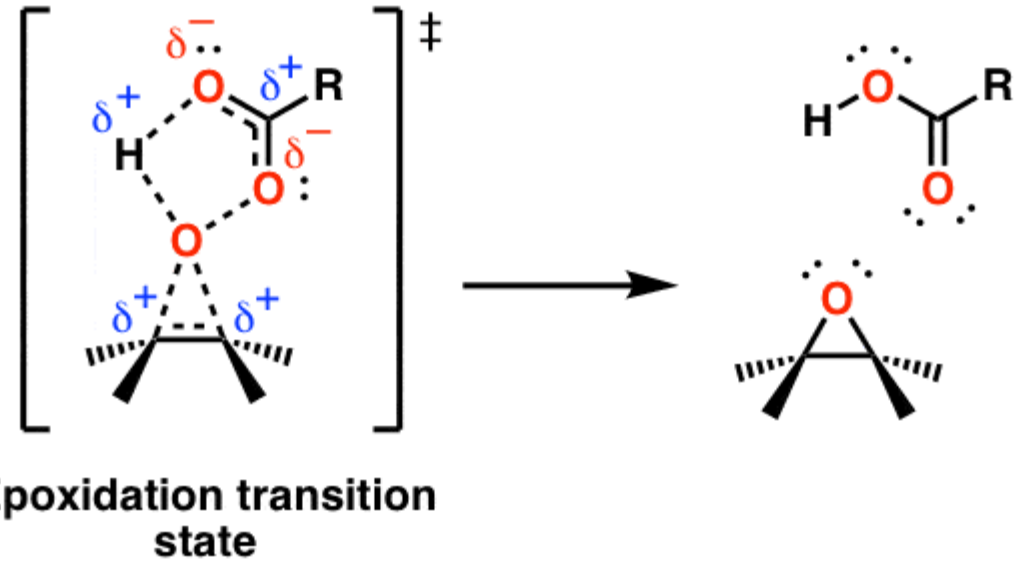
Treatment of alkenes with hydrogen gas and a "noble" metal catalyst such as palladium (Pd) or platinum (Pt) [nickel, rhodium, ruthenium and other metals also find use] results in the addition of two atoms of hydrogen to the same face of the alkene. Under these conditions, the alkene and hydrogen gas are both "adsorbed" on to the surface of the metal.

In the transition state for this reaction, each of the two hydrogen atoms are delivered to the same face of the alkene. The rate of the reaction is surface area dependent: dispersing the metal on finely divided carbon (charcoal) drastically improves the reaction rate, hence the use of charcoal (finely divided carbon)

3. Epoxidation Of Alkenes With Peroxyacids Such As *meta*-Chloroperoxybenzoic Acid (*m*-CPBA)



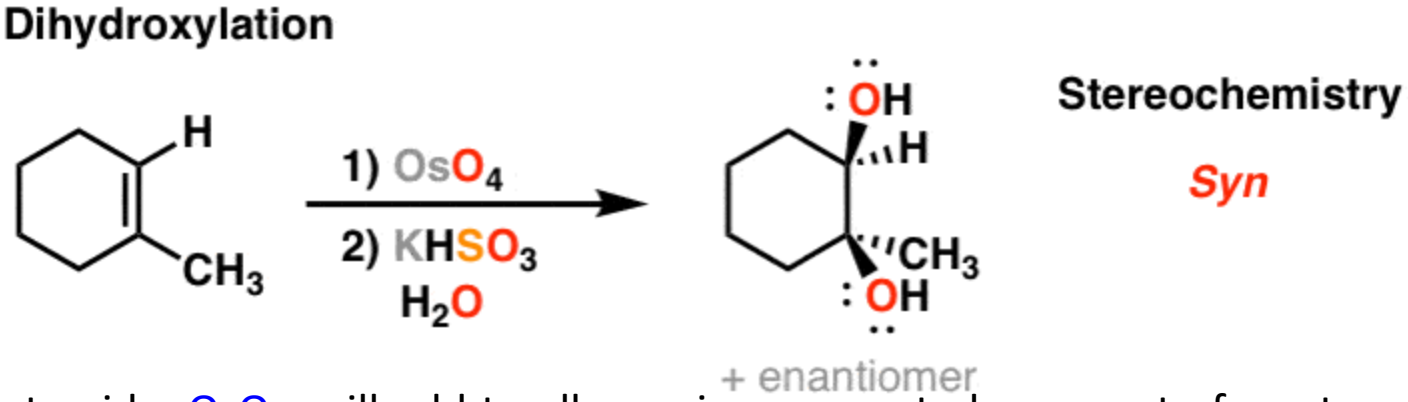
Treatment of an alkene with a peroxyacid such as *m*-CPBA results in formation of an epoxide ("oxirane"). This also occurs through a concerted transition state:



Epoxidation transition state

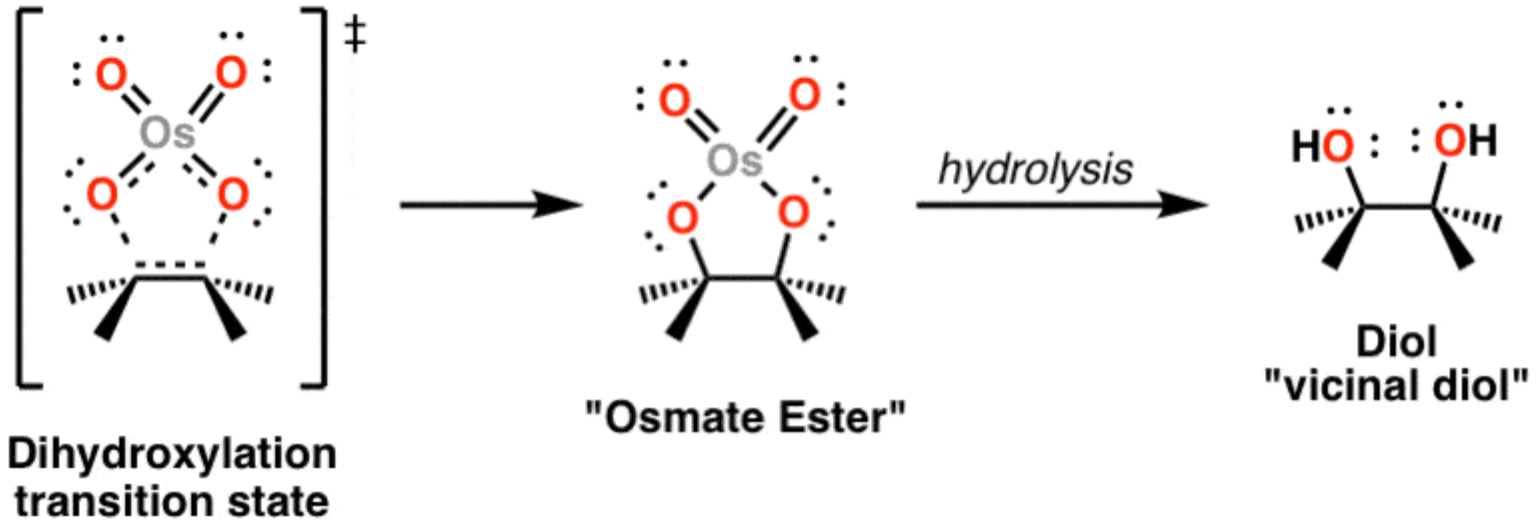
Note that as the (weak) O–O bond breaks, the proton from the peroxy acid is picked up by the (former) carbonyl oxygen.

4. Dihydroxylation Of Alkenes With Osmium Tetroxide (OsO4)

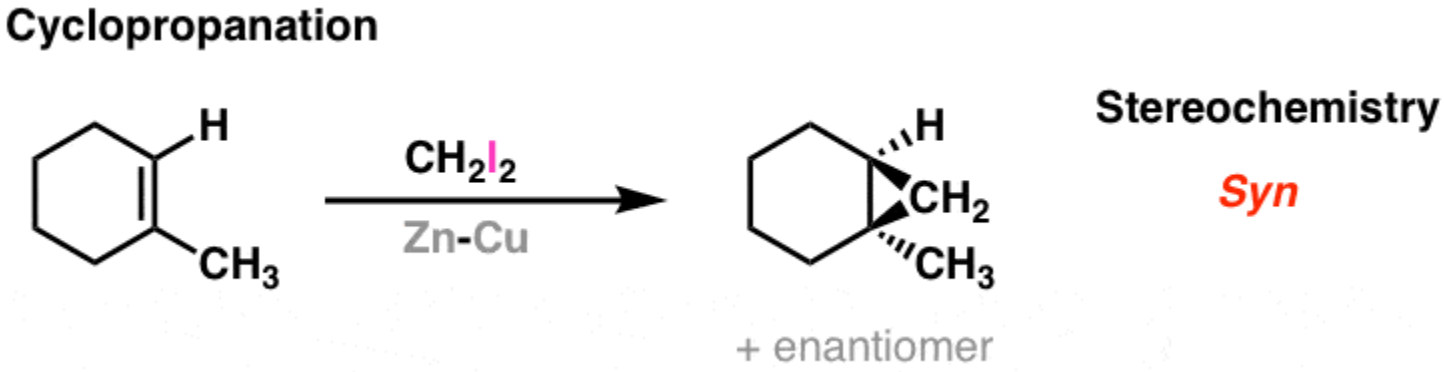


Osmium tetroxide, OsO_4, will add to alkenes in a concerted process to form two new C-O bonds. The stereochemistry is also syn.

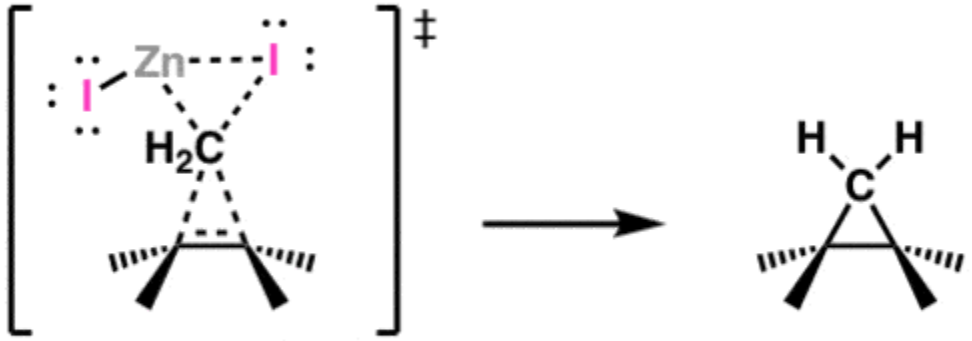
An intermediate in this reaction is a cyclic compound containing osmium, called an *osmate ester*. The second step shown in grey ($KHSO_3$, H_2O) results in breakage of the O-Os bonds and formation of the alcohols. This is called "hydrolysis". $KHSO_3$ is a reducing agent and aids in the workup of the toxic osmium.



5. Cyclopropanation Of Alkenes With The Simmons-Smith Reagent (Zinc-Copper Couple)

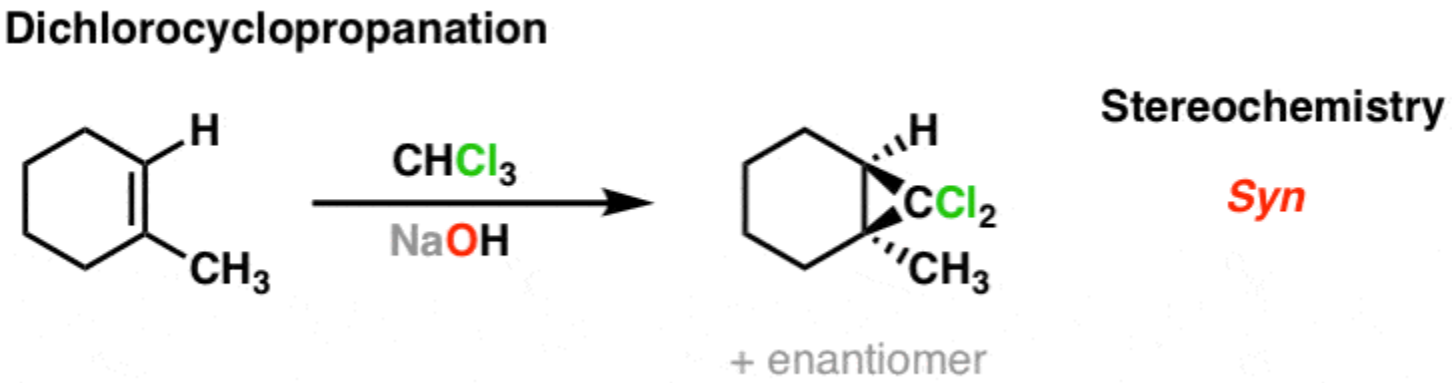


In a reaction sometimes known as the "Simmons-Smith reaction", diiodomethane (CH_2I_2) and zinc-copper couple ("Zn-Cu') form a "carbene" (actually, a carbenoid to be more precise). Alkenes add to this species to give cyclopropanes. The stereochemistry of the addition is **syn**. Here is the transition state generally drawn for this reaction:

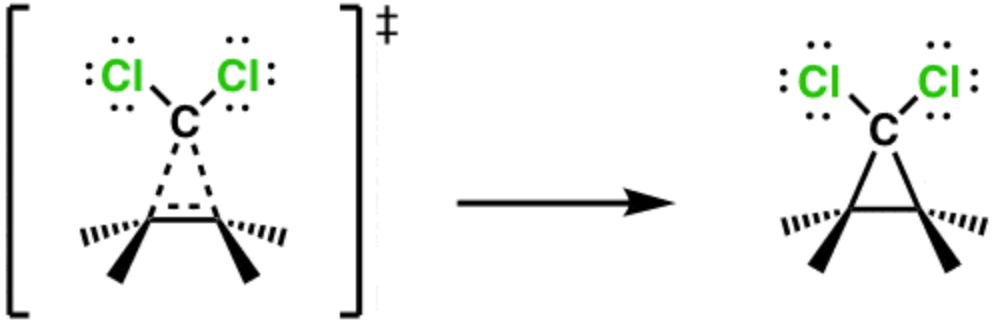


Cyclopropanation transition state

6. Dichlorocyclopropanation Of Alkenes With Chloroform And Base (Giving Dichlorocarbene)



When treated with strong base, chloroform ($CHCl_3$) is deprotonated to give its conjugate base. Loss of chloride ion from this species results in $Cl_2C:$, otherwise known as a "dichlorocarbene". As in the reaction above, alkenes can add to this carbene to give a cyclopropane. The reaction proceeds through this transition state (empty p orbital and orbital lobe containing lone pair of electrons not shown)

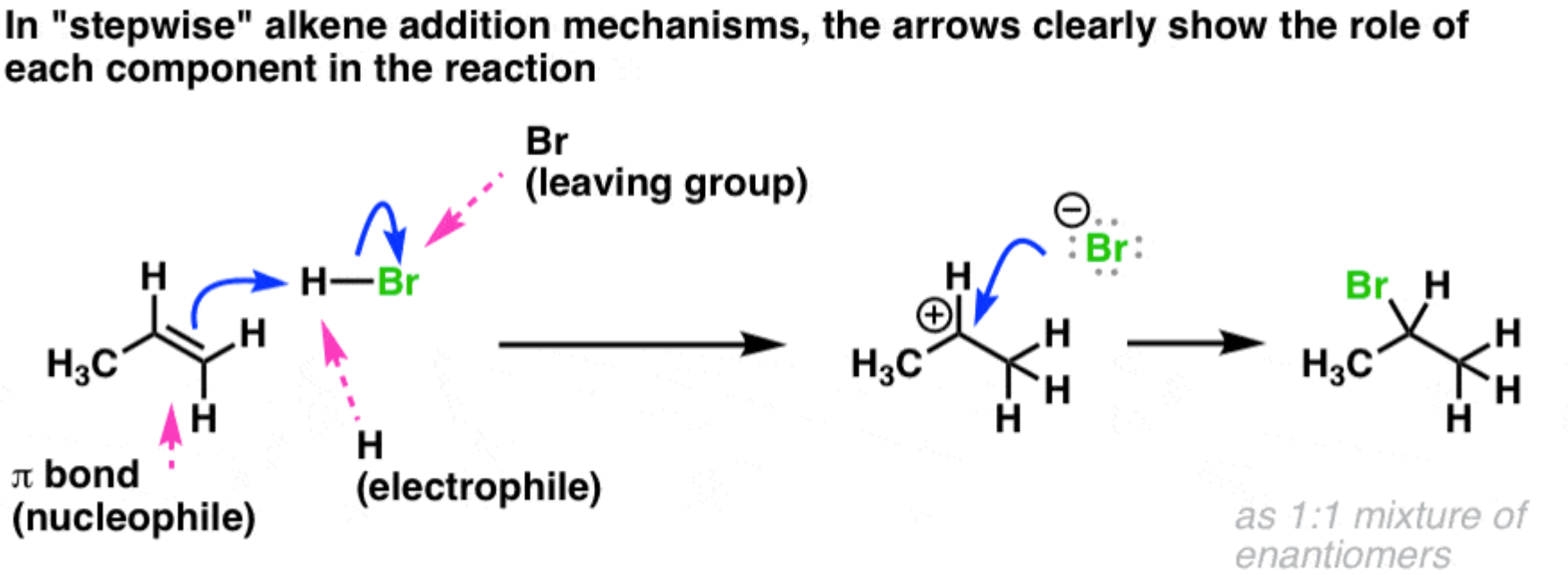


Dichlorocyclopropanation transition state

28-04-2020 Bromonium Ion Formation: A (Minor) Arrow-Pushing Dilemma

1. Identify The Nucleophile And Electrophile In This Reaction

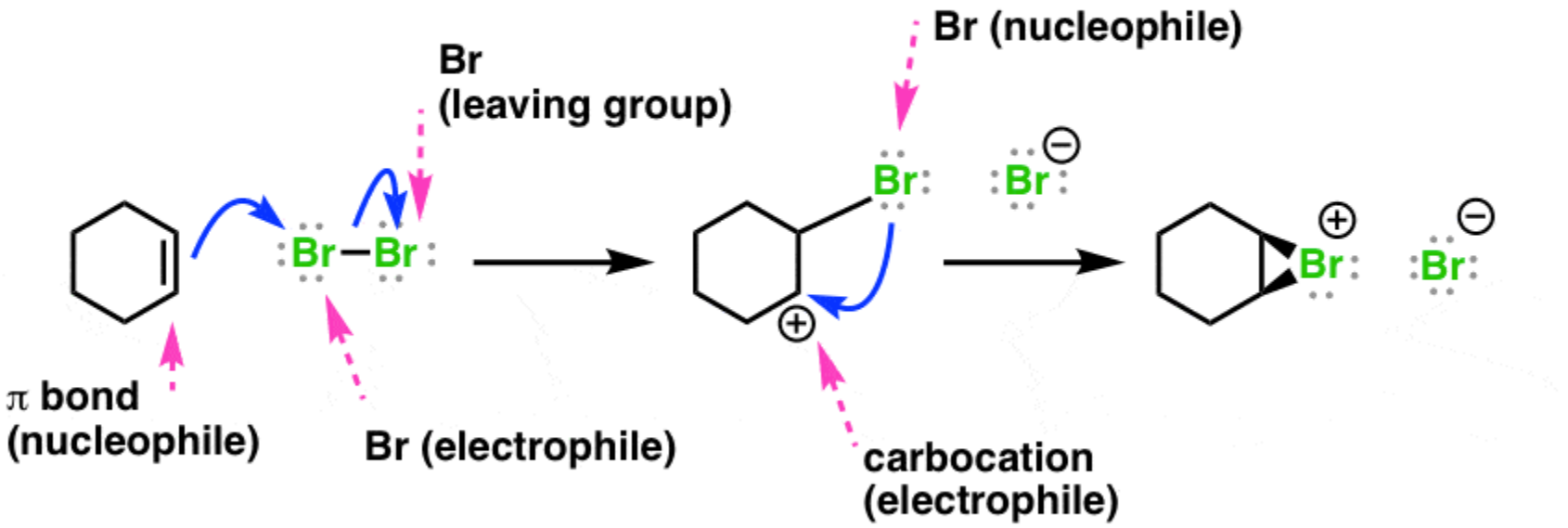
Electrons flow from areas of high electron density to areas of low electron density. The arrow pushing formalism has been crystal clear up till now in helping us identify which atom/group in a reaction is the nucleophile, which is the electrophile, and which is the leaving group. Here's an example:



2. In Bromonium Ion Formation From Alkenes, Is Br_2 A Nucleophile Or Electrophile?

Ideally, we'd like to be able to draw all of our mechanisms like this. Take the formation of a bromonium ion through addition of Br_2 to an alkene. Based on every single arrow-pushing example we've seen up until now, it might seem reasonable to draw the mechanism like this:

Although we might like to draw the mechanism for formation of a bromonium ion like this, with every component clearly delineated....

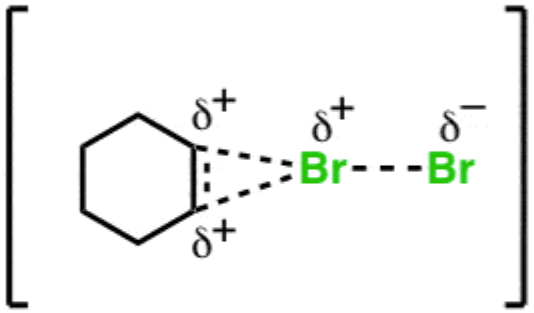


… this doesn't correspond to reality!

There's just one problem with the way this mechanism is drawn, above. It implies the existence of a free carbocation. **And that doesn't correspond to reality.** We know that free carbocations aren't involved in brominations. So even though it might be more "convenient" to draw the mechanism this way, we must throw it out and try something else.

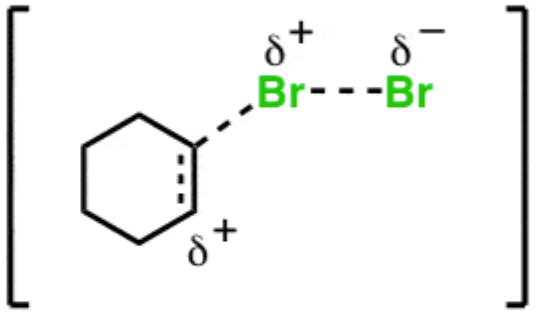
3. In Bromonium Ion Formation, Bromine Atom In Br_2 Actually Serves As Both Nucleophile *And* Electrophile!

The transition state for addition of Br_2 to alkenes is consistent with a *concerted* mechanism, not a stepwise mechanism*:



Transition State

not



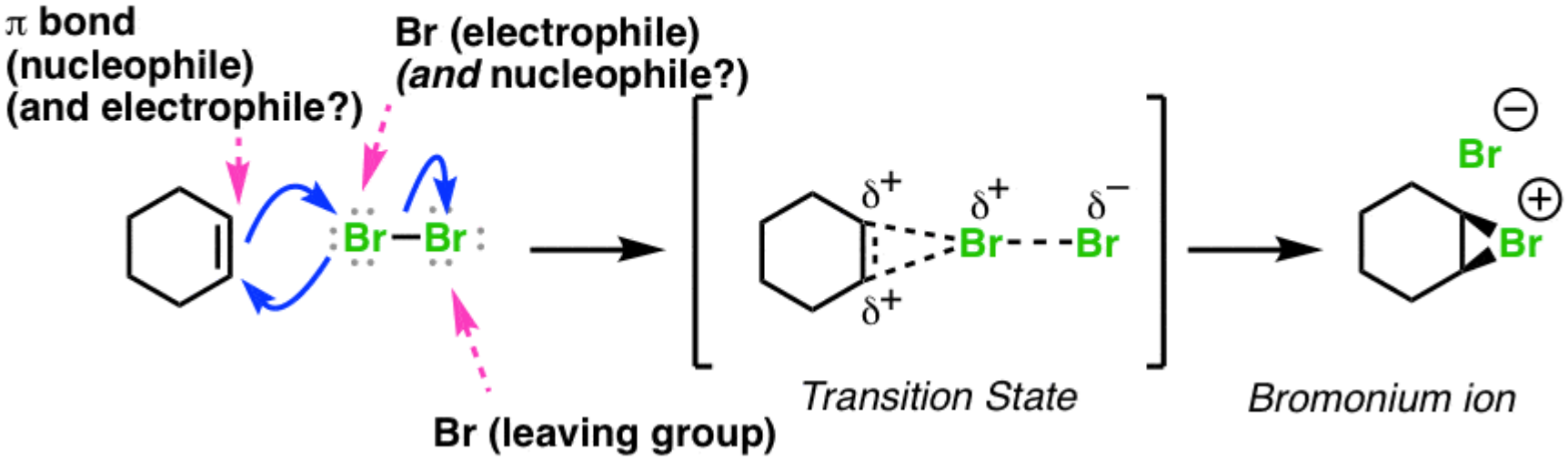
Transition State

* according to calculations, and experimental observations. Some exceptions exist for situations where a very stable carbocation may be formed (e.g. 4-methoxystyrene)

So how might we adapt what we know about the mechanism of bromination to the curved arrow formalism? Here's one attempt.

Follow the arrows?

Defining *atoms* as nucleophiles/electrophiles is difficult in concerted transition states. This makes following "electron flow" more difficult.



4. Summary: Arrow Pushing In Bromonium Ion Formation

For concerted reactions of alkenes, we're going to have to give up our cherished habit of being able to clearly trace the flow of electrons from nucleophile –> electrophile –> leaving group. It's the price we pay for making our curved arrow mechanisms accurately portray reality.

A Fourth Alkene Addition Pattern – Free Radical Addition

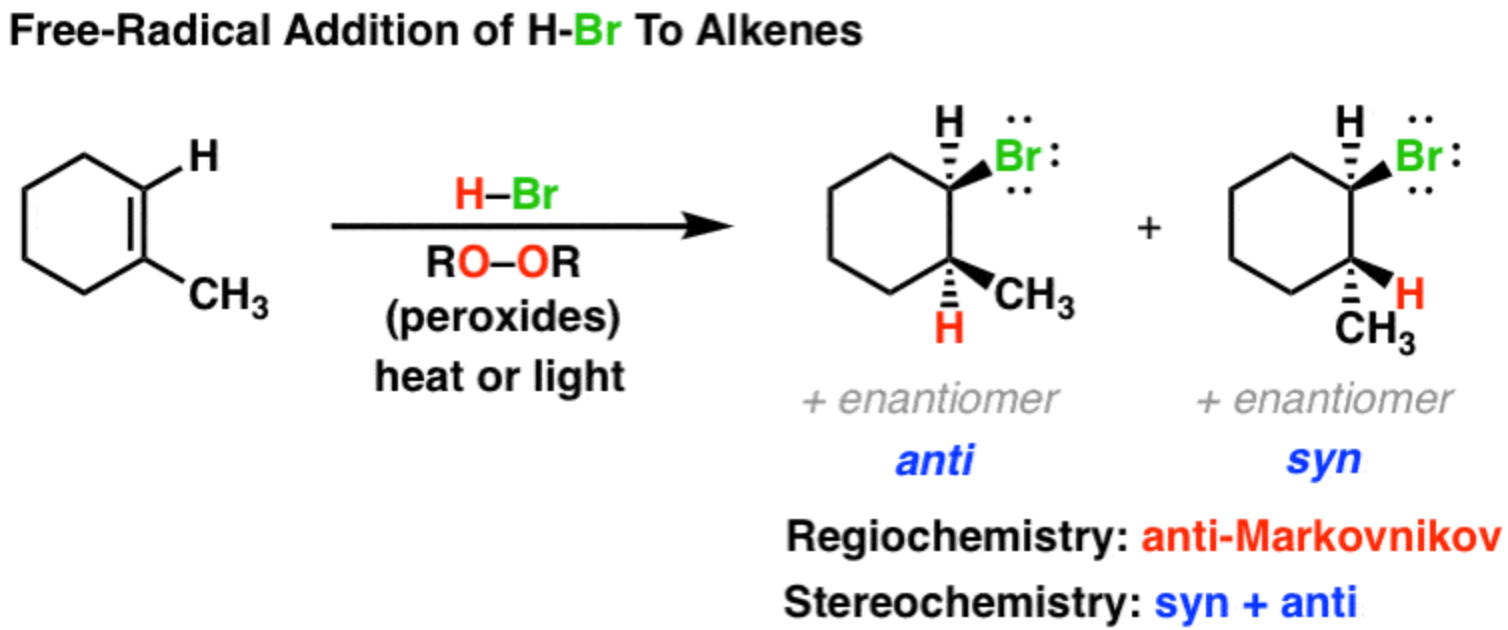
Free Radical Addition Of HBr To Alkenes With ROOR (Peroxides)

We've seen that there are three major alkene reactivity patterns [**carbocation**, **three membered ring**, and **concerted**], but there are two minor pathways as well. This post discusses one of them: free-radical addition of HBr to alkenes, which shows the opposite regioselectivity (anti-Markovnikov) than "normal" addition of HBr to alkenes (Markovnikov) which follows the "carbocation" pathway.

1. Free Radical Addition Of HBr To Alkenes Leads To "Anti-Markovnikov" Products

As discussed previously, alkenes normally react with HBr to give products of "Markovnikov" addition; the bromine ends up on the most substituted carbon of the alkene, and the hydrogen ends up on the least substituted carbon. However, something interesting happens when the same reaction is performed in the presence of peroxides and heat / light: the pattern of addition changes!

Instead of Br ending up on the **most** substituted carbon of the alkene, it ends up on the least. [The stereochemistry of the reaction, however, is unchanged: it still gives a mixture of "syn" and "anti" products.]



This so-called "anti-Markovnikov" addition is intriguing. What difference could the presence of peroxides, and furthermore heat (or light) make to this reaction?

2. An Outline Of The Free Radical Mechanism For Addition Of HBr To Alkenes In The Presence Of ROOR (Peroxides)

This reaction occurs through a **free-radical process**. (For a primer on free radical chemistry, you might want to check out this chapter). Here is an outline of the mechanism:

- Peroxides contain a weak oxygen-oxygen bond [approximately 35 kcal/mol; compare to C-H at approx 100 kcal/mol]
- Heating leads to **homolytic** fragmentation of this bond – that is, the bond breaks such as to leave one unpaired electron on each atom. Strong sources of light [e.g. a floodlight or other source of light radiation which reaches into the near UV] can also serve to sever this bond.
- The resulting highly reactive alkoxy radical can then abstract a hydrogen from H-Br, giving a **bromine** radical. **The bromine radical is the species that adds to the alkene.**
- Addition to the alkene will preferably occur in such a way that the **most stable** free radical is formed [in the case above, the tertiary radical]. **That's why bromine ends up on the least substituted carbon of the alkene.** (See: *3 Factors Which Stabilize Free Radicals*)
- This tertiary radical then removes hydrogen from H-Br, liberating a bromine radical, and the cycle continues.

3. Initiation Of The Free-Radical Process Through Homolytic Cleavage Of ROOR (Peroxides) By Heat Or Light

Only a trace [catalytic] amount of peroxide is required to get the reaction started, although of course at least one molar equivalent of HBr is required to result in full addition of HBr to the alkene.

In the first step, addition of energy (in the form of heat or light) leads to homolytic fragmentation of the weak O–O bond to generate two new free radicals. "Homolytic" means that the bond is broken such that each atom receives the same ("*homos*" = Greek for *"same"*) number of electrons.

Step 1: *Initiation*

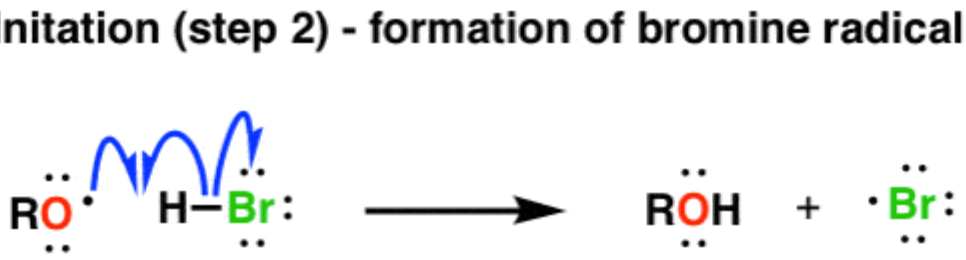
The **singly barbed arrows** depict the movement of single electrons; two alkoxy radicals are formed. Since there is a net increase in the number of radicals (0 →2) this is an initiation step.

Common "peroxides" for this purpose are t-butyl peroxide or benzoyl peroxide. * [Note 1]. Alternatively other free-radical "initiators" such as AIBN (Azobisisobutyronitrile) can also be used.

Only a catalytic amount of peroxides are used to initate this reaction (typically 10-20 mole %, although more can be used, especially when added batchwise).

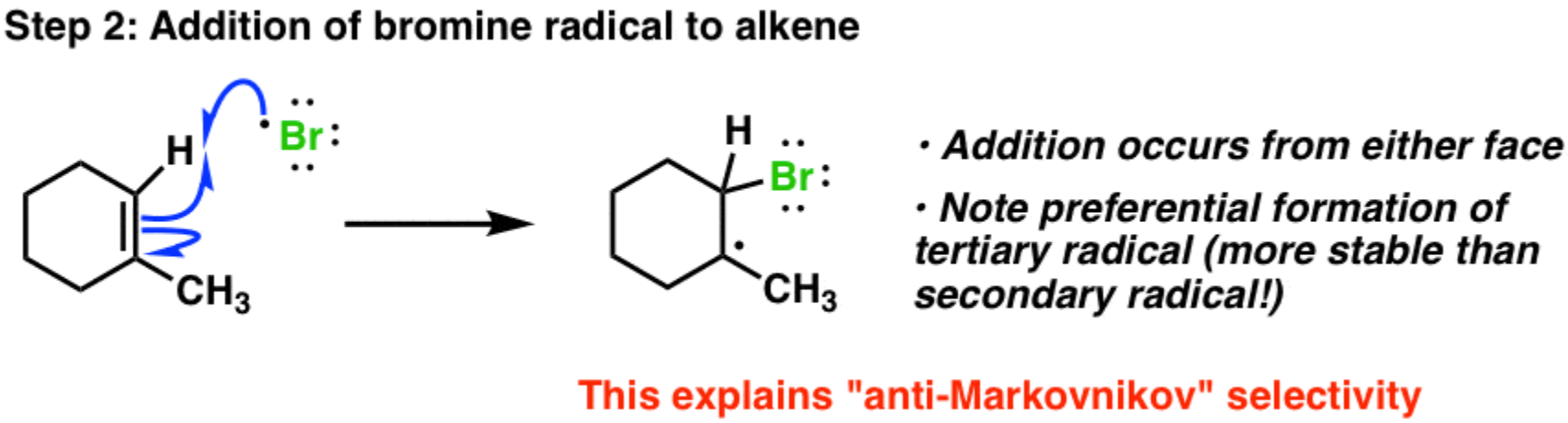
4. Formation Of The Bromine Radical From The Alkoxide Radical And HBr

In the next step, one of the oxygen radicals from step 1 removes a hydrogen from H–Br in another homolytic process.



Here, we're forming an H–O bond (bond dissociation energy of 102 kcal/mol for H–O in CH_3OH) and breaking an H–Br bond (bond dissociation energy of 87 kcal/mol) , so a difference in energy of about 15 kcal/mol makes this process essentially irreversible. (Note: since this process does not change the number of free radicals, it is technically a propagation step)

5. Propagation Step #1 : Addition Of Bromine Radical To The Alkene Occurs So As To Give The Most Stable Carbon Radical



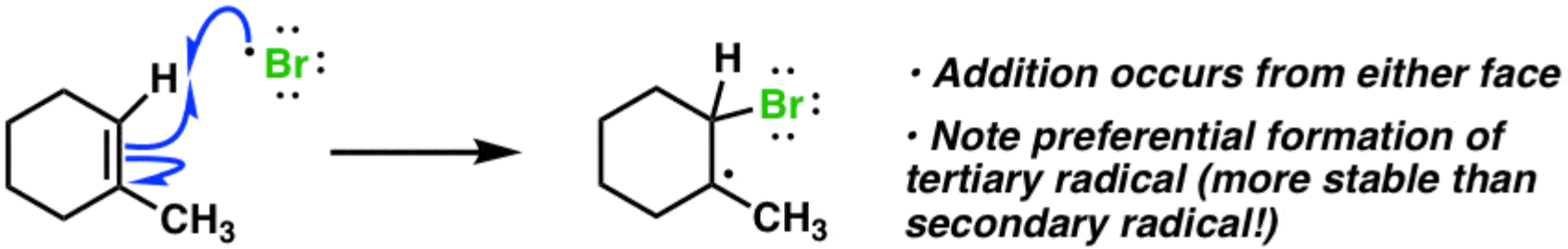
Once formed, the bromine radical can then add to the alkene.
In a relatively “flat” alkene such as 1-methylcyclohexene, addition of the radical will occur with equal probability from either face.
The question is, *which* atom of the double bond does the free radical attack? The bond could break two different ways, after all.

- Attack of the bromine radical on the more substituted carbon would result in a new free radical on a **secondary** carbon.
- Attack of the bromine radical on the less substituted carbon would result in a new free radical on a **tertiary** carbon.

Free radicals are electron-deficient species and are stabilized by adjacent electron donors. The more stable free radical intermediate is the **tertiary** free radical, and that is why addition occurs predominantly at the less substituted carbon (i.e. the carbon attached to the fewest number of carbons).

This explains the “anti-Markovnikov” selectivity of the reaction.

Step 2: Addition of bromine radical to alkene



This explains "anti-Markovnikov" selectivity

6. Propagation Step #2: The Resulting Carbon Radical Removes A Hydrogen Atom From H–Br, Regenerating The Bromine Radical

In a second propagation step in the main sequence, the resulting carbon radical removes a hydrogen from another equivalent of H–Br, giving the final addition product.

Alkyl free radicals are sp^2-hybridized, and are shallow pyramids that invert easily.

H–Br, therefore, can react on either face of the free radical [note 2]. If it attacks on the same face as the Br, then we obtain a *"syn"* product. If it attacks on the opposite face of the Br, then the product is *"anti"*.

A mixture of both will be obtained. The reaction is not stereoselective.

Abstraction of hydrogen from H-Br to give addition product

- ***addition can occur from either face***

This accounts for mixture of "syn" and "anti" products

A bromine radical is generated by this process, which can then add to another equivalent of alkene (propagation step #1).

7. The Termination Step

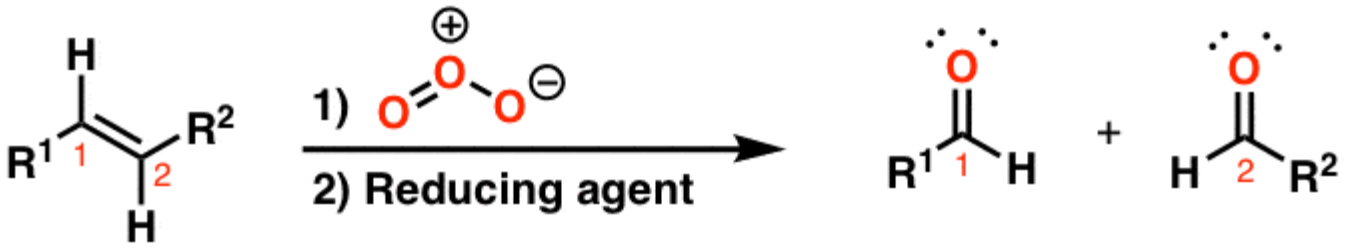
When the concentration of HBr and alkene become low relative to the concentration of free radical, **termination** can occur. This could occur through a variety of specific pathways involving recombination of two free radicals to generate a new bond.

Alkene Reactions: Ozonolysis

1. Ozone (O_3) Is A Powerful Oxidant For Cleaving Alkenes To Carbonyl Compounds

Ozone does more than absorb UV radiation in the upper atmosphere and cause breathing problems in traffic-clogged cities. It's a powerful oxidant, and since its discovery in the mid 1800's by (Schönbein) has found use in the cleavage of carbon-carbon multiple bonds. Here's the pattern for the reaction of alkenes with ozone:

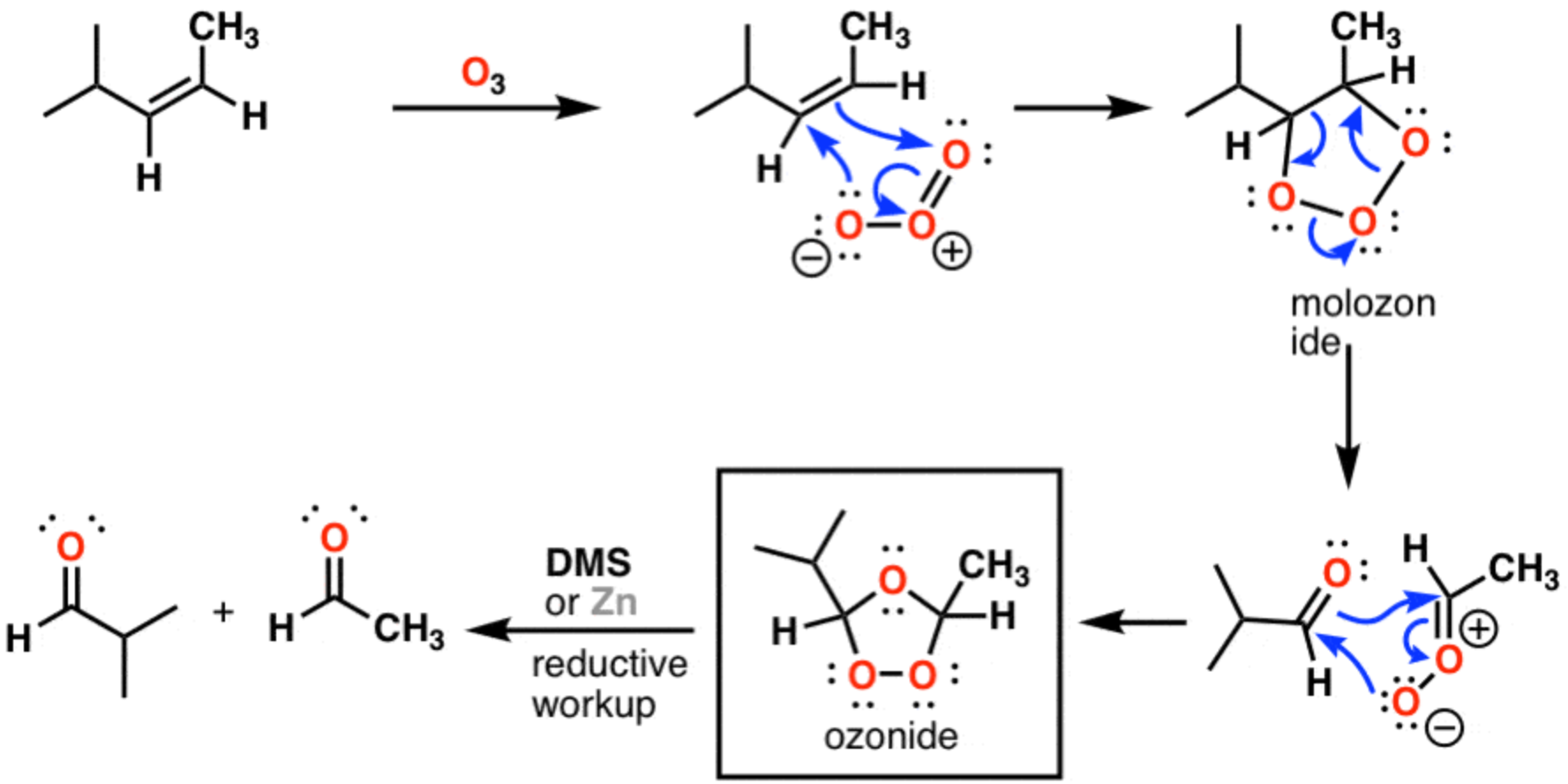
Ozonolysis of alkenes with reductive workup



(common reducing agents are zinc (Zn) or dimethyl sulfide $(CH_3)_2S$)

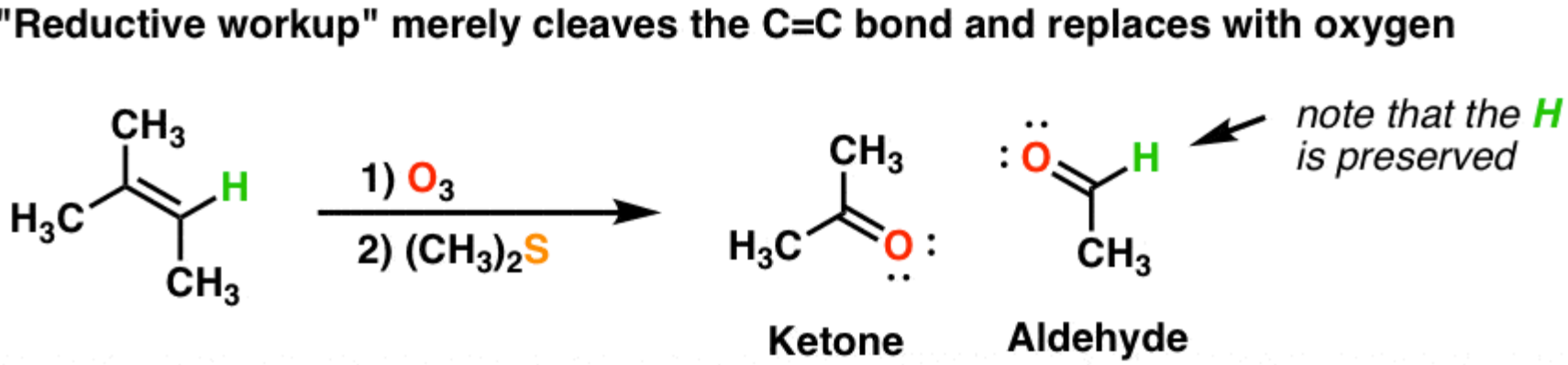
Note that the carbon-carbon double bond is broken and we are forming a carbon-oxygen double bond on each of the two carbons that originally composed the alkene. The second step in ozonolysis is called the "workup". There are two different types of "workup", and the most common is referred to as "reductive workup". In this step, we add a reducing agent (commonly zinc metal or dimethyl sulfide) that decomposes the intermediate formed at the end of the ozonolysis reaction (called an "ozonide" by the way). If you're wondering where the third oxygen of ozone went – it's now attached to what used to be our reducing agent (making either zinc oxide (ZnO) or dimethyl sulfoxide (DMSO). [For more details / mechanism everything is written out in this post.]

How it works: Oxidative cleavage of alkenes



2. Ozonolysis With "Reductive Workup" – All C–H Bonds Are Preserved

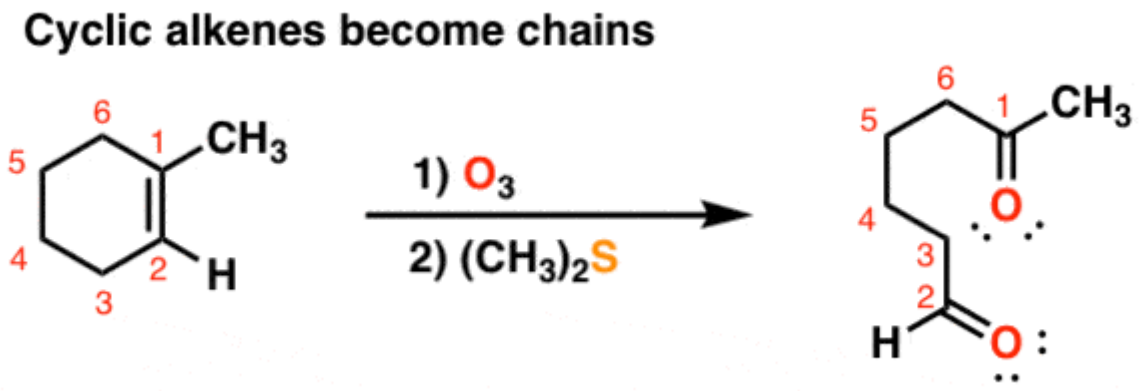
Using "reductive workup" preserves all other aspects of the molecule save the double bond. So if we start with, say, a trisubstituted alkene, as in the example below, we will end up with a ketone and an aldehyde. [What happens if the alkene carbon is attached to two hydrogens? It becomes formaldehyde, which is then further converted to carbon dioxide]



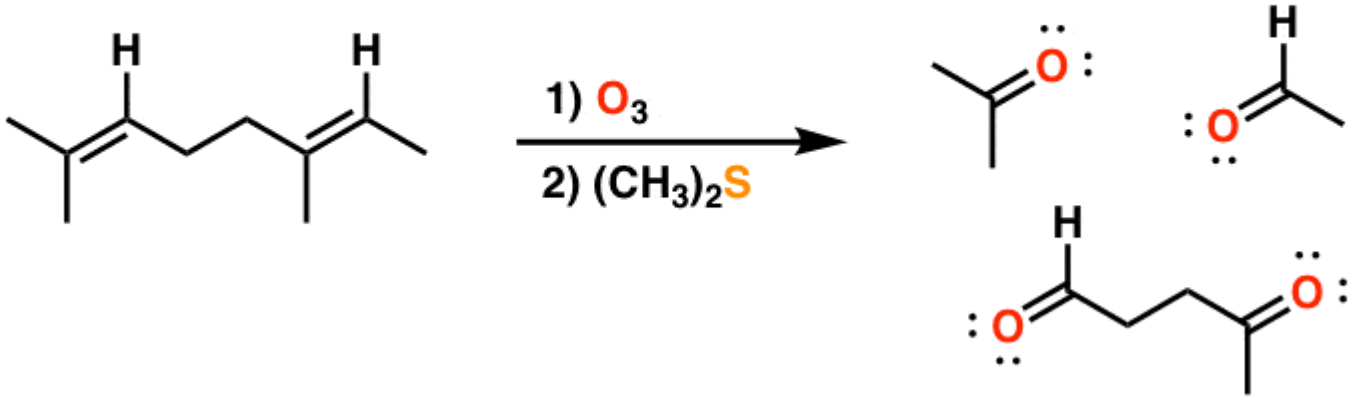
Note that although I've written $(CH_3)_2S$ as the reductant here, it's essentially interchangeable with Zn for our purposes.

3. Ozonolysis Of A Ring Results In A Chain With Two Carbonyls

An interesting consequence of ozonolysis is that if the alkene is within a ring, you end up with a chain containing two carbonyls:



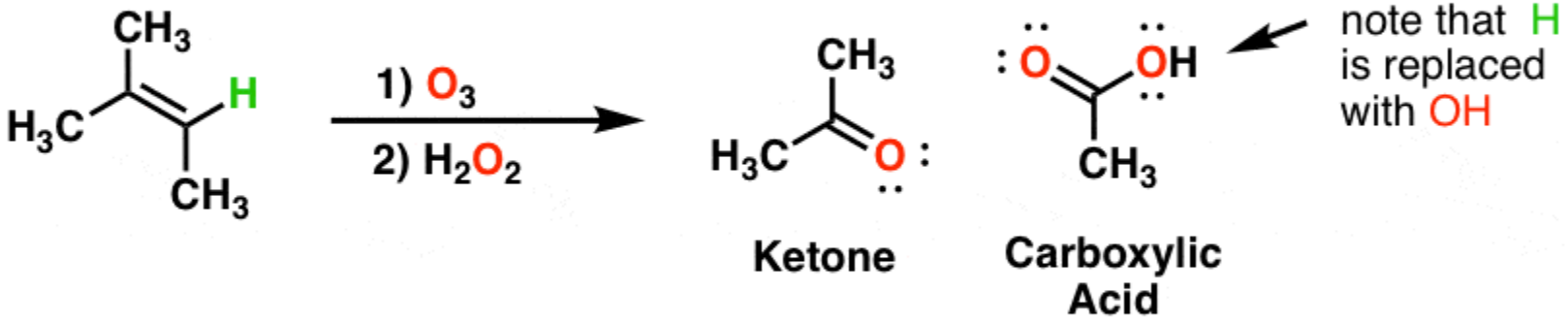
4. Ozonolysis Of A Compound With Multiple Bonds Results In Several Fragments



5. Ozonolysis With Oxidative Workup Converts Aldehydes To Carboxylic Acids

This isn't the end of the story with ozonolysis. There's a second type of workup that can be used, referred to as **oxidative workup**. Instead of using Zn or $S(CH_3)_2$, if we use the oxidant hydrogen peroxide [H_2O_2], any aldehydes that form will be oxidized to give carboxylic acids. Like in the example below – notice that the green C-H bond is oxidized to C-OH [but all the other hydrogens remain intact].

"Oxidative workup" oxidizes sp^2 hybridized C–H bonds to C–OH as well as cleaving C=C



Typical oxidant used for "oxidative workup" is H_2O_2 ; this oxidizes any aldehydes to carboxylic acids

The same process can be performed by replacing O_3 with hot, acidic $KMnO_4$

Summary: Three Key Families Of Alkene Reaction Mechanisms

1. Alkene Reaction Family #1 – The Carbocation Pathway

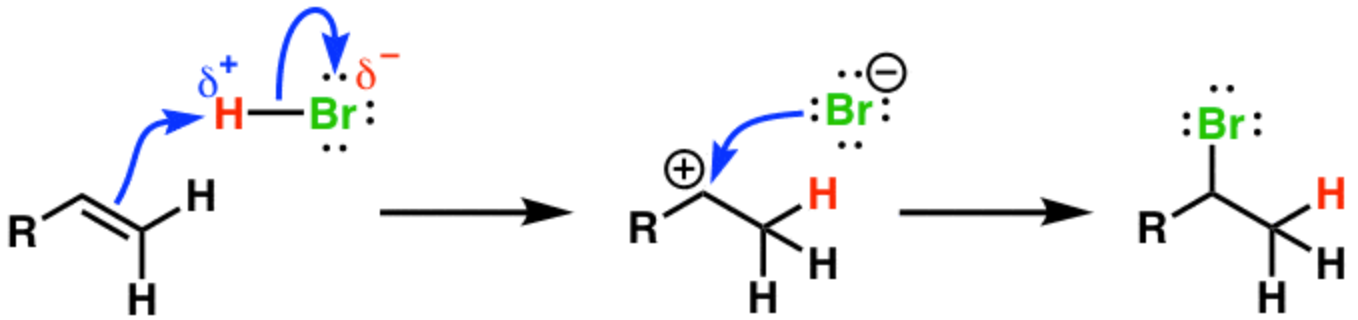
In the Carbocation Pathway, the alkene acts as a nucleophile and attacks an electrophile, resulting in the formation of a carbocation. The regioselectivity is Markovnikov and the stereochemistry of the reaction is a mixture of syn and anti products. Since carbocations are formed, be alert for rearrangements ! This is the only family where this can happen.

Pattern 1: The Carbocation Pathway

- Attack of alkene upon acid gives carbocation
- Carbocation attacked by nucleophile

(Sometimes this is followed by an acid-base reaction)

Example: addition of H–Br to alkenes



Regiochemistry: Markovnikov-Selective.
[**hydrogen** ends up bonded to the **less** substituted carbon of the alkene]

Stereochemistry: Syn + Anti (mixture)

Reactions in this category:

Addition of H–Cl
Addition of H–Br
Addition of H–I

Addition of $H_3O^{\oplus}$ (sometimes written as H_2O/H_2SO_4)

Note: since this reaction goes through a carbocation, **rearrangements are possible.**

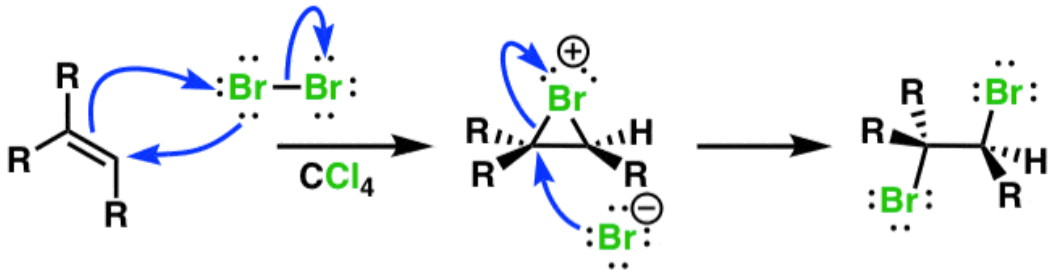
2. Alkene Reaction Family #2 – The 3-Membered Ring Pathway

In the so called "3-membered ring pathway" the alkene attacks an electrophile and forms a 3-membered ring intermediate. This intermediate is then attacked at the most substituted carbon by a nucleophile via a backside attack, giving rise to anti stereochemistry:

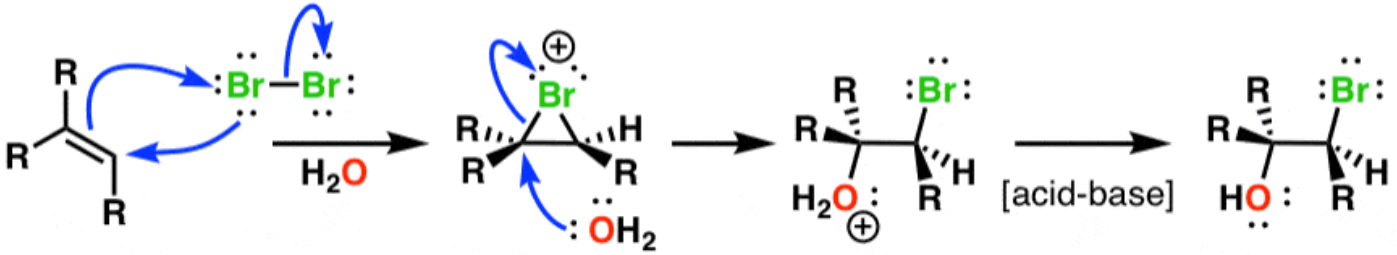
Pattern 2: The 3-Membered Ring Pathway

- Proceed through formation of a 3-membered ring cation
- Nucleophile attacks backside of most substituted carbon, opening the ring

Example 1: addition of Br_2 to alkenes



Example 2: Addition of Br_2/H_2O



Regiochemistry: Markovnikov-Selective (where relevant)
e.g. with Br_2/H_2O, water adds to the **most** substituted carbon of the alkene.

Stereochemistry: Anti. The two groups add to opposite faces of the alkene.

Reactions in this category:

Addition of halogens: Cl–Cl, Br–Br, I–I

Addition of halogens in the presence of nucleophilic solvents e.g. Br_2/H_2O, Br_2/ROH

Oxymercuration: $Hg(OAc)_2$, H_2O, then $NaBH_4$

Oxymercuration (with an alcohol as solvent) $Hg(OAc)_2$, ROH, then $NaBH_4$

Opening of epoxides under acidic conditions

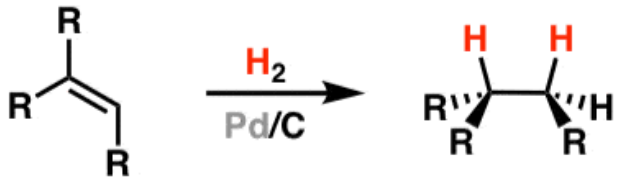
3. Alkene Reaction Family #3 – The Concerted Pathway

The "concerted" pathway is not meant to describe a single reaction mechanism, but it does describe similar consequences. In this class of reaction the regioselectivity is generally not relevant (except for hydroboration with BH_3, which is anti-Markovnikov). The stereochemistry of the reaction is syn, meaning the two new bonds form on the same face of the alkene.

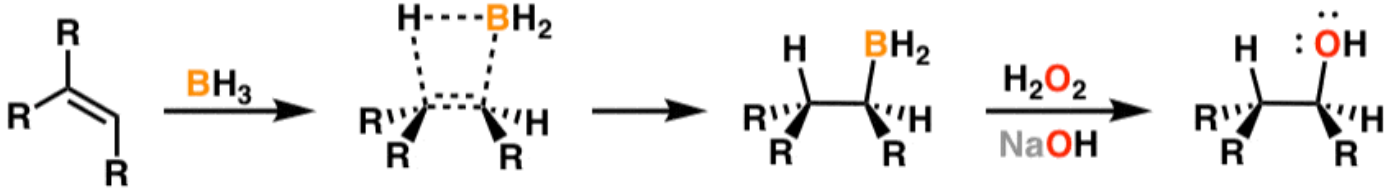
Pattern 3: The "Concerted" Pathway

Although these reactions do not share a common mechanism, they each form two new bonds on the same side of the alkene, a consequence of a "concerted" reaction mechanism.

Example 1 - hydrogenation



Example 2 - hydroboration



Regiochemistry: anti-Markovnikov-Selective (for BH_3). Note how hydrogen adds to the **most** substituted end of the alkene, and OH ends up on the **least** substituted end.

Stereochemistry: Syn. The two bonds are formed on the same side of the alkene

Reactions in this category: Hydroboration: BH_3, then H_2O_2/NaOH

Hydrogenation: Pd/C, H_2

Epoxidation: RCO_3H (e.g. mCPBA)

Dihydroxylation: OsO_4

Cyclopropanation: CH_2I_2, Zn-Cu

Dichlorocyclopropanation $CHCl_3$, NaOH

4. Two Miscellaneous Minor Alkene Reaction Families: Oxidative Cleavage of Alkenes And Free-Radical Addition To Alkenes

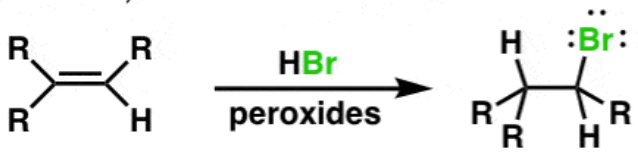
In addition there is a fourth pathway which goes through a free radical addition of HBr in the presence of peroxides. The regiochemistry is anti-Markovnikov and the stereochemistry is a mixture of syn and anti.

Finally in the presence of strong oxidants such as KMnO4 or O3 alkenes undergo a reaction called oxidative cleavage which results in the complete breakage of C=C to form carbonyl compounds.

Two Miscellaneous (but important) classes of reaction:

Radical addition of HBr

• Addition of HBr to alkenes in the presence of a radical initiator (peroxides)

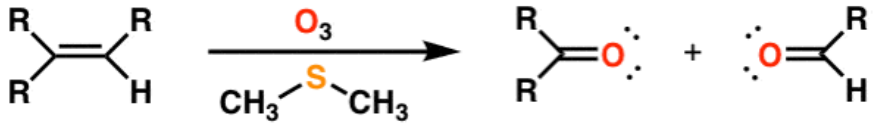


Regiochemistry: anti-Markovnikov-Selective.
Note that the H adds to the most substituted end of the alkene.

Stereochemistry: Syn + Anti
H and Br do not add exclusively "syn" or "anti" across the alkene.

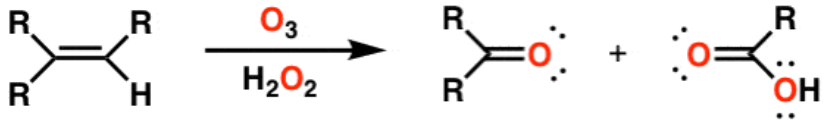
Oxidative cleavage:
• Addition of ozone (O_3) leads to cleavage of the carbon-carbon double bond
and formation of two new carbon-oxygen double bonds.

Ozonolysis (Reductive workup)



[or Zn, with H^+]

Ozonolysis (Oxidative Workup)



alternatively, $KMnO_4$ can be used to give the same products

and the C-H bond is replaced with a C-OH bond

Alkyne Reactions

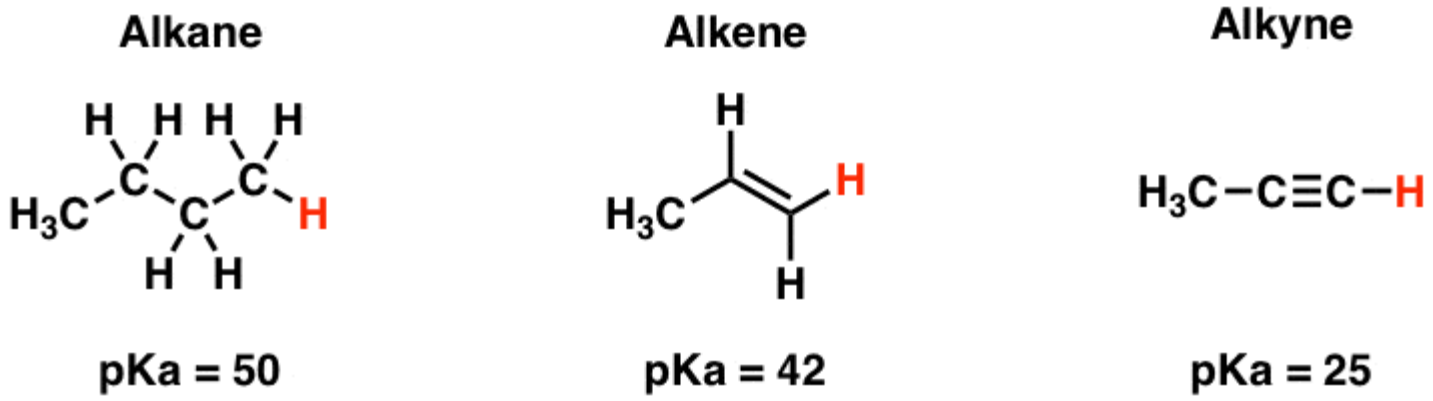
Acetylides from Alkynes, And Substitution Reactions of Acetylides

1. Alkynes Are Unusually Acidic. Deprotonation of Alkynes Gives "Acetylides"

Acidity of a compound is related to the stability of the conjugate base.

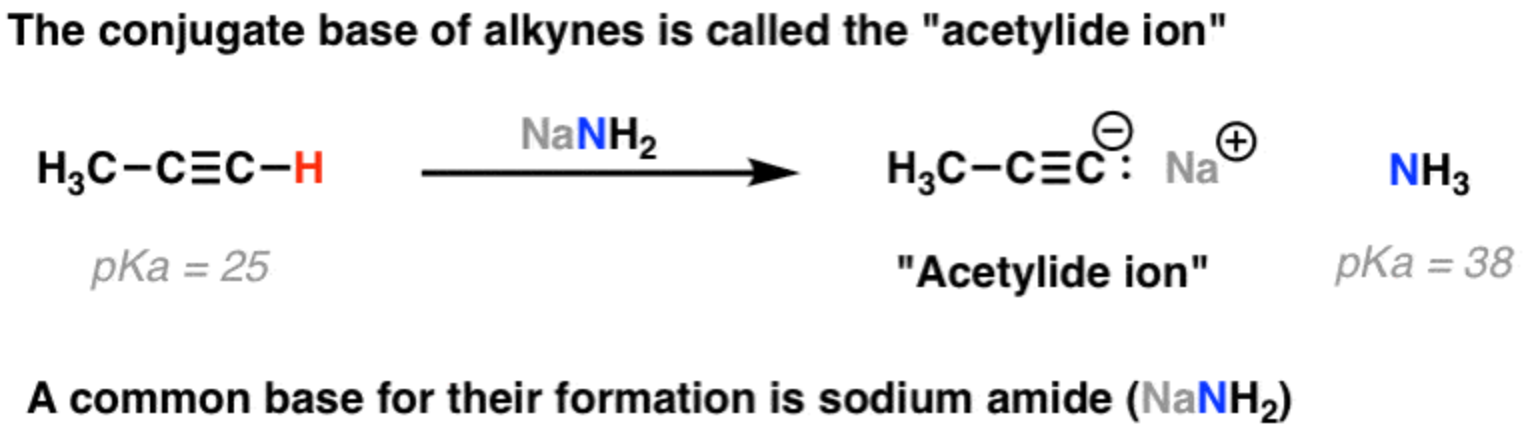
In an alkyne, where the carbon is sp hybridized, the lone pair resides in an orbital with 50% s character [the 2s orbital is closer to the positively-charged nucleus than the 2p orbital, increasing stability]. Compare that to alkenes (sp^2, 33% s-character) and alkanes (sp^3, 25% s character) and we have an explanation as to why alkynes have a pKa of 25, which is a factor of 10^{17} more acidic than your typical alkene (pKa about 42) and 10^{25} more acidic than alkanes (pKa 50).

Alkynes are relatively acidic hydrocarbons:



This means that alkynes can be deprotonated without resorting to heavy artillery (i.e. organolithium bases, or Schlösser's base – not that you probably need to know about that particular reagent) required to deprotonate alkenes. Instead, readily available sodium amide ($NaNH_2$) the conjugate base of ammonia (pKa 38) can be used, which is a big plus for convenience.

Deprotonation of alkynes with a strong base yields the conjugate base, often referred to as an "acetylide" :



So that's certainly one way in which the chemistry of alkynes is distinct from that of alkenes: **alkynes can be readily deprotonated.**

2. Alkylation of Acetylides With Alkyl Halides via Substitution

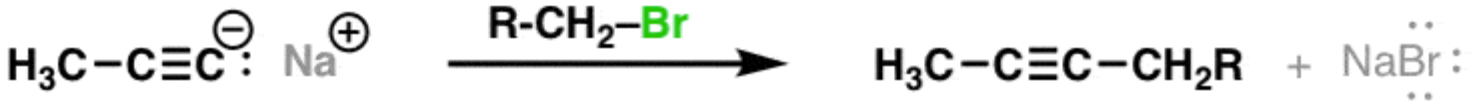
The conjugate base is a stronger nucleophile. And almost every reaction in organic chemistry involves the attack of a nucleophile upon an electrophile. So one logical application of being able to deprotonate alkynes into acetylide ions is that **they are excellent nucleophiles and we can combine them with various electrophiles.**

One of the simplest and yet most **powerful** reactions in terms of generating a diverse array of functional groups is the S_N2 reaction, in which a nucleophile attacks a carbon with a good leaving group (alkyl halides or sulfonates). The "big barrier" to the S_N2 is **steric hindrance** so the reaction works particularly well for methyl and primary alkyl halides (secondary alkyl halides are a bit iffy in this context).

Here's an example of how the S_N2 can be applied to alkynes.

Acetylide ions are strong bases and good nucleophiles

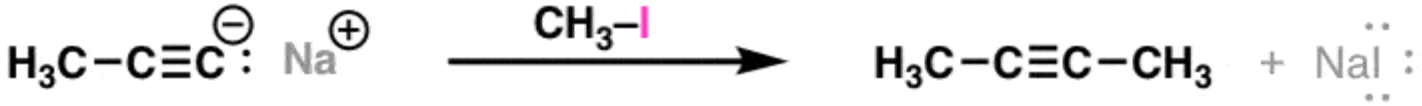
Notably useful: They can perform an S_N2 reaction with alkyl halides



Acetylide ion

Form	Break
C–C	C–Br

Specific Example:



Note: works best for primary (and methyl) alkyl halides

It's a typical substitution reaction: we're forming and breaking a bond on the same carbon.

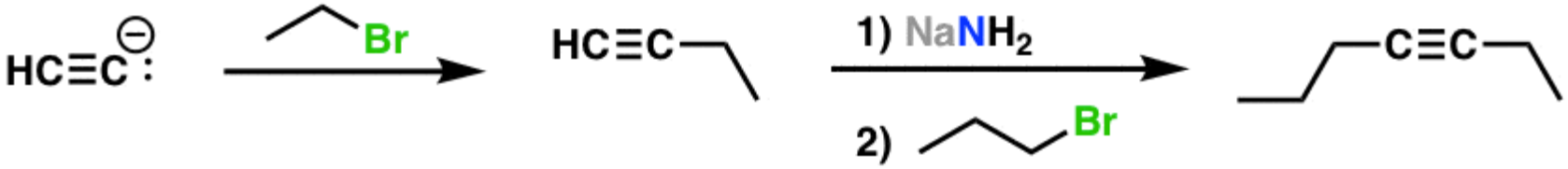
Now comes the important part. This S_N2 reaction is particularly useful.

3. Why Is This So Important? Because It Forms A New Carbon-Carbon Bond!

Notice the **type** of bond that's being formed here: **we're forming a carb0n-carbon bond.** If you've read previous posts leading up to this one, scratch your head for a moment: can you think of any examples where we're forming a carbon-carbon bond? Probably not! [one example is cyanide ion with an alkyl halide].

Note that in these reactions a carbon-carbon bond is formed

Therefore, these reactions can be used for **extending the carbon chain**



Note that the second alkyl halide can be different from the first; we can make unsymmetrical alkynes.

Why is this important? Consider that organic chemistry is the study of carbon containing molecules. The reaction of acetylides with alkyl halides, therefore, **is a way of extending the carbon skeleton of the molecule.** We haven't yet learned any other reactions that perform this function nearly as well.

Partial Reduction of Alkynes To Obtain Cis or Trans Alkenes

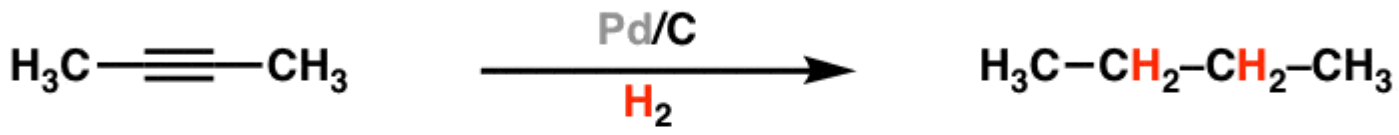
1. Hydrogenation of Alkynes With Pd-C and H_2 Gives Alkanes

The reduction of alkenes by hydrogen in the presence of a metal catalyst ("catalytic hydrogenation") is a time-honoured reaction recognized by Sabatier's receipt of the Nobel Prize for Chemistry in 1904. Incidentally, the products of this reaction are a part of our daily lives – modern margarine is produced from hydrogenation of vegetable oils for example [Trans-fats are an unfortunate byproduct of catalytic hydrogenation].

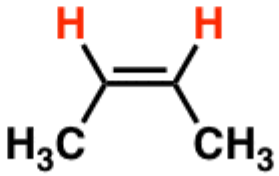
Bearing two carbon-carbon π bonds, alkynes may likewise be hydrogenated. Under conditions used for the hydrogenation of alkenes, both bonds are reduced, producing alkanes.

[It's reasonable to think that you could prevent over-reduction simply by only using one molar equivalent of hydrogen gas; in practice, this doesn't work very well]

Hydrogenation of an alkyne with Pd/C and H_2 gives the alkane



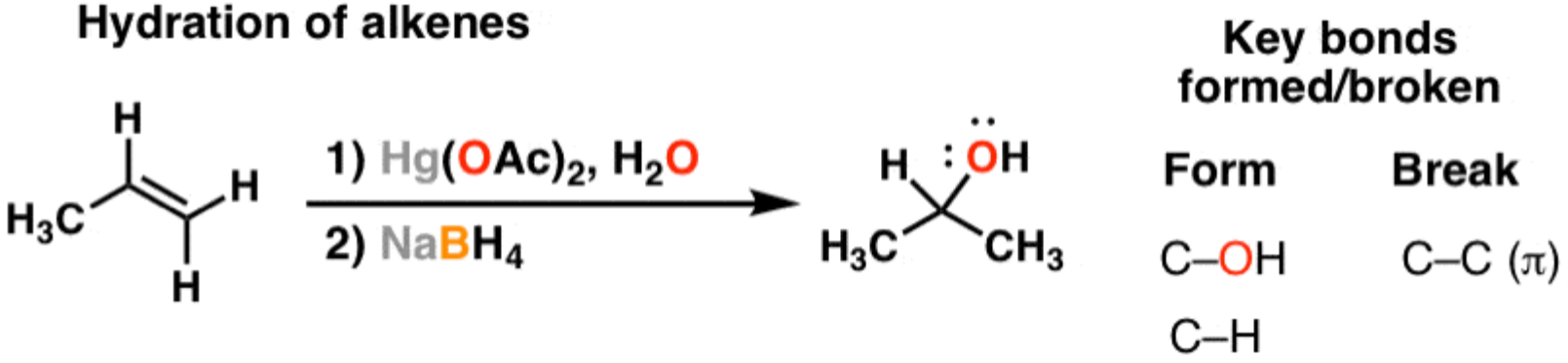
proceeds *via*



Hydroboration and Oxymercuration of Alkynes

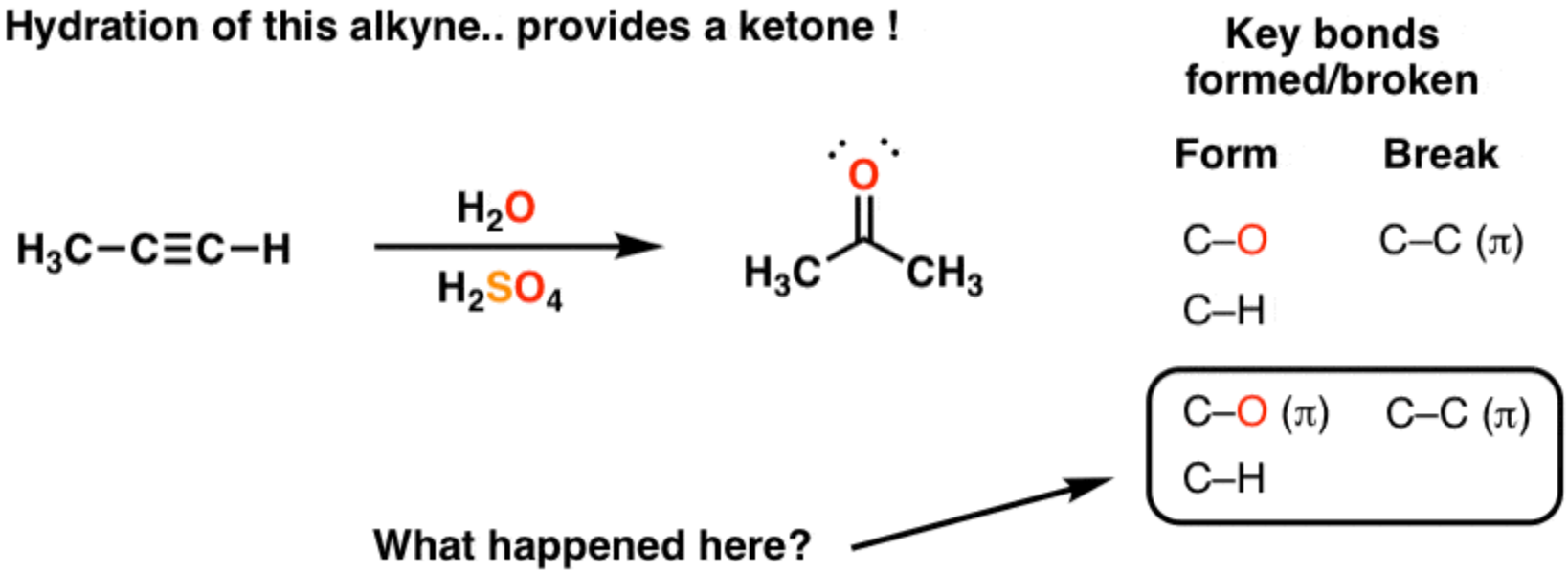
1. Hydration of Alkenes Gives Alcohols

We have talked about the **hydration of alkenes** . This can be done either with aqueous acid, or with mercury and water ("oxymercuration"). Looking at the reaction with alkenes, the pattern is fairly straightforward: break a C-C π bond, and form a C-H and C-OH bond. Also recall that the oxygen ends up on the most substituted carbon ["Markovnikov" selectivity].



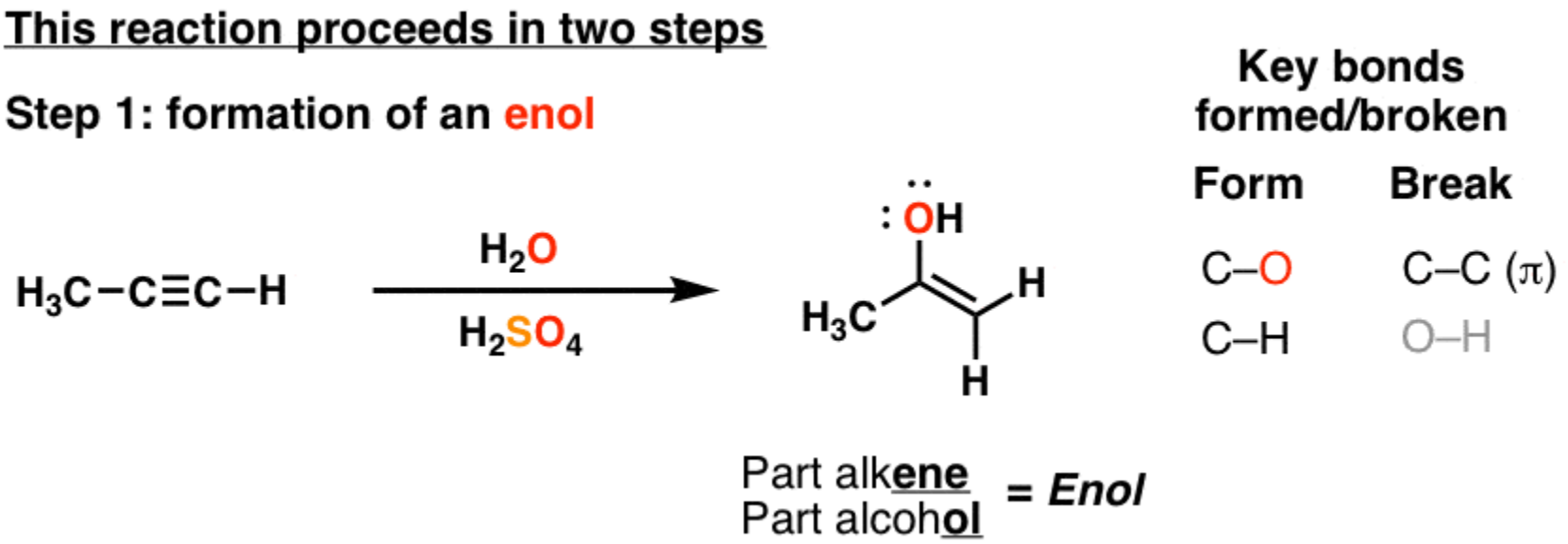
2. Hydration of Alkynes With Aqueous Acid Gives… Ketones??… What?!

o what happens when we try this reaction on alkynes? We might expect to observe the same pattern, right? After all, it's just a simple addition reaction.
Well… here's what we actually observe. We get… a **ketone** !?



3. The First Step In The Hydration of Alkynes Is Formation Of An "Enol"

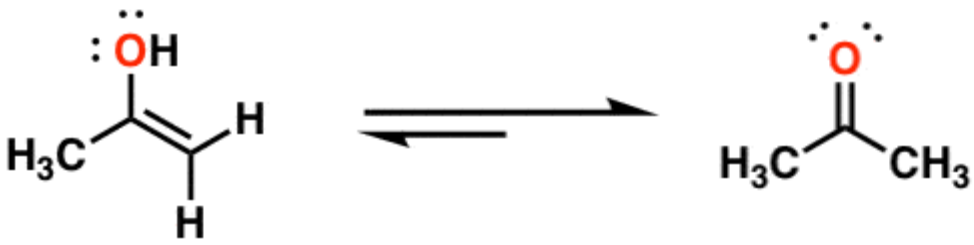
If you monitor this reaction closely – one way to do it is in an NMR tube – it's actually possible to observe the first product of this reaction, which is the one shown below. We call this an "enol", by the way – kind of like a spork (half spoon half fork) it is part alkene, part alcohol.



4. The "Enol" Is Converted To A Ketone Through A Process Called "Tautomerization"

Over time, this enol spontaneously converts into the ketone. Note that the two have the same molecular formula – they are *constitutional isomers.* And they are in equilibrium with each other. We call these constitutional isomers which interconvert, "tautomers". This equilibrium generally favors formation of the ketone due to the strong C-O π bond (compared to C-C π).

Step 2: Conversion of enol to ketone through *tautomerism*

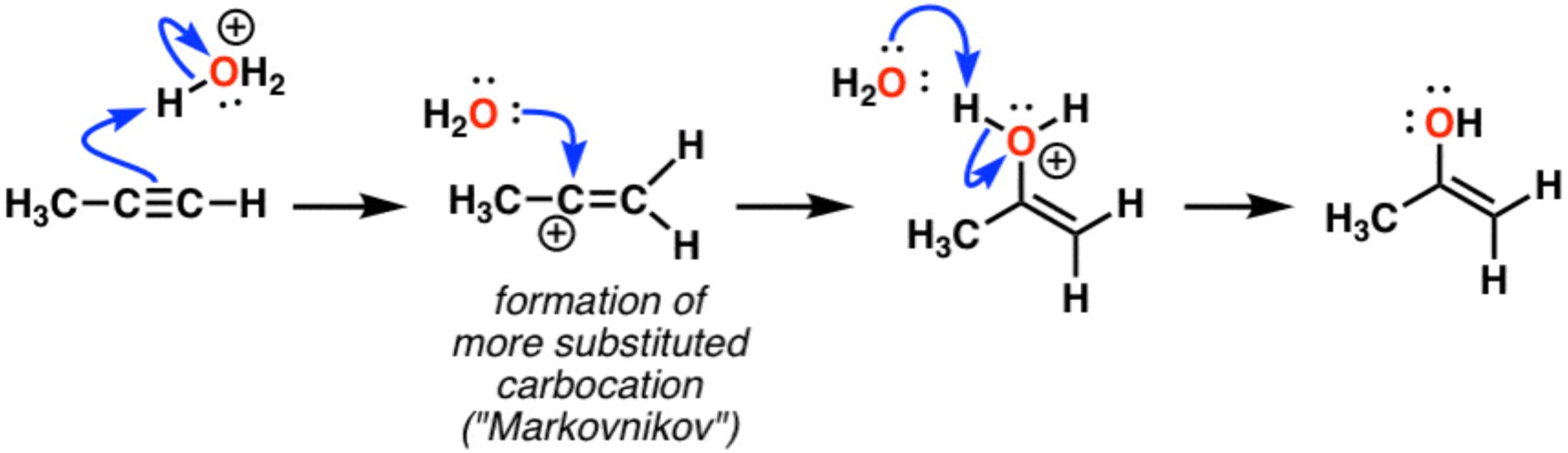


Form	Break
C–O	C–C (π)
C–H	O–H

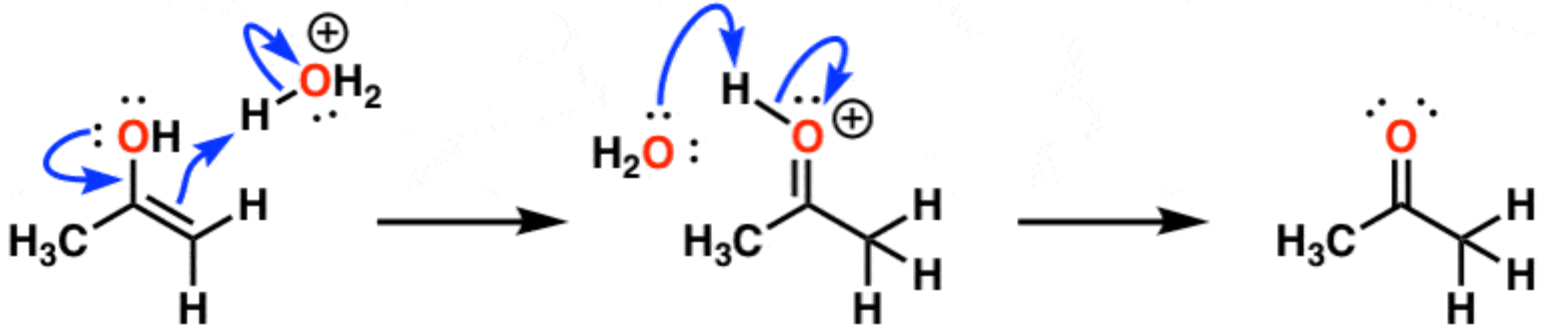
Equilibrium favors ketone

Hydration of Alkynes - The Mechanism

Step 1 - Enol formation



Step 2 - Tautomerization



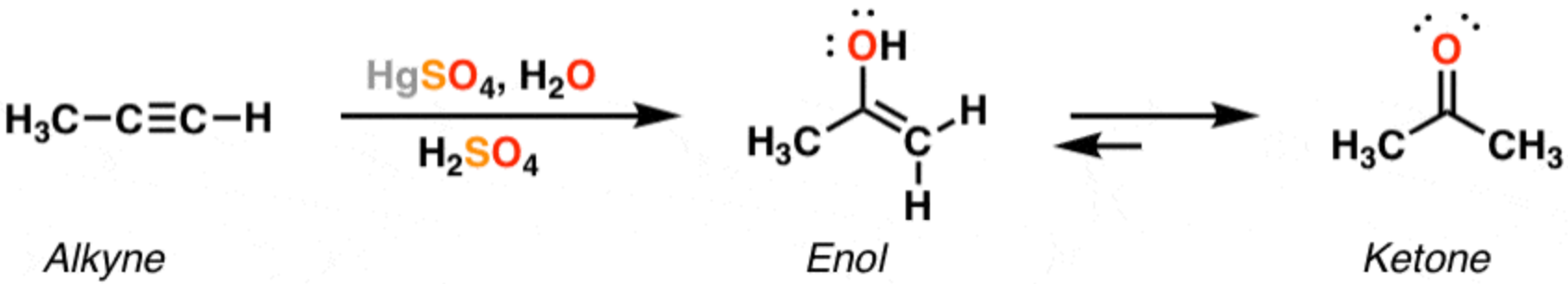
Protonate carbon

Deprotonate oxygen

5. Alkynes Can Also Be "Hydrated" via Oxymercuration

There's another way to "hydrate" alkynes, just like there was with alkenes. We can also perform the same reaction with mercury, water and strong acid [sulfuric acid, H_2SO_4 is the usual acid of choice]. For interesting reasons we wont get into at the moment, NaBH4 is not generally needed here; it is sufficient to merely have water and acid present.

Oxymercuration of alkynes produces the same result as hydration



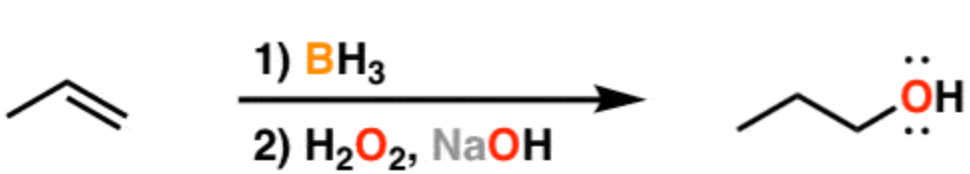
6. Hydroboration Of Alkynes Occurs With "Anti-Markovnikov Selectivity", Giving Aldehydes From Terminal Alkynes

There's also hydroboration. Remember how it performs "anti-Markovnikov" hydration of alkenes?

Likewise, we can use the same reaction to perform "anti-Markovnikov" hydroboration of alkynes. *[Note: while BH_3 is sometimes written for this, it's not strictly correct to do so. [Why? Double addition.] Instead often use sterically hindered boranes, such as disiamyl borane or 9-BBN that both increase the proportion of addition to the less substituted carbon and also prevent a second hydroboration reaction.]*

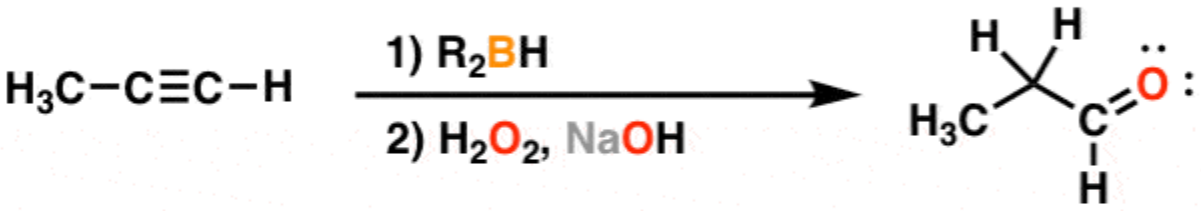
Just as in the cases above, we initially obtain an enol. However, under the reaction conditions, keto-enol tautomerism results in formation of the aldehyde.

Bottom line here: if we start with a "terminal" alkyne, that is an alkyne where one of the carbons is attached directly to H – then we will obtain **ketones** with H_3O+/H_2SO_4 or via oxymercuration, and **aldehydes** via hydroboration.



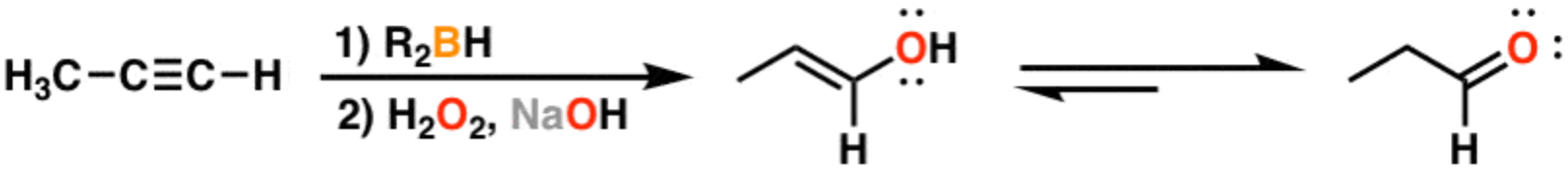
Form	Break
C–H	C–C (π)
C–OH	

Hydroboration of terminal alkynes produces *aldehydes*



note: disiamyl borane or 9-BBN are often used in place of BH_3

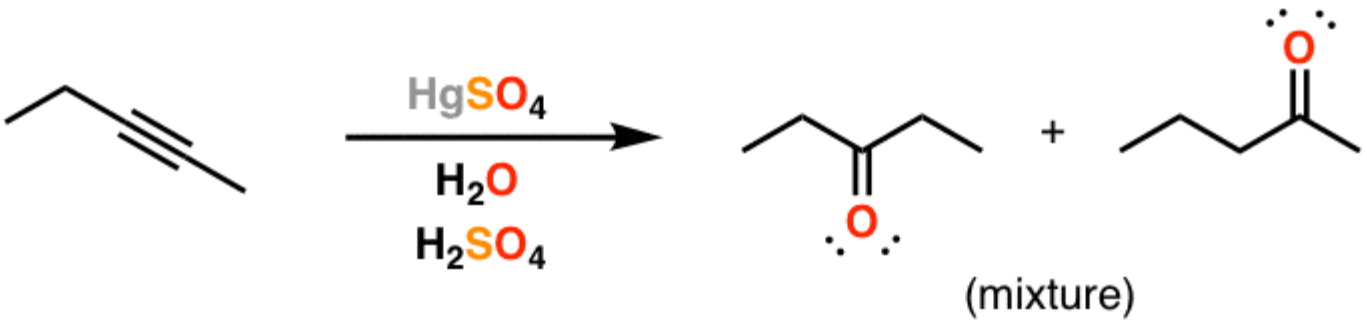
This reaction also proceeds through an enol which tautomerizes to the aldehyde. Note that the oxygen ends up on the least substituted carbon of the double bond



Enol

7. Depending On The Alkyne, Mixtures Of Products Can Be Obtained

One final note: if we use an alkyne where both ends are directly attached to carbon, we will obtain a mixture of products. That's just "Markovnikov's rule" – remember that if each carbon in the multiple bond is attached to an identical number of hydrogens, then we can't determine which is the "most substituted" for our purposes. Like in this example.



Alkyne Hydrohalogenation – Addition of HX To Alkynes – HCl, HBr, and HI

In the previous three posts on alkynes we've introduced some new reactions that are specific to alkynes (versus alkenes):

1. Deprotonation (and subsequent substitution),

2. Partial reduction to alkenes, and

3. Formation of aldehydes and ketones through net "hydration".

1. Addition of Hydrogen Halides To Alkynes (Once) – Hydrohalogenation

The three major examples in this category are the reaction of hydrohalic acids (H-Cl, H-Br, and H-I) with alkynes. If you recall, when added to alkenes, these reagents were:

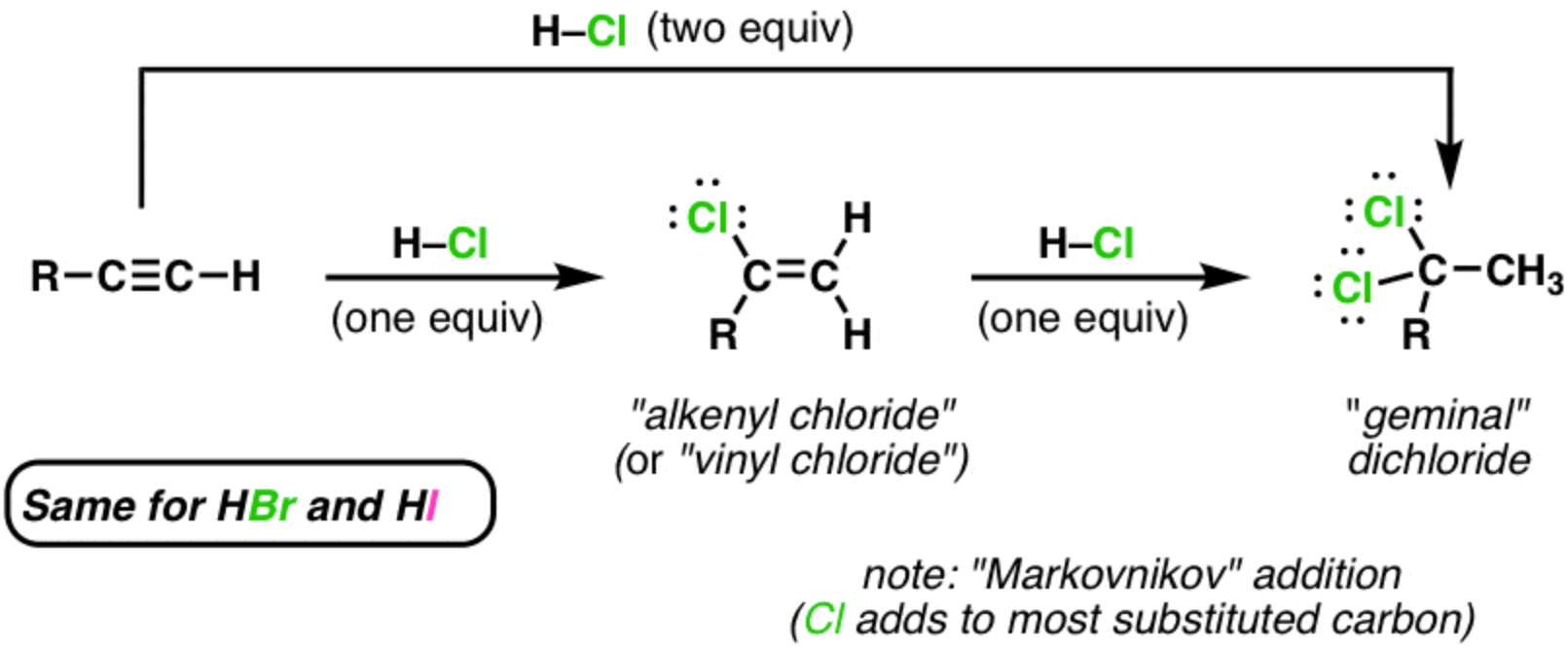
1. attacked by the π bond of the alkene to give a carbocation (on the most substituted carbon, giving "Markovnikov" regioselectivity) followed by
2. attack of halide ion on the carbocation.

Since alkynes merely differ from alkenes in the addition of a second π bond, we would expect that these reactions would also work for alkynes as well – **and they do**!

Addition of Acids To Alkynes

One equivalent of acid gives the alkenyl halide ("vinyl halide")

Two equivalents of acid gives the "geminal dihalide"



If we treat an alkyne with a single equivalent of H–Cl [**note – we'll just use H-Cl in all of these examples, but HBr and HI work in exactly the same way**] we end up forming an alkenyl chloride. Note that the chlorine atom ends up attached to the most substituted carbon of the alkene [**"Markovnikov" regioselectivity**].

2. Addition Of A Second Equivalent Of HX To An Alkyne

You might be wondering if it's possible to for this π bond to react with a **second equivalent** of H-Cl. The answer is yes. [Note – it **is** possible to just "stop" the reaction at this stage if we use just one equivalent, because the product (alkenyl chloride) is less reactive towards HCl than the starting alkyne].

Indeed, if we add a second equivalent of H-Cl, it adds to either side of the C-C π bond, giving us the product where two chlorine atoms are on the same carbon. By the way, we call this a **"geminal" dichloride** (think Latin – "gemini" = twins).

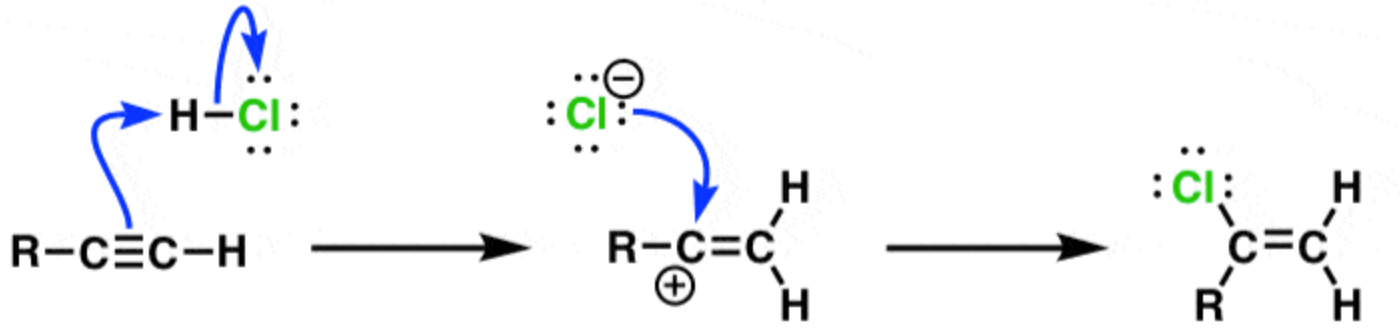
We can also get this product if we simply add two equivalents of H-Cl to the starting alkyne.

3. Addition of Hydrogen Halides To Alkynes – The Mechanism For Hydrohalogenation

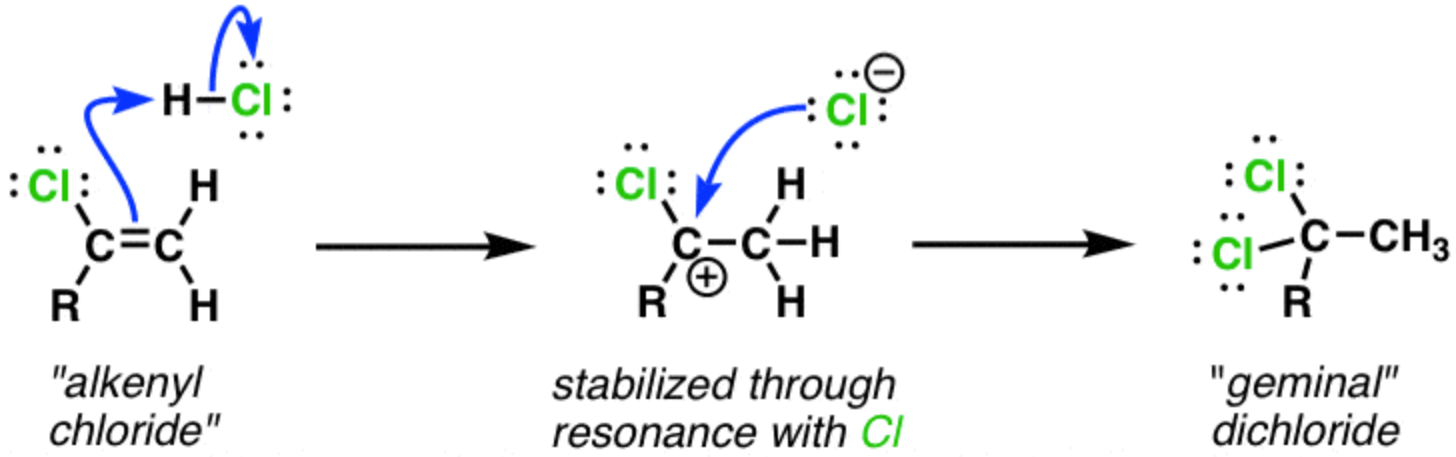
Halogenation of Alkynes: How It Works

Mechanism still proceeds through a carbocation

Addition of first equivalent:



Addition of second equivalent:



4. Comparing Alkenes and Alkynes In The “Carbocation Pathway”

It’s probably worth tying back this post to the post on alkenes and the carbocation pathway, noting the similarities and differences between the chemistry of alkenes and alkynes. Hopefully this table will prove useful:

The Carbocation Pathway - Comparing Alkenes and Alkynes

Similarities

- Hydrogen halides add to most substitued carbon of π bond ("Markovnikov")
- Proceeds through carbocation intermediate

Differences

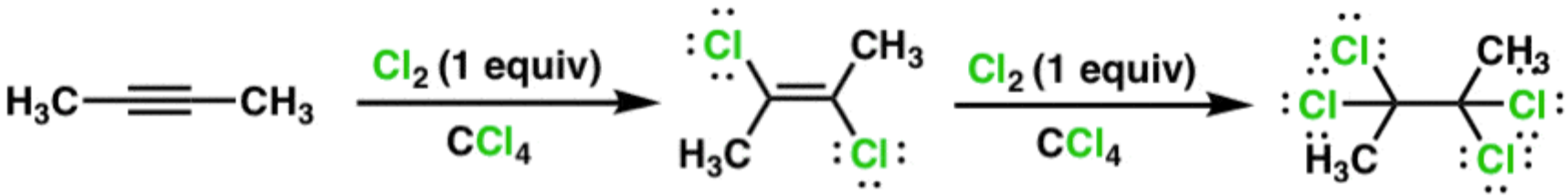
- Hydrogen halides can add *twice* (giving "geminal" dihalides)
- Hydration [H_2O, H_2SO_4] gives *ketones* (via the enol)

Alkyne Halogenation: Bromination, Chlorination, and Iodination of Alkynes

1. Halogenation of Alkynes With Cl_2, Br_2, and I_2

Well, happily for us, **the reaction of alkynes with electrophiles such as Cl_2, Br_2, and I_2 *does* give very similar results to what is observed with alkenes.** For example, treatment of an alkyne with 1 equivalent of Cl_2 provides a dichlorinated alkene with the two chlorides opposite to each other. If a second equivalent of Cl_2 is added, the tetrachloro derivative will form.

Chlorination of alkynes gives the *trans* alkene
A second equivalent of Cl_2 gives the tetrachloro alkane



trans product obtained

CCl_4 (carbon tetrachloride) is solvent

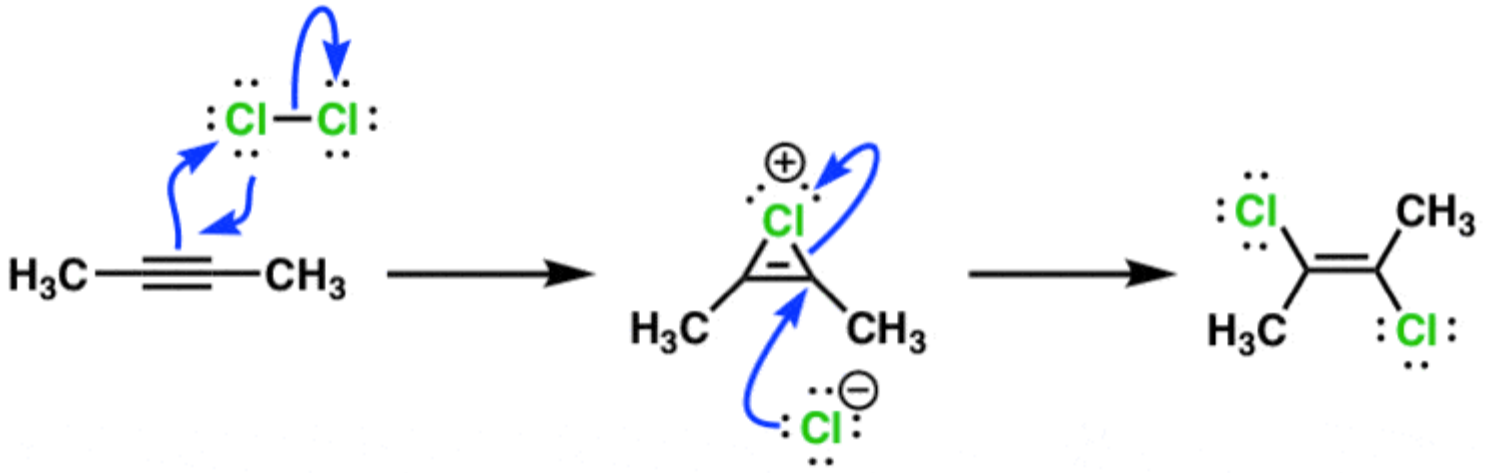
Also works for Br_2 and I_2

2. Halogenation of Alkynes Also Proceeds Through A Bridged-Ion Intermediate, Providing *Trans* Products

Just as with alkenes, a π bond from the alkyne can act as a nucleophile, attacking Cl_2 and giving rise to a bridged intermediate. In the next step, chloride ion attacks the carbon from the back face, leading to the trans product.

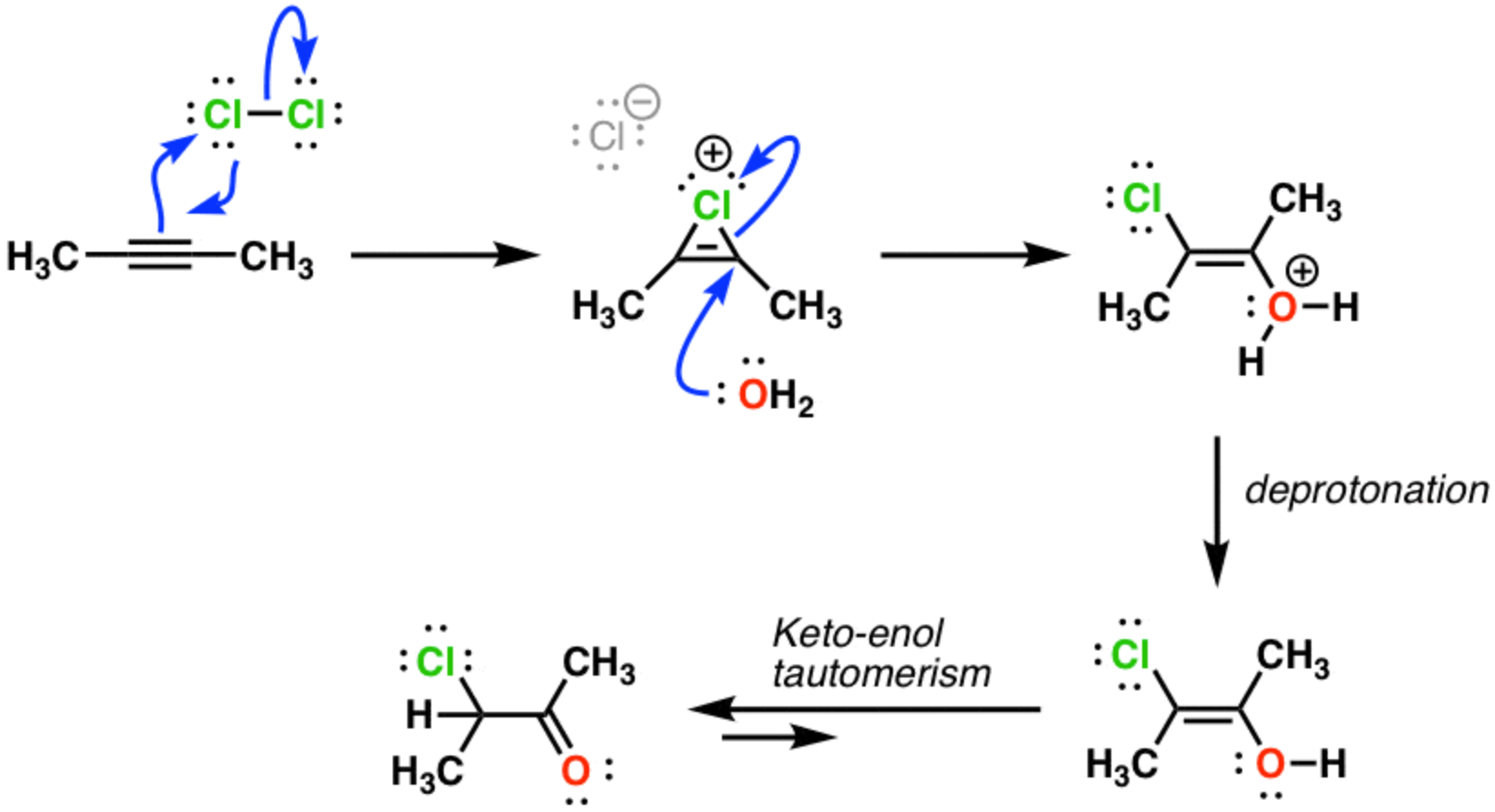
How does this work?

Proposed mechanism:



bridged-ion intermediate

Similar mechanism for Br_2 and I_2


Cl
Cl
H3C
CH3
Cl
Cl
H3C
CH3
OH2
Cl
CH3
H3C
O
H
H
deprotonation
Keto-enol
tautomerism
Cl
H
CH3
H3C
O
Cl
CH3
H3C
O
H

Alkyne Reaction Mechanisms That Pass Through A “Concerted” Pathway – Cyclopropanation, Hydrogenation, Hydroboration

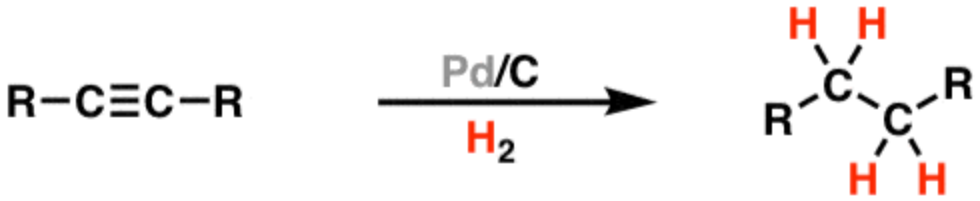
1. The “Concerted” Pathway for Alkynes: Hydrogenation and Hydroboration

Two major reactions in the “concerted” pathway that work for alkynes are **hydrogenation** and **hydroboration**. However, as we’ve already seen, each of these reactions comes with a twist when applied to alkynes.

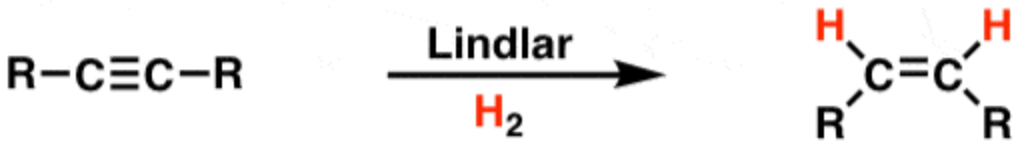
With **hydrogenation**, treatment of an alkyne with a late metal catalyst such as Pd-C (or platinum on carbon, among others) in the presence of hydrogen leads not just to one hydrogenation, but **two**. The product is an alkane. It’s possible to get the reaction to stop “halfway” by using a less reactive catalyst such as “Lindlar’s catalyst” or by using nickel boride. This provides the *cis* alkene. Alternatively (although this doesn’t really count as a “concerted” mechanism, one can obtain the *trans* alkene through the use of sodium in ammonia (Na/NH_3).

The "Concerted Pathway for Alkynes" - What Works?

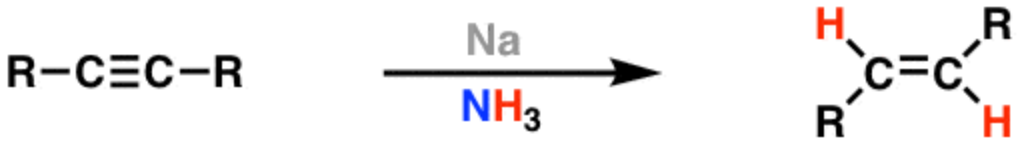
1. Hydrogenation (although Pd/C / H_2 adds *twice* to alkynes)



Note: partial hydrogenation can be achieved using Lindlar's catalyst or nickel boride to give syn hydrogenation



The anti product can be formed using Na/NH_3 (although this is not a concerted reaction)



Lindlar's catalyst is a palladium catalyst poisoned with traces of lead and quinoline, that reduce its activity such that it can only reduce alkynes, not alkenes. It always gives the *cis*-alkene, in contrast to Na/NH_3, which gives the *trans* alkenes. Lindlar's catalyst doesn't really have a "structure". Like Raney nickel, it's basically a metal that has been modified in a very particular way to provide a certain desirable set of properties. Sometimes you might see it written as $Pd\text{-}CaCO_3\text{-}PbO_2$, but it's usually just written "Lindlar".

Similar or the same as: There's a whole family of poisoned catalysts that are similar. You might also see Ni–B (nickel boride), $Pd\text{-}CaCO_3$, palladium on barium sulfate, $Pd\text{-}CaCO_3$-quinoline and others enlisted to do the same task.

Reduction Of Alkynes To *cis*-Alkenes With Lindlar's Catalyst