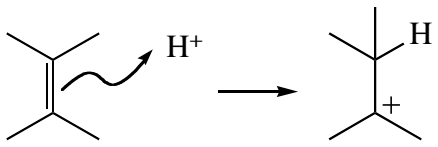
# Chapters 9–10. Additions across C=C π Bonds.

We've learned a number of different substitution and elimination reactions of alkyl halides. We've learned that compounds with lone pairs are nucleophiles, and alkyl halides are electrophiles. Now we're going to learn the reactions of a different class of nucleophiles: the C=C π bond in alkenes and alkynes.

## *10.1. Reactivity of Alkenes.*

The C=C π bond of an alkene is higher in energy than the C—H or C—C σ bond. As a result it can act as a nucleophile towards various electrophilic species.

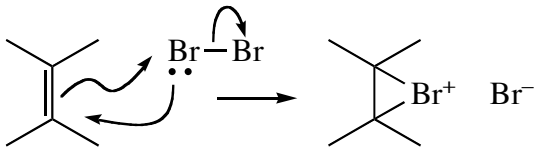
When a C=C π bond acts as a nucleophile, one of the C atoms takes the π electrons away from the other C and uses them to make a bond to the electrophile. The other C atom either becomes electron-deficient:




The top C takes the pair of electrons from the π bond and uses it to make a σ bond to the H.

The lower C has a pair of electrons taken away and becomes electron-deficient.

or it gets a pair of electrons from the electrophile at the same time as the electrophile is getting a pair of electrons from the π bond:




The top C takes the pair of electrons from the π bond and uses it to make a σ bond to one Br, displacing the other Br as a leaving group.

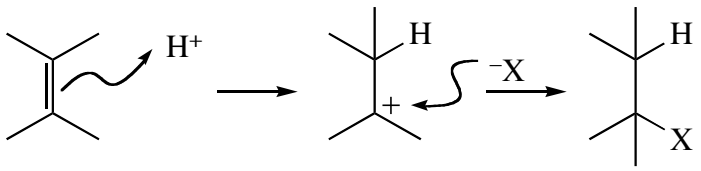
The electrophilic Br uses a lone pair to make a bond to the lower C to replace the π electrons that were taken away.

Note the balance of charge in both examples! Because the C=C π bond is lower in energy than a lone pair (it is, after all, a bond, not an unshared, nonbonding pair of electrons), it reacts only with very strong electrophiles and not at all with alkyl halides (except under circumstances you will learn next semester).

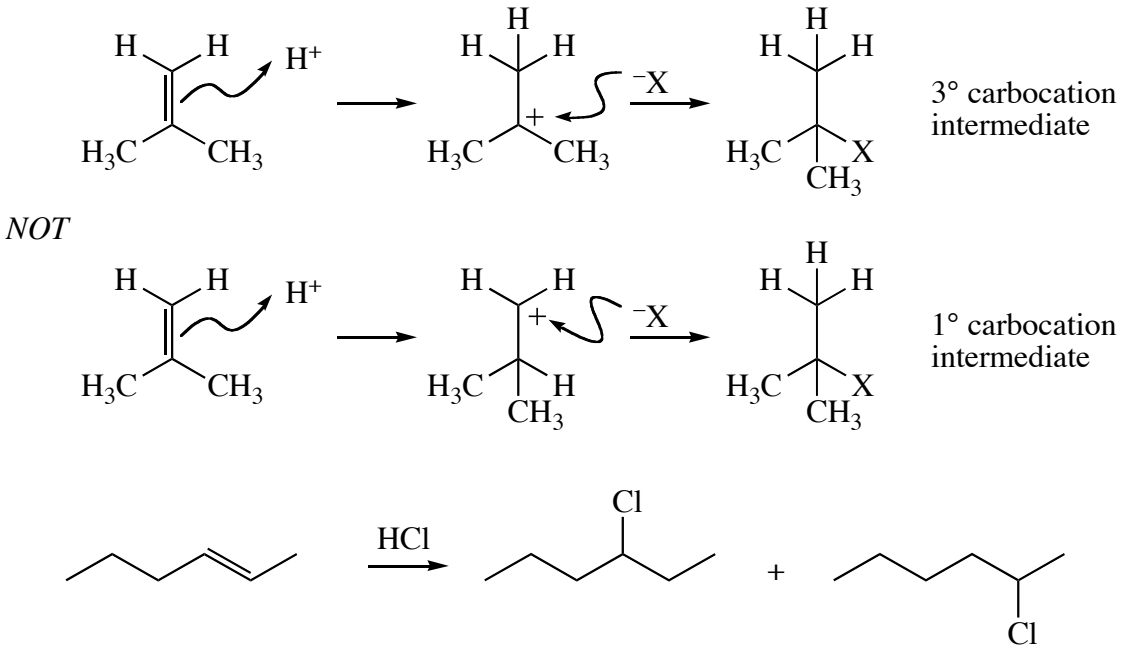
## *10.2. Addition of Strong Acids HX to Alkenes to give Alkyl Halides.*

Alkenes C=C react with strong acids HX to give alkyl halides H—C—C—X. HX can be HF, HCl, HBr, or HI, although HCl and HBr are used most often. Alkenes also react with carboxylic acids to give esters H—C—C—$O_2$CR.

When alkenes react with HX, they do so in a two-step mechanism. Alkenes are nucleophiles, so the first step in their reaction with HX must involve reaction with an electrophile. Acids are electrophiles because they give up $H^+$. The first step in the reaction of an alkene with HX, then, is addition of $H^+$ to the alkene to give a carbocation intermediate. The carbocation is an electrophile, of course, so the next step is combination with a nucleophile. The nucleophile is $X^-$, the conjugate base of the acid. In fact, the second step of the mechanism is the same as the second step in the $S_N1$ mechanism. Here you just have a different way of generating the carbocation intermediate.

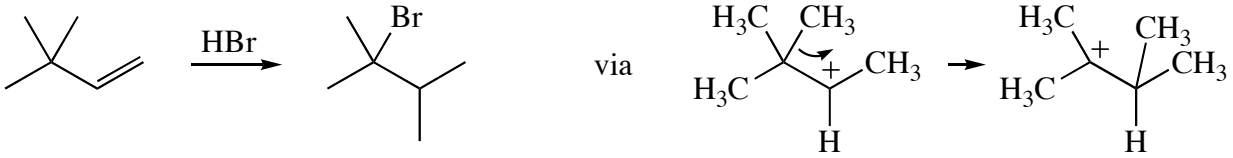



Suppose an alkene that has different substituents on each C. In principle we can obtain two products. The major product is the one where the nucleophile has added to the C better able to bear a positive charge, in many cases the more substituted C. This rule, called *Markovnikov's rule*, derives directly from the fact that the reaction proceeds through a high-energy carbocation, so the faster reaction is the one that gives the lower energy carbocation intermediate. Another way of formulating Markovnikov's rule is that the C with more H atoms gets another one (them that has, gets more). If the two carbocations are about equal in energy, you will get a mixture of regioisomers.

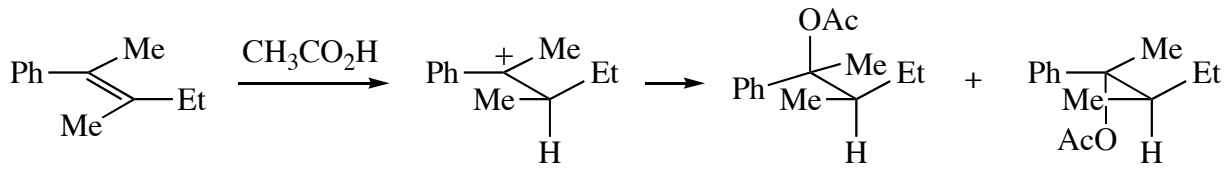



The carbocation intermediates in HX addition reactions are the same as the carbocation intermediates in $S_N1$ and E1 reactions, and as such they can undergo rearrangements. Again, the rearrangements occur to give more substituted carbocations, so again, 2° carbocations are most prone to undergo

rearrangement, 3° carbocations tend not to undergo rearrangement, and 1° carbocations can't be formed in the first place.



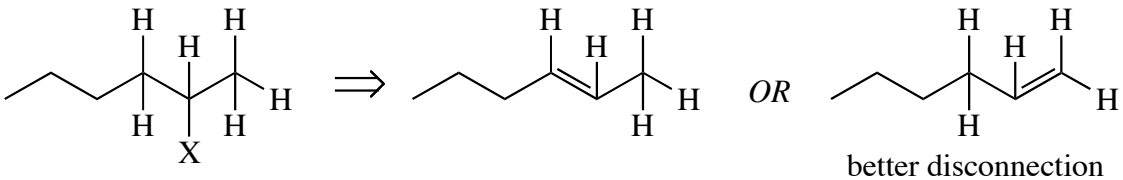

Alkenes are of course flat, whereas the product alkyl halides are not, so the question arises, do the H and the X add to the same face of the alkene (called *syn addition*), to opposite faces (*anti addition*), or is a mixture of products obtained? When the alkene reacts with $H^+$, a carbocation is obtained. Suppose the $H^+$ adds to the bottom face of the alkene. The carbocation is planar, and the top face of the carbocation is no different from the bottom face, so the $X^-$ can add to either face. As a result, a mixture of products is obtained. The addition, therefore, is *nonstereospecific*. We will shortly see additions that *are* stereospecific.




Another way of thinking about the addition of HX to an alkene is that it is the reverse of E1 elimination of HX from an alkyl halide.

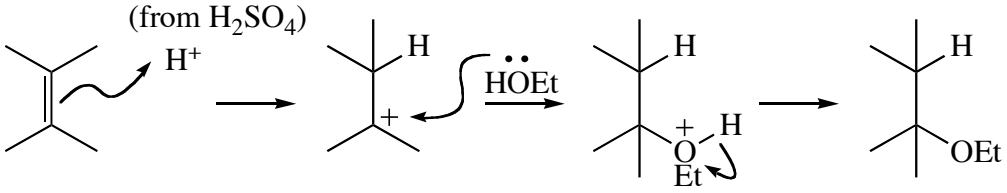
HX also adds to alkynes to give haloalkenes, but the intermediate C(sp) carbocations derived from alkynes are much higher in energy than the C($sp^2$) carbocations derived from alkenes, so the reaction is much more difficult and less widely used than the addition to alkenes. It's covered in Hornback, but I don't expect you to know it.

You have already learned how to make alkyl halides from alcohols. Now you know how to make alkyl halides from alkenes. (You also know how to make alkenes from alkyl halides!) If you want to make an alkyl halide from an alkene, disconnect the X—C bond and a C—H bond on the adjacent C. If you have a choice of C's from which to remove H, take the H off the C with more H's. (Otherwise, you may have regiochemistry problems when you go in the forward direction.) Then put a double bond between the C's from which you removed atoms. As always, make sure that the forward reaction gives you the desired product by Markovnikov's rule.

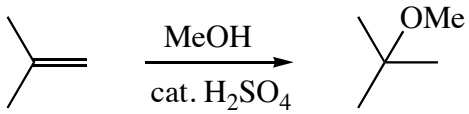


### *10.3. Addition of $H_2O$ or ROH to Alkenes to give Alcohols or Ethers.*

Alkenes C=C are not sufficiently good nucleophiles to react with weak acids such as $H_2O$ and EtOH. However, we have seen that alkenes will react with strong acids to give carbocations, and we have seen that $H_2O$ and EtOH will add to carbocations to give alcohols and ethers. We can combine these two behaviors as follows: Alkenes C=C will react with $H_2O$ or ROH to give alcohols H–C–C–OH or ethers H–C–C–OR *in the presence of a catalytic amount of a very strong acid* such as $H_2SO_4$. In the case of $H_2O$ as the nucleophile, the reaction is called *hydration*. The mechanism of this reaction is exactly the same as the reaction of HX with alkenes, with the exception that because the nucleophile is neutral and protic, the last step after addition of the nucleophile to the carbocation is loss of $H^+$ from O to give the neutral product.




The gasoline additives MTBE and ETBE are made in this way from isobutylene (2-methylpropene).

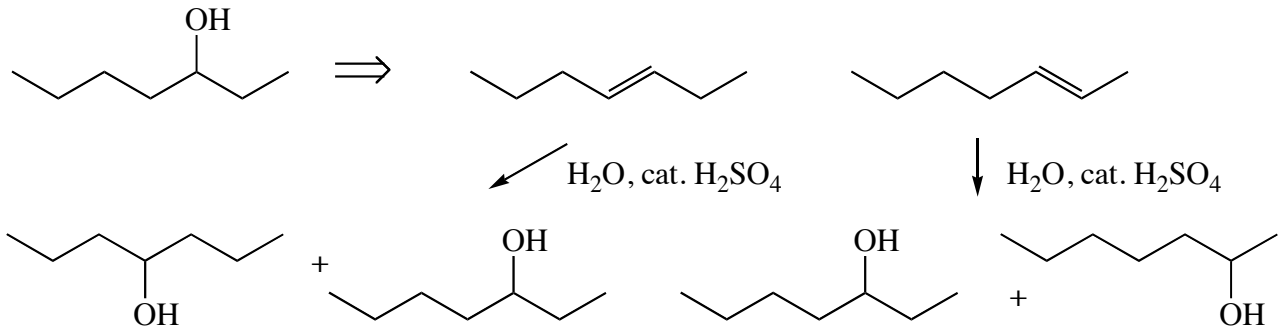



As in the addition of HX, these reactions follow Markovnikov's rule, they are nonstereospecific, and when a 2° carbocation intermediate is formed, it can undergo rearrangement reactions. The disconnection of an alcohol to an alkene is done the same way as the disconnection of an alkyl halide to an alkene.

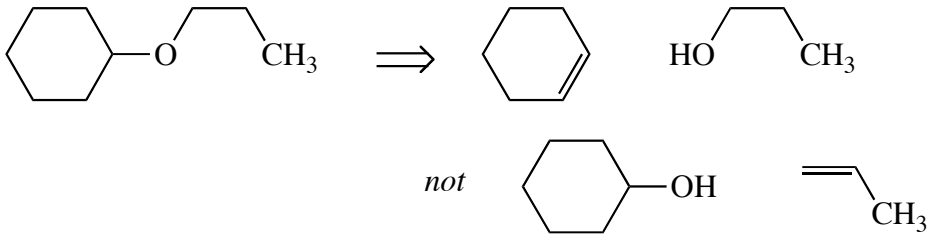
As before, another way of thinking about the addition of $H_2O$ or ROH to an alkene is that it is the reverse of E1 elimination of $H_2O$ or ROH from an alcohol or ether.

So we can make alcohols from alkyl halides, and now from alkenes by acid-catalyzed hydration. How do we choose which method to use? The answer is, you choose the method that is most selective for your target and begins from permissible starting materials. For example, you would not want to prepare 3-heptanol by hydration of an alkene, because each of the possible starting materials, 2-heptene and 3-heptene, can give two different, equally low-energy carbocation intermediates, and therefore no matter what starting material you chose you would end up with a mixture of products. It would be better to prepare the alcohol from 3-bromoheptane, *if* it is a permissible starting material. On the other hand,

sometimes an alkene is the *only* permissible starting material; in that case, you must make the alcohol from an alkene, even if the reaction is not very selective. (Most organic compounds these days are derived from petroleum, so if you look back far enough, your starting material is *always* an alkene.)



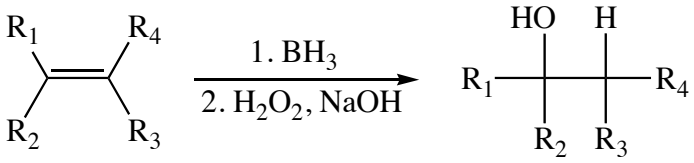

Ethers can now be prepared from an alcohol and an alkyl halide or from an alcohol and an alkene. The disconnection of the ether is the same, but the electrophilic partner, instead of getting a halogen atom, instead gets a double bond between the electrophilic atom and its neighbor. Because these reactions occur under acidic conditions, it is better to make the electrophilic C the more substituted one (3° better than 2° better than 1°).

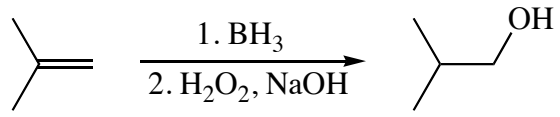


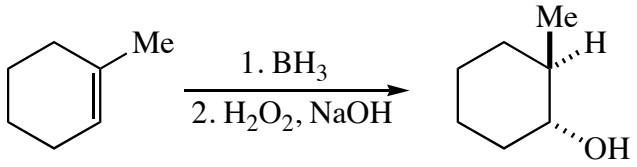

As before, you need to be able to work both backwards and forwards. In the forward direction, remember that 2° carbocations tend to rearrange.

### *10.4. Hydroboration to give Alcohols.*

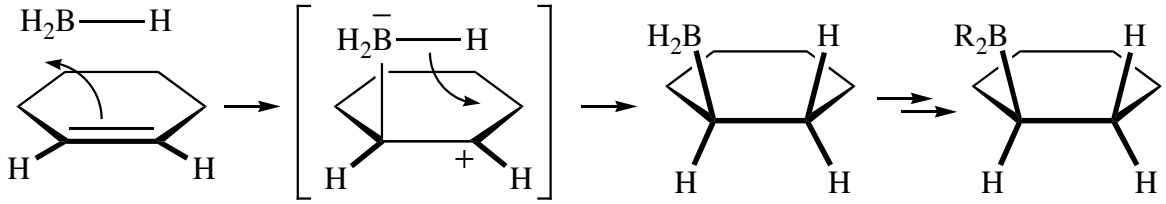
The hydration reaction results in overall Markovnikov addition of $H_2O$ to the alkene. A different way of converting alkenes to alcohols utilizes a sequence of two reactions called *hydroboration* and *oxidation*. The most common hydroborating reagent is $BH_3$, borane, which in the gas phase and in some solvents exists as a dimer, $B_2H_6$. When an alkene is treated with borane, a stable compound called a *trialkylborane* is formed by an *addition* reaction. This species can be isolated and characterized, but usually it is allowed to react immediately with $H_2O_2$ and NaOH as soon as it is formed. The C–B bonds are *substituted* with C–O bonds to give an alcohol as a product. The overall transformation is both regio- and diastereoselective: when an unsymmetrical alcohol is used, the *anti-Markovnikov* product is obtained, and the H and the OH are added in a *syn* fashion, i.e. to the *same side* of the double bond.



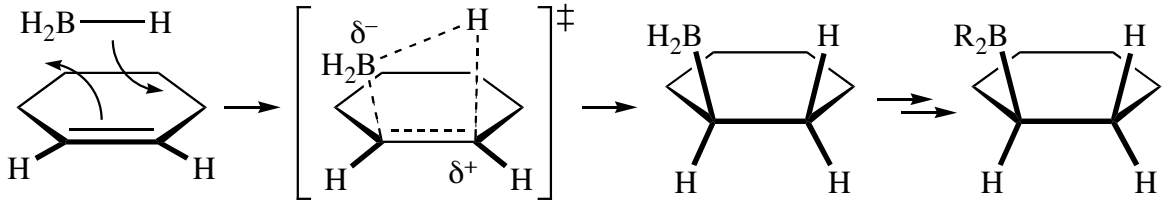



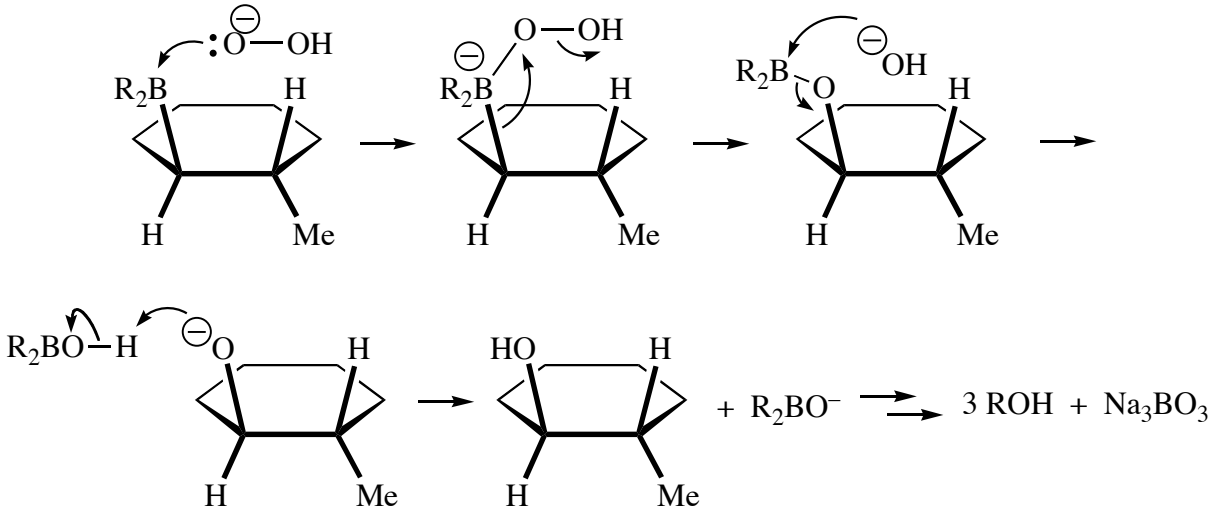

We'll look at the mechanism of the addition of borane to a symmetrical alkene first. The reactivity of borane is electrophilic, because boron is electron-deficient. The electron-rich alkene C1=C2 can use its π electrons to form a C1–B bond. When this happens, C2 becomes electron-deficient; at the same time the borane develops a formal negative charge. Boron is electropositive, and it doesn't enjoy having a formal negative charge, so it wants to lose a pair of electrons. The B–H σ bond can then act as a σ bond nucleophile toward the developing carbocation at C2. The pair of electrons in the B–H bond move away from B and form a new bond to C2. B becomes electron-deficient again, while C2 regains its octet. When all is done, the C1=C2 π bond and a B–H bond have broken, and C1–B and C2–H bonds have formed. After the first B–H bond of $BH_3$ adds, the next two B–H bonds can add in the same manner, eventually giving a trialkylborane. Thus, one only needs 1/3 equivalent of $BH_3$ to hydroborate one equivalent of alkene.




The mechanism of the reaction of borane with alkenes is not really two steps as shown. Actually, the formation of the two new bonds occurs simultaneously (*concertedly*) with the cleavage of the two old bonds. There is no discrete carbocationic intermediate. A better way of drawing the mechanism of the reaction is shown below. This drawing shows that all bonds are made and broken simultaneously, but it also shows how the C1–B bond forms *before* the C2–H bond does. Thus, the mechanism of this reaction is better described as pericyclic than as polar.

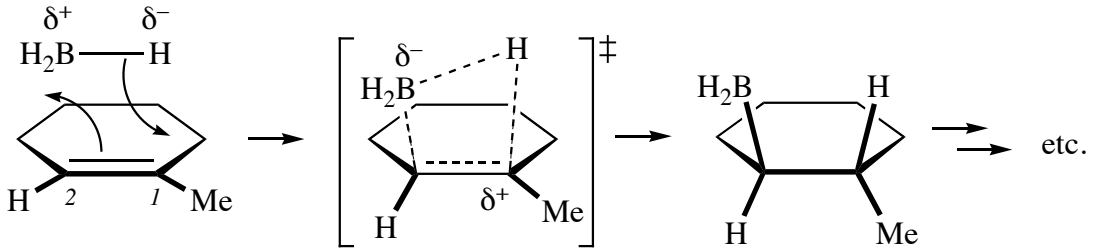


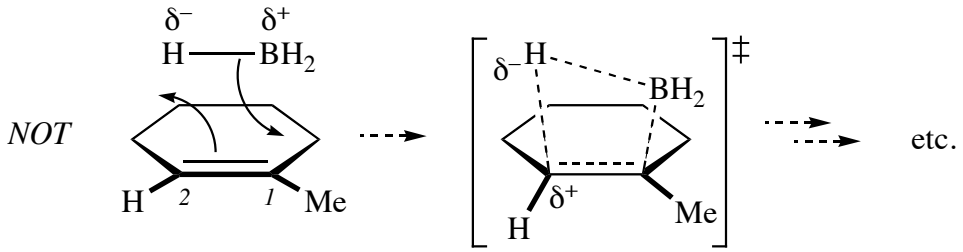
Once the trialkylborane is obtained, it is converted into an alcohol by treatment with $H_2O_2$ and NaOH. The reaction does not proceed without $H_2O_2$. In this substitution reaction, the O–O and C–B bonds are broken, and new C–O and B–O bonds are formed. The mechanism is as follows. We need to form a B–O bond. Since B is electrophilic, it must be attacked by a nucleophile. Either $HO^-$ or $HOO^-$ (by deprotonating hydrogen peroxide) could add to B to give an eight-electron negatively charged boron species (borate). Since the reaction doesn't proceed without $H_2O_2$, let's add $HOO^-$. Now the B has an octet, but it is electropositive and doesn't appreciate having a formal negative charge. It would like to lose a pair of electrons. This makes one of the C–B bonds into a σ bond nucleophile. The O–O bond is electrophilic, with $OH^-$ acting as a leaving group, so the nucleophilic C–B bond can take its pair of electrons away from B and slide it over to O, expelling $HO^-$ as a leaving group. This is a 1,2-shift. (One could in principle have the C–B bond attack O2 instead of O1, but 1,3-shifts are much less favorable than 1,2-shifts.) Now we have broken the C–B bond and formed the C–O bond. Our final product is an alcohol, though, and we still have a B–O–C linkage where we want an H–O–C linkage. The hydroxide ion that was just displaced from O comes back and displaces alkoxide ion from the B to give alkoxide, which upon protonation gives the alcohol. This whole procedure is repeated with each alkyl group on B until finally one equivalent of alcohol and 1/3 equivalent of boric acid are obtained. This step is called *oxidation*.



Now let's look at the mechanism with 1-methylcyclohexene. Only *trans*-2-methylcyclohexanol is obtained. We want to explain both the *regioselectivity* and the *stereoselectivity*. First, the regioselectivity. The observed product after the two steps is apparently the anti-Markovnikov product. Evidently B adds only to C2 and H to C1. Why? H is more electronegative than B, so the B–H bond is

polarized with δ⁻ on H and δ⁺ on B. This is opposite from Brønsted acids like H–Br, which has δ⁺ on H and δ⁻ on B. The more electronegative element in the B–H bond, H, adds to the more substituted C. When B is replaced by O in the oxidation step, the overall result *appears* to be anti-Markovnikov addition, because we've replaced electropositive B with electronegative O.



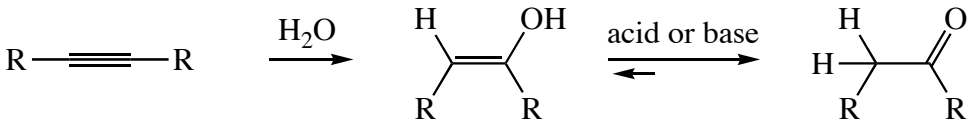

Now the stereoselectivity. Since the addition of the B–H bond to the alkene is concerted, both B and H must add to the same face of the cycloalkene. This is a *stereospecific* reaction, because the nature of the mechanism makes it possible to obtain only one stereoisomer. (A *stereoselective* reaction can give two products, but one is obtained in higher proportion because of differences in transition state energies leading to the two products.) The 1,2-alkyl shift also occurs stereospecifically. The C–O bond is formed concerted with C–B bond breakage, so that if the B is *trans* to a group on the ring in the borane, the O is *trans* to it in the alcohol. Together the stereospecific nature of these two steps determines the stereospecific nature of addition of boranes to alkenes.

*Big take-home message: If we want to make a 1° alcohol from an alkene, we need to do anti-Markovnikov addition of $H_2O$ across the C=C π bond, so we should do hydroboration / oxidation. If we want to make a 3° alcohol from an alkene, we need to do Markovnikov addition of $H_2O$ across the C=C π bond, so we should do acid-catalyzed hydration.* We can make 2° alcohols either way, but hydroboration / oxidation is usually better, because rearrangements can happen during hydration. However, when making a 2° alcohol, whatever method you choose, you have to be careful that your reaction runs with the correct regioselectivity in the forward direction.

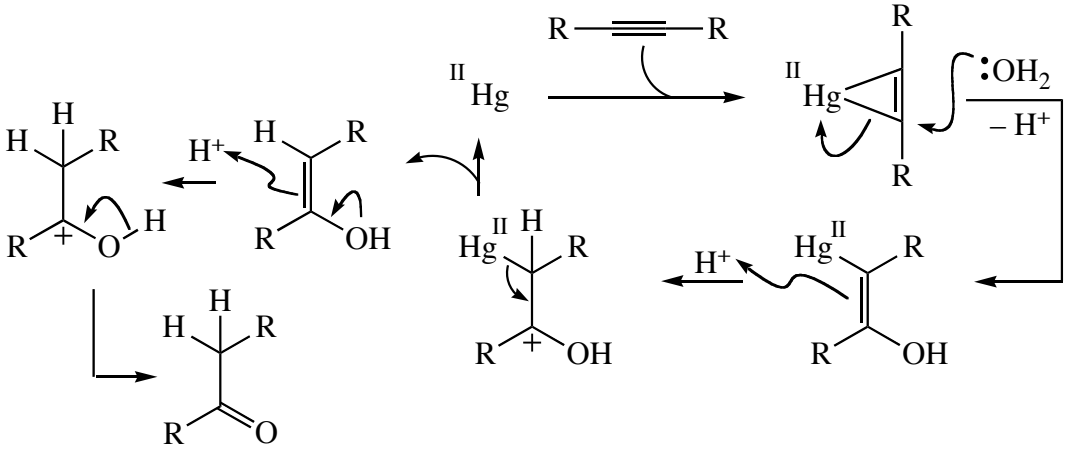
### *10.5. Hydration of Alkynes to give Ketones or Aldehydes*

We have learned how to carry out addition of $H_2O$ across an alkene to give an alcohol. We have learned

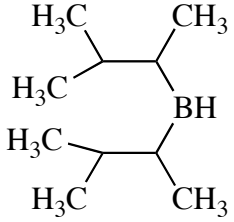
how to do it both in Markovnikov ($H_2O$, $H_2SO_4$) and anti-Markovnikov ($BH_3$, then $H_2O_2$) fashion. If we carry out addition of $H_2O$ across an alkyne, the product is an alkenol, more commonly known as an *enol*. It happens that enols isomerize rapidly to carbonyl compounds by transfer of the H atom from the OH group to the C atom that already bears an H. This isomerization is catalyzed by both acid and base. The addition of $H_2O$ to an alkyne constitutes a route to aldehydes or ketones. A happy consequence of the isomerization reaction is that there is no need to worry about the stereochemistry of the reaction. The ultimate product, the carbonyl compound, has no additional stereochemical elements.




The reagents used to add $H_2O$ across alkynes are slightly different from those used to add $H_2O$ across alkenes. Addition of $H_2O$ itself requires not only catalytic $H_2SO_4$, but also catalytic $HgSO_4$. The reason is that the carbocation obtained by attack of an alkyne on $H^+$ is very high in energy. By contrast, when $Hg^{2+}$ reacts with an alkyne, it makes a *mercurinium* ion, perfectly analogous to the bromonium ion that we have already seen. $H_2O$ then opens up the mercurinium ion to make an alkene with Hg and OH groups on adjacent C atoms. The Hg atom is replaced with $H^+$ in a two-step reaction to give the enol, which then isomerizes in two steps to the carbonyl compound.



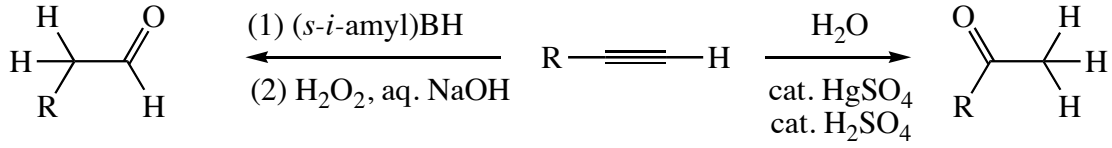

Hydroboration of alkynes with $BH_3$ is not very selective. Instead, a very bulked-up borane called disiamylborane is used. Disiamylborane has one H and two 1,2-dimethylpropyl groups attached to B. The oxidation step, using $H_2O_2$ and aqueous NaOH, is unchanged, except that in the final step, after the O–B bond is cleaved, the product *enolate* picks up a $H^+$ on C, not on O.




disiamylborane

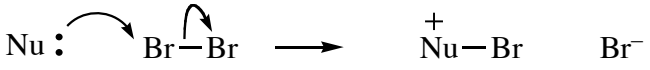
(s-*i*-amyl)$_2$BH

If a symmetrical alkyne, RC≡CR, is the substrate, it makes no difference whether Hg-catalyzed hydration or hydroboration–oxidation is used to add $H_2O$ across the π bond. If an internal alkyne, RC≡CH, is used, though, we have a question of regioselectivity. As you might expect, Hg-catalyzed hydration proceeds with Markovnikov regioselectivity, giving a methyl ketone (ketone on position 2 of an alkane), whereas hydroboration–oxidation proceeds with anti-Markovnikov regioselectivity, giving an aldehyde.

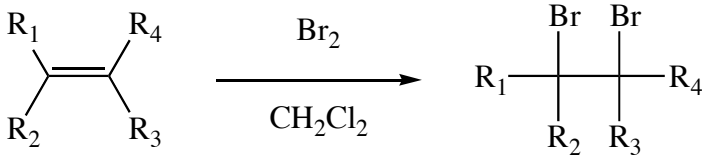



### *10.6. Addition of $X_2$ to Alkenes and Alkynes to give 1,2-Dihalides.*

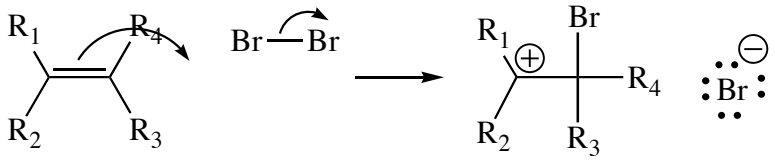
We have mentioned that alkenes and alkynes are not sufficiently good nucleophiles to react with alkyl halides. However, they are sufficiently good nucleophiles to react with elemental halogens, $X_2$. Elemental halogens are fundamentally electrophilic: the two electronegative elements are both tugging on the electrons in the σ bond. However, the bond does not break spontaneously to give $Br^+$ and $Br^-$, because the former is a very high-energy species (an electron-deficient electronegative atom). Instead, a nucleophile attacks Br1 directly. Since Br1 already has its octet, a bond to Br1 must break at the same time as the new bond forms. As a result the Br1–Br2 bond breaks simultaneously, with Br2 acting as a *leaving group*.

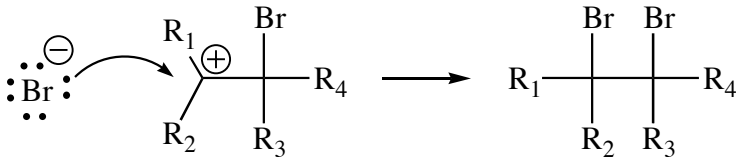



Alkenes react with $Br_2$ and $Cl_2$ to give 1,2-dihaloalkanes, or 1,2-dihalides. This addition reaction is usually run in a non-nucleophilic solvent like dichloromethane.

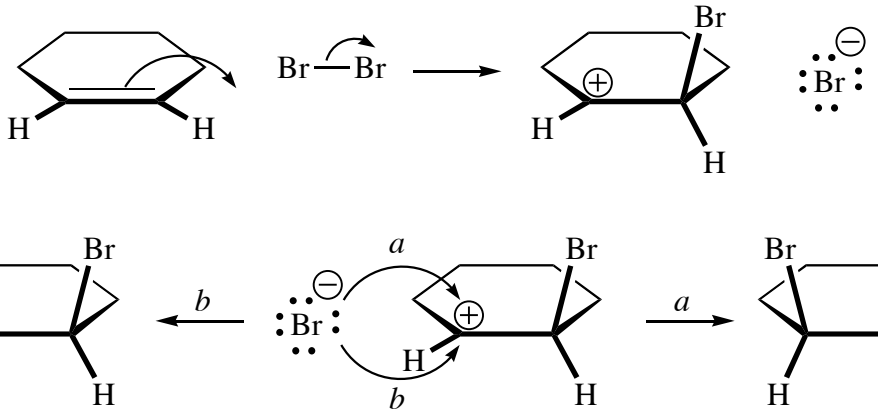



The mechanism begins with alkene attack on $Br_2$, just the same as alkene attack on $H^+$ earlier. Once attack occurs, a carbocation and $Br^-$ is generated. Then $Br^-$, a nucleophile, adds to the carbocation to give the observed product.

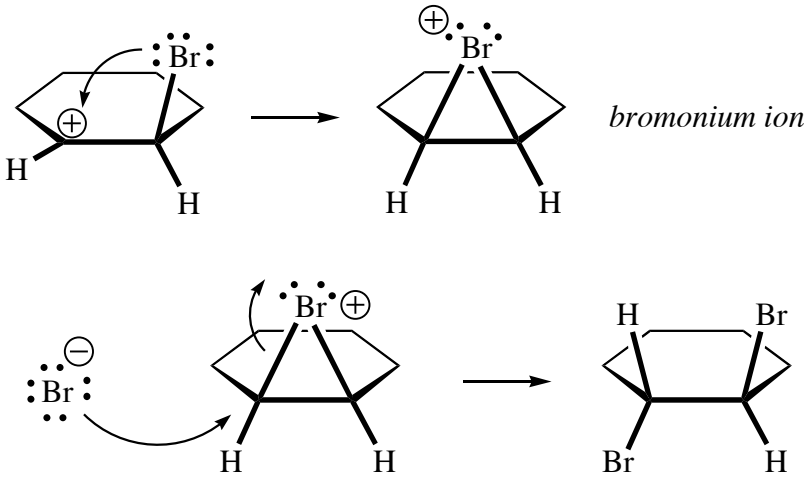





We can get information about whether mechanisms are correct by considering the experimentally observed regioselectivity and stereoselectivity of the reaction and seeing whether the proposed mechanism explains these aspects of the reaction correctly or at all. In the present reaction, since we are adding the same group to both atoms of the double bond, we needn't consider regioselectivity. How about stereoselectivity? Let's see what product we get from the reaction of cyclohexene with $Br_2$. In the first step we would get a carbocation with a Br atom on the neighboring carbon. This carbocation could combine with $Br^-$ to give two possible diastereomers. The $Br^-$ could attack from the same face of the ring as Br resides to give a *cis* product, or it could attack from the opposite side to give a *trans* product. Since a Br atom is larger than a H atom, we would expect to get more *trans* than *cis,* but not a whole lot more. In fact, we get exclusively *trans*. Our mechanism doesn't explain this fact. How can we modify the mechanism so that it explains it?




It happens that we had an incorrect structure for the intermediate carbocation. Imagine the Br atom in the carbocation reaching over and forming a bond to the electron-deficient carbon atom using one of its lone pairs. This gives a three-membered ring called a *bromonium ion*. (Note: the bromonium ion and the 2-halocarbocation are structural isomers, not resonance structures, since they have different atom-to-atom connections.) The Br atom has a formal positive charge. The C atom is no longer electron-deficient, but it is still electrophilic, because the $Br^+$ atom, which is electronegative, wants to leave and have its lone pair back to itself again. The $Br^-$ comes along and attacks the C atom; as its electrons come in to the C atom, other electrons must leave so that the C atom doesn't gain more than an octet; the ones that leave are in the C–$Br^+$ bond, which go back to Br. The $Br^-$ attacks from *opposite* the bond that breaks. We obtain *trans*-1,2-dibromocyclohexane as product. This is called overall *anti* addition, because the two Br atoms add to opposite sides of the double bond. An acyclic substrate will also undergo *anti* addition.



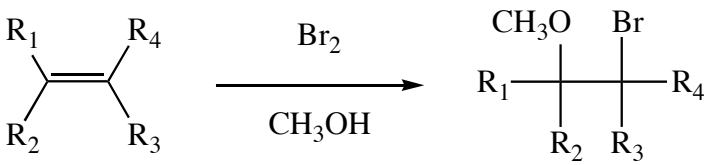

I've drawn the $Br^-$ ion attacking the left-hand C atom in the bromonium ion. It could equally well attack the right-hand C atom. The bromonium ion is achiral, and the product is chiral, so the product is obtained as a racemic mixture. One enantiomer is obtained from attacking one C of the bromonium ion, and the other is obtained from attacking the other C.

One synthetic use of the halogenation of alkenes is that the products can be converted to alkynes by two elimination reactions. Thus, alkynes can be prepared from alkenes by a two-step sequence: halogenation, then elimination.

Alkynes also react with $X_2$. The product is a 1,2-dibromoalkene, and the halogen atoms are trans to one another. If one equivalent of $X_2$ is added, the reaction stops there. If excess $X_2$ is added, the dihaloalkene can react further to give a tetrahaloalkane.

### *10.7. Cohalogenation. 2-Haloalcohols, 2-Haloethers.*

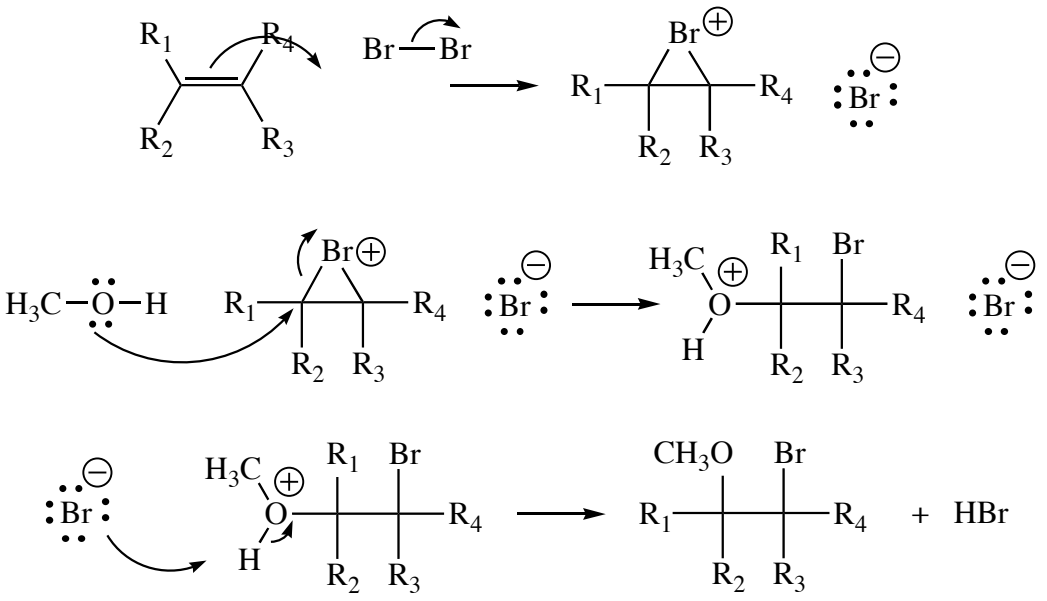
So far we've seen nucleophilic $Br^-$ attack the electrophilic bromonium ion to give a dibromide. Any other nucleophile might attack the bromonium ion to give a different product. This addition reaction is called *cohalogenation*. Cohalogenation is most commonly conducted by adding $Br_2$ to an alkene in water, an alcohol, or a carboxylic acid as solvent. For example, if we add $Br_2$ to an alkene in methanol, we obtain a product in which a $CH_3O-$ group is incorporated into the product instead of a Br– group. This product is called a 2-bromoether.



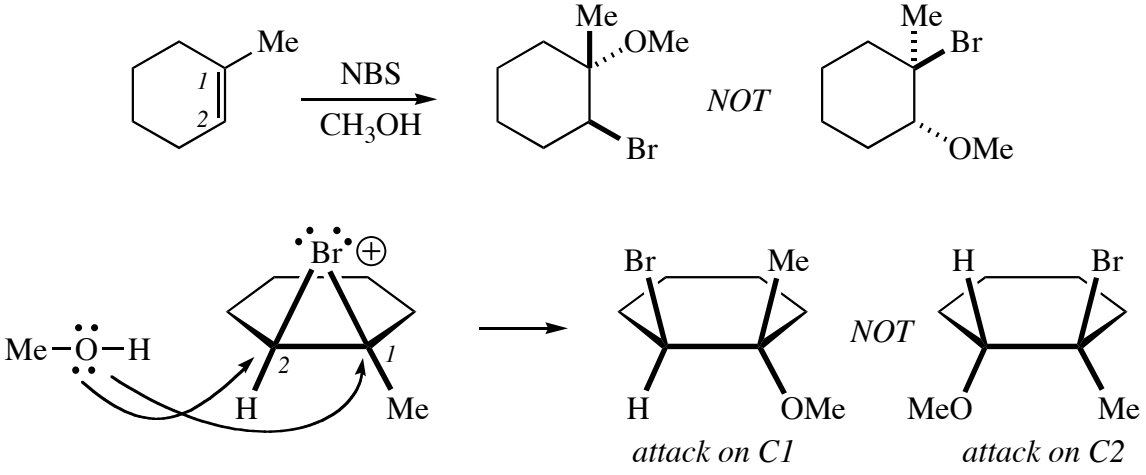

The first part of the mechanism is the same as halogenation; a bromonium ion is formed. Then, instead

of $Br^-$ acting as a nucleophile toward the bromonium ion, the alcohol solvent acts as a nucleophile. The O attacks C and displaces Br to give a cationic, electron-saturated intermediate. Finally, the O atom is deprotonated to give the product.

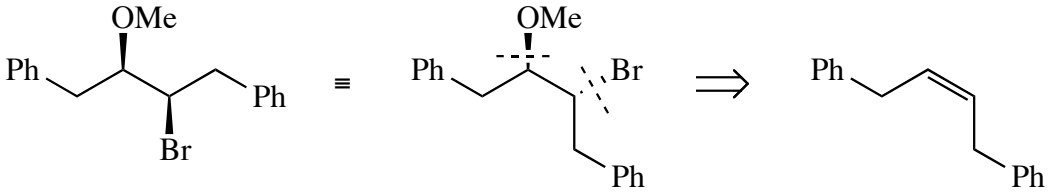
Mechanism:




When we make 2-haloethers and 2-haloalcohols, we are adding one group to one of the C atoms of the double bond and a different group to the other. The question of regioselectivity now arises. For example, what happens if we use 1-methylcyclohexene as a substrate? Remember that we said that 3° carbocations were more stable than 2° ones. We can imagine that in the bromonium ion, the C1–$Br^+$ bond is weaker than the C2-$Br^+$ bond, because C1 is better able to bear a positive charge. Since the C1–$Br^+$ bond is weaker, this bond is more prone to cleavage. Therefore MeOH attacks C1, Markovnikov addition takes place, and the product is 1-bromo-2-methoxy-2-methylcyclohexane (the second one as drawn). Note that *both* regioisomeric products that might be obtained have Br and OMe in a *trans* relationship.

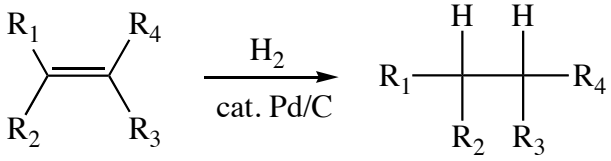


The cohalogenation reaction gives us a new retrosynthetic strategy. A molecule with a bond between C($sp^3$) and a heteroatom can be disconnected at that bond. The heteroatom gains an H in the starting material. *If the C atom adjacent to the electrophilic C bears a halogen, then remove the halogen from the adjacent C, and place a π bond between the electrophilic C and the one that bore the halogen.* If the alkene that you obtain retrosynthetically has E/Z isomers, you need to be careful that the alkene that you draw has the stereochemistry that gives you the correct diastereomer of the product.

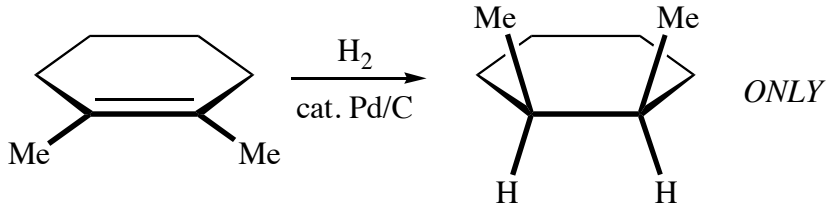



### *10.8. Catalytic Hydrogenation. Alkynes to Alkenes to Alkanes.*

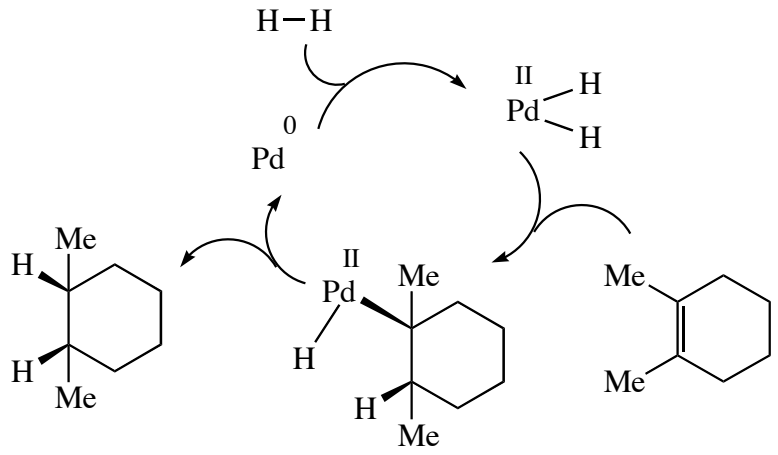
We can hydrogenate alkenes by allowing them to react with $H_2$ in the presence of a noble metal catalyst like Pd on charcoal (Pd/C) or $PtO_2$. This is called a *reduction*. It is an overall *addition* reaction.



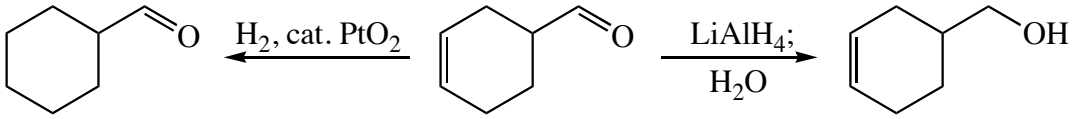

Suppose we start with 1,2-dimethylcyclohexene. Two stereoisomeric products are possible: *cis*- or *trans*-1,2-dimethylcyclohexane. In fact, the reaction is stereospecific. Only the *cis* isomer is obtained. Note that the *less* stable isomer is obtained.




The mechanism of the reaction explains the stereochemistry. The mechanism is completely different from mechanisms we have studied up until now. It begins by Pd(0) inserting itself between the two H atoms in $H_2$, in a reaction called *oxidative addition*, to give a Pd(II) complex with two Pd–H bonds. In the second step, one of the Pd–H bonds reacts with the alkene in an insertion reaction, just like the one we saw with the B–H bond in hydroboration, to give a new Pd(II) compound with one Pd–C and one Pd–H bond. The insertion reaction is concerted, with both new σ bonds forming simultaneously, so it is syn. In the final step, the two groups attached to Pd gain a new σ bond to one another, in a reaction called *reductive elimination*, and release Pd(0) to restart the catalytic cycle.

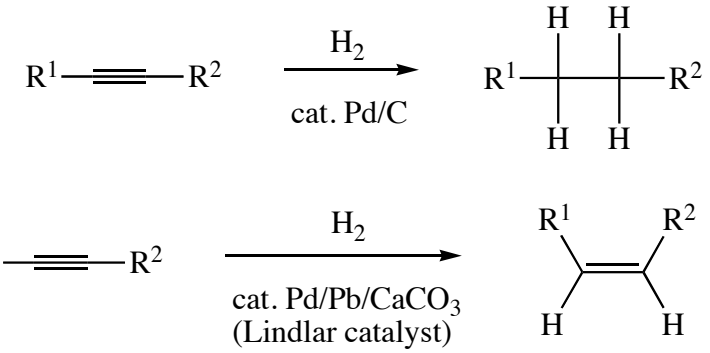



Catalytic hydrogenation is a useful reaction because it usually reduces only *unpolarized* π bonds like C=C π bonds. Polarized π bonds like C=O π bonds are reduced with other reagents such as lithium aluminum hydride, $LiAlH_4$. (The reduction of C=N π bonds is intermediate in difficulty and depends partly on the nature of the groups attached to C and N.) This is called *chemoselectivity*. The fact that $LiAlH_4$ reduces only polarized π bonds and $H_2$/Pd reduces only unpolarized π bonds means that a compound that contains both of these kinds of functional groups can be selectively transformed into two different products, depending on the choice of reagent.

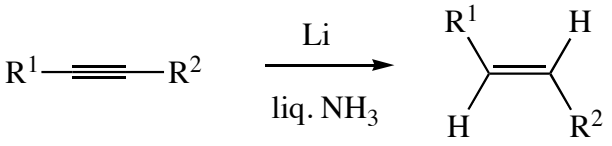


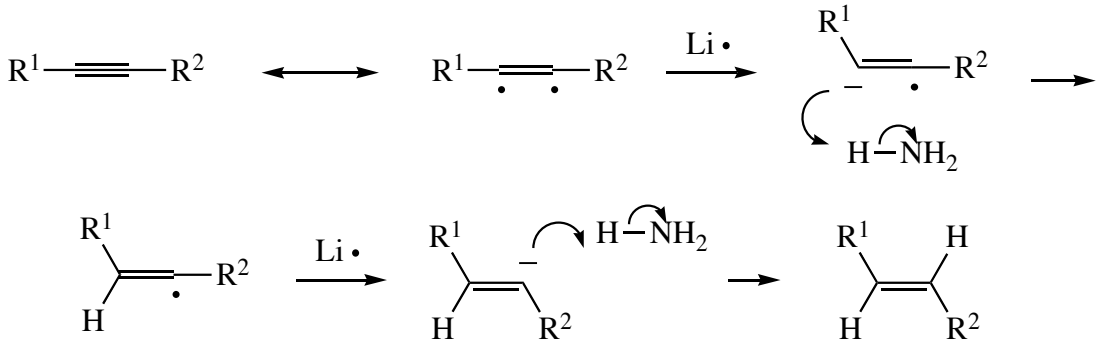

Catalytic hydrogenation has often been used to determine how many of the degrees of unsaturation of a compound with a given formula are due to the presence of C=C π bonds, since cycloalkanes don't react with $H_2$. E.g., if the compound $C_6H_{10}$ (two degrees of unsaturation) reacts with 1 equivalent of $H_2$, it must have one ring and one π bond.

Alkynes can also be catalytically hydrogenated. Addition of $H_2$ across an alkyne gives an alkene. We know that alkenes can be reduced to alkanes, so it seems that it should not be possible to stop the reduction at the alkene stage, and alkynes should be reduced directly to alkanes. This is true if a catalyst such as Pd/C is used. However, the second π bond in an alkyne is higher in energy than the first π bond, so if a weaker catalyst is used, the reaction can be stopped at the alkene stage. The catalyst best used is Lindlar catalyst, which is Pd contaminated with Pb. Syn addition of the two H's to the alkyne is observed; i.e., a cis alkene is obtained.

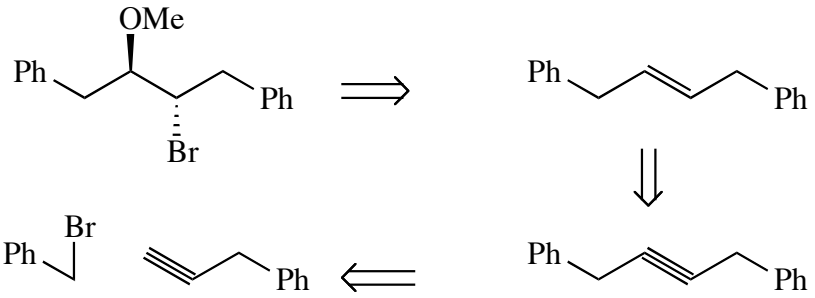



What if you want a trans alkene? In that case, you cannot use catalytic hydrogenation. Instead, you use Li or Na metal in liquid ammonia. The mechanism of this reaction begins with the realization that an alkyne can be drawn in its 1,2-diradical form, RC≡CR ↔ R$\dot{C}$=$\dot{C}$R. Li metal really, really wants to give up its lone electron to become $Li^+$, so it donates an electron to the alkyne. That converts the alkyne into a radical anion, R$\bar{C}$=$\dot{C}$R. The anionic C atom deprotonates the solvent $NH_3$ to give RCH=$\dot{C}$R. Now a second electron transfer occurs to give RCH=$\bar{C}$R. When the radical C picks up its electron, it goes from sp hybridization to $sp^2$ hybridization, and when it does that, the R group swings to the side of the H atom. Finally, the last H atom is picked up to give RCH=CHR in the trans stereochemistry.



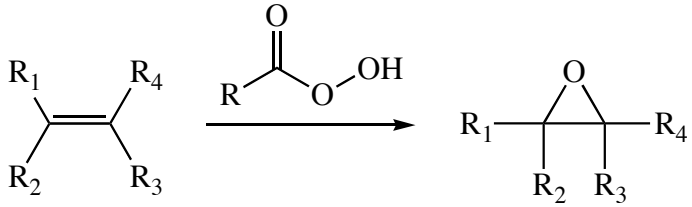




So, retrosynthetically, a cis alkene can be made from an alkyne, a trans alkene can be made from an alkyne, and any compound with a $CH_2CH_2$ group can be made from an alkyne. These reactions are exceedingly important, because so far the alkylation of an alkyne with an alkyl halide is the only way we know how to make a new C–C bond, and making C–C bonds is the essence of organic chemistry. If you have a target compound that should be made from starting materials containing fewer C atoms, so you need to make a C–C ond, you know that if you can retrosynthetically introduce a CH=CH or $CH_2CH_2$ linkage into your target, you can convert that linkage into a C≡C linkage, which you can then use to make C–C bonds.

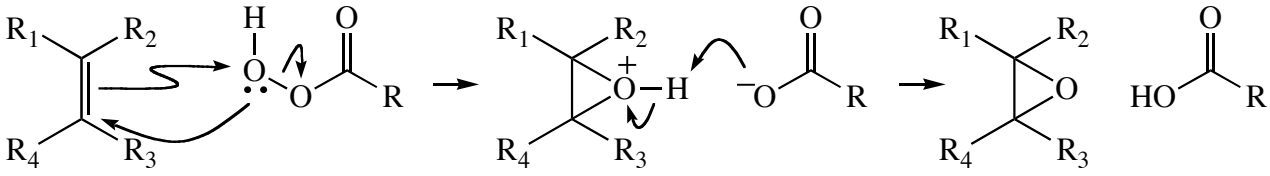



### *10.9. Oxidation of Alkenes. Epoxides, 1,2-Diols, Carbonyls.*

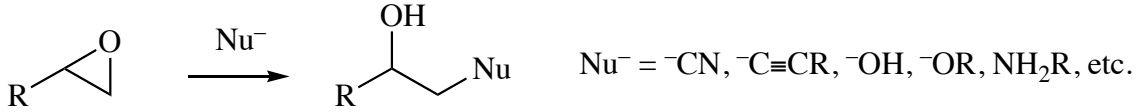
When alkenes are treated with a peracid, $RCO_3H$, an epoxide is obtained. The peracid used most often in the lab is called mCPBA, but any peracid, even peracetic acid, AcOOH, will work. A peracid is related to a carboxylic acid, but instead of an OH group attached to the carbonyl there is an OOH group.




Alkenes are nucleophiles, so peracids should be electrophiles. In fact, as in $Br_2$, the two electronegative O atoms are fighting over the pair of electrons in the σ bond between them. The CO group attached to one O helps it win the battle, so the O atom attached to H is even more electron-poor. The alkene attacks it, displacing a carboxylate anion, and the O being attacked uses its lone pair to make a bond back to one of the alkene C's to give a protonated epoxide. The carboxylate then deprotonates the O to give the products.

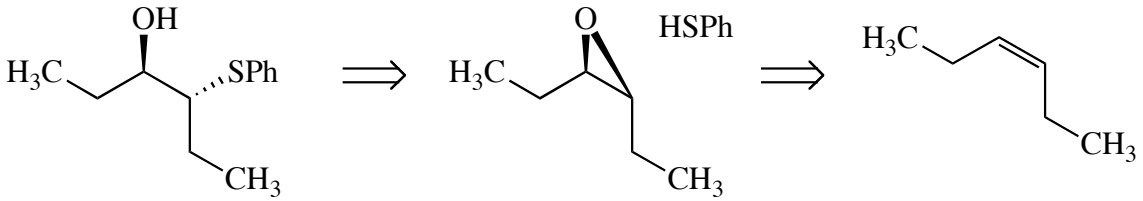



The C atom of an ether is normally not electrophilic because the C–O bond is very strong. In an epoxide, though, the C–O bond is so strained that it becomes very electrophilic. As a result, under basic conditions, epoxides react with nucleophiles by an $S_N2$ process to give alcohols. If the epoxide is unsymmetrical, the nucleophile attacks the *less hindered* C atom of the epoxide. The nucleophiles that can be used to open up epoxides are the usual suspects: $^-CN$, $^-C{\equiv}CR$, $^-OR$, $NH_2R$, $^-SR$, etc.



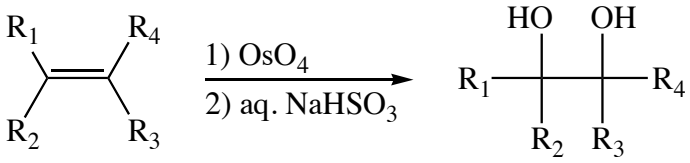

The epoxidation reaction therefore gives us a new retrosynthetic strategy. A molecule with a bond

between C($sp^3$) and a heteroatom or between C($sp^3$) and C(sp) can be disconnected at that bond. The nucleophile gains an H in the starting material. *If the C atom adjacent to the electrophilic C bears an OH group, then connect the O of the OH group to the electrophilic C* (and remove the H from the O). If not, attach a regular leaving group (Br or OTs) to the electrophilic C. If the electrophilic C atom is stereogenic, its configuration must be *inverted* in the starting material. The epoxide can be made from an alkene that has a double bond between the two C atoms of the epoxide. The stereochemistry of the epoxide is *preserved* in the alkene starting material.

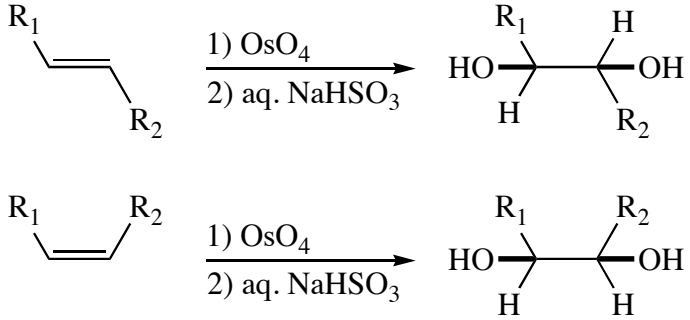



We will now learn two other *oxidation* reactions whose mechanisms are too complex to discuss. You must simply memorize these reactions. It is important to learn them because they accomplish useful functional group transformations.

When alkenes are treated with one equivalent of $OsO_4$ (osmium tetroxide) and then aqueous $NaHSO_3$, a 1,2-diol is formed. This reaction is called *dihydroxylation*. The overall reaction is an addition reaction.



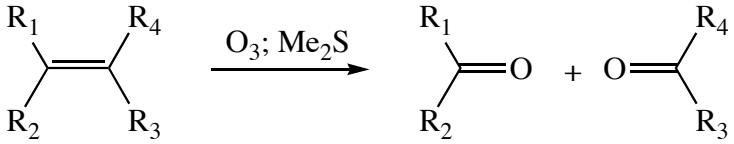

There are no regiochemical issues in dihydroxylations, because the same group is added to each atom of the former π bond. The stereochemistry of the reaction is stereospecifically *syn*; both OH groups add to the same side of the double bond. Only the *cis* diastereomer is obtained from a cyclic substrate. A *trans* alkene gives a single diastereomeric product; the corresponding *cis* alkene also gives a single product, different from the one derived from the *trans* alkene.




This reaction is very mild, very selective for C=C bonds, and proceeds in high yields. The problem with it is that $OsO_4$ is extraordinarily toxic and volatile (evaporates easily). To get around this problem, we

usually use a *catalytic* amount of $OsO_4$ in conjunction with a stoichiometric amount of another oxidizing agent that regenerates $OsO_4$ after it has reacted and allows it to react again. Also, people generally run the oxidation in the presence of pyridine, because it goes faster under these conditions. For our purposes, though, stoichiometric $OsO_4$ without pyridine is just fine for making 1,2-diols.

The C=C double bond in alkenes can be *oxidatively cleaved* and replaced with two C=O double bonds. This can be done in several ways. We will learn only one: ozonolysis. When an alkene is treated with ozone, $O_3$, and then a mild reducing agent like $Me_2S$, two ketones or aldehydes are obtained. The overall transformation is not easily classified; it is the result of an addition *and* an elimination, or you might see it as a substitution. Other reducing reagents besides $Me_2S$ can be used, e.g. Zn, $Ph_3P$, and even $H_2$ and a catalyst. Ozone has been in the news a lot recently; it's good to have it in the stratosphere, where it abosrbs harmful UV light, and it's bad to have it at ground level, where it causes smog. It also happens to be a very useful organic reagent.




The mechanism of this reaction is well-known, and it is in the book if you are interested, but I do not expect you to know it. Oxidative cleavages of alkenes have neither regiochemical nor stereochemical issues.

So, if you see a carbonyl compound, you now know three ways to make it:

- If it is an aldehyde, make it by hydroboration–oxidation of a terminal alkyne. Retrosynthetically, replace the $CH_2CH(=O)$ group with a C≡CH group.
- If it is a 2-alkanone (a methyl ketone), make it by Hg-catalyzed hydration of a terminal alkyne. Retrosynthetically, replace the $C(=O)CH_3$ group with a C≡CH group.
- If it is an alkynone of the form $RCH_2C(=O)R$, where the two R groups are identical, make it from an internal alkyne by either method. Retrosynthetically, replace the $CH_2C(=O)$ group with a C≡C group.
- Any type of aldehyde or ketone C=O can be made from an alkene. Retrosynthetically, replace the carbonyl O in RR´C=O with CRR´ or $CH_2$.
- A diketone, dialdehyde, or keto aldehyde RC(=O)–X–C(=O)R´ (X is a linking group) can be made from a cycloalkene. Retrosynthetically, remove the two O atoms and join the two carbonyl C atoms with a double bond.