

Lecture 25A • 12/02/11

[alkene lab – spectrum][

exam review – Sn1/Sn2/E1/E2: mechanism, fill-in-the-blank; electrophilic additions: simple – HBr, carbocation, acid catalyst/water or alcohol, Markovnikov addition, carbocation shifts, order of addition; cyclic: oxymercuration/demercuration, alkoxymercuration/demercuration, halohydrin and alcohol variation; hydroboration/oxidation: anti-Markovnikov addition; free radical halogenation]

Hydroboration

With the reaction of borane•THF, you're first going to form an alkyl tribromide. From that, an attack by hydrogen peroxide [is] possible – actually, not hydrogen peroxide itself, but the peroxide ion; separately, we can have hydroxide that reacts with hydrogen peroxide to deprotonate it. It turns out hydrogen peroxide is more acidic than water; that's why two reagents are listed second, so that you can form that hydrogen peroxide ion. The hydrogen peroxide ion ends up attacking the boron, but that intermediate then decomposes. It's exactly that decomposition step that is the most curious step in this reaction. You can rationalize it in one main way: in terms of thermodynamics. We've now made boron that is negatively charged, which isn't un favorable, per se, but to flip that around, you could say that boron is isolatable when it is not charged, so it would be possible for this to lose a bond in this intermediate. The oxygen-oxygen bond, the peroxide bond, is a weak bond. On top of that, an oxygen-carbon bond would be preferable to an oxygen-oxygen bond. Additionally, boron-oxygen bonds are way more favorable than boron-carbon bonds, because boron is such a strong electrophile because it has an incomplete octet unless it makes a negatively-charged structure like this. The point of mentioning all of these items is to explain why it is that we can have an alkyl shift – just like we can have a hydride shift, we can have alkyl shifts. This alkyl shift occurs because of thermodynamic, because the formation of this new carbon-oxygen bond is more favorable than the carbon-boron that had been there previously.

When I showed you the first part of this mechanism, where we made the trialkylborane, [it was ok to just abbreviate] and say that it happens two more times; [you can] do the same thing here. At the end of that process, we now have a trialkoxyborane, which then continues further to react. Besides from the hydrogen peroxide ion you have, there is hydroxide around that could attack. You might say: why couldn't have a hydroxide attack before? I could have, but it wouldn't have produced any useful intermediates; the reaction would have just gone in reverse. But at this point, what can effectively occur is you have a swap between the alkoxy group and hydroxy. Boron can be neutrally charged by only having three bonds, so after hydroxide attacks, imagine an alkoxide comes off. If that occurs, then that alkoxy group can deprotonate this boron-oxygen-hydrogen system, which is favorable because boron loves getting electrons. Notice that the product we produce is exactly what we want. This happens two more times, so you end up with three of these alcohols per equivalent of the borane that is used originally. There's three phases to this reaction: first making the trialkylborane; next, hydrogen peroxide oxidizing the compound; then finally, hydroxide decomposing that intermediate to release the alcohol.

Let me show you one more example of the hydroboration reaction so we can get at stereochemistry. The four-center transition state is what we use to explain regiochemistry, but [now we need to see] stereochemistry. I'll use the same example that we've been using all along. On reaction with borane, remember that that is a syn addition. It's syn addition because it's not possible to form that four-centered transition state with one leg of the square pointing one direction, and the other leg point 180° in the opposite way; all of the atoms have to be in close proximity to each other. After the very first attack occurs, we're going to end up with two intermediates, where, because boron ends up acting as the electrophile, it is boron that's going to end up at the less-substituted position. Because the double bond is flat, we'll get enantiomers that this point. Of course, this is on the first attack, because [borane] can add multiple times – three times per molecule; I'm only showing this much of it to emphasize the fact we have syn addition. It's syn because ... if I took one of the corners of the square and put it down here where my pinky is, could you physically make a square any more? It's not physically possible; that's why it has to be syn addition.

Let's summarize the six aspects of the reaction. The utility is to convert an alkene into an alcohol. The reagents – this is a case where you do have to use the 1/2: first borane, second hydrogen peroxide and sodium hydroxide. Conditions, absolutely no water, because water is going to destroy the borane. The mechanism is kinda hard to classify, cause you don't form a carbocation. You also don't formally form a carbanion. This reaction is due, however, to an electrophile, so if I was going to classify it somehow, I'd call it cationic. In terms of stereochemistry, it is syn addition, and because the alkene is flat, you form enantiomers. In terms of regiochemistry, the very first step of this reaction, you might argue, is in line with Markovnikov addition, if you focus on the fact that boron, which is the electrophile, ends up at the less substituted position, which is normally what happens in electrophilic addition. But, the term Markovnikov versus anti-Markovnikov is more typically used to describe where things substituted. If you look at the product of this reaction, the alcohol that you make, that ends up at the less-substituted position, so this is termed anti-Markovnikov addition. Because we don't even have an intermediate, and because we don't even have an intermediate, we just have this four-centered transition state, there's no rearrangement.

[exam: radical halogenation]

Hydrogenation. Very commonly used reaction. It doesn't have a mechanism that you need to be responsible for, but you need to know a little bit about how the reaction occurs to understand the stereochemistry that occurs. Hydrogenation normally involves either a platinum or palladium catalyst. Why? Because those two metals react particularly well with hydrogen; a hydrogen molecule, then can end up getting split up and adsorbed onto the surface of that catalyst. The catalyst, then, acts as a support on which an alkene can then react. Hydrogen and alkene reacting with each other is a thermodynamically-favorable process, it's an exothermic reaction, so thermodynamically it wants to happen. But kinetically, you have an alkene which is usually a liquid, sometime a solid, less frequently a gas – generally a liquid, trying to react with hydrogen that is a gas, so there's a kinetic barrier to the reaction, but what ends up happening is the metal, the catalyst, ends up splitting hydrogen before it tries to react with the alkene, so it's activating the hydrogen. First, the hydrogen settles onto that metal catalyst, and then the alkene reacts with the hydrogen. Since the alkene is approaching the metal surface, and the two hydrogens are pointing up the same way from the metal surface, both of those hydrogens effectively end up adding to the same side of the double bond, which means that hydrogenation is a syn addition. Again even though you don't know the mechanism, you should know this aspect of how the catalyst is involved. Hydrogen can be adsorbed onto the surface of palladium or platinum metal. Once adsorbed, the hydrogen is made more reactive and can then react with an alkene. Since the alkene is approaching the metal surface with both hydrogens pointed the same direction, the hydrogens add with syn addition.

To show an example of hydrogenation, let's use that asymmetric alkene. No 1s or 2s here; the platinum or palladium needs to be there the same time as the hydrogen. Since the double bond is flat, you're going to get addition at both faces, so you're going to end up with two products. Filling out the six aspects of this reaction, the utility is to convert alkenes to alkanes. Reagents – hydrogen and either palladium or platinum. Conditions [none at the moment]. As far as mechanism, not really classifiable, since it's not matching any other mechanism that we'll learn because it involves the catalyst. We can talk about the stereochemistry; there is syn addition, and we form enantiomers. In terms of regiochemistry, there is none, because you're adding the same atom to either side of the double bond, so there's no structural effects. What you could say, at least, though, is that there are no rearrangements. The hydrogen's being provided by the metal surface, and even if it's not simultaneous, the way that it occurs, there's never a formal carbocation that forms, so you never have the possibility of migration occurring.

The last reaction – another way of making epoxides. As a reminder, we did see a reaction of this sorts, where we took an alkene, reacted it with bromine and water. That reaction's going to produce a halohydrin. If you react it with sodium hydride, hydride tends to be basic more than it is nucleophilic, and so it is able to deprotonate the -OH group. If that occurs, then you have a nucleophile immediately next door to the leaving group, so you get intramolecular [substitution] and you form the epoxide. But there is another epoxidation reaction. One of the main reagents used to do this reaction is called MCPBA, which stands for meta-chloroperoxybenzoic acid. Benzoic acid is benzene with a carboxylic acid functional group; peroxybenzoic acid is where there one more oxygen involved; meta-chloro, meta is the position two positions away from the carboxylic acid group, so there is meta-chloroperoxybenzoic acid. Why does this compound have some unusual reactivity? Because of the peroxide bond. Whether we do this as analysis of formal charge or oxidation state, how we break the bonds and count electrons, or whether we just fall back to the rule that we blindly followed in Chem 1A, which is that in peroxides, what is the oxidation state of oxygen? -1, which indicates in some ways that it doesn't have, in its own self, as many electrons as it might, given that oxygen is the second-most electronegative element. But in this compound, it's bound with itself. Were it to react with anything else except itself or fluorine, it effectively ends up with more electrons, which would lower its oxidation state. Both of these singly-bound oxygens have a -1 oxidation state, and therefore can oxidize another molecule to become -2 oxidation state, because that which oxidizes becomes reduced. Oxidation means to take electrons; if it takes electrons, it's going to get that -2 oxidation state.

Let's see what the mechanism looks like. The reactive part of the molecule is the second oxygen; why? Because it doesn't have any form of conjugation possible with the carbonyl that's over next door, so of the two oxygens, the one out closer to the hydrogen is more reactive. The double bond can attack that oxygen, again because that's going to initiate the reduction of that oxygen. In response, that weak oxygen-oxygen bond can break. The lone pair that would come from that bond would collapse back towards the carbonyl, in a form of resonance. If that were to happen, you'd push open the carbonyl. It turns out that it's actually close enough in proximity, that because you've made acetate, which is a base, it can pull off the hydrogen over here, which if it pulls off that hydrogen, there's this last oxygen-hydrogen bond that has to go somewhere, which is right back to the alkene. It is a cyclic-style reaction. Let me go over the logic of it one more time. The oxygen close to the hydrogen is the one more likely to attack, cause it's not in conjugation at all with the double bond. When it's attacked, this weak oxygen-oxygen bond breaks. If you think about what's left over right at that moment, it's acetate. Acetate has a resonance structure, which is what I've shown by this bond falling back to attack the carbonyl, but nearby is a hydrogen which initially was acidic, so acetate can pull off that hydrogen, which causes a back attack onto the alkene, which forms the peroxide. If they didn't happen at the same time, then you'd show it as separate steps. Only all of the arrows drawn at the same time in a step occur simultaneously. The by-product that's left over is meta-chlorobenzoic acid; we have one less oxygen.

I want to show you two gotcha examples of elimination. Let's say that we have something like the following: a tertiary alkyl halide, and I have sodium hydroxide. The tertiary alkyl halide, that can't undergo S_N2 . Because we have sodium hydroxide, which is a strong base, that means there's not the opportunity for S_N1 . What's the only kind of reaction that's going to be possible? Tertiary substrate, so it can't be S_N2 ; strong base, so it can't be S_N1 .

Remember that the only time that E1 can happen is also the only time that Sn1 can happen, cause they go through the same intermediate. If it's not Sn2 or Sn1 or E1, the only reaction left is E2. Given that we don't have one of those kinetic bases, that we don't have t-butoxide, what's going to be the most likely product? Where do I draw the double bond: here, cause that makes the most thermodynamically favored product – it also makes the product that can't physically form. This is the major product of the reaction. Why? Eliminations can only occur if you have synperiplanar or antiperiplanar geometry between the leaving group and the hydrogen that's being pulled off. Let's take this molecule and draw chair structures for it. Here's the hydrogen and the chlorine, and in this configuration, it's neither synperiplanar or antiperiplanar, which means the reaction can't occur. Let's say that I do a ring flip – still, the hydrogen and chlorine are not synperiplanar or antiperiplanar. Even after the ring flip, it's still true that the hydrogen and chlorine are not synperiplanar or antiperiplanar, so elimination from that position is not possible.

In a sense, it's a kind of trick question, because if I had just said this statement about what Zaitsev elimination is, then you hopefully were thinking: what's the most substituted alkene. What I've drawn is not the most substituted alkene, but it's the only one that can form, because that carbon that I've drawn the double bond to does have a hydrogen that can become synperiplanar or antiperiplanar. Ring flips at room temperature happen all the time; because they can happen, that's why we have to consider them; we have to consider both possibilities. Only if you were at low enough temperature where you're locked into one configuration or the other would you ignore that ring flips happen. Just because one version can't do it doesn't mean that the other one can't do it either. Previously, we [examined] two sets of molecules – two molecules where we ring flipped each one. In one case, where we had trans geometry between the leaving group and hydrogen, one of the ring flipped versions allows elimination, the other doesn't. When we had cis, which is what we had with this case, in fact, then it was exactly what we had here: neither of the forms allows elimination – unless there's a double bond somewhere else in the molecule. If something prevents the ring from flipping, and it doesn't start out in the right configuration in the first place, it never will eliminate.

Last case: let's say that we have a molecule like this – our first example of a bicyclic compound. Let's say with the way that I've drawn the hydrogens here that we're not worried about stereochemistry at all. Let's say that there's enough steric hinderance here that, even with a small base, let's say that only elimination occurs. Which one of the two products, based off of the two hydrogens that I've indicated there, do you think will be the major product to form? Terminal is where you have the double bond at the end of the molecule; opposite of that would be internal. Terminal double bonds have less hyperconjugation cause you only have one substituent, and internal double bonds have at least two substituents, so they have more hyperconjugation. To the right, that alkene would be more favorable than this alkene. But wouldn't the second alkene I just drew be the more substituted one, so it'd be thermodynamically more favored? It's a trick question – this molecule can't exist. Why not? Because if you have these three other carbons in a small enough structure like this, where this sp²-hybridized carbon is trying to be a part of, that sp²-hybridized carbon has to be planar. Because it's got these three other connections that are not in the plane – if you were to try to build this molecule, the top point on either of these two on the right, aren't anywhere near close to planar with each other, so it's just physically impossible for that planar position to form. This is what's known as a Bredt's rule violation. Bredt's rule involves what are known as bridgehead carbons. Those are carbons that are at the junction of two or more fused rings. Notice that this is really a compound that could be viewed as the combination of two rings that are each sharing three carbons with each other. That little peak up at the top we can think of as a bridge from one side of the molecule to the other. Where you enter the bridge, the position here that's circled where we're talking about elimination, that is the bridgehead. Bredt's rule says that, unless the ring size is sufficiently large, elimination is not possible at bridgehead positions, because the carbon cannot become planar.

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- 1) utility: alkene → alcohol
 - 2) reagents: 1) BH₃•THF 2) H₂O₂, NaOH
 - 3) conditions: no water!!!
 - 4) mechanism:
 - 5) stereochemistry: syn addition; enantiomers
 - 6) regiochemistry: anti-Markovnikov; no rearrangements

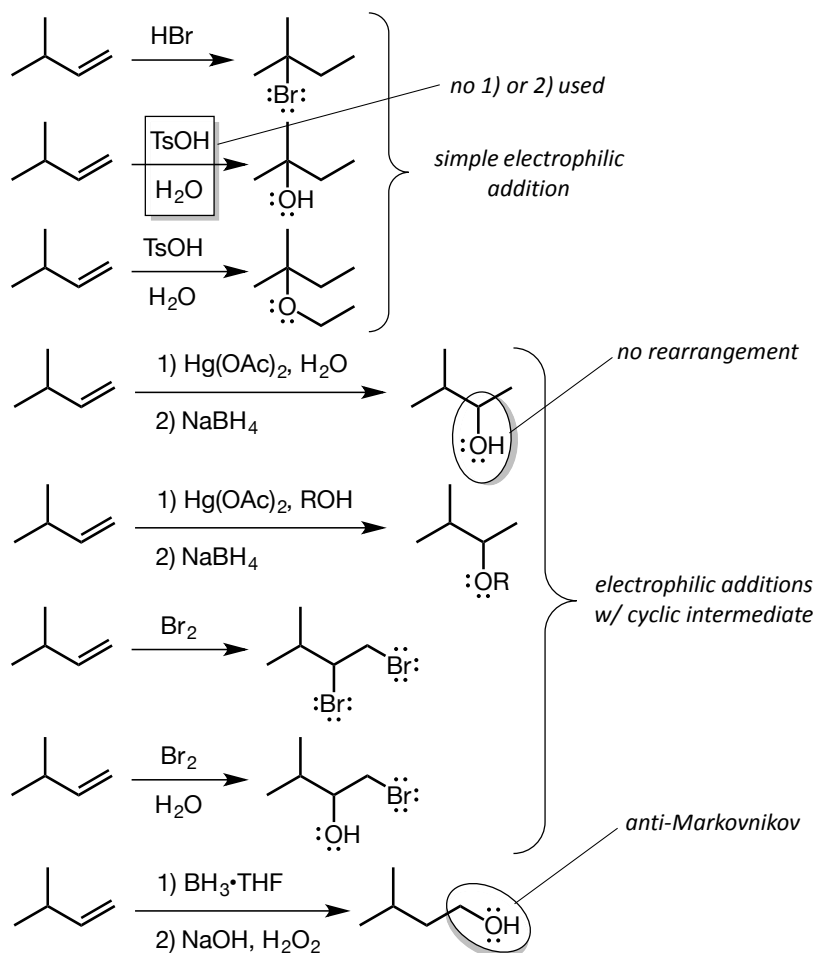
Hydrogenation – Hydrogen can be adsorbed onto the surface of Pd or Pt. Once adsorbed, the hydrogen becomes more reactive and can then be reacted with an alkene. Since the alkene is approaching the metal surface with both hydrogens pointed in the same direction, the hydrogens add w/ syn addition.

- 1) utility: alkenes → alkanes
- 2) reagents: H₂ and Pt or Pd
- 5) stereochemistry: syn addition; enantiomers
- 6) regiochemistry: no rearrangements

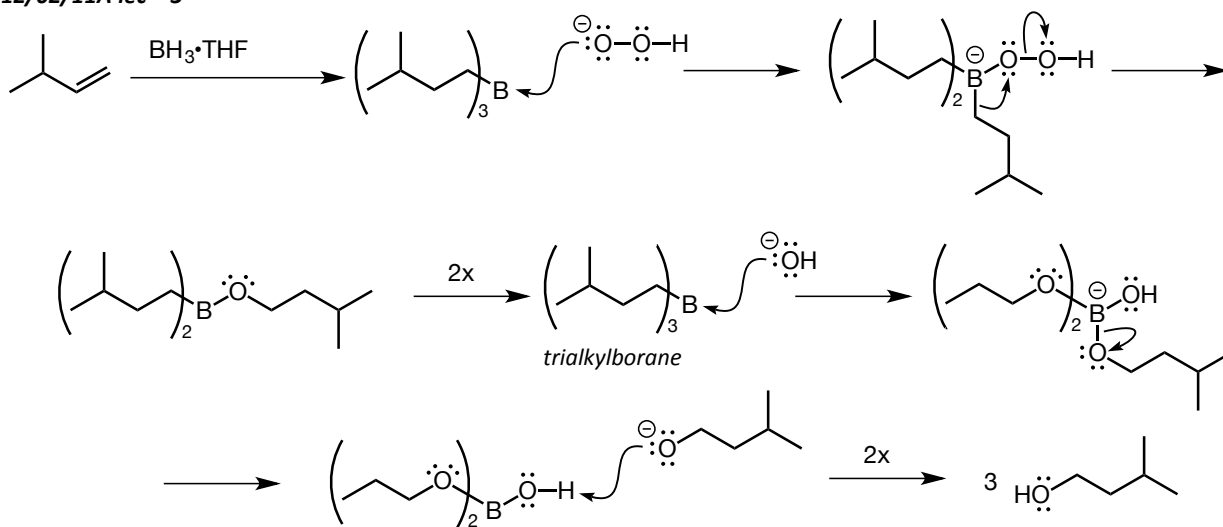
Bredt's rule – Unless the ring size is sufficiently large, elimination is not possible @ bridgehead positions because the carbon cannot become planar.

Structures

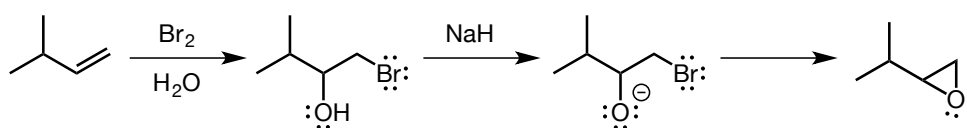
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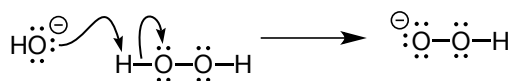
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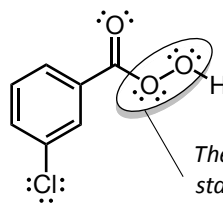
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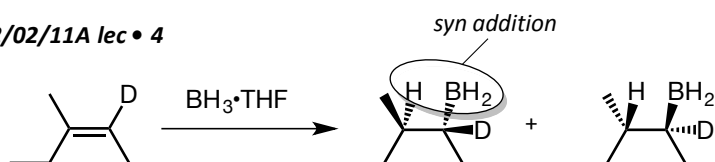


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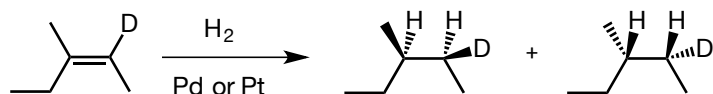


These oxygens have a -1 oxidation state and therefore can oxidize another molecule to become -2 O.S.

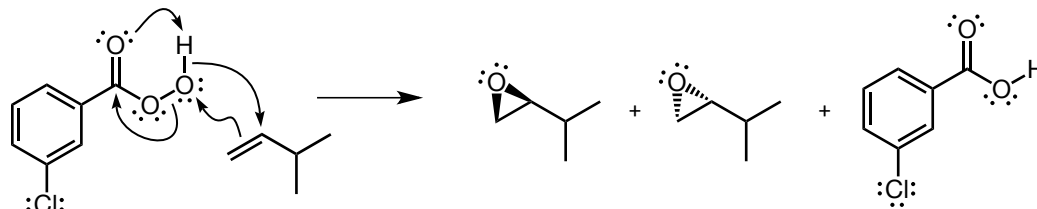
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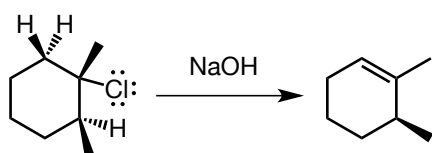
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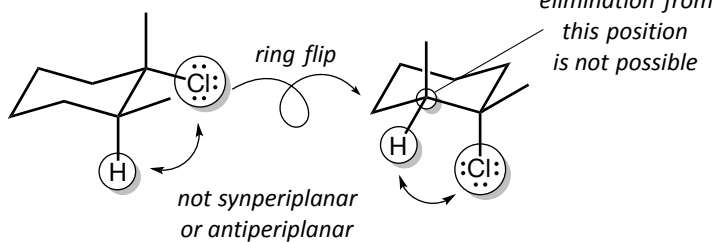
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