Lecture 27A • 12/09/11

Exam

Question 1 – Mechanism

You were shown some of the potential products, [and] you were supposed to circle which one of the products was most likely to form. You needed to write the mechanism for that reaction, and then use that mechanism to explain why is it that particular product formed in greatest proportion.

First problem: reaction of an alkene with tosic acid and water. The most common mistake was using tosic acid for something other than just being an acid catalyst. Remember that one of the big advantages of tosic acid is the fact that its counterion, the tosylate, is the cojugate of a strong acid, meaning it's going to be non-nucleopilic. After the H+ reacts with the alkene that's coming from that tosic acid, the tosylate is not going to react. [Tosic acid] is just there to be a source of H+; otherwise, it's going to be water that adds in for the attack. It would be OK to show just H+ being attacked by the alkene; if you did show the tosylate, then there were two arrows that you had to use: the first arrow to show the alkene attacking H; second arrow to show the dissociation of that hydrogen-oxygen bond, cause hydrogen can only have one bond at a time, unless it's one of these strange borane complexes. It is at that point that you end up with a tertiary carbocation. It is extraordinarily unlike that you're going to end up with a secondary carbocation. Some of you showed the secondary forming and then showed a hydride shift to the tertiary position. It wouldn't really want to do that; it would end up at the tertiary position to begin with. That's because the tertiary position is far more stabilized by hyperconjugation than the secondary position. That is, in fact, the basis of Markovnik addition. This is the more stable intermediate, which is why in the long run, the answer to this question is for the alcohol to end up at that most substituted position. At this point, water can come in to attack, because the carbocation is planar, we're [could end up] with two possibilities[, but there is no stereocenter]. Initially, we end up with the positively-charged oxygen; deprotonation occurs, and you end up with an alcohol plus its enantiomer.

Moving to the second one. You had hydroxide, heat, and a tertiary substrate, which means E2 elimination. It cannot be E1 because we do have a base. Because of that base, it's going to cause the hydrogen to be pulled off actively. When writing this mechanism, if you showed the hydrogen being removed separately from the leaving group coming off, that's an incorrect mechanism; they had to be shown simultaneously. [Hydroxide does not directly attack the leaving group;] that's an Sn2 reaction, that's substitution. Attacking th leaving group does not make an alkene, and attacking the leaving group's not possible cause it's a tertiary substrate. Instead, you had to show a hydrogen next door to the leaving group being attacked instead. Hydrogen gets removed; that pair of electrons can fall back towards the leaving group; leaving group comes off. The product I've shown in this case is this one, which turns out to be the most favorable product because you have four alkyl groups on this molecule, where all of the others examples had two or three. This is the most stable due to the most hyperconjugation with the neighboring alkyl groups. [partial credit for showing the least substituted product] We did have a reaction where we used t-butoxide to do elimination. If we have bulky base like t-butoxide, then that does cause the thermodynamically less-stable product to form. But we didn't have that in this case, we did just have the small-ion hydroxide, so it will be the thermodynamic that would be the one most likely formed.

Next problem. Chlorine and light – this is one of two radical reactions that you learned this [quarter]. There are three phases to this reaction. The first is you have to form chlorine radical, so you have to show the dissociation of that chlorine-chlorine bond. This is a radical process, so notice that all of the arrow are single-headed arrows – not the usual double-headed arrows like we have in all the other reactions from the quarter. This is slightly different. You form that chlorine radical, which does not directly add into an alkane - the first thing that happens, in fact, is a hydrogen is pulled off the alkane. Since there's two electrons in that bond between carbon and hydrogen, and since only one electron's going to be shown at a time using these radical arrows. You have to have two arrows for that bond; additionally you have to show the electron from chlorine interacting, so there's a total of three arrows that are necessary. At this point, you don't have the product; you have another radical, which normally does not attack a chlorine radical; it attacks another full molecule of fluorine. Again there's going to be three arrows total: two for the chlorine molecule to show where the electrons in that bond are going, one from the radical itself. That will produce the product, along with regenerating the chlorine radical, which then could react to finish off this reaction, now, with some other radical.

There were three phases to this: there's the initiation; the two propagation steps, and then the termination step. The product I have shown is the most likely one to form. Yes, it is true that the tertiary position is the most reactive, but there's only one hydrogen at that position. If all the hydrogens had exactly the same reactivity, it matters how many hydrogens that you have in place as far as how likely is it that a certain product's going to form. Both of those factors, in fact, mattering at the same time: how reactive is one hydrogen, versus how many of the hydrogens there are. You put the two together, and this secondary product ends up being the most favorable. [There is] a relative population of the different products of three for this methyl group reacting, 6 for the other methyl groups reacting, five for the tertiary, and then eight for the secondary.

Last mechanism: cyclohexene reacting with bromine to form a dibromide. It is critical that light is not listed as a reagent. Since light is not listed, that means that this is electrophilic addition and not free-radical halogenation. In an electrophilic addition, [the] double bond attacks, makes a ring with bromine. One of the bromides gets kicked off, and you form a cyclobromonium ion. The bromide ion then comes back to attack that cyclobromonium ion, and we end up, therefore, with a vicinal dihalide that's trans. Why is it trans? It's to do stereochemistry, nothing to do with sterics – it's the fact that that ring, that cyclobromonium ion, does not open until the halogen attacks. The whole point of this reaction is you don't form a carbocation. Because you don't go through that planar intermediate, instead you have this cyclic intermediate where you have a simultaneous attack of bromide as the ring opens, that's why you end up having anti addition overall to the double bond.

Problem 2

We have four molecules. You were asked: why is it that none of these four molecules can undergo bimolecular elimination. For none of these, the correct answer would be: substitution happens instead, cause it doesn't ask about substitution, it asks: why can't elimination occur. For molecule A, elimination does not occur because on one position, there's no hydrogens; on the other, that's a bridgehead position. Elimination's not possible from bridgehead positions cause it's not possible to make a planar carbon at that point. Molecule B, I'm going to write in one of the hydrogens and point out that that hydrogen is cis to the leaving group. In cyclohexane rings, when we have two groups that are vicinal and they're cis, it is never possible to get both of them anitperiplanar, so elimination can't happen, cause you never get the correct geometry.

For the third molecule, [the statement: elimination cannot occur because elimination from primary positions is not favorable; is only true for unimolecular elimination. For bimolecular elimination, there's no problem with it being a primary substrate. The problem is, there's no hydrogens at the carbon where elimination would occur. Yes, there's hydrogens on the same carbon as the bromine, but those are the hydrogens removed; it's the hydrogens one position over that end up getting removed. The last molecule has nothing to do with whether something is synperiplanar or antiperiplanar, because realize that you have all single bonds. Even if it's not in the right position to begin with, just a simple rotation and you would, in theory, have the right geometry. Problem is, hydroxide is not a leaving group. Even less so, the methyls are absolutely not a leaving group, so no reaction can occur.

You can't do E1, because E1 requires the formation of a carbocation, and you can't make a carbocation at a primary position. But, E2, you never make a carbocation, cause the hydrogen gets removed at the same time the leaving group comes off. That can easily happen if you have a primary substrate. In fact, if we had this reaction: let's say that I used a hindered base to ensure that substitution's not going to happen, the only reaction that's going to happen is that base will pull off a hydrogen, that bond will kick back towards the leaving group, and you're eliminate. You'll make a terminal alkene, and yes, terminal alkenes may not be as favorable as other kinds of alkenes, but it's the only one that could form in this case. There's nothing wrong with a primary substrate for E2; the only problem's for E1, cause you can't make a carbocation.

Fill-in-the-blank problems

Question 1: something reacts with this nucleophile to make a sulfide. What kind of substrate do we have? Primary substrate. It's not as strong of a base, but it is a strong nucleophile. Why? Because it's ionic, and it has sulfur. When you have a neutral nucleophile, that's almost always going to end up being weak, whereas most of the strong nucleophiles are charged. Since we have sodium, which is an ion, that makes it an ionic compound. Sulfur, ionic, is even a stronger a nucleophile than oxygen ionic. Put all of that together, that means this is going to be Sn2. If it's Sn2 and we're trying to back up and figure out what the substrate would have been, inversion of configuration occurs. At the very least, I'm going to invert that deuterium. Then, a reaction can't happen if you don't have a leaving group, so you have to put something else in here – it could have a been a halogen, it could have been a mesylate, it could have been a tosylate, but you had to have something. The bromide was the most common answer; that's why I'm showing it here.

Next problem: an alkene reacting with something make an alcohol. Borane is anti-Markovnikov addition, so if I had used borane, it would actually put the alcohol at the least substituted position, so that's the wrong alcohol. If you showed water, water all by itself is not strong enough to react with an alkene; you have to have some kind of acid catalyst. If you just list tosic acid, tosic acid is a solid that doesn't have water in it, so you do have to show both water and H+ – problem is, that's the wrong answer, because if you took this original molecule and reacted it with H+ and water, you'd get a carbocation shift, and so you end up with a tertiary. So, the only correct answer was mercury acetate and water, followed by sodium borohydride. If you did not show the 1) and 2), that's a wrong answer, cause not putting the 1) and 2) means all of those reagents participate at the same time, so you had to show them as being two different steps. This is exactly the case of why we have something like the oxymercuration-demercuration reaction, because it does let you put the alcohol at the most substituted position of the double bond without it then having rearrangement.

Next problem: this was just being able to recognize the reagents. [flashcards][learn by teaching] Let's say you're trying to figure out what hyperconjugation is: how would you get up in front of the class and teach the topic of hyperconjugation?

What's important? Where does it show up? How does it happen? What does it affect? You'll put all those ideas together as soon as you try to open your mouth and explain it to someone else, cause as soon as you do, you'll figure out what you don't know.

MCPBA is this molecule. MCPBA is one of our reagents for making epoxides. There really is a stereocenter at that secondary position, so you really do need to show two different products. [The] primary position is not a stereocenter; I've gone ahead and used a wedge and a dash just to match what is at the secondary position. If I had drawn these end ones with plain lines, that technically would have been correct.

Next one: something reacts with t-butoxide to make an alkene. Let me write down three of the most common answers, I'll show you which one would have been correct: halogen next door to the methyl group; halogen on the same position as the methyl group; halogen on the methyl group. That last one definitely can't be right, cause the only product that you would get from elimination is a terminal alkene. How do I know it's elimination? I'm using a hindered, strong base; that's why I know it's E2. What about either of these other two choices? It's not going to be the second one, either, because this is a hindered base, and it's exactly this situation, where you have a bulky, hindered base that's going to cause the less-substituted product to form, because it's kinetically easier. The only correct answer is the first one. It didn't have to be bromine; it did have to be a leaving group, though. [should have showed correct stereochemistry]

Bromine and light. Br2 does not react with alkanes; Br2 reacts with alkenes. It is bromine radical that reacts with an alkane, and the only way you get that is you have bromine in the presence. This is, in fact, the only product we could get cause where those four methyl groups are attached, there's no hydrogen there, so there's only one possible product.

Next one: cis alkene reacting with D2 and platinum; that is simple hydrogenation. Because it could add to one face or the other of the double bond, we're going to have two enantiomeric products. If you showed stereochemistry, you had to write hydrogens in on whatever the deuteriums where not on, because if you show a dash or a wedge and you don't write hydrogen, it means a methyl group.
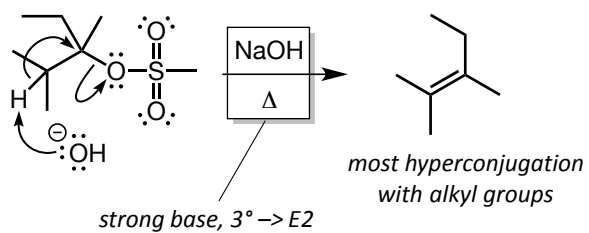
Next one: something reacts with borane•THF first, and then hydrogen peroxide [and] sodium hydroxide to make an alcohol – that is a hydroboration. Hydroboration occurs by adding to the least substituted position. Let's look at some possible [substrates]. The first one, if you did hydroboration-oxidation, you'd get this: the alcohol would be on the ring itself, so that would be the wrong answer. The last one, if we did hydroboration-oxidation there, you'd end up with the alcohol at the end of the molecule, so it's also incorrect. The middle one is the only correct answer, because the less substituted position is the secondary position, where is exactly where we want that alcohol.

Two more problems. First, an allyl halide reacts with something to make an allyl ether. This is an Sn1 reaction. What does that mean the answer has to be? Ethanol. It cannot be anything ionic, because if it were, it would cause E2, cause you can't have a [basic] nucleophile with a tertiary substrate and avoid E2.

Last reaction: alkene reacting with bromine and water – that is going to form a halohydrin. In this case, there aren't stereocenters, so you don't need to show stereochemistry. The alcohol is going to end up at the most-substituted position, because bromine is the electrophile and therefore going to end up at the last-substituted position.

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NaOH

Δ

strong base, 3° –> E2

*most hyperconjugation
with alkyl groups*

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