## Lecture 22B • 11/22/11

E2 reaction stereochemistry

We had seen one example where the leaving group and the hydrogen being pulled off were trans to each other on that ring. What would happen if you had a similar molecule where those hydrogen and leaving group were cis to each other instead. Let's investigate that.

We had a compound like this where next to the leaving group on one side we had two methyl groups, which means there's no removable hydrogen at that position, so elimination will not occur from that side. On the other side of the leaving group, we have a hydrogen and then a methyl group, so there's only one hydrogen that could be removed on that other side. The question I had posed is: would that elimination be able to occur?

Let's draw a chair structure for this. There's our two methyl groups. We could write bromine in the axial position and then its hydrogen in the equatorial position. That's going to mean that the hydrogen on the next carbon over is in the equatorial position, while the methyl group is in the axial position. That's one possible chair structure. We could draw the ring-flipped version as well. There's our two methyl groups. There's bromine still pointed up, but now in the equatorial position, which will force the hydrogen axial. [In this] other version we have the hydrogen axial, which is going to put the methyl group equatorial. Do we either have synperiplanar or antiperiplanar geometry in either one of these cases? Let's see if we can determine that.

What if we were to make a rotomer diagram looking along this bond axis. What would this look like as a Newmann projection? The bonds that are closer to us will be the ones that we write with lines going through all the way to the center. The ones that are further behind, behind this virtual disc, will not be drawn all the way through. Bromine in the back is pointed up; the hydrogen is pointed down and to the right. In the front, the methyl group is pointed down, and the hydrogen is up. I could just, for simplicity, connect these other two substituent positions because they're just the ring. [model sets] Let's do the same type of projection for the ring-flipped version. This one's going to be a little bit tougher one to visualize. I'm going to visualize it from here. From that perspective, the hydrogen's going to be pointed straight down. We're going to have the bromine pointed out to our left. Realize that if we're looking at the molecule from this side, bromine is actually kinda pointed out this direction at us; with the way that I've written it on the paper, it's hard to visualize. We'll then have the rest of the ring going off to the right. In back, it's a little bit easier to see: the methyl group will be pointed down to the left; the hydrogen will be pointed straight up. We'll have the rest of the ring pointed out the other direction. In either case, the dihedral angle between the hydrogen that can be removed versus the leaving group is 60°. You have to have either 0° or 180° in order for elimination to occur.

When we have the removable hydrogen and the leaving group trans to each other, then one of the ring flip versions did have a 180° angle. [homework, do similar Newmann projections]. When you do that, you will find one of them is not 180° but the other one is. Elimination will not occur in this compound because it never can achieve the correct geometry.

Let me briefly introduce the E1 mechanism. Let me show you the mechanism for an E1 eliminaton. E1 is called E1 because it's unimolecular, meaning only one reagent is present in the rate-limiting step. It's exactly the same initial rate-limiting step as we have for Sn1, which has an immediate important consequence: since it is exactly the same intermediate as the Sn1 reaction, it is impossible to have an E1 reaction without at least the possibility of forming substitution products as well. Similarly, you can't have an Sn1 reaction without there being the possibility of E1 occurring as well, again because they both go through exactly the same intermediates. SInce the exact same intermediate is formed at the beginning of both the Sn1 and E1 reactions, they'll always occur together. As far as which one are you going to end up with more happening, it's going to depend on primarily solvent, maybe the size of the nucleophile, or temperature. I say maybe the size of the nucleophile because recognize that the rate-limiting step of this reaction doesn't depend on the nucleophile, but you could argue that there's some kind of secondary effect afterwards.

Focusing on the elimination mechanism for the moment, once the carbocation forms, you're going to have a more active overlap with neighboring sigma bonds; you'll have hyperconjugation. You could imagine that, what if that intensified so much that the electrons from that hydrogen just end up completely overlapping with the p orbital? If we had some kind of weak nucleophile come along and pull the hydrogen off, we'll form a triple bond.

Let's briefly cover those six aspects of a reaction. In terms of utility, an alkyl halide or [a] sulfonate forming an alkene. The reagents: weak, non-basic nucleophiles. If you had basic nucleophiles, E2 would happen instead. As fas as conditions, same as Sn1: polar, protic sovlents. You have the mechanism up above. More substituted alkenes are formed preferentially. In terms of regiochemistry, more substituted alkenes form. [In terms of] sterochemistry, recognize that carbocation shifts can occur. They wouldn't in this example that I showed you because you have a tertiary that would much rather be tertiary than a primary possibly forming. But, in other cases, you could have migration.

For question 1 – this was the question about the three different types of carbocations. You had the same original molecule, but you have shone a primary versus secondary versus tertiary carbocation. You were told that the tertiary carbocation forms more rapidly than the secondary versus the primary. You're asked to explain this behavior. This is hyperconjugation. I'll do the answer which was the most common answer which was to do the carbocation fo compound C, the tertiary carbocation itself. So, sp2 hybridization on that central carbon, which means it's going to have a p orbital on it. Sp3 hybridization for all the other carbons; so, we'll have two methyl groups, and then an ethyl group . Shouldn't forget the hydrogens that are there. It makes sense to show the hyperconjugation that's going to occur to make this a stronger diagram for supporting the answer, which is: for this tertiary carbocation, because we do have three different neighbors that the overlap can occur with, that provides more stabilization than if we had had a secondary carbocation or a primary carbocation.

If you drew [a primary or a secondary carbocation instead], figuring out which neighbors does the overlap actually occur with [can be tricky]. Notice I have not drawn this hyperconjugation interaction connecting to the last carbon on the right there; it's really too far away for it to have an interaction with the p orbital, so it's only the neighbors that really are on the next atom over that are going to have the possibility for hyperconjugation. Also, hypercojugation, all the examples that's we've seen so far, all involve only one p orbital; it's the interaction with neighboring sigma bonds. [This is different from] conjugation [where you draw a] p orbital on each of the carbons; but those p orbitals don't exist if you have sp3 hybridization. Be careful that you are making a difference between conjugation an hyperconjugation. [grading scale]

The second problem. You were given the allyl anion, and you were asked to draw a SMOG for the allyl anion; let's do that first. That gets to the heart of the problem: although we write the structure using either one of these resonance structures, they are actually the incorrect structure for the molecule. You can' use these to generate your SMOG, cause that SMOG would not reflect what allyl's true structure is. In fact, it has sp2 hybridization on all three of the carbons. Since there's sp2 hybridization on each of the carbons, you're going to have not hypercojugation, but conjugation in this case. Again, we don't want to forget the hydrogens. That's the SMOG. You're asked to explain how an why neither resonance structure correctly show the structure of this anion. The how you can express in a couple of different ways: one, the electron pairs, the negative charge, isn't really localized on any one particular carbon, as the resonance structures have it. One of the carbons of the structure is sp3 hybridized and the other two are sp2 hydridized, but that's exactly where the structure fails to describe really what the allyl ion looks like. That's because line structure, which are a form of Lewis dot structures, are incapable of showing delocalized electrons; it's a writing system that can only handle bonds between two atoms. [grading scale]

Third question; the mechanism question. You have two starting materials, one of which was a primary alkyl halide, one of which was a tertiary alkyl halide. You were told that the primary alkyl halide reacts with sodium hydroxide, and you were told that the tertiary reacts with water. You were asked to write complete mechanisms for both of these reactions. With the primary substrate, that's the Sn2 reaction; you were required to know the Sn1 and Sn1 mechanisms, and this is almost or identical to the example that had been in class. For the Sn2 mechanism, it's concerted, and because it's concerted, that means that you're going to have inversion of configuration. [grading scale] Let's draw the mechanism for the second one. Here, the bromine leaves first, forms a carbocation; water comes in to attack. Recognize that neutral water has an almost zero quantity of H+ and hydroxide; that trace amount that forms so quickly recombines again that it's not really an appreciable quantity to be a reactant. H2O is never, ever the same thing as H+ and OH-, at least within organic chemistry reactions. It really is going to be water that attacks in the second case. When it attacks, you end up forming a stereocenter[; this means the enantiomer will also be present]. I'll just draw one product at first. The most commonly missed arrow is the deprotonation of the oxygen; the hydrogen comes off, but the arrow does not show which way the hydrogen goes; it shows which way the electrons go, and the electrons go back to the oxygen. Once that deprotonation occurs, we have a neutral alcohol. Now, at this point, I'll go ahead and write in both of the products.

Number four was the reaction coordinate diagram problem. [answer to question four tied partly to answer in question 3] For the first reaction, there is only going to be one transition state, because it is a concerted reaction. You were told in the problem that it's exothermic, so you had to make sure, and it would have been fine to assume that energy was in terms of enthalpy, but you had to make sure, then, that that product was going to be lower in energy than your reactants. You were asked to label reactants and product, and you were also asked to label the transition state(s), which there's only one in this case, and the activation energy, which there's only one of in this case. If the mechanism had three steps in it, then your reaction coordinate diagram should also have three steps in it. You were only told that the overall reaction is exothermic, so in some ways you would not have been able to correctly place the energy levels for the intermediates, except, the first step of the reaction is the formation of a carbocation [and] is, therefore, a bond-breaking event, so at the very least your first intermediate should have been higher than the reactants in energy. Because the first step is also the rate-limiting step, you needed to makes sure that you showed the first step having the largest activation barrier. The position of the second intermediate you might not have known. So, we have a reactant, a product, and two intermediates. The intermediates are the local minima, these species that form just for a moment in solution. The tops of the cures, those are the transition states. Here are the two transition states. Now there are three forward activation energies. Notice that the activation energy is written either from the reactant or the intermediate that it's immediately preceding that transition state. You don't write each activation energy in comparison to the original reactant; you only do that for the first transition state.

There are three steps. The first step is the nucleophile comes off; that would be the largest activation barrier. The second step would be attack of the water; that's that activation barrier there. And then you have the dissociation of water, so third reaction step. I showed you an example of iodide being the nucleophile; that did not have a third, deprotonation step, so that doesn't have a third hump on the reaction coordinate diagram. Because we do have that bond dissociation energy, we do have a third step. The number of transition states equals [the] number of reaction steps.

The other part of the question is the fact that both the nucleophile and the substrate, their concentrations matter for the rate of the first reaction, but only the concentration of the substrate matters for the rate of the second reaction. That's because of what's in the rate-limiting step. For the first reaction, there's only one step, so automatically, both of the reactants are found in the rate law, so automatically both of them have an effect on the rate of the reaction. For the second one, it's only that first toughest step, the rate-limiting step, the formation of that carbocation, that is going to control the rate of the reaction. Since only the substrate matters for forming that carbocation, that's why only the substrate affects the rate of the reaction.

Number five; stereochemistry. As we can see from the Sn2 mechanism, we're only going to make one product, but you can't say that just because it has a stereocenter, that's why the solution is optically active, because you could have a meso compound. Meso compounds have stereocenters, but are achiral, so you do have to say it does have a stereocenter but you also have to specifically say that it is chiral, which is why it is optically active. For reaction B, the reason that you don't see optical activity there is because you have a racemic mixture, where you have exactly 50/50 balance of both enantiomers. Since the optical rotation of one cancels out the other, that's why you end up with an optically inactive solution.

Number six was naming. First one, cyclohexane derivative. This is cyclohexanol; it is an alcohol, so the alcohol functional group ending, because there's only one of that most important functional group, you don't actually use the number, so this name is going to end in just cyclohexanol. You've got three substituents: a deuterium, and then two methyl groups. The 'd' in deuterium comes lower than the 'm' in methyl; even though you're going to say 'dimethyl', even with that 'di', it would still come after deutero, but you don't even look at the 'di' to alphabetize, you look at the 'm' in methyl. We're going to list deutero first, methyl second. Since the alcohol is the most important functional group, numbering starts from that position, so we're going to have 2-deutero-4,4-dimethyl. That would almost be complete, but we do have stereocenters, we've two of them. The top one isn't a trick question, but does appear to be a stereocenter because you've got dashes and wedges, but since they're both methyl groups, since you've got two of exactly the same substituent, that means it isn't really a stereocenter. Position one and position two we need to determine. For position one, oxygen's more important than carbon, so it's automatically priority one. Then we have two halves of the ring; they're different from each other: the left half has a deuterium, the right half doesn't. Deuterium has precedence over hydrogen, so it looks like it's R, but the least important group is actually pointed towards us, so we have to reverse what we see, so it's actually S. For the other stereocenter, we have two carbons and a deuterium attached; we have a carbon with an oxygen, and we have a carbon without an oxygen. The carbon with the oxygen's more important than the carbon without the oxygen; then we have the deuterium. That one is also S. So the full name is (1S, 2S)-2-deutero-4,4-dimethylcyclohexanol.

The other problem: another alcohol. The longest carbon chain here is seven carbons long; it's going to be some form of heptane, but it's going to be an alcohol, so it's a heptanol, except we have three alcohols, so it's a heptanetriol. There's two different ways that we play around with these base names, something like hexane. If we have an alkene or an alkyne, it's the -ane part of the name that changes. We could go from hexane to hexene to hexyne. When we have an alcohol, you're changing what comes after that. For alcohols, the 'n' like in hexane, pentane is always there. If you had a single alcohol, that would be hexanol; you drop 'e' just so the 'e' and the 'o' don't clash. If you have a triol, that means you're going to have the full name: heptanetriol. The lowest position we could number would be if we gave the righthand most alcohol the one number, so this is going to be heptane-1,3,3-triol. Now we need to worry about the substituents. There's an ethyl substituent and two methyl substituents. Even though it's dimethyl, the 'di' part doesn't get alphabetized. We're going to put ethyl first, and then the two methyls. Ethyl, the five position; two and four for the methyls.

We do have stereocenters again; we only have two stereocenters. Where the two methyls are connected, that's the same substituent, so it won't be a stereocenter. Where the two –OH groups are connected, same substituent, also no stereocenter. So it's going to be positions two and four that are chiral. Each of those has four different substituents. Let's handle position two first. We've got a carbon with two oxygens, a carbon with one oxygen, and a carbon with no oxygen. It looks S, but the least important group is pointed towards us, so it's really R, so that's 2R. Then, for position four, we have carbon with alcohols, we have carbon with just carbon, and then you have carbon with just hydrogen. That looks R, but the least important group is pointed at you, so it's really S. So the full name is (2R, 4S)-5-ethyl-2,4-dimethylheptane-1,3,3-triol.

Equilibrium: esterification. Very common reaction where you take a carboxylic acid and cook it up in a heavy amount of alcohol with a little bit of an acid catalyst, which I did put in there as well. The type of reaction that you leave overnight and come back the next day and you have your ester. Your first asked to give the three definitions of equilibrium; it's where you have no apparent change in the concentrations of reactants or products; where you've reached the lowest-energy point of the system; and where the rates of the forward and reverse reactions are equal to each other. You were then asked how could you affect this reaction to push this to making products, to force the reaction to go to completion.

The answer that nearly everybody gave is to remove products, which is what you did in one of your labs. By removing products, what happened? You lowered Q below K, which is the concentration argument. I'm making this argument because you were asked to explain Le Châtelier's effect in the context of those three definitions of equilibrium that you had given. The three definitions were about concentration, rates, and energy; you needed to refer to each one of those. For concentration, you drop the concentration of products down, makes Q lower than K so more products want to form to reestablish equilibrium concentrations. In terms of rate, if you drop the amount of products then your forward reaction rate's going to increase [by comparison], but not your reverse one, so it's again going to move the reaction forward. Then, in terms of energy, if equilibrium is the lowest-energy point of the system, then if you do anything to disturb the equilibrium, automatically you're going to be higher in potential energy, so the reaction's going to go towards lower energy again.

What about the catalyst? You were asked why adding a catalyst will not change the balance of products and reactants found at equilibrium. Because, the catalyst affects activation energy; it affects how fast the reaction's going to occur, but it actually doesn't change what the reactant is and what the product is. At equilibrium, that balance depends on what is the energy of the reactants and products, so it's really Hess's law. Hess's law says that it doesn't matter how a reaction occurs, it's still going to have the same overall energy change. SInce energy change is related to equilibrium, that's why the catalyst has no effect on equilibrium. You could also add a whole bunch of alcohol. If you keep adding to the reactants side, that's going to push it to products as well. If you add product, that will make it go back to reactant. In real life, the alcohols that you tend to esterify with tend to be cheap and the acid more expensive, so you tend to use the alcohol as the one that's in excess. Temperature would have an effect, but we'd have to know exactly what's the energy of the reactants or products to know how temperature would change the balance.

[quiz 3]

The first question, the three factors were hybridization, induct effects, and resonance effects; exactly the three things we had talked about in lecture. For example, the difference between the alkane and alkyne, that was hybridization; that was the only thing that was present. Between the alkane and the alcohol, that's the inductive effect, because oxygen can tolerate that negative charge, versus carbon which isn't as electronegative so it's not as good at pulling electrons away. Then, you have that alcohol versus the carboxylic acid, where yes, you put a second oxygen on there, but you have resonance. Once that hydrogen from the acid comes off, you have resonance stabilization, which is why it would want to come off in the first place.

Let's do those five pairs of reactions. First one: primary alkyl halide with sodium hydroxide; secondary alkyl halide with sodium hydroxide. You were responsible for knowing the six aspects of those different reactions, Sn1 versus Sn2. One of those aspects is to recognize that Sn2 is a reaction that prefers primary versus secondary substrates and prefers strong nucleophiles. If you look at sodium hydroxide, that is a strong, basic nucleophile, so it's going to encourage Sn2 reaction. Since we have a primary versus secondary substrate, you might remember that we discussed steric hinderance as the reason why primaries are more reactive. It is going to be the first reaction that is the faster one. The product of the reaction then would be this, where the hydroxide's going to substitute for the bromine, and you're going to have inversion of configuration. This is Sn2, because we have a strong, basic nucleophile, and primary is faster than secondary because of less steric hinderance.

The next pair: again, you had a primary and a secondary, but now you have a weak nucleophile; you have water instead. That's a characteristic of the Sn1 reaction. Secondary carbocarbocations, which is what you form in an Sn1 reaction, are more stable than primary carbocations, so that's going to mean that the first reaction is the more rapid one. For the products, implicit in this is, what is the stereochemistry of the products? You would get two of them. This is Sn1; we have a weak, non-basic nucleophile, so secondary's faster than primary because of hyperconjugation.

The third pair is where this question of is it the same or not comes up. What you might have been tempted to look at first is the difference between the oxygen and the sulfur. What's the rate-limiting step of this Sn1 reaction? How do we know it would have been Sn1? Because, again, we have a weak nucleophile. The only thing that affects reaction rate is the substrate itself. Since it's the same substrate in both cases, it's the same reaction rate. Sn1, because it's a weak, non-basic nucleophile; since it's the same substrate, it's the same rate.

The fourth pair: this is going to be Sn2, because we have [a] strong nucleophile nucleophile. The point of this question is it's going to be a stronger nucleophile than oxygen because of polarizability. Sulfur: bigger, squishier than oxygen, more polarizable, that's going to be the better nucleophile. That will be the product for that one. You get a ether or a sulfide.

The last pair of reactions was with a mesylate being substituted with sodium hydroxide and fluoride with sodium hydroxide. Fluoride is the conjugate of a weak acid; it is the one halogen that we have discussed being a poor leaving group because it comes from a weak acid. A mesylate, that is the conjugate base of a strong acid. In terms of leaving group ability, the stronger the acid it comes from, the conjugated, the better leaving group it's going to be. Since this is an Sn2 reaction, even an Sn1 reaction, for both cases it would be the mesylate that would be the better group, so it'd be the faster reaction. It is Sn2 in this case because we have strong, basic nucleophile and a primary substrate.

Mesylate, a good leaving group; fluoride, since it's basic, is a bad leaving group. The product's structure in this case would be this. [solvent would affect the nucleophile, but solvent isn't specified, and the leaving group would still be the same]

Sn2 versus Sn1 versus E2 versus E1

Think about the things that can influence which one of these things is going to happen. It's not really going to be the leaving group, because if you change one leaving group versus the other, technically that can cause a change in distribution of products if you've got elimination going on, but the nucleophile's also involved, and if you're using the same nucleophile, the leaving group really isn't one of the strong factor. It is the substrate and what kind of nucleophile that you're trying to use. It might be easier to first think about substitution versus elimination instead of trying to tackle all four distinctions at once. Substitution's going to happen if you don't have something that's trying to get in there and grab that proton, especially if we're talking about Sn2 versus E2. Sn2, nucleophile has to attack, you just gotta make sure it's not basic enough that it's not going to pull off a proton instead. We did discover, though, that Sn1 can't happen without the chance of E1 and vice versa. There's always going to be his footnote that we gotta make; in any discussion about Sn1 and E1, remember both of them could, in theory, happen. If we're focusing on the Sn2 versus E2 reactions, let's just take a couple of examples to work with and maybe build a small table.

Ethyl bromide with sodium hydroxide, primary substituent, primary leaving group – about as sterically unhindered as you can get, other than having a methyl group. I've shown this as the major product. Is elimination technically possible? Yes, if, somehow, hydroxide, being basic, is able to rip a proton off over here; there's nothing that would prevent that from happening, but it would be a ver minor product in this case, because substitution is not difficult. What if we had something like this, though? This is actually the tough case: what to do about secondaries. Secondary's [are] in between good and bad for Sn1, and it's between good and bad for Sn2. It's also in between Sn2 versus E2, because there's enough steric hinderance now where you would have slowed substitution down enough that elimination becomes a non-zero possibility. So, if you had just hydroxide, one of the smallest basic nucleophiles that you could have, it is possible to get more Sn2 than E2, so I'm going to write for the major product in this case that we're going to get substitution – but I'm going to acknowledge the fact that, with that extra bit of steric hinderance, we're also going to have the possibility of elimination. Primary is going to be Sn2; secondary's going to be Sn2 and E2 – unless you've got a hindered nucleophile. We saw this ion, the t-butoxide ion, when we were talking about eliminations. This t-butoxide ion is itself so hindered that it's really not going to have a chance to substitute. Yes, when we first when through the Sn1/Sn2 reactions, for Sn2 we talked about how steric hinderance of the substrate has an influence, but now we're focusing on the nucleophile. In this case, the product is almost exclusively going to be E2. Secondary with bulky base is E2. Tertiary doesn't do Sn2, so it you have a basic nucleophile, the only thing possible is E2.

These are the four examples we have to worry about if we're dealing with basic nucleophiles. But what if you have non-basic nucleophiles? Let's break these cases down. Primary alkyl halide with water – technically, you might get a trace of Sn2, just a litte, itty, bitty bit. Water is not basic, so that reaction's really not favorable, so it would just have to be a time-exposure thing, where you leave the compounds in for a long time before you really encourage any Sn2 to occur. Sn1 flat out won't happen. You will get a product, but big asterix here: it is a slow Sn2 reaction. For anything else, it's Sn1 and E1. For anything besides primary, secondary or tertiary that means, you're going to have Sn1 and E1, if you have a non-basic – and let's intensify that – weak nucleophile. [how much differentiation is a student responsible for] Primary will be slow, slow, slow Sn2. We have a secondary alkyl halide and we have water. It's going to be much more like that, if substitution occurs, it's going to just be Sn1; it's not a basic nucleophile, so Sn2 is not very likely. Because Sn1 has the same intermediate as E1, you will get some quantity of the alkene as well. Secondary will be E1 and Sn1. Usually if you have a non-hindered nucleophile, you might get a bit more substitution, just because if it's not all that big, it can get in there and substitute at the carbocation. Generally, if you have a bulky nucleophilie, you might have a little bit more elimination. Even in that bulky nucleophile case, because it's not basic, the carbocation has time to sit around and form and maybe persist, you will get substitution. It's very nucleophile, and solvent (and maybe a little bit temperature) dependent. Here we'll have substitution and elimination. This was for the cases of non-basic nucleophiles. Let me summarize the factors that I gave at the beginning of this: that is the substrate and how basic and bulky the nucleophile is that will determine which one of the reaction mechanisms occurs.

The last thing I want to show you, then, is leading up to a type of problem you're going to have on all exams from now on. It's what is known as the fill-in-the-blank problem. For example, let's say that you have something like this: let's say that you have a tosylate that I show reacting with something but that something is not shown, and I show an ether as a product. In this type of question, then, I would ask you what should go in the blank. What should go in the blank in this case? What compound would go in the blank? NaOH? Strong nucleophile? Would this undergo Sn2? No, because it's a tertiary substrate, so you can't use strong nucleophiles, you can't use hydroxide, because you would get elimination instead. If you see something like this, you have to analyze it and say: oh, tertiary substrate, but substitution, the only possible reaction is Sn1, which means whatever our answer is is going to have to be a weak, non-basic nucleophile. [Instead of hydroxide] we use water instead, that would give us an alcohol instead of an ether as a product, so the other consideration is what's the carbon structure of the product. We have two new carbons in the product that really weren't in the reactant, so we're going to want a two-carbon compound to be our nucleophile, which means the answer is ethanol.

Let's do another example where I have the product missing instead of the reagent. CN is the cyanide ion. Figure out if you can write a Lewis dot structure for the cyanide ion. Carbon, four valence electrons; nitrogen, five valence electrons; negatively charged ion, so 1 + 4 + 5 gives us ten electrons total. We have carbon and nitrogen; the only way we could squeeze ten electrons out those is to make a triple bond between the carbon and nitrogen and put a lone pair on each. Nitrogen's going to be neutral if we do that, carbon's going to be negatively charged. This is a basic nucleophile, it's relatively strong. Carbon's going to be the business end of it, so you'll form new carbon-carbon bonds – which is a hugely important trick. What we're going to find out is that the formation and breaking of carbon-carbon bonds are some of the most important reactions in organic chemistry. There are many more reactions that transform functional groups, but to combine and cleave carbon bonds, that's a bit rarer. This is a sneaky way of doing it because we're just doing a substitution, but it makes a carbon-carbon bond. The only way to put the negative charge on nitrogen would be to make a quadruple bond. Hydrogen cyanide has a pKa of [9.25]; that [the conjugate]'s not as good a base as hydroxide, but it's a stronger base than fluoride is. If that is a basic nucleophile, what kind of reaction's going to happen? Sn2. Why? Primary substrate. So, a combination of primary substrate and basic nucleophile that's not very hindered, so it's going to be Sn2. So the product's going to be this. This functional group is known as a nitrle. Nitriles can be converted into other carboxylic acid derivatives. This is our sneaky way of introducing a carbon-carbon bond to later make carboxylic acid derivatives, which can be used to make aldehydes and ketones, which can then be used to make alkenes and alkynes. If you used a really hindered base, yes, you could get elimination; but, we didn't in this case, so that's why the major product's substitution.

One more example. Something reacts with potassium t-butoxide to make this compound. What kind of reaction would have occurred? E2. Why? Because we made an alkene; that's one of the big clues that elimination happened instead of substitution. The other clue is that there's nothing that looks like either a nucleophile or a leaving group on the end molecule. E2 would occur – why E2 and not E1? Has to do with the nucleophile: what kind of nucleophile is it? It's bulky, it's tertiary; it's basic. Remember, potassium, that's an ion, so even though I wrote it as [R–]OK, it really oxygen minus, so it's a hindered, bulky, basic nucleophile, which means it's E2 instead of E1. That means we have to work backwards and figure out where to put the halogen. If I want to make sure this is the only product formed, then that means I would not want to put the halogen where my pen is right now, because if you eliminated that alkene, you could have elimination in two different directions. If you wanted to ensure that you only get this product, you want to make sure that the leaving group is at this top position. If we had had the leaving group here – we won't worry about stereochemistry in this case – even if we used sodium hydroxide, that's a tertiary substrate, so even sodium hydroxide could cause elimination. It would cause the formation of two products. Because of that, this is not the ideal location for the leaving group, since two products can be formed. Instead, we'll put the leaving group at the top position. The leaving group and the hydrogen being removed need to be trans to each other, so once we put that leaving group up there, we would technically have a number of choices – one choice would be this, which is fine, because the correct elimination geometry is possible. Another choice would be its enantiomer; you still have the correct geometry possible. But if I look at its diastereomer – I'll write the hydrogen explicitly to show that they're cis. This would not be a correct answer, because the correct elimination geometry is not possible. This is the new type of product you'll have on exam three, where the reagent, the product, or the substrate may be missing.

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Elimination will not occur in this compound since the leaving group and the hydrogen removed will never attain the correct geometry (periplanar [0°] or antiperiplanar [180 °])

E1 – Since the exact same intermediate is formed at the beginning of both the Sn1 and E 1 reactions, they will always occur together.

1. utility: alkyl halide -> alkene
2. reagents: weak, non-basic nucleophiles
3. conditions: polar, protic solvents
5/6 –> more substituted alkenes form
6) regiochem: carbocation shifts can occur

Sn2 vs Sn1 vs E2 vs E1 – The type of reaction that occurs depends on the structure of the substrate and the basicity and bulkiness of the nucleophile.
This reaction is a substitution rxn on a 3° substrate. Only Sn1 is possible, so a weak, non-basic nucleophile must be used.

$H_2O \neq H^+ + OH^-$

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Structures

Identical to those from lecture 22A (11/22/11)