Lecture 26B • 12/06/11

Hydrogenation of alkynes

Let's start with plain hydrogen and platinum (or palladium). An alkyne's got two pi bonds, so you might imagine that if you were to hydrogenation, you might be able to take an alkyne and react one of the pi bonds and make an alkene, which is in fact true. The problem is that an alkene itself is reactive to exactly the same conditions, so there isn't really a way to stop the reaction using the normal platinum or palladium catalyst at the alkene, instead you go all the way to the alkane. If you just have plain hydrogenation conditions, you can't say: let's hope that only one molecule of hydrogen's going to react and we'll make the alkene instead; no, we're going to take it all the way down to the alkane.

But, there is a way to get around this, which is to make a less-reactive version of the catalyst, what's known as a poisoned catalyst. There is a particular catalyst known as Lindlar's catalyst. There's different formulations, but essentially it contains lead sulfate or some other lead salt, along with a nitrogen-based compound called quinoline. It's specifically used because it has reduced reactivity, so it does let you selectively reduced an alkyne to an alkene. Remembering the geometry, the way that hydrogenation reaction works, we have a metal surface where, in this case, an alkyne will come down to react with hydrogen that had already been adsorbed on that metal surface. Same situation again where the two hydrogens would end up adding to the same face of that pi bond, but now instead of it being syn addition to a double bond, this is a triple bond we're talking about. What that's going to leave is a pi bond, but since both the hydrogens add into the same face of that pi bond, you're going to therefore make a cis alkene. If we have platinum or palladium [along with the poisoning reagents], and then hydrogen, if we hydrogenation, we specifically get a cis alkene. Since hydrogen is added to the same face of the pi bond, partial hydrogenation of an alkyne using a poisoned or deactivated catalyst will produce a cis alkene. Or, if we end up with a situation where you have to call it E or Z instead, it would still be that the two hydrogens would add to the same face of that pi bond.

Wouldn't it be nice, though, if we also had a way to make a trans double bond? It turns out there is a way to do so. It involves a redox reaction, because it involves sodium metal and ammonia liquid. As a side note, sodium amide, which is $NaNH_2$, that's an extremely basic compound. The nitrogen itself, when it's neutral, tends to be a little bit basic; in this case, because we've actually taken a hydrogen off it, that makes it even more basic. That compound, however, is not the same thing as sodium comma ammonia; comma just means you're listing another reagent. Ammonia itself, in fact, is cooled down to be liquified, and then the sodium is just dissolved in it. [blue color?] In ammonia, sodium will lose electrons, so that's acting as a reducing agent.

The first step of the mechanism is the following: one electron from sodium is going to add into the triple bond – more specifically, it's going to add into the antibond of one of the pi bonds of that triple bond. Sodium metal is a reducing agent and acts as a source of electrons. In the first step of this reduction, the electron is added in to the antibond of one of the pi bonds. What you end up forming is going to be negatively charged, therefore, but also have a radical, because we started with an even number of electrons, we've added just one into the system, so it's going to be something called a radical anion. This anion is extremely basic, because we have a negative charge on an sp2-hybridized orbital, which alkanes are less acidic that alkenes are less acidic than alkynes, because in an alkyne once you lose that hydrogen, the lone pair that's there will be in an sp-hybiridized orbital versus sp2 versus sp3. The more s character you have, the more favorable it is for that negative charge. We do have just an sp2-hybridized orbital here, so it's not the most favorable. And, ammonia, even though it is not an acid by any means – ammonia itself is a base – it will be attacked by this ion because it's basic enough.

Let me bring your attention to this radical. Technically, what is the hybridization of the carbon at this point? How many sigma bonds are at that double bond position where the radical is? Only two, because you already have double bond, so that's one pi bond, one sigma bond. You had a carbon-carbon bond; that's the second sigma bond. We have a radical there, which means we have a hydrogen missing, so there's no other bond there. Remember that single electrons do no count towards either VSEPR theory or hybridization because they don't have the repulsive force of a pair of electrons. And, since we only have two sigma bonds, there's only two pairs that are going to repel each other, so what geometry does that produce? Linear. I've kinda drawn it misleadingly, drawing it with a bend to it, but it doesn't truly exist yet, because we only have sp-hybridization. I'm point that out because that's the key feature of the next step of this mechanism: because we have a radical, but because we have a source of electrons in solution due to that sodium, another electron gets added into the system – this time not into an antibond, though, to pair up with the radical that we just made.

Now, once you've added that extra electron in, what's going to happen to the hybridization at that position? What's it going to become? Sp2, because we now have a third pair of electrons that's going to be doing repelling. Now that methyl group I have there has to more one way or the other; it can't stay linear. Which way is it going to want to move: to be cis, on the same face as the ethyl group; or does it want to be trans, opposite. Which one thermodynamically would be preferred? Trans. That is exactly what happens. That is why we end up with a trans alkene in this process. When it gains that electron, it's now again basic, and so, one more time, ammonia will be attacked by it.

So, three types of hydrogenation: plain hydrogenation, where we use exactly the same catalyst as we would for alkenes; the altered hydrogenation, where we use Lindlar's catalyst.

[why doesn't an alkene undergo the radical process?] Once you add that electron in, if you think about a pi bond, you've got one orbital that can have two electrons, that's the bonding orbital; you have another orbital that's normally empty, that's where the electrons are going into. If you put that electron in there, you basically have a bond order of 1/2, which is not tenable, so what ends up happening is that bond splits. You have three electrons that are trying to be stuffed into this bond; when it does collapse, two of the electrons end up on one atom, one of the electrons ends up on the other. The two that end up on one atom, that instantly makes it basic, so you rapidly get a neutralization reaction. You still have the extra electron left, so that molecule gets reduced by sodium again, cause there's still more electrons floating around in solution. That makes an anion that again gets neutralized. The stereochemistry is controlled by that last step, where you make the last anion, because it would rather be trans than cis.

Let me show you why this set of reactions, these different hydrogenations, can be really useful. We're going to see our first true example of a carbon-carbon bond-forming reaction. [sodium cyanide a sneaky way of introducing a carbon-carbon bond] Let's say that we have a terminal alkyne – terminal meaning that the last carbon of the chain is one of the carbons of that triple, which is going to mean there's exactly one hydrogen at the end of the molecule. If we take a strong base – sodium amide, NaNH2, [is] one of the most common ones used as an example – you could deprotonate a terminal alkyne and make what is called an acetylide ion – a negatively-charged triple bond. There are relatively easy to produce, because compared to just plain hydrocarbons, alkynes are relatively acidic. The reason that these can be useful is although they are very, very basic, they are small and compact enough that you could do Sn2 substitution, as long as you're using a primary substrate. If we had some other molecule with a leaving group on it, [the] triple bond would be able to attack, and we make a new carbon-carbon bond.

Note how I've drawn the product here: one common mistake would be to take the carbon where the leaving group was and start from there to draw the triple bond – but that means that you would end up with five carbons in your product's structure if you drew it that way, cause you'd miss the bond that is formed between where the leaving group was and the triple bond, which is exactly the bond that this green arrow is pointing to. Count carbons carefully whenever you're using alkynes. This process is called alkylation – adding an alkyl group. Alkylation is possible using primary substrates. If you tried to use a secondary, you'd just get elimination, cause the acetylide ions are very basic. If you did it with a tertiary, the only thing possible is elimination, so it'd be a useless reaction.

You start out with stilbene dibromide; that's the short name for this compound. You've taken an alkene and reacting it with Br2 in the absence of light; remember that if you have Br2 and light, that's going to be free radical halogenation. Bromine without light, then that's elecrophilic addition. We started with an alkene, made this dibromide. What you could react this with is that same sodium amide that I just mentioned a moment ago, but use two equivalents, because we have a hydrogen and a bromine that are, currently, antiperiplanar to each other. Even if they weren't, since the single bond does rotate, they could come into being antiperiplanar from each other. But what would happen if we had just the first elimination occur? What I'm putting in the dotted lines here does not exist as an isolatable intermediate, cause the reaction just continues. What you end up with first, are one pair of hydrogen and bromine get eliminated, would be an alkene – that still has a hydrogen and bromine, which if they're in the trans configuration as they are in this example – why, because trans would be far more favorable in terms of thermodynamics. If they're trans, there's still going to be an antiperiplanar relationship between the two. What you can get is yet another elimination. This is still an E2 elimination, but now what it produces is an alkyne.

There's this general set of steps that can be used: if you start with an alkene, you can react it with bromine without light to make a vicinal dibromide. That dibromide, you can react with a strong base, do a double elimination, and end up with an alkyne.

Chlorine and bromine both can do that double addition, so could use chlorine to get this elimination to occur as well. Bromine eliminates a little bit more cleanly, so if you can use bromine, it's a little bit better in this specific case.

Hydroboration of alkenes

Let's again work with a terminal alkyne of some sorts. Let's say that we used borane and THF, and let's imagine that only one addition to the borane happens, cause as we learned, each hydrogen on the borane can react. After just one step, we would end up with what? What would be the geometry of addition of borane to a triple bond: is it a syn addition, or is it an anti addition? Syn; why? That four-centered transition state – it's physically impossible for you to have a square where one bond is pointing one way and one bond is pointing the other. The hydrogen and the boron add to the same face as the triple bond. The whole point of saying that is you're going to end up with a cis configuration on the [double] bond because of that. After one addition, hydrogen goes to the less-substituted position – same reasoning as before. We'll have one hydrogen that starts out there already. Notice it's not necessarily the cis product that you're going to end up with, because the hydrogen was already there, the R group was already there, and they're both pushed away at the same time.

That means the hydrogen's gonna end up itself being cis with the alkyl group that's there, but we can't help it. Thermodynamically, it might want to be the other way around, but it's not possible in this reaction.

Here's a problem with this hydroboration: there's two other hydrogens on the boron that can react, but can't the alkene itself react with yet another molecule of borane? The answer's yes. What you could end up with is an absolute mess of all these different borons and carbons all networked to each other. In order to do hydroboration, we have to use a slightly different reagent. The alkene can react with a separate molecule of borane. Additionally, the hydrogen's on the boron already added would continue to react with other alkenes and alkynes. The result would be a messy network of carbon and boron bonds.

But, we could still do this reaction if we use a different reagent. The solution to the problem: use a hindered borane derivative. [name] Notice the unusual way that I'm writing it; it makes it a little bit easier to remember – it kinda looks like the letter pi, where one end of it I've attached to boron. Notice that part of that structure's in parentheses. What that means is there's two bonds to boron, each one of which has this substituted alkyl group. There is also one hydrogen that's present on the boron. What this causes is two things: first, only one hydrogen per boron is going to react, so once we make that first intermediate that has the alkene, the only thing that could continue to react is nothing, because with all of these alkyl groups there, it prevents having yet another borane adding into the same molecule. So, there's only one reactive hydrogen per molecule, and, sterically, it prevents any other reactions occurring anyway. This is the modified reagent.

I'll just show a mechanistic step once for this. Boron attacks; hydrogen attacks backwards. Remember that this is the origin of that four-centered transition state – the fact that both of these things simultaneously. Let me point out the two notes here: there's no more hydrogens to react on the boron, and there's too much steric hindrance for further reaction. Overall, here's what would occur: take an alkyne, react it with this modified borane reagent. You'll end up producing, after oxidation of that boron, this product, which is called an enol. It's called an enol because it has an alkene and an alcohol together on the same molecule. The term enol could be used generally to describe any molecule that has both an alcohol and an alkene, but there's something particularly special that occurs if you have the alcohol on the same position as an alkene, if you had the alcohol vinyl to the alkene [vinyl enols], because thermodynamically these molecules can't exist.

This process I'm about to show you is called tautomerization. Before showing you the mechanism, let me show you the transformation that's going to occur. Notice the arrow that I've used between the two here – a reversible reaction arrow. These two structure are not resonance structures, although they kinda have that feel to it; in fact, the intermediate is going to involve resonance. This is formally a reaction. Notice what's going on – we are losing a carbon-carbon double bond, but gaining a carbon-oxygen double bond. Notice also that we're losing the oxygen-hydrogen single bond, but ending up with a new carbon-hydrogen single bond. If you calculate the energy differences of those four things – how much energy it would take to get rid of the carbon-carbon double bond, how much energy is released when you make the carbonyl, how much energy would be needed to pull the hydrogen off of oxygen, how much energy do you get back when you put it on the carbon – to go from the left to the right is, overall, an exothermic reaction – exothermic enough that it happens very rapidly in solution, whether you have base or acid. Let me highlight what's lost and what's gained.

Tautomerization is not resonance. It involves the loss of two bonds and formation of two bonds. Overall, the process is exothermic for forming the carbonyl. This specific type of tautomerization – cause there's not only one, but this is one of the most common ones – this is called the keto-enol tautomerization. Let me show you the mechanism that would be applicable in this case, because we have basic conditions that are being used. In the basic version, hydroxide reactions to pull off a hydrogen from the -OH group. This happens for two reasons: one, alcohols in general are roughly the same acidity as water, so in reverse that means hydroxide is roughly the same basicity as other alkoxides. On top of that, once we pull the hydrogen off, there's resonance that's possible, so pull that hydrogen off, we end up with an alkoxide that can undergo resonance. It's exactly at that point where we're leaning towards changing the types of bonds that are present, because resonance structures aren't real structures, they're different aspects of representing a real structure. It's not truly correct to say that the bonds are forming and breaking at this point, but the process completes [with] hydrogen being attacked. When the oxygen does form it's double bond, it pushes the carbon-carbon double bond open, forming a carbanion, which normally not favorable but can happen because there is resonance. What will happen now is that water – not H+ – get's attacked.

You know you want to add H+ on, so you could understandably put H+ there – except that we're in [a solution with sodium hydroxide] right now, so there's no way an H+ could exist in solution all on it's own. We can show water, however – the conjugate of sodium hydroxide – being involved; that's what I've done here. What this means, though, overall, is that if you have a terminal alkyne, if you react it first with this hindered borane, followed by sodium hydroxide and hydrogen peroxide, you're going to end up with an aldehyde. If, instead, you have an internal alkyne, and you react it with the same set of reagents, then you'll form a ketone. Which R group will the ketone be closer to? Sometimes that can't actually be controlled, so it work best if you have a symmetric alkyne.

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Since hydrogen is added to the same face of the pi bond, partial hydrogenation of an alkyne using a "poisoned" (deactivated) catalyst will produce a cis alkene.

NaNH2 ≠ Na, NH3

Sodium metal is a reducing agent and acts as a source of electrons. In the first step of the mechanism, an electron is added to the antibond of one of the pi bonds.
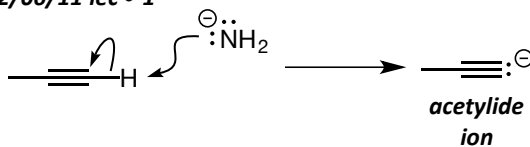
Alkylation (adding an alkyl group) is possible using 1° substrates (2° undergoes E2)

The alkene can react with a separate molecule of borane; additionally, the hydrogen on the boron already added would continue to react with other alkenes & alkynes. The result would be a messy network of carbon & boron bonds. Solution: use a hindered borane derivative.
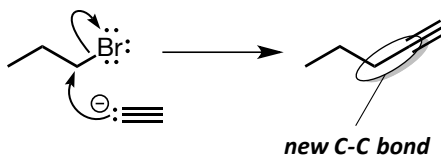
Tautomerization is not resonance. It involves the loss of two bonds (C=C, O-H) and the formation of two bonds (C-H, C=O). Overall, the process is exothermic for forming the C=O.
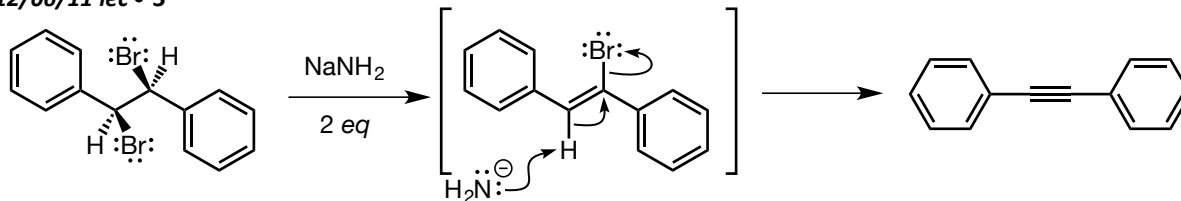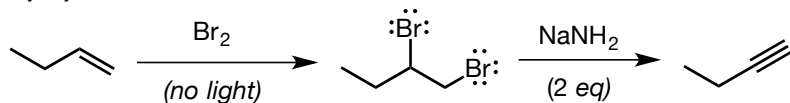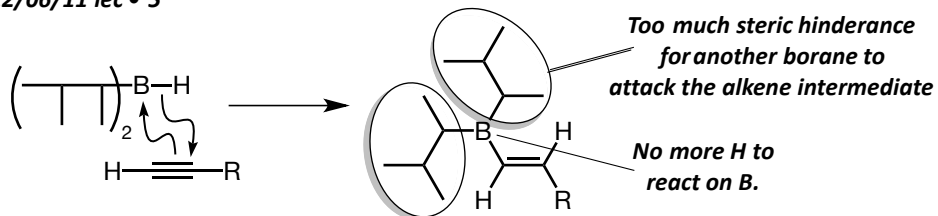
Structures

12/06/11 lec • 1

acetylide
ion

12/06/11 lec • 2

new C-C bond

12/06/11 lec • 3

NaNH₂

2 eq

12/06/11 lec • 4

Br₂

(no light)

NaNH₂

(2 eq)

12/06/11 lec • 5

*Too much steric hinderance
for another borane to
attack the alkene intermediate*

*No more H to
react on B.*

12/06/11 lec • 6