Lecture 19A • 03/12/12

Activators versus deactivators

Let's look at a generalized electrophilic addition. Let's do two reactions in parallel. Let's take plain old benzene. [For nitration,] we have nitric and sulfuric acids. Sulfuric acid protonates the nitric acid, ends up making that really reactive NO2+, which the benzene then attacks, then we reform the aromatic ring. Let's do the same reaction with phenol. Technically, we would get two products out. You do not have to worry, at this level of o-chem, about predicting how much ortho versus para that you're going to get. You need to know that this is an ortho/para-director, but you don't have to predict percentage of the mixture that you're going to end up with. On a synthesis problem, you can just ignore the fact that you get two different products. I'll arbitrarily choose the para one in this case.

Let me go back and expand to write a mechanism; I'm going to ignore the formation of NO2+. When [attack occurs], you must show one of the double bond going to nitrogen opening up, cause nitrogen can only have four bonds to it. Where the nucleophile ends up, that's where the hydrogen is that's going to get eliminated; it's the other position that ends up with the + charge. Something comes along – I'll call it B for a generalized base – removes that hydrogen, and we end up forming the benzene ring. From the perspective of benzene, this is a two-step reaction. Yes, there's the steps before it, where we make the NO2 species, but if we ignore that, if we look only at benzene, let's see if we can look at a reaction coordinate diagram for that reaction.

I'll call the first one with benzene reaction A, and i'll call the second one with phenol reaction B. Reaction A, we have this kind of reaction coordinate diagram. The reaction, let's presume, is exothermic. There is going to be one intermediate to this reaction. The intermediate should be at much higher energy, because we're breaking the aromaticity of the benzene ring; that's the whole reason why benzene's not reactive in most alkene reactions, anyways. In fact, that's the whole point of that hydrogenation discussion that we had, where we looked at a single double bond, versus what would happen, in theory, if we had two double bonds versus three, and we saw that in benzene, it was so much more stable, compared to the three double bonds, and we said that's because of aromaticity. All that stability, you'd have to add all of that energy in in order to break apart the benzene ring. The intermediate's going to be at a much higher energy.

Let's draw in parallel just a portion of the reaction coordinate diagram for reaction B. I'm going to place phenol arbitrarily at the same energy as benzene is. They are not [likely] at the same energy, though, because they are not isomers. If you wanted to be technical about it, we could look at heats of formation and figure out, on a more absolute scale, where, energetically, the two compounds would lie. What would the effect of the phenol lone pair be on getting to that intermediate? Breaking benzene apart, that's rate-limiting step of the reaction. [RLS – rate-limiting step] Why is it the rate-limiting step? Cause it's got the largest activation barrier. For benzene to be reformed, that's trivial; it wants to be formed, that's not a tough transition state to get to; to break benzene open, that's a huge barrier. What about phenol? It's got this lone pair that's adding electron density to the benzene ring. The whole difficulty of the reaction is to break open the benzene ring, but if you're providing it electron density, that's exactly the electron density it needs to go out and attack that electrophile to start the process. Another way of saying it, is: once you did have that attack occur and you did end up with a positive charge, anything that could delocalize the positive charge is going to make it energetically more favorable. Energetically more favorable means that, by comparison, if we look at the magnitude of te activation energies that we're going to end up with, we're going to have a relatively smaller activation energy. Due to electron density being donated by the substituent on phenol, the activation energy to reach the intermediate – EaB – is lower than in the similar reaction with unsubstituted benzene (EaE). Since the electron density from phenol is stabilizing the carbocation and making the attack on the electrophile easier. If you looked at the Arrhenius expression, you would say that the lower activation energy ends up causing a higher rate, and so that's how we end up calling thing like phenol activators; it's an activator because it speeds up the rate of the reaction.

Is an ortho/para director always an activator. Oxygen, it has this lone pair, it delocalizes; that's what's stabilizing this compound. But isn't oxygen the second more-electronegative element on the periodic table? In so many other situations, we talk about oxygen being an electron withdrawing group (if we were in NMR right now, we'd be talking about how it would cause large chemical shift. If we were talking about pKa values, we would say heteroatoms like oxygen make hydrogen dissociation easier because we're pulling electron density away from the hydrogen. Those are just two examples, but if we had those two examples of oxygen acting as electron withdrawer, then how come it's an activator here? The answer is: it gives more than it takes. Oxygen has good orbital overlap with carbon, so the resonance that oxygen undergoes provides a good amount of electron density. It really does activate the reaction. Yes, it's electronegative, it is pulling some electron density away, but it donates more than it withdraws, so, overal, oxygen-type groups like this are activators. Even though oxygen is electronegative and will withdraw electron density by induction, it also has good orbital overlap with carbon, and it provides more electron density through delocalization than it withdraws by induction.

If we have a p orbital on oxygen, a p orbital on carbon [on sp3 on each], if we imagine that that's how the delocalization's occurring, the size of those p orbitals is enough the same that they get as much overlap as they could, a similar amount of overlap as you would have in a carbon-carbon double bond. Carbon-carbon, they're exactly the same atoms, so their orbitals are going to overlap the best. The halogens, if you have something like bromine, much bigger atom, orbitals are much bigger shapes on bromine, and so, percentage-wise, as far as how much it overlaps with the carbon's orbitals, there's a missmatch there in size. The overlap occurs, you still have delocalization, but it's not as favorable, because there's not as much chance for those atoms to inter.

Imagine that we had another graph where we had an electron withdrawing group. Ignoring whether ortho, meta, or para's going to form, pulling electron density off of this ring is going to increase the activation energy. If you're increasing activation energy, it's going to slow the reaction down. There's two different effect: delocalization places more electron density at certain places on the molecule; that's why ortho/para versus meta substitution occurs. Separately, as far as the rate of reaction, more electron density is being pulled away than provided. It's being provided, though in specific places. The specific places, that explains the substitution pattern, the regiochemistry. The fact that it, overall, is pulling electron density away, that's why it slows the reaction down, and halogens are known as deactivating ortho-para directors.

Here's a carbon-oxygen versus carbon-chlorine double bond. Chlorine double bonds? Does it want to form chlorine double bonds? Remember, this is in a resonance structure. Let's say that we have some electrophilic reaction that had occurred, and we had a chlorine on there initially. One resonance structure that's possible shows delocalization using chlorine, but it would make a double bond directly out of the chlorine. We would have the same thing with oxygen present [only drawing one set of resonance structures]. Chlorine – larger atom, larger orbitals. We can see that that causes a less-favorable orbital overlap with carbon. Yeah, carbon's small, but therefore it's orbital doesn't fully overlap with chlorine. The percentage of overlap is related to bond strength and the ability to delocalize, so there's a poor overlap, due to mismatch in orbital size. For carbon and oxygen, they're more similar, so better overlap because they're similar in size.

Let me go back and tell the story about chlorine again. Halogens are ortho/para directors, but are deactivators. Resonance involving the halogen, [which] puts more electron density at the ortho and para positions. Let's say we had something like chlorobenzene. Even before reaction, realize, on paper at least, we could write this resonance structure. It's a horrible resonance structure; we took a compound that was neutral and we created a split ion out of it. But, notice that that negative charges is going to be at the ortho position, and if I wrote one more resonance structure, I could show it skips over the meta position and ends up at para instead. This is why, regardless of their activating and deactivating capability, halogens are always ortho/para directors. Resonance involving a halogen will always put more electron density at the ortho/para positions, regardless of the overall activating or deactivating effect of the halogen. If we have chlorine, bromine, or iodine, these atoms are large, so they have poor orbital overlap. They're not as electronegative as fluorine, but they're more electronegative, they withdraw more electron density, due to induction than they do provide back through resonance. Since halogens – chlorine, bromine, and iodine – are larger than carbon, they have poorer orbital overlap, so they don't provide as much electron density as they withdraw due to induction, so they are deactivators. In the case of fluorine, it's only a slightly different than the size of carbon. It is similar enough in size to carbon that it has good overlap – but, it's the most electronegative element on the periodic table, so it again withdraws more than it donates. We have three classifications of substituents: we have ortho/para directors and meta directors versus activators and deactivators.

Ortho/para directors. What are some good ortho/para directors? Phenol; aniline; anisole. Alcohols, amines, ethers. Halogens – they are ortho/para directors, but they are deactivators. They are the only functional group that you're going to learn that is a deactivator. Let's go back to the activating ortho/paras. Styrene, alkenes; thiols. Toluene – you're not going to have delocalization or conjugation, but what could you have? Hyperconjugation. That hyperconjugation is enough of an effect that it does make an alkyl group an activator. [Toluene] is an ortho/para director and an activator due to hyperconjugation. Let's go over to the other column – deactivators that are meta directors. Nitro. What are some other functional groups that withdraw electron density? Carbonyls. So, benzaldehyde or other aldehydes. Or, we could have acetophenone or other ketones. There's all sorts of functional groups with carbonyls in them; for example, methyl benzoate, an ester. Why are these electrons withdrawing groups? Because the carbonyl carbon is very delta +; that's going to do exactly the same thing as the nitro would do. Even though it's not a real positive, it would put a delta positive next to the ring, where that position right next to the ring wouldn't want to form a positive charge. Would all esters be meta directors? Would they all be deactivators? No. Why not? It depends on [the position of the carbonyl]. What if we did this? That's an ester, but now the oxygen is next to the benzene ring. The carbonyl will pull electron density away; this is not as good an activator as having an ether or an alcohol. But because you do have that lone pair there, it is able to able to delocalize, it is an ortho/para director. [reverse ester, phenolic ester] Can we think of any other electron-withdrawing groups? Sulfonate. As long as it's the sulfur connected to the benzene ring, then it's a deactivator. Nitrile.

We have ortho/para directors. [mechanism] What's the difference between something being an ortho/para director and it being an activator or deactivator. Resonance has to do with what's happening with the lone pairs, regardless of whether overall the lone pair's being given or taken. Resonance, you're still going to cause electron density at certain places; as a separate issue, some things donate electron density, some things withdraw electron density.

Those that donate are activators, those that withdraw are deactivators. Normally, since providing electrons through resonances is giving electron density, ortho/para directors are normally activators. Since functional groups that would deactivate the ring do so by withdrawing electron density, which also usually means the functional group's got a real positive or a delta positive right where the benzene ring connects, that will also cause it to be a meta director. But then there's the halogens that are in this in-between space. They give electron density through resonance, so they're ortho/para directors, but they induct more electron density than they give, so they're deactivators. [example of ortho/para activating and deactivating directors, and meta directors]

Frontier orbital chemistry – pericyclic reactions

Here's the story we're going to discuss. Is the starting material that I drew aromatic? No. Obviously not, because it's not cyclic. You might have been tempted to wonder, just because it does have the right number of double bonds, but because it's not a ring, it's not aromatic. But, you can imagine that, even though it doesn't have that bridge making it the ring, one p orbital on one side of that gap may still want to interact with another p orbital on the other side of the gap. In fact, that ends up being the case – this reaction undergoes a mechanism where we could write it like this: one of the double bonds from one side attacks the double bond on the other side, which pushes that double bond over, which pushes that double bond over. Notice that this is a cyclic mechanism. But it's not a true ring that it's happening in, so that's why it's called a pericyclic reaction. The end product is a diene. I've done this reaction twice. In one case, we're going to discuss if just heat is use to cause the reaction to occur, versus if light causes the reaction occurs. Why do we need to talk about these at two different reaction conditions? Because one of the products is optically active, and one of them is not. Which one is which? The left one is not active – it's meso. The other one's optically active.

Why is there this difference in reactivity? We are going to get into a discussion of ground versus excited states. What [are] the three filling rules for electrons in orbitals? Lowest energy up – that's the Aufbau principle. No two electrons can have the same four quantum numbers[, or,] if you have two electrons in an orbital, that's possible, but only if they have opposite spin – that's the Pauli exclusion principle. What's the third one? Hund's rule, which says that, if you have a bunch of degenerate orbitals – which means they're all the same energy – that one electron goes into each before you pair the electrons up, so you maximize spin. That's all true, only in one situation – the one we call the ground state. Implicit in that is the ground electronic state, which is the lowest-energy electron configuration. Imagine that I have some system that has four molecular orbitals to it. It could be something like the butadiene system. We want to show that electrons are filled according to the normal rules – I put them in the lowest energy orbitals first. There are no degenerate orbitals, so I don't worry about Hund's rule; and I pair electrons, but only I had put one electron in.

What if I hit it with a photon? One electron can absorb that photon and jump up to a higher energy level. If you have the right energy, there's multiple levels that electron, in theory, can be bumped up to, if there were multiple levels available – which there are in this case. If I go up to the very next level, just to the next one, then this is what we call the first excited state. Let's imagine that only one photon of the right amount of energy was absorbed. That first excited state is the next-lowest energy. Why do we care about whether a molecule's going to be in the ground or excited electronic states? That's the difference between something being done with heat versus light. If you kept the reaction in the dark, then the electrons are going to be in one configuration. If you expose them to UV light, it's likely that – at the moment a reaction occurs, or the way that enough energy's given so the reaction occurs – will be in this electronic state. The shape of the orbital is going to be different, depending on where the electrons are going to be [– more correctly,] the most energetic electrons, the ones that act like valence electrons. Whatever orbital they're in, that's going to shape how the reaction occurs.

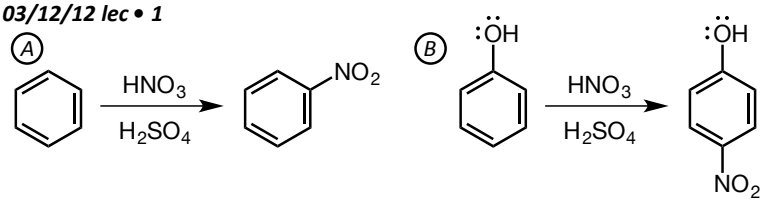
_____

Due to the electron density being donated by the –OH on phenol, the activation energy to reach the intermediate (EaB) is lower than in the similar rxn with unsubstituted benzene (EaA), since the electron density from phenol is helping to delocalize the carbocation formed & make the attack on the electrophile easier.
Lower Ea –> higher rate –> activator
– Even though oxygen is electronegative and will withdraw e- density by induction, it also has good orbital overlap with carbon, and it provides more e- density through delocalization than it withdraws by induction.
Halogens are o,p-directors but are deactivators
Resonance involving the halogen will always put more electron density @ the ortho & para positions, regardless of the overall activating or deactivating effect of the halogen.
Cl, Br, I –> Since these halogens are larger than carbon, they have poorer orbital overlap, so they do not provide as much e- density through resonance as they withdraw by inductions, so they are deactivators.
F –> Fluorine is similar in size to carbon so it has good orbital overlap, but it is the most electronegative element, so it withdraws more e- density than it donates, so it is a deactivator.

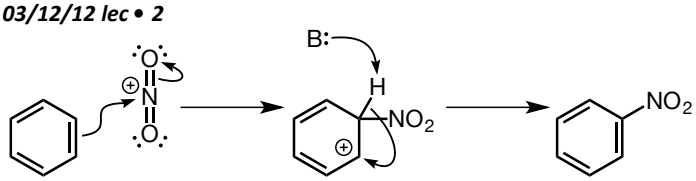
Frontier orbital theory –> pericylic rxn
_____

Structures *(remaining structures identical to lecture 21B)*

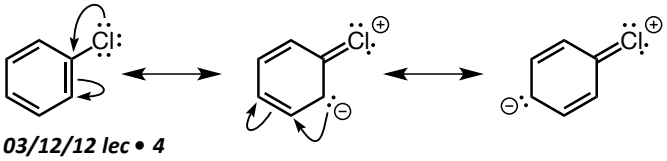
03/12/12 lec • 1



03/12/12 lec • 2



03/12/12 lec • 3



03/12/12 lec • 4