

Lecture 20A • 03/14/12

[Exam 3 – aromaticity and conjugation: activators and deactivators, ortho/para versus meta, aromatic/non-aromatic/anti-aromatic, MO theory]

[EAS – nitration, alkylation, acylation, sulfonation, halogenation]

Separate from resonance, there's whether the activation energy increases or decreases, based on the functional. For most of the ortho para directors, because they have lone pairs that can delocalize, they lower the activation energy of the reaction, and because they're doing that by having a lone pair, that's why they're also ortho/para directions. Halogens are the exception where, because of resonance, yet they prefer to substitute ortho/para, but they withdraw more by electronegativity than they donate, so that's why they're deactivators. Then, we have meta directors that, because it's an unfavorable charge combination and cause it's pulling electron density off of the ring, it's a meta director and slows the reaction down.

Reactivity of carbonyls. A carbonyl, we can react in two different ways. We can push electron density onto a carbonyl. Imagine that we're attacking it with a Grignard reagent, for example. That forces the carbonyl open, and that forces a negative charge onto oxygen. The other way a carbonyl could react is something like making an acetal, where first you start with an acid catalyst, which means you're trying to trick electron density coming off of the oxygen to then make the carbonyl more likely to be attacked. In one case, you're pushing electron density on; the other case, you're pulling electron density off. In that carbonyl example, when you're pushing it on, they're concerted reaction; when you're trying to tease it, it's a stepwise reaction. In other words, whether we're doing cationic or anionic, you get reverse patterns of behavior.

Take the idea of what we have with a benzene reaction, and the idea that if you flip from talking about cations to anions the behavior reverses, then let's see if we can explain the following behavior. [graduate students operate by food] Chlorobenzene with sodium methoxide – no reaction. Why does S_N2 not occur in this case? Steric hinderance – of what sort? You'd actually have to pass through the benzene ring; remember in S_N2 reactions, the nucleophile has to attack from exactly the opposite position of where the leaving group is. In this case, since the whole molecule's planar, that means that the leaving group would have to come through the benzene ring to attack chlorine, which, of course, it can't do; that's why S_N2 can't occur; that's one of the reasons. There's also another reason, which is that vinyl halides don't tend to do S_N2 reactions because the pi electron cloud repels the nucleophile.

Why does S_N1 not occur. If we took chlorine off and made a carbocation, would that carbocation be aromatic? Is the pi system actually affected by making a carbocation in this case? Is the chlorine part of the pi system? Then why would chlorine reacting affect the pi system? The pi system is this way; chlorine is sticking out perpendicular. If you make a new carbocation that would have an orbital left over that, therefore, would also be perpendicular, it doesn't affect the pi system. So yes, it's aromatic, but it's incredibly unfavorable. Why? Why is an alkyne more acidic than an alkene? Hybridization. sp , once it looks its hydrogen, that lone pair goes into a lower-energy orbital because it's sp instead of sp^2 or sp^3 . If a negative charge is favorable in an sp orbital, that means a positive charge is less favorable. An sp^2 carbocation is more favorable than an $[sp]$ than an $[s]$, cause the positive charge is more exposed, less stabilized, in an sp orbital. Besides that, what would the hybridization be at this position? sp . It should be linear: can you have a linear geometry in a six-membered ring? No, so due to geometry – the fact that it would want to be linear – and due to poor stabilization of the positive charge due to the hybridization of the orbital it ends up in, S_N1 won't happen.

How does that explain the fact that, if you put a nitro group either para or ortho to the chlorine, then when you react it sodium methoxide, you do get substitution? It can't be that we changed sterics in any way, cause we've now put a substituent even more in the way of the nucleophile. It doesn't change the fact that we have a pi cloud or a poor positive charge that'll form or the fact it wouldn't be linear if you made a positive charge, so what's change? In electrophilic aromatic substitution, we need electron density on the benzene ring to attack an electrophile. Now, the ring is being attacked by a nucleophile, and a ring is more attractive to a nucleophile if electron density is being pulled away from it. The nitro group, pulling electron density away, makes it more attractive to a nucleophile. But beyond that, it also can delocalize a negative charge. When you have a nitro group, it causes addition at the meta position if we're using an electrophile, because it avoids bad charge interaction. But look at what happens in this case by it being in the para position. First, methoxide attacks; it does not kick the chlorine off at first, the reaction's not possible. The reaction occurs from the front side. That'll push a double bond open, which we could show pushing another double bond open, on to the nitrogen. Nitrogen can only have four bonds. This is technically a reversible reaction, although once this intermediate forms, even though it can reverse, there's something more preferable that will occur. It is a bimolecular reaction, but it's not S_N2 . This is known as nucleophilic aromatic substitution.

Once you form this complex, it'll decompose again. Oxygen can attack the nitrogen, pushing the double bond back around the ring.. Once it gets to the position where the chlorine is, chlorine's a far better leaving group than methoxide, so the chlorine will be the one that comes off. That's not reversible, chlorine's not a base. We end up with the substituted compound. In the ortho and para positions, this set of resonance structures is possible; in the meta position, it's not. Let's see that to show the parallel but the reversal of roles that's going on.

In electrophilic substitutions, when you already had one substituent – one of the big differences in this reaction is I have two substituents that I'm playing with. In this [electrophilic substitutions], you only have one substituent that guiding where the next one will go. This is a case of one substituent changing the reactivity of the other one. In electrophilic reactions, nitro groups are electron withdrawers that [were] bad for the reaction, and it caused addition at the meta position. Here, having it in the para position is favorable, now, because we're having a nucleophile attack, so it's better if we can pull electrons off the benzene ring. The meta position is where the nitro causes electrophiles to go; the meta position is what fails to pull electron density off from the ring in this case. Everything is opposite. Why? Cause it's a nucleophilic versus an electrophilic reaction. [reference back to dual reactivity of carbonyl] We'll never be able to delocalize onto the NO₂. [will rxn with meta substituted compound occur at all?]

Pericyclic reactions

Here's one of the two situations that we have. We have this compound ... what is the name of that compound? Can we use cis or trans in naming this molecule? No, because we have more than one double bond that must use a term, and when you have to use more than one, you can't use cis and trans. (2E, 4Z, 6E)-octa-2,4,6-triene. This molecule, when heated, forms cyclohexadiene, and it forms a meso molecule, where the two methyl groups end up being cis relative to each other, which is what causes the molecule to be meso. Why is it that, under heat, why does this particular compound cyclize in this way? When you don't have light, electrons tend to be in the lowest-energy levels possible. When you do have light, an electron can absorb energy and move up to a higher energy level. What energy levels would even be involved in this reaction? These double bonds – it's not aromatic, cause it's not fully cyclic. But imagine that the two carbons on the right, the ones here and here, imagine that the p orbitals there were to somehow turn towards each other. A sigma bond is just when you have head-to-head overlap, not necessarily between any two specific types of orbitals. If you had these p orbitals that, for whatever reason, started to turn towards each other, if those p orbitals now were to be head-to-head with each other, that would turn into a sigma bond. Of course, for those p orbitals to turn, they'd have to break the bonds they're already part of. That, in turn, would mean they could interact with the p orbitals that are next to them. That's exactly what happens; this is a pericyclic reaction. If it's the pi system involved with this reaction, then maybe it's the pi system's orbitals that we need to look at.

There are six carbons, so six p orbitals that would be involved, so there are six molecular orbitals. Since it's linear, we're going to have 0, 1, 2, 3, 4, then 5 nodes. Bottom case is easy – no nodes, we shade all of the p orbitals the same way. One level up, one node. Two levels up, two nodes. These three are bonding orbitals. Why? When we look at the number of favorable and unfavorable interactions between p orbitals, more favorable than unfavorable below here. The bottom one, it's all favorable overlaps. This middle one, there's [four favorable] and one unfavorable. Above this, we have enough nodes that the number of nodes automatically outnumbers the number of favorable interactions that we have. Three nodes, four nodes, and five nodes – every other one opposite.

Notice this pattern: when we have an even number of p orbitals, the maximum number of nodes is odd. That means you'll always end up in this situation, where half of the orbitals generated are bonding, and then half of them are antibonding. If you have an odd number of p orbitals, then you end up in a situation where you have an even number of nodes, which means you can end up with an even number of favorable and unfavorable interactions, which means you generate a non-bonding orbital. For even numbers of p orbitals, always half are bonding and half are antibonding for the molecular orbitals that are made, and for odd-number systems, one orbital would be non-bonding, half the rest bonding, then the rest of those antibonding. For cyclic systems, there's a pattern as well. If you have $4n$ orbitals – something like cyclobutadiene – then you're going to have two orbitals non-bonding, half the rest bonding, and then the remaining antibonding. If you have $4n + 1$ – like cyclopentadiene – then you're going to have one more bonding than antibonding orbital. If you have $4n + 2$, then you'll have half bonding and antibonding, like benzene. And if you have $4n + 3$ – like the cycloheptatriene case – then you're going to have one more antibonding orbital than bonding.

What do we do with this mess? There's electrons in here.

Yes, the molecule's partially cyclic; it's curved cyclicly. But, the p orbitals themselves are still in a line; that's why we're using these linear diagrams to describe it.

Back to here, six orbitals that need electrons. How many electrons are we going to put in? Six, cause we have three double bonds. This is what is known as the highest occupied molecular orbital (HOMO), but in the ground state, where everything is in its lowest possible energy levels. That means this other orbital up here is going to be the lower unoccupied molecular orbital (LUMO). What's the whole point of this HOMO-LUMO theory? It's these highest-energy electrons that are the highest-energy electrons; they're the ones likely to react. The LUMO, that's the place where it's the lowest-energy place the electrons have to go. Why are we worrying about this at all in connection with this problem? If we think this is a pericyclic reaction, where one double bond pushes the next one pushes the next one, let's say it's this highest-energy pair of electrons that begins that process. That means that it is that particular molecular orbital that matters in this reaction.

Let's take the physical structure of the molecule and put on top of it a diagram of that molecular orbital. Notice that at gate here, the p orbitals are shaded on top the same. Realize that this is just one molecular orbital that's got a complicated structure but the ends of it have the same phase. If those two ends were going to rotate to form a sigma bond, in order to do it favorably in terms of wavefunction, they would have to turn opposite ways of each other. You might be confused and say you're turning the same way, because from our human perspective this hand's going to my interior, this is going to my interior. If you look in terms of clockwise versus counterclockwise, from your perspective, one arm is going clockwise, and one arm is going counterclockwise. They're moving in opposite directions. This is called disrotatory motion – the p orbitals twist in opposite directions. That is why you end up with the two methyl groups pointed the same way, and because there's an internal plane of symmetry, this compound is meso, so it's not optically active.

Why do things change when light is involved? What would the electronic structure of the first excited state look like? You still have to put six electrons in there. Excited state means you've bumped an electron up to a higher level than the filling rules would tell you that you should do. That means that this is the LUMO for the excited state, and this same one that used to be the LUMO is the HOMO for the excited state. What does that mean? Observe which orbital it is now that would have highest energy electron. It has a different orbital symmetry. Notice the one we did previously, the two ends had shading that was the same. Now, because we're one more node up, we've flipped the shading of the two ends. That means that the reaction's going to occur with the methyl groups now turning the same way as each other. The ends of the orbitals look like they're coming together and they look like they turn opposite ways from each other, but if, from your perspective, my left elbow is one of those p lobes that's going to react, and then my right hand, when they both turn the same direction, notice how one overlaps with the other, so they are turning the same direction. That is conrotatory. That does end up making the methyl groups relatively trans to each other, which is why we get an optically active material.

It does matter whether there's the presence of light. If there's only heat, the top one happens; when there is light, only the bottom one happens. There's actually a summary of these rules called the Woodward-Hoffmann rules. [rant against memorizing them] If you take the two p orbitals that end up being the sigma bond, you have two more p orbitals left over. Since it's not a cyclic system, it's not going to be aromatic. Technically, these four overlap, but that's exactly what you have in butadiene. By these two orbital no longer interacting with the pi system, the pi system shrinks, and you end up with a four p-orbital system, which means you have two double bonds. Another way to think of it is: this used to be a double bond, so take this away, and this bumps over and makes a double bond with this. This used to be a double bond, which means it gets bumped over to be with this, and this this goes away anyways because it's becoming part of the sigma bond. The methyl groups are turning opposite ways, but the end result [of both reactions] is the same in terms of the pi system.

Let me preview the Diels-Alder reaction. This is a reaction involving only one molecule, whereas the Diels-Alder reaction is a reaction involving two molecules. We're still going to use this frontier orbital theory to explain why Diels-Alder reactions occur the way that they do.

Sn2 – Cannot occur due to steric hinderance (the nucleophile would have to pass through the ring) and repulsion of the nucleophile by the pi cloud.

Sn1 – Cannot occur due to formation of vinyl carbocation (poor stabilization of + due to hybridization) and geometric constraints (would want to be linear).

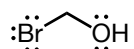
Nucleophilic Aromatic Substitution

When the nitro group is at the ortho or para positions, it is able to delocalize the - off the ring, but not in the meta position. ∴ The rxn is possible w/ the NO₂ @ ortho or para positions, but not likely or very slow @ the meta position.

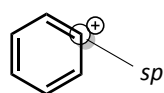
Either an electron moves from the HOMO of cyclopentadiene to the LUMO of the anhydride or an electron moves from the HOMO of the anhydride to the LUMO of the cyclopentadiene.

Structures (remaining structures identical to lecture 21B and lecture 22B)

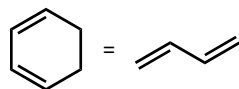
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