Lecture 18B • 03/02/12

[Previously,] we talked about the tropyliium ion. I showed you the fact that cyclohepta-1,3,5-triene has unusual behavior, in that it likes to lose H-. It was that starting molecule where I had circled the two hydrogens that were on that ring and we discussed the fact that, because the two hydrogens were there, that that particular carbon was sp3-hybridized [and] blocked full conjugation around the ring and therefore made it where it was not aromatic. We can see what happens once the hydride does come off. The starting material is not aromatic, but is the product aromatic? Yes it is, because it's cyclic, it's planar, each of those positions is sp2-hybridized, and there's nothing sterically that's going to prevent it from being planar. Because of the same fact that it's planar and it's sp2-hybridized at every position, it means that it is fully conjugated, and it has the right number of electrons. I asked you to generate a Frost circle for this to help prove that this is aromatic. That was partly so that you had a chance to grapple with another one of these odd-numbered systems, odd number of positions on the ring. How do you inscribe a heptagon? I'm sure that's not a shape that you're commonly familiar with from geometry. If you think of it this way: we did see the cyclooctatetraene case, and in that case, we had molecular orbitals that were just on that non-bonding line. If you look at benzene, that's case where you have orbitals just above and below, but not right on that non-bonding line. The seven case is somewhere right in between. What we end up with is three bonding, four anti-bonding orbitals. There has to be an uneven distribution in this case; you have an odd number of atoms. But, since we only have six pi electrons, it turns out that only those bonding molecular orbitals are filled. That's why this molecule's unusually stable.

The reason I point out that is because I want to bring up a thought problem. Is it aromatic, what I just wrote? Is is cyclic? Is it planar? Is it fully conjugated? Does it have 4n + 2 electrons? Does that mean it's aromatic? No. This would be more table than another tetra-charged molecule would be, because you do have electrons in a delocalized orbital – but not enough to keep this thing from falling apart. Putting four positive charges would not be favorable. This is an example of how not to blindly follow the 4n + 2, cause this does have two electrons – if n = 0, that means 4n + 2 = 2, which matches. But it doesn't have all of the bonding orbitals filled – that is the more complete way, the more sophisticated way to state that portion of the Hückel rules: that you only want to have the bonding orbitals filled. They're exactly filled, they're not missing electrons – missing electrons means missing a chance to stabilize the molecule. There are also no extra electrons, which is most cases would cause the molecule to be destabilize. Although this cation is delocalized and has 4n + 2 pi electrons, it is not aromatic, per se, since not all bonding orbitals are filled.

Let's return to talking about the different kinds of reactions. We [previously] saw the Friedel-Crafts acylation. Recall that, in Friedel-Crafts acylation, I had shown aluminum trichloride as a Lewis acid that can be used to induce the reaction to occur. It turns out that not just aluminum chloride works; iron tribromide and few other common compounds are also used as a Lewis acid. With an acylation, I used an acyl halide. Friedel-Crafts alkylation uses an alkyl halide. For example, we could have 1-chloropropane. The mechanism for the reaction is similar to the acylation mechanism. What should be the first step of this reaction? The Cl's going to attack the aluminum, because does aluminum have a full octect in this compound? No; that's why is such a strong electrophile. What's the next step? The carbon-chlorine bond breaks. There's some evidence that this happens. What do you think that evidence is? We just made a primary carbocation, didn't we? o primary carbocations like to exist? No. If you form a cation, and you really do form a carboncation, where you make an isolated positive charge, those positive charges, as we've seen in the past, can more around. Before it has a chance to react with benzene, a hydride shift occurs. That's the important feature about the alkylation reaction – you've got to be careful what you use as your starting material, because it might not end up being the same thing by the time the benzene ring attacks. To finish off the reaction, it's exactly the same as some of these other reactions we've seen, where the benzene ring opens up, attacks that electrophile. Where the electrophile ends up is not where the positive charge is. The next step would be for a hydrogen to be removed to reform the benzene ring. There are some variations of the Friedel-Crafts reaction.

We've had nitration, alkylation, acylation. There's two more. One is sulfonation, which is where you take a combination of sulfuric acid and sulfur trioxide. There are different ways to write the mechanism. Because we are in acidic conditions, this way makes sense to me: if we're in sulfuric acid – the only difference between sulfur trioxide and sulfuric acid is water, SO3 + H2O gives you H2SO4 – the sulfur trioxide can become protonated under those conditions, which could cause the sulfur-oxygen bond to open up under resonance, which generates our electrophile. [The next portion of the mechanism] is an identical copy of the same bit of mechanism we've seen in the last three reactions. Benzene reacts, and then a hydrogen is removed. As strange as it might seem, in this case it would have to be something like the hydrogen sulfate that would come along and deprotonate. The product is a sulfonic acid – benzenesulfonic acid. Would it be neat if we took toluene and did this reaction, cause then we could make p-toluenesulfonic acid, we could synthesize tosic acid.

The last reaction is halogenation. This particular set of reagents only works well with bromine and chlorine. [iodine?] It's very similar to the Friedel-Crafts reaction, where you start with chlorine or bromine, and you can use something like iron(III) trichloride if you were trying to do the reaction with chlorine, iron(III) tribromide if you were thrying to do the reaction with bromine. Similar, again, to the Friedel-Crafts [reaction], chlorine is going to donate into the Lewis acid, and you effectively end up with chlorine +. Chloride - is the way that chlorine wants to be; this is incredibly electron-deficient, so strong electrophile.

I want to move into another topic. We can easily explain, with a little bit of mechanism, the following two observations: if I take a molecule like phenol, and I put it under nitration conditions (sulfuric acid and nitric acid), we'll get two different products. The proportion of the products we get is unimportant at this level of o-chem. This reaction happens rapidly, and you do get almost entirely ortho- and para-nitrophenol. If we take a molecule like nitrobenzene and we react it under the same conditions, by far the only major product that forms is meta-dinitrobenzene. In the first case, we end up with ortho and para products, and the reaction's fairly fast. In the second case, we end up with only the meta product as the major product, and the reaction ends up being very slow. Why? Write out a mechanism. I'm going to start with nitric acid – imagine the sulfuric acid's already protonated it, imagine water's already nitric, so that I have the following: at this point, the first step of the reaction is for benzene to attack, but there are three possibilities, regiochemically, where that attack could occur: it could occur ortho, meta, or para. It will not attack ipso, meaning at the position itself. You can't have substitution here because you're already got the three bonds going to other carbons, and there's only the one bond that can go to oxygen, not another bond that can go to anything else. [aniline] Any benzene molecule that has an oxygen directly attached, a sulfur directly attached, a nitrogen with a lone pair directly attache, those molecules all have the same reactivity pattern, where they tend to react more quickly than benzene and they tend to form othro and para products. What if we had something like nitrobenzene or benzaldehyde or benzoic acid or anything that has an electron withdrawing group attached to the benzene, then what ends up happening is the reaction's slow and you get meta substitution instead. I'm about to show you a series of mechanisms that will demonstrate why does the top reaction not make meta, why does the next reaction not make ortho or para.

When phenol reacts, we've got three different places we can put it; let's write the mechanism for all three. First, I'll show reaction through the ortho position. Notice the arrow that I have going from the double bond up to oxygen. What happens when the attack occurs the way that I've written it? We end up with a positive charge right next to the oxygen, so doesn't that mean that the oxygen can delocalize, which is favorable. If we can delocalze the ion, that means it's easier to form, easier to form means faster reaction. Why is it faster because this particular ion is stabilized? Because the limiting step of nitration is the formation of the positive charge on the benzene ring. If you stabilize that positive charge, you lower the activation energy, which makes the reaction faster. This reaction is not over, but I've shown you all that I care about: the fact that we have resonance stabilization. Arene is a word used often to refer to an aromatic-style compound, something with benzene rings and such. Arenium means a positive-charged ion from something that used to be like benzene, which is exactly what we have. We have a benzene derivative that's been made positive, that's called the arenium ion.

Let's do the same nitration reaction again. Again, I'm skipping over the initial steps to show how I made the NO2+, cause it's not important to the argument that I'm making. We could put any electrophile here, in fact. Now, let's have it go through the meta position, the attack itself. Let's try to move that around the ring, the positive charge. Notice what happens: yes, we can move it around the ring, but we never get it right next to oxygen; we can get it to either side of oxygen, but it's not able to delocalize on the oxygen. There's nothing destabilizing this system, either. We had one case that was favorable, one case that is not unfavorable but is not favorable either.

Let's look at the last case, which is if we had para substitution. Now, if we make a resonance structure, try to push the charge around the ring, we'll be successful in doing so – not just successful pushing it around the ring, we actual get it onto oxygen, that positive charge. That again stabilizes the positive charge, making it easier to form, which is why the reaction ends up being more favorable. If we do either ortho substitution, that generates this more favorable cation. If we tried to do meta substitution, you don't get that favorable cation. That is why with something like phenol, you're only going to end up with ortho and para produc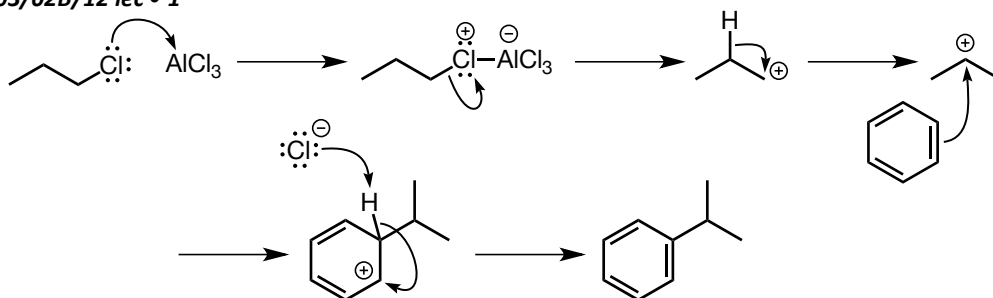ts. Phenol is an example of an ortho/para director, meaning that substitution is likely to occur almost exclusively at the ortho and para positions, due to the stability of the intermediate that forms, as opposed to the meta position, which is not stabilized.
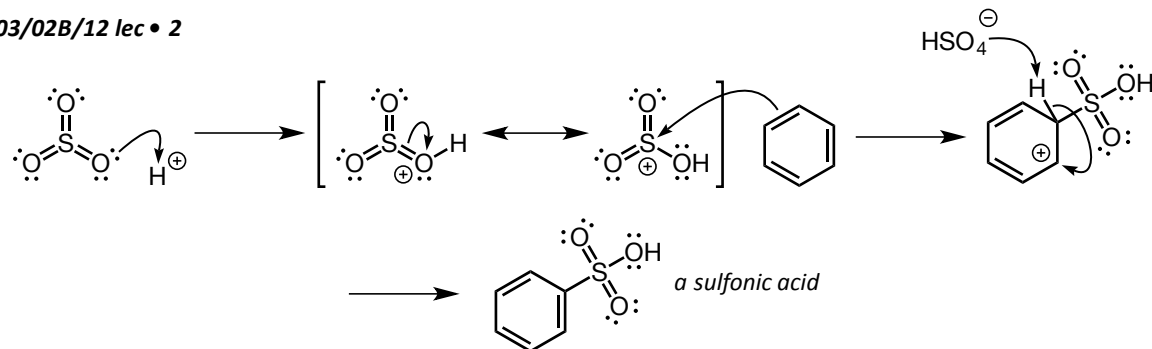
We're going to repeat the same story for nitrobenzene, and we're going to use the same rationalization to explain why does it only have meta substitution. Nitrobenzene reacting in a nitration reaction, starting out with the example of attack occurring at the ortho position. I'm going to write out the full structure of the nitro group that I started with. Look what we have at this point: there's the positive charge on what used to be the benzene ring that is right next door to the positive charge that's already there on the nitro group. Is it likely that these two positive charges are going to want to be this close to each other, the way I've drawn it. No; not favorable at all. What about the meta case? We can't really tell much, at least by the first structure I've written, because the positive charges are on opposite sides of the molecule. Let's show the delocalization. Now they're closer, but are they right next to each other, on adjoining positions? No, so there's some separation. Let's scoot it further around the ring. It's still not right next to it. Having two positive charges is still not great; it does slow the reaction down that we have something pulling electrons off the benzene ring, cause why would the benzene want to use its electrons want to use its electrons, which it wants to keep anyways, to attack something when they're getting pulled right off the ring by something that's already there before the attack even occurs. But this is not as bad as what we saw up above, at least.

Then, of course, there's one more case, the para case. Once we write even just the first resonance structure, we're going to again end up in a situation where we have two neighboring positive charges. Nitrobenzene is an example of a meta director, meaning that substitution is likely to occur almost exclusively at the meta position, since the intermediates formed by substitution at the ortho or para positions would be highly unfavorable.

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Regardless of where it ends up, the nitro group that was already on there to begin with is pulling electrons off the ring, which makes all three of these slower than if just benzene by itself reacted. In more complex cases, you can have multiple products, where there's competition as far as what's faster: a hydride shift, or attacking it. If the attacking can occur faster than the hydride shift, you could get a range of products.

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Bonding MOs are exactly filled

Although this cation is delocalized and has 4n + 2 pi e-, it is not aromatic since not all bonding orbitals are filled.

Friedel-Crafts alkylation

Sulfonation

Halogenation (Cl, Br)

Phenol is an example of an ortho-para director, meaning that substitution is likely to occur almost exclusively at the ortho & para positions due to the stability of the intermediate that forms, as opposed to the meta position, which is not stabilized.

Nitrobenzene is an example of a meta director, meaning that substitution is likely to occur only @ the meta position, since the intermediates formed by substitution @ the ortho and para positions would be highly unfavorable.

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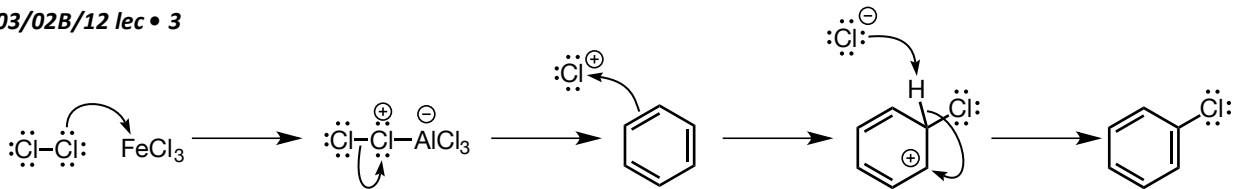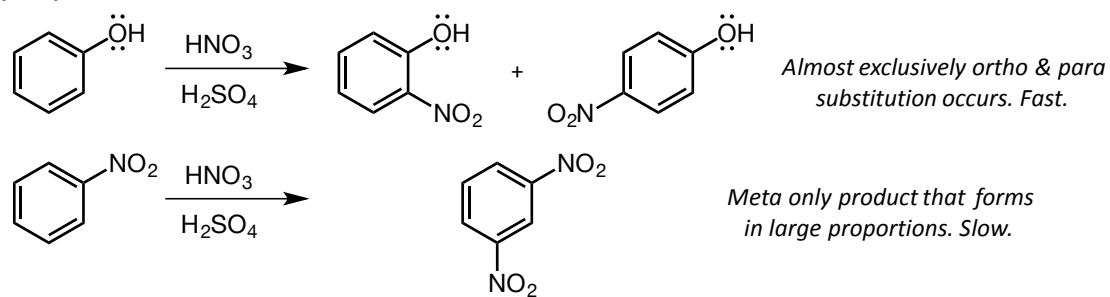**Structures** *(remaining structures identical to lecture 16A)*
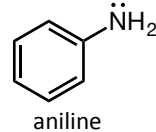
03/02B/12 lec • 1

03/02B/12 lec • 2

a sulfonic acid

03/02B/12 lec • 3

03/02B/12 lec • 4

+ *Almost exclusively ortho & para substitution occurs. Fast.*

Meta only product that forms in large proportions. Slow.

03/02B/12 lec • 5

aniline

ortho

resonance stabilization of the [arenium] ion

related to benzene

meta

no delocalization with oxygen

para

delocaliztion with oxygen

ortho

two + charges neighboring

related to benzene

two + charges neighboring

meta

two + never directly neighbors

para