



## Activating Groups

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### Transcript

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**Dr.Jessie Key:** So activating groups are groups that activate or enhance the ability of an electrophilic aromatic substitution to occur. When we perform a nitration and we use toluene, we see it undergoes nitration 25 times faster than when we just try and nitrate benzene. The methyl group is electron donating.

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**Dr.Jessie Key:** It is going to activate the ring by donating electron density through induction or more specifically through hyperconjugation. So having that methyl group there activates the ring, it makes it more nucleophilic. The reaction happens 25 times faster than if it's not there.

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**Dr.Jessie Key:** We also see that when we perform this reaction with toluene, that we do have certain regio selectivity as to where that group that we're adding gets placed. Here's an example: here we have toluene and you can see the reaction conditions. We have our nitric acid and sulfuric acid, so that's our typical nitration conditions.

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**Dr.Jessie Key:** and when we look at the products that we get, we see that there is 3 possible products. We could have that nitrogroup get added ortho to the methyl and that is the major product. We could have it added meta to the methyl, which is a very, very minor product.

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**Dr.Jessie Key:** Only 3% is meta compared to the 63% that was ortho. Then when we look at the last product, paranitration, we see that that's in the middle at about 34%. There's certain selectivity in that we do have a major product and that's a ortho then we have a minor product, para and then a very minor product and that's meta.

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**Dr.Jessie Key:** So the main reason that we're seeing this is because the position of the methyl group really affects the stability of the sigma complex. Where our methyl group is

compared to where the electrophile is going, that is going to affect the stability of that sigma complex intermediate that we go through. Here we have ortho attack.

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**Dr.Jessie Key:** On the left side of the screen in this diagram, you can see that we're showing the formation of this new bond to the nitrogen, in this black rectangle here, we have our 3 possible sigma complex resonance forms. When we look at these 3 resonance forms, you can see that there is that formal positive charge which is at different places along the ring. One of these forms, the one highlighted actually stabilizes that resonance form of the sigma complex by having this electron donating methyl group attached to the carbon that has a formal positive charge.

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**Dr.Jessie Key:** We have hyperconjugation from that methyl substituent stabilizing the carbocation intermediate. So this is why having an ortho placement of that nitro group is favored because we have one of our sigma complexes that gets additional stabilization by having that formal positive charge directly on the carbon where we have an electron donating group. But what if we have a meta attack?

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**Dr.Jessie Key:** There's a toluene and we're forming that bond to the nitrogen at the meta position relative to the methyl and we would get these three corresponding sigma complexes. When you look at these three sigma complexes and the position of the substituents relative to the position of the carbocation, none of these particular sigma complexes have that stabilization from the electron donating methyl. We have our methyl group on carbons other than the ones which get the formal positive charge in our resonance forms.

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**Dr.Jessie Key:** So there's no stabilized version of our resonance forms when we have meta attack. This is why we see meta being a very small minor product. Last scenario here, what if our substituents are para?

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**Dr.Jessie Key:** We can draw out the three sigma complexes that would arise from our para substitution of the nitro group. And you can see that as we walk through these three resonance forms, one of them, this one in the middle here, has that electron donating methyl group attached to the carbocation. This particular sigma complex has one resonance form which is stabilized.

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**Dr.Jessie Key:** That's why we do see a preference for para substitution compared to meta. So let's take a look at the energy diagrams of the step to form our sigma complex. Here we have these three energy diagrams, free energy on the Y and the reaction coordinate or time

or reaction progress, whichever one you want to use down here on the X axis, we're showing the scenarios here for ortho attack, meta attack, and para attack.

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**Dr.Jessie Key:** When we look at our ortho attack, you can see we have an intermediate amount of activation energy, and then we end up with our product energy about midway through the diagram here. When we look at the meta attack, it's much higher energy to perform the reaction, so much higher activation energy as well, the intermediate that we're left with is also a much higher energy, it's not stabilized by that electron donation. And then finally, looking at the para attack, we can see that it has a slightly lower activation energy than ortho and slightly lower, it looks like intermediate energy as well.

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**Dr.Jessie Key:** This difference between the ortho and para, again, is likely due to some amount of steric hindrance, although methyl groups and nitro groups are relatively small, so it's not as large of an obstacle or hindrance as we would see in other examples. So the main takeaway here, ortho and para attack reduce the activation energy and give us a more stable intermediate for this reaction. A meta attack does not reduce any of our activation energy and gives us a relatively high energy intermediate, but there are other types of activating groups besides alkyl groups.

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**Dr.Jessie Key:** One of these is the methoxy group. When we're looking at anisole, which has that methoxy, that O and then CH<sub>3</sub>, we see that it activates the ring about 400 times more than benzene. It's an even stronger activating group than toluene, which activated the ring about 25 times more than benzene.

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**Dr.Jessie Key:** But you may be asking yourself, how does this work when we look at methoxy group and we look at it in terms of electronegativity and the resulting induction, we would draw a bond dipole arrow like this one on the screen. Although the oxygen in our methoxy group is electron withdrawing by induction, it is electron donating through resonance. Here we have our methoxy attached to our ring.

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**Dr.Jessie Key:** We can draw another resonance form if we move a lone pair down to form a new pi bond, and that's going to kick one of the existing pi bonds in the ring over as a lone pair on the orthocarbon. So now we'll get this resonance form where we have a formal positive charge on our methoxy oxygen, and we also now have this lone pair and formal negative charge on the orthocarbon. We can walk this negative charge around the ring.

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**Dr.Jessie Key:** If we go from the lone pair here on this atom to form a new pi bond down here between the ortho and meta position, that's going to cause a pi bond that exists here between meta and para to come up as a lone pair on that paracarbon. We can keep moving

it around the ring, so from this form where we have the lone pair and formal negative charge on the para carbon, we can draw that forming a new pi bond between the para and meta carbon on the left side. That's going to cause that pi bond between the meta and ortho carbons on the left side to move up as a lone pair on that orthocarbon.

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**Dr.Jessie Key:** So we just saw that there are multiple resonance forms for our methoxy group, which allows us to stabilize this sigma complex intermediate. Notice again, that we're seeing this methoxy group would direct the substitution to ortho and para positions. A general rule is that all of our activators, whether it's through induction, like we saw with our toluene and the methyl group, or if it's activated by resonance, like we're seeing here with our methoxy, they all direct ortho and para.

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**Dr.Jessie Key:** If we did an ortho attack here, we could draw out the resonance forms of our sigma complex and we would actually have four of them now because we have that additional resonance from the methoxy group. I'm not going to go through each of these, but I will point out that we can get to that additional fourth one by bringing down the lone pair from the methoxy oxygen. Having this additional fourth sigma complex compared to having just three is itself a stabilizing thing.

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**Dr.Jessie Key:** That's where we see that extra activation, having now a fourth Sigma complex resonance form compared to the three that we had with toluene, that makes this much more stabilized and allows us to go through this reaction more readily. If you were to perform a meta attack and then try and draw the different resonance forms for our sigma complex, you would then see that we would only be able to draw three resonance forms. Then finally, if we drew a para substitution, again, we would get an additional form, like we saw with the ortho attack.

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**Dr.Jessie Key:** In both the ortho and para substitutions, we get an extra bonus resonance form, which gives us extra bonus stability in our sigma complex. So let's take a look at the free energy diagrams that we see here for our anisole nitration. Again, we have the three different free energy diagrams here, corresponding to our ortho, meta and para attack.

00:11:09:56 - 00:11:48:65

**Dr.Jessie Key:** We'll start here with ortho attack an intermediate level of activation energy and an intermediate level of energy for intermediate. When we look at the meta attack, much higher activation energy and much higher energy for our sigma complex intermediate, and then with our para attack, a little bit lower activation energy than the ortho and a little bit lower energy for our sigma complex intermediate, a little bit more stable intermediate for our para attack compared to the ortho. Again, that likely has something to do with some steric penalties, having this methoxy group right beside the nitro group.