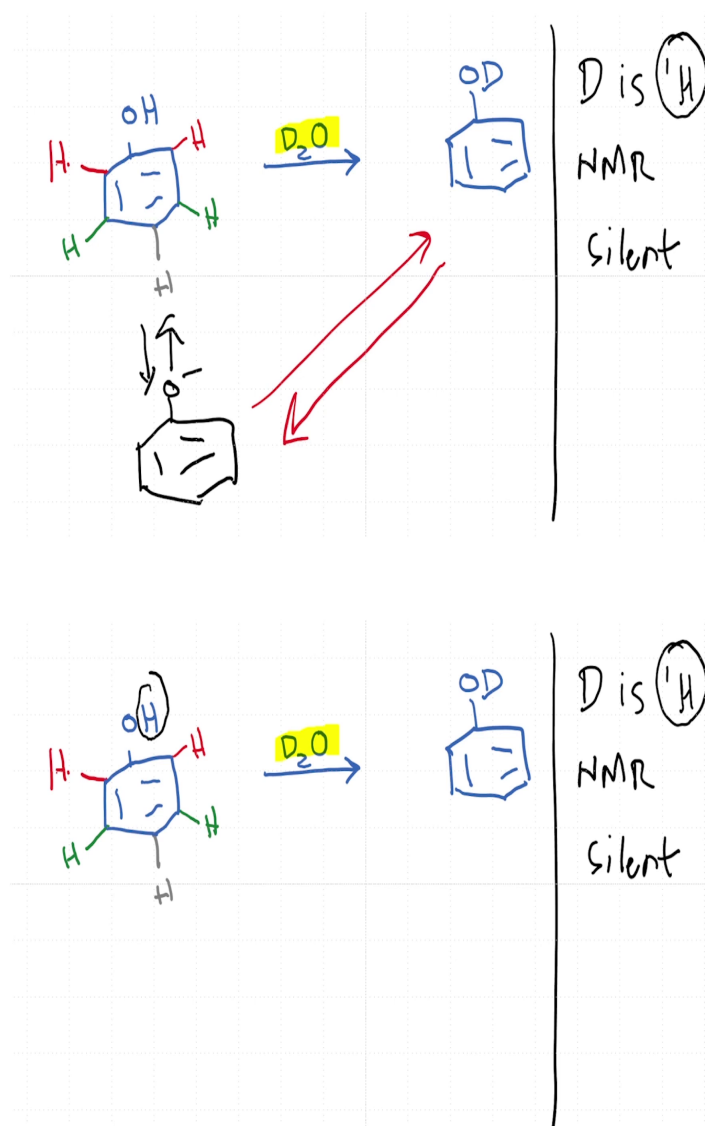


Introductory Organic Chemistry - II
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Indian Institute of Science Education and Research, Pune
Lecture 05

Electrophilic Aromatic Substitution - Part 1

So, in this lecture, we are going to look at a very important reaction known as the Electrophilic Aromatic Substitution. We already have a good idea about the way aromatic systems are going to react. And so, we will now look at some of these reactions in detail.

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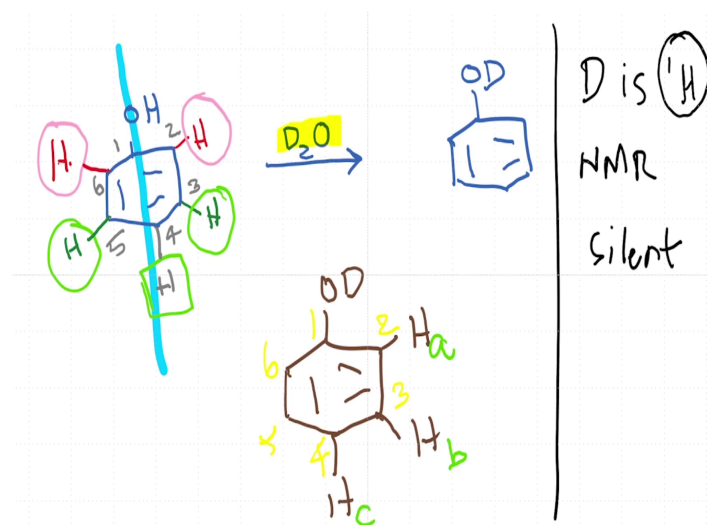
So, in the past couple of introductory lectures, we have seen the value of NMR, both Proton NMR, as well as Carbon NMR and how it is very useful for us to understand structure of molecules and what is the local environment, etcetera. So, now what I am going to do in the next minute or so, a couple of minutes or so, is to describe an NMR experiment that we do.

So, what we do is we take basically Phenol whose structure is shown here, it is Benzene with a hydroxyl group and we dissolve it in D_2O . D_2O , is basically deuterated water and deuterated water and, the concept that we need to understand which I will now discuss is that Deuterium is NMR silent, which means that under the conditions under which you do Proton NMR recording of Proton NMR spectrum, Deuterium is silent.

So, once you replace a Hydrogen with Deuterium that peak will disappear. So, when you add Phenol into D_2O , the peak area of Phenol is a little bit above around maybe 9, 10 or so. And so, in D_2O , what happens is that there is an equilibrium that is set up between this Phenol and Phenoxide and, once this equilibrium is set up, when it picks up the Deuterium, it goes back to, it goes to OD rather than OH. So of course, this is also going to be an equilibrium in this reaction.

So, gradually Phenol gets completely converted to deuterated phenol, so in the NMR spectrum, the peak that you would expect for OH does not show up and so you see only the remainder of the peaks.

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Now, coming to the remainder of the molecule, let us look at this one by one. So, when you look at Phenol in this position, let me just number the Carbon so that it is easy for us to follow it. So, this is 1, 2, 3, 4, 5 and 6. So, in Carbon number 1, where the hydroxyl group is there, there is no Hydrogen. So, there is nothing to worry about here. When we look at Carbon 2, there is a Hydrogen attached to it which I have shown in red.

And you will see that there is a plane of symmetry in this molecule and this plane of symmetry, sort of which I am going to just draw like this, sort of cuts the molecule into two. And therefore, this part of the molecule, the left-hand side of the molecule, is identical to the right-hand side of the molecule.

So, the one that I have circled now, these two Hydrogens are the same. So, the chemical environment is the same and therefore, they also show up in NMR as a single peak. The magnetic environment is also the same. Now, the next set of Hydrogens which are in green, are also the same.

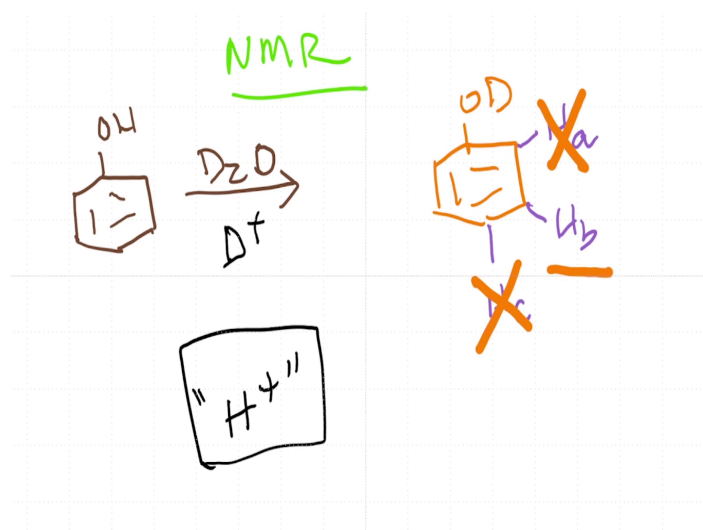
And lastly, there is one Hydrogen here that I am showing in the form of a square, that is a single Hydrogen anyway, and then it is distinct from the other Hydrogens. The other way to think about it is that if I assume that from Benzene, I am making Phenol, in my mind, the Hydrogen here is close to the Phenol and therefore the environment that it is going to experience is going to be different from this Hydrogen here, which is a little bit far away from the Phenol.

And lastly, this Hydrogen is in the 4 position, and therefore it must be experiencing a very different environment. And among these three Hydrogens, not just the Phenol but this Hydrogen is next to the pink Hydrogen here, I mean the Hydrogen is also next to this Hydrogen here, whereas this red Hydrogen is only next to the Phenol and the other Hydrogen.

So, there are many differences that you can sort of systematically work up. But at the end of it, what we realise is that the Phenol in D_2O has three distinct signals that we would expect to see, which I am going to label here as Ha, Hb and Hc. So just to be clear about the numbering, this is 1, 2, 3, 4, 5 and 6.

So, you are going to see three signals in the NMR spectrum. I am not going to draw out the NMR spectrum because it is a little complicated, and we have not done coupling for example, in NMR, so, that will be reserved for an advanced course, but suffice to say that you do see three signals in D_2O .

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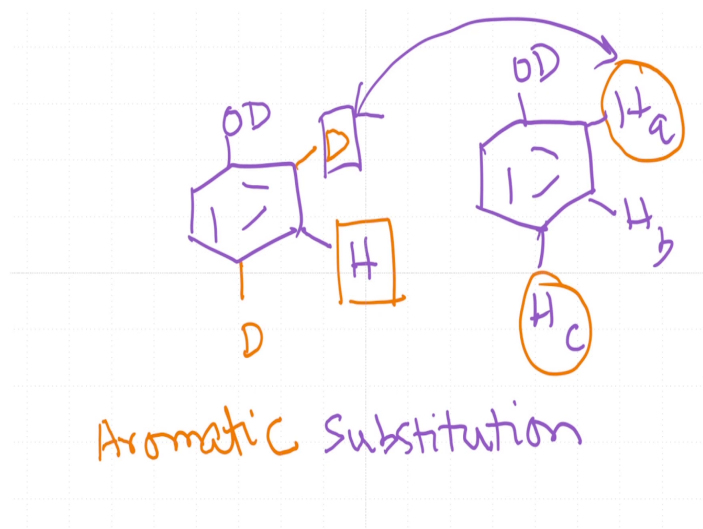


Now, the experiment that we want to do is, we take Phenol or Deuterated Phenol in D_2O and add some amount of D^+ . D^+ is basically the equivalent of H^+ , except that it is a Deuterium. Now, as we just discussed this, then you record the NMR spectrum, it is an NMR experiment.

And what you expect to see is essentially, the peaks that you expect to see are, this OH is going to be replaced by OD, so, that becomes NMR silent. Now, the H_a , H_b , and H_c are the three peaks that you expect to see. However, when you go and record the NMR spectrum, what ends up happening is that you do not see a peak for H_a , and you do not see a peak for H_c , but you only see a peak for H_b .

Now, remember that we discussed the formation, the replacement of Hydrogen by Deuterium and how that is going to have an effect on the absence of a signal. So, if Deuterium replaces Hydrogen, then it is going to become NMR silent.

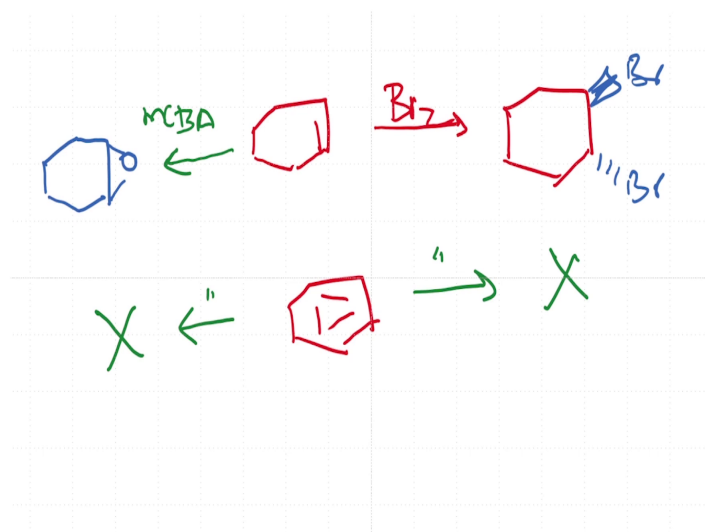
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So, one possible interpretation from this experiment is that under these conditions, this is actually forming a molecule like this. So, what happens if I just draw out the original structure that we had. So, as we discussed this H_a , H_b and H_c . So, now, this H_a is replaced by Deuterium, H_c is replaced by Deuterium, and so, therefore, you have only one signal in the NMR spectrum when you add D_2O and D^+ . So, this is a very important experiment, because this tells us that there is a substitution reaction that is happening.

So, first of all, the aromatic ring is involved. So, therefore, it is an Aromatic Reaction. The second key term is the substitution that is happening. So, you have Deuterium, that is replacing Hydrogen and therefore, it is a Substitution Reaction. So, as a reaction, we are going to call it an Aromatic Substitution reaction. Now, the mechanism of the reaction, or the way in which the reaction happens, we will understand that it is actually an Electrophilic Aromatic Substitution.

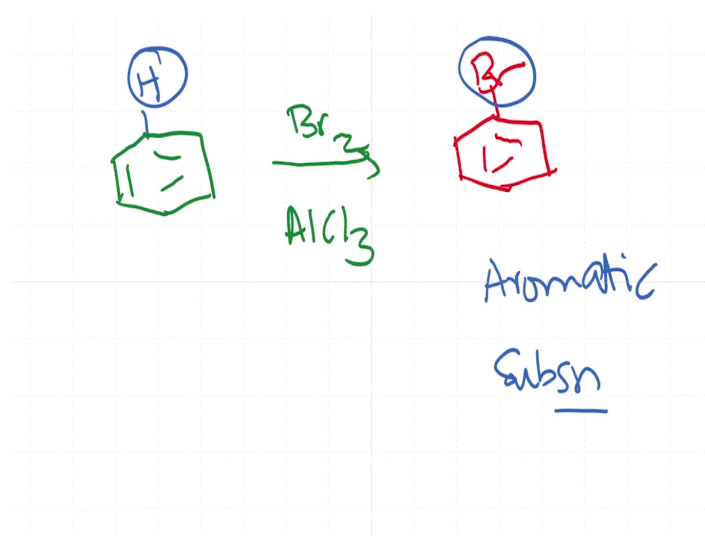
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So, now let us try and understand the mechanism of this reaction. So, before we get into the details of the mechanism, let me introduce another reaction to you. So, you all must be familiar that if we start with the cyclohexene and add Bromine to it, we get this 1,2-dibromo compound. And this is a very standard reaction that we are all quite familiar with.

Similarly, if you start with a peracid such as m-CPBA, we end up with the corresponding epoxide. So, these are all fairly well-established reactions of olefins, but when we do the same or expose Benzene to the same reaction conditions, that is Bromine or m-CPBA there is absolutely no reaction. So, Benzene is fairly stable and it really does not do the kind of reactions sometimes that olefins do very easily.

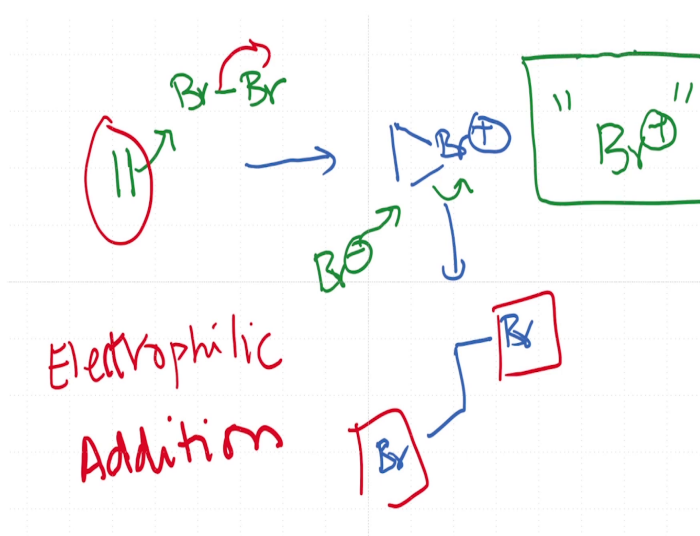
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You also would have studied it as a very special property of aromatic compounds, which is that $(4n + 2)$ pi electrons, etcetera. So, now how do we get Benzene to undergo bromination. If you want to do that, then what we need to do is basically take Bromine and add some Lewis acid like Aluminium Chloride, and this reaction goes fairly well, you get the product which is Bromobenzene.

Now, if I look at this reaction, we can clearly say that this is an aromatic substitution reaction, as we discussed in the previous case, because the Hydrogen here is being replaced by Bromine. Now, here comes the question about the mechanism. So, in order to understand the mechanism, let us first move to the reaction where we had the olefin.

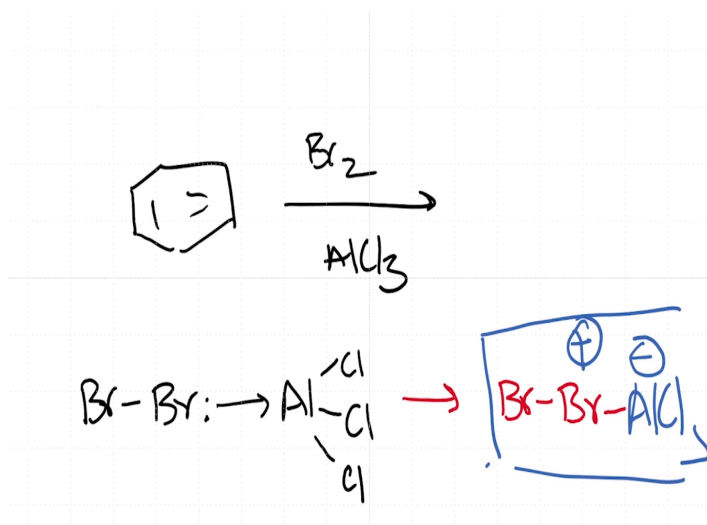
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So, we are all familiar with the bromination reaction. So, you have Br-Br and then this you can push arrows here and you get to be cyclic bromonium ion which then eventually gives you the dibromo product, through the addition of Br⁻. So, now similarly, this is called an Electrophilic Addition reaction, because if you see the Bromine has actually added on to the olefin here.

So, this is electrophilic because the olefin is reacting or the Carbon-based group is reacting as an electrophile. So therefore, it is an Electrophilic Addition reaction. And it is also called bromination epoxidation, whatever those reactions, they all come under electrophilic addition reactions. But the important point here is that there is an electrophile that is produced, which is essentially Br⁺. So, this is important that we understand because the active reacting group is not bromide, but it is Br⁺.

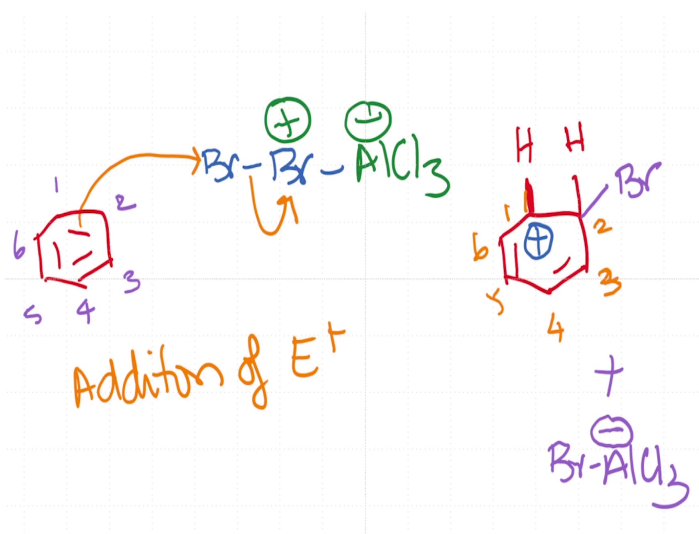
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Now, coming back to the aromatic substitution reaction that we have just encountered. So, in the case where we had Br_2 and AlCl_3 , what we can propose, based on our knowledge of chemistry so far, is that we can say that the Br which has a pair of electrons can coordinate with AlCl_3 .

Once this coordination happens, it is going to produce a complex such as this, where you have AlCl_3 and you are going to have full positive charge on Br and a negative charge on Aluminium. And what can happen is that this produces a very reactive species. So, this is the reactive electrophile that is going to react.

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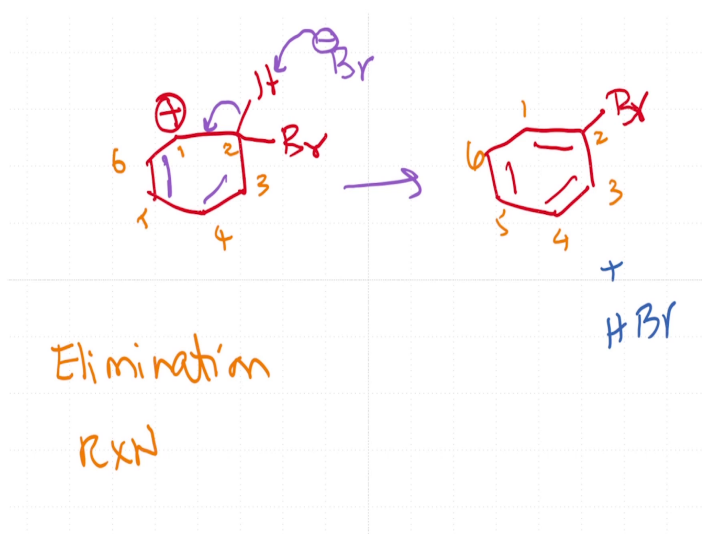
Now, let me move to the next slide, where we can discuss this in a bit of detail. So, let me just draw out the Benzene ring. And here is your Br-Br and AlCl₃, so there is a negative charge on Aluminium, there is a positive charge on Br because Br is donating electrons to Aluminium. Now, this is set up beautifully to do the electrophilic aromatic substitution reaction. Here is where it attacks, and then this kicks out this leaving group here. So, what I will do now is I will just number these Carbon so that it is easy for us to follow, this is 1, 2, 3, 4, 5, and 6.

So, if we just redraw the Benzene ring the way it is, now what is going on here is the bond between 1 and 2 is being broken and the new bond between 2 and Br is being formed. So let me just draw the new bond and as you can very clearly see, the by-product is Br-AlCl₃, and it has a negative charge because once this lone pair goes here, there is still a negative charge remaining.

So, the bond between Carbon-2 and Bromine is being formed. And there is the bond between 1 and 2 that is broken and that would result in a full positive charge on Carbon-1. The remaining bonds will continue, because you will get, the other double bonds are going to remain. And keep in mind that this Hydrogen over here remains at the 2 position.

So, let me just draw this Hydrogen out as well, so that it is easy for us to follow it. So, this is carbon 1, 2, 3, 4, and so on. So, these two Hydrogens, I mean, all the Hydrogens remain intact, so far, Hydrogen has not been lost. So, this is the step where this is called the addition of E⁺, which is the electrophile.

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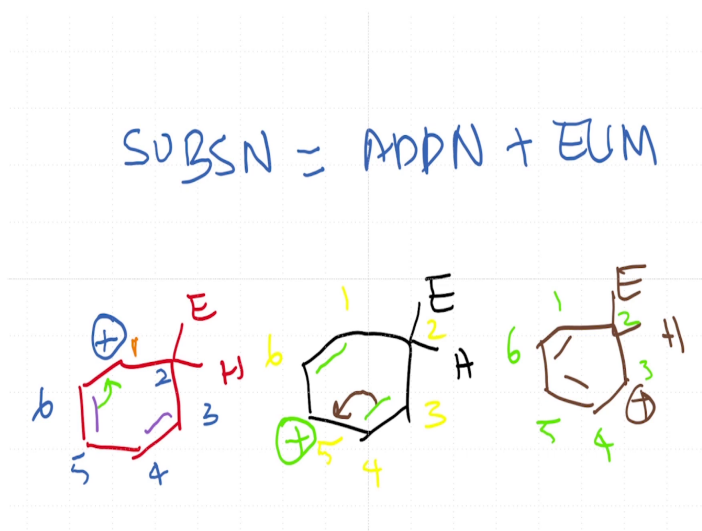


The next step, which I am going to draw out here, is the elimination reaction, which is the loss of a proton. So let us look at that step now. So, I am essentially drawing the same structure that I drew in the previous page. There is a positive charge here, keep in mind that this is 1, 2, 3, 4, 5, and 6, and there is a double bond here, there is a double bond here.

And there are resonating forms that we can look at later. But now imagine that there is either a bromide or water or something in the system that comes and attacks here and produces, reforms the double bond, then the product that you get is, this bond remains the same, this bond remains the same, carbon-bromine bond remains the same. And there is a new bond that has been formed here.

And HBr is lost, this could also be water or it could be any other nucleophile or base. So, if you see, if you look at it closely, you should be very careful with this because the numbering is very important. So, I am just keeping the numbering the same, just so that we understand the reaction outcome. So, there is now a bond that has been formed between carbon-1 and carbon-2, that is a double bond. So, this is actually an Elimination reaction.

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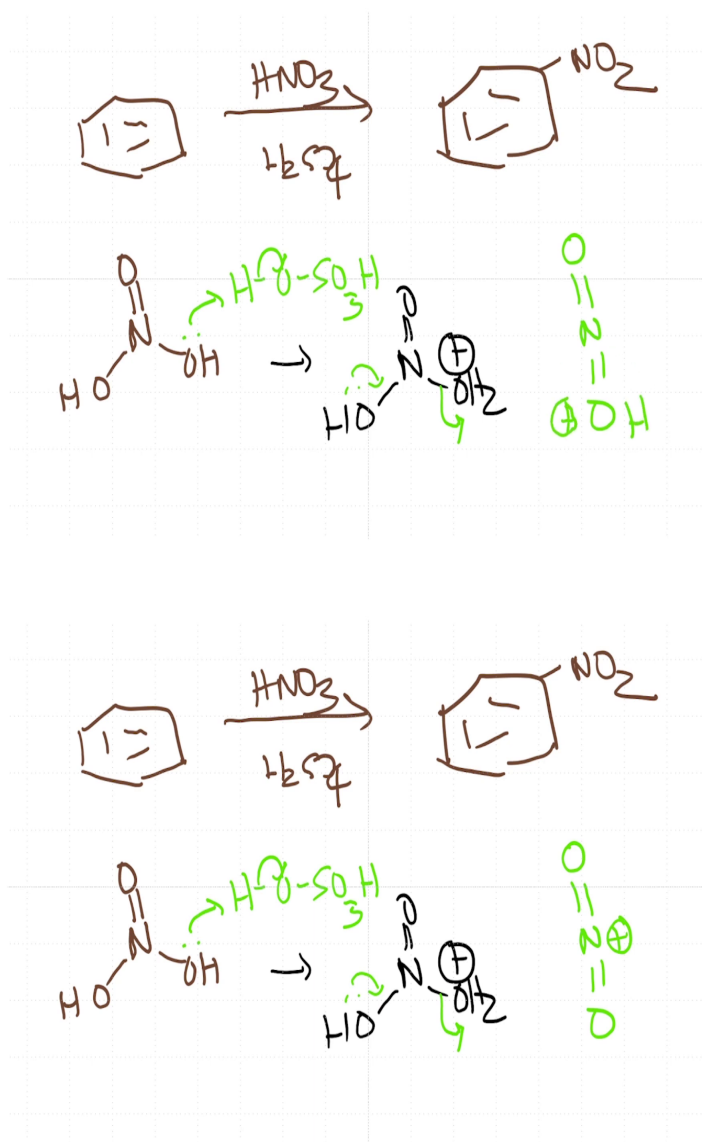


So therefore, this substitution reaction is actually a combination of the addition plus elimination. So, that is why this reaction mechanism is quite unique. Now, coming to the resonance forms. So, if I take a general structure, such as this, E and H, and I am just going to stick to the same numbering, I will just change this as 1, 2, 3, 4, 5, 6. And the positive charge is here, the double bond here, double bond here.

So, now you could draw a resonance form, wherein I am just going to put this positive charge outside so that it is easy for us to follow. And this becomes Carbon-1. So, one way to draw a resonance form is to push these electrons over here. So, when you push the electrons over there, the resulting structure has exactly the same structure except that there is a new double bond that is being formed here and there will be a positive charge here, this double bond remains intact.

So, just to complete the numbering, this is 1, 2, 3, 4, 5 and 6. And lastly, if you push these electrons over here, then you have full positive charge here, E, H and so on. So, again, if I stick to the same numbering, 1, 2, 3, 4, 5, and 6. So, these are the resonance forms that could happen in the intermediate that sort of stabilises the positive charge that is present.

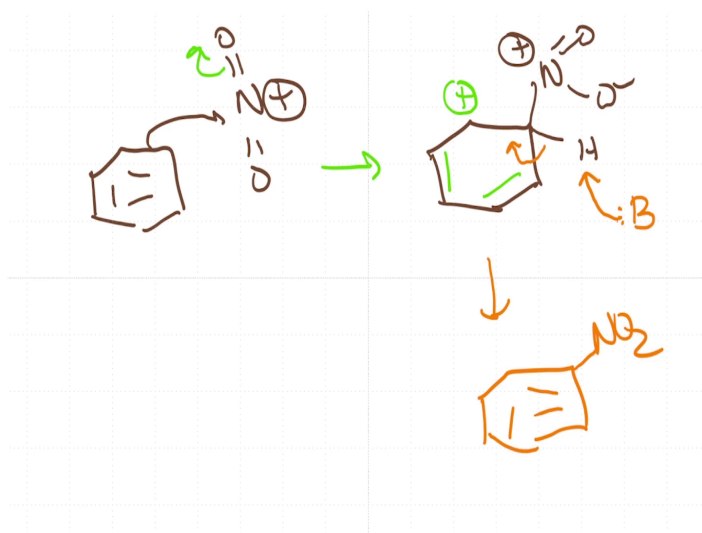
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Now, let us look at a slightly different reaction, which is basically the Nitration reaction. So again, this is something that we might have encountered earlier in our previous courses, but it is a very important reaction that we understand. So, when we add HNO_3 and H_2SO_4 , the product that we get here is Nitrobenzene.

So, let me just quickly write out the structure of HNO_3 . Now, what happens is that this picks up a proton from, likely from, H_2SO_4 and the product that is formed is actually $^+\text{OH}_2\text{N}=\text{OOH}$ and you can push arrows for water to leave and the electrophile that is going to be produced is NO_2^+ .

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Now, this NO_2^+ is the active nitrating agent and the reaction that it can undergo, it can mediate, is the reaction with the benzene ring. So, let us now draw that out, $\text{O}=\text{N}^+=\text{O}$, this can attack here, if this moves up and you get H, N double bond O, O^- and this Nitrogen continues to have a positive charge because it has four bonds and there is a full positive charge on this carbon, these two bonds remain the same.

Now, as we discussed earlier, you can propose that a base of some sort which could be HSO_3^- for example, comes in, picks up this proton and the final product that you want to get is Nitrobenzene. So, this is a fairly straightforward reaction mechanism, once we have understood the basics.