Essentials of Oxidation, Reduction and C-C Bond Formation
Application in Organic Synthesis
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Lecture -09
1,2-Ketone transpositions, Shapiro reaction and Dauben-Michno rearrangement
(a case of 1,3-enone transposition)

Hello everyone I hope you had the chance to go through the last classes that I discussed many aspects of oxidation reactions. So today we will have briefly first will go through the few points of the last classes, for example what we did was;

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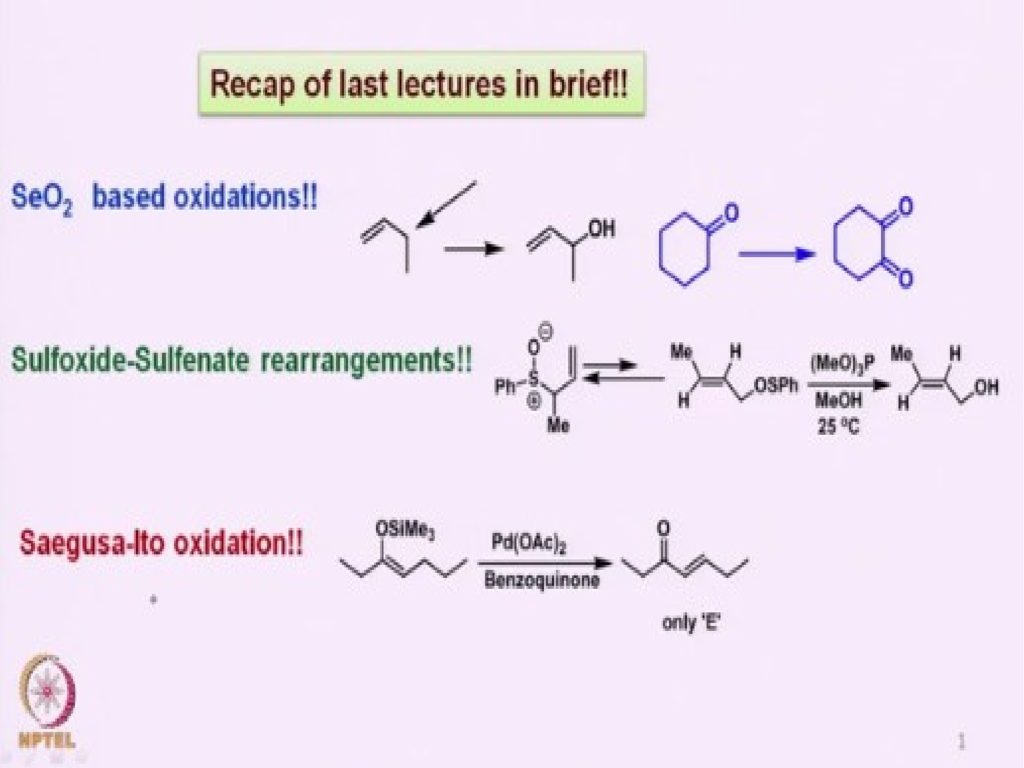

Recap of last lectures in brief!!

SeO_2 based oxidations!!

Sulfoxide-Sulfenate rearrangements!!

Saegusa-Ito oxidation!!

Selenium dioxide based oxidations here and then we also did the sulfoxide sulfenate rearrangements. Also we did in the case of selenium dioxide based oxidations conversion of ketones to diketones and also oxidation at the allylic position to go to allyl hydroxy group. Then we also did the Saegusa Ito oxidation where enol sillyl ether was converted to the corresponding enone.

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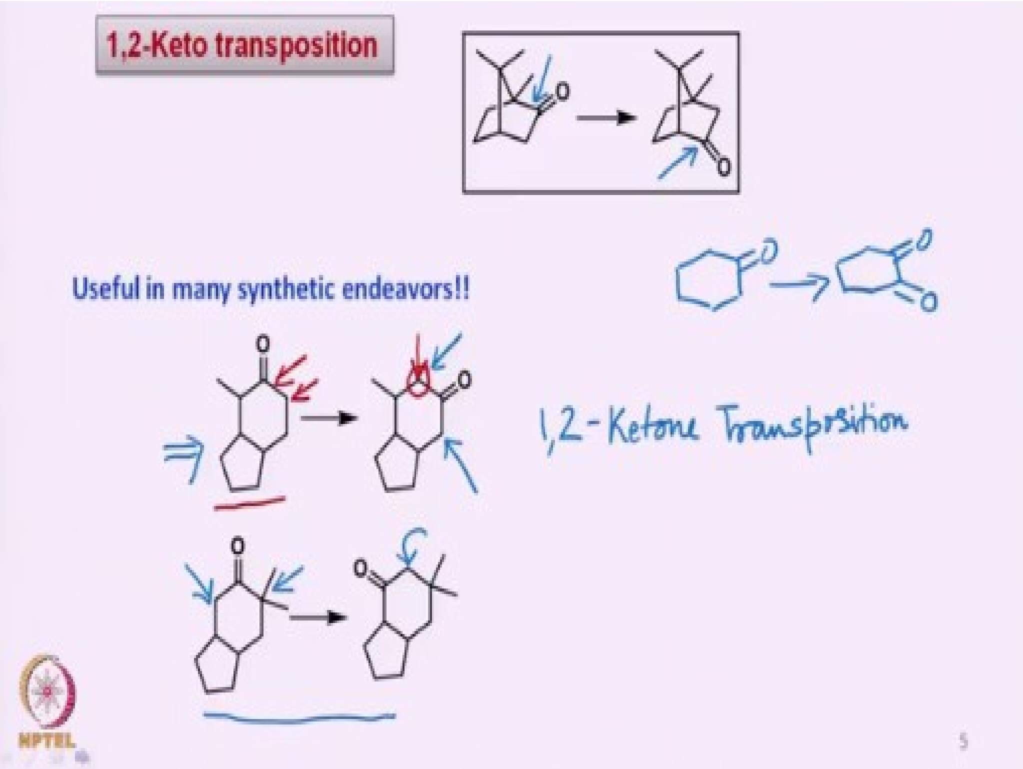

1,2-Keto transposition

Useful in many synthetic endeavors!!

1,2-Ketone Transposition

Now let us go to another topic today is that 1,2 keto transposition what we discussed in say earlier conversions using selenium dioxide was conversion of a ketone to a diketone. However another possibility and other requirement that happens in cases of many synthetic transformations is, how are we going to convert a ketone which is already present here to the next position which is here.

Now this is something very important and this is important mainly because what happens is in many of the transformations that are required is conversion of one keto position to the next keto position. For example in this case, if one takes an example of this kind and if one wants to carry out some transformations at this position, one possibility of course is directly you can functionalize this carbonyl group.

But if one wants to utilize both these hydrogens here therefore we need to convert this carbonyl group here to the next position here. Now once that is done then you now have two possibilities, one of course is the functionalization at this center now and the other is also at this center now, that you have a choice. So if somehow you can make this molecule, if somehow you have arrived at this molecule and if you want to convert the carbonyl group from this position to the next position then what are the ways.

So this is just an hypothetical example which I have shown. Similarly there is another example like this where if you have blocked this particular position of the alpha position of the carbonyl group. Then we can convert this ketone to the next carbon atom and once that is done then one can also then functionalize here the position next to the carbonyl group. So this is called 1,2 keto transposition, ketone transposition.

So what are the methods, there are of course several methods but we will take a one or two methods which are using the;

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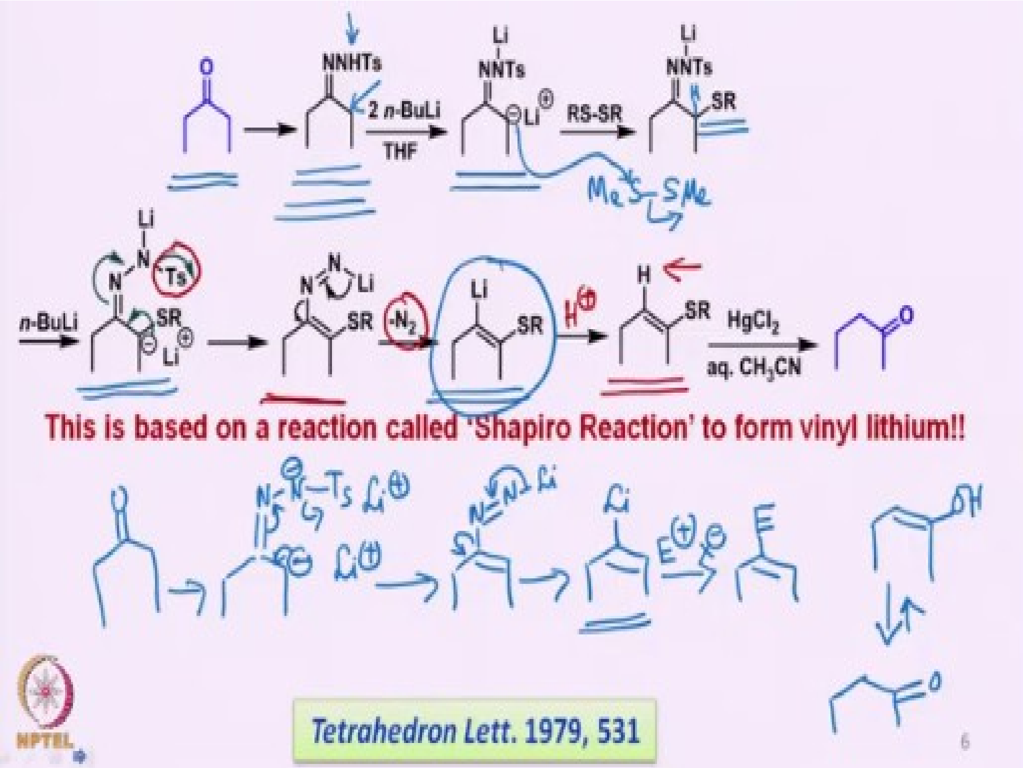

This is based on a reaction called 'Shapiro Reaction' to form vinyl lithium!!

Tetrahedron Lett. 1979, 531

Sulfur based or selenium based chemistry. One of the earlier methods was that one takes this carbonyl group here, for example which I have written 3- pentanone and if one converts into tosyl hydrazone like this and treats with two equivalents of butyl lithium, then of course you will first deprotonate the hydrogen which is attached to the nitrogen and of course you will deprotonate the hydrogen with the second butyllithium at the alpha position.

Leading to this diene anion that is you have anion here at this carbon and you have an anion at the nitrogen and when this is treated with any disulfide such as RSSR which is can be any of the disulfides say diphenyl disulfide or dimethyl disulphide, so you can have a choice of the disulfide that you would like to use it. Now once that happens this anion then reacts with the sulfur here and this breaks off and of course what you introduce is SR.

I have shown here methyl but we can have anything. Now you use one more equivalent of butyl lithium, so that you generate now another anion at from the hydrogen that is abstracted to form this anion, which is easily formed alpha to the sulfur and now that undergoes elimination, the way it is shown here that the tosyl group is a good leaving group and therefore it goes off with the movement of the negative charge to form this intermediate.

Now this intermediate then loses nitrogen as it is shown here to form this vinyl lithium, this is what is formed. Now during this process when the protonation occurs here then you get the corresponding hydrogen at this stage. Now this vinyl sulphide, this is a vinyl sulphide that can be easily hydrolyzed with the help of mercuric chloride Hg $^{++}$ and aqueous acetonitrile. Essentially what is happening in this particular case is the SR group being soft, the sulphur being soft interacts with the Hg^{++} and followed by the attack of water at this centre.

So essentially what you have is a complexation of the mercury onto the sulfur making this particular bond relatively weak and then the attack of the water then allows the formation of corresponding enol and which is what is basically nothing but so you have ketone formation. So you can start with one ketone, make the corresponding tosyl hydrazone here then treat with butyllithium to form an introduction essentially at the vinylic position is sulphur.

And once that has happened you can then hydrolyze it with the help of soft Hg^{++} in aqueous acetonitrile medium to hydrolyze the vinyl sulphide to the corresponding ketone. This is one of the earlier methods which is what is utilized and of course this is based on a reaction called Shapiro reaction, which forms vinyl lithium. So Shapiro reaction is nothing but similar fashion as tosyl hydrozone is there.

So once you have a tosyl hydrazone and you form a di anion from here. So you have a anion formation here and you will have anion formation here if you simply remove the nitrogen from here so what you have is a di anion like this and which is what then of course in these cases there will be $lithium^{+}$ and this loses the tosylate group as I showed earlier and to form this particular intermediate.

And this is the intermediate then that loses the nitrogen and then forms the corresponding vinyl lithium. Now this vinyl lithium is of course similar to the vinyl lithium that I showed here on the top except that in the top position we had SR group introduced, here we do not have an SR group introduced. So if one starts with a ketone like this and prepares the tosyl hydrazone and then finally gets the vinyl lithium.

Now you can react with any electrophile that is possible to react and that allows the introduction of say if you have an E plus as an electrophile and X minus of course is a counterion, then one can introduce the E here. So this is what is called the Shapiro reaction. So basically the method that I introduced on the top is nothing but an application of the Shapiro reaction for the conversion of one ketone to transpose into the second position.

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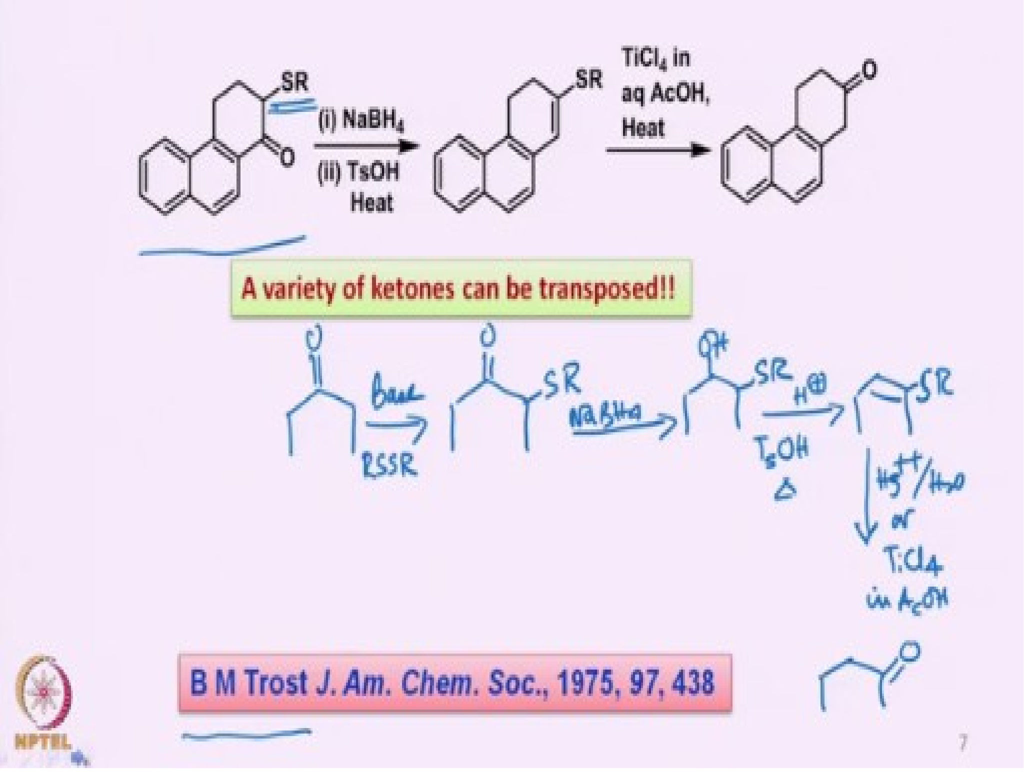

A variety of ketones can be transposed!!

B M Trost *J. Am. Chem. Soc.*, 1975, 97, 438

Now Barry Trost also has reported an interesting way of doing this kind of 1,2 ketone transposition where he took a ketone and introduced simply an SR group adjacent to the alpha position next to the ketone at the alpha position without making the tosyl hydrozone. So if one takes this kind of any keto group here, say like this and introduce by means of say a base and RSSR then you can introduce here SR.

And now you reduce it to the corresponding alcohol by means of say sodium borohydride and then you can eliminate it in terms of dehydration by say tosic acid, paratoluene sulfonic acid and you heat it so this elimination will give you this SR. And once this SR is formed one can also do hydrolysis either by Hg $^{++}$ or and water or as it is shown above is TiCl$_4$ in acetic acid. So one of some of the maze by which you can hydrolyze it and one can go to the corresponding ketone.

So this is the method that is also followed, it is relatively easy by simply reduction followed by dehydration and then rehydration or forming the hydrolysis of the corresponding vinyl sulphide to the corresponding ketone. So this is another method by which one can transpose a ketone to the second position.

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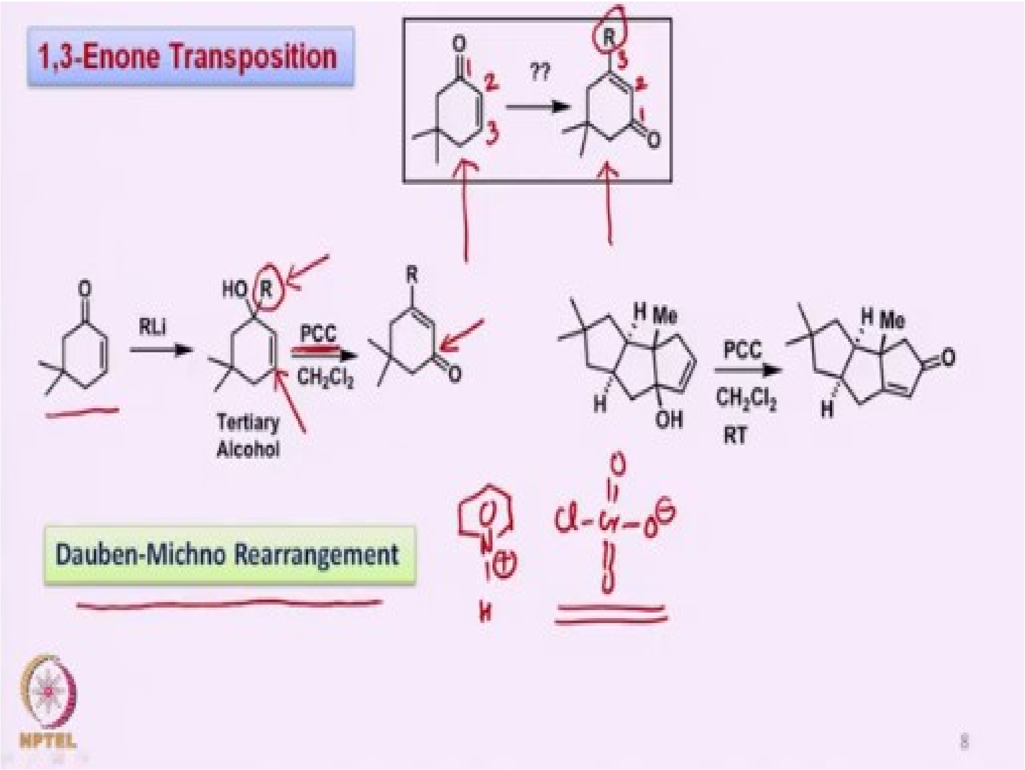
1,3-Enone Transposition

Dauben-Michno Rearrangement

Now there is an interesting reaction which is also required many times is how are you going to convert an enone of this type to another enone. This is a 1,3 enone transposition, so you have 1 position, 2 position and 3 position, now you have inverted it is 1, 2 and 3. Except that here we have introduced another R group at this position. So it is not a simple 1, 3 enone transposition but it is an a 1, 3 enone transition with an addition of an R group.

So if one starts with this enone here and introduce an R group such as this at the position onto the carbonyl carbon by reacting it with R lithium, say you have alkyl lithium or a aryllithium or whatever kind of R group that you want to introduce if you react it with a carbonyl group then it will form the corresponding allyl alcohol with an R group at the carbon holding the OH group. So now this allylic alcohol which is a tertiary allylic alcohol when it is reacted with say PCC which is pyridinium chlorochromate.

So you have here pyridinium chlorochromate and then what happens is that it forms an intermediate where a tertiary alcohol will be reacting with the electrophilic chromium here. But then since R group here, introduced R group is not a hydrogen anymore because we have used R lithium which is either alkyl or aryl, so that means no oxidation of the hydroxy group will occur at the carbon because it does not have any hydrogen left.

So as a result there is some type of migration or some type of rearrangement that occurs where the intermediate eventually comes and gets transformed in such a way that it reaches to the third carbon here or the vinylic carbon or the other end of the double bond which has one hydrogen. Now this is what is called a Dauben-Michno rearrangement.

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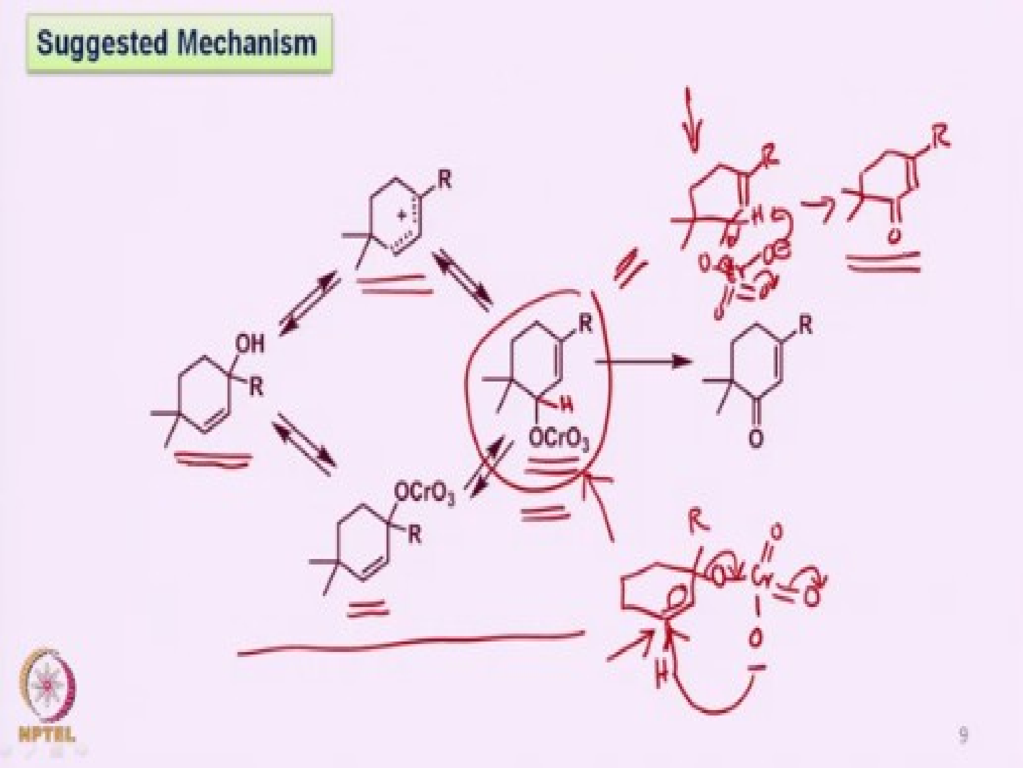

Suggested Mechanism

How does it happen is basically these are the kind of intermediates that are formed. So what happens is if you have an allyl alcohol of this type, then when the chlorochromate or any chromium based reagent reacts with this hydroxy group. So, in supposing if you have the pyridinium chlorochromate.

So, if you have an R group here, an OH group here, so this OH group will react with pyridinium chlorochromate and this is the intermediate that will form. Now you have one hydrogen here, so this part has come by reacting the tertiary alcohol to the pyridinium chlorochromate or any chromium reagent. Now this particular oxygen then interacts in this fashion and this breaks off to form an intermediate of this kind, where the oxygen of the chromium species now has come to this particular position.

Now since there is a hydrogen here, then of course oxidation of this particular species occurs in a fashion something like this, suppose you leave it as it is, then you have OCr Cr and O O O and then you have a hydrogen. So this will undergo oxidation and of course you will then be left out with the corresponding ketone where there is a double bond of course and R group. So this species which I have shown here is similar to this species and that undergoes oxidation to give to the corresponding enone.

So what we have done is we have transformed an allyl alcohol to this intermediate which undergoes a rearrangement, of course it can also go back from here to here or here to here. That is why there is an equilibrium same thing can happen here or this intermediate can be shown as somewhat like this where the chromate is coming out and then this species undergoes oxidation in the way I have shown here to the corresponding enone.

So this is one of the very popular methods of converting an alpha beta unsaturated ketone with an extra substitution to the corresponding 1,3 transposed enone.

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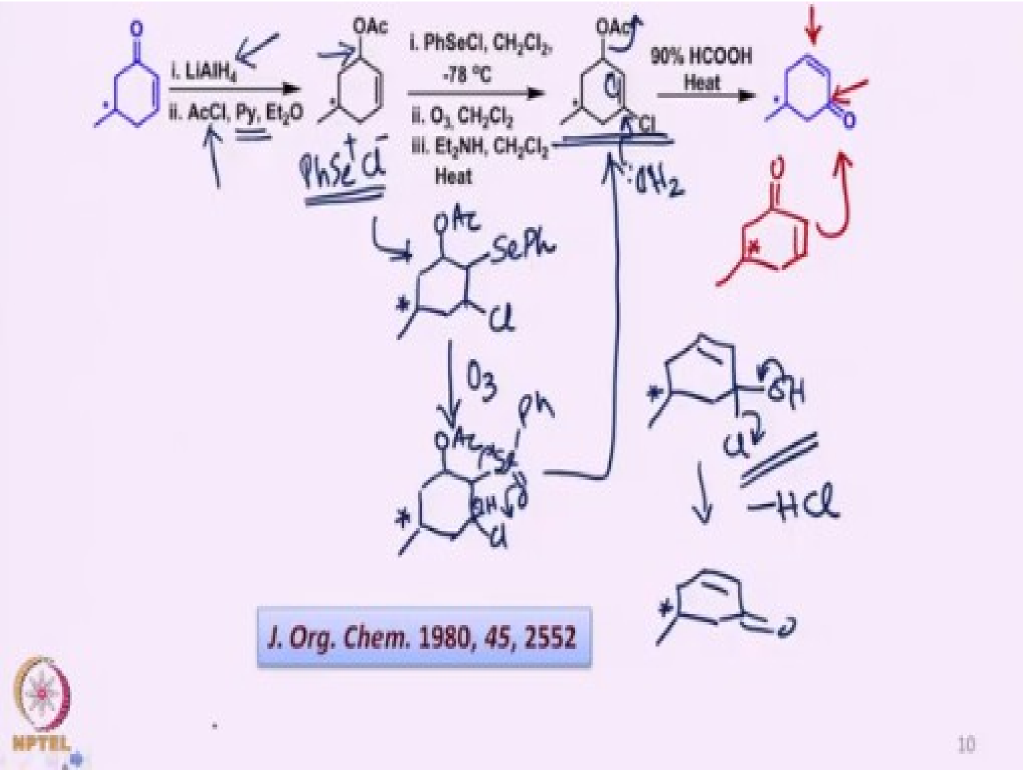

J. Org. Chem. 1980, 45, 2552

Now if one wants to do a simple 1,3 enone to the corresponding inverted 1,3 enone or transposed 1,3 enone, say for example you have this and you want to convert into this, where the ketone position is now changed from this position here ketone was here, now we have made it here. So one other method which was published in 1980 is that we reduce the ketone to the corresponding alcohol here and by lithium aluminum hydride and then you acetylate it by means of acetyl chloride and pyridine or we can use acetic anhydride to form the corresponding acetate.

When this allyl acetate is reacted with phenyl SeCl what one forms is an intermediate of this type chlorine here and Se phenyl. So essentially the double bond has interacted with phenyl Se$^+$ and Cl$^-$ to form this particular reagent that reacts to form this where selenium comes in on this position and Cl comes on this position. Now when ozone is reacted to, ozone is allowed to react to this intermediate what formed is selenoxide.

And you have one hydrogen here this undergoes elimination to form basically this. So you have an elimination here to give this double bond and then this double bond is reacted with 90% formic acid, so you get hydrolysis in this way and with the loss of acetate and this undergoes then loss of hydrochloric acid to form the corresponding ketone like this. So when formic acid and water and the acidic condition react with this particular compound.

There is an addition of water followed by that means you have water reacting like this and this going like this under the acidic conditions and of course you lose acetic acid. So, you form the corresponding this intermediate which is an unstable intermediate and looses hydrochloric acid to form the corresponding enol. So we will stop it at this stage here and then catch it up for the next topic in our next lecture.

So you go through these into important transpositions of 1,2 ketone transposition and enone transposition by both the ways one is substituted, one as well as the other non-substituted one and we will then look at some other oxidative transformations later on. So thank you.