

Molecular Rearrangements and Reactive Intermediates in Organic Synthesis

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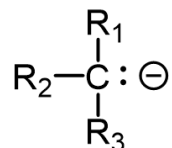
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Lecture 06: Carbanion

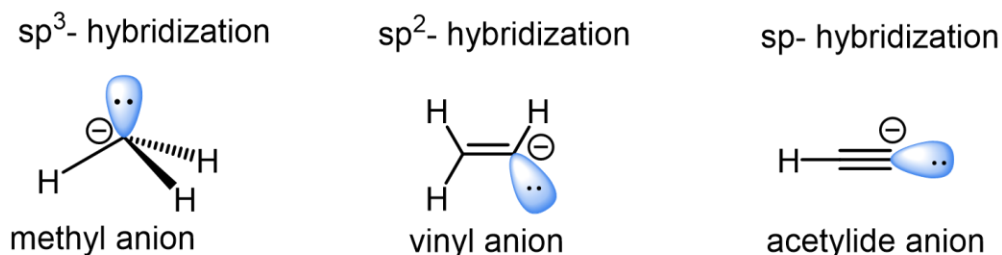
Welcome back to this online NPTEL certification course in molecular rearrangement and reactive intermediate. Last couple of classes we have learned about the carbocation, we learned about their structure, their reactivity and various different rearrangement reaction using carbocation. In today's class we are going to learn about carbanion. So, we are going to learn about first the structure and stability of carbanion. We are going to learn about the correlation of the pKa and the carbanion they are different pKa their stability, their reactivity. We are going to talk about some of the rearrangement reaction as well.

So, if you talk about the carbanion then the first thing is comes to our mind that the carbon with a negative charge. So, now if you think about so, if you talk about the carbon with a negative charge then if you remember when I was talking about carbocation I told you from this methane if you get as a H minus then you generate this CH₃ plus. Now from methane if you take a H plus then you generate CH₃ minus So, this is will be the methyl carbanion. So, now, you can see the carbanion what will have a carbon with a negative charge, it attached with it forming 3 other bonds. So, totally the carbon having the 8 electrons 6 are the bonding electrons and then there will be 2 electrons which are not bonding electrons and then carbanion are much more reactive species.



- A negatively charged carbon atom is called a carbanion.
- Carbon is tetravalent having three bonds and one lone pair of electrons in the outermost shell of carbon.
- They are commonly involved in nucleophilic reactions.

Now you can see there are in lot of different type of reaction which are done with carbanion. And now we are going to talk about different type of carbanion. So, if it is happening through this as I said from the from methane we call it methyl anion. So, now if you talk about this methyl anion geometry, so it is carrying a sp^3 hybridization. So, it has a pyramidal shape here. So, it has this electron pair which is carrying one of the sp^3 orbital actually have this electron pair there and it is forming the 3 bonds with the 3 hydrogens. Now, once you go to the vinyl anion now this will be a sp^2 hybridized, once you go to the acetylide anion it will be sp hybridized. So, what is happening in case of sp^2 and sp hybridization. So, they are actually have a planar structure, but in case of sp^3 it has a the pyramidal structure.



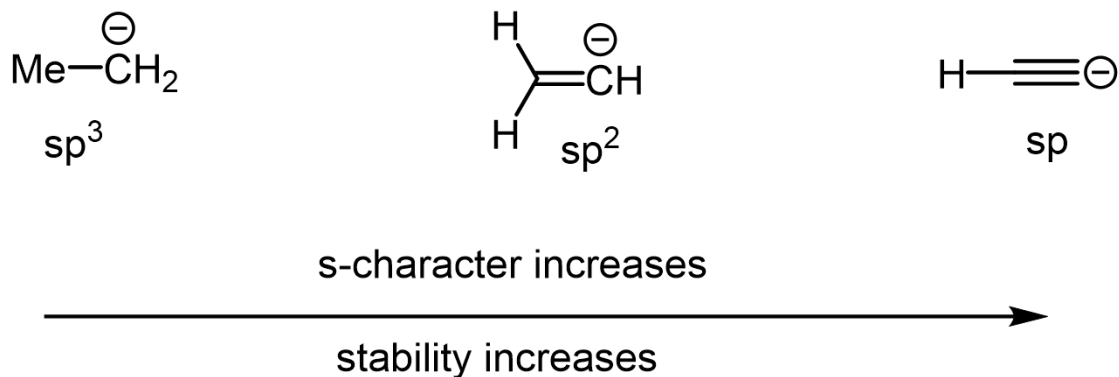
- Alkyl carbanion is sp^3 hybridized and pyramidal geometry whereas allyl and benzyl carbanion are planar with sp^2 hybridization.
- It is diamagnetic because all the electrons in the outermost orbit of carbon are paired.
- Vinyl and acetylide carbanions are sp^2 and sp hybridized respectively.

Now, we are going to try to understand about their stability. Now, going from sp^3 to sp^2 to sp what is happening they are the percentage of s character is getting increased. As the percentage of s character getting increase what is happening the electronegativity of the corresponding carbon is getting increased. As the electronegativity of the carbon is getting increased it has a tendency to attract the electron density more as it is stabilizing the electron density more that is why this carbon will be more stable compared to this one compared to this one. Now, we can see we can talk about the stability of a primary versus a secondary carbanion and secondary carbanion versus a tertiary carbanion.

So, what is happening here going from primary So, this is a primary to a secondary to a tertiary what is happening we are seeing that the stability actually getting decreased. So, going from primary to secondary to tertiary or if you say from tertiary to secondary to primary what we are seeing the stability getting increase. As the number of methyl group is getting increased from primary to secondary to tertiary what is happening the plus I effect

- Factors that decrease the electron density of carbon increase its stability.

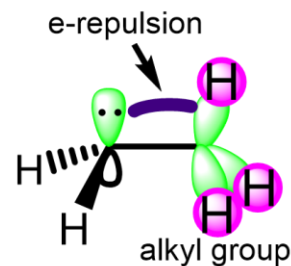
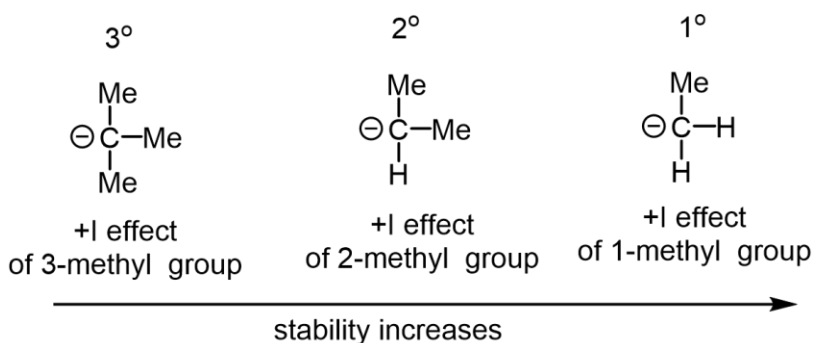
1. Electronegativity of carbanionic carbon:



will be more as number of plus I effect is getting increased the electron density will be more on the on this tert-butyl carbanion. So, as the more electron density will be there it will be more reactive, but it will be less stable.

2. Inductive Effect:

- -I effect increases the stability.
- Stability decreases with the increase of +I effect.

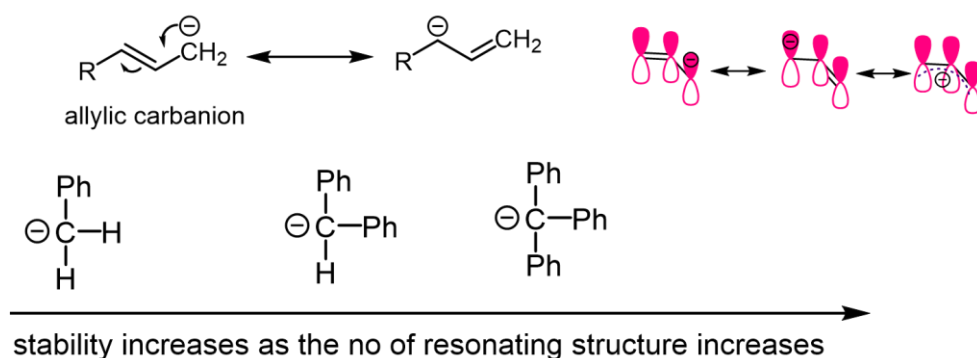


Now, once you bring some sort of a double bond or a phenyl ring like a benzylic or allylic, in that case we have learnt in case of carbocation also that there will be a stabilization through resonance. So, we can able to draw the resonance structure here. So, to show you that allylic carbonyl will be getting stabilized through this resonance structure and we can able to draw the resonance structure here as well. Very similarly for benzylic carbanion also the resonance structure is giving this corresponding benzylic carbanion better stability. Now, once you go from a mono benzylic like this one, di benzylic and then tri benzylic. What is happening? Going from mono to di to tri the

stability actually getting increased. Why that is happening? Because the number of resonance structure to stabilize this carbanion is getting increased from a mono to di to a tri benzylic carbanion.

3. Resonance:

- If a double bond is located α to the anionic carbon stability increases due to the resonance effect.
- This effect increases the stability of allylic and benzylic carbanions.

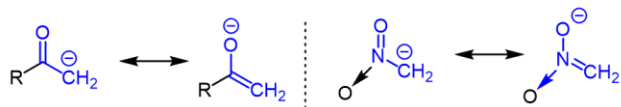


So, now we are going to talk about the carbanion where getting stabilized if there is an electron withdrawing group which is attached to this carbanion. So, here we have a carbanion which is alpha to the carbonyl group. ok. We have already learned this type of chemistry that once you have carbonyl group you treat a base you generate this alpha to the carbonyl carbanion and this is getting stabilized through the carbonyl group because through the resonance. It could be other electron withdrawing group like nitro, nitro can also stabilize this corresponding carbanion. Then means if you have electron withdrawing group then that particular carbanion will be more stabilized. Stabilization can be done by sulfur and phosphorus. So, we have learned about the sulfur ylide and the phosphorus ylide chemistry. If you remember at the time we have learned that the sulfur or phosphorus will be going to carry a positive charge and the corresponding carbon which is attached going to carry a negative charge. And that negative charge will be stabilized by sulfur or phosphorus because they have the vacant d orbital.

So, this electron can be transferred to the vacant d orbital to stabilize. Then the stability through the aromatic carbanion as I mentioned that is if you have a benzylic or some sort of aromatic it has a part of aromatic things attached then it can also stabilize through the resonance. Also if it is have a something like that if the carbanion will be part of an aromatic system. In that case like this cyclopentadienyl carbanion. So, which is getting stabilized it is a 6-pi electron system is getting stabilized because of the gaining aromaticity.

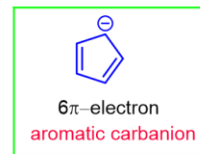
Now we are going to talk about some of this example here where you can see although this is a carbanion here, but the problem is this is this is anti-aromatic compound. So, compared to this one which is aromatic ok. So, aromatic will be a carbanion which is actually

4. Stabilization by C=O, NO₂, CN functional group:



5. Stabilization by Sulphur and Phosphorous:

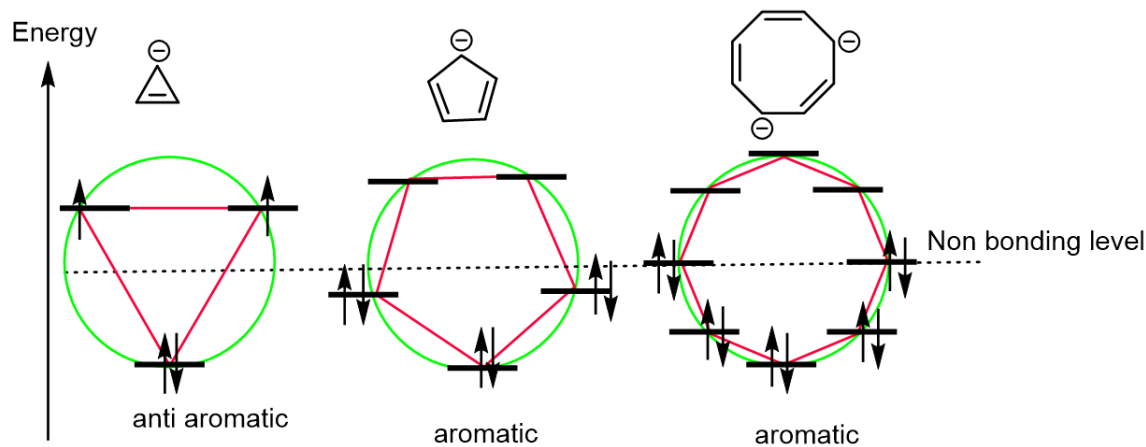
- Carbanion adjacent to sulphur or phosphorous can be stabilized through the delocalization of the electron into the vacant d orbital of these atoms.



6. Stability of Aromatic Carbanions:

- If anionic carbon is part of an aromatic system then it is known as aromatic carbanions and these are the most stable carbanions.

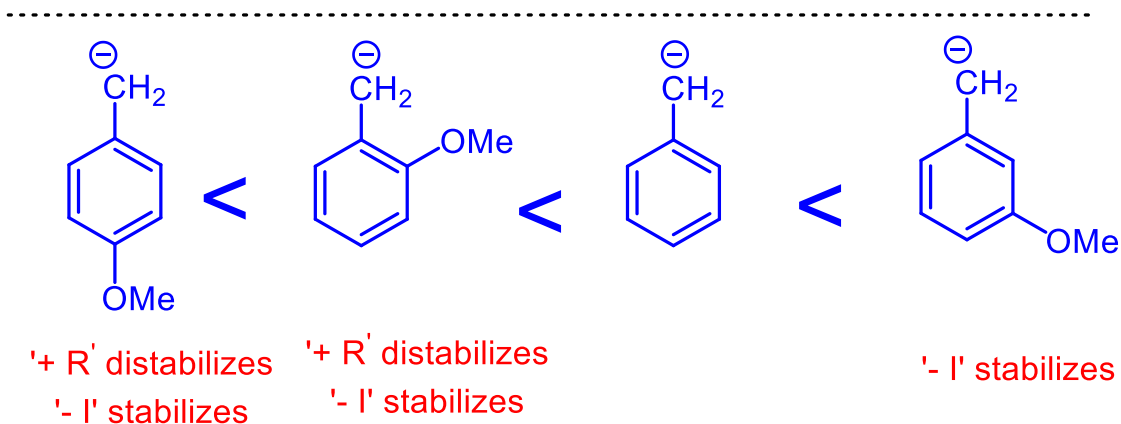
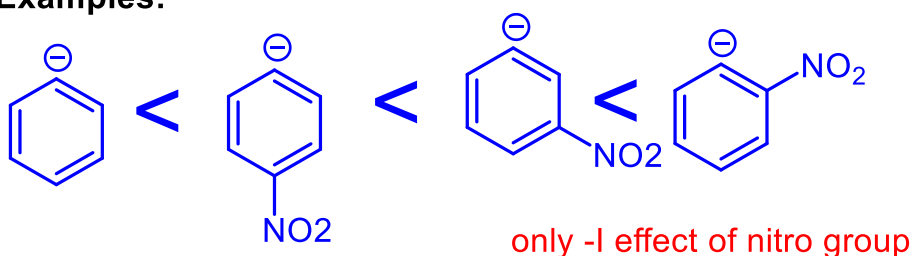
forming aromatic compounds will be more stable compared to the other carbanion which is forming a anti-aromatic compound ok. So, the stability will be aromatic, non-aromatic and anti-aromatic.



- Stability order: aromatic > non-aromatic > anti aromatic.

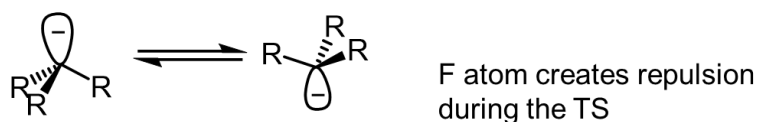
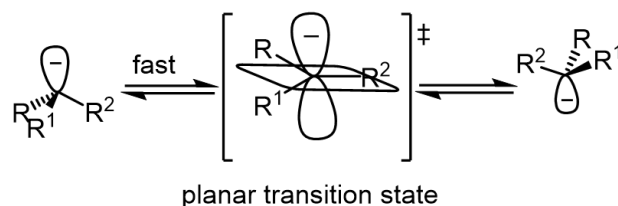
And now we are going to talk about the stability if you have an electron withdrawing or electron donating group. Suppose the carbanion is from here now the thing is now in case of benzene ring if the benzene ring will have attached with the electron withdrawing group versus electron donating group what is going to happen here. Now depending on the substitution of the nitro group you can see that in these cases where the nitro group is ortho to the carbanion is going to stabilize more through the minus I effect. So, now you can see there that in case of -OMe group here what is going to happen here? The -OMe group can have a plus R effect and a minus I effect. So, the plus R can actually destabilize the carbon ion and minus I is going to stabilize it. So, that is why you can see these particular compounds where your plus R is not operating only the minus I is operating is actually more stable compared to others.

Examples:



So, now we are going to talk about the other important factor is called the pyramidal inversion of carbanion. So, as the carbanion are isoelectronic to the ammonia and we have learned about the pyramidal inversion there which actually what happened is it actually goes for an inversion here where you can see the configuration which was here actually going to form the corresponding enantiomer after the pyramidal inversion.

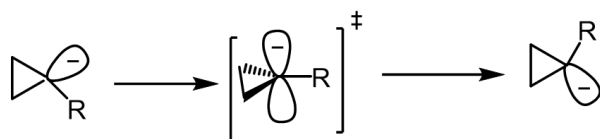
- sp^3 -hybridized carbanion (isoelectronic with NH_3) undergoes pyramidal inversion.
- pyramidal inversion allows its enantiomers to racemize



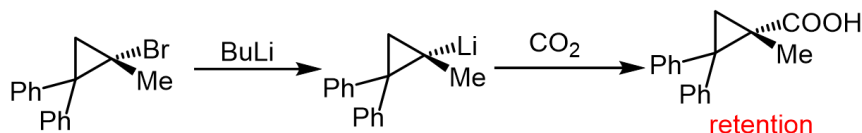
R = H; barrier = 2 kcal/mol
 R = F; barrier = 120kcal/mol

So now we are trying to learn that that while this inversion happens it actually goes through a planar transient state. So that means if it is going through a planar transient state here that means this R, R¹ and R² has to get some sort of a planarity to go to the corresponding inversion product. Now, you can see here if R equal to H the barrier for the pyramidal inversion is 2 kilo calorie per mole. Once R equal to fluorine the barrier is 120 kilo calorie per mole. So, why such a different in the barrier for this pyramidal inversion? Because during the transition state as it has to achieve the planarity there will be repulsion between this fluorine atom. As there is a repulsion because of the fluorine has this the lone pair which can repel each other and that will not allow it to bring to the planarity, that is why the barrier is higher here.

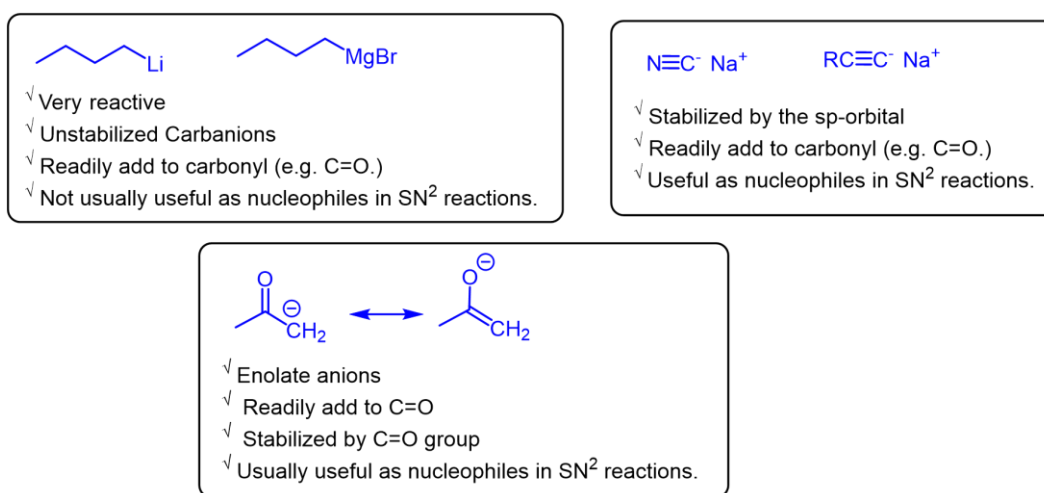
- Cyclopropyl anions and vinyl anions are generally considered configurationally stable.
- The transition state is highly strained therefore the slow rate of inversion.



sp^2 hybridization at transition state
 ideal angle 120° .
 But here it is 60° .



We are going to learn about other systems also there will be a problem. So, now, we are not talking about the lone pair repulsion, we are going to talk about some strain system. Now, if it is a cyclopropyl anion, now that the cyclopropyl has a bond angle of 60 degree. Now this anion to go for inversion it has to achieve a planarity to that it has to come to a angle of 120 degree which will be very difficult. to achieve that, that is why the cyclopropyl carbanion mostly do not go for this pyramidal inversion. And here is an example here, if you can start with this particular chiral compounds and go for a metal halogen exchange to generate this corresponding lithium, this lithium is still making the retention of this configuration, it can able to trap with CO₂ to the corresponding product. So, what we are seeing that if you are generating a cyclopropyl anion then it is going through a retention, we are not seeing a mixture of R and S.

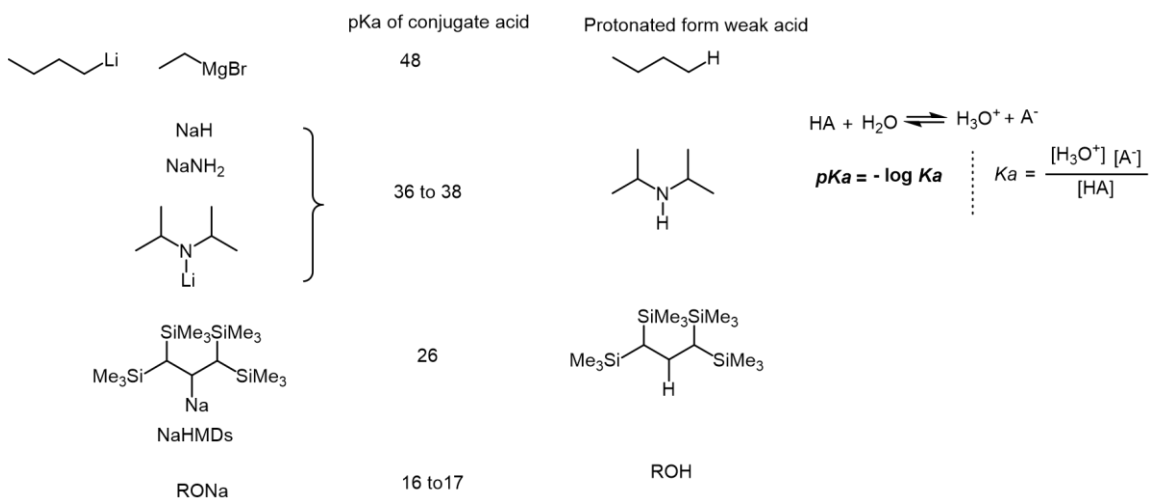


Now, I am going to talk about the types of carbanion. So, there are several different types of carbanion, one of the very reactive class of carbanion are organolithiums and Grignard reagent ok. So, organolithium and Grignard reagents are very reactive, they are very much unstabilized because you cannot see there is any other group attached to them that which can stabilize the carbanion and they can readily act to carbonyl and in many other functional groups and they are not useful for SN². Then I am going to talk about some of the stabilized carbanion like here which is actually carbanion in the SP carbon. As I said because of the higher electronegativity of the sp carbon it stabilize that carbanion and it is can be readily added to a carbonyl group and other functional group and it can also participate in a SN² reaction. The other one is very well known which is the enolate anions. So, anions can be very much stabilized through this carbonyl group resonance and now it can be readily add to carbonyl group and participate in various type of chemical transformations and of course, it go for the SN² reaction as well.

So, now I am going to say these different type of carbanion with their pK_a values. So, now I am talking about a pK_a of a base. So, generally if the definition of pK is a actually

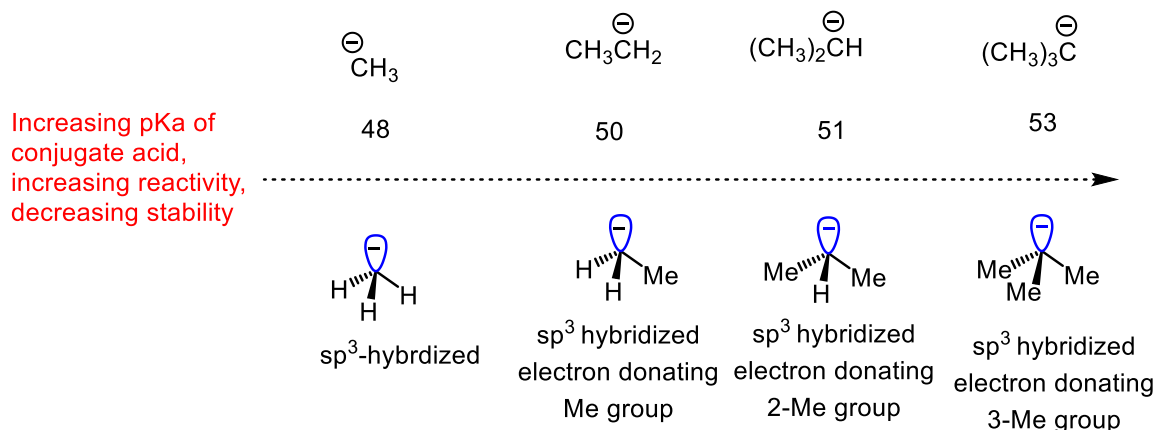
minus log K which is a nothing but the dissociation constant of HA to A minus and H plus. Generally we use pK to talk about that if we say have a pK lower digit that means, it is strongly acidic. In case of base what we try to represent that if a base is very strong then the conjugated acid will be very weak. Like we are talking about a butyl lithium which is a very strong base, now it is corresponding acid which is the protonated acid is butane is a very weak acid. So, we it has a pKa of 48. So, you can understand it is a very very weak acid. So, that means that the conjugate base will be very strong. Similarly, there are the LDA which is a very common base we have seen again have a pKa of 38 because of the protonated form is actually a weak acid. Again for NHMDS and for alkoxide which has a pKa around 16. So, what we are seeing here going from this alkoxide to NHMDS to LDA what we are observing? We are observing the pKa getting increased, because what is happening the base becoming stronger and stronger and stronger.

And we can see here also that we have a methyl carbanion, ethyl carbanion, isopropyl and tert-butyl. What we are seeing here the pKa value getting increased and as the number of methyl group is getting increased there will be plus I effect is will be more so that this type of carbanion will be more electron rich and more reactive compared to them. And then there are other type of carbanion here I told you that particular class of carbanion which is actually in part of the aromatic system which is getting stabilized to the resonance and then we have a carbanion here which is in the sp On the sp carbon then

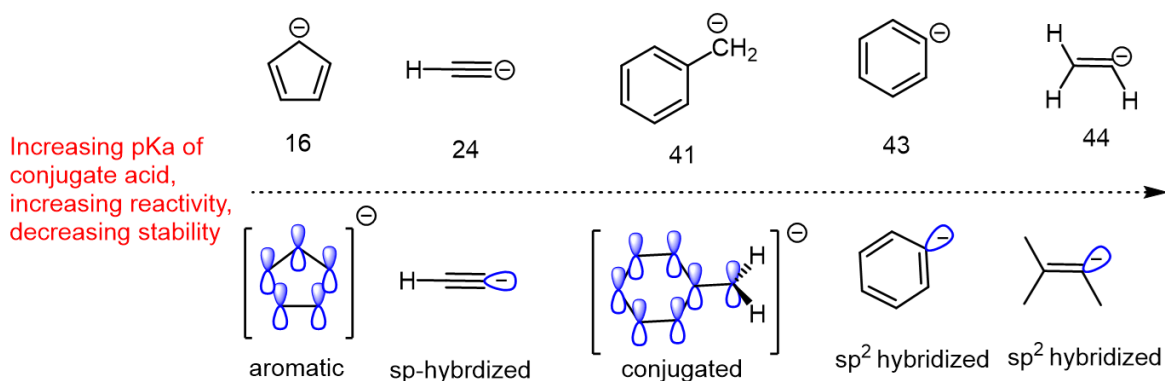


we have a some sort of a conjugations with the benzylic then we have this aryl carbon and vinyl. So, they are the more reactive carbon on here. So, going through this direction what we are seeing we are seeing the pKa value getting increased and the reactivity is getting increased as well. And this is another comparison here why I am putting this

slides here because this is another way to understand that generally we use pKa for showing for acid like you can see the carboxylic acid as a pKa of 5.

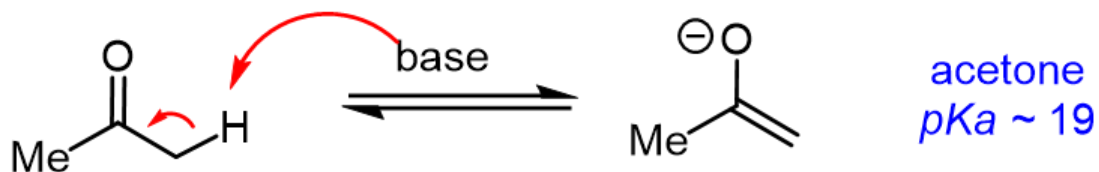
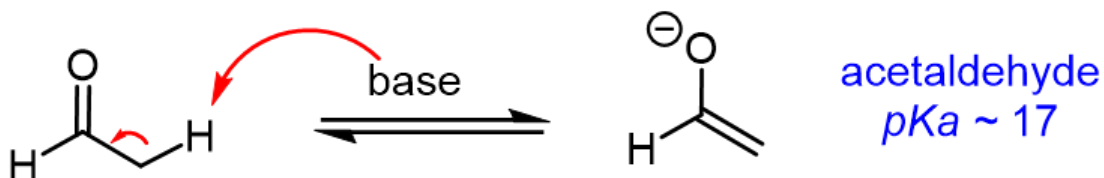
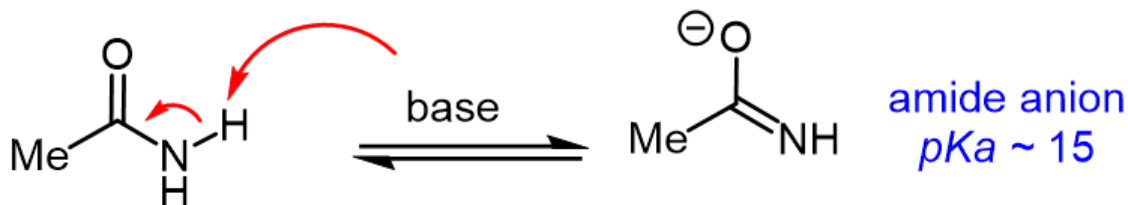
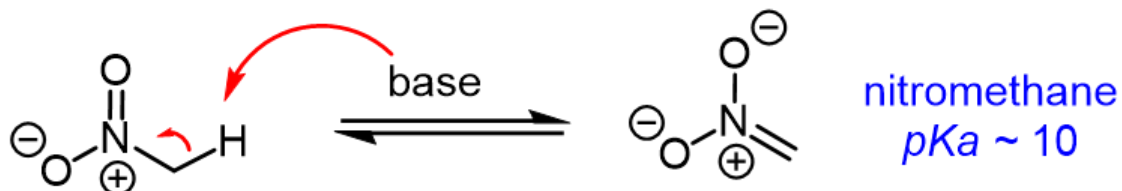
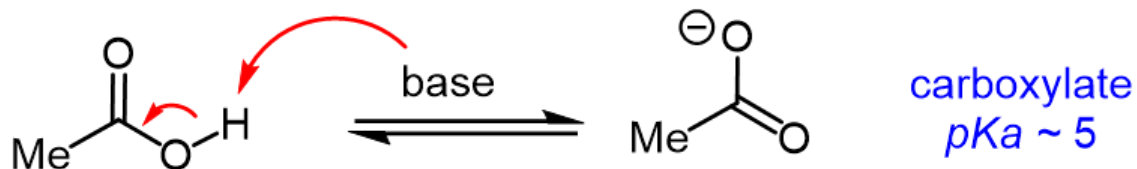


Comparison of pKa with stability



Now if you try to understand that which type of base we need to use going for a deprotonation, then we have to try to correlate the pKa of these type of compounds with the corresponding base. So, suppose we want to use deprotonated nitro methane. So, we know a nitro methane have a pKa of 10. That means, we need to find a base which will be lower than pKa or close to that which can able to deprotonate that. Very similar thing for amide anions and then we have learned about the acetaldehyde and acetone which you always use for different type of reactions and of course, you can use we have a large number of base we can use for this type of deprotonation.

➤ Comparison of pKa of different anions

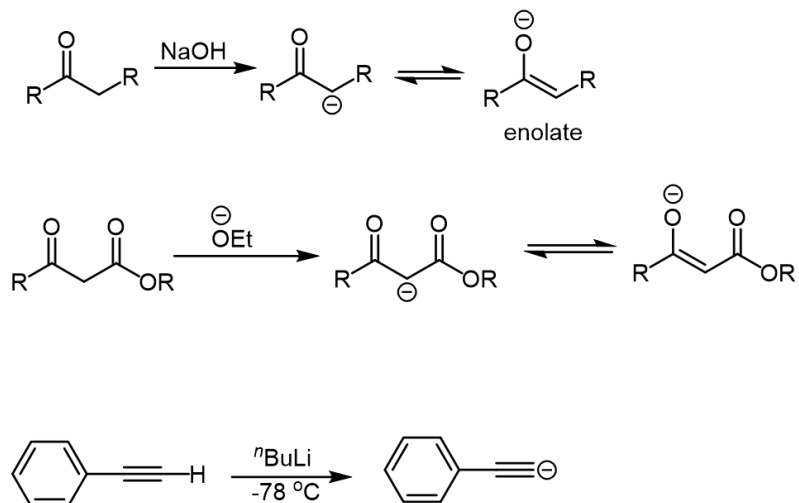


Even using alkoxide or using the HMDS, LDA which are often used for this deprotonation reaction. Here I am going to show you again the same thing which I was telling here, but the important thing is if you have a 1, 3-dicarbonyl. Then the proton here which are very much

acidic because once you abstract this proton then the corresponding carbon ion is getting stabilized here. because there are present of 2 different carbonyl group here because that is actually stabilizing the corresponding carbanion which is forming here ok. So, that in that case you can use a sodium ethoxide that will be enough to abstract this proton because that will have a pKa in the range of 16.

➤ **Proton abstraction:**

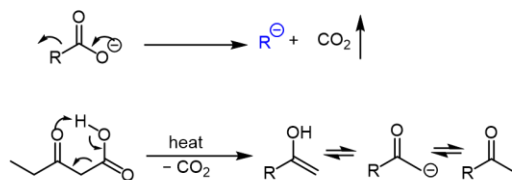
➤ When an acidic proton is abstracted by an appropriate base, a carbanion forms.



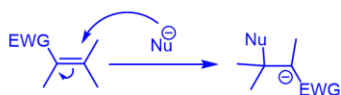
Then you have acetylene like a phenyl acetylene. Now, this acetylene proton has a pK_a around 26 that means, now you have to choose a base which have a pK_a you can see a you have to choose a base which have a pK_a more than that. That means, you have to choose a base which will be something like n -butyllithium which can be able to abstract this proton ok. Of course, you can also use LDA to abstract this proton as well.

➤ **Decarboxylation:**

➤ Decarboxylation of carboxylates can generate carbanions.

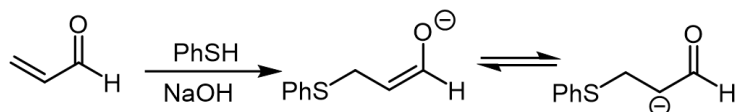


➤ **Nucleophilic addition to alkene or alkynes.**



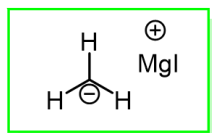
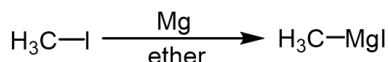
Now, we are going to talk about what are the different methods for the formation of carbanions. So, here you can see that we have learned about these types of things that form from acids once you heat up, particularly from this β -keto carboxylate. So, β -keto acids we call them β -keto acids. So, β -keto acids once you heat up what is going to happen is that they go through decarboxylation to form the corresponding ketone. So, that way what

is happening we are generating a carbanion here which is getting protonated. Then there is another method where you can have a nucleophile to an alpha,beta-unsaturated compound. Like once you have an alpha,beta-unsaturated compound like you have an alpha,beta-unsaturated compound there you are adding a nucleophile. What is happening here? The nucleophile can attack here and if you try to write there that you will be generating a double bond and a nucleophile here which can come back and generate a carbanion here in the alpha position. So, of course, which can get a proton or something here, but so I am talking about generation of this type of carbanion after addition of a nucleophile. And there is an example given here which I was trying to tell you in the previous slide to generate a carbanion. Then the other very common method we use in the laboratory to generate an organometallic compound like organolithium like RLi, RMgX then RZnX and then of course, organocopper and all these different things.

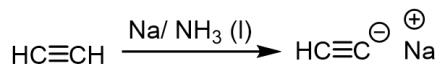


Formation of Organometallic compound:

- **Metal halogen exchange**, such as Li, Mg, Zn, etc. will react with an alkyl halide and form organometallic compounds where carbon is anionic in nature.



- **Deprotonation**

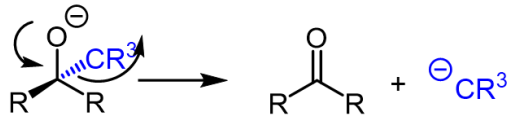


So, I think what is happening in case of organolithium you generally see a metal to halogen exchange happens from corresponding alkyl halide. So, we are going to talk about these types of organolithium, organomagnesium in very details towards the end of this course. We have a particular module which is dedicated for this synthesis and reactivity of organolithium, magnesium and corresponding zinc. So, here are other methods as I mentioned that you can do a deprotonation from acetylene to generate a corresponding carbanion.

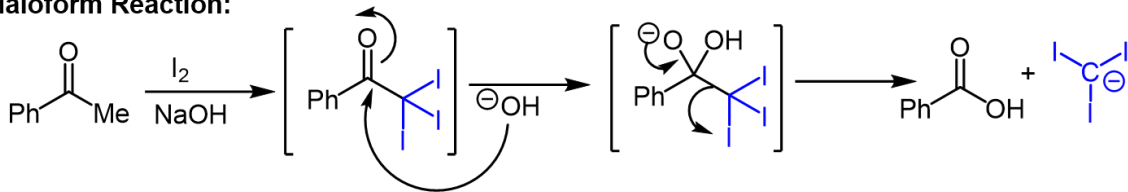
There is another type of method. So, we learn about the haloform reaction. So, in the haloform reaction what we have seen that there is a generation of some sort of a PCC like

Formation of Carbanions:

- When a group or atom departs from a carbon atom with its bonding pairs.



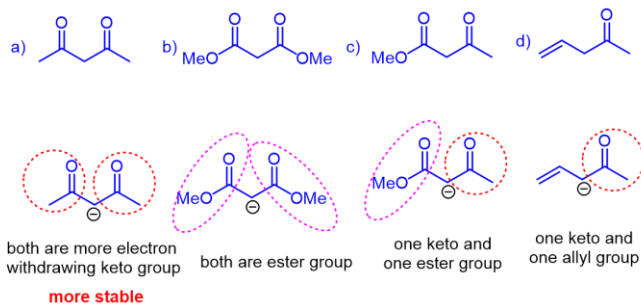
Haloform Reaction:



CR³ minus. What is happening? This particular group is actually getting out taking this 2electron pair this CR³. So, what is happening in case of haloform reaction in case of iodine and base this CH₃ will be replaced by CI₃. So, now, it is the base can attack here because it is getting very reactive to get rid of this as a CI₃ minus ok.

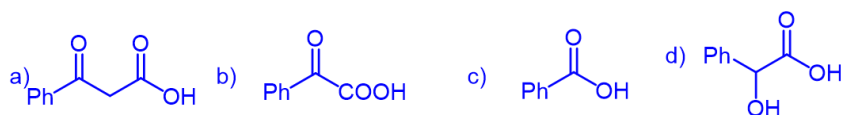
- ❖ Among the following compounds, the one that undergoes deprotonation most readily in the presence of a base, to form a carbanion is

GATE: 2003

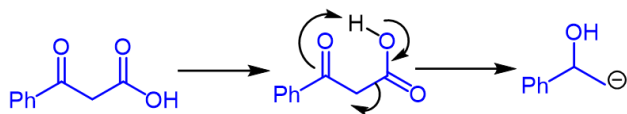


So, that is in case of haloform reaction we can generate this type of carbon So, now, there is a question in the GATE exam that among the following compounds the one that undergoes deprotonation most rapidly in the presence of base ok. So, now, if you see this A, B, C and D in case of A there is two normal compounds. So, in case of B there is a two esters here. So, we are talking about these protons because if the deprotonation happen then it is going to abstract these protons. So, now if there is 2 esters versus 1 ester, 1 carbonyl, 1 carbonyl, 1 type of a double bond. So, then what is happening here. So, this will be allylic versus allylic versus a carbonyl group here. So, now what is happening this will be actually going to. So, this is the compound which undergoes the deprotonation faster because this carbon will be getting more stabilized through this 2 carbonyl group. Then among the following acid which

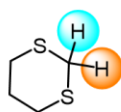
❖ Among the following acid which undergoes faster decarboxylation?



GATE: 2000



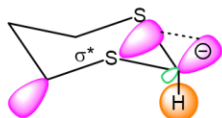
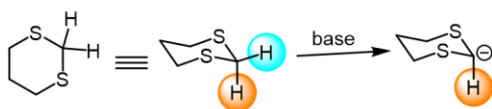
undergoes faster decarboxylation. As I told, you have to look for a beta keto acid that means you have to look for which one is a beta keto acid.



Which proton is more acidic?

1,3-Dithianes

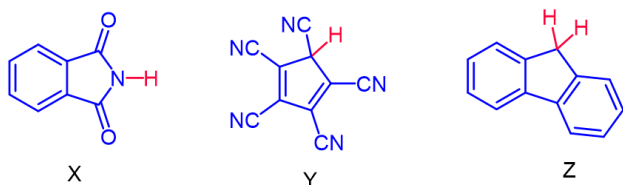
➤ Equatorial H is more acidic because the equatorial carbanion is delocalized into the C-S bond σ^* -orbital.



If you see this is the one actually a beta keto acid as I told you before the beta keto acid only goes for decarboxylation not the alpha. If you heat up alpha keto acid it will not go for decarboxylation. Then there is a question here that if you have this 1,3 dithiane which you always use for protection of carbonyl group for doing some other transformations. So, what is happening if you make this 1,3 dithiane then we have to try to understand there will be in this particular case there will be axial and equatorial proton. Now, which one is more acidic. you can see the equatorial one will be the more acidic. So, that will form the corresponding carbanion because this carbanion is getting stabilized giving electron density to the sigma star orbital of this carbon sulfur bond. So, this is the sigma star orbital which is getting which is giving the. So, which is getting electron density from this carbanion. Then there is another questions in the exam which will be the correct order of pk of the following compounds x, y and z. Now, if you look into x, y and z. So, one thing you have to try to understand that in case of in case of X it is just going to abstract this proton to form this type of carbanion. So, what we want to see first we have

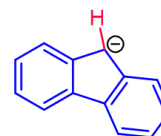
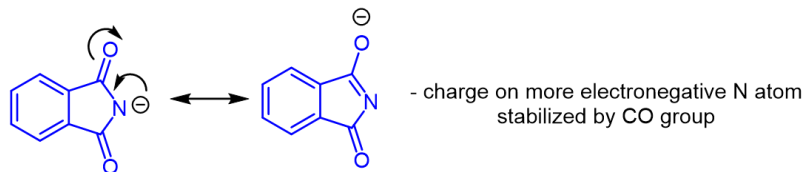
to find out which will be more acidic the pKa will be low and which will be less acidic the pKa will be high and then we

❖ The correct order of pKa of the following compounds X,Y,Z is

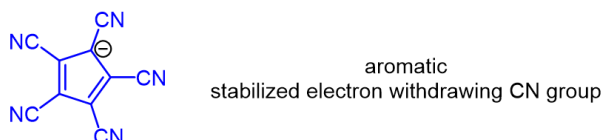


NET: 2016

- a) $X > Y > Z$ b) $Y > Z > X$ c) $Z > X > Y$ d) $Y > X > Z$

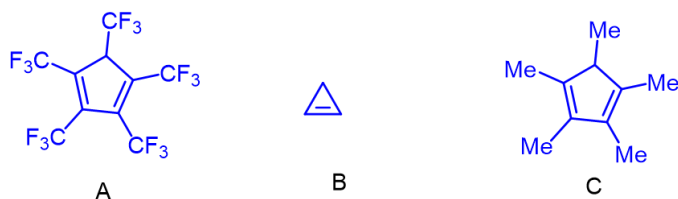


aromatic but less resonance energy



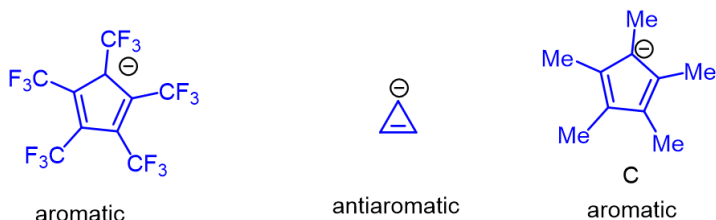
can ordered them accordingly. Now if you think about this particular carbanion which is the Y here after abstracting this proton to generate anion which will be getting very stabilized here because there are 5 cyano group here which is stabilizing that carbanion. So that means, this proton will be highly acidic. So that means, this pKa will be the lowest. So that means, this is the one which will be the last and then if you compare among these two. So, what is happening again if you compare X and Z in case of X this H is attached with the nitrogen. So, you have to understand if the X if the hydrogen attached with a atom like nitrogen or oxygen which can stabilize the corresponding carbon ion with having a carbonyl group attached with it, then it is going to be the one which will be the next acidity that means, this will be the number X here and then the next will be the Z ok. So, this will be the right answer. The correct order of acidity of the following compound here they are asking about acidity not pKa.

❖ The correct order of acidity of the following compounds A-C is



NET: 2011

- a) $B > C > A$ b) $C > B > A$ c) $A > C > B$ d) $A > B > C$

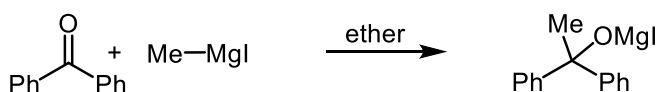


So, you have to be careful what they are asking. If they are asking acidity we will order them if they are asking pKa then we have to order them accordingly. So, based on acidity now first thing is we generally learn that if you compare acidity we have to go to corresponding carbanion and find out their stability. Now, if you find out this carbanion of course, this is aromatic compound, this is anti-aromatic compound and this is also aromatic. Now, if you compare between these two then you can see this is aromatic, but there is a negative charge which is getting stabilized because of this CF₃ group here. So, this will be the one and I think this is the proton will be highly acidic. So, the order will be A, C and B.

Reaction involving carbanion as nucleophile

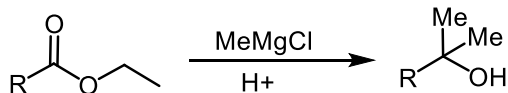
Nucleophilic addition:

Addition to aldehyde or ketone:



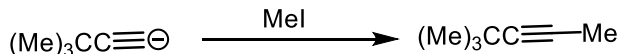
Nucleophilic acyl substitution:

Addition to ester or acid chlorides:



Substitution Reaction:

Addition to alkyl halides:



Now, we are going to talk about the reactions of carbanion as an intermediate. Of course, we are going to talk about a lot of these reactions of corresponding Grignard and lithium as I said in a different module, but again these are very reactive and act to a carbonyl compound to form this type of tertiary alcohols here. It can act to an ester once you act to an ester not only single methyl magnesium works, it actually two of them are here. Because it first forms a corresponding carbonyl then another methyl magnesium chloride attacks here to form this corresponding alcohol. It can go for a soft solution if you have a carbon and it can go for a soft solution to form this corresponding product.

And then I think there will be a lot of chemistry which was done of course, using the enolates which is the first it will be abstracting this proton as I was telling you and to formation of this. So, once it is formation from here once it is going for the corresponding

So, in this class I try to talk about the carbanion stability. and then which one will be more stable which will be less stable and then I talk about the different method of generation and in the next class I am going to talk about more about the rearrangement. And these are the reference very similar books which I mentioned in the previous class and thank you for coming to the class. I am looking forward to see you guys in the next class.