Molecular Rearrangements and Reactive Intermediates in Organic Synthesis

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Lecture 40: Organozinc

Welcome back to this NPTEL online certification course in molecular rearrangement and reactive intermediates. In the last couple of classes I talk about the organolithium, organomagnesium and in the last class I talk about organocopper and the today's class I am going to talk about organozinc. So, organozinc is also very important and you will find lot of the name reaction.

So, I want to start with the introduction and some of the structures and some of the different type of organozinc compounds, their preparation. What are the different method to prepare them, then I am going to talk about the reaction of organozinc compounds. So, first thing is the discovery.

Again, I think you know before I talk about any of these organometallic reagent. Now, I start with what is the first compound isolated and what is the timeline. So, again you are seeing that all these organometallic compounds I talk about organocopper and you have seen before the organolithiums and everything it was done in the 18th century. So, you have to understand that these types of organometallic compounds are present So, we found out in a long back and there is a rich history for this organometallic compounds.

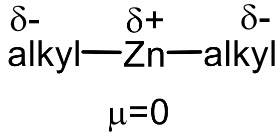
So, Edward Frankland prepared the first organozinc compound called diethylzinc. If you have not use this in the laboratory, this is a very volatile and a pyrophoric colorless compound. So, once you take this diethyl zinc and outside the air it will start catching fire. Again you can see here we are talking about a organozinc, again from the definition of organozinc there will be a zinc with organic part. So, this is a diethyl zinc it was synthesized from two equivalent of ethyl iodide and zinc.

$$2EtI \ + \ 2Zn \xrightarrow{\Delta} Et_2Zn + ZnI_2$$

So, it is from a zinc metal. Again, we are going to understand about this part little bit that what type of zinc and what are the different variation. Again, organozinc cases we are saying that zinc is (+2) oxidation here mostly and then it can adopt a different type of octahedral, tetrahedral and penta-coordinated geometries are well known. So, these are the different type of coordination geometry well known with organozinc.

And you can see the coordination geometry are guided by the electrostatic and steric interaction.

So, these are the two important factor which guide it will be octahedral, tetrahedral or the penta coordinate geometry. And again, 3D orbital of zinc is filled. So, the ligand field does not exist. I think if you know about the ligand field theory. The dialkyl zinc is monomeric with a linear coordination .



$$\overset{\delta-}{\text{alkyl}}-\overset{\delta+}{\text{Zn}}-\overset{\delta-}{\text{alkyl}}$$

$$\mu=0$$

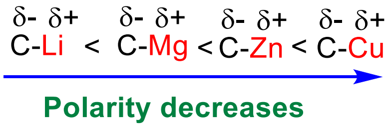
At the zinc atom possesses zero dipole moment you can see there is dialkyl zinc. So, it is possesses zero dipole moment So, now we are going to talk about the different things. So, here it is mentioned it is soluble in non-polar hexane solvent and it has a low affinity towards the etheral solvent. So, now we are going to learn about the preparation. We are going to see majorly the tetrahedral furan, that was used in the tetrahedral furan in the lab for the synthesis organo zinc also diethyl ether.

Sometime you will see the some sort of non polar solvent, but majorly you will see this type of etheral solvent. Again, the bond between the carbon-zinc, so again I think every time when I talk about this type of organometallic reagent, I talk about these important things, the difference in electronegativity. Because once you go from organolithium from Grignard to copper to zinc, in this direction what is happening?

C-M bond	Difference in electronegativity	% of ionic character= $\frac{E_C-E_M}{E_C} * 100$
C-Li	2.5-1.0=1.5	60
C-Mg	2.5-1.2=1.3	52
C-Cu	2.5-1.9=0.6	24
C-Zn	2.5-1.65=0.85	34

The difference in electronegativity between carbon and metal. So, this difference of electronegativity is getting decreased.

So, as the electronegativity is getting decreased, the polarity also getting decreased.

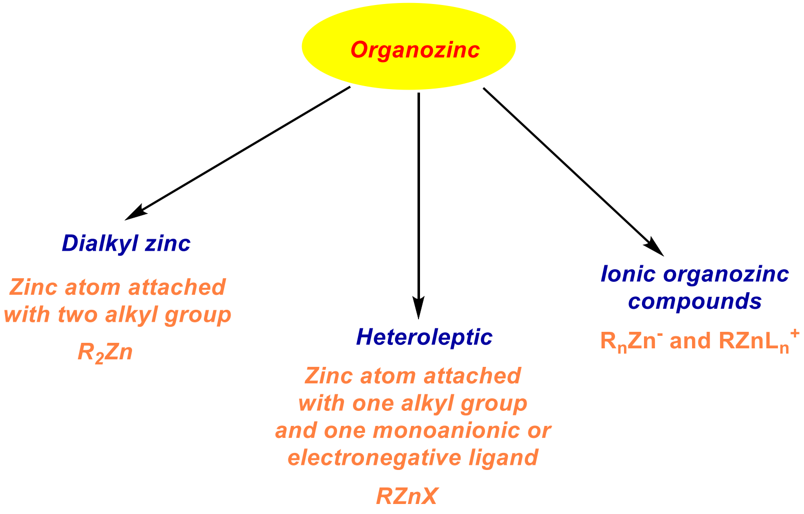


$$\overset{\delta-\ \delta+}{\text{C-Li}} < \overset{\delta-\ \delta+}{\text{C-Mg}} < \overset{\delta-\ \delta+}{\text{C-Zn}} < \overset{\delta-\ \delta+}{\text{C-Cu}}$$

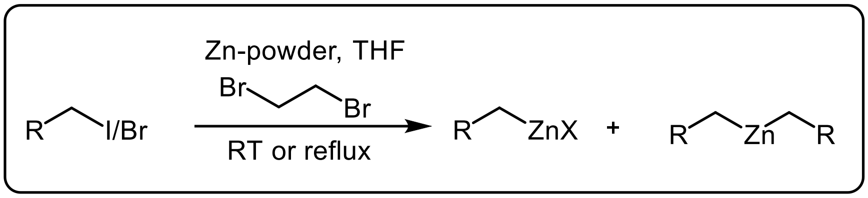
So, the polarity decreases going from lithium to magnesium to zinc to copper. So, all the other side what is getting decreased the percentage of ionic character. So, as the percentage of ionic character getting decreased. The organolithium will be the highest ionic character. Of course, the organosodium or organopotassium, will be more compared to this.

But in compared to the zinc, I think, the lithium has more percentage of ionic character. So, lithium will be more stronger in a reagent, in compared to zinc. And the zinc-alkyl bonds will be covalent bonds mostly. So, now we are going to talk about that there will be three different type of organozinc compound. we are going to deal in the today's class.

One is dialkyl zinc, you are going to see this particular class that you have a zinc with a dialkyl group here, you have a heteroleptic. So, zinc is attached with a one alkyl group and another one a mono anionic or an electronegative ligand. So, that is called RZnX, you going to see this class also and then there will be ionic organo zinc compound. So, this means there will be a charge, there will be negative charge on zinc. You have seen some of this diionic compound in case of copper.



So, first thing if you are making zinc, generally you know this is the condition used. So, it used in the beginning, now there is better method. If you take alkyl bromide or alkyl iodide, if you take a zinc dust. So, we take a zinc dust from a bottle most of the time that zinc dust is not activated, because what is happening we always menti in the preparation as a zinc powder. But in this zinc powder there is lot of times zinc oxide was there because over the time when you stay there it become a zinc oxide.



Zn powder can be activated by stirring with dilute HCl, then washing with distilled water,ethanol, and absolute diethyl ether before rigorous drying. This procedure removes oxides from the surface of zinc

Catalytic amount of iodine can activate the Zn-powder as well

So, there is a zinc oxide layer again this is some sort of a heterogeneous reaction happening here. So, to remove this zinc oxide layer sometime. What we do we start this with a dilute HCl and washing through distilled water, ethanol and absolute diethyl ether before a rigorous drying. This procedure removes the oxide from the surface of the zinc. So, that is the one thing we do before we start the organozinc synthesis.

The next thing we do we add some catalytic amount of this dibromo ethane. Again, why we add sometime this dibromo ethane or sometime we can also add iodine. Again you know what is the idea here, once adding these type of things this can forms the corresponding zinc bromide and ethylene. And in case this dibromo ethane and if use the corresponding iodine it can form the corresponding zinc iodide. After forming the zinc iodide or zinc bromide, then reaction is getting started.

So, that can help the reaction move fast. So, that is why people use this as a additives. Now there are the dialkyl zinc synthesis can be happen from the Grignard reagent. So, now we are talking about zinc dust. So, zinc dust was used as a source of zinc.

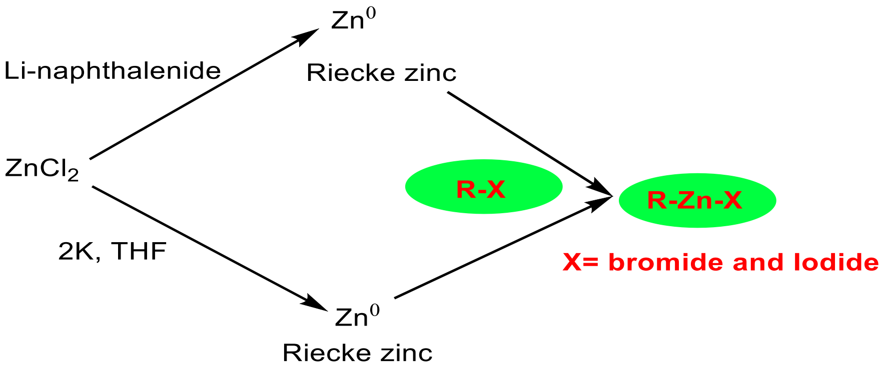
Now we are talking about zinc chloride. So, if you have a zinc chloride as a source of a zinc, you can treat with a organolithium or a Grignard that will end up making this corresponding compounds. So, if you treat with the corresponding Grignard reagent. then you end up getting to this dialkyl zinc. I am going to talk about also the reaction with the organolithium as well.

And there is another thing, from zinc chloride, can you make the oxidation state of Zinc is zero? That is the what we need? We need the zinc zero oxidation state for formation is organozinc reagent from this corresponding alkyl halides, which I talked about in the last slide. So, can you make a more reactive zinc reagent? That is called a Riecke zinc. How that was, prepared? That was prepared from a zinc chloride using lithium-naphthalenide. So, about the lithium-naphthalenide? Which is going to reduce the corresponding zinc chloride to zinc(0) oxidation state. And this is a very reactive zinc.

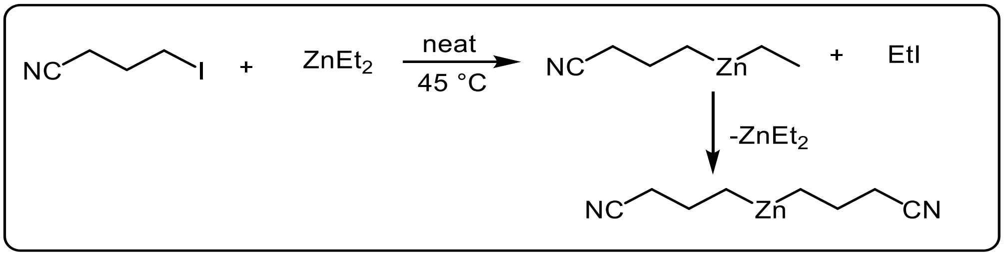
Dialkyl zinc formation:

$$2\ i\text{-BuMgBr} + \mathrm{ZnCl_2} \longrightarrow i\text{-Bu}_2\mathrm{Zn} + 2\ \mathrm{MgClBr}$$

Heteroleptic compound formation:



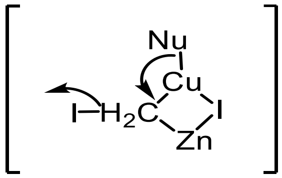
You can purchase the Riecke zinc. And now, if you take alkyl halide or alkyl bromide, the reaction happens very fast to form this corresponding organozinc reagent. Again, there is a functionalized, so this is a another very important thing you should understand. Then I am talking about a functionalized organozinc, I think in the previous class if I talk about a formation of a Grignard reagent or you have seen the synthesis organolithium. I never talk about that you can bring a cyanide in the starting material, because it can also get attacked.



But here in case of zinc you can carry some functional group act as nucleophile itself, so that is the advantage of using a organozinc reagent. And now if you treat a dialkyl zinc here, it is going to react in neat condition, both of them to form. So, there is ethyl in the one side and then this is the functional group in other side and there will be ethyl iodide. And slowly what is going to happen, the another equivalent of this corresponding iodide is going to interact with this and going to form this product. And you can take this for the further transformations.

You can use these for several different transformations. you can have some sort of insertion reaction here, you can have this nucleophile copper. So, that means, from the nucleophile copper if you use I-CH_2-ZnI, here this nucleophile can be there could be various different things here. and then you can able to make.

$$\text{Nu-Cu} + \text{I-CH}_2\text{-ZnI} \longrightarrow \text{Nu-CH}_2\text{-Cu}\bullet\text{ZnI}_2$$



Nu: CN, CH(R)CN, NR_2, S-alkyl, Ar, 2-theinyl, alkynyl, alkenyl

So, this nucleophile can able to have a migration from this copper to here this is a 1,2- shift happening this, for this nucleophile to get of this iodine to form this type of reagent which can be used for several different transformations.

So, you are generating this copper zinc reagent here. Literally organocopper with bind with this zinc iodide. it can happen there is a metal zinc transmetallation. As I was mentioning you have some other things like organotin, organomercury, organolead and antimony. Then they can go for a transmetallation with corresponding zinc reagent.

$$n\ \text{ZnR}_2 + 2\ \text{MX}_n \longrightarrow n\ \text{ZnX}_2 + 2\ \text{MR}_n$$

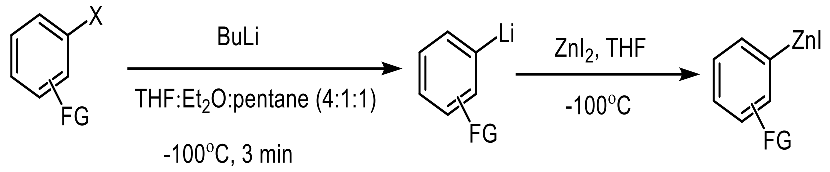
R= methyl, ethyl; M= Hg, Sn, Pb, Sb, As

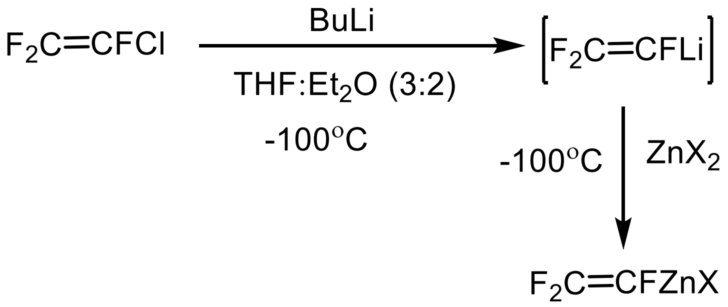
So if you have dialkyl zinc, this type of metal halide, is going to form that can able to go for a transmetallation and it can able to form this corresponding MR_n, that means you have getting different type of these corresponding organotin. Also, you can able to make all these different type of organotin or organolead, from these starting compound dialkyl zinc through the transmetalation reaction. So, again in 1864 Frankland reported that the original zinc compound easily can be prepared from the organomercury compound as well. So, you take organo mercury, also the zinc here, the trans metalation happening to make the organo zinc compound here. As I mentioned at the beginning that if you see that if you have butyllithium and corresponding organolithium here.

$$\text{HgR}_2 + \text{Zn} \longrightarrow \text{ZnR}_2 + \text{Hg}$$

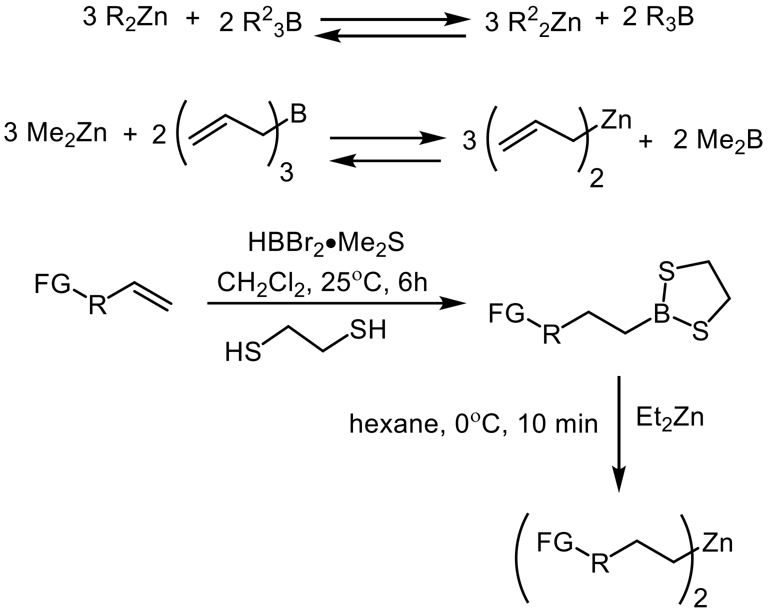
R= methyl, ethyl

Now, this organolithium we talk about this is a called metal to halogen exchange. And we have learned the generation of corresponding lithium, if you treat the corresponding zinc iodide it is going to form this allyl zinc iodide. You know there will be huge difference of the reactivity versus this lithium compounds versus this zinc. Again, you can see here in this corresponding fluorinated compound formation of the corresponding lithium and then it can treat with the zinc iodide to get the corresponding organozinc. It can be transmitted with a corresponding organoboron compound.

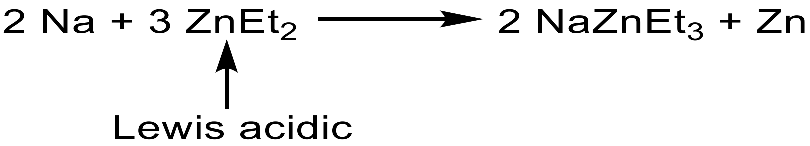




It was also become popular that if you have this organoboron compound which you can synthesize from a hydroboration. After hydroboration once you make this corresponding trialkyl boron compound that react with this dialkyl zinc. After that, the trans-methylation happen, you can see this vinyl group, trans-methylated vinyl group, now the zinc, you can able to make this, divinyl zinc, which can participate in the several different transformations. Another example here, again, there is a olefin here, so first hydroboration, and then you can see there is formation of this compounds. Now, you can have a some sort of protecting group for the boron, and then once you treat with dialkyl zinc, it can participate in a trans-methylation to form this functionalized organozinc compound.



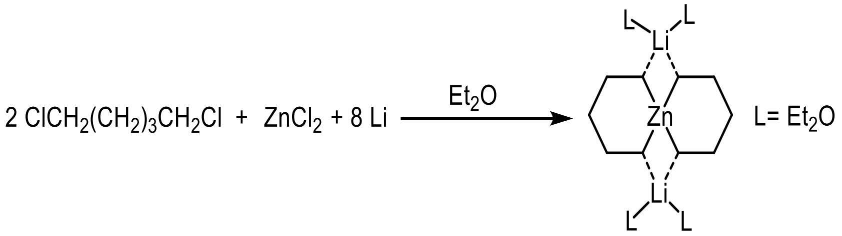
So, this can another way you can bring some functionalizable group. So, you have a functionalizable group like a cyano with a olefin here. So, you can go for a hydroboration and then that can transfer to the zinc to form this corresponding functionalized organo Zinc reagent. could be ionic organo zinc preparation if you take a sodium, sodium can take part in the reaction with dialkyl zinc to form $NaZnEt_3$. So, this can form a negative charge on the zinc with three ethyl group.



$$2\,Na + 3\,\underset{\substack{\uparrow \\ \text{Lewis acidic}}}{ZnEt_2} \longrightarrow 2\,NaZnEt_3 + Zn$$

So, you can see there is a tetra organozincates synthesis. Here happening from zinc chloride, lithium wire and corresponding halides. So, they can form this tetra organozincates because here both the side have a chlorine. So, they can now able to form this corresponding lithium. Then it is react with the corresponding zinc chloride and end up forming this. There is a formation of a triorganozincates as well. So, I think one of the important reaction, I already talk about this that if you have a CH_2I_2 and zinc activations can able to make this or if you treat with dialkyl zinc you can able to make this important species called zinc carbenoids. I think we talk about this carbon chemistry. We talk about the discovery by the Howard Ensign Simmons, that brings to the Simmons-Smith reaction.

So, this type of zinc carbenoid is very reactive, once this zinc carbenoid forms you can see here the mechanism.

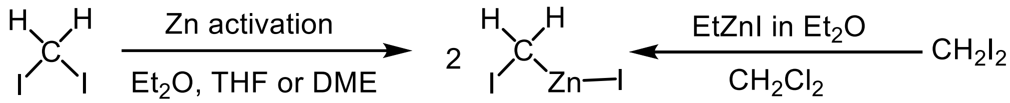


Tetraorganozincates

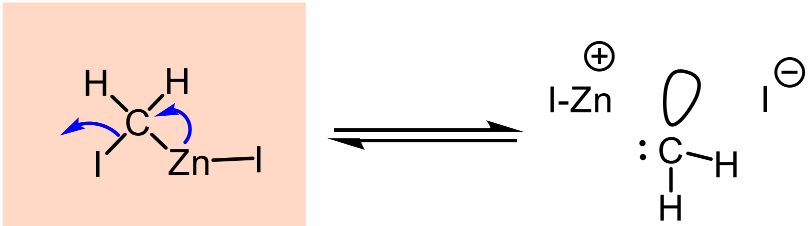
$$(Me_3SiCH_2)_2Zn + K \longrightarrow [(Me_3SiCH_2)_3Zn]K$$

Triorganozincates

Here it is going through this zinc copper you can go into the insertion first to form this type corresponding zinc carbenoid which can take part in the reaction with the olefin. Now, you can see here it is actually generating a some sort of a singlet carbene. So, through a butterfly-type transition state, it can give able to the corresponding compounds. Now, you can see here again the mechanism. If you use this zinc copper couple can be used to generation this corresponding carbenoids or you can use the corresponding dialkyl zinc, which I told you in the last slide.



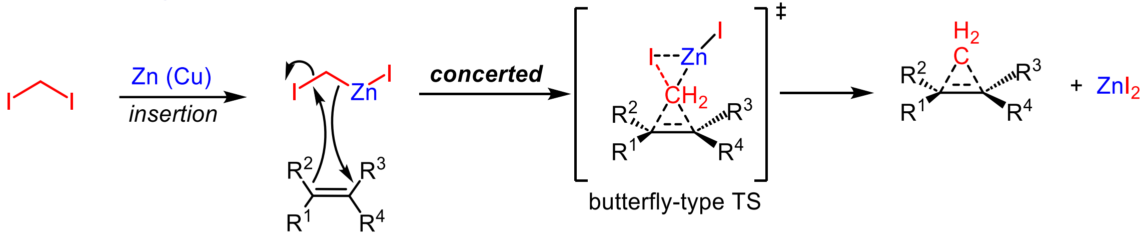
$$CH_2I_2 \xrightarrow[CH_2Cl_2]{Et_2Zn} EtZnCH_2I \text{ and/ or } Zn(CH_2I)_2$$



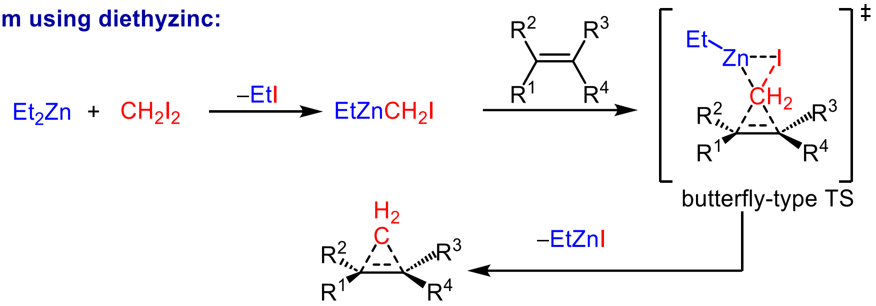
Zinc Carbenoids

There can also generate this type of the zinc carbenoids species which can able to go to the form these corresponding cyclopropane through formation of this corresponding butterfly like transition state.

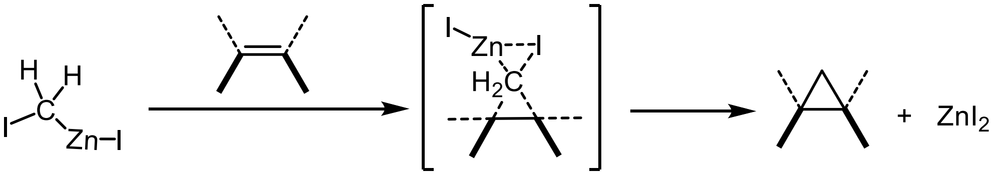
Mecahnism using Zn-Cu couple:



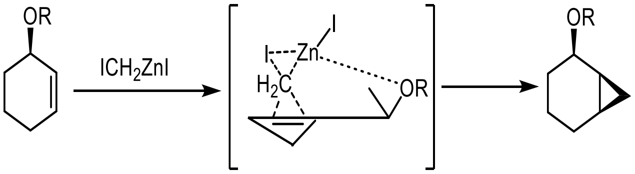
Mecahnism using diethyzinc:



So, here is the example again you can able to make a cyclopropane through this butterfly transition state, you can able to form this corresponding cyclopropane here. So, there is a example here that if you have a oxygen here I think I told you lot in the carbon part. So, you can go back to that part we talk about several different examples. So, that is why I am not discussing any more example after this you can see have oxygen which can coordinate with the zinc.



Butterfly transition state

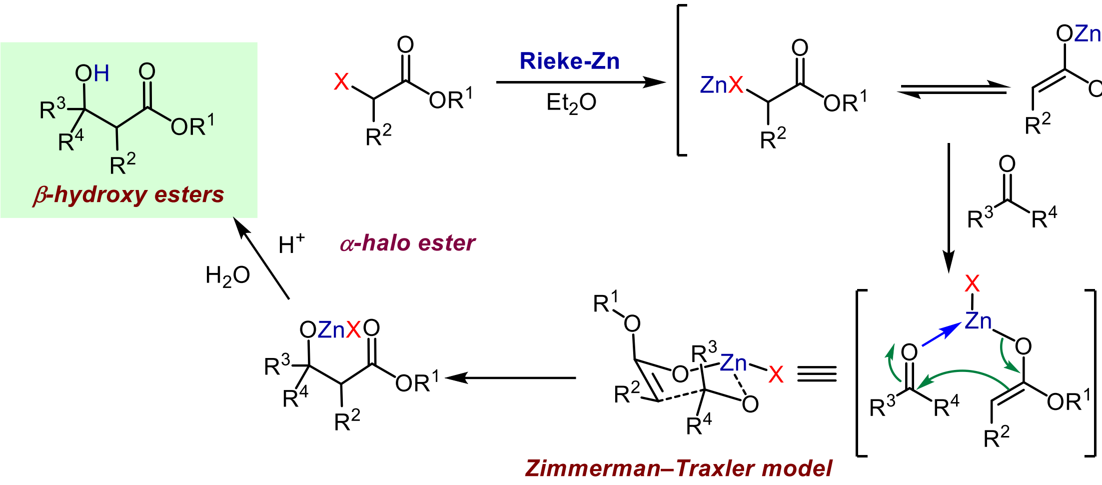


Then it can allow the cyclopropane formation on the same phase of this OH-group, that is why you end up getting this product as a major product, not this is down side, this is same side of this oxygen. One of the other important name reaction is the Reformatsky reaction. We learn about this lot and I think this comes also in the Net, Gate and other exams. So, if you have alpha halo esters.

So, these are alpha halo esters. Once you use the Rieke-zinc with them it is going to form first you can see there is a halogen. So, it is going to alkyl halide. So, it is going to form the corresponding zinc. Now you can think about if you have this and now you can think about this two molecules of it.

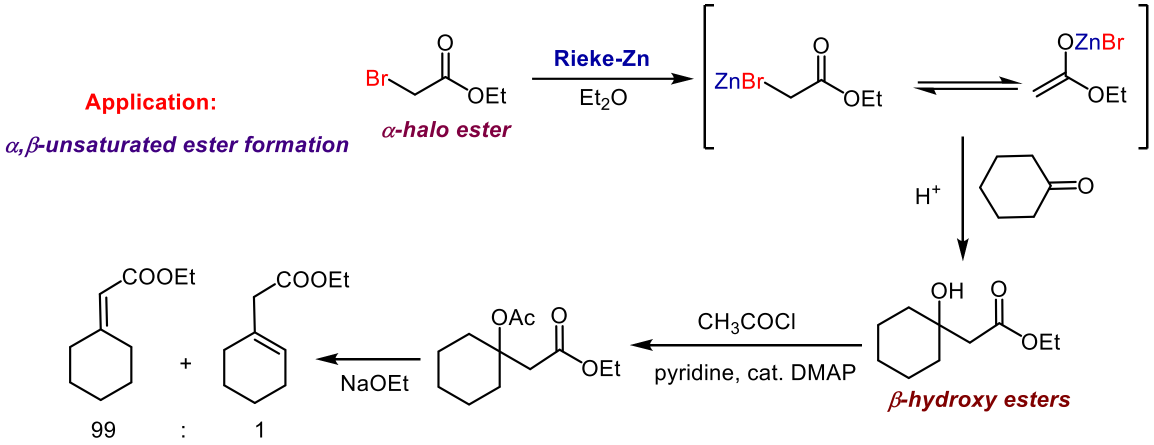
That means the other molecule will have a zinc here. you can think about the other molecule have a zinc and then you have this the R^2 here and then you have a -CO, -OR group. So, you can think this is a coordination between this oxygen and zinc and there is another zinc and this oxygen. So, now, this can allow to form some sort of a zinc enolate and now that can react with the corresponding carbonyl compound. So, six member Zimmermann-Traxler like transition state, it can able to form this compound here which can after treat with the H_2O molecule, it can generate a β-hydroxy ester.

So,



Starting from a α-halo ester you end up synthesizing a β-hydroxy ester .So, literally you see this is the part if you start here, halogen is gone from here and it is introduced this part, a reduced carbonyl compound.Again, there are several application, I have shown one of the important application here, if you take this α-halo ester, it will form the corresponding zinc, and then it is going for the generalization I have shown in the previous slide, now going to attack to the carbonyl compound from theβ-hydroxy ester, but after forming β-hydroxy ester, if you treat with the acid chloride like acetyl chloride and pyridine catalytic DMAP.

It will form the corresponding acetate. Now, if you use sodium ethoxide, it can have, two different products.

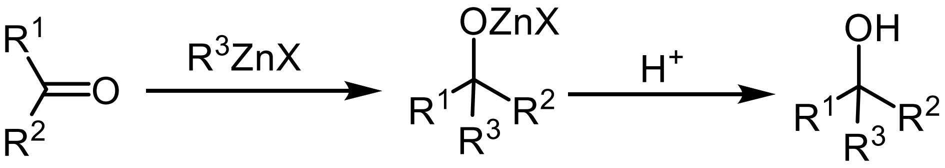


An alternative pathway to Horner–Wadsworth–Emmons (HWE) olefination of ketones

I think it can, the most acidic proton is this one. You can able to take this most acidic proton and it can go for elimination to get to this type of product with 99% selectivity. So, this is what is happening. This could be alternative pathway. So, if you write this conversion, what we have learned from here in this particular slide that what it is from cyclohexanone, it is giving this product. So, you can think about the Wittig reaction, I think that is the reaction you have learnt.

We are going to talk about that organosilicon and phosphorus. So, so this is a alternative to that reaction here, it can by using Reformatski condition also and then using this acetyl chloride and pyridine you can able to get and using sodium ethoxide you can also get to the very same product. Then the Barbier reaction, I talk about the Barbier reaction when I talk about this the single electron transfer reactions there. I talk about the samarium Barbier reactions and the other chemistry also with indium and others. So, here what is happening if you have this R³ZnX, if you have a carbonyl compound this can participate this can go for this 1 2- addition, after the protonation it can form this corresponding alcohol. You know several example, one of the example using this propazyli bromide.

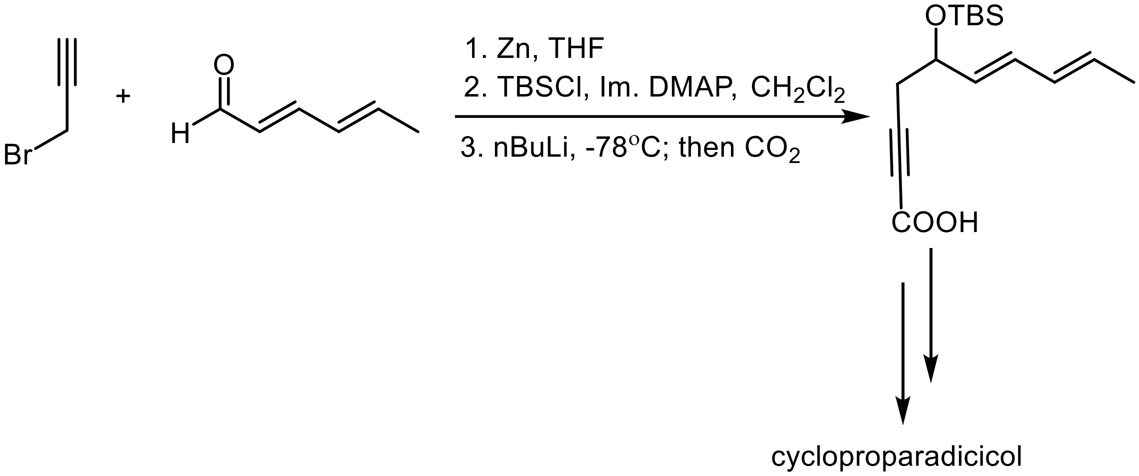
Barbier reaction



***via* a 1,2-addition.**

If you have propaxylic bromide you put the zinc it could be the Rieke-Zinc or it could be the corresponding zinc just with this additives you can able to make this corresponding organozinc reagent. Now if you treat to this corresponding aldehyde it will going to participate a Barbier coupling to form this corresponding alcohol which can be protected from this compound which can be finally after few step to convert to a very important compounds. So, what is the things here? The important thing here, what is the difference of this reaction compared to a Grignard and others reactions? Here, what you are happening, in case of Grignard, to make the Grignard first and then you have to add. If you want to add to a carbon compound or something.

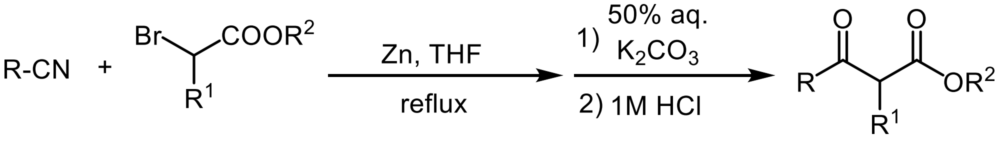
Application:



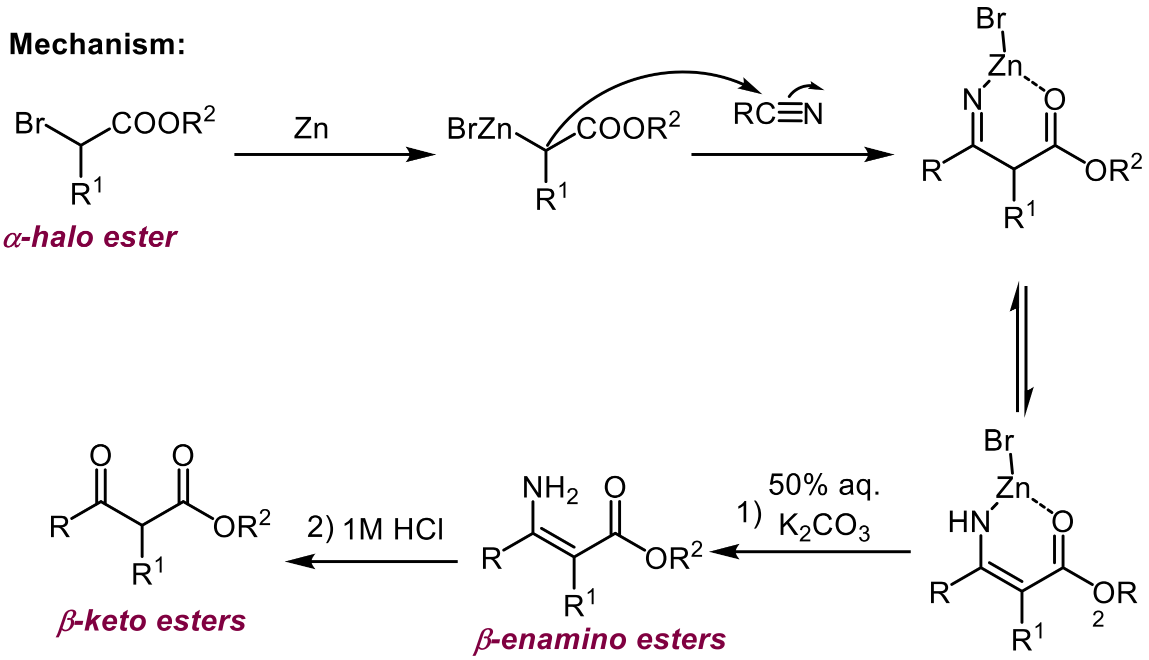
But here, you can take everything together. You can take this reagent, aldehyde and the zinc. There will be no interference. So, zinc will going to only react with the propylene bromide to make the organo zinc. Then, the reaction will happen with the aldehyde. Blaise reaction here again you have this α-bromoester, we have already learned about the α-bromoester to formation of the organozinc, but now you have this is nucleophile and change your electrophile.

Now the taken electrophile previously in case of reformatski was ketone, now it is a corresponding cyanide. We know that the Grignards or this lithium attack also cyanide here, similarly the organozinc also attack here. and it can form this type of chelation complex here and you treat with the K_2CO_3 and 1(M) molar HCl, it end up forming a β-keto ester. So, starting from the α-halo ester, you end up synthesizing a β-keto ester. Again what is happening if you understand there the halogen is gone this α-bromohalide and you end up this carbonyl group.

Blaise reaction



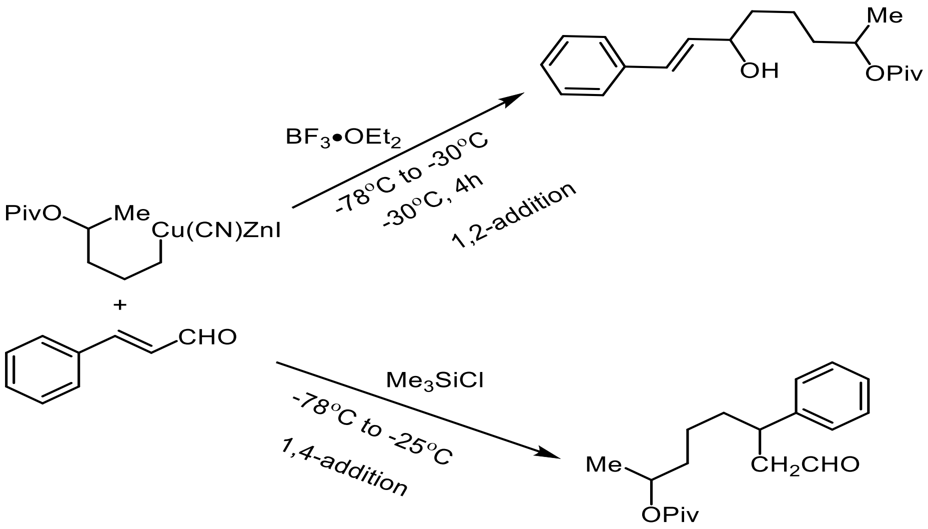
Mechanism:



So, remember if you give this conditions where you treat with the corresponding cyanide then you remember that you have to just introduce RCO group and replace the bromide and that will be the product . If you see this type of problem in the exam that is how you should solve this. Then you can see if you have this type of copper species which can be synthesized, I have mentioned using this zinc iodide and this copper and you have seen those type of species generation. The copper can go for this organocopper reagent, also we have learned it can go for some sort of a 1,4- addition, but if you use Lewis acid here. Then what is going to happen? Then you end up finding a 1, 2-addition happening, because activate this carbonyl more with a Lewis acid, now that particular carbon will be more electrophilic, that is why you see formation of this 1, 2 addition product.

Instead of the 1, 2 addition which is happening in other case. There is a enantioselective version of this 1, 2 addition reaction. We have learned this dialkyl zinc can add here, to the aldehyde. Now, can this reaction be asymmetric? Yes, if you use a chiral ligand. So, these (s)-1-phenyl-1-propanol, there are so many variation of this where you can see there will be nitrogen and oxygen, this type of ligands was developed, lot of them have a scheme and this is found very good for this reaction giving very high enantioselectivity. If you try to understand the transition state again you can see the corresponding transition state, the zinc is binding with both nitrogen and oxygen.

Addition of organozinc reagent to aldehyde:

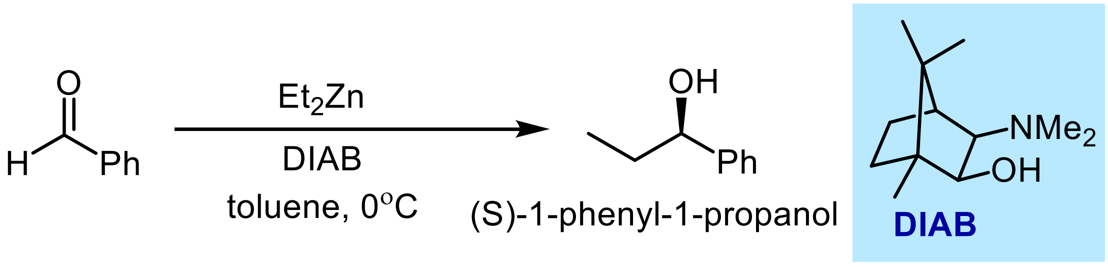


So, there will be two different zinc, So, you can see the one is binding with this amino alcohol here. So, this is the one and the other one is actually here which is binding with this corresponding with the substrate. So, this Zinc compound is binding with this oxygen and the substrate oxygen here.

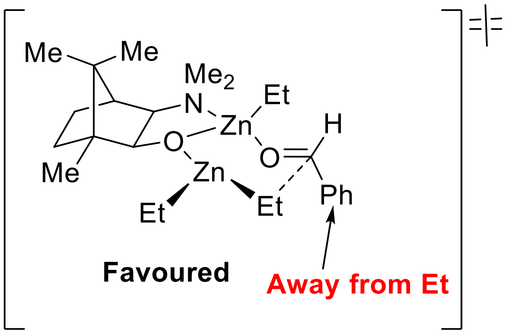
So, that is how you can see in this particular transition state, these are all kind of you know formation like a chelate and that is why this R group from the zinc going to transform to the particular phase of this carbonyl. So, using these chiral ligand, you are blocking one of the phase of this carbonyl group, to get to the product with a high enantioselectivity.

Enantioselective addition of organozinc reagent to aldehyde:

(-)-3-exo-(dimethylamino)isoborneol



One zinc atom is bound to the amino alcohol and another equivalent of dialkylzinc binds the oxygen



There are the reaction of functionalized organozinc reagent using copper salt.

So, you have a functionalized group you able to make them using the copper cyanide and LiX , you can able to make this RCuZnX and then you can use this type of reagents or use a dialkyl zinc here functionalized use copper cyanide and then you can able to make these reagent as well where you have a copper and a zinc. with the copper cyanide and zinc.

So, this can be used for several different transformations one of the things is showing here. If you have this corresponding aryl bromide, you first make corresponding zinc chloride.

So, you treat with the lithium naphthalenide and zinc chloride that will end up forming first. And now, if you treat with the copper cyanide, you are going to make this copper Cu(CN)ZnBr compound. And this is much more reactive compared to a normal organozinc reagent. So, it can now take part in acylation reaction with acyl chloride to form this product.

So, some of this reaction and some of this reagent was developed by Professor Nochels and he has lot of contribution development of different type of organozinc reagent.

Reactions of functionalized organozincs mediated by copper(I) Salts:

$$\text{FG-R} + \text{CuCN}\bullet\text{nLiX} \xrightarrow[0^{\circ}\text{C, 5 min}]{\text{THF}} \text{FG-RCu(CN)ZnX}\bullet\text{nLiX}$$

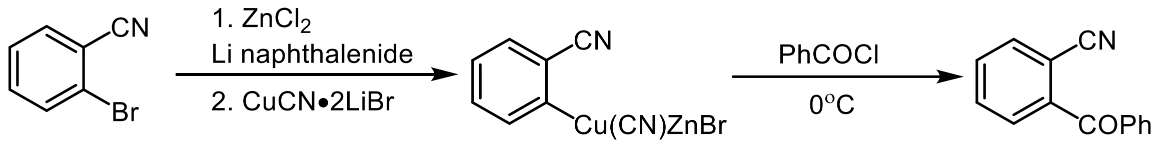
$$(\text{FG-R})_2\text{Zn} + \text{CuCN}\bullet\text{nLiX} \xrightarrow[0^{\circ}\text{C, 5 min}]{\text{THF}} \text{FG-RCu(CN)Zn(FG-R)}\bullet\text{nLiX}$$

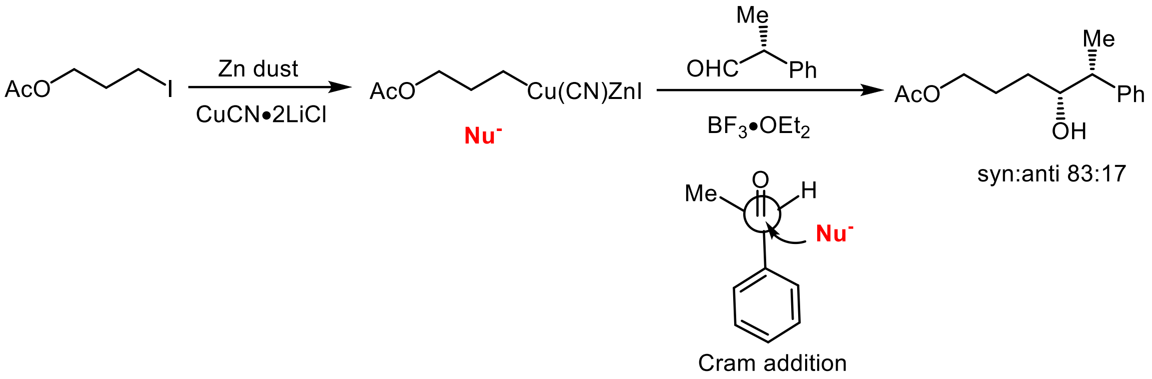
X=Cl, Br, I and n=1,2

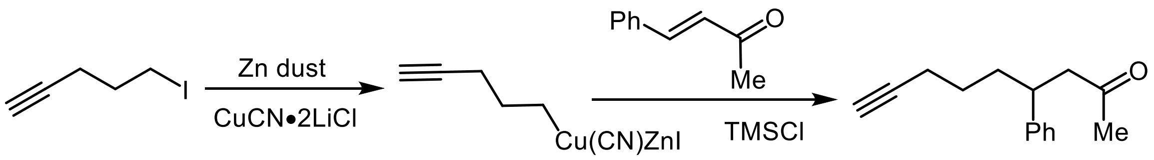
Again, there is a another example here if you make this corresponding organocopper zinc species as I mentioned use zinc dust then use the copper cyanide if you remember the copper cyanide effect when you make. When I talk about the formation of the organocopper reagent. So, very similar tricks are happening here forming this type of compound here, so forming this corresponding copper reagent, first they are forming corresponding zinc, now there is a trans-metalation happening to form the corresponding organocopper, and that is how they are able to keep this different type of functional group here. that can add to the corresponding aldehyde again there is a from the Crams rule it is going to attack.

So, there will be large, medium, small group are considered and it is going to nucleophile attack from where it will be a through where smaller or medium group that is how the nucleophile should be attacked, that are shown here to give it to this product as a major product.

Reactions of functionalized organozinc mediated by copper(I) Salts:







Again, there is another example here this corresponding iodo compounds, in case of zinc dust formation this organocopper species which can now take part in a 1,4-addition.

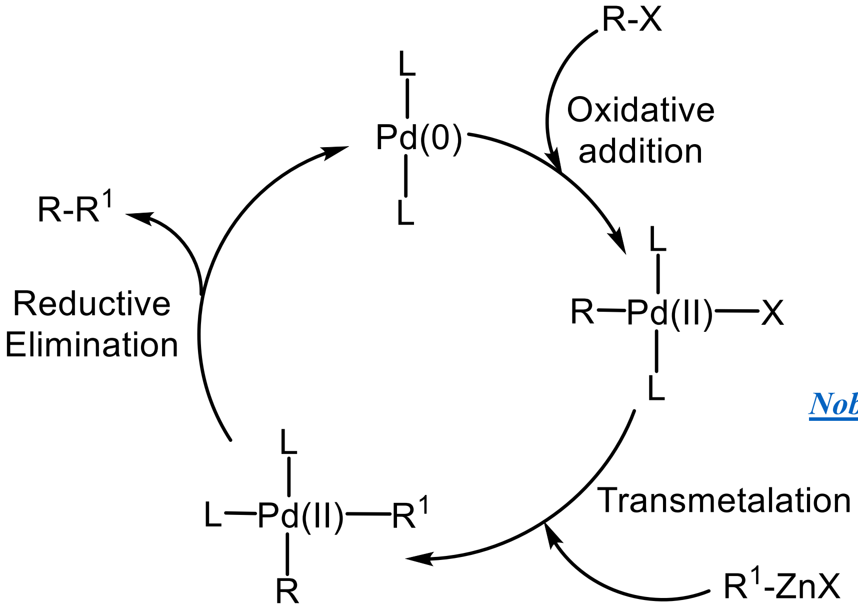
Since organocopper compounds you have learned in the previous lecture that it can take part in the 1,4-addition and TMSCl-reagent is also very important. So, sometime TMSCl is playing a very important role because it can also able to activate this carbonyl group. So, this can generate some sort of a (δ+) that can allow this type of 1,4-addition happening faster. Then there is another important cross coupling reaction, so I started about the Kumada coupling, Sonogashira coupling in the last class.

And now I am going to talk about another important coupling called Negishi coupling. So, Professor Ei-ichi Negishi, he was a faculty of Purdue University, so he received the Nobel Prize in 2010. So, there was Professor Heck and then you know Professor Suzuki. So, these three of them share the Nobel Prize for development of this cross coupling reaction. Again, you can use a palladium catalyst or nickel catalyst.

Negishi coupling:

$$R\text{-}X + R^1\text{-}ZnX \xrightarrow{PdL_n/NiL_n} R\text{-}R^1$$

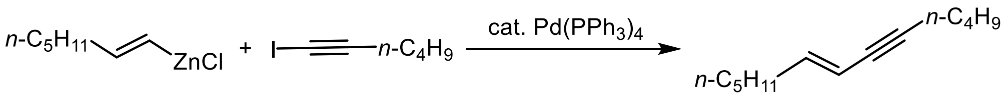
Ei-ichi Negishi

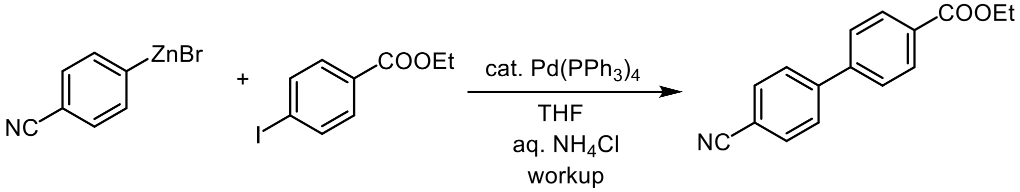


Nobel Prize in Chemistry in 2010

What do you have? You have organozinc and corresponding aryl halide. Of course, this reaction has gone, went to alkyl halide and there are lot of more scope, but I am going to only talk about the reaction some sort of aryl halide here. Now it can participate in oxidative addition that if you take a palladium(0), it will take for oxidative addition to make this palladium(II) complex, there will be a palladium(II) here and then there will be a trans-metalation with the corresponding zinc reagent first and then there will be reductive elimination to get to the corresponding product . Again, it is a very similar mechanism what you are seeing we are changing the trans metalation reagent. Here we are only changing the zinc. So, when it is a Grignard it is called Kumada coupling, when it is alkyne with a copper acetate it is the Sonogashira coupling and when it will be the Boron it is the Suzuki coupling, and when it is a zinc it is going to be the Negishi coupling.

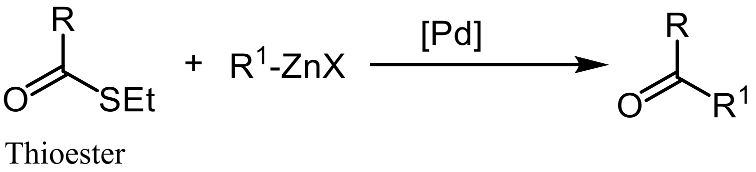
Here are some example here, you have this alkynyliodide and this corresponding vinyl zinc is going to take part in the negishi coupling with means palladium(0) to form this corresponding products. It can also use corresponding zinc bromide and allyl iodide also can form these biaryls. Another important coupling is the Fukuyama coupling. So, you can see it is the another version here instead of using these aryl iodide, here they are using a thioester. So, what is happening palladium first form can go for a oxidative addition reacting with the thioester here.

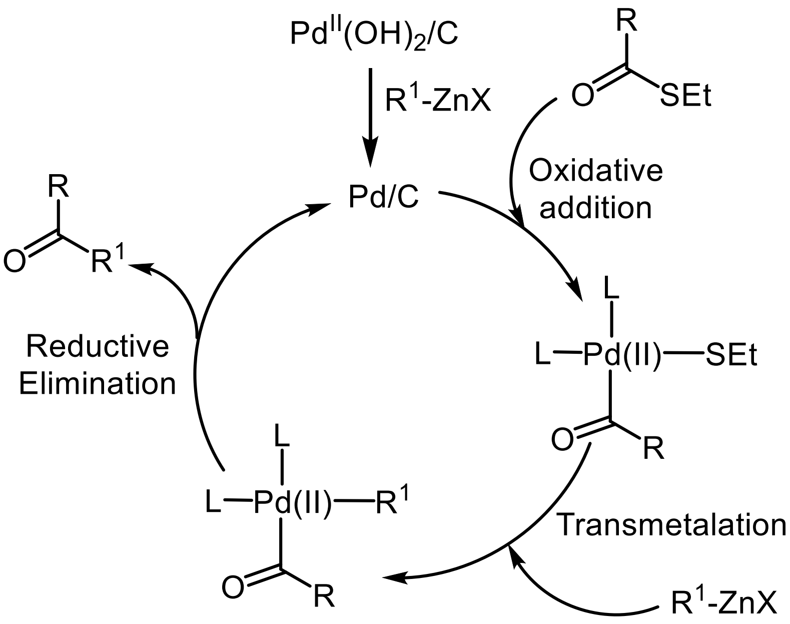




So, with the thioester it can go for oxidative addition then and then undergo trans-metalation happening with organozinc that is the very similar with the Negishi coupling then formation palladium(II) and then there will be reductive elimination happening. So, you end up from a thioester are making a corresponding ketone. you are replacing this SET with a R^1 here and mechanism will be very similar. So, oxidative addition, trans-metalation and reductive elimination takes place. There is an example of Fukuyama coupling given you have this it can also work with this alkyl zinc reagents.

Fukuyama coupling:

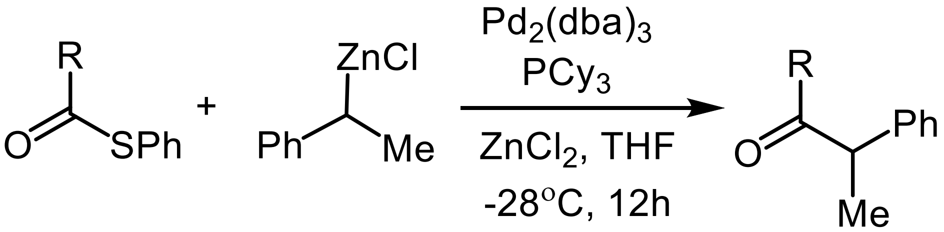




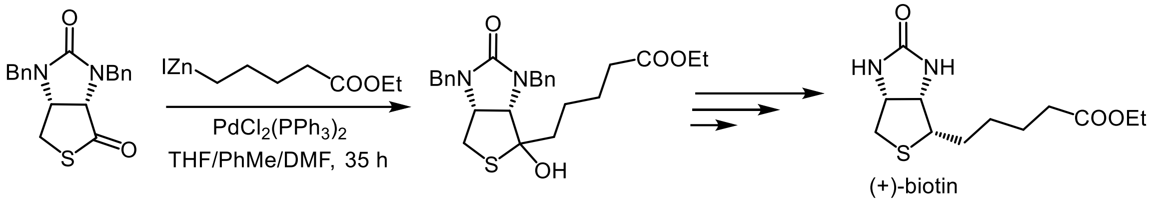
You can think that there is an example here with this corresponding thioester. So, you can see the thioester is reacting with this corresponding organozinc compounds in place of the palladium appropriate ligand to get this corresponding carbonyl compounds. There is another example you can see the alkyl zincs are participating in a trans-metalations reaction here in place of the palladium, what is happening again this corresponding thio esters. So, what is happening here the thio ester is actually in case of using this reagent. It actually forming this product after the first cross coupling and then this it can able to do remove the OH- group here to get the biotin which is a very important compound.

So, in the next slide we are going to talk about the reaction using the organozinc- copper reagent.

Fukuyama coupling:



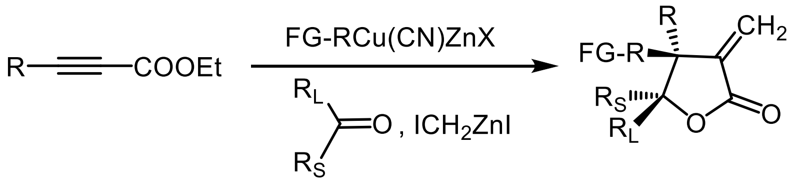
Application:



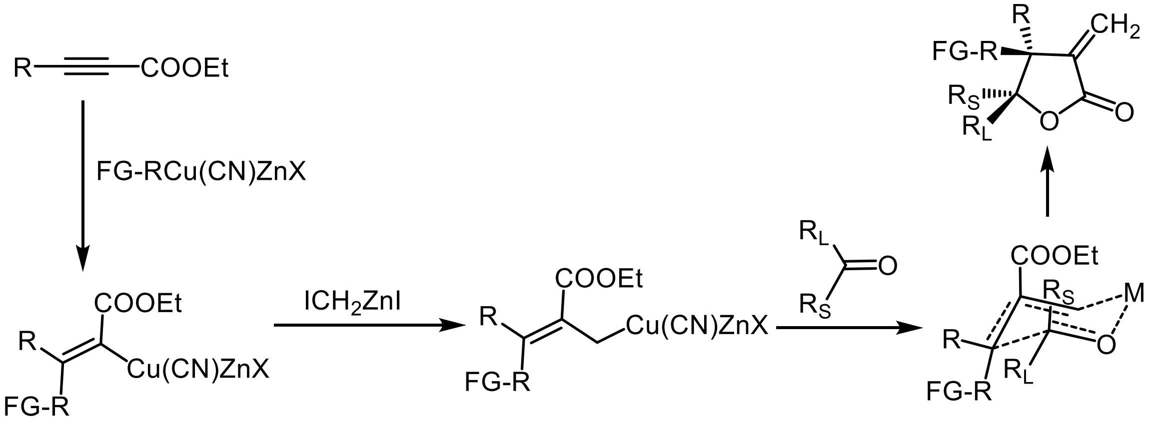
So, there is another important reaction, this alkyne here if you have this corresponding copper zinc you have learned about the carbocupration here to the corresponding acetylene. Here you have this alkyne it can go for a carbocupration here first. Again, you can see these the corresponding copper and this functional group add in the same fashion to the alkyne. Then you can you treat with the ICH_2ZnI, there will be a 1, 2-shift going to happen here.

So, there is a 1,2- shift happening for the formation of this type allylic copper species.

Using organozinc-copper reagent



Mechanism:



Now, this allyl copper species can participate a reaction with a carbonyl compound through a six membered transition state. They can form this type of cyclic furanone. Again, here are the references for these courses. I think please go through these references that can give you some of the important books for which introduce the organozinc chemistry.

And again, thank you so much for coming to the class and I am going to see you guys in the next class. Thank you.