

Molecular Rearrangements and Reactive Intermediates in Organic Synthesis

Prof. Santanu Panda

Department of Chemistry

Indian Institute of Technology, Kharagpur

Lecture 37 : Grignard

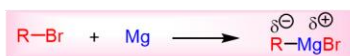
Welcome back to this NPTEL online certification course in molecular rearrangement and reactive intermediate. In the last couple of classes, we have been learning about the organo lithium. So, we have learned in the four lectures about the generation of organo lithium using several different strategies, one is the metal halogen exchange, then the trans-metalation, and then the deprotonation and there are several different types of reaction we talk about. In today's class, I am going to focus on another type of organo metal reagent called the Grignard reagent. So, we are going to talk about the generation of Grignard reagents and different types of reactivity. So, I am going to talk about the history of the Grignard reagent, and how the Grignard reagent was originally synthesized.

Some of the introduction tries to focus on the reactivity, then the nature of the Grignard reagent, the effect of the solvent and the different type of alkyl halides what will be their effect on the generation of Grignard reagent, and then their structure and mechanism. So, Victor Grignard in 1900 published the generation of Grignard reagent from magnesium and alkyl halide. He can synthesize R-MgBr which was called as a Grignard reagent.

➤ History of organomagnesium compounds:

- ✓ Discovered by French chemist Francois Auguste Victor Grignard (University of Nancy France).
- ✓ Who published it in 1900 and was awarded Noble Prize in Chemistry in 1912 for this work.

➤ First involves the preparation of an organo-
Magnesium reagents are-



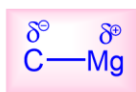
Victor Grignard

So, Victor Grignard received the Nobel Prize in chemistry in 1912 for this important work. Because Grignard reagent was found not only on a particular synthesis of a particular molecule, but it has a huge importance in organic synthesis. You will see that it

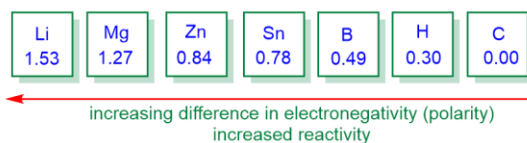
can be used for several different carbon-carbon bond-forming reactions. After the beginning of this organomagnesium chemistry, we are going to learn about the reactivity of organomagnesium in comparison to other metals like lithium, zinc, tin, and boron. So, first thing if you see about the organomagnesium reagent, I think as very similar to the organo lithium that we talked about also there will be a δ^- here and there will be δ^+ on the metal. So, that means, you will see you have already seen in the case of organolithium when you talk about the bonding between lithium and carbon, you have seen that the σ -bond electron density is actually on the carbon that a very similar thing happens once you have magnesium there. So, that means, the carbon has the (-) charge on it. It is kind of acting as a carbanion. Now if you go in this direction, what we are showing from this particular diagram below is that once you go in this direction, what we are saying the increasing difference in electronegativity with carbon. So, if you compare the carbon electronegativity with the different types of tin, zinc, magnesium, and lithium in this direction, what is happening? The difference in electronegativity with carbon is actually getting increased. So, as it is increasing in this direction what we are seeing, also we are seeing the % of metallic character is increasing and as well as the polarity.

➤ **Reactivity of Magnesium metal in the Grignard reagent:**

- ✓ Formation of the Grignard reagent is a heterogeneous reaction at the magnesium surface.
- ✓ Organomagnesium compounds is characterized by polarized carbon magnesium bond.
- ✓ Carbon atom bearing negative partial charge, usually called "Carbanions".



- ✓ The following scheme illustrates the difference in electronegativity between carbon and other elements based on Allred-Rochow scale:

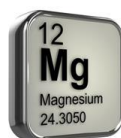


So, that is why you will see that the organolithium is the strongest one, then organomagnesium, then organozinc and organotin, and so on. I think I have talked about this in the organolithium chemistry as well. So, now I am going to talk about how you synthesize it. Suppose I think that is the important thing because if you are trying to go to the laboratory to synthesize the Grignard. So, then how you do that.

Generally, you found that we use magnesium turnings which mostly are commercially available or sometimes this comes in a bigger size, you have to cut in a small species. The next thing is, once you have done that you have to kind of try to wash this magnesium turning with the diluted HCl. So, to clean some of the magnesium oxide which is in the top of this magnesium turning because this reaction is some sort of a

heterogeneous reaction. It is happening on the surface of the magnesium. So, your reagent is mostly this alkyl and aryl halides. So, mostly you find that bromides and iodides. And then you have to use a dry solvent and that is mostly you use diethyl ether or THF. These are the two different solvents. So, diethyl ether or THF are the solvents you will find for the generation of Grignard reagents. And the next thing is once you are adding this thing together, you are adding this corresponding alkyl halide and then you are adding the solvent and you have the corresponding magnesium turnings.

➤ Experimental set-up in laboratory to formation of Grignard reagent:



Alkyl, aryl halide mostly bromide and iodide

All magnesium is coated with a passivating layer of magnesium oxide, which inhibits reactions with the organic halide. The oxide layer can also be broken up using ultrasound, using a stirring rod to scratch the oxidized layer off, or by adding a few drops of iodine or 1,2-Diiodoethane.

So, once you have this reagent, the first thing is the beginning of the reaction is a little bit slower. Because when the reaction is starting, the reaction is slower. So, in this time what is happening, because this reaction initially time is slow, people use some sort of an initiator. We call these initiators. So, there are different types of initiators you can use.

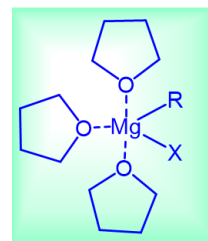
One is that you can use 1,2-diiodo ethane or 1,2-dibromo ethane. That is one you can use. So, you can see these are the 1,2 or you can have a bromo or you can have a iodo. So, why we are using this or you can use iodine also as an activator. So, these are things you can use a little bit in this mixture. So, that can initiate the reaction. How this is happening? We have mentioned here. There is a magnesium oxide layer which can be broken up. Also, you can use ultrasound to break up that layer or you can use a stirring to scratch it or you can use a few drops of iodine or diiodomethane or want to

dibromoethane. So, what is going to happen? Once you react this with the magnesium, this is going to generate the magnesium bromide or magnesium iodide depending on what you choose, plus you can see you will generate ethylene. So, you will see the ethylene will come out. So, once you add them, you will see ethylene will come out from the reaction. That is the time you understand ok, the reaction already started happening. And very similar thing once you use iodine also. It is going to clean this magnesium oxide because it is going to start reacting with the magnesium forming magnesium iodide. So, that is why these two initiators going to use for this reaction.

Once the reaction starts it is going to consume all the alkyl iodide and it is going to convert to the corresponding Grignard reagents. So, now as I mentioned there are two different solvents we use one is the THF, and another is ether and people found out that they can able to what type of coordination is there between this solvent and the Grignard reagents. So, it was found that in general if you have a THF then you can see three equivalents of THF bound with the magnesium forming some sort of a penta-coordinated complex, and in the case of ether it could be monomeric or it could be dimeric. That means, it could have just one magnesium with two ether here or it could be a two magnesium which has a halide with a bridge. So, this type of different complex you can find.

➤ In THF:

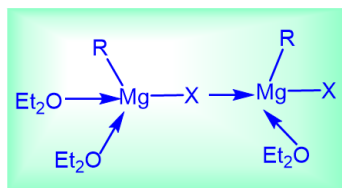
- ✓ RMgX ($\text{X} = \text{Cl}, \text{Br}, \text{I}$) are monomeric over a wide concentration range.
- ✓ For $\text{X} = \text{F}$, compounds are dimeric $[\text{RMgF}]_2$.



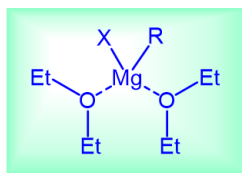
pentacoordinated

➤ In Et_2O :

- ✓ RMgX ($\text{X} = \text{Cl}, \text{F}$) are dimeric over a wide concentration range.
- ✓ For $\text{X} = \text{Br}, \text{I}$ association patterns are more complex.
- ✓ At low concentration, monomeric species exist.



dimer



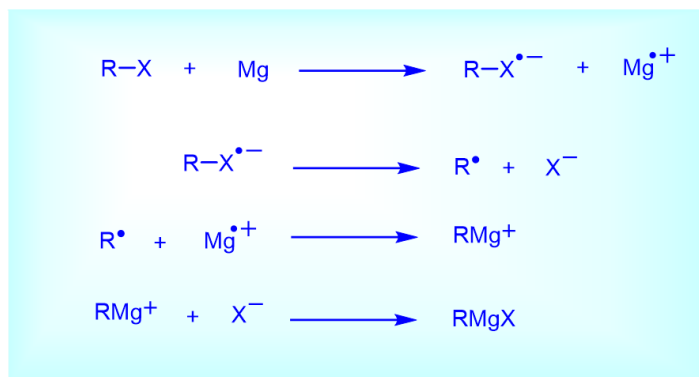
monomer

Not only that in the particular reaction when you are forming the Grignard reagent it has a link, I am going to come back to that discussion in a minute. So, first, we are going to

learn the mechanism. What is happening, once you add this alkyl halide with the magnesium turning? So, this reaction actually goes via a single electron transfer mechanism, SET. So, you might see sometimes the question comes what is the mechanism? How the Grignard reagent was synthesized? it is called single electron transfer.

So, I think I have already taught you guys some of the single electron transfer reagents. If you remember when I was talking about this birch reduction and acylion condensation, I talked about some of this. So, here you can see, what is happening. You have a magnesium. So, magnesium can give a single electron to the alkyl halide to form this $RX^{\cdot-}$. Now, there will be and then there will be Mg^+ . Now, there will be a homolytic cleavage between this R and X to generate R^{\cdot} and X^- .

- ✓ The synthesis of the Grignard reagent mechanism has two steps.
- ✓ These steps are: An electron radical on magnesium attacks the halogen.
- ✓ Putting the electron radical on the R group.
- ✓ Remaining radical on magnesium and radical on the R group form a bond.

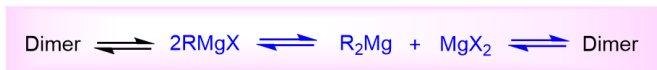
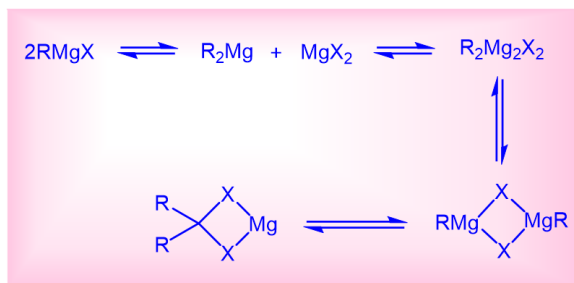


I think you can understand this nicely. Then R^{\cdot} is going to react with this $Mg^{\cdot+}$ to form $R-Mg^+$ and you have the X^- . So, that can form $R-MgX$. So, literally what is happening something like you have RX and the magnesium kind of got inserted between the R and X to form $RMgX$. So, now as I was telling you at the beginning once you have this, once you try to mix this alkyl halide and this corresponding magnesium turning, it is not only going to form $RMgX$, it can form a mixture of a couple of things, we call it as a Schlenk equilibrium.

So, it is kind of what we call it is Schlenk equilibrium. So, it was found out that depending on the R group, what type of R you are using, and what type of alkyl halide

you are using it is a primary, secondary, or tertiary you find there will be different equilibrium, means, the equilibrium of formation of R_2Mg . So, that is also present in the reaction.

- Organomagnesium halides i.e Grignard reagent $MgRX$ are generally tetrahedral.
- Also penta-coordinated trigonal bipyramidal species are found.
- Grignard reagents are associated with halogen bridges.
- This reagent remains complex structure with many species in equilibrium known as Schlenk equilibrium.

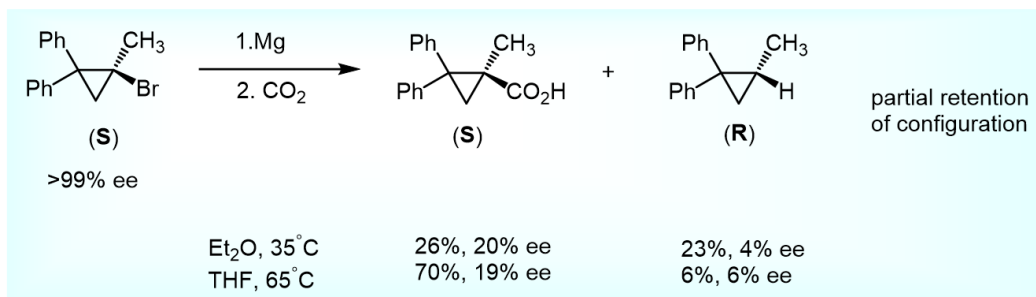


Once you mix them. So, the ratio of this equilibrium depends on the size of the R group. It can also form something like that, which is actually associated with a halogen bridge. So, there are two Grignard reagents associated with a halogen bridge or it can form this one as well. So, all these species are in a Schlenk equilibrium.

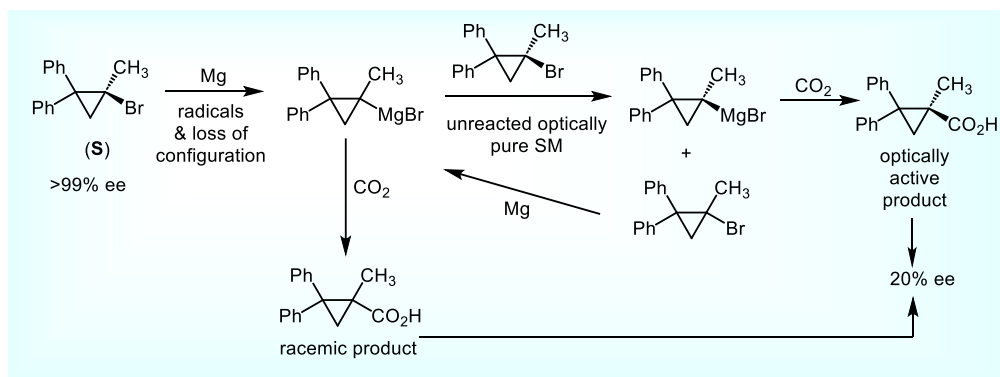
Now, the question comes that we have learned about is that once you are forming a Grignard reagent, what is happening, is going to a single electron transfer. So, is there any evidence for that? This is one important evidence comes from that if you start with this corresponding cyclopropyl bromide which is 99% ee, means it is a chiral compound. Now, if you treat with magnesium and then CO_2 . Once it is forming the corresponding carboxylic acid what we found it that you are getting first of all a mixture. So, you started with S, and now you are getting a mixture of S + R and you are seeing that in the case of ether 20% ee, in THF 19% ee. what is happening here? You are seeing a very poor ee which means, there is a racemization happening.

And that racemization does not matter with solvent, temperature, or reaction time, whatever you or the magnesium purity whatever you change, you are not able to change this scenario that you cannot able to. So, that means what is happening, is you are losing this stereochemistry once you form the Grignard reagent. Now, you try to understand what is happening. I think one of the important aspects as I told you before it is going

through radical and now once it is forming a radical, it can have an inversion. So, it can go to the, I am going to show you that structure in a minute.



- ✓ Solvent, temperature, reaction time and purity of Mg showed no significant effect on stereochemistry of the desired product.

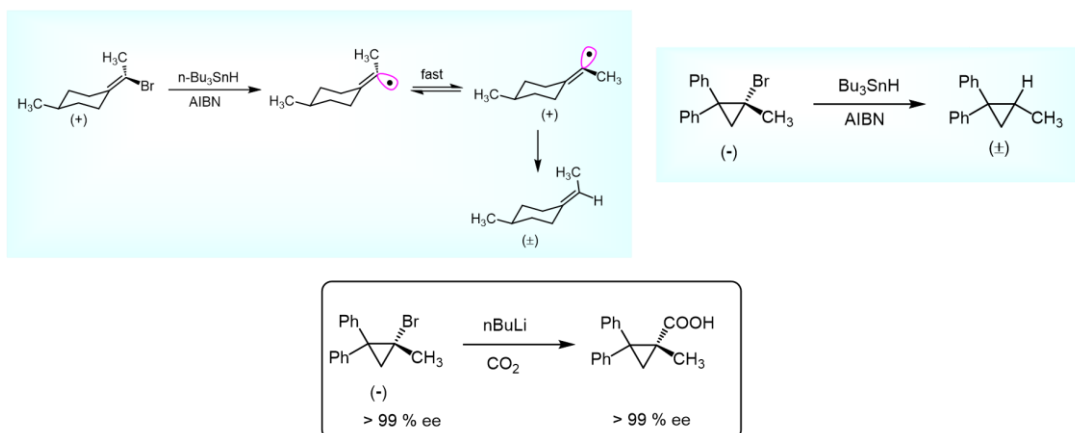


So, before that, I am going to tell you one important question, why partial retention? Of course, we know if there is a formation of a radical intermediate, there is a racemization we understand. But the question is why there is a partial retention. If you see in the previous slide we are still seeing some 20% ee, why not just 50:50? What they are saying is that once this Grignard formation is happening, there is in the reaction medium, there could be some unreacted optically pure starting material. So, this Grignard can now so, there could be a this Grignard can react with this corresponding bromide, this magnesium bromide can react with this corresponding bromide. So, there will be transfer of Grignard.

So, that is how, if there is some optically pure remaining then that can form Grignard from this corresponding Grignard reagent that is how some of the optical purity will be maintained there with most of the racemic material that you are forming. So, there will be a majorly racemic material which you are forming with that you will see some optically pure. Because, why it is happening as I am telling you, there will be some unreacted optically pure which can react with this one to form this Grignard which can be trapped with the CO₂, that is why you are seeing some 20% ee in the product. So, we try to now

explain to you why this is happening. If you go back to radical chemistry then you can see there. If you treat this particular compound with tributyl tin hydride and AIBN, if you remember I taught in radical chemistry, AIBN under heating, it is going to generate a radical which can go for a hydrogen atom transfer to generate a tin radical which can cleave this carbon-bromine bond to generate a radical species. So, now, once it is forming a radical species at the time what is happening your stereochemistry getting lost. That is how you end up getting a racemic mixture. You can see here clearly from there is another example here. From this chiral compound once you treat with the tributyl tin hydride and AIBN. What is happening here? There is inversion happening as I mentioned in the previous slide. You can see this radical can go for inversion. It can be on this site or it can be on the other site. So, very similar thing you can think about for cyclopropane.

- Both vinyl and cyclopropyl radicals are σ radicals i.e. easily inverted.
- So radicals lose their optical activity and formed racemic product.



It can have a scenario like this. you can have a radical like this or you can have a structure where CH_3 is here and your radical will be this side. If these are in equilibrium between this and this if these two things are in equilibrium formation of this and then what is going to happen from this, both the intermediate there will be a hydrogen transfer going to happen. So, once there is a hydrogen transfer is happening from the intermediate formation of this radical A or this species B then it can form this racemic product. So, that is happening here in this particular compound also you are seeing that it is losing the stereochemistry if you treat it with the tributyltin hydride and AIBN. But I think if you remember I talked about in the case of organolithium reagent once you are generating this anion, here you actually retain the stereochemistry.

Because these corresponding anion which is going to form is configurationally stable. I think I have already talked about that it cannot participate in the inversion because it

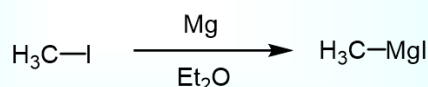
cannot achieve the planarity because that has to achieve for going to the for the inversion to happen.

So, now I am going to start with the alkyl one first. If you take alkyl iodide and magnesium and dry ether, you will end up getting the CH_3MgI . In general, if you make this Grignard reagent I think I am going to come back to another class where I am going to teach you how to titrate it. Suppose you make the solution now you have to find out what is the molarity of it.

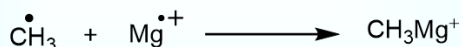
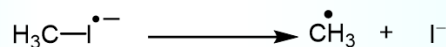
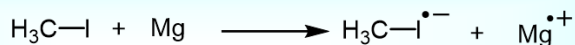
We generally used the iodine as a titrating agent, but I am going to teach you some other reagents. So, what is going to happen? Once you take iodine and the corresponding $\text{CH}_3\text{-MgI}$, what is going to happen? This Grignard reagent going to react with I_2 and it is going to consume the iodine. So, from there you can see how much iodine got consumed and you can find the amount of iodine got consumed from that we found the amount of Grignard reagent formed, and from that, you can find out the concentration. So, I am going to take a separate class. So, there are other methods as well for organolithium titration.

So, I will come back to that discussion later. So, what is happening here, again I think we are trying to explain you the very similar single electron transfer mechanism here. So, here a similar thing happens, magnesium is giving electrons and formation of this CH_3 radical and that is how it is forming the corresponding Grignard. Again it could be ethyl bromide very similar to methyl to form the Grignard, it could be a corresponding cyclohexyl bromide. So, that means, we are saying that there is a primary then there is a secondary. Again very similarly you can see here that will form the secondary radical.

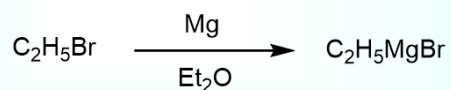
➤ From alkyl halide:



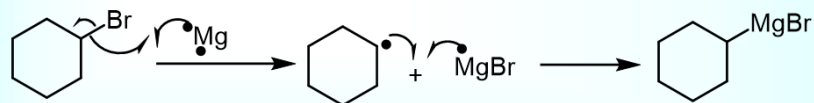
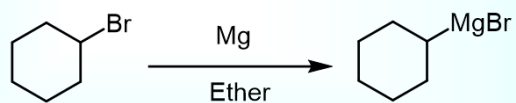
Mechanism:



➤ From ethyl bromide:



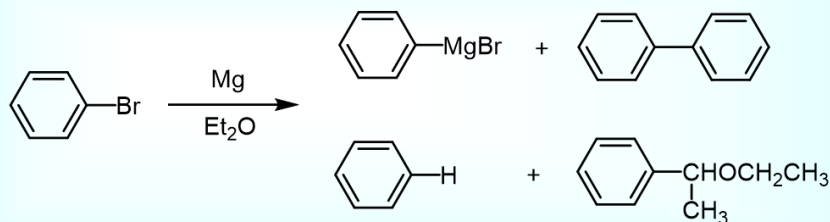
➤ From cyclohexyl bromide:



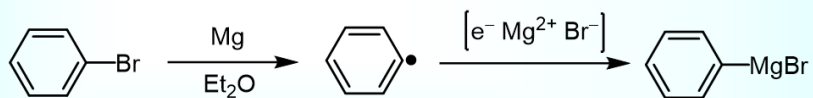
So, of course, if it is secondary the reaction rate will be little bit faster because you are forming a stable radical here.

➤ From aryl bromide:

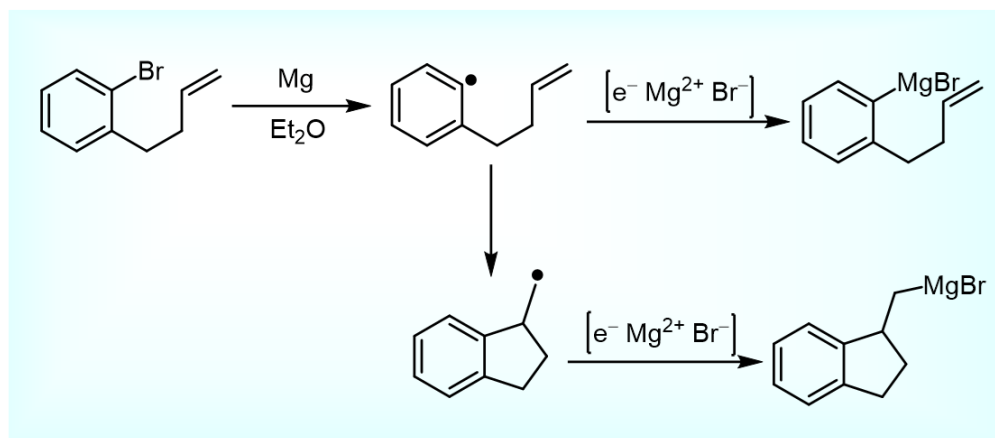
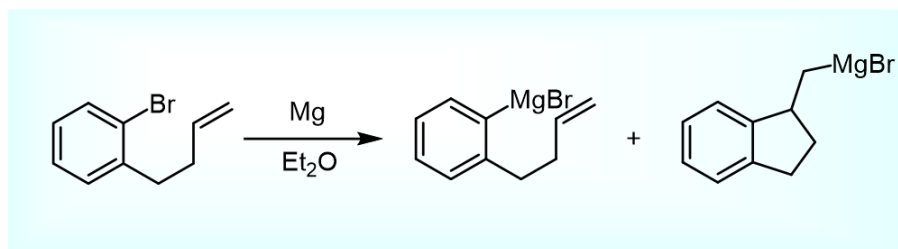
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❖ Radical mechanism:



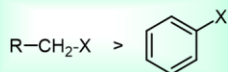
Now if you treat with the aryl bromide of course, it is going to so, aryl bromide or aryl iodide if you treat with magnesium and diethyl ether it is going to form the corresponding Grignard, but at the same time what is going to happen it can also form some sort of a dimer. some sort of Wurtz coupling going to happen or it can also be able to take a proton. As you can see these are indications. So, this is going through via a hydrogen atom transfer. I think I taught you that if you have a aryl radical, it can go for a hydrogen atom transfer from a solvent to convert to your ArH. And again I think that radical mechanism which you are talking we can have another proof here that if you have an aryl bromide and with this. So, if you have this vinyl group then it is going to participate in an intramolecular, I think I taught you guys that a 5 exo-trig. So, 5 exo trig cyclization going to happen. So, that is how you not only get this Grignard reagent as a product you also end up getting some of the product this cyclized compounds.



Why? Because the formation of this radical which can add here to the corresponding olefin to the 5 exo trig. It will form this one, then it will form the corresponding Grignard reagent. Again the reactivity order is if you have corresponding iodo vs bromo vs chloro. If you see most of the time I am saying iodo and bromo because those two alkyl halides or aryl halides are mostly used. You will see sometimes aryl chloride is also used or alkyl chloride is also used, but you will find very rarely the corresponding fluoride is used for this reaction. Again if you have this corresponding alkyl versus benzyl and aryl then the alkyl reaction rate is much faster corresponding to the vinyl or the aryl halide. Again I

think you can see there is an order which is given here. So, you can see again the 1° vs 2° then cycloalkyl, tertiary, aromatic. So, these are the different orders in what follows for the formation of the Grignard reagents. As I mentioned once you are forming this type of Grignard reagent RMgX, you have to understand very similar to the RLi, I think I taught you that it can act as a base or it can act as a nucleophile. That is the important thing here.

- ✓ Grignard reagents are chemical compounds with the general formula R-Mg-X.
- ✓ Relative reactivity of organohalides towards magnesium increases from fluorides to iodide.
- ✓ Fluorides are so unreactive that can only be transferred to Grignard reagents under special conditions.



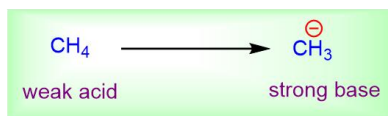
- ✓ The general influence of "R"- on the Grignard formation follows the order:



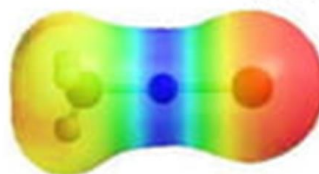
That means, you have a R actually as a (-). So, if it is a (-) you can think about from a methane it is forming. Finally, if once you make a Grignard you are literally forming this some sort of a CH₃⁻. So, you can think about CH₃MgX as an equivalent to CH₃⁻. once you form it can act as a strong base as well as a strong nucleophile.

➤ Nature of Grignard reagent:

- ✓ Grignard reagents are identical to organolithium reagents .
- ✓ Both are strong nucleophile and also act as a strong base.
- ✓ Forming a new carbon-carbon bonds.

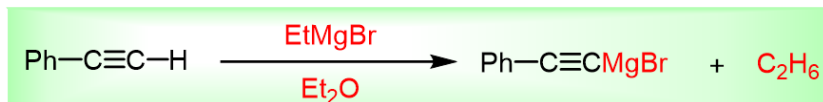
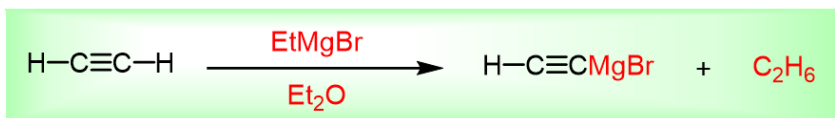


- ✓ It can taken out hydrogen ion from C-H bonds.



That means, it can abstract a proton from here. If you have an alkyne in that case what is going to happen, if you take a Grignard reagent it is going to abstract this CH proton to form this corresponding alkynyl Grignard reagent. I am going to come back to that discussion also. Here I think you can see on this page if you use an ethyl magnesium bromide, diethyl ether then what is going to happen? Here these are the acidic protons in the alkyne that are getting abstracted here first to form this corresponding alkynyl Grignard reagent. If you have a phenylacetylene here you use ethyl magnesium bromide in diethyl ether, then then this is going to abstract this proton here in the alkyne to form the corresponding alkynyl Grignard. So, what you have learned is that we have learned you can make alkyl Grignard bromide, and you can make some aryl Grignard from the aryl bromide and iodide and if you have an alkyne then you do not have to form the start from the corresponding iodo or bromo you can directly start from the corresponding alkyne.

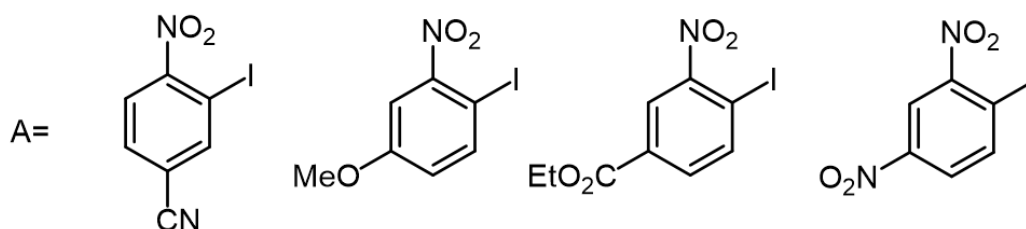
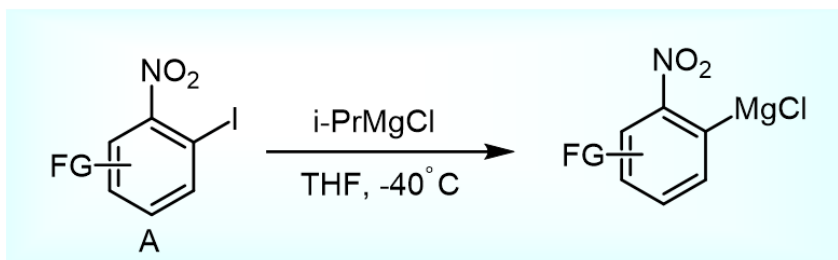
➤ Synthesis of acetylene magnesium bromide



And now you can via deprotonation using another Grignard reagent, another alkyl Grignard reagent you can able to make this corresponding alkynyl Grignard reagent. So, till now what I was talking about about this different aryl and alkyl Grignard reagent. One of the important things I should mention is that when you are forming a Grignard reagent, compared to organolithium there are methods where you can keep the functional group.

Suppose in your molecule you have a functional group. Here we have an example you have a functional group and we have an iodo bromo. So, now the question comes if you treat it with organolithium. As organolithiums are very reactive once you go for a metal halogen exchange then there is a chance that this functional group is also going to get attacked. Of course, we have learned that if you go to a very low temperature like -100°C , then it is possible to control. We have shown you some examples in the class, but here we are talking about that if you use isopropyl magnesium chloride.

➤ Synthesis of functionalized Grignard:

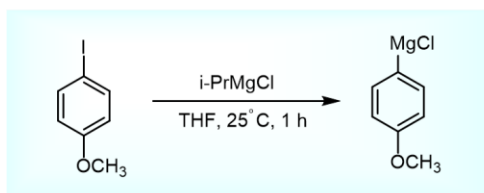
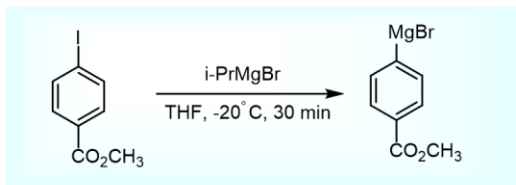


So, this reagent is also commercially available, if you get isopropyl magnesium chloride now you can be able to go for this metal halogen exchange. So, here again, you can see the metal halogen exchange is happening at -40°C , sometime this can be done at -25°C depending on the functional group and you can be able to cleanly convert this corresponding carbon iodine bond to carbon magnesium chloride. So, one of the things in this particular reaction always you have to start with the corresponding iodide mostly with the corresponding iodo. So, then what is happening, the isopropyl magnesium chloride can participate in the metal halogen exchange and it will not interact.

As you can see it is an isopropyl group is here. So, that is why what is going to happen as this is a bulkier group, this Grignard is even less reactive. So, that is why it is going to participate in a trans-metalation to introduce magnesium chloride here. You can see there are several different groups in this particular compound you have a nitro and cyano, it still works fine. I think Knochel groups from Germany actually developed this strategy. And there you have a nitro group here, of course, methoxy will be fine anyway, but here it is important you have a nitro you have an ester. So, in this case, if you try to react with the organolithium, I am sure it is ester will get attacked. Here you have 2 nitro groups, still surviving. Again there is an example again, you have an ester here and you have an iodide. So, now, using isopropyl magnesium chloride at -20°C in 30 minutes only this metal halogen exchange was done to form this corresponding magnesium bromide. So, this is showing a very the uniqueness of this reagent that isopropyl magnesium bromide

can be used for metal halogen exchange to get to the corresponding Grignard reagent keeping the functional group intact.

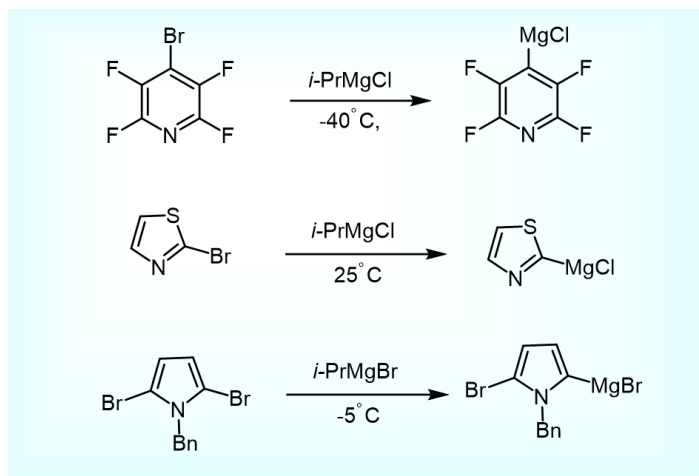
➤ **Synthesis of functionalised Grignard:**



Again there is an example here. You can also do this from the corresponding Grignard reagent. Not only this particular reagent works for sp^2 corresponding iodide, but if you have something like corresponding sp^3 like if you have a cyclopropyl group and you have a bromide. So actually this one started from the corresponding dibromide. So, what is going to happen, I think this could be chloride or the bromide depending on the group you have.

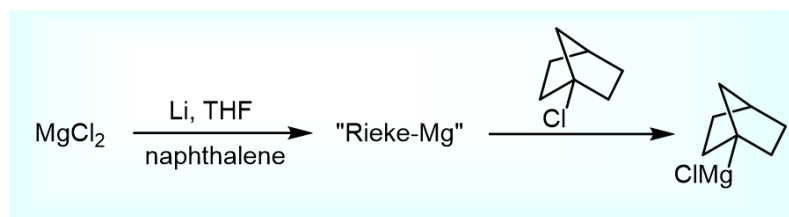
So, you can see it is actually leaving ester unreacted. It can also work with the vinyl system. Here you have a ketone and you have made the corresponding magnesium chloride using this isopropyl magnesium bromide. So, depending on the isopropyl, it could be isopropyl magnesium chloride or bromide I think both work for this type of reaction. Again some more examples here. In this particular heterocycle here this corresponding carbon bromine bond was replaced. So, there is a metal halogen exchange that happens to form this corresponding magnesium chloride. Then in the case of the heterocyclic ring where you see that here also the metal halogen exchange is possible to get to this corresponding Grignard agent. Again you can see sometimes the reaction can go up to 25°C without seeing any other side reaction which will be difficult if you try to do with organolithium. Because of organolithium, you have to always use very low temperatures. Here you have a 2-bromo here and if you use this corresponding isopropyl magnesium bromide at -5°C you can selectively go for a metal halogen exchange to get to this corresponding Grignard reagent.

➤ Synthesis of functionalised Grignard from heteroaromatics:

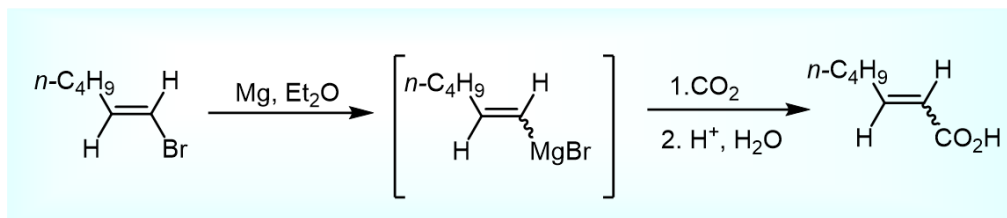


Now, we are going to talk about that in case of this magnesium turning as I was mentioning you guys that there is a magnesium oxide layer. So, that is why this reaction is slower, it took some time to form this corresponding Grignard reagent. So, there is an activated magnesium turning where you do not have the magnesium oxide, they started from the magnesium chloride using lithium and naphthalene which can give you an electron source if you remember. They can generate a compound called Rieke magnesium. So, this Rieke magnesium we are going to talk about a similar thing in the Rieke zinc.

❖ From activated magnesium turning in Et_2O or THF solvent:



❖ From alkenyl and phenyl bromides or iodides in THF:

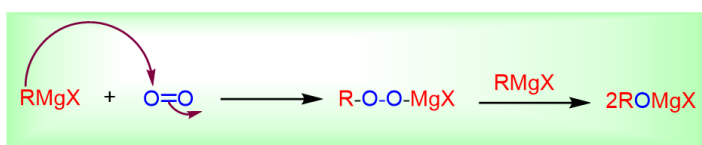


So, these are very very reactive magnesium species. It is just ready to react. So, these types of species are very fast going to react with corresponding alkyl chloride to form the corresponding Grignard reagent. If you think about if you have a tertiary alkyl halide. So, think about here what is happening? Now the corresponding alkyl chloride which was telling you is going to be less reactive corresponding to the bromide and iodide. Now it can participate in the Grignard reaction formation. Again here is an example here corresponding bromide can be also converted to the corresponding Grignard reagent.

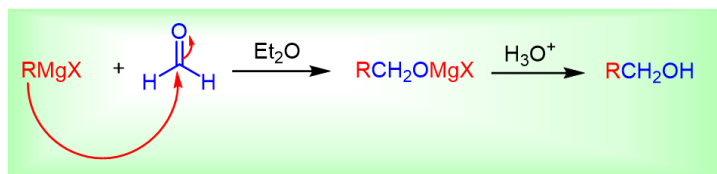
I was mentioning you as it is going through a radical intermediate. So, it might going to lose the stereochemistry which means, you might end up getting to a product that will be either *cis* or *trans*. So, you end up getting a mixture of the product that is the problem with the Grignard reagent which you see if you do the same reaction go for corresponding vinyl lithium, and do the reaction I can guarantee you this will end up giving you the corresponding COOH. Again I think I have already explained to you why that is happening for carbanion versus the radical chemistry. Again this reaction has to be done under an inert atmosphere you do not want oxygen to be present, if oxygen is present it is going to react with oxygen very similar to the corresponding in organo lithium, it is going to form the corresponding alcohol after once you treat with the H_3O^+ . It can also react with the corresponding aldehyde if you have formaldehyde or if you have any type of course, if you have water or acid or amine it is going to go for a proton abstraction.

❖ As a nucleophile:

Grignard reagent acts as a nucleophile and used for the preparation of different functional groups:



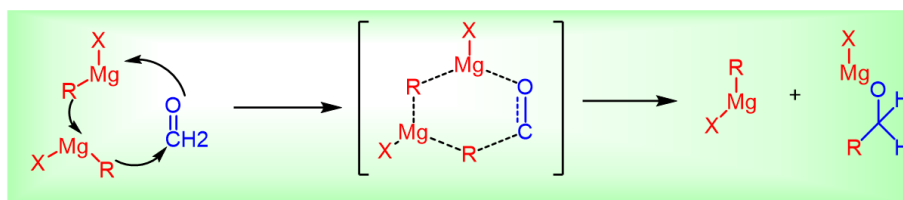
ROMgX then hydrolysed further to ROH in presence of water or acid.



And if you have formaldehyde we are going to discuss this part in the next class. We are

going to discuss more details about the reaction of the Grignard reagent with the carbonyl group. In general, what is happening? There is a 6-member transition formation that happens. So, again this depends on what type of Grignard you are using. If you have a smaller size Grignard, you can think about this type of 6-member transition state.

- The reaction proceeds via six membered T.S .
- One mole of Grignard reagent acts as Lewis acid and another mole acts as carbanion.



- One mole of Grignard reagent gets back which supports our mechanism of involvement of only one mole Grignard reagent for this reaction.

Now why because you can see here two equivalents of Grignard are actually participating. One of the Grignard reagents acts as a Lewis acid to activate this oxygen or I mean to form a coordination with the oxygen to activate the carbonyl group. Once it acts as a Lewis acid it can activate the carbonyl group. So, now the nucleophile attack going to happen from the other Grignard reagent. So, through a six-member transition state, it can form the corresponding alcohol like O-MgX which will convert to the corresponding alcohol after treated with water and there will be one Grignard will come out. So, what is going to happen when one of them only getting reacted to the product and one equivalent is coming back to the mechanism to start the next reaction.

So, in this part, I already told you that what is the definition of the Grignard reagent, how to prepare them, what are reactivity, and why different types of solvents are used, you have seen mostly THF and diethyl ether are used. And I talk about the different structures and then what are the different mechanisms, I talk about the radical mechanism, I give you some evidence to justify that. In the next class, I am going to talk about the different reactions of the Grignard reagent. Again these are the references you can follow. And again thank you for coming to the class and I am going to see you guys in the next class. Thank you.