Molecular Rearrangements and Reactive Intermediates in Organic Synthesis

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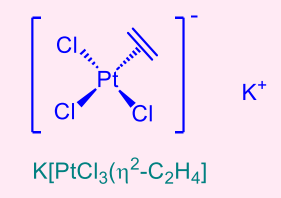
Lecture 32: Organolithium

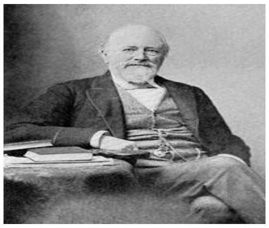
Welcome back to this NPTEL online certification course in molecular rearrangement and reactive intermediates. In the last couple of classes I have talk about the carbocation and then I talk about the carbonyl and then carbene, nitrene free radicals and also benzyne. Then I talking about you know organometallic compound. So, there are briefly I am going to talk about organolithium, then the Grignard reagent, organozinc and organocopper. But before I go and talk about them I am going to briefly introduce the history organometallic compounds. I am going to talk about some of the organometallic compounds and then I am going to take you to the organolithium compounds and their the basic concept, structure and some of the basic reactivity. So, lets start with the early discovery of the organometallic compounds.

It was 1760 when the Cadet was working on the cobalt-containing inks and then he found out later compound called cacodyl oxide and tetramethyldiarsine. So, here you can see the arsenic which methyl groups and there is a bond between them. And, then this is the other compound with the oxygen which is the cacodyl oxide.

$$As_2O_3 \; + \; 4\,MeCO_2K \longrightarrow [(AsMe_2)_2O] \; + \; [Me_2As\text{-}AsMe_2] \; + \; \cdots\cdots$$

And, then in 1827 it was the first π- complex which was the Zeise salt discovered, the platinum metal bind with the three chlorine atoms and π- bond. Then Frankland actually introduced the term organometallic in 1850 and also there are several organometallic compounds which are air and moisture sensitive was actually synthesized using mercury and tin like diethyl zinc, diethyl mercury. And then othe reagents. So, now I am going to define what is called organometallic briefly.





E.C. Frankland

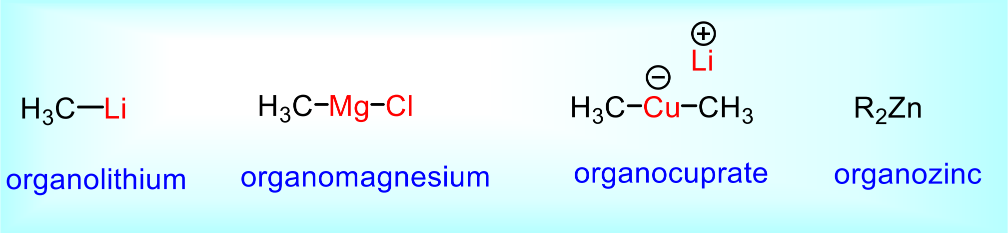
So, organometallic chemistry is the study of chemical compound containing at least one bond between a carbon atom and an organic compound. So, organometallic chemistry is the study of chemical compound containing at least one bond between a carbon atom and an organic compound.

❖ Definition:

- ➢ Organometallic chemistry is the study of chemical compounds containing at least one bond between a carbon atom of an organic compound and a metal.

  - ✓ OMC provide a source of nucleophilic carbon atoms.
  - ✓ React with electrophilic carbon to form a new C-C bond.

❖ Examples of organometallic compounds:



So, that is the important thing you see from the terminology an organo and metallic that means there will be an organic part attached with the carbon a metal. And then they provide a source of nucleophilic carbon atoms because you can see when it is attaching with the metal always the carbon is going to be electron-rich and act as the nucleophilic.

And so, what is going to happen it is going to found to another electrophilic carbon. So, that carbon which is nucleophilic in organometallic compound going to react with other carbon which is electrophilic in nature. So, they can form a bond.

Of course, there are a lot of different in organometallic compounds. you can think about the organometallic compounds from the main group elements or from the main block elements and they are from the transition metal elements.

So, then I am going to show some of the examples in this particular class talk about this four different type of organometallic compounds, one is the organolithium, organomagnesium or the Grignard reagent, organocopper and then organozinc reagent.

Of course, you know this metalloids like silicon, tin and boron containing compounds also called organometallic compounds. So, you are going to also see I am going to discuss about organoboron chemistry as well.

So, again you can classify them as a ionic organometallic compounds or covalent organometallic compounds. They are two different class. So, from the terminology you can clearly understand if it is ionic then what is going to happen you see there is mostly from the alkali and alkaline earth metals.

- Classification of OMC:
  - Ionic Organometallic Compounds
  - Covalent Organometallic Compounds

It means lithium, magnesium metals those are talking about here. And they have maximum ionic character that means these are mostly in the form of like Carbon atom bearing minus charge and Metals bearing (+) charge.

And then there is other type of organometallic compound is called covalent organometallic compound. You are going to find in a lot of these transition metal complex and you have studied there are actually in the class of covalent organometallic compounds.

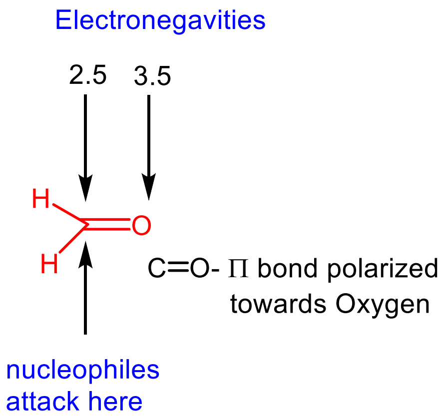
So, then I am going to try to give a brief idea about the differences about this type of organometallic compounds. So, you think about a carbon with a metal. So, lets try to understand about a covalent bond.

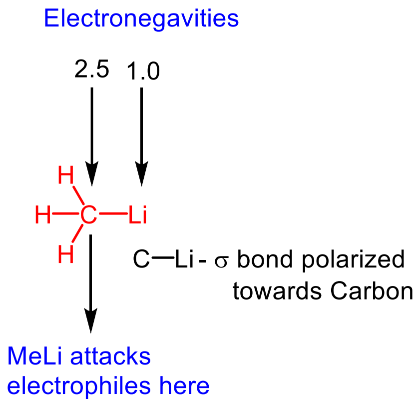
If you think about forming a bond between this and this is a covalent bond, then the polarity is the another important factors are consider. The polarity of the covalent bonds is a very important thing. And lets try to understand the basic carbonyl compound. So, if you think about a carbonyl carbon and an oxygen and if you try to think about the polarity then you always know that the oxygen has electronegativity of 3.5 and the carbon is 2.5 and there is a one electronegativity difference between the oxygen and carbon. So, because oxygen is more electronegative. So, what is going to happen? It is going to pull the electron density towards oxygen. So, you will see there will be some sort of a δ (+) charge in the carbon and δ (-) in the oxygen. Now, if you come to organometallic compound like organolithium or any type of carbon with a metal.

So, what you are going to see here generally in case of the lithium the carbon have electron density 2.5, lithium is 1.0. So, what is happening here? You see something reverse from this here what you are seeing here the carbon having actually a delta minus or a negative charge and the lithium is a delta(+) . And you can see there is a huge difference there is a 1.5 .

So, that means, the most of the electron density of this carbon lithium covalent bond actually lying on the carbon atom. So, that is why you see that in case of this type of methyl lithium it is mostly like a CH_3 -.

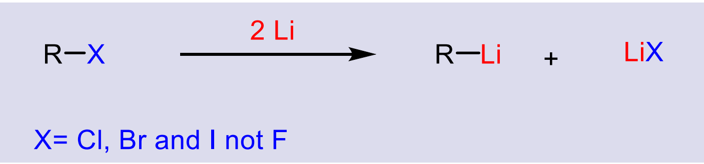
- Interactive display of polarity of organometallics:

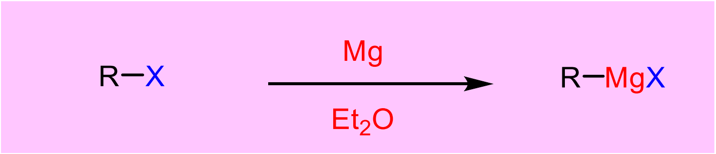




So, I am going to talk about in all these different types of as I mentioned I am going to talk about the organolithium reagents, their synthesis and can synthesize from this corresponding alkyl halide there are also in other methods. And then going to the Grignard reagent using magnesium how to make the Grignard reagents what are the different mechanisms for the synthesis of Grignard reagent. Then you know organocopper reagents of course, the one of the important one is the Gilman reagent, how you can make the Gilman reagent and what are the different reaction using Gilman reagent. Then about organozinc reagents what are the difference between these four about organolithium and organomagnesium which is more stronger or more weaker and if this is stronger the what are the difference between their reactivity. So, we are going to discuss all these different things in this particular topic. So, we are going to start with organolithium.

Formation of Organometallic compounds





$$R{-}X + 2Li \xrightarrow{\text{ether}} R{-}Li + LiX$$

$$2R{-}Li + CuI \longrightarrow R_2CuLi + LiI$$

$$R{-}X + 2\,Zn^0 \longrightarrow R_2Zn + ZnX_2$$

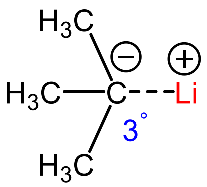
So, you can see first organolithium reagents is react with wide variety of organic substrate. As you can see this is a kind of a carbon with minus,, it can able to react with different compounds.

So, it can act as a base as well as it can act as a nucleophile depending on the structure. And then what is going to happen? So, most organolithium reagents are prepared by hydrocarbon solvent. So, as you see if your organometallic species is very reactive you want something polarizable group are there or something can be deprotonated.

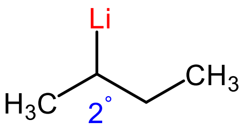
So, you want some sort of a solvent where it will be not going to react with the solvent . So, that is why hydrocarbon solvents are mostly used. If you are purchasing them from any sigma or any other supplier you will always see they are in the pentane or in the hexane solvent. And the important thing, you have an organolithium we are talking about tert-butyl lithium or tertiary lithium you can say secondary lithium and primary lithium.

So, if you have this primary to secondary to tertiary in the organolithium what is the difference between them? Lets talk about their pKa first, from the pKa value we can clearly see going this direction the pKa getting decreases. So, what is happening here? You can see from the structure wise this organolithium, tert-butyl lithium is bulkier compared to a n-butyl lithium or if I am going to write methyl lithium here.

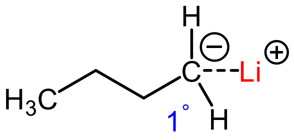
So, that pKa is around 48.



pK_a= 53



pK_a= 51



pK_a= 50

So, what is happening here in this direction you can see pKa is decreases that means, we know from that that if you have a base in the pKa decreases that means the basicity getting decreased. So, this way the basicity getting decreased from tert-butyl lithium to methyl lithium, but if you talk about the nucleophilicity or if you try to talk about the reactivity that will be reverse the reactivity will be highest in methyl lithium and then the n-butyl then the sec-butyl then the tert-butyl lithium. Because, only difference here the size is the another important factor if it is a bulkier then it mostly going to act as a base instead of a nucleophile. We are going to learn the molecular orbital diagram. So, this is nicely given in the Claydon book if you have following that book and go to the organometallic chapter you find that diagram is given.

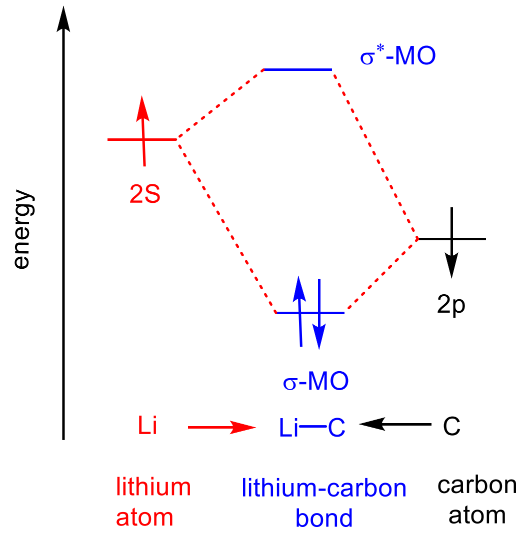
So, what they are talking about from this diagram that if you talk about this carbon and lithium bond. So, this is a covalent bond. So, if you think about this covalent bond here and try to go for the molecular orbital then what is happening?

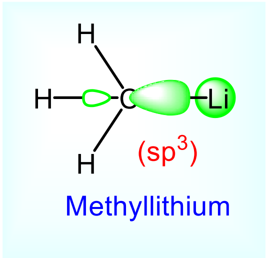
The 2s atomic orbital for the lithium and the 2p orbital from the carbon is forming this sigma bond here. So, now if you see about the energy difference this sigma electron density is mostly in this p orbital on that particular carbon.

So, that is also clearly seen from the molecular orbital that the sigma bond electron density is actually carbon.

- Orbital diagram for the C-Li bond of Organometallic compounds:

Example: Methyllithium





Because carbon is the one which is the closest one and lithium is far from here.

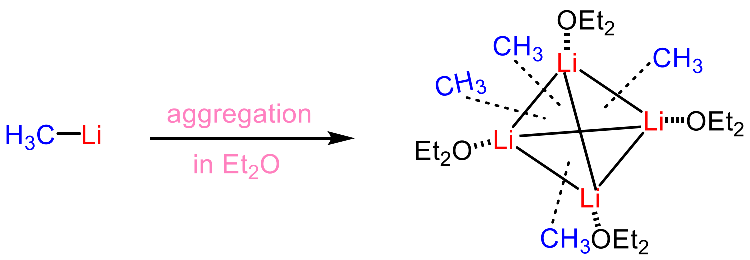
So, that is why you are going to see that the mostly the charges are actually on the top of the carbon the negative charge . So, the other important thing, about this is a question we always ask ourselves that when you talk about this in organo lithium reagent. We are talking about RLi, it could be a methyl lithium or it could be n-butyl lithium, the question always comes does it stay like n-butyl lithium or it has some other structure. So, we always see about once find in a solvent, also find in a aggregation.

So, they actually stay as a aggregation. What is the aggregation? Because the electropositive charges, electronegative charges. If using a diethyl ether, you can understand the ether oxygen can forms a bond with the lithium which is electropositive. So, it can be Lewis acid base in adducts, some sort of oxygen can give in lone pair forms adduct with the lithium. So, that is depending on the solvent you will find them they are forming different sort of aggregations.

So, that this type of aggregation depends on couple of things what solvent is there and what type of organometallic species we are talking about is it a primary organometallic lithium or an organometallic reagent versus a secondary versus a tertiary.

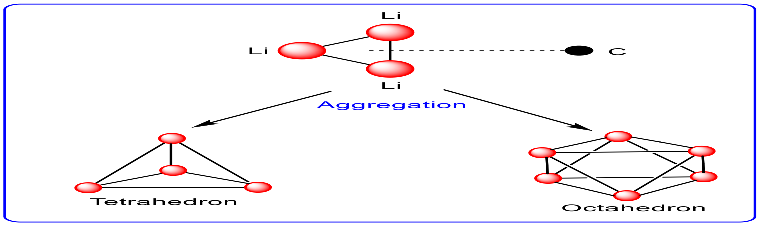
- ❖ Three general factors affect aggregation:
  - ✓ The electrostatic interaction between opposite charges.
  - ✓ The coordination sphere of lithium can be either solvent molecules or Lewis bases.

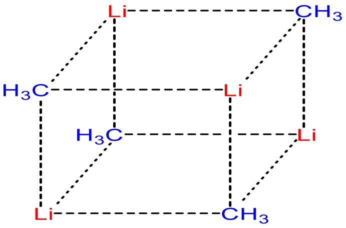
For example:



So, these all the factors are important. And then based on that are going to see couple of different things like tetrahedron or octahedron metal cores going to form. So, here Li_3-triangle going to form.

So, this is a lithium 3 triangle and then after the lithium 3 triangle you will see different type of solvent going to form these aggregates and form the different type of say this could be tetrahedron or could be octahedron or could be something like in case of methyl lithium you will end up seeing something like Cuban type clusters.





And now you are going to see that the why there are different shapes. Again I was telling you at the beginning the most of the cases you see the hexameric aggregates are found. But then the primary alkyl lithium turned out to be the tetrameric unit. Again I mentioned these shapes are mostly you cannot really predict that if you take this particular unknown lithium and you put the solvent you can say this will be tetramer or dimer. There is no such prediction or no such mode.

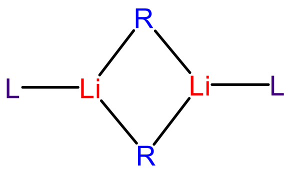
Cubane-type cluster

Mostly people have find out from the extra structure from the different aggregation from there we can able to write them it could be a more tetramer or it could be hexamer.So, you can see primary alkyl lithium mostly go for tetrameric unit. If you have a tertiary alkyl lithium or where alkyl groups are bulky it end of form a tetramer and a linear aggregation. If you have bulky it can form a linear aggregation and in lot of the times also find in case of the secondary or in case of the primary depending on the solvent. They can also form some sort of a hexamer aggregation as well.

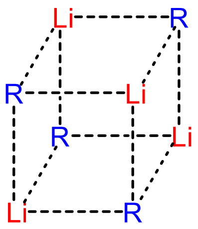
Aggregation of alkyllithium in solid state, solution and gas phase:

- Solubility of alkyllithium compounds in solvents plays an important role both synthesis and in synthetic applications.

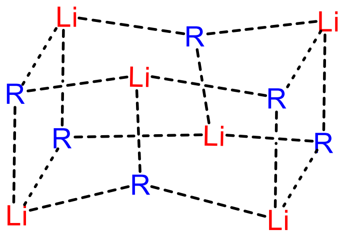
(monomer)



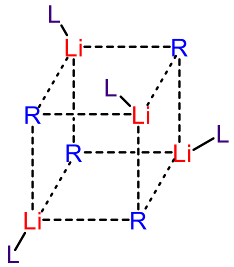
(dimer)



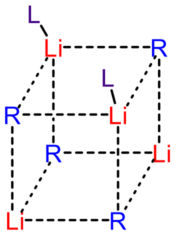
(tetramer)



(Hexamer)



Tetramer(4 ligands)



Tetramer(2 ligands)

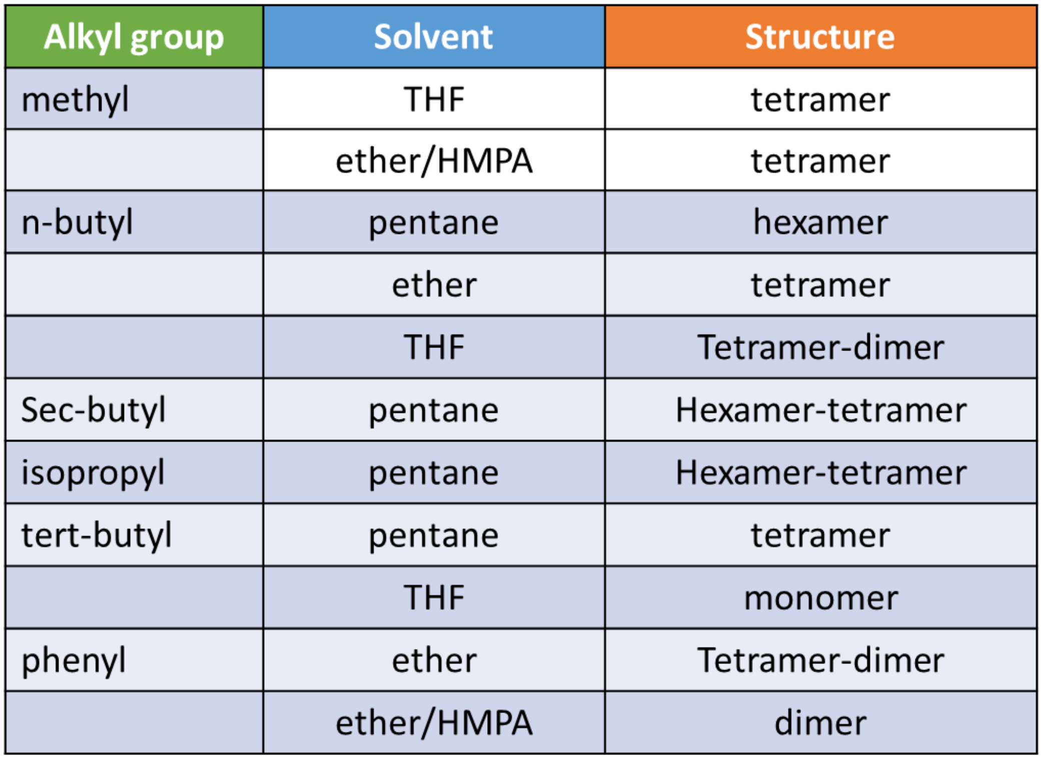
So, there is a list here you can see in case of methyl mostly seeing this tetramers in THF and HMP. So, there are list of some common solvents you are able to purchase them. In case of n-butyl there is a hexamer happening, in case of pentane solvent and an ether it is forming tetramers .

So, again these are the structure which was found from the X-ray and that is why it was written here. Again there is no hard and fast rule that whatever structure they are going to form.

Again depending on the solvent, you can see the same n-butyl lithium it can form a tetramer or it can form a hexamer. very similar thing happening in case of sec-butyl or in case of tert- butyl lithium. Sometime in the case of tert-butyl in the THF solvent. it can form a monomer depending on the solvent because what is going to happen in a solvent, is going to make another important thing here because depending on the solvent structure and depending on how the solvent is forming a coordination with lithium these shapes are also depending on that. Another important fact that always question arises that why organolithium reagent go to a low temperature like sometime minus, mostly are doing in -78°C.

Structure of alkyllithium in various solvent

- Organolithium reagents adopt structures in solution that differ from the solid state.
- Interaction between lithium ion and the carbanion centre are static or



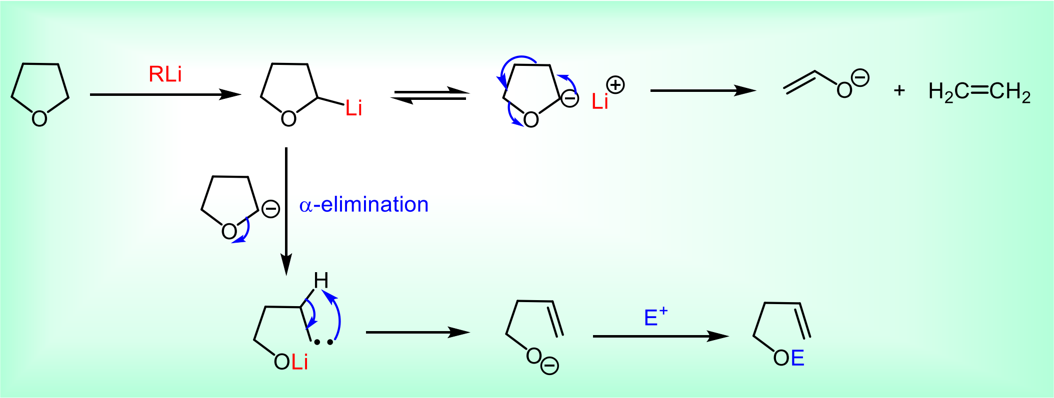
Alkyl group	Solvent	Structure
methyl	THF	tetramer
	ether/HMPA	tetramer
n-butyl	pentane	hexamer
	ether	tetramer
	THF	Tetramer-dimer
Sec-butyl	pentane	Hexamer-tetramer
isopropyl	pentane	Hexamer-tetramer
tert-butyl	pentane	tetramer
	THF	monomer
phenyl	ether	Tetramer-dimer
	ether/HMPA	dimer

So, one of the important fact is that for some solvent like tetrahydrofuran which might mostly use, you try to do organolithium chemistry in the lab. then this type of solvent areusing and increase the temperature, and also not doing a minus temperature but coming to a room temperature. So, I think this type of THF started breaking out. So, what happened when solvent is going to break down and form ethylene and lithium enolate some sort of an enolate going to form. So, it is going to break down through such mechanism and then it is going to form two species.

Why organolithium reagents are conducted at low temperature in solvent:

- ✓ All the solvents suffer to some extent to react with organolithium .
- ✓ Et_2O is stable over a period of days in the presence of BuLi at room temperature.
- ✓ THF is readily decomposed by organolithiums at this temperature.
- ✓ The products of this decomposition – ethylene and lithium enolate of acetaldehyde.

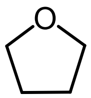
For example: In THF

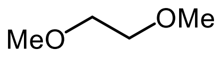


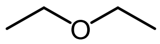
So, that is happen that is why try to do this reaction at very low temperature because do not want the solvent to be decomposed because this can also take part the entire reaction. And there is another mechanism also that it can form after the lithium formation happening.

So, first thing is with increase the temperature the proton going to abstract by organolithium reagents. So, that going to form this corresponding lithium and only can able to alpha elimination or it can form this type of species here in ethylene and this lithium ionised species or it can able to go for alpha elimination and then going to form this type of species. So, some common solvents are use for these organolithium reagents general diethyl ether in the lab or THF and DME.

- Mainly used solvent in organolithium reactions are:

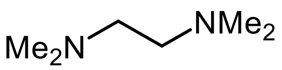

THF

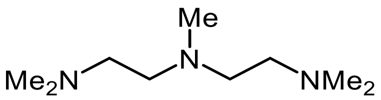

DME

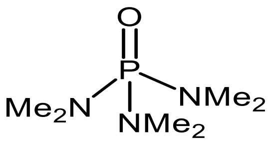

Diethylether

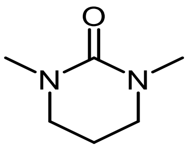
These are the very common solvent. And lot of the times see in the lab also using some additives in organolithium reaction like TMEDA. a tetramethyl ethylene diamine or it could be a pentamethyl. Since also use a HMPA or it could be DMPU. So, all the different type of additives are used.

- Importance of coordinating solvents:


TMEDA


PMDTA


HMPA


DMPU

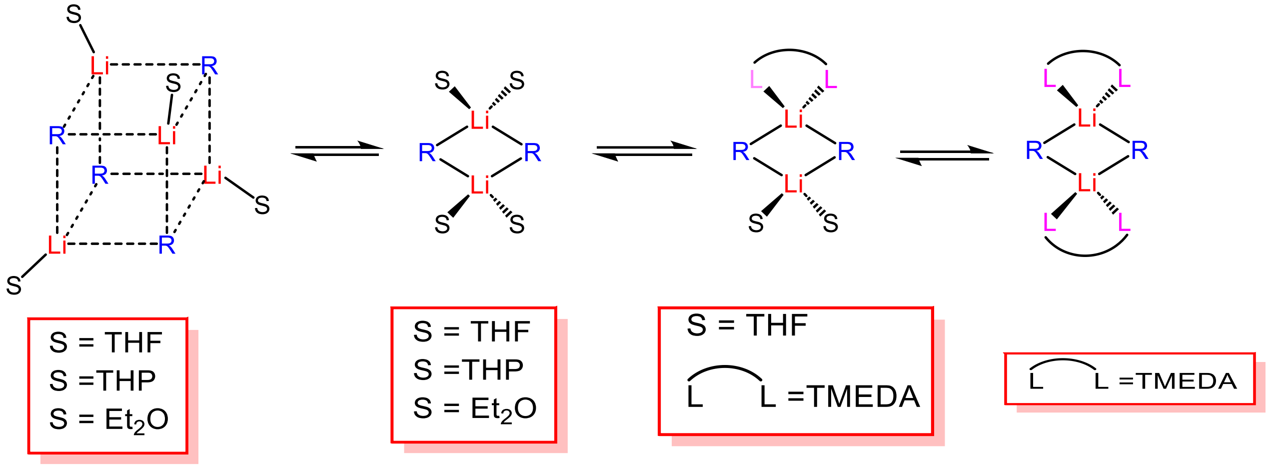
So, we can see. So, these are nitrogen-based compounds. So, we use in this type of compounds in the reaction as additives. So, now, the question comes why we have to use this additives in the reaction? What is the role of these additives? So, first we have understand that this type of organolithium reagents when we are finding in the corresponding solvent like mostly they are in the pentane or hexane. So, also used ether solvent. So, they are actually forming a aggregate that already talked about it.

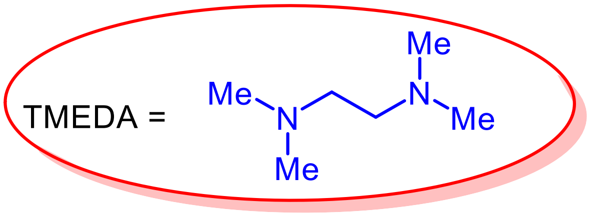
Now, if it is exist in the aggregate form then the lithium is not the reactive. So, what we try to use? We use this type of reagent like TMEDA or we have seen the HMPA. What is going to happen? These nitrogen going to make a complex with lithium metal.

So, these two nitrogen of TMEDA you can think about So, they can make a complex with lithium, once they will get the lithium out it can go for a decompression. That means, from the aggregate it can form a smaller complex and it will make the anion free for reacting.

Is TMEDA a good ligands for organolithium chemistry?

- ✓ Function as a donor ligand reduces the degree of aggregation.
- ✓ Increases nucleophilicity of these organolithium reagents.
- ✓ Acts as a good bidentate chelating ligand and forms a stable Li-TMEDA chelate structure.





That means organolithium will be much more reactive after forming this aggregation. It also does one important thing to stabilize it. So, that is the important thing, it actually acts as a bidentate thing. So, it forms a chelate with lithium metal and then increases the nucleophilicity. And there are different thing as I mentioned and again use them in a stoichiometric amount that is also another important thing.

Reactivity of Organolithium compounds:

- ✓ Organolithium compounds are ionic in nature.
- ✓ Due to small size of Li- cation posses greater polarising power.
- ✓ Organolithium derivatives are extremely reactive called Super Grignard reagent.
- ✓ Highly air and moisture sensitive, kept in inert atmosphere.

If using one equivalent of them, also use 1.5 equivalent in a little more. So that lithium got to form some sort of a chelate. So, these are the common thing to buy from store. So, it comes with a particular strength n--butyl lithium, sec-butyl lithium or phenyl lithium, tert-butyl lithium can able to buy from the store and they come with a particular strength and I am going to also teach in the later classes that also use some sort of a titration method. There are several different methods to titrate them that we have to find out what are the strength of this organolithium reagents.

So, again these are ionic in nature due to the small size of lithium metal, there is greater polarizing power and they are extremely reactive. So, again I think sometime they are not only pyrophoric. If we talk about the tert-butyl lithium these are also pyrophoric because they are very much reactive Again the reactivity of organolithium compounds towards the air and water. So, we are talk about that type of compounds are actually moisture sensitive and air sensitive. What that is mean? That means if we take the organolithium compound to a water what is going to happen? It is going to form lithium hydroxide and corresponding alkane.

So, that is why we have to make sure that of course, we can understand clearly this is a kind of some sort of a carbanion. So, if we take a water it is going to quench it. And if we take a oxygen what is going to happen?

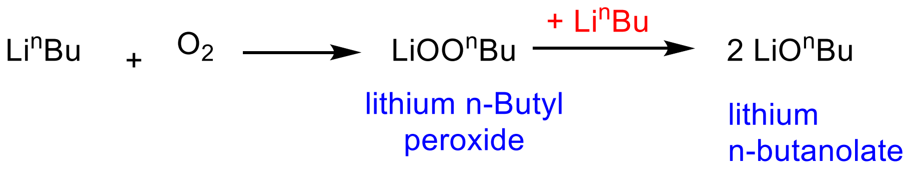
If we found oxygen with organolithium like n-butyl lithium it is going to form the lithium n-butyl peroxide and finally, it is going to make lithium n-butoxide or you can make the same compound as a lithium n-butanolate . That means, again we have to understand these compounds are react with the moisture as well as with the air. So, the other important parameter we should understand that once we are talking about different organometallic reagents, we talk about organopotassium is also there, organosodium, organolithium, organomagnesium.

➢ Reactivity of organolithium compounds towards air and water:

- ✓ Organolithium compounds are air and moisture sensitive.
- ✓ Reaction with alkyl lithium and water are exothermic in nature.

$$\mathrm{LiR} \;+\; \mathrm{H_2O} \longrightarrow \mathrm{LiOH} \;+\; \mathrm{RH}$$

➢ Reaction of alkyl lithium with molecular oxygen, initially formed lithium alkyl peroxide reacts with excess alkyllithium to alkanolate.



$$\mathrm{Li^{n}Bu} + \mathrm{O_2} \longrightarrow \mathrm{LiOO^{n}Bu} \xrightarrow{+\,\mathrm{Li^{n}Bu}} 2\ \mathrm{LiO^{n}Bu}$$

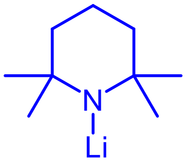
In this directions seeing the percentage of metallic character. As the percentage of metallic character increases from the magnesium to lithium to sodium to potassium, so reactivity getting increased. So, if we think about organic sodium compound versus organolithium compound then of course, sodium and potassium will be much more reactive compared to organolithium. And, again we found compared between organolithium with organomagnesium or the Grignard reagent, then organolithium will be much more reactive then compared to the organomagnesium because of the percentage of ionic character. Now, I am going to talk about that as I mentioned organolithium reagents, all cannot be act as a nucleophile, but they can act as a nucleophile or a base.

➢ Organolithium are more reactive than Organomagnesium:

Metal % of	K	Na	Li	Mg
ionic character	51	47	43	35

Reactivity increases

So, that is also depend on their size. So, that means, if we taking organolithium reagents like I mentioned LDA, TMP are lithiummetal based compounds. So, TMP is a tetramethyl pyrrolidine, then also we can also see LHMDS. So, here we can see what is the structure of lithium metal and the size of silicon. So, it is a hexamethyl disilane. So, again if we see this characteristic of this compound and here what we have isopropyl we always talk about these compounds.

	$i\text{-}Pr_2NLi$		$(Me_3Si)_2NLi$
	LDA	LTMP	LHMDS
pK_a of amine	38	37	30

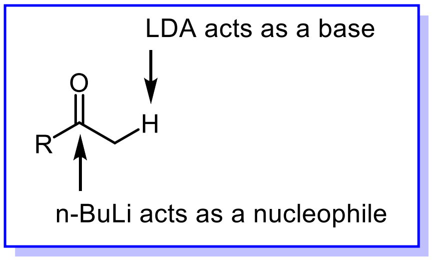
So, now see about this structure one of the important thing is these are really this you know next to the lithium this carbon has a hinder in case of lithium TMP or in case of LDA. We see there is a bulkier group or in case two silicon groups are here. So, because of this bulkier group, you know this type of organolithium species can see their pKa values. So, this is pKa 30, 37, 38 these are quite strong base.

So, these are commonly used for deprotonation. We will see this base are using for the deprotonation purpose, because bulky structure are mostly used as a base instead of a nucleophile. Again if we talk about n-butyllithium or methyl lithium you will see them what is going to happen. They mostly act as a nucleophile instead of a base because again organolithiums are very hard. So, they can able to go for 1,2- addition which going to explain also. So, first thing they actually participate many different reaction and they act as a base as previously mentioned.

❖ Chemoselectivity:

R_2NLi- are non-nucleophilic, strong bases

RLi- are powerful nucleophile as well as a strong base

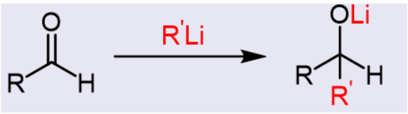


So, that means if we found out that some sort of an organo lithium reagents and an acidic proton like you have a proton this carboxylic acid then first thing will be deprotonation going to happen. And of course, if you use excess then it is going to also attack. So, if you take an aldehyde it is going to attack carbonyl carbon from the corresponding aldehyde. Then formed oxygen lithium substance. Then if you put water, it is going to form the corresponding alcohol.

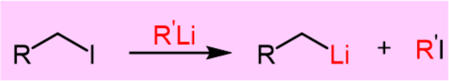
➢ Alkyl lithium participates in many reactions:

- ✓ As a base:

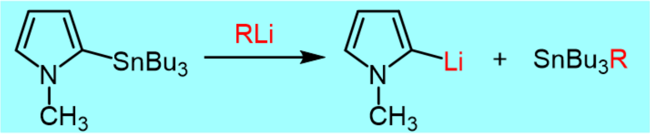
- ✓ Nucleophile:



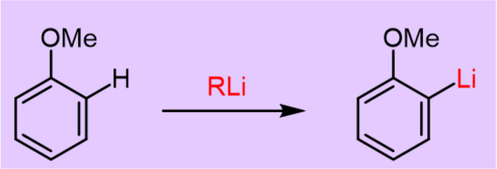
- ✓ Metal-halogen exchange:



- ✓ Metal-metal exchange:



- ✓ Ortho-lithiation:

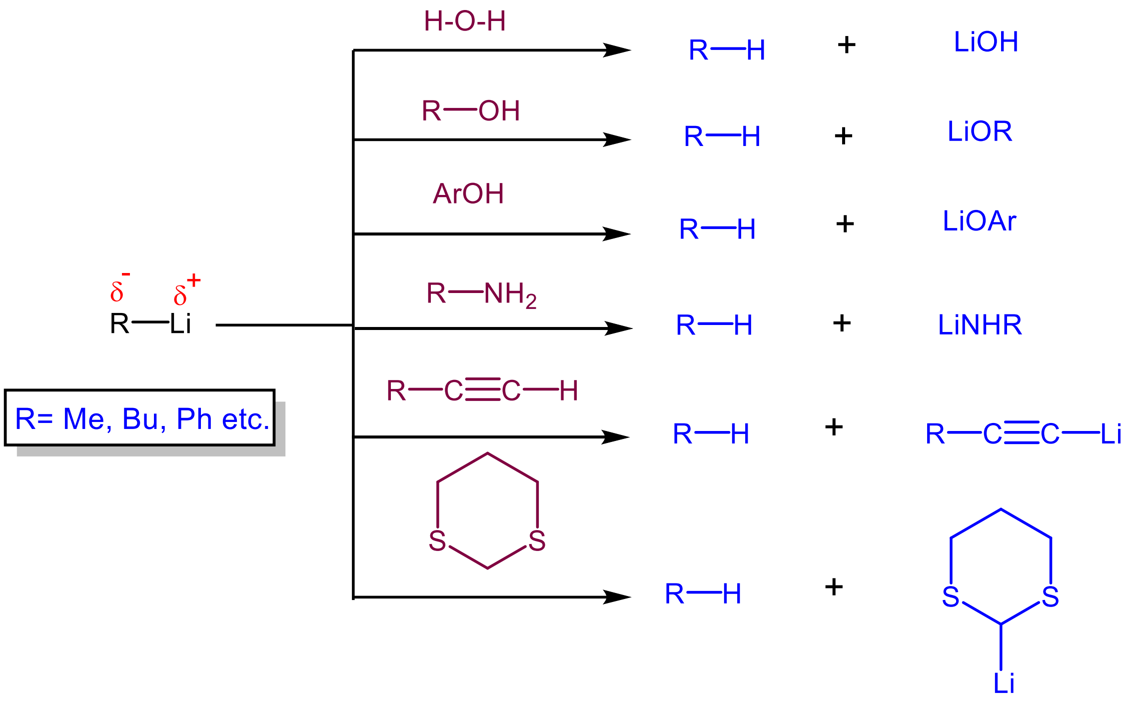


Again I am going to come back to some of this in a specific example. It can also react with an alkyl halide then it can go for a metal halogen exchange to generate a corresponding lithium. Then it can have a metal-metal exchange that means, it is a called some sort of a transmetalation can happen if you have a organo tin, then used organo lithium it can generate organolithium reagents through a trans metalation or it could be an ortho lithiation. Then if you have some sort of a directing group, like lone-pair containing -OMe group where oxygen atom coordinate with lithium metal through H-bond. So organolithium reagent can deprotonation from the next carbon to the directing group. Then this C-H bond going to get deprotonated to form this corresponding lithium containing substance.

So they are strong base, they can easily abstract a proton from water, alcohol. So, you can understand these are base. The basicity ranges from 30 starting from pKa 30 till it is going up to 55. So, that means there are a lot of these things, lot of these proton from in this range which all of them going to get deprotonated starting from water. So, you can see phenols, anilines or amines, alkynes and dithians products and all going to get deprotonated.

- ➢ As base:

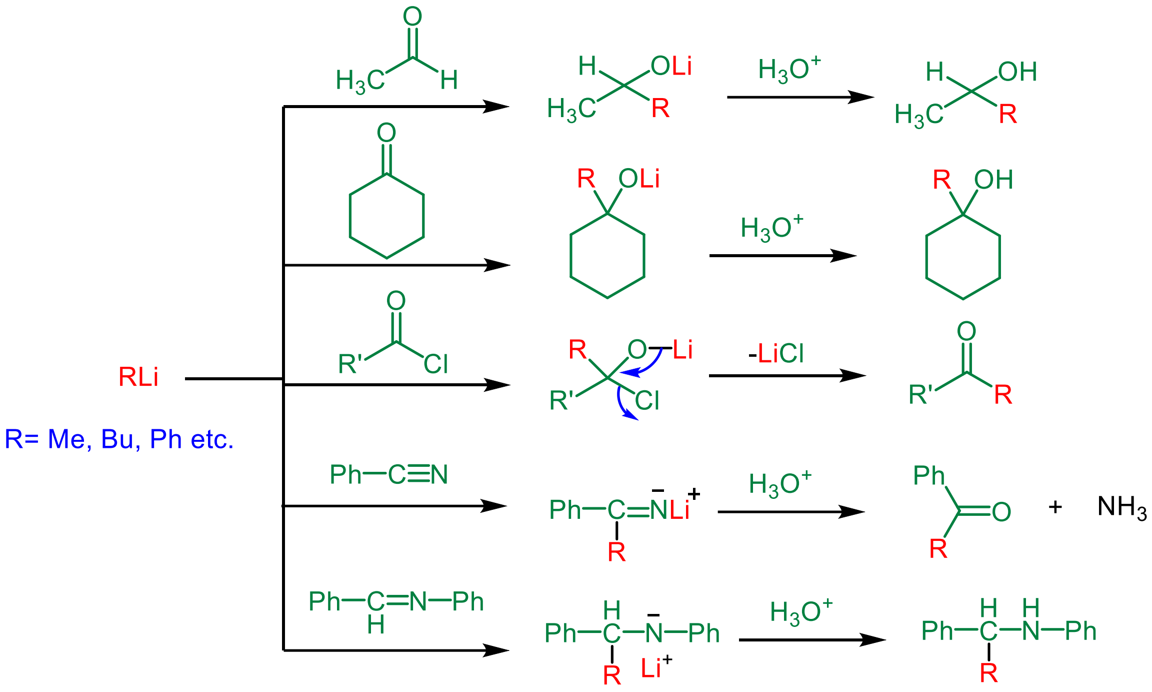
- ✓ They are strong base: Abstract acidic proton



They are also good nucleophile as I mentioned if you are using this type of alkyl lithiums they are very good nucleophiles. They are going to add to all this substance aldehydes, ketones and acid chloride, then it can also add to the cyanide and every cases in the former one you end up getting alcohols and you can add to acid chloride, it is not going to stop here. Then if we used one more lithium, getting the corresponding alcohol. If we take the cyanide, to form lithiated intermediate and further hydrolyze to give the corresponding ketone. It can also add up to the corresponding imine then it can protonate and then go to the corresponding amine.

- ➢ As nucleophile:

- ✓ They are Good nucleophile: Attacks on electrophilic centre



So, going to spend some time in this part and in the next lecture what are the different methods for the preparation. So, one of the important method for the synthesis of organolithium reagents, using metal halogen exchange methods or some books mentioned as an oxidative addition. So, let's try to understand what is happening. If we taking alkali halides and lithium wire, again you know purchase the lithium wire which can be sold as a lithium wire in kerosene. The reaction between lithium wire and alkali halides that can generate corresponding alkali lithium.

So, now you can think about why they are saying this is oxidative addition because change the oxidation state. So, that is why it is saying some sort of oxidative addition, but mostly this type of reaction is metal halogen exchange because at the end halogen is replaced and introduced lithium. So, there is some example here. you can have this in a cyclopropyl bromide it can metal lithium can also able to do instead the lithium.

Lithium wire you can also use. Another organo lithium reagent which can able to do the generating this type of organo lithium species. It can be corresponding bromobenzene can also same thing happen, to generate the corresponding phenyl lithium. Then there is a carbanion-halide exchange. So, suppose if you take corresponding organo lithium reagent and magnesium halide that can generate RMgX and lithiumhalide.

Thus, it can also react with the magnesium halides. Now, the most important method among all of this is the deprotonation.

You are going to see in a lot of this discussion about this topic. You are going to see there are lot of different protons because organolithium reagent act as a very strong base. It is going to deprotonate, a lot of the acidic proton you will see and then it is going to generate the corresponding in organolithium. After deprotonation, it will generate a negative charge on the carbon atom and a positive charge on the lithium metal.

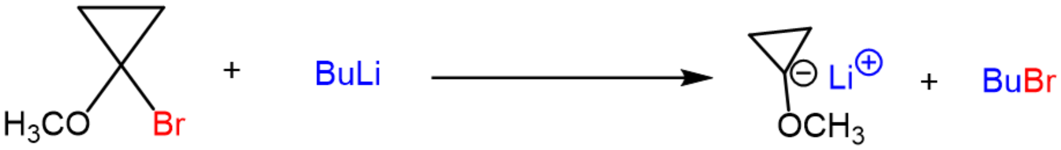
So, we are going to talk about this. So, there are different type of methods and you will see there will be different type of protons. It could be sp3 or sp2- hybridized. So, this proton could be attached with a sp2 carbon or with a sp3 carbon. So, we are going to discuss in detail this part.

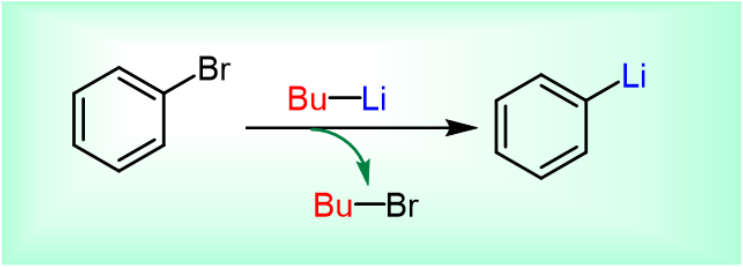
Then there will be a transmetallation, we are going to talk about them in the lot. So, we are going to discuss transmetallate with tin and some other like selenium metals. So, in this particular part I try to talk about the definition of organometallic compound, what are the difference between organo magnesium versus organo lithium versus a organo copper and organo zinc. Then also I try to talk about the important thing the polarity of the organo lithium compounds. Then also I talk about the one of the important thing about aggregation. organolithium reagents showing what are the different aggregated structures? Then the role of the additives TMEDA, what we use for the organolithium reaction.

The following methods can be adopted to prepare various organolithium compounds:

1. Oxidative- Addition or metal halogen exchange reaction:

$$R{-}X \; + \; 2\,Li \xrightarrow[-20^{\circ}C]{Et_2O} R{-}Li \; + \; LiX$$





2. Carbanion- halide exchange:

This reaction involve the interchange of the carbanion (alkyl / aryl) and halide groups present on two different metals.

$$\mathrm{Li{-}R} \quad + \quad \mathrm{Mg{-}X_2} \quad \xrightarrow{\text{ether}} \quad \mathrm{Mg(R)X} \quad + \quad \mathrm{LiX}$$

4. Deprotonation or Metal hydrogen exchange reactions(Metalation):

Due to polarization of the alkali metal carbon bond, the carbon atom bound to an alkali metal should be a strong base which is capable of abstracting Protons from more acidic hydrocarbons.

$$\mathrm{LiC_2H_5} \quad + \quad \mathrm{Ph_3CH} \quad \longrightarrow \quad \mathrm{LiCPh_3} \quad + \quad \mathrm{C_2H_6}$$

5. Transmetallation:

This route depends on the difference in the free energies of the formation Of the two species

$$\mathrm{2Li} \quad + \quad \mathrm{Mg{-}R_2} \quad \longrightarrow \quad \mathrm{2Li{-}R} \quad + \quad \mathrm{Mg}$$

Of course, the one of the important thing, you should understood in this class is the basicity versus nucleophilicity. So, depending on the organolithium reagents you can see one cases. it is going to abstract a proton and in other cases it is going to 1,2- addition. I am going to discuss this particular topic the preparation of organomeallic reagents. Again, these are the references here and again thank you for coming to the class and I am going to see you guys in the next class. Thank you.