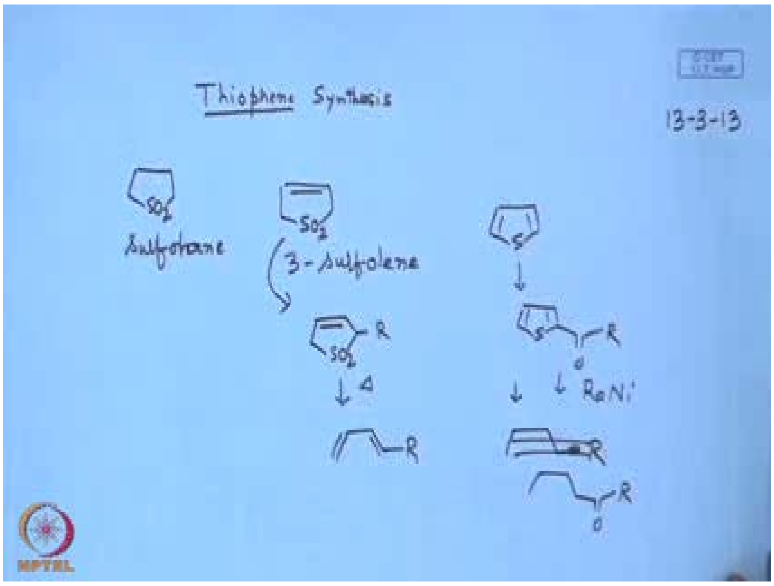
Heterocyclic Chemistry
Prof. D. R. Mal
Department of Chemistry
Indian Institute of Technology, Kharagpur

Lecture - 35
Thiophene Synthesis

(Refer Slide Time: 00:22)



Good afternoon. Today topic is synthesis of thiophene. And like previous topic, thiophene synthesis is an again an important idea, but you have to justify what of the importance; and very quickly let us have the little bit of the look at the importance of these categories of this compound. And you have any idea can you prompt me on this aspect, whether why they are so important thiophene? Where have you come across the important of thiophene. See like pyroles there are plenty of natural products, they are polymers etcetera. Furans they are very important reactive intermediates.

Similarly, I mean, so likewise they will thiophene actually do not figure in natural product. There are very few natural products which will have thiophene nucleus. And in the other hand, there are very useful as a polymer; if you remember last time I talked about there is a polymer called PEDOT. That poly ethylene dioxythiophene which is produced in tons and tons. And this polymer is of paramount importance in the field of organic transistors then organic light emitting diode what we called OLED. And then there are several applications actually as conducting polymers. And sometimes we called organic metals these poly thiophenes are known as organic metals.

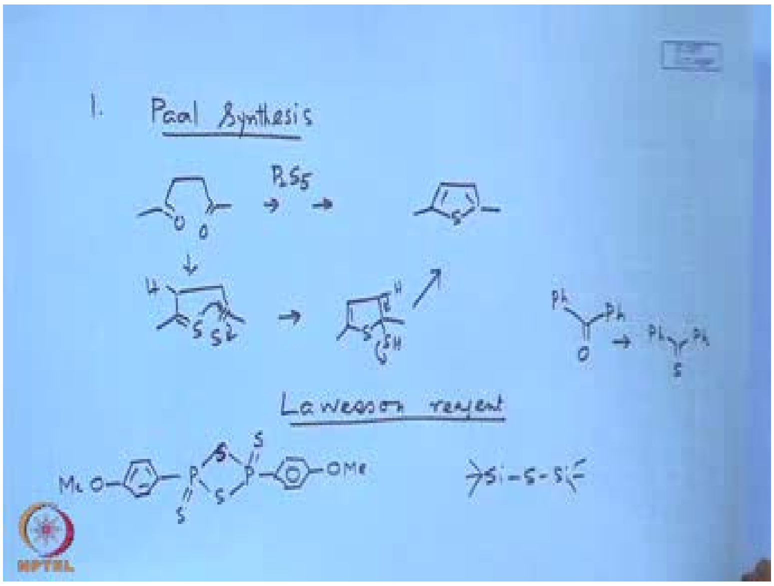
So, that means they are very important. In addition I think many of you know in large number of thiophene derivative are nice organic intermediates. And one of them is very popular solvent many of heard of material called sulfolane right this is sulfolane. What is it use for? It is basically organic solvent it is organic solvent. Then there is molecule also called it you know of which is nothing but it is known as I think many of you know what is it? It is sulfolane 3 sulfolane. And it is I mean there are ways to look at it this called solid burdinne in fact; burdinne can be combined to a sulphur dioxide to produce a nice solid. So, both the gases immediately react with each other and form the solid.

And, this can be stored in solid forms in for years in years in fact; if you like to see I have a bottle of this a big bottle quite nice powder. It is the basically, source of small scale depression of Burdines. So, one can just take this heat at around 140 degree; so you can get the Burdines otherwise, you have to by a big cylinder. So, when small scales one can quickly generate this one. And what else you can actually for example, you can derivatized by using LDA.

And, then alkyl halide you can convert this into this one. Then if you heat it of course, what will we get it? Will be getting the substituted Burdines. So, that means there is very important reactive source. And similarly, many of you probably know what can be done with this thiophene also is a nice starting point for Diels- Alder is not that popular though in thiophene case not very like furan case that is not very popular.

Because most of us know thiophene is most aromatic nucleus in this range. But what can be done in very quickly 1 or 2 steps. One can produce a branch or long chain alkenes how do you to produce? Not, yes, reduction. Actually, what one can do first you have to derivatized corresponding plus a you can produce something like this right. So, Friedel craft reactions kind of use. And it undergoes reactions at 2 positions. Then you do the reduction. And you can do the reaction let us say normally with RaNi. So, what we can get? We can get a product which would be looking like this. I say that means you have a long chain hydrocarbon kind of compound from this one of the materials.

(Refer Slide Time: 05:58)



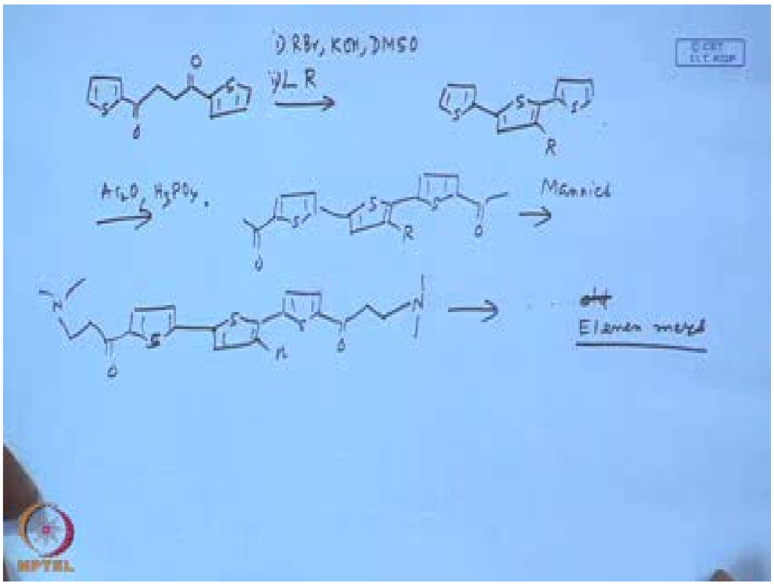
So, today what we do we will take up different synthetic methods and based on normally this starting material and based on normally this starting material. And if so the first one sometimes it is once again it is known as a Paal synthesis not there Paul knor anything like that Paal synthesis. So, the name tells you what should be the starting material right the starting material should be 1, 4- diketone. And then the reagent and that would give you in one step corresponding this small. And what is the reagent? The commonest reagent is I think many of you know P 2 O 5 right P 2 O 5, sorry P 2 S 5. And what are the so intermediates actually; there is an exchange of sulphur with the oxygen. So, what will we getting; will be getting I mean this is assume it is not isolated. Then like regular kind of thing so what will be getting; will be getting sort of an intermediate Thiol kind of thing.

And, then as usual for aromatization you lose H 2 S. So, we get this one only disadvantage with this method many of you could do not know it is little rest to carrier to reactive area ok. P 2 O 5 is reactive region number 1. Number 2 is inorganic material. So, it does not can to dissolve in organic solvent. So, it is sort of a like heterogeneous reaction. And the best way to circumvent this problem you have to use a sort of a hybrid kind of reagent. And the reagent which is popular in this area I do not know how many of you know of this reagent; this known as Lawesson reagent. And what is it? It is basically an organic molecule then couple to it P 2 S 5; and which starts from any soul.

Then, you will link to with phosphorus then again this sulphur then phosphorus again one more nucleus of anisole; and that would give rise to nice yellow crystalline solid. And anybody can do it; in fact we used to make in regular basis this compound; and it is known as thionosine reagent. That means, this reagent is very popular to convert corresponding ketone to corresponding thione like say let us say you have I mean benzophenone.

And, you want convert this into thiono benzophenone or thioketones of benzophenone; how do you do it? It is to perfectly alright. But this is base to a as I said it has nice to soluble in organic solvent, and it is manageable, and it is not that reactive. So, this is one of the best with two. And then you can also try with this let us say bis trimethyl silane sulphide like this one. This is also can be useful in the presence of P 2 S 5 ok. So, I will give gust 1 or 2 examples of this synthesis.

(Refer Slide Time: 09:44)



Why it is so useful? Like say if you start with a thiophene contain a compound; then again a ketone has to 1 4 and then once you have a thiophene. So, you do I will just now onward I will write L R Lawesson reagent. And so first thing what you do? If you start with this; and then react with RBR that means alkyl halide and KOH. And I tell you why need all these things and DMSO is a solvent, because you using KOH. And then I use this I mean Lawesson reagent. So, what we expect here? You can expect here that a again now thiophene derivative with 3 nuclei and this is R here. And then so what will you find? 3 different kinds of nuclei. Why you are doing so because as I just tell told you before to start with that oligo thiophenes are very useful as semiconductors; so conducting material.

So, this is the way one can make ((Refer Time: 11:06)). That means the lawesson reagent is useful for thiophene containing 1 4 di ketone. And but before we do the formation of thiophene what we do? We have done alkyl acyl with regular KOH and DMSO. We introduce a R group in the nucleus. The reason be so if you have a large alkyl group if the polymer would chemistry no it has an advantage; what is the advantage? Have alkyl side chain of monomer.

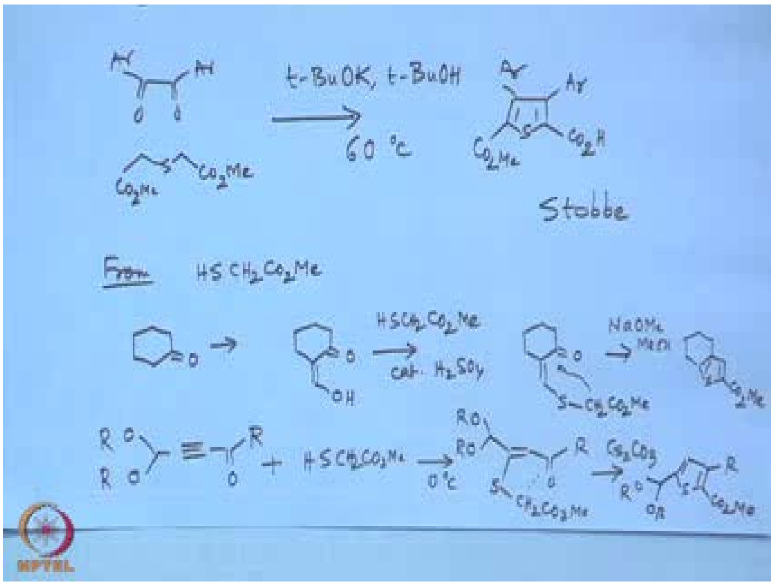
Student: ((Refer Time: 11:36))

Professor: Solubility, best thing would be say processability is the better term for the polymer chemistry. So, you can go on then let us say I mean they are all important let us say acetic anhydride and phosphoric acid; so what we can guess here? Acylacyl. so that means will we get this acylacyl done at 2 end the middle one of course, do not have any 2 and 5 positions are blocked. So, one can have the an acylacyls on the 2 end side right.

So, we can go on doing all these things; and what next in perform this onward you can do mannich reaction; I mean I am just giving 1 example how to grow on this original molecule with more thiophene nuclei. So, you can contact this into I will just very quickly right this thiophene and then this and you can just quickly do mannich reactions. So, all of us know mannich reactions would give you this co Lawasson by 1 carbon right. So, similarly, on this side also will give homologations this. Now, from here you can generate again 1 4 di ketone with michael addition with thiogen reaction; that is scatter reactions benzyl thiophene like be potassium cyanide.

So, one we do synthesis the benzoin kind of thing in case alpha beta ketone; it gives you 1 4 di ketone. So, then you go on doing this and eventually you get to the oligo mars. In this example what I was sighting it has produced 11 mars I think all of you understand; that mean that total of the11 nuclei of thiophene. So, that means this is the way that mean this is analogous to all others pyrrole and furan nucleus. This is only one thing to remember reagent; in this case what is the new we have learnt? Lawesson reagent.

(Refer Slide Time: 14:26)



The other way to go to this thiophene system is method called Hinesburg synthesis; it is nothing but it is a very simple synthesis based on aldol type of condensation. If you have 2 ketones, 1 2 di ketones for example, Ar and Ar; and so one can just think about a bis acetate thio bis acetate or thio di acetate; you can say. If you take thio di acetate with sulphur in this. So, that is what we have to remember that in this case di acetate and this reagent of course, all of you can guess what could be the reagent?

The reagent could be strong base and normally potassium tertiary butoxide and is used in permission with acid butanol. And the temperature here is around 60 centigrade. And all of you can guess what is the product? The product would be a thiophene. Here, Ar and Ar then as the methyl here; and a carboxylic acid little tricky though; and you see only one has got hydrogenation you got hydrolyzed the other and the remaining intact. If you have come across such things seen in very famous reactions in carbon elongation process; anybody know this reaction; Stobbe condensation. Never this reaction with benzaldehyde and

Student: ((Refer Time: 16:14))

Right succinctness. So, you get half ester ok. There are also similar reaction because in that we will get in that ok. And next thing that I think from now onwards what will we do? Will go by the sulphur containing compound used in the synthesis. The previous one was bis acetate thio acetate. And the next one thioglyconic acid. Thioglyconic acid means basically, all of us know glyconic acid is HS CH 2 ester ((Refer Time: 17:09)) is this one like ok. And then so what we can see here sulphur carbon sulphur and carbon that means 1 carbon is the provided for the nucleus; and this is one of the homonest starting material making this thiophenes like. I will give 1 example here, let us say if you have cyclohexanone and one can readily convert into this compound right. Homologuet compound I will not tell you may be comeback and ask you same question.

Now, if you react with this thioglycol ester methyl thioglycolate; in the presence of catalytic amount of sulphuric acid. So, what we expect here, get different then glycolic acid at set ra. Sulphur has propensity to undergo aldol condensation wrong or right? Normally, sulphur actually prefers to undergo conjugated additions, because of the last size; and it is so one would expect here; that means alpha beta positions would be effect by sulphur then followed by elimination of water.

So, you are expecting basically acid catalyzed condensations michael condensations kind of thing here. So, once you have this you can guess in the previous example what was it? It was Hinesburg method it was sort lot of like aldol condensations kind of thing. So, in this case if you use sodium methoxide once again methoxide means the other solvent is methanol; so what we expect? A kind aldol condensations kind of thing. So, we will get a fused thiophene and of course, one of the substituent is an ester here.

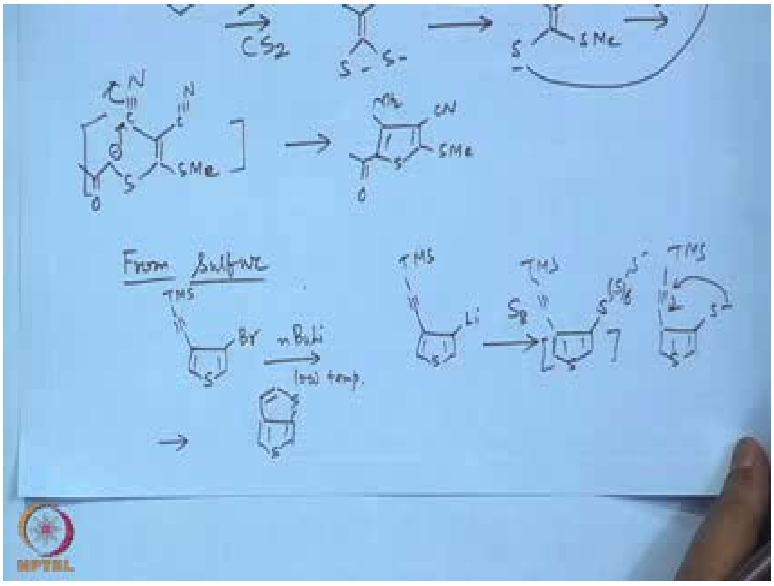
So, I mean this they are all somewhat like standard now for example, if you just extend this example; you can do the extension of this example of this like that was an alpha beta unsaturated compound. Now, we can start from this acetlenic compound; or in this example what I have here is basically one more substituent this side. Then react with thioglycolate methyl thioglycolate. And you do not have anything here by to reactive towards thioglycolic is so reactive at 0 degree centigrade. Then simply makes you can expect a Michael reactions with sulphur; then CH 2 and then here is an ester here. And then whatever you have before that is the other groups here. So, just a Michael addition. Now, you know the stages ready now so you do aldol condensations between carbon and the carbonyl of this like. And that would require a base in this particular example the base was cesium carbonate.

So, the product would be then you just you can write this thiophene unit. Then you have an ester which comes from a thioglycolic acid R and double bond. And then you have other substituents; what you had here? OR and OR that be ketone substituents. So, I mean and this is a standard protocol. Now, if you do not want to have the carboxylic acid like esters here; what we to do? We have to hydrolyse and the do de carboxylation. De carboxylation is not that easy, but it will decreases very high temperature cooper cool ((Refer Time: 21:19)) right that would gives you be a decarboxylation.

And, just to refresh your memory how do you compared this into hydroxy methylene compound? Who can tell me quickly? This one I am talking about this conversations; this standard actually that means a it is alpha formyl cyclohexanol. How do you make it? There are 2 ways to make it. One is to just take sodium hydride; and there are 3 methods. Then actually methyl formate or ethyl formate; you can use then di methyl carbonate you can use that would gives some aldehyde derivative.

Actually, gives ester derivative; base thing would be if you take di methyl carbonate that would give you corresponding ester derivative, but it is the aldehyde derivative. So, best thing would be the methyl formate or ethyl formate. So, what is other possible sulphur sources? We have seen P 2 S 5 Lawasson reagent; and then that thioglycolic ester, bis acetates. What are the other possible sulphur sources? Sulphur with carbon it is one of the cheapest ((Refer Time: 23:08)) good very good. So, will you look at it how is it used.

(Refer Slide Time: 23:14)



So, that means one can use there are plenty of examples C S 2 are exclusive I mean that is not extensively used in heterocyclic chemistry. So, if you take with start with what is that nitrile? Malono nitrile and I take potassium hydride, and then carbon di sulphide. You do not have actually take potassium hydride simple potassium hydroxyl would check I thing I made a mistake in some where here I should be potassium hydroxyl perfectly all right. Because ethyl malono nitrile is so active. So, what we expect here? kind of thing thio enolet. And then equivalent amount of alkyl halide in this case methyl Iodide. So, one can just selectively one of this S minus and then other remains as S minus. Next thing that we have here. In this example use this chloro acetone. And what is expected chloro acetone? And what is expected here? Unlike those furan synthesis; if you see try to recall it furan synthesis.

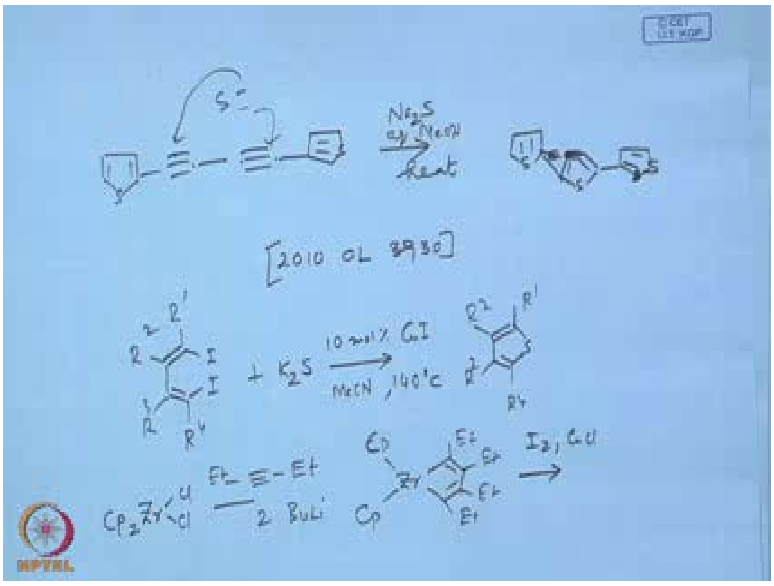
Normally, goes first with this aldol condensations sulphur you have a tendency is a softer nucleophile. So, actually it would displace chlorine; so what will expect? Then SMe then one sulphur then this is the acetone part of this; and then you have this is cyano and this is cyano this is know. And of course, once you have this then what next under the basic conditions actually this done in basic conditions what we expect in an would be form then this kinetic undergo this reaction. So, eventually after all this tautomerisation; now all these things isomerisation. So, will be getting in the this SMe here; and amino thiophene 3 amino thiophene and with acetyl side chain. So, what is new? I mean what Is to be known here; or what Is to be remember here? That mean the cyanide group is sufficiently reactive.

Normally, cyanide do not react carbon nucleophile; let us say if you have acetone nitrile if you do with malonate kind of things does not undergo any reactions. The probable the reaction should takes place elsewhere, but in this case in case inter molecular reaction. So, cyanide opens up to become an amine group and this is very frequently observed reactions in heterocyclic chemistry. There is cyanide could be a important source of amino group. So, if you have a requirement of amino substituted heterocycles. So, you can think of cyanide as the source of nitrogen. And let me next let us say just I give one more example actually form how elemental sulphur so how long elemental sulphur? How long you have been using this sulphur compound and sulphur carbon compound? Now, elemental sulphur also can be used to form thiophene.

And, this is case this like in this example what we see here; you start from thiophene and with an alkaline side chain alkaline again we have seen in before alkaline has been very good for heterocyclic synthesis, because of the cyclisation and this cyclisation. Now, if you treat this n butyl lithium of course, low temperature I will just write low temperature. I think by now many of you know what is expected reaction? Expected reaction should be lithiation or lithium exchange lithium halogen exchange; that is very fast reaction and lot of expect here. So, you will have this lithium halogen exchange. It is a very important reaction; and then if you take elemental sulphur is all of you know this structure right formula S 8. What we expect here? Let us say if you have a let us say Grignard reagent introduce a sulphur; what you get? S 8. So, initially what would do it would form S here right; then this 6 right.

So, basically it would form a sulphide then it breaks 6. It breaks down to this is unstable of course, this is unstable. So, what will be getting? Will be getting this S minus right; S minus and TMS. And then in the previous example in the furon cases we have seen this sort of this link place undergo 5 endo cyclysation. And the process of work of would give you a compound which is of course, would be known as thiopheno thiophene; that means I mean this have this strategy. Basically, introduction with lithium then contacting this into corresponding for minus and then process of basically acidic workup and de cyanolate; and the compound to giving the corresponding thiophene compound. And so what is the chemistry part? The chemistry part is that once you have S minus that undergo even inactivated alkanes to form the thiophene.

(Refer Slide Time: 30:40)



I will one of the example similar to the this one; for the example in this case if you have let us say thiophene like this and let us say other case exactly the it was something like this. Now, we matched this with sodium sulphide and aqueous methanol; of course, in this case little heat is requiring what we expect? What is the expectation? Normally, we do not see any reaction done with alkali and sulphur right sodium sulphide. But since a possibility of here linked to here of S minus. So, it would undergo reactions; and several will get what will get here? Will get a thiophene and this ((Refer Time: 31:43)) sorry in this case will get this here. so that means 1, 2, 3, 4. So, sulphur minus would attack here right.

And, then it will again that means there are 2 minuses; so it will undergo reactions with this sulphur minus. I think there is a mistake somewhere here it should be 2 types substituted the middle one should be 2 way substituted right. So, 1 2 S I think 2 types substituted thiophene that means di nucleo thiophene derivative would be produced. And there are other ways to use di sulphate kind of things. This worth published very recently this was in 2010 organic letters page 3930 and this is very similar to the biggest one; in this case sodium sulphide was used; and in this case potassium sulphide in the presence of tungsten metal. And the procedure goes like this or the methods looks like this; it starts from di ido compound starts from di ido compound. And then you have all kinds of R R groups; it could be 1 nucleus 1, 2, 3, 4 all kinds of basically di ido compounds.

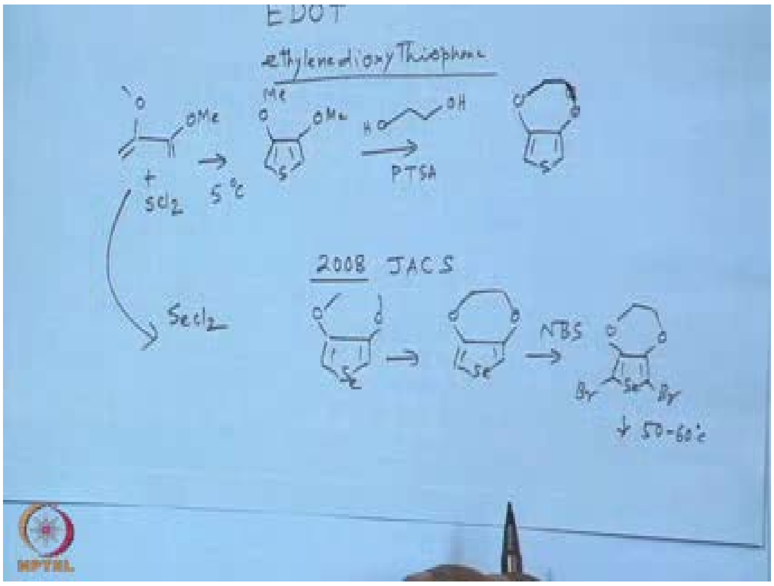
Now, since it is an s p 2 connected carbon connected iodine this not that reactive, but the source is this methyl of the sodium sulphide and this is a pottasiumsulphide I do not know why, but that work alone; so what have to do is you have to use catalyst. And of course, whenever you have couper that is chance to need a transition metal and this sketch transition cuprous added and temperature is around 140 degree centigrade.

This solvent is aceto nitrile; and yield is very good and the reaction is very general. So, what we can get is now this is highly tetra substituted thiophene mind it; getting a heavily substituted nucleus is very difficult is it being introduction of first one is second one, is ok third, fourth go on increase the a steric effect. So, this is the region where this sort of method sub are developed, but apparently one would think that this method is not that very great is it being reagent is pretty easy right. So, substrate that means the making the substrate is very difficult apparently. But there are way to out again this is the due to negishi. All of you have heard the name negishi; negishi coupling this same negishi he has a reagent named negishi reagent. That is C p 2 and zirconium you know zirconium replace in the periodic table; below titanium. And what is it famous for? Actually, in organic chemistry zirconium is very useful many a times it is used as substitute for hydro boration reagent.

Suppose, we want to do very selective hydro boration and you are unable to do so you can think about zirconium hydro croride. Actually, that was Cl and hydrogen just like hydro borating reagent it can undergo hydro zirconation. So, this reagent if now you react with alkenes this alkenes likes a ethyl and ethyl alkenes very easy to make. And use 2 equivalents of butyl lithium what you get is not a hetero cycle; it is a zirconium kind that means zirconium here. Then this is cyclo penta zirconium; zirconium cyclo penta diene you can say. And then this is Cp and Cp and then this one is should be ethyl and ethyl and ethyl here and ethyl here.

So, what next; so and then if you each iodine and cuprous chloride; you can get this well defined di ido substance. That means very easy to make and this also very easy to make that is not very difficult to make. So, that means there is a way out to this material. And will come back to some these problems for practice, but let me I think I give one more important many important way of getting monomer for the oligo thiophenes and thiophenes. What I say before there is a monomer called EDOT.

(Refer Slide Time: 37:35)



EDOT stands for ethylene dioxythiophene. What it is; it is a monomer for corresponding polymer. So, PDOT PEDOT means poly ethylene di oxy; and it would look like this sorry it would look like this. So, how do you make this? One cool. So, we have learnt quite a need of sulphur chemistry. And these thing that so how do you make this compound? This compound is again produced in tons and tons say conducting polymer. So, how do I know; that means the small one it will give you the 1 sorry 2 di substituted; the other from the thioglycolic acid; it will give you the carboxylic acid. You have to hydrolyse we have to plenty of furan rings de carboxylate all these things.

Student: ((Refer Time: 39:04))

Thiophene ok.

Student: ((Refer Time: 39:16))

Ok thiophene which method let us say

Student: ((Refer Time: 39:24))

S 8. Now, but here you have oxygen. So, that means what we have learned that is not enough; we have to learn little more that is the risk that is the logic I am trying to say. So, that means something else is required and in this case start with a di methoxy burodine. So, I think once you have defined one these starting material which provides 4 carbon atoms. So, what is the other reagent that we can think of now there is a reagent that would be given sulphur di chloride and it gives straight away di methoxy thiophene very easy looks good right and looks good. And see here the temperature of the reaction is only 5 degree centigrade you makes them these nice one; and what the next what is even more important many of us know that cyclization process is very fertile right; when the possibility cyclization.

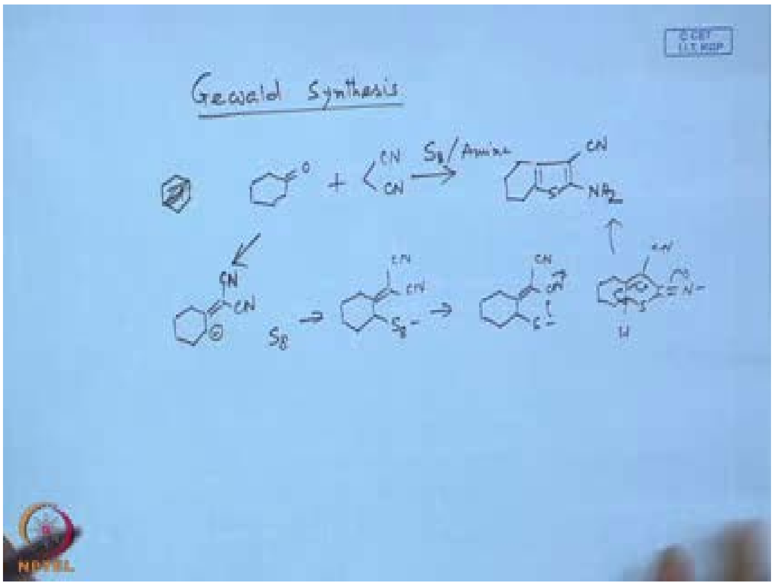
Because it is a intermolecular reaction and if you do this reaction with ethylene glycol in the presence of para toluene sulphonic acid; is just in no time will get this compound without any problem. Just basically, again displacement sort of addition elimination reaction eventually get this reaction. And reaction is so powerful that this known since 1990 around 95 version show, but then what can I do somewhat you publish this very similar work is known as Michael Bendikov in 2008. How can you extend this reaction to elsewhere? That is what we have to know; see when you say I am telling about thiophine thorough out the last know 20 minutes sorry 40 minutes may be ok.

So, but then you have to say something new. So, similarly we are the researchers, we are chemistry students; what should be say, what could be the next example that is what we have to think about. And what new chemistry you have learn for the example in this case what is this new thing we have learnt? It is a new reagent; we have never came across an reactions of sulfur dichloride right have you have not. So, like this; in the other area let us say material chemistry for example, what can I think about; like I know Amith is doing thiophene chemistry; and right Soroub is doing he is he is absent today; he is also doing thiophene chemistry. But how can you extend your work other area; guess?

And, he is published in that person who has followed this work what he did; selenium dichloride exactly same thing he has done. But then sorry selenium here; he has made this only thing he did not stop here; he develop the method for the polymerization. What he did he reacted with N B S and N B S would prompt it supply Brominum ion. But this what does it go? We have so many places actually it undergoes although N B S is known for brenzlicbromision right. But you do not have brenzliccarbon hydrogen so it under go nuclear bromination; you will have something like this; so the ((Refer Time: 44:10).

Now, that means that means our discussion was not restricted to thiophene also it can be insular offence; after this is pretty. But in this compound which unstable in fact unstable I mean but it gives very interesting compound just if you reached around 50 to 60 degree centigrade it undergo polymerization that they wanted. That means, polyselenophene wanted and of course it gives lot improve etcetera. So, we have let us say you have talked about most of the things except one more important thing where involved elemental sulfur.

(Refer Slide Time: 45:05)

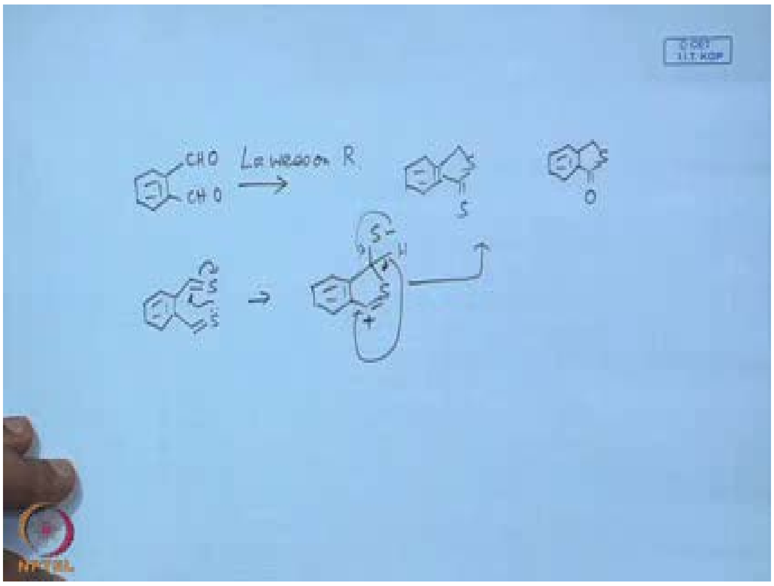


And, the method is known as known as Gewald synthesis where elemental sulfur is used. And the starting material are two it is ketone and malenonitrel then sulfur is used and amine is base. So, amine as base what will see the product that is form ((Refer Time: 45:37)) I thing one can thing about it; usually visualize it. In this case you have N H 2 and cyano N H 2 and cyano.

So, again amino thiophene what is to be noted that you are now deriving the amino group of the heterocyclic from cyano. So, cyano is a good source of amino; and what else? Now, elemental sulfur is incorporating this sulfur of the thiophene. So, what is the reaction? I think all of us can agree that in the ketones and ((Refer Time: 46:19)) would give you this sorry malenonitrel sorry malenonitrel would give something like this; Knoevengal kind of reactions; what next? How does this elemental sulfur undergoes incorporation? In the previous example you remember there is lithium compound lithium basically nuclephillically attracted the sulfur-sulfur bond opened up the chain to make the sulfur minus which decomposed to corresponding monosulphate.

But here what do you expect? Here, also very similar thing that was lithium carbon minus lithium in this case you do not have carbonyl here. But you can expect carbonyl here right; because it is an double bond to ((Refer Time: 47:17)) could be carbon ion. So, then of course then you have sulfur here and so you can think about this is C N; this is S 8 probably S eight minus and then slowly decomposes to this. And once you have monosulphide minus then you can go writing this I guess I thing all of us can right. So, it forms the imine right and then this deprotonation isomerization would give the corresponding this would give the amino ((Refer Time: 48:11)). So, lastly I think I should give a reaction very interesting reaction.

(Refer Slide Time: 48:24)



Let us see with the you can predict the reaction mechanism; this is a case of thedolite; I would say thinorthedeiolite is something like this which called theodolite. And we what have extensive long this; we have reagent inter method by which we can use naphthalene out of it. And that method has been adopted for photosynthesis that means theodolite can be nice class of reagent for making fine chemicals; other chemicals. So, that way we increase the important of the thiophine of the nucleus.

And, if you treat this again this well know reagent called Lawasson reagent; what we get is thiono; so because it is ketone is converted into sulfur thinorthedeiolite. So, how do what do you see here? So, what is the reagent, what is the reaction mechanism? Reaction mechanism that has been proposed little unlikely though it is not that straight forward. So, what is the first thing you think of in such and this reaction has been pretty general. You make take two more other aldehyde you will get similar compounds quite general reactions ok.

So, what is the first thing; you have to think about? First thing about Lawasson rearrangement reagent what does it do? It exchange this right with sulfur here and sulfur here. And of course and next thing so you thought it would give dithiono thino aldehyde are very difficult to make very difficult. I mean there are very few stable android here; then pretty unstable. So, then of course one can visualize this; so right this one would go this is sulphur here and there alright I think up to this looks.

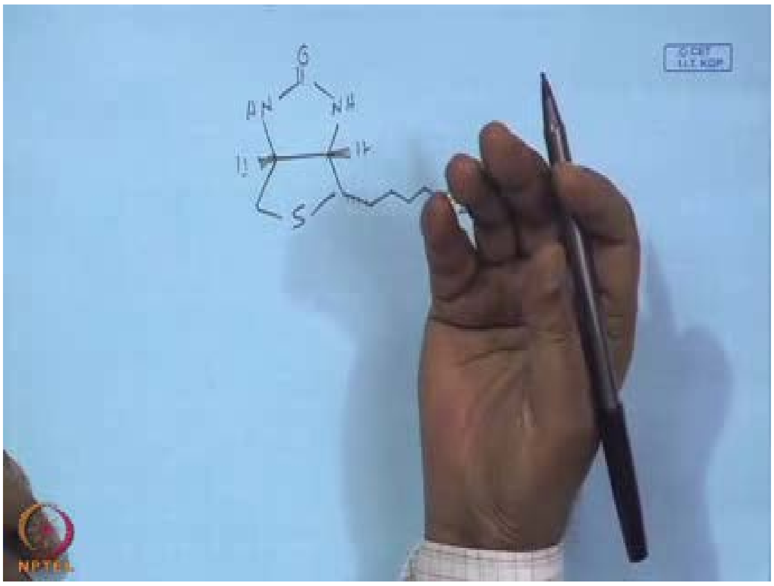
That means, intermolecular it forms a sort of a deuteron kind of thing or you can say light kind things; what next you can think of? Because this the product right this the product then the it has to be something like to be this hydrogen probably would be migrated to this one. So, if you lose this hydrate migration to this sort of benzylum ion benzyliccation here. So, you can get this compound; this the I mean ((Refer Time: 51:47)) propose mechanism but apparently looks. I mean there is not complaint about it but I have only one complaint about it what is the complaint; any complaint against this mechanism? What is the complaint? What is ((Refer Time: 52:16)) cook striking about this mechanism; you have one seen before. See, all this hydrates, carbonium ion everything they proceed in 1, 2 manner; I mean only occasionally you will see right 1, 3 that is quite I mean.

Then, normally it goes wrong through wrong classical ion etcetera. So, 1, 2 is more favor logically expected but 1, 3 may be intermolecular at the reaction is taking place; that is the possibility; that is not tested. So, summary time for summary; thiophine nucleus I have missed one point about thiophene about natural products example have you heard of the term called biotin? Who has heard the name biotin rise hand? Only 1 monolisa good Bindhu; what is it?

Student: ((Refer Time: 53:32))

No, you are chemist now right; when I say what is Quinine and you said natural product that is not enough; whenever you want to claim yours as you chemist. Then you have to tell me the structure or structural features. Monoslia what is biotin, structure? ((Refer Time: 53:54)) is thiophene derivative.

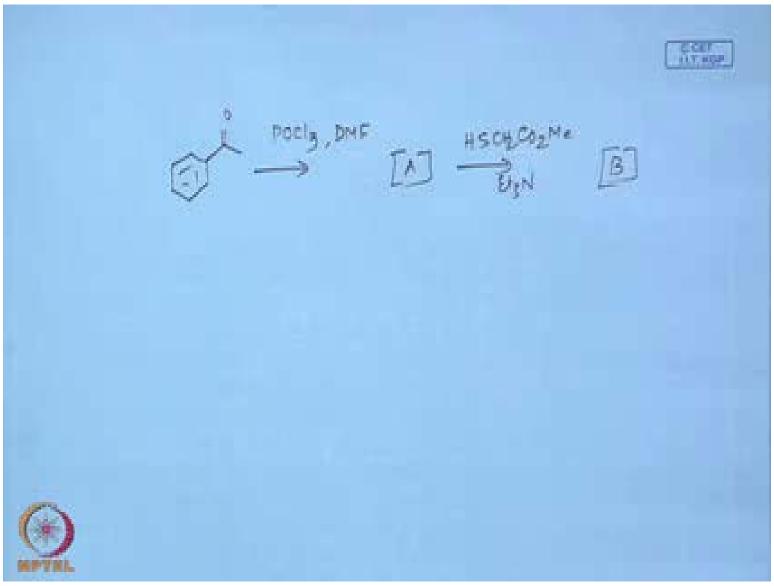
(Refer Slide Time: 54:02)



But well it is arguable some people can say it as an Imidazole derivative. Let us say something like this then you have 1, 2, 3, 4, 5 ((Refer Time: 54:24)) acid derivative. So, this that is it; so if there is an beta pretty easy to remember. But you know why it is so important that is we have to know. I can claim this thiophene derivative and if you look at the top portion you will saw an Imidazole derivative. But well that is depends on your advantage; for today I think this is thiophene derivative. And so but tell me what is the uses; actually it is very good actually is it is a good nutrient for human kind. In fact for animal also it is implied that animal health is improved if the sufficient quantity of biotin is present in animal food. Moreover many of we do not know if we lose hair there is a chance for especially girls.

So, you may lack of biotin content; you have to supplied food with biotin content there are many other things. For example, I mean some people say also it is good for whose are diabetic patient. So, summary in summarizing thing so we have seen all Paul syntheses that based on this P 2 S 5 and it is derivative by Lawasson rearrangement. Then thioglycolic acid is one of the important right; reagent from we can do elemental sulfur can be made use of. Then so di addosubtrate olefinicsubstrate of organotranstic metal can be used. And that also gives synthesis that is involves elemental sulfur; what else one more right; sulfur mono di chloride also can use for synthesizing substituted thiophene derivative fine. Let us see how much you learnt; test?

(Refer Slide Time: 56:37)



Tell me the answer of the sequence reaction we begin with acetophenon, P O C l 3, D M F; you get substrate here then thioglycolate, C H 2 let us say I will put it methyl ester of course may be ethyl amine little bit. So, you get a product B fine; right down the structure of the product B of course you give the structure of A also.

Student: ((Refer Time: 57:21))

You tell me the structure that is what the product B, B as well as A; A and B in.