# Heterocyclic Chemistry
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## Lecture - 13
## Radicals in Heterocyclic Chemistry – I

Good morning, so today we start with Radicals in Heterocyclic Chemistry, I do have to tell you that the organic chemistry began with radical chemistry. If you recall, that was the 1 st year first class the halogenation of alkanes, actually for alkanes there are not many reactions known in the literature. If you think about the alkane chemistry, we will have hardly hand full of organic reactions applicable to alkane chemistry. Because, all of us know that, CH bonds are not easily functionalizable so, one of the earliest and useful reaction is the halogenations of alkanes like chlorination, bromination, etcetera.

Similarly, the radical reactions in heterocyclic chemistry also is very useful and but, it is not talked well as a subject. And in heterocyclic chemistry, radical could be very useful provided, you know the subject, it can produce normally carbon radical, nitrogen radical, oxygen radicals. We are actually concerned about all these three radicals but, primary we are concerned about the radicals which are carbon means, carbon bearing radicals. And there is a our starting example should be from a set of reactions, I like to focus on the reaction conditions, which are applicable to the radical chemistry.

In the first slide, what I will do, I will just give you four different examples, four different experimental conditions and their corresponding products. That will tell you the types of the reactions you can achieve, types of the reasons you can use and of course, that also would set the example for the generation of carbon radicals. Then, we will go to a very broadly used radical reactions organic chemistry that is, minisci reactions, very briefly I told you when we talked about the specialty of nitrogen, let us look at set of examples.

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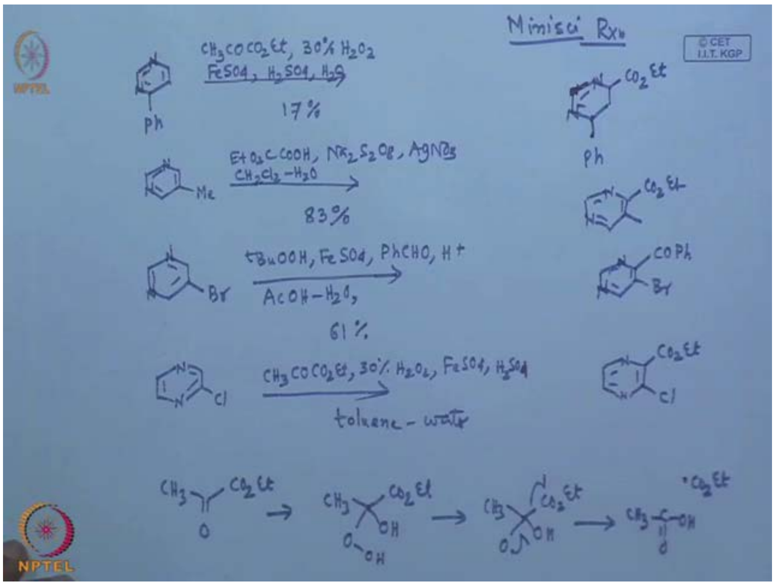

Like, this is a case of pyrimidine, you have substituted pyrimidine, you have this and then, you have to carefully note the reactions conditions. Reaction conditions are like this, all of us know what I am writing, if you do not know as I will just tell you later but, what is the nick name of the formula I wrote?

Student: ((Refer Time: 03:29))

Ethyl, no as a pretty well known in biochemistry

Student: ((Refer Time: 03:43))

Right, ethyl pyruvate and this is a reaction so, we can see here and the yield of the product, I will not write the product at the moment, yield of the product is 17 percent. Take another example, very similar to the one I wrote, once again this is pyrimidine but, it is a ethyl substituted one and the reaction conditions are quite similar it is a Et CO 2 and I think all of us know what it is, ethyl glyoxylate then, sodium paradyl sulphate, silver nitrate.

So, these are the recipe then, you have methylene fluoride and water and yield of the product what will be getting is 83 percent. Then, there is a another reaction I mean, all these actually leads to different publications then, in this case, what will find this set is a little different tertiary butyl hydroperoxide, ferrous sulphate then of course, ferrous sulphate means persulfate hydride then, benzaldehyde, sulphuric acid. So, all these is actually then, you have acetic acid and water and the yield of the product is 61 percent.

One more, this is not a pyrimidine, this is a pyrogen, this is a chloro once again, this is a ethyl pyruvate then, 30 percent which is commonly use hydrogen peroxide then, ferrous sulphate and of course, little sulfuric acid. I think sulfuric acid should be there and this solvent is toluene and water so, all these examples are actually belongs to reaction called minisci reaction. Minisci reaction word is, how do we define minisci reaction, minisci reactions are the radical reactions, radical lessons reactions of carbon radicals.

Carbon radicals two heterocyclic compounds, you have not the carbocyclic compounds it is a basically the domain of the heterocyclic chemistry and what are the products, that we have to find out. In the first case, the product is I mean, this skeletons remains as it is then, this nitrogen up here 1 3 nitrogen phenyl and what will find. In this case, you are introducing an ester group directly. Same thing, next example also would involve introduction of a direct ester group.

Next example so, what will find, in the next class again a pyramidine and the bromo and in this case, it is not the ester group, it is CO Ph group, asile group you can say and last one, all of you can guess, the product is again ester substituted. What is the chemistry, basically you have to first note how to produce the radical, if you look at the first one, it is a pyruvate and what is it required. See if you look at the reaction condition, all of the reaction conditions involve the presents of acid so, that is the clue of this, success of this menisci reaction.

Although this was observe by another French scientist quite few years ago Minisci observed that is the trick for the use of these radical reaction heterocyclic chemistry. In heterocyclic chemistry, radical was not very successful but, one of the scientist found that, if you alternate, reaction takes fasters and also the reactions become little more regio selective means, you can get one regioisomer preferentially. That is why, observation by one of the scientist called Dover or somebody from France and the subsequently menisci develop this in the late 1916.

So, but for us, we have to basically recognize the reaction conditions and the chemicals that are required. How to generate carbon radical from let us see ethyl pyruvate, if you look at the regent is hydrogen peroxide so, hydrogen peroxide missed at some point, the peroxide bond would be climbed. So, in this case it is proposed that, the pyruvate under the influence of acid that means, carbonate gets ((Refer Time: 10:02)), you get a sort of full hydro peroxide kind of the thing.

Then, you have ester group here then, all of us know what can happened next, this peroxide linkage would be broken so, you have oxygen up here then, you have I mean carboxyl ester here. What next, just basically this is where that means, this radical goes to this and the ester group comes here. So, what will find this is a CH 3 and this is OH and then, what appears to be that, you have a radical here at the ester carbonate. So, that means say, nice way of producing a ester radical, ester containing radical.

And of course, then the question is where to attach and all of us know, that the if you have a pyridine system, the carbon double bond nitrogen behaves like a shift base. So, it under goes addition to the electrophil that means, these are somewhat like you know nucleophilic radical compare to the pyridine system. So, if you go to the next one, the reaction condition is different, go to the next one what is the reaction condition, the glyoxylic acid monoester. Once again, this one of the earliest reaction condition found by minisci, all of these reagents are required. First of all, I think if I let us say, give you the mechanism that means, the reaction set here, the reaction condition here.

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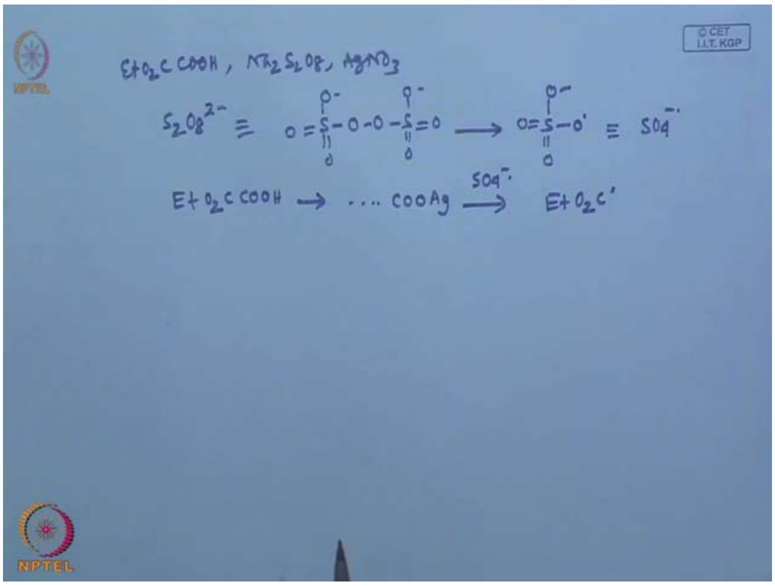

Eto 2 C and then, glyoxylic acid and sodium perdisulphate, silver nitrate and what else, I think I miss probably, acid also should be there because, nitrogen heterocycles, whenever

you have nitrogen heterocycles, you have always add an acid. And in this case, what happens this perdisulfate, if perdisulfate actually if you bond wise if you write, it would look like so, double bond oxygen like perdisulfate. So, you have I think, double bond oxygen minus oxygen minus and then, all of us can guess what happens, it breaks down to sulfate minus oxygen and this, which is equivalent to sulfate radical aline.

So, this is radical aline, actually what fix of one more electron to becomes sulfate from where so, simultaneously the glyoxylic acid, this is a trick here the hydrogen has to be replaced by not many metals, actually silver. If you recall, decarboxylation of carboxylic acids, how it perform, that not many methods that, if you can come up with a nice clean methods at low temperature that is, below 150 degree DMS or DMF temperature then, you can get a nice fabrication.

Just last 2, 3 years actually there are several fabrications, when you studied B.Sc you have to use copper quinoline, copper quinoline is one of the standard technique. If let us say, you have a benzoic acid, you want to convert benzoic acid to benzene, how do you do, very old literature, they used to heat with zinc oxide or zinc something like that I have, either zinc or zinc oxide. But then, it come down that if you use copper and quinoline at high temperature, you can get decarboxylation that is also useful in heterocyclic chemistry.

Then, many of you know there is a little bit deviation of ((Refer Time: 15:02)) reactions, that is not a truly decarboxylation reactions but, it along with that, brominate the carbon bearing the carboxylic acid. Then, what else, there not many methods and there is one more very recently has come that palladium. If you replace the hydrogen by palladium, there is a propensity, that this carboxyl group clave to produce the corresponding decarboxylated product.

In this case, this reaction is radically very specific to the silver, if you have a silver sort then, your sulfate radical that would immediately produce the corresponding decarboxylated carboxyl with radical that means, in this case ester radical. So, once you have the ester radical then, you know the product, this ester radical would act to the alpha position of the nitrogen.

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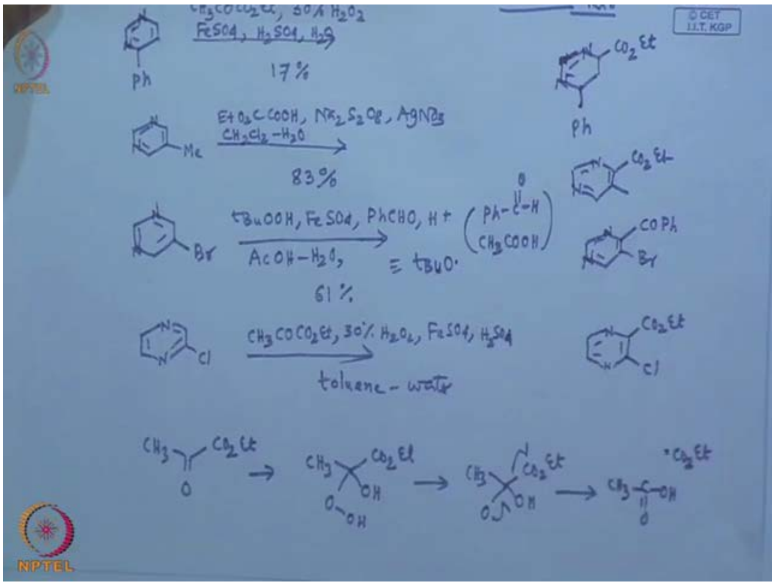

So then, let us say, I will come back to this, let us look at the one more, that this one third example, what is the third example. In this case, the combinations are as say butyl hydroperoxide, ferrous sulphate and all of us by now know this agent. So, it produce the oxygen radical then, there is a question, see there are two substrate possible here. You have in this case, benzaldehyde and you have carboxylic acid so, the carboxylic acid can form the corresponding ferrous salt and the benzaldehyde.

Now, the radical that is here you have this tertiary butyl oxy radical now, what sort of carbon radical do you expect. If you think of benzaldehyde actually, it can produce the radical here, after the extraction let me give you here, write here.

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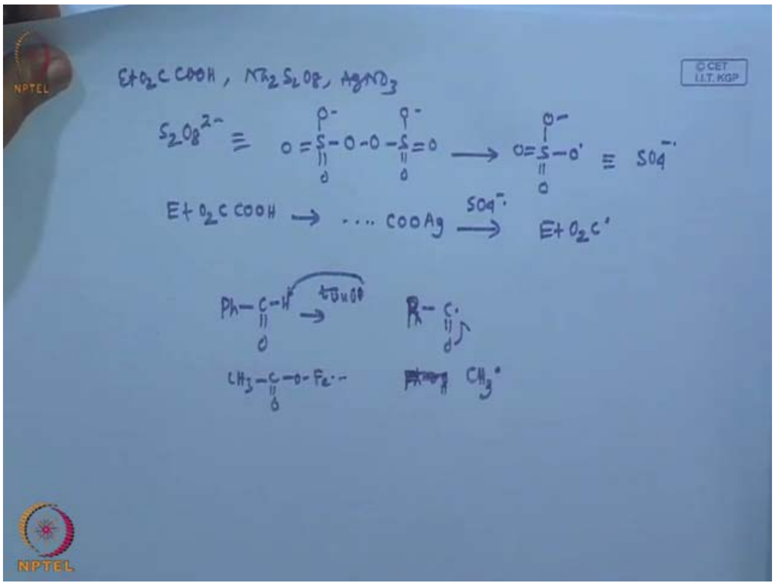

If you have benzaldehyde so, there is a possibilities that, the per radical would that tertiary butyl oxy radical, radical would abstract the proton and it can produce the corresponding CH so, oxy carbon radical. The other possibilities that it can, this salt is produced with iron salt and that can be oxydise to corresponding literal to methyl radical. So, these are the two possible that means, one aisle radical, one methyl radical now, you have to know, how to distinguish them, which one is more likely, since answer is known, yes it is the aisle radical.

What is the driving force, driving force is the once again the stability of the radicals, they like oxocarbenium and cations, carbon ion. And similarly here in this case, this iron carboxyl is not such a tool to the oxidation with tertiary butyl hydroperoxide. So, this reactions said or the reaction conditions without silver is nicely suited for radical fromation from the benzaldehyde, that we have to remember. That means, whenever you have the hydroperoxide reagents without silver, there is a likelywood, that would produce radical alpha tool oxygen sp we will have more examples, let us see look at the next one, the last one.

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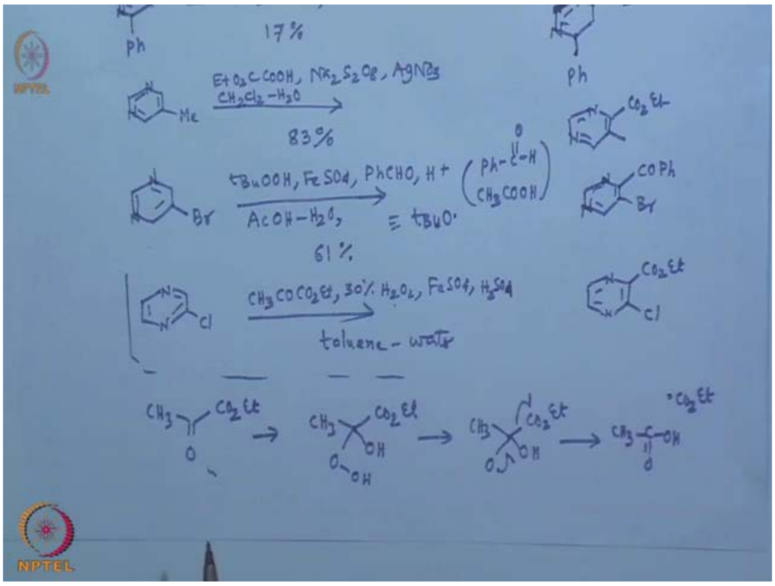

The last one that is a fourth example so, what is the fourth one means this one so now, you can quickly find it out that, you have a hydrogen peroxide perasufate. So, this combination means, you have to have hydroperoxide system and then, you have an ester group here, there is no carboxylic acid. That means, but show carboxylic acid should be all other radical should be generated through this hydro peroxide intermediates semi or hemi acetal of this carbonyl compounds and then, ether decomposing this.

So, this basically gives you rough idea about the types of the reaction conditions that are used in the minisci reactions. Then, may be will quickly, this is just an introduction and then, will very quickly go to little bit of the radical chemistry in general, why should we use radical chemistry. I have told you before, again just recapitulate, what is the use of radical reactions especially, those who will be doing bioorganic chemistry, physical organic chemistry, radical chemistry is very useful.

Biological system, all radical chemistry is very useful, many times people says super oxide, dismotivation all these things. And then inflammation, inflammation is one of the serious ((Refer Time: 20:43)) set, do you understand what is the meaning of the inflammations. Inflammations, swelling that is the basically the symptom but, in biological term, one common inflammation is due to a productions of prostaglandins. If you have headache have a severe itching, whatever many kinds of inflammations are there due to the production of prostaglandin in cells.

And then, that prostaglandin is produced from again a weak C 20 fatty acid, what is the name of the fatty acid [FL] I think you have studied all these thing. Krishna, arachidonic acid have you heard, if you have not heard you go to the any standard textbook Marison bhat's, Salman's you know anywhere, there is big nice chapter actually. Arachidonic acid actually gives rise to prostaglandin, most of the prostaglandin will have C 20 carbon.

This is due to the presence of whether superoxide dismutase, which causes decomposition or which introduce oxygen radicals although or which participate in a reduction of oxygen in the biological system. So, that mean, I am try to say, radical chemistry is very useful in biological system and elsewhere, many of you know polymer chemistry also. A series of I mean, lot of polymers are produced by radical chemistry but, what is the remarkable award polymer radical chemistry, what is its specialty, there are quite few specialty.

Let us see in fact, most of the organic chemistry loutery when you go, you dry THF by protein sodium and benzophenone, why benzophenone?

Student: That is the indicator.

Indicator, very good so, it indicates it also signify something.

Student: ((Refer Time: 23:12))

Radical could be of sufficient stability that means, if you remove moisture, if you remove oxygen rather then, it could be stable. There are many known by now, all of you know radical even could be stable in air that means, they are that sensitive. So, I mean, depending on the situation, it could be very sensitive to oxygen and water but, again there are cases where, radical could be very stable even in water, that is the beauty.

Biological system means, you have full of water only in body so, inspite of all, having all sorts of organic compounds also and then, plenty of water, the radical could be very stable. So that means, the radical reactions can be run in the presence of water, in the presence of oxygen I mean, many reactions are just done in the open flask. So, that is one of the major reasons, why radical chemistry should be popular or rater should be made popular.

Then, there are radical, as you have noted in the earlier reaction conditions, sulphuric acid deliberately added. What does it mean that means, radicals are inert to the acids so, similarly also, there are conditions where, they are also insensitive to bases. Then, most important from the chemistry point of view that, normally the radicals do not induce any elimination reaction, that is important. If have carbon ion and the beta position are having a living room then, eliminations are most likely reactions but, in case of radical, you do not see such things.

Disadvantage is very difficult to actually predict that means, we have understood carbonium very nicely you have understood. Carbonium very nicely but, radical chemistry not routinely understood so, what you have to do, you have little experience from the examples then, the typical patterns of the radical reactions. So, we have given a set of reactions then, have let me give you just that the reason, why you have to have something in mind let us say, I will give you set of precursors.

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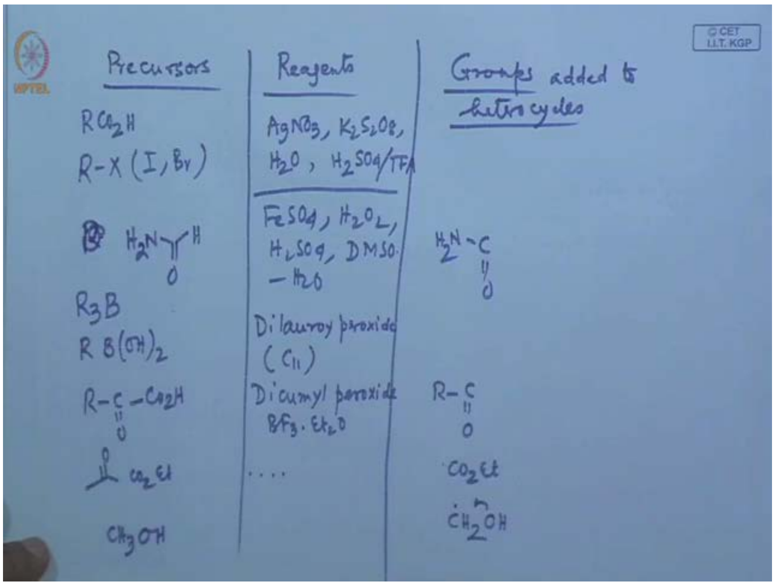

That R to be remember let us say, which are the precursor that are often used in the radical chemistry, precursors let us say then, I will write some of the reagents sets. We have already set some and then, we will have something and then, the groups that are added to the heterocycles groups. So, that is the reason you have there I mean, all of these basically are centered down the information some about the carbon radicals. For example, you want to produce carbon radical, a carboxylic acid is sufficient and what is the condition.

We have already said that, what should be condition now, by now all of us know what is the condition, carboxylic acid condition means, first thing that you have to come this is, it could be potassium paradyl sulphate, a sodium paradyl sulphate, ammonium paradyl sulphate. And then, one of this paradyl sulphate, potassium pardyl sulphate and what else, these are all inorganic compounds. So, you have to have water and so, and often always it is also sulphuric acid you can guess sulfuric acid or TFA.

We are meant for the heterocycles, the heterocyclic nitrogen are prognated so, the reaction becomes more regio selective. So, that is why, this is this and then, this silver salt is prone to oxidation with potassium paradyl sulphate. So, once you know this then, they are carboxyl acid could be taken as a substrate then, very fortunately or very importantly then, R X simple halides. How to generate radical from halides?

Student: ((Refer Time: 28:14))

No, you have an alkyl bromide let us say, R X means, it could be iodine, it could be bromine, how do you generate?

Student: ((Refer Time: 28:29))

Not really.

Student: ((Refer Time: 28:35))

Once again, you can use this pantone system, hydrogen peroxide and ferrous sulphate then of course, sulphuric acid has to be there and then, solvent is solvent, it could be DMSO and water. And only then, there are reactions conditions also R 3 that means, these are I am trying to basically least some of these alkyl radical generating precursors, this is one trialkyl radicals, trialkylborane. Trialkyl boranes also are very useful precursor for generation of R radical and earliest example should involve reaction of these tryalkyl boranes with oxygen, dependence of oxygen.

So, mechanism, do not ask me the mechanism, mechanism too complicated but, if you have that oxygen one time generation, it would generate the corresponding R radical.

And the latest one, this is the 2011 I mean, is quite interestingly boronic acid. Boronic acid, who discovered boronic acid, generation of boronic radical from boronic acid, one very young scientist, age below 40 ((Refer Time: 30:02)). Only last year, he had published these papers, in which he produce nice radicals from this boronic acids I mean, boronic acid had been known for suzuki reaction.

But, it came to his mind that, this could be also useful precursor and under the very similar conditions, I will give you examples very similar conditions. But, not silver nitrate just ammonium paradyl sulphate should be sufficient hopefully, I will little be appreciate. Then, you have already seen that, this pyruvic acid, if you have pyruvic acid then, it would give rise to, it will deliver this asile unit then, you have also seen that, if you have ethyl pyruvate and under the influence of ((Refer Time: 31:06)) conditions, it will provide the carboxylic acid.

Similarly, if you have say methanol and what should be the radical I mean, again fenton’s reagent and what is the substituent that to be provided by this, it is this CH 2 OH. This is to be noted actually, this is very important actually guideline, this is last example methanol would gives CH 2 OH that means, you have if you look at methanol have three different kinds of bonds, methanol has a bond CH bond, carbon oxygen bond and OH bond.

And among the three, which one is to weakest bond, this is true let us say, I will give you OH in water, OH in ethanol, C C carbon bond in ethane and let us say, CH bond in propane and C Br bond in ethyl bromine, all these things. You have studied in high school, honours level, which one is the weakest one, which one is the strongest one. Any idea, when I say strongest means, strongest in terms of homolytic cleavage so, often we talk about the homolytic cleavage because, that is easier to evaluate so, which one is the strongest bond?

Student: ((Refer Time: 32:46))

See, carbon carbon, good any other answer, any intelligent answer?

Student: ((Refer Time: 32:58))

No, we are talking about homolytic bond fission, radical chemistry means homolytic bond fission. We have to know because, we spent so much times in B.Sc, you learning you know what is bond decision, how do you evaluate and what are the different trends. And then, if you go to the ((Refer Time: 33:21)), etcetera the very important guideline actually I mean, the answer is lies in the first slide. When I said, the radical reactions are very useful especially, they can be carried out in water that means, if you have a carbon radical, it does not touch the water.

So, what that mean, actually I will give you the hints this morning, I forgot also but, today morning I had to copy the numbers. For water, the bond energy is 1 1 9 kilo calorie per mole whereas, carbon carbon bond energy what is the average value?

Student: ((Refer Time: 34:05))

No way, it is 88 aprox so similarly, carbon oxygen bond in methanol, it has a bond energy of 91.5, this is taken from Solomon’s book. So, this basically, tells you that, these are all radical reactions this pattern and obviously, the carbon hydrogen bond in methanol I do not have it but, that is produced low though, that is very low at the moment I could not get it but, it is low, simply because if you have a radical here, this should stabliate at by the oxygen loan pair.

And there are other kinds of system for example, many of you know, this is dilauroyl peroxide is one of the reagents o used in the radical generation corresponding lauric acid. Lauric acid means, how many carbon, you see commercially available and is very cheap, plenty. Actually, it has 11 carbon atoms then, there is also commonly used. Especially, by the polymer chemist, dicumyl peroxide, this is also pretty useful but, in combination with BF 3 etherate and I think now, we all understand the structure of dicumyl peroxide.

So, basically cause cumyl hydro peroxide dimerization to give the corresponding... so, these are the basically the substrate and these are the basically the reagents. And then, you have to have different combinations here and there, and the corresponding let us say, I will give you one example, may be evenly the amides could be let us say, permomides. For example, permomide could be also a substrate for radical generation and all of you can guess the group, that will be added to the heterocycle, is corresponding amide like ester directly, you can introduce an amide we gave you example a class before. From now onwards, let us look at some of the typical examples and the advantage like this was in last year's exam.

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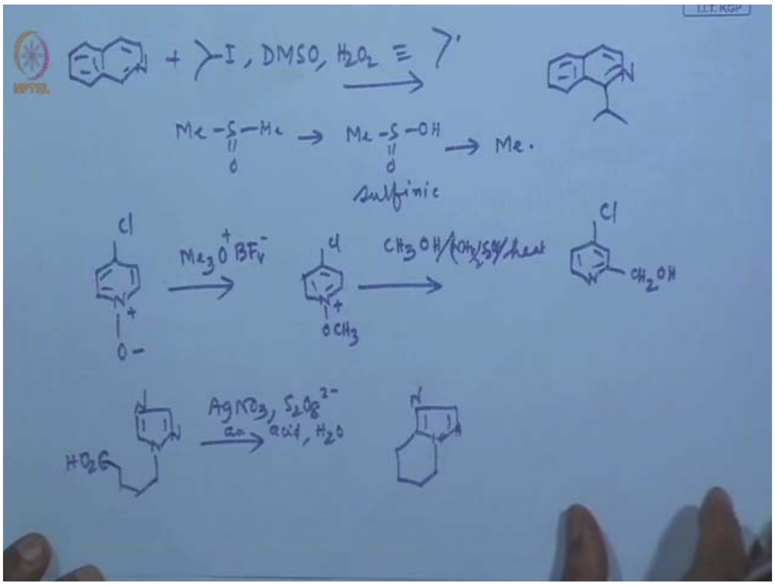

If you have isoquinoline and then, treat with this isopropyl iodide, DMSO and hydrogen peroxide so, what do you expect I mean, little difficult though. So, somewhere it will be some hydro peroxide will be generated actually, DMSO is this one then, it undergoes oxidization with hydrogen peroxide, it goes to sulfinic acid. Sulfiic acid, s i f i n i c and we have worked on sulfinic acid, there is unstable. If you freeze, it will stay there for month then, after that, it will be decomposes.

But, in the form of salt, it is pretty stable, it can be marketed, it can be shipped, it can be stored and so, this gives you corresponding alkyl group. If that is so, the top combination would give you, this is equivalent to isopropyl carbon radical and the reactions precedes nicely and all of us know the polarization is such that, the isopropyl group would be attaching the one position of isoquinoline. So, we have already with acetaldehyde, we have already said let me give you one more example, the radical reactions also could be useful for an oxides but, to make with useful, you have to o metholate first. O metholate can be done with trimethyloxonium tetrafluoroborate and this is all of us know, this is a salt but, you right what is the name?

Student: ((Refer Time: 39:44))

Right, Meerwein salt is more reactive than corresponding methyl added, methyl sulphate and it gives you this O metholated products. O metholated product CH 3 here and chlorine. Now, this is basically salt here now, if let us say particular combination now, methanol and I will not write, give you the answer and simply heat it, what you will get eventually. After all these dimetholization etcetera, what you will get, you will get nice introduction of direct introduction of CH 2 OH.

So, what is the missing reagent, we have given you all kinds of permutation combinations here. In this case, it is ammonium pyridine sulphate so, say basically peroxide kind of thing, in a sort of peroxide normally CH 2 OH is provided photo chemically by photochemical reaction. But, in this case, ammonium pyridine sulphate is sufficient, let me give you one more example, this is a azole with a three nitrogen then, it has a side chain and is a carboxylic acid side chain.

Now, it lead this with let us say silver nitrate, again pyridine sulfate and of course, an acid means to protonate the nitrogen and so, water has to be there because, inorganic salt. Most of the reactions are done in the mixture of water and inorganic solvent so, you can the guess, what is the product. So, this recipe silver actually, is meant to the suited for carboxylic acids. So, it will generate the decarboxylated carbon radical that means, radical would generated here at the alpha position.

And whenever you have a react ((Refer Time: 42:34)) intra molecular reaction so, the reaction would take place intra molecularly and all of us can look see that, it will form in this way. Also, it tells you something else that, even a five member ring can be functionalized by carbon radical. So long, we had been giving example on the six membered ring, this is another example I will use a radical for the functionalize of five members are not many low but, they could be useful, provided they have nitrogen in it. And let us say, I think we have given you many of these examples, let me give you one or two more this is the example, may be you can just take note.

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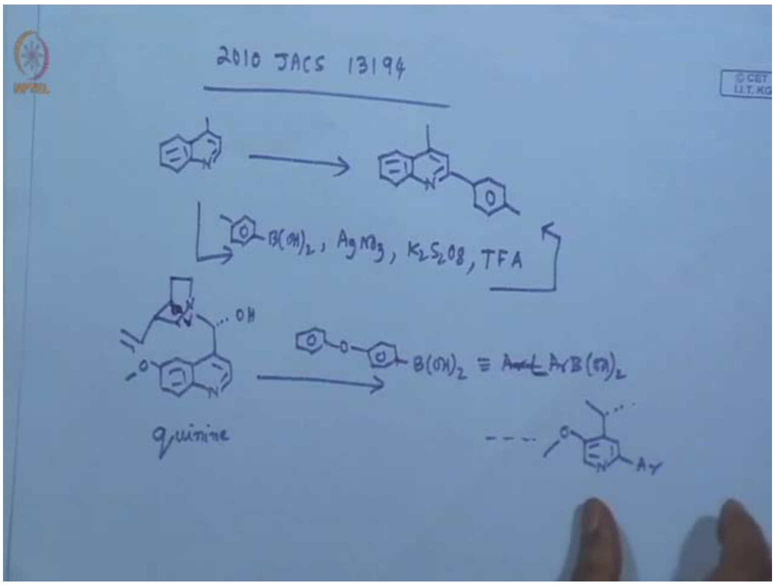

This was in 2010, JACS page number is 1 3 1, this paper is by Fillbaran, what he noted, he noted reaction if you begin with substrate like quinoline. And then, you can directly have phenyl substituted quinoline particularly, in this example, he could introduce the toulene portion if try to think about doing this transformations otherwise, without involving radical chemistry is, how do you do. This is may be using the ((Refer Time: 44:25)) reaction ((Refer Time: 44:27)) reaction corresponding toril lithium compound, that can add to these and then, you have oxidize, etcetera.

But then, there could be a serious problem in those sort of reaction, what could be the other side reaction ((Refer Time: 44:45)) for simple pyrole is perfect fluoride. But, for substituted pyridines or other quinoline derivatives.

Student: ((Refer Time: 44:55))

So, that is called lateral lithiation means, side chain lithiation, side change lithiation can takes place. So, Barone has of course, come up with this different kind of solution, he had used this corresponding boronic acid. And then, since such an acid like carboxylic acid also will require silver nitrate then, potassium paradyl sulphate and one more thing paradyls. Like carboxylic acid, he has used sodium silver nitrate, pardy sulfate is required for generating the sulphate ion radical and acid.

So, in this case, he has cleverly used trifluoroacetic acid and what you could get, you could get this compound, that to this come. So, I mean, if you look at say, very regio selective that means, only the two position is and that too directly you know one step so, that is the beauty. Let me give you one more example, this is a from a natural product, I think I will write this structure, the quinoline natural product and I think… Any guess, actually the two carbons here, two carbons, 2 2 2 as I obtain 2 2 2, as I obtain by cyclooctane.

What is it, I think all of you know, you have oxygen appear in this, this is two carbon this is two carbon, this is a here and here, this is two carbon. So, another is one nitrogen so, this is one as a 2 2 2 octane by cyclooctane. And then, you have a vinyl group, methoxy group, this is quinoline moiety and all of us know, what is the name you have to know, quinine. Now, if you just apply the borons reactions, borons reactions with a substrate, I do not know why he has chosen this substrate.

It is a substrate ((Refer Time: 48:14)) big one is diphenyl ether kind of linkage and the corresponding boronic acid and the recipe as before. So, as before, what equivalent to let us see, I write Ar B OH twice so, it will give H 2 I mean, you can just extrapolate. And what would be the product, the product would be Ar and then, rest it is so, you have oxygen of here, oxygen of here. That means, this is very remarkable example, why it is so important, why did I choose this example in especially, when you are try to do biochemistry or any other advanced chemistry, youhave to look for a reagent feature very selective.

When I say selective means of course, the selectivity fall under three different categories region, chemo and stereo so, three different categories. And least case, it is of course, regio as well there is no question of stereo but, it is varies chemo selective, vary chemo selective means, it did not reselect the radical that was generated from the Cl, the phenyl radical, it did not undergo addition to the double bond. Normally, you know the radical is undergo addition to the carbon carbon double bond, it did not then, what else would you have expected.

What are the problem would you have anticipated, one could have been this radical would generate the double bond I said. Then, if you recall the radicals, alpha to the nitrogen also is ready stable so, that could have been produced here and alpha to the oxygen as well as benzyl, that could have been also a possibility. All these possibilities have been not observed in this particular example, it has undergoes nice addition, this is a nucleophilic radical, it has undergoes addition to the corresponding product. Let me give you one or two more very important examples from medicinal chemistry some of you probably, are familiar with this.

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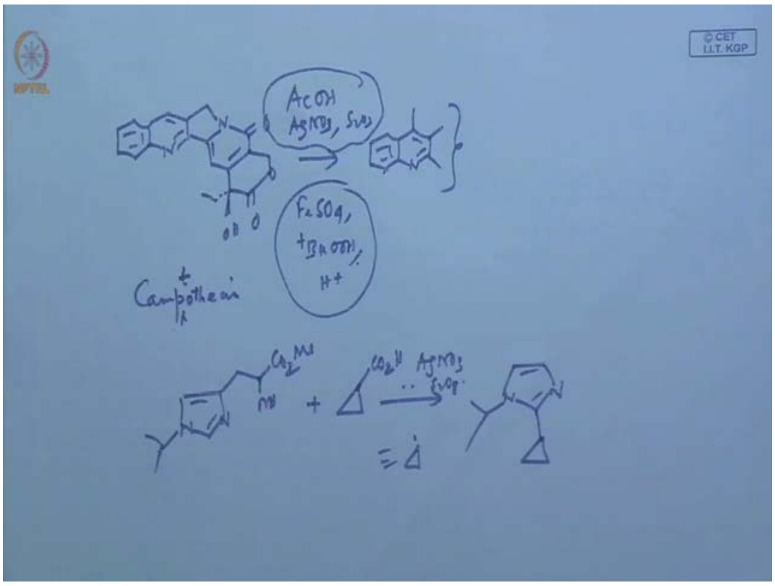

Again quinoline derivative is a anti cancer drug and what we will see it has so many functionalities and it has only one pyrole center and then, you have double bond nitrogen and this and then, you have nitrogen this. Actually I wish to know the name but, I do not know the spelling, it is known as campothesin probably. Ccampothesin I think, if I am incorrect I will correct it next class but, name is although important but for us, now reaction is important.

So, how do I or how do you functionalize this molecule and chemo selectively, regio selectively, if the methyl group at the four position of here so, rest remains as it is. So, what do you expect and what should be the recipe, what are the required chemical, now I got the name, it is camptothecin, this is anti cancer drug. Now, let us see many times actually to cellulize, you have to introduce something, you have to introduce nitrogen, you have to introduce a side chain and the one of the first step here is the introduction of the methyl group.

So, by now, all of us know, the recipe should be, the starting carbon source should be acetic acid, acetic acid give you the CH 3 radical. So, once you know acid that means, immediately you have to think about the silver salt and all these things but, that is what you would think and then, paradyl sulphate. But, in this example, alternatively if you recall another possibility also, this fenton's reagent said is also perfectly all right, ferrous sulphate then, tertiary butyl hydroperoxide and sulphuric acid is also equivalent also solve the purpose of producing these the CH 3 radical.

Let me give you one more example, this example is applicable to imidazole derivative with isopropyl group here and the nitrogen continue side change that means, NaH there is and the corresponding ester here. Now, what do you see, said you same thing that silver nitrate and then, paradyl sulphate and etcetera but, eventually what will get, you will get this imidazole that basically ester dean moiety. And then, you have this and what is this cyclopropane carboxylic acid so, this set of silver nitrate, paradyl sulfate, etcetera be equivalent to cyclopropyl radical.

So, that is the beauty that means, I mean nowhere in the chemistry, we have seen cyclopropyl radical. Cyclopropyl methyl radical are known but, this radical I would not that commonly used and so, you can generate that. Now, mind it that you have a five membered hydrocyclic imidazole and that can be functionalized and in this case, the middle one, the number 2 carbon is functionalize with a cyclopropyl. So, why do you see cyclopropyl moiety in medicinal chemistry but, many of you know norprosthetics, have you heard of norprosthetics.

They are basically this second generation, third generation of antibiotics, what are the heterocylic ((Refer Time: 56:16)), quinoline derivative. In market you will find, there is a cyclopropyl quinoline, the cyclopropyl can be plus in nitrogen and those are also very useful. Then, if you have real bulky radical, you can also make use of it in radical chemistry. And then, there are other usefulness of these radicals could be for the introduction of trifluoromethyl radical.

If you take trifluoromethyl iodide and use fenton's reagent, you can produce the corresponding radical and that radical can undergo addition too many heterocylcles I mean, in these examples, I having with me, it adds to the nucleic acid. Similarly, there are cases example, there are known examples where, you can also functionalize furan, many of us know furan is acid sensitive.

But, in that case, you have to change the reaction conditions so, what can I do, say all of these reactions actually involve use of acids because, you have to propionate the nitrogen and you have to make this heterocyle more regio selective. But, in case of furan, which are more I mean, very susceptive to acidic conditions then, you have to change over to something else. Recently, people have used phenyl boronic acid in the presence of something else, again different kind of oxidising agent, manganese triacetate.

So, in the next class, we will see some of these special cases like I mean, how to generate radicals from manganese triacetate and many of you probably know, phenyl hydrodium diacetate are flow exclusively these days. And then, in classical literature people used to use letetra acetate for example, you have cyclopentane 1 2 dicarboxylic acid, how do you produce cyclopentane from there letetra acetate the principle is basically.

Then, letetra acetyl also use for remote functionalizations, if you have an alcohol then, you use letetra acetate, you can make use of reactions in… I think, we will have little bit different kind of radical reactions, how to generate heterocyclic, these are all for the functionalization of the heterocycles. In the next class, we will have some examples for how to construct the heterocyclic ring by using…