Hetero Cyclic Chemistry
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Lecture - 7
Effects of Ring Nitrogen-A

Good morning, today's topic is effect of hetero atom in heterocyclic chemistry that can be categorized one in this lecture. This is one of the most important topics in heterocyclic chemistry reason being if you can understand very carefully the effect of hetero atoms on the reactivity and physical properties. Then you can master the heterocyclic chemistry very nicely without going to the each and every details of the particular reactions or particular class or particular topic. There are few points which have to be noted, the first thing that what kind of effect we are expecting.

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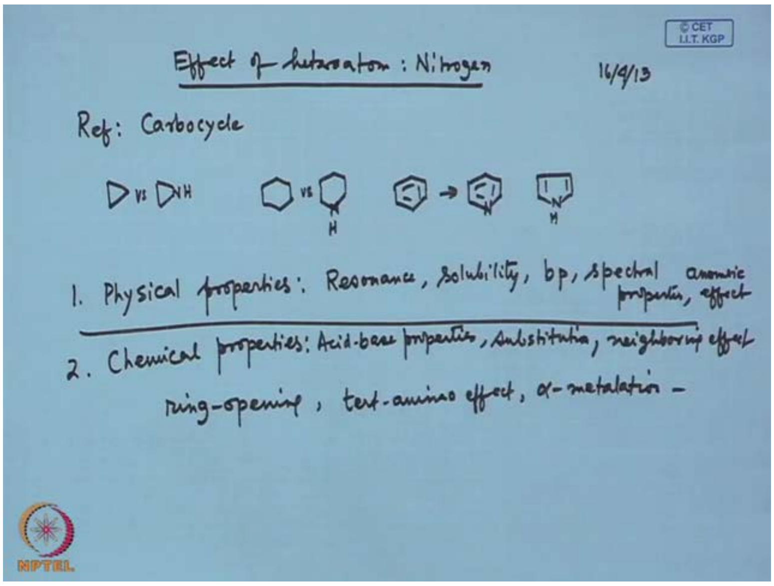

Effect of heteroatom : Nitrogen

16/4/13

Ref: Carbocycle

1. Physical properties: Resonance, solubility, bp, spectral properties, anomeric effect

2. Chemical properties: Acid-base properties, substitution, neighboring effect ring-opening, tert-amino effect, α-metalation –

Normally, in the area of effect of hetero atom in this case I will be talking about let us say nitrogen, maybe this this would be our main focus nitrogen and what we have to do? We have to compare the reactivity all other effects with the carbocycles that is important that means your reference or the backgrounds material would be the carbocycles. So, our reference would be carbocycles, then when you say, so then that means you have to first define what the carbocycles are. You would like to refer to one of them is cyclo hex propane because it is most strain and all of us know and then we will compare with cyclo hexane that is strain free.

Then, also one more which belongs to the aromatic compounds that is basically the benzene thing. Now, when we consider the effect of hetero atoms, when I say, so that means basically nitrogen sulphur and oxygen, now often I will just give the examples with nitrogen which can be extended to other hetero atoms, so when you let us say talk about the hetero atoms cyclo propane chemistry or the corresponding azardine chemistry.

Then, you have to basically compare cyclo propane azardine, similarly in case of cyclo hexane, all of you can guess just replace one C H 2 by N H and that would give you this one bipyridine likewise in case of aromatics. So, you have to compare with pyridine, so that means the transition is basically transition of knowledge or background of the knowledge would be based one benzene chemistry and you can also compare benzene with pyrole. So, likewise furan thiophene etcetera, so that means hetero atom is there, but the ring size is changed for both.

They are basically the representative members of as I told you in the last class it is a member phi excessive and phi deficient hetero atoms heterocyclic compounds. So, throughout the class, basically we will compare the chemistry of azardine or the three-member cycles or the strain system with cyclo propane. This cyclo cyclohexane should be compared to bipyridine and likewise benzene or all other heterocyclic compound should be. Now, this one means one other aromatic compound should be compared with the benzene, so given all the facts, let us say put together, you can divide the effects into two different categories.

What are the two different categories, the first one is physical property, this is very important though many of us ignore, we want to know the only the reactions, but that is not enough. Physical property is very important because you can extrapolate that to into chemical properties and then of course you can do all reactions in inventory absence. Then the chemical properties both the kinds, both the kinds would be useful when I say physical properties. Then I think you have to know what it is like say bonding is physical property, but since we are organic chemistry. I think we will start with resonance and solubility is very important especially in case of the heterocyclic chemistry.

To isolate the compound, purify the compound, you have to have your understanding of this solubility, and then boiling point of course that is good. Then what spectral property spectral properties spectral properties that is also important and what more what more and could be aromatic effect aromatic effect also is a kind of effect of the bonding etcetera, but that is that is manufactured elsewhere. These are the thing you have to think about whenever you come across a situation first think about the physical properties bonding properties.

Then, you extrapolate to the chemical properties and so all these properties would be manifested at in the chemical properties, when I say chemical properties means I think very first thing that we talk about is loud reaction, no acid base property. This is basically chemical properties though, so acid base properties, so that means whether acid base properties. That means whether the acid strength has increased or decreased etcetera, then of course all of us know. The next important thing in the area of especially heterocyclic chemistry is substitutions substitution.

Then, I think many of us know, I think in when you are talking about this called neighboring group affect this is all. So, that means here few things we have to remember though what is the area you want to explore or you want to remember or you want to know. Then there are few things special things for example, this is important in heterocyclic chemistry ring opening. So, ring opening is not very common in carbocyclic chemistry, but when you come to heterocyclic chemistry is ring opening.

Then, enclosing all these things is often encountered and then there are there is a special category, I think there are two kinds of special category that would be taken up in details in another full lecture. That is called amino effect amino effect or sometimes butyl amino effect, so this is one of the very important fascinating area where you can do all kinds of new molecules and lastly there is another important area that is called alpha metallization. I will give you one or two, I will give you one or two examples of alpha metallization, so that is also is important that we will talk about as you go proceed.

These are all that means these last two are important very uncommon though and that is particularly activated to the presence of a hetero atom. If you do not have the hetero atom do not like to I mean see such things, so let us take up the cases one by one for example, when you talk about the physical properties. That means the resonance, so what you know about the resonance I think all of us know resonance what to know about the resonance, I mean I can give you example.

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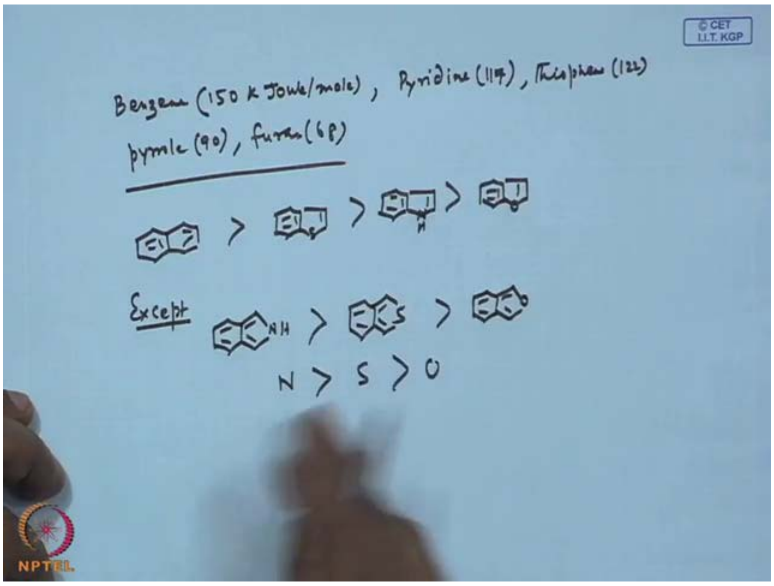

I mean benzene; all of us know resonance energy, and how much no joules joule is the SI unit, so I think should remember SI unit 150 kilojoules, 150 kilojoules per mole. So, likewise then pyridine how much one seventeen, and thiophene theophany 122 and then pyrole 90 and furan 68, so this will tell you something. So, that means, basically what you have to do to find out you have to find out the trend, you do not have to remember the value what is the trend the trend is, if you do not change the cycle the ring size the with increased ring the electro negativity.

This is important electro negativity all of us know among all this hetero atoms oxygen is the highest next highest is nitrogen then the then sulphur marginally electronegative than carbon. So, we know all these things that means and as usual from the data you can make out without changing the ring size that resonance energy decreases with the increase in the electronegative. Let us say from benzene to pyridine there is no change in size, but then resonance energy decreases and among this for example, thiophene furan and pyrole.

Again, this thiophene has the highest resonance energy followed by pyrole followed by furan this is true this, for example, let us say, now if you take fuse system for example, naphthalene, naphthalene will have higher resonance energy from benzyl thiophene. So, benzyl thiophene and pyrole is basically nothing but benzyl furan benzyl furan, so this is the order that means again it complies with these or trend previous trend that is electro negativity increases resonance energy decreases, but that is not always the case.

In certain cases, you will see there is a difference for example, if you take the isomers of the previous isomer of the previous examples. So, among these at least what has been found hmm this is iso indole, iso indole this is iso benzyl thiophene and this is iso benzyl furan. So, that means is the in this fusion is changed, they are named as iso series and what, you see here this is this is nitrogen this is sulphur and this is oxygen. So, there is bit of change here in the resonance energy that means that most places what you seen resonance energy is perfect, but in iso series.

Sometimes, you may have a difference in the resonance energy, next thing what solubility all of us know how we basically, how do you correlates solubility with the presence of the hetero atom. This is also very important solubility is a very serious concerned in medicinal chemistry because all the drugs have to be soluble in water. So, one of the major concern in development of a drug is to make it water soluble for example, there are many organic compounds many hetero atom continue organic compound medicines are known in the literature. They have been converted into salt; let us say some sort of salt means carboxylate sorry bi sulphite complex.

Then, hydrochloride complex, so hydrochloride salts, so that means they can be solubilized in water. So, that means and all of us know between nitrogen sulphur and oxygen of course nitrogen is most basic. It can undergo, so once you form this propionate nitrogen that can undergo hydrogen bonding with water. Hence, solubility increases that means an inane is not water soluble, but all of us know that if you had little bit of acid in it, then it undergoes solubilizations.

So, this is pretty common, but then you have to know this is only true for the nitrogen compounds oxygen or sulphur compounds. You have to remember and dipole movement dipole movement is also important dipole movement is also important because it can give you some idea about the boiling points, some idea about the boiling points.

There are quite a few examples that is the title movement increases boiling point increases. Then one more important point about the boiling point, how do you corrugate boiling point with other physical properties like dipole movement and molecular weights. These are the basically the two parameters option known, there are other points too, I mean boiling point, what are the factors dependent on boiling points. First is I think the commonly known parameter is molecular weight, if the molecular weight goes up, boiling point goes up, the second important point is packing geometry structure of the molecules.

If the alkene and trans alkenes between the trans alkenes which one has higher boiling point anybody knows, trans means nice stable arrangements. So, they can pack among themselves, so that means that Trans will have higher boiling point than the cis. The cis will value of boiling point, so likewise and if you have a if you know the dipole movement the dipole movement also induces rather can be attributed to the boiling point changes. If you have higher dipole movement boiling point to be higher, so these are the three important factors that there are no linear go relationships, but with little experience you can make out where dipole movement is important.

Here, dipole movement is not important, but in case of heterocyclic chemistry dipole movement is important because you are putting hetero atom. So, you are putting a carbon and hetero atom bond polarized, so automatically will have a dipole movement change and dipole movement change would induce the boiling point change. Let me give you just I think I have quite a few examples, but I will give you just one example.

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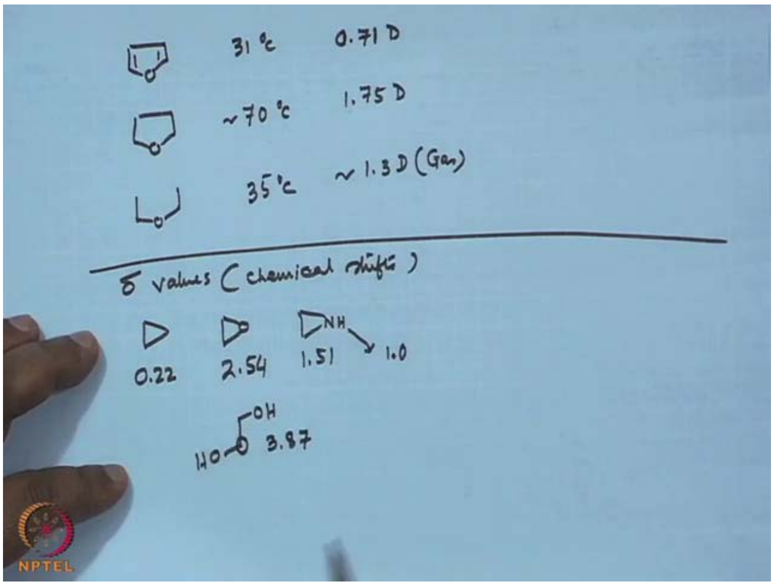

Let us say furan for example, furan is a boiling point is 31 degree, this is 31 degree boiling points and what is the dipole movement, dipole movement is 0.171 d y that is the dipole movement. Now, just think about this one think about this one tetrahydrofuran what is a boiling point t h f all this is will have boiling point, I will make it like this how is that 70 degree. So, why this boiling point, we have only increased 2 units, sorry 4 units of atomic weight. So, molecular weight has been increased by 4 units, but the boiling point has enormously doubled, more than double.

This can be attributed to a high dipole movement, high dipole movement, now what is this ether, so how much we have increased. So, that means from tetrahydrofuran to ether, what is the molecular weight increase only 2. So, that means boiling point should be around 70, but how much you get, let us see make it 35, so why the boiling point decreased, this is a clear case of dipole movement in fact, sorry I do not have the dipole movement in this.

I used to have there is a gas phase dipole movement, I do not remember exactly, but I can tell you it is definitely less than 1.751, let us say make it 1.3, maybe this is just guess and this is gas phase. You just look up the google, you will see the dipole movement is lesser than this one, so likewise you can have other examples. The other important things about these physical properties for a physical property, we are still talking about the physical properties, the chemical shifts in NMR. That means NMR determination is very important in heterocyclic chemistry, what we will find very interesting trend for example, what is the chemicals shift of this carbon.

So, that means basically the delta values, chemical shifts, we are comparing with the carbocycle compounds and what should be the chemical shift value. Let us say if you this one take a furan, sorry let us say oxygen for example, and in case of cyclo-propane this chemical shift value is 0.22 is less than aliphatic compound though linear aliphatic compound because of some reason, what is the reason. Suppose, alkane is one cyclo-propane will have very reduced chemical shift value 0.22 because of the sliding an isotropic effect sliding just reverse of the benzene, reverse of the benzene.

So, if this would create a sliding atmosphere so that the hydrogen goes to up field chemical shift value is reduced, but when you come go to the box side, basically you are increasing the electro negativity, so electro negativity. So, chemical shift value in this case box side could be 2.54 that is quite obvious, electro negativity in that means by placement of hetero atoms. You are increasing the electron density, sorry electro negativity of the atom and it pulls the electrons density towards oxygen. So, chemical shift increases, so likewise let us say a azardine, one would expect a this c h 2 2 up here between cyclopropane.

This is because it is less negative electro negative than this and it is 1.51, so what about this one N H, what should be the chemical shift value, see that is the thing that is what good. At least you have said so but it is not, it is one it is one again, this shielding because of this shielding current, it actually shields all the three members. For example, very clear cut way for example, ethylene dichol, for ethylene dichol what should be the chemical shift value at the circle carbon. Normally, if you have hetero atoms, the corresponding carbon hydrogen would have normally 3.5, but you have neighboring oxygen here, so this comes around 3.87.

Now, you see the difference what is the difference 3.87 goes to 3.54, sorry 2.54 that means drastically decreased when I say drastically means less than more than 1 ppm. So, why has it decreased, so this is also a nice test for whether you have, let us say you are handling with l cyclic compound. We are trying to make it a cyclic compound cyclic hetero cycle, this is especially the three membered ring, and you can very clearly see whether you have got the cyclized product or not based on this change in the electromagnet values. Once again, I mean because of this anisotropic effect of the cyclopropane ring system, so I will give you one more example just to emphasize that these chemical shifts distinctly different for heterocyclic compounds.

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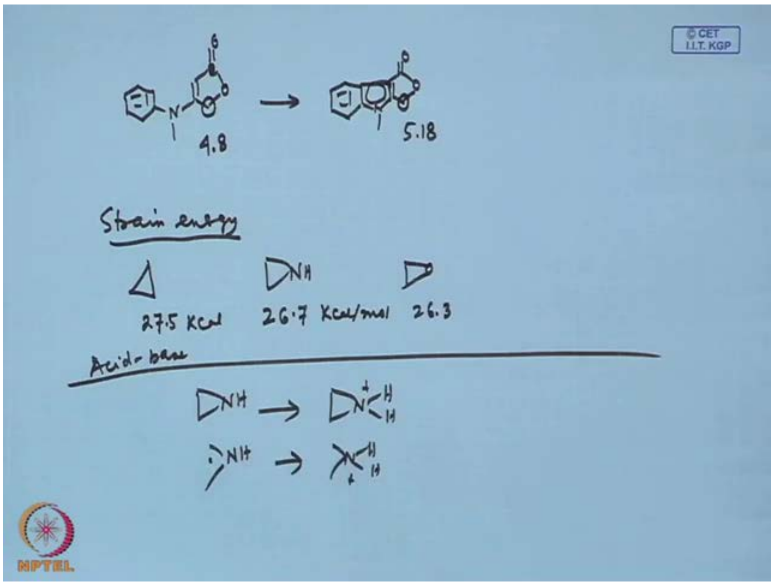

Let us say if you are thinking about let us say molecule of this kind, this is known compound and in this case methyl here and let us say you want to carry out a reaction of this kind, how do you know whether reaction has taken place. In aromatic portion, normally there are lot of quite a few pics, if it is divided, we have to do the integration, let us say I think I will straightaway come to the problem circle carbon hydrogen.

It appears at 4.8, now you have to predict these effect of hetero atom or other things here, these are circled C H 2, chemical shift after the cyclization, you do not have to give me the value, just tell me what is it, more or less than 4.8. So, you understood chemistry, basically we do not have to go through the book, you can predict with confidence whether it should be more than 4.8 or less than 4.8. You know NMR chemical shifts only thing we have to basically predict and with confident valued be increased valued be increased because this ring is aromatized, so when I say this heterocyclic ring, this heterocyclic ring aromatized.

So, when you have aromatic anisotropic effect would induce this, so it to the value increased and the exact value is actually 5.18. Now, this fourth, I think this is also you all know this is strain energy strain energy of a cyclic structure. So, normally cyclopropane is our again reference, what is the strain energy for cyclopropane, some of you probably know it is 275 kilocalorie. Then possibly external energy for cyclic azardine azardine, it is slightly less, I think I will just give you the data, it is just more or less comparable and this is 26.7 kilocalorie or more. So, likewise oxygen also will have very similar strain energy, what does it mean?

So, these are all the physical properties, strain energy etcetera as we see calculation bonding, it comes and then of course it is validated by the experimental results, but now what you see what is the manifestation, what is the manifestation? They undergo ring opening reactions; all of them undergo ring opening reactions. Now, depending on that, we have to know little bit of more chemistry, but one common chemistry is that all of these strain ring system would open up if the situation demands or situation is such that reaction would favor this thermodynamically favorable. It will undergo ring opening to give you the ring product and we will see more example, but maybe just where little quickly we can see some of these acid base properties.

For example, many of us know I have to know acid base properties are say between azardine, let us say acid base property means it is basically the chemical property. Now, one more we will talk about only the chemical properties acid base property in case of azardine. For example, what is the necessity, it is more than when I say, so that means in this case will be talking about let us say dimethyl amine. For example, dimethyl amine compared to dimethyl amine, what is the weather, it is basic more basic or less basic cyclic.

So, it should be more basic or less basic that means what you to do all of us know, so normally we talk about the corresponding this, now we have to show which one more stable. In this case, it is an open sense compound; it can readjust this structure according to used opinion. That means it becomes more stable, this less stable that means which one is more basic more basic no dimethyl amine dimethyl amine is more basic because it gets the stabilization on protonation. So, azardine is less basic that azardine is more basic aromatic amine that you have to remember.

That means the necessity of azardine is in between the aliphatic amines and aromatic amine. So, that means basically what we try to say presence of hetero atoms would induce this or rather change this azardine necessity. Let us look at some of these examples of this manifestation of strain the manifestation of strain. For example, let us say maybe I can just give you another example on this anomeric effect; you have studied anomeric in hetero rather in carbohydrate chemistry.

Anomeric effect is the basically the effect between the anomeric oxygen and the corresponding the substitutions. So, due to the anomeric effect, actual isomer becomes predominant will isomer compare to that, so that is also true for the nitrogen heterocycles, I will just give you an example here.

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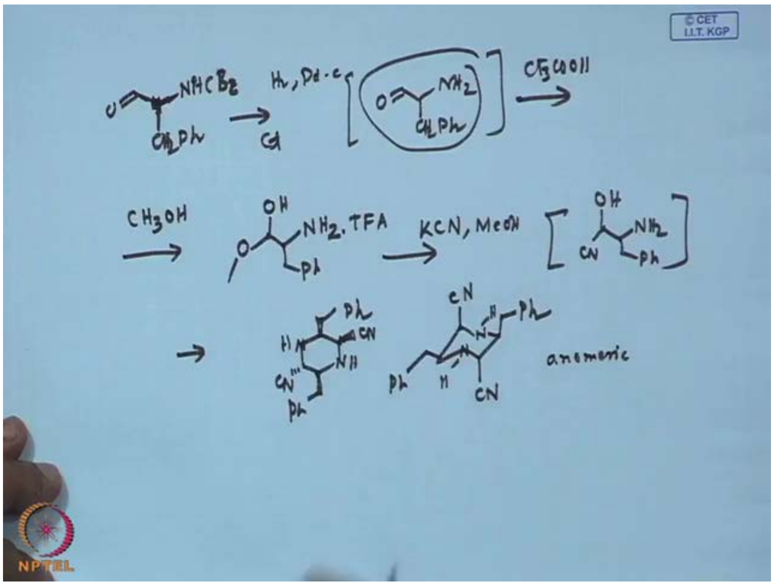

Someone wanted to make a free, sorry this is not nitrogen, this is carbon pre amino aldehyde pre amino aldehyde and this is C Bz, this is a productive group C Bz. Now, if you do the hydrogenation, peridium charcoal. So, what you are supposed to get, you are supposed to get this is N H 2 and this is C H 2 P H, C Bz means carbo oxy carboxy benzyl. So, this sort of compounds is not stable, simply because you have an aliphatic amine aromatic amine, so undergoes shift wise formation automatically undergoes polymerization.

They are not very stable and so to stabilize, actually the reaction was carried out in the presence of trifluoride, acetic acid. If you do, so what you will get you will get, actually you should know, you should have rather obtained corresponding trifluoride acetate salt, but that is also not stable, so what they did. So, after this reduction, they treated this with methanol, so result is this was N H 2 and this trifluoride acetate salt. Then this is the benzyl and then what you get a hemi acetone hemi acetone, so this is not a heterocyclic compound, but just sometime tell you this effect of the hetero atom.

It polymerizes aldehyde, but then when you treat this with potassium cyanide and methanol, one would expect that that expected product is what this is N H 2 and this would be cyanide hydrate just aldehyde iodide reactivates anhydride. It is not a product here, a product goes to which is like this cis and I think this is I think will see that whether it is Trans and this is cyanide. So, presence of hetero atom, what does it do presence of presence of this hetero atoms, actually makes this aldehydes also more reactive. So, you eventually it goes to the dimerization, but if you take this structure this excess is structure of this molecule, what you will find?

You will find a nice orientation and which would be would be like this hydrogen and this benzyl group is axial. This benzyl group is and that is because they are ceased to each other and what else, you will find this cyanide is now axial and this cyanide is axial. So, what does it mean, anomeric effect, so it is clear case of anomeric effect, anomeric effect means if you have a hetero atom in the cycle that you would know alter the confirmation. That will alter the confirmation of a substitute and alpha and due to the dipole interactions dipole repulsion.

Some people, I mean talk about this overlap with the anti-bonding orbitals, so that means the presence of this is basically this is again a manifestation on extrapolation of the physical properties. I will just give you one more example probably as I will skip some of the things.

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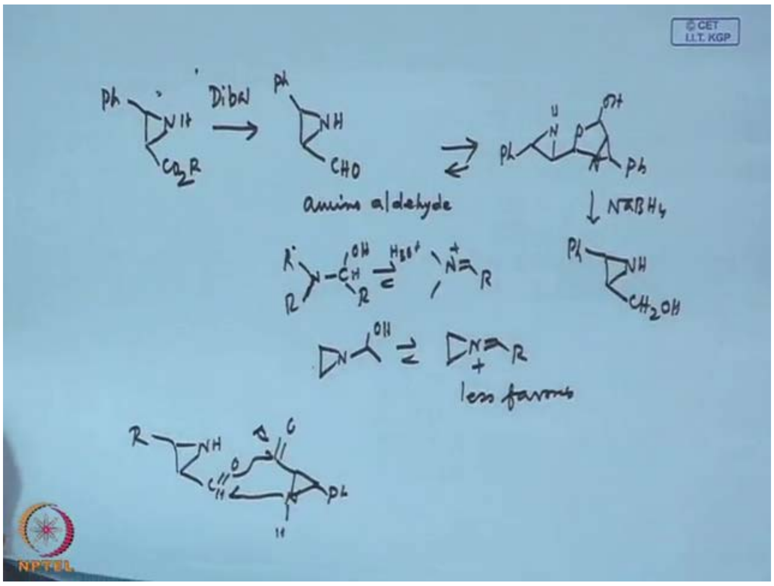

For example, if you let us say try to prepare amino aldehyde, let us say in this case you see here, now we are talking about the hetero cycle, let us know the hetero cycle. If you react to this with the Dibal and all of us know what is expected Dibal is so selective towards extra reduction to the aldehyde. So, you will get this, now what it is, it is a amino aldehyde write in the previous case it was not very stable. So, it got no further, it underwent further reactions, but in this case let us say if you want to stop this, is it possible or not. If you compare, let us say if you compare an open chain compound that that is what you have to do it is a cyclic compound.

Now, you see have to compare with open chain compound open chain compound if you have a amine, then let us say if you react with aldehyde. So, what you would expect, you will say amino aldehyde, write this is in presence of acid, it forms this ammonium iron here and then it undergoes ammonium iron. So, it undergoes all sort of reactions and this then you can do sodium borohydride this cyano borohydride, it can convert these into direct amine et cetera.

Now, it is a case here very few have azardine for example, a similar case let us take this is a hetero cycles. So, in this case, what you have to do, you have to say think about reactor intermediate of this kind, now whether this is possible or not. So, this is now tetra hydra, this is now tetra hydra, I mean nitrogen is constant with tetra hydra here, so that means it is approximately I mean let us say 109 could be etcetera. When you just like sp2 carbon atoms to flatten it this angle increases, so that means you have further increasing the strain that means this is less favorable.

This is less favorable than the previous example, so what it means that the you can actually isolate this compound. In reality, what you will actually it was not isolable, but it was sort of an, it undergoes it underwent dimerizations to the cyclic structures here, so it underwent cyclisation to this one.

So, it is essentially is a dimer of this one and what happens this nitro, one more azardine nucleus nitrogen attacks the aldehyde, it forms this OH here and OH undergoes further intramolecular addition to this aldehyde to give you this lactol kind of things. So, how do you know this this is for the isolable and if you simply just react with sodium borohydride, you can get the stable molecule of the stable amine this azardine and alcohol azardine alcohol.

So, this one is actually first is intra molecule, this second, so let us say if you just look at this here, this is aldehyde write and this is r and then you have nitrogen here ph and this is ch aldehyde. So, what it does, this this goes to this one and this goes to this one, the first is intermolecular, then second is intramolecular. So, basically it says dimerization that means that this is although a supposed to be stable, but it is not stable, but they can be I mean in equilibrium unlike the other example. So, that means what it says the adding strain has induced little stability to this azardine aldehyde that means that can be made use of some other transformations.

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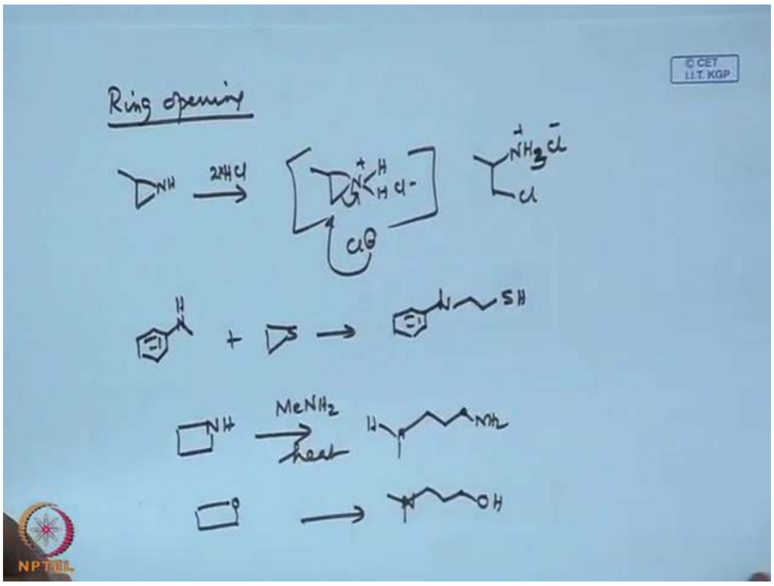

Then, other important area that is of course in heterocyclic especially in nonaromatic heterocyclic is ring opening. So, all of us know if you have for example, azardine here and if you treat this with 2 molecular, let us say 2 2 times of H Cl, 2 times of H Cl, what do you expect, so H Cl means acid based reaction. So, first people undergo protonation then what that means in the first step 1 1 would say this is a quadranization and this next step. So, this is this is how you have to predict that means that means our foundation is based on carbo cyclic chemistry. We know very good chemistry of the carbo cyclic compounds, so what next ring opening of course.

Now, that means strain energy, now the physical property tends to chemical property ring opening. Now, this chlorine, so the question is where it reacts this chlorine. Actually, this is a continued research, this is a topic of the continuity means today people are working on this ring opening, now this is activated. The proton has made this even more activated because there is a chance separation possible.

So, in this case is and there are all possible chlorine here and then here it depends on the balance of the electro balance of the substituent effect, but in this case it attacks this liquidation of 2 and what we get is now this one N H 2. Then once N H is formed, then it picks up one more molecules of H Cl, so eventually gives you basically this amino chloride. So, likewise for example, if you take even aromatic amine for example, aromatic amine here and take ethylene corresponding sulphur compounds, so what we are likely to just basically heat nothing else. We do not have to do anything heat and this three membered ring opens up and it to get the corresponding markup ton.

This is not restricted to three membered ring, if you have let us say what this name azardine, 4 membered ring azardine, now a methyl amine methyl amine and just heat it that means amine and amine. So, they should not react, they should be comfortable with each other, but the reaction it opens up and gives you the corresponding N H 2 here and N M. So, you get the di amine, so that means this is a pretty common phenomena. So, likewise you can also, I mean just think about this oxidant oxidants also would give you the corresponding methyl amine, sorry this is hydrogen, so you will have the corresponding amino alcohol.

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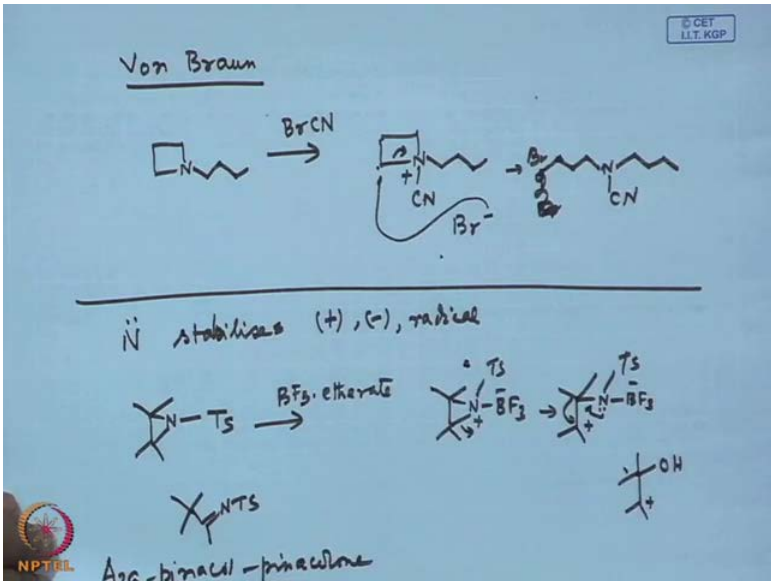

So, like this you can get all kinds of ring opening and one of the famous ring opening reactions, famous ring opening reactions, I think many of people would be knowing this is alkaloid chapters. Von Braun ring opening, it is a reaction with cyanogen bromide it is a reaction with cyanogen bromide. For example, if you take in butyl azardine in butyl azardine and then this is a particular reaction only reaction that is actually the used in this reaction. It is known as cyanogens bromide, so what do you expect, we have tertiary nitrogens here and what is expected out here.

Once again cyanogens bromide which one is positive which one is negative we are is no cyanogens bromide. So, bromide is negative, so that means intermediary between so hide hide is a negative, so that means cyanogens is pass and distinctly readily available and review whole reaction. They also multiply, in many cases is pretty useful in peptide chemistry, also in peptide chemistry if you have a cyclic structure, you can I think I have forgotten, it will also probably is used for disulphide form.

I do not know, you do you know i think over there may be and this could be is your cyanogens bromide in peptide chemistry, but in this case if you wants you have a quitrent nitrogen. Then what is next based bromide can attack this alpha of position this alpha position and this alpha position of these two are equivalent. So, then you have to decide which one would be attacked and obviously now you know the heterocyclic chemistry and you know the ring strength. So, this one would attack, so that the ring will open, so that means the product would be the product would be 1, 2, 3 nitrogen n butyl.

Then, you have synate and here you have left the bromide 1, 2, 3, sorry one more belong to less, so it should be bromide is here 1, 2, 3 nitrogen this butyl and this synate. So, this should a pretty common kind of reactions pretty useful reactions, then what else and there are other, let us say other imported reactions from this. This is reopening, this pretty useful, there are plenty of examples you can take it up and then I will just tell you one more important thing in case of heterocyclic chemistry effect of nitrogen push stabilized radical carbo cut ions and carbon irons.

This is important nitrogen can stabilized de alpha carbon ion alpha carbo cut ion alpha radical this is very important and you will see throughout these carbon nitrogen chemistry. That means nitrogen can know appears can stabilize nitrogen stabilize that ion and ion and radical this is important and for example, i mean it can it can also induced let us say Pinac Holy arrangement. For example, and that case it will be known as has pinac holy arrangement as Pinac Holy arrangement. So, you have take these is BFS and BF 3's etherate, so what would be expect is fine, then what see where is perfectly true.

So, use Pinac like in the previous example undergoes coordination, so nitrogen is quaternized, but n is quaternized and then what next, it will reopen find that is that is also perfectly correct. So, it will have reopening, so reopening we have 3, then minus and this now what it is these they have to that is important structure its intermediate as to be identified. If you recall, it is very similar to very similar to Pinac holy arrangements feel have a Pinac co Pinac arrangements. So, Pinac holy you have o h group here in this case you have nitrogen that is the b f into as Pinac code, so what you expect this methyl group migrates and this would quaternize and this is quaternized.

So, I missed, sorry you have tousle here tousle here and tousle so there is result should be there is a product you have n tousle. So, you have this corresponding image, the waves, this is the case of a two a Pinacol of the arrangements Pinacol. So, that is the one can say that basically nitrogen stabilizer is the alpha positive picture, let me tell you one more important this facility reactions again given by nitrogen.

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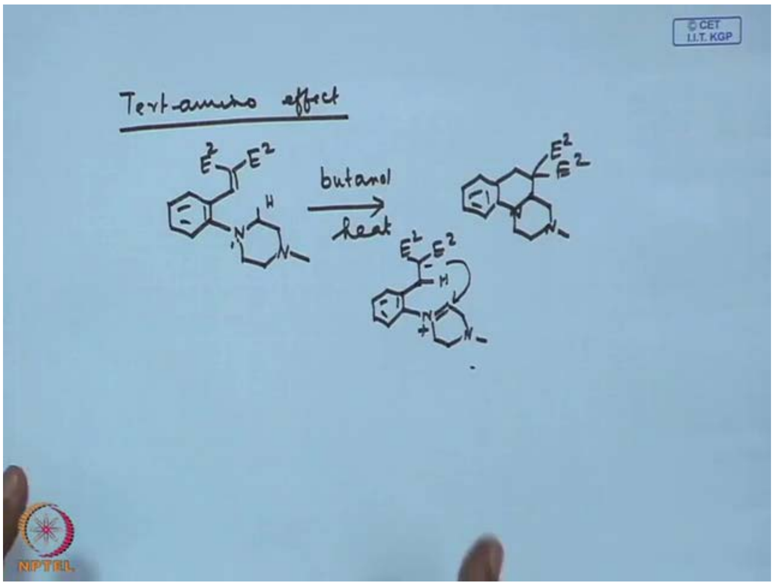

You have tertiary amino effect or are sometimes you call it as a butyl amino effect tertiary butyl amino effect and what is it, it is reactions of this kind these as to be sort of a biotic compounds. Then you should have activating groups and e 2 and e 2 and then a tertiary amino groups tertiary amino group. So, in this particular example you have one more tertiary amino group tertiary amino group, let us show that is the only a 1 of them could react which are would be react the reaction, so simple just take this molecule neutrol solvent butanol and and heat. So, what you expect, now only one would expect you have butanol and extract, so you expecting a transition fixed kind of reaction, but you do not see this trance establish and normally requires either acid or base.

In this case, what you have to recognize the presence of the hetro atom and at the same time also you have to rotate that this is a tertiary nitrogen. So, this is also tertiary nitrogen the reaction actually go to give you a new hetro cycle and this is nothing but this is sort of a rearranged to hetro cycle. That means and this is e 2 means a if a enlister it will be the this compound, so would you see what is the sayings do you see you see is basically alpha n nitrogen. What I said before this alpha nitrogen, it is this case, it is stabilizes the alpha carbon ion actually this hydrogen is shift at mechanistically this hydrogen is shifted are you can say.

So, many things happen, let us it is go to see that, so eventually as if what you can say one of these intermediate could be returned this way you can sit down and are it out as if this hydrogen shifted here. Then this attraction is formed this is shifted here formerly and this and what else it is a neutral compound. So, it is as to be neutral that means this is the negative charge in negative charge their this negative charge then intra molecularly attack this.

So, it is actually given the plenty of example plenty of examples and people are actually using this kinds of molecules and this way. So, you have more example in one of the latter classes I think I do not know what I talk about this ring of participations. All of you know nitrogen master, what is the nitrogen master what is the structure of features you have to a hetro atom c is to c is to and a living room. So, these all them is the basically the effect of the hetro atom on the reactivity.

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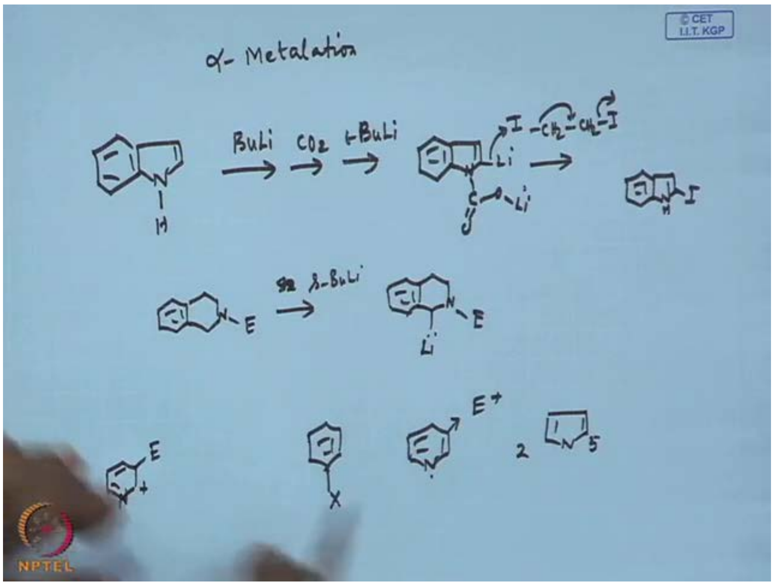

The last example I think I still you this alpha metalation alpha metalation, there are plenty of example and it is applicable to both saturated and unsaturated molecule, sorry boot saturated aromatic and non aromatic molecules. I will just give you one examples, it could facilitating c, if you begin with indole and I think first butyl lithium is given. Then carbon dioxide then again tertiary butyl lithium tertiary butyl lithium first one remove N H, convert this into salt, what next, it will actually be alpha positions. You see the trick that means the basically the term hydro atoms in dishes the alpha litigations.

Now, if you noted this with less a di hydro ethylene, so what you would expect will be getting is 2 because this is carbon ion. So, this is nice source of similarly, di and di bromo ethylene also is a source of this is the bromine in a in a metal essence of these symmetric reaction with metal spaces. So, you get the corresponding to the carbonic acid, you just put the carbon dioxide and I do not have the exact example. Now, there are quite a few examples, let us say if you is if you have for example, you have some electro liberalized group here.

If you can use secondary sec butyl lithium you can expect this litigation at the alpha position even for this is also true for the parallel odene pipel dene systems, but you have to have a carbonate on there. So, it can stabilize these correspondingly basis, but that is also driven by the stability of this nitrogen that means and each case there are two possible groups. All of us know that this is benzoic one, so if you and what else for summary physical properties, so you have to list the physical properties, you are resonance boiling point spectral properties etcetera and chemical property means acid base.

Next one is substitution you have not cover substitution see in case of benzene, now all of us know substitution is guided by independents of the groups. So, the heterocyclic chemistry in case of pyridine the substitution, electro substitution; for example, x plus referentially at no three position. So, that is what you have to remember, so the in case of benzene, let us say you know it depends on the substituent here, but in case of pyridine you can think about that.

We see the substituent may be so in case of this is meta, it determines basically and this is the most preferable position preferable position of the electro substituent reactions. If you have a 5, the 5 position is the most f referred one, so the one that means this one I can saw 2, 2, 2 or 2 or 5 and in case of pi roll, it is 3 positions, 3 positions. So, these are the these are the things you have remember and we can also if you go you have if you have forgotten what you have to do you have to write, what you write, you have let us say if have nitrogen here, you have to write the corresponding intermediate e.

So, this should be e and this should be plus now have to see if they whether you can write how many resonate structure, how many more resonate structure from there. This is one of the nice as to being, can we do calculations of these things, but they are somewhat not when you do and how do you do and all this things are there, but here is very conflict. So, you can predict very well the reactivity and other thing we have already said this never being who participations already known.

So, specific heading reactions I missed a point though heading of reaction can be assisted by like what you said, what you have seen by portal nation. It can be also assisted by quantization if your group nitrogen is quantization opens up. Then also like BSP is also characterized that and then other think sulphur group electron group presence of electrons group. Let us say this is a case of nitrogen and sulphur group that can open up and lastly I think since we can see here.

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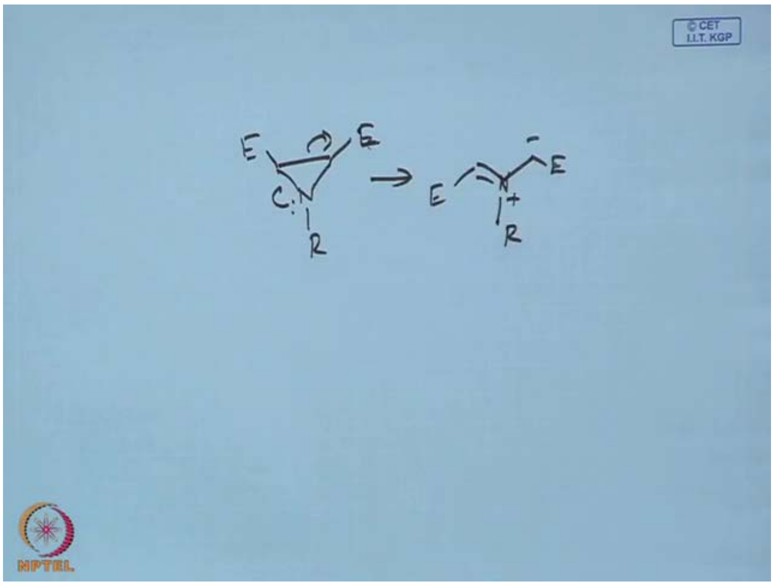

Let us say if you were here, so f a group, let us say r of an opens up to give you this, it is stimuli, this will delight dipole. So, 1, 3 dipole generated by a algorithm and this is where true for the also cases known, so if you are interested, I can give you a homework, no that is a homework and let us say I will skip it.