Heterocyclic Chemistry
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Lecture - 8
Effects of Ring Nitrogen-B

Before we take up this topic Effect of Ring Nitrogen, which is synonymous of the topic effect of heterocyclic, all other heteroatom on a different reactivities and structures, etcetera. If you recall, last time we classified two different kinds, one is the effects on the physical properties and second one is chemical properties. And just very quickly, let me give you a review questions and see, whether you can come up with the right answers to this problem.

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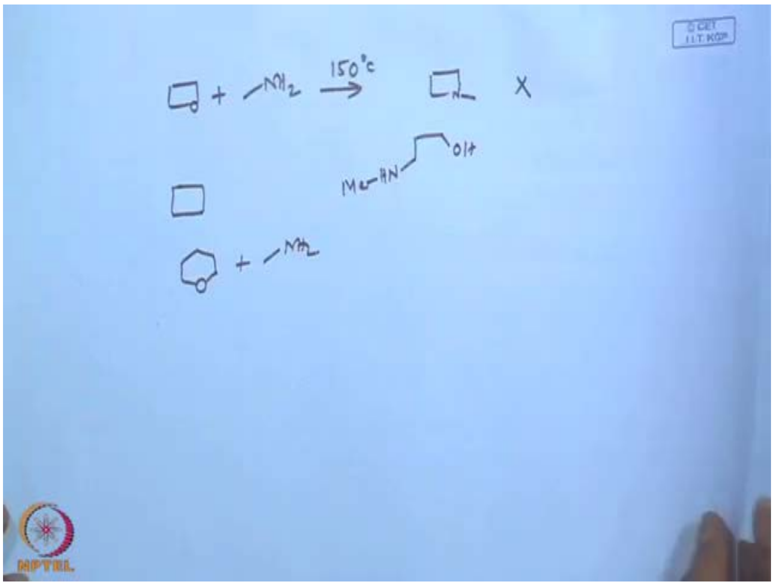

Let us say, if we mix these two reagent, this is oxidant and then, if you just heat it at some degree, 150 degree. So, what would you expect or from this reaction, do you expect a reaction first of all. That means, you have two different kinds of the hetero atom, the purest compounds where the study materials are oxidant and methyl amine. We just simply hit that, no catalyst, nothing.

Student: Ring opening followed by ((Refer Time: 01:47))

Ring opening followed by...

Student: ((Refer Time: 01:50))

By nitrogen, so that means, what you are suggesting that, the compound should be this, now we have to, that is a good suggestion though, but while answer obviously, is no. So, what does it reflects basically, it reflects these, the reaction product is this alcohol here and this NH and Me, so basically it is a ((Refer Time: 02:27)) product, that is what. So, simply because, all of us know there is I mean, you have two different kinds of atoms, the one of the better nucleophile is nitrogen all of us know and then, since the cycle is a four membered ring, so it should all open up.

So, this is a basically that means, on the other hand, if you think of similar reaction with a cyclobutane, you do not expect such reactions. So, that is the basically heteroatom that means, it imposes a strain and then, it will open I mean, the strain is responsible or the driving force for the reaction. But, similarly if you let us say, look at a reactions of these kinds, let us say the six membered ring will the similar reagent, so you do not expect it. So that means, it all depends all of us know, this six membered is more strength and four membered is less strength and so on.

So that means, this reopening, etcetera in the heterocyclic compounds depends on the ring size, that is what. So that means, hetero atoms, although the size of the ring imposes the strength, but the heteroatom gives the electrophilicity, electrophilicity means this weakening of the carbon hetero bonds. Whereas, in the previous, in the case of the cyclobutane, the carbon hetero bonds are very strong, this is just a example. Now, so next category is basically the effect of hetero atom, but we will exclusively talk about the effect of a nitrogen on chemical reactivity.

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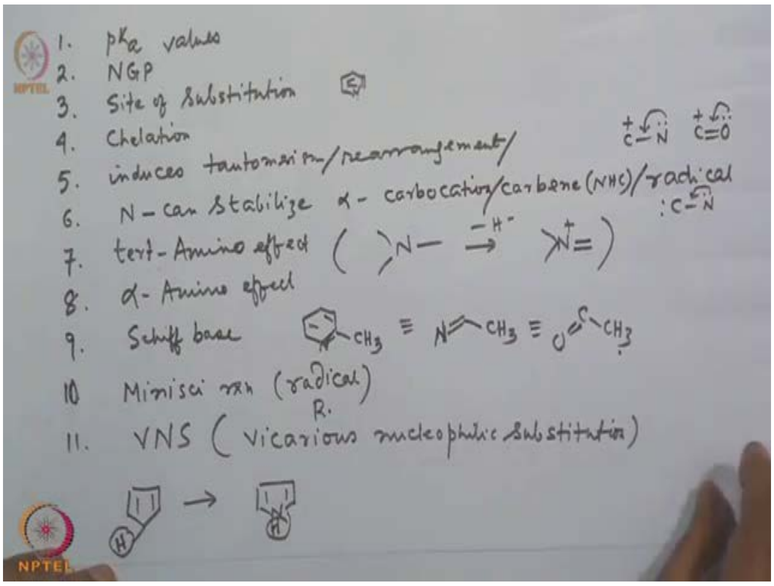

1. pKa values
2. NGP
3. Site of Substitution
4. Chelation
5. induces tautomerism/rearrangement/
6. N - can Stabilize α - carbocation/carbene (NHC)/radical
7. tert-Amino effect ($>N- \xrightarrow{-H^-} >\overset{+}{N}=$)
8. α- Amino effect
9. Schiff base
10 Minisci rxn (radical)
11. VNS (vicarious nucleophilic substitution)

So, how many kinds of the chemical reactivity are manifested by the hetero atom or dictated by hetero atoms. So, which one I mean, I have a list of something like 12 different items, maybe you can add, maybe you can subtract, maybe some of them are overlapping. But, we will systematically follow some of them and we give examples basically today, will classify the types of the effects of nitrogen and the reactivity. And then, give some suitable examples, most of them are the latest examples in literature, chosen from the current literature.

The first thing what you can think of, all of us know that, it alters the p K a value, p K a value of this compounds, that is to be important. So, wherever you have nitrogen, oxygen, the corresponding p K a value increases at the alpha position or at the nitrogen I mean, depending on the situations. So, this is a most often in the undergraduate you have seen, the discussion on p K a is taken up very early in the course, simply because the reactions, it is basically a chemical reaction. Decision of acid means, the chemical reactions, one the simplest possible chemical reactions and that gives you some clues about the reactivity of a molecule, so that is the reason.

So, similarly will have more examples on this, will come back just let us see what are the items, which are classified under this category that is, effect of nitrogen on the chemical reactivity. Other possibility, I think many of us know without writing, so well known to all of you, neighboring group participation. Third category could be site of the nuclear substitution I mean, when I talk about these actually, I am meaning to say, if we are beginning with molecule like pyridine.

So, you know that, actually the orientations or these positions of the nucleophilic or electrophilic atoms are governed by the nitrogen. So, all of us know that, so then it is also very important in our case, chelation. I think all of you know meaning of the chelation, chelation means, say formation of a ring and that too involving a metal, so you remember. And then also, sometimes it promotes the remote functionalization, normally the reaction takes place at the functional groups or at the alpha position or at the beta positions.

But, these chelations, etcetera all these can also promote reactions at a very remote place, let us say far away from the position of the heteroatom. And then, what else I mean, so when I say site of the substitution, actually it can also involve the nucleophilic substitution as well. So then, anything else, induces tautomerism, this is important factor, whenever you have a heteroatom, that is likely hood, that it can cause tautomerism. If you have non hetero like carbon, only pure carbon compound, carbon hydrogen compound, you do not see any tautomerism.

We see another cases, but strictly speaking, but at some point somewhere, the presence of heteroatom is a must. And so, that also sometimes induces the, heteroatom also the rearrangements then, what are the other possibilities, this actually the sixth.

Student: ((Refer Time: 08:26))

So, by induces tautomerism, so the rearrangements condensation reactions, basically the or you can say that, site of this substitution that is a important, site could be in the ring, it could be on the nitrogen. So, nitrogen that means, basically substitution or in addition whatever that taking pressure at the nitrogen ring, that comes under the site of the substitutions. Then, the next most important one is that, a nitrogen can stabilized, this is a very important one all of us know, I think know, but often we miss it, it can stabilize alpha carbocation, this is important.

What else, carbene like in NHC, so you can say then, what else radical, anything else, you can think of, carbon ion, no that is the exception, so the nitrogen cannot in fact, destabilizes the carbon ion. So, and very similar to this, I think I do not remember whether I taught this one, this is a very important one in a nitrogen heterocyclic and oxygen heterocyclic. There is a effect called, did I teach you in the 4 th year, tertiary amino effect.

I do not know whether you know or not, may be this time I taught, this is new batch, this is very interesting and you will find plenty of paper. Just write tertiary amino effect in Google, will find what it is, basically what it demands, as the name implies it requires a tertiary amine function. And what it does, actually it is a minus hydrate and so, you can understand what happens, minus hydrate means, this alpha position hydrogen is kicked out and it is forms an iminium salt.

So, this is the origin, actually where does the hydride go, hydride goes to a electrophilic positions within the molecule that is, intramolecular position. So, the reaction will give you more and more examples, so I am just basically listing the possible effects and etcetera.

Student: ((Refer Time: 11:24))

Carbon ion is stabilized by...

Student: ((Refer Time: 11:38))

I understand, no, but that is not a carbon ion, if the amine is on nitrogen, it is nitronion, if the ion is on carbon then, it is called carbon ion, but if the nitrogen...

Student: alpha...

Alpha, we are talking about the s p 3, that is a sort of, actually we are coming to that actually, there is a point, but I have put it in a different category, it is like a Schiff base, that is the next one. Then, these are the important one, any case we will give more examples, I will come in to your point, I have characterized some of the thing, may be I have missed, most of them are not in any book, I have just listed them. So, if you can add any additional effects anywhere, just I will list them, but I will try to include all the possible effects.

Then, you have another effect probably, I think all of us know, this is a alpha amino effect, essentially it is nothing but, alpha effect, how many of you know alpha effect. So, basically it is a enhanced effect, enhanced nucleophilicity of nitrogen bearing with an hetero atom next to it, like basically the higher reactivity of hydrogen with amine, over amine. Then, this next atom is basically that Schiff base property that is, the Schiff base property, that is what we are talking about actually.

So, Schiff base property means, if you have an amine, so this is pyridine let us say or let us say 2 methyl pyridine. So, this is equivalent to, will have more example, I think next class will have more examples on this type of the category. So, it would be looking like this, so it is an amine and that means, this molecule would act like an aldehyde, which equivalent to sort of an aldehyde. Let me see, as acetaldehyde oxygen has been replaced by nitrogen, so obviously, all these parallels are known.

That means, like acetaldehyde it forms the carbon ion, so that means, in this case this carbon ion is stabilized not only by the heteroatom, but it is the functional group of carbonyl pi bond and functional groups. To some extent you can argue, yes the carbon atom is stabilized by the heteroatom, but whenever we talking about this alpha stabilizer, actually this is the alpha anion is not that means, alpha in this case the number 6, when we talked about this, it is stabilized by the carbon cations.

And alpha carbocation means, if we have a system like, say you have a clusters here and you have a nitrogen of here then, this lone pair would stabilize this carbon ion just like you have seen in Friedel Crafts reactions. Friedel Crafts reactions what have seen, you have a carbocation and oxygen and then, this actually stabilize this. So, similarly if you have a carbine and then, nitrogen here, so this nitrogen always will also be stabilized, similarly radical also stabilized by nitrogen or with a alpha position.

Student: Sir.

Yes.

Student: ((Refer Time: 15:41))

((Refer Time: 15:45))

Student: ((Refer Time: 15:46))

Yes, right.

Student: ((Refer Time: 15:52))

Basicity.

Student: ((Refer Time: 16:01))

See, there are two items again, one is nucleophilicity, other is acidity, basicity, you have two different things. When we talked about nucleophilicity, most often we forget that, it is a kinetic parameters, most often we forget. I mean, most of the people do not differentiate and [FL] so, it is all depends on the, actually hydrogen peroxide which is more acidic than the water. That means, if the first p K a value of hydrogen peroxide is lesser than water, simply because just on the count of the electronegativity.

That means, you have an additional electronegative atom, so it is likely that, that is all, if we have corresponding hydrogen will be. And when you comes to nucleophilicity, you talk about transition state, when you talk about p K a and p K a, etcetera this is basically we talked thermodynamics. And so, then secondly, this is also the important one, what you will find, this is a special kind of reaction, Minisci reaction. What is the effect Minisci reaction, Minisci is an Italian scientist, the reaction was discovered long ago, some 100 years ago, but it was quite I mean, neglected.

But, recently people have began to react to this, this is a special kind of reaction, you will find it is a radical kind of reaction, it is a radical reaction and this reaction can be carried out in water and you can generate this alkyl radical. This alkyl radical acts to the heterocyclic compounds and this radical they are not like the, previously I said nitrogen radical stabilizes alpha radical. But, in this case, nitrogen radical itself is more stable and will give you more example from these.

And lastly, this is a reactions of an VNS, V stand for Vicarious and nucleophilic substitution reactions. I mean, I do not know many of you know the meaning of the Vicarious, the Vicarious is basically unusual, for us unusual reactions, that is all. And I mean, one can say ((Refer Time: 19:00)) reaction, I think all of you remember I do not have to say anything, if you have an pyridine, if you have an amine reaction, it gives the amine.

But, in this case, the molecule that is lost is corresponding hydride, kind of an unusual reactions. But, in vicarious substation reactions what you will find, the nucleophile would contain living group at the alpha carbon, alpha nucleophile. I will give you example little later maybe, so anything else can you think of, I think if you remember all these things then, if you have given a problem and you can immediately extrapolate that. Cyclohexane does not have a nitrogen then, pyridine has a nitrogen, so you can expect some of these reactions.

Now, let us say, we talk about let us say for example, cyclopentadiene you can talk about, now you going from cyclopentadiene, if you put the, substitute these things, so what sort of reactivity you will see, just compare the reactivity.

Student: ((Refer Time: 20:24))

So, this is diene, this is aromatic nucleus, now we would not go there, we just see that means, it has given the aromaticity, that it is covered in the first-class or a previous class, so let me see bonding, etcetera all this things. When I comes to reactivity that means, it can increase the acidity, so what is the acidity of this one, this hydrogen, many of you know I guess, acidity of this hydrogen. What should be the p k a value of this pyrrole and what is the p K a value of this cyclopentadiene, any idea anybody?

Student: ((Refer Time: 21:07))

p K a value all of all these circled hydrogen, how many of you know how many p K a values, this is important, at least you have to some knowledge.

Student: Acetic acid.

How much?

Student: 4.7

4.76, fine.

Student: ((Refer Time: 21:35))

How many compound?

Student: ((Refer Time: 21:38))

How much?

Student: ((Refer Time: 21:42))

Possible, I do not remember, but I can guess you are very close, so something like that you have to remember, these are very useful guide, I will tell you why.

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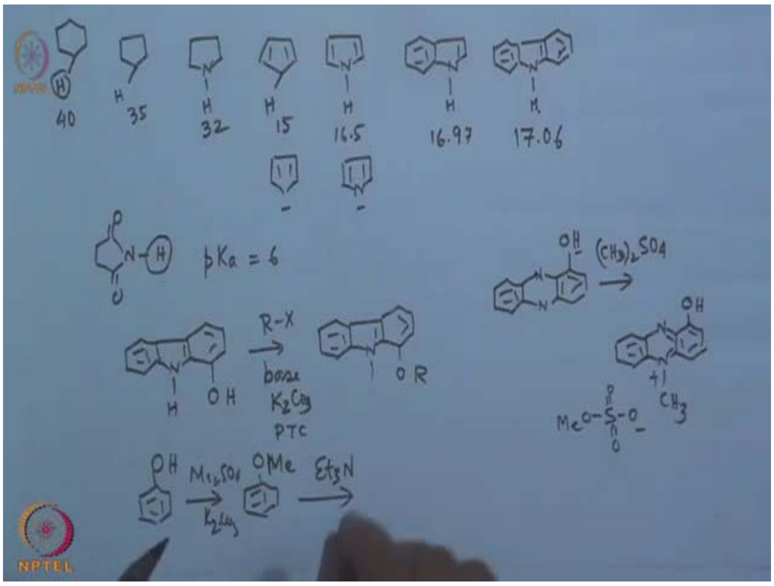

Let me give some of the data first, so our starting point in this case, since we are talking about the hydro cyclic compounds, so our starting point is cyclohexane let us say. What is the p K a value of this circled hydrogen?

Student: ((Refer Time: 22:09))

40, 40 is good enough, so then, this one cyclopentane, from the book H is 35, so these are all not very accurately in those lines, actually it is very difficult to determine. So, you have to take the values with the grain of salt and then, if you have a, that is now bi pyridine. So now, this is a game, actually basically we have replacing these carbon with nitrogen, now you have been quite obviously, what should be the p K a value, should be less than 35 or more than 35.

Student: Less than 35

So, that is it that means, it can alter, so you have some rough idea and in this case, this is not very significant. Now, come to this is a very important and see, this cyclopyridine is a very important molecule for all of us, for organic as well as for inorganic people. They do not say cyclopyridine, what they say, inorganic people they will never utter cyclopyridine, they will utter only Cp, they will say CP 1, CP 2, CP 3 all these things like eta 1, eta 2, eta 2, all these things.

So, but this is, I think as an organic chemist we have let to know this thing, p K a value, p k a value here...

Student: 15

So, black magic, do you know the meaning of black magic, coincidence.

Student: That is not sure.

Now, you sure, so I want to said that, then what should be the value here?

Student: ((Refer Time: 24:14))

What should be the value?

Student: ((Refer Time: 24:19))

That is what I thought, but so again there is a marginary difference that, the value given here is 16.5 mind it and in both the cases, important to note actually,. In both the cases, see normally how do I estimate k P a value, the quickest way is to see the stability of the conjugate base, that is the standard way. So, the conjugate base in this case is, this one and in this case it is obviously, it is this one. So, which one is more stable between the two?

Student: First one

Why?

Student: ((Refer Time: 25:16))

So, equivalent number equivalent structures are more, so even the nitrogen is more electron negative, but that is actually that higher acidity in this case is compensated with this equivalent structures. So, anything but for us, so that means, just replacing the nitrogen is not enough, we have to think about all other things. And now, let us static another molecule which a very well known molecule, let us say what is your guess now, indole. Take an indole, corresponding what should be p K a value?

Student: Less than 16.97

How is that, since it is 16.97, so is to very close, basically gives you an idea, the p K a value are very similar to each other. Now, come to another molecule, actually the molecules of our interest and superstition interest and so, let us see superstition know it, what is it, what should be the value then?

Student: ((Refer Time: 26:28))

And it forms on here, it can undergo dealkylations, it can break the tautomerism, so aromaticity, all these things. So that means, is very difficult to estimate actually, one can guess that, the two benzenes are there, so should be more acidic, all these things, but again you do not know, whether if your structures of the conjugative base could be different. So, sincerely again it is a very similar, so that means, the lesson what we get here from pyrrole to carbosol, the p K a value is very similar.

So, your standard number is, in this series what is the standard number?

Student: ((Refer Time: 27:18))

No, standard number is reference number you should remember.

Student: 15

Very good, so if you are handling is five membered hetero cycle, remember all is compare your basicity, acidity, etcetera to these things. Like say, now if I take imidazole for example, first should be the p K a value of the imidazole and hydrogen.

Student: Lesser

Less or at least it should be less than 15, because you have a additional electron negative atom present in that, if it is triazole, even more acidic. So, like these that means, you can extrapolate that means, one number you have to remember, that is 15. So, let us take another molecule for example, quickly just to have this idea about this sucenoid, it is a five membered heterocycle, but it has no structural similarity with the other molecules we discussed.

So, but when we talk about this NH, what should be the p K a?

Student: Less than 6

Our reference point is now 15.

Student: Less than 15.

This is actually the p K a here is 6, so acetic acid how much, you said four point something, pretty close. What does it means, you can just react this with potassium salt like you have made the potassium phthalimide, etcetera in the gavial amine synthesis. So that means, you can easily form a potassium salt structure and moreover, this compound I think those who have now practicing organic chemistry with MBS reactions, this is the by product from the MBS reactions and it is highly water soluble.

You remember in a last class, we talked about this solubility, heteroatom can cause solubility increases. So, and let us see now, but why do you study all these things, you have to make use of it in fact, we have very recently few years ago, couple of years ago, we had made use of this principle. We had a table problem in being an alkylations of a carbozole derivative, but in that case we had an OH group here. Our job was to, we wanted to selectively do this alkylation here, how do you do, whether it is possible or not, have you understood the problem.

Let us say R X, there are two labile hydrogen, NH hydrogen, OH hydrogen, no protection.

Student: ((Refer Time: 30:31))

[FL] first of all whether it is, no protection in fact, we did not do with the protection, let us say if you do this and a base, base normally many, I do not know whether you know or not, normally under this sort of alkylation of labile oxygen and nitrogen, potassium carbonate. Occasionally, people use PTC, Phase Transfer Catalyst, so these are the standard protocol. Now, let us say if we follow this standard protocol, which one would be alkylated first, answer.

Now that means, what we have to know, one more value.

Student: Phenol.

Phenol, what is the p K a value of phenol?

Student: 10

We had a good memory then, it is 10 actually of course, you are also pretty close 10, so now, know that the carbizole has 17. So, assuming both of them form anions, let us see nitrogen minus, oxygen minus and all of us know that, p K a value gives a good guideline to the nucleophilicity with the p K a is higher, nucleophilicity is higher, because conjugate basis, more nucleophilic that means, conjugate base of say, weaker acid is more nucleophilic.

So, in that case that means, NH should have been more nucleophilic and we would have obtained this NR here. In fact, this has a very competing reaction, we got three products, we got W alkylated, nitrogen alkylated, oxygen alkylated. So, how do we do, so what we did, we just basically check the rate of the reaction, whether mono alkylated is, nitrogen alkylated or oxygen alkylated is producing faster. And what you found that, oxygen alkylation is faster than nitrogen alkylation, although p Ka value is same as nitrogen, why, any idea.

P k a value suggest that, the nitrogen should be alkylated first, because of the nucleophilicity. But, in really, it is actually the oxygen that is getting alkylated first and this is a thing when you have also keep it in mind and no concentration effect under the conditions, potassium carbonate is not is strong base, is not a sufficient strong base to pullout this NH nitrogen. Like the difference between, many of you know like sodium carbonate and sodium bicarbonate reacting towards the phenolic OH group.

So, that sort of seeing, because of the assistant and assistant like sodium bicarbonate, does not react with phenolic OH. So, with potassium carbonate [FL], so potassium carbonate is sufficiently strong enough to pull this phenolic OH group in sufficient concentration and that could be one of the reason. That means, you have to be little cautious about the p K a value, that is just only p Ka value is not enough, that gives you some guidelines, but at the same time, these concentration effect is very important.

If you can produce a particular anion in sufficient concentration bases, that becomes more nucleophilic, the reaction is a bimolecular reaction and normally alkylation reactions are anionic alkylation reaction means, bimolecular reactions. So, eventually we could solve these, so by taking advantage of the higher nucleophilicity of this oxygen here, by virtue of having higher concentration under the conditions. And let me give you one more very related example, this is the old one, so benzo quinoxylene and if you have these then, you create this with dimethyl sulfate.

So, what you expect, dimethyl sulfate know.

Student: ((Refer Time: 35:33))

No, I did not do anything, just dimethyl sulfate nothing else, maybe adjust the solvent like normally we do methyl acetate, both are soluble in methyl acetate.

Student: n alkylation

n alkylation, so again you see the p K a value is pretty very high, but you have to be very careful that, you are not actually pulling out that hydrogen. So, under the room temperature normal conditions, what do you get, the product is this one. So that means, whatever the knowledge we have and I mean, we just if you just apply them and what you will find, this is CH 3 plus and what, and dimethyl sulfate. So, this mono sulfate, it should be minus, that is it and in fact, to give you clue, if you are going to be an organic chemist, what happens, let us say this typical reaction often we do.

If you are trying to do the ohm acylation for example, what you do, use dimethyl sulfate, potassium carbonate, etcetera. After the reaction is over what you do, take this crude reaction mixture and treat with something.

Student: ((Refer Time: 37:19))

No, sodium hydroxide can be used, but in most often we have many functional groups, so that can cause problems to other functional groups.

Student: ((Refer Time: 37:30))

Not really, see that is the problem, bicarbonate is not nucleophilic, the purpose is to destroy excess dimethyl sulfate.

Student: Water.

Water is not that soluble, it takes lot of time to get hydrolyzed, in fact dimethyl sulfate is purified by aqueous bicarbonate.

Student: Because of, we use the sulfuric acid.

Sulfuric acid, etcetera, so that is why that means, dimethyl sulfide is sufficiently stable to water. So, is just by adding water you cannot decompose, quick way I have given you the clue here, triethyl amine, this nitrogen is quadranized at room temperature, just in half an hour the reaction is complete. So then, it becomes a quadranized salt, ((Refer Time: 38:28)) quadranized salt you can just washout the water, solubility increases you can washout with the water. So, I mean, this is a nucleophilicity p K a sometimes very useful, but you have to just sit down and think about it.

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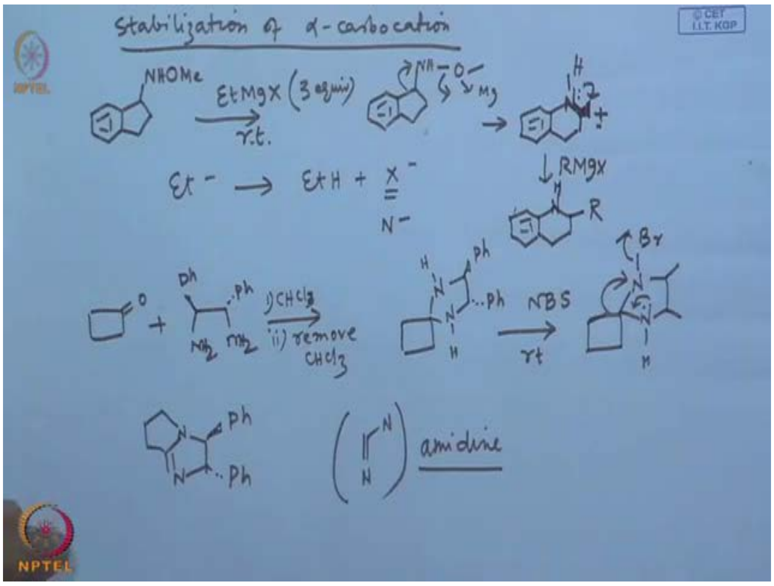


Let us see one more, now I mean, we have many many examples basically, this time in the case of let us say stabilization of alpha carbocation. Now, just I will give the example and first I will not give you the answer, you tell me what happens, this is a indane derivative with NH and OMe, X, the reaction at room temperature.

Student: ((Refer Time: 39:56))

NH, at least you have began to think that, it has the possibility [FL], but you have to again use a p K a value. Between CH and NH, which one is more acidic?

Student: NH

NH, fine that is CH means, that goes to around 40 and NH goes to close to 30, so that means, slightly more acidic. Now, you see, you have to think about the equilibrium, normally I think if you go to Solomon's book, you will find, if you are analyzing a reactions involving a carbon ion, the product that should be found, which should be an weaker carbon ion.

In this case, what is the carbon ion I mean, we think about E t minus, E t minus to start with then, it should go to a corresponding this one and it should produce something else that, the anion and X anion and that should be weaker than E t minus. But that means, in this case, if you are thinking of deproconation from the nitrogen that means, it should produce N minus. So, between N minus and CH minus, which one is weaker?

Student: CH minus

Which one is weaker base?

Student: CH minus

Is it so, p K a of ethane is how much, ethane is I said 440, NH is 30, so the p k a here is less, so corresponding...

Student: ((Refer Time: 42:21))

Which one is...

Student: Nitrogen is weaker base

Which one is most, let us say between the CH minus NH minus, which one is more stable?

Student: NH minus

So that means, low weaker base, so that means, it should be a good option, but what is the other possibility. So, it sits there, fine that is perfectly all right, it sits there then, what happens. Now, you have to predict a reaction, so when you holds the reaction what happens, we get the study material bag, that is it that means, there is no reaction. So, what else do we expect, anything else, of all these things you have...

Student: ((Refer Time: 43:33))

Benzoic...

Student: Hydrogen

Benzoic hydrogen almost equally I mean, strong enough as E t minus, so it will basically carbon ion and producing a carbon ion, there is a little difference in reactivity. Other possibility that, this in most cases in organic chemistry, you will find that the organic material is slightly acidic in nature, they undergo coordination with oxygen, nitrogen, etcetera. So, we are ignoring the oxygen also and magnesium, lithium, all this organic materials will have stronger affinities towards oxygen, especially magnesium.

So, let us say, we hope that also undergoes coordination with oxygen, so what next then we expect?

Student: ((Refer Time: 44:24))

So, actually one can expect that NH and then, oxygen and then, that coordinated to, let us say magnesium. So, what is expected, what next, if ir sits there no problem, you will get the study material bag, no reaction. There is a possibility that, this bond is pretty weak too many of you know, it can form a sort of a nitrenium ion, but all of us known nitrenium ions are not that stable, that existence is not sure not well proven. So, what you can expect, you can expect a synchronized migration.

So, if you put then, what would you see, if my migrates, this one become nitrogen, and this position become plus. What is the driving force, driving force is in these case, nitrogen oxygen bond is weakened by the coordination with magnesium followed by migration. Why the migration all of us know, the driving force for any reagent is the stabilization of the ion produced, carbocation that is produced. In this case, once this NH, this is nitrogen, now this lone pair stabilize this nitrogen, is that ok, any confusion, is that the justified.

So that means, you have a now nitrenium ion and so, what next then that means, at least some rearrangement has taken place, the counter cation should be neutralized. So, then we have R M g X, actually in this particular example, three equivalent of the Grignard reagent has been used and what you will get, you will get nice quinoline systems and this is R basically. So that means, from an indane derivative, nitrogen substitute indane derivative we are getting a tetra hydro quinoline system and there are plenty of examples and this has been done very recently.

So, it is just a typical example of the carbonol being stabilized by nitrogen, that is what you have to keep it in mind, let me give you one more example let us say, whether you can work out or not. Let us say, if you take a diamine, these diamines are very useful reagents.

Student: Sir

Yes

Student: ((Refer Time: 47:48))

See equivalent probably, I do not know I have to go to the original literature, I do not have detailed numbers with me, probably to pick up this NH hydrogen.

Student: ((Refer Time: 48:02))

To equivalent it is could be enough just I do not know, I have to just go to the literature, yes officially 2 is enough, but normally we do not count 2. For example, energy reduction is set all these things, officially it is one fourth of these, what we give lot of excess, maybe to make this reaction undergo after completion, that could be one of the reason. So, I have to see that, but yes may be one magnesium is already inactive due to coordination to oxygen maybe, the second one maybe fix up this NH hydrogen.

And third one as I mean, you can account for all these things, but exactly I do not know, but our trust here is to see I mean, what is the driving force for such a rearrangement such a nice simple reactions. Often see, we had the idea that, we would not react with a multiple bond, but it is a case here that, you do not have a multiple bond, but multiple bond is being generated in SITU and that is a undergoing reaction. Let us look at one more reactions where in a similar kind of stabilization, which possible probably, stabilization of the carbocation by nitrogen.

This is simple reaction, in this case you have 1 2 diamine, now just dip it for some time only two days in a solvent and then, says chloroform and then, that is the first step. The second step, just remove chloroform, so you get a product, so what is the product?

Student: ((Refer Time: 49:52))

Any idea, what is the product, just so actually all of us know, these are very first process, but that shift base permission is driven to the right by the removal of water. So, when you actually remove this solvent, first water is goes out and so, you will get a shift base kind of permissions, actually the product that is found in this case is your...

Student: ((Refer Time: 50:40))

Not vs, we say ketone, nitrogen are all ketone, so you get nitrogen, so imidazole derivative. So now, you know the names, once in hydrogen five membered ring, so spiro imidazole then obviously, this hydrogen here and hydrogen, such a simple reaction. Next what, next this reaction, again it treated with NBS and room temperature, you get a nice product here and grooming feed product. So, what could be the product, just room temperature, all these reactions are room temperature, room temperature remove the solvent in this thing.

NBS means, where is the NBS, NBS actually has two different kinds of reactivity, one is that is it generous the radical, number 2 is the bromonium ion, especially in presence of little bit of weak acids is bromonium ion is produced. And now, we can see that, in nbs, bromium is attached to nitrogen. In this case, you have an nitrogen of here and between the two nitrogen, we know which one is more nucleophilic, so that means n bromo compound would be formed and this, acceptable.

What next, n allow bonds of pretty weak bonds, you can brutalize, you can hydrolyzed you can do any kind of, because they are not very stable bonds, n chloro compounds, n bromo compounds, NBS perforate the pretty stable, it can be crystallized from waters. So, you know what not under radical conditions...

Student: ((Refer Time: 53:04))

That is it, but what is the driving force, first of all actually see different things here, three difference here, this is the weak bond number 1, this is a strange system number 2, this nitrogen lone pair stabilizes. So, we have three different factors, that is why the reaction is so fast, it takes place at room temperature and the product that you get is this one. So, again and how do you describe this product, the fused imidazole or anything else, do you see the functionality present in this molecule.

What is the name of the functional group, actually the title of the paper size is an name the paper, the preparation of this compound, bicyclic. This is the important nucleus though, this is the important functional group, what is it, in heterocyclic chemistry, it is a very important functional group?

Student: ((Refer Time: 54:32))

No, why do we see this, have you seen any molecule, small molecule?

Student: ((Refer Time: 54:39))

No, even a smaller molecule?

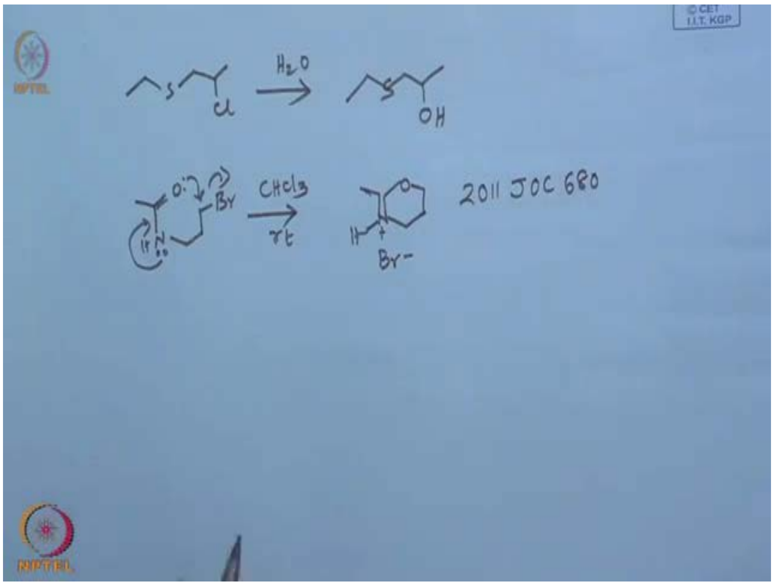
Student: Urea

Not really, close...

Student: ((Refer Time: 54:46))

So, this is actually amidine functionality, amidine functionality is a ((Refer Time: 54:55)) to powerful base. So, someone said, go divu, actually divu is a bicyclic amidine and that is the target actually, they did not produce divu, but they have produced many bicyclic amidine. So, will have very quickly, so similarly just I will have more example maybe, may be one more example, I think this is old example old example, let us see how much you remember.

(Refer Slide Time: 55:27)



What is this compound, it is a general name?

Student: Master

Sulphur master, so if you add water, what is your observation, Whalen reaction produce HCl and what it does, so all of us know that, NuvaRing participation. So, and what is meant by NuvaRing participation, it actually enhance the reaction rate, that is number 1, number 2 it can generate two different structures. I think I do not have to tell you, one more structure also is possible, once you form a three membered ring. At the same time, you have to mind it that, the three membered ring is getting strained, so it will open up that you have to remember.

That means, it forms a heterocyclic three membered ring system and forms, I mean it has two effects, it can give two products and reaction rate is enhanced. Similarly, if you put nitrogen in the place of sulphur, you can go to the same thing, similar effect you see, but what happens if you put oxygen?

Student: ((Refer Time: 56:54))

Yes or no?

Student: No.

Remember that, then I will give you just, this is the last example and this was published in last year by an Indian scientist, they desorbs this compound and left it at room temperature and they published just JOC paper, this is a simple bromo amide. What you think I mean, I have not written, I think you can guess, again a case of NuvaRing participation and you have now lone pair, that is actually stabilizing. And what he suggested, I do not know how far this is right, but news paper is accepted and he has got ((Refer Time: 58:01)) is fault only, which is quite obvious.

Now, after the publication, everything looks pretty obvious and if you are interested, you can go to this journal, this is 2011 JOC and the number 680 and if you are interested, the name of the scientist is E. N. Prabhakaran. So, we will have more example basically, see basically we identified 11 different reactivity profiles of heterocyclic compound or hydroatoms, so take care of those things.