Rate Processes

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Lecture No. # 19

Acid Base Catalysis (contd…)

Good morning everybody. So, today we will continue with specific acid base catalysis, general acid base catalysis and metal ion catalysis.

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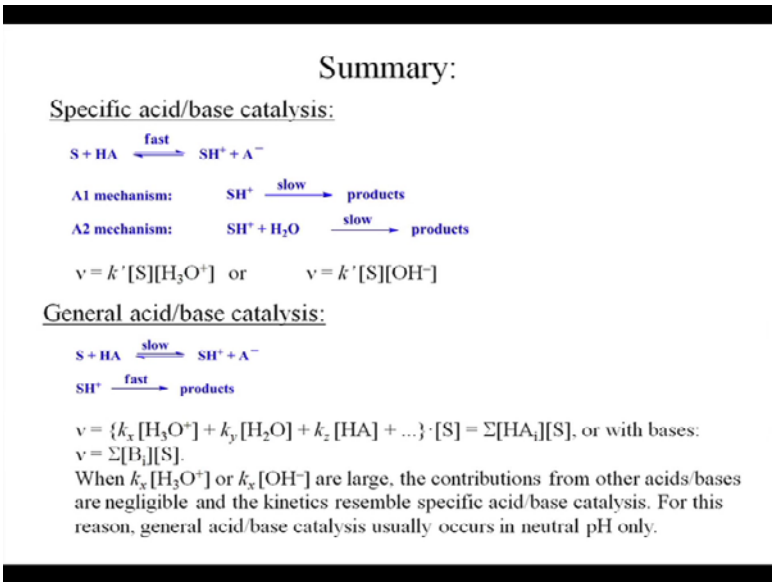

So, in our last lecture, we talked about this specific acid base catalysis, we discussed the general mechanisms for this specific acid base catalysis and also we talked about general acid base catalysis. We tried to distinguish between them that under what condition under what conditions maybe general acid base catalysis, gets converted to specific acid base catalysis. So, as I told you that for specific acid base catalysis; It has got a, you know, two types of mechanism: one is unimolecular, the other one is bimolecular, and for you general acid base catalysis.

It is a combination that is the, you are you are absorbed rate constant is is nothing but a combination of the contributions from your various catalysts. It maybe H 3 O plus; it

maybe your H 2 O; it maybe H A or it may be B minus. So, it is it is a summation of all the constituents, I mean constituent catalysts responsible for your for your absorbents and also when acid concentration or your O H minus concentration is is large then contribution from the other, other you know components become negligibly small and therefore the kinetics resemble specific acid base catalysis, but in general, you know general acid base catalysis usually occurs in in the in the vicinity of neutral p H.

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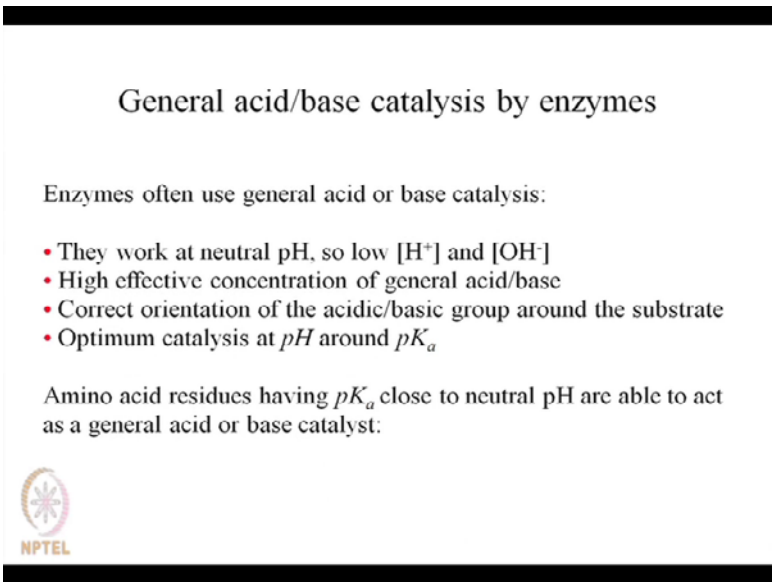

So, general acid base catalysis for enzymes, now enzymes often use a general acid or general base catalysis. And within our body, the p H is you know optimum, I mean the the p H of, I mean physiological p H is around 7 that is 7.4. So, around 7.4 or around 7, so, it is the it is the best you know region for the general acid base catalysis to take place. I mean best condition p H condition. Now, this enzymes work at neutral p H. So, low H plus or low O H minus concentration, high effective concentration of general acid or base. Since H plus and O H minus these are low. So, effectively concentrations of other general acids or general bases are you know effectively you know high. For your enzymes, what is happening that correct orientation of acidic or basic group around the substrate.

Since, the acidic or basic groups of the enzyme, though that that are you know responsible for a specific reaction to take place, that is you know the the if your your mechanism requires that certain groupings must be there. I mean, maybe basic group,

maybe acidic group, they should be oriented in a specific fashion. So that, the reaction will have the best, you know best yield or the reaction will be very effectively. You know carried out or it will proceed efficiently and optimum catalysis, at at p H 7 around p K a, I mean at p H around p K a.

So, so since, it is around p K a.We are we are around p K a. So, you know catalysis will be optimum that is the that is if your p H is I mean, p H of your medium is very close to p K a, p K a of the of the acidic or basic group, then what will happen that it will be the optimized condition for your catalysis to take place. It is not necessarily 7, but you know, if certain groups are are having you know p K a which is close to the p H of the medium then then you know catalysis will be optimum, because those groups are involved in proton transferring or maybe proton snatching. So, that is why p K a, p H around p K a, is a very important point to think of. Now, amino acid residues having p K a close to neutral p H that is close to neutral p H minus p H 7 are able to act as general acid or general base catalysts.

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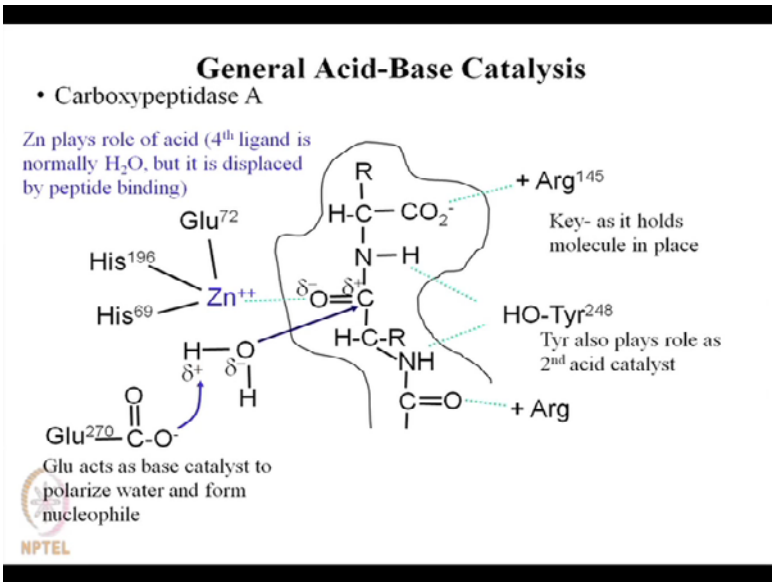

As for example, let us have I mean this an example of a, of a general acid base catalysis, that is Carboxypeptidase. So here, you see that it has got the zinc two plus and your, it basically peptidase. So, peptide bond you know break breaking. So, zinc plays role of an acid that is a fourth legend is normally H 2 O, but it is displaced by a peptide bond that is this peptide is is binding. So, water initially was there that is the fourth leading position

and the moment it is you know, this is your peptide is coming inside the pocket, then it is displaced; there is one argentine 145.

Which makes you know bond, with you know with this argentine plus, and this C O minus, there is a there is an interaction, there is tyrosine O H, there is a hydrogen bond formation. So, tyrosine plays role as second acid catalyst and there is a key, as it holds the molecule in place. So, it is the one which holds the molecule, there is another argentine, over here and glutei acid residue that is you see. It is acting as a base catalyst to polarize the water and form the nucleophile. So, so you know, it is acting as the base to maybe to snatch this proton or maybe it is not snatching the proton.

What happens that you know this bond is polarized, as a result of which this the nucleophilic strength, of this water is increased. So, that it attacks over here. So, it is you see. It is a very complicated phenomenon. It is not only that one molecule, one you know molecule, like say water is acting here. You see from this side you know this one is glutei acid, you know side chain then your zinc. So, zinc what is happening then that zinc is is you know polarizing. So, delta minus of this oxygen has, has an interaction with zinc two plus. So, that this bond you know, I mean this carbon becomes more electron deficient. So, it is a combined I mean, it is a much combined effect.

And it is an example of general acid base catalysis, that you see here, this water is taking part then glutei acid, is also taking part. So, not only one not only one molecular, one you know catalyst but it is a number. It is a combination of like sum over k. Into concentration of H 3 O, I mean k H 3 O plus, then concentration of k. I mean k H a concentration of H A like that. So, means your absorbed rate absorbed rate constant is a combination, of you know various factors, I mean various contributions from; maybe H 2 plus maybe from H A, maybe from water and So on…

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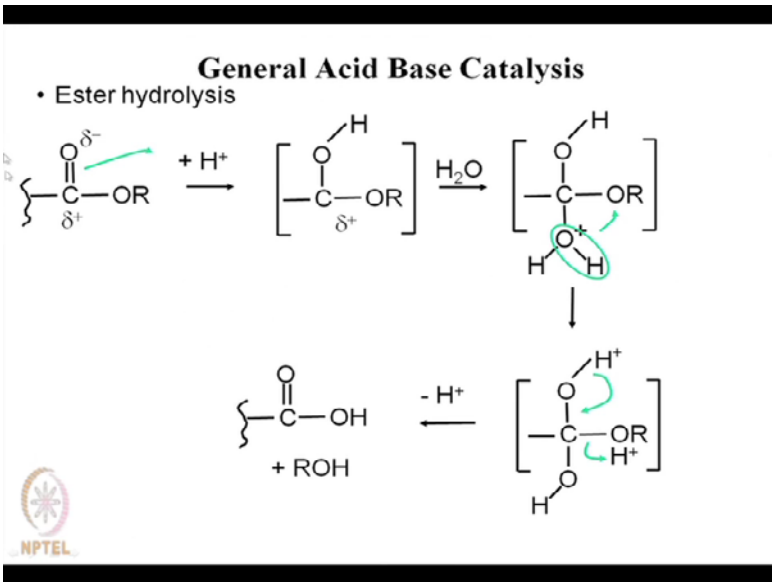

So, general acid base catalysis examples is, Ester hydrolysis you see another case simple chemical reaction, that you know this H plus, this is polarized then this bond; is polarized and then this prorogation, then water attacks then, this this one is formed, this intermediate is formed, then this bond pair is back fired and So, that this this bond is cleaved. So, minus H plus and followed by your you know product. So, you see that H plus has also water these two are taking part: So, it it is happening maybe you know, you know it it is it is a case of general acid base catalysis. So, water has also you know H plus is involved. So, it is not a specific acid base catalysis, it is a general acid base catalysis like your you sees like Carboxypeptidase.

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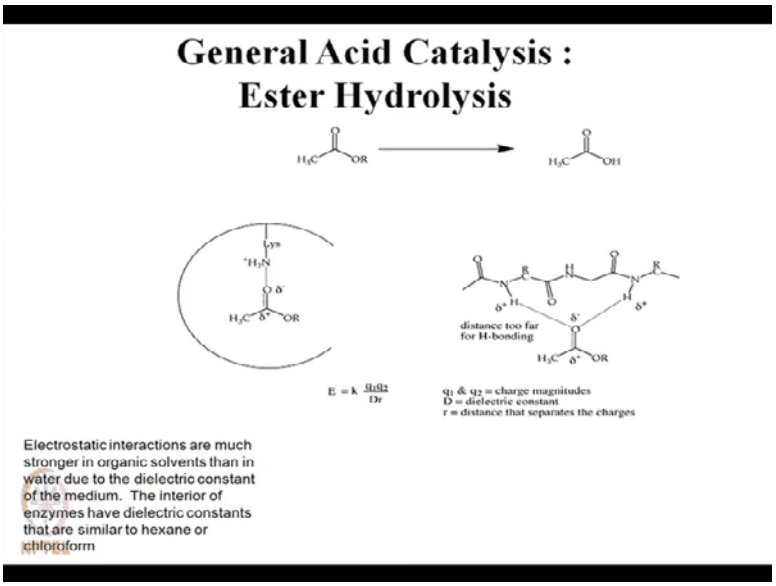

Next ester hydrolysis general, you know option that maybe, it is your enzyme and this is your C H 3 C O O R, this is your lysine then N H 2. So, this 1 N H 2 plus. So, it mixes a bond with your C O carbonyl off your ester. So, and then reaction takes place. So, you see here this C C H 3 C O O R. So, you see that there is one, there is one this H there is another H with delta plus, this is also with delta plus and this is delta minus. So, there is a there is and there is electrostatic interaction because this bonding maybe far. So for for hydrogen bonding. So, in that case since this oxygen and this hydrogen they are not in hydrogen bonding distances. So, maybe electrostatic interaction will will bind this or will attract this molecule inside the pocket.

So, electrostatic interactions are much stronger in organic solvents, than in water due to dielectric constant. And interior of the enzyme, you see interior of the enzyme and this interior of the enzyme. It is generally in most of the case, it is hydrophobic in nature or maybe, it is its polarity is less than water and its dielectric constant are similar hexane and or maybe chloroform in in certain cases. So, you see that it is the electrostatic q 1 q 2 by r. So, electrostatic energy. so, electrostatic energy When it is the dielectric constant. So, when dielectric constant is less. So, interaction energy is more.

So, interaction energy is more means, more of you know tight binding more tight binding and there is a tighter interaction. So, tighter interaction means, because of hydrogen bond, I mean because of electrostatic interaction. And since, the dielectric constant is

less therefore; it is tightly bound and then then reaction. Will take place like inside, why is inside is the enzyme interior of enzyme, enzymes have dielectric constant similar to hexane or chloroform. Because, it is hydrophobic you can you you can imagine, like it is like a like a micelle, inside of the normal micelle is you know like, you know hexane kind of thing, and outside is covered by water. So, so as if your molecule is si micellized, or as if means it is very similar to your micelle. So, as if you ester is micellized within your your catalyst within your within your enzyme.

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Prototropic groups of enzymes

Amino acid	Acidic group	Basic group	pK_a
N-terminus	α-NH_3^+	α-NH_2	7.8
C-terminus	α-COOH	α-COO^-	3.8
aspartic acid	β-COOH	β-COO^-	4.4
glutamic acid	γ-COOH	γ-COO^-	4.6
histidine	imidazolium ion	imidazole	7.0
cysteine	–SH	$–S^-$	8.7
tyrosine	$–C_6H_4OH$	$–C_6H_4O^-$	9.6
lysine	ε-NH_3^+	ε-NH_2	10.4
serine	β-OH	β-O^-	13
threonine	β-OH	β-O^-	13
arginine	$–NH–(C{=}NH_2^+)NH_2$	$–NH–(C{=}NH)NH_2$	12.5
peptide bond	R–CO–NH–R'	$R–CO–N^-–R'$	14.8

The pK_a is strongly influenced by its environment: *e.g.*, in enzymes the pK_a of lysine can drop to 7

It is around 4.4 glutei acid, it is around 4.6 glutei acid, acidic group and this is basic group histamine imidazolium ion and imidazole. It is around 7 cytosine S H to S minus, it is around 8.7 tyrosine; tyrosine means it is C 6 H 4 O H C 6 H 4 O minus ,it is 9.6 lysine 13 threonine it is C 6 H 4 O H and C 6 H 4 O minus, it is 9 point sorry it is it is lysine it is epsilon N H 3, plus and epsilon N H 2, it is 10.4 serine beta O H and beta O minus, it is it is 13 also argentines, it is 12.5 peptide bond.

It is 14.8 and you see histamine, has got very similar to you know 7. So, and also importantly it is not only that that these are some standard value, you know these numbers may change, depending on depending on the environment that is p K a value is strongly influenced by the environment, that is the environment in which these groupings are there as for example, in enzymes the p K a of lysine can drop to 7. So, you see lysine is 10.4 it may drop to 7 depending on which you, know groupings are there; as for

example, suppose if this N H 3 that is this extra proton, is stabilized that is if this charge is stabilized or this proton is stabilized by hydrogen bond or maybe if this charge is stabilized, by nearby some negative; groupings then maybe this one will be stabilized. So, these numbers will be changing. So, so it is very much environment dependent environment means.

Whether whether there is chance of hydrogen bond formation or whether there is additional charges additional charges means: maybe positive charge, maybe negative charge. So, whether that is going to stabilize out of these two, maybe one form or destabilize the other form. So, these are are important or essential things that maybe considered.

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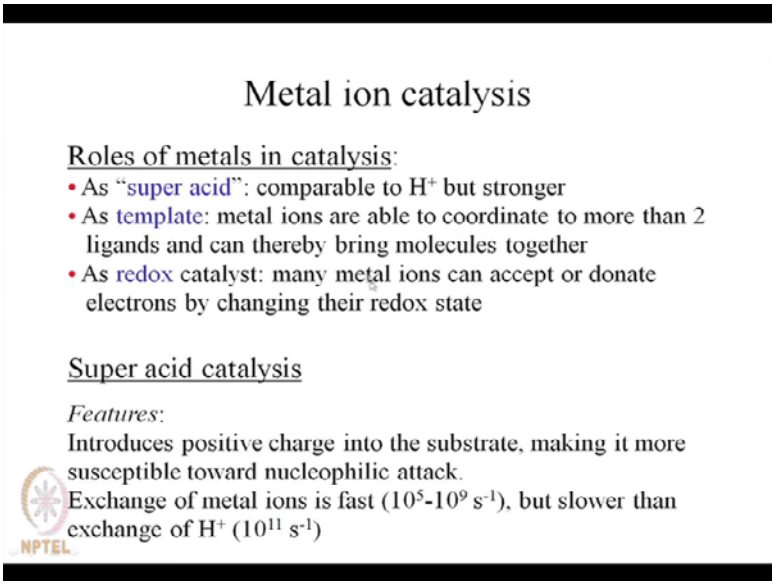

Next move onto metal ion catalysis: role of metals in catalysis, a super acid comparable to H plus, but it is stronger as template metal ions are able to. So, it is it is metal ion, can be can be called as super acid, it which is comparable to H plus, but it is stronger metal ion as template metal ions are able to co-ordinate, to more than two lagans, and can thereby bring molecules together. So, which is very important that is its proximity, is very important suppose, you want to bring two molecules together: So, that is important. So, if some if if a an entity has got option to bind, I mean maybe by electrostatic interaction, or maybe by hydrogen mono whatever, it has got the option to bind two entities: then these two entities come close to each, other for a facile reaction. So, that is

why metal ions are able to coordinate, to more than 2 legends and can thereby bring molecules together, as radix catalyst these metal ions, can be can be redox catalyst as well many metal ions can accept or donate electrons by changing the redox state.

So, it is not only not only doing like binding something, but do after binding maybe the metal ion in between can accept one electron or maybe can can donate one electron to this entity. So, what is happening that this metal ion itself can act as the redox entity? I mean redox couple that is maybe after getting, one electron it may get reduced or maybe giving, one electron to to another entity, it can you know get oxidized now, what are the features of super acid catalysis features: are like introduces positive charge into the substrate making, it more susceptible towards nucleophilic attack. So, suppose you have got an entity.

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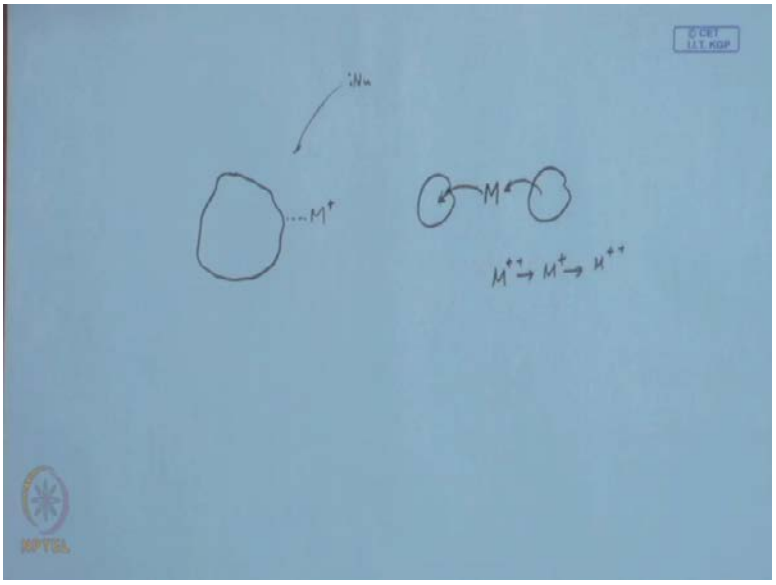

And suppose you know if this metal ion metal ion suppose M plus. So, if it binds to this means as a whole this entity becomes more positively charged. So, another nucleophile, having electrons will have better option for this better option to attack this. So, that is why it is told that it introduces positive charge, into the substrate. So, after binding the whole thing becomes the substrate, and thereby thereby you know, making it more susceptible towards, nucleophilic attack. And also exchange of metal ions is fast like 10 to power 5 to 10 to the power 9 per second, but it is slower than the exchange of H plus.

Because unit is it is the it is the lightest and is the smallest one, and it is it is exchanged, that is exchange of H plus, is is that is why, it is very fast than compared to your metal ions, but it is not that bad you know this exchange is not, I mean exchange rate is not that bad, you see it is 10 to the power of 5 to 10 to the power 9 per second, depending on the on the environment depending on the metal ion concerned, but although it is little little slower maybe, 10 to the power 9 is hundred times slower, but still you know since hydrogen plus is lightest.

So, it has always got the option to to exchange very fast

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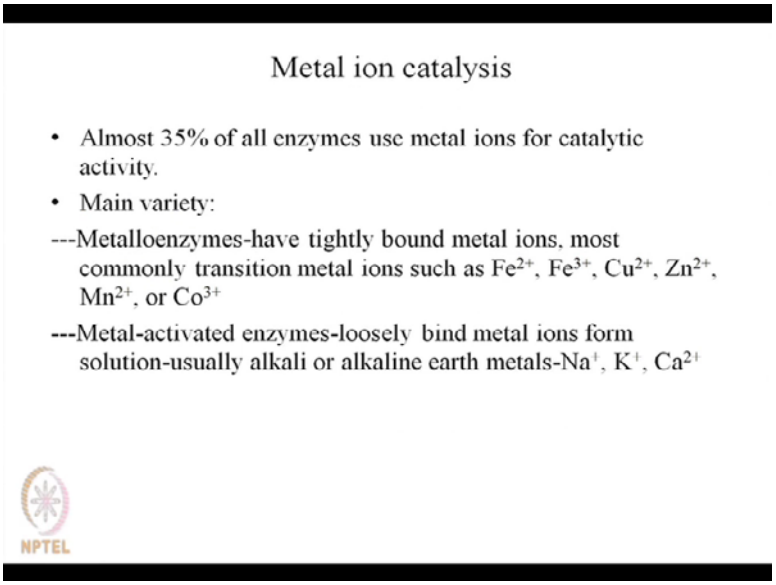

Metal ion catalysis for biological cases almost 35 percent of all enzymes, use metal ions for catalytic activity. So, one-third one third of almost one-third of the total enzyme populations use catalytic activity with metal ions. Now Main variety, Main varieties are like Metalloenzymes-have tightly bound metal ions, most commonly are the transition metal ions such as F e 2 plus, F e 3 plus, C u 2 plus, zinc 2 plus, M n 2 plus maybe cobalt 2 plus, cobalt 3 plus. So, tightly bound metal ions, metal enzymes are having tightly bound metal ions.

And another one is Metal-activated enzymes; these have loosely bound metal ions. From from solutions-usually alkali or alkaline earth metals like sodium plus, K plus or calcium 2 plus. So, this metal metal activated or metal ion activated enzymes-loosely bind metal ions from solutions and these these metal ions are sodium plus, potassium plus, calcium

plus, calcium 2 plus. So, these are second category is metal ion activated enzymes and the first category is metalloenzymes, that is having having tightly bound, firmly bound, metal ions within

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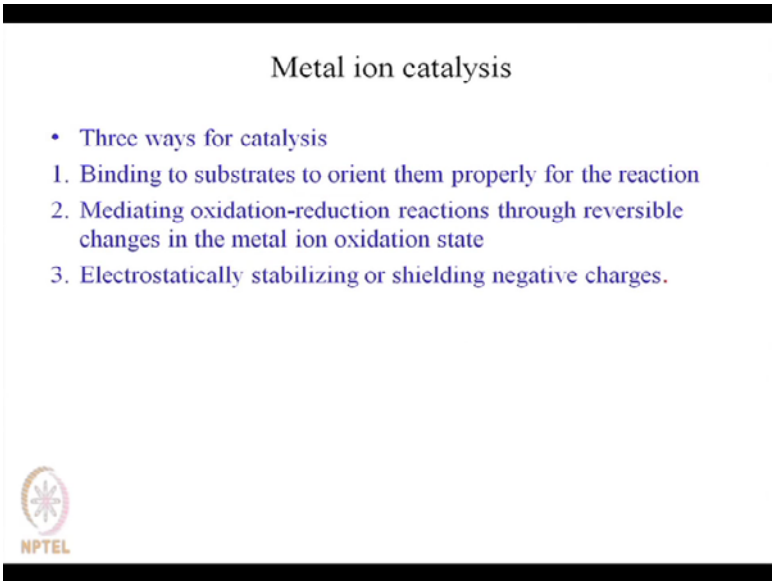

Metal ion catalysis, three ways for catalysis: binding to substrate, to orient them properly for reaction. So, first one is three ways means out of the three three ways one is the binding to substrates to orient them properly for reaction, second one is Mediating oxidation-reduction reactions through reversible changes in metal ion oxidation state. Third is Electrostatically stabilizing or shielding negative charges. So that means, for metal ion catalysis the first one is the binding to substrates to orient them properly for reaction. So, metal ion will bind to the substrate, so that, the substrate is properly oriented for the reaction to take place. Next is, it is mediating oxidation reduction reaction through reversible changes in metal ion oxidation state.

So, that means, maybe it is the mediator, suppose if it is a if it is a redox reaction then the metal ion is acting as your mediator. So, that means, maybe you have got, suppose you have got metal ion over here, you have got one entity over here, another entity over here. So, what is it is doing is maybe it is accepting one electron and maybe it is giving this electron over here. So, first step it is reduction, second step oxidation. So, reversibly it is

you know switching from say maybe M plus to M plus plus to M plus then to M plus plus. So, it is a reversible process.

So, reversibly it is doing like this, and so mediating oxidation-reduction reactions through reversible changes in metal ion oxidation states, third-one is electro statically stabilizing or shielding the negative charges, because it has got positive charges. So, electro statically it is shielding the or stabilizing the negative charges.

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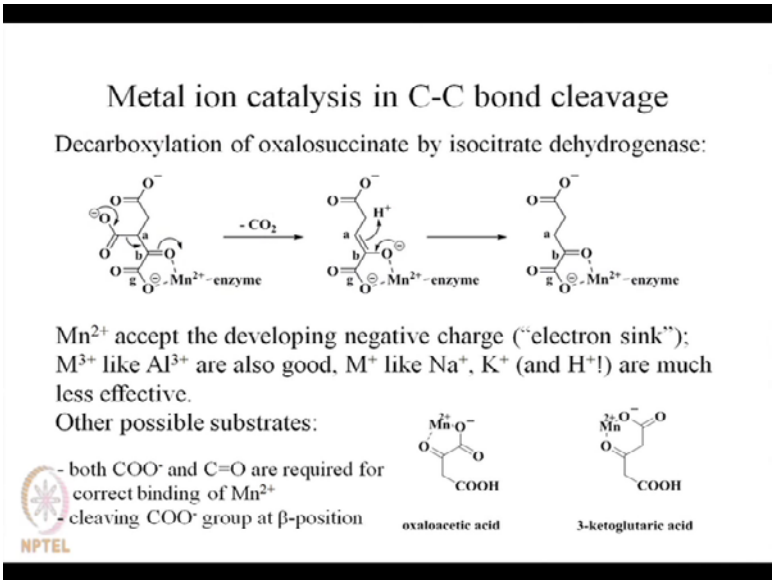

Let us have a have and one example metal ion catalysis in carbon-carbon bond cleavage, decarboxylation of oxalosuccinate by isocitrate dehydrogenase. So, it has got the Mn 2 plus and this is the enzyme part. So, Mn 2 plus binds over here, I mean makes a bond and then you know through this mechanism. You know this is this backfires and then it this bond formed, I mean breaks and ultimately decarboxylation occurs.

So, you see that this is minus CO 2. So, this this one will be this one will be you know will be going, I mean no not this one this will be going this carbon dioxide, Will be going out. So, this one is here and then it is given this bond pair is given to here. So, you see that this is this stabilizes this negative charges Mn 2 plus, stabilizes the negative charges, charge and what happens that since, it is polarized. Because of this 2 plus this one this carbon becomes electron deficient, because this oxygen has has an interaction with with Mn 2 plus.

So therefore, there is there is always an inward pull. So, that it helps this decarboxylation. So, so then it it comes out this carbon dioxide. It comes out and then it backfires then and then with a proton. It you know makes a bond. So, that this double bond becomes single bond and then finally you know this this goes out. So, M n 2 plus accept the developing negative charge. So, this developing negative charge means, it is it is backfiring. So, as if is electrons are are pushed from this region to this region. So, there is a developing negative charge. So, this one is accepting that developing negative charge. So, it is acting as Mn 2 plus is acting.

As if it is a sink for electron M 3 plus, like A l 3 plus, are also good M plus, like N a plus, K plus and H plus are much less effective. Other possible substrates, like you know this one similar. I mean substrates where Mn 2 plus is acting as electron C. So, both C O minus and C O are required for correct binding of Mn 2 plus. So, this C O O minus and C O these two are required you see this is C O O minus and C O this is C C O O minus and C O.

So, oxaloacetic acetate acid acid and this three ketoglutaric acid, these are also you know possible, you know substrates and cleaving the requirement is cleaving, C O O minus group at the beta position. So, this is your alpha position this is beta position. So, this one is beta is is cleaved. So, so this requires these are the requirements for Mn 2 plus to act as metal catalysis metal ion catalysis in C C bond cleavage.

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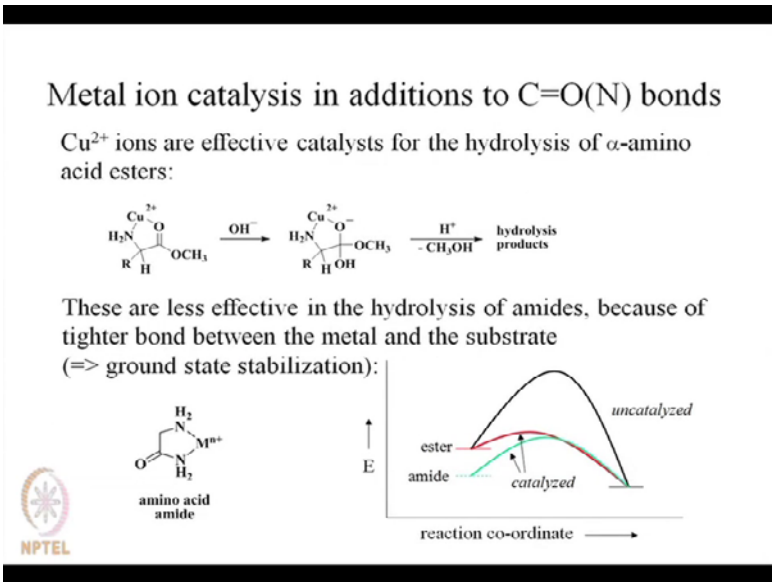

Metal ion catalysis in addition to C O or C N bonds. So, in that case copper 2 plus, you see copper ions are effective catalysts for hydrolysis of alpha amino acid esters, you see copper 2 plus does this you know binding, I mean bond formation then O H minus, attacks, Over here because now this bond is polarized. So, it attacks over here and then it is a five member intermediate then H plus is in presence of H plus, you know this one is taken out. So, hydrolysis product is formed. So, C H 3 O H is released. So, hydrolysis product is formed. So, these are less effective in hydrolysis are amides because of tighter bond between metal and the substrate.

Because, it is the ground state stabilization, so, for your unanalyzed reaction the you know unanalyzed reaction. It requires more energy but your catalyzed reaction for your ester this ester or maybe for your amide, now for your amide. It is this is less effective because, you know because tighter bond between metal and the substrate but anyway it is it is you know, it is you know it is you know effective in this reaction hydrolysis product. Because C O or C N, one this is metal and catalysis in addition to C O. Because you see here, it is basically an addition reaction to C O. First addition of O H minus and then maybe a because in presence because of the presence of H plus. It is it is dissociated but basically metal ion in presence of metal ion this addition reaction occurs.

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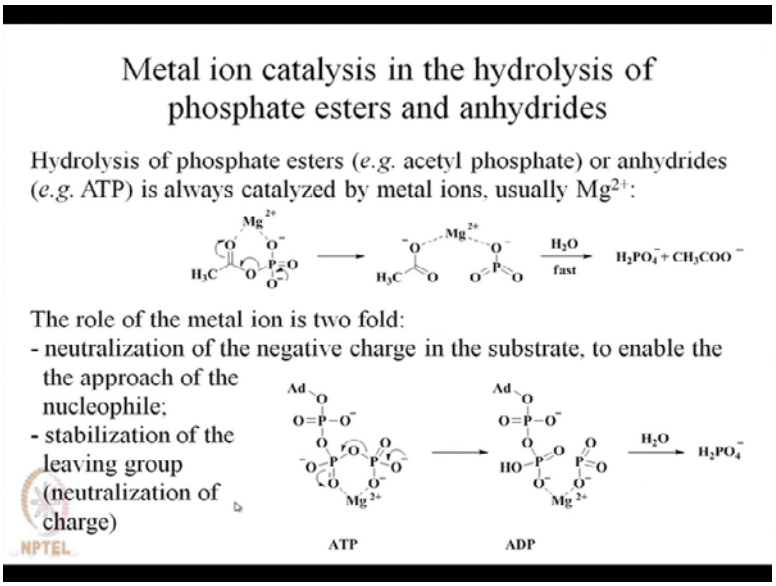

Next metal ion catalysis in hydrolysis of phosphate esters and anhydrosis-hydrolysis of phosphate esters as for example, acetyl phosphate or anhydrides, like ATP is always catalyzed by metal ions usually Mg 2 plus, you see this is the scheme that M g 2 plus, makes a bond between this one and that one like the other case, I talked about it is in one case. It is keno another case, it is carboxyl ate, here it is phosphate. So, bond formation and then subsequent reactions.

Will give rise to H 2 P O 4 and C H 3 C O O minus in presence of M g 2 plus. So, now here what is the role of metal ion that is M g 2 plus. So, it is it is effective for neutralization of negative charge in the substrate this negative charge. Because this has this has got two negative charges and it is 2 plus. So, negative charges in the substrate is neutralized to enable the approach of the nucleophile, because it is neutralized now a nucleophile can approach and stabilization of the leaving group neutralization of charge.

So, this is your leaving group this is your leaving group. So, their charges are also neutralized, you know in presence of water they form these two: So, leaving group stabilization, I mean is also important, over here for your ATP. See it is Mg 2 plus, adenosine triphosphate Mg 2 plus, making bond like this the similar disposition, you see is keno group phosphate this is also although this is if P O and phosphate then then this bond is cleaved this bond is cleaved and then in presence of water. It produces H 2 P O 4 minus.

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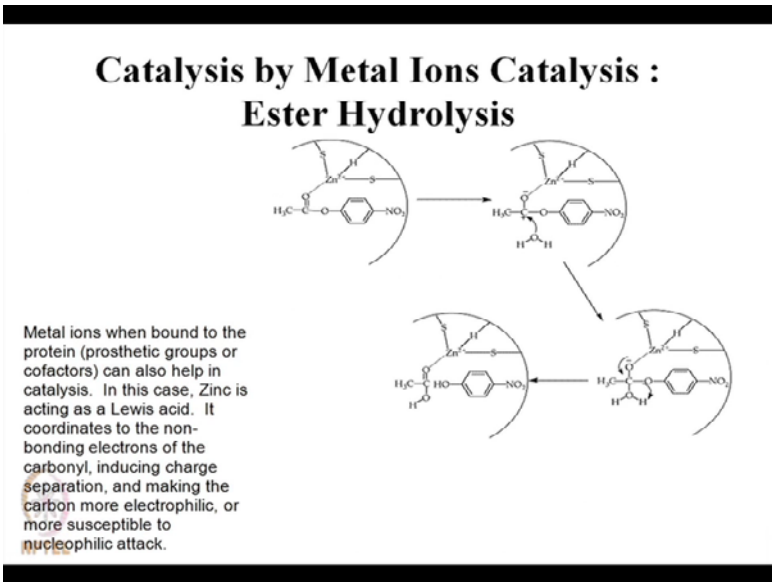

Ester Hydrolysis again, in in enzyme is it is a zinc containing enzyme this is your C H 3 C O O. So, in presence of zinc this bond is polarized. So, water now can attack because it is properly oriented and water now can attack. So, that is it becomes a trihydride intermediate and then this developing, I mean negative charge backfires and then this bond is cleaved this proton is taken up by this one. So, this bond is cleaved. So, metal ions when bound to protein prosthetic group or cofactors can also help in catalysis.

As in this case zinc is acting Lewis acid, zinc 2 plus. So, this lone pair is donated. So, it is acting as a Lewis acid, so therefore this bond is polarized. So, it coordinates to the nonbonding electrons of the carbonyl inducing charge separation. So, it is polarized and making the carbon more electrophonic. So, this carbon is more electrophonic or more susceptible to nucleophilic attack. So, nucleophilic attack means this water is your nucleophile.

So, it attacks. So, basically this bond is polarized in presence of the zinc 2 plus. So, metal ions metal ions do such you know thing metal ion catalysis ester hydrolysis, you know another case that this bound water with zinc this is your ester inside the pocket. So, this this one this lone pair, you know this proton is eliminated. So, here initially zinc 2 plus is bound to water is acting as a Lewis acid. So, therefore it is bound to water and then this

proton is removed from here. So, therefore it is z z n O H kind of thing and then this lone pair of z n O H. You know attacks this one and thereby this hydrolysis is taking place.

So, metal ion can make potential nucleophile also over here in earlier case you know electro philicity of this carbon is increased but here the nucleon philicity of your of your water in the form of O H is is increased and therefore, So, what happens that when coordinated zinc is present then, then it is acting as a good you know attacking agent. So, its electron pair is attacking, over here and therefore, a then thereby your hydrolysis is occur.

For example, when p K of water: example the p K a Soft water drops from 15.7 to 6 to 7. When it is coordinated to zinc or cobalt, the hydroxide ion is 4 orders, of magnitude more nucleophilic than water. So, because of this hydroxide ion formation. So, it is highly you know nucleophilic, than water because because it has got high charge density negative charge, density on oxygen. So, therefore, it will act as a as a good nucleophile compared to water of course.

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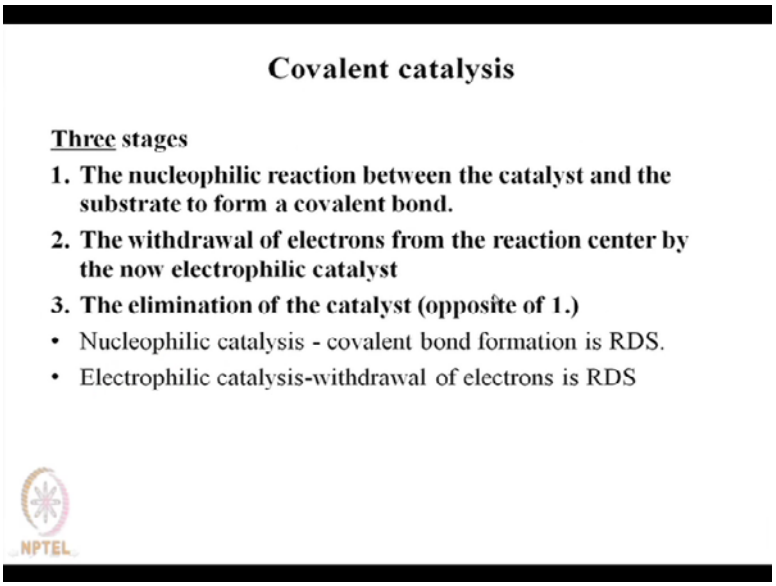

Now covalent catalysis, what is covalent catalysis? It has got three stages nucleophilic the nucleophilic reaction, between catalyst and the substrate to form a covalent bond the withdrawal of electron from, reaction center by the new electrophonic, catalyst and the third one is the elimination of catalyst that is the opposite of 1. And nucleophilic

catalysis the covalent bond formation in the rate determining, step electrophonic catalysis.

Withdrawal of electrons in rate determining, step now you see. So, there are three stages: The first stage is the nucleophilic reaction between catalyst and the substrate to form a covalent bond. So, there is a covalent bond formation catalyst and the substrate there is a covalent bond formation then withdrawal of electron from the reaction center, by the new electrophonic catalyst and then elimination. So, these are the three stages that we need to we we need to consider.

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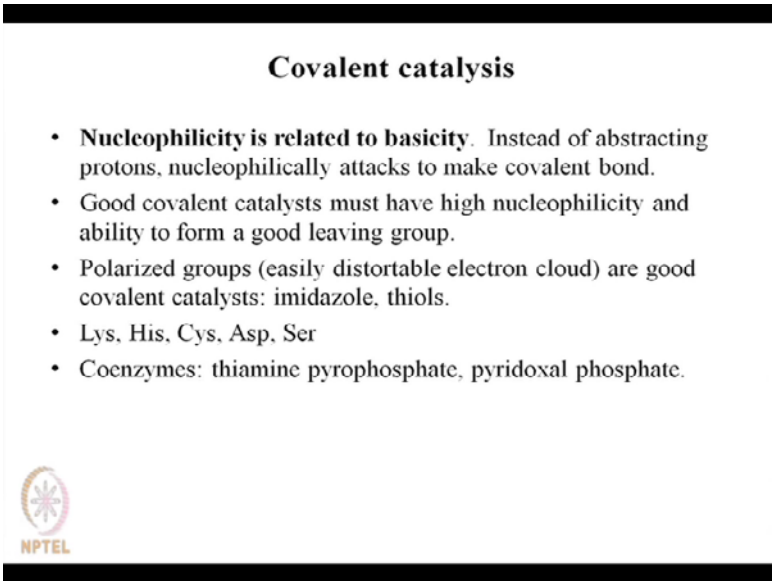

Now nucleophilicity is related to basicity but not exactly same thing but they are somehow related instead of abstracting the proton nucleophilically, it attacks and make covalent. So, so basicity has got relation to proton abstraction and nucleophilicity has got you know you know some connection to covalent bond formation. So, good covalent catalyst must have high nucleophilicity and ability to form a good leaving group.

For good covalent catalysis you know you need to have high nucleophilic, you know catalyst also polarized groups, like easily distortable electron cloud are good covalent catalyst, like imidazole trials etcetera. Like you know lysine histamine costing aspartic acid serine coenzymes, like thiamine pyrophosphate pyridoxal phosphate these are also you know good covalent catalysts. So, so in this case nucleophilicity is more important. So, and also polarization, I mean polarized groups are very important and leaving

character, leaving group character is also very important, while you know considering covalent catalyst that is for effective covalent catalysis.

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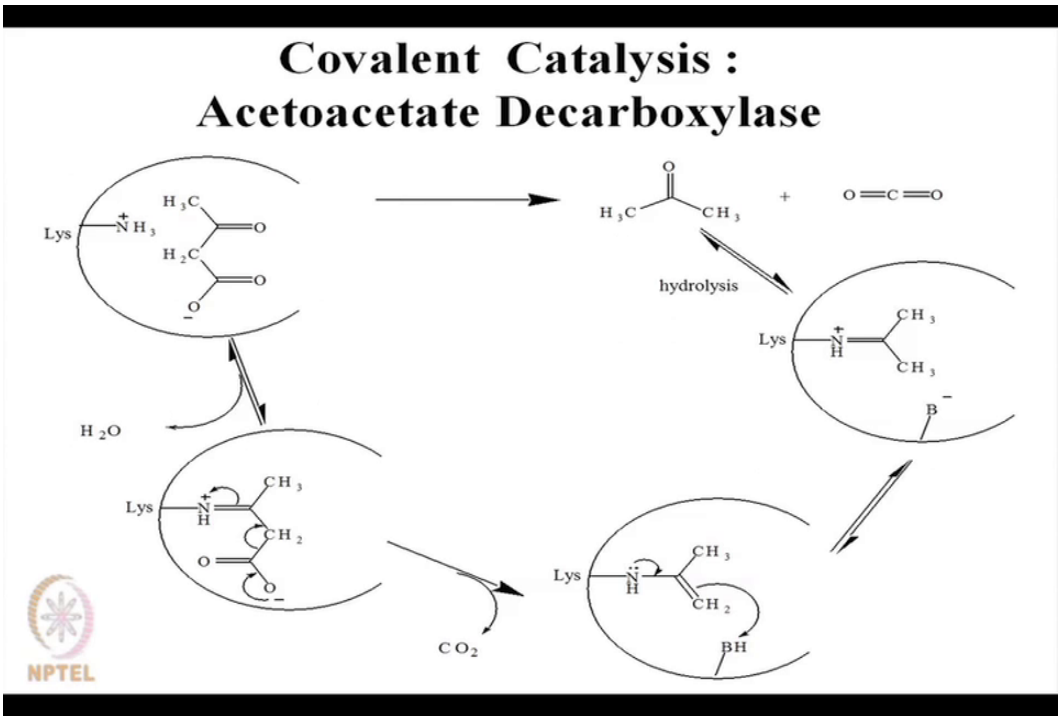

Now, an example covalent catalysis, acetoacetate decarboxylase, biacetoacetate d**ec**arboxy, covalent catalysis biacetoacetate decarboxylase, you see it has got lysine and N H 3 plus. So, this is your acetoacetate. So, what is the product? Product is C H 3 C O C H 3 acetone and then it is your carbon dioxide. So, what what are the steps steps is basically, when water is eliminated water is eliminated means this reacts with this one this carbonyl one not this one this carboxyl ate.

One will will not form any you know such bond. Because this is resonance stabilized, this is a resonance stabilized and generally this one makes, bond with this one these are very stable this C O O minus is very stable. So, therefore it will not react with this one. So, only this this one will react with this one. So, what happens that this C O and this N H 3 plus. So, one molecule of water is eliminated in in a in this equilibrium scheme.

So, so it attaches with this N H 3 plus then double bond then this one then this one backfires, why this one is backfiring, because this is N plus. So, this one has got tendency. So, there is there is a there is an outward pull of this electron, I mean pull of

this electron cloud this way because this is N plus. So, it is electronegative as also plus charge. So, this bond is polarized this way. So, that is why easily distortable electron cloud. So, what is happening that when this is backfired there is a pull there is and there is a pull of electron, I mean from this side to this side. So, this backfires then this bond cleaves this bond cleaves.

So, minus C O 2 so, this is your product and then you see there is another side group maybe B H plus, I mean B H. So, this B H proton is snatched by this C H 2. So this backfires, and then this one this C snatches this proton from here, thereby making B minus and this one and then in presence of water hydrolysis will take place, hydrolysis will take place to to give rise to your product. So, what happens is that there is a covalent bond formation first, as I told you that that the nucleophilic in the nucleophilic reaction between the catalyst, and the substrate to form a covalent bond, then withdrawal of electron from the reaction center, by then new electrophonic catalyst. You see the covalent bond formation then withdrawal of electron and thereby this bond is cleaved.

So, initially this bond formation, covalent bond formation then because of this N plus, this electron cloud is polarized this way, therefore there is a there is a outward pull of electron. So, therefore, this carbon is partly electron deficient. So, to to satisfy the electron deficiency there is a there is a tendency that this, this bond maybe if this bond is switched from here to here. So, its electron deficiency maybe, somehow you know you know satisfied, therefore this bond cleaves and carbon dioxide is released, and and following this scheme the reaction, I mean following this scheme your product is formed that is C H 3 C O C H 3, along with carbon dioxide. So, this is the schematic of covalent catalysis, where acetoacetate decarboxylase is the enzyme. Which decarboxylases, you know, you know decarboxylation occurs from acetoacetate.

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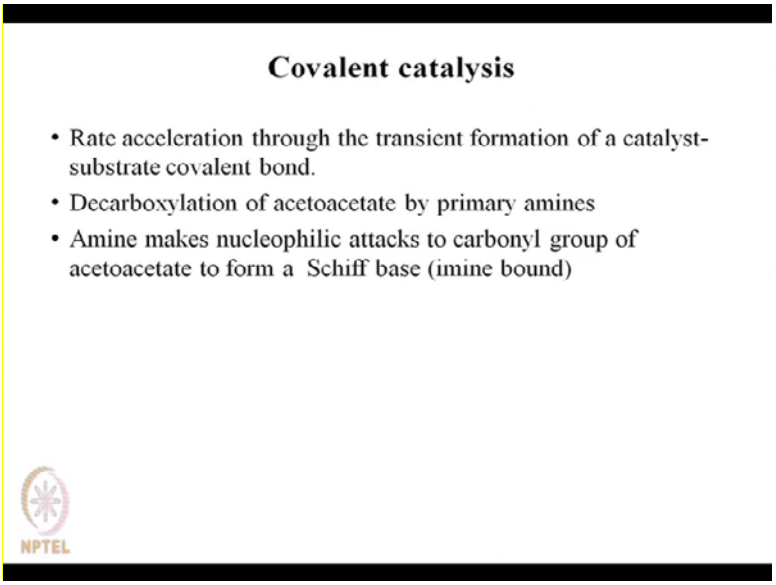

Now covalent catalysis so, rate acceleration, through transient formation of catalyst-substrate covalent bond formation. So, this covalent bond formation thereby reaction rate is accelerated, decarboxylation of acetoacetate by primary amines, amine makes nucleophilic attack to carbonyl group, or acetoacetate to form Schiff base, that is imines bond. So, this is this is what is happening you know this is a Schiff base, formation basically imines, formation and then, as I as I have shown to you how this reaction proceeds.

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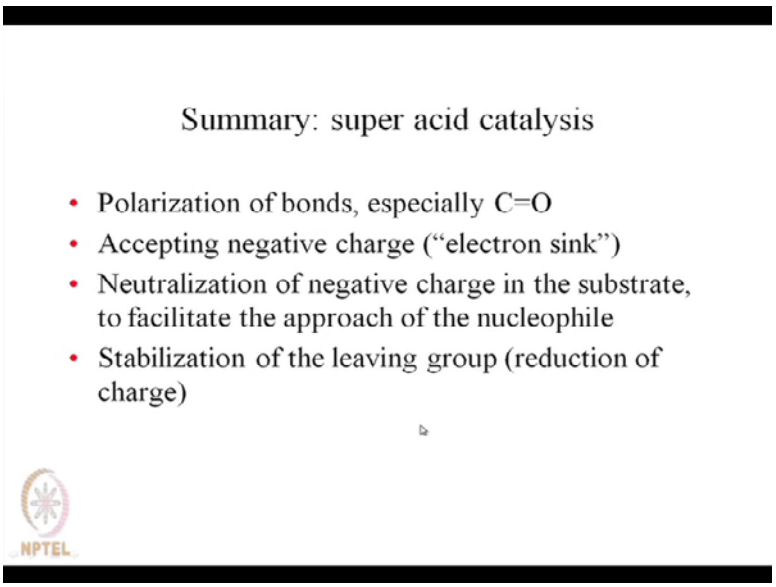

Summary: summary for super acid acid catalysis, polarization of bonds especially C O, accepting negative charge that is the electron sink neutralization of negative charge in the

substrate to facilitate the approach of the nucleophile and stabilization of leaving group reduction of charge. So, these are the are the summary for your super acid catalysis, as I already have you know told you metal ion catalysis, polarization of bond then accepting negative charge, neutralization of negative charge, in the substrate to facilitate the approach of nucleophile, and the stabilization of leaving group. So, these are the these are the points that you should think of,

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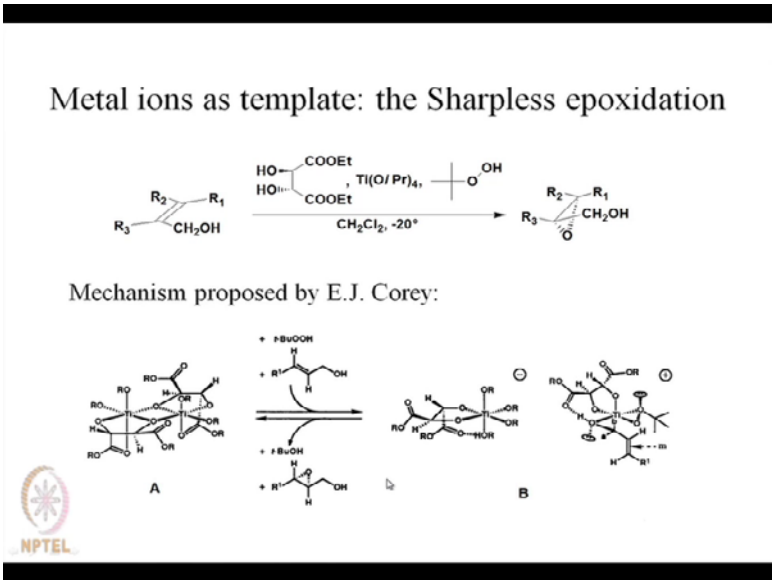

Next is metal ion as template in sharpness epoxidation you can maybe have a look at it is a mechanism proposed by E J Corey.

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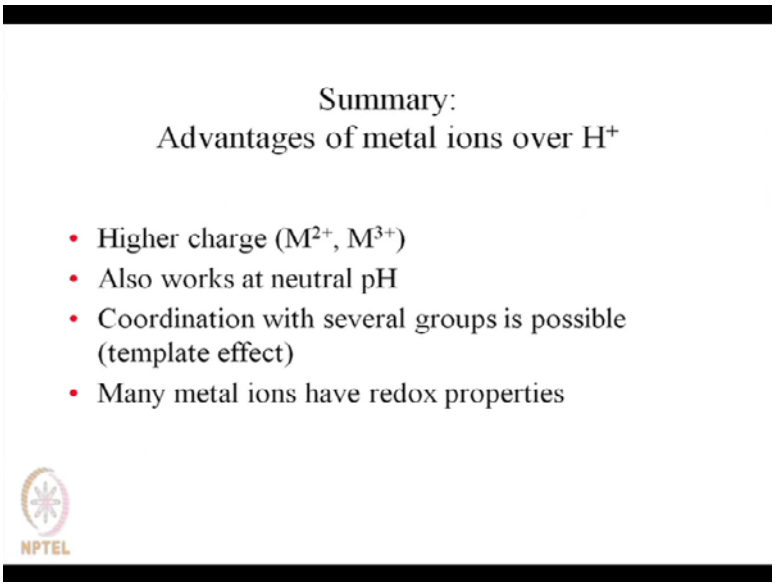

Next is advantages of metal ions over H plus, why are we looking for you know medallions, metal ion catalysis. Let us go back let us try to recap, this metal ion catalysis, another example is your M n, here it is your Mg 2 plus. So, you know you know what is the you know need of, or what is the importance of this metal ion catalysis? What is the advantage? Now metal ions, have higher charge higher charge means it is either it is M 2 plus, or M 3 plus, maybe C O 2 plus, maybe means some cases it is M n 2 plus, or maybe M g 2 plus, these work in their neutral p H range.

So, this is very important for enzymatic reaction. Since, you know our physiological p H is around seven. So, so it is the it is the neutral p H, so that means the catalyst, which can work effectively in this region, are very important. So, are of importance. So, that is why since this metal ions, metal ions are working or can work in in neutral p H range therefore, it is always advantages rather than H plus in presence of H plus, because in that case, if you have high H plus concentration then it will acidic.

So, for physiological requirement acidic p H. Will will not be very much accepteted, now it can coordinate, with several groups, which is called the template effect not only single group but also with more than one groups like you know in one case maybe, it is phosphate, another case it is you know C O or maybe as I told you that M n 2 plus. So, M n 2 plus - simultaneously binds with you know this C O O minus and also this C O.

As I showed to you earlier lets go back to it see M n 2 plus it binds with this one as also this one. So, it is an it is a it is called a template effect. So, if this template is present, then it will be effective in doing doing that, one and also since M n 2 plus, is is a high charge. So, it tends to stabilize this minus charge along with the along with the would be would be you know or incoming negative charge, because of this decarboxylation, there is there is a there is a developing negative charge. So, this developing negative is stabilized and only it is possible, because if such template is there.

So, that is why it is called the template effect and many metal ions have redox property. So, redox property means it is reversibly you know you know accepting electron to get reduced and then you know again this accepted electron is transferred to another entity and thereby it is again oxidized. So, reversibly it it is reduced oxidized reduced oxidized and the cycle is completed cycle is completed that means, the process of you know radix reaction occurs, via this metal ion. So, exploiting this redox property of the metal ions, we can we can you know, have interesting chemistry. So, what we have learnt out of such you know out of this discussion, here we have you know talked about general acid base catalysis then we moved onto metal ion catalysis.

So, why have we moved on because, they are these super acids are very very stronger maybe in some cases it is stronger or maybe comparable to H plus. So, they can be good you know catalysts and they have got very and these have got very you know good option for for carrying out you know radix reactions during its binding that is this metal ion, can accept or donate electrons by changing the redox state. So, exploiting that maybe, we can have have something extra, and also these as template metal ions are able to coordinate to to more than two legends, and can thereby bring molecules together or bring bring a specific confirmation that is very useful for the effective reaction.

Suppose we have got two groupings are like this, but when when metal ion is coordinating with maybe this group or maybe this group. So, maybe confirmation becomes like this that is parallel confirmation. So, what is happening, that maybe in this particular confirmation maybe the reaction is more effective well that is that is the rate is faster. So, this template effect is very important and also we have you know learnt covalent catalysis. Which happens via formation of you know covalent bond and then eventually eventually you know withdrawal of electron from the reaction (( )) followed by elimination of the catalyst leading to your product formation.

So, this covalent catalysis then super acid catalysis then acid base catalysis is very important not only in chemical reactions but also in biochemical reactions, you can this catalysis that is metal ion catalysis, maybe covalent catalysis. Can give rise to interesting results, interesting chemistry. So, with this I conclude for this session, I mean this lecture maybe we will take up kinetic isotope effect in chemical reaction in the in the next lecture. So, till then thank you.