**Fundamentals and Applications of Supramolecular Chemistry**

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**Week 03**
**Lecture 13**

W3L13_Factors affecting Chelate Effect,Thermodynamics of binding

Hello everybody. So, let us continue our discussion. In the last class, we were discussing about the role of cooperativity and the chelate effect. And here what we observed is that the chelate effect is an entropy effect, where the increase in the number of particles on the right hand side drives this particular process.

As you can see here, that we have started with hexamine nickel 2 plus, we have taken ethylenediamine as a ligand, this is a bidentate ligand, and during the process of this chemical reaction the monodentate ligand that is ammonia is consecutively stepwise being replaced by the bidentate ligand that is ethylenediamine, and forming the tris ethylenediamine nickel 2 complex and 6 ammonia molecules are removed from the primary coordination sphere of the metal ion and released into the bulk.

And the equilibrium constant for this process is reflected in the magnitude of log K which is 8.76. And what we observed is the number of particles on the right-hand side is 1 for the metal complex, 6 for the ammonia molecules.

So, the total number of particles is 7 and here the number of particles on the left-hand side, that is the reactants, is 1 for the hexamine nickel 2 complex, and 3 molecules for the bidentate ligand. So, totally there are 4 molecules.

So, then there is an increase in the number of particles when you go from the left-hand side to the right-hand side and therefore, this is reflected in and an increase in the entropy of the system and this is primarily reflected in the increase in the translational degrees of freedom.

Because now you have got more molecules in the bulk and ammonia molecules are moving around in the solution. So, overall, there is an increase in the entropy of the system therefore, the entropy change is positive.

And if you were to look at the overall Gibbs free energy change for the process you can also look at this process at room temperature in that case you will have delta G 0, delta H 0 and delta S 0 which comes from the enthalpy change and the entropic contributions and overall, this process must be reflected by delta G 0 less than 0.

So, as we see that the bonds on the left-hand side and the right-hand side are the same, there are 6 nickel-nitrogen bonds on the left-hand side and 6 nickel-nitrogen bonds on right hand side.

Therefore, in the absence of any solvent interactions, we are ignoring currently the role of the solvent. So, ignoring the role of the solvent, the enthalpy change on going from the reactants to the products is approximately equal to 0.

And therefore, the entire Gibbs free energy change contribution comes from the entropy term, which will decide the magnitude of delta G 0. This process is such that there is an increase in the number of rings on the right-hand side.

So, if you can see on the product side, you have got this one chelate ring, which is formed, this is a diamino ethane, it is a 5 membered ring, this is a 5 membered ring this is a 5 membered ring.

So, there are three 5 membered rings formed and this particular product is exceptionally stable, why, because in the case of the monodentate ligand they can be exchange of ammonia molecules between the bulk and the coordination sphere which is the first coordination sphere.

Where is here in the product side once a nickel-nitrogen bond is formed, the other nickel-nitrogen bond also forms in a facile way because it benefits from the enthalpy change. So, the formation of two nickel-nitrogen bonds is the driving force and this results in the formation of a cyclic system, cyclic loop which we call as a five-membered ring.

And because the ligand effectively encapsulates the metal ion here, this is referred to as the chelate effect. And three such rings contribute towards the overall stability of this chelate effect.

And then what we realized is that the entropy change for the process is around 33.4 into n joule mole inverse Kelvin inverse and where n is the number of rings formed in our particular case of tris ethylenediamine nickel 2 plus, n is equal to 3.

Therefore, the entropy change is approximately 100 joule mole inverse Kelvin inverse. And if we actually look at the thermodynamic data. Wherein we have reported delta G 0 values, delta H and delta S 0 values and this values are in kilo joule per mole, for delta G and delta H and for delta S this is joule mole inverse Kelvin inverse.

So, if you were to see the formation of the amine complex The delta G value is minus

52, delta S is minus 100 and the delta contribution is minus 163. For the formation of the tris ethylene diamine Nickel 2+ complex, the delta G for the process is 102, enthalpy change is 117 and entropy change is only 42.

Now, if you were to now combine these two complexes, that is the amine complex plus the ligand to form this particular complex, then the chelate effect can be quantified as the change in the value of delta G, change in the value of delta H and change in the value of entropy change. So, we are looking at delta of delta G, delta of delta H and delta of delta S and this value comes out to be minus 102 plus minus of minus 52 is plus 52 that is minus 50.

This is around minus 17 and this is a large positive quantity that is the product minus of that of the reactant which is plus 121 joule mole inverse Kelvin inverse which is comparable to the value which is reported from the calculation.

So therefore, we concluded that the chelate effect is an entropy effect and why because it is this term the delta of delta S which is responsible for the chelate effect being an entropy effect. So now keeping this in mind, people have now looked at the role of the size of the ring to examine the chelate effect.

So, the size of the ring is supposed to be a very important thing here and here what we have we can see that you can have for example, a 4 membered ring, you can have a 5 membered ring, you can have a 6 membered ring, 1, 2, 3, 4, 5, 6, 7 membered ring and so on and so forth. So, you can have a 4 membered ring, this is a 5 membered ring. So, now, we can see that we have got different 5 membered, we have got different size rings here.

For example, we can start with a 4 membered ring, we can have a 5 membered ring, we can have a 6 membered ring, we can also have a 7 membered ring. In the case of the 4 membered ring, there is strain in the system.

So, 4-membered rings are not relatively stable. The optimum stability is for actually for the 5-membered ring and mostly also observed for the 6-membered ring. These are the two systems where the chelate effect is operational to a maximum extent.

And then when you go to the 7-membered ring, the formation of these chelate rings becomes difficult and entropically unfavorable. Now, why is this so? So, say you started with this particular ligand, then you have increased the chain length by introducing a methylene group.

This is another possible orientation of the same, a diamino, say if X is equal to NH2, this is a diamino ethylene ligand and then we can have this particular ligand, which is going to now change its conformation and form the 6 membered ring.

So, you can see here that in order to form the cyclic chelate ring, there must be a change in the conformation of this particular ligand, because in reality, when this particular complex is formed in solution it exists in different conformation, this is the open conformation.

And there must be a change in the conformation because this must convert into this particular conformation and then this is more effective insulation.

And this change in conformation is entropically unfavorable because now you are actually restricting the motion of the ligand. So, initially in the open conformation the molecule was free to rotate and explore more degrees of freedom, but now when you have actually locked the ligand you have restricted its conformation degrees of freedom therefore, this is entropically unfavorable.

So, larger is the size of the ligand that means when you are going to the 6 membered or when you are going to the 7 membered rings where the number of carbon atoms increases, here the number of carbon atoms is 4, here it is 3 then you will have to bring about a greater change in the conformation, for it to bind effectively.

And therefore, statistically the probability of this folding into a more closed conformation to form the chelate ring is increasingly difficult because it has a entropic component associated with it. And therefore, the stability of the complexes decreases when we increase the size of the ring.

This is one factor which is responsible for the stabilization or the magnitude of the binding constant associated with the chelate effect. The next factor is, so this is the size of the ring. The next factor is the size of the metal cation.

Now, what has been observed is that when you are forming this particular close conformation the X atom for example, the nitrogen atom here or the oxygen or the sulfur or any lone pair donor atom is having the lone pairs and the lone pairs are oriented in this fashion. So, there is unfavorable electronic repulsion.

So, these X atoms will always try to approach each other because they have to go and capture the metal ion M N plus and eventually when the complex is formed these repulsions will stay.

These repulsions are not going to go away because the X atoms are going to approach the metal ion.

Obviously, most of the electron density is going to be donated to the metal center, but nevertheless these electronic repulsions are going to stay in the complex also, and one can minimize these repulsions, if one increases the size of the cation.

Because if you have a small cation, say for example, lithium ion then the two donor atoms will try to capture the lithium ion, by going closest towards it, and the closer the X atoms approach towards the smaller size lithium cation there is going to be increasing unfavorable repulsion between the lone pairs.

Therefore, small size cations do not get stabilized by the chelate effect. It is slightly larger size cations like sodium or potassium which have a more favorable binding constant in terms of the chelate effect.

And it has been observed that if you go for the six membered rings then what is important is that it would be best to have a metal atom whose size resembles that of the sp3 carbon in that of cyclohexane.

So, that there is no strain set up within the system. And in this regard, the small size cations like for example, $B^{3+}$ and $Be^{2+}$ form stable entities with these large sized ligands. And on the contrary if you were to take the large size cations for example, if you take calcium, strontium then the cations being large, they do not form very stable complexes with this particular ligands. So, overall to summarize the 5 membered ring forms the most stable complexes and 4 membered ring is a strained system, ok.

And if the size of the cation is small then we have to minimize the electronic repulsions between the lone pairs and therefore, 5 membered rings or 4 membered rings are not favored. If you really want to form a stable complex with the small size cations, then we utilize 6 membered rings or 7 membered rings.

And if you want to stabilize the large size cations, then the 5 membered ring is most favorable. And for the 6 membered and 7 membered rings, the large size cations do not form very stable complexes. It is a small size cations which forms most stable complexes.

So, overall these are the factors which affect or influence the magnitude of the chelate effect. And let us look at more examples now, which actually demonstrate the relevance of the chelate effect.

For example, we can now look at, example 2, we can now look at acetyl acetone ligand and complexes with metal ions. So, let us look at this particular ligand. This particular ligand acetyl acetone exists in the keto form and it is in equilibrium with the enol form and why is it stable, the enol form is because these is hydrogen bonding which stabilizes the enol form.

Now, in the presence of a base we abstract this acidic hydrogen and it forms the enolate and we know that the enolate is resonance stabilized. So, we use the resonance symbol

now. So, this is the acetyl acetonate ligand, and it can form octahedral complexes, distorted octahedral complexes with different trivalent cations.

For example, it can form with aluminium acac, chromium 3 plus, iron 3 plus, it can form cobalt 3 plus, it can form the metal acetyl acetonate, this is the neutral complex. Again if you were to see the structure of the complex, it will be seen that the metal ion in the 3 plus oxidation state forms this kind of very stable complexes, that is where the charge as well as the coordination is satisfied by the hard donor atoms oxygen and you can see that every ligand forms a cyclic loop, it forms a ring system.

So, there are three chelate rings which are formed in this particular process, and these are also 5 membered rings essentially. So, these are also stabilized by the chelate effect. So, the formation of aqueous complexes is again another demonstration of the operation of the chelate effect. Now, keeping these things in mind, the fact that the chelate effect is very important and the cooperativity amongst the donor atoms is also very, very important. People were now interested to look at the role of ligand in affecting host-guest complexation behavior.

So, now we know that the ligand plays a very important role in host-guest complexation. And it is very important to keep in mind that we discussed in the previous lecture that the next factor is that there is a very important role, which is the pre-organization of the ligand.

As we already saw in the case of chelate effect that every ligand has got conformational degrees of freedom, and if a ligand L has to bind to a guest molecule, then it must have the correct geometry or conformation so as to maximize the interactions with the guest atom or molecule.

In this case, this is a ligand is having a permanent dipole moment and this is having a charge. So, these are essentially ion-dipole interactions, and the ligand must have the correct conformation, the correct geometry.

So, that it is able to bind with the metal ions now with maximum efficiency and the overall stabilizing energy for this process must be negative. So, there are two important things which must be kept in mind here.

One is that you must have the correct conformation, and you also have to keep in mind that during the process of change in conformation you must also minimize the unfavorable lone pair-lone pair repulsions, between the donor atoms on the host molecule.

Why we have to minimize these unfavorable interactions, because these unfavorable interactions are going to be also present in the complex. So, when you form the MLn n plus, or you say this particular complex you form.

Then you will see that these unfavorable lone pair-lone pair repulsions are also going to be present in the complex. Therefore, now these also have to be minimized. So, overall we see that when you have the complexation process that there are two factors one is you have the energy which is necessary to bring about change in conformation.

So, energy change due to conformation and this is the binding energy is going to define the E total and we want that the E total be negative. That means the formation of the host-guest complexation process is a stabilizing process, where the final potential energy of the system is lowered and this comes from two terms.

That is the binding energy term, which has to be highly negative, such that you have maximized the donor-acceptor interactions. In this case, your donor are the lone pairs and the acceptor is the empty metal d orbitals or empty metal orbitals.

So, there are maximum donor-acceptor interactions such that there is a enthalpy change associated with the process which is highly negative and the binding energy becomes highly negative, and this is a positive term because energy has to be spent by the system in bringing about the conformation change.

So, this conformation change has an energetic penalty associated with it, and because both these terms contribute towards the overall E, it will be nice, if we can minimize this particular contribution and in order to minimize this contribution it is very important to have the ligand preorganized.

So, the ligand already has been put in a geometry or a conformation, where it is already pre-organized for binding, then this energy penalty will not be present.

In other words, during the process of synthesis of the ligand into a pre-organized geometry, this energy penalty would have been paid. That means, now when you are going to do the host guest binding, this energetic contribution, which is an unfavorable contribution will not play any role.

So, if the host is pre-organized then the overall E total or the stabilizing energy for the process is highly negative and this is what has been explored largely in supramolecular chemistry, that is how the degree of pre-organization of the host plays a very important role and what has been observed is that acyclic host versus cyclic host.

So, compared to acyclic host, the cyclic host, which have got a greater degree of pre-organization, they play a very important role in stabilization. So, let us now look at

what are the different kinds of host which have been observed to amplify the stabilization of the host-guest complexes.

Now, in this regard, the first one is we have got, so you have got a open conformation. And then you have added in a guest molecule. So, this is the guest molecule and finally the guest molecule has to get encapsulated by the host molecule.

So, this is one kind of binding and such kind of ligands which have got open conformation are referred to as podands. We will come to more examples of podands, later, but this is a schematic representation.

And then we can have a pre-organized ligand for example, already having a cyclic structure where these are the donor atoms. And then this is called a closed conformation and then we have the guest, so it forms a cyclic host. We can also have a bicyclic host.

And now we see that the stabilization that is the binding constant increases this is logK2, this is logK3 and this is logK1. So, overall, the binding constant has been found to increase.

So, there is an increase in the degree of host organization and there is an increase in the magnitude of the binding constant as well and this has been attributed primarily to, here it is the chelate effect.

And the additional stability conferred on the host-guest complex, because the presence of the closed conformation, or the cyclic conformation, is referred to as the macrocyclic effect, which is in addition to the chelate effect.

So, we have the chelate effect and the macrocyclic effect operational here. The chelate effect is because you are forming these rings here and here you will have the chelate effect and because you have a bicyclic host you will have the macrobicyclic effect.

So, more is the number of rings, more is the number of chelate rings, more is going to be the stabilization and more closed is going to be the conformation and more is going to be the stability of these complexes.

So, in the next class we will now take up more concepts related to the operation of these bicyclic and macrocyclic effects.

Thank you.