

Fundamentals and Applications of Supramolecular Chemistry
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Lecture 18

W4L18_Phase Transfer Catalyst, Kinetic and Thermodynamic Template Effect

So, hello, everybody. So, let us now continue our discussion from where we left off in the last lecture. So, in the last lecture, we were looking at the concept of phase transfer catalysts, where we aimed to investigate the nucleophilic substitution reaction in a halide-substituted compound when treated with this potassium salt of A minus.

In this case, my A is my acetate ion. And X is my chloride ion, is my chloro atom; in the presence of crown ether, we would like to see and investigate the replacement of X by the A species and the reaction kinetics of the process. Now, what has been observed is that when this reaction was done in the absence of crown ether, the reaction half-life was 685 hours.

When we added 18-crown-6, the reaction time drastically decreased to 3.5 hours. And in the presence of dibenzo-18-crown-6 and dicyclohexyl-18-crown-6, the reaction times were 9.5 hours and 1.5 hours, respectively. That means there is a special role for the crown ether in these processes, and this enhancement in the rates of the reaction via metal ion complexation with the macrocycle modifies the conformation of the macrocycle, with subsequent implications for reactivity.

So, we referred to this enhancement in the rate of the reaction in the sense that there is a catalyst that actually catalyzes this process, and the catalyst involved is the complexation of the metal ion with the macrocycle, which is the 18-crown-6, that effectively enhances the rate of the reaction.

Now, how does this take place? So, to start with, let us consider the reaction vessel in the following way: we have, say, this is the aqueous phase, and this is the chloroform phase. So, this is the organic solvent, and now what I am doing is that I have taken the corresponding potassium acetate, and it is in the aqueous phase.

You see that the cation and the anion are solvated; however, there exists ion pairing. Now, what the macrocycle does is encapsulate the potassium cation and form the crown ether complex, which then comes into the organic phase, allowing the acetate ion to be free to perform the chemical reaction.

So, initially, the potassium and the acetate ion are tightly held because of the electrostatic interactions, and these electrostatic interactions are also favorable in the polar phase.

However, when we add the crown ether, the crown ether sequesters or captures the potassium cation and freezes the acetate ion.

Now, this particular crown ether complex has a different conformation because we know that the crown ether complex, when it is uncomplexed, has a different conformation compared to the conformation it adopts when the oxygen atoms point towards the interior where the potassium ion binding takes place.

So, this particular conformation, where the exterior part is more non-polar, is more favorable in the organic phase; therefore, the potassium is removed from the vicinity of the acetate, the acetate is now freed up, and now the acetate, as a nucleophile, can attack the carbon electrophilic center and form the resulting product.

Now, once the product formation has taken place, it should be realized that the inorganic byproduct KCl is also formed. So, what happens is that now you see you have the crown ether, plus KCl, plus my organic product here in the reaction vessel. But the inorganic salt is not stable in the organic phase or in the organic solvent.

And therefore, now it comes back to the aqueous phase; the inorganic product and the crown ether are also not stable in the organic phase because they do not have the potassium cation, and they adopt a more polar conformation.

The polar conformation is most stabilized in the polar solvent; therefore, the uncomplexed crown ether now goes back to the aqueous phase. Again, it takes up the starting material; that is, it takes up the nucleophile that potassium acetate again brings into the organic phase, and the chemical reaction proceeds.

So, this transfer of the reactants from the aqueous phase to the organic phase in which the chemical reaction takes place is brought about by the potassium cation, and this leads to tremendous enhancements in the rates of the reaction, which is facilitated by the cation complexation.

Hence, this is reflected in the extremely short reaction half-life for the 18-crown-6 and even lower reaction times for the dicyclohexyl crown ether complex as well. So, this is a very interesting application of phase transfer catalysts, which are mediated by the crown ether complexes.

In this regard, the application of crown ethers in the presence of potassium ions is very, very important. It has also been realized that other cations do not bind very efficiently with crown ether; the binding is most efficient with the potassium ion.

So, keeping in mind that reaction rates are tremendously enhanced in the presence of the potassium cation, it has also been realized that to perform organic chemical

transformations, the potassium ion has been utilized to create a template that shall facilitate processes that govern intramolecular ring products, or we can say intramolecular cyclic products.

So, if you want to have a chemical reaction where there is competition between an intermolecular process and an intramolecular process, then the potassium ion has been utilized to create a template that facilitates processes that govern the formation of the intramolecular cyclic product in preference to the intermolecular products. Let us take a particular example.

For example, let us take this particular acyclic component and the corresponding dichloro compound and treat it in the presence of KOH, potassium hydroxide. Now, what potassium hydroxide does is act as a base, and what has been observed is that you have 1, 2, ok.

So, we have these two reactant partners: the dichloro compound and the dihydroxylated compound, along with the corresponding potassium cation, which kind of forms a template. This creates a template, and then what happens is that the nucleophilic reaction proceeds in a very enhanced fashion because the base generates the O minus, which attacks the electrophilic carbon. Again, it attacks the electrophilic carbon, chloride goes out, and two equivalent molecules of HCl are removed, resulting in the final product.

So, now you see we have got 12, 13, 14, 15, 16, and we have got the 18 crown 6. So, we have got the cyclic product. And if you do not add KOH, but instead add a simple base that is triethylamine, then a polymer is formed because, statistically, in the presence of triethylamine, we generate the O minus, it hits the electrophilic center, forms a carbon-carbon bond, and we get this linear polymer.

So, essentially, it leads to a reaction where I have an intermolecular process happening, and I get a long-chain polymer, while the possibility of a cyclic reaction taking place is very remote. This process is very difficult; obtaining the cyclic product is very challenging.

However, in the presence of the potassium ion, it creates the necessary template, which we can call the necessary playground, where the reacting partners can come very close to each other; these are the reacting partners. They can come very close to each other, and the functional groups that are supposed to react with each other are also in close proximity.

The SN2 reaction can take place, and the cyclic product formation happens in a very facile way. The rates of the reaction are tremendously enhanced, and the entire process is catalyzed by this template formation, which is referred to as the primary template effect.

And it is as if the close proximity of the reactants creates an intermediate, which thus facilitates the formation of the cyclic product, and this is referred to as the primary template effect.

And it has also been observed that this effect can be templated by other cations, like the alkali metals, such as sodium, or the alkaline earths, lanthanides, etcetera. So, different kinds of metal cations can actually catalyze this process, and this is referred to as a primary template effect or a kinetic template effect. This is referred to as the kinetic template effect because the processes that govern the formation of the product are of a kinetic nature.

Now, along the same lines, we have also got the formation of products that is governed by thermodynamics. So, we see that in the kinetic template effect, the actual formation of the complex with an arrangement of ligands around the metal center takes place, but in a thermodynamic template, it depends on the ability of a cation to pick up a ligand complementary to it from an equilibrating mixture of products such that the most favored product is also the thermodynamically stable one.

So, we looked at the kinetic template effect, and we now look at a thermodynamic template effect. It depends on the ability of a cation to pick up a specific ligand that is complementary to it from a mixture of more products that are in equilibrium with each other, such that the final obtained product is also the thermodynamically most stable one.

And let us look at one particular example where the formation of, or the demonstration of, the thermodynamic template effect has been relevant. For example, it has been observed that, let us take M tris(ethylenediamine), a dicationic complex treated with acetone, gives you this particular complex; and so to start with, we have the ethylene diamine ligand that is complexed with the metal ion.

So, for the ligand to complex with the metal ion, it forms an initial complex, but then we want first the ligand to react with acetone and therefore, decomplexation has to take place.

In other words, the metal-ligand bond has to break, and this is only possible if these are kinetically labile bonds and inert complexes; kinetically inert complexes do not contain labile bonds.

And therefore, those kind of complexes for example, if you consider $[Co(en)_3]^{3+}$ plus ok. In this particular case, the cobalt is a 3 plus cation; the cobalt-nitrogen bonds are kinetically inert, and therefore, they are not labile; because they are not labile, it is very difficult to undergo decomplexation, and hence, the reaction of the ethylene diamine with acetone does not take place.

And in this case of the thermodynamically template effect, we do not need, in some cases, the presence of the metal ion to template this particular process. So, for example, the final product does not necessarily need a metal ion to template this process.

Now, let us look at how this particular complex is formed. So, we have the ethylene diamine ligand, which is $\text{NH}_2\text{CH}_2\text{CH}_2\text{NH}_2$, and we have acetone. Acetone will react with the amine group to form the imine. So, it forms this particular ligand first. So, the reaction of ethylene diamine with two equivalents of acetone will give this particular ligand, which is actually in equilibrium with the starting material.

Now, another equivalent of this ligand will undergo cyclization in such a way that we will have a CH_2 , and here we will have a CH_2 minus, followed by the proton. So, the nucleophilic attack occurs because this is a base-catalyzed process, where you have the CH_2 minus that attacks the electrophilic site of C double bond N, and followed by the proton transfer, will give you the desired ligand NH.

And so now we also have the equilibrium of this final ligand. This is the intermediate ligand, and these are the starting ligands. So, now the thermodynamic template effect is such that you still have the metal ion present in solution, and now the metal ion can have an affinity for either this ligand or it can have an affinity for the solvent; it can be solvated by acetone molecules.

It forms an initial complex with ethylene diamine, and now it can be stabilized further by the chelate effect and macrocyclic effect, both of which stabilize the metal ion in this particular template or the final structure of the ligand, which is the thermodynamically most stable structure; that particular ligand is now picked up by the metal ion to form this particular complex.

And we have also realized that in the formation of this complex, it is not necessary for the metal ion to be present. As long as there is an equilibrium between the starting material and the different ligands being formed, or in this equilibrium mixture of ligands, the metal ion will pick up the corresponding most stable ligand and form the thermodynamically stable product.

So, this is a very interesting example of the thermodynamic template effect. And keeping this in mind, people have further explored this thermodynamic template effect to make different kinds of metal macrocycles, either containing the metal or not.

Now, depending on the size of the metal ion, we can achieve macrocycles of larger sizes as well. For example, we can consider a reaction in which this particular ligand is treated with this diamine that is bridged by two etheric oxygens.

And now we are going to take two different types of metal cations. We are going to take two differently sized metal cations. In one case, we are going to take manganese, iron, or magnesium.

In other case we are going to take barium 2 plus or lead 2 plus. In the first case, we are going to take both ligands in a 1 to 1 stoichiometry; that means one part of this and one part of that. In the second one, we are going to take in 2 to 2 stoichiometry, and it will be interesting to see what the final product obtained is.

In the first case, you will have the reaction of the amine group with the keto functionality to form this particular product, where now my metal ion sits and interacts with the nitrogens as well as the oxygens. And in the second case, it is going to form a much larger macro cycle.

This is a much larger-sized macro cycle in which my large cations like barium 2 plus or lead 2 plus are going to sit, whereas here the relatively smaller-sized cation is going to occupy.

So, the size of the macro cycle depends on the size of the cation that is templating this macrocyclic effect. So, this again demonstrates the operation of the thermodynamic template effect and the size of the template that is being formed.

The size of the ligand that is being formed again depends upon the size of the metal cation, which templates the formation of these kinds of final ligands. So, the next part here in this particular process is whether we can effectively remove the metal cation from the macrocycle and free it, and this can be done by adding ligands with which the metal ion complexes strongly.

For example, we can take KCl and the cyanide ion complexes with the metal cations, which are the divalent cations, very strongly bond to form this kind of species. So, if you have nickel, for example, then it will form $[\text{Ni}(\text{CN})_4]^{2-}$, or if you have lead—sorry, if you have nickel, it will form $\text{Ni}(\text{CN})_4^{2-}$; it is very specific for nickel, or if you have palladium or platinum, it will form the corresponding tetracyanopalladate or platinum complexes.

Therefore, the metal ion can be removed from the macrocycle, and the ligand can be obtained. So, all these results demonstrate to us the relevance of template effect, both kinetic as well as thermodynamic in the formation of larger size micro cycles. And with this, we have a complete overview of this class of ligands: the corands, the podands, the crown ethers, the cryptands, and we have also looked at the spherands.

In the next lecture, we will go on to the other classes of molecules that exhibit host-guest

complexation behavior. For example, we look at calixarenes, cyclodextrins, and so on and so forth.

Thank you.