Fundamentals and Applications of Supramolecular Chemistry
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Week 07
Lecture 32

W7L32_Nucleation Model, Kinetic and Thermodynamic Crystal, Phase Transitions

So, hello, everybody. So, let us continue our discussion today on the concept of nucleation and growth, and today we will be discussing the qualitative understanding of the crystal nucleation model.

And we discussed in the last class that the formation of the prenucleation aggregates means that there are a certain small number of nuclei that are formed, and now these nuclei have to grow further so that they can form the final crystal. We looked at the classical nucleation pathways, and we also looked at the non-classical nucleation pathways.

That is the one-step model and the two-step model, respectively, and we also looked at a case study of olanzapine, where we saw how the different dihydrates or polymorphs can form, depending on whether you have the crystallization of these dense droplets on the surface or you dissolve these droplets further in the bulk solution and then crystallize at the new phase.

In order to understand the process of nucleation, we realize that there are two important terms: one is the Gibbs free energy term associated with the volume change in the bulk crystalline material, and the second is the interfacial energy, where energy has to be spent to create the necessary surface for the formation of the crystal.

So, we now have to look at both these processes, and it is the cumulative combination of both these processes that decides the overall process of crystallization. So, here we define two quantities: delta Gv, which is the Gibbs free energy of the nucleus per unit volume, and delta Ga, which is the surface free energy per unit area of the nucleus. Here, we would like to look at this curve. So, we have delta G as a function of r.

This process of nucleation involves a certain activation barrier, and once you cross this barrier, the process of growth takes place in a facile way. Here, there are different regions we need to consider. So, there is an activation barrier, and when you reach this activation barrier, this represents rc. This is the critical size of the nuclei. At this particular point, the delta G is equal to 0, and at r, we call this rD.

So, at r greater than rD, ΔG° becomes less than 0. At r equal to rD, ΔG is equal to 0, and at r less than rD, ΔG° for the process is greater than 0. Because the creation of the surfaces needs energy, this is a term that is associated with delta Ga, and there is a volume term that is associated with delta Gv; it is actually a combination of both these processes that drives the overall process of nucleation and growth.

And as we know that the formation of the nucleus is essentially critical, it is only after it reaches the critical size rC that the Gibbs free energy change ΔG starts decreasing. So, the Gibbs free energy change starts decreasing in this region, goes to 0, and then becomes negative.

Therefore, it is important to consider the size of the nuclei present in all these regions. So, as I told you, initially there is an energy penalty because you have to create the surface, but there are also concentration fluctuations and thermal fluctuations.

So, in the regions between r and rC, the nuclei that are formed can also dissolve back into the solution because there is no barrier associated with the process. And that is the reason why, when you do the process of crystallization, we have to keep them steady and not disturb the crystallization vials, because the nuclei that are forming in solution will rapidly redissolve back into the bulk medium due to the necessary thermal agitation.

So, I am giving thermal agitation to the molecules or disturbing them or providing vibrations; then these nuclei again tend to dissolve back into the solution.

So, it is very important that we leave the crystallizations undisturbed for a sufficiently long period of time so that we get the right size of nuclei and then these nuclei can grow and give you the bulk crystal.

Now it was initially thought that for the nucleation to proceed satisfactorily, if nucleation proceeds satisfactorily, then only the growth process starts, because you have this critical size of the nuclei that is reached and now, they can start growing larger and create the crystal surfaces. More and more of these nuclei will be formed, and they will attach themselves to the crystal surface.

Now, in this case, you see that whenever the nucleus wants to go and attach itself to the crystal surface, it is the Gibbs energy change that is more negative because of the volume change due to the formation of the bulk crystalline material, but there is also a resistance because you have to create the surface.

So, when you have actually crossed this barrier and the volume changes are more, then the system does not respond negatively to the requirement of creation of surfaces.

So, you have a competition between volume change and surface change, and it so happens that the volume change dominates the positive energy necessary to create the surfaces. And so initially, it was thought that delta G should be less than 0, but that is not the case if you look at the region between rC and rD.

So, if you take, say, any particular radius, say rX here, you will see that the nuclei that are formed are thermodynamically unstable, but kinetically they are stable. Why? Because if they have to dissolve the nuclei in this region, they will face an increase in activation energy. Now there is a barrier.

So, you have this delta Gx and this is delta Gc. Now there is a barrier. Delta Gc minus delta Gx is greater than 0 because of this barrier. These will not be able to dissolve back now. That is why this distance rC is considered to be the critical size beyond which nucleation proceeds further, and as more and more nucleation happens and you cross delta G less than 0, the volume term takes over in a substantial way.

So, although these nuclei are unstable thermodynamically, they are stable kinetically; therefore, we are able to achieve the process of nucleation in a facile way, and the tendency to go back into the solution does not exist because of the relatively large activation barrier, depending upon where you are.

So, if you are in this region, say for example, then the activation barrier is very high. And as you go higher in r, the ability to dissolve back becomes less and less feasible. So, now we can look at a quantity which we can compute the maxima of these thermodynamic quantities; that means we can now compute what delta gC is because that is the barrier height, and to do that we will have to first see the terms that are involved in this process. So, in order to compute the barrier height, we will first look at delta G nucleation as a function of r.

We can write that it is a combination of two terms. We have the volume phase, multiplied by the Gibbs free energy of the nucleus per unit volume. So, this is delta Gv, and this is negative because it is associated with decreasing delta G, and the positive term is the $4\pi r^2$ delta Ga, which is the surface free energy per unit area of the nucleus.

And now, to get the position of the maxima, we will have to take the first derivative of delta G and r with respect to r, and that will give you minus 4 pi r squared times delta Gv plus 8 pi r delta Ga. And this is then set equal to 0, and from here we can conclude that $4\pi r^2 \delta Gv$ is equal to $8\pi r \delta Ga$.

So, r cancels, and this gives me the critical radius because now it is at r equal to rC. Thus, rC becomes equal to $2\delta Ga$ by δGv. So, now you see this is how you get the magnitude of rC; that is, it is the ratio of twice delta Ga to delta Gb.

So, the area term contribution that gives the free energy surface area is more important compared to the volume term. The ratio of this decides rC, and if you now put this value of rC into the original expression, then you will get the quantity which is called the Gibbs critical excess energy.

This is the excess energy, that is delta Gc, which will come out to be 16 by 3 pi delta Ga cube by delta Gv square. So, this is equation number 2; this is equation number 1. So, we see now that the activation barrier depends on the cube of delta Ga and is inversely proportional to the square of delta Gv; overall, these determine the magnitude of the barrier height or the activation barrier required for the process.

So, once the nucleus has become sufficiently large in size, there is a decrease in the free energy associated with the formation of the bulk crystalline material, and the interfacial energy does not become very significant now. And we also keep in mind that the concentration fluctuations are now present, which aid in the process of crystallization once the crystal size has been exceeded.

As we realized in the previous lecture, there is a metastable zone, and we have to cross this metastable zone and go into the labile zone. So, in the labile zone, the process of crystallization takes place because you have now increased the levels of supersaturation, and then crystallization proceeds in a facile way.

So, if you want to enhance the nucleation and growth, you need to increase the supersaturation of the system. Increasing the supersaturation of the system will decrease the activation barrier. When the activation barrier decreases, you need a lower magnitude of rC to achieve nucleation.

So, you can actually modulate or control the barrier height by increasing the supersaturation in the system, and that will also lead to more concentration fluctuations, which will statistically increase the probability of formation of more crystalline material at the expense of the energy necessary to create the additional surfaces.

So, now you see that as the activation energy and the critical size decrease, this process leads to spontaneous and rapid nucleation. Because now you are increasing the concentration of these critical nuclei, the pre-nucleation clusters are increasing, and this can lead to facile growth.

So, overall, we see that this is the very basic concept of the nucleation and growth mechanism in crystals. So, this also accounts for the fact that when you have a phase transition process, say one polymorph converting into another, it can proceed by the nucleation and growth mechanism, where the structure of the daughter phase is related to the structure of the mother phase, and the process happens gradually as a function of temperature.

And then there are some processes that happen due to dramatic changes in the structure, and the two polymorphs cannot be related to each other in terms of mapping the trajectory of how one form converted into the other.

And keeping this in mind, we now realize that the solution phase is actually the pathway to the formation of polymorphs, and just like in a chemical reaction, the reactant concentration is very important; in the formation of polymorphs, the nature, concentration, and role of the nuclei are extremely important.

So, we can now consider a solution phase where we have these nuclei. In these nuclei, we have these molecules that interact via intermolecular interactions. They interact through intermolecular interactions, and they form a high energy dense phase which is the nuclei.

Depending on the barrier to crystallization, whether it is small or large, we can have different kinds of polymorphs that can form. So, in this case, if the barrier is less, that means the activation energy is low; then we have got a kinetic crystal.

And we call this delta G kinetic, and this is the change compared to that of the parent phase or the solution phase from which the crystallization takes place. So, this is the delta G of kinetic, whereas you can have a much higher barrier, which is delta G of thermodynamic, and this will lead to the formation of the thermodynamic crystal.

So just like you have kinetic products and thermodynamic products that come out from the solution in an organic reaction or organic transformation, you can now have different polymorphs crystallizing out from the solution phase.

Depending on the structure of the nuclei and the changes happening in these nuclei, which actually lead to the crystallization of the kinetic crystal or the thermodynamic crystal, and depending on the conditions you provide for crystallization.

If you give very fast evaporation rates and high temperatures, then the tendency to get a kinetic crystal is high; but if you allow the system to equilibrate with the surroundings and gradually lower the temperature of the system very, very slowly, you significantly reduce the rates of evaporation; then statistically, you are promoting thermodynamic conditions of crystallization.

So, the barrier can be higher, but it will give you the thermodynamic crystal, and once the thermodynamic polymorph is formed, it will not convert into the kinetic polymorph. In this regard, what has been proposed is that when you get a kinetic crystal, there is now a competition between the maximization of hydrogen bonds and close packing. And it is the competition between these two sets of forces that decides the outcome of crystallization.

So, when close packing principles govern, this is in accordance with the rules of close packing as stated by A. Kitagorodsky. You will have more weak interactions, but close packing will prevail where you will essentially try to minimize the void space in the crystal, and you will get a highly dense solid.

Whereas, if you want to have the formation of supramolecular synthons that maximize highly directional and short hydrogen bonds, then the tendency to form a kinetic crystal is greater. And once this hydrogen bond array is formed in solution, it is quite stable, and it is very difficult to disrupt this hydrogen bonding structure and convert it back into the monomers, from where it can possibly go into the thermodynamic form where the close packing principles operate.

So, it is the competition between the maximization of hydrogen bonds and close packing that actually leads to kinetic and thermodynamic polymorphs. And also, there is one very important assumption of classical nucleation theory: it is that the arrangement of the molecules in the bulk crystal is very similar to that in the nuclei. In other words, whatever the surface free energy of the nuclei is, that is the same as that of the bulk crystal.

Now, this is a very, very limited approach because there are a lot of variations happening in the nuclei, and so assuming that the surface free energy of the nuclei of the molecules is the same as that in the crystal is an oversimplification. Because now what can take place is that the kinetic crystal can actually convert into a neighboring phase that has lower activation energy.

Then it can convert to another phase, and then it can finally convert to the thermodynamic phase. So, during the process of crystallization, it is not only the kinetic phase and the thermodynamic phase that are present. These are the ideal conceptualizations, but a kinetic crystal can convert into a thermodynamic crystal via sampling of the low energy minima.

So, these are the relatively lower energy minima before they convert into the thermodynamic crystal. And so, in that case, the assumption that the free energy of the molecules in the nuclei and that in the crystal phase, which is crystallizing out, is the same does not hold.

And this process of conversion from one form to the immediate form that exists in a lower kinetic minima is referred to as Oswald's rule of stages. So, we have this Oswald rule of stages, where the sample, actually, the nuclei explore slightly lower energy minima, then convert into the next lower energy minima, and finally transform into the thermodynamic crystal.

This is referred to as a series of continuous crystallization processes, each process mediating the formation of a new phase with a slightly lower free energy minimum compared to the one from which it initiated, eventually converting into the thermodynamic crystal.

And this thing is also very, very common when you take a kinetic crystal, dissolve it in a solution, and actually stir this mixture for a period of 2 to 3 days. The possibility of converting to the other polymorph is very high.

Now that you can access the neighboring polymorph. It can be another kinetic polymorph, and if you do this stirring for a long period of time very, very slowly, you might end up converting into the thermodynamic crystal as well. So, all these processes talk about the relevance of nucleation and growth.

Now, what we will discuss further is the fact that we have polymorphs. You have different crystalline phases, and now we would like to understand the concept of whether in solids one form can convert into another, and this happens due to the existence of the phenomenon of phase transitions.

So, we have looked at nucleation and growth mechanisms, we have looked at polymorphs, but now we would like to understand the thermodynamic relationship between the polymorphs. We would also like to understand the concept of phase transitions, where one structure converts into another.

And this process of converting one structure into another, proceeds through different mechanisms. Two very common mechanisms exist. For example, there is a nucleation growth mechanism where the new phase is formed at the expense of the parent phase slowly and stepwise, and then there is a process called displacive transition or martensitic transition where one phase converts into the other without any association with an activation barrier.

So, what is a phase transition? A phase transition is the process of transformation of a substance from one phase to another. And obviously, we are only considering structural changes here, and the two most important variables are pressure and temperature. And as I mentioned to start with, there are two types of phase transitions. So, I can write this as PT, which is different from pressure and temperature.

There are two types of phase transitions. Number 1, we have the nucleation and growth model, which is slow, and the nucleation step is the rate-controlling step or the rate-determining step, and it is a difficult and slow step. Whereas, on the other hand, you can also have martensitic and displacive phase transitions where these processes take place via a diffusionless pathway.

The activation barrier is very low, occurs spontaneously, and proceeds at a fast rate. So, you have slow processes and very fast processes. The martensitic and displacive phase transitions are relatively fast, whereas the nucleation and growth model is relatively slow.

And then what was also proposed at that time by a famous scientist called Buerger is that, according to Buerger's classification, phase transitions are of two types: the reconstructive and the displacive phase transitions.

In the case of the reconstructive phase transition, there is a major reorganization of the crystal structure. In which many bonds have to be broken and formed again. Reconstructive phase transition is one in which you actually disrupt the parent structure and then form the new crystal structure. For example, here we have the classical example of graphite, which is in equilibrium with that of diamond.

They have very different structures. Graphite consists of hexagonal sheets, whereas diamond contains four coordinated carbon atoms. So, in the case of graphite, we have the hexagonal sheets, and here we have the giant structure. This is 3D; this is 2D. Here, carbon is three-coordinated.

Here, carbon is four-coordinated. So, the structures are very different, and if you want to convert from graphite to diamond, there is a major reorganization of the structure as a whole. So, what essentially happens is why there is a barrier to the process.

There is a large barrier to the process because it involves breaking a large number of bonds and forming new bonds. So, although you can have a kinetically stable phase that can exist for a long period of time because the barrier involved in converting to the thermodynamic phase is very, very large.

So, for example, we know that diamond, which is formed at extremely high temperatures and pressures, is actually a kinetic phase; it is kinetically stable.

It is thermodynamically metastable, but the process of conversion from diamond to graphite does not take place so easily because of the large barrier involved. And, on the other hand, graphite is the most stable form of carbon at room temperature and pressure.

At 25 degrees centigrade and one atmospheric pressure, the graphite form is the most stable form, while diamond is the kinetic phase. So, we know that there is a kinetic factor here that actually does not allow for the diamond to graphite transition to take place.

So, that was about reconstructive phase transitions. Now, similarly, we can look at displacive phase transitions. In the case of a displacive phase transition, it is a distortion of the bonds only, rather than a breaking of bonds.

The structural changes are usually very small, and this is what makes the field of phase transitions very, very interesting and exciting because in many transformations of the displacive type, there are minor atomic rearrangements in the crystal structure. The magnitudes of the distortions are very small. Nevertheless, one form converts in a facile way into the new phase.

Also, because these are dispersive phase transitions, there exists a structural relationship between these forms. For example, we can consider SiO2, silica, which exists in different polymorphic forms like quartz, tridymite, and cristobalite.

So, quartz, tridymite, and cristobalite are the different forms of silica, and the conversion of one form into another involves displacive phase transitions. So, these essentially involve the distortions of the SiO4 tetrahedra. So, tetrahedra are the building blocks in the silicates or SiO2; first is how these tetrahedra are arranged, and then how you can actually distort these tetrahedra by making them undergo rotations because of the formation of the silicate chain.

They can undergo distortion by rotation of the silicate tetrahedra and give you different crystal structures, different crystalline phases of silica without the necessity to break and make new bonds. Let us look at one particular figure that illustrates the displacive phase transitions. For example, we have this kind of structure. Ok. And all you need to do is rotate, and that constitutes a displacive phase transition where you essentially now get.

So, you have this kind of arrangement. So, all you need to do is buckle the layers a little bit, distort some of these layers including rotating some bonds where you can rotate them along this direction, shear them along this direction, shear them along this direction, and this kind of displacive mode will result in giving you a new structure, a new rearrangement, a rearranged structure that has a different structure compared to the starting phase, and these are referred to as displacive phase transitions.

So, this constitutes Buerger's classification of phase transitions, and the fact that these are of two types. Now phase transitions are of different orders. We can have phase transitions that are of the first order, we can have phase transitions that are of the second order, and there is a change in the magnitude of the thermodynamic quantities when you look at these phase transitions.

And now in the next lecture, we will be looking at the thermodynamic classification of phase transitions, focusing on first-order and second-order phase transitions and how you characterize these, which are very important for understanding the relationship between polymorphs.

Thank you.