Fundamentals and Applications of Supramolecular Chemistry
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Lecture 48

W10L48_Supramolecular Amphiphiles-Structure and Applications

So, hello, everybody. Now, let us continue the discussion on the topic of micelle formation.

So, in the previous lecture, we were looking at the formation of micelles and the formation of different kinds of architectures involving the existence of amphiphiles.

Now, we are going to move on to the next topic, where we will look at the supramolecular association of individual amphiphiles, which, in turn, form a micelle that exhibits micelle-like properties.

So, now we are not really worried about a particular molecule, a covalently bonded backbone that has, say, polar heads and a non-polar head.

We are not going to talk about such specific amphiphiles, but now we are going to talk about an amphiphile that actually supramolecularly interacts with another amphiphile, and then this resultant structure exhibits micelle formation, vesicle formation, and so on and so forth.

So, now we are going to look at supramolecular amphiphiles and the resulting structures and topological connectivity of supramolecular amphiphiles. I have designated it as SA, and we have already seen that conventional amphiphiles have very complex aggregation pathways, and the same thing also holds for supramolecular amphiphiles.

And there is a very big library of both small molecules and polymeric supramolecular amphiphiles that are actually connected by NCIs, which I refer to as non-covalent interactions. So, now let us look at the different types of supramolecular amphiphiles.

Number 1 is the side-chain amphiphile, in which there is a hydrogen bond between the hydrophobic and hydrophilic portions of the amphiphile. So, let us now consider an example: There is a donor here, and here we have an acceptor.

So, this is the acceptor A, and this is the hydrophobic end; this is the hydrophilic end of the amphiphile, and now there exists hydrogen bonding between the donor and the acceptor. The donor comes from the hydrophobic portion of the amphiphile, and the interaction is with the acceptor, which is the hydrophilic portion of the amphiphile, giving rise to this side chain amphiphile. So, this is the first classification of supramolecular amphiphiles.

The second one is the double-chain amphiphile, where we have an amphiphile that has a donor region and an acceptor region here A, but you see it has a double chain. And they are now non-covalent interactions between the donor and the acceptor regions.

That is, there exist supramolecular interactions between the head and tail regions of the amphiphile. So, this is the head, this is the tail, this is the head, this is the tail. So, there exist now supramolecular interactions between the head and the tail regions of the amphiphiles.

The second, the third one is referred to as a bola form. The bola form has two hydrophilic head groups at the end of the hydrocarbon chain. So, if you look at the covalent connectivity only, it refers to the presence of two head groups, and these are connected by a hydrophobic chain. Thus, this constitutes a bola form. So, we have these two hydrophilic head groups that are connected by a hydrophobic alkyl chain.

We also have the corresponding supramolecular equivalent, where we can have the donor and the acceptor interacting via specific NCIs to give you the BOLA form. And when such an association takes place, these are referred to as BOLA amphiphiles.

They constitute a supramolecular linking arrangement, a supramolecular connectivity. Thus, this is referred to as a bola amphiphile, where you have supramolecular connectivity and two amphiphiles are connected by a supramolecular linking arrangement.

For example, we can have, this is the polar part; we have the acceptor, we have the donor, and then we have another donor compartment.

This is the polar part, and there are specific interactions between the donor and the acceptor to give you the bola amphiphile. The fifth one is referred to as the Gemini amphiphile, where we have got two surfactant molecules that are linked at their charged head groups.

So, the head is actually charged, and the surfactant molecules are linked at the charged head group. For example, let us take this particular amphiphile; this is positively charged, and this is negatively charged. So, there exist electrostatic interactions between these two surfactant molecules at the charged head groups; they are referred to as Gemini amphiphiles.

We can have another arrangement, where we have a positive charge and then there is a negative charge, which kind of insulates the positive charges, and this gives rise to a Gemini amphiphile.

And in all these cases of supramolecular association, it is the hydrogen bonding, the electrostatic interactions, the charge transfer interactions, or halogen bonding that stabilizes the supramolecular assembly.

And these supramolecular amphiphiles are of a highly tunable nature, and you can also reverse this phenomenon of association because of the dynamic nature of NCIs. So, the supramolecular amphiphile formation is both dynamic and reversible, keeping in mind that the interactions involved are non-covalent interactions.

So, with this background of supramolecular amphiphiles, let us take up some specific examples that represent the supramolecular amphiphiles.

For example, we will look at a complex that is formed between melamine and the quaternary salt of isocyanuric acid. And this particular supramolecular amphiphile was designed by T. Kunitake at Kyushu University.

So, let us look at the structure of this particular supramolecular amphiphile. So, now you can see the extensive hydrogen bonding that exists in this particular region, which is possible through N-H...O and one N-H...N hydrogen bond. So, this particular supramolecular amphiphile forms a transparent dispersion in water and gives a disc-like aggregate.

So, it has a disc-like aggregate and forms an ordered bilayer structure. Now, let us go to the next example. The next example: We will now look at the formation of a BOLA amphiphile. So, we are starting here with a plus in the vicinity of this aldehyde group; we now bring in an amine group. So, you see that the ends are positively charged, and if it were a pure covalent backbone, that would be a conventional bola amphiphile.

But now, that is what we are going to do: we are now going to form the covalent bond, and this depends upon the pH of the solution under pH-controlled conditions. More specifically, under basic conditions, it will form the corresponding imine.

And we have the positive charge here. So, this gives rise to a covalently bonded bola amphiphile. Under acidic conditions, we know that the imine bond is very sensitive to pH, and if you lower the pH of the solution, making it acidic, then it will again go back to the starting materials due to the breakage of the -C=N- bond.

And this particular property, where the C=N bond formation is controlled by the pH, can be used to deliver a drug, for example, in cells that thrive in an acidic environment, such as cancer cells.

So, in the case of cancer cells, the drug release at low pH can be performed, and this bola amphiphile has been known to form micelles in water. So, it forms micelles in water, and these micelles can now carry the drug molecule because the drug molecule has hydrophobic portions.

So, the hydrophobic portions interact with the micelles, and then the drug is transported. Wherever the conditions are low pH, which means acidic conditions, it breaks this particular -C=N- bond, and the drug can be released.

So, you have the micelle. And then you have the drug impregnated, the C=N bond breaks, the micelles are disrupted, and the drug can be released at the site of action. So, depending on the pH, we can control the C=N bond formation, and that can be utilized in drug delivery processes.

The third example we would like to take is a Gemini Amphiphile, considering 13 carbon atoms. So, we consider this particular Gemini Amphiphile, which now has positively charged head groups connected by a covalent backbone.

And this particular entity forms foams. So, if you take it in a vial, it will form foams in water. Therefore, it will be all white foams that it forms, and in the presence of cucurbit-[7]-urils, which are actually cylindrical, tub-shaped molecules. What these cucurbiturils do is separate the hydrophobic chains from each other to form these kinds of entities. So, the interactions are prevented.

So, this particular aggregation between the side chains, which was giving it the desired stacking property, is now prevented. These side chain interactions do not take place, and this increases the solubility of the amphiphile and prevents foaming.

So now you get this container, a transparent aqueous solution of the Gemini amphiphile. So, now the solution becomes transparent, and then you can actually reverse the process. Again, you can actually disengage these cucurbiturils by the addition of 1-adamantanamine hydrochloride.

So, if you add this particular compound, it will reform the starting material, which again starts foaming. The addition of this adamantamine hydrochloride is now able to capture these cucurbiturils very efficiently and then release this Gemini amphiphile, which again starts forming foams.

And this particular Gemini Amphiphile was developed by Zhe Zhang from Tsinghua University in China. Another example I would like to discuss here is the formation of reverse vesicles using pnictogen bonding. We now have antimony 3 salt, and it forms 1, 2, 3, 4, 5, 6, 7, 8, so there are 9 carbon atoms.

So, we have 9 carbon atoms, and this particular surfactant forms reverse vesicles, where the polar parts stick to each other and the non-polar parts are inside, with the non-polar parts on the outer side. So, we have the non-polar part, the polar, and then normally we have the non-polar and the polar in a typical vesicle. Here we again have the polar part sticking to the interior and the non-polar part protruding out into the exterior. So, the exterior and the interior have the non-polar hydrophobic part. This is referred to as a reverse vesicle.

So, via these nitrogen bonding contacts, it is able to form the reverse vesicles, and how does this happen? We have the non-polar part, and we have the antimony, and then the antimony is able to engage; we have another antimony here.

And so, this is able to engage in short contacts; similarly, this antimony is also able to engage in short contacts, and then this will continue here. So, this kind of pnictogen bonding contact can lead to the formation of these reverse micelles.

And then, we have already learned in the previous lecture that sonication can lead to the formation of these SUVs, which are the short unilamellar vesicles, which are actually analogous to inverse biological cells. So, as we looked at in the previous lecture, these small unilamellar vesicles can be formed by the process of sonication.

Here, we can also perform the process of sonication, and we can generate the inverse biological cells. So, with this background, we can now look at some of the important applications of these amphiphiles, and in this regard, it is important to first prepare the Langmuir-Blodgett film, which contains the monolayer formation, and then on this monolayer, you can put the next layer, which will form the bilayer. In this way, you can actually increase the orientation of these surfactant-like molecules at the water interface. So, how do we do that? We essentially have, what we take is a trough of water. We have the water molecules here, and we put in a substrate.

We will see that the surfactant molecules will start sticking to the surface. Now, you have a solid surface; this is the monolayer. At this point, you will see that you have the surfactant, the water, and the solid phases. This is called a three-phase contact. And now this is being pulled at a certain rate; this particular solid is being pulled at a certain rate.

So, when it is being pulled, the surfactant molecules now start forming the monolayer on top of this particular solid surface. The solid surface can be made of silicon, other metals, or all metal oxides, so it is polar, has an electropositive character, and therefore can interact with the polar regions of the amphiphiles of the surfactant molecules.

And this is the aqueous layer, which has been confined to this particular trough, and now once you have formed the first monolayer, you can again bring this monolayer in contact with this trough, which contains the surfactant molecules, and now the hydrophobic parts will stick to this particular monolayer and form the bilayer.

So, in this way, you can actually create a new monolayer, and this leads to the formation of a bilayer coating. In this regard, you will be able to create highly ordered structures where you are controlling the degree of orientation via molecular tuning of the hydrophobic chains.

Now, this particular technique was developed by the scientists, namely Langmuir and Catherine Blodgett, and therefore, this process is referred to as Langmuir-Blodgett film. So, this Langmuir-Blodgett film has now been applied to understand different interesting processes that happen at the interface.

Because these processes happen at the interface and involve the presence of self-assembled monolayers, we refer to these as surface self-assembled monolayers. That is, we call these SAMs, and the surface SAMs, which contain densely packed hydrophobic chains and are also constituted of an ordered structure, can now be utilized to do some interesting chemistry at the interface.

We compared these interfacial processes, and the rates are different; for example, different reactions at the interface occur in comparison to a process happening in the bulk.

In order to understand the effect of the interface on a particular property, for example, any chemical reactivity of a particular chemical reaction, these interfaces have been extensively utilized to understand different processes happening at the interface. This field was first developed in 1989 by George Whitesides.

And we have already heard about some of the most important applications, where we have assembled thiol molecules containing sulfur on the gold surface because of the favorable gold-sulfur bonds. These monolayers are able to align themselves on the gold surface, and then different chemical processes can be investigated.

Now, the thickness of the layer that is formed is equal to one molecule's thickness, and this thickness depends on the layer thickness, which depends on the length of the molecule and the contact angle the axis makes with the surface.

So, let us see this. We have now got a gold surface. We have got a sulfur-containing alkanethiol. Now, this is the layer thickness D, and this is the contact angle it makes with the surface.

And normally, the strength of these gold-sulfur interactions is comparable to that of hydrogen bonds; therefore, these thiol molecules are able to assemble in a very clean manner on these gold surfaces. Now, when this process of self-assembly takes place, there are some interesting steps; this does not happen in one step.

There are interesting sequences of steps that take place. Let us look at those two steps. Number one, the first step is the fast step. I am putting it in quotes and it takes minutes to achieve 80 to 90 percent thickness, as well as the magnitude of the contact angle.

This is the first step. So, this is the diffusion-controlled step. In the second step, which is a very slow step, it takes hours during which the final thickness and contact angle are reached. That is, it is only after a period of at least 24 to 48 hours, or 1 to 2 days, that this process is complete.

The final value of the thickness, or the converged value of the thickness, and the contact angle will be reached, involving the process of ordering and packing of the hydrophobic chain into a clean self-assembled monolayer on the surface. And when these steps are taking place, what is happening at the molecular level? Why is the first step very fast? Because it involves the formation of a large number of these gold-sulfur bonds.

So, the formation of this large number of stabilizing gold-sulfur bonds makes the process of coverage 80 to 90 percent complete. This is the interaction between the sulfur and the gold interface. And in the second step, what happened is actually the side chain interactions, the interactions between the hydrophobic chains, that need to accommodate all possible favorable contacts, so that we have a packed, tightly packed structure and overall dense and firm packing.

So, it is the interactions between the organic chains, the side chain interactions, that occur in the second step. So, this relates to the creation of a very, very favorable surface, and now these kinds of surfaces have been prepared and different kinds of applications have been performed.

For example, people have looked at modified phthalate units, where they have put different kinds of functional groups. For example, a redox probe allows you to study the redox properties between the gold surface and the receptor, which is a redox unit. You can also put different kinds of donor atoms on this hydrophobic chain and then study different kinds of binding affinities of anions, etc., and a whole new chemistry can be performed. And just to appreciate this particular aspect, one last example I would like to share with you.

So, we can now say, for example, we have a ferrocene unit, and we have now connected it with N-H, and here we have connected it with C=O. So, this is connected to the surface here, and now we can actually have the ferrocene unit; it contains iron.

So, we can now study the process of electron transfer, or the redox process, from the ferrocene to the gold surface. And we now put in an anion; the binding of the anion takes place, and the affinity is increased.

So, why is this affinity increased? Because if you were to consider the binding in the absence of the gold substrate, you would see that the sulfur-containing rings have conformational flexibility; they move a lot, and therefore the anion binding processes are weak.

But now, when you have assembled this particular unit on this gold surface, this ordering of this ligand leads to enhanced anion binding efficiency by several orders of magnitude in comparison to those receptors when you do not have the gold surface. And now, you can actually study the redox process, which will be different in the presence of anions compared to the case when you do not have the anions.

So, redox processes, anion binding affinities, and the enhancement of these anion binding affinities when you actually template the ligand on the gold surface form these favorable gold-sulfur contacts and therefore result in the pre-organization of this particular ligand by the modification of the surface to have enhanced binding affinities.

So, this is a very interesting application of self-assembled monolayers. So, with this, we can now close the discussion on this particular topic.

In the next lecture, we will go on to another fascinating class of molecules, which are called liquid crystals, and we will further look at their characteristics and properties.

Thank you.