Fundamentals and Applications of Supramolecular Chemistry
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W11L54_Principles and Applications of Supramolecular Photochemistry

So, hello everybody, today we are going to continue our discussion on supramolecular photochemistry.

So, we saw in the last lecture that the co-crystallization process using 1,3-dihydroxybenzene is able to bring the double bonds in bis-4-pyridyl ethylene into close proximity, and now, upon irradiation, they are able to undergo the [2+2] cycloaddition reaction to give the photo dimer.

Along the same lines, people have now used thiourea as a template to achieve the [2+2] photocyloaddition reaction. So, let us now look at this dimerization process where thiourea serves as a template. We have the 2 N-H bonds, and this forms an N-H...N hydrogen bond.

So, you see here that the thiourea molecules themselves form this hydrogen-bonded tape structure. Now, the next set of these molecules, which are going to come close to each other, and on irradiation, there will be photodimerization of the double bonds to give you the photodimer.

So, we can now pre-organize these reactant materials into suitable geometrical orientations so that the dimerization can take place in a facile way. The double bonds are now in close proximity; the separation is between 3.5 and 4 angstroms, the desired distance is achieved, and hence dimerization proceeds.

Now the next thing that we need to keep in mind is that the environment being created, or the template being created, is able to bring about certain reactions that otherwise do not take place in solution. So, most of these active species that contain isomerizable double bonds do not undergo cycloaddition reactions in solution.

However, when they are actually brought inside a reaction template, the reactant molecules come close to each other, and they are able to adopt the right orientation, allowing the dimerization reaction to proceed in a facile way.

When this work was performed by Gerhard Smith, he also proposed the concept of minimum movement of the molecules during the process of photodimerization. So, when the dimerization process is taking place and product formation is happening starting from the reactants via a particular transition state, which involves the activation of the molecules in the ground state by light taking them into the excited state, the reaction occurs and then product formation takes place.

During this entire chain of events, there may be changes in the shape of the molecule. If the shape of the molecule is large, then the lattice might not be able to accommodate this change, and product formation might not take place.

However, the product formation happens in a way that the final product involves minimum change in shape, and the final shape is able to be nicely accommodated in the whole structure of the parent lattice; then the corresponding reactions will proceed in a facile way.

So, the environment has a very important effect on bringing about these cycloaddition reactions of photodimerization. Let us look at the effect of the environment, for example, when you have a reactant molecule. It will give you the products, P1 and P2; say one is P1 and one is P2, of different shapes. So, the shape change can take place, and there is no problem in the gas phase.

In the solution phase, you have the reactant molecules and the solvent molecules. We can have this as the product, and we can also have that as the product. The solvent molecules can now change orientation; they can relax quickly.

So, the relaxation of the solvent can happen, and this allows for product formation in the liquid phase or the solution phase. Then, when you have a solid, the solid has a well-defined architecture; for example, the crystal structure has finite voids, and now you have the reactant molecule here.

There are two possibilities; for example, because the void is the same, it can change shape to this one. Okay. This change will not be accommodated because here you see that the shape becomes sufficiently large that it now creates sterics between the boundary of the template, which is the boundary within which the reaction has to take place. If the boundary is crossed, it puts a lot of stress on the crystalline system; therefore, this product formation does not take place.

Only this particular product, say for example P2, is formed; P1 is not formed, and therefore this rigid environment only allows certain shape changes.

This enclosed space is referred to as the reaction cavity. The enclosed space is referred to as the reaction cavity, which is the volume available within which the reaction is supposed to take place. This size is small in the case of crystals and cyclodextrins, which have intrinsic voids, and the size is large.

If you have micelles, zeolitic structures, or silica, which are large three-dimensional molecules, what has been observed is that if you have an isotropic liquid, then the free volume available is mobile. It is like a mobile phase; the solution phase is a mobile phase.

However, in crystals or organized media, it is essentially immobile. Thus, we have a limitation in terms of the free volume that is available. Let us look at this particular representation. We have the reactant molecule. So, this is the free space, the free space that is available for the reactant molecules to interact with each other.

This is the boundary that cannot be exceeded; this region is outside, and this is inside the reaction cavity. This is the overall diagram depicting a reaction cavity. Whatever you see here now, this region, which you see here, is the free volume.

In this case, you can see that the size of the free volume is important and what the overall shape of the free volume is. In this case, it is more like a spherical free volume shape, but this spherical shape can also change as a function of the template that actually creates the reaction cavity.

So, we have this boundary. We have a template that is created for the reaction to take place, and this defines the reaction cavity. So, it is also to be kept in mind that during the process of supramolecular dimerization, particularly in crystals, there will be minimal atomic motion.

If the atomic motion is large and the distortion is severe, then the product formation will not take place. However, if the product formation involves minimal atomic motion or minimal rearrangement of the positions in the final product, the reaction proceeds in a facile way.

So, the free space or the free volume allows for the necessary tolerance to be present in the system for the chemical reaction to take place, and this model is referred to as Cohen's reaction cavity model. Cohen was a scientist with whom Gerard Smith was working, and after the untimely death of Gerard Smith, it was Cohen who actually took his work forward.

He then started looking at the overall features of supramolecular reactions and proposed this reaction cavity model. So, in crystals, we see that the free volume is essentially immobile, whereas in isotropic liquids it is mobile. Therefore, in crystals, the template is

of a very rigid and organized nature.

Whereas in the case of micelles and all liquid crystals (LCs) that we have discussed, these have flexible structures, and free volume may become available as the reaction proceeds. So, it is to be kept in mind that this free volume also has to be optimized.

If you have a lot of free volume and a lot of free space, like you have in the case of gaseous reactions or in the case of liquid solution phases, then you might not get the desired selectivity. At the same time, if the void space, the free volume, is very small, confinement will not happen, and the reaction will not take place because there is no free volume available.

Now, depending upon whether we have a rigid and pre-organized cavity or whether we have a flexible cavity, we can define reaction cavities as hard and soft reaction cavities.

Therefore, crystals and zeolites have the hard reaction cavity, but micelles and liquid crystals have the soft reaction cavity. Similarly, we have a proposal for a time-independent reaction cavity, which essentially does not change its shape during the process of the reaction.

So, as the reaction proceeds, the overall shape of the free volume, the cavity that does not change its shape, changes during the process of product formation. So, the free volume cavity remains fixed as the reaction proceeds. We have, for example, this is the reaction cavity, this is my reactant, and this is the available free volume of the cavity.

During the process of photochemical irradiation, we will see that the product formation has occurred, but the free volume of the cavity remains the same. So, in other words, this cavity-free volume is intrinsic to the supramolecular system, whereas in the case of micelles and liquid crystals, we have a time-dependent reaction cavity where we initially might have, for example, the spherical free volume. This is the reactant.

And in the process of the photochemical reaction, this is fixed, but now you see, the shape of the free volume changes to accommodate the product. So, it was spherical here, but here it becomes less spherical, more of an ellipsoidal type of cavity.

So, the reaction cavity is now quite flexible; it is soft and able to accommodate the changes that happen during product formation. So, that is what makes it flexible, and that is why we call it "this is latent", that it is available, as per the requirement of the reaction. So, this is a latent cavity; that is, the cavity, or the free volume, will be available as the reaction proceeds.

And that is why the nature of this cavity is soft or flexible, which can accommodate the product very well due to changes in the shape and size of the product. The cavity is also flexible, so the free volume can change depending on the changes in the shape of the cavity as well.

In one case, it is intrinsic; in another case, it is a latent cavity, which is available as per the requirement of the reaction. And then there is another categorization of cavities; we call it the passive reaction cavity, and we have an active reaction cavity.

So, here in the case of a passive reaction cavity, you see we have the host structure, which is either the crystal or the supramolecular host-guest complexes. The interactions are weak and non-directional. Or practically, you can say that they do not exist.

There are not many important non-covalent interactions between the guest and the reaction host. Whereas, in the case of the active reaction cavity, there exists strong and directional interactions, between the guest and the host template, and this can actually influence the reaction outcome in profound ways.

So, now we are going to look at some important applications of the reaction cavity model, which is able to bring about certain photodimerization reactions. So, the next example is the dimerization of coumarin. Coumarin, if you look at the crystal structure and the orientation of the coumarin molecules, shows no photo reaction upon photoirradiation in the crystal.

So, it is a photostable molecule. However, when you actually template it with this chiral compound, on irradiation it will give you the chiral product. So, you see here that now this is the bottom part, and this is the top part. So, we have now got the anti-head-to-head arrangement. So, you see that these are anti to each other, and the head parts interact and form the photo dimer.

So, what does this chiral molecule do? This chiral molecule actually creates a hydrogen-bonded template, which brings the coumarin molecules in close proximity to each other, and they interact through pi-pi stacking interactions, which are favorable here, dispersive interactions, and then photoirradiation is able to create the photodimer.

So, this can actually provide the necessary template by which the coumarin molecules can undergo photodimerization. Now, let us take another interesting reaction, where we look at performing chemical reactions in micelles. So, we would like to look at this particular reaction. Upon photoirradiation, these two possibilities exist.

I call it product A; I call it product B. This is 3-en-butyl cyclopentanone. This is my heptenyl acetate. Now let us look at the reaction conditions and yields. So, when you do

it in methanol, this particular reaction produces 0 percent A and 100 percent B.

When you do it in cyclohexane, it is 0 percent A and 100 percent B. But when you do it in the presence of a micelle, that is, a potassium dodecanoate micelle, you get 70 percent of A and 30 percent of B.

So, you are now able to access product A, which is actually not formed at all when the reaction is performed in methanol or in the case of cyclohexane. So, there is a very profound role of the micelle. We know that a micelle is a species that has a polar head and a non-polar part.

The polar head is what is being solvated in water, and the non-polar head is buried deep as a hydrophobic interior. So, how does this reaction proceed? The reaction proceeds by bringing in the polar reactant molecules.

So, you have the polar parts, and you also have the non-polar parts. The non-polar parts of the reactant molecules are now buried within the hydrophobic code, whereas the polar parts are now brought into close proximity at the hydrophobic-hydrophilic interface.

So, we now have this micelle here. You say this is the surface of the micelle, and we have the surfactant molecules here. This is my surfactant molecule, and this is my hydrocarbon chain; you can have, say, another one here, and now my reactant molecules, assuming in this particular micelle.

So, the reaction template or the reaction cavities, provided by the micelle here, and I am now going to add. So, this is my n-butyl chain, and I also have the statistical possibility of another one here; then I can have another one here. Now, you see here that these two come close to each other and have the right orientation at the hydrophobic interface, and this is the hydrophilic interface.

So, these are the polar parts, which are actually solvated in a polar solvent, as we know. So, the micelles, which are present, the potassium dodecanoate micelle, now at the hydrophobic-hydrophilic boundary, will react with each other to give you this particular product. So, you can see the double bonds, and the OAc and the carbonyl group are syn to each other, and that gives you the desired A product in 70 percent yield.

So, this orientation effect at the interface is brought about by these micelles, which allow the chemical reaction to proceed in a very facile way. And thus, micelles, which are actually supramolecular aggregates stabilized by hydrophobic as well as hydrophilic interactions, steer these chemical reactions at very preferred rates, and the yield is actually enhanced as well.

So, you are able to get those products that are actually not achieved in other solvent systems. Now, let us take another example: another very interesting example of photodimerization in the solid state, in the case of cinnamic acid. So, we will compare the photodimerization in the solid state with aqueous solution. Ok. So, we will now see that in the case of cinnamic acid, when we do irradiation in the solid state, no dimerization is observed.

However, when you irradiate in aqueous solution, it undergoes cis-trans isomerization, where R is equal to the phenyl group. When we actually have a host, in this case, we are using cucurbiturils-8, and do the irradiation in aqueous solution, we are able to obtain the photodimer in aqueous solution, but we also have the cis-isomer, and this is a head-to-head alignment.

So, cucurbiturils actually give the desired molecular template by which cinnamic acid is able to orient itself inside the cucurbituril, which is actually functioning like a supramolecular barrel here, providing the necessary confinement to the molecules, allowing them to come close to each other, and the dimerization proceeds in a facile way. Let us look at this.

We have got this barrel-like structure. We have the carbonyl groups that are present on the cucurbiturils, and we now have our reacting molecules. So, you see that there are hydrogen bonds, O-H...O hydrogen bonds in this particular region, and these are essentially stabilized by hydrophobic interactions.

Now, see this very nice architecture. Both hydrogen bonds and pi...pi stacking interactions orient the molecules, which actually promote the head-to-head alignment of the molecules. So, the head-to-head alignment of the molecules, where the carboxylic groups now face each other, is stabilized by strong hydrogen bonds.

So, as I was telling you in the previous case, there can be an active cavity; there can be a passive cavity. So, this is an active cavity where there are strong hydrogen bonds, and it will interact with the host template, which will pre-organize the reacting molecules, and then you will have the dimerization.

So, the hydrogen bonds and the pi-pi stacking interactions orient the molecules, but it is actually the hydrophobic effects that stabilize this entire dimer inside the molecular vessel. So, you also have the role of hydrophobic effects, which are stabilizing these pi-pi interactions via the hydrophobic walls of the host structure.

So, this will lead to facial dimerization, and now you can put different substituents R here, where R is equal to 4-methoxy.

The percentage of dimer in cucurbiturils (I am writing it as CB) and the percentage of the cis product are 72 percent and 28 percent. When it is 3-OMe, it is approximately 72 percent, and when it is 2-OMe, it is 83 percent, which is 17 percent.

So, this is what has been reported in the literature: that we are able to achieve this photodimerization in aqueous solution in the case of cinnamic acid using cucurbiturils as a pre-organized host structure into which the molecules go, and in the reaction cavity, the reaction takes place.

The photodimerization takes place, which is templated by the active interactions, and hence the product is formed. So, in the next lecture, we will look at some more interesting case studies where this cavity plays a very important role.

We will also see, in some cases, how, because of the cage effect, unusual or unstable intermediates can now get stabilized for extended periods of time.

We will also look at some more interesting reactions that take place by photodimerization to form more interesting organic molecules.

Thank you.