Fundamentals and Applications of Supramolecular Chemistry
Deepak Chopra
Department of Chemistry
IISER Bhopal
Week 11
Lecture 53

W11L53_Applications of Molecular Barrels, Self Sorting Process

So, hello everybody. Now, let us continue our discussion further into the area of supramolecular reaction vessels. So, in the previous lecture, we looked at the enantioselective transformation, which was achieved using Fujita's octahedral cage, where the cage has been modified by introducing a chiral center in this particular cyclohexyl part. Because of the presence of chirality in this fragment, the overall cage provides the necessary chiral environment.

This is the first example of a coordination cage that is applied for an enantioselective reaction and allows for the [2+2] cycloaddition reaction using this set of reactants. So, this success with supramolecular cages has led people to decide to make supramolecular reaction vessels or these kinds of nanocages of larger dimensions, which also have broader architectures.

Instead of looking at triangles, people started looking at extended triangles, prismatic cages, larger prismatic cages, and square barrel-like structures by modifying the ligand backbone.

So, the modification of the ligand backbone became an important prerequisite to form these kinds of 3D barrels, which have more surface area available for effective encapsulation of the guest or substrate molecules to achieve the desired transformations to the products, given a set of reactants. So, now let us go to the next molecular barrel, which is actually a 3D barrel. In this regard, the following ligand has been taken.

This particular ligand has been considered. Now, we have these donor nitrogens that are available. So, we have got 1, 2, 3, 4, 5, and then these are the ones that can coordinate to the palladium centers. And the palladium part has this particular arrangement. So, we have the palladium center, which is the 2 plus, and this will lead to the formation of a barrel-like structure.

So, you can have coordination from palladium. So, we can have 1, 2, 3, 4, 5, 6. So, we have this particular ligand, which is called the tetra-imidazole-based tetraphenyl ligand.

It forms this kind of 3D barrel structure, where now you can see that these are the large π-surfaces available for interacting with the reactant molecules. And these have large pi-surface areas, allowing the reacting molecules to enter.

We can have chemical reactions that take place in these 3D barrels, and this particular 3D barrel, which I am referring to as H, now. So, you can see here that this particular surface is present, this particular surface is present, and the back surface is present.

So, we have this 3D barrel, which is used for the synthesis of xanthenes and tetralones, using this 3D barrel as a supramolecular catalyst, and this is a case of homogeneous catalysis. So, what are the reaction conditions? Now, we are going to consider the reactants here. This is one reactant plus this is the other reactant, and in the presence of this molecular barrel, H, 5 mole percent, and water, it gives rise to this product.

So, this is the tetra ketone, but it also forms the corresponding xanthene. This happens because of the intermolecular cyclization, and the water molecule that is formed in this reaction can easily be expelled because of the hydrophobic cavity.

So, that drives the reaction towards the right-hand side. And because we got both the products, the idea was to now obtain complete conversion of tetra ketones to xanthene. Then the reaction was performed at 60 degrees centigrade, which is at a relatively high temperature, and that led to the formation of 90 percent xanthene.

It is also important to keep in mind that during this reaction, the anion is generated at this particular site, which actually performs a reaction: the nucleophilic attack at the carbonyl reaction center. So, these kinds of anionic centers are also stabilized by interactions with Pd2+ centers, which are present in these 3D barrels.

So, these anions can be stabilized in the 3D barrels, and then the reactivity is enhanced by reaction with the electrophilic center. And it has been observed that this particular reaction does not take place in the absence of a catalyst, again demonstrating the versatility of this particular 3D barrel structure.

So, now you have modified the ligand backbone by creating this tetra-imidazole-based tetraphenyl ligand, a particular scaffold that facilitates this reaction.

Keeping this in mind, further modifications were made to these barrel-like structures, where people have now modified the ligand backbone further. So, they were now able to make this particular barrel.

This particular ligand was used, along with ferrocene, and we have the connection to PPh2Pd(OTf)2. In the presence of dry nitromethane for 3 hours at 50 degrees centigrade and in a nitrogen atmosphere, we were able to obtain this tetra-facial molecular barrel structure. We call this barrel G.

Now you can see that there are large π surfaces and therefore, it was useful, as it catalyzed an intermolecular Diels-Alder reaction. Let us see what the reaction is now. So, we have this particular substrate.

So, we have the diene part here. So, you can see very clearly that we now have the positioning, we have these 4 pi electrons, we have the 2 pi electrons, and they are in relative proximity to each other.

So that they can undergo reaction in the presence of 10 mole percent of the reaction barrel G, and when heated, it will give rise to the desired product, where you will now have the dimerization taking place.

So, you will have hydrogen here, you will have the hydrogen here, so you will have the cyclization here, and then this will lead to the formation of the product. So, you will see that the [4+2] cycloaddition reaction takes place. Once we have the cycloaddition, the product is formed, and we have this cis-fused product. The trans-fused product is also formed, but it is in a minor quantity.

So, when you take this substituent, which is benzylidene barbituric acid, and you have the reacting groups that are in proximity to each other, it gives rise to the intermolecular Diels-Alder reaction, and the rate of this reaction is seven-fold higher in comparison to the reaction when no catalyst is present.

So, this again demonstrates the relevance of the molecular barrel. Another interesting example we can consider is a multi-component self-sorted Pd7 nanocage. Now we are going to different kinds of barrels with different architectures to achieve the particular formation of this Pd7 nanocage. So, we consider this ligand as TIM; we call this TIMB; this is actually the 1,3,5-tris-(1-imidazolyl benzene), and TIM is 1,2,4,5-tetra-bis-imidazolyl benzene.

So, this is TIM. So, it forms a barrel-like structure, where the composition of the barrel is as follows: we have Pd 2+, which are 7 units; we have TIMB, which is 2 units; and TIM, which is 2 units, $(NO_3)_{14}\cdot 20H_2O$.

So, this represents a triangular kind of geometry, this represents a square kind of geometry, and I will represent this in this way, and now I need to stitch them all. So, we can do this in the following way. These are the two stitches of the square surfaces, and now I can further stitch the triangle here, and there is another triangle that is stitched here. And we can have the palladium centers 1, 2, 3, 4, 5, 6, and 7.

So, we can now have the stitching here and here. So, 1, 2, 3, 4, 5, 6, and 7. So, you can see that it forms this kind of boat-like barrel structure, where you have these triangles, and here you have the squares.

And this kind of boat-like barrel is referred to as a nano reactor. The nano reactor has been utilized for this molecular boat to perform the Knoevenagel condensation reaction with this particular molecular barrel, which I call F.

And, for example, we have now studied the condensation reaction with aldehyde. We take 12 mole percent of F in the presence of water for 72 hours at room temperature, and we get the product, okay. And Ar here can be phenanthryl, naphthyl, or phenyl.

So, we are able to achieve this Knoevenagel condensation reaction in the presence of this molecular barrel, which we refer to as a nano reactor, and this reaction takes place in quantitative yields to give you the desired products.

So, I hope I have been able to impress upon you the importance of supramolecular reaction vessels in enhancing reactivity profiles, these being very well exemplified cases of supramolecular catalysis.

We now extend our understanding of supramolecular chemistry to probing photochemical reactions, particularly in the solid state, and also compare the photochemical reactions involving supramolecular chemistry and the different non-covalent interactions in solution as well.

So, now we go on to the topic of supramolecular photochemistry, and we have given some introduction to supramolecular photochemistry during our discussion on crystal engineering. And so, we are aware that by utilizing strong hydrogen bonds, we are able to pre-organize the substrates in a certain way so that cycloaddition reactions can be performed in crystals as well. We would now like to continue and extend that argument further. So, to start with, there is a relevance to doing supramolecular chemistry in solids.

Solids provide the necessary environment for the molecules, allowing specific reactions and transformations to be achieved that otherwise do not happen in the solution state. So, there are certain photochemical reactions that can go to near completion, provided the reactant molecules are brought into the right orientation, and the right kind of environment is given to them, such that after the reaction takes place, if there is any change in shape, then there must be sufficient free volume also available for the product to be effectively included within the crystalline environment.

Because here we have a very tightly packed crystalline environment, the formation of the product can lead to changes in the three-dimensional structure that might require more space; therefore, the necessary volume must be available. Otherwise, it will be a highly strained system, and the product formation might not take place.

Another important advantage of the solid-state environment is that when there are certain reactive molecules, for example, certain molecules that form free radicals in the gas phase, and these free radicals are reactive, they can also be stabilized inside this kind of solid-state environment or supramolecular cages where the lifetime of these free radicals can be increased.

And because the molecules are now able to come into close proximity, we can actually promote phosphorescence and other luminescent processes of the molecules in the solid state, and these can be observed at room temperature.

And also, we can bring chirality into the molecule because we are now able to perform the cycloaddition reactions by making prochiral centers come close to each other, performing the chemical transformations, and creating the necessary chirality in the final structure via this solid-state environment.

So, to start with, if you consider a molecule AB that has a double bond and we shine light, then in solution, a large number of isomers can form. For example, we can have this as the product, we can have this as the product, or we can have this as the product. In total, there are 12 possibilities that exist.

So, there is no control over the reaction because you can have dimerization in so many possible ways. But now, if you want to control this particular dimerization process in a specific way, what was proposed by G. M. J. Schmidt was that when you take cinnamic acid and then photo-irradiate it in the solid state, it can lead to the formation of the centrosymmetric dimer, which is called alpha truxillic acid.

Here, the separation between the double bonds is 3.6 to 4.1 angstroms. On the other hand, when you have the beta form, this compound exists as different polymorphs. In the beta form, when the separation is 3.9 to 4.1 angstroms, it will give rise to beta-truxillic acid, and here you can see that there is mirror symmetry, which exists in the final product.

If you have the gamma form, then the separation between the double bonds is longer, and therefore no reaction takes place. Therefore, this particular form is photostable. So, these were the conditions that were very well described by G.M.G. Schmidt as necessary conditions to achieve a solid-state dimerization process.

That means we can have a crystalline environment, three-dimensional structures, or layered structures, where the double bonds are actually not in proximity to each other. So, if they are not in proximity, they will not dimerize.

If the arrangement of the double bonds in the crystal is such that they are not within a certain distance or proximity, then these reactions do not take place. So, the thing was that, okay, can we now modify the solid-state environment?

The modification of the solid-state environment was done by co-crystallizing these kinds of molecules, which have double bonds but do not have the pre-organization or the pre-orientation to bring the double bonds close to each other.

So, can we now utilize some templates that form strong hydrogen bonds with these molecules containing double bonds and bring them into close proximity so that we can achieve the dimerization process?

So, to understand this particular case, first we will consider the molecule trans-1,2-bis(4-pyridyl)ethylene, which we also refer to as 4,4'-BPE. It has been observed that bis-pyridyl ethylene, when it is photochemically irradiated in solution, leads to the cis isomer. So, essentially, there exists trans-cis isomerization in solution.

However, when you take this particular solid and photochemically irradiate it, there is no dimerization because the double bonds are not in proximity to each other to react.

So let us take this particular example. They have to come close to each other for them to react, and this arrangement is not present in the case of the parent compound. That means in the parent compound, it essentially has the gamma type of packing, where the distances are very, very long and therefore the dimerization does not take place.

So, here the distances are greater than 5.7 angstroms long, and therefore, no dimerization takes place. However, if you now co-crystallize this particular compound with 1,3-dihydroxybenzene, then we are able to bring them into position.

So, this dihydroxybenzene now brings these molecules close to each other; the distance is around 3.7 angstroms, and therefore, when you shine light, they undergo photochemical dimerization or the [2+2] cycloaddition reaction. Along the same lines, similar to that of dihydroxybenzene, people have also used thiourea as a template as well.

So, with this, we will stop this lecture. In the next lecture, we will take up more examples related to supramolecular photochemistry.

Thank you.