

Fundamentals and Applications of Supramolecular Chemistry
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Week 02
Lecture 10

W2L10_Compensation involving interactions in close packing of solids

So now let us continue our discussion. The next molecule we would like to look at is the crystal packing of pentane. So we looked at the crystal packing of propane, we looked at the crystal packing of butane and now we are looking at pentane. And in today's lecture we will try to now cover more examples so that we have a better understanding of the principles of supramolecular chemistry because we will now be heading towards the different systems and the applications.

So, with this set of examples you will be able to appreciate that given a molecule you should be able to predict the type of interactions the molecule will participate in and what kind of supramolecular architectures can possibly be present particularly in case of the solid state. So, now continuing our discussion on close packing, we can see the crystal packing of pentane now.

Again, you can see that there are 5 carbon atoms and there are CH₃, CH₂, CH₂, CH₂, CH₃ groups. So, again you have this one layer of molecules, where you can see that they translate along the b direction because this view is down the bc plane and a is perpendicular to the board.

The next layer of molecules again you see has got a slight displacement of the methyl groups such that you can maximize these H...H contacts favorable to close packing and then in case of the third layer again it is a repetition of the first layer where again you maximize these interactions.

So, you can see very clearly here that pentane has got an arrangement which is very similar to that of butane. Now we can go to the next molecule that is the crystal packing of hexane where we are now going to the higher homologues of the hydrocarbons, the alkanes.

So here we can see again 6 carbon atoms 1, 2, 3, 4, 5, 6 and the interesting part about these analysis is that these are all experimentally determined crystal structures that means experimentally this is the way the molecules interact with each other in the solid state.

And again, you can see that there exists, you know a layer of molecules, you see this

constitutes one layer and then this is the next layer of molecules again they are slightly displaced so as to maximize the H...H contacts.

So, you never get to have an opportunity where you have direct face-to-face interaction, rather, they are slightly displaced so that they can minimize the sterics and maximize the electronics and the subtle interplay of the electronics and the sterics is what governs the close packing of molecules.

So, I can write here subtle interplay of sterics and electronics is what governs close packing. So even in case of closed packing you would like to maximize the interaction, you would like to maximize the nucleus-electron attractions via the origin of dispersive interactions and minimize the steric repulsions.

Now let us go to the next case, heptane. So, in case of heptane, you can see, that this is the arrangement of the molecules in the solid state, this is the arrangement of the unit cell, the unit cell is down the a axis that is down the bc plane and here you can see that heptane C_7H_{16} , CH₃, 2, 3, 4, 5, 6, 7 and now you can see this particular arrangement of molecules where again you can see very clearly that the hydrogen is interacting with the carbon, so this forms nice H...C contacts, similar to what you observed in case of propane.

So, you have this particular layer of molecules, this is one layer and then this is the next layer of molecules. So again, you can see that the next layer of molecules approaches the first layer in a manner so as to maximize again here the interactions across the layers. So now you can see these are the H...H contacts.

Now these are the H...H contacts and here you can see that the methyl groups they face each other. The hydrogen...carbon interactions in this particular layer, but you also have the face-to-face CH₃ interactions, you have the H...H contacts between the layers. So, this tells you that the packing between the 1D chain of molecules is such that they try to maximize the H...H contacts between the layers.

So, you have one layer of molecules like this, you have another layer of molecules, they try to interact via the H...H contacts because the hydrogen atoms are the peripheral atoms, also the hydrogen atoms are the smallest in size. So, the atoms are able to approach each other more closely and that is what constitutes close packing.

So, the crystal packing of heptane again is a very nice representation of the interplay of H...C and H...H contacts to give the resulting solid. Now, let us see more examples. Now, this is a crystal structure of butane in a hydrocarbon. So, we have got a very complex hydrocarbon here, you can see that this is a flat planar system here, this is another flat planar system here. You have got butane, which is included in the crystal structure of the

compound of the hydrocarbon.

And you can see that the methyl groups are positioned in a way such that this hydrogen to this carbon separation is around 2.7 angstrom and this hydrogen to this carbon separation is around 2.65 angstrom.

Now these distances are from the crystal structure okay and so that tells you that the hydrogen to carbon distance and the carbon the hydrogen comes from CH this is from the butane and this is from the aromatic hydrocarbon this is from the hydrocarbon and this distance is 2.7 angstrom. And this is fairly close to the sum of the van der Waals radii.

Now because the van der Waals radius of carbon is around 1.7 plus hydrogen is 1.2, so around 2.9. So, this is in fact less than the sum of the van der Waals radii, tells you that there is a close interaction there is a close association and there is a substantially strong approach of the hydrogen towards the aromatic carbon and these distances are quite short.

Traditionally in CH...C contacts lie between 2.9 to 3.1 angstrom, but in this case the distance is quite short. So, this is shorter than the sum of the van der Waals radii, again telling you that CH... pi hydrogen bonds, and also you can see that the C-H...pi hydrogen bonds is quite directional, this is almost 180 degree.

So, although we have studied, we have appreciated that close packing interactions need not be very specific or directional, but in this case, we see that the C...H does try to have directionality with the pi system and that is around 180 degree. So given a chance, given the right environment, C-H...pi interactions can also be highly directional.

They also maximize their interactions with the pi surface. So, this talks about how a non-planar molecule like butane can also interact favorably by CH...C interactions to form the close packing in the crystal structure of this hydrocarbon.

And all these geometrical details can be obtained from the crystal structure determination, the directionality of the hydrogen bonds, the separation between the different non-covalent contacts between the different atoms in the crystal structure, all can be obtained very very accurately from X-ray crystallographic studies.

Now let us go to another very interesting example. These are the case studies to allow us to appreciate what is the role of hydrogen bonding and close packing, particularly dispersive interactions, involving the hydrophobic parts.

So now let us consider another organic molecule which has got a polar part. This is the polar part where the blue atoms are nitrogen, the red are oxygen, the black is carbon, and the greyish black is hydrogen.

This is the C-H, this is carbonyl group and this is N-H. So, it has a strong donor NH, it

has got a strong acceptor CO. So, to start with naturally, it will tend to form a favorable N-H...O hydrogen bond, this is the most favorable hydrogen bond.

So, once a structure is given to you a chemical structure, you must be able to predict the possible hydrogen bonds. That means, which is the most acidic donor, which is the most basic atom, which is an acceptor, so that it forms the strongest hydrogen bonds.

And, now when it forms this N-H...O hydrogen bonds, the polar part cannot interact face to face, so it rotates. So, this molecule as you can see, so if this molecule is in the plane, the other molecule completely rotates, almost 90 degree.

So, the orientation is almost like 90 degree, so this is the N-H...O hydrogen bond. Ok, and it cannot be like this because it is severe sterics. So, it completely rotates to maximize the N-H...O hydrogen bond and the orientation of the other groups now you can see this one is now perpendicular to the plane of the board and this long alkyl chain is perpendicular to the plane of this particular molecule.

So, the molecule which is in the plane is drawn for you, this is the molecule in the plane and this molecule is almost orthogonal to this particular plane. In maintaining this orthogonality, it tries to maintain the N-H...O hydrogen bond.

Now, what would have been preferred is also to have a close association of this alkyl chain with this alkyl chain, but the sterics are very severe because of this particular group. You know hitting each other and therefore the molecule rotates maintaining the N-H...O hydrogen bond because of the energetic stabilization because every hydrogen bond is associated with large stabilization energy and this rotates as a whole.

Now when this rotates as a whole there are there must be factors which also stabilize further this association of molecules otherwise this will not become a solid. So now in the next slide in the next figure I can show you how this dimer. Here, so you can see, this is the dimer which I showed you initially is now interacting with the other molecules. So now you can see here very clearly this is the perpendicular layer. This is in the plane, these are the parallel layers, ok.

And here you can see that the polar part is in the center, this is the polar part, this is the non-polar part, and you can see these are the hydrogen bonds. This is again, you can see there is a N...O contact, this is again hydrogen bond.

So, the polar parts involving particularly N-H...O hydrogen bonds, and N...O contacts. This is by and large present in the center and the nonpolar parts are present in the periphery and you can see that in between, the perpendicular alkyl chains are also present, which come to above the plane of the board.

So, essentially when you have a molecule which is a hydrophobic part, and the hydrophilic part, the hydrophilic part tends to associate together. So, say this is the hydrophilic layer and then you have got the hydrophobic layer. And then this can again repeat with the hydrophilic layer.

So, these layers are alternately arranged, now the hydrophobic layers and the hydrophilic layers telling you that whenever the hydrophilic parts interact with each other and the hydrophobic parts interact with themselves.

Therefore, there is hydrophilic-hydrophobic content present in the crystal structure of the molecule. And when this particular thing happens, it always wants to maximize the interactions which are present.

Now, let us take another example to demonstrate this interplay between hydrogen bonds and close packing. Now, let us look at the crystal packing of palmitic acid. In case of palmitic acid, you can see this is a long chain fatty acid, you can see this is the side chain, and here you have got the carboxylic acid.

So the carboxylic acid has got a carboxylic acid group which we have studied forms a dimer with another carboxylic acid. So the dimer of carboxylic acid which is represented here is also present here, is also present here. Now what is important is to see that this is experimentally realized atomic connectivity in the crystal structure. So, the next layer which is this layer is perpendicular.

So, this layer is perpendicular to the top layer. So, the top layer is like this, whereas the next layer is in the plane of the board, but overall, these two are perpendicular, then the next one comes like this.

So, you can see that the mutual orientation of the hydrophobic part with respect to each other is different and the mutual orientation of the hydrophilic part which is the polar part that is the carboxylic acid group is also different such that they have an orthogonal orientation and when they have this orthogonal orientation, they also maximize their association via this short C...O contact. So, you will see that there is a short C...O contact, this is the top layer, this is the bottom layer, and the separation is around 3.1 angstrom, which is quite short than the sum of the van der Waals radii.

Carbon is around 1.75, oxygen is around 1.5, so 1.75 plus 1.5 approximately I am saying, 3.3 angstrom, which is definitely much greater than 3 angstrom. 3 angstrom is the experimental value of the separation between the carbon and the oxygens and this we also can appreciate because carbon is electrophilic and oxygen is more nucleophilic in nature or having more electron density.

So, there are these nice short carbon...oxygen contacts which stabilize the packing of molecules along this particular direction you can see, and the same thing operates here.

You have this OH...O hydrogen bond and you also have a C...O contact and also when this association takes place you will see that there are favorable interactions between the hydrophobic part. This hydrophobic part and this hydrophobic part you can see the orientation of the CH₂ groups.

They are not face to face with each other, but there is some orientation dependence where they maximize the H...H contacts. Now if you now co-crystallize you now try to crystallize palmitic acid with niacinamide where niacinamide is a polar compound which has got polar functional groups. So niacinamide is represented here. It has got a pyridine-based system, which has got an amide functionality at the three position. So, this is the NH₂, this is the CO, this is the nitrogen. Nitrogen, pyridine nitrogen is a basic, is a basic atom, it has got basic character, therefore it can accept, it has got lone pairs and therefore it can accept hydrogen bonds.

And here we have got palmitic acid, which has got a hydrogen bond donor, this is the hydrogen bond acceptor. So now you can have hydrogen bonding between carboxylic acid O-H with the pyridine nitrogen of niacinamide and this O-H and hydrogen bond is what is responsible for the crystallization of niacinamide with palmitic acid together. And here again you can see that the central part here is the niacinamide which is the polar part. And the palmitic acid you can see this is the non-polar part. So, polar part is there, non polar part is also there, and you will see that in the polar region further you will see that niacinamide has got NH₂.

NH₂ means there are two proton donors there is nitrogen which is a proton acceptor there is also carbonyl which is a proton acceptor and you can see a maximization of all these hydrogen bonds in the crystal structure of palmitic acid with niacinamide where you can see this N-H...O hydrogen bonds, both the NH₂ donors are being utilized. To form the N-H...O hydrogen bonds and to form this polar arrangement and then this arrangement of niacinamide molecules is now connected with the carboxylic acid via the O-H...N hydrogen bond.

So, O-H...N hydrogen bonds between palmitic acid and niacinamide and N-H...O hydrogen bonds between the niacinamide molecules is what separates the hydrophobic parts from the hydrophilic parts. So, this is the hydrophobic part, this is the hydrophilic part, this is the polar region, these are the non-polar regions, they are well separated from each other in the solid state.

So this gives us a very strong support to the fact that non-polar parts always try to be

with each other and the polar parts always try to stick around with each other. And the combination of these is what gives rise to the crystal packing of the resulting solid. And it also allows you to appreciate the role of energetics, the strongest hydrogen bonds always try to dictate the crystal packing.

So, the primary reason for the stabilization of the primary factors of the strong hydrogen bonds and then the weaker interactions are present and because they are present in large numbers, why, because they operate over the entire length of the alkyl chain, these H...H contacts. Therefore, these dispersive interactions they operate over the entire length of the alkyl chain and the more is the length more is the area of contact between these alkyl chains more is going to be the dispersive interactions.

So, this also brings to us the important role of cooperativity that means in a compound when it packs or when it crystallizes it does so by maximizing all the possible interactions. We have hydrogen bonding interactions which try to be linear and we have close packing interactions which are non-specific and which lack directionality. So, the cooperative interplay about strong hydrogen bonds and weak interactions give rise to the final packing which is a very characteristic feature as observed in nature where packing is governed by these forces.

And now we will go to some other cases. For example, we can look at even simple molecules. If you are able to appreciate the packing of simple molecules, you will see that you will be able to realize that when small molecules pack or when they interact with hydrogen bonds, all the donors and acceptors are involved in the crystal packing. And slight modification in the molecule can entirely change the crystal packing.

This is something we will now look at. For example, let us look at formamide. Formamide is HCONH_2 . So, this has got two strong donors, N-H donor, this has got a strong acceptor.

So, it is expected to form N-H...O hydrogen bonds and this is what it does. So, here you have a dimer of formamide where you have N-H...O hydrogen bond and this is a centrosymmetric dimer there is a center of inversion here and then the other hydrogen involves in N-H...O hydrogen bond as well and in this way you have got this dimer, and you have got another dimer here.

So, you have got this nice association of molecules, you can see here both the N-H donors form N-H...O hydrogen bonds, this one forms N-H...O, this one forms N-H...O, this also forms N-H...O, this forms N-H...O. So, you have this association 1, 2, 3, 4, 5, 6. So, you have got this hexameric motif, you have got this hexameric motif. This hexameric motif further participates in extensive hydrogen bonding and it is like a

layered structure this is more like a sheet-like structure where all the molecules are approximately in a plane.

And now when you change the compound from formamide to acetamide, where you have replaced the hydrogen with a methyl group. Then you replace the hydrogen with the methyl group then the packing changes completely and you will see now that again it tries to maximize the hydrogen bonds.

So, this molecule is just like water. So, in case of water we have got 2 lone pairs and we have got 2 donors. So, it can form hydrogen bonds further with two donors the lone pairs and it has also got two donors by itself. So, it can have a tetrahedral arrangement.

Similarly, you see in case of acetamide the oxygen lone pairs form N-H...O hydrogen bonds and the N-H donors form N-H...O hydrogen bonds. So, this is a pseudo tetrahedral arrangement in acetamide. A pseudo tetrahedral where you can see a central acetamide molecule is tetrahedrally surrounded with four other acetamide molecules, primarily involving two N-H...O hydrogen bonds functioning as donors and additional N-H...O hydrogen bonds interacting with the lone pairs of the carbonyl group.

So, this gives rise to a pseudo tetrahedral arrangement of acetamide. Again, this is mimicking the fact that hydrogen bonds when non-covalent associations takes place they also tend to have geometrical arrangements which are similar to that of covalent bonds. So, just like methane which has got a covalent, suppose C-H covalent bonds, and it forms a tetrahedral arrangement or may say oxygen or water molecule or tetrahedral ammonia. Similarly, when hydrogen bonding association takes place, they tend to form tetrahedral arrangements which are mimicking or reminiscent of the covalent arrangements in covalently bonded species.

So, now in this example we will now demonstrate to you the crystal packing of the compound propanamide. So, propanamide $\text{CH}_3\text{CH}_2\text{CONH}_2$ and here you can see that the steric bulk increases, you have got an ethyl group, nevertheless it wants to maximize the hydrogen bonding, so you have the N-H...O hydrogen bond here.

And then again you have this N-H...O hydrogen bond. So, it is trying to maximize the hydrogen bonds and in this case it generates the packing of molecules and as you can see now the packing also takes place in such a way so as to allow sufficient space for the ethyl groups to be present.

And the ethyl groups are present in a way that they are orthogonally oriented with respect to each other. So, one ethyl group is in the plane, other is perpendicular to the plane and they have adopted different orientations so as to minimize the sterics. At the same time,

maximizing the hydrogen bonding interactions, so as to stabilize the molecular association.

So, what is important to realize is that a slight change in the chemical compound can alter the crystal packing, but the compound still tries to maintain the strong hydrogen bonds and then maximize the dispersive interactions coming from the weak C-H contacts which are present because of the hydrophobic parts of the molecule.

Towards the end of this lecture, now we will take up some more examples, on halogen bonding. Let us look at some more examples of halogen bonding, so that we will be able to complete this week's lectures, where we would have covered sufficient number of examples.

For example, let us try to look at how iodine and the solvent dioxan they will interact with each other. So, iodine plus dioxan. So, iodine we know has got a sigma hole which is along the iodine-iodine bond axis.

We know that we have studied the sigma hole here and so there is a region of electron deficiency. So, it will like to interact with the oxygen lone pair. And then the other oxygen lone pair will also interact with another iodine and in this way this will continue.

So, this forms a 1D chain of iodine...oxygen, iodine...oxygen contacts, these are halogen bonds which are mediated by iodine...oxygen contacts. The electrophilic region of iodine which is the sigma hole interacts with the lone pairs on oxygen, and this is the driving force.

We know that halogen bonds are highly stabilizing in nature and they are responsible for the molecular association of this binary system containing iodine and oxygen. The same concept can also be extended to bromine, where you can have bromine interacting with dioxan to form this particular association.

We can also take other examples. For example, we can go to di-iodobenzene, and then we can take this kind of a system which has got nitrogen lone pair and then nitrogen lone pair can interact with the sigma hole.

And from this kind of a molecular association, it is important to realize that in all these cases when you have strong halogen bond association this distance d which is the separation between the iodine and the nitrogen atoms is less than the sum of the van der Waals radii of iodine plus nitrogen.

This distance is quite short. There is a substantial reduction in the separation between the iodine and the nitrogen atoms at the equilibrium geometry which is shorter than the sum

of the van der Waals radii telling that there is a strong electrostatic control because of the sigma hole present on iodine.

And because of the sigma hole present on iodine the nitrogen lone pair, is able to interact with the sigma hole very strongly, such that there is substantial contraction in this distance which separates the nitrogen and the iodine atoms.

This is a very very characteristic feature of halogen bond and here this directionality again, phi is around 180 degree. So, the key feature about halogen bonds is that whenever they try to interact with each other they would like to maximize the directionality that is 180 degree.

So, this is a key feature of halogen bonding which is forming highly directional halogen bonds. And we can also take up now we can also take up some other examples. For example, we can now modify, we can also see whether we can modify the strength of the halogen bond. We can modify now the strength of the same halogen bond by the introduction of electron withdrawing groups.

So, if you put electron withdrawing groups, for example, if you put electron withdrawing groups, like fluoro, then fluorine is a strongly electron withdrawing group and therefore, it will enhance the electrophilic character on iodine. It will enhance the electrophilic character on iodine and therefore, the magnitude of the electrostatic potential will be raised.

And it will interact more strongly with the nitrogen lone pair thereby shortening the distance between iodine and nitrogen further. And this is what has been observed also that when you put electron withdrawing groups. This is what happens, that the iodine now approaches more closely to nitrogen.

Because of the electron withdrawing effect, the sigma hole magnitude is enhanced and therefore, there is strong electrostatics which operate and thereby nitrogen...iodine distance decreases. Now, this iodine near the fluorine atoms is more contracted or shortened. This distance is slightly longer because this is far away from the fluorine atoms. So, this is going to be this say, this is d_2 , this is d_1 , d_1 is going to be less than d_2 .

So this is another example of halogen bonding which is mediated by iodine...nitrogen contacts. I have already given you an example of iodine...oxygen halogen mediated contacts. So overall these are the set of examples we have which talk about all the kinds of interactions and now in the next lecture we will go to individual systems. We will start looking at the other concepts which are of importance in supramolecular chemistry.

Thank you.