Molecular Rearrangements and Reactive Intermediates in Organic Synthesis

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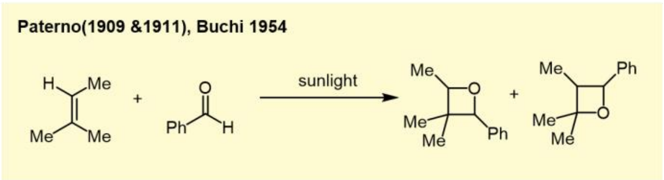
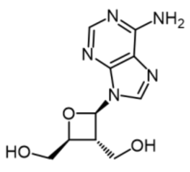
Lecture 20 : Radical Continued

Welcome back to this NPTEL online certification course in Molecular Rearrangement and Reactive Intermediates. We are still continuing in the Radical Chemistry. If you remember, in the last class, I talked about the photochemistry of carbonyl compounds, and I talked about the Norrish type-I and type-II reactions. And if you remember at the beginning, you have a carbonyl compound and once the UV ray fall on the carbonyl compound there is n to pi-star (π^*) orbital transition happen. So, now we are going to talk about another reaction which I already mentioned in the last class is the Paterno-buchi reaction. So, I am going to start with the Paterno-buchi reaction and then I am going to explain the enone- alkene cycloaddition and some of the [2+2] cycloaddition reaction using enone.

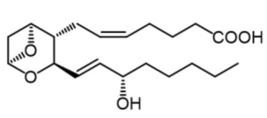
Then also I am going to talk about some of the Aza-paterno-buchi reactions and the di-pi-methane rearrangement. So, let us start with the Paterno-buchi reaction. So, it is actually a very important cycloaddition reaction between aldehyde or carbonyl or ketone with alkene. So, if you remember in the last class when I was talking about this, if you have a carbonyl compound you remember there was a n to pi-star (π^*) transition, we will talk about the different type of fate about it.

The photochemical cycloaddition between aldehydes and alkenes to form oxetanes is known as the Paterno-Büchi reaction





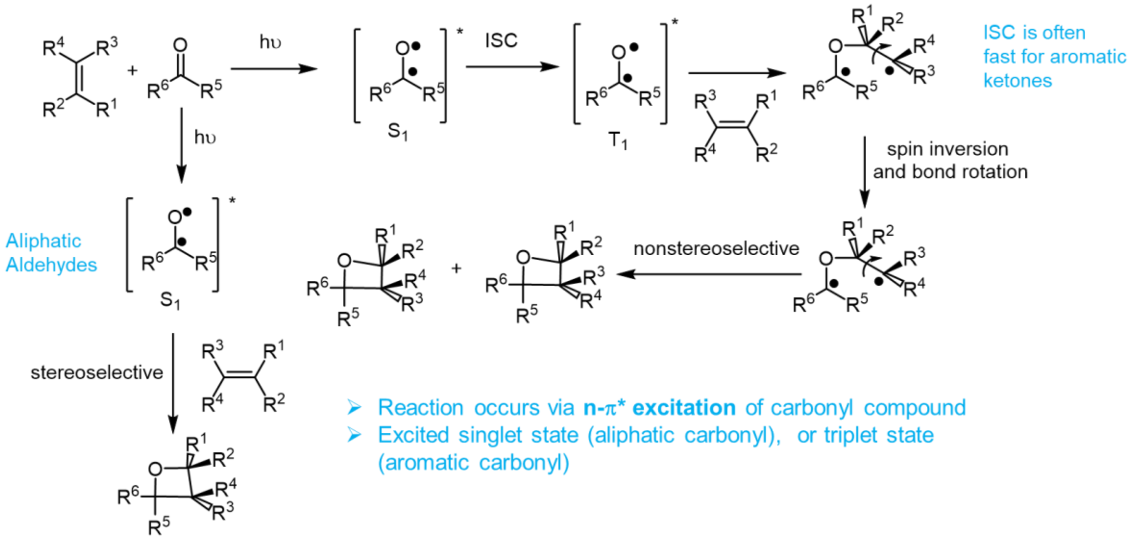
Oxetanocin



Thromboxane B2

So, in one case I talk about the Norris type-I reaction, if you remember there is a generation of acyl radical then there is a the type-II reaction where there is a hydrogen abstraction happening and then the formation of the 1, 4 diradical. S,o, here I am going to talk about another important chemistry where you can do cycloaddition with an olefin. So, that can able to form a important 4-member ring called oxetane. So, why we are interested about this chemistry because this oxetane is present in several type of natural products. So, you can see this 4-member oxygen containing ring here in this type of natural products.

So, now we are going to learn about the reaction mechanism. what is the mechanism of this Peterno-buchi reaction? So, there what is happening? first thing, once the n to pi-star (π*) transition happen from the carbonyl compounds. So, it is going to the excited single state. Given here from the excited single state, it can directly go for a stereoselective reaction with the olefin to form the product with high stereoselectivity. or it can go for a singlet to triplet through inter-system crossing.



ISC is often fast for aromatic ketones

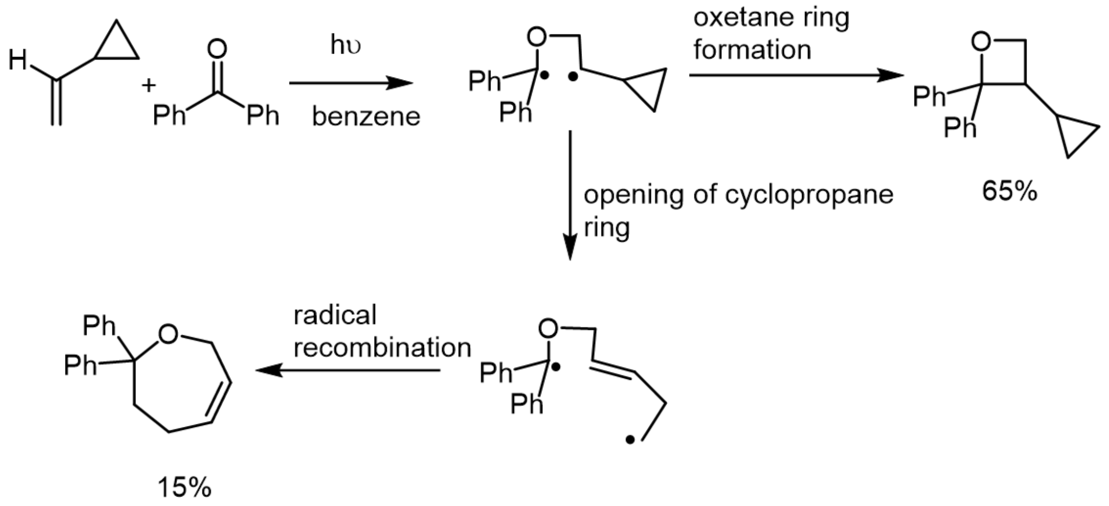
- Reaction occurs via **n-π* excitation** of carbonyl compound
- Excited singlet state (aliphatic carbonyl), or triplet state (aromatic carbonyl)

So, this radical can now add to the corresponding olefin, now it can form this 1,4-biradical. Now, here, there are two things happening. So, first thing is once this biradical formation happening in the triplet state, at the same time, there is a spin flip and at the same time there is a bond rotation happening. So, once that is happening, this reaction become non-stereo selective. So, you end up getting a mixture of products.

So, now the question comes: what type of compounds are favorable in this reaction? When it comes to aliphatic aldehydes, the Paterno-buchi reactions predominantly occur from the singlet state. In the case of aromatic ketones, you observe it is going through this type of formation of the biradical species, and then there is a non-stereoselective reaction. So, it is not only the one important factor that if you are going through triplet state then only you will always get a mixture of products, there are some other important factors also I am going to discuss. So, first important thing is that, this chemistry is happening due to the n-π* excitation of the carbonyl compound. The second thing is the excited state.

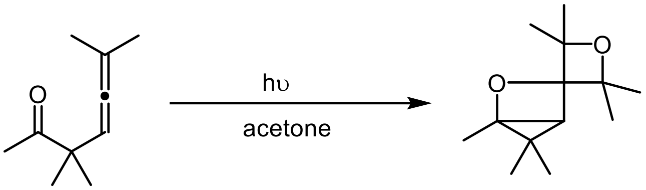
It can happen from the excited singlet state, as I mentioned, or from the triplet state in the case of an aromatic carbon compound. So, first thing is there is a formation of this type of biradical. So, now the question comes: is there any evidence for that, there is a biradical formation happening? So, now if the Paterno-buchi reaction happens between the benzophenone and this vinyl cyclopropane. then what is happening? here, after the formation of biradical, it can go to the corresponding product oxetane formation, or from there, there is a cyclopropane ring opening happening because cyclopropane is a strained ring. So, if you have a radical here, it will allow the ring-opening, formation of this radical.

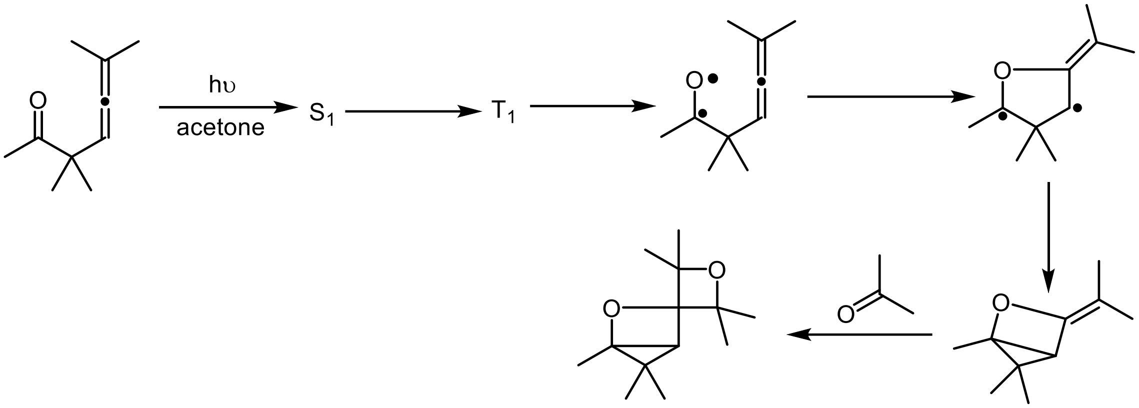
you



The formation of tetrahydrooxepine confirms the diradical formation

Now, there is a radical recombination between these two radicals. which can form this tetrahydroxepine. So, once the tetrahydroxepine is going to form here, the confirm that it is gone through some sort of a biradical formation. There are other evidence here in this particular reaction. So, there is an allene here and there is a carbonyl compound.



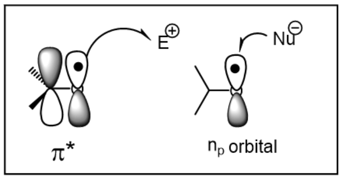


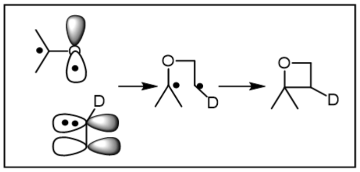
So, they have isolated this product. So, this is also kind of giving explanation for the formation of this type of biradical. So, first thing there is a n to pi-star (π*) transition happening from singlet to triplet through the inter system crossing. And then what is going to happen? you can see the first thing that is going to happen is this oxygen radical, and then it is going to react with this double bond here, formation of these radical species. Again this 1,4-biradical species which can form a bond here, and now what is going to happen? you can see there is a double bond here, and you have acetone in the reaction.

That is an important fact because once you have acetone in the reaction, it can also able to form oxygen radical and the carbon radical, which can do a recombination here. So, there will be another Peterno-buchi reactions with this olefin and the carbonyl group here to get to this product. So, as this product formation is happening this is kind of indicating that if this radical are not forming then how come this bond is forming here in between this carbon. So, so that is kind of an evidence for this biradical formation.

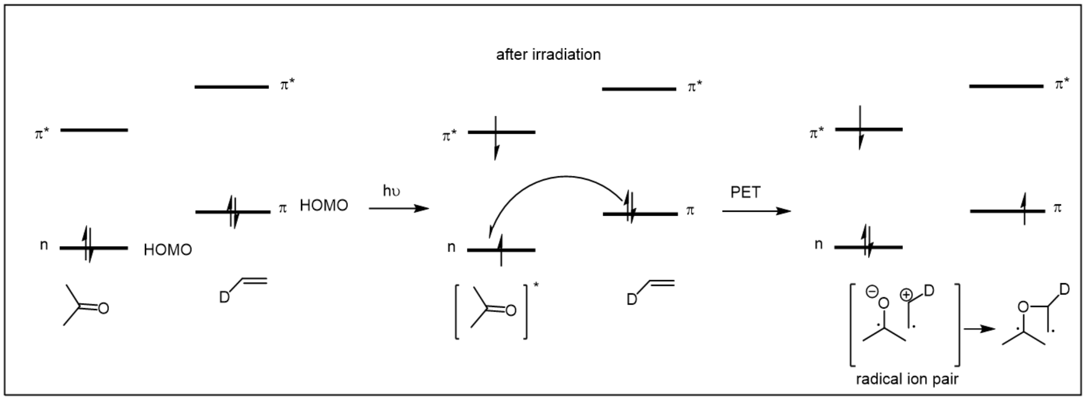
So, now we are going to learn about the important fact here that if you have a carbonyl compound here, as I mentioned, it could be aliphatic or aromatic. So, let me write R and R', and at the same time, you have an olefin here. So, the question comes whatever group that olefin has if the olefin has an electron-donating group or an electron-withdrawing group. depending on these, we are going to learn about the chemistry with the electron-donating group versus the electron-withdrawing group. Two different scenarios are going to happen. So, before going that, we are going to learn that once the n to π* transition happens, if you try to look into your n(p) orbital, which has a single electron and that is on the oxygen. So, now what is going to happen? that is actually electrophilic in nature.

Carbonyl compounds in their nπ * state possess an amphoteric character, since a) one electron lies in the π * orbital, so the system is globally electron-rich and b) the np orbital of the oxygen atom is electron-deficient.





perpendicular approach
diradical formation and
non-stereospecefic reaction



That means, it can only able to interact with a nucleophile or with a electron pair or with a pi(π)-electron cloud. Then now, in the π* case, what is happening is that, the π* is actually nucleophilic. So, now it can able to interact with an electrophile. So, that is a very important fact because based on that, you are going to see here that now, if you try to think about the reaction with an olefin having an electron-donating group. Now, if you try to think about your carbonyl compound, nπ*orbital n is your HOMO having this 2electron here.

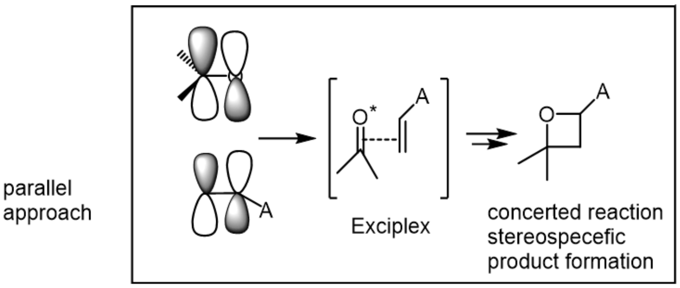
and if you have an electron-donating group, then your π-bond will be a little bit higher in energy. So, that will be the HOMO, and that is the pi-star(π*) orbital. Once you put hv, what is going to happen? from the n-orbital, it will go to the excited state. So, that is happening from n, it is going to the excited state. So, it is going to n to pi-star(π*) transition is happening.

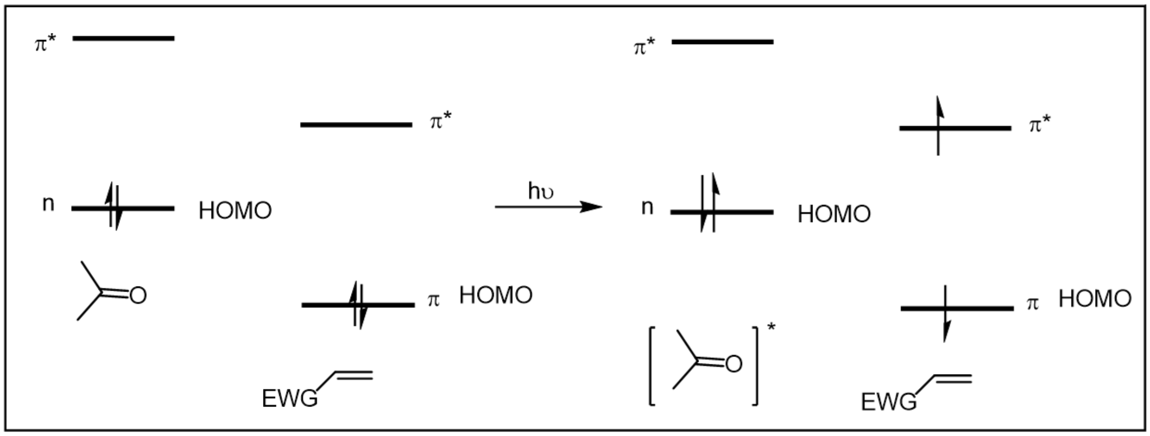
Then what is going to happen? now, if you look into it, you have a pi-electron here in the olefin, and you have this n-orbital. So, now, what is going to happen? Now, this n and pi(π) going to interact with each other. So, there will be a photo induced electron transfer going to happen from here to here. So, that can able to form this radical ion pair, at the end it is going to form this type of bi-radical species and then it is going to form to the corresponding product. So, now, the question is if you have this type of electron-donating group how they are going to interact.

So, the way we are trying to draw here. So, this is your n(p)-orbital and that is the pi(π) and we can draw here with a 1, 1 electron here. So, now what is going to happen? they are actually interacting in a perpendicular approach. So, that means, kind of a 90-degree approach. So, you see here this is your n, and that is your pi(π).

So, that is how they are actually forming this, then after the inter-system crossing, they are forming this biradical, and then from there, it is going to form the corresponding product. So, the thing is as it is forming a biradical that, this reaction is non-stereo specific as I mentioned at the beginning.

Now the question comes if you have electron-deficient or electron-poor alkane. So, now if you try to look into this molecular orbital picture here, you have this pi-star(π*) here, but now if you have electron-deficient one you can think about now what is going to happen it will decrease the π density. So, the π will be more stabilized for that particular double bond, and then there will be a π*. So, what is going to happen? after you shine the UV light, there is a error here it is going to go for this n to pi-star (π*) here and this will kind of remain here in pi-orbital(π).

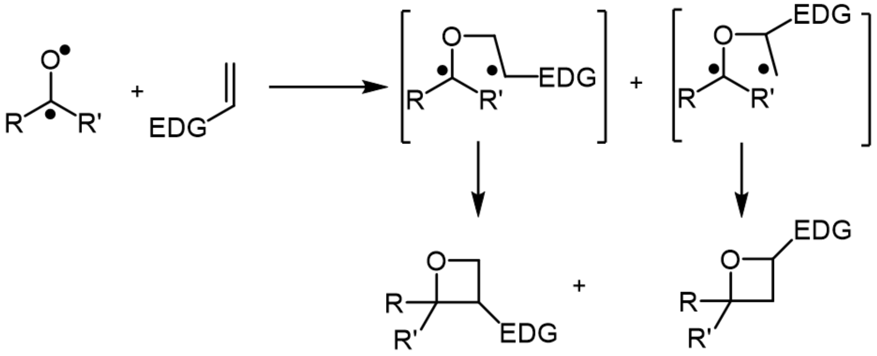


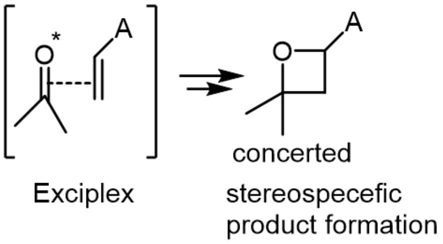


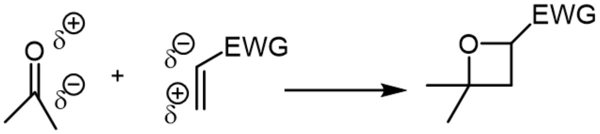
So, it will go for the n to pi-star (π*), and then the pi-star (π*) is going to interact with another pi-star(π*) because if you remember, I was talking about at the beginning, the pi star, like to interact with the electrophile. So, this two pi-star(π*) now going to interact. And now, once these two pi-star((π*)) going to approach to each other, they are going to approach in a parallel approach . And what is going to happen? They are going to form some sort of a exciplex. So, in exciplex, actually there are two conjugate molecules in the excited states, once they are forming this exciplex that mean and then one of them will be in the excited states and one of them in ground state.

So, the excited states of this ketone are forming exciplex with this double-bond compound. and then through a concerted reaction they are forming the product. So, that is why the reaction is stereospecific. So, if you have electron-withdrawing in olefin, then the reactions are mostly stereospecific.

So, now the important fact here that you can see here is that in the carbonyl case, you have oxygen and carbon, and so now, in the case of the electron donating group So, there are two different sides.







a complex formed between two different conjugated molecules (monomers) when one of which is in an excited state

So, is it going to happen from both the head or from the head and tail? What is going to happen here? So, because you can see there are two different possibility, let us try to write it down to simplify it. if you have a carbonyl group here and if you have an electron donating group, then what are the possibilities that are the two different oxetanes going to form? it can form this one with an electron donating group, or it can form the other one. Now, the question comes which one will be major and which one will be minor and the same thing if you have electron withdrawing group then what will be the scenario? So, now, if you try to understand that once you have these oxo-radical species, this can add here, and now the question comes: what are the different possibilities it can add here or it can add here?

So, that way, you will end up with two different scenarios here. So, there will be two different types of biradical we are talking about; in one case, you have this radical next to the electron-donating group here versus you have this primary radical. So, now, if look into it, this will be a more stable radical. So, this will end up giving this as a major maybe around 60 to 70% of the product and the rest will be the this product in case of electron- donating group. Now, if you come for the electron-withdrawing group, as we mentioned, it is going to form some sort of exciplex.

So, it is a complex form between two different conjugated molecule and one of which are in the excited state as I mentioned. So, now the thing is as the reaction is going through a concerted things we can think about some sort of zwitterionic species where, there is a δ+ and δ- . So, now the question comes if you think about this carbonyl group, we always know that if I have a carbonyl group , we are very familiar with that there will be δ- here δ+ here. So, but the important thing you have to understand. So, this is all about in the ground state.

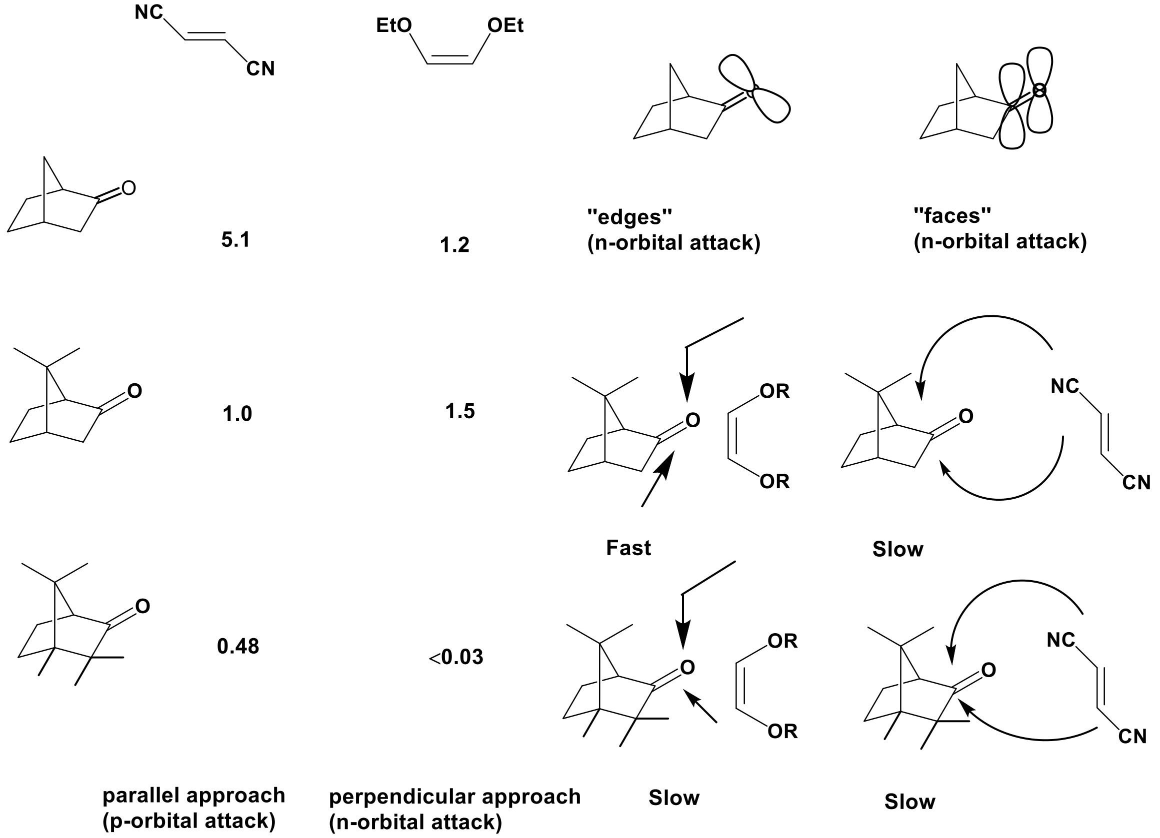
What is happening once you are going to the excited state? You have seen in the excited state, we are making this O• and then C•. So, now, the scenario is getting changed. once you are making this, now this this O• species. So, now, the oxygen center actually becoming a electrophilic because it is a oxygen with a radical species I have already mentioned that in the radical chemistry also. So, now, you have a scenario that, this will be a δ+ and this will be a δ- .

So, now if you think about this. you have a δ+ here and δ- here; now, for the electron withdrawing group, the electron withdrawing group pulls the electron density from this carbon more because it is going to take the electron density. So, that is how, if you try to draw the resonance structure, you can clearly see that. So, if you suppose you have some sort of a carbonyl group or something like that, then you will see that there will be a plus and there will be a minus here. If you try to draw, you will see there is a δ+ here in this carbon, and there will be δ- in this carbon. So, now, what is going to happen? this is the way they can form bonds.

So, that means the oxygen will be with this carbon, where you have an electron-withdrawing group, and the next carbon will be with the other side. So, that can give this product as a major product.

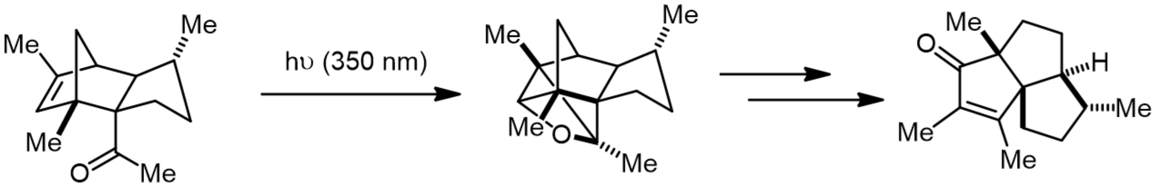
So, now, there is an important concept we just now learn about this perpendicular and the parallel approach. The important difference, as you have seen, is that in the case of the parallel approach, they have to approach from the top or the bottom faces, and the perpendicular approach you have seen in the case of the n(p) orbital and the π interaction. So, now, if you have one double bond that has an electron-withdrawing group and two cyano groups versus two OEt-groups.

that means they are electron-donating versus electron-withdrawing, and we are talking about the fluorescence quenching of these starting materials. So, what is happening here? Once you see that in this particular compound, we are seeing the quenching is higher in case the dicyano compound compared to the here one having two OEt groups. So, because what is going to happen? that once you have this carbonyl here, now this can come from the up or down which is happening very comfortably compared to the facial approach. But now what is going to happen? if you have a scenario that means, you try to bring some sort of a steric reason.

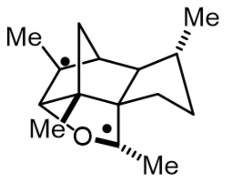


That means once you are try to bring a dimethyl group here, now you see the ratio is not great. So, there is not much selectivity between a perpendicular approach versus a parallel approach. But as soon as you bring this, dimethyl here, then dimethyl in this carbon, now what is going to happen? Now, this approach is becoming slow; what is going to happen? Now, this approach where is going to come in a perpendicular approach, so the perpendicular approach between this group is now slow here. once you are having this bulky group here, the perpendicular approach becoming slower. So, now what is going to happen? now this approach from that up and down up and down has not much effect here.

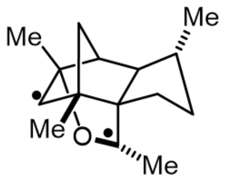
So, you will see this one still getting major and this is really minor here. So, you are seeing that once you are bringing the steric factor what is happening? the perpendicular approach getting actually affected much compared to the parallel approach in the electron deficient olefin. So, there is another important fact about the Paterno-buchi reactions that, in this case you have olefin and your carbonyl group. Once you put a hv, what is going to happen? You see the formation of the O• and the C•. Now, you have to understand there is two different possibility.



oxosilphiperfol-6-ene



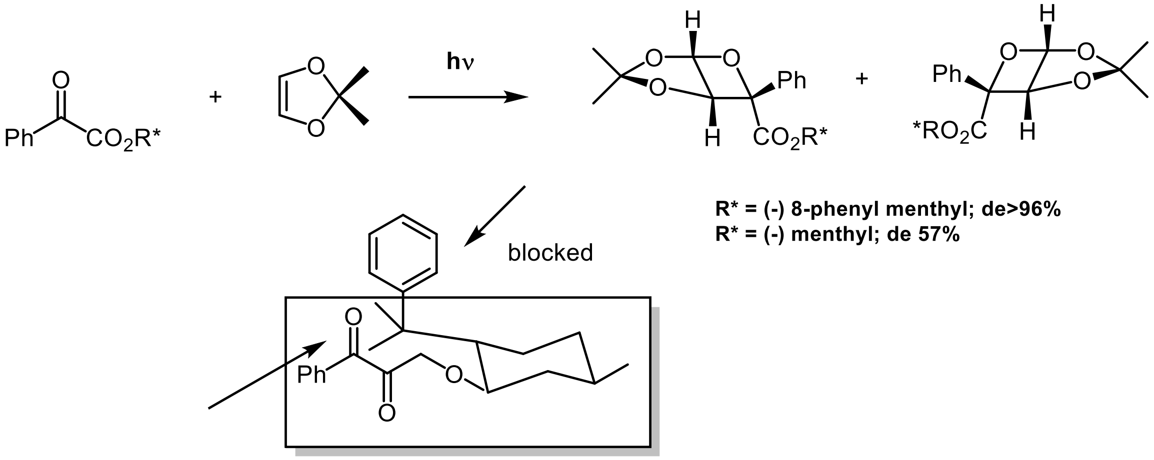
more stable radical



less stable radical

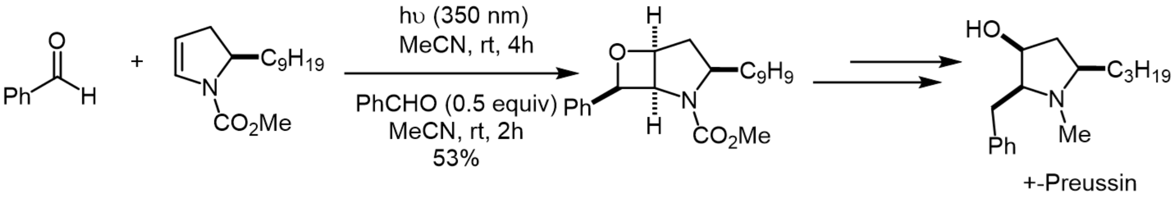
if you have a carbonyl here. So, what will be the regioselectivity? So, that is the important factor. we are trying to show you that there is a possibility that the oxygen forms a bond here and forms a radical here, and these two radicals combine, or the oxygen form a bond with this methyl radical here and then forms this radical, and they can combine. So, which will be the ideal scenario? Again, depending on which radical will be more stable here. So, you can see here this radical will be a tertiary and this will be a secondary.

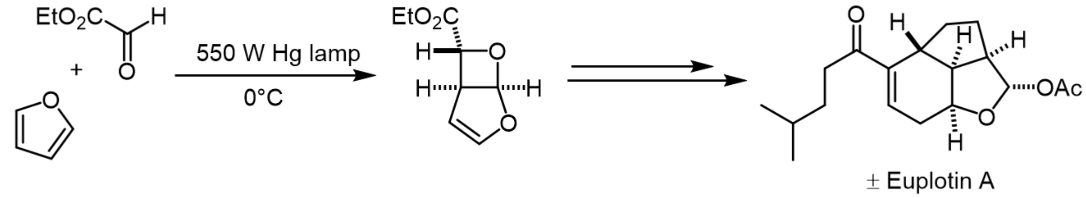
So, here, this will be the winner. That is how you end up getting to this product as a major product, which will be converted to a natural product after a few steps. the topic is enantiocontrol and the diastereocontrol. So, we now go to talk about that suppose if you want to make a diastereocontrol here with the ester group if you try to bring the 8-phenyl menthyl group here. Once you bring the menthol group what is going to happen? in the presence of this 8-phenyl menthol, you can clearly see that if if you have a carbonyl group, then carbonyl has two different phases, correct? So, that you have to control, and that can be controlled. Once you have this bulky group, then this facial approach or formation of the bond through that side is getting blocked.



So, now the only approach is remaining through this side. So, that is how you can able to control. So, you can improve the diastereoselectivity up to 96% using that.

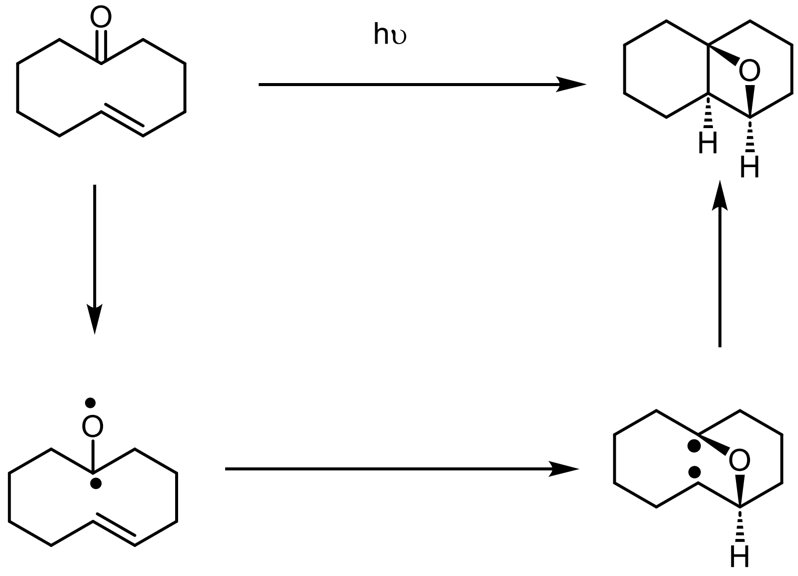
So, there are some more examples of the synthesis of important compounds. Again, you can see the Paterno-buchi reaction, which is a reaction with the benzaldehyde, and with this compound, you can get to a very high stereoselectivite product.





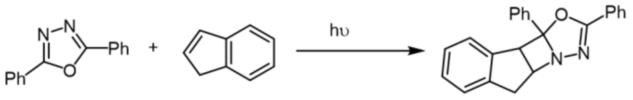
There is another example here with furan. This can also participate with the pattern, which is reactions, and you can see it can form the product with high stereoselectivity, which can convert to the natural product. Again there are more examples and there are also different aspects about the Paterno-buchi reaction. So, there is another important factor that once the diradical formation happens and finally, two bonds are formed, the steric also plays an important role. So, I think I have already given the reference of the Nicholas Turro book. I think it is a very good book for photochemistry. So, you can also go through that book there are some more examples. Also, there is a very good NPTEL lecture by Professor N. D. Pradeep Singh of our department; you can also definitely go through his lectures as well.

So, now I am going to show you another important example for the intramolecular version, you can see here again there is a formation of this O• and the C• which can able to form this bond to here to form finally, the oxidant. So, now, it is not always with the carbonyl. It can also happen with the imine, and once it happens with the imine, we call it an Aza-Paterno-Buchi reaction.



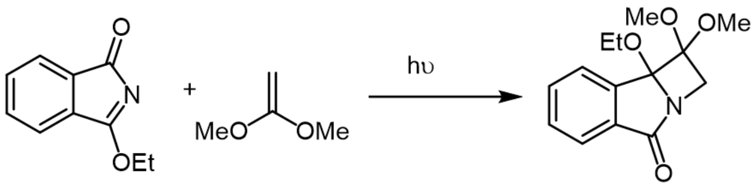
Again instead of what is going to happen? now you have a 4-membered ring with nitrogen. So, it can form azetine.

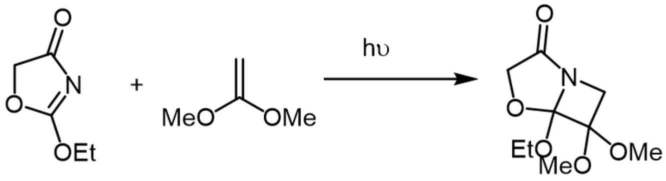
The **aza Paternò-Büchi** reaction is a [2+2]-cycloaddition reaction between imines and alkenes that is arguably the most atom-economical method to access 4- membered nitrogen-containing heterocycles



a conjugated electron-withdrawing group to be attached to the C-N double bond is necessary to cycloaddition to proceed.

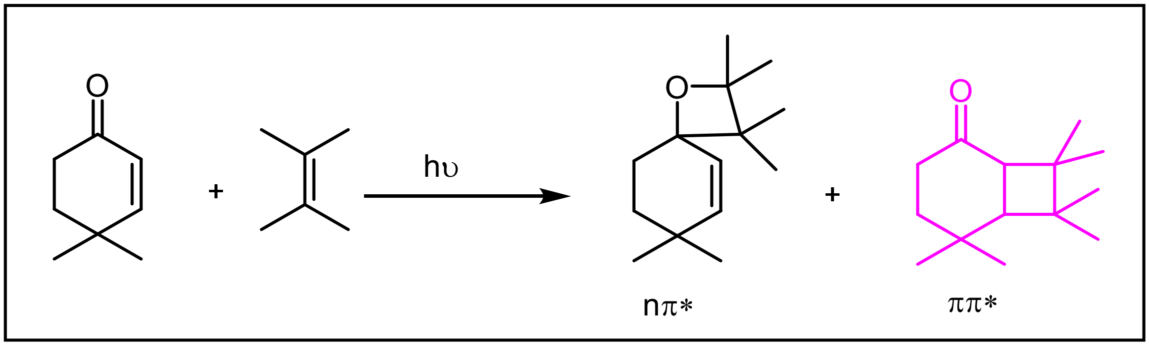
So, there are more examples here. We can see here it can: you have an imine here, and now you have a double bond with the electron donating group, and you have ended up making this product here.





I think you can also try to follow the concept which I have taught you for the formation of the why it is forming. this is not the other one. And now you can see another example here very similar substrates and we also end up getting to this sort of product here. So, now I am going to move to the Paterno-buchi reaction and I will give you more problem to solve during the homework.

So, the every week there is assignment you guys know already. So, I am going to give you some more problems there. So, now I am going to move to the Paterno-buchi and talk about another important photochemical reaction about the carbonyl groups this is the enone [2+2] cycloaddition.

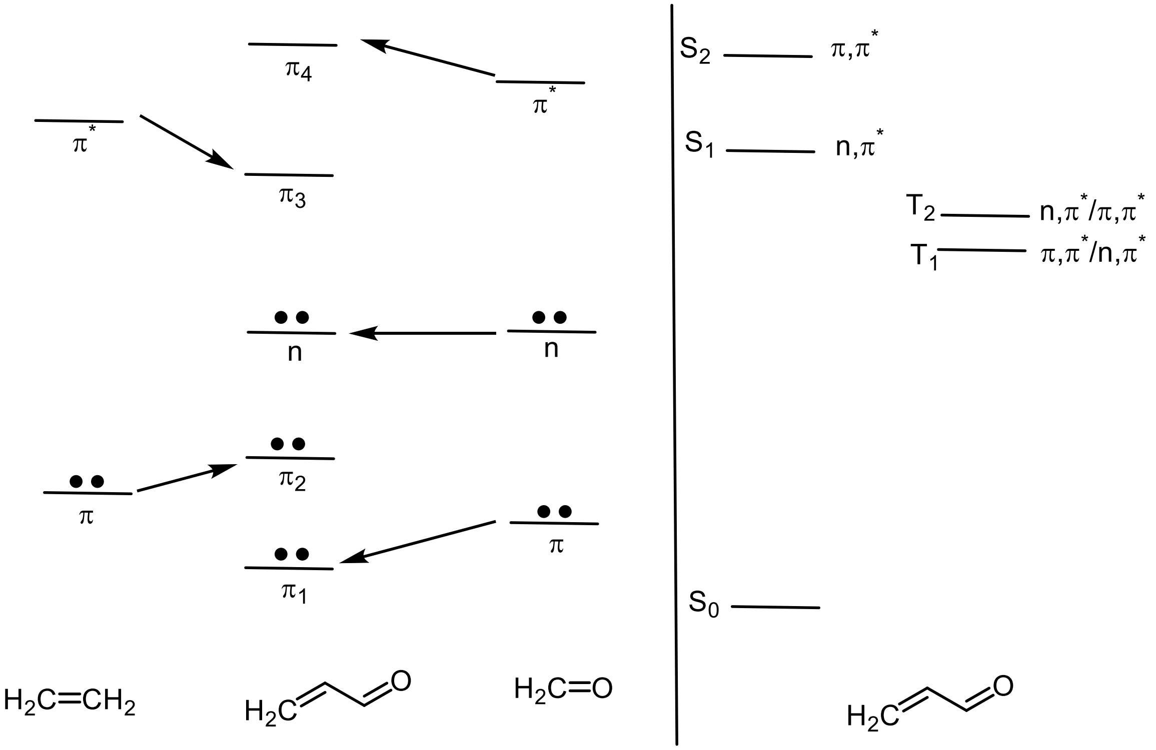


So, I think we have already seen that if you have a carbonyl group and if you have an olefin, then you end up getting to the Peterno-buchi product, and that is majorly happening from the nπ*.

So, I think it is happening from the nπ*. That is the first step. So, it could be a singlet or triplet depending on the substrate, but the nπ* transition is the important transition there.

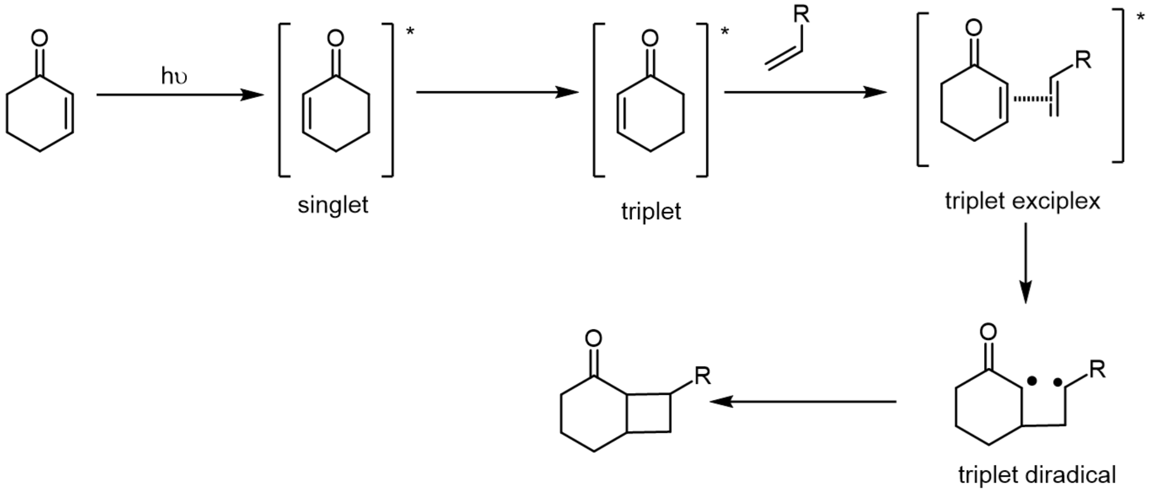
But now we are going to learn that, that, there is a double bond here in case of enone you can see there is a olefin also here. So, that olefin can also take part in a [2+2] cycloaddition here to form this product. So, now you are going to see here the major chemistry here with the enone [2+2] cycloaddition actually happening from the ππ* .

So, let us try to understand that if you have an olefin here, there is a π and π*. we already know that. And if you have a carbonyl group, we have seen that in the case of a carbonyl group, there is an n to π* transition that can happen, or there is a π to π* transition that can happen. But now, we will come to enone. So, enone is a mixture of the double bond and the carbonyl compound. So, what you are going to see here? Now, you are going to see not only one π bond, you are going to see there are two π bond, one is from the double bond here and then one is with the carbonyl.



So, there will be a π_1, π_2 and then there is a non-bonding electron. As the same time there will be this π* orbital as well. So, these will be the anti-bonding orbitals and these are going to the bonding orbital. And the important fact you are going to see in case of enone that once it will go for the inter system crossing. So, once it comes from S_2 to S_1. So, once it will go to the S_2 come to the S_1 and then it can go for a inter system crossing.

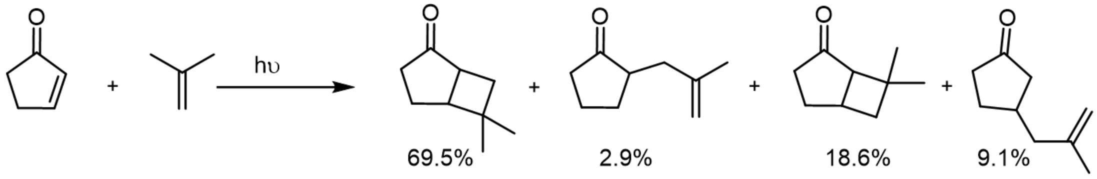
And now, it can have that, again you will see there will be nπ* and the ππ*, but in case of enone the nπ and ππ* gap is really small. So, lot of times you will see the ππ* will be the triplet, will be the lowest energy compared to the nπ* and some cases depending on the the structure of the enone you will see the $n\pi^*$ going to the lowest energy triplet state. So, now what is happening here? what is the mechanism of this type of enone [2+2] reaction? First, it is going to excite to the singlet, then it will be going to the triplet through the inter-system crossing, and then it is going to form an exciplex with the olefin. From there, it is going to form this triplet diradical, and then it is going to finally form the product. So, again, the low energy $\pi\pi^*$ state is responsible for this enone to undergo cyclization.

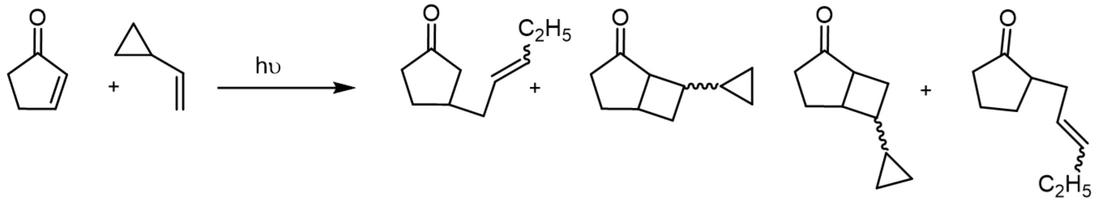


Low energy π-π^* state is responsible for enone to undergo cycloaddition

As I mentioned here, the $\pi\pi^*$ energy is major cases. You will see the lowest triplet state. So, we already know why the [2+2] does not happen thermally you must have already read in the photochemistry that if you try to draw the HOMO and LUMO . So, you have seen that already you knoe about the LUMO and HOMO in case of just [2+2] cycloaddition if this is your LUMO and this is my HOMO. So, what is going to happen here? you can see in one case you will see a bonding and the other case you will see anti bonding . So, that is how we see that [2+2] cycloaddition in case of enone it is happening photo chemically.

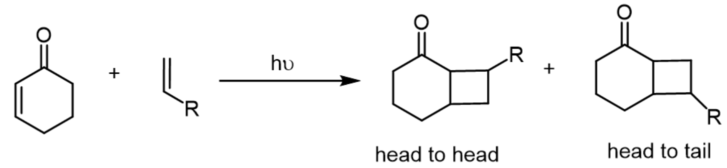
So, now, the involvement of the biradical in [2+2] cycloaddition. So, suppose if you do the reaction with this enone and this double bond here what is happening? you are going to see that it is not only giving you the product with the cyclobutane, but at the same time we are also isolating other products. We are isolating this product as 2.9 %, then this is the other regioisomer around 19%, and we are also getting through this product. and also, if you use a vinyl cyclopropane, a similar thing is happening. Not only are we getting the product, but also we are majorly getting to the ring opening of the cyclopropane.





So, this kind of indicate that why this is happening? So, this is definitely happening because you have a radical species here and you have a cyclopropane here. So, now, that is the scenario as I mentioned cyclopropane is a strain ring that is going to open up and once that is going to open up it is going to form this species here and at the same time it is going to form a double bond and then if you have a double bond here as you can see that can end up making to radical species here. So, now, what is going to happen? once you are forming this radical species they can go for the hydrogen atom abstraction and you can end up seeing this type of products here. So, that kind of indicates that there must be some sort of biradical formation that is how these types of products are isolated. and then you can see here the question comes also that why this product formation is happening ? the 2.9% or this 9.1%, why is this product coming from? now if you try to think about how these products are generating? then you have to try to think about this type of so now you can think about here that once you are forming this product let us think about here So, once you have a radical species like this instead of the radical recombination, what is happening? it can also go for hydrogen atom abstraction. So, this can go for hydrogen atom abstraction from this CH3 and once that is happening then this is also going for hydrogen atom abstraction to end up this product . this 9.1% also happening very similar mechanism, So, this kind of indicates that there is involvement of this 1,4-biradical.

Now, the question comes as you have asked that head to head or head to tail. So, what is happening here? Because if you have a carbonyl group in one side and then you have a CH_2 on the other side. So, here also you have R group one side and then nothing on the other side or you can have a substitution. So, there could be a head to head or head to tail product formation. how that is getting controlled. So, the question comes there is one important thing is steric and the electronic factor.

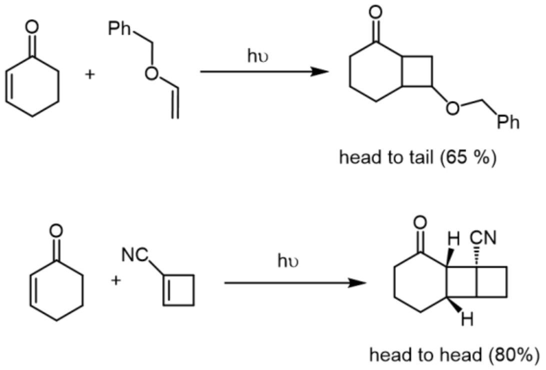


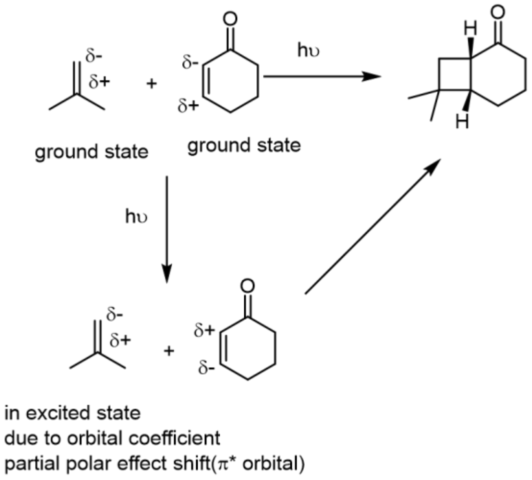
Selectivity for one of these isomers depends on both steric and electronic factors:

Steric interactions and electrostatic interactions between the excited enone and alkene.

In their excited state, the polarity of enones is reversed so that the β carbon possesses a partial negative charge. In the transition state for the first bond formation, the alkene tends to align itself so that the negative end of its dipole points away from the β carbon of the enone

So, we are going to explain them and then there is also how to understand why we are going to get to head to head or head to tail. So, what is the easy way to explain the product selectivity. Again you can have a two different scenario as I mentioned that you can have a olefin with electron donating group or olefin with electron withdrawing group. So, now, the question comes we are showing here if you have if you have a scenario where electron donating groups then you form this head-to-tail 65%, that means this is the major product, and if you have electron -a withdrawing group, then the head-to-head is the major product. Now, why that is happening? So, let us try to understand the difference here because we know that in the carbon cases once you have this n to π* transition this is going to form this species.

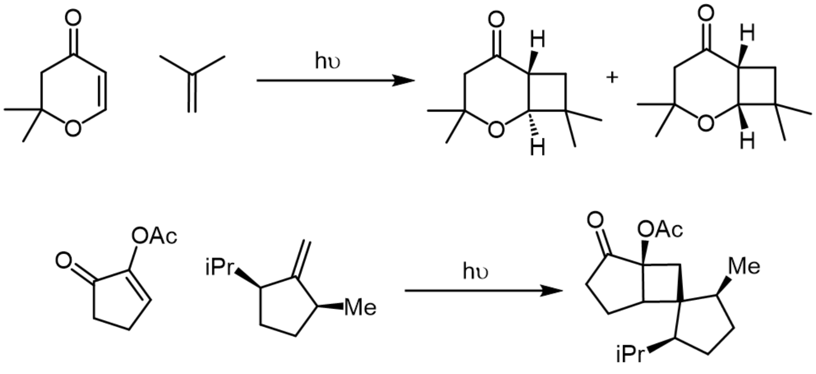




So now you can think about them also. You can draw them like these also. So, now if you look into it as you as I told you before that once it is forming O• that is where you can see is a δ+ and then if it is a if it is a δ+ this will be δ- then there is a δ+ and there will be δ- there is electron formation happening. If this is the scenario then you can think about that if this is my δ+ this is a δ- say then you can have a olefin suppose you have a olefin with electron donating group like here in case of oxygen. So, if you just think about oxygen then that this is giving electron density. So, that means, here you will see a δ- and here you will say δ+ correct. So, now, if you try to recombine them this side is going to add up here and this side is going to add up in this place.

So, that means, the oxygen part will be here. So, this will be going to head to tail and in very similar thing if you have a electron withdrawing group here if you have electron withdrawing group . that if you have a cyano or any other group that can pull electron density. this will be δ+, this will be δ-. So, now, it can this site is going to add here and the and the head is going to add here.

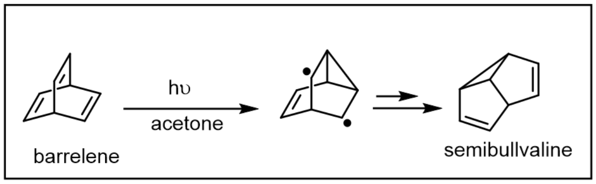
So, that is going to be a head-to-head addition. So, that can get to this product. Again, you can see some examples here? where the the diastereofacial selectivity is happening because you can see in this example here that you are getting to the this product. So, and this product and you can see that you can clearly see in this reaction that diastereofacial selectivity is maintained. Then there is another example here if you have isopropyl group and a methyl group then the reaction try to take place with this double bond in a such a way to avoid the strain with the isopropyl group. So, if you have the isopropyl group in this position, then this could have more interaction with the acetate compared to the methyl group.

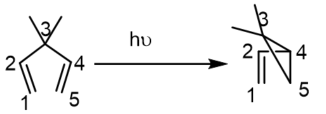


Diastereofacial selectivity is highly predictable in most cases. The less hindered faces of the enone and alkene react

We have learned about the enone-alkene cycloaddition. So, now we are going to move to another important reaction, which is di-pi-methane rearrangement. . So, what is a di-pi-methane rearrangement? A di-pi-methane rearrangement is a very important reaction. here, what is going to see? It is going to rearrange the non-conjugated olefin containing 2 π-systems. So, if you have a scenario here, you have a 2 π- system which are non-conjugated and then by a saturated carbon it has to separated by a saturated carbon and then it could be in aryl substitution.

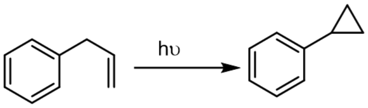
The di-π-methane rearrangement or Zimmerman rearrangement is a photochemical reaction that rearranges non-conjugated molecules containing two π-systems separated by a saturated carbon(sp^3) atom into an ene- or aryl-substituted cyclopropane, it was first observed in 1967 as a conversion of barrelene to semibullvaline.





1,4-diene

vinyl cyclopropane



allyl benzene

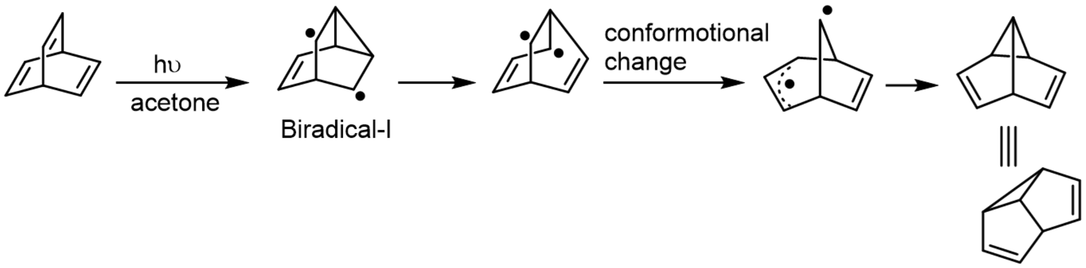
phenyl cyclopropane

So, now, what is going to happen? it can able to do some sort of rearrangement to form very important compounds like starting from 1, 4-diene you can end up making vinyl cyclopropane or starting from allyl benzene it can end up making a phenyl cyclopropane. So, it can also be said that this reaction is a Zimmerman rearrangement. Because the Zimmerman group in 1967 observed this important reaction from barrelene in presence of hv and acetone. it can convert to semibullvaline. So, so that is a very important transformation happening and we can see this reaction used in acetone in presence of the UV light, this conversion happen.

And so, so this is the initial discovery about the di-pi-methane rearrangement. Now, we are trying to understand the mechanism of this reaction. conversion of the barrelene to this particular compound. So, how this reaction is happening? You have to understand that an important thing in this reaction is that this rearrangement actually happens exclusively from the excited states. And then it can go via the singlet or triplet excited states depending on, if you are using sensitizer. If you are using sensitizer it is going from this excited state triplet and if you are not using the sensitizer it is mostly happening from the excited state singlet.

1. This rearrangement occurs exclusively in the excited state not in the ground state
2. Reaction goes via singlet or triplet excited state in the presence of a sensitizer

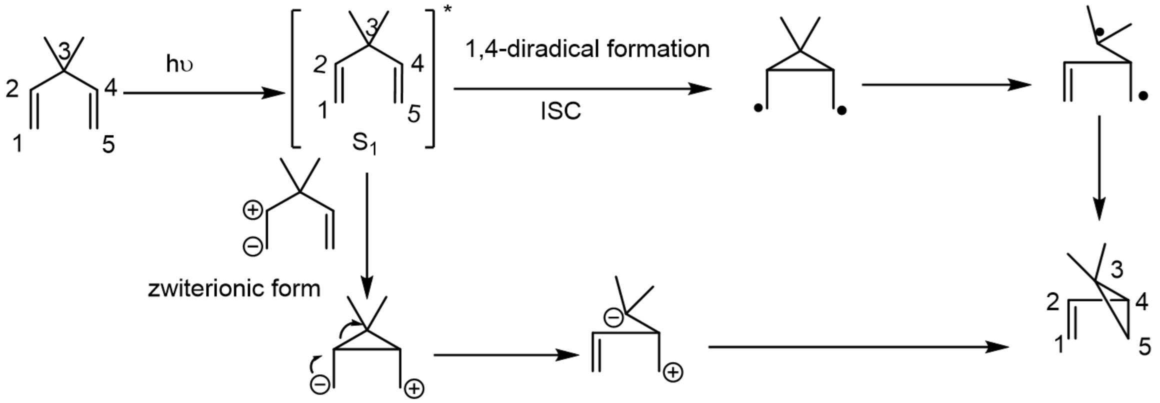
The conversion of barrelene to semibullvaline goes via a triplet excited state where acetone acts as a sensitizer. It transfers its energy from the excited triplet state to the substrate.



So, what is happening? I think this reaction also depends on the substrate. So, for some particular class of substrates this reaction happening from the excited state triplet as well. So, here you can see first the acetone, which actually acts as a sensitizer. acetone can actually go to the excited state triplet; it can transfer the energy to the starting material to convert the starting material to the excited state triplet to form this biradical. From the biradical, you can see here, it can now form this sort of biradical after cleavage.

So, it can move this way and form this biradical. Now, there is a conformational change happening, you can able to draw that, and now, if you think about it. So, this is literally going to form a radical here in the next stage, which there is a radical recombination because it is going to form a double bond and a radical that can recombine to form this product. So, important thing to remember that you need to use acetone for this reaction if you do not use acetone it is not going to form this product it is going to form something else. Now, we are trying to understand the mechanism of this reaction.

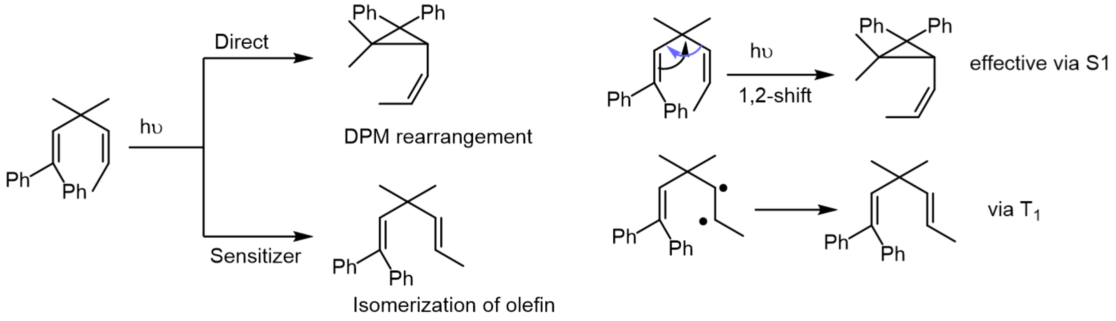
This reaction goes via a singlet excited state (zwitterionic mechanism) or via triplet excited state via a radical mechanism.



first thing, under the UV light, it is going to the excited singlet state. As I mentioned, if the reaction is happening from the excited singlet, then we generally try to write the mechanism in a zwitterionic form. you can think about this double bond as a plus-minus. And now you can try to push the arrow here and then form an anion here which can combine with this cation to form this corresponding vinyl cyclopropane. Now, if you have the other scenario, it can go from singlet to the triplet state to the inter-system crossing formation of this 1,4-bi-radical and then once you have this 1,4-diradical it can now have allow this cyclopropane ring opening because it is going to form the more stable tertiary radical and after that there is a radical recombination can happen to form this product.

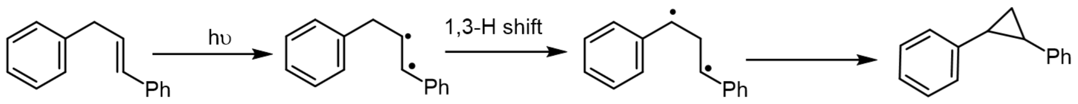
So, let us try to see a scenario here in this particular compound. So, there is a different product forms if you done in the presence or absence of the photosensitizer. So, in the presence of the sensitizer it is forming. what is happening? there is an isomerization happening. what is happening? it is a di-pi-methane rearrangement happening and you can observe it here.

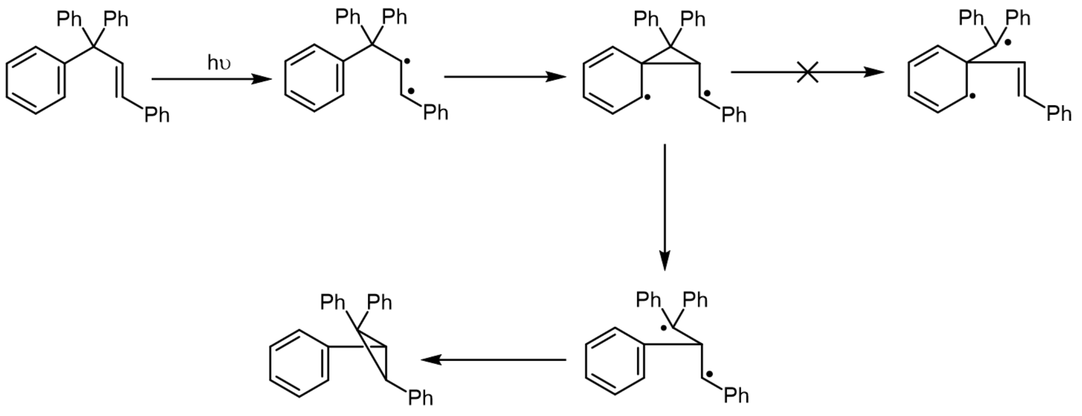
Different product formed if the reaction was done in the presence or absence of sensitizer



So, there is a 1,2 shift happening. So, you can see there is a 1,2 shift happening from this group to here and this pi-bond. So, there is a formation of a cyclopropane here. and this group is shifting here. So, there is a 1,2- shift happening and this is happening effectively from the single state. And now again in the in case of the triplet state what is happening in the triplet state there is a formation of that if you have a olefin that can also excited from the π to π^* that can also from this diradical species which can now able to.

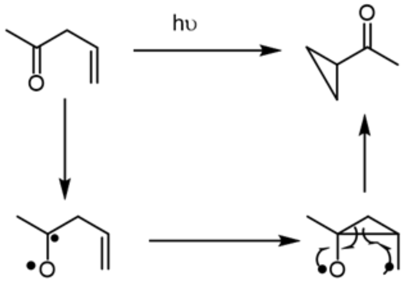
So, there is a bond rotation going to happen which can isomerize the olefin. There is another important example here in this particular compound. We can see the first formation of the biradical from this. If you pass the light from there, what is going to happen it can? So, there is a hydrogen here it can go for a 1,3 hydrogen shift to form this 1,3 biradical intermediate from there it can combine and form a cyclopropane as I mentioned at the beginning. Now it is not always going to form this 1,4-diradical it can also form a 1,3 diradical. So, now, if you have instead of this hydrogen if you remove the hydrogen and put 2 phenyl group here what is going to happen? Now, first thing is going to happen formation of this 2 radical now there is no hydrogen for the abstraction. So, what is going to happen this is a stable benzylic radical it is going to add to the aromatic ring and now after that what is going to happen you can you can see here this radical can also add here.

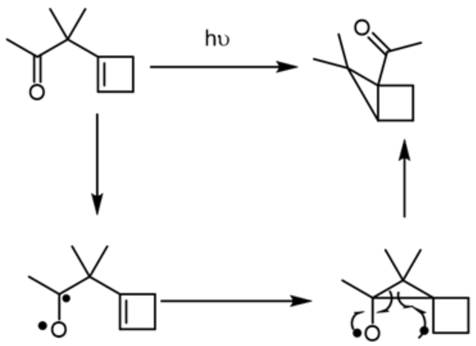




So, there is 2 different scenario this can add here to generate this radical. because I think I think one of the important thing, this is a more stable radical. So, this is less reactive. The homo benzylic radical is going to add here to the aromatic ring. it is a more reactive one going to generate this radical species here. The next thing what is going to happen now this is going to try to get aromaticity and once it will trying to get aromaticity it is going to generate a more stable diphenyl radical.

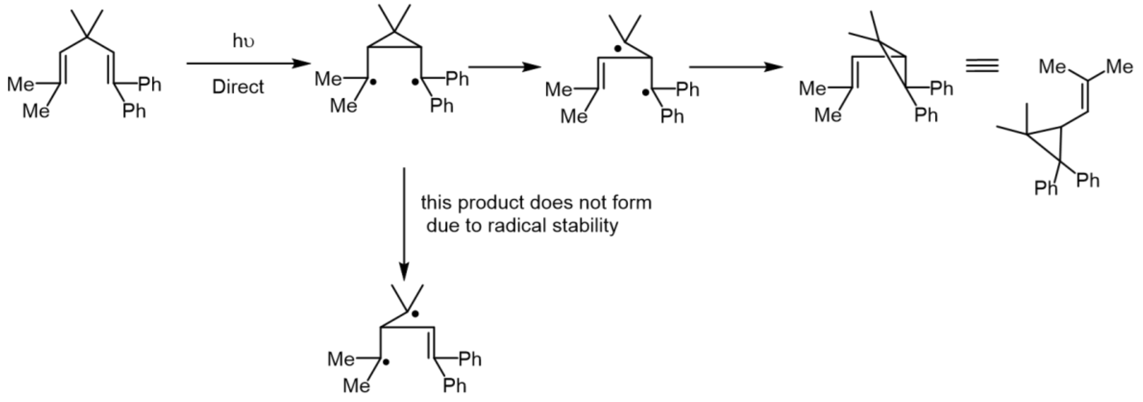
And, from there it can have a radical recombination very similar to the in the previous step. you can able to end up getting to this product. then there is a oxa-di-pi methane rearrangement, if you have carbonyl and if you have a double bond here then there will be a nπ* transition then this radical can able to add here to form this radical species. you can see here it can open the corresponding cyclopropane and generate a radical which can again recombine to form this species.





In this cases also the very similar thing happen. first this nπ* transition happen then you can see formation of the cyclopropane and formation of this 1,4-diradical species. And here what is happening? you can see there is again very similar thing this is going to get a cleave because the formation of this carbonyl compound is very important is going back to the carbonyl compound. it is a more stable product. So, that is why this cyclopropyl is going to cleave from this carbonyl to form this radical here, which is going to be, I think you can see here, the formation of this carbonyl. Then you end up making this radical, and then also you end up making this radical here, which is also your 2-methyl group, which is stabilizing it.

Then, finally, the radical recombination is going to get to this product. And if you have a scenario in one case you have a dimethyl, and you have a diphenyl here what is going to happen? first thing under the UV light it can form this cyclopropane and there is a formation of 1,4-diradical species. But now depending on the stability you can see this is a more stable one, compared to this one. So, so what is going to happen? because this is a more stable and that is going to remain.



The cleavage of the cyclopropylcarbinyl moiety, occurs so as to put the better radical stabilizing substituents on the radical center. Thus, these substituents become part of the cyclopropane ring in the product.

So, so that is not going to be more reactive. So, the one which is less stable here. that is going to open up the cyclopropane ring here to form this radical at the end these two radical going to go for recombination to form this product. But the other way it is not happening as I mentioned because of the stability of the radical. in this part, I have talked about the photochemical [2+2] cycloaddition; I talk about the enone-alkene cycloaddition. At the beginning, I talk about the Paterno-buchi reaction, the aza-paterno-buchi reaction.

at the end I talk about the di-pi-methane rearrangement. And actually, there is important reference books. you should definitely get this book by Nicolas Turro. It is a very good book for photochemical reactions. And then there are some other references and again thank you so much for coming to the class. I am going to see you guys in the next class.