Molecular Rearrangements and Reactive Intermediates in Organic Synthesis

Prof. Santanu Panda

Department of Chemistry

Indian Institute of Technology, Kharagpur

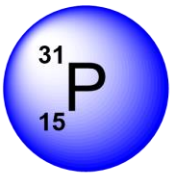
Lecture 54: Organophosphorus Chemistry

Welcome back to this NPTEL online certification course in molecular rearrangement and reactive intermediates. In the last couple of class i was started talking about the organosulfur chemistry previously and also talk about organosilicon chemistry and in today's class I am going to start with organophosphorus chemistry. These are the three different p-block element we want to cover in this course. In the today's class mainly to talk about the discovery of phosphorus. And different type of organophosphorus compound and then try to talk about some of the important reaction like Wittig reaction we are going to learn it is a very important reaction for the synthesis of olefin. We talk about the different selectivity modification of this reaction the Horner-Wadsworth-Emmons modification.

There are several other modifications of this reaction we are going to talk about apple reaction and finally, finish with the Staudinger reaction. So, first thing is the discovery of the phosphorous. So, Hennig brand in a 1669 he was an alchemist. So, I think it is a accidental discovery of phosphorous he was searching for something else and actually he found the phosphorous.

So, after i think the phosphorus actually is a group-15 and 3rd period p-block element having this $3s^2$ $3p^3$ in the outer cell. There are two different type of phosphorus we are going to come back in a minute one is the white another is the red. both having the different boiling point we are going to come back to their structure. Now talk about the oxidation state of the phosphorous starting from the 0 to +5 and the phosphorous are could be a trivalent or pentavalent so we are going to see some of these different type of compounds

Chemistry of Phosphorus



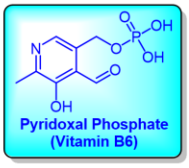
Hennig Brand (German merchant)
(1669)

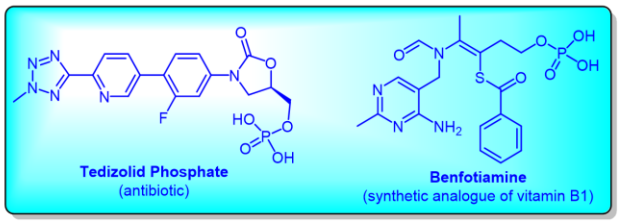
group:	15 (V A)
period:	3
block:	*p*
electronic configuration:	$[Ne]3s^2 3p^3$
m.p.:	white: 317.3 K red: 860 K
b.p.:	white: 553.7 K red: 860 K
density:	white: 1.823 g/cm^3; red: 2.2-2.34 g/cm^3; violet: 2.36 g/cm^3; black: 2.69 g/cm^3.
Electronegativity:	2.19
Oxidation state:	−3, 0, +1, +2, +3, +4, +5

I think phosphorous is present everywhere, inside the human body you can see there are flame retardants from fertilizers. And of course, the vitamin B6 pyridoxal phosphate there are the r n s has this the phosphate there are antibiotics and of course, there are a lots of-drugs where the phosphorus is present. So, mercury drugs are bioactive compounds and then there are lot of phosphorus specially the agrochemical is the most of the important thing the fertilizer and then there are also Phosphorus based reagent. And the other very important thing is Phosphorus based ligand if you see the Phosphine based ligands are play very important role for doing the different transition metal catalyst and also even in transition metal free carbon bond formation.

Uses of Phosphorus

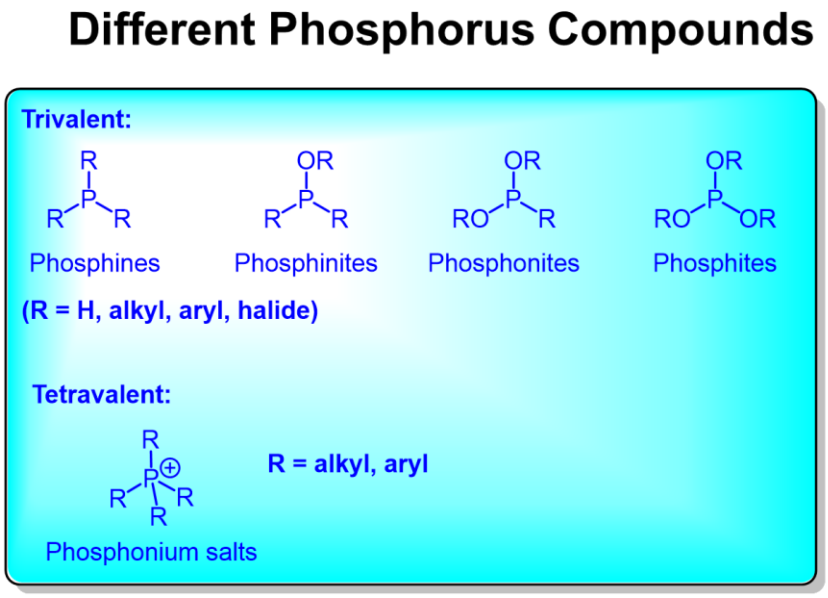
1. Phosphorus compounds are used as flame retardants.
2. Phosphorus is an essential mineral for the human diet (vitamin B6).
3. Phosphorus is a crucial element in different fertilizers.
4. Phosphorous is a key element in different phosphorus-based reagents and organophosphorus compounds.
5. Present in numerous drugs and bioactive molecules.





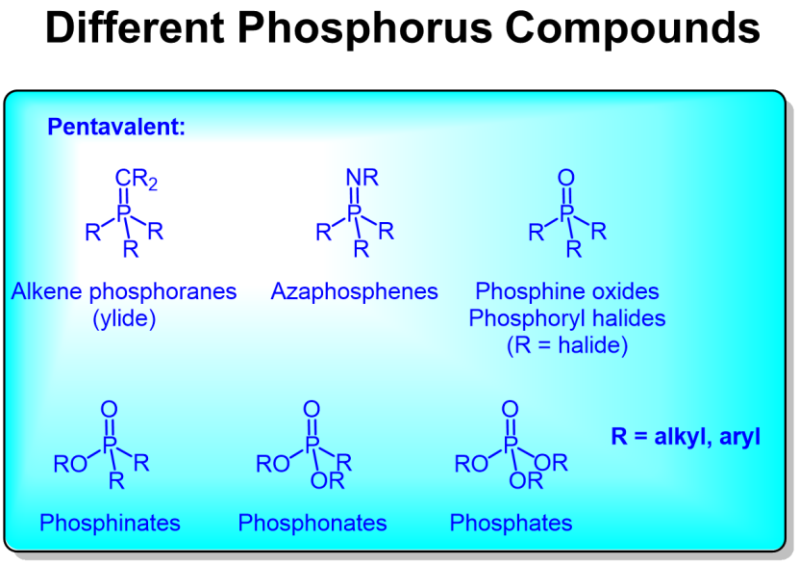
I am going to talk about the different phosphorus compound here are the list of different trivalent phosphorus compound like phosphine once the phosphorus having R (3-H, alkyl, aryl, halide) so these are the class of the compound called phosphine. and then there are Phosphinites.

when one of the R replaced by one oxygen this is called phosphinite then phosphonites 2R is replaced by 2 OR this is called phosphonites and finally, phosphite when 3 of these R group was replaced by 3 OR group. So, if you will see that all of them the important thing is from going to here and there you are giving more electron density into the phosphorous. So, if you think about the nucleophilicity wise then this one phosphite will be more nucleophilic and then we are going to talk about some of the tetravalent one. So, we talk about trivalent now we are going to talk about the tetravalent. then the the phosphonium salts.



So, if that the phosphines if react phosphines are also can participate nicely for the SN2 reaction with a alkyl iodide then you end up getting to $R'R_3P+$ So, we call this phosphonium salts we are going to talk about some of this also. and then from the phosphonium salt which I discussed in the previous slide if you give a base so what i was telling that if you have a phosphonium salt like this CH_2R and you have R or R' on phosphorus. in the phosphonium salt it is a plus on the phosphorus if you use a base then this can able to abstract this proton to generate a minus so that can form a double bond we call them as a ylide you have learned that if there is a plus and minus so this type of compound you can write them like these also $PR_3=CH_2R$ called phosphorus base ylide

then there are compound like azaphosphenes where your oxygen will be replaced by a NR group, oxygen replaced by a nitrogen then phosphine oxides this is another very important compounds and you will see lot of the phosphorus chemistry the byproduct will be phosphine oxides then phosphinates you can see another compound phosphinates having phosphor with the oxygen and then there will be one of R will be replaced by one of OR group so phosphine oxide if you replace one R by one of OR group this is called a phosphinates then phosphonate where you can see there are oxygen is present here but two of the R group replaced by two OR group when three of them will be replaced you will see these are called phosphate. again you can see that I think there are also phosphorous based acid like phosphoric acid also there are other different phosphorous compound most of them you will see in these two class either trivalent or pentavalent with very less amount structure you will see which has tetravalent like one we have already mentioned



So, that is the structure part now come to the oxidation state again the phosphorus having oxidation state from 0 to +5. So, if you see the elemental phosphorus, it having the 0-oxidation state once you go to the hypophosphorus acid and then once you come to the phosphine you will see it is a +3-oxidation state and once you come to phosphoric acid at the time you can see it is going to the +5-oxidation state.

So, this actually varies and you will see different type of reaction where you can able to convert a compound which are +3 oxidation state to +5 oxidation state of phosphorus.

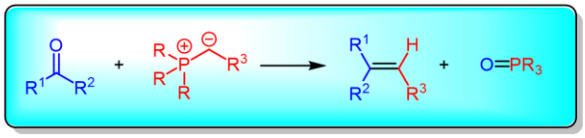
Oxidation States of Phosphorus

Oxidation state of Phosphorus	Example
0	P_4
+1	Hypophosphorus acid (H_3PO_2)
+3	Phosphorus acid (H_3PO_3), P_4O_6, Phosphine (PR_3, PX_3)
+5	Phosphoric acid (H_3PO_4), P_4O_{10}

I am going to start with the very important reaction developed by Professor Georg Wittig and it was a Wittig olefination reaction. So, we actually we talk about this ylide that we know one slide before that you can able to make the phosphonium salt correct we talk about that if you have a compound called this phosphonium salt. So, this is a phosphonium salt. and now if you use a base this is going to generate this ylide again in this ylide you will see the carbon having carbanion and phosphorus is a positive charge so that means this carbanion now can able to react with aldehyde we have already talked about lot of the sulfur based ylide chemistry I think you have seen that very similar type of reaction here this carbon going to attack through the corresponding aldehyde or ketone and from there we are going to talk about the details mechanism but at the end the triphenyl phosphine oxide going to eliminate through formation of a four member ring we end up getting to the corresponding-olefin.

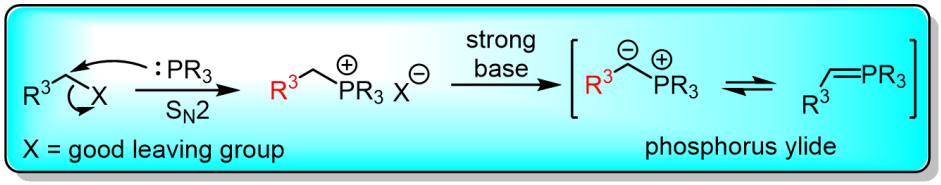
- The Wittig reaction or Wittig olefination is a chemical reaction of an aldehyde or ketone with a phosphorus ylide.
- This phosphorus ylide is known as Wittig reagent.
- Wittig reactions are most commonly used to convert aldehydes and ketones to alkenes.

Prof. Georg Wittig

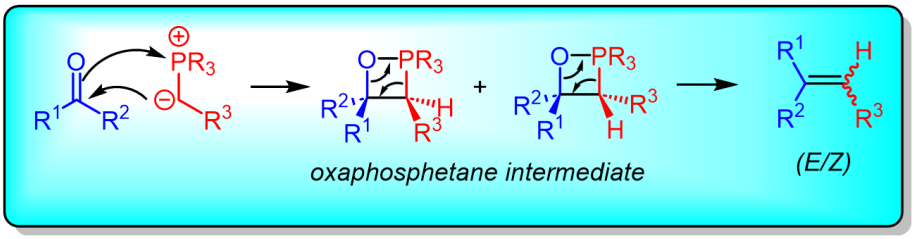


again as I was mentioning the first step how do you synthesize this type of ylide I think first step is the SN2 reaction trialkyl phosphines which are electron rich very good nucleophile going to participate in this reaction in this SN2 reaction to form the phosphonium then you have to use a strong base to abstract this proton correct to generate the phosphorus ylide again different type of base is used potassium tert-butoxide, n-BuLi there are different base can be used to generate the phosphorus ylide once you have ylide you can now add to the corresponding carbon compound the ketone or aldehyde which form the oxaphosphetane intermediate so this is the one important intermediate which is going to form ok so now again i think the you know the question comes what type of oxaphosphetane they are going to form going to form a threo or erythro so that again the very same problem we are going to talk about where you have seen in case of peterson olefination remember then when the nucleophile going to attack to the corresponding the carbonyl group which phase it is going to attack because it has corresponding when after that attacking happens the next step will be the formation of the oxaphosphetane intermediate from there it is going to form the corresponding olefin. So, I we are going to learn in a minute depending on which oxaphosphetane is going to going to form it is going to give you either E or Z olefin.

❖ The phosphorus ylide, usually generated in situ from the corresponding phosphonium salt.

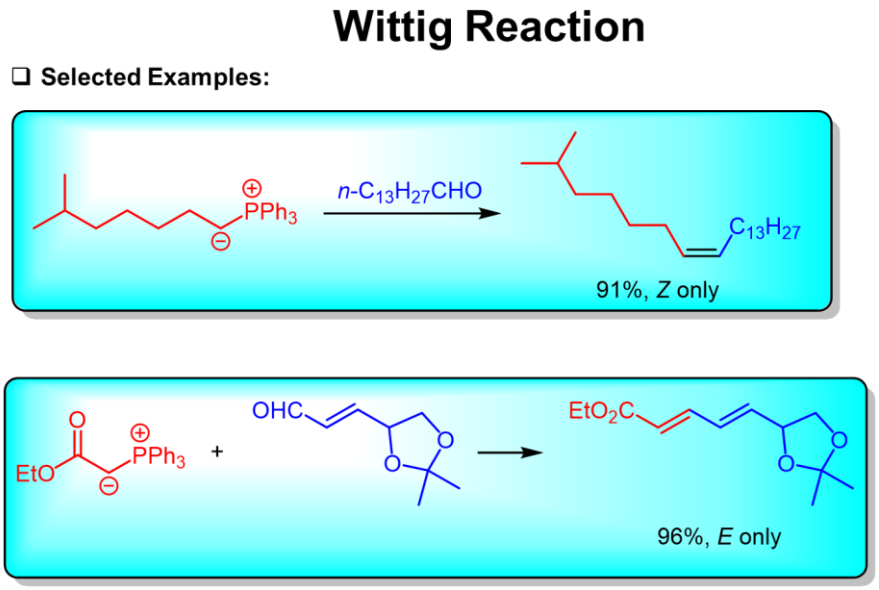


❑ **Mechanism:**



here you can see in this particular example we can see clearly this. So, we can see these ylide react with the corresponding aldehyde to form the Z olefin. But in case of the other cases where what we are seeing here once you are generating a ylide, but you have the carbanion which have a ester groups So, if you try to compare this carbanion A versus B

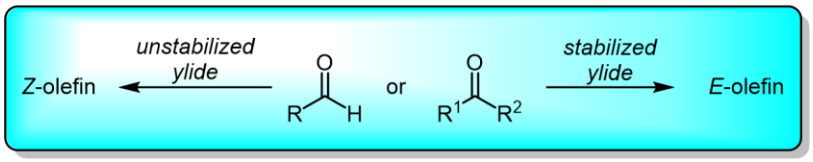
which one you think will be more stabilized? I am sure this the B will be the more stabilized carbanion because of the presence of the ester group. So, here what we are seeing once it is going to react with this aldehyde and form this corresponding olefin here we are seeing the 96% of the product, but E only product is formed. So, one case we are seeing the Z product one case we are seeing the E product formation happening. So, we can say the A can be a unstabilized there is not stabilizing group like not a electron withdrawing group except the triphenyl PPh_3 plus there is no other stabilizing group is there. here you have a stabilizing group so you can classify them stabilized versus non stabilized or unstabilized.



again you can s what is happening here we are seeing that if you have a stabilized ylide it is going to give E product as a major E-olefin as a major product if it is unstabilized ylide it is going to give you the Z olefin as a major product So, now we are going to learn why that is happening, why the stabilizing ylide giving and a different product compared to

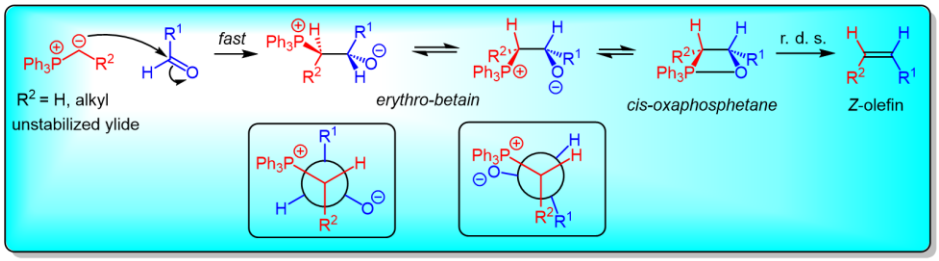
Stabilized vs Unstabilized Ylide

- When a conjugating or anion-stabilizing substituent adjacent to the negative charge is present, then the ylide is called a stabilized ylide.
- Other ylides are called unstabilized ylides
- **With stabilized ylides, the Wittig reaction is *E-selective*.**
- **With unstabilized ylides, the Wittig reaction is Z-selective.**



unstabilized ylide what is the difference? Again the difference comes again very similar to the peterson olefination the first step of attacking. When the attacking is happening there could be erythro vs thro there is two different reversible step in this reaction. One is the first step of the formation of the attacking of this nucleophile to this aldehyde or ketone and then the next thing is the next you know reversible thing is the oxaphosphetane intermediate formation so there is two different irreversible step now depending on so now the depending on the size and depending of this R^2, R^1 group and also the most important thing the depending on the stability of the ylide this two reversible step can be controlled but once it will go to the oxaphosphetane intermediate it will go to the irreversible step which is going to give you to the corresponding E or Z olefin so here to here what you are seeing if it is a unstabilized ylide you can see this is not a stabilized one so it is going to react fast so this is a very fast step one it is going to react first. So, the kinetics is going to take the major role here. It is going to go for formation of the cis-oxaphosphetane intermediate through the equilibrium. It is going to because this is a fast attacking happening So, this is going to form the cis-oxaphosphetane very fast and then from there it is going to go for. So, you can see there is a formation of this phosphorus oxygen bond and then carbon carbon double bond. So, this is going to get collapsed and then end up formation of So, again you can see in these cases the kinetics is going to take care. So, that is why you can see you are going to form the corresponding Z-olefin through this because this is going to be a Syn-elimination because these two phosphorus and the oxygen going to come from the same side they form triphenylphosphine oxide or trialkylphosphine oxide and then this is going to come out and form the corresponding olefin corresponding Z-olefin.

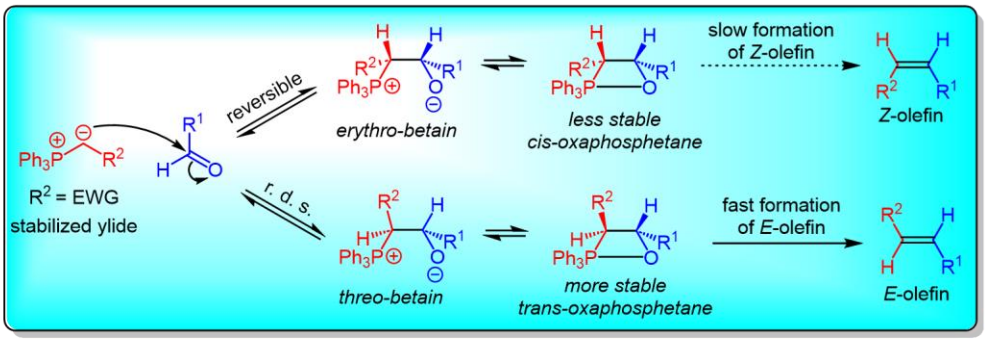
Synthesis of *Z*-Olefin



- In the case of unstabilized ylide, the betain formation is a very fast and irreversible process due to the higher reactivity of the ylide.
- Attack of the ylide on carbonyl will generate an *erythro*-betain.
- From the *erythro*-betain, *cis*-oxaphosphetane will form, which will undergo *syn*-elimination to form the *Z*-olefin (KCP).
- Here, elimination step is the rate determining step.

Now question comes what is happening if you have a stabilized one Now if you have a stabilized one the important thing become that there is two possibility because now the once it is going to attack here now that first thing is once attacking is happening here as the corresponding carbanion is a stabilized one so this is becoming a rate determining step and there is a two possibility now a formation of the oxaphosphetane intermediate it could be it try to form one of the oxaphosphetane which will be more stable so now the thermodynamics comes into the play as the ylide is more stabilized so once again is the steps as I mentioned this is a reversible so it will going to form the more stable which is trans of course if you think about these two in this two carbon where the substitution around this R^2 and R^1 once there is a trans the steric interaction will be less correct. So, this will be a more stable compared to the Cis. So, because there is a equilibrium here the equilibrium favors to formation of the more stable one. And once it is going towards the more stable one now this step is very fast. So, that's why once the equilibrium drives towards the trans-oxaphosphetane intermediate you will see the formation of the E-olefin. So, that's why the reaction goes towards formation of the E-olefin as a major in comparison to formation of the corresponding Z-olefin as you can see this is going through a less stable

Synthesis of *E*-Olefin



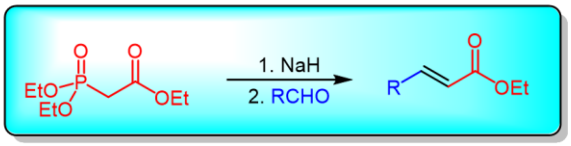
- In the case of stabilized ylide, the betain formation is slow and reversible process due to the stability of the ylide.
- The *cis*-oxaphsphetane is less stable, it decomposes to the starting material and forms the more stable *trans*-oxaphosphetane.
- From the *trans*-oxaphosphetane the *E*-olefin will form (TCP).

Cis-oxaphosphetane intermediate. so you can see the one as i mentioned so this stabilized ylide formation was discovered by horner-wadsworth-emmons so it is called a modified reaction so they have now we are going to talk about some of the wittig reaction variation which are again going to starting from a stabilized the phosphorus wittig so here what is going to happen? your stabilized phosphorus ylide going to form. Again you can see here the the the difference is once you are going to form a stabilized ylide you end up formation of the corresponding E-olefin again what is happening instead of trialkyl triallyl phosphine now you have this phosphonate ylide. So, we are moving from the phosphine ylide to a phosphonate ylide here. again you have the ester group and you have a phosphonate ylide here so that means now you have a phosphonate group so it is going to form the stabilized ylide which going to form the corresponding E-olefin. so in the next slide we are going to talk about some of the reaction where we are forming some sort of a phosphonate ylides so previously we talk about the formation of so you start with phosphine and then phosphonium and from there you form ylide now we are talking about phosphonate ylide here which are again stabilized ylide you see there are phosphonate group here and you have a ester group and this proton is getting abstracted to generate a anion here which is forming a phosphonate ylide. so phosphonate ylide are more nucleophilic and in less basic then corresponding phosphonium ylide ok as i mentioned before once this corresponding phosphonate ylides will be more nucleophilic because again once it is more nucleophilic it is going to react first and going to form the corresponding E-olefin through the mechanism i have discussed before again the one of the important thing here once you have a phosphonate group here you have a

phosphonate group is the electron withdrawing group you have a ester group now this proton in the middle will be much more acidic so you can use a sodium hydride which can able to abstract this proton and form the corresponding ylide and from there you can form the corresponding product so it is another example of a important things.

Horner-Wadsworth-Emmons Modification

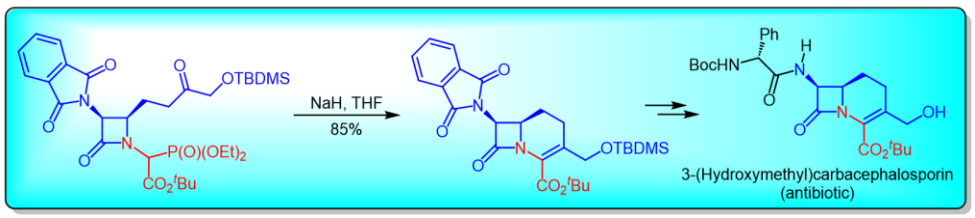
- The reaction of a stabilized phosphonte ylide with carbonyl compounds to form the *E*-olefin, the reaction is known as Horner-Wadsworth-Emmons reaction.
- The phosphonate ylides are more nucleophilic and less basic than phosphonium ylides used in the Wittig reaction.
- The reaction is used for the selective formation of *E*-olefin.



stabilized ylide there is a example here you can see from here they are forming formation of the corresponding phosphoryl ylide is going to form using sodium hydride and that can allow the formation of the olefin between this carbon group and this carbon. These two carbon can form a olefin here again this is a stabilized one. So, you end up forming this olefin and which can further convert to a antibiotic compound Now I am going to talk

Horner-Wadsworth-Emmons Modification

❑ **Synthetic application:**

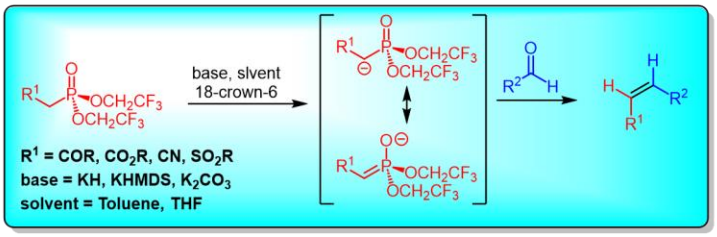


about some of the important modification. So, we talk about that the HWE modification and we are going to talk about another modification called still-gennari modification or SG modification. So, what they have done? I think what was the initial concept that once

you have this type of stabilized ylide So, the Horner's- wadsworth-emmons modification where you have learned that once you have this system once you have this phosphonates phosphonate ylide we talk about that those cases we always get to the corresponding E product but now the question comes can you change some of these so that it can end up formation of the z-olefin as i mentioned one of the advantage of this phosphonate ylide is they are more nucleophilic and this proton can be easily abstracted as i mentioned because of you have two electron with this carbon So, then I think the Still and Gennari actually introduced first the general way to prepare the Z-olefins where they have introduced the important thing is the trifluoro-ethyl(CH_2CF_3) group. So, instead of this OCH_2CH_3 they have to introduce this CF3 group here. So, again you can understand introducing CF3 means you introduce some sort of electron this electron withdrawing group this electron withdrawing group plays a very important role for the synthesis of corresponding Z- olefin because just by changing this group what you are bringing you are bringing the selectivity of the corresponding olefin product formation of course you have to use the base and 18-crown-6 always used to take the sodium or the potassium and which can now able to generate the corresponding ylide here, which can able to react with the aldehyde to form the corresponding Z alkene.

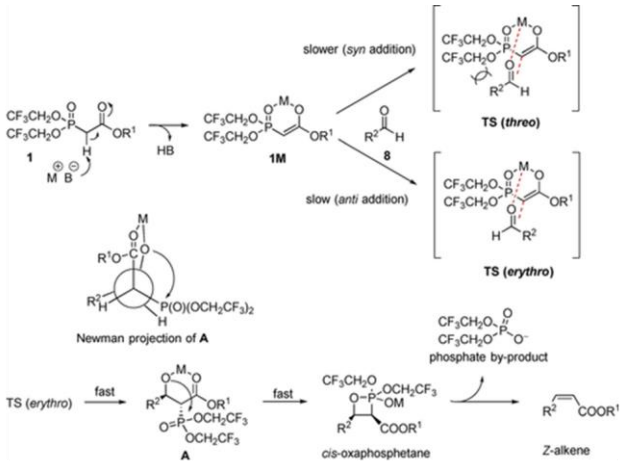
Still-Gennari Modification

- In 1983, W.C. Still and C. Gennari introduced the first general way to prepare *Z*-olefins from aldehydes by the modification of the phosphonate reagent used in the HWE olefination.
- An excellent method for the preparation of *Z*-α,β-unsaturated ketones and esters.
- Bis(trifluoroethyl)phosphonoesters used as the ylide source.



We are going to learn the the important concept here that why we are seeing the corresponding Z product here, what is the important thing. They are saying the one of the important thing is electron withdrawing character of the alkoxy group one of the crucial factor which affecting the stereoselectivity Of course, once you have electron withdrawing group here, the first thing is that you can use this formation of the corresponding of course, you can able to abstract this proton to form the corresponding enolate. Now, the enolate can be able to go for a syn addition or anti addition means depending on this if you are adding to the aldehyde the R^2 group can have steric effect

with this phosphorus. So, it will try to go through this anti addition forming the erythro product instead of the threo there is a steric class here. So, so that is why it is going to go for anti addition. So, once you have anti addition happening to formation of the corresponding erythro-product. So, you can see this is a Newman projection for this after the addition happen here. Now, that the next thing is what is happening there this oxygen here is going to form a bond with this phosphorous it is going to attack to the phosphorous and going to form the cis-oxophosphetane intermediate. Now because now this step is a very important step this is the one important step which is differentiating in compared to the the HWE modification. What is happening here? Because there is a phosphorous is attached with a group which are electron withdrawing group this step is much faster. again there is a some sort of a kinetics playing into the role instead of this getting into the equilibrium to the corresponding trans-oxophosphetane after the attacking happen this immediately form cis oxophosphatine and going to the corresponding Z-olefin which you you have seen in case of unstabilized one correct in case of unstabilized one we have seen that is going the reaction is happening first it is forming immediately through a through the kinetic control formation of the cis-oxophosphetane and going to the product here also you are controlling the reactivity by introducing electron withdrawing group in the phosphonate and again i think once you have electron withdrawing substitution occupy the apical positions which stabilize the penta-coordinated oxophosphetane intermediate go to the corresponding Z-alkene.



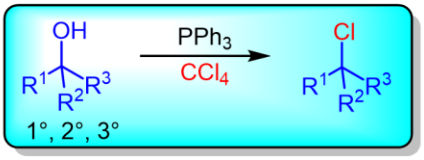
The electron-withdrawing character of the alkoxy group is one of the crucial factors affecting the stereoselectivity of the reaction. The electron-withdrawing substituents occupying the apical position stabilize the pentacoordinate oxaphosphetane intermediate, they thus push the reaction equilibrium towards product formation.

The other important reaction is the appel reaction which is a again you can able to convert the corresponding secondary primary alcohol to the corresponding alkyl halide using triphenyl phosphine and you can use a CCl_4 or CBr_4 Br_2 there are several different variation of that again this is a very important reaction. you can see mechanistically what is happening

Appel Reaction

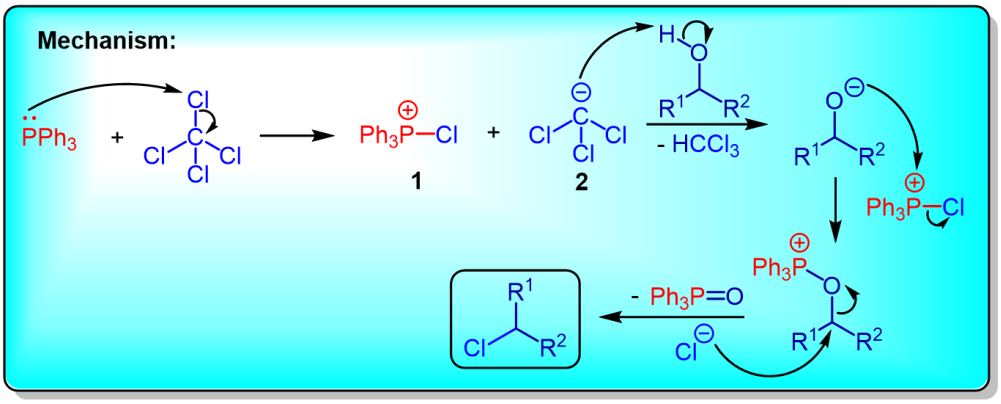
- The Appel reaction is an organic reaction that converts an alcohol into an alkyl chloride using triphenylphosphine and carbon tetrachloride.
- CBr_4, Br_2, CI_4, I_2, and MeI are also used.

Prof. Rolf Appel



Here the triphenyl phosphine nucleophilic attacking to the carbon tetrachloride (CCl_4) formation of this very important species here and then you have the at the same time you are generating this species you guys have seen there at the beginning when I was talking about the generation of I think we talk about the alpha elimination when in interest of the carbene. But here the α elimination is not happening because these two species one and two forming a tight ion pair. So, that is why they after this formation happening this minus can able to abstract this proton from OH group Now this O minus can immediately attack to the phosphorus which having the positive charge. Now once you have this species now this phosphorus actually bound with the oxygen correct. So, once is bind to the oxygen it is taking electron density from oxygen that is now it can act as a leaving group. So, the Cl minus can attack here to get rid of this and it can end up forming a triphenyl phosphine oxide which is stable product. so it is forming from a phosphine it is going to form a phosphine oxide you can see here its forming a more stable products here and it is going from a trivalent to a pentavalent phosphorus at the same time it is going to convert the corresponding alcohol to the corresponding alkyl halide There are some of the variation

Appel Reaction



- **1** and **2** present as a tight ion pair and that's why **2** didn't undergo α-elimination to form dichlorocarbene.
- Strong P=O bond formation is the driving force of the reaction.
- In the final step 1° and 2° alcohol reacts in a S_N2 fashion whereas 3° alcohol reacts in S_N1 fashion.

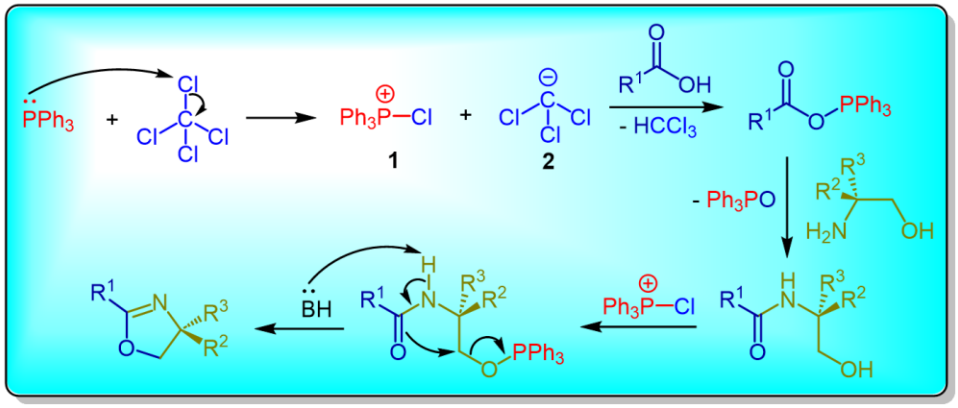
here apple reaction can also effective with the carboxylic acid instead of the alcohol if you use a carboxylic acid, but it can convert to corresponding oxazolines or thiazolines depending on whatever. So, I think once you have this you once you have acid here.

and after that what is going to happen you can remember the acid OH can very similarly alcohol attack to the this species. So, this can attack to this species after the formation of the O minus when this can able to after this proton formation of this. So, you can see you can think about these are very activated ester. So, the nucleophile can attack here in the carbonyl. So, you have this NH_2OH once you have this species it can attack here.

from the amide you have learned about very similar the amide formation where you take activate acid with the this type of DCC or EDC to form some sort of activated ester which get attacked by the amine from the amide but you have this OH group there which can react with another equivalent of this compound further this can attack through this oxygen to get rid of this as a triphenyl phosphine oxide to form this corresponding oxazolines you have a sulfur here it can form the corresponding thiazolines example here you have the OH group

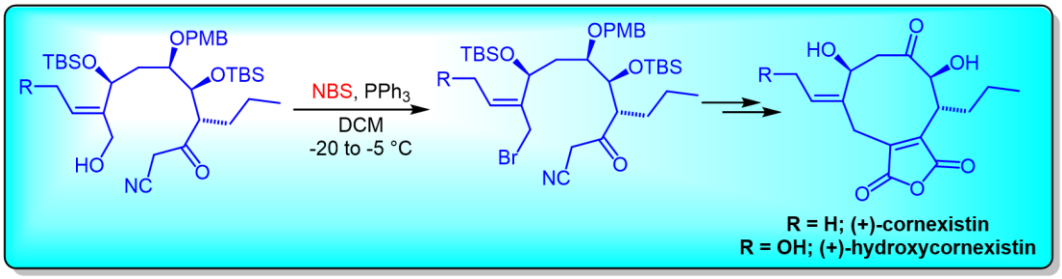
Appel Reaction

- The Appel reaction is also effective on carboxylic acids.
- Used to convert them to oxazolines and thiazolines.



here converting to the corresponding bromine and then going to convert to the corresponding natural product.

Appel Reaction



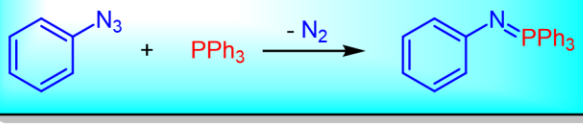
Another important reaction is a Staudinger reaction which is a conversion of what you are seeing you are seeing conversion a azide to the corresponding amine through this very important intermediate a phosphoiminium intermediate. we are going to talk about that from there you can see formation of the different different product in 1919 the professor staudinger and professor j meyer discovered this reaction using the triphenyl phosphine and a phenyl azide.

Staudinger Reaction

- In 1919, H. Staudinger and J. Meyer reported the reaction between phenyl azide and PPh_3, which afforded a novel compound, phosphinimine.
- Later on, the reaction was applied to different systems.
- The phosphinimine can be converted to amine, imine, amide and imidoyl halides.

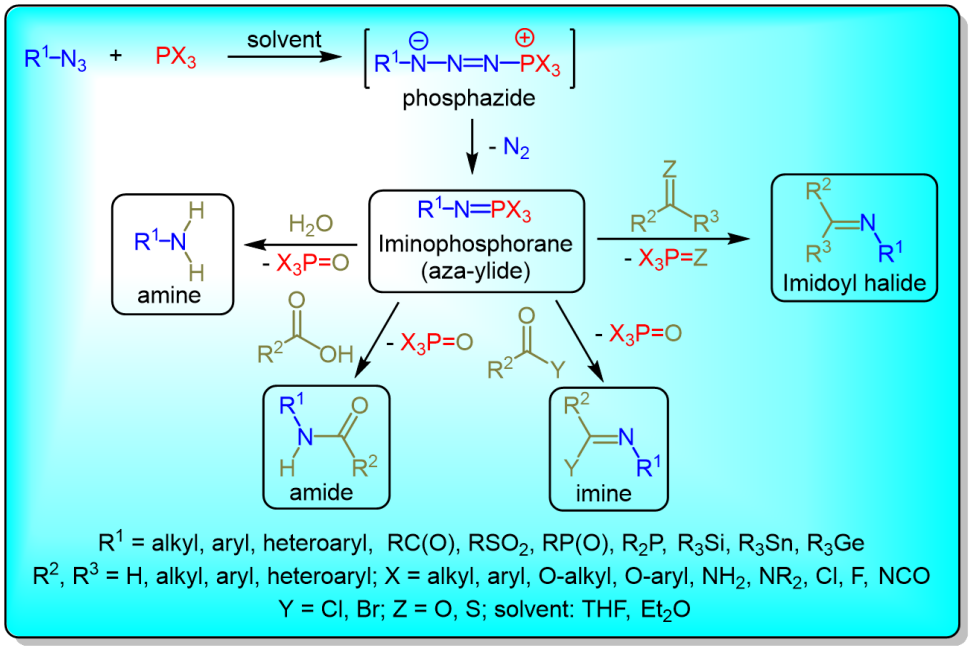
Prof. Hermann Staudinger

***Staudinger* (1919):**



again i think you can see this is going to first react with the azide and the triphenyl phosphine react from the phosphazide it from the phosphazied and then the N2 expansion happen to form the immunophosphorane or the (aza-ylide) or the immunophosphorus I think once you have the immunophosphorane from there once you treat with the water it is going to form the corresponding amine if you treat with the corresponding compound like thiswith a carbonyl group compound that can form the imidoyl halide. or then you have it can form the corresponding imine once you attack to the corresponding carbonyl compound it can form the imine or it can form the corresponding amide I think it can form amine or it can form amide or it can form a corresponding amine based on the different different reagent you choose here you choose acid here you choose water here you use corresponding carbonyl compound with a Y equal to corresponding i think it is a acid halide you use acid halide and here you have are used corresponding so your Z equal to here so you use a carbon compound or if you use a J equal to could be oxygen or sulphur that can generate the corresponding imidoyl compound I am going to talk about the mechanism of this reaction

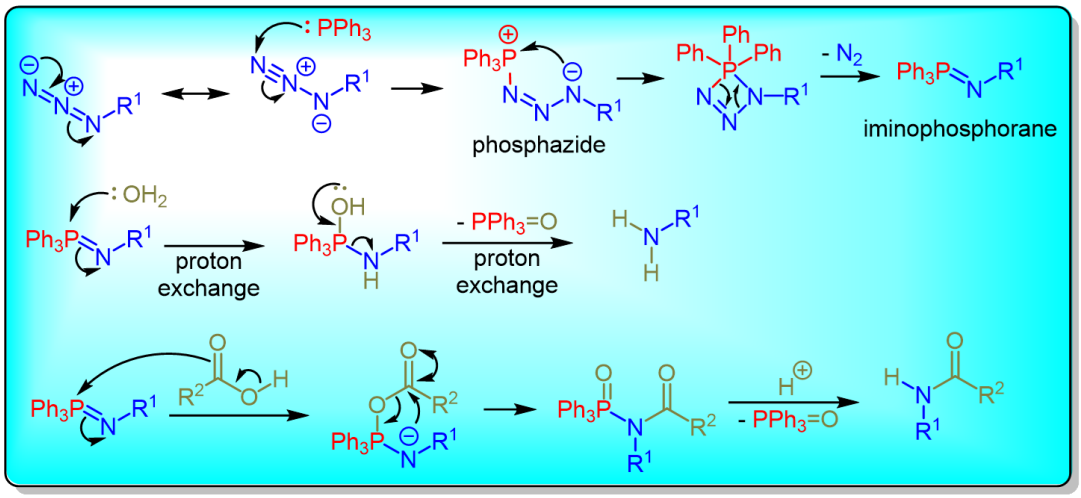
Staudinger Reaction



again first thing the triphenyl phosphine you can see phosphines are nucleophilic that can attack here to this nitrogen to form the corresponding phosphazide correct then the phosphazide can attack to the phosphorus and form through this four member transition state and N2 going to get out from a immunophosphorane once you have immunophosphorin the water can attack here and through the proton exchange and the the get rid of triphenyl phosphine oxide it can generate this corresponding amine. the acid can also attack here very similarly the oxygen can attack here and then you can see it is going to come back and going to form a phosphor oxygen double bond and the N minus can attack here first it is going to come back and then form a corresponding phosphine oxide, so phosphine oxide is going to get out and you end up formation of this corresponding amide

Staudinger Reaction

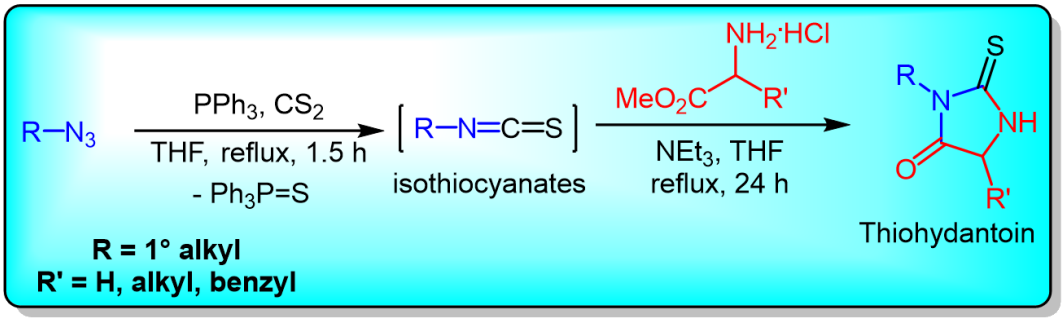
Mechanism:



another application if you used triphenylphosphine and with carbon disulphide (CS_2) you end up forming this isothiocyanate and which can again if you treat with this compound with a amino acid that can form the corresponding thiohydantoin so that is another

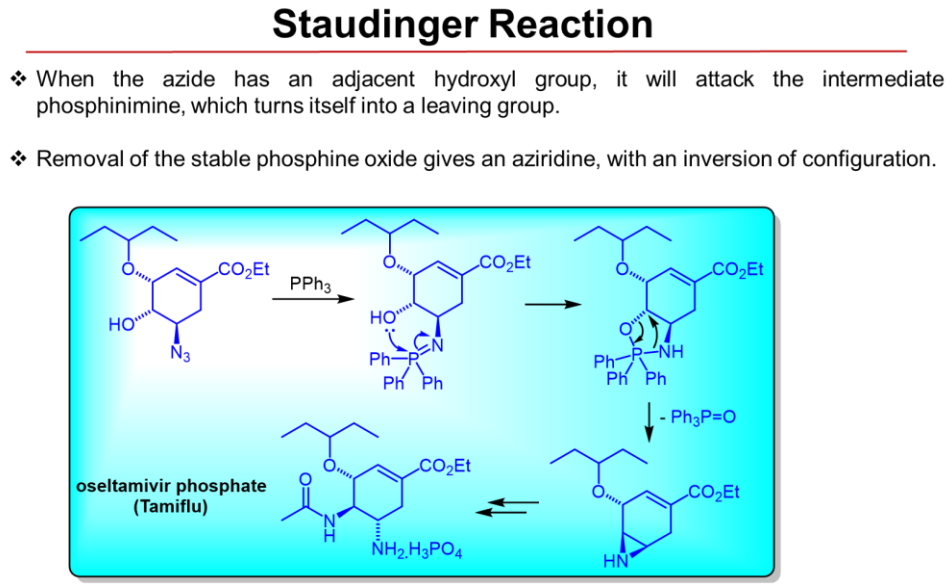
Staudinger Reaction

❖ **Synthetic Application:**



important application of this reaction again i think the mechanism will be very similar formation of this isothiocyanate going to happen by very similar first formation of the immunophosphorane then it is going to react with the carbon disulfide to form that

application of this reaction you can see there is azide here which finally going to convert to the corresponding amine you can see let's try to understand first thing is you have a corresponding alcohol here it is going to also play important role after formation of the immunophosphorane you have this internal alcohol which is going to attack phosphorous from here it is going to get rid of triphenyl phosphine oxide and form this azitidine and which can going to get open up to form this very important compound, very important drug which is called the tamiflu again you can see that there are a couple of important step here I think one of the important thing I should mention here that you can see the the amine stereochemistry actually retain here towards the end, but then in this compound at least in that the alcohol stereochemistry actually go on for inversion. Why it is happening? Because in this stage when you are forming this diphenylphosphine oxide bond this nitrogen attacking here. So, there is SN2 happening here that is why you see a inversion of the stereochemistry in this particular carbon. So in this part i talk about the discovery of the



phosphorus i talk about the very important wittig reaction and its selectivity. The HWE modification of this reaction then Still-Gennari modification, Appel reaction, and i talk about the Staudinger reaction from the reduction of azide to amine.

Again these are the test book you can able to find most of the things from the jonathan clayden books Again thank you so much for the coming to the class i am going to see you guys in the next class.