

**Chapter 8**  
**Organophosphorus**  
**Reactions**

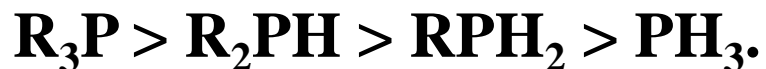
## CONSIDERATIONS

**Phosphorus compounds can be divided into three classes:**

**1. trivalent, 2. positively charged, and 3. pentavalent compounds.**

**The predominant role of trivalent phosphorus is that of a nucleophile.**

**The basicity of phosphines decreases according to substitution:**



**As  $H^-$  is much softer than the alkyl residue, the replacement of H by R would make the phosphorus atom harder and, hence, easier to combine with the proton.**

**Phosphines:  $R_3P$**

**Phosphites:  $(RO)_3P$**

**Phosphonium salt:  $[(RO)_3P-R]^+ [RO]^-$**

**Phosphinites:  $(R)_2POR'$**

**Phosphonites:  $(RO)_2PR'$**

**Phosphonate:  $(RO)_2P(O)(R)$**

**Phosphinates:  $(R)_2P(O)(OR)$**

**Trialkylphosphine oxides:  $(R)_3P(O)$**

**For  $R_3P$ , the nucleophilicity diminishes (1) along the series  $R = \text{alkyl} > \text{aryl} > \text{alkoxy}$ , and within the phosphite subgroup,  $R = \text{MeO} > \text{EtO} > \text{n-PrO} > \text{n-BuO}$ .**

**The progressive increase in hardness of the alkyl, aryl, and alkoxy groups makes the phosphorus correspondingly harder and less compatible with a soft acid.**

**The fact that the trialkylphosphites are still reactive toward alkyl halides (Michaelis-Arbuzov reaction) may be rationalized in the following manner.**

**The ground state energies of phosphites must be higher than phosphines by virtue of the negative contribution by the hard-soft interactions between the O and P atoms.**

**However, on going into the transition state of alkylation the phosphorus atom undergoes rehybridization and a valence change which can essentially be summarized as a soft to hard transformation.**

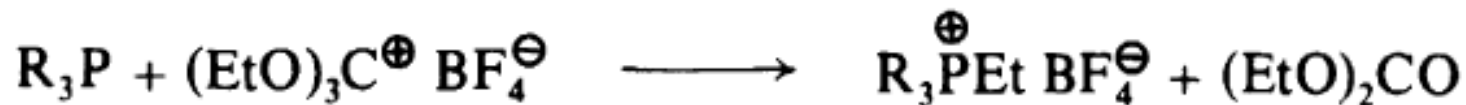
**The activation energies for such a process must be lower. Thus, both the elevated ground state energy and the decreased activation energy contribute to the ease of phosphite alkylation.**



# TRIVALENT PHOSPHORUS COMPOUNDS AS NUCLEOPHILES

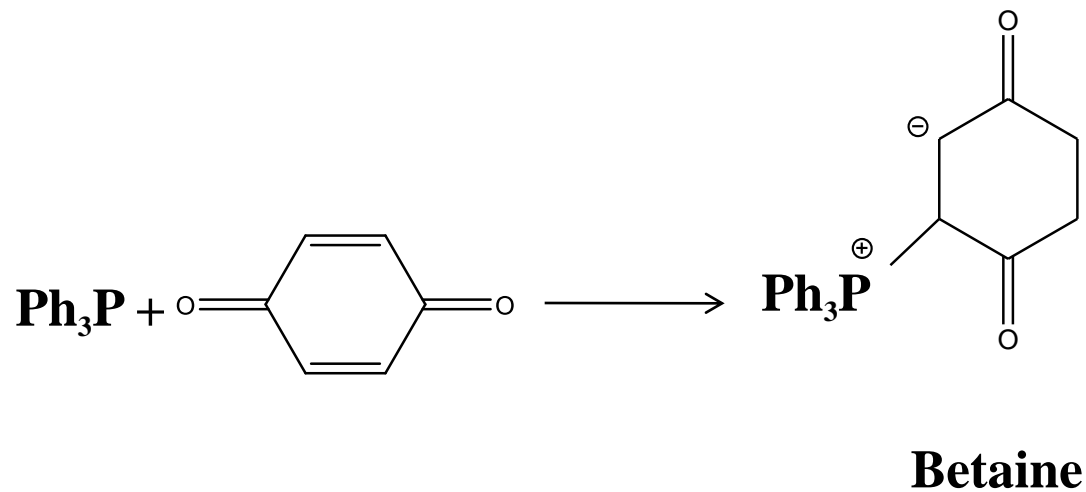
## Attack at Carbon:

Tertiary phosphines are rapidly quaternized by alkyl halides. During the reaction with the ambident triethoxycarbenium fluoroborate, phosphines seek the softer ethyl group.

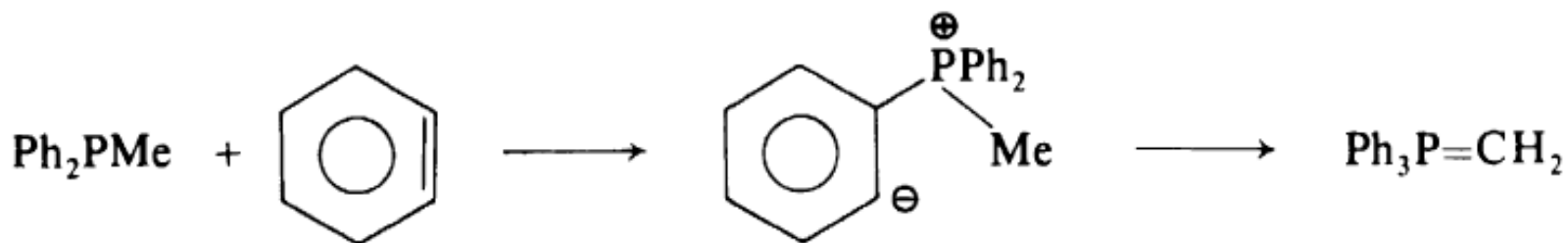
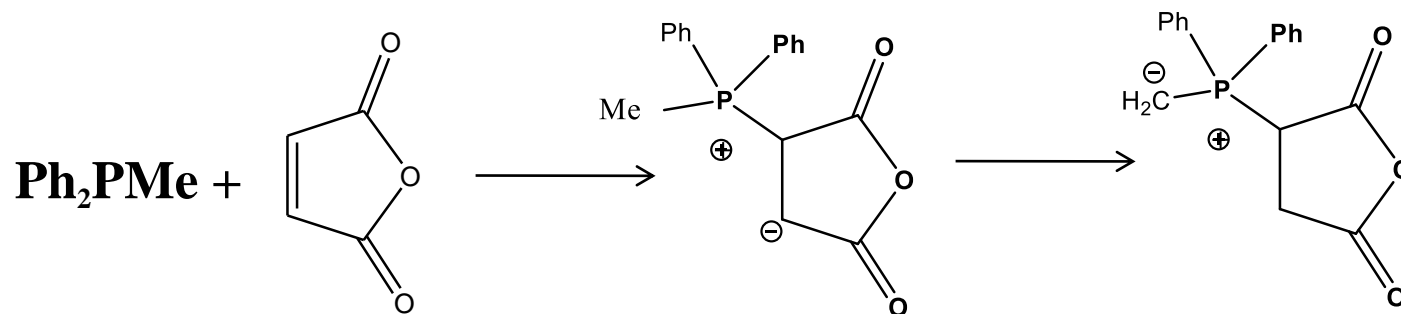




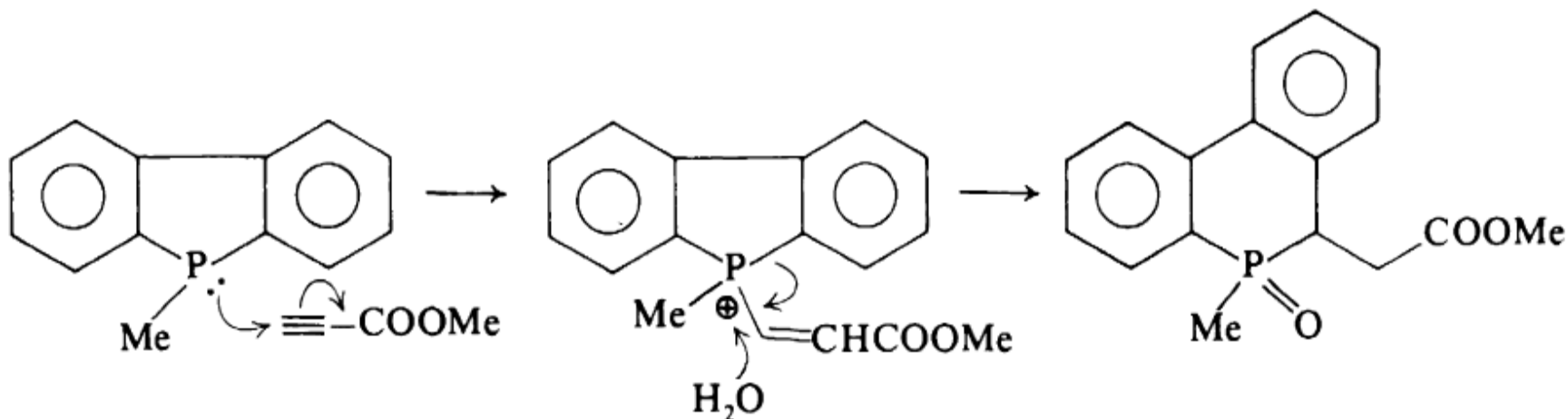
**Phosphines function as Michael donors in the betaine formation with benzoquinone.**



Similarly, ylides are produced from mixing phosphines with maleic anhydride and benzyne.



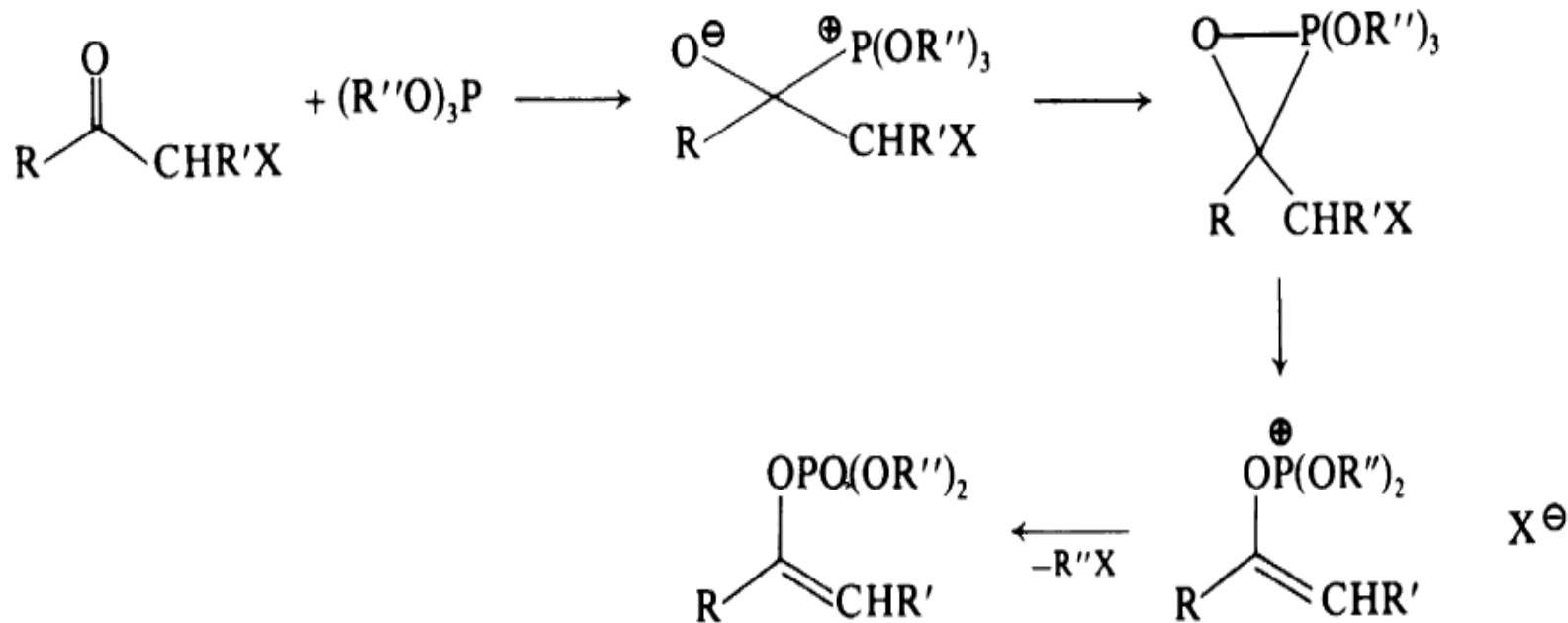
The ring expansion of 9-methyl-9-phosphafluorene on treatment with methyl propionate must be initiated by a Michael addition of the phosphine to the triple bond.

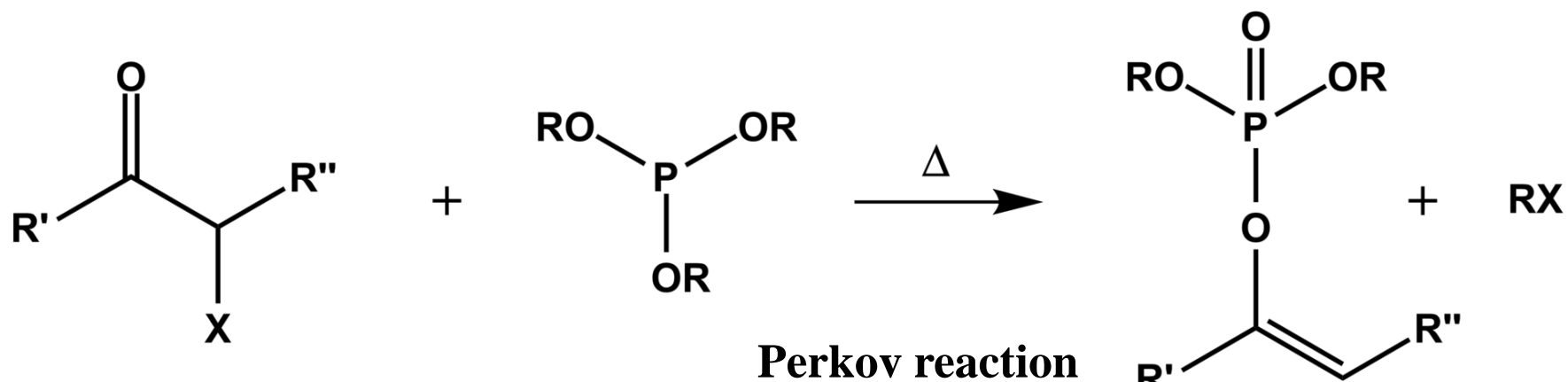


By virtue of their softness, phosphines readily intercept carbenes resulting in Wittig reagents.

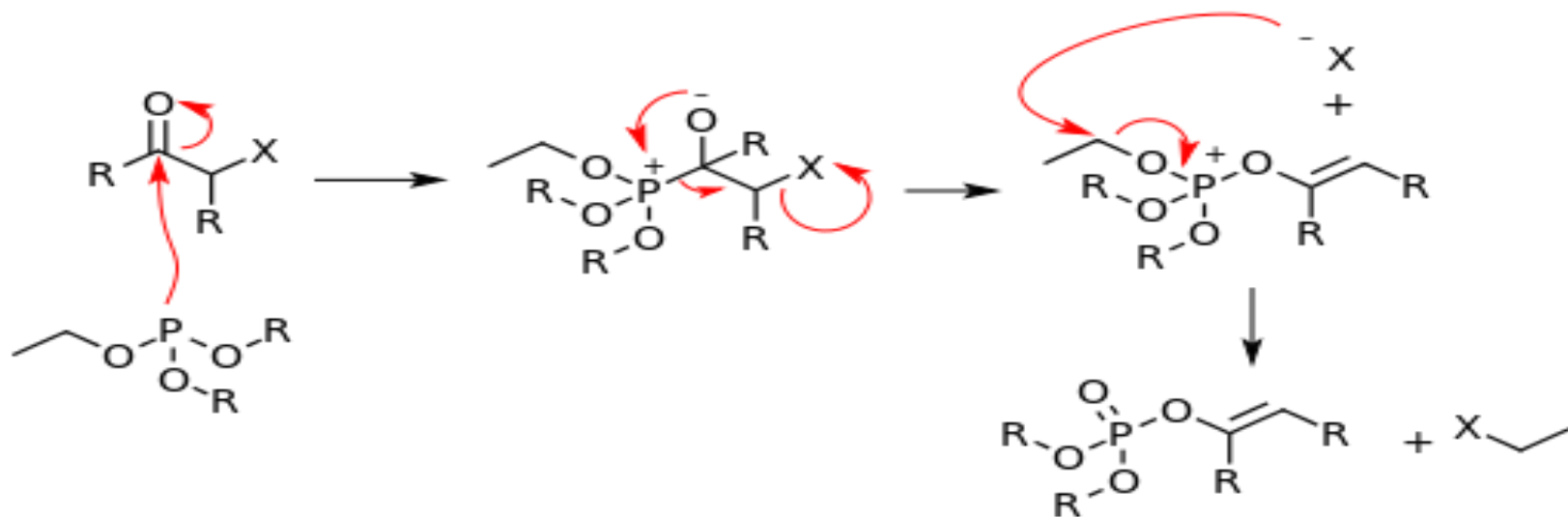


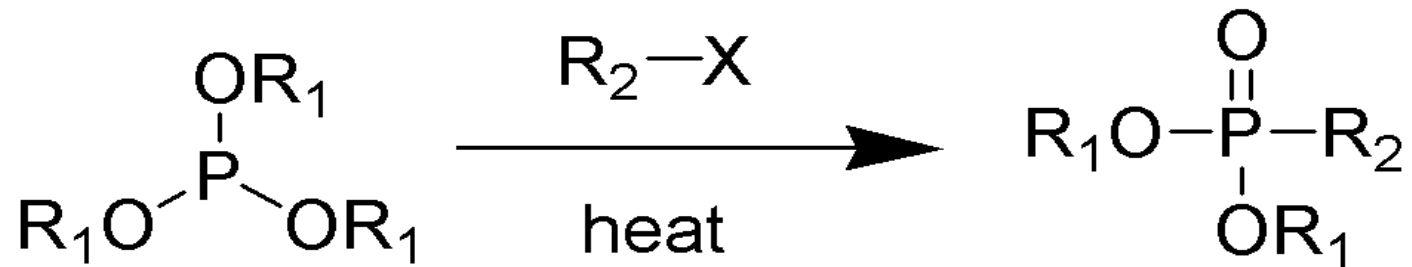
In the Perkov reaction, all evidence indicates that the addition of the phosphite to the carbonyl carbon is the first step. The Perkov pathway is favored over the competing Michaelis-Arbuzov reaction (attack on carbon of X) by the harder halide substrates.



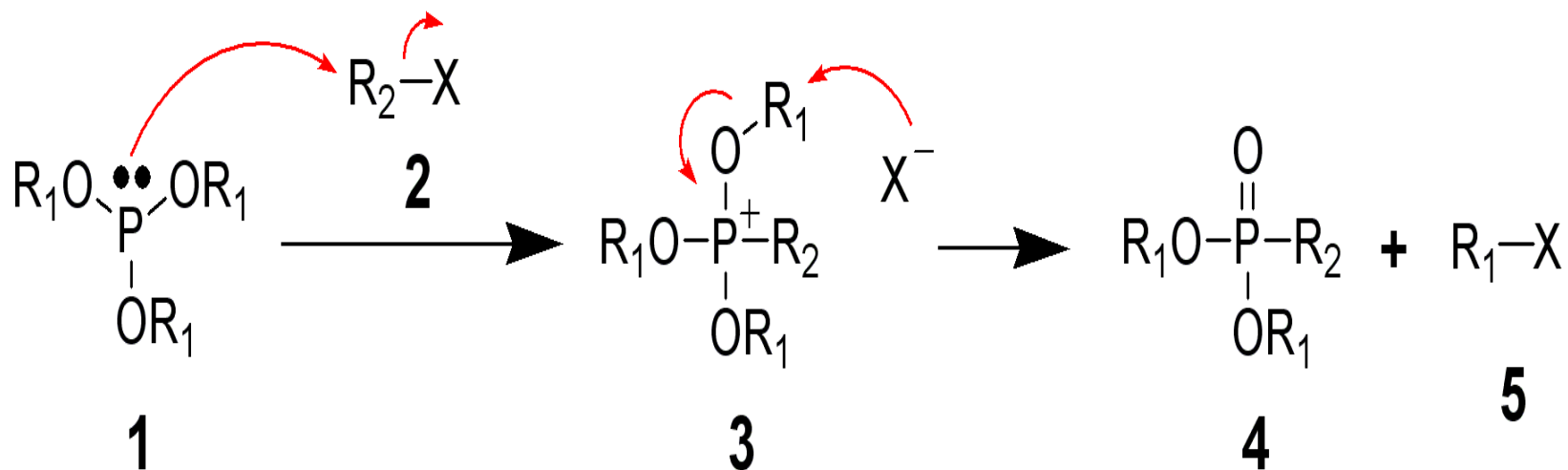


X = Br, Cl





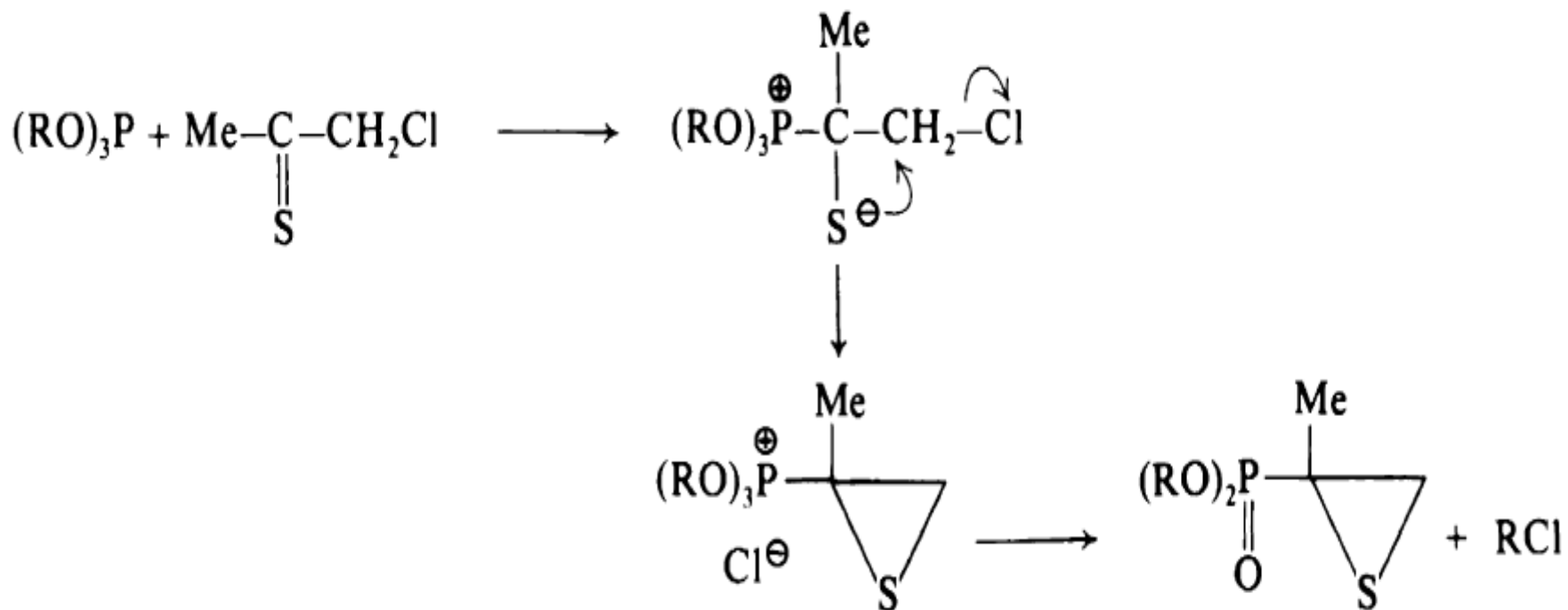
### Michaelis Arbusov reaction



**$\alpha$ -Phenylthiodeoxybenzoin (PhCOCH(SPh)Ph) reacts with (EtO)<sub>3</sub>P following the Perkov route, in contrast to the  $\alpha$ -ethylthio analog which furnishes a host of ketonic and vinylic products.**

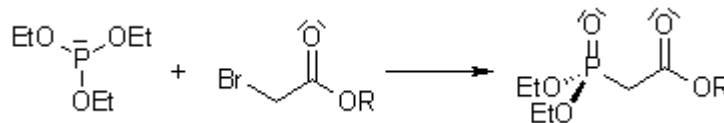
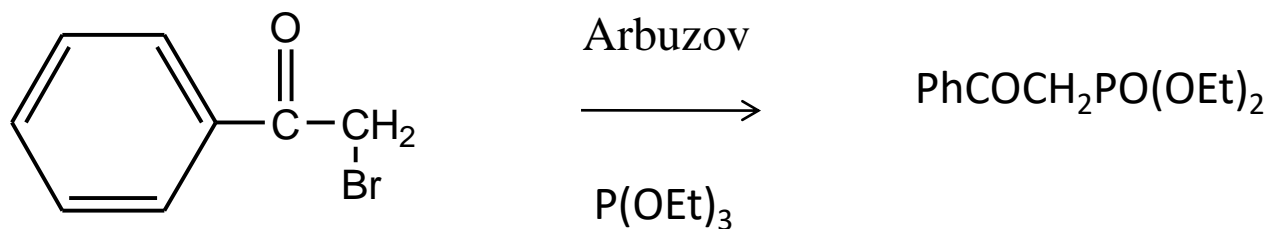
**It appears that, besides steric effects, the slight increase in hardness of the phenylthio sulfur drives the phosphorus atom to interact with the carbonyl.**

**In the Perkov reaction of  $\alpha$ -chlorothioacetone, decomposition of the intermediate zwitterion is determined by the softness of the sulfide anion.**





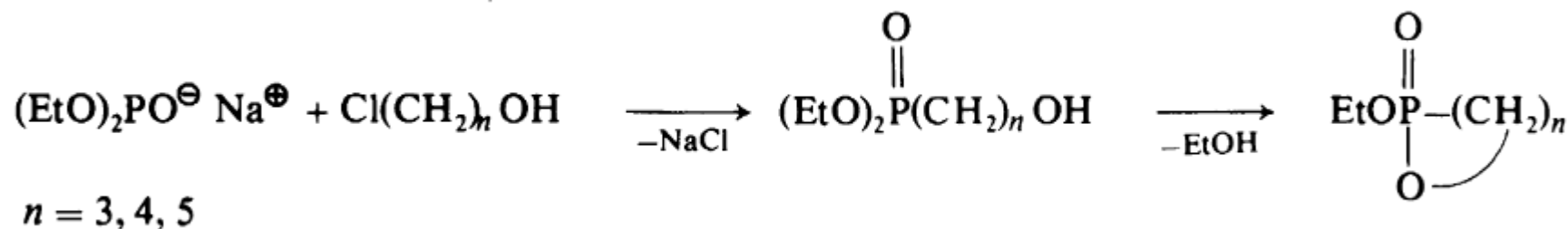
**The Arbusov reaction of substituted  $\alpha$ -bromoacetophenones shows a negative Hammett  $\rho$  value suggesting an initial attack on carbon during formation of the ketophosphonates.**



**Although phosphines seldom attack simple carbonyl compounds, Mark reported the formation of zwitterionic adducts from hexamethylphosphorous triamide ( $\text{P}[(\text{N}(\text{CH}_3)_2]_3$ ) with aldehydes.**

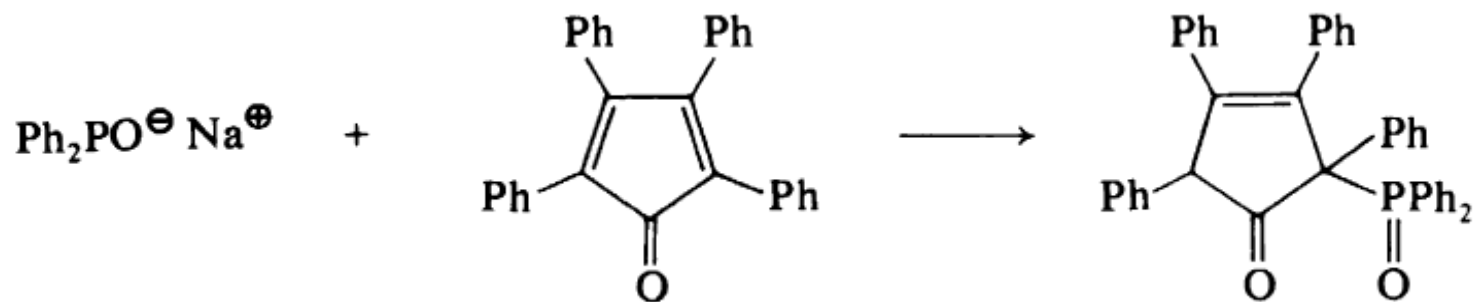
**Because the aldehydic carbon is softer than the ketone counterpart and the phosphorus of the triamide is harder than that of ordinary phosphines, the softness of these reactants are perhaps sufficiently compatible with each other.**

**Sodium diethylphosphonate combines with  $\omega$ -chloroalkanols of appropriate chain length to yield cyclic phosphonates. It is evident that the first P alkylation step is a soft-soft combination and that the ring closure involves a hard-hard interaction.**



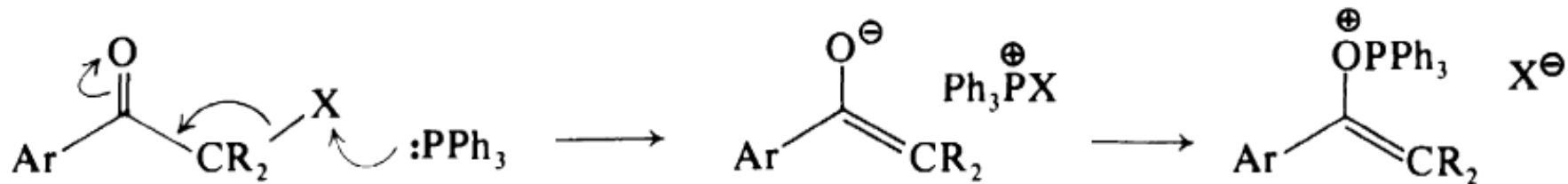
**A related report reveals that phosphites are generated by the reaction of triarylchloromethanes with silver diisopropylphosphite. This reaction is charge controlled.**

**The kinetic product of sodium diphenylphosphite addition to tetraphenylcyclopentadienone is a 1,4-adduct.**

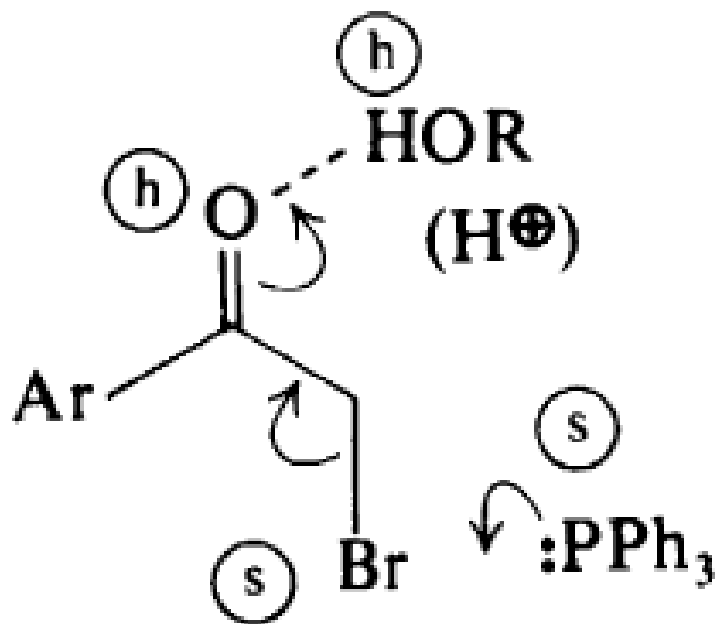


## Attack at Halogen:

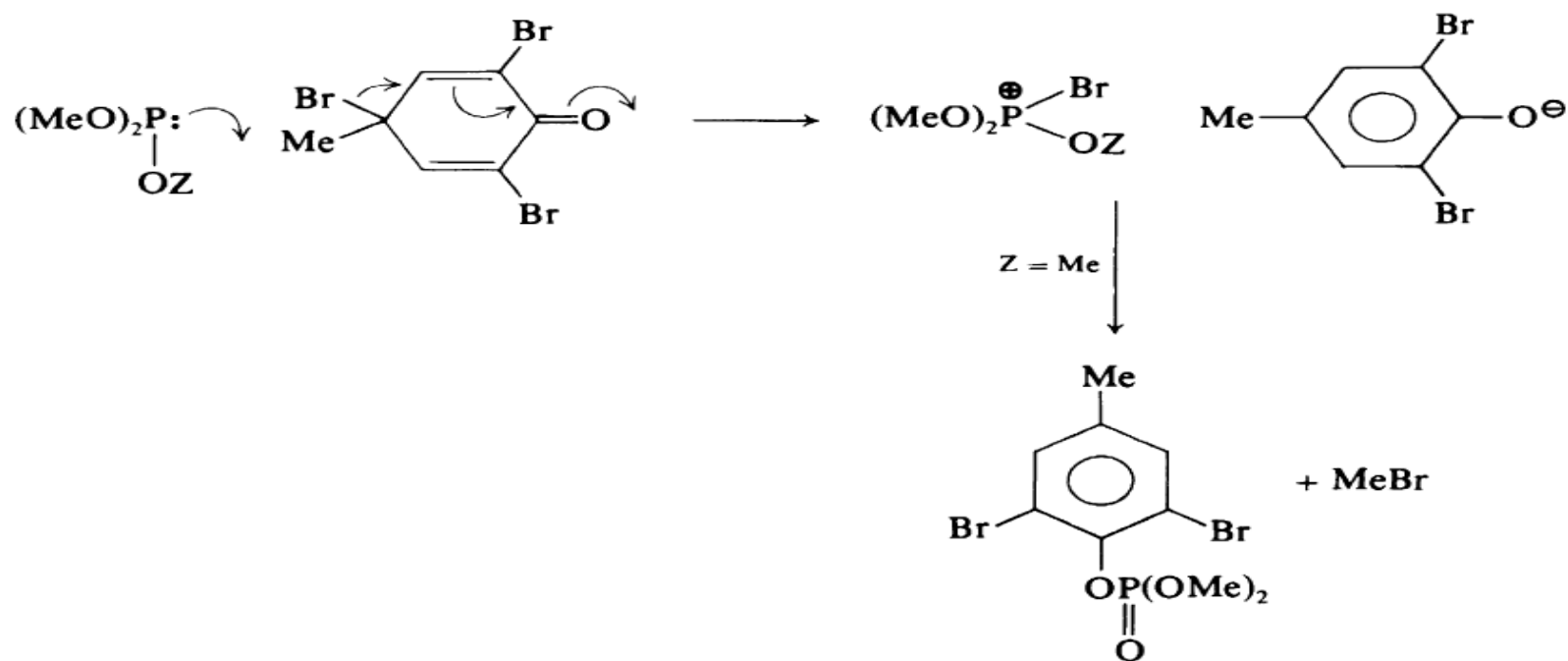
The change of venue from the Perkov and Arbuzov pathways concurs with the HSAB rationale as the phosphine P is softer than the phosphite P. Studies on enol phosphonium salt formation support this contention.



**The  $\alpha$ -chloroketones** fail to undergo a similar reaction.  
The catalyzed reaction conforms to Saville's rule.



The C-4 bromine of 2,4,6-tribromo-4-methylcyclohexa-2,5-dienone is very soft, and therefore it is readily extracted by trivalent phosphorus compounds. Rate studies with the 2,6-di-tert-butyl analog exclude the attack on oxygen.



**Dibromoketene** can be generated from trimethylsilyl tribromoacetate on treatment with  $\text{Ph}_3\text{P}$ . Many other trihaloacetic acid derivatives undergo similar dehalogenation reactions.

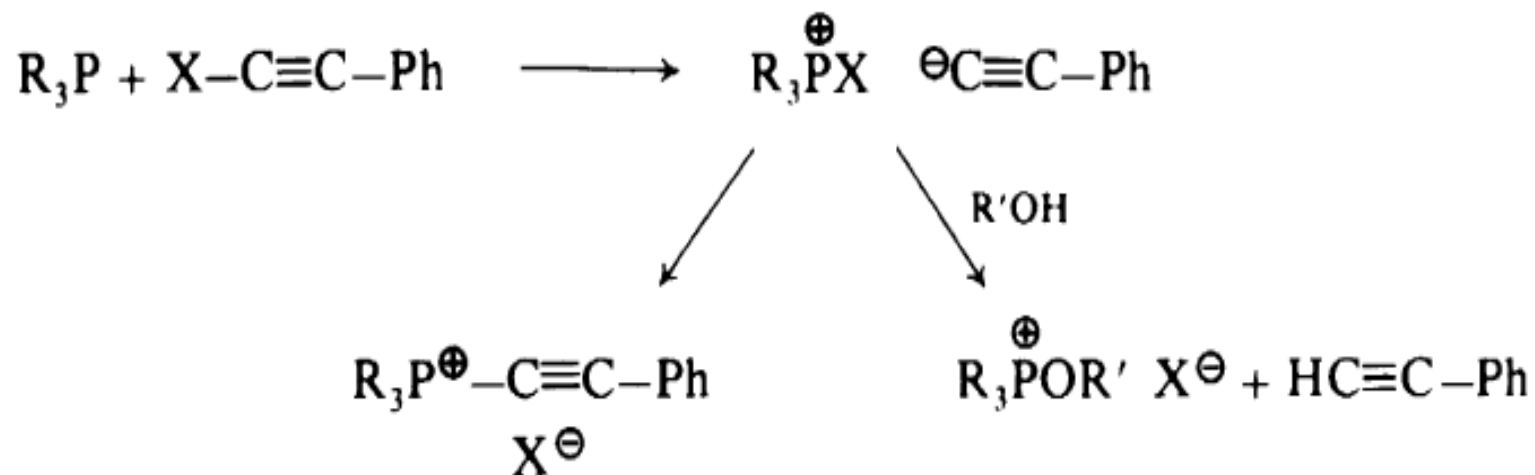




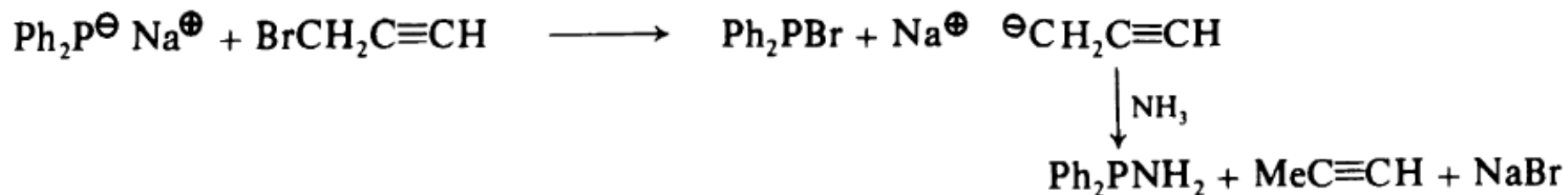




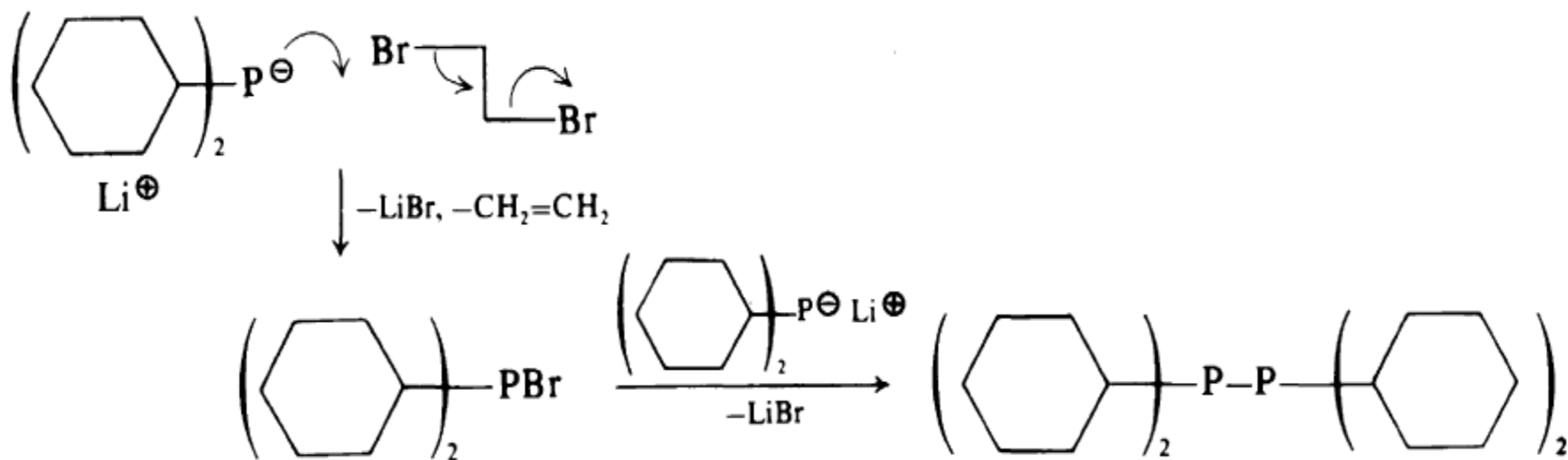
**The haloacetylenes** afford phosphonium salts or phosphonates when reacted with phosphines or phosphites, respectively. However, in the presence of a proton source, a net reduction to the acetylenes is observed.



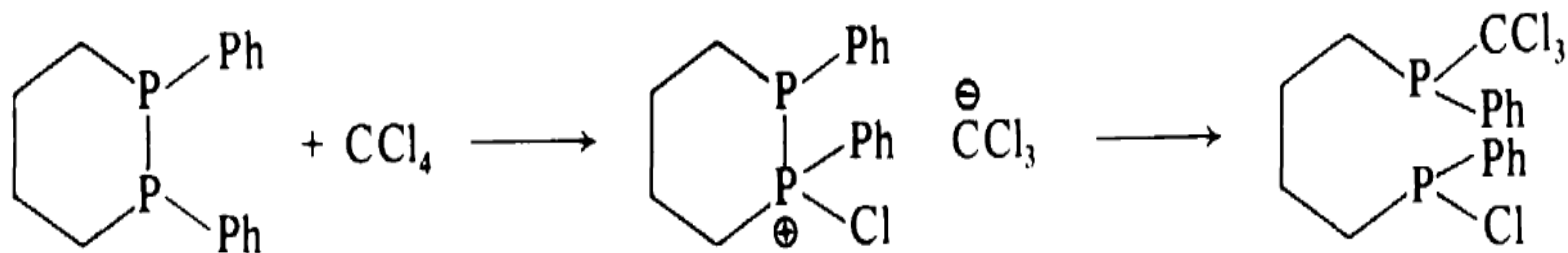
**The interaction between the softest species is overwhelmingly preferred. The propargylic carbon is apparently softer than the chlorine.**



It is of interest to note that the slightly harder diphenylphosphide elects to attack on the carbon atom ( $S_N2$ ).

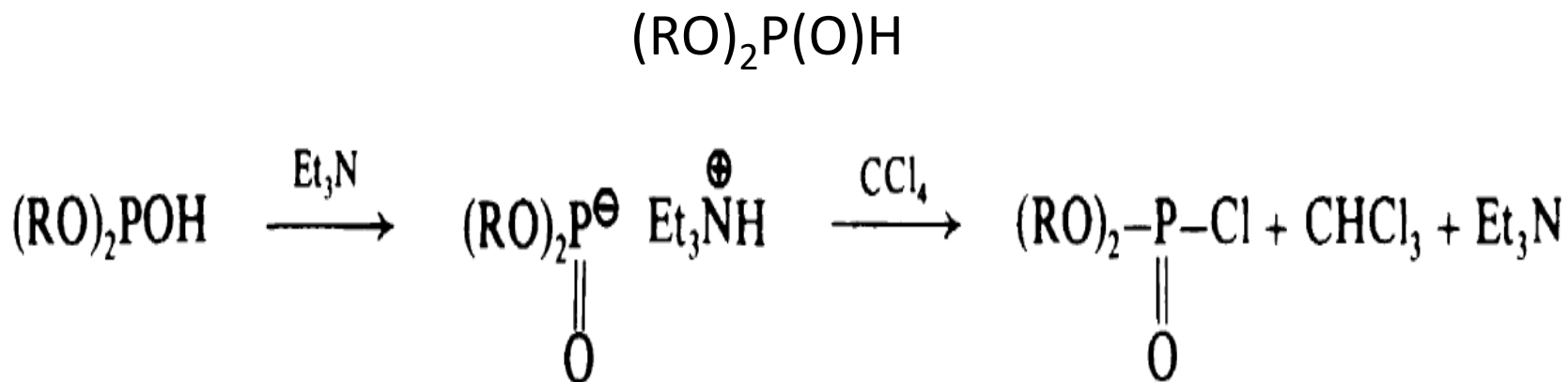


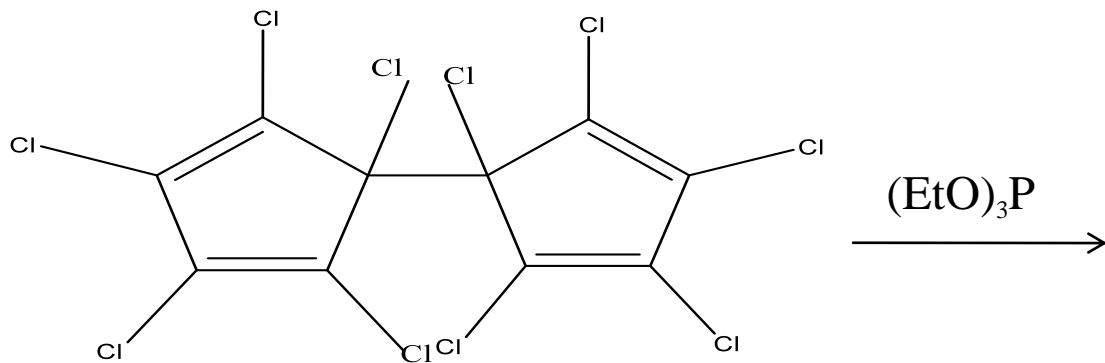
**Tetrahalomethanes react with phosphines in a 1 : 2 molar ratio to afford dihalomethylenephosphoranes and dihalophosphoranes. 1,2-Bis-(phenylphospha) cyclohexane is cleaved by carbon tetrachloride.**



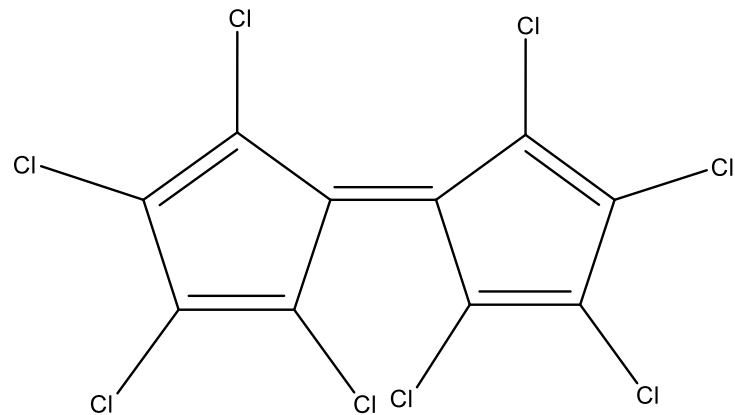
**A mixture of a dialkyl hydrogen phosphonate, triethylamine, and carbon tetrachloride is very effective for dehydration of aldoximes.**

**The actual reagent is formed by the deprotonation of the phosphonate (phosphite tautomer) by the hard amine, followed by  $\text{Cl}^+$  removal from  $\text{CCl}_4$  by the ensuing phosphonate ion.**

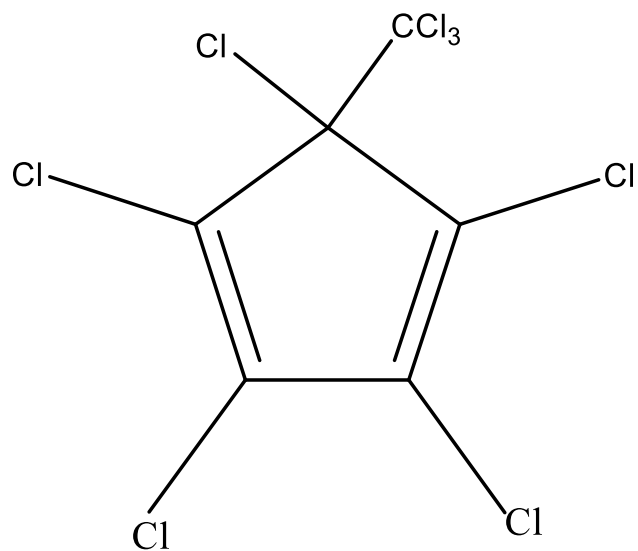




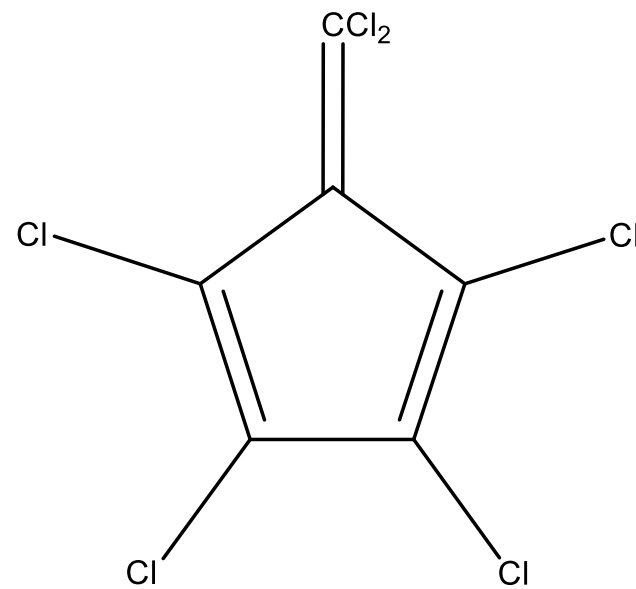
$(\text{EtO})_3\text{P}$



Perchlorofulvalene



$(\text{EtO})_3\text{P}$

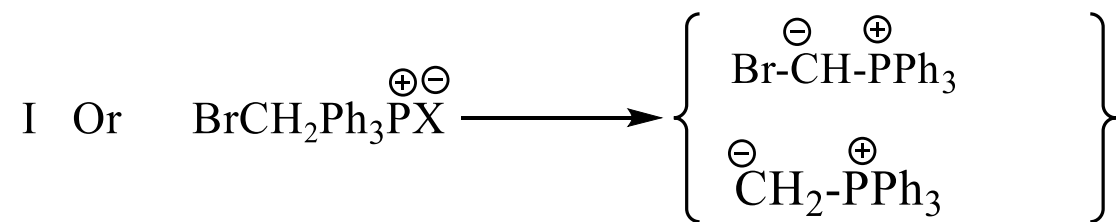
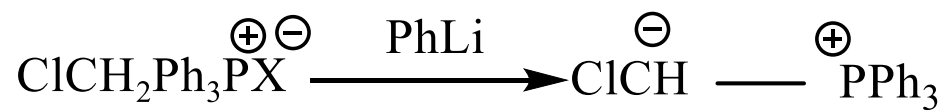
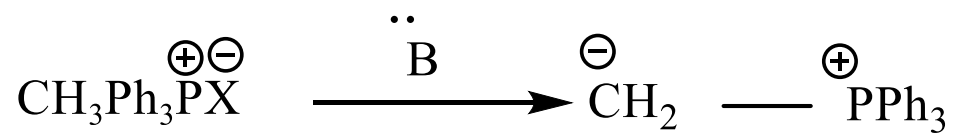


Perchlorofulvene

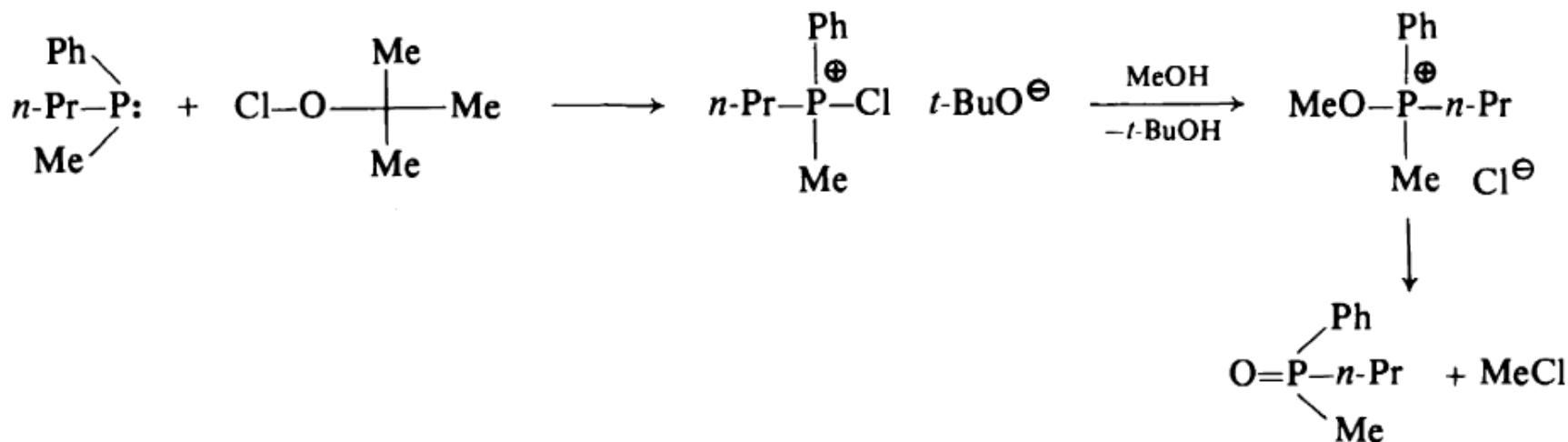
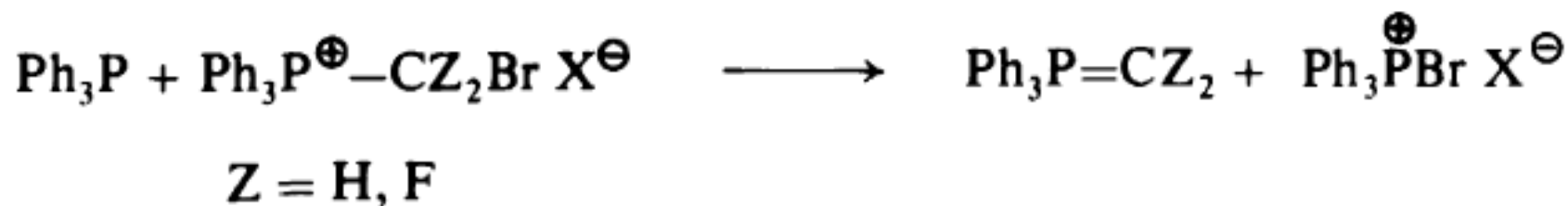


**Whereas the strong hard bases deprotonate alkyltriphenylphosphonium salts to generate the ylides, triphenylphosphine tends to abstract the soft bromine from bromomethyltriphenylphosphonium halides and the bromodifluoromethyl analog.**

**The chlorometho salt undergoes deprotonation only, while the bromometho and iodometho analogs give a mixture of ylides in which the halogen atom is either retained or lost.**



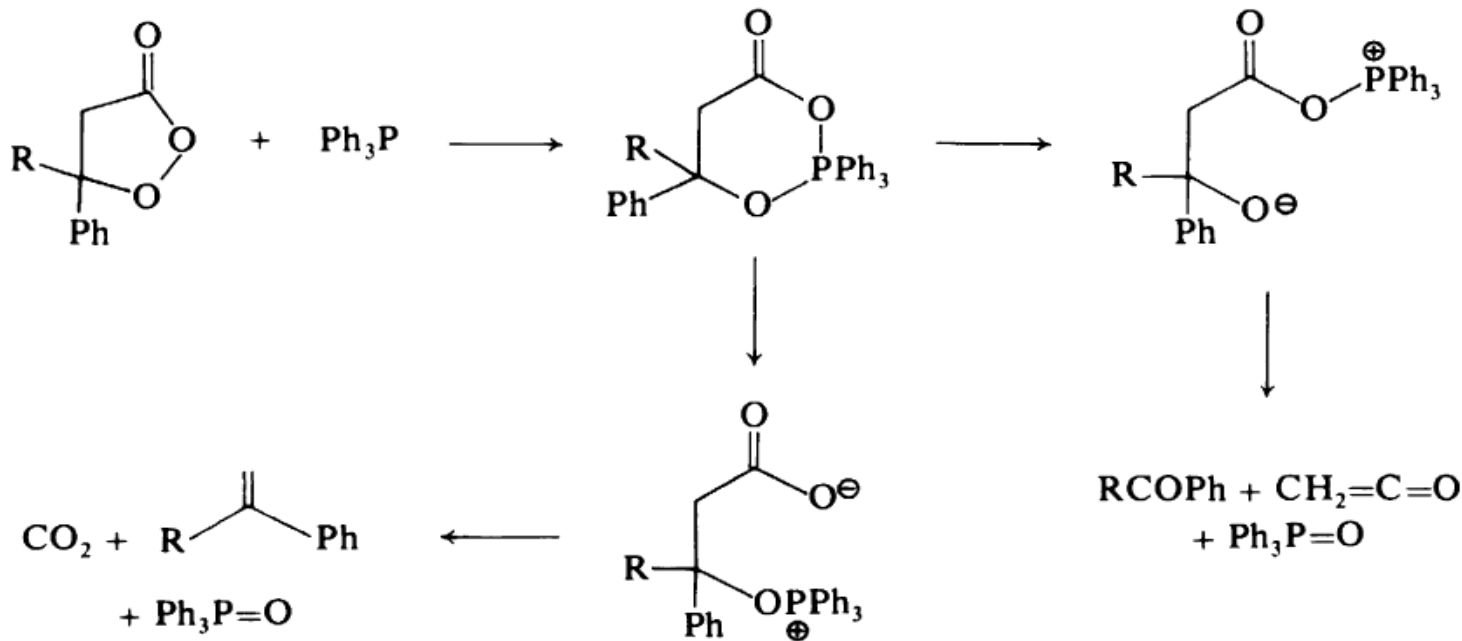
The higher proportion of  $\text{Ph}_3\text{P}=\text{CH}_2$  obtained from the iodomethyl compound, compared to the bromomethyl derivative, manifests the dual properties of organolithium compounds as being both basic and soft.



As anticipated, the N-halosuccinimides and alkyl hypohalites are reactive toward trivalent phosphorus compounds.

## Attack at Oxygen:

The fragmentation of  **$\beta$ -peroxylactones** promoted by phosphines yields two types of products. Diisopropyl peroxydicarbonate is similarly degraded. Here the phosphorane intermediate decomposes into a carbonate and a pyrocarbonate via different pathways.



**In contradistinction to the phosphine-peroxy compound reaction, an ionic mechanism is not operative in the corresponding amine reaction.**

**The hard amine bases are less prone to interact with the soft oxy center, rendering the alternative one-electron transfer process viable.**

**The existence of pentacovalent phosphorus intermediates during the deoxygenation of dialkyl peroxides with phosphites has been demonstrated by  $^{31}\text{P}$  nuclear magnetic resonance studies and isotope labeling techniques.**

**The corresponding adducts derived from phosphines are less stable because they lack full symbiosis.**

**Depending on the structure of the p-quinones and the nature of the trivalent phosphorus compounds being used, two types of products may result from their reactions. The initial attack is directed at either the O or the C of the quinones, and both sites are soft.**

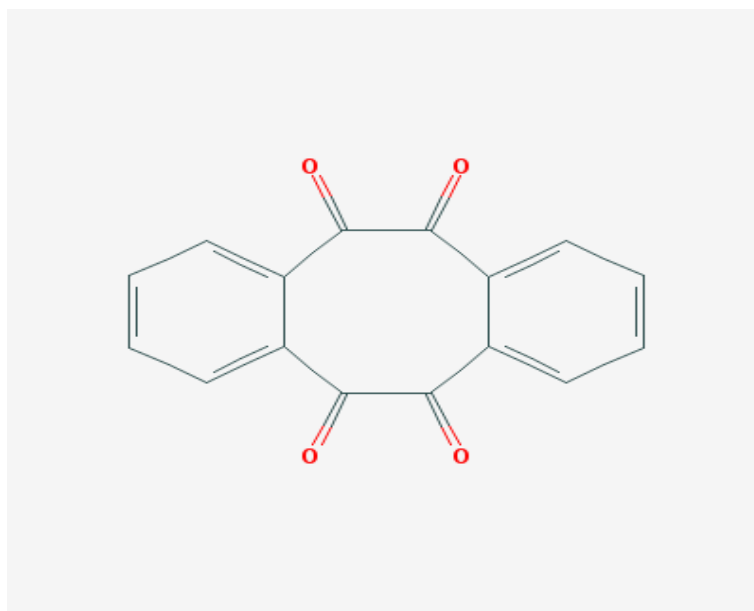
**Pentacovalent phosphorus cyclic adducts are produced by the addition of *o*quinones and  $\alpha$ -diketones to phosphites. The structure of one such biphilic adduct from phenanthraquinone has been determined by X-ray diffraction.**

**As previously mentioned, cyclopentadienones which possess a very soft oxygen acceptor site react vigorously with soft donors.**

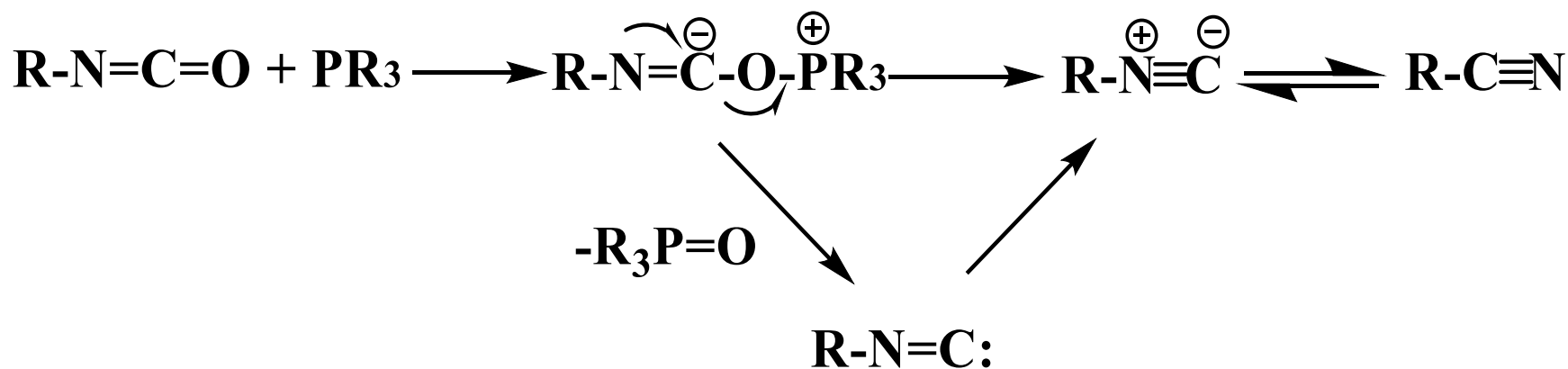
**Although stable adducts of these compounds with phosphines have been isolated, their reaction with phosphites is more complex. However, a soft-soft interaction is involved in each step.**



Phthalic anhydride is transformed into **diphthalyl** on heating with triethylphosphite. Diphenylketene undergoes deoxygenative rearrangement by the same treatment.

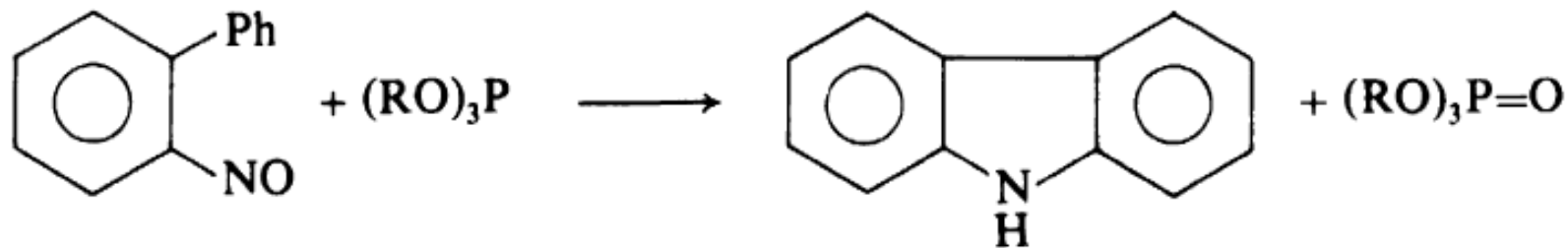


The analogous reaction of **isocyanates** furnishes **isonitriles**. In this case the intermediate disintegrates into a "carbene" which is stabilized by a neighboring nitrogen atom.



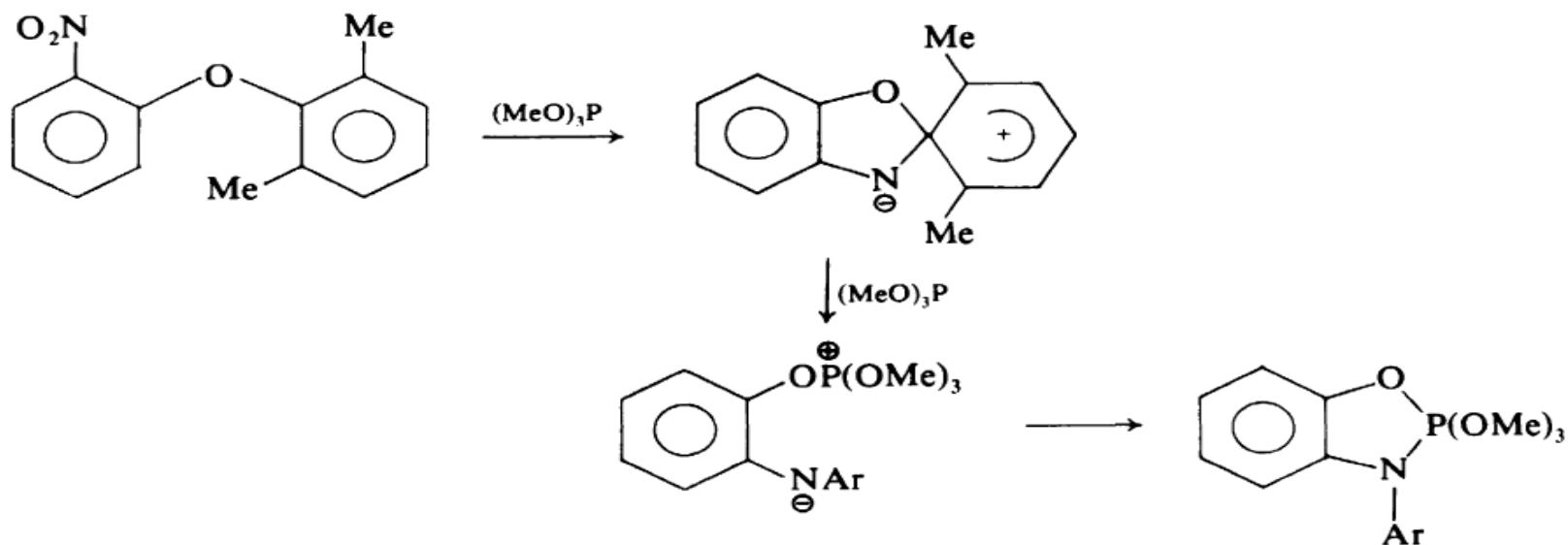


The internal trapping of the **nitrene** or the dipolar precursor leads to heterocyclic products. Thus, 2-nitrosobipheny affords **carbazole** in good yield.

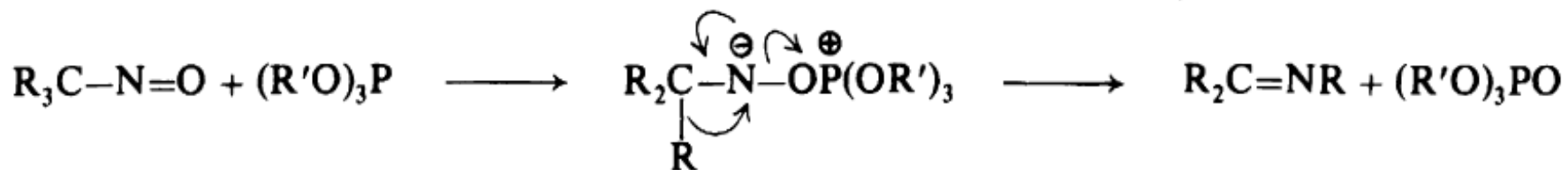


**Spirodienyl intermediates** are involved in the deoxygenation rearrangement of certain aromatic **nitroso** compounds.

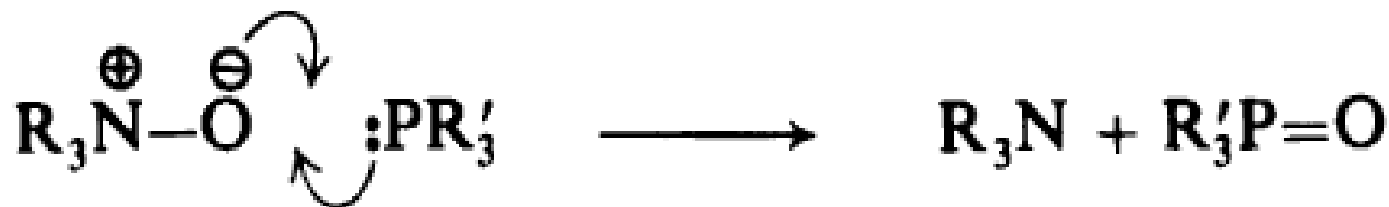
The phosphite reagent serves the dual function of removing oxygen atoms from the nitroso group and effecting O—C bond cleavage of the spiro species.



For the deoxygenation of **nitrosoalkanes**, arguments for a concerted migration-phosphate elimination pathway have been presented.



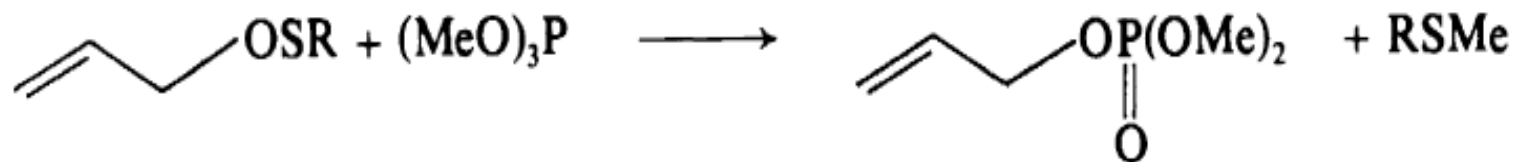
Semipolar oxygen may be removed by P(III) derivatives. However, the opposite reactivity order of these reagents to their usual nucleophilicities suggests that a **biphilic process** is involved in the reaction.



**The two reactivity sequences for the trivalent phosphorus compound reduction of dimethyl sulfoxide may indicate a change in the relative importance of  $\sigma$  and  $\pi$  donation during a biphilic attack on oxygen.**

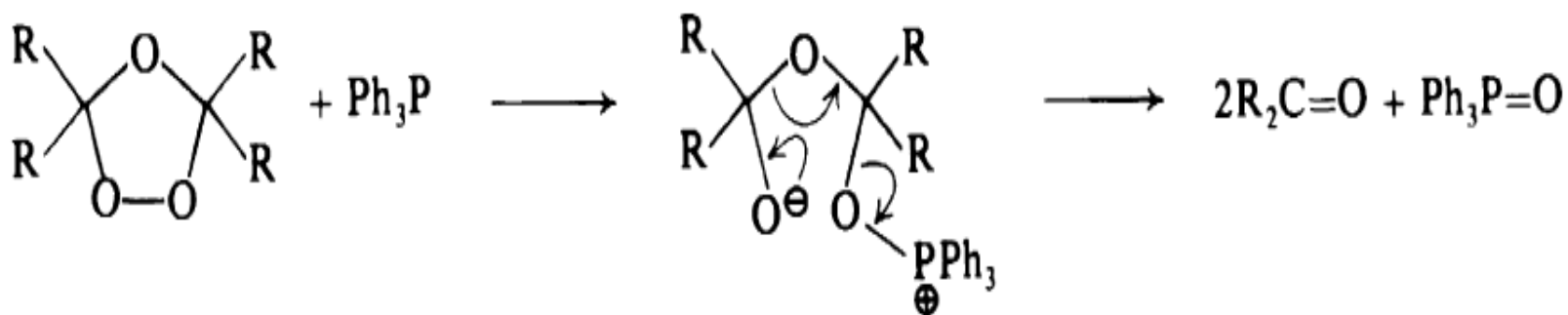


The cleavage of **allylic sulfenate** esters by phosphites may actually involve attack at sulfur, even though the products indicate otherwise.



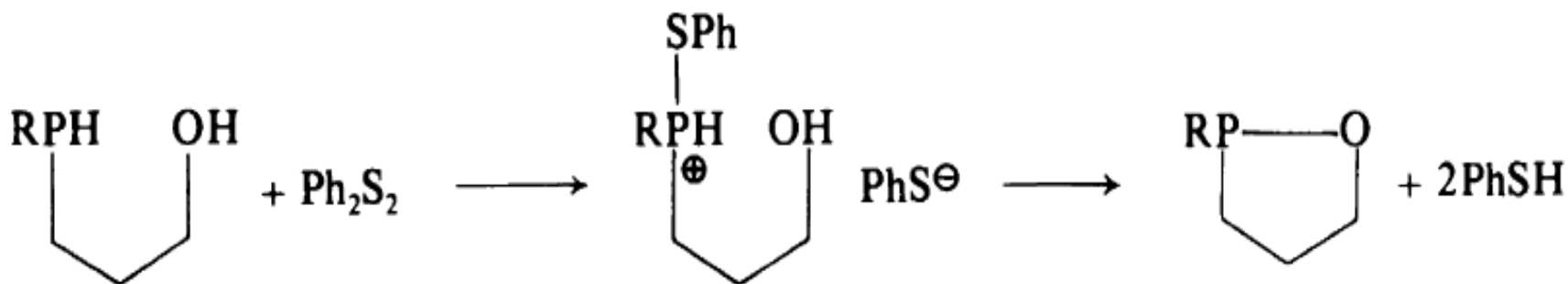


Phosphines and phosphites are readily oxidized by **ozone**. The 1:1 adducts have pentacovalent phosphorus structures. **Ozonides** are reductively cleaved by triphenylphosphine.

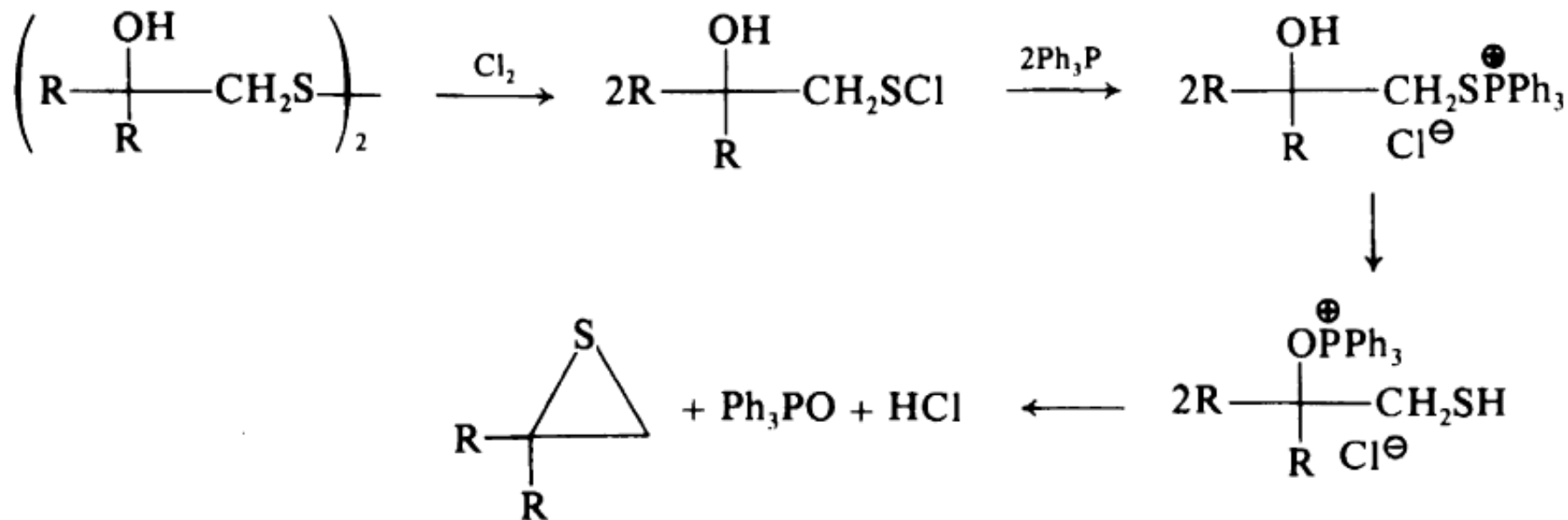




In the presence of water, triphenylphosphine reduces **diaryl disulfides to arenethiols** . An intramolecular version of this double displacement is shown below .

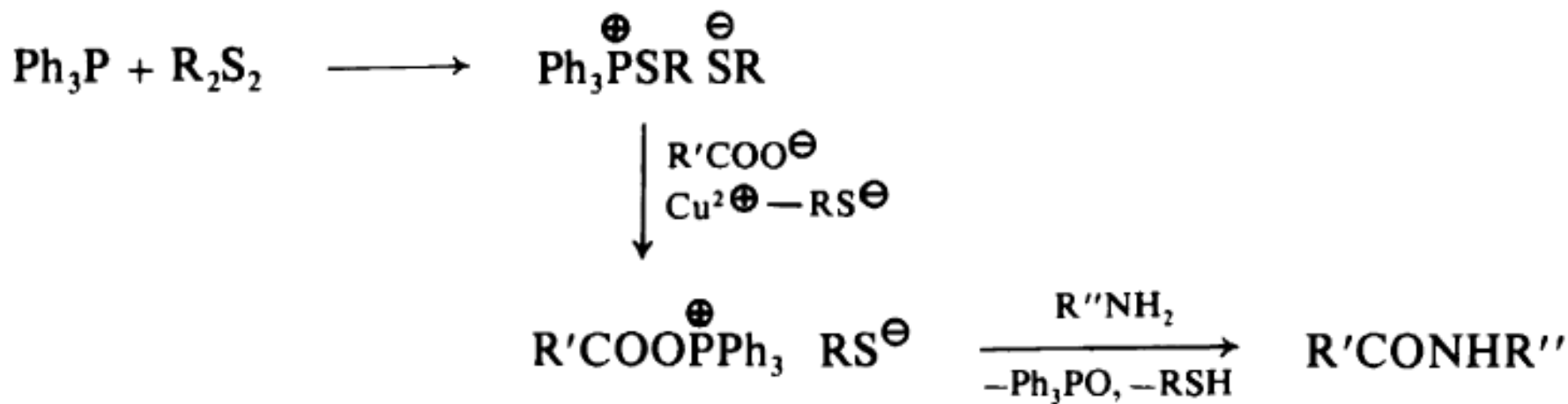


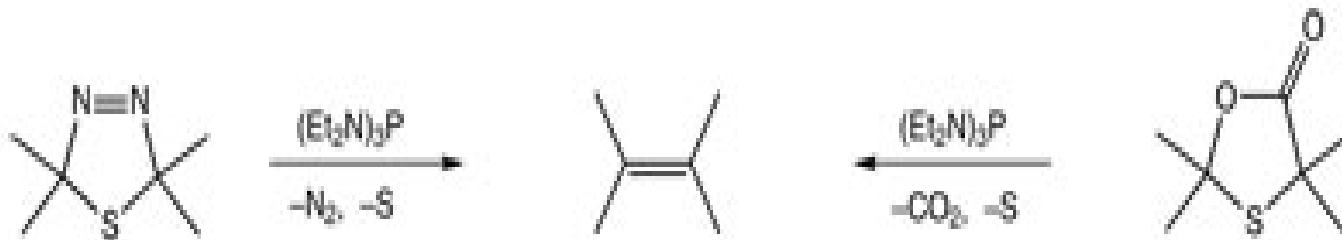
The formation of **thiiranes** by the following reaction illustrates another example consistent with the HSAB concept.



In a peptide synthesis based on redox condensation, triphenylphosphine-disulfide adducts are used to **activate the carboxyl group for the coupling with amines.**

The overall transformation consists of sequential soft-soft, hard-hard, and hard-hard interactions.





**Barton and co-workers have developed a useful olefin synthesis, which is particularly applicable to highly hindered alkenes. Hexaethylphosphoroustriamide is a key reagent for sulfur abstraction.**

**Like diacyl peroxides, diacyl disulfides are desulfurized readily by phosphines. Highly exothermic reactions occur when sulfenyl chlorides are treated with phosphites or phosphines. However, the site of initial attack (S or Cl) has not been determined.**

**Menthyl *p*-methylphosphinite is converted to a phosphonothioate on reaction with sulfenamides.**

**A sulfinato group is displaced from organic thiosulfonates by phosphites, whereas phenyl benzenethiosulfonate undergoes deoxygenation to give diphenyl disulfide by phosphines.**

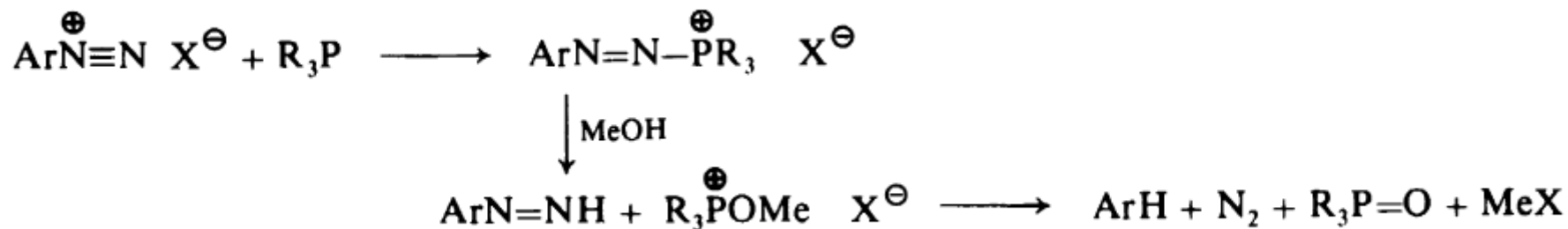
The dialkylphosphite ions can displace a sulfite ion from the Bunte salts in a straightforward process. Both the donor and the acceptor atoms are soft.



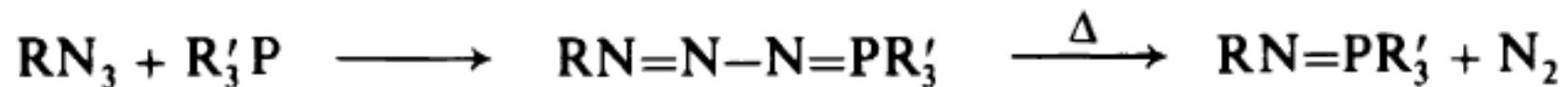


## Attack at Nitrogen

Aromatic diazonium salts are reduced by phosphines in protic solvents. The crucial steps can be summarized as soft-soft P:N and hard-hard O: P interactions.

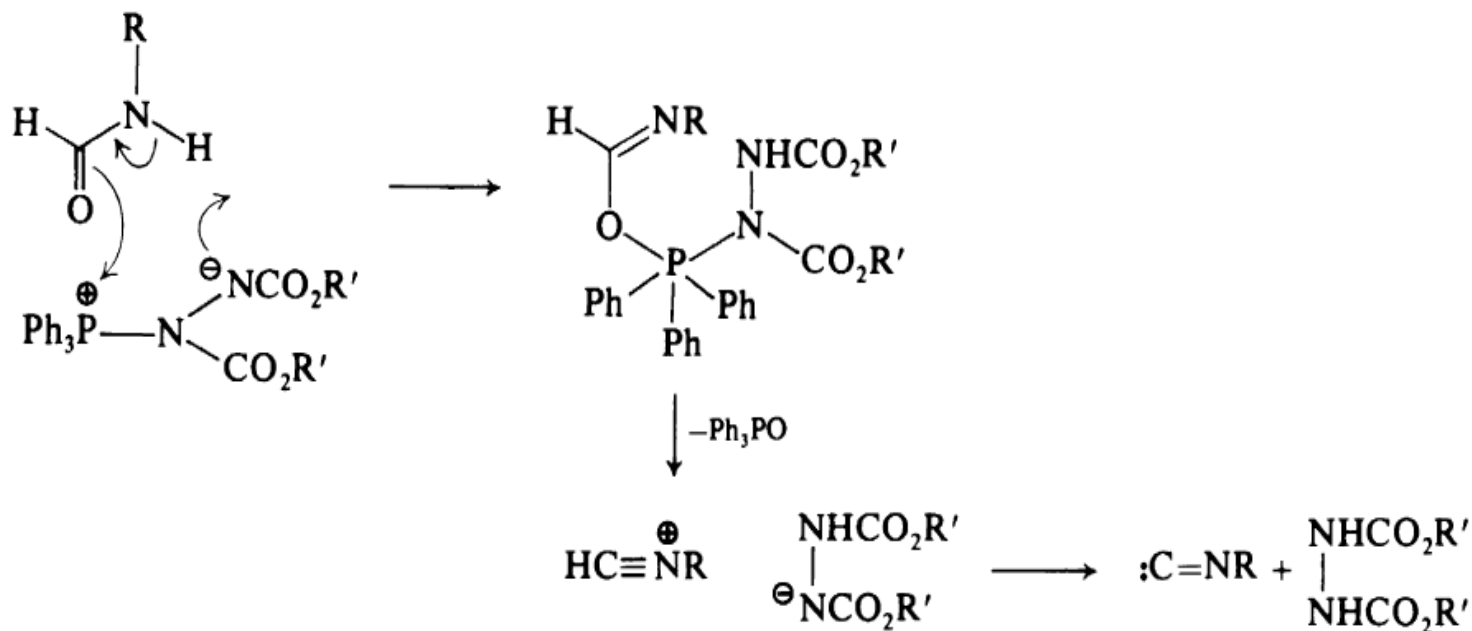


**Organic azides form adducts with phosphines which liberate nitrogen on heating.**



**The triphenylphosphine-azodi formate ester combination is a strong dehydrating system in the alkylation of imines by alcohols and the formation of aryl alkyl ethers.**

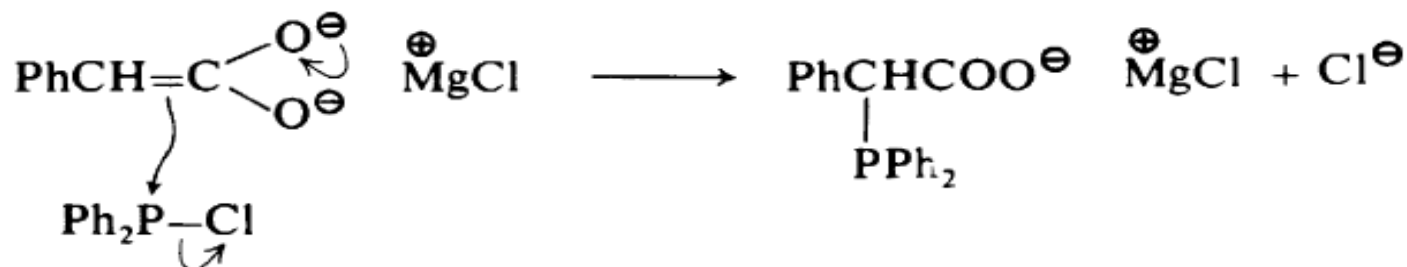
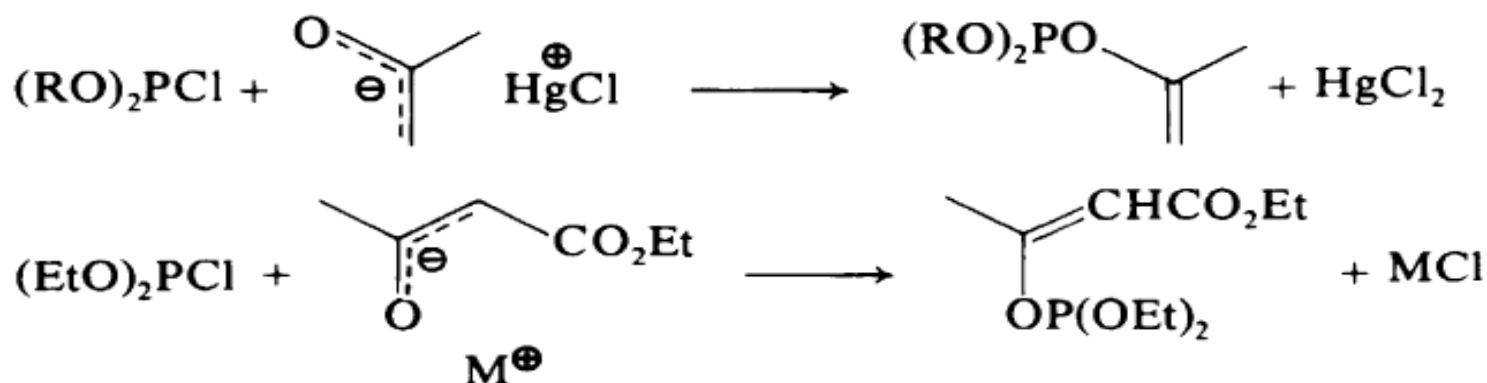
**The synthesis of isonitriles from formamides can be formulated according to the following interactions.**



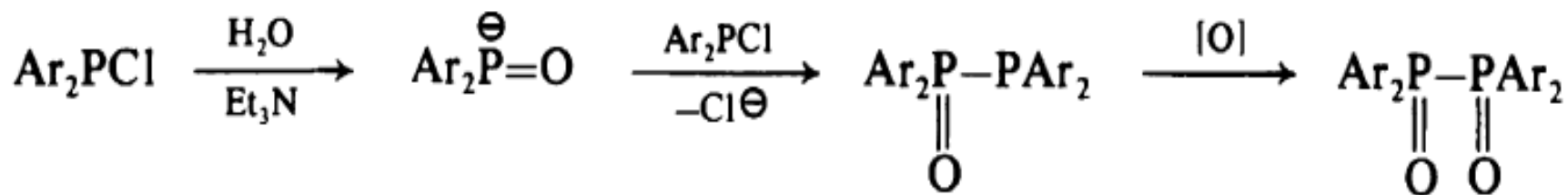
# NUCLEOPHILIC ATTACK ON THE PHOSPHORUS CENTER

## Trivalent Phosphorus

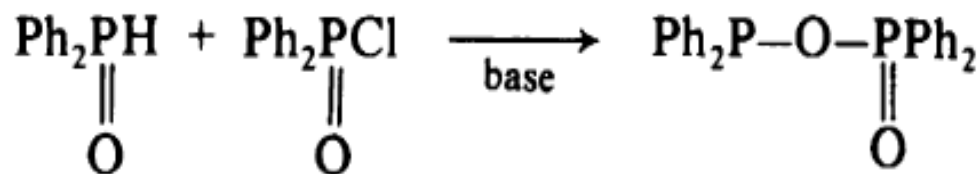
The dianion of phenylacetic acid is alkylated at the  $\alpha$  carbon. It appears that these processes are subject to symbiotic control.



The P—P bond is formed by electrophilic attack on the chlorophosphine by the conjugate base of the hydrolyzed molecule. This pattern of soft-soft P—P bond making is contrasted to the interaction between diphenylphosphine oxide and chlorodiphenylphosphonate. The phosphoryl chloride has a hard acceptor center.



tetraaryldiphosphine dioxides



chlorodiphenylphosphonate

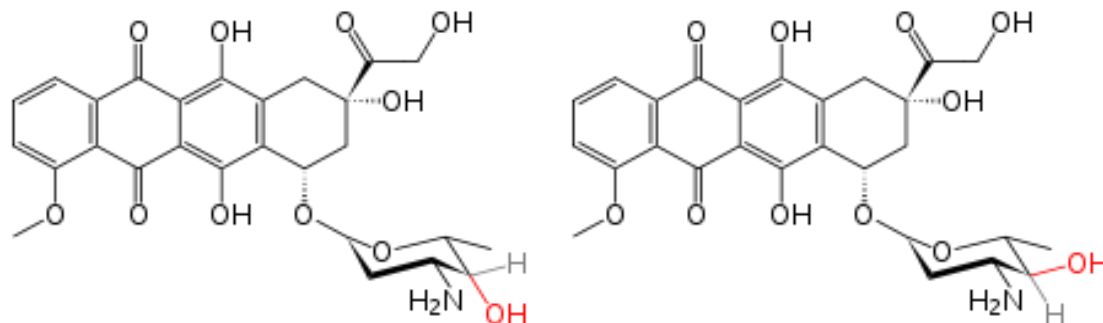
## Tetrahedral Phosphorus

**There are two types of P(V) compounds, i.e., the pentacovalent and the ionic phosphonium salts. The most familiar outcome of the attack at a pentacovalent phosphorus atom by nucleophiles is substitutive fragmentation.**

**On the other hand, there are numerous ways for a nucleophile to attack  $R_4P^+$  compounds: direct  $S_N2$  displacement, simple addition, and addition-elimination.**

**Many reactions, especially the biphilic processes, involve formation of  $R_4P^+$  compounds followed by a counter ion-initiated decomposition. The Arbuzov and Perkov reactions are representative.**

**The phosphine—carbon tetrachloride combination has proven to be a versatile dehydrating agent. Primary amides and aldoximes are converted into nitriles and the substituted ureas are transformed into carbodiimides. The reactive species  $R_3P^+CCl_3^-$  provides a strongly electrophilic locus for hard donors.**



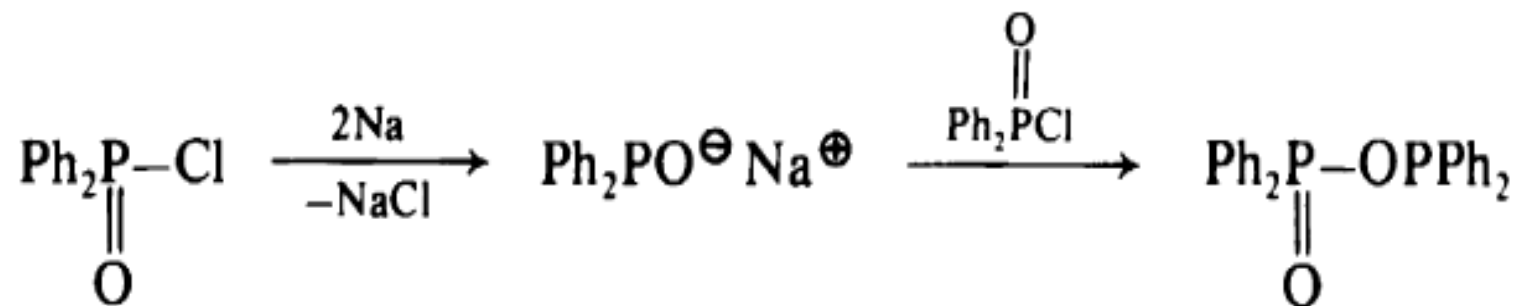
**The stereochemistry and reaction modes of dialkoxypyosphonium salts with various nucleophiles can be correlated with the HSAB principle.**

**Epimerization and P-O bond cleavage are associated with the hard bases. The soft bases generally effect C - O bond scission leading to products which retain the configuration of the phosphorus.**

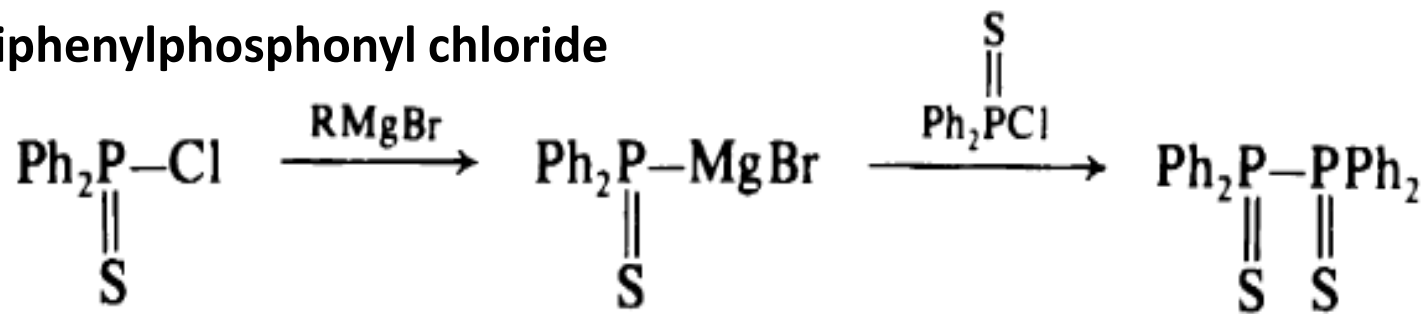




**The reductive dimerization** of the diphenylphosphonyl chloride and the thiophosphonyl chloride involves **soft-soft** and **hard-hard** interactions, respectively, between the anionic intermediates and the starting materials.

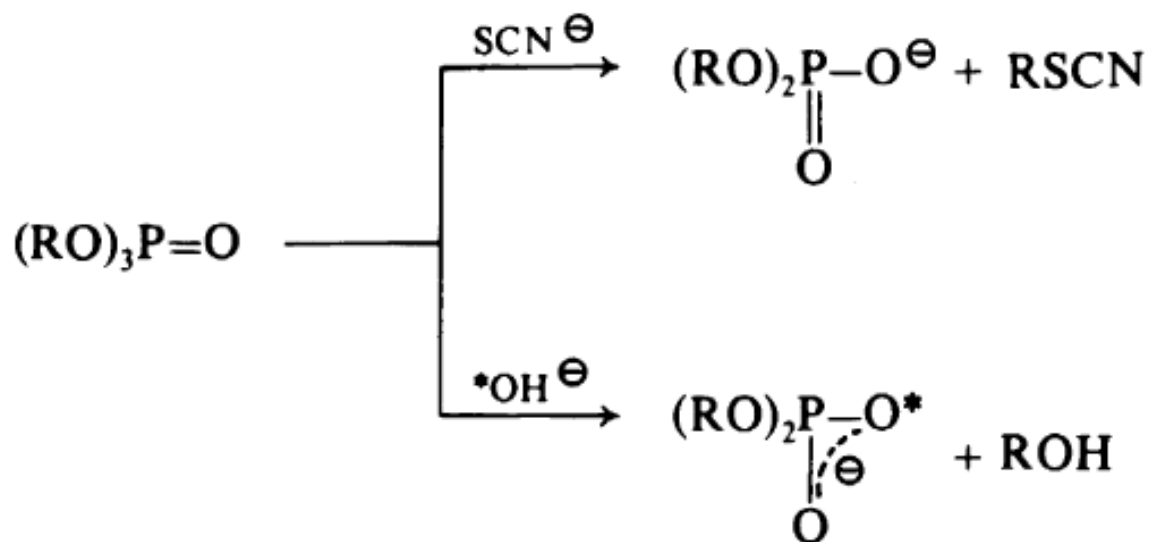


diphenylphosphonyl chloride



thiophosphonyl chloride

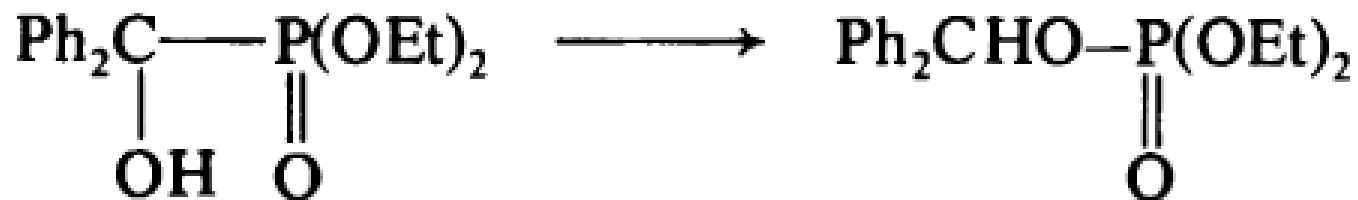
The dealkylation of the ambident trialkylphosphates using soft and hard bases follows separate pathways as expected.



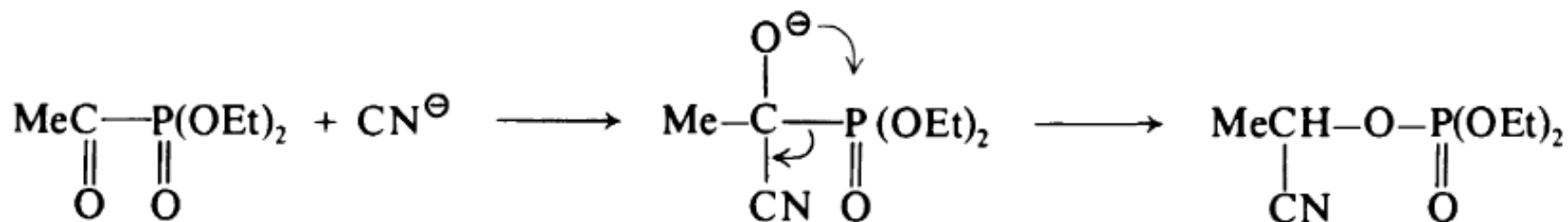
The hydrolysis of **acetoin phosphate** at pH 7.7-8.2 is extremely fast, whereas the hydrolysis of methyl acetoin methylphosphonate is 200 times slower.

Empirically it can be assumed that the P(V) atom of phosphates is harder than the phosphonates and, accordingly, the phosphates react faster with hard bases.

The  $\alpha$ -hydroxyalkylphosphonates undergo facile base-catalyzed mutation to the phosphates. The result mirrors the symbiotic stabilization of the transition state and the products.

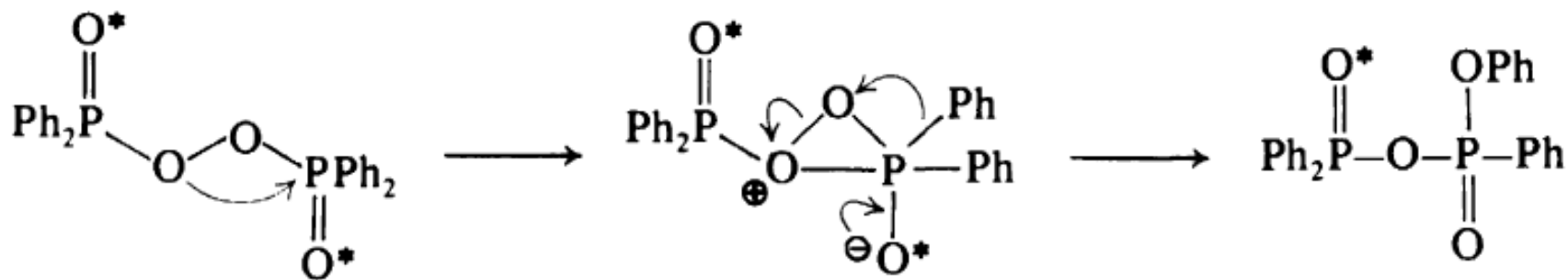


The  $\alpha$ -keto phosphonates are converted into similar compounds on treatment with the cyanide ion.



This is the mechanism for the thermal rearrangement of bis(diphenylphosphinyl) peroxide to an unsymmetrical anhydride.

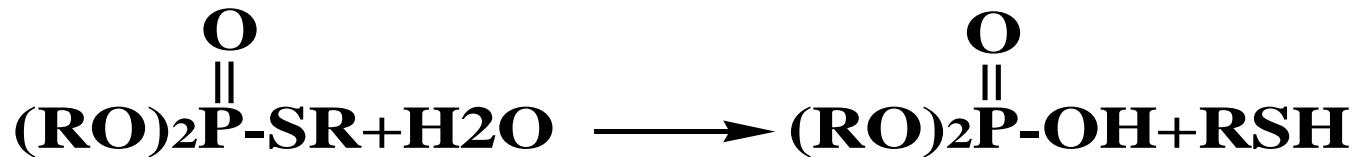
An intramolecular hard-hard interaction between oxygen and phosphorus atoms results in a zwitterion intermediate which collapses via migration of a phenyl group from P to O (soft) with a concomitant O-O bond fission.



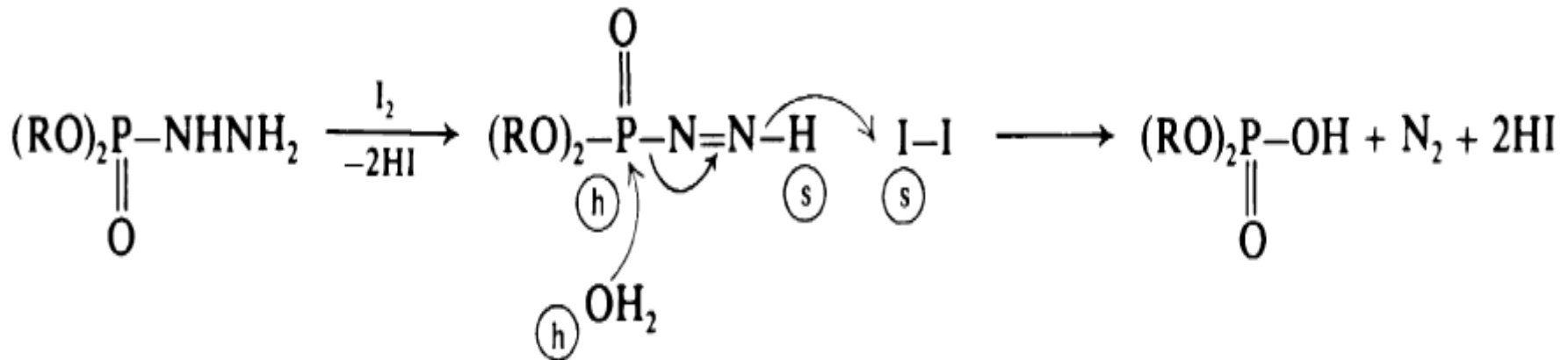
bis(diphenylphosphinyl) peroxide

The S-alkylphosphorothiolates are hydrolyzed and dialkylphosphorohydrazidates are hydrolytically deaminated with the aid of iodine.

The fragmentation step of the latter reaction is a perfect example of hard/soft cooperativity (Saville's rule).



S-alkylphosphorothiolates



dialkylphosphorohydrazidates

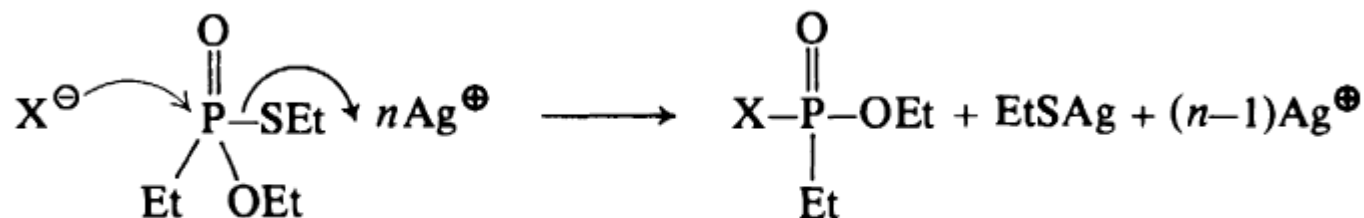


Phosphoro- and phosphinothiocyanatidates isomerize to the corresponding isothiocyanatidates at room temperature. The lability of the thiocyanatidates originates from a hard-soft pairing in these compounds.



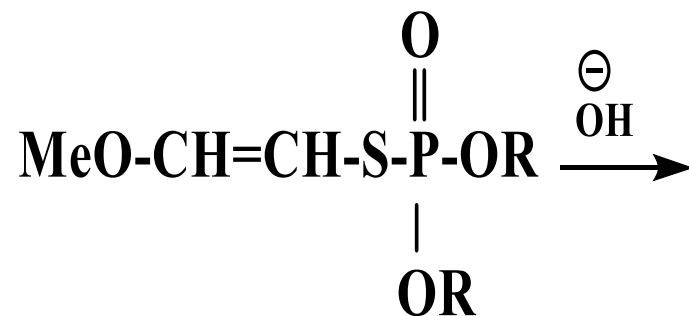
$\text{R}, \text{R}' = \text{R} \text{ or } \text{OR}$

**O,S-Diethyl ethylphosphonothioate reacts with water in the presence of silver and fluoride ions. The reaction proceeds according to Saville's generalization.**



**X = F, OH**

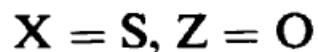
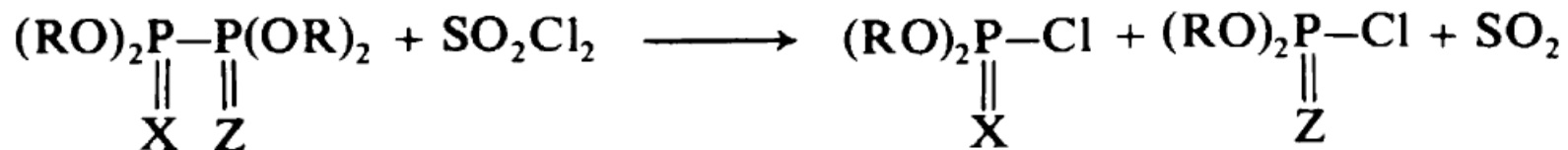
***O,S*-Ethylene *O*-methylphosphorothioate  
suffers P-S bond cleavage by hydroxide ion.  
The P(V)-S bond is weak because it is a hard-  
soft combination.**



**Teichmann and Hilgetag have summarized and discussed the various chemical aspects of the thiophosphoryl group in terms of the HSAB principle. The P=S group may behave as an electrophile (P end) or as a nucleophile (S end).**

Triarylphosphine sulfides form crystalline adducts with the soft halogens (ICl, IBr, I<sub>2</sub>). A facile cleavage of tetraalkyldiphosphine disulfides by halogens is precluded by S-X coordination.

Dithio- and monothiohypophosphates also react exothermically with sulfuryl chloride. However, the sulfur-free analogs must be heated to reflux in order to bring about fission of the P-P bond.

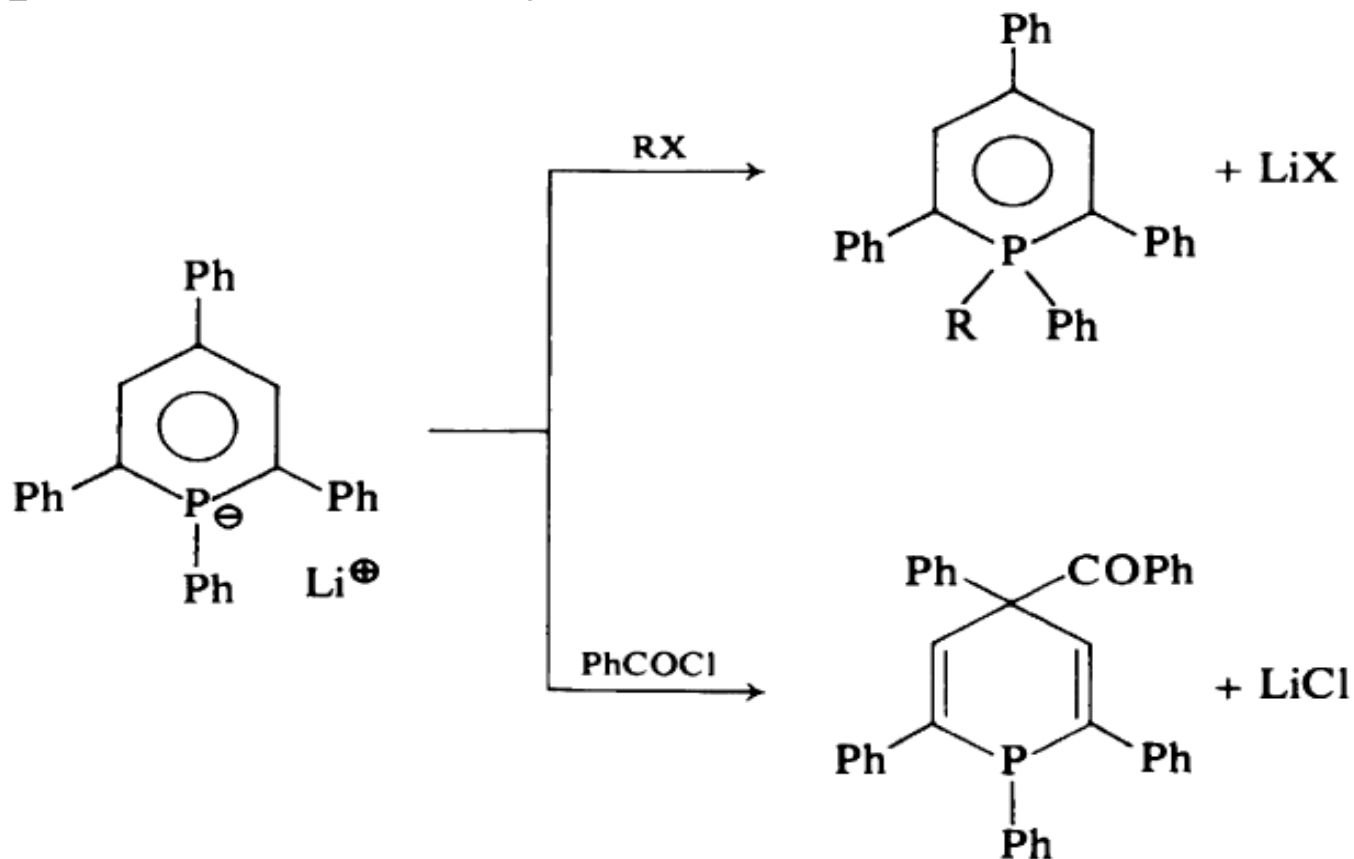


**Optically active phosphine sulfides are desulfurized by  $\text{LiAlH}_4$  to the parent phosphines with retained configurations.**

**The union of the soft hydride ion with the soft sulfur, instead of the hard pentavalent phosphorus of the thiophosphoryl function, is in keeping with the HSAB principle.**

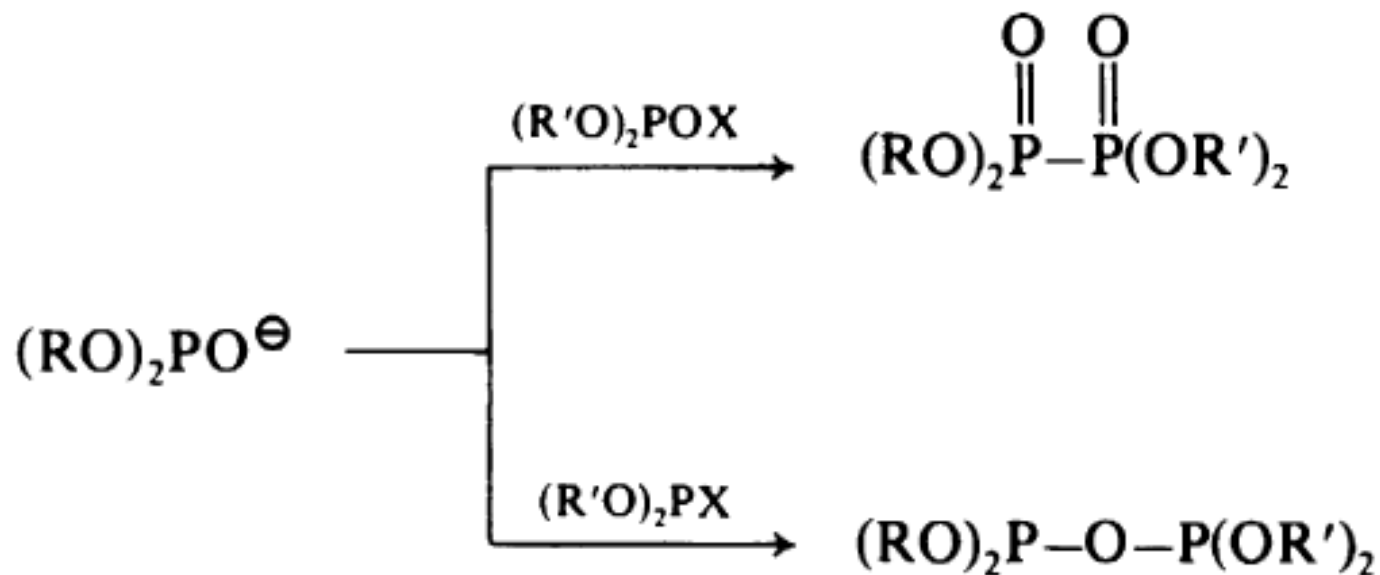


**Phosphabenzenes** fail to react with hard acids, yet they readily form  $\sigma$  complexes with soft metal compounds. The alkylation of 1,2,4,6-tetraphenylphosphabenzene anion takes place at P, while acylation occurs at the harder C-4.





**However, results contradictory to HSAB prognostication are known in reactions involving ambident ions, e.g.,**



**In such cases, the interpretation requires a knowledge of the nature of the transition state. Thus, P-phosphorylation is determined by a high P - O bond energy in the transition state which resembles the addition intermediate.**

**A thermodynamically stable product results. In the second reaction outlined above, the greater charge on oxygen dictates its high reactivity as the transition state is closer to the reactants.**