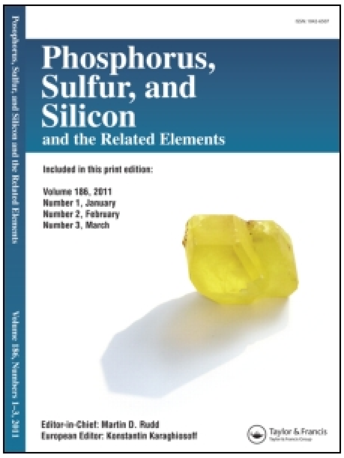

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REACTIONS OF DERIVATIVES OF PHOSPHORUS ACIDS WITH CARBONYL COMPOUNDS ACTIVATED BY ELECTRONEGATIVE GROUPS †

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T. Kh. GAZIZOV, and G. V. ROMANOV

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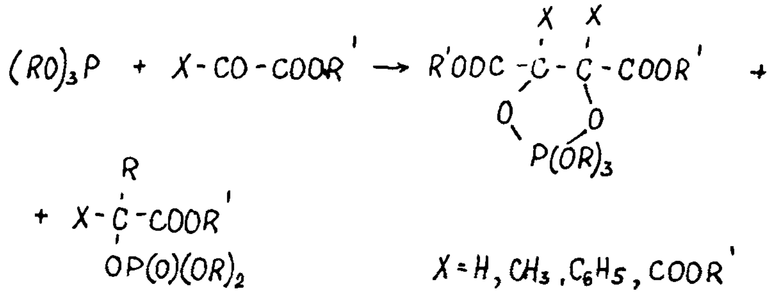
The Arbuzov reaction results in the synthesis of various phosphonic esters and is of great importance for the further development of the chemistry of organophosphorus compounds. Investigations of recent decades have shown that, besides halogen-containing organic compounds, different types of organic compounds of the electrophilic type which do not contain halogen atoms are capable of entering this reaction. Reactions with carbonyl compounds are especially interesting. This report presents the results of reactions of derivatives of tricoordinated phosphorus (trialkyl phosphites, amidophosphites, ester anhydrides, isocyanate phosphites) with carbonyl compounds. Special emphasis was placed on studying the reactions with carbonyl compounds activated by some electronegative groups. The regularities and mechanisms of these reactions were investigated depending on the structure of the carbonyl compounds, the derivatives of tricoordinated phosphorus and the reaction conditions.

Trialkyl phosphites react with esters of α-keto-carboxylic acids (pyruvic,[1-3] glyoxylic,[4] mesoxalic[4-6] and benzoyl formic[7]) even at low temperatures. These reactions are accompanied by a pronounced exothermic effect: according to the data of differential thermal analysis (dta) the temperature at which the effect starts lies within the interval of −60°C-40°C. As a result of such reactions, the corresponding 1,3,2-dioxaphospholanes are formed. Their formation is favored by low temperature and the use of polar solvents. At elevated temperatures and in the absence of the solvent, the yield of 1,3,2-dioxaphospholanes decreases and the formation of dialkyl-α-substituted alkyl phosphates is observed.



Unlike α-keto-carboxylates, the esters of α-keto-phosphonic acids show low reactivity in their reactions with trialkyl phosphites. 1,3,2-dioxaphospholanes with a pentacoordinated phosphorus atom are not formed in these reactions. The reactions proceed under more rigorous conditions and are accompanied by side processes. The interaction of triethyl phosphite with acetophosphonic ester at 100-200°C proceeds with the formation of an addition product: diethyl-(α-methyl-α-diethoxyphosphinyl)propyl phosphite, in a yield of ≈ 20%. With more rigorous conditions (130-140°) thermal decomposition of acetophosphonic ester is observed resulting finally in the formation of methyl-*bis*-(diethoxy phosphinyl)carbinol which undergoes phosphonate-phosphite rearrangement.[8]

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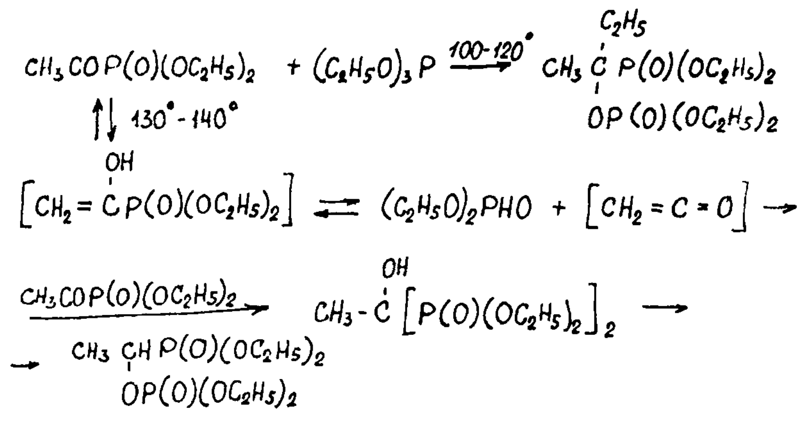
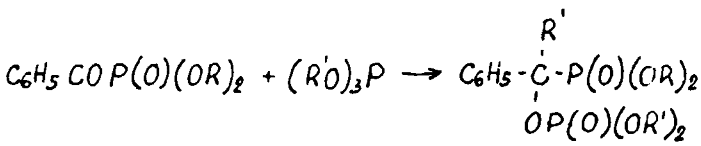
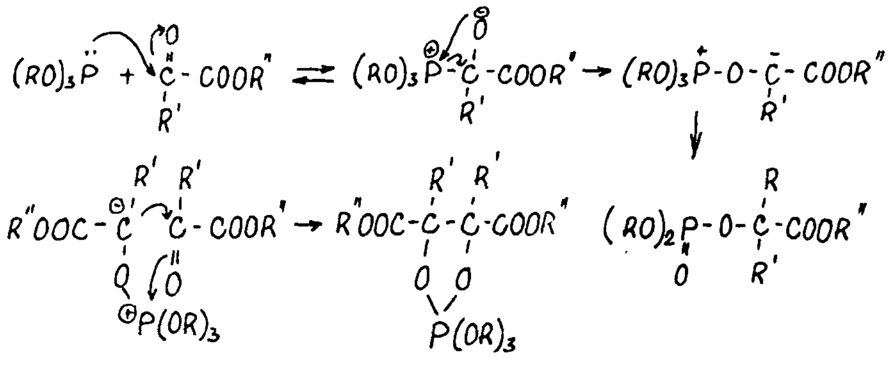
† Plenary Lecture. Vth International Conference of Organic Phosphorus Chemistry, Gdansk, Poland, September 1974.



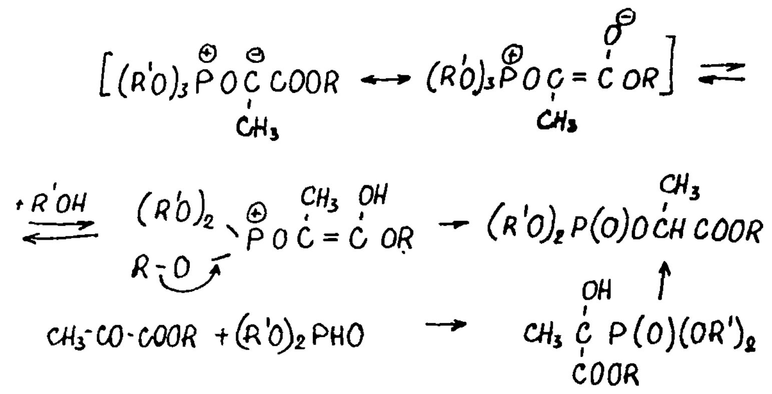
Trialkyl phosphites react with benzoyl phosphonic esters forming only addition products of phosphitic structure.[9]



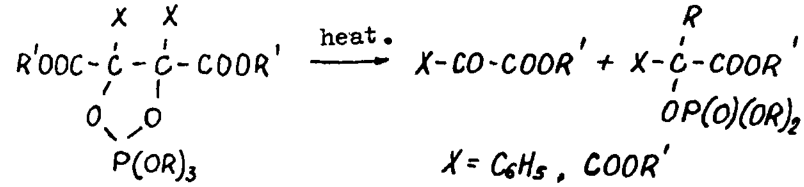
Concerning the mechanism of reactions between the esters of tricoordinated phosphorus acids with carbonyl compounds activated by some electronegative groups, we assume that they follow the general scheme which includes the initial nucleophilic attack of a tricoordinated phosphorus atom on the carbonyl group. The structure of the final products of the reaction is determined to a large extent by the nature of the initial products and the reaction conditions. The bipolar ion with a P–C bond formed at the initial stage of the reaction undergoes a rapid intramolecular rearrangement of the same type as in the reaction of nucleophilic substitution at the phosphonium center with the formation of a more thermodynamically stable bipolar ion having a P–O–C bond. Its further stabilization is possible in two directions: either a new bipolar ion is formed as a result of the carbon atom attacking the carbonyl group of the second molecule of the carbonyl compound which then passes over to 1,3,2-dioxaphospholane; or the bipolar ion passes over as a result of dealkylation in accordance with the second stage of the Arbuzov rearrangement, to the dialkyl-α-substituted alkyl phosphites.[10]



Under the same conditions the yield of dialkyl-α-substituted alkyl phosphonates increases as one passes from the pyruvic ester to the esters of glyoxylic and then to mesoxalic, benzoyl formic and acetophosphonic acids. The changes in direction of the reactions are evidently caused by the different character of intermediate bipolar ion polarization and by the spatial difficulties arising with the formation of 1,3,2-dioxaphospholanes. When performing the reaction in proton-donor solvents (acetic acid, methanol) the intermediate bipolar ions are transformed as a result of protonization with subsequent dealkylation intc phosphites. The phosphites formed are identical to those produced by the isomerization of dialkyl-α-oxy-α-carbalkoxyethyl phosphonates.[11]

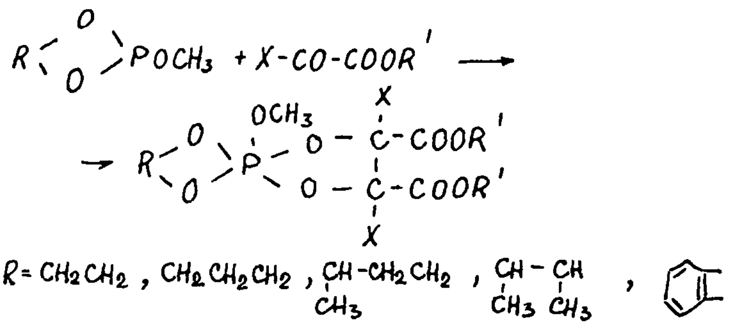


2:1 adducts of trialkyl phosphites with carbonyl compounds are capable of different transformations, including thermal dissociation, with the formation of a carbonyl compound and a 1:1 adduct. As already noted, 1,3,2-dioxaphospholanes in reactions with α-keto-esters are formed at low temperatures; 1:1 adducts of phosphatic structure under more rigorous reaction conditions. These adducts can be formed as a result of the thermal decomposition of 1,3,2,-dioxaphospholanes. We observed such thermal decompositions in the reaction of trialkyl phosphites with mesoxalic and benzoyl formic esters. When distilled in vacuum, 1,3,2-dioxaphospholanes decompose with the separation of the carbonyl compound and dialkyl-α-substituted alkyl phosphates.[7]

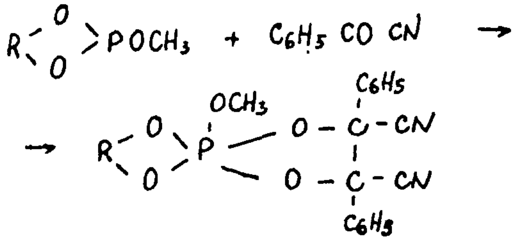


As one passes from acyclic to cyclic trialkyl phosphites, reactions with α-keto-carboxylates, irrespective of conditions, proceed in the direction of spiro-1,3,2-dioxaphospholane formation,[7,19] which have a high resistance to thermal effects. They are separated in pure form by vacuum distillation; no formation of 1:1 adducts is observed. The stability of spirodioxyphospholanes is increased as a result of strain decreases in the trigonal-bipyramidal configuration with pentacoordinated phosphorus due to the introduction of the second pentagonal cycle.

PMR spectra show that reactions of α-keto-carboxylates with alkylene glycol phosphites proceed with the formation of a mixture of two diastereomeric spiro-1,3,2-dioxaphospholanes similar to the reaction of trialkyl phosphites with aldehydes and α-keto-carboxylates.



According to the literature, unstable addition products of dioxaphospholanic structure are formed in a reaction of trialkyl phosphites with benzoyl cyanide and substituted benzoyls cyanides.[13] We believe that the use of cyclic phosphites could result in the formation of more stable spiro-1,3,2-dioxaphospholanes. Reactions of benzoyl cyanide with O-methyl ethylene-, 1,3-propylene-, 1,2-propylene-, 1,3-butylene-, and 2,3-butylene glycol phosphites proceed with the formation of spiro-1,3,2-dioxaphospholanes.

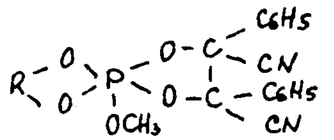


However, spiro-1,3,2-dioxaphospholanes formed during the reaction with benzoyl cyanide also turned out to be thermally unstable. To study the thermal decomposition of reaction products we used the dta method. Decomposition of reaction products starting at about 120°C is accompanied by an exothermal effect. The data of thermographic analysis are shown in the following table.

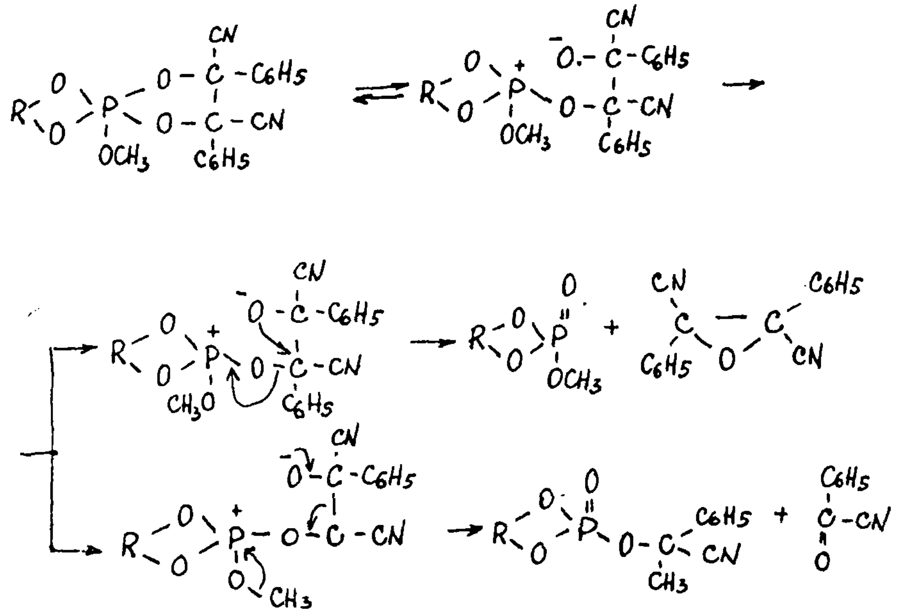
TABLE I
Thermographic analysis of reaction products of O-methyl glycol phosphites and benzoyl cyanide

Glycol phosphite	TSE °C[a]	TME °C[b]
$-CH_2-CH_2-$	120	152
$-\underset{CH_3}{CH}-CH_2-$	127	155
$-\underset{CH_3}{CH}-\underset{CH_3}{CH}-$	129	166
$-CH_2CH_2CH_2-$	112	142
$-\underset{CH_3}{CH}CH_2CH_2-$	128	156

[a] Temperature at start
[b] Temperature of maximum effect.



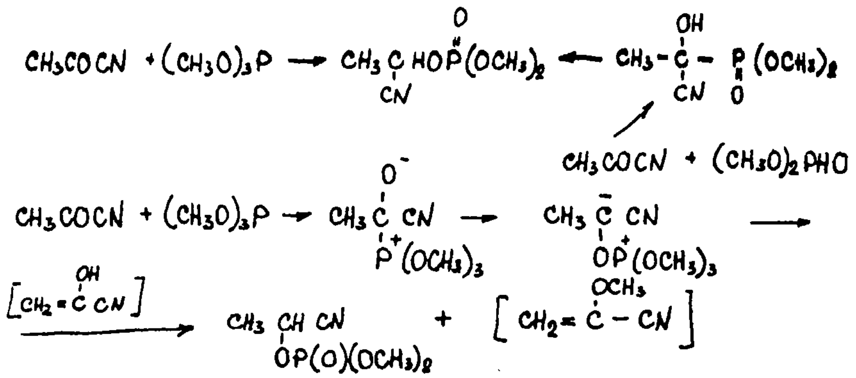
As is seen from the table, the temperature at which the effect starts (TSE), characterizing the stability of compounds, depends only slightly on the phosphite structure. However one can note the tendency for spirane stability to increase when a six-membered cycle is replaced by a five-membered one and when donor substituents are introduced. 1,3,2-dioxaphospholanes based on acyclic phosphites turned out to be much less stable. Thus the adduct of triethyl phosphite with benzoyl cyanide has TSE 90°C and the TME (temperature of maximum effect) 126°C. Analysis of spirane decomposition products shows that their thermal decomposition proceeds with the initial formation of *trans*-α, β-dicyano stilbene oxide to benzoyl cyanide and cyclic phosphates.

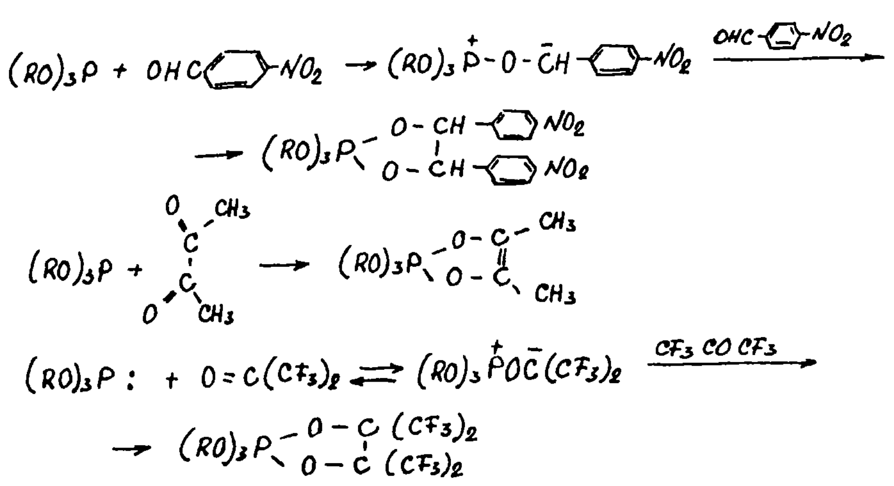


The reaction of trialkyl phosphites and alkylene glycol phosphites with pyruvonitrile proceeds in a different way. Irrespective of reaction conditions no formation of adducts with 1,3,2-dioxaphospholane is observed. When trimethyl phosphite reacts with pyruvonitrile, dimethyl-α-cyanoethyl phosphate is formed.

Phosphate formation is, evidently, the result of the protonization of the intermediate bipolar ion due to the enol form of pyruvonitrile. The reaction is accompanied by considerable gumming of the reaction mixture and the formation of low boiling compounds among which alkyl acetates and pyruvonitrile dimer have been identified.

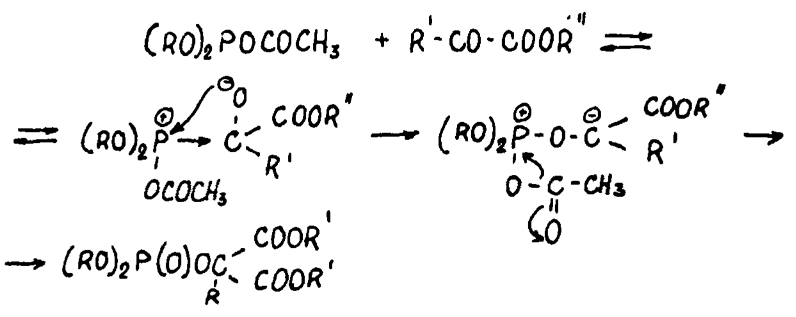
When studying the interaction of the derivatives of tricoordinated phosphorus with carbonyl compounds, the question about the site of the nucleophilic attack on the carbonyl group remains open. Along with our concept of the initial attack on the carbonyl group carbon atom,[1-9] there is a view, expressed by Ramirez, that the reactions of carbonyl compounds which have electron-acceptor substituents such as *p*-nitrobenzaldehyde can start with the nucleophilic attack of the phosphorus atom of phosphite on the positively charged oxygen atom of the carbonyl group.[14] Similar concepts have been developed with respect to the mechanism of reaction of phosphites with α-dicarbonyl compounds; though in this case the possibility of an initial attack on the carbonyl carbon atom was not excluded. The attack on the oxygen of the carbonyl group was also considered possible in reactions of phosphites with perfluoroacetone[15] and trifluoropyruvic esters.[16]

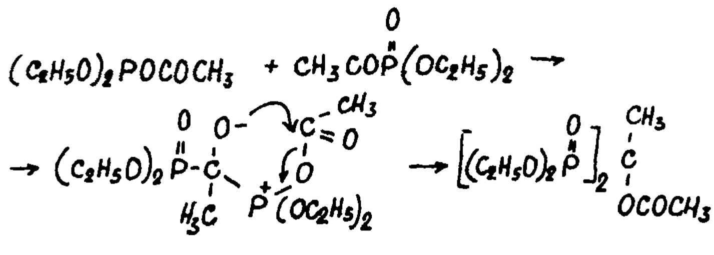




To investigate this question in greater detail we have studied the reactions of carbonyl compounds activated by electronegative substituents with derivatives of tricoordinated phosphorus having easily detachable groups. For these investigations mixed anhydrides of phosphorus and carboxylic acids and diethyl trimethylsilyl phosphite were used. Mixed anhydrides of phosphorus and carboxylic acids have lower reactivity in the reactions with α-aldehydo- and α-keto-carboxylates as compared to trialkyl phosphites. Reactions proceed in one direction only irrespective of reaction conditions (100°C, –5°C) with the formation of substituted α-acylalkyl dialkyl phosphates.[17] The course of these reactions is similar to that for trialkyl phosphites. The specific feature is that the carbanion center attacks the oxygen atom of the carbonyl and not the alkoxyl group as in the reaction for neutral phosphites. This process goes faster than the reaction with the second molecule of the carbonyl compound and no 1,3,2-dioxaphospholane formation is observed in reactions with ester anhydrides.

In the reactions of mixed anhydrides of diethyl phosphorus and carboxylic acids with α-ketophosphonates, acetates of alkyl *bis*(diethoxy phosphinyl)carbinols were obtained. In this case acetyl group migration proceeds faster than the phosphorus-phosphate rearrangement, and it becomes possible to detect a reaction product with a phosphorus-carbon bond which confirms the initial attack on the carbon atom of a carbonyl group.[18-19]





One could expect that in the reaction with diethyl trimethylsilyl phosphite it would also be possible (at least in a number of cases) to isolate the product without isomerization and further transformations. This is favored by the fact that the trimethylsilyl group splits off readily owing to the considerable ionic character of the Si–O bond (~ 50%), after the formation of the bipolar ion, resulting from the great difference in the electronegativity of the silicon and oxygen.[1,7] Reactions of diethyl trimethylsilyl phosphite with *p*-fluoro, *p*-chloro, and *p*-nitrobenzaldehydes result in the formation of diethyl α-trimethylsilyloxy-*p*-fluoro-, *p*-chloro-, or *p*-nitrobenzyl phosphonates;[20] reactions with dibutyl trimethylsilyloxy phosphinites proceed in a similar way. In all cases, products with a phosphorus-carbon bond are formed which excludes the possibility of the reaction proceeding with initial attack of phosphite on the oxygen atom of the carbonyl group. However the possibility cannot be excluded *a priori* that these reactions proceed with initial attack of the carbonyl oxygen of the aldehyde on the positively polarized silicon atom of the silyl phosphite. To check this assumption we performed reactions of diethyl trimethylsilyl phosphite with benzaldehyde/*p*-nitrobenzaldehyde and benzaldehyde/*p*-fluorobenzaldehyde mixtures.[20] In both cases, silyl phosphite reacts with *p*-nitro- and *p*-fluorobenzaldehydes only, benzaldehyde is recovered from the reaction mixture unchanged. This shows that the reactions follow scheme B and not A; i.e. with initial attack of phosphite on the carbon atom of the carbonyl group.

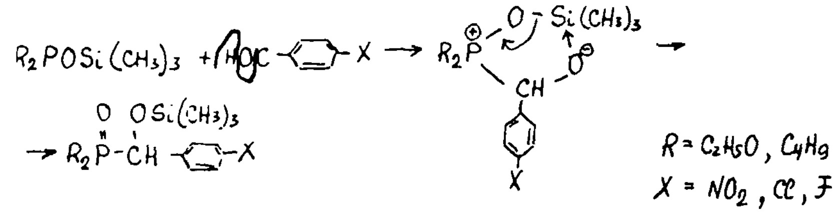
In reactions of diethyl trimethylsilyl phosphite with methyl and ethyl ethers as well as with pyruvonitrile, products of phosphonatic structure are formed: at the second stage of the reaction the trimethylsilyl group migrates to the oxygen atom. With benzoyl formic ethyl ester, however, diethyl trimethylsilyl phosphite forms diethyl α carboxy-α-trimethylsilylbenzyl phosphate. Apparently in this case, because of the α-carbon atom having two electronegative groups, favorable conditions for phosphonate-phosphate rearrangement arise; this is followed by the migration of the trimethylsilyl group.

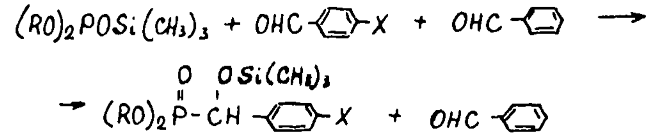
Diethyl trimethylsilyl phosphite reacting with benzoyl cyanide forms mixtures of products with phosphonatic and phosphatic structure.

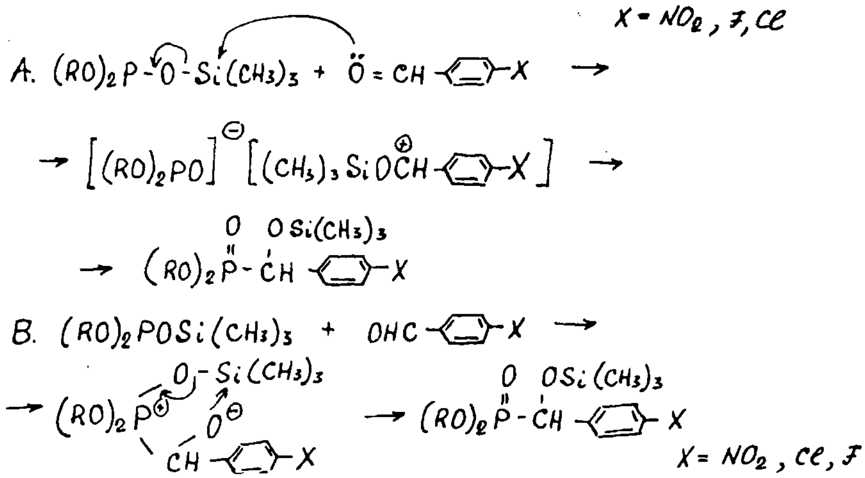
Interesting results were obtained when studying reactions of diphenylphosphine with esters of pyruvic,[21] benzoyl formic, aceto- and benzoylphosphonic acids and diacetyl. In all cases α-oxyalkyl phosphines were obtained and, therefore, stabilization of the bipolar ion by carbon-phosphorus bond formation during the reaction is due to the proton migrating from phosphorus to the oxygen atom.

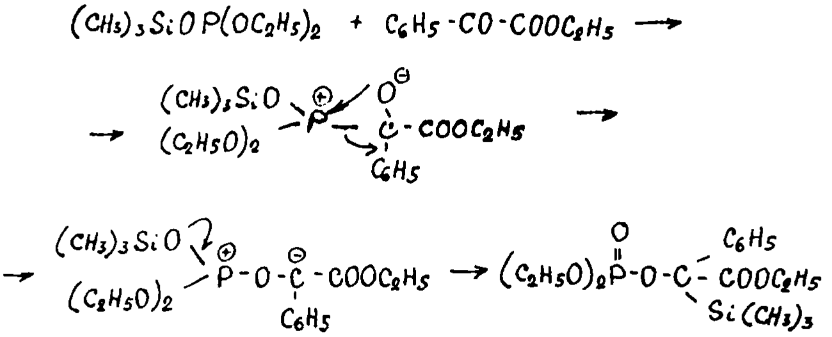
When tributyl- or triphenylphosphines react with pyruvic and levulinic acids in the presence of HCl or

CH_3COOH, stable α-hydroxy-α-methyl-carboxypropyl tributyl(phenyl)phosphonium salts separated. In both cases the phosphorus atom attacks the carbon atom of the carbonyl group.

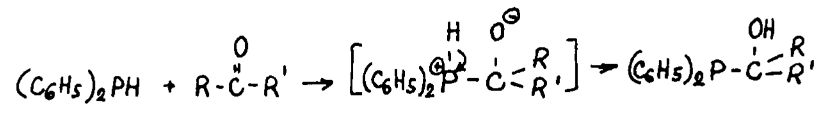




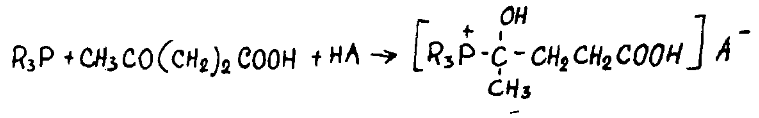




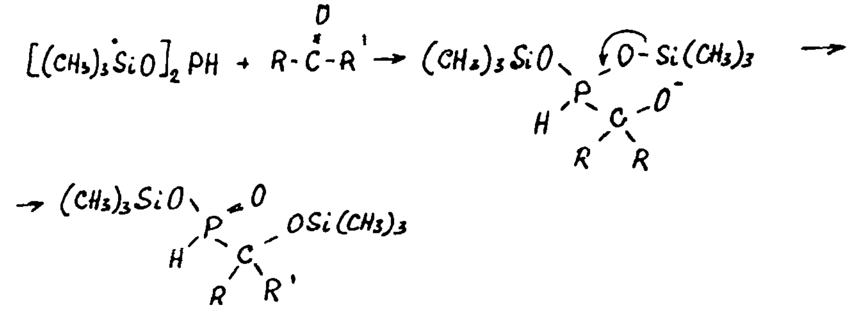
In reactions of such carbonyl compounds as aliphatic, aromatic and acyclic aldehydes and ketones with *bis*-(trimethylsilyl)-hypophosphite, the products formed are not α-hydroxyphosphines, as in the previous reactions, but trimethylsilyl(α-trimethylsilyloxy)alkyl phosphinates.[22] Evidently in these reactions stabilization of the bipolar ion is not due to the migration of the hydrogen atom but to the migration of the trimethylsilyl group and the formation, as a result of its departure, of an energetically favorable phosphoryl group.



$R = CH_3, C_6H_5$; $R' = COOAlk, COCH_3, P(O)(OC_2H_5)_2$

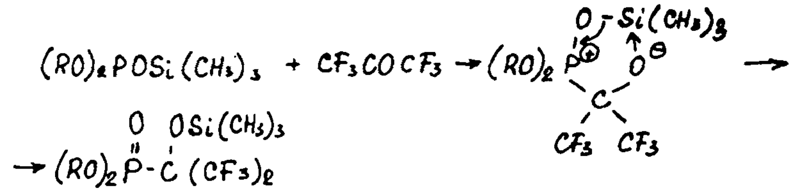


$R = n\text{-}C_4H_9, C_6H_5$; $A = Cl, CH_3COO$



Studying the reaction of diethyl trimethylsilyl phosphite with hexafluoroacetone (−25°C) containing positively polarized carbonyl carbon showed that the reaction proceeds exclusively with the formation of diethyl α trimethylsilyloxyhexafluoroisopropylphosphonate (96%).[23]

In this case the reaction evidently starts with the nucleophilic attack of the silyl phosphite phosphorus atom on the carbonyl carbon of hexafluoroacetone. Because of the high mobility of the trimethylsilyl group at the second stage of the reaction, the bipolar ion is stabilized and diethyl α-trimethylsilyloxyhexafluoroisopropylphosphonate is formed.

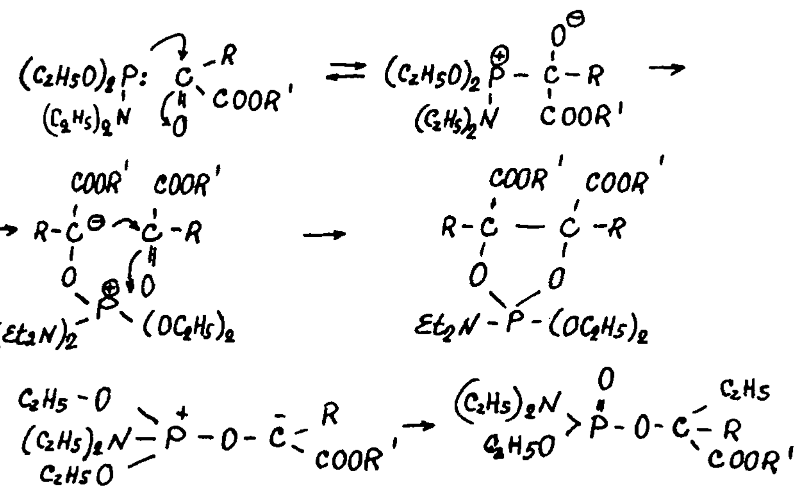


At elevated temperatures the reaction proceeds in the opposite direction and diethyl trimethylsilyl phosphite is formed. The reaction of diethyl trimethylsilyl and acetyl diethyl phosphites with 1,1,1-trifluoroacetone also proceeds with the formation of products which have phosphonatic structure. The resulting products are diethyl α,α,α-trimethylsilyloxy-α-(trifluoromethyl)methylphosphonate (67%) and diethyl α,α-acetoxy-α-(trifluoromethyl)methylphosphonate (52%) with δ^{31}P-15 and -12 ppm respectively. To extend these studies, we considered it of interest to investigate the reactions of dialkyl acyl phosphites and diethyl trimethylsilyl phosphite with chloral. Chloral, when reacting with phosphites, is known to form unsaturated phosphonic esters. In the reactions of dialkyl acyl phosphites with chloral, di- and monochloracetic aldehydes have been shown to form the corresponding phosphonates.[24,26] Chemical shifts of the phosphorus atom in these phosphonates are equal to −10, −14, −18 ppm respectively. In the reaction of chloral with diethyl trimethylsilyl phosphite, diethyl α-trimethylsilyloxy-β,β,β-trichlorethylphosphonate (δP^{31} − 13 ppm) is also formed.[27]

The fact that in the latter case the reaction proceeds not on the silicon but on the phosphorus atom was demonstrated with the reaction of diethyl trimethylsilyl phosphite with a mixture of chloral and acetaldehyde: chloral and not the acetaldehyde enters into the reaction. The results obtained by us show that reactions of various anhydrides of phosphorus acid containing an easily detachable radical start with the nucleophilic attack of the phosphorus atom on carbonyl carbon; subsequent stabilization of the bipolar ion formed, in most cases, is not accompanied by phosphonate-phosphate rearrangement and results in the formation of phosphonates.

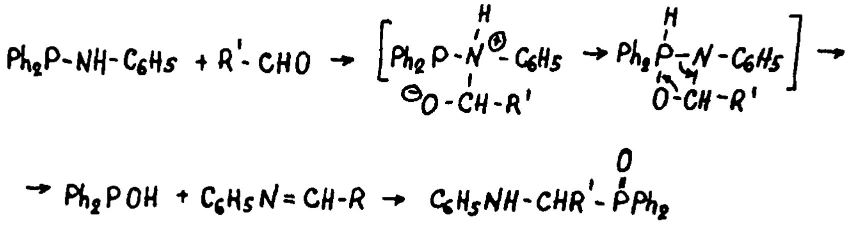
When the α-carbon atom of the carbonyl compound has strong electronegative groups, the migration of the ester radical can be preceded by the phosphonate-phosphate rearrangement; in this case too, the reaction proceeds on the carbonyl group carbon. The bipolar ion formed initially from neutral phosphites which have no easily detachable groups in their reactions with carbonyl compounds with activating electronegative substituents, evidently undergoes fast phosphonate-phosphate rearrangement and is transformed into the corresponding phosphate.

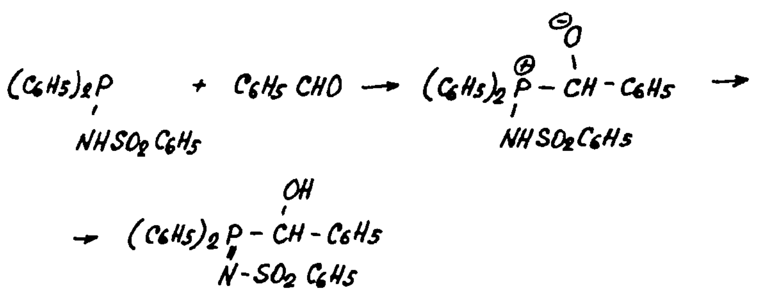
Reactions of carbonyl compounds with amides and isocyanates of phosphorus acids having a phosphorus-nitrogen bond are now considered. Reactions with carbonyl-containing compounds in multicenter nucleophilic systems such as P(III) amides, depending on the nature of the groups surrounding the phosphorus or nitrogen atoms, can proceed on the phosphorus atom, on the nitrogen atom, or on both reaction centers simultaneously. The reactions of dialkyl amidophosphites with the esters of α-aldehydo-, α-keto-carboxylic-, and α-keto-phosphonic acids proceed in a way similar to that of trialkyl phosphites. The reactions seem to start with the nucleophilic attack of the phosphorus atom on the carbon of the carbonyl group after which the reaction proceeds in two directions: addition of the second molecule of the carbonyl compound and the formation of 1,3,2-dioxaphospholanes; or the detachment of the alkoxyl group radical with the formation of phosphates. A slighter tendency to the formation of 1,3,2-dioxaphospholanes was observed in reactions with dialkyl amidophosphites as compared to those with trialkyl phosphites.[10]



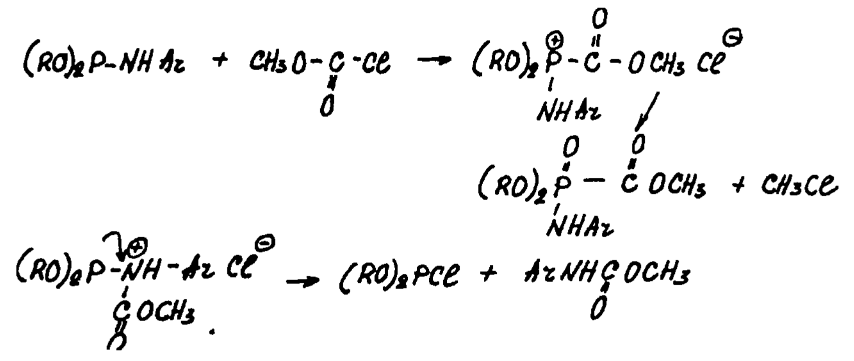
The reactions of anilides of dialkyl phosphorus and diaryl phosphinous acids that have a mobile hydrogen atom with carbonyl compounds, as has been shown by Evdakov and Hudson for saturated, and by us for unsaturated aldehydes, proceed with the participation of the nitrogen atom and result in the formation of α-aminophosphonates or oxides of α-aminoarylphosphines.[28]

One could expect the decrease of the nitrogen atom electron density to reduce the reactivity and the reaction to proceed on the other nucleophilic center, the phosphorus atom, yielding products with structure different from that of α-aminophosphonates. And indeed diphenyl phenylsulfophosphamid forms compounds with a phosphimide bond.[29]

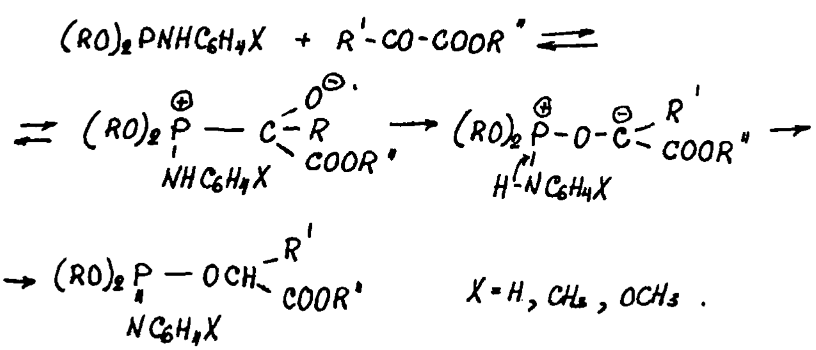




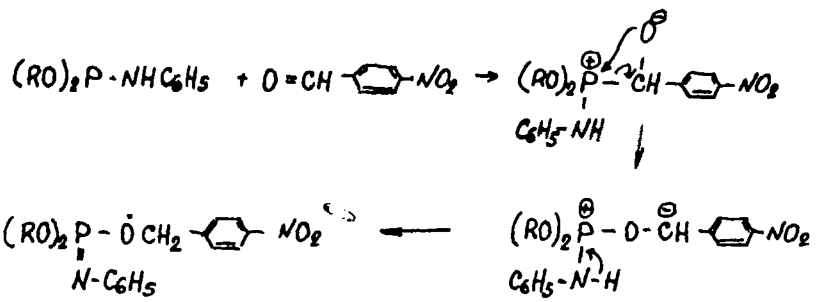
The interaction between dialkyl anilide phosphites and carboxylic chlorides is an interesting example of the reaction proceeding in such a dual direction. Evidently, in this case too, the interaction of amidophosphites with carboxylic chlorides proceeds in two directions simultaneously: the carbon atom of the carbonyl group is initially attacked by the phosphorus atom, thus forming anilidophosphinyl carboxylic ester; and on the nitrogen atom with the formation of methyl anilide carbonates and dialkyl phosphorus chlorides. The relation between the products formed in the reaction depends on the character of the substituents located at the phosphorus and the nitrogen atoms. An increase of electron density on the phosphorus atom results in raising the amount of phosphonate in the reaction.[30]



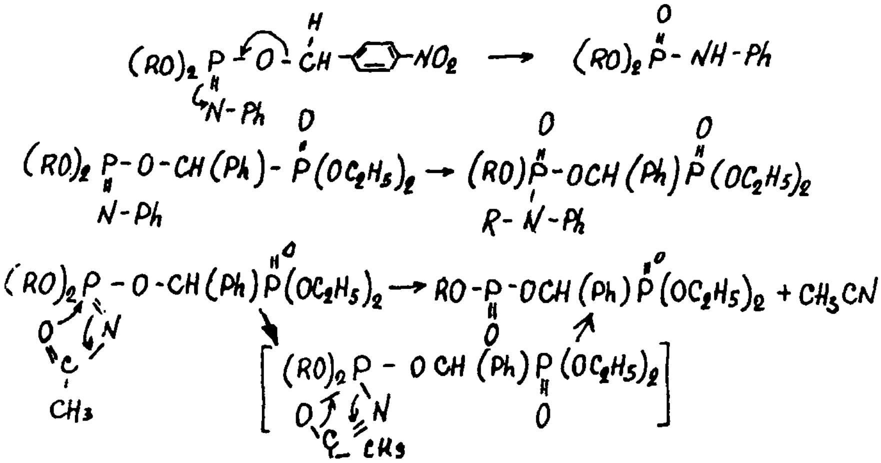
Formation of compounds with a phosphorus-oxygen bond is observed when anilides of P(III) acids react with compounds containing an activated carbonyl group. The fact that there is a mobile hydrogen atom in the anilide group causes proton migration from the anilide group to the negatively charged carbon atom which results in the formation of O,O-dialkyl-N-phenylimido phosphates.[31,32]



Reactions with α-keto-phosphonates[33] and β-nitrobenzaldehydes[34] proceed in a similar way.

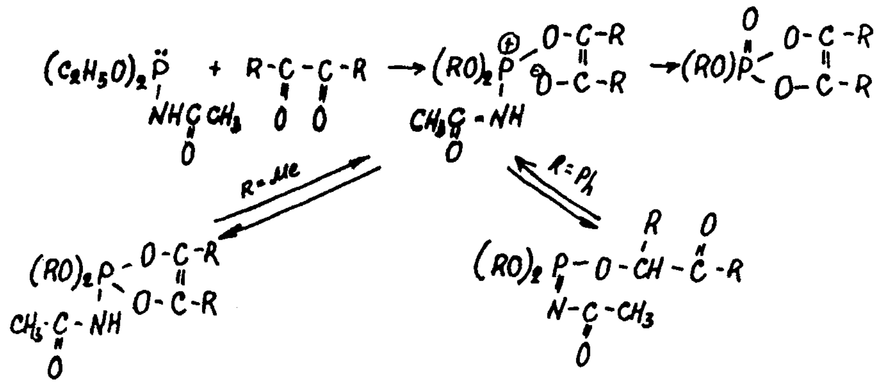


The imidophosphates formed readily undergo thermal transformations. Thus, N-tolylimido-O-*p*-nitrobenzyl phosphate decomposes with the migration of the mobile proton of the methylene group to the nitrogen atom of the phosphimide group with the formation of O,O-diethyl anilidophosphate even at room temperature. O,O-diethyl-α(O,O-diethyl phosphinyl)benzyl-N-phenyl imidophosphate at 170°, with the displacement of the alkoxyl radical, is transformed into O-ethyl-α-(O,O-diethyl phosphinyl)benzyl-N,N-ethyl phenyl amidophosphate. Similarly, N-acetylimidophosphate, under the same conditions, releases acetonitrile and is transformed into O,O-diethyl-α-(O,O-diethyl phosphonyl) benzyl phosphate.[33]



The direction in which the rearrangement proceeds is evidently determined by both the mobility of the hydrogen atom and the basicity of the nitrogen atom.

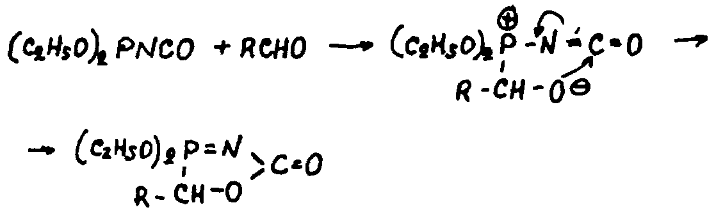
The reactions of amides of P(III) acids containing a mobile hydrogen atom with αdiketones proceed in a more complicated way. The phosphorus atom of the amidophosphite attacks the carbonyl group of the α-diketone with the formation of a bipolar ion having a phosphorus-oxygen bond. Its stabilization involves not only the migration of the mobile proton of the amide group, as a result of which imidophosphate is formed (as was the case for the reactions of amides of P(III) acids with an activated carbonyl group), but also the attack of the negatively charged oxygen atom on the phosphorus atom with cyclization to 1,3,2-dioxaphospholene. The way the reaction proceeds is determined by the nature of the carbonyl compound. For example, N-acetamidophosphite reacts with benzyl with the formation of the corresponding N-acetimidophosphate; in the case of diacetyl, the steric and polarization effects facilitate the attack of the negatively charged oxygen atom on the phosphorus atom and cyclization to 1,3,2-dioxaphospholene takes place.



Both of these processes are obviously reversible and the increase of temperature favors the reaction proceeding in the opposite direction – the transformation of imidophosphate and dioxaphospholene into an open bipolar structure with a phosphorus-oxygen bond. During distillation, N-alkylacetamide splits off and 1,3,2-dioxaphospholene with a tetracoordinated phosphorus atom is formed.

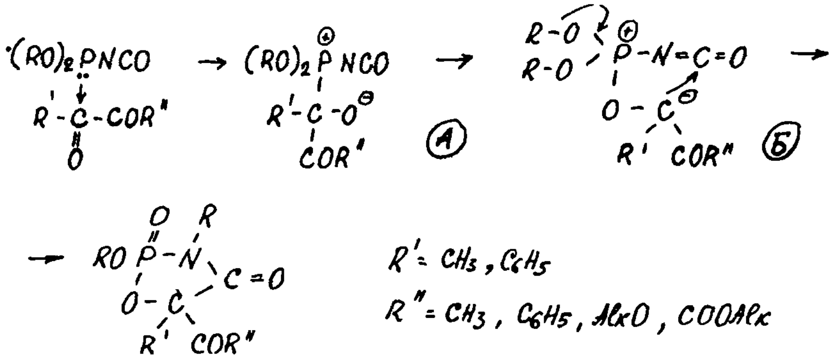
The way the reactions of carbonyl compounds with isocyanates of phosphorus acids proceed is quite interesting and unusual. The isocyanate group is capable of intramolecular interaction with the negatively charged end of the bipolar ion formed in the reaction.

We studied the reactions of diethyl isocyanate phosphite with benzaldehyde, *p*-chloro-, *p*-fluoro-, and *p*-methoxybenzaldehydes at a temperature of – 10° and obtained cyclic diethoxyalkyl phosphazocarbonates.[35]



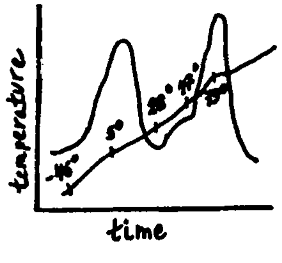
In view of the results obtained, it was of interest to study similar reactions with carbonyl-containing compounds in which the carbonyl group is activated by electron-attracting groups since in this case, just as in similar reactions with phosphites, one could expect phosphonate-phosphate rearrangement to take place. We studied the reactions of dialkyl isocyanate phosphites with α-diketones and esters of α-keto-carboxylic acids: diacetyl,[36] benzil,[36] esters of pyruvic,[37] benzoyl formic and α,β-diketo-butyric acids.[38] The reactions were carried out with different reactant ratios (1:1, 1:2), at different temperatures (+100, 0, – 10°) without a solvent and in solution. Under these conditions, adducts of one isocyanate molecule with one carbonyl compound molecule are formed. The chemical shift δ^{31} is equal to -9, -12 ppm. With acid hydrolysis of the benzoyl formate ester adduct, amygdalic acid has been separated.

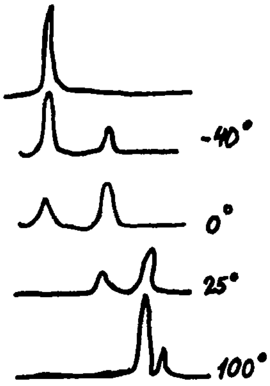
Along with the adducts formed in a yield of 60-70%, in all cases we observed the formation of dialkyl isocyanate phosphates (up to 15%) resulting from the oxidation of initial isocyanate by the carbonyl compound. Evidently, the reactions of dialkyl isocyanate phosphites with carbonyl compounds follow the general scheme proposed by us for a similar reaction with trialkyl phosphites in which 2-alkoxy-2-oxa-3-alkyl-5-substituted 2-phosphaoxazolidene-4-ones are formed.



As a result of the nucleophilic attack of the phosphorus atom of isocyanatophosphite on the electrophilic carbon atom of the carbonyl group, a bipolar ion A is formed. Since the adjacent carbon atom has an electronegative group which strengthens the positive charge on the phosphorus atom, this bipolar ion undergoes rapid isomerization into a more thermodynamically stable ion B with a P–O–C bond. Further stabilization of the bipolar ion into the final reaction product takes place with the participation of the isocyanate group. As a result of the carbanion attack on the carbon atom of the isocyanate group, cyclization of the five-membered structure takes place and subsequent dialkylation leads to the final reaction product.

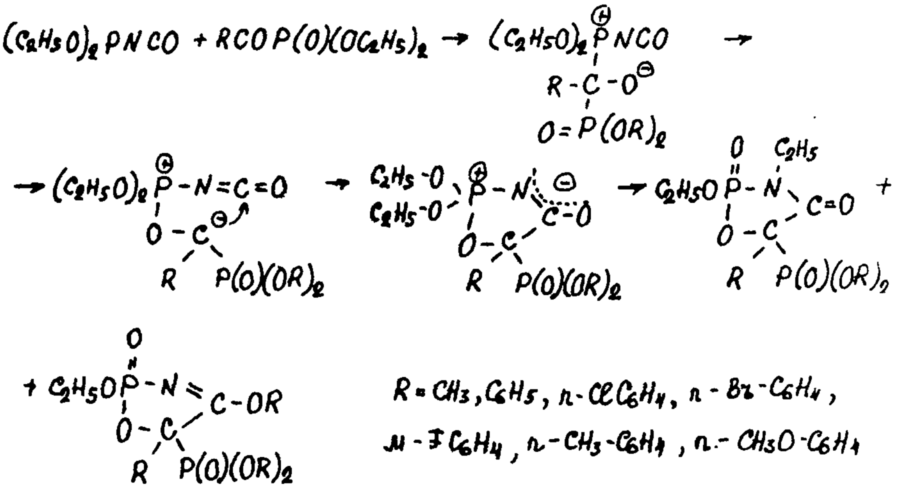
To study these reactions in greater detail, we applied dta, ir and ^{31}P nmr-spectroscopy.[38] Thermographic investigation was performed starting with an initial temperature of $-100°$.



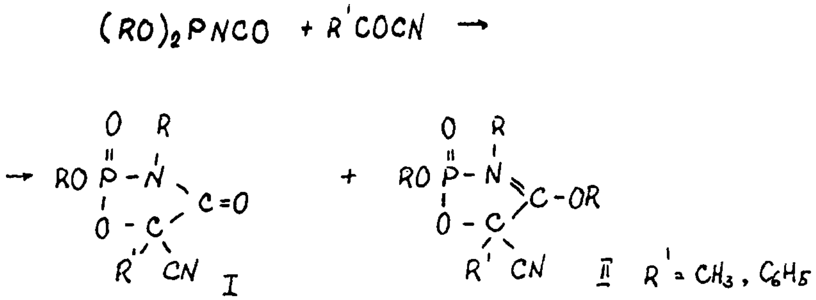


The thermograms show two exothermic effects. The thermograms reflect high reactivity of isocyanates: TSR lies below $-40°$. To assign the exo-effects observed, ir and ^{31}P nmr spectra were recorded with time and at different termperatures. When recording the ir spectra of the reaction mixture (as exemplified by diethyl isocyanatophosphite and pyruvic ethyl ester) rapid disappearance of the NCO group absorption band is observed in the condensed phase; in an 0.02M solution in CCl_4 a gradual decrease of the intensity of this band is observed with the progress of the reaction. The band disappears completely after the first exo-effect has been passed. In the ^{31}P nmr spectrum of the reagent mixture cooled with liquid nitrogen, there is one δ_P −122 ppm signal corresponding to the initial isocyanate. At −15°C, which corresponds to the temperature of the first exo-effect, and up to the temperature corresponding to the maximum another peak, δ_P −67 ppm, appears. With the further rise of temperature, the peak with δ_P −122 ppm decreases and completely disappears while the peak with δ_P −67 ppm increases. This peak may be assigned to the intermediate reaction product of a bipolar structure. Subsequently, the −67 ppm peak decreases and a peak at $\delta_P = -16$ ppm appears corresponding to the final reaction product. On termination of the second exo-effect, the −16 ppm signal remains in the spectrum as well as a small signal with −1 ppm corresponding to dialkyl isocyanate phosphate. Proceeding from these observations it can be concluded that the first exo-effect corresponds to the initial interaction of isocyanate with the carbonyl compound resulting in the formation of an intermediate having the structure of a bipolar ion. The nature of the second exo-effect is related to the formation of the final reaction product.

The reaction of esters of α-keto-phosphonic acids with isocyanates of dialkyl phosphites is very active. It should be noted that similar reactions with trialkyl phosphites, as we have seen, proceed slowly, require rigorous conditions, and are accompanied by the detachment of α-keto-phosphonates along the P—C bond.[39]

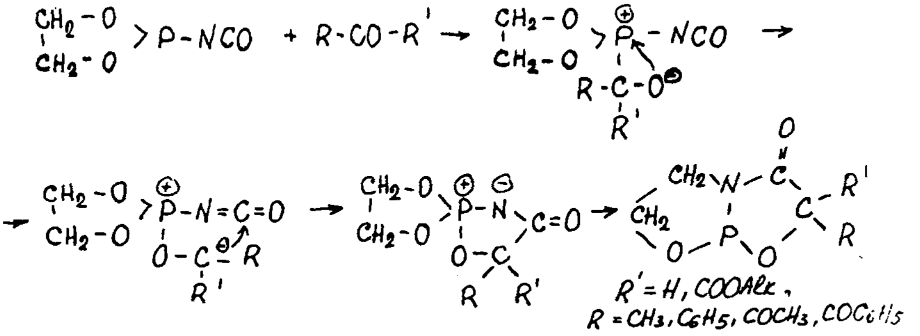


Reactions with aceto-, benzoyl- and substituted benzoyl phosphonic acids follow the general scheme described above. In these reactions however two isomeric compounds are formed: 2-alkoxy-2-oxo-3-alkyl-5-substituted-2-phosphaoxazolidinones (I); and 2,4-dialkoxy-2-oxo-5-substituted-2-phosphaoxazoles (II). Here the intermediate bipolar ion stabilization is the result of formation of a five-membered ring with the participation of the NCO-group and subsequent N- and O-alkylation. The compounds formed are derivatives of lactam-lactim tautomers. Reactions with highly reactive nitriles of α-keto-carboxylic acids proceed in a similar way. The reactions take place in methylene chloride solution below 0°.

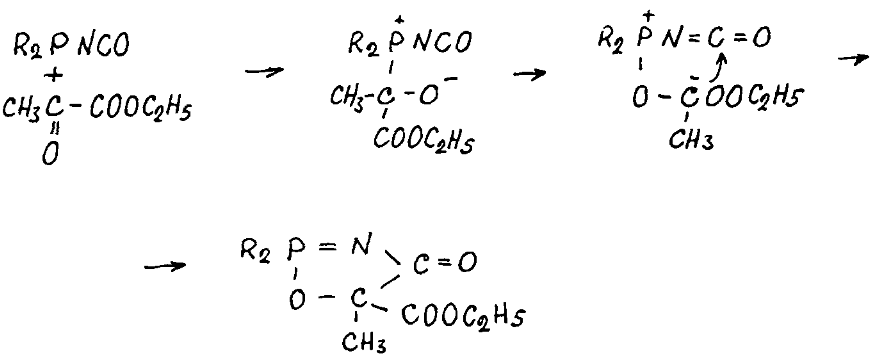


Phosphaoxazolidinones (I) and phosphaoxazoles (II) are a close-boiling mixture of compounds distilling in vacuum in a temperature interval of 5-10° without decomposing. In the ir spectra of the mixture, there are bands of the C = O group characteristic of I (1770-1800 cm^{-1}) and the C = N group characteristic of II (1645-1670 cm^{-1}). In the ^{31}P nmr spectra, two signals with δ_P −7 and +3 ppm are clearly observed. Isomer formation is confirmed by gas-liquid chromatography.

The reactions of alkylene glycol phosphorus isocyanates with α-diketones and α-keto- and α,β-diketo-carboxylates were also studied.[36,40] They proceed in a way similar to that of acyclic isocyanates, the process of intramolecular dealkylation in the intermediate bipolar ion is accompanied by opening of the ring which results in the formation of 1-aza-2,5-dioxo-5-phospha-4,6-dioxo-3-substituted-bicyclo[3,3,0] octanes and -[3,4,0] nonanes. Two exothermic effects are observed thermographically. They are at higher temperatures than those for acyclic isocyanates, which confirms the reduced reactivity of cyclic isocyanates.

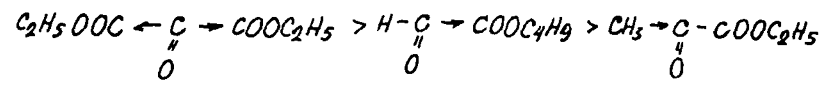


The reactions of tetraethyl isocyanate diamidophosphites and diphenyl isocyanate phosphonates with the ethyl ester of pyruvic acid proceeds with the formation of the corresponding phosphaoxazolones. The stabilization of the intermediate bipolar ion in this case results from cyclization and the formation of a phosphamide bond.[41]



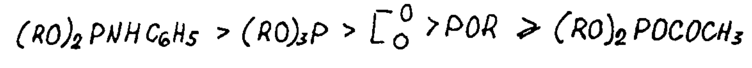
I should like to note in conclusion that in the reactions of carbonyl compounds with esters, ester amides, amides and ester anhydrides of phosphorus acid, whose nucleophilic properties are clearly manifested in a number of interactions, the limiting process is, in most cases, the nucleophilic attack of the phosphorus atom with an unshared electron pair on the electrophilic carbon center of the carbonyl group. This conclusion is supported by the regularities we observed when comparing the reactivity of these derivatives of tricoordinated phosphorus in their reactions with α-keto-carboxylates using the dta method.

The reactivity of carbonyl compounds is primarily determined by the deficit of electron density on the carbon atom of the carbonyl group and decreases in the series:



$$C_2H_5OOC \leftarrow \underset{\overset{\|}{O}}{C} \rightarrow COOC_2H_5 > H-\underset{\overset{\|}{O}}{C} \rightarrow COOC_4H_9 > CH_3 \rightarrow \underset{\overset{\|}{O}}{C} - COOC_2H_5$$

Reactivity increases when one passes from phosphites to N-arylamidophosphites and decreases appreciably for the cyclic derivatives and mixed anhydrides of phosphorus and carboxylic acids. The decrease in reactivity in the series:



$$(RO)_2PNHC_6H_5 > (RO)_3P > \left[\begin{smallmatrix}O\\O\end{smallmatrix}\right\rangle POR > (RO)_2POCOCH_3$$

can be associated with the decrease of electron density on the phosphorus atom resulting from the increased inductive (–I) effect of substituents and the decrease, in the same sequence, in the conjugation of substituents, $NHC_6H_5 > OR > OCOCH_3$, with the vacant phosphorus orbitals.

TABLE II

Thermographic study of the reactions of the derivatives of tricoordinated phosphorus with esters of α-ketocarboxylic acids, $R-CO-COOC_2H_5$

Phosphorus compound	R	TSR °C	TMR °C
$(C_2H_5O)_2PNHC_6H_5$	C_6H_5	– 66	– 31
$(C_2H_5O)_3P$	C_6H_5	– 57	– 1
	CH_3	– 50	– 2
O POC_2H_5 O	C_6H_5	– 26	– 8
$(C_2H_5O)_2POCOCH_3$	C_6H_5	– 23	– 5

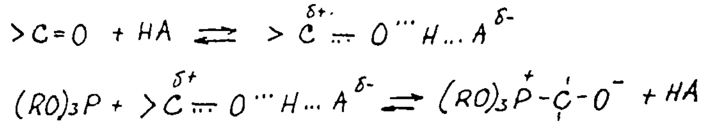
To obtain additional data on the influence of substituting groups in phosphites and carbonyl compounds on the rate and the mechanism of reaction, we applied the kinetic method of investigation. Reactions of benzoyl formic esters with trialkyl phosphites were studied under conditions leading only to the formation of 1,3,2-dioxaphospholanes. The rates were recorded with the help of uv spectroscopy, using the K band of benzoyl formic ester. Reactions were carried out in surplus phosphite with an initia concentration of carbonyl compound of 0.25 mol/l. Rate constants of the second order determined in n-hexane are shown in Table III.[42]

TABLE III

Sern. No.	Phosphite	$K_2^{20^\circ} \cdot 10^4$ l/mol.sec
1.	$(CH_3O)_3P$	3.2
2.	$(C_2H_5O)_3P$[a]	8.4
3.	$(n-C_3H_7O)_3P$	7.3
4.	$(n-C_4H_9O)_3P$	8.0
5.	$(iso\text{-}C_3H_5O)_3P$	10.3
6.	O POC_2H_5[b] O	3.1

[a] Ea 4.95 kc/mol ΔS – 55.70 en.un.
[b] In CH_3CN at 25°C.

Comparison of the data obtained shows that the reaction rate increases with increased electron-donor capacity of alkyl groups in phosphites. Reduced reactivity has been noted for phosphites with bulky substituents which is explained by the influence of not only induction but also steric effects of substituents on the reaction rate. Reaction acceleration has been shown in the presence of acetic acid which is caused by the activation of the carbonyl group due to the formation of a hydrogen bond with the acid.



$$>C=O + HA \rightleftarrows >\overset{\delta+}{C} \cdots O \cdots H \ldots A^{\delta-}$$

$$(RO)_3P + >\overset{\delta+}{C} \cdots O \cdots H \ldots A^{\delta-} \rightleftarrows (RO)_3\overset{+}{P}-\overset{|}{\underset{|}{C}}-O^{-} + HA$$

Reaction rate has been noted to increase with increased dielectric constant of the solvent.

The low activation energy shows that, at the stage determining the rate of reaction, large energy is not required and, probably, the P–C bond does not break. The transformation of the ion with a P–C bond into one with a P–O–C bond is taking place as a tricentral rearrangement with the nucleophilic attack of negatively charged oxygen on the phosphorus atom. The large negative activation entropy is indicative of a high degree of orientation in the transient state. Thus the data obtained are in agreement with the mechanism proposed above for these reactions.

The results obtained from kinetic studies are also in agreement with the data of the Japanese investigators Ogata and Yamashita, who studied the reactions of trialkyl phosphites with α-diketones and made it possible to express an opinion that the mechanism proposed can be of general character for the reactions of derivatives of tricoordinated phosphorus with carbonyl compounds.

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