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Phosphorylated Aldehydes†

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The review presents systematic data on the methods of synthesis and chemical properties of phosphorylated aldehydes. Attention has been concentrated on organophosphorus compounds containing the formyl group in the alkyl substituent linked to the phosphorus atom by a C-P bond. The phenomena of keto-enol tautomerism of phosphorylated aldehydes are described in greater detail, the influence of various factors on the position of the keto-enol equilibrium is assessed, and the geometrical structure of the enols formed is considered.
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I. INTRODUCTION

Aldehydes occupy one of the central positions in organic chemistry both as regards their reactivities and synthetic possibilities. Presumably phosphorylated aldehydes will in time occupy just as important a place in the chemistry of organophosphorus compounds. In view of the high reactivity of the aldehyde group, they may be considered as the starting materials for the synthesis of a wide variety of other organophosphorus compounds. On the other hand, compounds of this class are convenient for the investigation of many general theoretical problems in organic chemistry and the chemistry of organophosphorus compounds.

Although from the time of the publication of the first study[1] which laid the foundations of the research on phosphorylated aldehydes twenty years have elapsed, the accumulation of factual data in this field has been extremely slow. This is probably due to the lack of convenient methods of synthesis for compounds of this kind. However, in recent years the number of published investigations of this problem increased sharply. Together with the development of synthetic methods, studies have been made on the structures and reactivities of phosphorylated aldehydes.

Hitherto there have been no reviews in the literature dealing with phosphorylated aldehydes. This paper is a first attempt at a general and systematic account of the available data on this question. At the same time, we feel it would be useful to draw the attention of investigators to this interesting branch of organophosphorus chemistry.

The review is devoted to derivatives containing the formyl group in the alkyl substituent linked to phosphorus via C-P bonds but other formyl-containing organophosphorus compounds are also briefly considered.

II. METHODS OF SYNTHESIS OF PHOSPHORYLATED ALDEHYDES

The vast majority of methods for the preparation of compounds with a C-P bond are based on the interaction of phosphorus(III) acid esters with electrophilic agents. However, the high reactivity of the aldehyde group in relation to such esters hinders the direct introduction of the formyl-containing substituent at the phosphorus atom. Organometallic synthesis, frequently used to form C-P bonds, also cannot be used. Therefore the formyl group must be introduced or regenerated from derivatives after the formation of the C-P bond.

In 1952, Dawson and Burger[1] suggested for the first time that the fundamental method for the synthesis of organophosphorus compounds—the Arbuzov reaction—be used to synthesise phosphorylated aldehydes with a halogenoacetal as the electrophilic agent. The reaction of the diethylacetal of bromoacetaldehyde with triethyl phosphate yielded the diethylacetal of diethylphosphonoacetaldehyde, the acid hydrolysis of which led to diethoxyphosphonoacetaldehyde:

$$(EtO)_3P + BrCH_2CH(OEt)_2 \rightarrow (EtO)_2P(O)CH_2CH(OEt)_2 + EtBr$$

$$(EtO)_2P(O)CH_2CH(OEt)_2 \xrightarrow{H_2O(H^+)} (EtO)_2P(O)CH_2C(O)H + 2EtOH.$$

The authors failed to develop further this method (neither the phosphorylated acetal nor the aldehyde were isolated in a pure form; the latter was only identified in the form of its 2,4-dinitrophenylhydrazone), but their idea concerning the protection of the aldehyde group undoubtedly merited attention.

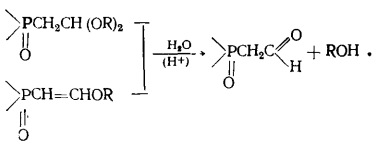
Detailed studies were made in our laboratory[2-8] of the reactions of halogenoacetals with phosphorus(III) acid esters followed by hydrolysis of the phosphorylated acetals to aldehydes up to the development of preparative procedures. Various phosphorus(III) acid esters (phosphites, aliphatic and aromatic phosphonites and phosphinites) together with a wide range of halogenoacetals were employed in the reactions. It was found that the influence of various factors [the nature of the phosphorus(III) acid ester and of the halogen in the halogenoacetals as well as the structure of the halogenoacetal] is determined by familiar relations typical for the Arbuzov reaction[9]. The temperature conditions in the reaction play a very significant role. At elevated temperatures phosphorylated aldehydes are degraded to the corresponding phosphorylated vinyl ethers:

$$>P(O)CH_2CH(OR)_2 \xrightarrow[-ROH]{t^\circ} >P(O)CH{=}CHOR$$

† Phosphonylated aldehydes (Editor of Translation).

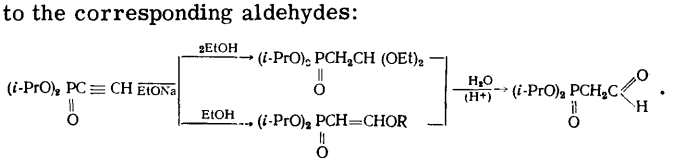
This type of degradation has also been noted in studies by other workers [10-12]. Probably the tendency of phosphorylated acetals to undergo reactions of this type is influenced, apart from the temperature factor, by the nature of the substituents at the phosphorus atom and the composition of the second component in the reaction mixture. Thus the reaction of tri-isopropyl phosphite with a chloroacetal (170°C) leads to the formation of a mixture of the phosphorylated acetal and alkoxyvinylphosphonate [10], while the interaction of a bromoacetal with trimethyl phosphite [11] and ethyl diphenylphosphinite [12] leads to the exclusive formation of the corresponding phosphorylated enolic ethers. It has been noted [11] that mainly ethoxyvinylphosphonate was formed in the study by Dawson and Burger [1].

The fact that phosphorylated acetals as a rule contain a mixture of the corresponding phosphorylated vinyl ethers is hardly a serious obstacle to the synthesis of phosphorylated aldehydes from them, since the hydrolysis of both the aldehydes and the vinyl ethers [10] leads to the formation of the same aldehydes:



In the hydrolysis of the phosphorylated acetal, a high concentration and a large excess of the acid should not be employed (to avoid the hydrolysis of the ester groups at the phosphorus atom). It is quite sufficient to use 5–7% HCl (80–90°C, hydroquinone). Naturally, as the electron-accepting phosphorus-containing group is removed further from the acetal group, the ease of hydrolysis increases. The excess acid and the volatile hydrolysis products should be removed *in vacuo* at relatively low temperatures. In the milder hydrolysis of phosphorylated acetals in the presence of ion exchangers, the yield of aldehydes increases [13].

The Michaelis–Bekker reaction can also be used to synthesise phosphorylated acetals [14]. Moreover, ethynylphosphonates react with alcohols in the presence of alkoxides with formation of a mixture of phosphorylated enolic ethers and acetals [10], the hydrolysis of which leads to the corresponding aldehydes:



The applicability of the method is limited by the availability of the ethynylphosphonate.

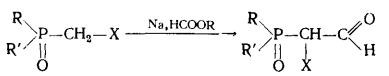
On the whole, one may say that the method of synthesising phosphorylated aldehydes via the corresponding acetals is general and has the advantage over the methods described below that it can be used to obtain products with various relative positions of the phosphorus atoms and the aldehyde groups as a function of the structure of the initial halogenoacetals and phosphorus(III) acid esters.

The genetic relation between vinylphosphonates and the corresponding phosphorylated acetals and the possibility of synthesising phosphorylated aldehydes on their basis was already noted above. The synthesis of vinylphosphonates was developed on the basis of the phosphorylation with phosphorus pentachloride of enolic [15] and dialkyl [16] ethers and acetals [17,18] as well as a number of other methods. It is clear that this method of synthesising phosphorylated aldehydes is based on the use of a fairly readily available class of compounds. The synthesis of phosphorylated aldehydes from the corresponding vinylphosphonates has also been thoroughly developed. Phosphorylated aldehydes belonging to the class of phosphonates [19-21], phosphonothionates [22,23], and phosphonothiolates [23,24] have been obtained by this procedure.

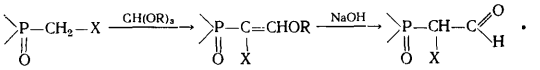
The hydrolysis of the corresponding alkoxyvinylphosphonates proceeds similarly to that of phosphorylated acetals but requires more severe conditions (particularly for phosphorothioic acid derivatives). This must be taken into account in the hydrolysis of acetals containing an admixture of a phosphorylated enolic ether. In practice the method is applicable only to the synthesis of α-phosphorylated aldehydes of the phosphonate series (in view of the availability of the initial enolic ethers).

In the synthesis of aldehydes with different relative positions of the formyl group and the phosphorus-containing substituent and also aldehydes belonging to the series of phosphinates and phosphine oxides, other procedures must be resorted to.

Many phosphorylated aldehydes have been obtained by the formylation of organophosphorus compounds with an active methylene group. The aldehydes synthesised include, together with the phosphorus-containing groups, other electron-accepting substituents in the α-position. Here one employs either direct formylation of the methylene group via the mechanism

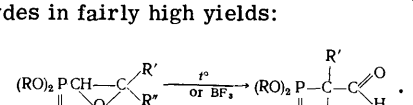


or the alkoxymethylene fragment is introduced by the initial interaction of the organophosphorus compound with orthoformic ester, this being followed by the alkaline hydrolysis of the condensation product:

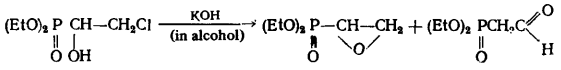


The active methylene group in phosphonoethylacetate [1,25,26], phosphonoacetone [25], benzylphosphonate [27], cyanomethylphosphonate [28], chloro- and bromo-methylphosphonates [29], diphenylbenzylphosphine oxide [12], and dibutylethoxycarbonylmethylphosphine oxide [30] was formylated by the first procedure. The formylation of dibenzylphosphinous acid proceeds at only one methylene group [31]. The synthesis of phosphorylated aldehydes with the preliminary introduction of the alkoxymethylene group has been achieved from cyanomethylphosphonate [26], phosphonoacetone [29], and dibutylphosphinylacetone [30]. The above reactions yielded phosphorylated aldehydes containing phenyl, chloro-, bromo-, cyano-, alkoxycarbonyl, and acyl groups next to the formyl group. Aldehydes of the above series proved suitable for the investigation of keto-enol tautomerism, which will be described below. The wide variety and large number of organophosphorus compounds with an active methylene group [32] suggest that methods of synthesising aldehydes on their basis will undergo a further successful development.

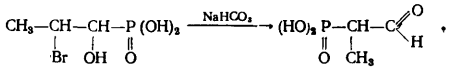
Thermal or catalytic isomerisation of oxiranylphosphonates ("epoxyvinylphosphonates") [33] leads to phosphorylated aldehydes in fairly high yields:



Both aliphatic [34] and cyclic [34,35] phosphorylated aldehydes can be obtained in this way. Oxiranylphosphonates without substituents in the oxiranyl group show little tendency to isomerisation of this kind [35]. Thus diethyl oxiranylphosphonate cannot be isomerised to phosphonoacetaldehyde either by heating or by treating with boron trifluoride-ether. However, phosphonoacetaldehyde is formed in a yield of up to 10% during the epoxidation of vinylphosphonate in methanol with hydrogen peroxide. It remains obscure whether this is a result of a rearrangement of the epoxide or of some other reaction between vinylphosphonate and hydrogen peroxide. Another method for the preparation of oxiranylphosphonate is dehydrochlorination of β-chloro-α-hydroxyethylphosphonate; here small amounts of phosphonoacetaldehyde are also formed together with the main reaction product—oxiranylphosphonate [36]:

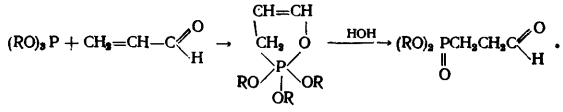


Dehydrobromination of β-bromo-α-hydroxypropylphosphonic acid with sodium bicarbonate yields α-phosphonopropionaldehyde as the main reaction product [37]:

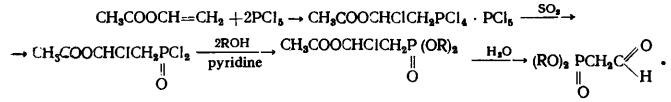


Thus oxiranylphosphonates or phosphorylated halogenohydrins can also be used to synthesise substituted phosphorylated aldehydes.

Apart from the methods of synthesis of phosphorylated aldehydes dealt with above, methods which have not hitherto found much application have been described in the literature. Of the studies of this series, the synthesis of aldehydes from compounds of the oxaphosphorane type [38,39] obtained as the result of the interaction of trialkyl phosphites with $\alpha\beta$-unsaturated carbonyl compounds should be mentioned:

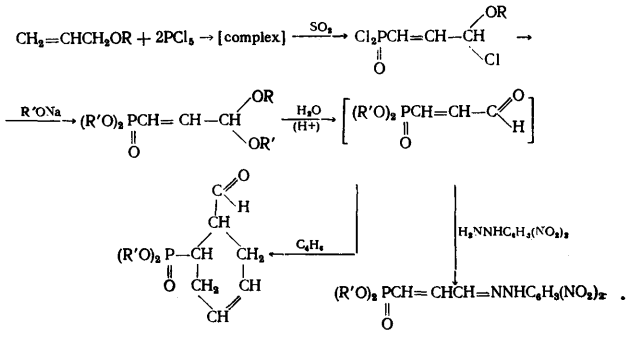


Treatment of the phosphorane with acetic acid also yields phosphonopropionaldehyde. The interaction of phosphoranes with alcohols leads to the acetals of the corresponding β-phosphonopropionaldehyde [40]. When crotonaldehyde reacts with triethyl phosphite in the presence of ethanol, the corresponding acetal is formed mixed with the enolic ether [41,42]. Phosphonoacetaldehydes have been obtained by the hydrolysis of β-acyloxy-β-chloroethylphosphonates [43-45]. The required starting materials were obtained by the low-temperature reaction of vinyl acetate with phosphorus pentachloride:



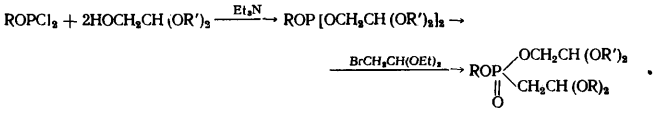
The ambiguous interaction between phosphorus pentachloride and enolic esters, shown by the studies of the same investigators, does not allow the synthesis of a wide variety of aldehydes by this procedure.

Unsaturated phosphorylated aldehydes have been obtained via the corresponding acetals [46]. The latter were synthesised from the products of the phosphorylation with phosphorus pentachloride of allyl ethers in accordance with the following scheme:



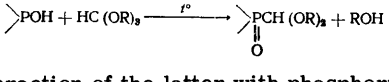
In view of their instability, phosphonoacroleins were not isolated in a free state and were identified only as their 2,4-dinitrophenylhydrazones. If the hydrolysis of the corresponding acetal is carried out in the presence of a conjugated diene, the phosphonoacrolein formed is involved in a Diels–Alder synthesis [46,47]. This reaction not only confirms the structure of the phosphonoacrolein but also constitutes a method for the synthesis of phosphorylated alicyclic aldehydes. Phosphonomethacrolein was obtained from methylallyl ether via the scheme described above [48] and, in contrast to its unsubstituted analogue, proved to be more stable and was isolated in a free state.

A method of synthesising phosphorylated diacetals based on the following general scheme has been developed in our laboratory: the phosphorus(III) acid chloride reacts with the acetal of glycolaldehyde to form the corresponding phosphorus(III) acid ester containing the acetal group in the ester moiety; the interaction of the latter via the Arbuzov reaction with the acetal of bromoacetaldehyde leads to the corresponding diacetals [49]:

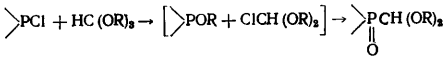


In the products synthesised, one of the acetal groups is contained in the alkyl substituent linked to the phosphorus atom and the other is in the ester moiety.

Compounds containing the formyl group attached directly to the phosphorus atom are still unknown. Possibly they cannot exist at all. We believe that the structure of the product quoted by Isamu [50] is unlikely. On the other hand, acetals of similar aldehydes are readily available and can be obtained in two ways: by the condensation of the partial esters of phosphorus(III) acid with orthoformic esters [51]:



or by the interaction of the latter with phosphorus(III) acid chlorides [52,53]:



Satisfactory yields of phosphorylated formals are achieved by the first method only in the reaction with dialkyl phosphites; acid phosphonites and secondary phosphine oxides

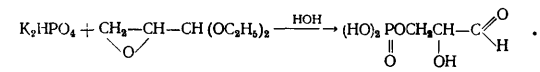
give extremely low yields of condensation products. The second method of synthesis—via phosphorus(III) acid chlorides—is more universal. The acetals of dimethylformamide (DMF) react with phosphorus(III) acid chlorides like orthoformic ester [54].

The hydrolysis of phosphonoformals does not lead to the corresponding aldehydes but involves the dissociation of the C–P bond [55] with formation of the initial dialkyl phosphite, alcohol, and alkyl formate.

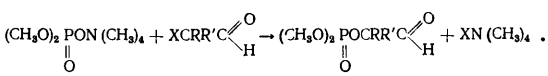
The structures of the phosphorylated aldehydes were confirmed in almost all cases by infrared spectroscopy and by the formation of 2,4-dinitrophenylhydrazones. In later investigations, NMR as well as infrared spectroscopy was employed.

Apart from the studies on phosphorylated aldehydes containing the formyl group in the substituent linked to the phosphorus atom by the C–P bond described above, mention has been made in the literature of compounds in which the formyl group is in the substituent linked to the phosphorus atom via a heteroatom (O, S, or N) and of phosphorus ylids and phosphonium salts. These studies on methods of synthesis cannot as yet be fitted into a definite system and therefore we shall confine ourselves to the enumeration of individual investigations in this field.

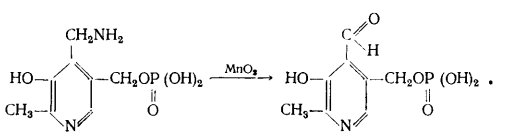
The interaction of the acetal of 2,3-epoxypropionaldehyde with dipotassium hydrogen phosphate followed by hydrolysis yielded glyceraldehyde phosphate [56]:



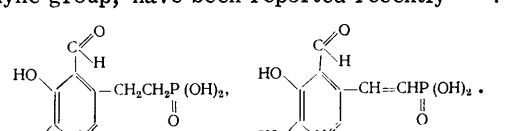
Another method of synthesising formyl-containing phosphates [57] consists in the interaction of the ammonium salts of phosphate esters with halogenoaldehydes:



Certain formyl-containing phosphates are interesting biologically active compounds. Pyridoxal phosphate [57-59], the synthesis of which involves the interaction of pyridoxamine with phosphoric acid followed by oxidation of the reaction product, is the most striking derivative of this kind:

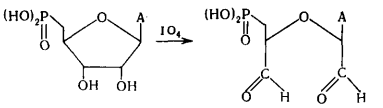


Phosphonic analogues of pyridoxal phosphate, in which the ester oxygen has been replaced by a methylene or methylidyne group, have been reported recently [60,61]:



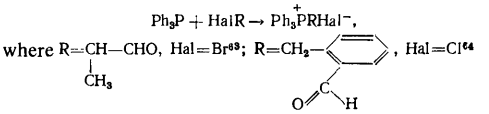
Their synthesis is based on the interaction of the corresponding pyridinealdehyde with phosphonate Wittig reagents, in particular with tetraethylmethylenediphosphonate. Esters of vinyl- and ethyl-phosphonic acids have been obtained by the oxidation of the hydroxymethylene group to the formyl group under mild conditions. The esters are hydrolysed by concentrated hydrochloric acid and phosphonic acid analogues of pyridoxal phosphate are isolated.

When adenosine monophosphate is oxidised by periodate, dialdehydes of the following type are formed [62]:



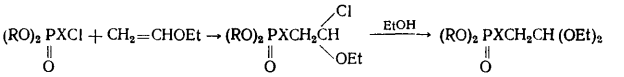
A = adenine residue

A series of phosphonium salts containing the aldehyde group are known [63,64]. Their synthesis is based on the interaction of triphenylphosphine with halogenoaldehydes:



Kirsanov and coworkers began the study of phosphazo-compounds with the aldehyde group in the aromatic ring, which are synthesised by the interaction of azidoaldehydes [65] or their oximes [66] with triphenylphosphine. In the latter case, the aldehyde was isolated by hydrolysing the oxime.

Acetals with the general formula $(RO)_2PXCH_2CH(OR')_2$, [67,68] where X = S or Se, are obtained according to the scheme



Acid hydrolysis of the acetal of the thio-derivative [67] led to the isolation of the corresponding aldehydes.

Several methods of synthesising aldehydes of the phosphorane type have been described, namely by the formylation of phosphinoalkylenes $Ph_3P{=}CH_2$ by *N*-formylimidazole [69] or ethyl formate [70] and also by the interaction of bromonitroethylenes with triphenylphosphine [71].

Compounds containing the formyl residue at a nitrogen atom linked to the phosphorus atom can be regarded as substituted formamides and are therefore not dealt with in the present review.

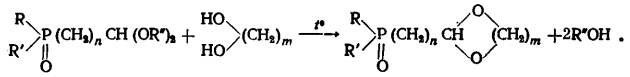
The foregoing discussion shows that many different types of synthesis of phosphorylated acetals and aldehydes have been described in the literature. The choice of a specific method for preparative purposes is determined mainly by the structure of the aldehyde to be synthesised and by the availability of the initial compounds. The advantages and disadvantages of individual methods have been stated in their discussion.

III. CHEMICAL PROPERTIES OF PHOSPHORYLATED ALDEHYDES

The chemical properties of phosphorylated aldehydes have been investigated much less than the methods of their synthesis. The limited number of studies in this field still precludes a broad general description of studies on the reactivity of compounds of this class and in the first place a description of the effects of electronic and steric factors on the course of nucleophilic addition reactions, which are most characteristic of the carbonyl group. Studies on keto-enol tautomerism of phosphorylated aldehydes, in which the mutual influence of the phosphorus-containing and formyl groups is clearly revealed, constitute an exception.

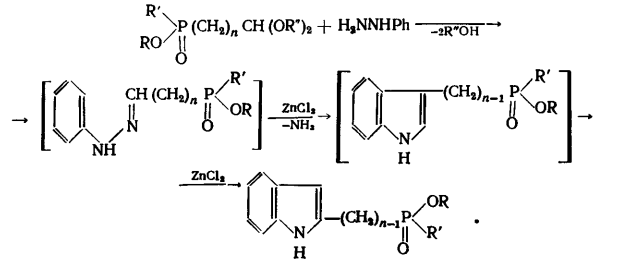
The first publications dealing with syntheses on the basis of phosphorylated aldehydes confirm their usefulness in this field. Certain reactions of phosphorylated aldehydes are described below. The most thoroughly investigated synthetic application of phosphorylated aldehydes is the synthesis of phosphorylated heterocyclic compounds with phosphorus in the side chain [72]. The first attempt to synthesise a phosphorylated aldehyde [1] was undertaken precisely with the aim of its subsequent employment to synthesise phosphorylated heterocycles. In many cases phosphorylated acetals were used successfully in the syntheses instead of phosphorylated aldehydes.

The reaction of phosphorylated acetals with diols yielded phosphorylated 1,3-dioxolanes [73], 1,3-dioxans [74], and polymethylene acetals [75]:



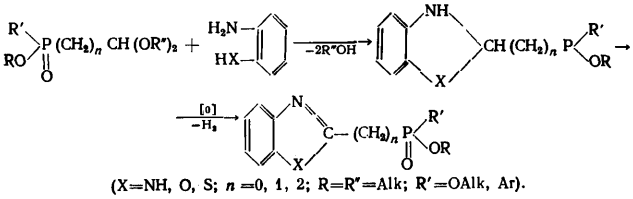
The reaction is carried out by heating equimolar amounts of the reactants with simultaneous distillation of the alcohol liberated. The phosphorylation of poly(vinyl alcohol) by phosphonoacetaldehyde can also be regarded as a transacetalisation reaction [76].

Phosphorylated acetals enter into a Fischer cyclisation reaction with arylhydrazines, forming phosphorylated indoles [5,77]:



It has been shown that the indoles phosphorylated in the 3-position, which are formed initially, isomerise to the 2-derivatives in the presence of an excess of zinc chloride.

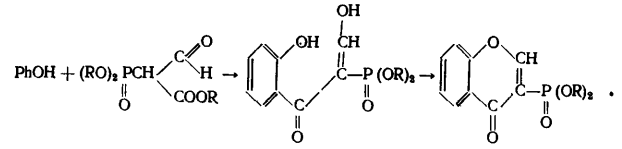
A wide range of phosphorylated heterocycles can also be obtained by the condensation of phosphorylated acetals with aromatic *ortho*-disubstituted compounds containing mobile hydrogen atoms, such as *o*-phenylenediamine, *o*-aminophenol, *o*-aminothiophenol, and others:



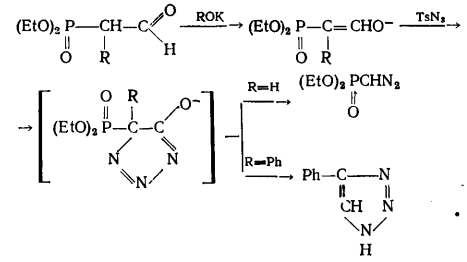
(X=NH, O, S; n =0, 1, 2; R=R″=Alk; R′=OAlk, Ar).

These reactions, which are common to the given classes of compounds, yielded respectively phosphorylated benzimidazoles [77,78], benzoxazoles [79], and benzothiazoles [80]. 2-Phosphorylated benzazoles are synthesised via a stage involving the formation of azolines [81]. The interaction of phosphorylated acetals with *o*-dihydroxy-derivatives of benzene and naphthalene resulting in the corresponding phosphorylated dioxoles takes place similarly [82]. Thus acetals of real phosphorylated aldehydes and derivatives known only in the acetal form (phosphorylated formals) have been used in the condensation reactions [77-82]. It has been found that, as the phosphorus-containing substituent moves further away from the acetal group, the rate of reaction increases, which can be accounted for by the decrease of the effect of the electron-accepting substituent on the mobility of the alkoxy-groups in the acetal moiety.

Substituted phosphorylated aldehydes also enter into a condensation reaction with monohydric phenols to form phosphorylated heterocycles [25]:

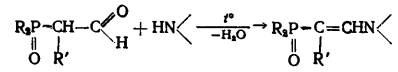


The ability of phosphorylated aldehydes to be converted comparatively readily into phosphorylated diazo-compounds greatly extends their synthetic possibilities, including the synthesis of heterocycles [83,84]:

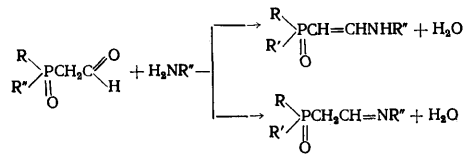


The free phosphonodiazomethane isolated [84] can be used for various organophosphorus syntheses.

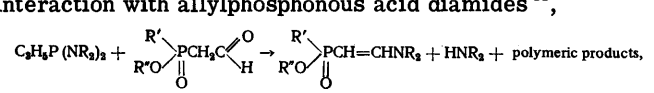
Phosphorylated enamines—a little known class of organophosphorus compounds—can also be obtained successfully from phosphorylated aldehydes. The interaction of equimolar amounts of the latter with cyclohexylamine in methanol [85] or with secondary aliphatic amines in toluene in the presence of catalytic amounts of toluene-*p*-sulphonic acid, accompanied by azeotropic distillation of water [86], gave satisfactory yields of phosphorylated enamines:



The interaction of phosphorylated aldehydes with primary amines leads to phosphorylated enamines, imines, or their mixtures depending on the structure of the amine employed [87]:

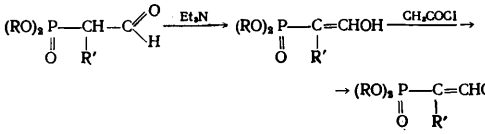


Virtually only enamines are formed when there is an electron-donating substituent at the nitrogen atom. When an electron-accepting substituent is present at the nitrogen atom, either a pure imine or a mixture of both products with the imine form predominating is formed. Whereas the direct interaction of secondary amines with phosphorylated aldehydes can involve either the keto- or the enolic form of the latter, the synthesis of phosphorylated enamines from the corresponding aldehydes via their interaction with allylphosphonous acid diamides [88],



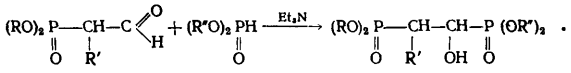
apparently involves the enolic form of the aldehydes.

Acylation of the enolic form of phosphorylated aldehydes by acetyl chloride in the presence of bases leads to β-acyloxyalkenylphosphonates [89]:



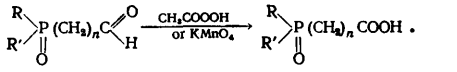
^{1}H NMR spectra have shown that the β-acyloxyvinylphosphonates, like the β-dialkylaminovinylphosphonates discussed above, have exclusively (or at least within the limits of the sensitivity of the ^{1}H NMR method) the *trans*-(P, O, or P, N) form. There are no specific data which would provide an answer to the question concerning the reason for the formation of only one geometrical isomer: either by the involvement in the reaction of only the *trans*-enolic form of the phosphorylated aldehyde or by the capacity of the *cis*-form of the corresponding derivative to isomerise readily under the reaction conditions to the energetically more favourable *trans*-form.

The extension of the familiar reactions of partial phosphorus(III) acid esters with aldehydes and ketones [90] to phosphorylated aldehydes leads to new possibilities in the synthesis of substituted ethylenediphosphonates [13,20]:

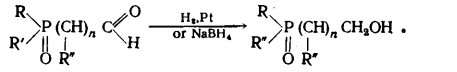


The reaction in the presence of a tertiary amine [13] or directly with dicyclohexyl phosphite salt [20] proceeds vigorously and reaches completion rapidly. On this basis, one may conclude that the aldehyde groups influenced by the electron-accepting phosphorus-containing substituent exhibit a fairly high electrophilic activity.

Phosphorylated aldehydes are oxidised by peracids [91] or by alkaline potassium permanganate [92] to the corresponding phosphorylated carboxylic acids:



The reduction of phosphorylated aldehydes over a platinum catalyst [27] or by sodium borohydride [93] leads to the corresponding hydroxy-derivatives in fairly high yields:



β-Aminoethylphosphonate has been obtained by the reduction of phosphonoacetaldehyde oxime in acetic anhydride [92].

Thus the data described show that the oxidation and reduction reactions of phosphorylated aldehydes and their derivatives can be used for preparative syntheses of organophosphorus compounds with functional groups.

The capacity of phosphorylated acroleins to undergo the Diels–Alder reaction [46,47] was mentioned above. The absence of a similar reaction involving phosphonomethacrolein has been explained [48] by the increased steric hindrance and by the electron-donating properties of the methyl groups, which reduce the electrophilicity of the C=C bond.

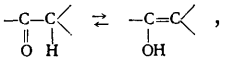
The diethylacetal of diethoxyphosphonoacetaldehyde has been used to synthesis olefins (via phosphonate carbanions). This acetal has been used successfully to synthesise cinnamaldehyde from benzaldehyde [94], but it did not react with steroid ketones [95].

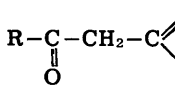
It has been noted [92] that, in an acid medium at an elevated temperature (90°C), phosphonoacetaldehyde decomposes with formation of acetaldehyde and inorganic phosphate. Possibly this constitutes one of the explanations of our earlier observation [2] that in the hydrolysis of phosphorylated acetals a high yield of aldehyde is achieved when volatile products and the excess volatile acid are removed from the hydrolysis product *in vacuo* before distillation. The high sensitivity of phosphorylated aldehydes to acids was also pointed out by Tavs [13]. On the other hand, a considerable excess of acid has been employed in many studies [19,20,23] involving the hydrolysis of phosphorylated enolic ethers without a significant decrease of the yield of the phosphorylated aldehyde.

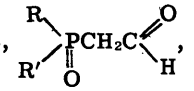
It follows from the data discussed that the properties characteristic of the aldehyde group are largely retained in phosphorylated aldehydes. This suggests that in future all the potentialities of the aldehyde group will be widely employed in organophosphorus synthesis.

IV. THE KETO–ENOL TAUTOMERISM OF PHOSPHORYLATED ALDEHYDES

The keto–enol tautomerism, involving the characteristic irreversible interconversion



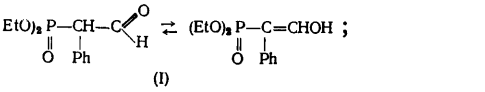
is very common and has been thoroughly investigated in organic chemistry. Mainly substances with two carbonyl groups separated by a methylene link were investigated in this field: β-diketones and β-ketoacid and malonic acid esters (β-dicarbonyl compounds) [96]. β-Ketoaldehydes with an unsubstituted methylene group, , have not been investigated in this connection in view of their low stability [97]. There are only isolated data [98,99] showing a somewhat higher stability of their keto-enol form. For further investigation of such tautomerism, it was of great interest to study other chemical series with structures close to that of β-ketoaldehydes.

Phosphorylated aldehydes are one such class of compounds. These include primarily phosphorus analogues of β-dicarbonyl compounds, , in which the C=O group has been replaced by the P=O group. The considerable similarity between the structures and properties of the two classes of compounds has been established for a long time and has been the subject of numerous investigations [32,100–102].

On the basis of these considerations, it was to be expected that α-phosphorylated aldehydes should exhibit keto–enol tautomerism. Presumably, apart from the principal external and structural factors determining the tautomeric equilibrium of β-dicarbonyl compounds, the P=O group also plays a significant role in phosphorylated aldehydes. It can exert an influence via the formation of hydrogen-bonded complexes with the hydrogen atom of the OH group of the enolic forms (which are more stable than in the case of the C=O group [103]) and via the involvement of the 3*d* orbitals of phosphorus in conjugation with the double bond of the enolic forms. Moreover, one cannot fail to

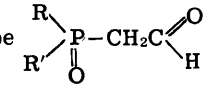
take into account the possible steric factors due to the larger bulk of the P=O group compared with that of the C=O group.

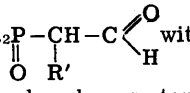
Indeed, in 1960 Tammelin and Fagalind [27] described the tautomeric properties of 2-diethoxyphosphonyl-2-phenylacetaldehyde (I), which they obtained,



(I)

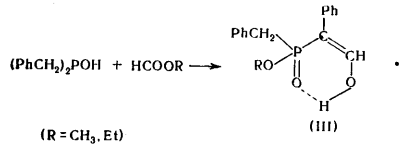
they resemble those of ethyl phenylformylacetate (II). Comparison of the infrared spectra and the dissociation constants of compounds (I) and (II) and also the spectrophotometric determination [on the basis of the colour of the complex with iron(III) chloride] of the keto–enol equilibrium constant and the rate of enolisation of compound (I) led the authors [104] to the conclusion that compounds (I) and (II) exist only in the keto- and *cis*-enolic forms in carbon tetrachloride and isopropyl alcohol solutions and that the *trans*-form is absent from such solutions. The infrared spectra of compound (I) showed the absorption bands of the OH group involved in an intramolecular hydrogen bond. At the same time the vibration frequency of the P=O group was displaced towards longer wavelengths, which indicated the formation of a hydrogen bond between them, while the enolisation of the phosphoryl group was not observed. The dissociation constants of compounds (I) and (II) were found to be very similar (pK_a = 7.09 and 7.21 respectively).

In subsequent studies dealing with the keto–enol tautomerism of α-phosphorylated aldehydes, two main trends were established. On the one hand, aldehydes without a second substituent at the α-carbon atom of the type  were investigated and the influence of substituents at the phosphorus atom on the position of the keto–enol equilibrium was elucidated. These investigations make it possible to estimate the intrinsic effect of the  groups, since in these cases it is not masked by the superposition of any other effect of substituents in the methylene group.

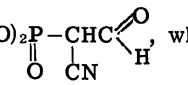
On the other hand, a study was made of the effect of substituents at the carbon atom in α-substituted aldehydes of the type  with retention of the same groups at the phosphorus atom. The substituents R′ were chosen mainly so that they could enter into conjugation with the π-electrons of the double bonds of the enols. At the same time, the introduction of the α-substituent can alter the molecular geometry, hindering the reverse transition into the keto-form, and hence can increase the general tendency towards enolisation. With this aim in view, groups possessing a considerable resonance component σ_R (CN, CH_3CO, COOR), together with a high negative inductive effect ($-I$), were employed as substituents in the first place. They make it possible to shift the equilibrium almost completely towards the enolic form. Next, substituents with lower values of σ^* (C_6H_5, Cl, Br) were introduced, and finally substituents exhibiting a positive inductive effect. In all these cases, the equilibrium was displaced towards the enolic form. The fact that substituents with opposite inductive effects (halogens [29] and alkyl groups [21]) caused an unambiguous shift of the equilibrium towards the enol cannot as yet be satisfactorily accounted for without additional investigations.

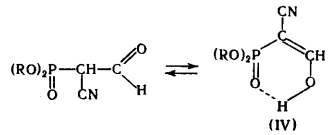
Thus, in studies of the second type, a decisive influence is attributed to the nature of the substituents at the α-carbon atom. The phosphoryl group influences the nature of the enolisation reaction (*cis*–*trans*-enolisation) and causes a slight shift of the equilibria. Naturally, particular investigations cannot always be definitely assigned to a particular type, since the data accumulated suggest quite clearly that the effect of the substituents at both the α-carbon atom and at the phosphorus atom is fairly important. In view of these findings, in later studies investigators attempted to take into account the overall effect of all the substituents present in the molecule. Chronologically, it is more convenient to consider initially the keto–enol tautomerism of substituted phosphorylated acetaldehydes.

In a further development of studies mentioned above [27,104], Arbuzov and coworkers [31] attempted to synthesise phosphorus-containing dialdehydes. However, they isolated alkoxybenzylphosphinylphenylacetaldehydes in the crystalline enolic forms (III) with stable cisoid configurations, which are sparingly soluble in organic solvents:



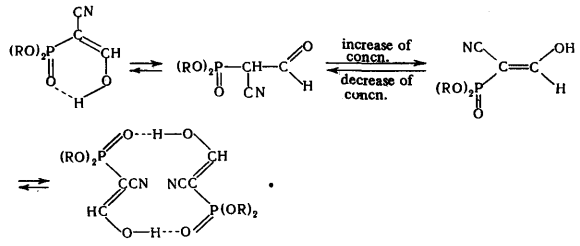
(III)

Kirilov and Petrov [28] investigated the tautomerisms of cyanoaldehydes of the type , where R = C_2H_5, n-C_3H_7, or n-C_4H_9, by infrared spectroscopy and by titration. However, the classical bromometric method proved to be unsuitable in view of the sensitivity of the aldehyde groups to bromine. A method involving the acidimetric titration of aqueous solutions of aldehydes with 0.01 M NaOH revealed the presence of up to 98% of the enolic form. On the basis of the literature data and the frequency shift of the OH and P=O groups in the infrared spectra, the authors suggest that a cisoid structure (IV) with an intramolecular hydrogen bond is characteristic of the enolic form and they explain the high stability of this bond by the considerable polarity of the P=O group:



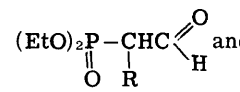
(IV)

The study of the infrared spectra of solutions of the aldehydes in carbon tetrachloride (at concentrations of 0.4 and 3.63%) led to the hypothesis that new enolic forms, namely the dimeric forms (V) and polymeric forms with an intermolecular hydrogen bond and involving *trans*-enols, appear in more concentrated solutions:

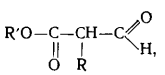


The dimeric structure is thought to be confirmed by the characteristic increase of the intensity of the absorption bands associated with the deformation vibrations of the bound OH group, with the concentration of the solution.

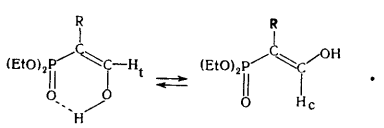
In a series of interesting studies, Kabachnik, Ioffe, and others [26,29,30,105-109] investigated by ^{1}H NMR the enolisation of α-substituted diethoxyphosphonoacetaldehydes



and compared it with the tendency towards enolisation in the corresponding substituted formylacetic esters:

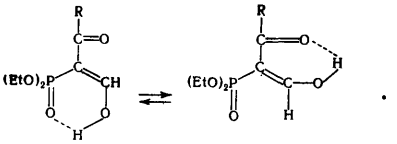


where R = CN, COOEt,[26] Ph, Cl, Br, or CH_3CO.[29] Particular attention was devoted to the elucidation of the nature of the hydrogen bonds. One should bear in mind that, owing to the lower thermodynamic stability of the *trans*-enolic form compared with the *cis*-enolic form [110], the *trans*-enolisation of open-chain formyl derivatives takes place extremely rarely and only under conditions such that structural factors or the solvent cause an additional stabilisation of the *trans*-form. One should also mention that hitherto there have been no reliably established instances of the *trans*-enolisation of open-chain β-dicarbonyl compounds with the exception of a small number of formyl derivatives [111,112]. The assignment of the tautomeric enolic forms to the *cis*-(VI) or *trans*-series (VII) was based on the vinyl proton signals in the ^{1}H NMR spectra. Integration of the signals made it possible to estimate the contents of the *cis*- and *trans*-isomers of the enolic forms relative to the P=O and OH groups:



cis (VI) *trans* (VII)

In addition, in acetyl- and ethoxycarbonyl derivatives there is a possibility of competition between two *cis*-enolic forms with chelation in different directions. Thus an intramolecular hydrogen bond can be formed with both C=O [formula (VIII)] and P=O groups [formula (IX)]:



P-*cis* (VIII) C-*cis* (VIII)

(R = CH_3, OEt)

The results of the investigations showed that, in the case of the ethoxycarbonyl derivative, the P-*cis*-form (VIII) is mainly involved in the equilibrium owing to the higher basicity of the P=O group compared with that of the carbonyl group. On the other hand, in the acetyl derivative the C-*cis*-form is dominant, probably due to the opposite changes in the basicities of the P=O and C=O groups. This enabled the authors to arrange the hydrogen bond acceptors in the following series in terms of their capacity for chelate-formation with the hydroxy-methylene group:

$$CH_3CO > (EtO)_2P(O) > COOEt$$

Determination of the proportions of the tautomeric forms in solvents of different polarities (carbon tetrachloride, dioxan, acetonitrile, and nitromethane) showed that, in solutions of phosphonic and carboxylic acids containing the CN, CH_3CO, and COOEt groups as α-substituents, the keto-form is absent (Table 1). This finding is probably related to the high acidity of the CH protons (Table 2) due to the appreciable inductive and mesomeric effect of the α-substituents.

According to the authors, the capacity for *trans*-enolisation is determined not so much by the steric effects as by the polar effects of the α-substituents. Thus, in acetonitrile esters containing chlorine and bromine exist in the *trans*-enolic and keto-forms but not in the *cis*-form. This phenomenon has been attributed to the inductive effect of the halogen atoms. The latter decrease the basicity of the P=O and C=O groups and reduce the energy of the hydrogen bond with a corresponding destabilisation of the pseudoaromatic ring of the *cis*-enolic form. On the other hand, in both acetonitrile and nitromethane the enolisation of carboxylic and phosphonic acids is similar, while in

Table 1. The content of the different forms (%) in solutions of diethyl formylmethylphosphonates and formylacetic esters [29].

R	RCH(CHO)COOEt									RCH(CHO)P(O)(OEt)$_2$								
	solvent									solvent								
	CCl_4			dioxan			CH_3CN			CCl_4			dioxan			CH_3CN		
	C	T	K	C	T	K	C	T	K	C	T	K	C	T	K	C	T	K
Ph	95	—	5*	92	—	8	90	—	10	85	—	15	95	—	5	93	—	7	89	—	11	85	—	15
Cl	10	80	10	16	70	14	—	80	20	—	75	25	—	82	18	—	73	27	—	67	33	—	62	38
Br	—	—	—	—	90	10	—	86	14	—	84	16	—	70	30	—	57	43	—	50	50	—	45	55
CN	—	—	—	60	40	—	52	48	—	16	84	—	46	54	—	37	63	—	31	69	—	14	86	—
CH_3CO	67	33	—	67	33	—	75	25	—	—	—	—	50	50	—	50	50	—	70	30	—	80	20	—
COOEt	100	—	—	—	—	—	—	—	—	—	—	—	81	19	—	84	16	—	74	26	—	73	27	—

C = *cis*-, T = *trans*-, K = keto.

*In $CDCl_3$.

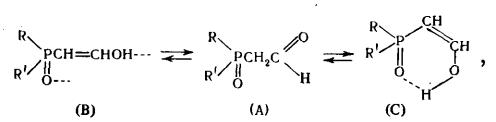
carbon tetrachloride and in dioxan differences are observed. For example, all three forms of chloroformylacetic ester are present in equilibrium, while the *cis*-enolic form of its phosphonic analogue is absent. Moreover, it has been shown that the *trans*-enolic form which predominates in the equilibrium is stabilised by intermolecular hydrogen bonds. In order to find the degree of association of the molecules, their molecular weights in benzene, dioxan, and acetonitrile were determined. It was discovered that carboxylic acid derivatives are monomeric, while phosphonic acid derivatives are associated in benzene but are converted into monomers during ebullioscopic determinations in acetonitrile. In the latter case, intermolecular hydrogen bonds are ruptured at the boiling point of the solvent. The results provide additional evidence in support of the above hypothesis concerning the intermolecular association of the enolic forms in solution, which stabilises them. The observations are also supported by infrared spectroscopic data [108].

Table 2. The pK_a values in water at 20°C. [29,109]

Compound	pK_a	Compound	pK_a
PhCH (CHO) COOEt	7.09	NCCH (CHO) COOEt	2.04
PhCH (CHO) P (O) $(OEt)_2$	7.21	NCCH (CHO) P (O) $(OEt)_2$	2.00
ClCH (CHO) COOEt	6.30	EtOOCCH (CHO) P (O) $(OEt)_2$	4.09
ClCH (CHO) P (O) $(OEt)_2$	6.11	CH_3COCH (CHO) P (O) $(OEt)_2$	3.68
BrCH (CHO) P (O) $(OEt)_2$	6.14	EtOOCCH (CHO) P (O) n-Bu_2	6.40

To confirm the dependence of the nature of the enolisation on the basicity of the C=O and P=O groups, a study was made [30] of the compounds n-Bu_2P(O)CH(R)CHO (R = COOEt or $COCH_3$). In contrast to the diethoxyphosphono-derivatives with the general formula $(EtO)_2$P(O)CH(R)CHO discussed previously, in the present case the enolic forms present in the equilibrium solution in acetonitrile have only the *cis*-configuration. They are stabilised by an intramolecular hydrogen bond, since the n-Bu_2P(O) group becomes a more basic chelating centre. It is extremely difficult to generalise these results and to find general relations governing the enolisation of phosphonoacetaldehydes, since in this case the overall effects of the α-substituents and the R(R′)P(O) groups operates. A characteristic pattern may be observed for each substituent and one of the above effects may become of primary importance if it is sufficiently powerful, as can be seen from halogeno- and cyano-derivatives. On the other hand, the interaction of all the effects enumerated creates different nuances in the type of enolisation which is a highly refined phenomenon [109].

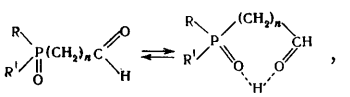
Therefore the study of unsubstituted phosphorylated aldehydes, where the complicating effect of α-substituents is removed and it is possible to follow the effect of the R(R′)P(O) group alone, is of special interest. The keto–enol tautomerism of unsubstituted phosphorylated aldehydes has been studied in a number of investigations [6-8,113-115]. In their approach to the solution of the problem of the relative amounts of tautomers in aldehydes of different classes of organophosphorus compounds (phosphonates, phosphinates, and phosphine oxides), Razumov and coworkers employed infrared, ^{1}H NMR, and ^{31}P NMR spectroscopic methods and to some extent polarography [6-8,113-115]. The following keto–enol equilibrium is observed in series of unsubstituted phosphorylated aldehydes:



(B) (A) (C)

where R = OAlk, C_2H_5, C_3H_5, or C_6H_5 and R′ = OAlk, C_2H_5, or C_6H_5.

Apart from the usual external factors (medium, temperature, and concentration), the equilibrium depends directly on the nature of the R(R′)P(O) group. In polarographic studies of the behaviour of phosphorylated acetaldehydes and propionaldehydes in neutral, alkaline, and acid aqueous solutions, it was found in the first place that their polarographic activity is due to the aldehyde group and not the phosphoryl group, since the latter is not reduced at the dropping mercury electrode. It was discovered that in a neutral aqueous medium aldehydes exist in the keto-form in equilibrium with the hydrated form:



where R = C_2H_5, C_6H_5, p-ClC_6H_4, p-$CH_3C_6H_4$, or OC_2H_5 and R′ = OC_2H_5.

The polarographically active form amounts to 11–12% for phosphinylacetaldehydes and 20–22% for phosphinylpropionaldehydes. In acid solutions, the equilibrium is displaced towards the enol and in alkaline solutions the enolic form is not detected, since it probably exists in the form of a polarographically non-reducible anion. A study was also made of the influence of the group R on the capacity of the aldehyde group to be hydrated and on the tendency towards enolisation. In phosphinylacetaldehydes, the effect is shown to a much greater extent than in phosphinylpropionaldehydes, but the effect is of the same type [113,114].

The employment of infrared and NMR spectroscopic methods in the study of the keto–enol equilibrium led to the discovery of many interesting relations governing the processes. Experiments were performed for many compounds of the series mentioned above. In each series ethoxy- and isopropoxy-groups were always present, which made it possible to follow the effect of only one substituent at the phosphorus atom. The study of the dependence of the position of the keto–enol equilibrium on the nature of the substituent showed that it is determined mainly by the basicity of the P=O group, which limits its capacity to form hydrogen bonds stabilising the enolic forms, and to a lesser extent by steric factors.

The basicity of the P=O group as a function of the nature of the substituent can be assessed from the chemical shifts $\delta^{31}P$ of the phosphorus nuclei, the energy of the π bond, and the shifts of the OH frequencies of the enolic forms in the infrared spectra. The latter also make it possible to establish that the acidity of the enolic forms is constant ($pK_a = 7.5 \pm 0.03$)‡ within the limits of the accuracy with which $\Delta\nu$(OH) is measured for the series investigated. The authors observed that, with increase of the basicity of the P=O group and the consequent increase of the hydrogen bond energy, there is a successive shift of the position of the keto–enol equilibrium towards the enol (Table 3). The aldehydes investigated can be arranged in the following sequence in terms of increasing amounts of the enolic form:

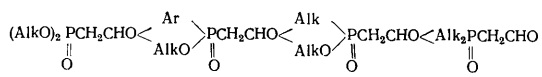
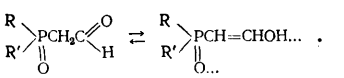


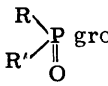
Table 3. The keto–enol equilibrium constants, free energies, π-bond energies, hydroxy-group frequency shifts, and the chemical shifts of the phosphorus nuclei of phosphorylated acetaldehydes[8]:

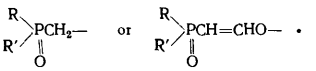


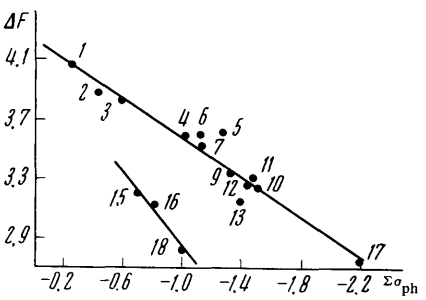
No.	R	R′	10^3K_e	ΔF	E_π, kcal mole^{-1}	$\Delta\nu$(OH) cm^{-1}	10^3K_e CCl$_4$ 0.2 M	CCl$_4$ 0.05 M	dioxan 0.1 M	hexane 0.1 M	δ^{31}P, p.p.m.
1	CH_3O	CH_3O	1.09	4.09	67.3	220					
2	EtO	C_2H_5O	1.475	3.88	66.9	260	1.06	0.117			−20
3	*i*-C_3H_7O	*i*-C_3H_7O	1.585	3.84	66.2	270	1.15	—			−18
4	C_3H_5	EtO	2.41	3.59	63.9	340	1.91	—			−44
5	C_3H_5	*n*-C_4H_9O	2.28	3.63	64.0	340	1.54	0.07	0.1	1.91	−43
6	C_3H_5	*i*-C_4H_9O	2.20	3.64	63.78	—	1.33	0.03	0.04	—	—
7	C_3H_5	*i*-C_5H_7O	2.75	3.52	63.8	350	2.22	—			−40
8	C_3H_5	s-C_4H_9O	3.14	3.46	63.7	360	1.75	0.12	0.05	1.93	—
9	Et	EtO	3.61	3.36	62.2	385	2.10[2]	0.132			−49
10	Et	*n*-C_4H_9O	4.01	3.28	62.2	390	1.02	—	0.29	1.90	−49.5
11	Et	*n*-C_5H_7O	4.34	3.26	62.2	390	2.39	0.147			−48.5
12	Et	*i*-C_4H_9O	4.23	3.24	61.7	393	2.42	1.82	1.03	2.86	−47.7
13	Et	*i*-C_5H_7O	5.15	3.15	61.6	397	2.98	0.197			−47.5
14	Et	s-C_4H_9O	6.36	3.02	59.9	430	4.91	3.81	0.83	2.16	−46
15	Ph	EtO	4.52	3.21	65.2	300	3.38				−34
16	Ph	*i*-C_5H_7O	5.46	3.12	64.2	320	3.31				−32
17	Et	Et	12.34	2.74	56.3	470					
18	Ph	Ph	8.9	2.82	57.5	420					

Table 3 shows that the keto–enol equilibrium constant, the basicity of the P=O group, and the charge on the phosphorus atom increase and the free energy and the π-bond energy decrease with increase of the positive inductive effect of the substituents and with decrease of the $p\pi$–$d\pi$ conjugation of the phosphorus atom with the surrounding atoms. The experimental ΔF are satisfactorily correlated with Kabachnik's constants for the substituents[116] (Fig. 1), i.e. the keto–enol equilibrium constant is directly related to the basicity of the P=O group and thereby demonstrates unambiguously the role of the latter as the decisive factor in this equilibrium.

‡ pK_a was determined from the $\Delta\nu$(OH) shift in triethylamine.

It follows from the foregoing that the transmission of the influence of the  group takes place via a hydrogen-bonded complex and not via the system





Variation of ΔF with $\Sigma\sigma_{ph}$ after Kabachnik; the numbers of the points in the graph correspond to the numbers of the compound in Table 3.

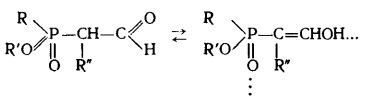
Structures with intramolecular (*cis*-) and intermolecular (*trans*-) hydrogen bonds (structures B and C) are characteristic of the enolic forms of phosphorylated acetaldehydes. The study of the nature of the hydrogen bonds by infrared spectroscopy showed that the undiluted compounds have structures with both configurations (B and C). For all the aldehydes investigated and the substances with the isopropoxy-group, the intramolecular hydrogen bond is stronger and the equilibrium constant is higher than for ethoxy derivatives. These findings can probably be accounted for not only by the higher basicity of the P=O group in the former compounds but also by the steric effect of the isopropoxy-residue, which leads to the proximity of the P=O and OH groups in the *cis*-positions of the enolic form (which can be seen also from the Stuart–Briegleb models).

To elucidate the type of enolisation of aldehydes, a study was made of their behaviour both in solvents with different polarities and basicities and as a function of temperature. Interesting observations were made. In non-polar solvents (carbon tetrachloride, dioxan, and hexane; in the last solvent only the aldehydes with high molecular weights are soluble), the equilibrium is displaced towards the keto-form, i.e. in a direction opposite to that for β-dicarbonyl compounds and phosphorylated ketones. Examination of the concentration variation in carbon tetrachloride (0.5, 0.05, and 0.005 M solutions) indicated a stabilisation of the enolic forms mainly by intermolecular association. On the other hand, in solutions the intermolecular hydrogen bonds present in the undiluted compounds and in more concentrated solutions are ruptured. Hence the presence of only one keto-form in 0.005 M solutions (Table 3, compounds 3, 4, 7, 10, 15, and 16) and of an insignificant amount of the *cis*-enolic form in certain cases become understandable.

When aldehydes are dissolved in a highly basic solvent (triethylamine), the situation changes. Here the equilibrium is displaced in the opposite direction—towards the enol with formation of a chelated structure involving powerful hydrogen bonds.

The study of the temperature variation of the keto–enol equilibrium showed that a change in temperature has a significant influence on the relative amounts of the forms [115]. With increase of temperature from 11° to 100°C, there is initially a transition from the *trans*-enol to the keto-form. This shift of the equilibrium is accompanied by a decrease of the content of the *trans*-enolic form and takes place up to temperatures in the range 50–75°C depending on the nature of the substituent at the phosphorus atom. A further increase of temperature to 95–100°C causes a shift towards the *cis*-enolic form.

Table 4. Keto–enol equilibrium constants, enthalpies, and entropies of phosphorylated aldehydes [115]:



R	R′	R″	$10^{-3}K_1$ temperature, °C							ΔH	ΔS	10^2K_2 (*cis* ⇌ *trans*) at 25°C
			11	25	35	50	60	75	95			
Et	EtO	H	—	3.50	—	2.51	—	2.97	4.65	9.06	19.1	1.26
Et	n-C_8H_7O	H	6.36	5.02	4.30	3.68	3.60	3.85	6.02	8.88	19.2	1.22
Et	s-BuO	H	10.6	7.78	6.20	4.48	4.32	3.63	5.04	9.72	23.0	0.96
Ph	EtO	H	5.44	4.71	4.45	3 97	3.86	3.88	4.21	7.84	13.7	—
C_6H_5	EtO	H	3.47	2.77	2.40	1.95	1.87	1.78	2.48	9.16	18.9	—
EtO	EtO	H	2.33	1.74	1.6	1.5	1.72	2.06	3.2	8.84	17.5	2.78
EtO	EtO	CH_3	100	3.33	—	15.1	14.0	7.78	5.16	10.92	29.8	—
EtO	EtO	Et	31.7	16.0	—	11.8	6.2	4.27	2.5	10.95	28.5	—

The study of the concentration and temperature variation of phosphorylated aldehydes containing an alkyl substituent in the methylene unit, $(C_2H_5O)_2P(O)CHRCHO$ ($R = CH_3$ or C_2H_5), showed that their enolisation has other characteristics (Table 4). Then, whereas in the undiluted state at 20°C they exist in the keto- and *trans*-enolic form (33 and 67% respectively for $R = CH_3$ and 25 and 75% respectively for $R = C_2H_5$), on dilution with carbon tetrachloride (0.05 and 0.005 M solutions) as well as on raising the temperature to 100°C, they are converted from the *trans*-enolic form into the keto-form alone (75 and 25% for $R = CH_3$ and 80 and 20% for $R = C_2H_5$).

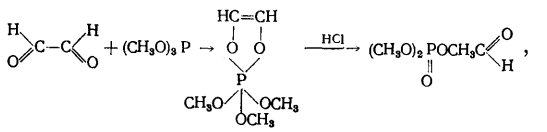
Thus the study of the tautomerism of phosphorylated aldehydes has led to the discovery of definite characteristics in their behaviour, which distinguish them from β-dicarbonyl compounds. These are as follows: firstly, α-phosphorylated aldehydes unsubstituted in the methylene group are stable keto–enol systems whose keto–enol equilibrium may be investigated; secondly, phosphorylated aldehydes are some of the few open-chain compounds capable of both *cis*- and *trans*-enolisation.

ADDENDUM

To make the review complete, mention must be made of a number of studies published recently when the manuscript of the review was with the editors. In addition to studies on the interaction of phosphorus(III) acid esters with the acetals of halogenoaldehydes, considered at the beginning of the review, Reichel and Jahns [117] examined the interaction of triethyl phosphite with the acetal of α-bromopropionaldehyde followed by hydrolysis of the Arbuzov reaction product to α-phosphonopropionaldehyde. In a continuation of the study reported previously [63], Reichel and Jahns [117] carried out a detailed synthesis of an aldehyde with a phosphonium structure.

Continuing their earlier investigations [54,55], Gross and Costisella [118] obtained data for the reactivities of phosphonoformals.

In addition to the earlier study by Ramirez et al. [119], who described the synthesis of aldophosphates according to the scheme



Kraus and Stürtz [120] extended the range of α-aldophosphates obtained by the method described above [57].

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