THE CHEMISTRY AND PROPERTIES OF ENOL PHOSPHATES

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I. INTRODUCTION

In 1934 Meyerhof and Lohmann (295), while investigating the enzymatic conversion of D-glyceric acid-3-phosphate to pyruvate and orthophosphate, observed the formation of a hitherto unknown organic phosphate. They succeeded in isolating the new intermediary compound and established its constitution as that of phosphoenol pyruvate (PEP). Thus, PEP represents the last phosphorylated three-carbon-atom compound, both in glycolysis and in fermentation, and also seems to play a role in the fixation of carbon dioxide (164).

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In view of the biochemical interest in PEP a convenient method of preparation was sought, since its isolation from biological material was rather difficult. However, despite the apparent simplicity of the molecule, the development of an efficient synthesis has been proved to be a difficult problem.

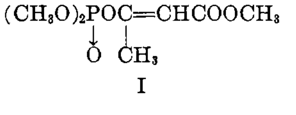
The first synthesis was accomplished by Kiessling (245, 246) by the action of pyruvic acid with phosphorus oxychloride (see page 620), and this procedure was the basis of improved techniques described more recently (322, 373, 374). However, the yields did not exceed 9 per cent. Another procedure, developed by Baer and Fischer (see page 618), was the dehydrohalogenation of a phosphoryl-β-chlorolactate, affording PEP in 10 per cent yield (63, 65).

Owing to these difficulties in the preparation of PEP, no other enol phosphates had been synthesized until about 1950. However, after Schrader's work during World War II became known, establishing that certain organophosphorus compounds were very potent insecticides, the interest in organophosphates developed tremendously. In the search for insecticides with better properties, several entirely new methods for the preparation of enol phosphates were discovered, leading not only to other syntheses of PEP but also to a large number of related enol phosphates.

It is the purpose of this review to describe these newly developed methods of preparing enol phosphates, covering the literature reported in *Chemical Abstracts* through 1960 and the more recent publications available to the author. The patent literature has been extensively searched, but only adequately characterized enol phosphates were considered in this review.

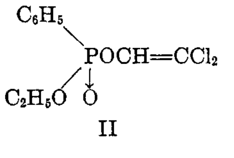
Nomenclature

The nomenclature used in this review is, in general, that established by the Committee on Nomenclature of the American Chemical Society (23). The name "enol phosphate" is used only as a generic name for vinyl esters of phosphoric acid (vinyl phosphates). Compounds substituted at the ethylenic double bond are named in the usual manner, numbering the carbon atom of the vinyl group attached to the phosphoryl moiety as 1. For example, compound I would be dimethyl 2-carbomethoxy-1-methylvinyl phosphate, although such names as dimethyl 1-carbomethoxy-1-propen-2-yl phosphate, methyl 3-(*O,O*-dimethylphosphoryloxy)-2-butenoate, and methyl 3-(dimethoxyphosphinyloxy)crotonate have also been used in the literature. A phosphonate such as II is named *O*-ethyl *O*-2,2-dichlorovinyl phenylphosphonate.



$$(CH_3O)_2\underset{\overset{\downarrow}{O}}{P}O\underset{\overset{|}{CH_3}}{C}{=}CHCOOCH_3$$

I



$$\overset{C_6H_5}{}\underset{\overset{\downarrow}{O}}{\overset{}{P}}OCH{=}CCl_2 \quad (C_6H_5)(C_2H_5O)P(O)OCH{=}CCl_2$$

II

II. Preparation of Enol Phosphates

A. THE PERKOW REACTION

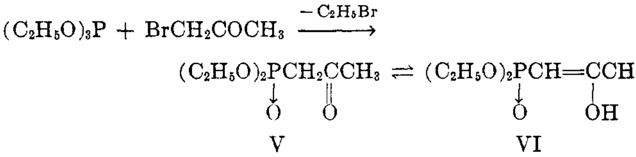
1. Historical development

A wide variety of organophosphorus compounds have been prepared by the Michaelis–Arbuzov reaction since it was first reported at the turn of the century (25–27, 296, 297), and the considerable body of experience which has accumulated since then has developed confidence in the normal course of the reaction (256, 257).

The mechanism of the reaction leading to the formation of a new carbon–phosphorus bond involves a nucleophilic attack by the phosphorus atom on the α-carbon of the alkyl halide, to give an intermediary trialkoxylalkylphosphonium halide (III), which decomposes by an S_N2 reaction to give a dialkyl alkylphosphonate (IV) and an alkyl halide (7, 39, 40, 43, 173, 186, 340). This reaction is not limited to alkyl halides.

$$(RO)_3P + R'X \rightarrow \underset{\text{III}}{[(RO)_3\overset{+}{P}R']X^-} \rightarrow \underset{\text{IV}}{(RO)_2P(O)R'} + RX$$

Aromatic and aliphatic acid chlorides were also found to undergo the Michaelis–Arbuzov reaction with formation of the corresponding phosphonates (256, 257). Several investigators have attempted to use α-halo aldehydes (29, 104, 105, 110, 112, 113, 266), α-halo ketones (35, 41, 44, 108, 137, 357), and α-halo esters (33, 34, 103, 107, 113, 182, 183, 205, 236, 254, 318, 339, 369) in the Michaelis–Arbuzov reaction. In all cases mentioned the products had been assumed to be phosphonates of the type expected from a normal course of the Michaelis–Arbuzov reaction. Only in the reaction of certain α-halo ketones with trialkyl phosphites have two reaction products been reported. In 1934 A. E. Arbuzov and Razumov found that diethyl benzoylmethylphosphonate, formed by the action of triethyl phosphite on ω-bromoacetophenone, had an unusually wide boiling range (35). From triethyl phosphite and bromoacetone Razumov and Petrov (357) obtained two isomeric products which analyzed for diethyl 2-oxopropylphosphonate (V), but which differed considerably in their physical properties. They concluded, from analogy to acetoacetates, that these substances were tautomeric forms of the phosphonate (V and VI).



$$(C_2H_5O)_3P + BrCH_2COCH_3 \xrightarrow{-C_2H_5Br} (C_2H_5O)_2\underset{\overset{\downarrow}{O}}{P}CH_2\underset{\overset{\|}{O}}{C}CH_3 \rightleftharpoons (C_2H_5O)_2\underset{\overset{\downarrow}{O}}{P}CH{=}\underset{\overset{|}{OH}}{C}CH_3$$

V VI

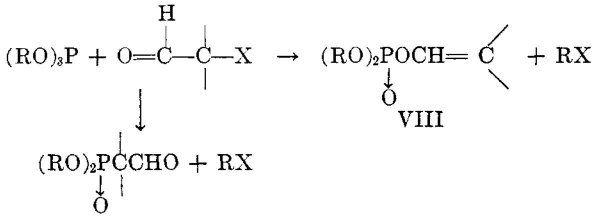
A study of the reaction between triethyl phosphite and α- and γ-bromoacetoacetates revealed that the phosphonates formed had very extended boiling ranges (41). In an attempt to investigate the assumed keto–

enol tautomerism of these compounds, numerous 2-oxoalkylphosphonates were synthesized from triethyl phosphite and α-bromo ketones (44), and the amount of enol was determined by the bromine titration method (45, 47). The results, however, did not support the presence of enol forms, since, for example, diethyl 1,1-dimethyl-2-oxopropylphosphonate (VII), in which enolization is unlikely, had an "enol content" of 23 per cent according to the consumption of bromine.

$$(C_2H_5O)_2P(O)C(CH_3)_2COCH_3$$

VII

These contradictory results could be understood when in 1952 Perkow (335) discovered that α-halo aldehydes did not react with trialkyl phosphites according to the Michaelis–Arbuzov reaction, although this had been repeatedly reported (29, 104, 105, 112, 113, 266), but that a new type of rearrangement occurred, yielding dialkyl vinyl phosphates (VIII) isomeric with the phosphonates (IX).



$$(RO)_3P + O{=}\overset{H}{\overset{|}{C}}{-}\underset{|}{\overset{|}{C}}{-}X \rightarrow (RO)_2\underset{\underset{O}{\downarrow}}{P}OCH{=}C\langle + RX$$

$$\downarrow$$

$$(RO)_2\underset{\underset{O}{\downarrow}}{P}\underset{|}{\overset{|}{C}}CHO + RX$$

VIII

IX

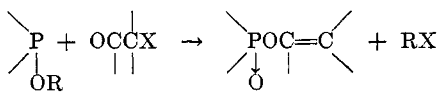
Concurrent work from other laboratories confirmed Perkow's discovery and showed that α-halo ketones and in some cases α-halo esters are also able to undergo this type of reaction. From 1955 on, the reaction has been studied extensively by many investigators, providing a considerable body of experimental material, which is the subject for the following discussion.

Several names have been used for this new type of reaction, such as "anomalous Arbuzov reaction" (341–352), "vinyl ester reaction" (18, 19), "Perkow rearrangement" (396, 397), "Perkow's synthesis" (70), and "Perkow reaction" (122, 123, 397). In this review, considering the priority of Perkow's publications, the name "Perkow reaction" is preferred. However, it should be mentioned that some of the work of the Shell Development Company concerning this reaction was done prior to 1950, as evidenced in a patent issued in 1960 (436).

2. Scope and limitations

(a) General conditions of the Perkow reaction

The most general formulation of this reaction may be given as follows:



$$\rangle\underset{OR}{\underset{|}{P}} + O\underset{|}{\overset{|}{C}}\underset{|}{C}X \rightarrow \rangle\underset{\underset{O}{\downarrow}}{P}O\underset{|}{C}{=}C\langle + RX$$

In this form the reaction proceeds with any derivative of trivalent phosphorus that carries at least one alkoxy group. The chief requirement of the structure of the organic halide is that the halogen atom must be attached to a carbon atom adjacent to an aldehyde, keto, or, in some cases, ester group.

The ease with which the reaction takes place is mainly dependent upon the nature of the α-halo carbonyl compound. The usual reactivity scale of I > Br > Cl applies to this reaction, as does an increase in the number of halogen atoms on the α-carbon atom. Generally, α-halo aldehydes are more reactive than α-halo ketones and α-halo esters.

The most reactive combinations of reactants take part in the reaction at room temperature, sometimes so violently that cooling and/or the use of a solvent as a moderator is necessary (e.g., in the reaction of triethyl phosphite with chloral, bromal, or 1,1,1-trichloroacetone). However, in most cases the reaction is carried out by mixing the reactants and warming the mixture to the required temperature, usually about 100–150°C.

The resulting products can be isolated in most cases by distillation *in vacuo* after stripping off the unreacted starting materials and the alkyl halide formed.

(b) Limitations of the Perkow reaction with respect to the α-halo carbonyl compound

(1) α-Halo aldehydes

Of the halogenated aldehydes which have been investigated, chloral and bromal reacted most readily with trialkyl phosphites (3, 15, 18, 70, 78, 157, 244, 299, 328, 333, 335, 380, 382, 387, 436, 454) and it was necessary to moderate the vigorous reaction by cooling or by using ether (70) or benzene (328, 335) as a solvent. The resulting dialkyl 2,2-dihalovinyl phosphates, isolated by distillation, were obtained in yields of 70–98 per cent (see table 25, page 635).

Dichloroaldehydes, e.g., dichloroacetaldehyde (18, 70, 72, 155, 258, 334) and 2,2,3-trichlorobutanal (18, 334), still reacted exothermically with trialkyl phosphites but less vigorously than chloral, whereas with α-chloroaldehydes, e.g., chloroacetaldehyde (18, 158, 435), the reaction temperature had to be raised to 110°C. in order to initiate the reaction.

The reactivity of α-halo aldehydes in the Perkow reaction thus decreases as the number of halogen atoms on the α-carbon atom decreases.

(2) α-Halo ketones

Whereas the Perkow reaction with various α-halo aldehydes was found to yield exclusively vinyl phosphates, the course of the reaction of trialkyl phosphites with α-halo ketones is not unequivocal. Both the Michaelis–Arbuzov reaction (formation of 2-oxoalkylphosphonates (X)) and the Perkow reaction (forma-

TABLE 1

Course of the reaction of trialkyl phosphites with haloacetones under different conditions

Trialkyl Phosphite	Haloacetone	Reaction Conditions	Ratio of Phosphonate (X)	Ratio of Vinyl phosphate (XI)	Total Yield of Reaction Products	Reference
			per cent	*per cent*	*per cent*	
$(CH_3O)_3P$	Bromoacetone	110–115°C.	44.5	55.5	71.0	(344)
	Chloroacetone	70–80°C.	5.3	94.7	70.5	(344)
		110–115°C.	16.5	83.5	80.0	(344)
$(C_2H_5O)_3P$	Iodoacetone	In ether	90.0	10.0	82.6	(344)
	Bromoacetone	In ether	19.9	80.1	66.3	(344)
		150–160°C.	80.0	20.0	81.8	(344)
		160°C.	70.0	30.0	80.0	(260)
	Chloroacetone	100–120°C.	6.1	93.9	60.0	(344)
		155–160°C.	11.9	88.1	75.6	(344)
		160–170°C.	14.0	86.0	89.0	(227)
$(C_4H_9O)_3P$	Bromoacetone	145–155°C.	64.7	35.3	71.6	(344)
	Chloroacetone	135–146°C.	13.7	86.3	61.0	(344)
$(iso\text{-}C_4H_9O)_3P$	Bromoacetone	150–155°C.	79.1	20.9	60.0	(344)
	Chloroacetone	115–125°C.	6.3	93.7	78.4	(344)
		150–160°C.	18.9	81.1	70.0	(344)

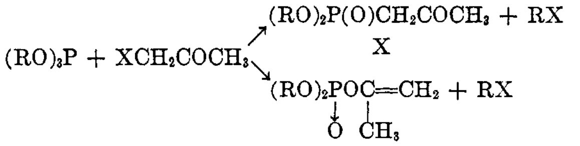
TABLE 2

Reaction of triethyl phosphite with ω-haloacetophenones (341)

Reaction of $(C_2H_5O)_3P$ with	Reaction Conditions	Ratio of Phosphonate (XIII)	Ratio of Vinyl phosphate (XII)	Total Yield
		per cent	*per cent*	*per cent*
ω-Chloroacetophenone	130–140°C.	—	100	90
ω-Bromoacetophenone	In ether	64	36	83
	150°C.	85	15	77.
ω-Iodoacetophenone	In ether	76	24	72

tion of vinyl phosphates (XI)) can take place. The nature and position of the halogen atom in the carbonyl compound and the temperature at which the experiment is carried out have a substantial effect on the course of the reaction.

This was well demonstrated by the results in the reactions of different trialkyl phosphites with chloro-, bromo-, and iodoacetones under varying conditions (table 1), yielding mixtures of *O,O*-dialkyl 2-oxopropylphosphonates (X) and dialkyl 1-methylvinyl phosphates (XI) (226, 260, 344).

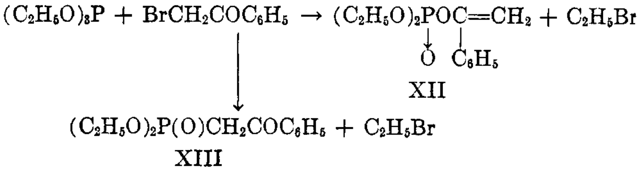


$$(RO)_3P + XCH_2COCH_3 \begin{array}{l} \nearrow (RO)_2P(O)CH_2COCH_3 + RX \\ \qquad\qquad X \\ \searrow (RO)_2\underset{\overset{\downarrow}{O}}{P}O\underset{\overset{|}{CH_3}}{C}{=}CH_2 + RX \end{array}$$

XI

As can be seen from table 1, the four trialkyl phosphites investigated gave the highest yields of vinyl phosphate (XI) when treated with chloroacetone at the lowest possible temperature at which the reaction would take place. Higher reaction temperatures increased the amount of the phosphonate (X), thus favoring the Michaelis–Arbuzov reaction. When bromoacetone was used as the halo component in the reaction, the amount of vinyl phosphate (XI) in the resulting mixture was greater, the lower the temperature was kept. With iodoacetone, however, the reaction products consisted predominantly of the phosphonate (X), even when the reaction was carried out at low temperature.

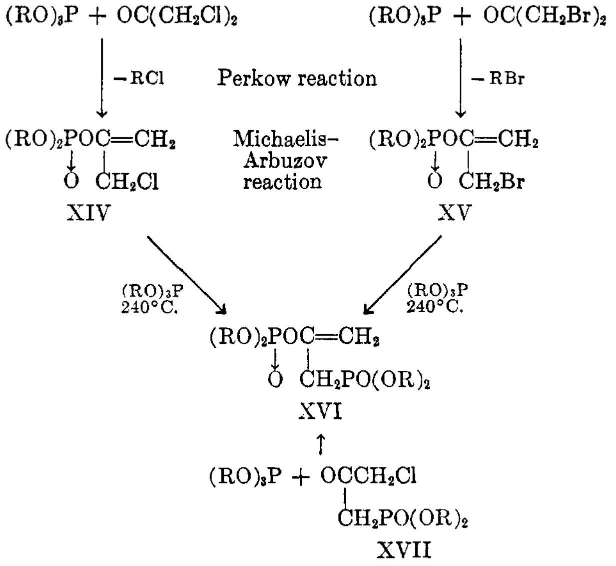
The same marked influence of the nature of the halogen and the temperature on the course of the reaction was observed in the reaction of triethyl phosphite with ω-chloro-, ω-bromo-, and ω-iodoacetophenones, as listed in table 2, yielding diethyl 1-phenylvinyl phosphate (XII) and *O,O*-diethyl benzoylmethylphosphonate (XIII) (341).



$$\begin{array}{l} (C_2H_5O)_3P + BrCH_2COC_6H_5 \rightarrow (C_2H_5O)_2\underset{\overset{\downarrow}{O}}{P}O\underset{\overset{|}{C_6H_5}}{C}{=}CH_2 + C_2H_5Br \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad \text{XII} \\ \qquad\quad \downarrow \\ (C_2H_5O)_2P(O)CH_2COC_6H_5 + C_2H_5Br \\ \qquad\quad \text{XIII} \end{array}$$

1,3-Dichloro-2-propanone and 1,3-dibromo-2-propanone also reacted according to the Perkow reaction at low temperature, forming the dialkyl 1-(halomethyl)vinyl phosphates (18, 342, 352). These can be used now as the halo component in a Michaelis–Arbuzov reaction, as was shown with the corresponding diethyl esters (XIV and XV, respectively; R = C_2H_5). Under somewhat stronger conditions (240°C.) they reacted with triethyl phosphite to give diethyl 1-(*O,O*-diethylphosphoryl)methylvinyl phosphate (XVI: R = C_2H_5), which could also be prepared by a direct Perkow reaction from triethyl phosphite and *O,O*-diethyl 3-chloro-2-oxopropylphosphonate (XVII: R = C_2H_5) (226, 352).

α-Halo ketones which have the halogen on a secondary carbon atom react to a significantly greater extent according to the Perkow reaction than those having the halogen on a primary carbon atom, as was

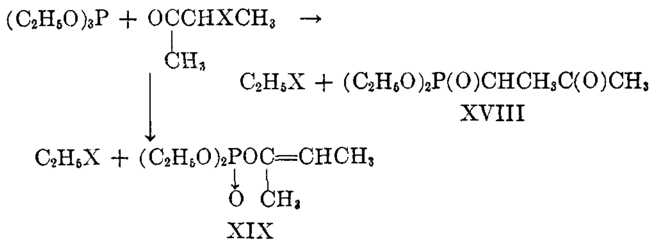


demonstrated by the reaction of triethyl phosphite with 3-chloro- and 3-bromo-2-butanones (table 3).

TABLE 3

Reaction of triethyl phosphite with 3-halo-2-butanones (345)

Reaction of $(C_2H_5O)_3P$ with	Reaction Conditions	Ratio of		Total Yield
		Phosphonate (XVIII)	Vinyl phosphate (XIX)	
		per cent	*per cent*	*per cent*
3-Chloro-2-butanone	90–100°C.	—	100	70
3-Bromo-2-butanone	In ether	9.3	90.7	65
	110–130°C.	18.8	81.2	65



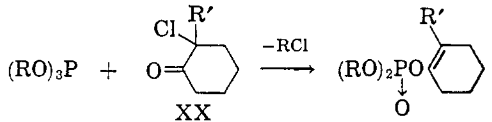
$$(C_2H_5O)_3P + OC(CH_3)CHXCH_3 \rightarrow C_2H_5X + (C_2H_5O)_2P(O)CHCH_3C(O)CH_3 \quad \text{XVIII}$$

$$\rightarrow C_2H_5X + (C_2H_5O)_2P(\rightarrow O)OC(CH_3){=}CHCH_3 \quad \text{XIX}$$

Only the vinyl phosphate (XIX) was isolated when the chloroketone was used in the reaction. The bromoketone, even at higher reaction temperatures, still yielded predominantly the vinyl phosphate (XIX), in contrast to the analogous reactions with bromoacetone (table 1) and bromoacetophenone (table 2), where the main products under these conditions are the phosphonates.

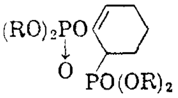
With the presence of more than one halogen atom in the α-position of the halo ketone, the reactions proceed exclusively or almost exclusively according to the Perkow reaction. Dichloromethyl, dibromomethyl, and tribromomethyl methyl ketones (342, 348, 352) yielded the corresponding dialkyl 2-halo-1-methylvinyl phosphates, in reaction with trialkyl phosphite below 60°C. Similar results were obtained with ω-substituted dichloro-, trichloro-, and tribromoacetophenones (345).

Of the cyclic halo ketones that have been investigated 2-halocyclohexanones gave the Perkow reaction very readily, as demonstrated by the high yields in which the corresponding dialkyl cyclohexenyl phosphates (XXI) were obtained from trialkyl phosphite and the 2-chloro derivatives of cyclohexanone (XX: R′ = H) (50, 52, 271, 341, 345), 2-methylcyclohexanone (XX: R′ = CH_3) (50), and 2-carbethoxycyclohexanone (XX: R′ = $COOC_2H_5$) (282, 310).

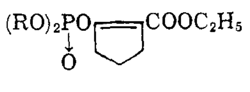


XX XXI

From 2,6-dibromocyclohexanone and triethyl phosphite, however, a range of products was obtained, from which the vinyl phosphate XXII (R = C_2H_5) was isolated in a yield of only 29 per cent (41).



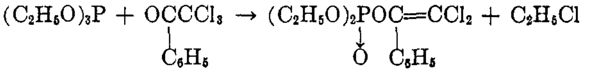
XXII



XXIII

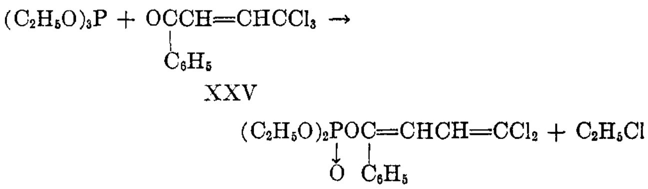
The reaction of 2-chlorocyclopentanone with triethyl phosphite has been carried out, and the product has been formulated as the *O,O*-diethyl cyclopentanonylphosphonate (44). The product, however, must contain at least some of the isomeric vinyl ester, since 2-carbethoxy-2-chlorocyclopentanone gave the vinyl phosphate (XXIII: R = CH_3) in a yield of 46 per cent (282, 308).

Halo carbonyl compounds which are vinylogs of α-halo ketones can also undergo the Perkow reaction, as demonstrated in the reaction of triethyl phosphite with ω,ω,ω-trichloroacetophenone (XXIV) (18, 244) and with its vinylog, phenyl 3,3,3-trichloropropenyl ketone (XXV) (18).



$$(C_2H_5O)_3P + OC(C_6H_5)CCl_3 \rightarrow (C_2H_5O)_2P(\rightarrow O)OC(C_6H_5){=}CCl_2 + C_2H_5Cl$$

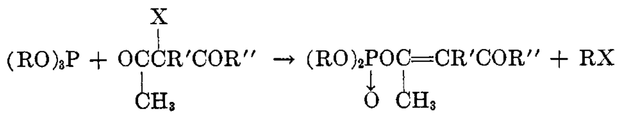
XXIV



$$(C_2H_5O)_3P + OC(C_6H_5)CH{=}CHCCl_3 \rightarrow$$
XXV
$$(C_2H_5O)_2P(\rightarrow O)OC(C_6H_5){=}CHCH{=}CCl_2 + C_2H_5Cl$$

(3) α-Halo dicarbonyl compounds

The α-halo derivatives of acetoacetates and acetoacetamide have been found to give the Perkow reaction very readily, with the formation of 2-carboxy and 2-carbamido derivatives of dialkyl 1-methylvinyl phosphates (XXVI).



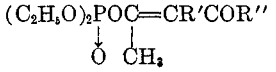
$$(RO)_3P + O\underset{CH_3}{C}\overset{X}{C}R'COR'' \rightarrow (RO)_2\underset{\overset{\downarrow}{O}}{P}O\underset{CH_3}{C}{=}CR'COR'' + RX$$

XXVI

Table 4 gives a survey of compounds of the general formula XXVI ($R = C_2H_5$), obtained by the action of triethyl phosphite with the corresponding α-halo dicarbonyl compound.

TABLE 4

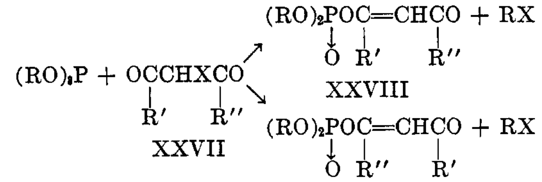
Vinyl phosphates obtained by the reaction of triethyl phosphite with derivatives of α-haloacetoacetates



$$(C_2H_5O)_2\underset{\overset{\downarrow}{O}}{P}O\underset{CH_3}{C}{=}CR'COR''$$

Vinyl Phosphate		Prepared from $(C_2H_5O)_3P$ and	Yield	References
R′	R″			
			per cent	
H	C_2H_5O	Ethyl α-chloroacetoacetate	76–91	(261, 271, 343, 402, 403)
H	$CH_3OCH_2CH_2O$	2-Methoxyethyl α-chloroacetoacetate	71.4	(319, 407)
H	$CH_3COOCH_2CH_2O$	2-Acetoxyethyl α-chloroacetoacetate	92.5	(319, 407)
H	$C_6H_5COOCH_2CH_2O$	2-Benzoyloxyethyl α-chloroacetoacetate	77.5	(319, 407)
Cl	C_2H_5O	Ethyl α,α-dichloroacetoacetate	63–80	(18, 261, 343)
C_2H_5	C_2H_5O	Ethyl α-chloro-α-ethylacetoacetate	75	(261)
H	C_6H_5NH	α-Chloroacetoacetanilide	?	(439)
H	p-$O_2NC_6H_5NH$	*N*-*p*-Nitrophenyl-α-chloroacetoacetamide	43	(439)
H	$(CH_3)_2N$	*N*,*N*-Dimethyl-α-chloroacetoacetamide	?	(439)
H	$C_6H_5(CH_3)N$	*N*-Methyl,*N*-phenyl-α-chloroacetoacetamide	71.5	(439)

Of the 2-halo-1,3-diketones the 3-chloro and 3,3-dichloro derivatives of 2,4-pentanedione gave most readily the corresponding dialkyl 2-acetyl-1-methylvinyl phosphates in yields of 60–80 per cent (261, 342, 343, 347). 2-Halo-1,3-diketones which bear different substituents at the 1- and 3-positions (XXVII) have two possibilities of reacting with trialkyl phosphites according to the Perkow reaction, giving either XXVIII or XXIX. In the case of α-benzoyl-α-chloroacetone the



$$(RO)_3P + O\underset{R'}{C}CHX\underset{R''}{C}O \nearrow (RO)_2\underset{\overset{\downarrow}{O}}{P}O\underset{R'}{C}{=}CH\underset{R''}{C}O + RX$$

$$(RO)_3P + O\underset{R'}{C}CHX\underset{R''}{C}O \searrow (RO)_2\underset{\overset{\downarrow}{O}}{P}O\underset{R''}{C}{=}CH\underset{R'}{C}O + RX$$

XXVII XXVIII XXIX

reaction proceeded with formation of dialkyl 2-acetyl-1-phenylvinyl phosphate (XXVIII: $R' = C_6H_5$, $R'' = CH_3$), as shown by the formation of methylglyoxal and benzoic acid upon ozonolysis and subsequent hydrolysis (311).

In the reaction of dibenzoylchloromethane with triethyl phosphite only 20 per cent of the diethyl 2-benzoyl-1-phenylvinyl phosphate was obtained together with a considerable amount of dibenzoylmethane (347), whereas the monobromo derivatives of dibenzoyl- and tribenzoylmethanes and of 1,3-indandione gave dibenzoylmethane, tribenzoylmethane, and 1,3-indandione, respectively, in yields of 60–75 per cent (38). Similar complications occurred when chloro- and dichlorodimedones were used (347). A radical mechanism has been considered for this anomalous course of the reaction, involving the reduction of the halogen-free diketomethyl radicals, formed in the first stage of the reaction, by hydrogen atoms of diethyl hydrogen phosphite or those of the solvent (38, 260, 347).

Compounds which have the α-halogen attached to a nitrogen atom may also undergo the Perkow reaction, as evidenced by the formation of diethyl 5-oxo-1-pyrrolin-2-yl phosphate from triethyl phosphite and *N*-chlorosuccinimide (212).

(4) α-Halo esters

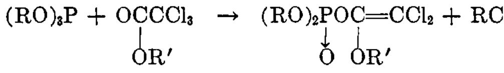
α-Halo esters were found to be considerably less reactive in reactions with trialkyl phosphites than halo aldehydes or halo ketones.

Trichloroacetates usually give a mildly exothermic reaction with trialkyl phosphites upon slight heating, yielding products which have been formulated as carbalkoxydichloromethylphosphonates (XXX), which would arise from the Michaelis–Arbuzov reaction (103, 106, 107, 113, 182, 205, 318, 339, 369).

$$(RO)_2P(O)CCl_2COOR$$

XXX

Later on, however, it was demonstrated with a large number of trichloroacetates that the Perkow reaction occurred with the formation of dialkyl 1-alkoxy-2,2-dichlorovinyl phosphates (XXXI) (9, 18, 125, 157, 181, 302, 303, 313, 396, 452).



$$(RO)_3P + O\underset{OR'}{C}CCl_3 \rightarrow (RO)_2\underset{\overset{\downarrow}{O}}{P}O\underset{OR'}{C}{=}CCl_2 + RCl$$

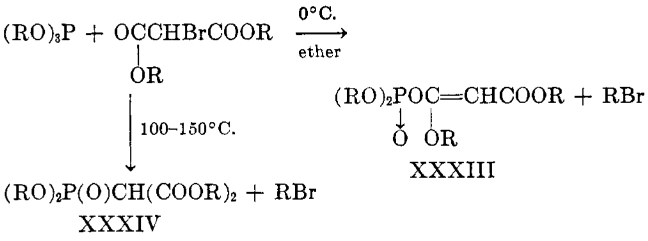
XXXI

Dichloroacetates, however, do not undergo the Perkow reaction. Ethyl dichloroacetate, for example, reacted only slowly with triethyl phosphite at 160°C. to afford a mixture boiling over a wide range from which no identifiable product could be isolated other than ethyl chloride (18).

Monohalo esters reacted completely according to the Michaelis–Arbuzov reaction. For example, ethyl chloroacetate gave a 76 per cent yield of *O,O*-diethyl carbethoxymethylphosphonate (XXXII) upon reaction with triethyl phosphite (44, 320, 396). Esters of bromoacetic (12, 26, 33, 356, 357), α-chloro- and α-bromopropionic (33, 44, 236), α,β-dibromopropionic (2), bromophenylacetic (10), and α-chloroisobutyric (44) acids reacted similarly. Certain derivatives of malonic acid, however, proved to be exceptions. Diethyl chloro- and dichloromalonates and ethyl chlorocyanoacetate underwent the Perkow reaction, giving the corresponding dialkyl 1-ethoxyvinyl phosphates (312). In the case of diethyl bromomalonate, either a Perkow or a Michaelis–Arbuzov reaction occurred, depending on the reaction conditions. Upon treatment with triethyl phosphite at 0°C. in ether as solvent the vinyl phosphate (XXXIII) was formed in 82 per cent yield (125), whereas the isomeric phosphonate (XXXIV) was obtained when the reaction was carried out at elevated temperatures without using a solvent (34, 254, 350).

$$(C_2H_5O)_3P + ClCH_2COOC_2H_5 \rightarrow (C_2H_5O)_2P(O)CH_2COOC_2H_5 + C_2H_5Cl$$

XXXII



$$(RO)_3P + \underset{OR}{\underset{|}{O}}CCHBrCOOR \xrightarrow[\text{ether}]{0°C.} (RO)_2\underset{O}{\underset{\downarrow}{P}}O\underset{OR}{\underset{|}{C}}{=}CHCOOR + RBr$$

XXXIII

$$\xrightarrow{100\text{–}150°C.} (RO)_2P(O)CH(COOR)_2 + RBr$$

XXXIV

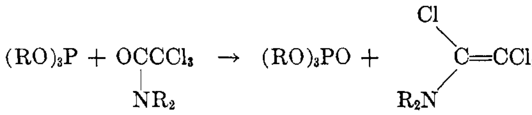
(5) α-Halo amides

The α-halo amides that have been investigated in their reactions with trialkyl phosphites did not undergo the Perkow reaction. With monohalo amides the Michaelis–Arbuzov reaction took place, as shown in the reactions of triethyl phosphite with chloroacetamide and numerous *N*-alkyl derivatives, leading to diethyl carbamidomethylphosphonates (XXXV) in yields of 70–85 per cent (67, 355, 396).

$$(C_2H_5O)_3P + ClCH_2CONR_2 \rightarrow C_2H_5Cl + (C_2H_5O)_2P(O)CH_2CONR_2$$

XXXV

Trihaloacetamides would be expected to yield vinyl phosphates in a manner analogous to trihaloacetates. However, no phosphates or phosphonates were isolated from the reaction of *N,N*-disubstituted trihaloacetamides with various trialkyl phosphites, although they may be formed as by-products. The major products of this reaction were trialkyl phosphate and trichlorovinylamines (XXXVI), formed by oxidation of the trialkyl phosphite with concomitant migration of a chlorine atom (397).

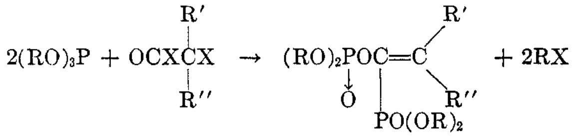


XXXVI

The competitive Perkow and Michaelis–Arbuzov reactions appeared to take place to some extent with triisopropyl phosphite, since isopropyl chloride was obtained in 37 per cent yield upon reaction with *N,N*-diethyltrichloroacetamide. Several mechanisms have been proposed (397) (see page 618).

(6) α-Halo acyl halides

Reactions of acyl halides with trialkyl phosphites have been found to proceed in accordance with the Michaelis–Arbuzov reaction, leading to the formation of *O,O*-dialkyl acylphosphonates (31, 32, 233). α-Halo acyl halides, however, reacting with two moles of trialkyl phosphite, gave both the Michaelis–Arbuzov and the Perkow reaction, forming dialkyl 1-(dialkylphosphono)vinyl phosphates (XXXVII) (66, 234, 346, 443).

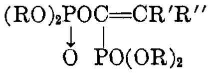


XXXVII

Table 5 lists the dimethyl and diethyl vinyl phosphates that have been prepared and that give enough evidence for generalizing this reaction. The reaction proceeds in two stages, as was shown in the case of

TABLE 5

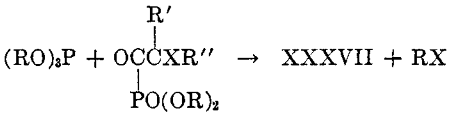
Vinyl phosphates obtained by the reaction of α-haloacyl halides with trimethyl and triethyl phosphites



$$(RO)_2\underset{O}{\underset{\downarrow}{P}}O\underset{PO(OR)_2}{\underset{|}{C}}{=}CR'R''$$

Vinyl Phosphate			Prepared from (RO)₃P and	Yield	Reference
R′	R″	R			
				per cent	
H	H	CH_3	Chloroacetyl chloride	86	(234)
				84	(346)
H	H	C_2H_5	Chloroacetyl chloride	86	(346)
				47	(234)
H	CH_3	C_2H_5	α-Bromopropionyl bromide	79	(346)
H	Cl	C_2H_5	Dichloroacetyl chloride	86	(443)
Cl	Cl	CH_3	Trichloroacetyl chloride	78	(346)
				53	(234)
Cl	Cl	C_2H_5	Trichloroacetyl chloride	79	(346)
				91	(443)
CH_3	CH_3	CH_3	α-Bromo-α-methylpropionyl bromide	92	(346)
CH_3	CH_3	C_2H_5	α-Bromo-α-methylpropionyl bromide	90	(346)

trichloroacetyl chloride and triethyl phosphite, which yielded considerable amounts of *O,O*-diethyl 2,2-dichloro-1-oxoethylphosphonate (R = C_2H_5; R′, R″, and X = Cl) besides the vinyl phosphate (70, 346). Thus, in the first phase of the reaction the halo acyl halide reacts with the phosphite to form the phosphonate (XXXVIII) (Michaelis–Arbuzov reaction), which, as a halo ketone, reacts readily with a second mole of phosphite according to the Perkow reaction.



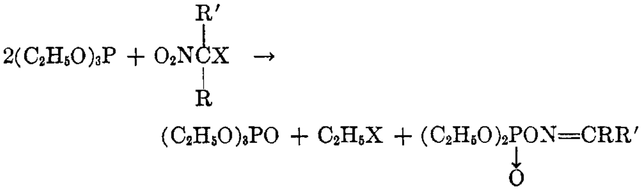
$$(RO)_3P + OC\overset{R'}{\underset{PO(OR)_2}{C}}XR'' \rightarrow XXXVII + RX$$

XXXVIII

(7) α-Halo nitroparaffins

The reaction of α-halo nitroparaffins with trialkyl phosphites has been studied repeatedly. A. E. Arbuzov (30) described the reaction of triethyl phosphite with α-bromonitro compounds, but only triethyl phosphate and ethyl bromide were isolated. Kamai (235) treated trichloronitromethane with trialkyl phosphates and reported the corresponding dialkyl phosphorochloridates as the only identifiable products.

Later on, Allen (16, 17) showed that the reaction of two moles of triethyl phosphite with several α-halo nitroparaffins (trichloronitromethane, 1,1-dichloro-1-nitroethane, and 1-bromo-1-nitropropane) leads to the formation of phosphoric esters of oximes (XXXIX) in yields of 63–73 per cent, besides alkyl halide, triethyl phosphate, and small amounts of phosphorochloridate and other unidentified products.



$$2(C_2H_5O)_3P + O_2N\overset{R'}{\underset{R}{C}}X \rightarrow (C_2H_5O)_3PO + C_2H_5X + (C_2H_5O)_2PO\underset{\overset{\downarrow}{O}}{N}{=}CRR'$$

XXXIX

Trimethyl phosphite and diethyl phenylphosphonite reacted in an analogous fashion. The structure of XXXIX is analogous to the vinyl phosphate structure, and it seems likely that the Perkow reaction and reaction of the nitro compounds proceed by the same mechanism, the latter, however, being complicated by the redox reaction. It is not apparent whether the nitro compound is first reduced to the nitroso compound, which reacts with additional phosphite, or whether the nitro compound forms an intermediate with the phosphite, which is then reduced by additional phosphite (16).

(c) Limitations of the Perkow reaction with respect to the phosphite

The Perkow reaction appeared to have about the same limitations with respect to the phosphite as the Michaelis–Arbuzov reaction. The general requirements for P(III) derivatives participating in the Perkow reaction are as follows: all three valences of the phosphorus atom must be occupied by groups other than H or OH; at least one of these must be an alkyl ester group, whose alkyl residue is capable of leaving as a carbonium ion (see the discussion of mechanism on page 616). Thus trialkylphosphines, triaryl phosphites, and phosphorotriamidites do not react, whereas all other P(III) derivatives of the general formula R′R″POR are able to undergo this reaction. Table 6 gives one standard example for each class of phosphorus compounds investigated. Detailed lists of numerous dialkyl vinyl phosphates that have been prepared from various phosphites are given in tables 21 to 33 (pages 633–642).

Trialkyl phosphites having different alkyl moieties usually eliminate the smallest group as alkyl halide. Ethyl dimethyl phosphite, for example, afforded methyl chloride and methyl ethyl 2,2-dichlorovinyl phosphate upon reaction with chloral (18). In phosphites containing one or two phenoxy groups, such as phenyl alkyl phosphite or diphenyl alkyl phosphite, the alkyl group is always removed as alkyl chloride (18). There is some indication that in a *p*-nitrophenyl dimethyl phosphite the nitrophenyl group can also be removed (403). The expected 1-halo-4-nitrobenzene, however, has not been isolated.

Phosphorous acid esters of tertiary alcohols would be expected to form an olefin instead of an alkyl halide, but no experimental evidence has yet been put forward.

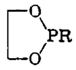
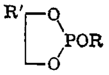
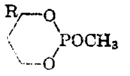
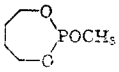
TABLE 6

2,2-Dichlorovinyl phosphates prepared from chloral and a tertiary phosphite

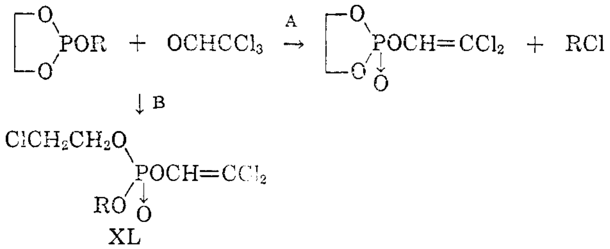
Reaction of Chloral with	Reaction Product	Yield	References
		per cent	
$(CH_3O)_3P$	$(CH_3O)_2P(O)OCH{=}CCl_2$	60–86	(18, 70, 328)
$(CH_3O)_2POC_2H_5$	$(CH_3O)(C_2H_5O)P(O)OCH{=}CCl_2$	67	(18)
$C_6H_5OP(OC_2H_5)_2$	$(C_6H_5O)(C_2H_5O)P(O)OCH{=}CCl_2$	84	(18)
$(C_6H_5O)_2POC_2H_5$	$(C_6H_5O)_2P(O)OCH{=}CCl_2$	100	(18)
$(CH_3)_2NP(OC_2H_5)_2$	$(CH_3)_2N(C_2H_5O)P(O)OCH{=}CCl_2$	43	(15)
$[(CH_3)_2N]_2POC_2H_5$	$[(CH_3)_2N]_2P(O)OCH{=}CCl_2$	67	(15, 18)
$C_2H_5P(OCH_3)_2$	$(CH_3O)C_2H_5P(O)OCH{=}CCl_2$	61	(364)
$(C_2H_5)_2POCH_3$	$(C_2H_5)_2P(O)OCH{=}CCl_2$	70	(364)
$[(CH_3)_2N]C_2H_5POCH_3$	$[(CH_3)_2N]C_2H_5P(O)OCH{=}CCl_2$	52	(364)

TABLE 7

Reaction of chloral with tertiary phosphites containing phosphorus in a ring system

Reaction of Chloral with	Reaction Products			References
	Retention of the ring		Ring cleavage	
	Alkyl halide	Alkylene 2,2-dichlorovinyl phosphate	Dialkyl 2,2-dichlorovinyl phosphate	
	*per cent*	*per cent*	*per cent*	
R = CH_3O	?	24	71	(18, 154, 157, 380, 384)
R = C_2H_5O	—	—	58	(18, 154, 380, 384)
R = $ClCH_2CH_2O$	?	?	87	(154, 380, 384)
R = CH_3S	?	?	52	(154, 380, 382, 384)
R = C_6H_5S	—	—	71	(154, 380, 382, 384)
R = $(CH_3)_2N$	—	—	67	(154, 380, 382, 384)
R = $(C_2H_5)_2N$	—	—	73	(18)
				
R = CH_3, R′ = H	68	54	?	(18)
R = CH_3, R′ = $CH_2OC_2H_5$	?	99	—	(18)
R = C_2H_5, R′ = H	22	?	?	(18)
R = C_2H_5, R′ = CH_2Cl	23	?	58	(436)
R = C_2H_5, R′ = $CH_2OC_6H_5$	24	?	68	(436)
				
R = H	65	?	?	(18)
R = CH_3	97	97	—	(18)
	45	?	?	(18)

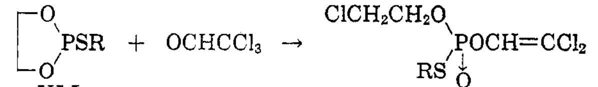
The Perkow reaction with P(III) derivatives containing phosphorus in a ring system can take place in two different ways. Either (A) elimination of alkyl halide occurs with retention of the ring or (B) cleavage of the ring occurs. This was demonstrated by the reactions of various ethylene tri- and tetramethylene phosphites with chloral.



XL

Alkyl ethylene phosphites usually undergo ring cleavage with chloral, as shown by the results listed in table 7, to give the corresponding alkyl 2-chloroethyl 2,2-dichlorovinyl phosphates (XL) in good yields. The only exception seems to be methyl ethylene phosphite, which gave both products, apparently owing to the fact that the methyl group and the ethylene group are attacked by the nucleophile (chloride ion) with comparable ease (see the discussion of mechanism on page 616). Substitution in or enlargement of the ring, however, increases its stability and thus favors the reaction to proceed with elimination of alkyl halide (course A). This is demonstrated by the results of the reaction of chloral with alkyl methylethylene phosphite and alkyl trimethylene and tetramethylene phosphites (table 7), which predominantly led to the formation of alkyl halide (18).

Trialkyl phosphorotrithioites, which do not undergo a normal Michaelis–Arbuzov reaction, also did not react with chloral to form dichlorovinyl phosphorodithiolothionates (18). The few trialkyl phosphorothioites that have been investigated readily participated in the Perkow reaction. *O,O*-Ethylene *S*-alkyl phosphorothioites (XLI) were found to give *O*-2-chloroethyl *O*-2,2-dichlorovinyl *S*-alkyl phosphorothiolates (XLII: R = CH_3, C_2H_5, C_6H_5) upon reaction with chloral (154, 380, 382). The *S*-alkyl group therefore is more stable against nucleophilic attack by the chloride ion than the ethylene ring.



XLI XLII

The products from the reaction of other dialkyl *S*-alkyl phosphites with chloral have been formulated as dialkyl dichlorovinyl phosphorothionates (XLIIIa) (383). It seems improbable, however, that in this case the *S*-alkyl group should be eliminated rather than one of the *O*-alkyl groups. Since no experimental evidence concerning the structure has been put forward, the reaction products might well be *O*-alkyl *O*-dichlorovinyl *S*-alkyl phosphorothiolates (XLIIIb).

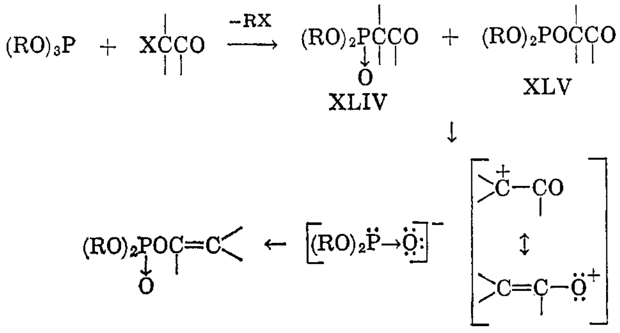
$$(RO)_2PSR + OCHCCl_3 \xrightarrow{-RCl} \underset{\text{XLIIIa}}{(RO)_2P(S)OCH{=}CCl_2} \text{ or } \underset{\text{XLIIIb}}{(RO)(RS)P(O)OCH{=}CCl_2}$$

Instead of phosphorus compounds, equivalent derivatives of arsenic and antimony can be used in the Perkow reaction, as shown by the synthesis of diethyl 2,2-dichlorovinyl arsenate and antimonate from chloral and triethyl arsenite and antimonite, respectively (333).

(d) Mechanism

Various mechanisms have been proposed for the Perkow reaction; although some seem rather improbable, the experimental material available does not allow one to establish the mechanism with certainty. The following discussion therefore is an attempt to evaluate the mechanisms proposed on the basis of theoretical considerations and the experimental findings available.

According to Perkow, Krockow, and Knoevenagel (334) the primary step of the reaction is the elimination of alkyl halide to give intermediates of the type of XLIV or XLV, which, owing to the inductive effect of the carbonyl group, are ionized to an ion-pair complex (XLVI) affording the vinyl phosphate:

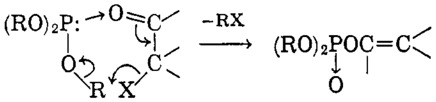


XLIV XLV

XLVI

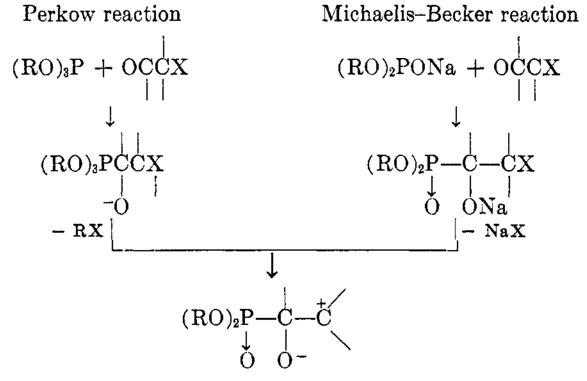
This mechanism is improbable, because it does not consider an initial attack by the nucleophilic phosphorus on the carbonyl carbon or the α-carbon atom, which in view of the mechanism of the Michaelis–Arbuzov reaction seems to be more likely than the hypothesis of an initial elimination of alkyl halide.

Pudovik (237, 265, 341) suggested that the Perkow reaction might proceed by way of a cyclic mechanism, the initial attack of the nucleophilic phosphorus on the carbonyl carbon being the driving force for the simultaneous electron shift:

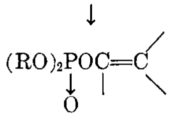


This formulation is unusual in that it represents the normally nucleophilic carbonyl oxygen as becoming electrophilic, which scarcely would result from the inductive effect of a single halogen atom. Also, the shift of the electrons would proceed via a sterically unfavored seven-membered ring.

Kreutzkamp and Kayser (260) proposed another mechanism, based on findings that the Michaelis–Becker reaction in some cases yielded vinyl phosphates (see page 620). Assuming a common intermediate for both reactions, the initial step of the Perkow reaction would be a nucleophilic attack by the phosphorus on the carbonyl carbon followed by elimination of alkyl halide and rearrangement of the bipolar ion (XLVII) to the vinyl phosphate:

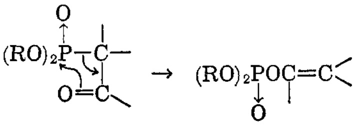


XLVII

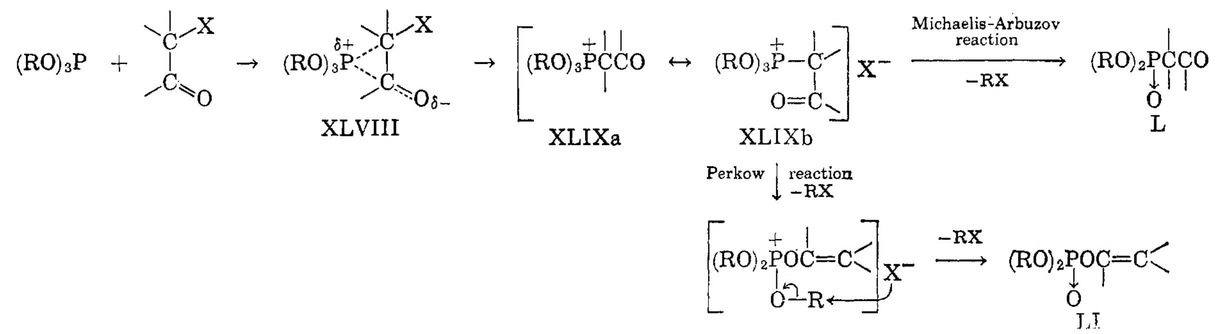


This mechanism, however, does not consider that the intermediate XLVII can readily form epoxyalkyl derivatives, compounds which have never been reported in the Perkow reaction, whereas their formation in the Michaelis–Becker reaction has been demonstrated (4, 5, 49, 50, 52, 53). Thus this formulation seems highly improbable.

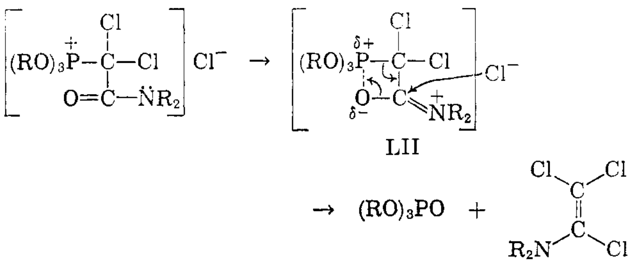
A very attractive mechanism appears to be the modification of the Spencer–Todd–Webb mechanism (395) by Cramer (123). The former postulated a "phosphonate-phosphate rearrangement" of the 2-oxoalkylphosphonate, formed by an initial Michaelis–Arbuzov reaction:



The assumption of the phosphonate as the precursor of the vinyl phosphate appears very questionable however, since none of the various 2-oxoalkylphosphonates that have been prepared showed a tendency to isomerize. Thus, it seems to be more likely to postulate the "phosphonate-phosphate rearrangement" as occurring prior to the phosphonate formation. This mechanism, as discussed by Cramer (123), involves an initial attack by the nucleophilic phosphorus on the α-carbon by way of a transition state (XLVIII) to give a phosphonium salt intermediate (XLIXa and XLIXb). From this either alkyl halide is eliminated directly with the formation of the phosphonate (XLIXa → L; Michaelis–Arbuzov reaction) or only after a "phosphonate-phosphate rearrangement" (XLIXb) to yield the vinyl phosphate (LI):

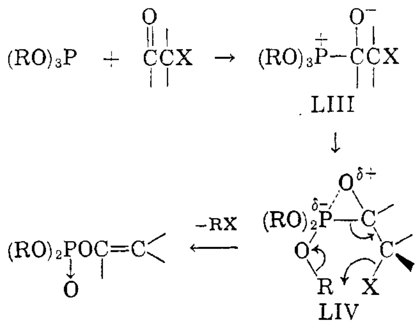


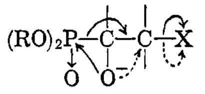
Support for this rearrangement is found in the Wittig reaction (375, 446), in which all available evidence necessitates a quasi-four-membered transition intermediate similar to XLIXb. Furthermore, this mechanism explains convincingly the increasing occurrence of the Michaelis–Arbuzov reaction in the order Cl < Br < I (for X in the halo carbonyl compound) by the corresponding increase of the nucleophilic reactivity of the halogen, which will favor direct elimination of alkyl halide (XLIXa → L). The formation of trichlorovinylamines and trialkyl phosphate, when trichloroacetamides are used in the Perkow reaction, can be explained by a complete Wittig reaction (LII), due to the electron support of the amino group and a subsequent nucleophilic attack of the chloride ion on the original carbon:



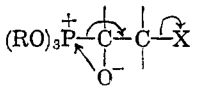
Allen and Johnson (18) and Kharasch and Bengelsdorf (244) independently proposed a mechanism for the Perkow reaction, which seems to comply with all the experimental data available. It involves an initial attack by the phosphorus on the carbonyl carbon to give an adduct (LIII), and a similar attack by the negatively charged oxygen on the phosphorus with intermediate formation of a quasi-three-membered ring (LIV). The subsequent cleavage of the carbon–phosphorus bond and the concomitant release of alkyl halide then result in the formation of the vinyl phosphate (see below).

This mechanism is closely related to the basic dehydrohalogenation of 1-hydroxy-2-haloalkylphosphonates (see page 619), where a similar intermediate is the precursor of the vinyl phosphate (LV) or the epoxyalkylphosphonate (LV, dotted arrows). In the Perkow reaction, however, the formation of epoxyalkyl derivatives is not favored, owing to the strongly electropositive phosphonium cation (LVI), which necessitates the nucleophilic attack by the oxygen on the phosphorus atom rather than on the adjacent carbon atom.



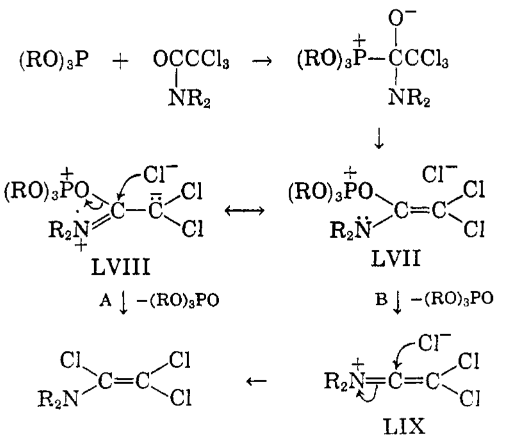


LV

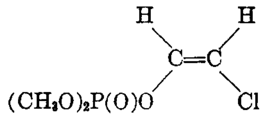


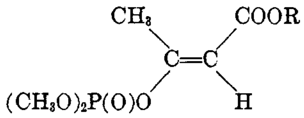
LVI

The increasing occurrence of the Michaelis–Arbuzov reaction in the order Cl < Br < I for the halogen of the halo component can be explained by the increase in the polarization of the carbon–halogen bond, which facilitates the elimination of the halide ion and thus favors the initial nucleophilic attack by the phosphorus on the α-carbon atom rather than on the carbonyl carbon. The fact that trichloroacetamides behave differently from their keto and, in particular, from their ester counterparts can be rationalized on the basis that the intermediate (LVII) is stabilized through resonance to a greater degree by nitrogen than by oxygen or carbon. Thus, the chloride ion would attack the iminium carbon atom (LVIII) rather than one of the phosphate ester groups (course A). An alternative route would be course B, the elimination of trialkyl phosphate (LVII → LIX) being the driving force for the formation of trichlorovinylamine (397).



An evaluation of the different mechanistic pathways on the basis of the few stereochemical data available does not seem to be fruitful at this time, since none of the mechanisms proposed provides a convincing explanation of the experimental findings that upon the reaction of trimethyl phosphite with dichloroacetaldehyde an isomeric mixture is obtained consisting mainly of the cis compound (LX, 80 per cent), whereas the reaction product from trimethyl phosphite and an α-chloroacetoacetate consists predominantly of the isomer having the two largest groups in the trans position (LXI) (see page 629). It is to be expected, however, that more detailed investigations of the stereochemical aspects of the Perkow reaction will furnish the material to establish with certainty the mechanistic course.

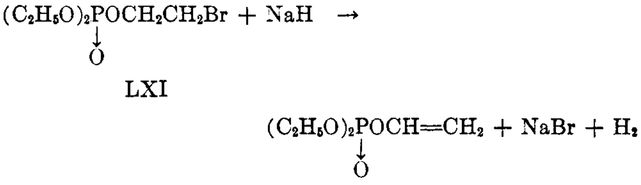

LX


LXI

B. DEHYDROHALOGENATION OF 2-HALOALKYL PHOSPHATES

This reaction, which has been successfully applied to the synthesis of vinylphosphonates from the corresponding 2-haloalkylphosphonates (1, 2, 11, 160, 177, 231, 255, 269), was found to be of rather limited use in the preparation of vinyl phosphates.

Diethyl vinyl phosphate (LXII) has been synthesized by the dehydrobromination of diethyl 2-bromoethyl phosphate (LXI) with sodium hydride in ether (19). Treatment of LXI with sodium *tert*-butoxide in tertiary butyl alcohol also led to LXII, which, however,

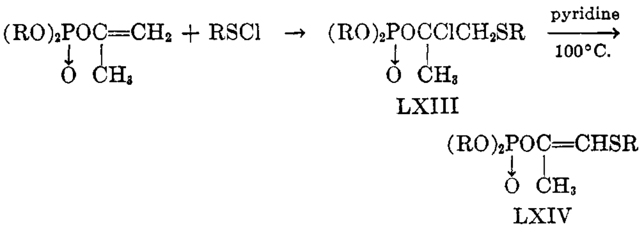


$$\underset{\text{LXI}}{\underset{\downarrow\atop \text{O}}{(C_2H_5O)_2P}OCH_2CH_2Br} + NaH \rightarrow \underset{\text{LXII}}{\underset{\downarrow\atop \text{O}}{(C_2H_5O)_2P}OCH{=}CH_2} + NaBr + H_2$$

was contaminated with diethyl *tert*-butyl phosphate formed by the partial alcoholysis of LXII (19). The product obtained by the dehydrochlorination of diethyl 2-chloroethyl phosphate with ethanolic potassium hydroxide was considered to be the vinyl phosphate (LXII) (422, 423). However, the product was recovered unchanged after being refluxed in 1 per cent aqueous hydrochloric acid for 3–6 hr., whereas LXII, prepared by the Perkow reaction, was hydrolyzed to the extent of 15 per cent after 6 hr. under milder conditions (85°C., 1 *N* hydrochloric acid–40 per cent ethanol) (271). Furthermore, the ease with which vinyl phosphates undergo alcoholysis in the presence of traces of alkali suggests that the product consisted mainly of triethyl phosphate. Later attempts to repeat this dehydrochlorination with ethanolic potassium hydroxide and other basic reagents were unsuccessful, yielding only ethanolysis and degradation products (19).

This method seems to give better results when anhydrous sodium carbonate is used as the dehydrohalogenation agent at elevated temperatures—*O,O*-divinyl phenylphosphonate was obtained in a 62 per cent yield from *O,O*-di-2-chloroethyl phenylphosphonate (423)—or when the chloroform solution of the 2-haloalkyl phosphate is treated with aqueous sodium hydroxide, as shown by the isolation of dibutyl 2,2-dichlorovinyl phosphate from dibutyl 2,2,2-trichloroethyl phosphate in 50 per cent yield (327).

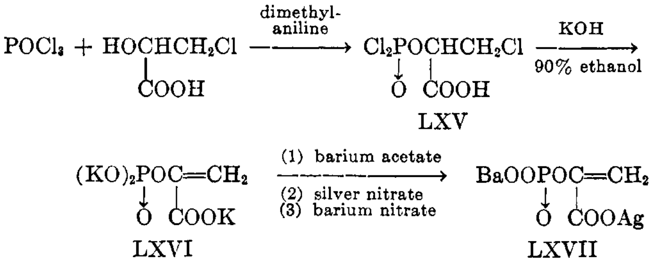
A number of dialkyl 2-alkylthio-1-methylvinyl phosphates (LXIV: R = CH_3 or C_2H_5) were prepared by the dehydrohalogenation with pyridine at 100°C. of 2-alkylthio-1-chloro-1-methylethyl phosphates (LXIII),



$$\underset{\downarrow\atop \text{O}}{(RO)_2P}O\underset{|\atop CH_3}{C}{=}CH_2 + RSCl \rightarrow \underset{\text{LXIII}}{\underset{\downarrow\atop \text{O}}{(RO)_2P}O\underset{|\atop CH_3}{C}ClCH_2SR} \xrightarrow[100°C.]{\text{pyridine}} \underset{\text{LXIV}}{\underset{\downarrow\atop \text{O}}{(RO)_2P}O\underset{|\atop CH_3}{C}{=}CHSR}$$

the intermediary products of the addition of alkylthio chloride to the ethylenic double bond of a dialkyl vinyl phosphate (143).

A dehydrochlorination also is involved in the synthesis of phosphoenol pyruvate (PEP) given by Baer and Fischer (63, 65). In this, the intermediate 2-chloroalkyl phosphorus compound (LXV), formed by the reaction of β-chlorolactic acid with phosphorus oxychloride in the presence of dimethylaniline, is treated with ethanolic potassium hydroxide at slightly elevated temperature, affording the potassium salt of PEP (LXVI). There were also obtained other organic phosphates, among which considerable amounts of ethyl dihydrogen phosphate, formed by the alcoholysis of PEP, might be expected. The overall yield of the silver barium salt of PEP (LXVII) did not exceed 10 per cent.



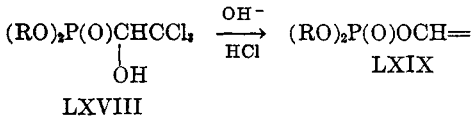
$$\mathrm{POCl_3 + HO\underset{|\atop COOH}{C}HCH_2Cl \xrightarrow{\text{dimethyl-aniline}} Cl_2\underset{\downarrow\atop O}{P}O\underset{|\atop COOH}{C}HCH_2Cl \xrightarrow[\text{90\% ethanol}]{\text{KOH}}}$$
$$\text{LXV}$$

$$\mathrm{(KO)_2\underset{\downarrow\atop O}{P}O\underset{|\atop COOK}{C}{=}CH_2 \xrightarrow[\text{(2) silver nitrate; (3) barium nitrate}]{\text{(1) barium acetate}} BaOO\underset{\downarrow\atop O}{P}O\underset{|\atop COOAg}{C}{=}CH_2}$$
$$\text{LXVI} \qquad\qquad \text{LXVII}$$

C. BASIC DEHYDROHALOGENATION OF 2-HALOALKYL-1-HYDROXYPHOSPHONATES

O,O-Dialkyl 2-haloalkyl-1-hydroxyphosphonates, readily accessible through the addition of 2-halo carbonyl compounds to dialkyl esters of phosphorus acid (4, 5, 6, 8, 49, 71, 111, 121, 129, 189, 190, 243, 273, 279, 280, 331) can undergo various reactions upon treatment with alkali, their course being dependent on the number of halogen atoms in the phosphonate and upon the reaction conditions.

Phosphonates of the type of LXVIII, having a 2,2,2-trichloro-1-hydroxyethyl moiety, were found to undergo rearrangement on treatment with alkali, leading to the corresponding enol phosphates (LXIX) by elimination of hydrogen halide and fission of the phosphorus–carbon bond (61, 70, 153, 274, 276, 294, 301, 331). The reaction is conducted by adding the base to a solution of the phosphonate in water, or, when it is water-insoluble, in alcohol, followed by gentle heating.



$$\mathrm{(RO)_2P(O)\underset{|\atop OH}{C}HCCl_3 \xrightarrow[\text{HCl}]{\text{OH}^-} (RO)_2P(O)OCH{=}CCl_2}$$
$$\text{LXVIII} \qquad\qquad \text{LXIX}$$

The kind of base used seems to be of minor importance, since, for example, the yields of dimethyl 2,2-dichlorovinyl phosphate, prepared from *O,O*-dimethyl 2,2,2-trichloro-1-hydroxyethylphosphonate under different basic conditions, are between 48 and 58 per cent (70, 153, 274, 276) (table 8). However, it is important that the reaction mixture be kept at pH 6–7 (addition of only the theoretical amount of alkali); otherwise considerable hydrolysis of the formed enol phosphate occurs. This is demonstrated by the data listed in table 9, which also show that the relatively low yields are due to hydrolysis, which cannot be completely eliminated.

TABLE 8

Dialkyl 2,2-dichlorovinyl phosphates (LXIX) prepared from the corresponding 2,2,2-trichloro-1-hydroxyethylphosphonates (LXVIII)

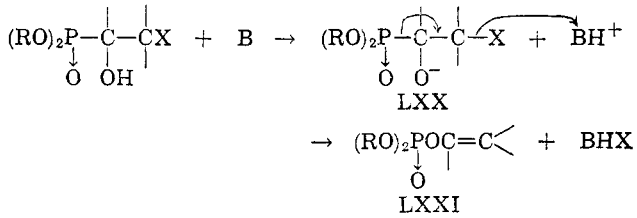
R	Base	Temperature	Yield	References
		°C.	per cent	
CH_3	NaOH	40	57	(70, 153, 276)
	NH_4OH	50–60	48	(153, 274)
	$(C_2H_5)_3N$	25–30	51	(153, 294)
	$NaOCH_3$	30	49	(153)
C_2H_5	NaOH	40	51	(70)
C_3H_7	$NaOCH_3$	40–50	36	(70)
iso-C_3H_7	$NaOCH_3$	40–50	26	(70)
C_4H_9	$NaOCH_3$	40–50	53	(70)

TABLE 9

Rearrangement of O,O-dimethyl 2,2,2-trichloro-1-hydroxyethylphosphonate to dimethyl 2,2-dichlorovinyl phosphate at varying pH values (30 min. at 70°C.) (301)

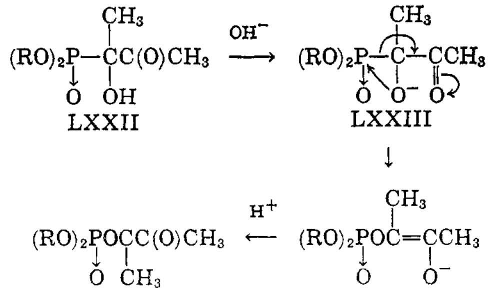
pH	Percentage Composition of the Reaction Mixture		
	Phosphonate	Vinyl phosphate	Hydrolysis products
	per cent	per cent	per cent
1	98.5	0.5	1
5	96.2	1.6	1.6
6	82.2	21.6	6.2
7	3.0	58.5	38.5
8	0	54.0	46.0

The mechanism of this rearrangement has been discussed by Bengelsdorf (72). The first step, involving the removal of a proton from the α-hydroxy group, leads to the intermediate LXX, which rearranges to the vinyl phosphate (LXXI) by a nucleophilic attack of the negatively charged oxygen atom on the phosphorus atom:



$$\mathrm{(RO)_2\underset{\downarrow\atop O}{P}{-}\underset{|\atop OH}{\overset{|}{C}}{-}\overset{|}{C}X + B \rightarrow (RO)_2\underset{\downarrow\atop O}{P}{-}\underset{|\atop O^-}{\overset{|}{C}}{-}\overset{|}{C}{-}X + BH^+}$$
$$\text{LXX}$$
$$\mathrm{\rightarrow (RO)_2\underset{\downarrow\atop O}{P}O\underset{|}{C}{=}C\!\!< + BHX}$$
$$\text{LXXI}$$

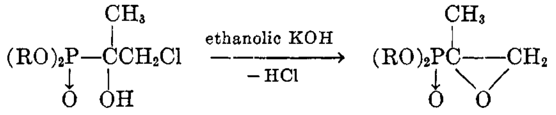
It was stated that the loss of a halide ion is a necessary event for this rearrangement to occur (72). However, the mere presence of electron-attracting groups, such as a carbonyl function at the α-position, is sufficient to cause rearrangement. Hence, *O,O*-dialkyl 1-hydroxy-2-oxoalkylphosphonates (LXXII), when treated with sodium ethoxide in ethanol, undergo an analogous rearrangement, as indicated in LXXIII, affording the corresponding trialkyl phosphates (264).



$$\mathrm{(RO)_2\underset{\downarrow\atop O}{P}{-}\underset{|\atop OH}{\overset{CH_3\atop |}{C}}C(O)CH_3 \xrightarrow{\text{OH}^-} (RO)_2\underset{\downarrow\atop O}{P}{-}\underset{|\atop O^-}{\overset{CH_3\atop |}{C}}{-}\underset{\|\atop O}{C}CH_3}$$
$$\text{LXXII} \qquad\qquad \text{LXXIII}$$
$$\downarrow$$
$$\mathrm{(RO)_2\underset{\downarrow\atop O}{P}O\underset{|\atop CH_3}{C}C(O)CH_3 \xleftarrow{\text{H}^+} (RO)_2\underset{\downarrow\atop O}{P}O\overset{CH_3\atop |}{C}{=}\underset{|\atop O^-}{C}CH_3}$$

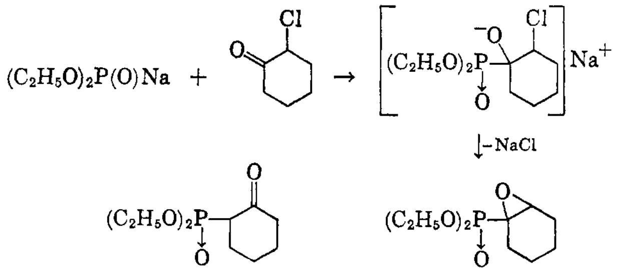
Whereas dialkyl 2,2,2-trichloro-1-hydroxyethylphosphonates yielded exclusively vinyl phosphates under alkaline conditions, the reaction with 1-hydroxyalkylphosphonates, which have fewer halogen atoms at the 2-position, can take several courses.

A number of dialkyl 2-chloro-1-hydroxy-1-methylethylphosphonates (LXXIV) were reported to give 1,2-epoxyalkylphosphonates (LXXV) rather than vinyl phosphates (4, 5, 37, 49).



LXXIV LXXV

Similarly, epoxy derivatives (LXXVII), as well as some 2-oxoalkylphosphonates (LXXVI), were obtained from diethyl sodium phosphite (sodium diethyl phosphonate) and the 2-chloro derivatives of cyclopentanone and cyclohexanone (50, 51–53).



LXXVI LXXVII

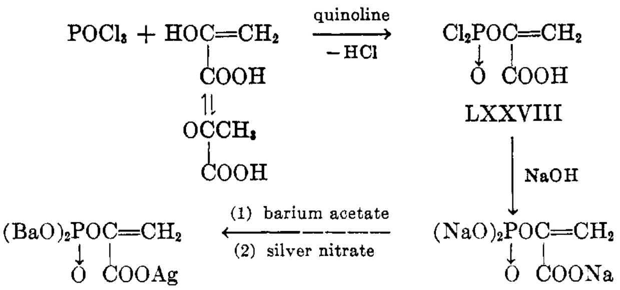
In other cases however, such as in the reactions of dialkyl sodium phosphite with 3-bromo-3-methyl-2-butanone, 2-chloro-2-methylcyclohexanone, α-bromocamphor (50, 52, 53), and methyl β-bromopyruvate (37, 129), the vinyl phosphates were major products.

These reactions have been incompletely studied and require considerable elucidation before the possible limitations can be profitably discussed.

D. PHOSPHORYLATION OF ENOLATES

A considerable number of organic phosphates have been prepared by the reaction of phosphoryl halides with either sodium alkoxide or alcohol in the presence of an organic or inorganic base (256). This method can also be applied to carbonyl compounds capable of forming an enolate with base.

The first application of this method was the synthesis of phosphoenol pyruvate (1-carboxyvinyl dihydrogen phosphate or PEP) by the interaction of pyruvic acid and phosphorus oxychloride in quinoline, followed by alkaline hydrolysis of the intermediate (LXXVIII) (245, 246). The yield of the silver barium salt of PEP (LXVII), however, did not exceed 9 per cent despite later improvements (322, 373, 374). Similarly the barium salt of 2-carboxy-1-methylvinyl dihydrogen phosphate was prepared from ethyl sodioacetoacetate and phosphorus oxychloride (240).

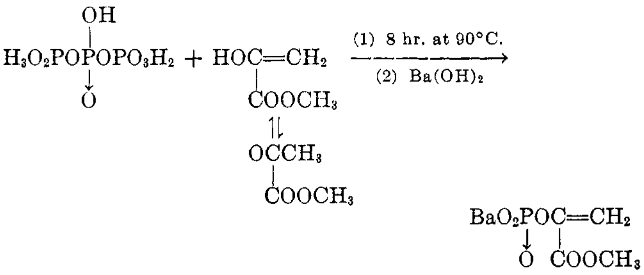


LXXVIII

LXVII

This reaction gave far better results when dialkyl phosphorochloridates and their thio analogs were used, either by treating them with the carbonyl compound in the presence of an acid-consuming agent (e.g., solid potassium carbonate), or directly with the alkali enolate (138, 179, 180, 192, 193, 282, 283, 309–311, 315, 316, 339, 378). Some representative dialkyl vinyl phosphates and phosphorothionates prepared by this method are listed in table 10.

Phosphorylation of an enol can also be accomplished by using polyphosphoric acid, as has been shown by the synthesis of some PEP derivatives. 1-Carbomethoxyvinyl barium phosphate (LXXXI), for example, was obtained in 47 per cent yield from methyl pyruvate and triphosphoric acid (102).



LXXXI

Related to the phosphorylation of enols is the reaction of phosphoryl chlorides with an excess of acetaldehyde in the presence of base (triethylamine), affording not only vinyl but also divinyl and trivinyl phosphates, which otherwise are difficultly accessible (178). Phosphorus oxychloride gave trivinyl phosphate (LXXXII). The other chlorides investigated were derivatives of phosphonic acids (LXXXIII); however, the corresponding phosphorochloridates would also be expected to enter the reaction. The yields did not exceed 35 per cent.

$$POCl_3 + 3CH_3CHO + 3R_3N \rightarrow PO(OCH{=}CH_2)_3 + 3R_3NHCl$$

LXXXII
Trivinyl phosphate

$$R'R''POCl + CH_3CHO + R_3N \rightarrow R'R''P(O)OCH{=}CH_2 + R_3NHCl$$

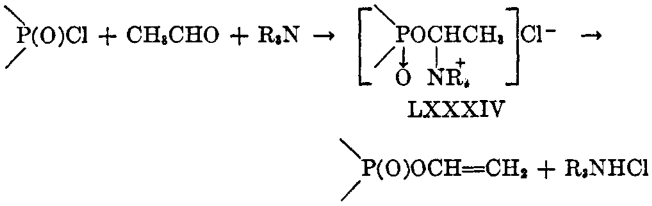
LXXXIII

TABLE 10

Dialkyl vinyl phosphates and phosphorothionates prepared from an alkali enolate of a ketone and a dialkyl phosphorochloridate

$(RO)_2P(X)OCR'{=}CR''R'''$					Prepared from $(RO)_2P(X)Cl$ and the Alkali Enolate of	Yield	References
X	R	R′	R″	R‴			
						per cent	
0	C_2H_5	CH_3	H	H	Acetone	50	(262)
0	C_2H_5	CH_3	H	$COOC_2H_5$	Ethyl acetoacetate	77	(378)
0	CH_3	C_6H_5	H	$COCH_3$	Benzoylacetone	58	(282, 311, 316)
0	C_2H_5	C_6H_5	H	$COCH_3$	Benzoylacetone	67	(282, 311, 316)
0	CH_3	CH_3	C_6H_5	CN	1-Cyano-1-phenyl-2-propanone	40	(309, 313)
0	CH_3	$—(CH_2)_3—$		$COOC_2H_5$	2-Carbethoxycyclopentanone	41	(310)
						98	(192)
0	C_2H_5	$—(CH_2)_3—$		$COOC_2H_5$	2-Carbethoxycyclopentanone	70	(310)
						89	(192)
0	CH_3	$—(CH_2)_4—$		$COOC_2H_5$	2-Carbethoxycyclohexanone	61	(310)
0	C_2H_5	$—(CH_2)_4—$		$COOC_2H_5$	2-Carbethoxycyclohexanone	71	(310)
0	C_2H_5	$—C(O)CH_2C(CH_3)_2CH_2—$		H	5,5-Dimethyl-1,3-cyclohexanedione	70	(262)
0	C_2H_5	$—CH_2C{=}CCH_2—$ $C_2H_5OOC \quad OPO(OC_2H_5)_2$		H	2,5-Dicarbethoxy-1,4-cyclohexanedione	68	(192)
S	CH_3	C_6H_5	H	$COOC_2H_5$	Ethyl benzoylacetate	35	(284, 309)
S	C_2H_5	C_6H_5	H	$COCH_3$	Benzoylacetone	63	(282, 311, 316)
S	C_2H_5	C_6H_5	H	$COOC_2H_5$	Benzoylacetone	35	(284, 309)
S	CH_3	CH_3	C_6H_5	CN	1-Cyano-1-phenyl-2-propanone	37	(309, 313)
S	C_2H_5	CH_3	C_6H_5	CN	1-Cyano-1-phenyl-2-propanone	41	(309, 313)
S	CH_3	CH_3	C_6H_5	$COOC_2H_5$	Ethyl α-phenylacetoacetate	21	(309)
S	CH_3	$—(CH_2)_3—$		$COOC_2H_5$	2-Carbethoxycyclopentanone	52	(283, 310)
S	C_2H_5	$—(CH_2)_3—$		$COOC_2H_5$	2-Carbethoxycyclopentanone	98	(192)
S	CH_3	$—(CH_2)_4—$		$COOC_2H_5$	2-Carbethoxycyclohexanone	44	(283, 310)
S	C_2H_5	$—(CH_2)_4—$		$COOC_2H_5$	2-Carbethoxycyclohexanone	53	(283, 310)

The mechanism of this reaction is believed to be the formation of a 1-chloroethyl ester followed by salt formation at the 1-position (LXXXIV); the salt decomposes to the vinyl ester by elimination of the amine hydrochloride (178). This mechanism does not seem very reasonable, however.



$$\rangle P(O)Cl + CH_3CHO + R_3N \rightarrow \left[\rangle \underset{\downarrow \atop O}{P}O\underset{| \atop \overset{+}{N}R_3}{C}HCH_3\right]Cl^- \rightarrow$$

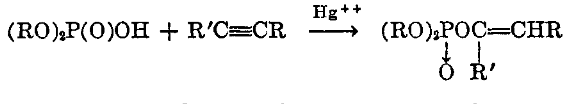
LXXXIV

$$\rangle P(O)OCH{=}CH_2 + R_3NHCl$$

E. MISCELLANEOUS METHODS

1. Catalytic addition of acetylene derivatives to dialkyl hydrogen phosphates

A novel method of preparing enol phosphates, similar to that described recently for the preparation of vinyl carboxylates (426), has been found in the mercuric ion-catalyzed addition of dialkyl hydrogen phosphates to acetylenic compounds (144, 288, 289, 299, 425). For example, diphenyl 1-ethoxyvinyl phosphate has been isolated from the reaction of ethoxyacetylene



$$(RO)_2P(O)OH + R'C{\equiv}CR \xrightarrow{Hg^{++}} (RO)_2\underset{\downarrow \atop O}{P}O\underset{| \atop R'}{C}{=}CHR$$

with diphenyl hydrogen phosphate in methylene chloride at 0°C. in the presence of mercuric acetate (425).

Numerous other enol phosphates (299) and enol phosphorothiolothionates (288, 289)—the latter prepared by using dialkyl hydrogen phosphorothiolothioates—have been reported, but no information concerning yields and data other than refractive indices is available.

2. Transesterification of vinyl carboxylates with phosphoric acid

A method for the preparation of vinyl esters of higher aliphatic acids by a mercuric ion-catalyzed, acid-exchange reaction between vinyl acetate and the aliphatic acid (287, 417) can also be used for the synthesis of enol phosphates, as was shown by the formation of vinyl dihydrogen phosphate from vinyl acetate and phosphoric acid. The yield of the pyridinium salt was 26 per cent (64).

$$H_3PO_4 + CH_3COOCH{=}CH_2 \xrightarrow{Hg^{++}} (HO)_2P(O)OCH{=}CH_2 + CH_3COOH$$

3. Oxidation of vinyl phosphites

The oxidation of some vinyl and divinyl phosphites (LXXXV) synthesized by the reaction of mercuri bis-acetaldehyde with the corresponding alkyl phosphorochloridites (307) have been studied, but owing to ready polymerization, no vinyl phosphates could be isolated upon treatment with oxygen. However, upon reaction with sulfur at elevated temperature, vinyl phosphorothioates (LXXXVI: R = C_2H_5, C_3H_7, or C_4H_9) were

TABLE 11

Chlorination of diethyl vinyl phosphates

Reaction of Chlorine with	Product	Boiling Point	Yield	References
		°C.	per cent	
$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}OCH{=}CH_2$	$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}OCHClCH_2Cl$	75–92/1 mm.	80	(157)
$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ CH_2Cl}}{C}{=}CH_2$	$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}OCCl(CH_2Cl)_2$	150–152/9 mm.	75	(352)
$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ CH_2Br}}{C}{=}CH_2$	$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ CH_2Br}}{C}ClCH_2Cl$	159/9 mm.	65	(352)
$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}OCH{=}CHCl$	$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}OCHClCHCl_2$	111–142/1 mm.	43	(19)
$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ CH_3}}{C}{=}CHCl$	$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ CH_3}}{C}ClCHCl_2$	147–148/11 mm.	85	(342, 352)
$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ C_6H_5}}{C}{=}CHCl$	$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ C_6H_5}}{C}ClCHCl_2$	162–163/1 mm.	53	(345)
$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ CH_3}}{C}{=}CHBr$	$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ CH_3}}{C}ClCHBrCl$	154–155/10 mm.	40	(352)
$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}OCH{=}CCl_2$	$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}OCHClCCl_3$	125–145/1.5 mm. 123–125/1.2 mm. 116–119/0.4 mm. 111/10^{-6} mm.	74 62 42 34	(19) (328) (70) (436)
$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ OC_2H_5}}{C}{=}CCl_2$	$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ OC_2H_5}}{C}ClCCl_3$	108/0.15 mm.	99	(442)
$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ CH_3}}{C}{=}CClCOOC_2H_5$	$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ CH_3}}{C}ClCCl_2COOC_2H_5$	65–70/0.05 mm.	70	(262)
$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ CH_3}}{C}{=}CBrCH_3$	$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{\vert\\ CH_3}}{C}ClCClBrCH_3$	164–165/10 mm.	92	(345)
$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}OCH{=}CHCH_2Cl$	$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}O(CHCl)_2CH_2Cl$	142–144/0.6 mm.	40	(334)

easily formed and isolated in yields of 50–80 per cent (307).

$$Hg(CH_2CHO)_2 + ClP(OR)_2 \rightarrow (RO)_2POCH{=}CH_2 + ClHgCH_2CHO$$

LXXXV

$$(RO)_2POCH{=}CH_2 + S \rightarrow (RO)_2P(S)OCH{=}CH_2$$

LXXXVI

4. Michaelis–Arbuzov reaction with dialkyl vinyl phosphites and alkyl divinyl phosphites

A number of dialkyl vinyl and alkyl divinyl phosphites have been shown to undergo the Michaelis–Arbuzov reaction very readily, giving the corresponding *O*-vinyl esters of phosphoric acid in good yields (278). The compounds that have been prepared are listed in table 30 on page 640.

$$(RO)_2POCH{=}CH_2 + R'X \rightarrow (RO)R'P(O)OCH{=}CH_2 + RX$$

5. Reaction of disulfides of phosphorodithioates with Grignard reagents

Disulfides of *O,O*-dialkyl phosphorodithioic acids were shown to react rapidly with Grignard reagents to give excellent yields of *O,O*-dialkyl phosphorothiolothionates (298). When vinylmagnesium bromide or derivatives thereof were used, *O,O*-dialkyl *S*-vinyl phosphorothiolothionates (LXXXVIII: R = CH_3 or C_2H_5), otherwise difficultly accessible, are formed (298).

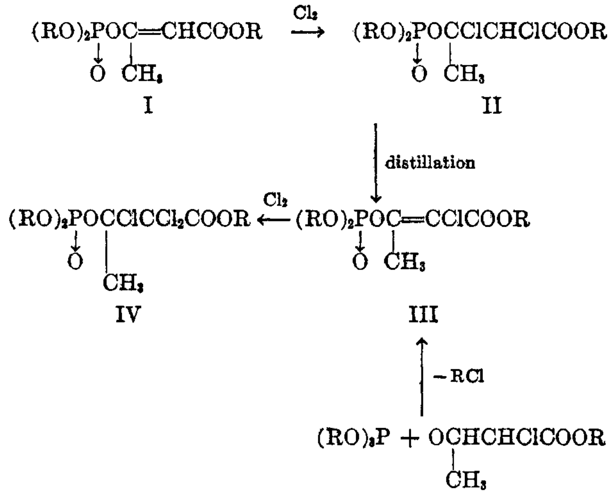
$$(RO)_2\underset{\substack{\downarrow\\ S}}{P}S\underset{\substack{\downarrow\\ S}}{S}P(OR)_2 + BrMgCH{=}CH_2 \rightarrow (RO)_2P(S)SCH{=}CH_2 + (RO)_2P(S)SMgBr$$

LXXXVII LXXXVIII

III. Reactions of Enol Phosphates

A. HALOGENATION

The addition of chlorine or bromine to the ethylenic double bond of dialkyl vinyl phosphates usually proceeds with great ease. Chlorination was carried out by introducing the calculated amount of chlorine into a solution of the phosphate in carbon tetrachloride (70, 159, 261, 308, 309, 313, 342, 345, 352). In a few cases, the addition of a little hydroquinone (19) has been found to enhance the reaction. The resulting dialkyl 1,2-dichloroalkyl phosphates were usually isolated by distillation (table 11), but with the higher alkyl analogs, distillation resulted in partial and sometimes complete decomposition to uncharacterized products or in the elimination of the elements of hydrochloric acid. The latter occurred in the case of diethyl 2-carbethoxy-1-methylvinyl phosphate (I: R = C_2H_5), which upon chlorination and subsequent distillation of II gave the vinyl phosphate (III), identical with the compound prepared directly from triethyl phosphite and α,α-dichloroacetoacetate. III could be converted to the trichloro derivative (IV) by further action of chlorine (261).



The bromination of dialkyl vinyl phosphates took place under conditions similar to those above, yielding the dibromoalkyl esters as brown oils, which could rarely be distilled without considerable decomposition (19, 157, 286, 310, 327, 328).

In a few cases, however, halogenations were found to take an anomalous course, entirely independent of the normal halogen addition, yielding an alkyl halide, a halogen-containing carbonyl compound, and other products of unknown nature (19).

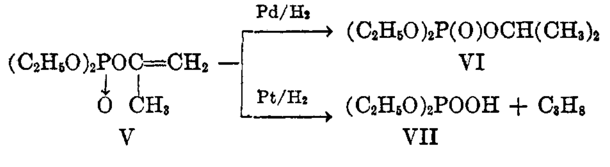
Analogous to the addition of halogen, ethylthio chloride was added to the ethylenic double bond, yielding dialkyl 1-chloro-2-ethylthioalkyl phosphates (143).

The mammalian and insecticidal toxicities of a number of dialkyl 1,2-dihaloalkyl phosphates have been investigated (159, 285, 328), from which the dimethyl 1,2-dibromo-2,2-dichloroethyl phosphate (Dibrom[2]) has found application in the field.

B. HYDROGENATION

Only limited data are available concerning the hydrogenation of vinyl phosphates, but it appears that the nature of the product is affected to a considerable extent by the catalyst and the solvent used.

Diethyl 1-methylvinyl phosphate (V) was found to be hydrogenated to diethyl isopropyl phosphate (VI) in the presence of 10 per cent palladium on charcoal, whereas with the use of a platinum catalyst, reductive cleavage of the enol ester group took place concurrently with remarkable ease, and diethyl hydrogen phosphate (VII) and, presumably, propane (226), were formed.

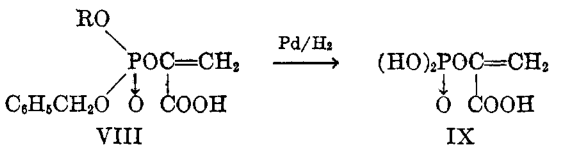


Such a reaction is analogous to the reductive cleavage of vinyl carboxylates with a platinum catalyst (223).

The hydrogenation of diethyl vinyl phosphate to triethyl phosphate in the presence of palladium chloride on charcoal took place readily in cyclohexane, whereas in dioxane no appreciable hydrogenation could be accomplished. A similar observation was made when Raney nickel in ether was used (19).

Attempted hydrogenation of diethyl 1-carbethoxyvinyl phosphate (PEP triethyl ester) and diethyl 2-carbethoxy-1-ethoxyvinyl phosphate with either Raney nickel or palladium on charcoal failed (125). This was probably due to the inactivation of the catalysts by these phosphates, since the hydrogenation of cinnamic acid was immediately stopped by addition of small amounts of these esters.

In contrast to these results, it has been found that benzyl ester groups in vinyl phosphates can be selectively removed under appropriate conditions by hydrogenation (129). The debenzylation of the dibenzyl ester of phosphoenol pyruvate (VIII: R = $CH_2C_6H_5$) and of the sodium salt of the monobenzyl ester (VIII: R = Na) gave good yields of phosphoenol pyruvate (IX) when palladium on charcoal in 50 per cent aqueous methanol was used and the hydrogenation was stopped after the consumption of the theoretical quantity of hydrogen. If the reaction was allowed to proceed beyond this point, the reduction of the ethylenic double bond took place at a rate one-twentieth that of the reductive debenzylation. However, an increase in the methanol content of the solvent caused a more rapid reduction of the double bond; consequently the yields of PEP (IX) were seriously impaired.



For the hydrogenation of PEP, a catalyst of freshly precipitated palladium in glacial acetic acid was found to complete the reaction within 3 min., yielding 1-carboxyethyl dihydrogen phosphate (245).

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[2] Trademark of California Spray-Chemical Corporation.

C. MONODEALKYLATION

Dialkyl vinyl phosphates were found to undergo monodealkylation when heated with alkali halides in suitable solvents for 5–20 min., giving in good yields the alkali salts of alkyl vinyl hydrogen phosphates (128, 129, 271, 395). This selective monodealkylation involving a nucleophilic attack by the halide ion on the alkyl moiety has been previously applied to various trialkyl phosphates (114, 132, 267, 455, 456), tetraalkyl pyrophosphates (123, 132), and dialkylphosphonates (12, 28). The sodium alkyl vinyl phosphates prepared in this manner, using sodium iodide in methyl ethyl ketone or acetone, are listed in table 12, in which it can be seen that methyl, ethyl, and benzyl groups are removed with equal ease.

$$(RO)_2P(O)OR + X^- \rightarrow (RO)_2P(O)O^- + RX$$

TABLE 12

Alkyl vinyl sodium phosphates prepared by monodealkylation of the corresponding dialkyl vinyl phosphates with sodium iodide

	NaO(RO)P(O)OCR′=CR″R‴				Yield	R_f values*	Reference
	R	R′	R″	R‴			
					per cent		
1.....	C_2H_5	H	H	H	42	0.64	(271)
2.....	C_2H_5	H	Cl	Cl	88	0.85	(271)
3.....	CH_3	CH_3	H	$COOCH_3$	70	?	(395)
4.....	C_2H_5	CH_3	H	$COOC_2H_5$	73	0.70	(271)
5.....	$C_6H_5CH_2$	COOH	H	H	64	?	(129)

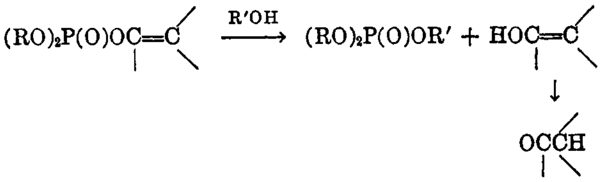
* Solvent: 2-propanol–water–ammonia (8:1:1, descending). Paper: Schleicher & Schüll, No. 2043b.

Application of this method, however, is limited to the relatively stable dialkyl vinyl phosphates. Attempted monodealkylation of 1-methylvinyl, 1-phenylvinyl, and 2,2-dichloro-1-ethoxyvinyl diethyl phosphates resulted in the removal of the ethyl group as well as the enol ester group. Ethyl phosphate and symmetrical diethyl pyrophosphate were the main products (271).

The sodium salts of 2,2-dichlorovinyl- and 2-carbethoxy-1-methylvinyl ethyl hydrogen phosphate (Nos. 2 and 4 in table 12) could be transformed into the corresponding acids by addition of the theoretical amount of hydrochloric acid without hydrolyzing the enol ester group. However, vinyl ethyl hydrogen phosphate, prepared similarly, contained considerable amounts of ethyl dihydrogen phosphate.

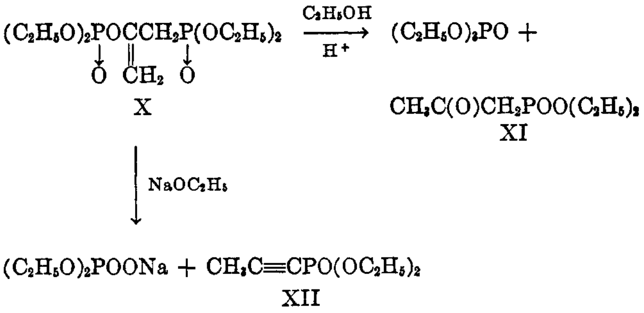
D. ALCOHOLYSIS (TRANSESTERIFICATION)

When dialkyl vinyl phosphates are heated in absolute alcohol in the presence of catalytic amounts of sodium alkoxide or *p*-toluenesulfonic acid, transesterification of the enol ester linkage occurs and the enol is liberated as a carbonyl compound. Since the isomeric phosphonates, which can also be formed during the preparation of enol phosphates by the Perkow reaction, are unable to react with these reagents under the same conditions, this method was used to confirm the structures of many of the newly prepared dialkyl vinyl phosphates (309, 310, 311, 313, 343, 345, 348, 349). The carbonyl compounds so formed were characterized as the semicarbazide, the 2,4-dinitrophenylhydrazone, or the dimedone derivative, and the corresponding trialkyl phosphates were easily obtained by distillation.



$$(RO)_2P(O)OC{=}C \xrightarrow{R'OH} (RO)_2P(O)OR' + HOC{=}C \rightarrow OCCH$$

In the presence of larger amounts of sodium alkoxide, however, the alcoholysis can take an alternative course leading to the formation of alkynyl derivatives (226). Hence, at room temperature in the presence of one molar equivalent of sodium ethoxide, diethyl 1-(diethylphosphonomethyl)vinyl phosphate (X) afforded not only the expected triethyl phosphate and *O,O*-diethyl 2-oxopropylphosphonate (XI), which are the reaction products when catalytic amounts of *p*-toluenesulfonic acid are used, but also diethyl hydrogen phosphate and diethyl propynylphosphonate (XII). The yield of XII increased to 69 per cent when the reaction was carried out at elevated temperature.



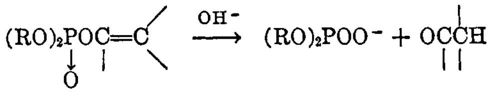
$$\underset{\text{X}}{(C_2H_5O)_2POCCH_2P(OC_2H_5)_2} \xrightarrow[H^+]{C_2H_5OH} (C_2H_5O)_3PO + \underset{\text{XI}}{CH_3C(O)CH_2POO(C_2H_5)_2}$$

$$\downarrow NaOC_2H_5$$

$$(C_2H_5O)_2POONa + \underset{\text{XII}}{CH_3C{\equiv}CPO(OC_2H_5)_2}$$

E. HYDROLYSIS

The alkaline hydrolysis of various dialkyl vinyl phosphates with 0.5 *N* potassium hydroxide at 80°C.



$$(RO)_2POC{=}C \xrightarrow{OH^-} (RO)_2POO^- + OCCH$$

or barium hydroxide at 100°C. was found to cleave only the enol ester linkage. With 0.5 *N* potassium hydroxide at 80°C. the hydrolysis can easily be followed by determining the consumption of base (one molar equivalent). Diethyl 2-carbethoxy-1-methylvinyl phosphate (XIII), however, consumed two moles of base, owing to simultaneous hydrolysis of the carbethoxy group (260, 261).

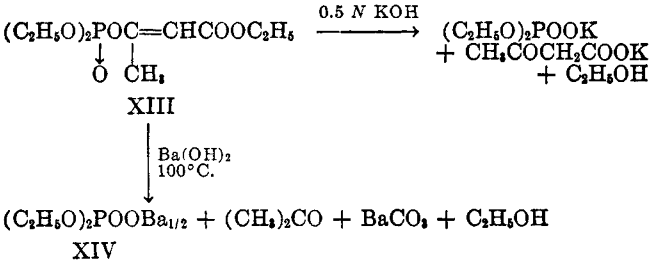
With barium hydroxide at 100°C. the corresponding barium salt of dialkyl hydrogen phosphate is formed in good yield. XIII, however, undergoes simultaneous

TABLE 13

Hydrolysis of dialkyl vinyl phosphates at pH 11 and 28°C. (96)

Vinyl Phosphate	Half-life	
	Trans isomer	Cis isomer
	hours	*hours*
$(CH_3O)_2P(O)OC(CH_3)=CHCOOCH_3$	1.8*	3.0*
$(C_2H_5O)_2P(O)OC(CH_3)=CHCOOC_2H_5$	3.4*	8.9*
$(C_2H_5O)_2P(O)OCH=CHCl$	6.0	11.0
$(CH_3O)_2P(O)OCH=CCl_2$	0.2	

* Cis and trans refer to these compounds as derivatives of *cis*- and *trans*-crotonate, respectively (see page 629).



$$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}O\underset{\underset{CH_3}{|}}{C}=CHCOOC_2H_5 \xrightarrow{0.5\ N\ KOH} (C_2H_5O)_2POOK + CH_3COCH_2COOK + C_2H_5OH$$

XIII

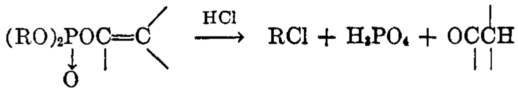
$$\xrightarrow[100°C.]{Ba(OH)_2} (C_2H_5O)_2POOBa_{1/2} + (CH_3)_2CO + BaCO_3 + C_2H_5OH$$

XIV

decarboxylation under these conditions, yielding, in addition to barium diethyl phosphate (XIV), acetone, barium carbonate, and ethanol (260, 261). Exact measurements of rates of hydrolysis at varying hydroxyl-ion concentrations have been made for a number of dialkyl vinyl phosphates (54, 94–96, 98). The half-lives of some, determined at pH 11 and 28°C., are listed in table 13.

Dialkyl vinyl phosphates show a remarkable stability toward water. Diethyl 1-phenylvinyl phosphate, for example, is hydrolyzed only to the extent of 11 per cent after 20 hr. at 100°C. in 30 per cent aqueous ethanol (341). An exception is diethyl 2-carbethoxy-1-ethoxyvinyl phosphate, which is readily hydrolyzed by water at room temperature (271).

The course of the acid hydrolysis of dialkyl vinyl phosphates is dependent upon the strength of the acid used. With hydrochloric acid (1:1) at 100°C. total hydrolysis of all ester groups occurs, forming mainly alkyl chloride, phosphoric acid, and the corresponding ketone (19, 341).



$$(RO)_2\underset{\underset{O}{\downarrow}}{P}O\underset{|}{C}=C\langle \xrightarrow{HCl} RCl + H_3PO_4 + OC\overset{|}{\underset{|\,|}{C}}H$$

Similar results were found for the hydrolysis with 30 per cent sulfuric acid at elevated temperatures (341, 344, 345, 348).

Under milder conditions, however, selective hydrolysis of the enol ester group can be effected, yielding the dialkyl hydrogen phosphate and the corresponding carbonyl compound. Table 14 lists the rates of hydrolysis of various diethyl vinyl phosphates with 0.1 *N* hydrochloric acid–40 per cent ethanol at 85°C., determined by titrating with sodium hydroxide the diethyl hydrogen phosphate formed (123, 271). With the exception of diethyl 2-carbethoxy-1-ethoxyvinyl phosphate (No. 1 in table 14), which hydrolyzes readily at 22°C. ($t_{1/2}$ = 1.74 hr. in 0.1 *N* hydrochloric acid–40 per cent ethanol), none of the investigated diethyl vinyl phosphates are hydrolyzed to any appreciable extent at room temperature.

TABLE 14

Rate of hydrolysis of diethyl vinyl phosphates in 0.1 N hydrochloric acid–40 per cent ethanol at 85°C. (271)

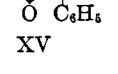
Diethyl Vinyl Phosphate	$K \times 10^3$ *	$t_{1/2}$
	min. $^{-1}$	*hours*
$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}O\underset{\underset{OC_2H_5}{\vert}}{C}=CHCOOC_2H_5$	130	0.1
$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}O\underset{\underset{CH_3}{\vert}}{C}=CH_2$	14.88	0.78
$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}O\underset{\underset{C_6H_5}{\vert}}{C}=CH_2$	6.46	1.79
$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}O\underset{\underset{OC_2H_5}{\vert}}{C}=CCl_2$	3.77	3.06
$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}O\underset{\underset{COOC_2H_5}{\vert}}{C}=CH_2$	2.38	4.86
$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}OCH=CCl_2$	1.34	8.56
$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}O\underset{\underset{CH_3}{\vert}}{C}=CHCOOC_2H_5$	0.99	11.71
$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}OCH=CH_2$	0.46	25.21
$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}O\underbrace{CH=CH(CH_2)_3CH_2}$	0.37	31.59
$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}OC_2H_5$	0.037	308.70

* *K* represents the unimolecular reaction constants, calculated with the formula

$$K = \frac{2.303}{t_2 - t_1}\log_{10}\frac{100}{100 - x}$$

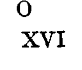
x being the percentage of hydrolyzed vinyl phosphate. The molecularity of the reaction has not been established.

The greater stability of the ethyl ester groups compared with the enol moiety was demonstrated by the following facts. The rate of hydrolysis of triethyl phosphate (No. 10 in table 14) was considerably smaller than that of the most unreactive vinyl phosphate (No. 9 in table 14). Semiquantitative measurements of the hydrolysis of diethyl 1-phenylvinyl phosphate (XV) and the isomeric *O,O*-diethyl benzoylmethylphosphonate (XVI) in 30 per cent ethanol–water at 140°C. showed that XV is hydrolyzed four to five times faster than XVI, the latter involving the saponification of an ethyl group (341).



$$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}O\underset{\underset{C_6H_5}{|}}{C}=CH_2$$

XV



$$(C_2H_5O)_2\underset{\underset{O}{\downarrow}}{P}CH_2COC_6H_5$$

XVI

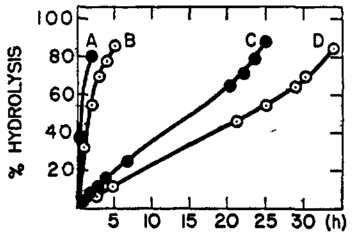


FIG. 1. The hydrolysis of diethyl 1-phenylvinyl phosphate at 85°C. (271). Curve A, 1 *N* hydrochloric acid–40 per cent ethanol. Curve B, 0.1 *N* hydrochloric acid–40 per cent ethanol. Curve C, 0.01 *N* hydrochloric acid–40 per cent ethanol. Curve D, water–40 per cent ethanol.

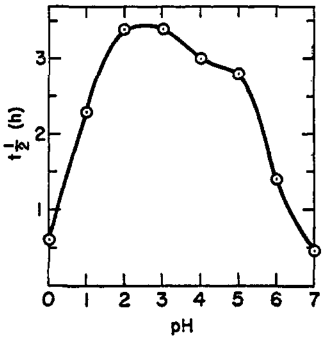


FIG. 2. The hydrolysis of dimethyl 2,2-dichlorovinyl phosphate at 70°C. (301).

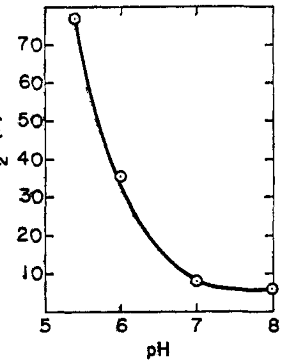


FIG. 3. The hydrolysis of dimethyl 2,2-dichlorovinyl phosphate at 37.5°C. (294).

In vinyl phosphates containing carbalkoxy groups, the concurrent hydrolysis of the carboxylic ester groups interfered considerably with the determination of the cleavage of the enol ester linkage. Thus the *K* values of these esters (Nos. 4, 5, and 7 in table 14), although based on measurements made during the first 60 per cent of the hydrolysis, are a little high, owing to hydrolysis of the carboxylic ester group.

Table 14 demonstrates that substitution of the vinyl group at the 1-position (Nos. 2, 3, and 5) increases the rate of the hydrolysis, the extent of which depends upon the nature of the substituent. The order of decreasing reactivity is $CH_3 > C_6H_5 > COOC_2H_5 > H$. The phosphates Nos. 1 and 4 in table 14 can be regarded as derivatives of a ketone, namely as ketene acylals, which as such possess a very reactive vinyl ester group. No. 1 was found to be the most reactive enol phosphate hitherto investigated.

There is no conformity as to whether the acid hydrolysis is acid catalyzed or not. Diethyl 1-phenylvinyl phosphate showed a considerable increase in the rate of hydrolysis with increase of the acidity. Under strongly acidic conditions (1 *N* to 0.1 *N* hydrochloric acid) the hydrolysis curves (figure 1, curves A and B) were of a regular exponential shape, but under weakly acidic and neutral conditions (figure 1, curves C and D) an increase of the rate, with progression of the hydrolysis, took place, owing to autocatalysis by the liberated diethyl hydrogen phosphate (271). The fact that some enol phosphates easily underwent acidolysis with dialkyl hydrogen phosphates (see page 627), whereas the less acidic carboxylic acids gave no reaction, also indicated an acid catalysis of cleavage of the enol phosphate bond.

The acid hydrolysis of dimethyl 2,2-dichlorovinyl phosphate, however, revealed a decrease in the rate of hydrolysis with increasing acidity, as demonstrated by figures 2 and 3. These discrepancies are thus far not explainable.

Concerning the type of cleavage of the enol phosphate bond during acid hydrolysis it would be expected, on the basis of theoretical reasons, that fission of the phosphorus–oxygen bond occurs, whereas hydrolysis of the trialkyl phosphate was shown to involve cleavage of the carbon–oxygen bond (69, 79). The formation of pyrophosphates as a result of the acidolysis of dialkyl vinyl phosphates with dialkyl hydrogen phosphates, however, indicates strongly cleavage of the phosphorus–oxygen bond of the enol ester group. Formation of salts of alkyl vinyl phosphates upon dealkylation with sodium iodide (page 624), in which the nucleophile (iodide ion) attacks the alkyl group rather than the double bond, also indicates that fission of the carbon–oxygen bond is not involved in the hydrolysis of the vinyl group. Furthermore, comparison of the relative rates of hydrolysis of ethyl and vinyl acetates (392, 393) and triethyl and diethyl vinyl phosphates (table 15) shows that the differences in the reactivity are considerably larger in the case of the diethyl phosphates (1:12.45) than in the case of the corresponding acetates (1:1.23). Since the hydrolysis of both of the acetates involves fission of an acyl–oxygen bond, the unexpected large difference in the rates of hydrolysis of the corresponding phosphates can only be explained by a different reaction mechanism, hydrolysis of the triethyl phosphate involving fission of a carbon–oxygen bond in the nonprotonated ethyl ester group and hydrolysis of the diethyl vinyl phosphate involving fission

TABLE 15

Comparative rates of hydrolysis of ethyl and vinyl acylates

Ester	$K \times 10^{-3}$	Relative Rate	Reference
	minutes		
$(C_2H_5O)_2P(O)OCH_2CH_3$	0.037	1	(271)
$(C_2H_5O)_2P(O)OCH{=}CH_2$	0.46	12.45	(271)
$CH_3C(O)OCH_2CH_3$	6.58	1	(393)
$CH_3C(O)OCH{=}CH_2$	8.13	1.23	(392)

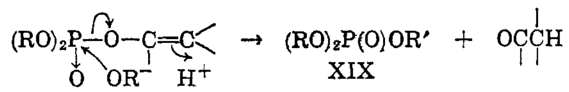
of a phosphorus–oxygen bond in the presumably protonated enol ester group. A possible mechanism of the acid hydrolysis of dialkyl vinyl phosphates, based on acid catalysis and fission of the phosphorus–oxygen bond, has been discussed (271).

The hydrolysis in either alkaline or acid medium of secondary phosphates containing a vinyl ester group has not yet been investigated. Nevertheless, it can be assumed from their acidolysis (page 627) that the cleavage of the enol ester group is easier than in the corresponding dialkyl vinyl phosphates (271).

Only three vinyl dihydrogen phosphates are known: the vinyl (XVII), 1-carboxyvinyl (PEP), and 2-carboxy-1-methylvinyl phosphates (XVIII). Whereas XVII seems to be extremely labile toward acids and the free acid could not be prepared from the salt without cleaving the enol ester linkage (64), PEP and XVIII are somewhat more stable. XVIII yielded acetone and carbon dioxide on heating with dilute acid (240). The unimolecular reaction constant of PEP during hydrolysis in 1 *N* hydrochloric acid at 100°C. is 3.5×10^{-3} ($t_{1/2} = 8.6$ min.) (65, 101, 102, 245, 366, 373).

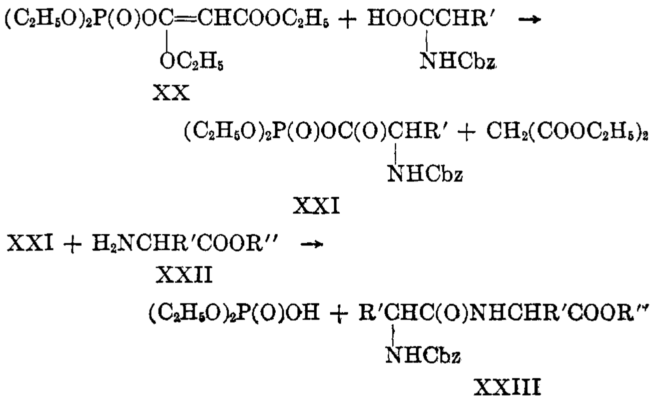
F. ACIDOLYSIS

Certain dialkyl vinyl phosphates react with carboxylic acids and substituted phosphoric acids with cleavage of the enol ester linkage yielding mixed anhydrides: namely, acyl phosphates (XIX: R′ = RC(O)) and pyrophosphates (XIX: R′ = (RO)$_2$P(O)).



In this acidolysis reaction the different enol phosphates showed, although this has not been established quantitatively, the same differences in reactivity as were found for the hydrolysis in 0.1 *N* hydrochloric acid. Diethyl 2-carbethoxy-1-ethoxyvinyl phosphate (XX), which was found to be the most acid-labile enol phosphate, reacted easily with carboxylic acids at room temperature, giving the corresponding acyl phosphates in good yields (123, 125, 130). Since the by-product in this reaction is diethyl malonate, which can easily be removed by distillation, the acidolysis of this vinyl phosphate represents a convenient method for the preparation of dialkyl acyl phosphates. Upon acidolysis of XX with alkyl dihydrogen phosphates the rather inaccessible P_1-diethyl P_2-alkyl pyrophosphates are formed (table 16). When nucleotides, such as thymidine 3′-phosphate or adenosine 3′-phosphate, are used in the acidolysis of XX, the diethyl thymidyl and adenyl pyrophosphates, initially formed, can undergo further reaction to form oligonucleotides (130, 131).

Also, a peptide synthesis can be derived from this reaction, which, by analogy with the enzymatic reaction (74, 215), involves the formation of anhydrides of phosphoric acid and amino acids (126, 127). XX readily reacted with *N*-blocked amino acids, giving the mixed anhydride (XXI), which without isolation yielded dipeptide derivatives (XXIII) in high yields on subsequent aminolysis with esters or salts of other amino acids (XXII). *N*-Carbobenzoxyglycylglycine



$$(C_2H_5O)_2P(O)O\underset{\underset{\text{XX}}{OC_2H_5}}{\underset{|}{C}}{=}CHCOOC_2H_5 + HOO\underset{NHCbz}{\underset{|}{C}}HR' \rightarrow$$

$$(C_2H_5O)_2P(O)OC(O)\underset{NHCbz}{\underset{|}{C}}HR' + CH_2(COOC_2H_5)_2 \quad \text{XXI}$$

$$\text{XXI} + \underset{\text{XXII}}{H_2NCHR'COOR''} \rightarrow$$

$$(C_2H_5O)_2P(O)OH + R'\underset{NHCbz}{\underset{|}{C}}HC(O)NHCHR'COOR'' \quad \text{XXIII}$$

Cbz = carbobenzoxy.

TABLE 16

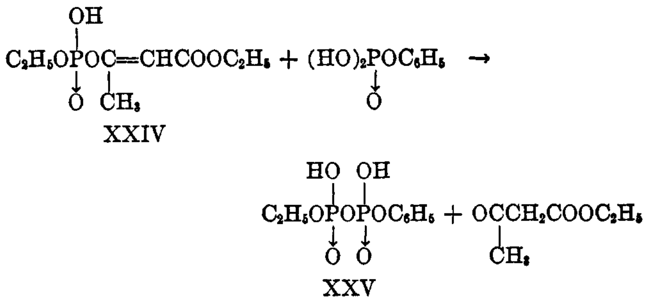
Acidolysis of diethyl 2-carbethoxy-1-ethoxyvinyl phosphate (XX) (12–15 hr. at 37°C.) (123, 125)

Acidolysis of XX with	Product	Yield	Boiling Point
		per cent	*°C.*
Acetic acid	$(C_2H_5O)_2P(O)OC(O)CH_3$	28	70/0.2 mm.
Propionic acid	$(C_2H_5O)_2P(O)OC(O)C_2H_5$	63	68/0.05 mm.
Butyric acid	$(C_2H_5O)_2P(O)OC(O)C_3H_7$	64	76–77/0.03 mm.
Valeric acid	$(C_2H_5O)_2P(O)OC(O)C_4H_9$	66	79/0.05 mm.
Caproic acid	$(C_2H_5O)_2P(O)OC(O)C_5H_{11}$	66.5	82–84/0.01 mm.
Benzoic acid	$(C_2H_5O)_2P(O)OC(O)C_6H_5$	55	110–111/0.01 mm.
p-Nitrophenol	$(C_2H_5O)_2P(O)OC_6H_4NO_2$-*p*	71	139–140/0.05 mm.
Diethyl hydrogen phosphate	$(C_2H_5O)_2P(O)OPO(OC_2H_5)_2$	85	105–106/0.05 mm.
Phenyl dihydrogen phosphate	$(C_2H_5O)_2P(O)OP(O)(OC_6H_5)OH$	?	—
Adenosine monophosphate	Sodium *O,O*-diethyl adenosine diphosphate	90	—

and *N*-carbobenzoxyglycyl-D,L-phenylalanine, for example, were synthesized in yields of 82 and 61 per cent by this method, using the corresponding amino acid derivatives (126, 127).

None of the other dialkyl vinyl phosphates hitherto investigated were found to be comparable to XX in their reactivity toward carboxylic and phosphoric acids. Diethyl 2,2-dichloro-1-ethoxyvinyl phosphate (124, 125, 271) and diethyl 2-carbethoxy-2-chloro-1-ethoxyvinyl phosphate (312), being ketene acylals like XX, underwent acidolysis in the same manner as XX; however, the reaction temperature had to be increased. In the acidolysis of 1-methyl-1-phenylvinyl phosphate and 1-carbethoxyvinyl diethyl phosphate with diphenyl hydrogen phosphate, the corresponding tetrasubstituted pyrophosphates could be detected on chromatograms, whereas with carboxylic acids apparently no reaction occurred (271).

Only limited data are available for the acidolysis of secondary phosphates containing an enol ester group. 2,2-Dichlorovinyl and 2-carbethoxy-1-methylvinyl ethyl hydrogen phosphates (XXIV) failed to react with benzoic acid, whereas with phenyl dihydrogen phosphate (5 hr. in acetonitrile at 80°C.) the expected pyrophosphate (XXV) was formed, as well as considerable amounts of P_1,P_2-diethyl and P_1,P_2-diphenyl pyrophosphates (271).



$$C_2H_5O\overset{OH}{\underset{\substack{\downarrow\\ O}}{P}}O\underset{CH_3}{C}{=}CHCOOC_2H_5 + (HO)_2\underset{\substack{\downarrow\\ O}}{P}OC_6H_5 \rightarrow$$

XXIV

$$C_2H_5O\overset{HO}{\underset{\substack{\downarrow\\ O}}{P}}O\overset{OH}{\underset{\substack{\downarrow\\ O}}{P}}OC_6H_5 + O\underset{CH_3}{C}CH_2COOC_2H_5$$

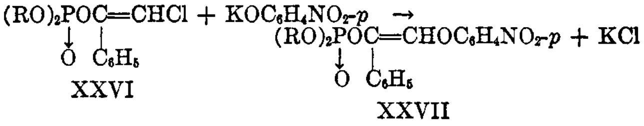
XXV

The reaction of phosphoenol pyruvate (PEP) with phosphoric acids, although having a very important role in carbohydrate metabolism—namely, the enzymatic acidolysis by adenosine monophosphate to form adenosine diphosphate and pyruvic acid—has not yet been achieved *in vitro*. The rather slow acidic hydrolysis of phosphoenol pyruvate (65, 101, 102, 245, 373) and its subsequent classification as intermediate between stable and labile organic phosphates (268) indicate that acidolysis *in vitro* would not proceed under conditions comparable to those *in vivo*.

G. SUBSTITUTION OF HALOGEN IN THE VINYL ESTER GROUP

Halogen in the 2-position of the vinyl group can be substituted without cleaving the vinyl ester linkage, as was shown by replacing chlorine with *p*-nitrophenoxy and ethylthio groups.

Dimethyl and diethyl 2-chloro-1-phenylvinyl phosphates (XXVI: R = CH_3, C_2H_5) gave, when heated with potassium *p*-nitrophenoxide, the corresponding 2-*p*-nitrophenoxy-1-phenylvinyl phosphates (XXVII) in yields of 27 and 38 per cent, respectively (308). In dialkyl 2,2-dichlorovinyl phosphates only one chlorine atom was substituted by a *p*-nitrophenoxy group (308), whereas upon treatment with potassium ethanethiolate both were replaced, giving a 2,2-di-(ethylthio)vinyl phosphate (XXVIII) (144).



$$(RO)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{C_6H_5}{C}{=}CHCl + KOC_6H_4NO_2\text{-}p \rightarrow (RO)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{C_6H_5}{C}{=}CHOC_6H_4NO_2\text{-}p + KCl$$

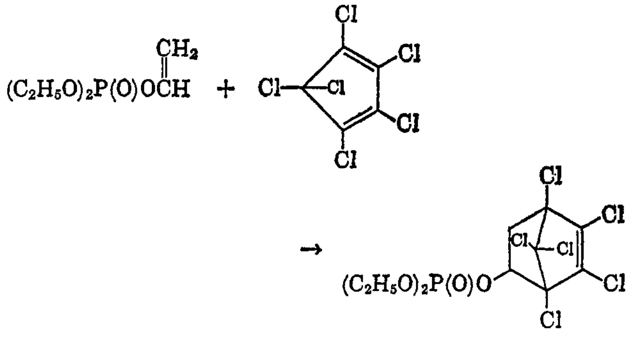
XXVI XXVII

$$(C_2H_5O)_2P(O)OCH{=}CCl_2 + 2KSC_2H_5 \rightarrow (C_2H_5O)_2P(O)OCH{=}C(SC_2H_5)_2 + 2KCl$$

XXVIII

H. DIELS–ALDER REACTION

By analogy with vinyl carboxylates, dialkyl vinyl phosphates also may participate in the Diels–Alder reaction, acting as the dienophile. This was demonstrated by the reaction of diethyl vinyl phosphate with hexachlorocyclopentadiene to give the adduct XXIX in 65 per cent yield (437). Other dienes have been used in this reaction, but the products were not characterized (437).



XXIX

I. POLYMERIZATION

Vinyl phosphates possess the ability to polymerize in a manner analogous to the vinyl esters of carboxylic acids. The polymerization conditions depend considerably on the nature of the vinyl phosphate (table 17). The triethyl ester of phosphoenol pyruvate readily polymerizes on prolonged standing and sometimes during distillation (271), whereas others require the addition of an initiator (e.g., dibenzoyl peroxide) and elevated temperatures (178, 435). Table 17 gives the conditions used for the polymerization of various vinyl phosphates and phosphonates containing a vinyl ester group and the properties of the polymers so formed. From these data it can be concluded that the esters containing one double bond form linear polymers of

TABLE 17

Polymerization of vinyl phosphates

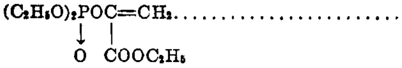
Vinyl Phosphate $RR'P(O)OCH{=}CH_2$ R	R′	Dibenzoyl Peroxide	Temperature	Time	Nature of Polymer	References
		per cent	°C.	hours		
C_2H_5O	C_2H_5O	?	Heating	2	Colorless viscous liquid	(435)
CH_3	C_4H_9O	1.45–1.84	50–70°C.	200	Yellow liquid	(178)
CH_3	$ClCH_2CH_2O$	1.5	50–70°C.	150	Soft yellow mass	(178)
CH_3	C_6H_5	1.5	50–80°C.	200	Yellow, thick liquid	(178)
$RP(O)(OCH{=}CH_2)_2$						
R = CH_3		1.4–1.9	50°C.	50	Yellow solid	(178)
R = C_2H_5		1.3	50–70°C.	100	Yellow solid	(178)
R = CH_2Cl		0.7	50°C.	30	Yellow solid	(178)
R = C_6H_5		1.2	50°C.	150	Black solid	(178)
R = C_6H_5		1–3	80°C.	?	Soft tacky solid	(422, 423)
R = $CH_2{=}CH_2$		0.7	70°C.	30	Yellow solid	(178)
R = $CH_2{=}CH_2O$		1	50–70°C.	5	Yellow solid	(178)
 $(C_2H_5O)_2\underset{\overset{\downarrow}{O}}{P}O\underset{\overset{\vert}{COOC_2H_5}}{C}{=}CH_2$		—	25°C.	Weeks	Light yellow, tacky solid	(271)
		1.5	25°C.	5	Light yellow, tacky solid	(271)

TABLE 18

Content of the α-isomer in dialkyl vinyl phosphates prepared by the Perkow reaction (96)

$(RO)_2P(O)OCR'{=}CR''COOR'''$ R′	R″	R‴	R	Amount of α-Isomer in Mixture
				per cent
CH_3	H	CH_3	CH_3	67
CH_3	H	C_2H_5	C_2H_5	67
CH_3	H	C_3H_7	C_2H_5	81
CH_3	H	C_4H_9	C_2H_5	80
CH_3	H	iso-C_4H_9	C_2H_5	86
CH_3	H	*tert*-C_4H_9	C_2H_5	86
CH_3	CH_3	C_2H_5	C_2H_5	89
CH_3	iso-C_5H_{11}	C_2H_5	C_2H_5	64
C_6H_5	H	C_2H_5	C_2H_5	88
$CH_2COOC_2H_5$	H	C_2H_5	C_2H_5	90
$COOC_2H_5$	H	C_2H_5	CH_3	78
$COOC_2H_5$	H	C_2H_5	C_2H_5	83
$COOC_2H_5$	CH_3	C_2H_5	C_2H_5	71
$COOC_2H_5$	C_2H_5	C_2H_5	C_2H_5	74

comparatively low molecular weight, whereas esters with two or three double bonds, polymerizing more rapidly, probably form crosslinked polymers, since they are insoluble in organic solvents.

Vinyl phosphates can also be used for copolymerization, as was shown with diethyl vinyl phosphate, which gave solid copolymers with styrene, methyl methacrylate, and acrylonitrile (422, 423).

J. OZONOLYSIS

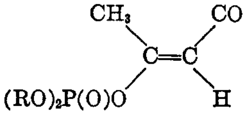
In order to confirm the presence of the ethylenic double bond in the enol phosphate ozonolysis has been applied, giving the corresponding carbonyl compounds (226, 311, 342, 344–346, 348).

IV. PHYSICAL PROPERTIES OF ENOL PHOSPHATES

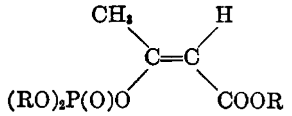
A. GEOMETRIC ISOMERISM

With di- or trisubstituted vinyl phosphates having different groups attached to the ethylenic double bond geometric isomerism is possible. Thus it would be expected that these compounds (with the exception of cycloalkenyl phosphates) accumulate as mixtures of the cis and trans isomers, their relative proportion depending on the steric requirements of the reaction used for preparation.

Experimental evidence was first put forth by Casida (94), who succeeded in separating a number of dialkyl 2-carbalkoxy-1-methylvinyl phosphates into the two isomers (I and II, respectively) by partition chromatography on silica gel columns. The materials eluted with organic solvents ("α-isomers") were less stable to hydrolysis (table 13) and were ten to one hundred times more toxic to insects and mammals (table 19) than the more water-soluble fractions, next eluted ("β-isomers"). Therefore, the corresponding α-isomers were assumed to have the *trans*-crotonate configuration[8] (II) (94, 95, 98).



I



II

Other investigators separated the isomeric mixture of the two dimethyl 2-carbomethoxy-1-methylvinyl phosphates by counter-current distribution in an ether–water system and arrived at the same conclusions as to the configuration of the two isomers from hydrolysis studies (395). More recent investigations, however, disproved these configurational assignments on the basis of nuclear magnetic resonance and infrared absorption spectra and other physical evidence (167, 405). In the case of dimethyl 2-carbomethoxy-1-

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[8] Trans refers to these compounds as derivatives of *trans*-3-oxycrotonate. Considering, however, the positions of the dialkyl phosphoryloxy and the carbalkoxy groups, as was done originally (94), the same isomer (I) has the cis configuration.

TABLE 19

Comparative toxicities of some dialkyl vinyl phosphates (*96*)

Item	Phosdrin® VII: R = CH_3			Ethylphosdrin VII: R = C_2H_5				$(C_2H_5O)_2P(O)OCH{=}CHCl$			DDVP
	Cis isomer* (I)	Trans isomer* (II)	Technical†	Cis isomer* (I)	Trans isomer* (II)	Technical		Cis isomer	Trans isomer	Technical	
						Shell OS 1808†	Shell NC 13‡				
LD_{50} (topical) for female housefly in mg./kg.	0.27	23	0.45	0.87	80	1.9	22.5	1	80	2.7	0.6
LD_{50} (systemic) for pea aphids in p.p.m.	—	—	0.8	—	—	15	100	—	—	12	3
LD_{50} (subcutaneous) for female white rat in mg./kg.	0.25	25	0.8	0.35	35	—	—	12	60	—	6
pI_{50} for blood cholinesterase§	6.1	4.4	—	7.8	5.9	—	—	5.9	4.9	—	3.7

* Referring to the isomeric compounds as derivatives of *cis*- and *trans*-crotonate, respectively.

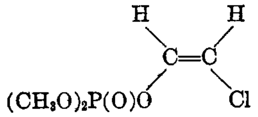
† Contains about 67 per cent of the cis isomer.

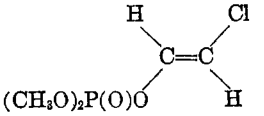
‡ Consists almost exclusively of the trans isomer.

§ The negative logarithm of the molar concentration of the inhibitor which results in 50 per cent whole blood cholinesterase inhibition.

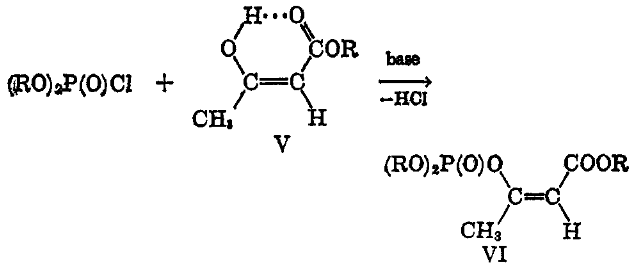
methylvinyl phosphate the α-isomer, predominating in the mixture and having the higher toxicity and hydrolytic reactivity, has the *cis*-crotonate structure (I: R = CH_3), whereas the less reactive β-isomer has the *trans*-crotonate configuration (II: R = CH_3). Thus it seems reasonable to assign the *cis*-crotonate structure also to the α-isomers of the other 2-carbalkoxy-1-methylvinyl phosphates that have been prepared (96). Table 18 lists the amounts of the α-isomer (*cis*-crotonate configuration) obtained from the isomeric mixtures which accumulate upon preparation by the Perkow reaction.

Assignment of configuration has also been made to a related pair of dimethyl 2-chlorovinyl phosphates. As revealed by the nuclear magnetic resonance spectrum the product, obtained by a Perkow reaction of dichloroacetaldehyde with trimethyl phosphite, consisted of a mixture of 80 per cent of the cis isomer (III) and 20 per cent of the trans compound (IV) (405).


III


IV

In contrast to this, enol phosphates prepared by the reaction of dialkyl phosphorochloridate and an enolate apparently consist almost exclusively of the isomer that has the two largest substituents in the cis position. Diethyl 2-carbethoxy-1-methylvinyl phosphate, prepared by this method, contained more than 90 per cent of the isomer with the *trans*-crotonate structure (VI: R = C_2H_5) (94, 96, 405). The reason is to be found in the stereochemistry of this reaction. The enol form of acetoacetate has been shown to have predominantly the *trans*-crotonate structure (V) (232). Thus, upon reaction with dialkyl phosphorochloridate the vinyl phosphate with the same configuration (VI) is formed.


V

VI

B. ABSORPTION SPECTRA

The infrared spectra of a considerable number of enol phosphates have been determined (18, 72, 94, 125, 129, 171, 226, 271, 276, 308–312, 395, 405). Generally, the phosphate ester group caused no profound change in the characteristics of the spectrum of the parent compound. In diethyl vinyl phosphates the absorption peak of the C=C stretching vibration normally occurred within the range 1660–1640 cm.$^{-1}$, the exact position depending upon the nature of the substituents. The absorption of the P=O group occurs in all hitherto investigated enol phosphates in the expected region of 1300–1250 cm.$^{-1}$, sometimes as doublets. Absorptions in the 1165–1155 cm.$^{-1}$ region, to be correlated with the POC_2H_5 groups, are very distinct in some cases (e.g., 1-methylvinyl, 1-phenylvinyl, and 2,2-dichlorovinyl diethyl phosphates) but show no constancy in position in others (271).

The infrared absorption spectra of the few, hitherto prepared alkyl vinyl hydrogen phosphates and vinyl dihydrogen phosphates show the same patterns as the fully esterified parent compound (271).

Ultraviolet absorption spectra have been reported only for 1-methylvinyl and 1,2-dimethylvinyl diethyl phosphates (46, 47), both showing an absorption maximum in the 2500-A. region.

C. PAPER CHROMATOGRAPHY

Enol phosphates can readily be chromatographed without decomposition, by using the usual solvent systems and developing with the molybdate reagent (224), followed by irradiation with ultraviolet light (68).

With 2-propanol–water–ammonia (8:1:1, descending) dialkyl vinyl phosphates usually show R_f values of about 0.9, with the exception of diethyl 2-carbethoxy-2-ethoxyvinyl phosphate, which is completely hydrolyzed by this solvent (271). The R_f values of alkyl vinyl phosphates are, as far as is known, within the range of 0.65–0.85 (see table 12, page 624). In some cases other solvent systems have also been used (13, 294, 394, 395).

Of the vinyl dihydrogen phosphates only PEP (1-carboxyvinyl dihydrogen phosphate) has been investigated in its chromatographic behavior. The R_f values in various solvents have been listed (73).

V. Insecticidal Properties of Enol Phosphates

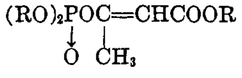
The development of organophosphorus insecticides is largely due to the work of Schrader prior to and during World War II. As early as 1947 he described two enol phosphates as quite effective insecticides (378, 379). In the course of the evaluation of thousands of phosphorus compounds for their insecticidal qualities (293) enol phosphates have found considerable attention. The insecticidal properties and merits of about two hundred dialkyl vinyl phosphates have been reported, of which, however, only three have been marketed in this country: Phosdrin®,[4] DDVP,[5] and Phosphamidon.

A detailed discussion and evaluation of the insecticidal qualities of the individual enol phosphates is beyond the scope of this review. Thus no attempt will be made at an exhaustive treatment of the available literature—well over one hundred and fifty papers have appeared on this matter—but only a rather brief description of the general features will be given.

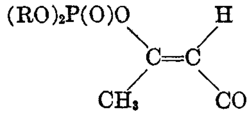
The excellent systemic, contact, and fumigant properties of Phosdrin® (VII: R = CH_3; Shell OS 2046) were first reported in 1953 by Shell Chemical Corporation (117, 118, 402). It has been marketed since 1956 (434) and has been applied frequently for economic control of insects. Excellent results in laboratory and field tests were obtained against insect pests such as *Homoptera* (aphid) (24, 81, 82, 117, 136, 187, 191, 230, 263, 391, 400–402, 433, 450), *Arachnida* (117, 210, 229, 239, 363, 388, 402, 429, 430, 434), and *Lepidoptera*, in particular the cabbage worm and cabbage looper (84, 242, 290, 386, 427, 428, 432, 448), the corn earworm (87, 88, 139, 152, 175, 176, 249, 389, 431), and the cotton leafworm (14, 136). However, it was used for the control of many other insect species such as *Diptera* (94, 96, 98, 117, 133, 134, 161, 162, 168, 169, 196, 204, 215, 216, 222, 241, 263, 385, 402), *Coleoptera* (24, 163, 174, 213, 253), *Heteroptera* (217, 291, 358, 385, 408, 433, 434), *Homoptera* (191, 326), *Lepidoptera* (60, 86, 90–92, 175, 176, 195, 200, 202, 208, 292, 327, 358, 362, 365, 424, 434), and *Thysanoptera* (203, 359, 360, 449). Phosdrin® is absorbed by the plant shortly after application and is rapidly translocated throughout the plant (98, 117, 118). It is much less persistent than most systemic insecticides, its insecticidal activity being negligible 24 hr. after application (98, 118, 146); thus it can be used close to harvest time without danger of hazardous residues. The effectiveness of Phosdrin® is not, therefore due to residual action, but rather to very high per cent of kill of the insects present at the time of application and to some ovicidal action (434). The tolerances for residues of Phosdrin® in many plants have been established (22).

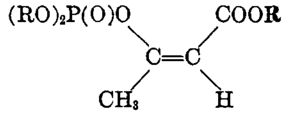
A comparative evaluation of the toxicities of Phosdrin® and fourteen other organophosphorus insecticides toward several insect species showed Phosdrin® to be about in the same range of effectiveness as paraoxon (diethyl *p*-nitrophenyl phosphate) and methyl parathion (dimethyl *p*-nitrophenyl phosphorothionate) and superior to malathion (dimethyl *S*-1,2-dicarbethoxyethyl phosphorothiolothionate) (263). The acute and chronic toxicity to mammals is similar to that of Systox® (a mixture of *O*,*O*-diethyl *O*-2-ethylthioethyl phosphorothionate and *O*,*O*-diethyl *S*-2-ethylthioethyl phosphorothiolate), parathion (diethyl *p*-nitrophenyl phosphorothionate), and Schradan (octamethylpyrophosphoramide) (96, 98, 207, 251, 252, 263, 300, 371, 434). The toxicity to honey bees, however, is relatively high (21, 415). In one case phytotoxic symptoms have been observed on plants (201).

More detailed studies revealed that technical Phosdrin®, prepared by the Perkow reaction, is essentially a mixture of the two geometrical isomers (see page 629), consisting of about two-thirds of the *cis*-crotonate isomer (I: R = CH_3) and one-third of the *trans*-crotonate isomer (II: R = CH_3) (167, 405).


$$\underset{\downarrow \atop O}{(RO)_2P}OC\underset{| \atop CH_3}{=}CHCOOR$$

VII


I


II

The *cis*-crotonate isomer was found to be 10 to 100 times more toxic to insects and mammals than the *trans*-crotonate isomer (table 19), emphasizing the importance of steric configuration in the specificity of action (94, 96, 98, 394, 395).

Ethylphosdrin[6] (VII: R = C_2H_5) was found to be generally less toxic to insects and mammals than Phosdrin® (94, 96, 98, 402, 438). The *cis*-crotonate isomer in this case (I: R = C_2H_5) also revealed a higher insecticidal and mammalian activity than the *trans*-crotonate isomer (II: R = C_2H_5) (table 19). Thus the technical

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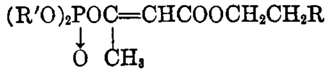
[4] Registered trademark of Shell Chemical Corporation.

[5] DDVP = dimethyl 2,2-dichlorovinyl phosphate.

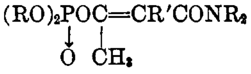
[6] Name suggested by the author.

product, prepared according to the Perkow reaction (Shell OS 1808) and containing about 67 per cent of the *cis*-crotonate isomer, had a considerably higher activity than the compound obtained from diethyl phosphorochloridate and the sodium enolate of ethyl acetoacetate (NC 13), which consisted almost exclusively of the *trans*-crotonate isomer (94, 96). Both compounds, Shell OS 1808 (20, 88, 239, 241, 270) and NC 13 (151, 378), have been widely tested.

Numerous analogs of Phosdrin® have been tested for their suitability as insecticides. Replacement of the alkyl group in the carbalkoxy moiety of Phosdrin® and ethylphosdrin by higher homologs, such as propyl and butyl, gave a decrease of the insecticidal activity (96, 402), whereas compounds of the type of VIII (R being an acyloxy or an acylamido group) are in the same effectivity range as Phosdrin® but have a longer period of persistence (319, 406, 407). Replacing the 2-carbalkoxy group by an *N*-substituted carbamido group led to useful systemic insecticides of the type of IX, of which Shell SD 3562 (IX: R = CH_3, R′ = H) (83, 116, 119, 147, 197, 317, 325, 389, 409, 439) and in particular Phosphamidon[7] (X) (62, 78, 147, 197, 206, 218, 220, 230, 304, 306, 317, 326, 354, 416, 450, 453) have quite promising insecticidal qualities. Compounds of the type of XI and XII (R = CH_3 or C_2H_5), differing from Phosdrin® in the alkyl substituents of the dialkyl phosphoryl group, have excellent properties as contact insecticides and are superior to Phosdrin® for certain uses (403, 438).


$(R'O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{|\\ CH_3}}{C}=CHCOOCH_2CH_2R$

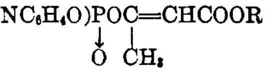
VIII


$(RO)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{|\\ CH_3}}{C}=CR'CONR_2$

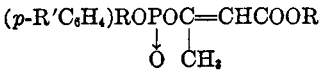
IX


$(CH_3O)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{|\\ CH_3}}{C}=CClCON(C_2H_5)_2$

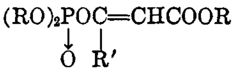
X


$(p\text{-}O_2NC_6H_4O)\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{|\\ CH_3}}{C}=CHCOOR$

XI


$(p\text{-}R'C_6H_4)RO\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{|\\ CH_3}}{C}=CHCOOR$

XII


$(RO)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{|\\ R'}}{C}=CHCOOR$

XIII

Modifying the substituent in the 1-position of the vinyl group in Phosdrin® gave no increase in the insecticidal activity, although the compounds tested [XIII, R′ being C_6H_5 (96, 308, 309), CH_2COOR (189), COOR (96), and other groups (308, 309, 311, 312)] were prepared by the Perkow reaction and thus predominantly consisted of the more toxic geometrical isomer (96).

Some thio analogs of Phosdrin® have also been investigated, but showed no apparent superiority over Phosdrin® (137, 308, 309, 311, 312)

The insecticidal behavior of DDVP (XIV: dimethyl 2,2-dichlorovinyl phosphate) has been thoroughly investigated, since it was first described in 1954–55 (70, 276, 286). Its insecticidal spectrum is wide, as shown by the studies made on many different insects. Against houseflies it showed an extremely high toxicity compared with other insects and mammals (54, 56) (table 19) and was therefore applied for their control in the form of contact sprays, dusts, or bait (54–59, 61, 96, 156, 219, 221, 222, 247, 248, 285, 286, 294, 390, 411, 418, 420, 436). It also was effective against houseflies which had developed resistance toward parathion (323, 324), malathion (89, 377), Diazinon (161, 323, 324), and DDT (61). Against the cigaret beetle DDVP has shown excellent results, and is now being used for their control in tobacco warehouses (149, 412–414, 418, 419, 445). It also has been applied for various insect species of *Diptera* (85, 133, 156, 162, 168, 169, 186, 214, 281, 321, 376, 398, 399), *Coleoptera* (24, 119, 141, 174, 219, 338, 361, 410), *Homoptera* (24, 54, 326, 436), *Lepidoptera* (54, 141, 172, 194, 338, 388, 436), *Orthoptera* (13, 54, 219, 418), and others (99, 115, 156, 272).

The mammalian toxicity of DDVP has been investigated very thoroughly (54, 57, 96, 149, 150, 170, 225, 250, 272, 285, 286, 370, 418, 420). In general it is more toxic than some of the commonly used chlorinated hydrocarbons, but has a significantly lower toxicity than TEPP[8] and parathion.

TABLE 20

Vinyl dihydrogen phosphates

Formula	Preparation	Derivatives
$CH_2=CHOPO_3H_2$......	From vinyl acetate and phosphoric acid in the presence of a Hg(II) salt (64)*	Pyridinium salt (64) Lithium salt (64)
$CH_2=\underset{\substack{\vert\\ COOH}}{C}OPO_3H_2$........	From pyruvic acid and $POCl_3$ (245, 246, 322, 373, 374)	Monosodium salt (131) Potassium salt (63, 65) Silver salt (63, 65, 102, 373, 374)
	From α-chlorolactic acid and $POCl_3$ (63, 65) From bromopyruvic acid and tribenzyl phosphite (131) From carbomethoxy-PEP (102)	Silver barium salt (63, 65, 245, 246, 322, 373, 374) Tricyclohexylammonium salt, m.p. 155–180°C. (d.) (447) Nicotinamide adduct of calcium salt (353)
$C_2H_5OOCCH=\underset{\substack{\vert\\ CH_3}}{C}OPO_3H_2$	From ethyl sodioacetoacetate and $POCl_3$ (240)	Sodium salt (240) Barium salt (240)
$HOOCCH=\underset{\substack{\vert\\ CH_3}}{C}OPO_3H_2$...	From 2-carbethoxy-1-methylvinyl disodium phosphate by deëthylation with sodium hydroxide (240)	Sodium salt (240)

* The free acid is highly unstable (64).

There is also substantial evidence that the toxic action of the widely used insecticide Dipterex (*O,O*-dimethyl 2,2,2-trichloro-1-hydroxyethylphosphonate) is

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[7] Registered trademark of Ciba Pharmaceutical Company.

[8] TEPP = tetraethyl pyrophosphate.

TABLE 21

Dialkyl vinyl phosphates

R in $(RO)_2P(O)OCH{=}CH_2$	Prepared by the Reaction		Boiling Point	n_D	Yield	References
	of	with				
			°*C.*		*per cent*	
C_2H_5	$(C_2H_5O)_3P$	Chloroacetaldehyde	79/5–7 mm.	1.4100 (35°C.)	67	(18, 158)
			48–50/0.2 mm.	1.4134 (20°C.)	69	(271)
			85.2–88.8/10 mm.	?	67	(435)
$ClCH_2CH_2$	$(ClCH_2CH_2O)_3P$	Chloroacetaldehyde	133–148	?	?	(158)
$CH_2{=}CH$	$PO(OC_2H_4Cl)_3$	$(C_2H_5)_3N$	84–85/10 mm.	1.4314 (20°C.)	30	(178)

TABLE 22

1-Substituted dialkyl vinyl phosphates

Compounds of the type $R'R''P(O)OCR'{=}CH_2$

R	R′	R″	Prepared by the Reaction		Boiling Point	n_D	Yield	References
			of	with				
					°*C.*		*per cent*	
CH_3	CH_3O	CH_3O	$(CH_3O)_3P$	Chloroacetone	84–86/10 mm.	1.4165 (20°C.)	67	(344)
CH_3	C_2H_5O	C_2H_5O	$(C_2H_5O)_3P$	Chloroacetone	65–66/1.5 mm.	1.4178 (25°C.)	75	(396)
					72–73/1 mm.	1.4135 (35°C.)	56	(18)
					96/12 mm.	1.4190 (20°C.)	94	(341, 342)
					57/0.6 mm.	1.4158 (25°C.)	80	(226)
CH_3	C_4H_9O	C_4H_9O	$(C_4H_9O)_3P$	Chloroacetone	125–126/5 mm.	1.4268 (20°C.)	53	(344)
CH_3	iso-C_4H_9O	iso-C_4H_9O	(iso-$C_4H_9O)_3P$	Chloroacetone	122–123/9 mm.	1.4245 (20°C.)	74	(344)
CH_3	iso-C_4H_9O	iso-C_4H_9O	(iso-$C_4H_9O)_2POC_2H_5$	Chloroacetone	122–123/9 mm.	1.425 (20°C.)	69	(348)
CH_3	C_2H_5O	C_6H_5O	$(C_2H_5O)_2POC_6H_5$	Chloroacetone	151.5–152/10 mm.	1.4845 (20°C.)	58	(348)
CH_3	C_4H_9	C_6H_5O	$(C_4H_9O)_2POC_6H_5$	Chloroacetone	166–167/9 mm.	1.4825 (20°C.)	49	(348)
CH_3	C_6H_5O	C_6H_5O	$C_4H_9OP(OC_6H_5)_2$	Chloroacetone	186/1.5 mm.	1.4583 (20°C.)	57	(348)
CH_3	C_3H_7O	$(C_2H_5)_2N$	$(C_3H_7O)_2PN(C_2H_5)_2$	Chloroacetone	105–106/5 mm.	1.4380 (20°C.)	51	(3)
CH_3	C_4H_9O	$(C_2H_5)_2N$	$(C_4H_9O)_2PN(C_2H_5)_2$	Chloroacetone	110–112/4 mm.	1.4340 (20°C.)	62	(3)
CH_3	$(C_2H_5)_2N$	$(C_2H_5)_2N$	$(C_2H_5)N_2POC_2H_5$	Chloroacetone	124–125/8 mm.	1.4520 (20°C.)	40	(348)
CH_2Cl	C_2H_5O	C_2H_5O	$(C_2H_5)O_3P$	α,α′-Dichloroacetone	76–89/1 mm.	?	82	(18)
					133.5–134.5/11 mm.	1.4435 (20°C.)	45	(352)
CH_2Cl	C_4H_9O	C_4H_9O	$(C_4H_9O)_3P$	α,α′-Dichloroacetone	154–155/11 mm.	1.4400 (20°C.)	82	(342)
CH_2Cl	C_2H_5O	$(C_2H_5)_2N$	$(C_2H_5O)_2PN(C_2H_5)_2$	α,α′-Dichloroacetone	120–122/3 mm.	1.4545 (20°C.)	78	(3)
CH_2Cl	C_3H_7O	$(C_2H_5)_2N$	$(C_3H_7O)_2PN(C_2H_5)_2$	α,α′-Dichloroacetone	142–143/10 mm.	1.4545 (20°C.)	75	(3)
CH_2Cl	C_4H_9O	$(C_2H_5)_2N$	$(C_4H_9O)PN(C_2H_5)_2$	α,α′-Dichloroacetone	144–146/5 mm.	1.4550 (20°C.)	67	(3)
CH_2Br	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	α,α′-Dibromoacetone	142.5–143/11 mm.	1.4622 (20°C.)	40	(342)
$COOC_2H_5$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	Ethyl bromopyruvate	104–108/0.4 mm.	1.4322 (25°C.)	74	(124)
					92–93/0.05 mm.			
COOH	$C_6H_5CH_2$	$C_6H_5CH_2$	$(C_6H_5CH_2O)_3P$	Bromopyruvic acid	75–78 (m.p.)	—		(129)
$PO(OCH_3)_2$	CH_3	CH_3	$(CH_3O)_3P$	Chloroacetyl chloride	128–130/vacuum	1.4400 (20°C.)	86	(234)
					141/1 mm.	1.4420 (20°C.)	84	(346)
$PO(OC_2H_5)_2$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	Chloroacetyl chloride	125–126/0.5 mm.	1.4396 (20°C.)	86	(346)
					132–135/1.5 mm.	1.4402 (20°C.)	47	(234)
$CH_2PO(OC_2H_5)_2$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	α,α′-Dichloroacetone	118–120/0.05 mm.	1.4459 (25°C.)	84	(226)
				1-Bromomethylvinyl diethyl phosphate	195–197/10 mm.	1.4440 (20°C.)	88	(352)
C_6H_5	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	ω-Chloroacetophenone	172/12 mm.	1.5020 (20°C.)	90	(341)
					106–107/0.1 mm.	1.5026 (20°C.)	81	(271)
OC_2H_5	C_6H_5	C_6H_5	$(C_6H_5O)_2POOH$	Ethoxyacetylene	100/0.0005 mm.	?	?	(425)

exerted through the *in vivo* formation of DDVP (140, 166).

A large number of analogs of DDVP have been prepared by varying the two alkoxy groups of the dialkylphosphoryl moiety and have been evaluated for their insecticidal properties. Replacement of the two methyl groups with higher homologs generally seems to decrease the insecticidal effectiveness, as shown by the decrease of toxicity in the order DDVP, ethyl-, propyl-, and isopropyl-DDVP against houseflies (61). However, these compounds have received some attention (156, 157, 165, 219, 226, 227, 270, 330, 332, 335, 436). Some newer developments in this field are Bayer 22684 (XV: R′ = Cl; "Mafu") (83, 135, 380, 382) and compounds of the type of XV (R′ = p-ClC_6H_4S, p-$CH_3C_6H_4S$) (80, 454) and XVI (R′ = CH_2Cl, COOH)

TABLE 23

2-Monosubstituted vinyl dialkyl phosphates

Compounds of the type $(R'O)_2P(O)OCH{=}CHR$

R	R′	Prepared by the Reaction		Boiling Point	n_D	Yield	References
		of	with				
				°*C.*		*per cent*	
Cl	CH_3	$(CH_3O)_3P$	Dichloroacetaldehyde	38–40/0.01 mm.	?	65	(155, 226)
Cl	C_2H_5	$(C_2H_5O)_3P$	Dichloroacetaldehyde	80/0.2 mm.	?	60	(334)
				121–122/11 mm.	1.4348 (25°C.)	53	(70)
				61/0.5 mm.	1.4342 (25°C.)	66	(72)
				110–114/10 mm.	1.4342 (20°C.)	67	(258)
				92–105/1–2 mm.	1.4276 (35°C.)	54	(18)
				116–118/10 mm.	1.4352 (20°C.)	?	(436)
Cl	$ClCH_2CH_2$	$(ClCH_2CH_2O)_3P$	Dichloroacetaldehyde	152–157/1 mm.	?	70	(18)
Cl	C_3H_7	$(C_3H_7O)_3P$	Dichloroacetaldehyde	94–100/0.1 mm.	1.4364 (25°C.)	56	(18)
Cl	iso-C_3H_7	(iso-$C_3H_7O)_3P$	Dichloroacetaldehyde	74–87/0.1 mm.	1.4307 (25°C.)	37	(18)
				89–91/0.3 mm.		45	(334)
Cl	C_4H_9	$(C_4H_9O)_3P$	Dichloroacetaldehyde	96/0.5 mm.	1.4392 (25°C.)	85	(77)
Cl	$C_4H_9\underset{\underset{C_2H_5}{\vert}}{C}HCH_2$	$(C_4H_9\underset{\underset{C_2H_5}{\vert}}{C}HCH_2O)_3P$	Dichloroacetaldehyde	156–173/0.1 mm.	1.4492 (25°C.)	82	(18)
$ClCH_2$	C_2H_5	$(C_2H_5O)_3P$	2,3-Dichloropropanal	115–118/0.8 mm.	?	41	(334)
				130/0.7 mm. (bath)	1.4518 (20°C.)	18	(435)
$ClCH_2$	iso-C_3H_7	(iso-$C_3H_7O)_3P$	2,3-Dichloropropanal	124/0.4 mm.	?	39	(334)
$ClCH_2$	iso-C_4H_9	(iso-$C_4H_9O)P$	2,3-Dichloropropanal	136–137/0.4 mm.	?	54	(334)
C_6H_5CHCl	C_2H_5	$(C_2H_5O)_3P$	2,3-Dichloro-3-phenylpropanal	Not distillable	?	100	(18)

TABLE 24

2,2-Disubstituted dialkyl vinyl phosphates

Compounds of the type $(RO)_2P(O)OCH{=}CR'R''$

R′	R″	R	Prepared by the Reaction		Boiling Point	Yield	References
			of	with			
					°*C.*	*per cent*	
Br	Br	C_2H_5	$(C_2H_5O)_3P$	Bromal	82/0.001 mm.	88	(436)
					139–40/1.5 mm.	70	(328, 333)
					ca. 100/0.15 mm.	48	(18)
Br	Br	iso-C_3H_7	(iso-$C_3H_7O)_3P$	Bromal	139–142/2.0 mm.	45	(328)
Br	Br	iso-C_4H_9	(iso-$C_4H_9O)_3P$	Bromal	159–160/1.5 mm.	20	(328)
Cl	CH_3CHCl	C_2H_5	$(C_2H_5O)_3P$	2,2,3-Trichlorobutanal	140–142/2 mm.	45	(334)
					ca. 80/0.01 mm.	49	(18)
CH_3	CH_3	C_2H_5	$(C_2H_5O)_3P$	2-Chloro-2-methylpropanal	112–113.5/10 mm.	73	(45)

(83, 387), which have insecticidal properties superior to those of DDVP in some aspects. Analogs of DDVP in which the two methoxy groups are replaced by amino (15), phenyl (157, 436), or ethylene groups (157) are also insecticidally active.

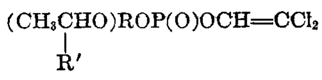
$(CH_3O)_2P(O)OCH{=}CCl_2$

XIV

DDVP

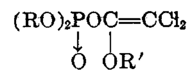
$(R'C_2H_4O)CH_3OP(O)OCH{=}CCl_2$

XV



$(CH_3\underset{\underset{R'}{\vert}}{C}HO)ROP(O)OCH{=}CCl_2$

XVI



$(RO)_2\underset{\underset{O}{\downarrow}}{P}O\underset{\underset{OR'}{\vert}}{C}{=}CCl_2$

XVII

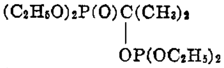
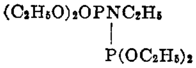
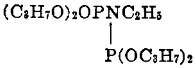
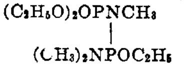
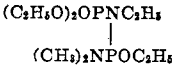
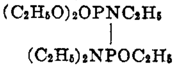
About fifty dialkyl 1-alkoxy-2,2-dichlorovinyl phosphates (XVII), which frequently have been formulated as the isomeric carbalkoxydichloromethylphosphonates, were reported to possess useful insecticidal potentialities (103–113, 181, 182, 303, 348, 339, 367–369). Only Chlorophan (XVII: R = CH_3, R′ = C_2H_5) (181, 211) and some 1-ethoxy and 1-phenoxy derivatives of XVII (312) have been tested in somewhat greater detail, showing appreciable toxicity to insects. Diethyl 2-chlorovinyl phosphate (XVIII, Shell OS 1836) has shown effectiveness as a systemic poison or fumigant with a relatively low mammalian toxicity (75, 117, 118, 156, 252, 254, 300). Its insecticidal activity is somewhat lower than that of Phosdrin® and DDVP, as demonstrated by the data given in table 19 (96).

Several cyclic enol phosphates, such as XIX and XX, and some of their thio analogs, were reported to have insecticidal qualities (179, 180, 192, 193, 198). However, their activity was considerably lower than that of Phosdrin® (96, 310). Pyrazoxon (XXI), on the other hand, has found use for the control of various insect pests (185, 199). Of the other types of enol phosphates that have been claimed to have insecticidal properties (78, 288, 289, 302, 315, 316, 421, 452) only diethyl 2,2-di(ethylthio)vinyl phosphate (XXII,

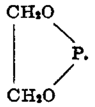
TABLE 25

2,2-Disubstituted dialkyl vinyl phosphates

Compounds of the type $RR'P(O)OCH{=}CCl_2$

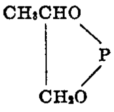
R	R′	Prepared by the Reaction of Chloral with	Boiling Point	n_D	Yield	References
			°C.		*per cent*	
CH_3	CH_3O	$(CH_3O)_3P$	81–82/1–2 mm.	1.4510 (20°C.)	94	(436)
			100–104/2.5 mm.	?	60	(328)
			120/14 mm.	1.4523 (25°C.)	86	(70)
			74–87/2 mm.	?	53	(18)
CH_3O	C_2H_5O	$(CH_3O)_2POC_2H_5$	80–96/1 mm.	?	67	(18)
C_2H_5O	C_2H_5O	$(C_2H_5O)_3P$	113–115/2 mm.	?	85–90	(328, 332, 335)
			132–133/14 mm.	1.4475 (25°C.)	97	(70)
			69–71/0.5 mm.	1.4498 (20°C.)	98	(245)
			114.5–115.0/5 mm.	1.4428 (35°C.)	57	(18, 156)
			112.7–113.5/5 mm.	1.4475 (20°C.)	80	(436)
C_3H_7O	C_3H_7O	$(C_3H_7O)_3P$	114/1.1 mm.	1.4440 (25°C.)	70	(70)
			109–123/3 mm.	?	75	(18)
iso-C_3H_7O	iso-C_3H_7O	(iso-$C_3H_7O)_3P$	106–108/0.8 mm.	?	72	(328)
			108–111/0.9 mm.	1.4422 (25°C.)	75	(70)
			96.5/2 mm.	1.4372 (35°C.)	62	(18)
			78–81/0.2–0.35 mm.	1.4422 (20°C.)	36	(436)
n-C_4H_9O	*n*-C_4H_9O	(*n*-$C_4H_9O)_3P$	128–129/1 mm.	1.4439 (20°C.)	83	(436)
			184–191/0.2 mm.	1.4487 (25°C.)	79	(70)
			107–121/0.5 mm.	?	80	(18)
iso-C_4H_9O	iso-C_4H_9O	(iso-$C_4H_9O)_3P$	125–127/0.5 mm.	?	?	(332)
			107–109.4/0.7 mm.	1.4465 (20)	?	(436)
C_6H_5O	C_6H_5O	$C_6H_5OP(OC_2H_5)_2$	116–130/0.5 mm.	?	84	(18)
			$110/5.10^{-5}$ mm.	1.5024	90	(436)
CH_3O	$C_4H_9OOCCH_2O$	$(CH_3O)_2POCH_2COOC_4H_9$	132–136/0.2 mm.	?	?	(387)
C_2H_5O	$C_4H_9OOCCH_2O$	$(C_2H_5O)_2POCH_2COOC_4H_9$	115–122/0.5 mm.	?	?	(387)
C_2H_5O	$C_2H_5OOCCH(CH_3)O$	$(C_2H_5O)_2POCH(CH_3)COOC_2H_5$	134–137/0.7 mm.	?	?	(387)
C_2H_5O	$(C_2H_5O)_2P(O)C(CH_3)_2$	 $(C_2H_5O)_2P(O)C(CH_3)_2$ $OP(OC_2H_5)_2$	162–164/1 mm.	1.4580 (20°C.)	52	(15)
C_2H_5O	$(CH_3)_2N$	$(CH_3)_2NP(OC_2H_5)_2$	90–91.5/3 mm.	1.4580 (20°C.)	43	(15)
C_4H_9O	$(CH_3)_2N$	$(CH_3)_2NP(OC_4H_9)_2$	103–104/2 mm.	1.4580 (20°C.)	56	(15)
CH_3O	$(C_2H_5)_2N$	$(C_2H_5)_2NP(OCH_3)_2$	116–117/3 mm.	1.4626 (20°C.)	60	(3)
C_2H_5O	$(C_2H_5)_2N$	$(C_2H_5)_2NP(OC_2H_5)_2$	112–114/3 mm.	1.4600 (20°C.)	62	(3)
iso-C_3H_7O	$(C_2H_5)N$	$(C_2H_5)_2NP$(O-iso-$C_3H_7)_2$	124/6 mm.	1.4580 (20°C.)	65	(3)
C_4H_9O	$(C_2H_5)_2N$	$(C_2H_5)_2NPOC_4H_9$	131–133/3 mm.	1.4590 (20°C.)	63	(3)
$(CH_3)_2N$	$(CH_3)_2N$	$[(CH_3)_2N]_2POC_2H_5$	90–115/1 mm.	1.4708 (35°C.)	67	(18)
			89.5–90/1 mm.	1.4785 (20°C.)	61	(15)
$(C_2H_5)_2N$	$(C_2H_5)_2N$	$[(C_2H_5)_2N]_2POC_2H_5$	115–125/1 mm.	?	74	(18)
C_2H_5O	$(C_2H_5O)_2OPNC_2H_5$	 $(C_2H_5O)_2OPNC_2H_5$ $P(OC_2H_5)_2$	164–165/2 mm.	1.4610 (20°C.)	70	(15)
C_3H_7O	$(C_3H_7O)_2PNC_2H_5$	 $(C_3H_7O)_2OPNC_2H_5$ $P(OC_3H_7)_2$	160–162.5/1 mm.	1.4580 (20°C.)	36	(15)
$(CH_3)_2N$	$(C_2H_5O)_2PNCH_3$	 $(C_2H_5O)_2OPNCH_3$ $(CH_3)_2NPOC_2H_5$	148–149/1 mm.	1.4700 (20°C.)	40	(15)
$(CH_3)_2N$	$(C_2H_5O)_2NC_2H_5$	 $(C_2H_5O)_2OPNC_2H_5$ $(CH_3)_2NPOC_2H_5$	145–145.5/1 mm.	1.4715 (20°C.)	51	(15)
$(C_2H_5)_2N$	$(C_2H_5O)_2NC_2H_5$	 $(C_2H_5O)_2OPNC_2H_5$ $(C_2H_5)_2NPOC_2H_5$	154–155/1.5 mm.	1.4690 (20°C.)	25	(15)
CH_3O	$ClCH_2CH_2O$	CH_3OX*	65–66/0.01 mm.	?	71.5	(154, 380)
C_2H_5O	$ClCH_2CHClCH_2O$†	C_2H_5OY'‡	$132/10^{-5}$ mm.	?		(436)
C_2H_5O	$ClCH_2CH_2O$	C_2H_5OX*	136/2 mm.	?	58	(154, 380)
C_2H_5O	$C_6H_5OCH_2CHClCH_2O$§	C_2H_5OY''‡	$132/10^{-5}$ mm.	?		(436)
$(CH_3)_2N$	$ClCH_2CH_2O$	$(CH_3)_2NX$*	137/2 mm.	?	67	(154, 380, 382)
$(C_2H_5)_2N$	$ClCH_2CH_2O$	$(C_2H_5)_2NX$*	113–123/0.2 mm.	?	73	(18)
$ClCH_2CH_2O$	$ClCH_2CH_2O$	$ClCH_2CH_2OX$*	169/2 mm.	?	87	(154, 380)
		$(ClCH_2CH_2O)_3P$	93–112/0.1 mm.	1.4820 (35°C.)	68	(18)
n-$C_6H_{13}O$	$ClCH_2CH_2O$	*n*-$C_6H_{13}OX$*	Not distillable	?	56	(154, 380, 382)
CCl_3CH_2O	$ClCH_2CH_2O$	CCl_3CH_2OX*	Not distillable	?	69	(154, 380, 382)
2,4-$Cl_2C_6H_3O$	$ClCH_2CH_2O$	2,4-$Cl_2C_6H_3OX$*	Not distillable	?	37	(154, 380, 382)
CH_3S	$ClCH_2CH_2O$	CH_3SX*	138/2 mm.	?	52	(154, 380, 382)
C_2H_5S	$ClCH_2CH_2O$	C_2H_5SX*	134/2 mm.	?	?	(154, 380, 382)
C_6H_5	$ClCH_2CH_2O$	C_6H_5SX*	174/2 mm.	?	71	(154, 380, 382)
—OCH_2CH_2O—		CH_3OX*	110–117/0.5 mm.	?	24	(18)
—$OCH(CH_3)CH_2O$—		CH_3OY‡	118–123/2 mm.	?	54	(18)
—$OCH(CH_3)CH_2CH_2O$—		CH_3OZ¶	132–140/1 mm.	?	97	(18)

* X =

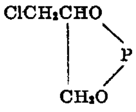


† R′ might be $(ClCH_2)_2CHO$.

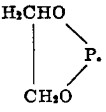
‡ Y =



Y′ =



Y″ =



§ R′ might be $C_6H_5OCH(CH_2Cl)CHO$.

¶ Z =

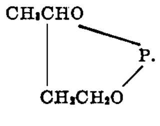
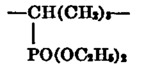


TABLE 26

1,2-Disubstituted dialkyl vinyl phosphates

Compounds of the type $(R''O)(R'''O)P(O)OCR{=}CHR'$

R	R′	R″	R‴	Prepared by the Reaction		Boiling Point	n_D	Yield	References
				of	with	°*C.*		*per cent*	
CH_3	CH_3	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	3-Chloro-2-butanone	112–113.5/110 mm.	1.4270 (20°C.)	?	(37)
						110–111.5/10 mm.	1.4274 (20°C.)	70	(345)
CH_3	Cl	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	α,α-Dichloroacetone	116.5–117/10 mm.	1.4370 (20°C.)	76	(329, 331, 342, 352)
CH_3	Cl	C_4H_9	C_4H_9	$(C_4H_9O)_3P$	α,α-Dichloroacetone	154–155/11 mm.	1.4400 (20°C.)	82	(342, 352)
CH_3	Cl	iso-C_4H_9	iso-C_4H_9	(iso-$C_4H_9O_3$)P	α,α-Dichloroacetone	139.5–140/9 mm.	1.4402 (20°C.)	63	(348)
CH_3	Cl	C_2H_5	C_6H_5	$(C_2H_5O)_2POC_6H_5$	α,α-Dichloroacetone	130–131/1 mm.	1.4972 (20°C.)	52	(348)
CH_3	Cl	C_4H_9	C_6H_5	$(C_4H_9O)_2OC_6H_5$	α,α-Dichloroacetone	55–56/3 mm.	1.4917 (20°C.)	61	(348)
CH_3	Br	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	α,α-Dibromoacetone	126–127/10 mm.	1.4540 (20°C.)	37	(352)
CH_3	$C(O)CH_3$	CH_3	CH_3	$(CH_3O)_3P$	3-Chloro-2,4-pentanedione	99–100/0.8 mm.	1.4500 (25.5°C.)	55	(282, 308)
						118–122/1.4 mm.	1.4488 (20°C.)	71	(259)
CH_3	$C(O)CH_3$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	3-Chloro-2,4-pentanedione	119–120/2 mm.	1.4489 (20°C.)	66	(343)
						101–103/1.0 mm.	1.4565 (19.5°C.)	68	(282, 308)
CH_3	$C(O)CH_3$	C_4H_9	C_4H_9	$(C_4H_9O)_3P$	3-Chloro-2,4-pentanedione	125–127/1 mm.	1.4510 (20°C.)	60–80	(347)
CH_3	$C(O)CH_3$	iso-C_4H_9	iso-C_4H_9	(iso-$C_4H_9O)_3P$	3-Chloro-2,4-pentanedione	137–138/2.5 mm.	1.4468 (20°C.)	80	(352)
CH_3	$C(O)NHC_6H_5$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	α-Chloroacetoacetanilide	81–81.5 (m.p.)	—	?	(439)
CH_3	$C(O)NHC_6H_4NO_2$-*p*	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	α-Chloro-*p*-nitroacetoacetanilide	143–144 (m.p.)	—	43	(439)
CH_3	$C(O)N(CH_3)_2$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	*N*,*N*-Dimethyl-α-chloroacetoacetamide	$132/10^{-5}$ mm.	1.4663 (20°C.)	?	(439)
CH_3	$C(O)N(CH_3)C_6H_5$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	*N*-Methyl,*N*-phenyl-α-chloroacetoacetamide	115–120/0.001 mm.	1.5164 (20°C.)	72	(439)
C_2H_5O	CN	CH_3	CH_3	$(CH_3O)_3P$	Ethyl chlorocyanoacetate	119–122/1.1 mm.	1.4332 (27°C.)	44	(312)
C_2H_5O	CN	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	Ethyl chlorocyanoacetate	124–126/1.0 mm.	1.4320 (21°C.)	51	(312)
$(C_2H_5)_2NC(O)CH_2$	Cl	CH_3	CH_3	$(CH_3O)_3P$	*N*,*N*-Diethyl-γ,γ-dichloroacetoacetamide	138–142/0.1 mm.	?	76	(78)
$(C_2H_5)_2NC(O)CH_2$	Cl	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	*N*,*N*-Diethyl-γ,γ-dichloroacetoacetamide	144/0.1 mm.	?	98	(78)
$PO(OC_2H_5)_2$	Cl	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	Dichloroacetyl chloride	120–130/0.07 mm.	?	86	(443)
$PO(OC_2H_5)_2$	CH_3	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	α-Bromopropionyl bromide	128–129/1.5 mm.	1.4450 (20°C.)	79	(346)
CH_3	CH_3S	CH_3	CH_3	$(CH_3O)_2P(O)OC(CH_3){=}CH_2$	CH_3SCl + pyridine	104–107/0.8–1.1 mm.	1.4726 (20°C.)	?	(143)
CH_3	CH_3S	C_2H_5	C_2H_5	$(C_2H_5O)_2P(O)OC(CH_3){=}CH_2$	CH_3SCl + pyridine	115–131/1–2 mm.	1.4656 (20°C.)	?	(143)
CH_3	C_2H_5S	CH_3	CH_3	$(CH_3O)_2P(O)OC(CH_3){=}CH_2$	C_2H_5SCl + pyridine	106–120/0.8 mm.	1.4737 (20°C.)	?	(143)
CH_3	C_2H_5S	C_2H	C_2H_5	$(C_2H_5O)_2P(O)OC(CH_3){=}CH_2$	C_2H_5SCl + pyridine	122–137/1.5 mm.	1.4648 (20°C.)	?	(143)
CH_3	C_3H_7S	C_2H_5	C_2H_5	$(C_2H_5O)_2P(O)OC(CH_3){=}CH_2$	C_3H_7SCl + pyridine	100–107/0.1–0.5 mm.	1.4657 (20°C.)	?	(143)
CH_3	$PO(OC_2H_5)_2$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	Diethyl 1-chloro-2-oxopropylphosphonate	161–162/1 mm.	1.4478 (20°C.)	39	(343)
$COOCH_3$	F	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	Methyl β-bromofluoropyruvate	135/1.3 mm.	?	50	(76)
$-(CH_2)_4-$		C_2H_5	C_2H_5	$(C_2H_5O)_3P$	2-Chlorocyclohexanone	143/11 mm.	1.4523 (20°C.)	89	(341)
 $\underset{PO(OC_2H_5)_2}{\underset{\vert}{-CH(CH_2)_3-}}$		C_2H_5	C_2H_5	$(C_2H_5O)_3P$	2,6-Dibromocyclohexanone	172.5–173.0/2.5 mm.	1.4652 (20°C.)	29	(50)
$-CH_2CHCH_3CH_2C(O)-$		C_2H_5	C_2H_5	$(C_2H_5O)_2P(O)Cl$	5-Methyl-1,3-cyclohexanedione	130–133/0.07 mm.	?	?	(198)
$-CH_2C(CH_3)_2CH_2C(O)-$		C_2H_5	C_2H_5	$(C_2H_5O)_2P(O)Cl$	5,5-Dimethyl-1,3-cyclohexanedione	110–112/0.002 mm.	?	?	(179)
						127–130/0.1 mm.	?	?	(198)
				$(C_2H_5O)_3P$	2-Chloro-5,5-dimethyl-1,3-cyclohexanedione	—	?	?	(347)

C_6H_5	Cl	CH_3	CH_3	$(CH_3O)_3P$	*ω,ω*-Dichloroacetophenone	125–135/0.3 mm.	1.5312 (28°C.)	51	(308)
C_6H_5	Cl	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	*ω,ω*-Dichloroacetophenone	139–140/0.5 mm.	1.5170 (20°C.)	80-90	(331, 345)
						130–139/0.4 mm.	1.5163 (24°C.)	61	(308)
						80/6 × 10^{-6} mm.	1.5148 (20°C.)	93	(436)
C_6H_5	C_6H_5	CH_3	CH_3	$(CH_3O)_3P$	*ω*-Chloro-*ω*-phenylacetophenone	165–166/0.15 mm.	1.5795 (25°C.)	42	(308)
C_6H_5	$C(O)CH_3$	CH_3	CH_3	$(CH_3O)_3P$	*α*-Benzoyl-*α*-chloroacetone	154–157/1 mm.	1.5256 (23.5°C.)	71	(311)
						138–139/1 mm.	1.5162 (20°C.)	60–80	(347)
C_6H_5	$C(O)CH_3$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	*α*-Benzoyl-*α*-chloroacetone	148–151/0.75 mm.	1.5157 (23.5°C.)	82	(311)
						170–172/2 mm.	1.5135 (20°C.)	60–80	(347)
C_6H_5	$C(O)C_6H_5$	CH_3	CH_3	$(CH_3O)_3P$	Dibenzoylchloromethane	—	1.5652	52	(311)
C_6H_5	$C(O)C_6H_5$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	Dibenzoylchloromethane	—	1.5730 (31°C.)	60	(311)
						208/3 mm.	1.5490 (20°C.)	20	(347)
C_6H_5	$CH{=}CCl_2$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	Phenyl 3,3,3-trichloropropenyl ketone	Not distillable	?	~100	(18)

TABLE 27

1,2-Disubstituted dialkyl vinyl phosphates

Compounds of the type $(R''O)(R'''O)\underset{\downarrow \atop O}{P}O\underset{| \atop R}{C}{=}CHCOOR'$

R	R′	R″	R‴	Prepared by the Reaction		Boiling Point	n_D	Yield	References
				of	with				
						°C.		*per cent*	
CH_3	CH_3	CH_3	CH_3	$(CH_3O)_3P$	Methyl *α*-chloroacetoacetate	106–107.5/1 mm.	1.4494 (20°C.)	68	(402)
CH_3	CH_3	CH_3	p-$O_2NC_6H_4$	$(p\text{-}O_2NC_6H_4O)_2POCH_3$	Methyl *α*-chloroacetoacetate	180–185/0.001 mm.	1.5280 (20°C.)	?	(403)
CH_3	CH_3	C_2H_5	p-$(CH_3)_2NC_6H_4$	$p\text{-}(CH_3)_2NC_6H_4O_2POCH_3$	Methyl *α*-chloroacetoacetate	154–156/0.001 mm.	1.5528 (27.5°C.)	63	(438)
CH_3	C_2H_5	CH_3	CH_3	$(CH_3O)_3P$	Ethyl *α*-chloroacetoacetate	118/1 mm.	1.4450 (28°C.)	58	(308)
CH_3	C_2H_5	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	Ethyl *α*-chloroacetoacetate	155–156/10 mm.	1.4451 (20°C.)	91	(343)
						123/1 mm.	1.4447 (20°C.)	76	(261)
CH_3	C_2H_5	C_2H_5	p-$O_2NC_6H_4$	$(p\text{-}O_2NC_6H_4O)_2POC_2H_5$	Ethyl *α*-chloroacetoacetate	195/0.001 mm.	1.5190 (22°C.)	?	(403)
CH_3	C_2H_5	C_2H_5	$CH_3OCH_2CH_2$	$CH_3OCH_2CH_2OP(OC_2H_5)_2$	Ethyl *α*-chloroacetoacetate	110/0.001 mm.	1.4481 (25°C.)	67	(319, 407)
CH_3	C_2H_5	iso-C_4H_9	iso-C_4H_9	$(iso\text{-}C_4H_9O)_3P$	Ethyl *α*-chloroacetoacetate	175/10 mm.	1.4445 (20°C.)	71	(342, 352)
CH_3	$CH_2CH_2OCH_3$	CH_3	CH_3	$(CH_3O)_3P$	2-Methoxyethyl *α*-chloroacetoacetate	100/0.001 mm.	1.4537 (25°C.)	68	(319, 407)
CH_3	$CH_2CH_2OCH_3$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	2-Methoxyethyl *α*-chloroacetoacetate	105/0.001 mm.	1.4497 (25°C.)	71	(319, 407)
CH_3	$CH_2CH_2OCH_3$	$CH_3OCH_2CH_2$	$CH_3OCH_2CH_2$	$(CH_3OCH_2CH_2O)_3P$	2-Methoxyethyl *α*-chloroacetoacetate	150/0.001 mm.	1.4535 (25°C.)	77	(319, 407)
CH_3	$CH_2CH_2OCOCH_3$	CH_3	CH_3	$(CH_3O)_3P$	2-Acetoxyethyl *α*-chloroacetoacetate	155–157/0.08 mm.	1.4580 (25°C.)	76	(319, 407)
CH_3	$CH_2CH_2OCOCH_3$	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	2-Acetoxyethyl *α*-chloroacetoacetate	150/0.001 mm.	1.4533 (25°C.)	93	(319, 407)
CH_3	$CH_2CH_2OCOC_6H_5$	CH_3	CH_3	$(CH_3O)_3P$	2-Benzoyloxyethyl *α*-chloroacetoacetate	160–165/0.001 mm.	1.5079 (25°C.)	78	(319, 407)
CH_3	$CH_2CH_2NHCOCH_3$	CH_3	CH_3	$(CH_3O)_3P$	2-Acetamidoethyl *α*-chloroacetoacetate	175–180/0.001 mm.	1.4785 (25°C.)	66	(406)
CH_3	$CH_2CH{=}CH_2$	CH_3	CH_3	$(CH_3O)_3P$	Allyl *α*-chloroacetoacetate				(395)
CH_3	$C_6H_5CH_2$	CH_3	CH_3	$(CH_3O)_3P$	Benzyl *α*-chloroacetoacetate	70/0.0005 mm.	1.5083 (16°C.)	79	(395)
CH_2COOCH_3	CH_3	CH_3	CH_3	$(CH_3O)_3P$	Dimethyl *α*-chloro-*β*-ketoglutarate	155–164/1.7 mm.	?	?	(189)
CH_2COOCH_3	CH_3	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	Dimethyl *α*-chloro-*β*-ketoglutarate	160–167/2 mm.	?	?	(189)
C_6H_5	C_2H_5	CH_3	CH_3	$(CH_3O)_3P$	Ethyl benzoylchloroacetate	149–157/0.65 mm.	1.5259 (24°C.)	65	(308)
C_6H_5	C_2H_5	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	Ethyl benzoylchloroacetate	151–153/0.35 mm.	1.5140 (22.5°C.)	69	(275, 308)
C_2H_5O	C_2H_5	C_2H_5	C_2H_5	$(C_2H_5O)_3P$	Diethyl bromomalonate	124–126/0.05 mm.	1.4513 (25°C.)	82	(124)
					Diethyl chloromalonate	137–140/0.3 mm.	1.4430 (27°C.)	70	(312)

TABLE 28

1,2,3-Trisubstituted dialkyl vinyl phosphates

Compounds of the type $(RO)_2P(O)OCR'{=}CR''R'''$

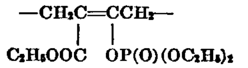
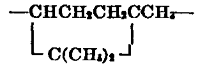
R′	R″	R‴	R	Prepared by the Reaction		Boiling Point	n_D	Yield	References
				of	with	°C.		per cent	
CH_3	Br	CH_3	C_2H_5	$(C_2H_5O)_3P$	3,3-Dibromo-2-butanone	147–148/10 mm.	1.4655 (20°C.)	38	(345)
CH_3	Br	Br	C_2H_5	$(C_2H_5O)_3P$	Tribromomethyl methyl ketone	145–148/2.5 mm.	1.4935 (20°C.)	18	(345)
CH_3	Cl	$CH_3C(O)$	CH_3	$(CH_3O)P$	3,3-Dichloro-2,4-pentanedione	115/2 mm.	1.4710 (20°C.)	60–80	(347)
CH_3	Cl	$CH_3C(O)$	C_2H_5	$(C_2H_5O)_3P$	3,3-Dichloro-2,4-pentanedione	135/3 mm.	1.4626 (20°C.)	63	(342, 343)
						118–123/1 mm.	1.4613 (20°C.)	?	(436)
CH_3	Cl	$CH_3C(O)$	C_4H_9	$(C_4H_9O)_3P$	3,3-Dichloro-2,4-pentanedione	138–139/2 mm.	1.4615 (20°C.)	60–80	(347)
CH_3	Cl	$CH_3C(O)$	iso-C_4H_9	(iso-$C_4H_9O)_3P$	3,3-Dichloro-2,4-pentanedione	150–151/4 mn.	1.4575 (20°C.)	80	(342, 343)
CH_3	Cl	$COOC_2H_5$	CH_3	$(CH_3O)_3P$	Ethyl α,α-dichloroacetoacetate	138–140/0.8 mm.	1.4620 (26°C.)	73	(308)
CH_3	Cl	$COOC_2H_5$	C_2H_5	$(C_2H_5O)_3P$	Ethyl α,α-dichloroacetoacetate	126–128/0.6 mm.	1.4559 (20°C.)	76	(261)
						120–128/1 mm.	?	68	(18)
						136/1 mm.	1.4572 (20°C.)	63	(343)
						123–126/0.15 mm.	?	62	(436)
CH_3	Cl	$COOC_2H_5$	iso-C_4H_9	(iso-$C_4H_9O)_3P$	Ethyl α,α-dichloroacetoacetate	154/1 mm.	1.4547	80	(343)
CH_3	Cl	$CON(C_2H_5)_2$	C_2H_5	$(C_2H_5O)_3P$	*N*,*N*-Diethyl α,α-dichloroacetoacetate	140/0.1 mm.	1.4718 (25°C.)	?	(78)
CH_3	C_2H_5	$COOC_2H_5$	C_2H_5	$(C_2H_5O)_3P$	Ethyl α-chloro-α-ethylacetoacetate	133–134/1.4 mm.	1.4470 (20°C.)	75	(261)
CH_3	$CH_2COOC_2H_5$	$COOC_2H_5$	CH_3	$(CH_3O)_3P$	Ethyl α-chloro-α-carbethoxy-β-oxovalerate	160/1.0 mm.	1.4549 (26.5°C.)	42	(308)
CH_3	C_6H_5	$COOC_2H_5$	CH_3	$(CH_3O)_3P$	Ethyl α-chloro-α-phenylacetoacetate	147–152/0.35 mm.	1.5070 (23.5°C.)	66	(308)
CH_3	C_6H_5	$COOC_2H_5$	C_2H_5	$(C_2H_5O)_3P$	Ethyl α-chloro-α-phenylacetoacetate	152–156/0.3 mm.	1.4963 (24°C.)	31	(309)
CH_3	C_6H_5	CN	CH_3	$(CH_3O)_2P(O)Cl$	1-Cyano-1-phenyl-2-propanone	155–160/0.3 mm.	1.5165 (26.5°C.)	40	(309, 313)
CH_3	C_6H_5	CN	C_2H_5	$(C_2H_5O)_2P(O)Cl$	1-Cyano-1-phenyl-2-propanone	143–145/0.2 mm.	1.5048 (26°C.)	10	(309)
CH_3	$—(CH_2)_2OOC—$		CH_3	$(CH_3O)_2P(O)Cl$	α-Acetyl-γ-hydroxybutyrolactone	153–156/0.5 mm.	1.4783 (24°C.)	?	(282, 315)
CH_3	$—(CH_2)_2OOC—$		C_2H_5	$(C_2H_5O)_2P(O)Cl$	α-Acetyl-γ-hydroxybutyrolactone	157–159/1.1 mm.	1.4071 (24°C.)	?	(282, 315)
CH_2F	F	$COOC_2H_5$	C_2H_5	$(C_2H_5O)_3P$	Ethyl α-bromo-α,γ-difluoroacetoacetate	128–130/1.1 mm.	?	50	(76)
$COOC_2H_5$	F	$COOC_2H_5$	C_2H_5	$(C_2H_5O)_3P$	Diethyl β-bromo-β-fluoro-α-oxosuccinate	155–157/1.2 mm.	?	50	(76)
C_6H_5	Cl	$C(O)CH_3$	CH_3	$(CH_3O)_3P$	α-Benzoyl-α,α-dichloroacetone	156–157/2.5 mm.	1.5223 (20°C.)	72	(347)
C_6H_5	Cl	$COOC_2H_5$	CH_3	$(CH_3O)_3P$	Ethyl benzoyldichloroacetate	150–153/0.8 mm.	1.5188 (25.5°C.)	59	(309)
C_6H_5	Cl	$COOC_2H_5$	C_2H_5	$(C_2H_5O)_3P$	Ethyl benzoyldichloroacetate	153–158/0.8 mm.	1.5068 (25.5°C.)	64	(309)
C_2H_5O	Cl	$COOC_2H_5$	CH_3	$(CH_3O)_3P$	Diethyl dichloromalonate	135–138/0.4 mm.	1.4381 (21°C.)	62	(312)
C_2H_5O	Cl	$COOC_2H_5$	C_2H_5	$(C_2H_5O)_3P$	Diethyl dichloromalonate	140–142/0.2 mm.	1.5387 (25°C.)	81	(312)
$(CH_3O)_2P(O)$	CH_3	CH_3	CH_3	$(CH_3O)_3P$	α-Chloro-α-methylpropionyl chloride	131–132/0.5 mm.	1.4580 (20°C.)	92	(346)
$(C_2H_5O)_2P(O)$	CH_3	CH_3	C_2H_5	$(C_2H_5O)_3P$	α-Chloro-α-methylpropionyl chloride	134–135/1.5 mm.	1.4503 (20°C.)	90	(346)
$—(CH_2)_3—$		$COOC_2H_5$	CH_3	$(CH_3O)_3P$	2-Carbethoxy-2-chlorocyclopentanone	133–136/1 mm.	1.4657 (27°C.)	46	(283, 310)
				$(CH_3O)_2P(O)Cl$	2-Carbethoxycyclopentanone	133–136/1 mm.	1.4657 (27°C.)	41	(310)
$—(CH_2)_3—$		$COOC_2H_5$	C_2H_5	$(C_2H_5O)_3P$	2-Carbethoxy-2-chlorocyclopentanone	132–137/1 mm.	1.4535 (26°C.)	76	(310)
				$(C_2H_5O)_2P(O)Cl$	2-Carbethoxycyclopentanone	132/137/1 mm.	1.4535 (26°C.)	70	(310)
						?	?	89	(192)
$—(CH_2)_4—$		$COOC_2H_5$	CH_3	$(CH_3O)P$	2-Carbethoxy-2-chlorocyclohexanone	135–140/0.15 mm.	1.4700 (30°C.)	71	(310)
				$(CH_3O)_2P(O)Cl$	2-Carbethoxycyclohexanone	135–140/0.15 mm.	1.4700 (30°C.)	61	(310)
$—(CH_2)_4—$		$COOC_2H_5$	C_2H_5	$(C_2H_5O)_3P$	2-Carbethoxy-2-chlorocyclohexanone	135–140/0.15 mm.	1.4640 (30°C.)	72	(310)
				$(C_2H_5O)_2P(O)Cl$	2-Carbethoxycyclohexanone	135–140/0.15 mm.	1.4640 (30°C.)	71	(310)
						?	?	49	(192)
 $—CH_2\underset{C_2H_5OOC}{C}{=}\underset{OP(O)(OC_2H_5)_2}{C}CH_2—$		$COOC_2H_5$	C_2H_5	$(C_2H_5O)_2P(O)Cl$	2,5-Dicarbethoxy-1,4-cyclohexanedione	—	?	68	(193)
$—CH_2C(CH_3)_2CH_2C(O)—$		Cl	C_2H_5	$(C_2H_5O)_3P$	2,2-Dichloro-5,5-dimethyl-1,3-cyclohexanedione	160–161/2.5 mm.	1.4818 (20°C.)	7	(347)
 $\underbrace{—CHCH_2CH_2CCH_2—}_{C(CH_3)_2}$		Br	C_2H_5	$(C_2H_5O)_3P$	Dibromocamphor	—	?	81	(18)

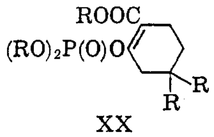
TABLE 29

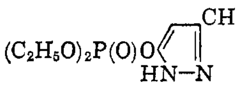
1,2,3-Trisubstituted dialkyl vinyl phosphates

Compounds of the type $(R'O)_2P(O)OCR{=}CCl_2$

R	R′	Prepared by the Reaction of $(R'O)_3P$ with	Boiling Point	n_D	Yield	References
			°*C.*		*per cent*	
CH_3O	CH_3	Methyl trichloroacetate	115–120/0.6 mm.	?	61	(181, 302)
CH_3O	C_2H_5	Methyl trichloroacetate	103.5–104.5/0.2 mm.	?	?	(181)
			139–142/7 mm.	1.4520 (20°C.)	27	(9)
CH_3O	C_3H_7	Methyl trichloroacetate	135–138/3 mm.	1.4526 (20°C.)	50	(9)
CH_3O	iso-C_3H_7	Methyl trichloroacetate	142–143/11 mm.	1.4478 (20°C.)	52	(9)
CH_3O	C_4H_9	Methyl trichloroacetate	145–146/3 mm.	1.4530 (20°C.)	69	(9)
CH_3O	iso-C_4H_9	Methyl trichloroacetate	130–132/1 mm.	1.4518 (20°C.)	63	(9)
CH_3O	C_2H_5	Methyl trichloroacetate	103.5–104.5/02 mm.	?	?	(181)
C_2H_5O	CH_3	Ethyl trichloroacetate	116–117/1 mm.	?	?	(181, 302)
			104/105/0.4 mm.	1.4479 (24°C.)	42	(312)
C_2H_5O	C_2H_5	Ethyl trichloroacetate	106–109/0.3 mm.	1.4438 (27°C.)	52	(312)
			91–92/0.2 mm.	1.4481 (25°C.)	51	(128)
			120–127/1 mm.	1.4437 (35°C.)	53	(18, 156)
			106/0.7 mm.	1.4495 (25°C.)	57	(396)
			103/0.5 mm.	1.4284 (20°C.)	40	(244)
			103/1 mm.	1.4284 (20°C.)	40	(9)
C_2H_5O	iso-C_3H_7	Ethyl trichloroacetate	117–118/2 mm.	1.4468 (20°C.)	45	(9)
C_2H_5O	C_4H_9	Ethyl trichloroacetate	145–147/2 mm.	1.4523 (20°C.)	49	(9)
C_2H_5O	iso-C_4H_9	Ethyl trichloroacetate	135–136/2 mm.	1.4499 (20°C.)	43	(9)
C_3H_7O	CH_3	Propyl trichloroacetate	122/0.2 mm.	?	?	(181)
iso-C_3H_7O	C_2H_5	isopropyl trichloroacetate	110/0.2 mm.	?	?	(302)
			130–131/2 mm.	1.4511 (20°C.)	26	(9)
iso-C_3H_7O	iso-C_3H_7	Isopropyl trichloroacetate	120–121/2 mm.	1.4445 (20°C.)	42	(9)
C_4H_9O	CH_3	Butyl trichloroacetate	122/0.3 mm.	?	?	(181)
C_4H_9O	C_4H_9	Butyl trichloroacetate	158–159/2 mm.	1.4530 (20°C.)	48	(9)
C_4H_9O	iso-C_4H_9	Butyl trichloroacetate	146–147/2 mm.	1.4498	53	(9)
iso-C_4H_9O	CH_3	Isobutyl trichloroacetate	120–123/0.4–0.5 mm.	?	?	(181, 302)
iso-C_4H_9O	C_2H_5	Isobutyl trichloroacetate	120–122/0.2 mm.	?	?	(181)
iso-C_4H_9O	iso-C_4H_9	Isobutyl trichloroacetate	144–146/2 mm.	1.4500 (20°C.)	33	(9)
iso-$C_5H_{11}O$	CH_3	Isoamyl trichloroacetate	116/117/0.15–0.2 mm.	?	?	(181, 302)
$C_6H_{13}O$	CH_3	Hexyl trichloroacetate	140–141/0.2 mm.	?	44	(302)
$C_4H_9CH(C_2H_5)CH_2O$	CH_3	2-Ethylhexyl trichloroacetate	142–143/0.3 mm.	?	?	(181)
$C_8H_{17}O$	CH_3	Octyl trichloroacetate	152–157/0.2 mm.	?	?	(181)
$CH_3OC_2H_4O$	CH_3	2-Methoxyethyl trichloroacetate	136–138/0.3 mm.	?	?	(181, 302)
$CH_3OC_2H_4$	C_2H_5	2-Methoxyethyl trichloroacetate	140–142/0.2 mm.	?	?	(811)
$C_2H_5OC_2H_4O$	CH_3	2-Ethoxyethyl trichloroacetate	131–132/0.15 mm.	?	?	(181, 302)
$C_4H_9OC_2H_4O$	CH_3	2-Butoxyethyl trichloroacetate	140–143/0.07 mm.	?	?	(302)
$CH_3COOC_2H_4O$	CH	2-Acetoxyethyl trichloroacetate	150–153/0.35 mm.	?	?	(181)
$CH_2OC(CH_3)_2OCCH_2O$	C_2H_5	1,2-*O*-Isopropylidene-3-glyceryl trichloroacetate	145–147/0.1 mm.	?	?	(181)
CH_3OOCCH_2O	CH_3	Carbomethoxymethyl trichloroacetate	148–150/? mm.	?	?	(303)
C_6H_5O	CH_3	Phenyl trichloroacetate	144–146/0.5 mm.	1.4932 (32°C.)	45	(312, 314)
C_6H_5O	C_2H_5	Phenyl trichloroacetate	154–156/0.9 mm.	1.4966 (33°C.)	59	(312, 314)
p-$O_2NC_6H_4O$	CH_3	*p*-Nitrophenyl trichloroacetate	150–155/0.3 mm.	1.5543 (28°C.)	36	(312, 314)
p-ClC_4H_4O	CH_3	*p*-Chlorophenyl trichloroacetate	123–125/0.5 mm.	1.4833 (30°C.)	45	(312, 314)
p-ClC_6H_4O	C_2H_5	*p*-Chlorophenyl trichloroacetate	149–153/0.4 mm.	1.5027 (30°C.)	56	(312, 314)
C_2H_5S	CH_3	Ethyl trichloroacetate	105/0.25 mm.	1.4940 (26°C.)	53	(452)
C_2H_5S	C_2H_5	Ethyl trichloroacetate	114/0.23 mm.	1.4810 (31°C.)	74	(452)
C_6H_5S	CH_3	Phenyl trichlorothioacetate	135/0.06 mm.	1.5486 (30°C.)	87	(452)
C_6H_5S	C_2H_5	Phenyl trichlorothioacetate	142/0.06 mm.	1.5336 (30°C.)	96	(452)
C_6H_5	C_2H_5	Trichloromethyl phenyl ketone	105–110/0.001	1.5195 (20°C.)	91	(244)
			145–146/2 mm.	1.5200 (20°C.)	54	(345)
			101/4 × 10^{-5} mm.	1.5188 (20°C.)	76	(436)
$(CH_3O)_2P(O)$	CH_3	Trichloroacetyl chloride	134–135/0.75 mm.	1.4770 (20°C.)	78	(346)
			155–156/1.5 mm.	1.4710 (20°C.)	53	(234)
$(C_2H_5O)_2P(O)$	C_2H_5	Trichloroacetyl chloride	132–133/0.5 mm.	1.4660 (20°C.)	79	(346)
			100–110/0.05 mm.	?	91	(443)

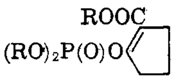
Hercules 3895) (83, 86, 144) and compounds of the type of XXIII (66, 147, 440) have been tested in somewhat greater detail.

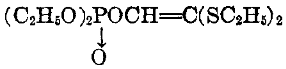

XX


XXI

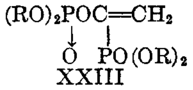
$(C_2H_5O)_2P(O)OCH{=}CHCl$

XVIII


XIX


$(C_2H_5O)_2\underset{\substack{\downarrow\\ O}}{P}OCH{=}C(SC_2H_5)_2$

XXII

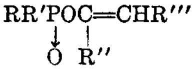

$(RO)_2\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{|\\ PO(OR)_2}}{C}{=}CH_2$

XXIII

TABLE 30

Alkyl vinyl phosphonates

Compounds of the type



$$RR'\underset{\substack{\downarrow\\ O}}{P}O\underset{\substack{|\\ R''}}{C}{=}CHR'''$$

R	R′	R″	R‴	Prepared by the Reaction of	Prepared by the Reaction with	Boiling Point	$n_D^{20°}$	Yield	Reference
						°C.		per cent	
C_6H_5	CH_3O	CH_3	H	$C_6H_5P(OCH_3)_2$	Chloroacetone	137–138/8 mm.	1.5120	44	(344)
C_6H_5	CH_3O	CH_3	$COOC_2H_5$	$C_6H_5P(OCH_3)_2$	Ethyl α-chloroacetoacetate	162–174/1 mm.	?	84	(438)
C_6H_5	$CH_2{=}CHO$	H	H	$C_6H_5P(O)Cl_2$	Acetaldehyde + $(C_2H_5)_3N$	110–111/1.5-2 mm.	1.5144	30–35	(178)
C_6H_5	CH_3	H	H	$C_6H_5(CH_3)P(O)Cl$	Acetaldehyde + $(C_2H_5)_3N$	102–104/2 mm.	1.5224	30–35	(178)
CH_3	$ClCH_2CH_2O$	H	H	$CH_3(ClCH_2O)P(O)Cl$	Acetaldehyde + $(C_2H_5)_3N$	96–98/3.5–4 mm.	1.4540	30–35	(178)
CH_3	C_4H_9O	H	H	$CH_3(C_4H_9O)P(O)Cl$	Acetaldehyde + $(C_2H_5)_3N$	63-65/2.5–3 mm.	1.4278	30-35	(178)
CH_3	$CH_2{=}CHO$	H	H	$CH_3P(O)Cl$	Acetaldehyde + $(C_2H_5)_3N$	64–65/8 mm.	1.4394	30–35	(178)
$ClCH_2$	$CH_2{=}CHO$	H	H	$ClCH_2P(O)Cl_2$	Acetaldehyde + $(C_2H_5)_3N$	66–67/1 mm.	1.4636	30–35	(178)
C_2H_5	$CH_2{=}CHO$	H	H	$C_2H_5P(O)Cl_2$	Acetaldehyde + $(C_2H_5)_3N$	60–61/5 mm.	1.4409	30–35	(178)
CH_3	C_2H_5	H	H	$(C_2H_5O)POCH{=}CH_2$	Iodomethane	82–83/25 mm.	1.4265	89	(278)
CH_3	C_3H_7	H	H	$(C_3H_7O)POCH{=}CH_2$	Iodomethane	79.5–80/8 mm.	1.4290	90	(278)
CH_3	C_4H_9	H	H	$(C_4H_9O)POCH{=}CH_2$	Iodomethane	79.5–80/3.5 mm.	1.4320	86	(278)
CH_3	$CH_2{=}CH$	H	H	$C_2H_5OP(OCH{=}CH_2)_2$	Iodomethane	62.5–63/6.5 mm.	1.4388	88	(278)
C_2H_5	C_2H_5	H	H	$(C_2H_5O)_2POCH{=}CH_2$	Iodoethane	69–69.5/6 mm.	1.4291	80	(278)
C_2H_5	C_4H_9	H	H	$(C_4H_9O)_2POCH{=}CH_2$	Iodoethane	95–96/7.5 mm.	1.4335	60	(278)
C_2H_5	$CH_2{=}CH$	H	H	$C_2H_5OP(OCH{=}CH_2)_2$	Iodoethane	66.5/7 mm.	1.4398	82	(278)
C_3H_7	$CH_2{=}CH$	H	H	$C_3H_7OP(OCH{=}CH_2)_2$	1-Iodopropane	71–71.5/3.5 mm.	1.4408	65	(278)
C_4H_9	C_4H_9	H	H	$(C_4H_9O)_2POCH{=}CH_2$	1-Iodobutane	83.5–84/1 mm.	1.4369	85	(278)
C_4H_9	$CH_2{=}CH$	H	H	$C_4H_9OP(OCCH{=}H_2)_2$	1-Iodobutane	71–72/2 mm.	1.4430	74	(278)
$CH_3C(O)$	C_2H_5	H	H	$(C_2H_5O)_2POCH{=}CH_2$	Acetyl chloride	76.5/2 mm.	1.4352	63	(278)
$CH_3C(O)$	C_3H_7	H	H	$(C_3H_7O)_2POCH{=}CH_2$	Acetyl chloride	67–68/1 mm.	1.4361	58	(278)
$CH_3C(O)$	C_4H_9	H	H	$(C_4H_9O)_2POCH{=}CH_2$	Acetyl chloride	91–92/1 mm.	1.4390	70	(278)
$C_6H_5C(O)$	C_3H_7	H	H	$(C_3H_7O)_2POCH{=}CH_2$	Benzoyl chloride	147–148/3 mm.	1.5168	83	(278)
$C_6H_5C(O)$	$CH_2{=}CH$	H	H	$C_2H_5OP(OCH{=}CH_2)_2$	Benzyl chloride	135–137/1 mm.	1.5315	50	(278)
C_2H_5	$CH_2{=}CH(CH_3)$	CH_3	H	$C_2H_5OP(OCH(CH_3){=}CH_2)_2$	Iodoethane	69.5–70/2 mm.	1.4470	82	(278)
$(CH_3)_2N$	CCl_3	H	H	$(CH_3)_2NPOCH_2CH_2O$	Tetrachloromethane	100–105/0.5 mm.	?	?	(444)

TABLE 31

Vinyl alkylphosphonates

Compounds of the type $RR'P(O)OCH{=}CCl_2$

R	R′	Prepared by the Reaction of Chloral with	Boiling Point	$n_D^{20°}$	Yield	References
			°C.		per cent	
C_2H_5	CH_3O	$C_2H_5P(OCH_3)_2$	65–66/0.5 mm.	1.4680	61	(364)
C_2H_5	C_2H_5O	$C_2H_5P(OC_2H_5)_2$	71–72/1 mm.	1.4637	68	(364)
C_2H_5	C_3H_7O	$C_2H_5P(OC_3H_7)_2$	83–86/0.5 mm.	1.4620	68	(364)
C_2H_5	iso-C_3H_7O	$C_2H_5P(O$-iso-$C_3H_7)_2$	73–74/0.5 mm.	1.4575	73	(364)
C_2H_5	C_4H_9O	$C_2H_5P(OC_4H_9)_2$	92–93/0.5 mm.	1.4624	69	(364)
C_2H_5	iso-C_4H_9O	$C_2H_5P(O$-iso-$C_4H_9)_2$	89–90/0.5 mm.	1.4570	73	(364)
C_2H_5	C_5H_{11}	$C_2H_5P(OC_5H_{11})$	100–101/0.5 mm.	1.4591	71	(364)
C_2H_5	$CH_2{=}CHCH_2$	$C_2H_5P(OCH_2CH{=}CH_2)_2$	76–78/0.5 mm.	1.4740	83	(364)
C_2H_5	$C_6H_5CH_2$	$C_2H_5P(OCH_2C_6H_5)_2$	132–133/0.5 mm.	1.5220	83	(364)
C_2H_5	$(CH_3)_2N$	$C_2H_5(CH_3O)PN(CH_3)_2$	80–82/2 mm.	1.4714	52	(364)
C_2H_5	C_2H_5	$(C_2H_5)_2POCH_3$	81–83/0.5 mm.	1.4810	70	(364)
C_6H_5	CH_3O	$C_6H_5P(OCH_3)_2$	80/10⁻⁴ mm.	1.5320	87	(436)
			125–137/1 mm.	?	73	(18, 156)
C_6H_5	C_2H_5O	$C_6H_5P(OC_2H_5)_2$	98/10⁻⁵ mm.	1.5242	95	(381, 436)
			131–144/2–3 mm.	?	68	(18)
p-ClC_6H_5	$(CH_3)_2N$	p-$ClC_6H_5(C_2H_5O)PN(CH_3)_2$	153/2 mm.	?	70	(381)

Concerning the mode of action of these insecticidally active dialkyl vinyl phosphates, it has been demonstrated, in particular with Phosdrin® (93–98, 100, 263, 300, 372, 394, 451) and DDVP[5] (54–59, 96, 149, 150, 188, 225, 250, 330, 336, 370, 419, 420), that their toxic action is the result of progressive inhibition of cholinesterase in mammals and in insects, where this system is physiologically important. Their mode of action, however, may also involve various other esterase enzymes, as shown in studies with houseflies, where different esterases compete for added DDVP (59). Insect cholinesterases also vary greatly in substrate specificity and susceptibility to inhibitors (93), possibly owing to different detoxication mechanisms. It has been proposed that the lability of the vinyl ester linkage might be an important feature in the extent to which inhibition of cholinesterase, that is, dialkyl phosphorylation of the enzymatically active sites (305), takes place (330); however, a comparison of the stability toward alkali of twenty-four dialkyl vinyl phosphates with their anticholinesterase activity and toxicity to rats and flies showed no distinct correlation (96).

VI. TABULAR SUMMARY OF THE ENOL PHOSPHATES

In this section the methods of preparation and the physicochemical data for the individual enol phosphates are given, covering those listed in *Chemical Abstracts* through 1960.

A. VINYL DIHYDROGEN PHOSPHATES

Table 20 lists the monoesters of phosphoric acid. A few alkyl vinyl hydrogen phosphates, previously prepared, are listed in table 12 (page 624).

B. DIALKYL VINYL PHOSPHATES

Only those compounds are listed in tables 21 through 33 that have been sufficiently characterized and adequately supported by experimental work. Some papers (35, 41, 44, 45, 48, 357) and numerous patents (103–108, 111–113, 182, 183, 205, 266, 339, 367, 368) describe *O,O*-dialkyl alkylphosphonates, prepared by the Michaelis–Arbuzov reaction, which in the light of the Perkow reaction, however, have to be formulated as the isomeric dialkyl vinyl phosphates. Those compounds, as well as vinylphosphonates of the structure $CH_2{=}CHPO(OR)_2$, are not included in the tables.

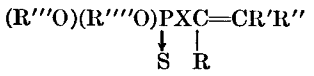
Several dialkyl vinyl phosphates have been prepared from the α-chloro, α-bromo, and α-iodo carbonyl compounds according to the Perkow reaction. Generally only the α-halo carbonyl compound that gave the best yield of the enol phosphate is listed. Owing to the large number of dialkyl vinyl phosphates known, the compounds have been grouped as follows:

(1) Unsubstituted dialkyl vinyl phosphates (table 21)
(2) 1-Substituted dialkyl vinyl phosphates (table 22)
(3) 2-Monosubstituted dialkyl vinyl phosphates (table 23)
(4) 2,2-Disubstituted dialkyl vinyl phosphates (tables 24 and 25)
(5) 1,2-Disubstituted dialkyl vinyl phosphates (tables 26 and 27)

TABLE 32

Dialkyl vinyl phosphorothioates

Compounds of the type



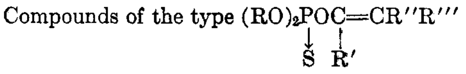
$$(R'''O)(R''''O)\underset{\substack{\downarrow\\ S}}{P}X\underset{\substack{|\\ R}}{C}{=}CR'R''$$

X	R	R′	R″	R‴	R⁗	Prepared by the Reaction		Boiling Point	n_D	Yield	References
						of	with				
								°C.			
O	H	H	H	C_2H_5	C_2H_5	$(C_2H_5O)_2POCH{=}CH_2$	Sulfur	82/7.5 mm.	1.4562	79	(307)
O	H	H	H	C_2H_5	$CH_2{=}CH$	$C_2H_5OP(OCH{=}CH_2)_2$	Sulfur	72–73/7 mm.	1.4634 (20°C.)	62	(307)
O	H	H	H	C_3H_7	C_3H_7	$(C_3H_7O)_2POCH{=}CH_2$	Sulfur	97/6 mm.	1.4581 (20°C.)	64	(307)
O	H	H	H	C_4H_9	C_4H_9	$(C_4H_9O)_2POCH{=}CH_2$	Sulfur	126–127/8 mm.	1.4575 (20°C.)	67	(307)
O	H	H	H	C_4H_9	$CH_2{=}CH$	$C_4H_9OP(OCH{=}CH_2)_2$	Sulfur	96/6 mm.	1.4654 (20°C.)	65	(307)
O	H	H	H	C_6H_5	$CH_2{=}CH$	$C_6H_5OP(OCH{=}CH_2)_2$	Sulfur	134–135/10 mm.	1.5268 (20°C.)	74	(307)
O	H	Cl	Cl	CH_3	CH_3	$(CH_3O)_2PSCH_3$	Chloral	70–71/1 mm.	?	?	(383)
O	H	Cl	Cl	C_2H_5	C_2H_5	$(C_2H_5O)_2PSC_2H_5$	Chloral	86–87/1 mm.	?	?	(383)
S	H	H	H	CH_3	CH_3	$(CH_3O)_2P(S)S_2$	Ethenylmagnesium bromide	74/77–2 mm.	1.5330 (25°C.)	58	(298)
S	H	H	H	C_2H_5	C_2H_5	$(C_2H_5O)_2P(S)S_2$	Ethenylmagnesium bromide	108–112/0.7 mm.	1.5120 (25°C.)	62	(298)
S	H	H	C_6H_5	C_2H_5	C_2H_5	$(C_2H_5O)_2P(S)S_2$	2-Phenylethenylmagnesium bromide	110–122/0.01 mm.	1.5820 (25°C.)	59	(298)
S	—OC_2H_4O—		H	C_2H_5	C_2H_5	$(C_2H_5O)_2P(S)SH$	1,2-Dichloro-*p*-dioxane	136–142/0.3–0.5 mm.	?	?	(142, 145)

TABLE 33

Dialkyl vinyl phosphorothioates

Compounds of the type



$$(RO)_2\underset{\overset{\downarrow}{S}}{P}O\underset{\overset{|}{R'}}{C}{=}CR''R'''$$

R′	R″	R‴	R	Prepared from $(RO)_2P(S)Cl$ and the Alkali Enolate of	Boiling Point	n_D	Yield	References
					°*C.*		*per cent*	
CH_3	H	$C(O)CH_3$	CH_3	2,4-Pentanedione	104/0.1 mm.	1.4859 (22°C.)	46	(282, 316)
CH_3	H	$C(O)CH_3$	C_2H_5	2,4-Pentanedione	110–115/0.3 mm.	1.4880 (24°C.)	?	(282, 316)
CH_3	H	$COOC_2H_5$	C_2H_5	Ethyl acetoacetate	139/12 mm.	?	?	(378)
C_6H_5	H	$C(O)CH_3$	CH_3	Benzoylacetone	154–157/1 mm.	1.5256 (23.5°C.)	?	(316)
C_6H_5	H	$C(O)CH_3$	C_2H_5	Benzoylacetone	150–152/0.2 mm.	1.5451 (26°C.)	63	(282, 311, 316)
C_6H_5	H	$COOC_2H_5$	CH_3	Ethyl benzoylacetate	156–159/0.3 mm.	1.5488 (25°C.)	35	(284, 309)
C_6H_5	H	$COOC_2H_5$	C_2H_5	Ethyl benzoylacetate	161/0.5 mm.	1.5348 (23.5°C.)	35	(284, 309)
CH_3	C_6H_5	CN	CH_3	1-Cyano-1-phenyl-2-propanone	143–147/1 mm.	1.5447 (26°C.)	37	(309, 313)
CH_3	C_6H_5	CN	C_2H_5	1-Cyano-1-phenyl-2-propanone	150–155/0.6 mm.	1.5334 (26.5°C.)	41	(309, 313)
CH_3	C_6H_5	$COOC_2H_5$	CH_3	Ethyl α-phenylacetoacetate	150–154/0.8 mm.	1.5211 (29°C.)	21	(309)
CH_3	C_6H_5	$COOC_2H_5$	C_2H_5	Ethyl α-phenylacetoacetate	145–150/0.8 mm.	1.4993 (23°C.)	20	(309)
$—(CH_2)_3—$		$COOC_2H_5$	CH_3	2-Carbethoxycyclopentanone	140–143/1.2 mm.	1.4995 (22°C.)	52	(310)
$—(CH_2)_3—$		$COOC_2H_5$	C_2H_5	2-Carbethoxycyclopentanone	131–135/0.9 mm.	1.4836 (28°C.)	?	(283)
$—(CH_2)_4—$		$COOC_2H_5$	CH_3	2-Carbethoxycyclohexanone	138–140/0.5 mm.	1.4980 (27°C.)	44	(283, 310)
$—(CH_2)_4—$		$COOC_2H_5$	C_2H_5	2-Carbethoxycyclohexanone	130–131/0.2 mm.	1.4900 (28°C.)	53	(283, 310)
CH_3	$—(CH_2)_2OOC—$		CH_3	α-Acetyl-γ-hydroxybutyrolactone	153–154/0.5 mm.	1.4796 (24°C.)	50	(282, 315)
C_2H_5	$—(CH_2)_2OOC—$		C_2H_5	α-Acetyl-γ-hydroxybutyrolactone	149–151/0.5 mm.	1.4699 (24°C.)	?	(282, 315)

(6) 1,2,3-Trisubstituted dialkyl vinyl phosphates (tables 28 and 29)
(7) Vinyl alkylphosphonates (tables 30 and 31)
(8) Dialkyl vinyl phosphorothioates (tables 32 and 33)

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