

Organophosphorus Analogues of Tropic Acid Esters

2. Tautomerism of Phenyl-diethoxyphosphoryl Acetaldehyde

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In part 1 of this investigation it has been proposed that phenyl-diethoxyphosphoryl acetaldehyde exists in both keto and enolic forms. Ethyl formyl-phenyl-acetate has in earlier literature been considered to exist in two enolic forms, *cis* and *trans*.

In this paper the structures of these compounds have been further elucidated by IR-spectra, protolytic titration with pK_a determination, and spectrophotometric determination of the coloured iron(III) complex concentration as a function of time. It has been confirmed that phenyl-diethoxyphosphoryl acetaldehyde in carbon tetrachloride and isopropanol solutions exists in keto and *cis* enolic forms. From IR-spectra it is evident that ethyl formyl-phenyl-acetate in carbon tetrachloride, besides existing in the enolic form, also exists in the keto form. In none of these two compounds has support been found for the existence of a *trans* enolic form or for enolization of the phosphoryl group.

In an earlier paper¹ the synthesis and properties of 2-phenyl-2-diethoxyphosphoryl ethanol has been described. An intermediate compound in this synthesis was phenyl-diethoxyphosphoryl acetaldehyde (for formulae see "Discussion"). This compound, which is closely related to ethyl formyl-phenyl-acetate, was shown to have the property of changing in refractive index and infrared spectrum, after distillation, during a period of eight days at room temperature. It was also pointed out in part 1 of this series¹ that an enolization evidently occurred which was a likely explanation of the observed phenomena. However, no consideration was given to the possibility of *cis-trans* isomerism of the enolic form. Such properties have been indicated by several authors^{2,3,4} in the case of ethyl formyl-phenyl-acetate. Another possibility for consideration is the enolization of the phosphoryl group. Investigations in order to obtain a more detailed description of phenyl-diethoxyphosphoryl acetaldehyde seemed thus an interesting study. Comparison of infrared spectra of phosphoryl and carbonyl analogues, determination of the keto-enol equilibrium and determination of the acid equilibrium constant of the enolic forms are the experiments chosen for this purpose.

EXPERIMENTAL

2,4-Dinitrophenylhydrazine was used as aldehyde carbonyl reagent.

Phenyl-diethoxyphosphoryl methane, phenyl-diethoxyphosphoryl acetaldehyde and 2-phenyl-2-diethoxyphosphoryl ethanol were prepared as described in part 1.

Ethyl phenyl-acetate was commercial (B.p. 90–91°/5 mm).

Ethyl formyl-phenyl-acetate was prepared analogously to the phenyl-diethoxyphosphoryl acetaldehyde. 1.5 moles of sodium were allowed to react with 2 moles of ethyl formate in 200 ml of ether, in a round bottomed flask fitted with a reflux condenser. One mole of ethyl phenyl-acetate in 250 ml of ether was added when all sodium had been consumed. The mixture was boiled for 4 h and then stirred at room temperature for 24 h, after which the ether solution was extracted with 2 × 200 ml of water. The pH of this extract was adjusted to 10 and the solution extracted with 3 × 100 ml of ether, the ether extracts being discarded. The aqueous solution was acidified with sulfuric acid to pH ~ 3 and percolated with ether for 12 h. The ether extract thus obtained was evaporated, giving a viscous residue. The residue was dissolved in benzene and the benzene evaporated; this operation was repeated twice. Finally, the product was distilled, the first 5 ml of distillate being discarded (B.p. 110°/6 mm Hg). Yield 55 %. $n_D^{25} = 1.5295$. (Found: C 68.9; H 6.3. Calc. for $C_{11}H_{13}O_3$ (192.2): C 68.8; H 6.3.)

Tropic acid ethyl ester was prepared by hydrogenation of ethyl formyl-phenyl-acetate, using sodium borohydride (SWS, Metal Hydrides Incorporated, Beverly, Mass.). 100 g of the sodium borohydride preparation (12.5 %) in 100 ml of water was neutralized with carbon dioxide to pH ~ 11. One mole of ethyl formyl-phenyl-acetate in 300 ml of methanol was added. Five min after the addition the mixture was hydrolysed with a dilute solution of hydrochloric acid. The methanol was evaporated under reduced pressure and the residual solution extracted with ether. The final product was obtained by fractional distillation of the ether extract (B.p. 145°/5 mm Hg). Yield 70 %. $n_D^{25} = 1.5192$. (Found: C 67.4; H 6.9. Calc. for $C_{11}H_{14}O_3$ (194.2): C 68.0; H 7.3.)

Infrared spectrophotometric measurements. The infrared spectra were recorded on a Perkin-Elmer spectrophotometer, Model 21, equipped with a rock salt prism. 0.2 M solutions in carbon tetrachloride were used, and the thickness of the cell was about 0.1 mm. In addition a 0.02 M solution of phenyl-diethoxyphosphoryl acetaldehyde in a 1.0 mm cell and a 0.2 M solution in isopropanol and cell thickness 0.1 mm were recorded. The following settings were used: resolution 927; response 2:1170; gain 5.7, suppression 3; speed about 1 μ /min; scale 5 cm/ μ .

Determination of dissociation constants. The dissociation constants of phenyl-diethoxyphosphoryl acetaldehyde and corresponding carbonyl analogue were determined at 25°C with a recording titrator⁵. The compounds were dissolved in 0.100 M potassium chloride and the concentration of the compounds was approximately 5.0 mM. Titration was performed in an atmosphere of nitrogen with 0.0990 M sodium hydroxide, which was added in 0.1 ml portions every third minute to permit the restoration of the keto-enol equilibrium. The pH-meter was standardized against two buffer solutions, 0.05 M potassium hydrogen *o*-phthalate (pH = 4.01) and 0.01 M borax (pH = 9.18).

The mixed dissociation constant is defined by

$$K'_a = \frac{a_{H^+} \times [E^-]}{[E] + [K]}$$

where $[E^-]$ is the concentration of the enolate ion and $[E]$ and $[K]$ the concentrations of the enolic and keto forms, respectively. In the actual pH-range a_{H^+} and a_{OH^-} can be neglected as terms and thus $[E^-] = [Na^+]$ and $[E] + [K] = C - [Na^+]$ are obtained, where C is the total concentration which was calculated from the titration curve. The equivalence point was obtained by plotting $\Delta V/\Delta pH$ against V (see Tables 1 and 2). The activity factor of the enolate ion, f_{E^-} , was estimated at 0.82⁶, and the thermodynamic dissociation constant was calculated from

$$pK_a = pK'_a - \log f_{E^-} = pK'_a + 0.09$$

Formation of iron (III) complex. At zero time one part of a 0.25 mM or 0.50 mM solution of phenyl-diethoxyphosphoryl acetaldehyde in isopropanol was added to one

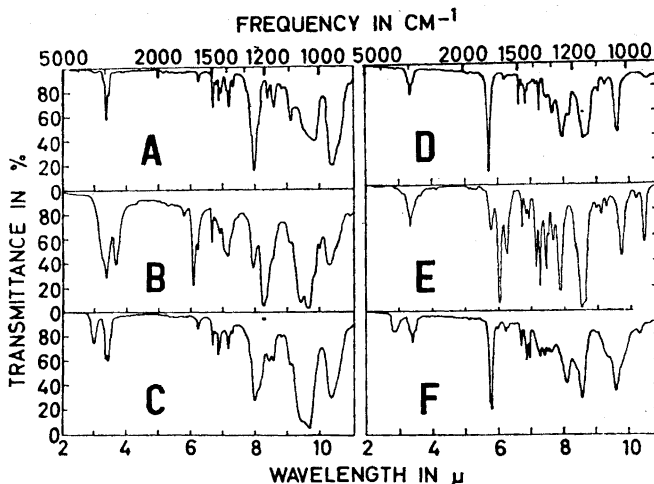


Fig. 1. Infrared absorption spectra of A. $\varphi\text{CH}_2\text{PO}(\text{OC}_2\text{H}_5)_2$; B. $\varphi\text{CH}(\text{CHO})\text{PO}(\text{OC}_2\text{H}_5)_2$; C. $\varphi\text{CH}(\text{CH}_2\text{OH})\text{PO}(\text{OC}_2\text{H}_5)_2$; D. $\varphi\text{CH}_2\text{COOC}_2\text{H}_5$; E. $\varphi\text{CH}(\text{CHO})\text{COOC}_2\text{H}_5$; F. $\varphi\text{CH}(\text{CH}_2\text{OH})\text{COOC}_2\text{H}_5$.

part of a 25 mM solution of iron(III) perchlorate in *isopropanol*. The optical density of the coloured complex was read at 4 500 Å at intervals until the development of colour terminated. A Beckmann spectrophotometer, Model B, with a 1 cm cell was used.

The molecular weight of phenyl-diethoxyphosphoryl acetaldehyde was determined with an isothermal distillation method using carbon tetrachloride as a solvent and azobenzene as a reference¹¹.

RESULTS

The following group frequency assignments can be made from the infrared spectra of the compounds^{7,8} (Fig. 1).

The 3 000 cm^{-1} region. The absorption bands at 3 015—2 875 cm^{-1} can be assigned to various CH stretching frequencies. The bands of the two carbinol derivatives (C and F) at 3 500—3 355 cm^{-1} can be ascribed to weakly hydrogen bonded OH frequencies, whereas the two bands of the aldehydes (B and E) at about 3 060 cm^{-1} and 2 730 cm^{-1} can probably be attributed to =C—H frequencies, and resonance stabilized intramolecular hydrogen bonded OH frequencies of the enolic forms, respectively.

Ten times dilution of solution B did not change the frequencies of its absorption bands in this region, nor did the relation between their densities change. Thus, only one O—H bond, which is intramolecular hydrogen bonded, has been found in B.

The 1 740—1 630 cm^{-1} region. The absorption band at about 1 730 cm^{-1} occurring in the spectra of phenyl-diethoxyphosphoryl acetaldehyde (B) and the three carbonyl derivatives (D, E, F) is ascribed to the C=O stretching frequencies and the very strong band of ethyl formylphenyl-acetate (E) at 1 660 cm^{-1} arises from a strongly hydrogen bonded C=O group. In the hydrogenated form (F) the C=O band occurs at 1 725 cm^{-1} indicating a much weaker hyd-

rogen bond than in (E). The band of (B) at $1\,635\text{ cm}^{-1}$ can probably be attributed to the C=C bond of the enolic form of (B). The corresponding band of the enolic form of (E) is presumably overlapped by the band at $1\,660\text{ cm}^{-1}$.

The 1 600—1 300 cm^{-1} region. The two bands occurring in all the spectra at $1\,600\text{ cm}^{-1}$ and at $1\,495\text{—}1\,490\text{ cm}^{-1}$ are caused by vibrations of the benzene nucleus. The $1\,600\text{ cm}^{-1}$ band is accentuated by the aliphatic C=C absorption in B and by C=O in E. Most of the other absorption bands in this region can be ascribed to C—H bending vibrations.

The 1 270—1 200 cm^{-1} region. At about $1\,250\text{ cm}^{-1}$ the three phosphorus compounds have an absorption band which originates from the P=O bond. Compound (B), however, shows an additional very strong band at $1\,200\text{ cm}^{-1}$ which probably originates from a hydrogen bonded P=O group. In this range absorption caused by the ester linkage C—O is also expected to occur (See D, E, F).

At lower frequencies absorption bands characteristic of C—OC, C—OP and CO—P bonds are found.

A change in infrared spectrum of phenyl-diethoxyphosphoryl acetaldehyde occurs when the compound is stored for a week at room temperature, as appears from Fig. 2. The absorption of the bands in the $3\,000\text{ cm}^{-1}$ region increases, especially that attributed to the hydrogen bonded band at $2\,730\text{ cm}^{-1}$, and the one attributed to H—C= at $3\,060\text{ cm}^{-1}$. The C=O band at $1\,725\text{ cm}^{-1}$ decreases and a new band ascribed to the C=C group appears at $1\,635\text{ cm}^{-1}$. The simultaneous increase of this band and the ones at $3\,060$ and $2\,730\text{ cm}^{-1}$ supports the assumption that the band at $1\,635\text{ cm}^{-1}$ is caused by vibrations of the C=C bond. The obvious increase of the absorption at $1\,410$

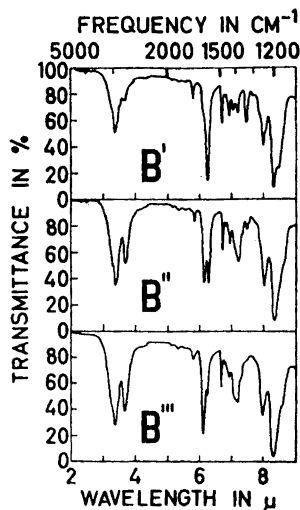


Fig. 2. Change in infrared absorption spectra from B' to B''' of phenyl-diethoxyphosphoryl acetaldehyde during a period of eight days after distillation. B''' represents the final stage.

Table 1. Dissociation constant of phenyl-diethoxy-phosphoryl acetaldehyde at 25°C
Total amount = 0.1899 mmoles.

V ml NaOH	pH	[E ⁻] mM	[E] + [K] mM	pK _a '
0.600	6.66	1.46	3.22	7.00
0.700	6.76	1.70	2.97	7.00
0.800	6.87	1.94	2.71	7.02
0.900	6.95	2.18	2.46	7.00
1.000	7.04	2.42	2.22	7.00
1.100	7.13	2.65	1.97	7.00
1.200	7.22	2.88	1.73	7.00
1.300	7.32	3.11	1.48	7.00

Mean value 7.00
pK_a = 7.09

cm⁻¹ may possibly arise from O—H bending vibrations, and moreover the band at 1 200 cm⁻¹ originating from the hydrogen bonded P=O group shows an increase in absorption.

At the *protolytic titration* of phenyl-diethoxyphosphoryl acetaldehyde and corresponding carbonyl analogue, it was observed that after every addition of alkali the pH, after an instantaneous increase, slowly decreased some tenths of units, and that equilibrium was reached after one to two min. This fact indicates a transformation of the compounds from a keto to an enolic form. The dissociation constants of the two compounds are given in Tables 1 and 2.

The *optical density of iron (III) complex*, after reaching a constant value, D_{∞} , has been found to be proportional to the concentration of phenyl-diethoxyphosphoryl acetaldehyde. The formation of the complex follows first-order kinetics as appears in Fig. 3. The quotient $a = D_0/(D_{\infty} - D_0)$, where D_0 is the optical density at the instant of mixing, and the rate constant of the complex formation, β , obtained from the slope of the line in Fig. 3, are

Table 2. Dissociation constant of ethyl formyl-phenyl-acetate at 25°C. Total amount = 0.1917 mmoles.

V ml NaOH	pH	[E ⁻] mM	[E] + [K] mM	pK _a '
0.601	6.78	1.47	3.26	7.13
0.700	6.88	1.71	3.01	7.13
0.801	6.97	1.94	2.76	7.12
0.900	7.06	2.18	2.51	7.12
1.000	7.15	2.42	2.26	7.12
1.100	7.24	2.65	2.01	7.12
1.200	7.33	2.88	1.77	7.12
1.300	7.43	3.12	1.53	7.12

Mean value 7.12
pK_a = 7.21

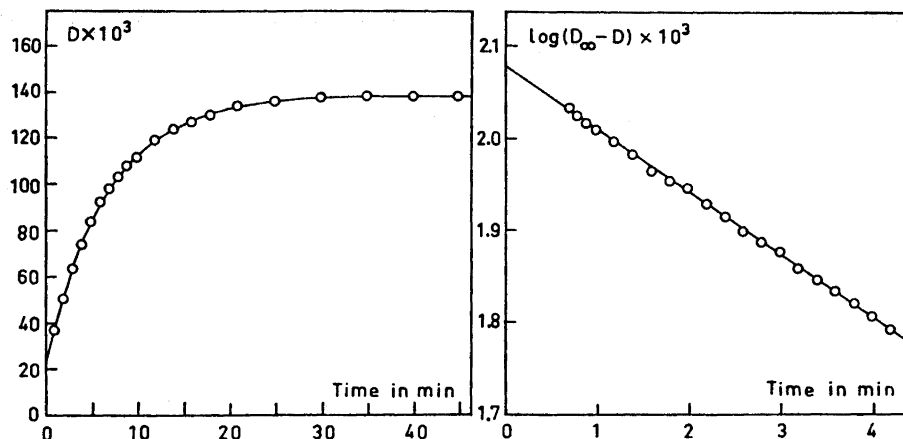


Fig. 3. Increase in optical density at 4 500 Å after addition of excess of iron(III) ions to an isopropanol solution of phenyldiethoxyphosphoryl acetaldehyde.

given in Table 3. For the significance of these constants see "Discussion".

The addition of 2,4-dinitrophenylhydrazine to phenyl-diethoxyphosphoryl acetaldehyde in alkaline solution produces a wine-red colour⁹.

The molecular weight of phenyl-diethoxyphosphoryl acetaldehyde was found to be 260 (Calc. 256.2).

DISCUSSION

An obstacle in determining the possible tautomeric forms of phenyl-diethoxyphosphoryl acetaldehyde was the fact that the enolic form did not consume bromine in aqueous solution. Such investigations have been made earlier² with the analogous ethyl formyl-phenyl-acetate, and the amount of enolic double bonds was found to exceed the amount of compound able to form iron(III) complex. The difference was interpreted as due to the presence of a *trans* enolic form.

Table 3. The constants of the keto-enol equilibrium, α , and enolization rate, β , of phenyl-diethoxy-phosphoryl acetaldehyde in isopropanol.

C	$\alpha = \frac{D_0}{D_\infty - D_0}$	$\beta \times 10^3 \text{ sec}^{-1}$
0.50	0.18	2.4
0.50	0.14	2.4
0.50	0.18	2.5
0.25	0.12	2.8
0.25	0.16	2.6
0.25	0.16	(3.7)

Mean value 0.16 2.5

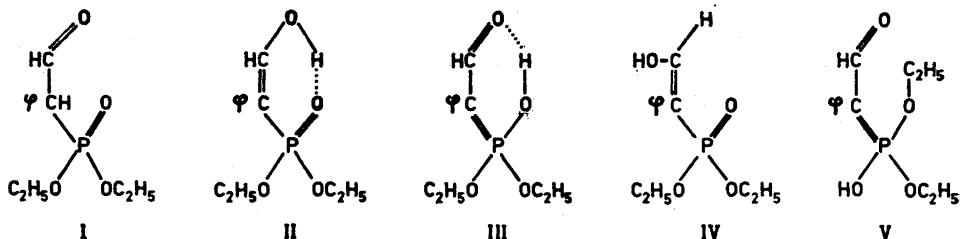


Fig. 4. *A priori* possible structures of phenyl-diethoxyphosphoryl acetaldehyde. Present experiments exclude III and V and give no support for IV.

The following is a discussion on how the results in this work support or exclude the *a priori* possible forms I—V (Fig. 4). Infrared spectra, especially B in Fig. 1 and Fig. 2, indicate that at least two of the forms given in Fig. 4 exist simultaneously in carbon tetrachloride solution. The discussion on the forms I—V is thus limited to the problem of which of these forms exist in considerable amounts. Influence of the solvent is realized but considered to cause only moderate changes in the concentration relations.

Formula I is the only form capable of showing simultaneously a carbonyl group and a slow neutralization, and thus represents one of the forms existing in considerable amounts.

Much more complicated than to demonstrate the presence of a keto form is the problem concerning which enol forms could be present. Here two oxygen atoms could act as proton acceptors and for each case one *cis* and one *trans* form have to be considered. Formulae II to V all have hydroxyl groups.

The content of C=C was shown to increase during enolization which indicates presence of II and IV. Formulae III and V show C=P and P—OH structures, but no absorption bands which could be attributed to these bonds have been observed. Moreover, phenyl-diethoxyphosphoryl acetaldehyde and ethyl formyl-phenyl-acetate show very similar pK_a values, indicating a carbonyl enolization. The pK_a -value itself (7.09) of the organic phosphorus compound is far above that which could be expected from a P—OH structure. It is thus reasonable to exclude formulae III and V.

Formulae II and IV now remain as possible forms, and the choice between these forms or their coexistence is mainly founded on the comparison of the infrared spectra in the 3000 cm^{-1} region at different concentrations. The *trans* form IV would most probably have been represented by two hydroxyl absorption bands, one for free hydroxyl and one for intermolecular hydrogen bonded hydroxyl. Such bands would also show changes in density and frequency, respectively, on dilution. None of these effects could be demonstrated. Only one band corresponding to an intramolecular hydrogen bonded hydroxyl group was found. It might be inferred that absorption bands from other types of hydroxyl groups are covered in the 3000 cm^{-1} region. Such covered bands are, however, unlikely because of the results from the dilution experiments, and also because of the proportional increase of the hydroxyl band to

the band ascribed to the =C—H group (Fig. 2). Furthermore the molecular weight obtained shows that no association occurs in carbon tetrachloride solution. The instantaneous formation of a coloured iron(III) complex also indicates a *cis* enolic group. Formula II must thus be considered to represent an existing form.

The kinetic results from the experiments with iron(III) complex (Fig. 3 and Table 3) can be given the following interpretations. Since the *trans* form can be excluded and the *cis* form is the only one capable of yielding a coloured complex instantaneously in the presence of excess of iron(III) ions, D_0 is proportional to the concentration of *cis* enol and enolate, [E], and D_∞ proportional to the total concentration, [E] + [K]. This gives

$$a = \frac{D_0}{D_\infty - D_0} = \frac{[E]}{[K]}$$

i.e. a is the equilibrium constant for $K \rightleftharpoons E$. Furthermore, under such conditions, the transformation of $K \rightarrow E$ is the rate determining step in the colour reaction, and β is thus the enolization rate constant.

Altogether, the present results give strong support to the view that phenyl-diethoxyphosphoryl acetaldehyde and ethyl formylphenyl-acetate exist in keto and *cis* enolic forms, and no support to the existence of a *trans* enolic form in either of the compounds. This conclusion is also supported by the opinion that the thermochemical stabilities of the keto and *cis* enolic forms are much higher than that of the *trans* enolic form¹⁰.

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