REACTIONS OF SOME 1,2-OXA-4-PHOSPHOLENE DERIVATIVES WITH ALCOHOLS AND AMINES

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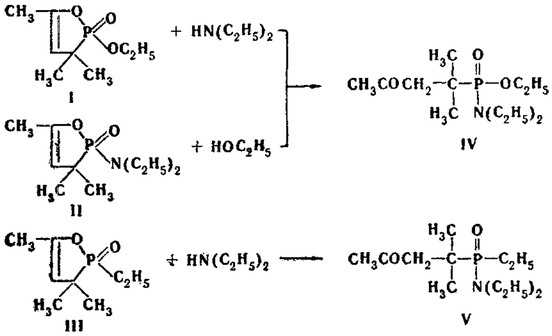
The reactions of P-alkyl and P-alkoxy derivatives of oxaphospholene with diethylamine and of oxaphospholene P-amide with alcohol proceed in a complex manner and included phosphorylation, alkylation, and salt formation.

It is known that 1,2-oxa-4-phospholene derivatives enter into reactions accompanied by ring formation. With water they form acids [1-4], while with alcohols they form symmetrical [3,5-8] or unsymmetrical [2,3,5,7] phosphonates and phosphinates [2,3,9]. The preparation of a monothiophosphonate was described in [7]. The synthesis of amides of phosphinic acids or of amidoesters of phosphonic acids via opening of the oxaphospholene ring has not been reported. Acyclic amidophosphates are formed from 1,3,2-dioxa-4-phospholenes [10]. We have shown [3] that esters of ketoalkylphosphinic and phosphonic acids have interesting biological properties. The preparation of their amide analogs seemed of natural interest in this plan.

Having three types of oxaphospholene derivatives (I-III) at our disposal, we decided to carry out the following reactions:



(1)

(2)

(3)

In contrast to the reactions of alcohols with I and III, which proceed smoothly [2,5], reactions (1)-(3) do not proceed at all under mild conditions, while under severe conditions they give complex mixtures.

Monitoring of the course of reactions (1) and (2) by gas-liquid chromatography demonstrated that diethyl ketobutylphosphinate is formed in both cases; in addition, amide II was recorded in the products of reaction (1), while ester I, diethylamine, and triethylamine were recorded in the products of reaction (2). The band at 870-880 cm^{-1}, which is characteristic for the oxaphospholene ring, in the IR spectra of the reaction mixtures vanishes (Fig. 1a) or becomes considerably less intense (Fig. 1b). The intensity of the absorption of the ring double bond at 1670-1690 cm^{-1} simultaneously decreases, and a carbonyl group band appears at 1710-1720 cm^{-1}. [The spectra of the starting cyclic ester and amide are presented in Fig. 2 (a and b).] The characteristic bands of ammonium absorption, complicated by some additional factors,

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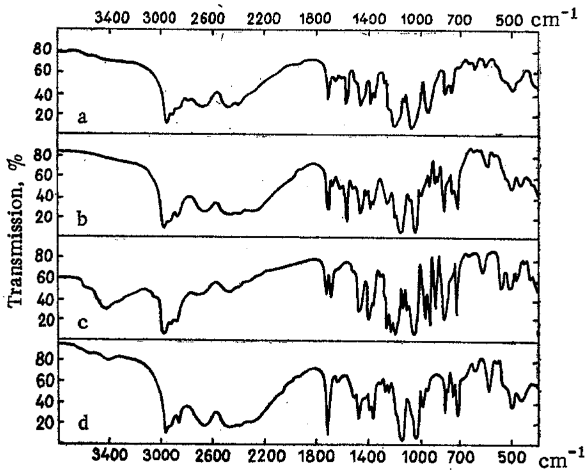


Fig. 1. IR spectra of the reaction products: a) 2-oxo-2-ethoxy-3,3,5-trimethyl-1,2-oxa-4-phospholene with diethylamine; b) 2-oxo-2-diethylamido-3,3,5-trimethyl-1,2-oxa-4-phospholene with ethanol; c) 2-oxo-2-ethyl-3,3,5-trimethyl-1,2-oxa-4-phospholene with diethylamine; d) ethyl 1,1-dimethyl-3-ketobutylphosphinate with diethylamine.

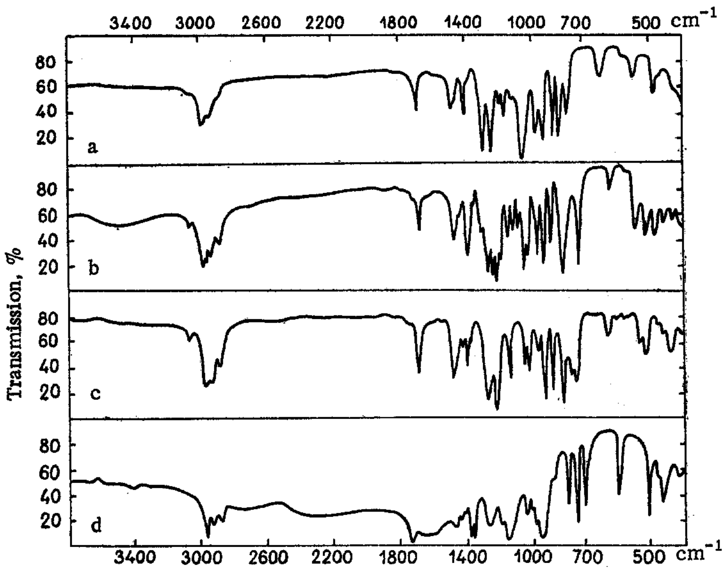


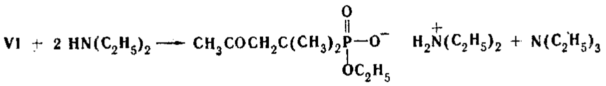
Fig. 2. IR spectra: a) 2-oxo-2-ethoxy-3,3,5-trimethyl-1,2-oxa-4-phospholene (I); b) 2-oxo-2-diethylamido-3,3,5-trimethyl-1,2-oxa-4-phospholene (II); c) 2-oxo-2-ethyl-3,3,5-trimethyl-1,2-oxa-4-phospholene (III); d) ethyl 1,1-dimethyl-3-ketobutylphosphinate (VII).

arise at 2000-3000 cm^{-1}. To confirm the correctness of this assignment, we recorded the IR spectra of the free ethyl 1,1-dimethyl-3-ketobutylphosphinate (Fig. 2d) and its mixture with diethylamine (Fig. 1d) both at room temperature and after heating to 160°. Heat treatment did not induce any visible changes. The ^{31}P NMR spectra change substantially in the course of the reactions. In the case of (1), the peak of the starting ester ($\delta = -50$ ppm) vanishes, and a signal appears at −24 ppm. In the case of (2), the signal of the starting amide at −53 ppm is retained along with a peak at −28 ppm.

We feel that the observed phenomena indicate the occurrence of the following processes:

$$\mathrm{II} + \mathrm{HOC_2H_5} \rightleftharpoons \mathrm{I} + \mathrm{HN(C_2H_5)_2} \tag{4}$$

$$\mathrm{I} + \mathrm{HOC_2H_5} \longrightarrow \underset{\mathrm{VI}}{\mathrm{CH_3COCH_2C(CH_3)_2PO(OC_2H_5)_2}} \tag{5}$$



$$\mathrm{VI} + 2\,\mathrm{HN(C_2H_5)_2} \longrightarrow \mathrm{CH_3COCH_2C(CH_3)_2}\underset{\displaystyle \mathrm{OC_2H_5}}{\overset{\displaystyle \mathrm{O}}{\overset{\|}{\mathrm{P}}}}\mathrm{{-}O^-}\ \ \mathrm{H_2\overset{+}{N}(C_2H_5)_2} + \mathrm{N(C_2H_5)_3} \qquad (6)$$

A reaction of the (5) type has been repeatedly described [2,3,5,9]. To confirm process (6), which has been reported for acyclic phosphinates [11, 12], we carried out the model reactions of diethylamine with the diethyl ester of 1,1-dimethyl-3-ketobutylphosphonic acid and the ethyl ester of ethyl 1,1-dimethyl-3-ketobutylphosphinic acid. The IR spectra of the reaction mixtures of the model and fundamental reactions were similar. In the first case, a signal appears at −28 ppm in the ^{31}P NMR spectrum.

By planning an experiment according to Scheme (3), we expected that a decrease in the number of reaction centers should simplify the occurrence of the reaction and facilitate the isolation of acyclic amide V. However, in this case also, the reaction does not proceed unambiguously. The starting compounds are recovered almost entirely under mild conditions. When the temperature is raised, processes similar to those indicated above, but occurring with the participation of exclusively the cyclic ester bond, are realized. The IR spectrum (Fig. 1c) contains oxaphospholene (875, 1680, 3060 cm^{-1}), acyclic carbonyl compound (1720 cm^{-1}), and secondary ammonium group bands (2000–3000 cm^{-1}). In addition to the signal of the starting cyclic phosphinate at −75 ppm, a signal at −40 ppm appears in the ^{31}P NMR spectrum. There is also a signal in this region for the products of the model reaction of diethylamine with ethyl 1,1-dimethyl-3-ketobutylphosphinic acid.

All of the facts presented demonstrate that the reactions proceed in a complex manner and include phosphorylation, alkylation, and salt-formation processes.

EXPERIMENTAL

Reaction of 2-Oxo-2-ethoxy-3,3,5-trimethyl-1,2-oxa-4-phospholene (I) with Diethylamine. A) A mixture of 9 g (0.05 mole) of I [13] and 3.6 g (0.05 mole) of diethylamine was heated in a sealed tube at 83-85° for 8 h. The volume of the reaction mixture did not change. The IR and ^{31}P NMR spectra did not register changes in the reaction mixture. Additional heating (at 115-117°) for 8 h reduced the volume by 1.5%. Distillation yielded 2 g of a volatile fraction with n_D^{20} 1.3923 (which, according to gas–liquid chromatography, proved to be diethylamine with a small amount of diethyl ether) and 5.2 g (58%) of starting I with bp 68-70° (0.02 mm) and n_D^{20} 1.4523.

B) A mixture of 7.3 g (0.04 mole) of I and 2.9 g (0.04 mole) of diethylamine was heated in a sealed tube at 140° for 8 h. The volume of the reaction mixture decreased by 10.5%. The reaction product became dark yellow and viscous. Found: N 5.41; P 11.7%. $C_{12}H_{26}NO_3P$. Calculated: N 5.3; P 11.6%. Distillation of the reaction product resulted in decomposition.

Reaction of 2-Oxo-2-diethylamino-3,3,5-trimethyl-1,2-oxa-4-phospholene (II) with Ethanol. A) A mixture of 25.4 g (0.12 mole) of II and 11 g (0.24 mole) of absolute ethanol in the presence of a catalytic amount of sodium ethoxide was heated in a sealed tube at 110° for 16 h. A water aspirator was used to separate a volatile fraction (13.0 g), which, according to GLC, proved to be a mixture of ethanol, diethylamine, and triethylamine. Column rectification made it possible to isolate 1 g of diethylamine with bp 55° and n_D^{20} 1.3872 and 8.6 g of ethanol with bp 78° and n_D^{20} 1.3632. Two fractions were isolated by vacuum distillation of the residue: 1) 1.8 g with bp 66-76° (0.02 mm), d_4^{20} 1.0578, and n_D^{20} 1.4595 (according to GLC, this fraction is a mixture of II, I, and VI); 2) 9.7 g of a product with bp 77° (0.02 mm), which crystallized on standing to give a substance with mp 55-57°. This product did not depress the melting point of starting II. The amount of II recovered was 38%.

B) A mixture of 11 g (0.05 mole) of II and 2.3 g (0.05 mole) of absolute ethanol in the presence of a catalytic amount of sodium ethoxide was heated in a sealed tube at 200° for 16 h. Workup of the reaction mixture gave 5 g of volatile reaction products with bp 72-75° and n_D^{20} 1.3945; according to GLC, this fraction consisted of diethylamine, ethanol, and triethylamine. The bulk of the mass decomposed during distillation.

Reaction of 2-Oxo-2-ethyl-3,3,5-trimethyl-1,2-oxa-4-phospholene (III) with Diethylamine. A) A mixture of 22.7 g (0.13 mole) of III [14] and 9.8 g (0.13 mole) of diethylamine was heated in a sealed tube at 120° for 8 h. Fractional distillation yielded 8.4 g (95%) of diethylamine with bp 55° and n_D^{20} 1.3873 and 18.5 g (82%) of starting III with bp 70-72° (0.02 mm) and n_D^{20} 1.4735.

B) A mixture of 10.8 g (0.06 mole) of III and 4.7 g (0.06 mole) of diethylamine was heated in a sealed tube at 160° for 8 h. Fractional distillation yielded 2.8 g (24%) of starting III with bp 72° (0.02 mm) and n_D^{20} 1.4732.

Reaction of Ethyl 1,1-Dimethyl-3-ketobutylphosphinic Acid (VII) with Diethylamine. A mixture of 0.8 g (0.004 mole) of VII [2] and 0.3 g (0.004 mole) of diethylamine was heated in a sealed tube at 160° for 6 h. When the compounds were mixed, a viscous, homogeneous liquid was formed and did not change its appearance during heating. The IR spectra of the reaction mixture before and after heating were identical.

Reaction of the Diethyl Ester of 1,1-Dimethyl-3-ketobutylphosphonic Acid (VI) with Diethylamine. A mixture of 3.7 g (0.016 mole) of VI [3] and 1.2 g (0.016 mole) of diethylamine was heated in a sealed tube at 160° for 6 h.*

Reaction of the Ethyl Ester of Ethy 1,1-Dimethyl-3-ketobutylphosphinic Acid (VIII) with Diethylamine. A mixture of 1.5 g (0.007 mole) of VIII [2] and 0.5 g (0.007 mole) of diethylamine was heated in a sealed tube at 160° for 16 h. Fractional distillation yielded 0.6 g (40%) of starting VIII with bp 85° (0.05 mm) and n_D^{20} 1.4590.

Except for VII, the IR spectra of all of the compounds were recorded as thin layers with a UR-10 spectrophotometer. The IR spectrum of a KBr pellet of VII was recorded. The chromatographic analysis was carried out with a Pye-104 chromatograph with a differential flame ionization detector in 200-cm-long glass columns with an inner diameter of 0.4 cm. The liquid phase was a mixture of fluorinated FS-328 silicone with neopentylene glycol succinate (5 : 1) applied in 3% quantities on silanized Chromosorb W (80-100 mesh). The gas-carrier (argon) flow rate was 30 ml/min. The phosphorus-containing compounds were analyzed at 180°, while the phosphorus-free volatile fractions were analyzed at 30°. The ^{31}P NMR spectra were recorded with a KGU-4 spectrometer with an operating frequency of 10.2 MHz at room temperature.

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