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NATURE OF ACID-CATALYZED ALCOHOLYSIS OF AMIDES OF TRIVALENT-PHOSPHORUS ACIDS

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ABSTRACT. To study the chemical nature of the acid catalysis of amides of trivalent-phosphorus acids (ATPA) alcoholysis the most important procedural problems have been solved. Simple and efficacious techniques for the purification of original ATPA from amine hydrohalides have been worked out. A precise and reliable way has been chosen to control the residual amount of amine hydrohalides in ATPA having been subjected to the various purification procedures. The nature of the dependence of alcoholysis rate constants for ATPA of different structures on the amine-hydrohalide concentration has been established. The general acid catalysis was established using the Brønsted equation, so that the process includes the formation of a catalytic H-complex incorporating substrate and catalyst on the whole. Amides P(III) of different types treated with anhydrous hydroborofluoric acid readily form the corresponding P-protonated salts. The conversions of corresponding products of complete protonation have been investigated. The structure of P-protonated salt 23 has been studied by means of X-ray analysis.

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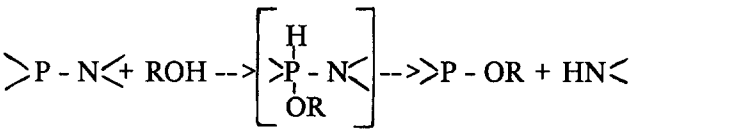
Phosphorylation of alcohols and phenols with ATPA[1] is characterized by high reaction rates, the ability to work with complex functionalized systems, the convenience and accessibility of the reactants. Owing to that, ATPA are actively employed nowadays in the synthesis of oligonucleotides[2],phospholipids[3],sugar derivatives[4], complex ligands for metallocomplexes[5], etc.

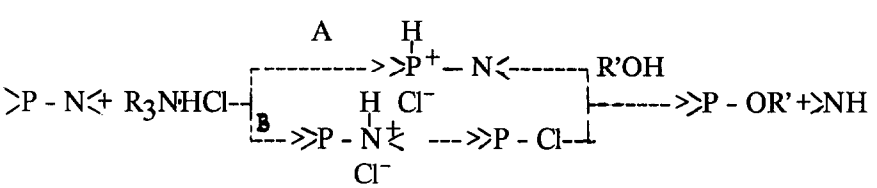
The reaction under consideration was discovered in the early 1960s[6,7], but its mechanism was remaining unclear for a long time. This reaction was regarded firstly as combination of consecutive addition and decomposition[7]:



In reality, however, the picture proved to be more complicated. As it was shown in our laboratory in 1966, ATPA exhibited a high phosphorylation ability only in the presence of either amine hydrohalides, that normally contaminate ATPA, or other acid catalysts[8,9]. The phenomenon of acid catalysis was observed further in other important reactions involving ATPA[10]. Thus, the investigation of acid catalysis turned into the determining factor in the development of researches on the ATPA-assisted phosphorylation of various nucleophiles.

In order to describe the nature of acid catalysis, a number of authors suggested schemes that included preliminary protonation of substrate at phosphorus (A) or nitrogen (B) atom.

As for the latter case, it was postulated that the phosphoammonium salt was converted into the halophosphite (phosphine), which was considered the actual phosphorylating agent[11]:



We have recently presented the data on the rates of deuteromethanolysis of 2-fluoro-1,3,2-dioxaphosphorinane in the present of various bases differing in the basicity and of that of 2-diethylamino(or imidazolyl-, N-ethylanilino-)-1,3,2-dioxaphosphorinanes catalyzed by hydrogen fluoride salts of different amines. The alcoholysis of the fluorophosphite in the presence of imidazole, N-ethylaniline proceeds slowly whereas alcoholysis of the P(III) amides catalyzed by imidazole and N-ethylaniline hydrofluorides occurs rapidly even at room temperature. Furthermore we have established similar catalytic activities for the amines hydrofluorides, hydrochlorides and hydrobromides. This would have been impossible if the reaction rate had been determined by halophosphite (phosphine) formation. Thus, the hypothesis concerning the formation of such an intermediate into the scheme of catalytic alcoholysis cannot be of common use[12]. A similar conclusion can be drawn from the data obtained by J.Szewczyk and L.D. Quin[13] in experiments on ATPA in the presence of ^{15}N-labelled amine hydrohalides.

The purpose of this work was to study the chemical nature of the catalysis of ATPA alcoholysis. To obtain reliable results, it was necessary to solve, at first, several important procedural problems that had been disregarded in the literature: (1) to work out simple and efficacious techniques for the purification of original ATPA from amine hydrohalides, (2) to choose a precise and reliable way to control the residual amount of amine hydrohalides in ATPA having been subjected to the various purification procedures and (3) to establish the nature of the dependence of the alcoholysis rate constants for ATPA different in the structure on the amine-hydrohalide concentration.

We chose initially three accessible phosphoamides which present neither stereochemical nor other complications. These were 2-diethylamino-5,5-dimethyl-1,3,2-dioxaphosphorinane (**1**), 2-diethylamino-1,3,2-dioxaphospholane (**2**), and tris(diethylamino)phosphine (**3**). All of the amides were obtained by the interaction of the corresponding chloroanhydrides and diethylamine, which was both the object of phosphorylation and the acceptor of hydrogen chloride. Thus, according to the synthesis technique, all the amides were contaminated with the same acid impurity, diethylamine hydrochloride, and possibly with chlorophosphites. To quantitatively evaluate the content of

chloride ions in phosphoamides, we used the method of potentiometric titration* , which allowed the residual chloride-ion content to be determined to within 5 $\mu g/l$[14]. Each of the amides was purified successively in four ways: twofold distillation (method *a*), after method *a* followed by water-washing of the benzene solution of the amide followed by the drying over calcium hydride and distillation over sodium (method *b*)[15], after method *b* followed by addition of butyl lithium and distillation over sodium (method *c*), and after method *c* followed by treatment with a concentrated alkali solution in the presence of ammonium salts with long-chain radicals on the phase transfer principle (method *d*) (see Experimental).

The results of the analysis are summarized in Table 1, suggesting that the simple twofold distillation of amides (method *a*) does not yield adequate purity whereas additional purification by method *b* and *c* reduces the amine-hydrochloride content significantly. The only exception is amide **3**, for which purification by method *b* does not allow amine hydrochloride to be essentially eliminated, which seems to be due to its higher basicity[16]. The purification by method *c* proved to be efficacious, because, in contrast to method *b*, the butyllithium treatment takes place in a homogeneous medium. This method was used

Table 1. The residual chloride-ion content in the amides (1-4) purified with different methods.

Method of purification	Chloride-ion content, mol/l			
	Amide 1	Amide 2	Amide 3	Amide 4
a	$1.2 \cdot 10^{-2}$	$2.1 \cdot 10^{-2}$	$1.8 \cdot 10^{-2}$	----
b	$5.3 \cdot 10^{-3}$	$4.8 \cdot 10^{-4}$	$0.9 \cdot 10^{-2}$	----
c	$1.2 \cdot 10^{-2}$	$3.2 \cdot 10^{-4}$	$1.3 \cdot 10^{-4}$	----
d	----	----	$1.2 \cdot 10^{-4}$	$1.6 \cdot 10^{-4}$

*The amount of amine hydrochlorides in the original ATPA may rise during alcoholysis on account of chlorophosphite impurities. To avoid inaccuracy, we hydrolyzed the ATPA sample before determining chloride ion, and only after that did we perform potentiometric titration (Fig.1).

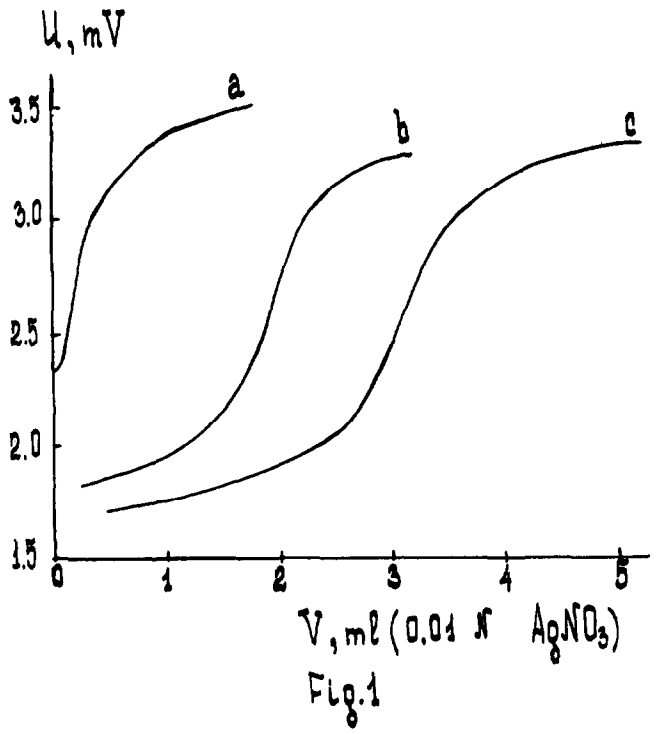
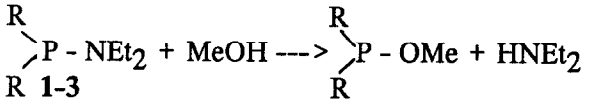


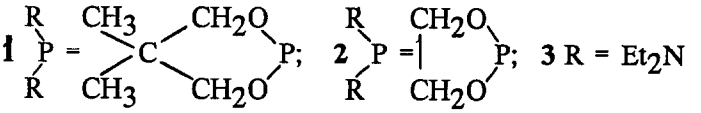
Figure 1. Potentiometric titration curves of amide (**3**) hydrolysis products. Curve (a): method *c*, 3.0517 g of amide used. Curve (b): method *a*, 1.0125 g of amine used. Curve (c): method *b*, 3.0824 g of amide used.

previously for purification of acidic ATPA only[17]. The purification by method *d* turned out especially simple and efficacious. This method was also used to refine other ATPA employed in this work - 2-ethylphenylamino-5,5-dimethyl-1,3,2-dioxaphosphorinane (**4**) and diethylaminodiisopropyl phosphine (**5**), allowing the residual amine-hydrochloride content to be reduced to about $1.2 \cdot 10^{-4}$mol/l.

The quantitative determination of the effect of amine hydrohalides on the alcoholysis rate for amides **1-3** of different types was a special problem. For this purpose, we determined the rate constant the first step of methanolysis as a function of the content of diethylamine hydrochloride within the concentration range to corresponding the purification by the methods *a-d*:



where



The reaction was conducted with an excess of methanol directly in the NMR spectrometer tube. The quantitative composition of the reaction mixtures was determined by integrating the signals from ^{31}P nuclei. The pseudo-first-order rate constants (k_I^{ψ}) were determined from the reduction in the concentration of the original amide by means of linearization in the coordinates $-\ln\{[\text{P-N}]/[\text{P-N}]_0\} = f(\tau)$, with $[\text{P-N}]_0$ being the initial concentration of the amide (Fig.2).

The k_I^{ψ} values were used to determine the second-order constant according to the equation $k_{II} = k_I^{\psi}/[ROH]$. Figure 3 shows the dependence of k_{II} on the concentration of amine hydrochloride for the various amides.

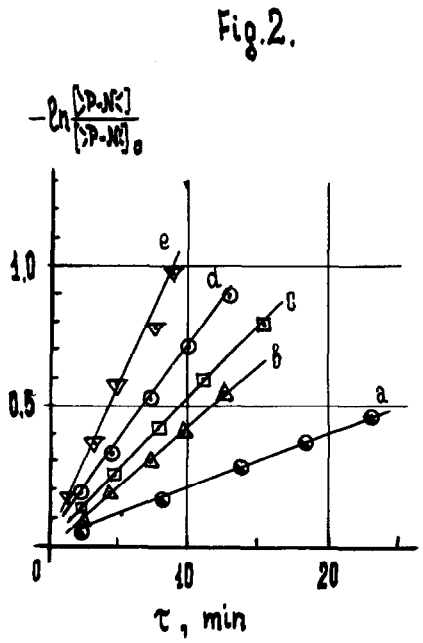
The data of the kinetic measurements can be described by the following equations[18]:

$$-\frac{d[\text{P-N}]}{d\tau} = k_{II}[\text{P-N}][ROH] \qquad (1)$$

$$k_{II} = k_0 + k_c[CAT] \qquad (2)$$

where k_0 is the rate constant for the reaction not catalyzed, k_c is the catalytic factor, which takes into account the strength of the activating action of amine hydrochloride, and [CAT] and [ROH] are the concentrations of salt and methanol, which are constant during the reaction.

As it was calculated by Eq. (2), the catalytic factors for amides **1-3** proved to be 0.34 (60°C), 0.33 (33°C), 0.1 (3°C) $l^2/(min \cdot mol^2)$, respectively. The linear dependence of k_{II} on the salt concentration is suggestive of the first order with respect to the catalyst concentration. Thus, what has been done by now is: general kinetic features have been



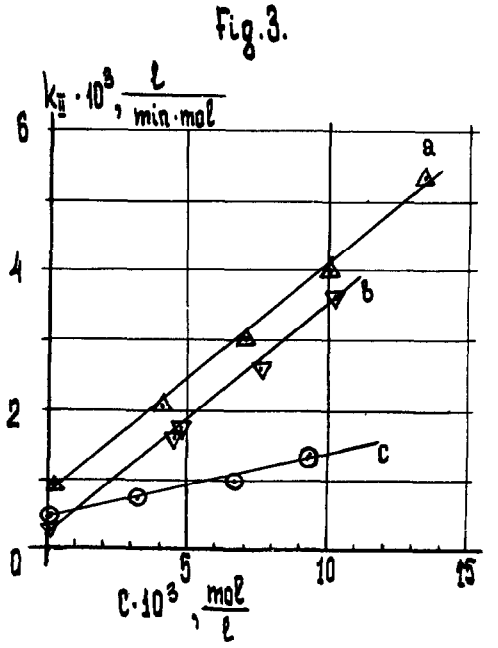
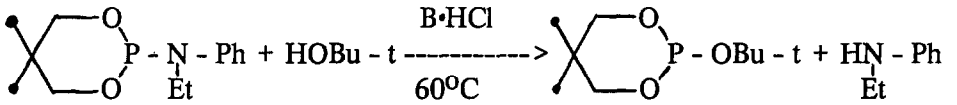


Figure 2. Determination of pseudo-first-order rate constants (k_I^{ψ}) in methanolysis of amide (**1**) containing $Et_2\overset{+}{N}H_2\bar{Cl}$ at different concentrations (*c*, mmol/l): a, 0.19; b 3.8; c, 6.8; d, 9.6; e, 13.1.

Figure 3. Dependence of k_{II} on the concentration, *c*, of amine hydrochloride in the reaction mixture for the variuos amides: a, amide **1**, 60°C; b, amide **2**, 33°C; c, amide **3**,3°C.

revealed in the acid catalysis of alcoholysis of amidophosphites; a reliable procedure has been offered for controlling the residual amine-hydrohalide content; the influence of amine hydrohalides on the ATPA alcoholysis rate has been estimated. All this made it possible conditions to elaborate the central issue in the acid catalysis of ATPA reactions, namely, to investigate the nature of the interaction of amine hydrohalides with ATPA.

The next stage of the work was devoted to studying the influence of the nature of amine hydrohalide on its catalytic activity in the reactions of ATPA alcoholysis. The experiment was performed in the "amide **4** (purified by method *d*) - tertiary butyl alcohol" system



The hydrochlorides of diethylamine (**6**), dimethylamine (**7**), triethylamine (**8**), trimethylamine (**9**), diethylbenzylamine (**10**), methylbenzylamine (**11**), N,N-diethylaniline (**12**), imidazole (**13**), and bromide of N,N'-dimethylimidazolium (**14**) were used as catalysts. Choosing amide **4** and catalysts **6-14**, we took into account that the basicity of the amines that were the conjugated bases of the catalysts should be no lower than that one of the amine produced by alcoholysis, i.e. N-ethylaniline. Otherwise, the catalyst would change during the reaction.

The use tertiary butyl alcohol was due to its moderate reactivity, making it possible to carry out alcoholysis during a time sufficient for the registration of kinetics by the NMR ^{31}P method. The reaction was performed with an excess of tertiary butanol directly in the NMR spectrometer tube. The quantitative composition of mixtures was determined by the integration of the ^{31}P signals in the NMR spectra.

The kinetic data were processed as described above using the Eqs.(1),(2). The concentrations of catalysts and tertiary butanol were constant during reaction and equal to $(2\text{-}14) \cdot 10^{-3}$ mol/l and 8 mol/l, respectively. Processed graphically, the data showed a linear dependence between $\lg k_c$ and acidity of salts **6-13**[**]. In the case of salts of secondary and tertiary amines, the dependence is expressed by two independent straight lines. The introduction of a statistical correction (S) unites the two lines into one (see Fig. 4). The statistical correction equals to the number of protons bonded to nitrogen in ammonium salts[19].

To analyze the data obtained the Bronsted equation was applied. For the process of interest it:

$$\lg(k_c/S) = \lg G_A - \alpha pK_a ,$$

where G_A and α are constants characterizing the reaction series. The slope α is a measure

[**] In addition, we report that the potentiometric measurements showed that values pKa of amine salts (**6-13**) in tert-bytanol were directly proportional to the values in water and value pH of the reaction mixture varied unessentially during reaction (the data are in press)

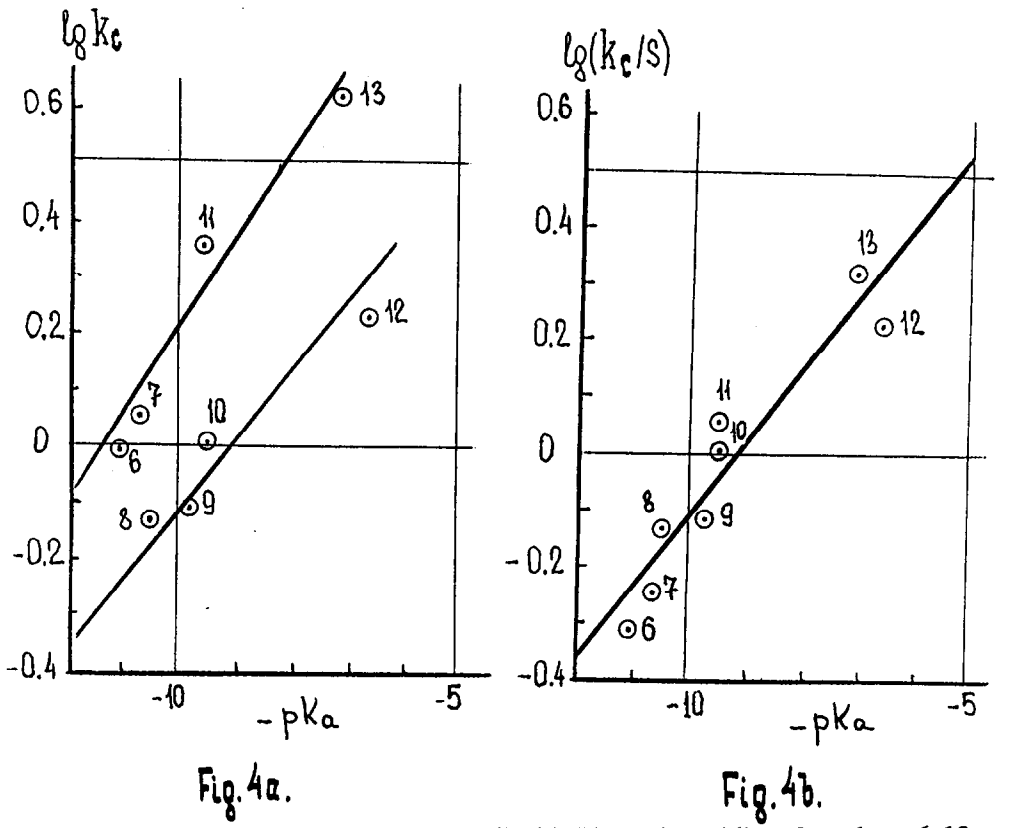


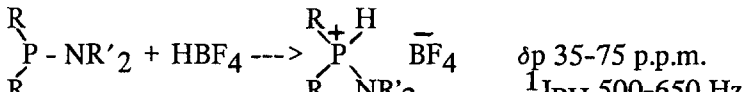
Figure 4. Dependence of $\lg k_C$ (a) and $\lg(k_C/s)$ (b) on the acidity of catalysts **6-13**.

of sensitivity of the reaction to the acid strength of general acid catalysts[19]. The value of α is not great and approximately equals to 0.13 ($r=0.95$), indicative of the *general acid catalysis* of phosphorylation. In this case, α is best interpreted as an approximate measure of the amount of change in the charge of the proton-donating or proton-accepting atom in the transition state[19]. Thus, the catalytic process includes the formation of catalytic H-complex rather than the protonation of substrate (formation of a phosphonium or phosphoammonium salt, as it was assumed formerly).

The above may have important stereochemical consequences. For instance, the reaction of racemic phosphoamide with the hydrochloride of an optically active amine will yield two catalytic complexes representing two diastereomers. These complexes may react

with an optically active alcohol at different rates. Hence, if the optically active reactants are appropriately chosen, the reaction of one mole of the optically active alcohol with two moles of racemic phosphoamide may lead to asymmetric induction. In virtue of what has just been said, we carried out the reaction between racemic 1.3-butylenephosphorous acid N-ethylanilide (**15**) (purified by method *d*) and 1,2;5,6-diisopropylidene-α-D-glucofuranose (molar ratio of reactants, 2:1) in the presence of racemic and optically active α-phenylethylamine hydrochloride. As it was shown using the NMR ^{31}P method in the case of racemic catalyst nearly equal amounts of the two diastereomers are produced. As to laevorotatory amine hydrochloride, one of the diastereomers is produced in 10% excess. The use of dextrorotatory amine hydrochloride gives a similar advantage in formation to the other of the diastereomers. Thus, it has been demonstrated that the use of optically active catalysts can result in stereoselectivity of the phosphorylation of nucleophiles with phosphorus acid amides.

So, we have shown that the reaction of phosphoamides with alcohols in the presence of catalytic amounts of amine hydrohalides includes the formation of catalytic H-complexes rather than protonation products. However, if a strong acid is used as catalyst, the formation of products of complete protonation can also be expected[20#]. Therefore, to imagine the general picture of the reactivity of phosphoamides, it was necessary to investigate the conversions of the corresponding products of complete protonation. We chose triaminophosphine (**3**) and trispiperidinophosphine (**16**), as well as diethylaminodiisopropylphosphine (**5**) and diethylamino- (**17**) and N-pyrrolyl- (**18**) ditertbutylphosphine as the objects of protonation. When treated with anhydrous hydroborofluoric acid, amides **3, 5, 16-18** readily form the corresponding salts, **19-23**:



3, 5, 16-18 **19-23**

δp 35-75 p.p.m.
$^1J_{PH}$ 500-650 Hz

where **3, 19** R = NR'_2 ; **5, 21** R = i-Pr, R' = Et ;

16, 20 R = NR'_2 = N◯ ; **17, 22** R = t-Bu, R' = Et ;

#A theoretical study of the effect of protonation on the phosphorus-nitrogen bond in aminophosphine is presented elsewhere [21].

18, 23 R = t-Bu, NR'_2 =

The protonation products are crystalline substances or oils. Their properties have been explored using the NMR ^{31}P and ^{1}H methods. In acetonitrile, chloroform, or dichloromethane solution, their spectra have doublet signals with a coupling constant $^{1}J_{PH}$ of 500-650 Hz. Without decoupling from protons the doublet converts into a singlet. It can be inferred that the protonation product is a quasiphosphonium salt, as presented in the reaction equation. This way we obtained the borofluorides of aminophosphoniums **19-23**. Their properties are listed in Table 2.

Table 2. NMR ^{31}P data of salts **19-23**.

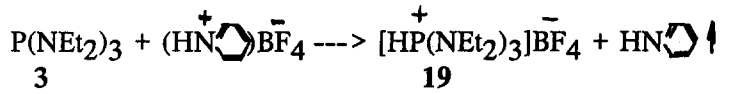
Compound	δ_P, p.p.m.(solvent);	$^{1}J_{PH}$,Hz
19, $HP(NEt_2)_3$ BF_4	38.3(CD_2Cl_2);	630
20, $HP(N$$)_3$ BF_4	35.8(CD_2CL_2);	632
21, $HP(i\text{-}Pr)_2NEt_2$ BF_4	69.2($CDCl_3$);	503
22, $HP(t\text{-}Bu)_2NEt_2$ BF_4	75.7($CDCl_3$);	504
23, $HP(t\text{-}Bu)_2$ N BF_4	70.1(CD_3CN);	516

The reaction between solution of these salts and bases stronger than phosphoamide leads to deprotonation. For example:

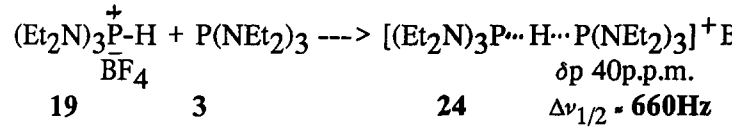
$$[HP(NEt_2)_3]BF_4 + NEt_3 \text{ ---> } P(NEt_2)_3 + (HNEt_3)BF_4$$
19 **3**

This phenomenon can be used to estimate approximately the basicity of phosphoamides: e.g., amide **18** turned out to be a weaker base than DMF. Dissolved in DMF ($pK_a^{25\,°C}$, H_2O=-1.5), its borofluoride, **23**, shows the NMR ^{31}P signal of amide **18** alone. At the same time, adding to salt **19** the equivalent amount of a base comparable in strength,

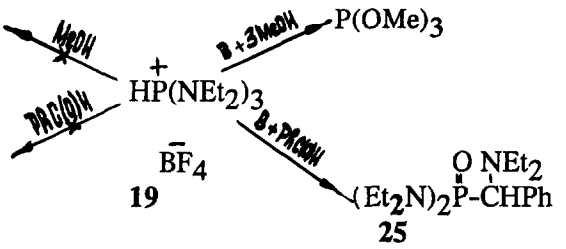
pyridine, causes a considerable broadening in the NMR ^{31}P signal, $\Delta\nu_{1/2}$ - 320 Hz, with the $^{1}J_{PH}$ coupling remaining constant. The fact that the pyridine does not deprotonate salt **19** enabled us to develop a new convenient technique for synthesizing quasiphosphonium salts **19, 20**. The procedure is based on the reaction of phosphoamide with the pyridine salt of HBF_4, with pyridine being distilled:



Thus , the base present in the solution of the quasiphosphonium salt will initiate give rise to proton-exchange processes. The base can also be represented by an appropriate phosphoamide. For instance, a broadened signal and absence of $^{1}J_{PH}$ coupling is observed in the case of the reaction between phosphonium salt **19** and an equimolecular amount of phosphoamide **3** (CH_2Cl_2, 27°C) That is indicative of the interaction of type **24** including proton exchange between the two P atoms:



We have also investigated certain reactions involving salt **19**. The salt has been shown to react with alcohols and carbonyl compounds only if bases, B (Et_3N, Py, $P(NEt_2)_3$), are present in the reaction mixture:



Apparently, the processes in question begin with the partial deprotonation of phosphonium salts under the action of base. The deprotonation yields the aforementioned hydrogen-bonded complexes, which react with nucleophiles, for example:

$$(Et_2N)_3\overset{+}{P}\text{-}H\ \underset{BF_4^-}{}\ +\ B \longrightarrow [(Et_2N)_3P\cdots\overset{+}{H}\cdots B]\ \underset{BF_4^-}{} \longrightarrow P(OMe)_3$$

19

We must note that the proton in the hydrogen-bonded complex performs two functions. On one hand it activates the phosphorus atom for the electrophilic reaction with alcohol and on the other hand it passes from the phosphorus to the nitrogen during the reaction of the adduct with alcohol and thereby promotes the cleavage of the P-N bond.

It should be emphasized that according to an X-ray study the hydrogen atom in quasiphosphonium salt is relatively strongly bonded to the phosphorus atom - the P-H bond length in **23** is 1.285(42) Å and is essentially shorter than ordinary P-H bond (1.42 - 1.44 Å). For that reason, the proton is not ready to carry out the second of above functions and it should be stressed that the salt **23** can be recrystallized even from methanol. This is also corroborated by the absence of prototropic processes in aminophosphonium salt **19** in the absence of bases at elevated temperatures. For example, raising the temperature of the 1 mol/l solution of salt **19** in protoactive dioxane up to 140°C does not lead to any appreciable broadening in the ^{31}P signal ($\Delta\nu_{1/2} \approx 9$ Hz).

It was previously shown that the quasiphosphonium salts incapable of prototropic processes do not undergo nucleophilic substitution (alcoholysis) [22]. We obtained, in addition, an alkylated analogue of salt **19**, tris(diethylamino)ethylphosphonium borofluoride **25**, and showed it not to undergo alcoholysis in the presence of triethylamine as well:

$$\underset{\mathbf{26}}{\overset{+}{E}tP(NEt_2)_3}\overset{-}{BF_4}$$

So, the phosphorylating system's capability of prototropic processes exerts the dominant influence on the phosphorylating ability of ATPA. The above observation allows the phosphorylating properties of systems involving ATPA to be prognosticated.

An X-ray Study of the Salt [t-$Bu_2\overset{+}{P}(H)N$⬚]$\overset{-}{BF_4}$ (**23**)

A general view of the cation (**23**) is shown in Fig.5 with atom numbering. The atomic coordinates and geometrical parameters are listed in Tables 3-5. The atomic coordinates and temperature factors, bond length and bond angles are deposited at the

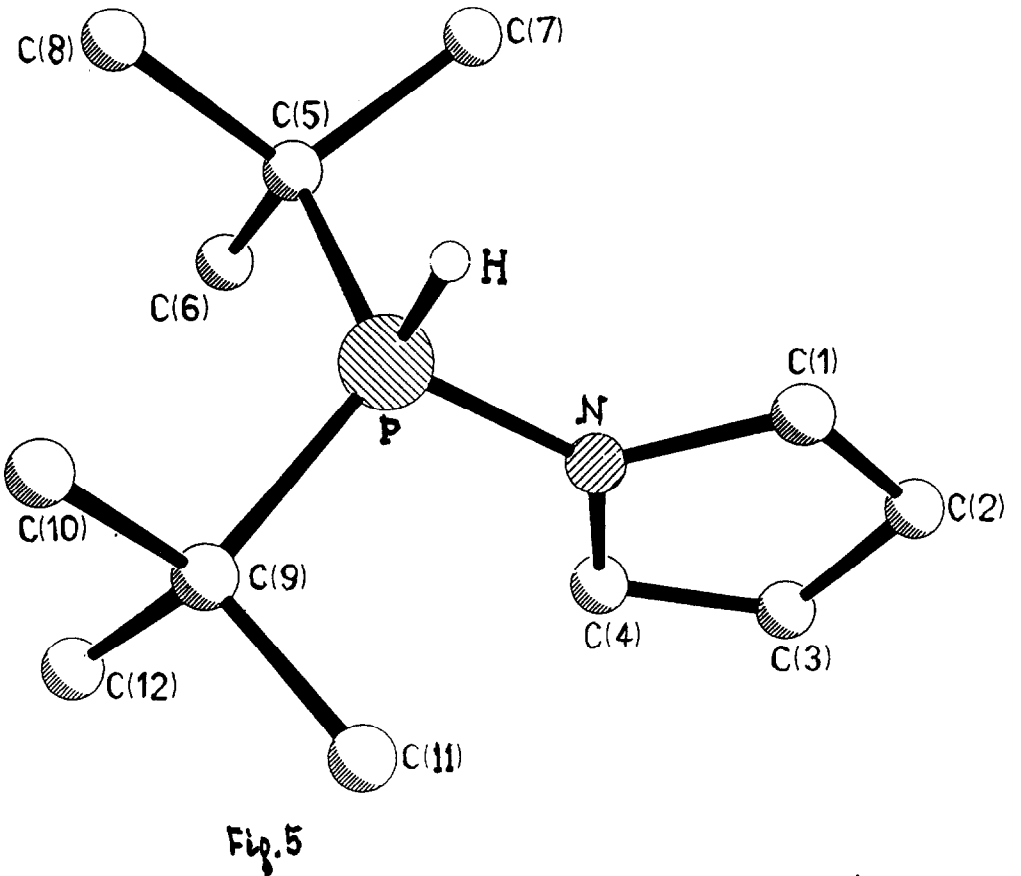


Fig.5

Figure 5. The general view of the cation in the crystal structure of [t-$Bu_2\overset{+}{P}(H)N$⬜]$\bar{B}F_4$ (**23**).

Cambridge Crystallographic Data Centre.

The crystal structure of (**23**) consists of isolated phosphonium cations [t-$Bu_2\overset{+}{P}(H)N$⬜] and $\bar{B}F_4$ anions. In accordance with our data (using the Cambridge crystallographic data base[23]), cations of a similar type, e.g. protonated derivatives of aminophosphines, have not been structurally characterized previously. As it follows from the data obtained, the protonation of aminophosphine (**18**)

Table 3. Atomic coordinates (10^4) and equivalent isotropic displacement coefficients ($A^2 \cdot 10^3$)

Atom	x	y	z	U(eq)
P	1823(1)	9862(1)	1714(1)	24(1)
N	2682(4)	10891(3)	1251(3)	28(1)
B	-4060(5)	9218(4)	-1234(3)	29(1)
F(1)	-3567(4)	8797(3)	-2039(2)	61(1)
F(2)	-3354(4)	8712(3)	-520(2)	63(1)
F(3)	-3665(4)	10231(2)	-1232(2)	59(1)
F(4)	-5785(3)	9134(3)	-1178(2)	57(1)
C(1)	2289(5)	11885(3)	1491(3)	32(1)
C(2)	3116(6)	12508(3)	926(3)	40(1)
C(3)	4046(6)	1923(4)	322(3)	40(2)
C(4)	3774(5)	10931(4)	513(3)	35(1)
C(5)	204(5)	9362(3)	977(3)	30(1)
C(6)	905(6)	8923(5)	102(3)	44(2)
C(7)	-929(7)	10283(5)	761(5)	49(2)
C(8)	-790(6)	8551(4)	1479(4)	40(2)
C(9)	3443(5)	9053(3)	2209(3)	31(1)
C(10)	2595(7)	8441(4)	2957(4)	43(2)
C(11)	4726(6)	9784(5)	2614(4)	51(2)
C(12)	4254(6)	8336(4)	1531(4)	46(2)
H	1088(48)	10189(37)	2424(28)	23(10)

Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor

occurs at the P rather than at N atom. The P-N bond length has a normal value of 1.668(4) Å and is only a little shorter than that in tripyrrolylphosphine (1.667(8) to 1.710(8) Å[24]). The coordination of the N atom is planar (the sum of the bond angles is 359.8(3)°). The P atom has a usual, slightly distorted tetrahedral coordination. The angle C(5)-P-C(9) involving two C atoms of tert-butyl groups is equal to 122.2(2)° and is the largest angle at this atom probably due to mutual repulsions of the two bulky radicals. Bond lengths in the pyrrolyl ring are close to those found in tripyrrolylphosphine[24]. Other geometrical parameters are usual[25].

Table 4. Bond lengths (Å)

P-N	1.668(4)	P-C(5)	1.820(4)
P-C(9)	1.832(4)	P-H	1.285(42)
N-C(1)	1.393(6)	N-C(4)	1.406(6)
B-F(1)	1.379(6)	B-F(2)	1.377(6)
B-F(3)	1.372(6)	B-F(4)	1.384(5)
C(1)-C(2)	1.349(6)	C(2)-C(3)	1.399(7)
C(3)-C(4)	1.355(7)	C(5)-C(6)	1.534(7)
C(5)-C(7)	1.548(8)	C(5)-C(8)	1.527(7)
C(9)-C(10)	1.534(7)	C(9)-C(11)	1.531(7)
C(9)-C(12)	1.527(7)		

Table 5. Bond angles (°)

N-P-C(5)	109.6(2)	N-P-C(9)	110.5(2)
C(5)-P-C(9)	122.2(2)	N-P-H	104.9(21)
C(5)-P-H	107.2(18)	C(9)-P-H	100.7(19)
P-N-C(1)	124.4(3)	P-N-C(4)	127.6(3)
C(1)-N-C(4)	107.8(4)	F(1)-B-F(2)	111.2(4)
F(1)-B-F(3)	109.1(4)	F(2)-B-F(3)	112.0(4)
F(1)-B-F(4)	107.7(4)	F(2)-B-F(4)	108.8(4)
F(3)-B-F(4)	107.8(4)	N-C(1)-C(2)	107.6(4)
C(1)-C(2)-C(3)	109.0(4)	C(2)-C(3)-C(4)	108.2(4)
N-C(4)-C(3)	107.4(4)	P-C(5)-C(6)	113.1(3)
P-C(5)-C(7)	104.9(3)	C(6)-C(5)-C(7)	109.3(4)
P-C(5)-C(8)	109.1(3)	C(6)-C(5)-C(8)	110.1(4)
C(7)-C(5)-C(8)	110.3(4)	P-C(9)-C(10)	106.7(3)
P-C(9)-C(11)	105.4(3)	C(10)-C(9)-C(11)	109.9(4)
P-C(9)-C(12)	113.1(3)	C(10)-C(9)-C(12)	110.1(4)
C(11)-C(9)-C(12)	111.5(4)		

Experimental

The NMR ^1H spectra were registered with a Bruker AM-400 spectrometer relative to an external standard, TMS. The solvents as well as methanol and tert-butanol were purified for kinetic measurements by conventional techniques[26].

An X-ray diffraction study was carried out with an automatic Siemens P3/PC four-cycle diffractometer (Mo Kα-radiation, graphite monochromator, $\theta/2\theta$ scanning, $2\theta < 50^o$) at 153 K. Crystals are orthorhombic, at 153 K: $a = 7.983(2)$, $b = 13.174(3)$,

$c = 14.916(3)$ Å, $V = 1568.7(6)$ Å^3, $d(\text{calc.}) = 1.266$ g/cm^3, $Z = 4$, space group $P2_12_12_1$. 1208 independent reflections with $|F| > 4\sigma(F)$ out of the total number of 1278, were used in calculations and refinement. The structure was solved by the direct method and refined in a full-matrix anisotropic-isotropic (for H-atoms) approximation to $R = 0.036$ and $R_W = 0.047$. All calculations were performed with the SHELXTL-PC programs.

Amidoesters **1,2** and amides **3,5,16** were obtained via the conventional techniques from the corresponding chloroanhydride and two (**1,2,5**) or six (**3,16**) equivalents of amine. The compounds produced had constants as described in the literature. Salts **6-13** were purified by diethylether precipitation from ethanol and stored in a vacuum exsiccator over P_2O_5.

Synthesis of aminophosphines **17,18** and salts **19-23,25** are described elsewhere[27].

Kinetic investigation of alcoholysis of amides of trivalent-phosphorus acids. The composition of reaction mixtures in the kinetic experiments was determined by the integration of the NMR $^{31}P\{H\}$ spectra with a Bruker WP-80 spectrometer at a frequency of 32.4 MHz. Spectrum registration conditions: frequency range 12 kHz, pulse duration 3 μs, number scans 64, pulse delay time 1 s. Sample thermostatting accuracy $\pm$ 0.5°C. Alcoholysis was performed with an excess of alcohol (methanol 20 mol/l, tert-butanol 8 mol/l), initial phosphoamide concentration 0.8 (**1, 3, 4**) or 1 (**2**) mol/l. The computation of pseudomonomolecular rate constants was based on the kinetic-curve portions confined to the 40-60% conversion of amides.

Potentiometric titration was performed using 0.01N $AgNO_3$ solution, following the recommendations,[14] on a pH-340 potentiometer (USSR) furnished with a chlorinated-silver indicator electrode made of a chlorinated silver wire 1 mm in diameter and a chlorinated-silver reference electrode, EVL-1MZ, filled with a saturated $Ba(NO_3)_2$ solution. Potential jump 1 mV. Experimental error 6%.

Synthesis of N-ethylanilides of cyclic phosphoesters. 0.2 mol of the chloroanhydride of corresponding acid were added to the solution of 0.2 mol N-ethylaniline in 180 ml triethylamine. On refluxing the reaction mixture within 5 hr, the precipitated triethylamine hydrochloride was filtered off, the solvent was removed in a vacuum, and the residue was distilled.

2-N-Ethylanilino-5,5-dimethyl-1,3,2-dioxaphosphorinane (**4**). Yield 31.9 g (63%), b.p. 114-115°C (1 mm), m.p. 40-41°C. NMR ^1H ($CDCL_3$, δ, p.p.m.): 0.79, 1.14 (2s, 6H, $C(CH_3)_2$), 1.09 (t,3H, $CH_2C\underline{H}_3$, $^3J_{HCNP}$ 7.0 Hz), 3.67 (m, 4H, $CH_{eq}O$, NCH_2), 3.83 (m, 2H, $CH_{ax}O$), 7.06-7.21 (m,5H, C_6H_5). NMR ^{31}P - {H} (δ, p.p.m.): 138.9. Found, %: C, 61.59; 8.22; P, 12.34. $C_{13}H_{20}NO_2P$. Calculated, %: C, 61.65; H, 7.96; P,12.23.

2-N-Ethylanilino-4-methyl-1,3,2-dioxaphosphorinane (**15**). Yield 27.8 g (58%), b.p. 107-111°C (1 mm), n^{20}_D 1.5410. NMR ^1H ($CDCl_3$, δ, p.p.m.) for the mixture of two geometric isomers: 1.07, 1.08 (2t, 3H, $NCH_2C\underline{H}_3$), 1.20, 1.28 (2d, CCH_3), 1.42, 1.68 (2m, 2H, CCH_2C), 3.47, 3.65 (2m, 2H, NCH_2), 4.16 (m, 3H, CH_2O, CH), 7.01, 7.27 (2m, 5H, C_6H_5). NMR ^{31}P - {H} (δ, p.p.m.): 139.4 and 128.8 (17:4, resp.). Found, %: C 60.16; H 7.85; P 13.18. $C_{12}H_{18}NO_2P$. Calculated, %: C 60.24; H 7.58; P 12.95.

Purification procedures for amidophosphites **1-4.**

a. Amidophosphites **1-3** obtained as described above were subjected to redistillation.

b. 0.2 mol of amide purified by procedure *a* were dissolved in 200 ml of benzene and washed 5 times, each time with 100 ml of distilled water. The benzene solution was dried by shaking over anhydrous Na_2SO_4 for 1 h, filtered, mixed with 5 g CaH_2, and kept for 12 h at 20°C. The solution was filtered, evaporated in vacuum, and the residue was distilled over 1 g of sodium. Yield 70%.

c. 0.1 mol of amide purified by procedure *b* was mixed with 3 ml of 10 % solution of butyl lithium in hexane, stirred for 1 h at 20°C, the solvent was removed in vacuum, and the residue was distilled over 0.5 g of sodium. Yield 90%.

d. Procedures of amide **3, 4** *purification in the conditions of phase transfer.* 0.048 mol of amide were added to the mixture of 50 ml of benzene, 11g (for **3**) or 2.2 g (for **4**) of triethylbenzylammonium hydroxide, and 50 ml of 50% solution of potassium hydroxide. The mixture was stirred for 2 h, the benzene layer was separated, the solvent was removed in a vacuum and the residue was distilled. Amide **3** yield 8.79 g (74%), b.p. 118-120°C (16 mm), n^{20}_D 1.4745; amide **4** yield 10.09 g (83%), b.p. 113-115°C (1mm), m.p. 39.6-41.2°C.

Preparation of samples for potentiometric titration. A sample of 1(± 0.1) g amidophosphite purified by procedure *a*, taken within a 0.0002 g accuracy, was mixed with 4 ml 5% HNO_3[$], stirred to obtain a homogeneous solution, and brought to pH 5-6 with concentrated HNO_3. When analyzing samples of amidophosphites purified by procedures *b, c, d* the amount of 5% HNO_3 was 3 times greater, the rest of the procedure being the same.

1,3-Dimethylimidazolium bromide (**14**). 9.5 g (0.1 mol) of ethyl bromide were bubbled for 1 h at 20°C into a solution of 3.10 g (0.0377 mol) N-methylimidazole in 10 ml of absolute ethanol. The reaction mixture was treated with 50 ml of diethyl ether, the precipitated crystals were filtered off, precipitated with diethyl ether from ethanol, and dried in vacuum exiccator over P_2O_5. Yield 2.95 g (44%), colourless hygroscopic crystals, m.p. 109-110°C. NMR ^1H (CD_2Cl_2, δ, p.p.m.): 4.04 (s, 6H, CH_3), 7.49 (s, 2H, CHCH), 10.29 (s, 1H, NCHN).

Reaction of racemic 1,3-butylenephosphorous acid N-ethylanilide (**15**) *with 1,2;5,6-diisopropylidene-α-D-glucofuranose (molar ratio of the reactants, 2:1) in presence of racemic and optically active (+), (-)-α-phenylethylamine hydrochloride.* A solution of 0.1087 g (0.4178 mmol) of glucofuranose in 0.7 ml of methylene chloride was added to 0.2000 g (0.8357 mmol of anilide (**15**) and 0.0050 g (0.0317 mmol) of racemic (a), dextrorotatory (b), or laevorotatory (c) α-phenylethylamine hydrochloride. NMR ^{31}P - {H} spectrum for the reaction mixture 24 h (20°C) after mixing: singlets at 139.9, 133.6, 133.4, 129.3, 128.7, 128.4 p.p.m. in ratio: a, 40:15:15:10:10:10; b, 45:14:12:7:14:12; c, 42:14:17:10:10:11, resp. (see Fig. 5).

Reaction of salt **19** *with triethylamine.* A solution of 0.282 g (0.841 mmol) of salt **19** in 0.6 ml of methylene chloride were mixed with 0.085 g (0.841 mmol) of triethylamine. NMR ^{31}P spectrum: the signal of triamide **3** at 118 p.p.m. Similar results were obtained with phosphonium salts **20-23**.

Reaction of salt **19** *with pyridine.* 0.8 ml solution of 0.476 g (1.42 mmol) of salt **19**in dioxane were mixed with 0.112 g (1.42 mmol) of pyridine. NMR ^{31}P -- {H} spectrum for the reaction mixture 5 min after mixing: a singlet at 38.8 p.p.m.: without decoupling from protons: a doublet $^1J_{PH}$ 630 Hz.

[$]Acetic acid was used for analyzing phosphorus acid anilides.

Reaction of amide **3** *with pyridinium borofluoride. Methanolysis.* 0.182 g (1.09 mmol) of pyridinium borofluoride were mixed with 0.269 g (1.09 mmol) of amide **3** in 0.5 ml of methylene chloride. NMR ^{31}P -- {H} spectrum for the reaction mixture 15 min after mixing: a singlet at 40.4 p.p.m. ($\Delta\nu_{1/2}$ ≈ 320 Hz); without decoupling from protons: a doublet $^{1}J_{PH}$ 630 Hz. Then 0.105 g (3.27 mmol) methanol was added. NMR ^{31}P -- {H} spectrum for the reaction mixture 5 min after adding: a singlet at 140 p.p.m. ($P(OMe)_3$).

Interaction of salt **19** *with amide* **3**.

a. *Salt-***19***-to amide-***3** *proportion 1:1. Methanolysis.* 0.640 g (1.909 mmol) of salt **19** were mixed with a solution of 0.472 g (1.909 mmol) of amide **3** in 0.5 ml of methylene chloride. NMR ^{31}P --{H} spectrum for the reaction mixture 5 min after mixing: a singlet at 43 p.p.m., $\Delta\nu_{1/2}$≈660 Hz (see Fig. 6). Then 0.367 g (11.45 mmol) methanol was added. NMR ^{31}P -- {H} spectrum for the reaction mixture 5 min after adding: a singlet at 140 p.p.m.

b. *Salt-***19***-to-amide-***3** *proportion 1:2.* 0.282 g (0.841 mmol) of salt **19** were mixed with a solution of 0.416 g (1.682 mmol) of amide **3** in 0.6 ml of methylene chloride. NMR ^{31}P -- {H} spectrum: two singlets at around 50 and 108 p.p.m. (see Fig. 6).

Reaction of salt **19** *with methanol.*

a. *In a solvent.* A solution of 0.251 g (0.749 mmol) of salt **19** in 0.6 ml of methylene chloride or dioxane was mixed with 0.072 g (2.247 mmol) of methanol. NMR ^{31}P -- {H} spectrum for the reaction mixture 10 min after mixing: a singlet at 38.3 (CH_2Cl_2) or 38.1 (dioxane) p.p.m.; without decoupling from protons: a doublet $^{1}J_{PH}$ 630 Hz. Then 0.0758 g (0.749 mmol) of triethylamine was added causing an exothermic reaction. NMR ^{31}P -- {H} spectrum for the reaction mixture 5 min after adding: a singlet at 140 p.p.m.

b. *Without a solvent.* 0.762 g (2.273 mmol) of salt **19** were mixed with 0.218 g (6.819 mmol) of methanol. NMR ^{31}P -- {H} spectrum for the reaction mixture 10 min after mixing: a singlet at 38.1 p.p.m.; without decoupling from protons: a doublet $^{1}J_{PH}$ 630 Hz. Then 0.230 g (2.273 mmol) of triethylamine were added causing an exothermic reaction. NMR ^{31}P -- {H} spectrum for the reaction mixture 5 min after adding: a singlet at 140 p.p.m.

Reaction of salt **19** *with benzaldehyde.* A solution of 0.285 g (0,850 mmol) of salt **19** in 0.3 ml of methylene chloride was mixed with 0.090 g (0.850 mmol) of benzaldehyde in 0.3 ml of methylene chloride. NMR ^{31}P -- {H} spectrum 10 min after mixing: a singlet at 39.0 p.p.m.; without decoupling from protons: a doublet $^{1}J_{PH}$ 630 Hz. Then 0.043 g (0.425 mmol) of triethylamine were added. NMR ^{31}P spectrum 3 min after adding: a singlet and two doublets at 20 p.p.m. ($^{1}J_{PH}$ 570 Hz), 31 p.p.m., 39 p.p.m. ($^{1}J_{PH}$ 630 Hz), corresponding to a mixture of phosphorous acid tetraethyldiamide, α-diethylaminobenzylphosphonic acid tetraethyldiamide (**25**), and salt **19** in a proportion of 2:3:5 (resp.) 24 h later the proportion was 3:10:0.

For identification, phosphonate **25** was produced by the procedure described elsewhere[28] and had constants as reported in the literature. NMR ^{1}H ($CDCl_3$, δ, p.p.m.): 0.7 (t, 6H, $PCNCH_2C\underline{H}_3$), 1.1 (t, 12H, $PNCH_2C\underline{H}_3$), 2.7 (m, 4H, $PCNCH_2$, $^{4}J_{PCNCH}$ 9.6 Hz), 3.2 (m, 8H, $PNCH_2$, $^{3}J_{PNCH}$ 9.6 Hz), 4.1 (d, 1H, PCH, $^{2}J_{PCH}$ 19.1 Hz). NMR ^{31}P -- {H} ($CDCl_3$, δ, p.p.m.): 31.

REFERENCES

1. E.E.Nifantyev, M.K.Gratchev. Usp.Khim., in press (in Russian).
2. M.D.Matteucci,M.H.Caruthers.J.Amer.Chem.Soc.,1981,**103**,3185; L.J.McBride, M.H.Caruthers. Tetrahedron Lett.,1983,**24**,245.
3. E.E.Nifantyev, D.A.Predvoditelev. Bioorgan.Khim.,1981,**7**,1285 (in Russian)
4. E.E.Nifantyev, M.P.Koroteev. In: Sov.Scientific Rev., Sect.B, New York, 1984,399.
5. E.E.Nifantyev, A.T.Teleshev, Yu.I.Blokhin. Usp.Khim., 1987,**56**,558 (in Russian).
6. R.Schliebs. Ger.Pat.1,079,022 (7 Apr. 1960) (Chem.Abstr. **55**, 14307i, 1961).
7. K.A.Petrov, E.E.Nifantyev, T.N.Lysenko, V.P.Evdakov. Zh.Obshch.Khim., 1961, **31**,2377 (in Russian)
8. E.E.Nifantyev, N.L.Ivanova, N.K.Blyznyuk. Zh.Obshch.Khim., 1966,**36**,765 (in Russian).
9. E.E.Nifantyev, N.L.Ivanova. Vestn.MGU, 1968,104 (in Russian).
10. E.E.Nifantyev, N.L.Ivanova, I.P.Gudkova, I.V.Shilov. Zh.Obshch.Khim., 1970,**40**,1420 (in Russian); E.S.Batiyeva, V.A.Alfonsov, A.N.Pudovik. Dokl.AN SSSR, 1988,**303**,632 (in Russian).

11. E.E.Nifantyev, T.V.Borisov. Zh,Obshch.Khim.,1985,**55**,1660 (in Russian)
12. E.E.Nifantyev, M.K.Gratchev, E.V.Borisov, A.R.Bekker. Phosphorus and Sulfur, 1987,**34**,105.
13. J.Szewczyk, L.D.Quin. J.Org.Chem., 1987,**52**,1190.
14. N.S.Frumina, N.F.Lisenko, M.A.Chernova. In: Chlorine, Nauka, Moscow, 1983 (in Russian).
15. Yu.G.Trishin, V.N.Chistokletov, A.A.Petrov. Zh.Obshch.Khim.,1983,**53**,664 (in Russian).
16. L.M.Epstein, Z.S.Novikova, L.D.Ashkinadze. L.M.Rubasheva, L.A.Kazitsina. Izv. Akad.Nauk SSSR, Ser.Chem., 1971, 963 (in Russian).
17. V.L.Foss, N.V.Lukashev, I.F.Lutsenko. USSR, Authorship Certificate No.827491 (15 May 1979). (Chem.Abstr. **95**,114208r, 1981).
18. E.V.Borisov, N.L.Ivanova, T.B.Aksenova, L.K.Vasyanina, M.K.Gratchev, A.R.Bekker, E.E.Nifantyev. Zh.Obshch.Khim., 1985,**55**,2270 (in Russian).
19. W.P.Jencks. Catalysis in Chemistry and Enzymology. New York, McGraw-Hill, 1969,p.170,173,241.
20. A.N.Pudovik, E.S.Batiyeva,E.N.Oficerov. Dokl.AN SSSR, 1977,**232,** 1092 (in Russian); O.Dahl. Tetrahedron Lett.,1982,**23**,1493; T.A.Van der Knaap, F.Bickelhaupt,Phosphorus and Sulfur,1984,**21**,227.
21. A.A.Korkin,E.N.Tsvetkov. Bull.Soc.Chim.Fr.,1988,335.
22. E.E.Nifantyev, N.L.Ivanova. Zh.Obshch.Khim.,1970,**40**,1492 (in Russian).
23. Cambridge Crystallographic Data Base. Release 1988.
24. J.L.Atwood, A.H.Cowley, W.H.Hunter, S.K.Mehrotra. Inorg.Chem.,1982,**21**,1354.
25. F.H.Allen, O.Kennard, O.G.Watson et al. J.Chem.Soc. Perkin Trans. II,1987,1.
26. A.J.Gordon, R.A.Ford. In: Chemist's Companion. A Handbook of Practical Data, Techniques and References, John Wiley, New York, 1972.
27. E.E.Nifantyev, M.K.Gratchev, S.Yu. Burmistrov, M.Yu.Antipin, Yu.T.Struchkov. Phosphorus and Sulfur, in press.
28. E.E.Nifantyev, I.V.Shilov. Zh.Obshch.Khim., 1971,**41**,2372 (in Russian).