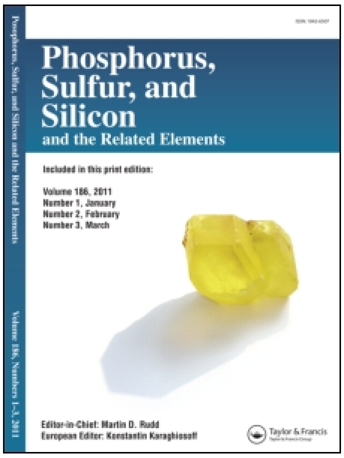

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IMPORTANCE OF AMINE HYDROHALIDES IN ALCOHOLYSIS OF PHOSPHOROUS ACID AMIDES

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The data are presented on the rates of deuteromethanolysis of 2-fluoro-1,3,2-dioxaphosphorinane **1** in the presence of various bases differing in the basicity and of that of 2-amino-1,3,2-dioxaphosphorinanes **2–4** catalysed by hydrogen fluoride salts of different amines. The alcoholysis of the fluorophosphite **1** in the presence of imidazole, N-ethylaniline and 2,6-di-tert-butyl-4-methylpyridine proceeds slowly whereas alcoholysis of the amidoesters **3, 4** catalysed by imidazole and N-ethylaniline hydrofluorides occurs rapidly even at room temperature. These data do not match the hypothesis that halophosphites are intermediates in the alcoholysis of amidophosphites in the presence of amine hydrohalides.

INTRODUCTION

During last years a significant interest to transformations of trivalent phosphorus acids' amides and first of all to their alcoholysis has arisen. Phosphorylation with phosphoamides found a wide use in the synthesis of many complex systems, especially natural compounds, phospholipides[1] and oligonucleotides.[2] The study of interactions of trivalent phosphorus acid amides and amidoesters with hydroxyl containing compounds previously performed, revealed some kinetic and stereochemical regularities and made it possible to suggest the existence of various intermediates: autoassociates, hydrogen-bonded complexes, phosphoranes and others.[3–5]

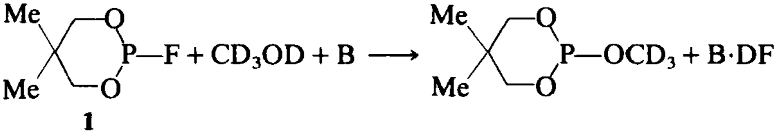
In addition, it has been shown that substitution of the amide group at a trivalent phosphorus atom, especially alcoholysis, is effectively catalysed by acidic substances including amine hydrohalides.[5,6] These compounds are usually present in amides and amidoesters not carefully purified. Unfortunately, up to date there is no common standpoint on the mechanism of acid catalysts action. The authors of the acid catalysis effect[7] have pointed out the importance of phosphoamide protonation, although other activation mechanisms are possible.[5]

Earlier experiment on thermal conversion of $(Et_2N)_3P$ with $Et_3N{\cdot}HCl$ (or $Et_2NH{\cdot}HCl$) to $(Et_2N)_2PCl$ was effected, and on the basis of the experiment it was concluded that in the reactions of trivalent phosphorus acid amides with nucleophiles in the presence of amine hydrohalides, haloanhydrides are formed as intermediates.[8] This mechanism was subjected to criticism but, unfortunately, the criticism was extended to the whole of acid catalysis.[9]

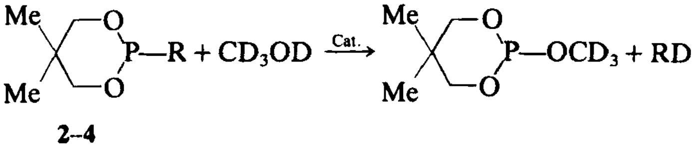
One of methods for solving the problem consists in a comparison of the reaction rates of phosphoamides and assumed intermediates, in particular halophosphites, with nucleophiles. It was demonstrated experimentally that chlorophosphites and bromophosphites react with nucleophiles, e.g. with alcohols in the presence of amines, faster than with phosphoamides. That was the reason why we began to work with fluorophosphites. The rates of alcoholysis of fluorophosphites and amidophosphites in the presence of amines hydrofluorides were compared.

RESULTS AND DISCUSSION

Unlike chloro- and bromophosphites, the fluorophosphite **1** proved to be a convenient object for studying the rates of deuteromethanolysis in the presence of different bases (Table I). It has been found that in the case of relatively strong bases, triethylamine, diethylamine, diisopropylethylamine, the reaction proceeds relatively fast (exps. 1–5) whereas the alcoholysis of the fluorophosphite **1** in the presence of relatively weak bases, imidazole, N-ethylaniline and 2,6-ditert-butyl-4-methylpyridine, occurs significantly slower (exps. 6–8). The rates of the reactions increase with increasing of base concentrations, but in the absence of amines, which are hydrogen fluoride acceptors, the latter breaks up the phosphorinane ring.



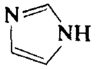
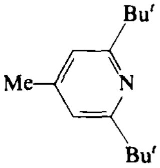
These data were compared with those on times of half reaction for the alcoholysis of amides **2–4** in the presence of different catalysts (Table II).



It turned out that in the case of amidoesters, formed from weak-base imidazole and N-ethylaniline, the deuteromethanolysis in the presence of the catalyst proceeds at a high speed even at room temperature (exps. 5, 6). It should be noted that in all experiments with amines hydrofluorides the formation of fluorophosphite **1** immediately after mixing the reagents was observed in the ^{31}P NMR spectra (δ^{31}P 113.3 ppm, $^{1}J_{PF}$ 1175 Hz). The concentration of **1** in the reaction mixture did not change actually up to checked conversion extents (~60%). The reaction is irreversible, which is evidenced by the absence of amidoester signal in ^{31}P NMR spectra of the reaction mixtures containing **1**, diethylamine, and excess deuteromethanol. In this work a possibility of the formation of chloro- and bromoanhydrides as intermediates in the alcoholysis with the use of amines hydrochlorides and hydrobromides as catalysts was not

TABLE I

Rates of deuteromethanolysis of 2-fluoro-5,5-dimethyl-1,3,2-dioxaphosphorinane **1** in the presence of different bases (B)

No. exps.	B	pKa[10] (H_2O)	Molar ratio [P—F]/[B]	$\tau^*_{1/2}$ min
1	Et_3N	11.0	1.0	36
2	Et_2NH	11.1	0.2	2
3	Et_2NH	11.1	0.5	11
4	Et_2NH	11.1	2.0	408
5	Pr^i_2NEt	—	1.0	33
6		7.0	0.5	239
7	Ph(Et)NH	5.0	0.5	†
8		4.0	1.0	†

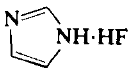
* Time of half reaction.

† No detectable products during 1 hr.

specially studied. Nevertheless, we have established similar catalytic activities for all studied hydrohalides (Table II). This would have been impossible if the reaction rate had been determined by halophosphite formation. Thus, the hypothesis about the proceeding of catalysed alcoholysis reactions via the formation of intermediate halophosphites[8,11] cannot be of a general character and in the case of amines hydrofluorides it was not confirmed experimentally. These facts and data[5] have to stimulate further investigations in the field of catalytic conversions of trivalent phosphorus acid amides.

TABLE II

The catalysts effect on the rate of deuteromethanolysis of amidoesters **2–4**

No. exps.	Compound	R	Catalysts (Cat.)	[Cat] · 10^2 mol/l	$\tau_{1/2}$ min
1	2	Et_2N	—	—	144
2	2	Et_2N	$Et_2HN \cdot HF$	1.6	50
3	2	Et_2N	$Et_2HN \cdot HCl$	1.7	26
4	2	Et_2N	$Et_2HN \cdot HBr$	1.6	27
5	3			3.0	<2*
6	4	Et(Ph)N	Et(Ph)HN·HF	3.0	<2*

* At 20°C.

EXPERIMENTAL

All experiments were carried out under nitrogen using dry solvents and pre-dried apparatus. The reactions were run with an excess of CD_3OD (reagents concentration 1.0 mol l^{-1}) at 60°C directly in an ampoule of the spectrometer.

Reagents. Fluorophosphite **1** and amidoesters **2–4** were prepared by the routine ways and purified by two- or threefold vacuum distillation while compound **2** was additionally purified by washing with water and drying over calcium hydride. Hydrofluorides were prepared by the common procedure, and the purity was controlled by titration with alcoholic alkali and amounted to 95–97% for diethylamine and imidazole and 85–95% for N-ehtylaniline.

Spectral data. ^{31}P NMR spectra were recorded with a Bruker WH-360 spectrometer. Chemical shifts are given relative to 85% H_3PO_4 external standard. The composition of the reaction mixture was determined by integration of the $^{31}P\{H\}$ spectra.

REFERENCES

1. E. E. Nifantyev and D. A. Predvoditelev, *Bioorgan. Khim.*, **7**, 1285 (1981).
2. M. D. Matteucci and M. H. Caruthers, *J. Amer. Chem. Soc.*, **103**, 3185 (1981); L. J. McBride and M. H. Caruthers, *Tetrahedron Lett.*, 245 (1983).
3. V. P. Evdakov, V. P. Beketov and B. I. Bryantzyev, *Zhur. Obshch. Khim.*, **46**, 1726 (1976).
4. M. T. Boisdon, C. Malavaud, F. Mathis and J. Barrans, *Tetrahedron Lett.*, 3501 (1977); O. Dahl, *Tetrahedron Lett.*, 3281 (1981); J. Nielsen and O. Dahl, *J. Chem. Soc. Perkin Trans. II*, 553 (1984).
5. E. V. Borisov, N. L. Ivanova, T. B. Aksenova, L. K. Vasyanina, M. K. Gratchev, A. R. Bekker and E. E. Nifantyev, *Zhur. Obshch. Khim.*, **55**, 2270 (1985).
6. E. E. Nifantyev, N. L. Ivanova and N. K. Bliznuk, *Zhur. Obshch. Khim.*, **36**, 765 (1966); E. E. Nifantyev and N. L. Ivanova, *Vestnik MGU*, **23**, 104 (1968).
7. E. E. Nifantyev and N. L. Ivanova, *Zhur. Obshch. Khim.*, **41**, 2192 (1971).
8. V. N. Eliseenkov, A. N. Pudovik, S. G. Fattahov and N. A. Serkina, *Zhur. Obshch. Khim.*, **40**, 498 (1970).
9. Yu. G. Grishin, V. N. Chistokletov and A. A. Petrov, *Zhur. Obshch. Khim.*, **53**, 664 (1983).
10. A. J. Gordon and R. A. Ford, The Chemist's Companion (Wiley-Interscience, New York, 1972); Russian Transl., Mir publishers, Moscow, 1976, p. 73.
11. E. S. Batyeva, V. A. Al'fonsov, G. Y. Zamaletdinova and A. N. Pudovik, *Zhur. Obshch. Khim.*, **46**, 2204 (1976).