Acid Hydrolysis of Organic Fluorophosphorus Compounds

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The acid hydrolysis of dimethoxy-, methoxyethyl- and diethyl
phosphoryl fluorides has been studied in different concentrations of
hydrochloric acid at 0° and 25°C. By calculation of the specific rate
constant, k_{H^+} it is necessary to correct for the organophosphorus acid
produced during the reaction. The pK-values of two of the organo-
phosphorus acids have been measured. These values are in reasonable
agreement with the values of the same acids reported by Hudson
and Harper [1]. The activation energies, E_A have been calculated. The
mechanisms of the acid hydrolysis of organic fluorophosphorus com-
pounds are discussed.

In a previous publication [2], the connection between the ability of hydrogen
bond formation with deuterium oxide of the phosphoryl group in organo-
phosphorus compounds and the acid hydrolysis of corresponding phosphorus
compounds was pointed out and discussed in some detail. In order to collect
more information on the acid hydrolysis of organophosphorus compounds three
organic fluorophosphorus compounds have been synthesized and their acid
hydrolysis studied in different low concentrations of hydrochloric acid. The
three compounds, dimethoxy-, ethylmethoxy- and diethylphosphoryl fluoride,
are the same which previously have been used for the study of the nucleophilic
reactions with hydroxyl ions and *iso*nitroso acetone [3]. Kilpatrick and Kilpat-
rick [4] have studied the acid hydrolysis of di*iso*propoxyphosphoryl fluoride
(DFP) by using a dilatometric method. In the present paper we have used the
ordinary titration method for determination of the acids produced during the
reaction.

THE KINETICS OF THE ACID HYDROLYSIS OF ORGANIC FLUOROPHOS-
PHORUS COMPOUNDS

The acid hydrolysis of dimethoxy-, methoxyethyl- and diethyl phosphoryl
fluorides was measured in hydrochloric acid in the concentration interval

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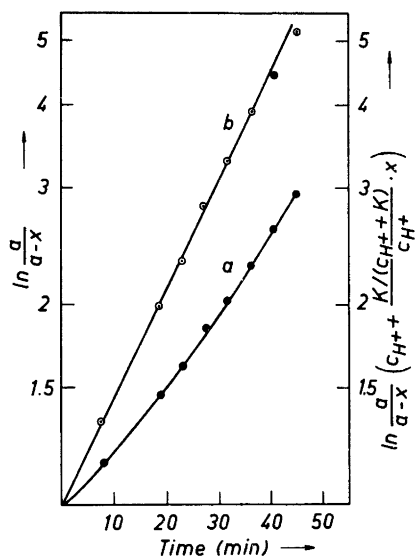* Present address: Chemical Institute, University of Bergen, Bergen, Norway.
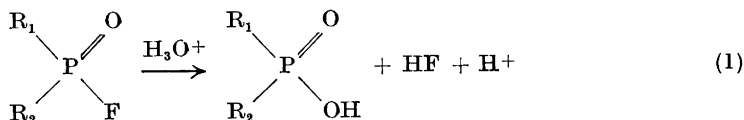
Fig. 1. The acid hydrolysis of dimethoxy-phosphoryl fluoride in 0.04 N HCl. a) The plot of the experimental values according to the first order rate equation. b) The plot of the experimental values according to eqn. (6).

0.01—0.1 N. In such low concentration of hydrochloric acid it was necessary to correct for the increase of hydrogen ions in the reaction solution due to the formation of free acids during the reaction:

$$\begin{array}{c}
\text{R}_1 \\
\diagdown \quad \text{O} \\
\text{P} \diagup \quad \xrightarrow{\text{H}_3\text{O}^+} \\
\diagup \quad \diagdown \\
\text{R}_2 \quad \text{F}
\end{array}
\qquad
\begin{array}{c}
\text{R}_1 \\
\diagdown \quad \text{O} \\
\text{P} \diagup \\
\diagup \quad \diagdown \\
\text{R}_2 \quad \text{OH}
\end{array}
\; + \; \text{HF} + \text{H}^+ \qquad (1)$$

In Fig. 1a is plotted the experimental values of the hydrolysis of dimethoxy-phosphoryl fluoride in 0.04 N HCl according to the first order rate equation, *i.e.* $\ln[a/(a—x)]$ as function of t. The curvature of the line is due to the catalysing effect of the organic phosphorus acid formed during the reaction. Hydrofluoric acid which has a pK of approximately 4.5 contributes so small amounts of hydrogen ions that its presence can be neglected. The three organophosphorus acids formed during the reaction have the following pK's: dimethoxyphosphorus acid, 1.29, methoxyethyl phosphorus acid, 2.0, and diethylphosphorus acid, 3.4[1].

If the amount of organic phosphorus fluoride hydrolysed after a time t is x the reaction can be described by the following equation:

$$\frac{\mathrm{d}x}{\mathrm{d}t} = k_{\text{H}^+} \, (c_{\text{H}^+} + c_{\text{h}}) \, (a—x) \qquad (2)$$

where k_{H^+} = specific rate constant of hydrogen ions, c_{H^+} = concentration of hydrogen ions due to the hydrochloric acid, c_{h} = contribution of hydrogen ions due to the organic phosphorus acid at the time t, and a = initial concentration of fluorophosphorus compound.

If the dissociation constant of the organic phosphorus acid is K the following equilibrium equation must be obeyed:

$$K = \frac{c_h(c_{H+} + c_h)}{x - c_h} \approx \frac{c_h \cdot c_{H+}}{x - c_h} \tag{3}$$

since in the present work $c_{H+} \gg c_h$. By rearrangement of eqn. (3) we get:

$$c_h = \frac{K}{c_{H+} + K} \cdot x \tag{4}$$

By inserting eqn. (4) in (2) we get for the rate of hydrolysis:

$$\frac{dx}{dt} = k_{H+} \left(c_{H+} + \frac{K}{c_{H+} + K} \cdot x \right) (a - x) \tag{5}$$

Upon integration of eqn. (5) the following rate equation is obtained:

$$k_{H+} \left(c_{H+} + \frac{K}{c_{H+} + K} \cdot a \right) = \frac{1}{t} \ln \frac{a}{a - x} \left(c_{H+} + \frac{K}{c_{H+} + K} \cdot x \right) \tag{6}$$

In Fig. 1b we have used the same experimental values as in Fig. 1a but in this case we have plotted

$$\ln \frac{a}{a - x} \left(\frac{c_{H+} + \dfrac{K}{c_{H+} + K} \cdot x}{c_{H+}} \right)$$

as function of t. The straight line which can be drawn through the calculated points shows that eqn. (6) can be used for the calculation of the specific rate constant k_{H+} when K is known. This was done in the case of dimethoxy — and methoxyethyl fluoride, but not diethylphosphoryl fluoride, since in the latter case the corresponding acid has as high a pK-value as approximately 3.4 [1], and the correction due to the formation of this acid during the reaction was found to be so small that the rate constants could be calculated according to the first order rate equation.

EXPERIMENTAL

Materials. The three organic fluorophosphorus compounds studied were synthesized according to previous descriptions [3]. All compounds are rather unstable in storage so freshly distilled products must always be used. The compounds are preferably kept in polyethylene bottles.

The hydrochloric acid solution used was prepared from constant boiling hydrochloric acid (B.D.H. Analar).

Kinetic measurements. These were performed in 250 ml Erlenmeyer flasks immersed in water of the desired temperature. A constant circulating water bath of $\pm$ 0.1°C accuracy was used for the measurements at 25°C; at 0°C the reaction flask was placed in water-ice mixture in a Dewar flask of 4 litres capacity.

The organic fluorophosphorus compound (0.5—0.9 g) was weighed into the Erlenmeyer flask. The flask was placed in the water bath for approximately 20 min, and the reaction started by quickly diluting the compound with 100 ml standardized hydrochloric acid which had been equilibrated beforehand in the same water bath.

After fixed intervals of time an aliquot of 10 ml of the reaction solution was transfered to an Erlenmeyer flask containing crushed ice. The total amount of acid was immediately titrated with standard 0.1 N sodium or barium hydroxide using cresol red as an

Table 1. Determination of dissociation constants of organic phosphorus acids. Temp 20°C.

Compound	Conc. of acid	Conc. of Na$^+$ present	Measured pH	K_a Calc.	pK_a Average

CH$_3$O   OH
  \ /
   P
  / ‖
CH$_3$O   O
	0.01806
	0.03612
	0.07224
	0.0903
		0
		0
		0
		0
			1.87
			1.65
			1.41
			1.33
				0.068
				0.049
				0.058
				0.065
					1.22

CH$_3$O   OH
  \ /
   P
  / ‖
C$_2$H$_5$ O
	0.0355
	0.0338
	0.0323
	0.0309
	0.0296
	0.0284
		0
		0.0047
		0.0091
		0.0131
		0.0166
		0.0200
			1.82
			1.91
			2.02
			2.15
			2.32
			2.54
				0.0124
				0.0140
				0.0137
				0.0135
				0.0128
				0.0110
					1.88

indicator. Eight or nine individual titrations were made for every rate constant calculated. The average error of the rate constant is approximately $\pm$ 5 %.

DETERMINATION OF pK-VALUES OF THE ORGANIC PHOSPHORUS ACIDS

The organic phosphorus acids were made from the corresponding chloride by shaking with an equivalent amount of silver oxide in water. The silver chloride was filtered off and the clear water solution was directly used for the determination of the dissociation constants. The measurements were performed with a Metrohm Potentiometer Model E 187. With this instrument pH-values are reproducible to $\pm$ 0.02 pH units. In the case of methoxyethylphosphorus acid the pH in the acid solution was determined in the presence of varying amount of sodium hydroxide. From the measured pH the pK was calculated according to the following formula:

$$K = \frac{c_{H^+}\left(c_{H^+} + c_{Na^+} - \dfrac{10^{-14}}{c_{H^+}}\right)}{c_{HA} - \left(c_{H^+} + c_{Na^+} - \dfrac{10^{-14}}{c_{H^+}}\right)}$$

where $c_{H^+} = \dfrac{a_{H^+}}{f_{H^+}}$ = concentration of hydrogen ions and c_{HA} = total concentration of organic phosphorus acid. The values of f_{H^+} were taken from the literature [5]. In Table I are summarized the calculated values of the dissociation constants of dimethoxy- and methoxyethyl phosphorus acids determined at different concentrations of acid and salt. The values are in reasonable agreement with the reported pK-values, 1.29 and 2.00, of the same compounds [1].

RESULTS AND AND DISCUSSION

In Table 2 are recorded the values of the rate constants at different acid concentrations of the acid hydrolysis of the three organic fluorophosphorus compounds studied. The values of k_{OH^-} are also included in the same table.

Table 2. Data from the acid hydrolysis of methoxy-, methoxyethyl- and diethylphosphoryl fluoride.

Compound	Specific rate constants, k_{H+} l mole^{-1} min^{-1} in different concentrations of HCl							k_{OH^-} l mole^{-1} sec^{-1} 25.1°C	E_A kcal/mole
	Temperature: 25°C						Temp. 0°C		
	0.01 N	0.02 N	0.03 N	0.04 N	0.06 N	0.099N	0.099		
CH_3O O $\diagdown\diagup$ P $\diagup\diagdown$ CH_3O F	—	0.502	—	0.437	0.435	0.401	0.0618	18.2	12.1 ± 1
CH_3O O $\diagdown\diagup$ P $\diagup\diagdown$ C_2H_5 F	—	0.500	—	0.476	0.476	0.437	0.0518	49.1	13.8 ± 1
C_2H_5 O $\diagdown\diagup$ P $\diagup\diagdown$ C_2H_5 F	2.62	2.24	2.25	2.06	—	—	0.289 (in 0.02 N HCl)	726	13.2 ± 1

. The substituents in these phosphorus compounds show a much smaller influence upon the rate of the acid catalysed hydrolysis than on the alkaline hydrolysis of the same compounds. In this respect the hydrolysis of organic fluorophosphorus compounds shows the same general tendency as the hydrolysis of esters of carboxylic acids [6]. From a theoretical point of view the acid catalysed reaction is more complex than the nucleophilic reaction with hydroxyl ions. The former involves an electrophilic attack of hydrogen ions probably on the oxygen of the phosphoryl group, and a nucleophilic attack of a water molecule on phosphorus. The rate determining step may be either the formation of a transition state with phosphonium structure:

$$R_1 \diagdown \quad \diagup OH$$
$$\overset{+}{P}$$
$$R_2 \diagup \quad \diagdown F \qquad\qquad (I)$$

or this step includes a bifunctional simultaneous attack of both the hydrogen ion and the water molecule forming a transition state with pentavalent structure:

$$H \diagdown \quad R_1 \quad R_2$$
$$\overset{+}{O} - - P - - F$$
$$H \diagup \quad | \quad\quad (II)$$
$$OH$$
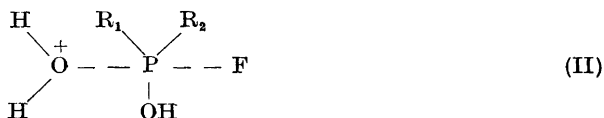
In the latter case we may expect that two opposing effects will contribute to the total picture of the reaction. The greater polarity of the phosphoryl group should favour a proton transfer from the water solution. If therefore the formation of the phosphonium structure (I) were the rate determining step, the rate of hydrolysis should be expected to increase steadily from the dimethoxy- to the diethyl phosphoryl fluoride in accordance with the increasing polarity of the P—O bond in the same series [3]. If on the other hand the pentavalent structure (II) is formed the stability of such a transition state may be expected to decrease from the dimethoxy to the diethyl compound in accordance with the decreasing negativity of the substituents in the same series [7]. The small differences in the rate constants of the acid hydrolysis of the three organic fluorophosphorus compounds thus seem to favour the hypothesis of a pentavalent structure of the transition state. In the same way if the phosphonium structure (I) represents the rate determining step, the acid hydrolysis of di*iso*propoxyphosphoryl fluoride ought to give a higher rate than the dimethoxy compound due to a stronger polarity of the P—O bond. From the measurements of Kilpatrick and Kilpatrick [4] we calculate that the k_{H+} of DFP at 25°C lies in the neighbourhood of 0.07 l mole^{-1} min^{-1}, and is thus approximately 1/7 of the k_{H+} of the dimethoxy compound. We therefore assume that the difference in k_{H+} is due to the entering of water in the rate determining step according to the pentavalent structure (II) of the transition state. In the case of DFP the bulky *iso*propoxy groups must be expected to give strong steric retardation during the formation of the transition complex.

As seen from Table 2 the specific rate constant, k_{H+}, decreases with increasing hydrogen ion concentration for the three organic fluorophosphorus compounds studied. The decrease can approximately be described by the equation: $k_{H+} = K \cdot [H^+]$ where K = constant. The magnitude of K in the hydrolysis of dimethoxy- and methoxyethyl phosphoryl fluoride is of the same order as observed for the K in hydrolysis of di*iso*propoxyphosphoryl fluoride (DFP) by Kilpatrick and Kilpatrick [4], but in the hydrolysis of diethylphosphoryl-fluoride K seems to be somewhat higher. This is in accordance with an explanation of the acid hydrolysis of phosphorus compounds put forward in a previous publication [2] according to which a stronger tendency of hydrogen bond formation of the substrate should favour a greater K-value.

REFERENCES

1. Hudson, R. F. and Harper, D. C. *J. Chem. Soc.* **1958** 1356.|
2. Aksnes, G. *Acta Chem. Scand.* **14** (1960) 1526.
3. Aksnes, G. *Acta Chem. Scand.* **14** (1960) 1515.
4. Kilpatrick, M. L. and Kilpatrick, M. *J. Phys. & Colloid. Chem.* **53** (1949) 1371.
5. Harned, H. S. and Owen, B. B. *The Physical Chemistry of Electrolytic Solutions.* Reinhold., New York 1943.
6. Hammet, L. P. *Physical Organic Chemistry*, McGraw-Hill Book Co. New York 1940, pp. 211—213.
7. Pauling, L. *Nature of the Chemical Bond*, Cornell University Press, New York 1948, p. 93.