102. *Kinetic Studies in the Phosphinyl Chloride and Phosphorochloridate Series. Part II.* Reaction of Di*iso*propyl Phosphorochloridate with Anionic Reagents.*

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The reactions of di*iso*propyl phosphorochloridate with a number of anions were studied in ethanolic solution. The reactions were of first order with respect to both the ester and the anion concentration. The effects of structural variations and of changes in solvent are in agreement with a simple bimolecular mechanism.

In continuation of our kinetic investigation of the phosphorochloridates (Part I *), we have studied the reactions of the *iso*propyl ester with ethoxide, phenoxide, thiophenoxide, fluoride, and acetate ions, all in ethanolic solution. These reactions are complicated by simultaneous solvolysis, and where necessary the observed rate constants were corrected for this reaction by Moelwyn-Hughes's method (*Proc. Roy. Soc.*, 1949, *A*, **196**, 540).

The reactions with thiophenoxide and acetate ions are probably slower that those with ethanol, for no increase in the rate is observed on addition of these ions to the solvolysis mixture. The order of reactivity can be written as $F^- > EtO^- > PhO^- > EtOH$, PhS^-, $CH_3\cdot CO\cdot O^-$. The reactions with ethoxide ion and fluoride ion were investigated in detail. They are irreversible, proceeding according to the equation $(RO)_2POCl + OEt^-$ (or F^-) $\longrightarrow (RO_2)PO(OEt)$ [or $(RO)_2POF$] $+ Cl^-$, are of first order with respect to both phosphorochloridate and reagent, and appear to be simple bimolecular substitution reactions. The rates for various initial concentrations of the reactants are shown in Table 1. From the temperature dependence of the reaction rates, the Arrhenius parameters were calculated and are given in Table 2.

Table 1. *Reaction of di*iso*propyl phosphorochloridate in dry alcohol at* 0°. (Second-order rate constants.)

With ethoxide ions.

Initl. concn. of $Cl\cdot PO(OPr^i)_2$, mole/l.	0·01	0·025	0·04	0·01
,, ,, OEt^-, mole/l.	0·02	0·02	0·02	0·097
k_2, l. mole⁻¹ sec.⁻¹	0·010	0·011	0·010	0·014

With fluoride ions.

Initl. concn. of $Cl\cdot PO(OPr^i)_2$, mole/l.	0·0063	0·0050	0·0052	0·0053	0·014
,, ,, F^-, mole/l.	0·0029	0·0064	0·0098	0·0098	0·023
k_2, l. mole^{-1} sec.$^{-1}$	0·034	0·031	0·027	0·033	0·027

Table 2. *Second-order rate constants at various temperatures for the reactions of di*iso*propyl phosphorochloridate, and the corresponding Arrhenius parameters.*

	k_2, l./mole^{-1} sec.$^{-1}$ at :				
Reagent	25°	0°	−8·5°	E, kcal./mole	$10^{-9}A$, l. mole^{-1} sec.$^{-1}$
NaOEt	0·11	0·010	0·0061	13·9	2·1
KF	0·23	0·030	—	12·9	0·64
NaOPh	—	0·003	—	—	—

Attempts to study the effects of changes of the alkyl group R were made but the rate of the reaction of diethyl phosphorochloridate was almost too fast to be measured and only approximate second-order rate constants were obtained. For reactions in ethanol at 0°, these were (in l. mole^{-1} sec.$^{-1}$) $k_2 = 0{\cdot}26$ for the reaction with ethoxide ions and $k_2 = 0{\cdot}28$ for that with fluoride ions. The reactions of the dimethyl ester were too fast to be measured at 0°. The effect of variations of the alkyl group is seen to be more marked with respect to reactions with anions than with neutral nucleophilic reagents (*J.*, 1953, 502).

The effect of change of solvent was studied by comparing the rate of reaction of di*iso*propyl phosphorochloridate with fluoride ion in dry ethanol and in 60% aqueous ethanol. In the latter, the rate of solvolysis is no longer negligible compared with the rate of reaction with fluoride ion, and special methods were required to obtain the rate of the latter reaction (cf. p. 510). It was found that the rate of the fluoride reaction in 60% aqueous

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* Part I, preceding paper.

ethanol at 25° is 0·039 l. mole^{-1} sec.$^{-1}$, *i.e.*, about six times slower than in dry ethanol (0·23 l. mole^{-1} sec.$^{-1}$). Only a small salt effect was observed for a reaction with ethoxide ion: in dry ethanol at $-8·5°$, the rate of reaction changed from 0·0062 without added salt to 0·0076 l. mole^{-1} sec.$^{-1}$ in the presence of 0·072 mole/l. of sodium perchlorate (the initial concentration of ethoxide ions was 0·023 mole/l. in each case).

EXPERIMENTAL

Materials.—Absolute ethanol and dialkyl phosphorochloridates were prepared as described in Part I (*loc. cit.*). Sodium ethoxide solutions were prepared by dissolving sodium in ethanol and standardised by titration with hydrochloric acid. Potassium fluoride solutions were prepared by dissolving anhydrous potassium fluoride (obtained by heating the acid fluoride in a platinum crucible to red heat) in the desired solvent and standardised by titration with thorium nitrate solution in 50% ethanol with sodium alizarinsulphonate as indicator (Willard and Winter, *Ind. Eng. Chem. Anal.*, 1933, **5**, 7). Sodium phenoxide and sodium thiophenoxide solutions were obtained by adding phenol or thiophenol in slight excess to a solution of sodium ethoxide of the desired concentration in ethanol. The equilibrium ethoxide + phenol (thiophenol) ⇌ ethanol + phenoxide (thiophenoxide) will be almost completely to the right. The total concentration of thiophenol and thiophenoxide was determined by titration with an alcoholic solution of iodine (Klason and Carlson, *Ber.*, 1906, **39**, 739). The concentration of thiophenoxide alone was determined by adding excess of standard hydrochloric acid solution and back-titrating with sodium hydroxide (methyl-orange).

Rate Measurements.—The rate of substitution of chlorine in dialkyl phosphorochloridates by ethoxide, phenoxide, and fluoride ions was followed by electrometric titration of chloride ions in samples of the reaction mixture, as described in Part I with the following modifications:

Reaction with ethoxide. Sodium ethoxide reacts with dialkyl phosphorochloridates to form sodium chloride and a trialkyl phosphate. Since the solubility of sodium chloride in absolute ethanol at 18·5° is only about 0·01 mole/l. (de Bruyn, *Z. physikal. Chem.*, 1892, **10**, 782), a homogeneous reaction mixture was obtained by preparing solutions so dilute that the solubility product of sodium chloride was not exceeded. The reactions were carried out in a measuring flask. At definite intervals samples of 5 or 10 ml. were withdrawn and introduced quickly into 20—25 ml. of a cooled solution of 95% ethanol containing a slight excess of sulphuric acid. Chloride ion was then titrated electrometrically with silver nitrate. For the more concentrated solutions, samples of the reaction mixture were introduced into tightly stoppered test-tubes and kept for measured times in the thermostat. The contents of the tubes were then poured quickly into ethanol containing sulphuric acid, the precipitated sodium chloride on the walls of the test-tube was washed out with small amounts of ethanol (altogether 25 ml. of ethanol were used), and the chloride was determined as above.

The following example of the reaction of di*iso*propyl phosphorochloridate (initially 0·0101 mole/l.) with sodium ethoxide (0·0219 mole/l.) in absolute ethanol at 0° illustrates the determination of second-order rate constants. The reaction was carried out in a measuring flask; samples of 10 ml. were withdrawn for every titration:

Time, sec.	0	154	332	570	967	1405	1750	2270	2966	∞
0·00919N-AgNO$_2$, ml.	1·33	1·65	1·91	2·27	2·88	3·63	4·01	4·56	5·25	10·94
10^4k_2	—	109	91	90	92	101	96	95	95	—

Mean: $k_2 = 0·0096 \pm 0·0005$ l. mole^{-1} sec.$^{-1}$.

This result, together with means of those of further runs under similar conditions, gave an average value of $k_2 = 0·010_4$, which is represented in Table 1. Other rate constants were determined similarly. The rate constants were calculated by the equation $k_2 = [2·303/t(b - a)] \times \log b(a - x)/a(b - x)$ in l. mole^{-1} sec.$^{-1}$, where a and b are the initial concentrations of phosphorochloridate and ethoxide ions and x is that of chloride ions at time t. Since the rate of solvolysis of di*iso*propyl phosphorochloridate in ethanol is so much less than the rate of reaction with sodium ethoxide, the former can be neglected in calculating the rate constants.

Reaction with phenoxide. The measurement of the rate was similar to that used for the ethoxide. However, since the phenoxide reacts much more slowly, it was necessary to introduce a correction for the simultaneous solvolysis, and Moelwyn-Hughes's method was used (*Proc. Roy. Soc.*, 1949, *A*, **196**, 540). Only a few runs were carried out; these were of rather low precision, but the approximate value of $k_2 = 0·003$ l. mole^{-1} sec.$^{-1}$ was obtained.

Reaction with fluoride. The solubility of potassium chloride in absolute ethanol is 0·011 mole/l. at 25° (McIntosh, *J. Phys. Chem.*, 1903, **7**, 350) and the reaction could be carried out homogeneously by working with solutions having a final chloride concentration lower than that value. For higher concentrations the test-tube method described above was used. An upper limit to the concentration was, however, imposed by the solubility of potassium fluoride in ethanol, *i.e.*, *ca.* 0·018 mole/l. at 20° (Germuth, *J. Franklin Inst.*, 1931, **212**, 346; Landolt–Börnstein's "Tabellen," III, 638). In view of the formation of toxic di*iso*propyl phosphorofluoridate (fluorophosphonate), pipettes were filled by slight suction with a water-pump. Samples were introduced into cold ethanol and titrated for chloride ions as above. The presence of fluoride did not interfere with the titration of chloride. The following example illustrates the determination of the rate constants:

Di*iso*propyl phosphorochloridate (initially 0·0052 mole/l.) in absolute ethanol at 25·14°. Reaction in a measuring flask; 10 ml. withdrawn for each titration.

Time, sec.	0	225	549	890	1215	1710	2140	2753	∞
0·00571N-$AgNO_3$, ml.	2·80	4·63	6·00	7·05	7·70	8·11	8·43	8·69	9·06
k_2, l. mole^{-1} sec.$^{-1}$ ...	—	0·22	0·22	0·21	0·25	0·23	0·24	0·23	—

Mean $k_2 = 0\cdot23 \pm 0\cdot01$ l. mole^{-1} sec.$^{-1}$.

A duplicate run (No. 81) gave a mean value of $k_2 = 0\cdot22$ l. mole^{-1} sec.$^{-1}$.

*Isolation of di*iso*propyl phosphorofluoridate from the reaction mixture.* Since potassium fluoride is so slightly soluble in ethanol, the preparation of the ester was modified as follows. Finely ground, dry potassium fluoride (12 g.; 0·2 mole) (obtained by heating the salt in a stainless-steel pot at 200—300°, breaking it into lumps, and grinding it while still hot in a mill) and absolute ethanol (200 ml.) were placed in a flask fitted with a dropping-funnel and connected to a downward condenser. The ethanol was brought to the boil and when distillation started di*iso*propyl phosphorochloridate (19 g., 0·05 mole) was added dropwise (10 minutes). The distillation was continued until most of the ethanol was removed. The residue was neutralised with a little barium carbonate and filtered. The filtrate was distilled; it had b. p. 84—88°/26 mm. (3·5 g.) (Found: F, 10·1; P, 16·5. Calc. for $C_6H_{14}O_3PF$: F, 10·3; P, 16·9%). Saunders and Stacey (*J.*, 1948, 699) give b. p. 82—83°/21 mm.

For the reaction of di*iso*propyl phosphorochloridate with fluoride ions in 60% aqueous ethanol the simultaneous solvolysis cannot be ignored. Moelwyn-Hughes's method (*loc. cit.*) of correction could not be rigorously applied to our runs in which only the rate of production of chloride ions was followed experimentally, leaving the instantaneous value of the fluoride-ion concentration unknown. By allowing the reactions to proceed to completion and then determining both fluoride and chloride ions, a value was deduced for the rate constant of the reaction with the first ion. The rate of evolution of chloride ion is given by $dx/dt = k_2(a - x)y + k_1(a - x)$, where a = initial concentration of di*iso*propyl phosphorochloridate, x and y are the instantaneous values for the concentration of chloride and fluoride ions, k_2 the desired rate constant, and k_1 the first-order rate constant for the solvolysis reaction. Similarly, the rate of production of fluoride ions is $-dy/dt = k_1(a - x)y$, whence $-dx/dy = 1 + k_1/k_2y$. Integrating, we obtain $k_2 = [2\cdot303k_1/(b - a - z)] \log (z/b)$, where b and z are the initial and final concentrations of fluoride ions. In one of our experiments carried in 60% aqueous ethanol at 25° (where $k_1 = 5\cdot8 \times 10^{-4}$ sec.$^{-1}$), $a = 0\cdot0121$ and $b = 0\cdot0149$ mole/l. After reaction, z was found to be 0·0096 mole/l. in solution. Therefore,

$$k_2 = \frac{2\cdot303 \times 5\cdot8 \times 10^{-4}}{0\cdot0149 - 0\cdot0121 - 0\cdot0096} \cdot \log \frac{0\cdot0096}{0\cdot0149} = 0\cdot038 \text{ l. mole}^{-1} \text{ sec.}^{-1}.$$

The value of k_2 obtained above, when compared with k_1, would indicate that Moelwyn-Hughes's method (*loc. cit.*) could be applied to our initial rate constants for the reaction of di*iso*propyl phosphorochloridate with fluoride ions in 60% ethanol, with an error not exceeding 15%. The application of this method to one of our runs is illustrated below. For the reaction of di*iso*propyl phosphorochloridate (initial concentration $a = 0\cdot035$ mole/l.) with fluoride ions (initially $b = 0\cdot10$ mole/l.) the observed first-order (drifting) constant at 6·5 minutes was $k_1' = 32\cdot4 \times 10^{-4}$ sec.$^{-1}$. At that time the amount of chloride ion produced was $x = 0\cdot029$ mole/l. Applying Moelwyn-Hughes's formula, *viz.*, $k_2 = (k'_1 - k_1)y$, and assuming $y = b - x$, *i.e.*, that the amount of fluoride disappearing is equal to chloride produced, we obtain, after substituting the appropriate values, $k_2 = (32\cdot4 - 5\cdot8) \times 10^{-4}/0\cdot071 = 0\cdot039$, in reasonable agreement with the value determined above.

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