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Organic Phosphorus Compounds. I. The Conversion of the Chloroaluminate Complexes, $[RPCl_3][AlCl_4]$, to Alkyl Alkylphosphonochloridates and Dialkyl Alkylphosphonates

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Phosphorus trichloride can be converted in methylene chloride solution in good yields by a simple one-batch procedure with alkyl chloride and aluminum chloride to the intermediate chloroaluminate complexes, $[RPCl_3][AlCl_4]$ (I) or $[RPCl_3][Al_2Cl_7]$, and by alcoholysis further to alkyl alkylphosphonochloridates or dialkyl alkylphosphonates. It is shown that the complexes I are converted by alcoholysis stepwise to $[RP(O)Cl][AlCl_4]$, $[RP(O)OR'][AlCl_4]$ and finally to $[RP(O)(OR')_2\cdot AlCl_3]$, all of which can be decomposed with water to yield $RP(O)Cl_2$, $RP(O)(OR')Cl$ and $RP(O)(OR')_2$, respectively, and hydrated aluminum salts.

Introduction.—The various methods described in the literature for the preparation of phosphonic acids and their derivatives[2] have been supplemented recently by a simple general procedure which utilizes the ready formation of complexes of the type $[RPCl_3]$ $[AlCl_4]$ (I) from equimolar amounts of alkyl chloride, aluminum chloride and phosphorus trichloride.[3-5]

Treatment of the complexes I in methylene chloride solution with 7–11 mole equivalents of water gives the corresponding alkylphosphonyldichloridates, $RP(O)Cl_2$ (II), generally in good yields.[3-5] Perren and Kinnear[5] also demonstrated by one example that the I can be converted directly with ethanol to the corresponding diethyl alkylphosphonate, in their example the ethylphosphonate, C_2H_5-$P(O)(OC_2H_5)_2$ (III).

The mechanisms proposed by Clay[3] and by Kinnear and Perren[4] for the formation of the dichlorides II differ with regard to the first step of the reaction. While Clay assumes that the first mole equivalent of water attacks the cation of the complex I forming by hydrolytic cleavage a $[RP(O)Cl]^+$ cation and thus a new ionic complex $[RP(O)Cl]$ $[AlCl_4]$ (IV), the British authors believe the first step of the hydrolysis to be a hydrolytic cleavage of the ionic complex I into $H[AlCl_4]$ and $RPCl_3\cdot OH$. The intermediate, having an unstable electron decet around the phosphorus atom, is then stabilized by elimination of HCl resulting in the formation of II.

Since ethanolysis of the complex $[C_2H_5PCl_3]$ $[AlCl_4]$ (V) is reported[5] to give III in 92% yield, while its hydrolysis resulted in the isolation of 82% of $C_2H_5P(O)Cl_2$ (VI), it appears that the complexes I can be utilized, at least in some cases, directly as starting materials for the synthesis of valuable organic phosphorus derivatives without the intermediate isolation of the dichlorides II. Clarification of the mechanism of the solvolysis of I would allow a proper selection of suitable conditions for the conversion to products other than II. Therefore, a study of the stepwise alcoholysis of I was undertaken. The results of this investigation enabled us to devise a useful method for the synthesis of alkyl alkylphosphonochloridates and dialkyl alkylphosphonates directly from the appropriate alkyl halides.

Summary of Results.—The complex $[CH_3PCl_3]$-$[AlCl_4]$ (VII), suspended in methylene chloride solution, deposited upon treatment with one mole equivalent of absolute methanol at 25° the less soluble crystalline complex $[CH_3P(O)Cl][AlCl_4]$ (VIII), the composition of which was established by independent synthesis and by analysis. The high thermal stability of the distillable complex VIII indicates strong complexing of its components.

The postulated breakdown of the complexes I into II and $H[AlCl_4]$ by which Kinnear and Perren[4] explain the hydrolysis to II seems to be disproved by the formation of the complex VIII from its components. The tendency of II to enter into complex formation with aluminum chloride is much too high to allow its coexistence with the weak complex $H[AlCl_4]$ in a solution. If the products II and $H[AlCl_4]$ existed at any time in the reaction mixture, complex formation to IV would occur with the elimination of hydrogen chloride. In other words, the first step of the hydrolysis appears to proceed in the fashion suggested by Clay[3] with the formation of IV.

The treatment of complex VII with two mole equivalents of methanol resulted in the formation of another complex with the elimination of hydrogen chloride. This new complex analyzes for a composition of an adduct of methyl methylphosphonochloridate, $CH_3P(O)(OCH_3)Cl$, and aluminum chloride and may possibly be formulated as $[CH_3P(O)OCH_3][AlCl_4]$. The reaction of VII with an additional, *i.e.*, with three, mole equivalent of methanol gave again a complex which could be isolated as a stable solid from the reaction mixture. The resulting product had the approximate composition $CH_3P(O)(OCH_3)_2\cdot AlCl_3$.

Conclusive evidence for the stepwise alcoholysis of I to new complex intermediates was obtained by ethanolysis of V in methylene chloride solution with one, two and three mole equivalents of absolute ethanol. The nuclear magnetic resonance (NMR) spectra of the resulting products were identical for all practical purposes with the spectra of the complexes prepared in methylene chloride solution from anhydrous aluminum chloride and VI, $C_2H_5P(O)(OC_2H_5)Cl$, (IX) and III, respectively. The chemical shift (δ) values for the various complexes, prepared by alcoholysis of V and by direct synthesis from the components, and also for the

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[1] To whom inquiries about this paper should be directed.

[2] G. M. Kosolapoff, "Organophosphorus Compounds," John Wiley and Sons, Inc., New York, N. Y., 1950, pp. 121–179.

[3] J. P. Clay, *J. Org. Chem.*, **16**, 892 (1951).

[4] A. M. Kinnear and E. A. Perren, *J. Chem. Soc.*, 3437 (1952).

[5] E. A. Perren and A. M. Kinnear, British Patent 707,961, April 28, 1954.

phosphorus-containing components of the complexes are listed in Table I.

TABLE I

NUCLEAR MAGNETIC RESONANCE SPECTRA[6]

P^{31} RESONANCE

Compound	Chemical shift, δ[a][b]
$[C_2H_5PCl_3][AlCl_4]$ (V)	−128.6
$[C_2H_5PCl_3][Al_2Cl_7]$ (XVI)	−128.6
$C_2H_5P(O)Cl_2$[c] (VI)	−53.0
$[C_2H_5P(O)Cl][AlCl_4]$ (X)[d]	−75.8
$[C_2H_5P(O)Cl][AlCl_4]$ (X)[e]	−77.4
$[C_2H_5P(O)OC_2H_5][AlCl_4]$[f]	−53.8
$[C_2H_5P(O)OC_2H_5][AlCl_4]$[g]	−54.5
$C_2H_5P(O)(OC_2H_5)Cl$ (IX)	−45.0
$[C_2H_5P(O)(OC_2H_5)_2 \cdot AlCl_3]$[h]	−31.0
$[C_2H_5P(O)(OC_2H_5)_2 \cdot AlCl_3]$[i]	−31.
$C_2H_5P(O)(OC_2H_5)_2$ (III)	−32.

[a] Chemical shift, $\delta = (H \text{ sample} - H_{H_3PO_4}) \times 10^6$, [illegible] PO4; the operating radio frequency for these measureme[illegible] was 17 megacycles. [b] The spectra were taken in me[illegible]ene chloride solution except where stated otherwise. [c] [illegible]iout solvent. [d] From V and one mole of absolute ethanol. [e] From VI and $AlCl_3$. [f] From V and two moles of absolute ethanol. [g] From IX and $AlCl_3$. [h] From V and three moles of absolute ethanol. [i] From III and $AlCl_3$.

That VI is not formed by alcoholysis of V with one mole equivalent of ethanol is clearly demonstrated by the differences of the chemical shift values between VI and its complex with aluminum chloride, $[C_2H_5P(O)Cl][AlCl_4]$ (X). The presence of VI in quantities of more than 2–3% of the total amount of phosphorus in the solution of the alcoholysis product of V with one mole of ethanol and of the product from VI and aluminum chloride would have been observed in the spectra of the two samples of complex X.

The chemical shifts of −53.8 and −54.5 observed for the solvolysis product of V with two mole equivalents of ethanol and for the reaction product of IX with aluminum chloride, respectively, again prove the identity of the reaction products. The smaller shift of −45.0 shown by IX seems to indicate that the conversion of a covalent P–Cl bond to an ionic bond results in a larger chemical shift. The same observation is made in the conversion of VI to X. The NMR spectrum of the reaction product of V with three moles of ethanol was identical with that of the synthetic complex obtained from III and aluminum chloride. The absence of a chemical shift to a more negative value upon complexing III can be regarded, on the basis of the foregoing observations, as indicative for the absence of a conversion of a covalent P–O bond to an ionic bond and can best be explained by the non-ionic structure $[C_2H_5P(O)(OC_2H_5)_2 \cdot AlCl_3]$ for the complex.

None of the conversion complexes formed by alcoholysis of I can be broken by the usual techniques, such as treatment with sulfuryl chloride, phosphorus oxychloride, triethylamine or fusion with sodium chloride, but requires hydration of the $[AlCl_4]^-$ anion to aluminum chloride hydrate and hydrogen chloride.

The reaction scheme involved in the alcoholysis, synthesis and cleavage of the various complexes is illustrated in Fig. 1.

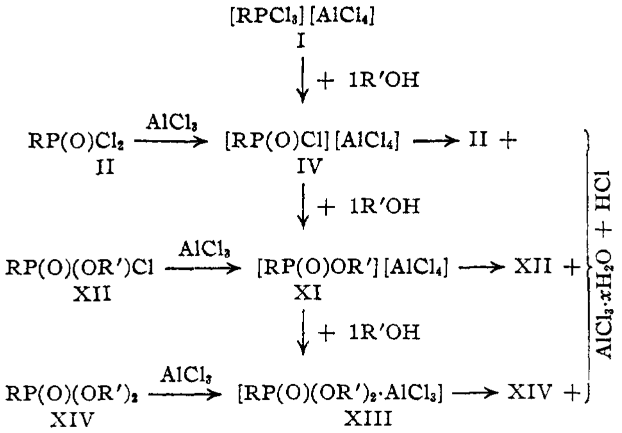

Fig. 1.

The first step of the alcoholysis of I (as well as of the hydrolysis) is the conversion to IV with the replacement of two chlorine atoms by one oxygen atom and the formation of alkyl chloride and hydrogen chloride. This reaction takes place in all probability by a nucleophilic displacement of a chloride ion on the phosphorus by the alkoxide ion followed by elimination of alkyl halide. A repetition of the nucleophilic displacement reaction on the cation of IV leads to the formation of the cation $[RP(O)OR']^+$ (XV). The conversion of IV to XI corresponds to the reaction of II with one mole equivalent each of an alcohol and a base leading to the chloridate XII. The role of the base is taken over in the system IV–R'OH by the displaced chloride ion which removes the proton as undissociated HCl. A similar situation prevails for the further alcoholysis of XI to XIII, except that here the nucleophilic attack of the alkoxide ion on the phosphorus atom of the cation XV results in a neutral molecule XIV, which forms an un-ionized complex with aluminum chloride. The chloride ion liberated from the anion $[AlCl_4]^-$ by the complexing is taken up by the proton originating from the alcohol.

Clay[3] and Kinnear and Perren[4] demonstrated that further treatment of the complex IV with one to fourteen moles of water (depending on the nature of the alkyl group) gives the corresponding II in good yields. The direct conversion of complex V with absolute ethanol until no further reaction occurred, followed by treatment with water,[5] showed that the isolation of the II is unnecessary for the synthesis of the phosphonates XIV. While the formation of XIV from II in acceptable yields requires the presence of two mole equivalents of a base as an acceptor for the liberated hydrogen chloride, no base is necessary in the conversion of I to XI and further to XIV. Complex V treated in methylene chloride solution with seven moles of ethanol (see run 5) and water added dropwise to the reaction mixture until the original gelatinous precipitate dissolved gave an 80% yield of III.

That not more than three mole equivalents of alcohol are actually required for the formation of III is demonstrated clearly by a run (no. 2) in which a

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(6) The NMR spectra reported in this paper were measured and interpreted by Messrs. Harold Finegold and G. F. Svatos employing the same instrumentation and technique as described by N. Muller, P. C. Lauterbur and Jerome Goldenson, THIS JOURNAL, **78**, 3557 (1956). The authors gratefully acknowledge this valuable help.

solution of V in methylene chloride was at first treated for conversion to $C_2H_5P(O)(OC_2H_5)_2 \cdot AlCl_3$ with three mole equivalents of ethanol and then for cleavage of the complex with sufficient water to give a clear, two-phase solution. The yield of III in this run was 76% of the theoretical.

Evidence for the stepwise conversion of the complex I to IV, XI and finally XIII (see Fig. 1) is not only obtained from the formation of the various complexes from their components but also from the conversion of IV by successive treatment with two different alcohols to complex XIII in which the two alkoxy groups can be identical or different, and its subsequent cleavage to yield the corresponding esters XIV in good yields (see runs 11 and 13). The high yields of XIV obtained in this manner appear to require the intermediate formation of a well-defined complex of the type XI in the first step and suggest the conversion of I directly to XII by treatment with two moles of an alcohol followed by cleavage of the intermediate complex XI with a limited amount of water. This reaction sequence permits the conversion of phosphorus trichloride through the readily obtainable complexes I in a simple one-batch method to the valuable alkylphosphonochloridates XII (see runs 14–17) in acceptable yields.

Since the first mole of alcohol in the reaction with the complex I serves merely the purpose of replacing two chlorine atoms of the cation by an oxygen atom, any inexpensive alcohol, such as methanol or ethanol, can be employed in the first step of the alcoholysis. For the preparation of phosphonochloridates or phosphonates, the introduction of the desired alkoxy group or groups on the phosphorus atom can then be accomplished by means of the appropriate alcohol. The feasibility of this procedure is, in principle, demonstrated by run 13 in which the complex $[iso\text{-}C_3H_7PCl_3][AlCl_4]$ was first treated with ethanol (20% deficiency) and then with isopropyl alcohol (20% excess) and finally hydrolyzed with a limited amount of water to yield 62% of di-isopropyl isopropylphosphonate.

The methods of Clay[3] and of Kinnear and Perren[4] for the preparation of the II use the complexes I which are prepared in solid form. It was found, however, that the I also are formed readily in dry methylene chloride and that the resulting solutions can be converted further without the actual isolation of the complexes I. This procedure had in some cases the added advantage that discoloration of the reaction mixture which is observed in the formation of the I from isopropyl chloride can be avoided entirely. In general the complexes I are formed readily by adding the appropriate alkyl chloride slowly to a stirred solution of phosphorus trichloride in the solvent containing the equivalent amount of anhydrous aluminum chloride in suspension. Completion of the complex formation is indicated by the disappearance of the aluminum chloride.

While the reaction products from equimolar quantities of phosphorus trichloride, aluminum chloride and alkyl chloride gave generally the solvolysis products of the I in good yields, it was observed that similar runs with ethyl chloride led consistently to yields below 50% of the theoretical (see run 3). A methylene chloride solution of the complex V (prepared from the components without solvent), on the other hand, could be converted in 62% yield to IX (run 15) and in 80% yield to III (run 5). When a solution of the complex from ethyl chloride (prepared in methylene chloride) was evaporated under reduced pressure, the residue was not the solid complex I. The ratio of PCl_3: C_2H_5Cl:$AlCl_3$ was 1:1:2 in the residual viscous oily product. The same liquid material also was obtained by shaking a mixture of the reactants in the molar ratio 1:1:2 without solvent in a pressure bottle until the aluminum chloride had dissolved.

The formation of 1:1:2 complexes is described by Perren and Kinnear[5] without indicating the physical state of the resulting products. However, these authors make the general statement that the amount of complex-forming agent is not critical in determining the course of the reaction but is of importance to ensure the formation of liquid complexes.

The structure of the liquid complex of the composition $[C_2H_5Cl \cdot PCl_3 \cdot 2AlCl_3]$ can be either $[C_2H_5PCl_3][Al_2Cl_7]$ (XVI) or $[C_2H_5PCl_2]^{++}[2AlCl_4]^{--}$ (XVII). Since the complexes V and XVI have the same cation in common, identical NMR spectra are to be expected if the 1:1:2 complex possesses structure XVI. A structure of the type XVII, however, would result in a different chemical shift of the phosphorus resonance as compared to complex V. The δ-value of -128.6 for both, the 1:1:1 and the 1:1:2 complex, rules out formula XVII.

The formation of the complexes I from the components seems to proceed through the intermediate complexes $[RPCl_3][Al_2Cl_7]$ which react further with one mole equivalent of phosphorus trichloride and alkyl halide. A mixture of equal molar quantities of methyl chloride, phosphorus trichloride and anhydrous aluminum chloride mixed at Dry Ice temperature forms, when allowed to come to room temperature in a sealed Pyrex tube, in an exothermic reaction a clear, colorless liquid which solidifies on further shaking spontaneously within a few seconds to a solid crystal cake consisting of VII.[7] A similar observation was made in the preparation of the complex V, except that here the further conversion of the primarily formed XVI to V required heating to 60° or continued shaking overnight.

While the higher alkyl chlorides form the complexes I readily in methylene chloride as a reaction medium, the reaction of ethyl chloride in solution with phosphorus trichloride and aluminum chloride led only to XVI. This accounts for the low yield of III from ethyl chloride in run 3, when calculated on the basis of complex V instead of XVI as actually required.

For preparative purposes, the alcoholysis of I with absolute ethanol was preferable to that with other alcohols because of the solubility of the intermediate complexes in methylene chloride. When methanol was used instead of ethanol for the alcoholysis reactions, white crystals separated from the solutions and subsequent decomposition of the in-

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(7) In one run of this type a very violent explosion occurred. In the preparation of the complex VII, the sealed tube should always be encased in a heavy steel pipe closed at the ends with steel screw caps.

TABLE II

ELEMENTAL ANALYSES OF NEW PHOSPHORUS COMPOUNDS

	Analyses, %							
	Calcd.				Found			
Compound	C	H	P	Cl	C	H	P	Cl
i-$C_3H_7P(O)(OC_2H_5)_2$	46.66	9.51	17.19	...	46.5	9.5	16.85	...
i-$C_4H_9P(O)(OC_2H_5)_2$	49.47	9.86	15.95	...	49.6	9.9	...	...
$C_6H_{11}P(O)(OC_2H_5)_2$[a]	54.43	9.89	13.95	...	54.2	9.6	14.05	...
i-$C_3H_7P(O)(OCH_3)_2$	39.47	8.61	20.36	...	38.9	8.3	20.36	...
i-$C_3H_7P(O)(OC_2H_5)OCH(CH_3)_2$	49.47	9.86	15.95	...	49.1	10.1	16.31	...
i-$C_3H_7P(O)[OCH(CH_3)_2]_2$	51.91	10.17	14.88	...	50.3	10.1	15.64	...
$CH_3P(O)(OC_2H_5)Cl$	25.28	5.65	21.74	24.88	24.6	5.6	21.58	25.97
$C_2H_5P(O)(OC_2H_5)Cl$	30.68	6.44	19.79	22.65	29.9	6.3	19.90	21.76
i-$C_3H_7P(O)(OC_2H_5)Cl$	35.20	7.10	18.16	20.78	34.8	7.2	18.57	20.02
$CH_3P(O)(OC_3H_7)Cl$	30.68	6.44	19.79	22.65	30.9	6.5	19.69	21.61

[a] Diethyl cyclohexylphosphonate, previously prepared by R. Graf, *Chem. Ber.*, **85**, 9 (1952), b. 148° (1.5 mm.).

termediate complexes with excess water resulted in the formation of gelatinous precipitates, insoluble in more water or acid, which had to be separated by centrifugation.

The yields of chloridates or dialkyl esters obtained in the various alcoholysis runs (see Tables III, IV and V) are not representative of optimum results but can be improved without doubt. It is interesting to note that, although the I from *t*-butyl chloride and from carbon tetrachloride can be hydrolyzed to give the corresponding II in good yields,[4,8] the alcoholysis of the *t*-butyl complex with excess ethanol followed by hydrolytic cleavage gave only *t*-butylphosphonodichloridate, while that of the trichloromethyl complex resulted in the formation of intractable products.

The analytical values of the new phosphorus compounds obtained in this investigation are listed in Table II.

Acknowledgment.—We are indebted to the personnel of the Analytical Research Branch, Chemical Research Division, for the performance of all elemental analyses reported in this paper.

Experimental

Preparation of the Chloroaluminate Complexes.—The solid complexes $[CH_3PCl_3][AlCl_4]$ (VII) and $[C_2H_5PCl_3][AlCl_4]$ (V) were prepared by the method of Kinnear and Perren.[4] Thus, 0.55 mole of anhydrous aluminum chloride and 0.50 mole of phosphorus trichloride was charged to a Pyrex glass pressure bottle of 350-cc. capacity and cooled in a Dry Ice–acetone-bath. To the cooled mixture was then added 0.60 mole of precooled methyl or ethyl chloride. The sealed pressure container was shaken mechanically overnight, during which time the reaction mixture solidified to a colorless crystal cake. The preparation of V was speeded up by shaking the mixture of the reactants for approximately 1 hr. until the aluminum chloride had dissolved and then heating for another hour to 60°.

The liquid complex $[C_2H_5PCl_3][Al_2Cl_7]$ (XVI) was prepared in a similar fashion by shaking a mixture of 0.5 mole of phosphorus trichloride, 1.0 mole of anhydrous aluminum chloride and 70 cc. of ethyl chloride in a pressure bottle at room temperature until a clear solution was obtained.

All complexes of type I with alkyl groups higher than ethyl were prepared in methylene chloride as the reaction medium. The preparation of the complex from isopropyl chloride, representative of the general procedure, is described in detail.

Dry methylene chloride (200 cc.) was placed in a 1-l., three-neck, round-bottom flask equipped with dropping funnel, mercury-sealed stirrer, pot thermometer and reflux condenser. The system was protected against atmospheric moisture by a drying tube charged with anhydrous calcium chloride. Phosphorus trichloride (68.5 g., 0.5 mole) and 64 g. (0.5 mole) of powdered, anhydrous aluminum chloride (Baker and Adamson, reagent grade, sublimed) were added successively to the solvent. The aluminum chloride remained undissolved in the mixture. The contents of the flask was then cooled to 0° and 44 g. (0.55 mole) of isopropyl chloride was added to the vigorously stirred mixture dropwise at such a rate as to maintain the temperature between 5 and 15°. Throughout the entire addition, the reaction vessel was immersed in an ice–water-bath. As the reaction progressed, the aluminum chloride went slowly into solution. The resulting colorless solution of $[(CH_3)_2CHPCl_3][AlCl_4]$ was allowed to warm to room temperature and used for further reactions.

Alcoholysis of the Chloroaluminate Complexes.—In general, a solution of the appropriate complex in dry methylene chloride (prepared either as described in the preceding paragraph or by dissolving the solid I in methylene chloride) was stirred vigorously and the desired amount of the alcohol was added without external cooling dropwise at such a rate as to keep the mixture refluxing gently. After the addition of the alcohol was completed, the mixture was refluxed for a period of 2–8 hr. and then cooled. The resulting solutions were treated further with vigorous stirring with water or dilute hydrochloric acid in order to break up the conversion complexes formed by alcoholysis.

Method A.—The hydrolytic cleavage of the intermediate complexes was accomplished by adding sufficient water to the methylene chloride solution at 10–20° to dissolve the gelatinous precipitate which was formed initially. The resulting liquid layers were separated and the heavy methylene chloride layer concentrated in a Rinco evaporator[9] under reduced pressure. The residual liquid product was fractionated under reduced pressure.

Method B.[10]—In an alternate procedure for the hydrolytic decomposition of the conversion complexes, water was added at −25° with vigorous stirring or with shaking in a separatory funnel to the complex solution (cooled occasionally by adding Dry Ice pellets) in an amount just sufficient to coagulate the initially formed, gelatinous aluminum salt. The resulting granular precipitate was filtered on a büchner funnel from the clear supernatant solution, and the filtrate was concentrated in a Rinco evaporator. The product was isolated by distillation of the liquid residue under reduced pressure.

Because of the sensitivity of the phosphonochloridates toward water, the complexes of type XI were cleaved exclusively by method B. The hydrolytic decomposition of complexes of type XIII can be carried out by either one of the two methods.

Preparation of Ethyl Isopropylphosphonochloridate.—The following procedure illustrates the general method for the conversion of alkyl halides to alkyl alkylphosphonochloridates.

Isopropyl chloride (0.55 mole) was added in the usual manner to 0.5 mole of phosphorus trichloride and 0.5 mole of anhydrous aluminum chloride in 700 cc. of methylene

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(8) K. C. Kennard and C. F. Hamilton, THIS JOURNAL, **77**, 1156 (1955).

(9) Rinco Instrument Co., Greenville, Ill.

(10) This method is an adaptation of the method described by W. T. Dye, Jr., THIS JOURNAL, **70**, 2595 (1948), for the processing of reaction mixtures from aromatic hydrocarbons, aluminum chloride and phosphorus trichloride.

chloride. To the resulting solution of the complex $[(CH_3)_2CHPCl_3][AlCl_4]$ was added dropwise with stirring over a period of 1 hr. 46 g. (1 mole) of absolute ethanol. Refluxing of the resulting colorless solution was continued with stirring for an additional period of 6 hr. After cooling to −25°, the solution was treated with water, in portions of approximately 5 cc., and shaken vigorously in a separatory funnel for several minutes after the addition of each portion. The addition of water was continued until the gelatinous precipitate, first formed, had coagulated to give a readily removable, granular mass. A total of 85 cc. of water was required in this operation. The methylene chloride solution was filtered rapidly from the coagulated aluminum salt through a Büchner funnel and the filter cake washed three times on the filter with 50-cc. portions of methylene chloride. The solvent was removed from the combined filtrates under reduced pressure and the residue distilled *in vacuo* to yield 67.4 g. (79%) of ethyl isopropylphosphonochloridate, b.p. 51–53° (1.9 mm.) (see Table III).

TABLE III

CONVERSION OF $[RPCl_3][AlCl_4]$ TO $RP(O)(OR')Cl$[a]

Run	R	R′	B.p. °C.	B.p. Mm.	$n^{25}D$	Yield calcd. on PCl_3, %
14	CH_3[b]	C_2H_5	33	0.9	1.4320	47.5
15	C_2H_5[c]	C_2H_5	55	2.4	1.4345	62
16	*i*-C_3H_7[d]	C_2H_5	53	1.9	1.4357	79
17	CH_3[e]	*n*-C_3H_7	46	1.0	1.4332	32.5

[a] All runs were carried out by alcoholysis of the appropriate complex I with two mole equivalents or less of the suitable alcohol and working up the reaction mixture by method B. [b] VII (0.5 mole) suspended in 1500 cc. of methylene chloride was treated with 41 g. (0.9 mole) of absolute ethanol during 1.5 hr., refluxed for a period of 6 hr. and finally hydrolyzed at −30° with 110 cc. of water. [c] V (0.3 mole) was dissolved in 750 cc. of methylene chloride, treated with 25.8 g. (0.56 mole) of absolute ethanol and the mixture stirred 2 days at room temperature and finally treated at −20° with 60 cc. of water. [d] This run is described in detail in the Experimental section. [e] To VII (0.5 mole) suspended in 1300 cc. of methylene chloride was added at 10–15° 60 g. (1 mole) of 1-propanol and the mixture refluxed for 1 hr. and treated at −30° with 110 cc. of water. A liquid distillation residue of 13.9 g. decomposed upon attempted distillation under high vacuum to form a gelatinous semi-solid.

Similar conversions of I to phosphonochloridates were performed with the complexes V and VII under varying conditions. The results of these runs are listed in Table III. No attempt was made to establish optimum conditions in the various runs.

Preparation of Diethyl Isopropylphosphonate.—The complex $[(CH_3)_2CHPCl_3][AlCl_4]$ was prepared by the general procedure in 400 cc. of methylene chloride from 1.1 moles of isopropyl chloride and 1.0 mole each of phosphorus trichloride and anhydrous aluminum chloride. Absolute ethanol (322 g., 7 moles) was added dropwise with stirring to the resulting solution of the complex at such a rate that gentle refluxing was maintained. After the alcohol addition was completed, the mixture was refluxed with stirring for an additional period of 3 hr. The colorless solution was then cooled to 20°, and 500 cc. of water was added slowly with stirring. During the addition, the temperature was maintained below 25° by cooling with ice-water. At the beginning of the addition of the water, a white solid precipitated from the reaction mixture. This precipitate, however, dissolved gradually upon further water addition and had completely disappeared after approximately 400 cc. of water had been added. The two colorless layers of the reaction mixture were separated, and the upper aqueous layer was extracted with three 50-cc. portions of methylene chloride. The combined methylene chloride layer and washings were evaporated under reduced pressure at room temperature and the liquid residue was distilled to yield 127.8 g. (71%) of diethyl isopropylphosphonate, b.p. 56° (1.8 mm.) to 58° (2.25 mm.), $n^{25}D$ 1.4161.

In the same fashion were prepared the diethyl alkylphosphonates listed in Table IV.

Preparation of Ethyl Isopropyl Isopropylphosphonate.—The complex $[(CH_3)_2CHPCl_3][AlCl_4]$ (0.5 mole) was prepared from isopropyl chloride and aluminum chloride in 250 cc. of methylene chloride in exactly the same manner as described for the preparation of diethyl isopropylphosphonate. The resulting solution was diluted with 500 cc. of dry methylene chloride and treated dropwise with 46 g. (1 mole) of absolute ethanol. The reaction mixture was then refluxed for a period of 4 hr. and subsequently treated in the usual manner with 60 g. (1 mole) of isopropyl alcohol. Refluxing of the reaction mixture was continued for a period 8 hr. Subsequent dropwise addition of 300 cc. of water precipitated a white solid which was brought back into solution by the addition of 50 cc. of concentrated hydrochloric acid. Separation of the methylene chloride layer and processing in the usual manner yielded 77% of ethyl isopropyl isopropylphosphonate (see run 11, Table V).

TABLE IV

CONVERSION OF $[RPCl_3][AlCl_4]$ TO $RP(O)(OC_2H_5)_2$[a,b]

Run	R	B.p. °C.	B.p. Mm.	$n^{25}D$	Yield, calcd. on PCl_3, %
1	CH_3[c]	44	1.5	1.4119[o]	83.5
2	C_2H_5[d]	54	1.6	1.4148[p]	76
3	C_2H_5[e]	45	0.93	1.4146	46
4	C_2H_5[f]	40	.75	1.4146	70
5	C_2H_5[g]	44	.9	1.4148	80
6	*i*-C_3H_7[h]	56	1.8	1.4159	71
7	*i*-C_3H_7[i]	51	0.65	1.4152	80
8	*i*-C_4H_9[k]	55	.7	1.4212	68
9	C_6H_{11}[l,m,n]	87	.8	1.4538	49

[a] Except where stated otherwise (runs 1 and 2), the alcoholysis of the I solution was carried out with 7 mole equivalents of absolute ethanol. [b] The solutions of the alcoholyzed complex were worked up by method A; all runs were performed in methylene chloride solution. [c] VII (0.25 mole) suspended in 500 cc. of methylene chloride was treated with 6 mole equivalents (1.5 moles) of absolute ethanol and the mixture refluxed for 3 hr. and decomposed with 200 cc. of water. [d] V (0.3 mole) in 150 cc. of methylene chloride was treated with 0.9 mole of absolute ethanol, refluxed for 8 hr. and hydrolyzed with 100 cc. of water. [e] Phosphorus trichloride (1 mole) and 1 mole of powdered, anhydrous aluminum chloride was treated at −10° with approximately 70 cc. of ethyl chloride, the mixture stirred for 2 hr. without cooling, treated with 420 cc. of absolute ethanol, refluxed for 8 hr. and decomposed with 60 cc. of concentrated hydrochloric acid in 400 cc. of water. [f] XVI from 0.5 mole of phosphorus trichloride, 1 mole of anhydrous aluminum chloride and 70 cc. of ethyl chloride in 300 cc. of methylene chloride was used. [g] Solid V (0.3 mole) dissolved in 150 cc. of methylene chloride; reflux time 3 hr.; decomposed with 100 cc. of water. [h] Described in detail in the Experimental section. [i] $[(CH_3)_2CHPCl_3][AlCl_4]$ (0.25 mole) was prepared in 150 cc. of methylene chloride from *n*-propyl chloride (see ref. 4); the final hydrolysis was carried out with 20 cc. of concentrated hydrochloric acid in 100 cc. of water. The infrared spectrum of the product was identical with that obtained of the product from run 6. [k] *n*-Butyl chloride (0.27 mole) (see ref. 4), 0.25 mole each of phosphorus trichloride and 100 cc. of solvent were employed; the final decomposition was performed with 100 cc. of water. [l] Cyclohexyl. [m] The complex I was prepared from 0.5-mole quantities each of cyclohexyl chloride, phosphorus trichloride and aluminum chloride in 200 cc. of solvent, treated with 3.8 moles of absolute ethanol, refluxed for 3 hr. and decomposed with 200 cc. of water. [n] See footnote *a* of Table II. [o] A. H. Ford-Moore and J. H. Williams, *J. Chem. Soc.*, 1465 (1947); b.p. 64° (4 mm.), $n^{16}D$ 1.4210. [p] B.p. 62° (2 mm.), $n^{18}D$ 1.4172 (Ford-Moore and Williams, ref. *o*).

Reaction of $[CH_3PCl_3][AlCl_4]$ with One Mole of Methanol.—To a vigorously stirred suspension of 107 g. (0.33 mole) of VII in 300 cc. of methylene chloride, maintained at 25° by cooling with water, was added dropwise in the course of 2 hr. a mixture of 10.6 g. (0.33 mole) of absolute methanol and 50 cc. of methylene chloride. After the addition of approximately one-half of the methanol–solvent mixture, the solid complex was completely dissolved. About 30 minutes after the methanol addition was complete, the clear, pale yellow solution became turbid and small colorless crystals separated. The reaction mixture was stirred for an additional 3 hr. and was allowed to stand at room temperature

TABLE V

CONVERSION OF $[(CH_3)_2CHPCl_3][AlCl_4]$ (XVIII) TO $(CH_3)_2CHP(O)(OR')_2$[a]

Run	R′	B.p. °C.	B.p. Mm.	$n^{25}D$	Yield, calcd. on PCl_3, %
10	CH_3[b]	71	5.5	1.4179	40
11	i-C_3H_7 and C_2H_5[c]	47	0.7	1.4138	77
12	i-C_3H_7[d]	38.5	0.25	1.4129	21
13	i-C_3H_7[e]	44	0.35	1.4148	62

[a] XVIII (0.5 mole) was prepared in all runs in the usual manner from isopropyl chloride in methylene chloride solution. [b] To XVIII (0.5 mole) in 150 cc. of solvent was added dropwise 64 g. (2 moles) of absolute methanol. After the addition of about 0.5 mole of methanol, a white solid began to precipitate. The alcoholysis mixture was refluxed for 4 hr. after the addition of the methanol was completed. The addition of 300 cc. of water to the mixture resulted in the formation of a gelatinous emulsion which was broken by centrifuging. [c] Described in detail in the Experimental part. [d] XVIII in 200 cc. of solvent was refluxed for 6 hr. with 2 moles of isopropyl alcohol. The white solid precipitate, formed upon the addition of 300 cc. of water, was dissolved by adding 100 cc. of concentrated sulfuric acid. In addition to the product, 33 g. of liquid distillation residue was obtained; on attempted distillation of the residue, decomposition occurred. [e] XVIII in 600 cc. of solvent was first treated with 18.4 g. (0.4 mole) of absolute ethanol in 50 cc. of solvent, refluxed for 1 hr., treated with 80 g. (1.33 moles) of isopropyl alcohol, refluxed for an additional 5 hr. and hydrolyzed at −10° with 110 cc. of water by method B.

overnight. About 200 cc. of the solvent was then removed by distillation at atmospheric pressure; the remainder was evaporated under reduced pressure, leaving a pale yellow, crystalline mass which weighed 93.5 g. The product which did not fume in air was pulverized to a light, crystalline powder. Recrystallization from methylene chloride after decolorizing with Norit yielded the complex VIII as a white, microcrystalline powder, m.p. 140–150° (not sharp). The complex VIII could be distilled without decomposition at a pressure of 5 mm.; at 242–245° a liquid distilled which solidified immediately in an attached air condenser.

Anal. Calcd. for CH_3AlCl_5OP: C, 4.5; H, 1.1; Al, 10.1; Cl, 66.6; P, 11.6. Found: C, 5.0; H, 1.6; Al, 9.6; Cl, 63.0; P, 11.6.

Reaction of Methylphosphonyldichloride with Aluminum Chloride.—To a solution of 25 g. of methylphosphonyldichloride in 150 cc. of methylene chloride was added 25 g. of aluminum chloride in portions. A vigorous exothermic reaction occurred keeping the solvent refluxing. After the initial reaction had subsided, the mixture was refluxed for an additional 30 minutes. The light brown solution was filtered to remove a small amount of solid and the filtrate was refrigerated overnight. The resulting deposit of fine, colorless crystals was filtered off, washed on the filter with a small amount of cold methylene chloride and dried in a vacuum desiccator; 93.9% yield.

Anal. Calcd. for CH_3AlCl_5OP: Al, 10.1; Cl, 66.6; P, 11.6. Found: Al, 10.3; Cl, 66.6; P, 12.8.

Reaction of $[CH_3PCl_3][AlCl_4]$ with Two Moles of Methanol.—To a suspension of 107 g. (0.33 mole) of VII in 250 cc. of methylene chloride was added dropwise in the course of 3 hr. a mixture of 21.0 g. (0.66 mole) of absolute methanol and 50 cc. of methylene chloride. After standing overnight, the solvent was removed from the clear, pale yellow solution under reduced pressure leaving 89.5 g. of a pale yellow, crystalline residue. The solid material was kept in a vacuum desiccator for 65 hr.; the loss of weight during this time was 9.5 g. The remaining 80 g. (91.9%) of product was recrystallized from methylene chloride to yield the complex $[CH_3P(O)OCH_3][AlCl_4]$ as colorless crystals.

Anal. Calcd. for $C_2H_6AlCl_4O_2P$: C, 9.2; H, 2.3; Al, 10.3; Cl, 54.2; P, 11.8. Found: C, 9.0; H, 2.4; Al, 10.4; Cl, 52.3; P, 11.9.

Preparation of Samples for NMR Spectra.—Solid V (0.3 mole) was dissolved with stirring at room temperature in 150 cc. of methylene chloride and a 2-cc. aliquot removed for determination of the NMR spectrum. The bulk of the solution was then treated with 13.8 g. (0.3 mole) of absolute ethanol in the usual fashion and refluxed for a period of 6 hr. The mixture, containing complex X, was cooled and another 2-cc. sample of the solution removed for NMR analysis. The alcoholysis was continued in two steps by adding each time a 0.3-mole portion of absolute ethanol and withdrawing at each step a sample for spectral analysis.

The solution used for the determination of the NMR spectrum of the complex $[C_2H_5P(O)(OC_2H_5)_2 \cdot AlCl_3]$ was prepared in the following manner. To a solution of diethyl ethylphosphonate (37 g., 0.22 mole) in 100 cc. of methylene chloride was added, after cooling to −78°, 30 g. (0.22 mole) of anhydrous aluminum chloride in two portions. An exothermic reaction took place upon each addition, but the temperature of the reaction mixture was maintained below 0° by cooling. The mixture was stirred below 0° until the aluminum chloride was dissolved and the stirring continued for an additional 2 hr. at room temperature. The trace amounts of insoluble material were allowed to settle by standing undisturbed overnight and an aliquot of the clear supernatant solution of the desired complex was removed for NMR analysis.

The spectra of III, VI, IX and the liquid complex XVI were determined without solvent.

Table I contains the chemical shifts exhibited by the various ethyl complexes and their phosphorus-containing components.

ARMY CHEMICAL CENTER, MD.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF VIRGINIA]

Monoesters and Ester-amidates of Aromatic Phosphonic Acids

BY ALFRED BURGER AND JAMES J. ANDERSON[1]

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Reaction of phosphonic acids with dicyclohexylcarbodiimide yields pyrophosphonic acids, $[RPO(OH)]_2O$, which with alcohols or phenol furnish the respective alkyl or phenyl hydrogen phosphonate esters. These in turn with dicyclohexylcarbodiimide give dialkyl pyrophosphonates, $[RPO(OR)]_2O$, which react with amines to render alkyl N-substituted phosphonamidates. The monoesters and ester-amidates of *p*-aminophenylphosphonic acid exhibited only negligible bacteriostatic activity. The biological observations are discussed in the light of ionization theories of analogous bacteriostatically active sulfanilamide derivatives.

In the course of their studies about the dependence of bacteriostatic activity of sulfanilamide derivatives on the relative negative character of the SO_2 group in these compounds, Bell and Roblin[2] expressed the view that the principles outlined by them should apply to any substance of the type p-$H_2NC_6H_4XO_2R$, provided its activity is inhibited by *p*-aminobenzoic acid. If the properties of the aromatic amino group are constant, activity in such compounds should be expressed by the negativity

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[1] Virginia-Carolina Chemical Corporation Fellow, 1955–1956.

[2] P. H. Bell and R. O. Roblin, Jr., THIS JOURNAL, **64**, 2905 (1942).