93. *Esters containing Phosphorus. Part I.*

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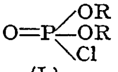
A convenient method for the preparation of dialkyl chlorophosphonates (dialkoxyphosphoryl chlorides) is the treatment of a dialkyl hydrogen phosphite with chlorine in the cold. The dialkyl chlorophosphonate, obtained in high yield, is readily identified by the formation of crystalline aminophosphonates with amines. The preparation of dialkyl hydrogen phosphites in high yield without the use of a tertiary base is described. Other methods of obtaining chlorophosphonates are also described.

We undertook, some three years ago, the preparation of substituted phosphoryl chlorides (I, R = alkyl) as intermediates in the preparation of certain compounds, the details of which will be published subsequently. Such compounds may be described as dialkoxyphosphoryl chlorides or, alternatively, as dialkyl chlorophosphonates. Three general methods for obtaining compounds of this type have already been described. (i) Phosphorus oxychloride on treatment with 3 mols. of an alcohol and 3 mols. of pyridine gives the trialkyl phosphate; this on further treatment with phosphorus oxychloride gives a mixture of dialkoxyphosphoryl chloride and monoalkoxyphosphoryl dichloride (II) (see Gerrard, J., 1940, 1464, who worked with *n*-butyl alcohol):


$O{=}P(OR)_2Cl$

(I.)

$$POCl_3 + 3C_2H_5{\cdot}OH + 3C_5H_5N = PO(O{\cdot}C_2H_5)_3 + 3C_5H_5N,HCl$$
$$2PO(O{\cdot}C_2H_5)_3 + POCl_3 = 3PO(O{\cdot}C_2H_5)_2Cl$$
$$PO(O{\cdot}C_2H_5)_3 + 2POCl_3 = 3PO(O{\cdot}C_2H_5)Cl_2 \quad \text{(II.)}$$

The disadvantage of this method, especially for large scale work, lies in the utilisation of large quantities of pyridine. Furthermore, with ethyl alcohol we find that some ethoxyphosphoryl dichloride (II) is always produced even under conditions favourable to the production of diethoxyphosphoryl chloride.

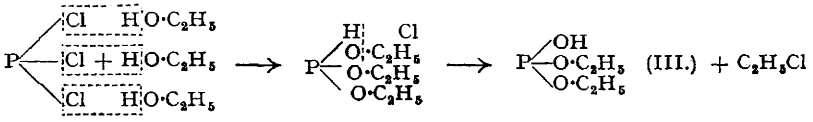
(ii) The action of ethyl alcohol on phosphorus oxychloride gives a mixture of diethoxyphosphoryl chloride, ethoxyphosphoryl dichloride, ethyl metaphosphate and other products. The diethoxyphosphoryl chloride is obtained impure and in poor yield (Walczynska, *Roczniki Chem.*, 1926, **6**, 110). We find that under favourable conditions the method is essentially one for preparing the alkoxyphosphoryl dichloride.

(iii) Phosphorus trichloride on treatment with 3 mols. of an alcohol and 3 mols. of pyridine gives the trialkyl phosphite (Milobedski and Sachnowski, *Chem. Zentr.*, 1918, I, 911). The latter on chlorination gives the dialkoxyphosphoryl chloride (Wichelhaus, *Annalen*, Suppl., **6**, 269):

$$PCl_3 + 3C_2H_5{\cdot}OH + 3C_5H_5N = P(O{\cdot}C_2H_5)_3 + 3C_5H_5N,HCl \quad . \; . \; . \; . \; . \; . \; . \; . \quad (A)$$
$$P(O{\cdot}C_2H_5)_3 + Cl_2 = PO(O{\cdot}C_2H_5)_2Cl + C_2H_5Cl \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (B)$$

Here again the disadvantage is the pyridine requirement in equation (A). Wichelhaus's directions were meagre and incomplete and an account is given in the Experimental Part of the preparation of diethoxy- and di*iso*propoxy-phosphoryl chloride by method (iii). The more readily accessible dimethylaniline can be used in place of pyridine in reaction (A), thus effecting a considerable economy for large scale work. We have found also that the production of a faint yellow coloration, due to a slight excess of chlorine, is probably a better indication of the end-point of reaction (B) than is the determination of the increase in weight of the reactants.

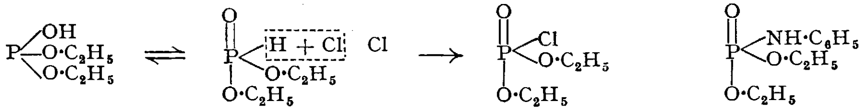
A still more economical method for large scale work was sought, and a further drawback of methods (i) and (iii) is that the complete removal of the tertiary base is sometimes difficult, particularly the elimination of traces of pyridine from triethyl phosphite. We therefore carried out the reaction between phosphorus trichloride and ethyl alcohol in the absence of a tertiary base and obtained a 93% yield of pure diethyl hydrogen phosphite (III).



$$PCl_3 + 3HO{\cdot}C_2H_5 \longrightarrow P(OH)(O{\cdot}C_2H_5)_3Cl \longrightarrow P(OH)(O{\cdot}C_2H_5)_2 \; \text{(III.)} + C_2H_5Cl$$

Milobedski (*Chem. Polski.*, **1917**, **15**, 34, 48) had previously made this compound, but he had 2 mols. of pyridine present during the addition of the alcohol. The compound was probably first made by Thorpe and North (**J.**, **1890**, **57**, 634) by the action of phosphorous anhydride on ethyl alcohol. Sachs and Levitsky (*J. Russ. Phys. Chem. Soc.*, **1903**, **35**, 211) and other workers have mentioned the action of phosphorus trichloride on alcohol, but details are generally incomplete and yields low. Nylén, however (*Ber.*, **1924**, **57**, 1029), obtained fair yields, but recommended the use of an atmosphere of carbon dioxide.

We have found that diethyl hydrogen phosphite [perhaps as the tautomeric diethyl phosphonate (IV), but this point will be discussed in a later communication] reacts very readily with chlorine to give the required diethoxyphosphoryl chloride (V) in 87% yield :



(IV.) (V.) (VI.)

The diethoxyphosphoryl chloride (diethyl chlorophosphonate) was characterised by the crystalline *diethyl anilinophosphonate* (VI) formed by the action of aniline. Michaelis and Schultze (*Ber.*, **1894**, **27**, 2572) prepared a compound by the action of alcohol on anilinophosphoryl dichloride, and to this they gave the formula (VI). This compound had m. p. 93°, was decomposed by water, and turned reddish-yellow in air. Our compound (m. p. 95·5—96·5°) was recrystallised from water and has remained colourless for 3 years. The compounds, therefore, are apparently not identical.

A similar set of reactions has been carried out in the *iso*propyl series. On account of our requirements for quantities of di*iso*propoxyphosphoryl chloride, the preparation of this compound and the intermediate di*iso*propyl hydrogen phosphite were examined in great detail. In the preparation of the hydrogen phosphite, the temperature of the reaction could be controlled by the presence of a solvent (ether or carbon tetrachloride). From the ethereal solution, the hydrogen chloride produced in the reaction was removed as far as possible by drawing air through the reaction mixture, and then ammonia; a considerable excess of the latter did not affect the yield. With carbon tetrachloride, however, the passage of ammonia could be omitted. Yields of di*iso*propyl hydrogen phosphite of the order of 90% were obtained in each case. Experiments were also carried out without a solvent, but in this case the temperature was kept down by cooling the reaction mixture in ice-salt. The best yields of the chlorophosphonate were obtained when chlorine was passed slowly into the hydrogen phosphite. In our largest scale preparations the chlorine was passed in through a rotating tube, the lower portion of which was bent at an angle and terminated by a bulb pierced with small holes. In this way the chlorine was distributed evenly to the entire liquid. A slight permanent yellow coloration due to excess of chlorine indicated the end of the reaction.

The removal of excess of chlorine and of hydrogen chloride is very necessary at the end of the reaction. The air for this purpose was thoroughly dried. Lead carbonate was essential for the complete removal of the hydrogen chloride.

If the hydrogen chloride were not completely removed, the chlorophosphonate was liable to decompose on distillation.

EXPERIMENTAL.

Use of Dimethylaniline in the Preparation of Triethyl Phosphite.—Phosphorus trichloride (151·2 g.), dissolved in an equal volume of dry ether, was added slowly from a dropping-funnel to a mixture of ethyl alcohol (151·8 g.) and dimethylaniline (399·3 g.) dissolved in dry ether (about 200 c.c.) and contained in a corked flask carrying a calcium chloride outlet tube. The mixture was well shaken and kept cold by immersion in water. Towards the end of the reaction, the mixture set to an almost solid mass, and was then kept at room temperature for 2 hours. The hydrochloride was filtered off, the filtrate dried over sodium sulphate, the ether distilled, and the residue fractionally distilled. Yield, 124 g. (73%), b. p. 48°/12·5 mm. (Found : C, 43·1; H, 9·2. Calc. for $C_6H_{15}O_3P$: C, 43·4; H, 9·0%).

Conversion of Triethyl Phosphite into Diethyl Chlorophosphonate.—Dry chlorine was passed through ice-cold triethyl phosphite (16·6 g.; 0·1 mol.) until a faint permanent green coloration was produced—this took place when the gain in weight was equal to that required by equation (B) (p. 380). Excess of gas was removed by bubbling dry air through the liquid under reduced pressure for 3 hours. The weight of product then indicated that none of the chlorophosphonate had been removed. After treatment with lead carbonate and filtration through kieselguhr, the product was distilled, and the fraction, b. p. 93—95°/18 mm., collected. Yield, 13·7 g. (80%) (Found : Cl, 20·3. Calc. for $C_4H_{10}O_3ClP$: Cl, 20·5%).

*Conversion of Tri*iso*propyl Phosphite into Di*iso*propyl Chlorophosphonate.*—This was carried out as for the ethyl compound. Yield, 70%; b. p. 41°/0·08 mm. (Found : Cl, 18·3. $C_6H_{14}O_3ClP$ requires Cl, 17·7%).

Diethyl Hydrogen Phosphite.—(a) *With ether as solvent.* Phosphorus trichloride (206·1 g.), dissolved in ether (600 c.c.), was slowly run into ethyl alcohol (207 g.) in a flask cooled in ice-water, air being meanwhile passed through the mixture to remove as much hydrogen chloride as possible. After 30 minutes, dry ammonia was passed in, the precipitated ammonium chloride removed, and ammonia again passed through the filtrate to ensure that all the hydrogen chloride had been removed. The ether was then distilled, and the residue distilled under reduced pressure. B. p. 87°/20 mm. Yield, 195 g. (93%).

(b) *With carbon tetrachloride as solvent.* To ethyl alcohol (207 g.), dissolved in carbon tetrachloride (225 c.c.), was slowly added phosphorus trichloride (206·1 g.) dissolved in carbon tetrachloride (150 c.c.).. Although heat was evolved, external cooling was unnecessary. The mixture was refluxed at 90° for 30 mins., and air then passed through it to remove hydrogen chloride and low-boiling liquid. On distillation, the main fraction had b. p. 73—74°/14 mm. Yield, 93% (Found : C, 35·0; H, 7·9. Calc. for $C_4H_{11}O_3P$: C, 34·8; H, 8·0%).

Diethyl Chlorophosphonate.—Diethyl hydrogen phosphite (97·2 g.) was cooled in ice-salt, and chlorine passed in until the liquid assumed a yellow coloration. Hydrogen chloride was evolved copiously. The product was distilled under reduced pressure. Yield, 105 g. (87%), b. p. 92°/17 mm. (Found : Cl, 20·55. Calc. for $C_4H_{10}O_3ClP$: Cl, 20·5%).

Diethyl Anilinophosphonate.—The chlorophosphonate (5·2 g.) was added slowly to aniline (5·6 g.) with cooling. After 1 hour, the mixture was extracted with boiling benzene, and the extract evaporated to a syrup, which crystallised. The crystals were washed with ether and recrystallised from water; m. p. 96·5°. They contained N and P, but no Cl (Found : C, 52·5; H, 7·4; N, 6·3. $C_{10}H_{16}O_3NP$ requires C, 52·4; H, 7·0; N, 6·1%). The m. p. of a mixture with the anilinophosphonate derived from chlorophosphonate made by the action of chlorine on triethyl phosphite was 95·5—96·5°.

*Di*iso*propyl Hydrogen Phosphite.*—(a) *With ether as solvent.* Dry *iso*propyl alcohol (180 g.; 3 mols.) was dissolved in dry ether (180 c.c.) and placed in a flask fitted so that dry air could be drawn through the mixture to remove as much hydrogen chloride as possible. Phosphorus trichloride (137·5 g.), dissolved in about half its volume of dry ether, was slowly run into the alcoholic solution, the flask being immersed in ice-water and shaken at intervals. The mixture was kept for ½ hour, with air bubbling through meanwhile, and then dry ammonia was passed through to precipitate ammonium chloride, which was removed. Ammonia was again passed through the filtrate to ensure the removal of all the hydrogen chloride. After filtration, the ether was distilled, and the fraction, b. p. 79°/14 mm., collected as a colourless mobile liquid miscible with water in all proportions. Yield, 148 g. (89%). B. p.'s were obtained as follows : 79°/14 mm., 80°/15 mm., 81°/16 mm., 82·5°/17 mm. (Found : C, 43·4; H, 9·1. Calc. for $C_6H_{15}O_3P$: C, 43·4; H, 9·0%).

(b) *With carbon tetrachloride as solvent.* The *iso*propyl alcohol (180 g.) was dissolved in carbon tetrachloride (180 c.c.) and phosphorus trichloride (137·5 g.), dissolved in carbon tetrachloride (*ca.* 40 c.c.), was run in, under the conditions stated above. The solution was kept for 1 hour and then subjected to reduced pressure in a Claisen flask. The temperature was raised slowly to remove hydrogen chloride and carbon tetrachloride; the residue distilled at 80—81°/16 mm. Yield, 146 g. (88%).

(c) *Without a solvent.* *iso*Propyl alcohol (90 g.) was placed in a 1-litre round-bottomed flask fitted with a water reflux condenser and calcium chloride tube. The flask was cooled in ice-salt and well shaken while phosphorus trichloride (68·8 g., 0·5 mol.) was added during 15 minutes. The temperature was then allowed to rise slowly to room temperature. Air was passed through the liquid, kept under reduced pressure, for 45 minutes, to remove as much hydrogen chloride as possible. On distillation a low-boiling fraction was obtained, followed by the main fraction at 80—81°/16 mm. The residue was small. Redistillation of the lower fraction gave a further small quantity of liquid, b. p. 80—81°/16 mm. Total yield, 72·7 g. (86·4%). Smaller yields were sometimes obtained when the scale of operation was increased.

*Di*iso*propyl Chlorophosphonate.*—Chlorine was slowly passed through the hydrogen phosphite (100 g.), in a flask cooled in ice-water and shaken at intervals, until a yellow coloration persisted. After 5 minutes, dry air was drawn through until the liquid was colourless, and then for about 1 hour longer. Dry powdered lead carbonate (*ca.* 15—20 g.) was then added in small quantities with shaking, and air drawn through the mixture for about 3 hours. The complete removal of the hydrogen chloride was usually manifested by the tendency of the lead salts to settle after shaking. A small quantity of kieselguhr was then added, and the mixture shaken. After filtration the liquid distilled at 95°/14 mm. as a mobile liquid, hydrolysed by water. Yield, 92 g. (76%) (Found : Cl, 17·6. $C_6H_{14}O_3ClP$ requires Cl, 17·7%). The *chlorophosphonate* was readily identified by formation of its aniline derivative.

*Di*iso*propyl Anilinophosphonate.*—Di*iso*propyl chlorophosphonate (6·0 g.; 0·03 mol.) was slowly added to aniline (5·6 g.; 0·06 mol.), the mixture being cooled in ice-water. After 1 hour, the product was extracted with boiling benzene. The undissolved aniline hydrochloride was removed, and the filtrate evaporated to give a syrup, which solidified. Recrystallised first from ether–light petroleum (b. p. 40—60°) and then from water, the *anilinophosphonate* formed white needles, m. p. 121—121·5° (Found : C, 55·7; H, 7·7; N, 5·6. $C_{12}H_{20}O_3NP$ requires C, 56·0; H, 7·8; N, 5·45%).

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