[Contribution from the Research Laboratory, Victor Chemical Works]

Tetraethyl Dithionopyrophosphate and Related Tetraalkyl Dithionopyrophosphates[1]

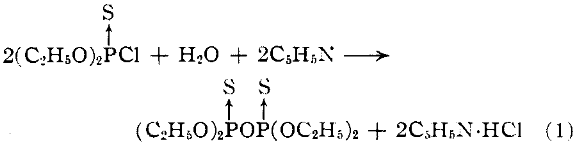
By A. D. F. Toy

A method has been developed for the synthesis of tetraalkyl dithionopyrophosphates by the action of a tertiary amine on a mixture of water and dialkyl thionochlorophosphates. A study of the mechanism of reaction indicates that the formation of a quaternary complex between the dialkyl thionochlorophosphate and the tertiary amine is necessary to initiate the reaction. As a consequence, only those tertiary amines which are sterically unhindered are suitable for this reaction. Side reactions involving decomposition of the quaternary complex compound tend to reduce the yields of the tetraalkyl dithionopyrophosphate, but may be minimized by controlling the temperature of reaction, the sequence, and the rate of the addition of reactants. Inorganic bases were found to be excellent substitutes for the tertiary amine, provided however, that a small amount of a sterically unhindered amine is used as a catalyst. The preparation and properties of tetraethyl, tetra-*n*-propyl, tetraisopropyl and tetra-*n*-butyl dithionopyrophosphates are described and toxicity data for these compounds included.

In connection with an extended study of the chemistry of the alkyl esters of pyrophosphoric acid, there have been investigated thus far the preparation and properties of various symmetrical[2] and unsymmetrical[3] tetraalkyl pyrophosphates. Differences in the degree of toxicity and in the rates of hydrolysis were found to depend on the nature of the alkyl groups. These research efforts have now been extended to include the tetraalkyl dithionopyrophosphates in order to evaluate the effect of replacement of two oxygen atoms by sulfur atoms.

Tetraethyl dithionopyrophosphate was first reported by Carius[4] who claimed to have prepared it by the action of concentrated sulfuric acid on triethyl thionophosphate and who described it as being rather soluble in water and subject to decomposition on distillation. Schrader[5] subsequently described this compound as a colorless material (b.p. 135° (2 mm.)). Although he gave some of its insecticidal properties, he did not describe its synthesis until later.[6,7]

Unsuccessful attempts were first made to prepare tetraethyl dithionopyrophosphate by the Carius procedure. It was finally synthesized by the controlled hydrolysis of diethyl thionochlorophosphate in the presence of pyridine (Equation 1). This reaction has since been reported also by Hall.[8] The reaction is analogous to that employed for the preparation of tetraethyl pyrophosphate.[2]



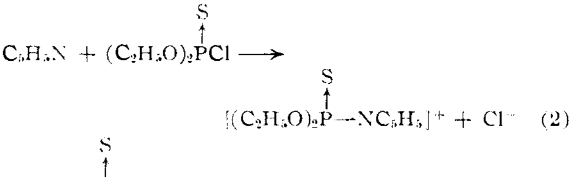
$$2(C_2H_5O)_2\overset{S}{\overset{\uparrow}{P}}Cl + H_2O + 2C_5H_5N \longrightarrow (C_2H_5O)_2\overset{S}{\overset{\uparrow}{P}}O\overset{S}{\overset{\uparrow}{P}}(OC_2H_5)_2 + 2C_5H_5N\cdot HCl \qquad (1)$$

This procedure may be used for the synthesis of all the tetraalkyldithionopyrophosphates, except the tetramethyl homolog.

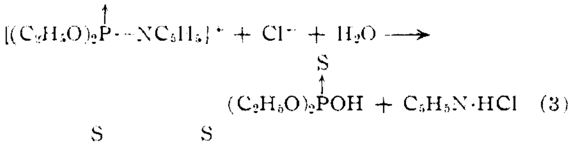
Mechanisms of Reaction

The mechanism of reaction is much more complicated and involved than that shown in the simple over-all Equation 1. It soon became apparent that pyridine serves other functions in the reaction in addition to the absorption of the hydrogen chloride. When pyridine was replaced with α-picoline, the yield of the product was not only found to drop appreciably, but the crude product was of such poor quality that its purification was very difficult. When the reaction was carried out using the structural isomers of α-picoline, such as the β- and γ-picolines in each of which the methyl radical is located farther away from the nitrogen atom, the yield and quality of the product were more nearly comparable with that obtained when pyridine was used. All three picolines have about the same order of basicity as shown by their ionization constants. The experimental results thus indicate that substitution in the α position to the nitrogen atom in the pyridine ring hinders this reaction. That steric hindrance caused by the α-substitution is responsible was verified when quinoline, in which the substitution starts at a position α to the nitrogen, was employed in the reaction. None of the desired product was isolated, while with isoquinoline a good yield of the product was obtained.

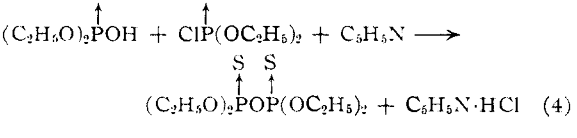
In view of these findings it is probable that the mechanism of the reaction involves as the first step, the formation of a quaternary complex between diethyl thionochlorophosphate and the tertiary amine (Equation 2). The quaternary compound undergoes hydrolysis to form diethyl thionophosphoric acid and pyridine hydrochloride. The acid then reacts in the presence of pyridine,



$$C_5H_5N + (C_2H_5O)_2\overset{S}{\overset{\uparrow}{P}}Cl \longrightarrow [(C_2H_5O)_2\overset{S}{\overset{\uparrow}{P}}{-}NC_5H_5]^+ + Cl^- \qquad (2)$$



$$[(C_2H_5O)_2\overset{S}{\overset{\uparrow}{P}}{-}NC_5H_5]^+ + Cl^- + H_2O \longrightarrow (C_2H_5O)_2\overset{S}{\overset{\uparrow}{P}}OH + C_5H_5N\cdot HCl \qquad (3)$$



$$(C_2H_5O)_2\overset{S}{\overset{\uparrow}{P}}OH + Cl\overset{S}{\overset{\uparrow}{P}}(OC_2H_5)_2 + C_5H_5N \longrightarrow (C_2H_5O)_2\overset{S}{\overset{\uparrow}{P}}O\overset{S}{\overset{\uparrow}{P}}(OC_2H_5)_2 + C_5H_5N\cdot HCl \qquad (4)$$

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(1) Presented before the Division of Organic Chemistry at the 118th Meeting of the American Chemical Society, Chicago, Ill., September, 1950.

(2) Toy, This Journal, **70**, 3882 (1948).

(3) Toy, *ibid.*, **72**, 2065 (1950).

(4) Carius, *Ann.*, **119**, 289 (1861).

(5) Schrader, P. B. Report 87923-R B.I.O.S. FR714, p. 31 (1947).

(6) Schrader, *Angew. Chem.*, **20**, 471 (1950).

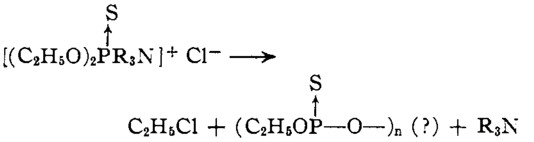
(7) Subsequent to the presentation of this paper Schrader summarized various methods used by him for the preparation of tetraalkyl dithionopyrophosphates. No experimental details are given, however, in his monograph entitled "Die Entwicklung neuer Insektizide auf Grundlage organischer Fluor- und Phosphor-verbindungen," Monographien Nr. 62, Verlag Chemie, G.m.b.H., Weinheim/Bergstr., 1951, pp. 43–44.

(8) Hall, "Agricultural Control Chemicals," Advances in Chemistry Series I, American Chemical Society, 1950, p. 156.

with unchanged diethyl thionochlorophosphate to form tetraethyl dithionopyrophosphate (Equations 3 and 4). This mechanism is proposed in view of the fact that a high steric factor in the heterocyclic amines which is unfavorable for the formation of the addition complex is also unfavorable for the production of tetraethyl dithionopyrophosphate.

The same phenomenon was also observed when the reaction was carried out using various aliphatic amines (Table I). With trimethylamine, which has a low steric requirement, a good yield of high purity tetraethyl dithionopyrophosphate was obtained. When the chain length of the alkyl groups in the amine was increased as in the case of triethylamine, thereby increasing the steric hindrance, the percentage yield was greatly decreased. This explanation is given further experimental basis by the work of Brown and Taylor[9] who have pointed out that α-picoline and triethylamine have similar steric effects, based upon the instability of the trimethylboron complexes.

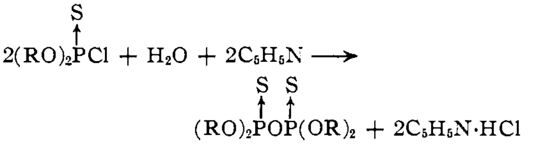
A side decomposition reaction was also observed which interferes greatly with the main reaction leading to the synthesis of tetraethyl dithionopyrophosphate. The decomposition reaction probably occurs as illustrated in Equation 5. Ethyl chloride has been identified by actual isolation and also as the quaternary ethyl ammonium chloride. The ethyl thionometaphosphate or the metaphosphate–base complex was not isolated. The products of decomposition are in many respects similar in nature to those obtained when dibenzyl chlorophosphate and tertiary amines react as reported by Clark and Todd,[10] and when dibutyl chlorophosphate and pyridine are heated together.[11] This decomposition phenomenon had also been observed previously in connection with a study of the use of amines as catalysts in the preparation of Parathion.[12] At room temperature the decomposition of the diethyl thionochlorophosphate–tertiary amine complex proceeds at a different rate with the different amines. The rate is much faster with triethylamine than with pyridine. The decomposition reaction is accelerated by a rise in temperature, so that even with pyridine the decomposition reaction becomes the predominant one at higher temperatures. Thus, even with the use of pyridine, the reaction for the synthesis of tetraethyl dithionopyrophosphate is preferably carried out at 35° to 50°. At a temperature below 35° the desired reaction proceeds very slowly; above 80° the decomposition due to the side reaction is sufficiently fast so that the yield is less and a product of poor quality is obtained.



$$[(C_2H_5O)_2\overset{S}{\overset{\uparrow}{P}}R_3N]^+\,Cl^- \longrightarrow C_2H_5Cl + (C_2H_5O\overset{S}{\overset{\uparrow}{P}}\text{—}O\text{—})_n\ (?) + R_3N \quad (5)$$

It is evident that the order of addition of the reactants is important. It would seem most desirable to introduce the tertiary amine slowly into a mixture of water and diethyl thionochlorophosphate, thus assuring a deficiency of the addition complex in the reaction mixture. The complex should then undergo hydrolysis immediately as it is formed to react with excess chlorophosphate to give the tetraethyl dithionopyrophosphate. Addition of the tertiary amine to the diethyl thionochlorophosphate before water is added would allow the decomposition reaction (Equation 5) to become competitive with the desired reaction. It might also be anticipated that the use of a reasonable excess of water (200–400%) should help the main reaction since the addition complex would then undergo the intermediate hydrolysis reaction more readily (Equation 3). These hypotheses were verified experimentally by use of dimethylbenzylamine. This tertiary amine was selected because, unlike pyridine, it forms an addition complex with diethyl thionochlorophosphate which has been shown to be very sensitive to the decomposition reaction. A great improvement in the yield as well as in the quality of the product was achieved when the recommended order of addition of reactants with the excess of water was followed. When pyridine was used as the tertiary amine, under the conditions chosen for the reactions, the decomposition reaction of the pyridine–diethyl thionochlorophosphate complex was sufficiently slow to permit the experimentally convenient addition of a solution of water and pyridine to the diethyl thionochlorophosphate.

Inorganic bases were also substituted for the organic bases, since the hydrolysis of the oxygen analog, diethyl chlorophosphate in the presence of sodium hydrogen carbonate gives good yields of tetraethyl pyrophosphate.[2] No product was obtained when diethyl thionochlorophosphate was allowed to react with sodium hydrogen carbonate, or with a dilute sodium hydroxide solution. It was discovered, however, that the reaction proceeds smoothly with inorganic bases provided that a small per cent. of pyridine is used as catalyst. The possible mechanism for this catalytic reaction is presented in Equations 6 and 7.



$$2(RO)_2\overset{S}{\overset{\uparrow}{P}}Cl + H_2O + 2C_5H_5N \longrightarrow (RO)_2\overset{S}{\overset{\uparrow}{P}}O\overset{S}{\overset{\uparrow}{P}}(OR)_2 + 2C_5H_5N{\cdot}HCl \quad (6)$$

$$2C_5H_5N{\cdot}HCl + Na_2CO_3 \longrightarrow 2C_5H_5N + 2NaCl + CO_2 + H_2O \quad (7)$$

Sodium carbonate gave best results, but other inorganic bases such as sodium hydrogen carbonate and sodium hydroxide were also found to be useful. The active agent is still believed to be pyridine. The inorganic base serves only to regenerate pyridine by reaction with pyridine hydrochloride. This hypothesis seems to be borne out by the fact that the reaction takes place more rapidly if the amount of pyridine is increased from 1 to 10%. Replacement of pyridine by sterically hindered tertiary amines such as triethylamine and α-picoline again results in formation of inferior products as was observed when these amines were used in the absence of the inorganic base. These results fur-

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[9] Brown and Taylor, THIS JOURNAL, **69**, 1332 (1947).

[10] Clark and Todd, *J. Chem. Soc.*, 2023 (1950).

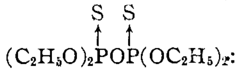
[11] Gerrad, *ibid.*, 1464 (1940).

[12] Toy and Beck, THIS JOURNAL, **72**, 3191 (1950).

ther substantiate the proposed mechanism of reaction to the effect that the formation of an addition complex between diethyl thionochlorophosphate and the tertiary amine is necessary to initiate the reaction.

Experimental

Tetraalkyl Dithionopyrophosphates. Tetraethyl Dithionopyrophosphate (a) Reaction in Presence of Pyridine.—In a 500-cc. 3-necked flask equipped with a stirrer, a thermometer and a dropping funnel was placed 188.5 g. (1 mole) of diethyl thionochlorophosphate (n^{25}_{D} 1.4700) to which was added slowly with stirring a solution of 84 g. (1.06 moles) of pyridine (commercial 2° grade) and 10 g. (0.555 mole) of water. The temperature of the addition was maintained at 38-40° by periodic cooling. Upon completion of the addition (40 minutes) the periodic cooling was continued until no further rise in temperature was observed (25 minutes). The stirring was continued without external cooling until the temperature had dropped to 32° (1 hour and 40 minutes). The reaction mixture was then heated to 38-40° for an additional two hours and allowed to stand at room temperature overnight. The thick white paste thus obtained was washed with 100 cc. of water. The immiscible organic layer was washed three additional times with 100-cc. portions of water (all three aqueous layers were neutral to methyl orange). The volatile contaminants were removed by first placing the product under reduced pressure at room temperature and then heating rapidly (11 minutes) to 100° (liquid temperature) at 1 mm. The residue weighed 147.1 g. (91.5%), n^{25}_{D} 1.4760. A 71.5-g. portion of the residue gave, upon distillation, a water-white liquid weighing 68.6 g. which corresponds to a distilled yield of 87.5%, b.p. 110-113° at 0.2 mm, n^{25}_{D} 1.4753, d^{25}_{4} 1.189. Solubility in water was found to be approximately 25 mg./l. The product is very stable to hydrolysis. Another 50-g. portion of the crude product was distilled in a simple Hickman pot still (bath temperature 96–100°, 0.004 mm.; distillation rate, 1 drop per 2 seconds). The distillate weighed 49.4 g. corresponding to an almost quantitative recovery, n^{25}_{D} 1.4758.



Anal. Calcd. for $(C_2H_5O)_2\overset{S}{\overset{\uparrow}{P}}O\overset{S}{\overset{\uparrow}{P}}(OC_2H_5)_2$: P, 19.3; S, 19.9. Found: P, 19.3; S, 19.8.

The undistilled product gave the same analytical results for phosphorus and sulfur.

When the reaction mixture was processed immediately after the two-hour heating period at 38-40°, approximately 3-4% of unreacted diethyl thionochlorophosphate was recovered in the distillate when the product was heated to 100° at 0.5 to 1 mm. to remove contaminants.

In the presence of ether as solvent, the condensation reaction proceeded very slowly at room temperature. After it had been heated to reflux for 7.5 hours at 40-45°, the yield of the distilled product was only 44.7% (n^{25}_{D} 1.4761). When the condensation reaction was carried out at 60° the undistilled product was rather impure (81%, n^{25}_{D} 1.4808). Raising the reaction temperature to 72-80° resulted in formation of a water-insoluble material equivalent only to a 31% yield. This product was very sirupy with n^{25}_{D} 1.5229 and decomposed on heating even under reduced pressure.

(b) Reaction in the Presence of Sodium Carbonate with Pyridine as Catalyst.—To 75.4 g. (0.4 mole) of diethyl thionochlorophosphate was added a mixture consisting of 2 g. (0.111 mole) of water and 3.3 g. (0.042 mole) of pyridine. The mixture was stirred for 10 minutes. The temperature increased from 24° up to 35°. To this mixture was added 23.3 g. (0.22 mole) of sodium carbonate. It was then cooled to 20° and 40 cc. of water added. The heat of hydration of sodium carbonate and then the heat of reaction caused the temperature to rise making it necessary to effect external cooling. The temperature of reaction was maintained at 38 to 40° by periodic cooling at first and by external heating later. After about an hour, carbon dioxide gas began to evolve. The reaction mixture became a thick paste and finally turned into a thin slurry. After about 3 to 3.5 hours no more gas was evolved. The mixture was heated for 30 minutes longer at 40° in order to complete the reaction. It was then cooled and washed with water. The oily residue obtained after heating to 105° at 1.5 mm. weighed 56.5 g. (87.7%), n^{25}_{D} 1.4768.

This reaction was also carried out using 2, 5 and 7.5% of pyridine as catalyst. Satisfactory results were obtained but the time required for the completion of reaction was much longer, the smaller the quantity of pyridine used.

Substitution of sodium hydrogen carbonate for sodium carbonate also produced satisfactory results in the presence of pyridine (81%, n^{25}_{D} 1.4760). Under identical conditions of reaction using sodium hydrogen carbonate as the inorganic base, but substituting α-picoline for pyridine, 72.5% of the starting material was recovered unchanged together with a small quantity of water-insoluble crude tetraethyl dithionopyrophosphate with n^{25}_{D} 1.4809. When 50% and 10% sodium hydroxide solutions were used instead of sodium hydrogen carbonate, with pyridine as catalyst, the yields of crude products obtained were 51.5% (n^{25}_{D} 1.4770) and 40% (n^{25}_{D} 1.4759), respectively. In these instances, some unreacted diethyl thionochlorophosphate was also recovered. When triethylamine was used unsatisfactory results were obtained with both 33% sodium hydroxide solution and sodium carbonate as the inorganic bases. The percentage recovery of unreacted diethyl thionochlorophosphate in these experiments amounted to 38.8 and 66.4%, respectively.

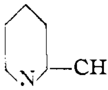
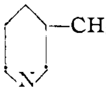
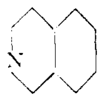
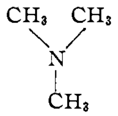
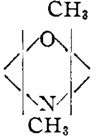
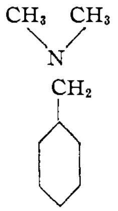
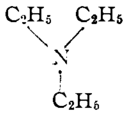
When 94.3 g. (0.5 mole) of diethyl thionochlorophosphate (n^{25}_{D} 1.4695) was heated with a slurry of 42 g. (0.5 mole) of sodium hydrogen carbonate in 30 cc. of water for three hours at 40 to 70°, there was no observable reaction. The oily layer recovered upon distillation weighed 84 g. (n^{25}_{D} 1.4692) and was shown by analysis to represent 89% of the diethyl thionochlorophosphate used in the original mixture. No tetraethyl dithionopyrophosphate was obtained when diethyl thionochlorophosphate was allowed to stand at room temperature overnight with an equivalent quantity of a 6.5% solution of sodium hydroxide and then heated with stirring for three hours from 50 to 70°. About 36% of the original diethyl thionochlorophosphate was recovered and the products of decomposition were water soluble compounds.

(c) Reaction of Triethyl Thionophosphate with 100% Sulfuric Acid (a Check on Carius's Procedure).—Forty grams each of triethyl thionophosphate and 100% sulfuric acid were mixed together slowly. The temperature of the mixing was maintained at 25° by means of an ice-bath. After one hour the mixture was poured on ice and then extracted with ether. The ether layer was first washed with an ice-cold solution of sodium hydrogen carbonate and then dried with anhydrous magnesium sulfate. Upon distillation, after the removal of ether, 13.7 g. of material was obtained having a b.p. of 63-70° at 1 to 0.5 mm., n^{25}_{D} 1.4505. There was practically no residue left, indicating no tetraethyl dithionopyrophosphate formation. When the above reaction was carried out using 87% phosphoric acid instead of 100% sulfuric acid, the triethyl thionophosphate was recovered unchanged.

(d) Reaction in Presence of Tertiary Amines Other than Pyridine.—The conditions of reaction employed using the various other tertiary amines in the synthesis of tetraethyl dithionopyrophosphate were similar to those described for pyridine. All the amines were freshly redistilled before use. The data are summarized in Table I. The reported yields are for the undistilled product after it had been heated to 100-110° at 1-2 mm. The extent of deviation of the index of refraction from 1.4758 gives some measure of the degree of contamination. Five grams (0.278 mole) of water was used in all of the experiments.

Other Tetraalkyl Dithionopyrophosphates. Tetra-*n*-Propyl Dithionopyrophosphate.—To 400 g. (1.845 moles) of di-*n*-propyl thionochlorophosphate was added a solution consisting of 15.7 g. (0.199 mole) of pyridine and 9.3 g. (0.516 mole) of water. The temperature rose to a maximum of 36°. The mixture was stirred for 20 minutes at a temperature below 36° and was then cooled to 20° by means of an ice-water-bath. Successive additions of 107.5 g. (1.015 mole) of sodium carbonate and 185 cc. of water were made. The temperature rose to 33°. The ice-water-bath was removed and the system was maintained at 37-39° for six hours by periodic cooling at first and subsequently by heating when no more heat was evolved. The mixture was stirred at room temperature overnight after which it had become a thin slurry. Four hundred cc. of water was added; the separated organic layer was washed with a total of 400

TABLE I

Amines	Amines, grams (mole)	$(EtO)_2\overset{S}{\overset{\vert}{P}}Cl$ grams (mole)	Yield, grams (%)	$n^{25}D$ product (amine)	Notes
	49.5 (0.532)	95.6 (0.507)	25.7 (31.5)	1.4812 (1.4980)	a
	49.5 (0.532)	95.6 (0.507)	73.1 (89.7)	1.4775 (1.5033)	
	49.5 (0.532)	95.6 (0.507)	71.6 (88.0)	1.4773 (1.5028)	
	68.6 (0.532)	95.6 (0.507)	None ...	.... (1.6230)	b
	68.9 (0.544)	95.6 (0.506)	75 92	1.4790 (1.6228)	c
	30.5 (0.518)	94.3 (0.50)	63.2 (78.5)	1.4769	d
	52 (0.515)	94.3 (0.5)	65.8 (81.5)	1.4804 (1.4335)	e
	54 (0.4)	75.4 (0.40)	45.2 (70.2)	1.4812 (1.5000)	f
	41.6 (0.412)	75.4 (0.40)	15.7 (24.4)	1.4763	g

[a] The reactions with pyridine, β- and γ-picoline, were accompanied by an immediate exothermic reaction; in contrast, when α-picoline and water were added to the diethyl thionochlorophosphate, only a minor heat effect was observed, and the reaction seemed to proceed very slowly. The latter reaction mixture was allowed to stand at room temperature for three days in order to achieve a more complete reaction. On washing the product with water considerable ethyl chloride gas was evolved. The product was washed with 5% sodium hydrogen carbonate solution and with several portions of water to remove free acid. When the reaction was carried out under conditions used for pyridine, but without standing at room temperature for three days, the yield was even lower. [b] There was 17 g. of residue left after heating at 0.5 mm. to 110°. The index of refraction was 1.5155 and analysis showed the residue to contain 10.4% N. Obviously it was not the desired product. [c] Thirty-seven grams of the residue, upon distillation in a Hickman still yielded 34.7 g. of distillate, $n^{25}D$ 1.4770. This corresponds to an over-all distilled yield of 86.5%. [d] Trimethylamine is a gas at the temperature of reaction. It was introduced by bubbling slowly into the reaction mixture. [e] The crude product, upon redistillation, gave a distillate ($n^{25}D$ 1.4766) corresponding to an over-all final yield of 54%. [f] In another experiment using identical quantities of reactants the amine was added very slowly (six hours) to the mixture of water and diethyl thionochlorophosphate. The yield of the undistilled product was increased to 52 g. (80.7%), $n^{25}D$ 1.4788. Further improvement in yield was achieved by carrying out the reaction under conditions identical to those for the preceding experiment except that a 455% excess of water was used. The yield of the product amounted to 54.3 g. (84.4%), $n^{25}D$ 1.4766. [g] The acidic contaminants were removed by repeated washings with 5% sodium hydrogen carbonate solutions and with water.

cc. of water. Upon heating to 75° at 1 mm. a residue was obtained which weighed 333.2 g. (95.5%), $n^{25}D$ 1.4718.[13]

Anal. Calcd. for $(n\text{-}C_3H_7O)_2\overset{S}{\overset{\uparrow}{P}}O\overset{S}{\overset{\uparrow}{P}}(OC_3H_7\text{-}n)_2$: P, 16.4; S, 16.9. Found: P, 16.6; S, 17.1.

A 25-g. portion of the crude product was distilled in the Hickman still (bath temperature 109–110°, 0.008 mm.; distillation rate, one drop/2–3 sec.). The yield of the distillate was 24.2 g. (91.6%); $n^{25}D$ 1.4712. Analytical results and rate of hydrolysis of the distilled product were found to be substantially identical with values for the crude product.

In another experiment the compound was prepared by the action of 324.8 g. (1.5 moles) of di-*n*-propyl thionochlorophosphate with 14 g. (0.78 mole) of water and 122 g. (1.55 moles) of pyridine at 36–38°. The crude product weighed 265.5 g. (93.7%), $n^{25}D$ 1.4722. A 50-g. portion, upon distillation in the Hickman still, weighed 47.9 g. (90%), $n^{25}D$ 1.4713.

Tetraisopropyl Dithionopyrophosphate.—To 108.2 g. (0.5 mole) of diisopropyl thionochlorophosphate ($n^{25}D$ 1.4601) was added a mixture consisting of 4.6 g. (0.266 mole) of water and 40.7 g. (0.515 mole) of pyridine. The reaction conditions were the same as those employed in the synthesis of the ethyl ester. Some unreacted diisopropyl thionochlorophosphate was recovered. The residue, representing the crude product, weighed 75 g., $n^{25}D$ 1.4633. A 25-g. portion of the residue was distilled in the Hickman still (bath temperature 102–103°, 0.004 mm.; rate, one drop/sec.). The distillate weighed 21 g. (65%), $n^{25}D$ 1.4620 and d^{25}_4 1.093. This material was found to undergo less than 1% hydrolysis after shaking a 0.02 *M* solution of it in contact with water for three days.

Anal. Calcd. for $(i\text{-}C_3H_7O)_2\overset{S}{\overset{\uparrow}{P}}O\overset{S}{\overset{\uparrow}{P}}(OC_3H_7\text{-}i)_2$: P, 16.4; S, 16.9. Found: P, 16.4; S, 17.2.

Tetra-*n*-butyl Dithionopyrophosphate.—This compound was prepared by the action of 230.5 g. (0.944 mole) of di-*n*-butyl thionochlorophosphate with a mixture of 9.45 g. (0.525 mole) of water and 81.4 g. (1.03 moles) of pyridine under conditions described in preceding experiments. After thorough washing with water, the organic layer was heated to 110° at 1 mm. The resulting crude product weighed 196 g., $n^{25}D$ 1.4692.

Anal. Calcd. for $(n\text{-}C_4H_9O)_2\overset{S}{\overset{\uparrow}{P}}O\overset{S}{\overset{\uparrow}{P}}(OC_4H_9\text{-}n)_2$: P, 14.3; S, 14.75. Found: P, 14.4; S, 15.1.

A 50-g. sample was distilled in the Hickman still (bath temperature 117–120°, 0.005 mm.; rate, one drop/2–4 sec.). The distillate weighed 45.1 g. (87%), $n^{25}D$ 1.4690 and d^{25}_4 1.068.

Reaction of Diethyl Thionochlorophosphate with Tertiary Amines.—The amines listed in Table I, as well as pyridine, were added in molar ratios to diethyl thionochlorophosphate. In some cases reaction occurred immediately. After 16 hours at 40°, the reaction mixture containing α-picoline and the one containing quinoline remained free-flowing fluids; the mixture prepared from triethylamine consisted of an upper fluid layer and a viscous lower layer. After standing for a longer period of time, the α-picoline and then the quinoline reaction products also separated into two layers. The reaction products containing pyri-

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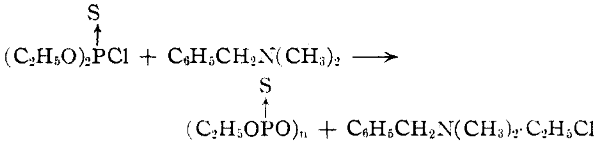
[13] Though many of the samples prepared gave the correct elemental analysis, hydrolysis tests revealed a maximum of 3–6% of hydrolyzable components. A check on the original reactants showed that the di-*n*-propyl thionochlorophosphate used as reactant contained a few per cent. of an isomeric compound O,S-di-*n*-propyl chlorophosphate. It is suggested that the hydrolyzable contaminant in the final product is probably a small quantity of O,O,O,S-tetra-*n*-propyl monothionopyrophosphate.

dine, β-picoline, γ-picoline and isoquinoline, eventually changed into homogeneous, extremely viscous materials, while the reaction products containing dimethylbenzylamine and N-methylmorpholine, became taffy-like solids.

A more thorough study was carried out on the reaction between dimethylbenzylamine and diethyl thionochlorophosphate. When equivalent quantities of these freshly redistilled reactants were sealed together in a flask under anhydrous conditions, crystalline precipitates formed almost immediately at room temperature. The crystal formation was rather slow at −27°, but at 0° the whole reaction mixture appeared to be a solid after 2–3 days. Samples containing these reactants were sealed and placed in a refrigerator at 0 ± 1°. One sample was removed after 138 hours; upon repeated washing with dry hexane to remove the unreacted materials there remained an insoluble residue, representing 74% by weight of the original reactants. It was a slightly sticky solid. Washing with absolute ether resulted in the removal of a major portion of the phosphorus and sulfur content. The ether wash followed by an acetone wash removed completely the phosphorus and sulfur content from the residue. The white acetone insoluble residue thus obtained was found to be dimethylethylbenzylammonium chloride.

Anal. Calcd. for $[(CH_3)_2(C_2H_5)(C_6H_5CH_2)N]Cl$: Cl, 17.8; N, 7.0. Found: Cl, 18; N, 7.0.

The quantity obtained represented 27.2% by weight of the original reactants, or a 44% yield if the reaction as represented in Equation 8 was the only reaction.



$$(C_2H_5O)_2\overset{S}{\overset{\uparrow}{P}}Cl + C_6H_5CH_2N(CH_3)_2 \longrightarrow (C_2H_5O\overset{S}{\overset{\uparrow}{P}}O)_n + C_6H_5CH_2N(CH_3)_2\cdot C_2H_5Cl$$

Both the ether and acetone solutions yielded, upon removal of the solvent, clear viscous oils which were only slightly soluble in water. Upon shaking with water the oil obtained from the ether solution was neutral to methyl orange, but became acidic on standing. No definite compound formation was determined from the elemental analysis.

Another sample of original reaction mixture was processed as described after 88 hours at 0 ± 1°. The yield of the dimethylethylbenzylammonium chloride corresponded to only 19.5% of the theory based upon the reaction represented by Equation 8.

Toxicity and Other Properties.—The toxicity of this series of compounds was determined by intraperitoneal injection in white mice, counting only those animals which died within the first hour after the injection. The LD_{50} for the tetraethyl ester was found to be 8 mg./kg. The compound is rather toxic, in agreement with the data reported by Schrader. Under identical testing conditions both of the propyl esters, as well as the *n*-butyl ester, were found to be relatively non-toxic to the white mice. As much as 7 to 9 g./kg. were required to cause a fatality in mice within one hour after injection. The tetraethyl ester[14] which was introduced commercially for evaluation as an insecticide in 1947 has been found in aerosol formulations to be even more effective than Parathion, for the control of many insects, especially greenhouse pests, such as spider mites, aphids, whiteflies and mealy bugs.[15] Preliminary reports from Dr. Robert Metcalf[16] of the Citrus Experiment Station, Riverside, California, to whom the homologous compounds were submitted have indicated that in spite of the low toxicity to mice the propyl esters are still fairly toxic to insects including mites, aphids and thrips. Recently Gersdorff and Mitlin[17] showed that the tetra-*n*-propyl dithionopyrophosphate is $^1/_{20}$ as toxic to houseflies as Parathion, but three times as toxic as pyrethrin.

In field tests on plants which had been sprayed with tetraethyl dithionopyrophosphate, the residual toxicity lasted only 10–14 days. It was at first thought that this loss in the toxicity was due to the gradual oxidation of the thiono group to the oxo group with resulting increased susceptibility to hydrolysis. However, when oxygen was bubbled through the liquid in a Vycor flask at 40–50° under intense ultraviolet light no appreciable change in the chemical properties occurred after 50 hours. The loss of toxicity in the field is probably due to gradual evaporation of the thin film or due to as yet undetermined causes.

The stability of pure tetraethyl dithionopyrophosphate at 100° was shown by the change in acidity, expressed in cc. 0.1 *N* NaOH/g., after heating for a period of time. This acidity was measured on the sample both before and after shaking with water (0.02 mole of compound suspended in 1 liter of water) for eight days.

Time of heating, hours	Acidity, cc. 0.1 *N* NaOH/g.	
	Initial	After shaking in H_2O
0	0.1	1.1
2	0.2	1.3
46	2.6	3.1

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(14) Victor Chemical Works, under the name of ASP47.

(15) Smith and Fulton, *Florists Exchange Hort. Trade World*, [2] **115**, 14, 19 (1950).

(16) Private communication.

(17) Gersdorff and Mitlin, *J. Econ. Entomol.*, **43**, 562 (1950).