Hexaethyl Tetraphosphate and Tetraethyl Pyrophosphate

S. A. Hall and Martin Jacobson

Bureau of Entomology and Plant Quarantine, United States Department of Agriculture, Beltsville, Md.

HE preparation of socalled hexaethyl tetraphosphate was first described by Schrader (20). The product was used in a formulation called Bladan (9, 12, 22) used by the Germans during World War II as a very effective substitute for unobtainable nicotine insecticides. The discovery of this material as an insecticide came about as an offshoot of research on toxic warfare agents by chemists of the I. G. Farbenindustrie working at Elberfeld and Leverkusen, Germany (9). Hexaethyl tetraphosphate is highly toxic not only to many species of insects but also to warm-blooded animals. In

Tetraethyl pyrophosphate was found to be the principal biologically active ingredient of so-called hexaethyl tetraphosphate which is a mixture. Mixtures containing varying proportions of tetraethyl pyrophosphate, ethyl metaphosphate, triethyl orthophosphate, and probably pentaethyl triphosphate were made by reacting triethyl orthophosphate with phosphorus oxychloride or with phosphoric anhydride. The hygroscopic liquid reaction products-important commercially as insecticides-were examined as to physical properties, effect of moisture, hydrolysis products, and biological activity; the latter was found to depend on the proportion of the reactants and conditions of the reaction. Tests useful in classifying these products were developed. Tetraethyl pyrophosphate was isolated from the mixtures and also prepared by independent syntheses. It hydrolyzed spontaneously in water to diethyl orthophosphoric acid as a first order reaction for which rates were determined at two temperatures and the Arrhenius heat of activation was calculated.

(1)

the presence of moisture it hydrolyzes rapidly to form relatively nontoxic products. Entomological tests made in this country (4, 13, 21, 23) have indicated that it is a promising insecticide, especially against mites and aphids (18).

Schrader (20) prepared hexaethyl tetraphosphate by reacting phosphorus oxychloride with triethyl orthophosphate at about 150° C. according to the following equation:

$$POCl_3 + 3(C_2H_b)_3PO_4 \longrightarrow 3C_2H_bCl + (C_2H_b)_8P_4O_{13}$$

Thurston (25) has recently described a new method adopted by the Germans for making hexaethyl tetraphosphate from phosphorus oxychloride and ethyl alcohol according to the following equation:

$$POCl_3 + 9C_2H_5OH \longrightarrow 9HCl + 3C_2H_5Cl + (C_2H_5)_6P_4O_{13}$$
(2)

The new process is operated at about the same temperature as the original Schrader process, but under a reduced pressure of 120 to 150 mm. of mercury in order to remove rapidly the hydrogen chloride evolved, which would otherwise react with the alcohol to form larger quantities of ethyl chloride.

The reaction product (4) is a light amber hygroscopic liquid completely miscible in water and in a wide variety of organic solvents, including acetone, alcohol, ether, chloroform, carbon tetrachloride, ethyl acetate, diacetone alcohol, glycerol, benzene, toluene, xylene, and alkylated naphthalenes. It is insoluble in ligroin and other paraffin fractions, such as kerosene.

Schrader considered the product to be the hexaethyl ester of tetraphosphoric acid, to which he ascribed (20) structure I (Figure 1).

The authors have concluded that hexaethyl tetraphosphate of empirical formula $(C_2H_\delta)_6P_4O_{13}$ does not possess a definite structure, nor is it probable that it actually contains the hexaethyl ester of tetraphosphoric acid, either a straight-chain form or the branched chain proposed by Schrader. The evidence in the early literature (8, 17, 19) that tetraphosphoric acid or its sodium salt was successfully prepared is unconvincing and has been refuted by the thorough investigations of Partridge *et al.* (16), who have shown that the highest member of the system $NaPO_2$ - $Na_4P_2O_7$ existing as a crystalline individual is sodium triphosphate (often called tripolyphosphate), $Na_5P_3O_{10}$.

The work in this laboratory with so-called hexaethyl tetraphosphate indicates that it is essentially a mixture of esters containing ethyl metaphosphate, triethyl orthophosphate, and tetraethyl pyrophosphate. Pentaethyl triphosphate (which has not yet been isolated) is a possible constituent. When hexaethyl tetraphosphate is poured onto crushed ice and the resulting ice water solution is

immediately extracted with chloroform, there is obtained, on removal of the chloroform, approximately 40% by weight of a liquid extractive with physical properties approaching those of tetraethyl pyrophosphate. This extractive is distillable under vacuum to the extent of 60 to 70% before decomposition commences as evidenced by the evolution of ethylene. The distillate thus obtained is approximately two thirds tetraethyl pyrophosphate and one third triethyl orthophosphate. Because triethyl orthophosphate and ethyl metaphosphate, as well as monoethyl and diethyl orthophosphoric acids (hydrolytic decomposition products of hexaethyl tetraphosphate) are all relatively noninsecticidal, it is be'ieved that tetraethyl pyrophosphate is the active insecticidal ingredient of the mixture called hexaethyl tetraphosphate. This theory is further supported by the fact that tetraethyl pyrophosphate itself has been found to be three to five times more active biologically than hexaethyl tetraphosphate. Moreover, it was found that, by simply increasing the proportion of triethyl orthophosphate in the Schrader process as indicated in Equation 3, a product of empirical formula $(C_2H_5)_4P_2O_7$ is obtained, which is even more active than hexaethyl tetraphosphate:

$$5(C_2H_5)_3PO_4 + POCl_3 \longrightarrow 3C_2H_5Cl + 3(C_2H_5)_4P_2O_7$$
(3)

The product obtained by this modified Schrader process is not pure tetraethyl pyrophosphate, but a nondistillable mixture (nondistillable tetraethyl pyrophosphate) containing a higher percentage of active ingredient than is obtained when 3 moles (Equation 1) instead of 5 moles of triethyl orthophosphate are reacted with 1 mole of phosphorus oxychloride.

Another method for making end products similar to those obtained by the Schrader process was patented by Woodstock (27). It is illustrated by the following equations:

$$2(C_2H_5)_{3}PO_4 + P_2O_5 \longrightarrow (C_2H_5)_{6}P_4O_{13}$$
(4)

$$4(C_2H_5)_3PO_4 + P_2O_5 \longrightarrow 3(C_2H_5)_4P_2O_7$$
 (5)

Hexaethyl tetraphosphate made by this method (Equation 4) has been found to exhibit essentially the same biological activity

(21) as the product of corresponding empirical composition made by the original Schrader process (Equation 1).

However, the product (nondistillable tetraethyl pyrophosphate) made by Woodstock's method (Equation 5) has been found to be appreciably less active biologically than the product of corresponding empirical composition made by the modified Schrader method (Equation 3). Woodstock has pointed out that the so-called nondistillable tetraethyl pyrophosphate made by his process may be heated with stirring to 160° C. for 1 hour to increase substantially its tetraethyl pyrophosphate content and hence its biological activity. The authors have since experimentally confirmed Woodstock's observation.

The Schrader process yields liquid products of a characteristic light amber color. The Woodstock process yields colorless liquid products which are slightly turbid. This turbidity is dissipated upon heating to about 160 °C. for ten minutes. With Woodstock hexaethyl tetraphosphate this short period of heating gives the liquid a pale amber hue exactly like that of a common grade of Schrader-process hexaethyl tetraphosphate. Both processes give mixtures as end products which cannot be distilled under vacuum (0.1 mm. of mercury) without decomposition. Physical properties of these products are given, together with corresponding analytical and empirical test data, in Table I.

TETRAETHYL PYROPHOSPHATE

The compound tetraethyl pyrophosphate, according to Nylèn (15), possesses the structure II (Figure 1) corresponding to the established structure of inorganic pyrophosphates. Balarev (2) proposed the structure III (Figure 1) for tetraethyl pyrophosphate in order to account for the ease with which his ester (which he believed was pure) split out on heating triethyl orthophosphate (structure IV, Figure 1), and ethyl metaphosphate (structure V) which in turn decomposed to ethylene and metaphosphoric acid (structure VI).



Figure 1. Structures and Degradation Products of Hexaethyl Tetraphosphate and Tetraethyl Pyrophosphate

According to Arbuzov and Arbuzov (1), tetraethyl pyrophosphate, a pure vacuum-distillable compound, was first prepared by them, although earlier investigators (2, 5, 7, 19) described what they thought to be the pure ester, which they prepared from silver pyrophosphate and ethyl iodide. Balarev (3) also prepared his ester from equimolecular quantities of triethyl orthophosphate (structure IV, Figure 1) and ethyl metaphosphate (structure V). This is suggestive of the later Woodstock process (27). The Arbuzovs (1) obtained a mixture containing at least five components which resulted from a complicated reaction of uncertain course between bromine and diethyl sodium phosphite suspended in ligroin. They subjected this reaction product to numerous fractionations under vacuum in a short column of their own design and obtained in their highest boiling fraction (144-145°C. at 3-mm. pressure) a yield of 7.6% tetraethyl pyrophosphate. They also describe a modified procedure wherein chlorine was used in place of bromine in the reaction, and their yield of tetraethyl pyrophosphate was increased to 21% based on the weight of diethyl phosphite used. Their modified procedure was repeated by the authors who were unable to separate in pure form tetraethyl pyrophosphate from the reaction mixture.

The density and refractive index of the ester described by the Arbuzovs are substantially in accordance with what was found in this laboratory for tetraethyl pyrophosphate prepared as described. The Arbuzovs report that the ester dissolved in water (equimolecular proportions) with slight absorption of heat; the temperature was lowered by about 2°C. The authors cannot confirm this. Mixed in the same way with an equimolecular proportion of water, their purest fraction of tetraethyl pyrophosphate showed a definite temperature rise of 0.5° C. When it was mixed in the ratio of 2 ml. of ester to 1 ml. of water, the temperature rise was 2.8° C. The Arbuzovs described the ester as being stable in water, as evidenced by heating a solution of 4.3 grams of the ester with 0.267 gram of water in a test tube by immersion in a Woods metal bath at 175° C.; they report that the water distilled leaving the ester unchanged. This is contrary to the experience of the authors with tetraethyl pyrophosphate. As indicated by hydrolysis rate studies, the ester would be appreciably hydrolyzed by even momentary contact with water vapor at temperatures near 175°C.

Distillable tetraethyl pyrophosphate was obtained in this laboratory by vacuum fractionation of the product obtained from the following reaction between diethoxy phosphoryl chloride and triethyl orthophosphate at about 150 °C. in the presence of a little copperbronze powder as a catalyst:

$$(C_2H_5O)_2POCl + (C_2H_5)_3PO_4 \longrightarrow C_2H_5Cl + (C_2H_5)_4P_2O_7$$
 (6)

Ethyl chloride was collected in a dry-ice trap almost quantitatively.

The reaction shown in Equation 6 probably takes place in the Schrader process (see Equations 1 and 3). In this connection McCombie *et al.* (14) pointed out that the reaction between phosphorus oxychloride and triethyl orthophosphate results in the formation of diethoxyphosphoryl chloride and of monoethoxy phosphoryl dichloride as follows:

$$POCl_{3} + 2(C_{2}H_{5}O)_{3}PO \longrightarrow 3(C_{2}H_{5}O)_{2}POCl$$
(7)

$$2\text{POCl}_3 + (\text{C}_2\text{H}_5\text{O})_3\text{PO} \longrightarrow 3\text{C}_2\text{H}_5\text{OPOCl}_2 \tag{8}$$

On the supposition that all three reactions take place in the Schrader process, one is led to conclude that conditions favoring the formation of the diethoxyphosphoryl chloride (Equation 7) to the exclusion of the monoethoxyphosphoryl dichloride would result (by Equation 6) in a better yield of tetraethyl pyrophosphate. Thus, in carrying out the reaction expressed in Equation 3, the slow addition of phosphorus oxychloride to triethyl orthophosphate held at reaction temperature (about 150 ° C.) would yield a product of higher tetraethyl pyrophosphate content. Preliminary experiments indicated that this indeed appears to be the case; a product of appreciably higher biological activity was obtained in this manner by the authors. A further series of experiments along these lines is in progress.

TABLE I. PHYSICAL PROPERTIES AND TESTS OF TYPICAL PRODUCTS

										Temp.	Color Te	sts
Product	Equa- tion No.	Phosph Calcd.	orus, % Found	Ethox Caled.	ryl, % Found	Refrac- tive Index, n_{D}^{25}	Sp. Gr., d ²⁵ ₂₅	Viscos- ity, Cp. at 25° C.	Temp. of Ethylene Evolution, °C. ^a	Rise with Water, °C.	With isophorone	With alcoholic methyl orange
$\begin{array}{c} Hexaethyl & tetraphosphate, \\ (C_2H_5)_6P_4O_{13} \end{array}$												
Schrader process Woodstock process	1 4	$24.47 \\ 24.47$	25.20 26.28	53.4	$\begin{array}{c} 53.2 \\ 51.8 \end{array}$	$\begin{smallmatrix}1.4265\\1.4275\end{smallmatrix}$	$1,2833 \\ 1.2895$	$\substack{31.5\\29.2}$	$140-160 \\ 148-170$	$egin{array}{c} 24.5\ 23.9 \end{pmatrix}$	Amber	Red
rophosphate, (C ₂ H ₅) ₄ P ₂ O:	7	01.95	. 02.02	69 1	61 1	1 (100	1 0001	0.0	100 104	10.0		
Woodstock process	э 5	$\begin{array}{c} 21.35\\ 21.35\end{array}$	$23.96 \\ 22.25$	62.1 62.1	$61.1 \\ 61.7$	1.4180 1.4160	1.2081 1.1837	$\frac{8.0}{5.6}$	180 - 194 183 - 195	10.2 13.3	Deep yellow	Red
aqueous hexaethyl tetra- phosphate Tetraethyl pyrophosphate.			21.65		59.6	1.4190	1,2071	9.7	172-190	6.5	Deep yellow	Red
$(C_2H_5)_4P_2O_7$ Purified fraction	6	21.35	21.86	62.1	61.7	1.4170	1.1845	5.1	208-213	2.8	No color change	Yellow
^a The lower temperature is	the poi	nt of inci	oient evolu	ition; at	the high	er temperatu	re, evoluti	ion is at a	rate of 1 bul	oble per	5 seconds.	

Tetraethyl pyrophosphate was also obtained by vacuum fractionation of the reaction product (5, 7) obtained from silver pyrophosphate and ethyl iodide:

$$Ag_4P_2O_7 + 4C_2H_5I \longrightarrow 4AgI + (C_2H_5)_4P_2O_7$$
(9)

The yield of a distillable fraction of tetraethyl pyrophosphate is lower by this method; the former reaction (Equation 6) is a more satisfactory preparative method.

A third method has already been mentioned in connection with the isolation of distillable tetraethyl pyrophosphate from socalled hexaethyl tetraphosphate. In carrying out this method one may use as starting material any of the products-whether of empirical composition $(C_2H_5)_4P_6O_{13}$ or $(C_2H_5)_4P_2O_7$ —obtained by either the Schrader or Woodstock methods (Equations 1, 3, 4, 5). Ordinarily the tetraethyl pyrophosphate that these products contain cannot be isolated by direct vacuum fractionation because of decomposition which appears to be catalytic. The substance responsible for this effect is apparently largely removable by partition between water and chloroform; it has not been isolated and identified. It appears to be present in hexaethyl tetraphosphate, because the addition of the latter to pure distillable tetraethyl pyrophosphate will, on attempted vacuum distillation, cause typical decomposition to triethyl orthophosphate and ethyl metaphosphate, which further decomposes to ethylene and metaphosphoric acid. Neither ethyl metaphosphate nor metaphosphoric acid alone, when added to distillable tetraethyl pyrophosphate, produced this effect to the same degree.

To obtain distillable tetraethyl pyrophosphate by the chloroform extraction method, the nondistillable product was stirred (either hexaethyl tetraphosphate or nondistillable tetraethyl pyrophosphate) with four times its weight of crushed ice and extracted immediately with chloroform. After the extract was dried by passing through a short tube (5 cm.) packed with alternate layers of dried cotton and anhydrous sodium sulfate, the chloroform was distilled to obtain the extractive. It was found that 60 to 70% of the extractive from hexaethyl tetraphosphate (either Schrader or Woodstock process) was distillable at approximately 0.1-mm. pressure before ethylene evolution commenced. A typical distillate contained 70% of tetraethyl pyrophosphate and 30% of triethyl orthophosphate which could be readily separated by vacuum fractionation.

The best fraction of tetraethyl pyrophosphate obtained in this laboratory by refractionation in a short open-tube column boiled between 104° and 110° .C. at 0.08-mm. pressure. Its wide boiling range might be due to the slight but ever present tendency of the ester when vacuum distilled to split out a very small percentage of triethyl orthophosphate. Attempted vacuum fractionation through a 40-cm. column packed with glass helices resulted in complete decomposition, and pure triethyl orthophosphate was obtained at the still head.

Tetraethyl pyrophosphate is a water-white, mobile liquid, completely miscible in water and in the organic solvents listed for hexaethyl tetraphosphate. It is also insoluble in ligroin and kerosenes of low aromatic content.

The molecular weight of the ester was determined by the Signer method, as described by Clark (β) , in which anhydrous ether was used as the solvent and purified azobenzene as the reference standard: molecular weight, calculated, 290; found, 293. Other physical properties and analytical data are given in Table I.

Jones *et al.* (11) determined the density and refractive index of tetraethyl pyrophosphate, which they evidently succeeded in preparing by the Arbuzovs' complex reaction (1). They calculated the molecular refraction by both the Gladstone-Dale and Lorenz-Lorentz equations. A comparison of their data with that of the authors follows:

Density	Refractive Index	${f Molecular}$ Refraction ^a	Reference
$d_{20} = 1.1846$	$n_{\rm D}^{20} = 1.4222$	$[R_G] = 103.43$ $[R_L] = 62.28$	Jones et al. (11)
$d_{25} = 1.1810$	$n_{\rm D}^{25} = 1.4170$	[RG] = 102.46 [RL] = 61.79	Authors

 a Gladstone-Dale formula $[RG]=(n-1)M/d;\;$ Lorenz-Lorentz formula $[RL]=(n^2-1)\;M/(n^2+2)d.$

HYDROLYS1S

The German chemists who developed hexaethyl tetraphosphate as an insecticide stated that in water solution or finely dispersed in the presence of atmospheric moisture it was completely hydrolyzed in 24 hours to ethyl alcohol and orthophosphoric acid (\mathcal{G}) . The authors found that this was not the case. At ordinary temperatures neither ethanol nor more than a trace of orthophosphoric acid is formed as a hydrolysis product. This finding was verified as follows:

A solution of 10 grams of hexaethyl tetraphosphate in 40 ml. of water was aerated, and the issuing air stream was bubbled through a gas-absorbing bottle containing potassium dichromate-nitric acid reagent (24). No trace of ethanol was detectable by this sensitive reagent, even after the solution had been left to stand in a stoppered flask for 4 days at about 25° C. Orthophosphoric acid, determined colorimetrically, was present in the freshly prepared solution only to the extent of 0.05%. After standing 4 days the orthophosphoric acid content had increased to 0.2%; this suggested that it was produced by the slow hydration of traces of metaphosphoric, pyrophosphoric, or triphosphoric acid originally present in the hexaethyl tetraphosphate.

The hydrolysis of hexaethyl tetraphosphate gave a mixture composed of monoethyl orthophosphoric acid (structure VII, Figure 1) and diethyl orthophosphoric acid (structure VIII, Figure 1). The monoethyl orthophosphoric acid was identified by its brucine salt, which melted at $206-208^{\circ}$ C. The salt obtained from the hydrolysis products of hexaethyl tetraphosphate did not depress the melting point of the brucine salt, $C_2H_5OPO_3H_2$.- $C_{23}H_{26}O_4N_2$.4H₂O, prepared from authentic monoethyl orthophos-

phoric acid. Wagner-Jauregg et al. (26) report the melting point of this salt as 211-214°C.

Pure tetraethyl pyrophosphate hydrolyzes (15) to diethyl orthophosphoric acid (structure VIII, Figure 1). This is a strong monobasic acid which may be readily determined by titration with standard alkali using phenolphthalein as indicator.

The rate of hydrolysis of a purified fraction The rate of hydrolysis of a purihed fraction of tetraethyl pyrophosphate was determined for $0.005 \ M$ solutions (0.145%) in distilled water at 25.0° and 38.0° C. The rate was also de-termined at 38.0° C. for a $0.020 \ M$ solution (0.580%). A thermostatically controlled bath, held constant within $\pm 0.03^{\circ}$, was used. Zero time was taken at the instant the measured vol-ume of water (at 25.0° or 38.0° C.) was added to an Erlenmeyer flask containing the weighed sample of ester. After an initial mixing by shaksample of ester. After an initial mixing by shaksample 0.0-ml. aliquots (5.0-ml. aliquots in the case of the 0.020 M solution) were transferred by pipet to a small flask (both kept at approximate bath temperature) and rapidly titrated with 0.0298 Nsodium hydroxide solution. The time rating was taken at the end point of the titration. The hydrolysis data are given in Table II. The logarithm of the concentration of tetra-

the logarithm of the concentration of tetra-ethyl pyrophosphate was plotted against time (Figure 2) and the best straight line drawn by inspection through the points. The slope of the line was multi-plied by -2.303 to give the rate constant, k, with the following results: At 25.0° C., 1.70×10^{-3} min.⁻¹; at 38.0° C., 3.50×10^{-3} min.⁻¹. The hydrolysis reaction is of the first order. No difference, within the limits of error, was found in the slopes of the lines at two different concentrations (0.005 M and 0.020 M)at 38.0° C.

TABLE II. HYDROLYSIS RATE DATA FOR TETRAETHYL

		PYROPHOSPHA	TE .	
Time Elapsed, Minutes	0.0298 <i>N</i> NaOH, Ml.	M1. $\times \frac{0.0298}{2}$ = a, Millimoles	0.100 - a = c, Millimoles	$\log (c \times 10^2)$
		At 25.0° C., 0.00	5 M	1
$\begin{array}{c} 9\\ 16\\ 25\\ 45\\ 77\\ 137\\ 257\\ 317\\ 317\\ 437\\ 498\\ 614\\ 737\\ 856\\ 1050\\ 1234\\ 1409\\ \end{array}$	$\begin{array}{c} 0.50\\ 0.59\\ 0.70\\ 0.88\\ 1.25\\ 1.82\\ 2.40\\ 3.12\\ 3.53\\ 3.88\\ 4.04\\ 4.52\\ 4.98\\ 5.68\\ 5.93\\ 6.13 \end{array}$	$\begin{array}{c} 0.\ 0075\\ 0.\ 0088\\ 0.\ 0104\\ 0.\ 0131\\ 0.\ 0186\\ 0.\ 0271\\ 0.\ 0358\\ 0.\ 0419\\ 0.\ 0465\\ 0.\ 0526\\ 0.\ 0526\\ 0.\ 0674\\ 0.\ 0674\\ 0.\ 0674\\ 0.\ 0742\\ 0.\ 0742\\ 0.\ 0784\\ 0.\ 0884\\ 0.\ 0884\\ 0.\ 0884\\ 0.\ 0913\\ \end{array}$	$\begin{array}{c} 0.0925\\ 0.0912\\ 0.0896\\ 0.0869\\ 0.0814\\ 0.0729\\ 0.0642\\ 0.0535\\ 0.0474\\ 0.0422\\ 0.0398\\ 0.0326\\ 0.0258\\ 0.0216\\ 0.0154\\ 0.0154\\ 0.0164\\ 0.0087\\ \end{array}$	$\begin{array}{c} 0.9661\\ 0.9600\\ 0.9523\\ 0.9390\\ 0.9106\\ 0.8027\\ 0.8075\\ 0.7284\\ 0.6758\\ 0.6758\\ 0.6253\\ 0.5999\\ 0.5132\\ 0.4116\\ 0.3345\\ 0.1875\\ 0.0645\\ -0.0605 \end{array}$
		At 38.0° C., 0.00	5 M	
$5 \\ 20 \\ 34 \\ 49 \\ 64 \\ 94 \\ 247 \\ 471 \\ 549 \\ 602 \\ 666 \\ 666 \\ 666 \\ 666 \\ 666 \\ 60 \\ 20 \\ 60 \\ 20 \\ 2$	$\begin{array}{c} 0.75\\ 0.85\\ 1.06\\ 1.32\\ 1.60\\ 2.20\\ 2.63\\ 4.06\\ 5.47\\ 5.81\\ 5.94\\ 6.16\end{array}$	$\begin{array}{c} 0.0112\\ 0.0127\\ 0.0158\\ 0.0197\\ 0.0238\\ 0.0328\\ 0.0328\\ 0.0392\\ 0.0605\\ 0.0815\\ 0.0885\\ 0.0885\\ 0.0918\\ \end{array}$	$\begin{array}{c} 0.0888\\ 0.0873\\ 0.0842\\ 0.0803\\ 0.0762\\ 0.0672\\ 0.0608\\ 0.0395\\ 0.0185\\ 0.0134\\ 0.0115\\ 0.0082\\ \end{array}$	$\begin{array}{c} 0.9484\\ 0.9410\\ 0.9253\\ 0.9047\\ 0.8820\\ 0.8274\\ 0.7839\\ 0.5966\\ 0.2672\\ 0.1271\\ 0.0607\\ -0.0862 \end{array}$
		At 38.0° C., 0.020) <i>M</i>	
5 13 30 90 161 242 344 412	$\begin{array}{c} 0.57\\ 0.76\\ 1.10\\ 2.30\\ 3.29\\ 4.19\\ 4.85\\ 5.55 \end{array}$	$\begin{array}{c} 0.0085\\ 0.0113\\ 0.0164\\ 0.0343\\ 0.0490\\ 0.0624\\ 0.0723\\ 0.0827 \end{array}$	$\begin{array}{c} 0.0915\\ 0.0887\\ 0.0836\\ 0.0657\\ 0.0510\\ 0.0376\\ 0.0277\\ 0.0173\\ \end{array}$	$\begin{array}{c} 0.9614\\ 0.9479\\ 0.9222\\ 0.8176\\ 0.7076\\ 0.5752\\ 0.4425\\ 0.2381 \end{array}$



Figure 2. Rate of Hydrolysis and Changes in pH of Tetraethyl **Pyrophosphate Solutions**

Substituting the values of the two rate constants in the Arrhenius equation integrated between two values of k,

$\log_{10}k_2/k_1 = E/4.576 (T_2 - T_1/T_2 \times T_1)$

where T_1 and T_2 are the respective absolute temperatures and E is the heat of activation in calories per mole, a value for E of 10.3 kg. cal. per mole is obtained. This value is approximate since the rate constants were determined at only two tempera-tures, but it may be used in the equation to calculate the approximate rate constants at other temperatures. The rate constant, have rate constants at other temperatures. The rate constants, t, at a given temperature may be substituted in the first order reaction equation, $t = 2.303/k \log_{10}c_0/c$, to find the time, t, in minutes for a given fraction to hydrolyze, where c_0/c is the ratio of initial concentration to the concentration at time t. Concenof initial concentration to the concentration at time i. Concentration, since it is a ratio in this equation, may be expressed in any unit. The time intervals at 25.0° and 38.0° C. for tetraethyl pyrophosphate to hydrolyze 10, 50 (half-life), 90, and 99% are as follows:

	Time Interval, Hours			
Hydrolysis, %	At 25.0° C.	At 38.0° C.		
10 50 90 99	$ \begin{array}{c} 1.0 \\ 6.8 \\ 22.6 \\ 45.2 \end{array} $	$0.5 \\ 3.3 \\ 11.0 \\ 21.9$		

The change in pH at the two temperatures of 0.005 M solutions of tetraethyl pyrophosphate is also shown in Figure 2. The pH data were obtained with a Beckman pH meter while the hydrolysis studies were in progress.

PHYSICAL PROPERTIES

Specific gravity determinations were made with an Ostwald pycnometer. Refractive index was obtained with an Abbe re-fractometer. Viscosity was determined with an Ostwald viscometer. Table I gives the properties of typical products made by the Schrader and Woodstock methods, of purified tetraethyl pyrophosphate used in the rate studies, and also of a chloroform extractive of hexaethyl tetraphosphate from ice water solution.

EFFECT OF MOISTURE ON PHYSICAL PROPERTIES

All the products described, including pure tetraethyl.pyrophosphate, are hygroscopic liquids. To preserve their activity it is important to protect them from moisture during manufacture and storage. Moisture has a marked effect upon viscosity, as would be expected from the viscous nature of the hydrolysis products, diethyl orthophosphoric acid and monoethyl orthophosphoric acid. The effect of added moisture on the physical properties of

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Moisture, %	Refractive Index, $n_{\rm D}^{25}$	Sp. Gr., d25	TABLE III Viscosity, Cp. at 25° C.	EFFECT OF AI Temp. of Ethylene Evolution, °C. ^a	Temp. Rise with Water, °C.	Color Tests With isophorone	With alcoholic methyl orange		
	Hexaethyl Tetraphosphate (Schrader Process)								
$\begin{array}{c} 0.0 \\ 0.1 \\ 0.5 \\ 1.0 \\ 2.0 \end{array}$	1.42651.42701.42601.42651.42651.4265	$1.2833 \\ 1.2844 \\ 1.2831 \\ 1.2812 \\ 1.2806$	31.5 34.2 37.2 44.3 62.6	$140-160\\140-160\\140-161\\140-160\\139-161$	$\begin{array}{c} 24.5\\ 20.8\\ 19.1\\ 15.9\\ 13.2 \end{array}$	Amber	Red		
,	Tetraethyl Pyrophosphate (Commercial Distillable)								
0.0 0.1 0.5 1.0 2.0	 1.4170 1.4170 1.4168 1.4165 1.4152 	$1.1904 \\ 1.1911 \\ 1.1903 \\ 1.1901 \\ 1.1885$	$\begin{array}{c} 6.3 \\ 6.5 \\ 6.9 \\ 8.2 \\ 12.8 \end{array}$	$197-204 \\193-204 \\191-203 \\191-203 \\191-203 \\191-203 \\$	3.0 2.8 3.4 4.6 4.8	No color change Slight deepening of color Deepening of color	Yellow Orange Red		

^a The lower temperature is the point of incipient evolution; at the higher temperature, evolution is at a rate of 1 bubble per 5 seconds.

hexaethyl tetraphosphate and tetraethyl pyrophosphate is shown in Table III. Each sample, after addition of the calculated amount of water, was brought to equilibrium by heating at 100° C. for 90 minutes. The approximate rate constant for tetraethyl pyrophosphate hydrolysis at this temperature is 5.53 imes 10^{-2} . Substituting this value in the first-order reaction equation gives a value of 83 minutes for 99% hydrolysis. Accordingly, heating at 100° C. for 90 minutes is sufficient to give mixtures of unchanging physical properties. On the basis of 1 mole of water reacting with 1 mole of tetraethyl pyrophosphate (molecular weight 290.2), 6% absorption of moisture would result in the complete destruction of the active ester if it is assumed that equilibrium is completely in the direction of diethyl orthophosphoric acid formation. Determinations above 2% moisture content were not made because samples of higher moisture content than this have not been encountered in practice.

EMPIRICAL TESTS

In the work with commercial samples of hexaethyl tetraphosphate and tetraethyl pyrophosphate, it was found that certain empirical tests may be applied by which these products may be rapidly classified as to their nature. The results are given in Tables I and II.

TEMPERATURE OF ETHYLENE EVOLUTION. A side-arm test tube containing sufficient sample to cover the bulb of a thermometer (inserted through a 1-hole stopper) is clamped and immersed in a heating bath of clear Arochlor (chlorinated diphenyl) so that the first microbubbles of ethylene gas issuing from the sample may be observed with a magnifying glass. The side arm of the test tube is connected by rubber tubing to a short length of 8-mm. glass tubing immersed in water for observation of issuing gas bubbles. The temperature at which the first microbubbles form was called the point of incipient ethylene evolution. The higher temperature at which ethylene was evolved at the rate of 1 bubble every 5 seconds was also recorded. When the heating was carried much above this point, ethylene evolution increased at a rapid rate. Of the products tested pure tetraethyl pyrophosphate exhibited the highest temperature of ethylene evolution.

TEMPERATURE RISE WITH WATER. Two milliliters of sample were transferred by pipet to a 150 \times 15 mm test tube. A thermometer was inserted, and 1 ml. of water (at the same temperature as the sample) was added by pipet to form an upper layer. The two layers were rapidly stirred together with the thermometer and the highest temperature rise noted. Results by this procedure are reproducible within 2%. Pure tetraethyl pyrophosphate gave the least temperature rise (2.8° C.) and ethyl metaphosphate the highest (47° C.). COLOR TESTS. With isophorone: One milliliter of sample was mixed with 5 ml. of isophorone (redistilled, pale yellow) in a test tube send immersed in a steam bath or in holing water for 10

Color Tests. With isophorone: One milliliter of sample was mixed with 5 ml. of isophorone (redistilled, pale yellow) in a test tube and immersed in a steam bath or in boiling water for 10 minutes. No color change took place with pure tetraethyl pyrophosphate. A deep color was given by hexaethyl tetraphosphate and also by ethyl metaphosphate. With methyl orange: To several drops of sample in a small test tube there was added 1 drop of a saturated (0.2%) solution of methyl orange in absolute ethanol. A yellow color was given only by tetraethyl pyrophosphate that contained less than 1% of moisture.

ANALYSES

Phosphorus was determined by a colorimetric method especially adapted to these products (10). Ethoxyl determinations were made by a modified semimicro Zeisel method as described by Clark (β)

SUMMARY AND CONCLUSIONS

So-called hexaethyl tetraphosphate is a nondistillable liquid mixture of empirical composition $(C_2H_5)_6P_4O_{13}$, composed essentially of tetraethyl pyrophosphate, ethyl metaphosphate, and triethyl orthophosphate; pentaethyl triphosphate may be a constituent of the mixture.

Contrary to statements made by its German discoverers, hexaethyl tetraphosphate hydrolyzes at ordinary temperatures, not to ethyl alcohol and orthophosphoric acid but to a mixture of diethyl and monoethyl orthophosphoric acids.

Nondistillable liquid products of empirical composition $(C_2H_b)_{\delta}P_4O_{1s}$ —corresponding to hexaethyl tetraphosphate—may be readily made by the original Schrader process from phosphorus oxychloride and triethyl orthophosphate (or, as recently modified, by substituting ethanol for the triethyl orthophosphate) and also by the Woodstock process from phosphoric anhydride and triethyl orthophosphate. Made by either process, products of this empirical composition have essentially the same physical properties and the same order of biological activity.

Nondistillable liquid products of empirical composition $(C_2H_5)_4P_2O_7$ —corresponding to tetraethyl pyrophosphate—may also be made by either the Schrader or Woodstock method. The products have similar physical properties when made by either process. The activity may be still further enhanced by simple modification of the Schrader process.

Distillable tetraethyl pyrophosphate (essentially a pure compound) was prepared by two different methods and was also isolated from nondistillable products, including hexaethyl tetraphosphate. It is three to five times as active as hexaethyl tetraphosphate and appears to be the active ingredient of all the nondistillable products described. In water it hydrolyzes spontaneously to diethyl orthophosphoric acid and follows a first-order reaction for which the rates were determined at 25.0° and 38.0° C. The Arrhenius heat of activation was calculated, and from these the approximate rate constants at other temperatures may be calculated. The change in pH of 0.005 M solutions of tetraethyl pyrophosphate was also followed.

The physical properties of the products, including the compound tetraethyl pyrophosphate, were determined. The molecular weight of tetraethyl pyrophosphate was determined in ether by the Signer method; its molecular refraction was also determined.

Because of their hygroscopic nature, the effect of added moisture upon the physical properties of hexaethyl tetraphosphate and tetraethyl pyrophosphate was studied. The effect is especially marked on viscosity.

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Empirical tests-temperature of ethylene evolution, temperature rise with water, and colors with isophorone and with alcoholic methyl orange—are described as useful in classifying typical commercial products.

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Propellents for Low-Pressure Liquefied Gas Aerosols

R. A. Fulton

Bureau of Entomology and Plant Quarantine, United States Department of Agriculture, Beltsville, Md.

A study has been made of a number of mixtures of liquefied gases as low-pressure propellents suitable for use in liquefied gas aerosols. They include chloro- and fluoroderivatives of methane and ethane such as methylene chloride, dichlorodifluoromethane (Freon 12), difluoroethane (Genetron 100), and monochlorodifluoroethane (Genetron 101).

ECENTLY there has been considerable interest in the development of low-pressure aerosol formulas (1, 3) with the same efficiency as those using dichlorodifluoromethane (Freon 12) as the propellent. The high-pressure formulas in general use require a special container to meet regulations of the Interstate Commerce Commission. The containers approved for aerosol use are ICC 9 (a refillable container) and ICC 40 (a nonrefillable container). The manufacture of these containers is an expensive process and increases the cost of the insecticide. Can manufacturers are now (2) developing low cost containers for use with reduced-pressure formulas.

Most of the aerosol formulas in use contain 2% pyrethrum extract (20% pyrethrins) and 3% DDT. These formulas were thoroughly tested for the armed forces, and at the close of hostilities, containers bearing commercial labels appeared on the market. The propellent gas in all the so-called high-pressure containers is dichlorodifluoromethane (Freon 12). This liquefied gas exerts a pressure of approximately 85 pounds per square inch gage at room temperature.

If the pressure of the aerosol formula is reduced to below 25 pounds per square inch at 70° F. an approved ICC container is not required. Tariff No. 4 of the Interstate Commerce Commission, par. 300, defines a liquefied gas as one exerting a total pressure exceeding 25 pounds per square inch at 70° F. An exemption request filed with the Interstate Commerce Commission to permit an aerosol formula with a gage pressure not exceeding 40 pounds per square inch at 70° F. to be used in light containers was granted July 28, 1947.

A number of combinations of solvents and liquefied gases were studied to determine the pressure characterization of the resulting solution. Several combinations of liquefied gases were found to be effective as propellents. However, some did not produce aerosols which would meet all requirements of the U.S. Department of Agriculture for acceptable formulas. The more effective of the combinations tested were as follows: trichlorofluoromethane (Freon 11) and dichlorodifiuoromethane (Freon 12); methylene chloride and dichlorodifluoromethane (Freon 12); pentane, Freon 11, and Freon 12; deodorized kerosene (Deobase) and Freon 12; propane and methylene chloride; methylene chloride, Freon 12, and carbon dioxide; 1,1-difluoroethane and Freon 11; and 1,1,1-chlorodifluoroethane and Freon 12.

Combinations of Freon 11 and Freon 12 were tested in a number of low-pressure formulas, 25 to 40 pounds per square inch at 70° F., containing pyrethrum extract and DDT in various ratios, and the resulting aerosols appeared to be satisfactory. Freon 11 was a better solvent for DDT than Freon 12, and the amount of auxiliary solvent, such as cyclohexanone and unsaturated hydrocarbons, could be reduced. With mixtures of Freon 11 and Freon 12 it was necessary to avoid the use of the high-boiling fractions of the unsaturated hydrocarbons which caused such mixtures to separate; this increased the vapor pressure in proportion to the amount of solvent added."