[Contribution from the Chemical Research Laboratories, The Lubri-Zol Corp., Cleveland, Ohio]

Chemistry of the Aliphatic Esters of Thiophosphoric Acids. I

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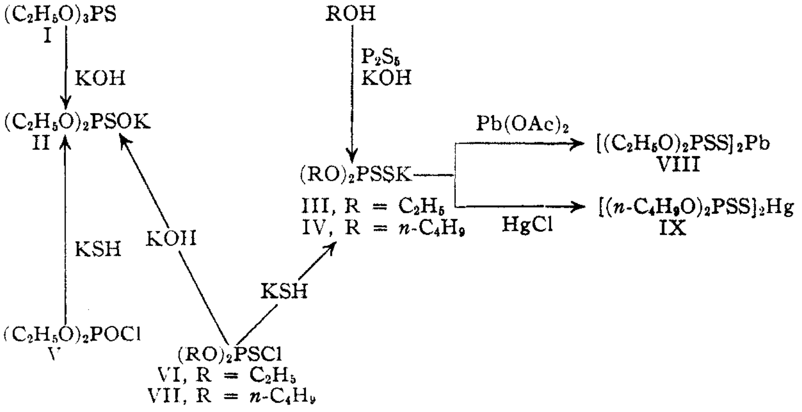
For some time we have been interested in the chemistry of the esters of thiophosphoric acids. A review of the work that has been done in this field indicated the need for a systematic structural study.

In 1912 P. S. Pistschimuka[1] published a paper in which he briefly reviewed the chemical literature previous to the beginning of our own work in this field. His three papers appearing in 1908, 1911[2] and 1912[1] constitute the outstanding contributions since the beginning of the century.

Discussion

A brief outline of the reactions carried out in this investigation is shown in the diagram. Compounds I[1] and V[3] are reported in the literature. Pistschimuka reported a salt similar to II, produced by the hydrolysis of I. Salt formation was indicated at the oxygen atom.

We obtained a potassium salt II by three different methods, as indicated in the diagram. The product obtained by each method melted at 197°. The mixed melting points showed no depression. Consequently II may be (a) potassium diethyl thionophosphate,[4] (b) potassium O,O-diethylthiolphosphate or (c) the salt of a thiophosphate acid whose structure must be explained by resonance. In the latter case only one potassium salt would exist.



Pistschimuka isolated a lead salt of a diethyl dithiophosphoric acid, produced from the reaction of phosphorus pentasulfide and ethanol, m. p. 74°. He was unable to determine the positions of the sulfur atoms in this salt because of the fact that he could not obtain the intermediate diethyl chlorothionophosphate, VI. Pistschimuka states that this chloro compound probably does not exist, in spite of the fact that Carius[5] claimed to have synthesized it. Carius, however, did not support his claim by published analyses and physical data.

We have isolated the lead salt VIII from the reaction product of potassium hydrosulfide and VI. It was obtained as white needles, m. p. 74°. This synthesis leaves no doubt as to the position of the sulfur atoms in VIII. Compound VIII was also isolated from the reaction product of phosphorus pentasulfide and ethanol. A mixed melting point of the salts obtained by the two methods showed no depression.

To further substantiate these results the acid product obtained from the reaction of n-butanol and phosphorus pentasulfide was converted to a mercuric salt IX. A mercuric salt was also prepared from the reaction product of potassium hydrosulfide and VII. The salt obtained by either method melted at 61–62°. A mixed melting point showed no depression.

As a consequence of this work we choose to write the reaction of aliphatic alcohols and phosphorus pentasulfide as follows

$$4ROH + P_2S_5 \longrightarrow 2(RO)_2PSSH + H_2S$$

In addition to VI and VII, three other new chloro compounds were prepared: S,S-diethyl chlorodithiophosphate, $(C_2H_5S)_2POCl$ (X); diethyl chlorotrithiophosphate, $(C_2H_5S)_2PSCl$ (XI); and n-butyl dichlorothionophosphate, n-$C_4H_9OPSCl_2$ (XII). Carius[5] mentioned X and XI but again failed to characterize these compounds. The present report, therefore, constitutes the first characterization of VI, VII, X, XI and XII appearing in the chemical literature.

Attempts to prepare salts from X and XI by use of potassium hydroxide or potassium hydrosulfide have been unsuccessful to date.

Experimental

Part A. Ethyl Compounds

Triethyl Thionophosphate (I) (TWM).—Thiophosphoryl chloride (0.5 mole) was added dropwise to a well-cooled sodium ethoxide solution (from 1.5 g.-atoms of

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(1) P. S. Pistschimuka, *J. Russ. Phys.-Chem. Soc.*, **44**, 1406–1554 (1912).

(2) P. S. Pistschimuka, *J. prakt. Chem.*, **84**, 746–760 (1911); *Ber.*, **41**, 3854 (1908).

(3) Wichelhaus, *Ann.*, Spl., **6**, 263 (1870); J. Walczynska, *Roczniki Chem.*, **6**, 110–119 (1926).

(4) The nomenclature employed in this paper is proposed by Dr. Mary Magill of the A. C. S. Nomenclature Committee.

(5) L. Carius, *Ann.*, **119**, 291 (1861).

sodium and 500 cc. of ethanol). After stirring for four hours the sodium chloride was filtered off and washed with absolute alcohol. The alcohol solution was concentrated to a small volume under vacuum and 500 cc. of benzene added. This solution was washed with water, dried and concentrated. The light yellow residue was fractionated through a three-foot column. The water-white product coming over at 105–106° (20 mm.) weighed 69 g. The yield was 70% of the theoretical amount.

Anal. Calcd. for $C_6H_{15}O_3PS$: P, 15.65; S, 16.16. Found: P, 14.7; S, 16.4.

Diethyl Chlorophosphate (V) (TWM).—A solution of pyridine (2 moles), absolute ethanol (2 moles) and 200 cc. of benzene was added dropwise to a cooled solution of phosphorus oxychloride in 700 cc. of benzene. The temperature of the reaction mixture was held below 20°. After stirring for three hours the pyridine hydrochloride was filtered off and washed twice with dry benzene. The filtrate and washings were then distilled through a fourteen inch, vacuum-jacketed column packed with glass helices. The desired product came over at 61–63° (2.5 mm.). The yield was 41.5 g. or 24% of the theoretical amount.

This material decomposes readily when heated above 95°.

For purposes of identification the diethyl chlorophosphate was converted to the phenylhydrazide melting at 113–114°.

Anal. Calcd. for $C_{10}H_{17}N_2O_3P$: N, 11.4; P, 12.7. Found: N, 12.2; P, 13.1.

Diethyl Chlorothionophosphate (VI) (GRN).—This compound was prepared in a manner similar to V, using thiophosphoryl chloride in place of phosphorus oxychloride. A yield of 24.4% of the product boiling at 96–99° (25 mm.) was obtained.

For purposes of identification the chloride was converted to the phenylhydrazide melting at 68–69°.

Anal. Calcd. for $C_{10}H_{17}N_2O_2PS$: N, 10.76; P, 11.9; S, 12.3. Found: N, 10.9; P, 11.6; S, 12.4.

S,S-Diethyl Chlorodithiophosphate (X) (GRN).—This compound was prepared in a manner similar to V, using ethyl mercaptan in place of ethanol. A 23.7% yield of product boiling at 145–150° (22 mm.) was obtained.

This material appears to be a mild vesicant.

For purposes of identification the chloride was converted to the phenylhydrazide melting at 106.5–107°.

Anal. Calcd. for $C_{10}H_{17}N_2OPS_2$: N, 10.14. Found: N, 10.1.

Diethyl Chlorotrithiophosphate (XI) (TWM).—A solution of pyridine (2 moles) in 200 cc. of naphtha (60–90°) was added dropwise to a cooled solution of thiophosphoryl chloride (1 mole) and ethyl mercaptan (2.2 moles) in 500 cc. of naphtha. After stirring for four hours the pyridine hydrochloride was filtered off and the naphtha removed under vacuum. The light yellow residue was fractionated through a three-foot column. The desired product came over at 110–113° (2 mm.). The yield was 56 g. or 25.3% of the theoretical amount.

Anal. Calcd. for $C_4H_{10}ClPS_3$: Cl, 16.08. Found: Cl, 16.3.

This material showed the properties of a vesicant.

Attempts to prepare a phenylhydrazide derivative of diethyl chlorotrithiophosphate were unsuccessful.

Potassium Diethyl Thionophosphate or Potassium O,O-Diethyl Thiolphosphate (II)

(a) **From Diethyl Chlorophosphate and Potassium Hydrosulfide** (GRN).—To an alcoholic solution of potassium hydrosulfide (0.409 mole, from potassium ethoxide and hydrogen sulfide) was added dropwise diethyl chlorophosphate (0.2 mole) in 50 cc. of dry ethyl ether. The reaction mixture warmed appreciably and was allowed to stand until it returned to room temperature. The potassium chloride was filtered off and the filtrate concentrated to a volume of 75 cc. A double volume of ether was added, the solution cooled, and the crystalline product filtered off. One recrystallization from ethanol gave 7.5 g. or 18% of the theoretical amount, m. p. 196–197°

(b) **Hydrolysis of Triethyl Thionophosphate** (TWM).—Triethyl thionophosphate (0.151 mole) was added to 150 cc. of absolute ethanol containing potassium hydroxide (0.16 mole). After a six-hour reflux period the reaction mixture was filtered and the filtrate concentrated to one-third of the original volume. From the cooled solution the product separated as fine white needles, m. p. 197–197.5°. The yield was 15.4 g. or 73.7% of the theoretical amount.

Anal. Calcd. for $C_4H_{10}O_3PSK$: S, 15.39; P, 14.89; K, 18.77. Found: S, 15.3; P, 15.5; K, 18.6.

A mixed melting point of this salt with the product of (a) gave no depression.

(c) **Hydrolysis of Diethyl Chlorothionophosphate** (TWM).—Diethyl chlorothionophosphate (0.111 mole) was added dropwise to 150 cc. of absolute ethanol containing potassium hydroxide (0.218 mole). The reaction mixture warmed until the ethanol began to reflux. After stirring for two hours the potassium chloride was filtered off and the filtrate concentrated to one-fourth the original volume. Addition of dry ether caused the product to separate as white needles. Recrystallization from absolute ethanol gave needles melting at 197°. The yield was 5 g. or 21.6% of the theoretical amount.

A mixed melting point of this salt with the product of (a) gave no depression.

Potassium O,O-Diethyl Thiolthionophosphate (III) (GRN).—Diethyl chlorothionophosphate (0.122 mole) was added dropwise to an alcoholic solution of potassium hydrosulfide (0.244 mole, from potassium ethoxide and hydrogen sulfide). The reaction mixture warmed until the ethanol began to reflux. After stirring for two hours the potassium chloride was filtered off and the filtrate concentrated to one-fourth the original volume. Upon addition of a triple volume of ether the product separated as platelets, m. p. 152–153°.

Recrystallization from a mixture of absolute ethanol and ether (1:2) gave 6.5 g. of fine white needles, m. p. 156–157°. The yield of recrystallized material was 23.6% of the theoretical amount.

A few of these crystals exposed to the atmosphere liquefied in about three minutes.

Lead O,O-Diethyl Thiolthionophosphate (VIII) (TWM).—To an aqueous solution of potassium O,O-diethyl thiolthionophosphate (0.028 mole) was added a calculated amount of lead acetate in water. The white oil which separated from the solution solidified upon cooling in an ice-chest. Recrystallization from ether resulted in thick prismatic needles, m. p. 74°.

Anal. Calcd. for $C_8H_{20}O_4P_2S_4Pb$: S, 22.18; P, 10.73; Pb, 35.84. Found: S, 21.8; P, 10.5; Pb, 34.7.

Part B. *n*-Butyl Compounds

***n*-Butyl Dichlorothionophosphate** (GRN).—*n*-Butanol (4 moles) was added dropwise to thiophosphoryl chloride (4 moles) at a temperature of 80°. The temperature was raised to 100–120° and held there for five hours. Liberated hydrogen chloride and unreacted thiophosphoryl chloride were removed by distillation and the water-white product distilled at 81–82° (10 mm.). The yield was 298 g. or 30.5% of the theoretical amount.

Anal. Calcd. for $C_4H_9OPSCl_2$: Cl, 34.25. Found: Cl, 34.8.

Di-(*n*-butyl) Chlorothionophosphate (GRN).—Pyridine (1.58 moles) was added to a solution of 700 cc. of naphtha (60–90°), *n*-butanol (1.56 moles), and *n*-butyl dichlorothionophosphate (1.44 moles) at such a rate that the temperature did not rise above 40°. After stirring for six hours the pyridine hydrochloride was filtered off and the naphtha removed under vacuum. The residue was distilled from a Claissen flask at 92–115° (2 mm.) and fractionated through a three-foot column. The fraction coming over at 95–98° (2 mm.) was taken as the product. The yield was 37.5 g. or 23.3% of the theoretical amount.

The analysis for chlorine was 1.7% high indicating an impure sample. The sample, however, was considered sufficiently pure for the next synthesis.

Mercuric Di-(*n*-butyl) Thiolthionophosphate from Di-(*n*-butyl) Chlorothionophosphate (IX) (GRN).—Di-(*n*-butyl) chlorothionophosphate (0.123 mole) was added dropwise to an alcoholic solution of sodium hydrosulfide (0.245 mole, from sodium ethoxide and hydrogen sulfide). After refluxing for two hours the alcohol solution was concentrated to a few milliliters. An excess of water was added and the water insoluble material removed by several extractions with ethyl ether. Addition of an aqueous solution of mercuric chloride resulted in the separation of a white oil and mercuric sulfide. The oil was extracted with ether, the solution dried and evaporated. The crystalline mass was taken up in methanol and filtered through a talc pad to remove last traces of mercuric sulfide. Long prismatic needles separated from the cooled solution, m. p. 61–62°.

Di-(*n*-butyl) Thiolthionophosphate (GRN).—Phosphorus pentasulfide (2 moles) was added in small portions to *n*-butanol (8 moles) at 70–80°. The temperature rose gradually until the reaction became violent. The flask was finally heated by an oil-bath at 100–110° for two hours. The reaction was accompanied by a copious evolution of hydrogen sulfide. Titration of the reaction product in a benzene–isopropanol mixture (1:1) indicated the solution was approximately 80% di-(*n*-butyl) thiolthionophosphate.

Mercuric Di-(*n*-butyl) Thiolthionophosphate from the Reaction Product of *n*-Butanol and Phosphorus Pentasulfide (IX) (GRN).—The reaction product (0.5 mole) of *n*-butanol and phosphorus pentasulfide was neutralized with a 10% solution of sodium hydroxide. The aqueous solution was washed twice with ethyl ether then treated with an aqueous solution of mercuric chloride (0.25 mole). The water-white oil which separated was taken up in ether, the solution dried, and evaporated in a large dish. The crystalline product melted at 56–57°. One recrystallization from methanol produced long white needles melting at 61–62°.

A mixed melting point with mercuric di-(*n*-butyl) thiolthionophosphate obtained from di-(*n*-butyl) chlorothionophosphate showed no depression.

Anal. Calcd. for $C_{16}H_{36}O_4P_2S_4Hg$: P, 9.06; S, 18.7; Hg, 29.20. Found: P, 9.06; S, 18.4; Hg, 28.5.

Apparatus

All melting points were taken on a Fisher melting point block.

The fractionating column employed was a three-foot column with a total reflux head. The column was externally heated and packed with glass helices.

Acknowledgment.—We are indebted to Dr. C. F. Prutton for continued interest during the course of this investigation.

Summary

1. Five acid chlorides of the thiophosphoric acid esters have been synthesized and identified in the chemical literature for the first time.

2. Certain new metallic salts and phenyhydrazide derivatives of dialkyl thiophosphoric acids have been synthesized.

3. The probability of the existence of resonance in the diethyl thionophosphate ion (or O,O-diethyl thiolphosphate ion) has been indicated.

4. The chief product obtained from the reaction of phosphorus pentasulfide with aliphatic alcohols has the O,O-dialkyl thiolthionophosphate structure. This is demonstrated by a comparison of the metallic salts of the phosphorus pentasulfide reaction product with corresponding salts obtained by unequivocal syntheses through the acid chloride intermediates.

CLEVELAND 17, OHIO RECEIVED MAY 31, 1945

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Reaction of Tetraacetylglucosyl Chloride with Aromatic Hydrocarbons in the Presence of Aluminum Chloride

BY CHARLES D. HURD AND WILLIAM A. BONNER[1]

In view of the widespread use of anhydrous aluminum chloride in organic chemistry, the very limited application of this catalyst to the carbohydrate series is rather surprising. The earliest study involving anhydrous aluminum chloride in the sugar series was in 1901 when Von Arlt[2] and Skraup and Kremann[3] showed that chloroform solutions of sugar acetates yielded the acetylated glycosyl chlorides if treated with aluminum chloride and phosphorus pentachloride. Hudson and Johnson[4] and Brauns[5] later extended the same reaction. A new observation was disclosed in 1926 by Kunz and Hudson[6] who found that aluminum chloride not only functioned as a chlorinating agent, but also served as catalyst for the inversion of certain of the asymmetric centers within the sugar molecule. In this reaction lactose octaacetate yielded heptaacetylneolactosyl chloride. By hydrolytic and oxidation methods[7] these investigators proved neolactose to be 4-(β-D-galactosyl)-D-altrose. The isomerization of lactose (4-(β-D-galactosyl)-D-glucose), therefore, affected positions 2 and 3 of the glucose part of the molecule. Hudson[8] noticed similar inversions of the second and third carbon atoms in the reducing sugar unit when cellobiose octaacetate was employed. More recently this reaction has been employed[9] as a means of preparing altrose.

The purpose of the present investigation was to ascertain whether hemiacetal halides in the sugar series could be induced to react with aromatic hydrocarbons in a manner analogous to the Friedel–Crafts reaction

$$RX + HAr \xrightarrow{AlCl_3} RAr + HX$$

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[1] Corn Products Refining Company Fellow, 1941–1944.

[2] Von Arlt, *Monatsh.*, **22**, 144 (1901).

[3] Skraup and Kremann, *ibid.*, **22**, 375 (1901).

[4] Hudson and Johnson, THIS JOURNAL, **38**, 1226 (1916).

[5] Brauns, *ibid.*, **44**, 401 (1922).

[6] Kunz and Hudson, *ibid.*, **48**, 1978, 2435 (1926).

[7] Kunz and Hudson, *ibid.*, **48**, 2435 (1926).

[8] Hudson, *ibid.*, **48**, 2002 (1926).

[9] Richtmyer and Hudson, *ibid.*, **57**, 1716 (1935); Hockett and Chandler, *ibid.*, **66**, 627 (1944).