aspiration. The residue was taken up in benzene–ether, washed with 5% potassium hydroxide and with water until neutral, then dried over sodium sulfate. The solvent was removed by aspiration and the residue topped at 60° (0.3 mm.). The tan liquid product weighed 66.8 g. (84% yield).

Anal. Calcd. for $C_{10}H_{24}O_4P_2S_4$: S, 32.0; P, 15.3. Found: Br, 0.1; S, 32.1; P, 15.5; $n^{20}D$ 1.5368.

Reaction of Zinc Chloride with O,O-Diethyl Hydrogen Phosphorodithioate in Benzene.—A mixture of 100 g. of a 39% solution of O,O-diethyl hydrogen phosphorodithioate in benzene and 2.72 g. (0.02 mole) of crushed, anhydrous zinc chloride was stirred and refluxed, and the hydrogen chloride evolved titrated continuously with sodium hydroxide using phenolphthalein indicator. Nitrogen was passed through the system to ensure the prompt removal of hydrogen chloride. In 30 minutes about 75% of the theoretical quantity of hydrogen chloride was evolved and after 40 more minutes, 100%. When about 50% of the hydrogen chloride was evolved, the mixture became homogeneous.

Acknowledgment.—Grateful acknowledgment is made to Dr. R. M. Speck, Mr. G. Buntin, Dr. K. Brack, Dr. D. L. Christman and Dr. R. T. Hall of the Hercules Research Center and to Dr. E. N. Woodbury, Dr. K. D. Ihde and Mr. H. M. Taft of the Hercules Agricultural Chemical Laboratory for their contributions to this work.

WILMINGTON, DEL.

[CONTRIBUTION FROM THE RESEARCH CENTER, HERCULES POWDER CO.]

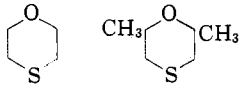
New Organophosphorus Derivatives of *p*-Thioxane and 2,6-Dimethyl-*p*-thioxane with Insecticidal and Acaricidal Activity

BY A. H. HAUBEIN[1]

RECEIVED MAY 15, 1958

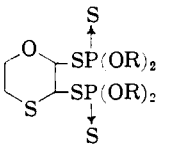
Several new organophosphorus derivatives of *p*-thioxane (I) and 2,6-dimethyl-*p*-thioxane (II) have been synthesized and found to have insecticidal and acaricidal activity. These compounds were prepared by reaction of the corresponding chloro-*p*-thioxanes with ammonium O,O-diethyl phosphorodithioate in acetone solution or with O,O-diethyl hydrogen phosphorodithioate in benzene solution using catalytic quantities of anhydrous zinc chloride. The synthesis of the chloro-*p*-thioxanes is described. Chlorination of *p*-thioxane in refluxing carbon tetrachloride produced 2,3-dichloro-*p*-thioxane (XVI). Chlorination at −10° in carbon tetrachloride produced an insoluble sulfonium chloride which rearranged at 0 to 25° to give 3-chloro-*p*-thioxane (XX) and hydrogen chloride. 3-Chloro-*p*-thioxane eliminates hydrogen chloride in refluxing benzene to produce thioxene, a new route to this compound. Hydrogen chloride added to thioxene to give 2-chloro *p*-thioxane. Some structure–activity relationships of the organophosphorus compounds are postulated.

During the course of the synthesis of compounds related in structure to 2,3-*p*-dioxanedithiol S,S-bis-(O,O-diethyl phosphorodithioate),[2] a number of organophosphorus derivatives of *p*-thioxane (*p*-oxathiane) (I) and 2,6-dimethyl-*p*-thioxane (2,6-dimethyl-*p*-oxathiane) (II) were found to have insecticidal and acaricidal activity. The compounds, the general formulas of which are given below, were

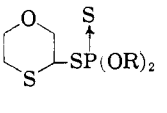


I II

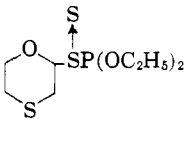
prepared and tested to determine the effect of structure on biological activity.



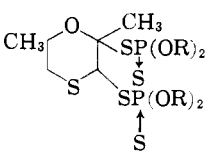
III, R = CH_3
IV, R = C_2H_5
V, R = i-C_3H_7



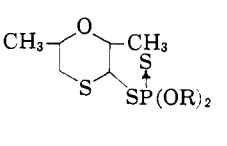
VI, R = CH_3
VII, R = C_2H_5
VIII, R = i-C_3H_7



IX



X, R = CH_3
XI, R = C_2H_5
XII, R = i-C_3H_7

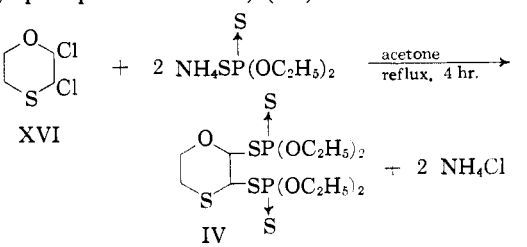


XIII, R = CH_3
XIV, R = C_2H_5
XV. R = i-C_3H_7

(1) Presented in part before the Division of Agricultural and Food Chemistry at the 133rd Meeting of the American Chemical Society, San Francisco, Calif., April, 1958.

(2) Also known as Delnav, a registered trademark of Hercules Powder Co.

The esters were synthesized from the corresponding chlorothioxanes by treatment with the ammonium salt of the dialkyl hydrogen phosphorodithioate in refluxing acetone as illustrated by the preparation of 2,3-*p*-thioxanedithiol S,S-bis-(O,O-diethyl phosphorodithioate) (IV).



XVI IV

Other salts such as pyridine, sodium or potassium may be used successfully in this reaction provided a suitable solvent is employed.[3] The free acid may be used in refluxing benzene, employing anhydrous zinc chloride as catalyst.[4]

The 2,3-dichloro-*p*-thioxane (XVI) was prepared by chlorinating *p*-thioxane (I) in refluxing carbon tetrachloride. The product was isolated by vacuum distillation. During this operation it was difficult to maintain constant pressure because of elimination of hydrogen chloride. Once distilled, however, the product was thermally stable and could be fractionated readily. The distillate is water-white and reacts with the moisture of the air to liberate hydrogen chloride. On storage at 0°, crystals slowly form which, when recrystallized from ether–petroleum ether mixture, gave white crystals, m.p. 40.5–41°. These darken on storage unless care is taken to exclude moisture.

(3) A. H. Haubein, U. S. Patents 2,725,331 (1955) and 2,766,167 (1956).

(4) R. M. Speck, U. S. Patent 2,815,350 (1957).

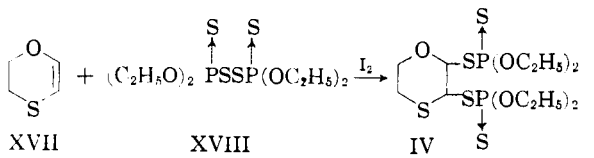
The reaction of XVI with silver acetate in benzene produced a crystalline 2,3-*p*-thioxanediol diacetate, m.p. 73.4–74°. With the phenyl Grignard reagent a crystalline 2,3-diphenyl-*p*-thioxane, m.p. 95–95.5°, was formed using the procedure used for the preparation of 2,3-diphenyl-*p*-dioxane from 2,3-dichloro-*p*-dioxane.[5]

The dichlorothioxane was assigned the structure 2,3-dichloro-*p*-thioxane (XVI) because it liberated iodine from potassium iodide in acetone solution.[6] Also hydrolysis produced one mole of glyoxal characterized as the 2,4-dinitrophenylosazone as in the case of 2,3-dichloro-*p*-dioxane.[7] Furthermore, chlorine was added to thioxene (XVII) to produce a dichlorothioxane whose infrared absorption spectrum was identical with XVI.

The phosphate ester IV obtained from 2,3-dichloro-*p*-thioxane was a tan, semi-viscous, non-distillable liquid. Biological tests were conducted with the crude material. It could be purified by partition chromatography. Using an acetonitrile–heptane-on-Celite system it gave a chromatogram which shows two major peaks which represent 12 and 75% of the crude product. Infrared spectra of these two materials indicate they might be *cis* and *trans* isomers as was found in the corresponding dioxane derivative.[8] No further work has been done on the stereochemistry of the disubstituted compounds.

Hydrolysis to the osazone using the procedure of Dunn[9] showed the ester IV to contain 89% of the 2,3-isomer.

The ester IV was also synthesized by the addition of the disulfide XVIII to thioxene XVII in the presence of catalytic amounts of iodine, a reaction described by Diveley, *et al.*[8]

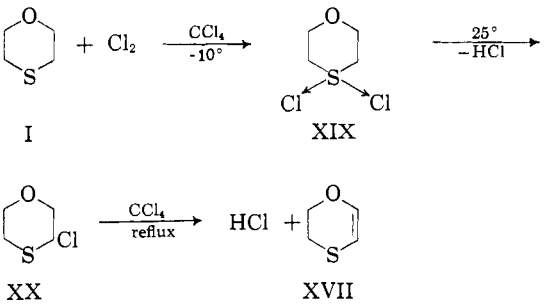


XVII XVIII IV

In like manner, 2,6-dimethyl-2,3-*p*-thioxanedithiol S,S-bis-(O,O-diethyl phosphorodithioate) (XI) was prepared from 2,6-dimethyl-2,3-dichloro-*p*-thioxane which in turn was obtained by chlorinating dimethyl-*p*-thioxane in refluxing carbon tetrachloride solution. The chlorinated product liberates iodine from potassium iodide in acetone solution and is hydrolyzed to pyruvic aldehyde characterized as the 2,4-dinitrophenylosazone.[10]

Chlorination of *p*-thioxane (I) in carbon tetrachloride at −10° produces a precipitate of the sulfonium chloride XIX which rearranges at 0 to 25° to liberate a mole of hydrogen chloride. 3-Chloro-*p*-thioxane (XX) was the structure assigned to the product by analogy with the low temperature chlorination and rearrangement of mustard gas.[11]

3-Chloro-*p*-thioxane eliminates hydrogen chloride so readily it cannot be isolated by distillation. In refluxing carbon tetrachloride or benzene it is dehydrohalogenated to thioxene.



I XIX

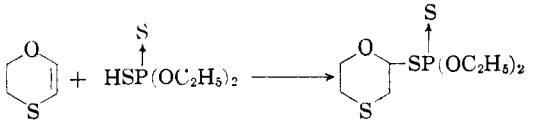
XX XVII

This material was characterized by hydrolysis to β-hydroxyethylmercaptoacetaldehyde, identified as the 2,4-dinitrophenylhydrazone as reported by Parham, *et al.*[12] This is a relatively simple method of preparing thioxene. The thioxene prepared by this method will contain thioxane as a contaminant.

3-*p*-Thioxanethiol S-(O,O-diethyl phosphorodithioate) (VII) prepared from 3-chloro-*p*-thioxane (XX) was a yellow, non-distillable liquid whose chromatogram shows a major peak which represents 75% of the crude product.

The addition of O,O-diethyl hydrogen phosphorodithioate (XXI) to thioxene produced a phosphorodithioate ester (IX) which was different from the 3-isomer VII. The infrared absorption spectra of these compounds differ in the 9.1 and 9.4 μ region, respectively. The absorption at 9.8 and 10.4 μ is attributed to the $-\overset{\downarrow}{\underset{S}{SP}}(OC_2H_5)_2$ group.[13]

The ester IX was assigned the structure 2-*p*-thioxanethiol S-(O,O-diethyl phosphorodithioate), since the acid adds to ethylenic double bonds as a mercaptan[14] and since alcohols are known to add to thioxene to produce 2-alkoxy-*p*-thioxanes.[12] As



XVII XXI IX

further proof of the structure of the ester IX, hydrogen chloride was added to thioxene. Again the chlorothioxane XXII formed eliminated hydrogen chloride too readily to be isolated, but reaction with ammonium diethyl phosphorodithioate in acetone solution resulted in a product whose infrared spectrum was identical with the O,O-diethyl hydrogen phosphorodithioate-thioxene adduct (IX).

(5) R. K. Summerbell and H. E. Lunk, THIS JOURNAL, **79**, 4802 (1957).

(6) H. Finkelstein, *Ber.*, **43**, 1530 (1910).

(7) J. Boeseken, F. Tellegen and P. C. Henriquez, *Rec. trav. chim.*, **50**, 909 (1931).

(8) W. R. Diveley, A. H. Haubein, A. D. Lohr and P. B. Moseley, THIS JOURNAL, **81**, 139 (1959).

(9) C. L. Dunn, *J. Agr. Food Chem.*, **6**, 203 (1958).

(10) C. Bulow and F. Seidel, *Ann.*, **439**, 55 (1924).

(11) W. E. Lawson and T. P. Dawson, THIS JOURNAL, **49**, 3119 (1927).

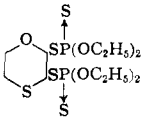
(12) W. E. Parham, I. Gordon and J. D. Swalen, *ibid.*, **74**, 1824 (1952).

(13) R. A. McIvor, G. A. Grant and C. F. Hubley, *Can. J. Chem.*, **34**, 1611 (1956).

(14) G. R. Norman, W. M. Le Suer and T. W. Mastin, THIS JOURNAL, **74**, 161 (1952).

TABLE I

PESTICIDAL TOXICITY OF ORGANOPHOSPHORUS DERIVATIVES OF *p*-THIOXANE AND *p*-DIOXANE[a]



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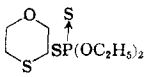
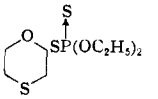
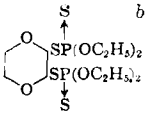


VII



IX



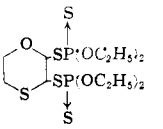
XXIII[b]

Pest	Concn., %	Kill, %	Kill, %	Kill, %	Kill, %
House fly	0.1	92	100	0	94
(*Musca domestica*)	.05	24	100	..	21
	.025	..	64	..	6
Pea aphid	.1	100	100	90	100
(*Macrosiphum*	.025	95	100	0	80
pisi)	.01	55	100	..	..
Two-spotted mite	.05	100	100	100	100
(*Tetranychus*	.005	100	100	30	100
bimaculatus)	.001	90	64	..	100
	.0005	44	53	..	100

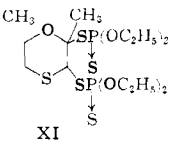
[a] Contact spray tests were used to determine toxicity. [b] Prepared by Diveley, *et al.*[8]

TABLE II

PESTICIDAL TOXICITY OF BIS-(DIETHYL PHOSPHORODITHIOATE) OF *p*-THIOXANE AND 2,6-DIMETHYL-*p*-THIOXANE



IV



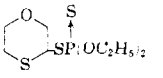
XI

Pest	Concn., %	Kill, %	Kill, %
Mexican bean beetle[a]	0.1	90	100
(*Epilachna varivestis* Muls)	.05	50	100
Two-spotted mite[b] (*Tetranychus bimaculatus*)	.0005	40	100

Contact spray tests used to determine toxicity. [b] Cut-stem systemic test used to determine toxicity.

TABLE III

PESTICIDAL TOXICITY OF MONO(DIETHYL PHOSPHORODITHIOATES) OF *p*-THIOXANE AND 2,6-DIMETHYL-*p*-THIOXANE



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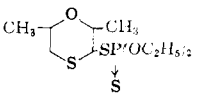
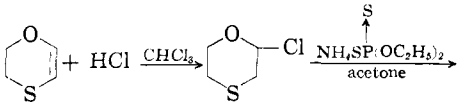


XIV

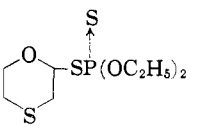
Pest	Concn., %	Kill, %	Kill, %
Housefly[a]	0.1	100	100
(*Musca domestica*)	.025	64	100
Pea aphid[b] (*Macrosiphum pisi*)	.0005	0	100

[a] Contact spray tests used to determine toxicity. [b] Cut-stem systemic test used to determine toxicity.

Unlike thioxane in the low temperature chlorination and rearrangement reaction, 2,6-dimethyl-*p*-thioxane produced a stable 3-chloro-2,6-dimethyl-



XVII XXII



IX

p-thioxane that could be distilled. This material would not eliminate hydrogen chloride when refluxed with trimethylamine in toluene. Reaction of 3-chloro-2,6-dimethyl-*p*-thioxane with O,O-diethyl ammonium phosphorodithioate in acetone solution produced the phosphorodithioate ester XIV.

The toxicities of the O,O-diethyl phosphorodidithioate esters of *p*-thioxane (I) and 2,6-dimethyl-*p*-thioxane (II) to insects and mites, shown in Tables I, II and III, indicate certain structure–activity relationships which have been postulated as: 1. The *p*-thioxane compounds IV and VII are more toxic to flies and aphids but less toxic to mites than the *p*-dioxane derivative XXIII. 2. The *p*-thioxane compound in which the phosphorodithioate ester group is located in the 3-position (VII) is more toxic than the compound containing the 2,3-vicinal bis-phosphorodithioate ester group (IV). 3. The *p*-thioxane compound containing the phosphorodithioate ester group in the 3-position (VII) is more toxic than the compound with the ester

group in the 2-position (IX). 4. The 2,6-dimethyl-*p*-thioxane phosphorodithioate esters (XI and XIV) are more toxic than the corresponding *p*-thioxane compounds (IV and VII).

Experimental

2,3-Dichloro-*p*-thioxane (XVI).—Chlorine, at a rate of 35 g. per hr., was passed into a solution of 208 g. (2.0 moles) of *p*-thioxane (Thiokol Chemical Corporation) in 400 ml. of carbon tetrachloride at reflux. Under these conditions all the chlorine reacted. After 284 g. (4.0 moles) of chlorine had been added, solvent was removed under aspirator vacuum at 60°. The residue which weighed 350 g. was given a simple distillation at 18 mm. A fraction weighing 249 g. was collected which boiled at 91–104°. This material was fractionally distilled to give 169 g. of liquid, b.p. 55–57° (0.1 mm.). On standing at 0° for several weeks this material crystallized. The crystals were recrystallized twice from ether–petroleum ether mixture (1:3) to give 96 g. of white crystals of XVI, m.p. 40.5–41°.

Anal. Calcd. for $C_4H_6Cl_2OS$: Cl, 41.1; S, 18.5. Found: Cl, 41.2; S, 18.4.

The crystals become dark on exposure to air because of reaction with moisture, with liberation of hydrogen chloride. The crystals liberate iodine from potassium iodide in acetone.[6] An approximate 50-mg. sample was cleaved and hydrolyzed in the presence of mercuric chloride and 2,4-dinitrophenylhydrazine according to Dunn[9] to give 98.8 % of the theoretical amount of the 2,4-dinitrophenylosazone of glyoxal.

2,3-Diphenyl-*p*-thioxane.—An 8-g. (0.05 mole) sample of 2,3-dichloro-*p*-thioxane was treated with phenylmagnesium bromide as described by Summerbell and Lunk.[5] The crude product did not crystallize. After distillation, a fraction, wt. 5.7 g., b.p. 157–178° (1.0 mm.), solidified. Crystallization from aqueous alcohol gave a material of m.p. 95–95.5°.

Anal. Calcd. for $C_{16}H_{16}OS$: S, 12.5. Found: S, 12.5.

2,3-*p*-Thioxanediol Diacetate.—An 8-g. (0.05 mole) sample of 2,3-dichloro-*p*-thioxane was treated with silver acetate in benzene according to the procedure of Summerbell and Lunk.[5] The product (7.7 g.) was obtained as a viscous liquid which slowly crystallized. Recrystallization from hexane gave white crystals, m.p. 73.4.°

Anal. Calcd. for $C_8H_{12}O_5S$: S, 14.6. Found: S, 14.9.

2,3-Dichloro-2,6-dimethyl-*p*-thioxane.—Chlorine, at a rate of 35 g. per hour, was passed through 66 g. (0.5 mole) of 2,6-dimethyl-*p*-thioxane, b.p. 104–105.1°, $n^{20}D$ 1.4870 (Thiokol Chemical Corporation), in 250 ml. of carbon tetrachloride at reflux. The chlorine completely reacted at this rate. After 71 g. (1.0 mole) of chlorine was added, solvent was removed under aspirator vacuum at 60°. The residue was given a simple distillation at 18 mm. and the fraction, wt. 35 g., b.p. 73–92°, collected and fractionated to give 11 g., b.p. 61–63° (0.4 mm.).

Anal. Calcd. for $C_6H_{10}Cl_2OS$: S, 15.9; Cl, 35.3. Found: S, 16.4; Cl, 34.9.

This fraction liberated iodine from potassium iodide in acetone solution.[6] Cleavage and hydrolysis in the presence of mercuric chloride and 2,4-dinitrophenylhydrazine[9] gave an orange precipitate of the 2,4-dinitrophenylosazone of pyruvic aldehyde which melted above 250° and gave a typical blue color with aqueous sodium hydroxide.[10]

Anal. Calcd. for $C_{15}H_{12}N_8O_8$: N, 25.9. Found: N, 25.6.

3 Chloro-*p*-thioxane (XX).—A 52-g. (0.5 mole) sample of *p*-thioxane in 150 ml. of carbon tetrachloride was cooled to −10° and chlorine was added through a sintered sparge tube at a rate of 15 g. per hr. No hydrogen chloride was evolved. A white solid formed which was presumed to be the sulfonium chloride of *p*-thioxane by analogy with mustard gas.[11] After 32 g. (0.45 mole) of chlorine had reacted,[15] the chlorine sparge was replaced by nitrogen and the off-gas collected in water and titrated with standard base. The stirred suspension was allowed to warm to room temperature. Hydrogen chloride was evolved and the solution became homogeneous. After 3 hr. at room temperature hydrogen chloride evolution had virtually ceased. 0.5 mole having been evolved. The 3-chloro-*p*-thioxane dehydrohalogenated so readily that it could not be isolated, but was used in solution immediately for further reactions.

p-Thioxene (XVII).—To a 104-g. (1.0 mole) sample of *p*-thioxane (I) in 500 ml. of carbon tetrachloride at −10° was added 78 g. (1.1 moles) of chlorine. After one mole of chlorine had reacted the suspension became yellow, indicating unreacted chlorine. No hydrogen chloride, however, was evolved.[15] The suspension was filtered in the absence of moisture through a sintered glass jacketed funnel kept at −10 to −15°. The precipitate was washed three times with cold (−10°) carbon tetrachloride, to remove any unreacted thioxane, and suspended in 200 ml. of benzene. The suspension was allowed to warm to room temperature during which time the solid went into solution and hydrogen chloride was evolved. After the hydrogen chloride evolution diminished (2 hr.), the solution was heated to reflux and hydrogen chloride was again evolved. After 4 hr. at reflux hydrogen chloride evolution ceased. The solution was distilled through a Vigreux column 20 cm. long and the cut, 36 g., b.p. 52–55° (28 mm.,), was fractionated again. The cut, b.p. 47–48° (19 mm.), $n^{20}D$ 1.5209, contained a maximum of 20% of thioxane according to infrared absorption. A sample was hydrolyzed with aqueous sulfuric acid in the presence of 2,4-dinitrophenylhydrazine to give yellow crystals of β-hydroxyethylmercaptoacetaldehyde 2,4-dinitrophenylhydrazone, m.p. 73–74°.[12]

2-Chloro-*p*-thioxane (XXII).—A 40-g. sample of thioxene containing 50% thixoane dissolved in 100 ml. of chloroform was saturated with dry hydrogen chloride at −10°. The solution was sparged with nitrogen at 0° for 1 hr. The 2-chloro-*p*-thioxane dehydrohalogenated so readily it could not be isolated and so was used in solution immediately upon its preparation.

3-Chloro-2,6-dimethyl-*p*-thioxane.—A 71-g. (0.54 mole) sample of 2,6-dimethyl-*p*-thioxane (II) in 100 ml. of carbon tetrachloride was cooled to −10° and 36 g. (0.5 mole) of chlorine was added. During the addition a tacky solid formed, but no hydrogen chloride was evolved. The suspension was sparged with nitrogen at 25° for 2 hr. during which time hydrogen chloride was evolved and the solid went into solution. A simple distillation gave 58 g. of distillate, b.p. 39–70° (0.3 mm.), which was fractionated through a Vigreux column 20 cm. long. A fraction was collected with b.p. 95–96° (15 mm.), wt. 18 g.

Anal. Calcd. for $C_6H_{11}ClOS$: Cl, 21.4; S, 19.2. Found: Cl, 21.6; S, 19.6.

Ammonium O,O-Diethyl Phosphorodithioate.—A solution containing 194 g. (1.0 mole) of 96% O,O-diethyl hydrogen phosphorodithioate[16] in 300 ml. of benzene was cooled in a water-bath and saturated with ammonia. Since the ammonium salt is soluble in excess ammonia the solution was sparged with nitrogen for 2 hr. The solid was filtered and air-dried, wt. 157 g.

2,3-*p*-Thioxanedithiol S,S-Bis-(O,O-diethyl Phosphorodithioate) (IV). Ammonium Salt Procedure.—To 5 g. 0.03 mole) of 2,3-dichloro-*p*-thioxane (XVI) dissolved in 50 ml. of acetone was added a solution of 13 g. (0.065 mole) of ammonium O,O-diethyl phosphorodithioate in 50 ml. of acetone. The resulting solution was refluxed for 4 hr., during which ammonium chloride precipitated. After cooling, the suspension was poured into water, extracted with benzene, and the benzene layer dried over anhydrous sodium sulfate. Solvent was removed at reduced pressure and the residue topped at 80° (0.5 mm.) to leave 12 g. (85% yield) of yellow, semi-viscous liquid.

Anal. Calcd. for $C_{12}H_{26}O_5P_2S_5$: P, 13.1; S, 33.9. Found: P, 12.8; S. 33.7.

The chromatogram of this material according to the procedure of Diveley, *et al.*,[8] showed the presence of two major constituents representing 12 and 75% of the crude product. Cleavage–hydrolysis of the material according to Dunn[9] gave 89% the theoretical quantity of osazone.

Pyridine Salt Procedure.—A 36-g. (0.21 mole) sample of 2,3-dichloro-*p*-thioxane was treated with 0.42 mole of the pyridine salt of O,O-diethyl hydrogen phosphorodithioate as

(15) Sometimes hydrogen chloride begins to be evolved when about three-fourths of the theoretical quantity of chlorine has been added. If this happens, the chlorine addition is stopped. The product will then contain unreacted thioxane.

(16) J. H. Fletcher, J. C. Hamilton, I. Hechenbleikner, E. I. Hoegberg, B. J. Sertl and J. T. Cassaday, THIS JOURNAL, **72**, 2461 (1950).

described by Diveley, *et al.*[8] The product was obtained as a dark liquid, wt. 63 g. (64% yield).

Anal. Calcd. for $C_{12}H_{26}O_5P_2S_5$: S, 33.9. Found: S, 33.2.

Catalytic Procedure.—A 17-g. (0.1 mole) sample of 2,3-dichloro-*p*-thioxane was treated with O,O-diethyl hydrogen phosphorodithioate in refluxing benzene using anhydrous zinc chloride as catalyst according to the procedure described by Speck.[4] A 51% yield of product was obtained.

Anal. Calcd. for $C_{12}H_{26}O_5P_2S_5$: S, 33.9. Found: S, 33.0.

Disulfide Method.—Bis-(diethoxyphosphinethioyl) disulfide (XVIII) prepared by the method of Bartlett, *et al.*,[17] was added to 5 g. (0.05 mole) of thioxene according to the procedure of Diveley, *et al.*[8] A 76% yield of 2,3-*p*-thioxanedithiol S,S-bis-(O,O-diethyl phosphorodithioate) (IV) was obtained.

Anal. Calcd. $C_{12}H_{26}O_5P_2S_5$: S, 33.9. Found: S, 33.9.

2,6-Dimethyl-2,3-*p*-thioxanedithiol S,S-bis-(O,O-diethyl phosphorodithioate) (XI) was prepared by the ammonium salt method by treating 5 g. (0.025 mole) of 2,3-dichloro-2,6-dimethyl-*p*-thioxane with 11 g. (0.054 mole) of ammonium O,O-diethyl phosphorodithioate in refluxing acetone. The product was a viscous yellow oil, wt. 9.1 g., 72% yield.

Anal. Calcd. for $C_{14}H_{30}O_5P_2S_5$: P, 12.4. Found: P, 11.5.

3-*p*-Thioxanethio S-(O,O-Diethyl Phosphorodithioate) (VII).—A solution of 3-chloro-*p*-thioxane (XX) in carbon tetrachloride was prepared by adding 35 g. (0.5 mole) of chlorine to 57 g. (0.55 mole) of thioxane in 150 ml. of carbon tetrachloride at −10°. The suspension was sparged at 5 to 10° with nitrogen until no more hydrogen chloride was evolved (2 hr.). To this was added a solution of 0.49 mole of the pyridine salt of O,O-diethyl hydrogen phosphorodithioate in 250 ml. of benzene. The reaction mixture was stirred at room temperature for 2 hr. and refluxed for 4 hours. The product, isolated in the manner described for the pyridine method, was a yellow liquid, wt. 120 g. (85% yield). The chromatogram of this material as determined by the method of Diveley, *et al.*,[8] shows this material to be 75.6% of one constituent.

(17) J. H. Bartlett, H. W. Rudel and E. B. Cyphers, U. S. Patent 2,705,694 (1955).

Anal. Calcd. for $C_8H_{17}O_3PS_3$: P, 10.7; S, 33.3; Cl, 0.0. Found: P, 11.2; S, 33.8; Cl, 0.3.

2-*p*-Thioxanethiol S-(O,O-Diethyl Phosphorodithioate) (IX). From 2-Chloro-*p*-thioxane (XXII).—To the solution of 2-chloro-*p*-thioxane in chloroform prepared above was added a solution of 0.2 mole of the pyridine salt of O,O-diethyl hydrogen phosphorodithioate (XXI) in 100 ml. of benzene. The reaction mixture was stirred for 2 hr. at room temperature and 4 hr. at reflux. The product was isolated as described for the pyridine method to give 41 g. of yellow liquid whose infrared absorption curve was identical with the product obtained by the addition of O,O-diethyl hydrogen phosphorodithioate to *p*-thioxene.

Anal. Calcd. for $C_8H_{17}O_3PS_3$: P, 10.7; S, 33.3. Found: P, 11.5; S, 32.9.

From Thioxene (XVII).—To 10 g. of thioxene containing 50% thioxane (0.05 mole thioxene) in 50 ml. of benzene was added 3 drops of triethylamine and 10 g. (0.051 mole) of 96% O,O-diethyl hydrogen phosphorodithioate. The solution was refluxed for 4 hr. Titration of an aliquot of the solution with standard base to phenolphthalein end-point showed that 0.047 mole of acid had reacted. The reaction mixture was washed with 10% aqueous base and with water, and dried over anhydrous sodium sulfate. Solvent was removed at 18 mm. to a pot temperature of 60°. The residue was topped at 80° (0.5 mm.) to leave a yellow liquid residue of 8 g. (62% yield).

Anal. Calcd. for $C_8H_{17}O_3PS_3$: P, 10.7. Found: P, 11.3.

2,6-Dimethyl-3-*p*-thioxanethiol S-(O,O-Diethyl Phosphorodithioate) (XIV).—Using the pyridine procedure 29 g. of 3-chloro-2,6-dimethyl-*p*-thioxane was treated with 0.2 mole of the pyridine salt of O,O-diethyl hydrogen phosphorodithioate XXI. The product was a yellow liquid, wt. 39 g. (71% yield).

Anal. Calcd. for $C_{10}H_{21}O_3PS_3$: P, 9.8; S, 30.3. Found: P, 10.4; S, 30.5.

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[CONTRIBUTION FROM THE CHEMICAL CORPS, CHEMICAL RESEARCH DIVISION, CHEMICAL WARFARE LABORATORIES]

Organic Phosphorus Compounds. V.[1] The Preparation of O-Alkyl Alkylphosphonothioic Acids

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The preparation of O-alkyl alkylphosphonothioic acids by limited hydrolysis of the corresponding O,O-dialkyl alkylphosphonothioates with alcoholic alkali was studied in order to determine the optimum reaction conditions. The O-alkyl alkylphosphonothioic acids were also prepared in good yield by the hydrolysis of the corresponding O-alkyl alkylphosphonochloridothioates with aqueous alkali.

The recent resolution of O-ethyl ethylphosphonothioic acid into its optical antipodes[3] which permits the synthesis of the pure enantiomorphs of a number of sulfur-containing organophosphorus inhibitors of cholinesterase and their study in the stereospecific, irreversible inactivation of the enzyme[4] made it desirable to have available a series of O-alkyl alkylphosphonothioic acids.

Kabachnik and co-workers[5] describe the first four members of the series of O-ethyl alkylphosphonothioic acids, $[RP(O)(S)OC_2H_5]H$, where R represents methyl, ethyl, *n*-propyl and *n*-butyl. These homologous monoacids were prepared by a limited, alkaline hydrolysis of the corresponding O,O-diethyl alkylphosphonothioates, $RP(S)(OC_2H_5)_2$ (I). Since our interest was mainly directed toward homologous members of the two series, $CH_3P(O)(OR)SH$ (II) and $C_2H_5P(O)(OR)SH$ (III), in which the R groups were lower alkyl

(1) Paper IV of this series, THIS JOURNAL, **80**, 5937 (1958).

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(3) H. S. Aaron, T. M. Shryne and J. I. Miller, THIS JOURNAL, **80**, 107 (1958).

(4) H. S. Aaron, H. O. Michel, B. Witten and J. I. Miller, *ibid.*, **80**, 456 (1958).

(5) M. I. Kabachnik, N. I. Kurochkin, T. A. Mastryukova, S. T. Ioffe, E. M. Popov and N. P. Rodionova, *Doklady Akad. Nauk S.S.S.R.*, **104**, 861 (1955); *C.A.*, **50**, 11240*a* (1956).