curic thiophosphate could be prepared in fairly good yield even under vigorous reaction conditions, substitution of some functional

group on phenyl group greatly hindered this reaction.

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Studies on the Organophosphorus Insecticides

Part IV. Synthesis and Toxicity of Phosphorates and Phosphorothioates Containing 1-Phenyl-2-acyl-vinyl Group

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The reaction of O,O-dialkyl phosphorochloridates*¹⁾ or phosphorochloridothioates with sodium salts of benzoylacetone and the reaction of trialkyl phosphites with α -chloro-benzoylacetone or acetophenone were attempted with a view to prepare the low toxic phosphorus insecticides containing acyl-vinyl group. It was found that the products did not have a phosphonate-form but a phosphate-form and the phenyl-acyl-vinyl group had linkage with phosphorus atom by the enol-form of next carbonyl group of the phenyl-group.

During a course of an investigation of organophosphorus insecticides, the present author¹⁾ found that the phosphorates containing 1-phenyl-2-carboethoxy-vinyl (II) or 1-methyl-2-phenyl-2'-carboethoxy-vinyl groups (III) are lower toxic than 1-methyl-2-carboethoxy-vinyl phosphate (I) in Phosdrin type phosphorates, though their activity are almost of the same degree (see Table I).

G. Schrader²⁾ also reported that O,O-diethyl-s-phenyl-cyanomethyl phosphorodithioate (V) is lower than O,O-diethyl S-phenyl-cyanomethyl phosphorodithioate (IV) (see Table I).

The present author reported already that the phosphorates containing acetyl-vinyl group (VI), (VII) have good insecticidal activity and high toxicity^{1,3)}. So, it was considered that the introduction of phenyl group into the above phosphorates (VI), (VII) will bring the lowering of the toxicity of the compounds in these series. Then, at first, the reactions of O,O-dialkyl phosphorochloridate (VIII, Y=O) or phosphorochloridothioate (VIII, Y=S) with sodium salt of benzoylacetone⁴⁾ (IX) and, next, the reaction of trialkyl phosphite with γ -chloro-benzoylacetone⁵⁾ (X) were attempted according to the follow-

*1) The phosphorous compounds in this paper were named according to the Drake Committee's Reports (*Chem. Eng. News*, **30**, 4515 (1952)).

1) Y. Nishizawa, *Bull. Agr. Chem. Soc. Japan*, **24**, 261 (1960).

2) G. Schrader, D.R.P., Nr. 1,024,509.

3) Y. Nishizawa, Jap. Pat., Announced No. *Showa* 32-2919 (1960).

4) L. Claisen, *Ber.*, **38**, 695 (1905).

5) A.K. Macbeth, *J. Chem. Soc.*, **123**, 1128 (1923).

FIG. 1. The Infrared Spectrum of O, O-Diethylo-(1-phenyl-2-acetyl-vinyl) phosphoroate (XIa₃)

(XII).

1) The products of the method-A showed strong infrared absorption at 1625 cm⁻¹ which is characteristic absorption spectrum of ethylenic double bond and the absorption spectrum of carbonyl group shifted to 1680 cm⁻¹. It was considered⁶⁾ that this shift occurred by the carbonyl group conjugated with some unsaturated group (see Fig. 1).

2) Alcoholysis of the products of the method-A by sodium alcoholate in an alcoholic solution gave trialkyl phosphorate or phosphorothioate and benzoylacetone. The melting point of copper salt of the benzoylacetone coincided with that of starting benzoylacetone and mixed melting point did not depress. These results showed that the products have phosphorate or phosphorothioate form⁷⁾ (XI).

3) The products of the method-B showed the same infrared absorption spectrum as that of the method-A and the alcoholysis of the products of method-B gave benzoylacetone which has not the chlorine atom.

Then, the formula of the products had to be determined to be (XIa) or (XIb).

4) The infrared absorption spectra of the products showed the absorption of styryl radical at 1588 cm⁻¹ ⁶⁾ (see Fig. 1).

5) The ozonization of the products gave the methyl glyoxal and the benzoic acid.

These results showed that the styryl radical is contained in the products.

The above experimental facts showed that the formula of the products is (XIa).

These products must have geometrical isomers but they are not yet separated. These products did not show the expected lower

6) U.J. Bellamy, *The Infra-red Spectra of Complex Molecules* (1958.)

7) A.N. Pudovik, *J. Gen. Chem. USSR*, **26**, 1605 (1956).

TABLE III. THE ACTIVITY AND THE TOXICITY OF NEW PHOSPHORUS COMPOUNDS

No.	Topical application towards hibernating larvae of rice stem borer (<i>Chilo suppressalis</i> WALKER)		Oral Toxicity towards Mice LD ₅₀ mg/kg
	Kill (%)	γ/larva	
XIa ₁	0	20	78
XIa ₂	100	0.67	13
XIa ₃	100	2	14
XIa ₁	50	6.7	120
XIa ₂	10	20	66
XVII	40	20	>1000
VI	90	6.7	55
VII	70	6.7	24

toxicity but the activity was higher than methyl-acetyl-vinyl phosphorates (VI), (VII) (see Table III).

The phenyl-benzoyl-vinyl phosphorates (XV) were prepared by the above method-B, namely, the reaction of trialkyl phosphite (IX) which ω-chloro-ω-benzoyl-acetophenone⁸⁾ (XIV).

These products (XV) shown the weaker toxicity than the products (XIa) but did not show the activity towards the insects.

The *p*-acetyl-vinyl-phenyl phosphorothioate (XVII) was also prepared by the above method-A, namely, the reaction of O,O-diethyl

phosphorochloridate with potassium salt of *p*-hydroxy-benzalacetone¹⁰⁾ (XVI). This prod-

uct showed the weakest toxicity and activity in this series. The above two compounds (XV), (XVII) could not be distilled without the decomposition, so, the products were purified by silica-gel column-chromatography.

The yield, the physical constants and the microanalytical data of the new phosphorus compounds were shown in Table II, and the activity and the toxicity were also shown in Table III.

EXPERIMENTAL

1) The preparation of O,O-diethyl O-(1-phenyl-2-acetyl-vinyl) phosphorothioate (XIa₁) by the method-A.

To a suspension of 12.6 g (0.2 M) of sodium ethoxide in 300 ml of anhydrous benzene, there was added gradually 32.4 g (0.2 M) of benzoylacetone. The solution became to sirup after two hours with stirring at 50°C and then 37.7 g (0.2 M) of O,O-diethyl phosphorochloridothioate was added to the reaction mixture and refluxed for eight hours at 80°C. The reaction mixture was cooled, washed with water and dried over anhydrous sodium sulfate. After removal of the benzene, the residual oil was distilled at 150~152°C/0.2 mmHg.

The distilled phosphorothioate was dissolved in 200 ml of chloroform and treated with silica-gel column. The pure phosphorothioate was obtained 18.8 g (63%); n_D^{26} 1.5451.

Anal. Calcd. for C₁₄H₁₈O₃PS; P, 10.4; S, 10.7%.

Found.; P, 10.8; S, 10.5%

2) The preparation of O,O-dimethyl O-(1-phenyl-2-acetyl-vinyl) phosphorate (XIa₂) by method-B

Twelve point four grams of trimethyl phosphite was

8) This was prepared by the same manner as A.K. Macbeth's method⁹⁾, namely, the reaction of ω-benzoyl acetophenone⁹⁾ with sulfaryl chloride in ether solution. m.p. 93~94°C (recryst. from ethanol).

9) L. Claisen, *Ber.* **38**, 696 (1905).

10) J.S. Buck, *J. Chem. Soc.*, **121**, 1101 (1922).

added gradually to a solution of 19.7 g (0.1 M) of 2-chloro-benzoylacetone in 50 ml of ether with stirring and sufficient cooling. The temperature of the reaction mixture was raised to 40°C. After refluxing for one hour, the ether was distilled off, and the residual colorless oil was fractionated in vacuo, b.p. 154~157°C/1 mmHg. Yielded 19.2 g. $n_D^{23.5}$ 1.5256.

Anal. Calcd. for $C_{15}H_{15}O_5P$; P, 11.5%

Found.; P, 11.6%

3) The preparation of O,O-diethyl O-(*p*-acetylvinyl-phenyl) phosphorothioate (XVII)

A mixture of 32.4 g (0.2 M) of *p*-hydroxy-benzalacetone, 27.6 g of anhydrous potassium carbonate and 100 ml of methyl isobutyl ketone was heated at about 100°C. Carbon dioxide and water were eliminated and the water was removed from the reaction mixture by azeotropic distillation, and then the reaction mixture was cooled at 60°C. There was added gradually 37.7 g (0.2 M) of O,O-diethyl phosphorochloridothioate to the mixture by stirring. After putting of the phosphorochloridothioate in excess, stirring was further continued for 8 hours at 60~80°C to complete the reaction. Water was added to dissolve the precipitated inorganic salt and organic layer was separated, washed with water and dried over anhydrous sodium sulfate. After removal of the methyl isobutyl ketone in vacuo, 51.3 g of this red oily product was obtained. For further purification, the crude product was purified by column-chromatography using active carbon and alumina, obtaining a pale yellow oily product having a refractive index n_D^{24} 1.5700.

Anal. Calcd. for $C_{14}H_{18}O_4PS$; P, 9.9; S, 10.2%

Found.; P, 10.1; S, 10.5%

4) Alcoholysis of O,O-diethyl O-(1-phenyl-2-acetylvinyl) phosphorate (XIa₃)

To a solution of sodium alcoholate prepared from 2.3 g of sodium in 200 ml of absolute alcohol was added to 29.8 g of O,O-diethyl O-(1-phenyl-2-acetylvinyl) phosphorate (XIa₃) at room temperature. After refluxing for one hour, the reaction mixture was neutralized with 6.0 g of acetic acid and the alcohol was evaporated.

Ether and water were added to the residue, the ether layer was washed with water and shaken with saturated aqueous solution of copper acetate, the crystals were obtained, yield 16.5 g. These crystals melted at 194~195°C (from methyl alcohol). A mixture of the crystals and the authentic specimen¹¹⁾

which was prepared by benzoylacetone and solution of copper acetate melted at 195~196°C.

Anal. Calcd. for $(C_{10}H_8O_2)_2Cu \cdot CH_3OH$; C, 60.34; H, 5.26%

Found.; C, 60.71; H, 5.44%

Ether solution after separating the copper salt was washed with water and dried over anhydrous sodium sulfate. After removal of the ether, the residual oil was distilled in vacuo, triethyl phosphorate was obtained at 100~105°C/25 mmHg. Yield 9.6 g n_D^{21} 1.4060.

Anal. Calcd. for $C_8H_{18}O_4P$; P, 17.0%

Found.; P, 17.2%

Alcoholysis of O,O-diethyl O-(1-phenyl-2-acetylvinyl) phosphorothioate gave the same results, namely, benzoylacetone and triethyl phosphorothioate (b.p. 94~95°C/15 mmHg) were obtained.

5) Ozonization of O,O-diethyl O-(1-phenyl-2-acetylvinyl) phosphorate (XIa₃).

Ozonized oxygen (0.1~0.05% ozone) was passed for 24 hours into a solution of 8.4 g of the phosphorate (XIa₃) in 20 ml of dry carbon tetrachloride cooled with a mixture of ice and salt. After suction-filtering of the solvent in vacuo, the ozonides were decomposed with water while heating on a boiling water for five hours. The water solution was cooled, white crystals of benzoic acid was separated. Yielded 2.1 g. m.p. 121°C.

To the filtrate solution, there was added sulfuric acidic alcohol solution of phenylhydrazine, phenylhydrazone of methyl glyoxal was precipitated, yield 4.4 g. m.p. 147~148°C.

Anal. Calcd. for $C_{15}H_{18}N_4$; C, 71.43; H, 6.35; N, 22.22%

Found.; C, 71.66; H, 6.18; N, 22.80%

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11) W. Wislicenus, *Ber.*, **35**, 545 (1902).