

of clay, and we can recognize the quantitative relation between the lowering of acidity and decomposition. From this result, hydrogen ions H^+ are supposed to have large effect upon the decomposition.

8. From the result as abovementioned, we shall be able to consider the stabilization mechanism by addition of stabilizers which author recommended, such as polyoxyethylene alkyl ether, polyoxyethylene dialkyl phenyl ether, polyoxyethylene phenyl ether, and polyoxyethylene alkyl phenyl ether. I presume that non-covalent electron pairs in the molecule of the compound used as a stabilizer might preferably seize hydrogen ions to prevent them

from reacting with malathion and methyl parathion.

9. Moisture in both kieselguhr and bentonite is much and the latter contains much alkali metals and alkaline earth metals. Talc is less acidic than clay and pH value is >7 under various influence of Mg^{++} , Fe^{+++} free bond, alkali impurities etc. Therefore, it is very difficult to judge the decomposition rate by acidity only.
10. Author could not find out the regularity between acidity of mineral carrier and decomposition rate, but we can suppose for H^+ to be an important factor of decomposition of organophosphorus dust insecticide.

Synthesis of Dialkyl Azophenyl Phosphates and Related Compounds. Studies on Organophosphorus Compounds. II*. By Yuji NAGAE, Tomoo WATANABE** (Institute of Agricultural Chemicals, Toa Agricultural Chemicals Co., Ltd.) Received April 24, 1958. *Botyu-Kagaku*, **23**, 89, 1958.

16. **Dialkyl Azophenyl Phosphate 及び関聯化合物の合成** 有機燐化合物の研究 第2報 永江祐治・渡辺智夫 (東亜農薬株式会社 農薬研究所) 33. 4. 24 受理

Dialkyl 置換-phenyl phosphate 及び thiophosphate の殺虫効果に就ては既に多くの報告があるが phenyl 基を azophenyl 基にかえた場合の殺虫効果に及ぼす影響を知る為に、新に 12 種の dialkyl 4'-置換 azophenyl phosphate 及び thiophosphate (一般式 $(RO)_2P(X)OC_6H_4-N=N-C_6H_4-Y$; $R=CH_3, C_2H_5$; $X=O, S$; $Y=H, Cl, NO_2$) を合成した。此等の化合物はすべて着色結晶でその中の 4 種は対応 azophenol との附加化合物を与えた。

Metcalf et al.¹⁾ studied on the insecticidal effectiveness of many dialkyl substituted phenyl phosphates and thiophosphates, and they found that there were general correlations between their chemical structures and biological properties as follows. (1) Compounds with phosphoryl groups were more active than those with thiophosphoryl groups. (2) Methyl and ethyl esters were more active than their higher homologs. (3) Presence of nitro groups on an aromatic ring was required for high effectiveness, and the maximum effectiveness was associated with nitro group in the *para* position. (4) Introduction of methylene or imine between benzene nucleus and phosphorus atom destroyed effectiveness.

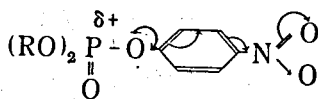
Lately, Fukuto et al.²⁾ found that there were rather precise correlations between hydrolysis constants, frequencies of phosphorus-oxygen-carbon stretching vibrations, inhibition of fly-brain cholinesterase, biological activities of dialkyl substituted phenyl phosphates and Hammett's constants (σ values) of *meta* or *para* substituents of their benzene nuclei. From these data, compounds containing such substituents with favorable σ values as *p*-nitro or *p*-cyano were highly active.

If the hydrolysis of these compounds and phosphorylation of cholinesterase by them are due to E effect of *para*-substituents (e.g. Equations 1 and 2), dialkyl 4'-substituted azophenyl phosphates and thiophosphates containing substituents

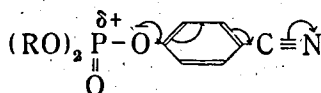
* Previous report (reported at the meeting of the Assoc. Plant Protection of Kyushu in 1956, in press) is to be Part 1 of this series.

** Kozu, Odawara, Kanagawa-ken.

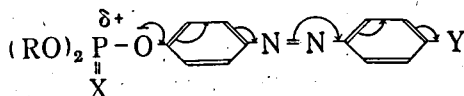
with favorable E effect, will be also active to insects as shown in Equation 3.



(Equation 1)



(Equation 2)



(Equation 3)

To ascertain this, we have synthesized twelve new compounds of dialkyl azophenyl phosphates and related compounds. These compounds were obtained in high yields as colored crystals by the interaction of dialkyl chlorophosphates or thiophosphates and appropriate azophenols in the presence of anhydrous sodium carbonate in acetone, and the experimental results are shown in Table 1. Some of them formed addition compounds with the starting azophenols as shown by the elemental analysis and partition paper chromatography described in the experimental part.

Biological properties of these chemicals are reported in elsewhere³. In brief, (1) compounds with 4'-nitro groups were the most active, and 4'-chloro or no 4'-substituted compounds, especially the latter, were less active, (2) phosphoryl and thiophosphoryl groups did not show any apparent differences, (3) there was no obvious correlation between methyl and ethyl esters.

Experimental*

Dialkyl chlorophosphates. Dimethyl and diethyl chlorophosphate were prepared by the chlorination of dialkyl phosphites with sulfur chloride as described by Fitzer et al⁹. Dimethyl chlorophosphate: bp 73° at 14 mm. Diethyl chlorophosphate: bp 83° at 12 mm.

Dialkyl chlorothiophosphates. Dimethyl and diethyl chlorophosphate were prepared from phosphorus pentasulfide and appropriate alcohols as described by Fletcher et al⁵. Dimethyl chlorothiophosphate: bp 66° at 16 mm. Diethyl

chlorothiophosphate: bp 85° at 10 mm.

Azophenols. Azophenols were prepared by

the coupling of phenol with appropriate diazonium salts. They were used without any purifications. Azophenol: mp 149-150°. 4'-Chloroazophenol: mp 157°. 4'-Nitroazophenol: mp 213°.

General Procedure for dialkyl azophenyl phosphates and thiophosphates and their 4'-substituted derivatives.

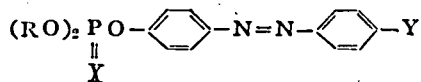
A mixture of equimolar quantities (usually 0.1 mole) of appropriate dialkyl chlorophosphate or thiophosphate, azophenol or 4'-substituted azophenol, and anhydrous sodium carbonate in acetone (100-200 cc per 0.1 mole) was stirred and heated at reflux for three to five hours. After cooling to the room temperature, the reaction mixture was filtered to remove sodium chloride and sodium bicarbonate. The filtrate was concentrated in vacuo to remove acetone. The residue was dissolved in ether, washed with dilute sodium carbonate and water, dried over anhydrous sodium sulfate, and then ether was distilled off. Crude product was obtained as crystals in quantitative yield, and purified by crystallization from n-hexane or methanol. Experimental data are given in Table 1.

Partition paper chromatography.

Compounds I~IV were paper-chromatographed using Toyo Filter Paper No. 51, silicone oil (Silicone KF-54, from Shinetsu Chemical Co., Ltd.) as stationary phase and the upper layer of the mixture of chloroform, alcohol and water (10:10:6) as mobile solvent by ascending method. In each case, two spots were obtained, and their colors were deepened by spraying 5% alcoholic potassium hydroxide. One spot corresponding to phosphate or thiophosphate was detected by spraying Hanes-Ischerwood reagent followed by ultra-violet radiation⁶. Experimental data are given in Table 2.

* All melting points are uncorrected.

Table 1. Synthesis of dialkyl azophenyl phosphate and related compounds



No.	R	X	Y	Mp (°C)	Yield (%)	Formula	Crystal Form	N% Calcd.	N% Found	P% Calcd.	P% Found
I	CH ₃	O	H	88-90	40	C ₁₄ H ₁₅ N ₂ O ₄ P 1/2 C ₁₂ H ₁₀ N ₂ O	Yellow prisms	10.37	10.25	7.65	7.36
I	C ₂ H ₅	//	//	48-50	48	C ₁₆ H ₁₉ N ₂ O ₄ P 1/2 C ₁₂ H ₁₀ N ₂ O	//	9.69	10.01	7.16	7.14
II	CH ₃	//	Cl	127-129	45	C ₁₄ H ₁₄ ClN ₂ O ₄ P 1/2 C ₁₂ H ₉ ClN ₂ O	//	9.22	9.78	6.81	6.67
IV	C ₂ H ₅	//	//	132-134	53	C ₁₆ H ₁₈ ClN ₂ O ₄ P 1/2 C ₁₂ H ₉ ClN ₂ O	//	8.66	9.00	6.39	6.01
V	CH ₃	//	NO ₂	99-101	62	C ₁₄ H ₁₄ N ₃ O ₆ P	Red needles	11.96	11.41	8.83	9.04
IV	C ₂ H ₅	//	//	73-76	67	C ₁₆ H ₁₈ N ₃ O ₆ P	//	11.08	10.66	8.18	8.24
VI	CH ₃	S	H	45-47	96	C ₁₄ H ₁₅ N ₂ O ₃ PS	Yellow prisms	8.69	8.68	9.62	10.01
VII	C ₂ H ₅	//	//	50-52	98	C ₁₆ H ₁₉ N ₂ O ₃ PS	//	8.06	8.05	8.85	9.28
K	CH ₃	//	Cl	79-80	87	C ₁₄ H ₁₄ ClN ₂ O ₃ PS	//	7.85	7.81	8.69	8.46
X	C ₂ H ₅	//	//	50-52	99	C ₁₆ H ₁₈ ClN ₂ O ₃ PS	//	7.28	7.43	8.06	8.47
N	CH ₃	//	NO ₂	90-92	99	C ₁₄ H ₁₄ N ₃ O ₅ PS	Red prisms	11.53	11.54	8.44	8.48
II	C ₂ H ₅	//	//	73-75	94	C ₁₆ H ₁₈ N ₃ O ₅ PS	//	10.63	10.33	7.84	7.49

a) Nos. I~VI were recrystallized from n-hexane, and VII~II from methanol.

Table 2. Partition paper chromatography of dialkyl azophenyl phosphate and related compounds.

Compound No.	a) Rf	b) Rf
I	0.05,	0.46
I	0.02,	0.46
Azophenol		0.45
II	0.05,	0.21
IV	0.02,	0.22
4-Chloro- azophenol		0.23

a) Sprayed with 5% alcoholic potassium hydroxide.

b) Sprayed with Hanes-Ischerwood reagent, followed by UV radiation.

Summary

Dialkyl 4'-substituted azophenyl phosphates and thiophosphates with general formula (RO)₂P(X)-OC₆H₄-N=N-C₆H₄-Y were synthesized by the reaction of 4'-substituted azophenols with dialkyl chlorophosphates or thiophosphates in the presence of anhydrous sodium carbonate in acetone. Twelve new compounds were obtained as colored

crystals. When X=O, and Y=H or Cl, addition compounds with 1/2 mole of the starting azophenols were obtained.

Acknowledgement

We wish to express our thanks to Ph. Dr. Kizo Hiratsuka, Head of this Institute, for his kind encouragement and guidance during this work. Our thanks are also due to Mr. Ken'ichi Kojima and his assistants for bioassay and helpful discussions concerning this work.

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