kurze Zeit mit Zn-Staub in Eisessig vorsichtig erwärmt. Beim Einrühren in Wasser fällt ein Gemisch von VII und XII(= der VII entsprechende Thioäther) aus. Mit CH_2Cl_2 lässt sich im Falle von Va das VIIa-Isomere extrahieren, das nach dem Umkristallisieren bei 205° schmilzt. Vb liefert VIIb vom Schmp. 195° (aus Alkohol).

VIIa	$C_{14}H_{14}O_3S$ (262, 3)	S Ber. 12, 2	Gef. 12, 3
VIIb	$C_{14}H_{14}O_3S$ (262, 3)	S Ber. 12, 2	Gef. 12, 0
XII	$C_{14}H_{14}O_2S$ (246, 3)	S Ber. 13, 0	Gef. 13, 2

Das in beiden Fällen als zweites Reduktionsprodukt mitentstandene XII schmilzt bei 125° (aus Methanol).

Oxydation von VIIa und VIIb: Mehrstdg. Erhitzen von VIIa und b mit Peressigsäure führt in beiden Fällen zum Sulfon VIII vom Schmp. 186° (aus Toluol), das auch aus der *trans*-IVa entsprechenden SO_2-Verbindung und Cyclopentadien synthetisiert werden kann.

$C_{14}H_{14}O_4S$ (278, 3) aus VIIa:	S Ber. 11, 5	Gef. 11, 2
aus VIIb:	S Ber. 11, 5	Gef. 11, 5
synthetisiert:	S Ber. 11, 5	Gef. 11, 4

Reduktion von VIa und VIb: 3stdg. Kochen von VI a bzw. b mit aktiviertem Zn-Staub in Eisessig führt in beiden Fällen zu einem Thioäthergemisch, das in IX vom Schmp. 60° (in organ. Lösungsmitteln leicht löslich) und Hydroxydihydro-IX vom Schmp. 151-152° (aus Toluol) zerlegt werden kann.

IX	$C_{14}H_{14}O_2S$ (246, 3)	S Ber. 13, 0	Gef. 13, 2
	$C_{14}H_{16}O_3S$ (264, 3)	S Ber. 12, 1	Gef. 12, 3

Persäure-Oxydation von IX führt zu einem Sulfon vom Schmp. 181°, welches das andere *trans*-Isomere von VIII ist.

Der *Deutschen Forschungsgemeinschaft* und dem *Verband der Chemischen Industrie* sei für die Förderung dieser im März 1960 experimentell abgeschlossenen Untersuchungen bestens gedankt. Vorliegende Arbeit ist im Juni und Juli zahlreichen Stellen als Manuskript zugänglich gemacht worden.

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Synthesis of Acyl Phosphorates and their Biological Activities. Yoshihiko NISHIZAWA, Masataka NAKAGAWA and Toshio MIZUTANI (Sumitomo Chem. Co. Ltd., Osaka) Received Nov. 12, 1960. *Botyu-Kagaku*, **26**, 4, 1961. (in English)

2. Acyl Phosphorate 類の合成とその毒性

西沢吉彦, 仲川政位, 水谷俊夫(住友化学工業株式会社 大阪製造所研究部) 35. 11. 12 受理.

有機リン殺虫剤の研究途上において, 著者等は数種の Acyl Phosphorate 類を合成し, その毒性, 殺虫力を比較検討した. これらの化合物は一般に Dipterex よりやや強い殺虫力を示したが, 温血動物に対して非常に毒性が強いことが明らかとなつた.

G. Schrader[1] reported already that O, O-diethyl-O-acetyl phosphorate* (I) is the biological active phosphorate. After that, no one had reported in detail about the degree of biological activities of the phosphorate (I) and the analogues comparing with the commercial insecticides.

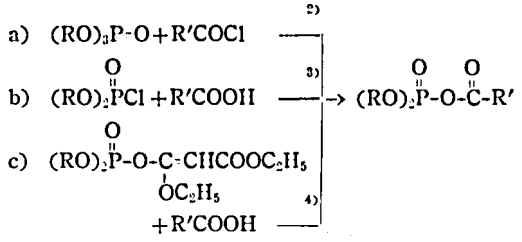
The present authors prepared some acyl phosphorates to understand clearly the biological activities of the acyl phosphorates towards warm blood animals and insects, and it is considered that these data would be of value upon the studies

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

of the organophosphorus insecticides.

1) Preparation of acyl phosohorates.

Acyl phosphorates were prepared by the following three methods



The yield of the products by the method (a) was the highest and almost all phosphorates were prepared by this method. All of the products were liquid and purified by distillation under reduced pressure. The proof of structure of these compounds was given by the microanalytical data, the infrared absorption spectra and the alkaline hydrolysis, namely, the IR-spectra of the products showed the streching vibration bands of carbonyl group at 1755 cm^{-1}, P=O group at 1300 cm^{-1}, P-O-C_2H_5 group at 1150 cm^{-1} and $-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{P}}-$ group at970 cm^{-1} [5] (see Fig. 1). The alkaline hydrolysis of benzoyl phosphorate (VI) gave benzoic acid.

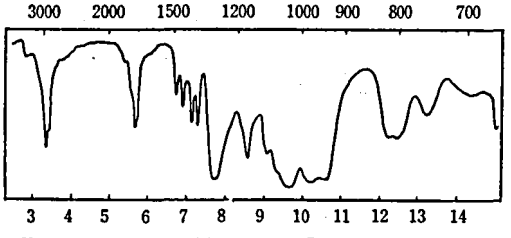


Fig. 1 Infrared Absorption Spectrum of O. O-Diethyl-O-chloroacetyl phosphorate (II).

2) The biological activities of acyl phosphorates

Topical test was conducted by using *Ephestia cautella* as follows; each compound was dissolved into acetone to prepare a series of acetone solutions containing from 0.067 to 2% of the compounds (g/cc). Each 1/1000 cc of these solutions was applied to the body of the insect by means of micrometer syringe and, after keeping it for 3 days at 25°C, the kill percent was calculated. The insect utilized in this test had almost the same body weights and each solution was applied to a group of these twenty bodies in order to calculate the mean fatal per cent.

For comparing the activity of synthetic samples with that of the commercial insecticides, Dipterex[6] (O, O-dimethyl-(1-hydroxy-2, 2, 2-trichloro-ethyl) phosphonate) wes tested at the same time.

The toxicity of acyl phosphorate towards warm-blood animals was tested by oral administration to mice; each test emulsion was prepared by dilution of 50% emulsifiable concentrate composed of 50 parts active ingredient and 50 parts polyethylene glycol nonylphenyl ester by weight.

Each emulsion thus prepared was given into the stomach of mice by metalic tube. The volume of instilment was 0.5 ml per 10g of body weight of mice and each consentration of the solution was applied to a group of five bodies of mice.

After keeping it for seventy two hours, the symptoms of poisoning was observed. Rough LD_{50} (mg/kg) value was calculated according to the Litchfield and Wilcoxon's method, and then by

Table I Yields, physical constants, and microanalytical data of acyl phosphorates.

$(C_2H_5O)_2\overset{O}{\overset{\|}{P}}-O-\overset{O}{\overset{\|}{C}}-R$

No.	R	Yield (%) (a-method)	b. p. °C	b. p. mmHg.	n_D (t°C)	Phosphorus (%) Calcd.	Phosphorus (%) Found	Chlorine (%) Calcd.	Chlorine (%) Found	Carbon (%) Calcd.	Carbon (%) Found	Hydrogen (%) Calcd.	Hydrogen (%) Found
I	CH_3-	48	119	1.0	1.4230(24)	15.81	15.65	——	——	36.73	36.81	6.63	6.57
II	$ClCH_2$-	51	114~115	0.9	1.4191(29)	13.45	13.21	15.40	15.53	31.24	31.39	5.21	5.50
III	Cl_2CH-	43	125~126	1.2	1.4508(27)	11.70	11.78	26.79	26.90	27.17	27.35	4.15	4.41
IV	Cl_3C-	38	132~134	1.0	1.4182(25)	10.35	10.55	35.56	35.39	24.03	24.25	3.33	3.30
V	$CH_2=CH(CH_2)_8$-	40	139~140	1.0	1.4358(29)	9.69	9.81	——	——	56.25	56.11	9.06	8.93
VI	C_6H_5	61	119~120	0.9	1.4854(29.5)	12.02	12.36	——	——	51.16	51.35	5.81	5.63

Table II The biological activities of acyl phosphorates.

$$(C_2H_5O)_2\overset{O}{\overset{\|}{P}}-O-\overset{O}{\overset{\|}{C}}-R$$

No.	R	*Ephestia cautera* (topical method) kill %				Oral Toxicity towards Mice LD_{50} mg/kg
		20γ/worm	6.7γ/worm	2γ/worm	0.68γ/worm	
I	CH_3-	100	100	55.6	30.0	2.0
	Dipterex	70	30	10	20	
II	$ClCH_2$-	100	80	10	10	2.0
	Dipterex	90	50	0	0	
III	Cl_2CH-	70	40	20	10	15.0
	Dipterex	90	50	0	0	
IV	Cl_3C-	90	80	10	0	4.3
	Dipterex	80	20	10	0	
V	$CH_2=(CH_2)_8$-	80	40	0	0	6.2
	Dipterex	90	50	0	0	
VI	C_6H_5-	90	50	0	0	6.3
	Dipterex	90	80	0	0	

changing the concentration of the solution near the value, the true LD_{50} value was determined by repeating the above experimental processes.

The results of the biological activities of acyl phosphorates are shown in Table II.

It may be summarized from Table II that the activities towards insect of acyl phosphorates are a little higher than that of Dipterex and the toxicities towards mice are very higher than that of Dipterex.

Experimental

1) Preparation of acyl phosphorates.

The following examples illustrate the preparation of acyl phosphorates. Other compounds prepared are shown in Table I and their biological activities are shown in Table II.

Caution : All of the phosphorates are powerful cholinesterase inhibitors and therefore highly toxic.

2) Preparation of O, O -diethyl-O-trichloroacetyl phosphorate (IV) by the method (a).

A mixture of 27.3g (0.15M) of triethyl phosphorate, 16.4g (0.1M) of trichloroacetyl chloride and 2 drops of triethylamine was heated at 110~130°C for 4 hours. And then, the product was distilled under a reduced pressure, b.p. 132~134°C/1 mmHg, yielded 12.9g (48% from trichloroacetyl chloride), n_D^{25} 1.4182.

Anal. Found. P, 10.55 ; C, 24.25 ; H, 3.30 ; Cl, 35.39

Calcd. for $C_6H_{10}O_5Cl_3P$, P, 10.35 ; C, 24.03 ; H, 3.33 ; Cl, 35.56

3) Preparation of O, O-diethyl-O-trichloroacetyl phosphorate (IV) by the method (b).

A solution of 32.6g (0.2M) of trichloroacetic acid in 100 ml of acetone was neutralized by 16.8g of sodium hydrogen carbonate in small quantity of water. Water was distilled off by azeotrope with acetone, 50 ml of acetone was added further and then 34.5g of O, O-diethyl phosphorochloridate were added. A mixture was refluxed for 5 hours. The precipitate was filtered off, the filtrate was concentrated and then residual oil was distilled under a reduced pressure, b.p. 132~133°C/1 mmHg. Yield 13.6g (23%), n_D^{25} 1.4183.

Anal. Found, C, 23.91 ; H, 3.51 ; Cl, 35.38
Calcd. for $C_6H_{10}O_5Cl_3P$, C, 24.03 ; H, 3.33 ; Cl, 35.56

The infrared absorption spectrum of this product was coincided with that of the method (a).

4) Hydrolysis of O. O-diethyl-O-benzoyl phosphorate (VI).

To 50 ml of 0.05N aqueous solution of sodium hydroxide, were added 2.6g of (VI) and heated for 3 hrs. A solution was acidified by hydrochloric acid and then concentrated. White crystals were precipitated and filtered off (0.8g). The crystals were recrystalized from water and melted at 121°C. A mixture of the crystals with the authentic benzoic acid melted at 121~122°C.

Anal. Found, C, 68.66 ; H, 5.05
Calcd. for $C_7H_5O_2$, C, 68.85 ; H, 4.92

Summary

Several acyl phosphorates were prepared and their biological activities were tested. These acyl phosphorates showed a little higher activity towards insect than Dipterex and the toxicities of these acyl phosphorates towards mice were also higher than that of Dipterex.

Acknowledgement

The authors wish to thank the Sumitomo Chem. Co., Ltd. for permission to publish this work. They are indebted to coworkers in the pesticidal, the biological and the analytical sections in this laboratory.

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An Attempt to Reduce and Increase Insecticide-Resistance in *D. melanogaster* by Selection Pressure. Genetical and Biochemical Studies on Negatively Correlated Cross-Resistance in *Drosophila melanogaster* I. Zenichi Ogita (Department of Genetics, Faculty of Medicine, Osaka University, Osaka, Japan). Received Nov. 22, 1960. *Botyu-Kagaku*, **26**, 7, 1961. (in English)

3. Selection pressure によって殺虫剤抵抗性を減少させ増加させる試み キイロショウジョウバエにおける negatively correlated cross-resistance の遺伝生化学的研究 I.

荻田善一 (大阪大学医学部 遺伝学教室) 35. 11. 22 受理

キイロショウジョウバエの第Ⅱ染色体上65±附近にある優性の DDT 抵抗性遺伝子の存在は，BHC, parathion および phenylurea (PU) に対して交叉抵抗性 (cross-resistance) を与えるが，phenylthiourea (PTU) に対しては逆に異常な非抵抗性 (逆相関交叉抵抗性 negatively correlated cross-resistance) をもたらす．また第Ⅲ染色体上 50 ±附近にある硫酸ニコチン抵抗性の遺伝子の存在は，これらの薬剤に対して交叉抵抗性をもたらすことをすでに報告した．したがって，PTU-selection pressure によっては DDT, BHC, parathion に対して非抵抗性でニコチンに対して抵抗性の系統をもたらし，PU-selection pressure はこれらの薬剤に対して抵抗性の系統をもたらすことを暗示した．実際，DDT 抵抗性と非抵抗性の系統からなる混合 population に PTU-selection pressure を働かせることによって DDT 抵抗性遺伝子を追い出し，生き残った系統は DDT, BHC, parathion 非抵抗性で硫酸ニコチン抵抗性であった．また PU-selection pressure より生き残った系統には，DDT, BHC, parathion 抵抗性と硫酸ニコチン抵抗性を同時にもたらすことを証明した．

The cross-resistance pattern of *Drosophila melanogaster* to DDT, BHC, and parathion is negatively correlated with its resistance to phenylthiourea(PTU), but is positively correlated with phenylurea(PU)-resistance. As a result of the genetical analyses in previous papers, the following working hypothesis was introduced by the author: "The dominant PTU-susceptibility and dominant PU-resistance may be a pleiotropic expression of the dominant gene for resistance to DDT, BHC and parathion at locus *65*± on the 2nd chromosome; and the dominant factor for PTU- and PU-resistance on the 3rd chromosome is a pleiotropic expression of the dominant gene for resistance to nicotine sulfate at locus *50*±.
The present investigation has aimed to test the hypothesis by means of applying selection pressure with PTU and PU to synthetic populations consisting of several strains resistant to DDT, BHC and parathion, and strains susceptible to those insecticides.