RESIDUE REVIEWS

VOLUME 60

Sumithion

RESIDUE REVIEWS

Residues of Pesticides and Other Contaminants in the Total Environment

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Foreword

"Sumithion" is the tradename owned by Sumitomo Chemical Co., Ltd., Japan, and given to *O,O*-dimethyl *O*-(3-methyl-4-nitrophenyl) phosphorothioate while its generic name registered at ISO and BSI is "fenitrothion."

It is an organophosphorous insecticide having a broad range of insecticidal spectrum comparable to that of methyl parathion, and its toxicity to mammals and fish is low enough to make its handling of less concern.

In 1959 the pesticide research group of Sumitomo Chemical Co., Ltd. was successful in synthesizing Sumithion, which had been code-numbered S-1102-A. Since then, the pesticide staffs of the company have been using their constant efforts in evaluation and practical development of the insecticide in various fields of application under different conditions of the world.

Today, Sumithion is an insecticide most extensively used in Japan, being indispensable for field crops, industrial crops, and forestry protection besides public health purposes. In many other countries of the world, usage of Sumithion is now so extended that it has come to be known as a typical organophosphorus insecticide together with methyl parathion and malathion.

Much of the information accumulated on Sumithion is here published by the members of Sumitomo engaged in the research and development of the compound.

Identical compounds are now produced and sold by Farbenfabriken Bayer AG, under the tradename of "Folithion," by Cheminova under the tradename of "Novathion," and by the Czechoslovakian state organization under the tradename of "Metation." Many other tradenames are also given to this product by distributing companies, such as "Accothion" (American Cyanamid Co.), "Agrothion" (Imperial Chemical Industries), "Danathion" (Nordisk Alkali), "Nuvanol" (Ciba-Geigy Limited), "Polowadophos" (Poland), "Sumiféne" (PEPRO), etc. In this review, the name "Sumithion" is mainly used, meaning fenitrothion originating from Sumitomo Chemical Co., Ltd. unless otherwise identified.

Ahead of other things the history of Sumithion research will be referred to, as it represents the pesticide research history in general of Sumitomo Chemical Company.

Sumitomo's pesticide work started in 1954 when the company began production of parathion and methyl parathion licensed from the American Cyanamid Co. and Farbenfabriken Bayer AG. The introduction of these chemical pesticides to the modernizing agricultural technology of Japan contributed a great deal in her postwar necessity to increase rice production. On the other hand, however, these pesticides caused frequent cases of accidents because of their high acute toxicities towards mammals.

Since then, the main target of Sumitomo's pesticide research group has been to find compounds that must be highly active towards target pests but with low toxicity towards mammals. After a three-years' screening trial, the group arrived at S-1102-A, Sumithion. It is surprising enough that the substitution of the 3-hydrogen in the 4-nitrophenyl group in methyl parathion with a methyl radical lowers the acute mammalian toxicity to one-fiftieth or -sixtieth, maintaining the insecticidal effect.

During the early years of the 1960s, Sumithion entered Japan's pesticide market where methyl parathion was mostly used, and steadily grew. Since 1971 when the Japanese Government finally prohibited the use of parathion and methyl parathion due to their high acute toxicities, Sumithion has completely taken over the role of parathion. Rather, its low toxicity allowed Sumithion to broaden its usage to cover such fields where parathion could not be used.

In Japan, Sumithion is used mainly for the control of rice stem borers, fruit worms, and tea leaf worms, among many other agricultural pest insects, and also as household, sanitary, veterinary, and forest insecticides. Outside Japan it is also used for the protection of rice and tea in Southeastern Asia; wheat in the Middle and Near East; coffee and fruits in Africa: cotton, wheat, coffee, and pasture in South America; and forest and fruits in North America.

Especially promising on the world-wide scale is its control of vector insects in connection with malaria and other epidemics. The World Health Organization (WHO) of the United Nations has long been testing the compound for possible malaria-control purposes. The test is now at the final stage with such satisfactory results that make this company expect the WHO recommendation in this field in the near future.

Sumitomo Chemical Co., Ltd. expresses thanks to the Vector Biology Control department of the World Health Organization for permission to refer to their data. Sumitomo Chemical Co., Ltd. also expresses gratitude to all companies, institutes, and personnel concerned for the concentrated efforts used for the research and development of the present compound.

For the research and development
staffs of The Pesticides Division,
Sumitomo Chemical Co., Ltd.

Osaka (Japan) 1974 Takashi Ohno

Preface—Cumulative Indexes

Volume 10 of "Residue Reviews" contained the cumulative indexes of volumes 1–10, with the Comprehensive and Cumulative Subject-Matter Index consisting of individual subject units prepared by the authors themselves but correlated, integrated, and cross-referenced by the editors. In contrast, volumes 11–59 contained individual index units prepared solely by the editors, who assume all responsibility for omissions; in a book series of such varied subject-matter content there will undoubtedly be many such omissions, especially since the frequency of use of editor-selected sub-entries has been greatly increased to aid literature searchers.

As with volumes 10, 20, 30, 40, and 50, this present volume 60 contains an abbreviated ten-volume table of subjects covered for ready reference, a ten-volume author index, and the comprehensive ten-volume cumulative and detailed subject-matter index. The present subject-matter or "Subject" index contains more detail for most of the volumes than is found in the original and individual index units to permit more exhaustive searches of all volumes. Major aspects or facets of a common subject such as DDT or dieldrin are accommodated by subentries where appropriate, casual, illustrative, or tabular mention of one of these common subjects is simply paginated after the simple subject entry.

It is sincerely hoped the user of "Residue Reviews" will find this three-way cumulative index both convenient and useful.

In addition, there is a cumulative list of the contents, by short titles, individually for all sixty volumes, with dates of publication.

Department of Entomology
University of California
Riverside, California
January 6, 1976

F.A.G.
J.D.G.

SUMITHION[*]

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[*] Manuscript received January 1, 1974; accepted May 1, 1975.

Chapter 1

Chemistry of Sumithion

By

YOSHIHIKO NISHIZAWA

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I. Introduction

Many researchers have investigated a series of chlorophenyl phosphorothioates[1] for the purpose of obtaining new insecticides. As the results of their efforts, Ronnel[2] and VC-13[3] have been developed. Chlorthion[4] and Dicapton[5] were found, in a series of chloronitrophenyl phosphorothioates, as low toxicity insecticides.

On the other hand, many attempts were made in agricultural chemicals, especially in the field of herbicides and insecticides, to replace the chlorine atoms of those compounds by methyl groups. These methyl

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[1] The chemical names of organophosphorus compounds mentioned are based upon the Drake Committee Report [Chem. Eng. News **30**, **4515** (1952)].

[2] *O,O*-Dimethyl *O*-(2,4,5-trichlorophenyl) phosphorothioate, Dow Chemical Co.

[3] *O,O*-Diethyl *O*-(2,4-dichlorophenyl) phosphorothioate, Virginia-Carolina Chemical Co.

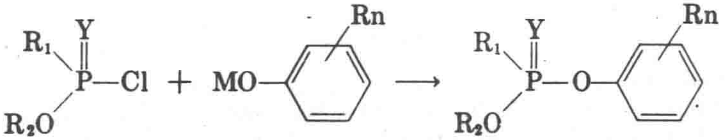
[4] *O,O*-Dimethyl *O*-(3-chloro-4-nitrophenyl) phosphorothioate, Farben Fabriken Bayer A.G.

[5] *O,O*-Dimethyl *O*-(2-chloro-4-nitrophenyl) phosphorothioate, American Cyanamide Co.

analogues also had some biological activities, although they were generally lower than those of parent chloro-compounds.

Thus, in Sumitomo Chemical Co., Ltd., some attempts were made for the purpose of developing new insecticides from a series of the methylphenyl phosphorothioates instead of chlorophenyl phosphorothioates. Although no one had reported on this series, when this work was begun SCHRADER (1960) had also reported independently on 3-methyl-4-methylmercaptophenyl phosphorothioate (Lebaycid) as a low toxicity insecticide.

All of the compounds were prepared from phosphorochloridothioate and substituted phenols or their alkaline metal salts by the following scheme:



where R_1 is phenyl or alkoxy group, R_2 is alkyl group, R_n is substituent, M is hydrogen atom or alkaline metal atom, Y is oxygen or sulfur atom.

The products were purified either by distillation or by column chromatography. The yields were generally between 80 and 90% but fell to between 40 and 50% on purification by the column chromatography. The products were tested for their biological activities towards mice and about ten kinds of insects. As a result, it was found that the products had broad spectra of activities.

II. Attempts to synthesise methylphenyl phosphorothioates

a) Preparation of methylphenyl phosphorothioates

The methylphenyl phosphorothioates shown in Table I were prepared. The activities of these compounds towards insects were generally lower than those expected by the present authors, but a few compounds had a considerable degree of activity towards houseflies. 3,5-Dimethylphenyl phosphorothioate (Ii) had comparatively high activity towards the rice stem borer (*Chila suppressalis* Walker), as high as Dipterex.[6]

b) Preparation of methylchlorophenyl phosphorothioates

At the next step, phosphorothioates having a methylchlorophenyl group were prepared. However, these compounds also proved to have

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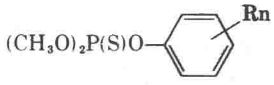
[6] *O,O*-Dimethyl-(2,2,2-trichloro-1-hydroxyethyl) phosphonate, Farbenfabriken Bayer A.G.

Table I. *Physical constants of O,O-dimethyl O-substituted phenyl phosphorothioates.*



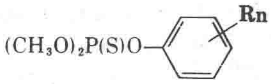
		bp		
No.	R_n	°C	mm Hg	n_D(t°C)
Ia	2-Me	112 ~ 113	0.06	1.5304(24)
Ib	3-Me	109 ~ 110	0.05	1.5301(22)
Ic	4-Me	113 ~ 114	0.08	1.5284(22)
Id	2,3-diMe	108 ~ 110	0.1	1.5310(25)
Ie	2,4-diMe	113 ~ 115	0.1	1.5290(23)
If	2,5-diMe	121 ~ 122	0.1	1.5289(24)
Ig	2,6-diMe	110 ~ 113	0.07	1.5297(24)
Ih	3,4-diMe	116 ~ 118	0.08	1.5332(23)
Ii	3,5-diMe	116 ~ 118	0.1	1.5296(23)
Ij	2,4,6-triMe	—	—	1.5165(23.5)
Ik	3,4,5-triMe	—	—	1.5350(22.5)

low activities like the series of methylphenyl phosphorothioates. Their physical constants are shown in Table II.

c) *Preparation of methylnitrophenyl, methylcyanophenyl, or methylthiocyanophenyl phosphorothioates and their biological activities*

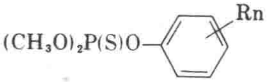
All the compounds examined in this series and their biological activities are shown in Table III. As it is clear from Table III, 2-methyl-4-

Table II. *Physical constants of O,O-dimethyl O-substituted phenyl phosphorothioates.*



		bp		
No.	R_n	°C	mm Hg	n_D(t°C)
IIa	2-Cl-6-Me	110 ~ 112	0.07	1.5417(24)
IIb	4-Cl-2-Me	113 ~ 115	0.15	1.5391(22)
IIc	2-Cl-4,5-diMe	118 ~ 119	0.2	1.5418(25)
IId	4-Cl-2,3-diMe	117 ~ 119	0.2	1.5436(25)
IIe	4-Cl-2,5-diMe	117 ~ 118	0.2	1.5410(21)
IIf	4-Cl-2,6-diMe	119 ~ 120	0.25	1.5432(25)
IIg	2,4-diCl-5-Me	118 ~ 119	0.2	1.5517(26)
IIh	2,4-diCl-6-Me	109 ~ 111	0.05	1.5514(25)
IIi	2,4-diCl-3,5-diMe	—	—	1.5544(25)
IIj	2,4-diCl-3,5,6-triCl	—	—	1.5637(24)

Table III. *Physical constants of O,O-dimethyl O-substituted phenyl phosphorothioates and their biological activities.*



No.	R$_n$	n$_D$(t°C)	Oral toxicities, mice[a] (LD$_{50}$, mg/kg)	*Callosobruchus chinensis* Linne, dipping method (LC$_{50}$)
IIIa	2-Me-4-NO$_2$	1.4900(33)	920	×50,000
IIIb	3-Me-4-NO$_2$[b]	1.5528(25)	870	×60,000
IIIc	3-Me-6-NO$_2$	1.5428(33.5)	1,200	×230
IIId	4-Me-3-NO$_2$	1.5316(30.5)	—	×250
IIIe	4-Me-2-NO$_2$	1.5466(25)	—	inactive
IIIf	2-Me-5-NO$_2$	1.5500(25)	—	inactive
IVa	4-CN[c]	1.5404(32.5)	1,020	×42,000
IVb	2-Me-4-CN	1.5404(28.5)	>1,000	×320
IVc	3-Me-4-CN	1.5415(24.5)	500	×7,600
Va	4-SCN	1.5660(33.5)	6	×250
Vb	2-Me-4-SCN	1.5703(23.5)	112	×220
Vc	3-Me-4-SCN	1.5778(23.5)	93	×270

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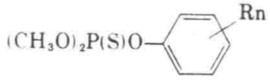
[a] Conducted according to Y. NISHIZAWA [Botyu-Kagaku **26**, **4** (1961)].
[b] bp 140 ~ 145°C/0.1 mm with decomposition.
[c] bp 119 ~ 120°C/0.09 mm with decomposition, mp 14 ~ 15°C.

nitrophenyl, 3-methyl-4-nitrophenyl and 3-methyl-4-cyanophenyl phosphorothioates (IIIa) (IIIb) (IVc) have good insecticidal activities although their toxicities were very low towards mice. Morever, it was very interesting for the present authors that 4-cyanophenyl phosphorothioate (IVa), which was prepared as a standard compound for the purpose of discussing the effect of 3-methyl group in series IV, showed a high activity and an unexpectedly low toxicity; so did that of 3-methyl-4-cyanophenyl phosphorothioate (IVc).

O,*O*-Diethyl-*O*-(4-cyanophenyl) phosphorothioate (IXa) had already been prepared by SCHRADER (1952) but it had high toxicity and weaker activity than parathion (see Table VI) so no studies on 4-cyanophenyl phosphorothioates have been reported thereafter.

However, the coworkers in the pesticidal section in this Laboratory found that 4-cyanophenyl phosphorothioate (IVa) had good insecticidal activity towards the rice stem borer and the possibility to become the new low toxicity organophosphorus insecticide. Of course, at the same time, other compounds (IIIa) (IIIb) (IVc) in this series also showed high activities towards the rice stem borer, although their toxicities were

Table IV. *Physical constants of O,O-dimethyl-O-substituted phenyl phosphorothioates and their biological activities.*



No.	R_n	n_D(t°C)	Oral toxicities, mice (LD_{50}, mg/kg)	*Callosobruchus chinensis* Line, dipping method (LC_{50})
VIa	2-MeO-4-NO_2	1.5625(22)	750	×50,000
VIb	3-MeO-4-NO_2	1.5627(24)	150	×52,000
VIc	3-MeO-6-NO_2	1.5732(24)	1,000	×450
VId	3-BzO-4-NO_2	mp 120°C	—	inactive
VIe	3-BzO-6-NO_2	mp 115°C	—	inactive
VIIa	2-Cl-4-CN	mp 65°C	490	×100,000
VIIb	3-Cl-4-CN	1.5553 (30.5)	500	×170,000

outstandingly low. On the other hand, the compounds in the thiocyanophenyl series showed lower activities but their toxicities were higher.

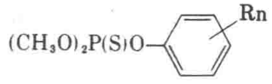
d) Preparation of methoxynitro-, benzoyloxynitro- or chloro-cyanophenyl phosphorothioates and their biological activities

It was well known from Chlorthion and Dicapton that the introduction of a chlorine atom into nitrophenyl phosphorothioates reduced their toxicities. But at the same time, they become inferior in their insecticidal activities, especially towards the rice stem borer. Now, it becomes clear from the above-mentioned factos that the introduction of a methyl group into nitrophenyl phosphorothioates reduced only their toxicities but not their activities. So, as the next step, it was considered that the introduction of some other groups might reduce only their toxicities, and methoxy-, benzoyloxy-nitrophenyl, or chloro-cyanophenyl phosphorothioates were prepared as shown in Table IV.

2-Methoxy- or 3-methoxy-4-nitrophenyl phosphorothioates (VIa) (IVb) and 2-chloro or 3-chloro-4-cyanophenyl phosphorothioates (VIIa) (VIIb) showed, also, good insecticidal activities and low toxicities but they had lower activities towards the rice stem borer compared with that of 3-methyl-4-nitrophenyl phosphorothioate (IIIb) or 4-cyanophenyl phosphorothioate (IVa) (see Table V).

Low toxicity organophosphorus compounds which were chosen from the above studies are shown in Table V. It is clear from Table V that all compounds having high activities towards Azuki bean weevils do not always have high activities towards the rice stem borer.

Table V. *Biological activities of O,O-dimethyl-O-substituted phenyl phosphorothioates.*



		Oral toxicities, mice	Post-test towards 2nd generation larvae of rice stem borer (*Chilo suppressalis* Walker) (spray 4 days later from the encroachment)			
No.	R_n	(LD_{50}, mg/kg)	1/2,000	1/4,000	1/8,000	1/16,000
IIIa	2-Me-4-NO_2	920	19.4%	10.1%	—	—
IIIb	3-Me-4-NO_2	870	100	100	100%	100%
VIa	2-MeO-4-No_2	750	94.7	48.8	—	—
VIb	3-MeO-4-NO_2	150	95.6	82.2	—	—
IVa	4-CN	1,020	100	100	100	97.2
IVb	2-Me-4-CN	1,000	20.3	22.3	—	—
IVc	3-Me-4-CN	500	100	100	77.5	—
VIIa	2-Cl-4-CN	490	100	90	74.0	—
VIIb	3-Cl-4-CN	500	100	100	100	82.3

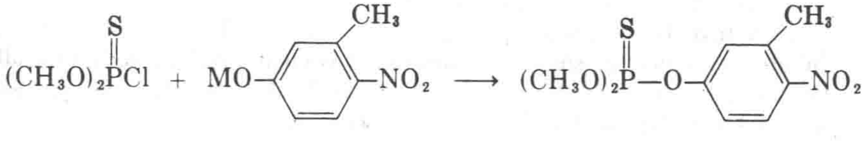
e) Preparation of O,O-dialkyl homologues of 3-methyl-4-nitrophenyl and 4-cyanophenyl phosphorothioates and their biological activities

It became clear from the above studies that 3-methyl-4-nitrophenyl and 4-cyanophenyl phosphorothioates (IIIb) (IVa) had an outstanding characteristic showing low toxicities and high activities at the same time. The present authors attempted to prepare *O,O*-dialkyl homologues of these two compounds (IIIb) (IVa) in order to study the effects of the *O,O*-dialkyl group in this series. The results are shown in Table VI.

As is evident from Table VI, the *O,O*-diethyl homologues showed good activity but at the same time their toxicity also was very high. *O,O*-Dipropyl, diisopropyl, dibutyl, and diamyl homologues showed weak toxicities and activities, and no compounds were found which were better as insecticides than the two compounds (IIb) (IVa).

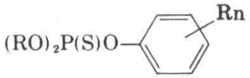
III. Chemical properties of Sumithion

Sumithion is prepared in good yield from 3-methyl-4-nitrophenol or its alkaline metal salt and *O,O*-dimethyl phosphorochloridothioate:



Sumithion

Table VI. *Physical constants of O,O-dialkyl O-substituted phenyl phosphorothioates and their biological activities.*



No.	R	R_n	bp		n_D(t°C)	Oral toxicities, mice (LD_{50}, mg/kg)	*Callosobruchus chinensis* Linne, dipping method (LC_{50})
			°C	mm Hg			
VIIIa	C_2H_5	—	—	—	1.5280(33)	17.5	×190,000
VIIIb	n-C_3H_7	—	—	—	1.5270(23)	117	inactive
VIIIc	iso-C_3H_7	3-Me-4-NO_2	mp 49°C		—	700	inactive
VIIId	n-C_4H_9	—	—	—	1.5208(24)	213	inactive
VIIIe	n-C_5H_{11}	—	—	—	1.5158(25)	81	inactive
IXa	C_2H_5[6]	—	143 ~ 145	0.2	1.5263(31)	7.0	×72,000
IXb	n-C_3H_7	—	129 ~ 130	0.03	1.5199(23)	80	×2,200
IXc	iso-C_3H_7	4-CN	124 ~ 125	0.15	1.5137(24)	335	×90
IXd	n-C_4H_9	—	140	0.04	1.5123(20)	103	inactive
IXe	n-C_5H_{11}	—	—	—	1.5082(25)	43.5	inactive

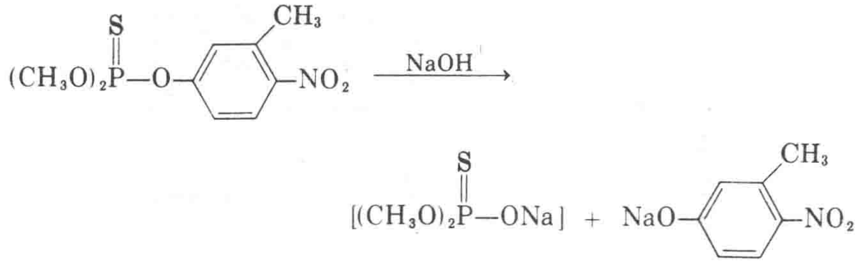
(*M* is a hydrogen atom or an alkaline metal atom.)

The distillation of Sumithion causes its isomerization even under reduced pressure and produces *O*-methyl *S*-methyl-*O*-(3-methyl-4-nitrophenyl)phosphorate, but does not cause an explosion contrary to the behavior of methylparathion.

Pure Sumithion is obtained by silica gel column chromatography in carbon tetrachloride solution and shows the refractive index n_D^{25} 1.5528 and the specific gravity d_4^{25} 1.3227.

Sumithion is, in a pure state, pale yellow in color and easily soluble in alcohols, ethers, ketones, esters, or cyclic hydrocarbons and barely soluble in aliphatic hydrocarbons and water.

The stability of Sumithion in alkaline aqueous solution was studied by colorimetric determination of 3-methyl-4-nitrophenol liberated during incubation with sodium hydroxide solution and was compared with that of methyl and ethylparathion:



The hydrolysis did not proceed proportionally with time, but the process was represented by a second-order reaction and, under the conditions tested, first-order relative to the concentration of organophosphorus compound and first-order relative to the sodium hydroxide. The second-order rate constant and the half-life times of methyl- and ethyl-parathion and Sumithion are shown in Tables VII and VIII.

It is clear from Tables VII and VIII that Sumithion is one-half time more stable than methylparathion.

The infrared spectrum and the ultraviolet spectrum of Sumithion are shown in Figures 1 and 2, respectively. Frequency of the P-O-C (aromatic) stretching vibration of Sumithion is 1,233 cm^{-1}, although that of methylparathion is 1,215 cm^{-1}; therefore, it may be considered that the distance of the P-O-C (aromatic) linkage of Sumithion is shorter than that of methylparathion (see Fig. 1).

In ultraviolet spectra, the λ max [ϵ max of methylparathion is at 273 (9,474μ) but that of Sumithion is at 268.5 (6,756μ)]. This difference in the wavelength and the molecular extinction coefficient of absorption maximum shows clearly that the steric hindrance between methyl group and

Table VII. *Second-order rate constant*[a] *of Sumithion in alkaline solution.*

Compound	Temperature	
	30°C	40°C
Me-parathion	0.375	0.895
Et-parathion	0.125	0.329
Sumithion	0.255	0.622

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[a] $k_2t = 2.303/b-2a \cdot \log(b-2x)a/(a-x)b$; k_2 is second-order rate constant $\text{min}^{-1} \cdot \text{mol}^{-1}$; a is initial concentration of organophosphorus compound, $1 \sim 3 \times 10^{-3}$ mol; and b is initial concentration of sodium hydroxide, 0.01*N* as 40% ethanolic solution.

Table VIII. *Half-life times of Sumithion in alkaline solution.*

Compound	Temperature	
	30°C	40°C
Me-parathion	210 min	84 min
Et-parathion	490 min	250 min
Sumithion	272 min	123 min

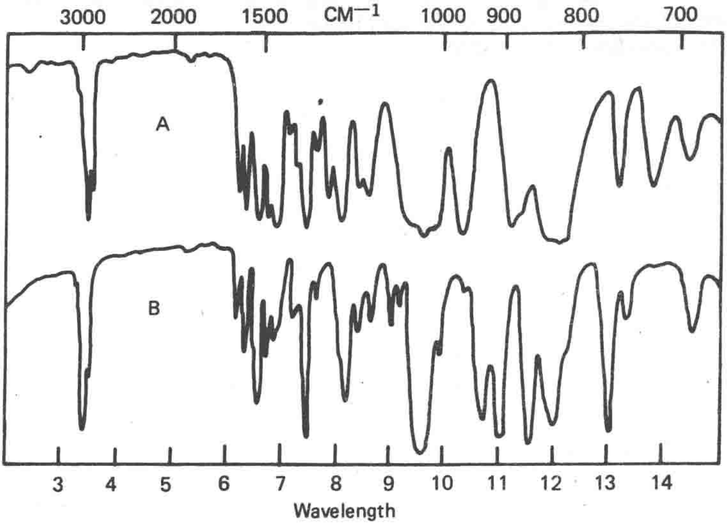

Fig. 1. Infrared absorption spectra of sumithion and methylparathion (in Nujol, by Shimadzu IR Infrared Spectrophotometer): A = Sumithion and B = methylparathion.

nitro group in the phenyl group of Sumithion is relatively larger (see Fig. 2).

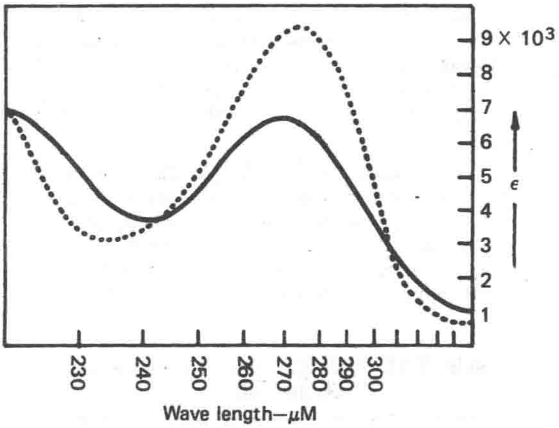

Fig. 2. Ultraviolet absorption spectra of Sumithion and methylparathion (in ethanol, by Shimadzu RS-27 Recording Spectrophotometer): —— Sumithion and ---- methylparathion.

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SCHRADER, G.: Die Entwicklung neuer Insektizide auf Grundlage organischer Fluor- und Phosphor-Verbindungen, p. 59 (1952).

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