Chemical Structure and Acaricidal Activity of 3-Alkylthiophenyl 4-Nitrophenyl Ethers[†]

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Many 4-nitro diphenylether derivatives with R-S(O)_x-substituents were systematically synthesized and their pesticidal activities were investigated. 3-*n*-Propylthiophenyl 4-nitrophenyl ether and its sulfoxide analog exhibited remarkable acaricidal and chlorosis-inducing activities on the young leaves of plants. For all compounds with the substituent at the 4 position in the 3-*n*-propylthio (and -sulfinyl) phenyl group, chlorosis-inducing activity vanished and an acaricidal activity stronger than that of the parent compound appeared. Evidence that the acaricidal and chlorosis-inducing activities are greatly influenced by the size of the 4-substituent and the hydrophobicity of R in the 3-R-S(O)_x-substituent is presented.

A number of derivatives of 4-nitro diphenylether are known to possess herbicidal activity. NIP (2, 4-dichlorophenyl 4-nitrophenyl ether), CNP (2, 4, 6-trichlorophenyl 4-nitrophenyl ether), and Chlomethoxynil (2, 4-dichlorophenyl 3-methoxy-4-nitrophenyl ether) are the widely used herbicides in our country. We systematically synthesized many 4-nitro diphenylether derivatives bearing alkylthio, alkylsulfinyl, or alkylsulfonyl radicals and investigated both herbicidal and acaricidal activities of these compounds.

Table I shows that the acaricidal activities are remarkable in the *m*- and *p*-alkylthio and alkylsulfinyl derivatives, but not in the *o*-isomers nor in any of the alkylsulfonyl derivatives. Of these compounds, 3-*n*-propylthiophenyl 4-nitrophenyl ether and its sulfoxide analog ($x = 1$) were the most active. However, they induced severe chlorosis on the young leaves of plants. Thus, new derivatives which possess high acaricidal activity, but do not produce chlorosis were investigated. We found that 3-*n*-propylthiophenyl 4-nitrophenyl ethers with an appropriate substituent at the

4 position of the 3-*n*-propylthiophenyl group ($x = 0$) and their sulfoxide analogs ($x = 1$) did not induce chlorosis and showed even higher activity than the parent compound against *Tetranychus urticae* and *Panonychus citri*.

MATERIALS AND METHODS

1. Synthesis

Four typical preparations are given below. Results are shown in Table II.

Method A. 4-Chloro-3-*n*-propylthiophenyl 4-nitrophenyl ether (9). 4-Chloro-3-(*n*-propylthio) phenol¹⁾ (5.0 g, 0.0247 mole) and 85.5% potassium hydroxide (1.7 g, 0.0258 mole) were dissolved in N,N-dimethylacetamide (50 ml) above 90°C. 4-Chloronitrobenzene (3.9 g, 0.0247 mole) was added to this solution below 90°C and the mixture was stirred at 140~150°C for 3hr. After cooling, the reaction mixture was poured into water (200 ml) and extracted twice with benzene. The combined organic layers were washed with 5% sodium hydroxide solution, 5% hydrochloric acid solution, and water, then dried over sodium sulfate. Evaporation of the solvent left a crystalline residue, which was recrystallized from ethyl alcohol to give 7.4 g (88.2%) of 9, pale yellow crystals, mp 90~91°C.

Method B. 4-Chloro-3-*n*-propylsulfinylphenyl 4-nitrophenyl ether (10). Thirty percent hydrogen peroxide solution (2.5 g, 0.0257 mole) was added at 8~10°C to a mixture of 4-chloro-3-*n*-propylthiophenyl 4-nitro-

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TABLE I. RESULTS^{a)} FROM SCREENING TEST OF ON *Tetranychus urticae* AND *Panonychus citri*

Isomer	R	x											
		0				1				2			
		T.u. ^{b)}		P.c. ^{c)}		T.u.		P.c.		T.u.		P.c.	
		a ^{d)}	e ^{e)}	a	e	a	e	a	e	a	e	a	e
<i>meta</i> (I)	CH ₃	C	D	D	D					C	D	D	C
	C ₂ H ₅			B	B	D	D	D	D	C	D	D	C
	<i>n</i> -C ₃ H ₇	C	A	C	B	C	B	A	A	C	D	C	C
	<i>iso</i> -C ₃ H ₇	B	C	C	D	C	D	D	C	C	D	D	D
	<i>n</i> -C ₄ H ₉	C	C	A	A	D	D	C	D	D	D		
	<i>n</i> -C ₅ H ₁₁	C	C	C	C	C	D	D	C	C	D	D	C
	<i>n</i> -C ₆ H ₁₃	C	D	A	C	C	D	A	C	D	D	D	D
	CH ₂ =CH·CH ₂	D	D	C	D	D	D	C	C	D	D	D	D
<i>para</i> (II)	CH ₃			C	C	C	D	D	C			D	C
	C ₂ H ₅	B	C	A	B	C	D	C	C	D	D	C	C
	<i>n</i> -C ₃ H ₇	C	D	C	A	D	D	D	B	D	D	C	C
	<i>n</i> -C ₄ H ₉	C	D	A	C	C	D	C	A	D	D	C	C
	CH ₂ =CH·CH ₂	C	D	A	C	C	D	D	D	C	D	D	D
<i>ortho</i> (III)	CH ₃	D	D	C	D					D	D	C	C
	<i>n</i> -C ₃ H ₇	D	D	C	D	D	D	C	C	D	D	C	C

^{a)} Activities are classified as A, B, C and D: A=the most active and D=inactive. A test compound was prepared as a 20% emulsifiable solution and was diluted with water to 400 ppm. The leaf-dipping method was used for these tests.

^{b)} *Tetranychus urticae*. ^{c)} *Panonychus citri*. ^{d)} Adults. ^{e)} Eggs.

phenyl ether (9) (3.2 g, 0.0094 mole) and glacial acetic acid (50 ml). After 5 hr at room temperature, the reaction mixture was poured into water (100 ml) and extracted three times with benzene. The combined organic layers were washed with 5% sodium carbonate solution, then with water and dried over sodium sulfate. Evaporation of the solvent left a crystalline residue. Recrystallization from ethyl alcohol gave 3.1 g (95.9%) of **10**, pale yellow crystals, mp 86~86.5°C.

Method C. 4-Chloro-3-*n*-propylsulfonylphenyl 4-nitrophenyl ether (**11**). 4-Chloro-3-*n*-propylthiophenyl 4-nitrophenyl ether (9) (4.0 g, 0.0118 mole) was dissolved in glacial acetic acid (40 ml), to which 30% hydrogen peroxide solution (4.0 g, 0.0353 mole) was added at 8~10°C. The mixture was heated at 90°C for 3 hr, then cooled, and poured into water (100 ml). The precipitates were filtered and recrystallization from ethyl alcohol gave 4.1 g (93.5%) of **11**, pale yellow crystals, mp 61~61.5°C.

Method D. 4-Nitro-3-*n*-propylthiophenyl 4-nitrophenyl ether (**14**)

Preparation of 5-chloro-2-nitrophenyl n-propyl sulfide.

n-Propylmercaptan (50 g, 0.657 mole) in dioxane (100 ml) was added to a solution of 2,4-dichloronitrobenzene (132.2 g, 0.689 mole) and potassium carbonate (90.7 g, 0.657 mole) in dioxane (100 ml) and N,N-dimethylacetamide (60 ml) below 50°C. The mixture was heated for 12 hr at 80°C, then cooled, poured into water (2 liters), and extracted twice with benzene. The combined organic layers were washed with 10% sodium hydroxide solution, 5% hydrochloric acid solution, and water, then dried over sodium sulfate. Evaporation of the solvent left a crystalline residue. Recrystallization from methyl alcohol gave 115 g (75.6%) of yellow crystals, mp 74.5~5°C. *Anal.* Found: C, 46.66; H, 4.23; N, 6.17. Calcd. for C₉H₁₀ClNO₂S: C, 46.66; H, 4.35; N, 6.04%. ((This product was identified as 5-chloro-2-nitrophenyl *n*-propyl sulfide, not as 3-chloro-4-nitrophenyl *n*-propyl sulfide, using the following sequence. By the reaction with sodium methoxide, this compound (5-chloro-2-nitrophenyl *n*-propyl sulfide) gave the methoxy derivative (5-methoxy-2-nitrophenyl *n*-propyl sulfide), which was reduced to the amino derivative (2-amino-5-methoxyphenyl *n*-propyl sulfide). Applying the Sand-

TABLE II. RESULTS OF THE SYNTHESIS OF

No.	R	Y	x	Method	Yield (%)	mp or n_D^{25} (°C)	Formula	Calcd.			Found		
								C	H	N	C	H	N
1	<i>n</i> -C ₃ H ₇	H	0	A	95.3	52 ~ 53	C ₁₅ H ₁₈ NO ₃ S	62.26	5.23	4.84	62.25	5.19	4.64
2	<i>n</i> -C ₃ H ₇	H	1	B	88.9	38.5 ~ 40.5	C ₁₆ H ₁₈ NO ₃ S	59.00	4.95	4.59	58.87	5.02	4.62
3	<i>n</i> -C ₃ H ₇	H	2	C	101 ~ 102	101 ~ 102	C ₁₇ H ₁₈ NO ₃ S	56.06	4.71	4.36	56.02	4.69	4.17
4	<i>n</i> -C ₃ H ₇	4-CH ₃	0	A	76.9	79 ~ 79.5	C ₁₆ H ₁₇ NO ₃ S	63.34	5.65	4.62	63.45	5.69	4.60
5	<i>n</i> -C ₃ H ₇	4-CH ₃	1	B	90.5	49.5 ~ 50.5	C ₁₇ H ₁₇ NO ₃ S	60.17	5.37	4.39	60.21	5.22	4.57
6	<i>n</i> -C ₃ H ₇	4-CH ₃	2	C	94.5	60 ~ 61	C ₁₈ H ₁₇ NO ₃ S	57.30	5.11	4.18	57.46	4.99	4.01
7	<i>n</i> -C ₃ H ₇	4-Br	0	A	74.1	88 ~ 89	C ₁₆ H ₁₇ BrNO ₃ S	48.93	3.83	3.80	48.77	3.54	3.92
8	<i>n</i> -C ₃ H ₇	4-Cl	1	B	88.9	77.5 ~ 78.5	C ₁₆ H ₁₄ BrNO ₃ S	46.89	3.67	3.65	46.62	3.42	3.90
9	<i>n</i> -C ₃ H ₇	4-Cl	0	A	88.2	90 ~ 91	C ₁₆ H ₁₄ ClNO ₃ S	55.55	4.34	4.31	55.71	4.26	4.47
10	<i>n</i> -C ₃ H ₇	4-Cl	1	B	95.9	86 ~ 86.5	C ₁₆ H ₁₃ ClNO ₃ S	52.86	4.14	4.11	52.75	4.09	3.98
11	<i>n</i> -C ₃ H ₇	4-Cl	2	C	93.5	61 ~ 61.5	C ₁₆ H ₁₂ ClNO ₃ S	50.49	3.95	3.93	50.52	3.82	4.11
12	<i>n</i> -C ₃ H ₇	4-C ₂ H ₅	0	A	95.2	1.6122	C ₁₇ H ₁₉ NO ₃ S	64.33	6.03	4.41	64.25	6.04	4.26
13	<i>n</i> -C ₃ H ₇	4-C ₂ H ₅	1	B	91.3	1.5942	C ₁₇ H ₁₉ NO ₃ S	61.24	5.74	4.20	61.21	5.73	4.18
14	<i>n</i> -C ₃ H ₇	4-NO ₂	0	D	64.0	97 ~ 98	C ₁₆ H ₁₄ N ₂ O ₆ S	53.89	4.22	8.38	54.19	4.34	8.19
15	<i>n</i> -C ₃ H ₇	4-NO ₂	1	B	41.4	151 ~ 152	C ₁₆ H ₁₄ N ₂ O ₆ S	51.43	4.03	7.99	51.40	4.13	8.20
16	<i>n</i> -C ₃ H ₇	4-OCH ₃	0	A	88.6	119 ~ 120	C ₁₆ H ₁₇ NO ₃ S	60.17	5.37	4.39	60.18	5.34	4.56
17	<i>n</i> -C ₃ H ₇	4-OCH ₃	1	B	89.2	111 ~ 112	C ₁₆ H ₁₇ NO ₃ S	57.30	5.11	4.18	57.12	4.96	4.07
18	<i>n</i> -C ₃ H ₇	4-OCH ₃	2	C	73.6	100 ~ 100.5	C ₁₆ H ₁₇ NO ₃ S	54.69	4.88	3.99	54.53	4.79	4.16
19	<i>n</i> -C ₃ H ₇	4-OC ₄ H ₉ (<i>n</i>)	0	A	70.0	81.5 ~ 82.5	C ₁₉ H ₂₃ NO ₃ S	63.14	6.41	3.88	63.13	6.60	3.86
20	<i>n</i> -C ₃ H ₇	4-OC ₄ H ₉ (<i>n</i>)	1	B	85.8	67 ~ 68	C ₁₉ H ₂₃ NO ₃ S	60.46	6.14	3.71	60.64	6.34	3.98
21	<i>n</i> -C ₃ H ₇	4-OC ₄ H ₉ (<i>n</i>)	2	C	84.5	76 ~ 76.5	C ₁₉ H ₂₃ NO ₃ S	58.00	5.89	3.56	58.05	6.02	3.50
22	CH ₃	4-CH ₃	0	A	79.8	90.5 ~ 91.5	C ₁₆ H ₁₆ NO ₃ S	61.08	4.76	5.09	61.16	4.71	5.42
23	C ₂ H ₅	4-CH ₃	0	A	78.0	92 ~ 92.5	C ₁₆ H ₁₆ NO ₃ S	62.26	5.23	4.84	62.27	5.17	4.72
24	<i>n</i> -C ₄ H ₉	4-CH ₃	0	A	80.6	61	C ₁₇ H ₁₉ NO ₃ S	64.33	6.03	4.41	64.44	6.32	4.18
25	<i>n</i> -C ₅ H ₁₁	4-CH ₃	0	A	44.4	59	C ₁₈ H ₂₁ NO ₃ S	65.23	6.39	4.23	65.03	6.29	4.03
26	<i>n</i> -C ₅ H ₁₁	4-CH ₃	0	A	52.8	43 ~ 44	C ₁₈ H ₂₁ NO ₃ S	66.06	6.71	4.06	66.09	6.89	3.94
27	iso-C ₃ H ₇	4-CH ₃	0	A	95.5	1.6132	C ₁₆ H ₁₇ NO ₃ S	63.34	5.65	4.62	63.35	5.51	4.38
28	iso-C ₄ H ₉	4-CH ₃	0	A	78.1	1.6100	C ₁₇ H ₁₉ NO ₃ S	64.33	6.03	4.41	64.37	5.99	4.35
29	CH ₂ =CHCH ₂	4-CH ₃	0	A	75.5	84.5 ~ 85	C ₁₆ H ₁₅ NO ₃ S	63.77	5.02	4.65	63.86	4.89	4.48
30	CH ₂ =CCH ₂	4-CH ₃	0	A	79.3	88 ~ 89	C ₁₆ H ₁₃ NO ₃ S	64.20	4.38	4.68	64.26	4.14	4.54
31	<i>n</i> -C ₃ H ₇	5-CH ₃	0	A	49.8	40 ~ 41	C ₁₆ H ₁₇ NO ₃ S	63.34	5.65	4.62	63.43	5.50	4.45
32	<i>n</i> -C ₃ H ₇	6-CH ₃	0	A	90.0	1.6135	C ₁₆ H ₁₇ NO ₃ S	63.34	5.65	4.62	63.60	5.49	4.43

meyer reaction, the latter was finally converted to the chloro derivative (2-chloro-5-methoxyphenyl *n*-propyl sulfide), whose physical properties were identical with an authentic sample prepared from methyl iodide and 2-chloro-5-hydroxyphenyl *n*-propyl sulfide.¹⁾⁾)

Preparation of 4-nitro-3-n-propylthiophenyl 4-nitrophenyl ether (14). A mixture of 5-chloro-2-nitrophenyl *n*-propyl sulfide (10 g, 0.043 mole), 4-nitrophenol (6.0 g, 0.043 mole), potassium carbonate (7.2 g, 0.052 mole) and *N,N*-dimethylacetamide (40 ml) was refluxed for 5 hr. After cooling, the reaction mixture was poured into water (200 ml) and extracted twice with benzene. The combined organic layers were sequentially washed with 5% sodium hydroxide solution, 5% hydrochloric acid solution, and water, then dried over potassium sulfate. Evaporation of the solvent left a crystalline residue. Recrystallization from methyl alcohol gave 9.2 g (64.0%) of **14**, yellow crystals, mp 97~98°C.

2. Biological tests

Every active ingredient of chemical grade was used for the biological test as a 20% emulsifiable solution prepared by mixing the active ingredient, xylene, isopropylalcohol and polyoxyethylenealkylphenol in a ratio of 20: 20: 35: 25.

1) *Determination of acaricidal activity against Tetranychus urticae.* Fifteen female adults of *Tetranychus urticae* were infested on the first leaves (two leaves), cut into squares (2 cm×2 cm), of dwarf *Phaseolus vulgaris* grown in a porous pot. After one day, the leaves were dipped into the test solution diluted to a concentration of 0.04% with water. These insects were then raised in a greenhouse at 25°C.

Dead adults were counted through a binocular microscope two days after treatment. The survivors were removed and the deposited eggs were counted. Unhatched eggs were counted one week later.

2) *Determination of acaricidal activity against Panonychus citri.* Pairs of leaves of dwarf *Citrus natsudaidai* seedlings grown in a porous pot were excised. "Tangle-foot" (pine resin) was applied to the petiole of the two leaves. Fifteen female adults of *Panonychus citri* per one leaf were infested. After one day, a test solution diluted to 0.04% with water was sprayed on the leaves for 20 sec in a pot placed on a turn-table (16 rpm) using a compressor-spray-gun (1.5 kg/cm²). The pot was then placed in a greenhouse at 25°C. The mortalities of adults and eggs were measured as described above.

3) *Determination of LC₅₀ against Tetranychus urticae* Cotyledons of dwarf *Phaseolus vulgaris* were cut into squares (2 cm×2 cm) and placed on an agar gel in a petri dish with their backs upwards. Twenty female adults of *Tetranychus urticae* were placed on the cotyledons. After one day, dead and unhealthy mites were removed and 7 ml of a test solution diluted to a given concentration was sprayed on the squares with a turning spray tower of the "Mizuho-style" (280 mmHg). Two days after treatment, mortality was measured through a binocular microscope and the LC₅₀ was calculated using Bliss' probit method.

RESULTS

1. 4-Substituted-3-n-propylthiophenyl 4-nitrophenyl ethers, sulfoxide and sulfone deriva-

TABLE III. RESULTS^{a)} FROM SCREENING TEST OF

ON *Tetranychus urticae* AND *Panonychus citri*

Y	x											
	0				1				2			
	T.u.		P.c.		T.u.		P.c.		T.u.		P.c.	
	a	e	a	e	a	e	a	e	a	e	a	e
CH ₃	A	A	A	A	A	A	A	A	C	D	D	D
C ₂ H ₅	A	A	A	A	A	A	A	A				
Br	A	A	D	C	A	A	A	A				
Cl	A	A	D	C	A	A	A	A	D	D	C	C
H	C	A	C	B	C	B	A	A	C	D	C	C
NO ₂	D	D	D	D	D	C	D	D				
OCH ₃	C	C	D	D	C	C	A	C	C	C	D	D
OC ₄ H ₉ (n)	D	D	D	C	D	D	C	D	D	D	D	C

^{a)} See notes under Table I.

tives (IV)

As shown in Table III, most of the sulfide ($x=0$) and the sulfoxide ($x=1$) derivatives exhibited remarkable acaricidal activities, but all the sulfone ($x=2$) derivatives showed low activities. Activities of the sulfides against *T. urticae* were A class against both adults and eggs when Y =methyl, ethyl, bromine or chlorine. The activity of the parent compound (Y =hydrogen) was A class only against eggs and was C class against adults. Other compounds (Y =methoxy, nitro or *n*-butoxy) showed low activities. The activities of the sulfides, where Y =methyl or ethyl against *P. citri* were evaluated as A class. The parent compound (Y =hydrogen) showed B class activity only against eggs, as against *T. urticae*. Thus, the selective action of the sulfides against the two species depends on substituent Y . The activities of the sulfoxides against *T. urticae* were quite similar to those of the sulfides. But sulfoxides with hydrogen, methyl, ethyl, chlorine or bromine as Y were highly active against both the adults and eggs of *P. citri*. The sulfoxide with methoxy as Y was

TABLE IV. MITICIDAL ACTIVITY^{a)} OF AGAINST FEMALE *Tetranychus urticae*

Y	$r_V^b)$	$\sigma^c)$	x	
			0	1
			LC ₅₀	LC ₅₀
CH ₃	1.97	-0.170	7ppm	6ppm
Br	1.85	0.232	11	6
Cl	1.75	0.227	13	11
C ₂ H ₅		-0.151	45	16
H	1.20	0.000	130	188
NO ₂	2.59	0.778	} 0% mortality at 200 ppm	
OCH ₃		-0.268		
OC ₄ H ₉ (n)				

^{a)} The test compound was prepared as a 20% emulsifiable solution and was diluted with water to serial concentrations.

The leaf-disk method was used for these tests. LC₅₀ was calculated by Bliss' probit method.

^{b)} Van der Waals radii.³⁾

^{c)} Hammett's substituent constants.⁴⁾

active only against the adults. The sulfoxides have a great selective toxicity against *P. citri* when compared with the toxicity of the sulfides. Since the activities of the sulfides and sulfoxides against the adults of *T. urticae* seemed to depend on the substituent Y , a structure-activity correlation was quantitatively studied. The compounds investigated and their miticidal activities (LC₅₀) are shown in Table IV. The Hansch approach²⁾ gave no clear correlation between $-\log \text{LC}_{50}$ and σ , π or the combination of σ and π of the substituent Y . However, as

FIG. 1. Correlation between Miticidal Activity ($-\log \text{LC}_{50}$) v.s. Female *Tetranychus urticae* and the Physicochemical Parameters, r_V and σ .

shown in Fig. 1, a high correlation was found between $-\log LC_{50}$ and the combination of van der Waals radii (r_v) and σ . This correlation indicates that the activity is greatly influenced by the size of substituent Y. The activity of the sulfide is more dependent on size than is that of sulfoxide. When the methyl radical was moved from the 4- position to the 3- or 2- position, activity decreased drastically (Table V). This large depression in activity cannot be explained by the term σ or π . Therefore the substituent Y at the 4-position is thought to

TABLE V. MITICIDAL ACTIVITY^{a)} OF AGAINST FEMALE *Tetranychus urticae*

Position	Mortality (%)	
	100 ppm	200 ppm
6-CH ₃	0	0
5-CH ₃	11	11
4-CH ₃	100	100
Control	0	0

^{a)} See note^{a)} of Table IV.TABLE VI. MITICIDAL ACTIVITY^{a)} OF AGAINST FEMALE *Tetranychus urticae*

R	π^b	Mortality (%)		
		50ppm	100ppm	200ppm
CH ₃	0.50		8	12
CH $\equiv$ C·CH ₂	0.90 ^{a)}	37	89	97
C ₂ H ₅	1.00	92	98	100
CH ₂ =CH·CH ₂	1.20 ^{c)}	92	100	100
iso·C ₃ H ₇	1.30	90	97	100
n·C ₃ H ₇	1.50	100	100	100
iso·C ₄ H ₉	1.80	73	98	100
n·C ₄ H ₉	2.00		53	89
n·C ₆ H ₁₁	2.50		8	24
n·C ₆ H ₁₃	3.00		18	31
Control			0	0

^{a)} See note^{a)} of Table IV.^{b)} Hansch's hydrophobic substituent constants.⁵⁾^{c)} π values were estimated using their additive nature.^{6,7)}

fit on a site of limited size. This specified site, if any, should be very small in the system of chlorophyll synthesis, because only the parent compound induced chlorosis.

2. 3-(*R-S*)-4-Methylphenyl 4-nitrophenyl ethers (VI)

4-Methylphenyl 4-nitrophenyl ether derivatives with the alkylthio, allylthio, or propynylthio radical substituted at the 3-position were studied to clarify the effect of the aliphatic group binding to sulfur on acaricidal activity. Results in Table VI indicate that the activity is closely related to the hydrophobic parameter (π) of the aliphatic group, R.

DISCUSSION

The above study of structure-activity-relationships strongly suggests that the mode of action against adult mites by 4-(Y)-3-(alkylthio)phenyl 4-nitrophenyl ethers and their sulfoxides involves fitting of the 4-substituent Y on a specified site and the hydrophobic binding of the alkyl radical on a lipoprotein site. The same explanation can be given for the action against eggs. Differences in susceptibility against the same chemical toxicant have often been observed between *T. urticae* and *P. citri*.^{8~10)} Therefore, it is not strange that the sulfoxides show distinctly higher activity against *P. citri* than against *T. urticae*. The sulfides and sulfoxides exhibited exactly the same order of activity against *T. urticae*. Sulfides and sulfoxides and/or sulfones are known to show the relationship of substrate-metabolites. The insecticidal activity of the *p*-methylthiophenyl phosphates is almost as high as the activities of the corresponding methylsulfinyl and methylsulfonyl analogs.¹¹⁾ This indicates that the methylthio radical is smoothly metabolized to active methylsulfinyl and/or methylsulfonyl radicals in the insects.¹¹⁾ Nevertheless, the sulfoxides are more active than the sulfides against *P. citri*. Since thio, sulfinyl and sulfonyl radicals differ in their physicochemical properties,⁷⁾ differences in activities should appear among the sulfides,

sulfoxides and sulfones, unless the change of $S \rightarrow SO \rightarrow SO_2$ corresponds to an activating metabolism. The fact that the activity of the sulfides against *T. urticae* adults is equal to that of the sulfoxides is possibly due to the rapid activating metabolism of $S \rightarrow SO$. The activity of the sulfides against *P. citri* adults is lower than that of the sulfoxides. This weak sulfide activity against *P. citri* is possibly attributable to the slow metabolism of $S \rightarrow SO$. Further work is necessary to confirm the reason for the similarity or dissimilarity in activity between the sulfides and sulfoxides. The inactivity of the sulfones seems to be due to their weak hydrophobic bonding to the sites of action because of the negative π value of the sulfonyl radical, or to a disturbance in the fixation of the molecule on the sites of action due to the considerable bulkiness of the sulfonyl radical.

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