

## Chemical and Biological Behaviour of Fenthion Residues\*

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*Previous experiments at the University of California Citrus Research Center and Agricultural Experiment Station indicated that compounds incorporating the methylthiophenyl group—such as the insecticide fenthion—were highly susceptible to oxidation. Since the stability of fenthion and the properties of its degradation products have an important bearing not only on the efficacy of the insecticide but also on its toxicity to mammals under operating conditions, studies on the chemical and biological behaviour of fenthion and its residues have recently been carried out at the Center.*

*The activity of fenthion against susceptible and resistant houseflies and mosquitos was compared with that of its principal oxidation products. Most of these products were similar to fenthion in their activity against houseflies, but appeared to be much less water-stable since they were considerably less effective against mosquito larvae. Stability tests showed that, in the presence of sunlight and air, fenthion was completely transformed into its sulfoxide and sulfone oxidation products within one to three days, and that these products were rapidly decomposed to non-insecticidal compounds. Upon heating, fenthion was rapidly isomerized to the S-methyl isomer.*

The insecticide *O,O*-dimethyl *O*-3-methyl-4-methylthiophenyl phosphorothionate or fenthion<sup>4</sup> has proved of especial interest because of its prolonged residual action to flies and mosquitos and its comparatively low mammalian toxicity. Fenthion is effective as a mosquito larvicide at dosages as low as 1-2 ounces per acre (7-14 mg per m<sup>2</sup>) (Lewallen & Gjullin, 1960) and has an oral LD<sub>50</sub> to the male rat of 215 and to the female rat of 615 mg per kg and a dermal toxicity of 500 mg per kg (Francis & Barnes, 1963). Previous experience in our laboratory has shown that compounds incorporating the

methylthiophenyl group are highly susceptible to oxidative reactions forming the corresponding sulfoxide and sulfone (Benjamini, Metcalf & Fukuto, 1959a, 1959b). Therefore it seemed of importance to examine the stability of fenthion when exposed to sunlight, air, and heat; and to characterize the insecticidal and anticholinesterase activity of its possible oxidation products.

Schrader (1960) has described some of the chemical and insecticidal properties of fenthion and its oxidation products, and the efficacy of this compound in controlling flies and mosquitos has been described by Jung, Kükenthal & Techman (1960). However, the authors of both these papers ascribe to fenthion an extraordinary chemical stability, which is not in accord with the results of the experiments reported here or with the facile oxidizability of the methylthio group to sulfoxide and sulfone.

The metabolism of fenthion in rats has been studied by Brady & Arthur (1961), who found that the compound was rapidly oxidized to sulfoxide and sulfone and to the sulfoxide and sulfone of the oxygen analogue. The oxygen analogue was also suggested as the predominant chloroform-soluble extractive of the faeces. These compounds were rapidly hydrolysed and, after three days, the urine

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<sup>4</sup> Fenthion is the common name designated by the International Organization for Standardization (ISO) for this compound, which is also known as Bayer 29493, S1752 or Baytex.

and faeces contained from 96% to 99% of the radioactive material, largely as dimethyl phosphorothioic acid in the urine and as dimethyl phosphoric acid in the faeces.

#### MATERIALS AND METHODS

The work described in this paper was largely carried out with  $^{32}\text{P}$ -labelled *O, O*-dimethyl *O*-3-methyl-4-methylthiophenyl phosphorothionate (fenthion), kindly supplied by Dr Gerhard Schrader of Farbenfabriken Bayer, Leverkusen, Germany. The activity of the preparation was approximately 14.8 counts per second per microgram as measured by gas flow counter at the beginning of the experiments and the material as analysed by paper chromatography was approximately 93% pure, with about 6% of an impurity that appeared by paper chromatography to be the *S*-methyl isomer (*O*-methyl *S*-methyl *O*-3-methyl-4-methylthiophenyl phosphorothiolate).

Paper chromatography was carried out on strips of filter-paper, using three systems:

(1) Whatman No. 1 paper impregnated with propylene glycol from a 50% solution in absolute ethanol and oven-dried at 80°C for 10 minutes: the solvent used was a mixture containing 70 parts of hexane (Skellysolve B) and 30 parts of toluene by volume, saturated with propylene glycol (Benjamini, Metcalf & Fukuto, 1959a);

(2) Whatman No. 1 paper with a solvent comprising 85 parts of acetonitrile and 15 parts water by volume (Kaplanis et al., 1959); and

(3) Whatman No. 1 paper with a solvent comprising 3 parts of isopropanol and 1 part of concentrated ammonium hydroxide (Plapp & Casida, 1958). Quantitative evaluation of the component spots of the chromatograms was carried out by serial counting of  $^{32}\text{P}$  activity and by radioautography (Fukuto & Metcalf, 1954).

The location of the spots of some of the model compounds was also determined by spraying the chromatograms with 5% 2,4-dibromo-*N*-chloroquinoneimine and heating (Menn, Erwin & Gordon, 1957) and by bio-assay of 1-cm sections of the paper strips using mosquito larvae. The compounds were evaluated for biological activity by topical application to female houseflies using susceptible (NAIDM), chlorinated-hydrocarbon resistant (SP) and organophosphorus resistant (SC) strains, and against the larvae and adults of susceptible *Culex pipiens quinquefasciatus* Say and resistant *Anopheles albimanus* Wied. (Metcalf & Georghiou, 1962).

#### *O, O*-Dimethyl *O*-3-methyl-4-methylsulfinylphenyl phosphorothionate

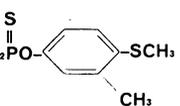
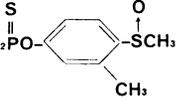
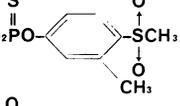
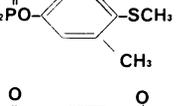
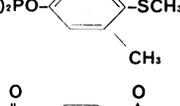
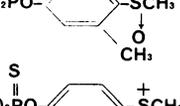
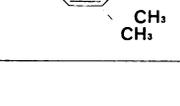
3-methyl-4-methylsulfinylphenol was prepared by heating 3-methyl-4-methylthiophenyl acetate with one equivalent of hydrogen peroxide in acetone. The oxidized acetate was hydrolysed in 10% sodium hydroxide and liberated with hydrochloric acid; the melting-point of the product, after recrystallization from benzene, was 111-113.5°C.

A mixture containing 6 g of 3-methyl-4-methylsulfinylphenol, 5.7 g of dimethyl phosphorothionochloridate, 3.8 g of anhydrous powdered sodium carbonate, and 45 ml of acetone was stirred and heated under reflux for 6 hours. The mixture was poured into water, the product was taken up in benzene, washed with dilute sodium hydroxide and with water, and dried over anhydrous sodium sulfate. The product was then distilled in a falling-film molecular still at 105°C (0.3 mm). This compound was extremely sensitive to heat and some decomposition appeared to take place even at this distillation temperature, as evidenced by a darkening of the product. Elemental analysis was not entirely satisfactory; calculated for  $\text{C}_{10}\text{H}_{15}\text{O}_4\text{PS}_2$ ; C = 40.81, H = 5.14; found, C = 39.62, H = 5.18. The infrared spectrum of the compound showed a strong sulfoxide shoulder (1070  $\text{cm}^{-1}$ ), a strong peak for P-O-aromatic (1235  $\text{cm}^{-1}$ ) and a very strong peak for P-O-aliphatic (1030  $\text{cm}^{-1}$ ).

#### *O, O*-Dimethyl *O*-3-methyl-4-methylsulfonylphenyl phosphorothionate

3-methyl-4-methylsulfonylphenol was also prepared from 3-methyl-4-methylthiophenyl acetate, but using two equivalents of hydrogen peroxide in acetic acid. A mixture of 4 g of the sodium salt of 3-methyl-4-methylsulfonylphenol and 3.2 g of dimethyl phosphorothionochloridate was stirred and heated in methanol for several hours. The product was worked up in the same manner as the above sulfinyl ester. The product was collected at 170°C (0.5 mm) in the falling-film molecular still. The product solidified upon standing and was recrystallized from Skellysolve B; its melting-point was 69-73°C. Elemental analysis: calculated for  $\text{C}_{10}\text{H}_{15}\text{O}_5\text{PS}_2$ ; C = 38.70, H = 4.86; found, C = 39.10, H = 4.65. The infrared spectrum of the product showed strong sulfone absorption (1160 and 1328  $\text{cm}^{-1}$ ), strong P-O-aromatic absorption (1238  $\text{cm}^{-1}$ ) and strong P-O-aliphatic absorption (1050  $\text{cm}^{-1}$ ).

TABLE 1  
SOME PROPERTIES OF FENTHION AND ITS OXIDATION PRODUCTS

Compound	Approx. $R_f$ by system (1)	Topical $LD_{50}$ for <i>Musca domestica</i> ( $\mu\text{g}$ per female)			$LC_{50}$ for mosquito larvae (p.p.m.)		$LC_{50}$ for mosquito adults ( $\mu\text{g}$ per $\text{cm}^2$ )		$I_{50M}$ for fly-head ChE
		NAIDM	SP	SC	<i>Culex</i>	<i>Anopheles</i>	<i>Culex</i>	<i>Anopheles</i>	
I. 	0.93	0.046	0.25	0.68	0.0045	0.016	1.2	1.3	$2.6 \times 10^{-4}$
II. 	0.08-0.14	0.048	0.25	1.6	0.015	0.072	0.43	4.1	$5.2 \times 10^{-7}$
III. 	0.23-0.40	0.072	1.6	>10	0.11	0.25	>16	>16	$2.9 \times 10^{-4}$
IV. 	0.65	0.026	0.15	0.26	0.034	0.20	7.0	>16	$1.3 \times 10^{-7}$
V. 	0.01	0.036	0.71	1.3	0.17	0.37	>16	>16	$9.3 \times 10^{-7}$
VI. 	0.11	0.035	0.68	1.5	0.19	0.57	>16	>16	$1.1 \times 10^{-7}$
VII. 	0	5.8	>10	>10	0.6	—	—	—	$1.6 \times 10^{-4}$

*O,O*-Dimethyl *O*-3-methyl-4-methylthiophenyl phosphorothionate methosulfate.

This compound was prepared by treating fenthion in anhydrous diethyl ether with an equimolar quantity of dimethyl sulfate. The precipitate was collected and washed several times with ether.

The other compounds listed in Table 1 were supplied by Dr G. Schrader. They were purified by molecular distillation and their identity was confirmed by infrared spectrophotometry and by elemental analysis.

RESULTS

*Toxicity of fenthion and oxidation products to insects*

Some biological properties of fenthion and its oxidation products are listed in Table 1. All of the

fenthion oxidation products are of approximately the same degree of toxicity to the susceptible NAIDM housefly and to the chlorinated-hydrocarbon resistant (SP) and organophosphorus resistant (SC) strains, with the exception of the sulfone (III), which was significantly less active, especially against the resistant strains. Fenthion (I) was outstandingly active against the mosquito larvae and adults, suggesting that the oxidation products are less stable in water and perhaps are less soluble in the lipids of the mosquito tarsi. The quaternary sulfonium salt of fenthion (VII), with its formal positive charge, is obviously deficient in toxicity, due in all probability to its failure to penetrate through the lipid sheath of the insect nerve (Heath & Vandekar, 1957).

TABLE 2  
PERCENTAGE OF TOTAL  $^{32}\text{P}$  IN VARIOUS DEGRADATION PRODUCTS OF FENTHION EXPOSED TO APRIL SUNLIGHT

$R_f$	Time of exposure (days)					Probable identity
	0	1	2	4	7	
A. Chromatographed on propylene glycol paper with hexane: benzene						
0.85-0.93	93	65	17	trace	trace	$\text{P}=\text{S}-\text{SCH}_3$
0.65-0.77	6	7	11	12	9	<i>S</i> -methyl isomer
0.23-0.32	1	10	31	29	10	$\text{P}=\text{S}-\text{SO}_2\text{CH}_3$
0.08-0.1	trace	5	17	31	25	$\text{P}=\text{S}-\text{SOCH}_3$
0.0	0	13	24	28	56	$\text{P}=\text{O}-\text{SOCH}_3$ ; $\text{P}=\text{O}-\text{SO}_2\text{CH}_3$ (hydrolysis products)
B. Spot $R_f$ 0.0 rechromatographed on untreated paper with acetonitrile: water						
0.93		4.7	6.5	8.6	9.0	$\text{P}=\text{O}-\text{SOCH}_3$
0.72		2.2	3.1	trace	trace	
0.30		0.5	trace	1.9	trace	
0.19		0.6	1.7	1.7	trace	
0.11		0.8	5.3	10.2	9.0	
0.05		2.6	6.7	1.7	28.6	dimethyl phosphoric acid
0.0		1.4	1.0	3.9	9.5	

The  $I_{50}$  values for the inhibition of fly-head cholinesterase (ChE) (Table 1) show that pure fenthion (molecularly distilled) is, like parathion, a weak inhibitor and must therefore exert its toxic action by *in vivo* oxidation to the corresponding phosphate (IV) and its further sulfoxide and sulfone oxidation products (V) and (VI), which are much more reactive with cholinesterase (Benjamini, Metcalf & Fukuto, 1959a). The anticholinesterase activity of the fenthion oxygen analogue ( $I_{50} = 1.3 \times 10^{-7}\text{M}$ ) approached that of para-oxon ( $I_{50} = 2.6 \times 10^{-8}\text{M}$ ). The introduction of the polar electron-withdrawing methylsulfinyl (II) and methylsulfonyl (III) groups into the fenthion type compound greatly enhances the anticholinesterase activity. It proved impossible to purify completely the sulfoxides II and V because of their tendency to form internal redox systems (Benjamini, Metcalf & Fukuto, 1959a) and the presence of impurities may account for the seemingly aberrant values obtained with these two compounds. The extraordinary anticholinesterase activity of the fenthion methylsulfonium salt can be accounted for only if this compound had partially isomerized to the *S*-methyl isomer.

It is of interest that the  $I_{50}$  values for these compounds against fly-brain ChE are significantly higher than those recorded by Francis & Barnes (1963) for human red-cell cholinesterase.

#### *Paper chromatographic separation of fenthion oxidation products*

The compounds in Table 1 could be separated by paper chromatography using solvent system (1), giving the approximate  $R_f$  values shown in Table 1. When  $^{32}\text{P}$  fenthion was treated with 30% hydrogen peroxide in acetone or with bromine water, rapid oxidation occurred and paper chromatographic separation of the products showed the presence of relatively large amounts of the sulfoxide (II) ( $R_f = 0.10-0.15$ ) and the sulfone (III) ( $R_f = 0.35-0.40$ ).

#### *Effect of exposure to light and air*

The results of the exposure of 10 microlitres of  $^{32}\text{P}$  fenthion, spread as a film over one half of a 9-cm Petri dish, to April sunlight are given in Table 2. It is evident that this compound is very unstable under these conditions and after two to three day's exposure is transformed into at least 11 phosphorus-containing compounds, separable by

TABLE 3  
PERCENTAGE OF TOTAL  $^{32}\text{P}$  IN VARIOUS DEGRADATION PRODUCTS OF FENTHION  
EXPOSED TO LIGHT AND AIR

$R_f$ by system (1)	Time of exposure (days)						
	0	1	2	4	5	7	14
A. Fluorescent light at 21°C							
0.95	93	92	88	80	—	81	61
0.65-0.77	6	5	9	8	—	7	0
0.23-0.32	1	3	2	5	—	9	30
0.08-0.1	trace	trace	trace	trace	—	trace	trace
0.0	0	0	1	7	—	3	9
B. Sunlight in October							
0.95	83.5	82.2	66.6	—	52.5	3.9	0.8
0.65-0.77	11.4	8.7	4.3	—	3.2	trace	0
0.23-0.32	trace	trace	trace	—	2.1	7.2	13.8
0.08-0.1	trace	6.3	15.8	—	31.2	63.1	39.1
0.0	5.1	2.8	13.3	—	11.0	25.8	46.3

the two systems of paper chromatography. The principal reactions are certainly those of oxidation to form the sulfoxide (II) ( $R_f = 0.08-0.14$ , by system (1)) and the sulfone (III) ( $R_f = 0.23-0.40$ , by system (1)). An appreciable amount of a compound ( $R_f = 0.65$ ) which appeared to be the *S*-methyl isomer was present in the starting material. This compound does not seem to be formed by exposure of fenthion to light and air, nor could its formation be detected by nuclear magnetic resonance (NMR) spectrometry (Fukuto, Hornig & Metcalf, 1963). The formation of sulfoxide and sulfone derivatives is apparently largely a function of light intensity, as shown in Table 3. In an identical experiment conducted in October sunlight, the rate of oxidation was noticeably slower, though relatively very large amounts of sulfoxide formed after several days. In a repetition of this experiment in intense July sunshine, under outdoor temperatures in excess of 100°F (38°C), only 4% of the original fenthion remained after a single 10-hour exposure. In another experiment, where the plate with the fenthion film was placed 18 inches (45 cm) below a bank of six 100-watt daylight fluorescent lamps in a constant-temperature room at 21°C, the oxidation of fenthion was relatively slow, as shown in Table 3. This is in accord with the lengthy residual action of the compound against adult mosquitos when applied in comparatively sheltered locations.

Schrader (1960) states that fenthion is more stable to the action of light and air than parathion. However, a similar experiment, in which 10 micro-litres of  $^{32}\text{P}$ -labelled parathion were exposed to July sunlight in half a Petri dish and then submitted to paper chromatographic analysis, showed that after 1 day's exposure 77% of the total  $^{32}\text{P}$  remained as intact parathion, as compared with the 4% of fenthion remaining unaffected after 10 hours' exposure under similar conditions.

The largest fraction of  $^{32}\text{P}$  fenthion decomposition products obtained after several days' exposure to sunlight consists mainly of predominantly water-soluble products, as was demonstrated by elution and rechromatography of Spot  $R_f$  0.0 of the propylene glycol system (1), using the acetonitrile and water system (2). Seven phosphorus-containing compounds were resolved (Table 2) and similar results were obtained with the isopropanol-ammonia system (3). The compounds at  $R_f$  0.0 of system (1) were subjected to paper electrophoresis at 400 volts on Whatman No. 1 paper with a buffer of 0.066 M,  $\text{Na}_2\text{HPO}_4$ . All of the spots except the least water-soluble spot,  $R_f$  0.93, migrated towards the anode, thus indicating that they are ionic products. From experiments with model compounds it appears that the major products,  $R_f$  0.05 and 0.11, are dimethyl phosphoric and dimethyl phosphorothioic acids, and that the product  $R_f$  0.93 is fenthion oxygen

TABLE 4  
PERCENTAGE OF TOTAL  $^{32}\text{P}$  IN VARIOUS DEGRADATION PRODUCTS OF FENTHION  
HEATED IN A SEALED TUBE AT  $140^\circ\text{C}$

$R_f$ by system (1)	Time of heating (minutes)					Probable identity
	0	15	45	180	420	
0.85-0.93	86.0	74.0	75.1	27.0	10.3	$\text{P}=\text{S}-\text{SCH}_3$
0.65-0.77	7.7	16.7	14.5	24.1	3.1	S-methyl isomer
0.23-0.32	2.9	4.4	2.6	2.1	trace	$\text{P}=\text{S}-\text{SO}_2\text{CH}_3$
0.08-0.1	trace	trace	trace	0	0	$\text{P}=\text{S}-\text{SOCH}_3$
0.0	3.4	5.1	7.8	46.8	86.6 <sup>a</sup>	$\text{P}=\text{O}-\text{SOCH}_3$ ; $\text{P}=\text{O}-\text{SO}_2\text{CH}_3$ (hydrolysis products)

<sup>a</sup> This spot, eluted and rechromatographed by system (2), gave the following spots:  $R_f$  0.72, 39.8%  $^{32}\text{P}$ ;  $R_f$  0.30, 32.0%;  $R_f$  0.11, 14.7%;  $R_f$  0.05, trace;  $R_f$  0.0, trace.

analogue sulfoxide (V)—dimethyl 3-methyl-4-methyl-sulfinylphenyl phosphate.

#### Effect of heat

The heating of  $^{32}\text{P}$ -labelled fenthion in a sealed tube under nitrogen for various periods, followed by paper chromatographic analysis, indicated a very rapid breakdown of the parent compound, as shown in Table 4. The major product formed,  $R_f$  0.65-0.77 on propylene glycol paper, is believed to be the S-methyl isomer—O-methyl S-methyl O-3-methyl-4-methylthiophenyl phosphorothiolate. The formation of this compound has been confirmed by NMR spectrometry, which showed the appearance of  $\text{CH}_3\text{SP}$  phosphorus resonance<sup>1</sup> peaks after the parent compound had been heated at  $140^\circ\text{C}$  for 5 hours. Similar transformations are known to occur with parathion and methyl parathion (Metcalf & March, 1953) and O, O-diethyl O-p-methyl-sulfinylphenyl phosphorothionate and its dimethyl analogue (Benjamini, Metcalf & Fukuto, 1959a). As shown in Table 4, no appreciable amounts of sulfoxide or sulfone oxidation products were found in the heat-treated product in addition to the small amounts present in the starting material, and this is to be expected because of the exclusion of oxygen. Paper chromatography of the spot  $R_f$  0.0, using solvent mixture (3), showed the presence of major components at  $R_f$  0.11, 0.30, and 0.72 and trace

constituents at  $R_f$  0.0 and 0.05. These components, which comprised nearly all of the material after 420 minutes, are further decomposition products of the S-methyl ester of fenthion, probably with the loss of the aryl moiety.

#### Metabolism of fenthion in cotton plants

In order to gain an idea of the behaviour of fenthion in a biological environment, the material was introduced as a systemic insecticide into cotton plants by applying 10 microlitres of the radio-labelled material to the stems of plants grown at constant temperature and under standard fluorescent light.

Fenthion was absorbed and translocated in substantial amounts and the total radioactivity reached a concentration equivalent to 968 p.p.m. in the upper leaves after two days. The chloroform/water partition ratio of the radioactivity in the leaves declined from 2.94 at two days to 0.85 at 4 and 0.14 at 10 days, indicating the progressive degradation into predominantly water-soluble hydrolytic products. Paper chromatograms of the chloroform-extractable radioactivity showed the presence of three principal components, with  $R_f$  values corresponding to the intact fenthion and its sulfoxide and sulfone, and the proportion of the oxidation products increased with time as the fenthion decreased. The rapid oxidizability of fenthion in the plant environment is qualitatively similar to that shown by demeton, phorate and other thioether insecticides (Metcalf, Fukuto & March, 1957).

<sup>1</sup> When fenthion was heated for 5 hours at  $140^\circ\text{C}$ , phosphorus NMR showed the presence of two types of compounds, (RO)<sub>2</sub>RSP=O and (RO)<sub>2</sub>P=S, in the ratio of approximately 2 : 1.

TABLE 5  
PERCENTAGE OF TOTAL  $^{32}\text{P}$  IN CHLOROFORM  
EXTRACTIVES FROM SUSCEPTIBLE (NAIDM STRAIN)  
AND RESISTANT (SC STRAIN) HOUSEFLIES TOPICALLY  
TREATED WITH 12.3 MICROGRAMS OF FENTHION

$R_f^a$	After 2 hours		After 4 hours	
	NAIDM strain	SC strain	NAIDM strain	SC strain
0.0	18 %	16 %	25 %	18 %
0.19	8 %	11 %	9 %	8 %
0.45	trace	trace	trace	trace
0.77	74 %	73 %	66 %	74 %
$\text{H}_2\text{O}/\text{HCCl}_3$ value	1.28	1.04	3.4	5.2
Percentage absorbed . . . .	60	47	83	78

<sup>a</sup>  $R_f$  values are low because of interfering lipids co-extracted from fly.

#### *Metabolism of fenthion in susceptible and resistant houseflies*

As assessed on the basis of the  $\text{LD}_{50}$  in  $\mu\text{g}$  per fly, female houseflies of the resistant SC strain were about 15 times as resistant to fenthion as the susceptible NAIDM strain (Table 1). Uniformly aged females of both strains were topically treated on the prothorax with 12.3  $\mu\text{g}$  of  $^{32}\text{P}$  fenthion. After 2- or 4-hour intervals, the external radioactivity was removed by washing in acetone and the flies were homogenized in water and the radioactivity partitioned in chloroform. The results of paper chromatography of the chloroform-soluble radioactivity are given in Table 5. The fenthion penetrated more slowly into the resistant strain and it appeared that there was somewhat more rapid degradation of the fenthion-type esters into partial hydrolysis products, as shown by the increasing  $\text{H}_2\text{O}/\text{HCCl}_3$  partition values. The combined effects of these factors probably account for the mild degree of resistance displayed. In both strains of flies, fenthion was the major component of chloroform-soluble  $^{32}\text{P}$  after two and four hours, with lesser amounts of com-

pounds showing the paper chromatographic characteristics of the sulfoxide and sulfone. Thus the oxidative metabolism in the housefly followed the same sequence as in the cotton plant.

The degree of resistance shown by the Chlorthion-malathion resistant strain (i.e., the ratio  $\text{LD}_{50}$  SC :  $\text{LD}_{50}$  NAIDM) to the various compounds in Table 1 is of particular interest. The ratio for fenthion (I) is 15 : 1 and that for fenthion oxygen analogue (IV) is 10 : 1. However, the ratios for the sulfoxides are 33 : 1 (PS-SO) and 36 : 1 (PO-SO), and those for the sulfones > 140 : 1 (PS-SO<sub>2</sub>) and 43 : 1 (PO-SO<sub>2</sub>). Since the oxidized compounds are more susceptible to destructive hydrolysis, this information is in agreement with that given in Table 5, which indicates that the SC flies seem to detoxify the fenthion products more rapidly than the NAIDM flies.

#### SUMMARY AND CONCLUSIONS

The experiments reported here demonstrate that fenthion, like other thioether insecticides which have been carefully examined, is readily oxidized as a surface residue or in the tissues of plants and animals to sulfoxide and sulfone derivatives. These oxidation products have a similar insecticidal activity against houseflies when applied topically, but are apparently much less water-stable than fenthion, as shown by their decreased activity against mosquito larvae. The oxygen analogues of the sulfoxide and sulfone of fenthion are highly active anticholinesterases and appear to be the ultimate products of lethal synthesis in insects.

Light appears to be the most important factor in catalysing oxidation, and under bright sunlight virtually all the fenthion in thin films was oxidized within 1 to 3 days' exposure. In addition to oxidation products, the exposure to light and air results in the formation of a number of non-toxic, predominantly water-soluble ionic phosphorus esters.

Fenthion subjected to heating in the absence of air rapidly forms the *S*-methyl isomer and a number of ionic phosphorus esters. In plant and insect tissues fenthion is rapidly oxidized to the sulfoxide and sulfone derivatives.

#### RÉSUMÉ

Les expériences effectuées par les auteurs démontrent que, comme les autres thioesters qui ont été soigneusement examinés, le fenthion est facilement oxydé et transformé en sulfoxyde et dérivés sulfonés, qu'il se trouve à l'état de

résidu superficiel ou dans les tissus végétaux ou animaux. Ces produits d'oxydation gardent leur activité insecticide vis-à-vis des mouches domestiques lorsqu'une application locale est effectuée, mais semblent beaucoup moins stables

dans l'eau si l'on en juge par la baisse de leur activité à l'égard des larves de moustiques. Les analogues oxygénés du sulfoxyde et du sulfone du fenthion sont des anticholinestérasés hautement actives et apparaissent comme les produits finals de synthèse létale chez les insectes.

La lumière semble être le facteur catalysant le plus important de cette oxydation et au grand soleil la quasi totalité du fenthion appliqué en couche mince a été oxydé après une exposition de 1 à 3 jours. Cette exposi-

tion à la lumière et à l'air a entraîné, outre l'oxydation, la formation d'un certain nombre d'esters phosphoriques ionisés non toxiques, surtout hydrosolubles.

Lorsqu'il est soumis à la chaleur en l'absence d'air, le fenthion forme rapidement l'isomère *S*-méthyl et plusieurs esters phosphoriques ionisés. A l'intérieur des tissus des plantes et des insectes, le fenthion est rapidement oxydé et transformé en sulfoxyde et dérivés sulfonés.

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